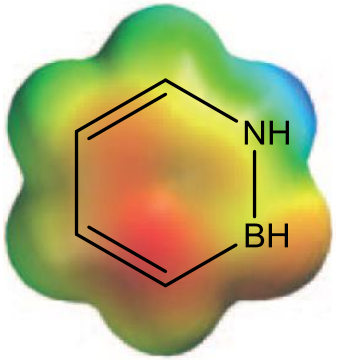
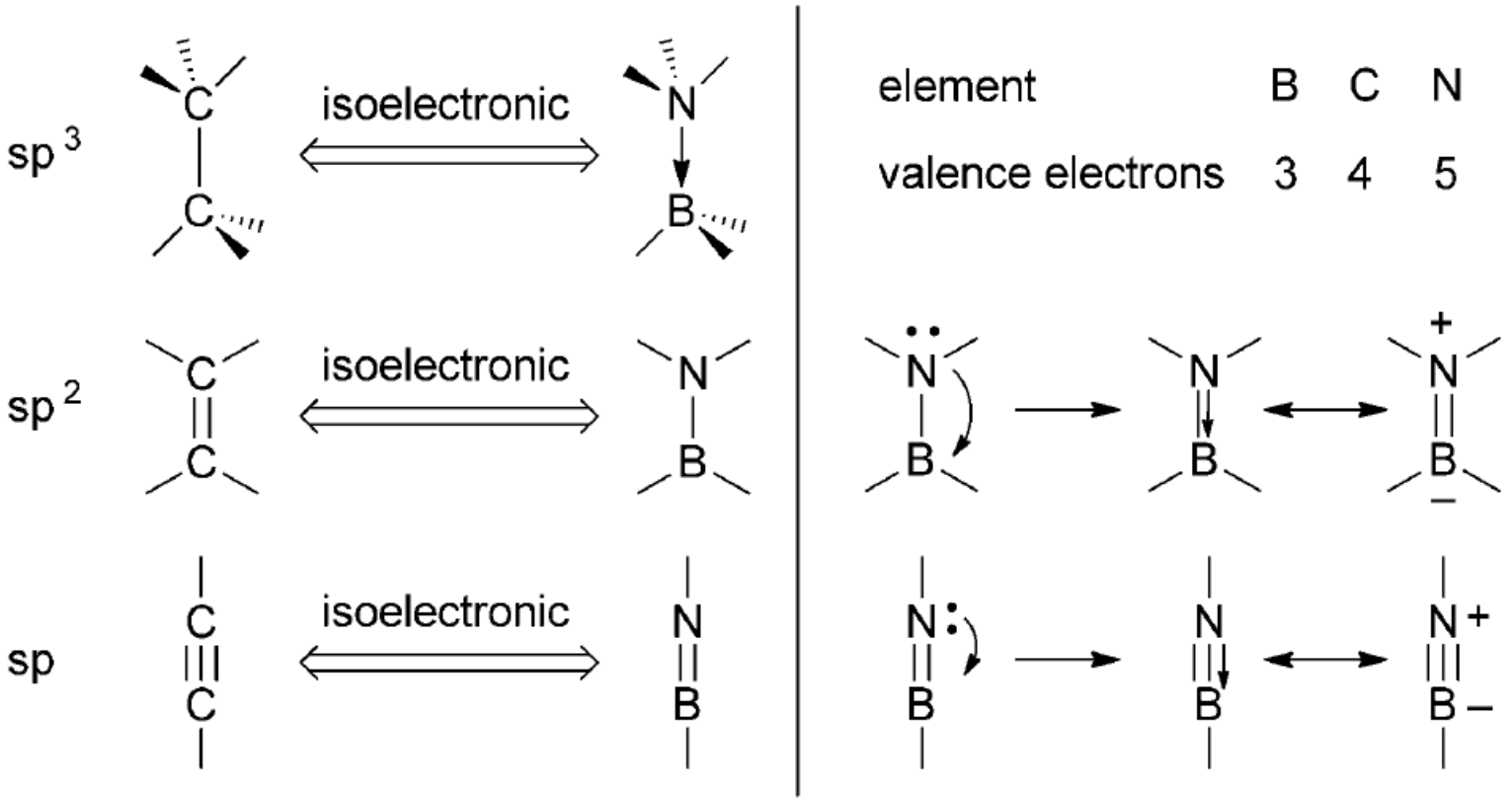


Azaborine

Synthesis, Structure and Reactivity

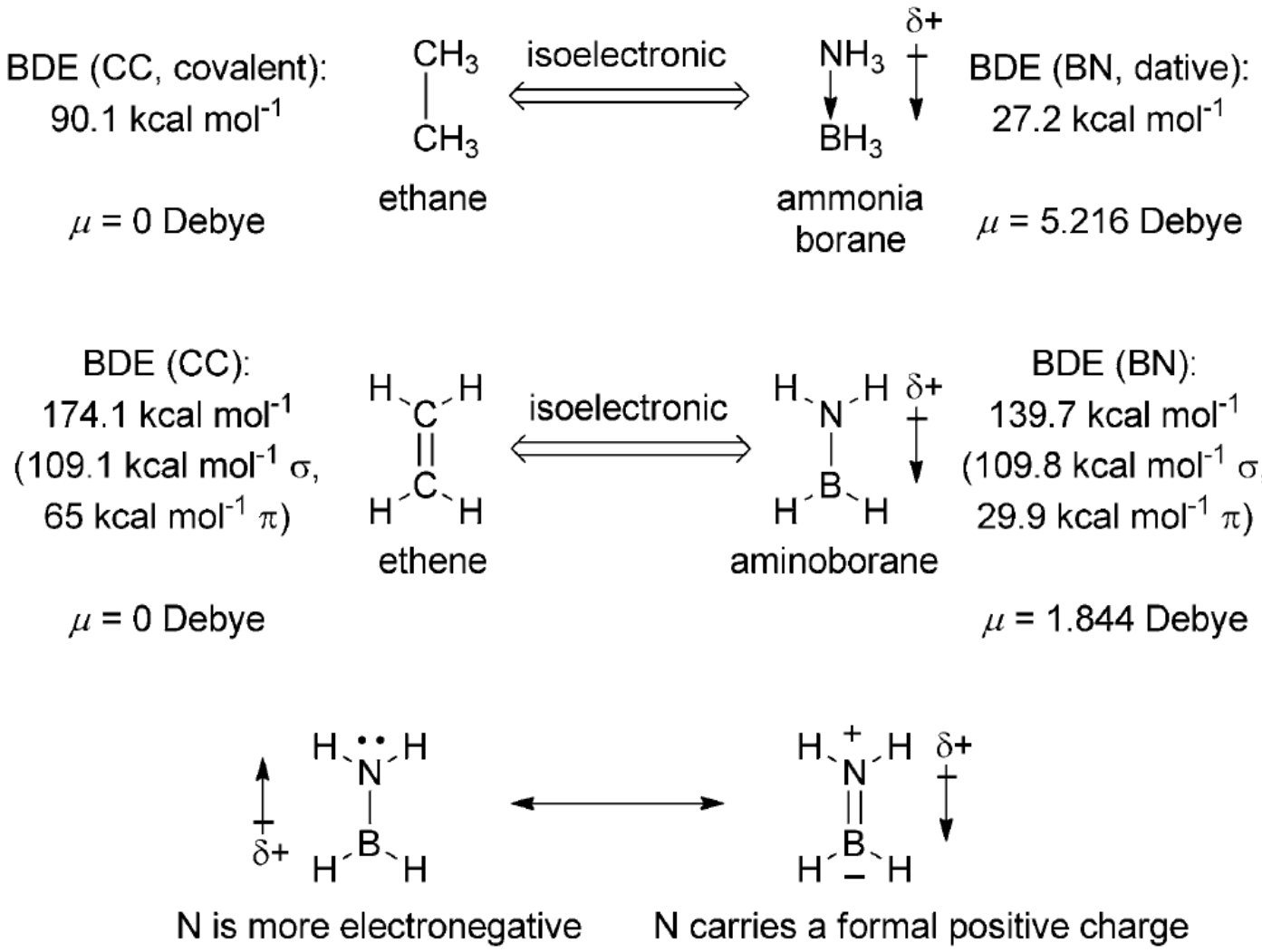
Chengpeng Wang
Dong Group Meeting
University of Texas at Austin
1/27/2016

Boron-Nitrogen Bonding



Liu, S.-Y. *et. al. Angew. Chem. Int. Ed.* **2012**, *51*, 6074-6092.

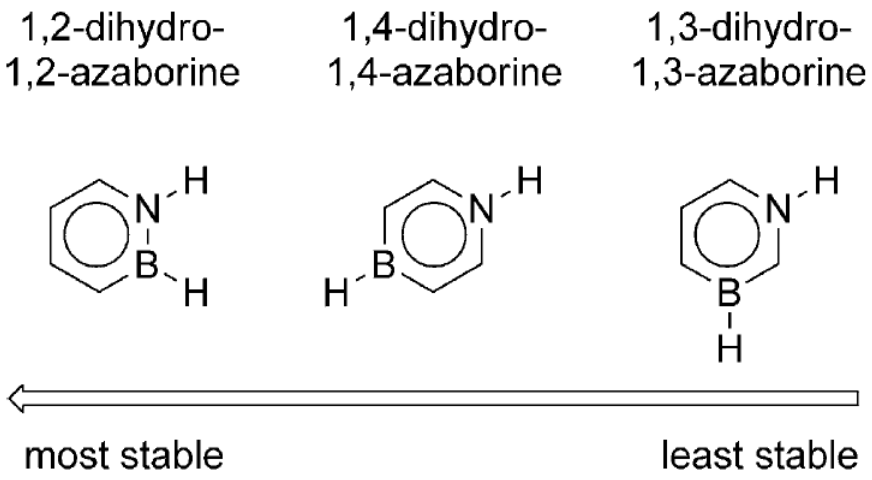
Boron-Nitrogen Bonding



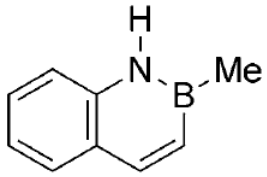
Liu, S.-Y. *et. al. Angew. Chem. Int. Ed.* **2012**, *51*, 6074-6092.

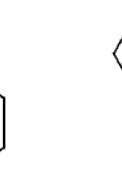
Azaborines

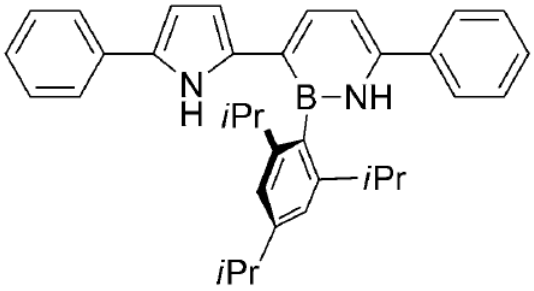
Monocyclic azaborines

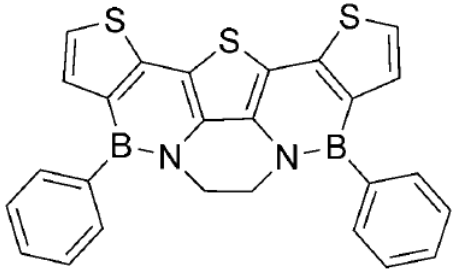


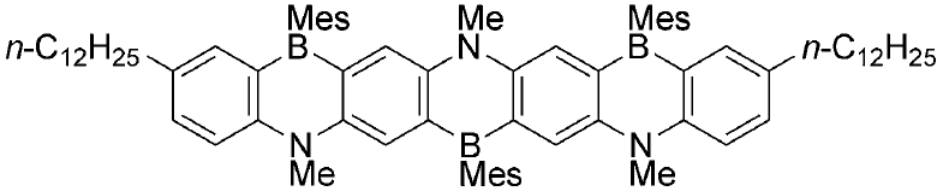
Fused polycyclic azaborines
And materials



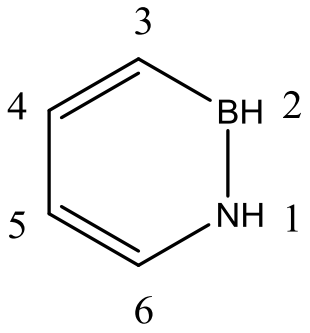




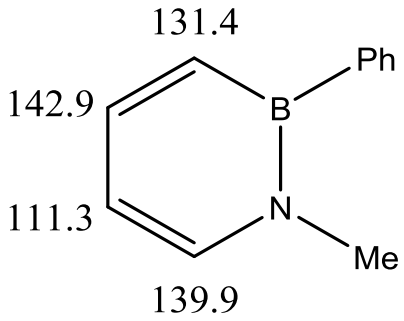




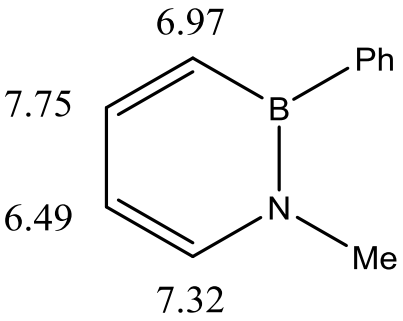
NMR Data of 1,2-Azaborine



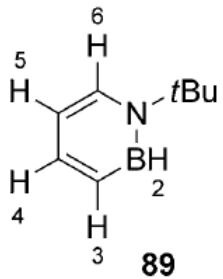
^{13}C spectrum



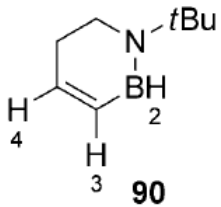
^{1}H spectrum



Ashe, A. J. *et. al. Organometallics* **2001**, *20*, 5413-5418.



89



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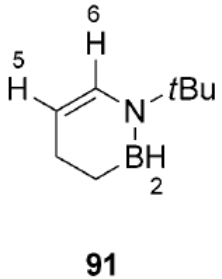

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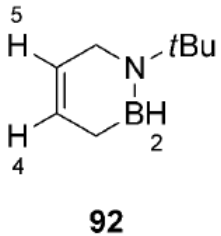
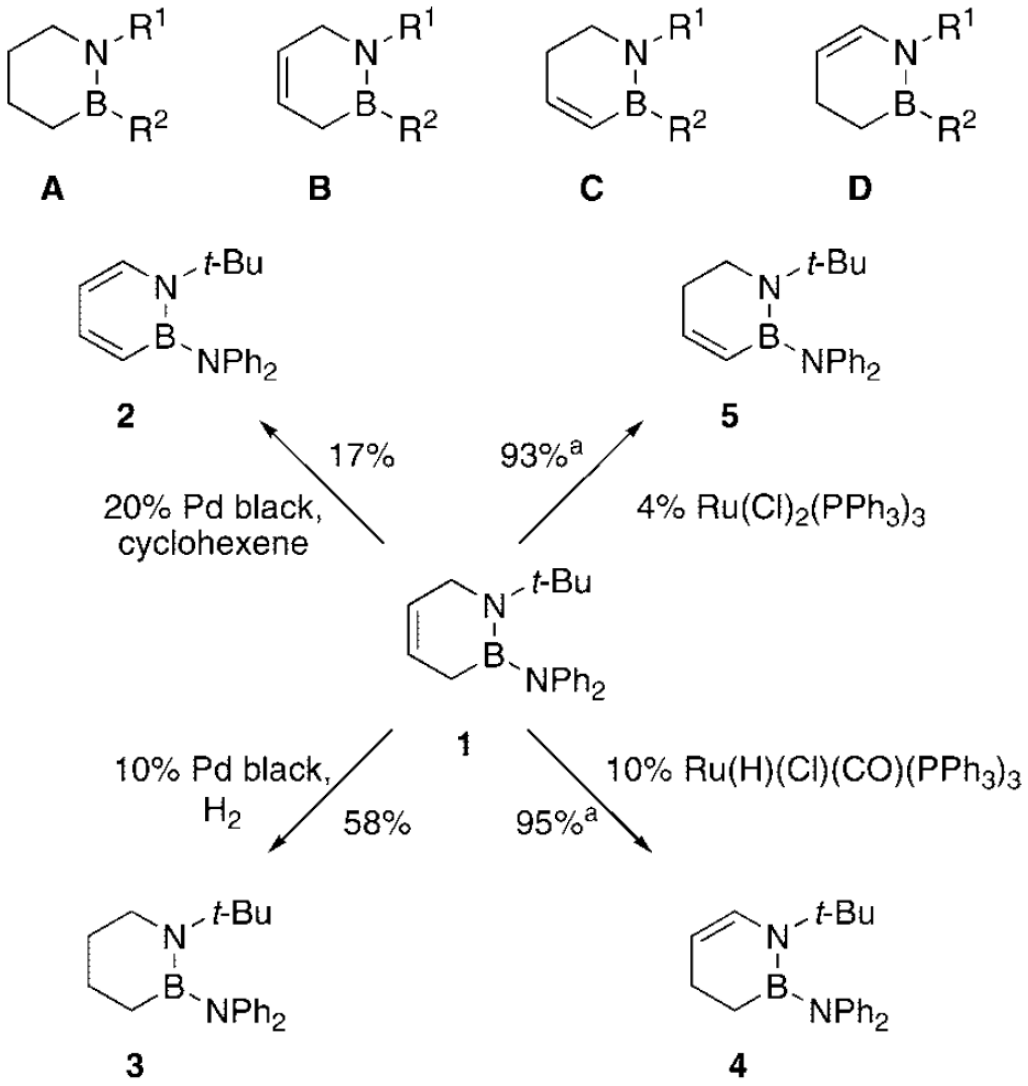


92

	89	**90**	**91**	**92**
H_{B2}	5.23	4.45 (0.78)	4.91 (0.32)	4.75 (0.48)
H_{C3}	6.84	5.91 (0.93)	–	–
H_{C4}	7.54	6.55 (0.99)	–	5.71 (1.83)
H_{C5}	6.38	–	5.02 (1.36)	5.62 (0.76)
H_{C6}	7.63	–	6.21 (1.42)	–

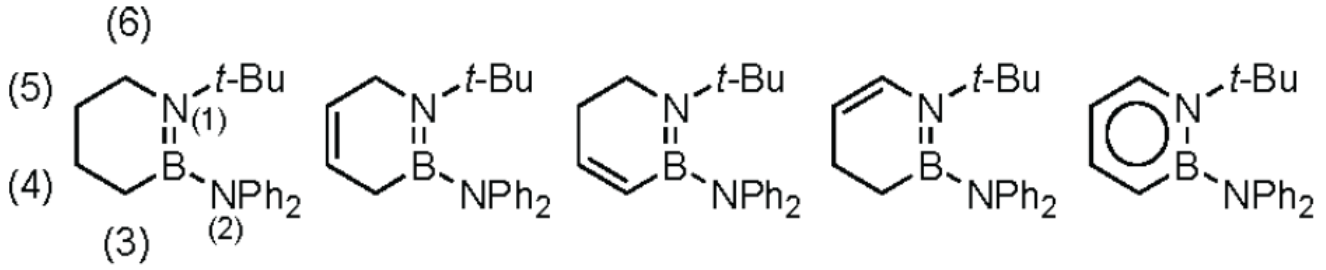
Liu, S.-Y. *et. al. Angew. Chem. Int. Ed.* **2012**, *51*, 6074-6092.

Structure of 1,2-Azaborine



Liu, S.-Y. *et. al. J. Am. Chem. Soc.* **2008**, *130*, 7250-7252.

Structure of 1,2-Azaborine

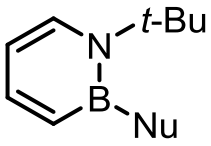


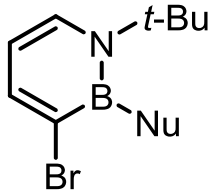
	3	1	5	4	2
N(1)–B	1.403(2)	1.405(2)	**1.407(2)**	**1.417(3)**	**1.446(2)**
B–C(3)	1.584(3)	1.590(2)	**1.559(2)**	1.579(4)	**1.518(2)**
C(3)–C(4)	1.511(3)	1.493(2)	**1.338(2)**	1.504(4)	**1.363(2)**
C(4)–C(5)	1.511(3)	1.319(2)	1.479(2)	1.494(4)	1.412(2)
C(5)–C(6)	1.508(3)	1.493(2)	1.503(2)	**1.319(3)**	**1.356(2)**
C(6)–N(1)	1.479(2)	1.477(2)	1.479(2)	**1.432(3)**	**1.383(2)**
B–N(2)	1.488(2)	1.478(2)	1.483(2)	1.480(3)	1.486(2)
planarity[a]	0.226	0.164	0.199	0.183	0.048

[a] Root mean square deviation of intra-ring atoms from the least-squares plane (in Å).

Liu, S.-Y. *et. al. J. Am. Chem. Soc.* **2008**, *130*, 7250-7252.

Stability of 1,2-Azaborine





O_2 stability

Nu	% material remaining at 4 h[a]	Nu	% material remaining at 4 h[a]
Bu	46	Bu	60
Ph	82	Ph	93
H	86	H	91
CCPh	92	CCPh	98
Cl	91	Cl	85
OEt	86	OEt	94

0.1 M substrate in benezene-*d*6 exposed to 2.5 mL of oxygen gas in a sealed tube at 50 °C.

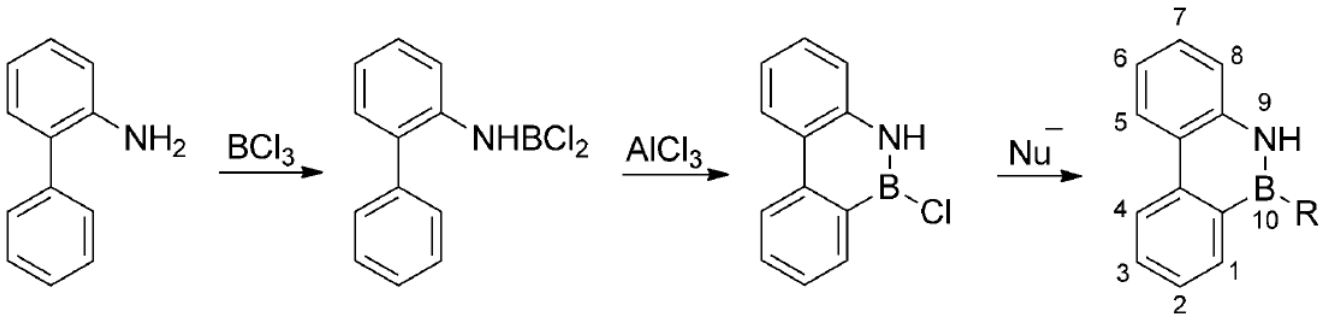
water stability

Bu	98	Bu	99
Ph	99	Ph	97
H	97	H	99
CCPh	97	CCPh	97
OEt	97	OEt	97
Cl	0	Cl	0

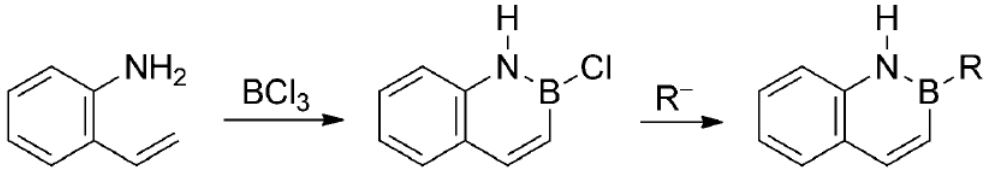
0.17 M substrate in DMSO-d_6 containing two equivalents of water at room temperature.

Liu, S.-Y. *et. al. Mol. Biosyst.* **2009**, *5*, 1303-1305.

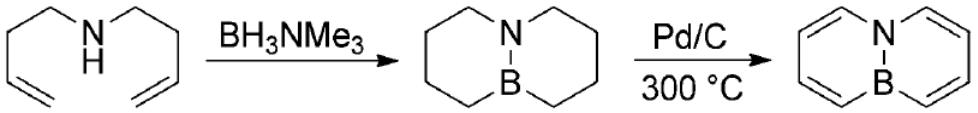
Early Synthetic Work



Dewar, M. J. S. *et. al. J. Chem. Soc.* **1958**, 3073-3076.

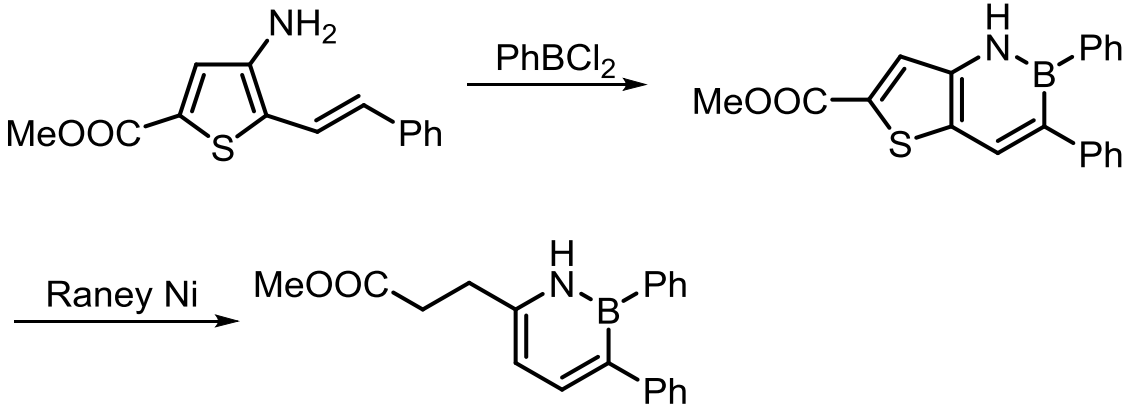


Dewar, M. J. S. *et. al. J. Chem. Soc.* **1959**, 2728-2730.

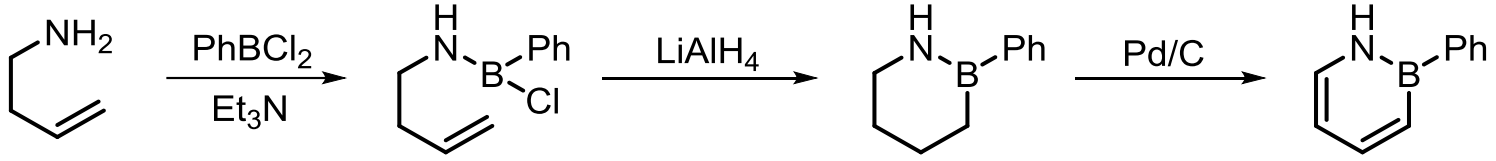


Dewar, M. J. S. *et. al. J. Am. Chem. Soc.* **1964**, *86*, 5698-5699.

Early Synthetic Work

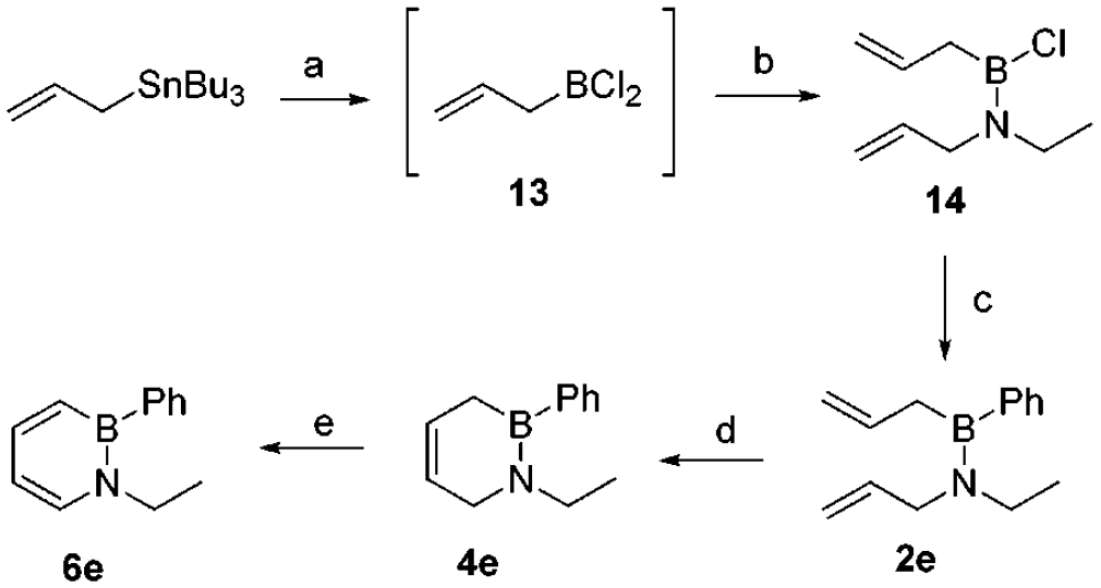


Dewar, M. J. S. *et. al. J. Am. Chem. Soc.* **1962**, *84*, 3782.



White, D. G. *J. Am. Chem. Soc.* **1963**, *85*, 3634-3636.

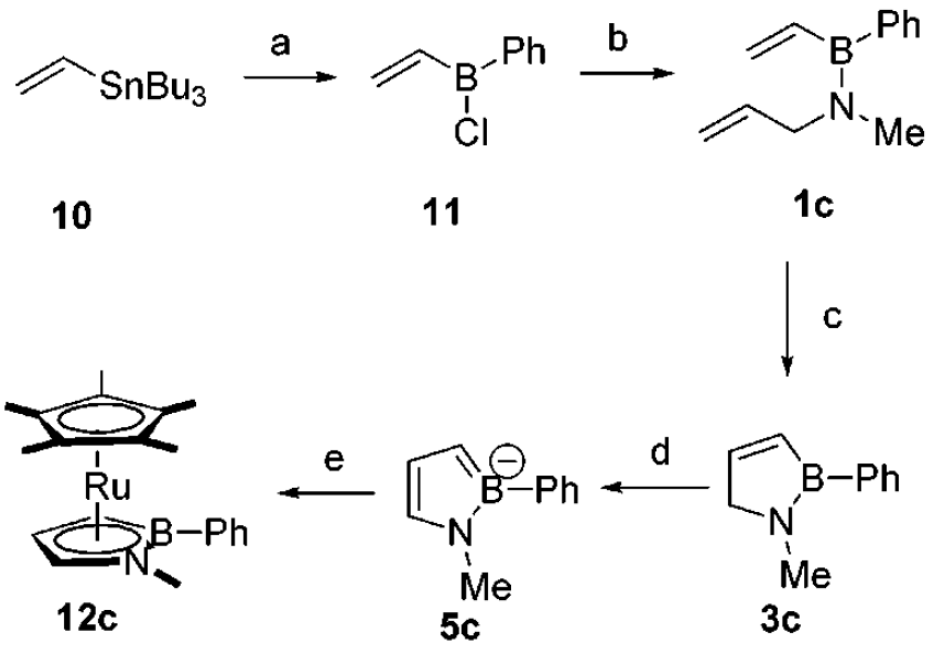
Synthesis of 1,2-Azaborine



[a] Key: (a) BCl_3, pentane; (b) $(C_3H_5)EtNH$, Et_3N; (c) PhLi; (d) $(Cy_3P)_2(PhCH)RuCl_2$; (e) DDQ, pentane.

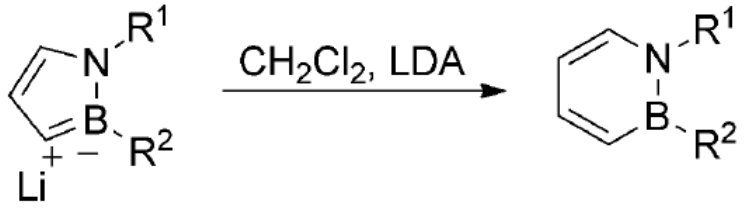
Ashe, A. J. *et. al. Org. Lett.* **2000**, *2*, 2089-2091.

Synthesis of 1,2-Azaborine



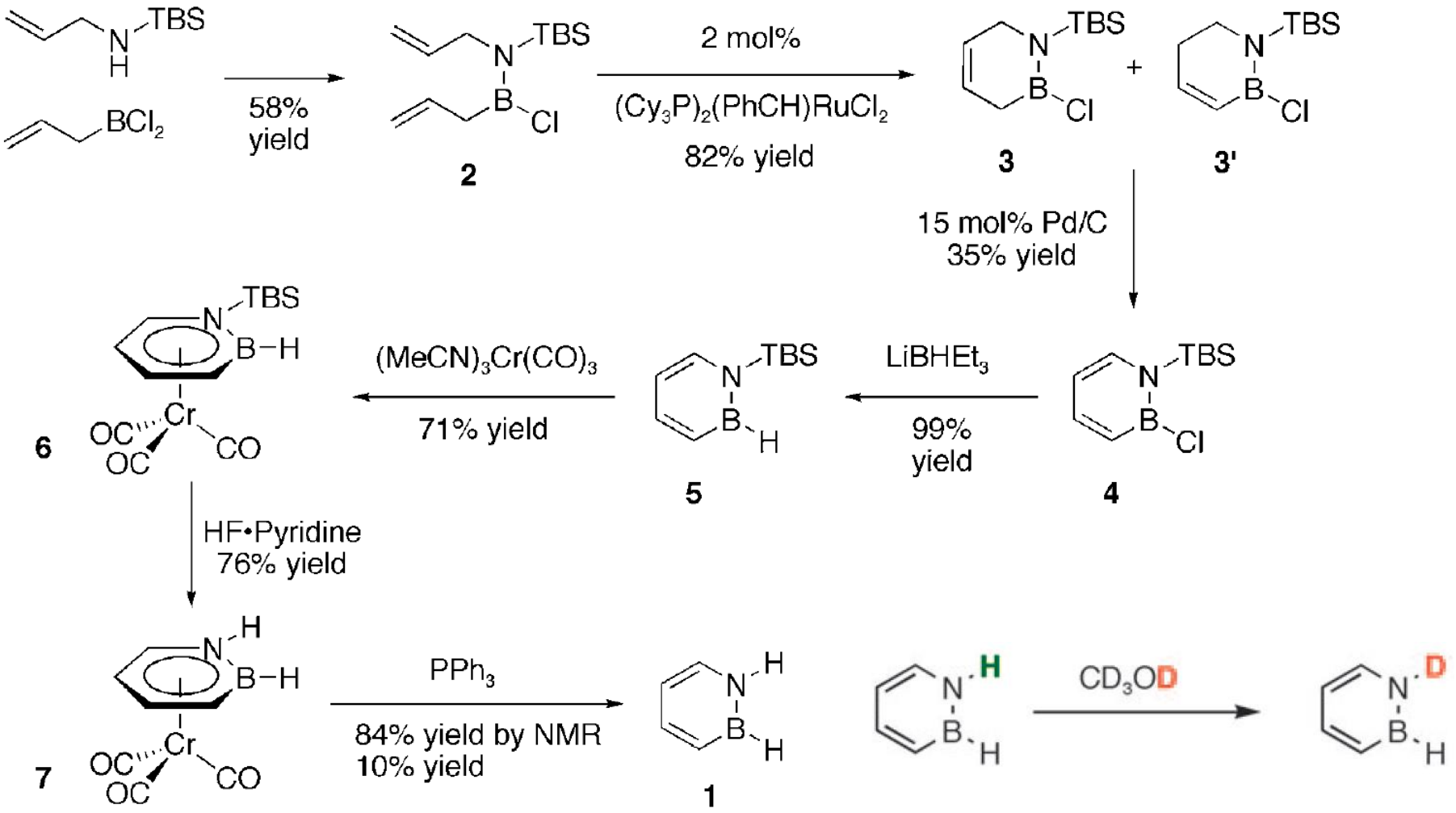
[a] Key: (a) $PhBCl_2$, pentane; (b) $(C_3H_5)MeNH$, Et_3N; (c) $(Cy_3P)_2(PhCH)RuCl_2$, CH_2Cl_2; (d) LDA; (e) $[Cp^*RuCl_4]$.

Ashe, A. J. *et. al. Org. Lett.* **2000**, *2*, 2089-2091.



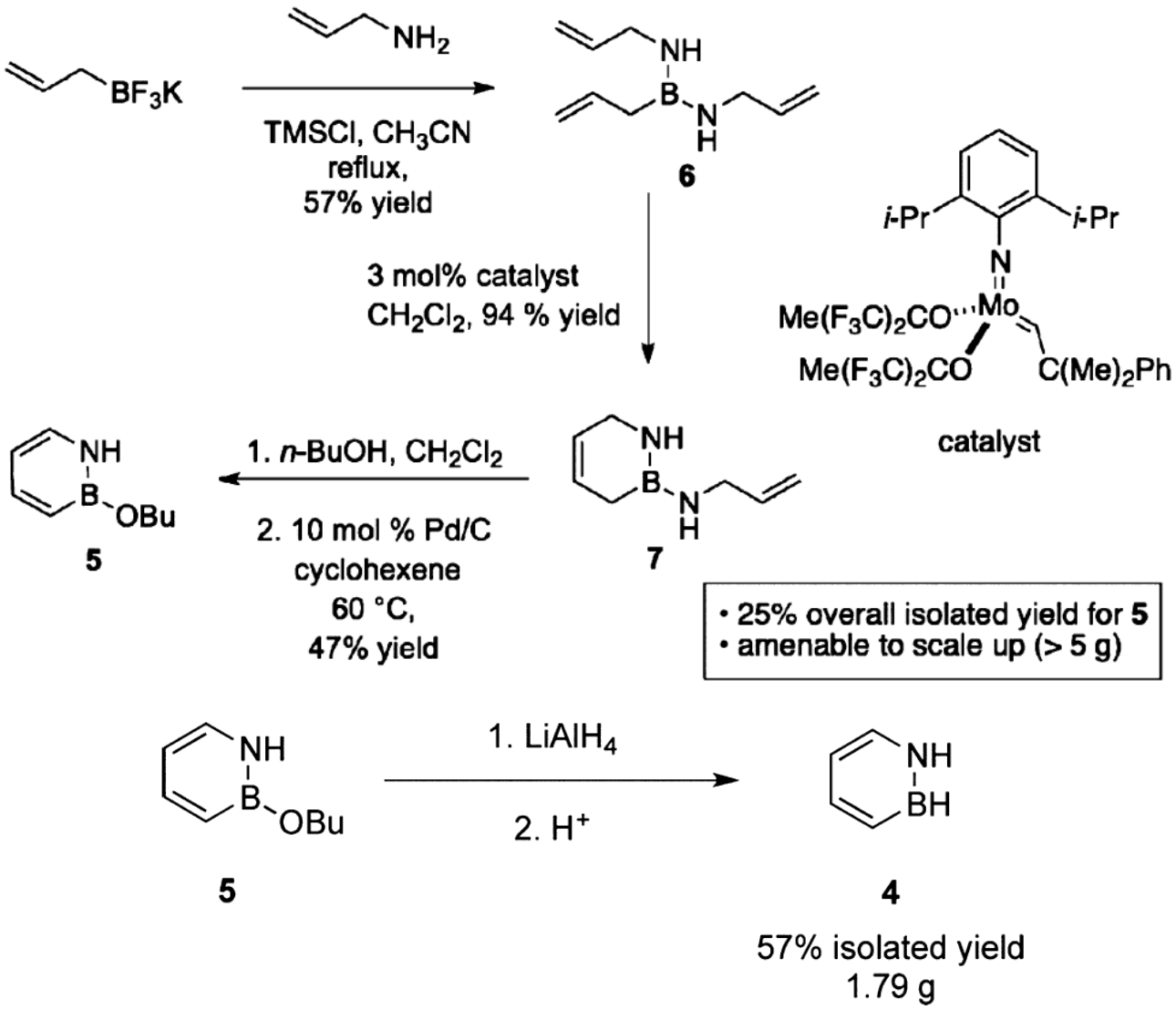
Ashe, A. J. *et. al. Organometallics* **2001**, *20*, 5413-5418.

Synthesis of 1,2-Azaborine



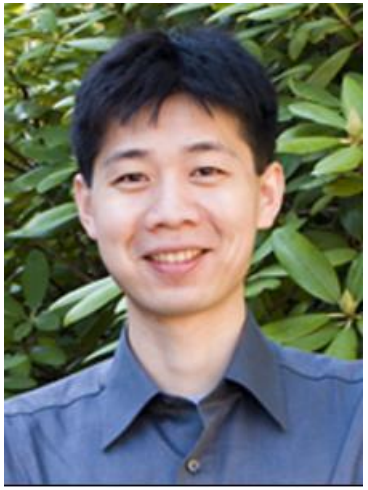
Liu, S.-Y. *et. al. Angew. Chem. Int. Ed.* **2009**, *48*, 973-977.

Synthesis of 1,2-Azaborine



Liu, S.-Y. *et. al. J. Am. Chem. Soc.* **2013**, *135*, 12908-12913.

About Shih-Yuan Liu



BS: Vienna University of Technology (Austria), 1995-1998.

PhD: MIT, with Prof. Gregory C. Fu, 1998-2003.

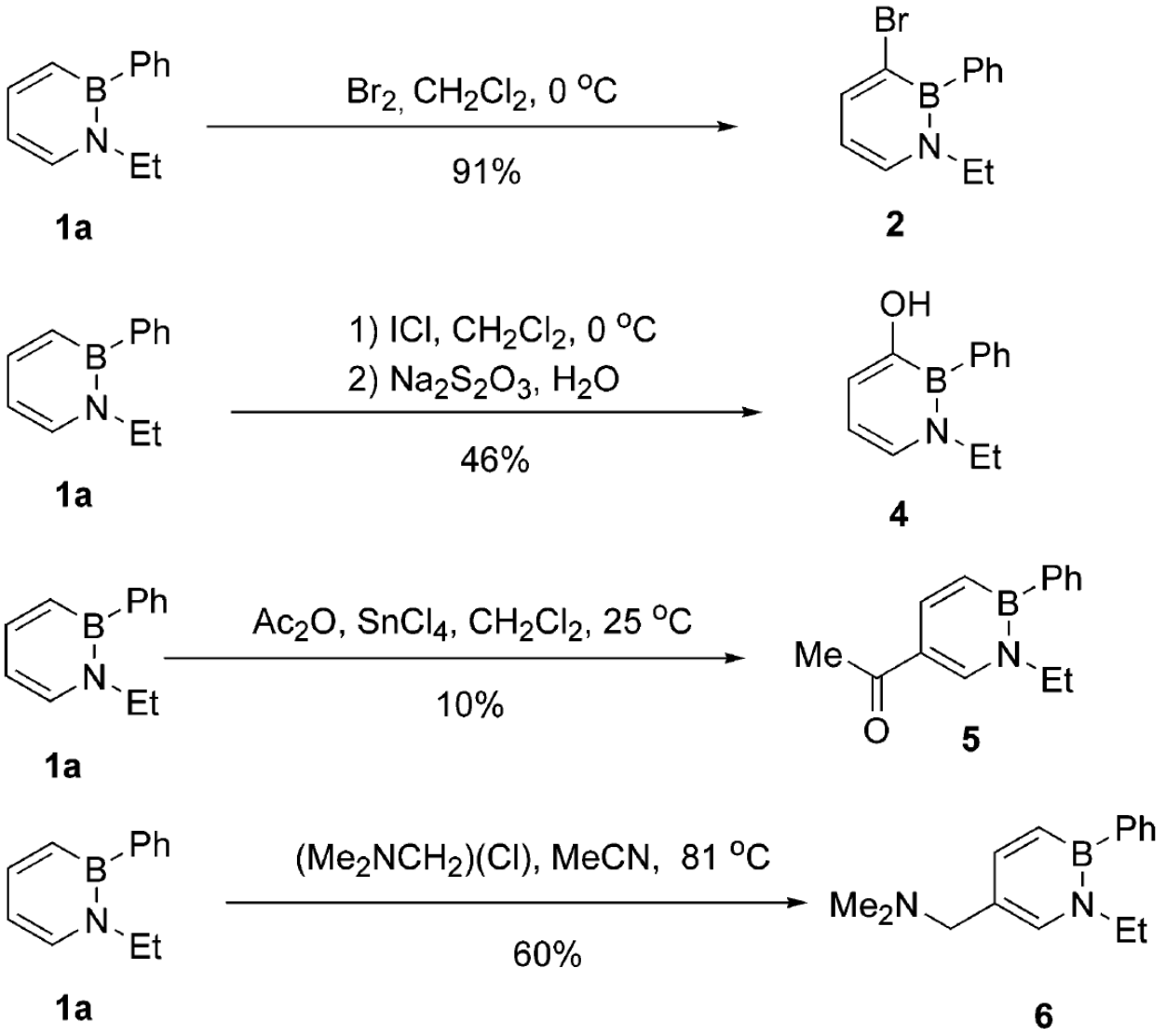
Postdoc: MIT, with Prof. Daniel G. Nocera, 2003-2006.

Assistant Professor: University of Oregon, 2006-2012.

Associate Professor: University of Oregon, 2012-2013.

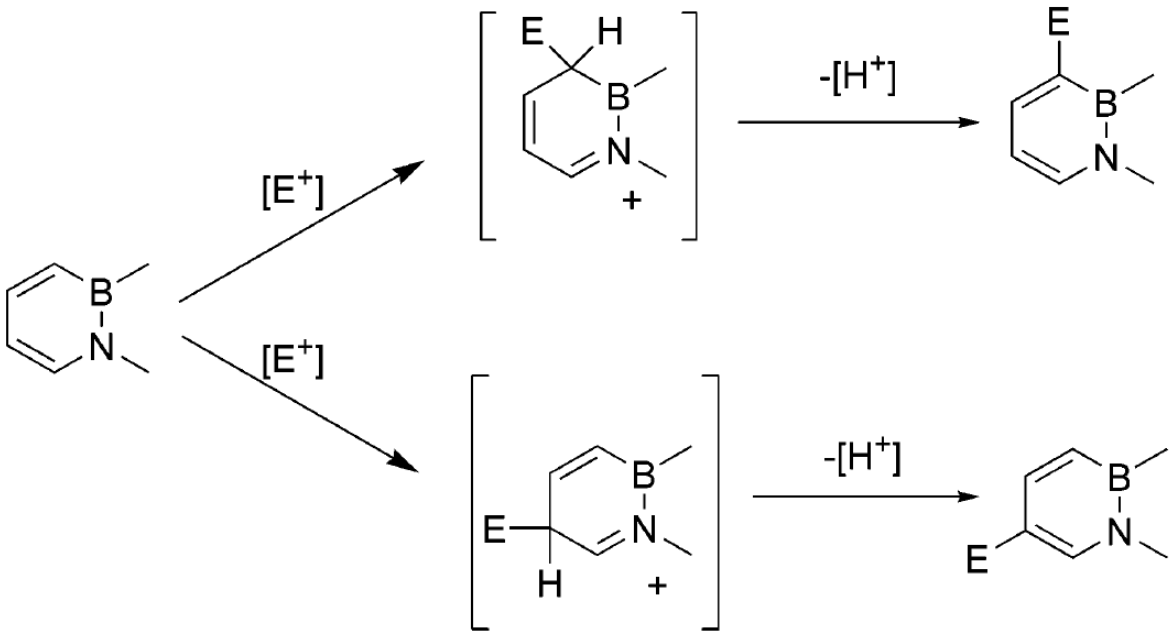
Professor: Boston College, 2013-now.

Electrophilic Substitution



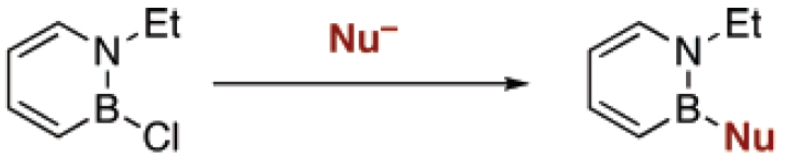
Ashe, A. J. *et. al. Org. Lett.* **2007**, *9*, 679-681.

Electrophilic Substitution



Ashe, A. J. *et. al. Org. Lett.* **2007**, *9*, 679-681.

Nucleophilic Substitution

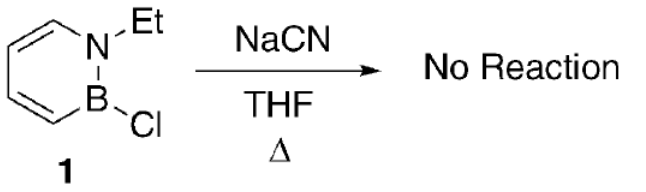


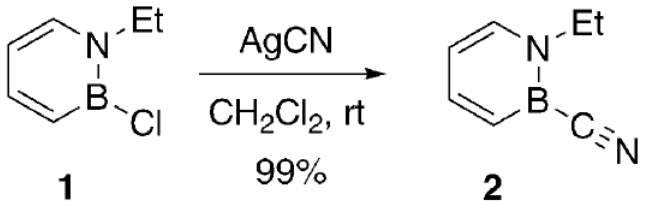
4 **5**

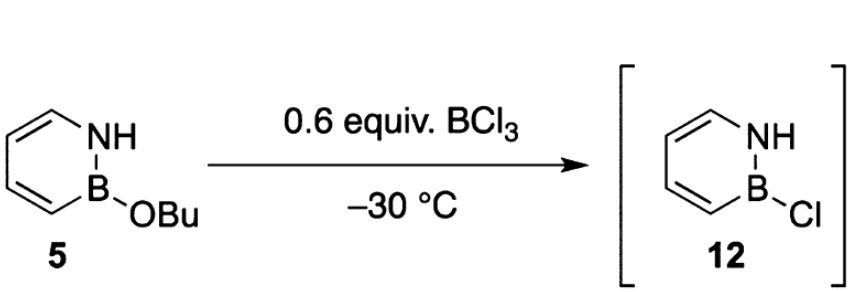
entry	nucleophile (**Nu**)	product	yield (%)[a]
1	Li–**Bu**	**5a**	79
2	Li–**vinyl**	**5b**	50
3	BrMg–**Ph**	**5c**	76
4	BrMg—≡—**Ph**	**5d**	83
5	Li–**NMe_2**	**5e**	66
6	K–**SBn**	**5f**	80
7	K–**O*t*Bu**	**5g**	71
8	$LiBEt_3$–**H**	**5h**	92

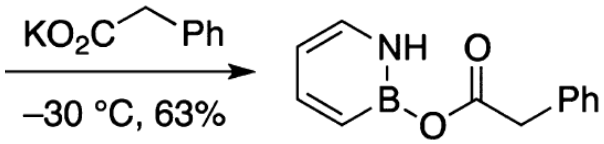
Liu, S.-Y. *et. al. Org. Lett.* **2007**, *9*, 4905-4908.

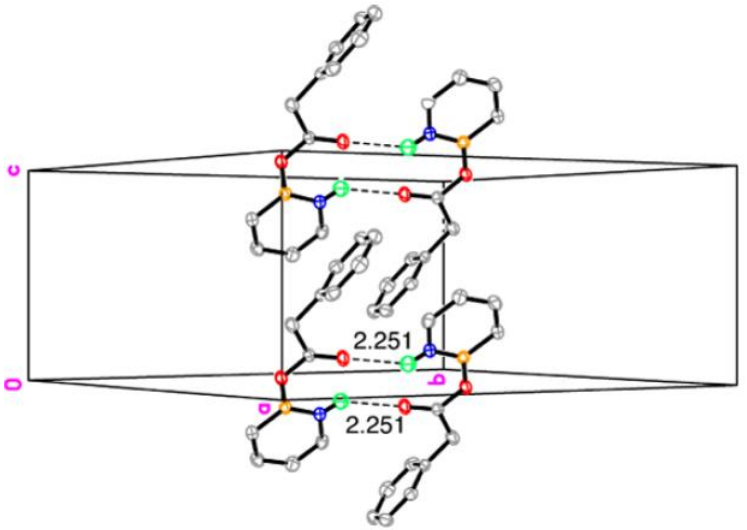
Nucleophilic Substitution





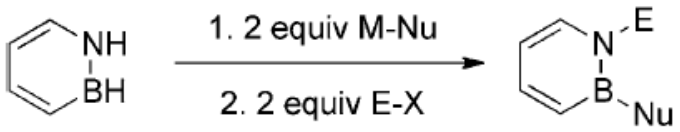






Liu, S.-Y. *et. al. Chem. Commun.* **2010**, 779-781.
Liu, S.-Y. *et. al. J. Am. Chem. Soc.* **2013**, *135*, 12908-12913.

Nucleophilic Substitution

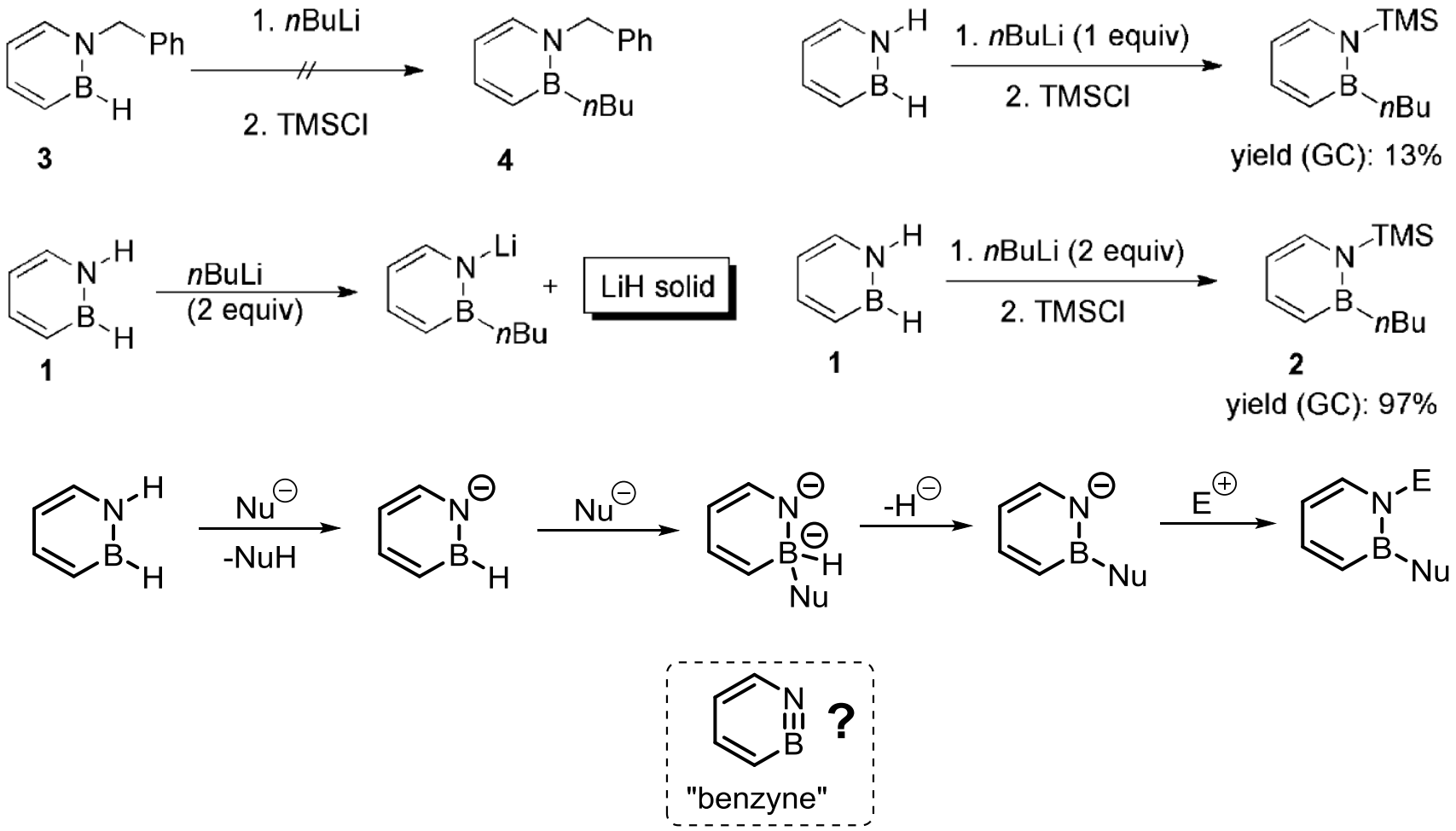


Entry	M–Nu	E–X	Yield [%][b]
1	Na–O*t*Bu	H–Cl	63
2	K–Oallyl	H–Cl	79
3	Li–*t*Bu	H–Cl	81
4	Li–*n*Bu	H–Cl	80
5	Li–Ph	H–Cl	98
6	BrMg–vinyl	H–Cl	59
7	BrMg–≡–Ph	H–Cl	71
8	Li–*n*Bu	TMS–Cl	89
9	Li–*n*Bu	Me–I	67
10	Li–*n*Bu	H–Cl	60

Liu, S.-Y. *et. al. Angew. Chem. Int. Ed.* **2011**, *50*, 8157-8160.

Nucleophilic Substitution

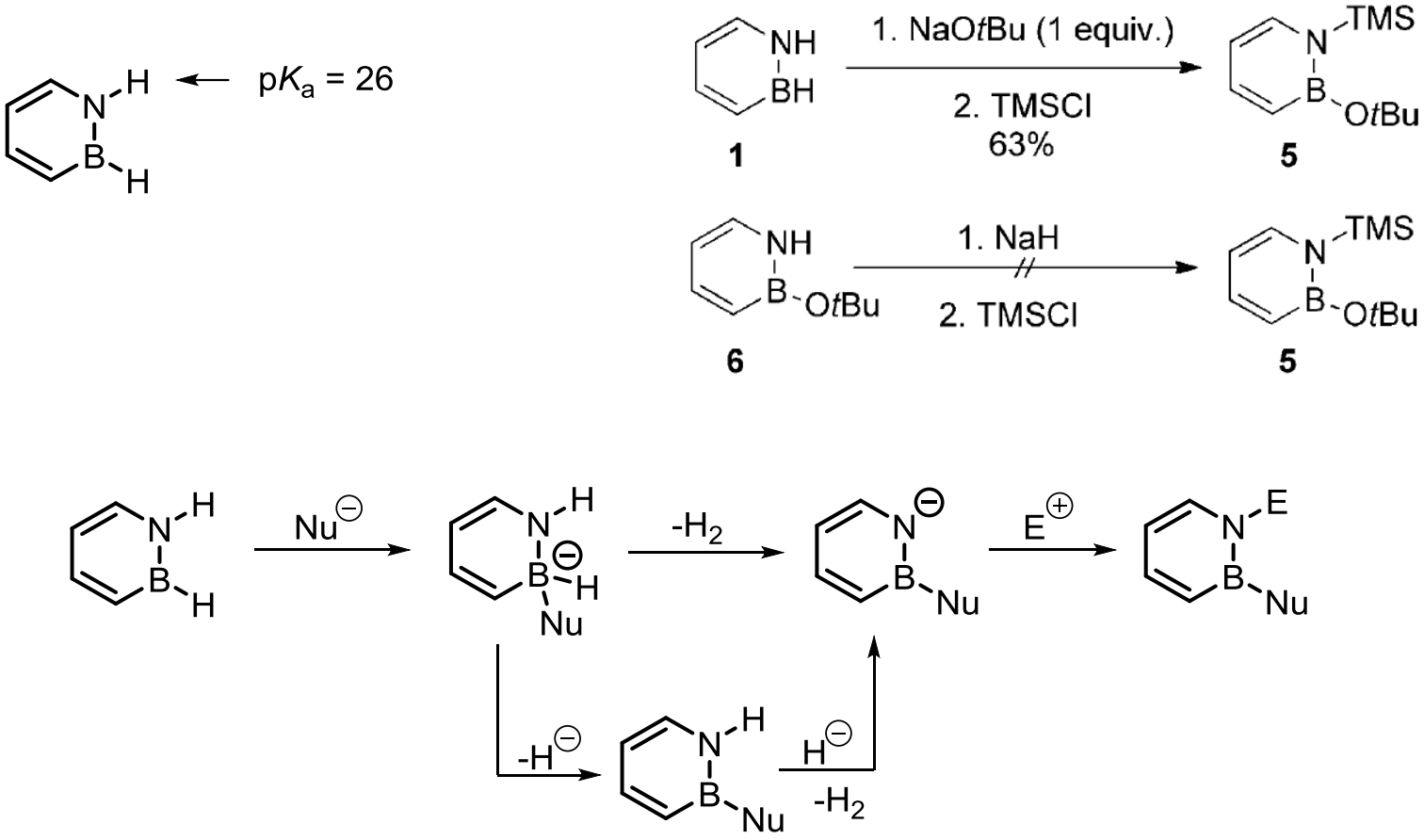
Mechanistic studies using *n*BuLi as nucleophile



Liu, S.-Y. *et. al. Angew. Chem. Int. Ed.* **2011**, *50*, 8157-8160.

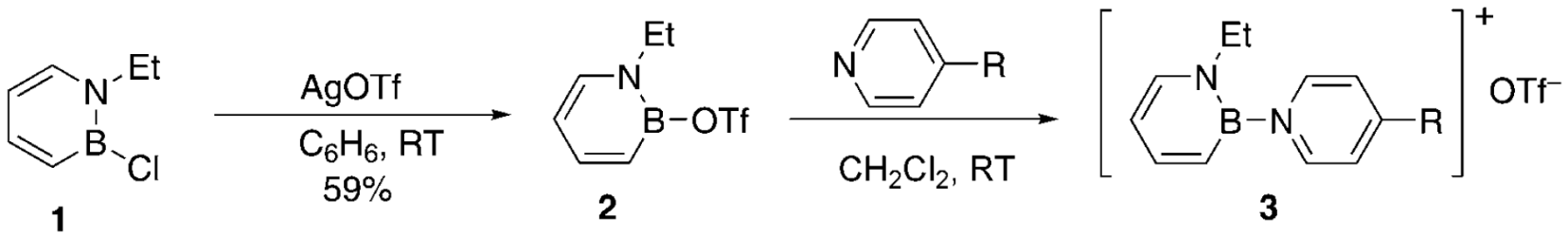
Nucleophilic Substitution

Mechanistic studies using NaO*t*Bu as nucleophile

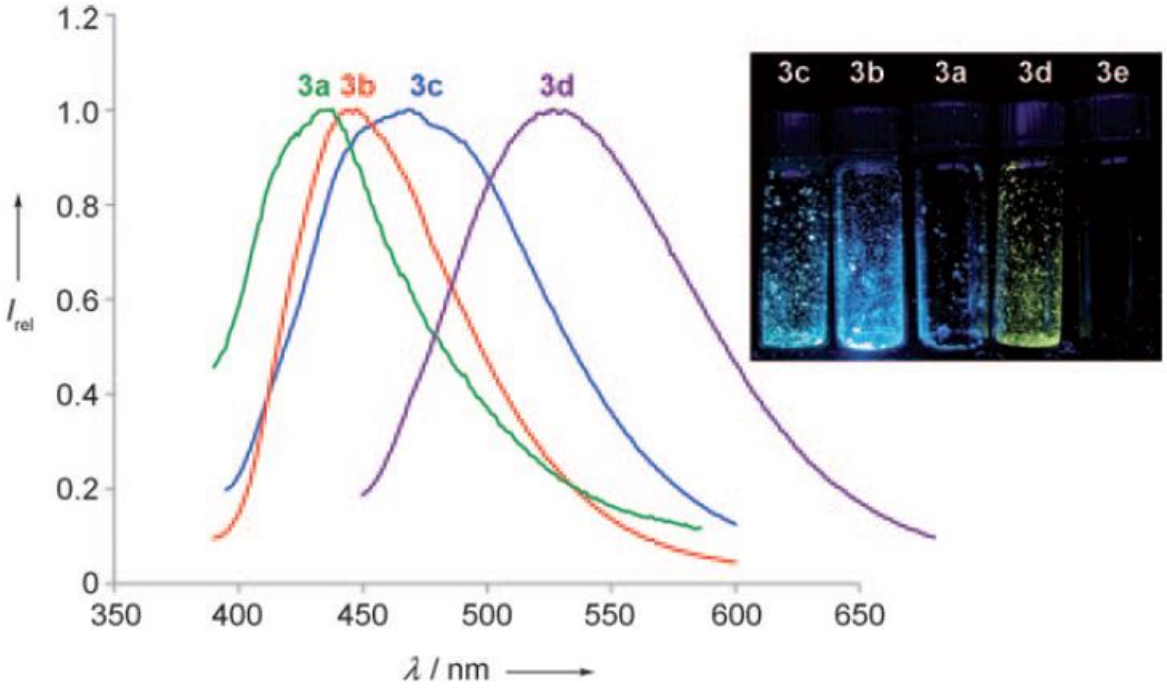


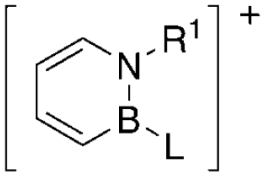
Liu, S.-Y. *et. al. Angew. Chem. Int. Ed.* **2011**, *50*, 8157-8160.

1,2-Azaborine Cation



3a (R = Me, 95%)
3b (R = Ph, 97%)
3c (R = H, 95%)
3d (R = CF_3, 90%)
3e (R = NMe_2, 98%)

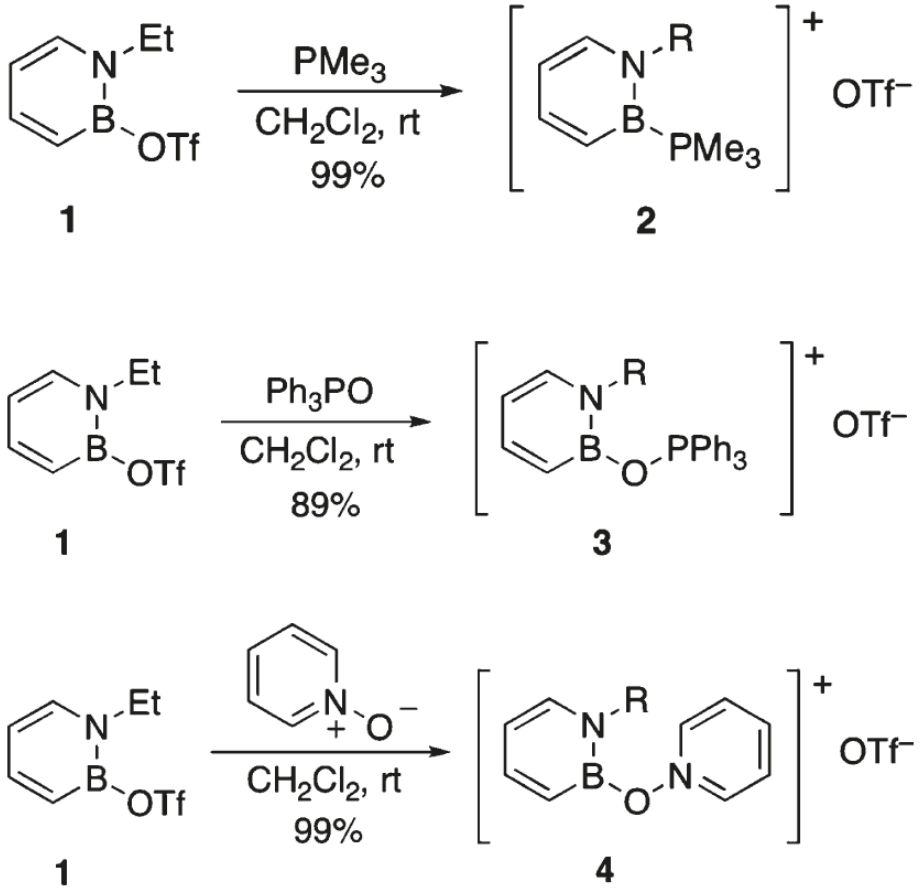




1,2-azaborine cation
L = neutral nucleophile

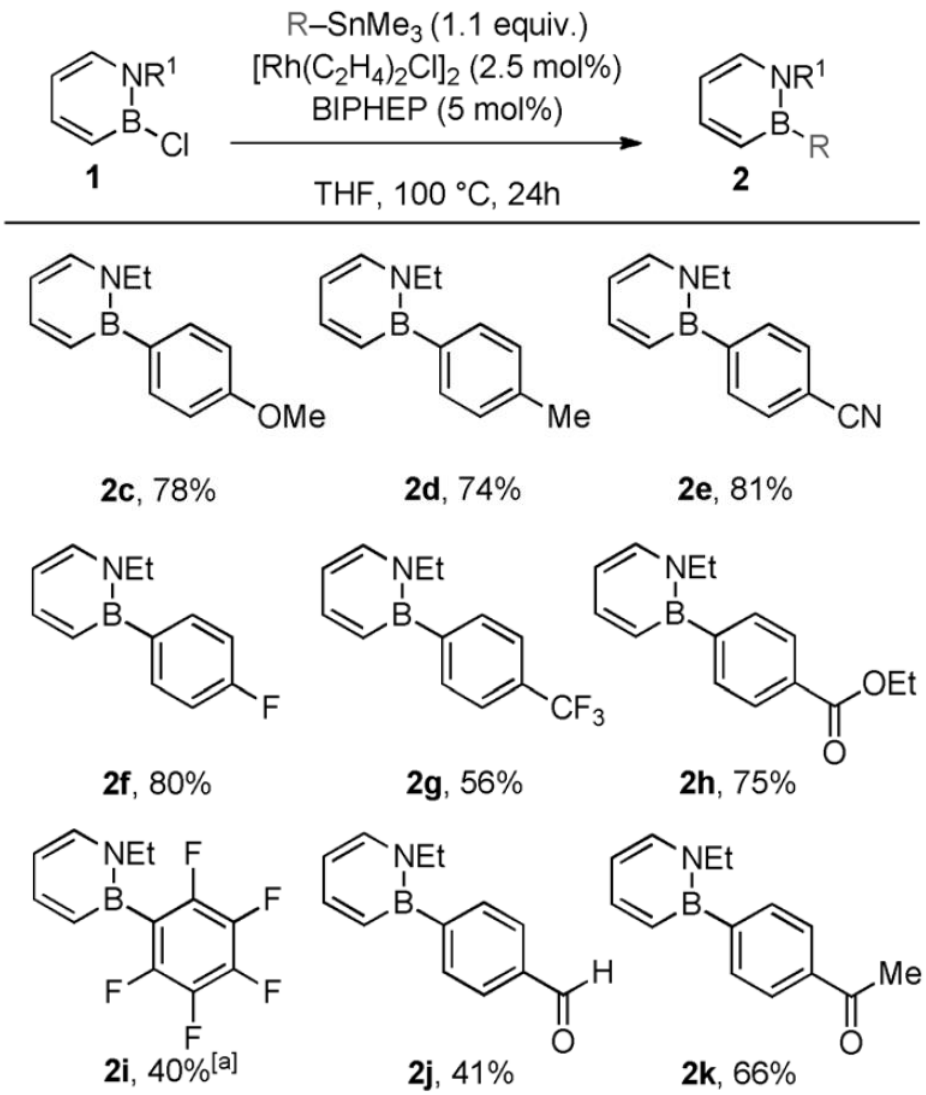
Liu, S.-Y. *et. al. Angew. Chem. Int. Ed.* **2010**, *49*, 7444-7447.

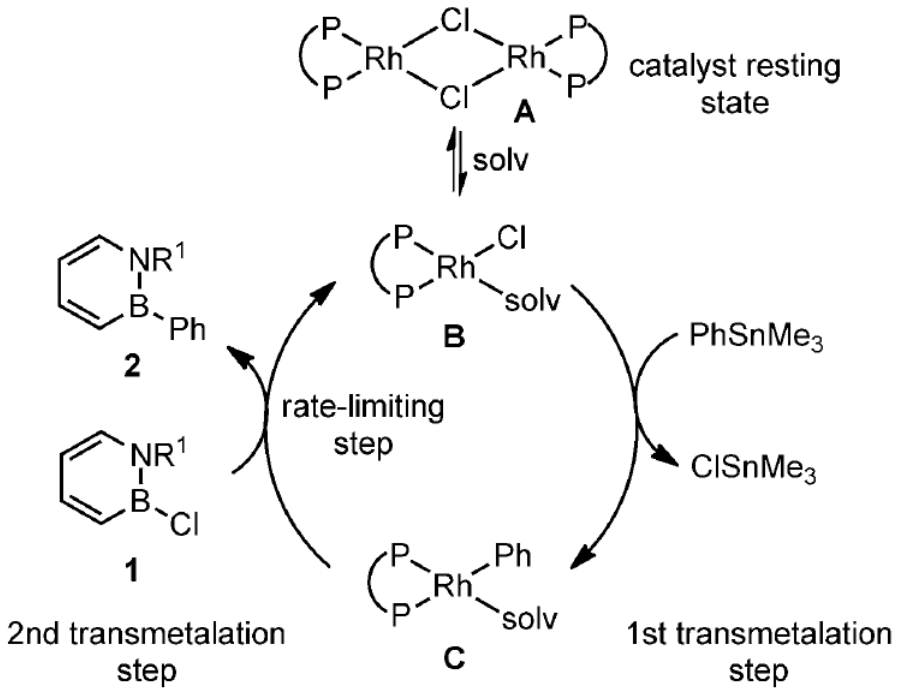
1,2-Azaborine Cation



Liu, S.-Y. *et. al. Organometallics* **2011**, *30*, 52-54.

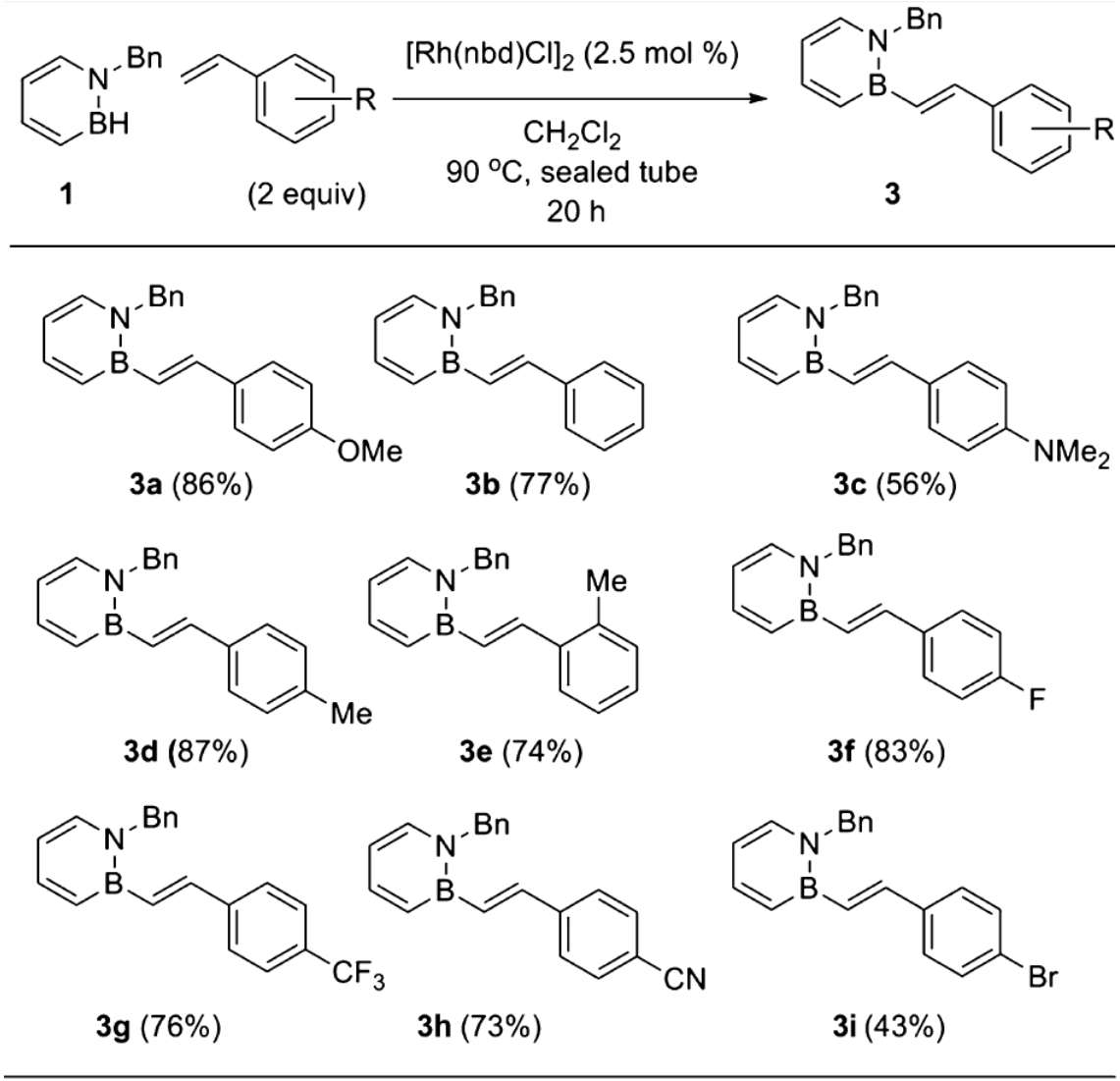
Functionalization of 1,2-Azaborine





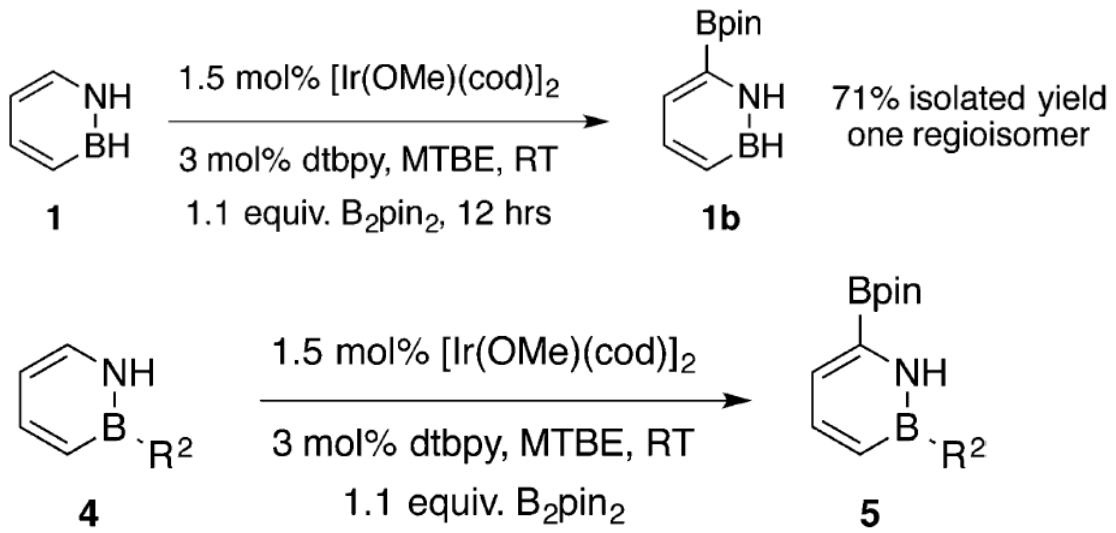
Liu, S.-Y. *et. al. Angew. Chem. Int. Ed.* **2013**, *52*, 9316-9319.

Functionalization of 1,2-Azaborine



Liu, S.-Y. *et. al. Org. Lett.* **2014**, *16*, 3340-3343.

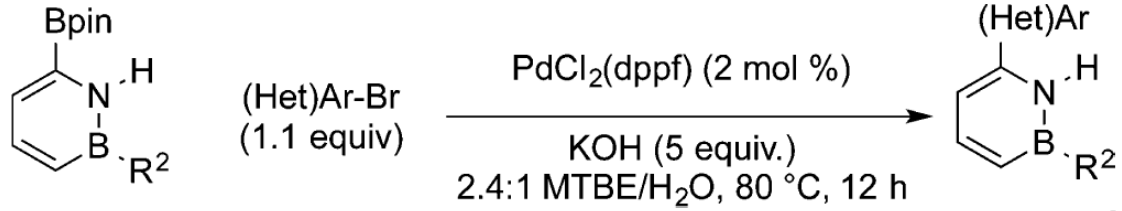
Functionalization of 1,2-Azaborine

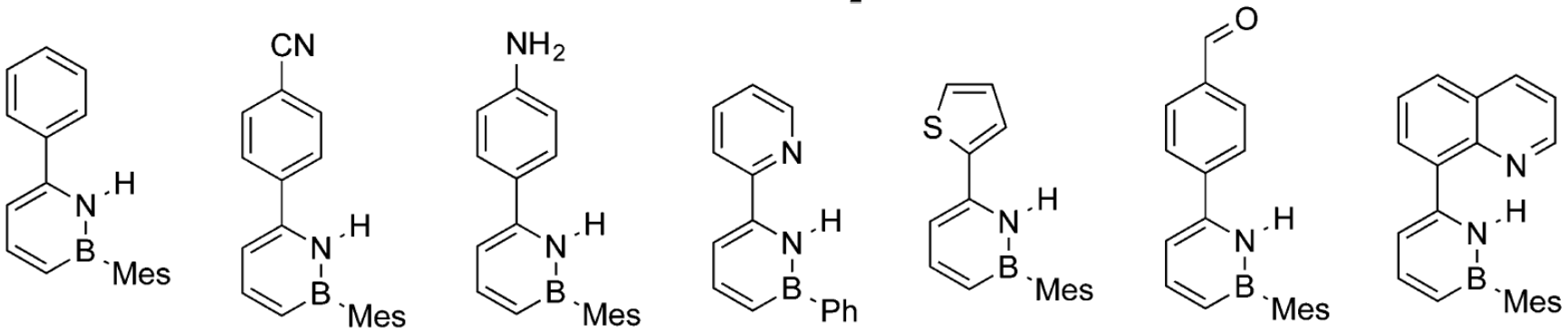


entry	substrate	product	yield[a] (%)
1	**4a** (R^2 = Me)	**5a**	67[b]
2	**4b** (R^2 = *n*-Bu)	**5b**	86
3	**4c** (R^2 = Mes)	**5c**	92
4	**4d** (R^2 = O-*n*-Bu)	**5d**	66

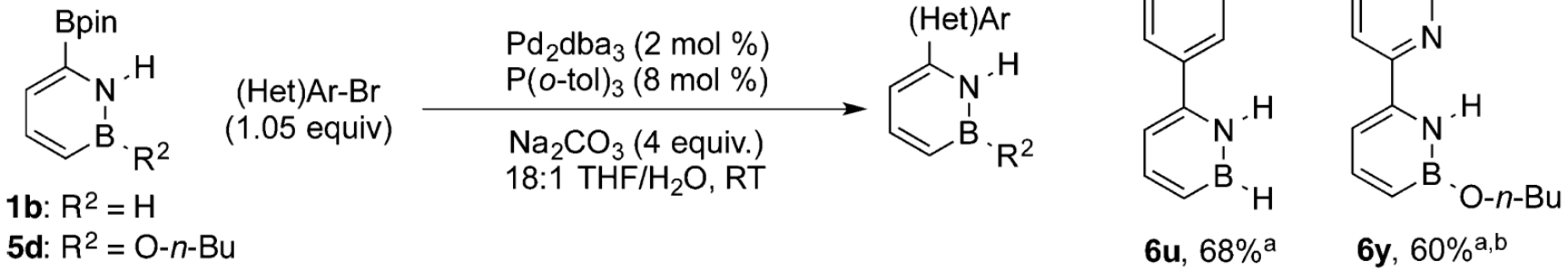
Liu, S.-Y. *et. al. J. Am. Chem. Soc.* **2015**, *137*, 5536-5541.

Functionalization of 1,2-Azaborine





6a, 90% **6f**, 80% **6k**, 86% **6p**, 80% **6m**, 80% **6d**, 75% **6t**, 86%

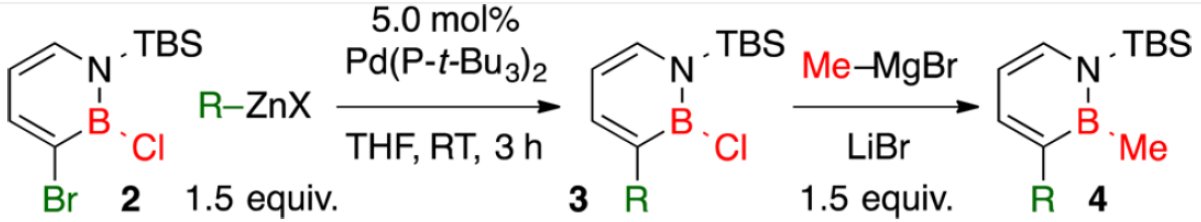


1b: R^2 = H
5d: R^2 = O-*n*-Bu

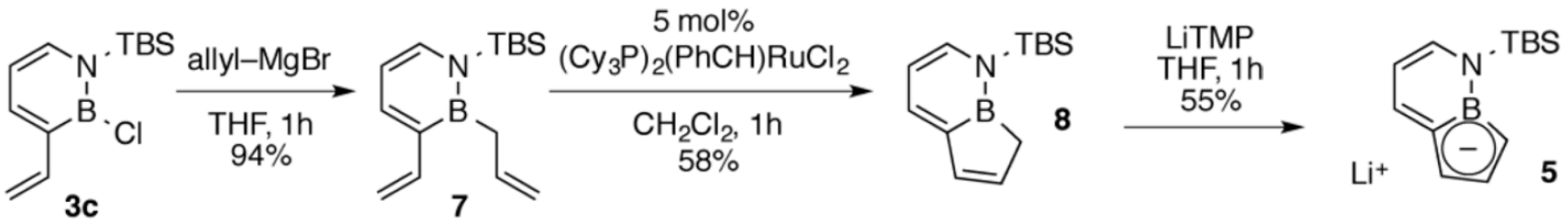
6u, 68%[a] **6y**, 60%[a,b]

Liu, S.-Y. *et. al. J. Am. Chem. Soc.* **2015**, *137*, 5536-5541.

Functionalization of 1,2-Azaborine

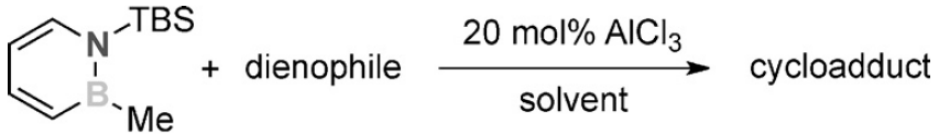


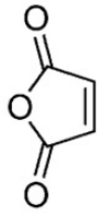
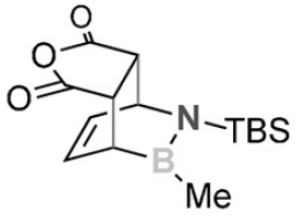
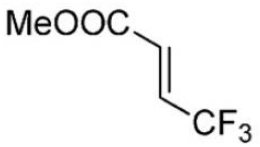
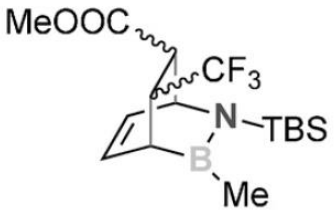
entry	R–ZnX	3, yield (%)[a]	4, yield (%)[b]
1	*n*-Pr–ZnBr	**3a**, 87	**4a**, 76
2	1-phenylvinyl–ZnBr	**3b**, 97	**4b**, 97
3	vinyl–ZnBr	**3c**, 69[c]	**4c**, 51[d]
4	2-(1,3-dioxan-2-yl)ethyl–ZnBr	**3d**, 69	**4d**, 66
5	4-chlorophenyl–ZnI	**3e**, 83	**4e**, 50
6	3,4,5-trifluorophenyl–ZnBr	**3f**, 91	**4f**, 89[e]

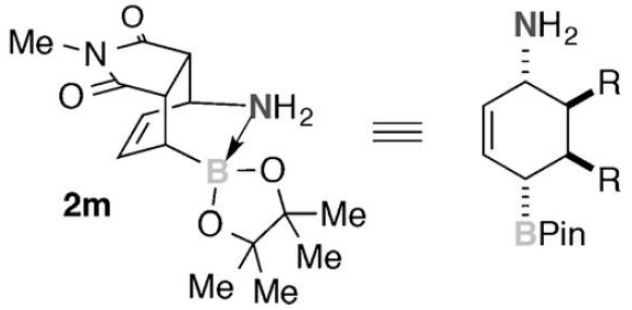


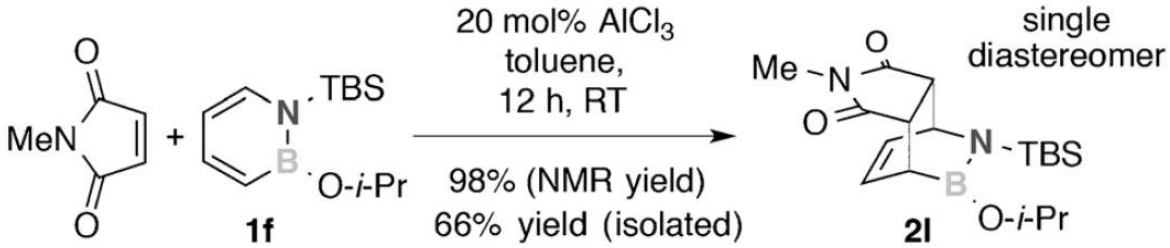
Liu, S.-Y. *et. al. J. Am. Chem. Soc.* **2015**, *137*, 8932-8935.

Diels-Alder Reaction



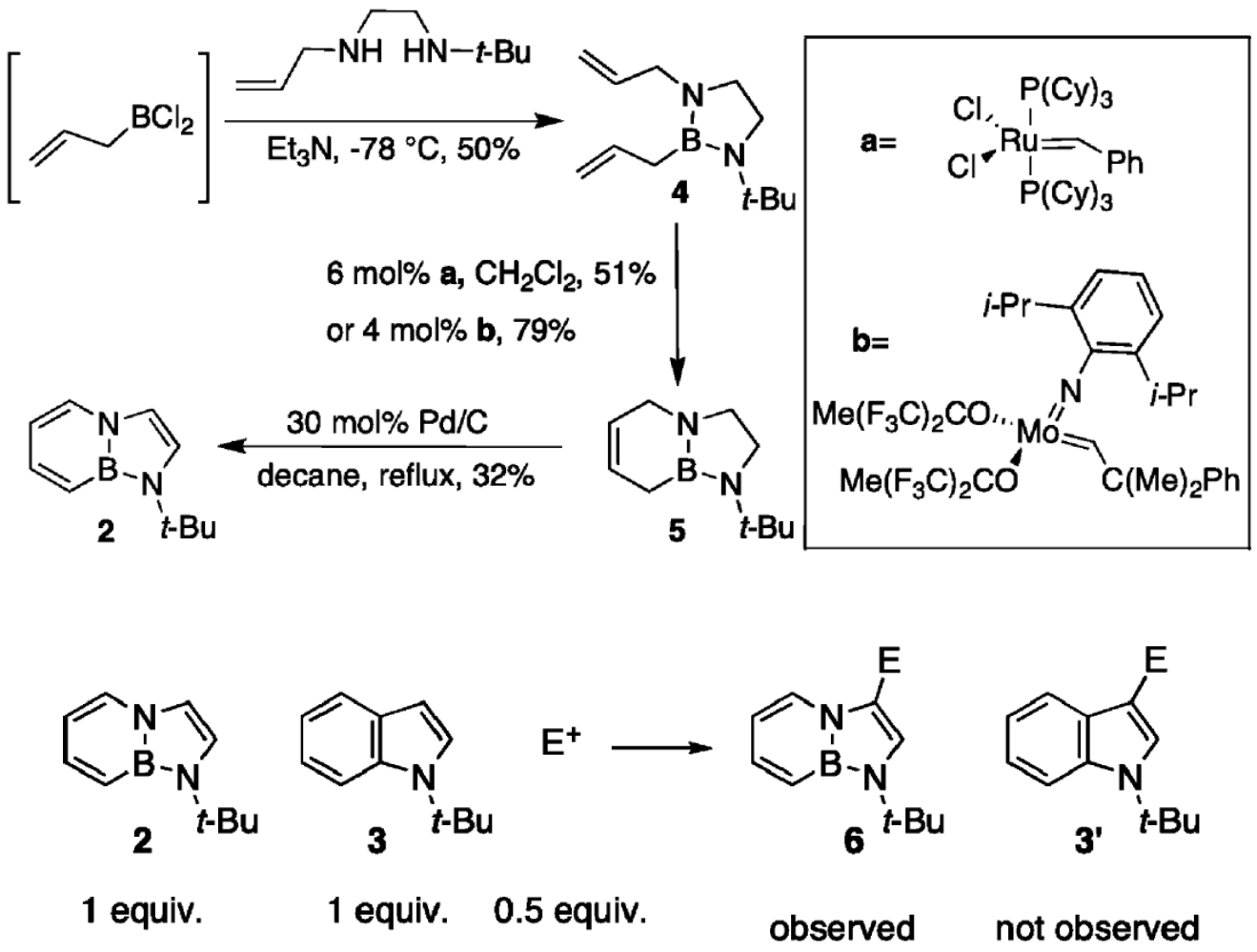
dienophile	cycloadduct		yield (%)
		**2a**	96[a] (7) >95:5 d.r.
		**2k**	90[b] (37) 1.1:1 d.r. single regioisomer





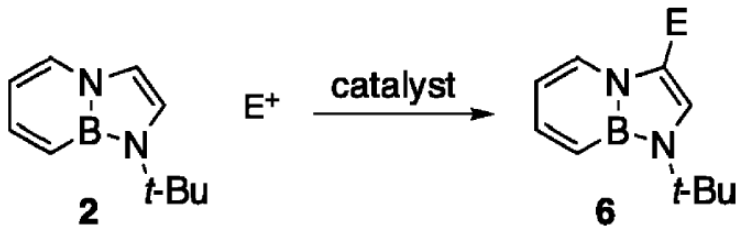
Liu, S.-Y. *et. al. Angew. Chem. Int. Ed.* **2015**, *54*, 7823-7827.

BN-Indole



Liu, S.-Y. *et. al. J. Am. Chem. Soc.* **2010**, *132*, 16430-16432.

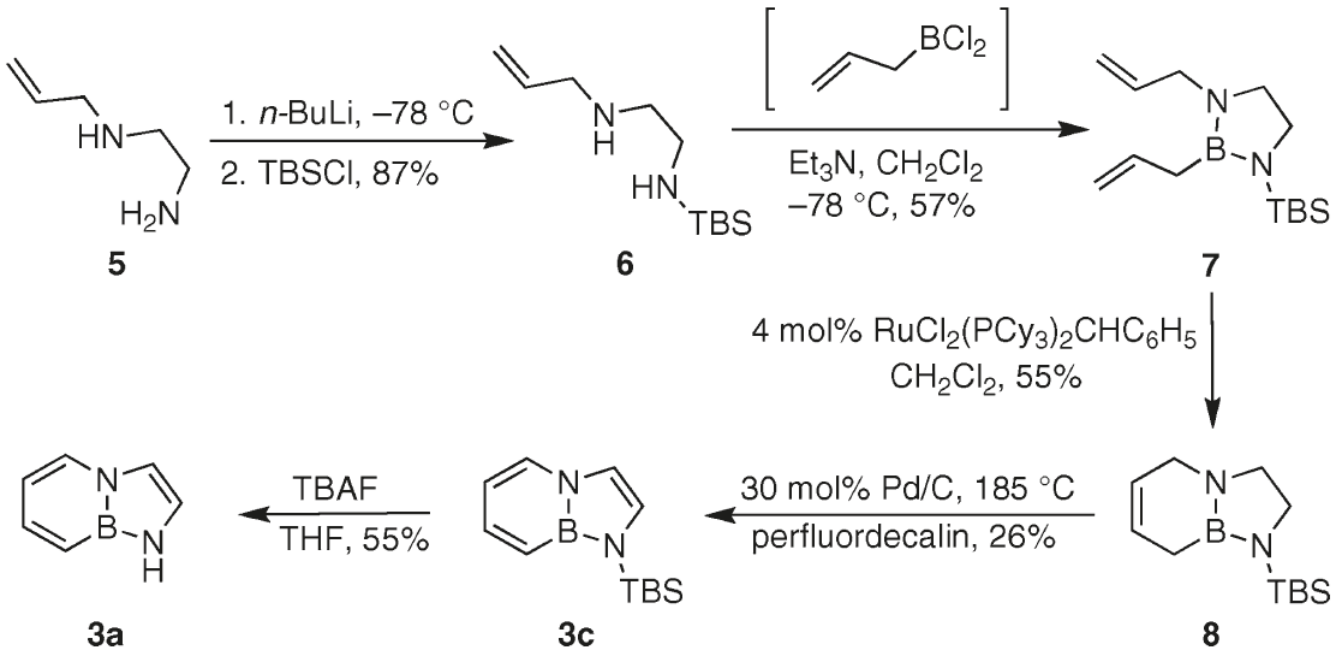
BN-Indole

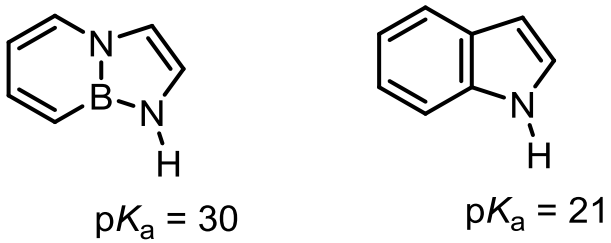


entry	electrophile (E^+)	catalyst	3-substituent (E)	product	yield (%)
1	Br_2	-	Br	**6a**	39
2	$NMe_2^{\oplus}\ Cl^{\ominus}$, H, H	-	NMe_2	**6b**	53
3	O	$ZrCl_4$	O	**6c**	57
4	CD_3OD/ D_2O	-	D	**6d**	39[a]
5	O, Cl, Me	Et_2AlCl	O, Me	**6e**	23

Liu, S.-Y. *et. al. J. Am. Chem. Soc.* **2010**, *132*, 16430-16432.

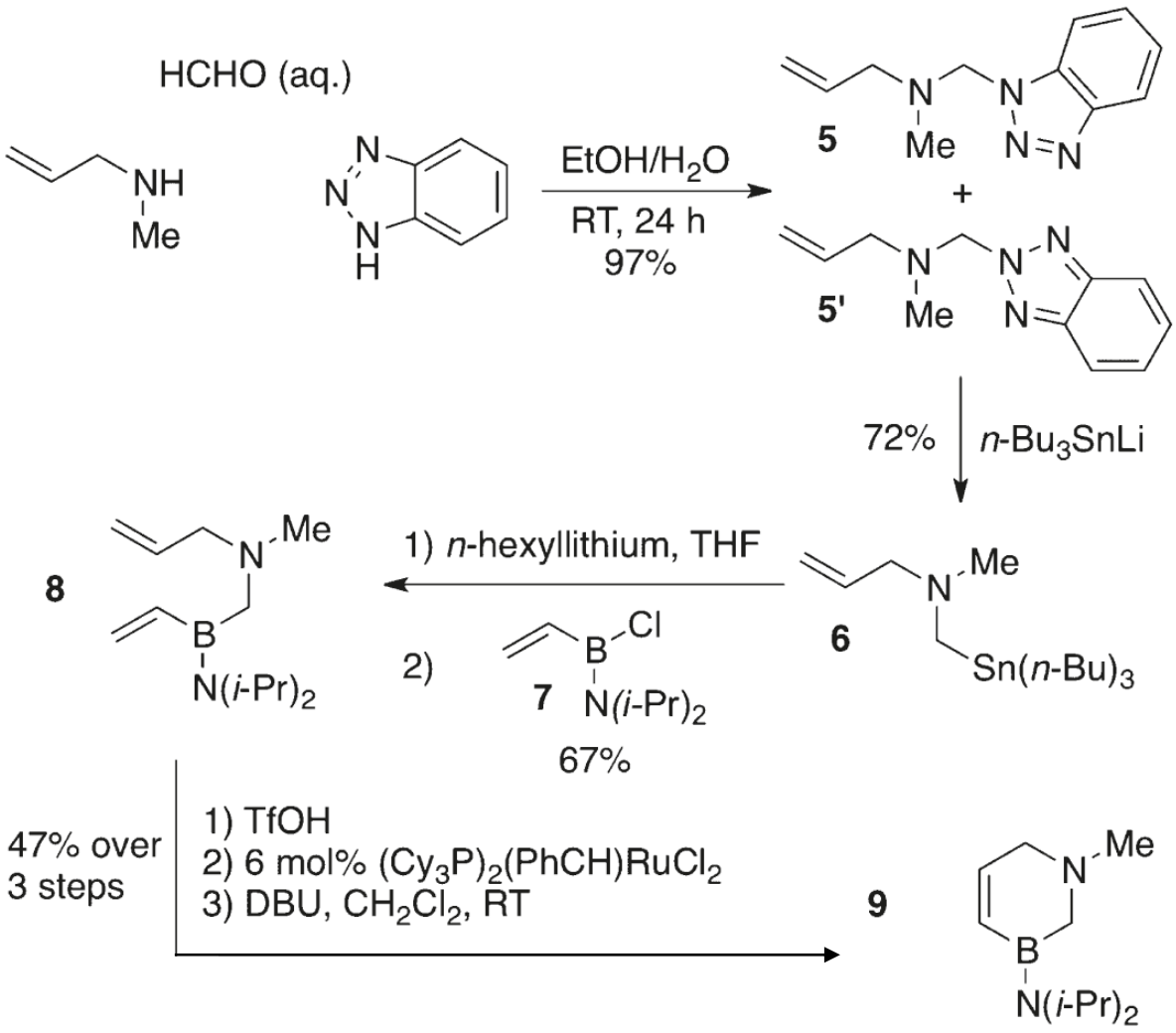
BN-Indole





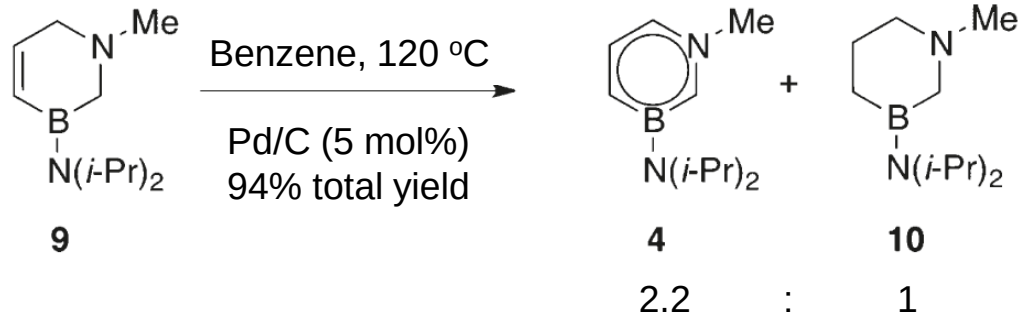
Liu, S.-Y. *et. al. J. Am. Chem. Soc.* **2011**, *133*, 11508-11511.

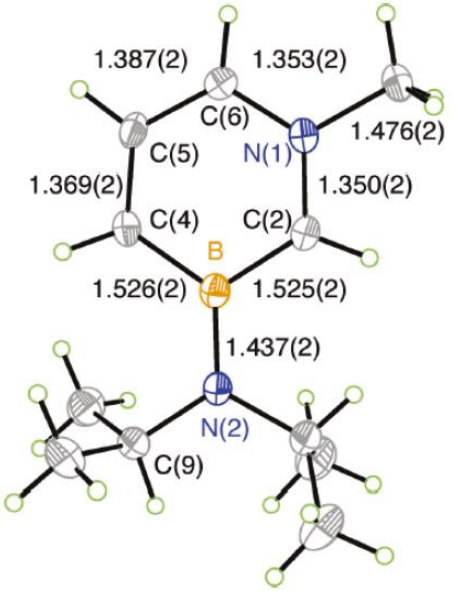
1,3-Azaborine

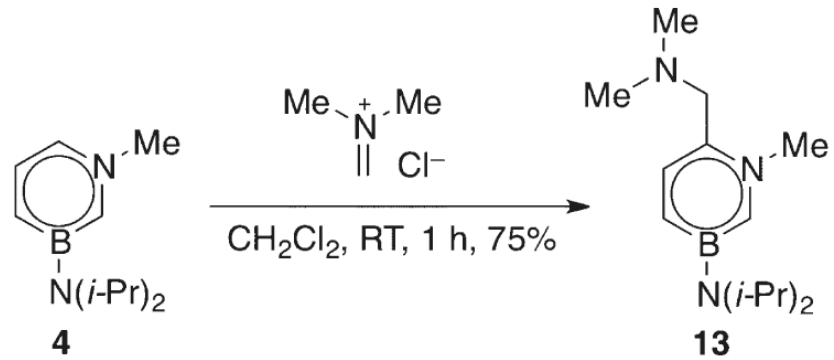


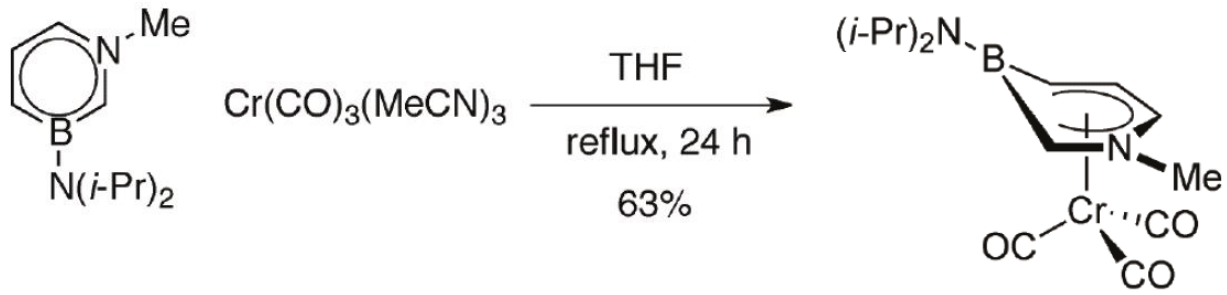
Liu, S.-Y. *et. al. J. Am. Chem. Soc.* **2011**, *133*, 20152-20155.

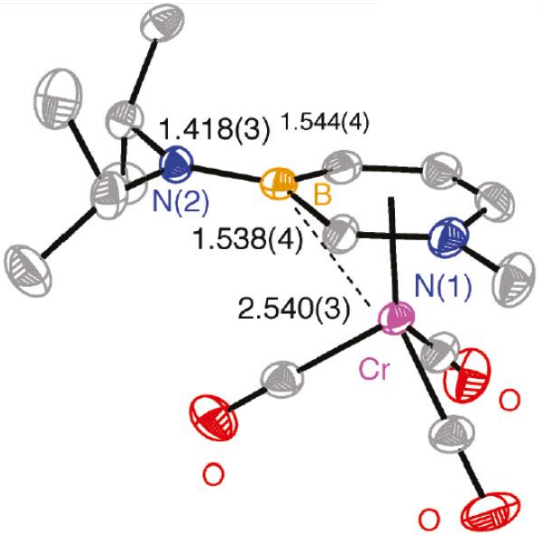
1,3-Azaborine





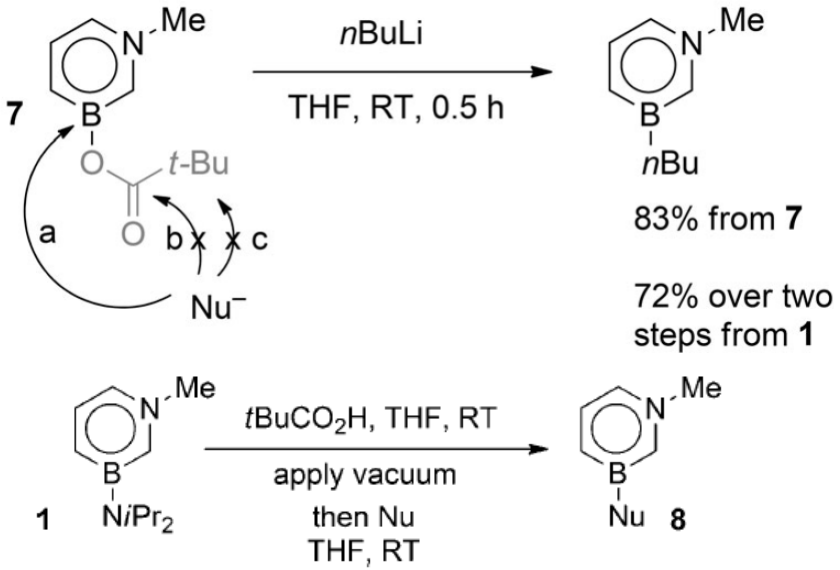






Liu, S.-Y. *et. al. J. Am. Chem. Soc.* **2011**, *133*, 20152-20155.

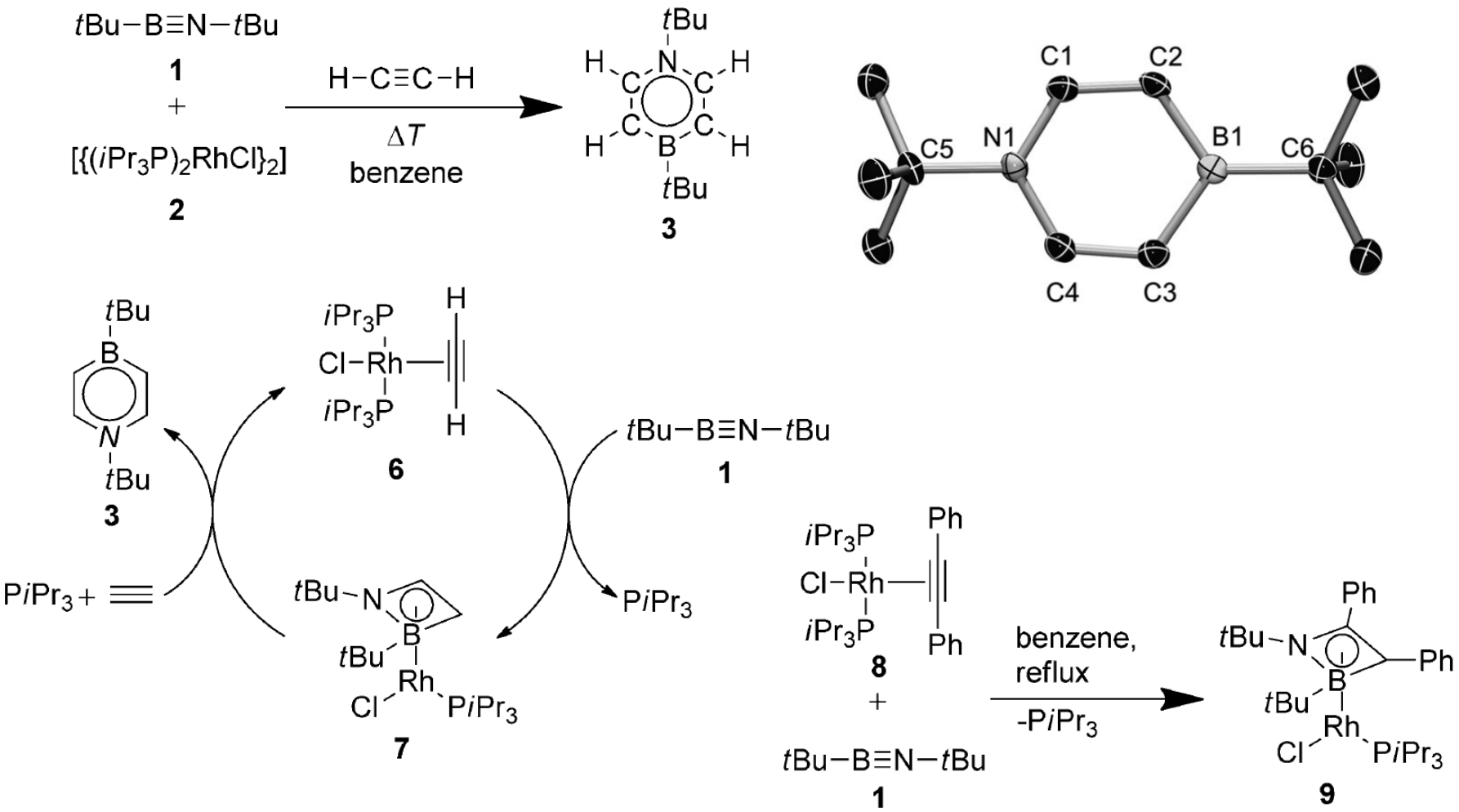
1,3-Azaborine



Entry	Nucleophile (Nu)	Product	Yield [%][a]
1	*n*BuLi	**8a**	80
2	CH_2=CHMgBr	**8b**	76
3	PhMgBr	**8c**	94
4	Ph—≡—MgBr	**8d**	89
5	mesityllithium	**8e**	87
6	PhOLi	**8f**	99
7	*t*BuOK	**8g**	99
8	$KN(SiMe_3)_2$	**8h**	69
9	CsF	**4**	81
10	Et_3N/MeOH[b]	**3**	96

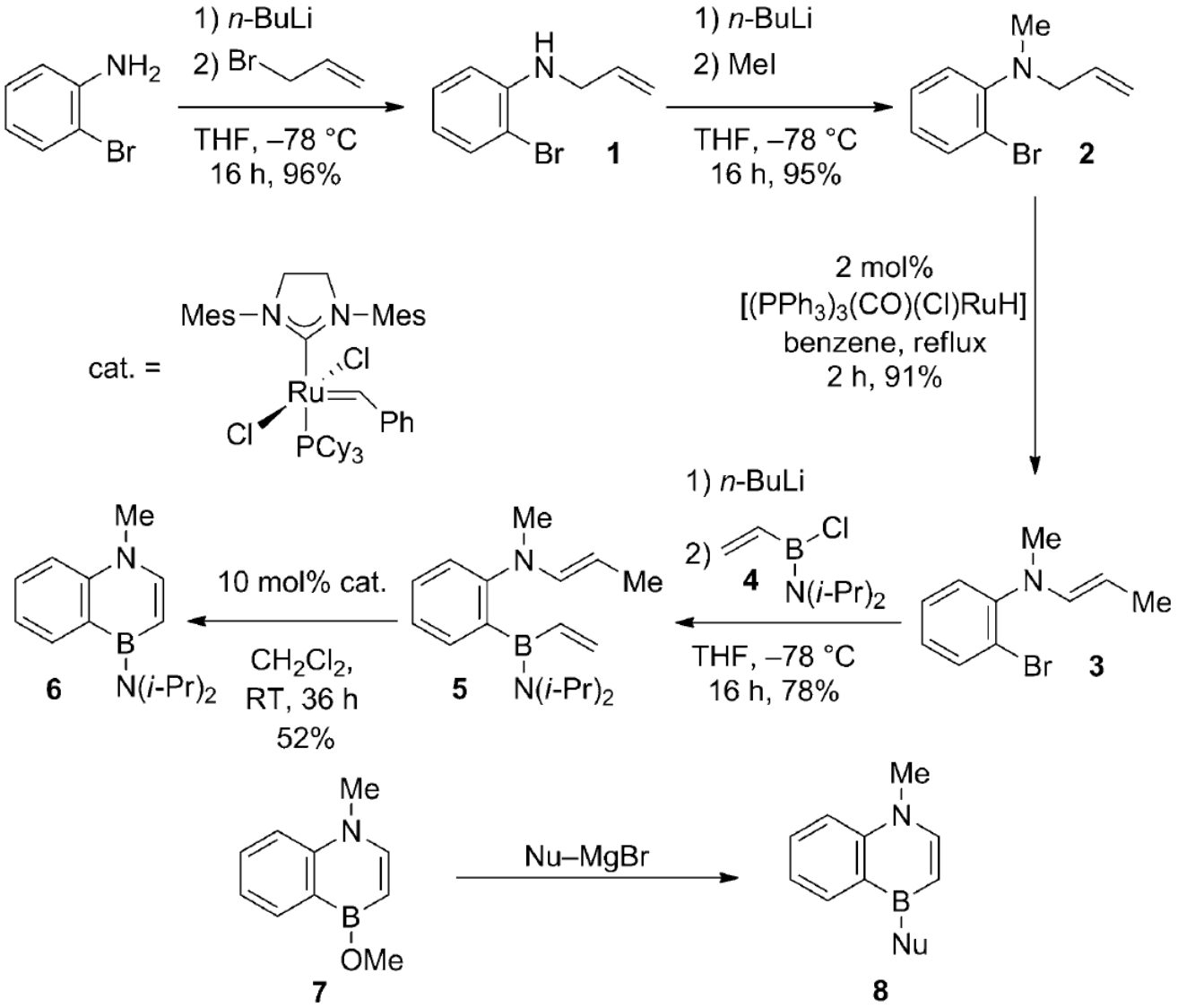
Liu, S.-Y. *et. al. Angew. Chem. Int. Ed.* **2013**, *52*, 7527-7531.

1,4-Azaborine



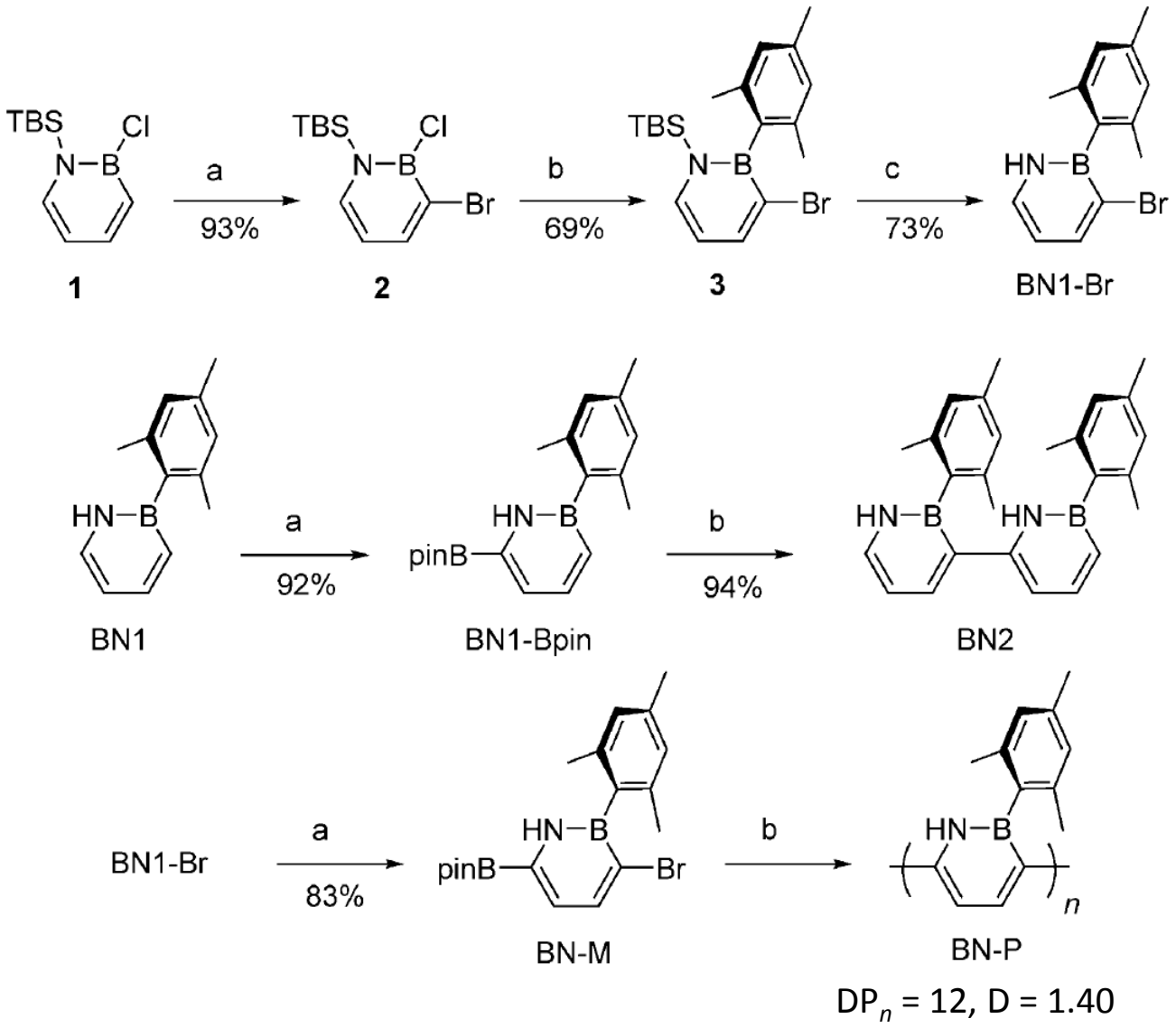
Braunschweig, H. *et. al. Angew. Chem. Int. Ed.* **2012**, *51*, 10034-10037.

1,4-Azaborine



Liu, S.-Y. *et. al. Angew. Chem. Int. Ed.* **2014**, *53*, 6795-6799.

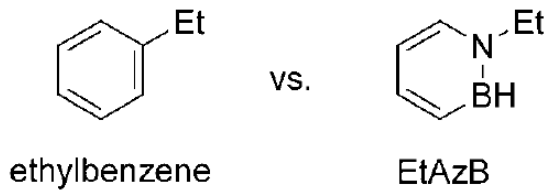
Polymerization



DP_n = 12, D = 1.40

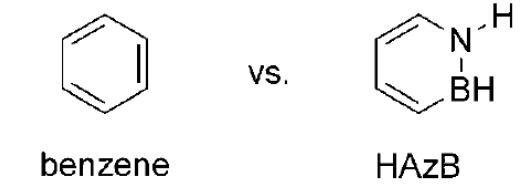
Liu, S.-Y. *et. al. Angew. Chem. Int. Ed.* **2015**, *54*, 11191-11195.

Biological Research

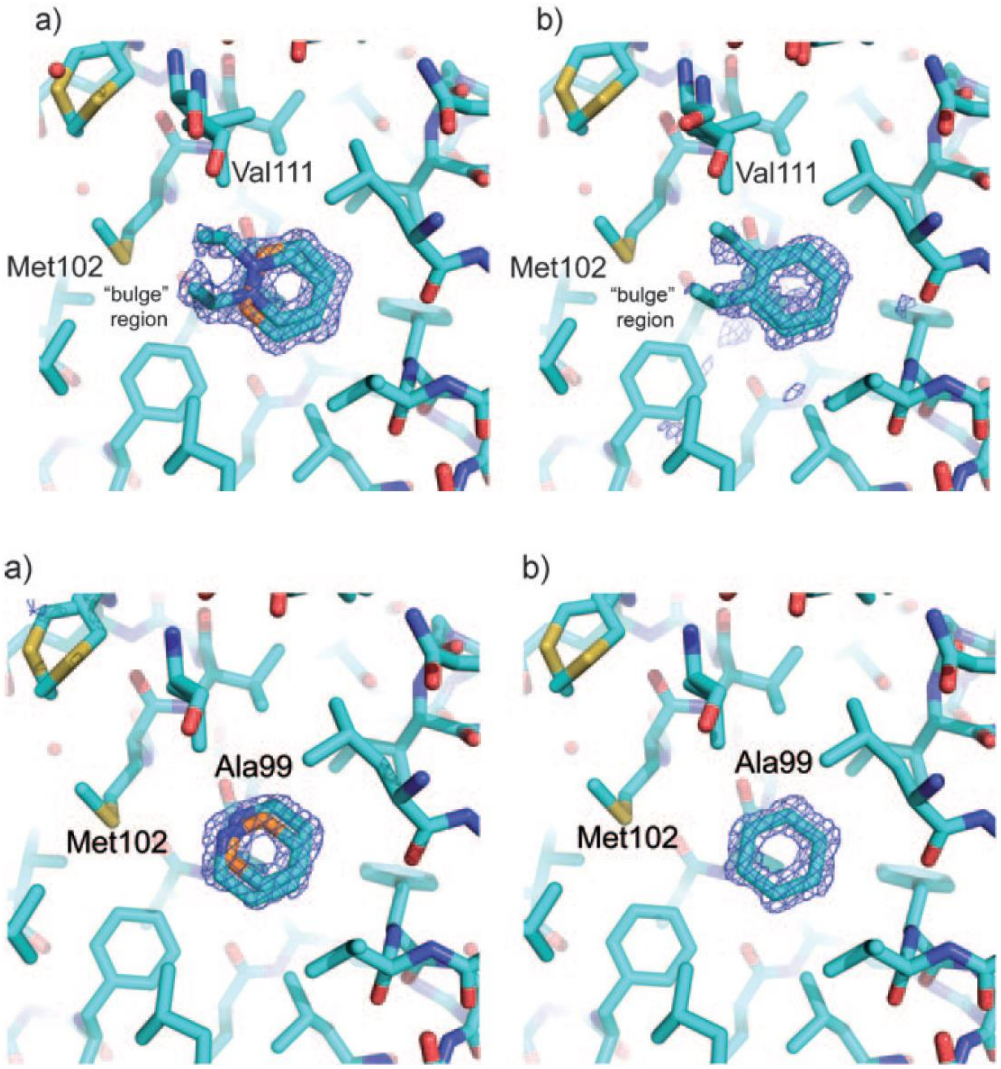


ethylbenzene EtAzB

Hydrophobic pocket of the L99A mutant of T4 lysozyme

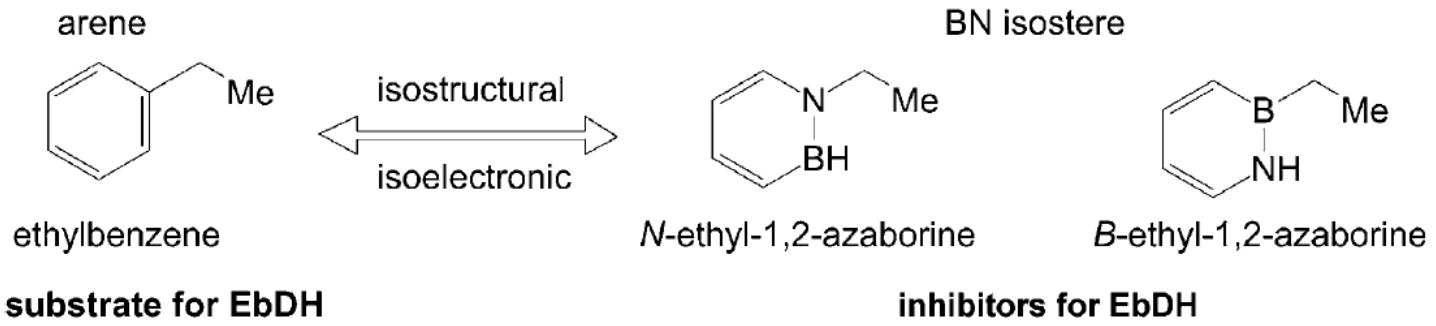


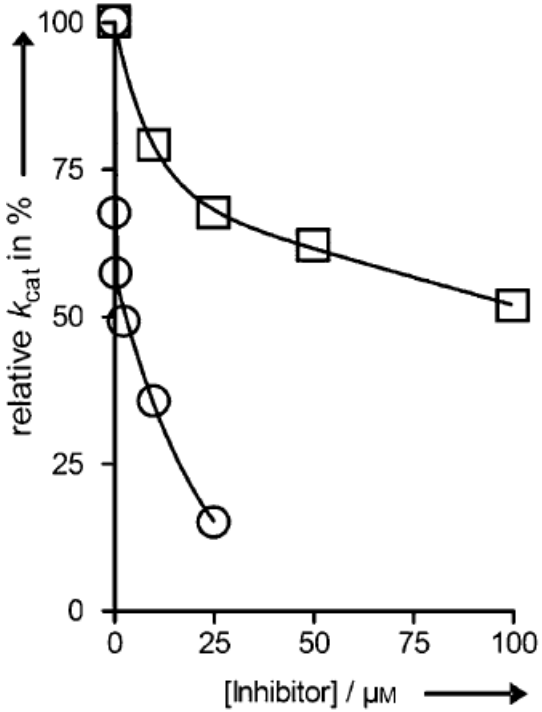
benzene HAzB



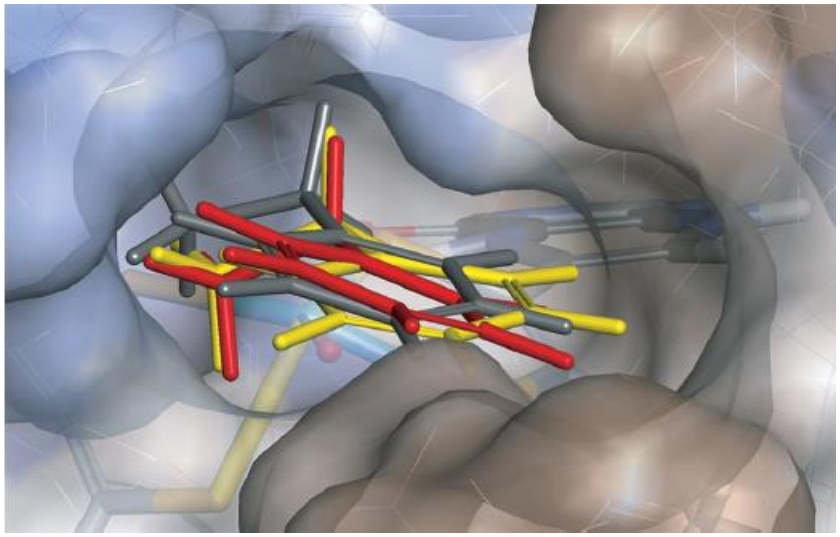
Metthews, B. W.; Liu, S.-Y. *et. al. Angew. Chem. Int. Ed.* **2009**, *48*, 6817-6819.

Biological Research



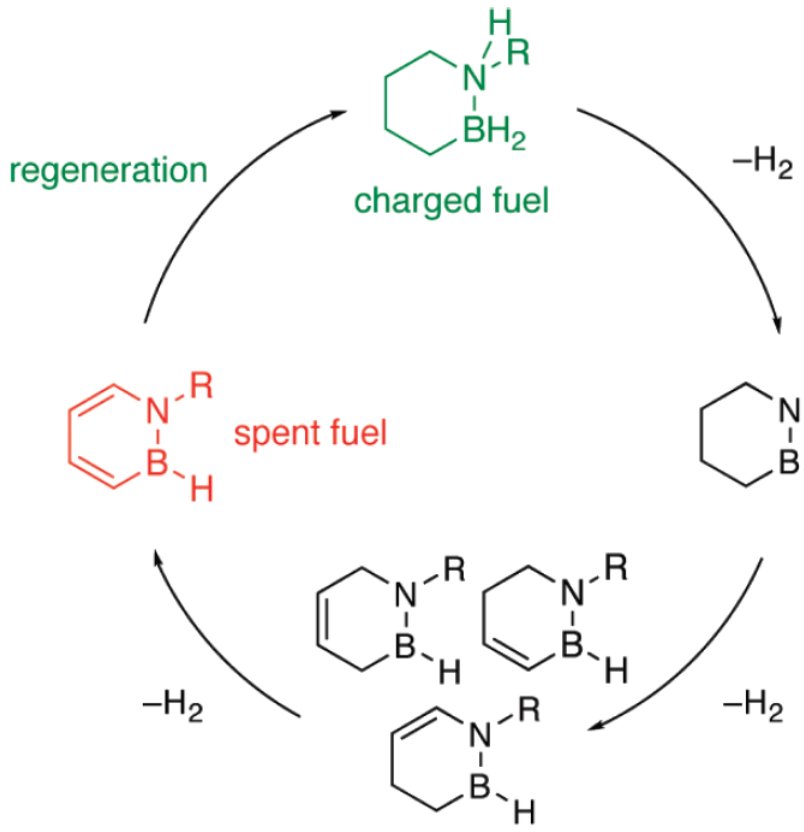


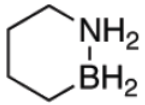
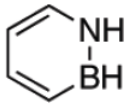
Strong inhibitors for the hydroxylation of ethylbenzene by ethylbenzene dehydrogenase (EbDH)



Liu, S.-Y.; Heider, J. *et. al. Angew. Chem. Int. Ed.* **2013**, *52*, 2599-2601.

Hydrogen Storage Potential



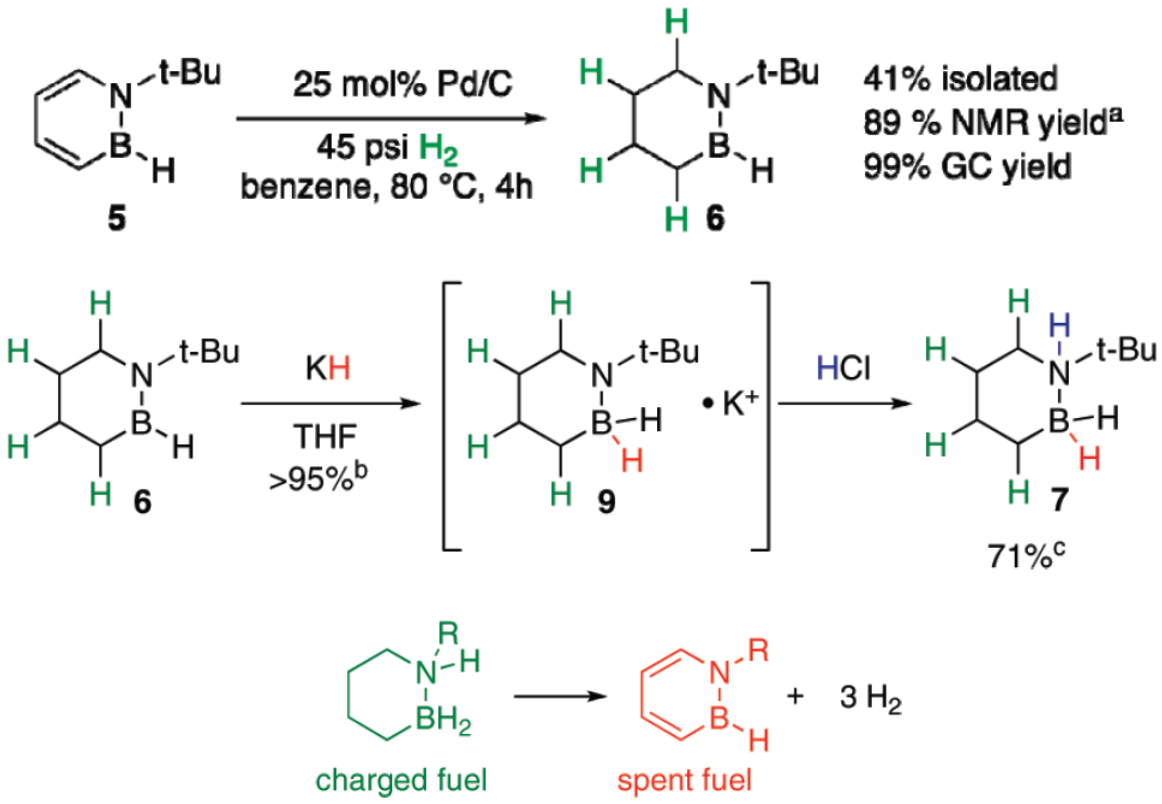
				ΔH (kcal/mol)	ΔG (kcal/mol)
(1)	$H_3N–BH_3$	→	$H_2N–BH_2$ + H_2	–5.1	–13.6
(2)	$H_3C–CH_3$	→	$H_2C=CH_2$ + H_2	32.6	23.9
(3)		→	 + 3 H_2	27.9	1.9

1
7.1 wt.% H_2

2
1,2-dihydro-
1,2-azaborine

Liu, S.-Y. *et. al. J. Am. Chem. Soc.* **2010**, *132*, 3289-3291.

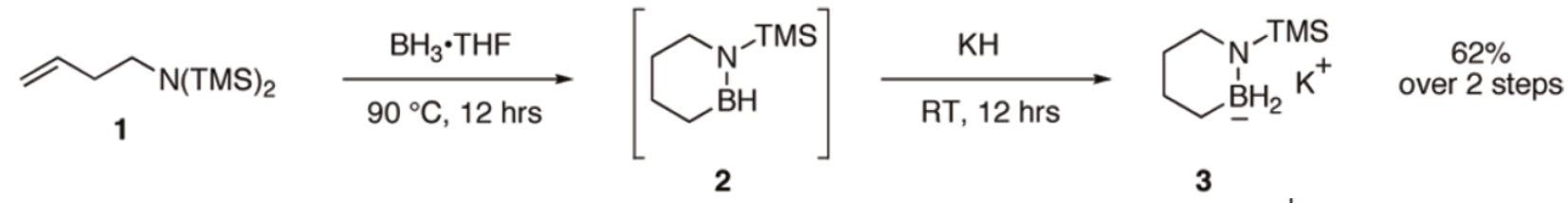
Hydrogen Storage Potential

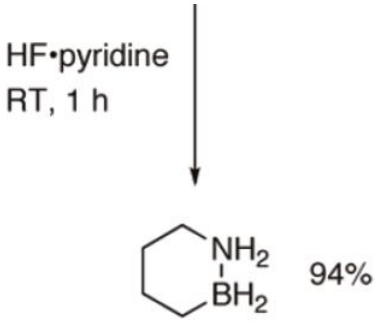


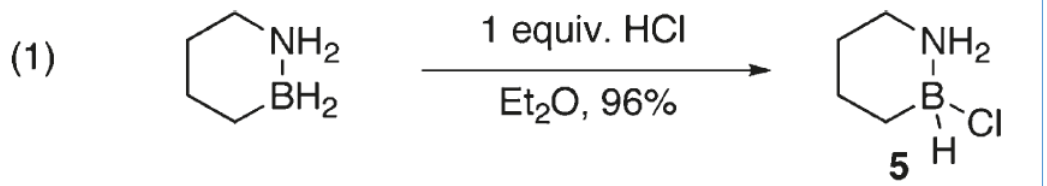
entry	R	ΔH (kcal/mol)	ΔG (kcal/mol)
1	H	23.5	−2.3
2	Me	26.0	−0.3
3	*t*-Bu	25.2	−0.4

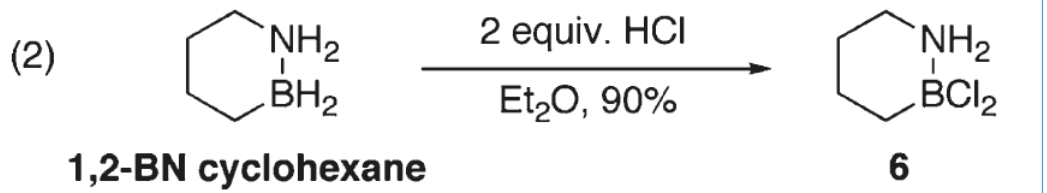
Liu, S.-Y. *et. al. J. Am. Chem. Soc.* **2010**, *132*, 3289-3291.

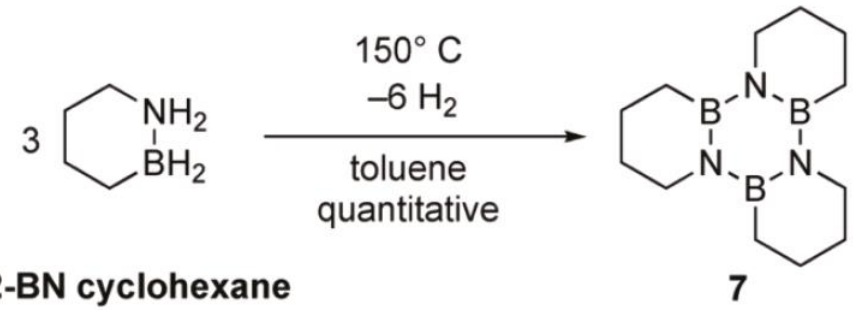
Hydrogen Storage Potential

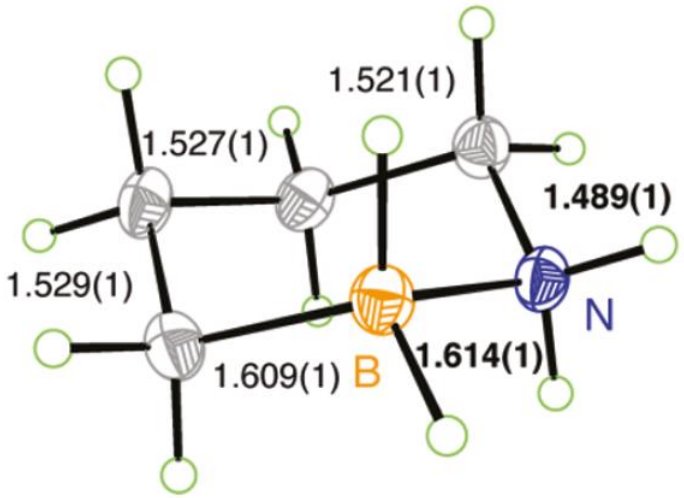






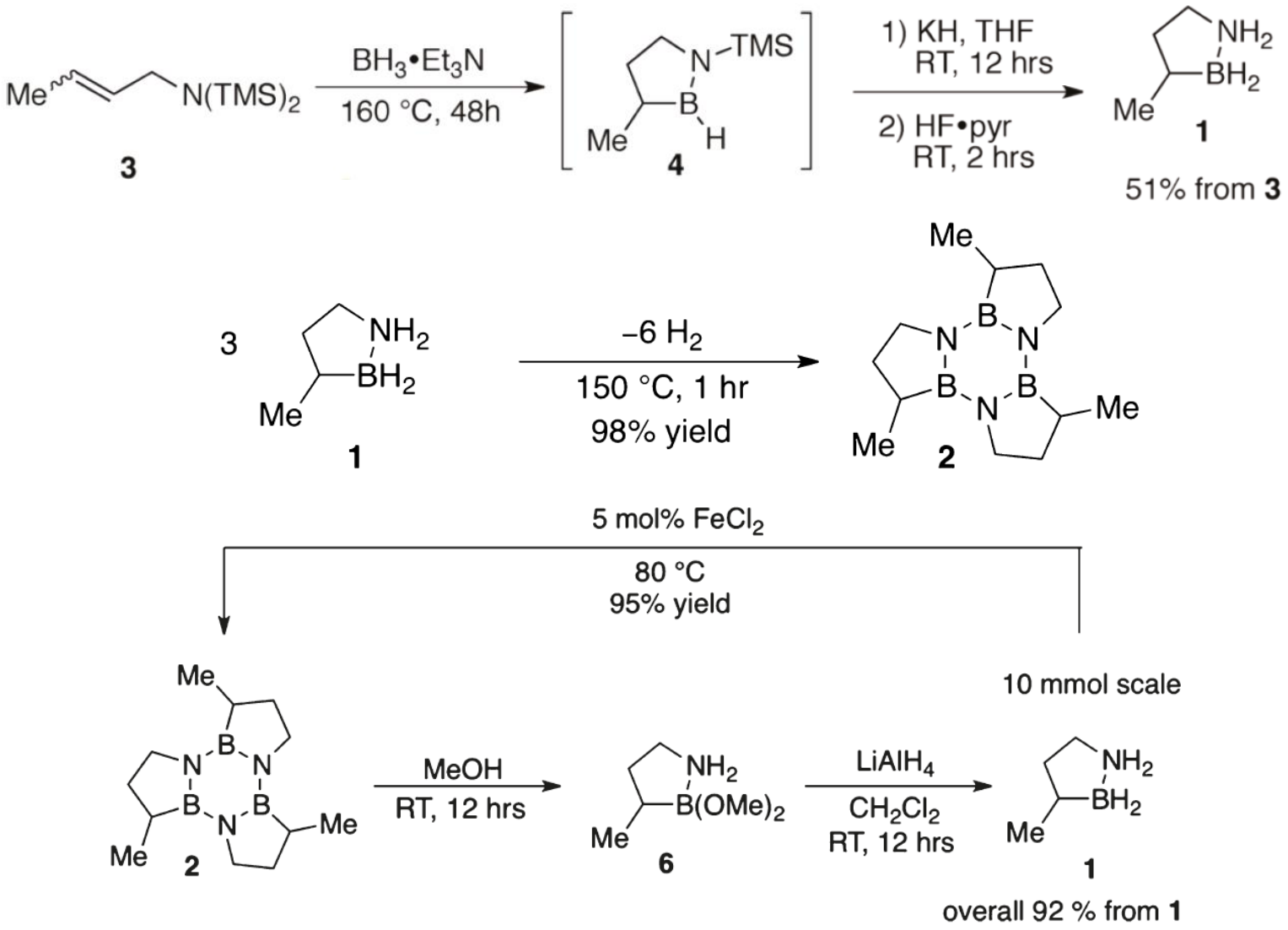






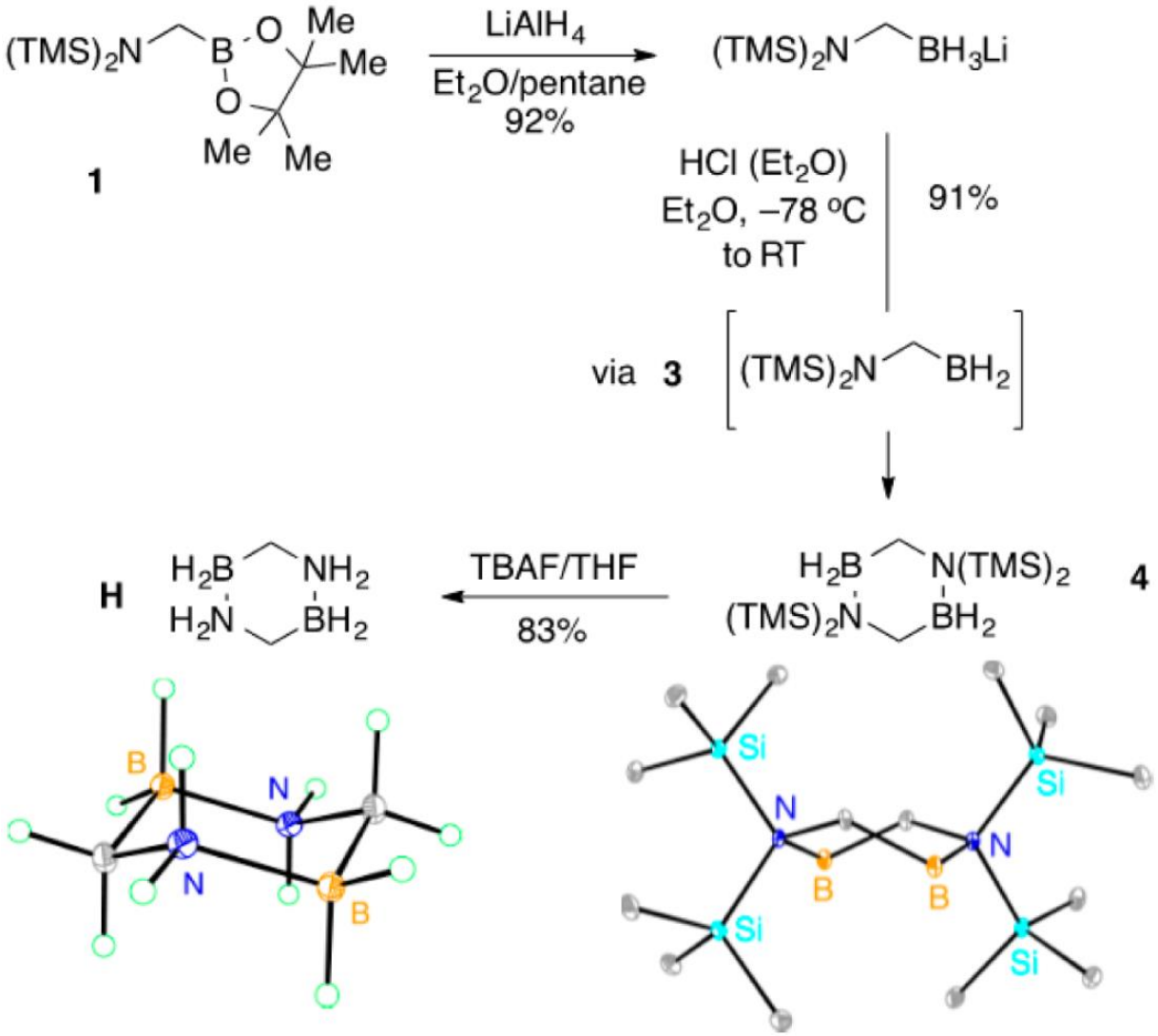
Liu, S.-Y. *et. al. J. Am. Chem. Soc.* **2011**, *133*, 13006-13009.

Hydrogen Storage Potential



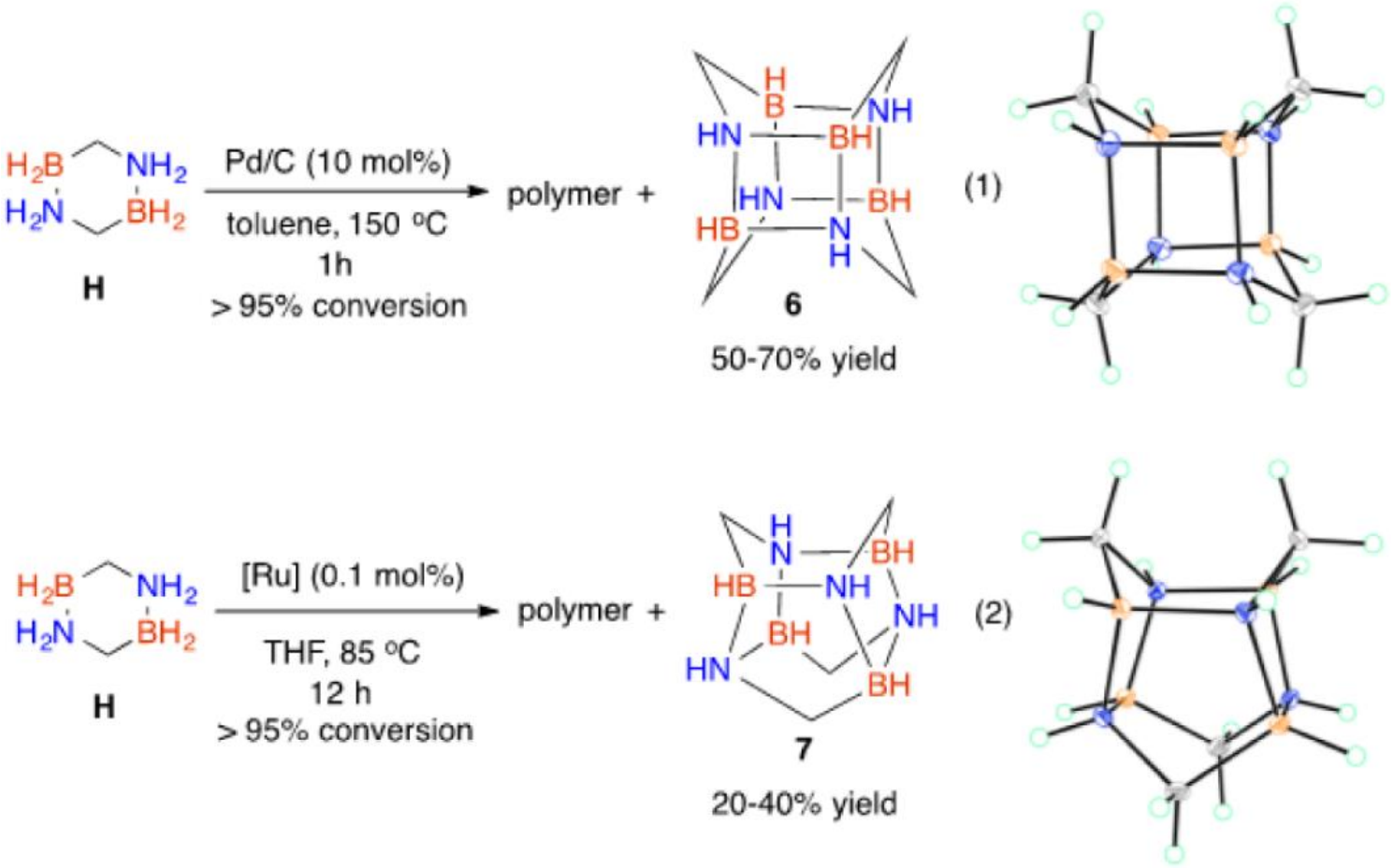
Liu, S.-Y. *et. al. J. Am. Chem. Soc.* **2011**, *133*, 19326-19329.

Hydrogen Storage Potential



Liu, S.-Y. *et. al. J. Am. Chem. Soc.* **2015**, *137*, 134-137.

Hydrogen Storage Potential

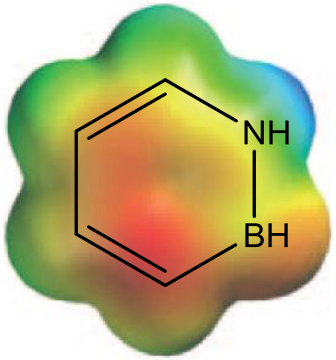


Liu, S.-Y. *et. al. J. Am. Chem. Soc.* **2015**, *137*, 134-137.

Summary

Synthesis and reactivity research towards azaborines remain under-developed.

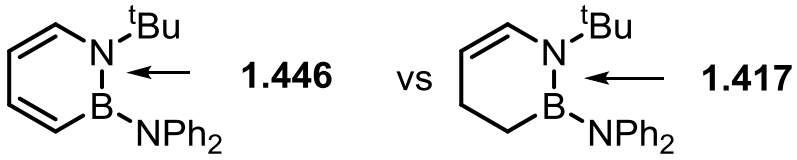
Azaborines have potential applications in materials, hydrogen storage and biological researches.



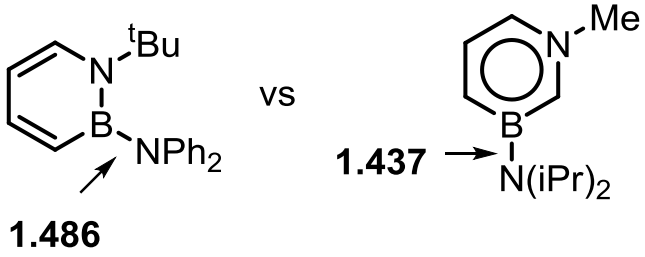
Thank you for your attention!

Key #1

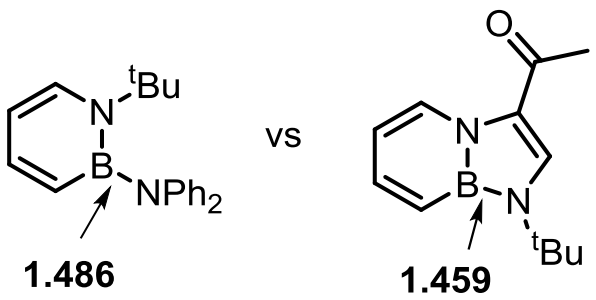
(a) endocyclic B-N bond



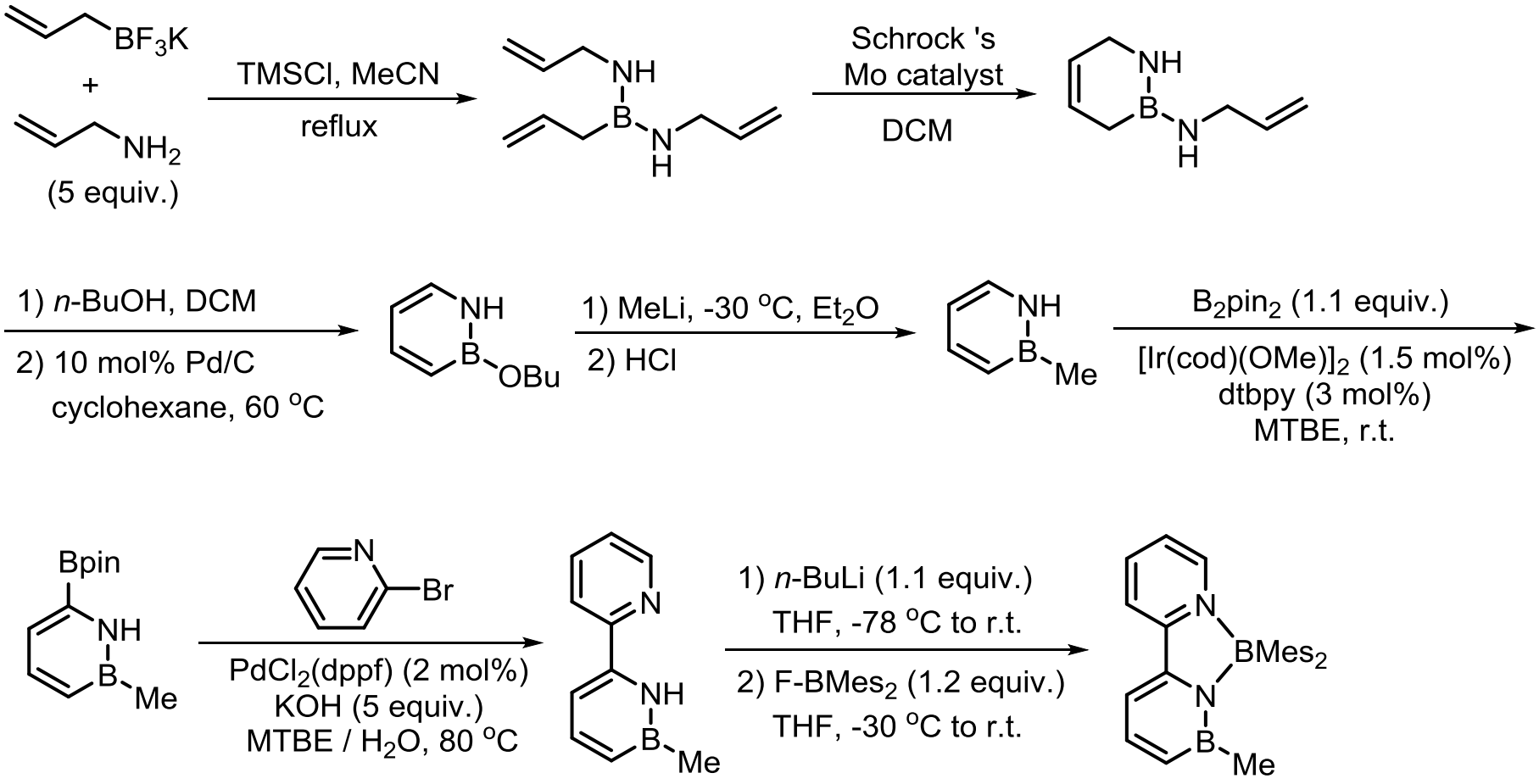
(b) exocyclic B-N bond



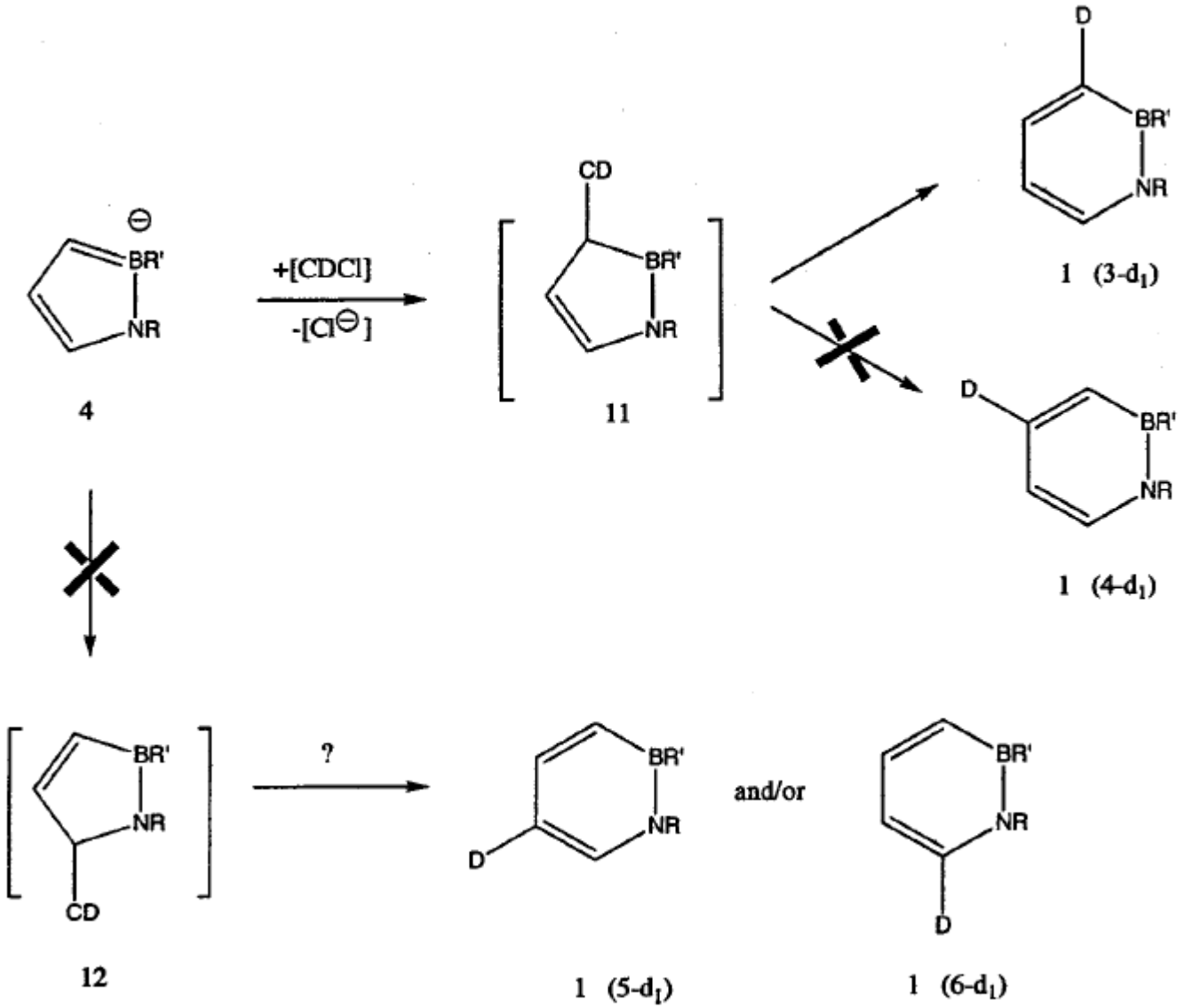
(c) exocyclic / indole B-N bond



Key #2


BF3K
+
NH2
(5 equiv.)
TMSCl, MeCN
reflux
NH
B
N
H
Schrock 's
Mo catalyst
DCM
NH
B
N
H
1) n-BuOH, DCM
2) 10 mol% Pd/C
cyclohexane, 60 °C
NH
B
OBu
1) MeLi, -30 °C, Et2O
2) HCl
NH
B
Me
B2pin2 (1.1 equiv.)
[Ir(cod)(OMe)]2 (1.5 mol%)
dtbpy (3 mol%)
MTBE, r.t.
Bpin
NH
B
Me
N
Br
PdCl2(dppf) (2 mol%)
KOH (5 equiv.)
MTBE / H2O, 80 °C
N
NH
B
Me
1) n-BuLi (1.1 equiv.)
THF, -78 °C to r.t.
2) F-BMes2 (1.2 equiv.)
THF, -30 °C to r.t.
N
BMes2
N
B
Me

Key #3



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