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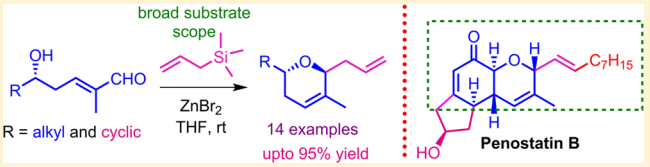
Highly Stereocontrolled Synthesis of *trans*-2,6-Disubstituted-5-methyl-3,6-dihydropyrans: Stereoselective Synthesis of the Bicyclic Core of Penostatin B

D. Srinivas Reddy,[†] Birakishore Padhi,[†] and Debendra K. Mohapatra*[,†]

[†]Natural Products Chemistry Division, CSIR−Indian Institute of Chemical Technology, Hyderabad 500 007, India

Supporting Information

ABSTRACT: An efficient, mild, and highly diastereoselective strategy for the synthesis of *trans*-2,6-disubstituted-5-methyl-3,6-dihydropyran ring systems has been developed starting from δ-hydroxy α-methyl α,β-unsaturated aldehydes and allyltrimethylsilane in the presence of a catalytic amount of $ZnBr_2$ in a highly diastereoselective manner with excellent yield. The versatility of the above method was also demonstrated for the construction of the bicyclic core present in penostatin B in a concise and highly stereoselective manner.



INTRODUCTION

Polysubstituted di- and tetrahydropyrans are important structural motifs that are found in many natural products and have diverse and potent biological activities.[1−11] The double bond present in the dihydropyran ring system provides a functional handle for further manipulation and organic transformation in natural product synthesis. Because of their importance in organic synthesis, substantial efforts have been made to develop methods for the construction of di- and tetrahydropyrans.[12] However, the stereocontrolled synthesis of these cyclic ethers and related heterocycles is still a challenging and interesting task. 2,6-Disubstituted-dihydropyrans are attractive targets, particularly with regard to controlling the syn and anti disposition of the substitution. Some of the natural products bearing a *trans*-2,6-disubstituted-5-methyl-3,6-dihydropyran ring system such as penostatin A, B, C, and D,[13] 4,5-deoxyneodolabbeline,[14] and methyl sarcophytoate[15]are shown in Figure 1. Similarly, some of the natural products containing the *cis*-2,6-disubstituted-5-methyl-3,6-dihydropyran ring system such as ambruticin S,[16] jerangolid D,[17] and funiculosin[18] show potent antifungal properties (Figure 1). As part of our research program on the total synthesis of di- and tetrahydropyran-containing natural products,[19] it was deemed important to study and develop new strategies for their rapid, efficient, and versatile synthesis. To reach this goal, a general and concise route toward dihydropyran, which would allow a broad spectrum of substituents at any position of the heterocyclic ring system, was sought after.[20,21] Although several methods are already precedent in the literature for the synthesis of 2,6-disubstituted-dihydropyrans including our recent protocol,[19d] to the best of our knowledge, there is no general report[22] for the preparation of the *trans*-2,6-disubstituted-5-methyl-3,6-dihydropyrans ring system.

Herein, we report an efficient, mild, versatile, and highly stereoselective zinc bromide-catalyzed tandem isomerization followed by C−O and C−C bond formation reaction to synthesize *trans*-2,6-disubstituted-5-methyl-3,6-dihydropyran ring systems starting from δ-hydroxy-α-methyl-α,β-unsaturated aldehydes and allyltrimethylsilane. The cis-fused dihydropyran ring systems could be obtained easily by isomerization with ^{t}BuOK in anhydrous THF.[23] We have demonstrated the application of this protocol for an efficient and concise stereoselective synthesis of the bicyclic core of penostatin B.

Benzyl-protected glycidol prepared from epichlorohydrin and benzyl alcohol using NaH in dry THF was used as the starting material for the preparation of δ-hydroxy-α-methyl-α,β-unsaturated aldehydes. The hydrolytic kinetic resolution of the terminal epoxide using Jacobsen's catalyst[24] (*S*,*S*)-Co^{III}(Salen)(OAc) for 24 h at room temperature afforded chiral epoxide **10** in 44% yield (~98% ee).

The enantiomeric excess was determined by chiral HPLC analysis. The chiral epoxide **10** was then treated with vinylmagnesium bromide in the presence of CuI at −20 °C to produce homoallyl alcohol **11** in 86% yield (Scheme 1).[25] The terminal olefin was subjected to Jin's one-step dihydroxylation followed by oxidation protocol[26] to afford aldehyde **12** in 88% yield. The aldehyde **12** was reacted with 2-(triphenylphosphoranylidene)propanal to obtain the desired δ-hydroxy-α-methyl-α,β-unsaturated aldehyde **13** in 82% yield with the *E*-isomer as the only product. After developing a general synthetic strategy for the preparation of δ-hydroxy-α-methyl-α,β-unsaturated aldehydes, the synthesis of *trans*-2,6-disubstituted-5-methyl-3,6-dihydropyran ring system was undertaken.

RESULTS AND DISCUSSION

As per our earlier report, we envisaged that the same reaction conditions could be further applied to the synthesis of the

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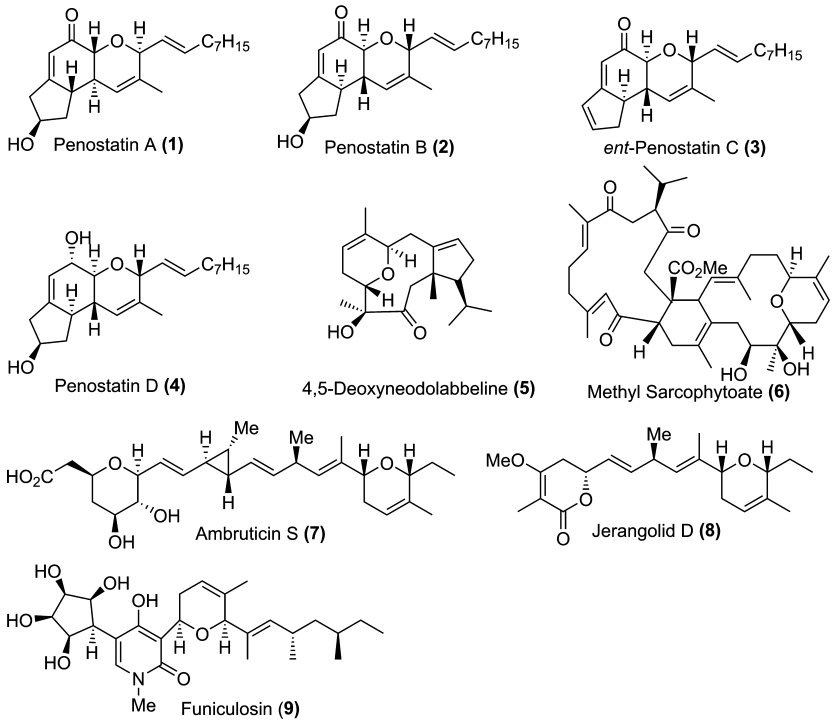
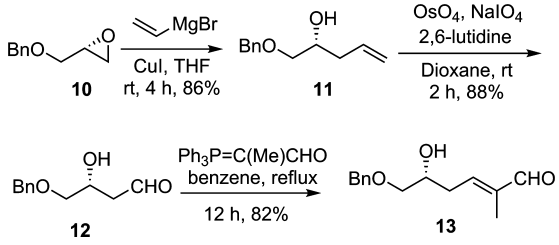


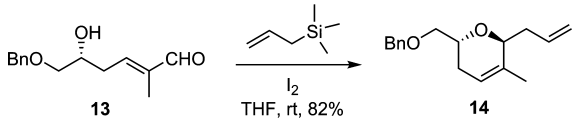
Figure 1. Structures of *trans*- and *cis*-2,6-disubstituted-5-methyl-3,6-dihydropyran containing natural products.

Scheme 1. Synthesis of δ-Hydroxy-α-methyl-α,β-unsaturated Aldehyde



common *trans*-2,6-disubstituted-5-methyl-3,4-dihydropyran ring system to provide a practical access to the above natural products. We began our study by using 10 mol % of iodine for the conversion of δ-hydroxy-α-methyl-α,β-unsaturated aldehyde to *trans*-2,6-disubstituted-6-methyl-3,4-dihydropyran. After 24 h at room temperature, the reaction provided the expected *trans*-2,6-disubstituted-5-methyl-3,6-dihydropyran **14** in 54% yield (Scheme 2). The ^{1}H and ^{13}C NMR of the product

Scheme 2. Synthesis of *trans*-2,6-Disubstituted-5-methyl-3,6-dihydropyrans



revealed a single diastereomer. The stereochemistry of the product at this stage was confirmed by NOE experiments. In ^{1}H and ^{13}C NMR of the crude product (flash column chromatography), no cis diastereomer was detected. To optimize the reaction conditions, screenings were performed on different parameters, such as solvents, temperature, and catalyst concentration. Initially, the reaction was performed in different solvent systems such as CH_2Cl_2, Et_2O, *tert*-butyl methyl ether (TBME), DME, and THF at room temperature with 10 mol % of molecular iodine. Among them, THF was found to be superior to other solvents. Next, the reaction was carried out at room temperature at reflux conditions. Heating was found to be detrimental, leading to intractable mixtures of products. The reaction was then carried out carefully under the influence of different concentrations of the catalyst at room temperature with THF as the solvent. The use of 20 mol % of molecular iodine (based on the δ-hydroxy-α-methyl-α,β-unsaturated aldehyde) gave the best result with a high yield of 82% in 1 h time (Scheme 2). Increasing the molecular iodine concentration did not help much in improving the yield, and reduction of the reaction time instead led to an intractable mixture of compounds. However, no reaction was observed in the absence of iodine after a long time (48 h). As already a precedent in the literature,[27] it is noteworthy to mention here that, with 20 mol % and the previously mentioned concentration of the catalyst, some of the sensitive functional groups (*tert*-butyldimethylsilyl (TBS), PMB, Boc, and acetonide) were getting deprotected. At this juncture, we postulated the use of a mild Lewis acid, which will not affect the sensitive protecting groups even under stoichiometric conditions. During the screening, $ZnBr_2$ was found to be suitable for the purpose. Accordingly, δ-hydroxy-α-methyl-α,β-unsaturated aldehyde was treated with $ZnBr_2$ and allyltrimethylsilane in THF at room temperature to obtain the expected *trans*-2,6-disubstituted-5-methyl-3,4-dihydropyran **14** in 95% yield in 2 h. With optimal reaction conditions in hand, the generality and versatility of tandem isomerization followed by C−O and C−C bond formation reaction was explored via screening of a variety of structurally diverse δ-hydroxy-α-methyl-α,β-unsaturated aldehyde (Table 1) with regard to protecting groups. Use of a stoichiometric amount of the $ZnBr_2$ did not affect the sensitive protecting groups (TBS, PMB, Boc, and acetonide) at room temperature and provided the expected products in good

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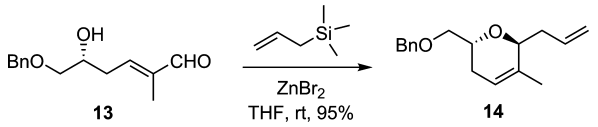
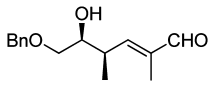
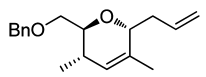
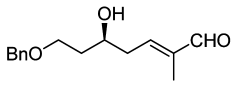
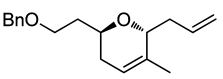
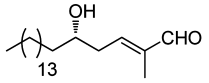
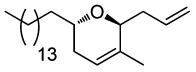
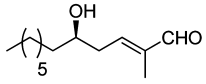
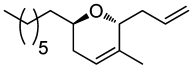
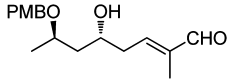
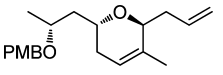
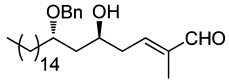
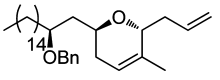
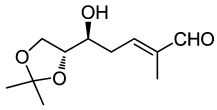
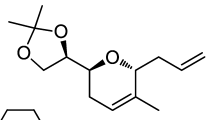
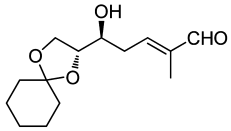
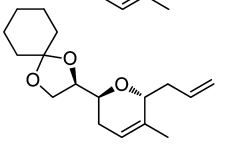
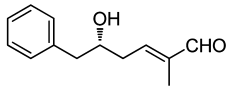
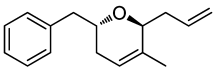
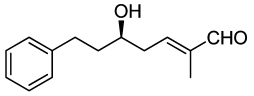
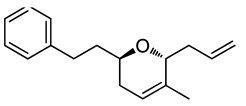
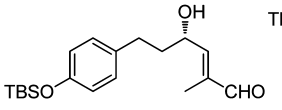
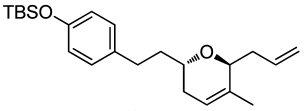
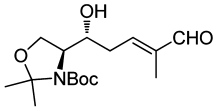
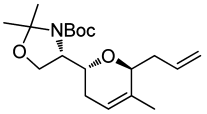
Table 1. Synthesis of *trans*-2,6-Disubstituted-5-methyl-3,6-dihydropyrans



Entry	Unsaturated aldehydes (**13**)	Product (**14**)	t[min]	Yield [%][a]
a			50	92
b			60	95
c			75	90
d			60	94
e			45	88
f			60	92
g			45	94
h			45	90
i			30	92
j			30	88
k			60	86
l			60	85

[a]$ZnBr_2$, allylTMS, THF, rt.

yields with a high level of selectivity. It is noteworthy to mention here that the reaction could be conducted on a gram scale without a reduction of isolated yield.

To predict the formation of the *trans*-2,6-disubstituted-5-methyl-3,6-dihydropyran from *δ*-hydroxy-*α*-methyl-*α*,*β*-unsaturated aldehyde following catalytic pathways, we postulated like earlier that the product could be generated with the activation of aldehyde and isomerization[28] by in situ formation of a catalytic amount of TMSBr[29] followed by subsequent formation of an oxocarbenium intermediate (path A) in which the stereoelectronic and/or steric factors dictate the direction of the incoming nucleophile (Figure 2). To test the viability of the proposed reaction pathways (path A), it was expected that the reaction of a *δ*-hydroxy-*α*-methyl-*α*,*β*-unsaturated aldehyde in the presence of a catalytic amount of TMSBr should generate the corresponding *trans*-2,6-disubstituted-5-methyl-3,6-dihydropyran.

As per our postulation, when 5 mol % of TMSBr was added instead of $ZnBr_2$ at room temperature, the reaction was completed in 20 min, which strongly supported our proposed

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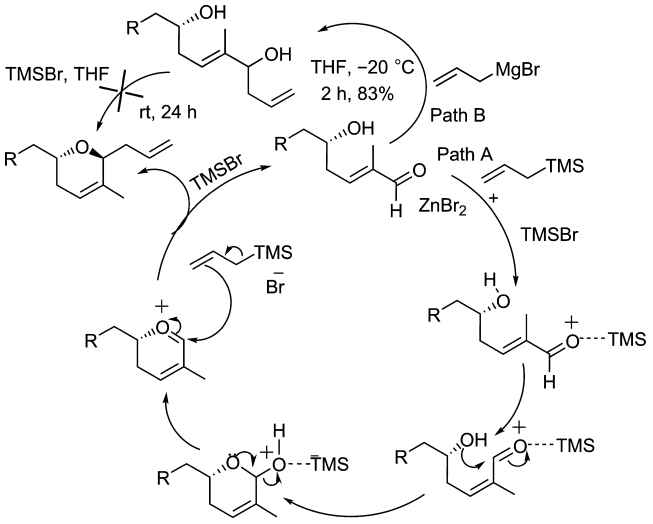
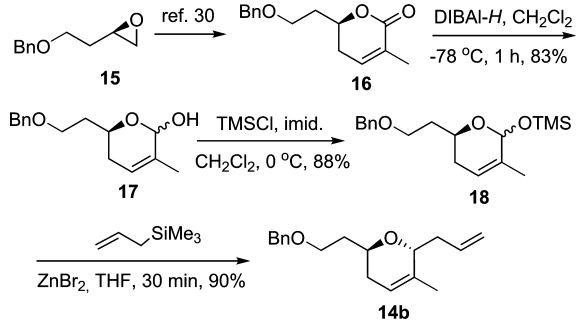


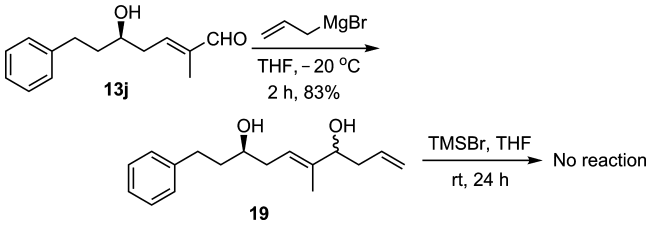
Figure 2. Plausible mechanistic cycle.

mechanism. Similarly, the reaction of a δ-hydroxy-α-methyl-α,β-unsaturated aldehyde in the presence of a catalytic amount of TMSBr led to formation of TMS-protected lactol in 15 min, which strongly holds up for the isomerization.[28] To further ascertain the mechanistic pathways, TMS-protected lactol **18** was synthesized following a standard protocol[30] and treated with allyltrimethylsilane and a catalytic amount of $ZnBr_2$ to afford the expected allylated compound **14b** in 90% yield in 30 min (Scheme 3). To verify the second mechanistic pathway

Scheme 3. Controlled Experiment



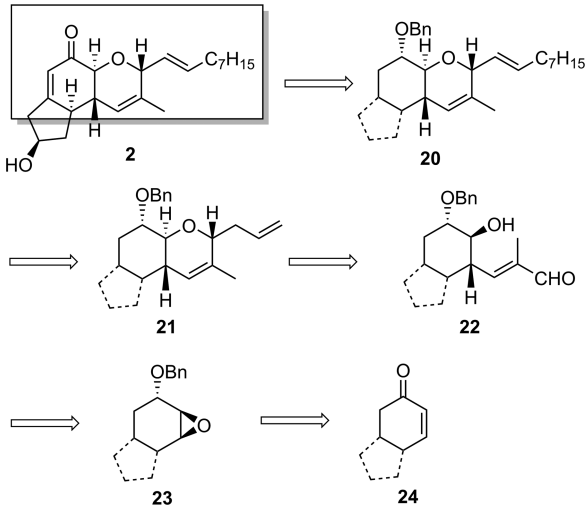
(path B), the diol compound **19**[30] was prepared by standard Grignard reaction followed by treatment of **19** with either TMSBr or $ZnBr_2$, which gave no expected product.



To examine the synthetic utility and generality of this novel methodology for the synthesis of complex biologically active natural products, the penostatin B, a natural product possessing tricyclic fused ring systems, was taken as a representative example. Penostatin A and B were isolated from *Penicillium* sp. separated from green alga *Enteromerpha intenstinalis* by Numata and co-workers in 1996.[13] All the penostatins except penostatin D exihibits significant cytotoxicity against P388 cells. Snider and Liu[31] reported the synthesis of (±)-5-deoxypenostatin A using an intramolecular Diels−Alder reaction to construct the dihydropyran ring. Later in 2001, Shishido and co-workers[32] synthesized (±)-penostatin B by applying a relay ring-closing metathesis protocol. As only one total synthesis of (±)-penostatin B is reported so far, we thought of developing a general and flexible approach toward a stereoselective total synthesis applying our earlier developed method. Initially, the synthetic utility of this strategy was demonstrated for a highly stereoselective synthesis of the bicyclic core of penostatin B.

According to our retrosynthetic analysis, the bicyclic core of penostain B could be constructed by cross-metathesis of **21** with 1-nonene. Advance intermediate **21** could be achieved from trisubstituted aldehyde **22** by $ZnBr_2$-catalyzed tandem isomerization followed by C−O and C−C bond formation reaction (Scheme 4). The trisubstituted aldehyde **22** in turn could be prepared starting from commercially available 2-cyclohexenone (**24**).

Scheme 4. Retrosynthetic Analysis



The synthesis was begun from commercially available 2-cyclohexenone (**24**), which was treated with $LiAlH_4$ in THF to obtain the corresponding racemic allyl alcohol **25** in 80% yield. Compound **25** was subjected to a Sharpless kinetic resolution[33] to furnish the enantiomerically pure epoxy alcohol **26** in 45% yield. The hydroxyl group was protected as its benzyl ether with benzyl bromide in the presence of NaH in THF at room temperature to afford **23** in 95% yield (Scheme 5). Considering the lengthy reaction sequences, an alternative concise protocol was sought. In this context, commercially available 2-cyclohexenone (**24**) was reduced with (*R*)-CBS catalyst to afford the allyl alcohol[34] and was protected as its benzyl ether. Homoallyl alcohol was treated with *m*-CPBA to obtain compound **23** (97% de as per HPLC) in good overall yield. The benzyl-protected epoxy compound **23** was treated with vinyl magnesium bromide in the presence of a catalytic amount of CuI in anhydrous THF to get homoallyl alcohol **27** in 85% yield.[35]

The double bond present in compound **27** was oxidatively cleaved following Jin's one-pot[26] reaction with OsO_4, $NaIO_4$, and 2,6-lutidine in 1,4-dioxane at room temperature to afford the corresponding aldehyde **28** that was immediately treated with 2-(triphenylphosphoranylidene)propionaldehyde in ben-

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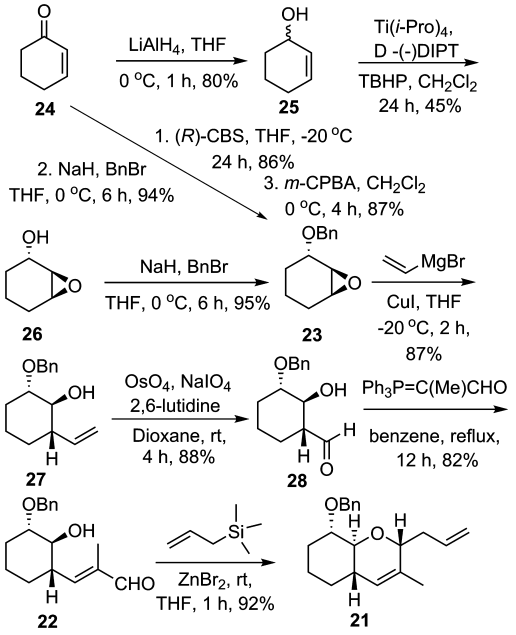
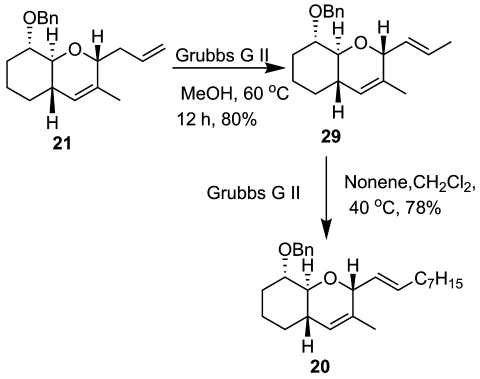
Scheme 5. Synthesis of Bicyclic Compound 21



zene under reflux conditions to furnish δ-hydroxyl-α-methyl-α,β-unsaturated aldehyde. With the required compound **22** in hand, the stage was set to perform the key $ZnBr_2$-catalyzed tandem isomerization followed by C−O and C−C bond formation reaction. Aldehyde **22** was treated with 20 mol % $ZnBr_2$ in anhydrous THF at room temperature under inert atmosphere to produce the bicyclic *trans*-fused **21** in 92% yield.

Our next aim was to attach the appendage to cyclic compound **21**, which was carried out by exposing it to Grubbs' second-generation catalyst for the isomerization[36] of allyl to propenyl followed by cross-metathesis[37] (Scheme 6).

Scheme 6. Synthesis of the Bicyclic Core of Penostatin B



Cyclic compound **21** was treated with 10 mol % Grubbs' second-generation catalyst in methanol at 60 °C to afford isomerized compound **29** (*E*/*Z* = 9:1) with 80% yield. The isomerized compound **29** again treated after purification with 10 mol % Grubbs' second-generation catalyst in dichloromethane at 40 °C to furnish the cross-metathesis product **20** in 78% yield.

CONCLUSIONS

In conclusion, an efficient, robust, mild, and versatile $ZnBr_2$-catalyzed method for tandem isomerization followed by C−O and C−C bond formation reaction for the synthesis of *trans*-2,6-disubstituted-5-methyl-3,6-dihydropyran compounds starting from δ-hydroxy-α-methyl-α,β-unsaturated aldehydes has been developed in good to excellent yield and with high diastereoselectivity. In addition, the reaction was conducted in gram scale, highlighting its possible industrial application. The potential of employing this methodology toward the total synthesis of natural products is intriguing as *C*-glycosides constitute a major component of many natural products. The synthetic utility of this strategy was demonstrated by achieving a short and stereoselective synthesis of the bicyclic core of tricyclic penostatin B. Further progress toward the total synthesis of penostatin B and other related natural products (syn-fused) such as ambruticin S and jerangolid D is in progress and will be reported in due course.

EXPERIMENTAL SECTION

General Methods. Experiments that required an inert atmosphere were carried out under argon in flame-dried glassware. Et_2O and THF were freshly distilled from sodium/benzophenone ketyl and transferred via syringe. Dichloromethane was freshly distilled from CaH_2. Tertiary amines were freshly distilled over KOH. Commercially available reagents were used as received. Unless detailed otherwise, "workup" means pouring the reaction mixture into brine, followed by extraction with the solvent indicated in parentheses. If the reaction medium was acidic (basic), an additional washing with 5% aqueous $NaHCO_3$ (aqueous NH_4Cl) was performed. Washing with brine, drying over anhydrous Na_2SO_4, and evaporation of the solvent under reduced pressure followed by chromatography on a silica gel column (60−120 mesh) with the indicated eluent furnished the corresponding products. Where solutions were filtered through a Celite pad, the pad was additionally washed with the same solvent used, and the washings were incorporated to the main organic layer. ^1H and ^{13}C NMR chemical shifts are reported in ppm downfield from tetramethylsilane, and coupling constants (*J*) are reported in hertz (Hz). High-resolution mass spectra were run by the electron impact mode (ESIMS, 70 eV) or by the FAB mode (*m*-nitrobenzyl alcohol matrix), using an orbitrap mass analyzer. IR data were measured with oily films on NaCl plates (oils) or KBr pellets (solids) and are given only for molecules with relevant functional groups (OH, C═O). Specific optical rotations $[\alpha]_D$ are given in 10^{-1} deg cm^2 g^{-1} and were measured at 25 °C. The following abbreviations are used to designate signal multiplicity: s = singlet, d = doublet, t = triplet, q = quartet, quin = quintet, m = multiplet, and br = broad.

General Procedure for δ-Hydroxyl-α-methyl-α,β-unsaturated Aldehydes. To a stirred solution of β-hydroxy aldehydes (1.0 mmol) in toluene (3.0 mL) was added 2-(triphenylphosphoranylidene)propionaldehyde (1.5 mmol). The solution was then heated at 85 °C for 12 h. After cooling, the solvent was removed under reduced pressure and the remaining oil was triturated with cold hexane. The insoluble triphenylphosphine oxide was precipitated out. The reaction mixture was filtered through a sintered funnel (washing with cold hexane), and the filtrate was concentrated to obtain the crude product, which on purification was performed using flash chromatography (hexane/ethyl acetate = 1:1) to obtain δ-hydroxyl-α-methyl-α,β-unsaturated aldehyde in 75−80% of isolated yield.

General Procedure for Iodocyclization. To a stirred solution of δ-hydroxyl-α-methyl-α,β-unsaturated aldehyde (1.0 mmol), iodine (0.2 mmol) and allyltrimethylsilane (1.5 mmol) were added in THF (6 mL) at 0 °C and allowed to come to room temperature. After completion of the reaction (monitored by TLC; 30−60 min), the reaction mixture was quenched with a saturated solution of $Na_2S_2O_3$ (3 mL) and diluted with ethyl acetate (10 mL). The organic layer was separated and the aqueous layer was extracted with ethyl acetate (2 × 10 mL). The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography using 2−5% ethyl

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acetate/hexane as eluent to obtain the cyclized product in 70−82% of isolated yield.

General Procedure for $ZnBr_2$-Catalyzed Cyclization. To a stirred solution of δ-hydroxyl-α-methyl-α,β-unsaturated aldehyde (1.0 mmol), $ZnBr_2$ (0.2 mmol) and allyltrimethyl silane (1.5 mmol) were added in THF (8 mL) at room temperature. After completion of the reaction (monitored by TLC; 30−60 min), the reaction mixture was quenched with a saturated solution of $NaHCO_3$ (5 mL) and diluted with ethyl acetate (10 mL). The organic layer was separated and the aqueous layer was extracted with ethyl acetate (2 × 10 mL). The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography using 2−5% ethyl acetate/hexane as eluent to obtain the cyclized product in 85−95% of isolated yield.

*(R,E)-6-(Benzyloxy)-5-hydroxy-2-methylhex-2-enal (**13**).* Colorless liquid (130 mg, 77%), $[\alpha]_D^{25}$ −9.6 (*c* 1.0, $CHCl_3$). IR (neat): υ_{max} 3433, 2966, 2864, 2843, 1680, 1453, 1219, 1055, 1032 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 9.41 (s, 1H), 7.41−7.29 (m, 5H), 6.60 (td, *J* = 6.0, 1.5 Hz, 1H), 4.57 (s, 2H), 4.01 (m, 1H), 3.58−3.38 (m, 2H), 2.55 (t, *J* = 6.7 Hz, 2H), 1.75 (s, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 195.2, 155.1, 137.5, 128.4, 127.9, 127.1, 73.5, 73.0, 72.4, 36.8, 15.5, 9.4. ESI-MS for $C_{14}H_{18}O_3$: *m*/*z* $[M + Na]^+$ 257. ESI-HRMS: *m*/*z* calcd for $C_{14}H_{19}O_3$ $[M + H]^+$: 235.1328. Found: 235.1316.

*(2R,6S)-6-Allyl-2-((benzyloxy)methyl)-5-methyl-3,6-dihydro-2H-pyran (**14**).* Colorless liquid (85 mg, 82%), $[\alpha]_D^{25}$ +2.6 (*c* 3.0, $CHCl_3$). IR (neat): υ_{max} 3417, 2929, 2357, 1719, 1451, 1274, 1219, 1110 cm^{-1}. ^1H NMR ($CDCl_3$, 500 MHz): δ 7.36−7.26 (m, 5H), 5.97 (m, 1H), 5.50 (m, 1H), 5.17−5.04 (m, 2H), 4.54 (AB_q, *J* = 12.0, 5.2 Hz, 2H), 4.08 (m, 1H), 3.96 (m, 1H), 3.59−3.45 (m, 2H), 2.50−2.29 (m, 2H), 2.10−1.91 (m, 2H), 1.63 (s, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 138.3, 135.4, 135.1, 128.1, 127.4, 127.3, 119.0, 116.4, 75.7, 73.1, 72.3, 66.4, 36.4, 27.4, 19.7. ESI-HRMS: *m*/*z* calcd for $C_{17}H_{22}O_2$ $[M + Na]^+$: 281.1505. Found: 281.1512.

*(4R,5S,E)-6-(Benzyloxy)-5-hydroxy-2,4-dimethylhex-2-enal (**13a**).* Colorless liquid (85 mg, 75%) $[\alpha]_D^{25}$ −13.2 (*c* 0.8, $CHCl_3$). IR (neat): υ_{max} 3433, 2966, 2864, 2843, 1680, 1453, 1219, 1055, 1032 cm^{-1}. ^1H NMR ($CDCl_3$, 500 MHz): δ 9.39 (s, 1H), 7.39−7.27 (m, 5H), 6.33 (dq, *J* = 7.7, 1.3 Hz, 1H), 4.53 (s, 2H), 3.71 (td, *J* = 4.1, 3.0 Hz, 1H), 3.52 (dd, *J* = 6.4, 3.0 Hz, 1H), 3.37 (m, 1H), 2.88 (m, 1H), 1.76 (d, *J* = 1.3 Hz, 3H), 1.16 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 195.2, 155.1, 137.5, 128.4, 127.9, 127.1, 73.5, 73.4, 72.4, 36.8, 15.5, 9.41. ESI-HRMS: *m*/*z* calcd for $C_{15}H_{20}O_3$ $[M + NH_4]^+$: 266.1756. Found: 266.1753.

*(2S,3S,6R)-6-Allyl-2-((benzyloxy)methyl)-3,5-dimethyl-3,6-dihydro-2H-pyran (**14a**).* Colorless liquid (60 mg, 92%) $[\alpha]_D^{25}$ −32.9 (*c* 1.5, $CHCl_3$). IR (neat): υ_{max} 3428, 2964, 2925, 2361, 1452, 1218, 1103, 1022 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 7.40−7.27 (m, 5H), 6.98 (m, 1H), 5.50 (dt, *J* = 2.2, 1.5 Hz, 1H), 5.16−5.04 (m, 2H), 4.54 (AB_q, *J* = 21.9, 12.0 Hz, 2H), 4.01 (m, 1H), 3.62−3.43 (m, 2H), 2.51−2.28 (m, 2H), 2.13 (m, 1H), 1.63 (s, 3H), 0.88 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 138.3, 135.5, 134.1, 128.2, 127.5, 127.4, 126.4, 116.5, 76.1, 73.2, 70.6, 69.1, 36.1, 30.9, 19.7, 13.6. ESI-HRMS: *m*/*z* calcd for $C_{18}H_{25}O_2$ $[M + H]^+$: 273.1849. Found: 273.1829.

*(R,E)-7-(Benzyloxy)-5-hydroxy-2-methylhept-2-enal (**13b**).* Pale yellow oil (150 mg, 80%) $[\alpha]_D^{25}$ −9.2 (*c* 1.8, $CHCl_3$). IR (neat): υ_{max} 3443, 2961, 2921, 2851, 1681, 1612, 1513, 1246, 1140, 1032 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 9.43 (s, 1H) 7.39−7.28 (m, 5H), 6.63 (td, *J* = 6.0, 1.3 Hz, 1H), 4.54 (s, 2H), 4.06 (m, 1H), 3.80−3.64 (m, 2H), 3.28 (br s, 1H), 2.54 (dd, *J* = 6.7, 0.9 Hz, 2H), 1.92−1.97 (m, 2H), 1.75 (s, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 195.1, 150.4, 140.7, 137.5, 128.5, 127.9, 127.7, 73.4, 70.6, 69.0, 36.7, 36.0, 9.4. ESI-MS for $C_{15}H_{20}O_3$: *m*/*z* $[M + Na]^+$ 271. ESI-HRMS: *m*/*z* calcd for $C_{15}H_{20}O_3Na$ $[M + Na]^+$: 271.1304. Found: 271.1307.

*(2R,6S)-6-Allyl-2-(2-(benzyloxy)ethyl)-5-methyl-3,6-dihydro-2H-pyran (**14b**).* Colorless liquid (110 mg, 95%) $[\alpha]_D^{25}$ −31.5 (*c* 0.6, $CHCl_3$). IR (neat): υ_{max} 2915, 2857, 2359, 2342, 1453, 1219, 1100, 1059 cm^{-1}. ^1H NMR ($CDCl_3$, 500 MHz): δ 7.35−7.25 (m, 5H), 5.92 (m, 1H), 5.49 (m, 1H), 5.12−5.03 (m, 2H), 4.41 (AB_q, *J* = 11.9, 7.4 Hz, 2H), 4.02 (m, 1H), 3.86 (m, 1H), 3.66−3.55 (m, 2H), 2.44−2.30 (m, 2H), 1.97−1.92 (m, 2H), 1.81−1.76 (m, 2H), 1.63 (s, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 138.3, 135.2, 135.1, 128.1, 127.5, 127.3, 119.6, 116.1, 75.7, 73.1, 72.3, 66.4, 36.2, 35.6, 31.1, 19.7. ESI-HRMS: *m*/*z* calcd for $C_{18}H_{24}O_2$ $[M + Na]^+$: 295.1668. Found: 295.1658.

*(S,E)-5-Hydroxy-2-methylicos-2-enal (**13c**).* Colorless liquid (80 mg, 77%), $[\alpha]_D^{25}$ −3.2 (*c* 1.5, $CHCl_3$). IR (neat) υ_{max} 3419, 2924, 2853, 2351, 1692, 1515, 1188, 1062, 1029 cm^{-1}. ^1H NMR ($CDCl_3$, 500 MHz): δ 9.43 (s, 1H), 6.60 (td, *J* = 6.0, 1.5 Hz, 1H), 3.81 (quin, *J* = 6.0 Hz, 1H), 2.56−2.45 (m, 2H), 1.76 (s, 3H), 1.57−1.38 (m, 3H), 1.37−1.15 (m, 24 H), 0.88 (t, *J* = 6.7 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 195.1, 150.4., 140.9, 70.9, 37.7, 36.8, 31.9, 29.6, 29.5, 29.3, 25.6, 22.6, 14.1. ESI-HRMS: *m*/*z* calcd for $C_{21}H_{41}O_2$ $[M + H]^+$: 325.3101. Found: 325.3088.

*(2S,6S)-6-Allyl-5-methyl-2-pentadecyl-3,6-dihydro-2H-pyran (**14c**).* Colorless liquid (55 mg, 90%), $[\alpha]_D^{25}$ −30.4 (*c* 0.9, $CHCl_3$). IR (neat): υ_{max} 2922, 2852, 2359, 2341, 1456, 1058 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 5.94 (m, 1H), 5.49 (m, 1H), 5.14−5.04 (m, 2H), 4.02 (d, *J* = 9.0 Hz, 1H), 3.67−3.58 (m, 1H), 2.47−2.28 (m, 2H), 2.02−1.82 (m, 3H), 1.64 (s, 3H), 1.55−1.36 (m, 4H), 1.35−1.21 (m, 26H), 0.88 (t, *J* = 6.9 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 135.8, 135.2, 119.8, 116.2, 75.9, 67.0, 36.4, 35.6, 31.9, 31.2, 29.6, 29.3, 25.7, 22.6, 9.8, 14.1. ESI-HRMS: *m*/*z* calcd for $C_{24}H_{43}O$ $[M - H]^+$: 347.3308. Found: 347.3293.

*(R,E)-5-Hydroxy-2-methyldodec-2-enal (**13d**).* Yellow liquid (60 mg, 75%) $[\alpha]_D^{25}$ −14.2 (*c* 1.2, $CHCl_3$). IR (neat): υ_{max} 2925, 2854, 1687, 1401, 1219, 1051 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 9.44 (s, 1H), 6.63 (m, 1H), 3.84 (m, 1H), 2.59−2.46 (m, 2H), 1.77 (s, 3H), 1.57−1.41 (m, 4H), 1.38−1.21 (m, 12H), 0.89 (t, *J* = 6.7 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 195.1, 150.6, 70.9, 37.4, 36.8, 31.7, 29.4, 29.2, 25.6, 22.6, 14.1, 9.4. ESI-HRMS: *m*/*z* calcd for $C_{13}H_{25}O_2$ $[M + H]^+$: 213.1849. Found: 213.1840.

*(2R,6R)-6-Allyl-2-heptyl-5-methyl-3,6-dihydro-2H-pyran (**14d**).* Colorless liquid (45 mg, 94%), $[\alpha]_D^{25}$ −6.8 (*c* 1.0, $CHCl_3$). IR (neat): υ_{max} 2955, 2925, 2855, 2357,1640, 1455, 1123, 1058 cm^{-1}. ^1H NMR ($CDCl_3$, 500 MHz): δ 5.93 (m, 1H), 5.49 (m, 1H), 5.12−5.03 (m, 2H), 4.02 (d, *J* = 9.1 Hz, 1H), 3.67−3.57 (m, 1H), 2.44−2.31 (m, 2H), 1.99−1.86 (m, 3H), 1.64 (s, 3H), 1.60 (m, 1H), 1.55−1.37 (m, 4H), 1.33−1.22 (m, 10H), 0.88 (t, *J* = 6.8 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 135.8, 135.2, 119.8, 116.2, 75.9, 66.9, 36.4, 35.6, 33.4, 31.8, 31.2, 25.7, 22.6, 19.8, 14.0. ESI-HRMS: *m*/*z* calcd for $C_{16}H_{28}O$ $[M + NH_4]^+$: 254.2478. Found: 254.2476.

*(5R,7R,E)-5-Hydroxy-7-((4-methoxybenzyl)oxy)-2-methyloct-2-enal (**13e**).* Colorless liquid (100 mg, 77%), $[\alpha]_D^{25}$ +10.3 (*c* 2.5, $CHCl_3$). IR (neat): υ_{max} 3409, 2924, 2360, 1687, 1400, 1219, 1034 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 9.42 (s, 1H), 7.26 (d, *J* = 8.6 Hz, 2H), 6.88 (d, *J* = 8.6 Hz, 2H), 6.61 (td, *J* = 5.9, 1.2 Hz, 1H), 4.60−4.35 (m, 2H), 4.13 (m, 1H), 3.88 (m, 1H), 3.80 (s, 3H), 2.55−2.45 (m, 2H), 1.78−1.70 (m, 4H), 1.64 (m, 1H), 1.27 (d, *J* = 6.2 Hz, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 195.1, 159.3, 150.7, 140.5, 130.0, 129.3, 113.9, 71.9, 70.1, 67.4, 55.2, 42.1, 36.8, 18.9, 9.4. ESI-HRMS: *m*/*z* calcd for $C_{17}H_{24}O_4$ $[M + Na]^+$: 315.1566. Found: 315.1553.

*(2S,6R)-6-Allyl-2-((R)-2-((4-methoxybenzyl)oxy)propyl)-5-methyl-3,6-dihydro-2H-pyran (**14e**).* Colorless liquid (82 mg, 88%), $[\alpha]_D^{25}$ −5.7 (*c* 2.0, $CHCl_3$). IR (neat): υ_{max} 2930, 2359, 2341,1513, 1247, 1219, 1062 cm^{-1}. ^1H NMR ($CDCl_3$, 500 MHz): δ 7.26 (d, *J* = 8.6 Hz, 2H), 6.86 (d, *J* = 8.6 Hz, 2H), 5.95 (m, 1H), 5.49 (m, 1H), 5.12−5.03 (m, 2H), 4.55−4.33 (AB_q, *J* = 11.8, 7.4 Hz, 2H), 4.03 (m, 1H), 3.93 (m, 1H), 3.81 (m, 1H), 3.79 (s, 3H), 2.45−2.31 (m, 2H), 1.94−1.89 (m, 2H), 1.67 (m, 1H), 1.64 (s, 3H), 1.60−1.54 (m, 2H), 1.21 (d, *J* = 6.2 Hz, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 159.0, 136.1, 135.0, 131.1, 129.1, 119.9, 116.1, 113.7, 76.2, 71.7, 70.2, 63.8, 55.5, 43.8, 36.3, 31.5, 20.1, 19.9. ESI-HRMS: *m*/*z* calcd for $C_{20}H_{28}O_3$ $[M + Na]^+$: 339.1930. Found: 339.1918.

*(5R,7R,E)-7-(Benzyloxy)-5-hydroxy-2-methyldocos-2-enal (**13f**).* Pale yellow viscous liquid (55 mg, 75%), $[\alpha]_D^{25}$ −16.2 (*c* 1.6, $CHCl_3$). IR (neat): υ_{max} 2923, 1401, 1219, 1033, 772 cm^{-1}. ^1H NMR ($CDCl_3$, 500 MHz): δ 9.43 (s, 1H), 7.40−7.28 (m, 5H), 6.61 (td, *J* = 6.2, 0.9 Hz, 1H), 4.56 (AB_q, *J* = 16.2, 11.5 Hz, 2H), 4.13(m, 1H), 3.72 (m, 1H), 3.14 (br s, 1H), 2.56−2.45 (m, 2H), 1.81 (m, 1H), 1.75 (m, 1H), 1.73−1.49 (m, 5H), 1.36−1.18 (m, 23H), 0.88 (t, *J* = 6.7 Hz,

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3H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 195.1, 150.5, 140.6, 137.4, 130.1, 128.4, 127.8, 76.9, 71.1, 67.5, 39.1, 36.9, 33.0, 31.8, 29.5, 29.6, 29.2, 25.4, 22.6, 14.0. ESI-HRMS: m/z calcd for $C_{30}H_{50}O_3$ $[M + Na]^+$: 481.3652. Found: 481.3640.

*(2R,6S)-6-Allyl-2-((R)-2-(benzyloxy)heptadecyl)-5-methyl-3,6-dihydro-2H-pyran (**14f**).* Colorless liquid (40 mg, 92%), $[\alpha]_D^{25}$ −11.3 (*c* 1.0, $CHCl_3$). IR (neat): υ_{max} 2923, 2853, 2356, 1614, 1459, 1065 cm^{-1}. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.37−7.27 (m, 5H), 5.92 (m, 1H), 5.50 (m, 1H), 5.13−5.01 (m, 2H), 4.51 (AB_q, J = 27.9, 11.3 Hz, 2H), 4.03 (m, 1H), 3.93 (m, 1H), 3.70 (m, 1H), 2.43−2.26 (m, 2H), 1.98−1.86 (m, 2H), 1.64 (s, 3H), 1.63−1.53 (m, 6H), 1.29−1.21 (m, 24H), 0.88 (t, J = 6.7 Hz, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 139.1, 136.1, 135.0, 128.2, 127.6, 127.3, 119.9, 116.1, 76.1, 76.0, 70.9, 64.1, 41.0, 36.3, 34.0, 31.9, 31.6, 29.9, 29.7, 29.6, 29.3, 24.7, 22.6, 19.9, 14.1. ESI-HRMS: m/z calcd for $C_{33}H_{54}O_2$ $[M + Na]^+$: 505.4016. Found: 505.3999.

*(S,E)-5-((R)-2,2-Dimethyl-1,3-dioxolan-4-yl)-5-hydroxy-2-methylpent-2-enal (**13g**).* Colorless liquid (72 mg, 80%), $[\alpha]_D^{25}$ −2.2 (*c* 3.0, $CHCl_3$). IR (neat): υ_{max} 2360, 1680, 1219, 772 cm^{-1}. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 9.43 (s, 1H), 6.66 (td, J = 6.0, 1.1 Hz, 1H), 3.19−3.24 (m, 2H), 3.56−3.61 (m, 2H), 2.63−2.44 (m, 2H), 1.77 (s, 3H), 1.66−1.56 (m, 6H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 195.0, 149.8, 141.0, 109.9, 77.7, 70.6, 64.8, 36.1, 34.5, 25.0, 23.6, 9.3. ESI-HRMS: m/z calcd for $C_{11}H_{18}O_4$ $[M + Na]^+$: 237.1105. Found: 237.1128.

*(2S,6R)-6-Allyl-2-((R)-2,2-dimethyl-1,3-dioxolan-4-yl)-5-methyl-3,6-dihydro-2H-pyran (**14g**).* Colorless liquid (50 mg, 94%), $[\alpha]_D^{25}$ −4.1 (*c* 1.0, $CHCl_3$). IR (neat): υ_{max} 2923, 2852, 2352, 1642, 1452, 1384, 1219, 1065 cm^{-1}. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 5.89 (m, 1H), 5.54 (m, 1H), 5.14−5.05 (m, 2H), 4.09−4.01 (m, 2H), 3.98−3.91 (m, 2H), 3.56 (m, 1H), 2.46−2.31 (m, 2H), 2.23−2.01 (m, 2H), 1.65 (s, 3H), 1.60 (s, 6H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 135.6, 134.9, 119.2, 116.5, 109.6, 77.7, 75.9, 68.6, 67.0, 36.5, 36.3, 34.7, 28.0, 25.1, 24.0, 23.7, 19.8. ESI-HRMS: m/z calcd for $C_{14}H_{22}O_3$ $[M + Na]^+$: 261.1468. FoundL 261.1488.

*(S,E)-5-Hydroxy-2-methyl-5-((R)-1,4-dioxaspiro[4.5]decan-2-yl)-pent-2-enal (**13h**).* Yellow liquid (130 mg, 76%), $[\alpha]_D^{25}$ −5.1 (*c* 2.1, $CHCl_3$). IR (neat): υ_{max} 3447, 2922, 2852, 1720, 1681, 1642, 1407, 1334, 1251, 1098, 1043 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 9.44 (s, 1H), 6.65 (td, J = 6.0, 1.1 Hz, 1H), 4.12−4.00 (m, 2H), 3.99−3.87 (m, 2H), 2.69−2.42 (m, 2H), 1.78 (s, 3H), 1.68−1.55 (m, 8H), 1.48−1.37 (m, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 195.0, 149.6, 141.0, 109.9, 77.7, 70.6, 64.7, 36.1, 34.5, 32.6, 29.6, 25.0, 23.9, 23.6, 9.3. ESI-HRMS: m/z calcd for $C_{14}H_{22}O_4$ $[M + Na]^+$: 277.1416. Found: 277.1411.

*(R)-2-((2S,6R)-6-Allyl-5-methyl-3,6-dihydro-2H-pyran-2-yl)-1,4-dioxaspiro[4.5]decane (**14h**).* Colorless liquid (105 mg, 90%), $[\alpha]_D^{25}$ −4.8 (*c* 1.0, $CHCl_3$). IR (neat): υ_{max} 3422, 2926, 2859,1219, 1049 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 5.89 (m, 1H), 5.54 (m, 1H), 5.17−5.03 (m, 2H), 4.09−4.00 (m, 2H), 3.99−3.90 (m, 2H), 3.60 (t, J = 6.8 Hz, 1H), 2.41−2.33 (m, 2H), 2.15−2.01 (m, 1H), 1.96−1.85 (m, 1H), 1.65 (s, 3H), 1.63−1.53 (m, 9H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 135.6, 134.9, 119.2, 116.5, 109.6, 77.7, 75.9, 68.6, 67.1, 61.3, 36.5, 36.3, 34.8, 28.0, 25.1, 24.0, 23.7, 19.8. ESI-HRMS: m/z calcd for $C_{17}H_{27}O_3$ $[M + H]^+$: 279.1954. Found: 279.1951.

*(S,E)-5-Hydroxy-2-methyl-6-phenylhex-2-enal (**13i**).* Pale yellow liquid (220 mg, 77%), $[\alpha]_D^{25}$ +3.6 (*c* 1.1, $CHCl_3$). IR (neat): υ_{max} 3417, 2923, 2360, 1682, 1402, 1219, 1055, 1079 cm^{-1}. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 9.43 (s, 1H), 7.38−7.18 (m, 5H), 6.65 (t, J = 7.1 Hz, 1H), 4.06 (m, 1H), 2.92−2.72 (m, 2H), 2.64−2.52 (m, 2H), 1.76 (s, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 195.0, 150.1, 140.9, 137.5, 129.3, 128.7, 126.8, 71.6, 43.0, 36.4, 9.4. ESI-HRMS: m/z calcd for $C_{13}H_{16}O_2$ $[M + Na]^+$: 227.1042. Found: 227.1041.

*(2S,6R)-6-Allyl-2-benzyl-5-methyl-3,6-dihydro-2H-pyran (**14i**).* Colorless liquid (170 mg, 92%), $[\alpha]_D^{25}$ −2.2 (*c* 1.5, $CHCl_3$). IR (neat): υ_{max} 3417, 2929, 2357, 1719, 1451, 1274, 1219, 1110 cm^{-1}. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.30−7.18 (m, 5H), 5.70 (m, 1H), 5.48 (m, 1H), 4.96−4.91 (m, 2H), 4.04 (d, J = 8.1 Hz, 1H), 3.89 (m, 1H), 2.87 (m, 1H), 2.70 (m, 1H), 1.36−2.25 (m, 2H), 2.90−1.90 (m, 2H), 1.63 (s, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 138.8, 135.5, 135.3, 129.3, 128.1, 126.0, 119.5, 116.1, 76.1, 68.5, 42.0, 36.4, 30.7, 19.7. ESI-MS for $C_{16}H_{20}O$: m/z $[M + Na]^+$ 251. ESI-HRMS: m/z calcd for $C_{16}H_{20}O$ $[M + Na]^+$: 251.1406. Found: 251.1417.

*(R,E)-5-Hydroxy-2-methyl-7-phenylhept-2-enal (**13j**).* Pale yellow liquid (180 mg, 79%), $[\alpha]_D^{25}$ −2.4 (*c* 0.8, $CHCl_3$). IR (neat): υ_{max} 3426, 2924, 1678, 1641, 1402, 1219, 1051 cm^{-1}. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 9.42 (s, 1H) 7.35−7.17 (m, 5H), 6.60 (td, J = 6.2, 0.9 Hz, 1H), 3.86 (quin, J = 6.0 Hz, 1H), 2.90−2.65 (m, 2H), 2.61−2.55 (m, 2H), 1.90−1.82 (m, 2H), 1.76 (s, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 195.2, 150.7, 141.2, 140.5, 128.2, 128.1, 125.7, 69.7, 38.6, 36.7, 31.7, 9.4. ESI-HRMS: m/z calcd for $C_{14}H_{18}O_2$ $[M + Na]^+$: 241.1212. Found: 241.1249

*(2R,6R)-6-Allyl-5-methyl-2-phenethyl-3,6-dihydro-2H-pyran (**14j**).* Colorless liquid (140 mg, 88%) $[\alpha]_D^{25}$ −8.7 (*c* 1.6, $CHCl_3$). IR (neat): υ_{max} 2922, 2852, 1729, 1456, 1376, 1285, 1092, 1037 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.33−7.14 (m, 5H), 5.98 (m, 1H), 5.49 (m, 1H), 5.17−5.03 (m, 2H), 4.07 (d, J = 8.2 Hz, 1H), 3.69 (m, 1H), 2.90−2.78 (m, 1H), 2.62 (m, 1H), 2.42−2.36 (m, 2H), 1.98−1.90 (m, 2H), 1.85 (m, 1H), 1.75 (m, 1H), 1.65 (s, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 142.1, 135.7, 135.0, 128.1, 125.4, 119.5, 116.1, 75.6, 66.3, 37.2, 36.2, 32.0, 31.0, 19.7. ESI-HRMS: m/z calcd for $C_{17}H_{23}O$ $[M + H]^+$: 243.1743. Found: 243.1748.

*(S,E)-7-(4-((tert-Butyldimethylsilyl)oxy)phenyl)-5-hydroxy-2-methylhept-2-enal (**13k**).* Colorless liquid (74 mg, 78%), $[\alpha]_D^{25}$ +6.4 (*c* 1.4, $CHCl_3$). IR (neat): υ_{max} 3432, 2927, 2360, 1684, 1399, 1219 cm^{-1}. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 9.42 (s, 1H),7.04 (d, J = 8.4 Hz, 2H), 6.76 (d, J = 8.4 Hz, 2H), 6.60 (dt, J = 6.0, 1.13 Hz, 1H), 3.89 (quin, J = 6.2 Hz, 1H), 2.81−2.50 (m, 4H), 1.87−1.77 (m, 2H), 1.76 (s, 3H), 0.98 (s, 9H), 0.18 (s, 6H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 195.1, 153.7, 150.2, 133.8, 129.1, 120.0, 70.1, 39.0, 36.9, 31.1, 29.6, 25.6, 9.46, −4.4. ESI-HRMS: m/z calcd for $C_{20}H_{32}O_3Si$ $[M + Na]^+$: 371.2012. Found: 371.2023.

*(4-(2-((2S,6S)-6-Allyl-5-methyl-3,6-dihydro-2H-pyran-2-yl)ethyl)-phenoxy)(tert-butyl)dimethylsilane (**14k**).* Colorless liquid (50 mg, 86%), $[\alpha]_D^{25}$ −8.4 (*c* 1.0, $CHCl_3$). IR (neat): υ_{max} 2922, 2853, 1732, 1609, 1462, 1255, 1168, 1101, 1051 cm^{-1}. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.05 (d, J = 8.5 Hz, 2H), 6.76 (d, J = 8.5 Hz, 2H), 5.96 (m, 1H), 5.48 (m, 1H), 5.14−5.05 (m, 2H), 4.06 (m, 1H), 3.66 (m, 1H), 2.77 (m, 1H), 2.56 (m, 1H), 2.41−2.33 (m, 2H), 1.98−1.90 (m, 2H), 1.86−1.66 (m, 2H), 1.64 (s, 3H), 0.97 (s, 9H), 0.17 (s, 6H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 153.5, 135.9, 135.2, 135.0, 129.1, 119.8, 119.6, 116.3, 75.9, 66.6, 37.5, 36.4, 31.3, 31.1, 25.6, 19.8, 18.1, −4.4. ESI-HRMS: m/z calcd for $C_{23}H_{36}O_2Si$ $[M + H]^+$: 373.2557. Found: 373.2535.

*(S)-tert-Butyl-4-((R,E)-1-hydroxy-4-methyl-5-oxopent-3-en-1-yl)-2,2-dimethyloxazolidine-3-carboxylate (**13l**).* Colorless liquid (90 mg, 75%), $[\alpha]_D^{25}$ +10.3 (*c* 2.5, $CHCl_3$). IR (neat): υ_{max} 3432, 2927, 2361, 1685, 1508, 1400, 1219 cm^{-1}. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 9.43 (S, 1H), 6.73 (m, 1H), 4.20 (brs, 1H), 4.10 (m, 1H), 4.05−3.95 (m, 2H), 3.94−3.80 (m, 2H), 2.62−2.39 (m, 2H), 1.76 (s, 3H), 1.61 (m, 3H), 1.53−1.45 (m, 12H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 195.0, 154.5, 151.3, 140.5, 94.5, 81.6, 72.6, 65.0, 62.0, 32.4, 28.2, 26.3, 23.8. ESI-HRMS: m/z calcd for $C_{16}H_{27}O_5N$ $[M + Na]^+$: 336.1781. Found: 336.1767.

*(S)-tert-Butyl-4-((2R,6S)-6-allyl-5-methyl-3,6-dihydro-2H-pyran-2-yl)-2,2-dimethyloxazolidine-3-carboxylate (**14l**).* Colorless liquid (70 mg, 85%), $[\alpha]_D^{25}$ +36.7 (*c* 1.5, $CHCl_3$). IR (neat): υ_{max} 2922, 2853, 1730, 1700, 1460, 1379, 1209, 1044 cm^{-1}. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 5.89 (m, 1H), 5.52 (d, J = 12.2, 1H), 5 0.18−5.04 (m, 2H), 4.18 (d, J = 7.9 Hz, 1H), 4.09 (d, J = 7.9 Hz,1H), 3.92 (m, 1H), 3.86−3.68 (m, 2H), 2.46−2.30 (m, 2H), 2.11 (m, 1H), 1.91 (m, 1H), 1.64 (s, 3H), 1.57 (s, 3H), 1.51−1.43 (m, 12H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 152.7, 135.9, 135.0, 119.7, 116.8, 93.6, 79.9, 76.5, 66.6, 63.9, 60.2, 36.3, 29.6, 28.4, 27.2, 24.6, 19.8. ESI-HRMS: m/z calcd for $C_{19}H_{31}NO_4$ $[M + Na]^+$: 360.2145. Found: 360.2135.

*(R)-6-(Benzyloxymethyl)-5,6-dihydro-2H-pyran-2-ol (**17**).* Lactone (1.0 g, 4.0 mmol) was dissolved in CH_2Cl_2 (15 mL) and cooled to −78 °C under nitrogen atmosphere. DIBAL-*H* (3.5 mL, 4.8 mmol, 1.4 M in toluene) was slowly added to it over a period of 10 min at −78 °C. After 30 min of stirring at the same temperature, TLC was checked and showed complete consumption of the starting material. The

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reaction was quenched by slow addition of a saturated solution of sodium potassium tartrate (40 mL), diluted with CH_2Cl_2 (50 mL), and allowed to stir at room temperature for an additional 2 h to get two separated layers. The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 40 mL). The combined organic layer was washed with brine (2 × 75 mL), dried over anhydrous Na_2SO_4, and evaporated to dryness under vacuum, which on silica gel column chromatography (ethyl acetate/hexane = 1:4) produced the desired lactol **17** (0.83 g, 83%) as a colorless liquid. $[\alpha]_D^{25}$ −36.2 (*c* 1.0, $CHCl_3$). IR (neat): υ_{max} 3444, 2926, 1683, 1384, 1251, 1098, 1026 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 7.37−7.25 (m, 5H), 5.63 (m,1H), 5.17 (m, 1H), 4.55−4.44 (m, 2H), 4.07 (m, 1H), 3.66−3.56 (m, 2H), 2.02−1.92 (m, 2H), 1.92−1.80 (m, 2H), 1.68 (s, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 138.3, 132.1, 128.3, 127.7, 127.5, 127.4, 122.9, 93.4, 72.9, 67.0, 64.2, 35.6, 30.8, 18.9. ESI-HRMS: *m*/*z* calcd for $C_{15}H_{20}O_3$ $[M + Na]^+$: 271.1304. Found: 271.1295.

*(R)-(6-(Benzyloxymethyl)-5,6-dihydro-2H-pyran-2-yloxy)-trimethylsilane (**18**).* To a stirring solution of lactol **17** (0.5 g, 2.0 mmol) in dry CH_2Cl_2 (15 mL) was added imidazole (0.27 g, 4.0 mmol) at 0 °C under nitrogen atmosphere. After 20 min, a solution of TMSCl (0.4 mL, 3.0 mmol) was added dropwise. After completion of the reaction (monitored by TLC), water (20 mL) was added to the reaction mixture and two layers were separated. The aqueous layer was extracted with CH_2Cl_2 (2 × 25 mL), and the combined organic layer was washed with brine (2 × 30 mL), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure to get the crude product, which was purified by flash column chromatography over silica gel (ethyl acetate/hexane = 1:20) to furnish the desired TMS-protected lactol **18** (0.56 g, 88%) as a colorless liquid. $[\alpha]_D^{25}$ −12.2 (*c* 1.0, $CHCl_3$). IR (neat): υ_{max} 2942, 1723, 1454, 1098, 1064 cm^{-1}. ^1H NMR ($CDCl_3$, 500 MHz): δ 7.37−7.26 (m, 5H), 5.65−5.56 (m, 1H), 5.08 (m, 1H), 4.51 (dd, *J* = 11.7, 26.4 Hz, 2H), 4.07 (m, 1H), 3.55 (m, 2H), 2.00−1.89 (m, 2H), 1.89−1.79 (m, 2H), 0.18 (s, 6H), 0.16 (s, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 138.3, 132.2, 128.3, 127.5, 127.4, 123.0, 93.4, 72.9, 67.0, 64.2, 35.7, 30.8, 18.9, 1.3. ESI-HRMS: *m*/*z* calcd for $C_{18}H_{28}O_3Si$ $[M + Na]^+$: 343.1699. Found: 343.1693.

*(2R,6S)-6-Allyl-2-(benzyloxymethyl)-3,6-dihydro-2H-pyran (**19**).* To a stirred solution of TMS-protected lactol (0.3 g, 0.93 mmol) and allyltrimethylsilane (0.3 mL, 1.87 mmol) in THF (8 mL) was added zinc bromide (41 mg, 0.18 mmol) at 0 °C under nitrogen atmosphere, and the solution was allowed to come to room temperature. After completion of the reaction (as indicated by TLC) (30 min), the reaction mixture was quenched with a saturated solution of $NaHCO_3$ (5 mL) and diluted with ethyl acetate (10 mL). The organic layer was separated and the aqueous layer was extracted with ethyl acetate (2 × 10 mL). The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (ethyl acetate/hexane = 1:20) to obtain the *C*-allylated product **14b** (0.23 g, 90%).

*(1R,2S,6S)-7-Oxabicyclo[4.1.0]heptan-2-ol (**26**).* Molecular sieves (4 Å, 12.0 g) were added to a stirred solution of $Ti(O^iPr)_4$ (3.1 mL, 11.2 mmol) and D-(−)-diisopropyl tartrate (3.34 mL, 14.2 mmol) in CH_2Cl_2 (60 mL) at −20 °C, and the reaction mixture was stirred vigorously for 30 min. Allyl alcohol **25** (10.0 g, 102.0 mmol) dissolved in CH_2Cl_2 (40 mL) was added to the reaction mixture at the same temperature and stirred again for 30 min followed by addition of *tert*-butyl hydroperoxide (6M, 10.1 mL, 61.1 mmol). The stirring was continued at the same temperature for 24 h. After completion of the reaction (monitored by TLC), the reaction mixture was filtered through Celite and washed with CH_2Cl_2 (3 × 50 mL). The filtrate was quenched with water (23.0 mL) followed by addition of 20% NaOH solution (60 mL). The mixture was saturated with NaCl and stirred at room temperature for 3 h. The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (2 × 100 mL). The combined organic layer was washed with brine (2 × 150 mL), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified on silica gel column chromatography (ethyl acetate/hexane = 1:4) to afford epoxy alcohol **26** (5.1 g, 44%) as a colorless liquid. $[\alpha]_D^{27}$ −4.8 (*c* 2.5, $CHCl_3$). IR (neat): υ_{max} 3388, 2933, 1219, 1059, 1032 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 4.02 (br s, 1H), 3.38−3.30 (m, 2H), 2.07 (m, 1H), 1.93−1.63 (m, 3H), 1.63−1.29 (m, 2H), 1.28−1.16 (m, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 67.0, 55.4, 55.3, 28.5, 22.9, 18.4. ESI-HRMS: *m*/*z* calcd for $C_6H_{11}O_2$ $[M + H]^+$: 115.0753. Found: 115.0754.

*(1S,2S,6S)-2-(Benzyloxy)-7-oxabicyclo[4.1.0]heptanes (**23**).* Alcohol **26** (5.0 g, 43.8 mmol) in THF (30 mL) was added slowly to a suspension of NaH (2.6 g, 65.7 mmol) in anhydrous THF (30 mL) at 0 °C. After 20 min, benzyl bromide (5.25 mL, 44.2 mmol) was added dropwise at 0 °C. The reaction mixture was stirred for 6 h at room temperature. After completion (monitored by TLC), the reaction mixture was quenched with ice-cooled water (40 mL) and diluted with ethyl acetate (50 mL). The organic layer was separated and the aqueous layer was extracted with ethyl acetate (3 × 50 mL). The combined organic layers were dried with Na_2SO_4, concentrated under reduced pressure, and purified by silica gel column chromatography (ethyl acetate/hexane = 1:6) to afford compound **23** (7.7 g, 87%) as a colorless liquid. $[\alpha]_D^{27}$ −13.6 (*c* 1.0, $CHCl_3$). IR (neat): υ_{max} 2952, 2357, 1454, 1219, 1074 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 7.43−7.26 (m, 5H), 4.70 (m, 2H), 3.80 (m, 1H), 3.31 (dd, *J* = 2.2 1.5 Hz,1H), 3.27 (dt, *J* = 3.7, 1.5 Hz, 1H), 1.86−1.77 (m, 2H), 1.80−1.49 (m, 2H), 1.23 (m, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 138.3, 128.1, 127.4, 127.3, 74.2, 69.8, 53.8, 53.1, 24.6, 22.7, 19.4. ESI-HRMS: *m*/*z* calcd for $C_{13}H_{16}O_2$ $[M + Na]^+$: 227.1042. Found: 227.1041.

*(1S,2S,6S)-2-(Benzyloxy)-6-vinylcyclohexanol (**27**).* To a solution of **23** (5.0 g, 24.4 mmol) in anhydrous THF (60 mL) under nitrogen atmosphere, CuI (0.41 g, 2.44 mmol) was added and the resulting mixture was stirred at 25 °C for 30 min. It was cooled to −20 °C, C_2H_3MgBr (85.4 mL, 1.0 M in THF) was slowly added, and the reaction mixture was stirred at the same temperature for 30 min. It was then slowly warmed to room temperature. After 1 h (monitored by TLC), it was quenched with saturated NH_4Cl solution (50 mL) and diluted with ethyl acetate (75 mL). The organic layer was separated and the aqueous layer was extracted with ethyl acetate (3 × 60 mL). The combined organic layers were washed with brine (2 × 150 mL), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure to afford the crude product, which on purification by column chromatography over silica gel using (ethyl acetate/hexane = 1:5) furnished the desired product **27** (4.8 g, 86%) as a colorless liquid. $[\alpha]_D^{27}$ −9.1 (*c* 1.6, $CHCl_3$). IR (neat): υ_{max} 3434, 3064, 2933, 2357, 1639, 1454, 1219, 1094 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 7.42−7.26 (m, 5H), 6.82 (m, 1H), 5.15−5.05 (m, 2H), 4.50 (AB_q, *J* = 47.5 Hz, 12.1 Hz, 2H), 3.80 (m, 1H), 3.32 (m, 1H), 2.39 (m, 1H), 2.08 (m, 1H), 1.75 (m, 1H), 1.58 (m, 1H), 1.55 (m, 1H), 1.32−1.14 (m, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 140.9, 138.6, 128.4, 128.3, 127.6, 127.5, 115.2, 76.9, 74.3, 70.8, 44.4, 29.9, 27.6, 19.1. ESI-MS for $C_{15}H_{20}O_2$: *m*/*z* $[M + Na]^+$ 255. ESI-HRMS: *m*/*z* calcd for $C_{15}H_{21}O_2$ $[M + H]^+$: 233.1536. Found: 233.1523.

*(2S,3S)-3-(Benzyloxy)-2-hydroxycyclohexanecarbaldehyde (**28**).* To a stirred solution of **27** (4.0 g, 17.2 mmol) in 1,4-dioxane and water (3:1) (40 mL), 2,6-lutidine (4.0 mL, 34.4 mmol) and OsO_4 (84 mg, 0.33 mmol) followed by $NaIO_4$ (14.6 g, 68.8 mmol) were sequentially added at room temperature and stirred for 4 h at room temperature. After completion of the reaction (monitored by TLC), 1,4-dioxane was removed under reduced pressure and the residue was was diluted with CH_2Cl_2 (50 mL). The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (2 × 50 mL). The combined organic layer was quickly washed with 1 N HCl (2 × 75 mL) to remove excess 2,6-lutidine followed by brine (2 × 75 mL). The organic layer was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to get the crude aldehyde, which on purification through a short silica gel column (ethyl acetate/hexane = 1:1) afforded aldehyde **28** (3.4 g, 85%) as a colorless liquid.

*(E)-3-((1S,2S,3S)-3-(Benzyloxy)-2-hydroxycyclohexyl)-2-methylacryl aldehyde (**22**).* To a stirred solution of **28** (3.0 g, 12.8 mmol) in toluene (64 mL, 0.2M) was added 2-(triphenylphosphoranylidene)-propionaldehyde (6.1 g, 19.2 mmol), and the solution was heated at 85 °C for 12 h. After completion of the reaction (monitored by TLC), the reaction mixture was cooled and the solvent was removed under reduced pressure. The remaining oil was triturated with cold hexane

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(40 mL), and the insoluble triphenylphosphine oxide was precipitated out. The precipitate was filtered, and the solid mass was rinsed with hexane (2 × 40 mL). The filtrate was concentrated to give an oil, which underwent purification by flash chromatography over silica gel (ethyl acetate/hexane = 1:6) to obtain **22** (2.59 g, 74%) as a colorless liquid. $[\alpha]_D^{27}$ −20.4 (*c* 4.5, $CHCl_3$). IR (neat): υ_{max} 3434, 2928, 1685, 1453, 1219, 1091 cm^{-1}. ^1H NMR ($CDCl_3$, 500 MHz): δ 9.41 (m, 1H), 7.41−7.29 (m, 5H), 6.40 (dd, *J* = 8.4, 1.0 Hz, 1H), 4.50 (AB_q, *J* = 47.6, 12.1 Hz, 2H), 3.84 (m, 1H), 3.46 (dd, *J* = 7.0, 2.9 Hz, 1H), 2.99 (m, 1H), 2.16 (m, 1H), 1.77 (s, 3H), 1.74−1.59 (m, 2H), 1.51 (m, 1H), 1.38(m, 1H), 1.20 (m, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 195.3, 156.6, 139.9, 138.1, 128.3, 127.6, 127.5, 76.5, 74.4, 70.7, 40.6, 29.3, 27.2, 18.6, 9.5. ESI-HRMS: *m*/*z* calcd for $C_{17}H_{22}O_3$ $[M + Na]^+$: 297.1461. Found: 297.1455.

*(2R,4aS,8S,8aS)-2-Allyl-8-(benzyloxy)-3-methyl-**4a,5,6,7,8,8a**-hexahydro-2H-chromene (**21**).* Zinc bromide (0.32 g, 1.44 mmol) was added to a stirred solution of δ-hydroxyl-α-methyl-α,β-unsaturated aldehyde **22** (2.0 g 7.2 mmol) and allyltrimethyl silane (1.72 mL, 10.8 mmol) in THF (30 mL) at room temperature. After completion of the reaction (monitored by TLC), the reaction mixture was quenched with a saturated solution of $NaHCO_3$ (20 mL) and diluted with ethyl acetate (40 mL). The organic layer was separated and the aqueous layer was extracted with ethyl acetate (2 × 40 mL). The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to give a pale yellow oil, which on purification by silica gel column chromatography (ethyl acetate/hexane = 1:19) afforded the cyclized product **21** (1.95 g, 90%). $[\alpha]_D^{27}$ +3.2 (*c* 2.0, $CHCl_3$). IR (neat): υ_{max} 3067, 3029, 2930, 2858, 1640, 1495, 1452, 1373, 1102, 1085, 1029 cm^{-1}. ^1H NMR ($CDCl_3$, 500 MHz): δ 7.43−7.20 (m, 5H), 5.96 (m, 1H), 5.36 (m, 1H), 5.13−5.02 (m, 2H), 4.70 (AB_q, *J* = 21.9, 12.8 Hz, 2H), 4.13 (m, 1H), 3.80 (m, 1H), 3.23 (dd, *J* = 8.3, 1.5 Hz, 1H), 2.55 (m, 1H), 2.43−2.30 (m, 2H), 1.97 (m, 1H), 1.71(m, 1H), 1.63 (s, 3H), 1.60 (m, 1H), 1.50−1.22 (m, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 139.5, 136.0, 134.4, 127.2, 126.9, 126.2, 115.6, 76.7, 75.1, 74.9, 71.0, 36.6, 33.6, 30.6, 29.5, 20.2, 19.4. ESI-HRMS: *m*/*z* calcd for $C_{20}H_{26}O_2$ $[M + Na]^+$: 321.1825. Found: 321.1816.

*(2R,4aS,8S,8aS)-8-(Benzyloxy)-3-methyl-2-((E)-prop-1-en-1-yl)-**4a,5,6,7,8,8a**-hexahydro-2H-chromene (**29**).* To a solution of **21** (1.0 g, 3.35 mmol) in MeOH (8 mL) was added second-generation Grubbs' catalyst (0.28 g, 0.33 mmol) at room temperature. The suspension was then heated at 60 °C. After 15 min the insoluble catalyst was dissolved, and the resulting orange−brown solution was stirred for 12 h at the same temperature. After completion of the reaction, MeOH was evaporated. The residue was purified by column chromatography over silica gel using (ethyl acetate/hexane = 1:19) to give predominately (*E*)-alkene **29** (0.8 g, 80%) as a colorless liquid. $[\alpha]_D^{25}$ −9.2 (*c* 2.5, $CHCl_3$). IR (neat): υ_{max} 3406, 2925, 2854, 1721, 1273, 1219, 1067 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 7.43−7.20 (m, 5H), 5.73−5.55(m, 2H), 5.39 (m,1H), 4.69 (AB_q, *J* = 34.7, 12.0 Hz, 2H), 4.44 (d, *J* = 6.0 Hz, 1H), 3.83 (dt, *J* = 3.0, 2.2 Hz, 1H), 3.26 (dd, *J* = 7.5, 2.2 Hz, 1H), 2.58 (m, 1H), 1.99 (m, 1H), 1.80−1.69 (m, 5H), 1.61−1.54 (m, 4H), 1.49−1.25 (m, 3H), 1.01(dt, *J* = 9.0, 3.7 Hz, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 139.6, 133.2, 129.0, 128.8, 128.0, 127.2, 126.9, 77.8, 75.7, 75.5, 71.2, 33.6, 30.7, 29.5, 20.2, 19.7, 17.8. ESI-HRMS: *m*/*z* calcd for $C_{20}H_{27}O_2$ $[M + H]^+$: 299.2005. Found: 299.1999.

*(2R,4aS,8S,8aS)-8-(Benzyloxy)-3-methyl-2-((E)-non-1-en-1-yl)-**4a,5,6,7,8,8a**-hexahydro-2H-chromene (**20**).* Isomerized alkene **29** (0.2 g, 0.67 mmol) and 1-nonene (4.37 mL, 3.35 mmol) were dissolved in CH_2Cl_2 (10 mL), and argon gas was purged through it for 10 min. Grubbs' second-generation catalyst (28 mg, 0.03 mmol) was added to it at room temperature and again degassed for 10 min. The reaction mixture was allowed to stir for 8 h. After completion of the reaction (monitored by TLC), solvent was removed under reduced pressure and directly purified by column chromatography over silica gel (ethyl acetate/hexane = 1:49) to afford cross-product **20** (0.19 g, 78%) as a colorless liquid. $[\alpha]_D^{25}$ −5.3 (*c* 0.8, $CHCl_3$). IR (neat) υ_{max} 2925, 1219, 1033, 772 cm^{-1}. ^1H NMR ($CDCl_3$, 500 MHz): δ 7.41−7.21 (m, 5H), 5.68−5.53 (m, 2H), 5.39 (m,1H), 4.77 (d, *J* = 12.3 Hz, 1H), 4.62 (d, *J* = 12.3 Hz, 1H), 4.44 (d, *J* = 6.4 Hz,1H), 3.83 (m, 1H), 3.26 (dd, *J* = 7.7, 2.2 Hz, 1H), 2.58 (m, 1H), 2.14−1.95 (m, 3H), 1.79−1.61 (m, 3H), 1.59 (s, 3H), 1.47−1.21 (m, 14H), 1.02−0.83 (m, 5H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 139.6, 134.5, 133.3, 132.1, 128.0, 127.5, 127.3, 127.2, 126.9, 126.2, 77.8, 75.7, 75.4, 71.2, 35.5, 33.6, 32.3, 31.6, 30.7, 29.5, 29.1, 28.8, 22.6, 20.3, 19.8, 14.0. ESI-HRMS: *m*/*z* calcd for $C_{26}H_{38}O_2$ $[M + NH_4]^+$: 400.3217. Found: 400.3205.

*(3R,E)-6-Methyl-1-phenyldeca-5,9-diene-3,7-diol (**19**).* To a stirred solution of unsaturated aldehyde **13j** (0.2 g, 0.91 mmol) in THF (10 mL) was added allyl magnesium bromide (2.73 mL, 2.73 mmol, 1.0 M in diethyl ether) at −78 °C, and the reaction mixture was stirred for 2 h at −20 °C. After completion of the reaction (monitored by TLC), the reaction mixture was quenched with a saturated solution of NH_4Cl (15 mL) and diluted with ethyl acetate (20 mL). The organic layer was separated and the aqueous layer was extracted with ethyl acetate (2 × 20 mL).The combined organic layer was washed with brine (20 mL), dried over anhydrous Na_2SO_4, and evaporated under reduced pressure. The crude product was purified by silica gel chromatography (ethyl acetate/hexane = 1:1) to afford diastereomeric mixture **19** (190 mg, 83% over two steps) as a colorless oil. $[\alpha]_D^{25}$ −16.2 (*c* 1.0, $CHCl_3$). IR (neat): υ_{max} 3398, 2925, 2856, 1723, 1445, 1047 cm^{-1}. ^1H NMR ($CDCl_3$, 500 MHz): 7.31−7.14 (m, 5H), 5.74 (m, 2H), 5.46 (m, 1H), 5.20−5.04 (m, 2H), 4.09 (m, 1H), 3.65 (m, 1H), 2.87−2.62 (m, 2H), 2.39−2.28 (m, 2H), 2.27−2.18 (m, 2H), 1.83−1.73 (m, 2H), 1.64 (s, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 142.0, 139.8, 134.6, 128.4, 128.3, 125.8, 121.8, 121.6, 117.8, 76.3, (76.2), 70.8, (70.7), 39.8, 38.5, 38.4, 35.5, 32.1, 12.1, (12.0). ESI-HRMS: *m*/*z* calcd for $C_{17}H_{24}O_2$ $[M + NH_4]^+$: 278.2114. Found: 278.2108.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Copies of ^1H and ^{13}C NMR spectra for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: mohapatra@iict.res.in.

Notes

The authors declare no competing financial interest.

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