Substrate-Dependent Stereospecificity in Samarium-Mediated Allylic Benzoate Reductions

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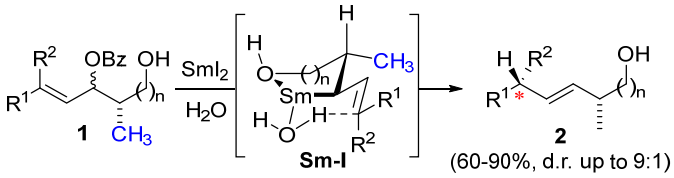
1. Abstract. A series of experiments were performed to determine if $SmI_2(H_2O)_n$ reductions of allylic benzoates was stereospecific to alkene geometry. The results indicate that for alkyl-substituted alkenes, the reaction is stereospecific (i.e. the *cis*- and *trans*-isomers select for the opposite major diastereomer). However, the introduction of a phenyl substituent causes the reaction to become non-stereospecific, both *cis*- and *trans*-isomers converging to the same major diastereomer. A potential rationale is presented based on stabilization of a proposed organosamarium intermediate by the phenyl group that allows for isomerization of alkene geometry to a sterically preferred *trans*-configuration at the transition state. The data provide further insights into the mechanism of this reaction, the nature of allylic organosamarium complexes, and the unique reactivity of benzene rings in samarium-mediated transformations.

2. Introduction.

The ability to generate stereogenic carbons with absolute control of their three-dimensional arrangement is a requirement for many compelling synthetic targets. A variety of methods have been and continue to be developed for this purpose,[1] serving not only as a testament to the often critical importance of stereochemistry to function,[2,3] but also the lack of any single solution to this important problem. Our group has been working on the development of samarium diiodide (SmI_2)-mediated allylic benzoate reductions for stereoselective asymmetric carbon atom synthesis.[4,5] For instance, treatment of compounds of type **1** with SmI_2 and water ($SmI_2(H_2O)_n$) results in the formation of products **2** featuring a newly generated carbon stereocenter (*) in high yield and diastereomeric ratios (d.r.) up to 9:1 (Scheme 1).[5] All data compiled at this stage, points to a mechanism involving formation of a chelated organosamarium intermediate (**Sm-I**), followed by intramolecular protonation by a samarium-bound water molecule. The absolute configuration of the major stereoisomer from these reactions is consistent with a model wherein the stereodirecting CH_3-group (blue, Scheme 1) gears the facial selectivity of the protonation event by assuming a sterically preferred position at the transition state.

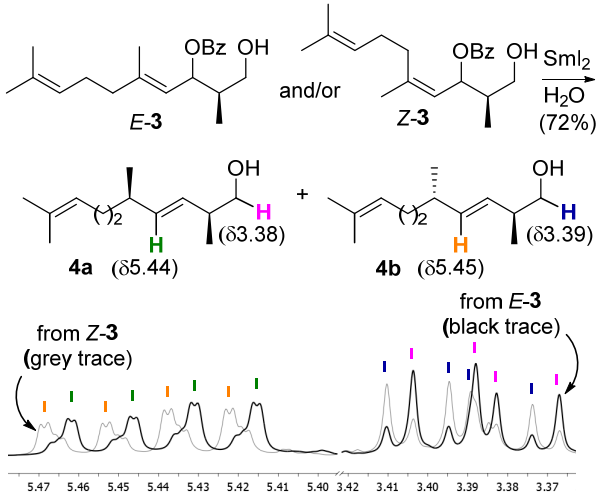
Scheme 1. Regio- and diastereoselective allylic benzoate reductions with $SmI_2(H_2O)_n$ via organosamarium intermediate **Sm-I**.



Based on this mechanism, opposite alkene configurations should lead to different major diastereomers (i.e. the reaction would be stereospecific with respect to alkene geometry). This is attractive since it would allow for access to both configurations of the newly formed stereocenter by manipulating the alkene geometry of the starting material. As an initial experiment to test for alkene stereospecificity, we reported that the reduction of *E*-**3** and *Z*-**3** with $SmI_2(H_2O)_n$ was stereospecific (i.e.

major product = **4b** from *E*-**3**, and major product = **4a** from *Z*-**3**), evidenced by opposing major/minor signals in the ^{1}H NMR spectra of the crude product mixture (Scheme 2).

Scheme 2. Results from initial alkene stereospecificity experiments with *cis*/*trans* isomers *E*-**3** and *Z*-**3**. Colored lines indicate signals for those same colored hydrogens on the structures shown in the ^{1}H NMR spectrum of the product mixture. Note that the major/minor diastereomer obtained is opposite depending on whether *E*-**3** or *Z*-**3** was used indicating that reduction of this substrate is stereospecific to alkene geometry.

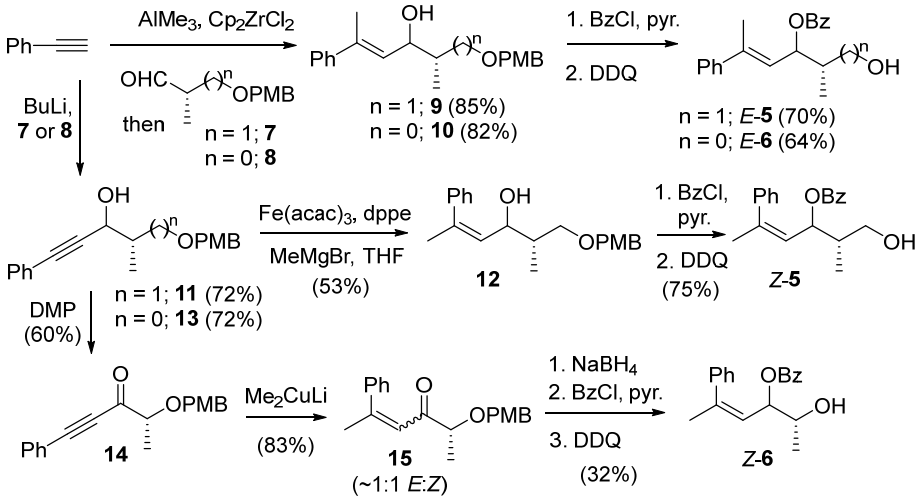


Herein we report results from additional investigations into the alkene stereospecificity of $SmI_2(H_2O)$ reductions of allylic benzoates. The results indicate that stereospecificity in these reactions is dependent on the nature of the alkene substituents. A potential rationale is provided based on both electronic and steric considerations of the proposed organosamarium intermediate.

3. Results and Discussion.

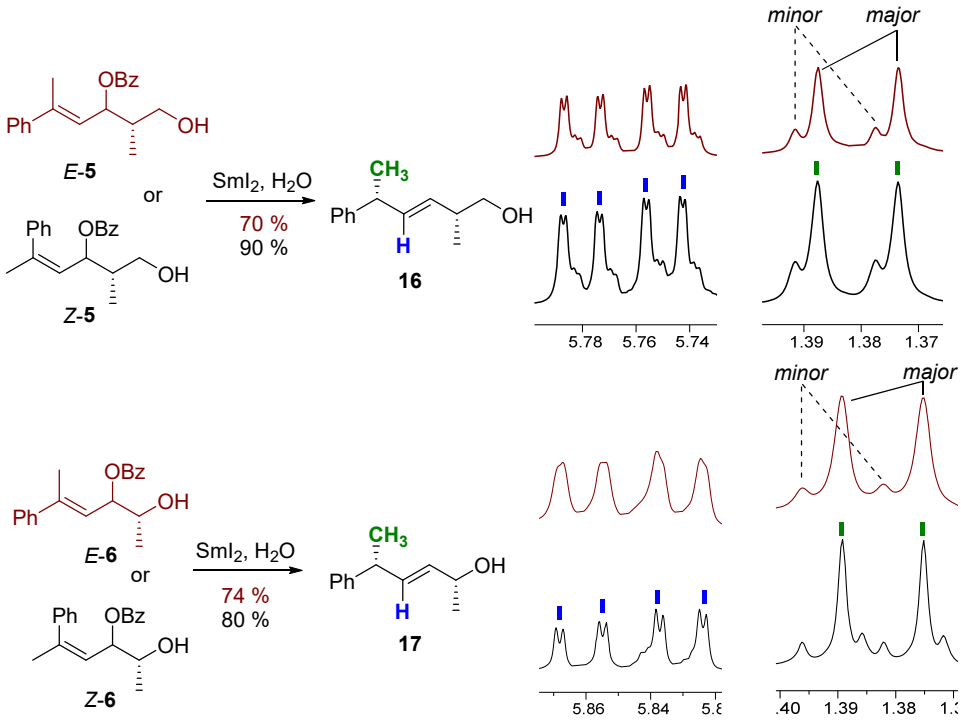
To further investigate alkene stereospecificity in these reactions, two additional sets of *cis*/*trans* isomers were synthesized. As outlined in Scheme 3, *trans*-isomers *E*-**5** and *E*-**6** were prepared as previously described[4] by zirconium-promoted carboalumination[6] of phenyl acetylene followed by addition into aldehydes (*S*)-**7**[7] and (*R*)-**8**[8] providing **9** and **10** respectively. Benzoylation of the secondary alcohol in **9** and **10** followed by removal of the PMB group with DDQ completed our synthesis of *E*-**5** and *E*-**6**. For the *cis*-isomer of compound **5** (*Z*-**5**), an iron-catalyzed carbometallation[9] was performed on propargyl alcohol **11**. Using the reported conditions (0.2 equiv. $Fe(acac)_3$, 0 °C, 7h), only trace amounts of the desired product **12** was observed, presumably due to steric deactivation by the large phenyl alkyne substituent. However, by increasing the equivalents of $Fe(acac)_3$ (1.0 equiv.) and methyl Grignard (MeMgBr) as well as longer reaction times (15 h, -20 °C), useful quantities of **12** were obtained. Benzoylation and PMB-removal then completed our synthesis of *Z*-**5**. Given the challenges encountered with the iron-carbometallation reaction, we opted for an alternative synthesis of *Z*-**6**. Instead, propargyl alcohol **13** was oxidized to the corresponding ynone **14** with Dess-Martin periodinane (DMP). Methyl cuprate addition[10] then gave a partially separable mixture of *cis*- and *trans*- enones **15**. After reduction with sodium borohydride ($NaBH_4$), benzoylation, and PMB-group removal, pure *Z*-**6** could be isolated by flash chromatography on silica.

Scheme 3. Synthesis of *cis*-/*trans*-isomers **5** and **6** for subsequent alkene stereospecificity investigations.



Samarium reductions of both isomers of compounds **5** and **6** were performed, and the crude mixtures were analyzed by NMR (Scheme 4). Somewhat surprisingly, the results revealed that reduction of these compounds was non-stereospecific to alkene geometry. More specifically, both *E*-**5** and *Z*-**5** produced compound **16** with comparable yield and identical d.r. (75:25) in favor of the (2*R*,5*R*)-isomer.[11] Similarly, *E*-**6** and *Z*-**6** converged to (2*R*,5*R*)-**17** as the major product.[11]

Scheme 4. $SmI_2(H_2O)_n$ reductions of both *cis*- and *trans*-isomers of compounds **5** and **6**. Analysis of the crude product mixtures by ^1H NMR revealed that these reactions were non-stereospecific to alkene geometry (i.e. the same major diastereomer was obtained from the *trans*-isomer (red trace) and *cis*-isomer (black trace)). Colored lines indicate signals for those same colored hydrogens on the structures shown.



One possible explanation for these results is that the organosamarium intermediate exists as a pi-allyl complex wherein bond rotation is possible.[12,13] Results from our group and others have indicated η^3-behavior for certain samarium complexes.[14-16] Reduction of *Z*-**5** or *Z*-**6** could lead initially to the formation of a chelated η^3 organosamarium intermediate **Sm-II** (Figure 1). Isomerization of these η^3 complexes to the corresponding η^1 complexes[17] **Sm-III** would allow for C-C bond rotation. Isomerization could then occur into the energetically preferred η^3 complexes **Sm-IV**. In this way, the *cis*- and *trans*-substrates converge to the same organosamarium intermediate and ultimately the same major product diastereomer.

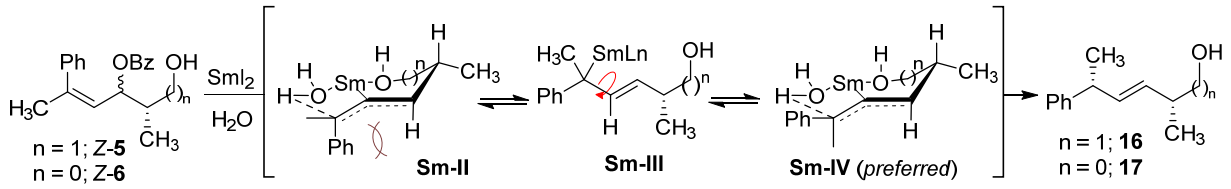
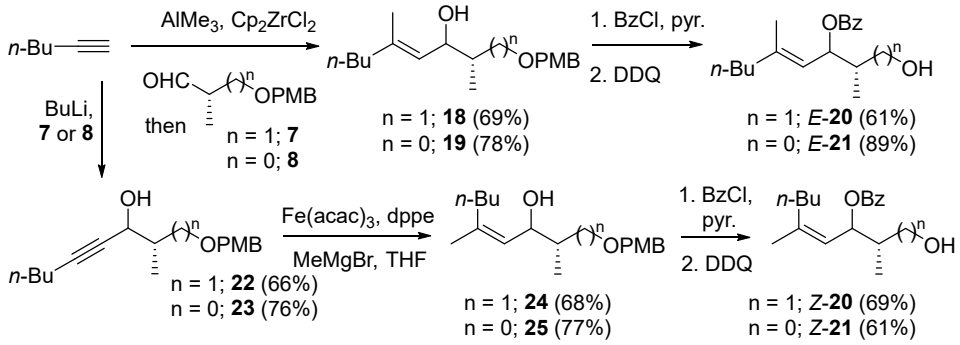


Figure 1. Possible rationale for non-stereospecific reductions of compounds **5** and **6** wherein bond rotation can occur from organosamarium intermediate **Sm-III**.

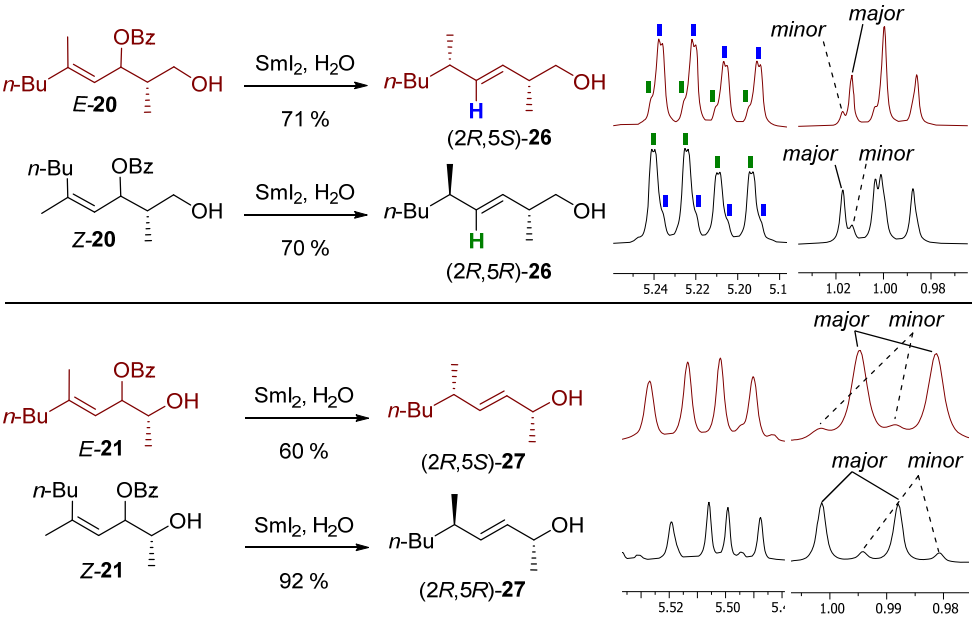
We hypothesized that if the steric difference between the two alkene substituents is small, as in compounds *E*-**3** and *Z*-**3** (*ref.* Scheme 2) perhaps there is insufficient steric preference to cause a rotation around the pi allyl intermediate thereby resulting in a stereospecific reaction. To test this theory, two additional sets of *cis/trans* isomers containing methyl and *n*-butyl alkene substituents with different chelation sizes were synthesized and tested (Scheme 5). The synthesis of the *trans* isomers was accomplished by zirconium-catalyzed carboalumination[6] of *n*-hexyne followed by addition to the corresponding aldehydes (*S*)-**7** and (*R*)-**8**. The resulting secondary alcohols **18** and **19** were acylated with benzoyl chloride and the PMB-group was removed with DDQ, affording the desired *trans* substrates *E*-**20** and *E*-**21**. The *cis* isomers were synthesized from propargyl alcohols **22** and **23**, prepared by lithiation of 1-hexyne followed by addition to aldehydes (*R*)-**7** and (*R*)-**8**. Iron-catalyzed carbometallation[9] of these substrates proceeded more readily and in higher yield (68% and 77% respectively), supporting our assumption that this chemistry is sensitive to sterically demanding alkynes. The resulting *cis*-alkene-containing secondary alcohols **24** and **25** were then benzoylated and the PMB group was removed to yield the desired *cis* substrates *Z*-**20** and *Z*-**21**.

Scheme 5. Synthesis of *cis*/*trans* isomers of compounds **20** and **21** containing sterically similar alkene substituents.



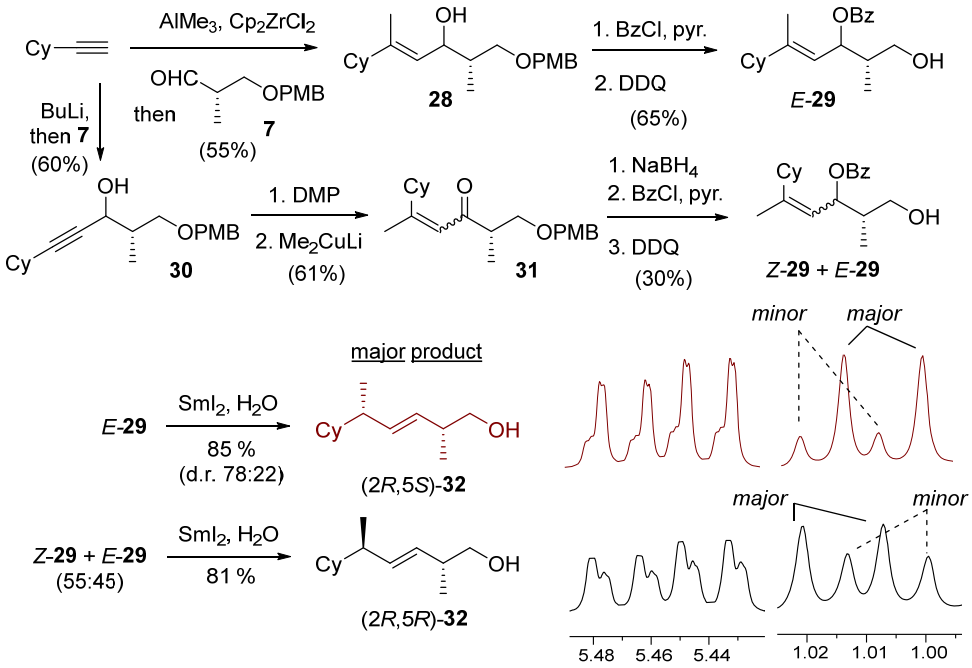
Each pair of *cis* and *trans* methyl/butyl isomers was reduced with $SmI_2(H_2O)$ and the resulting product mixtures were analyzed by NMR (Scheme 6). As predicted, these compounds containing sterically similar alkene substituents proved stereospecific with respect to alkene geometry. Compound *E*-**20** produced a mixture of alcohol **26** enriched in the (2*R*,5*S*)-stereoisomer, whereas *Z*-**20** gave primarily the (2*R*,5*R*)-diastereomer.[18] Similarly, compound *E*-**21** selected for (2*R*,5*S*)-**27**, whereas *Z*-**21** gave mostly (d.r. 7.5:1) (2*R*,5*R*)-**27**.[18]

Scheme 6. $SmI_2(H_2O)_n$ reductions of both *cis*- and *trans*-isomers of compounds **20** and **21**. Analysis of the crude product mixtures by ^1H NMR revealed that these reactions were stereospecific to alkene geometry. Colored lines indicate signals for those same colored hydrogens on the structures shown.



These results suggested that a steric mismatch of alkene substituents would in turn cause a loss in stereospecificity with respect to alkene geometry by inducing bond rotation upon formation of the initial organosamarium complex. To test this, a pair of *cis/trans* isomers was synthesized containing a large cyclohexyl group (Cy) along with a methyl alkene substituent (Scheme 7). The *trans* substrate was again prepared using a zirconium catalyzed carboalumination,[6] in this case using cyclohexyl acetylene, followed by addition to aldehyde (*S*)-**7** to form the secondary alcohol **28**. The secondary alcohol in **28** was then benzoylated and the crude product was treated with DDQ to remove the PMB group and give the cyclohexyl/methyl *trans* substrate *E*-**29** in 65% yield for the two steps. Unfortunately, attempts to synthesize the *cis*-isomer (*Z*-**29**) by iron-catalyzed carbometallation of propargyl alcohol **30** failed, again supporting the premise that this reaction is optimal for less sterically encumbered substrates. Instead, alcohol **30** was oxidized to the corresponding ketone allowing for conjugate methyl cuprate addition, giving enone **31** in 70% yield over the two steps as a ~1:1 mixture of *cis/trans* isomers. Reduction of the ketone in **31** with $NaBH_4$, benzoylation, and PMB-group removal, gave a mixture of *E*-**29** and *Z*-**29** that were partially separable by chromatography on silica gel. Contrary to our prediction, reduction of both isomers of **29** revealed that the reaction with these substrates was stereospecific with respect to alkene geometry. The reaction with pure *E*-**29** gave primarily (2*R*,5*S*)-**32** (d.r.78:22),[20] whereas a mixture enriched in *Z*-**29** clearly selected for the 5*R*-**32** diastereomer

Scheme 7. Synthesis and $SmI_2(H_2O)_n$ reductions of both *cis*- and *trans*-isomers of compound **29**. NMR analysis showed that these reactions were stereospecific to alkene geometry despite containing sterically different cyclohexyl (Cy) and methyl alkene substituents.



The only difference between compound **29** (stereospecific reaction) and **5** (non-stereospecific, *ref.* Scheme 4) is a cyclohexyl vs a phenyl group. The Flowers group has reported unique results for samarium reactions of substrates containing a phenyl group, with a change in diastereoselectivity for β-hydroxyketone reductions with a $SmI_2/H_2O/Et_3N$ mixture.[21] The authors postulated that the electron deficient Sm^{3+} was interacting with the pi system of a nearby benzene ring leading to a different major diastereomer. Evans et al. have also reported agostic interactions with *ortho* C-H bonds of benzene in certain samarium complexes.[22,23] For our particular system, these types of interactions could favor formation of the η^1 isomer **Sm-III** wherein bond rotation can occur leading to a loss in stereospecificity (Figure 2). Alternatively, it may be that **Sm-III** has a greater contribution to the overall structure of the organosamarium due to stabilization of the samarium-bound carbanion by the phenyl ring.[24] While it has yet to be determined what exactly is causing this change in alkene stereospecificity, it is clear that nearby benzene rings can impact samarium-based reactions.

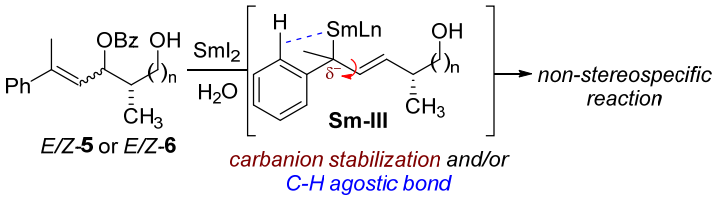
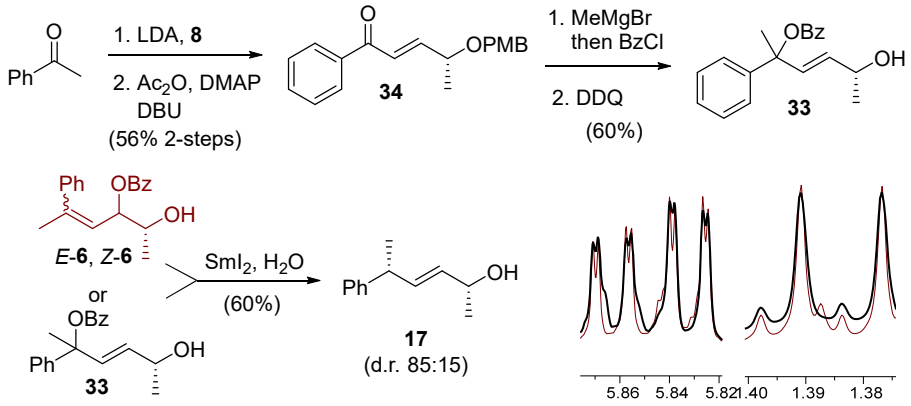


Figure 2. Possible rationale for non-stereospecific reductions of substrates containing a phenyl substituent. An agostic C-H bond and/or carbanion (δ^-) stabilization by the phenyl ring may favor formation of **Sm-III** wherein bond rotation can occur (red arrow) resulting in a non-stereospecific reaction.

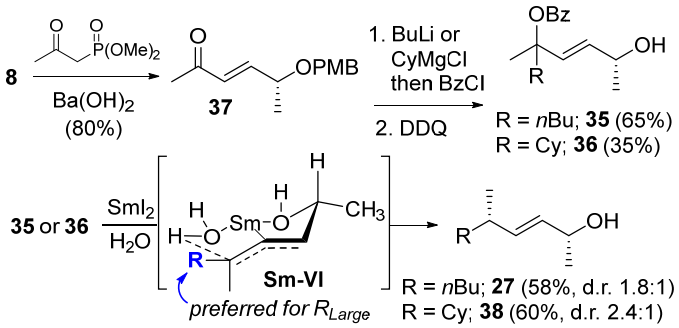
Current results show *cis*- or *trans*-phenyl substituted substrates lead to the same major product in similar yields and diastereoselectivity. It is thought that this lack of alkene stereospecificity arises from an η^3- η^1- η^3 isomerization of the organosamarium complex that allows for rotation and convergence which is promoted through stabilization by the phenyl ring. This suggested that switching the locations of the benzoyl ester and alkene in the starting material would have no effect on the outcome (e.g. diastereoselectivity) of the reaction, providing access to the same equilibrium of organosamarium intermediates (**Sm-II** – **Sm-IV**, *ref.* Figure 1).[25] To test this theory, compound **33** was synthesized starting with an aldol condensation reaction between acetophenone and aldehyde (*R*)-**8** to produce α,β-unsaturated ketone **34** (Scheme 8). Methyl Grignard addition, *in situ* acylation of the resulting alkoxide with benzoyl chloride, and deprotection of the secondary PMB-protected alcohol gave the tertiary benzoate substrate **33** in 60% overall yield. As predicted, samarium reduction of **33** gave identical results (60% yield, d.r. 85:15) to those obtained for the isomeric compounds *E*-**6** and *Z*-**6**.

Scheme 8. Synthesis and SmI_2 reduction of tertiary benzoate **33**. Treatment of **33** with $SmI_2(H_2O)_n$ produced **17** with identical results to those obtained from isomeric compounds *E*-**6** and *Z*-**6** as indicated by ^{1}H NMR (black trace = product mixture from **31**; maroon trace = product mixture from **6**).



For non-phenyl containing compounds, a tertiary allylic benzoate might "force" samarium to form an η^1 complex where rotation is possible. We reasoned this might lead to diminished diastereoselectivity, particularly for those substrates containing groups with little steric differentiation. Along these lines, compounds **35** and **36** were prepared from a common methyl enone **37** by 1,2-addition, *in situ* benzoylation, and PMB-group removal (Scheme 9). Treatment of tertiary allylic benzoates **35** and **36** with $SmI_2(H_2O)_n$ resulted in their clean conversion to the expected products **27** and **38** respectively. As predicted, the reduction of compound **35** containing sterically similar *n*-butyl and methyl groups proceeded with low diastereoselectivity, giving **27** as a 1.8:1 mixture of diastereomers (compared to 7.3:1 from **21**). Moreover, the major diastereomer obtained from **35** was the same as that obtained from *E*-**21** (i.e. (2*R*,5*S*)-**27**, *ref.* Scheme 6), consistent with our mechanistic model involving intramolecular protonation from a chelated organosamarium intermediate **Sm-VI** wherein the larger alkene substituent occupies a sterically preferred position. Slightly higher diastereoselectivity was obtained for **38** from the sterically mismatched methyl/cylohexyl substrate **36** (2.4:1), perhaps reflective of a larger preference for the cyclohexyl group to occupy the *trans*-position in intermediate **Sm-VI**. The diastereoselectivity, however, was still lower than what was observed for the phenyl substrate **33** (5.7:1), again suggestive of a unique role for phenyl substituents in these reactions.

Scheme 9. Synthesis and SmI_2 reductions of non-phenyl containing tertiary allylic benzoates **35** and **36**. Higher diastereoselectivity was observed for **38** containing sterically different cyclohexyl (Cy) and methyl groups, presumably due to a greater preference for formation of the **Sm-VI** conformer wherein this group occupies a less sterically hindered position.



4. Conclusion.

To summarize, the alkene stereospecificity of SmI_2-mediated allylic benzoate reductions is dependent on the nature of the groups attached to the alkene. The reduction of substrates containing alkyl substituents, irrespective of their size, is stereospecific. The stereochemistry of the major product from these reactions is consistent with a mechanism involving intramolecular protonation from a chelated organosamarium intermediate. When a phenyl group is introduced, however, the reaction becomes non-stereospecific (i.e. both *cis*- and *trans*-phenyl substrates converge to the same major diastereomer). This change in stereospecificity could be explained by stabilization of an η^1-samarium complex by the phenyl ring, allowing for C-C bond rotation and subsequent isomerization of alkene geometry. Results from the use of tertiary allylic benzoate substrates in these reactions to directly access the proposed η^1-organosamarium intermediate responsible for bond rotation provides some support for this conclusion. However, the higher d.r. from the phenyl-containing compound within this class of substrates points to unique reactivity of benzene rings in these reactions. Additional experiments are ongoing to better understand the phenyl effect in allylic organosamarium systems, ultimately aimed at the development of a robust and versatile method for asymmetric carbon atom synthesis.

5. Experimental Section.

5.1 General information. All reactions were carried out under N_2 in flame-dried glassware unless otherwise specified. The solvents used were dried by passing the solvent through a column of activated alumina under nitrogen immediately prior to use. Samarium(II) iodide was prepared according to the method of Procter.[26] All other reagents were purchased and used as received unless otherwise mentioned. TLC analysis used 0.25 mm silica layer fluorescence UV254 plates. Flash chromatography: silica gel (230-400 mesh). NMR: Spectra were recorded on a Varian Mercury 300 or Bruker 500 spectrometer in the solvents indicated; chemical shifts (δ) are given in ppm, coupling constants (J) in Hz. The solvent signals were used as references ($CDCl_3$: δc = 77.0 ppm; residual $CHCl_3$ in $CDCl_3$: δH = 7.26 ppm; C_6D_6: δc = 128.0 ppm; residual C_6H_6 in C_6D_6: δH = 7.16 ppm). MS (EI): Bruker MaXis Impact mass spectrometer. Spectral data listed is for a mixture of stereoisomers unless specifically labelled to the contrary.

5.2 Procedures.

General procedure for zirconium-catalyzed carboalumination: To a schlenk tube filled with dichloromethane (DCM) (0.3 M relative to alkyne) and Cp2ZrCl2 (0.1 eq) at -20 ^{o}C was added trimethyl aluminum (2.0 eq) dropwise resulting in a yellow solution which was stirred for 10 min. Deionized H2O (1.0 eq) was then added dropwise turning the solution a darker shade of yellow which was then stirred for another 10 min. The reaction was then warmed to room temperature for ten min and then cooled to 0 ^{o}C. Phenyl acetylene (1.0 eq) was added dropwise and the solution was stirred for 40 min at 0 ^{o}C. The aldehyde (0.8 eq) was then added dropwise and the mixture was stirred for 1 h at 0 ^{o}C. The reaction was quenched slowly with cold H2O and then aq. HCl, and extracted with DCM (3x). The combined organic extracts were dried over MgSO4 and concentrated *in vacuo*.

General procedure for acetylide formation and addition to aldehydes: To a Schlenk tube filled with tetrahydrofuran (THF) (0.2 M relative to alkyne) and terminal alkyne (1.0 eq) at -78 ^{o}C was added a solution of *n*-butyllithium (1.2 eq) dropwise and stirred for 30 minutes. Aldehyde (0.8 eq) was then added dropwise and stirred at -78 ^{o}C for one hour. The cold reaction mixture was poured to a seporatory flask containing saturated aq. ammonium chloride and extracted using ethyl acetate (3x). The combined organic extracts were dried over $MgSO_4$, and concentrated *in vacuo*.

General procedure for iron-catalyzed carbometalation of propargylic alcohols: Methylmagnesium bromide (25 equiv) was added dropwise to a solution of iron(III) acetylacetonate (1.0 eq), 1,2-bis(diphenylphosphino)ethane (1.0 eq), alkyne (1.0 eq) and THF (0.08 M relative to alkyne) at -78 ^{o}C. The resulting brown mixture was warmed to -20 ^{o}C and stirred for 15 h at this temperature. After cooling to –78 ^{o}C, the reaction was quenched slowly with isopropyl alcohol and then saturated aq. NH_4Cl. The mixture was extracted with ethyl acetate (3x) and the combined organic extracts were dried over $MgSO_4$ and concentrated *in vacuo*.

General Procedure for alcohol benzoylation: Pyridine (2 equiv.) was added to a schlenk tube containing substrate (1 equiv.) in DCM (0.2 M relative to substrate). The mixture was then cooled to 0 oC followed by the addition of benzoyl chloride (1.2 equiv.). The reaction was allowed to warm to rt for 15 h., before quenching with aq. NaHCO3 and extracting with DCM (3x). The combined organic extracts were dried over MgSO4 and concentrated *in vacuo*.

General procedure for DDQ removal of a PMB: Substrate was added to a round bottom containing a 50:50 mixture of DCM:pH 7 buffer (0.1 M relative to substrate). The reaction mixture was cooled to 0 oC and stirred vigorously at which time DDQ (3 equiv.) was added portion wise over 30 min. The reaction was stirred vigorously for 1 h. and then quenched with aq. NaOH (1.0 M) and extracted with DCM (3x). The combined organic extracts were washed with brine (2x), dried over MgSO4, and concentrated *in vacuo*

General procedure for $SmI_2(H_2O)_n$ reductions: To a dry schlenk tube containing a solution of SmI2 in THF (0.1 M, 7 equiv.) was added degassed nano-pure H2O (105 equiv.) turning the solution a deep red color. The solution was stirred for 5 min. before the substrate (1 equiv) was then added. After 30 min. the reaction was quenched with aq. NaHCO3 and extracted with EtOAc (3x). The combined organic extracts were dried over MgSO4, and concentrated *in vacuo*.

Compounds 4a and 4b. A mixture of *E*-**3** and *Z*-**3** (0.06 g, 0.16 mmol) was subjected to the general procedure for $SmI_2(H_2O)_n$ reductions. Purification by flash chromatography on silica (10:1 to 4:1 hexanes:ethyl acetate) gave a mixture of **4a** and **4b** (0.022 g, 72 %, R_f. = 0.53 in 4:1 Hex:EtoAc). See Scheme 2 for d.r. values.

IR (ATR) of **4a** and **4b** mixture: 3345, 3022, 2957, 2917, 2869, 2850, 1453, 1376, 1263, 1033, 970 cm^{-1}.

*Spectral data for **4a**.* ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.41 (ddd, *J* = 15.5, 7.8, 1.0 Hz, 1H), 5.21 (ddd, *J* = 15.4, 7.9, 1.0 Hz, 1H), 5.11 (tp, *J* = 7.1, 1.4 Hz, 1H), 3.47 (dd, *J* = 10.4, 5.6 Hz, 1H), 3.35 (dd, *J* = 10.5, 7.8 Hz, 1H), 2.30 (hept, *J* = 14.0, 7.1 Hz, 1H), 2.10 (p, *J* = 7.0 Hz, 1H), 1.94 (q, *J* = 7.3 Hz, 2H), 1.68 (s, 3H), 1.59 (s, 3H), 1.30 (q, *J* = 7.4 Hz, 2H), 0.99 (d, *J* = 4.2 Hz, 3H), 0.98 (d, *J* = 4.2 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 138.41, 131.28, 130.52, 124.62, 67.30, 39.77, 37.12, 36.40, 25.81, 25.71, 20.92, 17.68, 16.76.

*Spectral data for **4b**.* ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.41 (ddd, *J* = 15.5, 7.7, 1.0 Hz, 1H), 5.21 (ddd, *J* = 15.5, 7.9, 1.0 Hz, 1H), 5.09 (tp, *J* = 7.1, 5.7, 2.8, 1.4 Hz, 1H), 3.47 (dd, *J* = 10.4, 5.6 Hz, 1H), 3.36 (dd, *J* = 10.4, 7.8 Hz, 1H), 2.30 (hept, *J* = 6.6 Hz, 1H), 2.11 (p, *J* = 7.0 Hz, 1H), 1.94 (q, *J* = 7.6 Hz, 2H), 1.68 (s, 3H), 1.59 (s, 3H), 1.30 (q, *J* = 7.7 Hz, 2H), 0.99 (d, *J* = 3.5 Hz, 3H), 0.97 (d, *J* = 3.5 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 138.30, 131.32, 130.47, 124.56, 67.34, 39.73, 37.12, 36.40, 25.87, 25.71, 20.74, 17.67, 16.68.

HRMS (ESI+): Calcd for $C_{13}H_{24}ONa^+$ $[M+Na]^+$: 219.1725. Found 219.1728.

(2S,E)-1-((4-methoxybenzyl)oxy)-2-methyl-5-phenylhex-4-en-3-ol (9). Prepared according to the general procedure for zirconium catalyzed carboalumination using aldehyde **7** (0.98 g, 4.0 mmol). Purification by flash chromatography on silica (10:1 to 4:1 hexanes:ethyl acetate) gave **9** (1.31 g, 85%, R_f = 0.65 in 1:1 Hex:EtOAc) as a clear and colorless oil.

IR (ATR): 3145, 3026, 2975, 2971, 2896, 2805, 1435, 1367, 1236, 1031, 977 cm^{-1}.

Spectral data for the major diastereomer. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43 (d, *J* = 7.1 Hz, 2H), 7.34 (t, *J* = 7.3 Hz, 2H), 7.29 (t, *J* = 8.7 Hz 3H), 6.91 (d, *J* = 8.6 Hz, 2H), 5.78 (dq, *J* = 8.9, 1.4 Hz, 1H), 4.50 (d, *J* = 11.7, 1H), 4.51 (m, 1H), 4.47 (d, *J* = 11.7Hz, 1H), 3.83 (s, 3H), 3.66 (dd, *J* = 9.3, 4.3 Hz, 1H), 3.51 (dd, *J* = 9.3, 7.6 Hz, 1H), 2.12 (d, *J* = 1.4 Hz, 3H), 2.03 (qd, *J* = 7.4, 4.3 Hz, 1H). 0.93 (d, *J* = 7.1 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 159.27, 143.22, 137.42, 129.87, 129.50, 129.34, 128.15, 127.10, 125.88, 113.84, 74.49, 73.11, 73.10, 55.25, 39.34, 16.52, 13.45.

HRMS (ESI+): Calcd for $C_{21}H_{26}O_3Na^+$ $[M+Na]^+$: 349.1780. Found 349.1771.

(2*S*,*E*)-1-hydroxy-2-methyl-5-phenylhex-4-en-3-yl benzoate (*E*-5). Compound **9** (1.2 g, 3.68 mmol) was subjected to the general procedure for alcohol benzoylation. The general procedure for DDQ removal of the PMB was then performed on the crude benzoylation product obtained. Purification by flash chromatography on silica (10:1 hexanes:ethyl acetate) gave ***E*-5** (0.80 g, 70%, R_f. = 0.18 in 4:1 Hex:EtOAc) as a clear and colorless oil.

IR (ATR): 3420, 3060, 3032, 2964, 2922, 2880, 1714, 1450, 1268, 1110, 932, 711 cm^{-1}.

Spectral data for the major isomer: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.07 (dd, *J* = 8.3, 1.2 Hz, 2H), 7.57 (t, *J* = 7.4 Hz, 1H), 7.45 (t, *J* = 7.7 Hz, 2H), 7.42 (dd, *J* = 7.2, 1.3 Hz, 2H), 7.33 (t, *J* = 7.7 Hz, 2H), 7.28 (t, *J* = 7.2 Hz, 1H), 5.95 (dd, *J* = 9.4, 8.1 Hz, 1H), 5.84 (dq, *J* = 9.4, 1.4 Hz, 1H), 3.68 (qd, *J* = 11.3, 4.6 Hz, 2H), 2.23 (d, *J* = 1.4 Hz, 3H), 2.15 (m, 1H), 1.10 (d, *J* = 7.0 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 166.48, 142.73, 140.69, 133.05, 130.20, 129.67, 128.38, 128.25, 127.54, 125.96, 124.33, 73.31, 64.09, 40.55, 16.88, 12.92.

HRMS (ESI+): Calcd for $C_{20}H_{22}O_3Na^+$ $[M+Na]^+$: 333.1467. Found 333.1472.

(2*R*,*E*)-2-((4-methoxybenzyl)oxy)-5-phenylhex-4-en-3-ol (10). Prepared according to the general procedure for zirconium-catalyzed carboaluminations using aldehyde **8** (0.500 g, 2.6 mmol). Purification by flash chromatography on silica (10:1 to 4:1 hexanes:ethyl acetate) gave the corresponding **10** (0.688 g, 82%, R_f diastereomer$_\alpha$ = 0.30; R_f diastereomer$_\beta$ = 0.20 in 4:1 Hex:EtoAc) as a clear oil and partially separable mixture of diastereomers (d.r = 58:42).

IR (ATR): 3328, 3058, 3016, 2928, 1268, 1110, 932, 711 cm^{-1}.

Spectral data for diastereomer α: ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 7.40 (dd, *J* = 8.6, 1.5 Hz, 2H), 7.33 (t, *J* = 7.1 Hz, 2H), 7.30 (d, *J* = 8.7 Hz, 2H), 7.27 (t, *J* = 7.3, 1H) 6.90 (d, *J* = 8.7 Hz, 2H), 5.70 (dq, *J* = 8.9, 1.4 Hz, 1H), 4.66 (d, *J* = 11.3 Hz, 1H), 4.43 (d, *J* = 11.3 Hz 1H), 4.38 (dd, *J* = 8.9, 7.7 Hz, 1H), 3.82 (s, 3H), 3.50 (dq, *J* = 7.7, 6.2 Hz, 1H), 2.13 (d, *J* = 1.4 Hz, 3H), 1.20 (d, *J* = 6.2 Hz, 3H).

^{13}C NMR ($CDCl_3$, 126 MHz): δ = 159.32, 142.98, 139.81, 130.21, 129.48, 128.18, 127.30, 126.40, 125.88, 113.92, 78.64, 72.44, 70.91, 55.26, 16.90, 15.52.

Spectral data for diastereomer β: ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 7.40 (dd, *J* = 8.7, 1.4, 2H), 7.32 (t, *J* = 7.19 Hz, 2H), 7.29 (d, *J* = 8.6 Hz, 2H), 7.27 (t, *J* = 7.5 Hz, 1H), 6.89 (d, *J* = 8.7 Hz, 2H), 5.80 (dq, *J* = 8.4, 1.3 Hz, 1H), 4.62 (dd, *J* = 8.4, 3.6 Hz, 1H), 4.62 (d, *J* = 11.7, 1H), 4.50 (d, *J* = 11.7, 1H), 3.81 (s, 3H), 3.66 (qd, *J* = 6.4, 3.5 Hz, 1H), 2.08 (d, *J* = 1.4 Hz, 3H), 1.20 (d, *J* = 6.3 Hz, 3H).

^{13}C NMR ($CDCl_3$, 126 MHz): δ = 159.26, 143.03, 138.24, 130.57, 129.53, 129.31, 128.23, 127.26, 126.55, 125.89, 113.88, 77.19, 70.92, 70.62, 55.31, 16.56, 14.42.

HRMS (ES+): *m/z* $[335.1623]^+$ calcd for $C_{20}H_{24}O_3Na^+$ $[M+Na]^+$; found: 335.1612.

(2R,E)-2-hydroxy-5-phenylhex-4-en-3-yl benzoate (*E*-6). Compound **9** (0.371 g, 1.18 mmol) was subjected to the general procedure for alcohol benzoylation. The general procedure for DDQ removal of the PMB was then performed on the crude benzoylation product obtained. Purification by flash chromatography on silica (10:1 to 4:1 hexanes:ethyl acetate) gave ***E*-6** (0.281 g, 80% over two steps) as an oil.

IR (ATR): 3450, 3062, 3031, 2976, 2929, 1712, 1600, 1583, 1450, 1266, 1110, 1025, 963, 909, 709 cm^{-1}.

Spectral data for diastereomer α: ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 8.07 (dd, *J* = 8.3, 1.2 Hz, 2H), 7.57 (t, *J* = 7.3 Hz, 1H), 7.45 (t, *J* = 8.1 Hz, 2H), 7.41 (dd, *J* = 8.4, 1.5 Hz, 2H), 7.32 (t, *J* = 7.1 Hz, 2H), 7.27 (t, *J* = 7.3 Hz, 1H), 5.77 (m, 2H), 4.10 (p, *J* = 6.3 Hz, 1H), 2.29 (d, *J* = 1.2 Hz, 3H), 1.30 (d, *J* = 6.4 Hz, 3H).

^{13}C NMR ($CDCl_3$, 126 MHz): δ = 166.01, 142.54, 141.90, 133.09, 130.16, 129.66, 128.41, 128.27, 127.68, 125.96, 122.37, 69.74, 18.81, 17.07.

Spectral data for diastereomer β: ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 8.07 (dd, *J* = 8.3, 1.2 Hz, 2H), 7.57 (t, *J* = 7.3 Hz, 1H), 7.45 (t, *J* = 8.1 Hz, 2H), 7.43 (dd, *J* = 8.4, 1.3 Hz, 1H), 7.33 (t, *J* = 7.1 Hz, 2H), 7.28 (t, *J* = 7.3 Hz, 1H), 5.91 (dq, *J* = 9.3, 1.3 Hz, 1H), 5.85 (dd, *J* = 9.3, 4.0 Hz, 1H), 4.15 (qd, *J* = 6.5, 4.1 Hz, 1H), 2.25 (d, *J* = 1.3 Hz, 3H), 1.31 (d, *J* = 6.4 Hz, 3H).

^{13}C NMR ($CDCl_3$, 126 MHz): δ = 165.94, 142.47, 142.03, 133.06, 130.15, 129.64, 128.39, 128.25, 127.66, 125.95, 122.37, 121.60, 76.73, 75.88, 69.59, 18.19, 16.90.

HRMS (ES+): *m/z* $[319.1310]^+$ calcd for $C_{19}H_{20}O_3Na^+$ $[M+Na]^+$; found: 319.1314.

(4*R*)-4-((4-methoxybenzyl)oxy)-1-phenylpent-1-yn-3-ol (11). Prepared according to the general procedure for acetylide formation and attack of aldehyde using phenyl acetylene (0.10 mL, 1.03 mmol) and aldehyde **7** (0.150 g, 0.77 mmol). Purification by flash chromatography on silica (4:1 hexanes:ethyl acetate) gave **11** (0.165 g, 72%), as a clear yellow oil and a mixture of diastereomers (d.r = 82:18).

IR (ATR): 3350, 3026, 3013, 2967, 2931, 1610, 1538, 1405, 1267, 1101, 1052, 936, 911, 710 cm^{-1}.

Spectral data for the major of diastereomer: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47 (m, 2H), 7.33 (td, *J* = 4.7, 3.0 Hz, 5H), 6.93 (m, 2H), 4.66 (d, *J* = 11.6 Hz, 1H), 4.55 (d, *J* = 11.5 Hz, 1H), 3.83 (s, 3H), 3.78 (qd, *J* = 6.3, 3.7 Hz, 1H), 2.56 (d, *J* = 5.9 Hz, 1H), 1.37 (d, *J* = 6.3 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 159.33, 131.79, 130.21, 129.42, 128.45, 128.26, 122.59, 113.91, 87.06, 86.04, 76.63, 70.79, 65.55, 55.31, 14.77.

HRMS (ES+): *m/z* $[311.1647]^+$ calcd for $C_{20}H_{23}O_3$ $[M+H]^+$; found: 311.1639.

(4*R*)-4-((4-methoxybenzyl)oxy)-1-phenylpent-1-yn-3-ol (13). Prepared according to the general procedure for acetylide formation and attack of aldehyde using phenyl acetylene (0.10 mL, 1.03 mmol) and aldehyde **8** (0.150 g, 0.77 mmol). Purification by flash chromatography on silica (4:1 hexanes:ethyl acetate) gave **13** (0.165 g, 72%), as a clear yellow oil and a mixture of diastereomers (d.r = 82:18).

IR (ATR): 3345, 3018, 3010, 2976, 2826, 1600, 1513, 1232, 1116, 1025, 964, 921, 750 cm^{-1}.

Spectral data for the major of diastereomer: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47 (m, 2H), 7.33 (td, *J* = 4.7, 3.0 Hz, 5H), 6.93 (m, 2H), 4.66 (d, *J* = 11.6 Hz, 1H), 4.55 (d, *J* = 11.5 Hz, 1H), 3.83 (s, 3H), 3.78 (qd, *J* = 6.3, 3.7 Hz, 1H), 2.56 (d, *J* = 5.9 Hz, 1H), 1.37 (d, *J* = 6.3 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 159.33, 131.79, 130.21, 129.42, 128.45, 128.26, 122.59, 113.91, 87.06, 86.04, 76.63, 70.79, 65.55, 55.31, 14.77.

HRMS (ES+): *m/z* [319.1310]$^+$ calcd for $C_{19}H_{20}O_3Na$ [M+Na]$^+$; found: 319.1313.

(2*S*,*Z*)-1-((4-methoxybenzyl)oxy)-2-methyl-5-phenylhex-4-en-3-ol (12)

Prepared according to the general procedure for iron-catalyzed carbometalation of propargylic alcohols using propargylic alcohol **11** (0.125 g, 0.402 mmol). Purification by flash column chromatography on silica (4:1 hexanes ethyl acetate) gave **12** (0.069 g, 53 %) as a yellow oil.

IR (ATR): 3345, 3018, 3010, 2976, 2826, 1600, 1513, 1232, 1116, 1025, 964, 921, 750 cm^{-1}.

Spectral data for major diastereomer: ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.37 – 7.33 (m, 2H), 7.30 – 7.25 (m, 3H), 7.25 – 7.22 (m, 2H), 6.93 – 6.85 (m, 2H), 5.50 (dq, *J* = 9.7, 1.5 Hz, 1H), 4.43 (d, *J* = 8.3 Hz, 2H), 3.98 (dd, *J* = 9.6, 8.0 Hz, 1H), 3.82 (s, 3H), 3.53 (dd, *J* = 9.3, 4.3 Hz, 1H), 3.38 (dd, *J* = 9.3, 8.0 Hz, 1H), 2.09 (d, *J* = 1.5 Hz, 3H), 1.92 (dddd, *J* = 12.4, 7.9, 4.9, 2.7 Hz, 1H), 0.78 (d, *J* = 7.0 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ = 159.28, 141.51, 140.32, 129.86, 129.40, 129.33, 129.30, 129.26, 128.68, 128.24, 128.21, 128.18, 128.16, 127.90, 127.84, 127.18, 126.88, 126.85, 113.87, 113.83, 113.80, 74.99, 73.84, 73.04, 72.95, 55.28, 39.05, 26.08, 25.88, 13.78, 12.07.

HRMS (ES+): *m/z* [349.1174]$^+$ calcd for $C_{21}H_{26}O_3Na$ [M+Na]$^+$; found: 349.1778.

(2*S*,*Z*)-1-hydroxy-2-methyl-5-phenylhex-4-en-3-yl benzoate (*Z*-5)

Prepared according to the general benzoylation procedure using **12** (0.0693 g, 0.212 mmol). The general procedure for DDQ removal of the PMB was then performed on the crude benzoylation product obtained. Purification by flash chromatography on silica (10:1 to 4:1 hexanes:ethyl acetate) gave ***Z*-5** (0.0233 g, 35% over two steps) as an oil.

IR (ATR): 3345, 3018, 3010, 2976, 2826, 1600, 1513, 1232, 1116, 1025, 964, 921, 750 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.13 (dd, *J* = 8.4, 1.3 Hz, 2H), 8.05 (ddd, *J* = 14.0, 8.4, 1.4 Hz, 2H), 7.66 – 7.55 (m, 2H), 7.52 – 7.43 (m, 6H), 7.40 – 7.35 (m, 4H), 7.28 (m, 4H), 5.74 (d, *J* = 2.1 Hz, 2H), 5.63 (dq, *J* = 9.6, 1.4 Hz, 2H), 5.52 (dd, *J* = 9.6, 7.7 Hz, 2H), 3.49 (t, *J* = 4.6 Hz, 2H), 3.46 (dd, *J* = 11.6, 5.7 Hz, 1H), 3.39 (dd, *J* = 11.6, 8.1 Hz, 1H), 2.13 (d, *J* = 1.5 Hz, 3H), 2.13 (d, *J* = 0.7 Hz, 3H), 2.06 – 1.93 (m, 2H), 1.00 (dd, *J* = 7.0, 3.8 Hz, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ = 166.24, 143.00, 142.06, 140.93, 133.69, 133.02, 130.37, 130.19, 129.72, 129.68, 129.53, 129.01, 128.51, 128.47, 128.43, 128.39, 128.37, 128.27, 127.61, 127.49, 127.47, 127.35, 127.32, 123.85, 123.59, 74.11, 72.79, 64.49, 63.86, 41.08, 40.67, 26.20, 12.98, 11.08.

HRMS (ES+): *m/z* [333.1461]$^+$ calcd for $C_{20}H_{22}O_3Na$ [M+Na]$^+$; found: 333.1668.

(*R*)-4-((4-methoxybenzyl)oxy)-1-phenylpent-1-yn-3-one (14). To a flask containing compound **13** (0.165 g, 0.556 mmol) dissolved DCM (3 mL) at room temperature and open to air was added sodium bicarbonate (223 mg, 2.78 mmol) and Dess-Martin periodinane (353 mg, 0.834 mmol). The solution was

stirred at room temp for 1 h before quenching with aq. NaOH (1M, 15 mL) and extracting with MTBE (3 x 15 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated *in vacuo*. Purification by flash chromatography on silica (10:1 hexanes:ethyl acetate) gave **14** (0.0982 g, 60%), as an oil.

IR (ATR): 2984, 2976, 2850, 1685, 1616, 1550, 1245, 1110, 1032, 976, 921, 717 cm^{-1}.

$[\alpha]_D$ = +10.5 (*c* 0.4, $CHCl_3$)

^1H NMR (500 MHz, $CDCl_3$) δ = 7.66 – 7.56 (m, 2H), 7.52 – 7.46 (m, 1H), 7.46 – 7.38 (m, 2H), 7.38 – 7.33 (m, 2H), 6.89 (s, 2H), 4.73 (d, *J* = 11.2 Hz, 1H), 4.50 (d, *J* = 11.2 Hz, 1H), 4.14 (q, *J* = 6.9 Hz, 1H), 3.83 (s, 3H), 1.51 (d, *J* = 6.9 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ = 190.08, 159.45, 133.30, 130.98, 129.70, 129.62, 128.67, 119.86, 113.89, 94.08, 86.25, 80.61, 71.91, 55.31, 17.95.

HRMS (ES+): *m/z* $[295.1329]^+$ calcd for $C_{19}H_{19}O_3$ $[M+H]^+$; found: 295.1328.

(*R*)-2-((4-methoxybenzyl)oxy)-5-phenylhex-4-en-3-one (15)

A Schlenk tube was charged with copper (I) iodide (0.095 g, 0.50 mmol) and THF (2 mL). The solution was cooled to -30 °C and MeLi (1.6 M, 0.63 mL) was added dropwise. After stirring for 30 minutes at -30 °C the solution was cooled to -78 °C and **14** (0.0982 g, 0.334 mmol) was added dropwise turning the solution yellow. The reaction was left for 1 hour at -78 °C, quenched with saturated aq. NH_4Cl (15 mL) and extracted with DCM (3 x 15 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated *in vacuo*. Purification by flash chromatography on silica (10:1 hexanes:ethyl acetate) gave the oil **15** (0.0858 g, 83 %), as a 50:50 *cis*/*trans* mixture.

IR (ATR): 2984, 2972, 1686, 1645, 1576, 1232, 1111, 1032, 976, 921, 717 cm^{-1}.

$[\alpha]_D$ = +5.5 (*c* 0.4, $CHCl_3$)

Spectral data for mixture of cis/trans isomers. IR (ATR): 2976, 2967, 2895, 1692, 1630, 1545, 1230, 1116, 1074, 985, 910, 740 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$) δ = 7.53 (dd, *J* = 6.6, 3.0 Hz, 2H), 7.42 (q, *J* = 2.9 Hz, 3H), 7.36 (qd, *J* = 7.6, 6.4, 3.6 Hz, 3H), 7.31 – 7.25 (m, 4H), 7.23 – 7.18 (m, 2H), 6.94 – 6.86 (m, 5H), 6.56 (d, *J* = 1.8 Hz, 1H), 4.57 (d, *J* = 11.3 Hz, 1H), 4.52 (d, *J* = 11.2 Hz, 1H), 4.46 (d, *J* = 11.4 Hz, 1H), 4.35 (d, *J* = 11.3 Hz, 1H), 4.02 (q, *J* = 6.9 Hz, 1H), 3.85 (t, *J* = 7.2 Hz, 1H), 3.83 (s, 3H), 3.82 (s, 3H), 2.63 – 2.60 (m, 3H), 2.24 (d, *J* = 1.4 Hz, 3H), 1.40 (d, *J* = 6.9 Hz, 3H), 1.33 (d, *J* = 6.9 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ = 203.14, 201.41, 159.40, 156.73, 155.80, 142.52, 140.89, 129.95, 129.88, 129.66, 129.58, 129.37, 128.59, 128.14, 128.05, 126.98, 126.59, 121.22, 119.35, 113.91, 113.89, 81.42, 80.42, 71.72, 71.53, 55.31, 53.48, 29.73, 27.78, 18.65, 18.27, 17.93.

HRMS (ES+): *m/z* $[333.1467]^+$ calcd for $C_{20}H_{22}O_3Na$ $[M+Na]^+$; found: 333.1461.

(2R,Z)-2-hydroxy-5-phenylhex-4-en-3-yl benzoate (*Z*-6)

Prepared according to the general benzoylation procedure using **15** (0.060 g, 0.192 mmol). The crude product was then subjected to the general procedure for removal of a PMB group with DDQ. Purification by flash column chromatography on silica (4:1 hexanes:ethyl acetate) gave ***Z*-6** (0.0317 g, 56 % over two steps) as an oil.

IR (ATR) 3332, 2956, 2922, 2872, 2857, 1457, 1378, 1033, 969, 728 cm^{-1}.

Spectral data for major diastereomer: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.04 (dd, *J* = 8.3, 1.4 Hz, 2H), 7.57 (tt, *J* = 7.4, 1.3 Hz, 1H), 7.45 (t, *J* = 7.6 Hz, 2H), 7.36 (tt, *J* = 7.7, 1.5 Hz, 2H), 7.31 – 7.27 (m, 3H), 5.66 (dq, *J* = 9.6, 1.5 Hz, 1H), 5.42 (dd, *J* = 9.6, 3.7 Hz, 1H), 3.99 (qd, *J* = 6.4, 3.7 Hz, 1H), 2.12 (d, *J* = 1.5 Hz, 3H), 1.17 (d, *J* = 6.4 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 165.29, 144.68, 140.99, 133.16, 130.52, 129.82, 128.53, 127.66, 127.49, 122.21, 121.04, 77.36, 69.14, 26.51, 17.22.

HRMS (ES+): *m/z* $[319.1305]^+$ calcd for $C_{19}H_{20}O_3Na$ $[M+Na]^+$; found: 319.1308.

(2*R*,5*R*,*E*)-2-methyl-5-phenylhex-3-en-1-ol (16). Compounds ***E*-5** or ***Z*-5** (0.05 g, 0.16 mmol) were subjected to the general procedure for $SmI_2(H_2O)_n$ reductions. Purification by flash chromatography on silica (10:1 to 4:1 hexanes:ethyl acetate) gave **16** (27 mg, 90%; 21 mg, 70%; clear colorless oil, R_f. = 0.3 in 4:1 Hex: EtOAc) as a 76:24 mixture of diastereomers.

IR (ATR): 3360, 3083, 3061, 3025, 2961, 2925, 2871, 1950, 1876, 1803, 1716, 1601, 1492, 1415, 1373, 1272, 1029, 971, 760, 698.

Spectral data for the major isomer: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38 (t, *J*=4.7 Hz, 1H), 7.30 (t, *J*=6.9 Hz, 2H), 7.20 (d, *J* = 8.0 Hz, 2H), 5.74 (ddd, *J* = 15.5, 6.8, 1.1 Hz, 1H), 5.33 (ddd, *J* = 15.5, 7.9, 1.4 Hz, 1H), 3.47(m, 2H), 3.38 (dd, *J* =10.6, 8.1, 1H) 2.36 (hept, *J* = 7.0 Hz, 1H), 1.36 (d, *J* = 7.0 Hz, 3H), 1.01 (d, *J* = 6.9 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 146.04, 136.89, 131.00, 128.43, 127.07, 126.06, 67.35, 42.27, 39.66, 21.48, 16.60.

HRMS (ES+): Calcd for $C_{13}H_{18}O^+$ $[M]^+$: 190.1358. Found 190.1358.

(2*R*,5*R*,*E*)-5-phenylhex-3-en-2-ol (17). Compounds ***E*-6** or ***Z*-6** (0.05 g, 0.17 mmol) were subjected to the general procedure for $SmI_2(H_2O)_n$ reductions. Purification of the crude product mixture by flash chromatography on silica (4:1 hexanes:ethyl acetate) gave **17** (16 mg, 54%; 18 mg, 60%; clear colorless oil, R_f. = 0.3 in 4:1 Hex: EtOAc)) as a mixture of diastereomers (d.r. 84:16).

IR (ATR): 3462, 3062, 2956, 2929, 2871, 1714, 1600, 1578, 1450, 1315, 1266, 1111, 1068, 962, 709 cm^{-1}.

Spectral data for the major diastereomer: ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 7.30 (t, *J* = 7.6 Hz, 2H), 7.22 – 7.18 (m, 3H), 5.82 (ddd, *J* = 15.4, 6.7, 1.1 Hz, 1H), 5.56 (ddd, *J* = 15.5, 6.6, 1.4 Hz, 1H), 4.30 (p, *J* = 6.4 Hz, 1H), 3.46 (p, *J* = 7.0, 6.4 Hz, 1H), 1.36 (d, *J* = 7.0 Hz, 3H), 1.28 (d, *J* = 6.4 Hz, 3H).

^{13}C NMR ($CDCl_3$, 126 MHz): δ = 145.56, 135.41, 132.87, 128.44, 127.16, 126.16, 68.87, 41.83, 23.42, 21.17.

HRMS (ES+): *m/z* [159.1174]$^+$ calcd for $C_{12}H_{15}$ [M-OH]$^+$; found: 159.1175.

(2*S*,*E*)-1-((4-methoxybenzyl)oxy)-2,5-dimethylnon-4-en-3-ol (18). Prepared according the general zirconium-catalyzed carboalumination using 1-hexyne (0.069 mL, 0.60 mmol) and aldehyde **8** (0.100 g, 0.48 mmol). Purification by flash chromatography on silica (10:1 to 4:1 hexanes:ethyl acetate) gave **18** (0.11 g, 69%), as a colorless oil and partially separable mixture of diastereomers (d.r = 86:14).

IR (ATR): 3425, 2928, 2867, 1610, 1574, 1410, 1375, 1254, 1131, 1079, 971, 867, 710 cm^{-1}.

Spectral data for major diastereomer: ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.28 (d, *J* = 8.6 Hz, 2H), 6.90 (d, *J* = 8.5 Hz, 2H), 5.18 (dq, *J* = 9.1, 1.4 Hz, 1H), 4.48 (s, 2H), 4.30 (td, *J* = 8.4, 1.0 Hz, 1H), 3.83 (s, 3H), 3.58 (dd, *J* = 9.3, 4.5 Hz, 1H), 3.48 (dd, *J* = 9.3, 7.7 Hz, 1H), 3.16 (d, *J* = 2.5 Hz, 1H), 2.03 (p, *J* = 7.7 Hz, 2H), 1.91 (hd, *J* = 7.2, 4.4 Hz, 1H), 1.68 (d, *J* = 1.4 Hz, 3H), 1.41 (hd, *J* = 7.5, 2.2 Hz, 2H), 1.31 (h, *J* = 7.2 Hz, 2H), 0.92 (t, *J* = 7.2 Hz, 3H), 0.83 (d, *J* = 7.0 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 159.27, 139.21, 130.04, 129.32, 126.15, 113.84, 74.76, 73.06, 72.78, 55.28, 39.43, 39.27, 29.97, 22.37, 16.68, 14.00, 13.39.

HRMS (ES+): *m/z* [329.2087]$^+$ calcd for $C_{19}H_{30}O_3Na^+$ [M+Na]$^+$; found: 329.2089.

(2R,E)-2-((4-methoxybenzyl)oxy)-5-methylnon-4-en-3-ol (19). Prepared according the general zirconium-catalyzed carboalumination using 1-hexyne (0.373 mL, 3.25 mmol) and aldehyde **7** (0.500 g, 2.6 mmol). Purification by flash chromatography on silica (10:1 to 4:1 hexanes:ethyl acetate) gave **19** (0.60 g, 78%), as a colorless oil and partially separable mixture of diastereomers (d.r = 56:44).

IR (ATR): 3420, 2980, 2928, 1614, 1570, 1265, 1110, 932, 886, 711 cm^{-1}.

Spectral data for diastereomer α: ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 7.29 (d, *J* = 8.3 Hz, 2H), 6.91 (d, *J* = 8.7 Hz, 2H), 5.13 (dq, *J* = 9.0, 1.3 Hz, 1H), 4.64 (d, *J* = 11.4 Hz, 1H), 4.42 (d, *J* = 11.3 Hz, 1H) 4.21 (dd, *J* = 9.0, 8.0 Hz, 1H), 3.82 (s, 3H), 3.39 (dq, *J* = 8.0, 6.2 Hz, 1H), 2.04 (t, *J* = 7.7 Hz, 2H), 1.71 (d, *J* = 1.4 Hz, 3H), 1.42 (m, 2H), 1.31 (h, *J* = 7.3 Hz, 2H), 1.13 (d, *J* = 6.2 Hz, 3H), 0.92 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR ($CDCl_3$, 126 MHz): δ = 159.22, 141.64, 130.31, 129.37, 123.08, 113.84, 78.91, 72.09, 70.80, 55.20, 39.38, 29.79, 22.29, 16.97, 15.36, 13.92.

Spectral data for diastereomer β: ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 7.27 (d, *J* = 8.7 Hz, 2H), 6.88 (d, *J* = 8.7 Hz, 2H), 5.20 (dq, *J* = 8.5, 1.3 Hz, 1H), 4.57 (d, *J* = 11.5 Hz, 1H), 4.47 (d, *J* = 11.1 Hz, 1H) 4.46 (dd, *J* = 8.3, 3.9 Hz, 1H), 3.81 (s, 3H), 3.55 (qd, *J* = 6.4, 3.4 Hz, 1H), 2.01 (t, *J* = 7.0 Hz, 2H), 1.64 (d, *J* = 1.4 Hz, 3H), 1.39 (p, *J* = 7.5 Hz, 2H), 1.29 (m, 2H), 1.12 (d, *J* = 6.4 Hz, 3H), 0.89 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR ($CDCl_3$, 126 MHz): δ = 159.17, 140.08, 130.70, 129.20, 122.97, 113.81, 77.32, 70.50, 70.37, 55.28, 39.39, 29.91, 22.34, 16.66, 14.17, 13.97.

HRMS (ES+): *m/z* [315.1936]$^+$ calcd for $C_{18}H_{28}O_3Na^+$ [M+Na]$^+$; found: 315.1944.

(2*S*,*E*)-1-hydroxy-2,5-dimethylnon-4-en-3-yl benzoate (*E*-20). Prepared according to the general benzoylation procedure using **18** (0.058 g, 0.19 mmol). The crude product was then subjected to the general procedure for removal of a PMB group with DDQ. Purification by flash column chromatography on silica (10:1 to 4:1 hexanes:ethyl acetate) gave ***E*-20** (0.034 g, 61 % over two steps) as a colorless oil.

IR (ATR): 3467, 2978, 2929, 2871, 1600, 1578, 1450, 1315, 1266, 1111, 1068, 962, 709 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.06 (dd, *J* = 8.3, 1.4 Hz, 2H), 7.58 (tt, *J* = 7.5, 1.3 Hz, 1H), 7.46 (t, *J* = 7.8 Hz, 2H), 5.78 (dd, *J* = 9.4, 8.3 Hz, 1H), 5.29 (dq, *J* = 9.4, 1.3 Hz, 1H), 3.64 (dd, *J* = 11.4, 4.5 Hz, 1H), 3.60 (dd, *J* = 11.4, 4.5 Hz, 1H), 2.07 (tt, *J* = 7.1, 1.0 Hz, 2H), 2.02 (pt, *J* = 8.3, 7.0, 4.5 Hz, 1H), 1.80 (d, *J* = 1.3 Hz, 3H), 1.43 (dddd, *J* = 11.0, 9.3, 5.2, 2.4 Hz, 2H), 1.31 (dddd, *J* = 15.8, 14.4, 7.3, 1.8 Hz, 2H), 1.05 (d, *J* = 7.0 Hz, 3H), 0.92 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ = 166.55, 142.68, 132.96, 130.88, 129.67, 128.01, 121.31, 73.35, 64.25, 40.43, 39.41, 29.88, 22.31, 16.99, 13.96, 12.96.

HRMS (ES+): *m/z* [313.1774]$^+$ calcd for $C_{18}H_{26}O_3Na^+$ [M+Na]$^+$; found: 313.1778.

(2*R*,*E*)-2-hydroxy-5-methylnon-4-en-3-yl benzoate (*E*-21). Prepared according to the general benzoylation procedure using **19** (0.431 g, 1.3 mmol). The crude product was then subjected to the general procedure for removal of a PMB group with DDQ. Purification by flash column chromatography on silica (10:1 to 4:1 hexanes:ethyl acetate) gave ***E*-21** (0.344 g, 89 % over two steps) as an oil.

IR (ATR): 3462, 3062, 2956, 2929, 2871, 1714, 1600, 1578, 1450, 1315, 1266, 1111, 1068, 962, 709 cm-1.

^{1}H NMR (CDCl3, 500 MHz): δ = 8.05 (dd, *J* = 8.5, 1.3 Hz, 4H), 7.55 (t, *J* = 7.4 Hz, 2H), 7.44 (t, *J* = 7.7 Hz, 4H), 5.66 (dd, *J* = 9.2, 4.4 Hz, 1H), 5.57 (dd, *J* = 9.5, 7.2 Hz, 1H), 5.32 (dq, *J* = 9.2, 1.3 Hz, 1H), 5.20 (dq, *J* = 9.5, 1.3 Hz, 1H), 4.03 (qd, *J* = 6.3, 4.2 Hz, 1H), 3.97 (p, *J* = 6.6 Hz, 1H), 2.06 (t, *J* = 7.6 Hz, 2H), 2.04 (t, *J* = 7.3 Hz, 2H), 1.84 (d, *J* = 1.4 Hz, 3H), 1.81 (d, *J* = 1.4 Hz, 3H) 1.40 (m, 4H), 1.29 (p, *J* = 7.4 Hz, 4H), 1.24 (d, *J* = 6.5 Hz, 3H), 1.22 (d, *J* = 6.5 Hz, 3H), 0.89 (t, *J* = 7.3 Hz, 3H), 0.88 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (CDCl3, 126 MHz): δ = 166.05, 165.96, 144.48, 144.07, 132.97, 132.95, 130.44, 130.42, 129.64, 129.63, 128.37, 119.36, 118.42, 76.80, 75.83, 69.74, 69.54, 39.50, 39.46, 29.86, 29.80, 22.32, 22.30, 18.73, 18.12, 17.20, 17.09, 13.94.

HRMS (ES+): *m/z* [319.1310]$^+$ calcd for $C_{19}H_{20}O_3Na^+$ [M+Na]$^+$; found: 319.1314.

(2*S*)-1-((4-methoxybenzyl)oxy)-2-methylnon-4-yn-3-ol (22). Prepared according to the general procedure for acetylide formation and attack of aldehyde using 1-hexyne (0.132 mL, 1.15 mmol) and aldehyde **8** (0.200 g, 0.960 mmol). Purification by flash chromatography on silica (10:1 to 4:1

hexanes:ethyl acetate) gave **22** (0.183 g, 66%), as a clear yellow oil and a mixture of diastereomers (d.r = 72:28).

IR (ATR): 3413, 3081, 3057, 3027, 2955, 2928, 2255, 1612, 1512, 1494, 1462, 1374, 1248, 1143, 1077, 1001, 834, 807, 774, 756, 731, 695 cm^{-1}.

Spectral data for major diastereomer: ^{1}H NMR (500 MHz, CDCl3) δ 7.28 (td, *J* = 6.1, 2.6 Hz, 2H), 6.90 (dd, *J* = 8.3, 1.6 Hz, 2H), 4.49 (d, *J* = 11.3 Hz, 1H), 4.45 (d, *J* = 11.6 Hz, 1H), 4.40 (m, 1H), 3.82 (s, 3H), 3.66 (dd, *J* = 9.3, 4.5 Hz, 1H), 3.46 (dd, *J* = 9.3, 6.9 Hz, 1H), 3.06 (d, *J* = 5.0 Hz, *O*H), 2.23 (td, *J* = 7.0, 2.0 Hz, 2H), 2.05 (dqd, *J* = 13.7, 6.9, 4.4 Hz, 1H), 1.53 – 1.46 (m, 2H), 1.43 (p, *J* = 7.1 Hz, 2H), 1.04 (d, *J* = 7.0 Hz, 3H), 0.93 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 159.30, 129.93, 129.37, 113.83, 86.31, 79.00, 73.33, 73.17, 67.08, 55.28, 38.71, 30.87, 21.95, 18.42, 13.60, 12.89.

HRMS (ES+): *m/z* $[313.1780]^+$ calcd for $C_{18}H_{26}O_3Na^+$ $[M+Na]^+$; found: 313.1782.

(2R)-2-((4-methoxybenzyl)oxy)non-4-yn-3-ol (23). Prepared according to the general procedure for acetylide formation and attack of aldehyde using 1-hexyne (0.132 mL, 1.15 mmol) and aldehyde **7** (0.19 g, 0.960 mmol). Purification by flash chromatography on silica gave **23** (0.2 g, 76%), as a clear yellow oil and a mixture of diastereomers (d.r = 72:28).

Spectral data matched that previously reported by Maezaki et al.[27]

(2*S*,*Z*)-1-((4-methoxybenzyl)oxy)-2,5-dimethylnon-4-en-3-ol (24). Prepared according to the general procedure for iron-catalyzed carbometalation of propargylic alcohols using alcohol **22** (0.183 g, 0.629 mmol). Purification by flash column chromatography on silica (10:1 to 4:1 hexanes:ethyl acetate) gave **24** (0.13 g, 68 %) as a colorless oil.

IR (ATR): 3347, 3082, 3058, 3028, 2954, 2927, 2855, 1598, 1495, 1471, 1462, 1387, 1360, 1250, 1153, 1089, 1028, 1005, 833, 774, 755, 694 cm^{-1}.

Spectral data for major diastereomer. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.28 (dd, *J* = 7.3, 1.6 Hz, 2H), 6.90 (d, *J* = 8.6 Hz, 2H), 5.24 (dd, *J* = 9.1, 1.4 Hz, 1H), 4.51 – 4.43 (m, 3H), 3.83 (s, 3H), 3.51 (dd, *J* = 9.8, 6.5 Hz, 1H), 3.43 (dd, *J* = 9.1, 5.2 Hz, 1H), 2.09 (dd, *J* = 16.8, 8.3 Hz, 2H), 2.00 (tdd, *J* = 7.0, 5.2, 3.9 Hz, 1H), 1.74 (d, *J* = 1.4 Hz, 3H), 1.54 – 1.26 (m, 4H), 0.96 – 0.88 (m, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ = 159.26, 159.22, 139.75, 139.58, 130.27, 130.06, 129.36, 129.30, 129.26, 126.79, 125.48, 113.83, 113.79, 74.68, 73.44, 73.04, 72.98, 72.37, 70.62, 55.28, 39.19, 39.18, 32.04, 32.01, 30.51, 30.48, 23.59, 23.49, 22.83, 22.81, 14.05, 14.03, 13.68, 12.21.

HRMS (ES+): *m/z* $[329.2093]^+$ calcd for $C_{19}H_{30}O_3Na^+$ $[M+Na]^+$; found: 329.2097.

(2*R*,*Z*)-2-((4-methoxybenzyl)oxy)-5-methylnon-4-en-3-olol (25). Prepared according to the general procedure for iron-catalyzed carbometalation of propargylic alcohols using alcohol **23** (0.100 g, 0.362

mmol). Purification by flash column chromatography on silica (10:1 to 4:1 hexanes:ethyl acetate) gave **25** (0.082 g, 77 %) as a colorless oil.

IR (ATR): 3456, 3080, 3055, 3028, 2956, 2870, 1611, 1585, 1512, 1443, 1418, 1366, 1301, 1246, 1173, 1079, 1032, 987, 909, 819, 757, 732, 696 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$) δ 7.27 (d, *J* = 8.6 Hz, 2H), 6.88 (d, *J* = 8.6 Hz, 2H), 5.23 – 5.16 (m, 1H), 4.57 (d, *J* = 11.5 Hz, 1H), 4.47 (d, *J* = 11.7 Hz, 1H), 4.44 (dd, *J* = 8.8, 3.3 Hz, 1H), 3.80 (s, 3H), 3.52 (qd, *J* = 6.4, 3.3 Hz, 1H), 2.10 – 1.96 (m, 2H), 1.72 (d, *J* = 1.4 Hz, 3H), 1.44 – 1.35 (m, 1H), 1.34 – 1.23 (m, 3H), 1.13 (d, *J* = 6.4 Hz, 3H), 0.89 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 159.34, 140.91, 130.82, 129.37, 123.58, 113.96, 77.48, 70.62, 70.09, 55.41, 32.33, 30.63, 23.67, 22.91, 14.26, 14.17.

HRMS (ES+): *m/z* $[315.1936]^+$ calcd for $C_{18}H_{28}O_3Na^+$ $[M+Na]^+$; found: 315.1944.

(2*S*,*Z*)-1-hydroxy-2,5-dimethylnon-4-en-3-yl benzoate (*Z*-20). Prepared according to the general benzoylation procedure using **18** (0.072 g, 0.24 mmol). The crude prouct was then subjected to the general procedure for removal of a PMB group with DDQ. Purification by flash column chromatography on silica (10:1 to 4:1 hexanes:ethyl acetate) gave ***Z*-20** (0.058 g, 69 % over two steps) as a colorless oil.

IR (ATR): 3340, 3167, 2978, 2826, 1612, 1532, 1447, 1328, 1216, 1150, 1076, 985, 770 cm^{-1}.

Spectral data for major diastereomer: ^1H NMR (500 MHz, $CDCl_3$) δ = 8.06 (dt, *J* = 8.8, 1.7 Hz, 2H), 7.58 (tt, *J* = 7.4, 1.3 Hz, 1H), 7.46 (t, *J* = 7.8 Hz, 2H), 6.02 (dd, *J* = 9.1, 4.0 Hz, 1H), 5.43 (dd, *J* = 9.1, 1.8 Hz, 1H), 3.67 – 3.42 (m, 2H), 2.46 (d, *J* = 7.3 Hz, *O*H), 2.25 (ddd, *J* = 13.5, 9.4, 5.8 Hz, 1H), 2.15 (ddd, *J* = 13.3, 9.3, 5.9 Hz, 1H), 2.04 (dddd, *J* = 13.3, 8.8, 6.8, 2.9 Hz, 1H), 1.78 (d, *J* = 1.5 Hz, 3H), 1.48 – 1.26 (m, 4H), 1.02 (d, *J* = 6.9 Hz, 3H), 0.91 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 166.68, 142.37, 132.99, 130.39, 129.68, 128.38, 121.50, 71.58, 64.66, 41.11, 32.30, 30.31, 23.52, 22.77, 14.00, 11.13.

HRMS (ES+): *m/z* $[313.1774]^+$ calcd for $C_{18}H_{26}O_3Na^+$ $[M+Na]^+$; found: 313.1778.

(2*R*,*Z*)-2-hydroxy-5-methylnon-4-en-3-yl benzoate (*Z*-21). Prepared according to the general benzoylation procedure using **25** (0.10 g, 0.35 mmol). The crude product was then subjected to the general procedure for removal of a PMB group with DDQ. Purification by flash column chromatography on silica (10:1 to 4:1 hexanes:ethyl acetate) gave ***Z*-21** (0.058 g, 61 % over two steps) as a colorless oil.

IR (ATR): 3345, 3064, 2987, 2826, 1612, 1545, 1440, 1334, 1167, 1030, 976, 750 cm^{-1}.

Spectral data for the major diastereomer: ^1H NMR (500 MHz, $CDCl_3$) δ 8.05 (dt, *J* = 8.4, 1.7 Hz, 2H), 7.56 (tt, *J* = 7.2, 1.2 Hz, 1H), 7.44 (t, *J* = 7.8 Hz, 2H), 5.69 (dd, *J* = 9.5, 4.3 Hz, 1H), 5.32 (dd, *J* = 9.3, 1.5 Hz, 1H), 4.00 (qd, *J* = 6.4, 4.2 Hz, 1H), 2.30 (ddd, *J* = 13.4, 10.0, 5.3 Hz, 1H), 2.14 (ddd, *J* = 13.4, 9.7, 5.7 Hz, 1H), 1.79 (d, *J* = 1.4 Hz, 3H), 1.52 – 1.29 (m, 4H), 1.25 (d, *J* = 6.5 Hz, 3H), 0.90 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 166.02, 145.18, 133.05, 130.51, 129.73, 128.44, 119.05, 75.44, 69.65, 32.61, 30.55, 23.74, 22.91, 18.24, 14.08.

HRMS (ES+): *m/z* $[299.1618]^+$ calcd for $C_{17}H_{24}O_3Na^+$ $[M+Na]^+$; found: 299.1622.

(2*R*,5*S*,E)-2,5-dimethylnon-3-en-1-ol (2*R*,5*S*-26). Prepared according to the general procedure for $SmI_2(H_2O)_n$ reductions using ***E*-20** (0.034 g, 0.12 mmol). Purification by flash column chromatography on silica (10:1 to 4:1 hexanes:ethyl acetate) gave **2*R*,5*R*-26** (0.014 g, 71 %; colorless oil) as a 75:25 mixture of diastereomers.

IR (ATR): 3450, 2975, 2826, 1624, 1545, 1417, 1340, 1287, 1226, 1175, 1130, 1065, 970 cm^{-1}.

Spectral data for the major diastereomer: ^{1}H NMR (500 MHz, $CDCl_3$): δ = 5.43 (ddd, *J* = 15.5, 7.7, 1.1 Hz, 1H), 5.21 (ddd, *J* = 15.4, 7.9, 1.2 Hz, 1H), 3.50 (ddd, *J* = 10.4, 8.0, 5.5 Hz, 1H), 3.37 (ddd, *J* = 10.5, 7.9, 4.2 Hz, 1H), 2.32 (tddd, *J* = 7.9, 6.7, 5.5, 1.1 Hz, 1H), 2.10 (h, *J* = 6.7 Hz, 1H), 1.39 (dd, *J* = 8.1, 4.3 Hz, 1H), 1.35 – 1.21 (m, 6H), 1.00 (t, *J* = 6.8 Hz, 6H), 0.90 (t, *J* = 7.0 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 138.70, 130.21, 67.33, 39.77, 36.80, 36.77, 29.67, 22.78, 20.80, 16.68, 14.10.

HRMS (ES+): *m/z* $[171.1743]^+$ calcd for $C_{11}H_{23}O^+$ $[M+H]^+$; found: 171.1744.

(2*R*,5*R*,*E*)-2,5-dimethylnon-3-en-1-ol (2*R*,5*R*-26). Prepared according to the general procedure for $SmI_2(H_2O)_n$ reductions using ***Z*-20** (0.023 g, 0.079 mmol). Purification by flash column chromatography on silica (10:1 to 4:1 hexanes:ethyl acetate) gave **2*R*,5*R*-26** (0.010 g, 70 %; colorless oil) as a 76:24 mixture of diastereomers.

IR (ATR): 3352, 3056, 2959, 2926, 2870, 1600, 1580, 1492, 1451, 1367, 1303, 1208, 1108, 1031, 908, 732, 699 cm^{-1}.

Spectral data for the major diastereomer: ^{1}H NMR (500 MHz, $CDCl_3$) δ = 5.44 (ddd, *J* = 15.6, 7.7, 1.1 Hz, 1H), 5.22 (ddd, *J* = 15.5, 7.9, 1.1 Hz, 1H), 3.50 (ddd, *J* = 10.6, 7.5, 5.4 Hz, 1H), 3.37 (ddd, *J* = 10.5, 7.9, 3.2 Hz, 1H), 2.32 (dddd, *J* = 14.6, 7.9, 5.5, 1.2 Hz, 1H), 2.11 (hept, *J* = 6.4 Hz, 1H), 1.39 (dd, *J* = 8.0, 4.2 Hz, *O*H), 1.34 – 1.23 (m, 6H), 1.01 (d, *J* = 6.9 Hz, 3H), 0.99 (d, *J* = 6.9 Hz, 3H), 0.91 (t, *J* = 6.9 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ = 138.74, 130.19, 67.30, 39.75, 36.77, 36.76, 29.57, 22.78, 20.91, 16.75, 14.11.

HRMS (ES+): *m/z* $[193.1568]^+$ calcd for $C_{11}H_{22}ONa^+$ $[M+H]^+$; found: 193.1568.

(2*R*,5*S*,E)-5-methylnon-3-en-2-ol (2*R*,5*S*-27). Prepared according to the general procedure for $SmI_2(H_2O)_n$ reductions using ***E*-21** (0.030 g, 0.11 mmol). Purification by flash column chromatography on silica (10:1 to 4:1 hexanes:ethyl acetate) gave **2*R*,5*S*-27** (0.010 g, 60 %; colorless oil) as a 90:10 mixture of diastereomers.

IR (ATR) 3347, 2958, 2925, 2871, 2857, 1606, 1457, 1371, 1258, 1150, 1123, 1060, 969, 730 cm^{-1}.

Spectral data for the major diastereomer: ^1H NMR ($CDCl_3$, 500 MHz): δ = 5.54 (dd, *J* = 15.4, 6.9 Hz, 1H), 5.48 (dd, *J* = 15.4, 6.0 Hz, 1H) 4.28 (p, *J* = 6.3 Hz, 1H), 2.11 (p, *J* = 6.6 Hz, 1H), 1.29 (m, 6H), 1.28 (d, *J* = 6.3 Hz, 3H), 0.99 (d, *J* = 6.8 Hz, 3H), 0.90 (t, *J* = 7.0 Hz, 3H).

^{13}C NMR ($CDCl_3$, 126 MHz): δ = 136.99, 132.24, 69.03, 36.56, 36.14, 29.48, 23.49, 22.79, 20.40, 14.08.

HRMS (ES+): *m/z* $[139.1487]^+$ calcd for $C_{10}H_{19}$ [M-OH]$^+$; found: 139.1482.

(2*R*,5*R*,*E*)-5-methylnon-3-en-2-ol (2*R*,5*R*-27). Prepared according to the general procedure for $SmI_2(H_2O)_n$ reductions using ***Z*-21** (0.0109 g, 0.0398 mmol). Purification by flash column chromatography on silica (10:1 to 4:1 hexanes:ethyl acetate) gave **2*R*,5*R*-27** (0.0057 g, 92 %; colorless oil) as an 86:14 mixture of diastereomers.

IR (ATR): 3350, 2958, 2926, 1600, 1580, 1492, 1451, 1367, 1303, 1208, 1108, 1031, 908, 732, 699 cm^{-1}.

Spectral data for the major diastereomer: ^1H NMR (500 MHz, $CDCl_3$) δ 5.53 (dd, *J* = 15.4, 6.7 Hz, 1H), 5.48 (dd, *J* = 15.4, 5.8 Hz, 1H), 5.48 (dq, *J* = 5.8ff, 2.5 Hz, 1H), 2.11 (dtq, *J* = 6.7, 6.4, 3.6 Hz, 1H), 1.29 (m, 6H), 1.28 (d, *J* = 6.4, 3H), 1.00 (d, *J* = 6.7 Hz, 3H), 0.91 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 137.08, 132.29, 69.11, 36.58, 36.21, 29.50, 23.57, 22.78, 20.46, 14.10.

HRMS (ES+): *m/z* $[157.1592]^+$ calcd for $C_{10}H_{21}O$ [M+H]$^+$; found: 157.1592.

(2S,E)-5-cyclohexyl-1-((4-methoxybenzyl)oxy)-2-methylhex-4-en-3-ol (28). Prepared according to the general procedure for zirconium-catalyzed carboalumination using cyclohexyl acetylene (0.078 mL, 0.60 mmol) and aldehyde **7** (0.100 g, 0.480 mmol). Purification by flash chromatography on silica (10:1 to 4:1 hexanes:ethyl acetate) gave **28** (0.19 g, 55%) as a colorless oil.

IR (ATR): 3436, 3055, 2963, 2873, 1599, 1597, 1512, 1441, 1365, 1255, 1108, 1032, 909, 732 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$) δ = 7.30 – 7.26 (m, 2H), 6.90 (d, *J* = 8.6 Hz, 2H), 5.17 (d, *J* = 9.0 Hz, 1H), 4.48-4.40 (m, 2H), 4.31 (t, *J* = 8.3 Hz, 1H), 3.83 (s, 3H), 3.58 (dd, *J* = 9.2, 4.5 Hz, 1H), 3.47 (dd, *J* = 9.3, 7.6 Hz, 1H), 3.11 (bs, *O*H), 1.94 – 1.83 (m, 2H), 1.81 – 1.73 (m, 2H), 1.73 – 1.67 (m, 2H), 1.66 (d, *J* = 1.3 Hz, 3H), 1.28 (dddt, *J* = 19.9, 16.5, 7.5, 3.9 Hz, 3H), 1.18 (tdd, *J* = 14.3, 6.1, 2.5 Hz, 3H), 0.83 (d, *J* = 7.0 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ = 159.40, 144.17, 129.45, 124.59, 113.97, 74.85, 73.18, 72.78, 55.42, 47.51, 39.47, 32.04, 31.94, 26.84, 26.51, 15.33, 13.51.

HRMS (ES+): *m/z* $[355.2244]^+$ calcd for $C_{21}H_{32}O_3Na$ [M+Na]$^+$; found: 355.2246.

(2*S*,*E*)-5-cyclohexyl-1-hydroxy-2-methylhex-4-en-3-yl benzoate (*E*-29). Prepared according to the general benzoylation procedure using **28** (0.116 g, 0.349 mmol). The general procedure for DDQ removal of the PMB was then performed on the crude benzoylation product mixture obtained. Purification by

flash chromatography on silica (10:1 to 4:1 hexanes:ethyl acetate) gave ***E*-29** (0.074 g, 65% over two steps) as an oil.

IR (ATR): 3459, 3083, 3060, 3080, 2958, 2930, 2884, 1712, 1600, 1583, 1493, 1450, 1387, 1314, 1266, 1176, 1109, 1069, 1025, 920, 710 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$) δ = 8.06 (dd, *J* = 8.5, 1.5 Hz, 2H), 7.59 (m, 1H), 7.46 (t, *J* = 7.7 Hz, 2H), 5.79 (dd, *J* = 9.4, 8.4 Hz, 1H), 5.29 (dt, *J* = 9.4, 1.3 Hz, 1H), 3.64 (dd, *J* = 11.3, 4.4 Hz, 1H), 3.61 (d, *J* = 12.0 Hz, 1H), 2.03 (m, 1H), 1.92 (ddd, *J* = 13.7, 10.8, 2.6 Hz, 1H), 1.79 (d, *J* = 1.4 Hz, 3H), 1.76 (d, *J* = 2.6 Hz, 2H), 1.74 – 1.66 (m, 2H), 1.35 – 1.11 (m, 6H), 1.04 (d, *J* = 7.0 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ = 166.57, 132.96, 129.69, 128.37, 119.65, 73.31, 64.24, 47.43, 40.55, 31.80, 31.79, 26.62, 26.59, 26.30, 15.51, 12.96.

HRMS (ES+): *m/z* $[339.1931]^+$ calcd for $C_{20}H_{28}O_3Na$ $[M+Na]^+$; found: 339.1934.

(4S)-1-cyclohexyl-5-((4-methoxybenzyl)oxy)-4-methylpent-1-yn-3-ol (28). Prepared according to the general procedure for acetylide formation and attack of aldehyde using cyclohexyl acetylene (0.225 mg, 2.07 mmol) and aldehyde **7** (0.175 g, 2.28 mmol). Purification by flash chromatography on silica (10:1 to 4:1 hexanes:ethyl acetate) gave **28** (0.4 g, 60%), as a clear yellow oil and a mixture of diastereomers (d.r = 75:25).

IR (ATR): 3419, 2915, 2858, 1611, 1585, 1512, 1493, 1452, 1362, 1246, 1173, 1076, 908, 819, 730, 697 cm^{-1}.

Spectral data for the major diastereomer: ^1H NMR (500 MHz, $CDCl_3$): δ = 7.25 (d, *J* = 10.8 Hz, 2H), 6.87 (d, *J* = 10.6 Hz, 2H), 4.47 (d, *J* = 11.5 Hz, 1H), 4.43 (d, *J* = 11.5 Hz, 1H), 4.40 (m, 1H), 3.80 (s, 3H), 3.64 (dd, *J* = 9.3, 4.5 Hz, 1H), 3.43 (dd, *J* = 9.3, 6.8 Hz, 1H), 2.95 (d, *J* = 5.3 Hz, 1H), 2.39 (m, 1H), 2.03 (qd, *J* = 6.8, 4.6 Hz, 1H), 1.81 - 1.72 (m, 2H), 1.72 - 1.63 (m, 2H), 1.50 (m, 1H), 1.46 – 1.36 (m, 2H), 1.35 – 1.24 (m, 2H), 1.02 (d, *J* = 6.9 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 159.25, 130.09, 129.27, 113.83, 113.81, 73.45, 73.05, 66.54, 55.27, 39.63, 32.68, 29.00, 25.89, 24.83, 13.18.

HRMS (ES+): *m/z* $[317.2117]^+$ calcd for $C_{20}H_{29}O_3Na$ $[M+Na]^+$; found: 317.2119.

(*S*)-1-cyclohexyl-5-((4-methoxybenzyl)oxy)-4-methylpent-1-yn-3-one. To a flask containing compound **28** (0.36 g, 2.28 mmol) dissolved DCM (3 mL) at room temperature and open to air was added sodium bicarbonate (0.285 mg, 3.42 mmol) and Dess-Martin periodinane (0.7 g, 1.71 mmol). The solution was stirred at room temp for 1 hour before quenching with aq. NaOH (1M, 35 mL) and extracting with MTBE (3 x 35 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated *in vacuo*. Purification by flash chromatography on silica (10:1 hexanes:ethyl acetate) gave the corresponding ynone (0.22 g, 60%), as an oil.

IR (ATR): 2926, 1700, 1610, 1583, 1493, 1450, 1373, 1314, 1266, 1175, 1111, 1068, 1025, 909, 758, 733, 711 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.28 – 7.25 (m, 2H), 6.92 – 6.87 (m, 2H), 4.47 (s, 2H), 3.83 (s, 3H), 3.76 (dd, *J* = 9.3, 6.8 Hz, 1H), 3.56 (dd, *J* = 9.3, 5.7 Hz, 1H), 2.87 (h, *J* = 6.8 Hz, *O*H), 2.57 (tt, *J* = 9.1, 3.9 Hz, 1H), 1.87 – 1.80 (m, 2H), 1.76 – 1.68 (m, 2H), 1.52 (dtt, *J* = 12.2, 8.7, 3.2 Hz, 3H), 1.42 – 1.32 (m, *J* = 3.7 Hz, 3H), 1.21 (d, *J* = 7.1 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ = 190.13, 159.20, 130.22, 129.27, 113.74, 99.02, 79.69, 72.88, 71.14, 55.27, 49.06, 31.61, 29.14, 25.63, 24.63, 13.35.

HRMS (ES+): *m/z* $[315.1955]^+$ calcd for $C_{20}H_{27}O_3$ $[M+H]^+$; found: 315.1954.

(*S*)-5-cyclohexyl-1-((4-methoxybenzyl)oxy)-2-methylhex-4-en-3-one (31). A Schlenk tube was charged with copper (I) iodide (0.112 g, 0.588 mmol) and THF (2 mL). The solution was cooled to -30 °C and a 1.6M solution of MeLi in ether was added dropwise. After stirring for 30 minutes at -30 °C the solution was cooled to -78 °C and (*S*)-1-cyclohexyl-5-((4-methoxybenzyl)oxy)-4-methylpent-1-yn-3-one. (0.123 g, 0.392 mmol) was added dropwise turning the solution yellow. The reaction was left for 1 hour at -78 °C, quenched with saturated aq. NH_4Cl (15 mL) and extracted with DCM (3 x 15 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated *in vacuo*. Purification by flash chromatography on silica (10:1 hexanes:ethyl acetate) gave the oil **29** (0.079 g, 61%), as a 50:50 cis/*trans* mixture.

IR (ATR): 2978, 2926, 1702, 1620, 1538, 1495, 1430, 1372, 1175, 1110, 1032, 910, 768, 733, 711 cm^{-1}.

Spectral data for the cis isomer: ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.25 (dd, *J* = 8.7, 2.3 Hz, 2H), 6.88 (d, *J* = 8.6 Hz, 2H), 6.12 (t, *J* = 1.2 Hz, 1H), 4.47 (d, *J* = 11.7 Hz, 1H), 4.43 (d, *J* = 11.7 Hz, 1H), 3.82 (s, 3H), 3.68 (dd, *J* = 9.3, 7.3 Hz, 1H), 3.43 (ddd, *J* = 9.2, 6.1, 3.0 Hz, 1H) 2.86 (m, *J* = 6.4 Hz, 1H), 2.13 (d, *J* = 1.2 Hz, 3H), 1.98 (tt, *J* = 11.3, 3.4 Hz, 1H), 1.79 – 1.67 (m, 4H), 1.45 – 1.13 (m, 6H),1.11 (d, *J* = 7.0 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ = 203.28, 202.34, 164.95, 164.24, 159.13, 130.47, 129.33, 129.21, 122.92, 121.06, 113.80, 113.72, 72.87, 72.85, 72.09, 72.04, 55.27, 49.06, 47.56, 47.46, 40.54, 31.41, 30.95, 30.91, 26.43, 26.24, 26.22, 26.12, 21.21, 18.03, 13.97, 13.95.

HRMS (ES+): *m/z* $[331.2268]^+$ calcd for $C_{21}H_{31}O_3$ $[M+H]^+$; found: 331.2268.

(2*S*,*Z*)-5-cyclohexyl-1-hydroxy-2-methylhex-4-en-3-yl benzoate (*Z*-29). Ketone **31** (0.06 g, 0.184 mmol) was dissolved with methanol (1 mL) in an open air flask. Sodium borohydride (20 mg, 0.55 mmol) was added to the stirring mixture. The reaction was left for 1 h at room temperature, quenched with saturated aq. NH_4Cl (15 mL) and separated with ethyl acetate (3 x 5 mL). The combined organic extracts were dried over $MgSO_4$ and extracted *in vacuo*. The crude reaction mixture was then subjected to the general benzoylation procedure and subsequently the general procedure for removal of a PMB group with DDQ. Purification by flash column chromatography on silica (10:1 to 4:1 hexanes:ethyl acetate) gave ***Z*-29** as a partially separable mixture of cis/*trans* isomers (0.052 g, 42 % over three steps) as a colorless oil.

IR (ATR): 3352, 2964, 2925, 2869, 1710, 1580, 1493, 1452, 1424, 1303, 1208, 1108, 1031, 973, 840, 800, 700 cm^{-1}.

Spectral data for the major diastereomer of the cis-isomer: ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.07 (ddd, *J* = 8.5, 2.4, 1.3 Hz, 2H), 7.63 – 7.53 (m, 1H), 7.46 (t, *J* = 7.8 Hz, 2H), 6.08 (dd, *J* = 8.9, 4.2 Hz, 1H), 5.34 (dq, *J* = 9.0, 1.5 Hz, 1H), 3.52 (t, *J* = 7.9, 5.9 Hz, 1H), 3.50 (dd, *J* = 7.9, 4.6 Hz, 1H), 2.60 (tq, *J* = 11.1, 3.2 Hz, 1H), 2.43 (dd, *J* = 8.2, 5.0 Hz, 1H), 2.04 (m, 1H), 1.79 (m, 1H), 1.71 (d, *J* = 1.5 Hz, 3H), 1.72 – 1.67 (m, 1H), 1.60 – 1.49 (m, 2H), 1.41 – 1.26 (m, 4H), 1.20 – 1.12 (m, 2H), 1.02 (d, *J* = 6.9 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ = 166.62, 166.48, 147.49, 146.66, 132.97, 132.94, 130.47, 130.43, 129.67, 128.37, 121.21, 120.81, 72.26, 71.15, 64.68, 64.14, 41.16, 40.60, 40.40, 31.11, 30.99, 30.94, 26.39, 26.30, 26.14, 26.12, 19.68, 19.65, 13.24, 11.23.

HRMS (ES+): *m/z* $[339.1931]^+$ calcd for $C_{20}H_{28}O_3Na$ $[M+Na]^+$; found: 339.1936.

(2*R*,5*S*,*E*)-5-cyclohexyl-2-methylhex-3-en-1-ol (2*R*,5*S*-32). Prepared according to the general procedure for $SmI_2(H_2O)_n$ reductions using compound ***E*-29** (0.068 g, 0.214 mmol). Purification of the crude product mixture by flash chromatography on silica (10:1 to 4:1 hexanes:ethyl acetate) gave **2*R*,5*S*-32** (0.034 g, 81 %) as an oil.

IR (ATR): 3384, 3056, 2928, 1600, 1583, 1494, 1450, 1381, 1068, 1025, 907, 757, 696 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$) δ = 5.45 (ddd, *J* = 15.4, 8.3, 1.0 Hz, 1H), 5.19 (ddd, *J* = 15.4, 8.0, 1.0 Hz, 1H), 3.50 (dd, *J* = 10.0, 5.7 Hz, 1H), 3.37 (dd, *J* = 10.4, 8.0 Hz, 1H), 2.34 (pp, *J* = 6.7, 1.2 Hz, 1H), 1.96 (h, *J* = 6.8 Hz, 1H), 1.77 – 1.63 (m, 4H), 1.40 (m, 1H), 1.27 – 1.08 (m, 4H), 1.01 (d, *J* = 6.8 Hz, 3H), 0.98 (d, *J* = 6.9 Hz, 3H), 0.97 – 0.87 (m, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ = 137.09, 130.91, 67.27, 42.92, 42.41, 39.79, 30.38, 30.35, 26.53, 17.71, 16.61.

HRMS (ES+): *m/z* $[197.1900]^+$ calcd for $C_{13}H_{25}O$ $[M+H]^+$; found: 197.1901.

(2*R*,5*R*,*E*)-5-cyclohexyl-2-methylhex-3-en-1-ol (2*R*,5*R*-32). Prepared according to the general procedure for $SmI_2(H_2O)_n$ reductions using compound ***Z*-29** (0.068 g, 0.21 mmol). Purification of the crude product mixture by flash chromatography on silica (10:1 to 4:1 hexanes:ethyl acetate) gave **2*R*,5*R*-32** (0.034 g, 81 %) as an oil.

IR (ATR): 3384, 3056, 2928, 1600, 1583, 1494, 1450, 1381, 1068, 1025, 907, 757, 696 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$) δ = 5.46 (ddd, *J* = 15.3, 8.2, 0.7 Hz, 1H), 5.19 (ddd, *J* = 15.4, 8.0, 0.7 Hz, 1H), 3.50 (dt, *J* = 11.1, 6.0 Hz, 1H), 3.37 (t, *J* = 9.3 Hz, 1H), 2.33 (heptq, *J* = 6.7, 1.1 Hz, 1H), 1.96 (h, *J* = 6.9 Hz, 1H), 1.77 – 1.62 (m, 4H), 1.38 (OH, 1H), 1.28 (s, 1H), 1.22 (tq, *J* = 12.7, 3.2 Hz, 2H), 1.15 (dt, *J* = 11.3, 2.5 Hz, 2H), 1.01 (d, *J* = 6.8 Hz, 3H), 0.98 (dd, *J* = 6.8, 0.7 Hz, 3H), 0.93 (ddd, *J* = 12.0, 8.4, 4.0 Hz, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ = 137.28, 130.98, 67.33, 43.06, 42.48, 39.86, 30.42, 30.38, 26.65, 17.94, 16.79.

HRMS (ES+): *m/z* $[197.1900]^+$ calcd for $C_{13}H_{25}O$ $[M+H]^+$; found: 197.1902.

(4*R*)-3-hydroxy-4-((4-methoxybenzyl)oxy)-1-phenylpentan-1-one. To a dried Schlenk flask, dry THF (3.2 mL) and diisopropyl amine (0.203 mL, 1.45 mmol) were added under nitrogen. The mixture was cooled to -78 °C and *n*-BuLi (2.5 M, 0.463 mL) was added dropwise. The solution was then warmed to 0 °C and stirred for 10 minutes. The mixture was then cooled to -78 °C and acetophenone (0.116g, 0.965 mmol) was added dropwise. The reaction was stirred for 1 h at -78 °C before adding aldehyde **8** (0.138 g, 0.772 mmol). The mixture was stirred for another hour at -78 °C before quenching with saturated aq. NH_4Cl (15 mL) and extracting with DCM (3 x 15 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated *in vacuo*. Purification by flash chromatography on silica (10:1 to 4:1 hexanes:ethyl acetate) gave the corresponding aldol product (0.108 g, 48 %), as a ~1:1 mixture of diastereomers.

IR (ATR): 3352, 3056, 3026, 2964, 2925, 2869, 1600, 1580, 1493, 1452, 1424, 1303, 1208, 1108, 1031, 973, 840, 800, 700 cm^{-1}.

Spectral data for the major diastereomer: ^1H NMR (500 MHz, $CDCl_3$) δ = 7.95 (dt, *J* = 8.4, 1.2 Hz, 2H), 7.61 – 7.55 (m, 1H), 7.47 (td, *J* = 7.8, 7.4, 1.5 Hz, 2H), 7.30 – 7.25 (m, 2H), 6.88 (t, *J* = 8.5 Hz, 2H), 4.63 (d, *J* = 11.4 Hz, 1H), 4.41 (d, *J* = 11.4 Hz, 1H), 4.28 – 4.23 (m, 1H), 3.81 (s, 3H), 3.64 (qd, *J* = 6.3, 4.4 Hz, 1H), 3.16 (d, *J* = 5.2 Hz, 1H), 1.30 (d, *J* = 6.3 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ = 200.12, 159.26, 137.00, 133.34, 130.49, 129.49, 128.61, 128.21, 113.84, 76.05, 70.71, 70.47, 55.26, 41.14, 15.15.

HRMS (ES+): *m/z* $[337.1416]^+$ calcd for $C_{19}H_{22}O_4Na[M+Na]^+$; found: 337.1414.

(*R*,*E*)-4-((4-methoxybenzyl)oxy)-1-phenylpent-2-en-1-one (34).

To a dried flask containing THF (3.2 mL) and (4*R*)-3-hydroxy-4-((4-methoxybenzyl)oxy)-1-phenylpentan-1-one (0.0483 g, 0.159 mmol) at 0 °C, DMAP (0.175 g, 1.43 mmol) and acetic anhydride (0.150 mL, 1.59 mmol) were added. The mixture was then allowed to warm to room temperature and stirred for 40 minutes. DBU was then added at room temperature and the reaction was stirred for 1 h before quenching with brine (15 mL) and extracting with MTBE (3 x 15 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated *in vacuo*. Purification by flash chromatography on silica (10:1 hexanes:ethyl acetate) gave **34** (0.025 g, 56 %), as an oil.

IR (ATR): 2958, 2873, 1687, 1623, 1493, 1476, 1450, 1367, 1269, 1175, 1110, 1040, 910, 711 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$) δ = 7.86 (dd, *J* = 8.4, 1.4 Hz, 2H), 7.53 – 7.46 (m, 1H), 7.40 (dd, *J* = 8.3, 7.0 Hz, 2H), 7.21 (d, *J* = 8.6 Hz, 2H), 7.00 (dd, *J* = 15.6, 1.2 Hz, 1H), 6.90 (dd, *J* = 15.5, 5.6 Hz, 1H), 6.82 (d, *J* = 8.6 Hz, 2H), 4.48 (d, *J* = 11.5 Hz, 1H), 4.37 (d, *J* = 11.5 Hz, 1H), 4.20 – 4.11 (m, 1H), 3.73 (s, 3H), 1.29 (d, *J* = 6.6 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ = 190.70, 159.29, 149.65, 137.71, 132.92, 130.29, 129.29, 128.64, 128.62, 124.90, 113.91, 74.08, 70.63, 55.31, 20.83.

HRMS (ES+): *m/z* $[319.1310]^+$ calcd for $C_{19}H_{20}O_3Na[M+Na]^+$; found: 319.1310.

(5*R*,*E*)-5-hydroxy-2-phenylhex-3-en-2-yl benzoate (33)

A dried flask containing **34** (0.022 g, 0.0749 mmol) and THF (1 mL) was cooled to 0 °C and a solution of methyl magnesium bromide (3.0 M, 0.037 mL) was added dropwise. The reaction was stirred at 0 °C for 1 h before adding benzoyl chloride (0.017 mL, 0.15 mmol). The mixture was then allowed to warm to room temperature and stirred for 15 h. The reaction was quenched with saturated aq. NH_4Cl (15 mL) and extracted with DCM (3 x 15 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated *in vacuo*. The crude reaction mixture was then subjected to the general procedure for DDQ removal of PMB protecting group. Purification by flash chromatography on silica (10:1 to 4:1 hexanes:ethyl acetate) gave the oil **33** (0.017 g, 60%).

IR (ATR): 3459, 3083, 3060, 3080, 2958, 2930, 2884, 1712, 1600, 1583, 1493, 1450, 1387, 1314, 1266, 1176, 1109, 1069, 1025, 920, 710 cm^{-1}.

Spectral data for the major diastereomer: ^1H NMR (500 MHz, $CDCl_3$) δ = 8.15 – 8.11 (m, 2H), 8.10 – 8.06 (m, 2H), 7.66 – 7.60 (m, 1H), 7.60 – 7.54 (m, 1H), 7.52 – 7.42 (m, 10H), 7.37 (ddd, *J* = 8.0, 6.3, 1.2 Hz, 2H), 7.31 – 7.26 (m, 2H), 6.26 (dd, *J* = 15.7, 1.2 Hz, 2H), 5.90 (ddd, *J* = 15.8, 6.2, 1.3 Hz, 2H), 4.44 (pdd, *J* = 6.3, 2.3, 1.3 Hz, 2H), 2.05 (s, 3H), 2.04 (s, 3H), 1.35 (d, *J* = 6.4 Hz, 3H), 1.33 (d, *J* = 6.1 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ = 171.21, 164.91, 143.96, 134.36, 134.27, 133.71, 133.47, 133.40, 132.88, 132.86, 131.32, 130.29, 130.20, 129.61, 129.36, 128.71, 128.58, 128.49, 128.44, 128.38, 128.31, 127.35, 126.01, 125.19, 125.15, 124.65, 83.27, 68.46, 68.40, 26.17, 26.11, 23.31, 23.27.

HRMS (ES+): *m/z* $[314.1751]^+$ calcd for $C_{19}H_{24}O_3N$ $[M+NH_4]^+$; found: 314.1752.

(*R*,*E*)-5-((4-methoxybenzyl)oxy)hex-3-en-2-one (37). To a flask containing $Ba(OH)_2$ (0.40 g, 1.28 mmol) that had been activated by heating to 130 °C under vacuum for 2 hr. and then cooled to room temperature, was added THF (2.1 mL) and dimethyl acetylmethylphosphonate (0.085 g, 0.51 mmol) and the mixture was stirred for 1 h. Aldehyde **7** (0.083 mg, 0.43 mmol) was then added as a solution in 40:1 THF:H_2O (3.4 mL) and the reaction was stirred for 15 h. The reaction was quenched with aq. $NaHCO_3$ (15 mL) and filtered through Celite with MTBE (15 mL). The layers were separated and the organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Purification by flash chromatography on silica (10:1 hexanes:ethyl acetate) gave **37** (0.08 g, 80%) as an oil.

IR (ATR): 2978, 2923, 1695, 1515, 1493, 1476, 1450, 1367, 1269, 1175, 1110, 1040, 912, 765 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$) δ 7.25 (d, *J* = 8.6 Hz, 1H), 6.88 (d, *J* = 8.7 Hz, 1H), 6.68 (dd, *J* = 16.1, 6.2 Hz, 1H), 6.21 (dd, *J* = 16.2, 1.2 Hz, 1H), 4.48 (d, *J* = 11.4 Hz, 1H), 4.39 (d, *J* = 11.5 Hz, 1H), 4.11 (pd, *J* = 6.4, 1.3 Hz, 1H), 3.80 (s, 2H), 2.28 (s, 2H), 1.32 (d, *J* = 6.6 Hz, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 198.53, 159.26, 148.20, 130.28, 130.09, 129.25, 113.85, 73.77, 70.50, 55.26, 27.11, 20.68.

HRMS (ES+): *m/z* $[257.1154]^+$ calcd for $C_{14}H_{18}O_3Na$ $[M+Na]^+$; found: 257.1155.

(2R,E)-2-hydroxy-5-methylnon-3-en-5-yl benzoate (35). To a solution of **37** (0.11 g, 0.50 mmol) in THF (2.5 mL) at – 78 °C was added *n*-BuLi (2.5 M, 0.24 mL) and the mixture was stirred for 1 h. Benzoyl chloride (0.12 mL, 0.10 mmol) was then added and the reaction was allowed to slowly warm to room

temperature and stirred for 15 h. The reaction was quenched with aq. NH_4Cl (25 mL) and extracted with MTBE (2 x 25 mL). The combined organic extracts were dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The crude product was the subjected to the general procedure for removal of a PMB. Purification by flash chromatography on silica (10:1 to 4:1 hexanes:ethyl acetate) the gave **35** (0.09 g, 65%) as a ~1:1 mixture of diastereomers.

IR (ATR) 3400, 3059, 3031, 2931, 2876, 1712, 1600, 1583, 1493, 1450, 1380, 1314, 1266, 1175, 1107, 1068, 1025, 908, 731 cm^{-1}.

^1H NMR (500 MHz, C_6D_6) δ 8.19 (m, 4H), 7.14 – 7.04 (m, 6H), 5.94 (dd, *J* = 15.7, 1.3 Hz, 1H), 5.93 (dd, *J* = 15.9, 1.0 Hz, 1H), 5.73 (dd, *J* = 15.9, 3.7 Hz, 1H), 5.71 (dd, *J* = 15.9, 4.5 Hz, 1H), 4.08 (m, 2H), 2.08 – 1.84 (m, 4H), 1.63 (s, 6H), 1.40 – 1.20 (m, 8H), 1.13 (d, *J* = 7.0 Hz, 3H), 1.12 (d, *J* = 7.0 Hz, 3H), 0.84 (t, *J* = 7.2 Hz, 6H).

^{13}C NMR (126 MHz, C_6D_6) δ 165.12, 165.09, 133.96, 133.91, 133.37, 133.29, 132.60, 132.59, 129.78, 83.25, 83.21, 68.20, 68.13, 40.33, 40.18, 33.79, 32.30, 30.14, 30.08, 30.00, 29.82, 29.79, 29.59, 29.30, 26.23, 24.98, 24.38, 24.24, 23.61, 23.26, 23.08, 14.33, 14.17.

HRMS (ES+): *m/z* $[277.1804]^+$ calcd for $C_{17}H_{26}O_3$ $[M+H]^+$; found: 277.1805.

(5*R*,*E*)-2-cyclohexyl-5-hydroxyhex-3-en-2-yl benzoate (36). To a solution of **37** (0.057 g, 0.25 mmol) in THF (2.5 mL) at – 78 °C was added CyMgCl (1.0 M, 0.50 mL) and the mixture was stirred for 20 min before warming to 0 °C for 1 h. Benzoyl chloride (0.06 mL, 0.50 mmol) was then added and the reaction was allowed to slowly warm to room temperature and stirred for 24 h. The reaction was quenched with aq. NH_4Cl (15 mL) and extracted with MTBE (2 x 15 mL). The combined organic extracts were dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The crude product was the subjected to the general procedure for removal of a PMB. Purification by flash chromatography on silica (10:1 to 4:1 hexanes:ethyl acetate) the gave **36** (0.026 g, 35%) as a ~1:1 mixture of diastereomers.

IR (ATR) 3405, 2931, 2887, 1710, 1605, 1581, 1490, 1454, 1387, 1311, 1267, 1172, 1107, 1068, 1025, 908, 731 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$) δ 7.99 (m, 4H), 7.54 (m, 2H), 7.43 (m, 4H), 5.90 (dd, *J* = 15.9, 6.4 Hz, 2H), 5.70 (dd, *J* = 15.1, 6.1 Hz, 1H), 5.68 (dd, *J* = 16.0, 5.7 Hz, 1H), 4.38 (m, 2H), 1.95 (m, 2H), 1.90 – 1.65 (m, 8H), 1.65 (s, 6H), 1.31 (d, *J* = 6.4 Hz, 3H), 1.30 (d, *J* = 6.2 Hz, 3H), 1.28 – 1.20 (m, 8H), 1.19 – 1.00 (m, 4H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 165.26, 165.19, 133.90, 132.61, 132.57, 132.29, 131.82, 131.79, 129.44, 128.30, 85.84, 85.77, 68.66, 68.54, 47.07, 27.39, 27.33, 27.29, 26.54, 26.52, 23.43, 23.38, 20.57, 20.46.

HRMS (ES+): *m/z* $[325.1780]^+$ calcd for $C_{19}H_{26}O_3Na$ $[M+Na]^+$; found: 325.1786.

(2*R*,5*S*,*E*)-5-cyclohexylhex-3-en-2-ol (38). Prepared according to the general procedure for $SmI_2(H_2O)_n$ reductions using compound **36** (0.026 g, 0.08 mmol). Purification of the crude product mixture by flash chromatography on silica (10:1 to 4:1 hexanes:ethyl acetate) gave **38** (0.094 g, 60%; clear oil) as a 2.4:1 mixture of diastereomers.

IR (ATR): 3347, 2958, 2925, 2871, 2857, 1606, 1457, 1371, 1258, 1150, 1123, 1060, 969, 730 cm^{-1}.

Spectral data for the major diastereomer: ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.53 (dd, *J* = 15.6, 8.7 Hz, 1H), 5.44 (dd, *J* = 15.6, 6.5 Hz, 1H), 4.27 (m, 1H), 3.20 (bs, *O*H), 2.39 (m, 1H), 1.76 – 1.60 (m, 6H), 1.59 – 1.44 (m, 5H), 1.26 (d, *J* = 7.2 Hz, 3H), 0.95 (d, *J* = 6.9 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 135.61, 133.08, 69.13, 43.00, 41.84, 30.42, 30.25, 26.99, 26.67, 26.64, 23.56, 17.35.

HRMS (ES+): *m/z* $[165.1638]^+$ calcd for $C_{12}H_{21}$ $[M\text{-}OH]^+$; found: 165.1639.

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$CHCl_3$); from ***Z*-20** $[\alpha]_D$ = +7.6 (*c* 0.8, $CHCl_3$); from ***E*-21** $[\alpha]_D$ = –12.2 (*c* 1.0, $CHCl_3$); from ***Z*-21** $[\alpha]_D$ = +10.2 (*c* 0.6, $CHCl_3$).

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