Tetrahedron 69 (2013) 5468–5475

Contents lists available at SciVerse ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Enantiodivergent hydroboration reactions of a racemic allenylsilane with diisopinocampheylborane and Curtin–Hammett controlled double asymmetric crotylboration reactions of (*S*)-*E*-α-phenyldimethylsilyl(*d*diisopinocampheyl)-crotylborane

Ming Chen, William R. Roush *

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

ARTICLE INFO

Article history:
Received 27 February 2013
Received in revised form 20 April 2013
Accepted 22 April 2013
Available online 28 April 2013

Keywords:
Enantiodivergent hydroboration
Mismatched double asymmetric crotylboration
Curtin–Hammett control

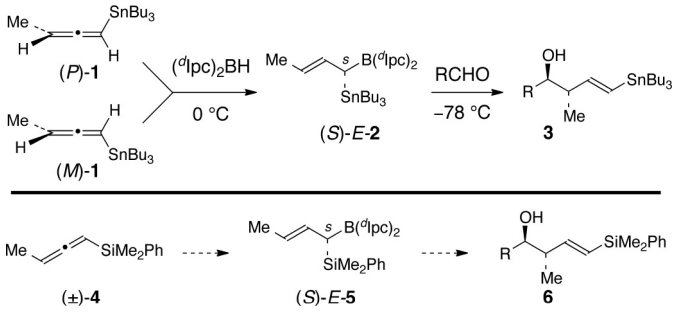
ABSTRACT

The enantiodivergent hydroboration reactions of racemic allenylsilane (±)-**4** with (^{d}Ipc)$_2$BH and subsequent crotylboration of achiral aldehydes with the product crotylborane (*S*)-*E*-**5** at −78 °C provide (*E*)-δ-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.

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 α-functionalized allylmetal reagents (specifically, non-racemic α-substituted allylmetal reagents) provide homoallylic alcohols with a functionalized olefin unit, however the preparation of such reagents, in particular enantioenriched α-substituted crotylmetal reagents, remains largely underdeveloped.[2] Therefore, development of enantioselective methods for the synthesis of chiral, non-racemic α-functionalized allylmetal reagents remains an important objective in methodology development.

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 (±)-**1** with (^{d}diisopinocampheyl)borane [(^{d}Ipc)$_2$BH] provides the enantioenriched α-tributylstannyl crotylborane, (*S*)-*E*-**2**. Subsequent crotylboration reactions of aldehydes with (*S*)-*E*-**2** give (*E*)-δ-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 (±)-**1** proceeds in an enantioconvergent manner, with both enantiomers of the racemic allene (±)-**1**—(*P*)-**1** and (*M*)-**1**—being converted into the same crotylborane intermediate, (*S*)-*E*-**2**. Therefore,



Scheme 1. Enantioconvergent and enantioselective hydroboration of Racemic Allenylstannane (±)-**4**) and proposed enantioselective hydroboration of racemic allenylsilane (±)-**4**.

* Corresponding author. Tel.: +1 561 228 2450; fax: +1 561 228 3052; e-mail address: roush@scripps.edu (W.R. Roush).

0040-4020/$ – see front matter © 2013 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.tet.2013.04.098

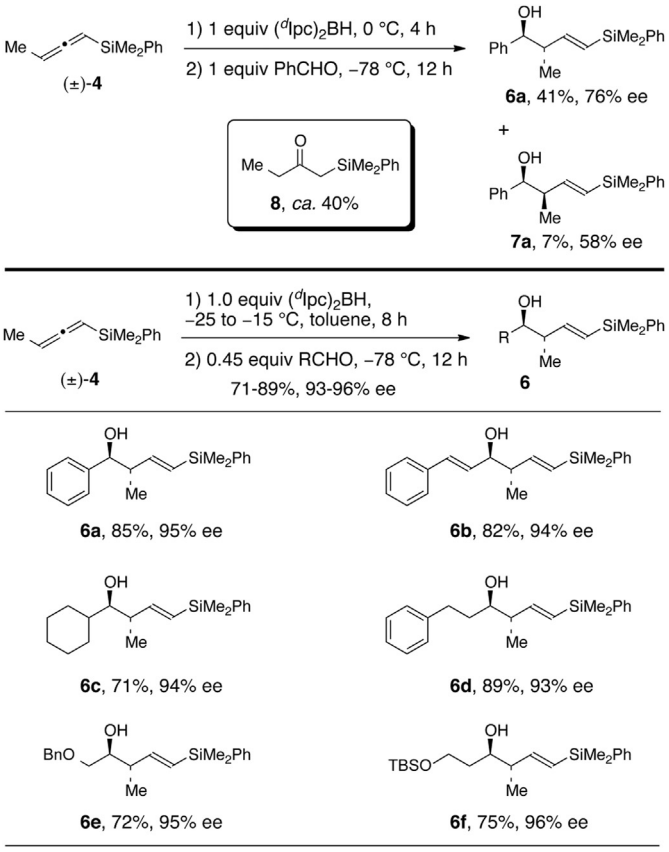
the synthesis of an enantiomerically pure allenylstannane precursor is not required to access (*E*)-δ-stannyl-*anti*-homoallylic alcohols **3** with high enantioselectivity and high chemical efficiency.

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 (±)-**4** as the substrate. If so, the α-silyl-crotylborane (*S*)-*E*-**5** that would be generated would provide access to enantioenriched (*E*)-δ-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 (±)-**4** with $(^d\text{Ipc})_2$BH.[6]

2. Results and discussion

In initial experiments, treatment of racemic allenylsilane (±)-**4**[7] with $(^d\text{Ipc})_2$BH (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 by-product **8** (ca. 40%) was also identified. After extensive evaluation of several reaction parameters,[6] we determined that when the hydroboration of racemic allene (±)-**4** was carried out with $(^d\text{Ipc})_2$BH (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 protiodesilylation (TBAF, DMSO, 80 °C) and comparison of the spectroscopic properties of the derived *anti*-homoallylic alcohol with an authentic sample.[6]

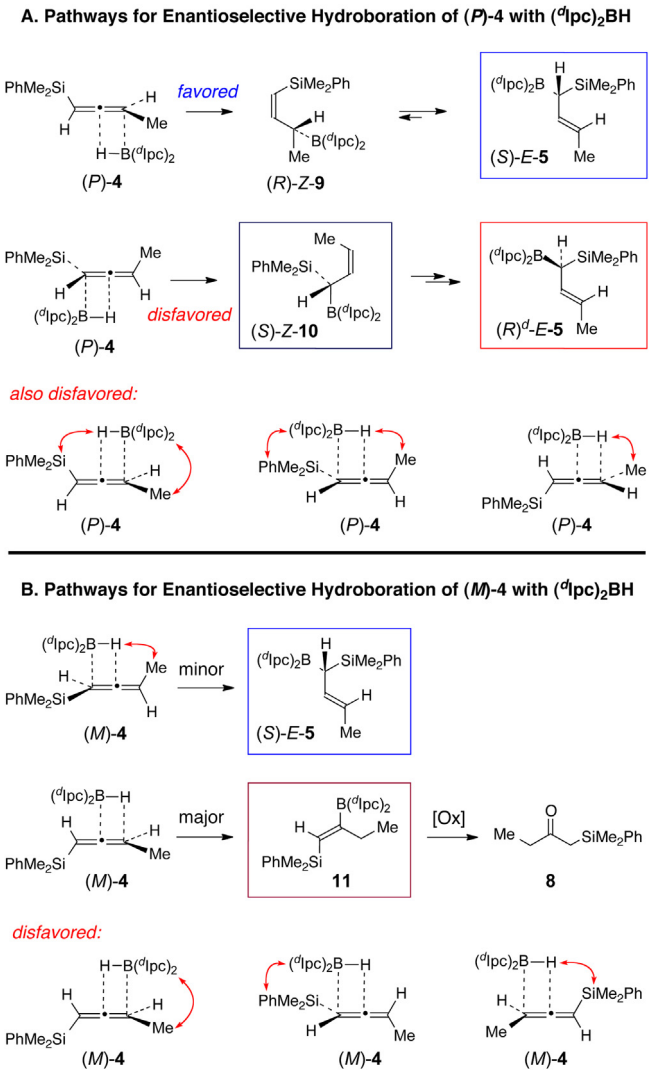
In contrast to our previously reported enantioconvergent hydroboration of allenylstannane (±)-**1**,[4a] the data in Scheme 2 for the hydroboration of racemic allenylsilane (±)-**4** with $(^d\text{Ipc})_2$BH suggest that this reaction proceeds via an enantiodivergent pathway. As illustrated in Scheme 3 (Panel A), hydroboration of allenylsilane enantiomer (*P*)-**4** with $(^d\text{Ipc})_2$BH occurs preferentially on the *re*-face of the methyl substituted olefin of (*P*)-**4**, *anti* to $PhMe_2Si$– 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 $(^d\text{Ipc})_2$BH.[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 $PhMe_2Si$– 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-boratropic 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 $(^d\text{Ipc})_2$BH, as illustrated in the third line of Panel A (Scheme 3), are either mismatched with respect to the enantiofacial selectivity of $(^d\text{Ipc})_2$BH [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.



Scheme 2. Synthesis of (*E*)-δ-silyl-*anti*-homoallylic alcohols **6**.

Hydroboration of allene enantiomer (*M*)-**4** with $(^d\text{Ipc})_2$BH is stereochemically mismatched when hydrogen adds to the central allenyl carbon atom.[4a,9] The hydroboration transition states presented in the third line of Panel B (Scheme 3) are mismatched with respect to the enantioselectivity of $(^d\text{Ipc})_2$BH (first two transition structures, third line, Panel B) or because the hydroboration occurs on the sterically hindered face of allene (*M*)-**4** (third transition structure, third line, Panel B). The hydroboration pathway presented in the first 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 $PhMe_2Si$– group to give vinylborane **11**, the precursor to ketone **8** (as indicated in the second 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 $(^d\text{Ipc})_2$BH,[4a,9] and is also favored in that the hydroboration occurs on the less hindered face of the allene, *anti* to the distal bulky $PhMe_2Si$– group. Hence, the hydroboration of (*M*)-**4** to give **11** appears to be stereochemically matched.

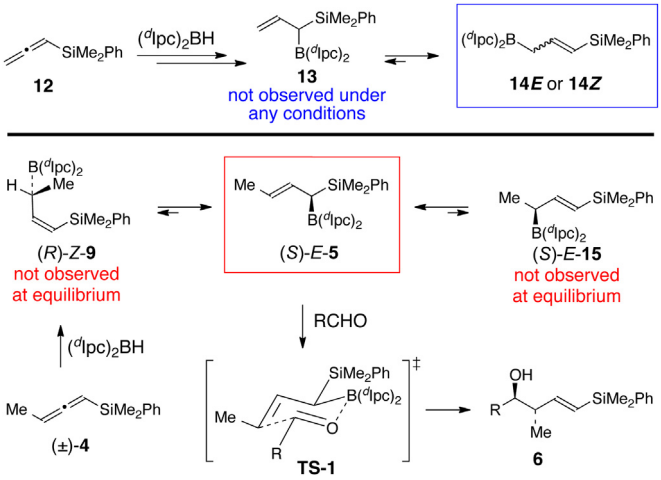
The rates of hydroboration of the two enantiomers of racemic allenylsilane (±)-**4** with $(^d\text{Ipc})_2$BH are comparable, as indicated by the fact that the allene recovered from experiments in which $(^d\text{Ipc})_2$BH is the limiting reagent (0.45 equiv) is nearly racemic (<10% ee).[6] Therefore, 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.



Scheme 3. Proposed enantiodivergent hydroboration–isomerization pathways for the two enantiomers of racemic allenylsilane (±)-**4**.

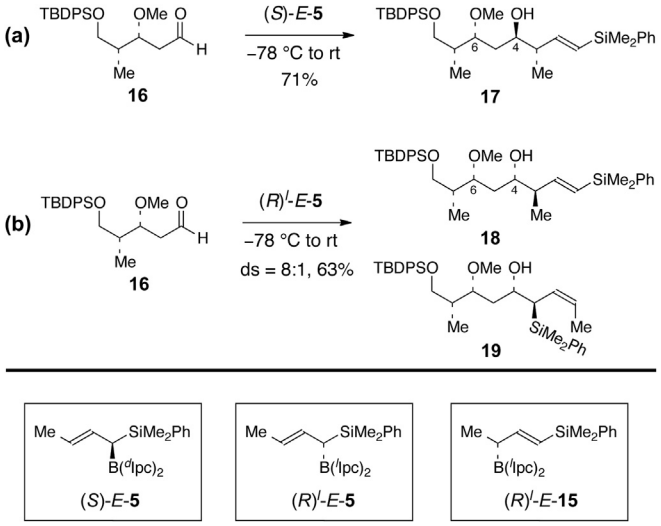
Evidence in support of this analysis, deriving from studies of the hydroboration of enantiomerically pure allenylsilanes (*P*)-**4** and (*M*)-**4** with $(^{d}Ipc)_2BH$, and ^1H NMR studies of the hydroboration reactions of (*P*)-**4** or (*M*)-**4** with $(^{d}Ipc)_2BH$ (demonstrating the significant 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 $(^{d}Ipc)_2BH$ are the (*E*)- or (*Z*)-γ-silyl-allylboranes, **14*E*** or **14*Z*** (depending on the temperature of the hydroboration reaction),[10] the product resting state for the hydroboration of the 3-methyl substituted allenylsilane **4** with $(^{d}Ipc)_2BH$ is (*E*)-α-silyl-crotylborane (*S*)-*E*-**5**. Indeed, ^1H NMR studies of the hydroboration reaction of (*P*)-**4** with $(^{d}Ipc)_2BH$ 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 $PhMe_2Si$– group and the adjacent boron atom (analogous to a silyl-stabilized β-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 $(^{d}Ipc)_2B$– 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 $PhMe_2Si$– group to give (*E*)-δ-silyl-*anti*-homoallylic alcohols **6** (Scheme 4).



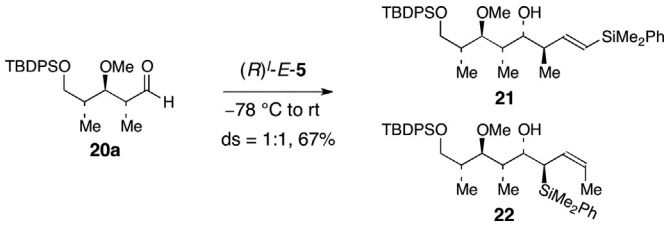
Scheme 4. Comparison of hydroboration–isomerization pathways for allenylsilanes **12** and (±)-**4**.

To evaluate the potential of crotylborane (*S*)-*E*-**5** as a reagent for organic synthesis, double asymmetric reactions[12] with several representative chiral aldehydes were studied. First, double asymmetric reactions of β-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 $(R)^{l}$-*E*-**5** [generated from allene (±)-**4** and $(^{l}Ipc)_2BH$] 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 $(R)^{l}$-*E*-**15**, which was not detected in our NMR analysis of hydroboration reaction mixtures (vide supra).



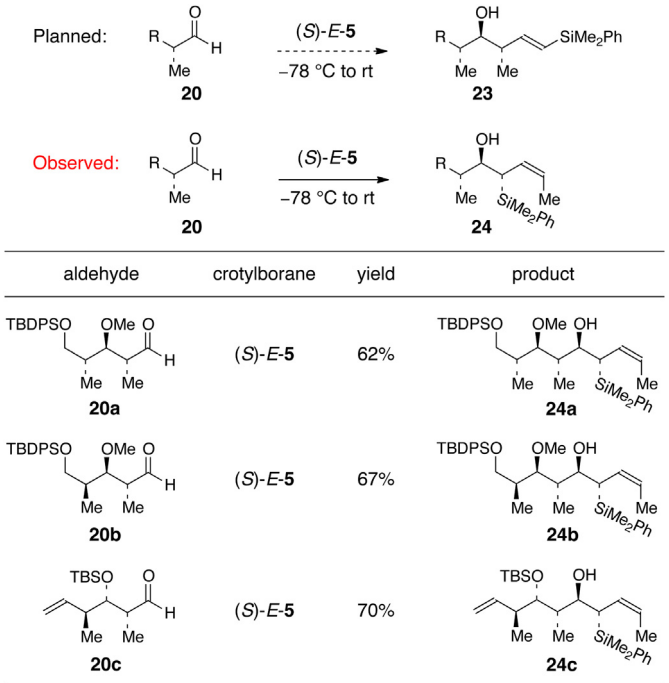
Scheme 5. Double asymmetric reactions of β-methoxylaldehyde **16** with reagents (*S*)-*E*-**5** and $(R)^{l}$-*E*-**5**.

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}-*E*-**5** provided a 1:1 mixture of the expected crotylation product **21** and the crotylsilane regioisomer **22** (Scheme 6).

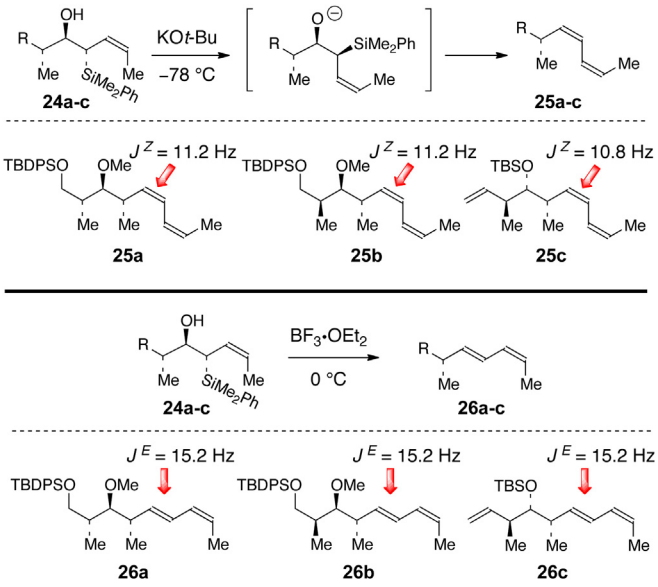


Scheme 6. Matched double asymmetric reaction of chiral aldehyde **20a** with (*R*)^{l}-*E*-**5**.

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^{Z}=10.8 Hz). The relative stereochemistry of the newly generated stereocenters in β-hydroxyl-crotylsilanes **24** was 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



Scheme 7. Mismatched double asymmetric crotylboration reactions of chiral aldehydes **20** with (*S*)-*E*-**5**. These reactions were performed by treating (±)-4 with (^{d}Ipc)$_2$BH (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 ($NaHCO_3$, H_2O_2) at 0 °C prior to product isolation.



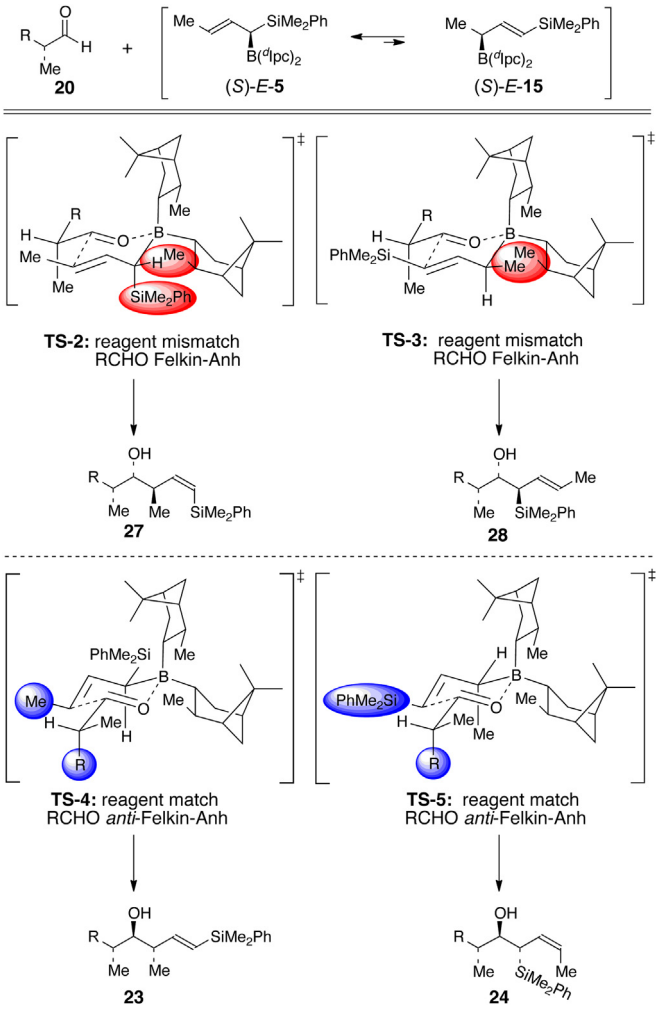
Scheme 8. Base and acid mediated Peterson elimination reactions of β-hydroxy-crotylsilanes **24**.

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 $BF_3{\cdot}OEt_2$ 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 $PhMe_2Si$– 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-boratropic shift.[16] ^{1}H 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 control[17] with (*S*)-*E*-**5** funneling to the more reactive intermediate (*S*)-*E*-**15** (with respect to aldehydes **20a**–**c**) to give the (*Z*)-*anti*-β-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 crotylborations 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}Ipc)$_2$B– 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}Ipc)$_2$B– units of reagents (*S*)-*E*-**5** and (*S*)-*E*-**15**.[13] However, the conformation of the aldehyde α-stereocenter in **TS-4** and **TS-5** is opposite to what is predicted by the Felkin–Anh model and *gauche*-pentane interactions[18] between the methyl or PhMe$_2$Si 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 PhMe$_2$Si group is in a more hindered position, adjacent to the bulky (^{d}Ipc)$_2$B– group in **TS-4**. Therefore, crotylborane (*S*)-*E*-**5** funnels to the more reactive intermediate (*S*)-*E*-**15** via a reversible 1,3-boratropic 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*-β-hydroxyl-crotylsilanes **24**.



Scheme 9. Transition state analyses of mismatched double asymmetric crotylboration of aldehydes **20** with crotylboranes (*S*)-*E*-**5** and (*S*)-*E*-**15**.

3. Conclusion

We have developed an enantioselective synthesis of (*E*)-δ-silyl-*anti*-homoallylic alcohols **6** via an enantiodivergent hydroboration–crotylboration reaction sequence that originates with the enantioselective hydroboration of allenylsilane (±)-**4** with (^{d}Ipc)$_2$BH. 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-boratropic shift, reacts with aldehydes **20** faster than (*S*)-*E*-**5** and provides (*Z*)-*anti*-β-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

4.1. 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 (^{1}H NMR) spectra were recorded on a commercial instrument at 400 MHz. Carbon-13 nuclear magnetic resonance (^{13}C NMR) spectra were recorded at 100 MHz. The proton signal for residual non-deuterated solvent (δ 7.26 for $CHCl_3$) was used as an internal reference for ^{1}H NMR spectra. For ^{13}C NMR spectra, chemical shifts are reported relative to the δ 77.36 resonance of $CHCl_3$. Coupling constants are reported in Hertz. 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 F_{254} 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 $KMnO_4$. 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.

4.2. (1*S*,2*S*,*E*)-4-(Dimethyl(phenyl)silyl)-2-methyl-1-phenylbut-3-en-1-ol (6a)

Crystalline (^{d}Ipc)$_2$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 (2 mL) was added slowly to the flask and the mixture (suspension) was cooled to −25 °C (~10 min). 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}Ipc)$_2$BH 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 $NaHCO_3$ (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 (2 mL) was added, the organic layer was separated and the aqueous layer was extracted with Et_2O (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:Et_2O=200:1 to 10:1), which provided homoallylic alcohol **6a** (57 mg, 85% yield) as a colorless oil. $[\alpha]_D^{26.8}$ −83.8° (*c* 1.15, $CHCl_3$); 85% yield; 95% ee; ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 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); ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 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 cmC^{-1}; HRMS (ESI) *m*/*z* for $C_{19}H_{24}OSiNa$ [M+Na]$^+$ calcd 319.1494, found 319.1500.

4.3. (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: $[\alpha]_D^{26.7}$ −24.3° (*c* 1.41, $CHCl_3$); 78% yield; 95% ee; ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 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); ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 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 cmC^{-1}; HRMS (ESI) *m*/*z* for $C_{21}H_{26}OSiNa$ [M+Na]$^+$ calcd 345.1651, found 345.1653.

4.4. (1*R*,2*S*,*E*)-1-Cyclohexyl-4-(dimethyl(phenyl)silyl)-2-methylbut-3-en-1-ol (6c)

A colorless oil: $[\alpha]_D^{26.6}$ −19.3° (*c* 1.86, $CHCl_3$); 71% yield; 94% ee; ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 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); ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 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 cmC^{-1}; HRMS (ESI) *m*/*z* for $C_{19}H_{30}OSiNa$ [M+Na]$^+$ calcd 325.1964, found 325.1971.

4.5. (3*R*,4*S*,*E*)-6-(Dimethyl(phenyl)silyl)-4-methyl-1-phenylhex-5-en-3-ol (6d)

A colorless oil: $[\alpha]_D^{26.4}$ −4.61° (*c* 0.97, $CHCl_3$); 89% yield; 93% ee; ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 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); ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 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 cmC^{-1}; HRMS (ESI) *m*/*z* for $C_{21}H_{28}OSiNa$ [M+Na]$^+$ calcd 347.1807, found 347.1805.

4.6. (2*S*,3*S*,*E*)-1-(Benzyloxy)-5-(dimethyl(phenyl)silyl)-3-methylpent-4-en-2-ol (6e)

A colorless oil: $[\alpha]_D^{26.7}$ −16.1° (*c* 0.91, $CHCl_3$); 75% yield; 96% ee; ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 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); ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 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 cmC^{-1}; HRMS (ESI) *m*/*z* for $C_{21}H_{28}O_2SiNa$ [M+Na]$^+$ calcd 363.1756, found 363.1755.

4.7. (3*R*,4*S*,*E*)-1-((*tert*-Butyldimethylsilyl)oxy)-6-(dimethyl(phenyl)silyl)-4-methyl-hex-5-en-3-ol (6f)

A colorless oil: $[\alpha]_D^{26.7}$ −11.5° (*c* 1.35, $CHCl_3$); 72% yield; 95% ee; ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 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, $CDCl_3$) *δ* 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 cmC^{-1}; HRMS (ESI) *m*/*z* for $C_{21}H_{38}O_2Si_2Na$ [M+Na]$^+$ calcd 401.2308, found 401.2301.

4.8. (4*S*,5*R*,6*S*,7*S*,8*S*,*Z*)-7-((*tert*-Butyldimethylsilyl)oxy)-4-(dimethyl(phenyl)silyl)-6,8-dimethyldeca-2,9-dien-5-ol (24c)

Crystalline (^{d}Ipc)$_2$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 min). Racemic allenylsilane (±)-**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}Ipc)$_2$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 (3×5 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. $[\alpha]_D^{27.1}$ −25.6° (*c* 1.78, $CHCl_3$); 70% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 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 (br s, 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, $CDCl_3$) δ 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 cmC^{-1}; HRMS (ESI) *m*/*z* for $C_{26}H_{46}O_2Si_2Na$ $[M+Na]^+$ calcd 469.2934, found 469.2941.

4.9. (4*S*,5*R*,6*S*,7*R*,8*R*,*Z*)-9-((*tert*-Butyldiphenylsilyl)oxy)-4-(dimethyl(phenyl)silyl)-7-methoxy-6,8-dimethylnon-2-en-5-ol (24a)

A colorless oil: $[\alpha]_D^{27.2}$ −15.8° (*c* 1.82, $CHCl_3$); 62% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 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, $CDCl_3$) δ 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 cmC^{-1}; HRMS (ESI) *m*/*z* for $C_{36}H_{52}O_3Si_2Na$ $[M+Na]^+$ calcd 611.3353, found 611.3361.

4.10. (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° (*c* 3.16, $CHCl_3$); 67% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 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); ^{13}C NMR (100 MHz, $CDCl_3$) δ 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 cmC^{-1}; HRMS (ESI) *m*/*z* for $C_{36}H_{52}O_3Si_2Na$ $[M+Na]^+$ calcd 611.3353, found 611.3358.

4.11. (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° (*c* 1.35, $CHCl_3$); 71% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 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); ^{13}C NMR (100 MHz, $CDCl_3$) δ 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 cmC^{-1}; HRMS (ESI) *m*/*z* for $C_{35}H_{50}O_3Si_2Na$ $[M+Na]^+$ calcd 597.3196, found 597.3194.

4.12. (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° (*c* 0.98, $CHCl_3$); 63% yield; 8:1 dr; ^{1}H NMR (400 MHz, $CDCl_3$) δ 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); ^{13}C NMR (100 MHz, $CDCl_3$) δ 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 cmC^{-1}; HRMS (ESI) *m*/*z* for $C_{35}H_{50}O_3Si_2Na$ $[M+Na]^+$ calcd 597.3196, found 597.3214.

Acknowledgements

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

References and notes

1. (a) Roush, W. R. In *Comprehensive Organic Synthesis*; Trost, B. M., Ed.; Pergamon: Oxford, UK, 1991; Vol. 2, p 1; (b) Yamamoto, Y.; Asao, N. *Chem. Rev.* **1993**, *93*, 2207; (c) Denmark, S. E.; Almstead, N. G. In *Modern Carbonyl Chemistry*; Otera, J., Ed.; Wiley-VCH: Weinheim, Germany, 2000; p 299; (d) Chemler, S. R.; Roush, W. R. In *Modern Carbonyl Chemistry*; Otera, J., Ed.; Wiley-VCH: Weinheim, Germany, 2000; p 403; (e) Denmark, S. E.; Fu, J. *Chem. Rev.* **2003**, *103*, 2763; (f) Lachance, H.; Hall, D. G. *Org. React.* **2008**, *73*, 1; (g) Yus, M.; Gonzáles-Gómez, J. C.; Foubelo, F. *Chem. Rev.* **2011**, *111*, 7774.
2. (a) Pietruszka, J.; Schone, N. *Angew. Chem., Int. Ed.* **2003**, *42*, 5638; (b) Pelz, N. F.; Woodward, A. R.; Burks, H. E.; Sieber, J. D.; Morken, J. P. *J. Am. Chem. Soc.* **2004**, *126*, 16328; (c) Sieber, J. D.; Morken, J. P. *J. Am. Chem. Soc.* **2006**, *128*, 74; (d) Ito, H.; Ito, S.; Sasaki, Y.; Matsuura, K.; Sawamura, M. *J. Am. Chem. Soc.* **2007**, *129*, 14856; (e) Peng, F.; Hall, D. G. *J. Am. Chem. Soc.* **2007**, *129*, 3070; (f) Chen, M.; Roush, W. R. *Org. Lett.* **2010**, *12*, 2706; (g) Althaus, M.; Mahmood, A.; Suarez, J. R.; Thomas, S. P.; Aggarwal, V. K. *J. Am. Chem. Soc.* **2010**, *132*, 4025; (h) Kliman, L. T.; Mlynarski, S. N.; Ferris, G. E.; Morken, J. P. *Angew. Chem., Int. Ed.* **2012**, *51*, 521; (i) Ferris, G. E.; Hong, K.; Roundtree, I. A.; Morken, J. P. *J. Am. Chem. Soc.* **2013**, *135*, 2501.
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, W. R. *J. Am. Chem. Soc.* **2011**, *133*, 5744; (b) Chen, M.; Ess, D. H.; Roush, W. R. *J. Am. Chem. Soc.* **2010**, *132*, 7881; (c) Han, J.-L.; Chen, M.; Roush, W. R. *Org. Lett.* **2012**, *14*, 3028.
5. (a) Sun, H.; Abbott, J. R.; Roush, W. R. *Org. Lett.* **2011**, *13*, 2734; (b) Yin, M.; Roush, W. R. *Tetrahedron* **2011**, *67*, 10274; (c) Chen, M.; Roush, W. R. *Org. Lett.* **2012**, *14*, 426; (d) Chen, M.; Roush, W. R. *Org. Lett.* **2012**, *14*, 1556; (e) Chen, M.; Roush, W. R. *Org. Lett.* **2012**, *14*, 1880; (f) Chen, M.; Roush, W. R. *J. Org. Chem.* **2013**, *78*, 3.
6. Chen, M.; Roush, W. R. *Org. Lett.* **2013**, *15*, 1662.
7. (a) Marshall, J. A.; Maxson, K. *J. Org. Chem.* **2000**, *65*, 630; (b) Fleming, I.; Waterson, D. *J. Chem. Soc., Perkin Trans. 1* **1984**, 1809; (c) Fleming, I.; Newton, T. W.; Roessler, F. *J. Chem. Soc., Perkin Trans. 1* **1981**, 2527.
8. (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.
9. (a) Brown, H. C.; Zweifel, G. *J. Am. Chem. Soc.* **1961**, *83*, 486; (b) Zweifel, G.; Brown, H. C. *J. Am. Chem. Soc.* **1964**, *86*, 397.
10. Chen, M.; Roush, W. R. *Org. Lett.* **2011**, *13*, 1992.

11. (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; (f) Stewart, P.; Chen, M.; Roush, W. R.; Ess, D. *Org. Lett.* **2011**, *13*, 1478.
12. Masamune, S.; Choy, W.; Petersen, J. S.; Sita, L. R. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 1.
13. Brown, H. C.; Bhat, K. S. *J. Am. Chem. Soc.* **1986**, *108*, 293.
14. (a) Hoffmann, R. W. *Angew. Chem., Int. Ed. Engl.* **1987**, *26*, 489; (b) Hoffmann, R. W.; Dahmann, G.; Andersen, M. W. *Synthesis* **1994**, 629; (c) Chemler, S. R.; Roush, W. R. *J. Org. Chem.* **1998**, *63*, 3800; (d) Chemler, S. R.; Roush, W. R. *J. Org. Chem.* **2003**, *83*, 1319; (e) Chen, M.; Roush, W. R. *J. Am. Chem. Soc.* **2012**, *134*, 3925.
15. (a) Peterson, D. J. *J. Org. Chem.* **1968**, *33*, 780; (b) Ager, D. J. *Org. React.* **1990**, *38*, 1.
16. (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) Wang, K. K.; Gu, Y. G.; Liu, C. *J. Am. Chem. Soc.* **1990**, *112*, 4424; (f) Fang, G. Y.; Aggarwal, V. K. *Angew. Chem., Int. Ed.* **2007**, *46*, 359; (g) Canales, E.; González, A. Z.; Soderquist, J. A. *Angew. Chem., Int. Ed.* **2007**, *46*, 397; (h) Kister, J.; DeBaillie, A. C.; Lira, R.; Roush, W. R. *J. Am. Chem. Soc.* **2009**, *131*, 14174; (i) Chen, M.; Handa, M.; Roush, W. R. *J. Am. Chem. Soc.* **2009**, *131*, 14602; (j) Ess, D. H.; Kister, J.; Chen, M.; Roush, W. R. *Org. Lett.* **2009**, *11*, 5538.
17. (a) Seeman, J. I. *Chem. Rev.* **1983**, *83*, 83; (b) Halpern, J. *Science* **1982**, *217*, 401; (c) Landis, C. R.; Halpern, J. *J. Am. Chem. Soc.* **1987**, *109*, 1746.
18. (a) Roush, W. R. *J. Org. Chem.* **1991**, *56*, 4151; (b) Cherest, M.; Felkin, H.; Prudent, N. *Tetrahedron Lett.* **1968**, *18*, 2199; (c) Anh, N. T.; Eisenstein, O. *Nouv. J. Chim.* **1977**, *1*, 61.
19. (a) Blumenkopf, T. A.; Overman, L. E. *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.
20. (a) Miura, K.; Hosomi, A. *Synlett* **2003**, 143; (b) Yu, C.-M.; Youn, J.; Jung, H.-K. *Bull. Korean Chem. Soc.* **2006**, *27*, 463; (c) Evans, D. A.; Aye, Y. *J. Am. Chem. Soc.* **2006**, *128*, 11034; (d) Ilardi, E. A.; Stivala, C. E.; Zakarian, A. *Org. Lett.* **2008**, *10*, 1727; (e) Nishimoto, Y.; Kajioka, M.; Saito, T.; Yasuda, M.; Baba, A. *Chem. Commun.* **2008**, 6396; (f) Bates, R. H.; Chen, M.; Roush, W. R. *Curr. Opin. Drug Discovery Dev.* **2008**, *11*, 778; (g) Aikawa, K.; Hioki, Y.-T.; Mikami, K. *J. Am. Chem. Soc.* **2009**, *131*, 13922.
21. For select reviews of Hiyama coupling: (a) Denmark, S. E.; Liu, J. H.-C. *Angew. Chem., Int. Ed.* **2010**, *49*, 2978; (b) Denmark, S. E.; Sweis, R. F. In *Metal Catalyzed Cross-coupling Reactions*, 2nd ed.; de Meijere, A., Diederich, F., Eds.; Wiley-VCH: Weinheim, Germany, 2004, Chapter 4; (c) Hiyama, T. In *Metal Catalyzed Cross-coupling Reactions*; Diederich, F., Stang, P. J., Eds.; Wiley-VCH: Weinheim, Germany, 1998, Chapter 10 and references cited therein.