Published in final edited form as:

Tetrahedron. 2013 July 1; 69(26): 5468–5475. doi:10.1016/j.tet.2013.04.098.

Enantiodivergent Hydroboration Reactions of a Racemic Allenylsilane with Diisopinocampheylborane and Curtin-Hammett Controlled Double Asymmetric Crotylboration Reactions of (*S*)-*E*- α -phenyldimethylsilyl(*d*-diisopinocampheyl)-crotylboration

Ming Chen and William R. Roush*

Department of Chemistry, The Scripps Research Institute, Florida, 130 Scripps Way, Jupiter, FL 33458, USA

Abstract

The enantiodivergent hydroboration reactions of racemic allenylsilane ($\pm$)-**4** with (*d*₁pc)₂BH and subsequent crotylboration of achiral aldehydes with the product crotylboration (*S*)-*E*-**5** at –78 °C provide (*E*)-silyl-*anti*-homoallylic alcohols **6** in 71–89% yield and with 93–96% ee. Intriguingly, mismatched double asymmetric crotylboration reactions of enantioenriched chiral aldehydes **20** with (*S*)-*E*-**5** proceed under Curtin-Hammett control to give *anti*- β -hydroxylcrotylsilanes **24** as the only products.

Keywords

Enantiodivergent hydroboration; Mismatched double asymmetric crotylboration; Curtin-Hammett control

1. Introduction

The asymmetric crotylation reaction of carbonyl compounds is one of the most widely utilized methods to synthesize stereochemically defined acyclic molecules.¹ However, for many synthetic applications the terminal vinyl groups embedded in the homoallylic alcohol products must be transformed into other functional groups via several step reaction sequences. Carbonyl crotylation with γ -functionalized allylmetal reagents (specifically, non-racemic β -substituted allylmetal reagents) provide homoallylic alcohols with a functionalized olefin unit, however the preparation of such reagents, in particular enantioenriched β -substituted crotylmetal reagents, remains largely underdeveloped.² Therefore, development of enantioselective methods for the synthesis of chiral, non-racemic γ -functionalized allylmetal reagents remains an important objective in methodology development.

© 2013 Elsevier Ltd. All rights reserved.

*Corresponding author. Tel.: +1-561-228-2450; fax: +1-561-228-3052; roush@scripps.edu.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

We envisioned that allene hydroboration reactions with chiral borane reagents could provide an exceedingly simple means to access chiral, non-racemic α -functionalized allylborane reagents.³ Several chiral, non-racemic crotylboranes have been developed recently in our laboratory by using this strategy.⁴ For example, as shown in Scheme 1, the enantioselective hydroboration of racemic allenylstannane ($\pm$)-**1** with (*d*Ipc)₂BH provides the enantioenriched α -tributylstannyl crotylborane, (*S*)-**E-2**. Subsequent crotylboration reactions of aldehydes with (*S*)-**E-2** gives (*E*)- α -stannyl-*anti*-homoallylic alcohols **3** in good yields and with excellent enantioselectivity.^{4a} The vinylstannane unit in homoallylic alcohols **3** can be used in a variety of subsequent transformations.⁵ Importantly, the enantioselective hydroboration of allenylstannane ($\pm$)-**1** proceeds in an enantioconvergent manner, with both enantiomers of the racemic allene ($\pm$)-**1** —(*P*)-**1** and (*M*)-**1**—being converted into the same crotylborane intermediate, (*S*)-**E-2**. Therefore, the synthesis of an enantiomerically pure allenylstannane precursor is not required to access (*E*)- α -stannyl-*anti*-homoallylic alcohols **3** with high enantioselectivity and high chemical efficiency.

In our continuing efforts to expand the scope of enantioselective allene hydroboration reactions for the synthesis of α -functionalized allylboranes, we envisioned that an analogous enantioconvergent reaction might be possible using racemic allenylsilane ($\pm$)-**4** as the substrate. If so, the α -silyl-crotylborane (*S*)-**E-5** that would be generated would provide access to enantioenriched (*E*)- β -silyl-*anti*-homoallylic alcohols **6** (Scheme 1). The vinylsilane unit of **6** is as useful for many subsequent transformations as is the vinylstannane unit of **3**. We describe here the results of our studies on the enantioselective hydroboration of racemic allenylsilane ($\pm$)-**4** with (*d*Ipc)₂BH.⁶

2. Results and Discussion

In initial experiments, treatment of racemic allenylsilane ($\pm$)-**4**⁷ with (*d*Ipc)₂BH (1 equiv) in toluene at 0 °C for 4 h, followed by addition of benzaldehyde (1 equiv) at –78 °C provided a 5:1 mixture of *anti*-homoallylic alcohol **6a** (76% ee) and the *syn* isomer **7a** (58% ee) in 41% and 7% yield, respectively (Scheme 2, top panel). Intriguingly, a ketone byproduct **8** (ca. 40%) was also identified. After extensive evaluation of several reaction parameters,⁶ we determined that when the hydroboration of racemic allene ($\pm$)-**4** was carried out with (*d*Ipc)₂BH (1 equiv) in toluene at –25 °C to –15 °C for 8 h, followed by treatment of the resulting crotylborane with 0.45 equiv of aldehyde at –78 °C, homoallylic alcohols **6a–f** (93–96% ee) were obtained in 71–89% yields (based on the aldehyde as limiting reagent) from both aromatic and aliphatic aldehydes (Scheme 2, bottom panel). Ketone **8** was also formed in these reactions. The absolute stereochemistry of homoallylic alcohols **6** was assigned by using the modified Mosher ester analysis.⁸ The *anti*-stereochemistry of **6d** was verified by protidesilylation (TBAF, DMSO, 80 °C) and comparison of the spectroscopic properties of the derived *anti*-homoallylic alcohol with an authentic sample.⁶

In contrast to the our previously reported enantioconvergent hydroboration of allenylstannane ($\pm$)-**1**,^{4a} the data in Scheme 2 for the hydroboration of racemic allenylsilane ($\pm$)-**4** with (*d*Ipc)₂BH suggest that this reaction proceeds via an enantiodivergent pathway. As illustrated in Scheme 3 (Panel A), hydroboration of allenylsilane enantiomer (*P*)-**4** with (*d*Ipc)₂BH occurs preferentially on the *re*-face of the methyl substituted olefin of (*P*)-**4**, *anti* to PhMe₂Si- to give intermediate (*R*)-**Z-9** (first equation of Panel A). We presume that this reaction is stereochemically matched,^{4a,9} since the enantioselectivity of this step parallels the enantioselectivity known for the hydroboration of (*Z*)-olefins with (*d*Ipc)₂BH.^{4a,9} Subsequent 1,3-shift of the boryl unit of (*R*)-**Z-9** gives crotylborane (*S*)-**E-5**. On the other hand, hydroboration of (*P*)-**4** with opposite regioselectivity on the olefin adjacent to the PhMe₂Si- group (second equation, Panel A) leads to the diastereomeric reagent (*S*)-**Z-10**

which can isomerize to (*R*)^d-*E*-**5** via a sequence of reversible 1,3-borotropic shifts. Crotylboration of aldehydes with (*R*)^d-*E*-**5** will give the enantiomeric alcohol product, *ent*-**6**. During the optimization of this hydroboration sequence,⁶ we observed that the pathway summarized in the second equation in Panel A of Scheme 3 is suppressed when the hydroboration is performed at temperatures below -25 °C. Other pathways for the hydroboration of allene (*P*)-**4** with (^dIpc)₂BH, as illustrated in the third line of Panel A (Scheme 3), are either mismatched with respect to the enantiofacial selectivity of (^dIpc)₂BH [as determined by the hydroboration of (*Z*)-olefins^{4a,9}] or mismatched in that hydroboration reaction occurs on the sterically disfavored face of the allene.

Hydroboration of allene enantiomer (*M*)-**4** with (^dIpc)₂BH is stereochemically mismatched when hydrogen adds to the central allenyl carbon atom.^{4a,9} The hydroboration transition states presented in the 3rd line of Panel B (Scheme 3) are mismatched with respect to the enantioselectivity of (^dIpc)₂BH (first two transition structures, 3rd line, Panel B) or because the hydroboration occurs on the sterically hindered face of allene (*M*)-**4** (third transition structure, 3rd line, Panel B). The hydroboration pathway presented in the 1st line of Panel B (Scheme 3) is also disfavored (addition to the more hindered face of the allene) and constitutes a minor pathway leading to crotylborane (*S*)-*E*-**5** from allene (*M*)-**4**.⁶ However, the enantioselective hydroboration of (*M*)-**4** can proceed with boron adding to the central allenyl carbon atom, *anti* to the PhMe₂Si- group to give vinylborane **11**, the precursor to ketone **8** (as indicated in the 2nd line of Panel B, Scheme 3). The sense of hydroboration in the conversion of (*M*)-**4** to **11** is consistent with the enantioselectivity of hydroboration of (*Z*)-olefins by (^dIpc)₂BH,^{4a,9} and is also favored in that the hydroboration occurs on the less hindered face of the allene, *anti* to the distal bulky PhMe₂Si- group. Hence, the hydroboration of (*M*)-**4** to give **11** appears to be stereochemically matched.

The rates of hydroboration of the two enantiomers of racemic allenylsilane (±)-**4** with (^dIpc)₂BH are comparable, as indicated by the fact that the allene recovered from experiments in which (^dIpc)₂BH is the limiting reagent (0.45 equiv) is nearly racemic (<10% ee).⁶ Therefore, the transformation presented in Scheme 2 is not a kinetic resolution. Rather, the fact that the enantioselective hydroboration of the two enantiomers of **4** proceed with different modes of addition to produce two structurally distinct intermediates, (*S*)-*E*-**5** and **11**, respectively, is critical to the success of this reaction for the synthesis of homoallylic alcohols **6** with high enantioselectivity.

Evidence in support of this analysis, deriving from studies of the hydroboration of enantiomerically pure allenylsilanes (*P*)-**4** and (*M*)-**4** with (^dIpc)₂BH, and ¹H NMR studies of the hydroboration reactions of (*P*)-**4** or (*M*)-**4** with (^dIpc)₂BH (demonstrating the significant production of **11** in the hydroboration of (*M*)-**4**) was included in our preliminary communication but is not repeated here.⁶

It is worth noting that, while the resting state of the products of hydroboration of monosubstituted allenylsilane **12** with (^dIpc)₂BH are the (*E*)- or (*Z*)-silyl-allylboranes, **14E** or **14Z** (depending on the temperature of the hydroboration reaction),¹⁰ the product resting state for the hydroboration of the 3-methyl substituted allenylsilane **4** with (^dIpc)₂BH is (*E*)-silyl-crotylborane (*S*)-*E*-**5**. Indeed, ¹H NMR studies of the hydroboration reaction of (*P*)-**4** with (^dIpc)₂BH shows that (*S*)-*E*-**5** is produced cleanly. Other crotylborane species such as (*R*)-*Z*-**9** or (*S*)-*E*-**15** are not observed (Scheme 4). Presumably a combination of the hyperconjugative effect between the PhMe₂Si- group and the adjacent boron atom (analogous to a silyl-stabilized carbocation)¹¹ and steric effects account for (*S*)-*E*-**5** being the only observed (and most stable) crotylborane product of the hydroboration of (*P*)-**4**. Steric repulsion between the methyl group and the (^dIpc)₂B- unit in either (*R*)-*Z*-**9** or (*S*)-*E*-**15** destabilizes these two species at equilibrium. Subsequent crotylboration of achiral

aldehydes with (*S*)-*E*-**5** proceeds through the chair-like transition state **TS-1** with pseudo equatorial placement of the PhMe₂Si- group to give (*E*)-*3*-silyl-*anti*-homoallylic alcohols **6** (Scheme 4).

To evaluate the potential of crotylborane (*S*)-*E*-**5** as a reagent for organic synthesis, double asymmetric reactions¹² with several representative chiral aldehydes were studied. First, double asymmetric reactions of α -alkoxy aldehyde **16** were explored (Scheme 5). The matched^{1a,13} double asymmetric reaction of **16** and reagent (*S*)-*E*-**5** provided **17** with a 4,6-*anti* relationship between the new hydroxyl group and the methoxyl substituent of aldehyde **16**, in 71% yield and with >20:1 diastereoselectivity. The mismatched double asymmetric reaction of **16** using the enantiomeric reagent (*R*)-*L*-**5** [generated from allene ($\pm$)-**4** and (*i*Lpc)₂BH] provided the 4,6-*syn* diastereomer **18** as the major product of an 8:1 product mixture. Surprisingly, the minor product (**19**) was determined by ¹H NMR analysis to be a crotylsilane regioisomer. As will be discussed subsequently, crotylsilane adducts such as **19** derive from crotylboration reactions of (*R*)-*L*-**5** which was not detected in our NMR analysis of hydroboration reaction mixtures (vide supra).

The formation of crotylsilane products such as **19** became much more prominent in studies of double asymmetric reactions of α -methyl branched chiral aldehydes, of interest as precursors to the di- and tri-propionate fragments found in many polyketide natural products.¹⁴ For example, the matched double asymmetric reaction of aldehyde **20a** with reagent (*R*)-*L*-**5** provided a 1:1 mixture of the expected crotylation product **21** and the crotylsilane regioisomer **22** (Scheme 6).

Strikingly, crotylsilane adducts **24** proved to be the exclusive products of the mismatched double asymmetric reactions presented in Scheme 7. The originally targeted *anti*, *anti*-stereotriads **23**¹⁴ were not detected in any of these experiments. The absolute stereochemistry of the secondary hydroxyl groups of homoallylic alcohols **22** and **24** was assigned by using the modified Mosher ester analysis.⁸ The olefin geometry of crotylsilanes **22** and **24** was *Z* (*J*_H = 10.8 Hz). The relative stereochemistry of the newly generated stereocenters in β -hydroxyl-crotylsilanes **24** were assigned by using both base and acid mediated Peterson elimination reactions.¹⁵ As shown in Scheme 8, addition of **24a** to a THF solution of KO^{*t*}Bu at 0 °C provided the *syn*-elimination product **25a**. Similar results were obtained with **24b** and **24c** (Scheme 8). The coupling constant between the two vinyl protons of the newly formed olefin in (*Z*, *Z*)-diene **25** is 10.8–11.2 Hz, which is consistent with a (*Z*)-olefin. On the other hand, treatment of β -hydroxyl-crotylsilane **24a** with BF₃•OEt₂ at –78 °C provided *anti*-elimination product (*E*, *Z*)-diene **26a**. Dienes **26b** and **26c** were obtained under similar elimination reactions from **24b** and **24c**, respectively (Scheme 8). The coupling constant of the two vinyl protons in the newly formed olefin is 15.2 Hz, which is consistent with an (*E*)-olefin. Based on these data, the products obtained from the mismatched double asymmetric crotylboration reactions of aldehydes **20** with (*S*)-*E*-**5** are (*Z*)-*anti*- β -hydroxyl-crotylsilanes **24**.

We focus on the attempted mismatched double asymmetric reactions of Scheme 7 in the following discussion. Assuming that these mismatched crotylboration reactions proceed through a chair-like transition state,¹ the surprising results in Scheme 7 indicate that *the dominant reactive crotylborane intermediate involved in these mismatched double asymmetric crotylborations is (S)-E-15, with the PhMe₂Si- group positioned distal to the boron atom* (Scheme 4). (An analogous reagent must also be involved in the chemistry summarized in Schemes 5b and 6, but to a lesser extent as compounds **19** and **22** are not the dominant products of those reactions). Although it is expected that (*S*)-*E*-**5** can equilibrate with (*S*)-*E*-**15** via a reversible 1,3-borotropic shift.¹⁶ ¹H NMR studies on the hydroboration of single enantiomer allenylsilanes (*P*)-**4** and (*M*)-**4** indicate that the amount of (*S*)-*E*-**15** in

the equilibrium mixture is negligible (not observed). Hence, these data suggest that: (1) the rate of the mismatched double asymmetric crotylboration of aldehydes **20a–c** with (*S*)-**E-15** (Scheme 7) is much faster than the rate of crotylboration with (*S*)-**E-5**; and (2) the rate of equilibration between (*S*)-**E-5** and (*S*)-**E-15** is much faster than the rates of the mismatched double asymmetric crotylboration of aldehydes **20** with these crotylboranes. Therefore, these reactions proceed under Curtin-Hammett control¹⁷ with (*S*)-**E-5** funneling to the more reactive intermediate (*S*)-**E-15** (with respect to aldehydes **20a–c**) to give the (*Z*)-*anti*-3-hydroxyl-crotylsilanes **24**. Although, Curtin-Hammett controlled transformations are well documented in the literature,¹⁷ to the best of our knowledge this behavior has not previously been observed in reactions of allylboration reagents.

Further analysis of this Curtin-Hammett controlled mismatched double asymmetric crotylboration is presented in Scheme 9. There are four possible transition states for the crotylboration of enantioenriched aldehydes **20a–c** with crotylborane species (*S*)-**E-5** and (*S*)-**E-15**, **TS-2** to **TS-5**. Among these, **TS-2** and **TS-3**, which lead to formation of **27** and **28**, respectively, operate under Felkin-Anh control.¹⁸ However, the arrangement of the crotyl group in **TS-2** and **TS-3** is mismatched with respect to the enantiofacial selectivity of the (*d*₁pc)₂B– group.¹³ Owing to the unfavorable non-bonding steric interactions in the transition states (shown in red), **TS-2** and **TS-3** are likely disfavored. Hence, the rates of crotylboration via these two transition states are comparatively slow. On the other hand, **TS-4** and **TS-5**, which lead to the formation of **23** and **24**, respectively, incorporate the proper sense of asymmetric induction deriving from the (*d*₁pc)₂B– units of reagents (*S*)-**E-5** and (*S*)-**E-15**.¹³ However, the conformation of the aldehyde –stereocenter in **TS-4** and **TS-5** is opposite to what is predicted by the Felkin-Anh model and gauche-pentane interactions¹⁸ between the methyl or PhMe₂Si group of the crotyl units and the R group of the aldehydes could occur in these two transition states (indicated in blue). Considering the relatively longer Si–C bond (estimated to be 1.85 Å) compared to a C–C bond (1.54 Å),¹⁰ the steric repulsion in **TS-5** is attenuated compared to **TS-4**, which likely renders **TS-5** [crotylboration of **20** with (*S*)-**E-15**] to be the most favored transition state for the mismatched double asymmetric crotylboration of aldehyde **20**. Moreover, the PhMe₂Si group is in a more hindered position, adjacent to the bulky (*d*₁pc)₂B– group in **TS-4**. Therefore, crotylborane (*S*)-**E-5** funnels to the more reactive intermediate (*S*)-**E-15** via a reversible 1,3-borotropic shift under the reaction conditions and the mismatched double asymmetric crotylboration reactions of aldehydes **20** proceed under Curtin-Hammett control via transition state **TS-5** with pseudo axial placement of the methyl group to give (*Z*)-*anti*-3-hydroxyl-crotylsilanes **24**.

3. Conclusion

We have developed an enantioselective synthesis of (*E*)-3-silyl-*anti*-homoallylic alcohols **6** via an enantiodivergent hydroboration-crotylboration reaction sequence that originates with the enantioselective hydroboration of allenylsilane (±)-**4** with (*d*₁pc)₂BH. Under optimized conditions, homoallylic alcohols **6** were obtained in 71–89% yield and with excellent enantioselectivity from racemic allenylsilane (±)-**4** and achiral aldehydes. The preparation of an enantiomerically pure allenylsilane is not required to produce highly enantioenriched homoallylic alcohol products **6**. In addition, the silyl substituted olefin unit embedded in the homoallylic alcohol products is suitable for use in a variety of subsequent transformations.^{19–21} A Curtin-Hammett controlled mismatched double asymmetric crotylboration of chiral aldehydes **20a–c** was discovered, in which reagent (*S*)-**E-5** isomerizes to the less stable, but more reactive transient reagent (*S*)-**E-15**. Specifically, the transient reagent (*S*)-**E-15**, deriving from (*S*)-**E-5** via a reversible 1,3-borotropic shift, reacts with aldehydes **20** faster than (*S*)-**E-5** and provides (*Z*)-*anti*-3-hydroxyl-crotylsilanes **24** as

the products instead of the expected vinylsilanes **23**. Synthetic applications of this methodology will be reported in due course.

4. Experimental

General Experimental Details

All reaction solvents were purified before use. Tetrahydrofuran, dichloromethane, diethyl ether and toluene were purified by passing through a solvent column composed of activated A-1 alumina. Unless indicated otherwise, all reactions were conducted under an atmosphere of argon using flame-dried or oven-dried (140 °C) glassware. The term “concentrated under reduced pressure” refers to the removal of solvents and other volatile materials using a rotary evaporator with the water bath temperature below 40 °C, followed by removal of residual solvent at high vacuum (< 0.2 mbar). Enantiomeric excesses were determined by the Mosher method.⁸

Proton nuclear magnetic resonance (¹H NMR) spectra were recorded on a commercial instrument at 400 MHz. Carbon-13 nuclear magnetic resonance (¹³C NMR) spectra were recorded at 100 MHz. The proton signal for residual non-deuterated solvent (7.26 for CHCl₃) was used as an internal reference for ¹H NMR spectra. For ¹³C NMR spectra, chemical shifts are reported relative to the 77.36 resonance of CHCl₃. Coupling constants are reported in Hz. Infrared (IR) spectra were recorded as films on a commercial FTIR instrument. Optical rotations were measured using a quartz cell with 1 mL capacity and a 10 cm path length. Melting points were determined on a hot stage melting point apparatus and are uncorrected. High resolution mass spectra were recorded on a commercial high resolution mass spectrometer.

Analytical thin layer chromatography (TLC) was performed on Kieselgel 60 F₂₅₄ glass plates precoated with a 0.25 mm thickness of silica gel. The TLC plates were visualized with UV light and/or by staining with Hanessian solution (ceric sulfate and ammonium molybdate in aqueous sulfuric acid) or KMnO₄. Column chromatography was generally performed using Kieselgel 60 (230–400 mesh) silica gel, typically using a 50–100:1 weight ratio of silica gel to crude product.

(1*S*,2*S*,*E*)-4-(dimethyl(phenyl)silyl)-2-methyl-1-phenylbut-3-en-1-ol (**6a**)—

Crystalline (*d*₁pc)₂BH (143 mg, 0.50 mmol) was weighed into a round bottom flask containing a stir bar in a glove box. (Note: The crystalline borane should be crushed and pulverized to fine powder with a glass rod in order to ensure efficient hydroboration). The flask was capped with a rubber septum and removed from the glove box. And then the flask was placed in a cold bath (–25 °C). Toluene (2 mL) was added slowly to the flask and the mixture (suspension) was cooled to –25 °C (~10 mins). Racemic allenylsilane (±)-**4**² (94 mg, 0.5 mmol) was added neat via a microliter syringe. This mixture was stirred for 4 h at –25 °C, and slowly warmed to –15 °C for 4 h, during which time the solid (*d*₁pc)₂BH dissolved to leave a colorless solution. The reaction mixture was cooled to –78 °C and freshly distilled benzaldehyde (24 mg, 0.225 mmol) was added at –78 °C dropwise to the reaction mixture via microliter syringe. The mixture was stirred for 12 h at –78 °C. MeOH (0.1 mL) was added to the –78 °C solution and the reaction was allowed to warm to 0 °C. To the 0 °C mixture was added saturated NaHCO₃ (0.5 mL) followed by slow addition of 30% H₂O₂ (1.0 mL). The reaction was stirred vigorously for 5 h at room temperature. Brine (2 mL) was added, the organic layer was separated and the aqueous layer was extracted with Et₂O (3 × 3 mL). The combined organic extracts were dried over anhydrous magnesium sulfate, filtered, and concentrated under reduced pressure. Purification of the crude product was performed by flash column chromatography (gradient elution: hexane:Et₂O = 200:1 to 10:1), which provided homoallylic alcohol **6a** (57 mg, 85% yield) as a colorless oil. [*α*]_D^{26.8}

= -83.8° (*c* 1.15, CHCl₃); 85% yield; 95% ee; ¹H NMR (400 MHz, CDCl₃) 7.27–7.49 (m, 10H), 6.12 (dd, *J* = 18.8, 7.6 Hz, 1H), 5.94 (d, *J* = 18.4 Hz, 1H), 4.42 (dd, *J* = 7.6, 3.6 Hz, 1H), 2.52–2.57 (m, 1H), 2.07 (d, *J* = 2.8 Hz, 1H), 0.90 (d, *J* = 6.8 Hz, 3H), 0.35 (s, 6H); ¹³C NMR (100 MHz, CDCl₃) 150.5, 142.7, 139.0, 134.1, 130.9, 129.3, 128.5, 128.1, 127.9, 127.1, 78.1, 49.2, 16.6, -2.14, -2.17; IR (neat) 3400, 3067, 2959, 2929, 1614, 1493, 1453, 1427, 1327, 1247, 1112, 1070, 1022, 998, 843, 822, 731, 699 cm⁻¹; HRMS (ESI) *m/z* for C₁₉H₂₄OSiNa [M+Na]⁺ calcd 319.1494, found 319.1500.

(1*E*,3*R*,4*S*,5*E*)-6-(dimethyl(phenyl)silyl)-4-methyl-1-phenylhexa-1,5-dien-3-ol (6b)—A colorless oil: [*α*_D^{26.7} = -24.3° (*c* 1.41, CHCl₃); 78% yield; 95% ee; ¹H NMR (400 MHz, CDCl₃) 7.52–7.50 (m, 2H), 7.23–7.38 (m, 7H), 7.22–7.25 (m, 1H), 6.58 (d, *J* = 15.6 Hz, 1H), 6.19 (dd, *J* = 16.0, 7.2 Hz, 1H), 6.10 (dd, *J* = 18.8, 7.2 Hz, 1H), 5.95 (dd, *J* = 18.8, 0.8 Hz, 1H), 4.09–4.11 (m, 1H), 2.40–2.48 (m, 1H), 1.78 (d, *J* = 3.2 Hz, 1H), 1.07 (d, *J* = 6.8 Hz, 3H), 0.35 (s, 6H); ¹³C NMR (100 MHz, CDCl₃) 150.2, 139.1, 137.1, 134.1, 131.9, 130.7, 130.5, 129.3, 128.9, 128.1, 128.0, 126.8, 76.4, 47.6, 16.1, -2.1; IR (neat) 3400, 3067, 2960, 1614, 1494, 1450, 1427, 1317, 1247, 1113, 1069, 1023, 998, 967, 844, 829, 732, 695 cm⁻¹; HRMS (ESI) *m/z* for C₂₁H₂₆OSiNa [M+Na]⁺ calcd 345.1651, found 345.1653

(1*R*,2*S*,*E*)-1-cyclohexyl-4-(dimethyl(phenyl)silyl)-2-methylbut-3-en-1-ol (6c)—A colorless oil: [*α*_D^{26.6} = -19.3° (*c* 1.86, CHCl₃); 71% yield; 94% ee; ¹H NMR (400 MHz, CDCl₃) 7.49–7.52 (m, 2H), 7.33–7.36 (m, 3H), 6.08 (dd, *J* = 18.8, 7.6 Hz, 1H), 5.83 (d, *J* = 18.8 Hz, 1H), 3.11–3.16 (m, 1H), 2.39–2.48 (m, 1H), 1.72–1.83 (m, 3H), 1.60–1.69 (m, 2H), 1.42 (d, *J* = 4.4 Hz, 1H), 1.36–1.41 (m, 1H), 1.06–1.26 (m, 5H), 1.04 (d, *J* = 6.8 Hz, 3H), 0.34 (s, 3H), 0.33 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) 150.8, 139.3, 134.1, 130.1, 129.3, 128.1, 79.0, 44.0, 40.8, 30.4, 27.3, 26.88, 26.86, 26.5, 17.2, -2.1, -2.2; IR (neat) 3435, 3068, 2924, 2852, 1613, 1449, 1427, 1247, 1113, 1067, 999, 844, 827, 730, 699 cm⁻¹; HRMS (ESI) *m/z* for C₁₉H₃₀OSiNa [M+Na]⁺ calcd 325.1964, found 325.1971.

(3*R*,4*S*,*E*)-6-(dimethyl(phenyl)silyl)-4-methyl-1-phenylhex-5-en-3-ol (6d)—A colorless oil: [*α*_D^{26.4} = -4.61° (*c* 0.97, CHCl₃); 89% yield; 93% ee; ¹H NMR (400 MHz, CDCl₃) 7.49–7.52 (m, 2H), 7.33–7.37 (m, 3H), 7.27–7.31 (m, 2H), 7.17–7.21 (m, 3H), 6.04 (dd, *J* = 18.8, 7.6 Hz, 1H), 5.90 (dd, *J* = 18.8, 0.8 Hz, 1H), 3.43–3.47 (m, 1H), 2.85 (ddd, *J* = 14.0, 10.0, 5.2 Hz, 1H), 2.68 (ddd, *J* = 13.6, 9.6, 6.8 Hz, 1H), 2.29–2.34 (m, 1H), 1.80–1.86 (m, 1H), 1.66–1.74 (m, 1H), 1.57 (d, *J* = 4.0 Hz, 1H), 1.05 (d, *J* = 6.8 Hz, 3H), 0.34 (s, 6H); ¹³C NMR (100 MHz, CDCl₃) 150.3, 142.6, 139.1, 134.1, 130.7, 129.3, 128.8, 128.7, 128.1, 126.1, 74.2, 47.4, 36.4, 32.5, 16.3, -2.1; IR (neat) 3391, 3066, 3020, 2957, 2923, 1613, 1454, 1427, 1248, 1113, 1068, 1023, 998, 843, 827, 731, 698 cm⁻¹; HRMS (ESI) *m/z* for C₂₁H₂₈OSiNa [M+Na]⁺ calcd 347.1807, found 347.1805

(2*S*,3*S*,*E*)-1-(benzyloxy)-5-(dimethyl(phenyl)silyl)-3-methylpent-4-en-2-ol (6e)—A colorless oil: [*α*_D^{26.7} = -16.1° (*c* 0.91, CHCl₃); 75% yield; 96% ee; ¹H NMR (400 MHz, CDCl₃) 7.49–7.52 (m, 2H), 7.28–7.38 (m, 8H), 6.14 (dd, *J* = 18.8, 7.6 Hz, 1H), 5.85 (dd, *J* = 18.8, 1.2 Hz, 1H), 4.55 (s, 2H), 3.70–3.75 (m, 1H), 3.53 (dd, *J* = 9.6, 3.2 Hz, 1H), 3.42 (dd, *J* = 9.6, 7.6 Hz, 1H), 2.42–2.47 (m, 1H), 2.25 (d, *J* = 3.2 Hz, 1H), 1.06 (d, *J* = 7.2 Hz, 3H), 0.34 (s, 6H); ¹³C NMR (100 MHz, CDCl₃) 150.1, 139.3, 138.4, 134.1, 129.3, 129.2, 128.8, 128.09, 128.07, 73.8, 73.7, 72.8, 43.7, 16.2, -2.1, -2.2; IR (neat) 3401, 3068, 2959, 2929, 2873, 1722, 1614, 1454, 1428, 1372, 1316, 1248, 1114, 1028, 998, 842, 826, 733, 699 cm⁻¹; HRMS (ESI) *m/z* for C₂₁H₂₈O₂SiNa [M+Na]⁺ calcd 363.1756, found 363.1755.

(3*R*,4*S*,*E*)-1-((*tert*-butyldimethylsilyl)oxy)-6-(dimethyl(phenyl)silyl)-4-methylhex-5-en-3-ol (6f)—A colorless oil: [*α*_D^{26.7} = -11.5° (*c* 1.35, CHCl₃); 72% yield; 95% ee; ¹H NMR (400 MHz, CDCl₃) 7.50–7.53 (m, 2H), 7.33–7.36 (m, 3H), 6.14 (dd, *J* = 18.8,

7.2 Hz, 1H), 5.83 (dd, J = 18.8, 1.2 Hz, 1H), 3.86–3.91 (m, 1H), 3.78–3.84 (m, 1H), 3.72–3.76 (m, 3H), 3.08 (d, J = 2.0 Hz, 1H), 2.30–2.35 (m, 1H), 1.59–1.65 (m, 2H), 1.06 (d, J = 6.8 Hz, 3H), 0.91 (s, 9H), 0.33 (s, 6H), 0.08 (s, 6H); ^{13}C NMR (100 MHz, CDCl_3) 150.9, 139.5, 134.1, 129.2, 128.8, 128.1, 75.1, 63.0, 46.8, 35.9, 26.2, 18.5, 15.8, –2.05, –2.08, –5.1; IR (neat) 3436, 3069, 2956, 2930, 2858, 1614, 1471, 1463, 1428, 1253, 1088, 997, 837, 778, 731, 699 cm^{-1} ; HRMS (ESI) m/z for $\text{C}_{21}\text{H}_{38}\text{O}_2\text{Si}_2\text{Na}$ $[\text{M}+\text{Na}]^+$ calcd 401.2308, found 401.2301

(4S,5R,6S,7S,8S,Z)-7-((tert-butylidimethylsilyl)oxy)-4-(dimethyl(phenyl)silyl)-6,8-dimethyldeca-2,9-dien-5-ol (24c)—Crystalline

(d^tIpc) $_2\text{BH}$ (143 mg, 0.50 mmol) was weighed into a round bottom flask containing a stir bar in a glove box. (Note: The crystalline borane should be crushed and pulverized to fine powder with a glass rod in order to ensure efficient hydroboration). The flask was capped with a rubber septum and removed from the glove box. And then the flask was placed in a cold bath (–25 °C). Toluene (1 mL) was added slowly to the flask and the mixture (suspension) was cooled to –25 °C (~10 mins). Racemic allenylsilane ($\pm$)-**4** (94 mg, 0.5 mmol) was added neat via a microliter syringe. This mixture was stirred for 4 h at –25 °C, and slowly warmed to –15 °C for 4 h, during which time the solid (d^tIpc) $_2\text{BH}$ dissolved to leave a colorless solution. The reaction mixture was cooled to –78 °C and freshly prepared aldehyde **20c** (51 mg, 0.2 mmol) was added at –78 °C to the reaction mixture via microliter syringe. The mixture was stirred for 4 h at –78 °C and slowly warmed to ambient temperature and kept stirring for 8 h. The reaction mixture was then cooled to 0 °C with ice bath. To the 0 °C mixture was added saturated NaHCO_3 (0.5 mL) followed by slow addition of 30% H_2O_2 (1.0 mL). The reaction was stirred vigorously for 5 h at room temperature. Brine (5 mL) was added, the organic layer was separated and the aqueous layer was extracted with Et_2O (3 $\times$ 5 mL). The combined organic extracts were dried over anhydrous magnesium sulfate, filtered, and concentrated under reduced pressure. Purification of the crude product was performed by flash column chromatography (gradient elution: hexane: Et_2O = 500:1 to 10:1), which provided alcohol **24c** (62 mg, 70% yield) as a colorless oil. $[\text{D}]_{\text{D}}^{27.1} = -25.6^\circ$ (c 1.78, CHCl_3); 70% yield; ^1H NMR (400 MHz, CDCl_3) 7.55–7.59 (m, 2H), 7.28–7.35 (m, 3H), 5.93 (ddd, J = 17.2, 10.0, 8.0 Hz, 1H), 5.56 (ddq, J = 11.2, 11.2, 1.6 Hz, 1H), 5.45 (dq, J = 11.2, 6.8 Hz, 1H), 4.88–4.94 (m, 2H), 3.86 (d, J = 10.0 Hz, 1H), 3.68 (t, J = 3.2 Hz, 1H), 3.12 (bs, 1H), 2.33–2.41 (m, 1H), 2.14 (dd, J = 11.2, 2.0 Hz, 1H), 1.71–1.80 (m, 1H), 1.31 (dd, J = 6.8, 1.6 Hz, 3H), 0.98 (d, J = 7.2 Hz, 3H), 0.90 (s, 9H), 0.65 (d, J = 7.2 Hz, 3H), 0.35 (s, 3H), 0.31 (s, 3H), 0.04 (s, 3H), 0.03 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) 141.6, 139.5, 134.5, 129.0, 127.8, 126.6, 122.9, 114.6, 80.6, 73.4, 42.3, 40.9, 33.0, 26.3, 20.3, 18.0, 13.5, 13.3, –3.1, –3.4, –3.9, –4.1; IR (neat) 3500, 3070, 2957, 2930, 2859, 1641, 1471, 1463, 1427, 1372, 1252, 1113, 1024, 837, 733, 700 cm^{-1} ; HRMS (ESI) m/z for $\text{C}_{26}\text{H}_{46}\text{O}_2\text{Si}_2\text{Na}$ $[\text{M}+\text{Na}]^+$ calcd 469.2934, found 469.2941.

(4S,5R,6S,7R,8R,Z)-9-((tert-butylidiphenylsilyl)oxy)-4-(dimethyl(phenyl)silyl)-7-methoxy-6,8-dimethylnon-2-en-5-ol (24a)—A colorless oil: $[\text{D}]_{\text{D}}^{27.2} = -15.8^\circ$ (c 1.82, CHCl_3); 62% yield; ^1H NMR (400 MHz, CDCl_3) 7.58–7.71 (m, 6H), 7.31–7.44 (m, 9H), 5.61 (ddq, J = 11.2, 11.2, 1.6 Hz, 1H), 5.45 (dq, J = 11.2, 6.8 Hz, 1H), 3.98 (t, J = 1.6 Hz, 1H), 3.70 (dd, J = 10.0, 5.6 Hz, 1H), 3.60 (d, J = 9.2 Hz, 1H), 3.52 (dd, J = 10.0, 2.4 Hz, 1H), 3.34 (s, 3H), 3.00 (dd, J = 7.2, 4.0 Hz, 1H), 2.20 (bd, J = 11.2 Hz, 1H), 1.91–1.97 (m, 1H), 1.76–1.82 (m, 1H), 1.31 (dd, J = 6.8, 1.6 Hz, 3H), 1.04 (s, 9H), 0.96 (d, J = 6.8 Hz, 3H), 0.62 (d, J = 6.8 Hz, 3H), 0.38 (s, 3H), 0.32 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) 139.7, 136.0, 135.95, 134.5, 134.3, 134.2, 129.9, 128.9, 127.9, 127.7, 126.9, 122.6, 91.4, 75.5, 65.5, 61.1, 40.1, 40.0, 32.7, 27.3, 19.6, 15.7, 15.4, 13.4, –3.1, –3.2; IR (neat) 3470, 3070, 2960, 2931, 2858, 1471, 1427, 1391, 1244, 1112, 1072, 840, 821, 737, 701 cm^{-1} ; HRMS (ESI) m/z for $\text{C}_{36}\text{H}_{52}\text{O}_3\text{Si}_2\text{Na}$ $[\text{M}+\text{Na}]^+$ calcd 611.3353, found 611.3361.

(4*S*,5*R*,6*S*,7*R*,8*S*,*Z*)-9-((*tert*-butyldiphenylsilyl)oxy)-4-(dimethyl(phenyl)silyl)-7-methoxy-6,8-dimethylnon-2-en-5-ol (24b)—A colorless oil: $[\alpha]_D^{26.9} = -1.58^\circ$ (c 3.16, CHCl₃); 67% yield; ¹H NMR (400 MHz, CDCl₃) 7.60–7.67 (m, 6H), 7.31–7.45 (m, 9H), 5.69 (ddq, $J = 11.2, 11.2, 1.6$ Hz, 1H), 5.44 (dq, $J = 10.8, 6.8$ Hz, 1H), 4.32 (dd, $J = 2.4, 1.2$ Hz, 1H), 3.68 (bd, $J = 8.4$ Hz, 1H), 3.47–3.56 (m, 2H), 3.384 (s, 3H), 3.38 (dd, $J = 8.8, 1.6$ Hz, 1H), 2.22 (dt, $J = 11.6, 2.0$ Hz, 1H), 1.80–1.85 (m, 1H), 1.69–1.75 (m, 1H), 1.31 (dd, $J = 6.8, 1.6$ Hz, 3H), 1.05 (s, 9H), 0.72 (d, $J = 6.8$ Hz, 3H), 0.62 (d, $J = 6.4$ Hz, 3H), 0.40 (s, 3H), 0.34 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) 139.7, 135.91, 135.89, 134.6, 134.1, 134.0, 130.0, 128.9, 128.01, 128.0, 127.7, 127.0, 122.5, 87.5, 75.4, 66.7, 61.3, 40.4, 39.0, 32.9, 27.2, 19.6, 14.6, 13.4, 10.2, –3.2; IR (neat) 3468, 3070, 3016, 2960, 2931, 2858, 1471, 1428, 1392, 1245, 1112, 1071, 823, 738, 701 cm^{–1}; HRMS (ESI) m/z for C₃₆H₅₂O₃Si₂Na [M+Na]⁺ calcd 611.3353, found 611.3358.

(3*S*,4*R*,6*R*,7*R*,*E*)-8-((*tert*-butyldiphenylsilyl)oxy)-1-(dimethyl(phenyl)silyl)-6-methoxy-3,7-dimethyloct-1-en-4-ol (17)—A colorless oil: $[\alpha]_D^{27.1} = -5.35^\circ$ (c 1.35, CHCl₃); 71% yield; ¹H NMR (400 MHz, CDCl₃) 7.65–7.67 (m, 4H), 7.49–7.52 (m, 2H), 7.32–7.43 (m, 9H), 6.08 (dd, $J = 18.8, 7.6$ Hz, 1H), 5.85 (d, $J = 18.8$ Hz, 1H), 3.67 (dd, $J = 10.0, 5.6$ Hz, 1H), 3.54–3.64 (m, 2H), 3.52 (dd, $J = 10.0, 6.4$ Hz, 1H), 3.33 (s, 3H), 2.16–2.25 (m, 1H), 2.18 (d, $J = 4.0$ Hz, 1H), 1.89–1.95 (m, 1H), 1.55–1.61 (m, 1H), 1.45–1.52 (m, 1H), 1.06 (s, 9H), 1.00 (d, $J = 7.2$ Hz, 3H), 0.95 (d, $J = 6.8$ Hz, 3H), 0.33 (s, 6H); ¹³C NMR (100 MHz, CDCl₃) 150.6, 139.3, 136.0, 135.95, 134.2, 134.17, 134.12, 129.9, 129.2, 128.1, 128.0, 80.0, 72.1, 65.9, 58.6, 47.6, 39.2, 35.9, 27.2, 19.6, 16.5, 12.8, –2.08, –2.1; IR (neat) 3459, 3070, 2959, 2931, 2858, 1614, 1471, 1462, 1427, 1247, 1112, 998, 825, 737, 701 cm^{–1}; HRMS (ESI) m/z for C₃₅H₅₀O₃Si₂Na [M+Na]⁺ calcd 597.3196, found 597.3194.

(3*R*,4*S*,6*R*,7*R*,*E*)-8-((*tert*-butyldiphenylsilyl)oxy)-1-(dimethyl(phenyl)silyl)-6-methoxy-3,7-dimethyloct-1-en-4-ol (18)—A colorless oil: $[\alpha]_D^{27.2} = 8.25^\circ$ (c 0.98, CHCl₃); 63% yield; 8:1 dr; ¹H NMR (400 MHz, CDCl₃) 7.64–7.68 (m, 4H), 7.49–7.52 (m, 2H), 7.31–7.44 (m, 9H), 6.10 (dd, $J = 18.8, 7.2$ Hz, 1H), 5.81 (dd, $J = 18.8, 0.8$ Hz, 1H), 3.70 (dd, $J = 10.0, 6.0$ Hz, 1H), 3.60–3.65 (m, 1H), 3.51–3.56 (m, 2H), 3.30 (s, 3H), 3.21 (d, $J = 1.6$ Hz, 1H), 2.27–2.34 (m, 1H), 1.95 (ddd, $J = 13.2, 6.8, 3.6$ Hz, 1H), 1.43–1.52 (m, 2H), 1.06 (s, 9H), 1.04 (d, $J = 6.8$ Hz, 3H), 0.88 (d, $J = 6.8$ Hz, 3H), 0.321 (s, 3H), 0.317 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) 150.8, 139.5, 136.0, 135.94, 134.2, 134.13, 130.0, 129.2, 128.8, 128.1, 128.0, 83.4, 75.1, 65.4, 57.8, 46.9, 38.4, 34.5, 27.3, 19.6, 15.5, 12.4, –2.04, –2.09; IR (neat) 3435, 3070, 2959, 2930, 2858, 1462, 1427, 1247, 1112, 1082, 824, 737, 700 cm^{–1}; HRMS (ESI) m/z for C₃₅H₅₀O₃Si₂Na [M+Na]⁺ calcd 597.3196, found 597.3214.

Acknowledgments

Financial support provided by the National Institutes of Health (GM038436) is gratefully acknowledged. We thank Eli Lilly for a predoctoral fellowship to M. Chen.

References

- (a) Roush, WR. Comprehensive Organic Synthesis. Trost, BM., editor. Vol. 2. Pergamon Press; Oxford: 1991. p. 1(b) Yamamoto Y, Asao N. Chem Rev. 1993; 93:2207.(c) Denmark, SE.; Almstead, NG. Modern Carbonyl Chemistry. Otera, J., editor. Wiley-VCH; Weinheim: 2000. p. 299(d) Chemler, SR.; Roush, WR. Modern Carbonyl Chemistry. Otera, J., editor. Wiley-VCH; Weinheim: 2000. p. 403(e) Denmark SE, Fu J. Chem Rev. 2003; 103:2763. [PubMed: 12914480] (f) Lachance H, Hall DG. Org React. 2008; 73:1.(g) Yus M, Gonzles-Gmez JC, Foubelo F. Chem Rev. 2011; 111:7774. [PubMed: 21923136]
- (a) Pietruszka J, Schone N. Angew Chem, Int Ed. 2003; 42:5638.(b) Pelz NF, Woodward AR, Burks HE, Sieber JD, Morken JP. J Am Chem Soc. 2004; 126:16328. [PubMed: 15600327] (c) Sieber JD,

- Morken JP. *J Am Chem Soc.* 2006; 128:74. [PubMed: 16390128] (d) Ito H, Ito S, Sasaki Y, Matsuura K, Sawamura M. *J Am Chem Soc.* 2007; 129:14856. [PubMed: 17988133] (e) Peng F, Hall DG. *J Am Chem Soc.* 2007; 129:3070. [PubMed: 17315879] (f) Chen M, Roush WR. *Org Lett.* 2010; 12:2706. [PubMed: 20476769] (g) Althaus M, Mahmood A, Suarez JR, Thomas SP, Aggarwal VK. *J Am Chem Soc.* 2010; 132:4025. [PubMed: 20192266] (h) Kliman LT, Mlynarski SN, Ferris GE, Morken JP. *Angew Chem, Int Ed.* 2012; 51:521.(i) Ferris GE, Hong K, Roundtree IA, Morken JP. *J Am Chem Soc.* 2013; 135:2501. [PubMed: 23390951]
3. For a recently review on allenes in asymmetric synthesis: Yu S, Ma S. *Angew Chem, Int Ed.* 2012; 51:3074.
4. (a) Chen M, Roush WR. *J Am Chem Soc.* 2011; 133:5744. [PubMed: 21449594] (b) Chen M, Ess DH, Roush WR. *J Am Chem Soc.* 2010; 132:7881. [PubMed: 20496899] (c) Han JL, Chen M, Roush WR. *Org Lett.* 2012; 14:3028. [PubMed: 22646839]
5. (a) Sun H, Abbott JR, Roush WR. *Org Lett.* 2011; 13:2734. [PubMed: 21510632] (b) Yin M, Roush WR. *Tetrahedron.* 2011; 67:10274. [PubMed: 22711935] (c) Chen M, Roush WR. *Org Lett.* 2012; 14:426. [PubMed: 22148850] (d) Chen M, Roush WR. *Org Lett.* 2012; 14:1556. [PubMed: 22372693] (e) Chen M, Roush WR. *Org Lett.* 2012; 14:1880. [PubMed: 22409510] (f) Chen M, Roush WR. *J Org Chem.* 2013; 78:3. [PubMed: 22703288]
6. Chen M, Roush WR. *Org Lett.* 2013; 15:1662. [PubMed: 23534391]
7. (a) Marshall JA, Maxson K. *J Org Chem.* 2000; 65:630. [PubMed: 10813988] (b) Fleming I, Waterson D. *J Chem Soc, Perkin Trans 1.* 1984:1809.(c) Fleming I, Newton TW, Roessler F. *J Chem Soc, Perkin Trans 1.* 1981:2527.
8. (a) Dale JA, Mosher HS. *J Am Chem Soc.* 1973; 95:512.(b) Ohtani I, Kusumi T, Kashman Y, Kakisawa H. *J Am Chem Soc.* 1991; 113:4092.
9. (a) Brown HC, Zweifel G. *J Am Chem Soc.* 1961; 83:486.(b) Zweifel G, Brown HC. *J Am Chem Soc.* 1964; 86:397.
10. Chen M, Roush WR. *Org Lett.* 2011; 13:1992. [PubMed: 21410173]
11. (a) Davis DD, Gray CE. *J Org Chem.* 1970; 35:1303.(b) Jerkunica JM, Traylor TG. *J Am Chem Soc.* 1971; 93:6278.(c) Wierschke SG, Chandrasekhar J, Jorgensen WL. *J Am Chem Soc.* 1985; 107:1496.(d) Lambert JB, Wang GT, Finzel RB. *J Am Chem Soc.* 1987; 109:7838.(e) Lambert JB, Wang GT, Teramura DH. *J Org Chem.* 1988; 53:5422.(f) Stewart P, Chen M, Roush WR, Ess D. *Org Lett.* 2011; 13:1478. [PubMed: 21323387]
12. Masamune S, Choy W, Petersen JS, Sita LR. *Angew Chem, Int Ed Engl.* 1985; 24:1.
13. Brown HC, Bhat KS. *J Am Chem Soc.* 1986; 108:293.
14. (a) Hoffmann RW. *Angew Chem, Int Ed Engl.* 1987; 26:489.(b) Hoffmann RW, Dahmann G, Andersen MW. *Synthesis.* 1994:629.(c) Chemler SR, Roush WR. *J Org Chem.* 1998; 63:3800.(d) Chemler SR, Roush WR. *J Org Chem.* 2003; 68:1319. [PubMed: 12585871] (e) Chen M, Roush WR. *J Am Chem Soc.* 2012; 134:3925. [PubMed: 22332989]
15. (a) Peterson DJ. *J Org Chem.* 1968; 33:780.(b) Ager DJ. *Org React.* 1990; 38:1.
16. (a) Hancock KG, Kramer JD. *J Am Chem Soc.* 1973; 95:6463.(b) Kramer GW, Brown HC. *J Organomet Chem.* 1977; 132:9.(c) Hoffmann RW, Zeiss HJ. *J Org Chem.* 1981; 46:1309.(d) Henriksen U, Snyder JP, Halgren TA. *J Org Chem.* 1981; 46:3767.(e) Wang KK, Gu YG, Liu C. *J Am Chem Soc.* 1990; 112:4424.(f) Fang GY, Aggarwal VK. *Angew Chem, Int Ed.* 2007; 46:359.(g) Canales E, González AZ, Soderquist JA. *Angew Chem, Int Ed.* 2007; 46:397.(h) Kister J, DeBaillie AC, Lira R, Roush WR. *J Am Chem Soc.* 2009; 131:14174. [PubMed: 19775159] (i) Chen M, Handa M, Roush WR. *J Am Chem Soc.* 2009; 131:14602. [PubMed: 19778012] (j) Ess DH, Kister J, Chen M, Roush WR. *Org Lett.* 2009; 11:5538. [PubMed: 19899749]
17. (a) Seeman JI. *Chem Rev.* 1983; 83:83.(b) Halpern J. *Science.* 1982; 217:401. [PubMed: 17782965] (c) Landis CR, Halpern J. *J Am Chem Soc.* 1987; 109:1746.
18. (a) Roush WR. *J Org Chem.* 1991; 56:4151.(b) Cherest M, Felkin H, Prudent N. *Tetrahedron Lett.* 1968; 18:2199.(c) Anh NT, Eisenstein O. *Nouv J Chim.* 1977; 1:61.
19. (a) Blumenkopf TA, Overman LE. *Chem Rev.* 1986; 86:857.(b) Fleming I. *Org React.* 1989; 37:57.(c) Fleming I, Barbero A, Walter D. *Chem Rev.* 1997; 97:2063. [PubMed: 11848898]
20. (a) Miura K, Hosomi A. *Synlett.* 2003:143.(b) Yu CM, Youn J, Jung HK. *Bull Korean Chem Soc.* 2006; 27:463.(c) Evans DA, Aye Y. *J Am Chem Soc.* 2006; 128:11034. [PubMed: 16925415] (d)

- Ilardi EA, Stivala CE, Zakarian A. *Org Lett.* 2008; 10:1727. [PubMed: 18386904] (e) Nishimoto Y, Kajioaka M, Saito T, Yasuda M, Baba A. *Chem Commun.* 2008:6396.(f) Bates RH, Chen M, Roush WR. *Curr Opin Drug Discovery Dev.* 2008; 11:778.(g) Aikawa K, Hioki YT, Mikami K. *J Am Chem Soc.* 2009; 131:13922. [PubMed: 19788326]
21. For select reviews of Hiyama coupling: Denmark SE, Liu JHC. *Angew Chem, Int Ed.* 2010; 49:2978.Denmark SE, Sweis RF. In *Metal Catalyzed Cross-Coupling Reactions (2)*. de Meijere A, Diederich F. Wiley-VCHWeinheim2004; Chapter 4Hiyama T. *Metal Catalyzed Cross-Coupling Reactions*. Diederich F, Stang PJ. Wiley-VCHWeinheim199810 and references cited therein

Scheme 1.

Enantioconvergent and Enantioselective Hydroboration of Racemic Allenylstannane (±)-4 and Proposed Enantioselective Hydroboration of Racemic Allenylsilane (±)-4

Scheme 2.
 Synthesis of (*E*)- -Silyl-*anti*-homoallylic Alcohols **6**

A. Pathways for Enantioselective Hydroboration of (*P*)-4 with (*d*₁pc)₂BH B. Pathways for Enantioselective Hydroboration of (*M*)-4 with (*d*₁pc)₂BH **Scheme 3.**

Proposed Enantiodivergent Hydroboration-Isomerization Pathways for the Two Enantiomers of Racemic Allenylsilane ($\pm$)-4. (A) Pathways for enantioselective hydroboration of (*P*)-4 with (*d*₁pc)₂BH, (B) Pathways for enantioselective hydroboration of (*M*)-4 with (*d*₁pc)₂BH,

Scheme 4.
Comparison of Hydroboration-Isomerization Pathways for Allenylsilanes **12** and $(\pm)\text{-4}$

Scheme 5.

Double Asymmetric Reactions of 4-Methoxypentanal **16** with Reagents (*S*)-*E*-5 and (*R*)-*E*-5.

Scheme 6.

Matched Double Asymmetric Reaction of Chiral Aldehyde **20a** with $(R)^L$ -E-5.

Scheme 7.

Mismatched Double Asymmetric Crotylboration Reactions of Chiral Aldehydes **20** with (*S*)-*E*-5

Reactions were performed by treating ($\pm$)-**4** with (*d*Ipc)₂BH (1 equiv) in toluene at -25°C and warming to -15°C over 8 h followed by the addition of aldehydes **20** (0.4 equiv) at -78°C . The mixture was then allowed to warm to room temperature and stirred for 12 h. The reactions were subjected to a standard workup (NaHCO₃, H₂O₂) at 0°C prior to product isolation.

Scheme 8. Base and Acid Mediated Peterson Elimination Reactions of 3-Hydroxy-crotylsilanes **24**

Scheme 9.
 Transition State Analyses of Mismatched Double Asymmetric Crotylboration of Aldehydes **20** with Crotylboranes **(S)-E-5** and **(S)-E-15**