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Chemoenzymatic synthesis of (+)-totarol, (+)-podototarin, (+)-sempervirol, and (+)-jolkinolides E and D

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Abstract—The enzymatic resolution products [(1*R*,4a*R*,8a*R*)-1,2,3,4,4a,5,6,7,8,8a-decahydro-5,5,8a-trimethyl-2-oxo-*trans*-naphthalene-1-methanol-2-ethylene acetal (8a*R*)-**7** (98% ee) and {acetate of (1*S*,4a*S*,8a*S*)-1,2,3,4,4a,5,6,7,8,8a-decahydro-5,5,8a-trimethyl-2-oxo-*trans*-naphthalene-1-methanol-2-ethylene acetal} (8a*S*)-**9** (>99% ee)] obtained by the lipase-catalyzed enantioselective acetylation of (±)-**7** in the presence of vinyl acetate as an acyl donor were converted to the α,β-unsaturated ketones (8a*R*)-**6** and (8a*S*)-**6**, respectively. Concise syntheses of (+)-totarol **1**, (+)-podototarin **2** and (+)-sempervirol **3** were achieved based on Michael reactions between (8a*S*)-**6** and the appropriate β-keto ester followed by aldol condensation. The first chiral syntheses of (+)-jolkinolides E **4** and D **5** were achieved from (5*R*,10*R*,12*R*)-12-hydroxypodocarpa-8(14)-en-13-one **15** derived from (8a*R*)-**6**.

1. Introduction

Many natural products contain the podocarpane skeleton, including (+)-totarol **1**,[1] (+)-podototarin **2**,[2] (+)-sempervirol **3**,[3] and (+)-jolkinolides E **4**[4] and D **5**[4] (Scheme 1). To synthesize these compounds, the construction of the C-ring of the chiral podocarpane skeleton is necessary. This can be achieved by a Michael reaction between chiral α,β-unsaturated ketone **6** and a β-keto ester followed by an aldol condensation. We previously reported that the lipase-assisted resolution of racemic primary alcohol (±)-**7**, derived from (±)-β-keto ester **8**, gave (8a*S*)-acetate **9** (49%, >99% ee) and (8a*R*)-primary alcohol **7** (49%, 98% ee).[5] This enzymatic resolution method was found to be effective, with an estimated *E*-value of 921. Chiral (8a*S*)- and (8a*R*)-**6** could be obtained from (8a*S*)-**9** and (8a*R*)-**7**, respectively. Herein we report concise syntheses of (+)-**1**, (+)-**2**, (+)-**3** from (8a*S*)-**9**, and the first synthesis of (+)-**4** and (+)-**5** from (8a*R*)-**7**.

2. Results and discussion

2.1. Syntheses of (+)-totarol 1 and (+)-podototarin 2

(+)-Totarol **1**,[1] a rare tricyclic diterpene phenol possessing an isopropyl group at the C(14) position, was first isolated as a major constituent of the heartwood of *Podocarpus totara* G. Benn and can also be isolated from a variety of other sources. It has been shown to have antibacterial activity against gram-positive bacteria, particularly methicillin-resistant *Staphylococcus aureus* (MRSA), with an MIC of 2.7 μM in vitro.[6] The structure of **1** was deduced on the basis of chemical and spectroscopic analysis,[7] while the absolute structure was determined by ORD measurement and by direct correlation with dehydroabietic acid.[8] (+)-Podototarin **2** was also isolated from the heartwood of *Podocarpus totara*,[2] and its structure was determined based on the synthesis from natural (+)-**1**.[9] The total synthesis of (+)-**1** was achieved by intramolecular cyclization of a chiral phenethylcyclohexene congener derived from (*R*)-(−)-α-cyclocitral[10] and also by conversion of natural products such as manool[11] or zamoranic acid.[12] Straightforward syntheses of (+)-**1** and (+)-**2** are shown in Scheme 2.

The consecutive treatment of the previously reported (8s*S*)-**7**[5] with 10% HCl and *p*-TsOH gave α,β-unsaturated ketone

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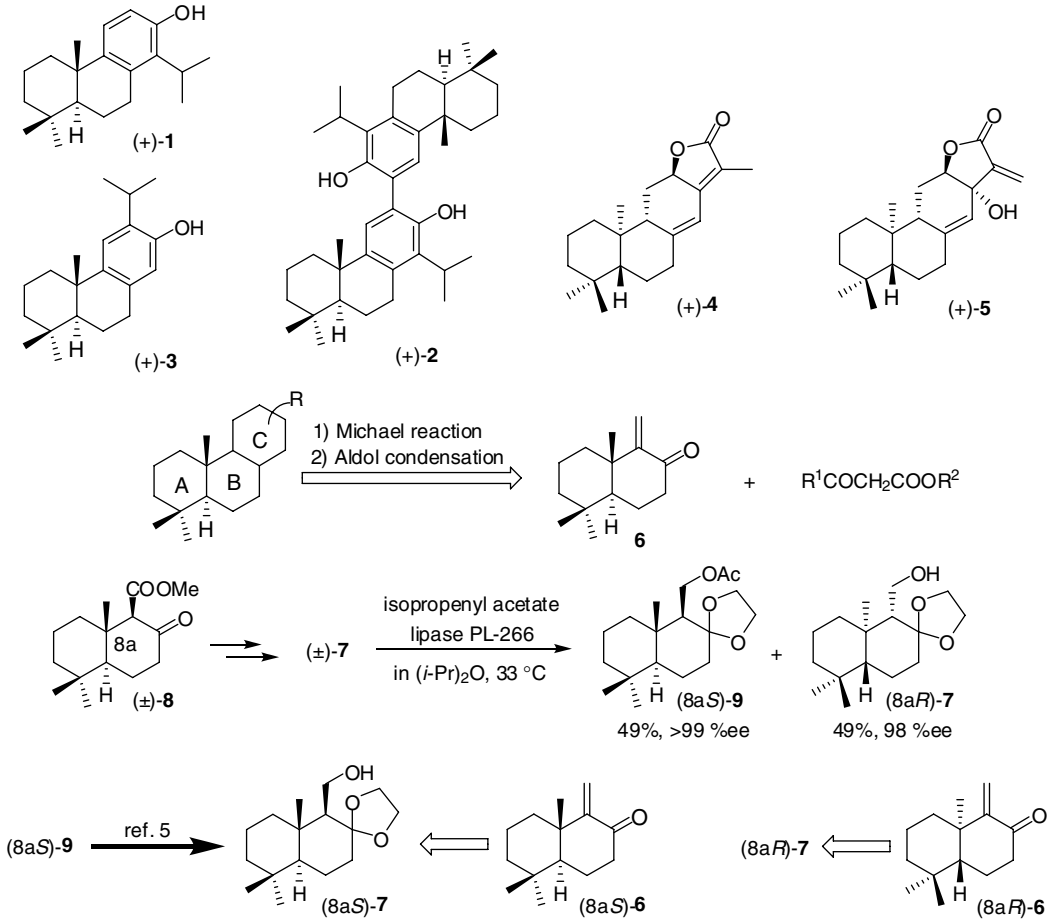
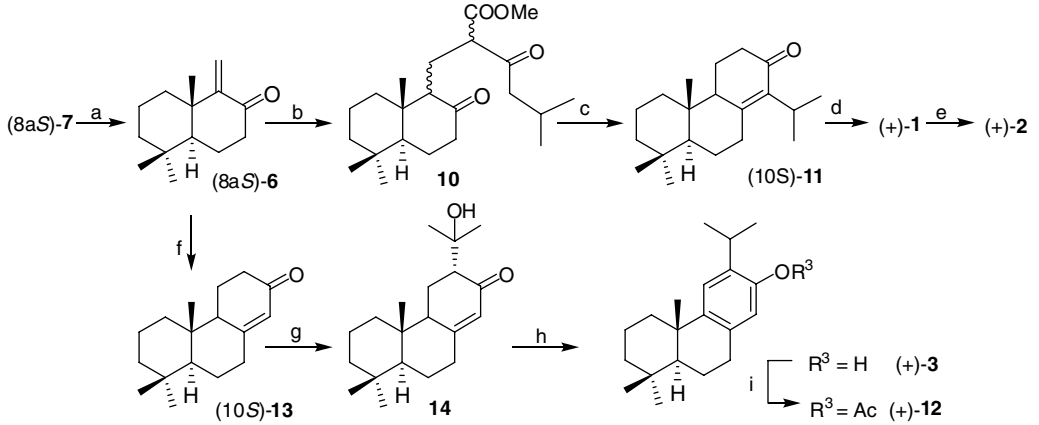


Scheme 1.



Scheme 2. Reagents and conditions: (a) (1) 10% HCl/MeOH, (2) *p*-TsOH/PhH; (b) methyl 5-methyl-3-oxohexanoate/NaOMe/MeOH; (c) (1) 1 M NaOH/MeOH, (2) 5 M HCl, 100 °C; (d) $CuBr_2$/LiBr/MeCN; (e) aq KOH/$K_3[Fe(CN)_6]$/PhH; (f) (1) methyl acetoacetate/NaOMe/MeOH, (2) 5 M NaOH, (3) 5 M HCl; (g) (1) LDA/THF, (2) acetone/0.5 M $ZnCl_2$/THF; (h) $CeCl_3{\cdot}7H_2O$/NaI/MeCN (i) Ac_2O/pyridine.

(8a*S*)-**6** in quantitative yield; this was used for the subsequent reaction without further purification. A Michael reaction of (8a*S*)-**6** with the anion obtained from the reaction of methyl 5-methyl-3-oxohexanoate[13] with NaOMe gave a 2:1 diastereomeric mixture of **10** in quantitative yield. Alkaline hydrolysis of **10** followed by treatment with 5 M HCl gave the aldol condensation product (10*S*)-**11** in 55% overall yield. Treatment of **11** with $CuBr_2$ and LiBr gave the product (+)-totarol **1** in 76% yield. The physical data of synthetic (+)-**1** (mp 123–124 °C and ^{1}H NMR) were in agreement with those of the reported (+)-**1** (mp 129–130 °C and ^{1}H NMR).[12] The specific rotation $\{[\alpha]_D^{27} = +41.9$ (*c* 1.0, $CHCl_3)\}$ of synthetic (+)-**1** was also in accordance with that of the previously reported sample $\{[\alpha]_D^{25} = +41.2$ (*c* 0.4, $CHCl_3)\}$.[12] Oxidation of (+)-**1** with alkaline potassium ferricyanide $[K_3Fe(CN)_6]$ by the reported procedure[9b] gave (+)-**2** in 45% yield. The specific rotation ($[\alpha]_D^{27} = +73.5$ (*c* 1.0, $CHCl_3$)) of the synthetic

(+)-**2** was in accordance with that of natural (+)-**2** {$[\alpha]_D^{24} = +76.1$ (*c* 1.0, $CHCl_3$)}.[2c]

2.2. Syntheses of (+)-sempervirol 3

(+)-Sempervirol **2**,[3] a rare tricyclic diterpene phenol possessing an isopropyl group at the C(12) position, was isolated from Cupressus sempervirens. Total syntheses of racemic **3** and its acetate (±)-**12** have been achieved by intramolecular cyclization of an α,β-unsaturated ketone congener obtained by condensation of β-cyclocitral with 4-isopropyl-3-methoxybenzyl chloride,[14] while the synthesis of natural (+)-**3** was accomplished by a novel conversion of methyl 12-bromodehydroabietate.[15] A straightforward synthesis of (+)-**3** from (8a*S*)-**6** is shown in Scheme 2. A Michael reaction of (8a*S*)-**6** with the anion obtained from the reaction of methyl acetoacetate with NaOMe gave a Michael addition product, which was subjected to alkaline hydrolysis followed by treatment with 5 M HCl to afford the aldol condensation product (10*S*)-**13** in 46% overall yield. Lithiation of (10*S*)-**13** followed by treatment with acetone in the presence of 0.5 M $ZnCl_2$ gave aldol product **14** in 59% overall yield. Finally, treatment of **14** with a combination of $CeCl_3$ and NaI, followed by dehydration and aromatization, afforded (+)-**3** in 82% overall yield. The ^{1}H NMR data of synthetic (+)-**3** were identical to those reported for the natural sample.[14b] The specific rotation {$[\alpha]_D^{23} = +54.2$ (*c* 1.0, $CHCl_3$)} of synthetic (+)-**3** was also in accordance with that of natural (+)-**3** ($[\alpha]_D = +60.2$ ($CHCl_3$)).[14b] Acetylation of (+)-**3** gave its acetate (+)-**12** in quantitative yield; the physical data of synthetic (+)-**12** (mp 88 °C and ^{1}H NMR) were in agreement with those of the previously reported sample of (+)-**12** (mp 92–94 °C and ^{1}H NMR).[14b] In addition, the specific rotation {$[\alpha]_D^{23} = +49.7$ (*c* 1.0, $CHCl_3$)} of synthetic (+)-**12** was in agreement with that of the previously reported sample {$[\alpha]_D = +55.4$ ($CHCl_3$)}.[14b]

2.3. Syntheses of (+)-jolkinolides E 4 and D 5

Jolkinolides A, B, C, D **5** and E **4** are diterpenoids, which were originally isolated from the roots of *Euphorbia Jolkini* Boiss.[4] The absolute structures of these compounds were determined by a chemical transformation to ferruginol, which possesses an abietane-type skeleton; the stereostructure of **5** was also confirmed by X-ray crystallographic analysis.[15] Jolkinolide D **5** exhibits cytotoxicity, inhibits tumor invasion into the basement membrane, and induces apoptosis in tumor cells.[15] A total synthesis of racemic **4** was achieved based on the intramolecular Wittig–Horner reaction.[16] We carried out the first total synthesis of the enantiomer of **5** from abietic acid.[17] Total syntheses of natural jolkinolodes **4** and **5** have not been reported. Straightforward syntheses of (+)-**4** and (+)-**5** from (8a*R*)-**6** are shown in Scheme 3.

Consecutive treatment of the previously reported compound (8a*R*)-**7**[5] with 10% HCl and *p*-TsOH gave α,β-unsaturated ketone (8a*R*)-**6** in quantitative yield. A Michael reaction of (8a*R*)-**6** with the anion obtained from the reaction of methyl acetoacetate with NaOMe gave a Michael addition product, which was subjected to alkaline hydrolysis followed by treatment with 5 M HCl to afford the aldol condensation product (10*R*)-**13** in 46% overall yield. Lithiation of (10*R*)-**13** followed by treatment with trimethylsilyl chloride gave a silyl enol ether, which underwent treatment with *m*-chloroperbenzoic acid (MCPBA) followed by desilylation with tetrabutylammonium fluoride (TBAF) to afford α-hydroxy ketone **15** in 51% overall yield. Esterification of **15** with 2-(diethylphosphono)propanoic acid in the presence of 4-dimethylaminopyridine (DMAP) and 1,3-dicyclohexylcarbodiimide (DCC), as reported previously,[16] gave ester **16**, which was treated with NaH to afford (+)-jolkinolide E **4** in 48% yield. The ^{1}H NMR data of synthetic (+)-**4** were identical to those of the previously reported sample[4] and the specific rotation {$[\alpha]_D^{21} = +337$ (*c* 0.6, $CHCl_3$)} of the synthetic (+)-**4** was also in agreement with that previously reported {$[\alpha]_D^{20} = +340$ (*c* 0.45, $CHCl_3$)}.[4] Silylation of **15** followed by treatment with a dianion derived from 2-iodoallyl alcohol, as reported previously,[17] gave (−)-**18** 27% overall yield from **15**, $[\alpha]_D^{28} = -40.7$ (*c* 0.15, $CHCl_3$) and (−)-**19** (32% overall yield from **15**, $[\alpha]_D^{30} = -27.3$ (*c* 0.64, $CHCl_3$)), whose ^{1}H NMR data were identical with those of the previously reported samples of **18** and **19**.[17] Desilylation of the obtained product (−)-**19** gave triol (−)-**20** (93% yield, $[\alpha]_D^{30} = -76.8$ (*c* 0.1,$CHCl_3$)), which was treated with MnO_2 to afford jolkinolode D (**5**) in 82% yield. The physical data (mp 190.5 °C and ^{1}H NMR) of the synthetic (+)-**5** were in agreement with those of the previously reported sample (mp 200–201 °C and ^{1}H NMR).[4] and the specific rotation {$[\alpha]_D^{21} = +301$ (*c* 0.5, $CHCl_3$)} of synthetic (+)-**5** was in agreement with that of natural (+)-**5** {$[\alpha]_D^{20} = +360$ (*c* 0.28, $CHCl_3$)}.[4]

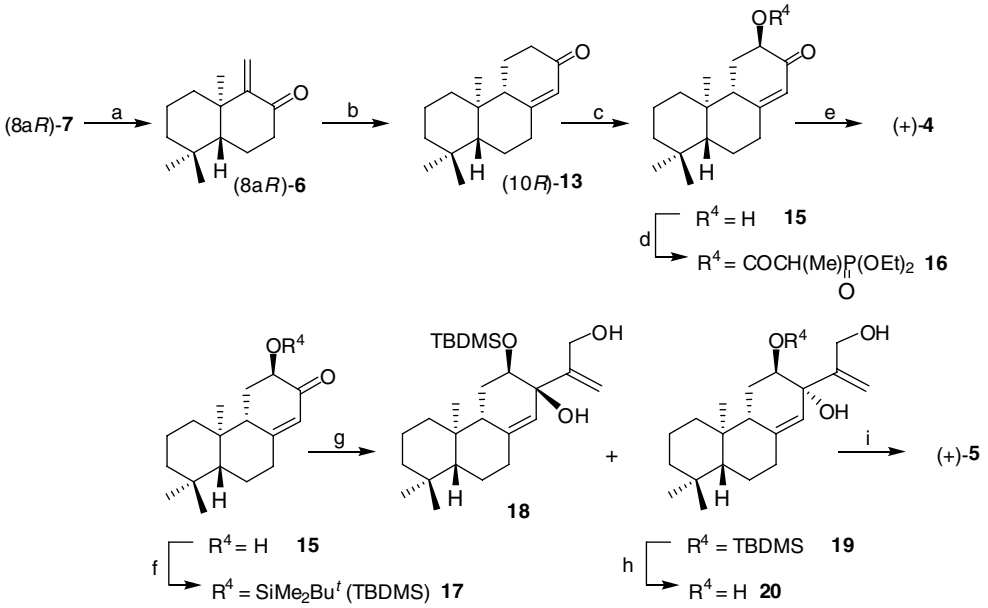
3. Conclusion

The enzymatic resolution products [(1*R*,4a*R*,8a*R*)-1,2,3,4,4a,5,6,7,8,8a-decahydro-5,5,8a-trimethyl-2-oxo-*trans*-naphthalene-1-methanol-2-ethylene acetal (8a*R*)-**7** (98% ee) and {acetate of (1*S*,4a*S*,8a*S*)-1,2,3,4,4a,5,6,7,8,8a-decahydro-5,5,8a-trimethyl-2-oxo-*trans*-naphthalene-1-methanol-2-ethylene acetal} (8a*S*)-**9** (>99% ee)] were obtained based on the lipase-catalyzed enantioselective acetylation of (±)-**7** in the presence of vinyl acetate as an acyl donor. The obtained (8a*S*)-**9** and (8a*R*)-**7** were converted to α,β-unsaturated ketones (8a*S*)-**6** and (8a*R*)-**6**, respectively. Concise syntheses of (+)-totarol **1**, (+)-podototarin **2**, and (+)-sempervirol **3** were achieved based on Michael reactions between (8a*S*)-**6** and the appropriate β-keto ester followed by aldol condensation. The first chiral syntheses of (+)-jolkinolides E **4** and D **5** were achieved using (5*R*,10*R*,12*R*)-12-hydroxypodocarpa-8(14)-en-13-one **15** derived from (8a*R*)-**6**.

4. Experimental

4.1. General

All melting points were measured on a Büchi 535 melting point apparatus and are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded on Bruker AV400M digital NMR



Scheme 3. Reagents and conditions: (a) (1) 10% HCl/MeOH, (2) *p*-TsOH/PhH; (b) (1) methyl acetoacetate/NaOMe/MeOH, (2) 1 M NaOH/MeOH, (3) 5 M HCl; (c) (1) LDA/TMSCl/THF, (2) MCPBA/CH_2Cl_2; (d) 2-(diethylphosphono)propanoic acid/DMAP/DCC/CH_2Cl_2; (e) 60% NaH/DME; (f) TBDMSCl/imidazole/DMF; (g) 2-iodoallyl alcohol/*t*BuLi/Et_2O; (h) TBAF/THF; (i) MnO_2/CH_2Cl_2.

spectrometer in $CDCl_3$. High-resolution mass spectra (HRMS) and the fast atom bombardment mass spectra (FAB MS) were obtained with a JEOL JMS 600H spectrometer and JEOL GC-Mate spectrometer (matrix; *m*-nitrobenzylalcohol). IR spectra were recorded with a JASCO FT/IR-4100 spectrometer. Optical rotations were measured with a JASCO P-1020 digital polarimeter. All evaporations were performed under reduced pressure. For column chromatography, silica gel (KANTO Silica Gel 60N, spherical, neutral, 40–50 mM) was employed.

4.2. (+)-Totarol 1

(i) To a solution of (8a*S*)-**7** (0.98 g, 3.65 mmol) in MeOH (50 mL) was added 10% aqueous HCl (15 mL) at 0 °C and the reaction mixture was stirred for 2 h at 0 °C. The reaction mixture was diluted with ice-water and extracted with AcOEt. The organic layer was washed with saturated $NaHCO_3$ and brine, and dried over Na_2SO_4, after which it was evaporated to give a crude oil. To a solution of the crude oil in benzene (50 mL) was added *p*-toluenesulfonic acid (*p*-TsOH, 0.14 g, 0.73 mmol) and the reaction mixture was stirred for 1 h at 50 °C. The reaction mixture was diluted with ice-water and extracted with AcOEt. The organic layer was washed with saturated $NaHCO_3$ and brine, and dried over Na_2SO_4, and evaporated to give a crude oil (8a*S*)-**6** (0.753 g, quantitative yield), which was used for the next reaction without further purification. (8a*S*)-**6**: ^{1}H NMR: δ 0.92 (3H, s), 0.96 (3H, s), 1.02 (3H, s), 1.25 (1H, dd, $J = 12.6$, 5.0 Hz), 1.40 (1H, dd, $J = 12.6$, 3.0 Hz), 1.44–1.53 (2H, m), 1.57–1.64 (2H, m), 1.73–1.80 (2H, m), 1.93–2.00 (1H, m), 2.33 (1H, ddd, $J = 17.0$, 12.6, 7.6 Hz), 2.67 (1H, ddd, $J = 17.0$, 5.5, 2.0 Hz), 5.01 (1H, d, $J = 1.2$ Hz), 5.54 (1H, d, $J = 1.2$ Hz).

(ii) To a solution of methyl 5-methyl-3-oxohexanoate[13] (0.693 g, 4.4 mmol) and NaOMe (0.237 g, 44 mmol) in MeOH (5 mL) was added dropwise a solution of (8a*S*)-**6** (0.753 g) in MeOH (5 mL) at rt and the reaction mixture was stirred for 16 h at the same temperature. The reaction mixture was diluted with ice-water and extracted with AcOEt. The organic layer was dried over Na_2SO_4 and evaporated to give a residue, which was chromatographed on silica gel (50 g, *n*-hexane–AcOEt = 4:1) to give a 2:1 diastereomeric mixture of **10** (1.330 g, quantitative yield) as a pale yellow oil. **10** (major product): IR (KBr): 2958, 1748, 1712, 1463, 1435, 1366, 1238, 1189 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.70 (3H, s), 3.51–3.46 (1H, m), 2.49 (1H, d, $J = 6.6$ Hz), 2.47–2.37 (2H, m), 2.33–1.96 (5H, m), 1.93–1.87 (1H, m), 1.87–1.79 (1H, m), 1.71–1.58 (1H, m), 1.57–1.49 (2H, m), 1.47–1.41 (2H, m), 1.31–1.19 (2H, m), 0.95 (3H, d, $J = 3.0$ Hz), 0.94 (3H, d, $J = 3.0$ Hz), 0.92 (3H, s), 0.85 (3H, s), 0.73 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 212.0, 205.4, 170.4, 61.4, 57.4, 54.0, 52.1, 50.9, 42.6, 42.3, 41.7, 38.8, 33.7, 33.4, 24.3, 23.8, 22.3, 22.3, 21.7, 20.9, 18.9, 14.6; (minor product) ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.71 (3H, s), 3.58–3.53 (1H, m), 2.49 (1H, d, $J = 6.6$ Hz), 2.47–2.37 (2H, m), 2.33–1.96 (5H, m), 1.93–1.87 (1H, m), 1.87–1.79 (1H, m), 1.71–1.58 (1H, m), 1.57–1.49 (2H, m), 1.47–1.41 (2H, m), 1.31–1.19 (2H, m), 0.95 (3H, d, $J = 3.5$ Hz), 0.94 (3H, d, $J = 2.0$ Hz), 0.93 (3H, s), 0.84 (3H, s), 0.73 (3H, s); HREI-MS: *m*/*z*: calcd for $C_{22}H_{36}O_4$: 364.2614. Found: 364.2616.

(iii) To a solution of **10** (1.1 g, 3.0 mmol) in MeOH (50 mL) was added 1 M aqueous NaOH (9 mL) and the reaction mixture was stirred for 4 h at 100 °C. After cooling, to the above reaction mixture was added 5 M aqueous HCl (5 mL) and the reaction mixture was stirred for 6 h at 100 °C. The reaction mixture was diluted with ice-water

and extracted with AcOEt. The organic layer was washed with saturated $NaHCO_3$ and brine, and dried over Na_2SO_4. Evaporation of the organic solvent gave a crude oil, which was chromatographed on silica gel (50 g, *n*-hexane–AcOEt = 4:1) to give (10*S*)-**11** (4.476 g, 55%) as a pale yellow oil. (10*S*)-**11**: IR (KBr): 2924, 2868, 1712, 1663, 1459, 1366, 1238, 1189 cm^{-1}; ^1H NMR: δ 0.74 (3H, s), 0.86 (3H, s), 0.92 (3H, s), 0.80–1.11 (3H, m), 1.13 (3H, d, $J = 7.0$ Hz), 1.19 (3H, d, $J = 7.0$ Hz), 1.38–1.69 (6H, m), 1.75–1.83 (1H, m), 1.86–1.96 (2H, m), 2.07 (1H, dd, $J = 9.6$, 5.5 Hz), 2.17 (1H, ddd, $J = 14.6$, 14.6, 5.6 Hz), 2.33 (1H, ddd, $J = 9.6$, 9.6, 4.6 Hz), 3.08–3.20 (2H, m). ^{13}C NMR: δ 14.6, 18.9, 19.7, 20.4, 21.8, 22.0, 22.5, 26.6, 31.4, 33.4, 33.5, 37.9, 38.7, 39.9, 41.8, 52.9, 54.5, 140.1, 157.0, 199.6. HREI-MS: *m*/*z*: calcd for $C_{20}H_{32}O$: 288.2453. Found: 288.2453.

(iv) To a solution of (10*S*)-**11** (0.07 g, 0.24 mmol) in MeCN (2.4 mL) were added $CuBr_2$ (0.108 g, 0.48 mmol) and LiBr (0.021 g, 0.24 mmol) and the reaction mixture was stirred for 6 h at rt. The reaction mixture was diluted with water and extracted with AcOEt. The organic layer was washed with brine, and dried over Na_2SO_4. Evaporation of the organic solvent gave a crude oil, which was chromatographed on silica gel (20 g, *n*-hexane–AcOEt = 5:1) to give (+)-**1** (0.053 g, 76%) as a colorless solid. (+)-**1**: mp 123–124 °C (*n*-hexane); $[\alpha]_D^{27} = +41.9$ (*c* 1.0, $CHCl_3$); IR (KBr): 3587, 3460, 2940, 1586, 1455, 1372, 1266, 1176 cm^{-1}; ^1H NMR: δ 0.91 (3H, s), 0.95 (3H, s), 1.17 (3H, s), 1.22 (1H, dd, $J = 13.6$, 4.5 Hz), 1.26 (1H, dd, $J = 12.6$, 2.0 Hz), 1.30–1.38 (1H, m), 1.33 (3H, d, $J = 7.0$ Hz), 1.35 (3H, d, $J = 7.0$ Hz), 1.44–1.48 (1H, m), 1.56–1.75 (3H, m), 1.88–1.94 (1H, m), 2.19–2.26 (1H, m), 2.74 (1H, ddd, $J = 19.2$, 11.1, 7.6 Hz), 2.94 (1H, dd, $J = 17.1$, 6.6 Hz), 3.29 (1H, ddd, $J = 21.1$, 14.1, 7.0 Hz), 4.41 (1H, s), 6.51 (1H, d, $J = 8.4$ Hz), 7.00 (1H, d, $J = 8.4$ Hz). ^{13}C NMR: δ 19.4, 19.5, 20.3, 20.4, 21.6, 25.2, 27.1, 28.7, 33.2, 33.3, 37.7, 39.6, 41.6, 49.6, 114.3, 123.0, 131.0, 134.0, 143.2, 151.9. HREI-MS: *m*/*z*: calcd for $C_{20}H_{30}O$: 286.2297. Found: 286.2302. Anal. Calcd for $C_{20}H_{30}O$: C, 83.86; H, 10.56. Found: C, 83.49; H, 10.58.

4.3. (+)-Podototarin 2

To a solution of (+)-**1** (0.04 g, 0.14 mmol) in benzene (1 mL) was added KOH solution (KOH; 0.039 g, H_2O; 1.5 mL) and $K_3[Fe(CN)_6]$ solution ($K_3[Fe(CN)_6]$; 0.077 g, H_2O; 1.5 mL) and the reaction mixture was stirred for 1 h at rt and 40 min at 100 °C. The reaction mixture was diluted with 5 M aqueous HCl (5 mL) and extracted with AcOEt. The organic layer was washed with brine, and dried over Na_2SO_4. Evaporation of the organic solvent gave a crude oil, which was chromatographed on silica gel (10 g, *n*-hexane–AcOEt = 10:1) to give (+)-**2** (0.018 g, 45%) as a colorless solid. (+)-**2**: mp 210.0 °C; $[\alpha]_D^{27} = +73.5$ (*c* 1.0, $CHCl_3$); IR (KBr): 3532, 2934, 1453, 1359, 1223, 1118 cm^{-1}; ^1H NMR: δ 0.92 (6H, s), 0.96 (6H, s), 1.20 (6H, s), 1.35 (6H, d, $J = 7.8$ Hz), 1.37 (6H, d, $J = 7.8$ Hz), 1.15–1.76 (14H, m), 1.91–1.97 (2H, m), 2.16–2.23 (2H, m), 2.80 (1H, ddd, $J = 18.6$, 11.0, 8.6 Hz), 2.99 (1H, dd, $J = 17.1$, 6.0 Hz), 3.15–3.40 (2H, m), 5.07 (2H, br s), 7.00 (2H, s). ^{13}C NMR: δ 19.3, 19.4, 20.2, 20.2, 21.6, 25.3, 27.7, 28.8, 33.2, 33.3, 37.8, 39.8, 41.6, 49.6, 120.8, 124.4, 132.0, 135.0, 143.3, 150.0. HREI-MS: *m*/*z*: calcd for $C_{40}H_{58}O_2$: 570.4437. Found: 570.4418. Anal. Calcd for $C_{40}H_{58}O_2 \cdot 1.5H_2O$: C, 80.35; H, 10.28. Found: C, 80.58; H, 9.86.

4.4. (+)-Sempervirol 3

(i) To a solution of methyl acetoacetate (2.1 g, 18 mmol) and NaOMe (0.973 g, 18 mmol) in MeOH (40 mL) were added dropwise a solution of (8a*S*)-**6** (3.09 g, 15 mmol) in MeOH (10 mL) for 2 h at rt and the reaction mixture was stirred for 16 h at the same temperature. To the above reaction mixture was added 5 M aqueous NaOH (11 mL) at rt and the reaction mixture was stirred for 10 h at the same temperature. After cooling, to the above reaction mixture were added 5 M aqueous HCl (15 mL) at rt and the reaction mixture was stirred for 1 h at the same temperature. The reaction mixture was diluted with ice-water (200 mL) and extracted with AcOEt. The organic layer was washed with saturated $NaHCO_3$ and brine, and dried over Na_2SO_4. Evaporation of the organic solvent gave a crude oil, which was chromatographed on silica gel (50 g, *n*-hexane–AcOEt = 4:1) to give (10*S*)-**13** (1.7 g, 46%) as a pale brown oil. (10*S*)-**13**: $[\alpha]_D^{22} = +39.7$ (*c* 1.0, $CHCl_3$); IR (KBr): 2908, 1659, 1613, 1457, 1387, 1220, 1173 cm^{-1}; ^1H NMR: δ 0.81 (3H, s), 0.88 (3H, s), 0.93 (3H, s), 1.07–1.25 (3H, m), 1.42–1.58 (4H, m) 1.70–1.78 (3H, m), 1.97–2.09 (2H, m), 2.17–2.32 (2H, m), 2.40 (1H, ddd, $J = 15.6$, 4.2, 4.2 Hz), 2.54 (1H, dd, $J = 15.1$, 4.5 Hz), 5.88 (1H, s). ^{13}C NMR: δ 15.3, 18.7, 20.5, 22.0, 22.0, 33.4, 33.6, 35.6, 36.8, 39.0, 39.3, 41.8, 51.7, 53.9, 125.8, 165.8, 199.9. HREI-MS: *m*/*z*: calcd for $C_{17}H_{26}O$: 246.1984. Found: 246.1987.

(ii) To a solution of diisopropylamine (83 μL, 0.6 mmol) in THF (1 mL) was added 1.6 M *n*-BuLi in *n*-hexane solution (380 μL, 0.6 mmol) at −78 °C and the reaction mixture was stirred for 30 min at the same temperature. To the generated lithium diisopropylamide (LDA) solution was added a solution of (10*S*)-**13** (0.123 g, 0.5 mmol) in THF (1 mL) at −78 °C and the reaction mixture was stirred for 20 min at the same temperature. To the above reaction mixture was added 0.5 M $ZnCl_2$ in THF solution (1 mL), acetone (0.1 mL) and THF (0.5 mL) at −48 °C and the reaction mixture was stirred for 20 min at −48 °C and for 1 h at 0 °C. The reaction mixture was diluted with saturated NH_4Cl solution (30 mL) and extracted with AcOEt. The organic layer was washed with brine, and dried over Na_2SO_4. Evaporation of the organic solvent gave a crude oil, which was chromatographed on silica gel (10 g) to afford the recovery (10*S*)-**13** (0.026 g, 21%) from *n*-hexane–AcOEt = 4:1 elution and **14** (0.090 g, 59%) as a colorless oil from *n*-hexane–AcOEt = 2:1 elution. **14**: $[\alpha]_D^{23} = -125.2$ (*c* 1.0, $CHCl_3$); IR (KBr): 3452, 2924, 1647, 1460, 1389, 1230, 1167 cm^{-1}; ^1H NMR: δ 0.86 (3H, s), 0.92 (3H, s), 0.96 (3H, s), 1.17 (3H, s), 1.21 (3H, s), 1.13–1.25 (3H, m), 1.42–1.64 (4H, m), 1.74–1.83 (1H, m), 1.84–1.93 (2H, m), 2.12–2.32 (3H, m), 2.49 (1H, ddd, $J = 13.6$, 4.3, 2.2 Hz), 2.57 (1H, dd, $J = 12.1$, 5.6 Hz), 4.75 (1H, br s), 5.89 (1H, s). ^{13}C NMR: δ 16.1, 19.0, 21.8, 23.1, 23.9, 24.6, 28.4, 33.5, 33.7, 36.7, 40.0, 41.9, 42.2, 50.4, 52.2, 55.0, 73.0, 125.4, 166.9, 203.3. HREI-

MS: *m*/*z*: calcd for $C_{20}H_{32}O_2$: 304.2402 (M^+). Found: 304.2412.

(iii) A mixture of $CeCl_3 \cdot 7H_2O$ (0.335 g, 0.9 mmol) and NaI (0.135 g, 0.9 mmol) in MeCN (3 mL) was stirred for 14 h at 100 °C. After cooling, to the reaction mixture was added a solution of **14** (0.090 g, 0.3 mmol) in MeCN (2 mL) and the reaction mixture was stirred for 30 h at the same temperature. The reaction mixture was diluted with ice-water (200 mL) and extracted with Et_2O. The organic layer was washed with brine, and dried over Na_2SO_4. Evaporation of the organic solvent gave a crude oil, which was chromatographed on silica gel (10 g, *n*-hexane–AcOEt = 3:1) to give (+)-**3** (0.07 g, 82%) as a colorless oil. (+)-**3**: $[\alpha]_D^{23} = +54.2$ (*c* 1.0, $CHCl_3$); IR (KBr): 3399, 2924, 1616, 1508, 1460, 1416, 1241, 1160 cm^{-1}; ^1H NMR: δ 0.92 (3H, s), 0.93 (3H, s), 1.17 (3H, s), 1.24 (6H, d, $J = 7.0$ Hz), 1.20–1.28 (1H, m), 1.32 (1H, dd, $J = 12.6$, 2.5 Hz), 1.39 (1H, dd, $J = 13.1$, 4.0 Hz), 1.44–1.50 (1H, m), 1.56–1.88 (4H, m), 2.28 (1H, d, $J = 13.1$ Hz), 2.71–2.88 (2H, m), 3.13 (1H, ddd, $J = 20.6$, 14.1, 7.0 Hz), 4.43 (1H, s), 6.42 (1H, s), 7.07 (1H, s). ^{13}C NMR: δ 19.0, 19.3, 21.6, 22.7, 22.8, 25.0, 27.2, 30.0, 33.3, 33.4, 37.5, 39.1, 41.7, 50.7, 114.9, 122.4, 131.8, 133.7, 142.8, 150.2. HREI-MS: *m*/*z*: calcd for $C_{20}H_{30}O$: 286.2297. Found: 286.2299.

(iv) To a solution of (+)-**3** (0.02 g, 0.07 mmol) in pyridine (0.5 mL) was added Ac_2O (0.009 g, 0.08 mmol) and the reaction mixture was stirred for 16 h at rt. The reaction mixture was diluted with water and extracted with AcOEt. The organic layer was washed with 1 M aqueous HCl, saturated $NaHCO_3$ and brine, and dried over Na_2SO_4. Evaporation of the organic solvent gave a crude oil, which was chromatographed on silica gel (5 g, *n*-hexane–AcOEt = 4:1) to give (+)-**12** (0.023 g, quantitative yield) as colorless prisms. (+)-**12**: mp 88.0 °C; $[\alpha]_D^{23} = +49.7$ (*c* 1.0, $CHCl_3$); IR (KBr): 2932, 1760, 1497, 1462, 1368, 1216, 1190 cm^{-1}; ^1H NMR: δ 0.92 (3H, s), 0.94 (3H, s), 1.178 (3H, d, $J = 7$ Hz), 1.178 (3H, s), 1.182 (3H, d, $J = 7$ Hz), 1.20–1.28 (1H, m), 1.33 (1H, dd, $J = 12.4$, 2.3 Hz), 1.38 (1H, dd, $J = 13.1$, 3.8 Hz), 1.42–1.50 (1H, m), 1.54–1.88 (4H, m), 2.29 (3H, s), 2.74–2.90 (2H, m), 2.93 (1H, ddd, $J = 20.7$, 13.6, 6.8 Hz), 6.64 (1H, s), 7.16 (1H, s). ^{13}C NMR: δ 19.0, 19.3, 21.0, 21.6, 23.0, 23.2, 25.0, 27.6, 29.9, 33.3, 33.4, 37.8, 38.9, 41.7, 50.2, 121.7, 122.6, 134.0, 136.8, 145.5, 148.0, 169.9. HREI-MS: *m*/*z*: calcd for $C_{22}H_{32}O_2$: 328.2402. Found: 328.2403.

4.5. (+)-Jolkinolide E 4

(i) To a solution of (8a*R*)-**7** (0.98 g, 3.65 mmol) in MeOH (50 mL) was added 10% aqueous HCl (15 mL) at 0 °C and the reaction mixture was stirred for 2 h at 0 °C. The reaction mixture was diluted with ice-water and extracted with AcOEt. The organic layer was washed with saturated $NaHCO_3$ and brine, and dried over Na_2SO_4, and evaporated to give a crude oil. To a solution of the crude oil in benzene (50 mL) was added *p*-toluenesulfonic acid (*p*-TsOH, 0.14 g, 0.73 mmol) and the reaction mixture was stirred for 1 h at 50 °C. The reaction mixture was diluted with ice-water and extracted with AcOEt. The organic layer was washed with saturated $NaHCO_3$ and brine, dried over Na_2SO_4, and evaporated to give a crude oil (8a*R*)-**6** (0.753 g, quantitative yield), which was used for the next reaction without further purification.

(ii) To a solution of methyl acetoacetate (2.1 g, 18 mmol) and NaOMe (0.973 g, 18 mmol) in MeOH (40 mL) was added dropwise a solution of (8a*R*)-**6** (3.09 g, 15 mmol) in MeOH (10 mL) for 2 h at rt and the reaction mixture was stirred for 16 h at the same temperature. To the above reaction mixture was added 5 M aqueous NaOH (11 mL) at rt and the reaction mixture was stirred for 10 h at the same temperature. After cooling, to the above reaction mixture was added 5 M aqueous HCl (15 mL) at rt and the reaction mixture was stirred for 1 h at the same temperature. The reaction mixture was worked up in the same way as for (8a*S*)-**6** to afford (8a*R*)-**13** (1.7 g, 46%) as a pale brown oil. (8a*R*)-**13**: $[\alpha]_D^{29} = -41.7$ (*c* 0.22, $CHCl_3$). Spectral data (IR, ^1H and ^{13}C NMR) of (8a*R*)-**13** were identical with those of (8a*S*)-**13**.

(iii) To a solution of diisopropylamine (0.68 mL, 4.8 mmol) in THF (2 mL) was added 1.6 M *n*-BuLi in *n*-hexane solution (3 mL, 4.8 mmol) at −78 °C and the reaction mixture was stirred for 30 min at the same temperature. To the generated lithium diisopropylamide (LDA) solution was added a solution of (8a*R*)-**13** (0.222 g, 0.9 mmol) in THF (2 mL) at −78 °C and the reaction mixture was stirred for 1 h at the same temperature. To the above reaction mixture was added trimethylsilyl chloride (TMSCl; 0.8 mL, 4.6 mmol) and the reaction mixture was stirred for 2 h at rt. The reaction mixture was diluted with Et_2O (20 mL) and the organic layer was washed with saturated $NaHCO_3$ and brine, and dried over Na_2SO_4. Evaporation of the organic solvent gave a crude enol ether (0.7 g), which was used for the next reaction without further purification. To a solution of a crude enol ether (0.7 g) in CH_2Cl_2 (20 mL) was added 65% *m*-chloroperbenzoic acid (MCPBA; 0.8 g, 3 mmol) at −40 °C and the reaction mixture was stirred for 3 h at the same temperature. The reaction mixture was filtered and the filtrate was condensed to afford a residue. To a solution of this residue in CH_2Cl_2 (10 mL) was added 1 M tetrabutylammonium fluoride (TBAF) in THF solution (6 mL) at rt and the reaction mixture was stirred for 6 h at rt. The reaction mixture was diluted with saturated $NaHCO_3$ and CH_2Cl_2 and the organic layer was washed with 1 M aqueous HCl and brine, and dried over Na_2SO_4. Evaporation of the organic solvent gave a crude oil, which was chromatographed on silica gel (10 g, *n*-hexane–AcOEt = 3:2) to give **15** (0.12 g, 51%) as a pale yellow oil. **15**: $[\alpha]_D^{30} = +159.8$ (*c* 1.0, $CHCl_3$). IR (KBr): 3397, 2929, 1613, 1265, 1068, 871 cm^{-1}; ^1H NMR: δ 0.86 (3H, s), 0.92 (3H, s), 1.00 (3H, s), 1.13–1.30 (3H, m), 1.42–1.65 (4H, m), 1.78–2.02 (3H, m), 2.23–2.31 (1H, m), 2.48–2.56 (1H, m), 3.55 (1H, s), 4.31 (1H, dd, $J = 13.0$, 6.5 Hz), 5.92 (1H, s). ^{13}C NMR: δ 16.4, 19.1, 21.7, 24.0, 29.4, 33.6, 33.8, 37.1, 40.0, 42.0, 42.3, 51.5, 55.0, 69.3, 121.5, 167.6, 199.8. HREI-MS: *m*/*z*: calcd for $C_{20}H_{32}O$: 288.2453. Found: 288.2453.

(iv) To a solution of **15** (0.055 g, 0.21 mmol) in CH_2Cl_2 (1 mL) was added 4-dimethylaminopyridine (DMAP; 0.029 g, 0.24 mmol), 2-(diethylphosphono)propanoic acid

(0.046 g, 0.22 mmol) and 1,3-dicyclohexylcarbodiimide (DCC; 0.05 g, 0.24 mmol) and the reaction mixture was stirred for 30 min at rt. The reaction mixture was diluted with ice-water and extracted with AcOEt. The organic layer was washed with 1 M aqueous HCl, saturated $NaHCO_3$, brine, and dried over Na_2SO_4. Evaporation of the organic solvent gave the crude oil **16** (0.1 g), which was used for the next reaction without further purification.

(v) To a solution of **16** (0.1 g) in DME (2 mL) was added 60% NaH (0.01 g, 0.25 mmol) at 0 °C and the reaction mixture was stirred for 3 h at rt. The reaction mixture was diluted with saturated NH_4Cl and extracted with AcOEt. The organic layer was washed with saturated $NaHCO_3$, brine, and dried over Na_2SO_4. Evaporation of the organic solvent gave a crude oil, which was chromatographed on silica gel (10 g, *n*-hexane–AcOEt = 5:1) to give (+)-**4** (0.030 g, 48% from **15**) as colorless prism. (+)-**4**: mp 182.3 °C; $[\alpha]_D^{21} = +337$ (*c* 0.6, $CHCl_3$); IR (KBr): 2958, 1748, 1670, 1607, 1368, 1086, 1020 cm^{-1}; ^1H NMR: δ 0.86 (3H, s), 0.92 (3H, s), 0.93 (3H, s), 1.05–1.25 (3H, m), 1.36–1.63 (5H, m), 1.84 (3H, s), 1.80–1.88 (1H, m), 1.89–1.97 (1H, m), 2.15–2.25 (2H, m), 2.51 (1H, ddd, $J = 13.4$, 4.0, 2.3 Hz), 2.58 (1H, dd, $J = 13.4$, 6.2 Hz), 4.88 (1H, ddd, $J = 13.4$, 6.2, 1.5 Hz), 6.27 (1H, br s). ^{13}C NMR: δ 8.3, 16.8, 19.1, 21.8, 23.9, 27.6, 33.6, 33.9, 37.2, 39.7, 41.7, 42.0, 51.9, 55.3, 76.1, 113.9, 116.2, 152.3, 156.3, 175.4. HREI-MS: *m*/*z*: calcd for $C_{20}H_{28}O_2$: 300.2089. Found: 300.2095.

4.6. (+)-Jolkinolide D 5

(i) To a solution of **15** (0.105 g, 0.4 mmol) in DMF (2 mL) were added imidazole (0.17 g, 2.5 mmol) and ^{t}butyldimethylsilyl chloride (TBDMSCl; 0.19 g, 1.25 mmol) at rt and the reaction mixture was stirred for 2 h at rt. The reaction mixture was diluted with H_2O and extracted with Et_2O. The organic layer was washed with brine and dried over Na_2SO_4. Evaporation of the organic solvent gave a crude oil, which was chromatographed on silica gel (10 g, *n*-hexane–AcOEt = 50:1) to give (+)-**17** (0.113 g, 75%) as a pale yellow oil. Compound **17**; $[\alpha]_D^{30} = +16.7$ (*c* 0.1, $CHCl_3$); IR (KBr): 2938, 1676, 1471, 1262, 1123, 840 cm^{-1}; ^1H NMR: δ 0.05 (3H, s), 0.08 (3H, s), 0.82 (3H, s), 0.87 (12H, s), 0.93 (3H, s), 1.06–1.28 (3H, m), 1.40–1.55 (4H, m), 1.72–1.90 (3H, m), 1.99–2.07 (1H, m), 2.24–2.35 (2H, m), 2.52 (1H, ddd, $J = 15.0$, 4.5, 1.8 Hz), 4.07–4.15 (1H, m), 5.78 (1H, t, $J = 2$ Hz). ^{13}C NMR: δ −5.1, −4.7, 14.2, 15.4, 18.9, 22.0, 22.5, 25.8 (3C), 30.1, 33.5, 33.7, 36.0, 39.4 (2C), 41.9, 48.9, 54.2, 71.8, 122.9, 165.6, 197.8. FAB-MS: *m*/*z*: 377 (M^++1).

(ii) To a solution of 2-iodoallyl alcohol (0.04 g, 2.2 mmol) in Et_2O (2.5 mL) was added 1.5 M ^{t}BuLi in pentane solution (3.5 mL, 5.3 mmol) at −78 °C and the reaction mixture was stirred for 10 min at 0 °C. To the anion generated was added a solution of **17** (0.1 g, 0.27 mmol) in Et_2O (2.5 mL) and the reaction mixture was stirred for 3 h at 0 °C. The reaction mixture was diluted with MeOH (1 mL), H_2O and extracted with AcOEt. The organic layer was washed with brine and dried over Na_2SO_4. Evaporation of the organic solvent gave a crude oil, which was chromatographed on silica gel (10 g, *n*-hexane–AcOEt = 3:1) to give (−)-**18** (0.041 g, 36%) as a colorless oil and (−)-**19** (0.05 g, 43%) as a colorless prism in elution order. **18**; $[\alpha]_D^{28} = -40.7$ (*c* 0.15, $CHCl_3$); IR (KBr): 3420, 2931, 2858, 1461, 1387, 1251, 1085, 835 cm^{-1}; ^1H NMR: δ 0.12 (6H, s), 0.75 (3H, s), 0.86 (3H, s), 0.91 (12H, s), 1.07 (1H, dd, $J = 12.6$, 2.5 Hz), 1.10–1.75 (11H, m), 1.83–1.90 (1H, m), 2.05–2.16 (1H, m), 2.38 (1H, ddd, $J = 14.4$, 4.5, 1.5 Hz), 3.33 (1H, br s), 3.99 (1H, dd, $J = 5.0$, 1.5 Hz), 4.09 (1H, d, $J = 12.6$ Hz), 4.34 (1H, d, $J = 12.6$ Hz), 5.12 (1H, d, $J = 1.5$ Hz), 5.20 (1H, d, $J = 1.5$ Hz), 5.27 (1H, d, $J = 1.5$ Hz). ^{13}C NMR: δ −5.0, −4.2, 15.0, 18.2, 18.9, 22.1, 22.2, 25.4, 25.9 (3C), 33.4, 33.7, 35.0, 37.8, 39.1, 42.0, 46.6, 54.6, 64.6, 71.2, 76.2, 117.7, 123.5, 140.8, 150.0. HREI-MS: *m*/*z*: calcd for $C_{26}H_{46}O_3$:Si 434.3216. Found: 434.3222. **19**; mp 105.3 °C; $[\alpha]_D^{30} = -27.3$ (*c* 0.64, $CHCl_3$); IR (KBr): 3421, 2928, 2856, 1461, 1254, 1092, 835 cm^{-1}; ^1H NMR: δ 0.03 (3H, s), 0.08 (3H, s), 0.83 (3H, s), 0.85 (3H, s), 0.86 (9H, s), 0.90 (3H, s), 1.09–1.83 (12H, m), 1.90 (1H, t, $J = 6.5$ Hz), 2.07–2.17 (1H, m), 2.36 (1H, ddd, $J = 14.0$, 4.0, 1.5 Hz), 2.45 (1H, br s), 2.90 (1H, br s), 3.91 (1H, dd, $J = 7.6$, 3.5 Hz), 4.14 (1H, d, $J = 12.6$ Hz), 4.30 (1H, d, $J = 12.6$ Hz), 4.97 (1H, d, $J = 1.0$ Hz), 5.22 (1H, d, $J = 1.0$ Hz), 5.40 (1H, s). ^{13}C NMR: δ −4.6, −4.4, 15.4, 18.2, 19.1, 22.1, 22.5, 25.9 (3C), 26.4, 28.1, 29.8, 33.4, 33.7, 35.4, 38.6, 39.4, 42.1, 48.4, 54.6, 65.1, 73.7, 76.3, 116.6, 124.3, 142.0, 149.0. HREI-MS: *m*/*z*: calcd for $C_{26}H_{46}O_3SiNa$ 457.3114 (M^++Na). Found: 457.3116.

(iii) To a solution of **19** (0.085 g, 0.2 mmol) in THF (2 mL) was added 1 M tetrabutylammonium fluoride (TBAF) in THF solution (4 mL) at 0 °C and the reaction mixture was stirred for 1 h at rt. The reaction mixture was diluted with saturated NH_4Cl and extracted with AcOEt. The organic layer was washed with brine and dried over Na_2SO_4. Evaporation of the organic solvent gave a crude oil, which was chromatographed on silica gel (10 g, *n*-hexane–AcOEt = 1:1) to give **20** (0.058 g, 93%) as colorless plates. **20**: mp 130.4 °C; $[\alpha]_D^{30} = -76.8$ (*c* 0.1, $CHCl_3$); IR (KBr): 3191, 2948, 2841, 1486, 1364, 1046, 902 cm^{-1}; ^1H NMR: δ 0.81 (3H, s), 0.86 (3H, s), 0.90 (3H, s), 1.00–1.74 (11H, m), 1.85 (2H, dd, $J = 8.0$, 4.5 Hz), 2.00 (1H, t, $J = 8.0$ Hz), 2.12–2.22 (1H, m), 2.37 (1H, ddd, $J = 14.3$, 4.5, 2.0 Hz), 3.86 (1H, ddd, $J = 8.0$, 4.0, 1.0 Hz), 4.23 (1H, d, $J = 12.3$ Hz), 4.34 (1H, d, $J = 12.3$ Hz), 5.09 (1H, d, $J = 1.5$ Hz), 5.35 (1H, d, $J = 1.0$ Hz), 5.46 (1H, d, $J = 1.0$ Hz). ^{13}C NMR: δ 14.8, 18.9, 22.1, 22.4, 24.2, 33.4, 33.7, 35.5, 38.3, 39.0, 42.0, 46.7, 54.6, 64.4, 70.6, 75.1, 116.5, 122.6, 144.7, 149.9. HREI-MS: *m*/*z*: calcd for $C_{20}H_{32}O_3$: 320.2352. Found: 320.2354.

(iv) To a solution of **20** (0.032 g, 0.1 mmol) in $CHCl_3$ (2 mL) was added MnO_2 (Aldrich, 0.086 g, 0.1 mmol) at rt and the reaction mixture was stirred for 16 h at rt. To the above reaction mixture was again added MnO_2 (Aldrich, 0.086 g, 0.1 mmol) at rt and the reaction mixture was stirred for 8 h at rt. The reaction mixture was filtered with the aid of Celite and the filtrate was condensed to give a crude oil, which was chromatographed on silica gel (10 g, *n*-hexane–AcOEt = 1:1) to give (+)-**5** (0.026 g, 82%) as colorless prisms. (+)-**5**: mp 190.5 °C; $[\alpha]_D^{21} = +301$ (*c* 0.5,

$CHCl_3$); IR (KBr): 3450, 2936, 2837, 1748, 1382, 1273, 982 cm^{-1}; ^1H NMR: δ 0.80 (3H, s), 0.86 (3H, s), 0.90 (3H, s), 1.07–1.51 (7H, m), 1.59–1.67 (1H, m), 1.67–1.75 (2H, m), 1.92–1.99 (1H, m), 2.02 (1H, br s), 2.06–2.16 (1H, m), 2.22 (1H, ddd, $J = 15.0$, 6.0, 4.0 Hz), 2.28–2.35 (1H, m), 4.42–4.46 (1H, m), 5.15 (1H, d, $J = 1.5$ Hz), 5.81 (1H, s), 6.21 (1H, s). ^{13}C NMR: δ 15.1, 18.8, 21.3, 21.7, 22.1, 33.4, 33.6, 35.1, 37.6, 39.5, 41.8, 44.6, 53.9, 72.9, 81.1, 120.1, 120.8, 142.8, 145.0, 171.5. HREI-MS: *m*/*z*: calcd for $C_{20}H_{28}O_3$: 316.2039. Found: 316.2032.

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