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Lewis-acid catalyzed formation of dihydropyrans

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Dedicated to Professor Gilbert Stork whose seminal contributions have inspired generations of synthetic chemists

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ABSTRACT

A methodology is described for the synthesis of 2,6-disubstituted dihydro[2*H*]pyrans through a Lewis-acid catalyzed 6-*endo*-*trig* cyclization of β-hydroxy-γ,δ-unsaturated alcohols. Employing alkyl-substituted allylic diols and catalytic amounts of a Lewis acid, such as $BF_3{\cdot}OEt_2$, the corresponding *syn*-pyrans are formed highly diastereoselectively and in good yields. The described process is simple to execute, proceeds readily at ambient temperature, and is scalable.

1. Introduction

Polysubstituted di- and tetrahydropyrans are ubiquitous structural elements in biologically important natural products.[1] For example, natural products incorporating dihydropyranyl moieties include, among others, ambruticin S,[2] jerangolid A,[3] cacospongionolide,[4] 4,5-deoxyneodolabelline,[5] funiculosin,[6] laulimalide,[7] penitrem D,[8] scytophycin C,[9] sorangicin A,[10] swinholide A,[11] and wortmannilactone G[12] (Fig. 1). *Syn* or *anti* disposition of substituents on the pyran ring affects the three dimensional shape of the heterocyclic moiety and the biological activity of the molecule.

Although substantial efforts have been made to develop methods for the construction of di- and tetrahydropyrans,[13] the stereocontrolled synthesis of these cyclic ethers and related heterocycles is still a challenging and interesting task. 2,6-Disubstituted dihydro[2*H*]pyrans are attractive targets, particularly with regard to controlling the *syn*- and *anti*-disposition of the substituents.

As part of a research program on antifungal polyketides, we developed a novel synthesis of ambruticin S[14] and jerangolid A,[15] which include the same dihydro[2*H*]pyran harboring a trisubstituted double bond (Figs. 1 and 2). Our synthetic plan toward the construction of the dihydropyran ring was originally aimed at using a transition metal catalyzed methodology developed by Uenishi and others (Scheme 1).[16–19] Allylic diols undergo stereoselective 6-*exo*- or 6-*endo*-*trig* cyclization upon treatment with catalytic amounts of $Pd(CH_3CN)_2Cl_2$ forming tetrahydro- or dihydropyrans, respectively. Thus, reaction of β-hydroxy-γ,δ-unsaturated alcohols **2a**,**b** affords either 2,6-*syn*- or 2,6-*anti*-3,6-dihydro[2*H*]pyrans **1** via an overall *syn*-S_N2' type process, with the *syn*/*anti* selectivity being controlled by the relative configuration of the diol. A major advantage of this methodology is the absence of any by-products, as only water is eliminated during the cyclization.

In considering an approach to the trisubstituted dihydropyran ring in ambruticin S[2,14] and jerangold A,[3,15] we attempted Uenishi's Pd-catalyzed cycloetherification protocol (Fig. 2). Our initial experiments resulted in the formation of the desired products, albeit as a mixture of diastereomers. However, a cationic Pd-catalyzed cycloetherification led to the desired *syn*-isomer as the preponderant if not exclusive product. These results ultimately led to the exploration of a novel Lewis-acid catalyzed 6-*endo*-*trig* cyclization of β-hydroxy-γ,δ-unsaturated alcohols to give dihydro[2*H*]pyrans. Herein, we report our initial results, the optimization strategy, and substrate scope.

2. Results

A series of *E*- and *Z*-β-hydroxy-γ,δ-unsaturated alcohols was synthesized using three different synthetic approaches. The *E*-

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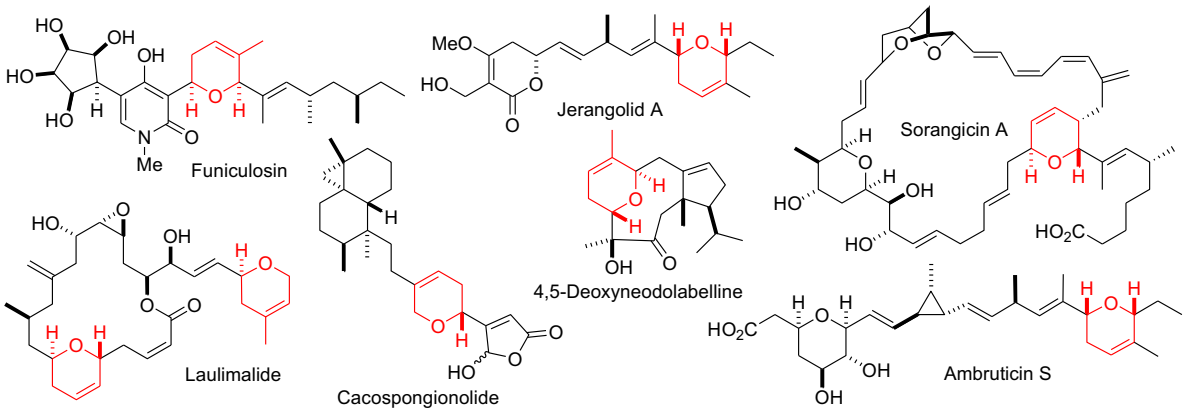


Fig. 1. Selected examples of dihydro[2*H*]pyran segment containing natural products.

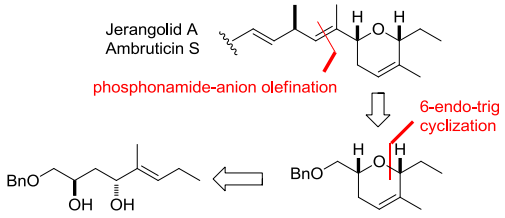
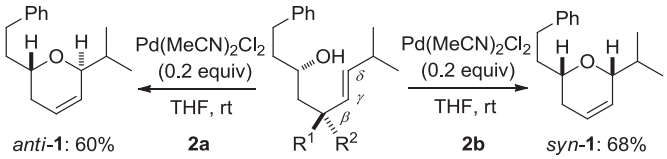


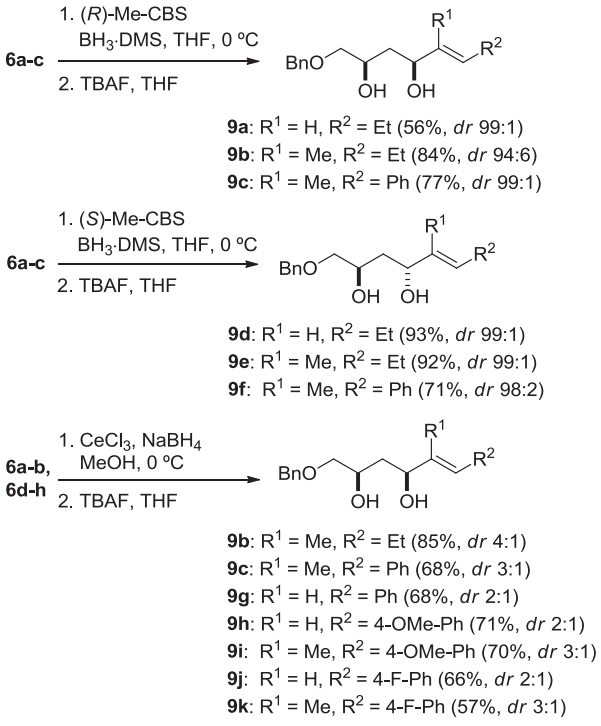
Fig. 2. Retrosynthesis of ambruticin and jerangolid.



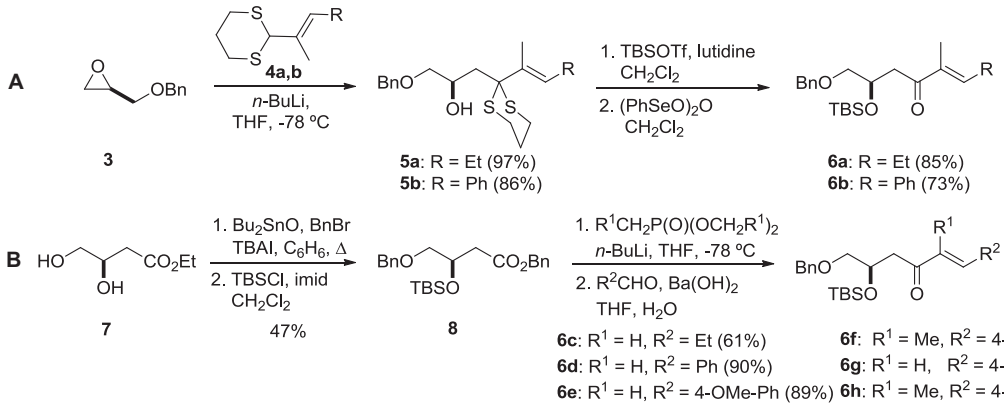
2a: R^1 = OH, R^2 = H
2b: R^1 = H, R^2 = OH

Scheme 1.

allylic diols were prepared either by route A or B as shown in Schemes 2 and 3. Thus, route A involved opening of (*R*)-glycidol benzyl ether (**3**) with dithiane **4a** or **4b**,[20] respectively, followed by unmasking of the enone system and stereoselective reduction. Protection of the hydroxyl group in dithiane adducts **5a**,**b** as TBS-



Scheme 3.

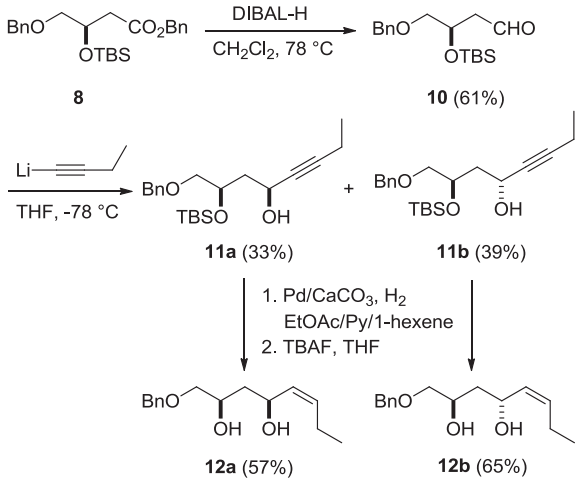


Scheme 2.

ethers proved to be necessary prior to unmasking the α,β-unsaturated system. The dithiane moiety could then be removed by treatment with benzeneseleninic anhydride[21] giving the relatively sensitive enones **6a** and **6b** in 85% and 73% yield, respectively (Scheme 2A). In route B, dihydroxy ester **7**,[22] readily available from D-malic acid, was used as the starting chiron (Scheme 2B). Conversion of the primary hydroxyl group into a benzyl ether derivative was achieved using Bu_2SnO and benzyl bromide, accompanied by concomitant transesterification. Protecting of the secondary hydroxyl group as the TBS-ether gave **8**, which was treated with the Li anion of dimethyl methylphosphonate or diethyl ethylphosphonate, respectively, to give the corresponding β-ketophosphonates. These were subsequently converted into α,β-unsaturated ketones **6c**–**h** using Paterson's protocol for the Horner–Wadsworth–Emmons olefination.[23]

Reduction of enones **6a**–**c** with either (*R*)-Me-CBS or (*S*)-Me-CBS followed by cleavage of the TBS-ether with TBAF furnished the diastereomerically pure diols **9a**–**f** (63–95% yield, dr 94:6–99:1) (Scheme 3). Alternatively, exposure of enones **6a**,**b** and **6d**–**h** to Luche reduction conditions followed by treatment with TBAF yielded diols **9b**,**c** and **9g**–**k** as mixtures of *syn*/*anti* diastereomers favoring the *syn*-diol.

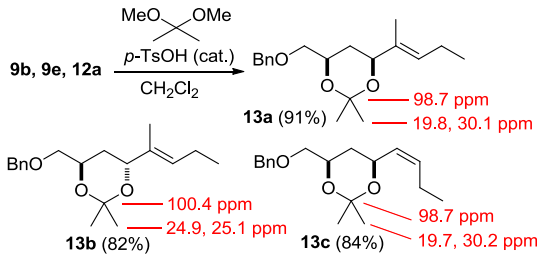
The *Z*-allylic diols **12a**,**b** were synthesized through alkyne addition to aldehyde **10**,[24] the latter being prepared from DIBAL-H reduction of benzyl ester **8** (61%, Scheme 4). Diastereomers **11a**,**b** thus obtained were separated and reduced under Lindlar conditions to provide diols **12a**,**b** in 19–25% yield (over 2 steps) as diastereomerically pure materials (Scheme 4).



Scheme 4.

The *syn*/*anti*-configuration of diols **9** and **12** was determined by ^{13}C NMR analysis of the corresponding acetonides **13** prepared from a few selected diols (Scheme 5).[25]

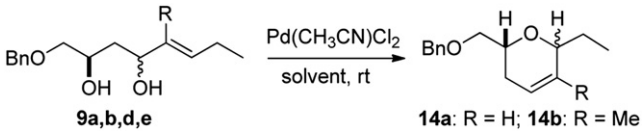
With a diverse set of allylic diols in hand, we were ready to study the 6-*endo*-*trig* cyclization and the formation of dihydropyrans.

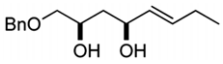
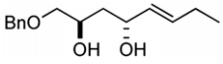
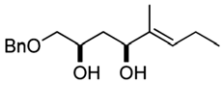
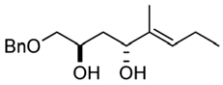
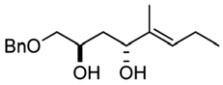
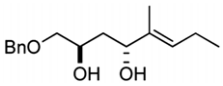
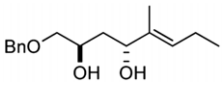
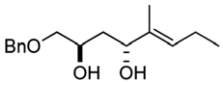
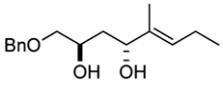


Scheme 5.

While cyclization of compounds **9a** and **9d** proceeded as expected under Uenishi's conditions ($Pd(CH_3CN)_2Cl_2$, THF) yielding the *anti*- or *syn*-dihydropyran **14a** selectively (Table 1, entries 1 and 2), we were surprised to find that the introduction of a vinylic methyl substituent was detrimental for selectivity. Thus, treatment of diols **9b** and **9e** with $Pd(CH_3CN)_2Cl_2$ in THF, both led to a 1.4:1 *syn*/*anti* mixture of dihydropyran **14b** (Table 1, entries 3 and 4). The selectivity could be improved to 6:1 favoring *syn*-**14b** by employing chlorinated solvents such CH_2Cl_2 or $CHCl_3$ (Table 1, entries 6 and 7). The use of acetonitrile as solvent led to a 7:1 selectivity, albeit accompanied by a low yield of **14b** (Table 1, entry 8).

Table 1
Formation of dihydropyrans **14** from allylic 1,3-diols **9** with $Pd(CH_3CN)_2Cl_2$

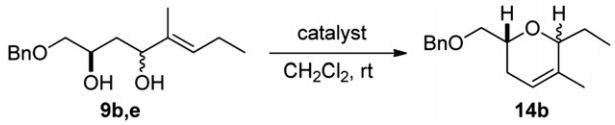


Entry	Diol	Solvent	Product	Yield (%)	*syn*/*anti*[a]
1		**9a** THF	**14a**	54	1:5
2		**9d** THF	**14a**	54	99:1
3		**9b** THF	**14b**	53	1.5:1
4		**9e** THF	**14b**	53	1.4:1
5		**9e** C_6H_6	**14b**	53	3:1
6		**9e** CH_2Cl_2	**14b**	56	6:1
7		**9e** $CHCl_3$	**14b**	57	6:1
8		**9e** CH_3CN	**14b**	21	7:1
9		**9e** Acetone	**14b**	67	3:1

[a] Determined by ^1H NMR.

Other dichloro palladium(II) complexes, such as $PdCl_2$ or $Pd(PPh_3)_2Cl_2$ failed to catalyze the conversion of diol **9e** to dihydropyran **14b** (Table 2, entries 2 and 3). Inspired by Gouverneur's study on the formation of pyranones from enones,[26] we also tested the cationic complex $Pd(CH_3CN)_4(BF_4)_2$ as catalyst in the reaction. Remarkably, *syn*-dihydropyran **14b** was formed in excellent *syn*/*anti* selectivity (>25:1) upon treatment of diol **9b** with $Pd(CH_3CN)_4(BF_4)_2$ (Table 2, entry 4). We considered the possibility that the Lewis acidity of the cationic Pd complex might induce the cyclization, and therefore tested the applicability of several other Lewis and Brønsted acids in the reaction, including $BF_3 \cdot OEt_2$ and TfOH.[27–29] Indeed, the desired

Table 2
Optimization and catalyst screening



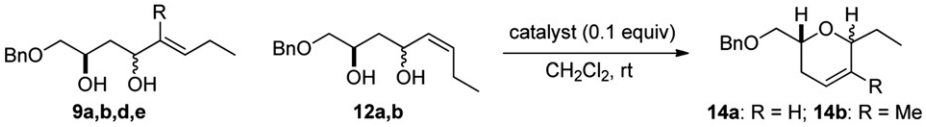
Entry	Diol	Catalyst (equiv)	Yield (%)	*syn*/*anti*[a]
1	**9e**	$Pd(CH_3CN)_2Cl_2$ (1.0)	56	6:1
2	**9e**	$PdCl_2$ (1.0)	—[b]	—
3	**9e**	$Pd(PPh_3)_2Cl_2$ (1.0)	—[b]	—
4	**9b**	$Pd(CH_3CN)_4(BF_4)_2$ (0.05)[c,d]	73	25:1
5	**9b**	$BF_3\cdot OEt_2$ (0.1)[c,d]	81	25:1
6	**9b**	$Fe(ClO_4)_2\cdot xH_2O$ (0.1)[c]	82	18:1
7	**9b**	$Cu(OTf)_2$ (0.1)[c]	40	25:1
8	**9b**	TfOH (0.1)[c]	63	15:1
9	**9b**	TsOH (0.1)[c]	44	7:1
10	**9b**	$AuCl_3$ (0.1)[c]	—[b]	—

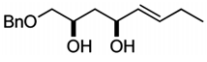
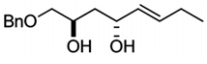
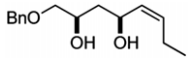
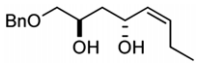
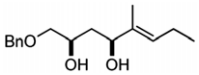
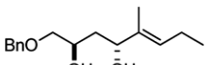
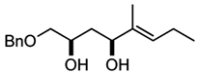
[a] Determined by ^1H NMR.
[b] No conversion observed.
[c] Using **9b** obtained from Luche reduction of **6a**, dr 4:1.
[d] Multigram scale reaction.

syn-dihydropyran **14b** was obtained in good to excellent selectivities, and moderate to good yields upon treatment of **9b** with Lewis acids. Thus, exposure of diol **9b** to $BF_3\cdot OEt_2$ led to the formation of **14b** in >25:1 *syn*/*anti* selectivity and 81% yield, while the use of $Fe(ClO_4)_2$ gave slightly lower selectivity (Table 2, entries 5 and 6). Copper(II) triflate provided **14b** highly selectively, albeit only in moderate yield (40%). We suspected that triflic acid generated from hydrolysis of $Cu(OTf)_2$ might be the active catalyst in this case, however, treatment of diol **9b** with TfOH gave **14b** with a diastereomeric ratio of only 15:1 (Table 2, entry 8). Surprisingly, $AuCl_3$ failed to catalyze the conversion of diol **9b** to **14b** (Table 2, entry 10). The cyclization proceeded smoothly on a multigram scale, using either $Pd(CH_3CN)_4(BF_4)_2$ or $BF_3\cdot OEt_2$ (Table 2, entries 4 and 5).

We next investigated the influence of the relative configuration of the starting diol on the selectivity of the cycloetherification. The diastereomeric diols **9a** and **9d** both yielded the same *syn*-dihydropyran **14a** in excellent diastereoselectivity (*syn*/*anti* >97:3) upon treatment with $BF_3\cdot OEt_2$ (Table 3, entries 1 and 2). The same outcome was observed in the case of the methyl-substituted analogues **9b** and **9e**. Using either $BF_3\cdot OEt_2$ or $Pd(CH_3CN)_4(BF_4)_2$, the *syn*-dihydropyran **14b** was formed in excellent selectivity (*syn*/*anti* >98:2) from both diols (Table 3, entries 7–10). Thus, the stereochemistry of the allylic alcohol was of no importance in the cyclization reaction, strongly suggesting a cationic mechanism. Consequently, for preparative purposes, we later applied Luche conditions ($NaBH_4$ and $CeCl_3$) for the reduction of enones **6** (Scheme 1 and 2) affording diastereomeric mixtures of diols **9**.

Table 3
Formation of *syn*-dihydropyrans **14** from alkyl-substituted allylic 1,3-diols **9** and **12**



Entry	Diol		Catalyst	Product	Yield (%)	*syn*/*anti*[b]
1		**9a**	$BF_3\cdot OEt_2$	*syn*-**14a**	75	97:3
2		**9d**	$BF_3\cdot OEt_2$	*syn*-**14a**	72	98:2
3		**12a**	$BF_3\cdot OEt_2$	*syn*-**14a**	76	99:1
4			$Pd(CH_3CN)_4(BF_4)_2$	*syn*-**14a**	41	98:2
5		**12b**	$BF_3\cdot OEt_2$	*syn*-**14a**	71	95:5
6			$Pd(CH_3CN)_4(BF_4)_2$	*syn*-**14a**	40	95:5
7		**9b**	$BF_3\cdot OEt_2$	*syn*-**14b**	76	99:1
8			$Pd(CH_3CN)_4(BF_4)_2$	*syn*-**14b**	72	98:2
9		**9e**	$BF_3\cdot OEt_2$	*syn*-**14b**	82	99:1
10			$Pd(CH_3CN)_4(BF_4)_2$	*syn*-**14b**	71	99:1
11		**9b**[a]	$Pd(CH_3CN)_4(BF_4)_2$	*syn*-**14b**	73	98:2

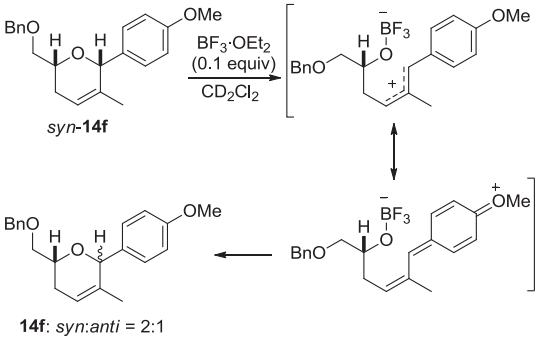
[a] Obtained from Luche reduction of **6a**, dr 4:1.
[b] Determined by HPLC.

Using a 4:1 mixture of diastereomers **9b** and **9e**, the same *syn* selectivity was obtained in the cycloetherification (Table 3, entry 11).

Additional evidence for a cationic mechanism was obtained from cyclization of diols **12a**,**b** featuring a *Z*-double bond. Indeed, subjecting the individual diastereomers of **12** to the conditions of cycloetherification ($BF_3{\cdot}OEt_2$ in CH_2Cl_2) afforded the same *syn*-product **14a** in excellent selectivity (*syn*/*anti* >95:5) and good yields (Table 3, entries 3 and 5). Usage of the cationic palladium complex $Pd(CH_3CN)_4(BF_4)_2$ resulted in the same selectivity, albeit a lower yield of **14a** (Table 3, entries 4 and 6).

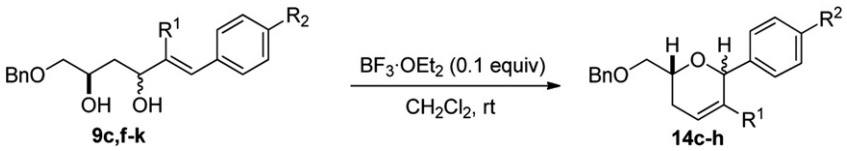
Further studies were conducted to test the effect of aryl substitution at the δ-position of the diol scaffold on the selectivity. Interestingly, when phenyl-substituted diol **9g** (dr 2:1) was subjected to the reaction conditions using $BF_3{\cdot}OEt$, dihydropyran **14c** was formed as a 3:1 mixture of diastereomers (Table 4, entry 1). A similar outcome was observed with diastereomerically pure diols **9c** and **9f**. In both cases, a 2:1 mixture of **14d** was obtained using $BF_3{\cdot}OEt$ as catalyst (Table 4, entries 3 and 5), favoring the *syn*-isomer. Electron-donating as well as electron-withdrawing substituents on the aryl moiety seemed to have no effect in combination with $BF_3{\cdot}OEt_2$. Thus, reactions of diol **9h** and diol **9j** provided the corresponding dihydropyrans in a 3:1 to 2:1 ratio of diastereomers, respectively (Table 4, entries 4 and 6). Likewise, diols **9i** and **9k**, bearing an additional methyl substituent on the double bond, yielded the corresponding dihydropyrans **14f** and **14h**, respectively, in similar ratios (Table 4, entries 5 and 7).

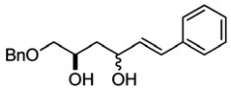
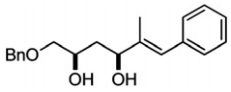
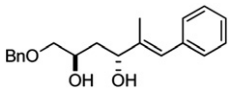
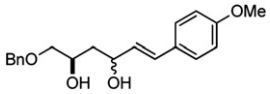
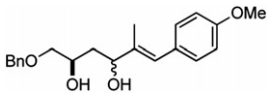
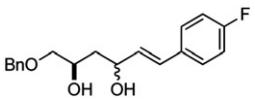
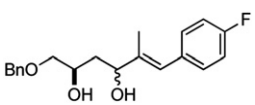
The alkyl substituted dihydropyrans **14a**,**b** are stable under the reaction conditions and do not epimerize through a ring-opening/ring-closing sequence when treated with $BF_3{\cdot}OEt_2$. Thus, no change in the *syn*/*anti* ratio was observed when diastereomerically pure *syn*-**14b** or *anti*-**14b** were subjected to the reaction conditions using $BF_3{\cdot}OEt_2$ even after several days. However, aryl-substituted dihydropyrans **14c**–**h** readily epimerize under the reaction conditions. For instance, treatment of diastereomerically pure *para*-methoxyphenyl substituted dihydropyrans *syn*-**14f** or *anti*-**14f** with $BF_3{\cdot}OEt_2$ gave a 2:1 *syn*/*anti* ratio of the recovered pyrans after <5 min of reaction time (Scheme 6).[30]



Scheme 6.

Table 4
Formation of *syn*-dihydropyrans **14** from aryl-substituted allylic 1,3-diols **9**

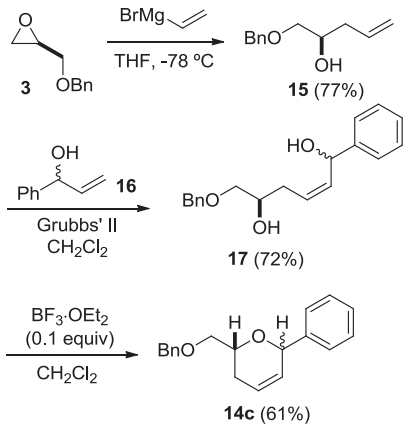


Entry	Diol		Product	R^1	R^2	Yield (%)	*syn*/*anti*[a]
1		**9g**	**14c**	H	H	82	3:1
2		**9c**	**14d**	Me	H	88	2:1
3		**9f**	**14d**	Me	H	81	2:1
4		**9h**	**14e**	H	OMe	85	2:1
5		**9i**	**14f**	Me	OMe	92	2:1
6		**9j**	**14g**	H	F	81	3:1
7		**9k**	**14h**	Me	F	78	2:1

[a] Determined by HPLC.

3. Discussion

The experimental data suggested that the stereochemistry of the allylic alcohol was of no consequence in the cyclization reaction. Therefore, the possibility of an ionic mechanism with formation of an allyl cation followed by cyclization of the adjacent hydroxyl group seemed likely.[27,28] Additional support for this hypothesis was provided by conversion of allylic diol **17** under standard cyclization conditions and comparison with diol **9g**. As expected, **17** and **9g** afforded the same product **14c** upon treatment of with $BF_3 \cdot OEt_2$, presumably via the same cationic intermediate (Scheme 7 and Table 4, entry 1).



Scheme 7.

On the basis of the experimental results we propose that after coordination of the allylic hydroxyl group by the Lewis-acid and subsequent partial or complete dissociation of the complexed group, an allylic cation is formed. This cation then undergoes face-selective attack by the adjacent hydroxyl group to yield dihydropyrans **14** (Table 1). It should be noted that the formation of the ethyl-substituted *syn*-dihydropyran **14b** proceeds in excellent yield and diastereoselectivity, even though the product is subject to $A_{1,2}$ strain experienced by the juxtaposition of the vicinal methyl and ethyl groups. The results can be rationalized considering a transition state model B leading to the preponderant formation of the *syn*-isomer **14b** via *re*-face attack of the hydroxyl group onto the allylic system (Fig. 3, R=Me).

Although *anti*-dihydropyran **14b** lacks $A_{1,2}$ strain, its formation would require the attacking hydroxyl group to approach the allylic system from the *si*-face of the allylic cation adopting an energetically disfavored eclipsed conformation. In addition, the *anti*-dihydropyran suffers from an energetic penalty associated with a 1,3-diaxial interaction (Fig. 3, transition state model C).

The diastereoselective formation of dihydropyran **14a** from *Z*-allylic alcohols **12a**,**b** can be rationized in a similar fashion. The allylic cation initially formed from **12a**,**b** presumably undergoes isomerization from an *anti*, *anti*-to a *syn*, *anti*-conformation in order to minimize allylic strain. *Re*-face attack of the δ-hydroxyl group then yields *syn*-dihydropyran **14a** (Fig. 3, transition state model A and B, R=H).

The aryl-substituted pyrans **14c**–**h** are most likely formed through an analogous mechanism, however, they subsequently isomerize under the reaction conditions to give a mixture of diastereomers. The diastereomeric ratios observed reflect the relative thermodynamic stabilities of the aryl-substituted dihydropyrans, with energetic penalties arising from $A_{1,2}$ strain and 1,3-diaxial repulsion in the *syn*- and *anti*-isomers, respectively.

In summary, we developed a novel synthesis of enantiomerically pure 2,6-disubstituted dihydropyrans, which are useful building blocks to access biologically active targets, such as ambruticin S[2,14]

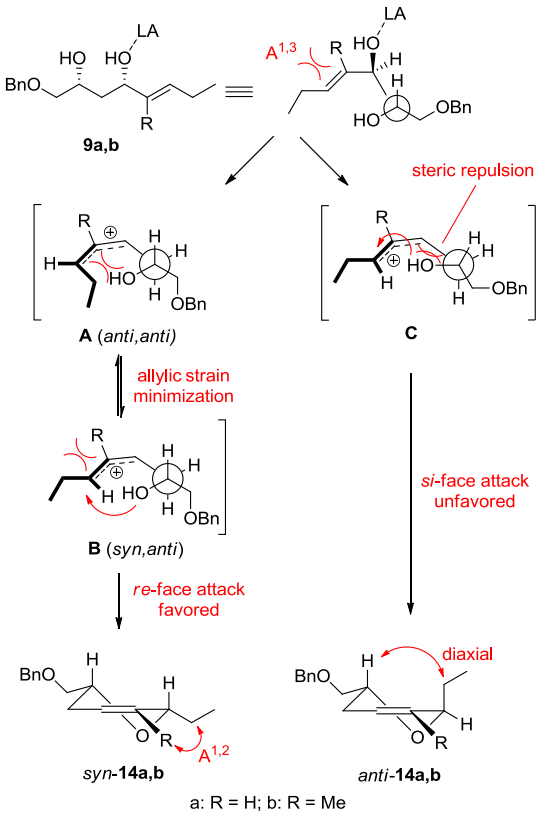


Fig. 3. Postulated mechanism for Lewis-acid catalyzed cycloetherification.

and jerangolid A.[3,15] The reaction proceeds through a Lewis-acid catalyzed 6-*endo*-*trig* cyclization of β-hydroxy-γ,δ-unsaturated alcohols. In case of alkyl-substituted allylic diols, the corresponding *syn*-dihydropyrans are formed in excellent diastereoselectivities. The described process is simple to execute, proceeds readily at ambient temperature, and is scalable. It is very attractive with respect to atom-economy, as water is the only by-product formed.

4. Experimental section

4.1. General information

All non-aqueous reactions were run in flame-dried glassware under a positive pressure of argon with exclusion of moisture from reagents and glassware using standard techniques for manipulating air-sensitive compounds. Anhydrous solvents were obtained using standard drying techniques. Unless stated otherwise, commercial grade reagents were used without further purification. Reactions were monitored by analytical thin-layer chromatography (TLC) performed on pre-coated, glass-backed silica gel plates. Visualization of the developed chromatogram was performed by UV absorbance, aqueous cerium ammonium molybdate, iodine, or aqueous potassium permanganate. Flash chromatography was performed on 230–400 mesh silica gel with the indicated solvent systems. Yields refer to chromatographically and spectroscopically (^1H and ^{13}C NMR) homogeneous materials. Reversed-phase HPLC analyses were performed using a C18 column (250×4.6 mm, 5 μM) and a 0.1% formic acid in water/acetonitrile gradient; UV detection at 254 nm. Melting points are uncorrected. Infrared spectra were recorded on an FT-IR spectrometer and are reported in reciprocal centimeters (cm^{-1}). Routine nuclear magnetic resonance spectra were recorded either on AV-300, ARX-400, or AV-400 spectrometer. Chemical shifts for ^1H NMR spectra are recorded in parts per million from tetramethylsilane with the solvent resonance as the

internal standard. Data are reported as follows: chemical shift, multiplicity (s=singlet, d=doublet, t=triplet, q=quartet, qn=quintet, m=multiplet, and br=broad), coupling constant in hertz, and integration. Chemical shifts for ^{13}C NMR spectra are recorded in parts per million from tetramethylsilane using the central peak of the solvent resonance as the internal standard. All spectra were obtained with complete proton decoupling. Optical rotations were determined at 589 nm at ambient temperature. Data are reported as follows: $[\alpha]_D$, concentration (c in g/100 mL), and solvent. High-resolution mass spectra were performed by the Centre régional de spectroscopie de masse de l'Université de Montréal using fast atom bombardment (FAB) or electrospray ionization (ESI) techniques. Low-resolution mass spectra were obtained using electrospray ionization (ESI).

4.2. Experimental procedures

*4.2.1. 2-((E)-Pent-2-en-2-yl)-1,3-dithiane (**4a**).* A mixture of 1,3-propanedithiol (7.50 mL, 75.0 mmol), boron trifluoride etherate (9.5 mL, 75.0 mmol), and glacial acetic acid (18.0 mL, 0.32 mol) in dichloromethane (125 mL) was cooled to −20 °C. To the vigorously stirred mixture was added slowly a solution of 2-methyl-2-pentenal (8.55 mL, 75.0 mmol) in CH_2Cl_2 (50 mL) while maintaining the temperature between −20 and −15 °C. The reaction mixture was stirred for 1 h at −20 °C, and then siphoned into ice-cold 10% aqueous KOH solution. The temperature was maintained below 5 °C during the quench. After dilution with diethyl ether, the organic phase was separated, washed with 10% KOH, water (3×), brine, and dried (Na_2SO_4). Concentration in vacuo yielded 13.9 g (99%) of the crude dithiane **4a** as a 10:1 mixture of *E*/*Z* isomers. The dithiane was used without further purification in the next step: ^1H NMR (400 MHz, $CDCl_3$, major isomer) δ 5.65–5.61 (m, 1H), 4.56 (s, 1H), 2.98–2.90 (m, 3H), 2.87–2.81 (m, 2H), 2.08–2.01 (m, 2H), 1.82–1.76 (m, 4H), 0.97 (t, J=7.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, major isomer) δ 132.3, 131.6, 55.3, 31.6, 25.5, 21.3, 14.9, 13.7; IR (film, NaCl) 2957, 2935, 2891, 1457, 1424, 1422, 1378, 1275, 1172, 745, 679 cm^{-1}; MS (ESI) calcd for $C_9H_{17}S_2$ $(M+H)^+$ 189.1, found 189.1.

*4.2.2. (E)-2-(1-Phenylprop-1-en-2-yl)-1,3-dithiane (**4b**).* The material was prepared from (*E*)-2-methyl-3-phenyl-2-propenal as a yellowish oil as described for **4a** (65% yield, 3:1 mixture of *E*/*Z* isomers): ^1H NMR (400 MHz, $CDCl_3$) δ 7.44–7.21 (m, 5H), 6.77 (br s, 1H, major isomer), 6.44–6.42 (m, 1H, minor isomer), 5.35 (br s, 1H, minor isomer), 4.76 (br s, 1H, major isomer), 3.07–2.80 (m, 4H), 2.19–2.05 (m, 4H), 1.97–1.84 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, major isomer) δ 137.0, 135.7, 129.1, 129.0, 128.1, 126.8, 55.8, 31.6, 25.4, 16.9; ^{13}C NMR (100 MHz, $CDCl_3$, minor isomer) δ 136.9(5), 134.8, 128.6, 128.4, 128.3, 126.9, 50.3, 30.7, 25.1, 20.7; IR (film, NaCl) 3054, 3023, 2897, 2827, 2339, 1953, 1897, 1645, 1598, 1575, 1493, 1422, 1379, 1274, 1248, 1171, 1111, 1075, 1020, 1003, 921, 866, 821, 741, 697, 678 cm^{-1}; MS (ESI) calcd for $C_{13}H_{17}S_2$ $(M+H)^+$: 237.1, found 237.2.

*4.2.3. (R,E)-1-(Benzyloxy)-3-(2-(pent-2-en-2-yl)-1,3-dithian-2-yl) propan-2-ol (**5a**).* To a −78 °C solution of dithiane **4a** (11.5 g, 61.0 mmol) in THF (60 mL) was added *n*-BuLi (33.3 mL of a 1.6 M solution in hexanes, 53.3 mmol) dropwise. The reaction mixture was stirred for 5 min at that temperature, warmed to 0 °C, and stirred for 30 min, before it was re-cooled to −78 °C. A solution of (*R*)-benzyl glycidol ether (**3**) (5.0 g, 30.5 mmol) in THF (40 mL) was then added slowly. The reaction mixture was stirred for 30 min and quenched by addition of saturated NH_4Cl solution. The aqueous layer was extracted with EtOAc, the combined organic phase dried (Na_2SO_4), and concentrated. The residue was purified by flash chromatography (hexanes/EtOAc, 10:1 to 4:1) to give 10.5 g (97%) of dithiane adduct **5a** as a colorless oil: ^1H NMR (400 MHz, $CDCl_3$) δ 7.39–7.25 (m, 5H), 6.05 (tq, J=7.1, 1.2 Hz, 1H), 4.55 (s, 2H), 4.07–3.98 (m, 1H), 3.44 (dd, J=9.6, 4.8 Hz, 1H), 3.39 (dd, J=9.6, 6.3 Hz, 1H), 2.88–2.65 (m, 5H), 2.25–2.04 (m, 4H), 2.00–1.88 (m, 2H), 1.77 (d, J=0.6 Hz, 3H), 1.04 (t, J=7.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.0, 133.8, 132.5, 128.3, 127.6, 127.6, 74.1, 73.2, 67.5, 58.3, 42.8, 27.3, 27.2, 25.0, 22.1, 14.0, 13.5; IR (film, NaCl) 2957, 2935, 2909, 2870, 1453, 1422, 1100, 1089, 736, 699 cm^{-1}; $[\alpha]_D$ −6.3 (c 1.58, $CHCl_3$); HRMS (ESI) calcd for $C_{19}H_{28}NaO_2S_2$ $(M+Na)^+$ 375.1423, found 375.1434.

*4.2.4. (R,E)-1-(Benzyloxy)-3-(2-(1-phenylprop-1-en-2-yl)-1,3-dithian-2-yl)propan-2-ol (**5b**).* The material was prepared from dithiane **4b** as a colorless oil as described for **5a** in 86% yield: ^1H NMR (400 MHz, $CDCl_3$) δ 7.44–7.26 (m, 11H), 4.58 (s, 2H), 4.17 (br s, 1H), 3.50 (dd, J=9.4, 3.9 Hz, 1H), 3.48–3.42 (m, 1H), 2.99–2.89 (m, 2H), 2.83–2.73 (m, 3H), 2.28 (dd, J=15.2, 7.5 Hz, 1H), 2.14 (d, J=15.0 Hz, 1H), 2.04 (s, 3H), 2.02–1.93 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.7, 136.3, 131.5, 128.7, 128.1, 127.8, 127.3, 126.4, 73.9, 72.9, 67.1, 58.8, 43.1, 27.3, 27.1, 24.7, 15.3; IR (film, NaCl) 3461, 3027, 2910, 1599, 1494, 1453, 1378, 1277, 1097, 1028, 909, 870, 745, 699 cm^{-1}; $[\alpha]_D$ −21.7 (c 0.40, $CHCl_3$); HRMS (ESI) calcd for $C_{23}H_{29}O_2S_2$ $(M+H)^+$: 401.1603, found 401.1600.

*4.2.5. (R,E)-1-(Benzyloxy)-2-((tert-butyldimethylsilyl)oxy)-5-methyloct-5-en-4-one (**6a**).* A cold (0 °C) solution of dithiane adduct **5a** (10.4 g, 29.5 mmol) and 2,6-lutidine (8.6 mL, 74.1 mmol) in CH_2Cl_2 (380 mL) was treated with TBSOTf (13.6 mL, 59.2 mmol) for 1 h. The reaction mixture was quenched with saturated NH_4Cl solution, the aqueous layer extracted with CH_2Cl_2, and the combined organic phase dried (Na_2SO_4) and concentrated. The residue was purified by flash chromatography (hexanes/EtOAc, 20:1 to 9:1) to yield 12.8 g (93%) of the TBS-dithiane adduct as a colorless oil: ^1H NMR (400 MHz, $CDCl_3$) δ 7.38–7.32 (m, 4H), 7.32–7.26 (m, 1H), 6.05–6.00 (m, 1H), 4.53 (d, J=12.2 Hz, 1H), 4.51 (d, J=12.4 Hz, 1H), 3.99–3.93 (m, 1H), 3.42 (dd, J=9.9, 4.1 Hz, 1H), 3.36 (dd, J=9.9, 5.6 Hz, 1H), 2.86–2.71 (m, 2H), 2.70–2.60 (m, 2H), 2.33 (dd, J=14.9, 6.4 Hz, 1H), 2.18–2.09 (m, 2H), 2.06 (dd, J=14.9, 3.9 Hz, 1H), 2.02–1.84 (m, 2H), 1.74 (s, 3H), 1.06 (t, J=7.5 Hz, 3H), 0.89 (s, 9H), 0.10 (s, 3H), 0.05 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.5, 134.1, 131.7, 128.2, 127.5, 127.3, 74.9, 73.1, 68.6, 58.6, 44.1, 27.5, 27.3, 26.0, 25.2, 22.2, 18.1, 14.2, 13.7, −4.0, −4.5; IR (film, NaCl) 2957, 2928, 2855, 1478, 1456, 1454, 1251, 1097, 1004, 836, 776, 733, 697 cm^{-1}; $[\alpha]_D$ −6.4 (c 0.94, $CHCl_3$); MS (ESI) calcd for $C_{25}H_{43}O_2S_2Si$ $(M+H)^+$ 467.3, found 467.3.

To a solution of the TBS-dithiane adduct (5.0 g, 10.7 mmol) in CH_2Cl_2 (140 mL) was added benzeneseleninic acid anhydride (70%, 5.51 g, 10.7 mmol) and propylene oxide (1 mL). The reaction mixture was stirred for 16 h at room temperature, and solid $NaHCO_3$ (5.0 g) was added. The solvent was removed and the residue purified by flash chromatography (hexanes/EtOAc, 10:1 to 4:1) to give enone **6a** (3.20 g, 79%) as a light yellowish oil: ^1H NMR (400 MHz, $CDCl_3$) δ 7.39–7.27 (m, 5H), 6.67 (dt, J=7.0, 0.9 Hz, 1H), 4.56 (s, 2H), 4.43 (dddd, J=7.4, 5.2, 5.2, 5.2 Hz, 1H), 3.49 (dd, J=9.8, 5.1 Hz, 1H), 3.42 (dd, J=9.7, 5.4 Hz, 1H), 2.95 (dd, J=15.3, 7.4 Hz, 1H), 2.82 (dd, J=15.3, 4.9 Hz, 1H), 2.27 (dq, J=7.4, 7.4 Hz, 2H), 1.78 (s, 3H), 1.10 (t, J=7.6 Hz, 3H), 0.86 (s, 9H), 0.07 (s, 3H), 0.02 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.3, 145.0, 138.3, 137.4, 128.3, 127.5, 127.4(7), 74.4, 73.2, 69.0, 42.0, 25.8, 22.4, 18.0, 13.0, 11.1, −4.6, −5.0; IR (film, NaCl) 2957, 2930, 2857, 1668, 1252, 1112, 836 cm^{-1}; $[\alpha]_D$ +28.5 (c 2.0, $CHCl_3$); HRMS (ESI) calcd for $C_{22}H_{37}O_3Si$ $(M+H)^+$ 377.2506, found 377.2526.

*4.2.6. (R,E)-6-(Benzyloxy)-5-((tert-butyldimethylsilyl)oxy)-2-methyl-1-phenylhex-1-en-3-one (**6b**).* The material was prepared from dithiane adduct **5b** via the corresponding TBS-dithiane adduct as a colorless oil as described for **6a** (71% overall yield). TBS-dithiane adduct: ^1H NMR (400 MHz, $CDCl_3$) δ 7.42–7.26 (m, 10H), 7.22 (br s, 1H), 4.52 (s, 2H), 4.14–4.08 (m, 1H), 3.46 (dd, J=9.9, 4.3 Hz, 1H), 3.42 (dd, J=9.9, 5.4 Hz, 1H), 2.97 (ddd, J=14.4, 11.5, 3.1 Hz, 1H), 2.88 (ddd, J=14.2, 11.3, 2.9 Hz, 1H), 2.74–2.66 (m, 2H),

2.44 (dd, J=14.9, 6.3 Hz, 1H), 2.16 (dd, J=14.9, 4.1 Hz, 1H), 2.09–1.90 (m, 5H), 0.91 (s, 9H), 0.14 (s, 3H), 0.09 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.5, 138.3, 136.2, 132.3, 129.1, 128.3, 128.2, 127.6, 127.4, 126.7, 75.0, 73.2, 68.6, 59.3, 44.6, 27.7, 27.6, 26.1, 25.2, 18.2, 15.8, −3.8, −4.2; IR (film, NaCl) 3061, 3027, 2952, 2928, 2899, 2855, 1947, 1807, 1633, 1599, 1575, 1495, 1471, 1462, 1454, 1422, 1410, 1361, 1329, 1278, 1252, 1213, 1098, 1028, 1003, 939, 908, 868, 835, 811, 777, 746, 698, 674 cm^{-1}; $[\alpha]_D$ −23.0 (c 0.38, $CHCl_3$); MS (ESI) calcd for $C_{29}H_{43}O_2S_2Si$ $(M+H)^+$: 515.3, found 515.3. Enone **6b**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (s, 1H), 7.46–7.41 (m, 4H), 7.38–7.34 (m, 4H), 7.34–7.27 (m, 2H), 4.59 (s, 2H), 4.55–4.47 (m, 1H), 3.55 (dd, J=9.7, 5.0 Hz, 1H), 3.48 (dd, J=9.7, 5.6 Hz, 1H), 3.12 (dd, J=15.4, 7.4 Hz, 1H), 3.01 (dd, J=15.4, 4.9 Hz, 1H), 2.08 (br s, 3H), 0.87 (s, 9H), 0.11 (s, 3H), 0.06 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.5, 139.1, 137.9, 137.7, 135.7, 129.4, 128.1, 128.0, 127.9, 127.3, 127.2, 74.0, 72.9, 68.8, 42.2, 25.5, 17.7, 12.8, −4.9, −5.2; IR (film, NaCl) 3063, 3030, 2954, 2928, 2886, 2856, 1950, 1667, 1626, 1575, 1495, 1471, 1462, 1454, 1388, 1361, 1323, 1303, 1252, 1207, 1091, 1048, 1029, 1005, 978, 939, 836, 811, 778, 736, 697 cm^{-1}; $[\alpha]_D$ +22.6 (c 0.42, $CHCl_3$); MS (ESI) calcd for $C_{26}H_{37}O_3Si$ $(M+H)^+$: 425.3, found 425.4.

*4.2.7. (R,E)-1-(Benzyloxy)-2-((tert-butyldimethylsilyl)oxy)oct-5-en-4-one (**6c**).* To a −78 °C solution of dimethyl methylphosphonate (38.0 mL, 351 mmol) in THF (150 mL) was added *n*-BuLi (116 mL of a 2.5 M solution in hexanes, 290 mmol). The reaction mixture was stirred for 1 h at −78 °C, after which a solution of benzyl ester **8** (24.0 g, 57.9 mmol) in THF (200 mL) was added to it. The reaction mixture was allowed to slowly warm to room temperature and stirred for 1 h. The mixture was quenched by addition of saturated NH_4Cl solution, concentrated in vacuo, and the remaining aqueous phase extracted with EtOAc. The combined organic phase was washed with brine, dried (Na_2SO_4), and concentrated. The crude β-ketophosphonate was used without further purification.

A solution of crude β-ketophosphonate in THF (120 mL) was treated with freshly activated[23] $Ba(OH)_2$ (14.9 g, 87.0 mmol) for 30 min at 0 °C, after which a solution of propionaldehyde (6.3 mL, 86.6 mmol) and water (6 mL) in THF (240 mL) was added to it. The reaction mixture was allowed to warm to room temperature and stirred for 2 h. Saturated NH_4Cl solution was added, and the mixture extracted with EtOAc. The combined organic phase was washed with brine, dried (Na_2SO_4), and concentrated in vacuo. The solvent was removed and the residue purified by flash chromatography (hexanes/EtOAc, 20:1 to 10:1) to give enone **6c** (13.27 g, 61% over 2 steps) as a light yellowish oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39–7.26 (m, 5H), 6.90 (dt, J=15.9, 6.4 Hz, 1H), 6.13 (dt, J=15.9, 1.6 Hz, 1H), 4.56 (s, 2H), 4.41 (dddd, J=6.8, 5.3, 5.3, 5.3 Hz, 1H), 3.42 (dd, J=9.7, 5.5 Hz, 1H), 3.49 (dd, J=9.7, 5.1 Hz, 1H), 2.81 (dd, J=15.2, 7.0 Hz, 1H), 2.76 (dd, J=15.2, 5.4 Hz, 1H), 2.26 (ddq, J=7.5, 6.3, 1.6 Hz, 2H), 1.09 (t, J=7.4 Hz, 3H), 0.87 (s, 9H), 0.08 (s, 3H), 0.05 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.0, 149.2, 138.2, 130.4, 128.2, 127.5, 127.4(6), 74.3, 73.2, 68.5, 44.8, 25.8, 25.5, 18.0, 12.2, −4.6, −5.0; IR (film, NaCl) 2956, 1669, 1627, 1462, 1361, 1252, 1112, 1005, 977, 836, 810, 778 cm^{-1}; $[\alpha]_D$ +31.4 (c 1.57, $CHCl_3$); MS (ESI) calcd for $C_{21}H_{35}O_3$ $(M+H)^+$: 363.2, found 363.2.

*4.2.8. (R,E)-6-(Benzyloxy)-5-((tert-butyldimethylsilyl)oxy)-1-phenylhex-1-en-3-one (**6d**).* The material was prepared from benzyl ester **8** as a light yellow oil as described for **6c** in 90% yield: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60–7.51 (m, 3H), 7.44–7.38 (m, 3H), 7.37–7.27 (m, 5H), 6.76 (d, J=16.3 Hz, 1H), 4.56 (s, 2H), 4.50–4.41 (m, 1H), 3.52 (dd, J=9.7, 5.0 Hz, 1H), 3.45 (dd, J=9.7, 5.6 Hz, 1H), 2.93–2.89 (m, 2H), 0.85 (s, 9H), 0.07 (s, 3H), 0.04 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.1, 143.1, 138.4, 134.7, 130.6, 129.1, 128.5, 128.4, 127.8, 127.7, 127.4, 74.4, 73.5, 68.9, 45.8, 26.0, 18.2, −4.4, −4.7; IR (film, NaCl) 3419, 3086, 3063, 3030, 2953, 2927, 2856, 1954, 1881, 1810, 1682, 1660, 1652, 1634, 1621, 1607, 1576, 1495, 1471, 1452, 1361, 1336, 1283, 1255, 1203, 1182, 1157, 1106, 1044, 1025, 979, 911, 878, 836, 811, 778, 743, 695 cm^{-1}; $[\alpha]_D$ +35.2 (c 0.42, $CHCl_3$); MS (ESI) calcd for $C_{25}H_{35}O_3Si$ $(M+H)^+$: 411.2, found 411.3.

*4.2.9. (R,E)-6-(Benzyloxy)-5-((tert-butyldimethylsilyl)oxy)-1-(4-methoxyphenyl)hex-1-en-3-one (**6e**).* The material was prepared from benzyl ester **8** as a light yellow oil as described for **6c** in 89% yield: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60–7.46 (m, 3H), 7.39–7.24 (m, 5H), 6.94 (d, J=7.5 Hz, 2H), 6.66 (d, J=15.5 Hz, 1H), 4.58 (s, 2H), 4.50–4.42 (m, 1H), 3.86 (s, 3H), 3.58–3.42 (m, 2H), 2.90 (d, J=5.8 Hz, 2H), 0.86 (s, 9H), 0.9 (s, 3H), 0.4 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.5, 161.2, 142.5, 137.9, 129.7, 127.9, 127.3, 127.2, 126.9, 124.8, 114.0, 74.0, 72.9, 68.5, 55.0, 45.2, 25.5, 17.7, −4.9, −5.2; IR (film, NaCl) 3543, 3064, 3033, 3005, 2954, 2929, 2896, 2856, 2031, 1682, 1658, 1651, 1601, 1574, 1512, 1470, 1463, 1455, 1422, 1360, 1329, 1305, 1254, 1204, 1172, 1112, 1031, 1005, 981, 939, 906, 831, 778, 736, 698, 661 cm^{-1}; $[\alpha]_D$ +31.1 (c 0.29, $CHCl_3$); HRMS (ESI) calcd for $C_{26}H_{37}O_4Si$ $(M+H)^+$: 441.2456, found 441.2458.

*4.2.10. (R,E)-6-(Benzyloxy)-5-((tert-butyldimethylsilyl)oxy)-1-(4-methoxyphenyl)-2-methylhex-1-en-3-one (**6f**).* The material was prepared from benzyl ester **8** as a colorless oil as described for **6c** in 60% yield: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.53 (br s, 1H), 7.41 (d, J=8.8 Hz, 2H), 7.37–7.26 (m, 5H), 6.95 (d, J=8.8 Hz, 2H), 4.57 (s, 2H), 4.53–4.43 (m, 1H), 3.86 (s, 3H), 3.52 (dd, J=9.7, 5.0 Hz, 1H), 3.46 (dd, J=9.7, 5.5 Hz, 1H), 3.08 (dd, J=15.3, 7.3 Hz, 1H), 2.97 (dd, J=15.3, 5.0 Hz, 1H), 2.07 (d, J=1.0 Hz, 3H), 0.85 (s, 9H), 0.08 (s, 3H), 0.03 (s, 3H); IR (film, NaCl) 3433, 2954, 2928, 2855, 1660, 1604, 1511, 1463, 1390, 1361, 1304, 1255, 1177, 1113, 1033, 833, 777, 735, 697 cm^{-1}; $[\alpha]_D$ +22.1 (c 0.40, $CHCl_3$); HRMS (ESI) calcd for $C_{27}H_{39}O_4Si$ $(M+H)^+$: 455.2612, found 455.2603.

*4.2.11. (R,E)-6-(Benzyloxy)-5-((tert-butyldimethylsilyl)oxy)-1-(4-fluorophenyl)hex-1-en-3-one (**6g**).* The material was prepared from benzyl ester **8** as a colorless oil as described for **6c** in 85% yield: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56–7.50 (m, 3H), 7.38–7.27 (m, 5H), 7.10 (dd, J=8.6, 8.6 Hz, 2H), 6.70 (d, J=16.2 Hz, 1H), 4.57 (s, 2H), 4.49–4.42 (m, 1H), 3.53 (dd, J=9.7, 5.0 Hz, 1H), 3.46 (dd, J=9.7, 5.6 Hz, 1H), 2.94–2.88 (m, 2H), 0.86 (s, 9H), 0.09 (s, 3H), 0.05 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.8, 165.4, 162.9, 141.7, 138.4, 131.0, 130.9, 130.3, 130.2, 128.5, 127.8, 127.7, 127.1, 127.0, 116.1, 74.4, 73.5, 68.9, 45.9, 25.9, 18.2, -4.4, -4.7; IR (film, NaCl) 2954, 2927, 2855, 1687, 1660, 1613, 1599, 1509, 1462, 1414, 1361, 1327, 1235, 1158, 1097, 981, 832, 778, 735, 697 cm^{-1}; $[\alpha]_D$ +31.3 (c 0.41, $CHCl_3$); MS (ESI) calcd for $C_{25}H_{34}FO_3Si$ $(M+H)^+$: 429.2, found 429.3.

*4.2.12. (R)-Benzyl 4-(benzyloxy)-3-((tert-butyldimethylsilyl)oxy)-butanoate (**8**).* A mixture of (*R*)-ethyl 3,4-dihydroxybutanoate[22] (21.5 g, 145 mmol) and dibutyltin oxide (36.1 g, 145 mmol) in benzene (200 mL) was heated under reflux for 18 h with azeotropic removal of water using a Dean–Stark trap. Benzyl bromide (43 mL, 362 mmol) and TBAI (2.5 g, 7.3 mmol) were then added and the mixture heated under reflux for another 21 h. After evaporation of all volatiles, the residue was purified by flash chromatography (hexanes/EtOAc, 4:1 to 2:1) to give (*R*)-benzyl 4-(benzyloxy)-3-hydroxybutanoate (28.47 g, 65%) as a yellowish oil.

To a cold (0 °C) solution of the hydroxyl benzyl ester (28.4 g, 94.6 mmol) in CH_2Cl_2 (140 mL) was added TBSCl (18.5 g, 122.7 mmol) and imidazole (9.7 g, 142.5 mmol). The reaction mixture was allowed to warm to room temperature and stirred overnight. After concentration in vacuo, the residue was purified by flash chromatography (hexanes/EtOAc, 20:1 to 8:1) to give benzyl ester **8** as a light yellow oil (28.3 g, 72%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42–7.29 (m, 10H), 5.15 (d, J=12.4 Hz, 1H), 5.10 (d, J=12.4 Hz, 1H), 4.56 (d, J=12.3 Hz, 1H), 4.53 (d, J=12.6 Hz, 1H), 4.40–4.33 (m, 1H), 3.51 (dd, J=9.6, 5.3 Hz, 1H), 3.41 (dd, J=9.6, 6.2 Hz, 1H), 2.71 (dd,

J=15.0, 4.7 Hz, 1H), 2.55 (dd, J=15.0, 7.7 Hz, 1H), 0.88 (s, 9H), 0.08 (s, 3H), 0.07 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.4, 138.1, 135.8, 128.5, 128.3, 128.2, 128.1, 127.6, 74.0, 73.3, 68.6, 66.2, 40.4, 25.7, 18.0, −4.5, −5.1; IR (film, NaCl) 2954, 2929, 2886, 2856, 1738, 1455, 1253, 1167, 1124, 1092, 1004, 836, 778, 736, 697 cm^{-1}; $[\alpha]_D$ +19.4 (c 2.03, $CHCl_3$); MS (ESI) calcd for $C_{24}H_{35}O_4Si$ $(M+H)^+$: 415.2, found 415.2.

*4.2.13. (2R,4S,E)-1-(Benzyloxy)oct-5-ene-2,4-diol (**9a**).* A solution of (*R*)-2-methyl-CBS-oxazaborolidine (0.60 mL of a 1 M solution in toluene, 0.60 mmol) in THF (5 mL) was treated with BH_3·DMS (0.15 mL, 1.58 mmol) at 0 °C for 15 min. A solution of enone **6c** (450 mg, 1.24 mmol) in THF (5 mL) was then added slowly at 0 °C and the reaction mixture stirred for 30 min at that temperature. After addition of saturated NH_4Cl solution, the aqueous layer was extracted with EtOAc, the combined organic phase dried (Na_2SO_4), and concentrated. Purification of the residue by flash chromatography (hexanes/EtOAc, 8:1) yielded 285 mg (63%, dr 99:1) of the *syn*-TBS-diol as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41–7.27 (m, 5H), 5.80 (dddd, J=15.4, 6.3, 6.3, 0.9 Hz, 1H), 5.49 (dddd, J=15.4, 6.7, 1.5, 1.5 Hz, 1H), 4.56 (br s, 2H), 4.36–4.28 (m, 1H), 4.07 (dddd, J=7.8, 5.0, 5.0, 5.0 Hz, 1H), 3.50 (dd, J=9.6, 5.0 Hz, 1H), 3.43 (dd, J=9.6, 5.7 Hz, 1H), 3.00 (br s, 1H), 2.13–2.03 (m, 2H), 1.84 (ddd, J=14.2, 4.5, 4.5 Hz, 1H), 1.75 (ddd, J=14.2, 8.0, 8.0 Hz, 1H), 1.03 (t, J=7.5 Hz, 3H), 0.93 (s, 9H), 0.13 (s, 3H), 0.10 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.9, 133.1, 131.4, 128.3, 127.6, 74.8, 73.3, 70.8, 70.7, 42.2, 25.8, 25.2, 18.0, 13.4, −4.2, −4.9; IR (film, NaCl) 3433, 2957, 2929, 2886, 2856, 1472, 1463, 1413, 1362, 1253, 1103, 1029, 1005, 969, 836, 810, 777, 735 cm^{-1}; $[\alpha]_D$ +14.3 (c 1.56, $CHCl_3$); MS (ESI) calcd for $C_{21}H_{40}NO_3Si$ $(M+NH_4)^+$: 382.3, found 382.2.

To a solution of the *syn*-TBS-diol (265 mg, 0.73 mmol) in THF (8 mL) was added TBAF (0.95 mL of a 1 M solution in THF). The reaction mixture was stirred for 2 h, and subsequently quenched by addition of saturated NH_4Cl solution. After evaporation of all volatiles and extraction of the remaining aqueous layer with EtOAc, the combined organic phase was dried (Na_2SO_4) and concentrated. Purification of the residue by flash chromatography (hexanes/EtOAc, 2:1 to 1:1) gave 162 mg (89%, dr 99:1) of *syn*-diol **9a** as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42–7.27 (m, 5H), 5.73 (dd, J=14.8, 6.6 Hz, 1H), 5.47 (dd, J=15.4, 6.8 Hz, 1H), 4.57 (br s, 2H), 4.41–4.29 (m, 1H), 4.11–4.01 (m, 1H), 3.51–3.38 (m, 2H), 3.30 (br s, 1H), 3.16 (br s, 1H), 2.12–2.01 (m, 2H), 1.74–1.60 (m, 2H), 1.01 (t, J=7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.8, 133.5, 131.2, 128.4, 127.7(4), 127.7, 74.3, 73.3, 72.7, 70.6, 39.8, 25.1, 13.3; IR (film, NaCl) 3390, 2962, 2915, 2872, 1454, 1102, 969 cm^{-1}; $[\alpha]_D$ −7.0 (c 1.65, $CHCl_3$); MS (ESI) calcd for $C_{15}H_{22}NaO_3$ $(M+Na)^+$: 273.1, found 273.1.

*4.2.14. (2R,4S,E)-1-(Benzyloxy)-5-methyloct-5-ene-2,4-diol (**9b**).* The material was prepared from enone **6a** by CBS reduction via the corresponding *syn*-TBS-diol as a colorless oil as described for **9a** (84% overall yield, dr 94:6). *syn*-TBS-diol: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41–7.29 (m, 5H), 5.48–5.43 (m, 1H), 4.55 (s, 2H), 4.21 (dd, J=8.6, 3.3 Hz, 1H), 4.05 (dddd, J=8.0, 5.4, 5.4, 4.7 Hz, 1H), 3.49 (dd, J=9.6, 5.0 Hz, 1H), 3.41 (dd, J=9.6, 5.7 Hz, 1H), 3.00 (br s, 1H), 2.12–1.99 (m, 2H), 1.85 (ddd, J=14.3, 4.4, 3.5 Hz, 1H), 1.73 (ddd, J=14.3, 8.3, 8.3 Hz, 1H), 1.63 (dd, J=1.9, 0.9 Hz, 3H), 0.99 (t, J=7.5 Hz, 3H), 0.92 (s, 9H), 0.13 (s, 3H), 0.10 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.0, 136.1, 128.3, 127.8, 127.6, 75.5, 74.8, 73.3, 71.4, 40.3, 25.8, 20.8, 18.0, 14.0, 11.6, −4.2, −4.9; IR (film, NaCl) 3436, 2957, 2929, 2857, 1472, 1455, 1362, 1252, 1092, 1029, 1005, 835, 776, 734, 697 cm^{-1}; $[\alpha]_D$ +3.8 (c 1.85, $CHCl_3$); MS (ESI) calcd for $C_{22}H_{38}NaO_3Si$ $(M+Na)^+$: 401.2, found 401.2. *syn*-Diol **9b**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38–7.27 (m, 5H), 5.42 (br t, J=7.0 Hz, 1H), 4.55 (s, 2H), 4.25 (dd, J=9.2, 3.6 Hz, 1H), 4.06–3.99 (m, 1H), 3.45 (dd, J=9.5, 4.1 Hz, 1H), 3.40 (dd, J=9.5, 6.9 Hz, 1H), 3.29 (br s, 1H), 2.99 (br s, 1H), 2.08–1.95 (m, 2H), 1.73–1.58 (m, 2H), 1.60 (dt, J=1.4, 0.8 Hz, 3H), 0.95 (t, J=7.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.8, 136.1, 128.4, 128.2, 127.8, 127.7, 77.5, 74.4, 73.3, 70.9, 37.9, 20.7, 14.0, 11.4; IR (film, NaCl) 3391, 2960, 2930, 2917, 2871, 1454, 1364, 1306, 1091, 1074, 1028, 999, 860 cm^{-1}; $[\alpha]_D$ −11.0 (c 1.7, $CHCl_3$); MS (ESI) calcd for $C_{16}H_{28}NO_3$ $(M+NH_4)^+$: 282.2, found 282.1.

Alternatively, diol **9b** was obtained from Luche reduction of enone **6a** as a colorless oil as a mixture of diastereomers (dr 4:1 by ^{1}H NMR).

*4.2.15. Procedure for the Luche reduction of **6a** and TBAF deprotection.* To a stirred solution of enone **6a** (13.27 g, 35.2 mmol) and cerium chloride heptahydrate (15.74 g, 42.2 mmol) in 300 mL of methanol was added sodium borohydride (1.6 g, 42.2 mmol) portionwise at 0 °C. The reaction mixture was stirred for 1 h at that temperature, after which acetone was added to destroy residual sodium borohydride. All volatiles were evaporated under reduced pressure and the residue was partitioned between water and CH_2Cl_2. The aqueous phase was extracted with CH_2Cl_2, the combined organic phase washed with brine, dried (Na_2SO_4), and concentrated in vacuo to give the crude TBS-diol (13.3 g) as an oil, which was used in the next step without further purification.

To a solution of the crude TBS-diol (12.3 g, 32.5 mmol) in THF (300 mL) was added TBAF (42.2 mL of a 1 M solution in THF, 42.2 mmol). The reaction mixture was stirred for 2 h, and subsequently quenched by addition of saturated NH_4Cl solution. After evaporation of all volatiles and extraction of the remaining aqueous layer with EtOAc, the combined organic phase was dried (Na_2SO_4) and concentrated. Purification of the residue by flash chromatography (hexanes/EtOAc, 4:1 to 1:1) gave 7.30 g (85% over 2 steps) of diastereomeric diols **9b** and **9e** as a colorless oil (**9b**:**9e**=4:1).

*4.2.16. (2R,4S,E)-1-(Benzyloxy)-5-methyl-6-phenylhex-5-ene-2,4-diol (**9c**).* The material was prepared from enone **6b** by CBS reduction via the corresponding *syn*-TBS-diol adduct as a colorless oil as described for **9a** (77% overall yield, dr 98:2). *syn*-TBS-diol: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38–7.26 (m, 9H), 7.24–7.19 (m, 1H), 6.58 (br s, 1H), 4.56 (s, 2H), 4.40–4.36 (m, 1H), 4.16–4.09 (m, 1H), 3.52 (dd, J=9.6, 4.9 Hz, 1H), 3.45 (dd, J=9.6, 5.9 Hz, 1H), 3.36 (d, J=1.6 Hz, 1H), 1.98 (ddd, J=14.4, 4.3, 3.1 Hz, 1H), 1.88 (d, J=0.9 Hz, 3H), 1.81 (ddd, J=14.5, 8.4, 8.4 Hz, 1H), 0.93 (s, 9H), 0.15 (s, 3H), 0.11 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.1, 138.0(3), 138.0, 129.1, 128.5, 128.2, 127.9, 126.4, 125.2, 75.8, 74.8, 73.6, 71.6, 40.6, 26.0, 18.2, 14.1, −4.0, −4.7; IR (film, NaCl) 3445, 3062, 3028, 2953, 2928, 2856, 1600, 1495, 1471, 1462, 1454, 1409, 1388, 1361, 1253, 1205, 1094, 1028, 1005, 960, 916, 835, 810, 777, 747, 697 cm^{-1}; $[\alpha]_D$ +13.9 (c 0.48, $CHCl_3$); MS (ESI) calcd for $C_{26}H_{38}NaO_3Si$ $(M+Na)^+$: 449.3, found 449.2. Diol **9c**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42–7.29 (m, 9H), 7.27–7.20 (m, 1H), 6.58 (br s, 1H), 4.60 (s, 2H), 4.50–4.44 (m, 1H), 4.18–4.11 (m, 1H), 3.55–3.50 (m, 1H), 3.49–3.43 (m, 1H), 3.24 (br s, 1H), 3.16 (br s, 1H), 1.92–1.87 (m, 3H), 1.83–1.76 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.8, 137.9, 137.7, 129.1, 128.6, 128.2, 128.0, 127.9, 126.5, 125.6, 77.8, 74.4, 73.6, 71.1, 38.3, 13.8; IR (film, NaCl) 3370, 3026, 2916, 2860, 1599, 1492, 1452, 1363, 1309, 1203, 1091, 1027, 1008, 918, 867, 748, 698 cm^{-1}; $[\alpha]_D$ +15.3 (c 0.52, $CHCl_3$); HRMS (ESI) calcd for $C_{20}H_{24}NaO_3$ $(M+Na)^+$: 335.1618, found 335.1621.

Alternatively, diol **9c** was obtained from Luche reduction of enone **6b** as a colorless oil as a mixture of diastereomers (dr 3:1 by ^{1}H NMR).

*4.2.17. (2R,4R,E)-1-(Benzyloxy)oct-5-ene-2,4-diol (**9d**).* To a cold (0 °C) solution of (*S*)-2-methyl-CBS-oxazaborolidine (1.84 mL of a 1 M solution in toluene, 1.84 mmol) in THF (10 mL) was added BH_3·DMS (0.17 mL, 1.83 mmol). The mixture was stirred for 15 min at that temperature, after which a solution of enone **6c** (607 mg,

1.67 mmol) in THF (10 mL) was added slowly. The reaction mixture was stirred for 30 min at 0 °C. After addition of saturated NH_4Cl solution, the aqueous layer was extracted with EtOAc, the combined organic phase dried (Na_2SO_4), and concentrated. Purification of the residue by flash chromatography using a short plug of silica gel (hexanes/EtOAc, 8:1) yielded 596 mg (98%, dr 99:1) of the *anti*-TBS-diol as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44–7.29 (m, 5H), 5.72 (dddd, J=15.4, 6.2, 6.2, 0.9 Hz, 1H), 5.49 (dddd, J=15.4, 6.5, 1.5, 1.5 Hz, 1H), 4.58 (d, J=12.1 Hz, 1H), 4.54 (d, J=12.1 Hz, 1H), 4.39–4.30 (m, 1H), 4.19–4.13 (m, 1H), 3.53 (dd, J=9.5, 5.7 Hz, 1H), 3.49 (dd, J=9.5, 6.2 Hz, 1H), 3.07 (d, J=1.7 Hz, 1H), 2.11–2.02 (m, 2H), 1.75–1.79 (m, 2H), 1.02 (t, J=7.5 Hz, 3H), 0.92 (s, 9H), 0.13 (s, 3H), 0.10 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.0, 132.7, 131.7, 128.3, 127.6, 73.6, 73.3, 69.9, 69.4, 41.0, 25.8, 25.1, 18.0, 13.4, −4.5, −5.0; IR (film, NaCl) 3426, 2978, 2929, 2878, 1467, 1457, 1455, 1424, 1402, 1361, 1253, 1092, 1054, 1033, 1011, 835, 777, 734 cm^{-1}; $[\alpha]_D$ +24.1 (c 1.73, $CHCl_3$); MS (ESI) calcd for $C_{21}H_{40}NO_3Si$ $(M+NH_4)^+$: 382.3, found 382.2.

To a solution of the *anti*-TBS-diol (800 mg, 2.20 mmol) in THF (30 mL) was added TBAF (2.90 mL of a 1 M solution in THF, 2.90 mmol). The reaction mixture was stirred for 2 h, and subsequently quenched by addition of saturated NH_4Cl solution. After evaporation of all volatiles and extraction of the remaining aqueous layer with EtOAc, the combined organic phase was dried (Na_2SO_4) and concentrated. Purification of the residue by flash chromatography (hexanes/EtOAc, 2:1 to 1:1) gave 525 mg (95%) of *anti*-diol **9d** as a light yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42–7.29 (m, 5H), 5.76 (ddt, J=15.4, 6.3, 1.0 Hz, 1H), 5.54 (ddt, J=15.4, 6.5, 1.5 Hz, 1H), 4.59 (s, 2H), 4.41 (ddd, J=7.3, 7.3, 3.7 Hz, 1H), 4.16 (dddd, J=8.7, 7.5, 3.6, 3.6 Hz, 1H), 3.53 (dd, J=9.5, 3.7 Hz, 1H), 3.44 (dd, J=9.4, 7.5 Hz, 1H), 2.75 (br s, 1H), 2.43 (br s, 1H), 2.12–2.03 (m, 2H), 1.76 (ddd, J=14.3, 8.7, 3.5 Hz, 1H), 1.65 (ddd, J=14.4, 7.9, 3.4 Hz, 1H), 1.01 (t, J=7.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.8, 133.0, 131.2, 128.4, 127.7, 127.6(8), 74.3, 73.2, 69.7, 67.7, 39.3, 25.1, 13.4; IR (film, NaCl) 3392, 2961, 2916, 1454, 1074, 968 cm^{-1}; $[\alpha]_D$ +3.5 (c 2.43, $CHCl_3$); MS (ESI) calcd for $C_{15}H_{22}NaO_3$ $(M+Na)^+$: 273.1, found 273.1.

*4.2.18. (2R,4R,E)-1-(Benzyloxy)-5-methyloct-5-ene-2,4-diol (**9e**).* The material was prepared from enone **6a** by CBS reduction via the corresponding *anti*-TBS-diol as a colorless oil as described for **9d** (92% overall yield, dr 99:1). *anti*-TBS-diol: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40–7.29 (m, 5H), 5.47–5.41 (m, 1H), 4.59 (d, J=12.1 Hz, 1H), 4.54 (d, J=12.1 Hz, 1H), 4.25 (dd, J=10.1, 1.9 Hz, 1H), 4.15 (dddd, J=5.8, 5.8, 5.8, 4.3 Hz, 1H), 3.53 (dd, J=9.5, 5.7 Hz, 1H), 3.50 (dd, J=9.5, 6.1 Hz, 1H), 2.92 (br s, 1H), 2.10–2.00 (m, 2H), 1.81 (ddd, J=14.1, 9.8, 4.2 Hz, 1H), 1.73 (ddd, J=14.3, 5.8, 2.9 Hz, 1H), 1.63 (s, 3H), 0.99 (t, J=7.5 Hz, 3H), 0.92 (s, 9H), 0.13 (s, 3H), 0.10 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.1, 136.5, 128.3, 127.6, 127.5(9), 127.1, 73.7, 73.6(8), 73.3, 69.9, 39.4, 25.8, 20.8, 18.0, 14.0, 11.8, −4.5, −5.0; IR (film, NaCl) 3426, 2978, 2929, 2878, 1467, 1457, 1455, 1424, 1402, 1361, 1253, 1092, 1054, 1033, 1011, 835, 777, 734 cm^{-1}; $[\alpha]_D$ +16.2 (c 1.62, $CHCl_3$). MS (ESI) calcd for $C_{22}H_{38}NaO_3Si$ $(M+Na)^+$: 401.2, found 401.2. *anti*-diol **9e**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38–7.27 (m, 5H), 5.44 (t, J=7.1 Hz, 1H), 4.56 (s, 2H), 4.27 (dd, J=7.1, 4.7 Hz, 1H), 4.10–4.03 (m, 1H), 3.51 (ddd, J=9.5, 3.7, 0.9 Hz, 1H), 3.41 (dd, J=9.3, 7.5 Hz, 1H), 2.86 (br s, 1H), 2.46 (br s, 1H), 2.07–1.98 (m, 2H), 1.70–1.64 (m, 2H), 1.59 (s, 3H), 0.96 (t, J=7.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.9, 136.2, 128.4, 127.8, 127.7, 127.4, 74.3, 73.9, 73.3, 67.9, 37.5, 20.7, 14.0, 12.0; IR (film, NaCl) 3400, 2960, 2930, 2871, 1454, 1396, 1089, 1073, 1028, 998 cm^{-1}; $[\alpha]_D$ +7.7 (c 2.37, $CHCl_3$); HRMS (ESI) calcd for $C_{16}H_{24}NaO_3$ $(M+Na)^+$: 287.1618, found 287.1611.

*4.2.19. (2R,4R,E)-1-(Benzyloxy)-5-methyl-6-phenylhex-5-ene-2,4-diol (**9f**).* The material was prepared from enone **6b** by CBS reduction via the corresponding *anti*-TBS-diol as a colorless oil as described for **9d** (71% overall yield, dr 98:2). *anti*-TBS-diol: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43–7.30 (m, 9H), 7.29–7.23 (m, 1H), 6.62 (br s, 1H), 4.63 (d, J=12.1 Hz, 1H), 4.59 (d, J=12.1 Hz, 1H), 4.49–4.43 (m, 1H), 4.29–4.22 (m, 1H), 3.63–3.56 (m, 2H), 3.30 (br s, 1H), 1.95–1.87 (m, 5H), 0.98 (s, 9H), 0.19 (s, 3H), 0.16 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.6, 138.1, 138.0, 129.1, 128.5, 128.1, 127.8, 126.3, 124.6, 74.0, 73.7, 73.5, 70.1, 39.7, 26.0, 18.2, 14.2, −4.3, −4.9; IR (film, NaCl) 3436, 3063, 3028, 2954, 2929, 2886, 2857, 1948, 1653, 1600, 1495, 1471, 1463, 1454, 1409, 1361, 1324, 1253, 1205, 1091, 1028, 939, 917, 836, 810, 777, 748, 698 cm^{-1}; $[\alpha]_D$ +10.2 (c 0.51, $CHCl_3$); MS (ESI) calcd for $C_{26}H_{38}NaO_3Si$ $(M+Na)^+$: 449.3, found 449.2. *anti*-diol **9f**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38–7.24 (m, 9H), 7.24–7.18 (m, 1H), 6.60 (br s, 1H), 4.58 (s, 2H), 4.50–4.43 (m, 1H), 4.19–4.11 (m, 1H), 3.55 (ddd, J=9.3, 3.1, 3.1 Hz, 1H), 3.45 (ddd, J=9.9, 7.6, 2.5 Hz, 1H), 2.71 (br s, 1H), 2.67 (br s, 1H), 1.85 (s, 3H), 1.83–1.76 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.2, 138.0, 137.8, 129.1, 128.6, 128.2, 128.0, 127.9, 126.5, 125.1, 77.4, 74.5, 73.6, 68.2, 37.6, 14.4; IR (film, NaCl) 3400, 3026, 2916, 2860, 1599, 1493, 1452, 1364, 1205, 1074, 1028, 1009, 919, 868, 748, 698 cm^{-1}; $[\alpha]_D$ +14.6 (c 0.42, $CHCl_3$); HRMS (ESI) calcd for $C_{20}H_{24}NaO_3$ $(M+Na)^+$: 335.1618, found 335.1612.

*4.2.20. (2R,E)-1-(Benzyloxy)-6-phenylhex-5-ene-2,4-diol (**9g**).* The material was prepared from enone **6d** as a colorless oil using the Luche reduction procedure (68% overall yield, dr 2:1): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.42–7.24 (m, 10H), 6.65 (dd, J=15.8, 0.7 Hz, 1H, minor isomer), 6.63 (d, J=15.8 Hz, 1H, major isomer), 6.28 (dd, J=15.4, 6.2 Hz, 1H, minor isomer), 6.23 (dd, J=15.8, 6.4 Hz, 1H, major isomer), 4.67–4.54 (m, 3H), 4.25–4.09 (m, 1H), 3.57–3.39 (m, 2H), 3.20 (br s, 1H, major isomer), 3.00 (d, J=1.68 Hz, 1H, minor isomer), 2.80–2.73 (m, 1H), 1.92–1.69 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$, major isomer) δ 137.9, 136.8, 131.8, 130.2, 128.7, 128.6, 128.0, 127.9, 127.8, 126.6(2), 126.6, 74.4, 73.6, 72.7, 70.9, 40.0; IR (film, NaCl) 3381, 3060, 3028, 2916, 2859, 1952, 1810, 1654, 1599, 1578, 1541, 1495, 1453, 1417, 1364, 1310, 1260, 1205, 1094, 1072, 1028, 967, 912, 854, 747, 707 cm^{-1}; HRMS (ESI) calcd for $C_{19}H_{22}NaO_3$ $(M+Na)^+$: 312.1461, found 321.1451.

*4.2.21. (2R,E)-1-(Benzyloxy)-6-(4-methoxyphenyl)hex-5-ene-2,4-diol (**9h**).* The material was prepared from enone **6e** as a colorless oil using the Luche reduction procedure (71% overall yield, dr 2:1): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42–7.30 (m, 7H), 6.90–6.85 (m, 2H), 6.59 (d, J=15.9 Hz, 1H, minor isomer), 6.58 (d, J=15.8 Hz, 1H, major isomer), 6.15 (dd, J=15.8, 6.1 Hz, 1H, minor isomer), 6.10 (dd, J=15.9, 6.6 Hz, 1H, major isomer), 4.63–4.54 (m, 3H), 4.26–4.18 (m, 1H, minor isomer), 4.17–4.10 (m, 1H, major isomer), 3.83 (s, 3H), 3.57–3.42 (m, 2H), 3.13 (br s, 1H, major isomer), 3.06 (br s, 1H, major isomer), 2.80 (br s, 1H, minor isomer), 2.73 (br s, 1H, minor isomer), 1.91–1.69 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, major isomer) δ 159.4, 137.9, 129.9, 129.6, 128.6, 128.0, 127.9, 127.8, 127.7(7), 114.1, 74.5, 73.6, 72.9, 70.8, 55.4, 40.1; IR (film, NaCl) 3390, 3063, 3031, 3004, 2918, 2857, 2056, 1886, 1651, 1607, 1577, 1512, 1463, 1454, 1421, 1365, 1301, 1250, 1207, 1175, 1105, 1032, 969, 910, 842, 816, 738, 699 cm^{-1}; HRMS (ESI) calcd for $C_{20}H_{24}NaO_4$ $(M+Na)^+$: 351.1567, found 351.1560.

*4.2.22. (2R,E)-1-(Benzyloxy)-6-(4-methoxyphenyl)-5-methylhex-5-ene-2,4-diol (**9i**).* The material was prepared from enone **6f** as a colorless oil using the Luche reduction procedure (70% overall yield, dr 3:1): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41–7.30 (m, 5H), 7.25–7.22 (m, 2H), 6.92–6.87 (m, 2H), 6.54 (br s, 1H, minor isomer), 6.50 (br s, 1H, major isomer), 4.59 (s, 2H), 4.48–4.42 (m, 1H), 4.21–4.09 (m, 1H), 3.83 (s, 3H), 3.58–3.42 (m, 2H), 3.34 (br s, 1H), 2.96–2.83 (m, 1H), 1.90–1.88 (m, 3H, major isomer), 1.88–1.86 (m, 3H, minor isomer), 1.83–1.74 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, major isomer) δ 158.1, 138.1, 137.9, 130.2(4), 130.2, 128.6, 127.9, 127.8(9), 125.1, 113.6, 77.9, 74.5, 73.5, 71.0, 55.3, 38.2, 13.6; IR (film, NaCl) 3391, 3063, 3031, 2915, 2860, 2058, 1607, 1574, 1520, 1463,

1454, 1417, 1365, 1298, 1250, 1178, 1109, 1034, 1007, 876, 830, 810, 738, 699 cm^{-1}; HRMS (ESI) calcd for $C_{21}H_{26}NaO_4$ $(M+Na)^+$: 365.1723, found 365.1726.

*4.2.23. (2R,E)-1-(Benzyloxy)-6-(4-fluorophenyl)hex-5-ene-2,4-diol (**9j**).* The material was prepared from enone **6g** as a colorless oil using the Luche reduction procedure (66% overall yield, dr 2:1): ^1H NMR (400 MHz, $CDCl_3$) 7.42–7.30 (m, 7H), 7.02 (dd, *J*=8.5, 8.5 Hz, 2H), 6.62 (d, *J*=15.9 Hz, 1H, minor isomer), 6.60 (d, *J*=15.9 Hz, 1H, major isomer), 6.20 (dd, *J*=15.9, 5.5 Hz, 1H, minor isomer), 6.15 (dd, *J*=15.8, 6.2 Hz, 1H, major isomer), 4.66–4.56 (m, 3H), 4.25–4.18 (m, 1H, minor isomer), 4.18–4.10 (m, 1H, major isomer), 3.57–3.40 (m, 2H), 3.30 (br s, 1H, major isomer), 3.01 (br s, 1H, major isomer), 2.86 (br s, 1H, minor isomer), 2.78 (br s, 1H, minor isomer), 1.92–1.69 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, major isomer) δ 164.1, 160.8, 137.9, 133.0, 132.9, 131.5(3), 131.5, 129.0, 128.6, 128.2, 128.1, 127.9, 115.7, 115.4, 74.4, 73.6, 72.6, 70.9, 39.9. IR (film, NaCl) 3392, 2917, 1601, 1509, 1454, 1228, 1158, 1093, 968, 815, 737, 698 cm^{-1}; HRMS (ESI) calcd for $C_{19}H_{21}FNaO_3$ $(M+Na)^+$: 339.1367, found 339.1366.

*4.2.24. (2R,E)-1-(Benzyloxy)-6-(4-fluorophenyl)-5-methylhex-5-ene-2,4-diol (**9k**).* The material was prepared from benzyl ester **8** using the olefination procedure as described for **6c** followed by Luche reduction as described for **9b** without purifying the enone intermediate **6h** (57% overall yield, dr 3:1): ^1H NMR (400 MHz, $CDCl_3$) δ 7.42–7.30 (m, 5H), 7.28–7.20 (m, 2H), 7.03 (dd, *J*=8.7, 8.7 Hz, 2H), 6.57 (br s, 1H, minor isomer), 6.53 (br s, 1H, major isomer), 4.59 (s, 2H), 4.49–4.41 (m, 1H), 4.21–4.09 (m, 1H), 3.59–3.41 (m, 2H), 3.23 (br s, 1H), 2.89 (br s, 1H), 1.89–1.74 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$, major isomer) δ 162.7, 160.3, 139.8, 137.9, 133.7, 133.6(6), 130.7, 130.6, 128.6, 128.0, 127.9, 124.5, 115.2, 115.0, 77.7, 74.4, 73.6, 71.2, 38.3, 13.8; IR (film, NaCl) 3445, 3031, 2916, 2849, 1605, 1507, 1454, 1400, 1222, 1156, 1096, 1057, 1028 cm^{-1}; MS (ESI) calcd for $C_{20}H_{23}FNaO_3$ $(M+Na)^+$: 353.3, found 353.3.

*4.2.25. (R)-4-(Benzyloxy)-3-((tert-butyldimethylsilyl)oxy)butanal (**10**).* To a cold (−78 °C) solution of benzyl ester **8** (337 mg, 0.81 mmol) in CH_2Cl_2 (20 mL) was added dropwise DIBAL-H (0.81 mL of a 1 M solution in CH_2Cl_2, 0.81 mmol). The reaction was stirred for 30 min at −78 °C, and subsequently quenched by addition of saturated NaK tartrate solution. The mixture was stirred at room temperature until two clear phases were obtained. After phase separation, the aqueous layer was extracted with CH_2Cl_2. The combined organic phase was washed (brine), dried (Na_2SO_4), and concentrated in vacuo. The residue was purified by flash chromatography (hexanes/EtOAc, 8:1) to give 152 mg (61%) of aldehyde **10** as a colorless oil: ^1H NMR (400 MHz, $CDCl_3$) δ 9.83 (dd, *J*=2.6, 2.1 Hz, 1H), 7.42–7.26 (m, 5H), 4.56 (s, 2H), 4.39 (dddd, *J*=6.3, 6.3, 5.2, 5.2 Hz, 1H), 3.54 (dd, *J*=9.5, 5.1 Hz, 1H), 3.43 (dd, *J*=9.6, 6.2 Hz, 1H), 2.69 (ddd, *J*=15.9, 5.1, 2.0 Hz, 1H), 2.61 (ddd, *J*=15.9, 6.6, 2.7 Hz, 1H), 0.89 (s, 9H), 0.10 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.4, 137.9, 128.4, 127.7, 127.6, 74.0, 73.4, 67.3, 48.9, 25.7, 18.0, −4.5, −5.0; IR (film, NaCl) 2954, 2929, 2894, 2857, 1728, 1472, 1463, 1454, 1362, 1254, 1103, 1028, 1005, 837, 811, 778, 736, 698 cm^{-1}; $[\alpha]_D$ +14.6 (*c* 1.81, $CHCl_3$); MS (ESI) calcd for $C_{17}H_{29}O_3Si$ $(M+H)^+$: 309.2, found 309.1.

*4.2.26. (2R)-1-(Benzyloxy)-2-((tert-butyldimethylsilyl)oxy)oct-5-yn-4-ol (**11**).* To a −78 °C solution of approximately 0.3 mL of 1-butyne (3.76 mmol) in THF (5 mL) was added *n*-BuLi (1.48 mL of a 1.6 M solution in hexanes, 2.37 mmol). The mixture was stirred for 30 min, and subsequently transferred to a −78 °C solution of aldehyde **10** (364 mg, 1.18 mmol) in THF (5 mL). The reaction mixture was allowed to slowly warm to room temperature, stirred for 30 min, and saturated NH_4Cl solution was added. The mixture was carefully extracted with CH_2Cl_2. The combined organic phase was washed with brine, dried (Na_2SO_4), and concentrated in vacuo. Purification of the residue by flash chromatography (hexanes/EtOAc, 8:1 to 4:1) yielded 142 mg (33%) of *anti*-propargylic alcohol **11b** as a colorless oil as the first fraction and 165 mg (39%) of *syn*-**11a** as a colorless oil as the second fraction. *syn*-**11a**: ^1H NMR (400 MHz, $CDCl_3$) δ 7.39–7.27 (m, 5H), 4.63–4.56 (m, 1H), 4.56 (d, *J*=1.6 Hz, 2H), 4.18–4.12 (m, 1H), 3.51 (dd, *J*=9.7, 5.2 Hz, 1H), 3.45 (dd, *J*=9.7, 5.7 Hz, 1H), 3.01 (br s, 1H), 2.24 (dq, *J*=7.5, 1.9 Hz, 2H), 1.98–1.94 (m, 2H), 1.16 (t, *J*=7.5 Hz, 3H), 0.92 (s, 9H), 0.13 (s, 3H), 0.10 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.8, 128.2, 127.6, 127.5, 86.9, 80.2, 74.7, 73.3, 69.5, 60.3, 43.1, 25.7, 17.9, 13.7, 12.3, −4.5, −5.0; IR (film, NaCl) 3410, 2954, 2928, 2884, 2856, 1471, 1462, 1454, 1361, 1252, 1127, 1088, 1029, 971, 836, 777, 698 cm^{-1}; $[\alpha]_D$ +19.5 (*c* 1.29, $CHCl_3$); MS (ESI) calcd for $C_{21}H_{35}O_3Si$ $(M+H)^+$: 363.2, found 363.2. *anti*-**11b**: ^1H NMR (400 MHz, $CDCl_3$) δ 7.40–7.27 (m, 5H), 4.63–4.57 (m, 1H), 4.55 (s, 2H), 4.24 (dddd, *J*=7.0, 5.6, 5.6, 4.3 Hz, 1H), 3.50 (dd, *J*=9.6, 5.4 Hz, 1H), 3.45 (dd, *J*=9.6, 5.9 Hz, 1H), 3.07 (d, *J*=5.3 Hz, 1H), 2.24 (dq, *J*=7.5, 2.0 Hz, 2H), 1.99 (ddd, *J*=14.3, 8.2, 4.3 Hz, 1H), 1.93 (ddd, *J*=14.3, 7.1, 3.9 Hz, 1H), 1.16 (t, *J*=7.5 Hz, 3H), 0.92 (s, 9H), 0.15 (s, 3H), 0.11 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.0, 128.3, 127.6, 86.3, 80.5, 74.0, 73.3, 69.4, 59.7, 41.9, 25.8, 18.0, 13.8, 12.3, −4.5, −5.0; IR (film, NaCl) 3425, 2956, 2928, 2891, 2856, 1471, 1462, 1454, 1388, 1361, 1319, 1253, 1205, 1120, 1090, 1005, 836, 811, 778, 736, 698 cm^{-1}; $[\alpha]_D$ +20.5 (*c* 1.03, $CHCl_3$); MS (ESI) calcd for $C_{21}H_{35}O_3Si$ $(M+H)^+$: 363.2, found 363.2.

*4.2.27. (2R,4S,Z)-1-(Benzyloxy)oct-5-ene-2,4-diol (**12a**).* To a solution of alkyne **11a** (165 mg, 0.46 mmol) in a mixture of EtOAc/1-hexene/pyridine (1 mL, 8:1:1) was added Lindlar-catalyst (5% Pd/$CaCO_3$/Pb, 20 mg). The reaction mixture was stirred for 8 h under an atmosphere of H_2 and subsequently filtered (Celite). Evaporation of all volatiles yielded the *cis*-alkene as a colorless oil, which was used without further purification.

To a solution of the crude reaction product in THF (4 mL) was added TBAF (0.83 mL of a 1 M solution in THF, 0.83 mmol). The reaction mixture was stirred for 1 h at room temperature, after which saturated NH_4Cl solution was added. After evaporation of all volatiles in vacuo, the residue was extracted with CH_2Cl_2. The combined organic phase was washed (brine), dried (Na_2SO_4), and concentrated. Purification of the residue by flash chromatography (hexanes/EtOAc, 2:1 to 1:1) yielded 66 mg (57%) of *syn-cis*-diol **12a** as a colorless oil: ^1H NMR (400 MHz, $CDCl_3$) δ 7.41–7.27 (m, 5H), 5.48 (ddd, *J*=10.8, 7.3, 7.3 Hz, 1H), 5.41–5.34 (m, 1H), 4.74 (ddd, *J*=8.7, 8.7, 4.0 Hz, 1H), 4.57 (s, 2H), 4.09–4.01 (m, 1H), 3.47 (dd, *J*=9.4, 3.9 Hz, 1H), 3.41 (dd, *J*=9.4, 7.1 Hz, 1H), 3.28 (br s, 1H), 3.10 (br s, 1H), 2.22–2.02 (m, 2H), 1.73 (ddd, *J*=14.2, 9.4, 9.4 Hz, 1H), 1.55 (ddd, *J*=14.3, 3.9, 2.9 Hz, 1H), 1.00 (t, *J*=7.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.3, 20.9, 39.8, 67.4, 70.4, 73.3, 74.4, 127.7, 127.7$_5$, 128.4, 131.3, 133.6, 137.8; IR (film, NaCl) 3369, 2963, 2933, 2872, 2913, 2872, 1455, 1096, 1005, 738, 698 cm^{-1}; $[\alpha]_D$ +47.9 (*c* 0.71, $CHCl_3$); MS (ESI) calcd for $C_{15}H_{26}NO_3$ $(M+NH_4)^+$: 268.2, found 268.1.

*4.2.28. (2R,4R,Z)-1-(Benzyloxy)oct-5-ene-2,4-diol (**12b**).* Following the procedure for the preparation of **12a**, *anti-cis*-diol **12b** was obtained as a colorless oil in 65% yield: ^1H NMR (400 MHz, $CDCl_3$) δ 7.41–7.29 (m, 5H), 5.48 (dd, *J*=11.0, 2.3 Hz, 1H), 5.43 (dd, *J*=10.9, 2.0 Hz, 1H), 4.80–4.73 (m, 1H), 4.58 (s, 2H), 4.19–4.12 (m, 1H), 3.52 (dd, *J*=9.5, 3.7 Hz, 1H), 3.43 (dd, *J*=9.4, 7.5 Hz, 1H), 3.09 (br s, 1H), 2.74 (br s, 1H), 2.18–2.02 (m, 2H), 1.68–1.63 (m, 2H), 0.99 (t, *J*=7.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.8, 133.2, 131.5, 128.4, 127.7$_4$, 127.7, 74.4, 73.3, 67.7, 64.9, 39.7, 20.9, 14.3; IR (film, NaCl) 3391, 3008, 2963, 2934, 2873, 1455, 1366, 1306, 1073, 1029, 964, 737, 699 cm^{-1}; $[\alpha]_D$ +25.0 (*c* 1.21, $CHCl_3$); MS (ESI) calcd for $C_{15}H_{26}NO_3$ $(M+NH_4)^+$: 268.2, found 268.1.

*4.2.29. (4R,6S)-4-((Benzyloxy)methyl)-2,2-dimethyl-6-((E)-pent-2-en-2-yl)-1,3-dioxane (**13a**).* To a solution of diol **9b** (47 mg,

0.18 mmol) in a mixture of 2,2-dimethoxypropane (1 mL) and CH_2Cl_2 (1 mL) was added *p*-toluenesulfonic acid monohydrate (3 mg, 0.016 mmol). The reaction mixture was stirred for 1 h at room temperature and subsequently quenched by addition of solid $NaHCO_3$. Filtration (Celite) and concentration gave 49 mg (91%) of *syn*-acetonide **13a** as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42–7.29 (m, 5H), 5.49–5.44 (m, 1H), 4.64 (d, J=12.2 Hz, 1H), 4.58 (d, J=12.2 Hz, 1H), 4.26 (dd, J=11.4, 2.5 Hz, 1H), 4.20–4.12 (m, 1H), 3.55 (dd, J=9.9, 5.8 Hz, 1H), 3.41 (dd, J=9.9, 4.9 Hz, 1H), 2.12–2.02 (m, 2H), 1.65 (dd, J=2.0, 1.1 Hz, 3H), 1.57–1.51 (m, 4H), 1.48 (s, 3H), 1.50–1.39 (m, 1H), 0.99 (t, J=7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.2, 134.3, 128.6, 128.3, 127.7, 127.6, 98.7, 74.0, 73.6, 73.4, 68.5, 32.4, 30.1, 20.8, 19.8, 13.9, 12.0; MS (ESI) calcd for $C_{19}H_{32}NO_3$ $(M+NH_4)^+$: 322.2, found 322.1.

*4.2.30. (4R,6S)-4-((Benzyloxy)methyl)-2,2-dimethyl-6-((E)-pent-2-en-2-yl)-1,3-dioxane (**13b**).* Following the procedure for the preparation of **13a**, *anti*-acetonide **13b** was obtained from **9e** as a colorless oil in 82% yield: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41–7.29 (m, 5H), 5.46–5.41 (m, 1H), 4.66 (d, J=12.2 Hz, 1H), 4.59 (d, J=12.2 Hz, 1H), 4.23 (dd, J=9.8, 6.0 Hz, 1H), 4.14–4.07 (m, 1H), 3.56 (dd, J=10.4, 6.4 Hz, 1H), 3.48 (dd, J=10.4, 4.2 Hz, 1H), 2.11–2.02 (m, 2H), 1.88–1.80 (m, 1H), 1.71–1.63 (m, 4H), 1.44 (s, 6H), 0.99 (t, J=7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.2, 133.7, 128.3, 128.2(5), 127.7, 127.5, 100.4, 73.3, 72.7, 71.4, 66.5, 32.6, 25.1, 24.9, 20.8, 13.9, 12.2; MS (ESI) calcd for $C_{19}H_{32}NO_3$ $(M+NH_4)^+$: 322.2, found 322.1.

*4.2.31. (4R,6S)-4-((Benzyloxy)methyl)-6-((Z)-but-1-en-1-yl)-2,2-dimethyl-1,3-dioxane (**13c**).* Following the procedure for the preparation of **13a**, *syn*-acetonide **13c** was obtained from **12a** as a colorless oil in 95% yield: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42–7.27 (m, 5H), 5.53 (dt, J=10.6, 7.2 Hz, 1H), 5.35 (dd, J=10.1, 8.5 Hz, 1H), 4.77–4.70 (m, 1H), 4.21–4.12 (m, 1H), 4.63 (d, J=12.2 Hz, 1H), 4.57 (d, J=12.2 Hz, 1H), 3.54 (dd, J=9.8, 5.8 Hz, 1H), 3.40 (dd, J=9.8, 5.0 Hz, 1H), 2.21–2.01 (m, 2H), 1.54 (s, 3H), 1.52–1.24 (m, 2H), 1.46 (s, 3H), 1.01 (t, J=7.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.6, 134.5, 129.8, 128.4, 127.8, 127.6, 98.7, 73.6, 73.5, 68.2, 65.1, 33.9, 30.2, 21.2, 19.7, 14.3; MS (ESI) calcd for $C_{18}H_{30}NO_3$ $(M+NH_4)^+$: 308.2, found 308.1.

*4.2.32. General protocol for the cyclization of monoallylic diols **9** and **12**.* To a solution of diol **9** or **12** in the given solvent (0.04–0.08 M) was added the catalyst (0.05–1.0 equiv) in one portion and the reaction mixture was stirred at room temperature overnight. After evaporation of all volatiles in vacuo, the residue was purified by flash chromatography (hexanes/EtOAc, 20:1 to 10:1). Dihydropyran *syn*-**14** was obtained as the first fraction and dihydropyran *anti*-**14** as the second one. The *syn*/*anti* ratio was determined by ^{1}H NMR or HPLC analysis of the crude reaction product after concentration in vacuo. The *syn*- and *anti*-assignments of the pyran products are based on NMR experiments, including 2D-NOESY.

*4.2.33. Lewis-acid catalyzed cyclization of diol **9b** on a multigram scale. Table 2, entry 4.* Treatment of diol **9b** (4.0 g, 15.1 mmol, dr 4:1) with $Pd(MeCN)_4(BF_4)_2$ (340 mg, 0.76 mmol) in CH_2Cl_2 (100 mL) for 18 h at room temperature gave 2.71 g (73%) of diastereomerically pure *syn*-pyran **14b** as a colorless oil after purification by flash chromatography (hexanes/EtOAc, 20:1 to 10:1). *Table 2, entry **5***. To a solution of diol **9b** (4.53 g, 17.1 mmol, dr 4:1) in CH_2Cl_2 (220 mL) was added $BF_3{\cdot}OEt_2$ (0.22 mL, 1.7 mmol) in one portion. The reaction mixture was stirred for 18 h at room temperature. After purification by flash chromatography (hexanes/EtOAc, 20:1 to 10:1), 3.40 g (81%) of diastereomerically pure *syn*-pyran **14b** was obtained as a colorless oil.

*4.2.34. (2R,6R)-2-(Benzyloxymethyl)-6-ethyl-3,6-dihydro-2H-pyran (syn-**14a**).* Using the general cyclization protocol, *syn*-**14a** was isolated as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44–7.26 (m, 5H), 5.84 (dddd, J=10.0, 4.8, 1.2, 1.2 Hz, 1H), 5.68 (dddd, J=10.2, 2.7, 1.3, 1.3 Hz, 1H), 4.68 (d, J=12.3 Hz, 1H), 4.61 (d, J=12.3 Hz, 1H), 4.17–4.10 (m, 1H), 3.90–3.83 (m, 1H), 3.60 (dd, J=10.3, 6.5 Hz, 1H), 3.50 (dd, J=10.3, 4.2 Hz, 1H), 2.11–1.90 (m, 2H), 1.66–1.57 (m, 2H), 0.99 (t, J=7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.4, 130.1, 128.3, 127.6, 127.5, 124.1, 75.7, 73.3, 73.2, 73.1, 28.3, 27.8, 9.3; IR (film, NaCl) 3030, 2963, 2921, 2857, 1454, 1366, 1185, 1123, 1098, 1063, 1013 cm^{-1}; $[\alpha]_D$ +29.6 (*c* 0.86, $CHCl_3$); MS (ESI) calcd for $C_{15}H_{21}O_2$ $(M+H)^+$: 233.2, found 233.1.

*4.2.35. (2R,6S)-2-(Benzyloxymethyl)-6-ethyl-3,6-dihydro-2H-pyran (anti-**14a**).* Using the general cyclization protocol, *anti*-**14a** was isolated as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44–7.26 (m, 5H), 5.85–5.79 (m, 1H), 5.78–5.73 (m, 1H), 4.64 (d, J=12.1 Hz, 1H), 4.60 (d, J=12.1 Hz, 1H), 4.12–4.08 (m, 1H), 3.97–3.94 (m, 1H), 3.60 (dd, J=10.1, 6.2 Hz, 1H), 3.52 (dd, J=10.1, 4.5 Hz, 1H), 2.07–2.01 (m, 2H), 1.73–1.65 (m, 1H), 1.58–1.52 (m, 1H), 1.02 (t, J=7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.4, 129.7, 128.3, 127.6, 127.5, 123.3, 74.0, 73.3, 72.8, 66.9, 29.7, 27.2, 10.4; IR (film, NaCl) 3032, 2961, 2919, 2851, 1454, 1105, 1058, 734, 697 cm^{-1}; $[\alpha]_D$ +46.6 (*c* 0.43, $CHCl_3$); MS (ESI) calcd for $C_{15}H_{21}O_2$ $(M+H)^+$: 233.2, found 233.1.

*4.2.36. (2R,6R)-2-(Benzyloxymethyl)-6-ethyl-5-methyl-3,6-dihydro-2H-pyran (syn-**14b**).* Using the general cyclization protocol, *syn*-**14b** was isolated as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42–7.34 (m, 4H), 7.34–7.27 (m, 1H), 5.60–5.56 (m, 1H), 4.68 (d, J=12.3 Hz, 1H), 4.61 (d, J=12.3 Hz, 1H), 4.12 (br s, 1H), 3.78 (dddd, J=10.2, 6.4, 3.8, 3.8 Hz, 1H), 3.60 (dd, J=10.3, 6.4 Hz, 1H), 3.50 (dd, J=10.3, 4.2 Hz, 1H), 2.10–1.88 (m, 2H), 1.83 (ddq, J=14.7, 7.4, 3.6 Hz, 1H), 1.63 (br s, 3H), 1.54 (ddq, J=14.2, 7.2, 7.2 Hz, 1H), 0.95 (t, J=7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.5, 135.4, 128.3, 127.6, 127.4, 120.1, 77.9, 73.3, 73.2, 72.8, 28.1, 25.5, 19.0, 8.4; IR (film, NaCl) 2964, 2934, 2858, 1454, 1368, 1118, 1062, 1028, 1005 cm^{-1}; $[\alpha]_D$ +74.7 (*c* 1.96, $CHCl_3$); HRMS (ESI) calcd for $C_{16}H_{22}NaO_2$ $(M+Na)^+$: 269.1512, found 269.1514.

*4.2.37. (2R,6S)-2-(Benzyloxymethyl)-6-ethyl-5-methyl-3,6-dihydro-2H-pyran (anti-**14b**).* Using the general cyclization protocol, *anti*-**14b** was isolated as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.44–7.28 (m, 5H), 5.51 (br s, 1H), 4.68 (d, J=12.1 Hz, 1H), 4.61 (d, J=12.1 Hz, 1H), 3.99–3.87 (m, 2H), 3.60 (dd, J=10.1, 6.1 Hz, 1H), 3.54 (dd, J=10.1, 4.4 Hz, 1H), 2.13–1.90 (m, 2H), 1.74–1.58 (m, 5H), 1.09 (t, J=7.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.4, 136.1, 128.2, 127.5, 127.4, 118.3, 77.5, 73.3, 73.0, 66.1, 27.6, 24.5, 19.9, 10.5; IR (film, NaCl) 2962, 2929, 2872, 1452, 1376, 1363, 1106, 1053, 1028, 994, 887, 735, 697 cm^{-1}; $[\alpha]_D$ +52.1 (*c* 0.95, $CHCl_3$); MS (ESI) calcd for $C_{16}H_{23}O_2$ $(M+H)^+$: 247.2, found 247.1.

*4.2.38. (2R,6S)-2-((Benzyloxy)methyl)-6-phenyl-3,6-dihydro-2H-pyran (syn-**14c**).* Using the general cyclization protocol, *syn*-**14c** was isolated as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43–7.29 (m, 10H), 5.99–5.91 (m, 1H), 5.78 (tdd, J=10.2, 2.7, 1.4 Hz, 1H), 5.28–5.23 (m, 1H), 4.67 (d, J=12.2 Hz, 1H), 4.59 (d, J=12.2 Hz, 1H), 4.07 (tdd, J=10.4, 6.1, 4.1 Hz, 1H), 3.69 (dd, J=10.2, 6.2 Hz, 1H), 3.56 (dd, J=10.2, 4.5 Hz, 1H), 2.29–2.16 (m, 1H), 2.15–2.03 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.6, 138.5, 130.4, 128.6, 128.5, 127.9, 127.7, 127.3, 124.2, 77.6, 73.8, 73.6, 73.3, 27.8; IR (film, NaCl) 3032, 2858, 1651, 1604, 1495, 1454, 1364, 1272, 1203, 1181, 1095, 1028, 910, 874, 807, 739, 698 cm^{-1}; $[\alpha]_D$ −51.0 (*c* 0.38, $CHCl_3$); MS (ESI) calcd for $C_{19}H_{20}NaO_2$ $(M+Na)^+$: 303.1, found 303.1.

*4.2.39. (2R,6R)-2-((Benzyloxy)methyl)-6-phenyl-3,6-dihydro-2H-pyran (anti-**14c**).* Using the general cyclization protocol, *anti*-**14c** was

isolated as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47–7.43 (m, 2H), 7.40–7.27 (m, 8H), 6.07–6.04 (m, 2H), 5.33 (br s, 1H), 4.54 (s, 2H), 3.90–3.81 (m, 1H), 3.57 (dd, J=10.3, 5.7 Hz, 1H), 3.50 (dd, J=10.3, 4.5 Hz, 1H), 2.30–2.18 (m, 1H), 2.09–1.99 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.1, 138.5, 128.4(3), 128.4, 128.0, 127.8, 127.7, 127.6(8), 127.6, 125.5, 74.1, 73.4, 72.8, 67.1, 27.5; IR (film, NaCl) 697, 734, 806, 868, 1028, 1069, 1196, 1260, 1362, 1452, 1494, 2922, 3031 cm^{-1}; $[\alpha]_D$ +48.7 (*c* 0.39, $CHCl_3$); HRMS (ESI) calcd for $C_{19}H_{20}NaO_2$ $(M+Na)^+$: 303.1356, found 303.1355.

*4.2.40. (2R,6S)-2-((Benzyloxy)methyl)-5-methyl-6-phenyl-3,6-dihydro-2H-pyran (syn-**14d**).* Using the general cyclization protocol, *syn*-**14d** was isolated as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42–7.29 (m, 10H), 5.74–5.70 (m, 1H), 5.07 (br s, 1H), 4.66 (d, J=12.2 Hz, 1H), 4.58 (d, J=12.2 Hz, 1H), 4.03–3.95 (m, 1H), 3.68 (dd, J=10.1, 6.1 Hz, 1H), 3.55 (dd, J=10.1, 4.6 Hz, 1H), 2.33–2.22 (m, 1H), 2.15–2.06 (m, 1H), 1.40 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.9, 138.5, 135.5, 128.4, 128.3, 128.0, 127.8, 127.6, 120.0, 81.7, 73.5, 73.4, 73.3, 28.4, 19.6; IR (film, NaCl) 3418, 3063, 3031, 2918, 2852, 1751, 1694, 1682, 1598, 1495, 1452, 1373, 1315, 1273, 1206, 1176, 1096, 1028, 912, 737, 714, 700 cm^{-1}; $[\alpha]_D$ −15.8 (*c* 0.38, $CHCl_3$); HRMS (ESI) calcd for $C_{20}H_{23}O_2$ $(M+H)^+$: 295.1693, found 295.1682.

*4.2.41. (2R,6R)-2-((Benzyloxy)methyl)-5-methyl-6-phenyl-3,6-dihydro-2H-pyran (anti-**14d**).* Using the general cyclization protocol, *anti*-**14d** was isolated as a white solid: mp 65–67 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44–7.23 (m, 10H), 5.83 (s, 1H), 5.08 (s, 1H), 4.49 (d, J=12.1 Hz, 1H), 4.46 (d, J=12.1 Hz, 1H), 3.81 (dt, J=9.5, 4.6 Hz, 1H), 3.50 (dd, J=10.3, 5.5 Hz, 1H), 3.43 (dd, J=10.3, 4.6 Hz, 1H), 2.30–2.19 (m, 1H), 2.13–2.04 (m, 1H), 1.66–1.61 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.9, 137.9, 132.7, 129.0, 128.0, 127.9, 127.8, 127.3, 127.1, 120.9, 78.1, 72.7, 72.3, 65.4, 27.3, 20.0; IR (film, NaCl) 3435, 3058, 3028, 2973, 2934, 2910, 2888, 2865, 2787, 1964, 1896, 1825, 1727, 1604, 1583, 1490, 1470, 1453, 1437, 1407, 1377, 1362, 1354, 1339, 1308, 1256, 1191, 1170, 1158, 1138, 1102, 1086, 1066, 1026, 1001, 973, 950, 939, 924, 911, 883, 860, 824, 796, 763, 742, 702 cm^{-1}; $[\alpha]_D$ +94.7 (*c* 0.51, $CHCl_3$); HRMS (ESI) calcd for $C_{20}H_{22}NaO_2$ $(M+H)^+$: 317.1512, found 317.1502.

*4.2.42. (2R,6S)-2-((Benzyloxy)methyl)-6-(4-methoxyphenyl)-3,6-dihydro-2H-pyran (syn-**14e**).* Using the general cyclization protocol, *syn*-**14e** was isolated as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41–7.26 (m, 7H), 6.93–6.87 (m, 2H), 5.97–5.90 (m, 1H), 5.75 (d, J=10.2 Hz, 1H), 5.19 (br s, 1H), 4.65 (d, J=12.1 Hz, 1H), 4.57 (d, J=12.2 Hz, 1H), 4.09–4.01 (m, 1H), 3.82 (s, 3H), 3.69–3.62 (m, 1H), 3.53 (dd, J=10.3, 4.7 Hz, 1H), 2.25–2.14 (m, 1H), 2.12–2.02 (m, 1H); IR (film, NaCl) 3437, 3010, 2918, 2851, 1723, 1613, 1586, 1514, 1463, 1455, 1365, 1303, 1247, 1216, 1174, 1092, 1036, 910, 877, 829, 755, 698, 667 cm^{-1}; $[\alpha]_D$ −18.1 (*c* 0.43, $CHCl_3$); HRMS (ESI) calcd for $C_{20}H_{23}O_3$ $(M+H)^+$: 311.1642, found 311.1640.

*4.2.43. (2R,6R)-2-((Benzyloxy)methyl)-6-(4-methoxyphenyl)-3,6-dihydro-2H-pyran (anti-**14e**).* Using the general cyclization protocol, *anti*-**14e** was isolated as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40–7.26 (m, 7H), 6.93–6.88 (m, 2H), 6.10–6.04 (m, 1H), 6.03–5.98 (m, 1H), 5.29 (br s, 1H), 4.55 (d, J=12.9 Hz, 1H), 4.52 (d, J=12.5 Hz, 1H), 3.86–3.80 (m, 1H), 3.83 (s, 3H), 3.55 (dd, J=10.3, 5.6 Hz, 1H), 3.51–3.47 (m, 1H), 2.30–2.19 (m, 1H), 2.09–2.00 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.2, 138.5, 133.2, 129.6, 128.4, 127.8, 127.8, 127.6, 125.4, 113.7, 73.8, 73.3, 72.8, 66.6, 55.4, 27.5; IR (film, NaCl) 3033, 2917, 2850, 2246, 1610, 1583, 1510, 1454, 1362, 1303, 1246, 1174, 1070, 1036, 909, 876, 834, 782, 732, 697, 680 cm^{-1}; $[\alpha]_D$ +45.9 (*c* 0.63, $CHCl_3$); HRMS (ESI) calcd for $C_{20}H_{22}NaO_3$ $(M+Na)^+$: 333.1461, found 333.1456.

*4.2.44. (2R,6S)-2-((Benzyloxy)methyl)-6-(4-methoxyphenyl)-5-methyl-3,6-dihydro-2H-pyran (syn-**14f**).* Using the general cyclization protocol, *syn*-**14f** was isolated as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39–7.23 (m, 7H), 6.92–6.86 (m, 2H), 5.72–5.66 (m, 1H), 5.00 (br s, 1H), 4.62 (d, J=12.2 Hz, 1H), 4.54 (d, J=12.2 Hz, 1H), 3.98–3.91 (m, 1H), 3.82 (s, 3H), 3.64 (dd, J=10.1, 6.1 Hz, 1H), 3.50 (dd, J=10.1, 4.7 Hz, 1H), 2.27–2.16 (m, 1H), 2.12–2.02 (m, 1H), 1.39–1.36 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.4, 138.5, 135.8, 133.2, 129.5, 128.5, 127.9, 127.7, 120.0, 113.9, 81.2, 73.5, 73.4(5), 73.4, 55.4, 28.4, 19.7; IR (film, NaCl) 3583, 3031, 2915, 2854, 1611, 1587, 1513, 1454, 1376, 1333, 1302, 1271, 1240, 1205, 1172, 1098, 1055, 1035, 950, 862, 827, 735, 697 cm^{-1}; $[\alpha]_D$ +73.2 (*c* 0.45, $CHCl_3$); HRMS (ESI) calcd for $C_{21}H_{24}NaO_3$ $(M+Na)^+$: 347.1618, found 347.1617.

*4.2.45. (2R,6R)-2-((Benzyloxy)methyl)-6-(4-methoxyphenyl)-5-methyl-3,6-dihydro-2H-pyran (anti-**14f**).* Using the general cyclization protocol, *anti*-**14f** was isolated as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36–7.22 (m, 7H), 6.93–6.87 (m, 2H), 5.81–5.76 (m, 1H), 5.02 (br s, 1H), 4.48 (d, J=13.0 Hz, 1H), 4.44 (d, J=12.5 Hz, 1H), 3.83 (s, 3H), 3.82–3.72 (m, 1H), 3.47 (dd, J=10.3, 5.3 Hz, 1H), 3.41 (dd, J=10.3, 4.6 Hz, 1H), 2.29–2.15 (m, 1H), 2.10–1.99 (m, 1H), 1.63–1.56 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.5, 138.5, 133.5, 131.6, 130.7, 128.4, 127.8, 127.6, 121.2, 113.7, 78.1, 73.2, 72.8, 65.6, 55.4, 27.9, 20.5; IR (film, NaCl) 3583, 2916, 2849, 2313, 1608, 1509, 1453, 1302, 1245, 1173, 1098, 1034, 868, 833, 696 cm^{-1}; $[\alpha]_D$ +79.5 (*c* 0.31, $CHCl_3$); HRMS (ESI) calcd for $C_{21}H_{25}O_3$ $(M+H)^+$: 325.1798, found 325.1809.

*4.2.46. (2R,6S)-2-((Benzyloxy)methyl)-6-(4-fluorophenyl)-3,6-dihydro-2H-pyran (syn-**14g**).* Using the general cyclization protocol, *syn*-**14g** was isolated as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41–7.30 (m, 7H), 7.04 (dd, J=8.4, 8.4 Hz, 2H), 5.99–5.91 (m, 1H), 5.73 (ddd, J=10.3, 2.5, 1.3 Hz, 1H), 5.22 (br s, 1H), 4.65 (d, J=12.2 Hz, 1H), 4.58 (d, J=12.2 Hz, 1H), 4.05 (qd, J=7.0, 3.8 Hz, 1H), 3.66 (dd, J=10.2, 6.3 Hz, 1H), 3.54 (dd, J=10.2, 4.3 Hz, 1H), 2.26–2.15 (m, 1H), 2.13–2.04 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.7, 161.3, 138.4, 137.4, 137.3(7), 130.1, 129.1, 129.0, 128.5, 127.9, 127.7, 124.5, 115.5, 115.3, 76.9, 73.9, 73.6, 73.3, 27.7; IR (film, NaCl) 3035, 2916, 2849, 1651, 1604, 1511, 1454, 1430, 1365, 1325, 1294, 1267, 1222, 1181, 1156, 1095, 1028, 1015, 911, 879, 832, 792, 736, 698, 658 cm^{-1}; $[\alpha]_D$ −58.3 (*c* 0.29, $CHCl_3$); HRMS (ESI) calcd for $C_{19}H_{20}FO_2$ $(M+H)^+$: 299.1442, found 299.1435.

*4.2.47. (2R,6R)-2-((Benzyloxy)methyl)-6-(4-fluorophenyl)-3,6-dihydro-2H-pyran (anti-**14g**).* Using the general cyclization protocol, *anti*-**14g** was isolated as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44–7.40 (m, 2H), 7.38–7.29 (m, 5H), 7.05 (dd, J=8.7, 8.7 Hz, 2H), 6.12–6.05 (m, 1H), 6.05–5.99 (m, 1H), 5.30 (br s, 1H), 4.55 (s, 2H), 3.84–3.78 (m, 1H), 3.57 (dd, J=10.3, 5.8 Hz, 1H), 3.50 (dd, J=10.3, 4.4 Hz, 1H), 2.24 (dddd, J=17.3, 9.9, 4.8, 2.4 Hz, 1H), 2.05 (ddd, J=17.6, 4.3, 4.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.7, 161.2, 138.4, 136.9, 136.9, 129.8, 129.7, 128.5, 127.7, 127.6, 127.5, 125.8, 115.3, 115.1, 73.4, 73.3, 72.7, 67.0, 27.4; IR (film, NaCl) 3035, 2916, 2849, 1602, 1506, 1454, 1362, 1264, 1223, 1157, 1075, 878, 838, 793, 736, 698, 680 cm^{-1}; $[\alpha]_D$ +86.2 (*c* 0.31, $CHCl_3$); HRMS (ESI) calcd for $C_{19}H_{19}FNaO_2$ $(M+Na)^+$: 321.1261, found 321.1258.

*4.2.48. (2R,6S)-2-((Benzyloxy)methyl)-6-(4-fluorophenyl)-5-methyl-3,6-dihydro-2H-pyran (syn-**14h**).* Using the general cyclization protocol, *syn*-**14h** was isolated as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37–7.28 (m, 7H), 7.03 (dd, J=8.6, 8.6 Hz, 2H), 5.69 (d, J=5.8 Hz, 1H), 5.03 (br s, 1H), 4.62 (d, J=12.2 Hz, 1H), 4.55 (d, J=12.3 Hz, 1H), 3.98–3.90 (m, 1H), 3.63 (dd, J=10.1, 6.2 Hz, 1H), 3.54–3.49 (m, 1H), 2.29–2.16 (m, 1H), 2.11–2.02 (m, 1H), 1.38–1.33 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.8, 161.4, 138.5, 136.8, 136.7(8), 135.4, 130.0, 129.9, 128.5, 127.9, 127.7, 120.3, 115.4, 115.2, 80.9, 73.5(4), 73.5, 73.3, 28.3, 19.6; IR (film, NaCl) 3445, 3031, 2916, 2849, 1728, 1605, 1509, 1454, 1366, 1294, 1266, 1222, 1156, 1096,

1057, 1028, 1015, 952, 900, 864, 831, 799, 751, 697, 666 cm^{-1}; $[\alpha]_D$ −37.6 (*c* 0.67, $CHCl_3$); HRMS (ESI) calcd for $C_{20}H_{25}FNO_2$ $(M+NH_4)^+$: 330.1864, found 330.1877.

*4.2.49. (2R,6R)-2-((Benzyloxy)methyl)-6-(4-fluorophenyl)-5-methyl-3,6-dihydro-2H-pyran (anti-**14h**).* Using the general cyclization protocol, *anti*-**14h** was isolated as a colorless oil: ^1H NMR (400 MHz, $CDCl_3$) δ 7.39–7.23 (m, 7H), 7.07 (dd, *J*=8.7, 8.7 Hz, 2H), 5.83–5.79 (m, 1H), 5.04 (br s, 1H), 4.50 (d, *J*=12.8 Hz, 1H), 4.46 (d, *J*=12.8 Hz, 1H), 3.75 (ddd, *J*=9.7, 4.5, 4.5 Hz, 1H), 3.49 (dd, *J*=10.3, 5.5 Hz, 1H), 3.42 (dd, *J*=10.3, 4.5 Hz, 1H), 2.27–2.17 (m, 1H), 2.12–2.03 (m, 1H), 1.62–1.59 (m, 3H); IR (film, NaCl) 3584, 2917, 2850, 1603, 1506, 1454, 1223, 1157, 1096, 871, 841 cm^{-1}; $[\alpha]_D$ +23.6 (*c* 0.47, $CHCl_3$); HRMS (ESI) calcd for $C_{20}H_{21}FNaO_2$ $(M+Na)^+$: 335.1418, found 335.1429.

*4.2.50. (R)-1-(Benzyloxy)pent-4-en-2-ol (**15**).* To a −78 °C solution of (*R*)-benzyl glycidol ether (**3**) (1.0 g, 6.1 mmol) in THF (20 mL) was added CuI (116 mg, 0.61 mmol) followed by vinyl magnesium bromide (6.4 mL of a 1.0 M solution in THF, 6.4 mmol). The reaction mixture was stirred for 2 h at −78 °C, slowly warmed to 0 °C, and stirred for one additional hour at that temperature. The mixture was quenched by addition of saturated NH_4Cl solution and concentrated under reduced pressure. The remaining aqueous phase was extracted with Et_2O, the combined organic phase dried ($MgSO_4$), and concentrated. The residue was purified by flash chromatography (hexanes/EtOAc, 10:1 to 2:1) to give 0.9 g (77%) of alcohol **15** as a colorless oil: ^1H NMR (400 MHz, $CDCl_3$) δ 7.42–7.30 (m, 5H), 5.85 (dddd, *J*=17.2, 10.0, 7.1, 7.1 Hz, 1H), 5.18–5.10 (m, 2H), 4.59 (s, 2H), 3.95–3.88 (m, 1H), 3.55 (dd, *J*=9.5, 3.4 Hz, 1H), 3.41 (dd, *J*=9.4, 7.5 Hz, 1H), 2.35 (d, *J*=3.3 Hz, 1H), 2.29 (dd, *J*=6.6, 6.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.1, 134.3, 128.6, 127.9, 127.8, 117.9, 74.0, 73.5, 69.9, 38.0; IR (film, NaCl) 3429, 3067, 3031, 2916, 2859, 1642, 1496, 1454, 1365, 1207, 1102, 997, 915, 737, 698 cm^{-1}; HRMS (ESI) calcd for $C_{12}H_{16}NaO_2$ $(M+Na)^+$: 215.1043, found 315.1036.

*4.2.51. 1-Phenylprop-2-en-1-ol (**16**).* To a 0 °C solution of benzaldehyde (3.8 mL, 36.4 mmol) in THF (27 mL) was added vinyl magnesium bromide (45 mL of a 1.0 M solution in THF, 45 mmol). The reaction mixture was allowed to warm to room temperature and stirred overnight. The mixture was quenched by addition of saturated NH_4Cl solution and concentrated under reduced pressure. The remaining aqueous phase was extracted with EtOAc, the combined organic phase dried ($MgSO_4$), and concentrated to give **16** as a light yellow (3.9 g, 79%). The crude material was used without further purification: ^1H NMR (400 MHz, $CDCl_3$) δ 7.42–7.39 (m, 4H), 7.38–7.31 (m, 1H), 6.08 (ddd, *J*=17.0, 10.3, 6.0 Hz, 1H), 5.37 (ddd, *J*=17.1, 1.4, 1.4 Hz, 1H), 5.23 (ddd, *J*=10.3, 1.3, 1.3 Hz, 1H), 5.21–5.17 (m, 1H), 2.75 (d, *J*=3.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.6, 140.3, 128.5, 127.7, 126.4, 115.1, 75.2; IR (film, NaCl) 3363, 3064, 3030, 2982, 2872, 1643, 1602, 1494, 1454, 1417, 1280, 1195, 1116, 1074, 990, 928, 835, 762, 700 cm^{-1}; MS (ESI) calcd for C_9H_9 $(M-OH)^+$: 117.1, found 117.1.

*4.2.52. (5R,Z)-6-(Benzyloxy)-1-phenylhex-2-ene-1,5-diol (**17**).* To a solution of alcohols **15** (27 mg, 0.14 mmol) and **16** (150 mg, 1.12 mmol) was added Grubbs' second generation catalyst (3.3 mg, 0.004 mmol) and the mixture was heated to reflux for 5 h. Concentration under reduced pressure followed by flash chromatography of the residue (hexanes/EtOAc, 2:1 to 1:1) gave diol **17** as a colorless oil as a mixture of diastereomers (30 mg, 72% yield, dr 1:1): ^1H NMR (400 MHz, $CDCl_3$) δ 7.41–7.29 (m, 10H), 5.82–5.76 (m, 2H), 5.22–5.18 (m, 1H), 4.57–4.54 (m, 2H), 3.90 (br s, 1H), 3.54–3.47 (m, 1H), 3.41–3.34 (m, 1H), 2.63–2.15 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.1, 138.0(1), 138.0, 135.7, 135.6, 128.64, 128.6, 128.0, 127.9, 127.7(3), 127.7, 127.6, 127.5, 126.3, 126.2(7), 75.1, 75.0, 74.0, 73.9, 73.5, 70.0, 36.4, 36.3; IR (film, NaCl) 3390, 3031, 2917, 2247, 1603, 1494, 1454, 1093, 909, 731, 697 cm^{-1}; HRMS (ESI) calcd for $C_{19}H_{22}NaO_3$ $(M+Na)^+$: 321.1461, found 321.1464.

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