

# Overview of Regioselective and Stereoselective Catalytic Hydroboration of Alkynes

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**Abstract.** Hydroboration of alkynes is of special interest to researchers since it is the most straightforward process for the synthesis of highly important vinyl borane synthetic intermediate compounds. It is significant in terms of both regioselectivity and stereoselectivity, since several positional isomers are formed during the process of hydroboration. Given the importance of this class of compounds, an extensive study has been carried out regarding catalytic condition development and detailed mechanistic studies for selectively obtaining a single isomer. This elaborate review comprehensively summarizes both the regioselective and stereoselective catalytic hydroboration of alkynes. It is aimed at giving readers accurate knowledge of the catalytic systems available for the hydroboration of certain alkynes. We anticipate that this inclusive review will encourage researchers to explore more new types of catalytic systems to achieve the remarkable process of hydroboration of alkynes.

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**Keywords:** Hydroboration; Alkynes; Regioselectivity; Stereoselectivity; Mechanistic overview

## 1 Introduction

Synthetically important organoborane reagents are highly popular due to their unique reactivity in various synthetic processes. They have been used for several years as synthetic intermediates in the introduction of various functional groups and carbon-carbon bond-forming processes. Well-known examples of this are the Suzuki-Miyaura coupling and Petasis borono-Mannich reaction.<sup>[1-3]</sup> The most straightforward strategy used to produce an organoboron compound is the hydroboration of unsaturated organic compounds. This calls to mind Brown and Rao's revolutionary discovery in 1956 of the hydroboration of an alkene moiety using sodium borohydride in the presence of aluminum chloride (Scheme 1a).<sup>[4,5]</sup> Two years after this discovery, R. Köster reported the hydroboration of alkenes using an alkyl borane reagent (Scheme 1b).<sup>[6]</sup> These landmark discoveries opened the door for researchers to access synthetically important organoborane intermediates and to use them in several important organic transformations. Given the significance of the hydroboration reaction, various unsaturated functionalities, such as alkenes, alkynes, carbonyls, imines, and nitriles, have been hydroborated over the years.<sup>[7-24]</sup> Among these, alkyne

hydroboration is of special interest as it enables researchers to achieve synthetically important alkenylborane compounds.<sup>[25,26]</sup> In this regard, pioneering work was done by Brown and Gupta in the hydroboration of alkynes with readily available reactive catecholborane, as reported in 1975.<sup>[27]</sup>



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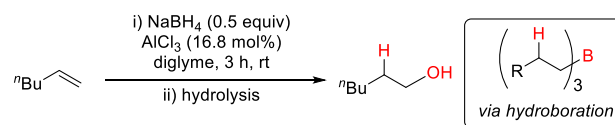
In the early days of research, conventional hydroboration reactions proceeded in a catalyst-free manner, through the addition of diborane ( $B_2H_6$ ), borane trihydride complexes ( $BH_3 \cdot L$ ;  $L$  = stabilizing adducts), or alkylboranes to unsaturated compounds. However, a major concern associated with this protocol was the lack of stability, high air sensitivity, and incompatibility with chromatographic purification of the resulting borane compounds, which limited the practical use of this process in organic synthesis. To address this issue, milder and air-stable dialkoxyborane compounds (HBpin: pinacolborane and HBcat: catecholborane) were introduced. Due to the reduction in electrophilicity, these dialkoxyborane compounds do not undergo catalyst-free transformations unless subjected to very high temperatures. In terms of a catalytic hydroboration reaction, Männig and Nöth first reported the Rh-catalyzed hydroboration of 1-hexyne using HBcat as the hydroboration reagent (Scheme 1c).<sup>[28]</sup> Subsequently, with the efficacy of the catalytic hydroboration reaction as well as the high stability and ease of purification of alkenylboronates being established, hydroboration of alkynes saw considerable progress, with various catalytic systems such as transition metals, base metals, and Lewis-acids or bases being used.

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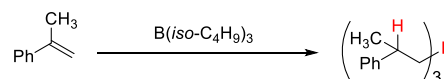


complexes using non-cyclopentadienyl-based ligands and their exploitation in homogeneous catalysis under ambient reaction conditions.

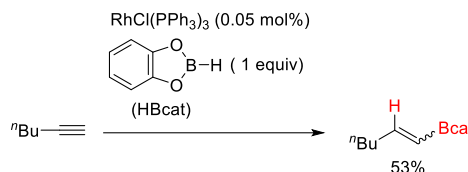
(a) Early discovery on hydroboration using  $NaBH_4$  and  $AlCl_3$  (Brown, 1956)



(b) Early discovery on hydroboration using trialkylborane (Koster, 1958)

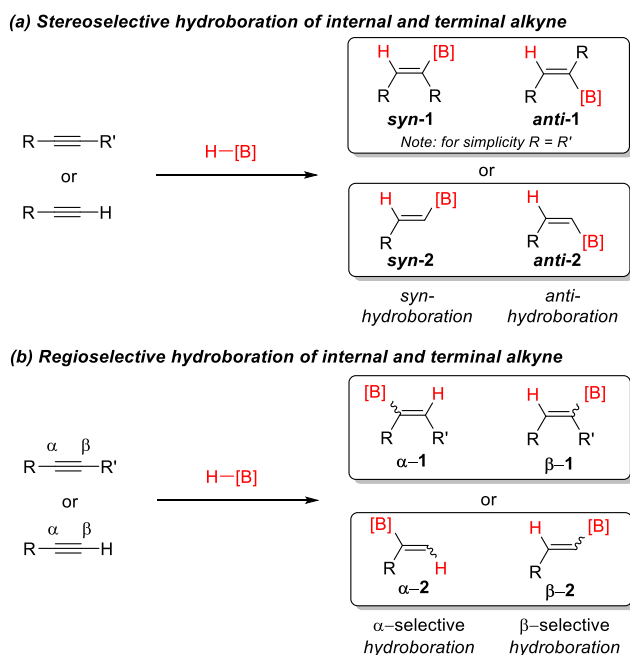


(c) Transition metal catalyzed hydroboration of alkyne (Noth, 1985)



**Scheme 1.** Early discoveries of hydroboration reaction using (a) sodium borohydride and (b) trialkylborane. (c) Early report of transition metal-catalyzed hydroboration of alkynes using HBcat.

The ability to control the regioselective and stereoselective orientation of afforded alkenylboranes places catalytic hydroboration of alkynes in the limelight. From a stereoselective point of view, hydroboration of alkynes can proceed in two ways, via *syn*-addition or *anti*-addition, affording either **syn-1/syn-2** or **anti-1/anti-2** respectively (Scheme 2a). Regioselectivity of the hydroboration of alkynes can also yield two forms of products, namely,  $\alpha$ -selective borylated product  **$\alpha$ -1/ $\alpha$ -2** or  $\beta$ -selective borylated product  **$\beta$ -1/ $\beta$ -2** (Scheme 2b). Regioselectivity and stereoselectivity of hydroboration of alkynes largely depends on the type of catalyst used. A well-known mechanism for achieving transition metal-catalyzed *syn*-hydroboration using HBpin is the generation of metal hydride and subsequent *syn*-hydrometallation. Conversely, the mechanism for obtaining *anti*-hydroboration often involves multiple steps. Notably, *anti*-hydroboration is uncommon and often difficult to control due to the isomerization process. Overall, *syn*- and *anti*-hydroboration mechanisms rely largely on catalysts. Keeping in mind the significance of this, in this review, we summarize the regio- and stereospecific hydroboration of alkynes. We believe that this overview will enable readers to explore the topic further, gaining greater insight into the mechanistic aspects of the specific hydroboration of alkynes.



**Scheme 2.** Stereo- and regioselective hydroboration of internal and terminal alkynes.

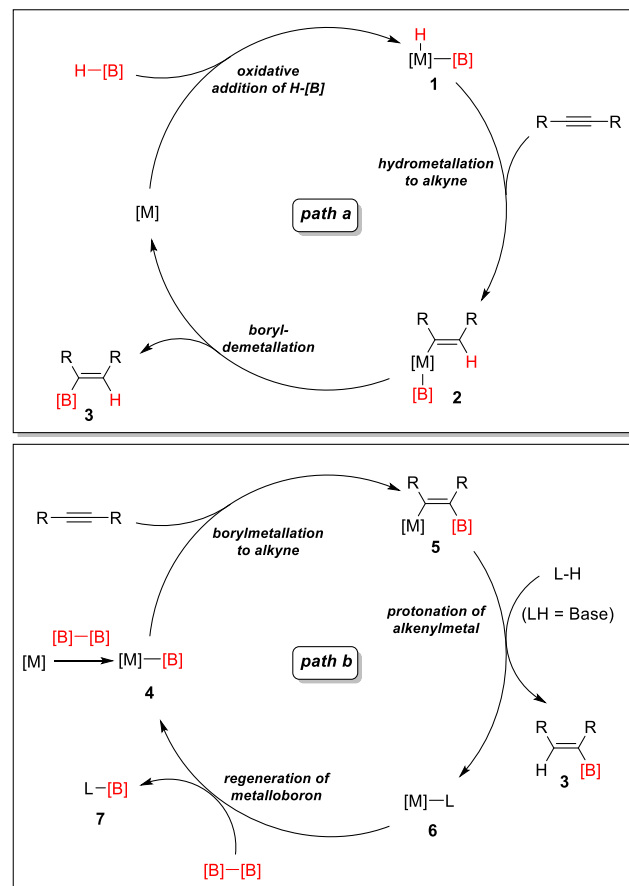
This review summary is based on the availability of published reports of regio- and stereoselective catalytic hydroboration of alkynes, containing detailed descriptions of *syn*-hydroboration and *anti*-hydroboration. Although a few previously published reviews summarize the hydroboration of unsaturated compounds, none of them dealt with selective alkyne hydroboration to provide a synthetically useful compound alkenylboron compounds.<sup>[7–24]</sup> Few review reports are also available which summarize the hydroelementation of olefins with specific catalysts<sup>[7,14,16,18–20,22,24]</sup> or specific substrates,<sup>[12]</sup> however, the reviews are too limited to a certain subject and touch very small area of mono-selective hydroboration of alkynes. Based on our observations, over the past few decades, regio- and stereoselective overview of alkyne hydroboration is a much-discussed topic. We believe that it should be comprehensively reviewed to collate all the relevant research in this field. This review covers reports published prior to 2021.

## 2 *syn*-Hydroboration of alkynes

### 2.1. Transition metal-catalyzed *syn*-hydroboration

The main attention of catalytic hydroboration of alkynes is the opportunity to control the stereochemistry of the products it affords. Metal catalysts play a key role in selectivity. There are two main mechanisms used to achieve the *syn*-hydroboration of alkynes catalyzed by metal precursors, as shown in Scheme 3. Initially, an oxidative addition to the metal center occurs to afford an M–H (as in **1**) or M–[B] (as in **4**) bond.

Subsequently, this metal hydride or M–[B] species is added to the alkyne moiety in a *cis*-manner, either via hydrometallation (path a) or boryl metallation (path b) to afford **2** or **5**, respectively. Later, boryl demetallation or protonation of alkenyl metal species provides the stereospecific *syn*-hydroborated product (Scheme 3).

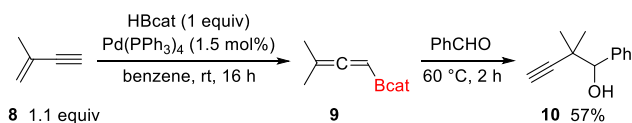


**Scheme 3.** Mechanistic aspect of *syn*-hydroboration of alkynes.

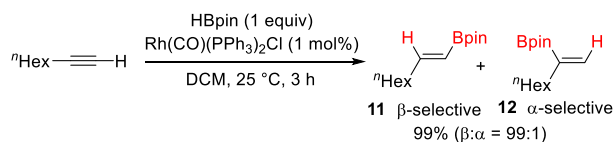
In a pioneering report on hydroboration of alkynes, Suzuki et al. described how conjugated enyne **8** undergoes selective hydroboration onto the alkyne moiety to afford allenic boronate **9** in the presence of Pd(PPh<sub>3</sub>)<sub>4</sub> as a catalyst. Upon quenching **9** with benzaldehyde, homopropargylic alcohol **10** was produced (Scheme 4a).<sup>[29]</sup> Using similar reaction conditions, a synthetic application of the Pd-catalyzed *syn*-hydroboration was reported for the synthesis of (*E*)-Doxepin.<sup>[30]</sup> In 1996, Pereira and Srebnik introduced an Rh-catalytic system for the  $\beta$ -selective *syn*-hydroboration of terminal alkynes using bench-top stable HBpin (Scheme 4b).<sup>[31]</sup> Their report revealed that a nickel catalyst [NiCp(PPh<sub>3</sub>)Cl] can work as efficiently as an Rh catalyst to afford the *E*-alkenylborane compound.<sup>[31]</sup> An application of the  $\beta$ -selective *syn*-hydroboration of terminal alkynes was reported using an immobilized heterogeneous Rh-catalytic system of ClRh[P(CH<sub>2</sub>CH<sub>2</sub>R<sub>6</sub>)<sub>3</sub>]<sub>3</sub> (R = (CF<sub>2</sub>)<sub>5</sub>CF<sub>3</sub>)<sub>3</sub>) in CF<sub>3</sub>C<sub>6</sub>F<sub>11</sub> solution. Significantly, the

catalyst was reused for up to three catalytic cycles with a high turnover number (TON).<sup>[32]</sup> Later, in 2004,  $\beta$ -selective *syn*-hydroboration of aromatic triyne was reported to afford the tris(boryl)vinyl product **14** (Scheme 4c).<sup>[33]</sup> Subsequently, Suzuki cross-coupling of multi-alkenylborane compounds led to a variety of substrates containing chromophore units to yield fluorescent dye-substituted products. Given the importance, further studies on Rh-catalytic systems for stereoselective hydroboration of alkynes were carried out,<sup>[34,35]</sup> showing that a rhodium hydride species could efficiently catalyze the selective hydroboration of 3,3,3-trifluoroprop-1-yne to produce *E*-selective product **15** (Scheme 4d).<sup>[35]</sup>

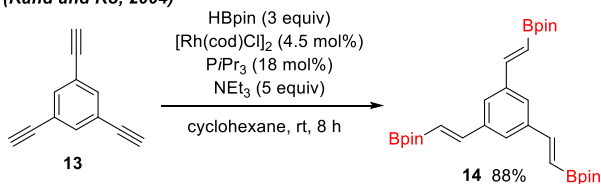
(a) Pd-catalyzed hydroboration of conjugated enyne (Suzuki, 1989)



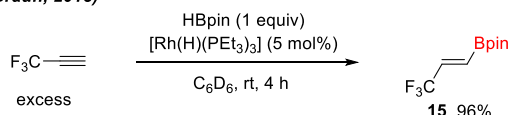
(b) Rh-catalyzed *syn*-hydroboration of terminal alkyne (Srebnik, 1996)



(c) Rh-catalyzed stereo-selective hydroboration of aromatic triyne (Kand and Ko, 2004)



(d) Rh-catalyzed stereo-selective hydroboration of 3,3,3-trifluoropropyne (Braun, 2018)

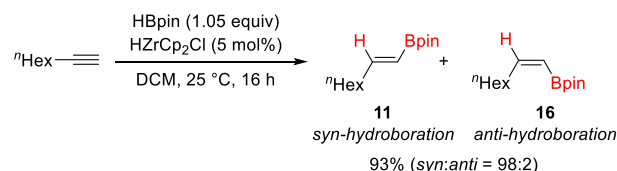


**Scheme 4.** (a) Early report of Pd-catalyzed stereoselective hydroboration. Rh-catalyzed hydroboration of (b) 1-octyne, (c) aromatic triyne, and (d) 3,3,3-trifluoropropyne.

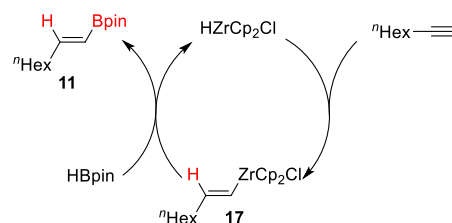
Apart from the Rh-catalytic systems, various other noble metals, for instance, Ir,<sup>[36,37]</sup> Ru,<sup>[38,39]</sup> Pt,<sup>[40]</sup> Au,<sup>[41]</sup> and Ag<sup>[42–44]</sup> proved their efficacy in the stereoselective hydroboration of alkynes. It is noteworthy that even a zirconocene hydride (HZrCp<sub>2</sub>Cl) efficiently catalyzed hydroboration of 1-alkyne, in which  $\beta$ -selective *syn*-hydroboration proceeded almost exclusively, affording a trace of an *anti*-hydroboration product (Scheme 5a).<sup>[45]</sup> Notably, in the case of internal alkynes, selectivity is retained. A simplified catalytic cycle proposed by the author suggests that hydrometallation followed by boryl demetallation is the key step in obtaining high stereoselectivity (Scheme 5b).<sup>[45]</sup> Recently, a Zr-catalyzed system was established for the  $\beta$ -selective

*syn*-hydroboration of terminal alkynes using diisopropylaminoborane (Scheme 5c).<sup>[46]</sup> In this reaction, a catalytic amount of Grignard reagent is required to catalytically transform the di-*iso*-propylamineborane complex (DIPAB; H<sub>3</sub>B←NH(*i*Pr)<sub>2</sub>) to di-*iso*-propylaminoborane (DIPOB; H<sub>2</sub>B–N(*i*Pr)<sub>2</sub>).

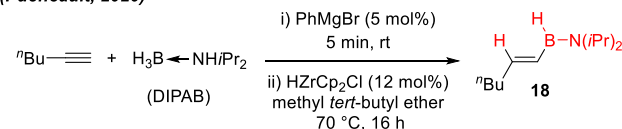
(a) Zr-catalyzed *syn*-hydroboration of terminal alkyne (Srebnik, 1995)



(b) Mechanism of Zr-catalyzed *syn*-hydroboration (Srebnik, 1996)



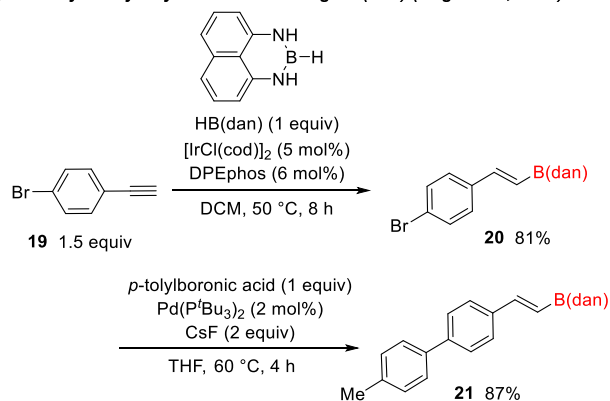
(c) Zr-catalyzed *syn*-hydroboration using diisopropylaminoborane (Pucheault, 2020)



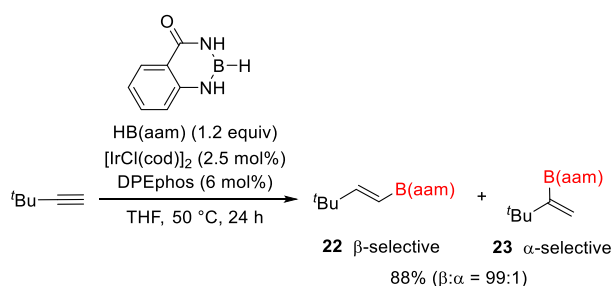
**Scheme 5.** (a) Zr-catalyzed *syn*-hydroboration and (b) its mechanism. (c) Stereoselective hydroboration of terminal alkyne catalyzed by Zr using diisopropylaminoborane.

Given the importance of alkenylborane compounds in synthetic organic chemistry, various protocols have been developed to finetune the stabilization of alkenylborane synthons. A notable contribution was made by Sugimoto et al. to the Ir-catalyzed *syn*-hydroboration of alkynes using naphthalene-1,8-diaminato (HB(dan)) (Scheme 6a). In the resultant product, the boronic acid moiety is masked by diamionaphthalene, which can easily be demasked in the presence of HCl (aq.) to give reactive boric acid. Significantly, the masked alkenylboronic acid contained a C(sp<sup>2</sup>)-Br bond (**20**) that easily experienced the Suzuki-Miyaura coupling reaction without disturbing the alkenylboron moiety (**21**, Scheme 6a).<sup>[36]</sup> This report was a significant contribution. Recently, Yoshida and coworkers synthesized anthranilamide-substituted borane [HB(aam)] as a stable and easy-to-handle substitute for HB(pin) for use in the Ir-catalyzed *syn*-selective hydroboration of terminal alkynes (**22**, Scheme 6b).<sup>[37]</sup>

(a) Ir-catalyzed *syn*-hydroboration using HB(dan) (Suginome, 2009)



(b) Ir-catalyzed *syn*-hydroboration using HB(aam) (Yoshida, 2019)

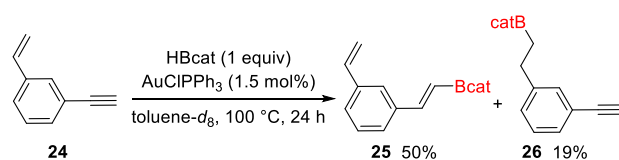


**Scheme 6.** Ir-catalyzed  $\beta$ -selective hydroboration of terminal alkynes using (a) HB(dan) and (b) HB(aam).

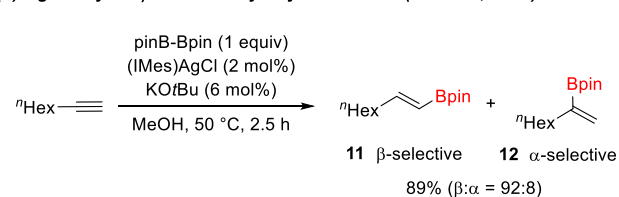
In 2009, Corma et al. reported the gold-catalyzed chemoselective hydroboration of alkynes. The authors showed that hydroboration occurred chiefly in terminal alkynes compared to terminal alkenes, yielding a substantial amount of **25** along with a minimal amount of **26** (Scheme 7a). They proposed that a gold-borane intermediate species was generated as an active species, rather than a gold-alkyne species.<sup>[41]</sup> In 2014, Yoshida et al. showed that an Ag-*N*-heterocyclic carbene complex has the qualities of a potent catalyst for the  $\beta$ -selective *syn*-hydroboration of terminal alkynes (Scheme 7b).<sup>[42]</sup> It was hypothesized that the reaction was triggered by the formation of borylsilver(I) species.<sup>[47]</sup> Subsequently, boryl metallation to alkynes proceeded largely in *syn*-fashion, followed by protonation by solvent MeOH, resulting in the hydroboration product (**11**). Recently, in two parallel reports, both the Rit and Bi working groups showcased that silver salt (AgSbF<sub>6</sub> or AgOAc) catalyzed the hydroboration of terminal alkynes using HBpin to exclusively yield *syn*-hydroborated *E*-alkenylborane **27** (Scheme 7c and 7d).<sup>[43,44]</sup> Unlike the previously reported reaction catalyzed by the Ag-*N*-heterocyclic carbene complex, the authors hypothesized that a radical pathway was involved, which resulted in the formation of an exclusive  $\beta$ -selective product. Apart from homogeneous catalytic systems, heterogeneous catalysts have also proved to be potent catalysts for the *syn*-hydroboration of alkynes. For instance, *N*-heterocyclic thione ligand-stabilized platinum nanoparticles displayed efficient reactivity in the hydroboration of terminal or internal

alkynes with significant selectivity for the *syn*-hydroborated product.<sup>[40]</sup> Hydroboration of terminal and internal alkynes using effective immobilization of Ru(CO)Cl(H)(PPh<sub>3</sub>)<sub>3</sub> in ionic liquids or in biphasic ionic liquid/supercritical CO<sub>2</sub> systems have also been reported, in which high *syn*-selectivity is maintained.<sup>[38,39]</sup>

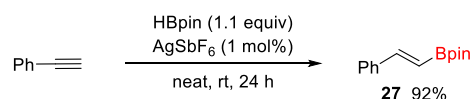
(a) Au-catalyzed stereo- and regio-selective hydroboration (Corma, 2009)



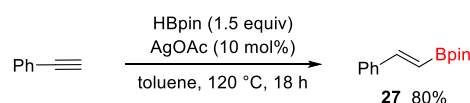
(b) Ag-catalyzed  $\beta$ -selective *syn*-hydroboration (Yoshida, 2014)



(c) Ag-catalyzed *syn*-hydroboration of terminal alkyne (Rit, 2019)

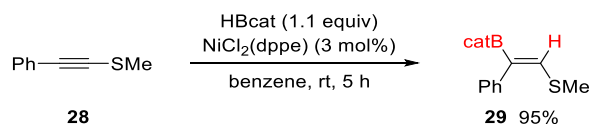


(d) Ag-catalyzed *syn*-hydroboration of terminal alkyne (Bi, 2019)



**Scheme 7.** (a) Au-catalyzed stereo- and position-selective hydroboration. (b–d) Ag-catalyzed stereoselective hydroboration of terminal alkynes.

3d transition metals are earth-abundant and demonstrate less toxic behavior, which makes them one of the prior choices for catalysis. In this regard, various first-row transition metals are also used as efficient catalysts in *syn*-selective hydroboration, for instance, Ti,<sup>[48,49]</sup> Mn,<sup>[50]</sup> Fe,<sup>[51–58]</sup> Co,<sup>[59–61]</sup> Ni,<sup>[62]</sup> Cu,<sup>[63–77]</sup> and Zn.<sup>[78]</sup>

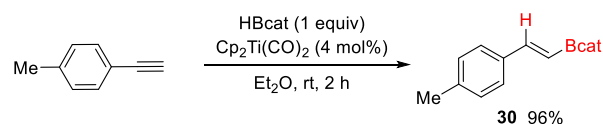


**Scheme 8.** Ni-catalyzed regio- and stereoselective hydroboration of thioacetylene (Miyaura and Suzuki, 1993).

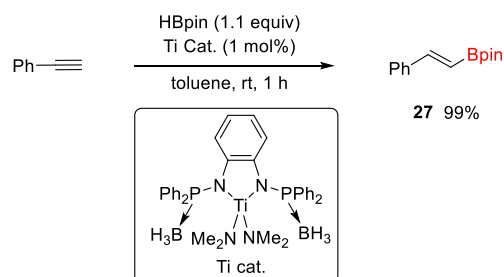
One of the early reports of regio- and stereoselective hydroboration of 1-(alkylthio)-1-alkyne (**28**) using HBcat and NiCl<sub>2</sub>(dppe) as catalysts (Scheme 8) was published by Miyaura and Suzuki in 1993.<sup>[62]</sup> Notably, hydroboration proceeded exclusively on the  $\beta$ -position with respect to the thioalkyl group. Unfortunately, this catalytic system did not show significant efficacy in

terms of selectivity when only an aliphatic or aromatic substituted alkyne (1-octyne or 1-phenyl-1-propyne) was used as the substrate.<sup>[62]</sup> Soon after, Hartwig et al. showcased a competent catalytic protocol for the *syn*-hydroboration of alkynes with HBcat using readily available dicarbonyltitanocene as a catalyst (Scheme 9a). In a plausible mechanism, it was shown that  $\sigma$ -bond metathesis proceeded with HBcat and metallacyclopene generated from the reaction between alkynes and the titanocene complex.<sup>[48]</sup> Very recently, Panda et al. synthesized a titanium(IV) complex supported by dianionic amidophosphine–borane ligands, which displayed high efficacy toward the  $\beta$ -selective *syn*-hydroboration of terminal alkynes (Scheme 9b).<sup>[49]</sup> Geetharani and coworkers also reported that a rare-earth metal of group 3 (Sc) works as an efficient catalyst in the *syn*-selective hydroboration of alkynes (Scheme 9c).<sup>[79]</sup> Commercially available Lewis acid Sc(OTf)<sub>3</sub> was used as a catalyst along with a catalytic amount of NaBHET<sub>3</sub>, which successfully *syn*-hydroborated a series of the terminal as well as internal alkynes. A general mechanism for *syn*-selective hydroboration of alkyne using Ti or Sc as the catalyst is postulated in Scheme 9d which is in principle different from the general mechanism presented in Scheme 3. At first, a metal-hydride **31A** is thought to be produced which added to alkyne in a *syn*-fashion via **31B**. In the last step, metal-alkene species **31C** reacted with another molecule of hydroboron compound to produce the *syn*-hydroborated product along with the regeneration of metal-hydride species.<sup>[49,79]</sup>

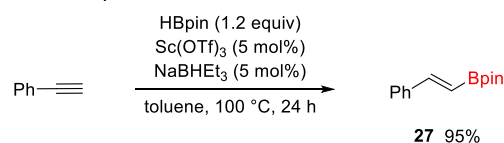
(a) *Ti*-catalyzed selective hydroboration of alkyne (Hartwig, 1996)



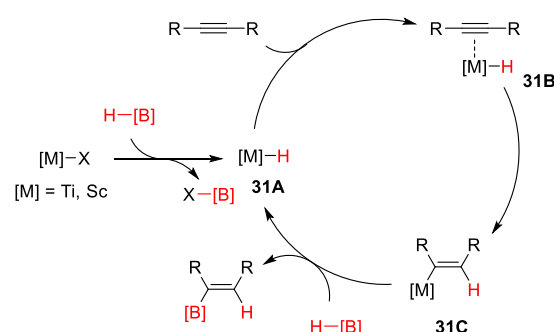
(b) *Ti*-catalyzed selective hydroboration of alkyne (Panda, 2020)



(c) Lewis acidic Sc(OTf)<sub>3</sub>-catalyzed selective hydroboration of alkyne (Geetharani, 2018)

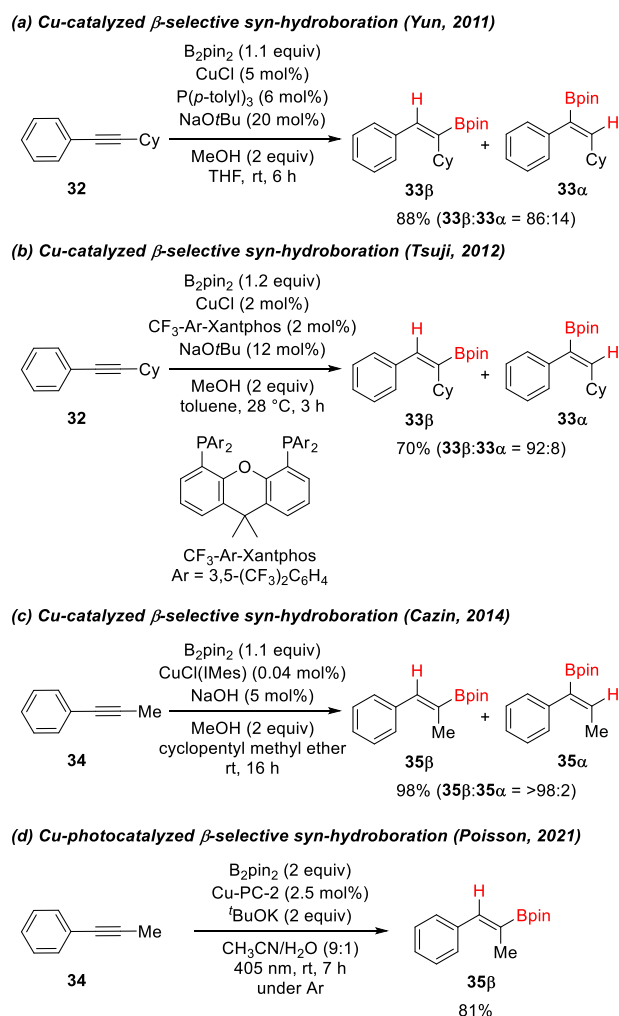


(d) General mechanism for *Ti* or *Sc* catalyzed hydroboration of alkyne

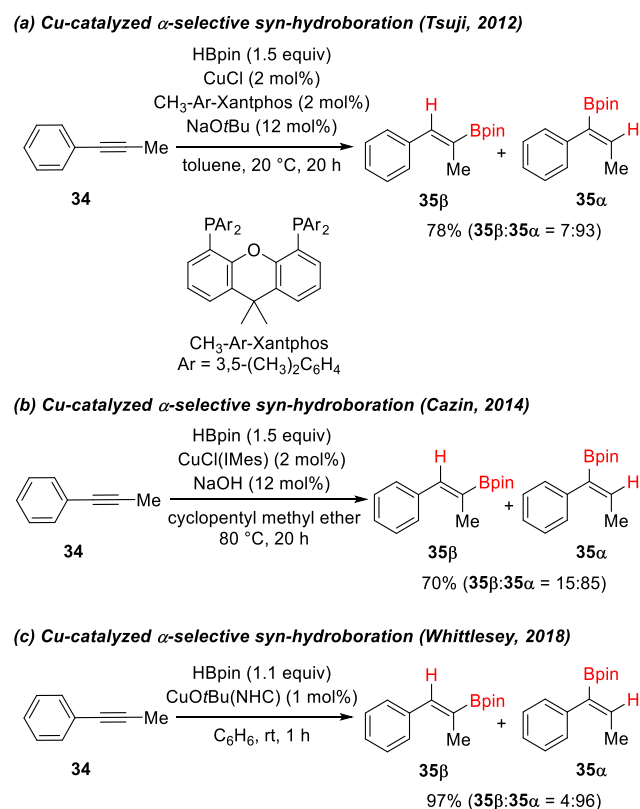


**Scheme 9.** (a) and (b) *Ti*-catalyzed *syn*-selective hydroboration of alkynes. (c) Sc(OTf)<sub>3</sub>-catalyzed *syn*-selective hydroboration. (d) General mechanism for *syn*-hydroboration of alkyne using *Ti* or *Sc* as catalysts.

Cu catalysts have contributed significantly to hydroboration of alkynes in a highly stereo- and regioselective manner.<sup>[63–77]</sup> It is worthy of mention that the  $\beta$ - or  $\alpha$ -selective borylation of aromatic substituted unsymmetrical internal alkynes (such as **32** or **34**) was achieved by varying the borylating reagents. The Yun, Tsuji, and Cazin groups independently reported a similar Cu-catalytic system using B<sub>2</sub>pin<sub>2</sub> as the borylating precursor to achieving  $\beta$ -selective *syn*-hydroboration products **33 $\beta$**  or **35 $\beta$**  (Scheme 10).<sup>[63,64,74]</sup> Likewise a Cu-photocatalytic system was also developed by Poisson et al for obtaining  $\beta$ -selective *syn*-hydroboration of internal alkynes with complete selectivity (Scheme 10d).<sup>[69]</sup> Conversely,  $\alpha$ -selective *syn*-hydroboration product **35 $\alpha$**  was obtained when HBpin was used in a Cu-catalytic system mentioned in Scheme 11.<sup>[64,74,77]</sup>

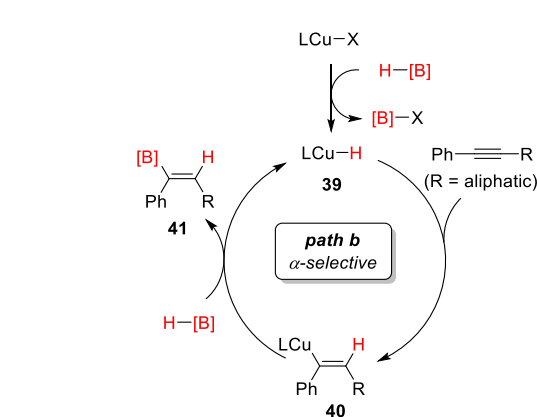
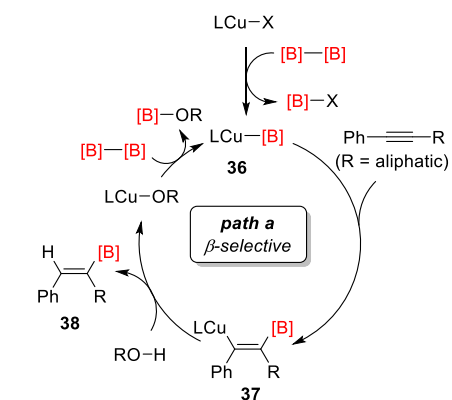


**Scheme 10.** (a)–(c) Cu-catalyzed  $\beta$ -selective *syn*-hydroboration of internal alkynes. (d) Cu-photocatalyzed  $\beta$ -selective *syn*-hydroboration of internal alkynes.



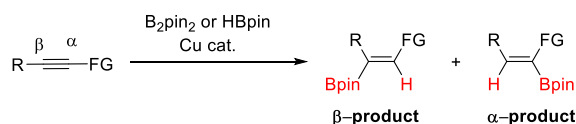
**Scheme 11.** (a)–(c) Cu-catalyzed  $\alpha$ -selective *syn*-hydroboration of internal alkynes.

Complementary  $\beta$ - and  $\alpha$ -selective *syn*-hydroboration proceed based on the use of borylating reagent. For clarity, two plausible catalytic cycles are presented in Scheme 12. A boryl copper species (**36**) is responsible for the  $\beta$ -selective product **38** (path a, Scheme 12), while a copper hydride species (**39**) was formed from the reaction between Cu-salt and HBpin, which is in charge of the formation of  $\alpha$ -selective product **41** (path b, Scheme 12). Following the formation of copper hydride **39**, hydrocupration to alkyne proceeded to yield **40**, which showed high regioselectivity owing to the directing effect of phenyl substitution. Later boryl demetallation afforded a high  $\alpha$ -selective *syn*-hydroborated product (**41**) (path b, Scheme 12).<sup>[64]</sup>

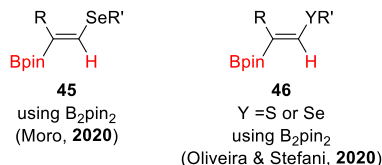
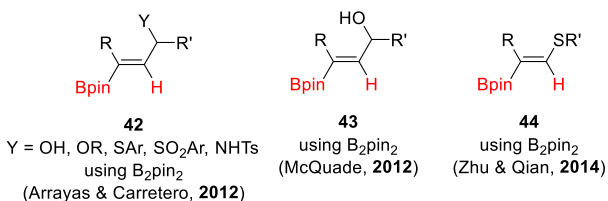


**Scheme 12.** Mechanistic differences in  $\beta$ - and  $\alpha$ -selective borylation of unsymmetrical aromatic substituted alkynes, using  $B_2pin_2$  and HBpin, respectively.

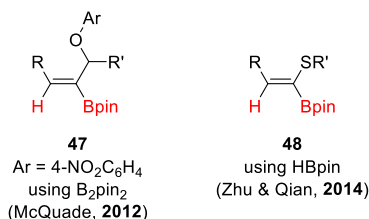
Substituted functional groups on alkynes have also contributed notably in controlling  $\alpha$ - or  $\beta$ -selective product formation in a Cu-catalytic system. In this regard, the Arrayás and Carretero group reported that the presence of a propargylic polar group, such as OH, OR, SAR,  $SO_2Ar$ , and NHTs allowed excellent  $\beta$ -selectivity ( $\beta$  to the propargylic function, as shown in **42**, Scheme 13).<sup>[70]</sup> McQuade et al. reported that regioselective *syn*-hydroboration of propargylic alcohols and ethers can also occur, providing either an  $\alpha$ - or  $\beta$ -selective product depending on the starting materials – propargylic alcohols (**43**) or ethers (**47**) and NHC ligand on the copper complex.<sup>[71]</sup> Chalcogen-substituted alkynes also control the regioselectivity of a *syn*-hydroboration reaction (as shown in **44–46** and **48**).<sup>[67,68,73]</sup> Given the importance of selective hydroboration reactions and considering the high efficacy of the copper catalytic system, a few heterogeneous Cu-catalytic systems have been reported in the hydroboration of alkynes with high *syn*-selectivity.<sup>[66,72,76]</sup>



#### $\beta$ -selective *syn*-hydroboration



#### $\alpha$ -selective *syn*-hydroboration

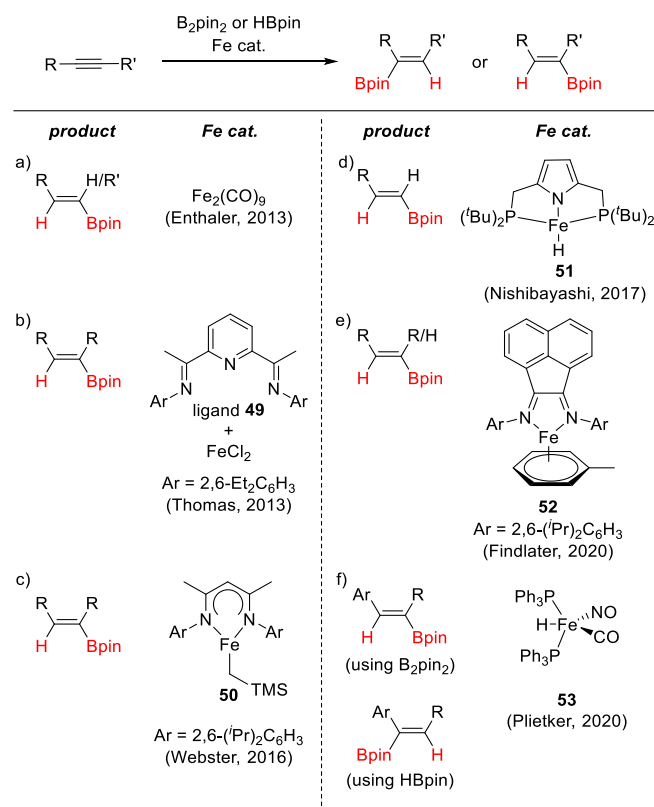


**Scheme 13.** Various Cu-catalyzed functional groups directed  $\alpha$ - or  $\beta$ -selective *syn*-hydroboration.

Bearing in mind the importance of earth-abundant metal catalysts in selective hydroboration reactions, Fe-based complexes have been widely studied. Notably, in 2013, Enthaler et al. reported the first example of a  $Fe_2(CO)_9$  catalytic system for the selective hydroboration of alkynes (Scheme 14a).<sup>[52]</sup> This protocol selectively provided *syn*-hydroboreated *E*-alkene as a product when terminal alkynes were used as the starting material. However, in the case of an unsymmetrical alkyne, a mixture of  $\alpha$ - and  $\beta$ -borylated products were obtained. In the same year, Thomas et al. reported a bench-stable iron complex in combination with a bis(imino)pyridine ligand, which upon activation with Grignard reagent, proved to be an efficient system for the *syn*-selective hydroboration of alkynes (Scheme 14b).<sup>[51]</sup> Later, Webster et al. introduced an alkylated iron complex (**50**) for the hydroboration of alkynes (Scheme 14c).<sup>[55]</sup> However, the report shows a narrow substrate scope for unsymmetrically substituted internal alkynes, as a mixture of products was obtained. An iron-hydride complex (**51**) supported by a pincer ligand was employed by Nishibayashi and coworkers for the *syn*-hydroboration of internal alkynes to afford *E*-alkene (Scheme 14d).<sup>[56]</sup> Recently, Findlater et al. presented a bis(2,6-diisopropylaniline)acenaphthene-ligated iron complex (**52**) for the hydroboration of terminal and internal alkynes (Scheme 14e).<sup>[57]</sup> Around the same



time, an iron-hydride complex (**53**) was used for the *syn*-hydroboration of unsymmetrical internal alkynes, which provided complementary regioselectivity based on the use of a boron source ( $B_2pin_2$  or HBpin; Scheme 14f).<sup>[58]</sup> Furthermore, stereoselective hydroboration of alkynes was achieved using iron nanoparticles or iron-based heterogeneous catalysts.<sup>[53,54]</sup>

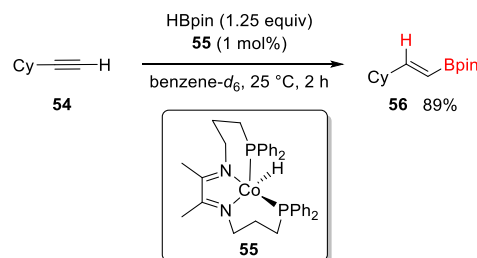


**Scheme 14.** (a)-(f) Various Fe-catalytic systems in *syn*-selective hydroboration.

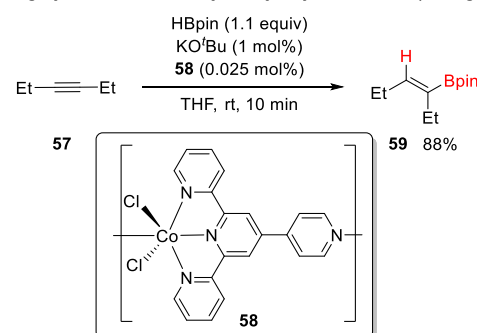
A cobalt-catalytic system was introduced by Trovitch et al. for *syn*-selective hydroboration using an  $\alpha$ -diimine cobalt hydride complex (**55**) as the catalyst. This protocol provides a decent substrate scope for terminal alkynes, affording *E*-alkenylboranes with high selectivity (Scheme 15a).<sup>[59]</sup> Later, in 2019, Zhang et al. introduced a bench-stable and inexpensive coordination polymeric cobalt complex (**58**) as a highly efficient catalyst in combination with  $KO^tBu$  for the stereoselective *syn*-hydroboration of the terminal as well as internal alkynes (Scheme 15b).<sup>[61]</sup> Notably, this catalytic system works efficiently even with very low catalyst loading and can provide a turnover frequency (TOF) of up to 47520 ( $h^{-1}$ ). Ge et al. reported a  $Co(acac)_2$ -catalyzed regio-divergent stereoselective *syn*-hydroboration of symmetrical or unsymmetrical 1,3-diynes in the presence of a bisphosphine ligand (dppf or xantphos). Remarkably, excellent  $\alpha$ -selectivity was obtained when dppf was used as a ligand along with the cobalt pre-catalyst. However, opposite selectivity ( $\beta$ -selective) was witnessed when xantphos was used as a ligand

(Scheme 15c).<sup>[60]</sup> A detailed experimental investigation suggested that  $Co(acac)_2/dppf$ -catalyzed hydroboration proceeds through a cobalt boryl intermediate to afford **61 $\alpha$** , while the hydroboration reaction catalyzed by  $Co(acac)_2/xantphos$  proceeds via a cobalt-hydride intermediate to provide **61 $\beta$**  in significant quantity.

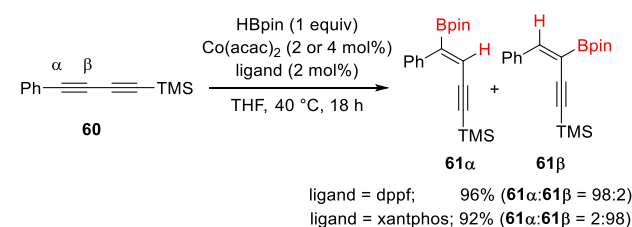
**(a) Co-catalyzed *syn*-hydroboration of terminal alkyne (Trovitch, 2017)**



**(b) Highly efficient Co-catalyzed *syn*-hydroboration (Zhang, 2019)**



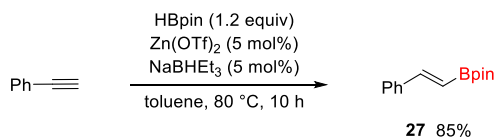
**(c) Co-catalyzed regio-divergent *syn*-hydroboration of 1,3-diyne (Ge, 2019)**



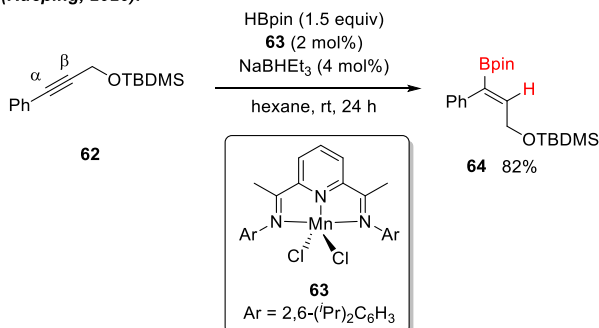
**Scheme 15.** Co-catalyzed *syn*-selective hydroboration of alkynes.

*Syn*-selective hydroboration of alkynes was reported using commercially available  $Zn(OTf)_2$  as a catalyst in combination with  $NaBHET_3$  (Scheme 16a).<sup>[78]</sup> A series of internal and terminal alkynes served as a substrate to yield the corresponding products in good quantity. Rueping et al. reported the hydroboration of propargylic alcohol (**62**) catalyzed by a manganese complex (**63**) to afford an  $\alpha$ -selective *syn*-hydroboration product (Scheme 16b).<sup>[50]</sup> Notably, along with propargylic alcohol, propargylic amines, and symmetrical internal alkynes participated efficiently in this Mn-catalyzed *syn*-hydroboration reaction to afford corresponding borylated alkenes. It was noted that the success of the reaction relies on the use of  $NaBHET_3$ , as it helped to form the catalytically active Mn species.

(a) Zn-catalyzed *syn*-selective hydroboration of alkyne (Geetharani, 2019)



(b) Mn-catalyzed  $\alpha$ -selective *syn*-hydroboration of propargylic alcohols (Rueping, 2020).

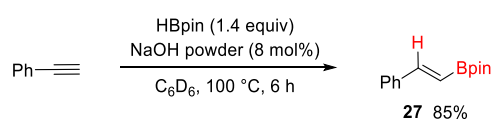


Scheme 16. (a) Zn- and (b) Mn-catalyzed *syn*-hydroboration of propargylic alcohols.

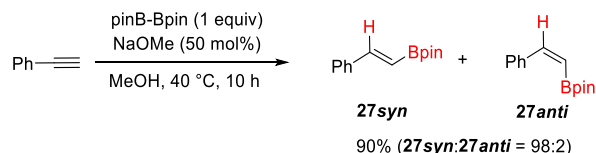
## 2.2. Alkali and alkaline earth metal-catalyzed *syn*-hydroboration

Having great worth of alkenyl organoboron compounds as synthetic intermediates, various catalysts have been designed for the selective hydroboration of alkynes. One of the finest contributions to this field was made when alkali and alkaline earth metals began to be used as catalysts. There are several advantages of using alkali and alkaline earth metal catalysts over transition metal catalysts, such as abundance, cost effectiveness, and easily separable techniques. The first selective hydroboration of alkynes, using a catalytic amount of NaOH, generated in-situ in the reaction mixture induced by NaOH, facilitated the reaction. However, this hypothesis has not been proven yet. Another report appeared just a year later, which dealt with NaOMe as an initiator in the *syn*-hydroboration of terminal as well as internal alkynes (Scheme 17b).<sup>[81]</sup> Notably, a trace of *anti*-hydroborated product was also obtained during this process.

(a) NaOH-catalyzed *syn*-hydroboration of alkyne (Wu, Liu and Zhao, 2017)

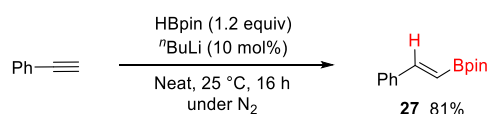


(b) NaOMe-induced *syn*-hydroboration of alkyne (Wen, 2018)

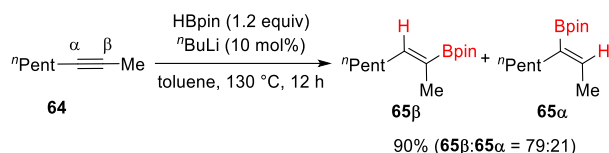


Scheme 17. (a) and (b) Sodium salt as catalysts in the *syn*-selective hydroboration of alkynes.

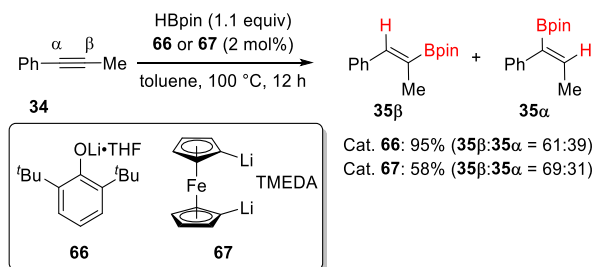
(a) *n*BuLi-catalyzed *syn*-hydroboration of alkyne (Bao and Xue, 2019)



(b) *n*BuLi-catalyzed *syn*-hydroboration of alkyne (Shi and Xu, 2019)



(c) Li compound-catalyzed *syn*-hydroboration of alkyne (Sen, 2019)

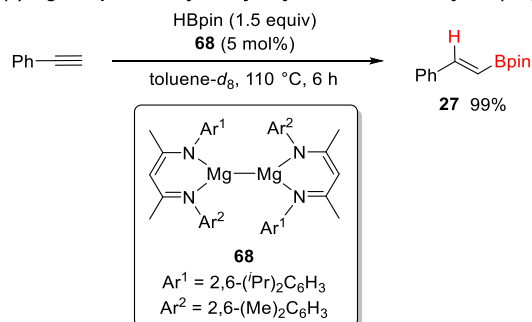


Scheme 18. (a)-(c) Lithium compounds as catalysts in the *syn*-selective hydroboration of alkynes.

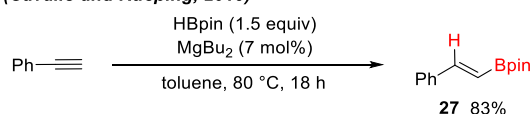
It was found that even organolithium compounds can catalyze the hydroboration of alkynes. The Bao/Xue and Shi/Xu groups independently reported that *n*-butyl lithium can efficiently catalyze the hydroboration of terminal (Scheme 18a)<sup>[82]</sup> as well as internal alkynes (Scheme 18b).<sup>[83]</sup> In the case of unsymmetrical internal alkynes, a mixture of products was obtained, with a major amount comprising 65 $\beta$ . The computational study suggested that a zwitterionic intermediate, generated from the reaction of HBpin and *n*BuLi, plays a key role in hydroboration.<sup>[82]</sup> Soon after, Sen et al. introduced another efficient catalytic system in which a Li compound (66 or 67) catalyzed terminal or internal alkynes during hydroboration (Scheme 18c). In the case of unsymmetrical

substituted internal alkynes, a mixture of products was obtained, with a higher portion constituted by the  $\beta$ -product (**35 $\beta$** ).<sup>[84]</sup>

(a) Mg complex-catalyzed *syn*-hydroboration of alkynes (Ma, 2018)



(b) MgBu<sub>2</sub>-catalyzed *syn*-hydroboration of alkynes (Cavallo and Rueping, 2019)

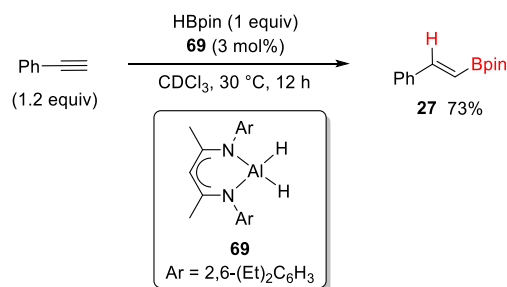


**Scheme 19.** (a) and (b) Mg-catalyzed *syn*-selective hydroboration of alkynes.

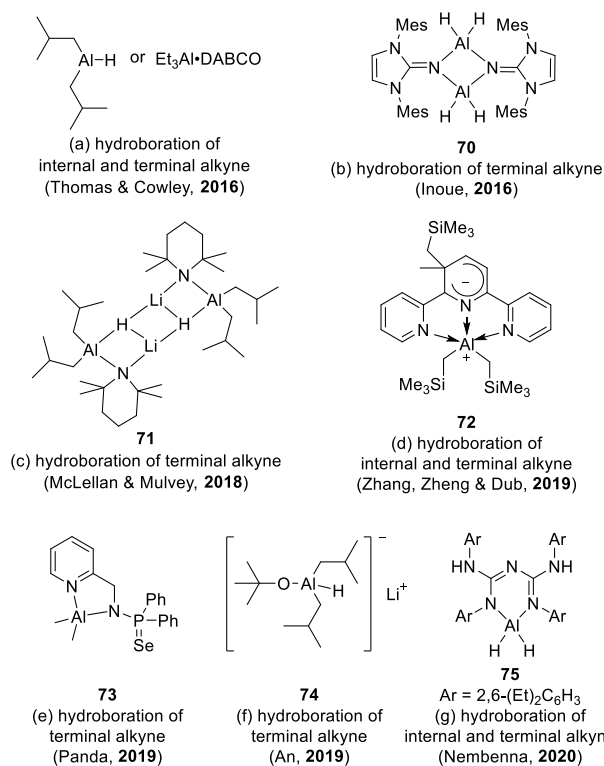
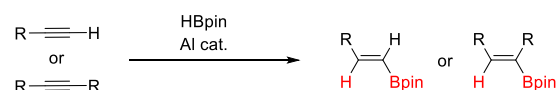
Ma et al. reported a di-magnesium complex (**68**) bearing an unsymmetrical  $\beta$ -diketimine ligand, which works as a reactive pre-catalyst in the *syn*-selective hydroboration of alkynes (Scheme 19a).<sup>[85]</sup> The authors discovered the involvement of a magnesium hydride species as a reactive intermediate based on experimental and computational evidence. Soon after, Cavallo, Rueping, and coworkers showed that readily available MgBu<sub>2</sub> can catalyze the same transformation with excellent *syn*-selectivity (Scheme 19b).<sup>[86]</sup> Along with terminal alkynes, various internal alkynes were also suitable candidates for this *syn*-hydroboration protocol.

### 2.3. Aluminum-catalyzed *syn*-hydroboration

As discussed in the first section, transition metal catalysts have contributed significantly to the selective hydroboration of alkynes. However, interest in sustainable chemical processes is growing and researchers are seeking replacements for transition metal catalysts. In this regard, the main group elements are comparable substitutes for transition metal catalysts. Aluminum-related compounds have contributed notably to the selective hydroboration of alkynes. In 2016, Roesky et al. first reported that an aluminum dihydride complex (**69**), bearing a  $\beta$ -diketiminate ligand, successfully catalyzed the *syn*-hydroboration of terminal alkynes (Scheme 20).<sup>[87]</sup> Various aromatic groups-substituted as well as aliphatic group-substituted terminal alkynes reacted smoothly to afford the *E*-alkene products.



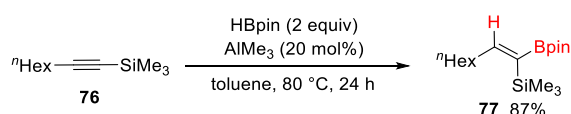
**Scheme 20.** Aluminum dihydride-catalyzed *syn*-hydroboration of terminal alkynes (Yang, Parameswaran, and Roesky, 2016).



**Scheme 21.** (a)-(g) Various aluminum complexes work efficiently in the *syn*-selective hydroboration of internal and terminal alkynes.

Following the pioneering report by Roesky et al.,<sup>[87]</sup> various other aluminum complexes were explored for stereoselective hydroboration. For instance, the Thomas and Cowley groups reported that commercially available aluminum hydride DIBAL-H or bench-stable Et<sub>3</sub>Al·DABCO efficiently catalyzes the *syn*-hydroboration of internal and terminal alkynes (Scheme 21a).<sup>[88]</sup> Inoue et al. reported an aluminum hydride (**70**) stabilized by *N*-heterocyclic imines as a catalyst in the hydroboration of terminal alkynes (Scheme 21b).<sup>[89]</sup> the McLellan and Mulvey groups

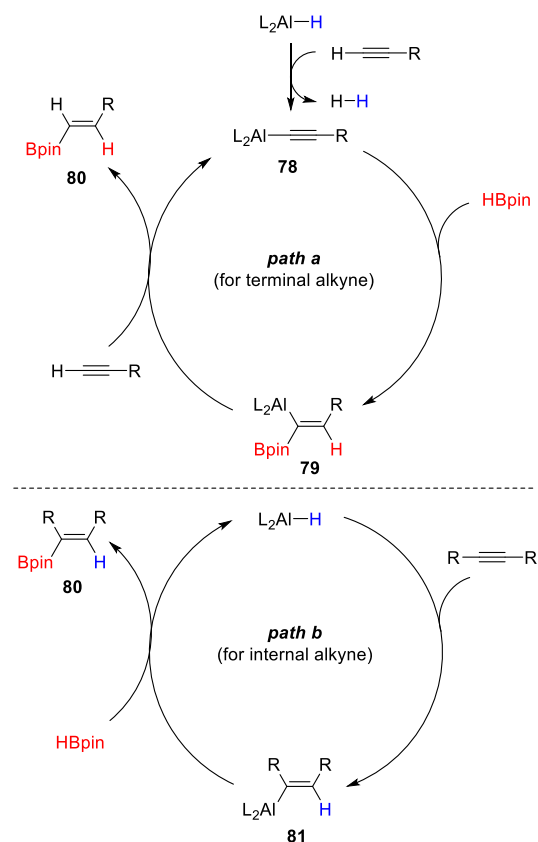
reported a neutral aluminum lithium complex (**71**), which functioned cooperatively as a catalyst in the hydroboration of terminal alkynes (Scheme 21c);<sup>[90]</sup> a zwitterionic aluminum complex (**72**) was introduced by Zhang, Zheng, and Dub in the efficient *syn*-hydroboration of internal or terminal alkynes with a high TON (up to 1000) (Scheme 21d);<sup>[91]</sup> Panda et al. introduced an aluminum complex (**73**) supported by a functionalized amidophosphine ligand for smooth hydroboration of terminal alkynes (Scheme 21e);<sup>[92]</sup> lithium di-*iso*-butyl-*tert*-butoxyaluminum hydride (LDBBA; **74**) was used by An et al. in the stereoselective hydroboration of terminal alkynes (Scheme 21f);<sup>[93]</sup> and very recently, Nembenna et al. reported that conjugated bis-guanidinate (CBG)-supported aluminum dihydride (**75**) proficiently catalyzed the *syn*-hydroboration of internal and terminal alkynes (Scheme 21g).<sup>[94]</sup> Since various aluminum catalytic systems have been developed for alkyne *syn*-hydroboration, it is now easier to search for the right choice of Al-catalyst for a certain substrate. Furthermore, progress in this field is ongoing. A notable example of aluminum complex catalysis was reported by Hong, Xu, and Shi in the regio- and stereoselective hydroboration of alkynylsilanes (Scheme 22).<sup>[95]</sup> In particular, they found that several alkynylsilanes, bearing various functional groups and heterocyclic substituents, formed hydroborated products smoothly in good yields and with high selectivity.



**Scheme 22.** Aluminum-catalyzed *syn*-hydroboration of alkynylsilanes (Hong/Xu/Shi, 2019).

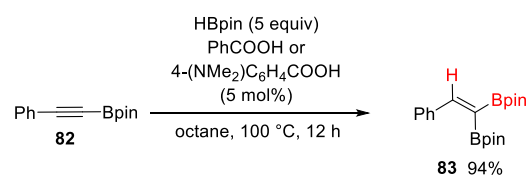
Considering the stereoselective accuracy of aluminum-catalyzed hydroboration of internal and terminal alkynes, establishing the general mechanistic aspect of such hydroboration is important (Scheme 23). In an aluminum complex-catalyzed hydroboration reaction, the aluminum hydride species, which mainly catalyzes the reaction, is either used or generated in-situ. In the case of a terminal alkyne, at first, deprotonation of the alkyne with aluminum hydride occurs, leading to the formation of aluminum acetylide (**78**) and a molecule of H<sub>2</sub>. Usually, this step is exothermic. The polarization of the C≡C bond in **78** resulted in a cycloaddition of HBpin bond to the C≡C bond in a *syn*-fashion via a four-membered transition state to form **79**. Again, a highly polarized bond of Al–C in **79** favors the  $\sigma$ -bond metathesis with another molecule of alkyne to yield the *syn*-hydroborated product **80** (*path a*, Scheme 23).<sup>[87]</sup> Conversely, in the case of internal alkynes, a different mechanism operates, in which the Al–H bond of aluminum hydride is inserted into the alkyne triple bond in a *syn*-fashion to produce an intermediate **81**.

Subsequently, in a reaction with HBpin, transmetalation occurs to form the desired *syn*-hydroborated product **80** along with the regeneration of aluminum hydride (*path b*, Scheme 23).<sup>[87,91,93,94]</sup>



**Scheme 23.** Mechanistic aspects of aluminum-catalyzed hydroboration of internal and terminal alkynes.

## 2.4. Metal-free catalytic *syn*-hydroboration

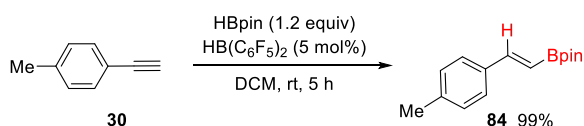


**Scheme 24.** A carboxylic acid-catalyzed *syn*-hydroboration of alkynes (Jin, 2014).

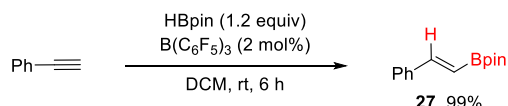
To eliminate the possibility of the incorporation of metals into a large-scale organic synthetic process, ongoing research focuses on the development of metal-free catalytic systems. Notably, selective hydroboration of alkynes has been achieved in several cases using various metal-free catalytic systems. An important report by Jin et al. was published in 2014, which dealt with benzoic acid derivatives as potential catalysts for hydroboration. Notably, the authors demonstrated that internal alkynes substituted with Bpin (**82**) reacted efficiently to afford the synthetically

important 1,1-diborylalkene **83** (Scheme 24).<sup>[96]</sup> This catalytic system applies to a wide range of alkynes, yielding the expected *syn*-hydroborated product with exclusive selectivity.

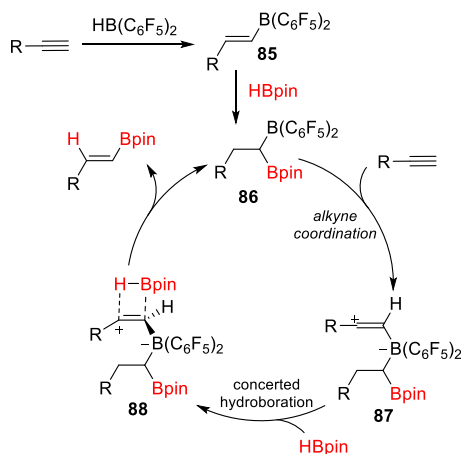
(a) Piers' borane-catalyzed hydroboration of alkyne (Stephan, 2016)



(b) B(C<sub>6</sub>F<sub>5</sub>)<sub>3</sub>-catalyzed hydroboration of alkyne (Melen, 2017)



(c) Proposed mechanism of Piers' borane-catalyzed hydroboration of alkyne (Stephan, 2016)



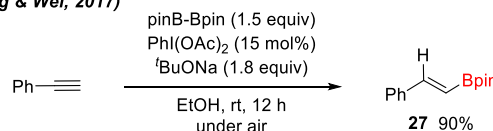
**Scheme 25.** (a) and (b) Borane-catalyzed *syn*-selective hydroboration of alkynes and (c) its mechanistic aspect.

In 2016, Stephan et al. proposed the use of Piers' borane as a catalyst in the *syn*-selective hydroboration of internal and terminal alkynes (Scheme 25a).<sup>[97]</sup> Recently, Melen et al. showed that B(C<sub>6</sub>F<sub>5</sub>)<sub>3</sub> also can be used for the same transformation, affording *syn*-selective products exclusively (Scheme 25b).<sup>[98]</sup> The mechanistic aspects of such borane-catalyzed alkyne hydroboration reactions are interesting. In the case of the former catalytic reaction, Piers' borane (HB(C<sub>6</sub>F<sub>5</sub>)<sub>2</sub>) acts as a pre-catalyst, which generates an unsymmetrical *gem*-diborylated species (**86**) through the concerted hydroboration of alkynes, as shown in Scheme 25c. This *syn*-1,2-hydroborated species (**86**) serves as a catalyst, which at first enables the electrophilic activation of alkynes, to form  $\sigma$ -complex **87**. Subsequently, concerted hydroboration of **87** proceeds in a *syn*-fashion via **88**. Thus, product release occurs along with regeneration of the active catalyst **86**.

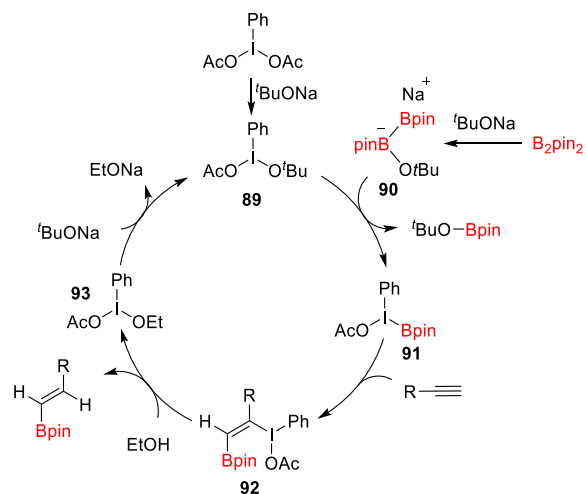
Another metal-free catalytic hydroboration system, which deals with the use of PhI(OAc)<sub>2</sub> as a catalyst, has been reported. Notably, various terminal alkynes

were hydroborated in good yields with excellent regio- and stereoselectivity (Scheme 26a).<sup>[99]</sup> A plausible mechanism for PhI(OAc)<sub>2</sub>-catalyzed hydroboration is given in Scheme 26b. At first, the intermediate **90** is generated with the reaction between B<sub>2</sub>pin<sub>2</sub> and NaO<sup>t</sup>Bu, which when reacted with the iodonium reagent (**89**) produces the key intermediate (**91**) containing the I–B bond. Subsequently, the addition of iodonium borane species (**91**) to alkynes proceeds in a *syn*-fashion to afford the intermediate **92**. Finally, the target *syn*-hydroborated product is released in the presence of ethanol as a hydrogen donor reagent. Very recently, a metal-catalyst free electrochemical hydroboration of terminal alkyne was reported by Jubault and Poisson et al (Scheme 26c).<sup>[100]</sup> The use of <sup>n</sup>Bu<sub>4</sub>NBF<sub>4</sub> as an electrolyte in MeOH, stainless steel electrodes (SSE) at both cathode and anode with a current of 10 mA and a total charge of 2 F.mol<sup>-1</sup> were crucial for achieving exclusive *syn*-hydroborated product in excellent yield.

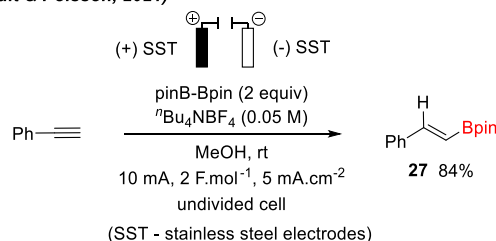
(a) PhI(OAc)<sub>2</sub>-catalyzed *syn*-hydroboration of terminal alkynes (Zhang & Wei, 2017)



(b) Proposed mechanism for PhI(OAc)<sub>2</sub>-catalyzed *syn*-hydroboration of terminal alkynes (Zhang & Wei, 2017)



(c) Electrochemical *syn*-hydroboration of terminal alkyne (Jubault & Poisson, 2021)



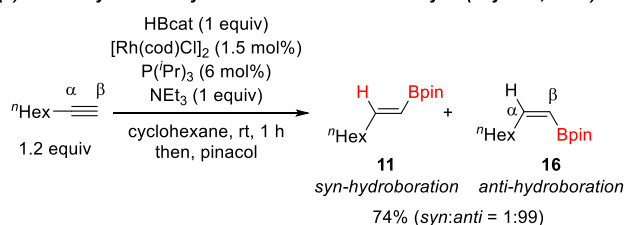
**Scheme 26.** (a) PhI(OAc)<sub>2</sub> as a catalyst in the *syn*-selective hydroboration of terminal alkynes and (b) its mechanistic aspects. (c) Metal catalyst-free electrochemical *syn*-hydroboration of terminal alkyne.

### 3. *anti*-Hydroboration of alkynes

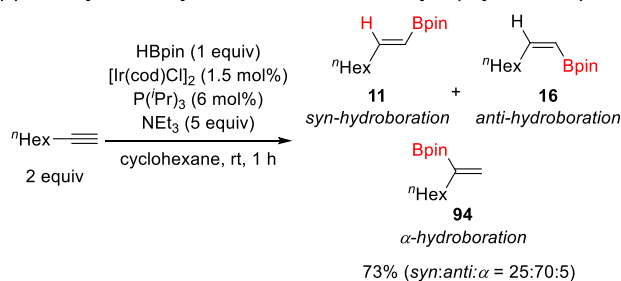
As already mentioned, hydroboration of alkynes is of high significance as it provides a reliable and straightforward means of synthesizing synthetically important alkenyl borane compounds. Hence, obtaining a single isomer as a product of hydroboration of an alkyne is important. Notably, compared to the occurrence of *syn*-hydroboration products, *anti*-hydroboration is rare, due to the *syn*-selective nature of hydroboration and relative thermodynamic instability of the *Z*-isomer (in the case of a product generated from terminal alkynes). Hence, non-classical *anti*-hydroboration of alkynes has been mainly reported in a transition metal catalytic system. In this section, we summarize reported catalytic protocols for the *anti*-hydroboration of alkynes, along with their mechanistic aspects.

#### 3.1. Transition metal-catalyzed *anti*-hydroboration

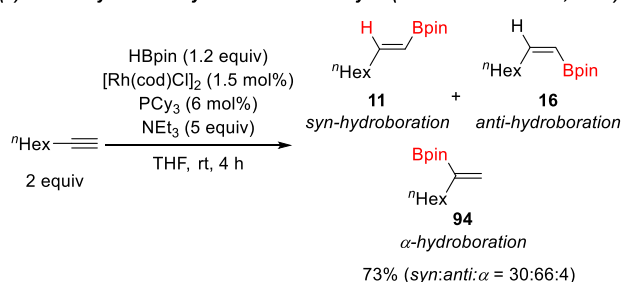
##### (a) Rh-catalyzed *anti*-hydroboration of terminal alkyne (Miyaura, 2000)



##### (b) Ir-catalyzed *anti*-hydroboration of terminal alkyne (Miyaura, 2000)



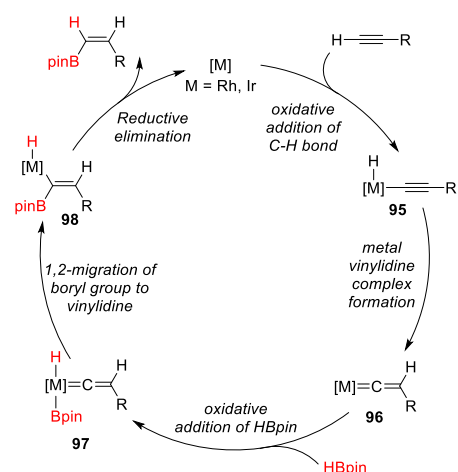
##### (c) Rh-catalyzed *anti*-hydroboration of alkyne (Carbo & Fernandez, 2012)



**Scheme 27.** (a) and (c) Rh- or (b) Ir-catalyzed *anti*-hydroboration of terminal alkynes.

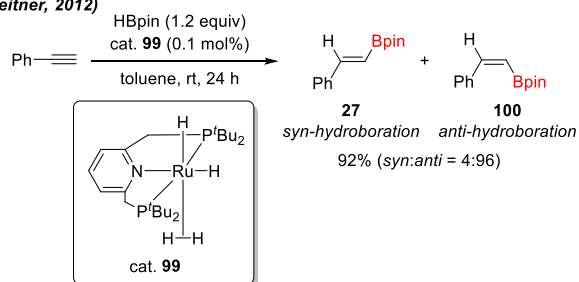
The first report of *anti*-hydroboration of terminal alkynes was published by Miyaura et al. in 2000 using rhodium (Scheme 27a) or iridium (Scheme 27b) as a catalyst.<sup>[101]</sup> Excellent *anti*-selectivity was obtained in the Rh-catalytic system; however, the Ir-catalyzed

reaction displayed only moderate selectivity. Using the Rh-catalytic system, several terminal alkynes were selectively hydroborated to afford the corresponding *Z*-alkenyl boranes. A similar catalytic study was reported by the Carbo and Fernandez group (Scheme 27c),<sup>[102]</sup> although poor selectivity was noted, compared to the earlier report. In the study by Miyaura et al., the authors carried out a deuterium-labeling experiment using 1-*d*<sub>1</sub>-1-octyne and found, surprisingly, that in the final compound (**16**), the deuterium atom had shifted to the  $\alpha$ -position. Based on this observation, the authors proposed a non-conventional mechanism, in which an oxidative addition of the terminal C–H bond to the metal center occurred, giving a metal hydride species (**95**). Subsequently, metal vinylidene complex **96** was formed through a hydrogen-shifting mechanism, followed by oxidative addition of HBpin to the metal center (**96**→**97**), 1,2-migration of boryl group to  $\alpha$ -carbon (**97**→**98**), and reductive elimination (**98**→[M]) to generate the product (Scheme 28).<sup>[101]</sup> The proposed mechanism was also supported by density functional theory (DFT) calculations.<sup>[102]</sup>

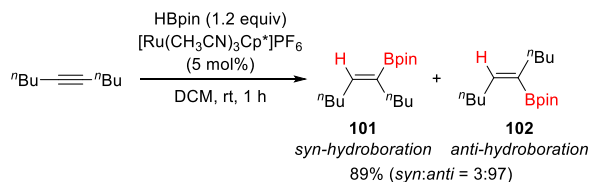


**Scheme 28.** A plausible mechanism for Rh- or Ir-catalyzed non-conventional *anti*-hydroboration of terminal alkynes (Miyaura, 2000).

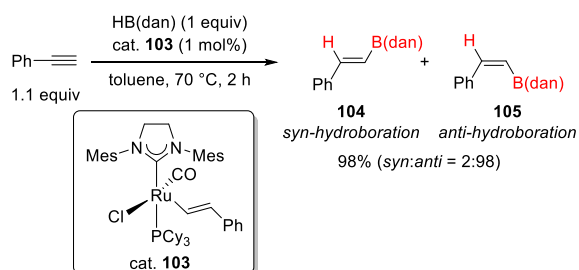
(a) Ru-catalyzed non-conventional anti-hydroboration of terminal alkyne (Leitner, 2012)



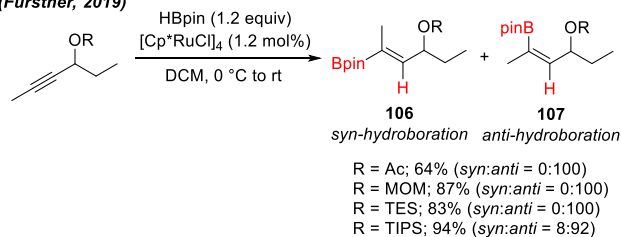
(b) Ru-catalyzed anti-hydroboration of internal alkyne (Furstner, 2013)



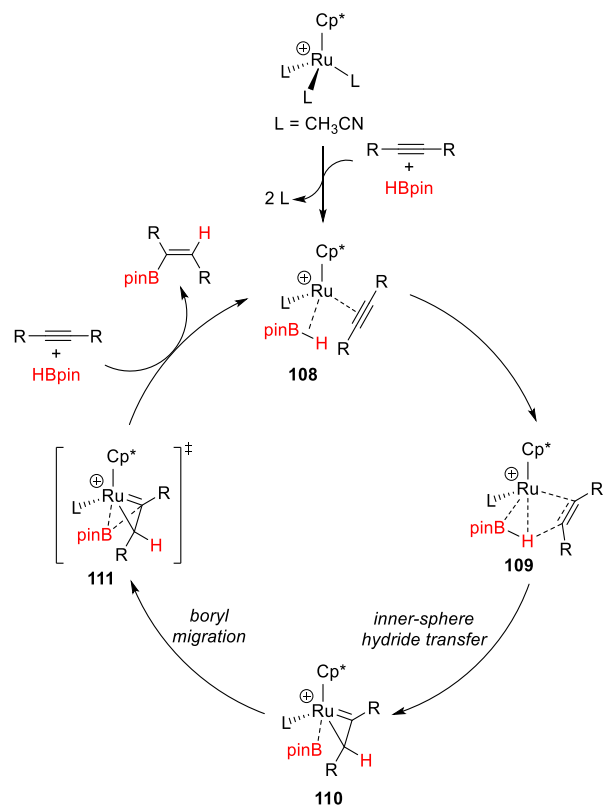
(c) Ru-catalyzed anti-hydroboration of terminal alkyne (Mutoh & Saito, 2019)



(d) Ru-catalyzed anti-hydroboration of secondary propargyl alcohols (Furstner, 2019)



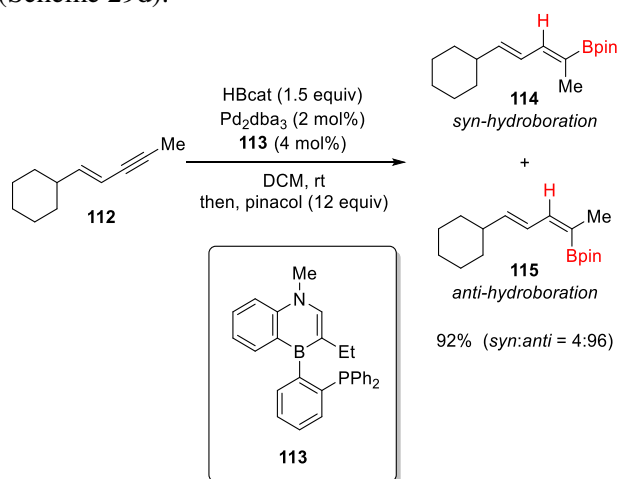
**Scheme 29.** (a)-(d) Ru-catalyzed *anti*-hydroboration of alkynes.



**Scheme 30.** A most plausible mechanism for Ru-catalyzed *anti*-hydroboration of internal alkynes (Zhang, Chung, and Wu, 2017).

In 2012, Leitner et al. introduced a ruthenium hydride pincer complex that efficiently catalyzed the unorthodox *anti*-hydroboration of terminal alkynes with a minimum catalyst loading (0.1 mol%) (Scheme 29a).<sup>[103]</sup> Based on the detection of plausible intermediates, it was proposed that rearrangement of coordinated alkynes to Z-vinylidene via hydrogen shifting is a key step in the catalytic cycle, as shown in the case of the Rh-catalytic system (Scheme 28). One year after this report, Furstner et al. reported the *anti*-selective hydroboration of internal alkynes using Ru complex  $[\text{Cp}^*\text{Ru}(\text{MeCN})_3]^+$  as the catalyst (Scheme 29b).<sup>[104]</sup> This report was the first to achieve *trans*-selective hydroboration of internal alkynes. A range of alkynes is selectively hydroborated in *anti*-fashion. In the report, the authors hypothesized that the alkyne moiety serves as a four-electron donor and holds a bonding interaction with the Ru center, which facilitates an inner-sphere hydride transfer to form the metallacyclopropene intermediate **110** (Scheme 30).<sup>[104]</sup> Subsequently, facile reductive boryl migration via transition state **111** helped to afford the *trans*-selective product. Detailed DFT calculations suggested that the *anti*-selectivity was determined in the oxidative hydrogen migration step, which is a rate-limiting step, and selectively formed the metallacyclopropene intermediate **110**.<sup>[105]</sup> Recently, the Mutoh and Saito group reported the hydroboration of terminal alkynes catalyzed by *N*-heterocyclic-carbene-ligated ruthenium complex **103**, using

HB(dan) as a hydroborating reagent (Scheme 29c).<sup>[106]</sup> A variety of terminal alkynes are selectively hydroborated to produce the desired *anti*-selective product. Mechanistic studies suggest that a distinctly different mechanism occurs, which involves the insertion of the alkyne into a Ru–B bond, followed by rapid isomerization to form a more stable component via a metallacyclopene intermediate. This mechanism is in line with the proposed mechanism reported for the *anti*-hydroboration of internal alkynes (Scheme 30). Furstner et al. further extended the Ru-catalyzed *anti*-hydroboration study to secondary propargyl alcohol derivatives, which in some cases provided the *trans*-hydroborated product exclusively (Scheme 29d).<sup>[107]</sup>

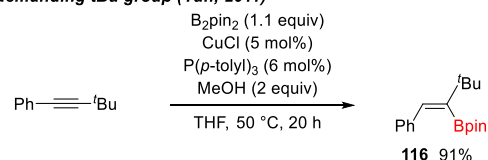


**Scheme 31.** 1,4-azaborine-based Phosphine ligated palladium-catalyzed *anti*-hydroboration of 1,3-enynes (Liu, 2016).

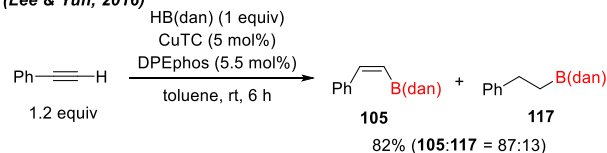
Liu et al. introduced a new type of mono-benzofused 1,4-azaborine phosphine ligand (**113**), which uniquely supports a Pd complex for stereoselective *anti*-hydroboration of 1,3-enynes (Scheme 31).<sup>[108]</sup> A range of internal and terminal 1,3-enynes are selectively *anti*-hydroborated to deliver dienylboronates (such as **115**). Detailed mechanistic exploration in terms of computational studies was carried out, showing a complicated pathway (different from the conventional mechanism) in which the coordination of the conjugated alkene to the metal center was recognized as a crucial event.<sup>[109]</sup>

Along with precious metal catalysts, a few novel complexes of earth-abundant first-row transition metals have also been used as catalysts. In 2011, Yun et al. briefly reported the *anti*-hydroboration of aryl and bulky *tert*-butyl group substituted internal alkyne (3,3-dimethylbut-1-yn-1-yl)benzene) to yield the corresponding product **116** (Scheme 32a). They realized that sterically demanding *t*Bu group and phenyl substitutions are crucial to achieving *anti*-hydroboration.<sup>[63]</sup> Later, the same group reported a Cu-catalyzed system with a combination of copper(I)-thiophene-2-carboxylate (CuTC) and DPEphos ligand to achieve the *anti*-hydroboration of terminal alkynes using HB(dan) (Scheme 32b).<sup>[110]</sup>

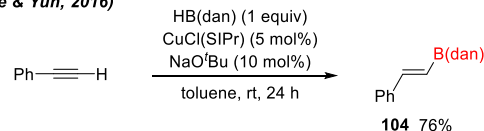
**(a) Cu-catalyzed *anti*-hydroboration of internal alkyne having sterically demanding *t*Bu group (Yun, 2011)**



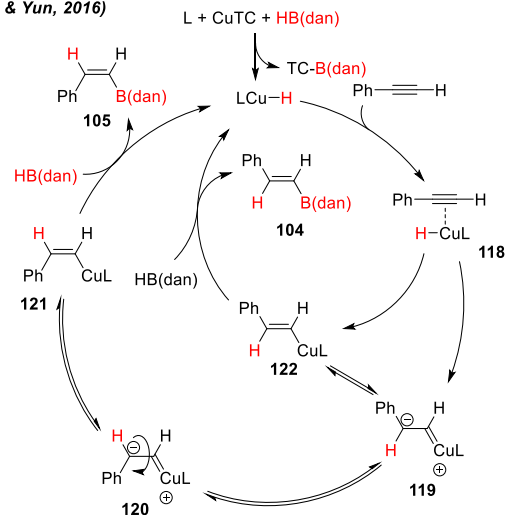
**(b) CuTC/DPEphos-catalyzed *anti*-hydroboration of terminal alkyne (Lee & Yun, 2016)**



**(c) SIPr•CuCl-catalyzed *syn*-hydroboration of terminal alkyne (Lee & Yun, 2016)**



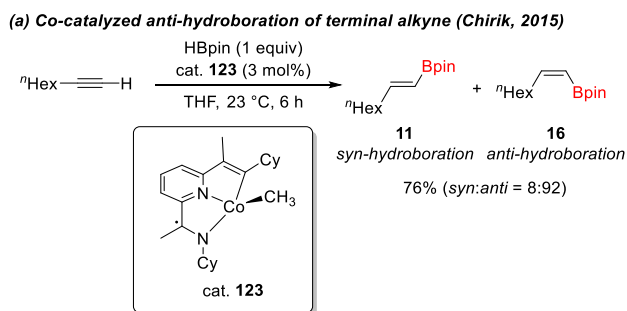
**(d) Mechanistic aspect for Cu/ligand-catalyzed hydroboration of alkyne (Lee & Yun, 2016)**



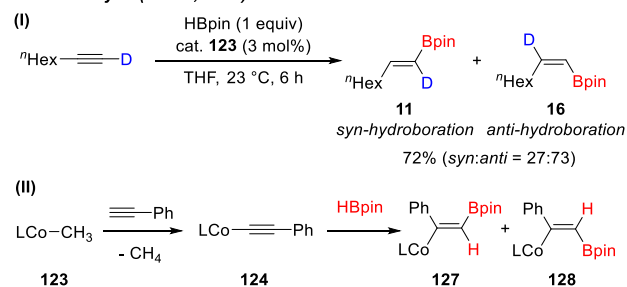
**Scheme 32.** (a) and (b) Cu-catalyzed *anti*-hydroboration of internal and terminal alkynes. (c) *syn*-Hydroboration reaction using a similar Cu-catalytic system. (d) A plausible mechanism for Cu-catalyzed *anti*-hydroboration.

It is also notable that when strong  $\sigma$ -donating ligands, such as the bulky *N*-heterocyclic carbene ligand (SIPr), were used, *syn*-hydroboration proceeded exclusively (Scheme 32c).<sup>[110]</sup> For the unusual *anti*-hydroboration reaction, the author proposed a plausible mechanism, as shown in Scheme 32d. At first, a copper-hydride species was generated, which upon reaction with alkyne, formed the intermediate (**119**). Subsequent C–C bond rotation via **120** generated **121**. In the last step,  $\sigma$ -bond metathesis of the organocopper intermediate and borane provided the desired product, either **105** (via **121**) or **104** (via **122**). The selectivity of the product was determined by the ligand (NHC or phosphine) used. Another important factor for determining the stereoisomer is the hydroborane reagent used, since HB(dan) prefers the alkenyl copper intermediate in which the phenyl group lies *cis* with Cu, to avoid the steric interaction (as shown in **121**).<sup>[110]</sup>

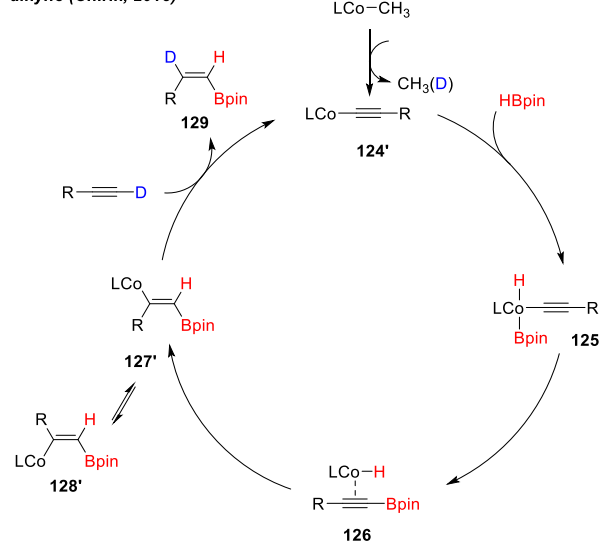




(b) Mechanistic consideration for Co-catalyzed *anti*-hydroboration of terminal alkyne (Chirik, 2015)



(c) Proposed mechanism for Co-catalyzed *anti*-hydroboration of terminal alkyne (Chirik, 2015)

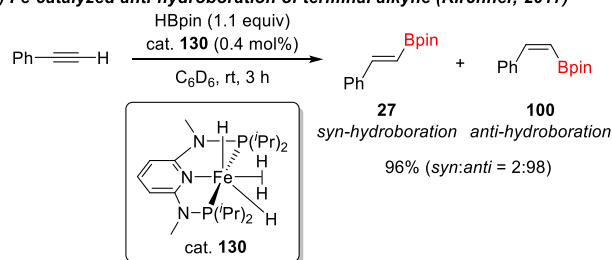


**Scheme 33.** (a) Co-catalyzed *anti*-hydroboration of terminal alkynes, (b) its mechanistic studies, and (c) plausible mechanism.

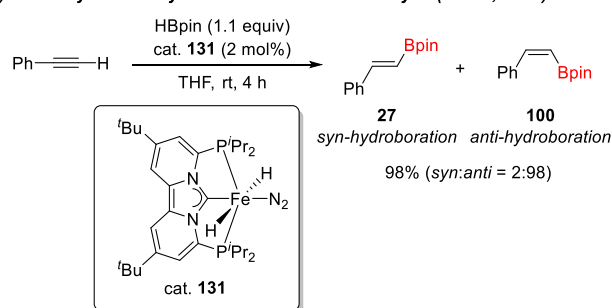
*anti*-Selective hydroboration of terminal alkynes was reported by Chirik et al. using a bis(imino)pyridine ligated Co complex (**123**) (Scheme 33a).<sup>[111]</sup> A unique and distinct reaction pathway was proposed for this reaction based on deuterium studies and control experiments (Scheme 33b). In the deuterium studies, it was observed that the terminal D-atom in 1-*d*<sub>1</sub>-1-octyne shifted to the 2-position in product **16** (Scheme 33b-I). However, in a controlled reaction between organocobalt compound **124** and HBpin, **127** and **128** were generated. It was detected that in **127** or **128**, the carbon bound to the cobalt is phenyl substituted, while the distal carbon is bound to the Bpin (Scheme 33b-II), which is completely unlike the previously reported mechanism via vinylidene (**97**→**98**, as shown in Scheme 28). Based on these

studies, the authors proposed that following the formation of cobalt acetylide (**124'**), oxidative addition of HBpin followed by reductive elimination resulted in the formation of alkynylboronate **126** (Scheme 33c). Subsequently, *syn*-hydrometallation resulted in the vinylic cobalt intermediate **127'**, which reacted with terminal alkynes to release the product and active cobalt species.<sup>[111]</sup> This catalytic cycle also supports the observation that the D-atom in product **16** came from another molecule of alkyne.

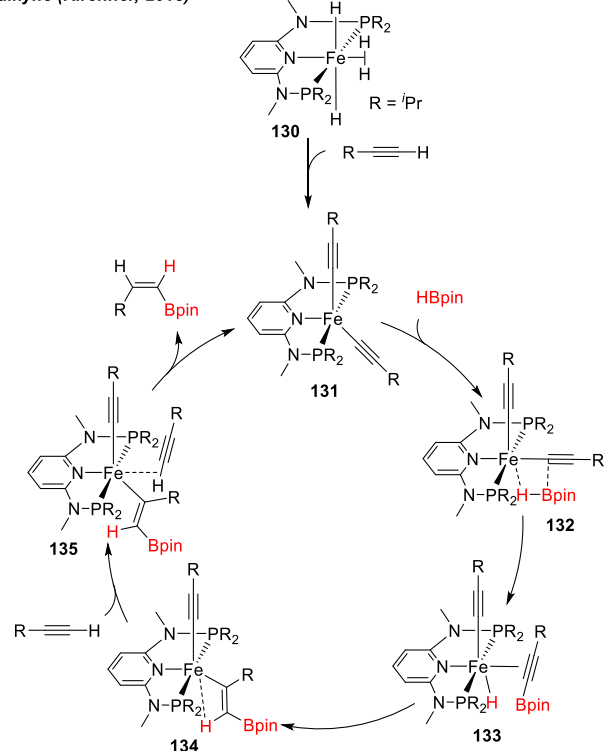
(a) Fe-catalyzed *anti*-hydroboration of terminal alkyne (Kirchner, 2017)



(b) Fe-catalyzed *anti*-hydroboration of terminal alkyne (Ruiter, 2020)



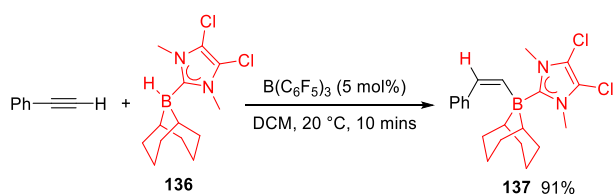
(c) Proposed mechanism for Fe-catalyzed *anti*-hydroboration of terminal alkyne (Kirchner, 2018)



**Scheme 34.** (a) and (b) Fe-catalyzed *anti*-hydroboration of terminal alkynes. (c) A plausible mechanism for Fe-catalyzed *anti*-hydroboration.

In 2017, a tridentate PNP pincer-type ligand ligated polyhydride Fe-complex (**130**) was introduced by Kirchner and coworkers for the stereoselective *anti*-hydroboration of terminal alkynes (Scheme 34a).<sup>[112]</sup> Their protocol covered a range of terminal alkynes to affords corresponding *Z*-alkenes in excellent yields and selectivity. In a successive report, the authors proposed a reaction mechanism (Scheme 34c)<sup>[113]</sup> based on computational studies and experimental evidence, which followed a pattern similar to the Co-catalytic system (as shown in Scheme 33c). Very recently, Rüter et al. developed an *N*-heterocyclic carbene-based PCP ligand ligated *trans*-dihydride iron complex (**131**), which efficiently catalyzed the *anti*-hydroboration of terminal alkynes to provide *Z*-alkenylborane compounds (Scheme 34b).<sup>[114]</sup>

### 3.2. Metal-free catalytic *anti*-hydroboration

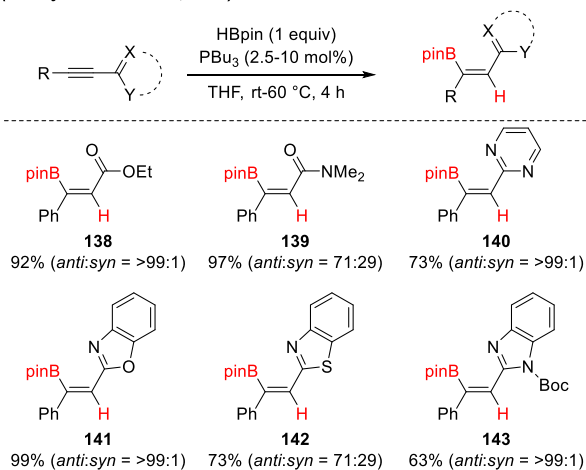


**Scheme 35.**  $B(C_6F_5)_3$ -catalyzed *anti*-hydroboration of the terminal alkyne (Ingleson, 2016).

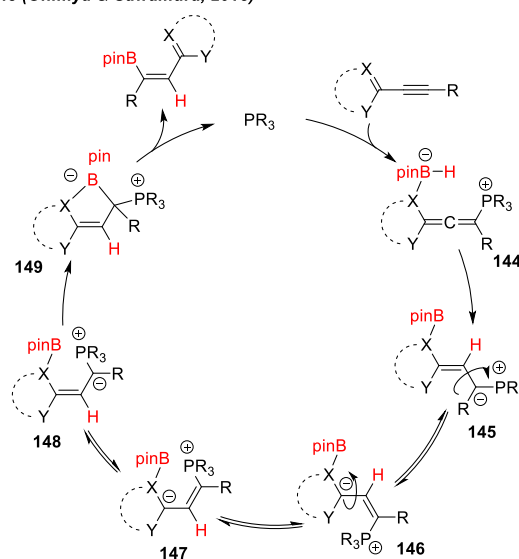
Although *anti*-hydroboration of alkynes is a rare transformation compared to the *syn* variant, there are a few reports in which borane or phosphines were used as efficient catalysts for this selective transformation. Incidentally, the first transition metal-free *trans*-hydroboration was reported by Ingleson et al. in 2016 using a catalytic amount of  $B(C_6F_5)_3$  and *N*-heterocyclic carbene coordinated hydroborane **136** (Scheme 35).<sup>[115]</sup> Notably, various terminal alkynes were selectively hydroborated in an *anti*-fashion to yield the corresponding product in excellent yield in a very short reaction time. Apart from the use of  $B(C_6F_5)_3$  as a catalyst in the *anti*-hydroboration reaction, phosphine also displayed impressive reactivity as a catalyst in the same transformation. Three parallel independent reports, published by the working groups of Ohmiya/Sawamura,<sup>[116]</sup> Vilotijevic,<sup>[117]</sup> and Santos<sup>[118]</sup> presented an attractive catalytic system in which a trialkylphosphine serves as an organocatalyst in the *anti*-hydroboration of alkynoic acid derivatives such as alkynoates (**138**), alkynylamides (**139**), adjacent pyrimidine (**140**), benzoxazole (**141**), benzothiazole (**142**), and benzoimidazole (**143**) group containing alkynes (Scheme 36a). It was hypothesized that the reaction started with the conjugate addition of phosphine to the electron-deficient alkyne moiety with the assistance of Lewis acidic activation of carbonyl or azole groups by HBpin (as shown in **144**, Scheme 36b). Later, hydride transfer to the allene moiety occurred, to form an ylide intermediate **145**. Subsequently, the resonance of the conjugated system, followed by C–C bond rotation,

easily led to a suitable position for the ylide carbon to attack the B center to form a five-membered intermediate (**149**). In the last step, elimination of phosphine and cleavage of B–X bond afforded the *anti*-hydroborated product. The concerted nature of the final phosphine elimination step is mainly responsible for obtaining high *trans*-selectivity.<sup>[116]</sup>

**(a) Phosphine-catalyzed *anti*-hydroboration of alkynoic acid derivatives (Ohmiya & Sawamura, 2018)**



**(b) Proposed mechanism for phosphine-catalyzed *anti*-hydroboration of alkyne (Ohmiya & Sawamura, 2018)**

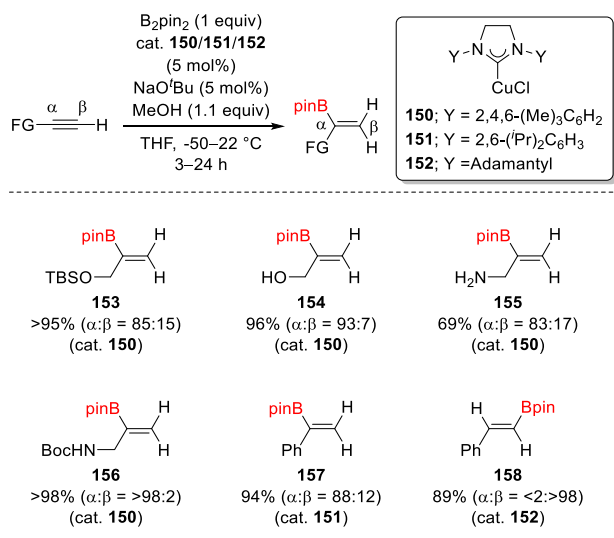


**Scheme 36.** (a) Phosphine-catalyzed *anti*-hydroboration of various alkynoic acid derivatives and (b) the plausible catalytic pathway.

## 4. $\alpha$ -Selective hydroboration of terminal alkynes

Considering the significance of vinyl borane compounds, several strategies have been employed to obtain the selective hydroboration product either via *cis*- or *trans* addition, which has already been discussed in the previous sections in detail. Reports discussed in previous sections dealt with the formation of  $\beta$ -borylated products when terminal alkyne was

used as a substrate. However, obtaining  $\alpha$ -vinyl boronated compounds via hydroboration of terminal alkynes is significantly limited. Methods reported to date for obtaining  $\alpha$ -selective hydroboration are limited to copper catalytic systems.<sup>[119–123]</sup> The pioneering report in this regard was published by Hoveyda et al. using *N*-heterocyclic carbene–ligated copper complexes (Scheme 37). Specifically, various propargyl alcohol (**153** and **154**) and amine-derived terminal alkynes (**155** and **156**) were reacted smoothly to afford the corresponding  $\alpha$ -borylated alkenes. Aryl-substituted terminal alkyne is also a suitable substrate for this transformation, giving the desired product **157** in high yield and with good selectivity. Based on mechanistic studies, it was anticipated that the desired  $\alpha$ -selectivity arises from the electronic and structural properties of the NHC ligand. Hence, aryl-substituted NHC-ligated copper complexes (**150** and **151**) were used for obtaining  $\alpha$ -selectivity, whereas, adamantyl group substituted NHC–Cu complex (**152**) provided  $\beta$ -borylated alkene (**158**) when phenylacetylene was used as a substrate (Scheme 37).<sup>[119]</sup>

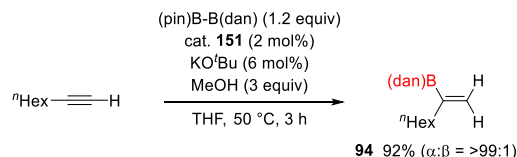


**Scheme 37.** NHC–Cu–catalyzed  $\alpha$ -selective hydroboration of terminal alkynes (Hoveyda, 2011).

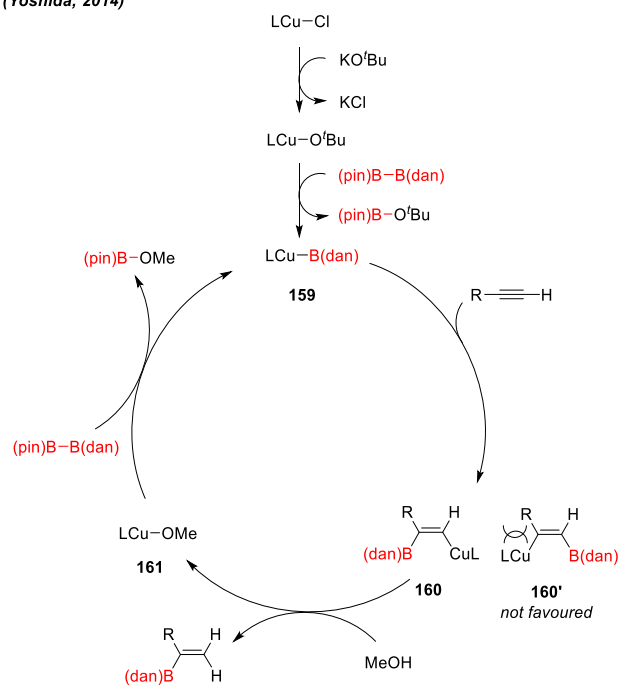
A few years later, Yoshida et al. introduced masked diborane [(pin)B–B(dan)] as a reagent for the Cu–NHC–catalyzed hydroboration of terminal alkynes, which eventually afforded the  $\alpha$ -borylated alkene (**94**) even when alkyl-substituted terminal alkyne was used as a substrate (Scheme 38a).<sup>[121]</sup> Notably, this protocol showed impressive selectivity and displayed a substrate generality, since alkyl-, aryl-, heteroatom-, and silyl-substituted terminal alkynes reacted smoothly to provide the corresponding  $\alpha$ -borylated product. The authors hypothesized that the use of masked borane is the key factor, since the Lewis acidity of B(dan) moiety in **159** is weakened, and the interaction between alkyne moiety and boron center is negligible. (This interaction is one of the factors for  $\beta$ -selective addition through a more stable cationic

transition state.) Therefore, a steric factor is the only remaining factor for determining position selectivity. Due to the bulkiness of the NHC ligand, it was expected that **160** would be preferred over **160'** as an intermediate, and hence the  $\alpha$ -selective product forms almost exclusively (Scheme 38b).<sup>[121]</sup>

(a) Cu-catalyzed  $\alpha$ -hydroboration with (pin)B–B(dan) (Yoshida, 2014)



(b) Proposed mechanism for Cu-catalyzed  $\alpha$ -hydroboration with (pin)B–B(dan) (Yoshida, 2014)

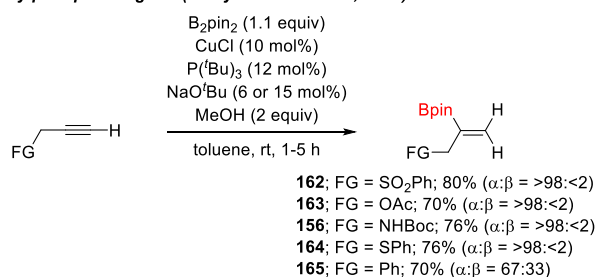


**Scheme 38.** (a) Cu-catalyzed  $\alpha$ -selective hydroboration of terminal alkynes using (pin)B–B(dan) and (b) its mechanistic aspects.

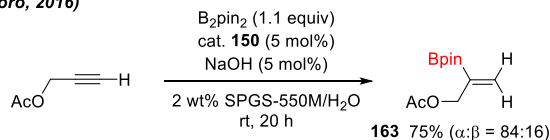
The Arrayas and Carretero research group also studied the  $\alpha$ -selective hydroboration of propargylic functional group–derived terminal alkynes (Scheme 39a).<sup>[120]</sup> Notably, propargyl-substituted sulfone (**162**), alcohol (**163**), amine (**156**), and sulfide (**164**) derivatives provided the smooth formation of  $\alpha$ -selective products. As expected, the hydroboration of 2-propynylbenzene did not give up-to-the-mark selectivity (**165**), which suggested that the polar functional group substitution contributed to high  $\alpha$ -selectivity. Another important point to note is that a bulky phosphine ligand was used in this case to provide a suitable steric interaction to accomplish high selectivity. Moro et al. later developed a similar catalytic transformation, which can work in the H<sub>2</sub>O medium in the presence of a surfactant SPGS-550M (Scheme 39b).<sup>[122]</sup> Recently, Jones and coworkers disclosed that *N*-heterocyclic carbene–ligated copper

hydroxide (Cu(IPr)(OH); IPr = 1,3-bis(2,6-diisopropylphenyl)-imidazol-2-ylidene) would work as a catalyst for  $\alpha$ -selective hydroboration of phenylacetylene in the absence of any additives (Scheme 39c).<sup>[123]</sup> Although reports of  $\alpha$ -selective hydroboration of terminal alkynes are scarce compared to  $\beta$ -selective hydroboration, research on the former is expected to flourish more in the coming decades.

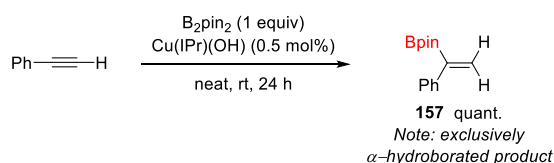
(a) Cu-catalyzed  $\alpha$ -hydroboration propargyl functionalized alkynes using bulky phosphine ligand (Arrayas & Carretero, 2013)



(b) Cu-catalyzed  $\alpha$ -hydroboration propargyl functionalized alkynes in water (Moro, 2016)



(c) NHC-Cu hydroxide as a catalyst for additive free  $\alpha$ -hydroboration terminal alkynes (Jones, 2019)



**Scheme 39.** Various catalytic systems for Cu-catalyzed  $\alpha$ -selective hydroboration of terminal alkynes.

## 5. Conclusion and future direction

In the past few decades, catalytic regioselective and stereoselective hydroboration of alkynes has been studied extensively in terms of reaction condition development, mechanistic exploration, and computational studies. Various catalytic systems have been employed from transition metal catalytic systems to alkali metal/alkaline earth metal, and Al-based catalytic systems. Even metal-free catalytic systems have been studied on several occasions to achieve selective hydroboration of alkynes. For readers to get an overview of the methods used in this selective transformation, this review summarizes reports of previous studies on the regioselective and stereoselective aspects of hydroboration. Three main types of selective hydroboration of alkynes are discussed in this review. (a) *syn*-Hydroboration, in which the addition of hydroborane proceeds via a *cis*-process. This is the most studied process in alkyne hydroboration. (b) *anti*-Hydroboration, where

hydrogen and boron moieties are added to an alkyne in a *trans*-fashion. Remarkably, a few pioneering reports have opened the window to this transformation and notable progress has been witnessed. (c)  $\alpha$ -selective hydroboration of terminal alkynes, which is still limited to the copper-catalytic system, was introduced by a pioneering report by Hoveyda et al.<sup>[119]</sup> Despite much progress, further advancement in this field depends on certain factors. These are: (a) alkenyl borane compounds are widely used in the synthesis of complex molecules in multi-step processes. If hydroboration of an alkyne can be performed even in the presence of impurities (generated from the last synthetic step), it would be a step-change in the economy of the processes; (b) given the ongoing interest in the reaction under continuous flow, hydroboration of alkynes is a probable candidate for improving productivity; (c) further industrial application is possible through the development of a more mild, practical, environmentally benign, metal-free protocol, which can be sustained in the presence of air and water. Overall, it is expected that more research will be reported in the coming years in terms of the development of new catalytic systems. We expect that in the future more efforts will be undertaken to establish new strategies to exclusively achieve a single isomer in an alkyne hydroboration process. We hope that this comprehensive review will help researchers to gather new ideas and stimulate them in undertaking more research in this field.

## 6. Data availability statement

The data that support the findings of this study are openly available in references.

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