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Diastereoselective Synthesis of Highly Substituted Tetrahydrofurans by Pd-Catalyzed Tandem Oxidative Cyclization–Redox Relay Reactions Controlled by Intramolecular Hydrogen Bonding

Joshua L. Brooks,[†] Liping Xu,[§,∥] Olaf Wiest,[∥,⊥] and Derek S. Tan*[,†,‡]

[†]Chemical Biology Program and [‡]Tri-Institutional Research Program, Memorial Sloan Kettering Cancer Center, 1275 York Avenue, Box 422, New York, New York 10065, United States

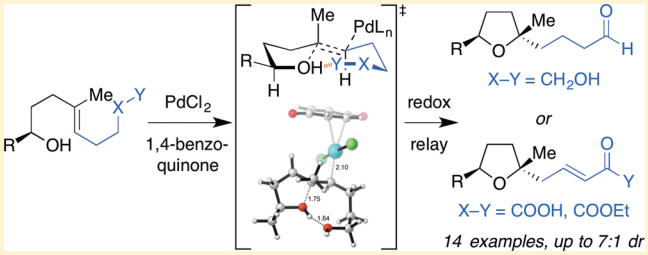
[§]School of Chemical Engineering, Shandong University of Technology, Zibo 255049, China

[∥]Lab of Computational Chemistry and Drug Design, Laboratory of Chemical Genomics, Peking University Shenzhen Graduate School, Shenzhen 518055, China

[⊥]Department of Chemistry and Biochemistry, University of Notre Dame, Notre Dame, Indiana 46556, United States

Supporting Information

ABSTRACT: Palladium-catalyzed oxidative cyclization of alkenols provides a convenient entry into cyclic ethers but typically proceeds with little or no diastereoselectivity for cyclization of trisubstituted olefins to form tetrahydrofurans due to the similar energies of competing 5-membered transition-state conformations. Herein, a new variant of this reaction has been developed in which a $PdCl_2$/1,4-benzoquinone catalyst system coupled with introduction of a hydrogen-bond acceptor in the substrate enhances both diastereoselectivity and reactivity. Cyclization occurs with 5-*exo* Markovnikov regioselectivity. Mechanistic and computational studies support an *anti*-oxypalladation pathway in which intramolecular hydrogen bonding increases the nucleophilicity of the alcohol and enforces conformational constraints that enhance diastereoselectivity. The cyclization is followed by a tandem redox-relay process that provides versatile side-chain functionalities for further derivatization.



INTRODUCTION

Highly substituted tetrahydrofurans are found in myriad natural products with diverse biological activities (Figure 1).[1] Among these are the macrocyclic norcembrenoids,[2] isolated from *Sinularia* soft corals and exemplified by the first identified family member, norcembrenolide (5-episinuleptolide),[2a,b] which inhibits production of the proinflammatory cytokine tumor necrosis factor-α.[2i] The plakortin family of polyketides,[3] isolated from *Plakortis* marine sponges, includes plakortone D,[3a] an activator of a Ca^{2+}-pumping ATPase involved in proper cardiac relaxation, and plakortether A,[3e] which exhibits selective cytotoxicity against a macrophage-like cell line. Other examples include squalene-derived polyethers such as venustratriol,[4] an antiviral natural product isolated from *Laurencia* red algae, and aplysqualenol A,[5] a potent antitumor and antiviral agent isolated from the *Laurencia*-consuming Caribbean sea slug *Aplysia dactylomela*.

A variety of methods have been developed for the synthesis of THFs.[6] Intramolecular oxypalladation of alkenols,[7,8] pioneered by Hosokawa and co-workers,[9] is a particularly powerful method for the construction of such oxygen heterocycles. Semmelhack later demonstrated that the resulting palladium–alkyl intermediate can be trapped with carbon monoxide in methanol to provide ester products (Figure 2).[10] Indeed, plakortone natural products have been synthesized using this approach

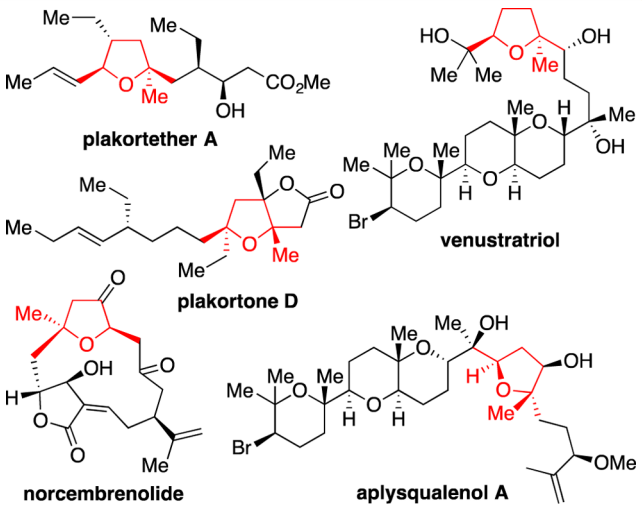


Figure 1. Natural products containing 1,1,4-trisubstituted tetrahydrofuran motifs.

via oxidative cyclization of tertiary alcohols onto 1,2-disubstituted olefins to form the THF ring with subsequent carbonylative

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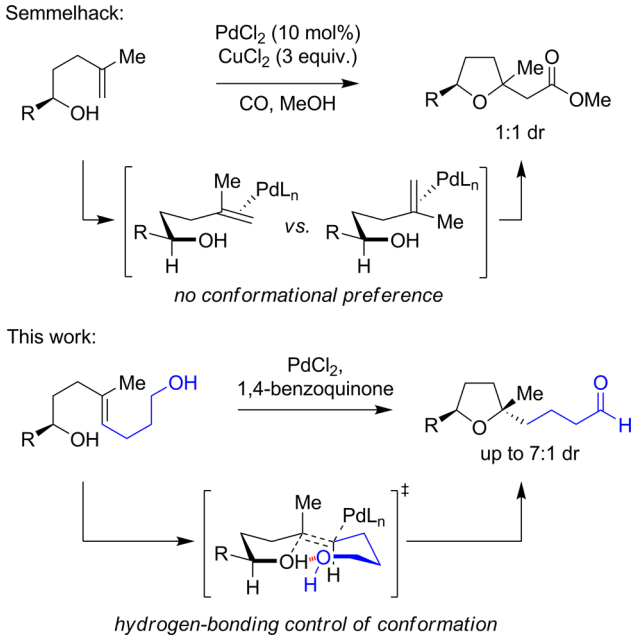


Figure 2. Models of diastereocontrol in intramolecular oxypalladations of alkenols to form 1,1,4-trisubstituted tetrahydrofurans.

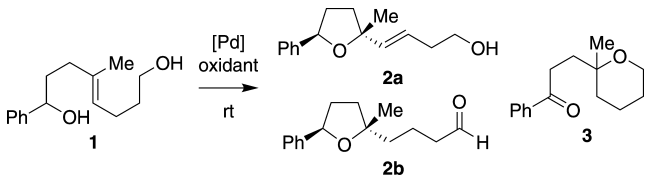
lactonization to form the fused ring system.[11] However, in the converse approach, Semmelhack found that cyclization of secondary alcohols onto 1,1-disubstituted olefins resulted, after carbonylation, in a 1:1 mixture of diastereomers. This was attributed to similar energies of the two competing 5-membered ring reactive conformations.[10]

We became interested in this problem in the context of our ongoing program on the synthesis of libraries based on underrepresented scaffolds from natural products.[12] Herein, we report a novel variant of this Pd-catalyzed oxidative cyclization in which intramolecular hydrogen bonding provides increased diastereoselectivity (up to 7:1 dr) in the conversion of trisubstituted alkenols to 1,1,4-trisubstituted THFs. The resulting Pd–alkyl intermediate then undergoes a tandem redox-relay reaction,[13] leading to synthetically useful side chain functionalities. A rationale for the observed diastereoselectivity is proposed based on mechanistic studies and computational modeling. The reaction accommodates a variety of substituent patterns and chelating functionalities.

RESULTS AND DISCUSSION

Reaction Discovery, Optimization, and Scope. In the course of exploratory studies of metal-catalyzed cyclizations of alkenols to access oxygen heterocycles, we discovered that $Pd(OAc)_2/Cu(OAc)_2$-mediated oxidative cyclization[9] of alkenediol **1** provided 1,1,4-trisubstituted THF **2a** with modest but non-zero 2:1 diastereoselectivity (Table 1, entry 1). Based on this unexpected result, we investigated other copper co-oxidants, but all led to either lower yields or decomposition of starting material (data not shown). Interestingly, use of a $PdCl_2/CuCl_2$ catalyst system led instead to 6-*endo* cyclization product **3** (entry 2). Returning to $Pd(OAc)_2$, we found that 1,4-benzoquinone (BQ) was also an effective co-oxidant (entry 3), while use of $Pd(TFA)_2$/BQ resulted in a much lower yield (entry 4). Strikingly, the combination of $PdCl_2$ and BQ resulted in increased 6:1 diastereoselectivity, a dramatic shift in reactivity, with aldehyde **2b** isolated in excellent yield (entry 5). The diastereomers were inseparable, but the stereochemical configuration of the major diastereomer was assigned by extensive 1D and 2D NMR analysis.[16] Notably, none of the expected β-hydride elimination product **2a** was observed. Formation of an aldehyde (**2b**) side chain, rather than an alkene (**2a**), in the product suggested that the initial oxidative cyclization was followed by a tandem redox-relay process (vide infra).

Table 1. Discovery and Optimization of Diastereoselective Tandem Oxidative Cyclization–Redox Relay Reaction[a]



entry	catalyst	oxidant	solvent	product	dr[b]	yield (%)
1	$Pd(OAc)_2$	$Cu(OAc)_2$[c]	THF	**2a**	2:1	86
2	$PdCl_2$	$CuCl_2$	THF	**3**	-	25
3	$Pd(OAc)_2$	BQ	THF	**2a**	2:1	87
4	$Pd(TFA)_2$	BQ	THF	**2a**	2:1	24
5	$PdCl_2$	BQ	THF	**2b**	6:1	94
6	$PdCl_2$, pyr[d]	BQ	THF	n.r.	-	-
7	$Pd(PPh_3)_2Cl_2$	BQ	THF	n.r.	-	-
8	$PdCl_2$[e]	-	THF	n.r.	-	-
9	$PdCl_2$	BQ	toluene	**2b**	6:1	91
10	$PdCl_2$	BQ	DCE	**2b**	3:1	88
11	$PdCl_2$	BQ	2-butanone	**2b**	2:1	92
12	$PdCl_2$	BQ	MeCN	**2b**	1:1	10
13	$PdCl_2$	BQ	EtOH	**2b**[f]	2:1	85

[a]Reaction conditions: alkenediol **1** (1 equiv) dissolved in THF at 0.1 M was added to a mixture of catalyst (5 mol %) and oxidant (1 equiv) and the mixture stirred at rt. [b]Inseparable mixture of diastereomers; dr determined by NMR integration of C5-H and/or C1-Me resonances; relative stereochemistry assigned by 1D NOE and 2D NOESY analyses.[16] [c]2 equiv of oxidant. [d]10 mol % of pyridine. [e]1 equiv of $PdCl_2$. [f]Isolated as corresponding diethyl acetal of **2b**. BQ = 1,4-benzoquinone; DCE = 1,2-dichloroethane; nr = no reaction; pyr = pyridine.

Addition of catalytic pyridine, which has been shown to increase catalytic efficiency in Wacker oxidations,[14] completely inhibited the reaction (entry 6). $Pd(PPh_3)_2Cl_2$ was also ineffective as a catalyst, resulting in no reaction (entry 7). No reaction was observed in the absence of 1,4-benzoquinone as a co-oxidant, even with stoichiometric $PdCl_2$ (entry 8). Evaluation of other solvents (entries 9–13) identified THF and toluene as the most effective with respect to both diastereoselectivity and yield.

With these conditions in hand, we next investigated the scope of the tandem oxidative cyclization–redox relay reaction. Reactions of other substituted alcohols revealed that diastereoselectivity correlated positively with the steric bulk of the cyclizing alcohol (*t*-Bu > Ph > isopropenyl > *n*-Bu > Me) (Table 2, entries 1–4, and Table 1, entry 5), reaching 7:1 dr for the *tert*-butyl-substituted substrate **4d**. Ester-substituted diol **4e** also underwent efficient cyclization, albeit with diminished 2:1 diastereoselectivity (entry 5). A triol substrate **4f** also cyclized to the corresponding THF with complete regioselectivity over

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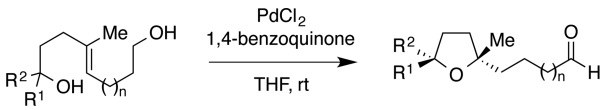
Table 2. Scope of the Diastereoselective Tandem Oxidative Cyclization–Redox Relay Reaction[a]



4a–j 5a–j

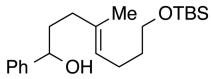
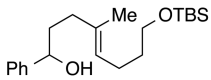
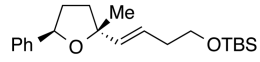
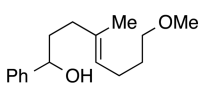
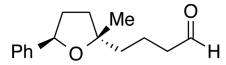
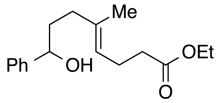
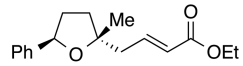
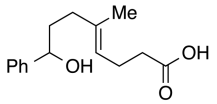
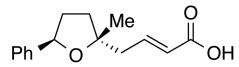
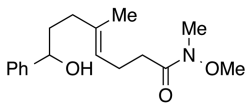
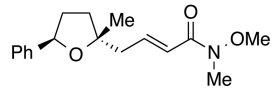
entry	substrate	R^1	R^2	n	product	dr[b]	yield (%)
1	**4a**	Me	H	1	**5a**	2:1	84
2	**4b**	*n*-Bu	H	1	**5b**	3:1	88
3	**4c**		H	1	**5c**	4:1	70
4	**4d**	*t*-Bu	H	1	**5d**	7:1	77
5	**4e**		H	1	**5e**	2:1	92
6	**4f**		H	1	**5f**	2:1	85
7[c]	**4g**	Me	Me	1	**5g**	na	84
8[c]	**4h**	Ph	Ph	1	**5h**	na	78
9	**4i**	Ph	H	0	**5i**	3:1	35
10	**4j**	Ph	H	2	**5j**	4:1	60

[a]Reaction conditions: alkenediol **4** (1 equiv) dissolved in THF at 0.1 M was added to a mixture of $PdCl_2$ (5 mol %) and 1,4-benzoquinone (1 equiv) and the mixture stirred at rt for 8 h. [b]Inseparable mixture of diastereomers; dr determined by NMR integration of C5-H and/or C1-Me resonances; relative stereochemistry assigned by 1D NOE and 2D NOESY analyses.[16] [c]Reaction carried out at 60 °C. na = not applicable.

tetrahydropyran formation (entry 6), although again with lower 2:1 diastereoselectivity (cf. entry 4). Notably, tertiary alcohols **4g** and **4h** were unreactive at 25 °C but underwent efficient oxidative cyclizations at 60 °C (entries 7 and 8). Variation in chain length for the distal (noncyclizing) alcohol led to somewhat decreased diastereoselectivies and yields (entries 9 and 10). Taken together, the observed decreases in diastereoselectivity in the presence of competing coordinating functionalities and with alternative chain lengths are suggestive of a role for the distal alcohol in transition-state organization.

Role of the Distal Alcohol on Diastereoselectivity and Reactivity. To gain further insights into the possible role of the distal alcohol in the reaction, we investigated substrates with related distal functionalities (Table 3). When the alcohol was capped as a TBS ether in substrate **6**, no reaction took place under our standard reaction conditions or upon heating to 60 °C (entry 1), consistent with a role for the distal alcohol in promoting the reaction. Further heating to 80 °C in 1,4-dioxane led to substrate decomposition to form a complex mixture. In contrast, when Hosokawa's original $Pd(OAc)_2$/$Cu(OAc)_2$ catalyst system was employed at 25 °C, the cyclization product **7** was isolated in 2:1 dr (entry 2), identical to the result obtained with the parent diol substrate **1** (Table 1, entry 1). This suggests that the distal alcohol does not impact reactivity or diastereoselectivity under Hosokawa's classical oxidative cyclization conditions.[9] When the distal alcohol was capped as a methyl ether in **8**, the $PdCl_2$/BQ reaction did proceed at 60 °C to form aldehyde **3** in modest yield and diastereoselectivity (Table 2, entry 3). We posit that the side-chain aldehyde is formed as a result of the subsequent redox relay process rather than via initial demethylation of the substrate **8** to reform diol **1** (vide infra). Ester, carboxylic acid, and Weinreb amide directing groups in **9**–**11**, respectively,

Table 3. Effects of Distal Functionalities on the Diastereoselective Tandem Oxidative Cyclization–Redox Relay Reaction[a,b]

entry	substrate	product
1	 **6**	no reaction (25–60 °C)[a] or complex mixture (80 °C)[c]
2[d]	 **6**	 **7** (82%, 2:1 dr)
3	 **8**	 **2b** (51%, 2:1 dr)
4	 **9**	 **12** (75%, 4:1 dr)
5	 **10**	 **13** (68%, 2:1 dr)
6	 **11**	 **14** (87%, 2:1 dr)

[a]Reaction conditions: substrate (1 equiv) dissolved in THF at 0.1 M was added to mixture of $PdCl_2$ (5 mol %) and 1,4-benzoquinone (1 equiv) and the mixture stirred at 60 °C for 8 h, except as otherwise noted. [b]Inseparable mixture of diastereomers; dr determined by NMR integration of C5-H and/or C1-Me resonances; relative stereochemistry assigned by 1D NOE and 2D NOESY analyses.[16] [c]Heated to 80 °C in 1,4-dioxane. [d]Reaction carried out with $Pd(OAc)_2$ (5 mol %) and $Cu(OAc)_2$ (2 equiv) and stirred at rt for 8 h.

were also effective under $PdCl_2$/BQ catalysis at 60 °C, yielding the corresponding α,β-unsaturated ester, acid, and amide products **12**–**14**, respectively (entries 4 and 5), albeit with modest diastereoselectivities.

Mechanistic Studies via Deuterium-Labeling Experiments. We next evaluated structural isomers of the parent alkene diol substrate **1** in the reaction (Figure 3). The isomeric diol **15**, in which the phenyl substituent is moved to the noncyclizing side chain bearing the distal alcohol, also underwent efficient cyclization with 5-*exo* Markovnikov regioselectivity to give phenyl ketone **16**. To probe the mechanism of the redox-relay process, we carried out the same reaction with the corresponding deuterium-labeled substrate **17**. Complete deuterium transfer to the α-carbon of the ketone in **18** was observed, consistent with a processive Pd–H migration mechanism leading directly to the carbonyl product rather than initial formation of an enol product followed by spontaneous tautomerization (vide infra).[13b,c]

Other $PdCl_2$-catalyzed oxypalladations have been shown to proceed via both *syn*- and *anti*-oxypalladation pathways.[15] To differentiate between these two possibilities, we synthesized

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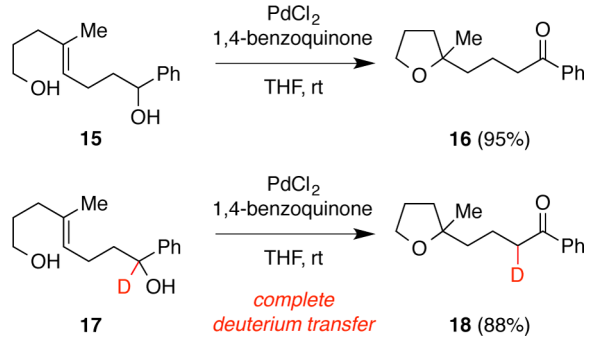

Figure 3. Deuterium-labeling experiment to probe mechanism of side-chain carbonyl formation.

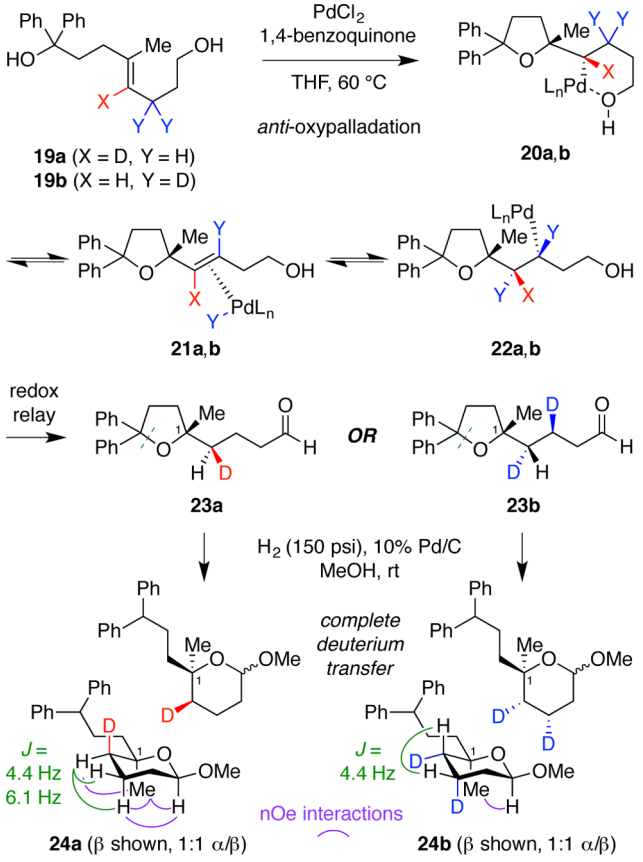

Figure 4. Deuterium-labeling experiments to differentiate between *syn*- and *anti*-oxypalladation mechanisms.

deuterium-labeled substrates **19a** and **19b** and subjected them to $PdCl_2$/BQ-catalyzed cyclization at 60 °C to yield THFs **23a** and **23b**, respectively, as single diastereomers (Figure 4 and Figure S1).[16] Relative stereochemical configurations were assigned by hydrogenolytic cleavage of the THF ring and conversion to cyclic acetals **24a** and **24b**, followed by ^{1}H NMR analysis of coupling constants and NOE interactions (Figure S2 and Figure S3).[16] This confirmed that the α-deuterium (adjacent to the THF ring) and C1-methyl group were *syn* in **23a** and *anti* in **23b**, consistent with the intermediacy of *anti*-oxypalladation intermediates **20a** and **20b**. In contrast, if a *syn*-oxypalladation mechanism were operative, the α-deuterium and C1-methyl group would be *anti* in **23a** and *syn* in **23b**, consistent with a *syn* relationship between the methyl group and the palladium in intermediate (cf. **20**).

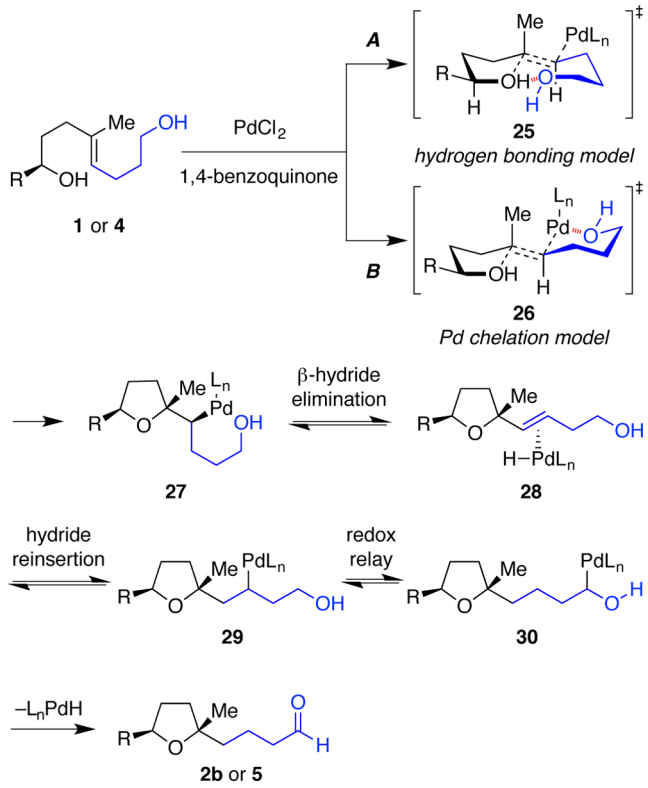

Figure 5. Proposed models for organization of *anti*-oxypalladation transition state by intramolecular hydrogen bonding (pathway A) or Pd chelation (pathway B) by the distal (noncyclizing) alcohol followed by tandem redox-relay reaction to generate an aldehyde side-chain functionality.

Computational Studies. The experimental results strongly suggest a role of the distal functionality in enhancing both reactivity and diastereoselectivity in the reaction. Moreover, inclusion of other potentially competing functionalities as solvent (Table 1, entries 11–13) or in the substrate (Table 2, entries 5 and 6, and Table 3, entries 4–6) leads to reduced diastereoselectivity. Thus, we considered two possible mechanistic hypotheses for a role of the distal hydroxyl functionality in organizing the transition state, leading to the unusual diastereoselectivity of this intramolecular oxypalladation (Figure 5). In one scenario, the distal functionality engages in an intramolecular hydrogen-bonding interaction with the cyclizing alcohol to organize the *anti*-oxypalladation transition state **25** (pathway A). Ess and co-workers have reported similar hydrogen-bonding interactions in Au^I- and Pd^{II}-catalyzed intramolecular cyclizations of allylic alcohols.[17] Alternatively, the distal functionality could chelate the Pd to organize the transition state **26** (pathway B). This chelation effect has been proposed to rationalize chirality transfer in oxypalladation reactions,[18] although experimental studies on a redox-relay Heck reaction[13f] have excluded chelation of the Pd. In both cases, 5-*exo* Markovnikov oxidative cyclization would be followed by a redox-relay process that, based on the deuterium-labeling experiment above (Figure 3), terminates with β-hydride elimination across the terminal C–O bond to form the observed aldehyde products (**2b** or **5**) directly.[13b,d]

To evaluate these mechanistic hypotheses, we carried out computational studies of the two putative reaction pathways by calculating the stereodifferentiating (diastereomeric) transition structures for the cyclization of alkene diol substrate **4a** at the M06/LanL2DZ+f/6-31g(d,p) level of theory.[16,19] For the

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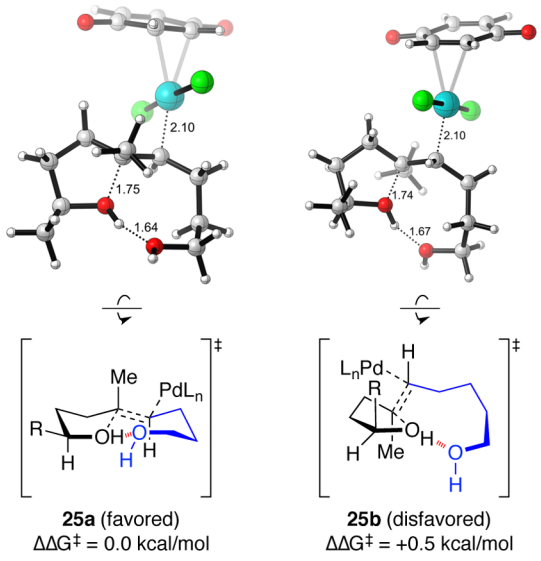

Figure 6. Stereodifferentiating transition structures **25a** and **25b** for the cyclization of **4a** (L_n = Cl_2(BQ)) with bond distances in Å.

Pd chelation model (**26**), attempts to locate transition structures for the direct attack of the cyclizing alcohol on the π-coordinated palladium were not successful. This suggests that the free hydroxyl group is not sufficiently nucleophilic to attack the Pd–olefin complex under these conditions. In agreement with previous work,[13d,f] this indicates that the distal (noncyclizing) alcohol does not chelate Pd. In contrast, in the hydrogen-bonding model (**25**), we were able to locate the transition structures **25a** and **25b** (Figure 6). Here, the distal hydroxyl group activates the cyclizing alcohol by an intramolecular hydrogen bond that increases the nucleophilicity of the hydroxyl group by partial deprotonation. It is noteworthy that, in contrast to the work of Ess and co-workers,[17] no dehydrative elimination is observed in our system. This is consistent with the experimental finding that elimination of the Pd from the carbon chain is disfavored compared to the chain-walking redox-relay process (Figure 3). It has been shown previously in redox-relay–Heck reactions[13b,d] that elimination is highly endergonic due to the instability of Pd bound to an electron-withdrawing ligand, suggesting a possible role for the BQ in controlling reactivity in our system. With the elimination pathways energetically unfavorable, the distal alcohol is converted into an aldehyde after a series of β-hydride elimination and reinsertion chain-walking steps.[13b]

Consistent with the experimentally observed 2:1 dr for oxidative cyclization of **4a** (Table 2, entry 1), transition structure **25a**, which leads to the *anti*-1,4-diastereomer **5a**, was calculated to be 0.5 kcal/mol lower in free energy than the diastereomeric transition structure **25b**.[19] Importantly, these calculated structures provide insights into the structural origin of the observed diastereoselectivity. In the favored transition structure **25a**, the methyl group α to the cyclizing alcohol is in a pseudoequatorial orientation relative to the forming five-membered ring. In contrast, this α-methyl group is an unfavorable pseudoaxial position in transition structure **25b**, inducing a 1,3-diaxial steric repulsion between the α-methyl group and an axial hydrogen atom. This is in agreement with the observation that diastereoselectivity increases as the size of this substituent increases (Table 2, entries 1–4). Nevertheless, the effect is modest due to the relatively small steric differences between the equatorial and axial positions in five-membered rings.[20]

CONCLUSION

Several features of this unusually diastereoselective tandem oxidative cyclization–redox relay reaction are notable. In particular, the choice of catalyst is critical to the outcome of the reaction. First, under $PdCl_2$/BQ catalysis herein, a hydrogen-bond accepting distal functionality is required for the oxidative cyclization reaction to proceed (Table 3, entry 1). In contrast, reaction with Hosokawa's classical $Pd(OAc)_2$/$Cu(OAc)_2$ catalyst system does not require a distal hydrogen-bonding functionality (Table 3, entry 2).

Second, under $PdCl_2$/BQ catalysis, diastereoselectivity of the oxidative cyclization is dependent upon tether length (Table 2, entries 9 and 10) and the electronics of the distal functional group (Table 3). This suggests that the distal functionality plays a critical role in organizing the transition state, as supported by our computational modeling studies (Figure 6). In contrast, under $Pd(OAc)_2$/$Cu(OAc)_2$ catalysis, the distal functionality does not appear to impact diastereoselectivity (Table 1, entry 1, vs Table 3, entry 2). This suggests that the 2:1 dr observed for oxidative cyclization of both **1** and **6** represents the inherent diastereoselectivity of the isolated THF-forming portion of the substrate. The 6:1 dr observed for oxidative cyclization of **1** under $PdCl_2$/BQ catalysis then indicates the increased diastereoselectivity attributable to the distal functionality.

Third, $PdCl_2$/BQ catalysis herein leads to aldehyde (or α,β-unsaturated carboxylate derivative) side chains via a putative tandem redox-relay process that follows the oxidative cyclization reaction.[13] In contrast, under $Pd(OAc)_2$/$Cu(OAc)_2$ catalysis, the tandem redox-relay process does not take place, and vicinal olefin side chains are formed via immediate β-hydride elimination of the initial alkyl-Pd intermediate (Table 1, entry 1 vs entry 5). The lack of reinsertion of Pd–H across the olefin in the latter case suggests rapid dissociation of the Pd–olefin complex and short lifetime of the resulting Pd–H species.[15] This may be due to differences between the Pd ligands in these two catalyst systems.

In conclusion, we have developed a novel variant of the classical Pd-catalyzed oxidative cyclization of alkenols in which use of a $PdCl_2$/BQ catalyst system and introduction of a distal hydrogen-bonding functionality into the substrate dramatically change the course of the reaction. The oxidative cyclization reaction proceeds via an *anti*-oxypalladation mechanism with 5-*exo* Markovnikov regioselectivity and a tandem redox-relay process converts distal side chain alcohols to aldehydes or ketones that are poised for further functionalization. In this tandem reaction, the distal hydrogen-bonding functionality enhances both reactivity and diastereoselectivity, and computational modeling studies suggest that this results from introduction of specific conformational constraints in the transition state. While the absolute diastereoselectivity of these reactions ranges from moderate to high depending on substrate structure, this transition-state organization increases diastereoselectivity well above the intrinsic levels observed under classical Hosokawa conditions that are not influenced by intramolecular hydrogen bonding. Further investigations of the scope and mechanism of this reaction, particularly the role of catalyst structure, and applications to natural product and library synthesis are ongoing.

EXPERIMENTAL SECTION

General Methods. All reactions were performed in flame-dried glassware under positive Ar pressure with magnetic stirring unless otherwise noted. Solvents were degassed with Ar and purified on a

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solvent drying system as described[21] unless otherwise indicated. Liquid reagents and solutions were transferred through rubber septa via syringes flushed with Ar prior to use. Cold baths were generated as follows: 0 °C, wet ice/water; −78 °C, dry ice/acetone.

NMR spectra were recorded on a 500 MHz NMR or 600 MHz NMR with a DCH CryoProbe at 24 °C in $CDCl_3$ unless otherwise indicated. Chemical shifts are expressed in ppm relative to TMS (^{1}H, 0 ppm) or solvent signals: $CDCl_3$ (^{13}C, 77.0 ppm); coupling constants are expressed in hertz. High-resolution mass spectra were obtained at the MSKCC Analytical Core Facility on an LC-TOF-MS by electrospray ionization (ESI).

Compounds not cited explicitly in the main text are numbered from **S1** below. Detailed synthetic schemes are shown in Figures S8−S25.

1. Synthesis of Diol Substrates. *1a. Synthesis of Ester Intermediate **S4** and Aldehyde Intermediate **S6**. tert-Butyl(pent-4-en-1-yloxy)diphenylsilane (**S1**).* In a 250 mL round-bottom flask, 4-penten-1-ol (6.00 mL, 58.1 mmol) and imidazole (7.90 g, 116 mmol, 2 equiv) were dissolved in CH_2Cl_2 (100 mL), and the solution was cooled to 0 °C. TBDPSCl (58.1 mL, 15.1 mmol, 1 equiv) was added slowly with stirring. The solution was allowed to warm to rt and stirred until complete conversion had occurred as judged by TLC. The mixture was quenched with 1 M HCl (100 mL), extracted with CH_2Cl_2 (3 × 50 mL), dried ($MgSO_4$), filtered, and concentrated by rotary evaporation to afford the crude product **S1** as a colorless oil (17.1 g, 91%) that was carried onto the next step without further purification. IR (neat) (cm^{-1}): 2929, 2857, 2337, 2271, 1671, 1015, 821, 737, 700, 614. ^{1}H NMR (600 MHz): δ 7.70−7.64 (m, 4H), 7.44−7.35 (m, 6H), 5.83−5.77 (m, 1H), 5.03−4.91 (m, 2H), 3.67 (t, J = 6.4 Hz, 2H), 2.15 (q, J = 6.4, 2H), 1.66 (quint, J = 6.4, 2H), 1.05 (s, 1H). ^{13}C NMR (151 MHz): δ 138.5, 135.6, 134.0, 129.5, 127.6, 114.5, 63.2, 31.78, 30.0, 26.8, 19.2. HRMS (ESI): m/z calcd for ($C_{21}H_{29}OSi$ [M + H]$^+$) 325.1988, found 325.1985.

*4-((tert-Butyldiphenylsilyl)oxy)butanal (**S2**).* In a 500 mL round-bottom flask, alkene **S1** (16.0 g, 49.3 mmol) was dissolved in CH_2Cl_2 (150 mL), and the solution was cooled to −78 °C. Ozone was bubbled through the solution until the blue color was persistent. The stream of ozone was replaced with oxygen until the blue color dissipated, and then the reaction was quenched with zinc powder (16.0 g, 246 mmol, 5 equiv) in acetic acid (50 mL), allowed to slowly warm to rt, and stirred overnight. The solution was concentrated by rotary evaporation to afford the crude product as a yellow oil. Purification by silica flash chromatography (9:1 hexanes/EtOAc) yielded aldehyde **S2** (15.3 g, 46.7 mmol, 95%) as a colorless oil. IR (neat) (cm^{-1}): 2936, 2862, 1729, 1431, 1112, 944, 826, 743, 706, 616. ^{1}H NMR (600 MHz): δ 9.79 (s, 1H), 7.65 (d, J = 6.5 Hz, 4H), 7.46−7.33 (m, 6H), 3.69 (t, J = 6.0 Hz, 4H), 2.55 (t, J = 1.7 Hz, 2H), 1.89 (quint., J = 6.0 Hz, 2H), 1.04 (s, 15H). ^{13}C NMR (151 MHz): δ 202.5, 135.5, 133.5, 129.7, 127.7, 62.9, 40.7, 26.8, 25.2, 19.2. HRMS (ESI): m/z calcd for ($C_{20}H_{27}O_2Si$ [M + H]$^+$) 327.1780, found 327.1769.

*6-((tert-Butyldiphenylsilyl)oxy)-2-methylhex-1-en-3-ol (**S3**).* In a 500 mL round-bottom flask, aldehyde **S2** (15.3 g, 49.3 mmol) was dissolved in THF (100 mL), and the solution was cooled to 0 °C. Isopropenylmagnesium bromide (1.0 M in THF, 93.5 mL, 46.7 mmol, 1 equiv) was added slowly via an addition funnel. Once addition was complete, the cooling bath was removed, and the solution was allowed to stir at rt until complete conversion had occurred as judged by TLC. The mixture was recooled to 0 °C and quenched with 1 M HCl (100 mL). The mixture was extracted with Et_2O (3 × 50 mL), dried ($MgSO_4$), filtered, and concentrated by rotary evaporation to afford the crude product as a yellow oil. Purification by silica flash chromatography (4:1 hexanes/EtOAc) yielded allylic alcohol **S3** (16.1 g, 43.7 mmol, 93%) as a yellow oil. IR (neat) (cm^{-1}): 3690−3147, 2936, 2862, 1431, 1111, 1001, 741, 704, 616. ^{1}H NMR (600 MHz): δ 7.69−7.63 (m, 4H), 7.43−7.33 (m, 6H), 4.94 (s, 1H), 4.83 (s, 1H), 4.06 (t, J = 6.4 Hz, 1H), 3.73−3.59 (m, 2H), 2.20 (s, 1H), 1.72 (s, 3H), 1.67−1.55 (m, 4H), 1.06 (s, 9H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 147.4, 135.5, 133.7, 129.6, 127.6, 110.9, 75.5, 63.9, 31.7, 28.5, 26.8, 19.2, 17.7. HRMS (ESI): m/z calcd for ($C_{23}H_{33}O_2Si$ [M + H]$^+$) 369.2250, found 369.2242.

*Ethyl (E)-8-((tert-Butyldiphenylsilyl)oxy)-4-methyloct-4-enoate (**S4**).* In a 50 mL round-bottom flask, allylic alcohol **S3** (3.00 g, 8.14 mmol), triethyl orthoacetate (15 mL), and propionic acid (60 μL, 0.81 mmol, 0.1 equiv) were added. The flask was equipped with a distillation head and heated to 140 °C, during which time ethanol was collected. Heating was continued at this temperature until complete conversion had occurred as judged by TLC. The mixture was cooled to rt and quenched with 1 M HCl (25 mL). The mixture was extracted with Et_2O (3 × 50 mL), washed with 1 M NaOH (10 mL), dried ($MgSO_4$), filtered, and concentrated by rotary evaporation to afford the crude product as a yellow oil. Purification by silica flash chromatography (9:1 hexanes/EtOAc) yielded ester **S4** (3.25 g, 91%) as a colorless oil. IR (neat) (cm^{-1}): 2956, 2858, 1735, 1445, 1428, 1156, 822, 737, 701, 649. ^{1}H NMR (600 MHz): δ 7.67 (d, J = 6.5 Hz, 4H), 7.45−7.33 (m, 6H), 5.12 (t, J = 1.4 Hz, 1H), 4.11 (q, J = 7.1 Hz, 2H), 3.64 (t, J = 6.3 Hz, 2H), 2.37 (t, J = 6.1 Hz, 2H), 2.30−2.24 (m, 2H), 2.07 (q, J = 7.4 Hz, 2H), 1.64−1.55 (m, 5H), 1.24 (t, J = 7.1 Hz, 3H), 1.05 (s, 9H). ^{13}C NMR (151 MHz): δ 173.5, 135.5, 134.0, 133.7, 129.5, 127.6, 124.8, 63.3, 60.2, 34.7, 33.2, 32.6, 26.8, 24.1, 19.2, 15.9, 14.3. HRMS (ESI): m/z calcd for ($C_{27}H_{39}O_3Si$ [M + H]$^+$) 439.2668, found 439.2663.

*(E)-8-((tert-Butyldiphenylsilyl)oxy)-4-methyloct-4-en-1-ol (**S5**).* In a 250 mL round-bottom flask, ester **S4** (2.00 g, 4.56 mmol) was dissolved in THF (50 mL), and the solution was cooled to 0 °C. $LiAlH_4$ (173 mg, 4.56 mmol, 1 equiv) was added slowly and the solution stirred at 0 °C until complete conversion had occurred as judged by TLC. The mixture was carefully quenched with 1 M HCl (25 mL). The mixture was extracted with Et_2O (3 × 10 mL), dried ($MgSO_4$), filtered, and concentrated by rotary evaporation to afford the crude product as a colorless oil. Purification by silica flash chromatography (4:1 hexanes/EtOAc) yielded alcohol **S5** (1.80 g, 4.53 mmol, 99%) as a colorless oil. IR (neat) (cm^{-1}): 3702−3114, 2933, 2858, 1589, 1470, 1428, 1107, 821, 737, 701, 612. ^{1}H NMR (600 MHz): δ 7.70−7.64 (m, 4H), 7.45−7.34 (m, 6H), 5.14 (t, J = 7.3 Hz, 1H), 3.65 (t, J = 6.4 Hz, 2H), 3.61 (t, J = 6.5 Hz, 2H), 2.08 (q, J = 7.4 Hz, 2H), 2.04 (t, J = 7.3, 2H), 1.69−1.58 (m, 5H), 1.27 (s, 3H), 1.05 (s, 9H). ^{13}C NMR (151 MHz): δ 135.6, 135.0, 134.1, 129.5, 127.6, 124.6, 63.4, 62.8, 35.9, 32.7, 30.7, 26.8, 24.2, 19.2, 15.8. HRMS (ESI): m/z calcd for ($C_{25}H_{37}O_2Si$ [M + H]$^+$) 397.2563, found 397.2558.

*(E)-8-((tert-Butyldiphenylsilyl)oxy)-4-methyloct-4-enal (**S6**).* In a 250 mL round-bottom flask, alcohol **S5** (1.85 g, 4.66 mmol) was dissolved in CH_2Cl_2 (100 mL), and PCC (2.01 g, 9.33 mmol, 2 equiv) was added. The solution was stirred at rt until complete conversion had occurred as judged by TLC. The mixture was filtered through a pad of silica with hexane/EtOAc 9:1 and concentrated by rotary evaporation to afford aldehyde **S6** (1.42 g, 3.60 mmol, 77%) as a colorless oil. IR (neat) (cm^{-1}): 2931, 2858, 1725, 1427, 1106, 822, 738, 701, 612. ^{1}H NMR (600 MHz): δ 9.73 (t, J = 1.9 Hz, 1H), 7.69−7.64 (m, 4H), 7.44−7.34 (m, 6H), 5.12 (t, J = 7.3 Hz, 1H), 3.64 (t, J = 6.3 Hz, 2H), 2.48 (td, J = 7.6, 1.9 Hz, 2H), 2.29 (t, J = 7.6 Hz, 2H), 2.08 (q, J = 7.3 Hz, 2H), 1.62−1.55 (m, 5H), 1.05 (s, 9H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 202.7, 135.6, 134.0, 133.3, 129.5, 127.6, 125.2, 63.3, 42.2, 32.5, 31.8, 26.8, 24.2, 19.2, 16.0. HRMS (ESI): m/z calcd for ($C_{25}H_{34}O_2NaSi$ [M + Na]$^+$) 417.2226, found 417.2212.

*1b. Synthesis of Diol Substrates **1** and **4a-d** from Aldehyde Intermediate **S6**. (E)-8-((tert-Butyldiphenylsilyl)oxy)-4-methyl-1-phenyloct-4-en-1-ol (**S7**).* In a 25 mL round-bottom flask, aldehyde **S6** (200 mg, 0.51 mmol) was dissolved in THF (5 mL), and the solution was cooled to 0 °C. PhMgBr (1.0 M in THF, 0.61 mL, 0.61 mmol, 1.2 equiv) was added dropwise with stirring. Once addition was complete, the solution was allowed to warm to rt, and stirring was continued until complete conversion had occurred as judged by TLC. The mixture was quenched with 1 M HCl (5 mL), extracted with Et_2O (3 × 5 mL), dried ($MgSO_4$), filtered, and concentrated by rotary evaporation to afford the crude product as a yellow oil. Purification by silica flash chromatography (4:1 hexanes/EtOAc) yielded benzylic alcohol **S7** (211 mg, 0.45 mmol, 88%) as a colorless oil. IR (neat) (cm^{-1}): 3683−3118, 3068, 2931, 2857, 1427, 1106, 821, 737, 699, 612. ^{1}H NMR (600 MHz): δ 7.68−7.64 (m, 4H), 7.42−7.30 (m, 11H), 5.12 (t, J = 7.0 Hz, 1H), 4.62 (dd, J = 7.8, 5.3 Hz, 1H),

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3.65 (t, J = 6.4 Hz, 2H), 2.11−2.04 (m, 3H), 2.02−1.95 (m, 1H), 1.91−1.81 (m, 1H), 1.81−1.74 (m, 1H), 1.62−1.55 (m, 5H), 1.05 (s, 9H). ^{13}C NMR (151 MHz): δ 144.7, 135.5, 134.9, 134.0, 129.5, 128.4, 127.5, 127.4, 125.9, 124.6, 74.3, 63.4, 37.2, 35.9, 32.6, 26.8, 24.1, 19.2, 16.0. HRMS (ESI): m/z calcd for ($C_{31}H_{40}O_2NaSi$ [M + Na]$^+$) 495.2695, found 495.2681.

*(E)-4-Methyl-1-phenyloct-4-ene-1,8-diol (**1**).* In a 10 mL round-bottom flask, protected alcohol **S7** (200 mg, 0.42 mmol) was dissolved in THF (4 mL) at rt. TBAF (1.0 M in THF, 0.85 mL, 0.85 mmol, 2 equiv) was added, and the solution was stirred until complete conversion had occurred as judged by TLC. The reaction mixture was concentrated by rotary evaporation. Purification by silica flash chromatography (1:1 hexanes/EtOAc) yielded diol **1** (96 mg, 0.41 mmol, 97%) as a colorless oil. IR (neat) (cm^{-1}): 3715−3092, 2932, 2864, 1720, 1496, 1059, 1033, 765, 703. ^{1}H NMR (600 MHz): δ 7.29−7.24 (m, 4H), 7.22−7.18 (m, 1H), 5.10 (t, J = 7.0, 1H), 4.56 (dd, J = 7.8, 5.3 Hz, 1H), 3.54 (t, J = 6.5 Hz, 2H), 2.08−1.90 (m, 1H), 1.85−1.78 (m, 1H), 1.77−1.70 (m, 1H), 1.57−1.49 (m, 5H). ^{13}C NMR (151 MHz): δ 144.8, 135.4, 128.4, 127.5, 125.9, 124.3, 74.3, 62.7, 37.2, 36.0, 32.7, 24.3, 16.0. HRMS (ESI): m/z calcd for ($C_{14}H_{20}O_2Na$ [M + Na]$^+$) 243.1361, found 243.1363.

*(E)-9-((tert-Butyldiphenylsilyl)oxy)-5-methylnon-5-en-2-ol (**S8**).* In a 25 mL round-bottom flask, aldehyde **S6** (100 mg, 0.25 mmol) was dissolved in THF (5 mL), and the solution was cooled to 0 °C. MeMgBr (1.0 M in THF, 0.30 mL, 0.30 mmol, 1.2 equiv) was added dropwise with stirring. Once addition was complete, the solution was allowed to warm to rt, and stirring was continued until complete conversion had occurred as judged by TLC. The mixture was quenched with 1 M HCl (5 mL), extracted with Et_2O (3 × 5 mL), dried ($MgSO_4$), filtered, and concentrated by rotary evaporation to afford the crude product as a yellow oil. Purification by silica flash chromatography (4:1 hexanes/EtOAc) yielded alcohol **S8** (102 mg, 0.25 mmol, 98%) as a colorless oil. IR (neat) (cm^{-1}): 3660−3131, 2930, 2858, 1469, 1427, 1106, 821, 735, 700, 612. ^{1}H NMR (600 MHz): δ 7.67 (d, J = 6.8 Hz 4H), 7.44−7.34 (m, 6H), 5.15 (t, J = 7.3 Hz, 1H), 3.76 (q, J = 6.2 Hz, 1H), 3.65 (t, J = 6.3 Hz, 2H), 2.12−1.98 (m, 4H), 1.63−1.67 (m, 4H), 1.56−1.47 (m, 1H), 1.18 (d, J = 6.2 Hz, 3H), 1.05 (s, 9H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 135.6, 135.3, 134.1, 129.5, 127.6, 124.4, 68.0, 63.4, 37.3, 36.1, 32.7, 26.8, 24.2, 23.4, 19.2, 15.9. HRMS (ESI): m/z calcd for ($C_{26}H_{39}O_2Si$ [M + H]$^+$) 411.2719, found 411.2719.

*(E)-5-Methylnon-4-ene-1,8-diol (**4a**).* In a 10 mL round-bottom flask, protected alcohol S8 (75 mg, 0.18 mmol) was dissolved in THF (2 mL) at rt. TBAF (1.0 M in THF, 0.37 mL, 0.37 mmol, 2 equiv) was added, and the solution was stirred until complete conversion had occurred as judged by TLC. The reaction mixture was concentrated by rotary evaporation. Purification by silica flash chromatography (1:1 hexanes/EtOAc) yielded diol **4a** (29 mg, 0.17 mmol, 92%) as a colorless oil. IR (neat) (cm^{-1}): 3667−3095, 2967, 2933, 2886, 1452, 1378, 1132, 1061, 737. ^{1}H NMR (600 MHz): δ 5.20−5.18 (m, 1H), 3.78 (sextet, J = 6.2 Hz, 1H), 3.63 (t, J = 6.5 Hz, 2H), 2.14−2.01 (m, 4H), 1.92 (s, 2H), 1.66−1.50 (m, 7H), 1.19 (d, J = 6.2 Hz, 3H). ^{13}C NMR (151 MHz): δ 135.7, 124.2, 68.0, 62.6, 37.2, 36.1, 32.6, 24.3, 23.4, 15.9. HRMS (ESI): m/z calcd for ($C_{10}H_{20}O_2Na$ [M + Na]$^+$) 195.1361, found 195.1357.

*(E)-12-((tert-Butyldiphenylsilyl)oxy)-8-methyldodec-8-en-5-ol (**S9**).* In a 25 mL round-bottom flask, aldehyde **S6** (100 mg, 0.25 mmol) was dissolved in THF (5 mL), and the solution was cooled to 0 °C. nBuLi (2.5 M in hexanes, 0.12 mL, 0.30 mmol, 1.2 equiv) was added dropwise with stirring. Once addition was complete, the solution was allowed to warm to rt, and stirring was continued until complete conversion had occurred as judged by TLC. The mixture was quenched with 1 M HCl (5 mL), extracted with Et_2O (3 × 5 mL), dried ($MgSO_4$), filtered, and concentrated by rotary evaporation to afford the crude product as a yellow oil. Purification by silica flash chromatography (4:1 hexanes/EtOAc) yielded alcohol **S9** (108 mg, 0.24 mmol, 94%) as a colorless oil. IR (neat) (cm^{-1}): 3683−3120, 2930, 2858, 1428, 1106, 1004, 822, 701, 612. ^{1}H NMR (600 MHz): δ 7.69−7.65 (m, 4H), 7.44−7.33 (m, 6H), 5.15 (t, J = 7.1 Hz, 1H), 3.66 (t, J = 6.3 Hz, 2H), 3.60−3.54 (m, 1H), 2.16−1.98 (m, 4H), 1.65−1.52 (m, 7H), 1.52−1.37 (m, 3H), 1.37−1.24 (m, 3H), 1.05 (s, 9H), 0.91 (t, J = 7.1 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 135.9, 135.5, 135.4, 134.1, 129.5, 127.6, 71.9, 63.4, 37.1, 36.0, 35.4, 32.7, 27.8, 26.8, 24.2, 22.8, 19.2, 15.9, 14.1. HRMS (ESI): m/z calcd for ($C_{29}H_{45}O_2Si$ [M + H]$^+$) 453.3189, found 453.3180.

*(E)-5-Methyldodec-4-ene-1,8-diol (**4b**).* In a 10 mL round-bottom flask, protected alcohol **S9** (100 mg, 0.22 mmol) was dissolved in THF (2 mL) at rt. TBAF (1.0 M in THF, 0.44 mL, 0.44 mmol, 2 equiv) was added, and the solution was stirred until complete conversion had occurred as judged by TLC. The reaction mixture was concentrated by rotary evaporation. Purification by silica flash chromatography (1:1 hexanes/EtOAc) yielded diol **4b** (29 mg, 0.17 mmol, 92%) as a colorless oil. IR (neat) (cm^{-1}): 3686−3076, 2860, 1378, 1055. ^{1}H NMR (600 MHz): δ 5.21 (t, J = 7.2 Hz, 1H), 3.65 (t, J = 6.5 Hz, 2H), 3.61−3.55 (m, 1H), 2.19−2.02 (m, 4H), 1.65−1.55 (m, 7H), 1.54−1.37 (m, 3H), 1.37−1.27 (m, 3H), 0.91 (t, J = 7.1 Hz, 3H). ^{13}C NMR (151 MHz): δ 135.9, 124.1, 71.9, 62.7, 37.2, 36.0, 35.4, 32.7, 27.8, 24.3, 22.8, 16.0, 14.1. HRMS (ESI): m/z calcd for ($C_{13}H_{26}O_2Na$ [M + Na]$^+$) 237.1831, found 237.1828.

*(E)-10-((tert-Butyldiphenylsilyl)oxy)-2,6-dimethyldeca-1,6-dien-3-ol (**S10**).* In a 25 mL round-bottom flask, aldehyde **S6** (100 mg, 0.25 mmol) was dissolved in THF (5 mL), and the solution was cooled to 0 °C. Isopropenylmagnesium bromide (0.5 M in THF, 0.61 mL, 0.30 mmol, 1.2 equiv) was added dropwise with stirring. Once addition was complete, the solution was allowed to warm to rt, and stirring was continued until complete conversion had occurred as judged by TLC. The mixture was quenched with 1 M HCl (5 mL), extracted with Et_2O (3 × 5 mL), dried ($MgSO_4$), filtered, and concentrated by rotary evaporation to afford the crude product as a yellow oil. Purification by silica flash chromatography (4:1 hexanes/EtOAc) yielded allylic alcohol **S10** (98 mg, 0.22 mmol, 88%) as a colorless oil. IR (neat) (cm^{-1}): 3660−3157, 2932, 2858, 1380, 1106, 899, 822, 736, 701, 612. ^{1}H NMR (600 MHz): δ 7.68−7.65 (m, 4H), 7.43−7.35 (m, 6H), 5.14 (t, J = 7.2, 1H), 4.93 (s, 1H), 4.84 (s, 1H), 4.03 (dd, J = 7.4, 5.5 Hz, 1H), 3.65 (t, J = 6.4 Hz, 2H), 2.08 (q, J = 7.5 Hz, 2H), 2.06−2.01 (m, 1H), 2.01−1.94 (m, 1H), 1.72 (t, J = 1.2 Hz, 3H), 1.65−1.56 (m, 7H), 1.05 (s, 9H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 147.5, 135.6, 135.0, 134.1, 129.5, 127.6, 124.5, 111.0, 75.7, 63.4, 35.7, 33.2, 32.7, 26.8, 24.2, 19.2, 17.6, 16.0. HRMS (ESI): m/z calcd for ($C_{28}H_{40}O_2SiNa$ [M + Na]$^+$) 459.2695, found 459.2710.

*(E)-5,9-Dimethyldeca-4,9-diene-1,8-diol (**4c**).* In a 10 mL round-bottom flask, protected alcohol **S10** (100 mg, 0.23 mmol) was dissolved in THF (2 mL) at rt. TBAF (1.0 M in THF, 0.46 mL, 0.46 mmol, 2 equiv) was added, and the solution was stirred until complete conversion had occurred as judged by TLC. The reaction mixture was concentrated by rotary evaporation. Purification by silica flash chromatography (1:1 hexanes/EtOAc) yielded diol **4c** (40 mg, 0.20 mmol, 88%) as a colorless oil. IR (neat) (cm^{-1}): 3667−3128, 2937, 2866, 1444, 1375, 1058, 899, 732. ^{1}H NMR (600 MHz): δ 5.20 (t, J = 7.1 Hz, 1H), 4.94 (s, 1H), 4.84 (s, 1H), 4.04 (t, J = 6.2 Hz, 1H), 3.64 (t, J = 6.5 Hz, 2H), 2.11−2.04 (m, 3H), 2.03−1.96 (m, 1H), 1.73 (s, 3H), 1.71−1.57 (m, 7H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 147.5, 135.5, 124.2, 111.0, 75.6, 62.7, 35.7, 33.1, 32.7, 24.3, 17.6, 16.0. HRMS (ESI): m/z calcd for ($C_{12}H_{22}O_2Na$ [M + Na]$^+$) 221.1517, found 221.1524.

*(E)-10-((tert-Butyldiphenylsilyl)oxy)-2,2,6-trimethyldec-6-en-3-ol (**S11**).* In a 25 mL round-bottom flask, aldehyde **S6** (100 mg, 0.25 mmol) was dissolved in THF (5 mL) and the solution was cooled to 0 °C. tBuMgBr (1.6 M in THF, 0.19 mL, 0.30 mmol, 1.2 equiv) was added dropwise with stirring. Once addition was complete, the solution was allowed to warm to rt, and stirring was continued until complete conversion had occurred as judged by TLC. The mixture was quenched with 1 M HCl (5 mL), extracted with Et_2O (3 × 5 mL), dried ($MgSO_4$), filtered, and concentrated by rotary evaporation to afford the crude product as a yellow oil. Purification by silica flash chromatography (4:1 hexanes/EtOAc) yielded alcohol **S11** (109 mg, 0.24 mmol, 95%) as a colorless oil. IR (neat) (cm^{-1}): 3677−3211, 1471, 1428, 1107, 822, 737, 701, 612. ^{1}H NMR (600 MHz): δ 7.67 (d, J = 6.5 Hz, 4H), 7.44−7.34 (m, 6H), 5.18 (t, J = 6.4 Hz, 1H), 3.66 (t, J = 6.3 Hz, 2H), 3.16 (d, J = 10.5 Hz, 1H), 2.24−2.19 (m, 1H),

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2.09 (q, J = 7.4 Hz, 2H), 2.05−1.97 (m, 1H), 1.66−1.53 (m, 7H), 1.38−1.29 (m, 1H), 1.05 (s, 9H), 0.89 (s, 9H). ^{13}C NMR (151 MHz): δ 135.6, 135.5, 134.1, 129.5, 127.5, 124.5, 79.6, 63.4, 37.2, 34.9, 32.7, 29.5, 26.8, 25.7, 24.2, 19.2, 15.9. HRMS (ESI): m/z calcd for ($C_{29}H_{45}O_2Si$ [M + H]$^+$) 453.3189, found 453.3184.

*(E)-5,9,9-Trimethyldec-4-ene-1,8-diol (**4d**).* In a 10 mL round-bottom flask, protected alcohol **S11** (100 mg, 0.22 mmol) was dissolved in THF (2 mL) at rt. TBAF (1.0 M in THF, 0.44 mL, 0.44 mmol, 2 equiv) was added, and the solution was stirred until complete conversion had occurred as judged by TLC. The reaction mixture was concentrated by rotary evaporation. Purification by silica flash chromatography (1:1 hexanes/EtOAc) yielded diol **4d** (37 mg, 0.17 mmol, 78%) as a colorless oil. IR (neat) (cm^{-1}): 3673−3092, 2951, 2889, 1711, 1445, 1364, 1062, 1010, 911, 733. ^{1}H NMR (600 MHz): δ 5.27−5.19 (m, 1H), 3.65 (dt, J = 79.9, 6.5 Hz, 2H), 3.17 (d, J = 9.0 Hz, 1H), 2.28−2.21 (m, 1H), 2.13−2.01 (m, 3H), 1.68−1.60 (m, 6H), 1.51 (s, 1H), 1.42 (s, 1H), 1.38−1.30 (m, 1H), 0.90 (s 9H). ^{13}C NMR (151 MHz): δ 135.9, 124.2, 79.6, 62.5, 37.2, 34.9, 32.7, 29.5, 25.8, 24.3, 15.9. HRMS (ESI): m/z calcd for ($C_{13}H_{26}O_2Na$ [M + H]$^+$) 237.1831, found 237.1832.

*1c. Synthesis of Diol Substrate **4e** from Aldehyde intermediate **S6**. Ethyl (E)-10-((tert-Butyldiphenylsilyl)oxy)-3-hydroxy-6-methyldec-6-enoate (**S12**).* In a 25 mL round-bottom flask, LDA was freshly prepared in THF (2 mL) at 0 °C from diisopropylamine (54 μL, 0.38 mmol, 1.5 equiv) and nBuLi (2.5 M in hexane, 0.15 mL, 0.38 mmol, 1.5 equiv). The flask was cooled to −78 °C, and EtOAc (50 μL, 0.38 mmol, 2 equiv) as a solution in THF (0.5 mL) was added dropwise with stirring. The solution was stirred at −78 °C for 30 min, and aldehyde **S6** (100 mg, 0.25 mmol) was added as a solution in THF (1 mL). Stirring was continued until complete conversion had occurred as judged by TLC. The mixture was quenched at −78 °C with the addition of satd aq NH_4Cl (5 mL). The mixture was extracted with Et_2O (3 × 10 mL), dried ($MgSO_4$), filtered, and concentrated by rotary evaporation to afford the crude product as a yellow oil. Purification by silica flash chromatography (4:1 hexanes/EtOAc) yielded **S12** (120 mg, 0.25 mmol, 98%) as a yellow oil. IR (neat) (cm^{-1}): 3712−3113, 2932, 2858, 1723, 1427, 1185, 1106, 821, 734, 701, 612. ^{1}H NMR (600 MHz): δ 7.67 (d, J = 6.6 Hz, 4H), 7.45−7.33 (m, 6H), 5.14 (t, 7.2 Hz, 1H), 4.16 (q, J = 7.1 Hz, 2H), 4,00−3.95 (m, 1H), 3.65 (t, J = 6.2 Hz, 2H), 2.99 (s, 1H), 2.49 (dd, J = 16.3, 3.3 Hz, 1H), 2.41 (dd, J = 16.3, 8.9 Hz, 1H), 2.18−2.00 (m, 4H), 1.63−1.55 (m, 6H), 1.55−1.48 (m, 1H), 1.27 (t, J = 7.2 Hz, 2H), 1.05 (s, 9H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 173.0, 135.5, 134.8, 134.0, 129.5, 127.6, 124.6, 67.8, 63.4, 60.6, 41.3, 35.6, 34.7, 32.7, 26.8, 24.2, 19.2, 15.9, 14.2. HRMS (ESI): m/z calcd for ($C_{29}H_{42}O_4NaSi$ [M + H]$^+$) 505.2750, found 505.2746.

*Ethyl (E)-3,10-Dihydroxy-6-methyldec-6-enoate (**4e**).* In a 10 mL round-bottom flask, protected alcohol **S12** (75 mg, 0.16 mmol) was dissolved in THF (2 mL) at rt. TBAF (1.0 M in THF, 0.31 mL, 0.31 mmol, 2 equiv) was added, and the solution was stirred until complete conversion had occurred as judged by TLC. The reaction mixture was concentrated by rotary evaporation. Purification by silica flash chromatography (1:1 hexanes/EtOAc) yielded diol **4e** (33 mg, 0.14 mmol, 86%) as a colorless oil. IR (neat) (cm^{-1}): 3640−3131, 2931, 1721, 1375, 1299, 1185, 1156, 1031, 879, 731. ^{1}H NMR (600 MHz): δ 5.20 (t, J = 7.3 Hz, 1H), 4.17 (q, J = 7.2 Hz, 2H), 4.03−3.94 (m, 1H), 3.64 (t, J = 6.5 Hz, 2H), 3.03 (s, 1H), 2.55−2.37 (m, 2H), 2.18−2.11 (m, 1H), 2.08 (q, J = 7.0 Hz, 3H), 1.67−1.59 (m, 7H), 1.58−1.49 (m, 1H), 1.28 (t, J = 7.1 Hz, 3H). ^{13}C NMR (151 MHz): δ 173.0, 135.2, 124.4, 67.7, 62.6, 60.7, 41.3, 35.6, 34.6, 32.6, 24.3, 15.9, 14.2. HRMS (ESI): m/z calcd for ($C_{13}H_{24}O_4Na$ [M + Na]$^+$) 267.1572, found 267.1568.

*1d. Synthesis of Triol Substrate **4f** from Geranyl Bromide. Dimethyl (E)-2-(3,7-Dimethylocta-2,6-dien-1-yl)malonate (**S13**).* In a 100 mL round-bottom flask, K_2CO_3 (2.55 g, 18.4 mmol, 2 equiv) was added, followed by a solution of geranyl bromide (2.00 g, 9.21 mmol) dissolved in DMF (40 mL). Dimethyl malonate (1.27 mL, 11.1 mmol, 1.2 equiv) was added and the solution stirred at rt until complete conversion had occurred as judged by TLC. The mixture was diluted with H_2O (50 mL) and extracted with Et_2O (3 × 20 mL). The combined organic layers were washed with H_2O (2 × 20 mL) and brine (20 mL), dried ($MgSO_4$), filtered, and concentrated by rotary evaporation to afford the crude product as a colorless oil. Purification by silica flash chromatography (9:1 hexanes/EtOAc) yielded diester **S13** (1.86 g, 6.93 mmol, 75%) as a yellow oil. IR (neat) (cm^{-1}): 2956, 2917, 1737, 1437, 1338, 1272, 1237, 1201, 1150, 1026, 687. ^{1}H NMR (600 MHz): δ 5.06 (q, J = 6.7 Hz, 2H), 3.73 (s, 6H), 3.38 (t, J = 7.7 Hz, 1H), 2.61 (t, J = 7.5 Hz, 2H), 2.04 (t, 2H), 1.98 (d, J = 6.2 Hz, 1H), 1.67 (s, 3H), 1.63 (s, 3H), 1.59 (s, 3H). ^{13}C NMR (151 MHz): δ 169.6, 166.9, 138.7, 131.5, 124.0, 119.4, 52.6, 52.4, 51.9, 41.1, 39.7, 27.6, 26.5, 25.7, 17.7, 16.0. HRMS (ESI): m/z calcd for ($C_{15}H_{24}O_4Na$ [M + Na]$^+$) 291.1572, found 291.1521.

*Methyl (E)-5,9-Dimethyldeca-4,8-dienoate (**S14**).* In a 50 mL round-bottom flask, LiCl (750 mg, 17.7 mmol, 5 equiv) was added, followed by a solution of diester **S13** (950 mg, 3.54 mmol) dissolved in DMSO (15 mL). The solution was heated to 150 °C until complete conversion had occurred as judged by TLC. The mixture was diluted with H_2O (20 mL) and extracted with Et_2O (3 × 20 mL). The combined organic layers were washed with H_2O (20 mL) and brine (20 mL), dried ($MgSO_4$), filtered, and concentrated by rotary evaporation to afford the crude product as a colorless oil. Purification by silica flash chromatography (9:1 hexanes/EtOAc) yielded ester **S14** (725 mg, 3.45 mmol, 97%) as a yellow oil. IR (neat) (cm^{-1}): 2919, 1739, 1437, 1162. ^{1}H NMR (500 MHz): δ 5.14−5.03 (m, 2H), 3.67 (s, 3H), 2.38−2.28 (m, 4H), 2.11−2.02 (m, 2H), 1.98 (t, J = 8.9 Hz, 2H), 1.68 (s, 3H), 1.62 (s, 3H), 1.60 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 173.8, 136.7, 131.4, 124.1, 122.2, 51.4, 39.6, 34.3, 26.6, 25.6, 23.5, 17.7, 15.9. HRMS (ESI): m/z calcd for ($C_{13}H_{22}O_2Na$ [M + Na]$^+$) 233.1517, found 233.1515.

*(E)-5,9-Dimethyldeca-4,8-dien-1-ol (**S15**).* In a 100 mL round-bottom flask, ester **S14** (700 mg, 3.33 mmol) was dissolved in THF (50 mL), and the solution was cooled to 0 °C. $LiAlH_4$ (126 mg, 3.33 mmol, 1 equiv) was added slowly and the solution stirred at 0 °C until complete conversion had occurred as judged by TLC. The mixture was carefully quenched with 1 M HCl (25 mL). The mixture was extracted with Et_2O (3 × 10 mL), dried ($MgSO_4$), filtered, and concentrated by rotary evaporation to afford the crude product as a colorless oil. Purification by silica flash chromatography (4:1 hexanes/EtOAc) yielded **S15** (580 mg, 3.18 mmol, 96%) as a colorless oil. IR (neat) (cm^{-1}): 3699−3125, 2924, 1723, 1449, 1379, 1055, 909, 732. ^{1}H NMR (600 MHz): δ 5.14 (t, J = 6.4 Hz, 1H), 5.09 (t, J = 5.8 Hz, 1H), 3.64 (t, J = 6.5 Hz, 2H), 2.12−2.04 (m, 4H), 1.99 (d, J = 6.3 Hz, 2H), 1.68 (s, 3H), 1.65−1.59 (m, 8H). ^{13}C NMR (151 MHz): δ 135.8, 131.4, 124.3, 123.8, 68.0, 62.7, 39.7, 32.7, 26.6, 25.7, 25.7, 25.6, 24.3, 17.7, 16.0. HRMS (ESI): m/z calcd for ($C_{12}H_{23}O$ [M + H]$^+$) 183.1749, found 183.1751.

*(S,E)-5,9-Dimethyldec-4-ene-1,8,9-triol (**4f**).* In a 100 mL round-bottom flask, diene **S15** (500 mg, 2.74 mmol) was dissolved in t-BuOH/H_2O (1:1, 50 mL), and the solution was cooled to 0 °C. AD mix-α (3.85 g, 1.4 g/mol) was added, and the solution was stirred at 0 °C until complete conversion had occurred as judged by TLC. The reaction was diluted with H_2O (50 mL) and extracted with Et_2O (3 × 25 mL), and the organic layers were pooled washed with 10% HCl (10 mL), brine (10 mL), and dried ($MgSO_4$), filtered, and concentrated by rotary evaporation to afford the crude product as a colorless oil. Purification by silica flash chromatography (1:1 hexanes/EtOAc) yielded **4f** (220 mg, 1.02 mmol, 37%) as a colorless oil. IR (neat) (cm^{-1}): 3682−3112, 2932, 2858, 1739, 1384, 1108, 821, 737, 700, 612. ^{1}H NMR (600 MHz): δ 5.24 (d, J = 6.8 Hz, 1H), 3.66 (t, J = 6.5 Hz, 2H), 3.38−3.32 (m, 1H), 2.30−2.21 (m, 2H), 2.14−2.03 (m, 4H), 1.70−1.55 (m, 8H), 1.47−1.36 (m, 1H), 1.21 (s, 3H), 1.16 (s, 3H). ^{13}C NMR (151 MHz): δ 124.6, 78.2, 73.0, 62.7, 36.8, 32.6, 29.6, 26.4, 24.3, 23.2, 15.9. HRMS (ESI): m/z calcd for ($C_{12}H_{24}O_3Na$ [M + Na]$^+$) 239.1623, found 239.1615.

*1e. Synthesis of Diol Substrates **4g,h** from Ester Intermediate **S4**. (E)-9-((tert-Butyldiphenylsilyl)oxy)-2,5-dimethylnon-5-en-2-ol (**S16**).* In a 25 mL round-bottom flask, ester **S4** (200 mg, 0.46 mmol) was dissolved in THF (5 mL), and the solution was cooled to 0 °C. MeMgBr (1.0 M in THF, 1.00 mL, 1.00 mmol, 2.2 equiv) was added dropwise with stirring. Once addition was complete, the solution was

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allowed to warm to rt, and stirring was continued until complete conversion had occurred as judged by TLC. The mixture was quenched with 1 M HCl (5 mL), extracted with Et_2O (3 × 5 mL), dried ($MgSO_4$), filtered, and concentrated by rotary evaporation to afford the crude product as a yellow oil. Purification by silica flash chromatography (4:1 hexanes/EtOAc) yielded alcohol **S16** (110 mg, 0.45 mmol, 98%) as a colorless oil. IR (neat) (cm^{-1}): 3695−3115, 2965, 2936, 2862, 1473, 1431, 1110, 912, 826, 736, 705, 616. ^1H NMR (600 MHz): δ 7.67 (d, J = 6.8 Hz, 4H), 7.45−7.33 (m, 6H), 5.15 (d, J = 5.7 Hz, 1H), 3.65 (t, J = 6.3 Hz, 2H), 2.11−1.99 (m, 4H), 1.64−1.57 (m, 5H), 1.57−1.51 (m, 2H), 1.34 (s, 1H), 1.22 (s, 8H), 1.05 (d, J = 2.2 Hz, 9H). ^{13}C NMR (151 MHz): δ 135.7, 135.6, 129.5, 127.6, 124.1, 71.1, 63.4, 42.0, 34.4, 32.6, 29.2, 26.8, 24.2, 19.2, 16.1. HRMS (ESI): m/z calcd for ($C_{27}H_{41}O_2Si$ [M + H]$^+$) 425.2876, found 425.2876.

*(E)-5,8-Dimethylnon-4-ene-1,8-diol (**4g**).* In a 10 mL round-bottom flask, protected alcohol **S22** (180 mg, 0.42 mmol) was dissolved in THF (2 mL) at rt. TBAF (1.0 M in THF, 0.85 mL, 0.85 mmol, 2 equiv) was added, and the solution was stirred until complete conversion had occurred as judged by TLC. The reaction mixture was concentrated by rotary evaporation. Purification by silica flash chromatography (1:1 hexanes/EtOAc) yielded diol **4g** (55 mg, 0.30 mmol, 69%) as a colorless oil. IR (neat) (cm^{-1}): 3727−3067, 2884, 1657, 1321, 1189, 1123, 1060, 966, 925. ^1H NMR (600 MHz): δ 5.20 (t, J = 7.2 Hz, 1H), 3.64 (t, J = 6.5 Hz, 2H), 2.13−2.04 (m, 4H), 1.64 (s, 3H), 1.63−1.60 (m, 2H), 1.60−1.55 (m, 2H), 1.23 (s, 6H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 136.2, 123.8, 71.1, 62.6, 41.9, 34.5, 32.7, 29.2, 24.3, 16.1. HRMS (ESI): m/z calcd for ($C_{11}H_{22}O_2Na$ [M + Na]$^+$) 209.1517, found 209.1518.

*(E)-8-((tert-Butyldiphenylsilyl)oxy)-4-methyl-1,1-diphenyloct-4-en-1-ol (**S17**).* In a 25 mL round-bottom flask, ester **S4** (200 mg, 0.45 mmol) was dissolved in THF (5 mL), and the solution was cooled to 0 °C. PhMgBr (1.0 M in THF, 1.00 mL, 1.00 mmol, 2.2 equiv) was added dropwise with stirring. Once addition was complete, the solution was allowed to warm to rt, and stirring was continued until complete conversion had occurred as judged by TLC. The mixture was quenched with 1 M HCl (5 mL), extracted with Et_2O (3 × 5 mL), dried ($MgSO_4$), filtered, and concentrated by rotary evaporation to afford the crude product as a yellow oil. Purification by silica flash chromatography (4:1 hexanes/EtOAc) yielded alcohol **S17** (220 mg, 0.40 mmol, 88%) as a colorless oil. IR (neat) (cm^{-1}): 3712−3254, 3068, 2931, 2858, 1592, 1187, 1107, 1003, 909, 822, 733, 698, 612. ^1H NMR (600 MHz): δ 7.69−7.63 (m, 4H), 7.46−7.23 (m, 14H), 7.26−7.18 (m, 2H), 5.08 (d, J = 7.1 Hz, 1H), 3.64 (t, J = 6.4 Hz, 2H), 2.39−2.34 (m, 2H), 2.06 (d, J = 7.4 Hz, 2H), 2.00−1.94 (m, 2H), 1.60 (s, 3H), 1.59−1.54 (m, 2H), 1.04 (s, 9H). ^{13}C NMR (151 MHz): δ 147.0, 135.5, 134.0, 129.5, 128.1, 127.5, 126.7, 125.9, 124.5, 78.5, 63.3, 40.0, 33.9, 32.6, 26.8, 24.2, 19.2, 16.2. HRMS (ESI): m/z calcd for ($C_{37}H_{44}O_2SiNa$ [M + Na]$^+$) 571.3008, found 571.3000.

*(E)-4-Methyl-1,1-diphenyloct-4-ene-1,8-diol (**4h**).* In a 10 mL round-bottom flask, protected alcohol **S17** (200 mg, 0.36 mmol) was dissolved in THF (2 mL) at rt. TBAF (1.0 M in THF, 0.73 mL, 0.73 mmol, 2 equiv) was added, and the solution was stirred until complete conversion had occurred as judged by TLC. The reaction mixture was concentrated by rotary evaporation. Purification by silica flash chromatography (1:1 hexanes/EtOAc) yielded diol **4h** (85 mg, 0.27 mmol, 75%) as a colorless oil. IR (neat) (cm^{-1}): 3709−3128, 2934, 2862, 1717, 1492, 1447, 1057, 1032, 944, 698. ^1H NMR (600 MHz): δ 7.42 (d, J = 6.6 Hz, 4H), 7.31 (t, J = 7.0 Hz, 4H), 7.22 (t, J = 7.3 Hz, 2H), 5.14 (t, J = 7.2 1H), 3.63 (t, J = 6.5 Hz, 2H), 2.43−2.36 (m, 2H), 2.06 (q, J = 7.3 Hz, 2H), 1.99 (dd, J = 9.9, 6.2 Hz, 2H), 1.65−1.56 (m, 5H). ^{13}C NMR (151 MHz): δ 146.9, 136.1, 128.1, 126.8, 126.0, 124.2, 78.5, 62.6, 40.0, 34.0, 32.6, 24.2, 16.2. HRMS (ESI): m/z calcd for ($C_{21}H_{26}O_2Na$ [M + Na]$^+$) 333.1831, found 333.1840.

*1f. Synthesis of Diol Substrate **4i** from 3-Buten-1-ol. (But-3-en-1-yloxy)(tert-butyl)diphenylsilane (**S18**).* In a 250 mL round-bottom flask, 3-buten-1-ol (1.00 g, 13.9 mmol) and imidazole (944 mg, 13.9 mmol, 2 equiv) were dissolved in CH_2Cl_2 (15 mL), and the solution was cooled to 0 °C. TBDPSCl (3.60 mL, 13.9 mmol, 1 equiv) was added slowly with stirring. The solution was allowed to warm to rt and stirred until complete conversion had occurred as judged by TLC. The mixture was quenched with 1 M HCl (10 mL) and extracted with CH_2Cl_2 (3 × 10 mL), dried ($MgSO_4$), filtered, and concentrated by rotary evaporation to afford the crude product as a colorless oil (4.24 g, 98%) that was taken onto the next step without further purification. IR (neat) (cm^{-1}): 2928, 2361, 1558, 1427, 1105, 822, 737, 700, 613. ^1H NMR (600 MHz): δ 7.76−7.62 (m, 4H), 7.48−7.31 (m, 6H), 5.91−5.76 (m, 1H), 5.10−4.97 (m, 2H), 3.71 (t, J = 6.7 Hz, 2H), 2.32 (q, J = 7.1, 6.3 Hz, 2H), 1.05 (s, 9H). ^{13}C NMR (151 MHz): δ 135.6, 135.4, 133.9, 129.5, 127.6, 116.3, 63.5, 37.2, 26.8, 19.2. HRMS (ESI): m/z calcd for ($C_{20}H_{27}OSi$ [M + H]$^+$) 311.1831, found 311.1821.

*3-((tert-Butyldiphenylsilyl)oxy)propanal (**S19**).* In a 250 mL round-bottom flask, alkene **S18** (1.50 g, 4.83 mmol) was dissolved in CH_2Cl_2 (50 mL), and the solution was cooled to −78 °C. Ozone was bubbled through the solution until the blue color was persistent. The stream of ozone was replaced with oxygen until the blue color dissipated, and then the reaction was quenched with triphenylphosphine (1.58 g, 6.04 mmol, 1.25 equiv), allowed to slowly warm to rt, and stirred for 0.5 h. The solution was concentrated by rotary evaporation to afford the crude product as a yellow oil. Purification by silica flash chromatography (9:1 hexanes/EtOAc) yielded aldehyde **S19** (1.40 g, 4.48 mmol, 92%) as a colorless oil. IR (neat) (cm^{-1}): 2959, 2934, 2724, 1729, 1470, 1426, 1095, 824, 745, 702, 613. ^1H NMR (600 MHz): δ 9.81 (t, J = 2.2 Hz, 1H), 7.69−7.63 (m, 4H), 7.47−7.36 (m, 6H), 4.02 (t, J = 6.0 Hz, 2H), 2.60 (td, J = 6.0, 2.2 Hz, 2H), 1.04 (s, 9H). ^{13}C NMR (151 MHz): δ 201.9, 135.5, 133.2, 129.8, 127.7, 58.3, 46.4, 26.7, 19.1. HRMS (ESI): m/z calcd for ($C_{19}H_{24}O_2NaSi$ [M + H]$^+$) 335.1443, found 335.1447.

*5-((tert-Butyldiphenylsilyl)oxy)-2-methylpent-1-en-3-ol (**S20**).* In a 25 mL round-bottom flask, aldehyde **S19** (1.00 g, 3.20 mmol) was dissolved in THF (5 mL), and the solution was cooled to 0 °C. Isopropenylmagnesium bromide (1.0 M in THF, 6.40 mL, 3.20 mmol, 1 equiv) was added slowly. Once the addition was complete, the cooling bath was removed, and the solution was stirred at rt until complete conversion had occurred as judged by TLC. The mixture was recooled to 0 °C and quenched with 1 M HCl (10 mL). The mixture was extracted with Et_2O (3 × 10 mL), dried ($MgSO_4$), filtered, and concentrated by rotary evaporation to afford the crude product as a yellow oil. Purification by silica flash chromatography (4:1 hexanes/EtOAc) yielded allylic alcohol **S20** (1.10 g, 3.10 mmol, 96%) as a yellow oil. IR (neat) (cm^{-1}): 3699−3144, 3053, 2937, 2779, 1720, 1431, 1111, 873, 743 706, 648. ^1H NMR (600 MHz): δ 7.68 (d, J = 7.0 Hz, 4H), 7.49−7.34 (m, 6H), 5.05 (s, 1H), 4.86 (s, 1H), 4.34 (dd, J = 7.1, 4.6 Hz, 1H), 3.91−3.85 (m, 1H), 3.81 (d, J = 3.2 Hz, 1H), 3.22 (s, 1H), 1.83−1.77 (m, 2H), 1.72 (s, 3H), 1.06 (s, 9H). ^{13}C NMR (151 MHz): δ 147.0, 135.5, 133.0, 129.8, 127.7, 110.5, 74.8, 62.8, 36.8, 26.8, 19.0, 18.3. HRMS (ESI): m/z calcd for ($C_{22}H_{31}O_2Si$ [M + H]$^+$) 355.2093, found 355.2083.

*Ethyl (E)-7-((tert-Butyldiphenylsilyl)oxy)-4-methylhept-4-enoate (**S21**).* In a 25 mL round-bottom flask, allylic alcohol **S20** (1.00 g, 2.82 mmol), triethyl orthoacetate (5 mL), and propionic acid (20 μL, 0.28 mmol, 0.1 equiv) were added. The flask was equipped with a distillation head and heated to 140 °C during which time ethanol was collected. Heating was continued at this temperature until complete conversion had occurred as judged by TLC. The mixture was cooled to rt and quenched with 1 M HCl (10 mL). The mixture was extracted with Et_2O (3 × 10 mL), washed with 1 M NaOH (10 mL), dried ($MgSO_4$), filtered, and concentrated by rotary evaporation to afford the crude product as a yellow oil. Purification by silica flash chromatography (9:1 hexanes/EtOAc) yielded ester **S21** (820 mg, 68%) as a colorless oil. IR (neat) (cm^{-1}): 2957, 2900, 1735, 1445, 1107, 701, 612. ^1H NMR (600 MHz): δ 7.71−7.63 (m, 4H), 7.45−7.35 (m, 6H), 5.15 (t, J = 7.2 Hz, 1H), 4.10 (q, J = 7.1 Hz, 2H), 3.62 (t, J = 7.0 Hz, 2H), 2.37 (d, J = 7.2 Hz, 2H), 2.34−2.22 (m, 4H), 1.56 (s, 3H), 1.22 (t, J = 7.1 Hz, 3H), 1.04 (h, 9H). ^{13}C NMR (151 MHz): δ 173.5, 135.6, 135.3, 134.0, 129.5, 127.6, 121.2, 63.6, 60.2, 34.7, 33.1, 31.5, 26.8, 19.2, 16.0, 14.2. HRMS (ESI): m/z calcd for ($C_{26}H_{36}O_3NaSi$ [M + Na]$^+$) 447.2331, found 447.2312.

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*(E)-7-((tert-Butyldiphenylsilyl)oxy)-4-methylhept-4-en-1-ol (**S22**).* In a 25 mL round-bottom flask, ester **S21** (500 mg, 1.18 mmol) was dissolved in THF (10 mL), and the solution was cooled to 0 °C. $LiAlH_4$ (45 mg, 1.18 mmol, 1 equiv) was added slowly and the solution stirred at 0 °C until complete conversion had occurred as judged by TLC. The mixture was carefully quenched with 1 M HCl (5 mL). The mixture was extracted with Et_2O (3 × 10 mL), dried ($MgSO_4$), filtered, and concentrated by rotary evaporation to afford the crude product as a colorless oil. Purification by silica flash chromatography (4:1 hexanes/EtOAc) yielded alcohol **S22** (405 mg, 1.06 mmol, 89%) as a colorless oil. IR (neat) (cm^{-1}): 3670−3134, 2893, 2858, 1470, 1170, 1087, 821, 804, 735, 700, 611. ^1H NMR (600 MHz, Chloroform-*d*) δ 7.70−7.65 (m, 4H), 7.44−7.34 (m, 6H), 5.17 (t, J = 6.7 Hz, 1H), 3.64 (t, J = 7.0 Hz, 2H), 3.59 (t, J = 6.5 Hz, 2H), 2.27 (q, J = 7.2 Hz, 2H), 2.04 (t, J = 7.4 Hz, 2H), 1.64 (quint, J = 6.7 Hz, 2H), 1.56 (s, 3H), 1.05 (s, 9H). ^{13}C NMR (151 MHz): δ 136.6, 135.6, 134.0, 129.5, 127.6, 120.8, 63.7, 62.7, 36.0, 31.5, 30.7, 26.8, 19.2, 16.0. HRMS (ESI): m/z calcd for ($C_{24}H_{35}O_2Si$ [M + H]$^+$) 383.2406, found 383.2422.

*(E)-7-((tert-Butyldiphenylsilyl)oxy)-4-methylhept-4-enal (**S23**).* In a 25 mL round-bottom flask, alcohol **S22** (250 mg, 0.65 mmol) was dissolved in CH_2Cl_2 (10 mL). PCC (140 mg, 0.65 mmol, 2 equiv) was added, and the solution was stirred at rt until complete conversion had occurred as judged by TLC. The mixture was filtered through a pad of silica with hexane/EtOAc 9:1 and concentrated by rotary evaporation to afford aldehyde **S23** (225 mg, 0.59 mmol, 90%) as a colorless oil. IR (neat) (cm^{-1}): 316, 3050, 2933, 2883, 1468, 1108, 1005, 858, 702, 647, 611. ^1H NMR (600 MHz): δ 9.73 (t, J = 1.9 Hz, 1H), 7.67 (dd, J = 8.0, 1.5 Hz, 4H), 7.44−7.34 (m, 6H), 5.16 (td, J = 7.2, 1.3 Hz, 1H), 3.63 (t, J = 6.9 Hz, 2H), 2.48 (td, J = 7.6, 1.9 Hz, 2H), 2.32−2.23 (m, 4H), 1.57 (s, 3H), 1.04 (s, 9H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 202.5, 135.7, 134.9, 133.9, 129.5, 127.8, 121.6, 63.5, 42.2, 31.8, 31.5, 27.5, 26.8, 26.8, 19.2, 16.2. HRMS (ESI): m/z calcd for ($C_{24}H_{33}O_2Si$ [M + H]$^+$) 381.2250, found 381.2234.

*(E)-7-((tert-Butyldiphenylsilyl)oxy)-4-methyl-1-phenylhept-4-en-1-ol (**S24**).* In a 25 mL round-bottom flask, aldehyde **S23** (200 mg, 0.52 mmol) was dissolved in THF (5 mL), and the solution was cooled to 0 °C. PhMgBr (1.0 M in THF, 0.66 mL, 0.66 mmol, 1.25 equiv) was added dropwise with stirring. Once addition was complete, the solution was allowed to warm to rt, and stirring was continued until complete conversion had occurred as judged by TLC. The mixture was quenched with 1 M HCl (5 mL), extracted with Et_2O (3 × 5 mL), dried ($MgSO_4$), filtered, and concentrated by rotary evaporation to afford the crude product as a yellow oil. Purification by silica flash chromatography (4:1 hexanes/EtOAc) yielded **S24** (220 mg, 0.47 mmol, 91%) as a colorless oil. IR (neat) (cm^{-1}): 3735−3131, 3050, 2931, 2893, 1892, 1822, 1724, 1108, 1086, 701, 612. ^1H NMR (600 MHz): δ 7.69−7.64 (m, 4H), 7.43−7.31 (m, 10H), 7.29−7.24 (m, 1H), 5.15 (t, J = 7.7, 6.8 Hz, 1H), 4.63 (t, J = 6.8, 6.0 Hz, 1H), 3.63 (t, J = 7.0 Hz, 2H), 2.26 (q, J = 7.1 Hz, 2H), 2.13−2.06 (m, 1H), 2.03−1.96 (m, 1H), 1.92−1.83 (m, 2H), 1.83−1.75 (m, 1H), 1.55 (s, 3H), 1.04 (s, 9H). ^{13}C NMR (151 MHz): δ 144.7, 136.5, 135.6, 134.0, 129.5, 128.4, 127.6, 125.9, 120.9, 115.2, 74.3, 63.7, 37.1, 35.9, 31.5, 26.8, 19.2, 16.1. HRMS (ESI): m/z calcd for ($C_{30}H_{38}O_2NaSi$ [M + Na]$^+$) 489.2539, found 489.2529.

*(E)-4-Methyl-7-phenylhept-3-ene-1,7-diol (**4i**).* In a 10 mL round-bottom flask, protected alcohol **S24** (150 mg, 0.33 mmol) was dissolved in THF (2 mL) at rt. TBAF (1.0 M in THF, 0.66 mL, 0.66 mmol, 2 equiv) was added and the solution was stirred until complete conversion had occurred as judged by TLC. The reaction mixture was concentrated by rotary evaporation. Purification by silica flash chromatography (1:1 hexanes/EtOAc) yielded diol **4i** (50 mg, 0.23 mmol, 69%) as a colorless oil. IR (neat) (cm^{-1}): 3722−3124, 2936, 2863, 1812, 1491, 1059, 1025, 760, 700, 613. ^1H NMR (600 MHz): δ 7.37−7.30 (m, 4H), 7.29−7.24 (m, 1H), 5.16 (t, J = 7.6 Hz, 1H), 4.63 (dd, J = 7.9, 5.1 Hz, 1H), 3.58 (t, J = 6.7, 5.6 Hz, 2H), 2.30−2.21 (m, 2H), 2.18−2.10 (m, 1H), 2.09−2.00 (m, 1H), 1.93−1.85 (m, 1H), 1.84−1.76 (m, 1H), 1.63 (s, 3H). ^{13}C NMR (151 MHz): δ 144.8, 138.1, 128.4, 127.5, 125.9, 120.5, 74.2, 62.3, 37.1, 36.1, 31.4, 16.2. HRMS (ESI): m/z calcd for ($C_{14}H_{20}O_2Na$ [M + Na]$^+$) 243.1361, found 243.1363.

*1g. Synthesis of Diol Substrate **4j** from 5-Hexen-1-ol. tert-Butyl(hex-5-en-1-yloxy)diphenylsilane (**S25**).* In a 250 mL round-bottom flask, 5-hexen-1-ol (1.00 g, 9.98 mmol) and imidazole (1.36 g, 20.0 mmol, 2 equiv) were dissolved in CH_2Cl_2 (10 mL), and the solution was cooled to 0 °C. TBDPSCl (2.60 mL, 9.98 mmol, 1 equiv) was added slowly with stirring. The solution was allowed to warm to rt and stirred until complete conversion had occurred as judged by TLC. The mixture was quenched with 1 M HCl (10 mL) and extracted with CH_2Cl_2 (3 × 10 mL), dried ($MgSO_4$), filtered, and concentrated by rotary evaporation to afford the crude product **S25** as a colorless oil (3.21 g, 95%) that was carried onto the next step without need for further purification. IR (neat) (cm^{-1}): 2929, 2857, 2361, 2337, 1558, 1427, 1105, 822, 700, 614. ^1H NMR (600 MHz): δ 7.70−7.64 (m, 4H), 7.44−7.34 (m, 6H), 5.79 (ddt, J = 16.9, 10.2, 6.6 Hz, 1H), 5.01−4.89 (m, 2H), 3.66 (t, J = 6.4 Hz, 2H), 2.03 (t, J = 7.2 Hz, 2H), 1.58 (quint, J = 6.9 Hz, 2H), 1.46 (quint, J = 7.8 Hz, 2H), 1.05 (s, 9H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 138.9, 135.6, 134.1, 129.5, 127.6, 114.3, 63.7, 33.5, 32.0, 26.8, 25.1, 19.2. HRMS (ESI): m/z calcd for ($C_{22}H_{31}OSi$ [M + H]$^+$) 339.2144, found 339.2132.

*5-((tert-Butyldiphenylsilyl)oxy)pentanal (**S26**).* In a 250 mL round-bottom flask, alkene **S25** (1.50 g, 4.43 mmol) was dissolved in CH_2Cl_2 (50 mL), and the solution was cooled to −78 °C. Ozone was bubbled through the solution until the blue color was persistent. The stream of ozone was replaced with oxygen until the blue color dissipated, then the reaction was quenched with triphenylphosphine (1.45 g, 5.54 mmol, 1.25 equiv), allowed to slowly warm to rt, and stirred for 0.5 h. The solution was concentrated by rotary evaporation to afford the crude product as a yellow oil. Purification by silica flash chromatography (9:1 hexanes/EtOAc) yielded aldehyde S26 (1.38 g, 4.05 mmol, 91%) as a colorless oil. IR (neat) (cm^{-1}): 2934, 2858, 2723, 1729, 1426, 1097, 1008, 702, 612. ^1H NMR (600 MHz): δ 9.74 (t, J = 1.8 Hz, 1H), 7.66 (dd, J = 8.0, 1.5 Hz, 4H), 7.44−7.36 (m, 6H), 3.67 (t, J = 6.2 Hz, 2H), 2.41 (td, J = 7.4, 1.8 Hz, 2H), 1.73 (quint, J = 7.4 Hz, 2H), 1.62−1.56 (m, 2H), 1.05 (s, 9H). ^{13}C NMR (151 MHz): δ 202.7, 135.5, 133.8, 129.6, 127.6, 127.6, 63.3, 43.5, 31.8, 26.8, 19.2, 18.5. HRMS (ESI): m/z calcd for ($C_{21}H_{28}O_2SiNa$ [M + Na]$^+$) 363.1757, found 363.1795.

*7-((tert-Butyldiphenylsilyl)oxy)-2-methylhept-1-en-3-ol (**S27**).* In a 25 mL round-bottom flask, aldehyde S26 (1.00 g, 2.94 mmol) was dissolved in THF (5 mL), and the solution was cooled to 0 °C. Isopropenylmagnesium bromide (1.0 M in THF, 5.87 mL, 2.94 mmol, 1 equiv) was added slowly. Once addition was complete, the cooling bath was removed, and the solution was allowed to stir at rt until complete conversion had occurred as judged by TLC. The mixture was recooled to 0 °C and quenched with 1 M HCl (10 mL). The mixture was extracted with Et_2O (3 × 10 mL), dried ($MgSO_4$), filtered, and concentrated by rotary evaporation to afford the crude product as a yellow oil. Purification by silica flash chromatography (4:1 hexanes/EtOAc) yielded allylic alcohol S27 (1.12 g, 2.93 mmol, 99%) as a yellow oil. IR (neat) (cm^{-1}): 3709−3167, 2933, 2859, 1710, 1469, 1427, 1107, 1000, 937, 898, 822, 739, 701, 612. ^1H NMR (600 MHz): δ 7.66 (d, J = 6.8 Hz, 2H), 7.45−7.33 (m, 8H), 4.92 (s, 1H), 4.82 (s, 1H), 4.03 (t, J = 6.5 Hz, 1H), 3.66 (t, J = 6.5 Hz, 2H), 1.70 (s, 3H), 1.64−1.56 (m, 2H), 1.56−1.48 (m, 2H), 1.48−1.40 (m, 1H), 1.40−1.30 (m, 1H), 1.04 (s, 9H). ^{13}C NMR (151 MHz): δ 147.5, 135.5, 134.02, 129.5, 127.6, 111.0, 75.9, 63.8, 34.6, 32.4, 26.8, 26.8, 21.8, 19.2, 17.4. HRMS (ESI): m/z calcd for ($C_{24}H_{34}O_2NaSi$ [M + Na]$^+$) 405.2226, found 405.2217.

*Ethyl (E)-9-((tert-Butyldiphenylsilyl)oxy)-4-methylnon-4-enoate (**S28**).* In a 25 mL round-bottom flask, allylic alcohol **S27** (1.00 g, 2.61 mmol), triethyl orthoacetate (5 mL), and propionic acid (20 μL, 0.26 mmol, 0.1 equiv) were added. The flask was equipped with a distillation head and heated to 140 °C during which time ethanol was collected. Heating was continued at this temperature until complete conversion had occurred as judged by TLC. The mixture was cooled to rt and quenched with 1 M HCl (5 mL). The mixture was extracted with Et_2O (3 × 5 mL), washed with 1 M NaOH (5 mL), dried ($MgSO_4$), filtered, and concentrated by rotary evaporation to afford the

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crude product as a yellow oil. Purification by silica flash chromatography (9:1 hexanes/EtOAc) yielded ester **S28** (0.85 g, 1.88 mmol, 71%) as a colorless oil. IR (neat) (cm^{-1}): 3051, 2929, 2857, 2775, 2337, 2270, 1735, 1372, 822, 667, 615. ^1H NMR (600 MHz): δ 7.67 (dd, J = 8.0, 1.5 Hz, 4H), 7.44−7.34 (m, 6H), 5.16−5.11 (m, 1H), 4.11 (q, J = 7.1 Hz, 2H), 3.65 (t, J = 6.4 Hz, 2H), 2.41−2.37 (m, 2H), 2.29 (dd, J = 9.2, 6.4 Hz, 2H), 1.96 (q, J = 7.3 Hz, 2H), 1.58 (s, 3H), 1.58−1.51 (m, 2H), 1.44−1.36 (m, 2H), 1.24 (t, J = 7.1 Hz, 3H), 1.04 (s, 9H). ^{13}C NMR (151 MHz): δ 173.5, 135.5, 134.1, 133.3, 129.5, 127.6, 125.4, 63.8, 60.2, 34.7, 33.3, 32.1, 27.6, 26.8, 25.9, 19.2, 15.9, 14.3. HRMS (ESI): m/z calcd for ($C_{28}H_{40}O_3NaSi$ [M + H]$^+$) 475.2644, found 475.2662.

*(E)-9-((tert-Butyldiphenylsilyl)oxy)-4-methylnon-4-en-1-ol (**S29**).* In a 25 mL round-bottom flask, ester **S28** (500 mg, 1.10 mmol) was dissolved in THF (10 mL), and the solution was cooled to 0 °C. $LiAlH_4$ (42 mg, 1.10 mmol, 1 equiv) was added slowly and the solution stirred at 0 °C until complete conversion had occurred as judged by TLC. The mixture was carefully quenched with 1 M HCl (10 mL). The mixture was extracted with Et_2O (3 × 10 mL), dried ($MgSO_4$), filtered, and concentrated by rotary evaporation to afford the crude product as a colorless oil. Purification by silica flash chromatography (4:1 hexanes/EtOAc) yielded alcohol **S29** (410 mg, 0.99 mmol, 90%) as a colorless oil. IR (neat) (cm^{-1}): 3667−3141, 2862, 2775, 1474, 1110, 805, 742, 704, 615. ^1H NMR (600 MHz): δ 7.71−7.62 (m, 4H), 7.45−7.34 (m, 6H), 5.20−5.11 (m, 1H), 3.65 (t, J = 6.5 Hz, 2H), 3.64−3.60 (m, 2H), 2.10−2.02 (m, 2H), 1.97 (q, J = 7.3 Hz, 2H), 1.72−1.62 (m, 2H), 1.62−1.49 (m, 5H), 1.47−1.37 (m, 2H), 1.36 (s, 1H), 1.05 (s, 9H). ^{13}C NMR (151 MHz): δ 135.6, 134.1, 129.5, 127.6, 127.6, 125.1, 63.8, 62.8, 36.0, 32.2, 30.7, 27.6, 26.9, 26.0, 19.2, 15.9. HRMS (ESI): m/z calcd for ($C_{26}H_{38}O_2SiNa$ [M + H]$^+$) 433.2539, found 433.2531.

*(E)-9-((tert-Butyldiphenylsilyl)oxy)-4-methylnon-4-enal (**S30**).* In a 25 mL round-bottom flask, alcohol **S29** (250 mg, 0.61 mmol) was dissolved in CH_2Cl_2 (10 mL). PCC (262 mg, 1.22 mmol, 2 equiv) was added, and the solution was stirred at rt until complete conversion had occurred as judged by TLC. The mixture was filtered through a pad of silica with hexane/EtOAc 9:1 and concentrated by rotary evaporation to afford aldehyde **S30** (220 mg, 0.54 mmol, 88%) as a colorless oil. IR (neat) (cm^{-1}): 3070, 2931, 2858, 1725, 1388, 1107, 822, 738, 701. ^1H NMR (600 MHz): δ 9.74 (s, 1H), 7.71−7.64 (m, 4H), 7.46−7.33 (m, 6H), 5.18−5.09 (m, 1H), 3.65 (t, J = 6.3 Hz, 2H), 2.50 (td, J = 7.5, 1.9 Hz, 2H), 2.31 (t, J = 7.5 Hz, 2H), 1.97 (q, J = 7.4 Hz, 2H), 1.58 (s, 3H), 1.55 (dd, J = 8.7, 6.3 Hz, 2H), 1.40 (quint, J = 7.6 Hz, 2H), 1.05 (s, 9H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 202.7, 135.7, 134.1, 132.9, 129.5, 127.8, 125.7, 63.8, 42.2, 32.2, 31.8, 27.6, 26.9, 25.8, 19.2, 16.1. HRMS (ESI): m/z calcd for ($C_{26}H_{36}O_2NaSi$ [M + H]$^+$) 431.2382, found 431.2390.

*(E)-9-((tert-Butyldiphenylsilyl)oxy)-4-methyl-1-phenylnon-4-en-1-ol (**S31**).* In a 25 mL round-bottom flask, aldehyde **S30** (200 mg, 0.49 mmol) was dissolved in THF (5 mL), and the solution was cooled to 0 °C. PhMgBr (1.0 M in THF, 0.61 mL, 0.61 mmol, 1.2 equiv) was added dropwise with stirring. Once addition was complete, the solution was allowed to warm to rt, and stirring was continued until complete conversion had occurred as judged by TLC. The mixture was quenched with 1 M HCl (5 mL), extracted with Et_2O (3 × 5 mL), dried ($MgSO_4$), filtered, and concentrated by rotary evaporation to afford the crude product as a yellow oil. Purification by silica flash chromatography (4:1 hexanes/EtOAc) yielded alcohol **S31** (130 mg, 0.27 mmol, 54%) as a colorless oil. IR (neat) (cm^{-1}): 3683−3183, 2930, 2857, 1454, 1428, 1107, 821, 737, 699. ^1H NMR (600 MHz): δ 7.66 (d, J = 6.5 Hz, 4H), 7.44−7.31 (m, 10H), 7.29−7.24 (m, 1H), 5.15 (t, J = 7.3 Hz, 1H), 4.64 (dd, J = 7.8, 5.3 Hz, 1H), 3.65 (t, J = 6.4 Hz, 2H), 2.13−2.06 (m, 1H), 2.04−1.93 (m, 3H), 1.93−1.85 (m, 1H), 1.84−1.76 (m, 1H), 1.63−1.51 (m, 5H), 1.40 (dq, J = 9.9, 7.6 Hz, 2H), 1.04 (s, 9H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 144.7, 135.5, 134.6, 134.1, 129.5, 128.4, 127.6, 127.5, 125.9, 125.1, 74.3, 63.8, 37.2, 36.0, 32.2, 27.6, 26.9, 26.0, 19.2, 16.0. HRMS (ESI): m/z calcd for ($C_{32}H_{42}O_2NaSi$ [M + H]$^+$) 509.2852, found 509.2862.

*(E)-4-Methyl-1-phenylnon-4-ene-1,9-diol (**4j**).* In a 10 mL round-bottom flask, protected alcohol **S31** (100 mg, 0.21 mmol) was dissolved in THF (2 mL) at rt. TBAF (1.0 M in THF, 0.41 mL, 0.41 mmol, 2 equiv) was added, and the solution was stirred until complete conversion had occurred as judged by TLC. The reaction mixture was concentrated by rotary evaporation. Purification by silica flash chromatography (1:1 hexanes/EtOAc) yielded diol **4j** (40 mg, 0.16 mmol, 78%) as a colorless oil. IR (neat) (cm^{-1}): 3677−3144, 3029, 2858, 1451, 1059, 911, 733, 699. ^1H NMR (600 MHz): δ 7.37−7.33 (m, 4H), 7.30−7.27 (m, 1H), 5.17 (t, J = 7.1 Hz, 1H), 4.66 (dd, J = 7.9, 5.3 Hz, 1H), 3.63 (t, J = 6.6 Hz, 2H), 2.16−2.08 (m, 1H), 2.06−1.97 (m, 4H), 1.94−1.86 (m, 1H), 1.85−1.78 (m, 1H), 1.61 (s, 3H), 1.56 (quint, J = 8.5 Hz, 2H), 1.40 (quint, J = 10.1 Hz, 2H), 1.32 (s, 1H). ^{13}C NMR (151 MHz): δ 144.7, 134.9, 128.4, 127.5, 125.9, 124.8, 74.4, 62.9, 37.2, 36.0, 32.3, 27.6, 25.9, 16.0. HRMS (ESI): m/z calcd for ($C_{16}H_{24}O_2Na$ [M + H]$^+$) 271.1674, found 271.1667.

*1h. Synthesis of TBS-Protected Substrate **6**. (E)-8-((tert-Butyldimethylsilyl)oxy)-4-methyl-1-phenyloct-4-en-1-ol (**6**).* In a 10 mL round-bottom flask, diol **1** (20 mg, 0.085 mmol) and imidazole (12 mg, 0.17 mmol, 2 equiv) were dissolved in CH_2Cl_2 (2 mL). The solution was cooled to 0 °C, and TBSCl (13 mg, 0.085 mmol, 1 equiv) was added. The solution was allowed to warm to rt and stirred until complete conversion had occurred as judged by TLC. The mixture was quenched with 1 M HCl (1 mL) and extracted with CH_2Cl_2 (3 × 1 mL), dried ($MgSO_4$), filtered, and concentrated by rotary evaporation to afford the crude product as a colorless oil. Purification by silica flash chromatography (4:1 hexanes/EtOAc) yielded TBS ether **6** (24 mg, 0.069 mmol, 80%) as a colorless oil. IR (neat): 3711−3103, 2933, 2858, 1602, 1450, 1254, 1059, 871, 835, 769, 699. ^1H NMR (600 MHz): δ 7.32−7.27 (m, 4H), 7.25−7.19 (m, 1H), 5.12 (t, J = 7.2 Hz, 1H), 4.58 (dd, J = 7.8, 5.3 Hz, 1H), 3.55 (t, J = 6.5 Hz, 2H), 2.10−2.02 (m, 2H), 2.02−1.92 (m, 3H), 1.89−1.80 (m, 1H), 1.80−1.71 (m, 1H), 1.56 (s, 3H), 1.50 (q, J = 6.6 Hz, 2H), 0.85 (s, 9H), 0.00 (s, 6H). ^{13}C NMR (151 MHz): δ 144.8, 134.9, 128.4, 127.4, 125.9, 124.6, 74.3, 62.7, 37.2, 35.9, 32.9, 26.0, 24.2, 18.3, 15.9, −5.3. HRMS (ESI): m/z calcd for ($C_{12}H_{22}O_3Na$ [M + Na]$^+$) 237.1467, found 237.1476.

*1i. Synthesis of Methyl Ether Substrate **8**. (E)-8-Hydroxy-4-methyl-1-phenyloct-4-en-1-one (**S32**).* In a 10 mL round-bottom flask, diol **1** (75 mg, 0.320 mmol) was dissolved in CH_2Cl_2 (3 mL) at rt. MnO_2 (690 mg, 8.0 mmol, 25 equiv) was added, and the solution was stirred until complete conversion had occurred as judged by TLC. The slurry was filtered through a pad of Celite, washed with CH_2Cl_2 (10 mL), and concentrated by rotary evaporation to afford the crude product as a colorless oil. Purification by silica flash chromatography (4:1 hexanes/EtOAc) yielded ketone **S32** (63 mg, 0.074 mmol, 85%) as a colorless oil. IR (neat): 3695−3140, 2931, 1818, 1491, 1379, 909, 729. ^1H NMR (600 MHz): δ 7.96 (dd, J = 7.1, 7.6 Hz, 2H), 7.56 (t, 1H), 7.47 (t, J = 7.7 Hz, 2H), 5.20 (tq, J = 7.2, 1.4 Hz, 1H), 3.64 (t, J = 6.5 Hz, 2H), 3.07 (t, J = 7.4 Hz, 2H), 2.42 (t, J = 7.9 Hz, 2H), 2.09 (q, J = 6.8 Hz, 2H), 1.68 (s, 3H), 1.60 (quint, J = 7.0 Hz, 2H). ^{13}C NMR (151 MHz): δ 200.1, 136.9, 134.6, 133.0, 128.6, 128.1, 124.5, 62.6, 37.3, 34.0, 32.6, 24.3, 16.2. HRMS (ESI): m/z calcd for ($C_{15}H_{21}O_2$ [M + H]$^+$) 233.1542, found 233.1549.

*(E)-8-Methoxy-4-methyl-1-phenyloct-4-en-1-one (**S33**).* In a 10 mL round-bottom flask, NaH (12 mg, 0.32 mmol, 1.5 equiv, as a 60% dispersion in oil) was suspended in THF (1 mL), and the solution was cooled to 0 °C. The alcohol **S32** (50 mg, 0.22 mmol) was added as a solution in THF (1 mL); once addition was complete, stirring was continued for 15 min, iodomethane (26 μL, 0.43 mmol, 2 equiv) was added, and the solution was stirred until complete conversion had occurred as judged by TLC. The reaction was quenched by the addition of 10% HCl (1 mL) and extracted with Et_2O (3 × 1 mL). The organic layers were combined, washed with brine, dried ($MgSO_4$), filtered, and concentrated by rotary evaporation to afford the crude product as a colorless oil. Purification by silica flash chromatography (9:1 hexanes/EtOAc) yielded methyl ether **S33** (42 mg, 0.17 mmol, 79%) as a colorless oil. IR (neat): 2923, 2857, 1685, 1597, 1448, 1357, 1289, 1203, 1117, 1037, 971, 742, 692. ^1H NMR (400 MHz): δ 8.00−7.94 (m, 2H), 7.56 (ddt, J = 7.9, 6.9, 1.3 Hz, 1H), 7.50−7.43 (m, 2H), 5.18 (tq, J = 7.2, 1.4 Hz, 1H), 3.35 (t, J = 6.6 Hz, 2H), 3.32 (s, 3H), 3.10−3.02 (m, 2H), 2.48−2.38

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(m, 2H), 2.11−2.01 (m, 2H), 1.67 (s, 3H), 1.63−1.57 (m, 2H). ^{13}C NMR (125 MHz): δ 200.2, 137.0, 134.4, 132.9, 128.6, 128.1, 124.5, 72.2, 58.6, 37.4, 34.1, 29.6, 24.4, 16.1. HRMS (ESI): m/z calcd for ($C_{16}H_{23}O_2$ [M + H]$^+$) 247.1698, found 247.1703.

*8-Methoxy-4-methyl-1-phenyloct-4-en-1-ol (**8**).* In a 10 mL round-bottom flask, ketone **S33** (40 mg, 0.16 mmol) was dissolved in EtOH (2 mL) at rt. $NaBH_4$ (6 mg, 0.16 mmol, 1 equiv) was added and the mixture stirred until complete conversion had occurred as judged by TLC. The reaction was quenched by the addition of 10% HCl (1 mL) and extracted with Et_2O (3 × 1 mL). The organic layers were combined, washed with brine, dried ($MgSO_4$), filtered, and concentrated by rotary evaporation to afford the crude product as a colorless oil. Purification by silica flash chromatography (4:1 hexanes/EtOAc) yielded alcohol **8** (36 mg, 0.14 mmol, 89%) as a colorless oil. IR (neat): 3720−3114, 2936, 2899, 1456, 1117, 1060, 1027, 775, 738, 699. ^{1}H NMR (400 MHz): δ 7.38−7.31 (m, 4H), 7.30−7.26 (m, 1H), 5.16 (tq, J = 7.2, 1.3 Hz, 1H), 4.66 (dd, J = 7.8, 5.4 Hz, 1H), 3.35 (t, J = 6.5 Hz, 2H), 3.32 (s, 3H), 2.16−2.08 (m, 1H), 2.08−1.99 (m, 3H), 1.97 (s, 1H), 1.94−1.85 (m, 1H), 1.85−1.78 (m, 1H), 1.65−1.54 (m, 5H). ^{13}C NMR (125 MHz): δ 144.7, 135.1, 128.4, 127.5, 125.9, 124.4, 74.3, 72.3, 58.6, 37.2, 36.0, 29.6, 24.4, 15.9. HRMS (ESI): m/z calcd for ($C_{16}H_{24}O_2Na$ [M + Na]$^+$) 271.1674, found 271.1666.

*1j. Synthesis of Ethyl Ester Substrate **9**. (E)-5-Methyl-8-oxo-8-phenyloct-4-enoic Acid (**S34**).* In a 50 mL round-bottom flask, diol **1** (400 mg, 1.71 mmol) was dissolved in acetone (17 mL), and the solution was cooled to 0 °C. Jones reagent (1.19 mL, 3.58 mmol, 3.0 M) was added over a period of 10 min, until the orange color persisted. Excess reagent was destroyed by addition of *i*-PrOH (5 mL), as indicated by the reappearance of a deep green color. The reaction was quenched by the addition of 10% HCl (10 mL) and extracted with Et_2O (3 × 20 mL). The organic layers were combined, washed with brine, dried ($MgSO_4$), filtered, and concentrated by rotary evaporation to afford the crude product as a colorless oil. Purification by silica flash chromatography (1:1 hexanes/EtOAc) yielded acid **S34** (360 mg, 1.46 mmol, 85%) as a colorless oil. IR (neat) (cm^{-1}): 3705−3107, 2861, 1705, 1683, 1410, 1204, 911, 842, 690, 655. ^{1}H NMR (600 MHz): δ 7.95 (d, J = 6.8 Hz, 6H), 7.56 (t, J = 6.8 Hz, 3H), 7.46 (t, J = 7.7 Hz, 2H), 5.18 (t, J = 6.7 Hz, 3H), 3.06 (dd, J = 8.4, 7.0 Hz, 2H), 2.40 (dd, J = 8.5, 6.6 Hz, 6H), 1.69 (s, 3H). ^{13}C NMR (151 MHz): δ 200.0, 179.0, 136.9, 135.8, 133.0, 128.6, 128.0, 122.7, 37.2, 34.0, 33.9, 23.2, 16.2. HRMS (ESI): m/z calcd for ($C_{15}H_{19}O_3$ [M + H]+) 247.1334, found 247.1325.

*Ethyl (E)-5-Methyl-8-oxo-8-phenyloct-4-enoate (**S35**).* In a 10 mL round-bottom flask, acid **S34** (100 mg, 0.41 mmol) was dissolved in benzene (4 mL) at rt. To this was added DMF (2 μL, 0.020 mmol, 5 mol %) followed by the dropwise addition of oxalyl chloride (35 μL, 0.41 mmol, 1 equiv) and the mixture stirred for 2 h. To this solution was added EtOH (47 μL, 0.81 mmol, 2 equiv) as a solution in pyridine (1 mL) and the solution stirred for 4 h. The reaction was quenched by the addition of 10% HCl (5 mL) and extracted with Et_2O (3 × 2 mL). The organic layers were combined, washed with brine, dried ($MgSO_4$), filtered, and concentrated by rotary evaporation to afford the crude product as a colorless oil. Purification by silica flash chromatography (hexanes/EtOAc 4:1) yielded ester **S35** (102 mg, 0.37 mmol, 91%) as a colorless oil. IR (neat): 3065, 2984, 2917, 1735, 1688, 1601, 1451, 1374, 1295, 1268, 1205, 1100, 974, 746, 695. ^{1}H NMR (600 MHz): δ 7.96 (d, J = 7.0 Hz, 2H), 7.56 (t, J = 7.0 Hz, 1H), 7.46 (t, J = 7.8 Hz, 2H), 5.20−5.14 (m, 1H), 4.12 (q, J = 7.1 Hz, 2H), 3.10−3.02 (m, 2H), 2.41 (t, J = 7.8 Hz, 2H), 2.35−2.30 (m, 4H), 1.69 (s, 3H), 1.25 (t, J = 7.1 Hz, 3H). ^{13}C NMR (151 MHz): δ 200.0, 173.3, 136.9, 135.4, 133.0, 128.6, 128.0, 123.0, 60.3, 37.3, 34.4, 33.9, 23.5, 16.2, 14.2. HRMS (ESI): m/z calcd for ($C_{17}H_{23}O_3$ [M + H]$^+$) 275.1647, found 275.1645.

*Ethyl 8-Hydroxy-5-methyl-8-phenyloct-4-enoate (**9**).* In a 10 mL round-bottom flask, ketone **S35** (40 mg, 0.15 mmol) was dissolved in EtOH (2 mL) at rt. $NaBH_4$ (5.5 mg, 0.15 mmol, 1 equiv) was added and the mixture stirred until complete conversion had occurred as judged by TLC. The reaction was quenched by the addition of 10% HCl (1 mL) and extracted with Et_2O (3 × 1 mL). The organic layers were combined, washed with brine, dried ($MgSO_4$), filtered, and concentrated by rotary evaporation to afford the crude product as a colorless oil. Purification by silica flash chromatography (hexanes/EtOAc 2:1) yielded ester **9** (42 mg, 0.17 mmol, 83%) as a colorless oil. IR (neat) (cm^{-1}): 3735−3131, 2980, 2915, 1731, 1450, 1374, 1181, 1035, 762, 701. ^{1}H NMR (600 MHz): δ 7.37−7.31 (m, 4H), 7.31−7.24 (m, 1H), 5.16−5.10 (m, 1H), 4.63 (t, J = 6.8 Hz, 1H), 4.11 (q, J = 7.1 Hz, 2H), 2.36−2.27 (m, 4H), 2.13−2.06 (m, 2H), 2.05−1.97 (m, 1H), 1.88 (dddd, J = 13.6, 9.2, 7.8, 5.7 Hz, 1H), 1.79 (dddd, J = 13.6, 9.6, 6.2, 5.3 Hz, 1H), 1.62 (s, 3H), 1.24 (t, J = 7.1 Hz, 3H). ^{13}C NMR (151 MHz): δ 173.4, 144.7, 136.2, 128.4, 127.5, 125.9, 122.8, 122.8, 74.2, 60.3, 37.1, 35.9, 34.4, 23.5, 16.0, 14.2. HRMS (ESI): m/z calcd for ($C_{17}H_{24}O_3Na$ [M + Na]$^+$) 299.1623, found 299.1624.

*1k. Synthesis of Carboxylic Acid Substrate **10**. 8-Hydroxy-5-methyl-8-phenyloct-4-enoic Acid (**10**).* In a 10 mL round-bottom flask, ketone **S34** (50 mg, 0.20 mmol) was dissolved in EtOH (2 mL) at rt. $NaBH_4$ (7.7 mg, 0.20 mmol, 1 equiv) was added and the mixture stirred until complete conversion had occurred as judged by TLC. The reaction was quenched by the addition of 10% HCl (1 mL) and extracted with Et_2O (3 × 1 mL). The organic layers were combined, washed with brine, dried ($MgSO_4$), filtered, and concentrated by rotary evaporation to afford the crude product as a colorless oil. Purification by silica flash chromatography (CH_2Cl_2/MeOH 9:1) yielded acid **10** (42 mg, 0.17 mmol, 83%) as a colorless oil. IR (neat) (cm^{-1}): 3677−3118, 3030, 2934, 1707, 1450, 1409, 1267, 1200, 1059, 1014, 915, 763, 699. ^{1}H NMR (600 MHz): δ 7.37−7.32 (m, 4H), 7.29−7.27 (m, 1H), 5.14 (t, J = 7.0 Hz, 1H), 4.64 (dd, J = 7.8, 5.3 Hz, 1H), 2.40−2.27 (m, 4H), 2.17−1.98 (m, 2H), 1.94−1.76 (m, 2H), 1.63 (s, 3H). ^{13}C NMR (151 MHz): δ 178.4, 144.6, 136.5, 128.5, 127.6, 125.8, 122.5, 74.2, 37.0, 35.8, 34.0, 23.2, 16.0. HRMS (ESI): m/z calcd for ($C_{15}H_{19}O_3$ [M + H]$^+$) 247.1334, found 247.1329.

*1l. Synthesis of Weinreb Amide Substrate **11**. 8-((tert-Butyldimethylsilyl)oxy)-N-methoxy-N,5-dimethyl-8-phenyloct-4-enamide (**S36**).* In a 10 mL round-bottom flask, acid **S34** (100 mg, 0.41 mmol) was dissolved in benzene (4 mL) at rt. To this was added DMF (2 μL, 0.020 mmol, 5 mol %) followed by the dropwise addition of oxalyl chloride (35 μL, 0.41 mmol, 1 equiv) and the mixture stirred for 2 h. To this solution was added *N*,*O*-dimethylhydroxylamine hydrochloride (79 mg, 0.81 mmol, 2 equiv) followed by pyridine (1 mL) and the solution stirred for 4 h. The reaction was quenched by the addition of 10% HCl (5 mL) and extracted with Et_2O (3 × 2 mL). The organic layers were combined, washed with brine, dried (MgSO4), filtered, and concentrated by rotary evaporation to afford the crude product as a colorless oil. Purification by silica flash chromatography (hexanes/EtOAc 4:1) yielded amide **S36** (105 mg, 0.36 mmol, 89%) as a colorless oil. IR (neat) (cm^{-1}): 2971, 2941, 1665, 1451, 1387, 1290, 1206, 1182, 1118, 1075, 998, 746, 696. ^{1}H NMR (600 MHz): δ 7.98−7.94 (m, 2H), 7.58−7.54 (m, 1H), 7.47 (t, J = 7.6 Hz, 2H), 5.19 (t, J = 6.0 Hz, 1H), 4.62 (s, 3H), 3.51 (t, J = 6.6 Hz, 2H), 3.36 (s, 3H), 3.10−3.03 (m, 2H), 2.42 (t, J = 7.6 Hz, 2H), 2.08 (quintp, J = 6.9 Hz, 2H), 1.67 (s, 3H). ^{13}C NMR (151 MHz): δ 200.1, 137.0, 134.4, 132.9, 128.6, 128.0, 124.4, 96.4, 67.3, 55.1, 37.4, 34.0, 29.7, 24.5, 16.2. HRMS (ESI): m/z calcd for ($C_{17}H_{24}NO_3$ [M + H]$^+$) 290.1756, found 290.1747.

*8-Hydroxy-N-methoxy-N,5-dimethyl-8-phenyloct-4-enamide (**11**).* In a 10 mL round-bottom flask, ketone **S36** (50 mg, 0.17 mmol) was dissolved in EtOH (2 mL) at rt. $NaBH_4$ (6.5 mg, 0.17 mmol, 1 equiv) was added and the mixture stirred until complete conversion had occurred as judged by TLC. The reaction was quenched by the addition of 10% HCl (1 mL) and extracted with Et_2O (3 × 1 mL). The organic layers were combined, washed with brine, dried ($MgSO_4$), filtered, and concentrated by rotary evaporation to afford the crude product as a colorless oil. Purification by silica flash chromatography (hexanes/EtOAc 2:1) yielded amide **11** (38 mg, 0.13 mmol, 75%) as a colorless oil. IR (neat): 3712−3113, 2932, 2857, 1641, 1450, 1386, 1317, 1178, 1060, 993, 916, 761, 700. ^{1}H NMR (400 MHz): δ 7.35 (d, J = 4.4 Hz, 4H), 7.31−7.24 (m, 1H), 5.19 (tq, J = 7.2, 1.3 Hz, 1H), 4.65 (dd, J = 7.9, 5.3 Hz, 1H), 3.67 (s, 3H), 3.17 (s, 3H), 2.45 (t, J = 7.6 Hz, 2H), 2.33 (q, J = 7.4 Hz, 2H), 2.15−2.08 (m, 1H), 2.07−1.99 (m, 1H), 1.94−1.85 (m, 1H), 1.86−1.77 (m, 1H), 1.64 (s, 3H). ^{13}C NMR (125 MHz): δ 144.8, 135.8, 128.4, 127.5, 125.9, 123.5,

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74.2, 61.2, 37.1, 35.9, 23.2, 16.0. HRMS (ESI): m/z calcd for ($C_{17}H_{25}NO_3Na$ [M + Na]$^+$) 314.1732, found 314.1732.

1m. Synthesis of Diol Substrate ***15****. Methyl (E)-2-Benzoyl-5,9-dimethyldeca-4,8-dienoate (****S37****).* In a 250 mL round-bottom flask containing K_2CO_3 (12.7 g, 92.1 mmol, 2 equiv) was added geranyl bromide (10.00 g, 46.0 mmol) dissolved in DMF (100 mL). Ethyl benzoylacetate (11.1 mL, 57.6 mmol, 1.22 equiv) was added and the solution stirred at rt until complete conversion had occurred as judged by TLC. The mixture was diluted with H_2O (100 mL) and extracted with Et_2O (3 × 50 mL). The combined organic layers were washed with H_2O (2 × 50 mL) and brine (50 mL), dried ($MgSO_4$), filtered, and concentrated by rotary evaporation to afford the crude product as a colorless oil. Purification by silica flash chromatography (9:1 hexanes/EtOAc) yielded ester **S37** (14.8 g, 45.0 mmol, 97%) as a colorless oil. IR (neat) (cm^{-1}): 2966, 1740, 1438, 1162, 834. ^{1}H NMR (600 MHz): δ 7.99 (d, J = 7.7 Hz, 2H), 7.62−7.55 (m, 1H), 7.47 (t, J = 7.8 Hz, 2H), 5.12 (d, J = 6.5 Hz, 1H), 5.03 (d, J = 6.5 Hz, 1H), 4.31 (t, J = 7.3 Hz, 1H), 4.14 (qd, J = 7.1, 2.2 Hz, 2H), 2.80−2.64 (m, 2H), 2.05−1.91 (m, 4H), 1.64 (s, 4H), 1.62 (s, 3H), 1.56 (s, 3H), 1.17 (t, J = 7.1 Hz, 3H). ^{13}C NMR (151 MHz): δ 195.1, 169.7, 138.3, 136.4, 133.4, 131.5, 128.7, 128.6, 124.0, 120.0, 61.3, 54.5, 39.7, 27.7, 26.5, 25.6, 17.7, 16.1, 14.0. HRMS (ESI): m/z calcd for ($C_{21}H_{29}O_3$ [M + H]$^+$) 329.2117, found 329.2126.

*(E)-5,9-Dimethyl-1-phenyldeca-4,8-dien-1-one (****S38****).*[22] In a 250 mL round-bottom flask containing LiCl (7.74 g, 183.0 mmol, 5 equiv) was added ester **S37** (12.0 g, 36.6 mmol) dissolved in DMSO (100 mL). The solution was heated to 150 °C until complete conversion had occurred as judged by TLC. The mixture was diluted with H_2O (100 mL) and extracted with Et_2O (3 × 50 mL). The combined organic layers were washed with H_2O (100 mL) and brine (50 mL), dried ($MgSO_4$), filtered, and concentrated by rotary evaporation to afford the crude product as a colorless oil. Purification by silica flash chromatography (9:1 hexanes/EtOAc) yielded ketone **S38** (8.58 g, 33.5 mmol, 92%) as a colorless oil. IR (neat) (cm^{-1}): 2968, 2915, 1685, 1597, 1448, 1270, 1180, 975, 911, 733, 690. ^{1}H NMR (600 MHz): δ 7.96 (d, J = 7.0 Hz, 2H), 7.55 (d, J = 7.3 Hz, 1H), 7.46 (t, J = 7.7 Hz, 2H), 5.19 (d, J = 7.1 Hz, 1H), 5.08 (d, J = 7.0 Hz, 1H), 3.00 (d, J = 8.3 Hz, 2H), 2.44 (q, J = 7.4 Hz, 2H), 2.06 (q, J = 7.3 Hz, 2H), 1.98 (d, J = 9.2 Hz, 2H), 1.67 (s, 3H), 1.63 (s, 3H), 1.59 (s, 3H). HRMS (ESI): m/z calcd for ($C_{18}H_{25}O$ [M + H]$^+$) 257.1900, found 257.1898.

*(E)-4-Methyl-8-oxo-8-phenyloct-4-enal (****S39****).*[23] In a 100 mL round-bottom flask, diene **S38** (8.50 g, 33.2 mmol) was dissolved in CH_2Cl_2 (30 mL), and the solution was cooled to 0 °C. *m*-CPBA (77%, 8.17 g, 36.5 mmol, 1.2 equiv) was added, and the solution was stirred at 0 °C until complete conversion had occurred as judged by TLC. The mixture was quenched with satd aq $Na_2S_2O_3$ (50 mL) and extracted with CH_2Cl_2 (3 × 20 mL). The organic fractions were pooled, washed with 1 M NaOH (20 mL) and brine (20 mL), dried ($MgSO_4$), filtered, and concentrated by rotary evaporation to afford the crude epoxide product as a colorless oil which was taken on to the next step without purification.

In a 250 mL round-bottom flask, the crude epoxide above was dissolved in THF/H_2O (9:1, 100 mL) and cooled to 0 °C. $NaIO_4$ (3.30 g, 19.9 mmol, 0.6 equiv) and HIO_4 (7.00 g, 36.5 mmol, 1.1 equiv) was added, and the solution was warmed to rt and stirred until complete conversion had occurred as judged by TLC. The mixture was quenched with satd aq $Na_2S_2O_3$ (50 mL) and extracted with Et_2O (3 × 50 mL). The organic fractions were pooled, washed with 1 M NaOH (50 mL) and brine (50 mL), dried ($MgSO_4$), filtered, and concentrated by rotary evaporation to afford the crude product as a gray oil. Purification by silica flash chromatography (19:1 hexanes/EtOAc) yielded aldehyde **S39** (5.05 g, 21.9 mmol, 66%) as a colorless oil. IR (neat) (cm^{-1}): 2927, 2898, 2360, 2342, 1723, 1685, 1449, 1253, 1105, 837, 743, 691. ^{1}H NMR (500 MHz): δ 9.75 (s, 1H), 7.96 (d, J = 8.2 Hz, 2H), 7.56 (d, J = 7.2 Hz, 1H), 7.47 (t, J = 7.9 Hz, 2H), 5.23 (t, J = 7.2 Hz, 1H), 3.01 (t, J = 7.3 Hz, 2H), 2.52 (t, J = 7.9 Hz, 2H), 2.45 (q, J = 7.3 Hz, 2H), 2.33 (t, J = 7.5 Hz, 2H), 1.66 (s, 3H). ^{13}C NMR (126 MHz): δ 202.4, 199.8, 137.0, 134.4, 133.0, 128.6, 128.0, 123.9, 42.1, 38.5, 31.7, 22.8, 16.1. HRMS (ESI): m/z calcd for ($C_{15}H_{18}O_2Na$ [M + Na]$^+$) 253.1204, found 253.1204.

*(E)-5-Methyl-1-phenyloct-4-ene-1,8-diol (****15****).* In a 50 mL round-bottom flask, keto aldehyde **S39** (1.50 g, 6.51 mmol) was dissolved in EtOH (20 mL) at rt. $NaBH_4$ (250 mg, 6.51 mmol, 1 equiv) was added and the mixture stirred until complete conversion had occurred as judged by TLC. The reaction was quenched by the addition of 10% HCl (10 mL) and extracted with Et_2O (3 × 10 mL). The organic layers were combined, washed with brine, dried ($MgSO_4$), filtered, and concentrated by rotary evaporation to afford the crude product as a colorless oil. Purification by silica flash chromatography (hexanes/EtOAc 2:1) yielded diol **15** (1.27 g, 5.42 mmol, 83%) as a colorless oil. IR (neat) (cm^{-1}): 3722−3118, 2934, 1450, 1058, 915, 759, 699. ^{1}H NMR (600 MHz): δ 7.31−7.24 (m, 4H), 7.23−7.17 (m, 1H), 5.11 (t, J = 6.0 Hz, 1H), 4.57 (dd, J = 7.9, 5.3 Hz, 1H), 3.55 (t, J = 6.5 Hz, 2H), 2.08−1.90 (m, 4H), 1.87−1.78 (m, 1H), 1.77−1.69 (m, 1H), 1.58−1.48 (m, 5H). ^{13}C NMR (151 MHz): δ 144.8, 135.4, 128.4, 127.5, 125.9, 124.9, 74.3, 62.7, 37.2, 36.0, 32.7, 24.3, 16.0. HRMS (ESI): m/z calcd for ($C_{15}H_{22}O_2Na$ [M + H]$^+$) 257.1517, found 257.1526.

1n. Synthesis of Carbinol Deuterium-Labeled Diol Substrate ***17****. (E)-8-Hydroxy-5-methyl-1-phenyloct-4-en-1-one (****S40****).* In a 25 mL round-bottom flask, diol **15** (200 mg, 0.85 mmol) was dissolved in CH_2Cl_2 (10 mL) at rt. MnO_2 (3.71 g, 42.7 mmol, 50 equiv) was added, and the solution was stirred until complete conversion had occurred as judged by TLC. The slurry was filtered through a pad of Celite, washed with CH_2Cl_2 (50 mL), and concentrated by rotary evaporation to afford the crude product as a colorless oil. Purification by silica flash chromatography (4:1 hexanes/EtOAc) yielded ketone **S40** (182 mg, 0.78 mmol, 91%) as a colorless oil. IR (neat) (cm^{-1}): 3664−3141, 2936, 1681, 1448, 1273, 1203, 1052, 750, 690. ^{1}H NMR (500 MHz): δ 7.97 (d, J = 7.1 Hz, 2H), 7.57 (t, J = 7.3 Hz, 1H), 7.48 (q, J = 7.6 Hz, 2H), 5.24 (t, J = 7.2 Hz, 1H), 3.63 (t, J = 6.3 Hz, 2H), 3.02 (t, J = 7.4 Hz, 2H), 2.45 (q, J = 7.4 Hz, 2H), 2.08 (t, J = 9.8 Hz, 2H), 1.79 (s, 1H), 1.76−1.65 (m, 5H). ^{13}C NMR (126 MHz): δ 200.1, 137.0, 136.0, 133.0, 128.6, 128.0, 123.2, 62.6, 38.6, 35.9, 30.7, 22.9, 15.9. HRMS (ESI): m/z calcd for ($C_{15}H_{20}O_2Na$ [M + Na]$^+$) 255.1361, found 255.1366.

*(E)-5-Methyl-1-phenyloct-4-ene-1-d-1,8-diol (****17****).* In a 10 mL round-bottom flask, ketone **S40** (50 mg, 0.22 mmol) was dissolved in EtOH (2 mL) at rt. $NaBD_4$ (18 mg, 0.43 mmol, 2 equiv) was added and the mixture stirred until complete conversion had occurred as judged by TLC. The reaction was quenched by the addition of 10% HCl (1 mL) and extracted with Et_2O (3 × 1 mL). The organic layers were combined, washed with brine, dried ($MgSO_4$), filtered, and concentrated by rotary evaporation to afford the crude product as a colorless oil. Purification by silica flash chromatography (hexanes/EtOAc 2:1) yielded diol **17** (48 mg, 0.20 mmol, 95%) as a colorless oil. IR (neat) (cm^{-1}): 3732−3102, 2932, 1447, 1059, 946, 759, 698. ^{1}H NMR (600 MHz): δ 7.39−7.32 (m, 4H), 7.31−7.24 (m, 1H), 5.20 (t, J = 5.9 Hz, 1H), 3.62 (t, J = 6.5 Hz, 2H), 2.14−2.00 (m, 4H), 1.84 (quint, J = 7.5 Hz, 1H), 1.78−1.71 (m, 1H), 1.67 (hept, J = 6.1 Hz, 2H), 1.59 (s, 3H). ^{13}C NMR (151 MHz): δ 144.6, 135.5, 128.4, 127.5, 125.9, 124.2, 73.8(t), 62.8, 38.8, 36.0, 30.7, 24.3, 15.9. HRMS (ESI): m/z calcd for ($C_{15}H_{21}DO_2Na$ [M + Na]$^+$) 258.1580, found 258.1578.

2. Oxidative Cyclization−Redox Relay Reactions. *2a. Representative Procedure for $PdCl_2$/BQ Oxidative Cyclization−redox Relay. 4-(2-Methyl-5-phenyltetrahydrofuran-2-yl)butanal (****2b****).* In a 5 mL round-bottom flask charged with $PdCl_2$ (1.9 mg, 0.011 mmol, 0.05 equiv) and 1,4-benzoquinone (46.1 mg, 427 mmol, 2.0 equiv) dissolved in THF (1 mL) was added diol **1** (50 mg, 0.22 mmol) as a solution in THF (1 mL). The solution was then stirred at rt until complete conversion had occurred as judged by TLC. The reaction mixture was quenched by the addition of 5% NaOH (2 mL) and extracted with Et_2O (3 × 1 mL). The organic layers were combined, washed with brine (1 mL), dried ($MgSO_4$), filtered, and concentrated by rotary evaporation to afford the crude product as a colorless oil. Purification by silica flash chromatography (hexanes/EtOAc 9:1) yielded tetrahydrofuran **2b** (46 mg, 0.20 mmol, 93%) as a colorless oil.

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The stereochemical configuration of the major diastereomer was assigned based on 1D NOE (Figure S4) and 2D NOESY analyses.[16]

*2b. Analytical Data for Alternative Products **2a** and **3**. (E)-4-(2-Methyl-5-phenyltetrahydrofuran-2-yl)but-3-en-1-ol (**2a**).* Prepared from diol **1** under the representative procedure above but with the alternative catalyst systems shown in Table 1. IR (neat) (cm^{-1}): 3732−3130, 2966, 2929, 2869, 1684, 1493, 1371, 1290, 1203, 1041, 972, 748, 698. ^{1}H NMR (600 MHz): δ 7.40−7.35 (m, 2H), 7.35−7.30 (m, 2H), 7.27−7.23 (m, 1H), 5.83−5.77 (m, 1H), 5.67 (dt, J = 15.5, 7.1 Hz, 1H), 5.05−4.97 (m, 1H), 3.68−3.55 (m, 2H), 2.36−2.27 (m, 2H), 2.10−2.01 (m, 2H), 1.95−1.87 (m, 2H), 1.44 (d, J = 7.5 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 143.5, 139.8, 139.2, 128.3, 127.3, 126.0, 125.8, 123.6, 123.3, 83.0, 82.8, 80.7, 62.0, 38.6, 37.8, 35.7, 35.0, 34.8, 31.6, 27.5, 26.9, 22.7, 14.2. HRMS (ESI): m/z calcd for ($C_{15}H_{20}O_2$ [M + Na]$^+$) 255.1361, found 255.1371.

*3-(2-Methyltetrahydro-2H-pyran-2-yl)-1-phenylpropan-1-one (**3**).* Prepared from diol **1** under the representative procedure above, but with the alternative catalyst systems shown in Table 1. ^{1}H NMR (600 MHz): δ 7.93 (d, J = 6.7 Hz, 1H), 7.51−7.46 (m, 1H), 7.39 (t, J = 7.7 Hz, 2H), 7.26 (quint, J = 7.5 Hz, 1H), 3.57 (dddd, J = 15.1, 11.4, 6.4, 4.4 Hz, 2H), 3.06−2.93 (m, 2H), 2.13 (ddd, J = 15.1, 9.9, 5.7 Hz, 1H), 1.69 (ddd, J = 14.4, 9.9, 6.0 Hz, 1H), 1.64−1.57 (m, 1H), 1.48−1.39 (m, 4H), 1.14 (s, 3H). ^{13}C NMR (151 MHz): δ 200.7, 137.1, 132.9, 128.6, 128.1, 72.3, 61.7, 35.6, 32.7, 32.6, 30.3, 29.7, 25.8, 23.8, 19.3.

*2c. Analytical Data for Tetrahydrofuran Products **2b**, **5a**−**j**, **12**−**14**, **16**, and **18**. 4-(2-Methyl-5-phenyltetrahydrofuran-2-yl)butanal (**2b**).* Prepared from diol **1** according to the procedure above. IR (neat) (cm^{-1}): 2933, 2862, 1450, 1058, 1030, 699, 535. ^{1}H NMR (600 MHz): δ 9.79 (t, J = 1.6 Hz, 1H), 7.38−7.30 (m, 4H), 7.26−7.20 (m, 1H), 4.96 (dd, J = 8.0, 6.4 Hz, 0.14H minor, C5-H), 4.91 (dd, J = 8.7, 5.8 Hz, 0.86H major, C5-H), 2.50 (t, J = 7.2 Hz, 2H), 2.33−2.26 (m, 1H), 2.00−1.87 (m, 2H), 1.87−1.82 (m, 1H), 1.82−1.72 (m, 2H), 1.71−1.59 (m, 2H), 1.35 (s, 3H). ^{13}C NMR (151 MHz): δ 202.7, 143.3, 128.3, 127.2, 125.8, 83.2, 81.1, 44.3, 40.8, 37.6, 35.6, 26.9, 17.3. HRMS (ESI): m/z calcd for ($C_{15}H_{21}O_2$ [M + H]$^+$) 233.1542, found 233.1545.

*4-(2,5-Dimethyltetrahydrofuran-2-yl)butanal (**5a**).* Prepared from diol **4a** according to the representative procedure above. IR (neat) (cm^{-1}): 2970, 2879, 1712, 1451, 1377, 1282, 1114, 713. ^{1}H NMR (600 MHz): δ 9.77 (t, J = 1.7 Hz, 1H), 4.11−4.05 (m, 0.29H minor, C5-H), 4.05−3.98 (m, 0.71H major, C5-H), 2.46 (t, J = 7.2 Hz, 2H), 2.02−1.95 (m, 1H), 1.83−1.75 (m, 1H), 1.75−1.64 (m, 2H), 1.57−1.44 (m, 4H), 1.23 (d, J = 6.0 Hz, 3H), 1.21 (s, 2H), 1.20 (s, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 202.7, 82.4, 75.0, 44.3, 40.8, 37.4, 33.8, 27.3, 21.8, 17.3. HRMS (ESI): m/z calcd for ($C_{10}H_{18}O_2$ Na [M + Na]$^+$) 193.1204, found 193.1195.

*4-(5-Butyl-2-methyltetrahydrofuran-2-yl)butanal (**5b**).* Prepared from diol **4b** according to the representative procedure above.

IR (neat) (cm^{-1}): 2958, 2869, 1710, 1459, 1376, 1110, 1038, 884, 742. ^{1}H NMR (600 MHz): δ 9.77 (t, J = 1.7 Hz, 1H), 3.96 (dd, J = 8.0, 6.4 Hz, 0.22H minor, C5-H), 3.85 (dq, J = 8.8, 6.1 Hz, 0.78H major, C5-H), 2.46 (t, J = 7.4 Hz, 2H), 1.99−1.92 (m, 1H), 1.82−1.73 (m, 1H), 1.72−1.66 (m, 2H), 1.66−1.56 (m, 3H), 1.56−1.44 (m, 2H), 1.44−1.37 (m, 1H), 1.37−1.23 (m, 4H), 1.19 (d, J = 2.7 Hz, 3H), 0.89 (t, J = 6.9 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 202.8, 82.0, 79.3, 44.3, 40.7, 37.1, 36.2, 31.8, 28.2, 27.1, 22.9, 17.3, 14.1. HRMS (ESI): m/z calcd for ($C_{13}H_{25}O_2$ [M + H]$^+$) 213.1855, found 213.1848.

*4-(2-Methyl-5-(prop-1-en-2-yl)tetrahydrofuran-2-yl)butanal (**5c**).* Prepared from diol **4c** according to the representative procedure above. IR (neat) (cm^{-1}): 2935, 2863, 1721, 1459, 1379, 1063, 902. ^{1}H NMR (600 MHz): δ 9.78 (t, J = 1.7 Hz, 1H), 5.00 (s, 1H), 4.79 (s, 1H), 4.37 (t, J = 7.1 Hz, 0.79H major, C5-H), 4.32 (t, J = 7.3 Hz, 0.21H minor, C5-H), 2.47 (td, J = 7.3, 1.7 Hz, 2H), 2.11−1.99 (m, 1H), 1.87−1.78 (m, 1H), 1.78−1.66 (m, 4H), 1.64−1.50 (m, 5H), 1.28−1.17 (m, 3H). ^{13}C NMR (151 MHz): δ 202.7, 145.7, 134.8, 110.2, 81.4, 44.3, 41.2, 37.0, 31.3, 25.8, 18.1, 17.4. HRMS (ESI): m/z calcd for ($C_{12}H_{21}O_2$ [M + H]$^+$) 197.1542, found 197.1549.

*4-(5-(tert-Butyl)-2-methyltetrahydrofuran-2-yl)butanal (**5d**).* Prepared from diol **4d** according to the representative procedure above. IR (neat) (cm^{-1}): 2967, 1723, 1458, 1371, 1313, 1261, 1135, 977, 883, 771, 703. ^{1}H NMR (600 MHz): δ 9.78 (t, J = 1.8 Hz, 1H), 3.63 (dd, J = 7.9, 6.7 Hz, 0.12H minor, C5-H), 3.55 (dd, J = 8.9, 5.4 Hz, 0.88H major, C5-H), 2.47 (td, J = 7.3, 1.7 Hz, 2H), 1.81−1.58 (m, 6H), 1.59−1.44 (m, 2H), 1.15 (s, 3H), 0.86 (s, 9H). ^{13}C NMR (151 MHz): δ 203.0, 87.3, 81.8, 44.3, 40.5, 37.2, 33.2, 26.7, 26.6, 25.9, 17.3. HRMS (ESI): m/z calcd for ($C_{13}H_{25}O_2$ [M + H]$^+$) 213.1855, found 213.1846.

*Ethyl 2-(5-Methyl-5-(4-oxobutyl)tetrahydrofuran-2-yl)acetate (**5e**).* Prepared from diol **4e** according to the representative procedure above. IR (neat) (cm^{-1}): 2941, 1711, 1450, 1380, 1280, 1111, 1067, 1025, 703. ^{1}H NMR (600 MHz): δ 9.77 (s, 1H), 4.35 (quint, J = 6.7 Hz, 0.37H minor, C5-H), 4.28 (dq, J = 8.1, 6.3 Hz, 0.63H major, C5-H), 4.14 (q, J = 7.1 Hz, 2H), 2.62 (ddd, J = 18.9, 15.1, 6.4 Hz, 1H), 2.51−2.38 (m, 3H), 2.22−2.04 (m, 1H), 1.90−1.77 (m, 1H), 1.77−1.65 (m, 5H), 1.59−1.42 (m, 1H), 1.32−1.23 (m, 3H), 1.21 (s, 2H), 1.20 (s, 1H). ^{13}C NMR (151 MHz): δ 202.7, 171.3, 82.9, 75.1, 60.4, 44.2, 41.4, 40.5, 36.9, 31.7, 27.0, 17.2, 14.2. HRMS (ESI): m/z calcd for ($C_{13}H_{22}O_4$ Na [M + Na]$^+$) 265.1416, found 265.1404.

*4-((2S,5R)-5-(2-Hydroxypropan-2-yl)-2-methyltetrahydrofuran-2-yl)butanal (**5f**).* Prepared from diol **4f** according to the representative procedure above. IR (neat) (cm^{-1}): 3648−3154, 2972, 2871, 1727, 1463, 1378, 1064, 706. ^{1}H NMR (600 MHz): δ 9.78 (t, J = 1.6 Hz, 1H), 3.79 (dd, J = 8.1, 6.6 Hz, 0.33H minor, C5-H), 3.74−3.69 (m, 0.67H major, C5-H), 2.48 (t, J = 7.4 Hz, 2H), 2.14 (s, 1H), 1.90−1.76 (m, 2H), 1.76−1.64 (m, 4H), 1.56−1.45 (m, 2H), 1.20 (s, 6H), 1.12 (s, 3H). ^{13}C NMR (151 MHz): δ 202.7, 85.8, 82.8, 70.6, 44.2, 40.6, 37.4, 27.6, 26.5, 24.0, 17.2. HRMS (ESI): m/z calcd for ($C_{12}H_{22}O_3$Na [M + Na]$^+$) 237.1467, found 237.1476.

*4-(2,5,5-Trimethyltetrahydrofuran-2-yl)butanal (**5g**).* Prepared from diol **4g** according to the representative procedure above, but at a reaction temperature of 60 °C. IR (neat): 2973, 2360, 2337, 1714, 1652, 1451, 1269, 1188, 1039, 984, 749, 699. ^{1}H NMR (600 MHz): δ 9.77 (t, J = 1.7 Hz, 1H), 2.45 (td, J = 7.3, 1.8 Hz, 2H), 1.94−1.83 (m, 2H), 1.83−1.74 (m, 2H), 1.75−1.65 (m, 2H), 1.59−1.43 (m, 2H), 1.26 (s, 3H), 1.21 (s, 6H). ^{13}C NMR (151 MHz): δ 202.8, 82.9, 80.9, 44.3, 41.9, 38.5, 36.9, 29.9, 29.5, 27.5, 17.5. HRMS (ESI): m/z calcd for ($C_{11}H_{20}O_2$Na [M + Na]$^+$) 207.1361, found 207.1354.

*4-(2-Methyl-5,5-diphenyltetrahydrofuran-2-yl)butanal (**5h**).* Prepared from diol **4h** according to the representative procedure above, but at a reaction temperature of 60 °C. IR (neat) (cm^{-1}): 3058, 2966, 2872, 1723, 1684, 1598, 1448, 1047, 1010, 699. ^{1}H NMR (600 MHz): δ 9.71 (t, J = 1.7 Hz, 1H), 7.43 (d, J = 7.7 Hz, 4H), 7.30−7.23 (m, 4H), 7.17 (q, J = 7.3 Hz, 2H), 2.73−2.66 (m, 1H), 2.66−2.59 (m, 1H), 2.41 (q, J = 7.2 Hz, 2H), 1.89−1.76 (m, 3H), 1.73−1.63 (m, 1H), 1.59−1.47 (m, 2H), 1.28 (s, 3H). ^{13}C NMR (151 MHz): δ 202.8, 148.0, 147.6, 128.0, 127.9, 126.5, 126.4, 125.8, 125.7, 88.0, 84.0, 44.2, 41.7, 38.6, 37.6, 26.4, 17.6. HRMS (ESI): m/z calcd for ($C_{21}H_{24}O_2$ Na [M + Na]$^+$) 331.1674, found 331.1670.

*3-(2-Methyl-5-phenyltetrahydrofuran-2-yl)propanal (**5i**).* Prepared from diol **4i** according to the representative procedure above. IR (neat) (cm^{-1}): 2934, 1713, 1685, 1450, 1281, 1114, 713. ^{1}H NMR (600 MHz): δ 9.80 (dd, J = 2.2, 1.5 Hz, 1H), 7.34−7.30 (m, 4H), 7.26−7.22 (m, 1H), 4.96 (dd, J = 8.4, 6.2 Hz, 0.37H minor, C5-H), 4.85 (dd, J = 8.6, 6.1 Hz, 0.73H major, C5-H), 2.68−2.52 (m, 3H), 2.36−2.29 (m, 1H), 2.04−1.83 (m, 4H), 1.36 (s, 2H), 1.32 (s, 1H). ^{13}C NMR (151 MHz): δ 202.4, 143.0, 128.3, 127.3, 125.8, 82.5, 81.0, 39.4, 37.5, 35.3, 33.3, 27.1. HRMS (ESI): m/z calcd for ($C_{14}H_{18}O_2$ Na [M + Na]$^+$) 241.1204, found 241.1204.

*5-(2-Methyl-5-phenyltetrahydrofuran-2-yl)pentanal (**5j**).* Prepared from diol **4j** according to the representative procedure above. IR (neat) (cm^{-1}): 2945, 1707, 1279, 1175, 1113, 711. ^{1}H NMR (600 MHz): δ 9.78 (t, J = 1.8 Hz, 1H), 7.38−7.29 (m, 4H), 7.25−7.20 (m, 1H), 4.95 (dd, J = 8.4, 6.1 Hz, 0.22H minor, C5-H), 4.90 (dd, J = 8.6, 5.8 Hz, 0.78H major, C5-H), 2.47 (td, J = 7.3, 1.7 Hz, 2H), 2.34−2.25 (m, 1H), 1.96−1.86 (m, 2H), 1.86−1.76 (m, 1H), 1.74−1.63 (m, 4H), 1.54−1.38 (m, 2H), 1.33 (s, 2.4H), 1.29 (s, 0.6H). ^{13}C NMR (151 MHz): δ 202.8, 143.4, 128.3, 127.2, 125.8, 83.3, 81.1, 43.9, 41.4,

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37.6, 35.6, 27.0, 24.2, 22.6. HRMS (ESI): m/z calcd for ($C_{16}H_{22}O_2$ Na [M + Na] $^+$) 269.1517, found 269.1520.

*(E)-tert-Butyldimethyl((4-(2-methyl-5-phenyltetrahydrofuran-2-yl)but-3-en-1-yl)oxy)silane (**7**).* Prepared from TBS ether **6** under the representative procedure above, but with the alternative catalyst systems shown in Table 3. ^{1}H NMR (600 MHz): δ 7.91 (d, J = 7.01 Hz, 0.6H), 7.50 (t, J = 6.64 Hz, 0.3H), 7.40 (t, J = 7.66, 0.6H), 7.34−7.29 (m, 1.5H), 7.26 (t, J = 7.25 Hz, 1.5H), 7.20−7.17 (m, 0.8H), 5.71−5.57 (m, 2H), 5.13 (t, J = 6.64 Hz, 0.28H minor, C5-H), 4.97−4.92 (m, 0.72H major, C5-H), 3.62−3.58 (m, 1.32H major, CH_2OSi), 3.54 (t, J = 7.66 Hz, 0.68H minor, CH_2OSi) 3.02−3.00 (m, 0.5H), 3.36 (t, J = 6.13 Hz, 0.5H), 2.28−2.21 (m, 2H), 2.01−1.96 (m, 1H), 1.94−1.91 (m, 0.4H), 1.87−1.79 (m, 1.5H), 1.49 (quint. J = 6.13 Hz, 0.6H), 1.39 (s, 0.80H minor, C1-Me), 1.35 (s, 2.20H major, C1-Me), 0.84 (s, 9H), 0.02 − −0.01 (m, 6H). ^{13}C NMR (151 MHz): δ 1.43.8, 1.43.1, 1.38.25, 1.37.6, 137.0, 134.1, 132.9, 128.6, 128.2, 18.1, 127.2, 126.1, 125.8, 124.8, 124.2, 124.1, 83.1, 82.8, 80.7, 80.4, 63.1, 62.6, 38.6, 37.5, 36.0, 35.0, 34.1, 32.9, 27.4, 26.9, 26.0, 24.2, 18.4, 16.2, −5.2. HRMS (ESI): m/z calcd for ($C_{21}H_{35}O_2$ [M + H]$^+$) 346.2328, found 346.2331.

*Ethyl (E)-4-(2-Methyl-5-phenyltetrahydrofuran-2-yl)but-2-enoate (**12**).* Prepared from hydroxy ester **9** according to the representative procedure above, but at a reaction temperature of 60 °C. Diastereomeric ratio of crude reaction product was 4:1, which increased to 10:1 following purification by silica gel chromatography. IR (neat): 3030, 2971, 2933, 2872, 1716, 1653, 1493, 1451, 1309, 1270, 1188, 1040, 985, 940, 749, 699. ^{1}H NMR (600 MHz): δ 7.38−7.26 (m, 4H), 7.28−7.22 (m, 1H), 7.03 (dt, J = 15.5, 7.7 Hz, 1H), 5.91 (dt, J = 15.6, 1.4 Hz, 1H), 5.03−4.97 (m, 0.09H minor, C5-H), 4.95 (dd, J = 8.7, 5.9 Hz, 0.91H major, C5-H), 4.20 (q, J = 7.1 Hz, 2H), 2.58−2.48 (m, 2H), 2.37−2.26 (m, 1H), 2.02−1.80 (m, 3H), 1.38 (s, 3H), 1.29 (t, J = 7.1 Hz, 3H). ^{13}C NMR (151 MHz): δ 166.4, 145.1, 143.0, 128.3, 127.3, 125.8, 124.1, 82.8, 81.3, 60.3, 44.3, 37.2, 35.4, 27.5, 14.3. HRMS (ESI): m/z calcd for ($C_{17}H_{22}O_3$ Na [M + Na] $^+$) 297.1467, found 297.1461.

*(E)-4-(2-Methyl-5-phenyltetrahydrofuran-2-yl)but-2-enoic Acid (**13**).* Prepared from hydroxy acid **10** according to the representative procedure above, but at a reaction temperature of 60 °C. IR (neat): 3772−3131, 3031, 2971, 2874, 2821, 2360, 1695, 1651, 1451, 1279, 1216, 1040, 986, 941, 909, 748, 698. ^{1}H NMR (600 MHz): δ 7.38−7.29 (m, 4H), 7.29−7.24 (m, 1H), 7.14 (dt, J = 15.5, 7.7 Hz, 3H), 5.93 (dt, J = 15.6, 1.4 Hz, 1H), 5.02−4.95 (m, 1H), 2.56 (dt, J = 7.6, 1.6 Hz, 2H), 2.37−2.26 (m, 1H), 2.02−1.84 (m, 3H), 1.38 (s, 2.03H major, C1-Me), 1.35 (s, 0.97H minor, C1-Me). ^{13}C NMR (151 MHz): δ 170.9, 148.1, 142.9, 128.4, 127.4, 125.8, 123.3, 82.7, 81.4, 44.9, 37.3, 35.2, 27.5. HRMS (ESI): m/z calcd for ($C_{15}H_{18}O_3$ Na [M + H] $^+$) 269.1154, found 269.1159.

*(E)-N-Methoxy-N-methyl-4-(2-methyl-5-phenyltetrahydrofuran-2-yl)but-2-enamide (**14**).* Prepared from hydroxy Weinreb amide **11** according to the representative procedure above, but at a reaction temperature of 60 °C. The 2:1 dr was determined based on relative peak integrations of the NMe, OMe, and C1-Me groups. Resonances for the minor diastereomer were also observable, but not resolved, for C5-H and the amide side chain β-H. IR (neat) (cm^{-1}): 2971, 2938, 1667, 1638, 1421, 1384, 1313, 1097, 1046, 1002, 705. ^{1}H NMR (600 MHz): δ 7.39−7.30 (m, 4H), 7.26−7.21 (m, 1H), 7.09−7.00 (m, 1H), 6.51 (d, J = 15.3 Hz, 1H), 5.01−4.93 (m, 1H), 3.71 (s, 2.07H major, NMe), 3.70 (s, 0.93H minor, NMe), 3.26 (s, 2.03H major, OMe), 3.25 (s, 0.97H minor, OMe), 2.63−2.53 (m, 2H), 2.38−2.27 (m, 1H), 2.06−1.97 (m, 1H), 1.96−1.79 (m, 2H), 1.39 (s, 2.03H major, C1-Me), 1.36 (s, 0.97H minor, C1-Me). ^{13}C NMR (151 MHz, $CDCl_3$): δ 143.4, 143.0, 128.3, 127.2, 125.9, 125.8, 121.6, 83.0, 82.8, 81.3, 80.3, 61.7, 44.7, 36.9, 35.5, 27.7. HRMS (ESI): m/z calcd for ($C_{17}H_{24}NO_3$ [M + H]$^+$) 290.1756, found 290.1761.

*4-(2-Methyltetrahydrofuran-2-yl)-1-phenylbutan-1-one (**16**).* Prepared from diol **15** according to the representative procedure above. IR (neat): 2925, 2856, 1686, 1452, 1376, 1105, 754, 700. ^{1}H NMR (600 MHz): δ 7.96 (d, J = 7.4 Hz, 2H), 7.56 (t, J = 7.9 Hz, 1H), 7.46 (t, J = 7.8 Hz, 2H), 3.84 (q, J = 7.8 Hz, 1H), 3.80 (q, J = 6.9 Hz, 1H), 3.00 (td, J = 7.1, 1.6 Hz, 2H), 1.98−1.86 (m, 2H), 1.84−1.74 (m, 3H), 1.70−1.52 (m, 3H), 1.21 (s, 3H). ^{13}C NMR (151 MHz): δ 200.3, 137.0, 132.9, 128.6, 128.0, 82.5, 67.2, 40.7, 38.9, 36.6, 26.1, 25.7, 19.6. HRMS (ESI): m/z calcd for ($C_{15}H_{21}O_2$ [M + H]$^+$) 233.1542, found 233.1546.

*4-(2-Methyltetrahydrofuran-2-yl)-1-phenylbutan-1-one-2-d (**18**).* Prepared from diol **17** according to the representative procedure above. IR (neat): 2965, 2870, 1682, 1597, 1449, 1373, 1268, 1178, 1045, 744, 692. ^{1}H NMR (600 MHz): δ 7.89 (d, J = 7.5 Hz, 2H), 7.48 (t, J = 7.1 Hz, 1H), 7.39 (t, J = 7.6 Hz, 2H), 3.77 (q, J = 7.8 Hz, 1H), 3.72 (q, J = 7.3 Hz, 1H), 2.90 (qq, J = 6.1, 3.5, 2.9 Hz, 1H), 1.94−1.79 (m, 2H), 1.77−1.64 (m, 3H), 1.67−1.54 (m, 2H), 1.57−1.49 (m, 1H), 1.13 (s, 3H). ^{13}C NMR (151 MHz): δ 200.4, 137.0, 132.9, 128.6, 128.0, 82.5, 67.2, 40.7, 38.7, 38.6, 38.4, 36.6, 26.1, 25.8, 19.5. HRMS (ESI): m/z calcd for ($C_{15}O_2H_{20}$ D [M + H] $^+$) 234.1604, found 234.1608.

3. Deuterium Labeling Experiments. *3a. Singly Vinylic Deuterium-Labeled Diol Substrate **19a** (→ **23a**, **24a**). 6-((tert-Butyldiphenylsilyl)oxy)-2-methylhex-1-en-3-one (**S41**).* In a 100 mL round-bottom flask, alcohol **S3** (1.00 g, 2.71 mmol) was dissolved in CH_2Cl_2 (30 mL). PCC (1.17 g, 5.43 mmol, 2 equiv) was added and the solution was stirred at rt until complete conversion had occurred as judged by TLC. The mixture was filtered through a pad of silica with hexane/EtOAc 9:1 and concentrated by rotary evaporation to afford ketone **S41** (0.95 g, 2.59 mmol, 95%) as a colorless oil. IR (neat) (cm^{-1}): 3070, 3049, 3016, 2931, 2858, 1678, 1470, 1427, 1107, 964, 794, 738, 701. ^{1}H NMR (600 MHz): δ 7.68−7.61 (m, 2H), 7.46−7.32 (m, 8H), 5.96 (s, 1H), 5.75 (s, 1H), 3.70 (t, J = 6.0 Hz, 2H), 2.80 (t, J = 7.4 Hz, 2H), 1.87 (s, 3H), 1.05 (s, 9H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 201.9, 144.4, 135.5, 133.8, 129.6, 127.7, 124.5, 63.1, 33.8, 27.3, 26.8, 19.2, 17.7. HRMS (ESI): m/z calcd for ($C_{23}H_{30}O_2SiNa$ [M + Na]$^+$) 389.1913, found 389.1908.

*6-((tert-Butyldiphenylsilyl)oxy)-2-methylhex-1-en-3-d-3-ol (**S42**).* In a 25 mL round-bottom flask, ketone **S41** (1.00 g, 2.73 mmol) was dissolved in MeOH (10 mL) at rt. $CeCl_3$·7(H_2O) (1.01 g, 2.73 mmol) was added with stirring, followed by $NaBD_4$ (114 mg, 2.73 mmol, 1 equiv). The solution was stirred until complete conversion had occurred as judged by TLC. The reaction was quenched by the addition of 10% HCl (10 mL) and extracted with Et_2O (3 × 10 mL). The organic layers were combined, washed with brine, dried ($MgSO_4$), filtered, and concentrated by rotary evaporation to afford the crude product as a colorless oil. Purification by silica flash chromatography (hexanes/EtOAc 4:1) yielded allylic alcohol **S42** (780 mg, 2.11 mmol, 77%) as a colorless oil. ^{1}H NMR (600 MHz): δ 7.69−7.64 (m, 2H), 7.45−7.40 (m, 4H), 7.40−7.35 (m, 4H), 4.95 (s, 1H), 4.84 (s, 1H), 3.71−3.65 (m, 2H), 1.72 (s, 5H), 1.67−1.54 (m, 4H), 1.05 (s, 9H). ^{13}C NMR (151 MHz): δ 147.4, 135.6, 133.7, 129.6, 127.6, 111.0, 75.1(t), 63.9, 31.6, 28.5, 26.8, 19.2, 17.7. HRMS (ESI): m/z calcd for ($C_{23}H_{32}DO_2Si$ [M + H]$^+$) 370.2311, found 370.2313.

*Ethyl (E)-8-((tert-Butyldiphenylsilyl)oxy)-4-methyloct-4-enoate-5-d (**S43**).* In a 25 mL round-bottom flask, allylic alcohol **S42** (780 mg, 2.11 mmol), triethyl orthoacetate (10 mL), and propionic acid (16 μL, 0.21 mmol, 0.1 equiv) were added. The flask was equipped with a distillation head and heated to 140 °C during which time ethanol was collected. Heating was continued at this temperature until complete conversion had occurred as judged by TLC. The mixture was cooled to rt and quenched with 1 M HCl (10 mL). The mixture was extracted with Et_2O (3 × 10 mL), washed with 1 M NaOH (10 mL), dried ($MgSO_4$), filtered, and concentrated by rotary evaporation to afford the crude product as a yellow oil. Purification by silica flash chromatography (9:1 hexanes/EtOAc) yielded ester **S43** (750 mg, 80%) as a colorless oil. ^{1}H NMR (600 MHz): δ 7.66 (d, J = 6.5 Hz, 2H), 7.44−7.34 (m, 8H), 4.11 (q, J = 7.1 Hz, 2H), 3.64 (t, J = 6.3 Hz, 2H), 2.39−2.34 (m, 2H), 2.28 (dd, J = 8.9, 6.2 Hz, 2H), 2.06 (t, J = 7.4 Hz, 2H), 1.67−1.50 (m, 5H), 1.24 (t, J = 7.2 Hz, 3H), 1.05 (s, 9H). ^{13}C NMR (151 MHz): δ 173.5, 135.6, 134.8, 134.1, 129.5, 127.6, 124.5 (t), 63.3, 60.2, 34.6, 33.2, 32.3, 26.8, 24.0, 19.2, 15.9, 14.3. HRMS (ESI): m/z calcd for ($C_{27}H_{38}DO_3Si$ [M + H]$^+$) 440.2731, found 440.2740.

*(E)-8-((tert-Butyldiphenylsilyl)oxy)-4-methyl-1,1-diphenyloct-4-en-5-d-1-ol (**S44**).* In a 25 mL round-bottom flask, ester **S43** (750 mg, 1.71 mmol) was dissolved in THF (10 mL), and the solution was

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cooled to 0 °C. PhMgBr (1.0 M in THF, 3.75 mL, 3.75 mmol, 2.2 equiv) was added dropwise with stirring. Once addition was complete, the solution was allowed to warm to rt, and stirring was continued until complete conversion had occurred as judged by TLC. The mixture was quenched with 1 M HCl (10 mL), extracted with Et_2O (3 × 10 mL), dried ($MgSO_4$), filtered, and concentrated by rotary evaporation to afford the crude product as a yellow oil. Purification by silica flash chromatography (4:1 hexanes/EtOAc) yielded alcohol **S44** (505 mg, 0.92 mmol, 54%) as a colorless oil. ^{1}H NMR (600 MHz): δ 7.69−7.63 (m, 4H), 7.45−7.33 (m, 10H), 7.31 (dd, J = 8.4, 7.1 Hz, 4H), 7.22 (t, J = 8.1 Hz, 2H), 3.64 (t, J = 6.3 Hz, 2H), 2.39−2.34 (m, 2H), 2.09−2.01 (m, 2H), 1.99−1.93 (m, 2H), 1.58 (tq, 5H), 1.04 (s, 9H). ^{13}C NMR (151 MHz): δ 147.0, 135.5, 134.8, 134.0, 129.5, 128.1, 127.6, 126.7, 126.0, 124.2 (t), 78.5, 63.4, 40.0, 34.0, 32.6, 26.8, 24.1, 19.2, 16.2. HRMS (ESI): m/z calcd for ($C_{37}H_{43}DO_2SiNa$ [M + Na]$^+$) 572.3068, found 572.3071.

*(E)-4-Methyl-1,1-diphenyloct-4-ene-5-d-1,8-diol (**19a**).* In a 10 mL round-bottom flask, protected alcohol **S44** (425 mg, 0.77 mmol) was dissolved in THF (8 mL) at rt. TBAF (1.0 M in THF, 1.55 mL, 1.55 mmol, 2 equiv) was added, and the solution was stirred until complete conversion had occurred as judged by TLC. The reaction mixture was concentrated by rotary evaporation. Purification by silica flash chromatography (1:1 hexanes/EtOAc) yielded diol **19a** (220 mg, 0.71 mmol, 91%) as a colorless oil. ^{1}H NMR (600 MHz): δ 7.41 (d, J = 8.1 Hz, 4H), 7.31 (t, J = 8.4 Hz, 4H), 7.22 (t, J = 7.3 Hz, 2H), 3.61 (t, J = 6.5 Hz, 2H), 2.45 (s, 1H), 2.42−2.35 (m, 2H), 2.05 (t, J = 7.4 Hz, 2H), 2.01−1.94 (m, 2H), 1.62 (s, 3H), 1.59 (quint, J = 7.3 Hz, 2H), 1.42 (s, 1H). ^{13}C NMR (151 MHz): δ 146.9, 136.0, 128.1, 126.8, 125.9, 123.8 (t), 78.5, 62.6, 40.0, 33.9, 32.6, 24.1, 16.2. HRMS (ESI): m/z calcd for ($C_{21}H_{25}DO_2Na$ [M + Na]$^+$) 334.1893, found 334.1890.

*4-(2-Methyl-5,5-diphenyltetrahydrofuran-2-yl)butanal-4-d (**23a**).* Prepared from diol **19a** according to the representative procedure in section 2a, but at a reaction temperature of 60 °C. ^{1}H NMR (600 MHz): δ 9.70 (s, 1H), 7.43 (d, J = 8.3 Hz, 4H), 7.26 (ddd, J = 8.1, 7.1, 4.9 Hz, 4H), 7.20−7.09 (m, 2H), 2.73−2.57 (m, 2H), 2.39 (qd, J = 7.6, 6.8, 1.8 Hz, 2H), 1.88−1.74 (m, 3H), 1.70−1.62 (m, 1H), 1.48 (dd, J = 12.2, 4.6 Hz, 1H), 1.27 (s, 3H). ^{13}C NMR (151 MHz): δ 202.7, 148.0, 147.6, 127.9, 127.9, 126.4, 126.4, 125.8, 125.7, 88.0, 83.9, 44.2, 41.2 (t), 38.6, 37.6, 26.3, 17.5. HRMS (ESI): m/z calcd for ($C_{21}H_{23}DO_2Na$ [M + Na]$^+$) 332.1737, found 332.1741.

*2-(3,3-Diphenylpropyl)-6-methoxy-2-methyltetrahydro-2H-pyran-3-d (**24a**).* In a 5 mL round-bottom flask, diphenyl THF **23a** (10 mg, 0.032 mmol) was dissolved in MeOH (2 mL), and 10% Pd/C (100 mg) was added. The flask was placed in a Parr reactor, pressurized to 150 psi with H_2, and stirred at rt for 12h. The mixture was filtered through a pad of Celite and washed with Et_2O and the solvent removed under reduced pressure to afford the product as a mixture of α- and β-isomers. The isomers were separated by preparative TLC (benzene/EtOAc 99:1) to yield methoxytetrahydropyran ***α*-24a** (4.7 mg, 0.014 mmol) and ***β*-24a** (4.3 mg, 0.012 mmol, 85%) as a colorless oils.

***α*-24a**. ^{1}H NMR (600 MHz): δ 7.31−7.23 (m, 8H), 7.20−7.15 (m, 2H), 4.42 (dd, J = 6.2, 3.0 Hz, 1H), 3.84 (t, J = 7.8 Hz, 1H), 3.41 (s, 3H), 2.12 (q, J = 7.9 Hz, 2H), 1.75−1.69 (m, 1H), 1.69−1.60 (m, 2H), 1.52−1.46 (m, 1H), 1.46−1.36 (m, 2H), 1.25 (s, 3H). ^{13}C NMR (151 MHz): δ 145.2, 144.9, 128.5, 127.8, 127.8, 126.1, 98.2, 74.5, 55.5, 51.9, 37.0, 35.0, 30.5 (t), 29.3, 26.6, 16.9. HRMS (ESI): m/z calcd for ($C_{22}H_{27}DO_2Na$ [M + Na]$^+$) 348.2050, found 348.2061.

***β*-24a**. ^{1}H NMR (600 MHz): δ 7.31−7.22 (m, 8H), 7.16 (dddd, J = 8.3, 7.0, 4.0, 1.7 Hz, 2H), 4.53 (dd, J = 8.6, 2.5 Hz, 1H), 3.85 (t, J = 7.0 Hz, 1H), 3.40 (s, 3H), 2.23−2.07 (m, 2H), 1.71 (tq, J = 4.1, 3.4 Hz, 2H), 1.61 (ddt, J = 11.7, 8.6, 4.5 Hz 1H), 1.58−1.53 (m, 2H), 1.49 (ddd, J = 13.6, 12.0, 4.9 Hz, 1H), 1.32 (tt, J = 6.1, 4.0 Hz, 1H), 1.17 (s, 3H). ^{13}C NMR (151 MHz): δ 145.4, 144.8, 128.4, 128.4, 127.9, 127.8, 126.1, 126.0, 98.3, 75.1, 55.6, 51.9, 42.2, 34.2 (t), 31.1, 29.4, 21.4, 18.1. HRMS (ESI): m/z calcd for ($C_{22}H_{27}DO_2Na$ [M + Na]$^+$) 348.2050, found 348.2050.

*3b. Doubly Allylic Deuterium-Labeled Diol Substrate **19b** (→ **23b**, **24b**). 4-((tert-Butyldiphenylsilyl)oxy)butanal-2,2-d_2 (**S45**).*[24] In a 10 mL round-bottom flask, aldehyde **S2** (1.00 g, 3.06 mmol) was suspended in D_2O (3 mL), and DMAP (37 mg, 0.306 mmol, 10 mol %) was added. The suspension was heated to 70 °C for 12 h. The reaction mixture was diluted with 1 M HCl (10 mL), extracted with Et_2O (3 × 10 mL), dried ($MgSO_4$), filtered, and concentrated by rotary evaporation to afford the crude product as a colorless oil. The product was purified by silica flash chromatography (9:1 hexanes/EtOAc) to yield diol **S45** (0.99 g, 0.303 mmol, 99%) as a colorless oil. ^{1}H NMR (600 MHz): δ 9.79 (s, 1H), 7.65 (d, J = 6.5 Hz, 2H), 7.45−7.34 (m, 8H), 3.69 (t, J = 6.0 Hz, 2H), 1.87 (t, J = 6.0 Hz, 2H), 1.04 (s, 9H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 202.8, 135.5, 134.8, 133.5, 129.7, 127.7, 127.7, 62.9, 40.0 (p), 26.8, 26.5, 25.1, 19.2. HRMS (ESI): m/z calcd for ($C_{20}H_{25}D_2O_2Si$ [M + H]$^+$) 329.1906, found 329.1912.

*6-((tert-Butyldiphenylsilyl)oxy)-2-methylhex-1-en-4,4-d_2-3-ol (**S46**).* In a 25 mL round-bottom flask, aldehyde **S45** (950 mg, 2.89 mmol) was dissolved in THF (5 mL), and the solution was cooled to 0 °C. Isopropenylmagnesium bromide (0.5 M in THF, 5.8 mL, 2.9 mmol, 1 equiv) was added slowly via syringe. Once addition of the Grignard was complete, the cooling bath was removed and the solution was allowed to stir at rt until complete conversion had occurred as judged by TLC. The mixture was recooled to 0 °C and quenched with 1 M HCl (10 mL). The mixture was extracted with Et_2O (3 × 10 mL), dried ($MgSO_4$), filtered, and concentrated by rotary evaporation to afford the crude product as a yellow oil. Purification by silica flash chromatography (4:1 hexanes/EtOAc) yielded allylic alcohol **S46** (850 mg, 2.29 mmol, 79%) as a yellow oil. ^{1}H NMR (600 MHz): δ 7.69−7.65 (m, 2H), 7.46−7.34 (m, 8H), 4.95 (s, 1H), 4.84 (s, 1H), 4.07 (s, 1H), 3.72−3.64 (m, 2H), 1.72 (s, 3H), 1.65−1.54 (m, 2H), 1.05 (s, 9H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 147.5, 135.6, 135.5 134.8, 133.7, 129.6, 127.7, 110.9, 75.5, 63.9, 31.0(p), 28.3, 26.8, 26.5, 19.2, 17.7. HRMS (ESI): m/z calcd for ($C_{23}H_{31}D_2O_2Si$ [M + H]$^+$) 371.2375, found 371.2358.

*Ethyl (E)-8-((tert-Butyldiphenylsilyl)oxy)-4-methyloct-4-enoate-6,6-d_2 (**S47**).* In a 50 mL round-bottom flask, **S46** (650 mg, 1.75 mmol), triethyl orthoacetate (5 mL), and propionic acid (13 μL, 0.18 mmol, 0.1 equiv) were added. The flask was equipped with a distillation head and heated to 140 °C during which time ethanol was collected. Heating was continued at this temperature until complete conversion had occurred as judged by TLC. The mixture was cooled to rt and quenched with 1 M HCl (10 mL). The mixture was extracted with Et_2O (3 × 10 mL), washed with 1 M NaOH (10 mL), dried ($MgSO_4$), filtered, and concentrated by rotary evaporation to afford the crude product as a yellow oil. Purification by silica flash chromatography (9:1 hexanes/EtOAc) yielded ester **S47** (470 mg, 61%) as a colorless oil. ^{1}H NMR (600 MHz): δ 7.66 (d, J = 6.2 Hz, 2H), 7.43−7.32 (m, 8H), 5.12 (s, 1H), 4.11 (q, J = 7.1 Hz, 2H), 3.64 (t, J = 6.3 Hz, 2H), 2.36 (q, J = 8.1 Hz, 2H), 2.28 (q, J = 7.6 Hz, 2H), 1.59 (s, 3H), 1.56 (t, J = 6.4 Hz, 2H), 1.24 (t, J = 7.1 Hz, 3H), 1.05 (s, 9H). ^{13}C NMR (151 MHz): δ 173.5, 135.6, 134.1, 133.8, 129.5, 127.6, 127.6, 124.8, 63.3, 60.2, 34.7, 33.3, 32.5, 26.9, 23.5 (p), 19.2, 15.9, 14.3. HRMS (ESI): m/z calcd for ($C_{27}H_{37}D_2O_3Si$ [M + H]$^+$) 441.2794, found 441.2794.

*(E)-8-((tert-Butyldiphenylsilyl)oxy)-4-methyl-1,1-diphenyloct-4-en-6,6-d_2-1-ol (**S48**).* In a 25 mL round-bottom flask, ester **S47** (200 mg, 0.45 mmol) was dissolved in THF (5 mL), and the solution was cooled to 0 °C. PhMgBr (1.0 M in THF, 1.00 mL, 1.00 mmol, 2.2 equiv) was added dropwise with stirring. Once addition was complete, the solution was allowed to warm to rt, and stirring was continued until complete conversion had occurred as judged by TLC. The mixture was quenched with 1 M HCl (5 mL), extracted with Et_2O (3 × 5 mL), dried ($MgSO_4$), filtered, and concentrated by rotary evaporation to afford the crude product as a yellow oil. Purification by silica flash chromatography (4:1 hexanes/EtOAc) yielded alcohol **S48** (75 mg, 0.14 mmol, 30%) as a colorless oil. ^{1}H NMR (600 MHz): δ 7.70−7.62 (m, 2H), 7.43−7.38 (m, 8H), 7.37−7.33 (m, 4H), 7.31 (dd, J = 8.4, 7.1 Hz, 4H), 7.24−7.20 (m, 2H), 5.08 (s, 1H), 3.64 (t, J = 6.3 Hz, 2H), 2.40−2.34 (m, 2H), 2.32 (s, 1H), 2.00−1.93 (m, 2H), 1.60 (s, 3H), 1.56 (t, J = 6.4 Hz, 2H), 1.04 (s, 9H). ^{13}C NMR (151 MHz): δ 147.0, 135.6, 135.5, 134.0, 129.5, 128.1, 127.6, 126.7, 126.0, 124.4, 78.5, 63.3, 40.0, 34.0, 32.4, 26.8, 23.5 (quint.), 19.2, 16.2.

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HRMS (ESI): m/z calcd for ($C_{37}H_{42}D_2O_2SiNa$ [M + Na]$^+$) 573.3134, found 573.3121.

*(E)-4-Methyl-1,1-diphenyloct-4-ene-6,6-d_2-1,8-diol (**19b**).* In a 10 mL round-bottom flask, protected alcohol **S48** (75 mg, 0.14 mmol) was dissolved in THF (2 mL) at rt. TBAF (1.0 M in THF, 0.27 mL, 0.27 mmol, 2 equiv) was added, and the solution was stirred until complete conversion had occurred as judged by TLC. The reaction mixture was concentrated by rotary evaporation. Purification by silica flash chromatography (1:1 hexanes/EtOAc) yielded diol **19b** (29 mg, 0.092 mmol, 68%) as a colorless oil. ^{1}H NMR (600 MHz): δ 7.41 (d, J = 7.3 Hz, 3H), 7.30 (t, J = 7.3 Hz, 4H), 7.22 (t, J = 7.3 Hz, 2H), 5.12 (s, 1H), 3.60 (t, J = 6.5 Hz, 2H), 2.42−2.35 (m, 2H), 2.03−1.94 (m, 2H), 1.62 (d, J = 1.4 Hz, 3H), 1.57 (t, J = 6.6 Hz, 2H). ^{13}C NMR (151 MHz): δ 147.0, 136.1, 128.2, 126.8, 126.0, 124.1, 78.5, 62.6, 40.1, 34.0, 32.4, 23.6 (p), 16.3. HRMS (ESI): m/z calcd for ($C_{21}H_{24}D_2O_2Na$ [M + Na]$^+$) 335.1956, found 335.1955.

*4-(2-Methyl-5,5-diphenyltetrahydrofuran-2-yl)butanal-3,4-d_2 (**23b**).* Prepared from diol **19b** according to the representative procedure in section 2a, but at a reaction temperature of 60 °C. ^{1}H NMR (600 MHz): δ 9.71 (s, 1H), 7.43 (d, J = 8.2 Hz, 2H), 7.26 (td, J = 7.6, 3.6 Hz, 4H), 7.17 (q, J = 7.3 Hz, 2H), 2.69 (dt, J = 13.3, 6.8 Hz, 1H), 2.63 (dt, J = 12.8, 7.3 Hz, 1H), 2.39 (t, J = 6.2 Hz, 2H), 1.90−1.76 (m, 2H), 1.66 (quint, J = 7.3 Hz, 1H), 1.54 (d, J = 12.2 Hz, 1H), 1.28 (s, 3H). ^{13}C NMR (151 MHz): δ 202.7, 148.0, 147.6, 127.9, 126.5, 126.4, 125.8, 125.7, 88.0, 84.0, 44.1, 41.2 (t), 38.6, 37.6, 26.4, 17.2 (t). HRMS (ESI): m/z calcd for ($C_{21}H_{22}D_2O_2Na$ [M + Na]$^+$) 333.1797, found 333.1800.

*2-(3,3-Diphenylpropyl)-6-methoxy-2-methyltetrahydro-2H-pyran-3,4-d_2 (**24b**).* In a 5 mL round-bottom flask, diphenyl THF **23b** (10 mg, 0.032 mmol) was dissolved in MeOH (2 mL) and 10% Pd/C (100 mg) was added. The flask was placed in a Parr reactor, pressurized to 150 psi with H_2, and stirred at rt for 12 h. The mixture was filtered through a pad of Celite and washed with Et_2O and the solvent removed under reduced pressure to afford the product as a mixture of α- and β-isomers. The isomers were separated by preparative TLC (benzene/EtOAc 99:1) to yield methoxytetrahydropyran ***α*-24b** (4.5 mg, 0.014 mmol) and ***β*-24b** (4.1 mg, 0.012 mmol, 85%) as a colorless oils.

***α*-24b**. ^{1}H NMR (600 MHz): δ 7.32−7.23 (m, 8H), 7.20−7.15 (m, 2H), 4.42 (dd, J = 6.3, 3.0 Hz, 1H), 3.84 (t, J = 7.8 Hz, 1H), 3.41 (s, 3H), 2.15−2.09 (m, 2H), 1.69−1.59 (m, 2H), 1.45 (s, 1H), 1.43−1.38 (m, 2H), 1.25 (s, 3H). ^{13}C NMR (151 MHz): δ 145.2, 144.9, 128.5, 127.8, 126.1, 98.2, 74.5, 55.5, 51.9, 37.0, 34.5 (t), 30.4, 29.3, 26.6, 16.6 (t). HRMS (ESI): m/z calcd for ($C_{22}H_{26}D_2O_2Na$ [M + Na]$^+$) 349.2113, found 349.2114.

***β*-24b**. ^{1}H NMR (600 MHz): δ 7.31−7.22 (m, 8H), 7.20−7.12 (m, 2H), 4.53 (dd, J = 8.6, 2.6 Hz, 1H), 3.85 (t, J = 7.1 Hz, 1H), 3.40 (s, 3H), 2.23−2.07 (m, 2H), 1.72 (ddd, J = 12.7, 4.5, 2.6 Hz, 1H), 1.67 (q, J = 4.5 Hz, 1H), 1.57 (td, J = 13.5, 12.0 Hz, 2H), 1.49 (td, J = 13.6, 12.0 Hz, 1H), 1.36 (d, J = 4.4 Hz, 1H), 1.17 (s, 3H). ^{13}C NMR (151 MHz): δ 145.4, 144.8, 128.4, 128.3, 127.9, 127.8, 126.1, 126.0, 98.3, 75.1, 55.6, 51.9, 42.2, 33.7 (t), 31.0, 29.4, 21.5, 17.7 (t). HRMS (ESI): m/z calcd for ($C_{22}H_{26}D_2O_2Na$ [M + Na]$^+$) 349.2113, found 349.2122.

*3c. Synthesis of Unlabeled Cyclic Acetals **24-H$_3$** for NMR Comparison. 2-(3,3-Diphenylpropyl)-6-methoxy-2-methyltetrahydro-2H-pyran (**24-H$_3$**).* In a 5 mL round-bottom flask, diphenyl THF, **5h** (10 mg, 0.032 mmol) was dissolved in MeOH (2 mL), and 10% Pd/C (100 mg) was added. The flask was placed in a Parr reactor, pressurized to 150 psi with H_2, and stirred at rt for 12h. The mixture was filtered through a pad of Celite and washed with Et_2O and the solvent removed under reduced pressure to afford the product as a mixture of α- and β-isomers. The isomers were separated by preparative TLC (benzene/EtOAc 99:1) to yield methoxytetrahydropyran ***α*-24-H$_3$** (4.5 mg, 0.014 mmol) and ***β*-24-H$_3$** (4.0 mg, 0.012 mmol, 81%) as a colorless oils.

***α*-24-H$_3$**. IR (neat) (cm^{-1}): 3060, 3026, 2935, 1736, 1599, 1493, 1451, 1373, 1261, 1225, 1202, 1156, 1123, 1066, 1034, 974, 914, 875, 802, 745, 700. ^{1}H NMR (600 MHz): δ 7.31−7.23 (m, 8H), 7.21−7.15 (m, 2H), 4.42 (dd, J = 6.3, 3.0 Hz, 1H), 3.84 (t, J = 7.8 Hz, 1H), 3.41 (s, 3H), 2.12 (ddd, J = 10.1, 8.3, 7.1 Hz, 2H), 1.73 (dddd, J = 10.6, 8.9, 5.4, 3.5 Hz, 1H), 1.69−1.59 (m, 2H), 1.49 (tdt, J = 12.6, 8.0, 4.1 Hz, 1H), 1.45−1.38 (m, 2H), 1.32−1.21 (m, 5H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 145.2, 144.9, 128.5, 127.8, 127.8, 126.1, 98.2, 74.6, 55.5, 51.9, 37.0, 35.0, 30.5, 29.3, 26.6, 17.0. HRMS (ESI): m/z calcd for ($C_{22}H_{28}O_2Na$ [M + Na]$^+$) 347.1987, found 347.1972.

***β*-24-H$_3$**. IR (neat) (cm^{-1}): 3060, 3026, 2942, 2872, 1736, 1674, 1599, 1493, 1451, 1377, 1263, 1229, 1160, 1119, 1079, 1033, 1004, 979, 909, 744, 701. ^{1}H NMR (600 MHz): δ 7.30−7.21 (m, 8H), 7.16 (qd, J = 6.7, 3.2 Hz, 2H), 4.53 (dd, J = 8.5, 2.4 Hz, 1H), 3.85 (dd, J = 8.7, 7.0 Hz, 1H), 3.40 (s, 3H), 2.22−2.07 (m, 2H), 1.71 (tq, J = 13.1, 4.2 Hz, 2H), 1.67−1.60 (m, 1H), 1.57−1.53 (m, 2H), 1.49 (ddd, J = 13.6, 12.0, 4.9 Hz, 1H), 1.55 (ddd, J = 13.7, 11.9, 4.8 Hz, 2H), 1.17 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 145.4, 144.8, 128.4, 128.4, 127.9, 127.8, 126.1, 126.0, 98.3, 75.2, 55.6, 51.9, 42.2, 34.2, 31.1, 29.4, 21.5, 18.2. HRMS (ESI): m/z calcd for ($C_{22}H_{28}O_2Na$ [M + Na]$^+$) 347.1987, found 347.1982.

4. Computational Studies. *4a. Computational Methods.* All calculations were performed using the M06[25] functional implemented in Gaussian09.[26] The Lanl2DZ[27] (augmented with one f-function[28]) and 6-31G(d,p) basis sets were used for Pd and all other atoms, respectively. Frequency calculations at the same level of theory at the optimized geometries were carried out to confirm the stationary points as minima (zero imaginary frequencies) or transition states (one imaginary frequency) and provided the thermal corrections to the single-point energies. Single-point calculations using the SDD basis set for Pd and the 6-311++G(d,p) basis set for all other atoms and the SMD solvent model with the parameters for THF were used to account for solvent effects.

*4b. Detailed Reaction Pathway for anti-oxypalladation of Diol Substrate **4a**.* We have calculated $PdCl_2$ with two 1,4-benzoquinone molecules coordinating to Pd and found that the *trans* conformation is energetically favored (**25a-Cat1**: 6.0 kcal/mol; **25a-Cat2**: 12.4 kcal/mol) (Figure 6 and Figure S5). The ligand-exchange step then forms **25a-INT1**. This is a exothermic step, and **25a-INT1** is −14.7 kcal/mol lower in free energy than **25a-Cat1**. The *anti*-oxypalladation step then takes place through **25a** to form **25a-INT2** (−0.4 kcal/mol). The activation barrier is 8.7 kcal/mol, and diastereoselectivity is determined by the *anti*-oxypalladation transition structures.

*4c. Transition Structures for anti-Oxypalladation of Diol Substrate **1**.* We have also calculated transition structures for the *anti*-oxypalladation step in the oxidative cyclization of phenyl-substituted diol **1** en route to tetrahydrofuran product **2b**, as well as the *tert*-butyl substituted diol **4d** en route to tetrahydrofuran product **5d**. In the first system, the energy difference between **25a-Ph** and **25b-Ph** is 0.5 kcal/mol, favoring **25a-Ph** that leads to the major diastereomer (Figure S6). Similary, in the second system, the energy difference between **25a-tBu** and **25b-tBu** is 0.6 kcal/mol, favoring **25a-tBu** that leads to the major diastereomer (Figure S7).

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b02053.

Complete experimental protocols and analytical data for all new compounds; details of computational methodology, including coordinates and energies for all described transition structures (PDF)

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: tand@mskcc.org.

ORCID

Joshua L. Brooks: 0000-0002-9404-8173

Notes

The authors declare no competing financial interest.

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