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TETRAHEDRON

Synthesis of Dendryphiellin C, a Trinor-sesquiterpene from a Marine Source

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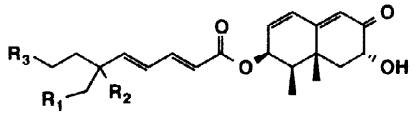
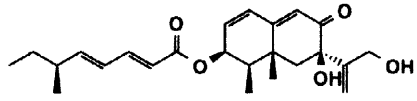
Abstract: Enantioselective synthesis of dendryphiellin C, isolated from cultures of *Dendryphiella sarina*, has been achieved in a convergent way such as coupling of a C9-branched carboxylic acid **10** with a trinor-eremophilane alcohol **11**. The latter was synthesized starting from a chiral building block, (1*S*,5*S*,6*R*)-5-hydroxybicyclo[4.1.0]heptan-2-one **16**, which was originally prepared in this group using biochemical transformation as a key step. The synthesis was completed through 12 steps from **16** in overall 2.4% yield.

Introduction

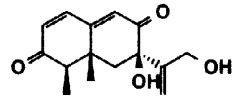
In the course of the screening of marine secondary metabolites from 1988 to 1990, Pietra *et al.* isolated from cultures of a marine deuteromycete, *Dendryphiella sarina* (Sutherland) Pugh *et* Nicot, a series of dendryphiellins A~G,[1a,b,c] which are classified into two groups, that is to say, eremophilanes (E~G) and trinor-eremophilanes (A~D). As the result of structural elucidation by Pietra *et al.*, it has come to light that they consist of an eremophilane or a trinor-eremophilane moiety and a branched C9 carboxylic acid, except for dendryphiellin G, all of which are rare as compounds of marine origin.



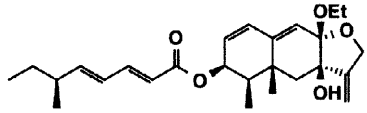
1 Dendryphiellin A R_1=R_2=H R_3=OH
2 B R_1=R_3=H R_2=OH
3 C R_1=R_2=R_3=H (6*S*)
4 D R_1=OH R_2=R_3=H



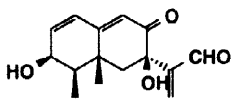
5 Dendryphiellin E



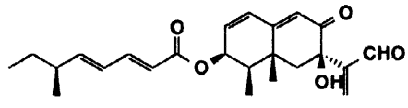
7 Dendryphiellin G



6 Dendryphiellin F



8 Bipolaroxin



9 KM-01

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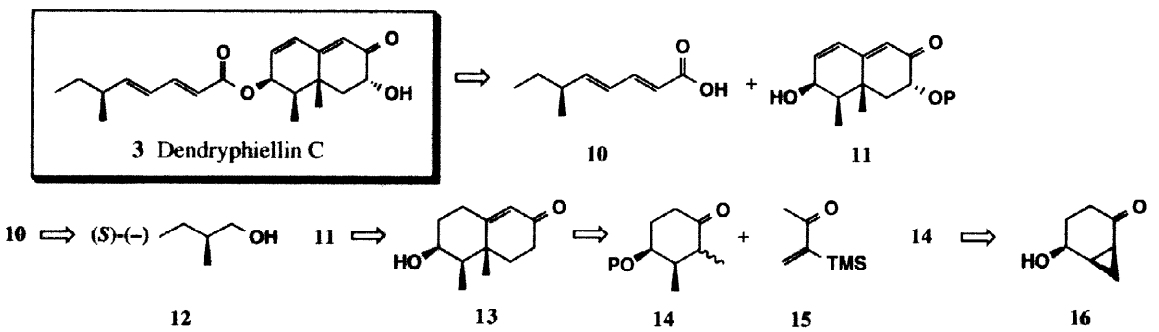
PII: S0040-4020(99)00407-X

So far, there has been no report about the physiological activities of dendryphiellins, while some other compounds with the same skeleton show remarkable activities. For example, bipolaroxin[2] **8** functions as a plant pathogenic toxin and KM-01[3] **9** as a brassinolide-inhibitor. So, we set about our investigation of the total synthesis of dendryphiellin C in order to establish a synthetic route to these valuable compounds.

Synthetic plan

As shown retrosynthetically in **Scheme 1**, the synthesis of **3** can be completed by coupling of the C9-branched carboxylic acid **10** with a protected trinor-eremophilane alcohol **11**.



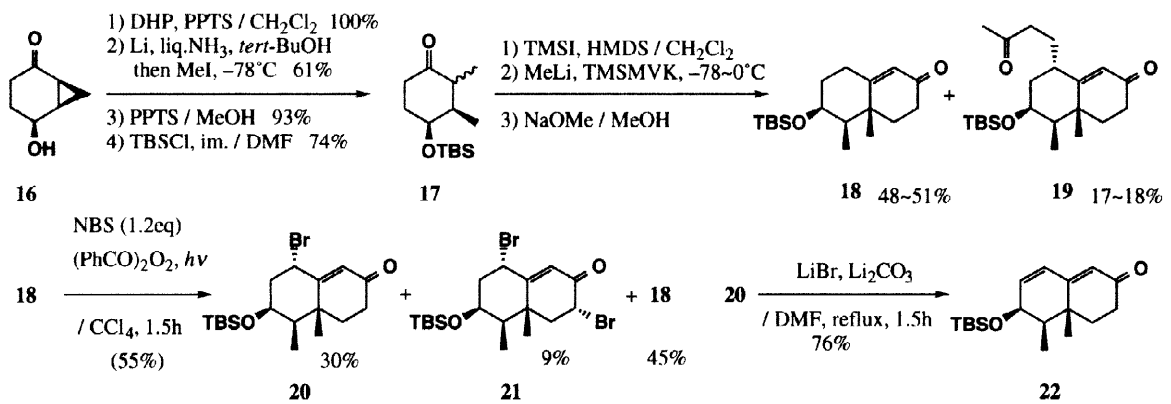
Scheme 1. Retrosynthetic Analysis of Dendryphiellen C

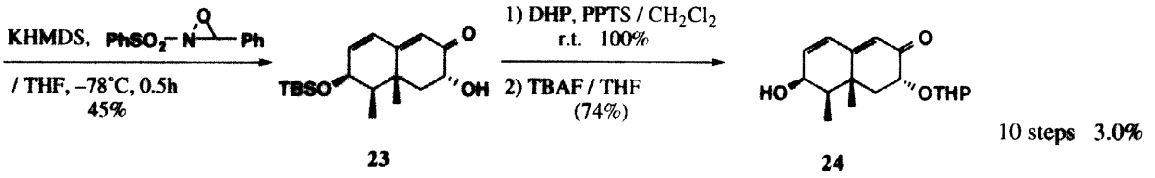
The acid **10** should be prepared from (*S*)-(−)-2-methylbutanol **12**.

Construction of **11** may be achieved by the Robinson-annelation reaction between **14** and **15**, followed by dehydrogenation and oxidation of the resulting **13**. The cyclohexane **14** can be derived from the chiral alcohol **16**, from which several bioactive molecules, e.g., sporogen-AO 1[4a], gigantenone[4b], phomenone[4b], phaseolinone[4b] and pironetin[4c], have already been synthesized in our laboratory.

Synthesis of the Trinor-eremophilane Moiety

We started our synthesis from (1*S*,5*S*,6*R*)-5-hydroxybicyclo[4.1.0]heptan-2-one **16**, which were available in large quantity through several step-operations from the known keto ester[4a], including reduction with baker's





Scheme 2. Preparation of the Trinor-eremophilane Skeleton

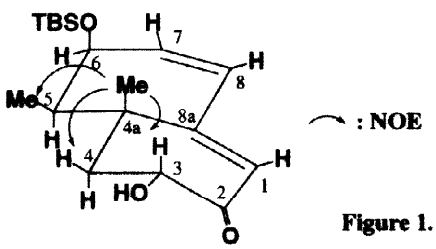
yeast[5].

After protection of the hydroxy group as a THP ether in order to increase solubility, reductive methylation of **16** by Stork's procedure[6] and the successive exchange of the protecting group gave dimethylcyclohexanone **17** regioselectively[7]. The cyclohexanone **17** was obtained as a diastereomeric mixture of *trans*- and *cis*-dimethyl isomers in a ratio of 3:1. Because the next step would be the enolization of the carbonyl group, we used the mixture directly.

The Robinson-annelation reaction of **17** with TMSMVK **15**[8] led to the octalone skeleton[9]; that is, at first treating with TMSI and HMDS, the more substituted thermodynamic enolate was trapped as a TMS enol ether[10] and then Michael addition was carried out under basic conditions, followed by aldol condensation. We got the desired octalone **18** in 48~51% yield together with 17~18% yield of **19**, which might be derived *via* randomized enolization and the following addition to TMSMVK.

The octalone **18** was brominated at the allylic position with NBS[11] to give monobromide **20** in 55% yield based on the recovery of **18**. When 2.2eq of NBS was used, the recovery of **18** could be reduced to 9%, but the yield of dibromide **21** increased up to 29% and that of **20**, on the contrary, decreased. So the use of a limited amount of NBS (1.2eq) and the reuse of the recovered **18** gave much better result.

Dehydrobromination of **20** with LiBr and Li_2CO_3[12] introduced a conjugated dienone system in the octalone ring to give **22** in 76% yield. Then, hydroxylation at the α–position of the carbonyl group was achieved on treatment of **22** with Davis' reagent[13] to give **23** in moderate yield.



C3-H : 4.36ppm (dd) *J*=5.7, 13.2Hz
C4-H (ax) : 1.58ppm (br.t) *J*=12.4, 13.2Hz
C4-H (eq) : 2.42ppm (dd) *J*=5.7, 12.4Hz

Figure 1. 300MHz Proton NMR Spectrum (in $CDCl_3$) of 23

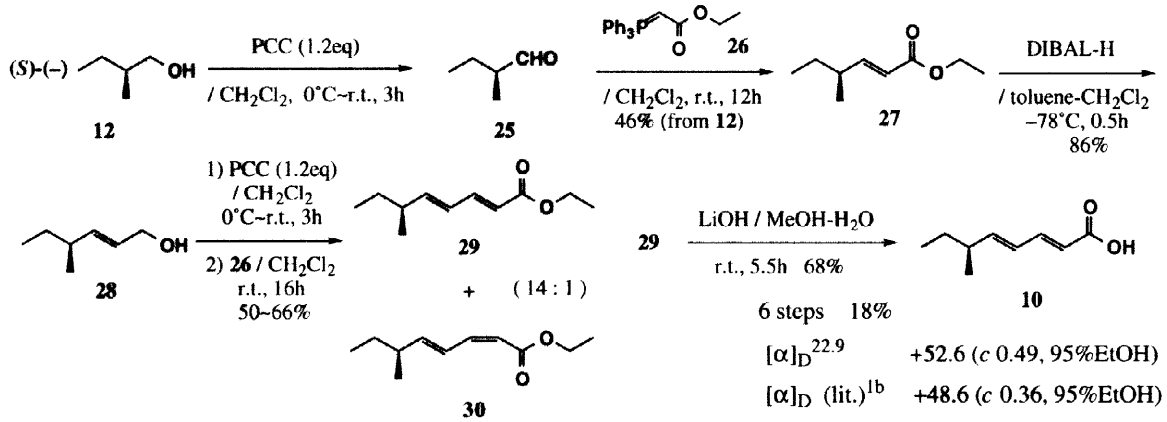
In a proton NMR spectrum of **23**, C3-H is observed at 4.36ppm as a double doublet peak (*J*=5.7Hz, 13.2Hz). A large coupling constant with one of the vicinal protons implies 1,2-diaxial relationship between these protons. Consequently, it was proved that the other vicinal proton at C4 and the newly-introduced hydroxy group at C3 are equatorial. When C4a-CH_3 was irradiated, peak enhancements were observed both at C3-H and equatorial C4-H. These data also support the equatorial orientation of the C3-hydroxy group as **Figure 1**, which

is rationalized *via* introduction of an oxygen function from the less hindered site.

Here, all of the required functional groups were furnished in the trinor-eremophilane skeleton. Protection of the hydroxy group as a THP ether, followed by removal of the TBS protecting group, afforded the alcohol **24** of the coupling half.

Preparation of the C9-Branched Carboxylic Acid

Next, the synthesis of the C9-branched carboxylic acid **10** was executed according to the reported procedure[1b] with slight modification.



Scheme 3. Synthesis of the C9-Branched Carboxylic Acid

Commercially available (*S*)-(–)-2-methylbutanol was treated with PCC to afford aldehyde **25**, which was immediately reacted with (carbethoxymethylene)triphenylphosphorane **26** to give unsaturated ester **27**. Reduction of **27** with diisobutylaluminum hydride gave an allylic alcohol **28**, which was subjected to similar processes to produce a separable mixture of the desired *EE* olefin **29** and the undesired *EZ* isomer **30** in a ratio of 14:1. Saponification of the purified ester **29** yielded the desired diene acid **10**. Specific rotation of the synthesized **10** is +52.6 and approximately accords with the reported value, +48.6[1b]. Our improved procedure is apparently simpler and more efficient in preparative scale.

Formation of the Ester Linkage and Synthesis of Dendryphiellin C

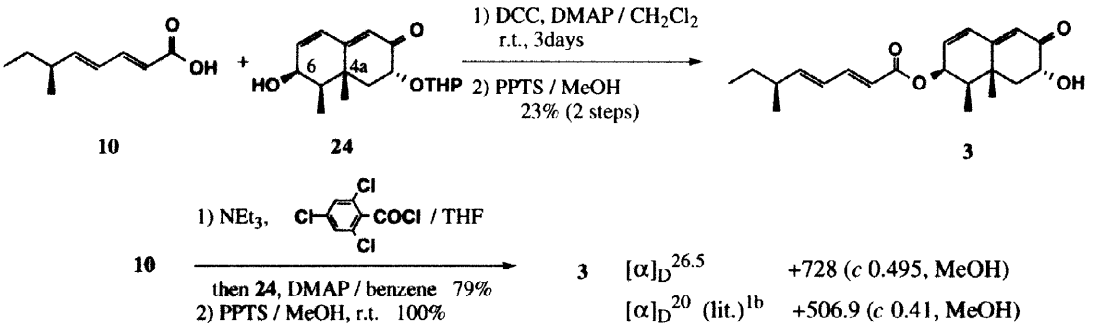
With (*S*)-6-methyloctanoic acid **10** and the properly protected trinor-eremophilane alcohol **24** in hand, we proceeded to the coupling process.

Using DCC and DMAP as coupling reagents, the reaction mixture was kept stirring at room temperature for 3 days, but the starting materials were not exhausted and the yield of the desired ester **3** was only 23%. This was most probably because the C6-OH group was sterically hindered due to 1,3-diaxial interaction between the C4a angular methyl group and the C6-OH group.

Fortunately, this problem was overcome by using Yamaguchi's esterification method[14] to improve the yield up

to 79%. Finally, removal of the THP protecting group afforded dendryphiellin C **3** quantitatively.

The absolute value of the observed specific rotation of the synthetic sample (+728) became much larger than that reported in literature (+506.9) but in the same plus sign. Other physical and spectroscopic data (^{1}H-NMR and ^{13}C-NMR) are in good accordance with those reported.



Scheme 4. Formation of the Ester Linkage

In conclusion, the convergent total synthesis of dendryphiellin C **3** has been accomplished starting from a versatile chiral building block, (1*S*,5*S*,6*R*)-5-hydroxybicyclo[4.1.0]heptan-2-one **16**, through 12 steps in overall 2.4% yield. In our synthetic plan, the target molecule was separated into two parts, one a C9-branched carboxylic acid **10** and the other, trinor-eremophilane moiety **11** whose skeleton could be constructed by Robinson-annelation reaction.

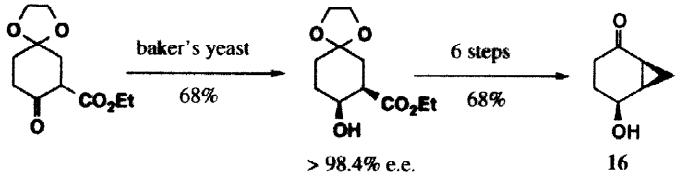
This method may be applicable to syntheses of other trinor-eremophilanes or eremophilanes with remarkable bioactivities as described in the introduction. Work along this line is now in progress in our laboratory and will be reported in due course.

EXPERIMENTAL SECTION

All b.p. and m.ps were uncorrected. IR spectra were measured as films for oils or as nujol-mal for solids on a Jasco FT/IR-230 spectrometer. ^{1}H-NMR spectra were recorded at 300 MHz on a BRUKER AC300 spectrometer or at 500 MHz on a JEOL JNM α-500 spectrometer as indicated. Chemical shifts are reported in parts per million (δ) relative to the residual solvent peak ($CHCl_3$:δ 7.26 or CH_3OH:δ 3.3). Coupling constants are reported in hertz (Hz). ^{13}C-NMR spectra were recorded at 75.5 MHz on a BRUKER AC300 spectrometer or at 125.7 MHz on a JEOL JNM α-500 spectrometer as indicated. Chemical shifts are reported in ppm (δ) relative to the residual solvent peak ($CHCl_3$:δ 77 or CH_3OH:δ 49). Optical rotations were measured on a Jasco DIP 1000 polarimeter. Silica gel chromatography was performed on Merk silica gel 60. Thin-layer chromatography was performed on Merk precoated glass-backed plates (silica gel 60 F_{254}).

Preparation of 16

According to the literature[4a], the ketone **16** was prepared from the corresponding keto ester through 7 steps in overall 46% yield.



THP ether of 16, (1*S*, 5*S*, 6*R*)-5-tetrahydropyranyloxybicyclo[4.1.0]heptan-2-one

A mixture of **16** (12.4g, 98.3mM), 2,3-dihydropyran (13.5g, 161mM) and pyridinium *p*-toluenesulfonate (1.1g, 4.5mM) in CH_2Cl_2 (200ml) was stirred overnight at room temperature. The reaction mixture was diluted with ether, washed with water, sat. $NaHCO_3$ soln and brine, dried over $MgSO_4$ and concentrated. The residual colorless oil was chromatographed over silica gel (450g) and eluted with *n*-hexane–EtOAc (9:1~6:1) to give 20.6g (98.0mM, quantitative) of THP ether of **16** as a colorless oil of a diastereomeric mixture, which was employed in the next step without any more purification; IR (film) νmax 3020 (m), 2960 (s), 2870 (s), 1695 (s), 1345 (s), 1255 (m), 1200 (s), 1155 (m), 1135 (s), 1115 (s), 1080 (s), 1030 (s) cm^{-1}; ^{1}H-NMR (300MHz, $CDCl_3$) δ 0.97~1.13 & 1.27~2.03 & 2.19~2.28 (14H), 3.37~3.43 (m) & 3.70~3.87 (m) & 4.17~4.30 (m) (3H), 4.60 (br) & 4.76 (br) (1H); ^{13}C-NMR (75.5Hz, $CDCl_3$) δ 8.19, 8.76, 19.35, 19.48, 20.29, 21.62, 22.71, 25.07, 25.72, 25.94, 26.17, 30.64, 30.70, 34.10, 34.46, 62.40, 67.87, 69.98, 96.45, 97.73, 207.11, 207.57.

(2*RS*, 3*R*, 4*S*)-2,3-Dimethyl-4-tetrahydropyranyloxycyclohexanone

To a blue solution of lithium (2.97g, 428mM) in liq. NH_3 (*ca.* 400ml) was added dropwise a solution of the above THP ether of **16** (9.00g, 42.8mM) and *t*-BuOH (3.17g, 42.8mM) in dry DME (80ml) at –78°C. After stirring for 30 min at –78°C, the blue solution was slowly quenched with MeI (77g, 540mM) and allowed to stand at ambient temperature in order to remove liq. NH_3. The residue was poured into sat. NH_4Cl soln (300ml) and extracted twice with ether (600ml). The combined ether layer was washed with water, sat. $NaHCO_3$ soln and brine, dried over $MgSO_4$ and concentrated. The residual orange oil was chromatographed over silica gel (270g) and eluted with *n*-hexane–EtOAc (15:1~10:1) to give 5.94g (26.2mM, 61%) of the title compound as a slightly yellowish oil of a diastereomeric mixture; $[\alpha]_D^{18.5}$ +40.4° (*c* 0.935, $CHCl_3$); IR (film) νmax 2940 (s), 2880 (s), 1715 (s), 1455 (m), 1380 (m), 1350 (m), 1200 (m), 1135 (s), 1120 (s), 1080 (s), 1035 (s), 1025 (s), 1005 (s), 980 (m) cm^{-1}; ^{1}H-NMR (300MHz, $CDCl_3$) δ 0.76~1.18 (6H), 1.55~2.83 (12H), 3.50~3.57 & 3.75~3.98 & 4.13~4.24 (3H), 4.69~4.81 (1H); ^{13}C-NMR (75.5Hz, $CDCl_3$) δ 11.49, 16.57, 17.11, 19.31, 19.91, 25.45, 28.20, 30.95, 31.09, 32.27, 35.86, 36.62, 44.09, 44.52, 45.76, 62.18, 63.02, 71.90, 78.10, 94.39, 101.53, 213.11, 213.40; Anal. Calcd for $C_{13}H_{22}O_3$: C, 68.99; H, 9.80. Found : C, 68.72; H, 9.84.

(2*RS*, 3*R*, 4*S*)-4-Hydroxy-2,3-dimethylcyclohexanone

A mixture of the above dimethyl derivative, (2*RS*,3*R*,4*S*)-2,3-dimethyl-4-tetrahydropyranyloxycyclohexanone (4.82g, 21.3mM) and pyridinium *p*-toluenesulfonate (535mg, 2.13mM) in MeOH (10ml) was stirred overnight at 60°C. The reaction mixture was concentrated and the residual oil was chromatographed over silica gel (130g) and

eluted with *n*-hexane–EtOAc (10:1~1:1) to give 2.82g (19.8mM, 93%) of the title compound as a slightly yellowish oil of a diastereomeric mixture. In the silica gel chromatography two diasteomers could be separated but a mixture was used in the next step. Spectroscopic data are mentioned respectively;

for **(2*R*, 3*R*, 4*S*)-4-hydroxy-2,3-dimethylclohexanone**; $[\alpha]_D^{19.2}$ +47.7° (*c* 0.645, $CHCl_3$); IR (film) νmax 3440 (br.s), 2970 (s), 2930 (s), 2880 (s), 1715 (s), 1695 (s), 1450 (s), 1430 (m), 1380 (s), 1350 (s), 1320 (m), 1305 (m), 1270 (m), 1210 (s), 1140 (s), 1105 (m), 1080 (m), 1040 (s), 1000 (s), 970 (m), 950 (s), 940 (s) cm^{-1} ; ^{1}H-NMR (300MHz, $CDCl_3$) δ 0.99 (d, *J*=6.7Hz, 3H), 1.11 (d, *J*=6.9Hz, 3H), 1.65 (d.d.q, *J*=2.2, 6.9, 11.5Hz, 1H), 1.85 (d.d.t, *J*=2.4, 4.7, 13.9Hz, 1H), 2.07 (br.s, 1H), 2.15 (d.d.d.d, *J*=2.8, 3.2, 6.2, 13.9Hz, 1H), 2.22 (d.d.d, *J*=2.8, 4.7, 13.9Hz, 1H), 2.56 (d.q, *J*=6.7, 11.5Hz, 1H), 2.75 (d.t, *J*=6.2, 13.9Hz, 1H), 3.94 (br, 1H); ^{13}C-NMR (75.5Hz, $CDCl_3$) δ 11.38, 16.64, 33.22, 35.68, 44.47, 45.06, 69.83, 213.32;

for **(2*S*, 3*R*, 4*S*)-4-hydroxy-2,3-dimethylclohexanone**; $[\alpha]_D^{20.1}$ +38.9° (*c* 0.400, $CHCl_3$); IR (film) νmax 3400 (br.s), 2970 (s), 2940 (s), 2880 (s), 1780 (m), 1770 (m), 1715 (s), 1455 (s), 1430 (s), 1380 (s), 1350 (s), 1290 (m), 1275 (m), 1250 (m), 1230 (m), 1140 (s), 1100 (s), 1025 (s), 990 (m), 950 (s) cm^{-1}; ^{1}H-NMR (300MHz, $CDCl_3$) δ 0.82 (d, *J*=7.1Hz, 3H), 1.01 (d, *J*=6.8Hz, 3H), 1.74 (br.s, 1H), 1.83~1.97 (m, 1H), 1.99~2.08 (m, 1H), 2.23~2.31 (m, 1H), 2.32~2.37 (2H), 2.63 (d.q, *J*=4.7, 6.8Hz, 1H), 4.31 (br.d.t, *J*=5.5, 11.1Hz, 1H); ^{13}C-NMR (75.5Hz, $CDCl_3$) δ 7.30, 11.95, 29.29, 38.13, 42.59, 46.61, 71.32, 211.73.

(2*R S*, 3*R*, 4*S*)-4-*tert*-Butyldimethylsilyloxy-2,3-dimethylcyclohexanone 17

A mixture of the above diastereomeric alcohol (2*RS*,3*R*,4*S*)-4-hydroxy-2,3-dimethylcyclohexanone (8.73g, 61.5mM), imidazole (12.54g, 184.2mM) and 90% *tert*-butyldimethylsilyl chloride (15.42g, 92.1mM) in DMF (90ml) was stirred overnight at room temperature. The reaction mixture was poured into water and extracted with ether. The ether layer was washed with water and brine, dried over $MgSO_4$ and concentrated. The residual oil was chromatographed over silica gel (480g) and eluted with *n*-hexane–EtOAc (50:1) to give 11.6g (45.2mM, 74%) of **17** as a colorless oil of a diastereomeric mixture of *trans*- and *cis*-dimethyl isomers in a ratio of 3:1, which could not be separated and was employed in the next step; $[\alpha]_D^{20.6}$ +40.1° (*c* 1.20, $CHCl_3$); IR (film) νmax 2960 (s), 2930 (s), 2880 (s), 2860 (s), 1715 (s), 1470 (m), 1460 (m), 1380 (m), 1360 (m), 1255 (s), 1140 (m), 1110 (s), 1080 (s), 1060 (s), 1020 (s), 840 (s), 775 (s); Anal. Calcd for $C_{14}SiH_{28}O_2$: C, 65.57; H, 11.00. Found : C, 65.65; H, 11.09; ^{1}H-NMR (300MHz, $CDCl_3$) for **(2*R*, 3*R*, 4*S*)-4-*tert*-butyldimethylsilyloxy-2,3-dimethylcyclohexanone** δ 0.07 (s, 6H), 0.92 (s, 9H), 0.97 (d, *J*=6.7Hz, 3H), 1.02 (d, *J*=6.8Hz, 3H), 1.58 (d.d.q, *J*=1.9, 6.8, 11.5Hz, 1H), 1.78 (d.d.t, *J*=2.0, 4.5, 13.8Hz, 1H), 2.02 (d.d.d.d, *J*=2.5, 3.2, 6.1, 13.8Hz, 1H), 2.19 (d.d.d, *J*=2.5, 4.5, 13.5Hz, 1H), 2.56 (d.q, *J*=6.9, 11.5Hz, 1H), 2.73 (br.d.t, *J*=6.1, 13.8Hz, 1H), 3.87 (br, *J*=1.9, 2.0, 3.2Hz, 1H): for **(2*S*, 3*R*, 4*S*)-4-*tert*-butyldimethylsilyloxy-2,3-dimethylcyclohexanone** δ 0.08 (s, 6H), 0.80 (d, *J*=7.1Hz, 3H), 0.88 (s, 9H), 1.00 (d, *J*=7.2Hz, 3H), 1.84~1.92 (m, 1H), 2.07~2.17 (m, 1H), 2.24~2.40 (m, 3H), 2.5~2.6 (1H), 4.17 (d.d.d, *J*=4.2, 6.2, 8.4Hz, 1H); ^{13}C-NMR (75.5Hz, $CDCl_3$) for **(2*R*, 3*R*, 4*S*)-4-*tert*-butyldimethylsilyloxy-2,3-dimethylcyclohexanone** δ –4.91, –4.49, 11.23, 17.32, 18.09, 25.80, 33.85, 35.84, 45.17, 45.32, 70.66, 213.37: for **(2*S*, 3*R*, 4*S*)-4-*tert*-butyldimethylsilyloxy-2,3-dimethylcyclohexanone** δ –4.91, –4.49, 8.13, 12.17, 18.09, 25.80, 30.26, 37.82, 43.04, 46.94, 71.68, 212.52;

Elution with *n*-hexane–EtOAc (40:1) gave 3.65g (15.1mM, 25%) of the monomethyl derivative, **(3*R*, 4*S*)-4-**

***tert*-butyldimethylsilyloxy-3-methylcyclohexanone** as a colorless oil; $[\alpha]_D^{17.9}$ +32.9° (*c* 1.01, $CHCl_3$); IR (film) *v*max 2955 (s), 2930(s), 2880 (s), 2860 (s), 1715 (s), 1470 (m), 1460 (m), 1365 (m), 1255 (s), 1140 (m), 1110 (s), 1085 (s), 1055 (s), 1020 (s), 975 (m), 890 (m), 840 (s), 775 (s); ^{1}H-NMR (300MHz, $CDCl_3$) δ 0.08 (s, 6H), 0.91 (s, 9H), 0.96 (d, *J*=6.8Hz, 3H), 1.76 (d.d.t, *J*=1.9, 4.6, 13.7Hz, 1H), 1.88~1.98 (m, 1H), 1.95~2.04 (m, 1H), 2.03~2.13 (m, 1H), 2.14 (m, 1H), 2.45 (br.t, *J*=13.3Hz, 1H), 2.61 (d.t, *J*=6.3, 13.7Hz, 1H), 3.88 (br, 1H); ^{13}C-NMR (75.5Hz, $CDCl_3$) δ –4.97, –4.54, 18.07, 18.35, 25.76, 33.15, 35.48, 38.47, 44.19, 69.23, 211.92; Anal. Calcd for $C_{13}SiH_{26}O_2$: C, 64.41; H, 10.81. Found : C, 64.42; H, 10.85.

(4a*R*,5*R*,6*S*)-6-*tert*-Butyldimethylsilyloxy-4,4a,5,6,7,8-hexahydro-4a,5-dimethyl-2(3*H*) naphthalenone 18

To a solution of **17** (1.92g, 7.50mM) in CH_2Cl_2 (40ml) was added hexamethyldisilazane (2.1ml, 9.8mM) and TMSI (1.2ml, 8.2mM). After stirring for 50 min at room temperature, the reaction mixture was diluted with *n*-hexane, filtered through florisil pad and concentrated to give the corresponding TMS enol ether. To the above enol ether in dry THF (43ml) was dropwise added MeLi (1.01M ether soln, 8.6ml, 8.7mM) at –78°C. The solution was allowed to reach room temperature, stirred for 30 min and recooled to –78°C. To this solution was added dropwise TMSMVK at –78°C. After being allowed to reach 0°C and stirred for 1 h at 0°C, the reaction mixture was diluted with ether. The organic layer was washed with sat. NH_4Cl soln and brine, dried over $MgSO_4$ and concentrated. To the above residue in MeOH (32ml) was added NaOMe (28% MeOH soln, 1.45g, 7.52mM). After stirring for 2 h at 50~60°C, the reaction mixture was diluted with ether (50ml) and the organic layer was washed with sat. NH_4Cl soln and brine, dried over $MgSO_4$ and concentrated. The residual oil was chromatographed over silica gel (75g) and eluted with *n*-hexane–EtOAc (40:1~30:1) to give 1.18g (3.82mM, 51%) of **18** as a slightly yellow oil. It solidified in standing at 5°C; $[\alpha]_D^{22.1}$ +147° (*c* 1.00, $CHCl_3$); IR (film) *v*max 2930 (s), 2860 (s), 1680 (s), 1665 (s), 1615 (s), 1470 (s), 1445 (s), 1430 (m), 1420 (m), 1370 (m), 1345 (m), 1320 (m), 1260 (s), 1220 (m), 1180 (m), 1105 (m), 1070 (s), 1045 (s), 1000 (m), 990 (s), 835 (s), 775 (s); ^{1}H-NMR (300MHz, $CDCl_3$) δ 0.06 (s, 3H), 0.07 (s, 3H), 0.92 (s, 9H), 1.00 (d, *J*=7.0Hz, 3H), 1.29 (s, 3H), 1.42 (d.q, *J*=2.5, 7.0 Hz, 1H), 1.56~1.70 (m, 2H), 1.90 (d.d.t, *J*=2.4, 4.7, 13.4Hz, 1H), 2.00 (d.d.d, *J*=2.8, 5.1, 13.3Hz, 1H), 2.08 (br.d.t, *J*=2.4, 3.3, 14.1Hz, 1H), 2.30 (br.d.d.d, *J*=2.8, 4.3, 17.1Hz, 1H), 2.46 (d.d.d, *J*=5.1, 14.8, 17.1Hz, 1H), 2.82 (d.d.t, *J*=1.5, 4.7, 14.1Hz, 1H), 3.86 (br.q, *J*=2.4, 2.5, 3.3Hz, 1H), 5.76 (br.d, *J*=1.5Hz, 1H); ^{13}C-NMR (75.5Hz, $CDCl_3$) δ –5.03, –4.59, 12.56, 18.03, 18.67, 25.80, 27.88, 33.61, 34.26, 36.33, 38.92, 46.75, 71.96, 123.81, 171.88, 199.71; Anal. Calcd for $C_{18}SiH_{32}O_2$: C, 70.07; H, 10.45. Found : C, 70.23; H, 10.47.

Elution with *n*-hexane–EtOAc (1:1) gave 468mg (1.24mM, 17%) of **19** as a slightly yellow oil.

(4a*R*,5*R*,6*S*,8*S*)-8-Bromo-6-*tert*-butyldimethylsilyloxy-4,4a,5,6,7,8-hexahydro-4a,5-dimethyl-2(3*H*)naphthalenone 20

A mixture of **18** (87mg, 0.29mM), NBS (60mg, 0.34mM) and benzoyl peroxide (a catalytic amount) in CCl_4 (3ml) was stirred and allowed to reflux under irradiation with a tungsten lamp of 185W for 1 h. The reaction mixture was diluted with ether and the organic layer was washed with sat. $NaHCO_3$ soln, water and brine, dried over $MgSO_4$ and concentrated. The residual yellow oil was chromatographed over silica gel (14g) and eluted with

CCl_4–EtOAc (100:1) to give 33mg (0.086mM, 30%) of **20** as a colorless needle, m.p. 56~62°C, together with 12mg (0.026mM, 9.2%) of **21** and 39mg (0.13mM, 45%) of recovered **18**; $[\alpha]_D^{21.2}$ +90.2° (*c* 0.410, $CHCl_3$); IR (film) *v*max 2960 (s), 2930 (s), 2900 (s), 2860 (s), 1680 (s), 1620 (s), 1470 (s), 1445 (s), 1370 (s), 1255 (s), 1220 (s), 1100 (s), 1070 (s), 1050 (s), 1000 (s), 950 (s), 940 (s), 910 (m), 870 (s), 835 (s), 780 (s); ^{1}H-NMR (300MHz, $CDCl_3$) δ 0.07 (s, 3H), 0.09 (s, 3H), 0.92 (s, 9H), 1.00 (d, *J*=6.9Hz, 3H), 1.32 (s, 3H), 1.49 (d.q, *J*=2.7, 6.9Hz, 1H), 1.72 (br.d.t, *J*=4.9, 13.5, 14.1Hz, 1H), 2.02 (br.d.d.d, *J*=3.3, 4.9, 13.5Hz, 1H), 2.15 (br.d.t, *J*=2.7, 13.1Hz, 1H), 2.32 (br.d.t, *J*=3.3, 4.9, 16.9Hz, 1H), 2.46 (d.d.d, *J*=4.9, 14.1, 16.9Hz, 1H), 2.54 (br.d.t, *J*=2.7, 4.5, 13.1Hz, 1H), 3.86 (br.q, *J*=2.7Hz, 1H), 5.23 (d.d.d, *J*=1.7, 4.5, 13.1Hz, 1H), 6.39 (d, *J*=1.7Hz, 1H); ^{13}C-NMR (75.5Hz, $CDCl_3$) δ –5.12, –4.74, 12.27, 17.94, 19.43, 25.72, 33.41, 37.05, 41.00, 46.29, 47.08, 48.13, 73.43, 126.26, 165.93, 199.35; Anal. Calcd for $C_{18}SiH_{31}O_2Br$: C, 55.80; H, 8.06. Found : C, 56.09; H, 7.86.

(4a*R*,5*R*,6*S*)-6-*tert*-Butyldimethylsilyloxy-4,4a,5,6-tetrahydro-4a,5-dimethyl-2(3*H*) naphthalenone 22

A mixture of **20** (51mg, 0.13mM), LiBr (23mg, 0.26mM) and Li_2CO_3 (29mg, 0.39mM) in DMF (2ml) was refluxed for 1.5 h. The reaction mixture was diluted with ether. The organic layer was washed with sat. NH_4Cl soln and brine, dried over $MgSO_4$ and concentrated. The residual oil was chromatographed over silica gel (10g) and eluted with *n*-hexane–EtOAc (80:1~60:1) to give 30mg (0.099mM, 76%) of **22** as a colorless oil. It solidified in standing at 5°C, m.p. 40~42°C; $[\alpha]_D^{20.4}$ +508° (*c* 0.580, $CHCl_3$); IR (nujol) *v*max 3035 (m), 2960 (s), 2930 (s), 2880 (s), 2860 (s), 1670 (s), 1630 (s), 1590 (m), 1475 (m), 1460 (m), 1445 (m), 1350 (m), 1255 (s), 1210 (m), 1110 (s), 1040 (s), 1000 (s); ^{1}H-NMR (300MHz, $CDCl_3$) δ 0.08 (s, 6H), 0.88 (s, 9H), 1.03 (d, *J*=7.1Hz, 3H), 1.24 (s, 3H), 1.62~1.73 (2H), 2.03 (d.d.d, *J*=2.1, 5.2, 13.1Hz, 1H), 2.41 (d.d.d, *J*=2.1, 5.2, 17.8Hz, 1H), 2.54 (d.d.d, *J*=5.2, 14.1, 17.8Hz, 1H), 4.09 (br.t, *J*=3.8Hz, 1H), 5.74 (s, 1H), 6.09~6.20 (2H); ^{13}C-NMR (75.5Hz, $CDCl_3$) δ –5.10, –4.07, 11.17, 17.98, 18.50, 25.71, 33.91, 34.47, 35.96, 42.31, 68.52, 124.85, 128.59, 137.25, 163.15, 199.78; Anal. Calcd for $C_{18}SiH_{30}O_2$: C, 70.53; H, 9.86. Found : C, 70.11; H, 9.80.

(3*R*,4a*R*,5*R*,6*S*)-6-*tert*-Butyldimethylsilyloxy-4,4a,5,6-tetrahydro-3-hydroxy-4a,5-dimethyl-2(3*H*)naphthalenone 23

To a solution of KHMDS (0.5M toluene soln, 0.48ml, 0.24mM) in dry THF (4.7ml) was added **22** (44mg, 0.15mM) in dry THF (1.6ml) at –78°C. The solution was allowed to stir for 30 min at –78°C followed by dropwise addition of 2-benzenesulfonyl-3-phenyloxaziridine (63mg, 0.24mM) in dry THF (4.7ml). After stirring for 20 min at –78°C, the reaction mixture was quenched with 2ml of sat. NH_4Cl soln at –78°C and extracted with ether. The ether layer was washed with sat. NH_4Cl soln, water and brine, dried over $MgSO_4$ and concentrated. The residue was chromatographed over silica gel (15g) and eluted with *n*-hexane–EtOAc (40:1~30:1) to give 21mg (0.065mM, 45%) of **23** as a colorless needle, m.p. 131~134°C; $[\alpha]_D^{18.7}$ +497° (*c* 0.220, $CHCl_3$); IR (nujol) *v*max 3470 (br.m), 2960(s), 2925 (s), 2860 (s), 1670 (s), 1630 (m), 1585 (m), 1375 (s), 1250 (m), 1230 (m), 1090 (m), 1050 (m); ^{1}H-NMR (300MHz, $CDCl_3$) δ 0.10 (s, 6H), 0.83 (s, 9H), 1.06 (d, *J*=7.0Hz, 3H), 1.34 (s, 3H), 1.58 (br.t, *J*=12.4, 13.2Hz, 1H), 1.70 (d.q, *J*=4.3, 7.0Hz, 1H), 2.42 (d.d, *J*=5.7, 12.4Hz, 1H),

3.58 (br.s, 1H), 4.07 (t, *J*=4.3Hz, 1H), 4.36 (d.d, *J*=5.7, 13.2Hz, 1H), 5.83 (s, 1H), 6.17 (d.d, *J*=4.3, 9.8Hz, 1H), 6.22 (d, *J*=9.8Hz, 1H); ^{13}C-NMR (75.5Hz, $CDCl_3$) δ –5.08, –4.11, 11.03, 17.98, 19.40, 25.70, 37.94, 42.50, 43.13, 67.85, 69.94, 121.67, 127.71, 138.02, 164.79, 199.82; Anal. Calcd for $C_{18}SiH_{30}O_3$: C, 67.03; H, 9.38. Found : C, 67.09; H, 9.31.

THP ether of 23, (3*R*,4a*R*,5*R*,6*S*)-6-*tert*-butyldimethylsilyloxy-4,4a,5,6-tetrahydro-4a,5-dimethyl-3-tetrahydropyranyloxy-2(3*H*)naphthalenone

A mixture of **23** (41mg, 0.13mM), 2,3-dihydropyran (130mg, 1.6mM) and pyridinium *p*-toluenesulfonate (10mg, 0.040mM) in CH_2Cl_2 (4ml) was stirred overnight at room temperature. The reaction mixture was diluted with ether, washed with sat. $NaHCO_3$ soln, water and brine, dried over $MgSO_4$ and concentrated. The yellow residue was chromatographed over silica gel (11g) and eluted with *n*-hexane–EtOAc (50:1~40:1) to give 52mg (0.13mM, quantitative) of THP ether of **23** as a colorless solid of a diastereomeric mixture; $[\alpha]_D^{27.9}$ +392° (*c* 2.60, $CHCl_3$); IR (film) *v*max 2930 (s), 2860 (s), 1730 (s), 1690 (s), 1680 (s), 1470 (m), 1460 (m), 1455 (m), 1260 (m), 1120 (s), 1070 (s), 1035 (s); ^{1}H-NMR (300MHz, $CDCl_3$) δ 0.09 (s, 6H), 0.89 (s, 9H), 1.06 (d, *J*=7.0Hz, 3H), 1.32 (s) & 1.35 (s) (3H), 1.55~1.89 (8H), 2.30 (d.d, *J*=5.4, 12.4Hz, 1H), 3.50~3.60 & 3.87~3.94 & 3.99~4.03 (2H), 4.06 (t, *J*=4.3Hz, 1H), 4.42~4.53 (1H), 4.81~4.82 (m) & 5.04~5.06 (m) (1H), 5.72 (s) & 5.77 (s) (1H), 6.11~6.20 (2H); ^{13}C-NMR (75.5Hz, $CDCl_3$) δ –5.12, –4.09, 11.12, 17.96, 18.86, 19.44, 19.62, 25.43, 25.68, 30.47, 37.77, 37.98, 40.89, 42.51, 61.74, 62.95, 67.92, 72.78, 95.69, 99.68, 123.79, 124.15, 127.79, 137.13, 137.29, 161.78, 162.65, 197.05, 199.00; Anal. Calcd for $C_{23}SiH_{38}O_4$: C, 67.94; H, 9.42. Found : C, 67.69; H, 9.49.

(3*R*,4a*R*,5*R*,6*S*)-4,4a,5,6-Tetrahydro-6-hydroxy-4a,5-dimethyl-3-tetrahydropyranyloxy-2(3*H*)naphthalenone 24

To a solution of the above THP ether of **23**, (3*R*,4a*R*,5*R*,6*S*)-6-*tert*-butyldimethylsilyloxy-4,4a,5,6-tetrahydro-4a,5-dimethyl-3-tetrahydropyranyloxy-2(3*H*)naphthalenone (91mg, 0.22mM) in dry THF (10ml) was added tetrabutylammonium fluoride (1M THF soln, 0.45ml, 0.45mM) at 0°C. After stirring for 10 min at 0°C and for more 1.5 h at room temperature, the reaction mixture was diluted with ether, washed with sat. NH_4Cl soln and brine, dried over $MgSO_4$ and concentrated. The yellow residue was chromatographed over silica gel (10g) and eluted with *n*-hexane–EtOAc (3:1) to give 44mg (0.15mM, 67%) of **24** as a slightly yellow gum of a diastereomeric mixture, which was employed in the next step without any more purification; $[\alpha]_D^{27.8}$ +465° (*c* 0.125, $CHCl_3$); IR (film) *v*max 3440 (s), 2940 (s), 2875 (s), 1680 (s), 1665 (s), 1630 (s), 1590 (m), 1455 (m), 1445 (m), 1390 (m), 1220 (m), 1200 (m), 1140 (s), 1120 (s), 1035 (s), 1020 (s), 975 (s); ^{1}H-NMR (300MHz, $CDCl_3$) δ 1.14 (d, *J*=7.1Hz, 3H), 1.30 (s) & 1.33 (s) (3H), 1.50~1.96 (8H), 2.11 (br.s, 1H), 2.31 (d.d, *J*=5.4, 12.3Hz, 1H), 3.49~3.56 & 3.86~3.93 & 4.09~4.21 (2H), 4.13 (t, *J*=4.1Hz, 1H), 4.45 (d.d, *J*=5.4, 13.4Hz) & 4.48 (d.d, *J*=5.4, 13.4Hz) (1H), 4.81 (br.t) & 5.02 (br.d.d) (1H), 5.74 (s) & 5.79 (s) (1H), 6.21~6.29 (2H); ^{13}C-NMR (75.5Hz, $CDCl_3$) δ 10.32, 18.73, 19.39, 19.61, 25.35, 30.43, 37.48, 37.69, 40.68, 41.98, 42.36, 61.67, 63.02, 67.39, 72.70, 95.57, 99.72, 124.08, 124.43, 128.50, 136.69, 161.29, 162.13, 196.99, 198.91.

Elution with *n*-hexane–EtOAc (15:1~10:1) gave 8mg (0.02mM, 9%) of recovered **23**. The yield of **24** based on the recovery of **23** was 74%.

(*S*)-2-Methylbutanal 25

To a mixture of 98% PCC (11.6g, 52.7mM) and silica gel (11.6g) in CH_2Cl_2 (90ml) was added (*S*)-2-methylbutanol **12** (4.0g, 45mM) in CH_2Cl_2 (20ml) at 0°C. After stirring for 3 h at 0°C ~ room temperature, the reaction mixture was filtered through florisil pad and washed with CH_2Cl_2. The combined CH_2Cl_2 layer (150ml) was employed in the next step without any purification; IR (film) νmax 2965(s), 2935 (s), 2880 (s), 1730 (s), 1460 (m), 1380 (m); ^{1}H-NMR (300MHz, $CDCl_3$) δ 0.91 (t, *J*=7.5Hz, 3H), 1.04 (d, *J*=7.0Hz, 3H), 1.39 (m, *J*=7.4, 7.5, 14.1Hz, 1H), 1.70 (m, *J*=7.5, 14.1Hz, 1H), 2.23 (m, *J*=1.6, 7.0, 7.4, 7.5Hz, 1H), 9.58 (d, *J*=1.6Hz, 1H); ^{13}C-NMR (75.5Hz, $CDCl_3$) δ 11.24, 12.75, 23.45, 47.68, 205.25.

Ethyl (2*E*,4*S*)-4-methyl-2-hexenoate 27

To the above **25** in CH_2Cl_2 was added 95% (carbethoxymethylene)triphenylphosphorane (16.6g, 45.3mM). After stirring overnight at room temperature, the reaction mixture was concentrated. The residual crude solid was chromatographed over silica gel (380g) and eluted with *n*-hexane–EtOAc (15:1~9:1) to give 3.3g (21mM, 46% from **12**) of **27** as a colorless oil; $[\alpha]_D^{20.6}$ +32.7° (*c* 0.910, benzene); IR (film) νmax 2965 (s), 2930 (s), 2875 (s), 1725 (s), 1715 (s), 1650 (s), 1460 (m), 1370 (s), 1350 (m), 1310 (s), 1290 (s), 1270 (s), 1240 (s), 1185 (s), 1160 (s), 1135 (s), 1095 (m), 1040 (s), 985 (s); ^{1}H-NMR (300MHz, $CDCl_3$) δ 0.84 (t, *J*=7.5Hz, 3H), 1.00 (d, *J*=6.8Hz, 3H), 1.25 (t, *J*=7.1Hz, 3H), 1.37 (br.quintet, *J*=7.2, 7.5Hz, 2H), 2.17 (br.septet, *J*=6.8, 7.2, 7.8, 1H), 4.14 (q, *J*=7.1Hz, 2H), 5.73 (d, *J*=15.7Hz, 1H), 6.82 (d.d, *J*=7.8, 15.7Hz, 1H); ^{13}C-NMR (75.5Hz, $CDCl_3$) δ 11.58, 14.24, 18.89, 28.74, 38.07, 60.11, 119.70, 154.43, 166.93; Anal. Calcd for $C_9H_{16}O_2$: C, 69.19; H, 10.32. Found : C, 69.42; H, 10.31.

(2*E*,4*S*)-4-Methyl-2-hexenol 28

To **27** (67mg, 0.43mM) in CH_2Cl_2 (2ml) was dropwise added diisobutylaluminum hydride (1.01M toluene soln, 0.48ml, 0.48mM) at –78°C. After stirring for 30 min at –78°C, the reaction mixture was quenched with MeOH (2ml) at –78°C, stirred at room temperature for 30 min, diluted with CH_2Cl_2 and filtered. The filtrate was concentrated. The residue was chromatographed over silica gel (20g) and eluted with *n*-hexane–EtOAc (20:1~8:1) to give 42mg (0.37mM, 86%) of **28** as a colorless oil; $[\alpha]_D^{21.7}$ +37.9° (*c* 0.570, $CHCl_3$); IR (film) νmax 3350 (br.s), 2960 (s), 2925 (s), 2875 (s), 1670 (m), 1640 (m), 1565 (m), 1455 (m), 1415 (m), 1380 (m), 1080 (m), 1015 (m), 970 (s); ^{1}H-NMR (300MHz, $CDCl_3$) δ 0.86 (t, *J*=7.3Hz, 3H), 0.98 (d, *J*=6.9Hz, 3H), 1.34 (quintet, *J*=7.3Hz, 1H), 1.40 (br.s, 1H), 2.05 (m, 1H), 4.09 (d, *J*=4.6Hz, 2H), 5.51~5.65 (m, 2H); ^{13}C-NMR (75.5Hz, $CDCl_3$) δ 11.67, 19.88, 29.47, 37.92, 63.90, 127.19, 139.01; Anal. Calcd for $C_7H_{14}O$: C, 73.63; H, 12.36. Found : C, 73.16; H, 12.39.

Ethyl (2*E*,4*E*,6*S*)-6-methyl-2,4-octadienoate 29

To a mixture of 98% PCC (2.47g, 11.2mM) and silica gel (2.5g) in CH_2Cl_2 (25ml) was added **28** (1.07g, 9.37mM) in CH_2Cl_2 (6ml) at 0°C. After stirring for 3 h at 0°C ~ room temperature, the solution was filtered through florisil pad and washed with CH_2Cl_2;

for **(2*E*, 4*S*)-4-methyl-2-hexenal**; ^{1}H-NMR (300MHz, $CDCl_3$) δ 0.90 (t, *J*=7.3Hz, 3H), 1.09 (d, *J*=6.7Hz, 3H), 1.46 (br.quintet, *J*=7.2, 7.3Hz, 2H), 2.36 (br.d.septet, *J*=0.8, 6.7, 7.2, 7.5Hz, 1H), 6.08 (d.d.d, *J*=0.8,

7.8, 15.6Hz, 1H), 6.74 (d.d, *J*=7.5, 15.6Hz, 1H), 9.50 (d, *J*=7.8Hz, 1H); ^{13}C-NMR (75.5Hz, $CDCl_3$) δ 11.50, 18.66, 28.65, 38.51, 131.41, 163.95, 194.28.

To the above (2*E*,4*S*)-4-methyl-2-hexenal in the combined CH_2Cl_2 solution was added 95% **26** (3.44g, 9.38mM). After stirring overnight at room temperature, the reaction mixture was concentrated. The yellow residue was chromatographed over silica gel (220g) and eluted with *n*-hexane–EtOAc (95:1) to give *ca.* 1g of a mixture of **29** and **30** as a colorless oil. This mixture was rechromatographed over silica gel (40g) and eluted with *n*-hexane–EtOAc (110:1) to give 60mg (0.33mM, 3.5%) of **30** and 850mg (4.66mM, 50%) of **29** both as a colorless oil; $[\alpha]_D^{22.6}$ +46.2° (*c* 1.83, $CHCl_3$); IR (film) *v*max 3420 (br.s), 2965 (s), 2930 (s), 2875 (m), 1715 (s), 1645 (s), 1620 (m), 1560 (m), 1460 (m), 1420 (m), 1370 (m), 1310 (m), 1260 (s), 1240 (m), 1230 (m), 1190 (m), 1145 (s), 1115 (m), 1045 (m), 1000 (m); ^{1}H-NMR (300MHz, $CDCl_3$) δ 0.86 (t, *J*=7.3Hz, 3H), 1.02 (d, *J*=6.8Hz, 3H), 1.28 (t, *J*=7.1Hz, 3H), 1.36 (quintet, *J*=7.3Hz, 2H), 2.16 (br.septet, *J*=6.8, 7.3, 7.5Hz, 1H), 4.19 (q, *J*=7.1Hz, 2H), 5.79 (d, *J*=15.3Hz, 1H), 6.00 (d.d, *J*=7.5, 15.2Hz, 1H), 6.13 (d.d, *J*=10.6, 15.2Hz, 1H), 7.26 (d.d, *J*=10.6, 15.3Hz, 1H); ^{13}C-NMR (75.5Hz, $CDCl_3$) δ 11.65, 14.29, 19.48, 29.28, 38.77, 60.13, 119.23, 126.69, 145.25, 150.14, 167.29; Anal. Calcd for $C_{11}H_{18}O_2$: C, 72.49; H, 9.95. Found : C, 72.27; H, 9.95;

for **ethyl (2*Z*,4*E*,6*S*)-6-methyl-2,4-octadienoate 30**; $[\alpha]_D^{22.9}$ +39.6° (*c* 0.705, $CHCl_3$); ^{1}H-NMR (300MHz, $CDCl_3$) δ 0.87 (t, *J*=7.3Hz, 3H), 1.03 (d, *J*=6.7Hz, 3H), 1.30 (t, *J*=7.1Hz, 3H), 1.38 (quintet, *J*=7.3Hz, 2H), 2.22 (br.septet, *J*=6.7, 7.3, 7.9Hz, 1H), 4.18 (q, *J*=7.1Hz, 2H), 5.57 (d, *J*=11.3Hz, 1H), 5.95 (d.d, *J*=7.9, 15.3Hz, 1H), 6.55 (t, *J*=11.3Hz, 1H), 7.34 (d.d, *J*=11.3, 15.3Hz, 1H); ^{13}C-NMR (75.5Hz, $CDCl_3$) δ 11.73, 14.30, 19.54, 29.35, 38.73, 59.82, 115.56, 125.29, 145.59, 151.21, 166.65.

(2*E*,4*E*,6*S*)-6-Methyl-2,4-octadienoic acid 10

To **29** (360mg, 1.98mM) was added LiOH (1.44g, 60mM) in MeOH–H_2O (4:1, 100ml) at 0°C. After stirring overnight at 0°C ~ room temperature, the solution was neutralized with AcOH and concentrated to remove MeOH. The residue was extracted with EtOAc three times. The combined EtOAc layer was dried over $MgSO_4$ and concentrated. The residual oil was chromatographed over silica gel (20g), eluted with *n*-hexane–EtOAc (100:1~30:1) to give a colorless oil. This oil was passed through LH-20 column (14mm i.d. x 32cm l.) developing with $CHCl_3$–MeOH (1:1) to give 206mg (1.34mM, 68%) of **10** as a colorless oil; $[\alpha]_D^{22.9}$ +52.6° (*c* 0.490, 95% EtOH); IR (film) *v*max 2960 (br.s), 2920 (s), 2880 (s), 2660 (m), 2560 (m), 1695 (s), 1680 (s), 1640 (s), 1620 (s), 1460 (m), 1420 (s), 1380 (m), 1310 (s), 1275 (s), 1160 (s), 1000 (s), 940 (m); ^{1}H-NMR (300MHz, $CDCl_3$) δ 0.87 (t, *J*=7.1Hz, 3H), 1.03 (d, *J*=6.8Hz, 3H), 1.38 (quintet, *J*=7.1Hz, 2H), 2.19 (septet, *J*=7.1Hz, 1H), 5.80 (d, *J*=15.3Hz, 1H), 6.06 (d.d, *J*=7.1, 15.2Hz, 1H), 6.18 (d.d, *J*=10.4, 15.2Hz, 1H), 7.35 (d.d, *J*=10.4, 15.3Hz, 1H), 10.6~10.9 (br.s, 1H); ^{13}C-NMR (75.5Hz, $CDCl_3$) δ 11.66, 19.39, 29.23, 38.84, 118.35, 126.59, 147.71, 151.64, 172.84; Anal. Calcd for $C_9H_{14}O_2$: C, 70.10; H, 9.15. Found : C, 69.53; H, 9.29.

THP ether of 3, (1*R*,2*S*,7*R*,8a*R*)-1,2,6,7,8,8a-hexahydro-1,8a-dimethyl-6-oxo-7-tetrahydro pyranyloxynaphthalen-2-yl (2*E*,4*E*,6*S*)-6-methyl-2,4-octadienoate

To **10** (15mg, 0.10mM) in dry THF (0.6ml) was added triethylamine (0.014ml, 0.10mM) and 2,4,6-

trichlorobenzoyl chloride (0.016ml, 0.10mM). The solution was stirred for 30 min at room temperature. After the removal of the triethylamine hydrochloride by filtration, the filtrate was concentrated to give a colorless residue. To this residue in dry benzene (0.3ml) was added a mixture of **24** (24mg, 0.083mM) and 4-dimethylamino pyridine (20mg, 0.17mM) in dry benzene (0.3ml). The reaction mixture was stirred for 1.5 h at room temperature and diluted with ether. The organic layer was washed with sat. NH_4Cl soln, water, sat. $NaHCO_3$ soln, water and brine, dried over $MgSO_4$ and concentrated. The yellow residue was chromatographed over silica gel (6g) and eluted with *n*-hexane–EtOAc (30:1~20:1) to give 28mg (0.066mM, 79%) of THP ether of **3** as a colorless oil of a diastereomeric mixture; $[\alpha]_D^{28.3}$ +624° (*c* 1.13, $CHCl_3$); IR (film) *v*max 2960 (s), 2920 (s), 2880 (s), 1715 (s), 1680 (s), 1640 (s), 1455 (m), 1380 (m), 1300 (m), 1260 (m), 1140 (m), 1120 (m), 1085 (m), 1070 (m), 1035 (m), 1010 (m); ^{1}H-NMR (300MHz, $CDCl_3$) δ 0.86 (t, *J*=7.3Hz, 3H), 1.02 (d, *J*=7.0Hz, 3H), 1.04 (d, *J*=7.0Hz, 3H), 1.35 (s) & 1.38 (s) (1H), 1.33~1.39 (m, 2H), 1.54~1.63 (m) & 1.67~1.77 (m) & 1.85~1.90 (m) (6H), 1.81 (t, *J*=13.0Hz, 1H), 1.95~1.97 (m, 1H), 2.17 (br.septet, *J*=7.0Hz, 1H), 2.33 (d.d, *J*=5.5, 13.0Hz, 1H), 3.49~3.55 (m) & 3.88~3.92 (m) & 4.18~4.22 (m) (2H), 4.49 (d.d, *J*=5.5, 13.0Hz) & 4.52 (d.d, *J*=5.5, 13.0Hz) (1H), 4.83 (br.t, *J*=3.0Hz) & 5.05 (d.d, *J*=2.5, 3.0Hz) (1H), 5.41 (br.t, *J*=5.0Hz, 1H), 5.78 (s) & 5.80 (s) (1H), 5.80 (d, *J*=15.4Hz, 1H), 6.02 (d.d, *J*=7.0, 15.5Hz, 1H), 6.15 (d.d, *J*=10.8, 15.5Hz, 1H), 6.23 (d.d, *J*=5.0, 9.5Hz, 1H), 6.33 (d, *J*=9.5Hz, 1H), 7.24 (d.d, *J*=10.8, 15.4Hz, 1H); ^{13}C-NMR (75.5Hz, $CDCl_3$) δ 10.09, 11.66, 18.76, 19.03, 19.30, 19.46, 19.63, 25.41, 29.22, 30.47, 37.39, 37.60, 38.82, 40.56, 41.02, 42.23, 61.68, 63.07, 68.36, 72.74, 95.58, 99.76, 118.68, 124.73, 125.10, 126.60, 130.40, 132.81, 145.93, 150.88, 161.03, 166.63, 198.69; Anal. Calcd for $C_{26}H_{36}O_5$: C, 72.87; H, 8.47. Found : C, 72.83; H, 8.48.

(1*R*,2*S*,7*R*,8a*R*)-1,2,6,7,8,8a-hexahydro-7-hydroxy-1,8a-dimethyl-6-oxonaphthalen-2-yl (2*E*,4*E*,6*S*)-6-methyl-2,4-octadienoate, dendryphiellin C 3

A mixture of the above THP ether of **3**, (1*R*,2*S*,7*R*,8a*R*)-1,2,6,7,8,8a-hexahydro-1,8a-dimethyl-6-oxo-7-tetrahydropyranyloxynaphthalen-2-yl (2*E*,4*E*,6*S*)-6-methyl-2,4-octadienoate (20mg, 0.046mM) and pyridinium *p*-toluenesulfonate (12mg, 0.048mM) in MeOH (1ml) was stirred overnight at room temperature. The reaction mixture was diluted with ether, washed with sat. $NaHCO_3$ soln and brine, dried over $MgSO_4$ and concentrated. The residue was chromatographed over silica gel (4g) and eluted with *n*-hexane–EtOAc (20:1~15:1) to give a colorless oil. This oil was passed through LH-20 column (14mm i.d. x 34cm l.) developing with $CHCl_3$–MeOH (1:1) to give 16mg (0.046mM, quantitative) of **3** as a colorless oil; $[\alpha]_D^{26.5}$ +728° (*c* 0.495, MeOH): *lit.*[1b] *$[\alpha]_D^{20}$ +506.9° (c 0.41, MeOH)*; IR (film) *v*max 3440 (br.s), 3040 (m), 2960 (s), 2920 (s), 2870 (s), 2860 (s), 1715 (s), 1670 (s), 1640 (s), 1630 (s), 1590 (m), 1460 (s), 1380 (m), 1300 (m), 1260 (m), 1230 (m), 1140 (m), 1090 (m); ^{1}H-NMR (300MHz, CD_3OD) δ 0.88 (t, *J*=7.3Hz, 3H), 1.04 (d, *J*=7.3Hz, 3H), 1.06 (d, *J*=7.3Hz, 3H), 1.36~1.42 (m, 2H), 1.40 (s, 3H), 1.67 (t, *J*=13.0Hz, 1H), 2.02 (d.q, *J*=4.8, 7.3Hz, 1H), 2.19 (br.septet, *J*=7.3Hz, 1H), 2.36 (d.d, *J*=5.5, 13.0Hz, 1H), 4.40 (d.d, *J*=5.5, 13.0Hz, 1H), 5.42 (br.t, *J*=4.8Hz, 1H), 5.85 (s, 1H), 5.85 (d, *J*=15.5Hz, 1H), 6.07 (d.d, *J*=7.3, 15.1Hz, 1H), 6.25 (d.d, *J*=10.4, 15.1Hz, 1H), 6.26 (d.d, *J*=4.8, 9.8Hz, 1H), 6.45 (d, *J*=9.8Hz, 1H), 7.27 (d.d, *J*=10.4, 15.5Hz, 1H); ^{13}C-NMR (75.5Hz, CD_3OD) δ 10.43, 12.09, 19.47, 19.96, 30.37, 38.84, 40.22, 42.44, 44.54, 69.93, 70.96, 119.74, 124.69, 128.15, 131.53, 134.12, 147.42, 152.08, 163.93, 168.20, 201.33; Anal. Calcd for $C_{21}H_{28}O_4$: C, 73.23; H, 8.19. Found : C, 73.13; H, 8.37.

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