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EFFICIENT SYNTHESIS OF THE NATURAL ENANTIOMER OF SPOROGEN-AO 1 (13-DESOXYPHOMENONE), A SPOROGENIC SESQUITERPENE FROM ASPERGILLUS ORYZAE†

TAKESHI KITAHARA,* HITOSHI KURATA and **KENJI MORI**

Department of Agricultural Chemistry, The University of Tokyo,
Yayoi 1-1-1, Bunkyo-ku, Tokyo 113, Japan.

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Abstract ---- An efficient total synthesis of (+)-sporogen-AO 1 (13-desoxyphomenone) **1** was achieved in 20 steps from ethyl (1R,2S)-5,5-ethylenedioxy-2-hydroxycyclohexanecarboxylate **3** in 8.3% overall yield. The optically active **3** with 98.4% e.e. was easily obtained in 74% yield by the reduction of the corresponding keto ester **4** with baker's yeast.

INTRODUCTION

Sporulation of fungi is an essential phenomenon for their own reproduction and deeply concerned with bio-production of important metabolites. In 1984, Marumo and his coworkers isolated 3 mg of an oily sporogenic substance from the culture broth of Aspergillus oryzae,[1] which is one of the most important fungi in Japanese fermentation industry to produce Japanese sake (rice wine), shoyu (soy-sauce), miso (fermented soybeans) and industrial enzymes, such as acylase, amylase and protease. They named it sporogen-AO 1 and determined its structure as depicted in 1,[2] which was identical with 13-desoxyphomenone, already isolated as a crystalline fungi- and phytotoxic elemophilane sesquiterpene from

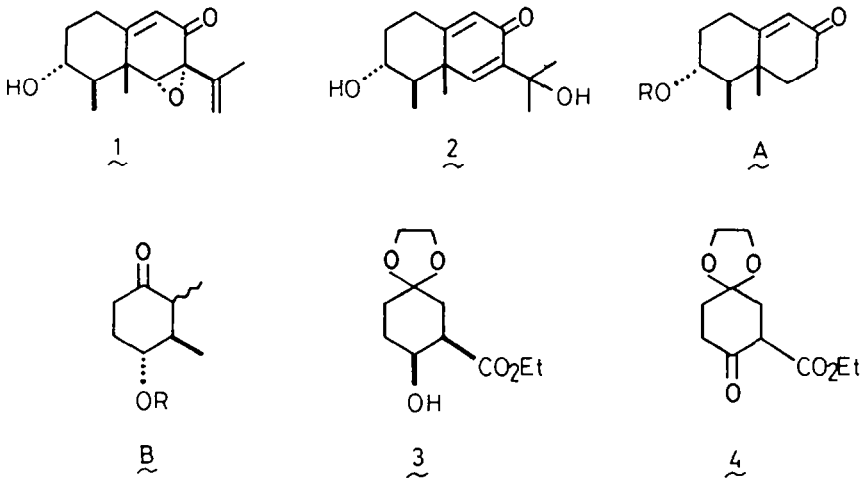
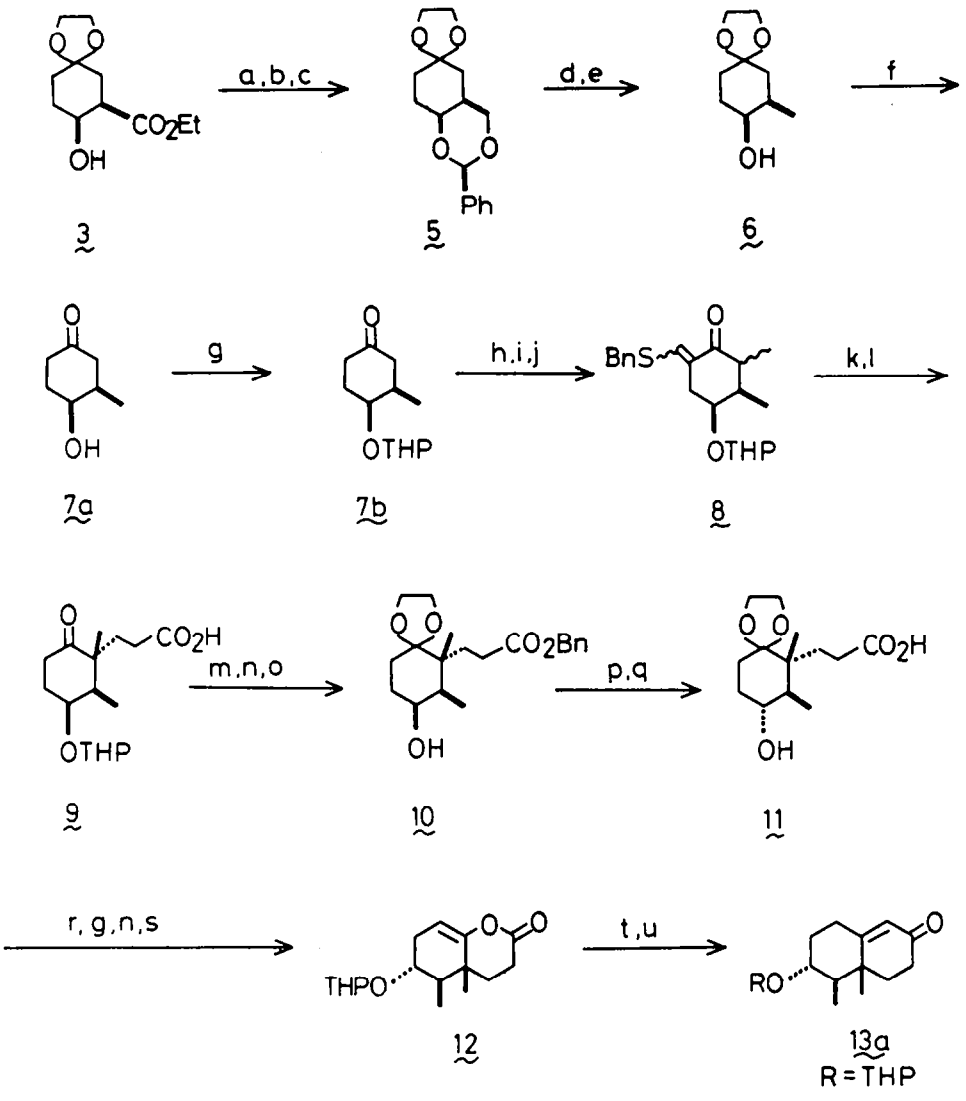


FIG. 1

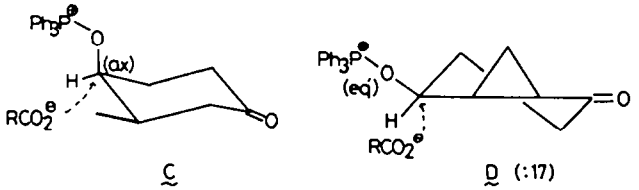
†Synthetic Microbial Chemistry Part 18. Part 17, K. Mori and M. Komatsu, Liebigs Ann. Chem. 1988, 107.

Dedicated to the Emeritus Professor M. Matsui on the occasion of his 70th birthday.



SCHEME I

a) Ac_2O, pyridine (quantitative); b) $LiAlH_4$, THF (95%); c) $PhCH(OEt)_2$, p-TsOH, CH_2Cl_2 (87%); d) NBS, AIBN, benzene (83%); e) $LiAlH_4$, THF (83%); f) Amberlite IR-120, H_2O (99%); g) DHP, p-TsOH, CH_2Cl_2 (90%); h) NaH, HCO_2Et, THF; i) LDA, MeI, THF-HMPA; j) p-TsCl, pyridine then BnSH (74%); k) t-BuOK, $BrCH_2CH_2CO_2Et$, t-BuOH; l) KOH, H_2O-diethylene glycol (69%); m) ethylene glycol, p-TsOH, benzene; n) LiOH, H_2O-MeOH; o) BnBr, $NaHCO_3$, DMF (53%); p) DMSO, $(COCl)_2$, Et_3N, CH_2Cl_2 (87%); q) Li/NH_3, t-BuOH; r) p-TsOH, MeOH; s) Ac_2O, AcONa (56%); t) MeLi, ether; u) KOH, H_2O-MeOH (55%)



C D (:17)

FIG II

Hansfordia pulvinata by Tirilly et al. in 1983.[3] This fungal metabolite showed significant philaspore formation-stimulating activity at a dose of 4.4 µg/disc. As detailed in the previous paper on the first synthesis of **1**,[4] we were interested in synthesizing sporogen-AO 1 to afford a sufficient amount for the biological study. Here, we wish to describe the short and efficient total synthesis of the natural enantiomer of sporogen-AO 1 **1**.

SYNTHETIC PLAN

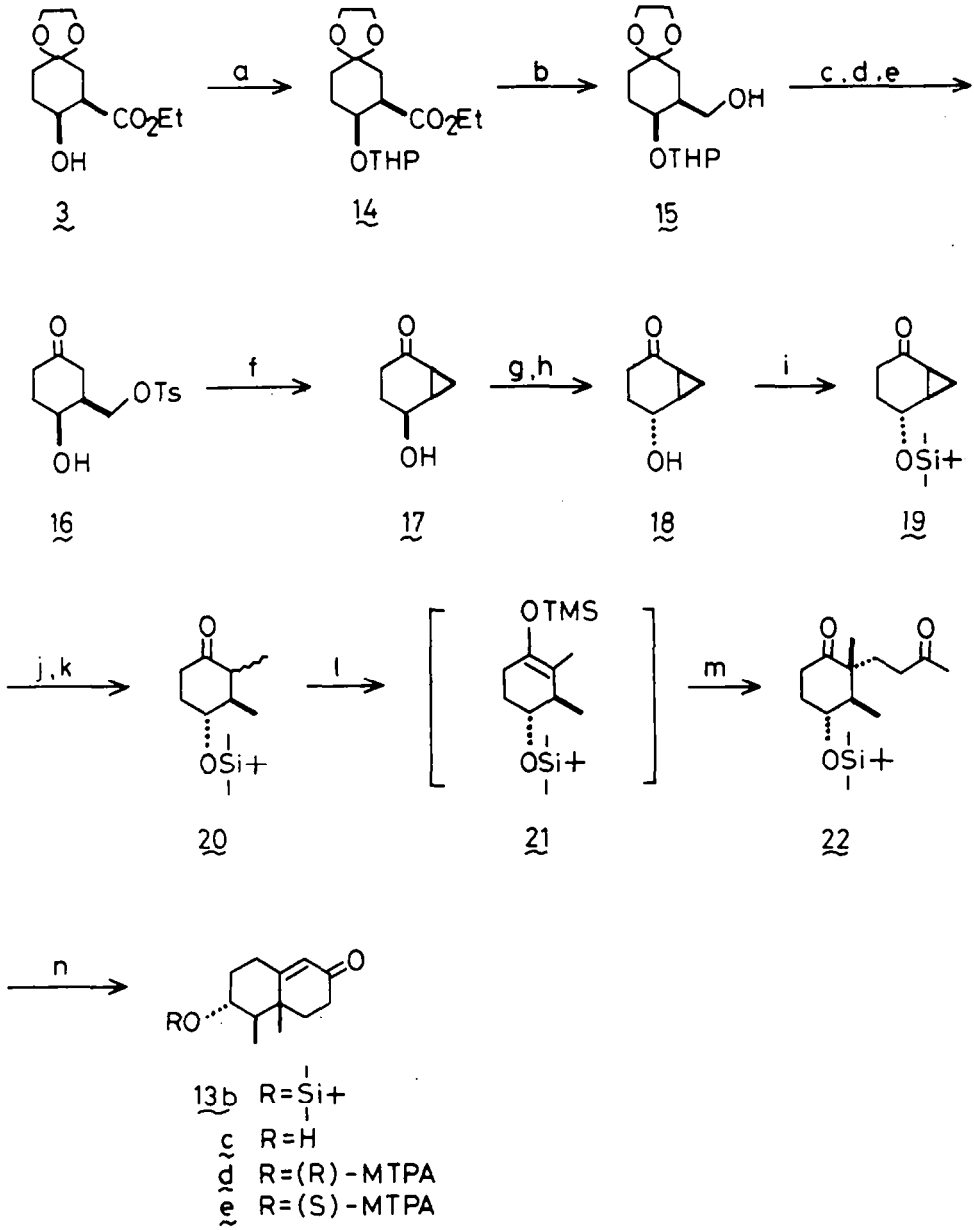
We selected the octalone **A**, which was used in the synthesis of (±)-petasitol **2** by Yamakawa et al.,[5] as the key intermediate. Addition of a three-carbon unit and formation of epoxide ring should give **1**. Problems were how to prepare **A** stereo- and regioselectively from the ketone **B** and to obtain **B** in optically active form. We reported the simple preparation of ethyl (1R,2S)-5,5-ethylenedioxy-2-hydroxycyclohexanecarboxylate **3** with 98.4% e.e. in 74% yield[6] by asymmetric reduction of the corresponding keto ester **4**[7] with baker's yeast. Using **3** as the starting material, reduction of ester to methyl group, regioselective introduction of methyl group and inversion of β-hydroxyl group were necessary to give **B**.

OXIDATION-REDUCTION ROUTE TO THE OCTALONE A

Scheme I shows overall route to the protected octalone **13a** (= **A**). Hanessian's fission of benzylidene group of **5** with NBS[8] and the following reduction with $LiAlH_4$ gave the methylcyclohexanol **6** in high yield. Acid hydrolysis of **6** gave the ketol **7a**. Mitsunobu inversion of the intermediate **3**, **6** or **7a**, however, did not yield the desired inversion product at all. Several attempts on the inversion of β-OH to α-OH were unfruitful and thus we turned to use the oxidation-reduction process. As the alcohol **7a** might racemize during oxidation-reduction step, inversion was carried out at a later stage. Formylation of the protected ketone **7b**, followed by treatment of its dianion with methyl iodide gave site-selectively alkylated product, which was converted to the benzylthiomethylene ketone **8**[10] in 74% yield. Second alkylation with several electrophiles including methyl vinyl ketone was fruitless, but only that with ethyl 3-bromopropanoate gave the desired product. Successive manipulation of protective groups gave the substrate **10** for the following oxido-reductive inversion. Swern oxidation[11] of **10** was followed by dissolving metal reduction to afford cleanly the α-oriented alcohol **15** as a sole product. Annulation was executed by Woodward's[12] and Piers'[13] procedure to give the octalone **13a**. This route required 23 steps from **3** with only 4.8% overall yield, because extra protections were necessary for selective introduction of alkyl groups and the oxido-reduction process. Thus, we re-examined the synthetic scheme from **3** to the octalone **A** especially on site-selective alkylation and the inversion of OH group.

IMPROVED ROUTE TO THE OCTALONE A VIA CYCLOPROPYL DERIVATIVE 17

We focused on the inversion of OH group first and employed the cyclopropyl carbinol **17** as the candidate for Mitsunobu inversion.[9] Preferred conformations of **C** and **D** for the inversion are depicted in Fig II. Apparently, quasi-equatorial OH in **17** is more favorable than axial OH in **7a** to form bulky phosphonium transition state and moreover, carbon bearing OH in **17** is more electronically activated by adjacent cyclopropane ring. Thus, the cyclopropyl intermediate **17** should be a much better substrate for the inversion both sterically and electronically. Preparation of **17** and its conversion to the octalone **13b** is shown in Scheme III. The hydroxy ester **3** was converted to the protected alcohol **14** in nearly quantitative yield which on tosylation gave an unstable tosylate. Direct conversion of the tosylate into the hydroxy ketone **16** with strong acid (35% $HClO_4$-Et_2O) was accompanied with by-products derived from THP group. Thus, stepwise hydrolysis was required to give the crystalline **16** in excellent yield. Treatment of **16** with t-BuOK in t-BuOH smoothly afforded the cyclopropyl ketone **17** in 79% yield. The first key step, Mitsunobu inversion of **17**, and successive methanolysis of the resulting benzoate gave the desired epimer **18** in 80% yield from **17**. The coupling constants of C_4-proton in **17** were 10, 6 and 4 Hz, while those in **18** was 5, 3 and 2 Hz in ^1H NMR spectra. This result demonstrated that our conformation analysis on **17** and **7a** was correct and the reaction proceeded with complete inversion. Birch reduction of the protected cyclopropyl ketone **19**



3 14 15 16 17 18 19 20 21 22

13b R=Si+
c R=H
d R=(R)-MTPA
e R=(S)-MTPA

SCHEME II

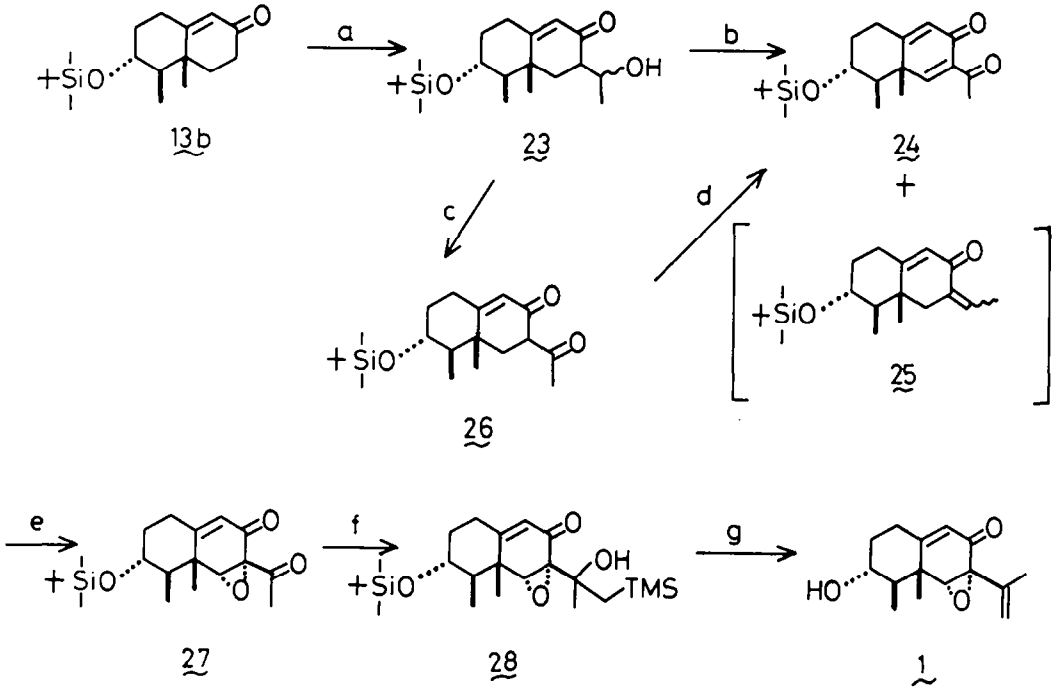
a) DHP, PPTS, CH_2Cl_2 (quantitative); b) $LiAlH_4$, ether (98%); c) p-TsCl, pyridine, DMAP; d) PPTS, MeOH; e) 35% $HClO_4$ aq, ether (85%); f) t-BuOK, t-BuOH (78%); g) Ph_3P, $PhCO_2H$, $(=NCO_2Et)_2$, benzene; h) LiOH, MeOH (80%); i) t-$BuMe_2SiCl$, imidazole, DMF (quantitative); j) Li/NH_3, t-BuOH; k) MeI, HMPA-DME (83%); l) TMSI, $(TMS)_2NH$, CH_2Cl_2; m) methyl vinyl ketone, $BF_3 \cdot OEt_2$, i-PrOH, CH_3NO_2 (56% or 68%); n) pyrrolidine, benzene (79%)

and trapping the enolate with methyl iodide[14] gave the site-selectively methylated cyclohexanone **20** in 83% yield.

The second key-step of our synthesis was how to introduce a four-carbon unit for regio- and stereoselective annulation. In the previous route (vide supra), methylene-blocking group had to be used for the regioselective methylation. As we have obtained **20** already, direct 1,4-addition reaction without protection of methylene group would be feasible with a more highly substituted enol or enolate. Michael-type addition under Lewis acid catalysis developed by Duhamel et al.[15] was the candidate. Thermodynamically more stable TMS enol ether **21** was prepared by treating **20** with TMSI-$(TMS)_2NH$ in CH_2Cl_2 at ambient temperature.[16] Starting material **20** was entirely recovered under House's standard procedure.[17] Treating **21** with methyl vinyl ketone in the presence of $BF_3 \cdot OEt_2$ and i-PrOH in nitromethane gave the diketone **22** as a sole addition product in 56% yield (efficiency, 68% based on the unrecovered **20**) along with the recovered **20** (16%). Cyclization of **22** with pyrrolidine gave the octalone **13b** in 79% yield. Recrystallization gave enantiomerically pure **13b**. This scheme required only 13 steps from **2** (10 steps shorter) and the overall yield of **13b** was improved to 22.3%, 5 times as high as that in the previous synthesis (vide supra and the reference[4]). Optical purity of **13b** was confirmed by HPLC analysis of the corresponding (R)- and (S)-MTPA esters **13d** and **13e** respectively derived via the hydroxyoctalone **13c**. It was shown to be 100% e.e. Thus, we entered the final stage of the synthesis.

CONVERSION OF THE OCTALONE **13b** INTO SPOROGEN-AO 1

The procedure reported by Marumo and Goto for the synthesis of simple analogs of sporogen-AO 1[18] was employed with some modification as to the introduction side chain and epoxide ring.



SCHEME III

a) LDA, CH_3CHO, THF (92%); b) DMSO, $SO_3 \cdot Py$, Et_3N; c) DMSO, $(COCl)_2$, Et_3N, CH_2Cl_2 (79%); d) DDQ, ether (83%); e) t-BuOOH, Triton B, THF (70%); f) $TMSCH_2MgCl$, ether; g) H_2SO_4, THF then HF, CH_3CN (88%)

Condensation of **13b** with acetaldehyde in the presence of LDA afforded the ketol **23** in 92% yield. One-step oxidation of **23** using DMSO-SO_3•C_5H_5N method[19] as reported by Marumo[18] gave the diene-dione **24** in rather poor yield (< 30%) with concomitant formation of the dienone **25** as an unseparable mixture. Stepwise procedure using Swern's oxidation[11] (79%) and dehydrogenation with DDQ (83%) gave much better result to yield **24**. Treatment of **24** with tert-butylhydroperoxide in the presence of Triton B[20] afforded the epoxide **27** in 70% yield. Although it was already known that carbonyl group in the side chain was convertible to exo-methylene group selectively in moderate yield (ca. 50%),[4] we applied Peterson-Chan reaction[21,22] for giving sporogen-AO 1 **1** in better yield. Addition of $TMSCH_2MgCl$[23] to **27** proceeded smoothly and selectively at 0°C for 5 min to give the adduct **28**, which without purification was treated with dilute sulfuric acid in THF[21] and then HF in acetonitrile to give natural (+)-sporogen-AO 1 **1** in 88% yield through 3 steps. Recrystallization gave both chemically and optically pure (+)-**1**, melting at 104-105°C, whose spectral and chiroptical data were completely indistinguishable with those of authentic sample.[4]

In conclusion, the efficient total synthesis of (+)-sporogen-AO 1 (13-desoxyphomenone) **1** was accomplished in 20 steps from ethyl (1R,2S)-5,5-ethylenedioxy-2-hydroxycyclohexanecarboxylate **3** in 8.3% overall yield. This enables us to afford sufficient amount of sporogen-AO 1 and other related elemophilane sesquiterpenes with remarkable phytotoxic activities, such as phomenone,[24] phaseolinone,[25] etc. Synthetic and biological studies on those analogs are in progress and will be reported soon.

EXPERIMENTAL

All b.ps and m.ps were uncorrected. IR spectra were measured as films for oils or as KBr disks for solids on a Jasco IRA-102 spectrometer. ^1H NMR spectra were recorded with TMS as an internal standard at 60 MHz on a Hitachi R-24A spectrometer or at 100 MHz on a JEOL JNM FX-100 spectrometer or at 400 MHz on a JEOL JNM GX-400 spectrometer. ^{13}C NMR spectrum was measured with TMS as an internal standard at 25 MHz on a JEOL JNM FX-100 spectrometer. Optical rotations were measured on a Jasco DIP 140 polarimeter. UV spectrum was measured on a Shimazu UV-160 spectrometer. CD spectrum was measured on a Jasco J-20C spectropolarimeter. Mass spectra were recorded on a JEOL DX-303 spectrometer at 70 eV. Merck Kieselgel 60 was used for SiO_2 column chromatography.

Ethyl (1R,2S)-5,5-ethylenedioxy-2-hydroxycyclohexanecarboxylate **3**. A mixture of sucrose (300 g) and dry yeast (200 g, Oriental Yeast Co.) in water (2 l) was stirred for 15 min at 30°C with aeration. To this was added a soln of **4** (15 g, 65.8 mmol) in EtOH (30 ml) and the fermentation was continued overnight at 30°C with stirring and aeration. Then $NaHCO_3$ (50 g) and EtOAc (500 ml) was added and the mixture was filterd through celite. The filtrate was saturated with NaCl and extracted with EtOAc (x5). The filter cake was washed thoroughly with EtOAc. The combined EtOAc soln was washed with brine, dried ($MgSO_4$) and concentrated. The residue was chromatographed over SiO_2 (400 g). Elution with hexane-EtOAc (4:1-1:1) gave 1-2 g of recovered **4** and 9-10 g of **3**, b.p. 117-118°C/0.35 Torr; n_D^{25} 1.4695; $[\alpha]_D^{23}$ +51.1° (c=1.02, $CHCl_3$); vmax 3500 (s), 2940 (s), 2890 (s), 1725 (s), 1440 (m), 1366 (m), 1275 (m), 1186 (s), 1140 (m), 1080 (s), 1035 (s), 993 (m), 943 (m), 900 (m), 864 (m), 815 (w), 788 (w), 762 (m), 712 (m) cm^{-1}; δ (60 MHz, $CDCl_3$) 1.27 (3H, t, J=7 Hz), 1.0-2.3 (6H, m), 2.12 (1H, ddd, J=11, 5 and 2 Hz), 3.03 (1H, br.s), 3.6-4.5 (5H, m), 4.10 (2H, q, J=7 Hz). (Found: C, 57.37; H, 7.80. Calc for $C_{11}H_{18}O_5$: C, 57.38; H, 7.88%).

Determination of the optical purity of **3**. Hydroxy ester **3** was converted to the corresponding (R)- and (S)-MTPA esters. HPLC analytical conditions are: Column normal phase, Nucleosil® 50-5, 4.6mm x 25cm; Eluent n-hexane-THF=10:1; Flow rate 1.2 ml/min (50 kg/cm^2); Detector UV 254nm; (R)-MTPA ester of **3**, Rt 20.1 min (0.9%), Rt 23.5 min (99.1%); (S)-MTPA ester of **3**, Rt 20.1 min (99.2%), Rt 23.5 min (0.8%). Therefore, the optical purity of **3** was determined to be 98.4% e.e.

Ethyl (1R,2S)-2-acetoxy-5,5-ethylenedioxycyclohexanecarboxylate. A mixture of **3** (28.0 g, 122 mmol), Ac_2O (23 g, 225 mmol) and 4-N,N-dimethylaminopyridine (200 mg) in pyridine (36 ml) was stirred overnight at room temp. The reaction mixture was quenched with water and extracted with ether. The extract was washed with ice-2N HCl (x3), water, sat $NaHCO_3$ soln and brine, dried ($MgSO_4$) and concentrated to give 33.1 g (quantitative) of acetate. An analytical sample was obtained by recrystallization from hexane-ether, m.p. 53.5-54.2°C; $[\alpha]_D^{23.2}$ +37.7° (c=1.07, $CHCl_3$); vmax 3020 (m), 3000 (s), 2980 (m), 2920 (m), 2900 (m), 1727 (s), 1480 (m), 1446 (m), 1440 (m), 1383 (m), 1370 (m), 1340 (w), 1333 (m), 1290 (s), 1280 (m), 1252 (s), 1220 (m), 1197 (s), 1143 (m), 1107 (w), 1083 (s), 1058 (m), 1042 (s), 1021 (m), 970 (m), 950 (m), 918 (m), 905 (m), 868 (m), 829 (w), 768 (w), 702 (m) cm^{-1}; δ (60 MHz, $CDCl_3$) 1.20 (3H, t, J=7 Hz), 1.2-2.2 (6H, m), 1.96 (3H, s), 2.70 (1H, m, hhw=18 Hz), 3.6-4.0 (4H, m), 4.02 (2H, q, J=7 Hz), 5.30 (1H, br, hhw=7 Hz). (Found: C, 57.49; H, 7.38. Calc for $C_{13}H_{20}O_6$: C, 57.36; H, 7.40%).

(1S,2S)-4,4-Ethylenedioxy-2-hydroxymethylcyclohexanol. To a stirred suspension of LAH (5.32 g, 140 mmol) in THF (100 ml) was added a soln of the acetate (18.0 g, 66 mmol) in THF (100 ml) at 0°C. After stirring for 1 h at 0°C, the reaction mixture was quenched by adding water (5.3 ml), 15% NaOH aq (5.3 ml) and water (15.9 ml). The precipitate was filterd through a celite pad and washed thoroughly with THF. The combined filtrate was dried ($MgSO_4$) and concentrated. The residue

was chromatographed over SiO_2 (200 g). Elution with CH_2Cl_2-MeOH (99:1-95:5) gave 11.8 g (95%) of diol, $n_D^{23.2}$ 1.4822; $[\alpha]_D^{23.2}$ +35.1° (c=1.67, $CHCl_3$); νmax 3430 (s), 2950 (s), 2900 (s), 1440 (m), 1360 (m), 1340 (m), 1310 (m), 1290 (m), 1230 (m), 1210 (m), 1146 (s), 1100 (s), 1077 (s), 1057 (s), 1030 (s), 993 (m), 963 (s), 920 (m), 880 (m), 856 (m), 830 (m), 800 (m), 768 (m), 703 (m), 680 (m) cm^{-1}; δ (60 MHz, $CDCl_3$) 1.1-2.3 (7H, m), 3.91 (4H, m), 3.4-4.3 (3H, m). HRMS: m/z Found: 188.1040. Calc for $C_9H_{16}O_4$: 188.1048.

(2R,4aS,8aS)-6,6-Ethylenedioxy-2-phenyl-1,3-dioxa-1,2,3,4,4a,5,6,7,8,8a-decahydronaphthalene 5. A mixture of the diol (11.8 g, 62.7 mmol), PhCH(OEt)$_2$ (12.4g, 68.9 mmol) and p-TsOH (100 mg) in CH_2Cl_2 (150 ml) was stirred for 3 h at room temp. The reaction mixture was diluted with ether (400 ml), washed with sat $NaHCO_3$ soln and brine, dried ($MgSO_4$) and concentrated. The residue was chromatographed over SiO_2 (400 g). Elution with hexane-EtOAc (19:1-7:3) gave 15.1 g (87%) of 5, m.p. 63-64°C; $[\alpha]_D^{23}$ +56.8° (c=1.18, $CHCl_3$); νmax 3080 (w), 3050 (m), 2970 (s), 2940 (s), 2860 (s), 2790 (m), 2700 (w), 1960 (w), 1820 (w), 1497 (m), 1460 (m), 1450 (s), 1440 (m), 1430 (m), 1393 (s), 1378 (m), 1363 (m), 1355 (s), 1340 (m), 1324 (m), 1316 (m), 1305 (m), 1279 (m), 1260 (m), 1235 (m), 1215 (m), 1173 (m), 1145 (s), 1123 (s), 1100 (s), 1085 (s), 1060 (m), 1040 (s), 1027 (s), 1008 (s), 983 (s), 966 (s), 948 (m), 934 (m), 900 (w), 885 (m), 842 (m), 805 (m), 768 (m), 762 (m), 750 (s), 737 (m), 700 (s), 690 (m), 663 (m) cm^{-1}; δ (60 MHz, CCl_4) 1.0-2.5 (7H, m), 3.5-4.1 (7H, m), 5.36 (1H, s), 7.1-7.6 (5H, m). (Found: C, 69.61; H, 7.23. Calc for $C_{16}H_{20}O_4$: C, 69.54; H, 7.30%).

(1S,2R)-2-Bromomethyl-4,4-ethylenedioxycyclohexyl benzoate. A mixture of 5 (15.1 g, 54.7 mmol), NBS (43%, 25 g, 60.4mmol) and AIBN (300 mg) in benzene (300 ml) was stirred for 1 h at 50°C. The reaction mixture was poured into water and extracted with ether. The extract was washed with water, sat $Na_2S_2O_3$ soln and brine, dried ($MgSO_4$) and concentrated. The residue was chromatographed over SiO_2 (400 g). Elution with hexane-EtOAc (19:1-7:3) gave 16.2 g (83%) of bromide, $n_D^{23.4}$ 1.5390; $[\alpha]_D^{23.4}$ +40.6° (c=1.15, $CHCl_3$); νmax 3090 (m), 3050 (w), 2980 (s), 2950 (s), 2900 (s), 1720 (s), 1603 (m), 1585 (m), 1495 (m), 1453 (m), 1440 (m), 1373 (m), 1350 (m), 1335 (m), 1315 (m), 1295 (m), 1270 (s), 1230 (m), 1205 (m), 1177 (m), 1112 (m), 1100 (m), 1070 (m), 1045 (m), 1027 (m), 1008 (m), 975 (m), 948 (m), 932 (m), 919 (m), 880 (w), 870 (w), 821 (m), 808 (m), 767 (w), 716 (s), 693 (m) cm^{-1}; δ (60 MHz, CCl_4) 1.0-2.7 (7H, m), 3.28 (2H, m), 3.9 (4H, m), 5.28 (1H, br.s, hhw=9 Hz), 7.3-7.6 (3H, m), 7.8-8.2 (2H, m). (Found: C, 53.70; H, 5.43. Calc for $C_{16}H_{19}O_4Br$: C, 54.09; H, 5.39%).

(1S,2R)-4,4-Ethylenedioxy-2-methylcyclohexanol 6. To a stirred suspension of LAH (1.90 g, 50.2 mmol) in THF (200 ml) was added a soln of the bromide (15.2 mmol, 45.6 mmol) in THF (100 ml) at 0°C. After stirring overnight at room temp, the reaction mixture was quenched by adding water (1.9 ml), 15% NaOH aq (1.9 ml) and water (5.7 ml). The precipitate was filtered through a celite pad and washed thoroughly with THF. The combined filtrate was dried ($MgSO_4$) and concentrated. The residue was chromatographed over SiO_2 (400 g). Elution with hexane-EtOAc (9:1-6:4) gave 6.1 g (83%) of 6, b.p. 82-84°C/0.1 Torr; m.p. 30-32°C; $[\alpha]_D^{19.6}$ +33.4° (c=1.0, $CHCl_3$); νmax 3430 (s), 2970 (s), 2945 (s), 2900 (s), 1480 (w), 1452 (m), 1440 (m), 1365 (m), 1343 (m), 1315 (w), 1296 (m), 1240 (m), 1216 (m), 1148 (m), 1117 (m), 1074 (s), 1054 (m), 1013 (m), 965 (s), 936 (m), 919 (w), 886 (m), 815 (m), 800 (w), 765 (m), 684 (m) cm^{-1}; δ (60 MHz, $CDCl_3$) 0.96 (3H, d, J=6 Hz), 1.2-2.3 (8H, m), 3.5-4.0 (5H, m). (Found: C, 62.80; H, 9.31. Calc for $C_9H_{16}O_3$: C, 62.76; H, 9.36%).

(3R,4S)-4-Hydroxy-3-methylcyclohexanone 7a. A mixture of 6 (6.0 g, 34.8 mmol) and Amberlite IR-120 (1 g) in water (100 ml) was heated under reflux for 3 h. After removing Amberlite IR-120, a small amount of $NaHCO_3$ was added and the reaction mixture was concentrated. The residue was dissolved in EtOAc, washed with water and brine, dried ($MgSO_4$) and concentrated. The residue was purified by distillation to give 4.40 g (99%) of 7a, b.p. 85-88°C/3 Torr; n_D^{15} 1.4734; $[\alpha]_D^{15}$ +26.0° (c=1.085, $CHCl_3$); νmax 3450 (s), 2960 (s), 2940 (s), 2910 (s), 2880 (s), 1710 (s), 1450 (m), 1420 (m), 1370 (m), 1350 (s), 1330 (s), 1300 (m), 1274 (m), 1233 (m), 1208 (m), 1134 (m), 1110 (m), 1075 (m), 1045 (m), 1017 (m), 988 (s), 960 (m), 950 (s), 875 (m), 838 (m), 808 (m), 755 (m) cm^{-1}; δ (60 MHz, $CDCl_3$) 1.05 (3H, d, J=6 Hz), 1.3-3.0 (8H, m), 3.95 (1H, br, hhw=9 Hz). HRMS: m/z Found: 128.0823. Calc for $C_7H_{12}O_2$: 128.0837.

(3R,4S)-3-Methyl-4-tetrahydropyranyloxycyclohexanone 7b. A mixture of 7a (4.4 g, 34.3 mmol), 2,3-dihydropyran (8.8 g, 104 mmol) and p-TsOH (200 mg) in CH_2Cl_2 was stirred overnight at room temp. The reaction mixture was diluted with ether, washed with sat $NaHCO_3$ soln and brine, dried ($MgSO_4$) and concentrated. The residue was chromatographed over SiO_2 (200 g). Elution with hexane-EtOAc (19:1-4:1) gave an oil. This was further purified by distillation to give 6.55 g (90%) of 7b, b.p. 100-103°C/3 Torr; $n_D^{21.5}$ 1.4696; $[\alpha]_D^{21.5}$ +33.4° (c=1.21, $CHCl_3$); νmax 2960 (s), 2890 (s), 1715 (s), 1453 (m), 1442 (m), 1420 (w), 1380 (w), 1346 (m), 1320 (w), 1300 (w), 1275 (m), 1260 (w), 1235 (w), 1203 (m), 1180 (m), 1157 (m), 1135 (m), 1120 (m), 1078 (m), 1035 (s), 1026 (m), 1007 (s), 976 (m), 952 (m), 928 (w), 906 (m), 886 (w), 870 (m), 842 (w), 813 (m), 757 (w) cm^{-1}; δ (60 MHz, CCl_4) 0.98 and 1.08 (total 3H, d, J=6 Hz), 1.2-3.0 (13H, m), 3.0-4.2 (3H, m), 3.5-3.9 (1H, m). HRMS: m/z Found: 212.1432. Calc for $C_{12}H_{20}O_3$: 212.1412.

(2RS,3R,4S)-6-Benzylthiomethylene-2,3-dimethyl-4-tetrahydropyranyloxycyclohexanone 8. To a stirred suspension of NaH (60%, 1.35 g, 33.8 mmol) in THF (70 ml) was added a mixture of 7b (6.50 g, 30.7 mmol) and HCO_2Et (6.5 ml). After stirring for 1 h at room temp, the reaction mixture was evaporated below 30°C and the remaining solvent was completely removed with vacuum pump. The residue was dissolved in THF (15 ml) and HMPA (15 ml) and to this was added at 0°C a LDA solution which was prepared from diisopropylamine (4.9 ml, 35 mmol) and n-BuLi (1.6 N, 22 ml, 35 mmol) in THF (20 ml). After stirring for 30 min at 0°C, MeI (90%, 2.6 ml, 40 mmol) was added and the mixture was stirred for further 1 h at 0°C. The reaction mixture was poured into water, acidified to pH 5 with AcOH and extracted with ether. The extract was washed with water and brine, dried ($MgSO_4$) and concentrated. The residue was dissolved in pyridine (40 ml) and to this was added portionwise p-TsCl (6.65 g, 35 mmol) at 0°C. After stirring for 3 h at 0°C, BnSH (5 ml, 40 mmol) was added and the stirring was continued overnight at room temp. The reaction mixture was poured into water, extracted with ether. The extract was washed with water and brine, dried ($MgSO_4$) and concentrated. The residue was chromatographed over SiO_2 (400 g). Elution with hexane-EtOAc (19:1-4:1) gave 8.2 g (74%) of 8, $n_D^{21.5}$ 1.5628; $[\alpha]_D^{21.5}$ -16.8° (c=1.0, $CHCl_3$); νmax 3060 (w), 3040 (w), 2960 (s), 2890 (s), 1707 (m), 1663 (s), 1600 (m), 1560 (s), 1545 (s), 1494 (m), 1451 (m), 1440 (m), 1375 (m), 1348 (m), 1304 (m), 1279 (m), 1240 (m), 1196 (m), 1190 (m), 1159 (m), 1130 (m), 1115 (m) 1095 (m), 1076 (m), 1052 (m), 1020 (m), 1005 (m), 975 (m), 922 (m), 868 (m), 808 (m), 745 (m), 700 (m) cm^{-1}; δ (60 MHz, CCl_4) 1.07 (6H, d, J=6 Hz), 0.6-2.8 (10H, m), 3.1-4.2 (5H, m), 4.59 (1H, br.s), 7.21 (5H, m), 7.34 (1H, br.s). (Found: C, 69.66; H, 7.89. Calc for $C_{21}H_{28}O_3S$: C, 69.96; H, 7.83%).

(1'R,2'R,3'S)-3-(1',2'-Dimethyl-6'-oxo-3'-tetrahydropyranyloxycyclohexane)propanoic acid 9. To a soln of 8 (5.0 g, 13.9 mmol) in t-BuOH (50 ml) was added portionwise t-BuOK (4.7 g, 42 mmol) at room temp. After stirring for 15 min at room temp, ethyl 3-bromopropanoate (7.5 g, 42 mmol) was added and the mixture was stirred for 2 h at room temp. The reaction mixture

was diluted with ether, washed with water and brine, dried ($MgSO_4$) and concentrated. The residue was roughly chromatographed over SiO_2 (200 g). Elution with hexane-EtOAc (19:1-4:1) gave a keto ester. A soln of the keto ester in 25% KOH aq (30 ml) and diethyleneglycol (30 ml) was heated under reflux for 24 h. The reaction mixture was diluted with water and extracted with ether (x2). Then the aqueous layer was acidified to pH 5 with AcOH and extracted with EtOAc. The EtOAc soln was washed with water and brine, dried ($MgSO_4$) and concentrated to give 2.86 g (69%) of **9**. This was employed for the next step without purification. IR and NMR spectrum of the corresponding methyl ester were as follows; νmax 2960 (s), 2890 (m), 1735 (s), 1707 (s), 1460 (m), 1440 (m), 1380 (m), 1360 (m), 1200 (m), 1170 (m), 1130 (m), 1115 (m), 1077 (m), 1025 (m), 978 (m), 955 (m), 912 (m) cm^{-1}; δ (60 MHz, $CDCl_3$) 0.8-1.3 (3H, m), 1.09 (3H, s), 1.3-2.8 (15H, m), 3.0-4.5 (3H, m), 3.65 (3H, s), 4.70 (1H, m).

Benzyl (1'R,2'R,3'S)-3-(6',6'-ethylenedioxy-3'-hydroxy-1',2'-dimethylcyclohexane)propanoate **10**. A mixture of **9** (1.04 g, 3.5 mmol), ethyleneglycol (500 mg, 8 mmol) and p-TsOH (cat. amount) in benzene (20 ml) was heated under reflux for 6 h with azeotropic removal of water. The reaction mixture was diluted with ether, washed with water, sat $NaHCO_3$ soln and brine, dried ($MgSO_4$) and concentrated. To the residue was added water (2 ml), MeOH (6 ml) and $LiOH\ H_2O$ (420 mg) and the mixture was stirred overnight at room temp. The reaction mixture was evaporated, acidified to pH 5 with AcOH and extracted with EtOAc. The extract was washed with water and brine, dried ($MgSO_4$) and concentrated to give a crude carboxylic acid. A mixture of the crude carboxylic acid, $NaHCO_3$ (600 mg) and BnBr (1.0 g, 6 mmol) in DMF (5 ml) was stirred overnight at 60°C. The reaction mixture was poured into water and extracted with ether. The extract was washed with water (x2) and brine, dried ($MgSO_4$) and concentrated. The residue was chromatographed over SiO_2 (30 g). Elution with hexane-EtOAc (9:1-1:1) gave 640 mg (53%) of unstable **10**. This was employed for the next step without further purification.

Benzyl (1'R,2'R)-3-(6',6'-ethylenedioxy-1',2'-dimethyl-3'-oxocyclohexane)propanoate. To a soln of oxalyl chloride (1.1 g, 8.6 mmol) in CH_2Cl_2 (5 ml) was added dropwise DMSO (1.12 g, 14.4 mmol) at -70°C. After stirring for 15 min at -70°C, to this was added a soln of **10** (1.0 g, 2.87 mmol) in CH_2Cl_2 (5 ml) and the mixture was stirred for further 1.5 h. Then Et_3N (2.9 g, 28.7 mmol) was added dropwise at -70°C and the temperature was gradually raised to 0°C. The reaction mixture was poured into water and extracted with ether. The extract was washed with water and brine, dried ($MgSO_4$) and concentrated. The residue was chromatographed over SiO_2 (40 g). Elution with hexane-EtOAc (19:1-7:3) gave 870 mg (87%) of ketone, m.p. 53.5-54.5°C; $[\alpha]_D^{23.7}$ +17.0° (c=1.0, $CHCl_3$); νmax 3080 (w), 3050 (w), 3040 (m), 2970 (s), 2940 (s), 2890 (s), 1728 (s), 1708 (s), 1665 (w), 1585 (w), 1498 (m), 1459 (m), 1424 (m), 1390 (m), 1372 (m), 1365 (m), 1347 (m), 1300 (s), 1280 (m), 1268 (m), 1238 (m), 1212 (m), 1194 (s), 1165 (s), 1138 (m), 1116 (m), 1082 (m), 1073 (m), 1045 (m), 1030 (m), 1018 (m), 1004 (m), 996 (m), 980 (m), 963 (m), 947 (m), 913 (m), 878 (m), 843 (w), 820 (w), 745 (s), 697 (s), 680 (w) cm^{-1}; δ (60 MHz, CCl_4) 0.81 (3H, s), 0.89 (3H, d, J=7 Hz), 1.0-3.0 (9H, m), 3.8-4.0 (4H, m), 4.98 (2H, s), 7.0-7.5 (5H, m). (Found: C, 69.06; H, 7.58. Calc for $C_{20}H_{26}O_5$: C, 69.34; H, 7.57%).

(1'R,2'R,3'R)-3-(6',6'-Ethylenedioxy-3'-hydroxy-1',2'-dimethylcyclohexane)propanoic acid **11**. To a blue soln of lithium (350 mg, 50 mmol) in liq NH_3 (ca. 30 ml) was added a soln of the ketone (870 mg, 2.5 mmol) and EtOH (276 mg, 6 mmol) in ether (5 ml) at -78°C. After stirring for 1 h at -78°C and for 1 h at -33°C, the reaction mixture was quenched with sat NH_4Cl soln. The aqueous layer was acidified to pH 5 with AcOH and extracted with EtOAc. The extract was washed with water and brine, dried ($MgSO_4$) and concentrated to give 650 mg of crude **15**, νmax 3600-3000 (br.m), 2970 (s), 2900 (m), 1710 (br.s), 1460 (m), 1445 (m), 1410 (m), 1373 (m), 1220 (s), 1185 (s), 1122 (m), 1097 (m), 1050 (br.s), 970 (m), 946 (m), 920 (m), 844 (m), 750 (m). This was employed for the next step without purification.

(4aS,5R,6R)-4a,5-Dimethyl-4a,5,6,7-tetrahydro-6-tetrahydropyranyloxy-2-chromanone **12**. A soln of **11** (650 mg, ca. 2.5 mmol) and p-TsOH (cat. amount) in MeOH (50 ml) was heated under reflux for 3 h with removal of water using molecular sieve 3A. The reaction mixture was evaporated and diluted with EtOAc. The EtOAc soln was washed with water, sat $NaHCO_3$ soln and brine, dried ($MgSO_4$) and concentrated to give 430 mg of keto ester, νmax 3480 (s), 2980 (s), 2970 (s), 2890 (m), 1735 (s), 1710 (s), 1460 (m), 1440 (m), 1380 (m), 1372 (m), 1320 (m), 1295 (m), 1195 (m), 1175 (m), 1103 (m), 1034 (m), 1000 (m), 955 (m), 893 (m), 845 (m), 760 (w) cm^{-1}; δ (60 MHz, $CDCl_3$) 1.04 (3H, s), 1.05 (3H, d, J=6 Hz), 1.2-1.8 (10H, m), 2.60 (3H, s), 2.85 (1H, dt, J=10 and 5 Hz). This was used for the next step without purification. A mixture of the crude keto ester (430 mg, ca. 1.9 mmol) and 2,3-dihydropyran (670 mg, 8.0 mmol) and pyridinium p-toluenesulfonate (cat. amount) in CH_2Cl_2 (10 ml) was stirred overnight at room temp. The reaction mixture was diluted with ether, washed with water, sat $NaHCO_3$ soln and brine, dried ($MgSO_4$) and concentrated. To the residue, MeOH (6 ml), H_2O (2 ml) and $LiOH{\cdot}H_2O$ (420mg, 10 mmol) was added and the mixture was stirred overnight at room temp. The reaction mixture was evaporated, diluted with water and extracted with ether. Then the aqueous layer was acidified to pH 5 with AcOH and extracted with EtOAc. The EtOAc soln was washed with water and brine, dried ($MgSO_4$) and concentrated to give 500 mg of keto acid. A mixture of the keto acid (500 mg, ca. 1.67 mmol) and AcONa (300 mg) in Ac_2O (30 ml) was heated under reflux for 2 h. Most of the Ac_2O was evaporated and the residue was diluted with ether. The ether layer was washed with water and brine, dried ($MgSO_4$) and concentrated. The residue was chromatographed over SiO_2 (15 g). Elution with hexane-EtOAc (9:1-7:3) gave 390 mg (56%) of **12**, $n_D^{22.3}$ 1.4962; $[\alpha]_D^{22.3}$ -66.4° (c=1.1, $CHCl_3$); νmax 2960 (s), 2890 (m), 1760 (s), 1690 (s), 1457 (m), 1423 (m), 1370 (m), 1354 (m), 1340 (m), 1261 (m), 1239 (m), 1205 (m), 1173 (m), 1135 (s), 1120 (m), 1077 (m), 1055 (m), 1025 (s), 978 (m), 958 (m), 940 (m), 937 (m) 905 (m), 885 (m), 870 (m), 847 (m), 817 (m), 803 (m), 735 (w) cm^{-1}; δ (100 MHz, $CDCl_3$) 0.97-1.20 (6H, m), 1.3-3.0 (13H, m), 3.3-4.2 (3H, m), 4.63 and 4.77 (total 1H, each, m), 5.20 (1H, dd, J=7 and 3 Hz). HRMS: m/z Found: 280.1708. Calc for $C_{16}H_{24}O_4$: 280.1675.

(4aR,5R,6R)-4,4a,5,6,7,8-Hexahydro-4a,5-dimethyl-6-tetrahydropyranyloxy-2(3H)naphthalenone **13a**. To a soln of **12** (360 mg, 1.29 mmol) in ether (10 ml) was added dropwise MeLi (1.4 M in ether, 1.5 ml, 2.1 mmol) at -25°C. After stirring for 1.75 h at -25°C, the reaction mixture was quenched with sat NH_4Cl soln and extracted with ether. The extract was washed with water and brine, dried ($MgSO_4$) and concentrated. To the residue, MeOH (20 ml) and 10% KOH aq (2 ml) was added and the mixture was heated under reflux for 2 h. The reaction mixture was evaporated, diluted with water and extracted with ether. The extract was washed with water and brine, dried ($MgSO_4$) and concentrated. The residue was chromatographed over SiO_2 (20 g). Elution with hexane-EtOAc (9:1-2:1) gave 195 mg (55%) of **13a**, n_D^{23} 1.5189; $[\alpha]_D^{23}$ +96.0° (c=1.1, $CHCl_3$); νmax 2950 (s), 2870 (m), 1675 (s), 1617 (m), 1460 (m), 1438 (m), 1418 (m), 1375 (m), 1348 (m), 1330 (m), 1264 (m), 1234 (m), 1218 (m), 1199 (m), 1180 (m), 1153 (m), 1126 (m), 1115 (m), 1073 (m), 1050 (m), 1025 (s), 972 (m) 945 (m), 910 (m), 900 (m), 880 (m), 865 (m), 839 (w), 810 (m), 770 (w), 725 (w), 679 (m) cm^{-1}; δ (100 MHz, $CDCl_3$) 1.01 and 1.12 (total 3H, each d, J= 7 Hz), 1.16 (3H, s), 1.2-2.7 (15H, m), 3.3-4.1 (3H, m), 4.64 and 4.82 (total 1H, br.t), 5.77 (1H, br.s). HRMS: m/z Found: 278.1862. Calc for $C_{17}H_{26}O_3$: 278.1882.

Ethyl (1R,2S)-5,5-ethylenedioxy-2-tetrahydropyranyloxycyclohexanecarboxylate **14**. A mixture of 3 (30.0 g, 130 mmol), pyridinium p-toluenesulfonate (1.5 g, 6 mmol) and 2,3-dihydropyran (18.0 g, 214 mmol) in CH_2Cl_2 (300 ml) was stirred overnight at room temp. The reaction mixture was diluted with ether (1 l), washed with water, sat $NaHCO_3$ soln and brine, dried ($MgSO_4$) and concentrated. The residue was chromatographed over SiO_2 (500 g). Elution with hexane-EtOAc (19:1-7:3) gave 40.95 g (quantitative) of **19**, n_D^{23} 1.4704; $[\alpha]_D^{23}$ +56.9° (c=1.6, $CHCl_3$); vmax 2950 (s), 2880 (s), 1735 (s), 1460 (m), 1440 (m), 1365 (s), 1350 (m), 1300 (m), 1280 (s), 1255 (s), 1185 (s), 1130 (s), 1115 (s), 1080 (s), 1035 (s), 1020 (s), 1000 (s), 983 (s), 947 (m), 920 (m), 904 (m), 867 (m), 815 (m), 762 (m), 725 (m) cm^{-1}; δ (100 MHz, $CDCl_3$) 1.28 and 1.29 (total 3H, each t, J=7 Hz), 1.3-2.35 (12H, m), 2.6-2.9 (1H, m), 3.3-4.5 (9H, m), 4.67 and 4.77 (total 1H, each m). (Found: C, 60.73; H, 8.26. Calc for $C_{16}H_{26}O_6$: C, 61.13; H, 8.34%).

(1S,2S)-5,5-Ethylenedioxy-2-tetrahydropyranyloxycyclohexanemethanol **15**. To a stirred suspension of LAH (5.0 g, 130 mmol) in ether (500 ml) was added dropwise a soln of **14** (40.95 g, 130 mmol) in ether (200 ml) at 0°C. After stirring for 1 h at 0°C, the reaction mixture was quenched by adding water (5.0 ml), 15% NaOH aq (5.0 ml) and water (15.0 ml). The precipitate was filtered through a celite pad and washed thoroughly with THF. The combined filtrate was dried ($MgSO_4$) and concentrated. The residue was chromatographed over SiO_2 (500 g). Elution with hexane-EtOAc (4:1-3:7) gave 34.65 g (98%) of **15**, $n_D^{23.5}$ 1.4833; $[\alpha]_D^{23.5}$ +31.7° (c=0.82, $CHCl_3$); vmax 3470 (br.s), 2960 (s), 2900 (s), 1440 (s), 1355 (m), 1315 (m), 1280 (m), 1250 (m), 1205 (m), 1185 (m), 1150 (s), 1135 (s), 1115 (s), 1075 (s), 1030 (s), 990 (s), 962 (m), 913 (m), 866 (m), 840 (w), 813(m), 767 (w), 716 (w) cm^{-1}; δ (100 MHz, $CDCl_3$) 1.2-2.3 (13H, m), 2.52 (1H, br.s), 3.3-4.3 (9H, m), 4.48 and 4.71 (total 1H, m). (Found: C, 61.34; H, 8.77. Calc for $C_{14}H_{24}O_5$: C, 61.74; H, 8.88%).

(1S,2S)-2-Hydroxy-5-oxocyclohexylmethyl-p-toluenesulfonate **16**. To a soln of **15** (5.44 g, 20 mmol) and 4-N,N-dimethylaminopyridine (244 mg, 2 mmol) in pyridine (7.9 g, 100 mmol) and CH_2Cl_2 (20 ml) was added p-TsCl (5.7 g, 30 mmol) with ice-cooling and the mixture was stirred for 2 days at 4°C. The reaction mixture was poured into water and extracted with ether. The extract was washed with ice-2N HCl (x2), water, sat $NaHCO_3$ soln and brine, dried ($MgSO_4$) and concentrated. The residue was roughly chromatographed over SiO_2 (200 g). Elution with hexane-EtOAc (9:1-1:1) gave 8.09 g (95%) of unstable tosylate, vmax (film) 3080 (s), 1595 (m), 1440 (m), 1360 (s), 1175 (s), 1072 (s), 1035 (s), 960 (s) cm^{-1}; This was employed for the next step without further purification.

A mixture of the tosylate (7.60 g, 17.8 mmol) and pyridinium p-toluenesulfonate (0.4 g) in MeOH (100 ml) was stirred for 1 h at 50°C. The reaction mixture was concentrated and the residue was dissolved in ether (300 ml). The ether layer was washed with water, sat $NaHCO_3$ soln and brine, dried ($MgSO_4$) and concentrated. The residue was roughly chromatographed over SiO_2 (100 g). Elution with hexane-EtOAc (8:2-1:1) gave 6.0 g of alcohol.

To a soln of the alcohol (6.0 g) in ether (30 ml) was added 35% $HClO_4$ aq soln (40 ml) at 0°C. After stirring for 1 h at 0°C, the reaction mixture was carefully poured into sat $NaHCO_3$ soln and ether. The ether layer was separated and the .cw8 aqueous layer was extracted with ether. The combined extract was washed with water and brine, dried ($MgSO_4$) and concentrated. The residue was chromatographed over SiO_2 (100 g). Elution with hexane-EtOAc (9:1-3:7) gave 4.52 g (85%) of **16**, m.p. 74-75°C; $[\alpha]_D^{23}$ +13.3° (c=1.25, $CHCl_3$); vmax 3400 (s), 3080 (w), 2960 (m), 2940 (m), 2910 (m), 1695 (s), 1595 (m), 1493 (m), 1460 (m), 1441 (m), 1410 (m), 1347 (s), 1292 (m), 1235 (m), 1210 (m), 1187 (s), 1176 (s), 1140 (m), 1120 (m), 1110 (m), 1095 (m), 1076 (m), 1052 (m), 1018 (m), 973 (s), 952 (s), 902 (m), 872(m), 853 (m), 825 (m), 806 (m), 790 (m), 706 (m), 697 (m), 662 (s) cm^{-1}; δ (100 MHz, $CDCl_3$) 1.5-3.0 (8H, m), 2.48 (3H, s), 3.7-4.4 (3H, m), 7.37 (2H, d, J=8 Hz), 7.71 (2H, d, J=8 Hz). (Found: C, 56.27; H, 6.08. Calc for $C_{14}H_{18}O_5S$: C, 56.35; H, 6.08%).

(1S,5S,6R)-5-Hydroxybicyclo[4.1.0]heptan-2-one **17**. To a soln of **16** (4.70 g, 15.8 mmol) in t-BuOH (100 ml) was added portionwise t-BuOK (5.6 g, 50 mmol) at room temp. After stirring for 1 h at room temp, the reaction mixture was neutralized with AcOH. The precipitate was filtered through a florisil pad, washed thoroughly with THF and the combined filtrate was concentrated. The residue was chromatographed over SiO_2 (50 g). Elution with CH_2Cl_2-MeOH (98:2-92:8) gave 1.56 g (78%) of **17**, n_D^{21} 1.5089; $[\alpha]_D^{21}$ -80.7° (c=1.37, $CHCl_3$); vmax 3400 (s), 3030 (m), 2955 (m), 2890 (m), 1670 (s), 1473 (m), 1405 (m), 1340 (m), 1250 (m), 1200 (m), 1062 (s), 1040 (s), 985 (m), 965 (m), 940 (m), 876 (m), 840 (m), 785 (w) cm^{-1}; δ (100 MHz, $CDCl_3$) 1.3-3.0 (9H, m), 4.43 (1H, ddd, J=10, 6 and 4 Hz). HRMS:m/z Found: 126.0658. Calc for $C_7H_{10}O_2$: 126.0681.

(1S,5R,6R)-5-Hydroxybicyclo[4.1.0]heptan-2-one **18**. To a soln of **17** (3.70 g, 29.3 mmol), PPh_3 (12 g, 45.8 mmol) and $PhCO_2H$ (5.8 g, 47.5 mmol) in benzene (60 ml) was added dropwise diethylazodicarboxylate (8.3 g, 47.7 mmol). After stirring for 2 h at room temp, the reaction mixture was poured into water and extracted with ether. The extract was washed with water, sat $NaHCO_3$ soln and brine, dried ($MgSO_4$) and concentrated. The residue was roughly chromatographed over SiO_2 (100 g). Elution with hexane-EtOAc (9:1-1:1) gave a benzoate, vmax (KBr) 3030 (m), 2940 (m), 1700 (s), 1670 (s), 1595 (m), 1450 (m), 1265 (s), 1172 (m), 1105 (s), 938 (m), 705 (s) cm^{-1}. This was employed for the next step without further purification.

A mixture of the benzoate (ca. 29.3 mmol) and $LiOH \cdot H_2O$ (2.4 g, 60mmol) in MeOH (100 ml) was stirred for 1 h at room temp. The reaction mixture was concentrated and the residue was dissolved in ether (300 ml). The precipitate was filtered through a florisil pad, washed thoroughly with THF and the combined filtrate was concentrated. The residue was chromatographed over SiO_2 (100 g). Elution with CH_2Cl_2-MeOH (98:2-92:8) gave 2.95 g (80%) of **18**, n_D^{23} 1.5096; $[\alpha]_D^{23}$ +5.96° (c=1.14, $CHCl_3$); vmax 3410 (s), 3030 (m), 2960 (m), 2905 (m), 1670 (s), 1465 (m), 1400 (m), 1357 (m), 1252 (m), 1207 (m), 1168 (m), 1113 (m), 1068 (m), 1010 (m), 983 (m), 946 (m), 937 (m), 890 (m), 865 (m), 830 (m), 760 (m) cm^{-1}; δ (100 MHz, $CDCl_3$) 1.0-1.4 (3H, m), 1.5-2.8 (6H, m), 4.45 (1H, ddd, J=5, 3 and 2 Hz). HRMS m/z Found: 126.0697. Calc for $C_7H_{10}O_2$: 126.0681.

(1S,5R,6R)-5-tert-Butyldimethylsilyloxybicyclo[4.1.0]heptan-2-one **19**. A mixture of **18** (0.91 g, 7.2mmol), imidazole (1.36 g, 20 mmol) and t-$BuMe_2SiCl$ (1.5 g, 10 mmol) in DMF (30 ml) was stirred overnight at room temp. The reaction mixture was poured into water and extracted with ether. The extract was washed with water (x2) and brine, dried ($MgSO_4$) and concentrated. The residue was chromatographed over SiO_2 (30 g). Elution with hexane-EtOAc (19:1-4:1) gave 1.73 g (quantitative) of **19**, m.p. 50-51°C; $[\alpha]_D^{23}$ +24.0° (c=1.06, $CHCl_3$); vmax 3060 (m), 2960 (s), 2940 (s), 2905 (s), 2860 (s), 1680 (s), 1470 (s), 1450 (w), 1400 (m), 1380 (m), 1365 (m), 1353 (m), 1342 (m), 1328 (m), 1313 (m), 1250 (s), 1215 (m), 1190 (m), 1173 (m), 1116 (m), 1104 (m), 1076 (s), 1060 (m), 1046 (m), 1029 (m), 1008 (m), 990 (m), 979 (m), 941 (m), 897 (m), 880 (m), 852 (m), 839 (s), 828 (s), 815 (m), 774 (s), 723 (m), 686 (m) cm^{-1}; δ (100 MHz, $CDCl_3$) 0.11 (3H, s), 0.12 (3H, s), 0.91 (9H, s), 0.95-1.3 (2H, m), 1.5-2.7 (6H, m), 3.37 (1H, q, J=3 Hz). (Found: C, 64.71; H, 10.06. Calc for $C_{13}H_{24}O_2Si$: C, 64.94; H, 10.06%).

(2RS,3R,4R)-4-tert-Butyldimethylsilyloxy-2,3-dimethylcyclohexanone **20**. To a blue soln of lithium (160 mg, 23 mmol) in liq NH_3 (ca. 50 ml) was added a soln of **19** (1.15 g, 4.8 mmol) and t-BuOH (355 mg, 4.8 mmol) in DME (10 ml) at -78°C. After

stirring for 30 min at -78°C, the blue soln was carefully quenched with MeI (2.5 ml, 40 mmol) and allowed to stand at room temp in order to dispel most of liq NH_3. To the residue, DME (10 ml) and HMPA (2.5 ml) was added and the mixture was stirred for further 1 h. The reaction mixture was poured into a cold sat NH_4Cl soln and extracted with ether. The extract was washed with water (x2), sat $NaHCO_3$ soln and brine, dried ($MgSO_4$) and concentrated. The residue was chromatographed over SiO_2 (30 g). Elution with hexane-EtOAc (19:1-7:3) gave 1.02 g (83%) of **20**, $n_D^{22.8}$ 1.4505; $[\alpha]_D^{22.8}$ -11.4° (c=1.15, $CHCl_3$); vmax 2970 (s), 2950 (s), 2900 (s), 2870 (s), 1715 (s), 1460 (m), 1382 (m), 1365 (m), 1310 (w), 1280 (w), 1255 (m), 1220 (w), 1205 (w), 1165 (m), 1140 (m), 1105 (m), 1067 (m), 1045 (m), 1030 (m), 1007 (m), 980 (m), 960 (w), 943 (m), 893 (m), 858 (m), 838 (m), 815 (m), 777 (m), 746 (w), 680 (m) cm^{-1}; δ (100 MHz, $CDCl_3$) 0.11 (6H, s), 0.7-1.2 (6H, m), 0.91 and 0.95 (total 9H, s), 1.5-2.3 (6H, m), 2.4-3.0 (1H, m). (Found: C, 65.48; H, 10.96. Calc for $C_{14}H_{28}O_2Si$: C, 65.62; H, 10.94%).

(2R,3R,4R)-4-tert-Butyldimethylsilyloxy-2,3-dimethyl-2-(3'-oxobutyl)cyclohexanone **22**. To a soln of **20** (1.55 g, 6.2 mmol) and hexamethyldisilazane (2 ml, 9.5 mmol) in CH_2Cl_2 (15 ml) was added TMSI (1.2 ml, 8.4 mmol) at 0°C. After stirring for 10 min at 0°C and for 1 h at room temp, the reaction mixture was diluted with hexane, filtered through a florisil pad and concentrated to give **21**. This was employed for the next step without purification.
To a soln of **21** (ca. 6.2 mmol) and methyl vinyl ketone (2 ml, 25 mmol) in CH_3NO_2 (30 ml) was added dropwise a soln of BF_3 OEt_2 (0.75 ml, 6.1 mmol) in 2-propanol (1.9 ml, 25 mmol) at -20°C. After stirring for 2 h at -20°C, the reaction mixture was quenched with sat $NaHCO_3$ soln and extracted with ether. The extract was washed with water and brine, dried ($MgSO_4$) and concentrated. The residue was chromatographed over SiO_2 (25 g). Elution with hexane-EtOAc (49:1-4:1) gave 270 mg (16%) of recovered **20** and 1.11 g (58%; 68% based on the unrecovered **20**) of **22**, $n_D^{24.4}$ 1.4655; $[\alpha]_D^{24.4}$ -3.17° (c=1.04, $CHCl_3$); vmax 2970 (s), 2940 (s), 2900 (m), 2870 (m), 1720 (s), 1710 (s), 1460 (m), 1420 (m), 1385 (m), 1360 (m), 1320 (w), 1285 (m), 1253 (m), 1160 (m), 1100 (m), 1070 (s), 1005 (m), 986 (m), 953 (m), 918 (m), 884 (m), 835 (m), 813 (m), 773 (m), 678 (m) cm^{-1}; δ (100 MHz, $CDCl_3$) 0.11 (6H, s), 0.92 (9H, s), 0.96 (3H, d, J=5 Hz), 1.04 (3H, s), 1.1-2.8 (9H, m), 3.14 (3H, s), 3.77 (1H, ddd, J=13, 9 and 4 Hz). (Found: C, 66.24; H, 10.52. Calc for $C_{18}H_{34}O_3Si$: C, 66.25; H, 10.43%).

(4aR,5R,6R)-6-tert-Butyldimethylsilyloxy-4,4a,5,6,7,8-hexahydro-4a,5-dimethyl-2(3H)naphthalenone **13b**. A mixture of **22** (5.10 g, 15.6 mmol) and pyrrolidine (3 ml) in benzene (120 ml) was heated under reflux for 2 h with azeotropic removal of water. The reaction mixture was filtered through a florisil pad and concentrated. The residue was chromatographed over SiO_2 (160 g). Elution with hexane-EtOAc (19:1-4:1) gave 3.78 g (79%) of **13b**. Recrystallization (pentane-ether) gave 2.64 g (70%) of pure **13b**, m.p. 36-37°C; $[\alpha]_D^{24.5}$ +88.7° (c=1.1, $CHCl_3$); vmax 2970 (s), 2950 (s), 2900 (s), 2875 (s), 1677 (s), 1620 (m), 1463 (m), 1446 (m), 1434 (m), 1388 (m), 1371 (m), 1360 (m), 1350 (m), 1335 (m), 1257 (m), 1237 (m), 1220 (m), 1200 (w), 1186 (m), 1125 (m), 1100 (m), 1074 (s), 1020 (m), 1007 (m), 961 (m), 952 (m), 940 (m), 918 (m), 890 (m), 868 (m), 860 (m), 834 (s), 814 (m), 775 (s), 706 (m), 685 (m), 666 (w) cm^{-1}; δ (100 MHz, $CDCl_3$) 0.10 (6H, s), 0.92 (9H, s), 0.99 (3H, d, J=6 Hz), 1.12 (3H, s), 1.15-2.5 (9H, m), 3.57 (1H, dt, J=10 and 4 Hz), 5.74 (1H, s). (Found: C, 69.79; H, 10.39. Calc for $C_{18}H_{32}O_2Si$: C, 70.13; H, 10.39%).

Determination of the optical purity of **13b**. **13b** was converted to the corresponding (R)-MTPA ester **13d** and (S)-MTPA ester **13e**. HPLC analytical conditions are: Column normal phase, Nucleosil® 50-5, 4.6mm x 25cm; Eluent n-hexane-i-PrOH=100:1; Flow rate 1.0 ml/min (30 kg/cm^2); Detector UV 254nm; **13d**, Rt 28.7 min (100%); **13e**, Rt 26.9 min (100%). Therefore, the optical purity of **13b** was determined to be 100% e.e.

(3RS,4aR,5R,6R,1'RS)-6-tert-Butyldimethylsilyloxy-4,4a,5,6,7,8-hexahydro-3-(1'-hydroxyethyl)-4a,5-dimethyl-2(3H)naphthale-

[redacted]

reaction mixture was quenched with sat NH_4Cl soln and extracted with ether. The extract was washed with water and brine, dried ($MgSO_4$) and concentrated. The residue was chromatographed over SiO_2 (170 g). Elution with hexane-EtOAc (19:1-3:1) gave 3.91 g (92%) of **23**, n_D^{23} 1.4924; $[\alpha]_D^{23}$ +105° (c=1.02, $CHCl_3$); vmax 3380 (m), 2970 (s), 2950 (s), 2900 (s), 2870 (s), 1665 (s), 1630 (m), 1462 (m), 1450 (m), 1435 (m), 1408 (m), 1385 (m), 1370 (m), 1360 (m), 1325 (w), 1280 (m), 1255 (m), 1218 (m), 1205 (m), 1186 (m), 1133 (m), 1100 (s), 1070 (s), 1017 (m), 1005 (m), 966 (m), 954 (m), 938 (m), 891 (m), 869 (m), 835 (s), 814 (m), 774 (m), 718 (m), 692 (m) cm^{-1}; δ (100 MHz, $CDCl_3$) 0.09 (6H, s), 0.92 (9H, s), 0.9-2.7 (12H, m), 3.57 (1H, dt, J=10 and 4 Hz), 3.8-5.0 (1H, m), 5.72 (1H, br.s). HRMS m/z Found: 352.2427. Calc for $C_{20}H_{36}O_3Si$: 352.2433.

(3RS,4aR,5R,6R)-3-Acetyl-6-tert-butyldimethylsilyloxy-4,4a,5,6,7,8-hexahydro-4a,5-dimethyl-2(3H)naphthalenone **26**. To a soln of oxalyl chloride (2.8 ml, 31 mmol) in CH_2Cl_2 (60 ml) was added dropwise DMSO (4.4 g, 56 mmol) at -70°C. After stirring for 15 min at -70°C, to this was added a soln of **23** (3.90 g, 11 mmol) in CH_2Cl_2 (30 ml) and the mixture was stirred for further 1 h. Then Et_3N (7.7 ml, 55 mmol) was added dropwise at -70°C and the temperature was gradually raised to 0°C. The reaction mixture was poured into water and extracted with ether. The extract was washed with water and brine, dried ($MgSO_4$) and concentrated. The residue was chromatographed over SiO_2 (170 g). Elution with hexane-EtOAc (19:1-17:3) gave 3.04 g (79%) of **26**, $n_D^{25.5}$ 1.5109; vmax 2970 (s), 2950 (s), 2900 (s), 2870 (s), 1720 (m), 1635 (br), 1460 (m), 1383 (m), 1362 (m), 1280 (m), 1253 (m), 1226 (w), 1191 (m), 1130 (m), 1100 (m), 1074 (s), 1007 (m), 955 (m), 892 (m), 880 (m), 866 (m), 847 (s), 818 (m), 778 (m), 745 (w), 680 (m) cm^{-1}; δ (100 MHz, $CDCl_3$) 0.09 (6H, s), 0.90 (9H, s), 0.90-1.1 (6H, m), 1.1-3.0 (11H, m), 3.54 (1H, dt, J=10 and 4 Hz), 5.95 (1H, br.s). This was employed for the next step without further purification.

(4aR,5R,6R)-3-Acetyl-6-tert-butyldimethylsilyloxy-5,6,7,8-tetrahydro-4a,5-dimethyl-2(4aH)naphthalenone **24**. A mixture of **26** (1.67 g, 4.77 mmol) and DDQ (1.36 g, 6.0 mmol) in ether (30 ml) was stirred for 2 h at room temp. The reaction mixture was diluted with ether (300 ml), washed with water (x3), sat $NaHCO_3$ soln and brine, dried ($MgSO_4$) and concentrated. The residue was chromatographed over SiO_2 (30 g). Elution with hexane-EtOAc (19:1-17:3) gave 1.40 g (83%) of **24**, $n_D^{23.5}$ 1.5017; $[\alpha]_D^{23.5}$ -28.8° (c=1.0, $CHCl_3$); vmax 2970 (s), 2950 (s), 2900 (m), 2870 (m), 1695 (s), 1664 (s), 1633 (m), 1597 (w), 1462 (m), 1440 (m), 1410 (m), 1387 (m), 1360 (m), 1283 (m), 1258 (s), 1213 (w), 1200 (w), 1140 (m), 1120 (m), 1104 (s), 1078 (s), 1020 (m), 1007 (m), 975 (w), 957 (s), 940 (w), 925 (w), 886 (s), 838 (s), 815 (m), 778 (m), 682 (m) cm^{-1}; δ (100 MHz, $CDCl_3$) 0.10 (6H, s), 0.89 (9H, s), 1.17 (3H, d, J=6 Hz), 1.22 (3H, s), 1.2-2.6 (5H, m), 2.57 (3H, s), 3.67 (1H, dt, J=10 and 4 Hz), 6.11 (1H, br.s), 7.64 (1H, s). (Found: C, 68.54; H, 9.21. Calc for $C_{21}H_{32}O_3Si$: C, 68.91; H, 9.20%).

(3S,4R,4aR,5R,6R)-3-Acetyl-6-tert-butyldimethylsilyloxy-3,4-epoxy-4,4a,5,6,7,8,-hexahydro-4a,5-dimethyl-2(3H)naphthalenone **27**. A mixture of **24** (1.20 g, 3.45 mmol), t-BuOOH (4.17 M in toluene, 3 ml, 12.5 mmol) and Triton B (40% in MeOH, 0.3 ml)

in THF (50 ml) was stirred overnight at room temp. The reaction mixture was poured into sat Na_2SO_3 soln and extracted with ether. The extract was washed with water and brine, dried ($MgSO_4$) and concentrated. The residue was chromatographed over SiO_2 (30 g). Elution with hexane-EtOAc (19:1-17:3) gave 880 mg (70%) of **27**, m.p. 61-62°C; $[\alpha]_D^{24.2}$ +196° (c=1.1, $CHCl_3$); νmax 2960 (s), 2945 (s), 2895 (s), 2870 (s), 1725 (s), 1713 (s), 1675 (s), 1630 (m), 1460 (m), 1435 (m), 1408 (m), 1385 (m), 1357 (s), 1337 (m), 1312 (w), 1290 (m), 1280 (m), 1255 (s), 1215 (w), 1196 (m), 1100 (s), 1078 (s), 1026 (w), 1004 (m), 985 (w), 976 (w), 955 (w), 940 (m), 920 (m), 888 (s), 836 (s), 815 (m), 771 (s), 740 (m), 714 (m), 687 (m) cm^{-1}; δ (100 MHz, $CDCl_3$) 0.10 (6H, s), 0.92 (9H, s), 1.20 (3H, d, J=7 Hz), 1.24 (3H, s), 1.3-2.7 (5H, m), 2.34 (3H, s), 3.50 (1H, s), 3.60 (1H, dt, J=10 and 4 Hz), 5.78 (1H, br.s). (Found: C, 65.93; H, 8.88. Calc for $C_{21}H_{32}O_4Si$: C, 65.88; H, 8.85%).

(3S,4R,4aR,5R,6R)-3,4-Epoxy-4,4a,5,6,7,8-hexahydro-6-hydroxy-3-isopropenyl-4a,5-dimethyl-2(3H)naphthalenone(sporogen-AO 1)

1. To a soln of **27** (100 mg, 0.27 mmol) in THF (2 ml) was added dropwise $TMSCH_2MgCl$ soln in ether (1M, 0.5 ml, 0.5 mmol) at 0°C. After stirring for 5 min at 0°C, the reaction mixture was quenched with sat NH_4Cl soln and extracted with ether. The extract was washed with water and brine, dried ($MgSO_4$) and concentrated to give **28**. This crude adduct was employed for the next step without purification.

A mixture of **28** (ca. 0.27 mmol) and conc H_2SO_4 (2 drops) in THF (10 ml) was stirred for 3 days at room temp. The reaction mixture was diluted with ether, washed with water, sat $NaHCO_3$ soln and brine, dried ($MgSO_4$) and concentrated. To the residue was added CH_3CN (2 ml) and 48% HF soln (0.08 ml). After stirring for 30 min at room temp, the reaction mixture was poured into sat $NaHCO_3$ soln and extracted with EtOAc. The extract was washed with water and brine, dried ($MgSO_4$) and concentrated. The residue was purified by preparative TLC (Merck Kieselgel 60 F-254 Art 5717, hexane-EtOAc=1:1) to give 60 mg (88%) of **1**, m.p. 104-105°C; $[\alpha]_D^{25}$ +262° (c=0.56, MeOH); UV (c=9.3x10^{-4} in MeOH) lgε=4.16 (λmax 243 nm); CD [at 24.5°C, c=0.023 in MeOH, Δε, (λ[nm])] -14.07 (219), +13.02 (247), +4.50 (334); νmax 3530 (s), 3090 (m), 3005 (m), 2990 (m), 2970 (m), 2940 (m), 2925 (m), 2900 (m), 2880 (m), 1655 (s), 1630 (m), 1615 (m), 1465 (m), 1455 (m), 1410 (m), 1390 (m), 1377 (m), 1365 (m), 1335 (m), 1260 (w), 1245 (m), 1235 (m), 1210 (m), 1181 (m), 1158 (m), 1120 (m), 1100 (w), 1035 (s), 1015 (m), 990 (w), 960 (m), 932 (m), 918 (m), 888 (m), 860 (w), 850 (m), 826 (w), 753 (m), 735 (m), 718 (w), 700 (m), 659 (m) cm^{-1}; ^1H NMR δ (400 MHz, $CDCl_3$) 1.228 (3H, s), 1.268 (3H, d, J=6.8 Hz), 1.440 (1H, dddd, J=14.5, 12.5, 11.0 and 4.5 Hz), 1.570 (1H, br.s), 1.815 (1H, dq, J=11.0 and 6.8 Hz), 1.873 (3H, t, J=1.2 Hz), 2.157 (1H, ddt, J=12.5, 5.0 and 2.8 Hz), 2.343 (1H, ddd, J=14.5, 4.5 and 2.8 Hz), 2.520 (1H, ddt, J=14.5, 5.0 and 2.0 Hz), 3.330 (1H, s), 3.627 (1H, dt, J=11.0 and 5.0 Hz) 5.106 (1H, q, J=1.2 Hz), 5.116 (1H, br), 5.765 (1H, d, J=2.0 Hz); ^{13}C NMR δ (25 MHz, $CDCl_3$) 11.3, 18.8, 19.8, 30.9, 35.2, 41.0, 44.3, 63.5, 68.3, 70.9, 114.4, 121.2, 139.1, 163.1, 192.8. (Found: C, 72.59; H, 7.87. Calc for $C_{15}H_{20}O_3$: C, 72.55; H, 8.12%).

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REFERENCES

1 S. Tanaka, K. Wada, M. Katayama and S. Marumo, Agric. Biol. Chem., **48**, 3189 (1984).
2 S. Tanaka, K. Wada, S. Marumo and H. Hattori, Tetrahedron Lett., **25**, 5907 (1984).
3 T. Tirilly, J. Kloosterman, G. Sipma and J. G. Kettenes-van den Bosch, Phytochem., **22**, 2082 (1983).
4 K. Mori and H. Tamura, Liebigs Ann. Chem., 97 (1988).
5 K. Yamakawa, I. Izuta, H. Oka, H. Sakaguchi, M. Kobayashi and T. Satoh, Chem. Pharm. Bull., **27** 331 (1979)
6 T. Kitahara, and K. Mori, Tetrahedron Lett., **26**, 451 (1985).
7 R. M. Lukes, G. I. Poos and L. H. Sarett, J. Am. Chem. Soc., **74**, 1401 (1952).
8 S. Hannessian and N. R. Plessas, J. Org. Chem., **34**, 517 (1978).
9 O. Mitsunobu, Synthesis, 1 (1981).
10 T. Takagi, Y. Nakahara and M. Matsui, Tetrahedron, **34**, 517 (1978).
11 A. J. Mancuso, S-L. Huang and D. Swern, J. Org. Chem., **43**, 2480 (1978).
12 R. B. Woodward, F. Sondheimer, D. Taub, K. Heusler and W. M. McLamore, J. Am. Chem. Soc., **74**, 4223 (1969).
13 E. Piers, R. W. Britton, W. de Waal, Can. J. Chem., **47**, 4307 (1969).
14 S. Torii, T. Inokuchi and K. Kawai, Bull. Chem. Soc. Jpn., **52**, 861 (1979) and references cited therein.
15 P. Duhamel, L. Hennequin, N. Poirier and J-M. Poirier, Tetrahedron Lett., **26**, 6201 (1985).
16 R. D. Miller and D. R. McKean, Synthesis, 730 (1979).
17 H. O. House, L. G. Czuba, M. Gal and H. O. Olmstead, J. Org. Chem., **34**, 2324 (1969).
18 S. Tamagami, M. Katayama, S. Marumo, M. Isobe and T. Goto, Abstract of papers, the Annual Meeting of the Agricultural Chemical Society of Japan. (Sapporo) p 231 (1985).
19 J. R. Parikl and W. von E. Doering, J. Am. Chem. Soc., **89**, 5505 (1967).
20 N. C. Yang and R. A. Finnegan, J. Am. Chem. Soc., **80**, 5845 (1958).
21 P. F. Hudrick and D. Peterson, J. Am. Chem. Soc., **97**, 1464 (1975) and references cited therein.
22 T. H. Chan and E. Chang, J. Org. Chem., **39**, 3264 (1974) and references cited therein.
23 C. R. Hauser and C. R. Hance, J. Am. Chem. Soc., **74**, 5091 (1952).
24 C. Riche, C.Pascard-Billy, M. Devys, A. Gaudemer, M. Barbier and J-F. Bousquet, Tetrahedron Lett., 2765 (1974).
25 T. K. Dhar, K. A. I. Siddiqui and E. Ali, Tetrahedron Lett., **23**, 5459 (1982).