ORGANIC LETTERS

2010
Vol. 12, No. 12
2706−2709

Highly (*E*)-Selective BF_3·Et_2O-Promoted Allylboration of Chiral Nonracemic α-Substituted Allylboronates and Analysis of the Origin of Stereocontrol

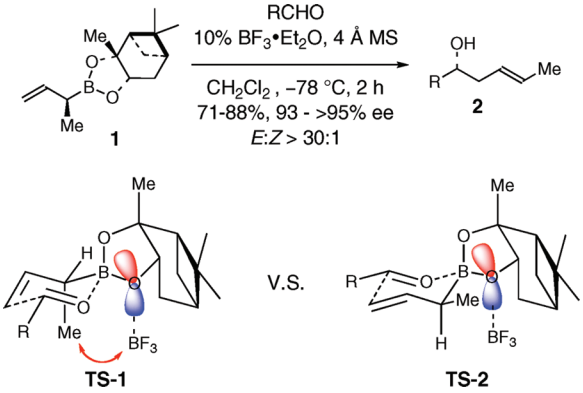
Ming Chen and William R. Roush*

Department of Chemistry, Scripps Florida, Jupiter, Florida 33458

roush@scripps.edu

Received March 30, 2010

ABSTRACT



***δ*-Methyl-substituted homoallylic alcohols 2 were prepared in 71−88% yield, *E*:*Z* >30:1 and 93% to >95% ee via BF_3·Et_2O-promoted allylboration with α-Me-allylboronate 1. The origin of high (*E*)-selectivity is proposed.**

The asymmetric carbonyl allylboration reaction is a valuable method for C−C bond formation. In the vast majority of cases that have been described, the asymmetric induction derives from the use of chiral auxiliaries attached to boron.[1,2] Although not as widely adopted in the literature, the addition of enantioenriched α-substituted allylboronates to carbonyl compounds is a useful alternative.[3−5] Pioneered by Hoffmann et al., carbonyl addition reactions of enantioenriched α-substituted allylboronates **3** proceed with near perfect chirality transfer.[3,4] A mixture of (*Z*)- and (*E*)-homoallylic alcohols **4** and **5** can be generated from two competing transition states **TS-3** and **TS-4** (Figure 1). The ratio of the two homoallylic alcohols depends in part on the electronic property of the

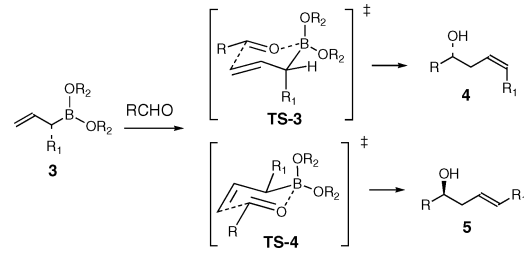


Figure 1. Competing transition states for carbonyl addition reaction of α-substituted allylboronates **3**.

(1) (a) Lachance, H.; Hall, D. G. *Org. React.* **2008**, *73*, 1. (b) Denmark, S. E.; Fu, J. *Chem. Rev.* **2003**, *103*, 2763. (c) Denmark, S. E.; Almstead, N. G. In *Modern Carbonyl Chemistry*; Otera, J., Ed.; Wiley-VCH: Weinheim, 2000; p 299. (d) Chemler, S. R.; Roush, W. R. In *Modern Carbonyl Chemistry*; Otera, J., Ed.; Wiley-VCH: Weinheim, 2000; p 403. (e) Yamamoto, Y.; Asao, N. *Chem. Rev.* **1993**, *93*, 2207. (f) Roush, W. R. In *Comprehensive Organic Synthesis*; Trost, B. M., Ed.; Pergamon Press: Oxford, 1991; Vol. 2, p 1.

(2) (a) Burgos, C. H.; Canales, E.; Matos, K.; Soderquist, J. A. *J. Am. Chem. Soc.* **2005**, *127*, 8044. (b) Canales, E.; Prasad, K. G.; Soderquist, J. A. *J. Am. Chem. Soc.* **2005**, *127*, 11572.

10.1021/ol1007444
Published on Web 05/17/2010

group at the α-position. When the α-substituent is a polar group,[3] such as an alkoxy group or halogen atom, allylboration proceeds predominately via **TS-3** to give (*Z*)-homoallylic alcohol **4**. Although the exact origin of the high (*Z*)-selectivity remains unclear, several factors, including steric effects, dipolar effects, and stereoelectronic minimization of $\pi-\sigma^*$ delocalization in the transition states, have been proposed[3l] and supported by computational studies.[4s] However, when the α-substitution is a nonpolar alkyl group,[4,5] a mixture of (*Z*)- and (*E*)-homoallylic alcohols **4** and **5** is often obtained. Until recently,[5l−n,9] synthetically useful selectivity has proven challenging to achieve with enantioenriched α-alkyl-substituted allyl- or (*E*)-crotylboronates.

Lewis or Brønsted acid promoted allylboration with allylboronate reagents is an important emerging topic in carbonyl allylation chemistry.[6,7] As demonstrated by Hall and coworkers, allylboration in the presence of a catalytic amount of a chiral, nonracemic Lewis or Brønsted acid provides homoallylic alcohols in high yields and excellent enantioselectivities.[8] However, Lewis or Brønsted acid promoted allylboration with enantioenriched, α-substituted allylboronates largely remains underdeveloped.[9] Recently, Hall reported the enantioselective synthesis and Lewis acid promoted allylborations of α-$TMSCH_2$-substituted allylboronates that generate (*E*)-δ-$TMSCH_2$-substituted homoallylic alcohols with excellent selectivities.[9c]

In connection with an ongoing problem in natural product synthesis, we had occasion to explore Lewis acid promoted allylborations of enantioenriched α-substituted allylboronates. We found and report herein that (*E*)-δ-methyl-homoallylic alcohols **2** are obtained in good yields and excellent enantioselectivities from $BF_3{\cdot}Et_2O$-promoted allylboration reactions of **1**.[10] In addition, we have found that δ-chloro-substituted homoallylic alcohols **14** can also be obtained in good yield and 3−6:1 (*E*)-selectivity from $BF_3{\cdot}Et_2O$-promoted allylboration reactions of **13**. The origin of (*E*)-selectivity in these reactions is proposed.

α-Methyl-substituted allylboronate **8** was prepared from methyl boronate **6**,[11] by using the Matteson homologation (Scheme 1).[12] Allylboration reactions of hydrocinnamaldehyde with **8** are summarized in Table 1. The noncatalyzed reaction provided a 1:1.4 mixture of ***ent*-2a** and **9** (entry 1). Similar results were obtained when the reaction was performed in the presence of 10% $Sc(OTf)_3$ (entry 2). When the reaction was

(3) For carbonyl addition with α-hetero atom substituted allylboronates: (a) Hoffmann, R. W.; Landmann, B. *Tetrahedron Lett.* **1983**, *24*, 3209. (b) Hoffmann, R. W.; Landmann, B. *Angew. Chem., Int. Ed.* **1984**, *23*, 437 (c) Hoffmann, R. W.; Dresely, S. *Angew. Chem., Int. Ed.* **1986**, *25*, 189. (d) Hoffmann, R. W.; Landmann, B. *Chem. Ber.* **1986**, *119*, 1039. (e) Hoffmann, R. W.; Landmann, B. *Chem. Ber.* **1986**, *119*, 2013. (f) Hoffmann, R. W.; Dresely, S. *Tetrahedron Lett.* **1987**, *28*, 5303. (g) Hoffmann, R. W.; Dresely, S.; Lanz, J. W. *Chem. Ber.* **1988**, *121*, 1501. (h) Hoffmann, R. W.; Dresely, S.; Hildebrandt, B. *Chem. Ber.* **1988**, *121*, 2225. (i) Hoffmann, R. W.; Dresely, S. *Synthesis* **1988**, 103. (j) Hoffmann, R. W.; Dresely, S. *Chem. Ber.* **1989**, *122*, 903. (k) Stürmer, R.; Hoffmann, R. W. *Synlett* **1990**, 759. (l) Hoffmann, R. W.; Wolff, J. J. *Chem. Ber.* **1991**, *124*, 563. (m) Beckmann, E.; Hoppe, D. *Synthesis* **2005**, 217. For synthetic applications: (n) Andersen, M. W.; Hildebrandt, B.; Dahmann, G.; Hoffmann, R. W. *Chem. Ber.* **1991**, *124*, 2127. (o) Andersoen, M. W.; Hildebrandt, B.; Hoffmann, R. W. *Angew. Chem., Int. Ed.* **1991**, *30*, 97. (p) Hoffmann, R. W.; Schlapbach, A. *Tetrahedron* **1992**, *48*, 1959. (q) Hoffmann, R. W.; Rohde, T.; Haeberlin, E.; Schafer, F. *Org. Lett.* **1999**, *1*, 1713. (r) Hoffmann, R. W.; Haeberlin, E.; Rohde, T. *Synthesis* **2002**, 207.

(4) For carbonyl addition with α-alkyl-substituted allylboronates: (a) Hoffmann, R. W.; Weidmann, U. *J. Organomet. Chem.* **1980**, *195*, 137. (b) Andersen, M.; Hildebrandt, B.; Koester, G.; Hoffmann, R. W. *Chem. Ber.* **1989**, *122*, 1777. (c) Hoffmann, R. W.; Ditrich, K.; Koester, G.; Stürmer, R. *Chem. Ber.* **1989**, *122*, 1783. (d) Hoffmann, R. W.; Sander, T. *Chem. Ber.* **1990**, *123*, 145. (e) Hoffmann, R. W.; Schlapbach, A. *Liebigs Ann.* **1991**, 1203. For synthetic applications: (f) Ditrich, K.; Bube, T.; Stürmer, R.; Hoffmann, R. W. *Angew. Chem., Int. Ed.* **1986**, *25*, 1028. (g) Hoffmann, R. W.; Ladner, W.; Ditrich, K. *Liebigs Ann.* **1989**, 883. (h) Stürmer, R.; Ritter, K.; Hoffmann, R. W. *Angew. Chem., Int. Ed.* **1993**, *32*, 101. (i) Hoffmann, R. W.; Rolle, U. *Tetrahedron Lett.* **1994**, *35*, 4751. (j) Hoffmann, R. W.; Stürmer, R. *Chem. Ber.* **1994**, *127*, 2511. (k) Stürmer, R.; Hoffmann, R. W. *Chem. Ber.* **1994**, *127*, 2519. (l) Hoffmann, R. W.; Rolle, U.; Goettlich, R. *Liebigs Ann.* **1996**, 1717. (m) Breitfelder, S.; Schlapbach, A.; Hoffmann, R. W. *Synthesis* **1998**, 468. (n) Rychnovsky, S. D.; Thomas, C. R. *Org. Lett.* **2000**, *2*, 1217. (o) Rolle, T.; Hoffmann, R. W. *Helv. Chim. Acta* **2004**, *87*, 1214. (p) Bahnck, K. B.; Rychnovsky, S. D. *Chem. Commun.* **2006**, *22*, 2388. (q) Bahnck, K. B.; Rychnovsky, S. D. *J. Am. Chem. Soc.* **2008**, *130*, 13177. (r) Smith, T. E.; Kuo, W.-H.; Balskus, E. P.; Bock, V. D.; Roizen, J. L.; Theberge, A. B.; Carroll, K. A.; Kurihara, T.; Wessler, J. D. *J. Org. Chem.* **2008**, *73*, 142. For computational studies: (s) Gennari, C.; Fioravanzo, E.; Bernardi, A.; Vulpetti, A. *Tetrahedron* **1994**, *50*, 8815.

(5) For recent development of α-substituted allylboronates: (a) Pietruszka, J.; Schone, N. *Angew. Chem., Int. Ed.* **2003**, *42*, 5638. (b) Pietruszka, J.; Schone, N. *Eur. J. Org. Chem.* **2004**, 5011. (c) Pietruszka, J.; Schone, N.; Frey, W.; Grundl, L. *Chem.−Eur. J.* **2008**, *14*, 5178. (d) Fernandez, E.; Pietruszka, J. *Synlett* **2009**, 1474. (e) Pelz, N. F.; Woodward, A. R.; Burks, H. E.; Sieber, J. D.; Morken, J. P. *J. Am. Chem. Soc.* **2004**, *126*, 16328. (f) Sieber, J. D.; Morken, J. P. *J. Am. Chem. Soc.* **2006**, *128*, 74. (g) Pelz, N, F.; Morken, J. P. *Org. Lett.* **2006**, *8*, 4557. (h) Burks, H. E.; Liu, S.; Morken, J. P. *J. Am. Chem. Soc.* **2007**, *129*, 8766. (i) Burks, H. E.; Kliman, L. T.; Morken, J. P. *J. Am. Chem. Soc.* **2009**, *131*, 9134. (j) Ito, H.; Kawakami, C.; Sawamura, M. *J. Am. Chem. Soc.* **2005**, *127*, 16034. (k) Ito, H.; Ito, S.; Sasaki, Y.; Matsuura, K.; Sawamura, M. *J. Am. Chem. Soc.* **2007**, *129*, 14856. (l) Fang, G. Y.; Aggarwal, V. K. *Angew. Chem., Int. Ed.* **2007**, *46*, 359. (m) Althaus, M.; Mahmood, A.; Suarez, J. R.; Thomas, S. P.; Aggarwal, V. K. *J. Am. Chem. Soc.* **2010**, *132*, 4025. (n) Binanzer, M.; Fang, G. Y.; Aggarwal, V. K. *Angew. Chem., Int. Ed.* **2010**, *49*, DOI: 10.1002/anie.201001223.

(6) (a) Kennedy, J. W. J.; Hall, D. G. *J. Am. Chem. Soc.* **2002**, *124*, 11586. (b) Ishiyama, T.; Ahiko, T.; Miyaura, N. *J. Am. Chem. Soc.* **2002**, *124*, 12414. For computational studies: (c) Sakata, K.; Fujimoto, H. *J. Am. Chem. Soc.* **2008**, *130*, 12519.

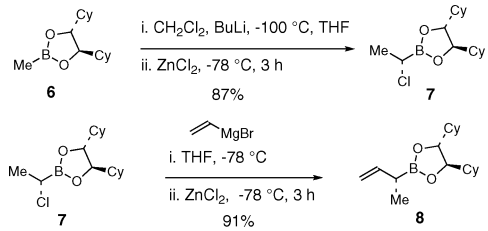
(7) (a) Wada, R.; Oisaki, K.; Kanai, M.; Shibasaki, M. *J. Am. Chem. Soc.* **2004**, *126*, 8910. (b) Lou, S.; Moquist, P. N.; Schaus, S. E. *J. Am. Chem. Soc.* **2006**, *187*, 12660. (c) Paton, R. S.; Goodman, J. M.; Pellegrinet, S. C. *Org. Lett.* **2009**, *11*, 37.

(8) (a) Lachance, H.; Lu, X.; Gravel, M.; Hall, D. G. *J. Am. Chem. Soc.* **2003**, *125*, 10160. (b) Kennedy, J. W. J.; Hall, D. G. *J. Org. Chem.* **2004**, *69*, 4412. (c) Rauniyar, V.; Hall, D. G. *J. Am. Chem. Soc.* **2004**, *126*, 4518. (d) Gravel, M.; Lachance, H.; Lu, X.; Hall, D. G. *Synthesis* **2004**, 1290. (e) Rauniyar, V.; Hall, D. G. *Angew. Chem., Int. Ed.* **2006**, *45*, 2426. (f) Rauniyar, V.; Hall, D. G. *Synthesis* **2007**, 3421. (g) Rauniyar, V.; Zhai, H.; Hall, D. G. *J. Am. Chem. Soc.* **2008**, *130*, 8481. (h) Rauniyar, V.; Hall, D. G. *J. Org. Chem.* **2009**, *74*, 4236.

(9) (a) Carosi, L.; Lachance, H.; Hall, D. G. *Tetrahedron Lett.* **2005**, *46*, 8981. (b) Carosi, L.; Hall, D. G. *Angew. Chem., Int. Ed.* **2007**, *46*, 5913. (c) Peng, F.; Hall, D. G. *J. Am. Chem. Soc.* **2007**, *129*, 3070. (d) Peng, F.; Hall, D. G. *Tetrahedron Lett.* **2007**, *48*, 3305. (e) Carosi, L.; Hall, D. G. *Can. J. Chem.* **2009**, *87*, 650.

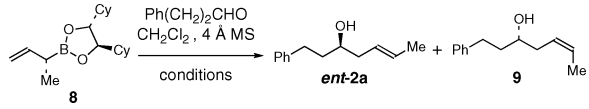
(10) For alternative approaches to δ-methyl-homoallylic alcohols: (a) Nokami, J.; Yoshizane, K.; Matsuura, H.; Sumida, S. *J. Am. Chem. Soc.* **1998**, *120*, 6609. (b) Sumida, S.; Ohga, M.; Mitani, J.; Nokami, J. *J. Am. Chem. Soc.* **2000**, *122*, 1310. (c) Nokami, J.; Anthony, L.; Sumida, S. *Chem.−Eur. J.* **2000**, *6*, 2909. (d) Nokami, J.; Ohga, M.; Nakamoto, H.; Matsubara, T.; Hussain, I.; Kataoka, H. *J. Am. Chem. Soc.* **2001**, *123*, 9168. (e) Nokami, J.; Nomiyama, K.; Matsuda, S.; Imai, N.; Kataoka, H. *Angew. Chem., Int. Ed.* **2003**, *42*, 1273. (f) Nokami, J.; Nomiyama, K.; Shafi, S. M.; Kataoka, K. *Org. Lett.* **2004**, *6*, 1261. (g) Shafi, S. M.; Chou, S.; Kataoka, K.; Nokami, J. *Org. Lett.* **2005**, *7*, 2957. (h) Kataoka, K.; Ode, Y.; Matsumoto, M.; Nokami, J. *Tetrahedron* **2006**, *62*, 2471. (i) Nokami, J.; Maruoka, K.; Souda, T.; Tanaka, N. *Tetrahedron* **2007**, *63*, 9016. (j) Loh, T. P.; Tan, K. T.; Hu, Q. Y. *Angew. Chem., Int. Ed.* **2001**, *40*, 2921. (k) Loh, T. P.; Tan, K. T.; Yang, J. Y.; Xiang, C. L. *Tetrahedron Lett.* **2001**, *42*, 8701. (l) Loh, T. P.; Hu, Q. Y.; Chok, Y. K.; Tan, K. T. *Tetrahedron Lett.* **2001**, *42*, 9277. (m) Loh, T. P.; Lee, C. L. K.; Tan, K. T. *Org. Lett.* **2002**, *17*, 2985. (n) Tan, K. T.; Chng, S. S.; Cheng, H. S.; Loh, T. P. *J. Am. Chem. Soc.* **2003**, *125*, 2958. (o) Lee, C. L. K.; Lee, C. H. A.; Tan, K. T.; Loh, T. P.; Cheng, H. S. *Org. Lett.* **2004**, *6*, 1281. (p) Lee, C. H. A.; Loh, T. P. *Tetrahedron Lett.* **2006**, *47*, 809. (q) Ramachandran, P. V.; Pratihar, D.; Biswas, D. *Chem. Commun.* **2005**, *41*, 1988. (r) Malkov, A. V.; Kabeshov, M. A.; Barlog, M.; Kocovsky, P. *Chem.−Eur. J.* **2009**, *15*, 1570.

Scheme 1. Synthesis of Allylboronate **8**



carried out in the presence of either 10% or stoichiometric BF_3•Et_2O, a 3:1 mixture of ***ent*-2a** and **9** was obtained (entries 3 and 4). Despite additional attempts to optimize this reaction, we were unable to achieve synthetically useful selectivity in allylboration reactions of **8**.

Table 1. Optimization for Allylboration Reactions with **8**

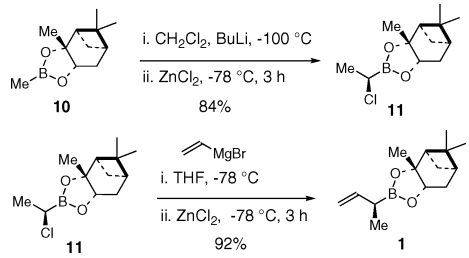


entry	conditions	***ent*-2a**:**9**[a]	yield (%)[b]
1	no catalyst, −78 °C to rt, 8 h	1:1.4	67
2	10% $Sc(OTf)_3$, −78 °C to rt, 8 h	1:1.5	63
3	10% BF_3•Et_2O, −78 °C, 2 h	3:1	78
4	100% BF_3•Et_2O, −78 °C, 2 h	3:1	71

[a] Based on ^{1}H NMR analysis of the crude reaction mixture. [b] Yield of isolated mixture of products.

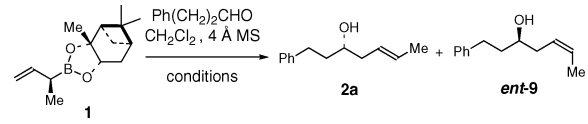
Pinanediol is a useful chiral director for the Matteson homologation.[13] We hoped that allylboronate **1** would provide access to the desired (*E*)-homoallylic alcohols with excellent selectivity based on Hall's work.[9c] Accordingly, allylboronate **1** was prepared with high diastereoselectivity from **10** (Scheme 2).[14]

Scheme 2. Synthesis of Allylboronate **1**



Results of allylboration of hydrocinnamaldehyde with reagent **1** are presented in Table 2. The reaction in the absence of Lewis acid gave a 1.5:1 mixture of alcohols **2a** and ***ent*-9** (entry 1). With the addition of 10% $Sc(OTf)_3$, a 3:1 mixture of **2a** and ***ent*-9** was obtained (entry 2).

Table 2. Optimization for Allylboration Reactions with **1**



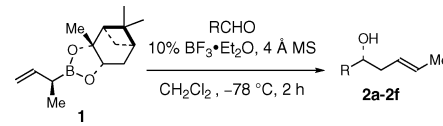
entry	conditions	**2a**:***ent*-9**[a]	yield (%)[b]
1	no catalyst, −78 °C to rt, 8 h	1.5:1	71
2	10% $Sc(OTf)_3$, −78 °C to rt, 8 h	3:1	64
3	10% BF_3•Et_2O, −78 °C, 2 h	>30:1	79
4	100% BF_3•Et_2O, −78 °C, 2 h	>30:1	68

[a] Based on ^{1}H NMR analysis of the crude reaction mixture. [b] Yield of isolated product(s).

Gratifyingly, when the reaction was carried out in the presence of 10% BF_3•Et_2O, (*E*)-homoallylic alcohol **2a** was obtained as the only product (*E*:*Z* > 30:1) in 94% ee and 79% yield (entry 3).

As summarized in Table 3, BF_3-mediated allylboration of a variety of aldehydes using **1** proceeded with near perfect

Table 3. Preparation of (*E*)-δ-Me-Homoallylic Alcohols **2a**−**2f**



entry	RCHO	product	yield (%)[a]	ee (%)[b]
1	$Ph(CH_2)_2CHO$	**2a**	79	>95
2	$PhCH_2CHO$	**2b**	88	>95
3	PhCHO	**2c**	75	94
4	CyCHO	**2d**	71	>95
5	$BnO(CH_2)_2CHO$	**2e**	84	93
6	$BnOCH_2CHO$	**2f**	73	95

[a] Yield of isolated (*E*)-homoallylic alcohols. [b] Enantiomeric purity and absolute stereochemistry of **2a**−**2f** were determined by using the Mosher ester analysis.[15]

chirality transfer. (*E*)-δ-Methyl-substituted homoallylic alcohols **2a**−**2f** were obtained in 93% to >95% ee and 71−88% yield. The correspoding (*Z*)-isomers were not detected in any of these experiments.

We suspect the high (*E*)-selectivity in these reactions originates from minimization of 1,3-*syn*-pentane interactions in the competing transition states.[16] As shown in Figure 2, it is conceivable that BF_3 will coordinate to the lower lone pair of electrons (in blue) of the oxygen atom distal to the angular methyl group to minimize steric interactions.[17] If so, **TS-1** is disfavored due to a 1,3-*syn*-pentane interaction

(11) (a) Matteson, D. S.; Man, H.-W. *J. Org. Chem.* **1994**, *59*, 5734. (b) O'Donnell, M. J.; Cooper, J. T.; Mader, M. M. *J. Am. Chem. Soc.* **2003**, *125*, 2370.

(12) (a) Midland, M. M.; Preston, S. B. *J. Am. Chem. Soc.* **1982**, *104*, 2331. (b) Tsai, D. J. S.; Matteson, D. S. *Organometallics* **1983**, *2*, 236.

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

(14) (a) Matteson, D. S.; Sadhu, K. M.; Peterson, M. L. *J. Am. Chem. Soc.* **1986**, *108*, 810. (b) Maurer, K. W.; Armstrong, R. W. *J. Org. Chem.* **1996**, *61*, 3106.

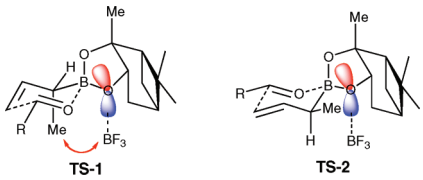


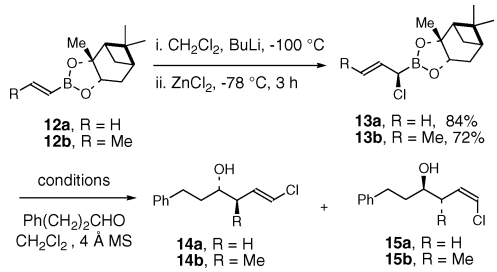
Figure 2. Competing transition states for BF_3-catalyzed aldehyde allylboration with α-methyl allylboronate **1**.

between the pseudoaxial methyl group and the BF_3 ligand; this interaction is absent in **TS-2**. Accordingly, product formation proceeds via **TS-2** and homoallylic alcohols with (*E*)-olefin geometry are obtained with excellent selectivity.

We were intrigued by the possibility that BF_3·Et_2O-promoted aldehyde allylboration could be used to induce (*E*)-selectivity with reagents that have much higher intrinsic preference for positioning of the α-substituent in a pseudoaxial position in the allylboration transition state. α-Chloro-substituted allylboronates, such as **13**, are known to give (*Z*)-δ-chloro-substituted homoallylic alcohols, e.g., **15**, with high (*Z*)-selectivity in allylboration reactions.[3]

The sensitive α-chloro-substituted allylboronates **13a** and **13b** were synthesized, and their allylboration reactions were explored (Table 4). The reaction of hydrocinnamaldehyde with **13a** in

Table 4. Allylboration with α-Cl-Allylboronates **13**



entry	substrate	conditions	**14:15**[a]	yield (%)[b]
1	**13a**	No catalyst, −78 °C to rt, 24 h	1:12	72
2	**13b**	No catalyst, −78 °C to rt, 24 h	1:10	70
3	**13a**	10% BF_3·Et_2O, −78 °C, 24 h	6:1	63
4	**13b**	10% BF_3·Et_2O, −78 °C, 24 h	3:1	52

[a] Based on ^{1}H NMR analysis of the crude reaction mixture. [b] Yield of isolated product(s).

the absence of BF_3·Et_2O provided (*Z*)-δ-chloro-homoallylic alcohol **15a** in 72% yield.[18] Similarly, crotylboration with **13b** gave alcohol **15b** in 70% yield.[18] In both cases, high (*Z*)-selectivity (≥10:1) was observed, consistent with Hoffmann's report.[3] However, when these reactions were performed in the presence of 10% BF_3·Et_2O, reagent **13a** provided a 6:1 mixture of δ-chloro-homoallylic alcohols **14a** and **15a**,[18] and reagent **13b** provided a 3:1 mixture of alcohols **14b** and **15b**.[18]

These data indicate that the strong preference of reagents **13** to react with aldehydes via a transition state analogous to **TS-5** (but lacking the BF_3 ligand) can be overridden in the presence of BF_3·Et_2O. As shown in Figure 3, **TS-5** is

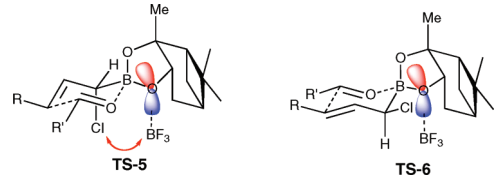


Figure 3. Competing transition states for BF_3-catalyzed aldehyde allylboration with α-chloro allylboronates **13**.

disfavored owing to the 1,3-*syn*-pentane interaction. In the competing (and now favored) transition state **TS-6**, the α-Cl substitution is positioned in a pseudoequatorial arrangement to minimize interactions with the chlorine substituent. Ultimately, these reactions lead to the formation of (*E*)-homoallylic alcohols **14** with 3−6:1 (*E*)-selectivity.

In summary, we have demonstrated the highly (*E*)-selective allylboration of aldehydes with reagent **1** in the presence of a catalytic amount of BF_3·Et_2O. (*E*)-δ-Methyl-substituted homoallylic alcohols **2** were prepared in 71−88% yield and excellent enantioselectivities. (*E*)-δ-Chloro-substituted homoallylic alcohols **14** were also obtained in good yields and 3−6:1 (*E*)-selectivity from reagents **13a**,**b**. We postulate that minimization of 1,3-*syn*-pentane interactions in the transition states is responsible for the (*E*)-selectivity of these reactions.

Acknowledgment. Financial support provided by the National Institutes of Health (GM038436 and GM026782) is gratefully acknowledged.

Supporting Information Available: Experimental procedures and spectroscopic data for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

OL1007444

(15) (a) Dale, J. A.; Mosher, H. S. *J. Am. Chem. Soc.* **1973**, *95*, 512. (b) Ohtani, I.; Kusumi, T.; Kashman, Y.; Kakisawa, H. *J. Am. Chem. Soc.* **1991**, *113*, 4092.

(16) (a) Roush, W. R. *J. Org. Chem.* **1991**, *56*, 4151. For recent examples where minimization of *syn*-pentane interactions plays an important role in stereoselectivity: (b) Liu, J.; De Brabander, J. K. *J. Am. Chem. Soc.* **2009**, *131*, 12562. (c) Jung, M. E.; Salehi-Rad, R. *Angew. Chem., Int. Ed.* **2009**, *48*, 8766. (d) Hashimoto, T.; Ito, J.-i.; Nishiyama, H. *Tetrahedron* **2008**, *64*, 9408. (e) Zhang, Y.; Sammakia, T. *J. Org. Chem.* **2006**, *71*, 6262. (f) Perkins, M. V.; Sampson, R. A.; Joannou, J.; Taylor, M. R. *Tetrahedron Lett.* **2006**, *47*, 3791.

(17) Coordination to the non-bonded electron pair (indicated in red) is disfavored owing to a 1,3-interaction with the angular methyl group. Coordination to the distal oxygen atom is disfavored for steric reasons.

(18) The enantiomeric purity of homoallylic alcohols **14** and **15** was ca.15−30% ee, presumably due to epimerization of the α-chloro center during preperations of reagents **13a** and **13b**. Matteson, D. S.; Erdik, E. *Organmetallics* **1983**, *2*, 1083.