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SYNTHESES OF OPTICALLY ACTIVE (+)- AND (-)-UNTENONE A

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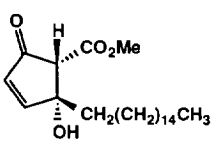
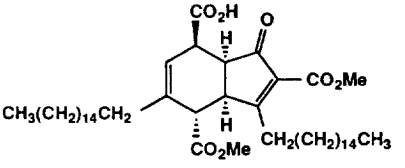
Abstract: Optically active (+)- and (-)-untenone were synthesized from (*S*)-4-[(*tert*-butyldimethylsilyl)oxy]-2-cyclopentenone and untenone A isolated from marine sponge was shown to be racemic.

Untenone A (**1**), which has been isolated from the Okinawan marine sponge *Plakortis* sp. is a unique oxylipin possessing a cyclopentenone and inhibits the cell proliferation of L1210 leukemia at IC_{50} 0.4 μg/ml.[1] Untenone A is considered a biosynthetic precursor of manzamenone A (**2**)[2] consisting of two molecular fatty acids, also obtainable from the Okinawan sponge *Plakortis* sp. Although the synthesis of (±)-untenone A[3] and (-)-untenone A[4] has been conducted, the absolute configuration of untenone A remains to be determined. The specific rotation observed for untenone A ($[\alpha]_D^{19}$ +0.2° (*c* 2.1, $CHCl_3$)) differed considerably with that for (-)-untenone A ($[\alpha]_D^{26}$ -73.3° (*c* 1.20, $CHCl_3$)). The authors were thus prompted to prepare both optically active (+)- and (-)-untenone A. The synthesis of (+)- and (-)-untenone A from (*S*)-4-[(*tert*-butyldimethylsilyl)oxy]-2-cyclopentenone and configuration of untenone A are presented in the following.



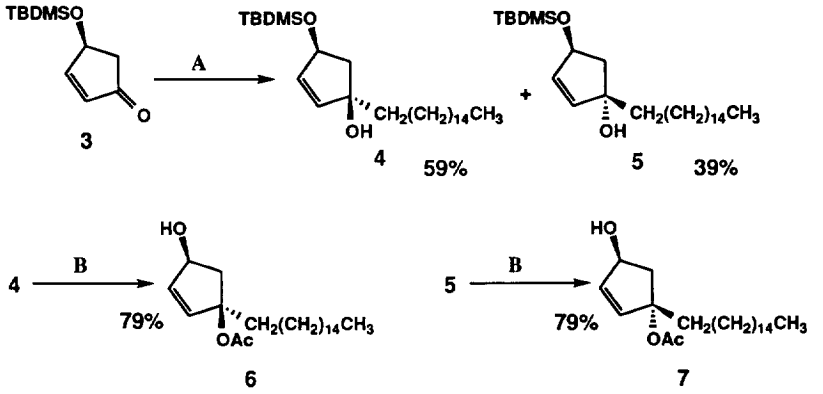
untenone A (1)



manzamenone A (2)

Reactions of (*S*)-4-[(*tert*-butyldimethylsilyl)oxy]-2-cyclopentenone (**3**), prepared from L-(+)-diethyl tartrate according to the established procedure,[5] with alkylsamarium (III) reagent,[6] prepared from 1-bromohexadecane and SmI_2, in THF at -78°C gave alcohols **4** and **5** in 59% and 39% yield, respectively.[7,8] The stereochemistry of these alcohols **4** and **5** was determined by observation of hydrogen bonding in acetoxy alcohols **6** and **7**. Acetoxy alcohols **6** and **7** were prepared from **4** and **5** by acetylation (Ac_2O, Py, 50°C) and deprotection of silyl ether (Bu_4NF, THF, r.t.). High dilution IR measurement of alcohol **6** in carbon

Scheme 1

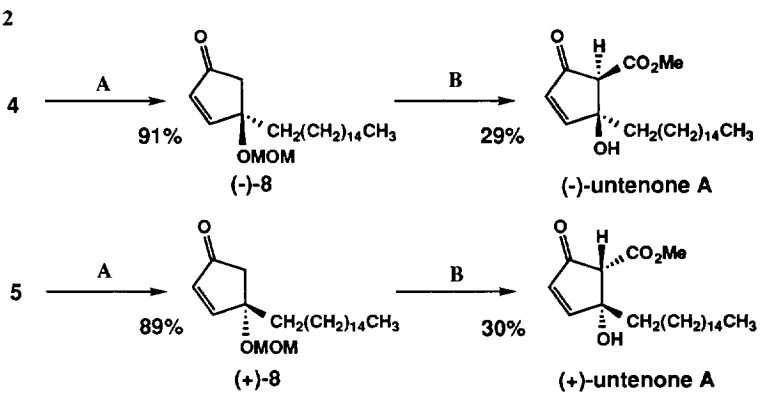


Reagents: A. $CH_3(CH_2)_{14}CH_2SmI_2$, THF - HMPA, -78°C; **B**. i) Ac_2O, Py, 50°C; ii) Bu_4NF, THF, r.t.

tetrachloride (5.0 x 10^{-3} M) showed absorption at 3520 cm^{-1} due to intramolecular hydrogen bonding between the hydroxy and acetoxy groups, indicating the *cis* configuration between these oxygen functional groups. The IR spectrum of alcohol **7** (5.0 x 10^{-3} M) disclosed absorption at 3620 cm^{-1} due to a free hydroxyl group, thus showing **7** to have the *trans* configuration.

The hydroxyl group of **4** was protected as methoxymethyl ether (MOM-Cl, $^{i}Pr_2NEt$, CH_2ClCH_2Cl, 50°C), followed by deprotection of silyl ether (Bu_4NF, THF, r.t.). Oxidation of the secondary alcohol with Jones reagent at 0°C gave enone (-)-**8**. Reactions of the lithium enolate, prepared from enone (-)-**8** and lithium diisopropylamide (LDA), with methyl cyanoformate[9] in the presence of hexamethylphosphoric triamide (HMPA) at -42°C gave β-keto esters as a diastereomeric mixture (3:2).[10] Without separating the

Scheme 2



Reagents: A. i) MOM-Cl, $^{i}Pr_2NEt$, CH_2ClCH_2Cl, 50°C; ii) Bu_4NF, THF, r.t.; iii) Jones Reagent, acetone, 0°C; **B**. i) LDA, THF - HMPA, -78°C, then $NCCO_2Me$, -42°C; ii) AcOH-c.HCl(50:1).

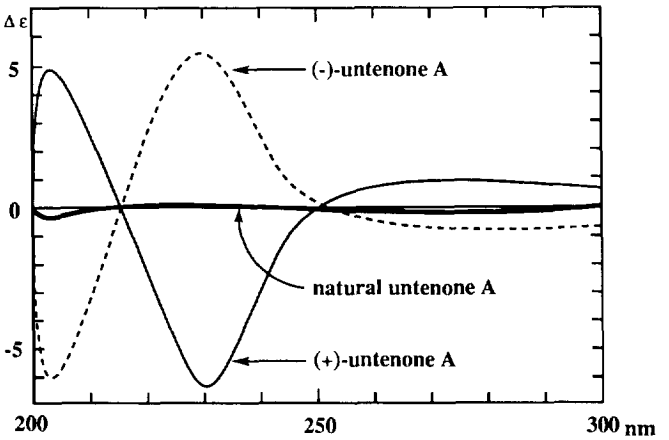


Fig. 1 CD spectra of (+)-, (-)- and natural untenone A

diastereomers, treatment of the β-keto esters with AcOH-c.HCl (50:1) at room temperature[11] gave (-)-untenone A ((-)-**1**)($[\alpha]_D^{26}$ -36.9° (*c* 0.90, $CHCl_3$), mp 77-78 °C) as a single isomer. Similarly, (+)-untenone A ((+)-**1**)($[\alpha]_D^{26}$ +36.7° (*c* 0.43, $CHCl_3$), mp 77-78 °C) was synthesized *via* enone (+)-**8** from the alcohol **5**. The NMR spectra of synthetic (+)-**1** and (-)-**1** were identical with those of natural untenone A. However, the specific rotation of untenone A ($[\alpha]_D^{19}$ +0.2° (*c* 2.1, $CHCl_3$))[1] differed from that of either enantiomer. The CD spectra of (-)-**1**, (+)-**1** and natural **1** are shown in Fig. 1. In (+)-**1**, the negative Cotton effect at 229 nm (Δε -6.2) and positive Cotton effect at 202 nm (Δε +4.8) were observed while the positive Cotton effect at 229 nm (Δε +5.4) and the negative Cotton effect at 202 nm (Δε -6.0) could be seen in (-)-**1**. However, natural untenone (**1**) was observed not to exert the Cotton effect. Untenone A, isolated from marine sponge, is thus clearly shown to be racemic.

Experimental

Melting points were measured on a Yazawa BY-2 micro melting point apparatus and uncorrected. Optical rotations were measured with a JASCO DIP-360 automatic polarimeter. Infrared (IR) spectra were recorded with a Perkin-Elmer FT-IR 1710 spectrometer or JASCO A-302 spectrometer. Ultraviolet (UV) spectra were recorded with a Hitachi 124 spectrophotometer. Circular dichroism (CD) spectra were measured with a JASCO J-720 spectropolarimeter. ^{1}H-NMR spectra were recorded with a Bruker AM-400 (400 MHz). Chemical shifts are given on a δ (ppm) scale with tetramethylsilane (TMS) as the internal standard (s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad). Electron impact mass (EIMS) spectra and high resolution mass spectra (HRMS) were obtained with a Hitachi M-80 or VG Auto Spec spectrometer. Elemental analysis was conducted using a Perkin-Elmer 242. Column chromatography was carried out on Merck Silica gel 60 (70-230 mesh). Tetrahydrofuran (THF) was distilled from sodium-benzophenone ketyl under argon. Hexamethylphosphoric triamide (HMPA) was distilled from calcium hydride under reduced pressure.

(1*R*, 4*S*)-4-[(*tert*-Butyldimethylsilyl)oxy]-1-hexadecyl-1-hydroxy-2-cyclopentene (4) and (1*S*, 4*S*)-4-[(*tert*-Butyldimethylsilyl)oxy]-1-hexadecyl-1-hydroxy-2-cyclopentene (5)

To a solution of 0.1 M SmI_2 (12.2 ml, 1.22 mmol) in THF was added HMPA (0.97 ml, 5.59 mmol). The solution was stirred at room temperature for 5 min and treated with 1-bromohexadecane (0.18 ml, 0.58 mmol). The resulting mixture was stirred at room temperature for 20 min and cooled to -78°C followed by the addition of a solution of (*S*)-4-[(*tert*-butyldimethylsilyl)oxy]-2-cyclopentenone (**3**) (50 mg, 0.23 mmol) in THF (1.5 ml). After 10 min, hexane (20 ml) and silica gel (2.7 g) were added and stirred at room temperature for 30 min. The resultant mixture was filtered through a plug of silica gel. The filtrate was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (eluted with hexane - acetone = 3 : 2) to give **4** (60 mg, 59 % yield) and **5** (40 mg, 39 % yield). Compound **4**: $[\alpha]_D^{26}$ -30.7° (*c* 1.16, $CHCl_3$); EIMS m/z (relative intensity) 438(M^+, 5), 420(20), 381(100), 213(44); Anal. Calcd for $C_{27}H_{54}O_2Si$: C, 73.91; H, 12.41. Found: C, 73.88; H, 12.52; IR (neat) 3423, 2927, 2855 cm^{-1}; ^{1}H-NMR (400MHz, $CDCl_3$) δ 0.08 (6H, s), 0.88 (3H, t, J=7.1 Hz), 0.89 (9H, s), 1.55 (28H, br m), 1.5 - 1.65 (2H, m), 1.70 (1H, dd, J=13.7, 3.6 Hz), 2.33 (1H, dd, J=13.7, 6.6Hz), 4.67 (1H, m), 5.80 (1H, dd, J=5.5, 2.0 Hz), 5.85 (1H, d, J=5.5 Hz). Compound **5**: $[\alpha]_D^{26}$ -21.4° (*c* 0.90, $CHCl_3$); EIMS m/z (relative intensity) 438(3), 420(10), 381(100), 213(81); Anal. Calcd for $C_{27}H_{54}O_2Si$: C, 73.91; H, 12.41. Found: C, 73.71; H, 12.56; IR (neat) 3344, 2925, 2853 cm^{-1}; ^{1}H-NMR (400MHz, $CDCl_3$) δ 0.07 (6H, s), 0.88 (3H, t, J=7.1 Hz), 0.89 (9H, s), 1.55 (28H, br m), 1.60 - 1.75 (2H, m), 1.78 (1H, dd, J=13.7, 4.2 Hz), 2.20 (1H, dd, J=13.7, 6.7Hz), 5.03 (1H, m), 5.80 (1H, dd, J=5.6, 1.1 Hz), 5.82 (1H, dd, J=5.6, 1.7 Hz).

(1*R*, 4*S*)-1-acetoxy-4-hydroxy-1-hexadecyl-2-cyclopentene (6)

To a solution of alcohol **4** (97 mg, 0.22 mmol) in pyridine (1.0 ml) were added Ac_2O (0.8 ml) and DMAP (3.0 mg, 0.02 mmol) and the mixture was stirred at 50°C for 1 h. The reaction mixture was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (eluted with hexane - Et_2O = 30 : 1) to give the acetate (104 mg, 98 % yield) as a colorless oil: $[\alpha]_D^{26}$ -19.9° (*c* 1.34, $CHCl_3$); EIMS m/z (relative intensity) 480(M^+, 0.1), 451(0.5), 423(10), 255(6), 117(100); Anal. Calcd for $C_{29}H_{56}O_3Si$: C, 72.44; H, 11.75. Found: C, 72.27; H, 11.76; IR (neat) 2926, 2855, 1737, 1250 cm^{-1}; ^{1}H-NMR (400MHz, $CDCl_3$) δ 0.08 (3H, s), 0.08 (3H, s), 0.88 (3H, t, J=7.1 Hz), 0.89 (9H, s), 1.25 (28H, br m), 1.89 (2H, m), 1.98 (3H, s), 1.99 (1H, dd, J=13.9, 5.1 Hz), 2.65 (1H, dd, J=13.9, 7.0 Hz), 4.68 (1H, m), 5.86 (1H, dd, J=5.6, 1.9 Hz), 6.10 (1H, dd, J=5.6, 1.3 Hz).

To a solution of the acetate (50 mg, 0.10 mmol) in THF (0.5 ml) was added 1.0M Bu_4NF (0.3 ml, 0.30 mmol) in THF followed by stirring at room temperature for 35 min. The mixture was diluted with Et_2O, washed with H_2O and saturated aqueous NaCl, dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (eluted with hexane - Et_2O = 3 : 1) to give alcohol **6** (31 mg, 81 % yield) as a colorless crystal: m.p. 47 - 48 °C; $[\alpha]_D^{26}$ +20.2° (*c* 0.94, $CHCl_3$); EIMS m/z (relative intensity) 306(73), 141(18), 123(7), 109(67), 96(100); Anal. Calcd for $C_{23}H_{42}O_3$: C, 75.35; H, 11.56. Found: C, 75.05; H, 11.56; IR (KBr) 3397, 2919, 2851, 1733, 1249 cm^{-1}; IR (CCl_4 5.0 x 10^{-3} M) 3520, 1730 cm^{-1}; ^{1}H-NMR (400MHz, $CDCl_3$) δ 0.88 (3H, t, J=6.7 Hz), 1.26 (28H, br m), 1.65 (1H, m), 1.76 (1H, m), 2.00 (3H, s), 2.15 (1H, dd, J=15.3, 2.2 Hz), 2.46 (1H, dd, J=15.3, 7.5 Hz), 4.66 (1H, m), 5.88 (1H, d, J=5.6, Hz), 6.06 (1H, dd, J=5.6, 2.3 Hz).

(1*S*, 4*S*)-1-Acetoxy-4-hydroxy-1-hexadecyl-2-cyclopentene (7)

To a solution of alcohol **5** (94 mg, 0.21 mmol) in pyridine (1.0 ml) were added Ac_2O (0.8 ml) and DMAP (3.0 mg, 0.02 mmol). After being stirred at 50°C for 1 h, the reaction mixture was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (eluted with hexane - Et_2O = 30 : 1) to give the acetate (87 mg, 85 % yield) as a colorless oil; $[\alpha]_D^{26}$ -48.5° (*c* 1.01, $CHCl_3$); EIMS m/z (relative intensity) 480(M^+, 0.1), 420(13), 350(68), 290(27), 117(100); Anal. Calcd for $C_{29}H_{56}O_3Si$: C, 72.44; H, 11.75. Found: C, 72.40; H, 11.87; IR (neat) 2926, 2851, 1737, 1251 cm^{-1}; ^{1}H-NMR (400MHz, $CDCl_3$) δ 0.08 (6H, s), 0.88 (3H, t, J=7.0 Hz), 0.89 (9H, s), 1.26 (28H, br m), 1.76 (1H, dd, J = 14.0, 4.3 Hz), 1.84 (1H, m), 1.95 (3H, s), 2.08 (1H, m), 2.50 (1H, dd, J=14.0, 6.7 Hz), 4.98 (1H, m), 5.89 (1H, dd, J=5.6, 1.8 Hz), 6.10 (1H, dd, J=5.6, 1.4 Hz).

To a solution of the acetate (87 mg, 0.073 mmol) in THF (0.3 ml) was added 1.0M Bu_4NF (0.22 ml, 0.22 mmol) in THF followed by stirring at room temperature for 2 h. The mixture was diluted with Et_2O, washed with H_2O and saturated aqueous NaCl, dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (eluted with hexane - Et_2O = 3 : 1) to give alcohol **7** (26 mg, 93 % yield) as a colorless crystal: m.p. 59 - 60 °C; $[\alpha]_D^{26}$ -40.0° (*c* 0.38, $CHCl_3$); EIMS m/z (relative intensity) 306(83), 288(9), 141(35), 109(65), 96(100); Anal. Calcd for $C_{23}H_{42}O_3$: C, 75.35; H, 11.56. Found: C, 75.06; H, 11.61; IR (KBr) 3442, 2917, 2850, 1726, 1698, 1250 cm^{-1}; IR (CCl_4 5.0 x 10^{-3} M) 3620, 1733 cm^{-1}; ^{1}H-NMR (400MHz, $CDCl_3$) δ 0.88 (3H, t, J=6.7 Hz), 1.26 (28H, br m), 1.79 (1H, dd, J = 14.5, 4.1 Hz), 1.86 (1H, m), 1.95 (3H, s), 2.07 (1H, m), 2.61 (1H, dd, J=14.4, 7.0 Hz), 5.02 (1H, m), 5.99 (1H, dd, J=5.6, 1.9 Hz), 6.20 (1H, dd, J=5.6, 1.3 Hz).

(*R*)-4-Hexadecyl-4-[(methoxymethyl)oxy]-2-cyclopentenone ((-)-8)

To a solution of alcohol **4** (611 mg, 1.39 mmol) in CH_2ClCH_2Cl (10 ml) were added diisopropylethylamine (0.97 ml, 5.56 mmol) and chloromethyl methyl ether (0.32 ml, 4.17 mmol). After being stirred at 60°C for 6 h, the reaction mixture was diluted with Et_2O, washed with H_2O and saturated aqueous NaCl, dried over anhydrous $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (eluted with hexane - Et_2O = 10 : 1) to give the ether (664 mg, 99 % yield) as a colorless oil; $[\alpha]_D^{26}$ -8.8° (*c* 1.00, $CHCl_3$); EIMS m/z (relative intensity) 482(M^+, 0.7), 421(12), 395(100), 257(47); Anal. Calcd for $C_{29}H_{58}O_3Si$: C, 72.14; H, 12.12. Found: C, 72.19; H, 12.32; IR (neat) 2926, 2855, 1105, 1033 cm^{-1}; ^{1}H-NMR (400MHz, $CDCl_3$) δ 0.07 (3H, s), 0.08 (3H, s), 0.88 (3H, t, J=7.0 Hz), 0.89 (9H, s), 1.25 (28H, br m), 1.5 - 1.65 (2H, m), 1.83 (1H, dd, J=14.1, 4.2 Hz), 2.31 (1H, dd, J=14.1, 7.2 Hz), 3.35 (3H, s), 4.62 (1H, d, J=6.8 Hz), 4.63 (1H, m), 4.76 (1H, d, J=6.8 Hz), 5.80 (1H, dd, J=5.7, 0.9 Hz), 5.83 (1H, dd, J=5.7, 1.8 Hz).

To a solution of the methoxymethyl ether (664 mg, 1.38 mmol) in THF (1.4 ml) was added 1.0M Bu_4NF (4.1 ml, 4.11 mmol) in THF and the mixture was stirred at room temperature for 40 min, diluted with Et_2O, washed with H_2O and saturated aqueous NaCl, dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (eluted with hexane - Et_2O = 5 : 1 to Et_2O) to give the alcohol (487 mg, 96 % yield) as white crystals; m.p. 39 - 40°C; $[\alpha]_D^{26}$ -25.2° (*c* 0.50,

$CHCl_3$); EIMS m/z (relative intensity) 323(3), 306(22), 143(100); Anal. Calcd for $C_{23}H_{44}O_3$: C, 74.93; H, 12.04. Found: C, 74.80; H, 11.75; IR (neat) 3430, 2916, 2851, 1099, 1034 cm^{-1}; ^{1}H-NMR (400MHz, $CDCl_3$) δ 0.88 (3H, t, J=6.7 Hz), 1.25 (28H, br m), 1.5 - 1.65 (2H, m), 1.93 (1H, dd, J=15.1, 2.0 Hz), 2.28 (1H, dd, J=15.1, 7.6 Hz), 3.39 (3H, s), 4.58 (1H, m), 4.59 (1H, d, J=7.6 Hz), 4.93 (1H, d, J=7.6 Hz), 5.74 (1H, d, J=5.6, Hz), 5.83 (1H, dd, J=5.6, 2.3 Hz).

To a cold (0°C) solution of the alcohol (435 mg, 1.18 mmol) in acetone (12 ml) was added dropwise the Jones reagent (about 0.4 ml) until the color of the reagent remained, and then 2-propanol was added. After being stirred for 5min, the mixture was diluted with Et_2O, washed with H_2O and saturated aqueous NaCl, dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (eluted with hexane - Et_2O = 5 : 1) to give enone (-)-**8** (487 mg, 96 % yield) as a colorless crystal: m.p. 49 - 50°C; $[\alpha]_D^{26}$ -22.9° (*c* 1.79, $CHCl_3$); EIMS m/z (relative intensity) 366(M^+, 10), 321(35), 305(22), 141(100); Anal. Calcd for $C_{23}H_{42}O_3$: C, 75.35; H, 11.56. Found: C, 75.24; H, 11.65; IR (KBr) 2916, 2855, 1715, 1088, 1029 cm^{-1}; UV (EtOH) λ_{max} 213 nm (ε 9113); CD (MeOH) λ_{ext} (Δε) 228 (+2.1), 204 (-1.7); ^{1}H-NMR (400MHz, $CDCl_3$) δ 0.88 (3H, t, J=6.6 Hz), 1.26 (28H, br m), 1.65 - 1.85 (2H, m), 2.43 (1H, d, J=18.6 Hz), 2.66 (1H, d, J=18.6 Hz), 3.36 (3H, s), 4.60 (1H, d, J=7.5Hz), 4.66 (1H, d, J=7.5 Hz), 6.19 (1H, d, J=5.7 Hz), 7.47 (1H, d, J=5.7 Hz).

(-)-Untenone A

To a cold (-78°C) solution of lithium diisopropylamide [prepared from diisopropylamine (306 μl, 2.19 mmol) and butyllithium (1.66 M in hexane, 1.33 ml, 2.19 mmol)] in THF (10 ml) was added dropwise a solution of the enone (-)-**8** (395 mg, 1.09 mmol) in THF (5.0 ml) and HMPA (380 μl, 2.19 mmol). After the mixture was stirred at -78°C for 30 min, methyl cyanoformate (173 μl, 2.19 mmol) was added and the system was stirred for 2 h at -42°C. The reaction mixture was poured into ether and saturated NH_4Cl solution. The organic layer was washed with water and saturated NaCl solution, dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (eluted with hexane - acetone - AcOH = 150 : 10 : 1) to give the β-ketoester (238 mg, 54 % yield) as a diasteremeric mixture (3 : 2). The mixtures was used for subsequent reactions without separation.

The above β-ketoester (150 mg, 0.368 mmol) was treated with AcOH-c.HCl (50:1) (2.5 ml) and stirred at room temperature for 10 min. The reaction mixture was diluted with ether, washed with saturated $NaHCO_3$ solution, water and saturated NaCl solution, dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The residue was chromatographed on silica gel column (eluted with $CHCl_3$ - AcOEt = 20 : 1) and recrystallized from hexane to give (-)-untenone A (75 mg, 54% yield) as a colorless crystal: m.p. 77 - 78°C; $[\alpha]_D^{26}$ -36.9° (*c* 0.90, $CHCl_3$); EIMS m/z (relative intensity) 380(M^+, 0.2), 361(2), 321(24), 156(100); HRMS: Calcd for $C_{23}H_{40}O_4$ (M^+) 380.2927: Found: 380.2934; IR (KBr) 3483, 2918, 2850, 1737, 1702 cm^{-1}; UV (MeOH) λ_{max} 209 nm (ε 7910); CD (MeOH) λ_{ext} (Δε) 229 (+5.4), 202 (-6.0); ^{1}H-NMR (400MHz, $CDCl_3$) δ 0.88 (3H, t, J=6.7 Hz), 1.2 - 1.6 (28H, br m), 1.69 (1H, m), 1.80 (1H, m), 3.46 (1H, s), 3.79 (3H, s), 6.18 (1H, d, J=5.7 Hz), 7.51 (1H, d, J=5.7 Hz); ^{13}C-NMR (100MHz, $CDCl_3$) δ 14.1, 22.7, 23.8, 29.3, 29.4, 29.5, 29.7(C x 7), 29.8, 31.9, 40.4, 52.8, 60.9, 79.9, 132.3, 167.0, 169.0, 200.0.

(*S*)-4-Hexadecyl-4-methoxymethyloxy-2-cyclopentenone ((+)-8)

To a solution of alcohol **5** (376 mg, 0.85 mmol) in CH_2ClCH_2Cl (10 ml) were added diisopropylethylamine (0.60 ml, 3.42 mmol) and chloromethyl methyl ether (0.20 ml, 2.56 mmol). After being stirred at 50°C for 5 h, the reaction mixture was diluted with Et_2O, washed with H_2O and saturated aqueous NaCl, dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (eluted with hexane - Et_2O = 10 : 1) to give the ether (407 mg, 99 % yield) as a colorless oil; $[\alpha]_D^{26}$ -31.8° (*c* 1.00, $CHCl_3$); EIMS m/z (relative intensity) 482(M^+, 3.4), 437(7), 395(100), 257(72); Anal. Calcd for $C_{29}H_{58}O_3Si$: C, 72.14; H, 12.12. Found: C, 72.09; H, 12.33; IR (neat) 2926, 2855, 1092, 1035 cm^{-1}; ^{1}H-NMR (400MHz, $CDCl_3$) δ 0.07 (6H, s), 0.88 (3H, t, J=7.1 Hz), 0.89 (9H, s), 1.26 (28H, br m), 1.68 (1H, dd, J=14.1, 4.2 Hz), 1.69 (2H, m), 2.34 (1H, dd, J=14.1, 6.9 Hz), 3.33 (3H, s), 4.52 (1H, d, J=7.1 Hz), 4.59 (1H, d, J=7.1 Hz), 4.96 (1H, m), 5.76 (1H, dd, J=5.7, 1.3 Hz), 5.90 (1H, dd, J=5.7, 1.9 Hz).

To a solution of the methoxymethyl ether (407 mg, 0.85 mmol) in THF (2.0 ml) was added 1.0M Bu_4NF (2.5 ml, 2.50 mmol) in THF and the mixture was stirred at room temperature for 40 min. The reaction mixture was diluted with Et_2O-CH_2Cl_2 (3 : 1), washed with H_2O and saturated aqueous NaCl, dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (eluted with hexane - Et_2O = 1 : 1) to give the alcohol (304 mg, 98 % yield) as a white crystal; m.p. 39 - 40 °C; $[\alpha]_D^{26}$ -21.9° (*c* 0.73, $CHCl_3$); EIMS m/z (relative intensity) 323(2), 306(7), 288(3), 143(51); anal. Calcd for $C_{23}H_{44}O_3$: C, 74.93; H, 12.04. found: C, 74.64; H, 12.08; IR (KBr) 3359, 2915, 2850, 1090, 1033 cm^{-1}; ^{1}H-NMR (400MHz, $CDCl_3$) δ 0.88 (3H, t, J=6.7 Hz), 1.26 (28H, br m), 1.70 (2H, m), 1.70 (1H, dd, J=14.5, 3.9 Hz), 2.46 (1H, dd, J=14.5, 7.2 Hz), 3.33 (3H, s), 4.52 (1H, d, J=7.3 Hz), 4.60 (1H, d, J=7.3 Hz), 4.98 (1H, m), 5.84 (1H, d, J=5.7, 1.3 Hz), 5.83 (1H, dd, J=5.7, 2.0 Hz).

To a cold (0°C) solution of the alcohol (304 mg, 0.83 mmol) in acetone (8.0 ml) was added dropwise the Jones reagent (about 0.3 ml) until the color of the reagent remained and then 2-propanol was added. After being stirred for 10 min, the mixture was diluted with Et_2O, washed with H_2O and saturated aqueous NaCl, dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (eluted with hexane - Et_2O = 5 : 1) to give enone (+)-**8** (279 mg, 92 % yield) as a colorless crystal: m.p. 50 - 51°C; $[\alpha]_D^{26}$ +23.2° (*c* 2.65, $CHCl_3$); EIMS m/z (relative intensity) 366(M^+, 7), 321(24), 304(15), 141(100); Anal. Calcd for $C_{23}H_{42}O_3$: C, 75.35; H, 11.56. Found: C, 75.24; H, 11.61; IR (KBr) 2916, 2855, 1715, 1088, 1029 cm^{-1}; UV (EtOH) λ_{max} 213 nm (ε 9110); CD (MeOH) λ_{ext} (Δε) 228 (-2.3), 204 (-1.4); ^{1}H-NMR (400MHz, $CDCl_3$) δ 0.88 (3H, t, J=6.6 Hz), 1.26 (28H, br m), 1.65 - 1.85 (2H, m), 2.43 (1H, d, J=18.6 Hz), 2.66 (1H, d, J=18.6 Hz), 3.36 (3H, s), 4.60 (1H, d, J=7.5Hz), 4.66 (1H, d, J=7.5 Hz), 6.19 (1H, d, J=5.7 Hz), 7.47 (1H, d, J=5.7 Hz).

(+)-Untenone A

To a cold (-78°C) solution of lithium diisopropylamide [prepared from diisopropylamine (77.5 μl, 554 μmol) and butyllithium (1.66 M in hexane, 337 μl, 554 μmol)] in THF (2.5 ml) was added dropwise a solution of enone (+)-**8** (100 mg, 260 μmol) in THF (1.0 ml) and HMPA (96 μl, 554 μmol). After the mixture was stirred at -78°C for 30 min, methyl cyanoformate (44 μl, 554 μmol) was added and the system was stirred for 2

h at -42°C. The reaction mixture was poured into ether and saturated NH_4Cl solution. The organic layer was washed with water and saturated NaCl solution, dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (eluted with hexane - acetone - AcOH = 150 : 10 : 1) to give the β-ketoester (60 mg, 54 % yield) as a diasteremeric mixture (3 : 2). The mixture was used for subsequent reaction without separation.

The above β-ketoester (60 mg, 140 μmol) was treated with AcOH-c.HCl (50:1) (1.0 ml) and stirred at room temperature for 10 min. The reaction mixture was diluted with ether, washed with saturated $NaHCO_3$ solution, water and saturated NaCl solution, dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The residue was chromatographed on silica gel column (eluted with $CHCl_3$ - AcOEt = 20 : 1) and recrystallized from hexane to give (+)-untenone A (28 mg, 55 % yield) as a colorless crystal: m.p. 77 - 78°C; $[\alpha]_D^{26}$ +36.7° (*c* 0.43, $CHCl_3$); CD (MeOH) λ_{ext} ($\Delta\varepsilon$) 229 (-6.2), 202 (+4.8).

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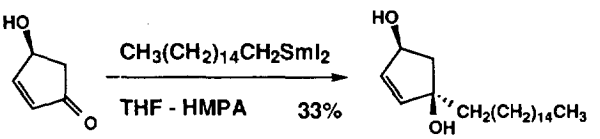

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