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A unified approach to the salicylaldehyde containing polyketide natural products: Total synthesis of *ent*-pyriculol, *ent*-epipyriculol, *ent*-dihydropyriculol, *ent*-epidihydropyriculol, sordariol, sordarial, 12-methoxy sordariol, and agropyrenol

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PII: S0040-4020(20)30523-8

DOI: https://doi.org/10.1016/j.tet.2020.131368

Reference: TET 131368

To appear in: *Tetrahedron*

Received Date: 24 March 2020

Revised Date: 22 June 2020

Accepted Date: 24 June 2020

Please cite this article as: Mahesh G, Raghavaiah J, Sudhakar G, A unified approach to the salicylaldehyde containing polyketide natural products: Total synthesis of *ent*-pyriculol, *ent*-epipyriculol, *ent*-dihydropyriculol, *ent*-epidihydropyriculol, sordariol, sordarial, 12-methoxy sordariol, and agropyrenol, *Tetrahedron* (2020), doi: https://doi.org/10.1016/j.tet.2020.131368.

A Unified Approach to the Salicylaldehyde Containing Polyketide Natural Products: Total Synthesis of *ent*-Pyriculol, *ent*-Epipyriculol, *ent*-Dihydropyriculol, *ent*-Epidihydropyriculol, Sordariol, Sordarial, 12-Methoxy Sordariol, and Agropyrenol

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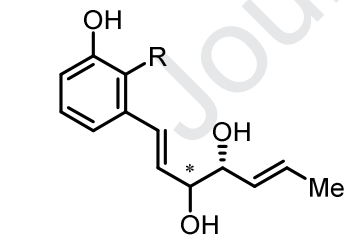
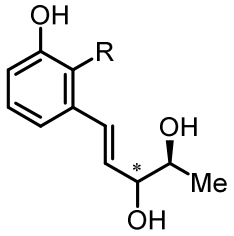


ent-pyriculol: R = CHO, * ◄ OH
ent-epipyriculol: R = CHO, * ····OH
ent-dihydropyriculol: R = CH_2OH, * ◄ OH
ent-epidihydropyriculol: R = CH_2OH, * ····OH



trans-sordariol: R = CH_2OH, * ····OH
trans-sordarial: R = CHO, * ····OH
12-methoxy sordariol: R = CH_2OMe, * ····OH
Agropyrenol: R = CHO, * ◄ OH

Abstract

Many fungal metabolites are salicylaldehyde containing polyketide natural products and are often isolated from the fungus culture broth. These metabolites commonly exhibit phytotoxicity,

however, some compounds exerted other biological activities including immunosuppressive activity. We have developed a unified synthetic strategy that provides easy access to *ent*-pyriculol, *ent*-epipyriculol, *ent*-dihydropyriculol, *ent*-epidihydropyriculol, sordariol, sordarial, 12-methoxy sordariol and agropyrenol.

Introduction

Certain organisms are essential in maintaining the ecological environment; for instance, fungi involve in decomposing dead wood/carbohydrates-structural materials, while leaving dead animals to bacteria. Several fungi live in symbiotic relations with plants, apparently the adaptation of green plants to life on land.[1] Conversely, fungi attack plants and cause huge loss to the crops, and they are also known to produce host-specific secondary metabolites with structurally distinctive and in certain cases exciting biological activities with a new mode of action. A culture broth of the rice blast fungus, *Pyricularia oryzae* Cavara produced myriad phytotoxic metabolites, and pyriculol (**1**) is the one isolated first in 1969 (Figure 1).[2] Later, structurally similar to pyriculol, epipyriculol (**2**),[3] dihydropyriculol (**3**),[4] epidihydropyriculol (**4**)[3] and pyriculone (**5**)[5] were isolated from the same fungus. Constitutional isomers (somewhat varying the framework of pyriculol) such as pyricyculariol (**6**),[6] dihydropyricullariol (**7**)[7] and pyricuol (**8**)[8] were isolated from *Magnaporthe grisea* (Hebert) Barr (the perfect stage of *Pyricularia oryzae* Cavara). In addition, monilidiol (**9**) and dechloromonilidiol (**10**) were obtained in an attempt to isolate a self-growth inhibitor from benomyl-ressistant strains of cherry brown rot fungus *Monilinia fructicola*.[9] Sordariol (**11**) and sordarial (**12**) were isolated from fungus Sordaria macrospora.[10] Further, **12** was also isolated from Gelasinospora heterospora and the absolute stereochemistry of it was determined by using Mosher's method.[11] Recently, Kong et. al isolated 12-methoxy sordariol (**13**) along with four novel sordariol dimers from the same

fungus (Figure 1), and these dimmers (bisordariols A-C) exhibited potent ABTS radical cation scavenging activities with 2-folds more potent than the positive trolox.[12] The *syn* diol compound, agropyrenol (**14**) was isolated from *Ascochyta agropyrina var*. Nana (a fungal pathogen of Elitrigia repens) and the absolute configuration of it (**14**) was determined as 3´R,4´R by using Mosher´s method,[13] but very recently, this was a revised as 3´S,4´S by using biphenyl chiroptical probes.[14a]

In fact these phytotoxic metabolites having salicylaldehyde-type moiety is a common feature. They were isolated often from fungus culture broth and are trivially differ in structure. From the activity standpoint, they are found to cause dark necrotic spots on rice leaves, a common symptom of rice blast fungus and the most destructive blast disease of rice plant in Asian countries.[2] Pyriculol and epipyriculol inhibited significantly against a spore germination bioassay while dihydropyriculol and epidydropuriculol showed no inhibition. However, dihydropyriculol was found to prompt root elongation of rice seedlings.[4] Monilidiol was active against *Staphylococcus aureus* and also shown phytotoxicity to cherry leaves by inducing dark necrotic spots.[9] Sordariol was not phytotoxic towards rice roots, but it induced browning on the rice leaves,[10a] and showed immunosuppressive activity.[11] Agropyrenol (**14**) was tested for phytotoxic activity,[13] and its derivatives were examined for phytotoxic, antimicrobial, and zootoxic activities. The results provided an important insights about the structure-activity relationship of **14**.[14b] This group of salicylaldehyde-type polyketide metabolites having phytotoxic/growth inhibitory activities as well as their potential use as novel natural herbicides[12] naturally attracted research groups to develop synthetic routes from the beginning of pyriculol's discovery. Watanabe group reported the first total synthesis of monilidiol (**9**) and dechloromonilidiol (**10**) in a stereo-controlled fashion.[15] Afterwards, the same group reported the first total synthesis and

absolute configuration of pyriculol (**1**)[16a] followed by all four stereoisomers of **1**, including epipyriculol (**2**).[16b] The synthesis of epipyriculol was accessed by Ley et. al starting from methyl L-tartrate, and this feat was achieved somewhat in less number of steps (17 steps versus 20 steps).[17] Before this, Kiyot et. al[18] reported the first synthesis of pyricuol in an achiral version (*rac*-**8**),[18a] and immediately thereafter asymmetric synthesis that revealed the absolute configuration of pyriculol (**8**).[18b] The same group[19] reported the first synthesis and absolute configuration of pyriculariol (**6**),[19a] subsequently the synthesis of both enantiomers of pyricuol (**8**) along with their plant growth inhibitory activity.[19b] The interest also aroused in biotechnology groups to find the plausible biosynthesis and biosynthetic intermediates including genome mining.[20]

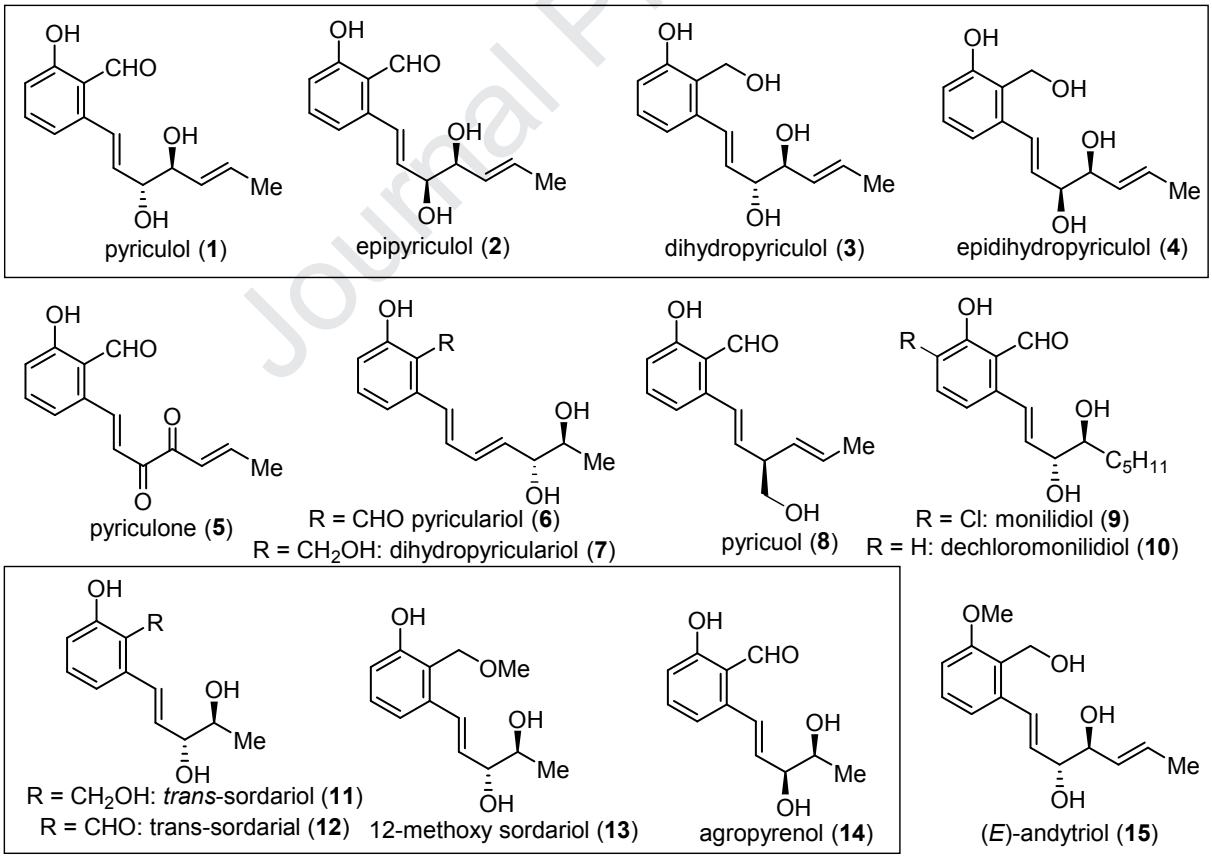


Figure 1. Salicylaldehyde-polyketide containing natural products (**1**-**15**) and synthetic targets **1**-**4** and **11**-**14**.

Almost a decade after the isolation of pyriculol (**1**), 2-methoxy-6-(3,4-dihydroxy-hepta-1,5-denyl)benzyl alcohol (**15**, andytriol) was isolated from static culture of the fungus *Aspergillus variecolor*.[21] It is structurally very similar to dihydropyriculol (**3**) and the presence of additional phenolic methyl ether in the salicylaldehyde moiety is the only difference. In 2002, varitriol and varioxirane were isolated from fungus *Emericella variecolor*, interestingly it was proposed that **15** could be a biosynthetic precursor for these natural products.[22] From the same fungus, varioxiranols A-G were isolated recently and some of them found to exert inhibitory effects against lipid accumulation at a dose of 10 μM.[23]

Because of our interest in the total synthesis of bioactive natural products,[24] we have developed a synthetic strategy to varitriol and varioxyrane based on the proposed biosynthetic pathway commencing from Sharpless kinetic resolution (SKR) of α-hydroxy ester (±)-**18**.[24f] In this approach, the epoxide obtained during the SKR was used in the synthesis of varitriol and varioxirane, and the unreacted allylic alcohol (-)-**18** was utilized in the synthesis of enantiomer of andytriol (*ent*-**15**) as shown in figure 2A.[24f] After our synthesis, Gracza et al. reported the first total synthesis of natural andytriol (**15**) from 2,3-*O*-isopropylidene D-ribose.[25]

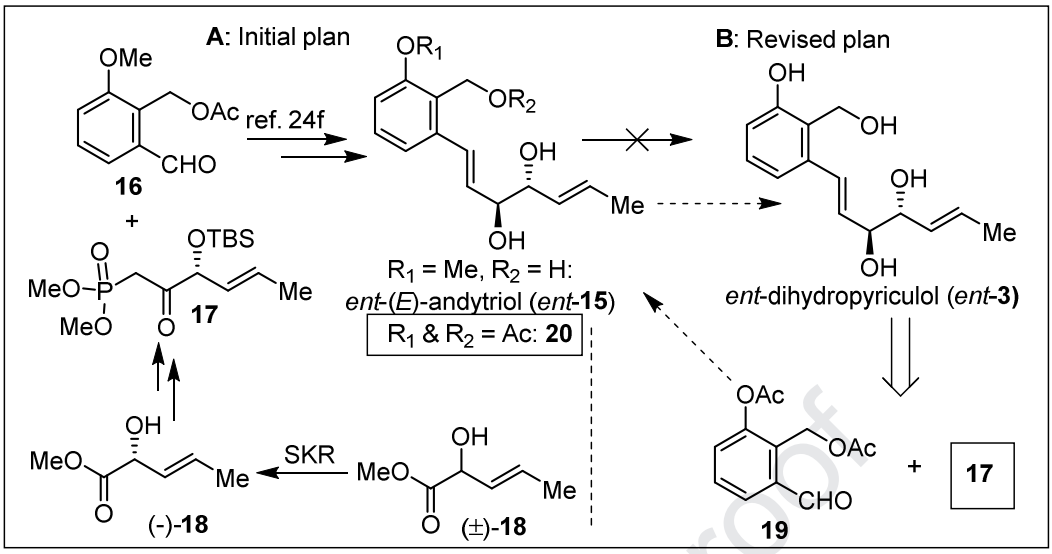


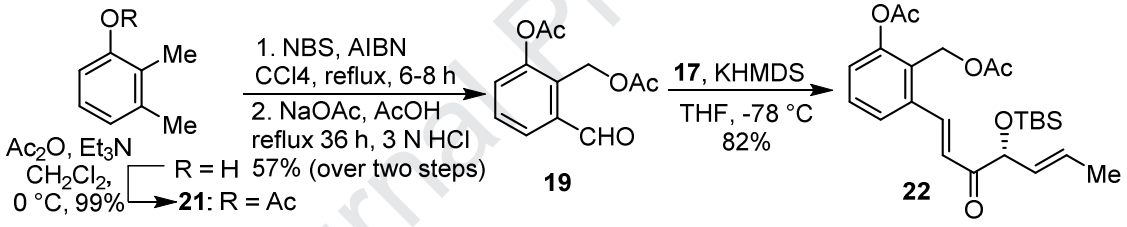
Figure 2. Synthetic plan for *enantiomer* of dihydropyriculol (*ent*-**3**) from ent-(*E*)-andytriol **15** (unsuccessful) and from **19** and **17** (successful)

Given interest with these natural products, we envisaged that the cleavage of phenolic methyl ether bond present in andytriol **15** could provide dihydropyriculol (**3**) and in the similar fashion transformations would allow us to achieve other salicylaldehyde-polyketide natural products of this class. However, our attempts in demethylating phenolic methyl ether of *ent*-**15** under various reaction conditions failed to produce the desired transformation, thwarting the access to *ent*-dihydropyriculol (*ent*-**3**) from this approach (Figure 2A). This could be attributed to the binding of hydroxyl groups (allylic and benzylic present in **15**) with demethylating agent such as BBr_3, resulted in a complex mixture. Then, we had to embark on revising the strategy and have contemplated replacing OMe group with an easily removable acetyl as a *O*-protecting group. This can be taken off along with the other acetyl group (benzyl acetate), eluding the additional deprotection step. Therefore the coupling of aromatic fragment **19** with ketophosphonate **17** (derived from **18** using (-)-DIPT in SKR), would provide compound **20** and subsequent deacetylation should result in the *ent*-dihydropyriculol (*ent*-**3**) as shown in Figure 2B. Herein, we

report the synthesis of enantiomers of **1**-**4** and natural podes of **11**-**14** by developing a novel strategy which is versatile and flexible in providing most of these salicylaldehyde-polyketide natural products of choice.

Results and Discussion

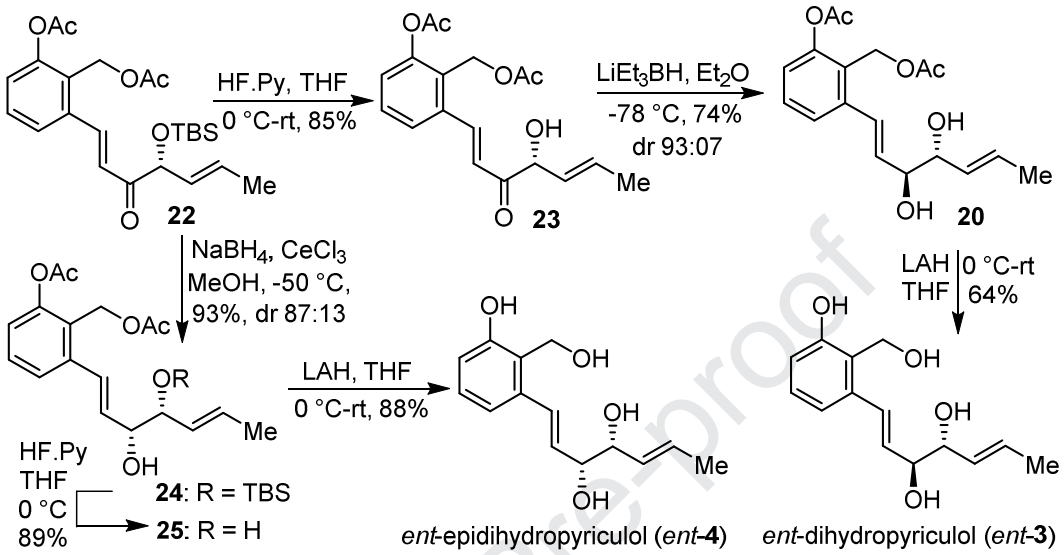
Accordingly, the acetyl group protected aromatic fragment **19** was commenced from the commercially available 2,3-dimethylphenol (R = H) which was subjected to acetylation with Ac_2O to give **21** in near quantitative yield (Scheme 1).[26] Then, two step reaction sequence of bromination/acetylation provided the compound **19** in 57% yield.[27] Subsequently, compound **19** was coupled with ketophosphonate **17** to obtain an advanced intermediate **22** in 82% yield.



Scheme 1. Synthesis of **19** and **22**

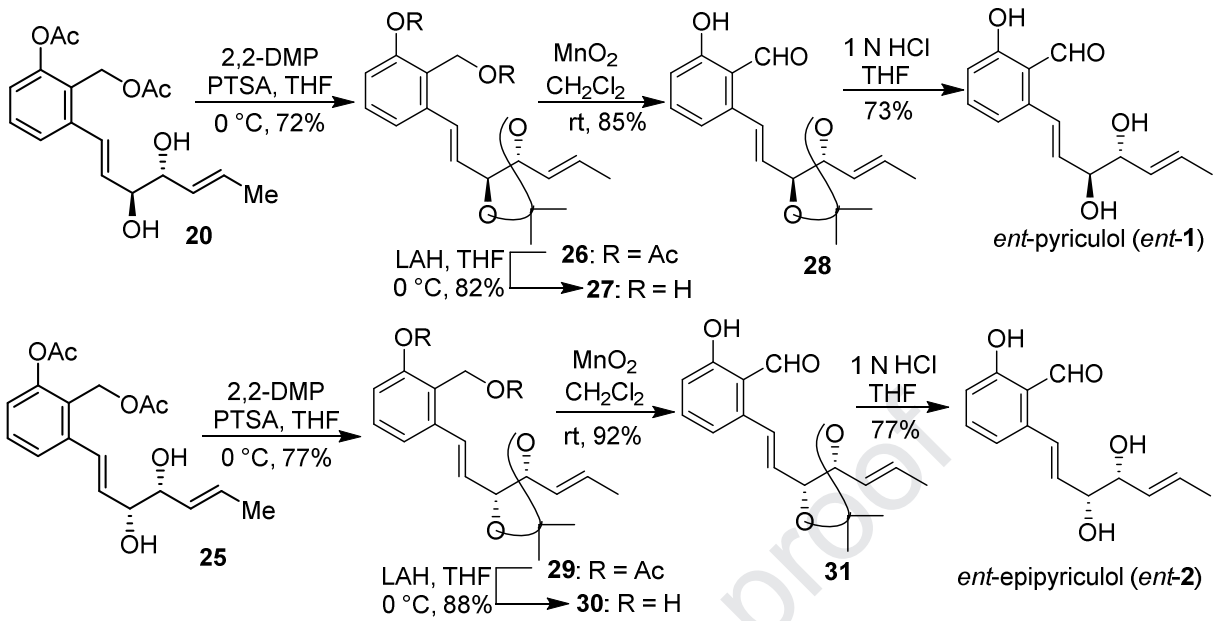
Having synthesized the intermediate **22**, the stage was set to convert it to the target molecules, shown in Schemes 2 and 3. Based on our previous results,[24f] the free α-hydroxy ketone **23** (obtained from **22** under silyl deprotection condition) was subjected to superhydride reduction to furnish the *anti*-diol product **20** in 74% yield and 93:07 dr. Subsequently, treatment of **20** with LAH cleaved both acetyls groups, obtaining the anticipated enantiomer of dihydropyriculol (*ent*-**3**) in 64% yield. Then, compound **22** was subjected to $NaBH_4$ reduction for *syn*-selectivity, affording **24** in 93% yield and 87:13 dr. Then, deprotection of TBS in **24** using HF.py followed

by acetyl groups deprotection (of **25**) using LAH resulted in enantiomer of epidihydropyriculol (*ent*-**4**) in 78% yield (two steps).



Scheme 2. Synthesis of enantiomer of epihydropyriculol (*ent*-**3**) and enantiomer of dihydropyriculol (*ent*-**4**)

Next, in order to obtain *ent*-pyriculol (*ent*-**1**) and *ent*-epipyriculol (*ent*-**2**), concealing of allylic alcohols in **20** and **25** was necessary to perform oxidation on benzyl alcohol. In this direction, acetonide protection was found to be suitable, therefore, **26** was prepared from reacting **20** with 2,2-DMP in the presence of catalytic amount of PTSA (Scheme 3). Then, acetyl groups were removed under LAH reduction, obtaining **27** in a yield of 82%. Benzylic oxidation of **27** with MnO_2 provided the corresponding aromatic aldehyde **28** and subsequent acidic treatment with 1 N HCl furnished the desired product, enantiomer of pyriculol (*ent*-**1**) in 73% yield (two steps). Following the same sequence of reactions, enantiomer of epipyriculol (*ent*-**2**) in 48% overall yield was achieved from **25**, *via* **29**-**31** as shown in Scheme 3.



Scheme 3. Synthesis of enatiomer of pyriculol (*ent*-**1**) and enantiomer of epipyriculol (*ent*-**2**)

After achieving the synthesis of pyriculol series, we consider the synthesis of sodariol, sordarial and agropyrenol. These natural products could be accessed from the intermediate **32** following the similar sequence of reactions mentioned above. The intermediate **32** would be obtained from a simple ketophosphonate **33** that in turn can be derived from the easily available (-)-methyl L-lactate (Figure 3).

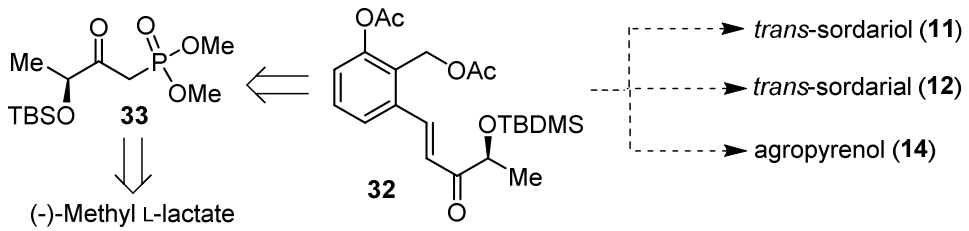
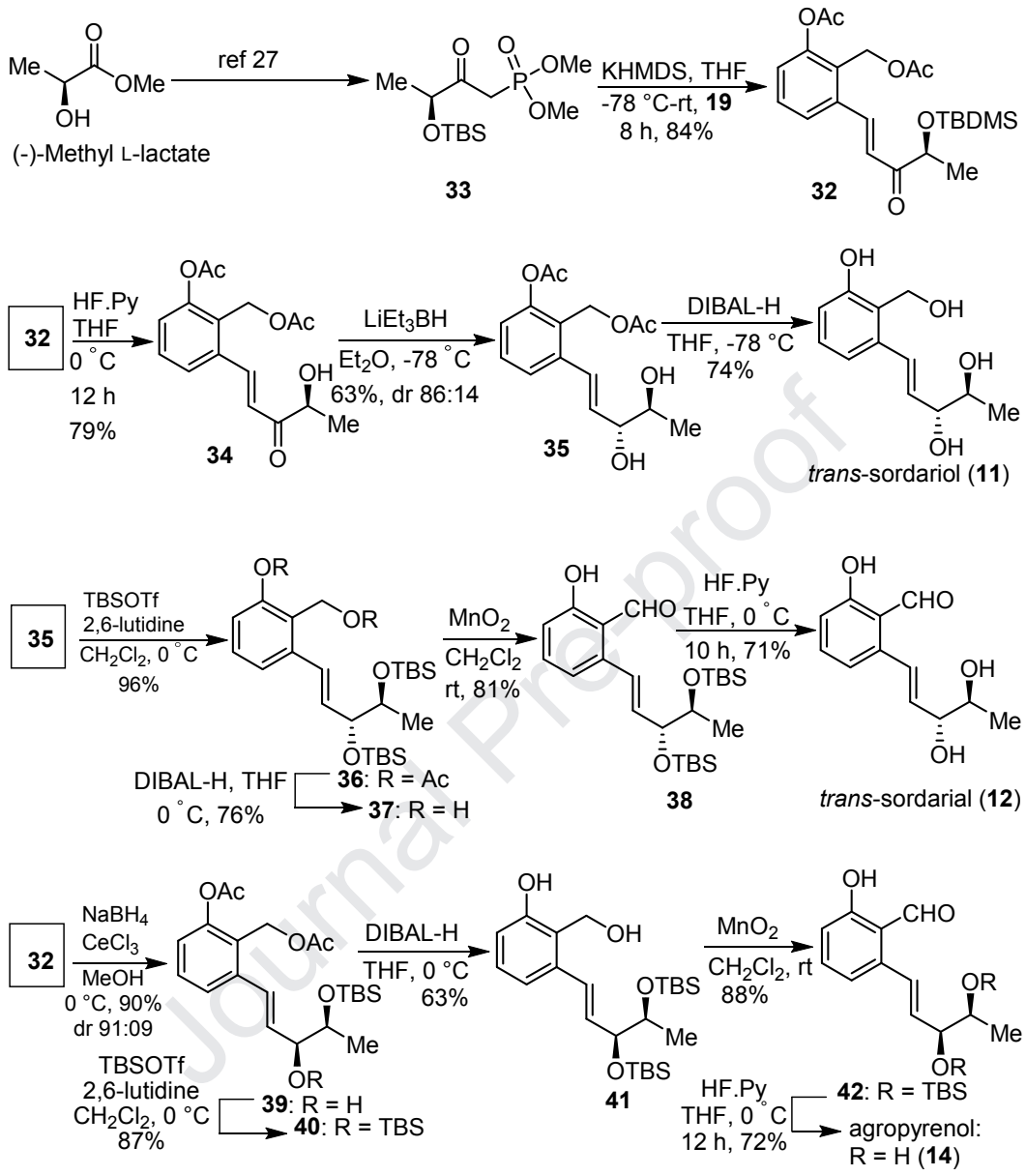


Figure 3. Synthetic plan for **11**, **12**, and **14**

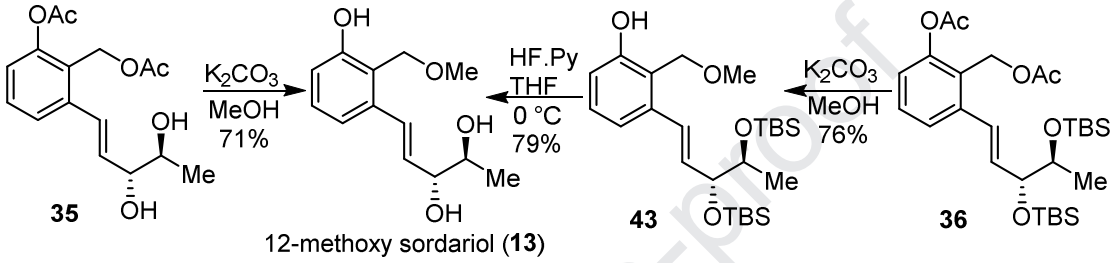
In this direction, methyl L-lactate was converted to keto-phosphonate **33** by following the literature procedure (Scheme 4).[28] Reacting keto-phosphonate **33** with aromatic aldehyde **19** afforded the advanced intermediate **32** in 84% yield, setting the stage to access the desired molecules. Reaction of **32** with HF.py resulted in **34** that was subjected to super hydride reduction to furnish the anticipated *anti*-diol product **35** in 63% yield and 86:14 dr. Subsequently, compound **35** was treated with DIBAL-H to yield *trans*-sordariol (**11**) in 74% yield. In order to achieve compound **12**, both hydroxyls of **35** were protected as TBS ether to obtain **36** in 96% yield. Treatment of diacetyl compound **36** with DIBAL-H resulted in the free benzylic alcohol **37** which upon MnO_2 oxidation afforded the corresponding aldehyde **38** in 61% yield (two steps). Removal of both silyl groups present in the **38** with HF.py furnished the desired natural product, *trans*-sordarial (**12**) in 71% yield. Next, compound **32** was subjected to $NaBH_4$ reduction to provide *syn*-diol **39** (dr 91:09) which upon further silylation afforded compound **40** in 78% yield (two steps). Subsequent DIBAL-H reduction on **40** provided acetyl free compound **41** that upon benzylic oxidation afforded **42** (55% yield in two steps). Finally, removal of both silyl groups delivered the agropyrenol (**14**) in 72% yield. The specific rotation of synthetic agropyrenol ($[\alpha]^{25}_D$: -43.0 (c 0.39, MeOH)) is resembled with the natural one ($[\alpha]^{25}_D$: -47.0 (c 0.5, MeOH)), supporting the revised absolute configuration reported recently.[14a]



Scheme 4. Synthesis of *trans*-sordariol (**11**), *trans*-sordarial (**12**), and agropyrenol (**14**)

Initially, we have isolated benzylmethyl ether containing product when attempted for deacetylation of **20**/**24** using K_2CO_3 in MeOH. Earlier, a similar transformation was observed in the literature, obtaining 3-(hydroxymethyl)-2-(methoxymethyl)phenol from (3-acetoxy-1,2-phenylene)bis(methylene) diacetate in an attempt to saponify acetate groups in aqueous methanol.[16b] Interestingly, this unexpected result became significant in this context as one of

these natural products, 12-methoxy sordariol (**13**), exists with benzyl methyl ether.[12] Indeed, reacting **35** with K_2CO_3 in MeOH furnished 12-methoxy sordariol (**13**) in 71% yield (Scheme 5). Alternatively, this was also achieved by reacting **36** with K_2CO_3 in MeOH to get **43** and subsequent silyl groups deprotection, obtained 12-methoxy sordariol (**13**) in 60% yield (over two steps). The spectral data of the synthetic one resembles with data of the natural products.



Scheme 5. Synthesis of 12-methoxy sordariol (**13**)

Conclusions

We have accomplished the total synthesis of *ent*-pyriculol, *ent*-epipyriculol, *ent*-dihydropyriculol, *ent*-epidihydropyriculol, sordariol, sordarial, 12-methoxy sordariol and agropyrenol from a unified approach. The total synthesis of agropyrenol supported the revised absolute configuration of this molecule. The synthesis of suitably protected aromatic fragment **19** facilitated the synthesis of these salicylaldehyde containing polyketide natural products of choice. Coupling of this intermediate with appropriate ketophosphonate and further necessary transformations can provide several natural products and their analogs for activity screening, which is underway in our laboratory.

Experimental Procedures:

2,3-Dimethylphenyl acetate (21):[25a] To a solution of 2,3-dimethylphenol (50 g, 0.409 mol) in CH_2Cl_2 (120 mL) at 0 ºC was added Et_3N (114 mL, 0.819 mol) followed by dropwise addition of Ac_2O (58 mL, 0.6135 mol). After completion of the reaction in 10 min (monitored by TLC), ice-cold water was added, and the aqueous layer was extracted by using CH_2Cl_2. The organic layer was washed with brine solution, dried over Na_2SO_4, concentrated under reduced pressure. The compound was purified by flash column chromatography to get compound **21** as yellow color liquid (66.5 g). Yield: 99%; R_f = 0.6 (10% EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.09 (dd, *J* = 7.7, 7.3 Hz, 1H), 7.03 (d, *J* = 7.3, 1H), 6.85 (d, *J* = 7.7, 1H), 2.31 (s, 3H), 2.28 (s, 3H), 2.07 (s, 3H); ^{13}C{H} NMR (100 MHz, $CDCl_3$): δ 169.5, 149.2, 138.5, 128.7, 127.5, 126.1, 119.4, 20.8, 20.1, 12.4; IR (Neat): ν_{max} 2931, 2858, 1753, 1463, 1372, 1253, 1141, 1060, 974, 829, 812, 776, 664; HRMS: (ESI-TOF) *m/z* calcd for $C_{10}H_{13}O_2$ $(M + H)^+$ 165.0928, found 165.0910.

2-Acetoxy-6-formylbenzyl acetate (19): To a solution of 2,3-dimethylphenyl acetate **21** (5 gm, 30.48 mmol) in CCl_4 (120 mL) was added NBS (16.1 gm, 91.46 mmol) and catalytic amount of AIBN (0.2 equiv, ~1.0 gm, 6.09 mmol). Then, the reaction mixture was refluxed for overnight (8-10 h), confirmed the formation of tribromo compound by ^{1}H NMR. The reaction mixture was filtered and washed with n-hexane for the elimination of excess NBS and other salts. The filtrate was concentrated and dried over vacuum until it became a powder. Without further purification, we proceeded to the next step.

To a solution of tribromo compound in anhydrous acetic acid (104 mL) was added NaOAc (8.5 gm, 103.7 mmol) portion-wise and refluxed for 36 h (the reaction mixture color turned to reddish black). Then, the reaction mixture brought to rt, filtered with a pad of silica gel. AcOH was evaporated on a rotary evaporator (bath temperature 70 □), diluted the reaction mixture with EtOAc and filtered. To the filtrate was added 3 N HCl, kept it for 3 h stirring and extracted with

EtOAc (3 times). The organic layer was concentrated under reduced pressure, and the crude product was purified by using silica gel column chromatography to get **19** as a colorless or light reddish liquid (4.1 gm). Yield: 57%; R_f = 0.5 (30% EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.30 (s, 1H), 7.80 (d, *J* = 7.8 Hz, 1H), 7.75 (t, *J* = 7.8, 1H), 7.36 (d, *J* = 7.8, 1H), 5.49 (s, 2H), 2.37 (s, 3H), 2.02 (s, 3H); ^{13}C{H} NMR (125 MHz, $CDCl_3$): δ 191.0, 170.5, 169.3, 150.2, 136.2, 130.0, 129.2, 129.0, 128.5, 55.7, 20.8, 20.7; IR (Neat): ν_{max} 2924, 1761, 1581, 1468, 1369, 1207, 1183, 1090, 1061, 1009, 925, 864, 778, 730, 597; HRMS: (ESI-TOF) *m/z* calcd for $C_{12}H_{13}O_5$ $(M + H)^+$ 237.07819, found 237.07575.

2-Acetoxy-6-((*S*,*E*,5*R*)-4-((*tert*-butyldimethylsilyl)oxy)-3-oxohepta-1,5-dien-1-yl) benzyl acetate (22): To a solution of *β*-Ketophosphonate **17**[24f] (3.7 g, 11.01 mmol) in THF (30 mL) at –78 °C was added KHMDS (1.0 M in THF, 12.1 mL, 12.1 mmol) dropwise. After 30 min at –78 °C, compound **19** (3.89 g, 16.51 mmol) dissolved in THF (15 mL) was added and stirred for 12 h. Then, the reaction was quenched by the addition of the water, and the product was extracted with EtOAc. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated in *vacuum*. The crude product was purified by using column chromatography on silica gel to give α,β-unsaturated ketone **22** (4.2 g) as a colorless oil. Yield: 86%; R_f = 0.5 (20% EtOAc/hexanes); $[\alpha]^{25}_D$: = +42.72 (c 1.65, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.02 (d, *J* = 15.9 Hz, 1H), 7.54 (d, *J* = 7.9 Hz, 1H), 7.40 (t, *J* = 7.9 Hz, 1H), 7.13 (dd, *J* = 1.0, 7.9 Hz, 1H), 7.11 (d, *J* = 15.9 Hz, 1H), 5.91 (ddd, *J* = 15.3, 6.7, 1.6 Hz, 1H), 5.50 (ddq, *J* = 15.3, 5.1, 1.6 Hz, 1H), 5.21 (ABq, *J* = 12.3 Hz, 2H), 4.66 (m, 1H), 2.34 (s, 3H), 2.02 (s, 3H), 1.73 (dd, *J* = 6.6, 1.5 Hz, 3H), 0.93 (s, 9H), 0.09 (s, 3H), 0.07 (s, 3H); ^{13}C{H} NMR (75 MHz, $CDCl_3$): δ 198.6, 170.5, 169.4, 150.1, 139.6, 137.3, 129.8, 128.8, 128.3, 127.4, 124.6, 124.3, 79.6, 56.9, 25.8, 20.8, 20.7, 18.3, 17.9, -4.7, -4.9; IR (Neat): ν_{max} 2924, 2853, 1766, 1733, 1637, 1579, 1468, 1371, 1224, 1202, 1184,

1046, 1025, 972, 753, 603; HRMS: (ESI-TOF) *m/z* calcd for $C_{24}H_{34}O_6Si$ (M + H) 447.2210, found 447.2197.

2-Acetoxy-6-((*R*,1*E*,5*E*)-4-hydroxy-3-oxohepta-1,5-dien-1-yl)benzyl acetate (23): To a solution of compound **22** (940 mg, 2.1076 mmol) in dry THF (12.6 mL) in a plastic vial at 0 ºC was added a solution of HF. py (70% solution in py, 2.5 mL, 5.5291 mmol) dropwise using a plastic syringe. Then, the reaction was allowed to rt and stirred for overnight. After completion of the starting material, the reaction was quenched with saturated aq $NaHCO_3$ solution by maintaining pH neutral. Then, the aqueous layer was extracted with EtOAc, and the organic layer was washed with water, brine, dried over Na_2SO_4, and concentrated under vacuum. The crude compound was purified by flash column chromatography to get compound **23 (**611 mg) as a light yellowish liquid. Yield: 85%; R_f = 0.3 (50% EtOAc/hexanes); $[\alpha]^{25}_D$: -52.88 (c 2.6, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.14 (d, *J* = 15.9 Hz, 1H), 7.53 (d, *J* = 8.0 Hz, 1H), 7.42 (t, *J* = 8.0 Hz, 1H), 7.17 (dd, *J* = 8.0, 1.0 Hz, 1H), 6.80 (d, *J* = 15.9 Hz, 1H), 6.03 (m, 1H), 5.44 (ddq, *J* = 15.2, 7.9, 1.6 Hz, 1H), 5.21 (s, 2H), 4.82 (d, *J* = 7.9 Hz, 1H), 3.89 (brs, 1H), 2.35 (s, 3H), 2.03 (s, 3H), 1.78 (dd, *J* = 6.6, 1.6 Hz, 3H); ^{13}C{H} NMR (100 MHz, $CDCl_3$) δ 197.9, 170.4, 169.4, 150.2, 140.9, 136.5, 132.6, 130.0, 127.7, 127.4, 124.9, 124.8, 124.2, 77.7, 56.8, 20.8, 20.7, 18.0; IR (Neat): ν_{max} 3449, 2954, 2926, 2854, 1770, 1738, 1468, 1374, 1224, 1202, 1185, 1091, 1046, 1024, 968, 863, 836, 777, 663; HRMS: APCI corona Full ms m/z: $(M + Na)^+$ calcd for $C_{18}H_{20}O_6Na$ 355.1152; found 355.1139.

2-Acetoxy-6-((1*E*, 3*S*, 4*R*, 5E)-3, 4-dihydroxyhepta-1, 5-dien-1-yl) benzyl acetate (20): To a solution of compound **23** (456 mg, 1.373) in dry ether (5.5 mL) at –78 ºC was added $LiEt_3BH$ (2.06 mL, 1.0 M in THF, 2.0602 mmol). The reaction mixture was stirred at –78 °C for 10 min and observed disappearing of starting material and formation of the complex on TLC.

Subsequently, the reaction was quenched with aq NH_4Cl solution and stirred for a long time to diminish the complex. The aqueous layer was extracted with EtOAc, and the organic layer was dried over Na_2SO_4 and concentrated in *vacuum*. The extracted compound was purified by using silica gel column chromatography (the complex was converted to product during column purification) to afford anti-diol **20** (338 mg, dr 93:07 based on the ^1H NMR) as a colorless liquid. Yield: 74%; R_f = 0.3 (50% EtOAc/hexanes); $[\alpha]^{26}_D$: +18.75 (c 0.23, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.37– 7.33 (m, 2H), 7.02 (m, 1H), 6.91 (dd, *J* = 15.7, 1.3 Hz, 1H), 6.03 (dd, *J* = 15.7, 6.7 Hz, 1H), 5.79 (m, 1H), 5.43 ddq, *J* = 15.2, 8.0, 1.6 Hz, 1H), 5.15 (s, 2H), 5.03 (ddd, *J* = 8.0, 6.7, 1.3 Hz, 1H), 4.90 (t, *J* = 8.0 Hz, 1H), 2.33 (s, 3H), 2.03 (s, 3H), 1.73 (dd, *J* = 6.6, 1.6 Hz, 3H); $^{13}C\{H\}$ NMR (100 MHz, $CDCl_3$): δ 170.7, 169.6, 150.08, 132.08, 130.2, 129.7, 129.0, 128.9, 124.6, 122.01, 75.6, 75.2, 57.5, 20.9, 20.8, 17.9; IR (Neat): ν_{max} 3405, 2922, 2852, 1764, 1735, 1638, 1580, 1467, 1373, 1225, 1204, 1185, 1044, 1025, 968, 756, 604; HRMS: (ESI-TOF) m/z: $(M + Na)^+$ calcd for $C_{18}H_{22}O_6Na$ 357.1313; found 357.1308.

***Enantiomer*-dihdropyriculol (*ent*-3):**[3,4,20a] To a solution of diacetyl compound **20** (37 mg, 0.110 mmol) in THF (1.1 mL) at 0 ºC was added LAH (12.6 mg, 0.332 mmol) in portion wise and stirred at rt till completion of the starting material (3 h). The reaction was quenched (slowly at 0 ºC) with saturated aq Na_2SO_4 and filtered through a sintered funnel. The aqueous layer was extracted with EtOAc, and the organic layer was washed with brine solution, dried over Na_2SO_4, and evaporated under reduced pressure. The crude product was purified by using silica gel column chromatography to get the enantiomer of dihydropyriculol (*ent*-**3**) (19 mg) as a gummy compound. Yield: 69%; R_f = 0.3 (80% EtOAc/hexanes); $[\alpha]^{24}_D$: -7.33 (c 0.40, MeOH); ^1H NMR: (300 MHz, CD_3OD + $CDCl_3$) δ 7.10 (t, *J* = 7.9 Hz, 1H), 6.97 (d, J = 8.0 Hz, 1H), 6.91 (d, *J* = 15.8 Hz, 1H) 6.76 (d, *J* = 8.0 Hz, 1H), 6.10 (dd, *J* = 15.8, 6.4 Hz, 1H), 5.78 (m, 1H), 5.55 (m,

1H), 4.84 (ABq, *J* = 12.6 Hz, 2H), 4.24 (m, 1H), 4.12 (m, 1H), 1.74 (d, *J* = 6.4 Hz, 1H); ^{13}C{H} NMR (75 MHz, CD_3OD + $CDCl_3$): δ 157.25, 138.98, 132.29, 130.69, 130.46, 130.07, 124.91, 119.62, 116.39, 76.97, 76.85, 58.48, 19.07; IR (Neat): ν_{max} 3375, 3019, 2918, 2855, 2360, 1639, 1609, 1569, 1450, 1328, 1310, 1237, 1193, 1163, 1081, 1045, 1009, 965, 845, 798, 750, 720, 666; HRMS: (ESI-TOF) m/z: $(M + Na)^+$ calcd for $C_{14}H_{18}O_4Na$ 273.1099; found 273.1097.

2-Acetoxy-6-((1*E*,3*R*,4*R*,5*E*)-4-((*tert*-butyldimethylsilyl)oxy)-3-hydroxyhepta-1,5-dien-1-yl)benzyl acetate (24): To a stirred solution of α,β-unsaturated ketone **22** (2.1 g, 4.706 mmol) in MeOH (28.2 mL) was added anhydrous $CeCl_3$ (5.2 g, 14.119 mmol) and allowed to stir for 30 min at rt. The reaction mixture was cooled to –50 °C and added $NaBH_4$ (178 mg, 4.7064 mmol) portion-wise and continued stirring for 20 min. After completion of the starting material (monitored by TLC), the reaction was quenched by the addition of water at the same temperature, slowly allowed to rt, and continued stirring for another 30 min. Then, the MeOH was evaporated with rotary evaporated and poured the reaction mixture into ice-cold water and extracted with EtOAc. Combined organic layers were washed with brine and dried over Na_2SO_4. The crude compound was purified by using silica gel column chromatography to get pure compound **24** (1.96 g, dr 87:13 based on the ^{1}H NMR) as a colorless liquid. Yield: 93% (dr 87:13); R_f = 0.4 (30% EtOAc/hexanes); $[\alpha]^{24}_D$: +7.53 (c 0.38, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37-7.29 (m, 2H), 6.99 (dd, *J* = 6.4, 2.7 Hz, 1H), 6.95 (dd, *J* = 15.8, 1.4 Hz, 1H), 6.09 (dd, *J* = 15.8, 5.7 Hz, 1H), 5.67 (m, 1H), 5.46 (ddq, *J* = 15.3, 7.6, 1.6 Hz 1H), 5.15 (s, 2H), 4.10 (t, *J* = 6.4 Hz, 1H), 3.97 (t, *J* = 6.9 Hz, 1H), 2.32 (s, 3H), 2.02 (s, 3H), 1.71 (dd, *J* = 6.4, 1.5 Hz, 3H), 0.91 (s, 9H), 0.08 (s, 3H), 0.06 (s, 3H); ^{13}C{H} NMR (100 MHz $CDCl_3$): δ 170.7, 169.6, 150, 139.8, 132.9, 130.6, 129.6, 129.3 ,127.8, 125.1, 124.4, 121.7, 77.6, 75.6, 57.5, 25.8, 20.9, 20.8, 18.1, 17.7, -3.8, -4.7; IR(Neat): ν_{max}3406, 2954, 2926, 2854, 1770, 1738, 1468, 1374,

1224, 1202, 1185, 1091, 1046, 1024, 968, 863, 836, 777, 738, 673; HRMS: (ESI-TOF) m/z: $(M + Na)^+$ calcd for $C_{24}H_{36}O_6SiNa$ 471.2183; found 471.2173.

2-Acetoxy-6-((1*E*,3*R*,4*R*, 5*E*)-3,4-dihydroxyhepta-1,5-dien-1-yl)benzyl acetate (25): Syn-diol **25** (929 mg) as a colorless liquid was prepared from compound **24** (1.4 g, 3.125 mmol) following the same procedure used for the synthesis of **23**. Yield: 89%; R_f = 0.3 (30% EtOAc/hexanes); $[\alpha]^{28}_D$: +23.63 (c 0.16, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34-7.30 (m, 2H), 7.0–6.96 (m, 2H), 6.10 (dd, *J* = 15.8, 6.0 Hz, 1H), 5.79 (m, 1H), 5.52 (ddq, *J* = 15.3, 7.0, 1.6 Hz, 1H), 5.15 (ABq, *J* = 12.3 Hz, 2H), 4.16 (t, *J* = 7.0 Hz, 1H), 3.99 (t, *J* = 7.0 Hz, 1H), 3.01 (brs, 1H), 2.78 (brs, 1H), 2.32 (s, 3H), 2.01 (s, 3H), 1.71 (dd, *J* = 6.5, 1.0 Hz, 3H); ^{13}C{H} NMR (100 MHz, $CDCl_3$)**:** δ 170.9, 169.7, 150.1, 139.5, 132.8, 129.9, 129.7, 129.5, 128.4, 125.2, 124.5, 121.9, 75.9, 75.5, 57.6, 20.9, 20.8, 17.9; IR (Neat): ν_{max} 3405,2922, 2852, 2337, 1764, 1735, 1638, 1605, 1580, 1467, 1373, 1225, 1204, 1185, 1078, 1044, 1025, 968, 756, 604; HRMS: (ESI-TOF) m/z: $(M + Na)^+$ calcd for $C_{18}H_{22}O_6Na$ 357.1313; found 357.1308.

Enantiomer of epidihydropyriculol (*ent*-4):[3] Enantiomer of epidyhydropyriculol *ent*-**4** (31.6 mg) as a light yellow liquid was prepared from *syn*-diol **25** (48 mg, 0.01437 mmol) following the same procedure used for the synthesis of *ent*-**3**. Yield: 88%; R_f = 0.3 (30% EtOAc/hexanes); $[\alpha]^{24}_D$: +19.67 (c 0.30, EtOH); ^{1}H NMR (300 MHz, $CDCl_3$ + CD_3OD) δ 7.11 (dd, *J* = 7.8, 7.1 Hz, 1H), 6.99 (brs, 1H), 6.95 (d, *J* = 7.1 Hz, 1H), 6.77 (d, *J* = 7.8 Hz, 1H), 6.09 (dd, *J* = 15.8, 6.5 Hz, 1H), 5.80 (dq, *J* = 15.3, 6.4 Hz, 1H), 5.56 (ddq, *J* = 15.3, 7.1, 1.6 Hz, 1H), 4.83 (ABq, *J* = 13.0 Hz, 2H), 4.15 (m, 1H), 4.01 (t, *J* = 6.9 Hz, 1H), 1.74 (d, *J* = 6.3 Hz, 3H); ^{13}C{H} NMR (75 MHz, CDCl3+CD3OD) δ 155.8, 137.7, 131.2, 129.8, 129.1, 128.7, 128.4, 123.5, 117.7, 114.4, 75.7, 75.5, 56.4, 17.2; IR (Neat): ν_{max} 3376, 3027, 1639, 1609, 1569, 1450, 1379, 1328, 1310, 1237,

1193, 1163, 1081, 1045, 1008, 965, 798, 749, 720; HRMS: (ESI-TOF) m/z: $(M + Na)^+$ calcd for $C_{14}H_{18}O_4Na$ 273.1099; found 273.1097.

2-Acetoxy-6-((E)-2-((4S,5R)-2,2-dimethyl-5-((E)-prop-1-en-1-yl)-1,3-dioxolan-4-yl)vinyl)benzyl acetate (26): To a solution of diol compound **20** (115 mg, 0.3443 mmol) in acetone (2.5 mL) was added 2,2-dimethoxypropane (DMP) (0.10 mL, 0.860 mmol) followed by catalytic amount of PTSA (5.9 mg, 0.034 mmol) and the reaction was stirred for overnight at rt. After completion of the starting material, the reaction was quenched with water, and the reaction mixture was extracted with EtOAc. The organic layer was washed with brine solution, dried over Na_2SO_4, and concentrated under reduced pressure. The compound was purified by flash column chromatography to get **26** (105 mg) as a colorless liquid. Yield: 82%; R_f = 0.6 (20% EtOAc/hexanes); $[\alpha]^{24}_D$: -57.40 (c 0.15, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38–7.32 (m, 2H), 7.01 (dd, *J* = 6.3, 3.0 Hz, 1H), 6.91 (dd, *J* = 15.7, 0.9 Hz, 1H), 6.05 (dd, *J* = 15.7, 7.4 Hz, 1H), 5.80 (m, 1H), 5.45 (ddq, *J* = 15.2, 8.3, 1.6 Hz, 1H), 5.15 (s, 2H), 4.75 (m, 1H), 4.65 (m, 1H), 2.33 (s, 3H), 2.03 (s, 3H), 1.72 (dd, *J* = 6.5, 1.6 Hz, 3H), 1.56 (s, 3H), 1.42 (s, 3H); ^{13}C{H} NMR (100 MHz, $CDCl_3$) δ 170.7, 169.6, 150.0, 139.4, 131.2, 130.7, 129.7, 129.1, 126.7, 125.2, 124.7, 122.0, 108.8, 80.1, 79.4, 57.5, 28.1, 25.5, 20.9, 20.8, 17.9; IR (Neat): ν_{max} 3019, 2927, 1735, 1469, 1372, 1214, 1186, 1048, 969, 929, 879, 743, 667; HRMS: (ESI-TOF) m/z: $(M + Na)^+$ calcd. for $C_{21}H_{26}O_6Na$ 397.1630; found 397.1621.

3-((*E*)-2-((4*S*,5*R*)-2,2-Dimethyl-5-((*E*)-prop-1-en-1-yl)-1,3-dioxolan-4-yl)vinyl)-2-(hydroxymethyl)phenol (27): Compound **27** (17.1 mg) as oil was prepared from compound **26** (27.2 mg, 0.072 mmol) following the same procedure used for the synthesis of ent-**3**. Yield: 81%; R_f = 0.4 (30% EtOAc/hexanes); $[\alpha]^{24}_D$: -26.9 (c 0.31, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (brs, 1H), 7.16 (t, *J* = 7.9 Hz, 1H), 6.92 (d, *J* = 7.9 Hz, 1H), 6.82 (d, *J* = 7.9 Hz, 1H), 6.75

(d, *J* = 15.5 Hz, 1H), 5.92 (dd, *J* = 15.6 Hz, 7.3 Hz, 1H), 5.80 (dq, *J* = 15.5 Hz, 6.5 Hz, 1H), 5.45 (ddq, *J* = 15.5 Hz, 8.2 Hz, 1.6 Hz, 1H), 4.98 (s, 2H), 4.72 (dd, *J* = 7.3, 6.9 Hz, 1H), 4.64 (dd, *J* = 8.2, 6.9 Hz, 1H), 2.22 (brs, 1H), 1.73 (dd, *J* = 6.5 Hz, 1.6 Hz, 3H), 1.55 (s, 3H), 1.42 (s, 3H); ^{13}C{H} NMR (100 MHz, $CDCl_3$): δ 156.5, 136.0, 132.1, 130.4, 129.0, 128.9, 126.7, 122.0, 118.9, 116.2, 109.0, 82.4, 81.8, 60.1, 27.1, 27.0, 17.9; IR (Neat): ν_{max} 3331, 2985, 2921, 2852, 1711, 1679, 1582, 1467, 1373, 1279, 1254, 1228, 1165, 1050, 994, 965, 879, 838, 809, 787, 756, 666; HRMS: APCI corona Full ms m/z: $(M + Na)^+$ calcd for $C_{17}H_{22}O_4Na$ 313.1410; found 313.1376.

2-((*E*)-2-((4*S*,5*R*)-2,2-dimethyl-5-((*E*)-prop-1-en-1-yl)-1,3-dioxolan-4-yl)vinyl)-6-hydroxybenzaldehyde (28): Benzyl alcohol compound **27** (17.1 mg, 0.058 mmol) was taken in dry CH_2Cl_2 (2.5 mL) and added MnO_2 (51.2 mg, 0.589 mmol, 10 equiv) and stirred for overnight (8-10 h) at rt. After completely disappearing the starting material (monitored by TLC), the reaction mixture was filtered through a pad of silica gel, concentrated and purified by flash column chromatography to give **28** as a viscous oil (14.4 mg). Yield: 85%; R_f = 0.5 (10% EtOAc/hexanes); $[\alpha]^{23}_D$: -29.9 (c 0.21, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) *δ* 11.86 (s, 1H), 10.29 (s, 1H), 7.46 (t, *J* = 8.0 Hz, 1H), 7.09 (d, *J* = 15.7 Hz, 1H), 6.92-6.87 (m, 2H), 6.00 (dd, *J* = 15.7, 6.7 Hz, 1H), 5.82 (dt, *J* = 13.0, 6.7 Hz, 1H), 5.45 (ddd, *J* = 15.7, 8.0, 1.6 Hz, 1H), 4.79 (t, *J* = 6.7 Hz, 1H), 4.72-4.67 (m, 1H), 1.75 dd, *J* = 6.7, 1.6 Hz, 3H), 1.44 (s, 6H); ^{13}C{H} NMR (100 MHz, $CDCl_3$) δ 195.1, 162.7, 141.8, 137.1, 132.9, 132.3, 127.4, 126.6, 118.8, 117.3, 109.2, 82.3, 81.2, 27.1, 26.9, 17.8; IR (Neat): ν_{max} 2955, 2921, 2851, 1737, 1648, 1452, 1377, 1329, 1236, 1164, 1052, 965, 841, 756, 722 HRMS: (ESI/TOF) m/z: $(M + H)^+$ calcd for $C_{17}H_{21}O_4$ 289.1436; found 289.1434.

Enatiomer of pyriculol (*ent*-1):[16b-c] Acetonide protected compound **28** was taken in a round bottom flask and added THF (0.2 mL) via syringe. The reaction mixture was cooled to 0 °C, added 1N HCl (0.1 mL, 2 equiv), and stirred for 3 h at rt. The reaction mixture was quenched with ice-cold water, and extracted with EtOAc. The organic layer was washed with brain solution, dried over Na_2SO_4, and concentrated using rotary evaporator. The crude compound was purified by using silica gel column chromatography to yield ent-**1** (11.9 mg) as yellow crystalline solid. Yield: 73%; MP: 96-98 ºC; R_f = 0.3 (50% EtOAc/hexanes); $[\alpha]^{25}_D$: -39.9 (c 0.05, MeOH); ^{1}H NMR (400 MHz, CDCl3): δ 11.85 (s, 1H), 10.31 (s, 1H), 7.45 (t, *J* = 8.0 Hz, 1H), 7.17 (d, J = 15.6 Hz, 1H), 6.91 (d, J = 8.0 Hz, 1H), 6.89 (d, J = 8.0 Hz, 1H), 6.11 (dd, J = 15.6, 5.7 Hz, 1H), 5.84 (m, 1H), 5.56 (ddq, J = 15.6, 7.2, 1.5 Hz, 1H), 4.38 (m, 1H), 4.23 (m, 1H), 2.27 (d, J = 4.5 Hz, 1H), 1.91 (d, J = 3.7 Hz, 1H), 1.75 (d, J = 6.5 Hz, 3H); ^{13}C{H} NMR (100 MHz, $CDCl_3$) δ 195.4, 162.7, 142.3, 137.0, 135.2, 130.6, 128.7, 126.6, 118.9, 117.1, 75.6, 74.7, 17.9; IR (Neat): ν_{max} 3374, 2921, 2852, 1642, 1610, 1569, 1451, 1329, 1310, 1238, 1193, 1164, 1082, 1009, 966, 924, 798, 751, 721; HRMS: (ESI/TOF m/z (M + Na) calcd for $C_{14}H_{16}O_4Na$ 271.0936; found 271.0940.

2-Acetoxy-6-((*E*)-2-((4*R*,5*R*)-2,2-dimethyl-5-((*E*)-prop-1-en-1-yl)-1,3-dioxolan-4-yl)vinyl)benzyl acetate (29): Compound **29** (216 mg) as a sticky oil was prepared from diol compound **25** (250 mg, 0.748 mmol) following the same procedure used for the synthesis of **26**. Yield: 77%; R_f = 0.6(20% EtOAc/hexanes); $[\alpha]^{28}_D$: +5.17 (c 0.29, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40 (d, J = 7.9 Hz, 1H), 7.34 (t, *J* = 7.9 Hz, 1H), 7.01 (dd, *J* = 7.9, 1.0 Hz, 1H), 6.97 (d, *J* = 15.7 Hz, 1H), 6.08 (dd, *J* = 15.7, 6.9 Hz, 1H), 5.82 (m, 1H), 5.50 (ddq, *J* = 15.2, 7.8, 1.6 Hz, 1H), 5.13 (ABq, *J* = 12.1 Hz, 2H), 4.27 (m, 1H), 4.14 (t, *J* = 8.0 Hz, 1H), 2.32 (s, 3H), 2.02 (s, 3H), 1.73 (dd, *J* = 6.5, 1.6 Hz, 3H), 1.48 (s, 3H), 1.47 (s, 3H); ^{13}C{H} NMR (100 MHz,

$CDCl_3$): δ 170.7, 169.6,150.0, 139.4, 131.2. 130.7, 129.7, 129.1, 126.7, 125.2, 124.7, 122.0, 108.8, 80.1, 79.4, 57.5, 28.1, 25.5, 20.9, 20.8, 17.9; IR (Neat): ν_{max} 3019, 2927, 1735, 1372, 1214, 1048, 969, 929, 743, 667; HRMS: (ESI-TOF) *m/z* calcd for $C_{21}H_{26}O_6Na$ $(M + Na)^+$ 397.1630, found 397.1621

3-((*E*)-2-((4*R*,5*R*)-2,2-dimethyl-5-((*E*)-prop-1-en-1-yl)-1,3-dioxolan-4-yl)vinyl)-2-(hydroxymethyl)phenol (30): Compound **30** (123 mg) as a colorless sticky oil was prepared from compound **29** (180 mg, 0.4781 mmol) following the same procedure used for the synthesis of compound **27**. Yield: 88%; R_f = 0.4 (30% EtOAc/hexanes); $[\alpha]^{28}_D$: +21.87 (c 0.16 $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (brs, 1H), 7.12 (t, *J* = 7.9 Hz, 1H), 6.94 (d, *J* = 7.5 Hz, 1H), 6.80 (d, *J* = 15.6 Hz, 1H), 6.79 (d, *J* = 7.5 Hz, 1H), 5.93 (dd, *J* = 15.6, 6.9 Hz, 1H), 5.82 (m, 1H), 5.48 (ddq, *J* = 15.2, 7.7, 1.6 Hz, 1H), 4.92 (s, 2H), 4.22 (ddd, *J* = 8.1, 6.9, 0.9 Hz, 1H), 4.12 (t, *J* = 8.0 Hz, 1H), 1.73 (dd, *J* = 6.6, 1.6 Hz, 3H), 1.47 (s, 3H), 1.46 (s, 3H); ^{13}C{H} NMR (100 MHz $CDCl_3$): δ 156.4, 136.0, 132.1, 130.5, 128.9, 128.8, 126.7, 122.2, 118.9, 116.1, 109.0, 82.4, 81.8, 59.8, 27.1, 27.0, 17.9; IR (Neat): ν_{max} 3331, 2985, 2921, 2852, 1711, 1605, 1582, 1467, 1373, 1279, 1254, 1228, 1165, 965, 838, 756, 627; HRMS: APCI corona Full ms m/z calcd for $C_{17}H_{23}O_4$ $(M + H)^+$ 293.1747, found 293.1715.

2-((*E*)-2-((4*R*,5*R*)-2,2-dimethyl-5-((*E*)-prop-1-en-1-yl)-1,3-dioxolan-4-yl)vinyl)-6-hydroxybenzaldehyde (31): Salicylaldehyde derivative **31** (68 mg) as a yellow color compound was prepared from benzylic alcohol compound **30** (75 mg, 0.256 mmol) following the same procedure used for the synthesis of **28**. Yield: 92%; R_f = 0.5 (10% EtOAc/hexanes); $[\alpha]^{28}_D$: +26.66 (c, 0.07, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.84 (s, 1H), 10.28 (s, 1H), 7.45 (t, *J* = 8.0 Hz, 1H), 7.17 (d, *J* = 15.6 Hz, 1H), 6.93 (d, *J* = 7.6 Hz, 1H), 6.89 (d, *J* = 8.4 Hz, 1H), 6.05 (dd, *J* = 15.6, 6.4 Hz, 1H), 5.85 (m, 1H), 5.51 (ddq, *J* = 15.2, 7.9, 1.6 Hz, 1H), 4.28 (ddd, 7.7,

6.4, 1.1 Hz, 1H), 4.14 (t, *J* = 8.2 Hz, 1H), 1.75 (dd, *J* = 6.5, 1.6 Hz, 3H), 1.48 (s, 3H), 1.47 (s, 3H); $^{13}C\{H\}$ NMR (100 MHz, $CDCl_3$): δ 196.1, 162.8, 141.9, 137.1, 132.9, 132.4, 127.5, 126.7, 118.9, 117.4, 117.3, 109.3, 82.4, 81.3, 27.1, 26.9, 17.9; IR (Neat): ν_{max} 2955, 2921, 2851, 1737, 1648, 1611, 1452, 1377, 1312, 1236, 1164, 1052, 965, 882, 756, 722; HRMS: (ESI-TOF) *m/z* calcd for $C_{17}H_{21}O_4$ $(M + H)^+$ 289.1436, found 289.1434.

Enantiomer of epipyriculol (*ent*-2):[16c] The enantiomer of epipyriculol (*ent*-**2**) (17.7 mg) as a yellow color sticky compound was prepared from compound **31** (24 mg, 0.0827 mmol) following the same procedure used for the synthesis of *ent*-**1**. Yield: 77%; R_f = 0.2 (50% EtOAc/hexanes); $[\alpha]^{26}_D$: +29.41 (c 0.08, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 11.85 (s, 1H), 10.29 (s, 1H), 7.44 (t, *J* = 8.0 Hz, 1H), 7.18 (d, *J* = 15.7 Hz, 1H), 6.90 (d, J = 7.2 Hz, 1H), 6.88 (d, *J* = 7.5 Hz, 1H), 6.08 (dd, *J* = 15.7, 5.5 Hz, 1H), 5.83 (dq, *J* = 15.7, 6.5 Hz, 1H), 5.55 (ddq, *J* = 15.3, 7.3, 1.6 Hz, 1H), 4.22 (t, *J* = 5.7 Hz, 1H), 4.03 (t, *J* = 7.0 Hz, 1H), 2.78 (brs, 1H), 2.36 (brs, 1H), 1.74 (dd, *J* = 6.5, 1.5 Hz, 3H); $^{13}C\{H\}$ NMR (100 MHz $CDCl_3$): δ 195.3, 162.5, 142.1, 136.9, 136.5, 130.4, 129.2, 126.1, 118.7, 117.2, 116.9, 75.9, 75.0, 17.7; IR (Neat): ν_{max} 3374, 3023, 2919, 2852, 1717, 1642, 1610, 1569, 1451, 1329, 1310, 1238, 1193, 1164, 1009, 966, 798, 751, 721; HRMS: (ESI-TOF) *m/z* $(M + Na)^+$ calcd for $C_{14}H_{16}O_4Na$ 271.0936, found 271.0940.

Dimethyl (*S*)-(3-((*tert*-butyldimethylsilyl)oxy)-2-oxobutyl)phosphonate (33):[27] To a solution of dimethyl methylphosphonate (5.1 g, 41.66 mmol) in dry THF (30 mL) under inert conditions at -78 □ was added *n*-BuLi (17.3 mL, 27.77 mmol) dropwise and stirred for 45 min at same the temperature. Next, (-)-methyl L-lactate (3.0 g, 13.88 mmol) in dry THF (25 mL) was cannulated drop wise to the reaction mixture. After completion of the starting material (15 min), the reaction was quenched with saturated aq NH_4Cl at -78 □ and left it to rt. The reaction mixture was extracted with EtOAc, and the organic layer was washed with brine solution, dried over Na_2SO_4,

and concentrated under reduced pressure. The product was purified by using silica gel column chromatography to afford **33** as a light yellow color liquid (3.6 g). Yield: 93%; R_f = 0.3 (50% EtOAc/hexanes); $[\alpha]^{26}_D$: +9.3 (*c* 0.3, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.24 (q, *J* = 6.8 Hz, 1H), 3.81 (d, $J_{P,H}$ = 11.2 Hz, 3H), 3.78 (d, $J_{P,H}$ = 11.2 Hz, 3H), 3.37 (dd, $J_{P,H}$ = 21.2, $J_{H,H}$ = 14.9 Hz, 1H), 3.25 (dd, $J_{P,H}$ = 21.2, $J_{H,H}$14.9 Hz, 2H) 1.32 (d, *J* = 6.8 Hz, 3H), 0.92 (s, 9H), 0.11 (s, 3H), 0.10 (s, 3H); ^{13}C{H} NMR (100 MHz, $CDCl_3$): δ 205.2 (d, J_{CP} = 6.8 Hz), 74.8 (d, J_{CP} = 3.2 Hz), 53.0 (d, J_{CP} = 6.3 Hz) 52.9 (d, J_{CP} = 6.3 Hz), 34.6 (d, J_{CP} = 135.2 Hz), 25.7, 20.2, 18.0, -4.6, -5.0; IR (Neat): ν_{max} 2955, 2929, 2855, 1721, 1463, 1254, 1134, 1030, 938, 836, 809, 779, 663; HRMS: (ESI-TOF) *m/z* calcd for $C_{12}H_{27}O_5NaSiP$ $(M + Na)^+$ 333.1263 found 333.1270.

(*S*,*E*)-2-Acetoxy-6-(4-((*tert*-butyldimethylsilyl)oxy)-3-oxopent-1-en-1-yl)benzyl acetate (32): *β*-Ketophosphonate **33** (3.5 g, 12.4 mmol) was dissolved in THF (30 mL) and cooled to –78 °C, then 0.5 M KHMDS (14.8 mmol, 30mL) was added dropwise. After 30 min at –78 °C, 2-acetoxy-6-formylbenzyl acetate (**19**) (14.89 mmol) dissolved in THF (20 mL) was cannulated dropwise. Then the reaction mixture was left to rt, and run for 12 h at rt. After completion of the reaction (monitored by TLC), it was quenched by the addition of water and extracted with EtOAc. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated by using rotary evaporator. The crude product was purified by using silica gel column chromatography to give α,β-unsaturated ketone **32** as a light yellow liquid (4.4 g). Yield: 84%; R_f = 0.6 (30% EtOAc/hexanes); $[\alpha]^{26}_D$: -38.02 (*c* 1.92, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.04 (d, *J* = 15.8 Hz, 1H), 7.55 (d, *J* = 7.4 Hz, 1H), 7.40 (t, *J* = 7.4 Hz, 1H), 7.22 (d, *J* = 15.8 Hz, 1H), 7.13 (d, *J* = 7.4, 1H), 5.22 (ABq, *J* = 12.3, 16.6 Hz, 2H), 4.34 (q, *J* = 6.8 Hz, 1H), 2.33 (s, 3H), 2.01 (s, 3H), 1.36 (d, *J* = 6.8 Hz, 3H), 0.92 (s, 9H), 0.10 (s, 3H), 0.08 (s, 3H); ^{13}C{H} NMR (125 MHz, $CDCl_3$): δ 201.5, 170.5, 169.4, 150.1, 139.7, 137.2, 129.9, 127.5, 124.5, 124.4, 123.7, 74.6, 56.8,

25.8, 21.1, 20.9, 20.7, 18.2, -4.7, -4.9; IR (Neat): ν_{max} 2954, 2929, 2856, 1772, 1742, 1719, 1614, 1469, 1368, 1222, 1183, 1119, 1089, 1025, 941, 833, 779, 673; HRMS: (ESI-TOF) *m/z* calcd for $C_{22}H_{32}O_6SiNa$ $(M + Na)^+$ 443.1866, found 443.1873.

(*S*,*E*)-2-Acetoxy-6-(4-hydroxy-3-oxopent-1-en-1-yl)benzyl acetate (34): Compound **34** as a light yellow colored liquid (0.790 gm) was prepared from compound **32** (1.42 g, 3.38 mmol) following the similar procedure used for the synthesis of **23**. Yield: 79%; R_f = 0.5 (50% EtOAc/hexanes); $[\alpha]^{25}_D$: +6.9 (*c* 1.81, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.11 (d, *J* = 15.8 Hz, 1H), 7.54 (d, *J* = 7.9 Hz, 1H), 7.41 (t, *J* = 7.9 Hz, 1H), 7.15 (d, *J* = 7.9 Hz, 1H), 6.79 (d, *J* = 15.8 Hz, 1H), 5.21 (s, 2H), 4.56 (m, 1H), 3.68 (d, *J* = 5.2 Hz, 1H), 2.34 (s, 3H), 2.01 (s, 3H), 1.44 (d, *J* = 7.1 Hz, 3H); ^{13}C{H} NMR (125 MHz, $CDCl_3$): δ 220.8, 170.4, 169.4, 150.2, 140.9, 136.4, 130.0, 127.6, 124.9, 124.7, 123.9, 71.9, 56.8, 20.8, 20.7, 20.4; IR (Neat): ν_{max} 3474, 2982, 1765, 1738, 1687, 1615, 1574, 1468, 1370, 1223, 1203, 1185, 1068, 1026, 979, 794; HRMS: (ESI-TOF) *m/z* calcd for $C_{16}H_{18}O_6Na$ $(M + Na)^+$ 329.1001, found 329.1006.

2-Acetoxy-6-((3*R*,4*S*,*E*)-3,4-dihydroxypent-1-en-1-yl)benzyl acetate (35): Anti-diol **35** as a colorless liquid (250 mg, dr 86:14) was prepared from compound **34** (397 mg, 1.297 mmol) following the procedure used for the synthesis of **20**. Yield: 63%; R_f = 0.4 (50% EtOAc/hexanes); $[\alpha]^{25}_D$: +9.2 (*c* 0.5, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39 (m, 1H), 7.34 (t, *J* = 7.8 Hz, 1H), 7.03-6.96 (m, 2H), 6.17 (dd, *J* = 6.6, 15.8 Hz, 1H), 5.17 (ABq, *J* = 12.0, 16.2 Hz, 2H), 4.27 (m, 1H), 3.96 (m, 1H), 2.33 (s, 3H), 2.02 (s, 3H), 1.19 (d, *J* = 6.4 Hz, 3H); ^{13}C{H} NMR (100 MHz, $CDCl_3$): δ 170.9, 169.6, 150.1, 139.3, 131.9, 129.8, 129.1, 125.2, 124.5, 122.0, 76.2, 70.3, 57.5, 20.9, 20.8, 17.8; IR (Neat): ν_{max} 3429, 2923, 1764, 1736, 1560, 1468, 1371, 1225, 1204, 1168, 1024, 971, 930, 738; HRMS: (ESI-TOF) *m/z* calcd for $C_{16}H_{20}O_6Na$ $(M + Na)^+$ 331.1158 found 331.1162;

***trans*-Sordariol (11):**[10a-b] To a solution of diacetyl compound **35** (31 mg, 0.1006 mmol) in dry THF (1.5 mL) at -78 ºC was added an excess amount of DIBAL-H (1.0 M solution in toluene, 1.0 mL, 1.0064 mmol) dropwise. The reaction was slowly brought to rt and stirred untill the completion of the starting material (~1 h, monitored by TLC). The reaction was quenched (slowly at 0 ºC) with saturated Rochelle salt ($KNaC_4H_4O_6$) solution, and stirred at rt for 4-6 h. The reaction mixture was extracted with EtOAc, and the organic layer was washed with brine solution, dried over Na_2SO_4, evaporated under reduced pressure. The crude product was purified by using silica gel column chromatography to get the *trans*-sordariol **11** as yellow sticky solid (16.7 mg). Yield: 74 %; R_f = 0.4 (10% $CH_3OH/CHCl_3$); $[\alpha]^{26}_D$: = +11.6 (*c*, 0.685, MeOH); ^{1}H NMR (400 MHz, CD_3OD): δ 7.07 (t, *J* = 8.0 Hz, 1H), 7.02 (brd, *J* = 8.1 Hz, 1H), 7.0 (brd, *J* = 15.0 Hz, 1H), 6.72 (dd, *J* = 8.0, 1.2 Hz), 6.17 (dd, *J* = 15.7, 6.8 Hz, 1H), 4.78 (s, 2H), 4.07 (ddd, *J* = 6.5, 5.0, 1.2 Hz, 1H), 3.77 (dq, *J* = 6.4, 6.5 Hz, 1H), 1.20 (d, 6.4 Hz, 3H); ^{13}C{H} NMR (100 MHz, CD_3OD): δ 157.3, 139.6, 132.5, 130.6, 129.7, 125.2, 118.9, 115.3, 78.0, 71.7, 56.5, 18.9; IR (Neat): ν_{max} 3321, 2923, 1638, 1580, 1467, 1274, 1074, 1014, 978, 648, 596; HRMS: APCI corona Full ms m/z calcd for $C_{12}H_{16}O_4Na$ $(M + Na)^+$ 247.0941, found 247.0917.

2-Acetoxy-6-((3*R*,4*S*,*E*)-3,4-bis((tert-butyldimethylsilyl)oxy)pent-1-en-1-yl)benzyl acetate (36): To a solution of compound anti-diol **35** (52 mg, 0.168 mmol) in CH_2Cl_2 at 0 ºC was added 2,6-lutidine (0.07 mL, 0.675 mmol) followed by TBSOTf (0.07 mL, 0.337 mmol). Upon completion of the reaction (15 min), it was quenched with ice-cold water and extracted with CH_2Cl_2. The organic layer was washed with brine solution, dried over Na_2SO_4, and evaporated under reduced pressure. The crude product was purified by using silica gel column chromatography to afford **36** as a colorless liquid (86.2 mg). Yield: 96%; R_f = 0.6 (5% EtOAc/hexanes); $[\alpha]^{23}_D$: (-)11.4691, (*c* 1.05, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39 (dd, *J*

= 1.1, 7.8 Hz, 1H), 7.34 (t, *J* = 7.8 Hz, 1H), 6.99 (dd, *J* = 1.3, 7.8 Hz, 1H), 6.86 (d, *J* = 15.8, 1H), 6.2 (dd, *J* = 5.9, 15.8 Hz, 1H), 5.16 (s, 2H), 4.09 (m, 1H), 3.76 (dt, *J* = 6.1, 11.2 Hz, 1H), 2.33 (s, 3H), 2.02 (s, 3H), 1.16 (d, *J* = 6.1 Hz, 3H), 0.92 (s, 9H), 0.87 (s, 9H), 0.10 (s, 3H), 0.05 (s, 3H), 0.05 (s, 3H), 0.02 (s, 3H); $^{13}C\{H\}$ NMR (125 MHz, $CDCl_3$): δ 170.7, 169.6, 150.0, 140.0, 136.3, 129.7, 126.4, 124.9, 124.1, 121.4, 78.2, 72.6, 57.3, 25.9, 20.9, 20.8, 19.8, 18.2, 18.1, -4.2, -4.4, -4.5, -4.5; IR (Neat): ν_{max} 2954, 2928, 2856, 1771, 1742, 1470, 1370, 1248, 1221, 1200, 1185, 1102, 1025, 971, 833, 810, 775, 672; HRMS: (ESI-TOF) *m/z* calcd for $C_{28}H_{48}O_6Si_2Na$ 559.2887 $(M + Na)^+$, found 559.2892;

3-((3*R*,4*S*,E)-3,4-Bis((*tert*-butyldimethylsilyl)oxy)pent-1-en-1-yl)-2-(hydroxymethyl)phenol (37): Compound **37** as white crystalline solid (59 mg) was prepared from diTBS compound **36** (93 mg, 0.173 mmol) following the procedure used for the synthesis of **11**. Yield: 76 %; M.P: 63-65 ºC; R_f = 0.4 (20% EtOAc/hexanes); $[\alpha]^{23}_D$: (-)20.6014 (*c* 0.66, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ 7.71 (brs, 1H), 7.15 (t, *J* = 7.8 Hz, 1H), 6.94 (d, *J* = 7.8 Hz, 1H), 6.79 (d, *J* = 7.8 Hz, 1H), 6.72 (dd, *J* = 1.6, 15.8 Hz, 1H), 6.11 (dd, *J* = 4.6, 15.8 Hz, 1H), 5.0 (s, 2H), 4.16 (ddd, *J* = 1.6, 4.6, 4.7 Hz, 1H), 3.83 (dq, *J* = 4.7, 6.2 Hz, 1H), 1.04 (d, *J* = 6.2 Hz, 3H), 0.94 (s, 9H), 0.90 (s, 9H), 0.09 (s, 3H), 0.08 (s, 6H), 0.07 (s, 3H); $^{13}C\{H\}$ NMR (125 MHz, $CDCl_3$): δ 156.5, 137.3, 132.9, 128.9, 126.9, 121.6, 118.9, 115.5, 75.7, 71.5, 60.6, 36.6, 25.9, 18.2, 18.1, 17.4, -4.5, -4.6, -4.6, -4.7; IR (Neat): ν_{max} 3269, 2954, 2928, 2856, 1581, 1468, 1251, 1101, 990, 832, 810, 774, 672; HRMS: (ESI-TOF) *m/z* calcd for $C_{24}H_{45}O_4Si_2$ $(M + H)^+$ 453.28934, found 453.28509;

2-((3*R*,4*S*,*E*)-3,4-bis((*tert*-butyldimethylsilyl)oxy)pent-1-en-1-yl)-6-hydroxybenzaldehyde (38): Aldehyde **38** as a colorless liquid (15.4 mg) was prepared from compound **37** (20 mg, 0.044 mmol) following the procedure used for the synthesis of **28**. Yield: 81%; R_f = 0.6 (5%

EtOAc/hexanes); $[\alpha]^{25}_{D}$: -11.7 (*c* 0.17, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 11.89 (s, 1H), 10.32 (s, 1H), 7.45 (t, *J* = 8.1 Hz, 1H), 7.05 (d, *J* = 15.8 Hz, 1H), 6.90 (d, *J* = 8.1 Hz, 1H), 6.87 (d, *J* = 8.1 Hz, 1H), 6.17 (dd, *J* = 5.8, 15.8 Hz, 1H), 4.10 (m, 1H), 3.77 (dq, *J* = 5.6, 6.0 Hz, 1H), 1.17 (d, *J* = 6.0 Hz, 1H), 0.93 (s, 9H), 0.86 (s, 9H), 0.11 (s, 3H), 0.06 (s, 3H), 0.05 (s, 3H), 0.01 (s, 3H); ^{13}C{H} NMR (100 MHz, $CDCl_3$): δ 195.3, 162.8, 142.8, 138.7, 137.1, 124.7, 118.6, 117.3, 116.7, 78.1, 72.6, 25.9, 25.8, 20.0, 18.3, 18.1, -4.2, -4.4, -4.5; IR (Neat): ν_{max} 2954, 2929, 2857, 1648, 1610, 1452, 1365, 1327, 1251, 1105, 1005, 834, 775, 722; HRMS: (ESI-TOF) m/z: $[M - H]^+$ calcd for $C_{24}H_{41}O_4Si_2$ 449.2543; found 449.2557.

***trans*-Sordarial (12):**[10b,11] *trans*-Sordarial (**12**) as a yellow sticky solid (2.8 mg) was prepared from compound **39** (8.0 mg, 0.0144) following the procedure used for the synthesis of **23**. Yield: 71%; R_f = 0.3 (50 % EtOAc/hexanes); $[\alpha]^{19}_{D}$: +16.43 (*c* 0.11 MeOH); ^{1}H NMR (400 MHz, $CDCl_3$): δ 11.87 (s, 1H), 10.34 (s, 1H), 7.46 (t, *J* = 8.0 Hz, 1H), 7.20 (d, *J* = 15.7 Hz, 1H), 6.94 (d, *J* = 8.0 Hz, 1H), 6.90 (d, *J* = 8.0 Hz, 1H), 6.17 (dd, *J* = 15.7, 6.1 Hz, 1H), 4.35 (brs, 1H), 4.02 (m, 1H), 2.27 (bs, 1H), 1.99 (bs, 1H), 1.22 (d, *J* = 6.4, 3H); ^{13}C{H} NMR (100 MHz, $CDCl_3$): δ 195.23, 162.85, 142.16, 137.22, 134.81, 126.93, 118.91, 117.36, 75.82, 70.28, 17.79; IR (Neat): ν_{max} 3401, 3344, 2924, 1637, 1451, 1237, 1060, 721, 674, 663; HRMS: (ESI-TOF) *m/z* $(M + Na)^+$ calcd for $C_{12}H_{14}O_4Na$ 245.0781, found 245.0784

2-Acetoxy-6-((3*S*,4*S*, *E*)-4-((*tert*-butyldimethylsilyl)oxy)-3-hydroxypent-1-en-1-yl)benzyl acetate (39): Compound **39** as a colorless liquid (424 mg, dr 91:9 based on the ^{1}H NMR)was obtained from α,β-unsaturated ketone **32** (470 mg, 1.119 mmol) following the procedure used for the synthesis of **24**. Yield: 90%; R_f = 0.4 (20% EtOAc/hexanes); $[\alpha]^{26}_{D}$: +4.7 (*c* 0.20, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39 (dd, *J* = 7.9, 1.1 Hz, 1H), 7.34 (t, *J* = 7.9 Hz, 1H), 7.01 (dd, *J* = 7.9, 1.1 Hz, 1H), 6.98 (d, *J* = 16.0 Hz , 1H), 6.12 (dd, *J* = 15.8, 6.4 Hz, 1H), 5.18 (ABq, *J* = 12.1

Hz, 2H), 4.03 (m, 1H), 3.78 (m, 1H), 2.72 (d, *J* = 4.1 Hz, 1H), 2.34 (s, 3H), 2.03 (s, 3H), 1.21 (d, *J* = 6.1 Hz, 3H), 0.92 (s, 9H), 0.12 (s, 3H), 0.11 (s, 3H); ^{13}C{H} NMR (100 MHz, $CDCl_3$): δ 170.7, 169.5, 150.0, 139.5, 133.3, 129.7, 128.3, 125.1, 124.2, 121.8, 72.0, 57.4, 25.8, 20.9, 20.8, 20.0, 18.0, -4.1, -4.7; IR (Neat): ν_{max} 3429, 2956, 2925, 2854, 1772, 1739, 1576, 1465, 1374, 1249, 1224, 1185, 1094, 970, 836, 776, 673; HRMS: (ESI-TOF) *m/z* calcdfor $C_{22}H_{34}O_6NaSi$ $(M + Na)^+$ 445.2022 found 445.2024.

2-Acetoxy-6-((3*S*,4*S*,*E*)-3,4-bis((*tert*-butyldimethylsilyl)oxy)pent-1-en-1-yl)benzyl acetate (40): Compound **40** as a colorless liquid (290 mg) was prepared from compound **39** (264 mg, 0.625 mmol) following the similar procedure (2,6-lutidine (~0.3 mL, 2.50 mmol) and TBSOTf (~0.3 mL, 1.25 mmol)) used for the synthesis of **36**. Yield: 87%; R_f = 0.7 (5% EtOAc/hexanes); $[\alpha]^{26}_D$: -35.21 (*c* 1.98, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.39 (dd, *J* = 1.0, 7.8 Hz, 1H), 7.34 (t, *J* = 7.8 Hz, 1H), 6.98 (dd, *J* = 1.1, 7.8 Hz, 1H), 6.92 (dd, *J* = 1.5, 15.8 Hz, 1H), 6.30 (dd, *J* = 4.0, 15.8 Hz, 1H), 5.15 (s, 2H), 4.30 (ddd, *J* = 1.8, 4.5, 4.5 Hz, 1H), 3.85 (dq, *J* = 4.5, 6.1 Hz, 1H), 2.33 (s, 3H), 2.01 (s, 3H), 1.05 (d, *J* = 6.1 Hz, 3H), 0.94 (s, 9H), 0.91 (s, 9H), 0.09 (s, 6H), 0.08 (s, 6H); ^{13}C{H} NMR (125 MHz, $CDCl_3$): δ 170.7, 169.6, 149.9, 140.6, 133.5, 129.7, 126.3, 124.8, 124.4, 121.2, 75.5, 71.5, 57.5, 25.8, 25.8, 20.9, 20.8, 18.1, 18.0, 17.3, -4.5, -4.6, -4.7, -4.8; IR(Neat): ν_{max} 2954, 2929, 2886, 2856, 1772, 1742, 1469, 1368, 1249, 1222, 1201, 1184, 1104, 1048, 1007, 970, 951, 834, 810, 775, 668; HRMS: (ESI-TOF) *m/z* calcd for $C_{28}H_{48}O_6Si_2Na$ 559.2887 $(M + Na)^+$, found 559.2892;

3-((3*S*,4*S*,*E*)-3,4-bis((*tert*-Butyldimethylsilyl)oxy)pent-1-en-1-yl)-2-(hydroxymethyl)phenol (41): Compound **41** as a white crystalline solid (118 mg) was prepared from compound **40** (222 mg, 0.4141 mmol) following the same procedure used for the synthesis of **11**. Yield: 63%; M.P: 60-61 ºC; R_f = 0.5 (20% EtOAc/hexanes); $[\alpha]^{26}_D$: -28.76 (*c* 0.52, $CHCl_3$); ^{1}H NMR (400 MHz,

$CDCl_3$): δ 7.76 (brs, 1H), 7.15 (t, *J* = 7.9 Hz, 1H), 6.94 (d, *J* = 7.9 Hz, 1H), 6.79 (d, *J* = 7.9 Hz, 1H), 6.73 (dd, *J* = 1.5, 15.7 Hz, 1H), 6.11 (dd, *J* = 4.5, 15.7 Hz, 1H), 5.0 (s, 2H), 4.24 (ddd, *J* = 1.7, 4.5, 4.5 Hz, 1H), 3.75 (dq, *J* = 4.5, 6.2 Hz, 1H), 2.42 (bs, 1H), 1.04 (d, *J* = 6.2 Hz, 3H), 0.94 (s, 9H), 0.90 (s, 9H), 0.09 (s, 3H), 0.08 (s, 3H), 0.08 (s, 6H); $^{13}C\{H\}$ NMR (125 MHz, $CDCl_3$): δ 156.5, 137.3, 133.0, 128.9, 126.9, 121.5, 118.9, 115.5, 75.7, 71.5, 60.6, 25.8, 18.2, 18.1, 17.4, -4.5, -4.6, -4.6, -4.7; IR (Neat): ν_{max} 3426, 3330, 2954, 2928, 2885, 2856, 1581, 1463, 1360, 1252, 1104, 1004, 950, 834, 774, 673; HRMS: (ESI-TOF) *m/z* calcd for $C_{24}H_{45}O_4Si_2$ $(M + H)^+$ 453.28934, found 453.28509.

2-((3*S*,4*S*,*E*)-3,4-bis((*tert*-butyldimethylsilyl)oxy)pent-1-en-1-yl)-6-hydroxybenzaldehyde (42): Aldehyde **42** as a colorless liquid (67.2 mg) was prepared from compound **41** (76 mg, 0.168 mmol) following the same procedure used for the synthesis of **28**. Yield: 88%; R_f = 0.3 (hexane); $[\alpha]^{23}_D$: -38.69 (*c* 0.235, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ 11.88 (s, 1H), 10.31 (s, 1H), 7.45 (t, *J* = 8.0 Hz, 1H), 7.10 (dd, *J* = 1.7, 15.6 Hz, 1H), 6.92 (d, *J* = 8.0 Hz, 1H), 6.86 (d, *J* = 8.0 Hz, 1H), 6.25 (dd, *J* = 4.1, 15.6 Hz, 1H), 4.31 (ddd, *J* = 1.8, 4.1, 4.8 Hz, 1H), 3.86 (qd, *J* = 4.8, 6.2 Hz, 1H), 1.05 (d, *J* = 6.2 Hz, 3H), 0.94 (s, 9H), 0.90 (s, 9H), 0.10 (s, 3H), 0.09 (s, 6H), 0.08 (s, 3H); $^{13}C\{H\}$ NMR (75 MHz, $CDCl_3$): δ 196.6, 162.7, 143.4, 137.1, 136.8, 124.6, 118.8, 117.4, 116.5, 75.4, 71.3, 25.8, 18.2, 18.0, 17.3, -4.5, -4.7, -4.8; IR(Neat): ν_{max}2954, 2929, 2885, 2857, 1648, 1610, 1452, 1365, 1327, 1251, 1105, 1005, 834, 775, 722; HRMS: (ESI-TOF) m/z: $[M - H]^+$ calcd for $C_{24}H_{41}O_4Si_2$ 449.2543; found 449.2557.

Agropyrenol (14):[13,14a] Agropyrenol (**14**) as a light yellow liquid (6.3 mg) was prepared from compound **42** (18.2 mg, 0.040 mmol) following the procedure used for **23**. Yield: 72%; R_f = 0.4 (80% EtOAc/hexanes); $[\alpha]^{25}_D$: -43.0 (c 0.39, MeOH); ^1H NMR (400 MHz, $CDCl_3$): δ 11.90 (s, 1H), 10.37 (s, 1H), 7.50 (t, *J* = 8.0 Hz, 1H), 7.27 (d, *J* = 15.6 Hz, 1H), 6.97 (d, *J* = 8.0 Hz, 1H),

6.94 (d, *J* = 8.0 Hz, 1H) 6.16 (dd, *J* = 15.6, 6.1 Hz, 1H), 4.15 (t, *J* = 6.1 Hz, 1H), 3.81 (quint, *J* = 6.1 Hz, 1H), 2.56 (brs, 1H), 2.26 (brs, 1H), 1.32 (d, *J* = 6.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 195.2, 162.8, 142.0, 137.2, 135.9, 126.9, 118.8, 117.4, 117.3, 77.0, 70.8, 19.3; IR(Neat): ν_{max} 3401, 3344, 2924, 1637, 1451, 1237, 1060, 721, 674, 663; HRMS: (ESI-TOF) *m/z* $(M + Na)^+$ calcd for $C_{12}H_{14}O_4Na$ 245.0781, found 245.0784.

12-Methoxy sordariol (13):[12] To a solution of diol **35** (35.2 mg, 0.1142) in MeOH (1.36 mL) at 0 ºC was added K_2CO_3 (157.9 mg, 1.1428 mmol) and stirred at room temperature for 12 h. After completion of the starting material (monitored by TLC), MeOH was evaporated and quenched the reaction with water at 0 °C. The aqueous layer was extracted with EtOAc (3 times), and the organic layer was washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The product was purified by using silica gel column chromatography to obtain 12-OMe sordarial (**13**) (19.3 mg) as a liquid. Yield: 71%; R_f = 0.6 (10% MeOH/$CHCl_3$); $[\alpha]^{25}_D$: -11.1 (*c* 0.09, MeOH); ^{1}H NMR (300 MHz, CD_3OD): δ 7.64 (brd *J* = 2.5 Hz, 1H), 7.10 (t, *J* = 7.9 Hz, 1H), 7.02 (d, *J* = 7.1 Hz, 1H), 6.91 (d, *J* = 15.8 Hz, 1H), 6.74 (d, *J* = 7.9 Hz, 1H), 6.16 (dd, *J* = 15.8, 6.8 Hz, 1H), 4.64 (s, 2H), 4.11 (dd, *J* = 6.8, 4.9 Hz, 1H), 3.81 (dq, *J* = 6.4, 4.9 Hz, 1H), 3.37 (s, 3H), 1.19 (d, *J* = 6.4 Hz, 1H); ^{13}C{H} NMR (100 MHz, CD_3OD): δ 157.7, 140.5, 132.5, 130.9, 130.6, 122.4, 119.1, 115.8, 78.1, 71.9, 66.9, 58.7, 19.1; IR(Neat): ν_{max} 3375, 2954, 2853, 2171, 2118, 1652, 1575, 1523, 1464, 1276, 1069, 971, 657; HRMS: Single Mass Analysis m/z calcd for $C_{13}H_{18}O_4Na$ $(M + Na)^+$ 261.1103, found 261.1103.

3-((3R,4S,E)-3,4-bis((tert-butyldimethylsilyl)oxy)pent-1-en-1-yl)-2-methoxymethyl)phenol (43): Compound **43** as a colorless liquid (32.6 mg) from **36** (51 mg, 0.095 mmol) following the same procedure used for **13** from **35**. Yield: 76%; R_f= 0.6 (20% EtOAC/ hexane); $[\alpha]^{25}_D$: -16.70 (*c*, 0.91 $CHCl_3$) ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.95 (s, 1H), 7.17, (t, *J* = 7.8 Hz, 1H), 6.94 (d, *J*

= 7.8 Hz, 1H), 6.80 (dd, *J* = 7.8, 0.8 Hz, 1H), 6.73 (dd, *J* = 15.6, 1.7 Hz, 1H), 6.11 (dd, *J* = 15.6, 4.6 Hz, 1H), 4.81 (s, 2H), 4.26 (td, *J* = 4.6, 1.7 Hz, 1H), 3.84 (dq, *J* = 6.2, 4.6, 1H), 3.45 (s, 3H), 1.05 (d, *J* = 6.2 Hz, 3H), 0.96 (s, 9H), 0.91 (s, 9H), 0.10 (s, 3H), 0.10 (s, 3H), 0.09 (s, 3H), 0.09 (s, 3H); $^{13}C\{H\}$ NMR (100 MHz, $CDCl_3$): δ 153.6, 138.2, 133.1, 128.4, 126.2, 121.6, 118.7, 113.7, 78.6, 72.7, 25.9, 25.9, 19.9, 18.3, 18.1, 11.3, -4.0, -4.4, -4.5; IR(Neat): ν_{max}3396, 2931, 2890, 2858, 1579, 1465, 1368, 1253, 1097, 832, 775, 730, 670; HRMS: (ESI-TOF) *m/z*calcd for $C_{25}H_{46}O_4NaSi_2$ $(M + Na)^+$ 489.2830, found 489.2832.

12-Methoxy sordariol (13): Compound **13** (9.5 mg) was synthesized from **43** (23 mg, 0.050 mmol) using the same procedure used for the synthesis of **23**. Yield: 79%; R_f = 0.6 (10% MeOH/$CHCl_3$)

Acknowledgements

We thank UGC-India for research fellowships (GM, and JR), and Indo-French Centre for Promotion of Advanced Research (IFCPAR, No. 5305-1) and the Ministry of Earth Sciences (MoES -2/DS/6/2007 PC-IV), New Delhi, India for financial support. We also thank Director CSIR-IICT for the support (IICT/Pubs./2020/092).

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A general strategy to access various salicylaldehyde-containing polyketide natural products is described. This approach is highly flexible in generating stereochemistry and attaining functional group oxidation of choice, providing easy access to *ent*-pyriculol, *ent*-epipyriculol, *ent*-dihydropyriculol, *ent*-epidihydropyriculol, sordariol, sordarial, 12-methoxy sordariol, and agropyrenol.

Declaration of interests

*The authors declare that they have no known competing financialinterestsor personal relationships that could have appeared to influence the work reported in this paper.

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