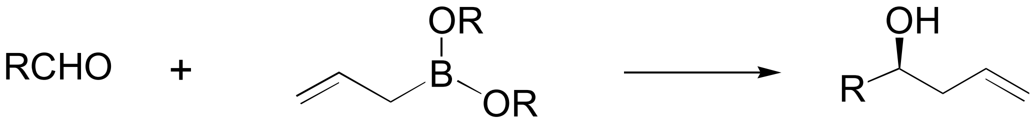
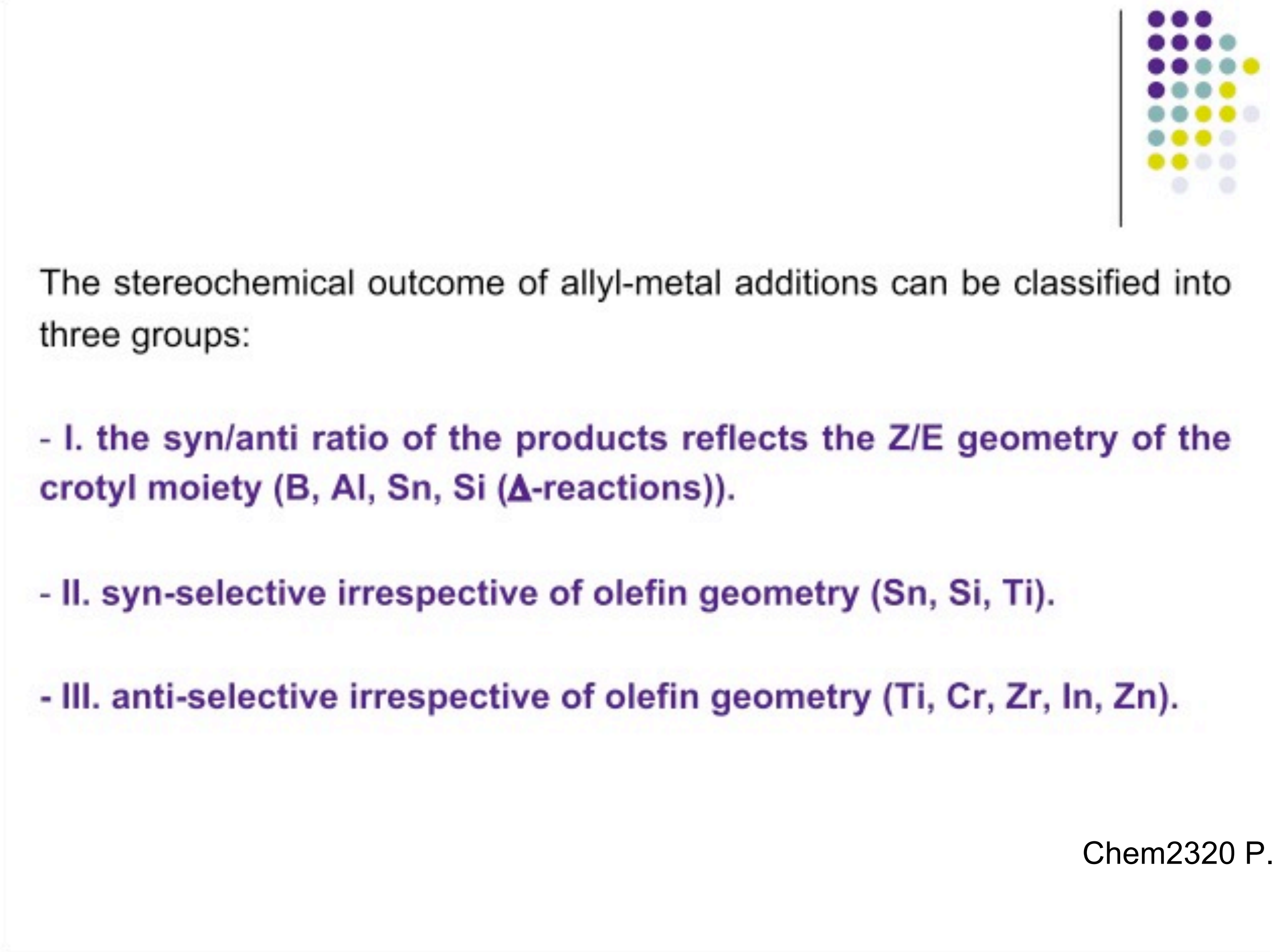
Catalytic Enantioselective Allyl- and Crotylboration of Aldehydes Using Chiral Diol•$SnCl_4$ Complexes. Optimization, Substrate Scope and Mechanistic Investigations



Vivek Rauniyar, Huimin Zhai, and Dennis G. Hall

J. Am. Chem. Soc. **2008**, *130*, 8481-8490.

Current lit.
06/28/08
Akira Nakamura



The stereochemical outcome of allyl-metal additions can be classified into three groups:

- **I. the syn/anti ratio of the products reflects the Z/E geometry of the crotyl moiety (B, Al, Sn, Si (Δ-reactions)).**

- **II. syn-selective irrespective of olefin geometry (Sn, Si, Ti).**

- **III. anti-selective irrespective of olefin geometry (Ti, Cr, Zr, In, Zn).**

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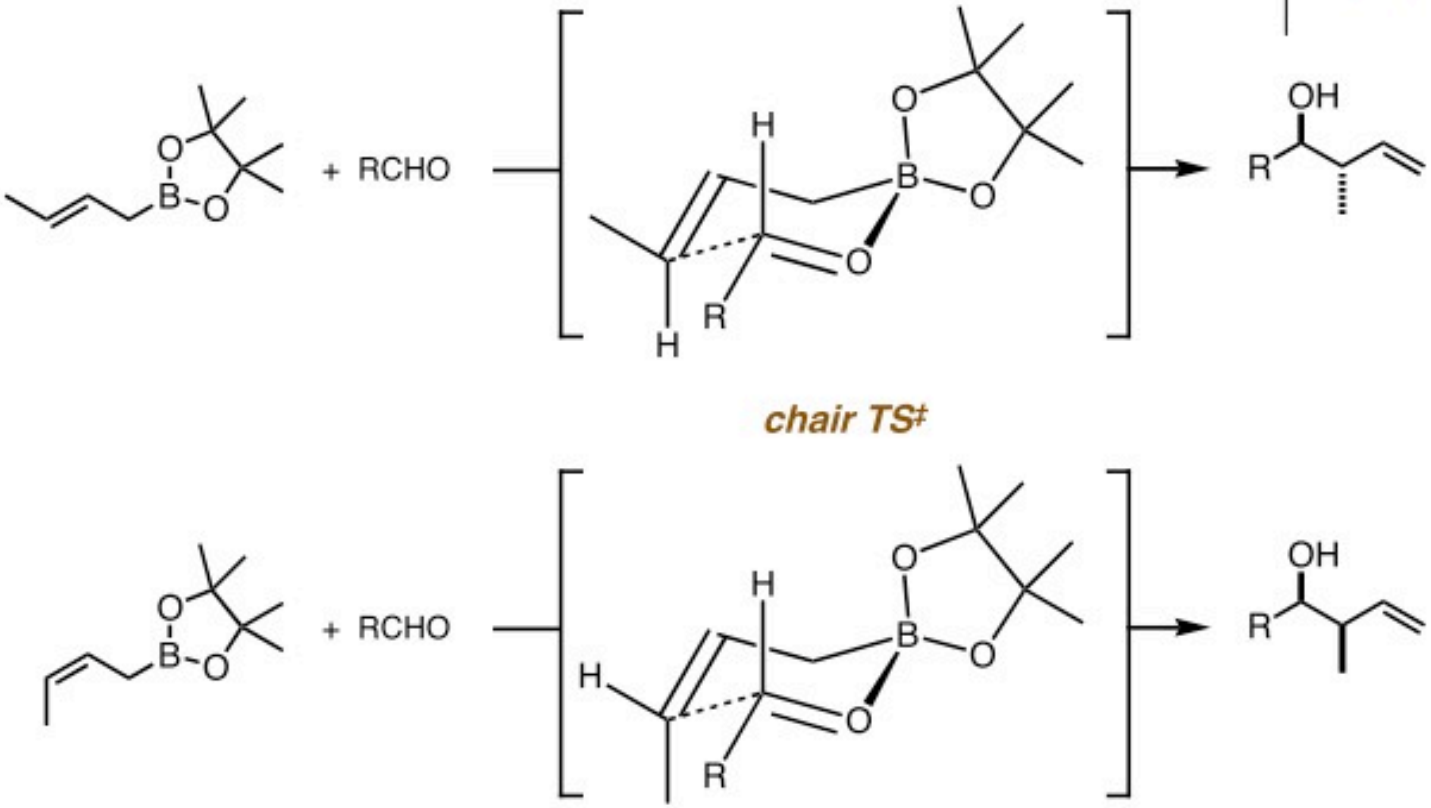
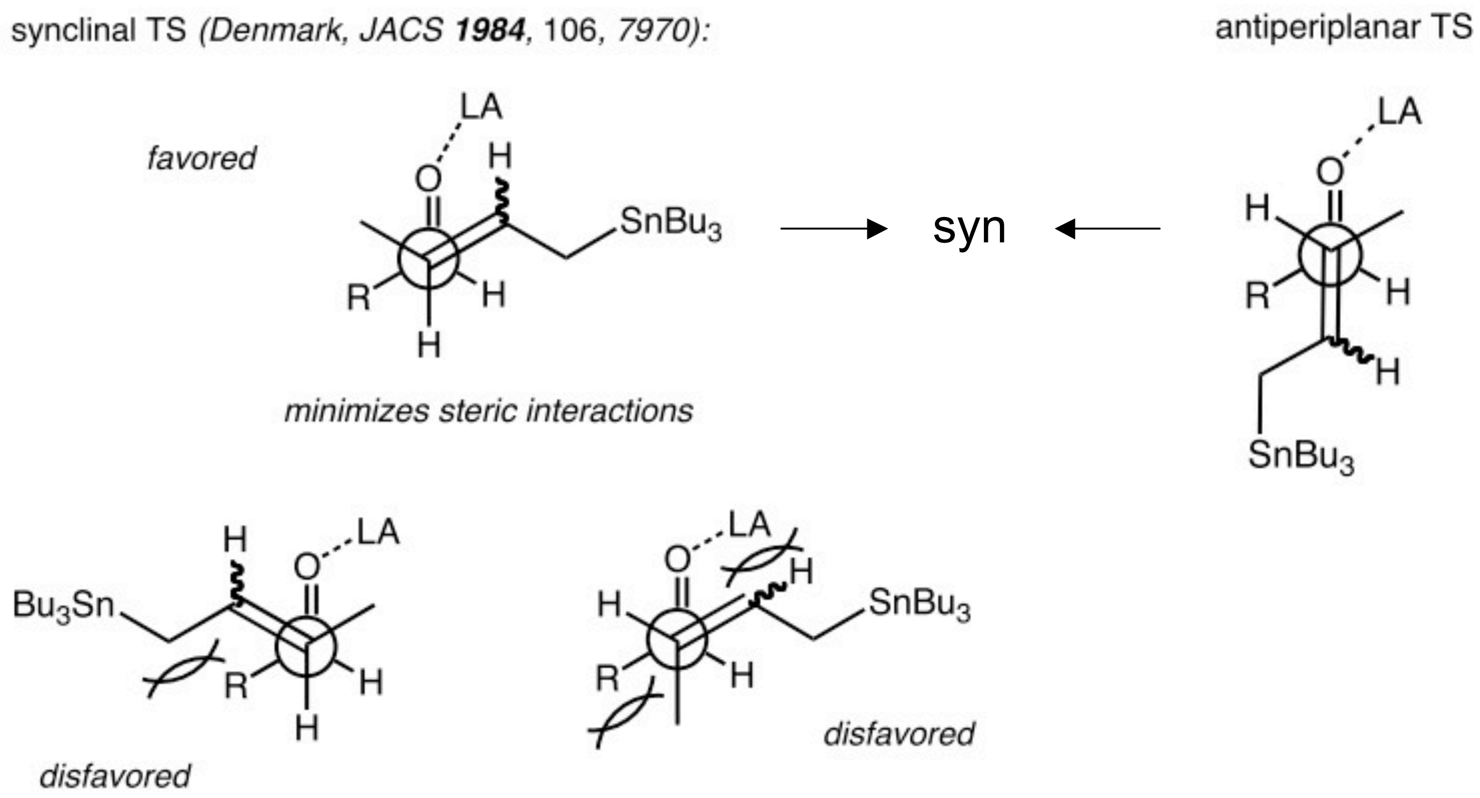
The Type I Reagents Mechanism

Hoffmann, 1979: Boronates are more configurationally stable



The Type II Reagents Mechanism



antiperiplanar vs. synclinal transition state: S. E. Denmark, *Helv. Chim. Acta* **1983**, *66*, 1655; *J. Am. Chem. Soc.* **1987**, *109*, 2512; *Tetrahedron* **1989**, *45*, 1053.

→ the LA influences the properties of the reaction taking place from the synclinal and antiperiplanar arrangements, with the former in general being the more important:

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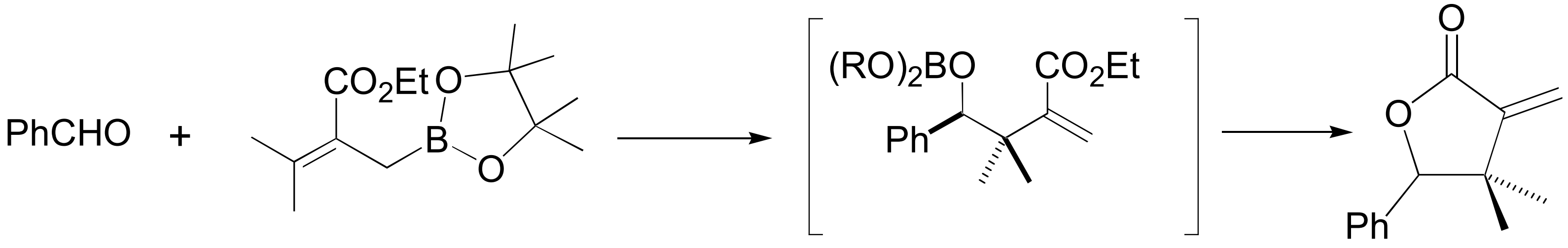
Acid Catalyzed Addition of Allylboronates



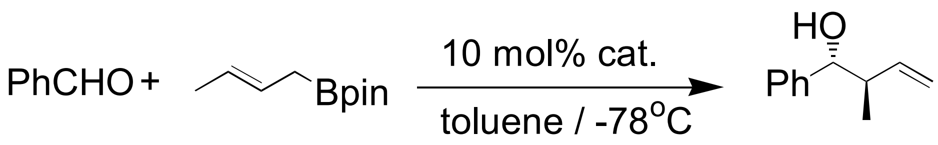
none	12 days at r.t.	84%
10% $Sc(OTf)_3$	6 h at r.t	93%

Dennis G. Hall. *JACS*. **2002**, *124*, 11586.

10% $Sc(OTf)_3$	16 h at 0 ^oC	< 5%
10% TFA	16 h at 0 ^oC	96%

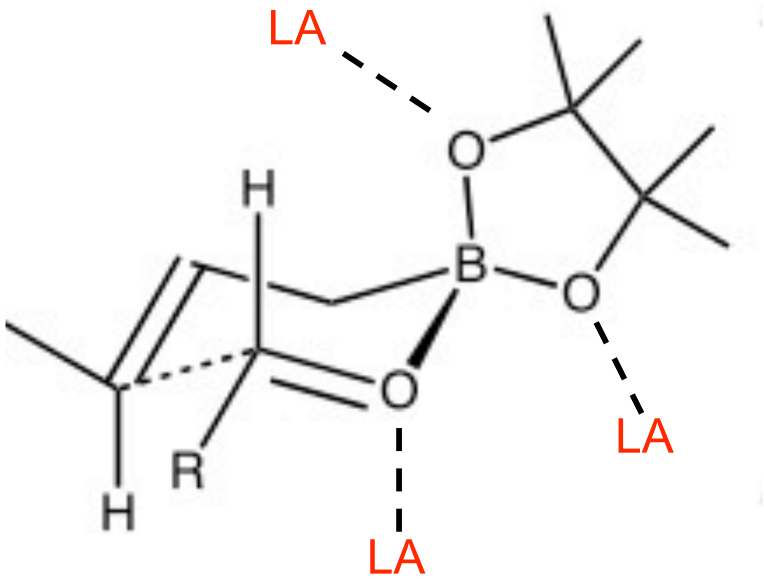
Dennis G. Hall. *JACS*. **2005**, *127*, 12808.

Acceleration Effect of Lewis Acid in Allylboration of Aldehydes



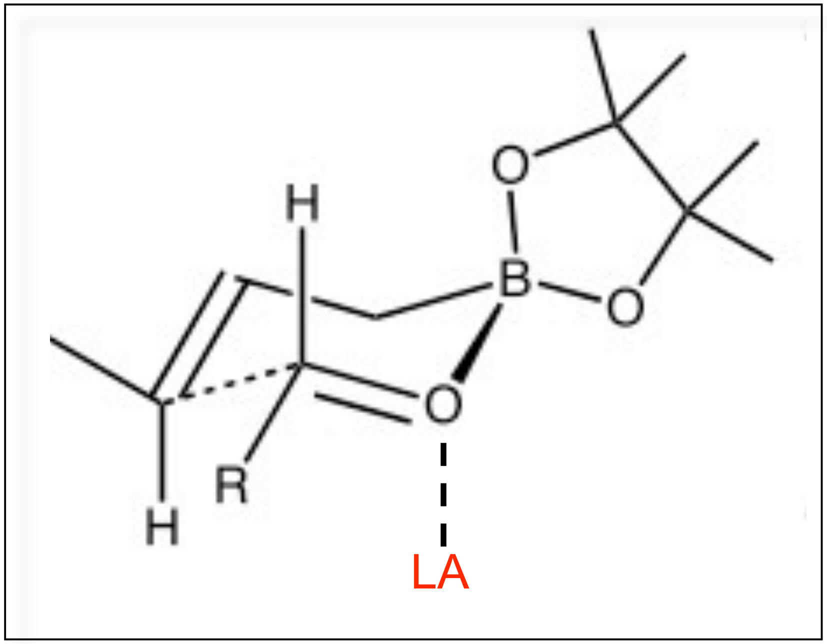
None	trace
$AlCl_3$	92% anti = 99%
$Sc(OTf)_3$	94% anti = 99%

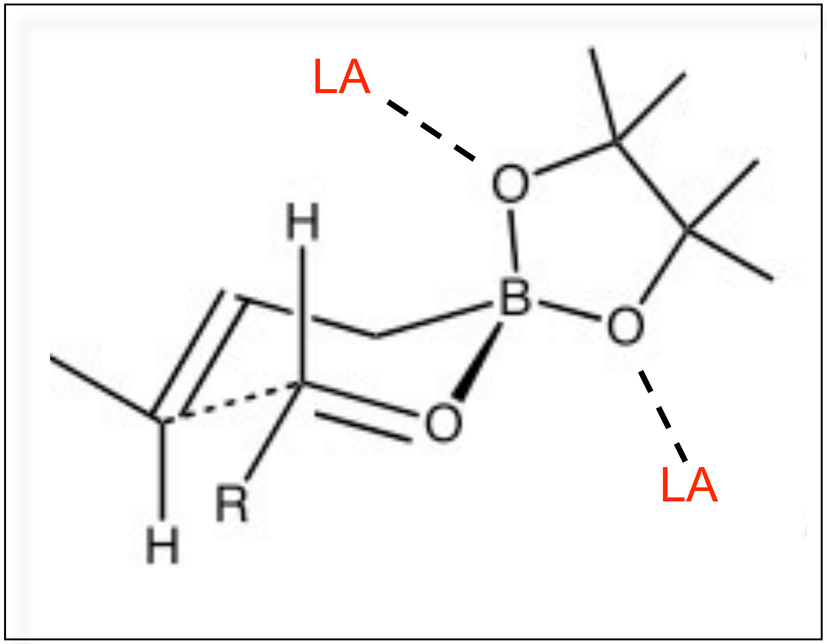
Miyaura. N. *JACS*. **2002**, *124*, 12414.



?

Investigation of Mechanism (Hypothsis)





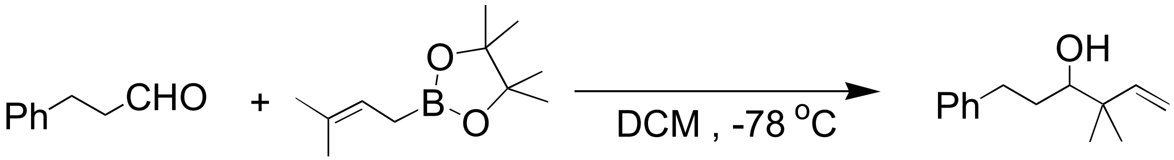
Double coordination

“superactivate” aldehyde

Suppress n_o-p_B overlap

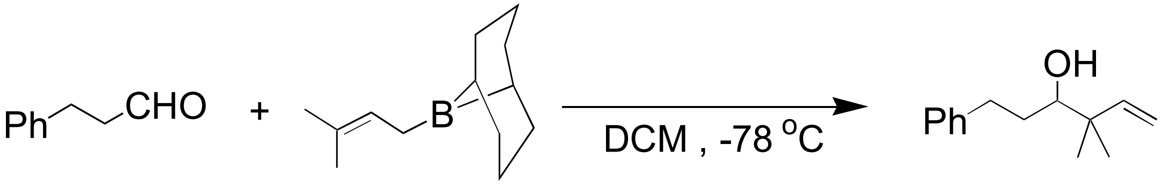
Increase the acidic character of B

Investigation of Mechanism (Result)

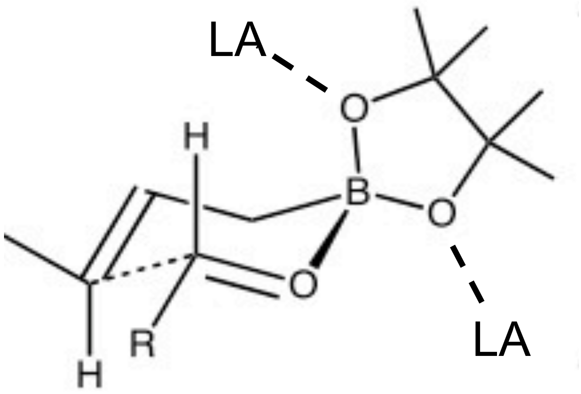


i) without LA
ii) 10% $Sc(OTf)_3$

accelerate >100 times

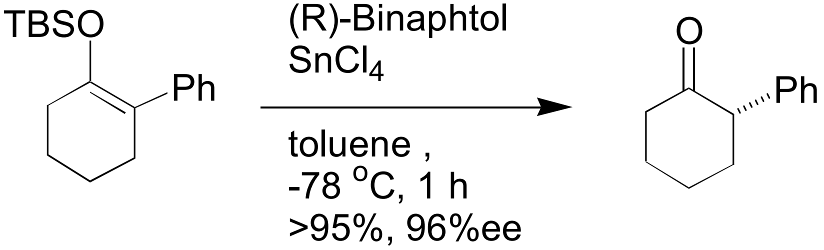


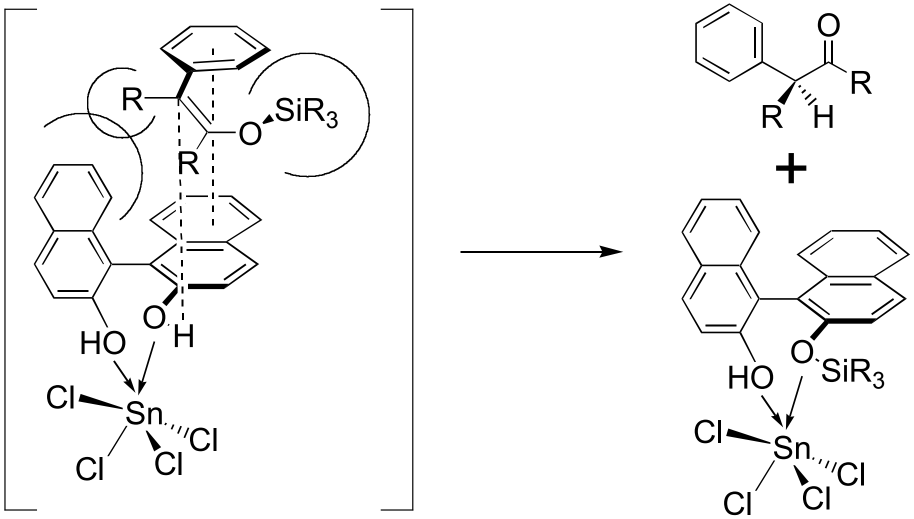
no acceleration observed



Dennis G. Hall. *JACS*. **2004**, *126*, 4518.

Yamamoto's Lewis acid assisted Brønsted acid system



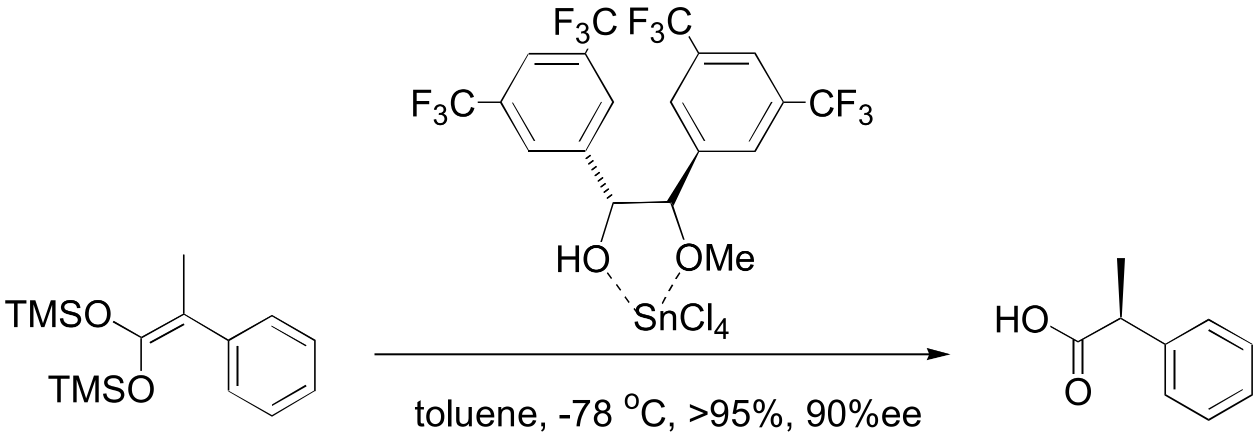


Yamamoto, H. *JACS*. **1994**, *116*, 11179.

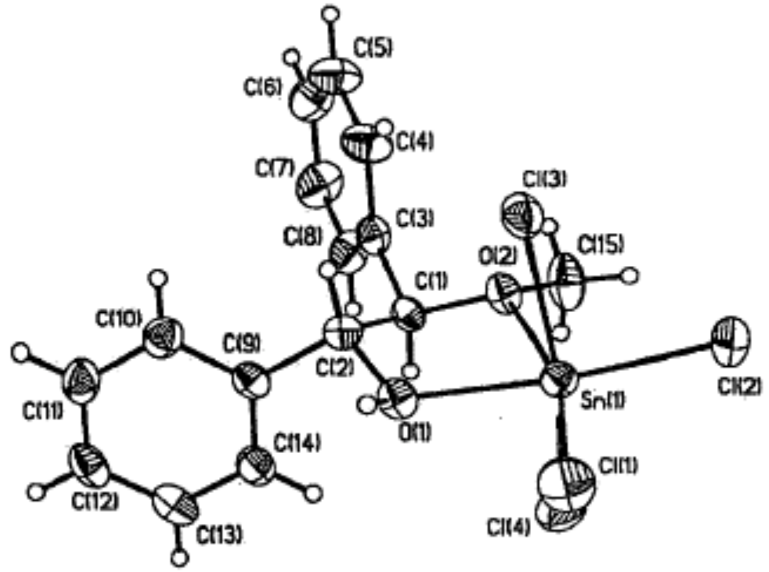
Proposed TS based on calculation

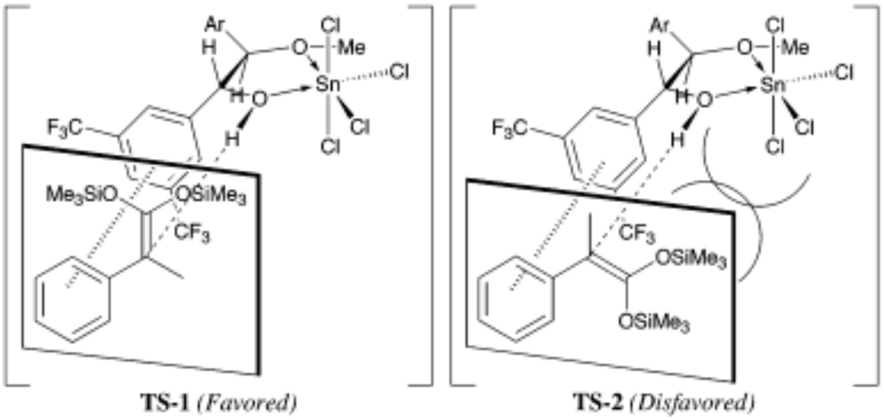
Yamamoto, H. *JACS*. **1999**, *121*, 4906.
Yamamoto, H. *JACS*. **2000**, *123*, 8120.

Investigation of Mechanism



toluene, -78 °C, >95%, 90%ee



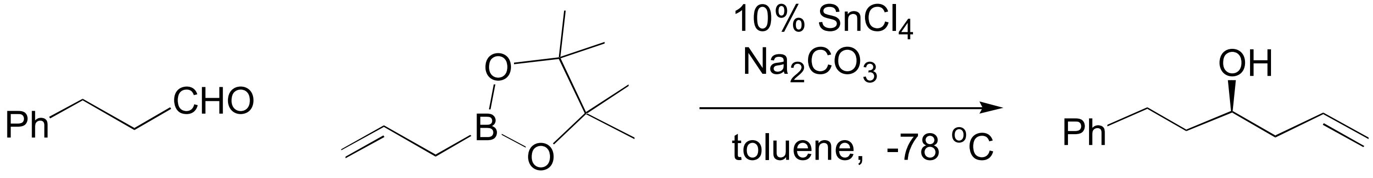


TS-1 *(Favored)* **TS-2** *(Disfavored)*

Linear π*- O-H bond interaction

Yamamoto, H. *JACS*. **2003**, *125*, 24.

Digest of Title Paper



85%, 78%ee

ACIE. **2006**, *45*, 2426.

99%, 95%ee

Title paper
Vivol ligand

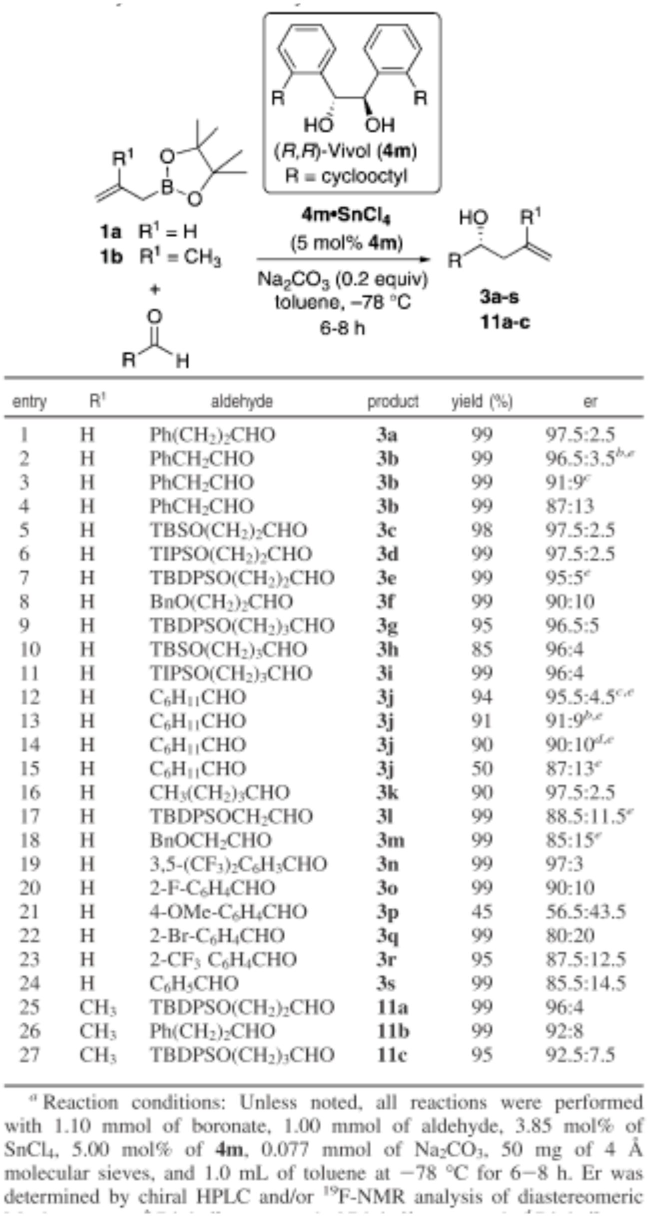
Background reaction

2% of product was observed -78 ^{o}C after 5 h

↓

A maximum ee wuold be approximately 96%

Substrate Scope of Vivol Ligand



entry	R^1	aldehyde	product	yield (%)	er
1	H	$Ph(CH_2)_2CHO$	**3a**	99	97.5:2.5
2	H	$PhCH_2CHO$	**3b**	99	96.5:3.5[b,e]
3	H	$PhCH_2CHO$	**3b**	99	91:9[c]
4	H	$PhCH_2CHO$	**3b**	99	87:13
5	H	$TBSO(CH_2)_2CHO$	**3c**	98	97.5:2.5
6	H	$TIPSO(CH_2)_2CHO$	**3d**	99	97.5:2.5
7	H	$TBDPSO(CH_2)_2CHO$	**3e**	99	95:5[e]
8	H	$BnO(CH_2)_2CHO$	**3f**	99	90:10
9	H	$TBDPSO(CH_2)_3CHO$	**3g**	95	96.5:5
10	H	$TBSO(CH_2)_3CHO$	**3h**	85	96:4
11	H	$TIPSO(CH_2)_3CHO$	**3i**	99	96:4
12	H	$C_6H_{11}CHO$	**3j**	94	95.5:4.5[c,e]
13	H	$C_6H_{11}CHO$	**3j**	91	91:9[b,e]
14	H	$C_6H_{11}CHO$	**3j**	90	90:10[d,e]
15	H	$C_6H_{11}CHO$	**3j**	50	87:13[e]
16	H	$CH_3(CH_2)_3CHO$	**3k**	90	97.5:2.5
17	H	$TBDPSOCH_2CHO$	**3l**	99	88.5:11.5[e]
18	H	$BnOCH_2CHO$	**3m**	99	85:15[e]
19	H	$3,5\text{-}(CF_3)_2C_6H_3CHO$	**3n**	99	97:3
20	H	$2\text{-}F\text{-}C_6H_4CHO$	**3o**	99	90:10
21	H	$4\text{-}OMe\text{-}C_6H_4CHO$	**3p**	45	56.5:43.5
22	H	$2\text{-}Br\text{-}C_6H_4CHO$	**3q**	99	80:20
23	H	$2\text{-}CF_3\ C_6H_4CHO$	**3r**	95	87.5:12.5
24	H	C_6H_5CHO	**3s**	99	85.5:14.5
25	CH_3	$TBDPSO(CH_2)_2CHO$	**11a**	99	96:4
26	CH_3	$Ph(CH_2)_2CHO$	**11b**	99	92:8
27	CH_3	$TBDPSO(CH_2)_3CHO$	**11c**	95	92.5:7.5

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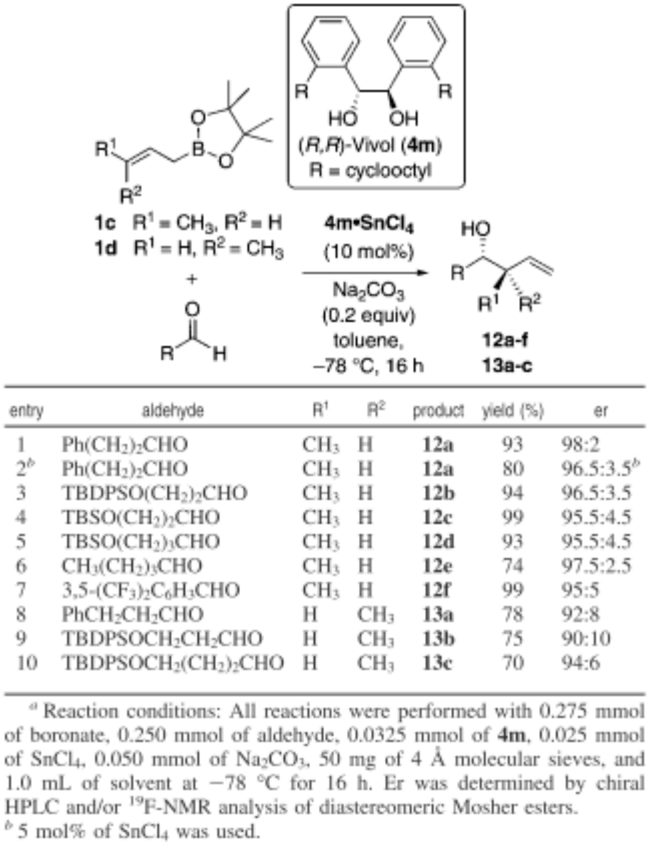
[a] Reaction conditions: Unless noted, all reactions were performed with 1.10 mmol of boronate, 1.00 mmol of aldehyde, 3.85 mol% of $SnCl_4$, 5.00 mol% of **4m**, 0.077 mmol of Na_2CO_3, 50 mg of 4 Å molecular sieves, and 1.0 mL of toluene at −78 °C for 6−8 h. Er was determined by chiral HPLC and/or ^{19}F-NMR analysis of diastereomeric



entry	aldehyde	R^1	R^2	product	yield (%)	er
1	$Ph(CH_2)_2CHO$	CH_3	H	**12a**	93	98:2
2[b]	$Ph(CH_2)_2CHO$	CH_3	H	**12a**	80	96.5:3.5[b]
3	$TBDPSO(CH_2)_2CHO$	CH_3	H	**12b**	94	96.5:3.5
4	$TBSO(CH_2)_2CHO$	CH_3	H	**12c**	99	95.5:4.5
5	$TBSO(CH_2)_3CHO$	CH_3	H	**12d**	93	95.5:4.5
6	$CH_3(CH_2)_3CHO$	CH_3	H	**12e**	74	97.5:2.5
7	$3,5\text{-}(CF_3)_2C_6H_3CHO$	CH_3	H	**12f**	99	95:5
8	$PhCH_2CH_2CHO$	H	CH_3	**13a**	78	92:8
9	$TBDPSOCH_2CH_2CHO$	H	CH_3	**13b**	75	90:10
10	$TBDPSOCH_2(CH_2)_2CHO$	H	CH_3	**13c**	70	94:6

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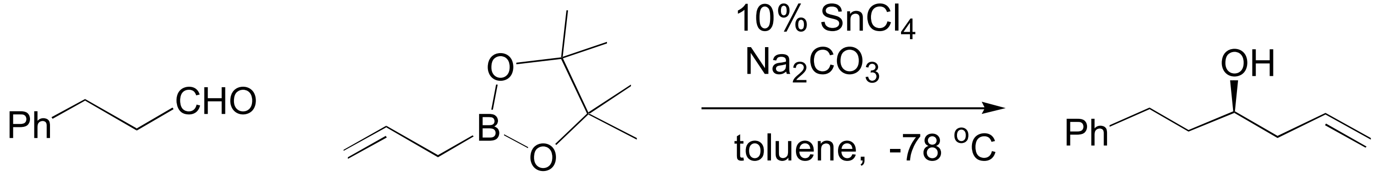
[a] Reaction conditions: All reactions were performed with 0.275 mmol of boronate, 0.250 mmol of aldehyde, 0.0325 mmol of **4m**, 0.025 mmol of $SnCl_4$, 0.050 mmol of Na_2CO_3, 50 mg of 4 Å molecular sieves, and 1.0 mL of solvent at −78 °C for 16 h. Er was determined by chiral HPLC and/or ^{19}F-NMR analysis of diastereomeric Mosher esters.

[b] 5 mol% of $SnCl_4$ was used.

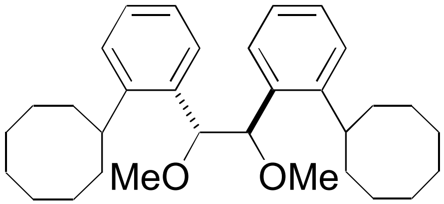
The enantioselectivity shown here is superior to that of the most popular stoichimetric reagents.

Investigation of Mechanism

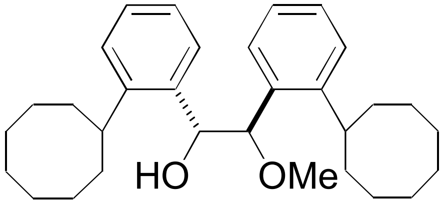
Truly Yamamoto's LBA system?



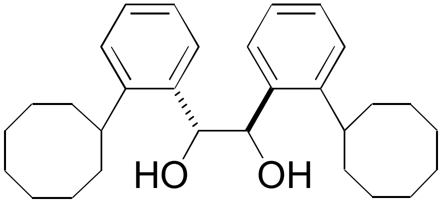
10% $SnCl_4$
Na_2CO_3
toluene, -78 °C



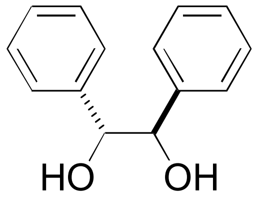
4 h <10% conversion, racemic



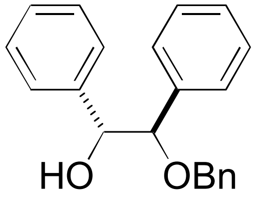
3 h 50% conversion, 85%ee



4h 99%, 95%ee



12 h, 37%ee



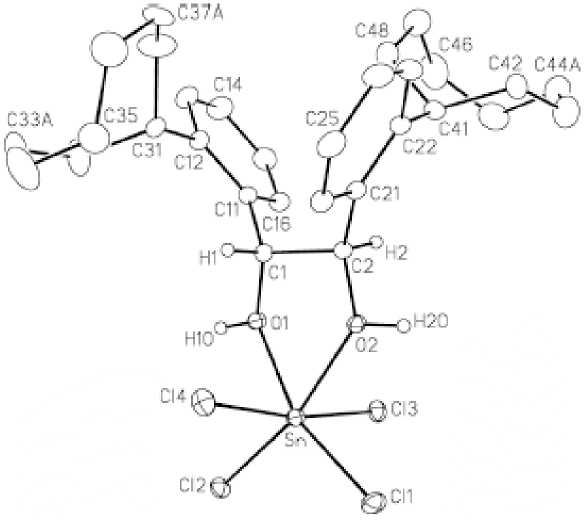
12 h, 62%ee

ACIE. **2006**, *45*, 2426.

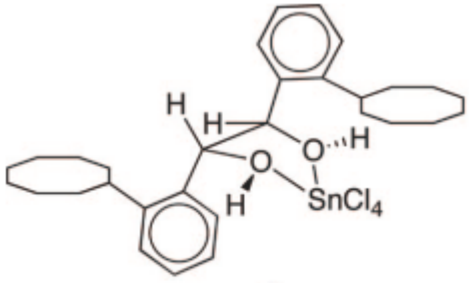
Yamamoto reported mono-protected diol ligands gave higher ee.

Yamamoto, H. *JACS*. **2000**, *122*, 8120.

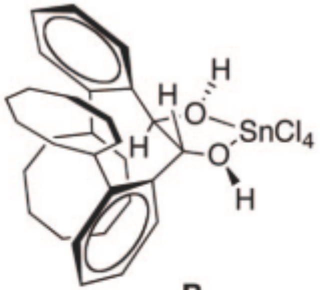
Farther Investigation of Mechanism



X-ray



A
"Extended"



B
"Stacked"

Stacked structure

Activate protons are pointing pseudoequatirial

↓

Rigid position

↓

Hold chiral information (?)

Conclusion

Vivol ligand – $SnCl_4$ system is

- **efficient catalyst for enantioselective allyl and crotylboration of aliphatic aldehyde.**

- **superior to well-established stoichiometric allylboration methods.**

- **hard to know the precise mechanism.**