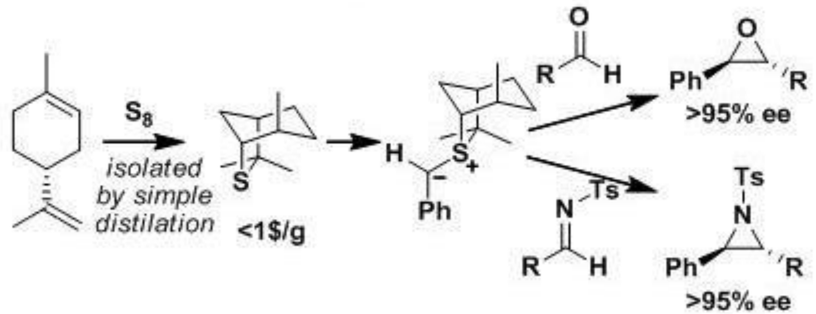
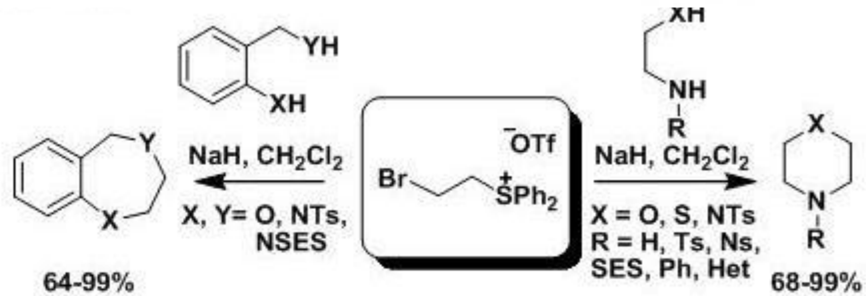
Homologation of Boronic Esters using OrganoLithium

Varinder Kumar Aggarwal*

Angew. Chem. Int. Ed., **2014**, *54*, 1082–1096.
Acc. Chem. Res., **2014**, *47*, 3174–3183
Chem. Eur. J., **2011**, *17*, 13124-13132.

Report: Zhe Dong
Advisor: Prof. Guangbin Dong
March 28th 2016

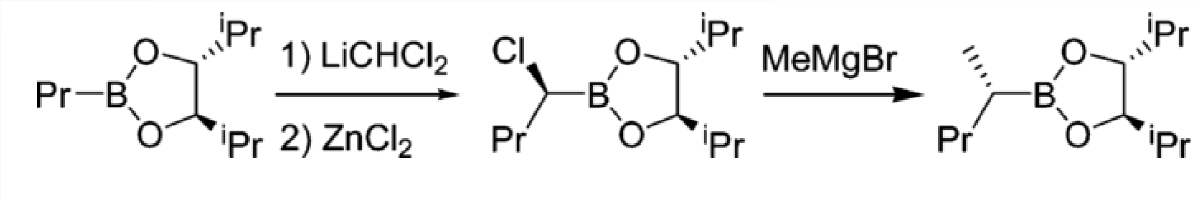




Varinder Kumar Aggarwal

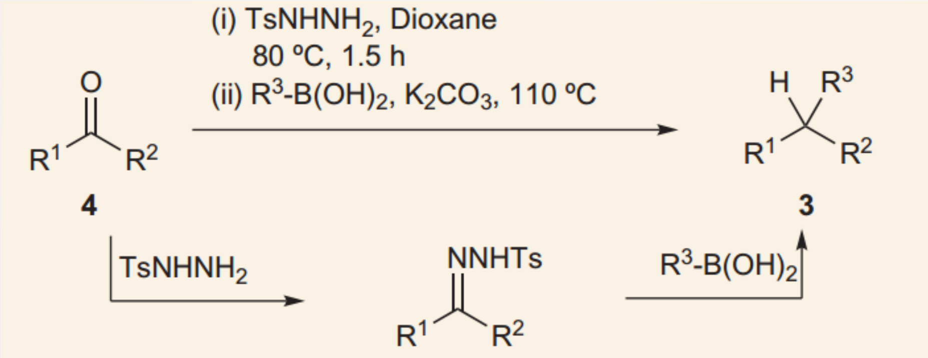
BS in chemistry, Cambridge University 1983
PHD : Prof. Stuart Warren Cambridge University 1983-1986
Prof. Gilbert Stork, Columbia University 1986-1988.
Lecturer in Chemistry, Bath University, 1988-1991.
Lecturer in Chemistry, Sheffield University (1991-1995)
Reader in Chemistry, Sheffield University (1995-1997)
Professor in Chemistry, Sheffield University (Oct. 1997-Sept. 2000).
Professor in Synthetic Chemistry, Bristol University (Sept. 2000 - present).

First Homologation of Boronic Esters

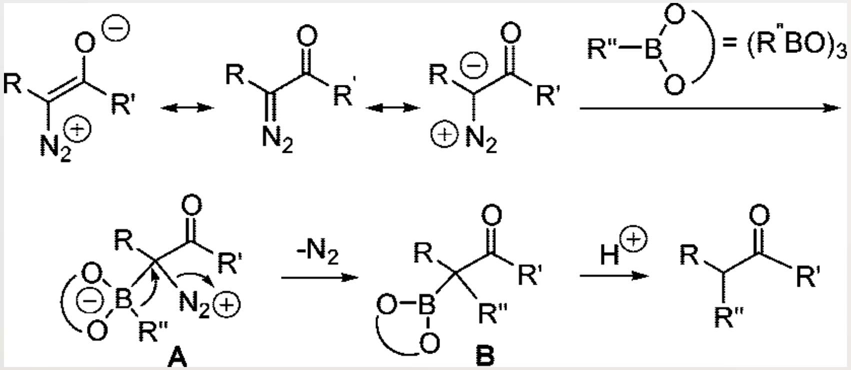


Matteson, D. S.; Ray, R. *J. Am. Chem. Soc.* **1980**, *102*, 7590

Carbene Insertion

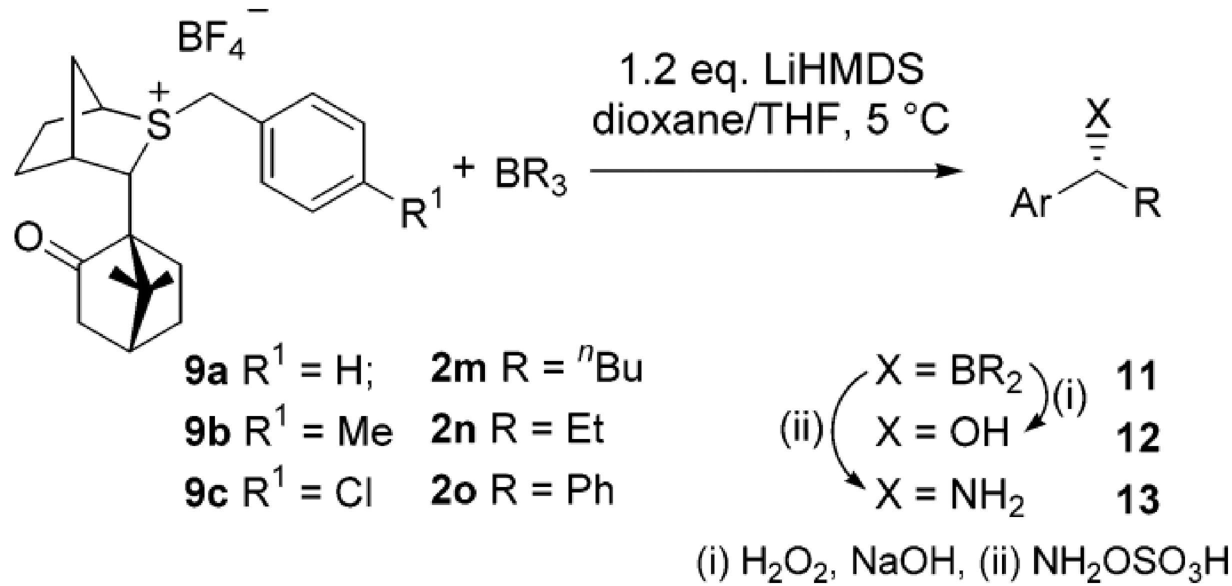


Barluenga, J.; Tomas-Gamasa, M.; Aznar, F.; Valdes, C. *Nat. Chem.* **2009**, *1*, 494



Peng, C.; Zhang, W.; Yan, G.; Wang, J. *Org. Lett.* **2009**, *11*, 1667.

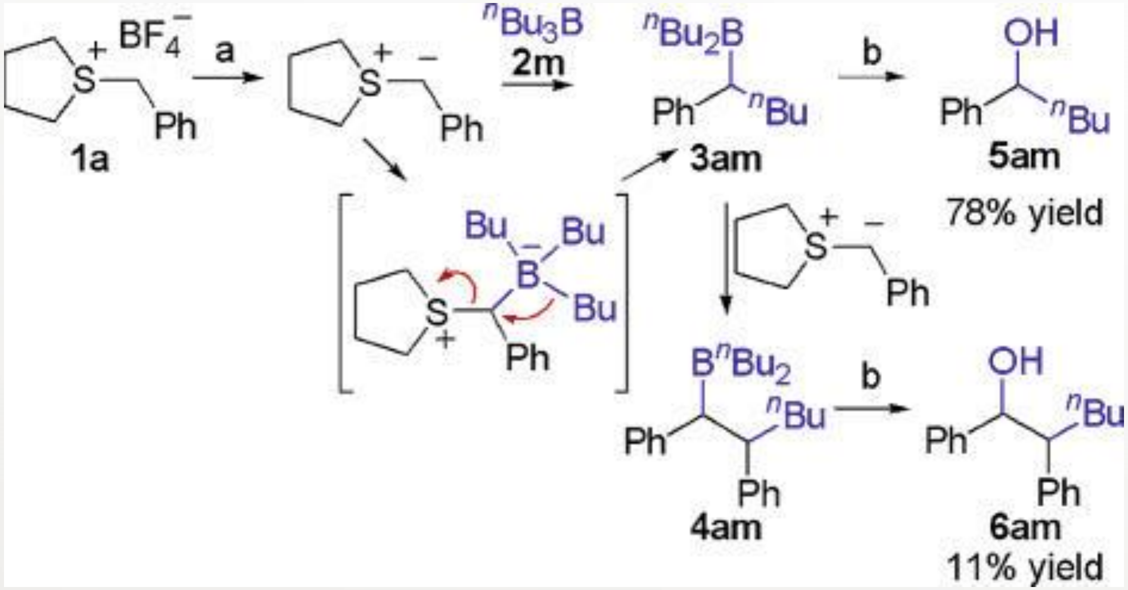
From
Carbene
To yilde



entry	R	Ar	X	product	yield[b]/ee[c] (%)
1	^{n}Bu	Ph	OH	**12am**	70/95
2	^{n}Bu	Ph	NH_2	**13am**	72/97[d]
3	Et	Ph	OH	**12an**	73/96
4	Et	Ph	NH_2	**13an**	68/97[d]
5	Ph	4-MeC_6H_4	OH	**12bo**	87/95
6	Ph	4-ClC_6H_4	NH_2	**13co**	68/96[d]

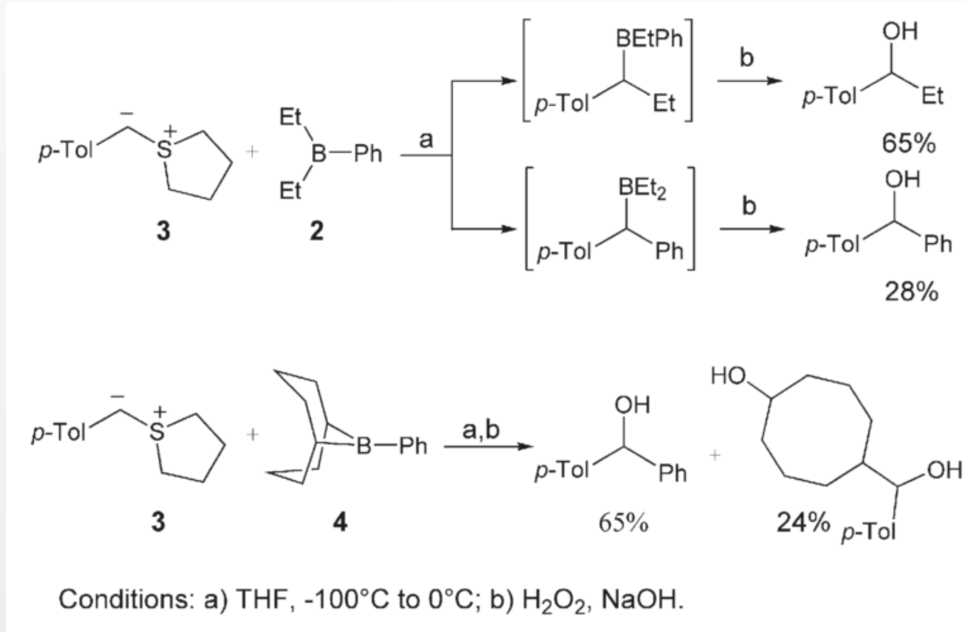
V. K Aggarwal, G. Yu Fang, A. Schmidt, *J. Am. Chem. Soc.*, **2005**, *127*, 1642-1643.

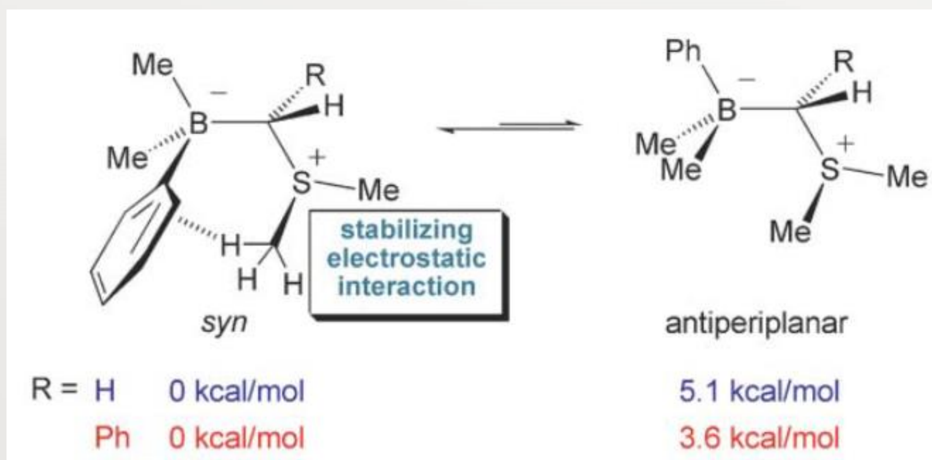
Mechanism Containing 1,2-metallate Migration



V. K Aggarwal, G. Yu Fang, A. Schmidt, *J. Am. Chem. Soc.*, **2005**, *127*, 1642-1643.

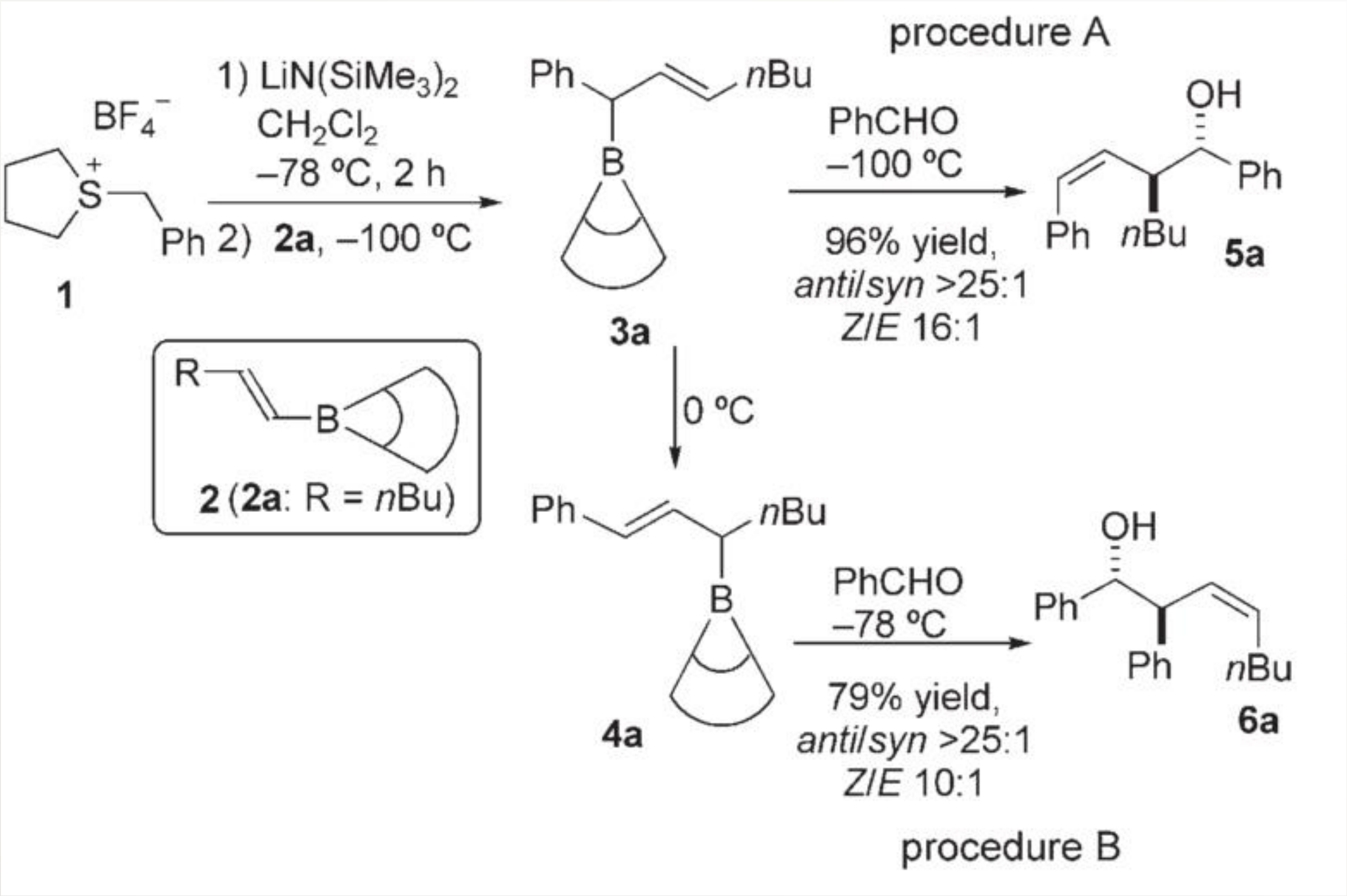
Selectivity of Asymmetric Borate for 1,2-metallate Migration





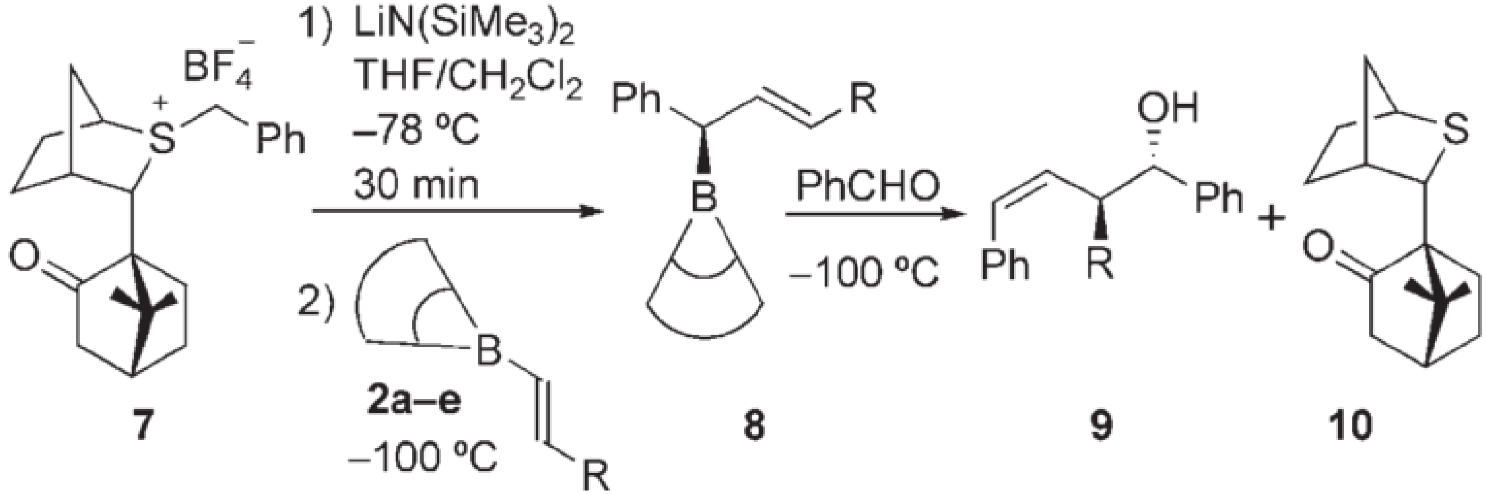
R. Robiette, G. Y. Fang, J. N. Harvey, V. K. Aggarwal, *Chem. Commun.*, **2006**, 741-743.

2+1 reaction : From vinyl Nuc to allyl Nuc



G. Y. Fang, V. K. Aggarwal, *Angew. Chem. Int. Ed.*, **2007**, *46*, 359-362..

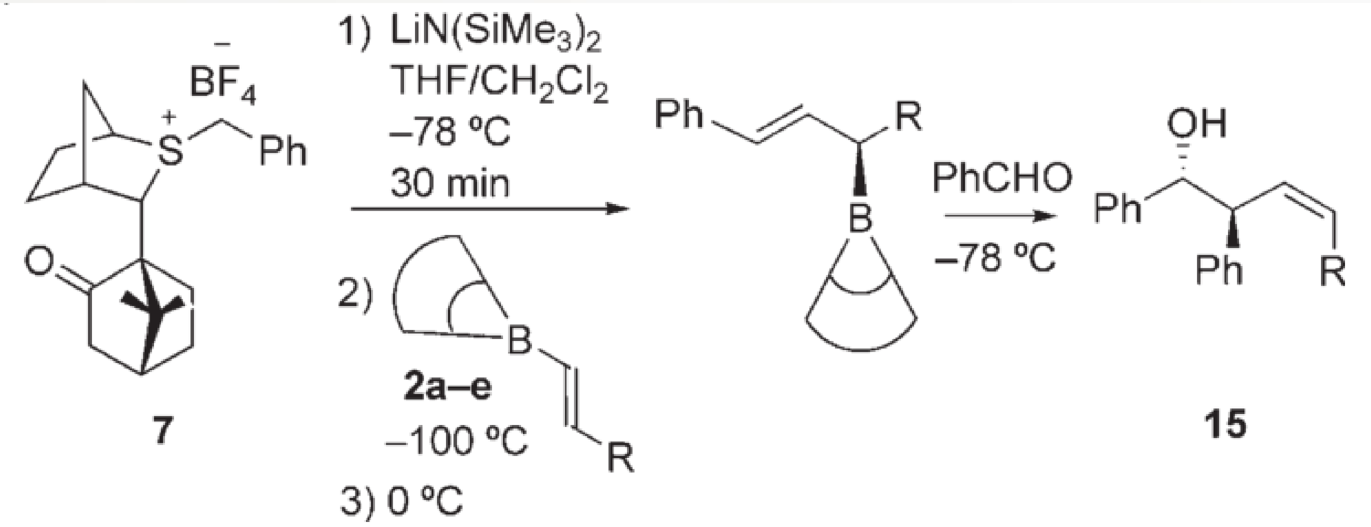
1,3 Asymmetric Crotylation



Entry	R	Yield (9) [%][a]	Z/E[b]	d.r. [%][b,c]	*ee* [%][c]
1	*n*Bu **a**	79	15:1	>95	>99
2	Me **b**	81	40:1	>95	>99
3	H **c**	61[d]	>40:1	>95	>99
4	$TMSOCH_2$[e] **d**	61[f,g]	>40:1	>95	>99
5	$AcOCH_2CH_2$ **e**	72[h]	>40:1	>95	>99

G. Y. Fang, V. K. Aggarwal, *Angew. Chem. Int. Ed.*, **2007**, *46*, 359-362..

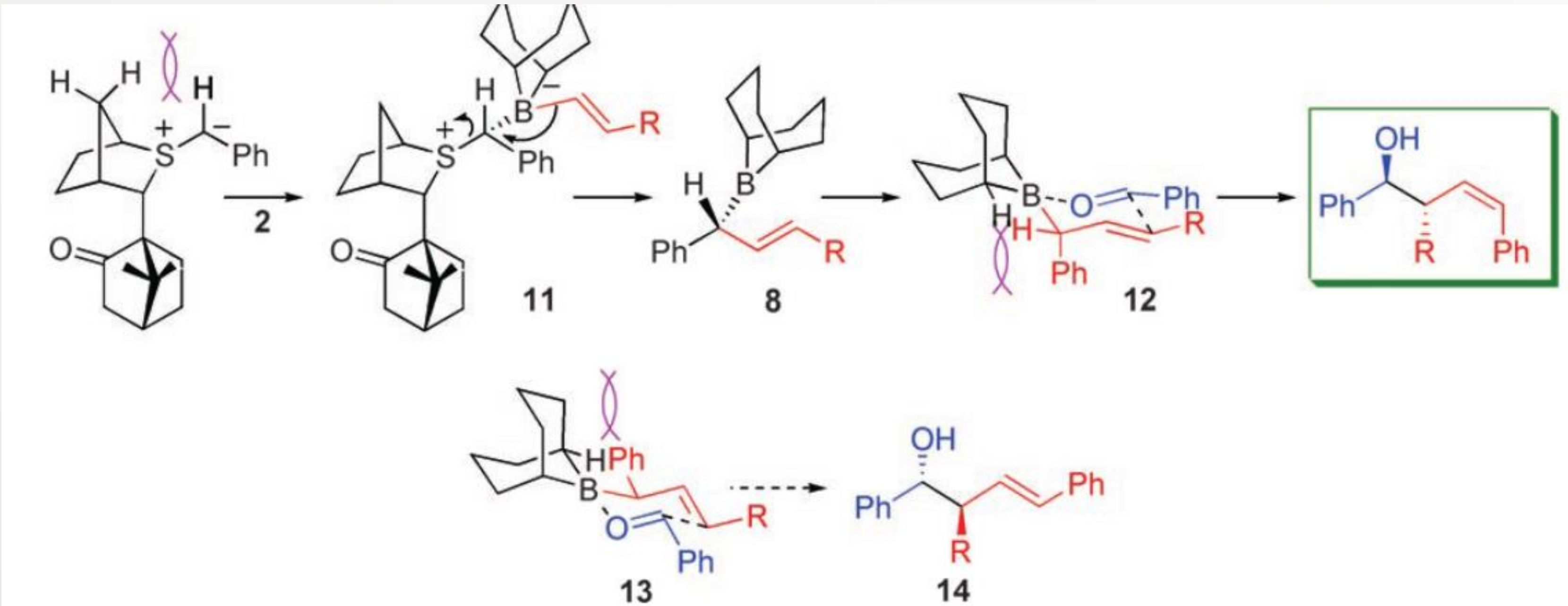
1,1 Asymmetric Crotylation



Entry	R	Yield (15) [%][a]	Z/E[b]	d.r. [%][b,c]	ee [%][c]
1	*n*Bu **a**	81	10:1	> 95	> 99
2	Me **b**	76	30:1	> 95	> 99
3	TMSOCH$_2$ **d**	49[d,e]	> 30:1	> 95	> 99
4	AcOCH$_2$CH$_2$ **e**	56[f]	13:1	> 95	> 99

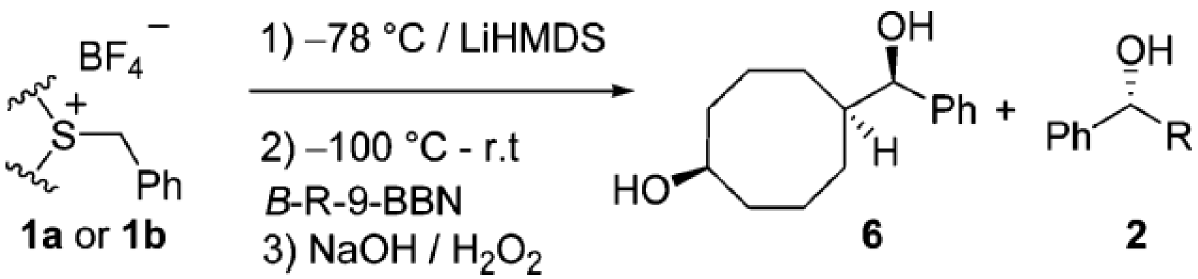
G. Y. Fang, V. K. Aggarwal, *Angew. Chem. Int. Ed.*, **2007**, *46*, 359-362..

Diastereoselectivity Model
Asymmetric Crotylation



G. Y. Fang, V. K. Aggarwal, *Angew. Chem. Int. Ed.*, **2007**, *46*, 359-362..

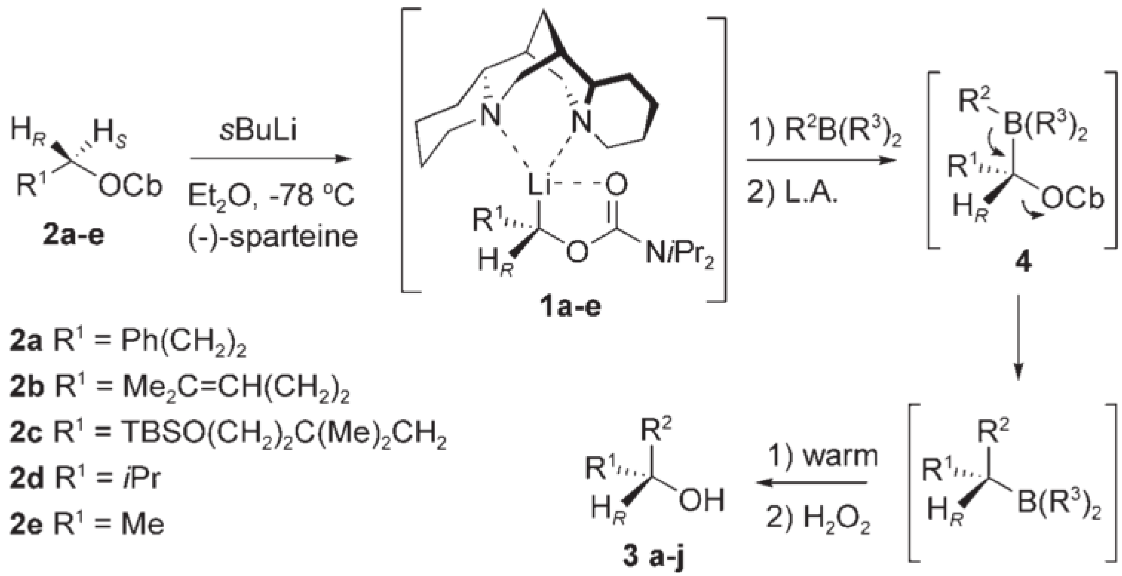
Selectivity of 9-BBN Borate for 1,2-metallate Migration



entry	sulfonium salt	*B*-R-9-BBN	yield of **6**	yield of **2**
1	**1b**	Hexyl (**7a**)	56%	41% (**2e**)
2	**1b**	Allyl (**7b**)	51%	39% (**2f**)
3	**1b**	Benzyl (**7c**)	51%	35% (**2g**)
4	**1b**	*i*-Pr (**7d**)	trace	77% (**2h**)
5	**1b**	Cyclopropyl (**7e**)	89%	trace
6	**1b**	Ph (**7f**)	trace	94%[a]
7	**1b**	1-Hexenyl (**7g**)	trace	21%[b] (**2i**)
8	**1b**	1-Hexynyl (**7h**)	92%	trace
9	**1a**	*i*-Pr (**7d**)	-	97%[c] (**2h**)
10	**1a**	1-Hexynyl (**7h**)	90%[d]	—

G. Y. Fang, O. A. Wallner, N. Di Blasio, X Ginesta, J. N. Harvey, V, K. Aggarwal, *J. Am. Chem. Soc.*, **2007**, *129*, 14632-14639.

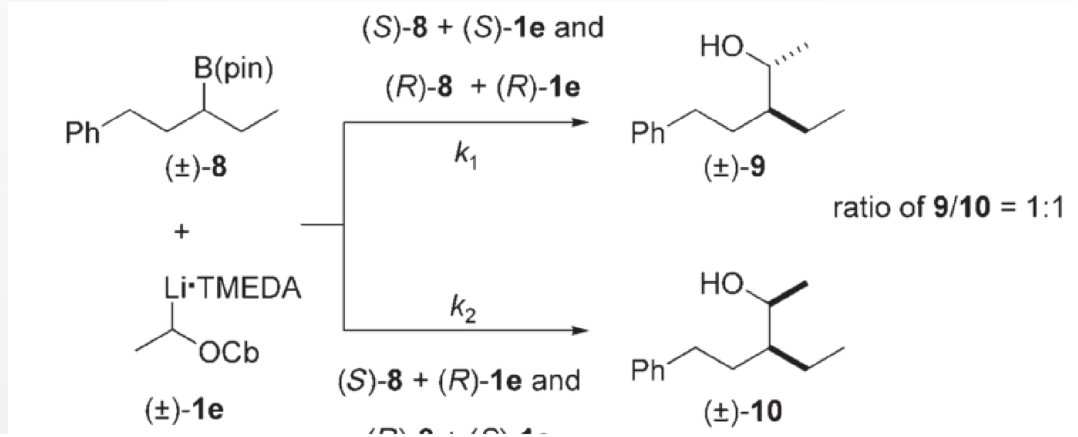
From Sulfur Yilde to Chiral Lithium Carbamate

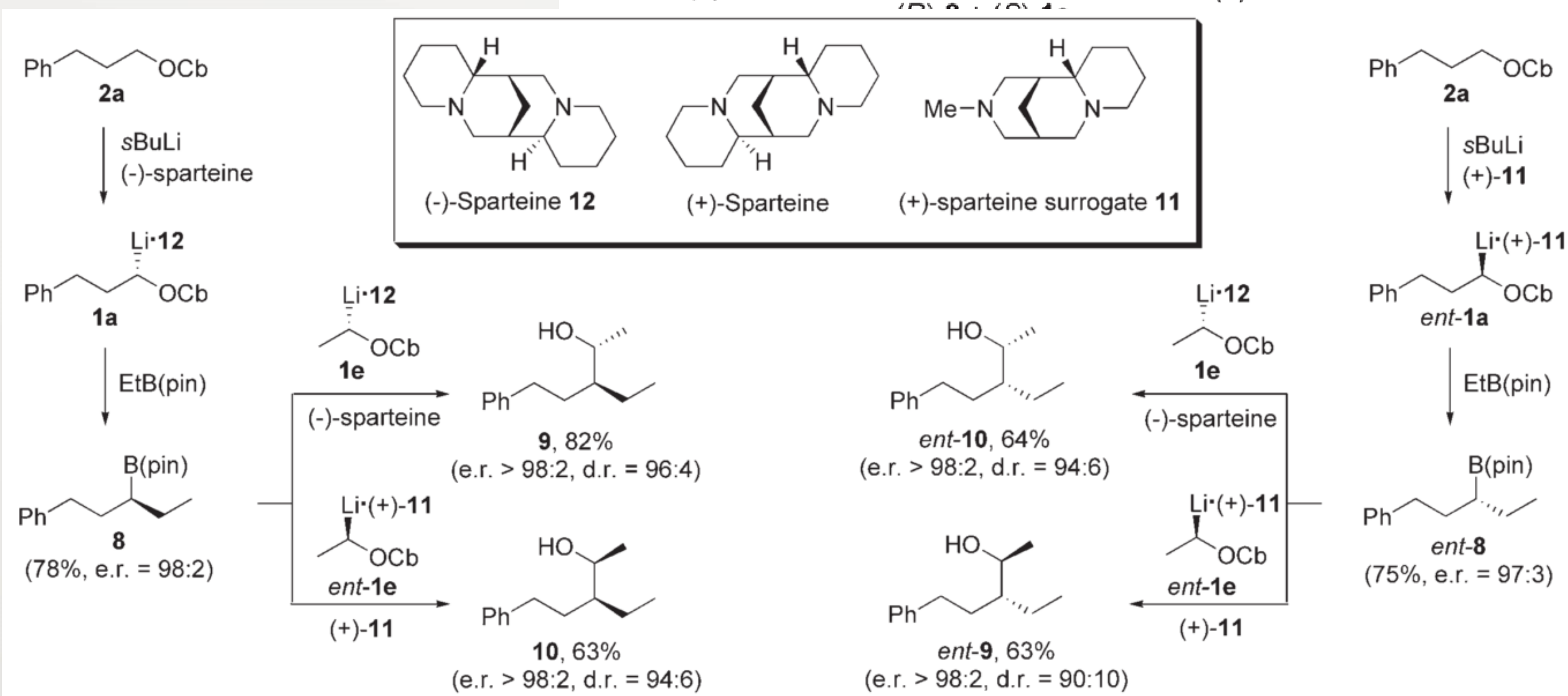


Entry	Carbenoid precursor	R^2	$(R^3)_2$	Lewis acid	Yield [%] (product)	e.r.[a]
1	**2a**	Et	Et	–	91 (**3a**)	98:2
2		*n*Hex	9-BBN	–	90 (**3b**)	98:2
3		*i*Pr	9-BBN	–	81 (**3c**)	98:2
4		Ph	9-BBN	–	85 (**3d**)	88:12
5		Ph	9-BBN	$MgBr_2$	94 (**3d**)	97:3
6		Et	pinacol	$MgBr_2$	90 (**3a**)	98:2

J. L. Stymiest, G. Dutheuil, A. Mahmood, V. K. Aggarwal, *Angew. Chem. Int. Ed.*, **2007**, *46*, 7491-7494.

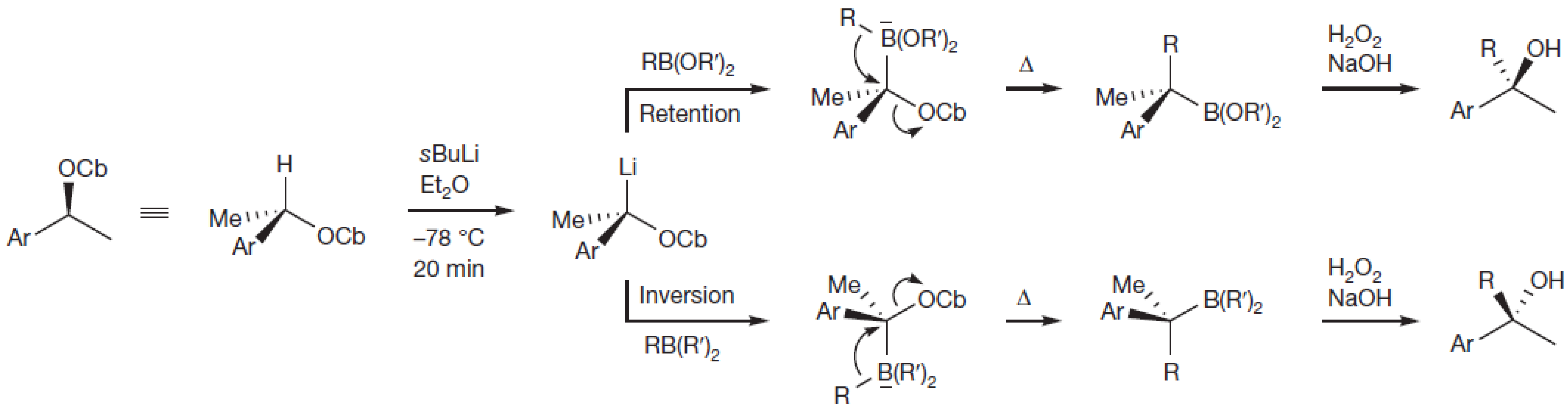
Stereodivergent Synthesis:

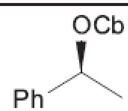
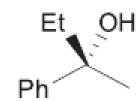
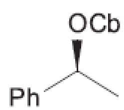
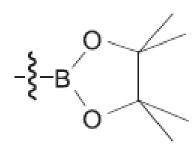
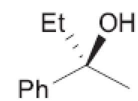
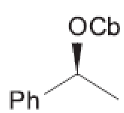
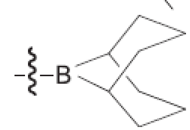
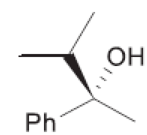
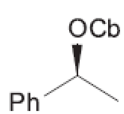
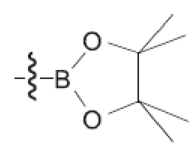
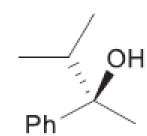




J. L. Stymiest, G. Dutheuil, A. Mahmood, V. K. Aggarwal, *Angew. Chem. Int. Ed.*, **2007**, *46*, 7491-7494.

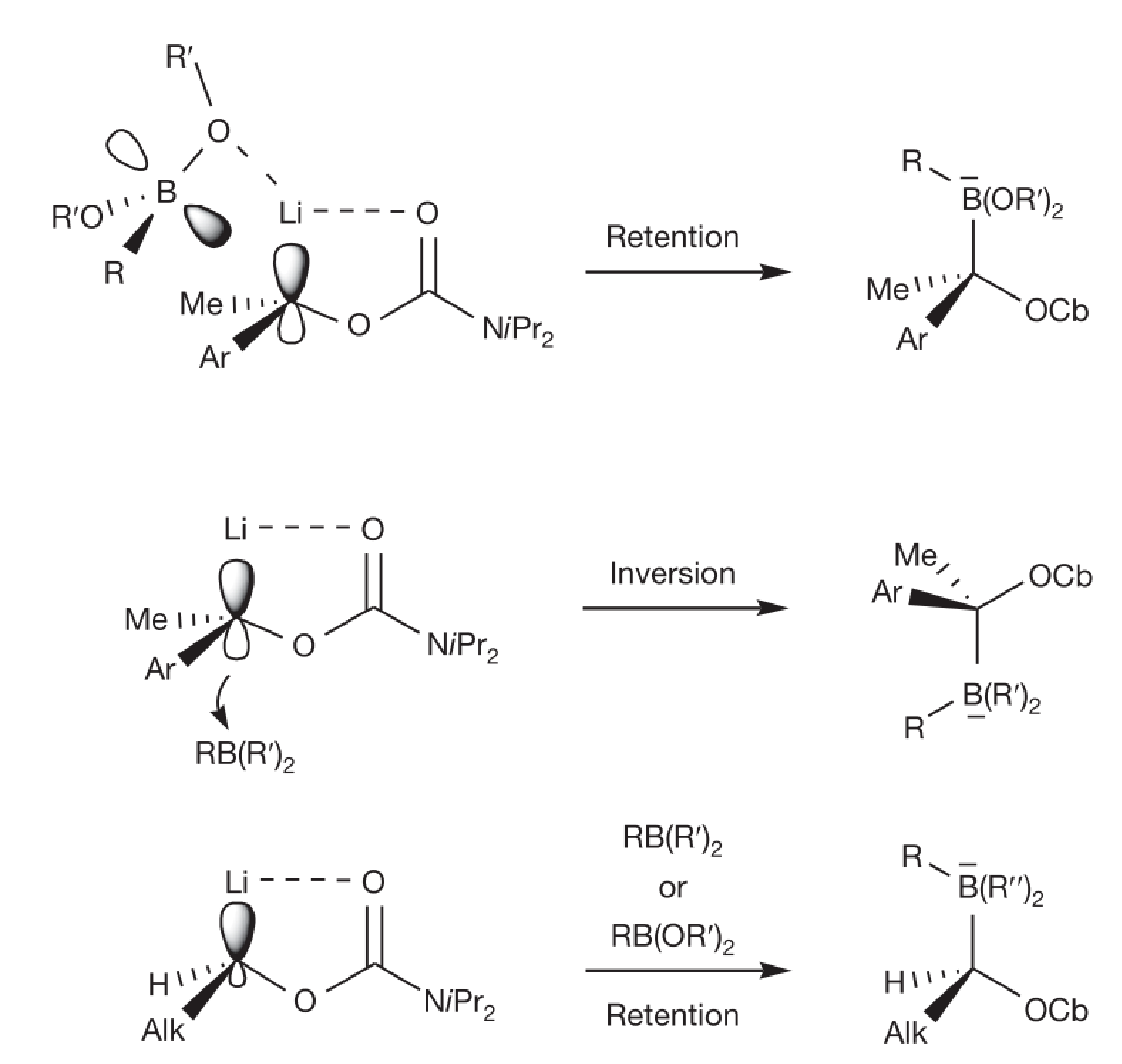
From Chiral Carbamate to Chiral Boronate



Entry	Carbamate (e.r.)	Migrating group, R	Borane/boronic ester component	Product	Yield (%) (e.r., S:R)
1	 (99:1)	Et			91 (99:1)
2	 (99:1)	Et			95 (1:99)
3	 (99:1)	*i*Pr			91 (98:2)*
4	 (99:1)	*i*Pr			80 (4:96)

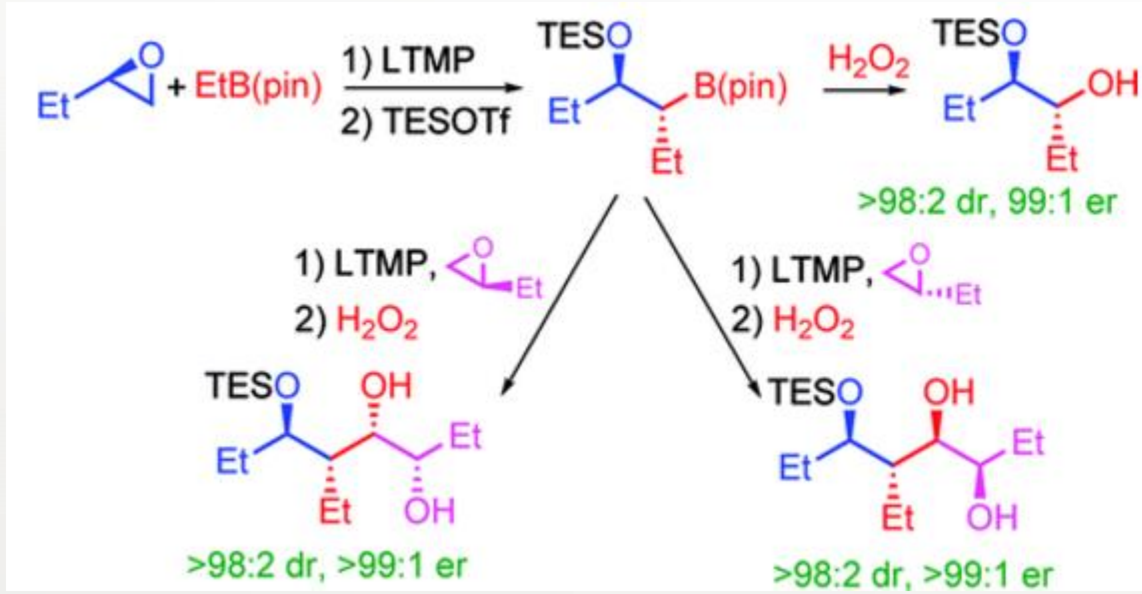
J. L. Stymiest, V. Bagutski, R. M. French, V. K. Aggarwal, *Nature,* **2008**, *456*, 778-782.

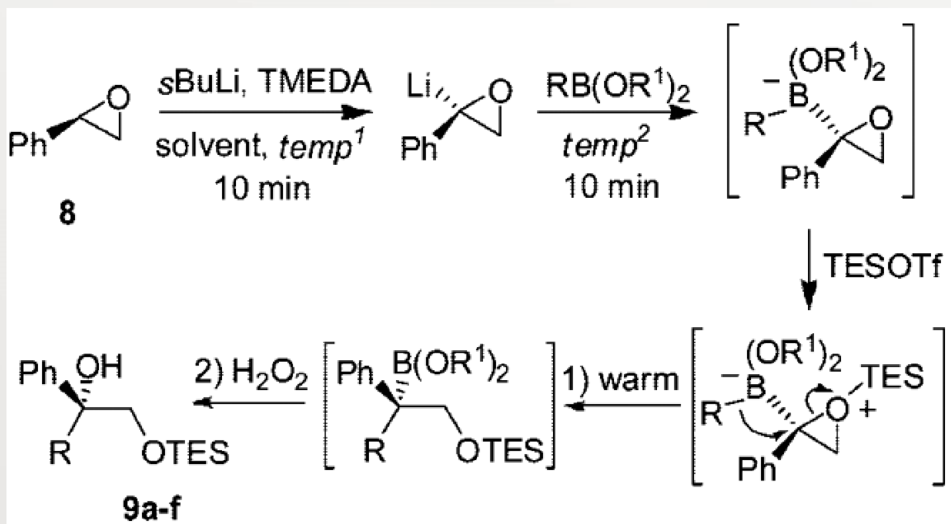
Explanation for Retention and Inversion



J. L. Stymiest, V. Bagutski, R. M. French, V. K. Aggarwal, *Nature,* **2008**, *456*, 778-782.

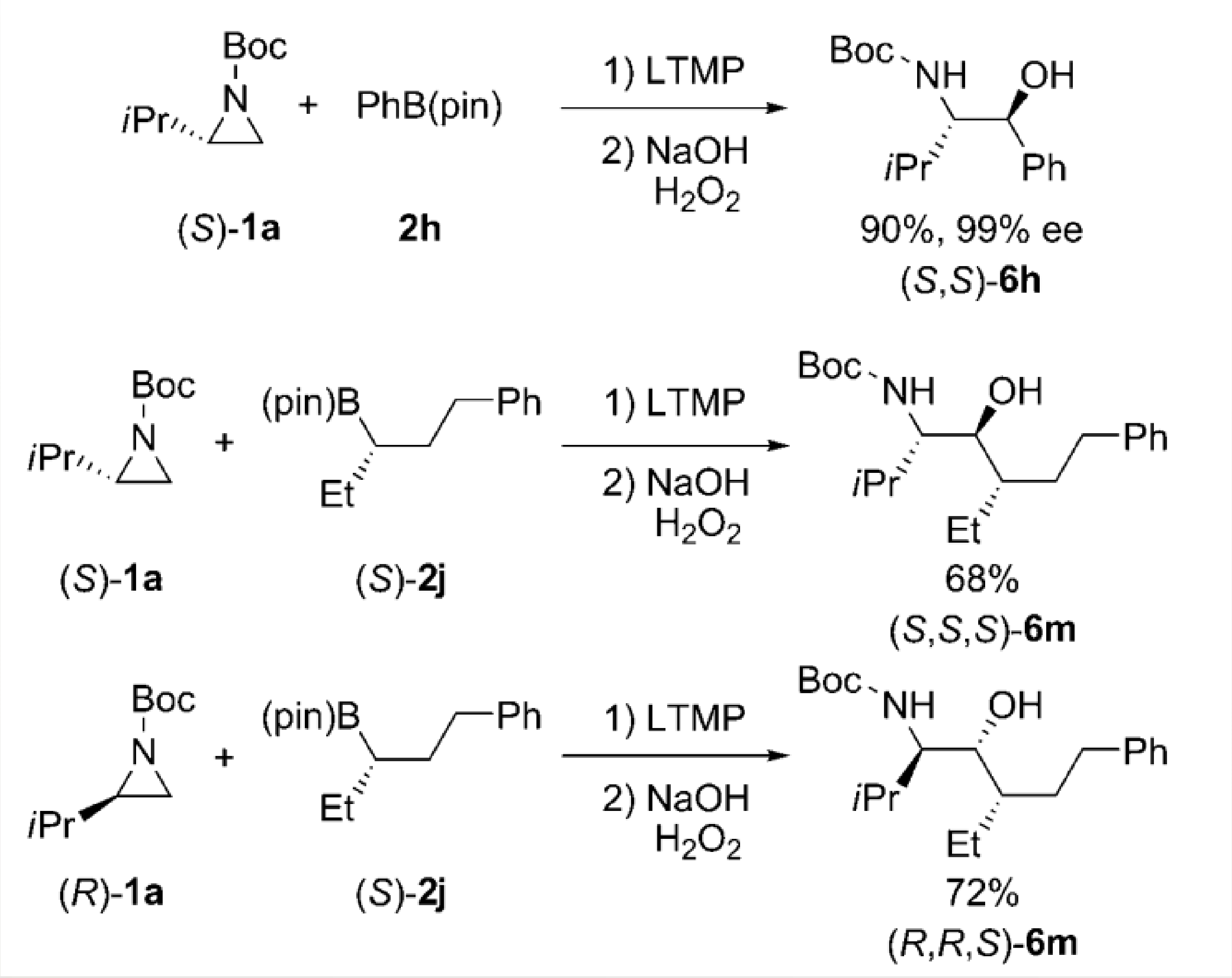
Chiral Lithium Generated From Chiral Epoxide



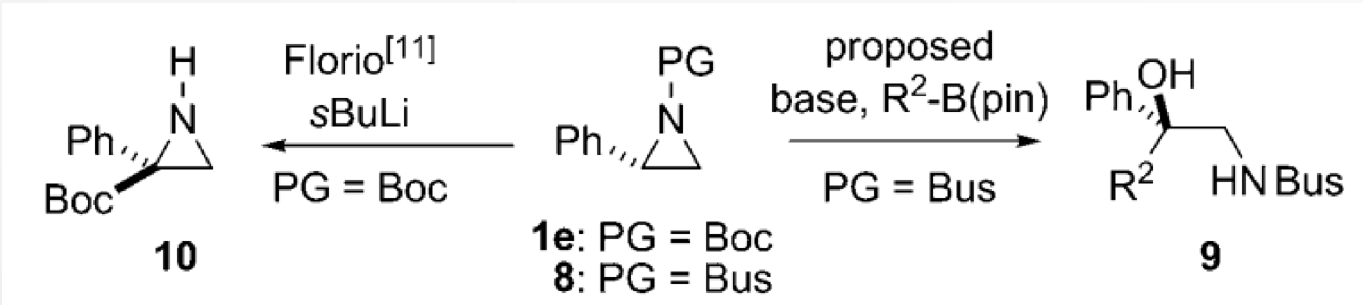


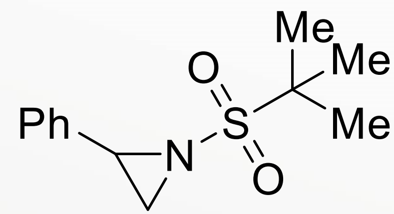
E. Vedrenne, O. A. Wallner, M. Vitale, F. Schmidt, V. K. Aggarwal, *Org. Lett.* **2009**, *11*, 165-168.

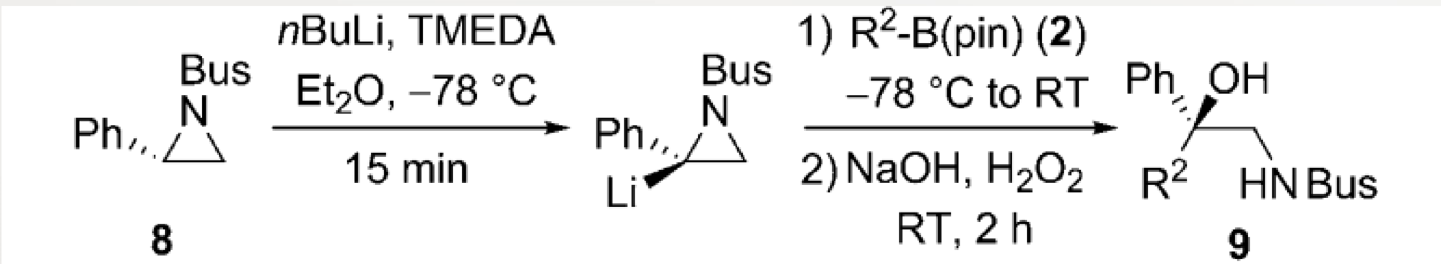
Chiral Lithium Generated From Chiral Azaridine



F. Schmidt, F. Keller, E. Vedrenne, V. K. Aggarwal, *Angew. Chem. Int. Ed.*, **2009**, *48*, 1149-1152.



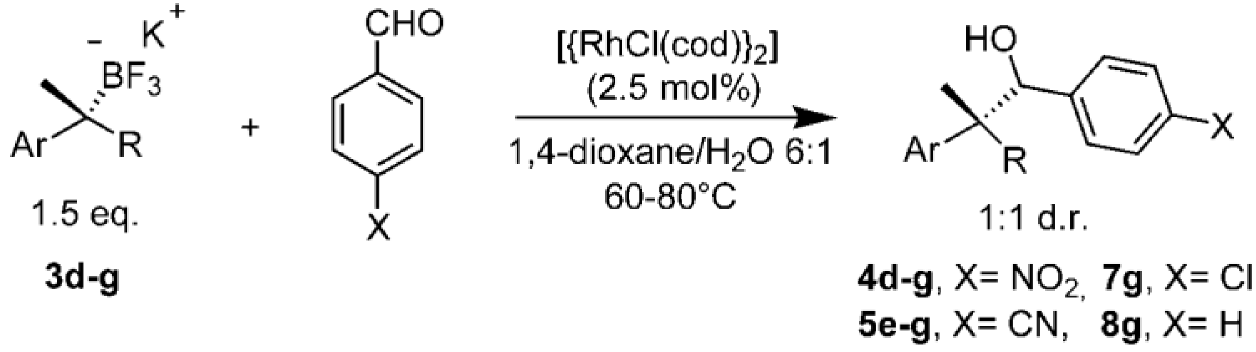




Entry	R^2 (boronic ester **2**)	Yield [%][b]	e.r.[c]
1	Cy (**2l**)[d]	84 (**9d**)	>99:1
2	allyl (**2j**)	87 (**9j**)	>99:1
3	*n*Bu (**2k**)	80 (**9k**)	>99:1

F. Schmidt, F. Keller, E. Vedrenne, V. K. Aggarwal, *Angew. Chem. Int. Ed.*, **2009**, *48*, 1149-1152.

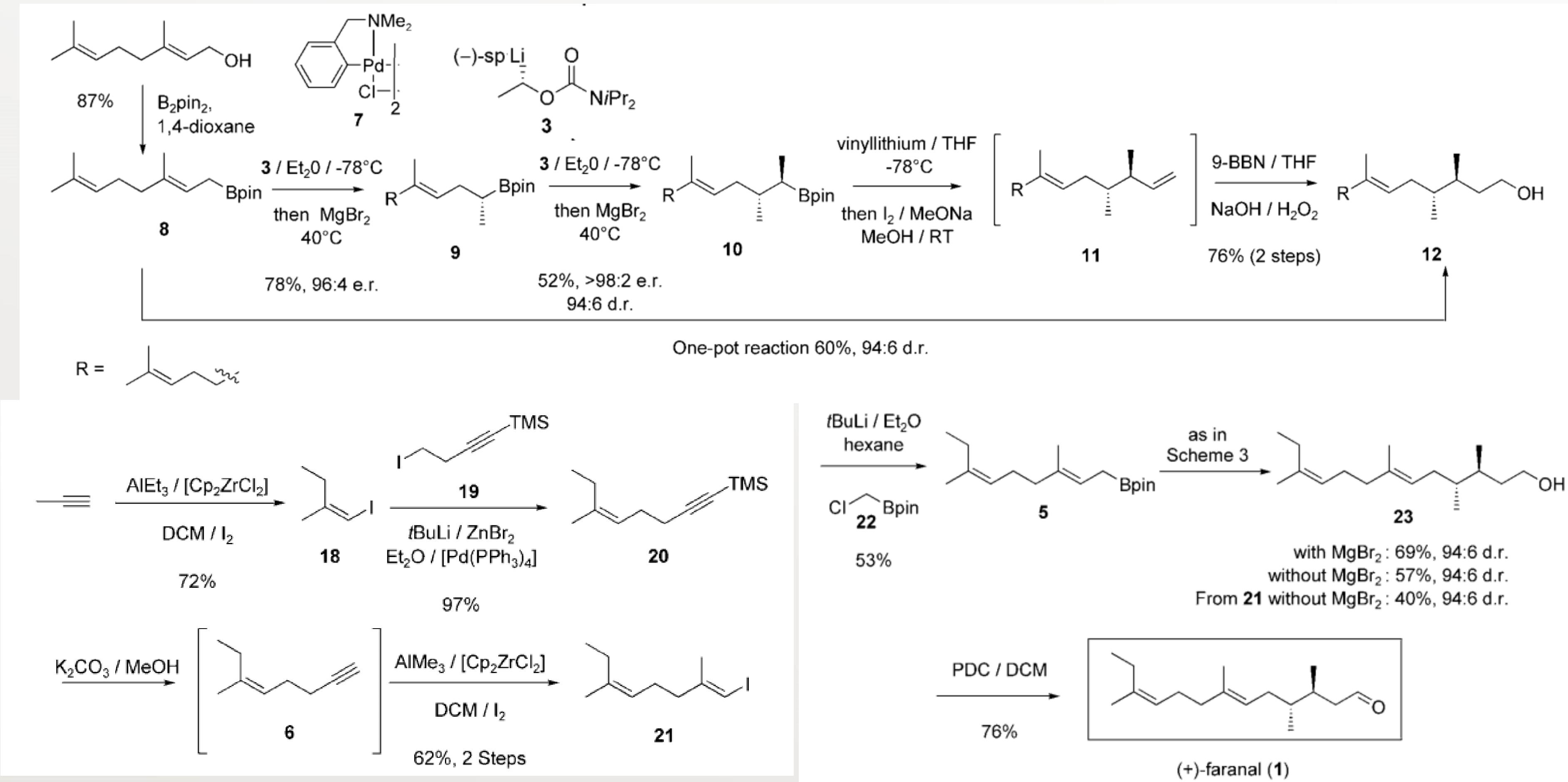
Rh(I) catalyzed Stereospecific Transfer to Form Quaternary Carbon



Entry	Trifluoroborate salt (**3 d–g**) Ar	R	X	*T* [°C]	*t* [h]	Yield [%][b]	Stereoret. [%][c]
1	Ph	*p*-ClC_6H_4	NO_2	60	6	**4d**, 84	>99
2	Ph	*p*-ClC_6H_4	NO_2	80	2	**4d**, 68	>99
3	*p*-$MeOC_6H_4$	Ph	NO_2	60	6	**4e**, 82	>99
4	*p*-$MeOC_6H_4$	Ph	CN	60	6	**5e**, 76	>99
5	*p*-$MeOC_6H_4$	*p*-ClC_6H_4	NO_2	60	20	**4f**, 89	>99
6	*p*-$MeOC_6H_4$	*p*-ClC_6H_4	CN	60	24	**5f**, 71	>99
7	Ph	Et	NO_2	80	2	**4g**, 87	>99
8	Ph	Et	CN	80	2	**5g**, 90	>99
9	Ph	Et	Cl	60	15[d]	**7g**, 44	>99
10	Ph	Et	H	60	15[d]	**8g**, 35	>99[e]

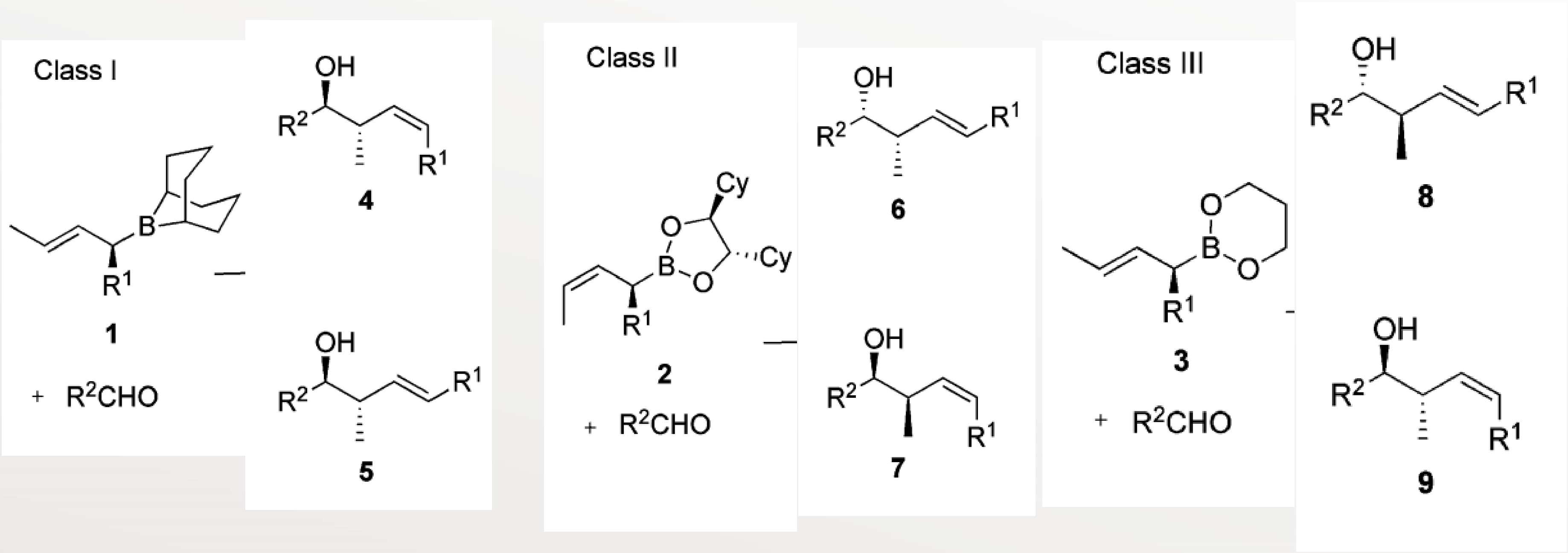
A. Ros, V. K. Aggarwal, *Angew. Chem. Int. Ed.*, **2009**, *48*, 6289-6292.

Total Synthesis of (+)-Faranal*



G. Dutheuil, M. P. Webster, P. A. Worthington, V. K. Aggarwal, *Angew. Chem. Int. Ed.*, **2009**, *48*, 6317-6319.

Stereodivergent Crotylation



M. Althaus, A. Mahmood, J. Ramón Suárez, S. P. Thomas, V. K. Aggarwal,*J. Am.Chem.Soc.*, **2010**, *132*, 4025-4028.

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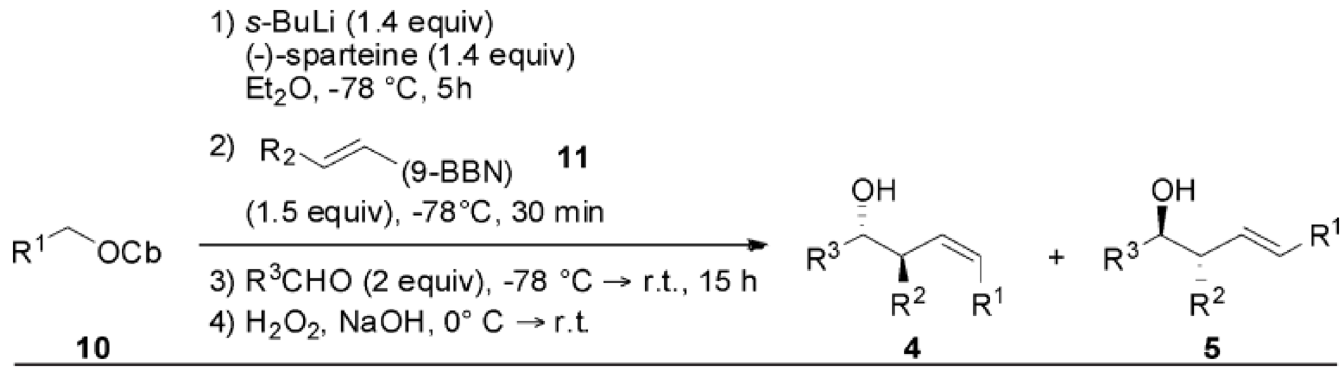
Class I Crotylation



entry	R^1	R^2	R^3	yield **4** (%)	er (**4**)	dr (**4**/**5**)
1	$Ph(CH_2)_2$	Me	Cy	84	96:4	>99:1
2	$Ph(CH_2)_2$	Me	Ph	82	97:3	>99:1
3	$Ph(CH_2)_2$	Bu	Ph	91	98:2	>99:1
4	$Ph(CH_2)_2$	Bu	Cy	78	98:2	>99:1
5	$Ph(CH_2)_2$	CH_2OSiMe_3	Ph	73	98:2	>99:1
6	$Ph(CH_2)_2$	Me	Bu	80	98:2	>99:1
7	*i*-Pr	Me	Ph	58	98:2	>99:1
8	*i*-Pr	Me	Cy	54	96:4	>99:1
9	*i*-Pr	Bu	Ph	60	95:5	98:2
10	Me	Me	Ph	88	60:40	>99:1
11	Me	Me	Cy	65	88:12	>99:1

M. Althaus, A. Mahmood, J. Ramón Suárez, S. P. Thomas, V. K. Aggarwal, *J. Am.Chem.Soc.*, **2010**, *132*, 4025-4028.

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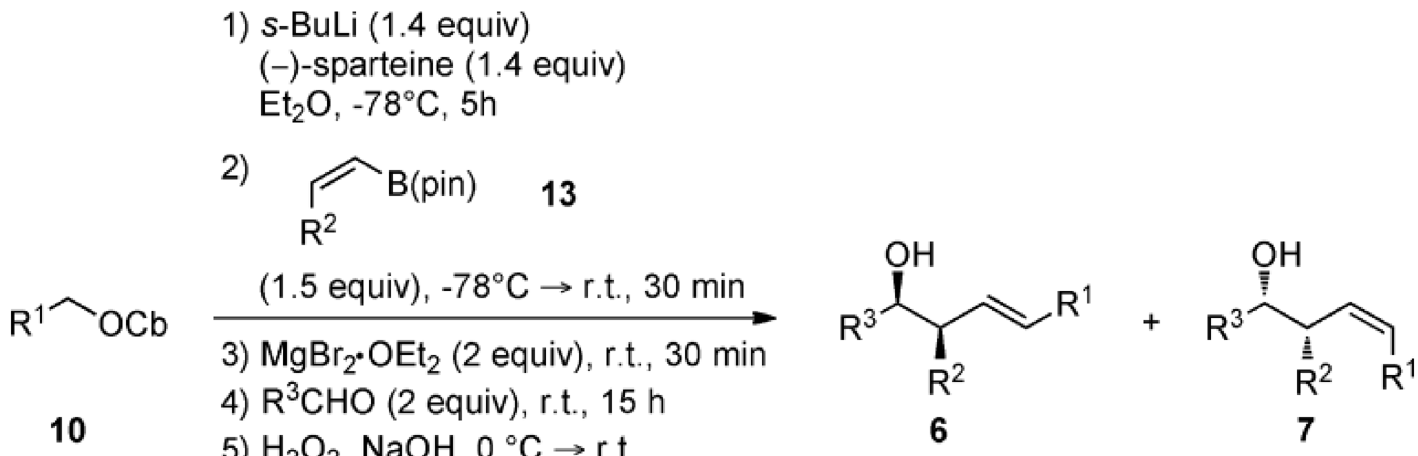
Class II Crotylation

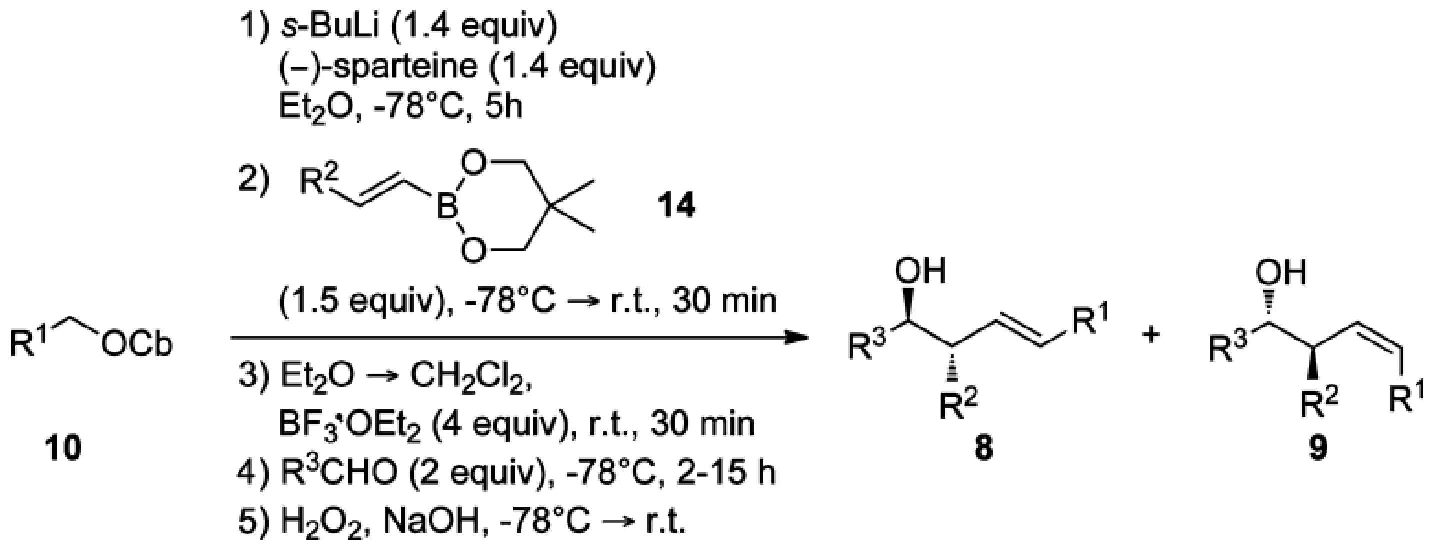


entry	R^1	R^2	R^3	yield **6** (%)	er (**6**)	dr (**6**/**7**)
1	$Ph(CH_2)_2$	Bu	Ph	54	99:1	>99:1
2	$Ph(CH_2)_2$	Me	Ph	46	99:1	>99:1
3[a]	$Ph(CH_2)_2$	Me	Cy	59	99:1	>99:1
4	Me	Me	Ph	56	99:1	>99:1
5[a]	Me	Me	Cy	46	99:1	>99:1

[a] Four equivalents of $MgBr_2 \cdot OEt_2$ used.

M. Althaus, A. Mahmood, J. Ramón Suárez, S. P. Thomas, V. K. Aggarwal, *J. Am.Chem.Soc.*, **2010**, *132*, 4025-4028.

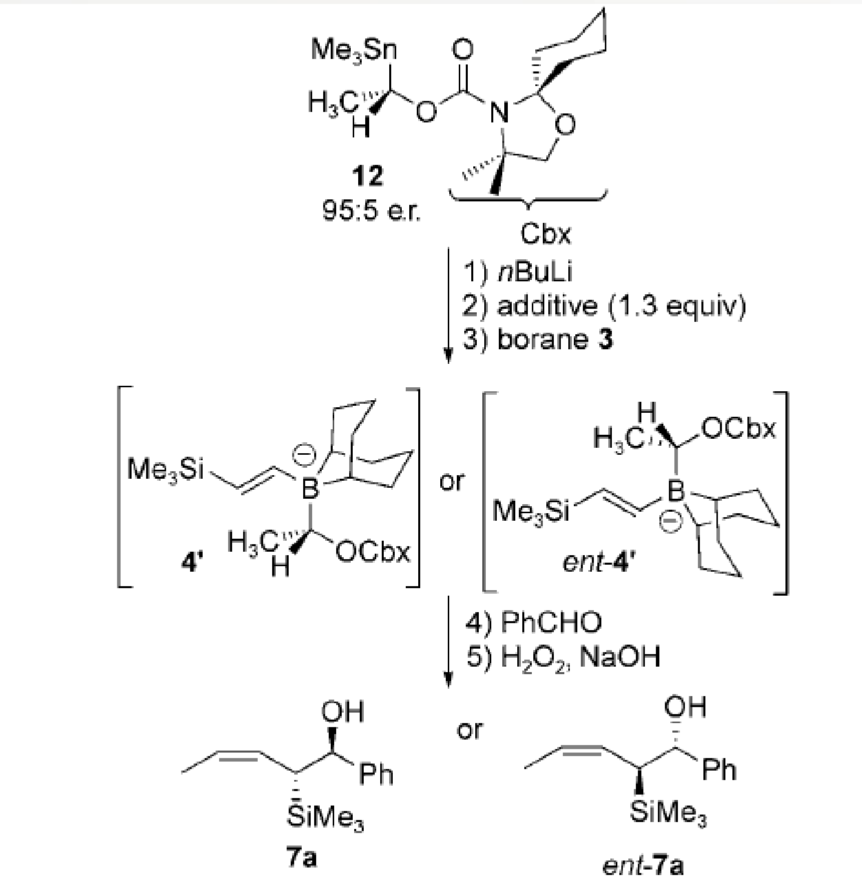
Class III Crotylation

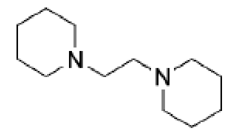
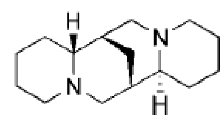
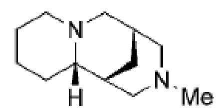


entry	R^1	R^2	R^3	yield **8** (%)	er (**8**)	dr (**8**/**9**)
1	$Ph(CH_2)_2$	Me	Ph	67	98:2	>99:1
2	$Ph(CH_2)_2$	Me	Cy	60	98:2	>99:1
3	$Ph(CH_2)_2$	Bu	Ph	58	99:1	>99:1
4	$Ph(CH_2)_2$	Bu	Cy	67	99:1	>99:1
5	Me	Me	Ph	51	95:5	>99:1
6	Me	Me	Cy	58	99:1	>99:1

M. Althaus, A. Mahmood, J. Ramón Suárez, S. P. Thomas, V. K. Aggarwal, *J. Am.Chem.Soc.*, **2010**, *132*, 4025-4028.

Unusual Inversion during 1,2 metallate migration



Entry	Additive	Stereochemical outcome	**7a**/*ent*-**7a**	Yield [%]
1	none	retention	94:6	95
2	TMEDA[a]	retention	91:9	78
3		retention	92:8	87
4		inversion	8:92	83
5		inversion	35:65	50
6		inversion	35:65	94

M. Binanzer, G. Y. Fang, V. K. Aggarwal, *Angew. Chem. Int. Ed.*, **2010**, *49*, 4264-4268.

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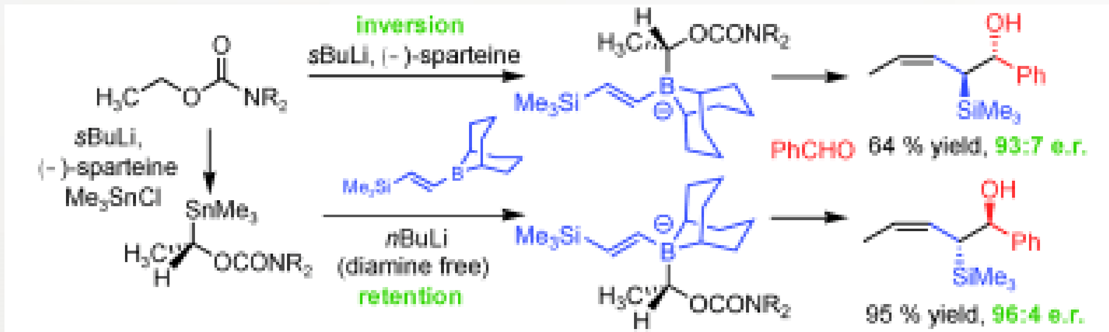
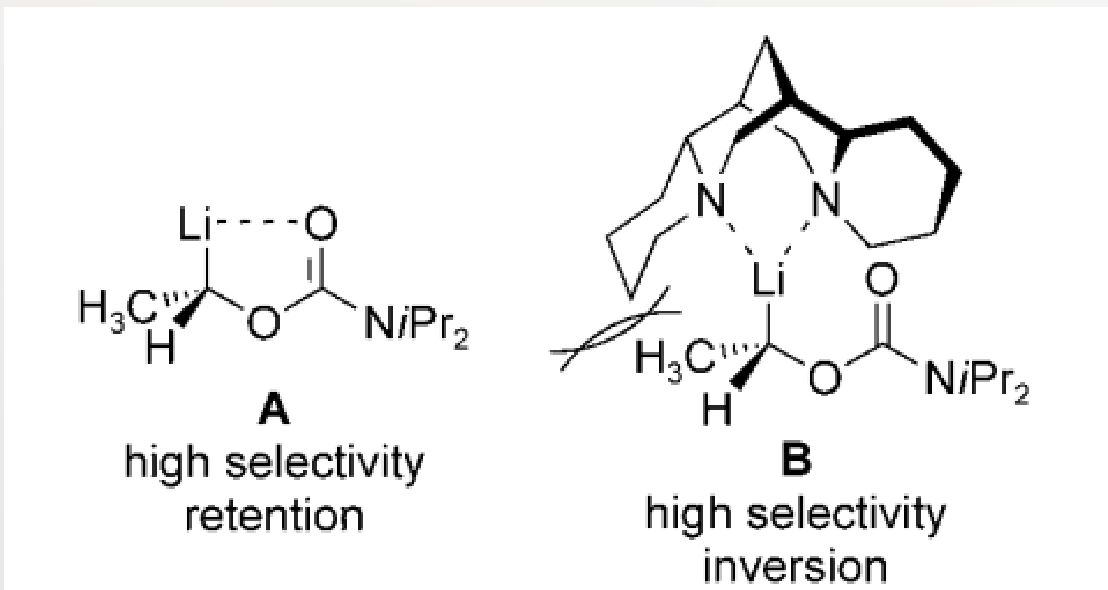
Unusual Inversion during 1,2 metallate migration





M. Binanzer, G. Y. Fang, V. K. Aggarwal,*Angew. Chem. Int. Ed.*, **2010**, *49*, 4264-4268.

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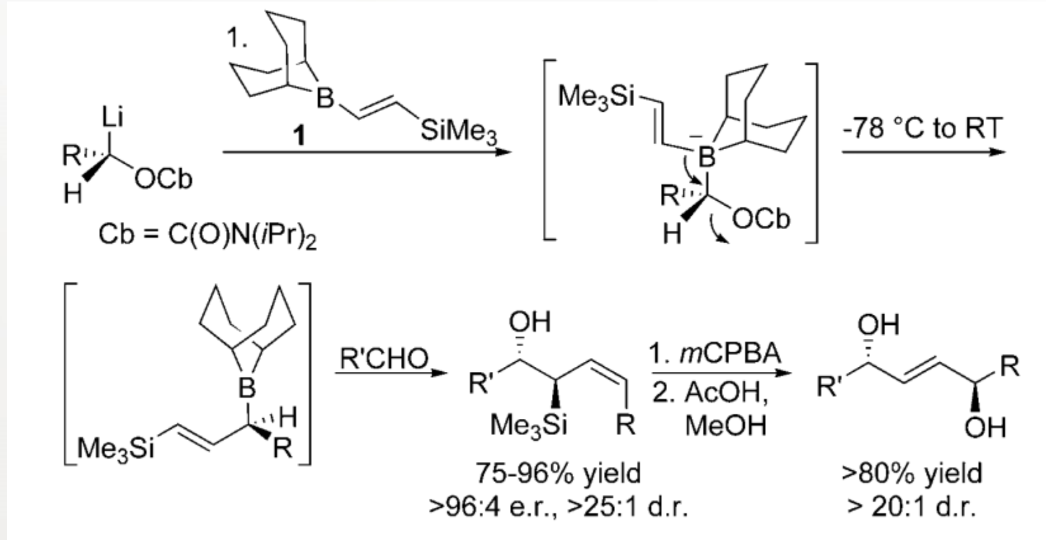
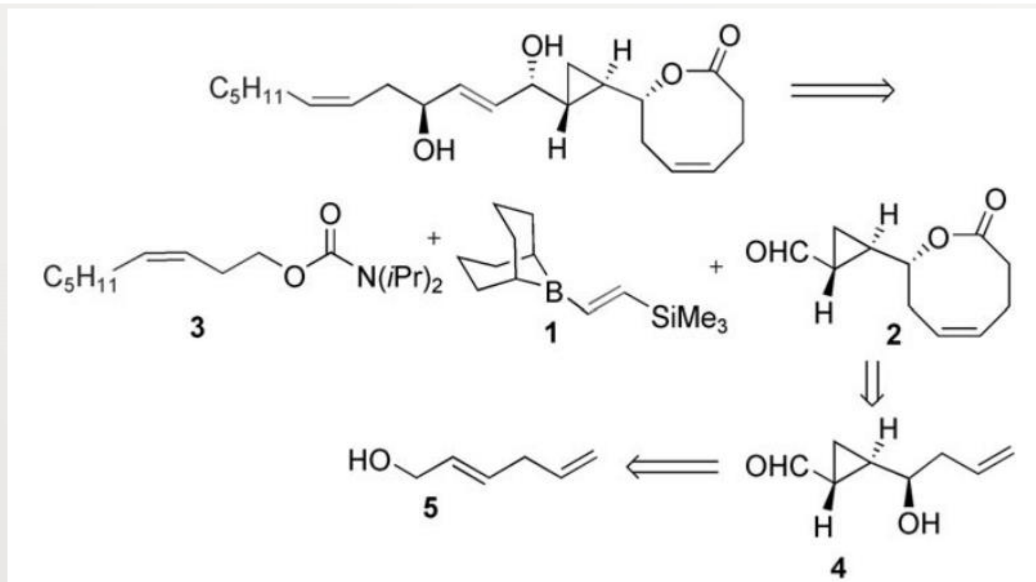
Total Synthesis of Solandelactone E:





V. Bagutski, R. M. French, V. K. Aggarwal, *Angew. Chem. Int. Ed.*, **2010**, *49*, 5142-5145.

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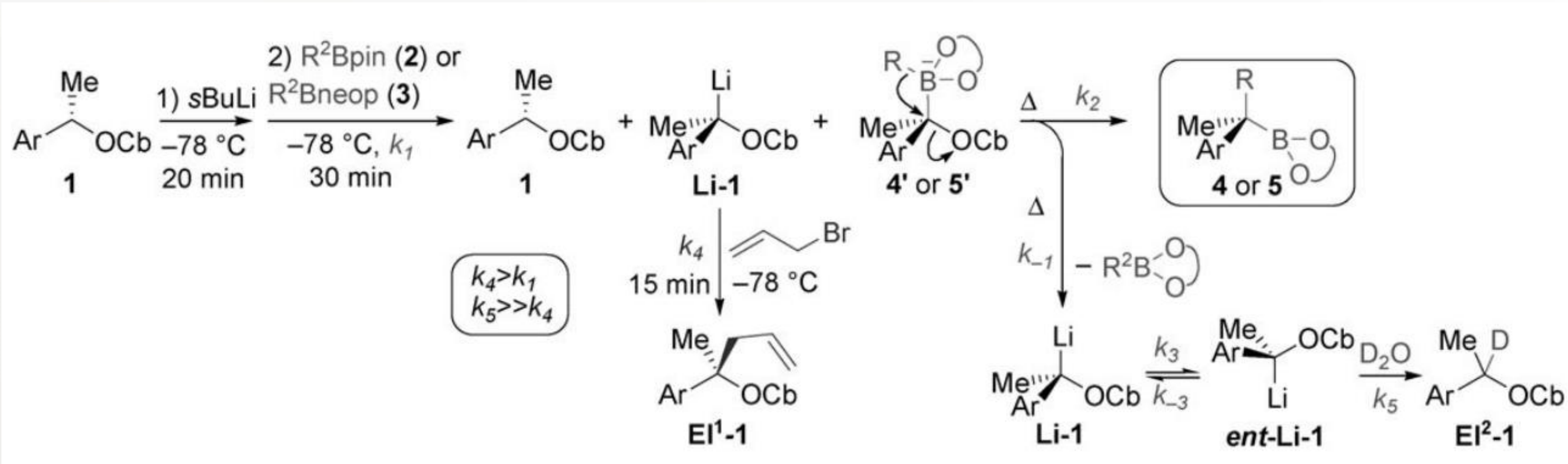
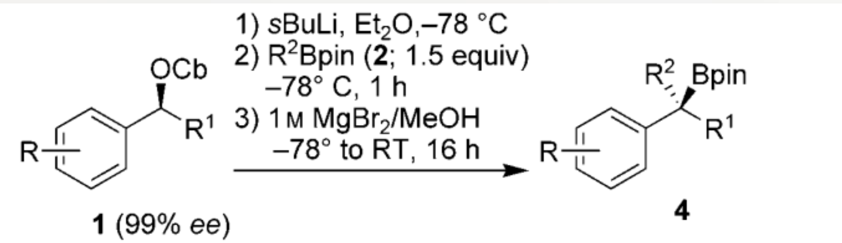


Improved 100% Charity Transfer



Entry	Substrate 1	R	R^1	R^2Bpin 2	R^2		Yield of 4 [%][a] (ee [%][b])
1	1a	H	Me	2c	iPr	4ac	92 (99)
2	1a	H	Me	2d	cHex	4ad	87 (99)
3	1b	H	Et	2a	Me	4ba	71 (99)
4	1b	H	Et	2c	iPr	4bc	74 (99)
5	1b	H	Et	2d	cHex	4bd	61 (99)
6	1b	H	Et	2e	cinnamyl	4be	91 (99)[c]
7	1b	H	Et	2f	4-BrC$_6$H$_4$	4bf	82 (99)[c]

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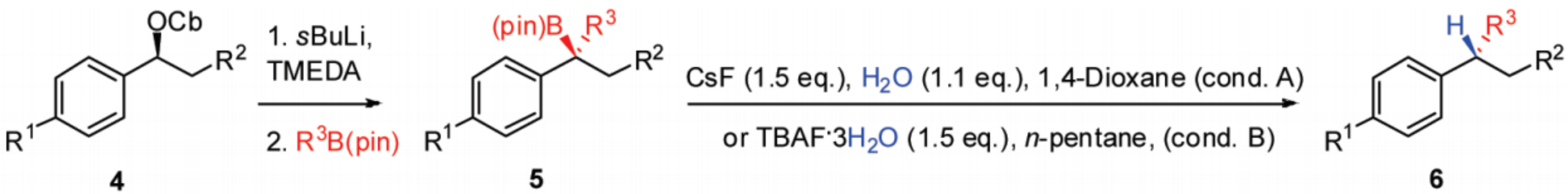
Stereospecific Proto-deboranlation



Entry	R^1	R^2	e.r. of carbamate	R^3	5[b] yield	5[b] e.r.	Conditions[c]	6 yield	6 e.r.	6 % es
1	H	H	**4a** 99.9:0.1	*p*-ClC_6H_4	**5a** 89%	99.7:0.3	A, 30 °C	**6a** 82%	97.3:2.7	98%
2	OMe	H	**4b** 99.5:0.5	Ph	**5b** 85%	98.3:1.7	A, 65 °C	**6b** 99%	98.1:1.9	99%
3	H	H	**4a** 99.9:0.1	2-furyl	**5c** 79%	99.0:1.0	A, 35 °C	**6c** 99%	97.9:2.1	98%
4	H	Me	**4c** 99.9:0.1	*p*-ClC_6H_4	**5d** 71%	99.4:0.6	A, 30 °C	**6d** 91%	98.7:1.3	99%
5	H	H	**4a** 99.9:0.1	Et	**5e** 68%	99.7:0.3	B, 45 °C	**6e** 97%	98.8:1.2	99%
6	Cl	H	**4d** 99.6:0.4	Et	**5f** 83%	99.4:0.6	B, 45 °C	**6f** 99%	98.9:1.1	99%
7	OMe	H	**4b** 99.9:0.1	Et	**5g** 88%	99.9:0.1	B, 45 °C	**6g** 90%	99.8:0.2	99%
8	H	H	**4a** 99.5:0.5	^{i}Pr	**5h** 98%	99.5:0.5	B, 45 °C	**6h** 96%	99.2:0.8	99%
9	H	H	**4e** *rac*	Vinyl	**5i** 57%	*rac*	B, 30 °C	**7** 91%	*E*:*Z* > 20:1[d]	-
10	H	H	**4a** 99.9:0.1	Allyl	**5j** 91%	99.6:0.4	B, 45 °C	**6j** 98%	99.5:0.5	99%
11	H	Me	**4c** 99.9:0.1	Allyl	**5k** 59%	99.9:0.1	B, 30 °C	**6k** 79%	99.9:0.1	99%

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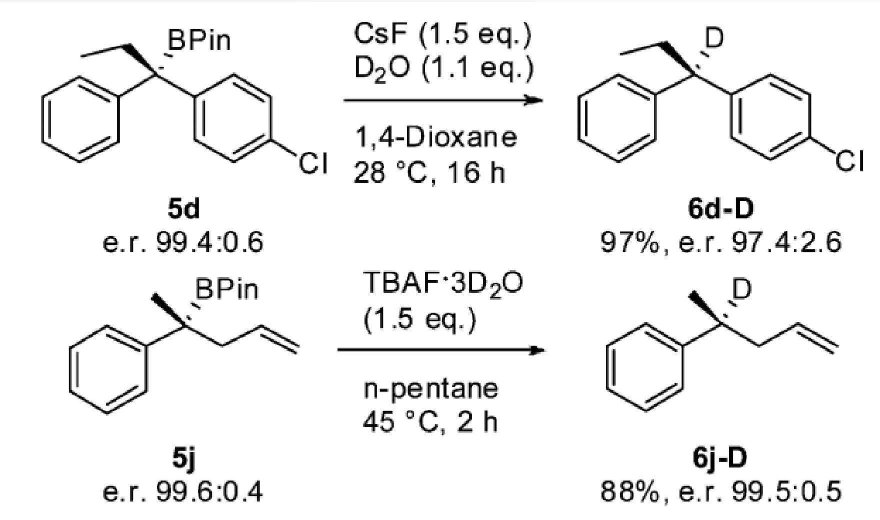
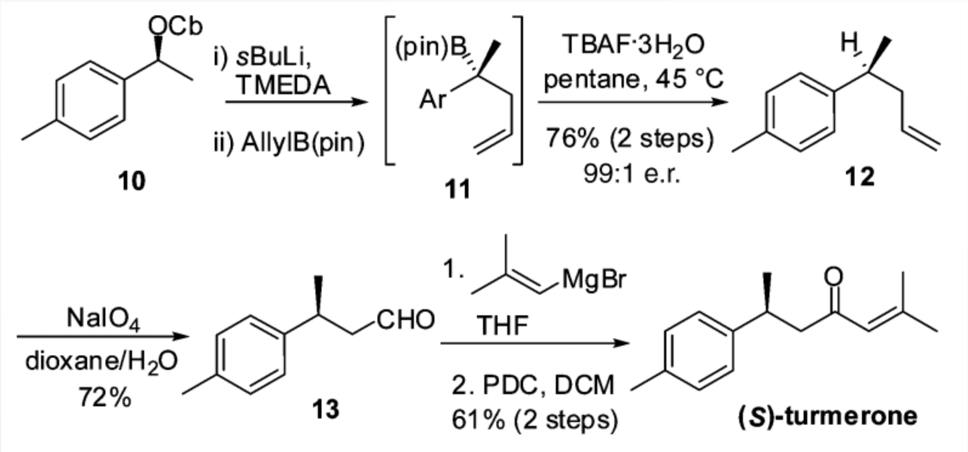
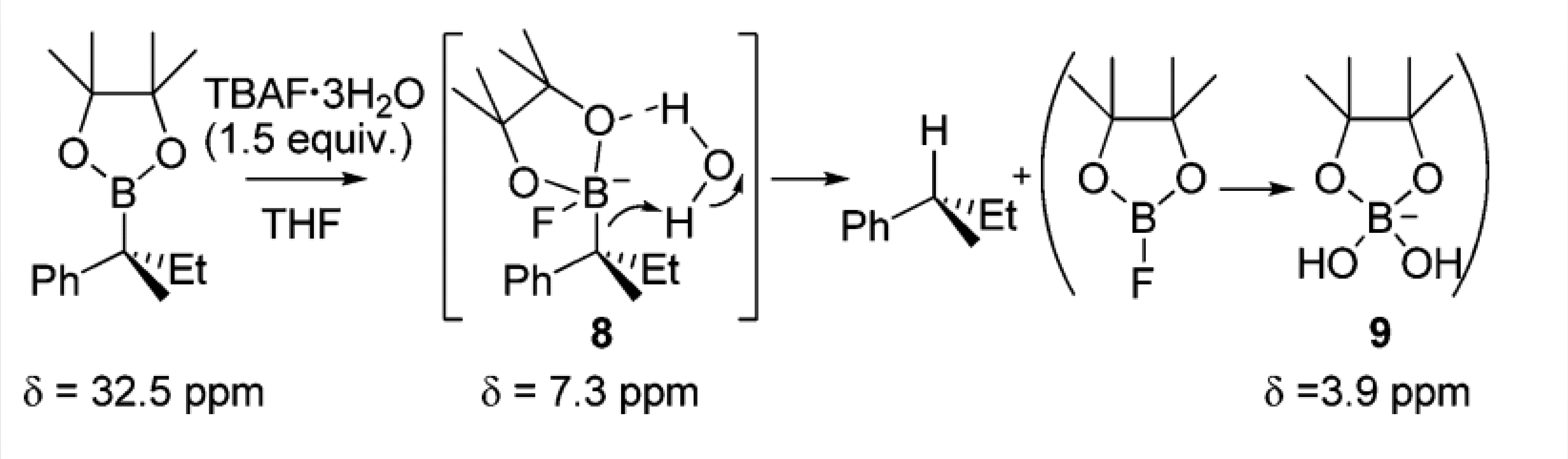
Stereospecific Proto-deboranlation







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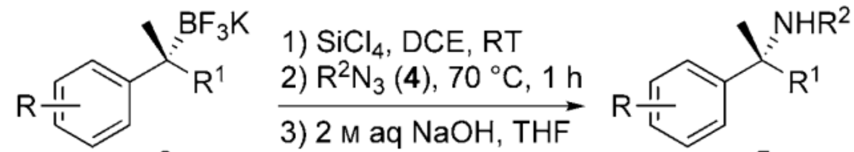
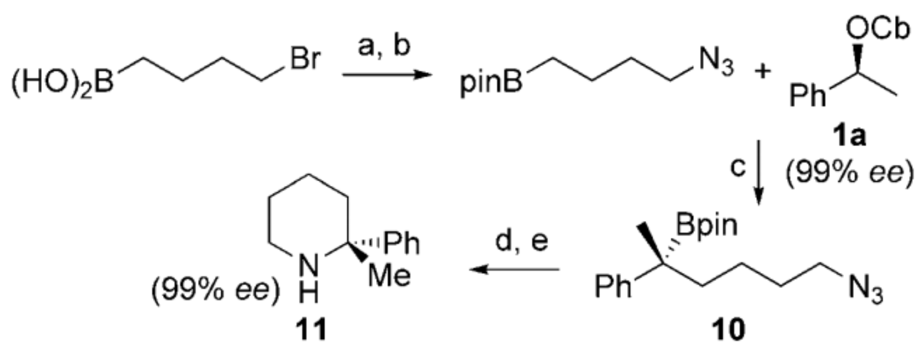
Chiral Amine From Chiral Boron

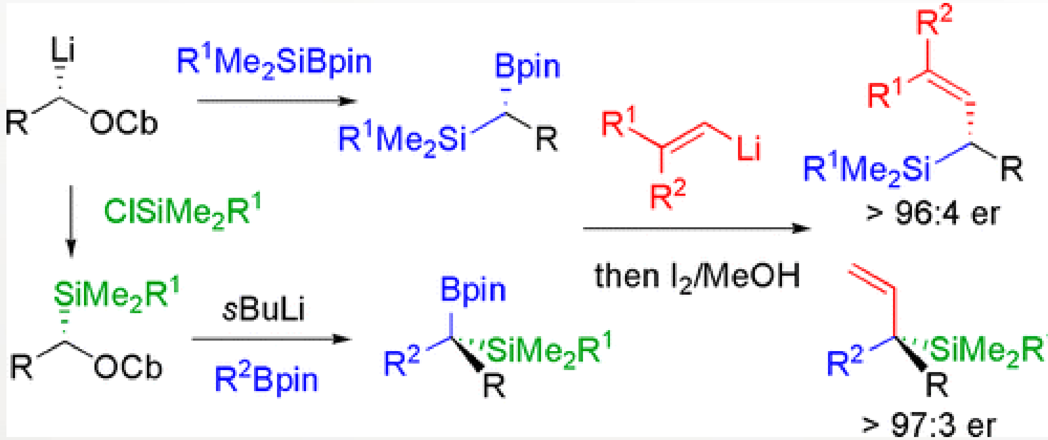


3 5

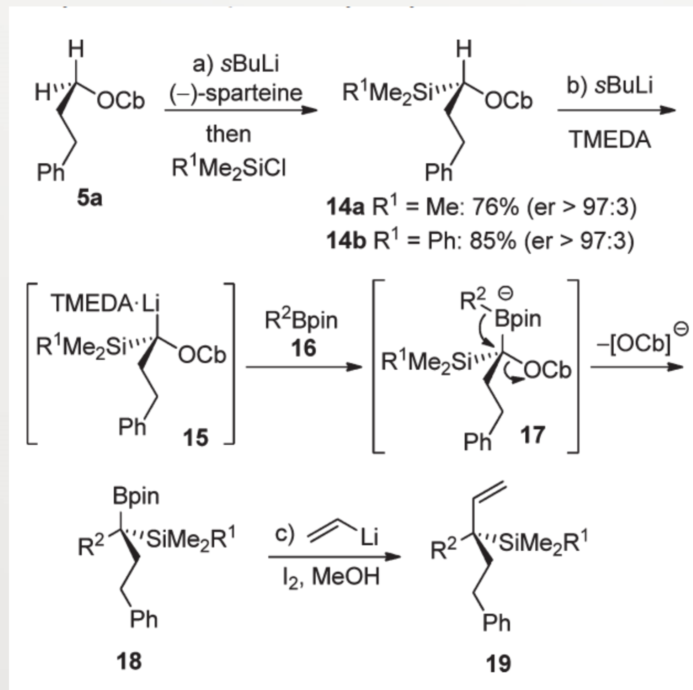
Entry	3[b]	R	R1	4	R2	5	Yield [%] (*ee* [%])[c]
1	**a**	H	Et	**a**	Bn	**aa**	94 (99)
2	**a**	H	Et	**b**	PMB	**ab**	73 (99)
3	**a**	H	Et	**c**	*c*PrCH_2	**ac**	89 (99)
4	**b**	H	*c*Hex	**a**	Bn	**ba**	78 (99)
5	**c**	4-Cl	*i*Pr	**a**	Bn	**ca**	76 (99)
6	**d**	2-F	*c*Hex	**a**	Bn	**da**	47 (99)
7	**e**	H	4-ClC_6H_4	**a**	Bn	**ea**	74 (99)
8	**f**	H	3-MeOC_6H_4	**a**	Bn	**fa**	69 (99)



V. Bagutski, T. G. Elford, V. K. Aggarwal.*Angew. Chem. Int. Ed.*, **2011**, *50*, 1080-1083

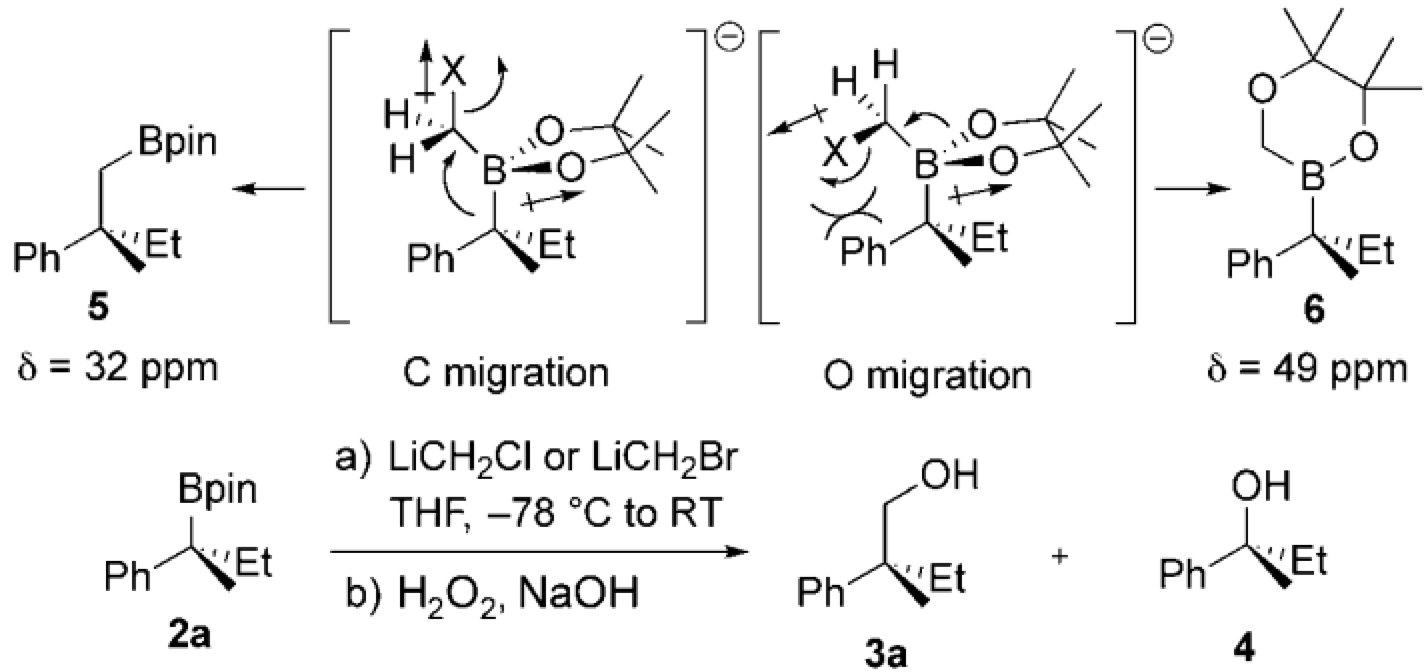


Using Zweifel Olefination To work up



V. K. Aggarwal, M. Binanzer, M. Carolina de Ceglie, M. Gallanti, B. W. Glasspoole, S. J. F. Kendrick, R. P. Sonawane, A. Vazquez-Romero, M. P. Webster. *Org. Lett.*, **2011**, *13*, 1490-1493

In-situ Cascade to form Quaternary Carbon



Entry	Reagent	Equiv	Yield **3a**	% O migration
1	$LiCH_2Cl$	2.2	71%	20%
2	$LiCH_2Cl$	4.0	63%	20%
3	$LiCH_2Br$	2.2	83%	5%

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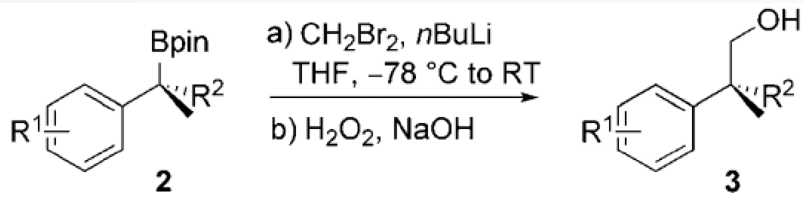
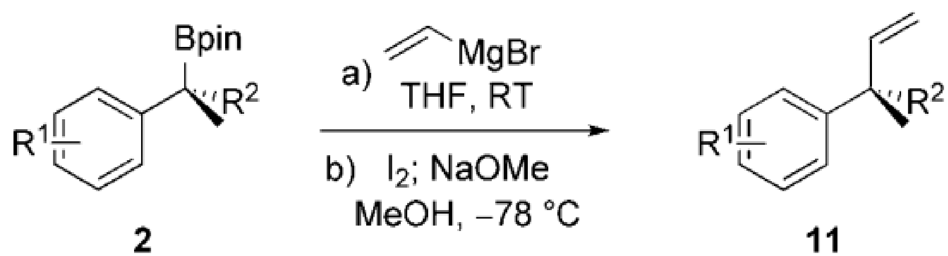
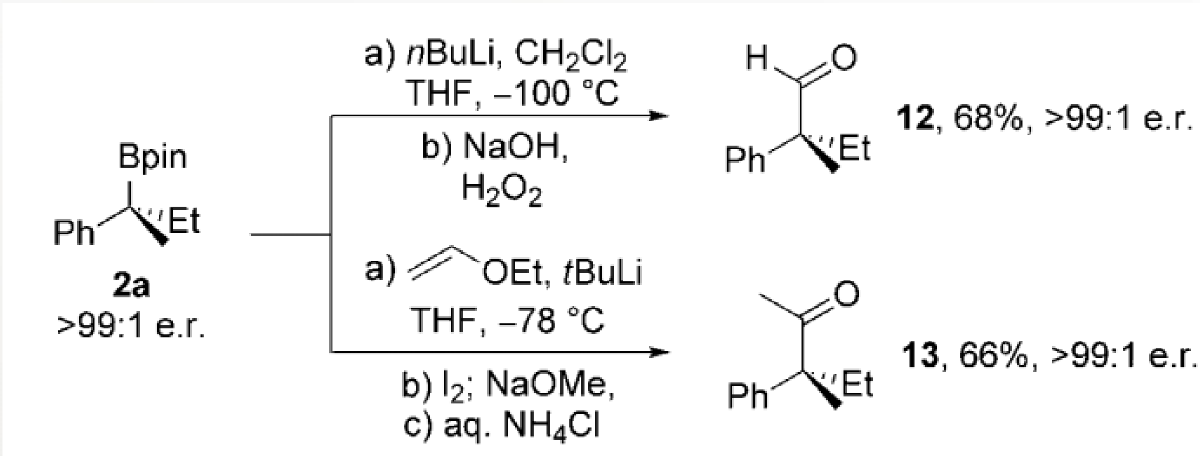
In-situ Cascade to form Quaternary Carbon

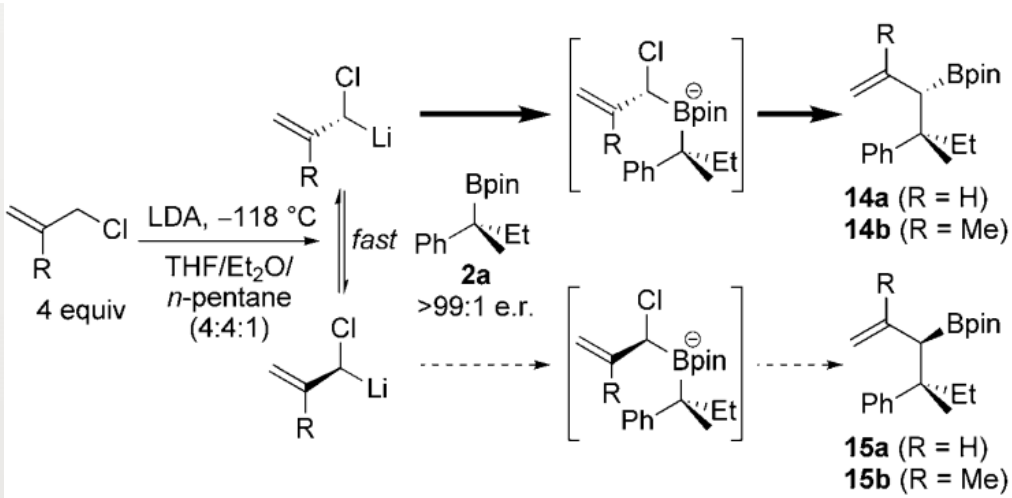


Entry		Boronic ester R^1	Boronic ester R^2	Boronic ester e.r.		Product Yield [%][b]	Product e.r.[c]
1	**2a**	H	Et	>99:1	**3a**	83	>99:1
2	**2b**	*p*Cl	Et	>99:1	**3b**	88	>99:1
3	**2c**	*p*MeO	Et	>99:1	**3c**	62	99:1
4	**2d**	H	allyl	>99:1	**3d**	82	>99:1
5	**2e**[d]	H	*i*Pr	>99:1	**3e**	37	>99:1
6	**2f**	*p*MeO	Ph	98:2	**3f**	41	98:2



R. P. Sonawane, V. Jheengut, C. Rabalakos, R. Larouche-Gauthier, H. K. Scott, V. K. Aggarwal, *Angew. Chem. Int. Ed.*, **2011**, *50*, 3760-3763.





	Yield (**14**+**15**)	d.r. (**14**:**15**)	e.r. (**14**)
a) R = H	73%	24:1	99:1
b) R = Me	96%	10:1	99:1

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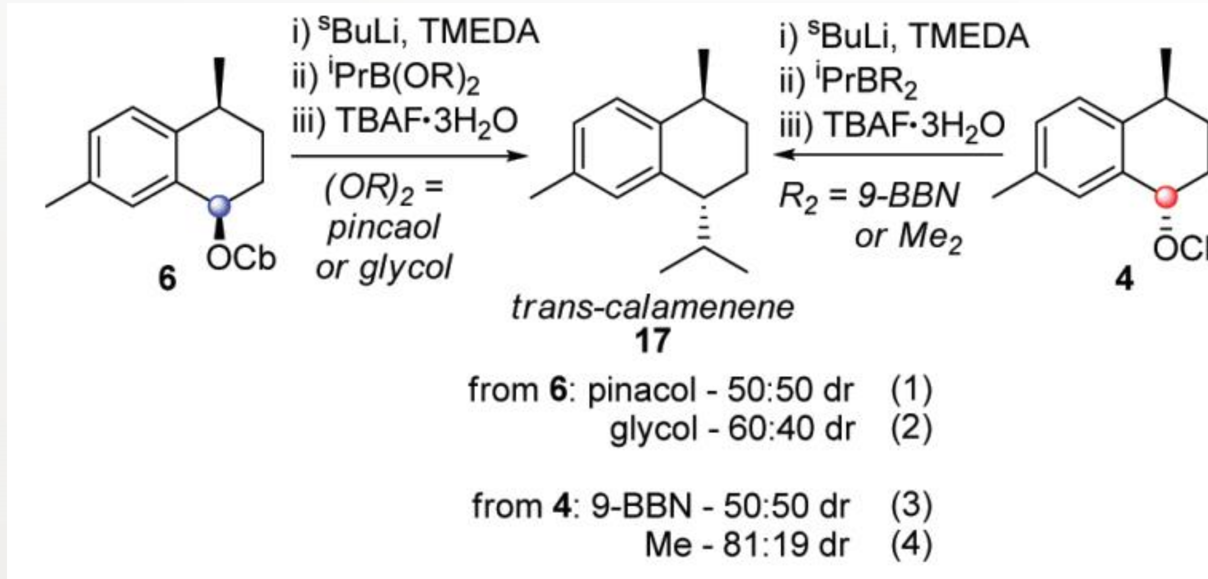
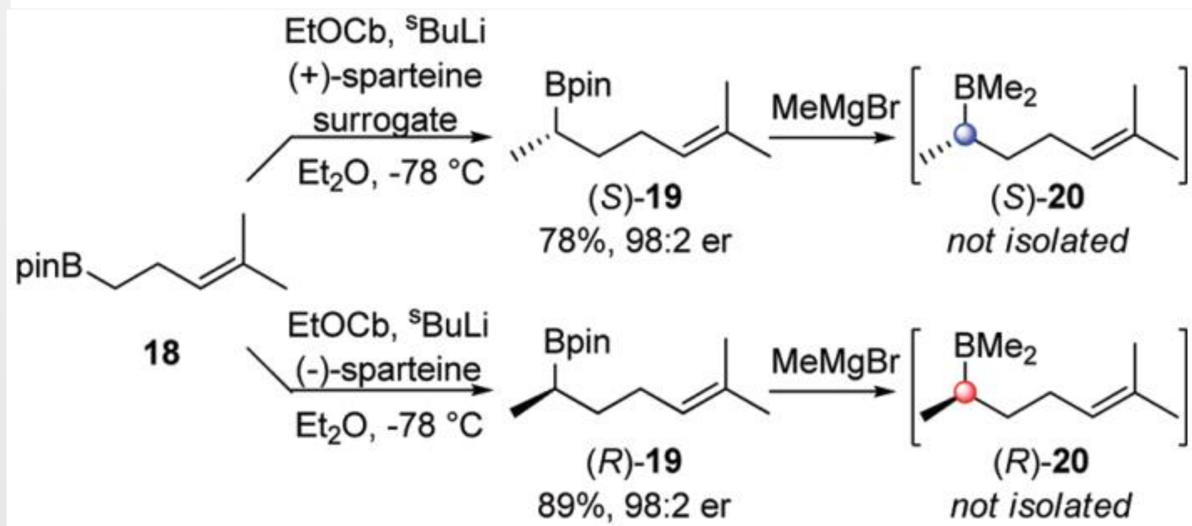
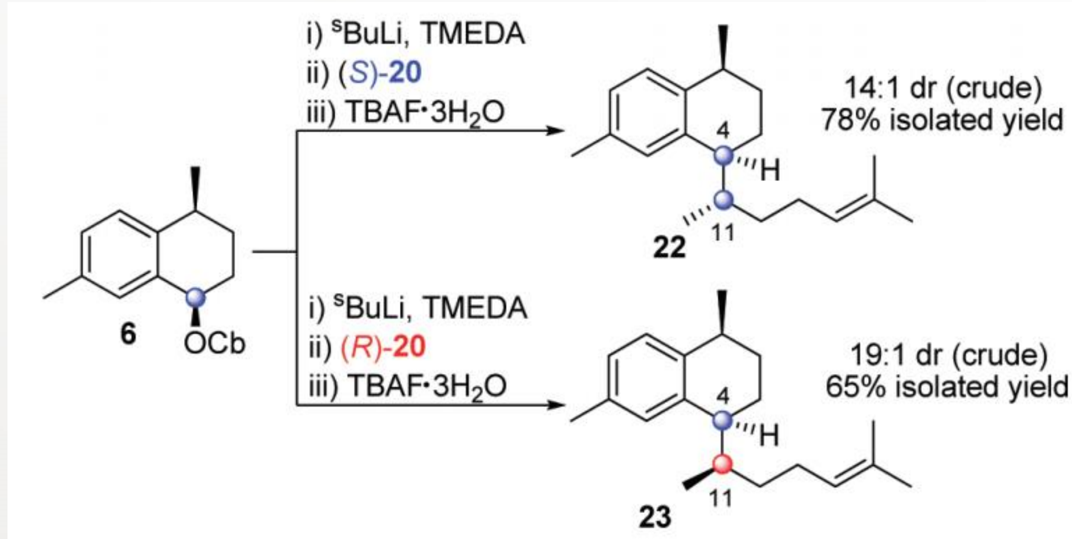
Total Synthesis of (+)-Erogorgiaene

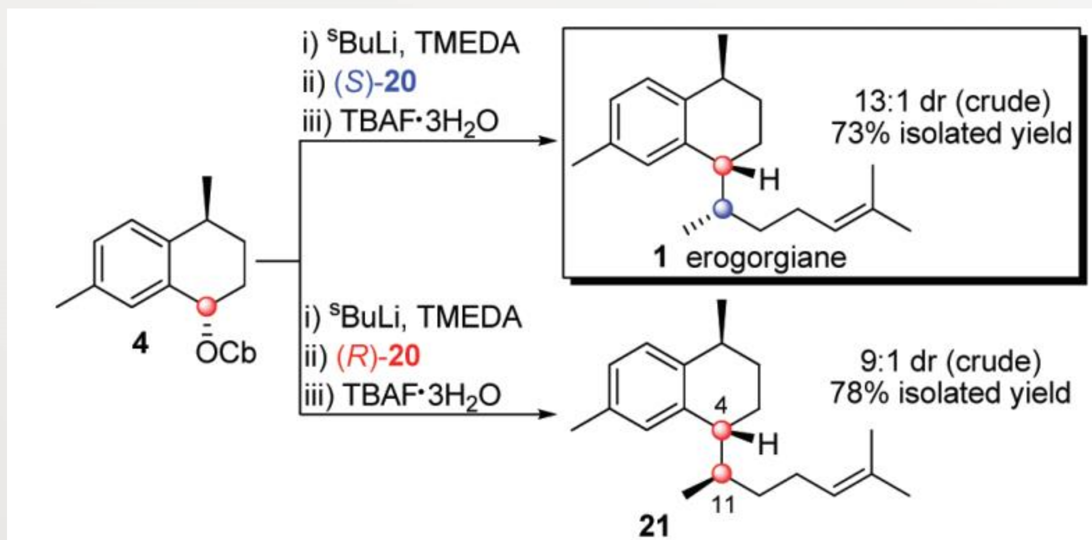




T. G. Elford, S. Nave, R. P. Sonawane, V. K. Aggarwal, *J. Am. Chem. Soc.*, **2011**, *133*, 16798-16801

Total Synthesis of (+)-Erogorgiaene





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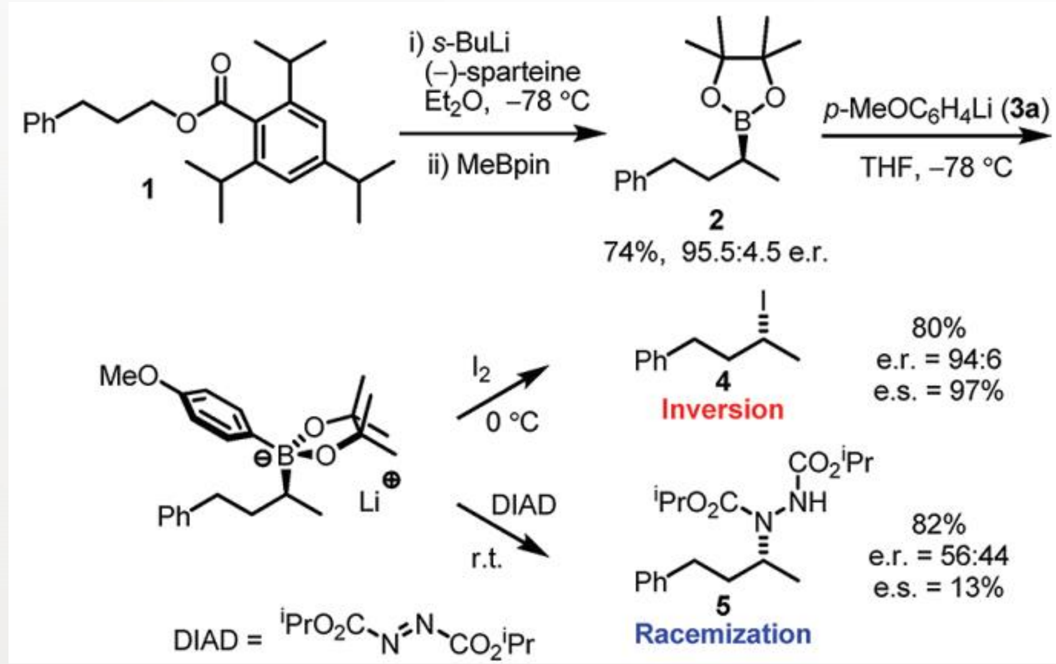
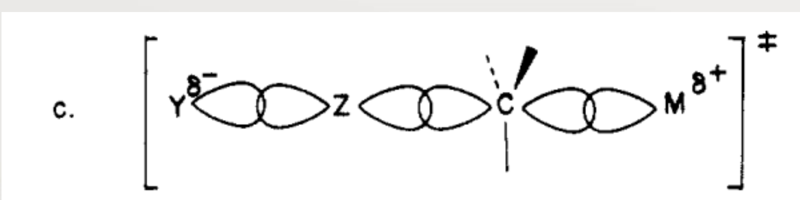
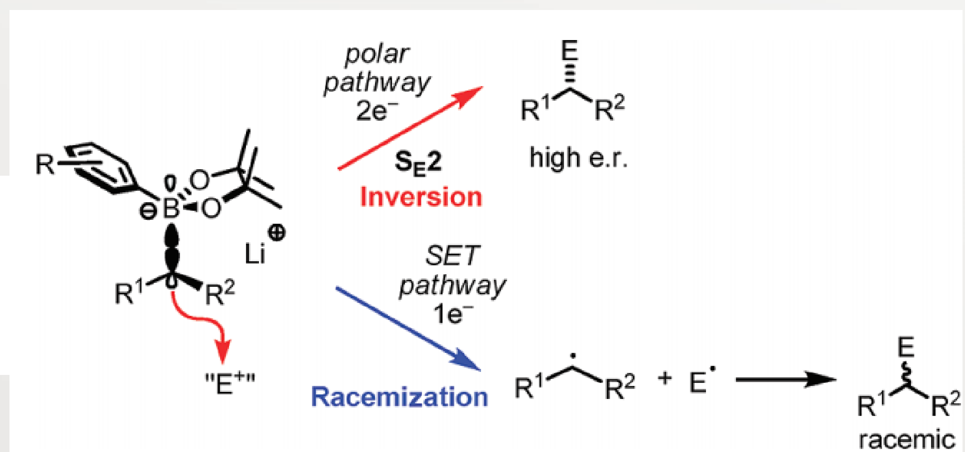
Chiral Organometallic Type Nucleophiles for Asymmetric Synthesis.



A type orbital for S_E2 Inservsion





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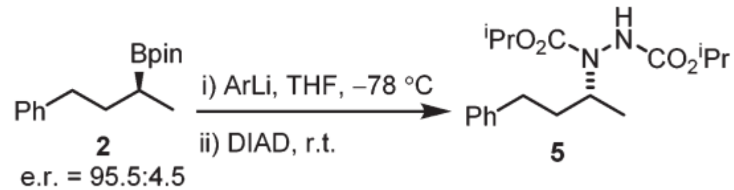
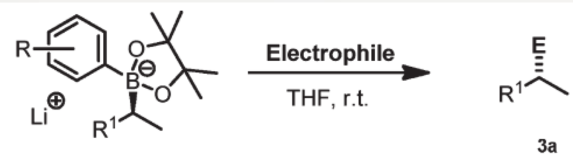
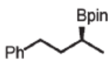
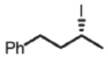
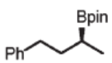
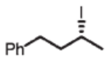
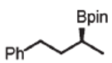
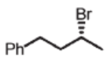
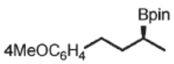
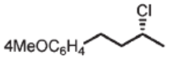
Activating group Effect.



entry	Ar	yield (%)	e.r.	e.s. (%)
1	4-$MeOC_6H_4$ (**3a**)	82	56:44	13
2	4-FC_6H_4	78	59:41	20
3	Ph	90	63:37	29
4	4-$CF_3C_6H_4$	85	70:30	44
5	3,5-$(CF_3)_2C_6H_3$ (**3b**)	74	80:20	66

Scope of electrophile



entry	boronic ester	electro-phile	product	3a yield (%)	3a e.s. (%)	3b yield (%)	3b e.s. (%)
1[b]		I_2		84	97	---	---
2		NIS		80	100	85	99
3		NBS		50	90	85	100
4[c,d]		TCCA		60	66	80	92

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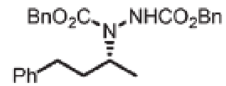
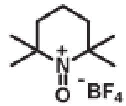
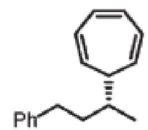
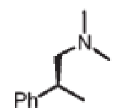
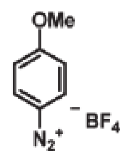
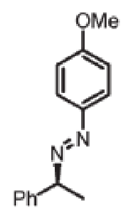
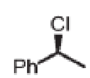
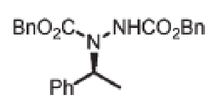
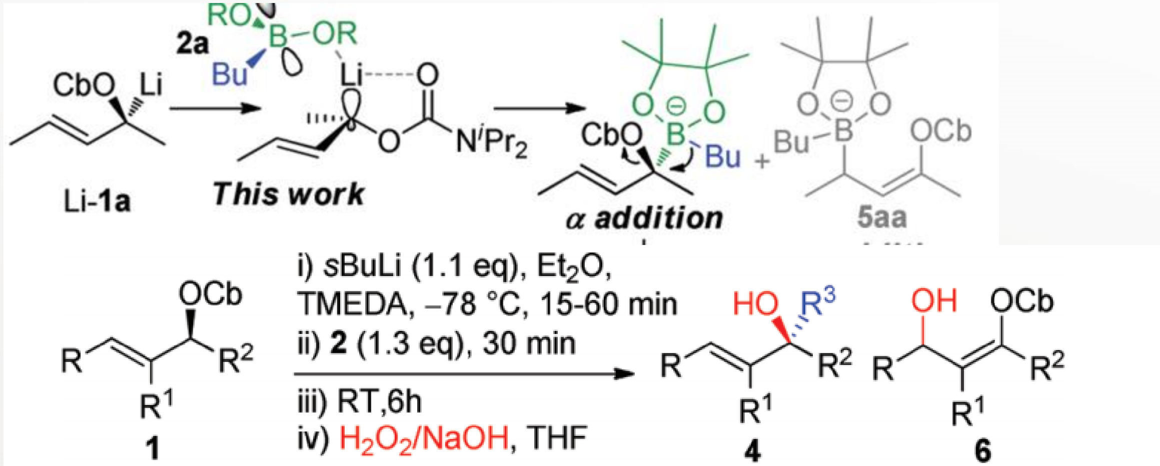
7[f]		DBAD		---	---	66	92
8[g]				---	---	64[h]	70
9				67	93	62	100
10				98	100	---	---
11				0	---	64	94
12[b]				0	---	44	100
13[e]		TCCA		52[i]	65	54[i]	96
14		DBAD		85	0	80	98

R. Larouche-Gauthier, T. G. Elford, V. K. Aggarwal,*J. Am. Chem. Soc.*, **2011**, *133*, 16794-16797

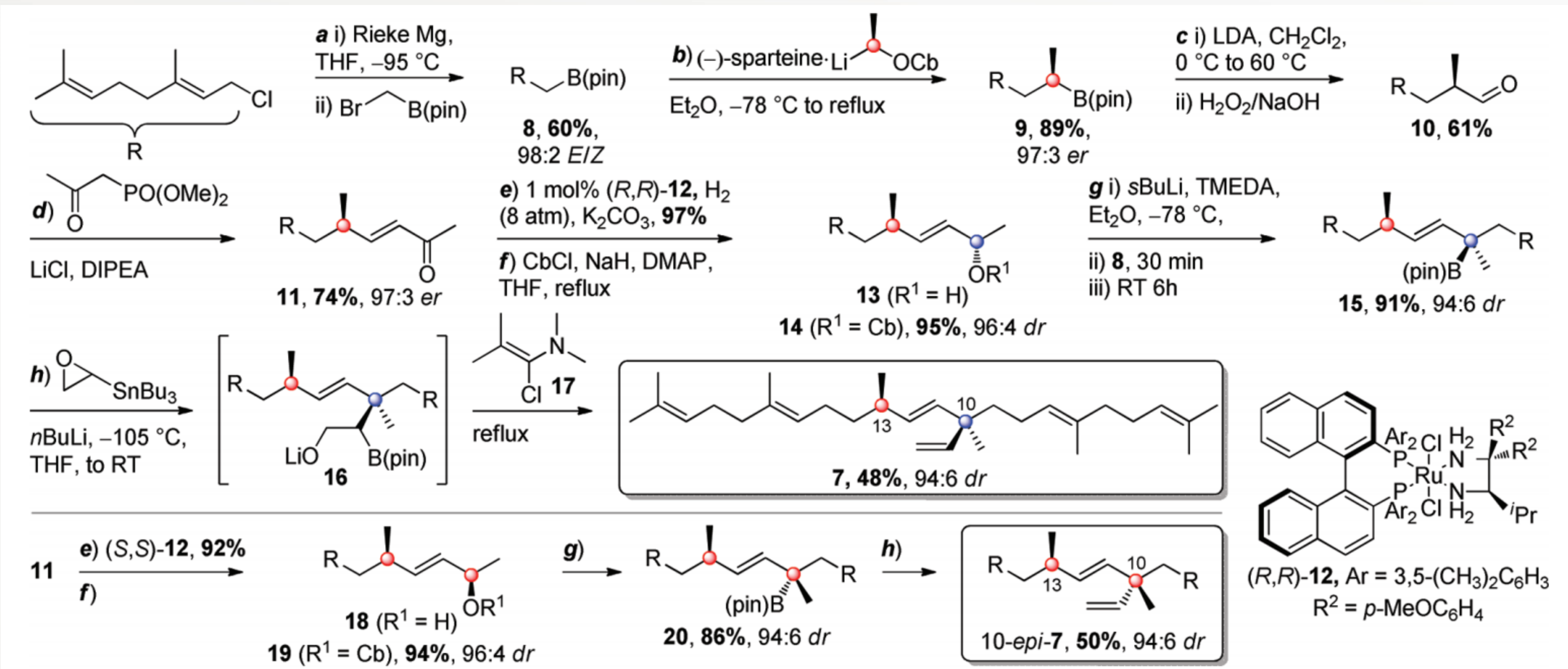
OrganoLithium From Chiral Secondary Allylic Carbamates



#	1 (er)[a]	R	R^1	R^2	R^3	4 / % (er)[b]		6 / %[b]
1	1a (>99:1)	Me	H	Me	*n*Bu 2a	4aa	75 (98:2)	c
2	1a (>99:1)	Me	H	Me	(CH$_2$)$_2$Ph 2b	4ab	92 (98:2)	c
3	1a (>99:1)	Me	H	Me	cHex 2c	4ac	76[d,e] (99:1)	c
4	1a (>99:1)	Me	H	Me	allyl 2d	4ad	77 (98:2)	7[f]

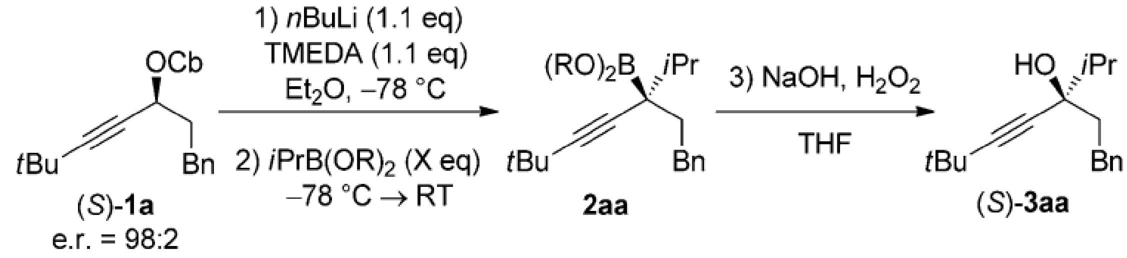
A. P. Pulis, V. K. Aggarwal, *J. Am. Chem. Soc.*, **2012**, *134*, 7570-7574

Total Synthesis of C30 Botryococcene.

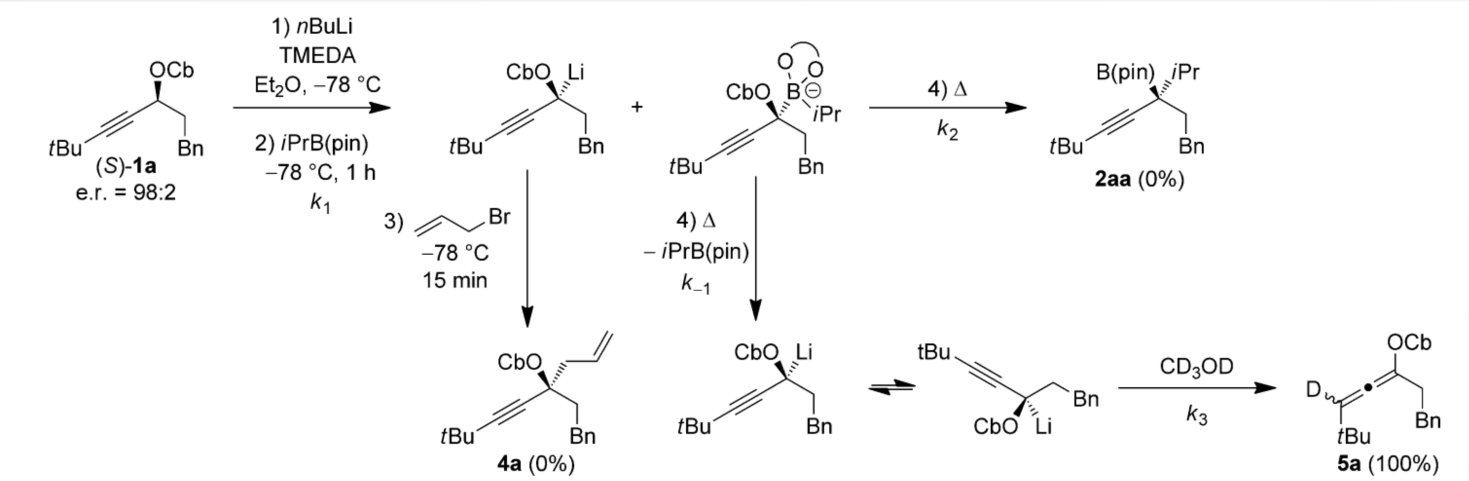


A. P. Pulis, V. K. Aggarwal, *J. Am. Chem. Soc.*, **2012**, *134*, 7570-7574

OrganoLithium From Chiral Secondary Propargyl Carbamates

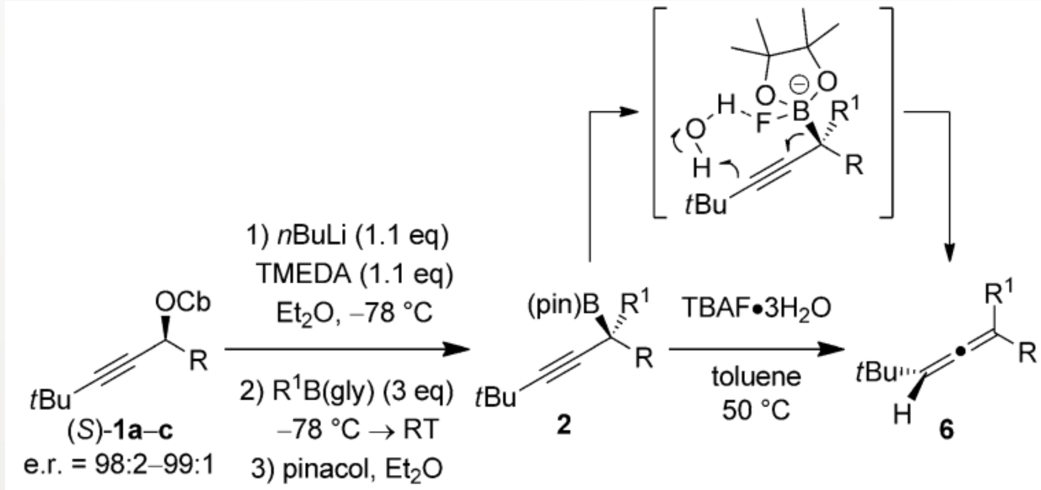


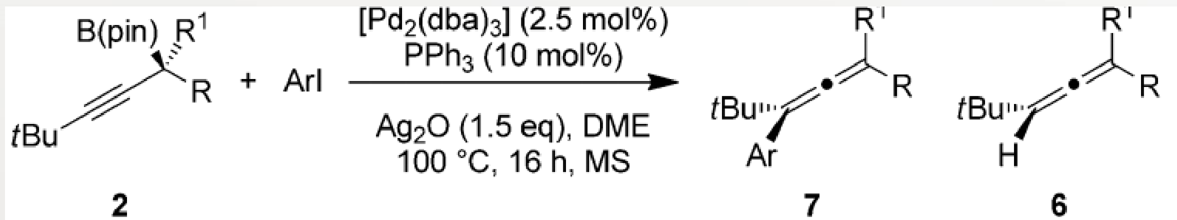
Entry	Diol [(OR)$_2$]	X [equiv]	Product	Yield [%]	e.r.[a]	e.s. [%][b]
1	pinacol	2	**2aa**	55[c]	51:49	2
2	pinacol	3	**2aa**	55[d]	52:48	4
3	neopentyl	2	**3aa**	51[d]	68:32	38
4	neopentyl	3	**2aa**	80[c]	89:11	81
5	ethylene glycol	2	**3aa**	48[d]	98:2	100



B. M. Partridge, L. Chausset-Boissarie, M. Burns, A. P. Pulis, V. K. Aggarwal, *Angew. Chem. Int. Ed.*, **2012**, *51*, *11795–11799*.

From
Propargyl
Borate
To chiral allene

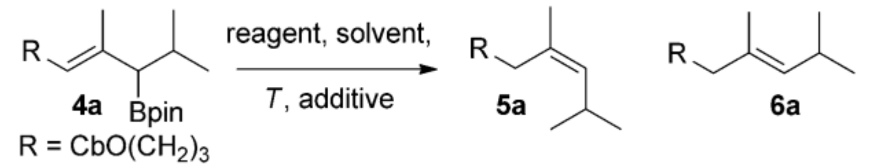




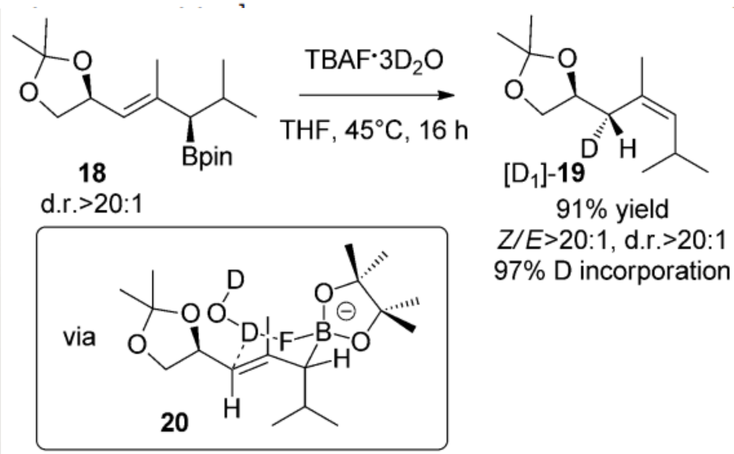
Entry	R	R^1	Ar	Ratio **7**:**6**[a]	Product (% yield)[b]	e.s. [%]
1	CH_2Bn **a**	Et **b**	Ph **a**	100:0	**7 aba** (83)	98
2	CH_2Bn **a**	Et **b**	pBrC$_6$H$_4$ **b**	90:10	**7 abb** (65)	98
3	CH_2Bn **a**	Et **b**	pAcC$_6$H$_4$ **c**	95:5	**7 abc** (80)	98
4	CH_2Bn **a**	Et **b**	pMeOC$_6$H$_4$[c] **d**	80:20	**7 abd** (72)	98

B. M. Partridge, L. Chausset-Boissarie, M. Burns, A. P. Pulis, V. K. Aggarwal, *Angew. Chem. Int. Ed.*, **2012**, *51*, *11795–11799*.

Fine tuning Of α and γ Seletivite Protonation Of Ally boron

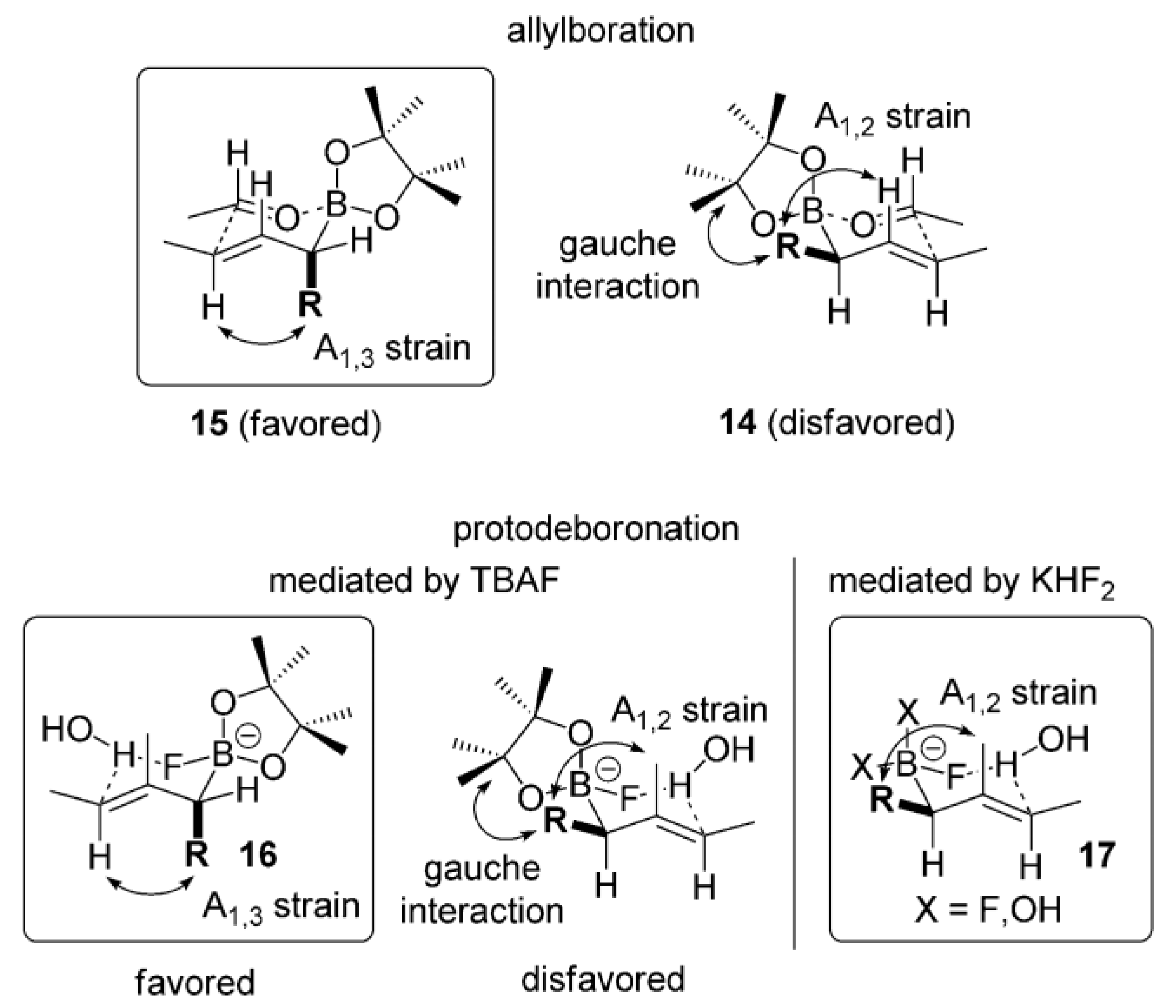


Ent.	Reagent	Solvent	T [°C]	Add.	5a:6a[a]	Yield [%][b]
1	TBAF·3 H_2O[c]	THF	45	–	>20:1	quant.
2	AcOH	neat	80	–	n.d.	42
3	AcOH	neat	120	–	5:1	85
4	CsF,[d] H_2O[e]	THF	45	–	–	trace
5	KHF_2[f]	MeOH/H_2O[g]	23	–	1:4	95
6	KHF_2[f]	MeOH/H_2O[g]	0	–	1:5	96
7	KHF_2[f]	MeOH/H_2O[g]	−30	TsOH[h]	1:7.5	94
8	KHF_2[f]	MeOH/H_2O[g]	−78	TsOH[h]	1:9	96



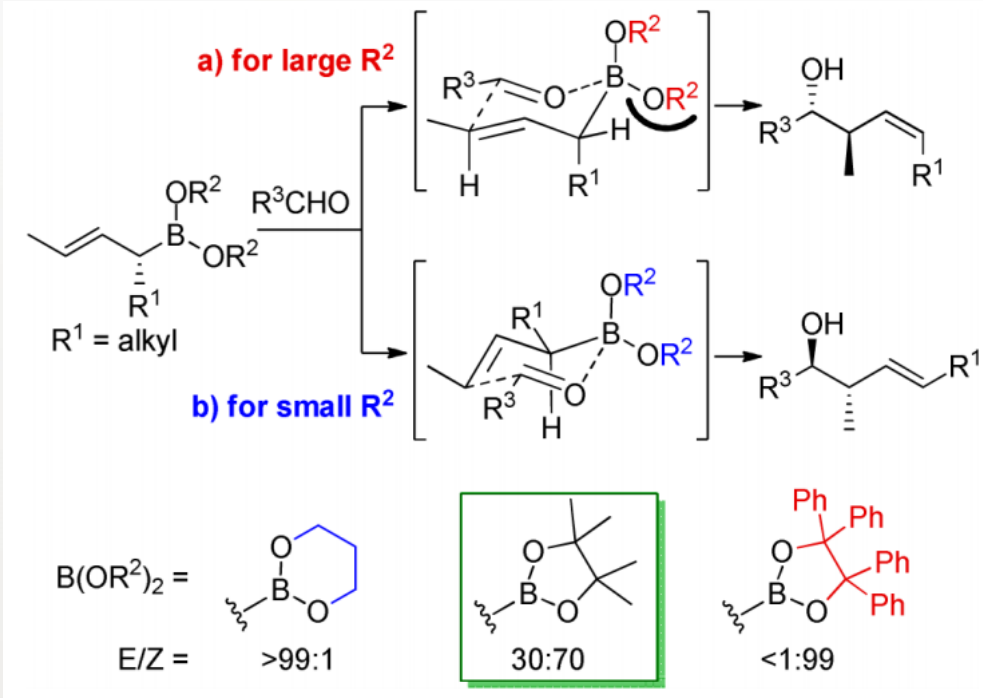
M. J. Hesse, C. P. Butts, C. L. Willis, V. K. Aggarwal, *Angew. Chem. Int. Ed.*, **2012**, *51*, *12444–12448*.

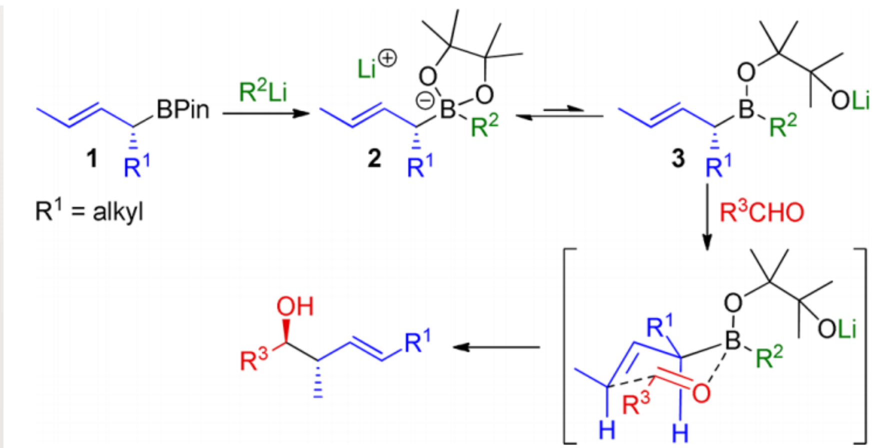
D.R. Model



M. J. Hesse, C. P. Butts, C. L. Willis, V. K. Aggarwal, *Angew. Chem. Int. Ed.*, **2012**, *51*, *12444–12448*.

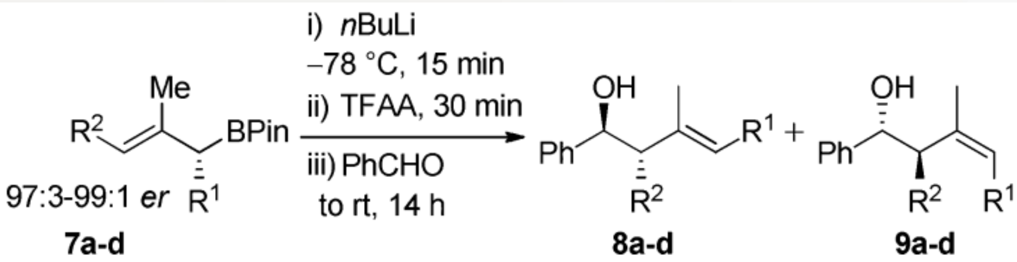
A new protocol For Roush-type Aldehyde Allylation



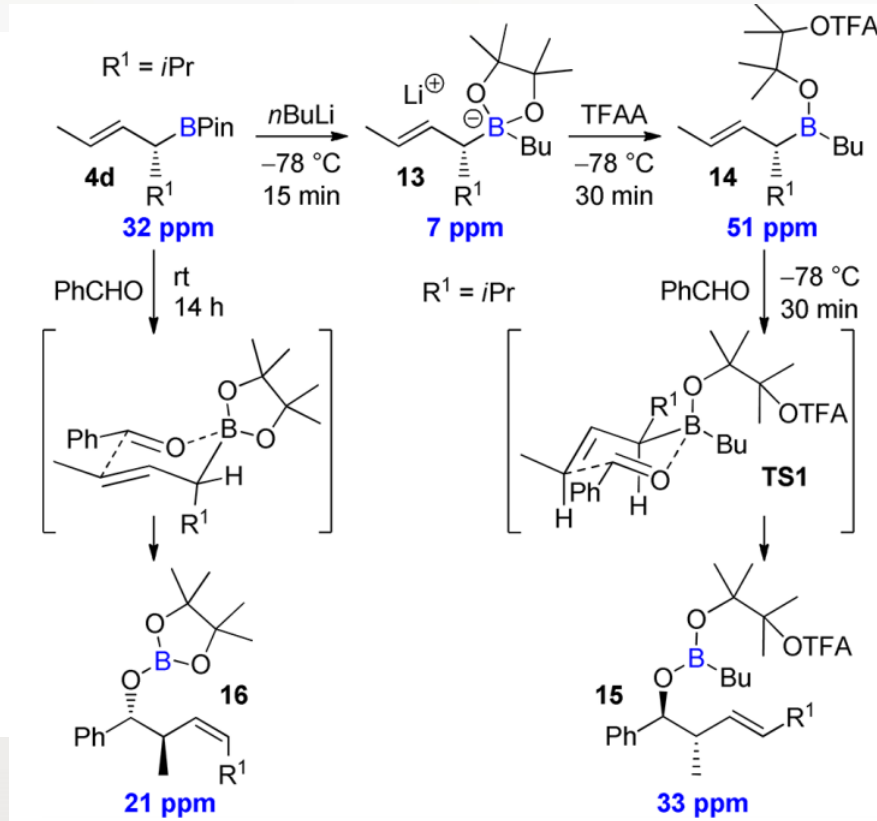


Jack L.-Y. Chen, Helen K Scott, Matthew J Hesse, Christine L. Willis, Varinder K. Aggarwal.*J. Am. Chem. Soc.*, **2013**, *135*, 5316–5319

Method A, directly mix together,
Method B, nBuLi and TFAA activation

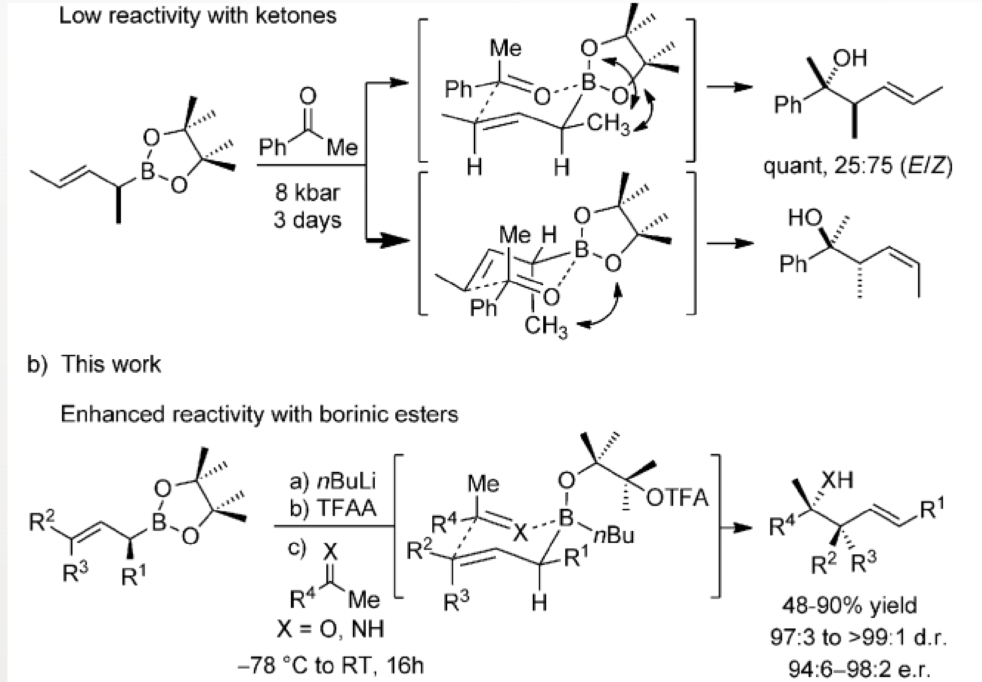


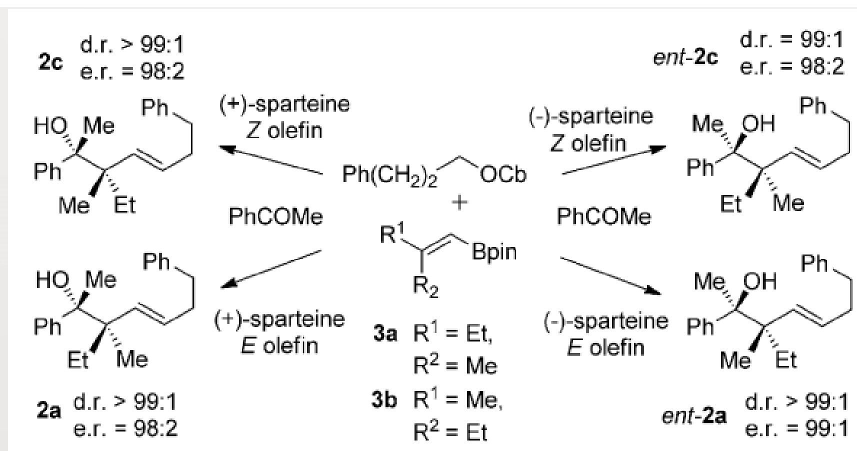
no.	7	R1	R2	cond.[a]	E/Z (8:9)	yield (8+9)	er[b]
1	7a	Me	Me	A	10:90	88	97:3
2				B	95:5	68	97:3
3	7b	iPr	Me	A	5:95	87	98:2
4				B	99:1	78	98:2
5	7c	iBu	Me	A	9:91	96	97:3
6				B	97:3	77	97:3
7	7d	iPr	H	A	5:95	80	99:1
8				B	97:3	72	99:1



Jack L.-Y. Chen, Helen K Scott, Matthew J Hesse, Christine L. Willis, Varinder K. Aggarwal. *J. Am. Chem. Soc.*, **2013**, *135*, 5316–5319

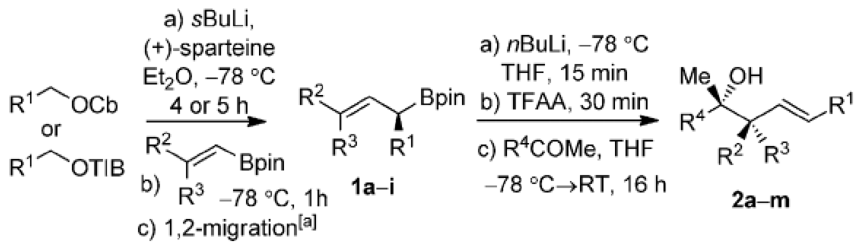
A new protocol For Ketone Allylation Seterodivergent Synthesis

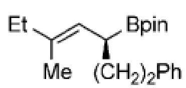
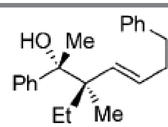
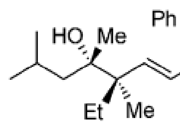
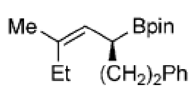
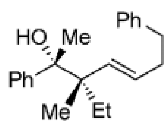
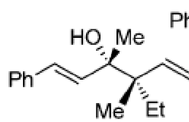


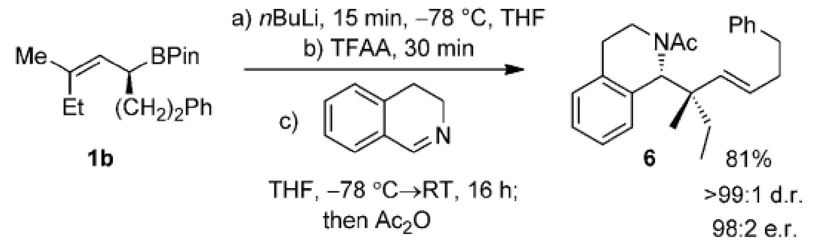


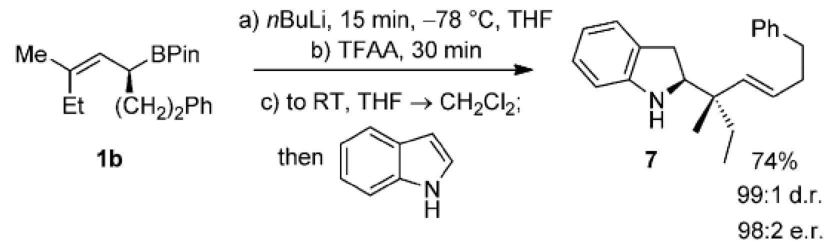
Jack L.-Y. Chen, Varinder K. Aggarwal. *Angew. Chem. Int. Ed.*, **2014**, *53*, 10992-10996

Ketone Allylation



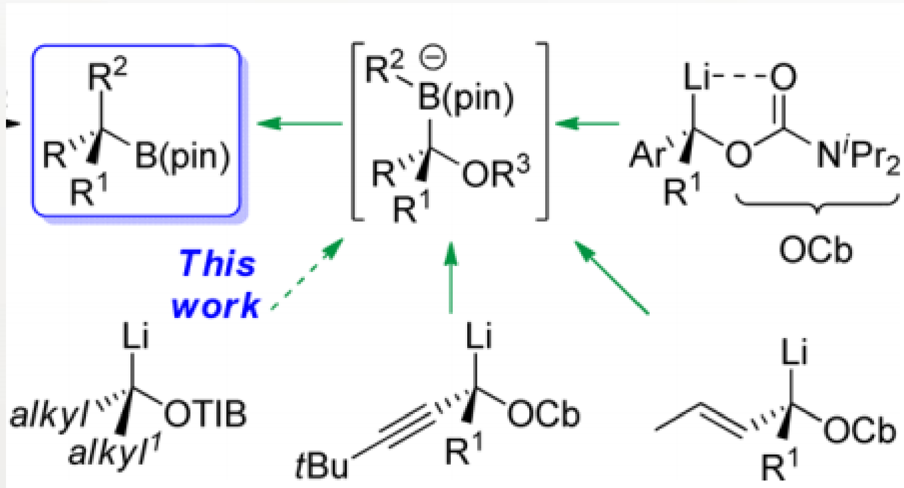
Entry	Li-B product	Yield[b]	Product	Yield[b]
1	 1a	77% 98:2 e.r.	 2a	87% >99:1 d.r.[c] 98:2 e.r.
2			 2b	80% >99:1 d.r.[c] 98:2 e.r.
3	 1b	74% 98:2 e.r.	 2c	83% >99:1 d.r.[c] 98:2 e.r.
4			 2d	88% 97:3 d.r.[c] 98:2 e.r.

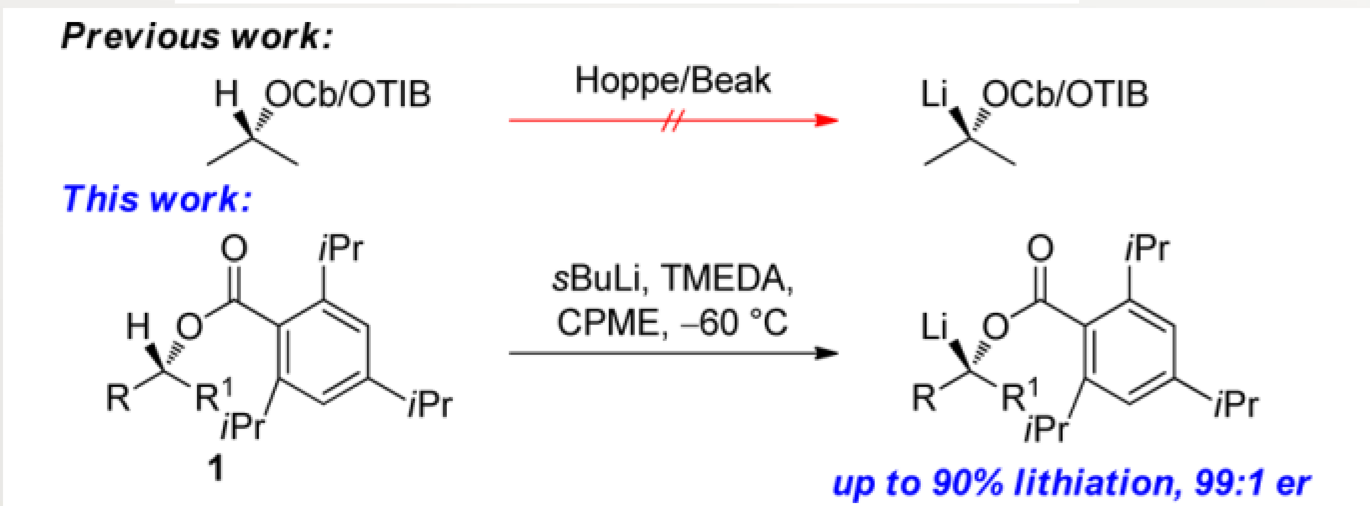




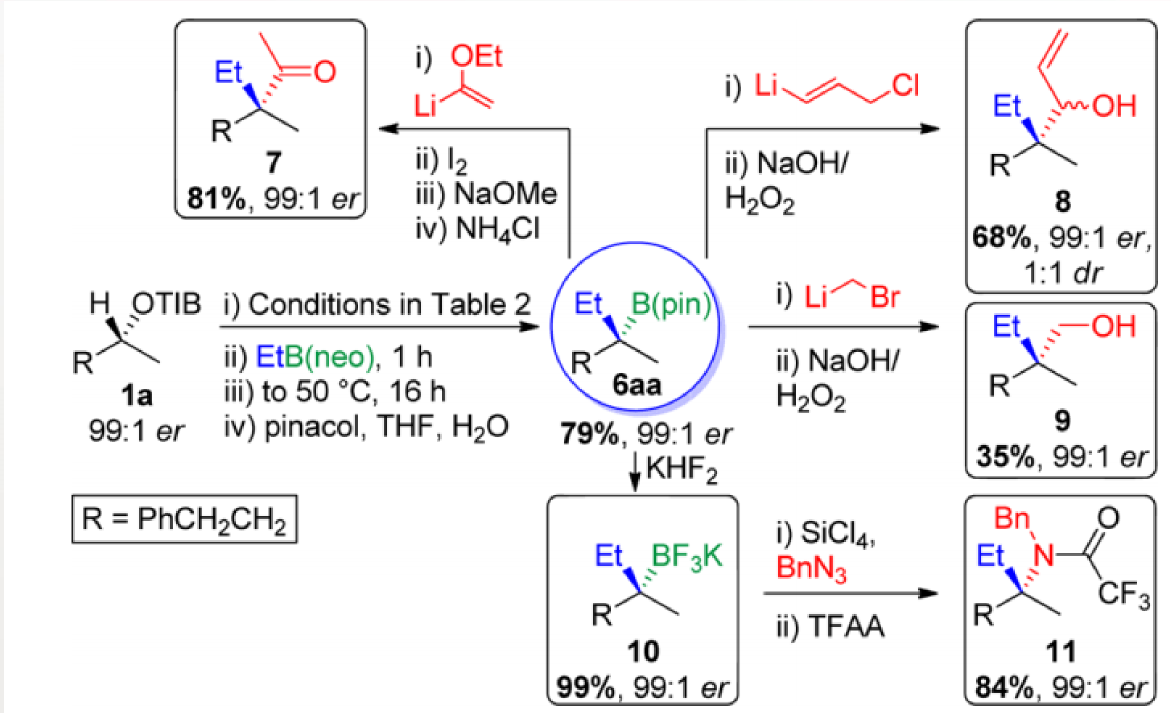
Jack L.-Y. Chen, Varinder K. Aggarwal.*Angew. Chem. Int. Ed.*, **2014**, *53*, 10992-10996

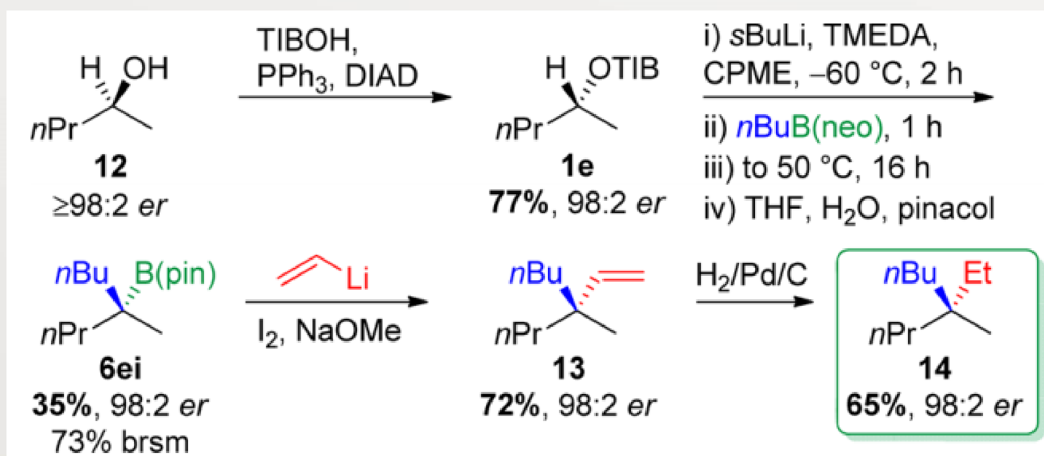
Generate the Chiral Lithium at Unactivated Position





Alexander P. Pulis , Daniel J. Blair , Eva Torres , and Varinder K. Aggarwal.*JACS*, **2013**, *135*, 16054–16057.

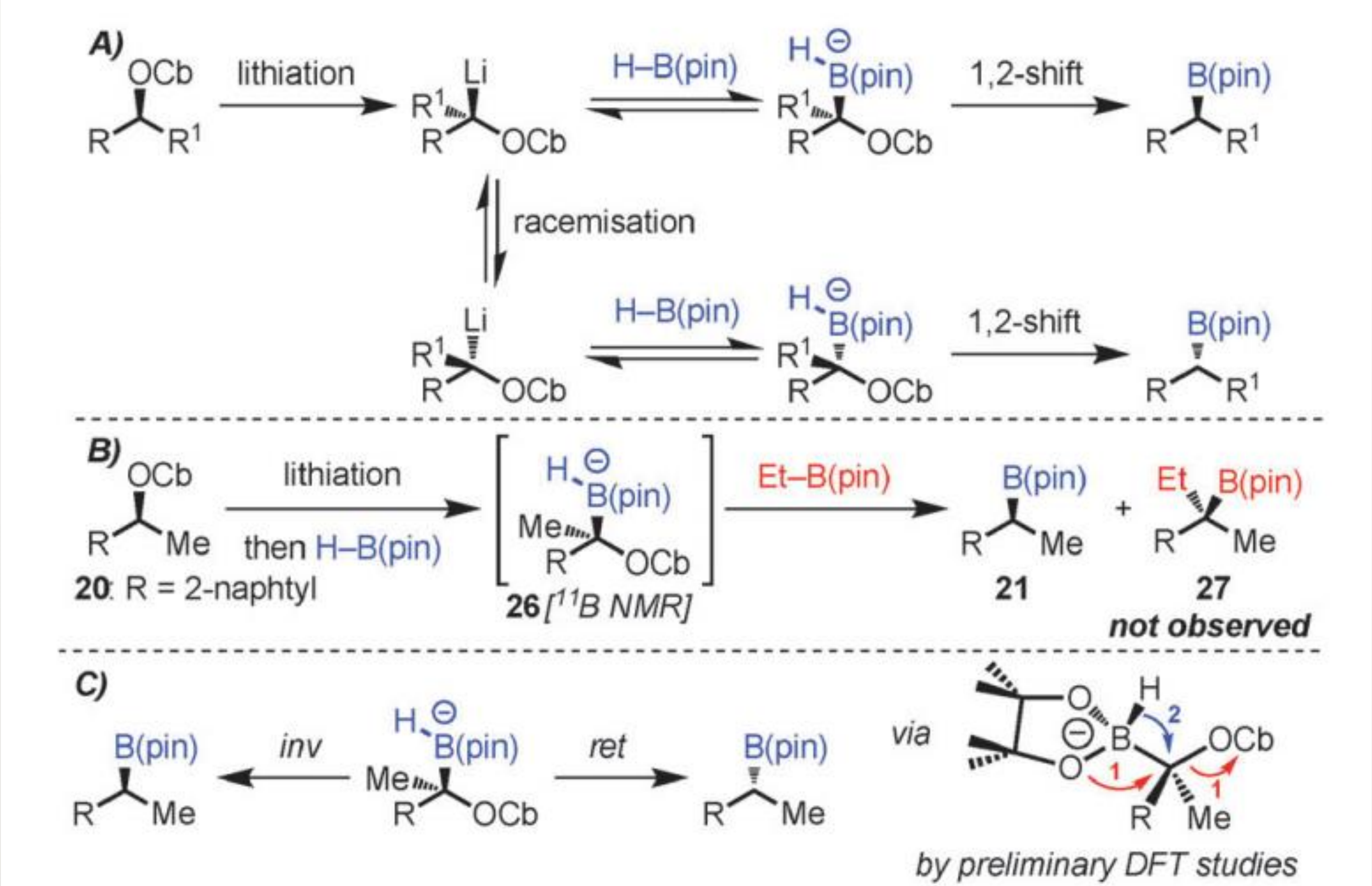




14 used to
Need 15 steps

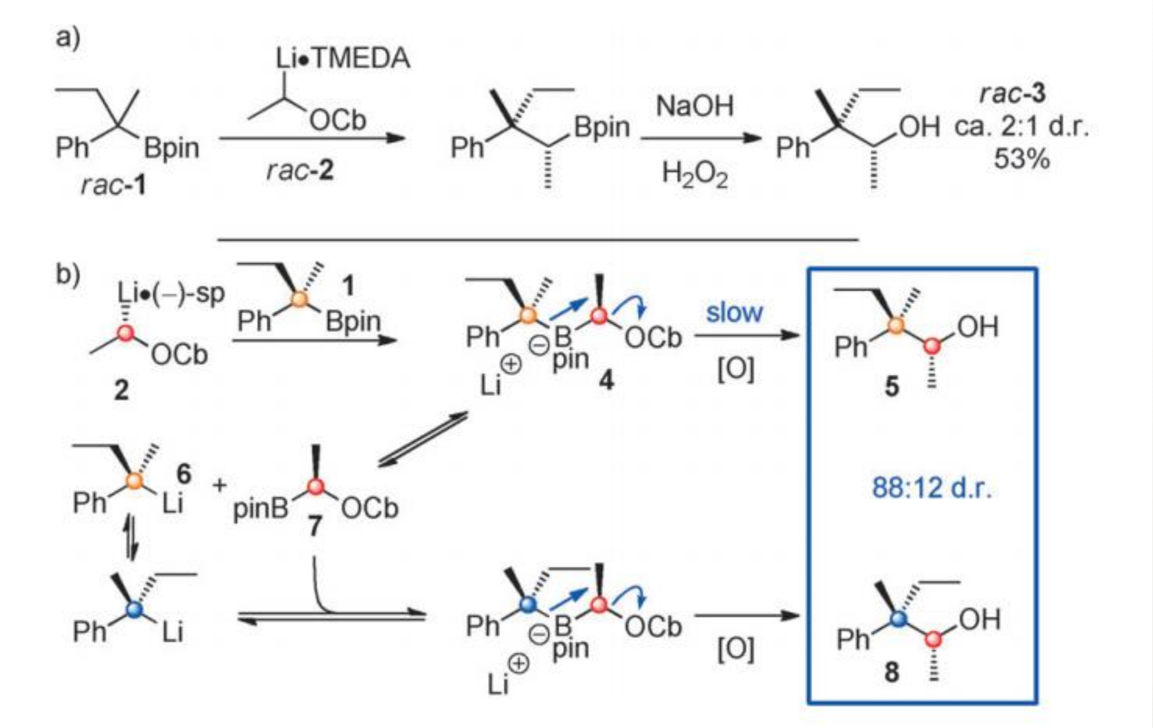
Alexander P. Pulis , Daniel J. Blair , Eva Torres , and Varinder K. Aggarwal.*JACS*, **2013**, *135*, 16054–16057.

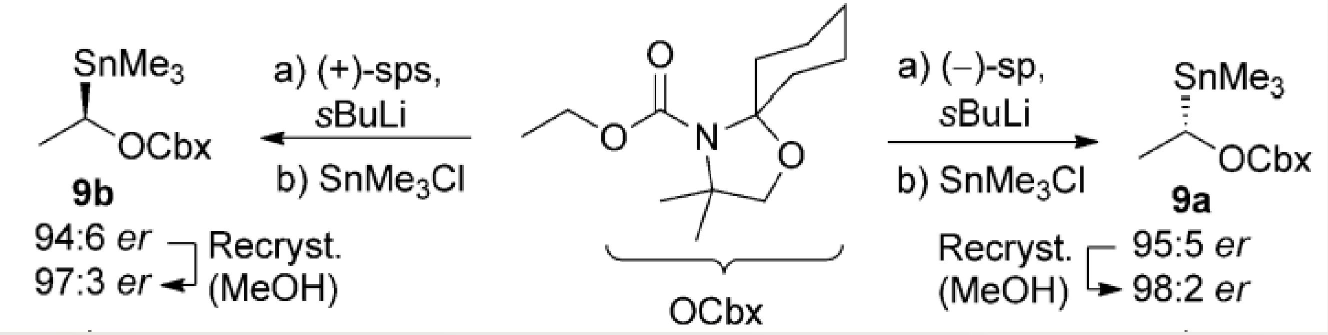
Transfer OH to Bpin



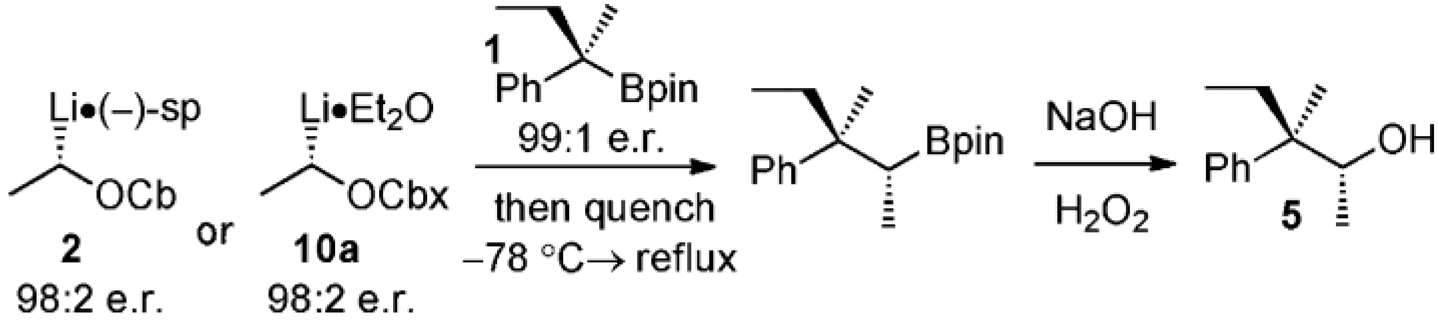
Stefan Roesner, Christopher A. Brown, Maziar M. Mohiti, Alexander P. Pulis, Ramesh Rasappan, Daniel J. Blair, Stefanie Essafi, Daniele Leonori and Varinder K Aggarwal. *Chem.Commun.*, **2014**, *50*, 4053-4055.

Quaternary Carbon Center formation



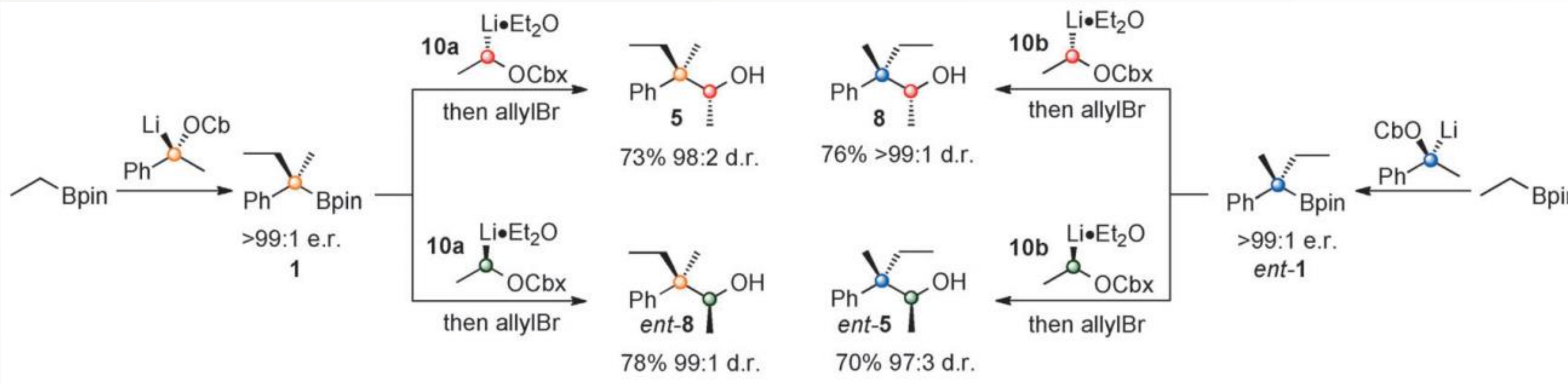


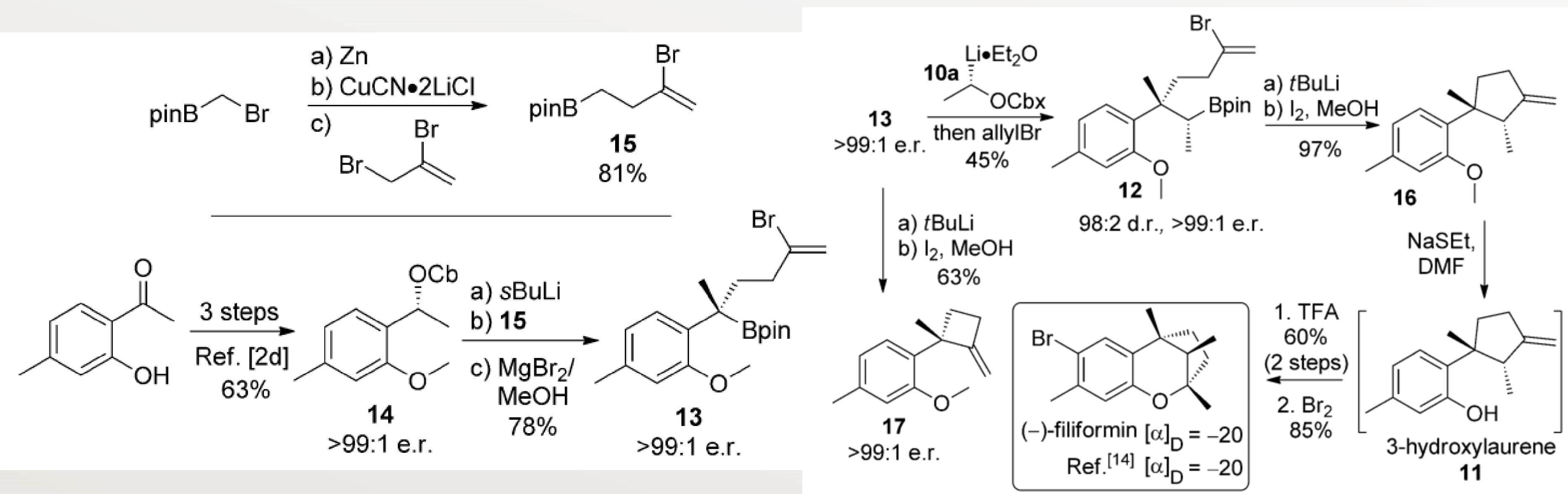
Daniel J. Blair, Catherine J. Fletcher, Katherine M. P. Wheelhouse, Varinder K. Aggarwal. *Angew. Chem. Int. Ed.*, **2014**, *53*, 5552–5555



Entry	Carbamate	Quench	d.r.[a]	e.r.[b]	Yield [%][c]
1	**2**		88:12 (**5**/**8**)	>99:1	n.d.
2[d]	**2**		88:12(**5**/**8**)	n.d.	n.d.
3	**2**	MeOH	98:2 (**5**/*ent*-**8**)	>99:1	28
4	**2**	$MgBr_2$/MeOH	98:2(**5**/*ent*-**8**)	>99:1	22
5	**2**	AllylBr	98:2 (**5**/*ent*-**8**)	>99:1	48
6	*ent*-**2**[e]	AllylBr	1:99 (**5**/*ent*-**8**)	>99:1	32[f]
7	**10a**	AllylBr	98:2 (**5**/*ent*-**8**)	>99:1	73

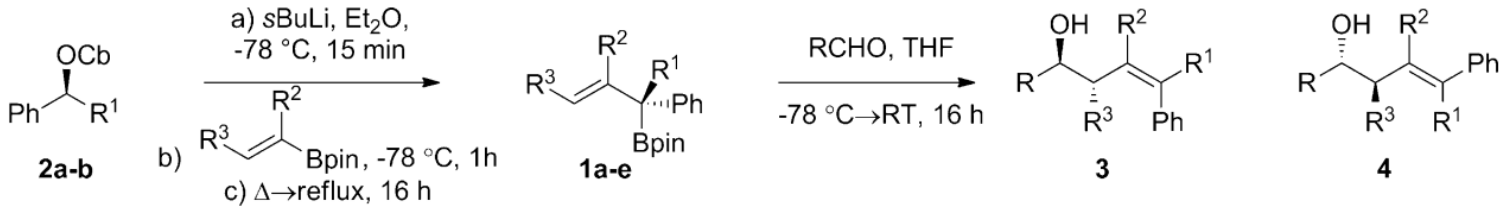
Daniel J. Blair, Catherine J. Fletcher, Katherine M. P. Wheelhouse, Varinder K. Aggarwal.*Angew. Chem. Int. Ed.*, **2014**, *53*, 5552–5555

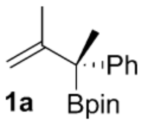
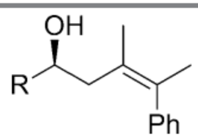
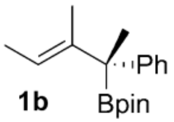
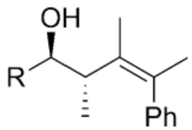
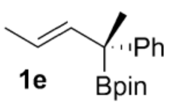
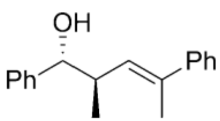


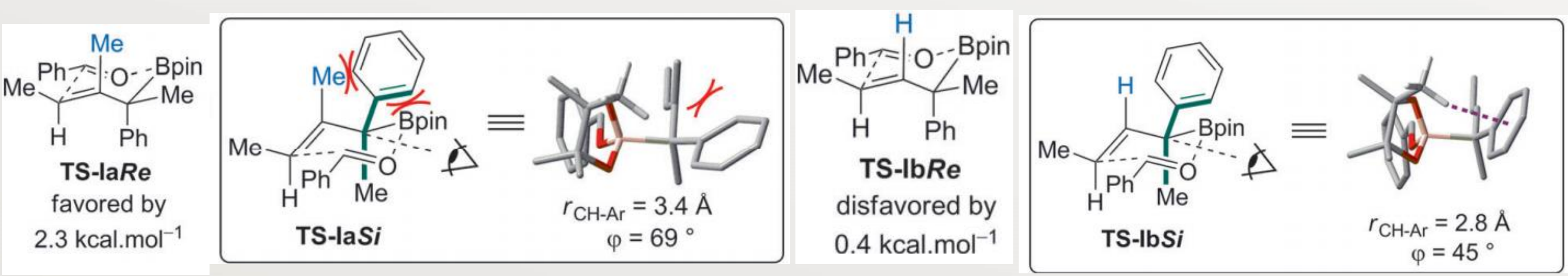


Daniel J. Blair, Catherine J. Fletcher, Katherine M. P. Wheelhouse, Varinder K. Aggarwal. *Angew. Chem. Int. Ed.*, **2014**, *53*, 5552–5555

1,1 di-substituted allyl Bpin in the crotylation

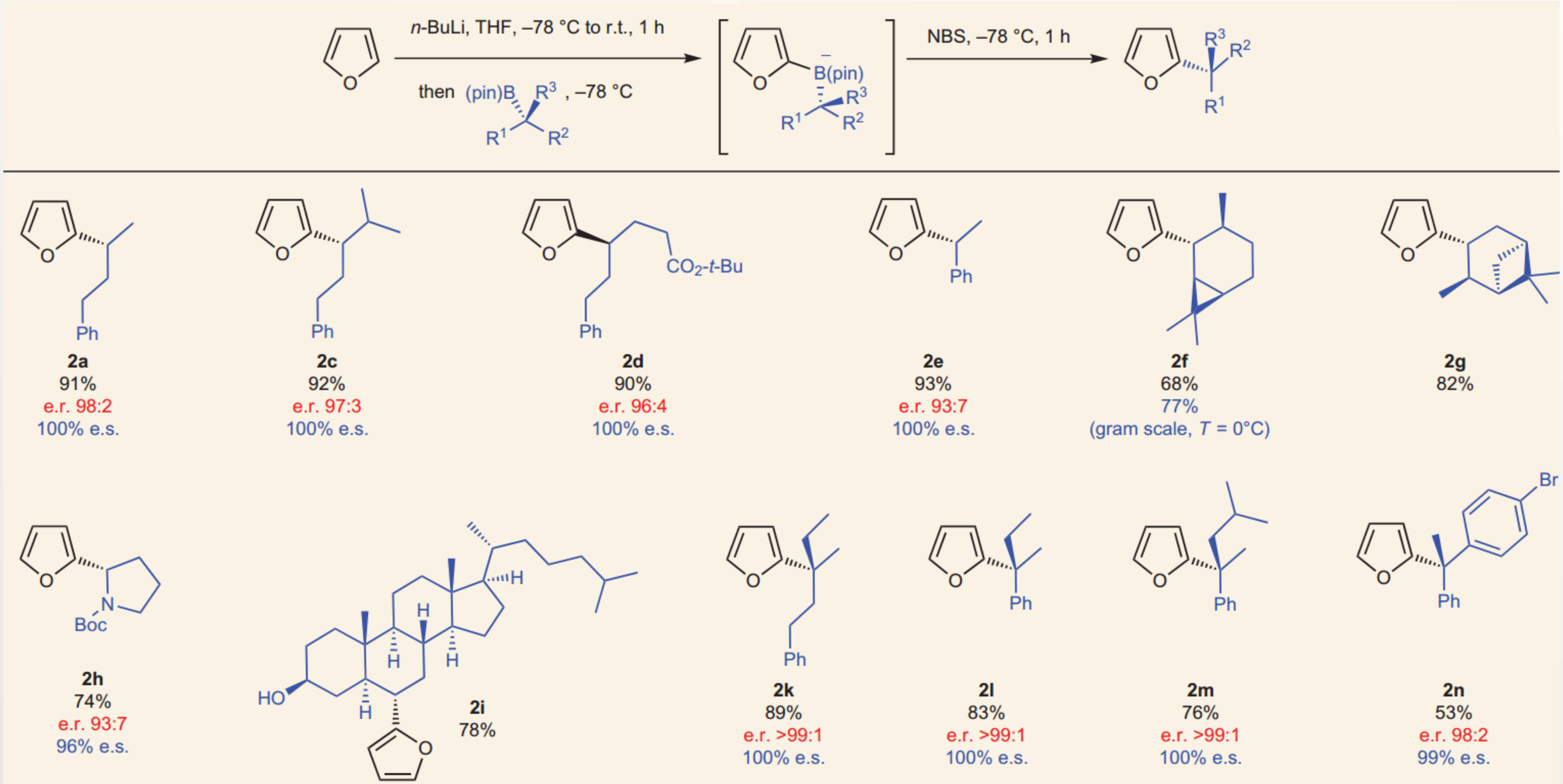


Entry	R¹	R²	R³	Yield [%][a]	1a–e	R		Yield [%][a]	d.r. (3:4)[b]	e.r.[b]
1	Me	Me	H	85	 1a	Ph 3aa		99	>99:1	>99:1
2	–	–	–	–		Cy 3ab		99	>99:1	>99:1
3	–	–	–	–		Me 3ac		98	>99:1	>99:1
4	Me	Me	Me	87 (85)[c]	 1b	Ph 3ba		99 (99)[c]	>99:1	>99:1
5	–	–	–	–		Cy 3bb		99	>99:1	99:1
6	–	–	–	–		Me 3bc		98	99:1	>99:1
9	Me	H	Me	90	 1e	Ph 3e		98	14:86	>99:1



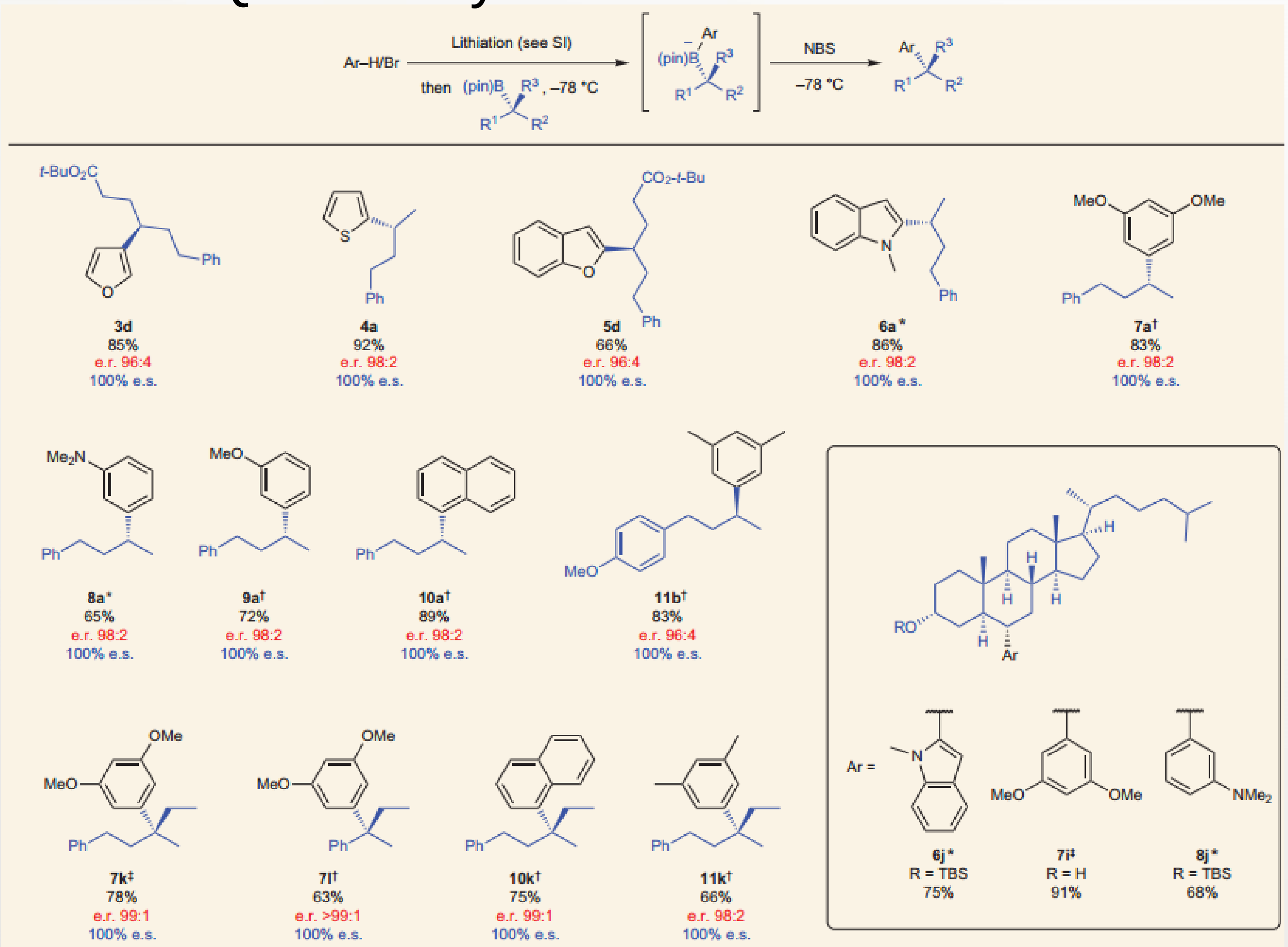
Matthew J. Hesse, Stéphanie Essafi, Charlotte G. Watson, Jeremy N. Harvey, David Hirst, Christine L. Willis, Varinder Aggarwal. *Angew. Chem. Int. Ed.*, **2014**, *53*, 6145–6149

Quaternary Carbon Center formation



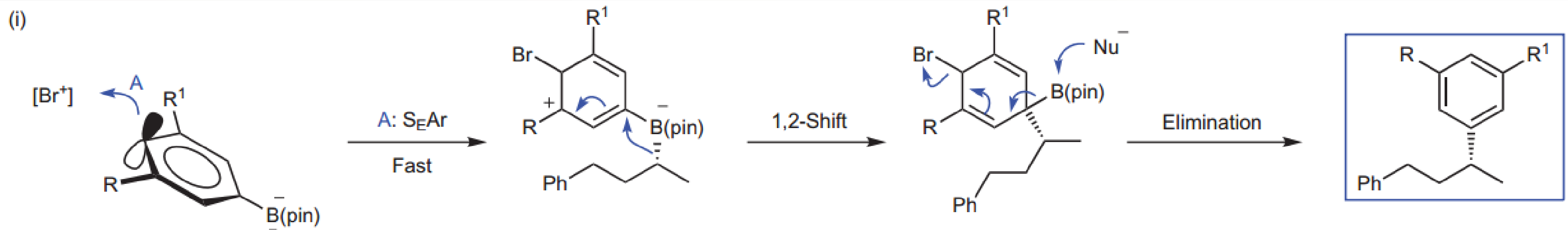
Amadeu Bonet, Marcin Odachowski, Daniele Leonori, Stephanie Essafi, Varinder Aggarwal. *Nat. Chem.*, **2014**, *6*, 584–589

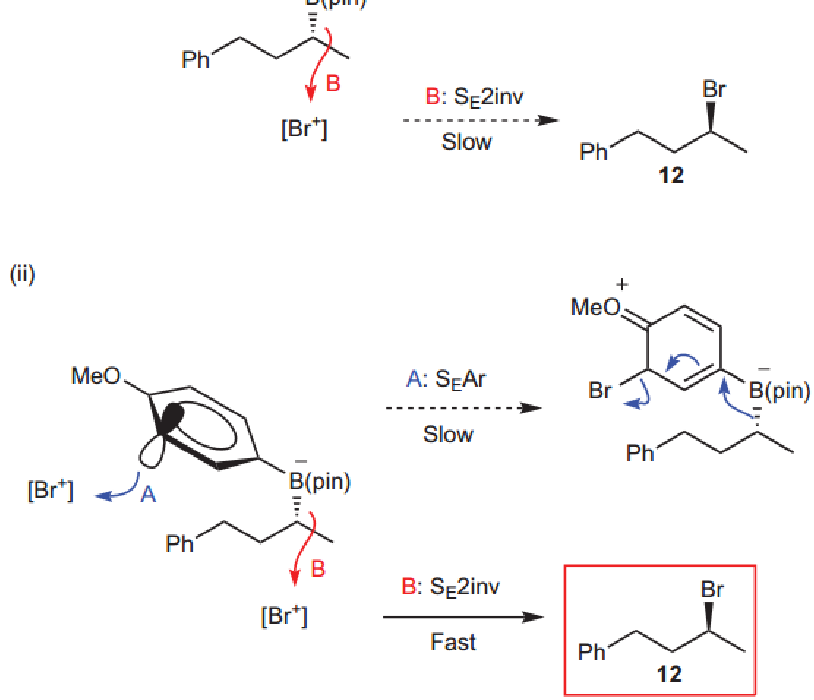
Quaternary Carbon Center formation



Amadeu Bonet, Marcin Odachowski, Daniele Leonori, Stephanie Essafi, Varinder Aggarwal. *Nat. Chem.*, **2014**, *6*, 584–589

Mechanism for Quaternary Carbon Center formation

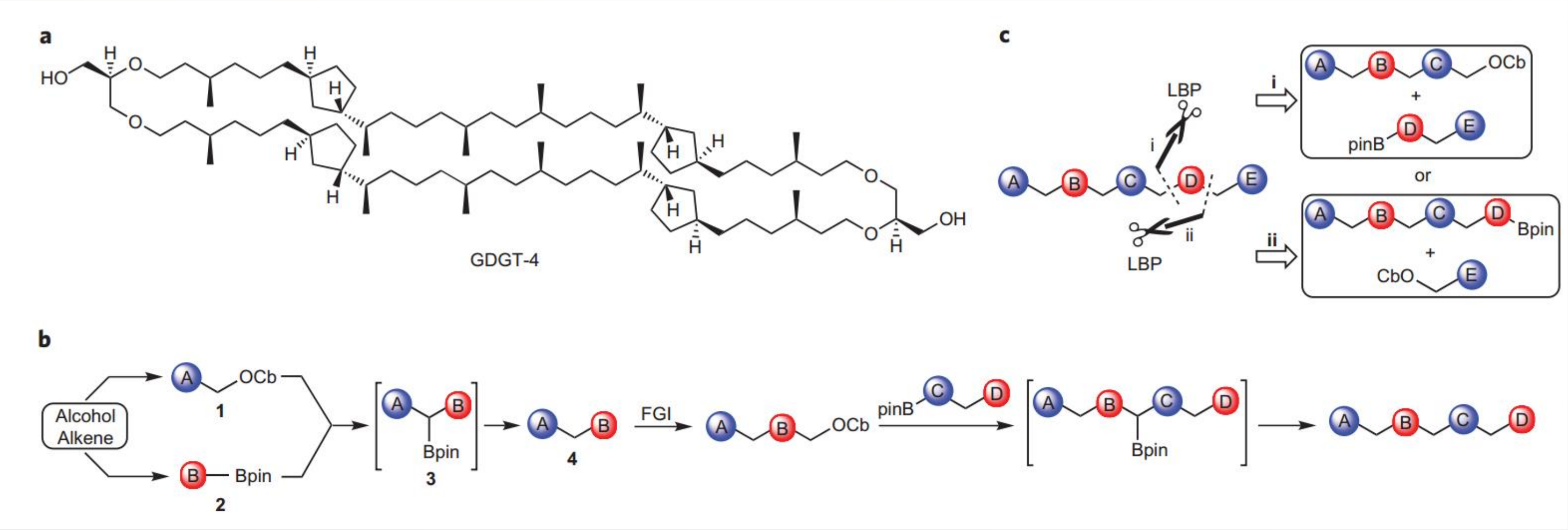


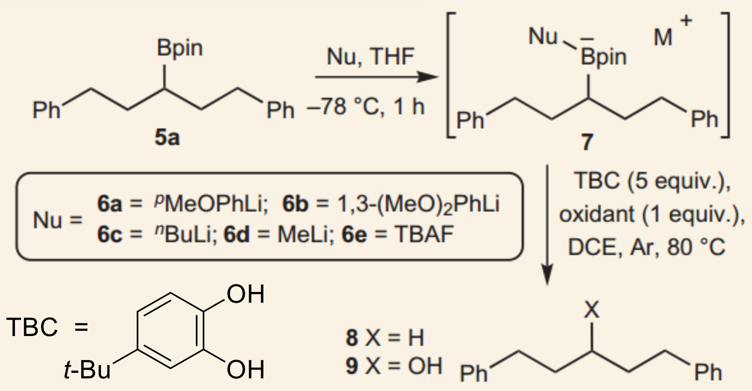


R	R1	Solvent	A:B*
MeO	MeO	THF	87:13
MeO	MeO	MeOH	99:1
MeO	H	THF	1:99
MeO	H	MeOH	99:1
Me	Me	THF	1:99
Me	Me	MeOH	99:1
Me	H	THF	1:99
Me	H	MeOH	28:72
H	H	THF	1:99
H	H	MeOH	1:99

Amadeu Bonet, Marcin Odachowski, Daniele Leonori, Stephanie Essafi, Varinder Aggarwal.
Nat. Chem., **2014**, *6*, 584–589

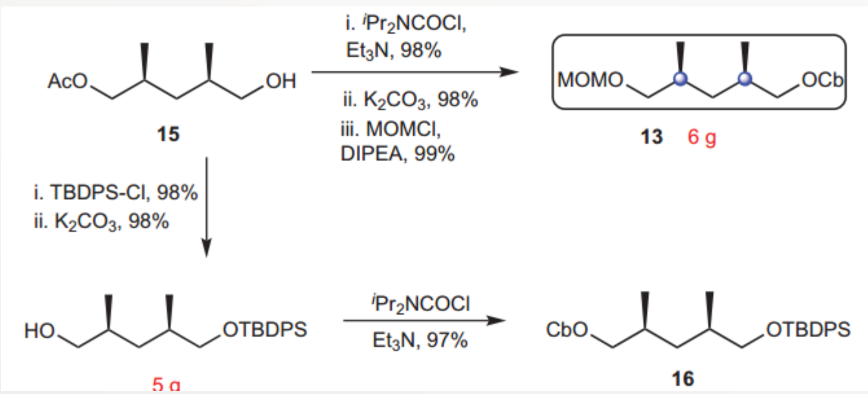
Remove the unactivate Bpin

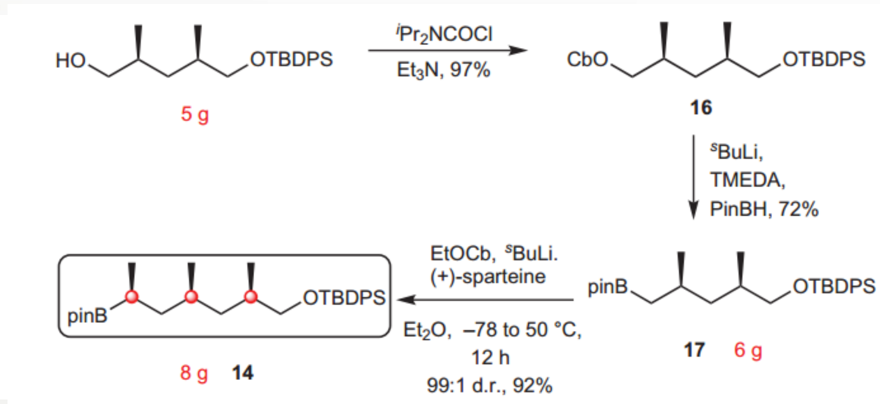


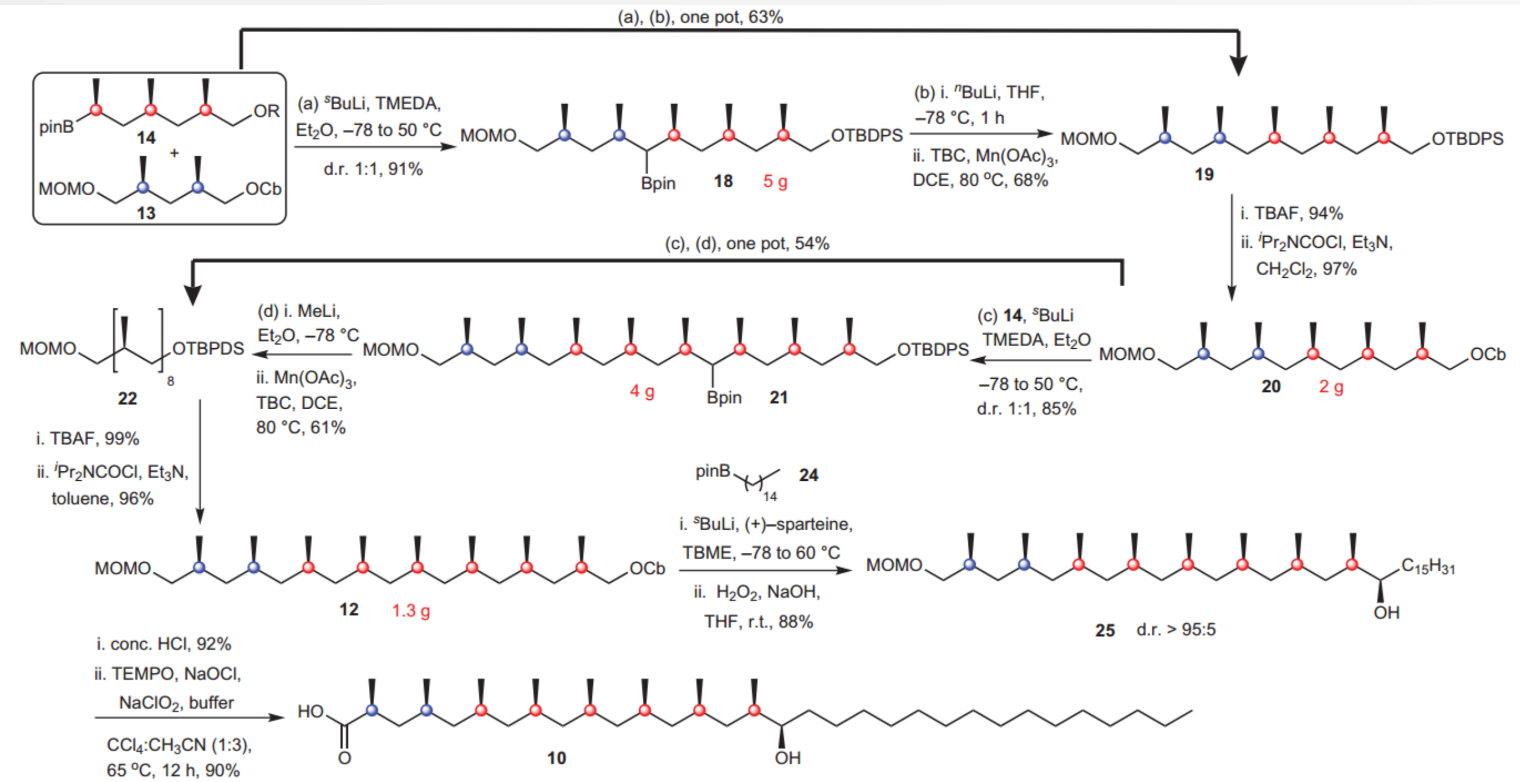


Entry	Nu	Oxidant	Time (h)	8:9	Yield (%)*
1†	**6a**	–	62	100:0	55
2‡	**6a**	–	40	92:8	72(65)
3‡	**6b**	–	40	95:5	85(78)
4‡	**6b**	Air	40	69:31	40
5	**6b**	$Cu(OAc)_2$	18	100:0	96(87)
6	**6b**	$Mn(OAc)_3$	18	100:0	96
7§,||	**6b**	$Cu(OAc)_2$	72	88:12	71
8	**6c**	$Cu(OAc)_2$	12	100:0	97(95)
9	**6c**	$Mn(OAc)_3$	12	100:0	98(97)
10	**6d**	$Mn(OAc)_3$	12	100:0	94
11||	**6e**	$Cu(OAc)_2$	12	100:0	72
12||	**6e**	$Mn(OAc)_3$	8 h	100:0	98(97)

Ramesh Rasappan, Varinder Aggarwal. *Nat. Chem.*, **2014**, *6*, 810–814

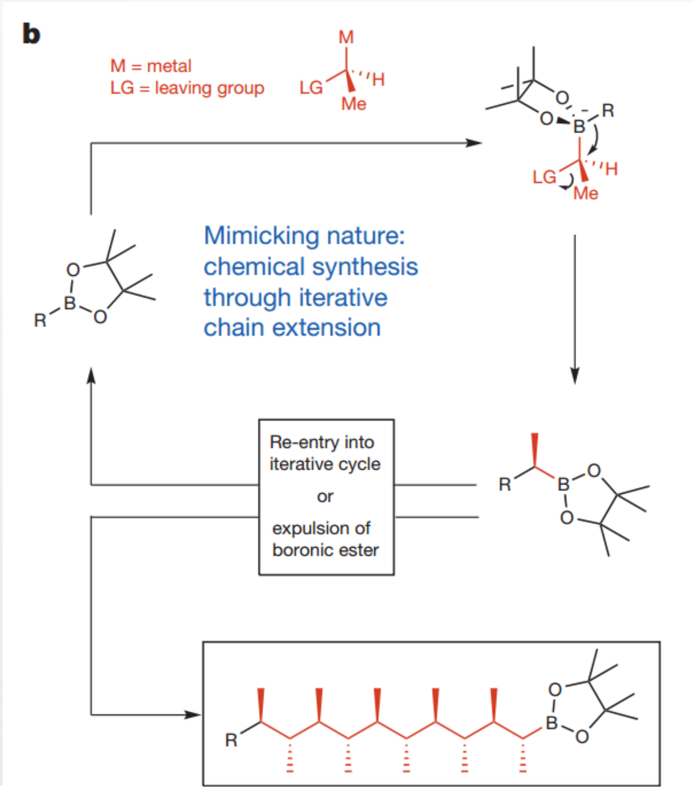


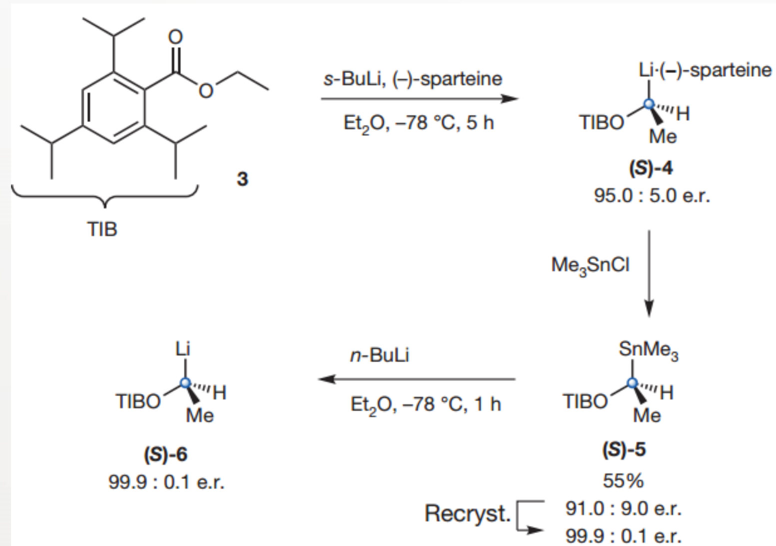


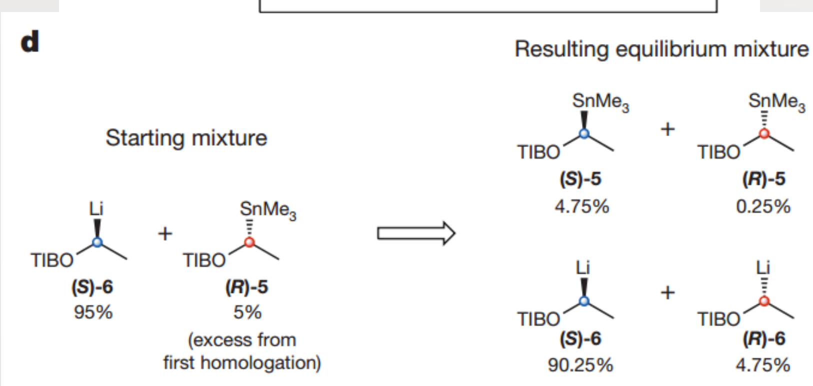


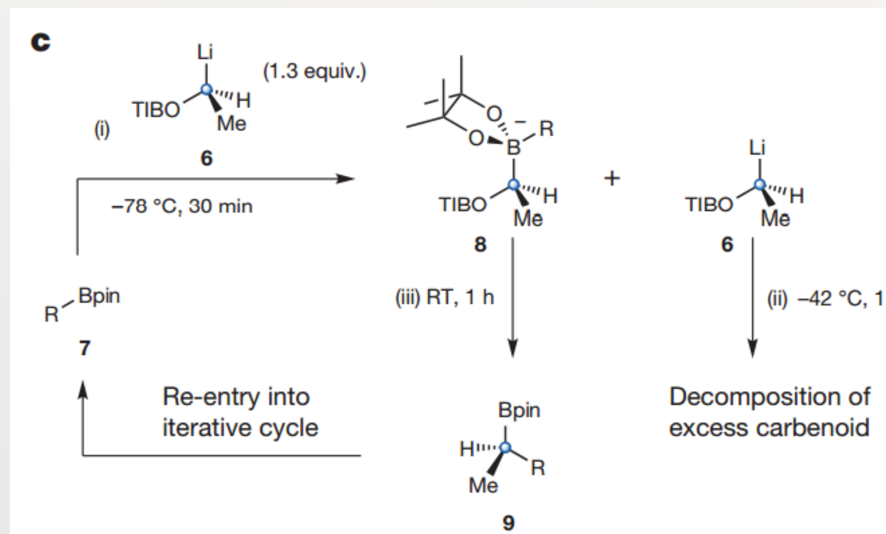
Ramesh Rasappan, Varinder Aggarwal. *Nat. Chem.*, **2014**, *6*, 810–814

Auto-synthesis



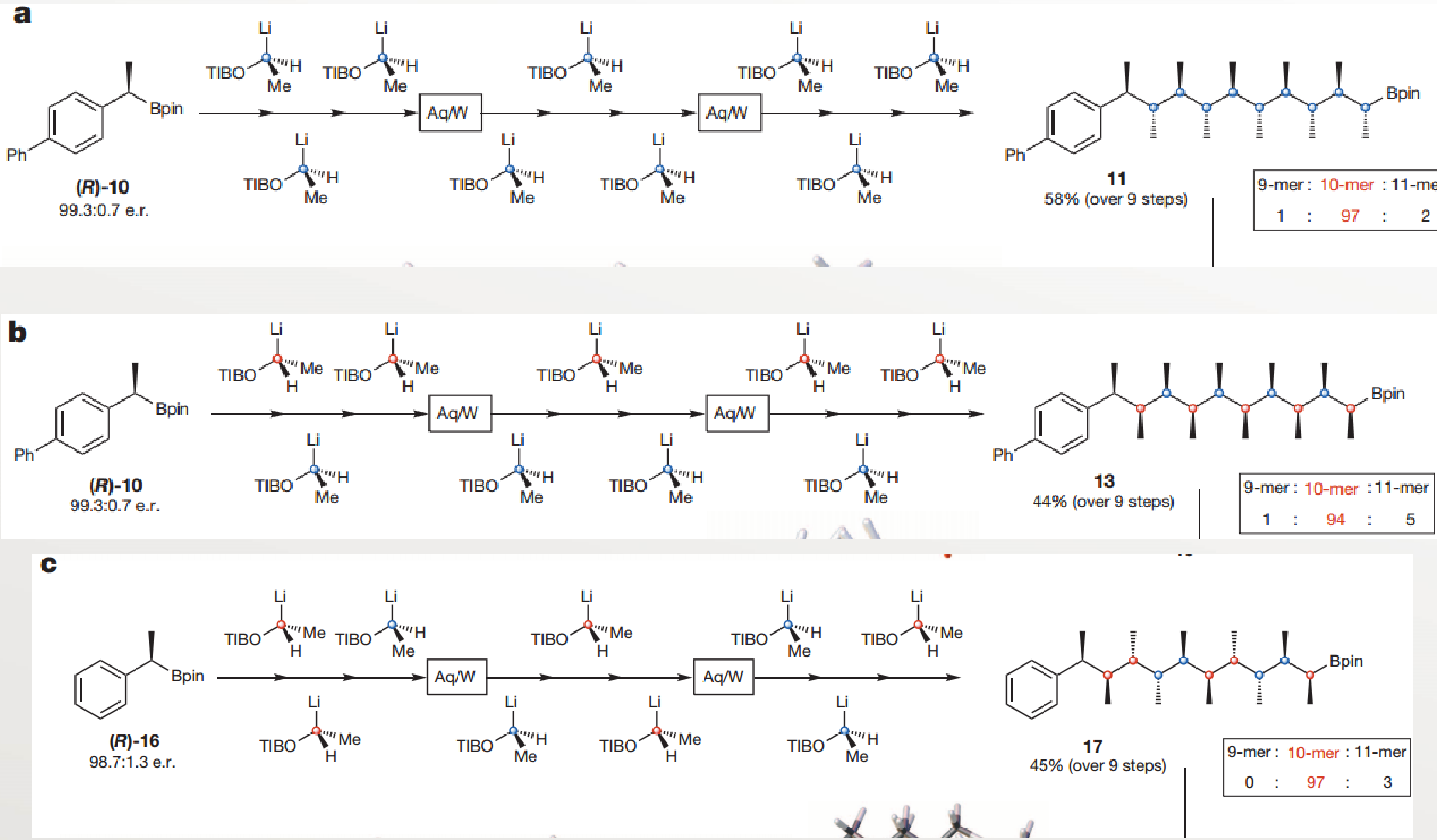






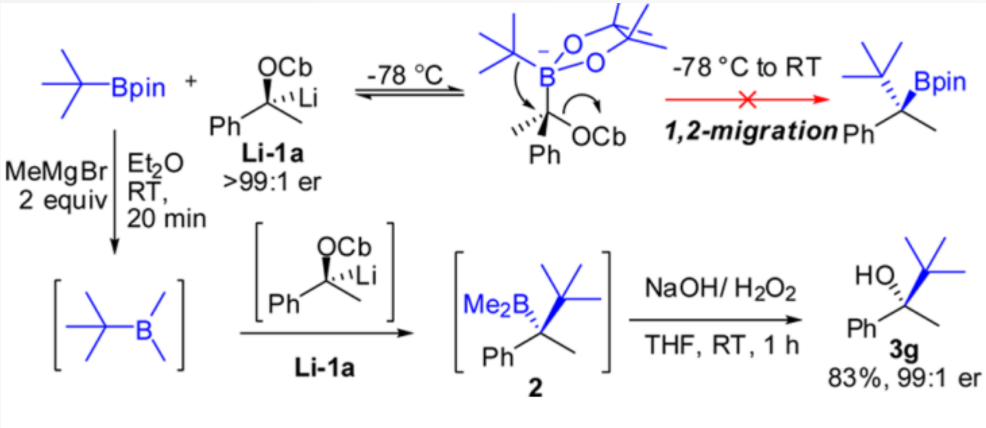
Matthew Burns, Stéphanie Essafi, Jessica R. Bame, Stephanie P. Bull, Matthew P. Webster, Sébastien Balieu, James W. Dale, Craig P. Butts, Jeremy N. Harvey, Varinder K. Aggarwal. *Nature*, **2014**, *513*, 183-188

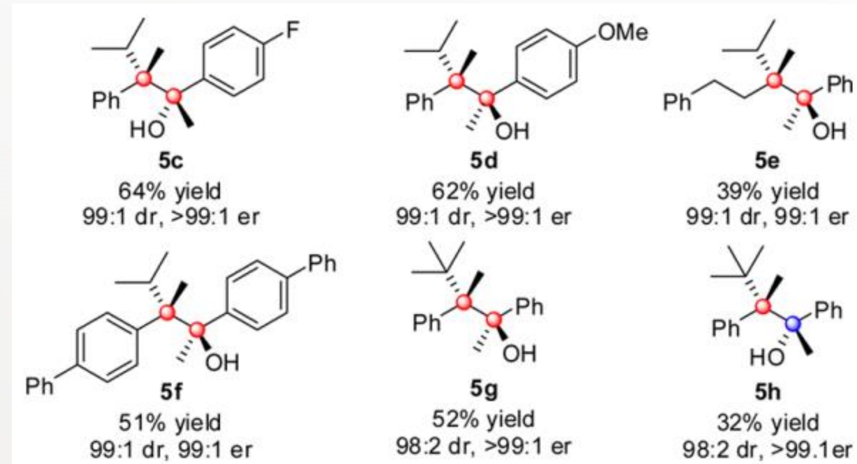
Only three example in the paper

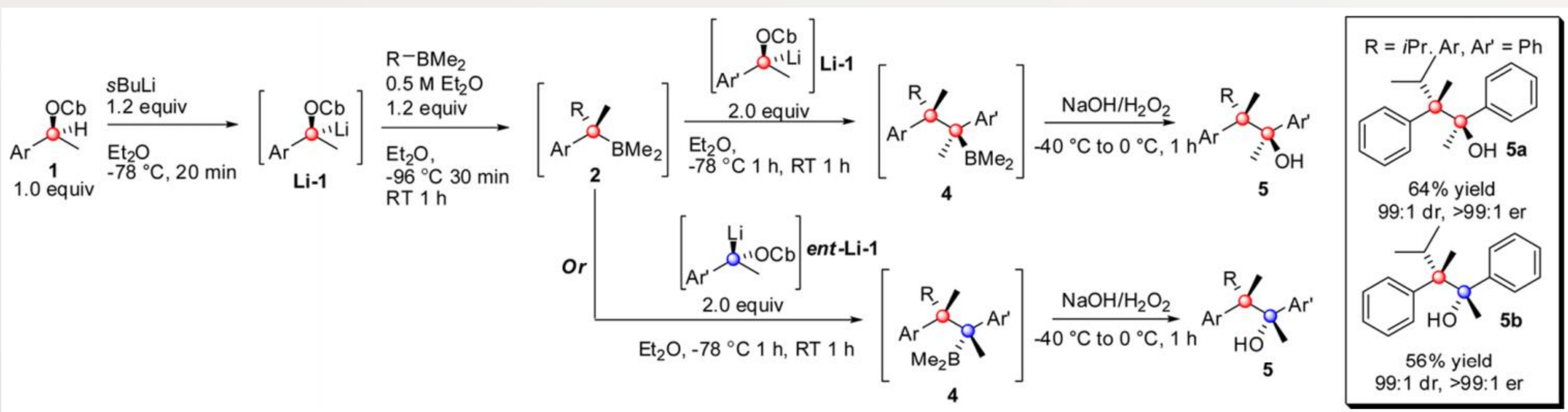


Matthew Burns, Stéphanie Essafi, Jessica R. Bame, Stephanie P. Bull, Matthew P. Webster, Sébastien Balieu, James W. Dale, Craig P. Butts, Jeremy N. Harvey, Varinder K. Aggarwal. *Nature*, **2014**, *513*, 183-188

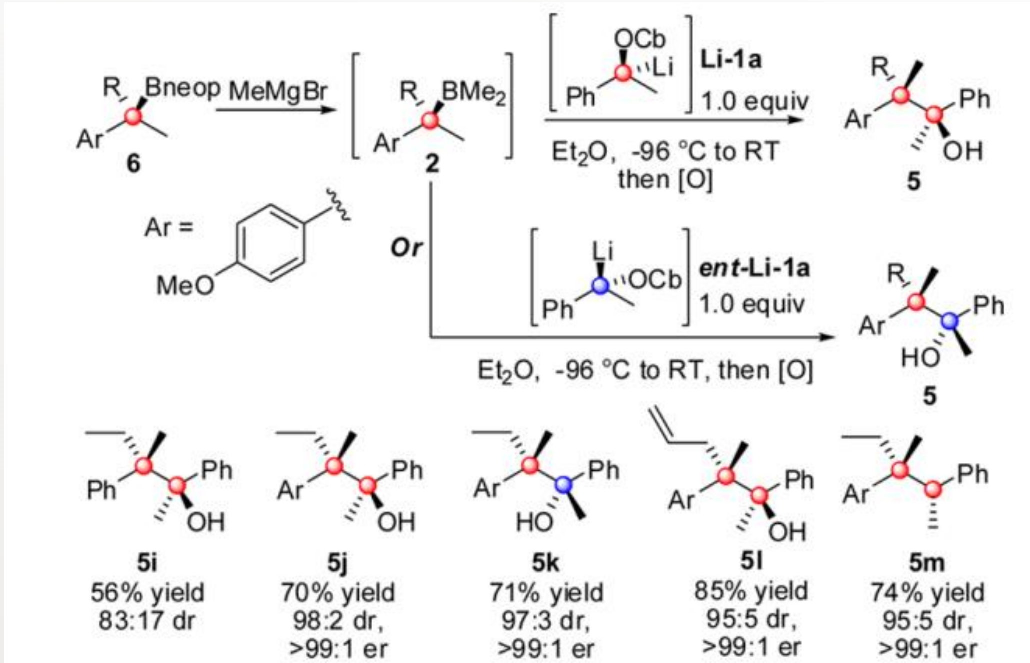
Vicinal Quaternary Carbon Center formation

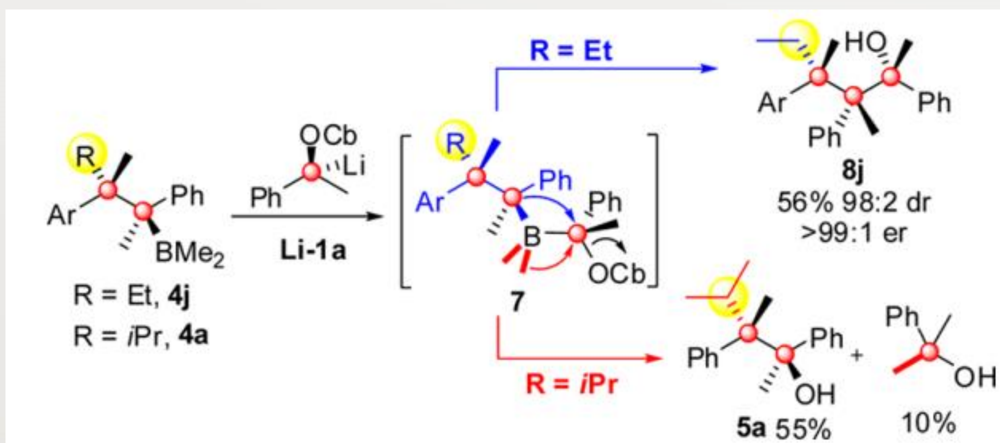






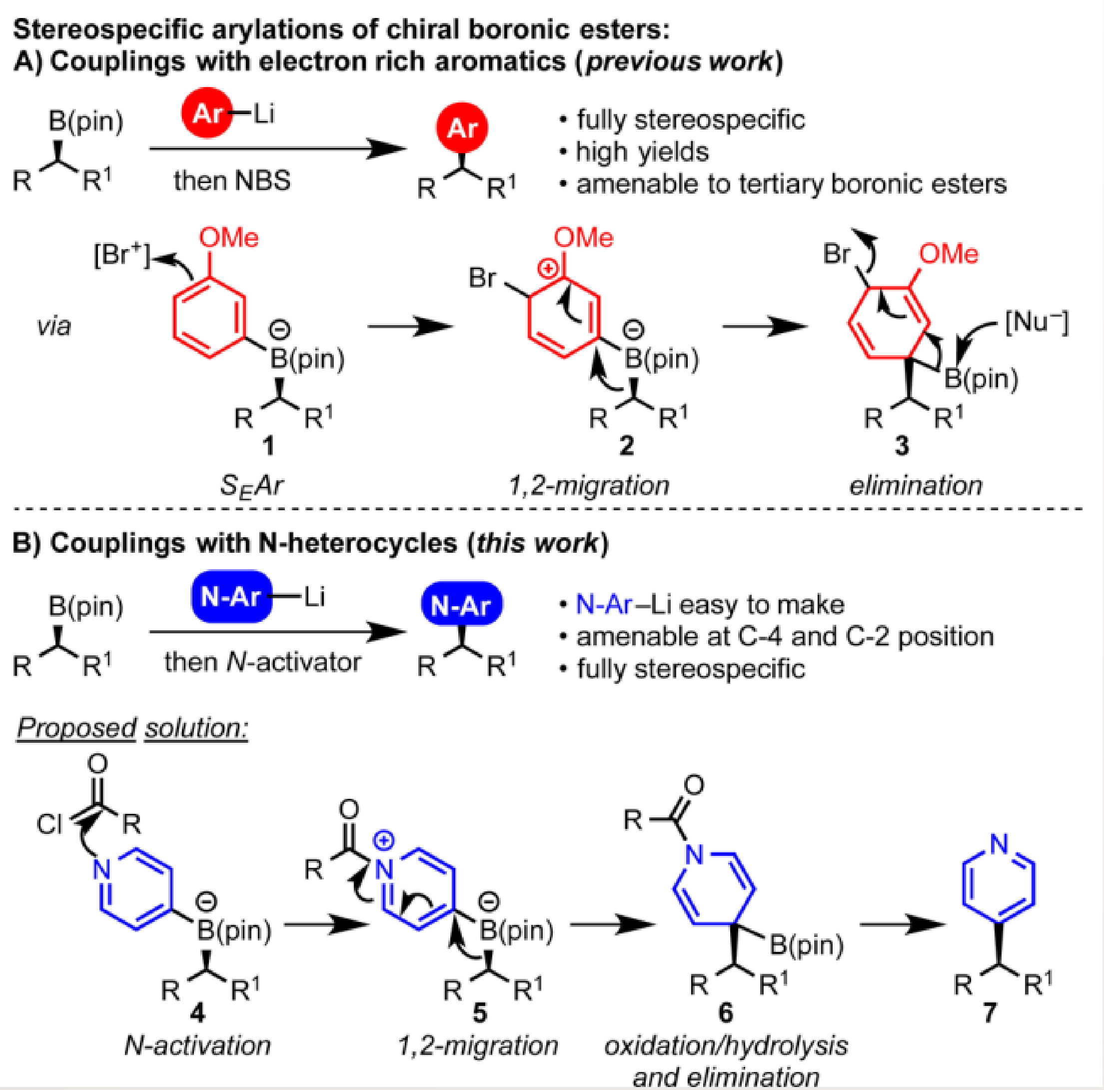
Charlotte G. Watson, Angelica Balanta, Tim G. Elford, Stéphanie Essafi, Jeremy N. Harvey, Varinder K. Aggarwal. *J. Am. Chem. Soc.*, **2014**, *136*, 17370-17373



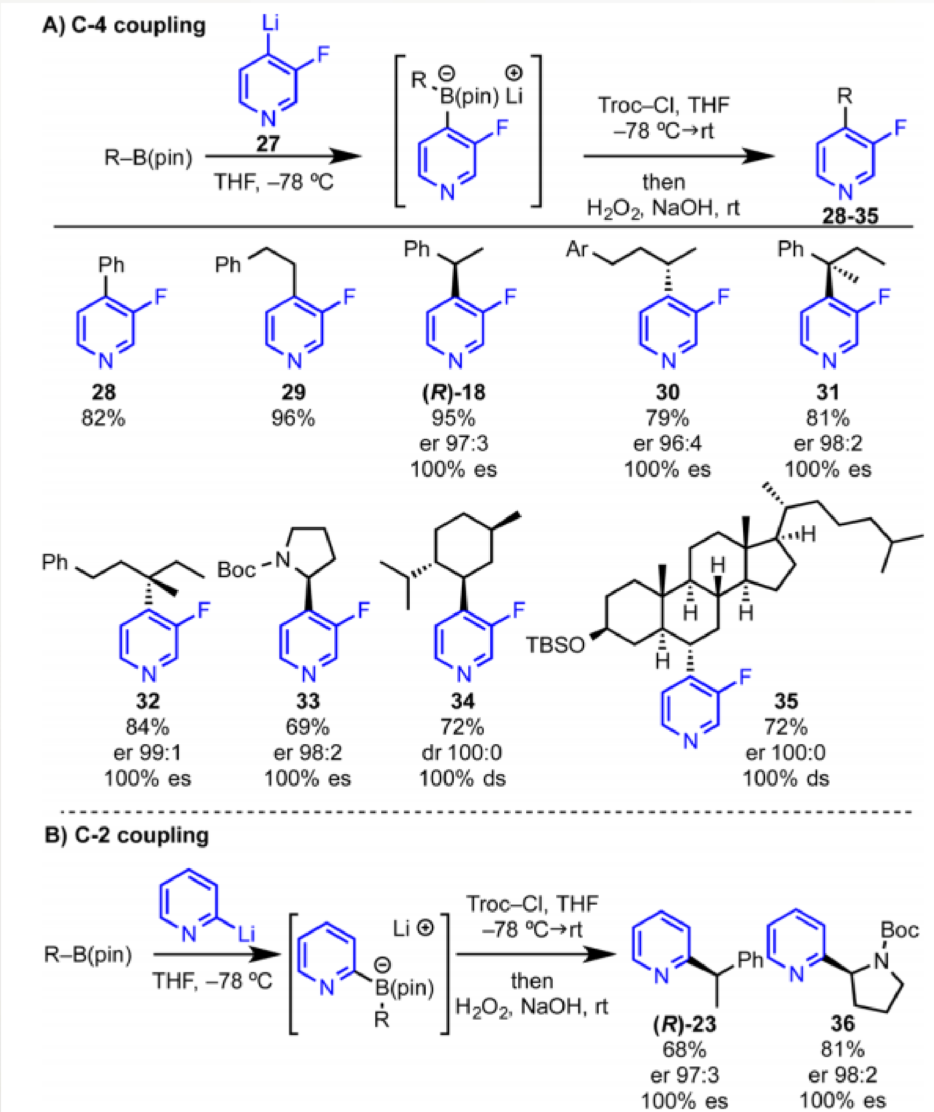


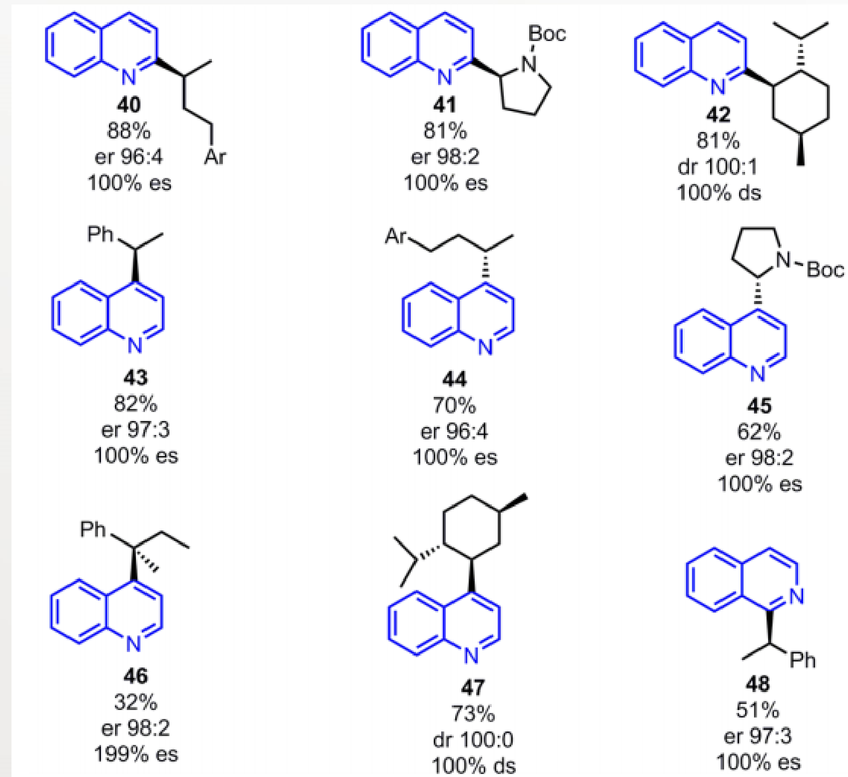
Charlotte G. Watson, Angelica Balanta, Tim G. Elford, Stéphanie Essafi, Jeremy N. Harvey, Varinder K. Aggarwal. *J. Am. Chem. Soc.*, **2014**, *136*, 17370-17373

C2/C4- alkylation of pyridine



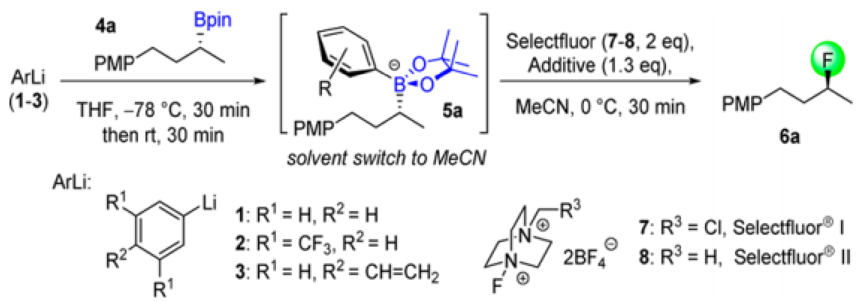
Josep Llaveria, Daniele Leonori, Varinder K. Aggarwal. *J. Am. Chem. Soc.*, **2015**, *137*, 10958–10961





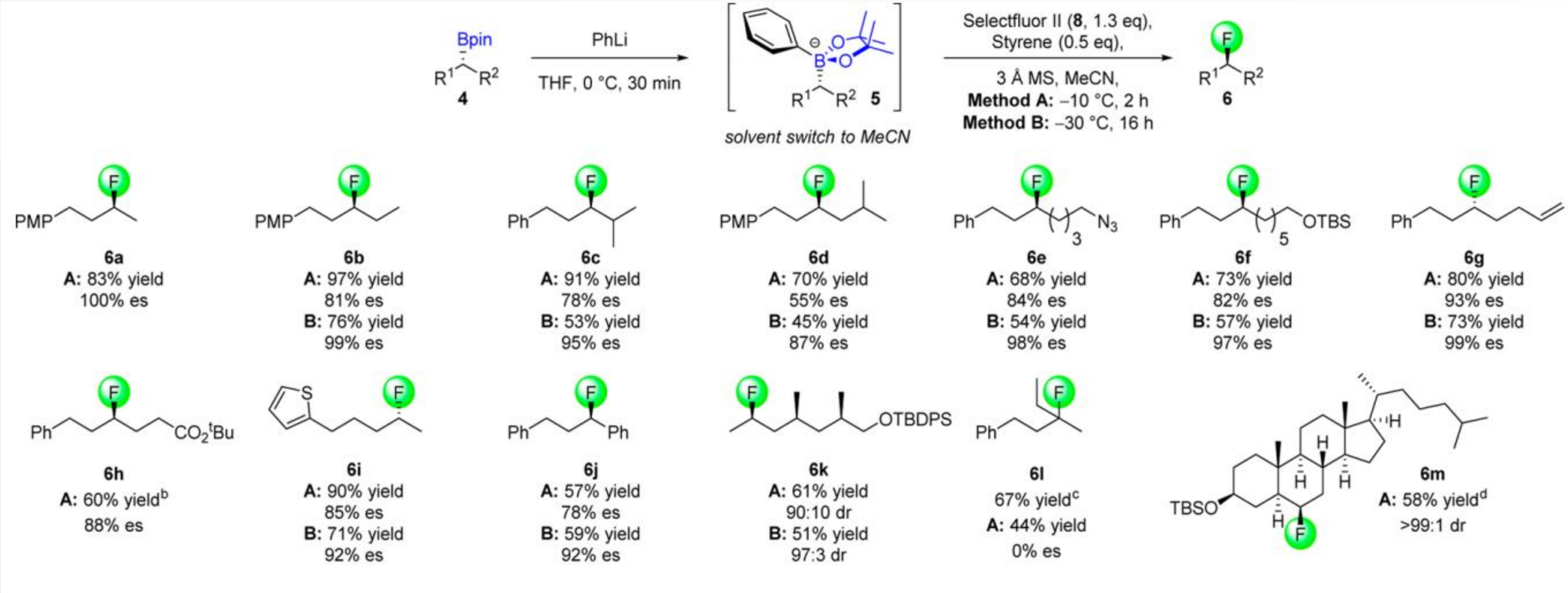
Josep Llaveria, Daniele Leonori, Varinder K. Aggarwal.*J. Am. Chem. Soc.*, **2015**, *137*, 10958–10961

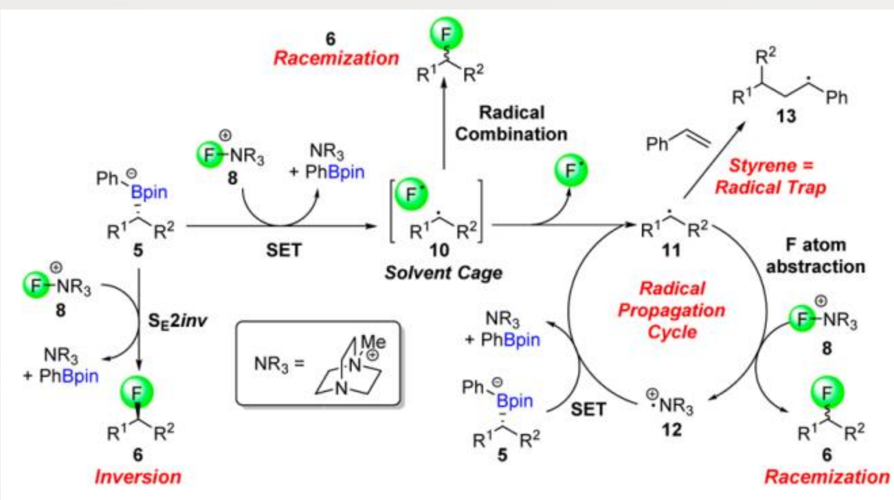
Chiral fluorine compound synthesis

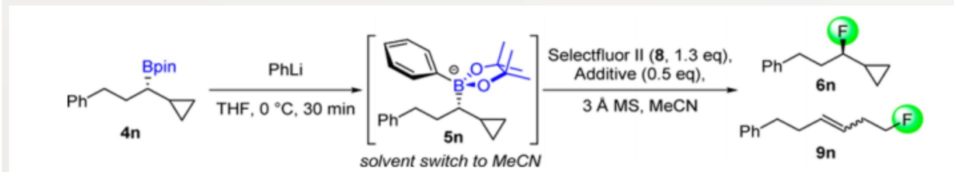


entry	ArLi	Selectfluor	additive	yield[b] (%)	es[c] (%)
1	**1**	Selectfluor I	none	78	37
2	**2**	Selectfluor I	none	61	47
3	**3**	Selectfluor I	none	61	59
4	**1**	Selectfluor I	styrene	81	89
5	**1**	Selectfluor I	4-MeO styrene	>99	74
6	**1**	Selectfluor I	4-CF_3 styrene	78	87
7	**1**	Selectfluor I	4-*tert*-butyl catechol[d]	67	24
8	**1**	Selectfluor I	1-octene	>99	78
9	**1**	Selectfluor I	toluene	72	46
10	**1**	Selectfluor I	*n*-octane	>99	33
11	**1**	Selectfluor I	styrene[e]	89	89
12	**1**	Selectfluor II	styrene[e]	72	94
13[f]	**1**	**Selectfluor II**	**styrene**[e]	**83**[g]	**100**
14[f]	**1**	Selectfluor II	none	72[g]	80

Christopher Sandford, Ramesh Rasappan, Varinder K. Aggarwal. *J. Am. Chem. Soc.*, **2015**, *137*, 10100–10103







entry	temp/°C (time)	additive	yield[b] (%)	ratio[c] 6n:9n	es[d] (6n) (%)
1	25 (1 h)	none	62	95:5	52
2	25 (1 h)	styrene	69	>99:1	56
3	−30 (16 h)	none	52	97:3	56
4	−30 (16 h)	styrene	74	>99:1	64

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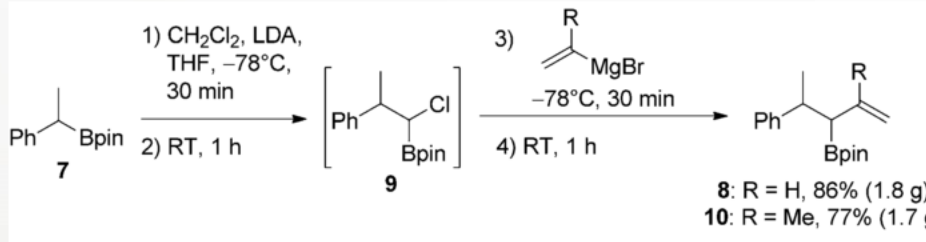
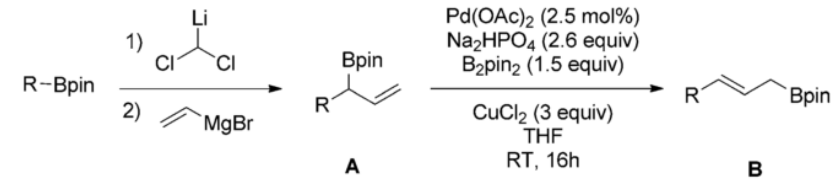
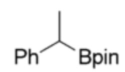
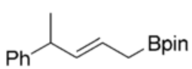
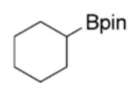
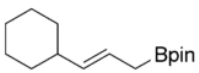
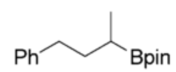
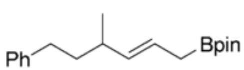
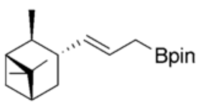
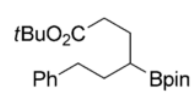
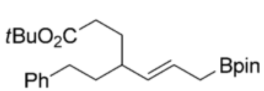
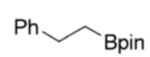
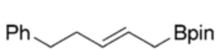
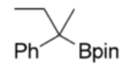
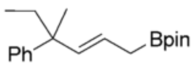
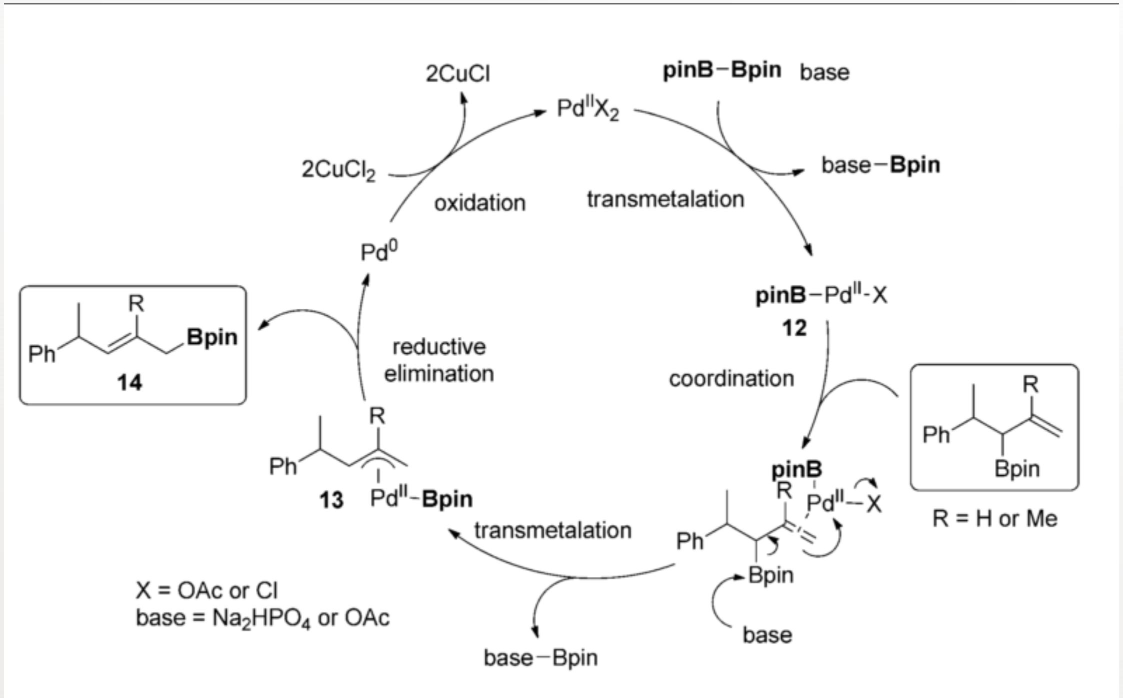
Pd-catalyzed Formal Three carbon Logation of Boronic Esters

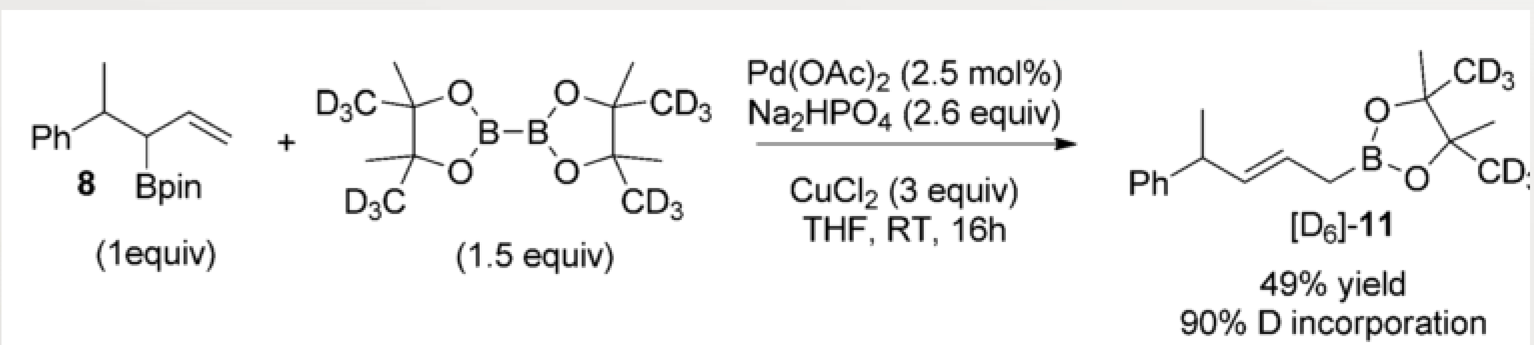




Substrate	Yield of A [%][a]	Yield of B [%][a]	E/Z[b]	Product
	86	79	>95:5	
	77	72	>95:5	
	86	84	>95:5	
	72	50	>95:5	
	65	64	>95:5	
	86	76	95:5	
	73[c]	79[d]	>95:5	

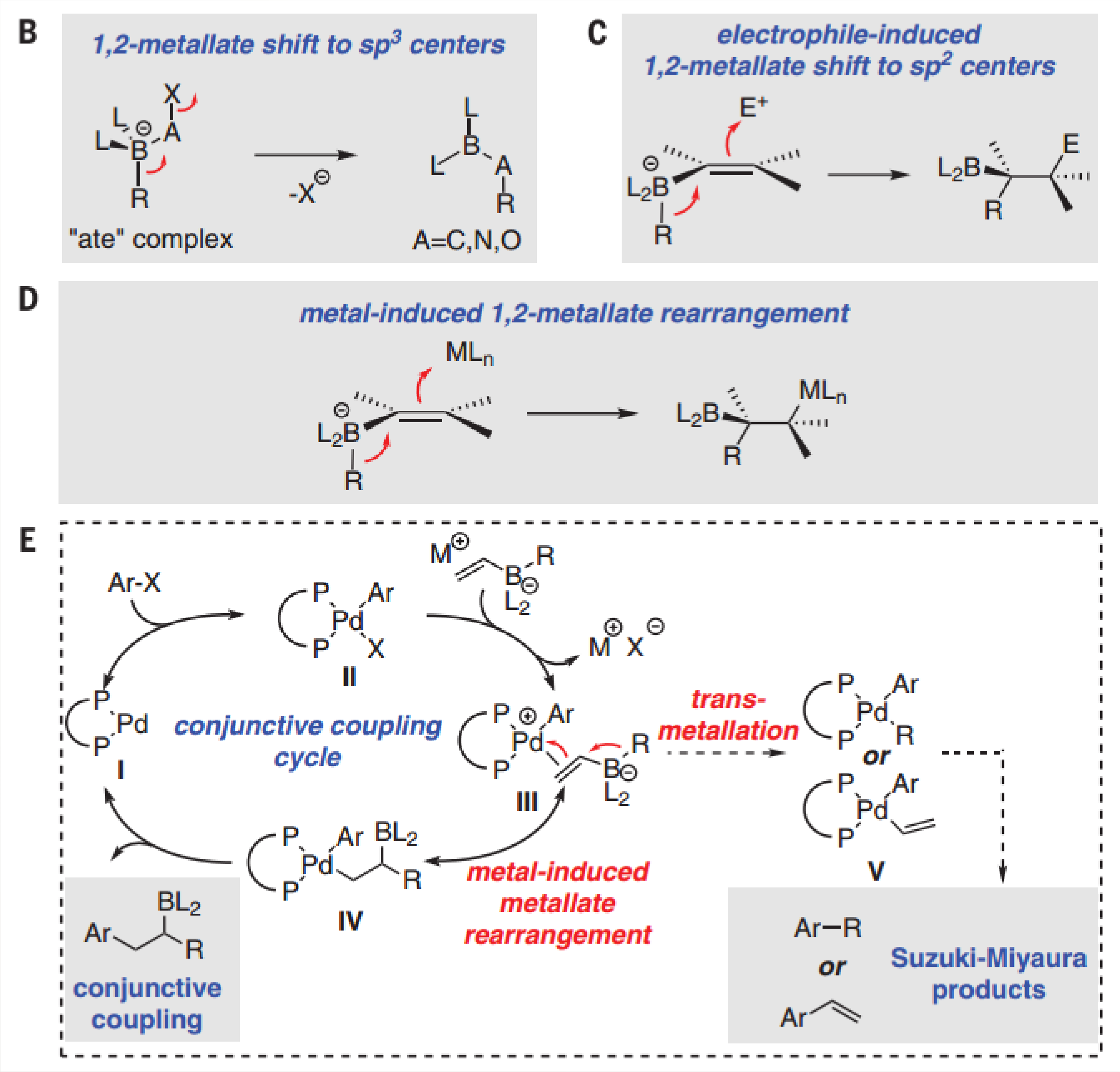
Phillip J. Unsworth, Dr. Daniele Leonori, Varinder K. Aggarwal. *Angew. Chem. Int. Ed.*, **2014**, *53*, 9846-9850



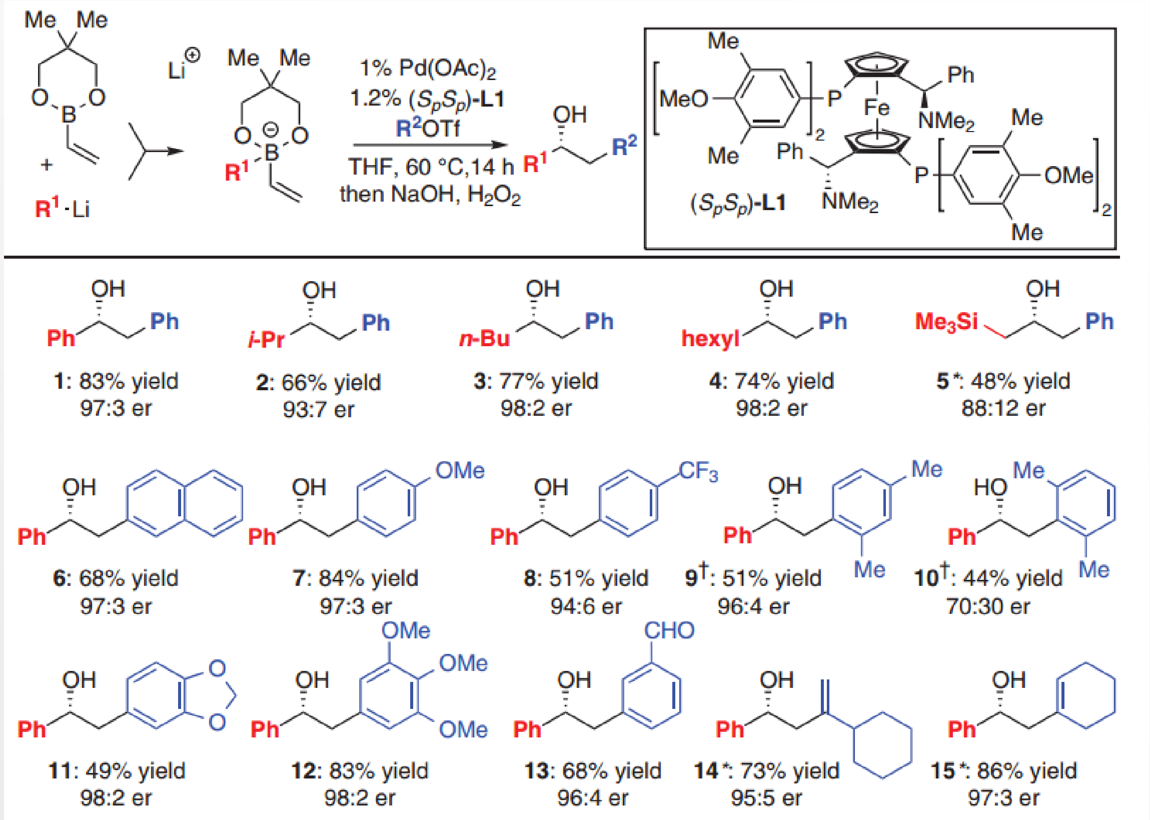


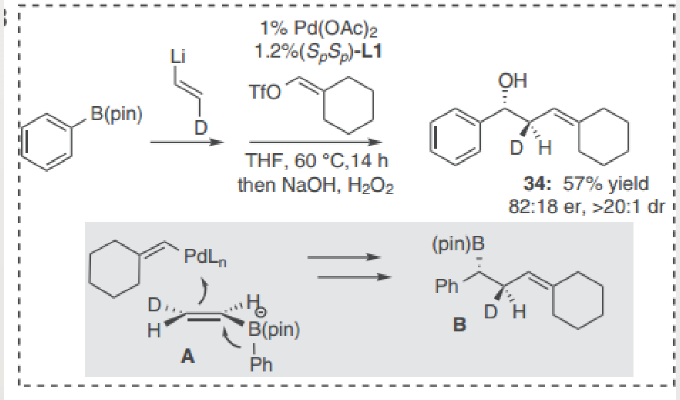
Phillip J. Unsworth, Dr. Daniele Leonori, Varinder K. Aggarwal. *Angew. Chem. Int. Ed.*, **2014**, *53*, 9846-9850

Merging the Metal catalysis And 1,2-metallate Migration



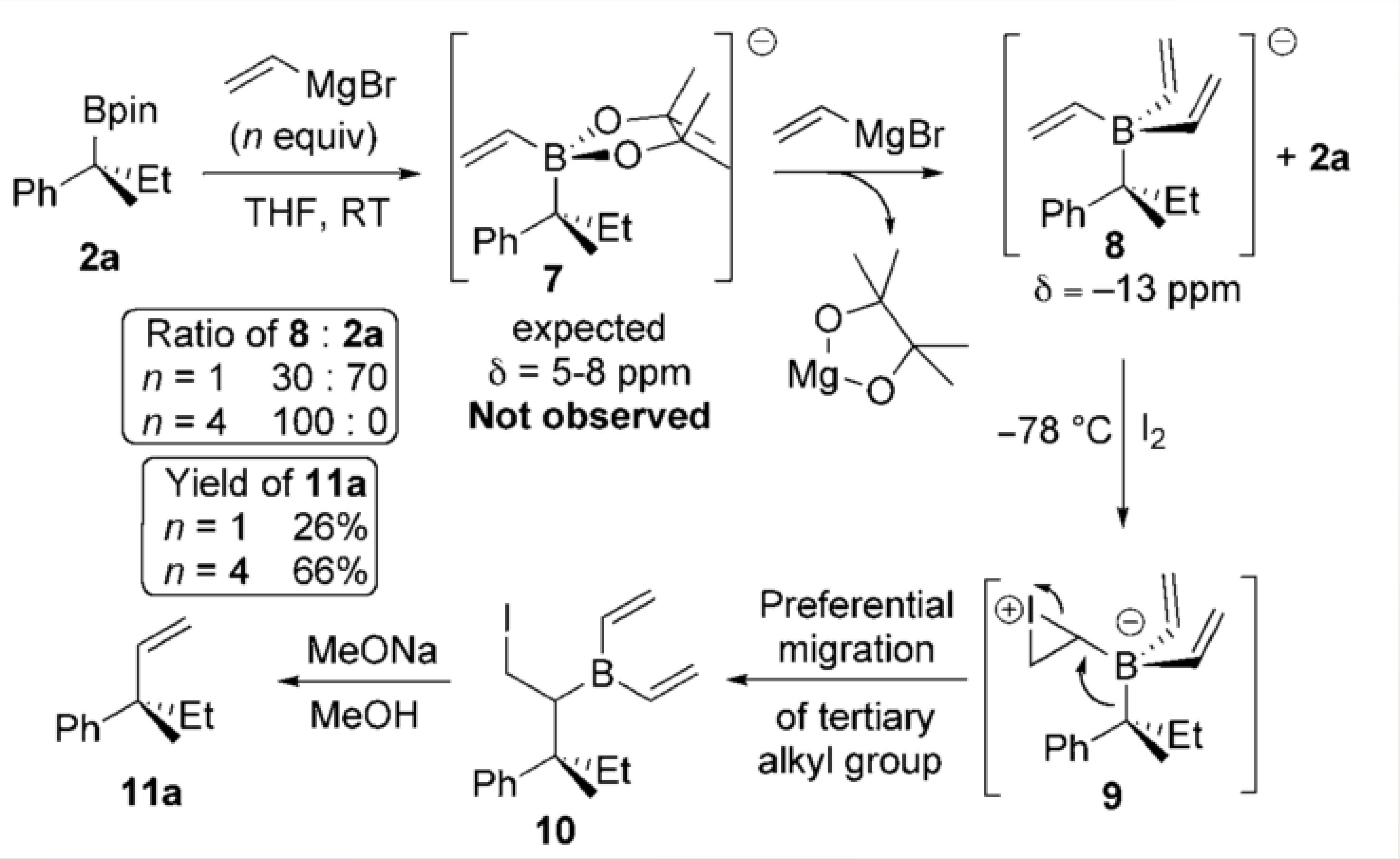
L. Zhang, G. J. Lovinger, E. K. Edelstein, A. A. Szymaniak, M. P. Chierchia and J. P. Morken, *Science*, **2016**, 351, 70.

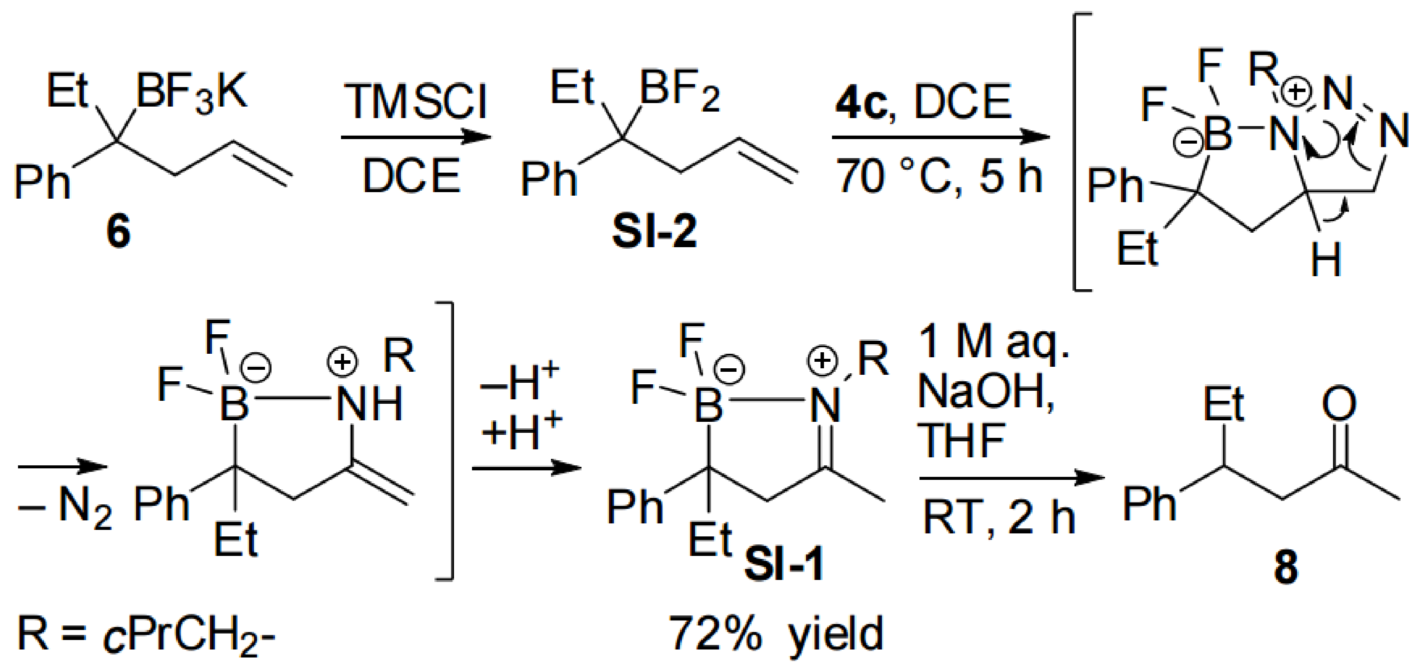


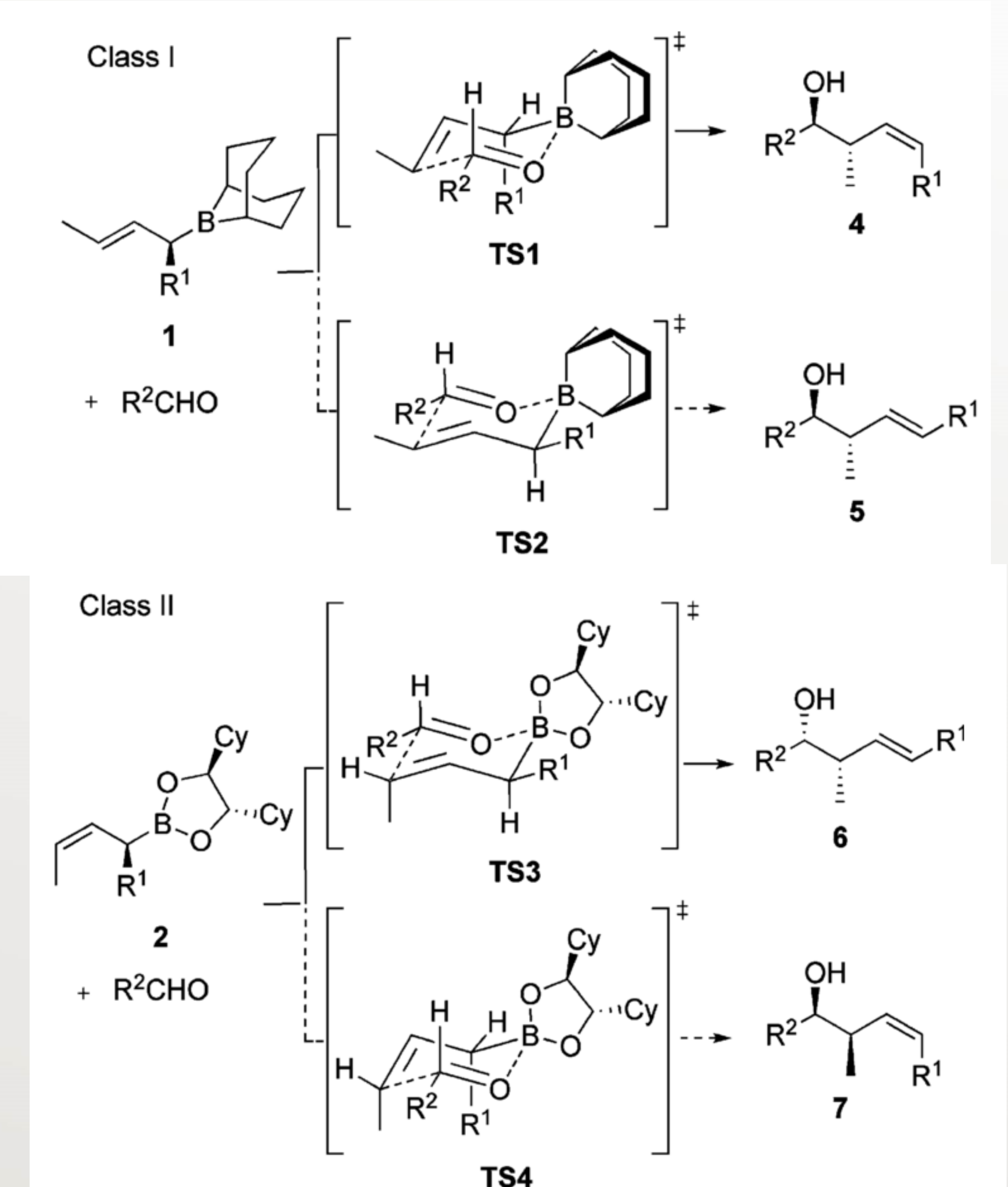


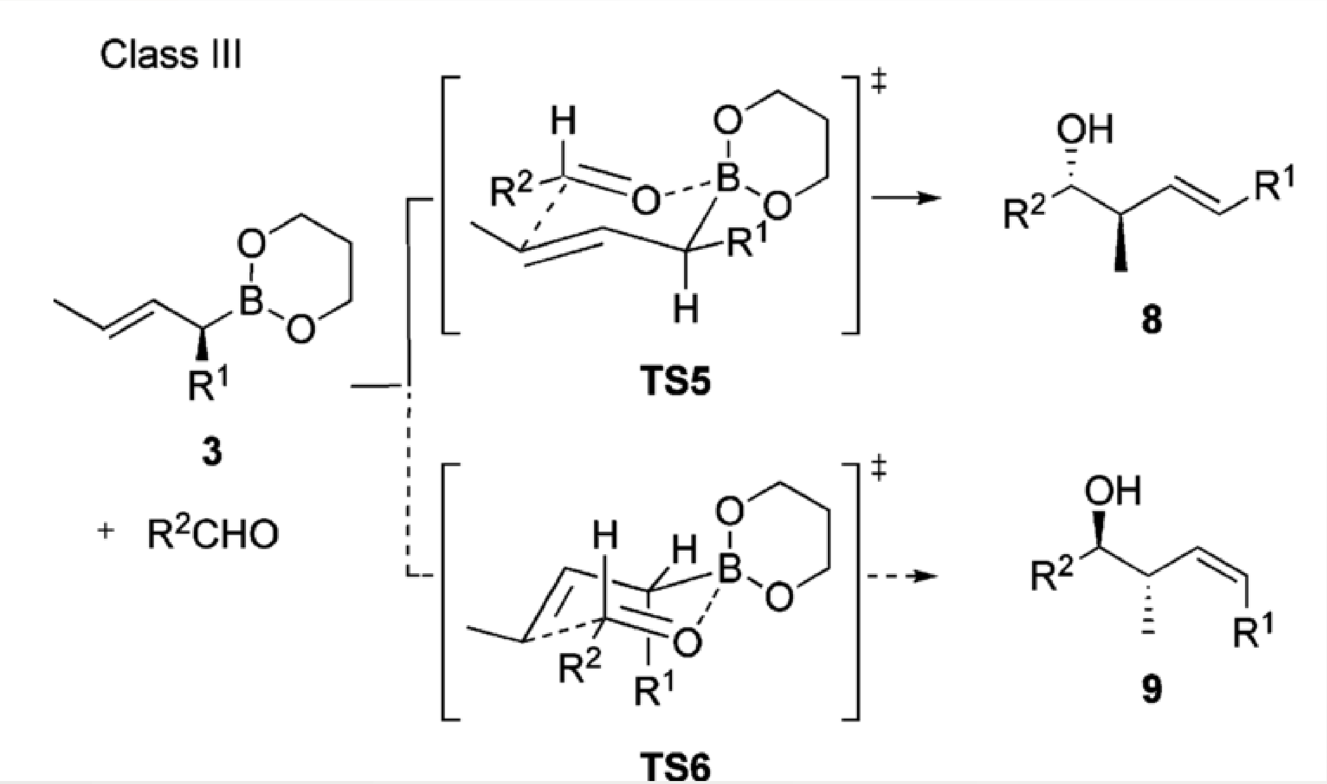
L. Zhang, G. J. Lovinger, E. K. Edelstein, A. A. Szymaniak, M. P. Chierchia and J. P. Morken, *Science*, **2016**, 351, 70.

Thank you for your attention


Bpin
Ph
Et
2a
MgBr
(n equiv)
THF, RT
B
O
O
Ph
Et
7
expected
δ = 5-8 ppm
Not observed
MgBr
O
Mg
O
B
Ph
Et
8
+ 2a
δ = –13 ppm
Ratio of 8 : 2a
n = 1 30 : 70
n = 4 100 : 0
Yield of 11a
n = 1 26%
n = 4 66%
–78 °C
I2
I
B
Ph
Et
9
Preferential
migration
of tertiary
alkyl group
I
B
Ph
Et
10
MeONa
MeOH
Ph
Et
11a


Et
BF_3K
Ph
6
TMSCl
DCE
Et
BF_2
Ph
SI-2
4c, DCE
70 °C, 5 h
F
F
R
N
N
N
B
Ph
Et
H
– N_2
F
F
B
R
NH
Ph
Et
–H^+
+H^+
F
F
B
R
N
Ph
Et
SI-1
1 M aq. NaOH, THF
RT, 2 h
Et
O
Ph
8
R = cPrCH_2-
72% yield


Class I
1
+ R²CHO
TS1
TS2
4
5
Class II
2
+ R²CHO
TS3
TS4
6
7


Class III
3
+ R2CHO
TS5
TS6
8
9