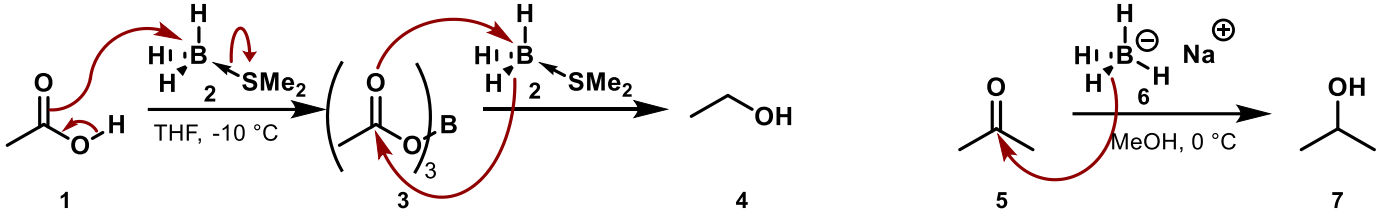
1,2-Metallate Rearrangements of Boron Ate-Complexes

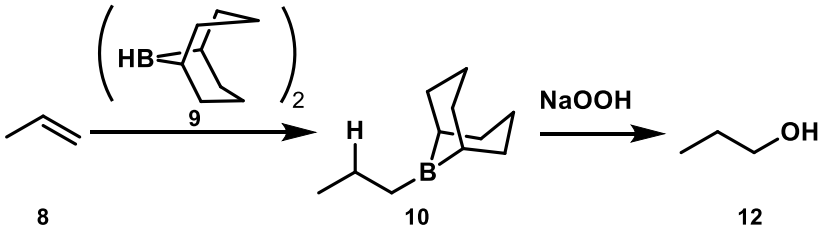
Matteson Chemistry and its Evolution

Boron in Synthesis

- Reductions using electrophil borane and nucleophilic borohydrides

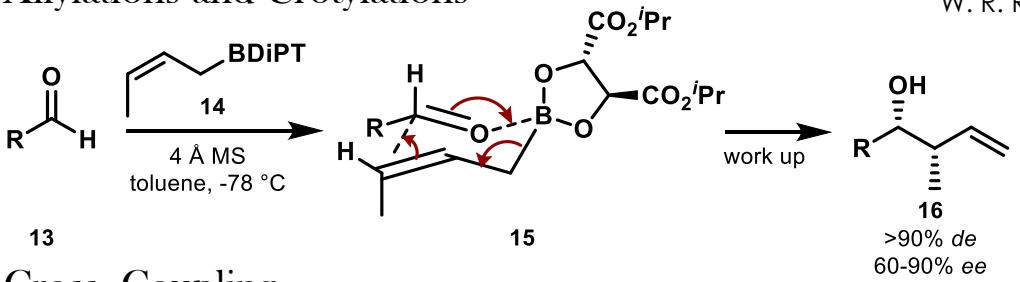


- Hydroboration



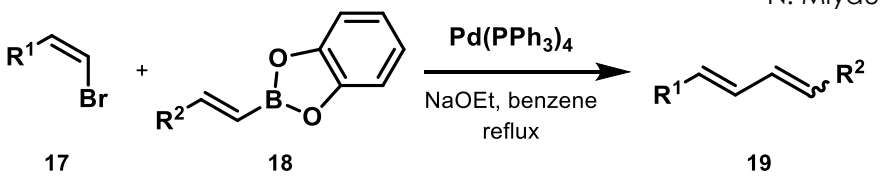
- Allylations and Crotylations

W. R. Roush *et al ., J. Am. Chem. Soc.* **1985**, *107*, 8186-8190.



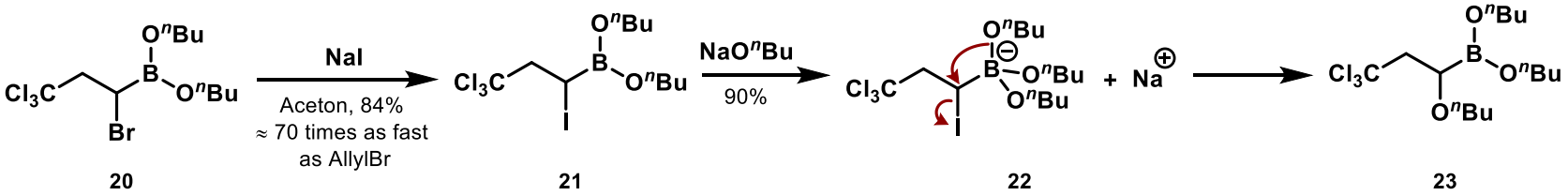
- Cross- Coupling

N. Miyaura, K. Yamada, A. Suzuki, *Tetrahedron Lett.* **1979**, *20*, 3437-3440.

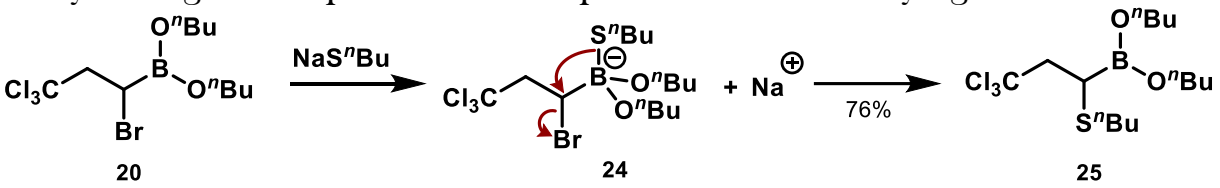


The 1,2-Boronate Rearrangement

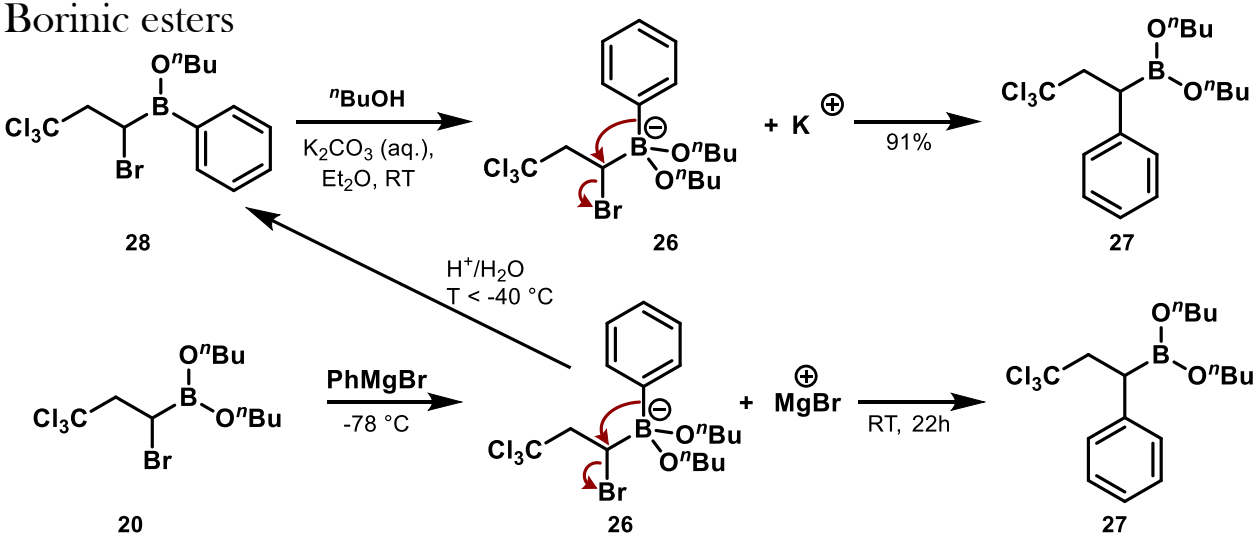
- Matteson 1963



- Only strong nucleophiles can compete with the butoxy ligand

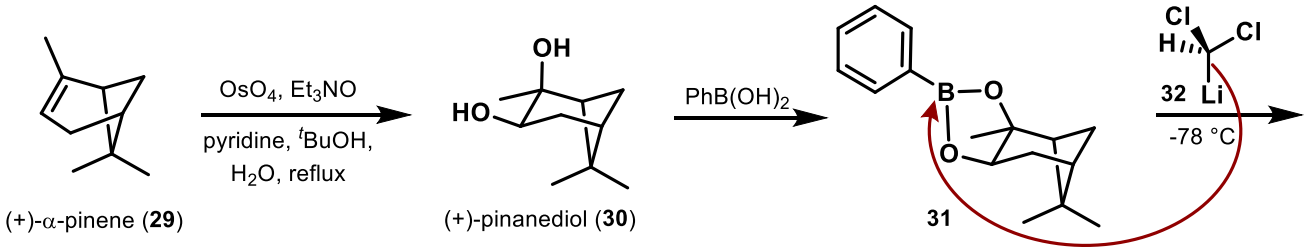


- Borinic esters

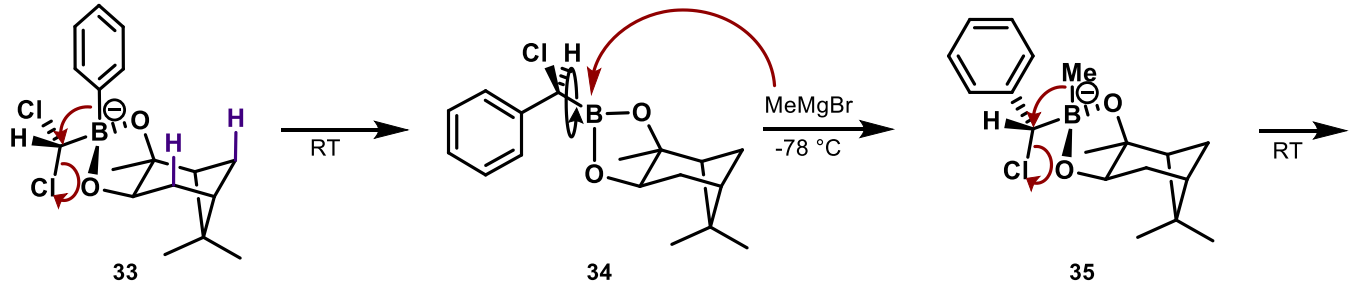


D. S. Matteson, R. W. H. Mah, *J. Org. Chem.* **1963**, *28*, 2171-2174.; D. S. Matteson, R. W. H. Mah, *J. Am. Chem. Soc.* **1963**, *85*, 2599-2603.

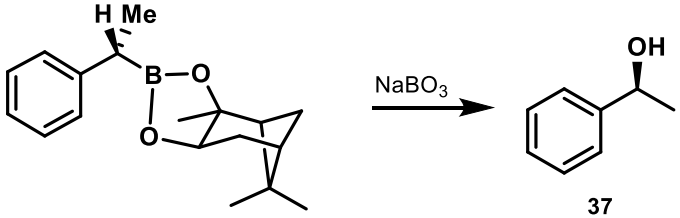
Substrate Control: Matteson Chemistry



(+)-α-pinene (**29**) (+)-pinanediol (**30**) **31**



33 **34** **35**

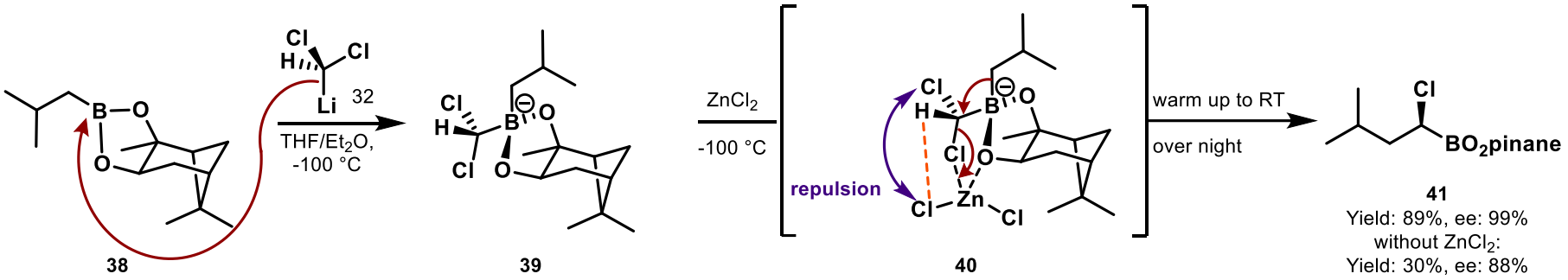


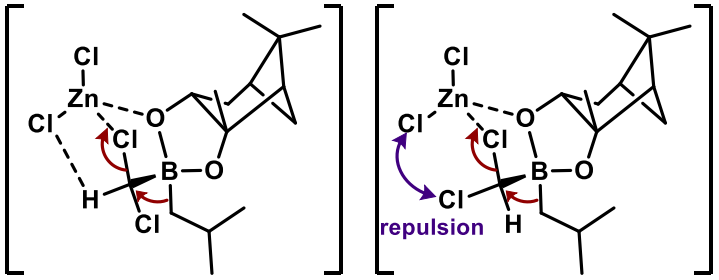
36 **37**
Yield: 94%
ee: 93,7%

- The attack of the carbon nucleophile approaches from the convex side of the molecule **31**
- The rearrangement requires anti- periplanar standing of the migrating- and the leaving group

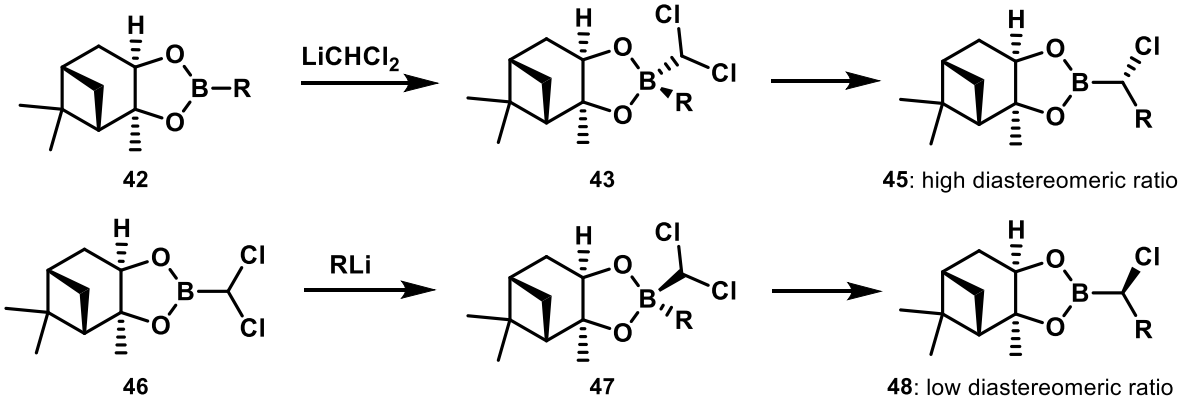
D. S. Matteson, R. Ray, *J. Am. Chem. Soc.* **1980**, *102*, 7590-7591.
R. Ray, D. S. Matteson, *Tetrahedron Lett.* **1980**, *21*, 449-450.

Homologation





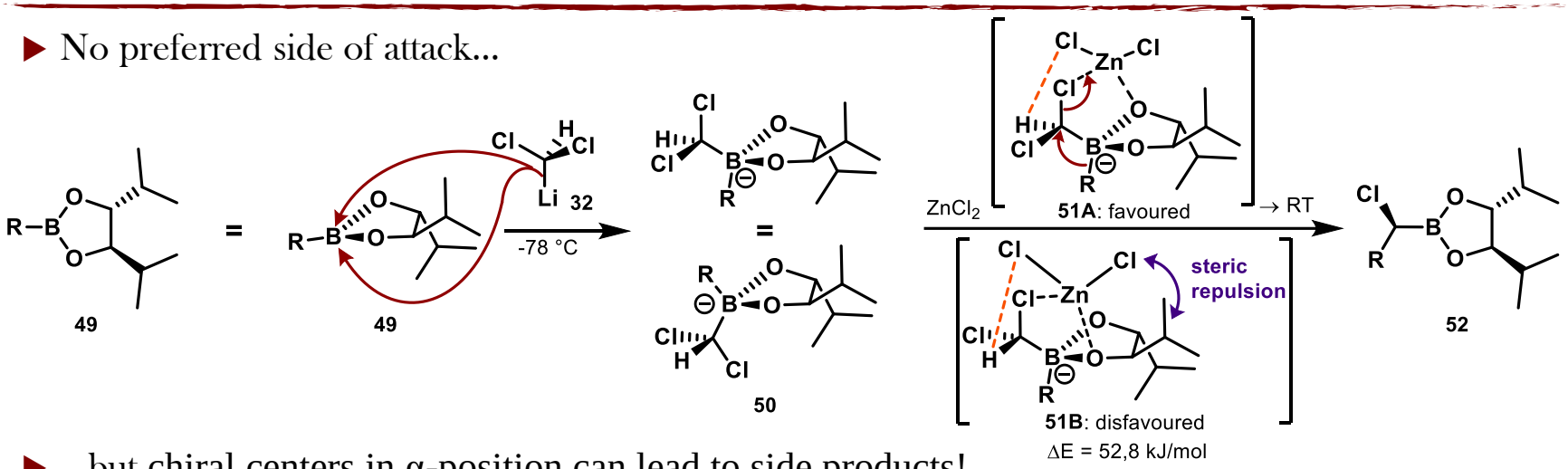
D. S. Matteson, K. M. Sadhu, *J. Am. Chem. Soc.* **1983**, *105*, 2077-2078.
E. J. Corey, D. Barnes-Seeman, T. W. Lee, *Tetrahedron: Asymmetry* **1997**, *8*, 3711-3713.



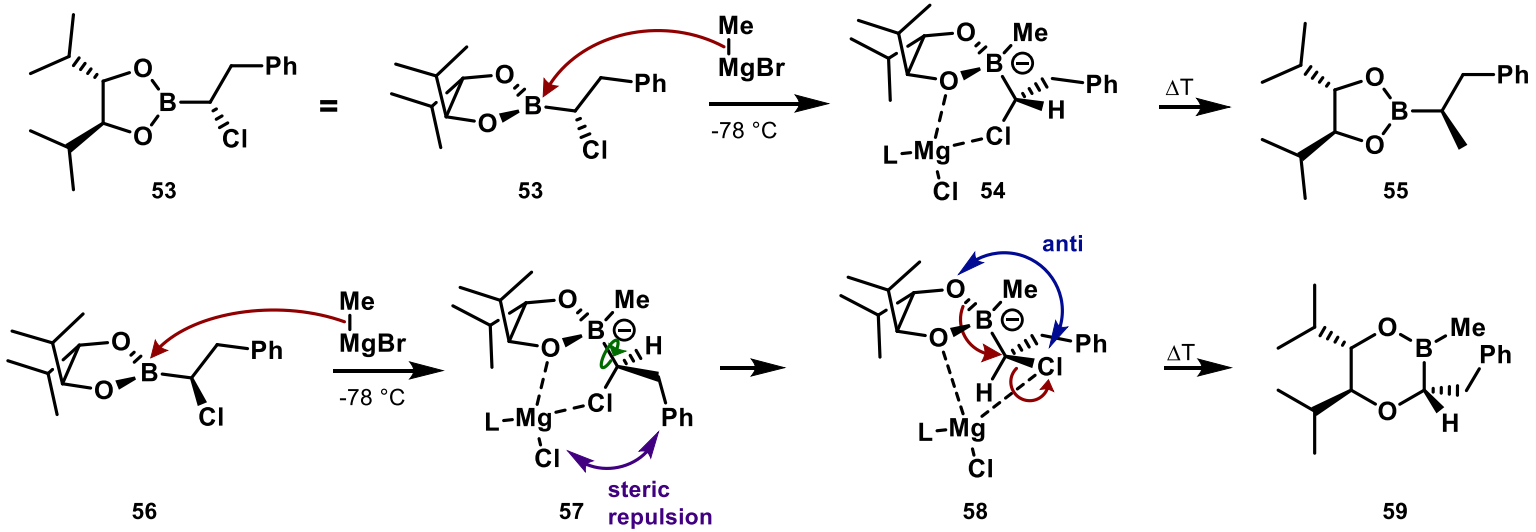
- $ZnCl_2$ and other Lewis acids bind to the less hindered oxygen atom facilitate the 1,2-rearrangement
- The order of addition can sometimes determine the diastereomeric ratio

C2-Symmetric Boronic esters

- No preferred side of attack...



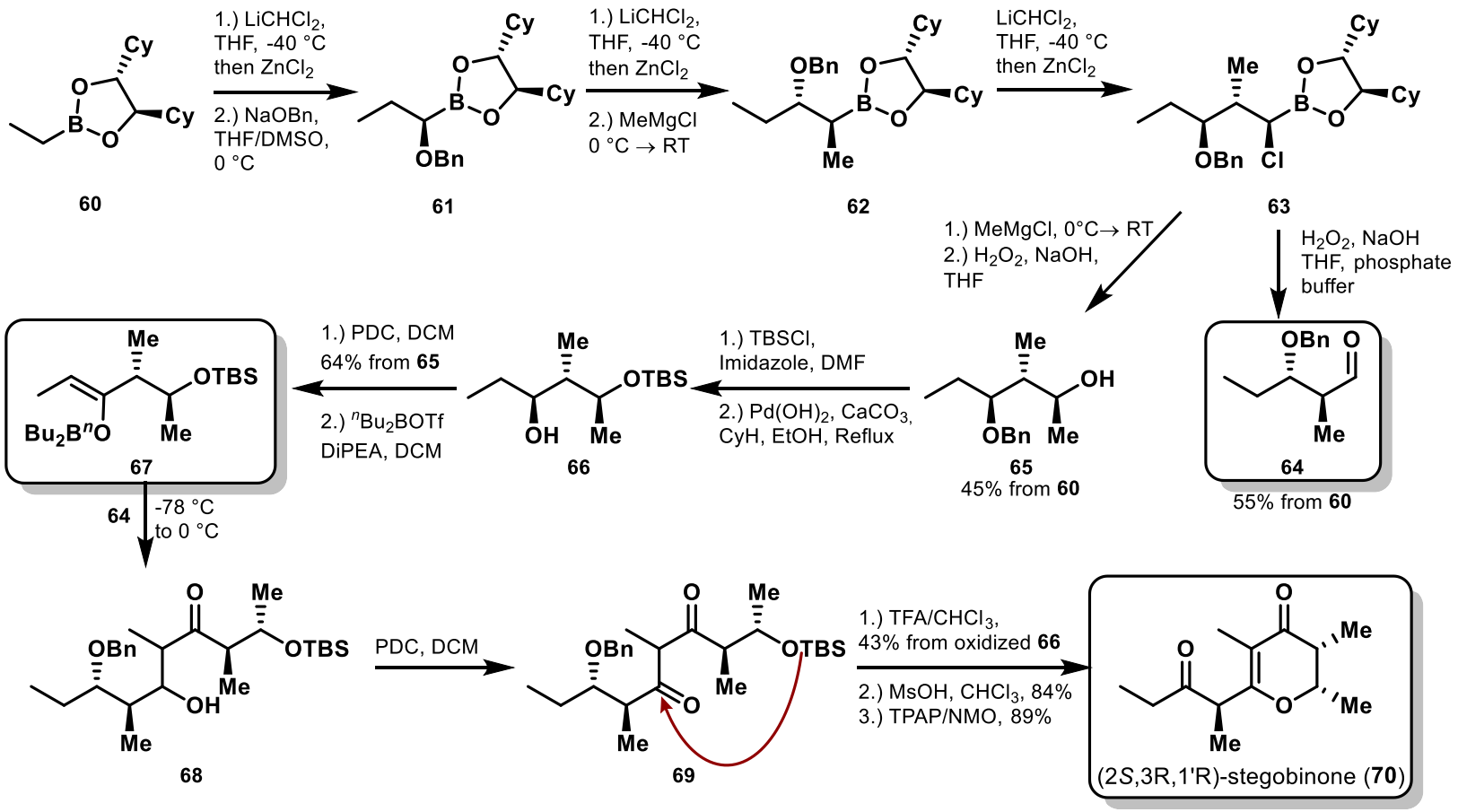
- ...but chiral centers in α-position can lead to side products!



Midland, M. M., J. Org. Chem. **1998**, *63*, 914–915.

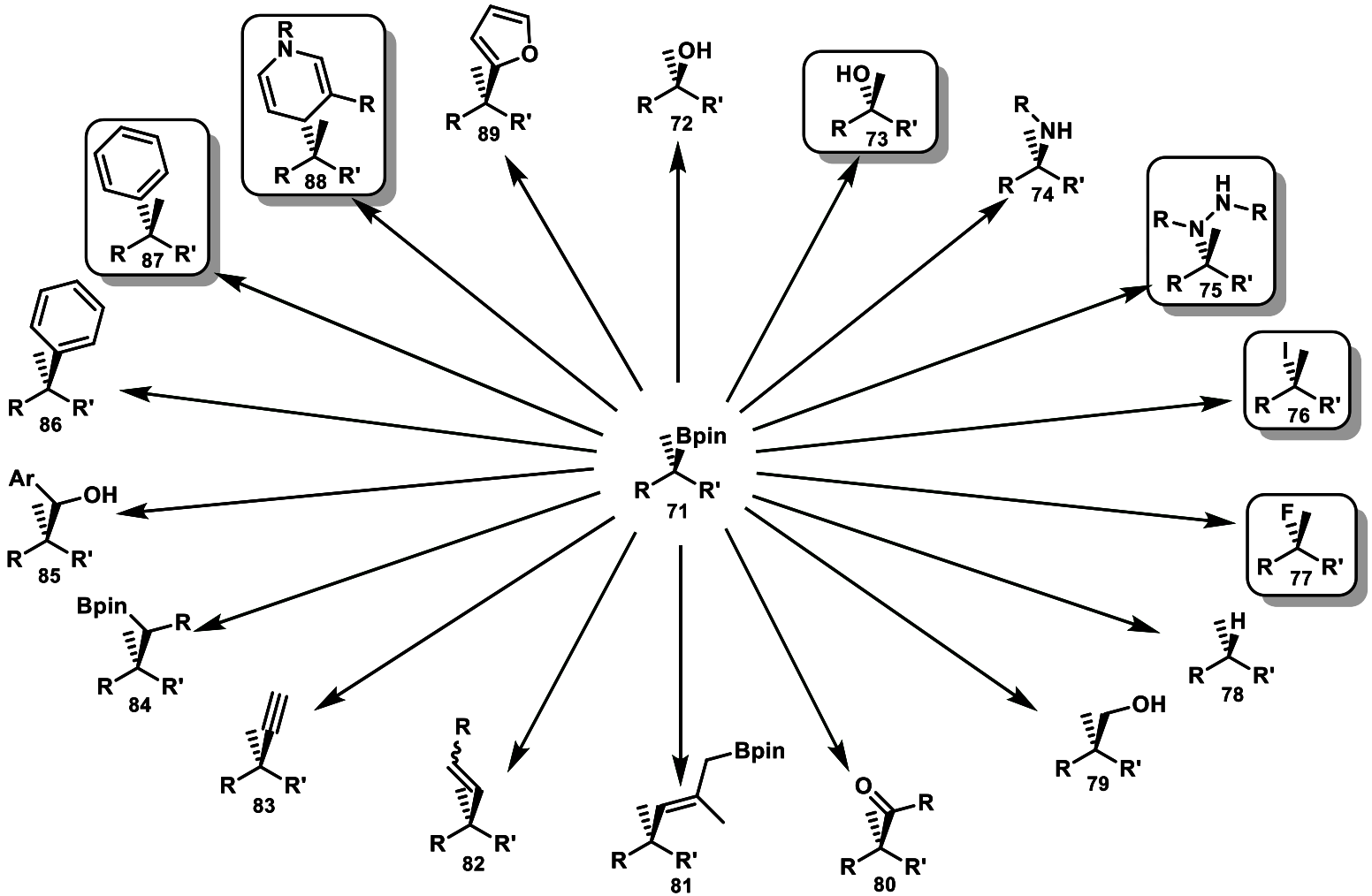
P. B. Tripathy, D. S. Matteson, *Synthesis* **1990**, *1990*, 200-206.

Administration in the Total Synthesis of (2S,3R,1'R)-Stegobinone



D. S. Matteson, H.-W. Man, O. C. Ho, *J. Am. Chem. Soc.* **1996**, *118*, 4560-4566.

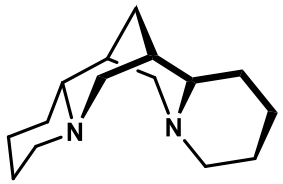
Functionalization of Chiral Boronic Esters - Scope



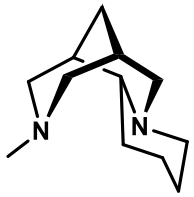
C. Sandford, V. K. Aggarwal, *Chem. Commun.* **2017**, *53*, 5481-5494.

Hoppe Chemistry

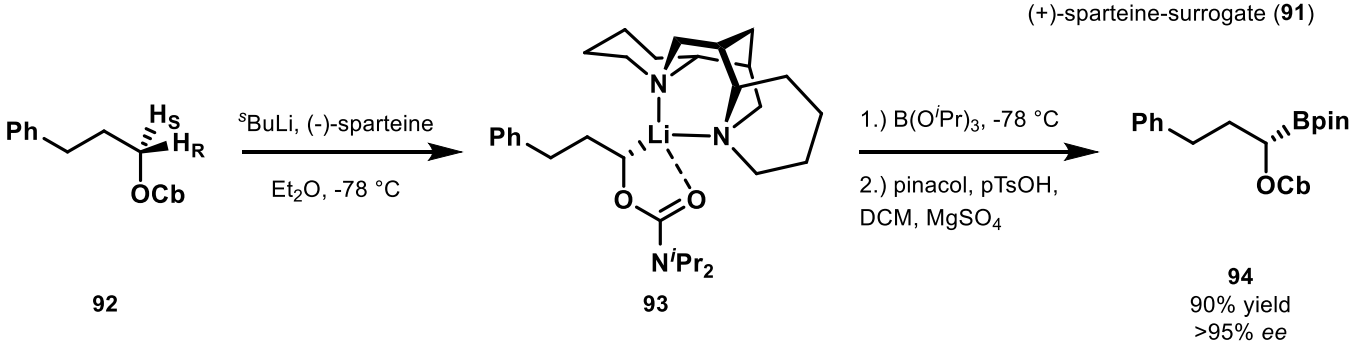
- (-)-Sparteine isolated from common broom and greater celandine and promotes abstraction of the *pro-(S)* proton
- (+)-Sparteine- surrogate is accessible through cytisine alcaloids from the golden chain (toxic plant of the year 2012!) promotes abstraction of the *pro-(R)* proton
- The configuration of the metal organic species is stable at -78 °C



(-)-sparteine (**90**)



(+)-sparteine-surrogate (**91**)



92

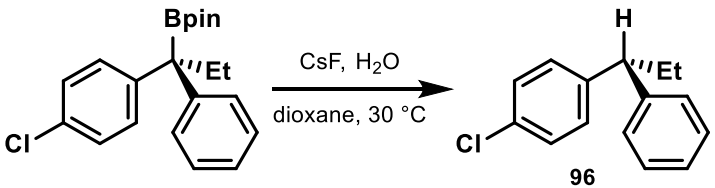
93

94
90% yield
>95% *ee*

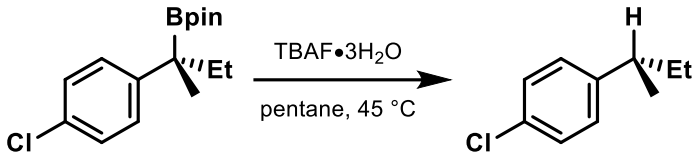
D. Hoppe, T. Hense, *Angew. Chem. Int. Ed.* **1997**, *36*, 2282-2316.
https://upload.wikimedia.org/wikipedia/commons/8/88/Laburnum_anagyroides_flowering.jpg
https://upload.wikimedia.org/wikipedia/commons/thumb/9/9a/Cytisus_scoparius_Habitus_2009April26_SierraMadrona.jpg/800px-Cytisus_scoparius_Habitus_2009April26_SierraMadrona.jpg
E. Beckmann, V. Desai, D. Hoppe, *Synlett* **2004**, *2004*, 2275-2280.

Protodeboronation and Homologation

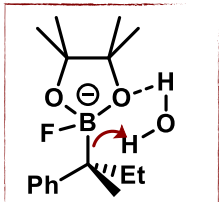
Protodeboronation



95 → 96
Yield: 91%, 99% es

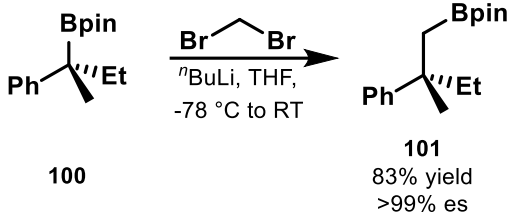


97 → 98
Yield: 99%, 99% es

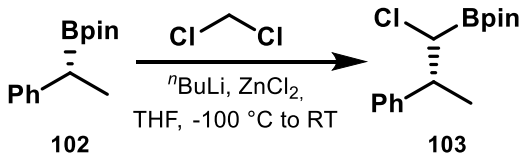


99

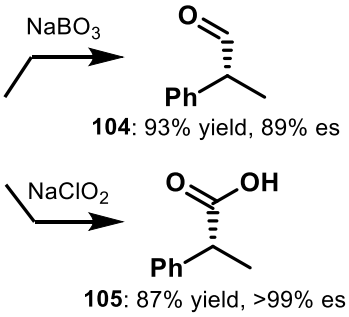
Homologation



100 → 101
83% yield
>99% es

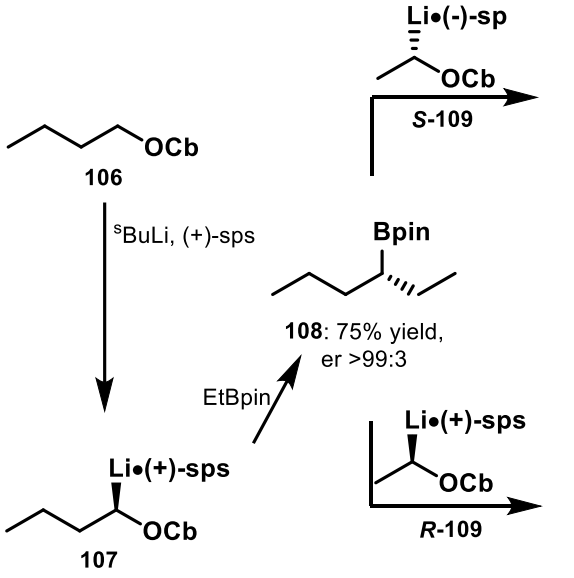


102 → 103



104: 93% yield, 89% es

105: 87% yield, >99% es



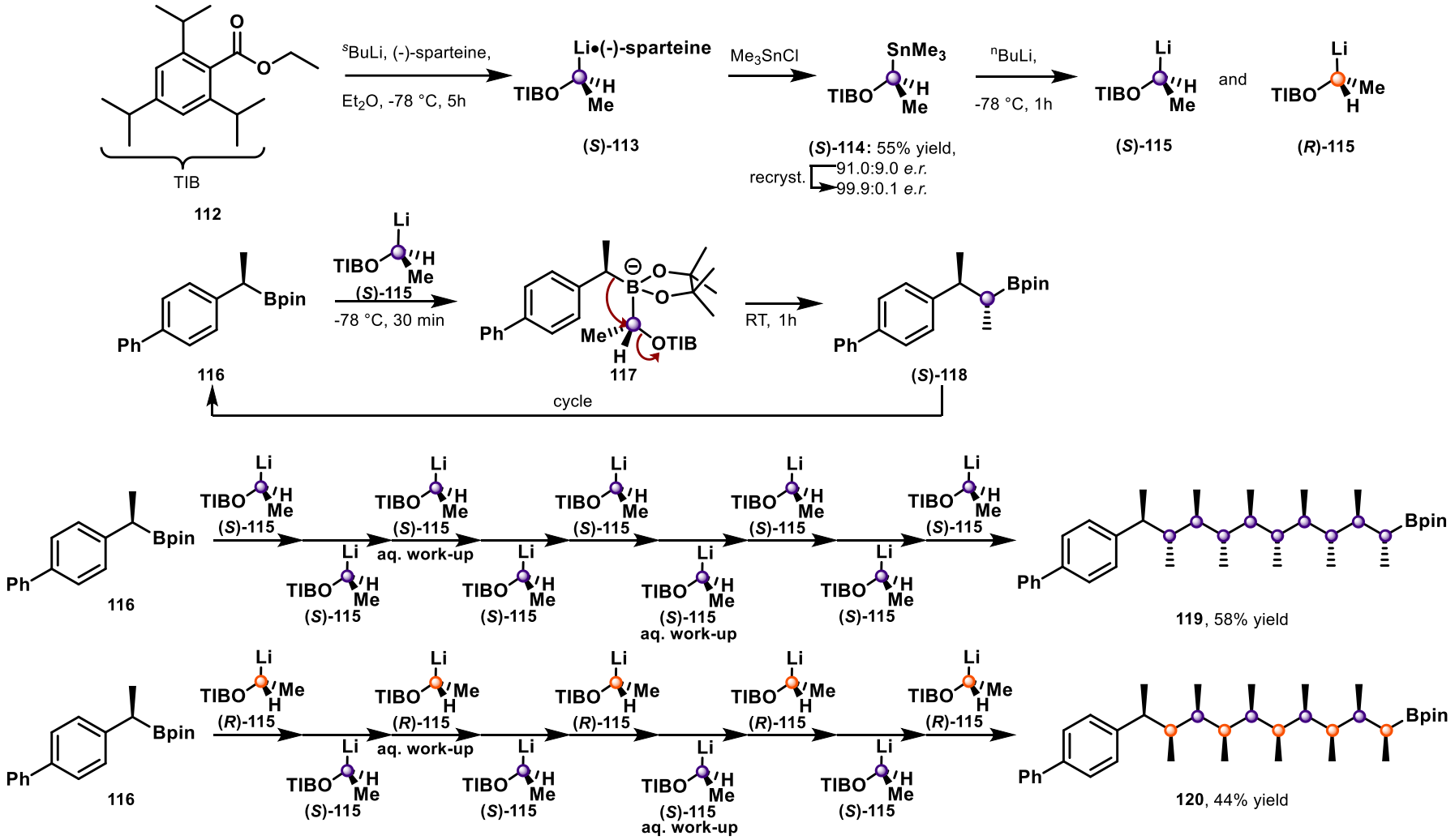
108: 75% yield, er >99:3

110: 64% yield, er >98:2, dr = 96:4

111: 63% yield, er >98:2, dr = 90:10

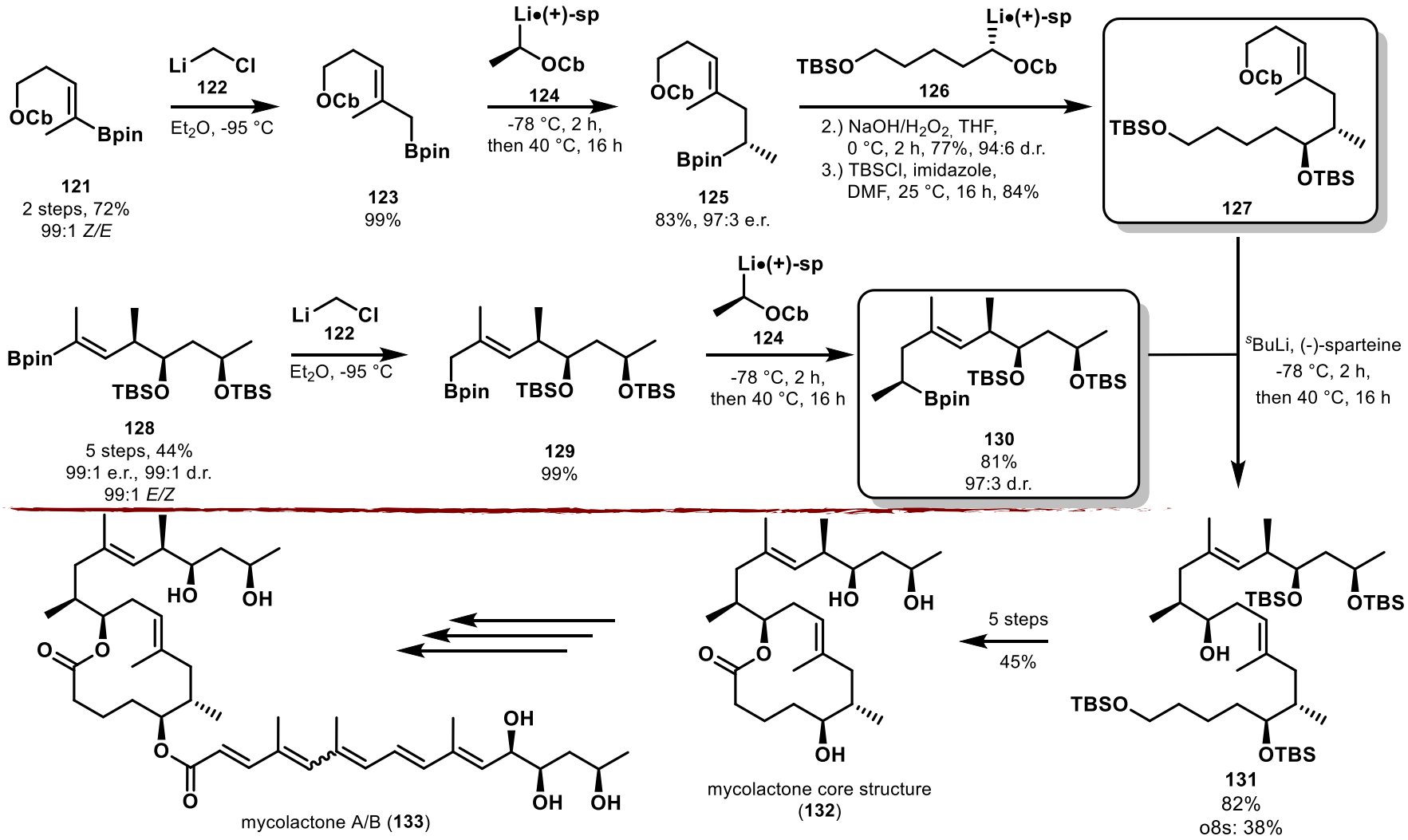
S. Nave, R. P. Sonawane, T. G. Elford, V. K. Aggarwal, *J. Am. Chem. Soc.* **2010**, *132*, 17096-17098.
J. Hesse Matthew, P. Butts Craig, L. Willis Christine, K. Aggarwal Varinder, *Angew. Chem. Int. Ed.* **2012**, *51*, 12444-12448.
A. Chen, L. Ren, C. M. Crudden, *J. Org. Chem.* **1999**, *64*, 9704-9710.
Aggarwal *et al.*, *Angew. Chem. Int. Ed.* **2011**, *50*, 3760-3763.
S. P. Thomas, R. M. French, V. Jheengut, V. K. Aggarwal, *The Chemical Record* **2009**, *9*, 24-39.

Building Block Synthesis



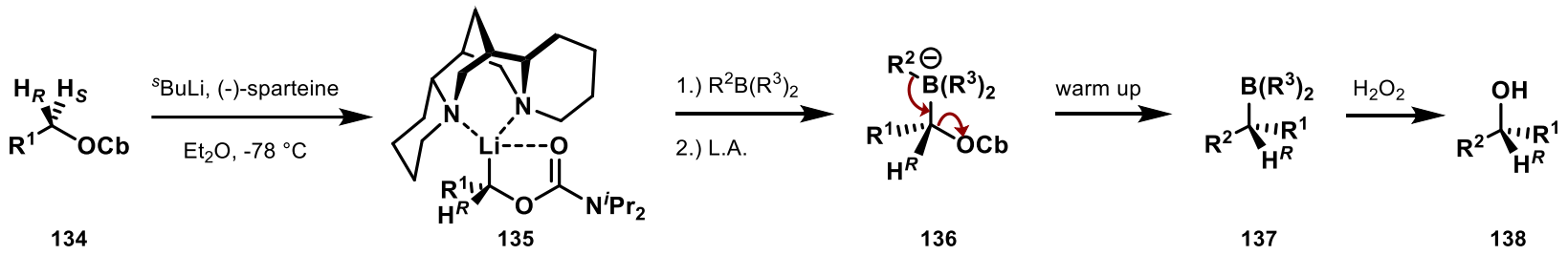
M. Burns, S. p. Essafi, J. R. Bame, S. P. Bull, M. P. Webster, S. b. Balieu, J. W. Dale, C. P. Butts, J. N. Harvey, V. K. Aggarwal, *Nature* **2014**, *513*, 183.

Application in the Synthesis of the Mycolactone Core



A. Brown Christopher, K. Aggarwal Varinder, *Chem. Eur. J.* **2015**, *21*, 13900-13903.

Synthesis of Secondary Alcohols

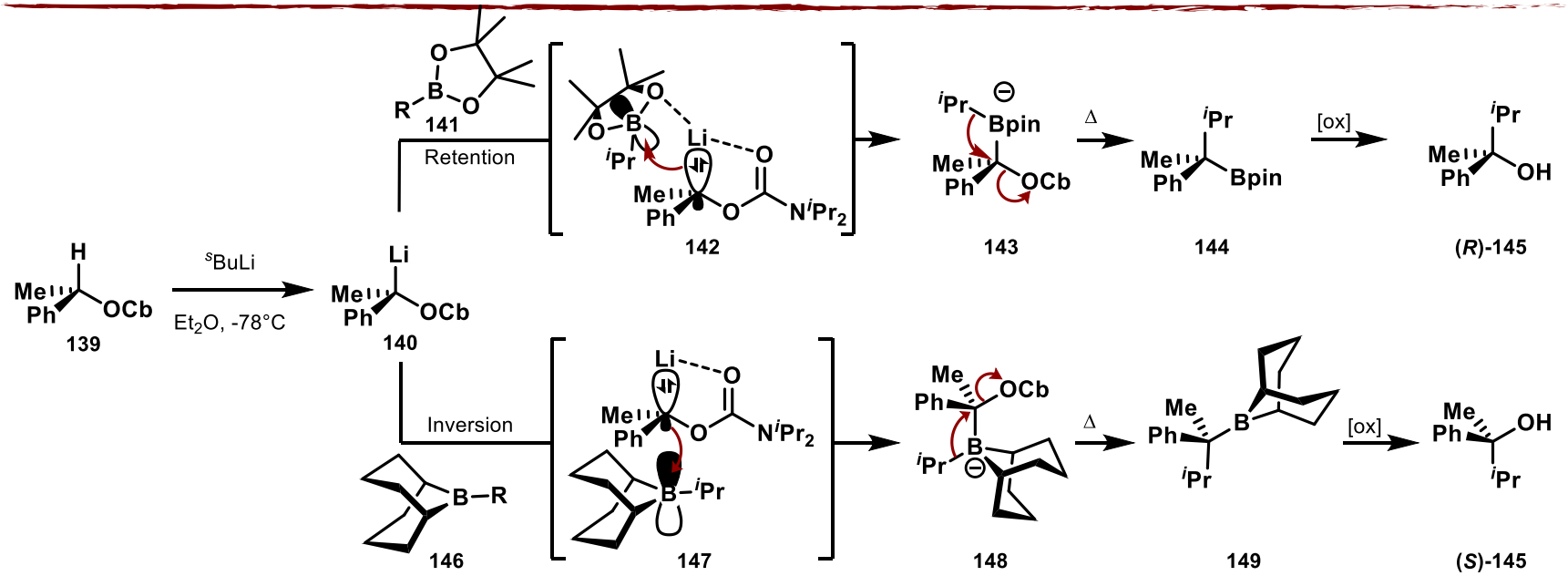


Entry	R^1	R^2	$(R^3)_2$	Lewis Acid	Yield	ee
1	$Ph(CH_2)_2$	Et	Et	-	91	98:2
2	$Ph(CH_2)_2$	^{i}Pr	„9-BBN“	-	90	98:2
3	$Ph(CH_2)_2$	^{n}Hex	„9-BBN“	-	81	98:2
4	$Ph(CH_2)_2$	Ph	„9-BBN“	-	85	88:12
5	$Ph(CH_2)_2$	Ph	„9-BBN“	-	94	97:3
6	$Ph(CH_2)_2$	Ph	Pinacol	$MgBr_2$	90	98:2
7	^{i}Pr	Ph	„9-BBN“	$MgBr_2$	68	96:4
8	^{i}Pr	Ph	Pinacol	$MgBr_2$	70	98:2

- 9-BBN does not migrate in contrast to other alkyl substituents
- Using 9-BBN, $MgBr_2$ increases ee (not for other boranes)
- Boranates rearrange already at -40 °C, boronates only with $MgBr_2$ in ether reflux
- Stereochemistry is retained in the borylation step

J. L. Stymiest, G. Dutheuil, A. Mahmood, V. K. Aggarwal, *Angew. Chem.* **2007**, *119*, 7635-7638.

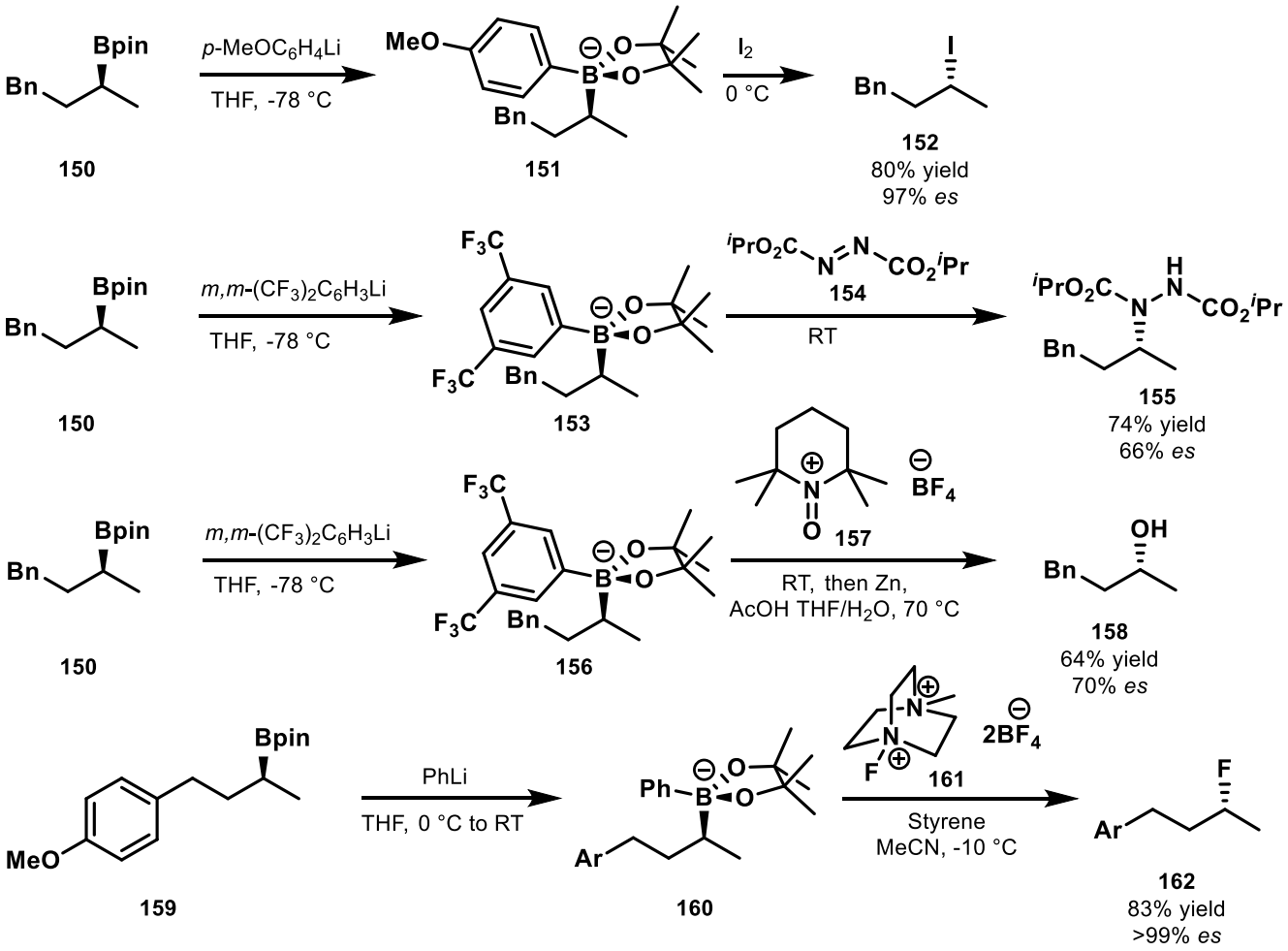
Synthesis of Tertiary Alcohols

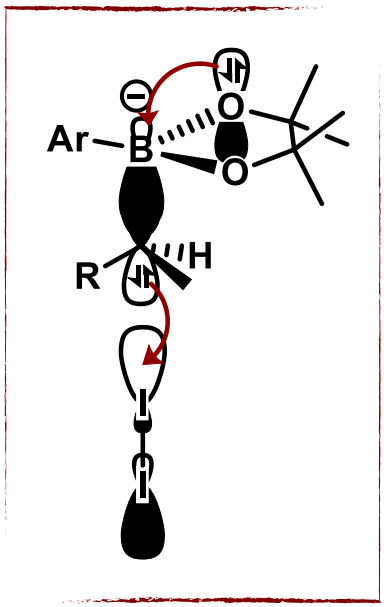


Entry	R	Ligand	Product	Yield	*er* ((*R*)-145/(*S*)-145)
1	Et	Pin	(*R*)-145	95%	99:1
2	^{i}Pr	Pin	(*R*)-145	80%	96:4
3	^{i}Pr	„9-BBN“	(*S*)-145	91%	2:98
4	^{n}Hex	Pin	(*R*)-145	85%	96:4
5	^{n}Hex	„9-BBN“	(*S*)-145	60%	2:98

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

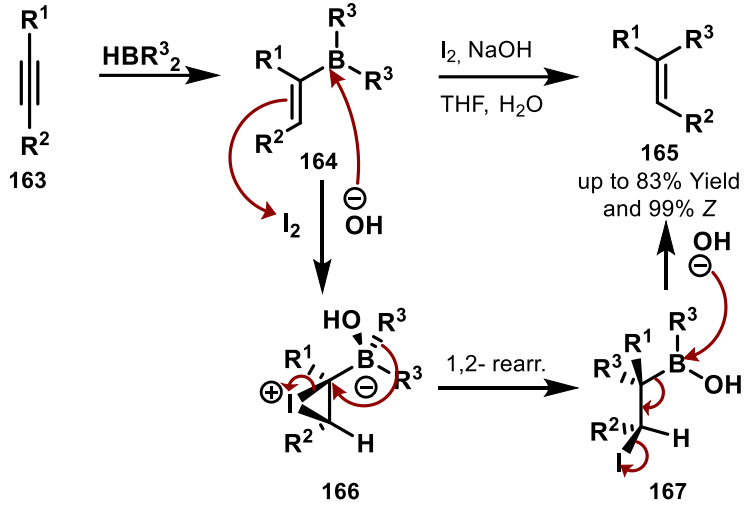
Inversion of configuration by S_E2inv pathway

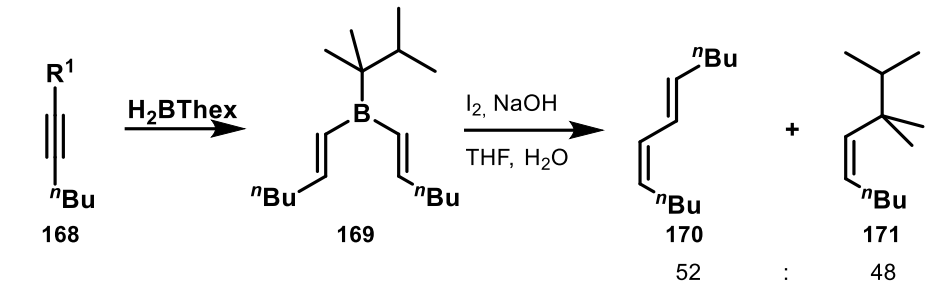


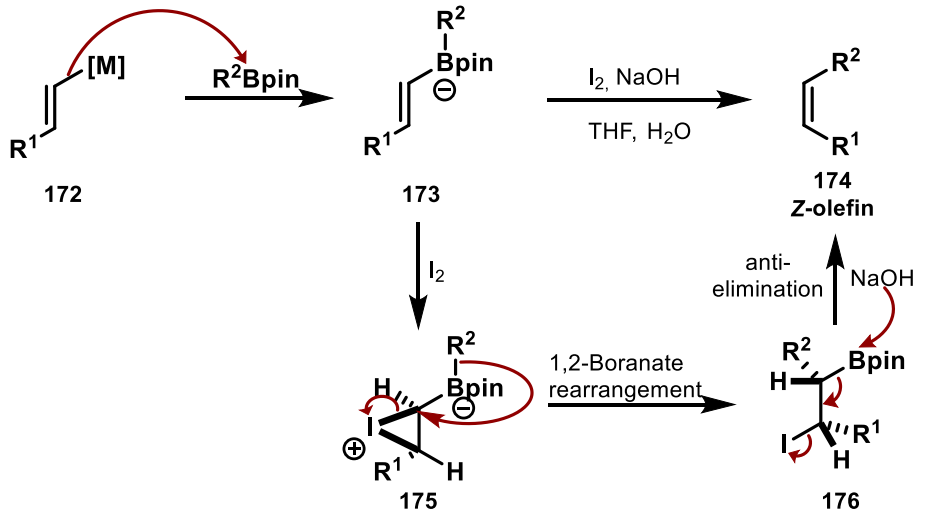


R. Larouche-Gauthier, T. G. Elford, V. K. Aggarwal, *J. Am. Chem. Soc.* **2011**, *133*, 16794-16797.
C. Sandford, R. Rasappan, V. K. Aggarwal, *J. Am. Chem. Soc.* **2015**, *137*, 10100-10103.

Zweifel Olefination



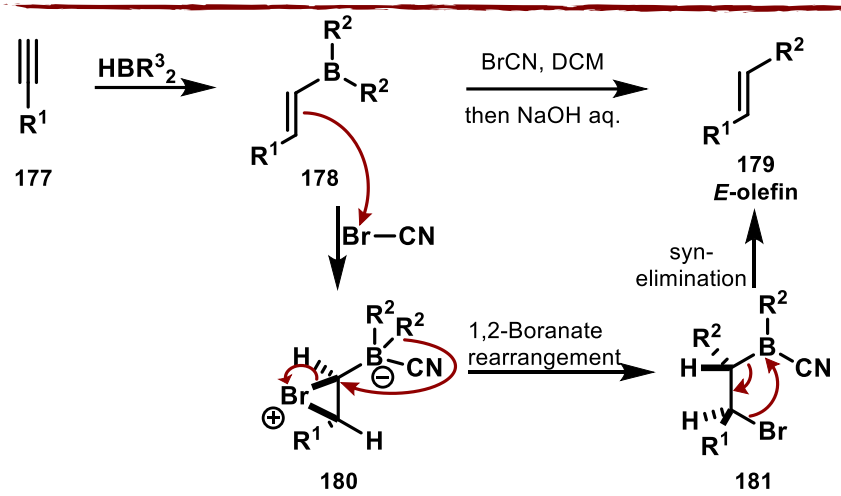




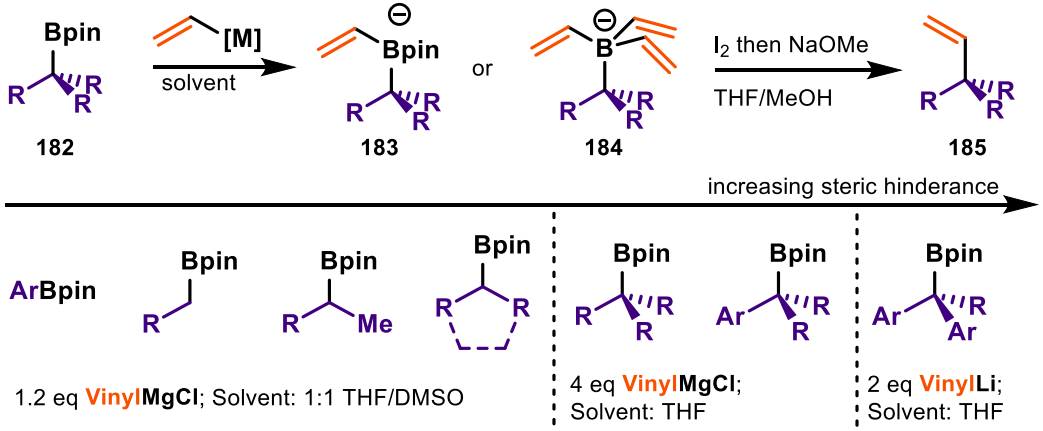
- Vinyl boranes or boronic esters form *cis*- substituted olefins in basic iodine solution
- A iodonium ion is formed and the hydroxide ions trigger the 1,2-boronate shift
- Organic moieties have similar tendency to migrate
- Modification by Matteson using vinyl lithium units

G. Zweifel, H. Arzoumanian, C. C. Whitney, *J. Am. Chem. Soc.* **1967**, *89*, 3652-3653.
G. Zweifel, N. L. Polston, C. C. Whitney, *J. Am. Chem. Soc.* **1968**, *90*, 6243-6245.
D. S. Matteson, P. K. Jesthi, *J. Organomet. Chem.* **1976**, *110*, 25-37.

Zweifel Olefination



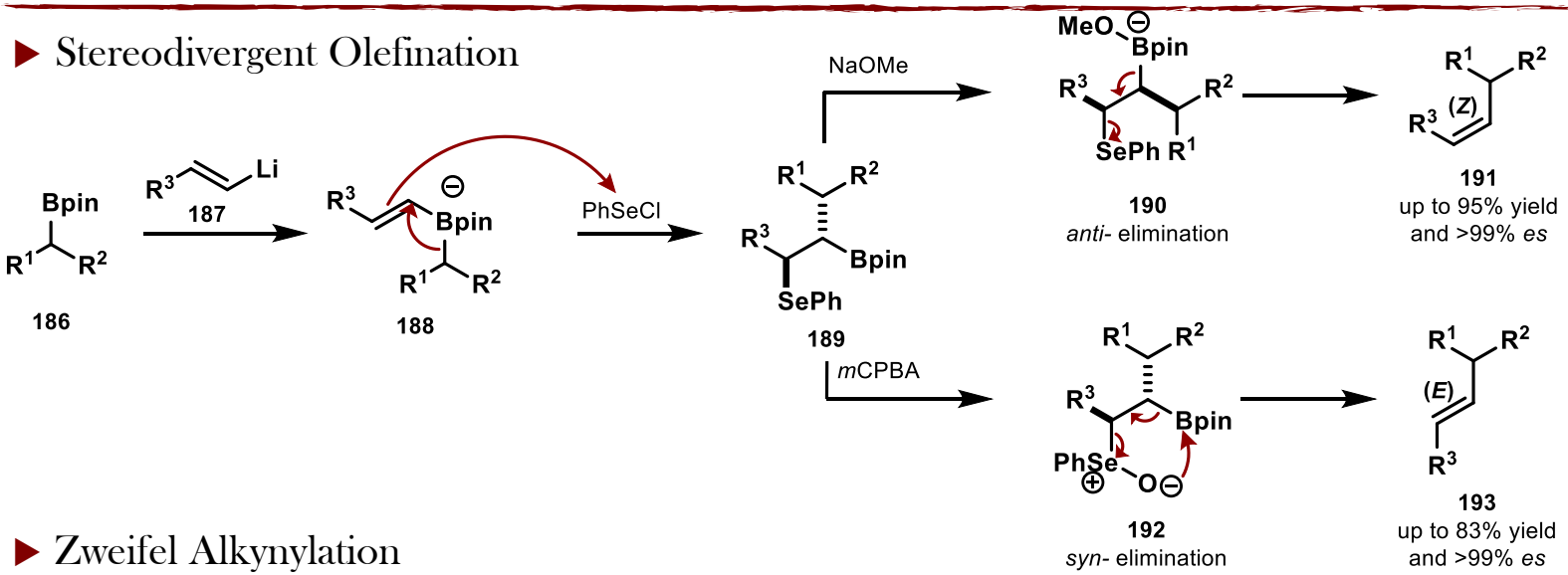
G. Zweifel, R. P. Fisher, J. T. Snow, C. C. Whitney, *J. Am. Chem. Soc.* **1972**, *94*, 6560-6561.



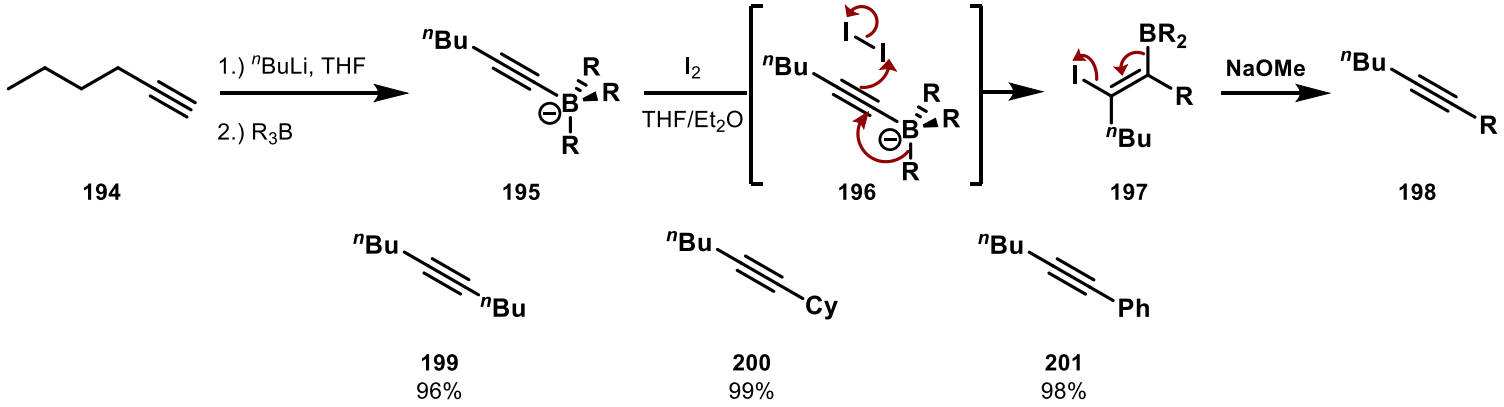
R. J. Armstrong, W. Niwetmarin, V. K. Aggarwal, *Org. Lett.* **2017**, *19*, 2762-2765.
Aggarwal *et al.*, *Angew. Chem. Int. Ed.* **2011**, *50*, 3760-3763.
M. Shimizu, *Angew. Chem. Int. Ed.* **2011**, *50*, 5998-6000.
G. J. Lovinger, M. D. Aparece, J. P. Morken, *J. Am. Chem. Soc.* **2017**, *139*, 3153-3160.

Zweifel Olefination

Stereodivergent Olefination



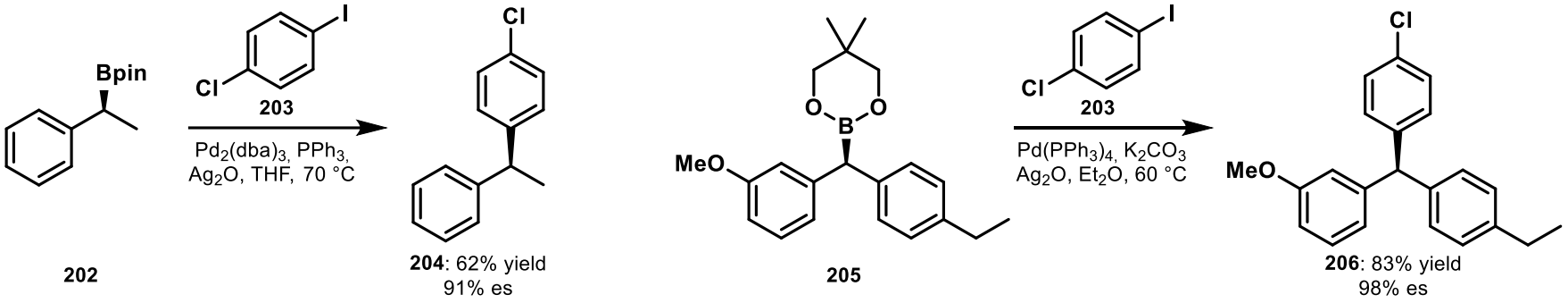
Zweifel Alkynylation



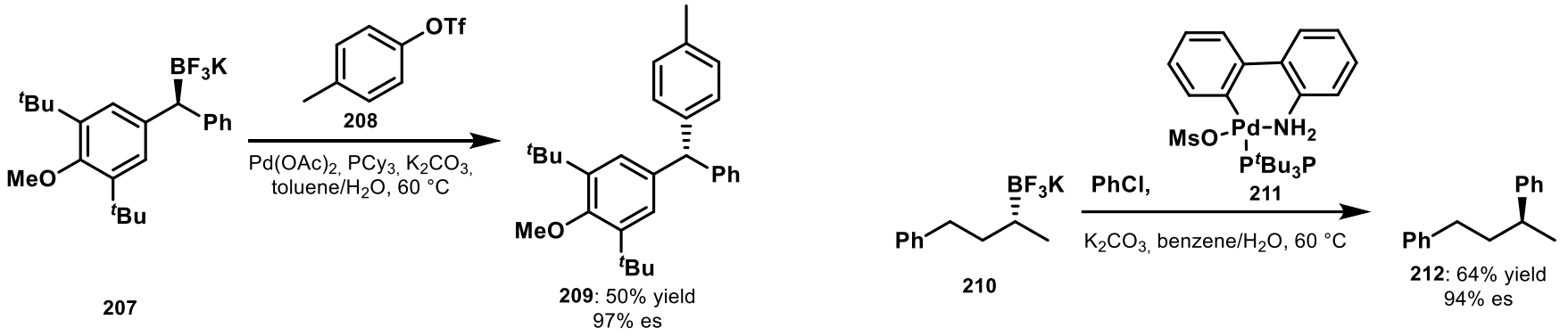
J. Armstrong Roly, C. García-Ruiz, L. Myers Eddie, K. Aggarwal Varinder, *Angew. Chem. Int. Ed.* **2016**, *56*, 786-790.
R. J. Armstrong, C. Sandford, C. Garcia-Ruiz, V. K. Aggarwal, Chem. Commun. **2017**, *53*, 4922-4925.
A. Suzuki, N. Miyaura, S. Abiko, M. Itoh, H. C. Brown, J. A. Sinclair, M. M. Midland, *J. Am. Chem. Soc.* **1973**, *95*, 3080-3081.

Retentive and Invertive Coupling

Retention



Inversion



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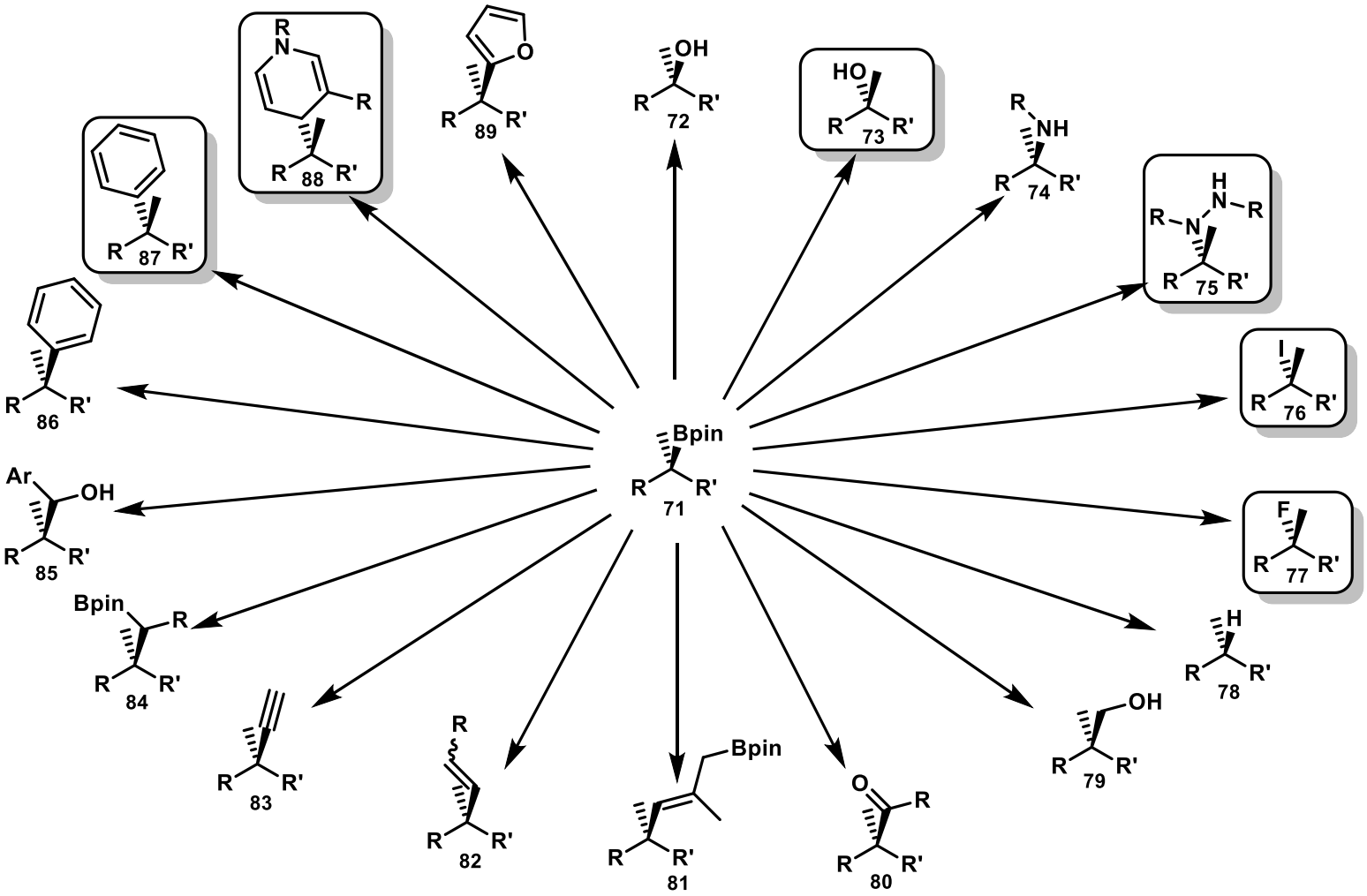
Conclusion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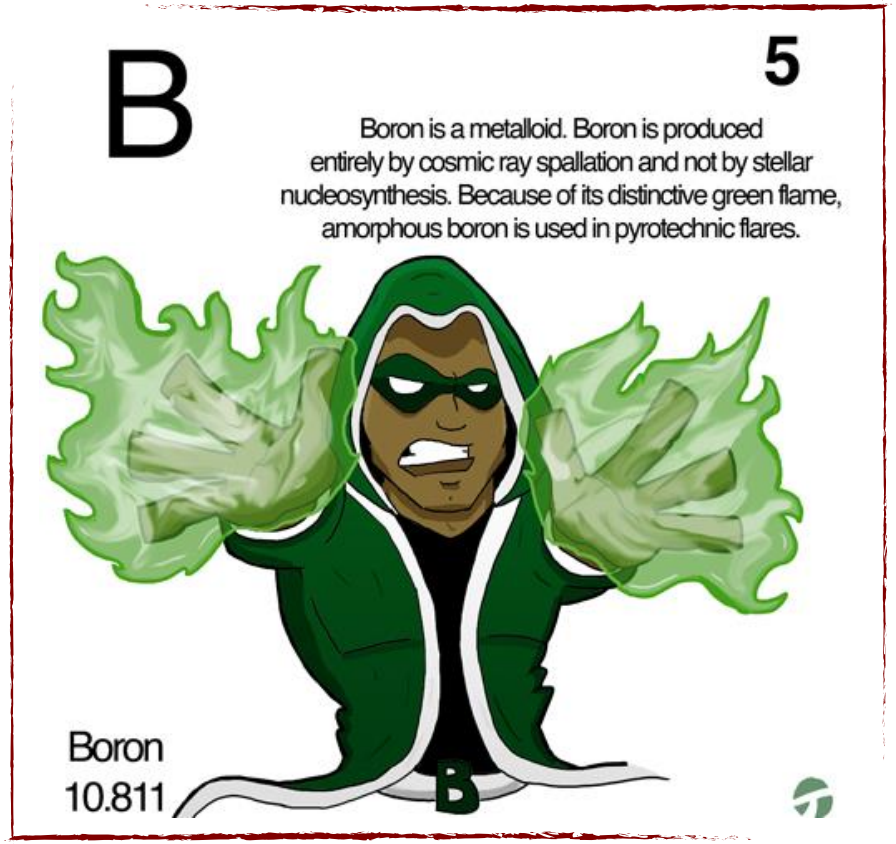
Thank you for your kind attention!

Questions?



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