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Enantioselective Syntheses of *syn*- and *anti*-β-Hydroxyallylsilanes Via Allene Hydroboration-Aldehyde Allylboration Reactions

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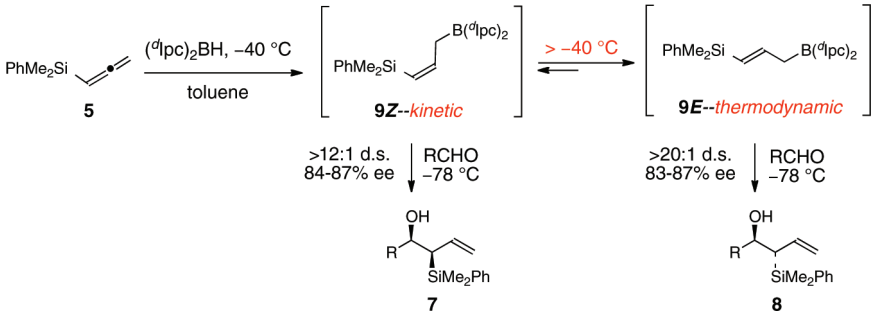
ABSTRACT



The kinetic hydroboration of allenylsilane 5 with $(^d\text{Ipc})_2$BH at −40 °C provides allylborane 9*Z* with ≥12:1 selectivity. When the hydroboration is performed at temperatures above −40 °C, 9*Z* isomerizes to the thermodynamically more stable allylborane 9*E* with >20:1 selectivity. Subsequent treatment of 9*Z* or 9*E* with aldehydes at −78 °C provides *syn*- or *anti*-β-hydroxyallylsilanes, 7 or 8, respectively.

Syn- and *anti*-β-hydroxyallylsilanes are versatile and important building blocks in organic synthesis[1] and have been used in syntheses of a variety of natural products.[2,3] Consequently, extensive efforts have been devoted to the stereocontrolled synthesis of β-hydroxyallylsilanes.[4−6] Aldehyde allylation using γ-silylallylmetal reagents is the most widely adopted procedure for the synthesis of *anti*-β-hydroxyallylsilanes.[7,8] Several enantioselective γ-silylallylboron[5] and titanium[6a,b] reagents have been developed. More recently, an important advance in the catalytic asymmetric synthesis of *anti*-β-hydroxyallylsilanes has also been achieved.[6c] However, compared to the methods available to prepare *anti*-β-hydroxyallylsilanes,

(1) (a) Fleming, I. *Org. React.* **1989**, *37*, 57. (b) Masse, C. E.; Panek, J. S. *Chem. Rev.* **1995**, *95*, 1293. (c) Fleming, I.; Barbero, A.; Walter, D. *Chem. Rev.* **1997**, *97*, 2063. (d) Chabaud, L.; James, P.; Landais, Y. *Eur. J. Org. Chem.* **2004**, 3173. (e) Bates, R. H.; Chen, M.; Roush, W. R. *Curr. Opin. Drug Discovery Dev.* **2008**, *11*, 778.

(2) (a) Sparks, M. A.; Panek, J. S. *J. Org. Chem.* **1991**, *56*, 3431. (b) Panek, J. S.; Yang, M. *J. Am. Chem. Soc.* **1991**, *113*, 9868. (c) Huang, H.; Panek, J. S. *J. Am. Chem. Soc.* **2000**, *122*, 9836. (d) Wu, J.; Chen, Y.; Panek, J. S. *Org. Lett.* **2010**, *12*, 2112. For recent applications: (e) Zhang, Y.; Panek, J. S. *Org. Lett.* **2009**, *11*, 3366. (f) Wrona, I. E.; Gozman, A.; Taldone, T.; Chiosis, G.; Panek, J. S. *J. Org. Chem.* **2010**, *75*, 2820.

(3) (a) Roberson, C. W.; Woerpel, K. A. *J. Org. Chem.* **1999**, *64*, 1434. (b) Smitrovich, J. H.; Woerpel, K. A. *Synthesis* **2002**, 2778. (c) Romero, A.; Woerpel, K. A. *Org. Lett.* **2006**, *8*, 2127. (d) Leonard, N. M.; Woerpel, K. A. *J. Org. Chem.* **2009**, *74*, 6915.

(4) (a) Chan, T. H.; Wang, D. *Chem. Rev.* **1995**, *95*, 1279. (b) Lombardo, M.; Trombini, C. *Chem. Rev.* **2007**, *107*, 3843 and references cited therein. (c) Yamamoto, Y.; Saito, Y.; Maruyama, K. *J. Chem. Soc., Chem. Commun.* **1982**, 1326. (d) Reetz, M. T.; Wenderoth, B. *Tetrahedron Lett.* **1982**, *23*, 5259. (e) Ikeda, Y.; Yamamoto, H. *Bull. Chem. Soc. Jpn.* **1986**, *59*, 657. (f) Landais, Y.; Mahieux, C.; Schenk, K.; Surange, S. S. *J. Org. Chem.* **2003**, *68*, 2779.

(5) For examples of enantioselective synthesis of β-hydroxyallylsilanes using γ-silylallylboron reagents: (a) Roush, W. R.; Grover, P. T.; Lin, X. *Tetrahedron Lett.* **1990**, *31*, 7563. (b) Barrett, A. G. M.; Malecha, J. W. *J. Org. Chem.* **1991**, *56*, 5243. (c) Hunt, J. A.; Roush, W. R. *Tetrahedron Lett.* **1995**, *36*, 501. (d) Roush, W. R.; Pinchuk, A. N.; Micalizio, G. C. *Tetrahedron Lett.* **2000**, *41*, 9413. (e) Lira, R.; Roush, W. R. *Org. Lett.* **2007**, *9*, 4315. (f) Kister, J.; DeBaillie, A. C.; Lira, R.; Roush, W. R. *J. Am. Chem. Soc.* **2009**, *131*, 14174. (g) Binanzer, M.; Fang, G. Y.; Aggarwal, V. K. *Angew. Chem., Int. Ed.* **2010**, *49*, 4264. (h) Robinson, A.; Aggarwal, V. K. *Angew. Chem., Int. Ed.* **2010**, *49*, 6673.

(6) For other examples of enantioselective synthesis of β-hydroxyallylsilanes using γ-silylallylmetal reagents, see: (a) Hafner, A.; Duthaler, R. O.; Marti, R.; Rihs, G.; Rothe-Streit, P.; Schwarzenbach, F. *J. Am. Chem. Soc.* **1992**, *114*, 2321. (b) Adam, J.-M.; Fays, L.; Laguerre, M.; Ghosez, L. *Tetrahedron* **2004**, *60*, 7325. (c) Han, S. B.; Gao, X.; Krische, M. J. *J. Am. Chem. Soc.* **2010**, *132*, 9153.

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stereoselective synthesis of the diastereomeric *syn*-β-hydroxyallylsilane isomers, and especially enantioselective syntheses of the syn isomers,[5e,7f] largely remains an unsolved problem due to the facile isomerization of (*Z*)- and (*E*)-γ-silylallylmetal reagents.[4,9,10] Therefore, development of a stereocontrolled method for synthesis of chiral, nonracemic (*Z*)-γ-silylallylmetal reagents and the corresponding *syn*-β-hydroxyallylsilanes via enantioselective aldehyde allylation remains an important goal. Accordingly, we have developed and report herein a simple, one step, diastereo- and enantioselective synthesis of *syn*-β-hydroxyallylsilanes via a highly stereoselective allene hydroboration-aldehyde allylboration reaction sequence.

We recently reported that hydroboration of allenylstannane **1** with diisopinocampheylborane [(^{d}Ipc)$_2$BH] initially forms (*Z*)-γ-stannylallylborane **2** as the kinetic product, and that **2** isomerizes rapidly through a highly diastereoselective 1,3-boratropic shift to give the thermodynamically stable α-stannylallylborane **3** (eq 1, Figure 1).[11d] Subsequent allylboration of aldehydes with **3** gave (*E*)-δ-stannyl-homoallylic alcohols **4** in good yields and excellent enantioselectivities. With the objective to synthesize the potentially environmentally benign (*E*)-δ-silyl-homoallylic alcohols **6**, we decided to study the hydroboration of allenylsilane **5**[12] (eq 2, Figure 1).

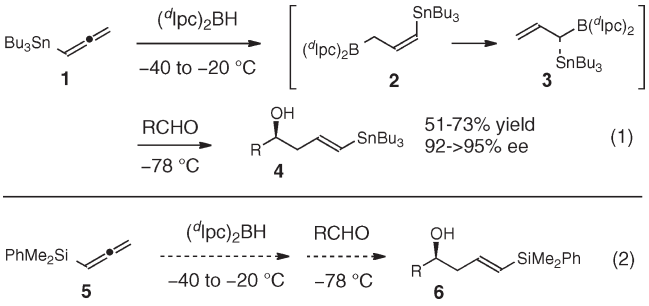


Figure 1. Hydroboration of allenylstannane **1** and planned hydroboration of allenylsilane **2** with (^{d}Ipc)$_2$BH.

In initial experiments, treatment of allenylsilane **5** with (^{d}Ipc)$_2$BH in toluene at −40 °C for 5 h followed by addition of hydrocinnamaldehyde at −78 °C provided the β-hydroxyallylsilane **7a** in 76% yield, 87% ee, and 14:1 d.s. and not the originally targeted homoallylic alcohol **6** (entry 1, Table 1). After careful comparison of the ^{1}H NMR spectra of the reaction product with the data reported in the literature for **7a**,[5e,7f] the major product was determined to be the *syn*-β-hydroxyallylsilane diastereomer (**7a**). The minor product is the *anti*- isomer **8a**. Application of this procedure to the (*Z*)-γ-silylallylboration of a variety of other aldehydes (entries 2−6, Table 1) provided *syn*-β-hydroxyallylsilanes **7b**−**7f** in 67−80% yields with ≥12:1 diastereoselectivities and 84−87% ee. The absolute stereochemistry of the secondary hydroxyl groups of **7a**−**7f** were assigned by using the modified Mosher ester analysis.[13] The regioisomeric (*E*)-δ-silyl-homoallylic alcohols **6** were not observed in these experiments.

The diastereoselectivity of this reaction sequence proved to be highly dependent on experimental conditions. When the hydroboration of **5** was performed at −20 °C followed by addition of hydrocinnamaldehyde at −78 °C, a 2:1 mixture of *syn*- and *anti*-β-hydroxyallylsilanes **7a** and **8a** was obtained in 81% yield. Similarly, when the hydroboration step was carried out at −30 °C, a 3:1 mixture of **7a** and **8a** was obtained in 77% yield. Hydroboration of **5** at −40 °C for 12 h also led to the formation of a 5:1 mixture of **7a** and **8a**. When the hydroboration step was carried out at temperatures below −40 °C (e.g., −50 °C for 5 h), the subsequent allylboration of hydrocinnamaldehyde at −78 °C provided **7a** as the only product, albeit in diminished yield (24%), owing to incomplete allene hydroboration.

These results indicate that at temperatures below −40 °C the kinetic hydroboration adduct **9*Z***, produced in the reaction of **5** with (^{d}Ipc)$_2$BH, *does not* rapidly isomerize to the thermodynamically more stable allylborane **9*E*** (Scheme 1). While the 1,3-boratropic shifts of the (^{d}Ipc)$_2$B− group is known to be slow for γ,γ-disubstituted allylboranes,[11b] this kinetically controlled hydroboration of allenylsilane **5** represents a rare case that a (*Z*)-γ-substituted allylborane

(7) For selected synthetic applications of β-hydroxyallylsilanes: (a) Micalizio, G. C.; Roush, W. R. *Org. Lett.* **2000**, *2*, 461. (b) Roush, W. R.; Dilley, G. J. *Synlett* **2001**, 955. (c) Heo, J.-N.; Micalizio, G. C.; Roush, W. R. *Org. Lett.* **2003**, *5*, 1693. (d) Shotwell, J. B.; Roush, W. R. *Org. Lett.* **2004**, *6*, 3865. (e) Tinsely, J. M.; Roush, W. R. *J. Am. Chem. Soc.* **2005**, *127*, 10818. (f) Tinsley, J. M.; Mertz, E.; Chong, P. Y.; Rarig, R.-A. F.; Roush, W. R. *Org. Lett.* **2005**, *7*, 4245. (g) Mertz, E.; Tinsley, J. M.; Roush, W. R. *J. Org. Chem.* **2005**, *70*, 8035. (h) Va, P.; Roush, W. R. *J. Am. Chem. Soc.* **2006**, *128*, 15960. (i) Huh, C. W.; Roush, W. R. *Org. Lett.* **2008**, *10*, 3371.

(8) For other selected applications of β-hydroxyallylsilanes: (a) Paterson, I.; Findlay, A. D.; Anderson, E. A. *Angew. Chem., Int. Ed.* **2007**, *46*, 6699. (b) Kishi, N.; Maeda, T.; Mikami, K.; Nakai, T. *Tetrahedron* **1992**, *48*, 4087. (c) Vincent, G.; Mansfield, D. J.; Vors, J.-P.; Ciufolini, M. A. *Org. Lett.* **2006**, *8*, 2791. (d) Beignet, J.; Jervis, P. J.; Cox, L. R. *J. Org. Chem.* **2008**, *73*, 5462. (e) Peroche, S.; Remuson, R.; Gelas-Mialhe, Y.; Gramain, J. C. *Tetrahedron Lett.* **2001**, *42*, 4617. (f) Ducray, R.; Ciufolini, M. A. *Angew. Chem., Int. Ed.* **2002**, *41*, 4688.

(9) (a) Hancock, K. G.; Kramer, J. D. *J. Am. Chem. Soc.* **1973**, *95*, 6463. (b) Kramer, G. W.; Brown, H. C. *J. Organomet. Chem.* **1977**, *132*, 9. (c) Hoffmann, R. W.; Zeiss, H. J. *J. Org. Chem.* **1981**, *46*, 1309. (d) Henriksen, U.; Snyder, J. P.; Halgren, T. A. *J. Org. Chem.* **1981**, *46*, 3767. (e) Brown, H. C.; Jadhav, P. K.; Bhat, K. S. *J. Am. Chem. Soc.* **1985**, *107*, 2564. (f) Wang, K. K.; Gu, Y. G.; Liu, C. *J. Am. Chem. Soc.* **1990**, *112*, 4424. (g) Gu, Y. G.; Wang, K. K. *Tetrahedron Lett.* **1991**, *32*, 3029. (h) Brown, H. C.; Narla, G. *J. Org. Chem.* **1995**, *60*, 4686. (i) Narla, G.; Brown, H. C. *Tetrahedron Lett.* **1997**, *38*, 219. (j) Fang, G. Y.; Aggarwal, V. K. *Angew. Chem.; Int. Ed.* **2007**, *46*, 359. (k) Canales, E.; González, A. Z.; Soderquist, J. A. *Angew. Chem.; Int. Ed.* **2007**, *46*, 397. (l) González, A. Z.; Román, J. G.; Alicea, E.; Canales, E.; Soderquist, J. A. *J. Am. Chem. Soc.* **2009**, *131*, 1269.

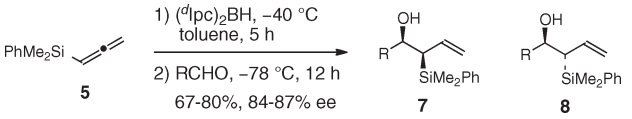
(10) One notable exception to the rapid isomerization of (*Z*)-and (*E*)-crotylborane isomers has been reported by Soderquist: Burgos, C. H.; Canales, E.; Matos, K.; Soderquist, J. A. *J. Am. Chem. Soc.* **2005**, *127*, 8044. Also see ref 5f.

(11) (a) Flamme, E. M.; Roush, W. R. *J. Am. Chem. Soc.* **2002**, *124*, 13644. (b) Chen, M.; Handa, M.; Roush, W. R. *J. Am. Chem. Soc.* **2009**, *131*, 14602. (c) Ess, D. H.; Kister, J.; Chen, M.; Roush, W. R. *Org. Lett.* **2009**, *11*, 5538. (d) Chen, M.; Ess, D. H.; Roush, W. R. *J. Am. Chem. Soc.* **2010**, *132*, 7881. (e) Stewart, P.; Chen, M.; Roush, W. R.; Ess, D. *Org. Lett.* **2011**10.1021/ol2001599. (f) Kister, J.; Nuhant, P.; Lira, R.; Sorg, A.; Roush, W. R. *Org. Lett.* **2011**, in press.

(12) (a) Myers, A. G.; Zheng, B. *Org. Synth.* **1999**, *76*, 178. (b) Li, Z.; Yang, C.; Zheng, H.; Qiu, H; Lai, G. *J. Organomet. Chem.* **2008**, *693*, 3771. (c) Fandrick, D. R.; Reeves, J. T.; Tan, Z.; Lee, H.; Song, J. J.; Yee, N. K.; Senanayake, C. H. *Org. Lett.* **2009**, *11*, 5458.

(13) (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.

Table 1. Synthesis of *syn*-β-Hydroxyallylsilanes **7** via Kinetically Controlled Hydroboration of Allenylsilane **5**[a]

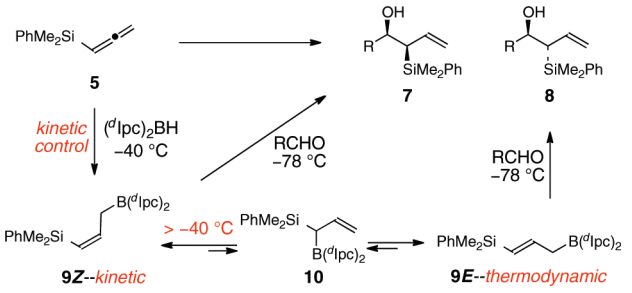


entry	RCHO	product	yield	d.s.	% ee[b]
1	$Ph(CH_2)_2CHO$	**7a**	76%	14:1	87
2	$PhCH_2CHO$	**7b**	70%	12:1	87
3	PhCHO	**7c**	80%	18:1	86
4	CyCHO	**7d**	67%	20:1	84
5	$TBSO(CH_2)_2CHO$	**7e**	71%	15:1	84
6	$TBSOCH_2CHO$	**7f**	72%	14:1	87

[a] Reactions were performed by treating **5** with $(^dIpc)_2BH$ (0.9 equiv) in toluene at −40 °C for 5 h, followed by the addition of RCHO (0.8 equiv) at −78 °C. The mixture was then allowed to stir at −78 °C for 12 h. The reactions were subjected to a standard workup ($NaHCO_3$, H_2O_2) at 0 °C prior to product isolation. [b] Determined by Mosher ester analysis.[13]

can be obtained in good Z/E ratio via hydroboration of a monosubstituted allene with dialkylboranes such as $(Ipc)_2BH$. Most (Z)-crotylboranes are configurationally unstable at temperatures above −60 °C.[9b] Allylboranes incorporating the Soderquist borane (10-TMS-9-borabicyclo[3.3.2]decanyl) auxiliary constitute the only general exception.[10]

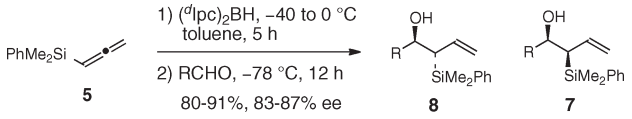
Scheme 1. Proposed Kinetic Hydroboration of **5** and Thermodynamically Controlled Allylborane Isomerization



As shown in Scheme 1, the kinetic adduct **9*Z*** can isomerize to the more stable allylborane **9*E*** through a reversible 1,3-boratropic shift[9,11] at temperatures above −40 °C, presumably via the intermediacy of **10**. Subsequent allylboration of aldehydes with **9E** should allow access to the diastereomeric *anti*-β-hydroxyallylsilanes **8** (which we have previously demonstrated by an alternative method).[5d] Indeed, when the hydroboration of allenylsilane **5** was performed at −40 °C with the solution being allowed to warm to 0 °C over 5 h, addition of hydrocinnamaldehyde to the resulting allylborane at −78 °C provided *anti*-β-hydroxyallylsilanes **8a** with >20:1 dr (**8a**:**7a**) in 87% yield and 86% ee (Table 2, entry 1). The hydroboration-isomerization-allylboration sequence was applied to a variety of aldehydes (Table 2). In all cases, *anti*-β-hydroxyallylsilanes **8a**−**f** were obtained in 80−91% yield and 83−87% ee with >20:1 diastereoselectivity.

To gain insight into the proposed reaction pathways, we carried out ^1H NMR studies of the hydroboration of allenylsilane **5** with $(^dIpc)_2BH$ at −20 and 0 °C.[14] As

Table 2. Synthesis of *anti*-β-Hydroxyallylsilanes **8** via Allene Hydroboration and Allylborane Isomerization[a]



entry	RCHO	product	yield	d.s.	% ee[b]
1	$Ph(CH_2)_2CHO$	**8a**	87%	>20:1	86
2	$PhCH_2CHO$	**8b**	90%	>20:1	87
3	PhCHO	**8c**	83%	>20:1	83
4	CyCHO	**8d**	80%	>20:1	86
5	$TBDPSO(CH_2)_2CHO$	**8e**	91%	>20:1	85
6	$TBSOCH_2CHO$	**8f**	87%	>20:1	84

[a] Reactions were performed by treating **5** with $(^dIpc)_2BH$ (0.9 equiv) in toluene at −40 °C and warmed to 0 °C over 5 h, followed by the addition of RCHO (0.8 equiv) at −78 °C. The mixture was then allowed to stir at −78 °C for 12 h. The reactions were subjected to a standard workup ($NaHCO_3$, H_2O_2) at 0 °C prior to product isolation. [b] Determined by Mosher ester analysis.[13]

illustrated in Figure 2, hydroboration of **5** with $(^dIpc)_2BH$ at −20 °C initially generates (Z)-γ-silylallylborane **9*Z*** (J = 12.8 Hz). Allylborane **9*Z*** isomerizes at −20 °C (monitored over 150 min) to (E)-γ-silylallylborane **9*E*** (J = 18.4 Hz). This isomerization is complete in about 60 min when the reaction mixture is allowed to warm to 0 °C. The fleeting intermediate α-silylallylborane **10** was not observed during these experiments.

Strikingly, while the hydroboration of allenylstannane **1** with $(^dIpc)_2BH$ provides α-stannylallylborane **3** as the most stable component of the equilibrating mixture,[15] the resting state of the hydroboration of allenylsilane **5** is (Z)- or (E)-γ-silylallylboranes, **9*Z*** or **9*E***, depending on the temperature of the hydroboration (Figure 3). Although it is well-known that both R_3Si- and R_3Sn- can stabilize a β−carbocation,[16] the capacity of these two groups to stabilize the β-carbocation is clearly different. For the intermediate α-stannylallylborane **3**, the hyperconjugative interaction between the Bu_3Sn- group and the boron

(14) We were not able to perform NMR studies at −40 °C due to the low solubility of $(^dIpc)_2BH$ in d_8-toluene at this temperature. $(^dIpc)_2BH$ is not fully soluble even at −20 °C, consequently signal resolution is poor at early stages of the reaction.

(15) See SI1 of ref 11d for details.

(16) (a) Davis, D. D.; Gray, C. E. *J. Org. Chem.* **1970**, *35*, 1303. (b) Jerkunica, J. M.; Traylor, T. G. *J. Am. Chem. Soc.* **1971**, *93*, 6278. (c) Wierschke, S. G.; Chandrasekhar, J.; Jorgensen, W. L. *J. Am. Chem. Soc.* **1985**, *107*, 1496. (d) Lambert, J. B.; Wang, G. T.; Finzel, R. B. *J. Am. Chem. Soc.* **1987**, *109*, 7838. (e) Lambert, J. B.; Wang, G. T.; Teramura, D. H. *J. Org. Chem.* **1988**, *53*, 5422.

atom (isoelectronic to a carbocation) must be strong enough to override the steric repulsion between the Bu_3Sn- and the $(^dIpc)_2B-$ units.[11e] The relatively long Sn−C bond (2.20 Å in **3**)[11e] might also be beneficial. On the other hand, for the intermediate α-silylallylborane **10**, it appears that the steric repulsion between the $PhMe_2Si-$ group and the $(^dIpc)_2B-$ unit overrides the hyperconjugative stabilization.[11e] The relatively shorter Si−C bond (estimated to be 1.85 Å) and the size of $PhMe_2Si-$ group presumably contribute to the steric effect, such that **9*Z*** or **9*E*** are much more stable than **10**. These conclusions are supported by a recent computational study.[11e]

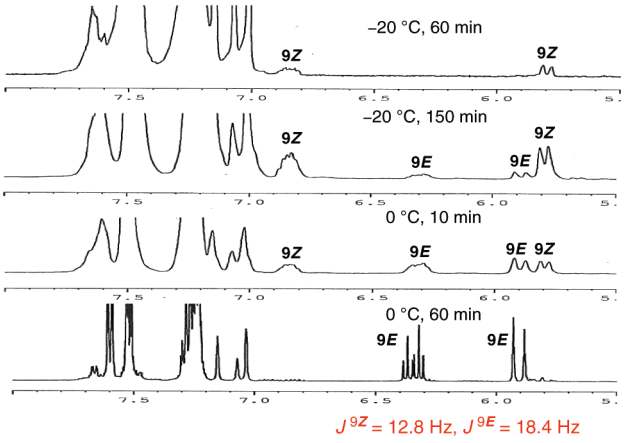


Figure 2. ^1H NMR studies of hydroboration of allenylsilane **5** in d_8-toluene. ^1H resonances in the olefinic region (8−5.5 ppm) are displayed in the partial spectra.

In conclusion, we have developed stereoselective syntheses of (*Z*)- and (*E*)-γ-silylallylboranes **9*Z*** and **9*E*** via hydroboration of allenylsilane **5** with $(^dIpc)_2BH$. At temperatures below −40 °C, the hydroboration reaction proceeds under kinetic control to give **9*Z*** with good selectivity. The normally facile 1,3-boratropic shift[9] is slow at −40 °C in the case of **9*Z***. However, isomerization readily occurs at temperatures above −40 °C, and complete isomerization of **9*Z*** to **9*E*** is observed at 0 °C. Thus, by appropriate control of the hydroboration conditions, highly diastereo- and enantioselective syntheses of either *syn*- or *anti*-β-hydroxyallylsilanes, **7** or **8**, can be achieved via aldehyde allylboration reaactions of **9*Z*** and **9*E***, respectively.

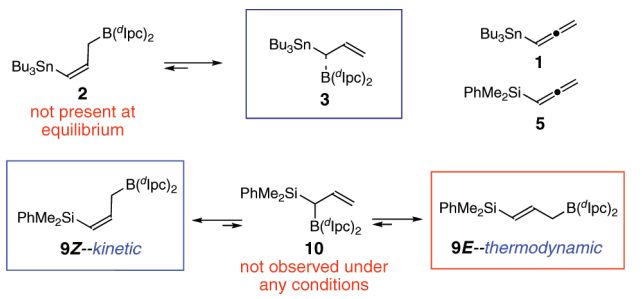


Figure 3. Comparison of the hydroboration-isomerization pathways for allenylstannane **1** and allenylsilane **5**.

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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.