ÉCOLE POLYTECHNIQUE
FÉDÉRALE DE LAUSANNE

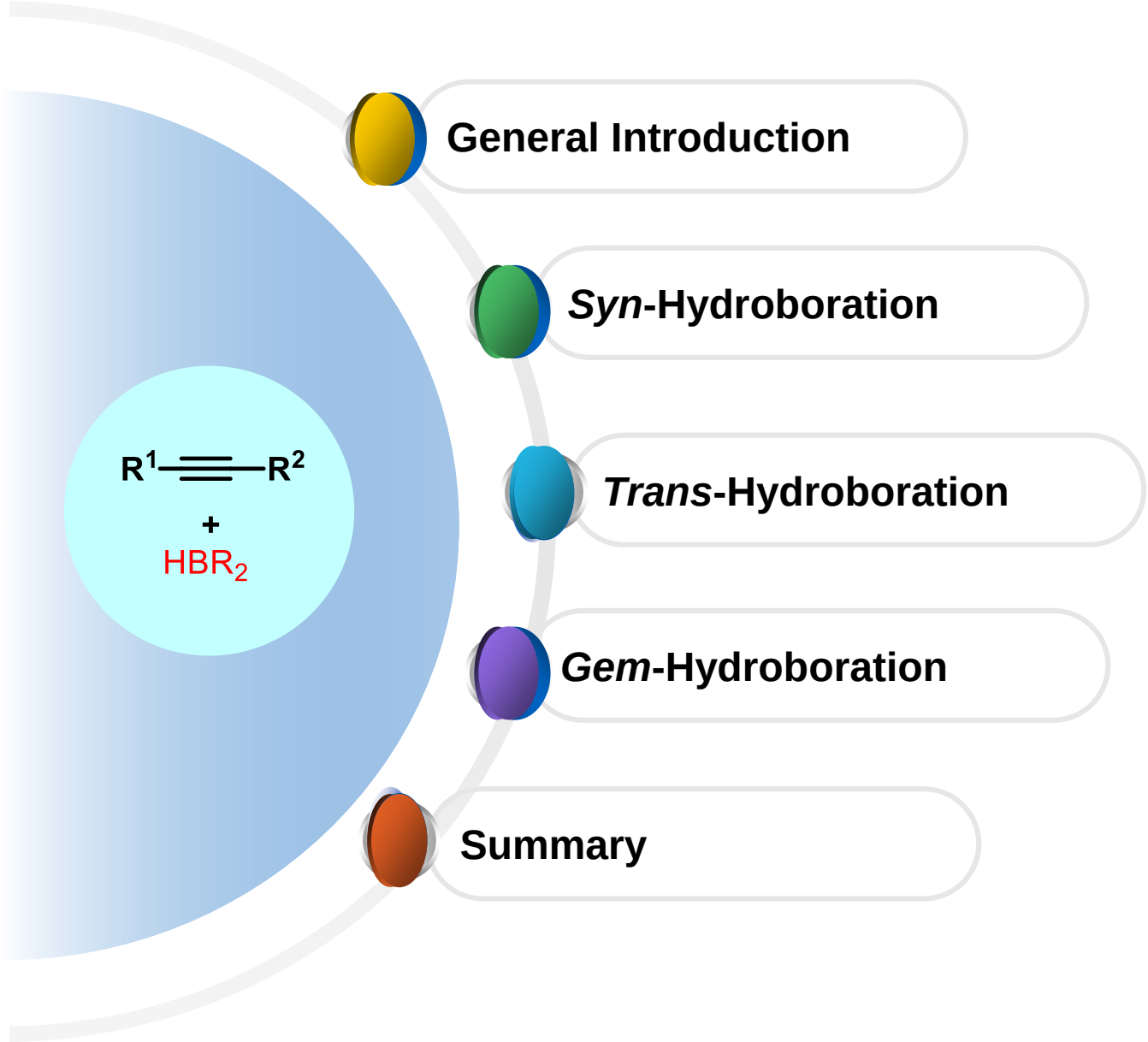
LABORATOIRE DE SYNTHESE
ET PRODUITS NATURELS

Group Seminar

Metal-catalyzed Hydroboration of Alkynes: Reaction Modes and Mechanistical Study

Speaker: Qiang Feng
Supervisor: Prof. Jieping Zhu
17-03-2022

Outlines

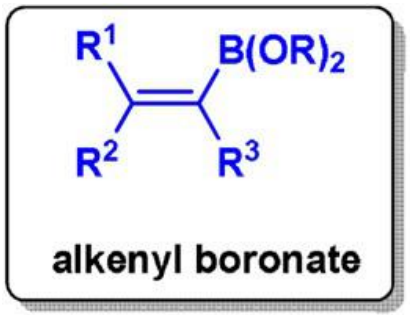


- General Introduction
- *Syn*-Hydroboration
- *Trans*-Hydroboration
- *Gem*-Hydroboration
- Summary

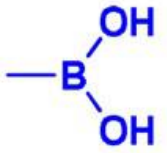
General Introduction

Alkenylboranates are versatile building blocks in organic synthesis (C-C formation, oxidation etc.)
Among the various methods for their synthesis, alkyne hydroboration represents the most straightforward approach.

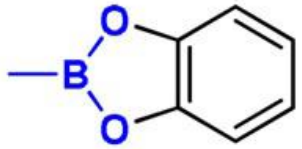
The most popular boron functional groups:



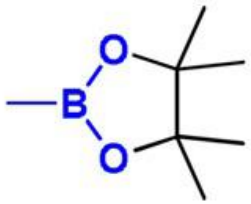
alkenyl boronate



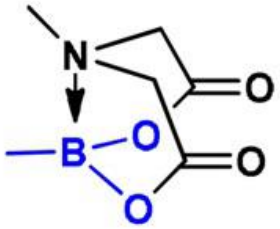
boronic acid



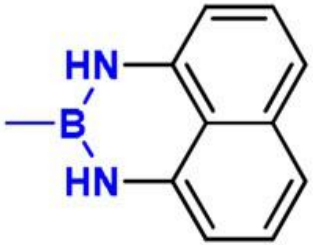
catechol boronic ester (Bcat)



pinacol boronic ester (Bpin)



MIDA boronate (BMIDA)

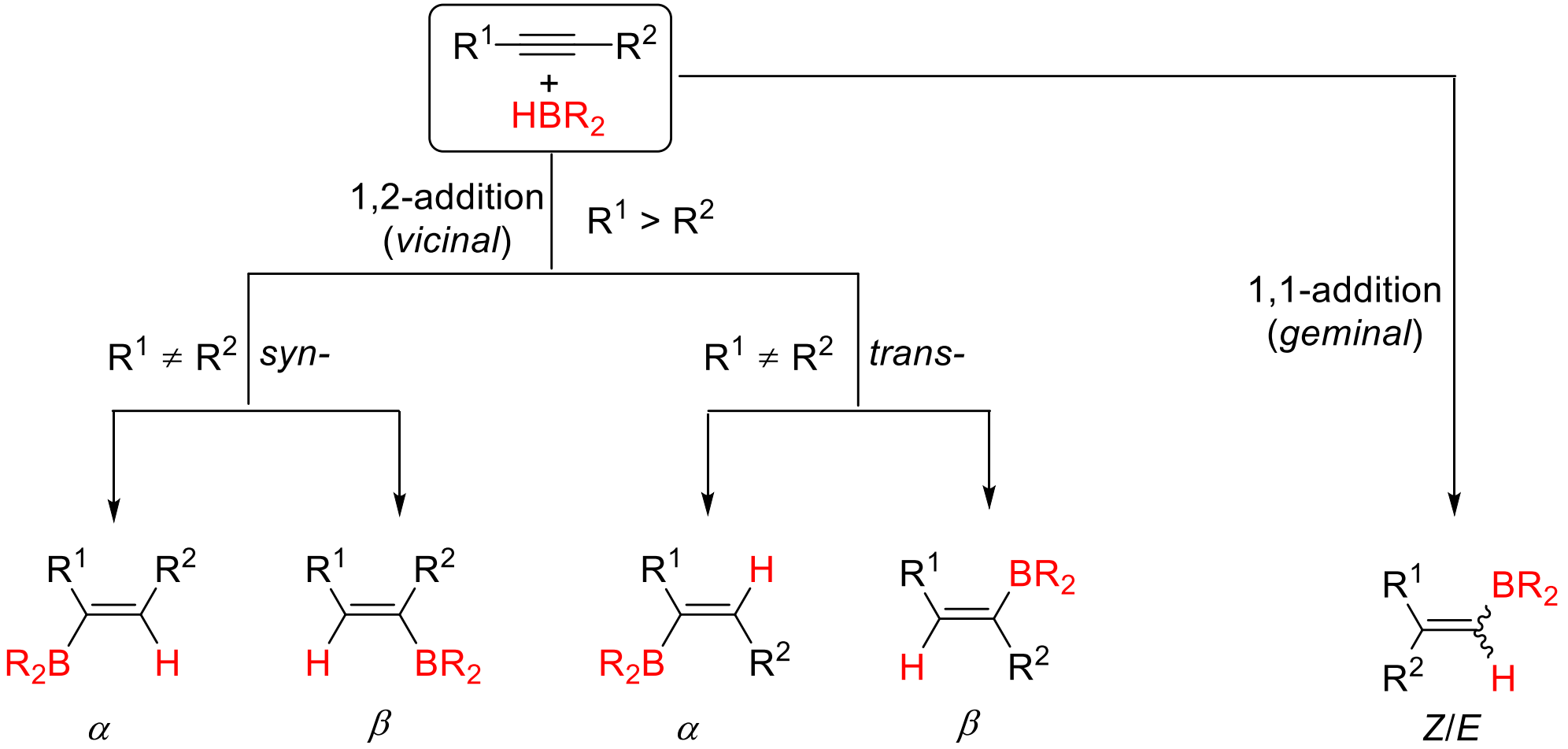


1,8-diaminonapthyl boronamide (Bdan)

Picture from: Carreras, J.; Caballero, A.; Pérez, P. J. *Chem. - Asian J.* **2019**, *14*, 329–343.

General Introduction

General reaction modes of alkyne hydroboration (regio- and stereo-):

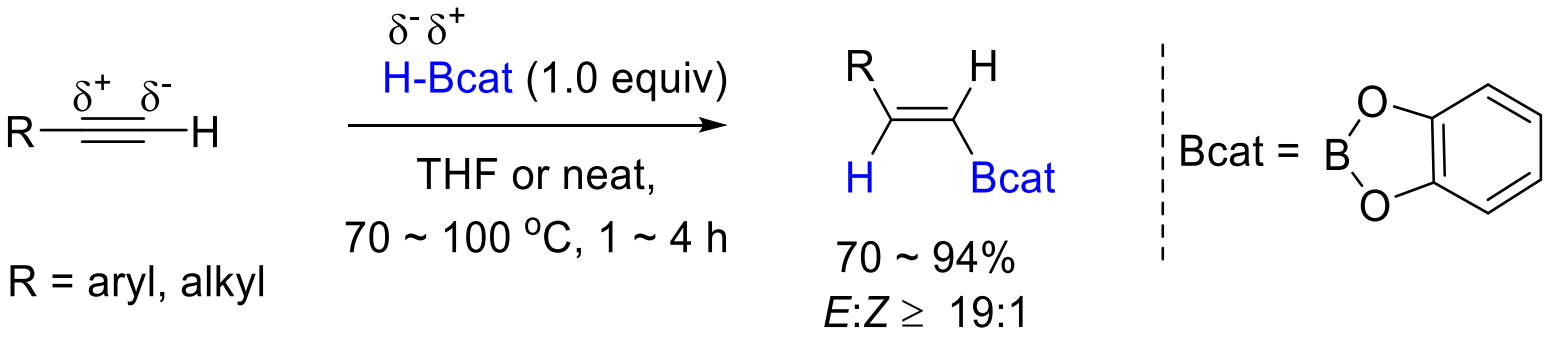


Majority: 1,2-hydroboration

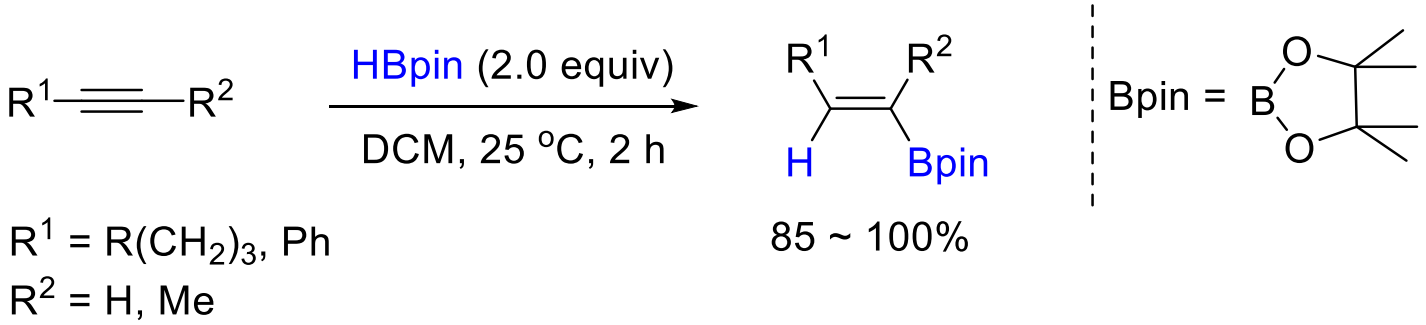
Relatively rare

General Introduction-pioneering works

Seminal Hydroboration of Alkynes (electronic attribute of substrates; small steric alkyne):



Brown, H. C.; Gupta, S. K. *J. Am. Chem. Soc.* **1972**, *94*, 4370–4371.

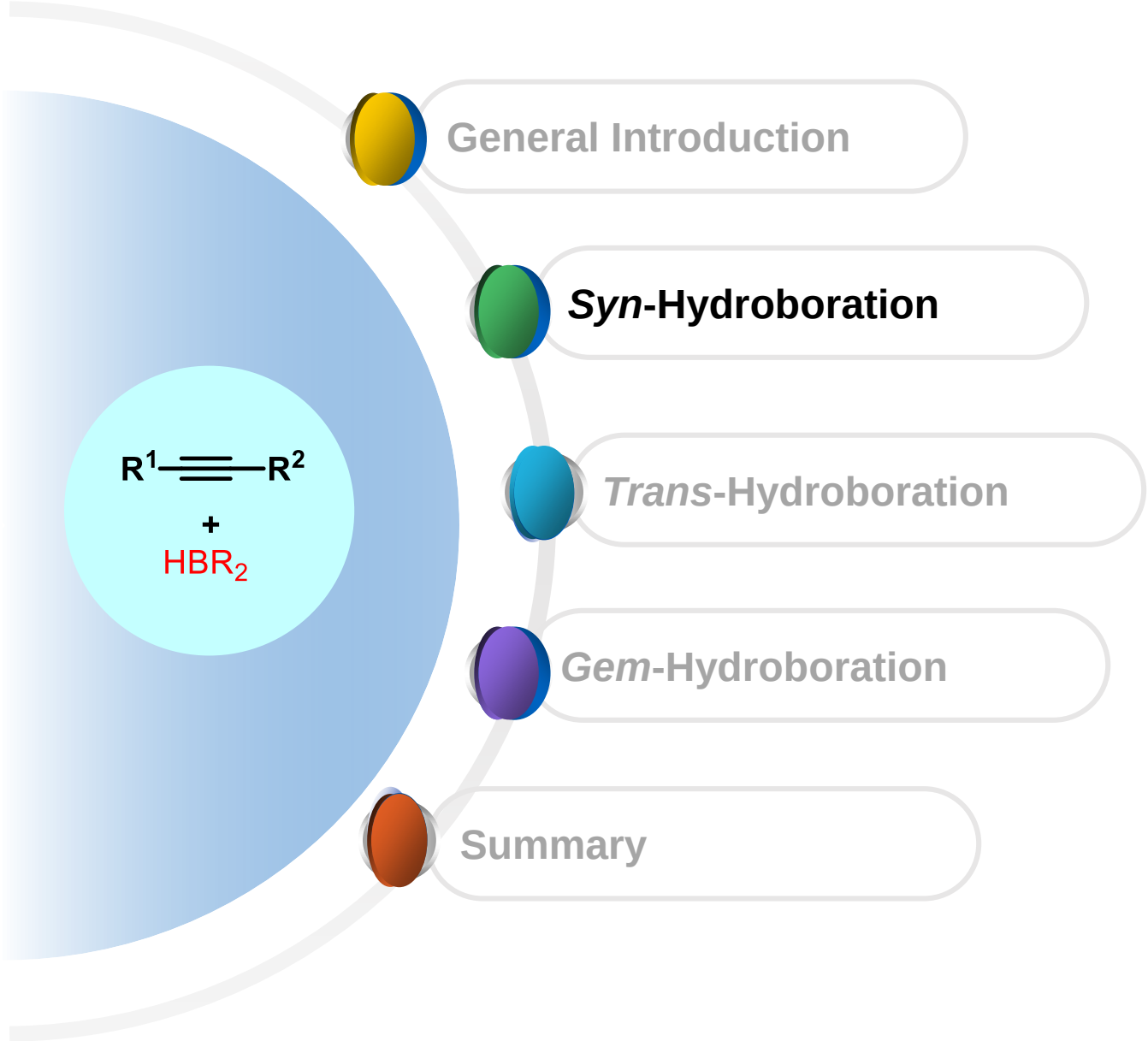


Tucker, C. E.; Davidson, J.; Knochel, P. *J. Org. Chem.* **1992**, *57*, 3482–3485.

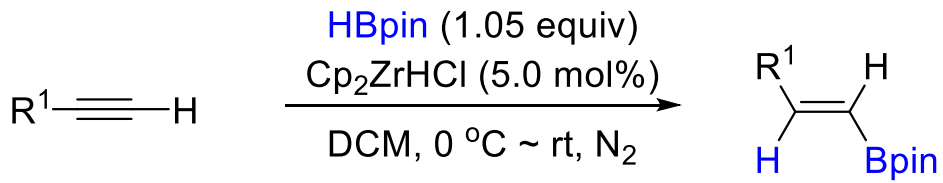
Selectivity control:

1. Substrates and boron reagent
2. Catalytic system (metal-catalysts: Zr-, Rh-, Ni-, Pd-, Cu-, Fe-, Al-, Co-, Ir-, and Ru- etc.)

Outlines

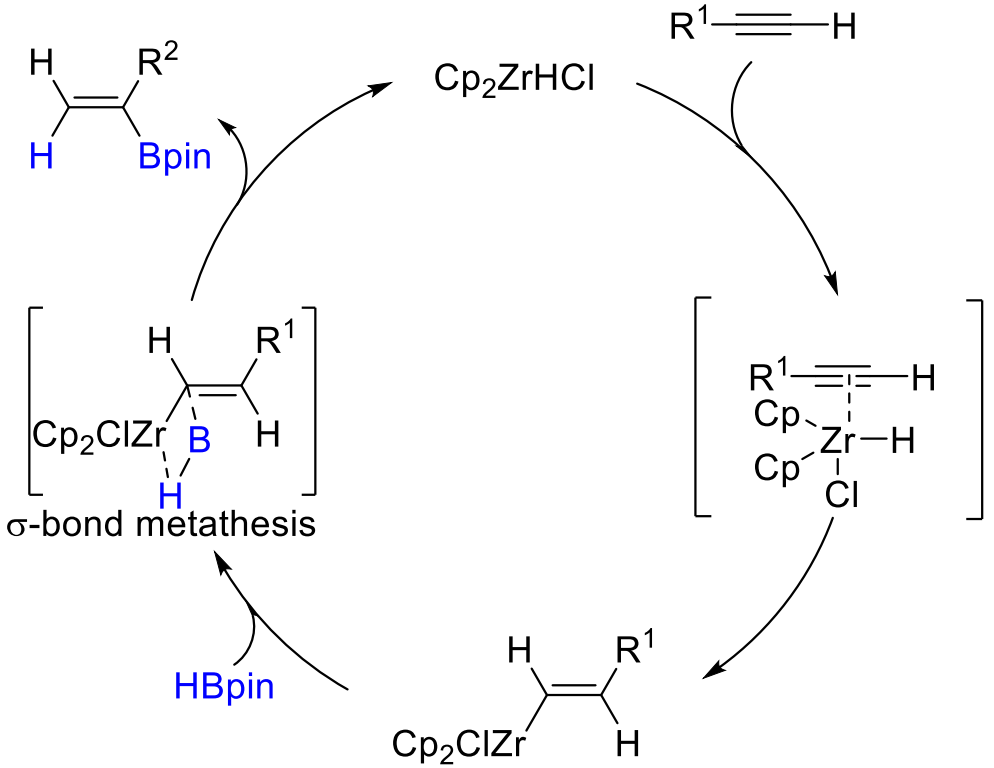

R^1—≡—R^2
+
HBR_2
General Introduction
Syn-Hydroboration
Trans-Hydroboration
Gem-Hydroboration
Summary

Syn-Hydroboration-(β-selectivity)



R^1 = alkyl (e.g. ^{t}Bu, ^{i}Pr), aryl, TMS

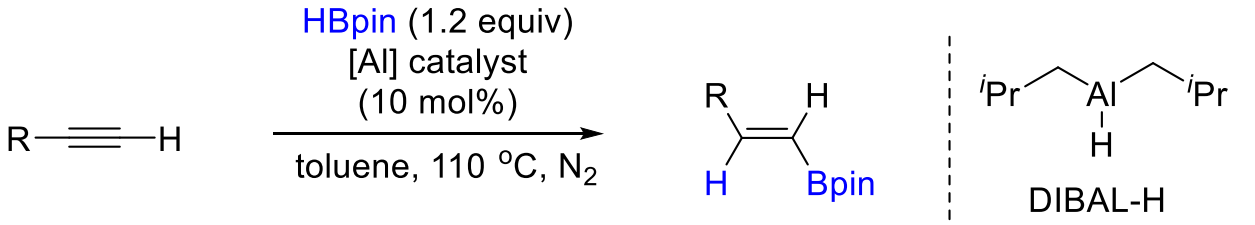
75 ~ 100%



1. Sterically bulky alkyne
2. A slight excess of HBpin

Pereira, S.; Srebnik, M. *Organometallics* **1995**, *14*, 3127−3128.

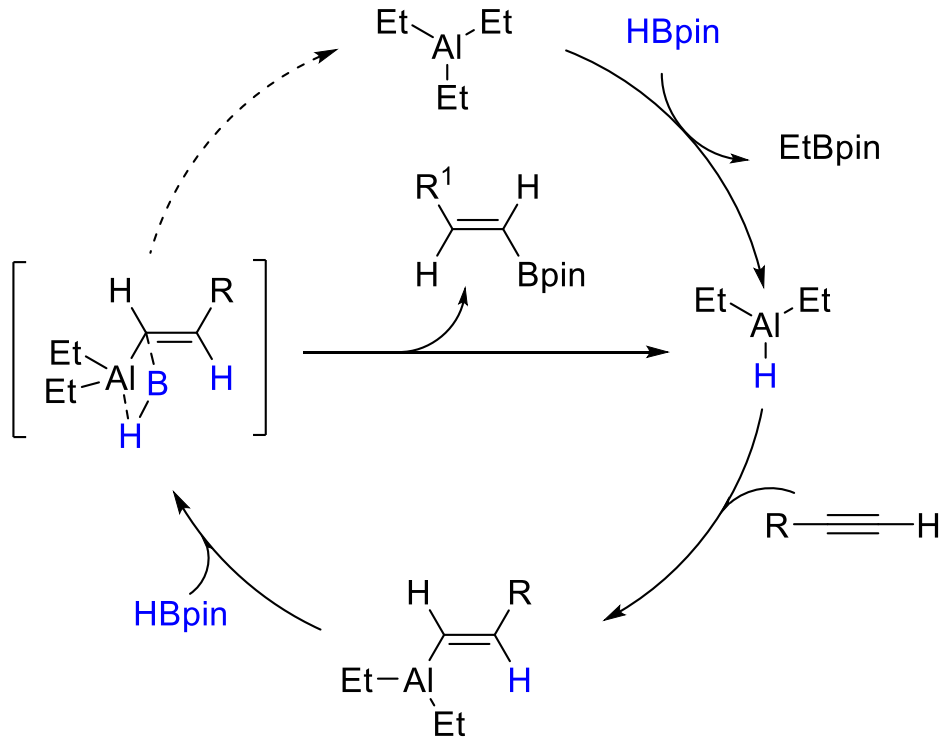
Syn-Hydroboration-(β-selectivity)



R = alkyl, aryl, alkenyl

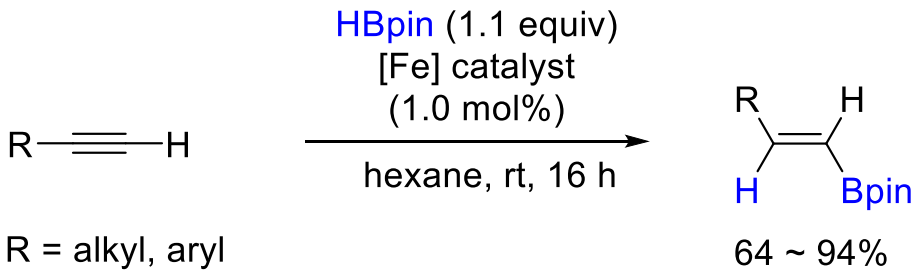
[Al] = DIBAL-H: 40 ~ 89%

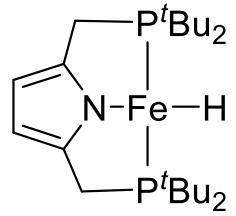
[Al] = $Et_3Al \cdot DABCO$: 35 ~ 84%

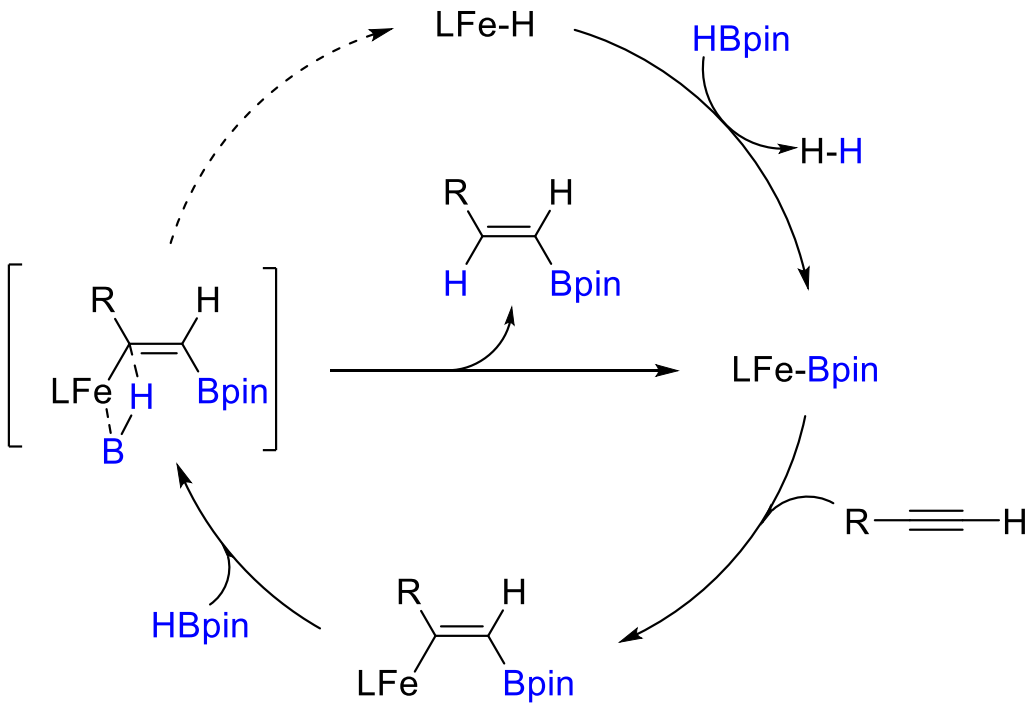


Bismuto, A.; Thomas, S. P.; Cowley, M. J. *Angew. Chem., Int. Ed.* **2016**, *55*, 15356−15359.

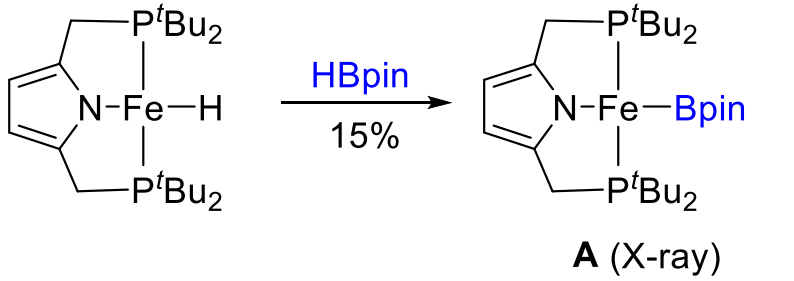
Syn-Hydroboration-(β-selectivity)

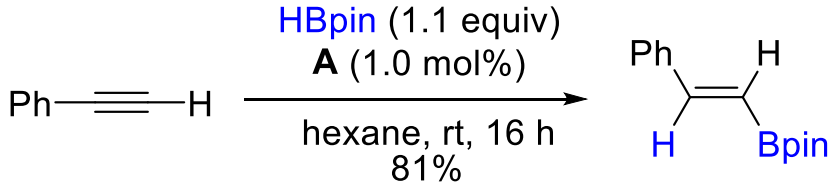






Control experiments:

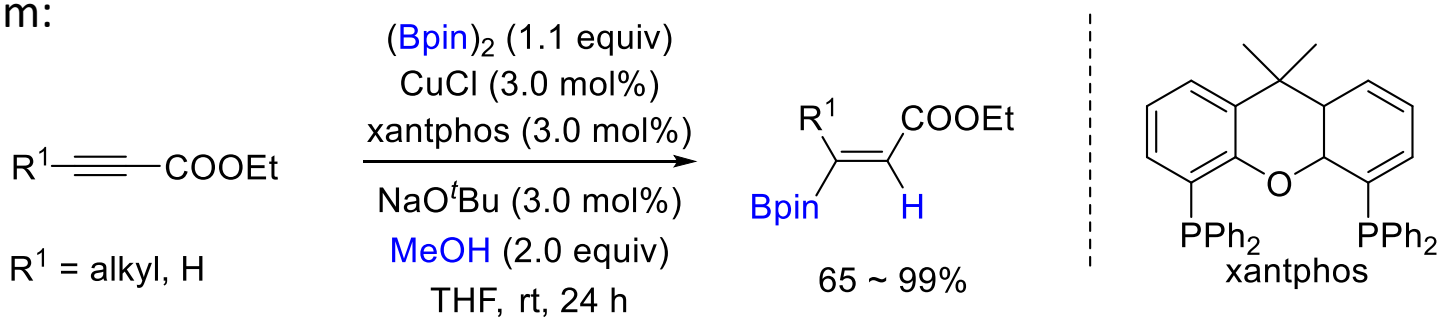


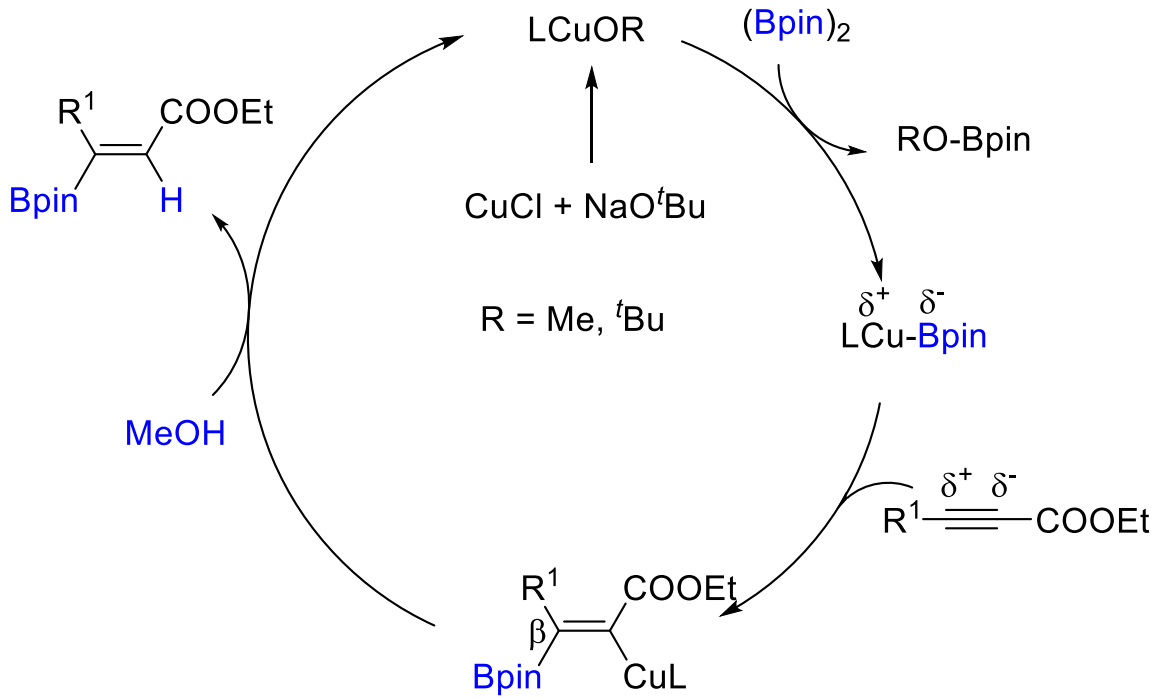


Nakajima, K.; Kato, T.; Nishibayashi, Y. *Org. Lett*. **2017**, *19*, 4323−4326.

Syn-Hydroboration-(β-selectivity)

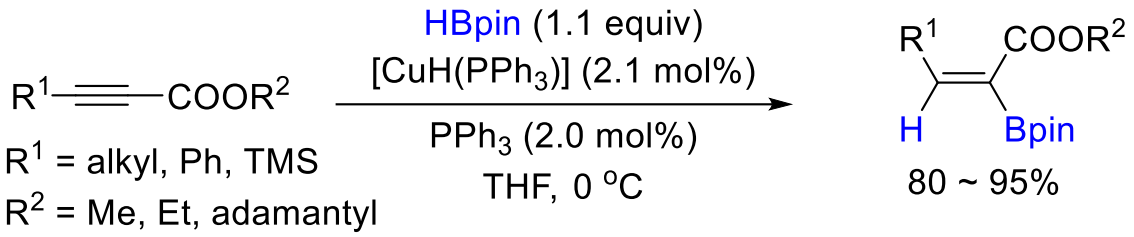
First Cu-catalytic system:

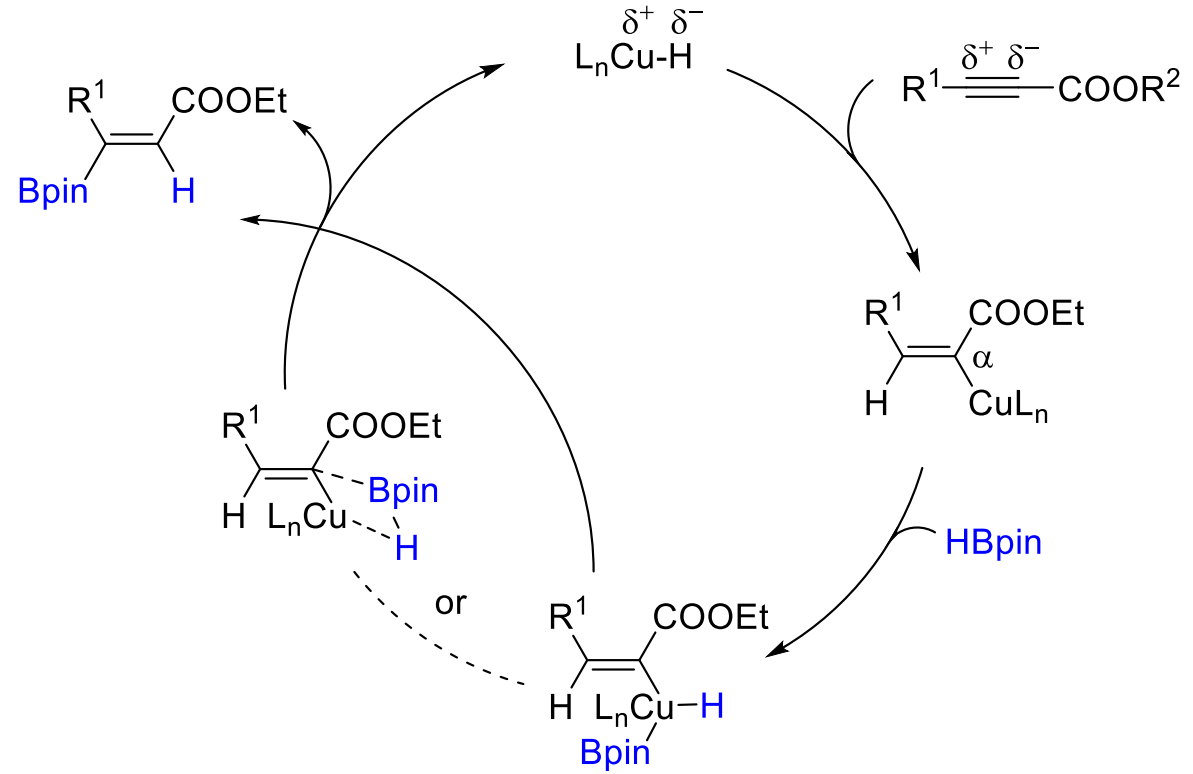




Lee, J.-E.; Kwon, J.; Yun, J. *Chem. Commun*. **2008**, 733–734.

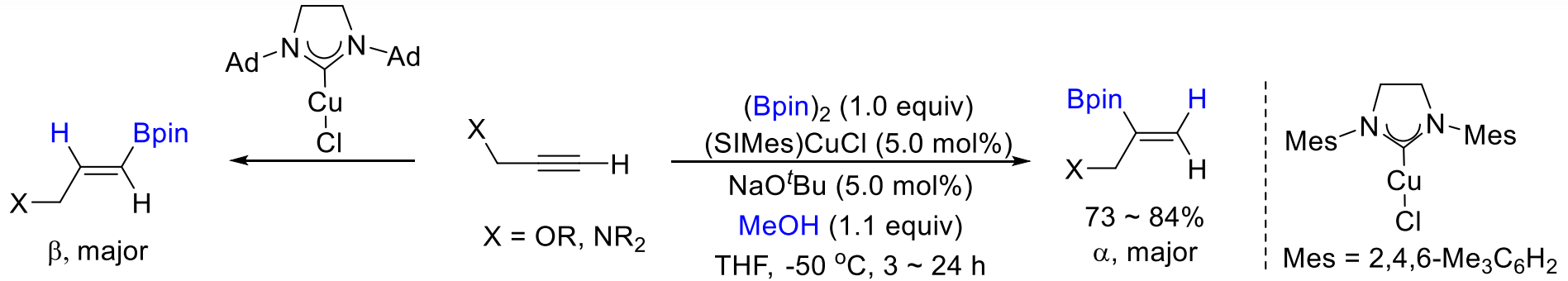
Syn-Hydroboration-(α-selectivity)



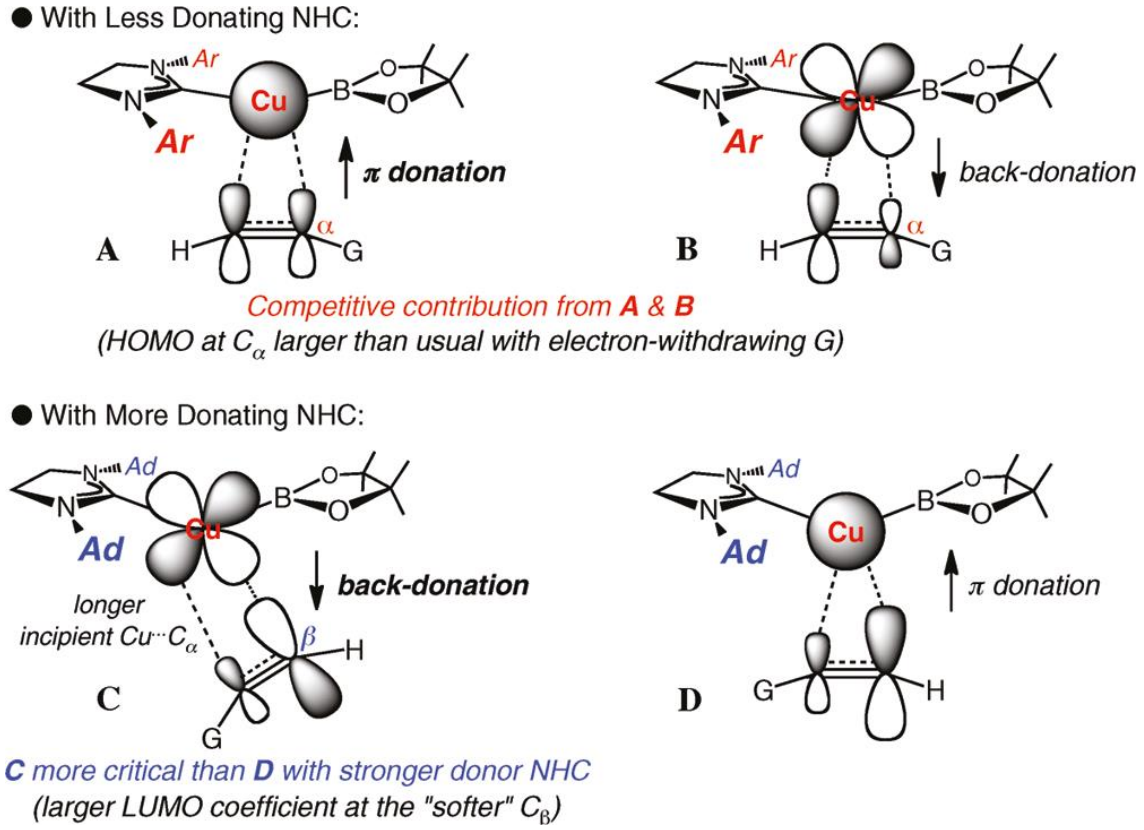


Lipshutz, B. H.; Boskovic, Z. V.; Aue, D. H. *Angew. Chem., Int. Ed.* **2008**, *47*, 10183–10186.

Syn-Hydroboration-(α-selectivity)

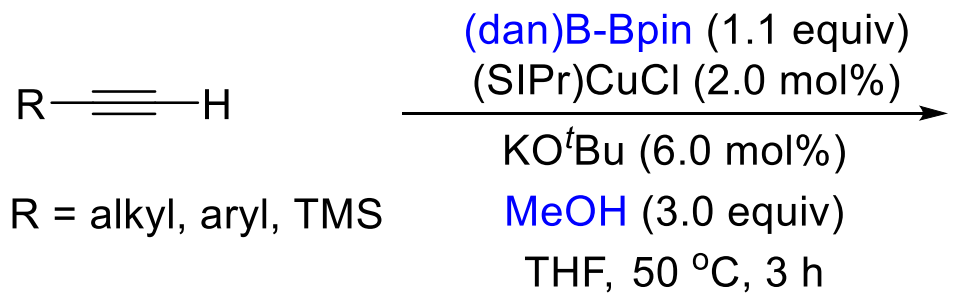


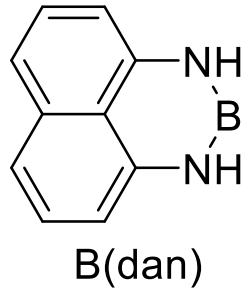
Selectivity:
electronic and steric attribute

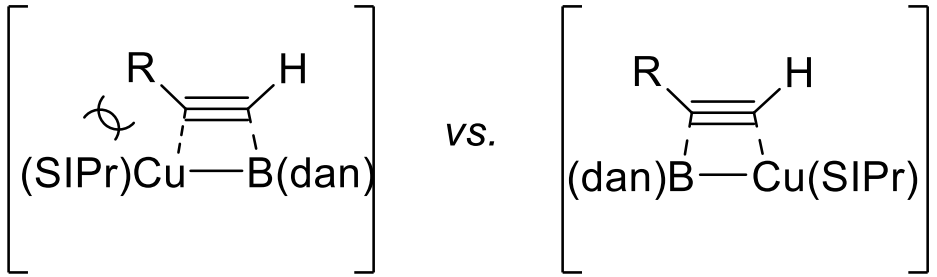


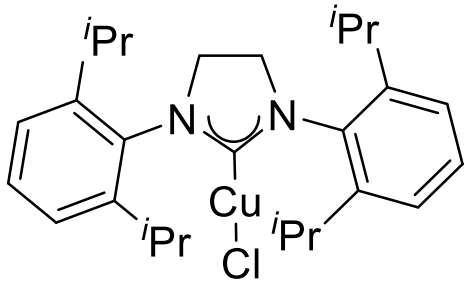
Jang, H.; Zhugralin, A. R.; Lee, Y.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2011**, *133*, 7859−7871.

Syn-Hydroboration-(α-selectivity)



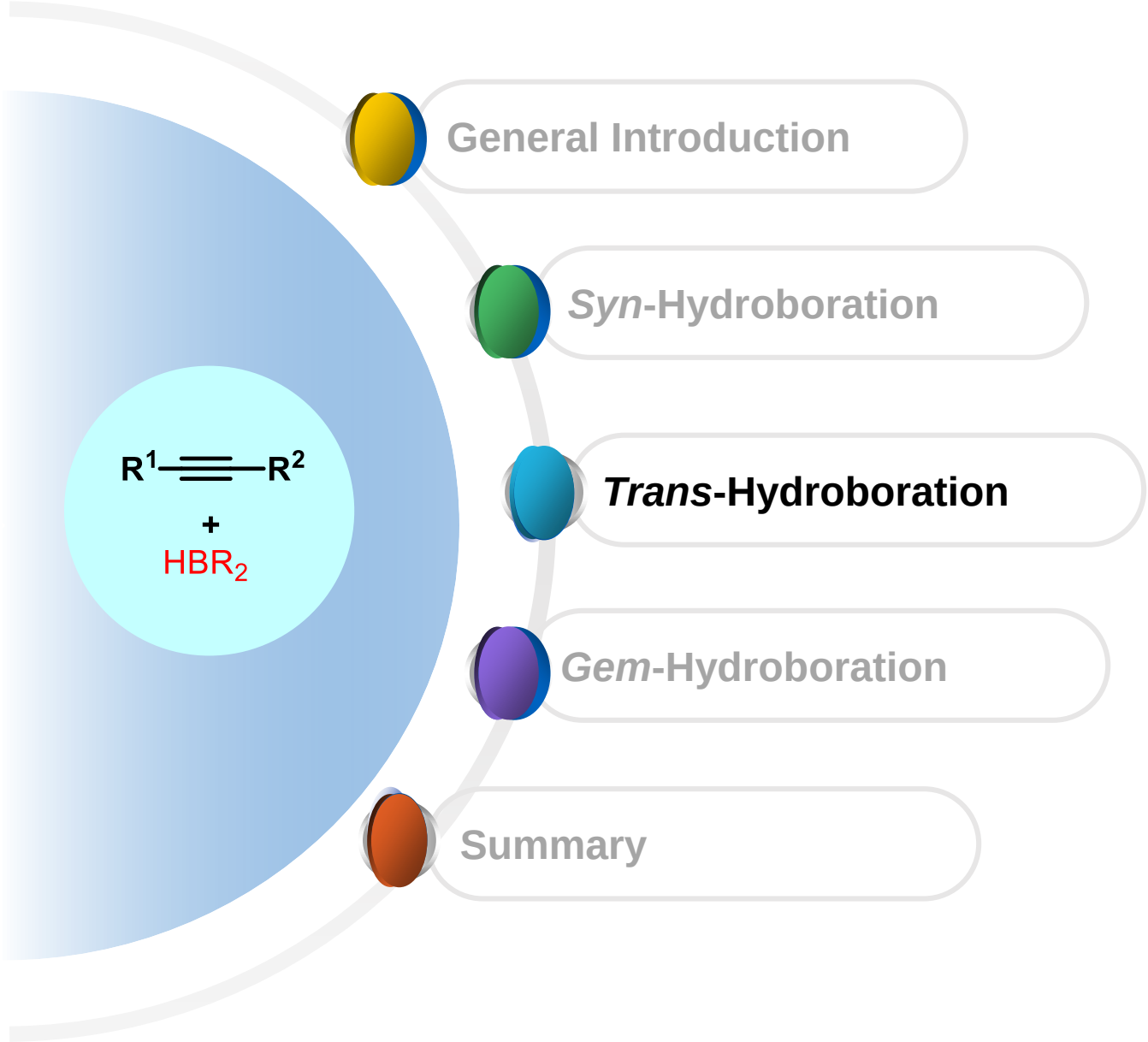






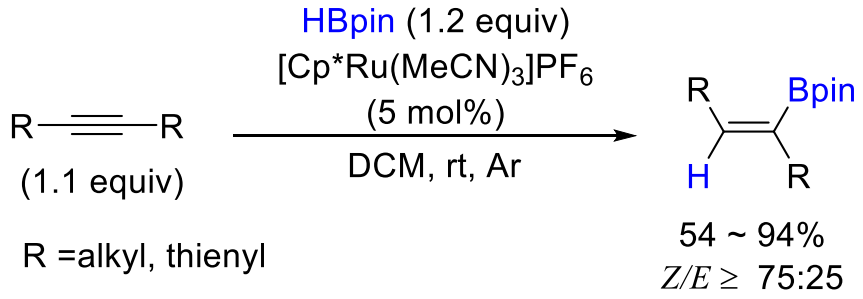
Yoshida, H.; Takemoto, Y.; Takaki, K. *Chem. Commun*. **2014**, *50*, 8299−8302.

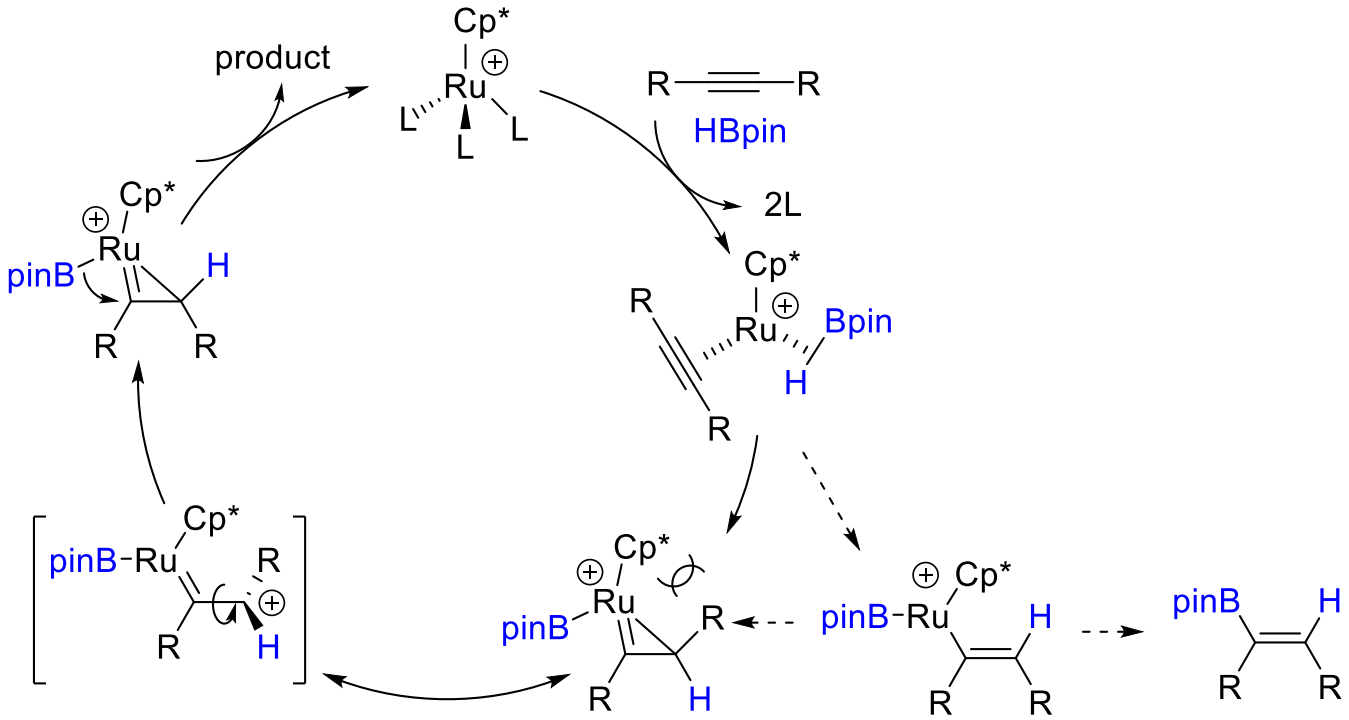
Outlines


R^1—≡—R^2
+
HBR_2
General Introduction
Syn-Hydroboration
***Trans*-Hydroboration**
Gem-Hydroboration
Summary

Trans-Hydroboration

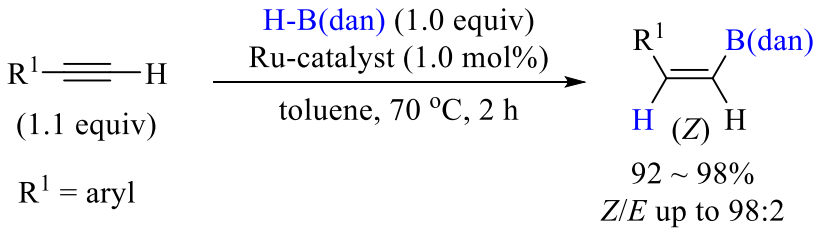
First example (internal alkyne):

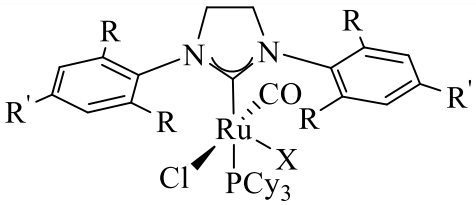


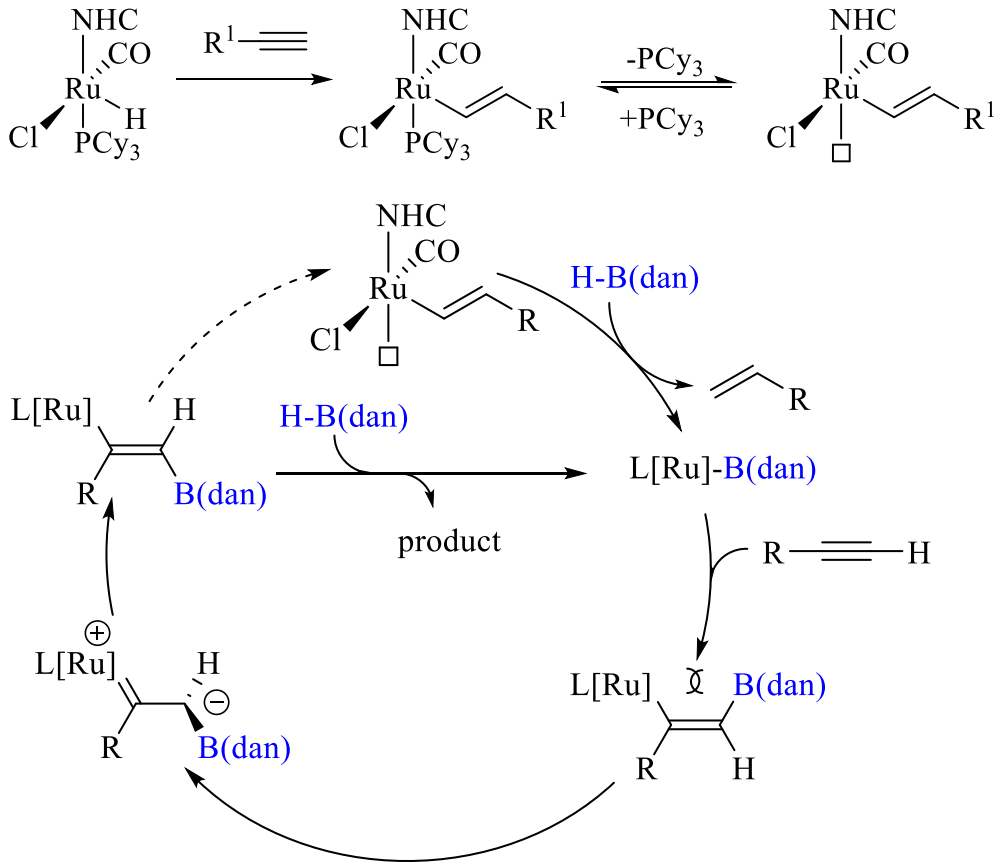


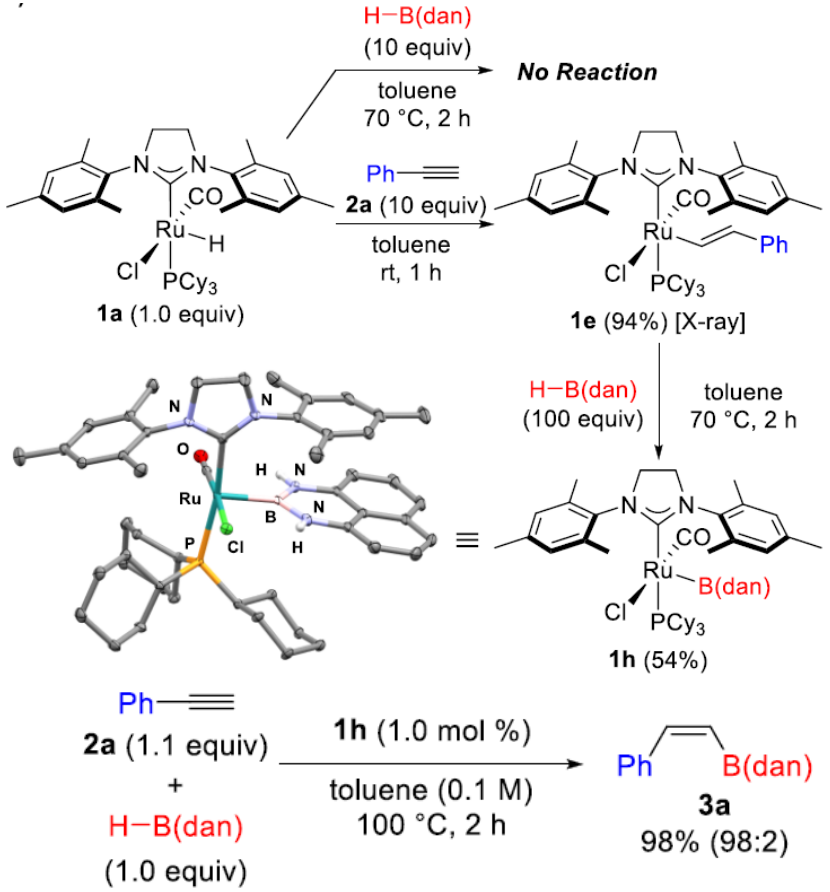
Sundararaju, B.; Fürstner, A. *Angew. Chem., Int. Ed.* **2013**, *52*, 14050−14054.

Trans-Hydroboration



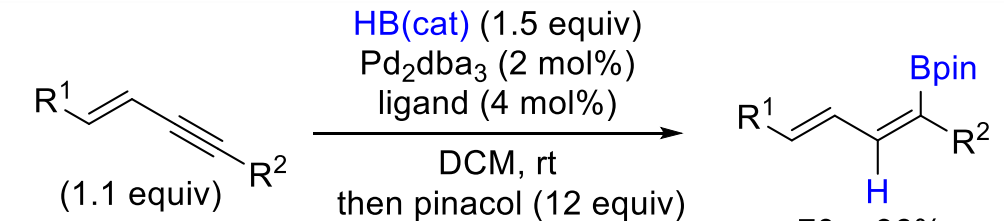




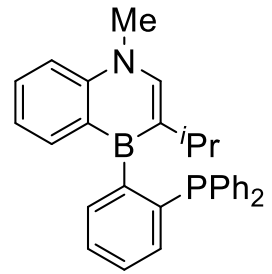


Yamamoto, K.; Mohara, Y.; Mutoh, Y.; Saito S. *J. Am. Chem. Soc.* **2019**, *141*, 17042−17047.

Trans-Hydroboration

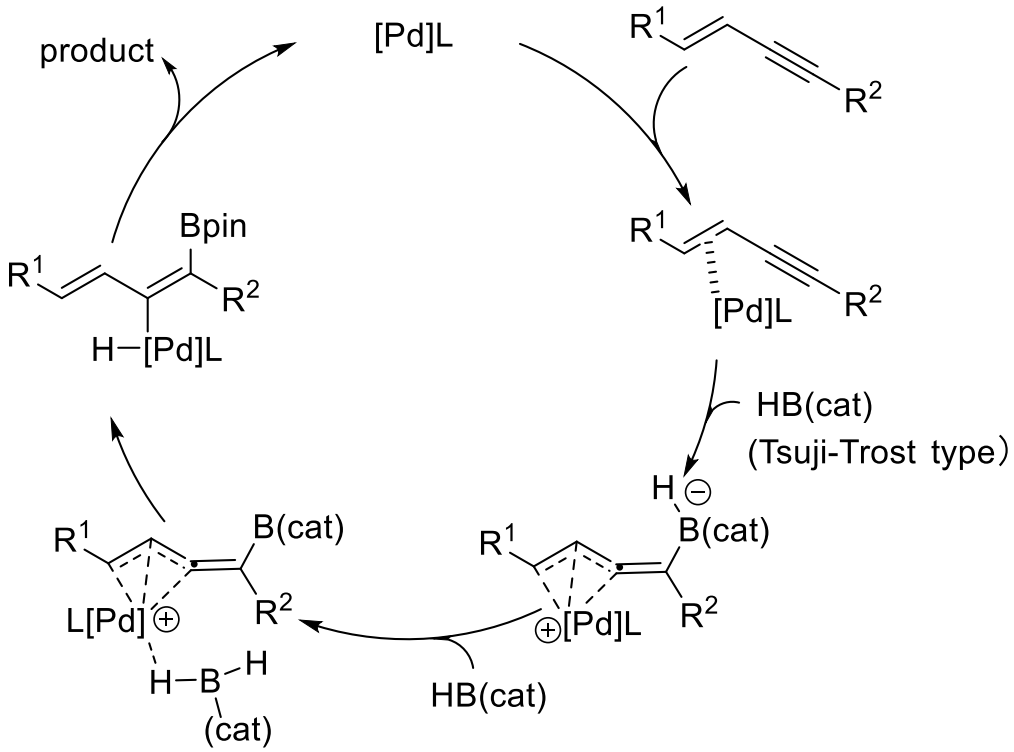


R^1 =alkyl, aryl, alkenyl



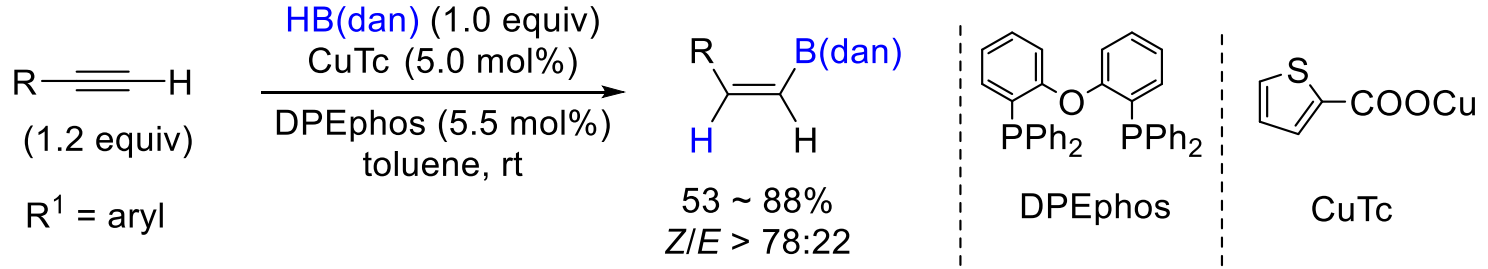
ligand

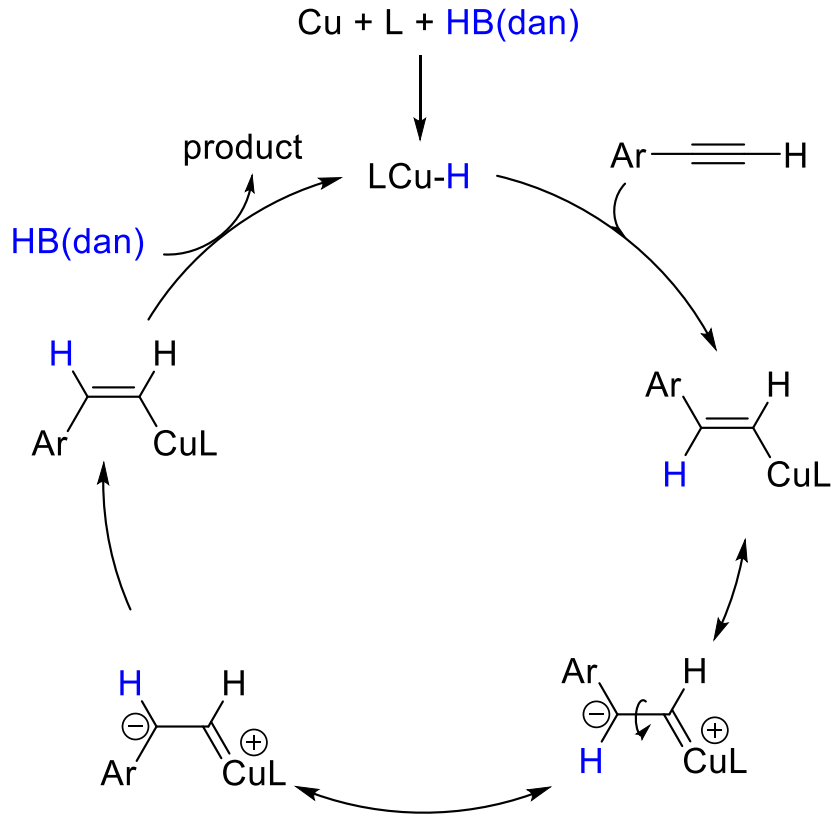
Unconventional H-B bond cleavage,
Outer-sphere mechanism



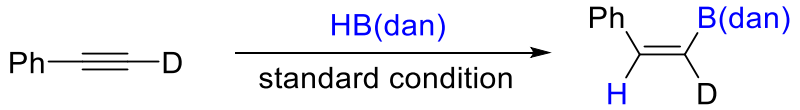
Xu, S.; Zhang, Y.; Li, B.; Liu, S.-Y. *J. Am. Chem. Soc.* **2016**, *138*, 14566−14569.

Trans-Hydroboration



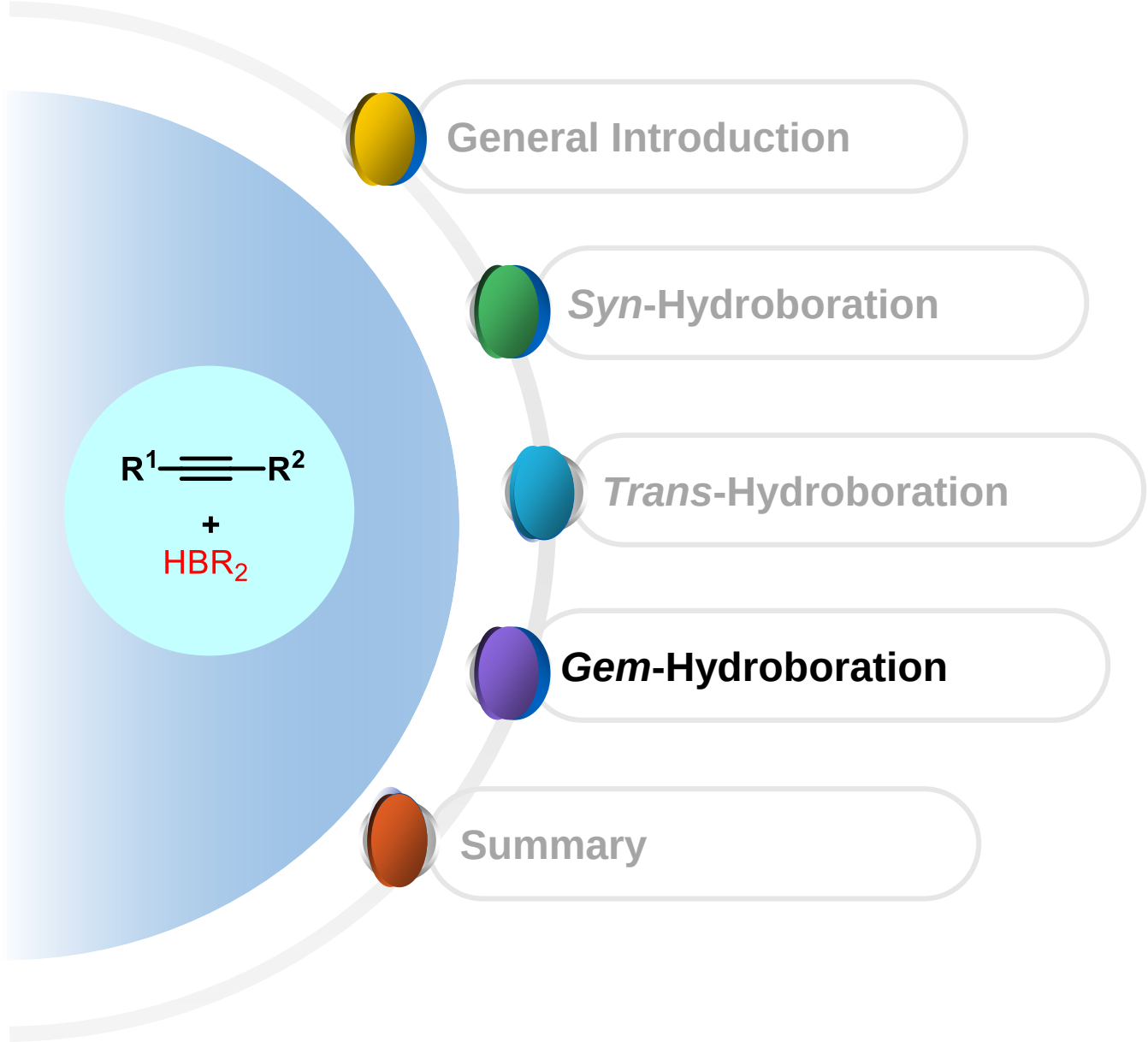


Deuterium labeling experiment:



Jang, W. J.; Lee, W. L.; Moon, J. H.; Lee, J. Y.; Yun, J. *Org. Lett.* **2016**, *18*, 1390−1393.

Outlines


R^1—≡—R^2
+
HBR_2
General Introduction
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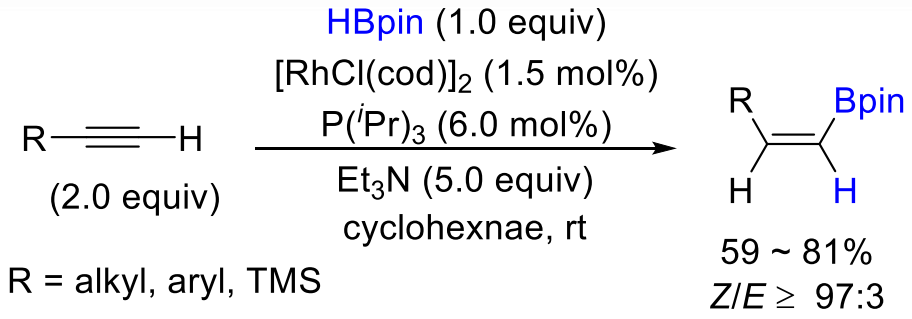
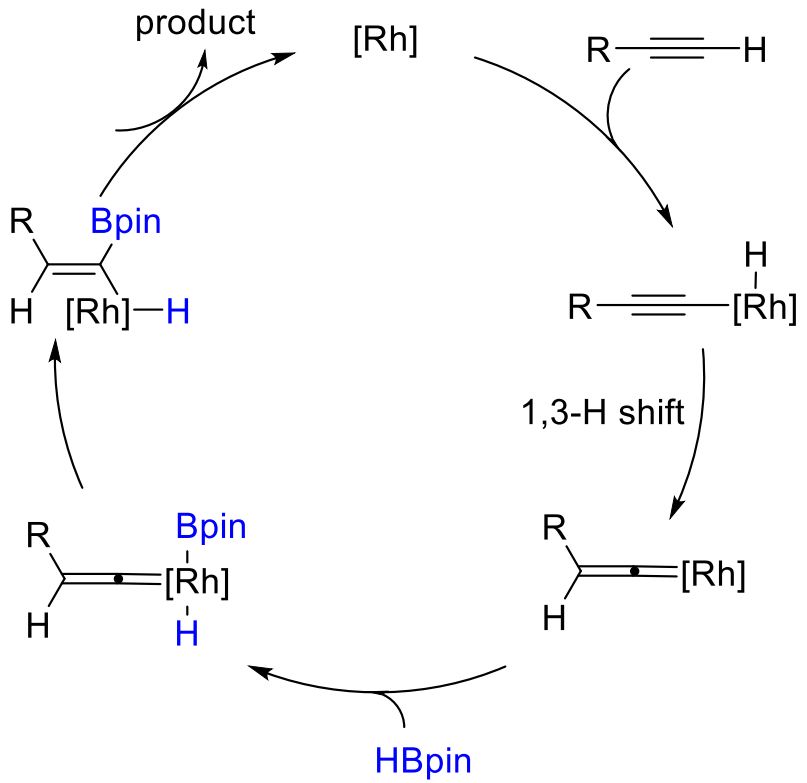
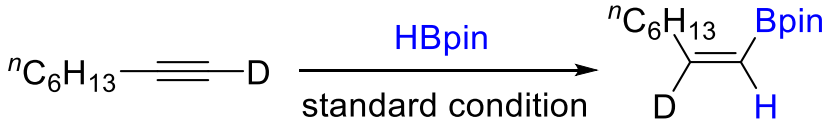
Summary

Gem-Hydroboration



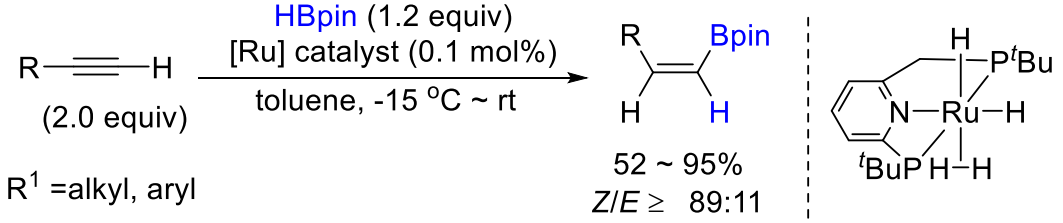


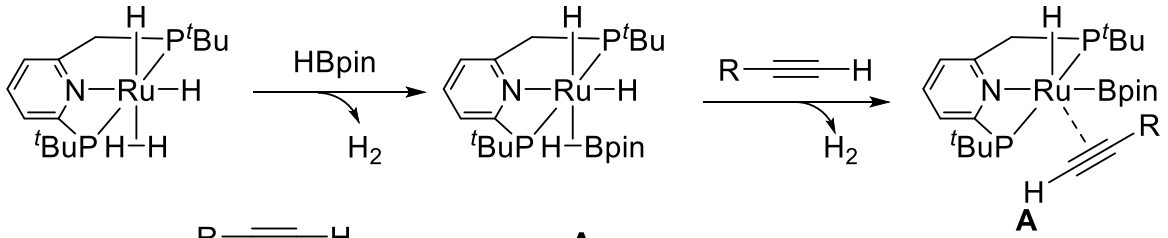
Deuterium labeling experiment:

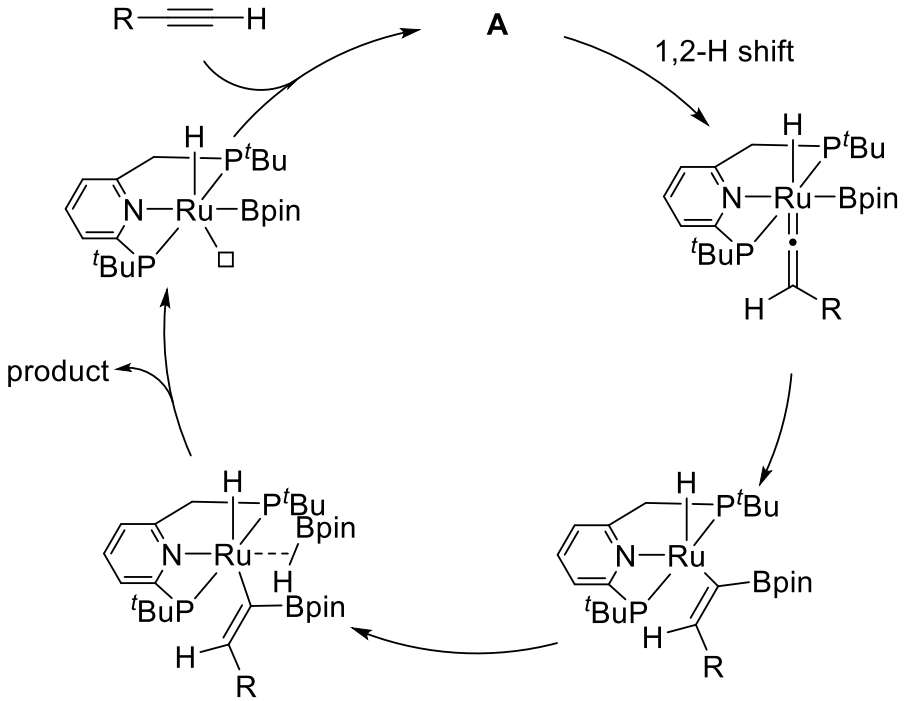


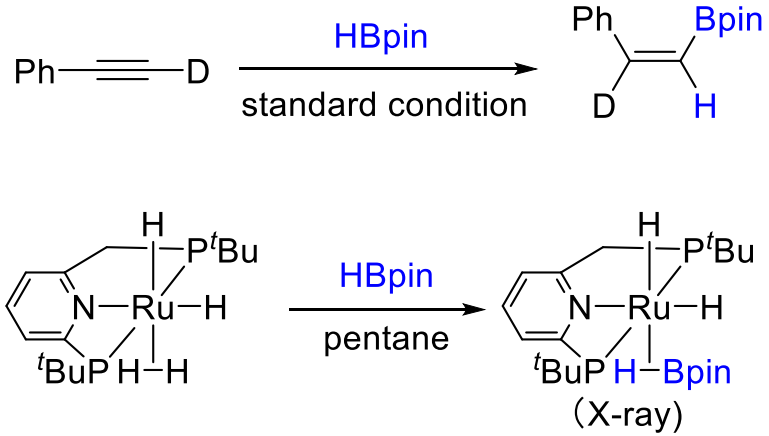
Ohmura, T.; Yamamoto, Y.; Miyaura, N. *J. Am. Chem. Soc.* **2000**, *122*, 4990−4991.

Gem-Hydroboration



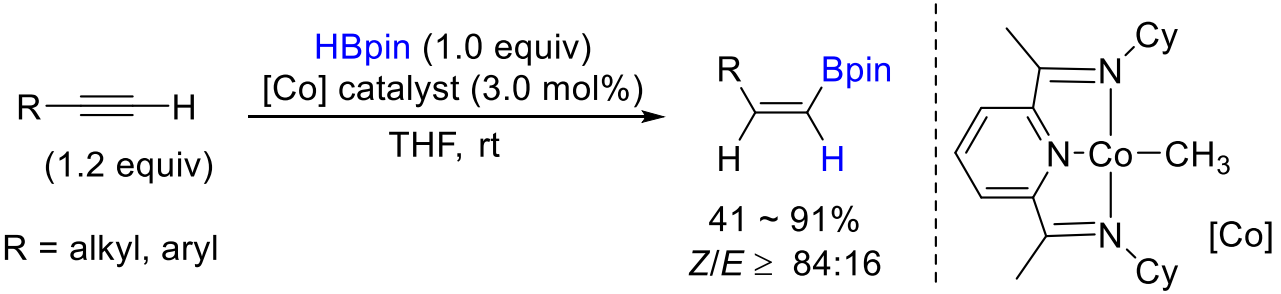


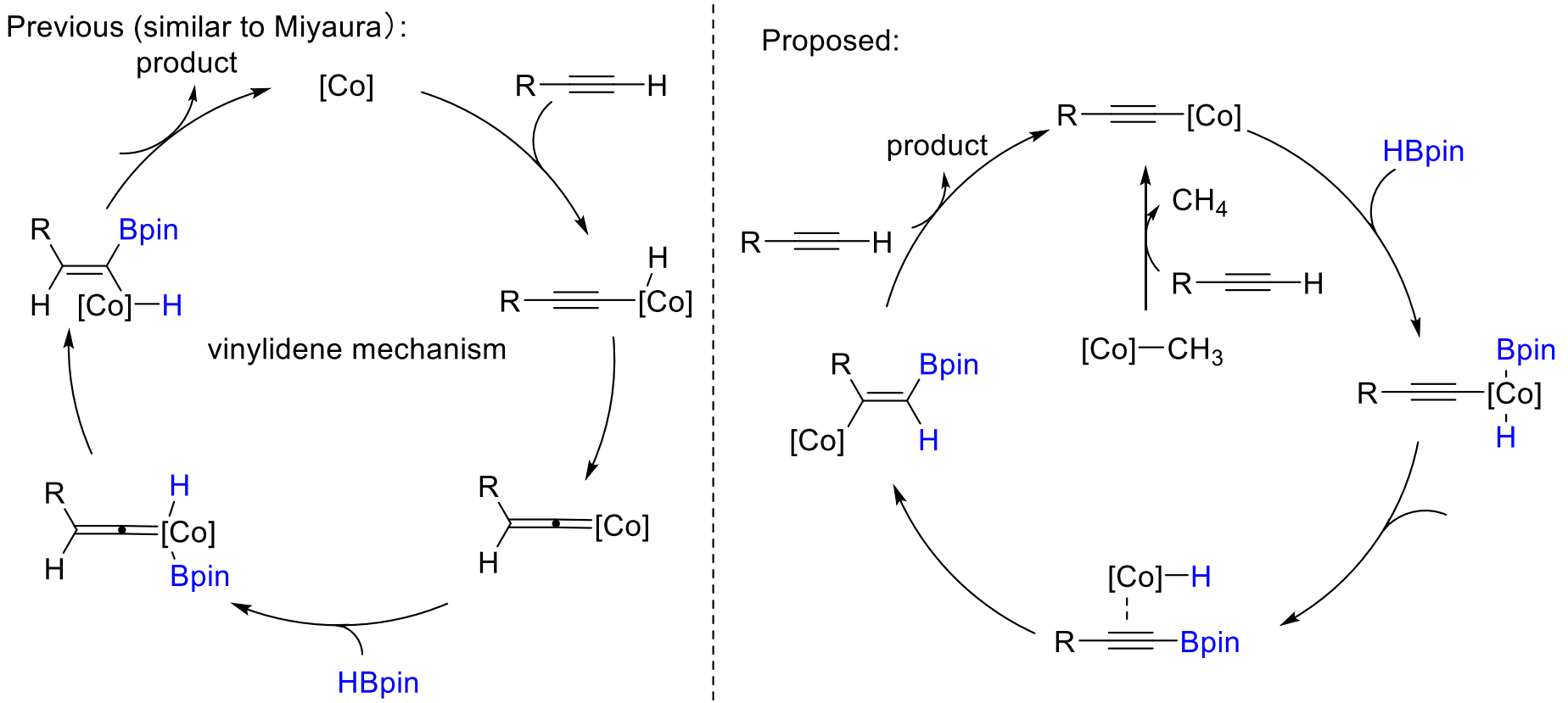




Gunanathan, C.; Hölscher, M.; Pan, F.; Leitner, W. *J. Am. Chem. Soc.* **2012**, *134*, 14349−14352.

Gem-Hydroboration

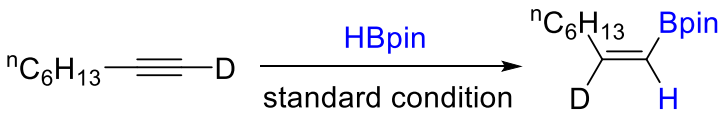


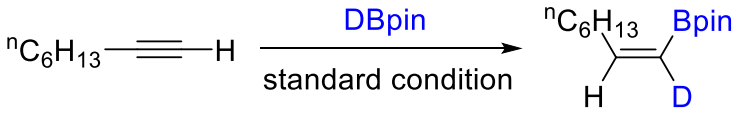


Obligacion, J. V.; Neely, J. M.; Yazdani, A. N.; Pappas, I.; Chirik, P. J. *J. Am. Chem. Soc.* **2015**, *137*, 5855−5858.

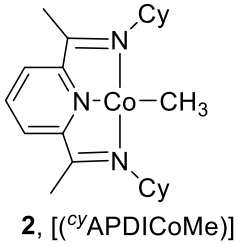
Gem-Hydroboration

Deuterium labeling experiment:

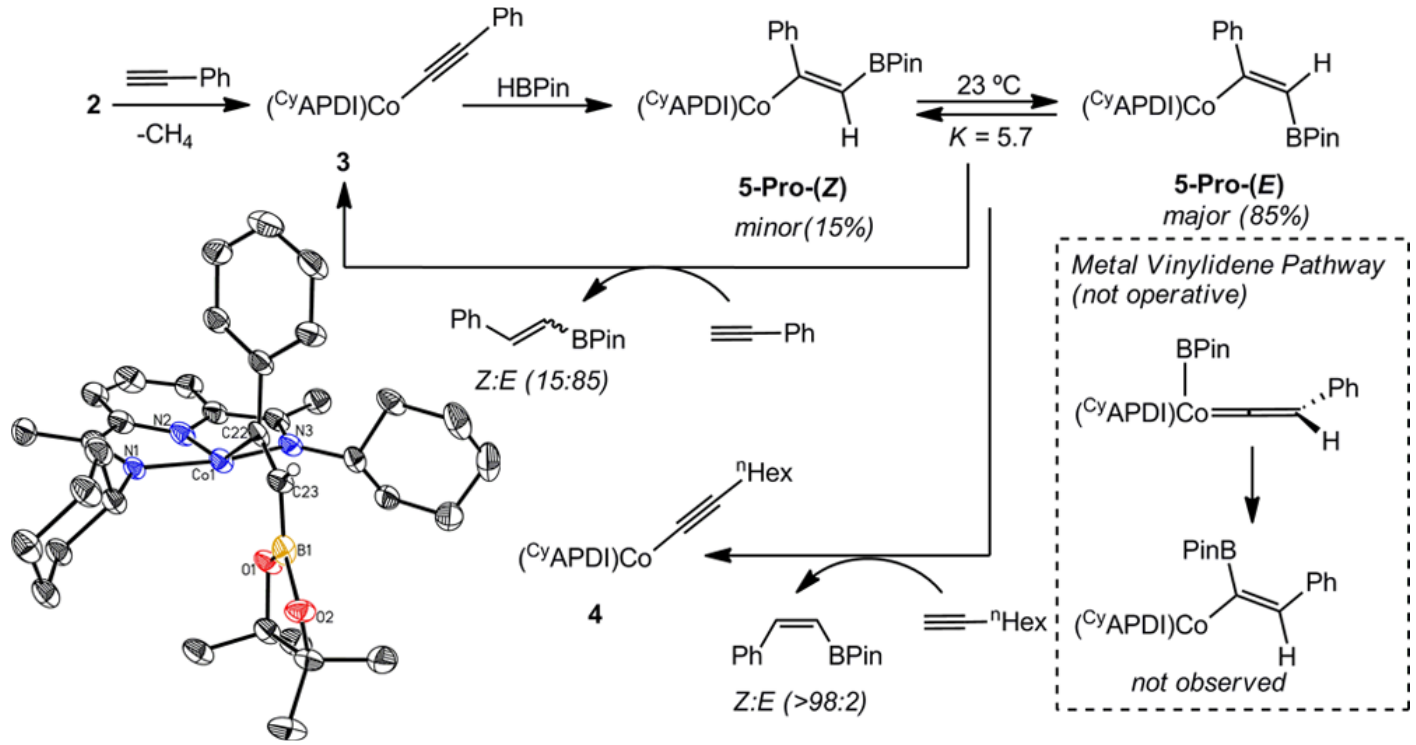




Stoichiometric experiment:

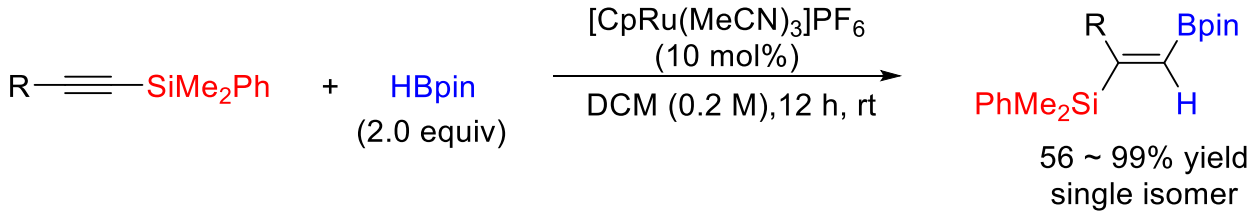


2, [(^{cy}APDICoMe)]



Obligacion, J. V.; Neely, J. M.; Yazdani, A. N.; Pappas, I.; Chirik, P. J. *J. Am. Chem. Soc.* **2015**, *137*, 5855−5858.

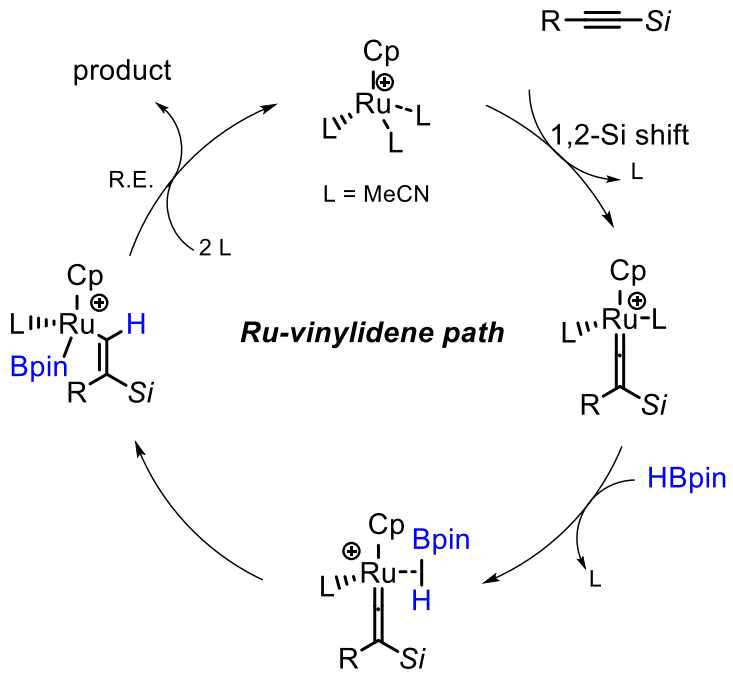
Gem-Hydroboration

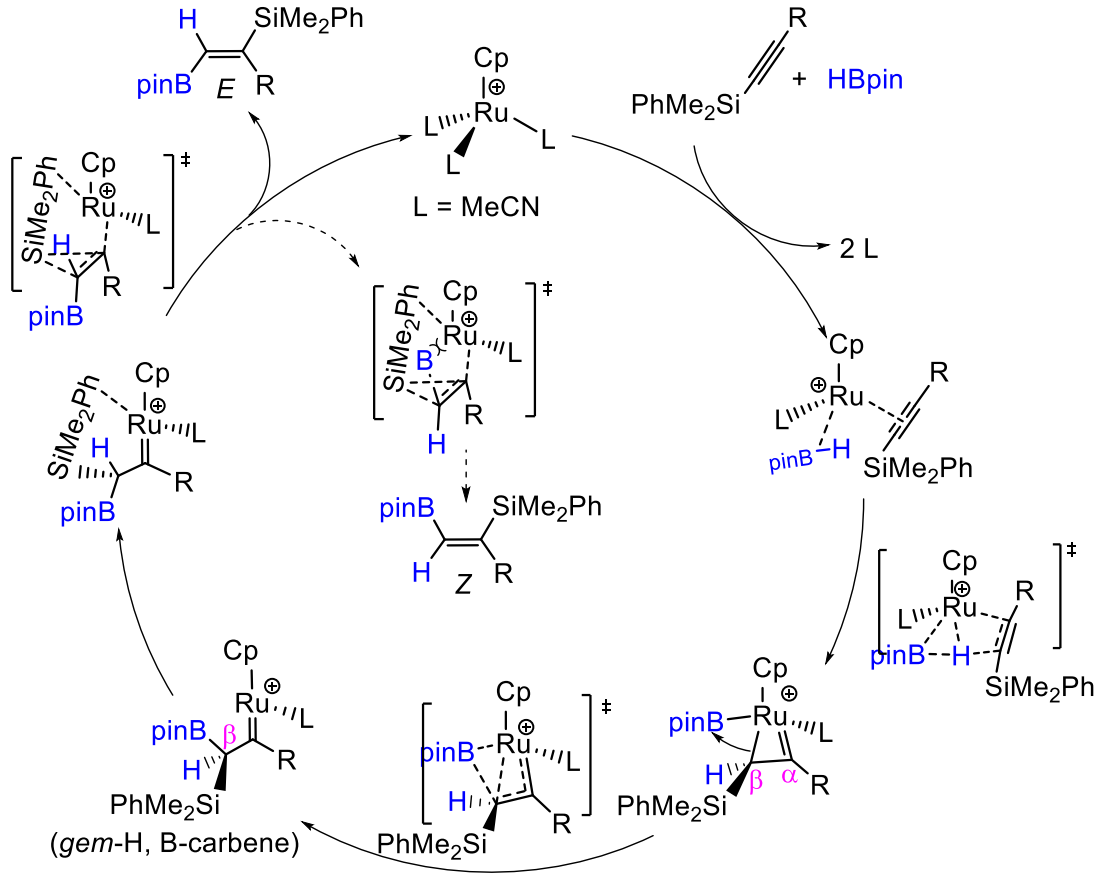


Why?

Regioselectivity: *gem*-addition

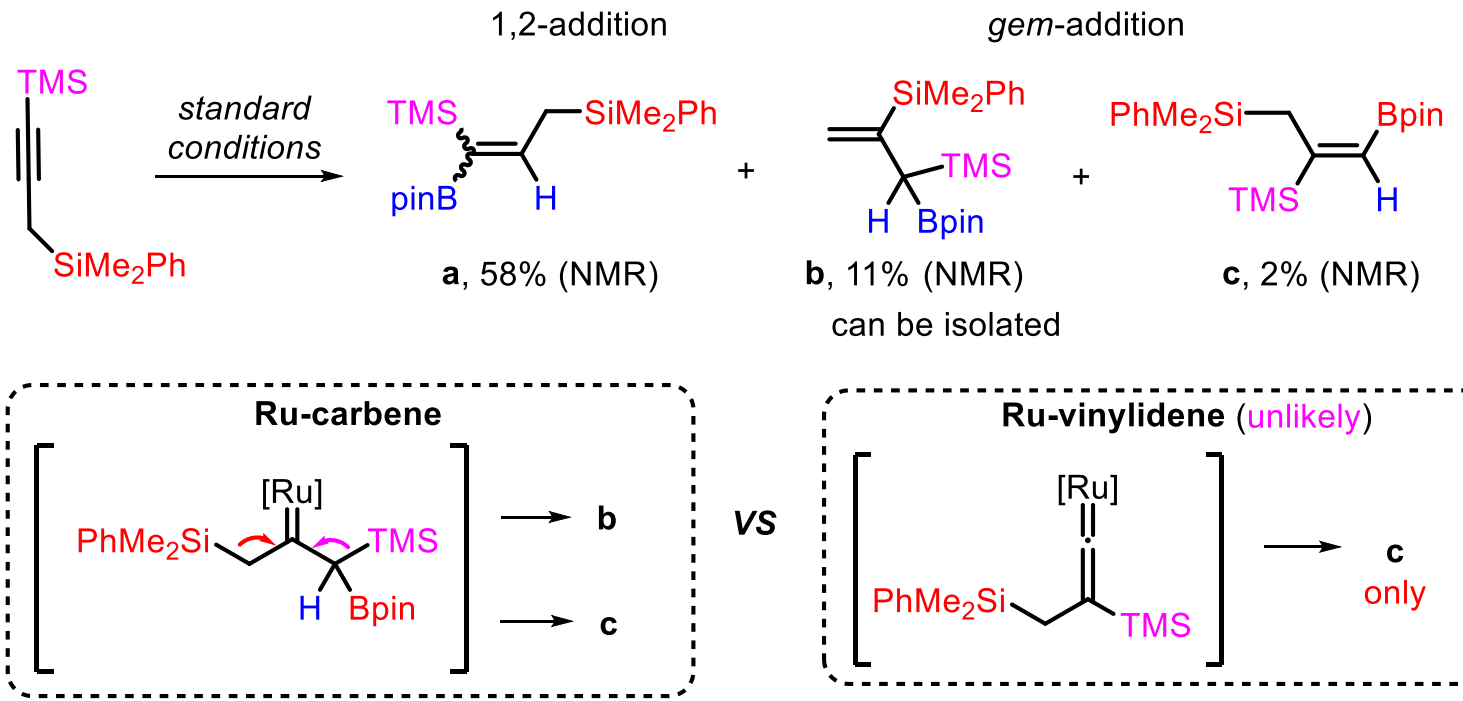
Stereoselectivity: *E*-isomer

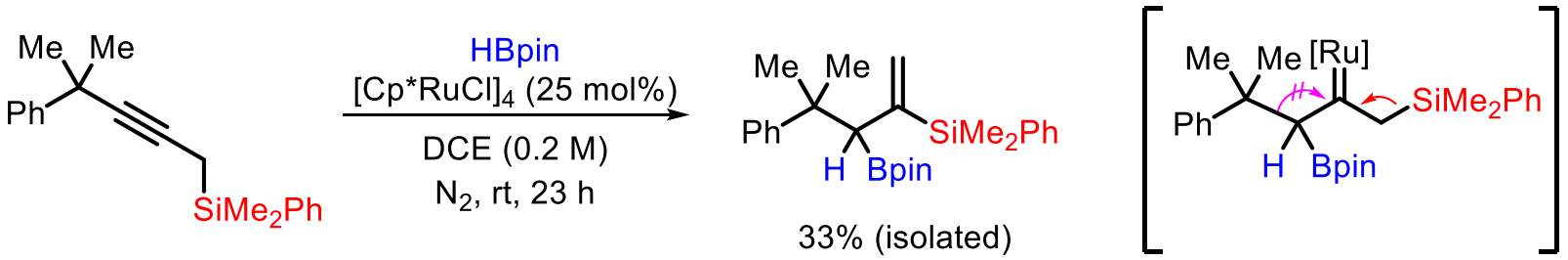




Feng, Q.; Wu, H.; Li, X.; Song, L.; Chung, L. W.; Wu, Y. D.; Sun, J. *J. Am. Chem. Soc.* **2020**, *142*, 13867−13877.

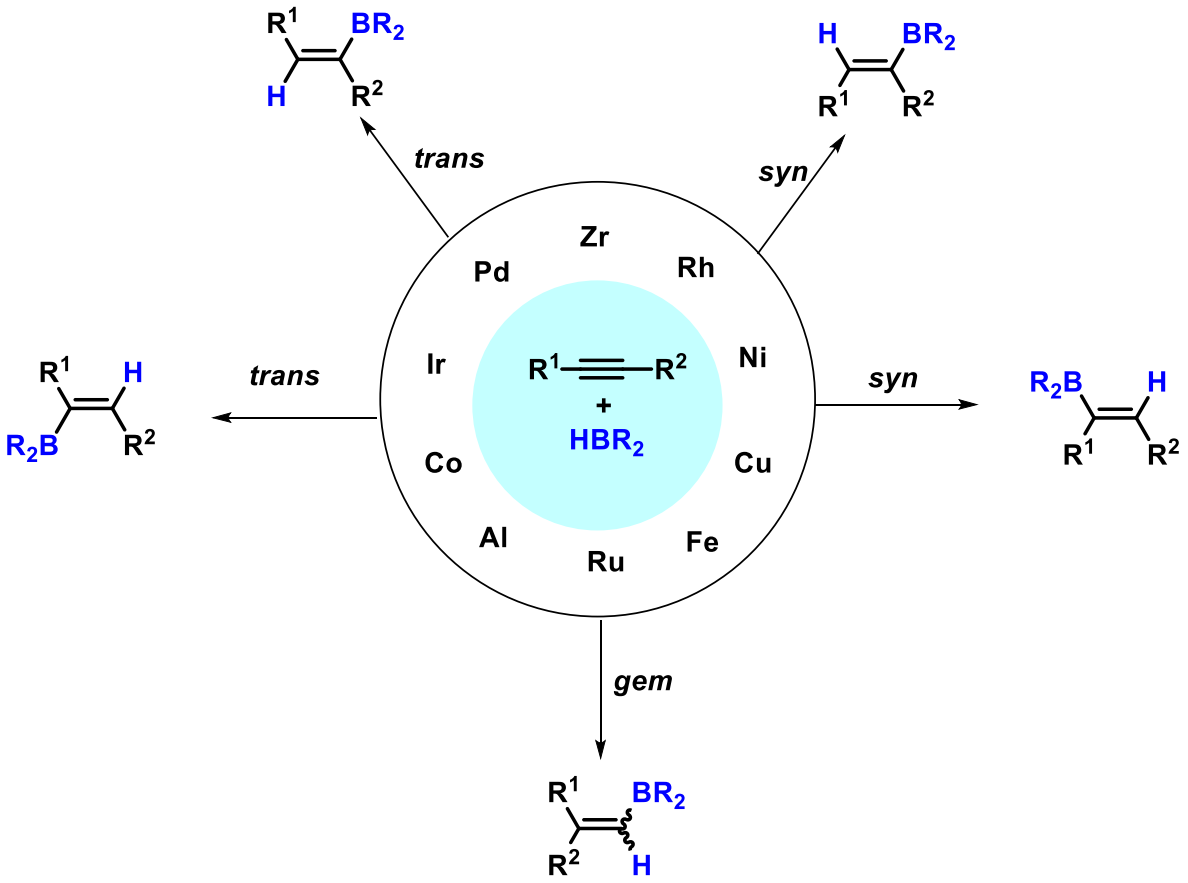
Gem-Hydroboration





Feng, Q.; Wu, H.; Li, X.; Song, L.; Chung, L. W.; Wu, Y. D.; Sun, J. *J. Am. Chem. Soc.* **2020**, *142*, 13867−13877.

Summary



In conclusion, the majority of current metal-catalyzed alkyne hydroboration have been 1,2-*syn*-addition. 1,2-*trans*-hydroboration and gem-hydroboration, especially, for unsymmetrical internal alkynes, still represent a much more challenging problem.

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Q & A