Pergamon

Tetrahedron, Vol. 53, No. 18, pp. 6313-6326, 1997

0040-4020/97 $17.00 + 0.00

PII: S0040-4020(97)00315-3

Enantiodivergent Synthesis of a Decalin Type of Chiral Building Blocks and Their Application to Terpenoid Synthesis

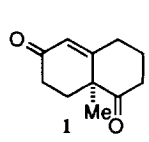
Naoki Toyooka, Akira Nishino, and Takefumi Momose*

Faculty of Pharmaceutical Sciences, Toyama Medical and Pharmaceutical University, Sugitani 2630, Toyama 930-01, Japan

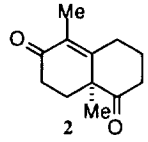
Abstract: An enantiomeric pair of a decalin type of chiral building blocks bearing an oxygenated angular substituent has been synthesized by the lipase-mediated ring differentiation of a *meso* decahydronaphthalene glycol system. Its synthetic utility has been demonstrated by the formal synthesis of (-)-polygodial, (-)-warburganal, (-)-drimenin, and (-)-elemol. © 1997 Elsevier Science Ltd.

A number of sesquiterpenoids having a decalin ring system with an angular methyl or with an oxygenated one are known, and some of them are reported to exhibit remarkable biological activities.[1] Although numerous reports[2] concerning their synthesis or synthetic approach starting with the enantiomeric Wieland-Miescher ketone **1** or its analog **2** have appeared, synthesis of the chiral building block for sesquiterpenoids having an oxygenated angular methyl has been reported only to a small extent.[3] A chiral decahydronaphthalene bearing an oxygenated angular carbon appendage such as the ester **3**, if readily available, would enable us to elaborate a versatile approach to the terpenoid synthesis. Our recent results[4] concerning the desymmetrization of the *meso* glycol system extending across the bridged bicyclic system prompted us to examine the desymmetrization of a decalin type of substrates as synthetic precursors.

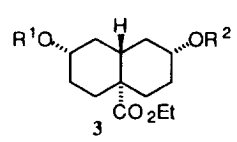
In this paper, we disclose a full detail of the enantiodivergent synthesis of a decalin type of chiral building blocks having an oxygenated angular appendage and their utility for the synthesis of some sesquiterpenoids.



1

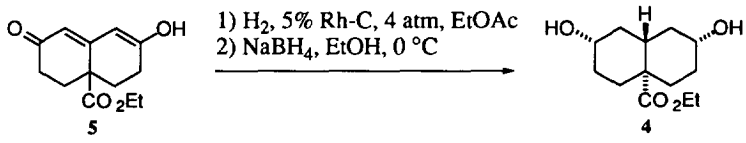


2



3

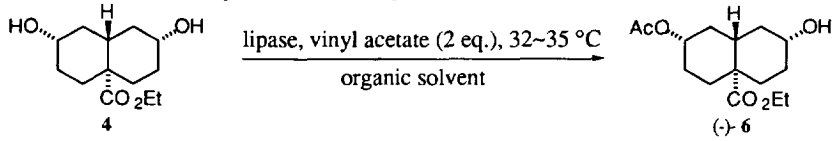
First, we examined the preparation of a substrate for enzymatic desymmetrization. As the starting material for this purpose, we chose a *meso* glycol (**4**) which was readily prepared from the ketone **5**[5] by a two-step sequence as shown below.



5 4

With the desired glycol **4** in hand, we next investigated its lipase-mediated ring differentiation. Of the lipase preparations used in this differentiation, the best result was obtained with an immobilized preparation of lipase[6] AK in *i*-Pr_2O to result in formation of an enantio-pure mono-acetate [(-)-**6**] in 96% isolated yield (Table 1).

Table 1 Lipase-mediated ring differentiation of the *meso* glycol **4**



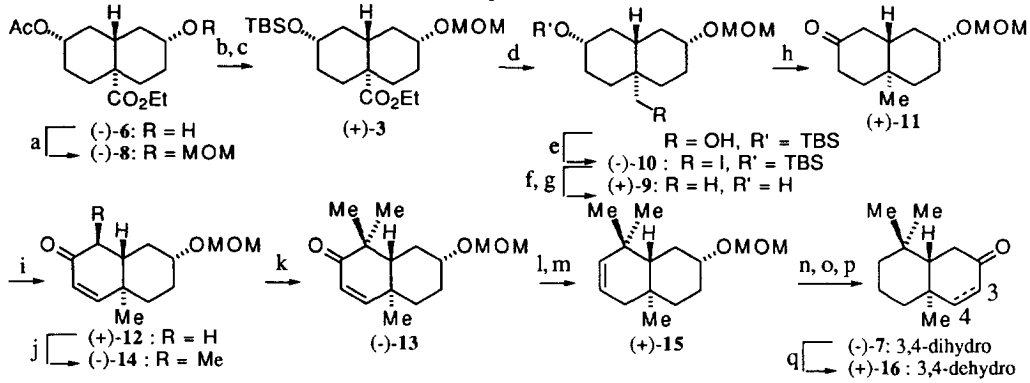
4 (-)-6

Lipase[a]	Solvent	Time (h)	Yield (%)[b]	Optical rotation ($[\alpha]^{26}_D$)[c]	Optical yield (% ee)
AK[d]	*i*-Pr_2O	12	96 (99)	-21.4	>99[e]
AK[d]	C_6H_6	12	39 (99)	-21.4	>99[f]
AK[d]	hexane	24	19 (99)	-21.2	99[f]
AK	*i*-Pr_2O	24	89 (99)	-21.2	99[f]
PS	*i*-Pr_2O	24	23 (99)	-20.9	98[f]
CCL	*i*-Pr_2O	24	10 (95)	-20.0	94[f]
CE	*i*-Pr_2O	24	6 (95)	-18.2	86[f]
AY	*i*-Pr_2O	24	17 (94)	-17.2	81[f]

a: Lipase AK (from *Pseudomonas fluorescens*), PS (from *Pseudomonas cepacia*), CE (from *Humicola lanuginosa*), and AY (from *Candida rugosa*) were supplied by Amano Pharmaceutical Co., Ltd. Lipase CCL (from *Candida cylindracea*) was purchased from the Sigma Chemical Co., Ltd. b: Yields in the isolated mono-acetate. Yields in parentheses are those based on the conversion rate. c: Optical rotations were determined in $CHCl_3$. d: Lipase immobilized on celite[6] was used. e: Determined after benzoylation of the mono-acetate by HPLC analysis using a column packed with CHIRALCEL AD (*i*-PrOH:hexane=1:30). f: Determined based on the value of the optical rotation.

To verify the absolute stereochemistry of (-)-**6**, we examined its conversion into a known decalone [(-)-**7**], a key intermediate for the chiral synthesis of (-)-polygodial and (-)-warburganal.[7] Protection of the hydroxyl in (-)-**6** with methoxymethyl (MOM) gave the ether (-)-**8** (96% yield), which was converted into the silyl ether (+)-**3** (**3**: R^1 = TBS, R^2 = MOM) through basic hydrolysis of (-)-**8** followed by protection of the resulting alcohol with *t*-butyldimethylsilyl (TBS) in 96% overall yield. The silyl ether (+)-**3** was transformed into the alcohol (+)-**9** in four steps. Thus, reduction of the ester group in (+)-**3** with $LiAlH_4$ (95%) followed by treatment of the resulting alcohol with I_2 and Ph_3P in boiling benzene provided the iodide (-)-**10** in 96% yield. Reduction of (-)-**10** with Zn in acetic acid and removal of the silyl protecting group with tetrabutylammonium fluoride (TBAF) afforded the alcohol (+)-**9** in 87% yield in two steps. Oxidation of (+)-**9** with pyridinium chlorochromate (PCC) gave the ketone (+)-**11** (92% yield), which was transformed into the enone (+)-**12** (76% yield) by using the Ito-Saegusa protocol.[8] Alkylation of (+)-**12** with MeI afforded (-)-**13** (53% yield in two steps *via* (-)-**14**, a single product, tentatively of 1β-methyl), which was converted to the octalin (+)-**15** (80% overall yield) by hydrogenation over Rh-C and subsequent Shapiro reaction of the resulting ketone. The octalin (+)-**15** was

converted into the decalone (-)-**7** in 90% overall yield in a three-step sequence. The spectral data for the synthetic (-)-**7** were in good accordance with those reported.[7]

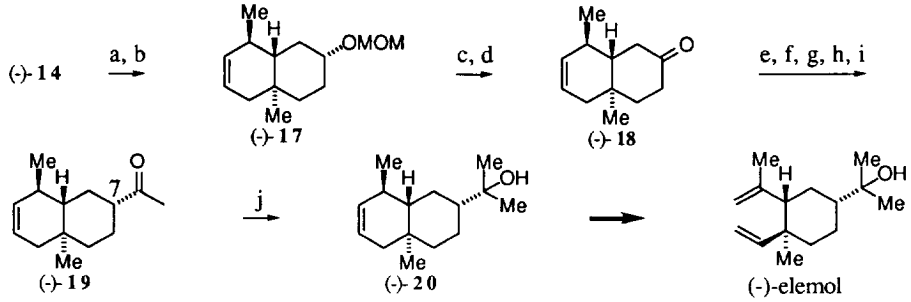


Scheme 1: *Reagents and conditions*: a: MOMCl, Hünig base (96%); b: K_2CO_3; c: TBSCl, DMAP, Et_3N (96% in 2 steps); d: $LiAlH_4$ (95%); e: I_2, Ph_3P, imidazole (96%); f: Zn, AcOH; g: TBAF (87% in 2 steps); h: PCC (92%); i: LDA, TMSCl then $Pd(OAc)_2$ (76%); j: LDA, MeI (86%); k: LDA, MeI (62%); l: H_2, 5% Rh-C (98%); m: $TsNHNH_2$, BF_3•Et_2O then MeLi (82%); n: H_2, 5% Pd-C; o: HCl, MeOH; p: PCC (90% in 3 steps); q: LDA, TMSCl then $Pd(OAc)_2$ (75%)

The Ito-Saegusa oxidation reaction[8] of the decalone (-)-**7** gave the octalone (+)-**16** (75% yield) a key intermediate for the chiral synthesis of (-)-drimenin.[9] The spectral data for the synthetic (+)-**16** were in good agreement with those reported.[9]

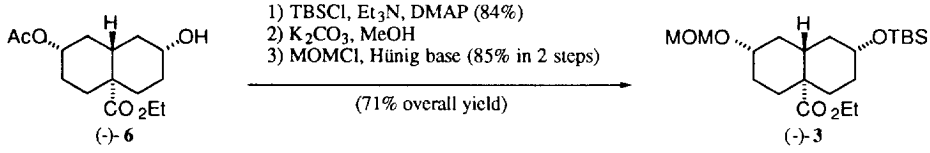
As another application of (+)-**3** to the sesquiterpenoid synthesis, we investigated the chiral synthesis of (-)-elemol,[10] a monocyclic sesquiterpene isolated from Manila *Elemi* oil and Java *Citronella* oil.

The ketone (-)-**14** was converted into the olefin (-)-**17** (86% overall yield) by hydrogenation and subsequent Shapiro reaction. Removal of the MOM protecting group in (-)-**17** with conc. HCl in MeOH followed by oxidation of the resulting alcohol with PCC gave the ketone (-)-**18** in 90% yield. The Wittig reaction of (-)-**18** afforded an enol ether as a mixture of the *E*- and *Z*-isomers in 75% combined yield. Hydrolysis of the enol ether with conc. HCl in MeOH gave a homologated aldehyde, which was alkylated by the Grignard reaction, and oxidation of the resulting alcohol with PCC gave a ketone as a 4:1 mixture of epimers at C-7. This mixture was epimerized into the more stable ketone (-)-**19** with K_2CO_3 in MeOH at room temperature. Finally, the Grignard reaction of (-)-**19** afforded the desired alcohol (-)-**20** in 75% yield. The synthetic alcohol (-)-**20** possessed the spectral properties (^1H, NMR, IR and mass) identical with those reported.[11] Transformation of (-)-**20** into elemol has already been reported.[11] Consequently, the present synthesis of (-)-**20** constitutes a chiral synthesis of (-)-elemol in a formal sense.



Scheme 2: *Reagents and conditions*: a: H_2, 5% Rh-C; b: $TsNHNH_2$, BF_3•Et_2O then MeLi (86% in 2 steps); c: c. HCl, MeOH; d: PCC (90% in 2 steps); e: $MeOCH_2P^+Ph_3Cl^-$, *n*-BuLi (75%); f: c. HCl. MeOH; g: MeMgBr; h: PCC (60% in 3 steps); i: K_2CO_3, MeOH (88%); j: MeMgBr (75%)

The enantiomer (-)-**3** was readily obtained in three steps from (-)-**6** in 71% overall yield.



In conclusion, we have performed the enantiodivergent synthesis of a decalin type of chiral building blocks (**3**) bearing an oxygenated angular carbon, less accessible so far but highly versatile building blocks, by lipase-mediated ring differentiation of the *meso* glycol **4**. The utility of this interesting molecule for the terpenoid synthesis has been demonstrated by its conversion into the decalone (-)-**7**, octalone (+)-**16**, and alcohol (-)-**20**, the intermediates for the chiral synthesis of (-)-polygodial, (-)-warburganal, and (-)-drimenin, and (-)-elemol, respectively. Further studies toward the chiral synthesis of more complex terpenoids bearing an oxygenated angular appendage, such as ajugarins, are under way in our laboratories, and the results will be described in due course.

Experimental

All melting points were determined on a Yanagimoto micro melting point apparatus and are uncorrected. Infrared spectra (IR) were recorded on a Perkin-Elmer 1600 series FT-IR spectrophotometer. ^1H and ^{13}C NMR spectra were taken on a JEOL JNM-GX 270 spectrometer at 270 and 67.9 MHz, respectively, with tetramethylsilane as an internal standard in $CDCl_3$ solution unless otherwise stated, and resonance patterns in ^1H NMR signals are shown as s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, and br = broad. Multiplicity of the ^{13}C NMR data was determined by distorsionless enhancement by a polarization transfer (DEPT) method (u = methyl or methine, d = methylene, s = quaternary carbons). EI-MS were obtained on a JEOL JMS D-200 mass spectrometer operating at 70eV. Elemental analyses were performed by the micro analytical laboratory of this University. Specific rotation was determined on a JASCO DIP-400 digital polarimeter. The solvents tetrahydrofuran and ether were distilled over metallic potassium or sodium.

Unless otherwise specified, all reactions were carried out in an oven-dried glassware under an atmosphere of argon. Column chromatography was performed on a silica gel [Fuji-Davison BW-200, Merck 60 (No 9385)].

Ethyl 2,7-Dihydroxydecahydronaphthalene-4a-carboxylate (4): To a solution of **5**[4] (3.0 g, 12.7 mmol) in EtOAc (50 mL) was added 5% Rh-C (100 mg), and the resulting suspension was hydrogenated at 4.5 atm for 10 h. The catalyst was removed by filtration through a celite pad, and the filtrate was evaporated to give a pale yellow oil, which was chromatographed on SiO_2 (30 g, hexane:acetone=30:1-10:1) to afford ethyl 2-hydroxy-7-oxodecahydronaphthalene-4a-carboxylate (1.56 g, 51%) as a colorless oil.

IR (neat): 3422, 2934, 2865, 1717, 1199, 1139 cm^{-1}; ^1H NMR δ 1.23-1.32 (5H, m, including δ 1.30, 3H, t, J = 7.1 Hz), 1.51-1.63 (1H, m), 1.65-1.79 (2H, m), 1.81-2.01 (2H, m), 2.17-2.40 (5H, m), 2.51 (1H, br), 3.03 (1H, t, J = 14.5 Hz), 3.60-3.71 (1H, m), 4.24 (2H, q, J = 7.1 Hz).

To a stirred solution of the keto alcohol obtained above (3.74 g, 15.6 mmol) in MeOH (30 mL) was added $NaBH_4$ (592 mg, 15.6 mmol) at 0 ℃, and the resulting solution was stirred at 0 ℃ for 0.5 h. The reaction was quenched with 10% aqueous acetic acid, and the solvent was removed. The residue was extracted with hot $CHCl_3$ (20 mL x 10), and the combined $CHCl_3$ layer was dried over $MgSO_4$ and evaporated to give a pale yellow solid, which was recrystallized from benzene:EtOH = 3:1 to afford **4** (3.12 g, 83%) as a colorless solid (mp 186~187 ℃).

IR (KBr): 3301, 3036, 2988, 2937, 2863, 1729, 1136, 1028 cm^{-1}; ^1H NMR δ 1.10-1.37 (8H, br m, including δ 1.27, 3H, t, J = 7.0 Hz), 1.70-1.80 (2H, m), 1.88-2.02 (4H, m), 2.11-2.18 (2H, m), 3.56-3.69 (2H, m), 4.17 (2H, q, J = 7.0 Hz); ^{13}C NMR (CD_3OD) δ 14.17 (u), 32.60 (d), 35.30 (d), 38.36 (d), 40.47 (u), 46.37 (s), 59.34 (d), 68.92 (u), 174.18 (s); HRMS Calcd. for $C_{13}H_{22}O_4$ 242.1517, Found 242.1484; *Anal.* Calcd. for $C_{13}H_{22}O_4$ C, 64.44; H, 9.15, Found C, 64.51; H, 8.91.

General procedure for lipase-mediated transesterification of *meso* glycol 4: Ethyl (2*S*,4a*R*,7*R*,8a*S*)-(-)-2-Acetoxy-7-hydroxydecahydronaphthalene-4a-carboxylate [(-)-6]: To a stirred suspension of **4** (121 mg, 0.5 mmol) and vinyl acetate (0.18 mL, 2.0 mmol) in the solvent (10 mL, see Table 1) was added a preparation of lipase AK (50 mg) immobilized on celite[6] (200 mg) or a lipase preparation (50 mg, see Table 1), and the resulting suspension was stirred at 32~35 ℃ for 12~24 h. After removal of enzyme by filtration through a celite pad, the filtrate was evaporated to give an oily residue, which was fractionated by column chromatography on SiO_2 (5 g) to afford the oily mono-acetate (-)-**6** in 96~6% yield along with the recovered starting glycol. The optical yield of (-)-**6** was determined, after benzoylation of the mono-acetate in a usual manner, by HPLC analysis using a column packed with CHIRALCEL AD (Daicel Chemical Co., Ltd., i-PrOH:hexane=1:30).

IR (neat): 3420, 2938, 2866, 1732, 1247, 1029 cm^{-1}; ^1H NMR δ 1.10-1.40 (7H, br m, including δ 1.28, 3H, t, J = 7.2 Hz), 1.65-2.20 (10H, m), 2.02 (3H, s), 3.64 (1H, br m), 4.17 (2H, q, J = 7.1 Hz), 4.72 (1H, br m); ^{13}C NMR δ 14.17 (u), 21.22 (u), 28.61 (d), 32.47 (d), 34.06 (d), 35.17 (d), 35.40 (d), 38.07 (d), 40.86 (u), 46.46 (s), 60.04 (d), 70.35 (u), 72.67 (u), 170.63 (s), 174.39 (s); HRMS Calcd. for $C_{15}H_{24}O_5$ 284.1624, Found 284.1656; *Anal.* Calcd. for $C_{15}H_{24}O_5$ C, 63.36; H, 8.51, Found C, 63.50; H, 8.44.

Ethyl (2*S*,4a*R*,7*R*,8a*S*)-(-)-2-Acetoxy-7-(methoxymethoxy)decahydronaphthalene-4a-carboxylate [(-)-8]: To a stirred solution of (-)-**6** (517 mg, 1.82 mmol) in CH_2Cl_2 (14 mL) were added MOMCl (0.27 mL, 3.64 mmol) and (*i*-Pr)$_2$EtN (Hünig base) (0.68 mL, 4.00 mmol) at 0 ℃, and the resulting

mixture was stirred at room temperature for 18 h. The reaction was quenched with H_2O (10 mL), and the organic layer was separated. The aqueous layer was extracted with CH_2Cl_2 (20 mL x 2), and the organic layer and extracts were combined, dried over $MgSO_4$, and evaporated to give a pale yellow oil, which was chromatographed on SiO_2 (20 g, hexane:acetone=25:1) to afford (-)-**8** (570 mg, 96%) as a colorless oil.

IR (neat): 2938, 1732, 1247, 1043 cm^{-1}; ^1H NMR δ 1.10-1.41 (8H, br m, including δ 1.27, 3H, t, J = 7.1 Hz), 1.71-2.20 (11H, br m, including δ 2.01, 3H, s), 3.35 (3H, s), 3.54 (1H, tt, J = 10.7, 5.1 Hz), 4.17 (2H, q, J = 7.1 Hz), 4.61-4.80 (3H, m, including δ 4.66, 2H, s); ^{13}C NMR δ 14.19 (u), 21.24 (u), 28.58 (d), 29.86 (d), 34.12 (d), 35.30 (d), 35.48 (d), 40.90 (u), 46.62 (s), 55.06 (u), 60.01 (d), 72.65 (u), 75.40 (u), 94.57 (d), 170.52 (s), 174.29 (s); HRMS Calcd. for $C_{17}H_{28}O_6$ 328.1886, Found 328.1918; *Anal.* Calcd. for $C_{17}H_{28}O_6$ C, 62.17; H, 8.59, Found C, 62.31; H, 8.57; $[\alpha]^{26}_D$ -5.0 (*c* 1.06, $CHCl_3$).

Ethyl (2*S*,4a*R*,7*R*,8a*S*)-(+)-2-[(1,1-Dimethylethyl)dimethylsiloxy]-7-(methoxymethoxy)-decahydronaphthalene-4a-carboxylate [(+)-3]: To a stirred solution of (-)-**8** (526 mg, 1.61 mmol) in MeOH (9 mL) was added K_2CO_3 (111 mg, 1.61 mmol) at 0 ℃, and the resulting suspension was stirred at room temperature for 1.5 h. The reaction was quenched with 10% AcOH, and the volatiles were removed. The residue was extracted with hot $CHCl_3$ (10 mL x 5), and the combined $CHCl_3$ layer was dried over $MgSO_4$ and evaporated to give a colorless oil, which was used directly in the next step. To a stirred solution of the oil obtained above in CH_2Cl_2 (15 mL) were added TBSCl (481 mg, 3.22 mmol), Et_3N (0.73 mL, 5.31 mmol) and *N*,*N*-dimethylaminopyridine (DMAP) (25 mg, 0.21 mmol) at 0 ℃, and the reaction mixture was stirred at room temperature for 17 h. The reaction was quenched with H_2O (10 mL), and the organic layer was separated. The aqueous layer was extracted with CH_2Cl_2 (20 mL x 2), and the organic layer and extracts were combined, dried over $MgSO_4$, and evaporated to give a pale yellow oil, which was chromatographed on SiO_2 (20 g, hexane:acetone=50:1) to afford (+)-**3** (613 mg, 96% in 2 steps) as a colorless oil.

IR (neat): 2931, 1729, 1198, 1137, 1100, 1043 cm^{-1}; ^1H NMR δ 0.03 (6H, s), 0.86 (9H, s), 1.05-1.29 (8H, br m, including δ 1.25, 3H, t, J = 7.1 Hz), 1.62-2.18 (8H, br m), 3.35 (3H, s), 3.45-3.65 (2H, br m), 4.14 (2H, q, J = 7.1 Hz), 4.64 & 4.67 (2H, ABq, J = 6.8 Hz); ^{13}C NMR δ -4.65 & -4.60 (each u), 14.22 (u), 18.10 (s), 25.83 (u), 29.92 (d), 33.07 (d), 35.50 (d), 35.79 (d), 35.85 (d), 38.84 (d), 41.24 (u), 46.71 (s), 55.09 (u), 59.90 (d), 71.49 (u), 75.76 (u), 94.58 (d), 174.49 (s); HRMS Calcd. for $C_{21}H_{40}O_5Si$ 400.2645, Found 400.2657; *Anal.* Calcd. for $C_{21}H_{40}O_5Si$ C, 62.96; H, 10.06, Found C, 62.95; H, 10.16; $[\alpha]^{26}_D$ +1.2 (*c* 1.19, $CHCl_3$).

(2*S*,4a*S*,7*R*,8a*S*)-(+)-2-[(1,1-Dimethylethyl)dimethylsiloxy]-4a-(hydroxymethyl)-7-(methoxymethoxy)decahydronaphthalene: To a stirred solution of (+)-**3** (350 mg, 0.88 mmol) in Et_2O (15 mL) was added $LiAlH_4$ (33 mg, 1.76 mmol), and the resulting suspension was refluxed for 15 h. After cooling, the reaction was quenched with 10% aqueous NaOH, and the mixture was filtered through a celite pad, and the filtrate was evaporated. The residue was extracted with $CHCl_3$ (10 mL x 5), and combined $CHCl_3$ layer was dried over $MgSO_4$ and evaporated to give a colorless oil, which was chromatographed on SiO_2 (10 g, hexane:acetone=10:1) to afford the alcohol (298 mg, 95%) as a colorless viscous oil.

IR (neat): 3446, 2933, 2856, 1098, 1040 cm^{-1}; ^1H NMR δ 0.02 (6H, s), 0.73-0.90 (11H, m, including δ 0.85, 9H, s), 1.25-1.98 (12H, br m), 3.34 (3H, s), 3.45-3.68 (2H, br m), 3.72 & 3.78 (2H, ABq, J = 11.2 Hz), 4.65 (2H, s); ^{13}C NMR δ -4.64 (u), 18.15 (s), 25.86 (u), 28.16 (d), 31.31 (d), 32.47 (d), 32.55 (d), 34.64 (d), 36.44 (s), 37.92 (d), 41.11 (u), 55.20 (u), 58.20 (d), 71.76 (u), 76.06 (u), 94.61 (d); HRMS Calcd. for

$C_{19}H_{38}O_4Si$ 358.2538, Found 358.2513; *Anal.* Calcd. for $C_{19}H_{38}O_4Si$ C, 63.64; H, 10.68, Found C, 63.46; H, 10.86; $[\alpha]^{26}_D$ +1.9 (*c* 1.16, $CHCl_3$).

(2*S*,4a*S*,7*R*,8a*S*)-(-)-2-[(1,1-Dimethylethyl)dimethylsiloxy]-4a-(iodomethyl)-7-(methoxymethoxy)decahydronaphthalene [(-)-10]: To a stirred solution of the alcohol obtained above (2.55 g, 7.12 mmol) in benzene (100 mL) were added imidazole (1.21 g, 17.8 mmol), Ph_3P (4.67 g, 17.8 mmol) and I_2 (3.61 g, 26.34 mmol), and the mixture was refluxed for 3 h. After cooling, the reaction was quenched with 10% aqueous $Na_2S_2O_3$ in satd. $NaHCO_3$ (30 mL), and the organic layer was separated. The aqueous layer was extracted with benzene (20 mL x 2), and the organic layer and extracts were combined, dried over $MgSO_4$, and evaporated to give a colorless oil, which was chromatographed on SiO_2 (100 g, hexane:acetone=40:1) to afford (-)-**10** (3.2 g, 96%) as a colorless oil.

IR (neat): 2931, 1101, 1040, 836 cm^{-1}; ^1H NMR δ 0.05 (6H, s), 0.81-1.02 (11H, m, including δ 0.88, 9H, s), 1.22-1.90 (11H, br m), 3.36 (3H, s), 3.40-3.62 (4H, br m), 4.67 (2H, s); ^{13}C NMR δ -4.65 & -4.68 (each u), 13.36 (d), 18.13 (s), 25.84 (u), 27.63 (d), 30.78 (d), 34.67 (s), 35.19 (d), 36.37 (d), 36.45 (d), 38.41 (d), 38.97 (u), 55.19 (u), 71.33 (u), 75.65 (u), 94.71 (d); HRMS Calcd. for $C_{19}H_{37}IO_3Si$ 468.1559, Found 468.1577; *Anal.* Calcd. for $C_{19}H_{37}IO_3Si$ C, 48.71; H, 7.96, Found C, 48.99; H, 7.83; $[\alpha]^{26}_D$ -3.9 (*c* 1.22, $CHCl_3$).

(2*S*,4a*S*,7*R*,8a*S*)-(+)-2-[(1,1-Dimethylethyl)dimethylsiloxy]-7-(methoxymethoxy)-4a-methyldecahydronaphthalene: To a stirred solution of (-)-**10** (2.99 g, 6.39 mmol) in AcOH (30 mL) was added zinc powder (17 g), and the resulting suspension was stirred at room temperature for 3 h. The reaction mixture was neutralized with satd. aqueous $NaHCO_3$ and then filtered. The aqueous layer was extracted with CH_2Cl_2 (50 mL x 4), and the combined CH_2Cl_2 layer was dried over $MgSO_4$ and evaporated to give a colorless solid, which was used directly in the next step. An analytical sample was obtained by column chromatography on SiO_2 (10 g, hexane:acetone=50:1) as a colorless solid (mp 38~40 ℃).

IR (KBr): 2931, 1149, 1104, 1043, 836 cm^{-1}; ^1H NMR δ 0.03 (6H, s), 0.87 (12H, s), 0.95-1.85 (13H, br m), 3.35 (3H, s), 3.48 (1H, tt, *J* = 11.2, 4.9 Hz), 3.54 (1H, tt, *J* = 10.5, 5.0 Hz), 4.66 (2H, s); ^{13}C NMR δ -4.64 (u), 15.79 (u), 18.17 (s), 25.89 (u), 28.49 (d), 31.67 (d), 32.52 (s), 35.04 (d), 38.38 (d), 39.15 (d), 39.25 (d), 41.15 (u), 55.06 (u), 72.03 (u), 76.29 (u), 94.57 (d); HRMS Calcd. for $C_{19}H_{38}O_3Si$ 342.2590, Found 342.2623; $[\alpha]^{26}_D$ +3.0 (*c* 1.12, $CHCl_3$).

(2*S*,4a*R*,7*R*,8a*R*)-(+)-2-Hydroxy-7-(methoxymethoxy)-4a-methyldecahydronaphthalene [(+)-9]: To a stirred solution of the silyl ether obtained above in THF (30 mL) was added TBAF (1.0 M in THF, 12.6 mL, 12.8 mmol), and the reaction mixture was stirred at room temperature for 6 h. The reaction was quenched with satd. aqueous NH_4Cl (20 mL), and the aqueous layer was extracted with CH_2Cl_2 (20 mL x 4). The combined CH_2Cl_2 layer was dried over $MgSO_4$ and evaporated to give a colorless oil, which was chromatographed on SiO_2 (60 g, hexane:acetone=10:1) to afford (+)-**9** (1.25 g, 87% in 2 steps) as a colorless oil.

IR (neat): 3396, 2930, 1149, 1106, 1083, 1032 cm^{-1}; ^1H NMR δ 0.88 (3H, s), 1.02-1.70 (11H, br m), 1.72-1.90 (3H, br m), 3.37 (3H, s), 3.45-3.65 (2H, br m), 4.68 (2H, s); ^{13}C NMR δ 15.71 (u), 28.41 (d), 31.16 (u), 32.45 (s), 34.91 (d), 37.82 (d), 38.96 (d), 38.99 (d), 40.98 (u), 55.06 (u), 71.08 (u), 76.15 (u), 94.48 (d); HRMS Calcd. for $C_{13}H_{24}O_3$ 228.1725, Found 228.1748; *Anal.* Calcd. for $C_{13}H_{24}O_3$ C, 68.38; H, 10.59, Found C, 68.34; H, 10.31; $[\alpha]^{26}_D$ +13.2 (*c* 1.09, $CHCl_3$).

(4a*S*,7*R*,8a*S*)-(+)-7-(Methoxymethoxy)-4a-methyldecahydronaphthalen-2-one [(+)-11]: To a stirred solution of (+)-**9** (1.23 g, 5.39 mmol) in CH_2Cl_2 (10 mL) was added PCC (2.33 g, 10.78 mmol), and the resulting suspension was stirred at room temperature for 4 h. The reaction mixture was chromatographed directly on SiO_2 (30 g, hexane:acetone=20:1) to afford (+)-**11** (1.12 g, 92%) as a colorless oil.
IR (neat): 2934, 1712, 1149, 1104, 1041 cm^{-1}; ^1H NMR δ 1.05-1.95 (12H, br m, including δ 1.09, 3H, s), 2.06-2.55 (4H, br m), 3.37 (3H, s), 3.53 (1H, tt, J = 10.9, 5.1 Hz), 4.68 (2H, s); ^{13}C NMR δ 14.87 (u), 28.15 (d), 32.47 (s), 35.04 (d), 37.85 (d), 38.15 (d), 39.88 (d), 42.49 (u), 44.35 (d), 55.06 (u), 75.33 (u), 94.58 (d), 210.78 (s); HRMS Calcd. for $C_{13}H_{22}O_3$ 226.1570, Found 226.1591; *Anal.* Calcd. for $C_{13}H_{22}O_3$ C, 68.99; H, 9.80, Found C, 69.01; H, 9.59; $[\alpha]^{26}_D$ +26.3 (*c* 1.23, $CHCl_3$).

(4a*S*,7*R*,8a*R*)-(+)-7-(Methoxymethoxy)-4a-methyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-2-one [(+)-12]: To a stirred solution of *i*-Pr_2NH (0.21 mL, 1.53 mmol) in THF (2 mL) were added *n*-BuLi (10% solution in hexane, 0.93 mL, 1.48 mmol) and hexamethylphosphoric triamide (HMPA) (0.26 mL, 1.53 mmol) at 0 ℃, and the mixture was stirred at 0 ℃ for 20 min. After cooling at -80 ℃, a solution of trimethylsilyl chloride (TMSCl) (0.38 mL, 3.06 mmol) and (+)-**11** (230 mg, 1.02 mmol) in THF (1 mL) was added to the reaction mixture, and the stirring was continued at -80 ℃ for 20 min. The reaction was quenched with satd. aqueous $NaHCO_3$ (5 mL), and the organic layer was separated. The aqueous layer was extracted with Et_2O (20 mL x 3). The organic layer and extracts were combined, dried over $MgSO_4$, and evaporated to give a pale yellow oil, which was used directly in the next step. To a stirred solution of the ether obtained above in MeCN (10 mL) was added $Pd(OAc)_2$ (229 mg, 1.02 mmol), and the resulting suspension was stirred at room temperature for 16 h. The insoluble material was removed by filtration, and the insoluble material was washed with CH_2Cl_2. The filtrate and washings were combined and evaporated to give a pale yellow oil, which was chromatographed on SiO_2 (22 g, hexane:acetone=30:1) to afford (+)-**12** (172 mg, 76%) along with the isomeric enone (36 mg, 16%) as a colorless oil, respectively.
(+)-**12**; IR (neat): 2938, 1681, 1148, 1107, 1041 cm^{-1}; ^1H NMR δ 1.05-2.02 (10H, br m, including δ 1.10, 3H, s), 2.06-2.55 (4H, br m), 3.38 (3H, s), 3.57 (1H, tt, J = 10.9, 5.3 Hz), 4.73 (2H, s), 5.85 (1H, d, J = 9.8 Hz), 6.78 (1H, d, J = 9.8 Hz); ^{13}C NMR δ 16.23 (u), 28.06 (d), 33.85 (d), 35.46 (s), 35.53 (d), 38.15 (d), 40.18 (u), 55.07 (u), 75.01 (u), 94.64 (d), 126.96 (u), 160.28 (u), 199.26 (s); HRMS Calcd. for $C_{13}H_{20}O_3$ 224.1410, Found 224.1398; *Anal.* Calcd. for $C_{13}H_{20}O_3$ C, 69.61; H, 8.99, Found C, 69.55; H, 9.05; $[\alpha]^{26}_D$ +13.5 (*c* 1.26, $CHCl_3$).
isomeric enone; IR (neat): 2940, 1676, 1619, 1149, 1105, 1044 cm^{-1}; ^1H NMR δ 1.27 (3H, s), 1.34-1.45 (1H, br m), 1.65-1.88 (4H, br m), 1.96-2.06 (1H, m), 2.30-2.65 (4H, br m), 3.39 (3H, s), 3.57 (1H, tt, J = 10.9, 4.9 Hz), 4.70 & 4.71 (2H, ABq, J = 7.1 Hz), 5.77 (1H, br s); ^{13}C NMR δ 21.81 (u), 28.35 (d), 33.73 (d), 35.07 (s), 37.25 (d), 38.30 (d), 39.38 (d), 55.17 (u), 75.72 (u), 94.85 (d), 125.58 (u), 166.75 (s), 198.98 (s); HRMS Calcd. for $C_{13}H_{20}O_3$ 224.1410, Found 224.1385; *Anal.* Calcd. for $C_{13}H_{20}O_3$ C, 69.61; H, 8.99, Found C, 69.69; H, 9.09; $[\alpha]^{26}_D$ +126.6 (*c* 0.77, $CHCl_3$).

(4a*S*,7*R*,8a*R*)-(-)-7-(Methoxymethoxy)-1,4a-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-2-one [(-)-14]: To a stirred solution of *i*-Pr_2NH (0.83 mL, 6.03 mmol) in THF (8 mL) were added *n*-BuLi (10% solution in hexane, 3.73 mL, 5.83 mmol) and HMPA (1.06 mL, 6.03 mmol) at 0 ℃, and the mixture was stirred at 0 ℃ for 20 min. After cooling at -80 ℃, a solution of (+)-**12** (900 mg, 4.02 mmol) in THF (4 mL) was added to the reaction mixture, and the stirring was continued at -80 ℃ for 30 min. To the

mixture was added MeI (0.75 mL, 12.06 mmol), and the reaction temperature was gradually raised to 0 ℃ for 2 h. The reaction was quenched with satd. aqueous NH_4Cl (30 mL). The organic layer was separated, and the aqueous layer was extracted with Et_2O (20 mL x 3). The organic layer and extracts were combined, dried over $MgSO_4$, and evaporated to give a pale yellow oil, which was chromatographed on SiO_2 (100 g, hexane:acetone=40:1) to afford (-)-**14** (525 mg, 55%, 86% conversion yield) as a colorless solid (mp 35~36 ℃) and the starting material (+)-**12** (331 mg, 37% recovered) as a colorless oil.

IR (KBr): 2940, 1676, 1106, 1039 cm^{-1}; ^1H NMR δ 1.12 (3H, s), 1.13 (3H, d, J = 6.4 Hz), 1.27-1.48 (2H, m), 1.56-1.66 (3H, m), 1.96-2.06 (2H, m), 2.29 (1H, dt, J = 12.8, 6.7 Hz), 3.39 (3H, s), 3.54 (1H, tt, J = 10.9, 4.9 Hz), 4.71 (2H, s), 5.85 (1H, d, J = 9.8 Hz), 6.72 (1H, d, J = 9.8 Hz); ^{13}C NMR δ 11.66 (u), 17.05 (u), 27.79 (d), 31.10 (d), 35.82 (s), 36.02 (d), 42.19 (u), 46.22 (u), 55.12 (u), 75.50 (u), 94.65 (d), 126.33 (u), 159.33 (u), 201.32 (s); HRMS Calcd. for $C_{14}H_{22}O_3$ 238.1567, Found 238.1532; *Anal.* Calcd. for $C_{14}H_{22}O_3$ C, 70.55; H, 9.31, Found C, 70.42; H, 9.43; $[\alpha]^{26}_D$ -26.9 (*c* 1.02, $CHCl_3$).

(4a*S*,7*R*,8a*R*)-(-)-7-(Methoxymethoxy)-1,1,4a-trimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-2-one [(-)-13]: According to the above procedure, (-)-**13** (130 mg, 42%, 62% conversion yield) was obtained from (-)-**14** (292 mg, 1.22 mmol) as a colorless oil, and the starting material (92 mg, 32%) was recovered.

IR (neat): 2943, 1708, 1241, 1145, 1107 cm^{-1}; ^1H NMR δ 1.05 (3H, s), 1.15 (3H, s), 1.19 (3H, s), 1.34-1.70 (5H, br m), 1.88-2.02 (2H, m), 3.40 (3H, s), 3.57 (1H, tt, J = 10.8, 4.9 Hz), 4.72 (2H, s), 5.86 (1H, d, J = 10.0 Hz), 6.74 (1H, d, J = 10.0 Hz); ^{13}C NMR δ 20.27 (u), 21.16 (u), 26.32 (u), 28.10 (d), 28.58 (d), 35.76 (s), 38.54 (d), 44.29 (s), 48.16 (d), 55.22 (u), 76.18 (u), 94.74 (d), 125.52 (u), 159.10 (u), 204.54 (s); HRMS Calcd. for $C_{15}H_{24}O_3$ 252.1725, Found 252.1710; *Anal.* Calcd. for $C_{15}H_{24}O_3$ C, 71.39; H, 9.59, Found C, 71.30; H, 9.48; $[\alpha]^{26}_D$ -0.7 (*c* 0.68, $CHCl_3$).

(4a*S*,7*R*,8a*R*)-(-)-7-(Methoxymethoxy)-1,1,4a-trimethyldecahydronaphthalen-2-one: To a solution of (-)-**13** (114 mg, 0.45 mmol) in EtOAc (10 mL) was added 5% Rh-C (50 mg), and the resulting suspension was hydrogenated at 4.5 atm for 8 h. The catalyst was removed by filtration through celite pad, and the catalyst was washed with CH_2Cl_2. The filtrate and washings were combined and evaporated to give the essentially pure ketone (112 mg, 98%) as a colorless oil , which was used directly in the next step. An analytical sample was obtained by column chromatography on SiO_2 as a colorless solid (mp 70~71 ℃).

IR (KBr): 2942, 1705, 1147, 1105, 1043 cm^{-1}; ^1H NMR δ 0.95-1.95 (18H, br m, including δ 1.03, 1.08, and 1.15, each 3H, each s), 2.32 (1H, ddd, J = 15.9, 5.0, 2.9 Hz), 2.71 (1H, ddd, J = 15.9, 13.8, 5.5 Hz), 3.39 (3H, s), 3.53 (1H, tt, J = 10.6, 4.7 Hz), 4.71 (2H, s); ^{13}C NMR δ 18.14 (u), 21.19 (u), 25.15 (u), 28.07 (d), 29.26 (d), 33.20 (s), 34.57 (d), 39.52 (d), 41.42 (d), 47.38 (s), 50.82 (u), 55.07 (u), 76.44 (u), 94.57 (d), 215.97 (s); HRMS Calcd. for $C_{15}H_{26}O_3$ 254.1880, Found 254.1843; *Anal.* Calcd. for $C_{15}H_{26}O_3$ C, 70.83; H, 10.03, Found C, 70.76; H, 10.22; $[\alpha]^{26}_D$ -28.2 (*c* 0.89, $CHCl_3$).

(4a*S*,7*R*,8a*R*)-(+)-7-(Methoxymethoxy)-1,1,4a-trimethyl-1,4,4a,5,6,7,8,8a-octahydronaphthalene [(+)-15]: To a stirred solution of the ketone obtained above (98 mg, 0.39 mmol) in benzene (1 mL) were added $TsNHNH_2$ (89 mg, 0.48 mmol) and one drop (catalytic amounts) of BF_3•Et_2O, and the resulting suspension was stirred at room temperature for 1 h. The reaction was quenched with satd. aqueous $NaHCO_3$ (1 mL), and the organic layer was separated. The aqueous layer was extracted with CH_2Cl_2 (10 mL x 2), and the organic extracts were combined, dried over $MgSO_4$, and evaporated to give a crude

tosylhydrazone. To a stirred solution of crude tosylhydrazone obtained above in THF (5 mL) was added MeLi (2.04 mL, 2.32 mmol, 1.14 mol/l in Et_2O) at 0 ℃, and the resulting mixture was stirred at room temperature for 2 h. The reaction was quenched with careful addition of satd. NaCl (5 mL), and the aqueous layer was extracted with Et_2O (10 mL x 3). The combined Et_2O layer was dried over $MgSO_4$ and evaporated to give an olefin, which was chromatographed on SiO_2 (5 g, hexane:acetone=50:1) to afford (+)-**15** (76 mg, 82%) as a colorless oil.

IR (neat): 3010, 2937, 1654, 1149, 1107, 1044 cm^{-1}; ^1H NMR δ 0.87 (3H, s), 0.95 (6H, br s), 1.38 (1H, td, J = 14.0, 3.5 Hz), 1.24-1.34 (2H, m), 1.27-1.57 (2H, br m), 1.75 (2H, br), 1.89 (2H, br m), 3.39 (3H, s), 3.47-3.57 (1H, m), 4.72 (2H, s); ^{13}C NMR δ 19.23 (u), 22.73 (u), 28.82 (d), 29.70 (d), 31.34 (u), 32.35 (s), 34.61 (s), 41.02 (d), 41.15 (d), 47.80 (u), 55.16 (u), 77.12 (u), 94.54 (d), 121.55 (s), 137.92 (s); HRMS Calcd. for $C_{15}H_{26}O_2$ 238.1931, Found 238.1919; *Anal.* Calcd. for $C_{15}H_{26}O_2$ C, 75.58; H, 11.00, Found C, 75.62; H, 10.98; $[\alpha]^{26}_D$ +42.1 (*c* 1.63, $CHCl_3$).

(4a*R*,8a*S*)-(-)-4a,8,8-Trimethyldecahydronaphthalen-2-one [(-)-7]: To a solution of (+)-**15** (62 mg, 0.26 mmol) in MeOH (6 mL) was hydrogenated over 5% Pd-C at 4 atm for 13 h. The catalyst was removed by filtration through a celite pad, and the filtrate was evaporated to give a crude decalin. To a stirred solution of the crude decalin obtained above in MeOH (1 mL) was added conc. HCl (1 drop), and the resulting mixture was refluxed for 1 h. After cooling, the reaction was quenched with satd. aqueous $NaHCO_3$, and the volatiles were removed. The residue was extracted with hot $CHCl_3$ (3 mL x 5), and combined $CHCl_3$ layer was dried over $MgSO_4$ and evaporated to give a colorless oil, which was used directly in the next step. To a stirred solution of the oil obtained above in CH_2Cl_2 (1 mL) was added PCC (84 mg, 0.39 mmol), and the resulting suspension was stirred at room temperature for 17 h. The reaction mixture was chromatographed directly on SiO_2 (5 g, hexane:acetone=50:1) to afford (-)-7 (46 mg, 90% in 3 steps) as a colorless solid (mp 30~32 ℃, lit.[5] 39 ℃).

IR (neat): 2925, 1712, 1456, 1418, 1387, 1367, 1292, 1263, 1245, 1204, 1189, 1158, 1124 cm^{-1}; ^1H NMR δ 0.78-1.95 (18H, br m, including δ 0.84, 3H, s, δ 1.12, 6H, s), 2.14-2.52 (4H, br m); ^{13}C NMR δ 18.26 (u), 18.66 (d), 20.53 (u), 32.31 (u), 33.37 (s), 33.60 (s), 38.15 (d), 38.96 (d), 40.83 (d), 41.58 (d), 43.86 (d), 52.38 (u), 212.63 (s); HRMS Calcd. for $C_{13}H_{22}O$ 194.1671, Found 194.1688; *Anal.* Calcd. for $C_{13}H_{22}O$ C, 80.35; H, 11.41, Found C, 80.50; H, 11.29; $[\alpha]^{26}_D$ -13.8 (*c* 1.49, $CHCl_3$), lit.[5] $[\alpha]_D$ -12.8 (*c* 1.0, $CHCl_3$).

(4a*S*,8a*S*)-(+)-4a,8,8-Trimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-2-one [(+)-16]: To a stirred solution of *i*-Pr_2NH (88 μL, 0.63 mmol) in THF (1 mL) were added *n*-BuLi (10% solution in hexane, 0.39 mL, 0.61 mmol) and HMPA (0.11 mL, 0.63 mmol) at 0 ℃, and the mixture was stirred at 0 ℃ for 20 min. After cooling at -80 ℃, a solution of Me_3SiCl (0.16 mL, 1.26 mmol) and (-)-**7** (81 mg, 0.42 mmol) in THF (1 mL) was added to the reaction mixture, and the stirring was continued at -80 ℃ for 15 min. The reaction was quenched with satd. aqueous $NaHCO_3$ (3 mL), and the organic layer was separated, the aqueous layer was extracted with Et_2O (10 mL x 3). The organic layer and extracts were combined, dried over $MgSO_4$, and evaporated to give a colorless oil, which was used directly in the next step. To a stirred solution of the silyl enol ether obtained above in MeCN (2 mL) was added $Pd(OAc)_2$ (94 mg, 0.42 mmol), and the resulting suspension was stirred at room temperature for 18 h. The insoluble material was removed by filtration, and the insoluble material washed with CH_2Cl_2. The filtrate and washings were combined and

evaporated to give a pale yellow oil, which was chromatographed on SiO_2 (6 g, hexane:acetone=40:1) to afford (+)-**16** (61 mg, 75%) and the isomeric enone (6.3 mg, 10%) as a colorless oil, respectively.

(+)-**16**: IR (neat): 2948, 1702, 1238, 1139, 1111 cm^{-1}; ^1H NMR δ 0.89 & 0.93 (each s, each 3H), 1.01-1.78 (br m, 10H, including δ 1.10, s, 3H), 2.33 (dd, J = 17.4, 13.8 Hz, 1H), 2.46 (dd, J = 17.4, 3.9 Hz, 1H), 5.77 (d, J = 9.8 Hz, 1H), 6.64 (d, J = 9.8 Hz, 1H); ^{13}C NMR δ 18.28 (u), 18.44 (d), 20.80 (u), 32.09 (u), 32.90 (q), 35.42 (d), 36.74 (q), 37.92 (d), 41.11 (d), 50.35 (u), 125.29 (u), 162.63 (u), 201.46 (s); HRMS Calcd. for $C_{13}H_{20}O$ 192.1514, Found 192.1530; *Anal.* Calcd. for $C_{13}H_{20}O$ C, 81.20; H, 10.48, Found C, 80.94; H, 10.63; $[\alpha]^{26}_D$ +25.0 (*c* 0.59, $CHCl_3$), lit.[7] $[\alpha]^{25}_D$ +7.4 (*c* 2.81, $CHCl_3$).

isomeric enone: IR (neat): 2942, 1679, 1144, 1102, 1033 cm^{-1}; ^1H NMR δ 0.89 & 0.93 (each s, each 3H), 1.01-1.78 (br m, 10H, including δ 1.10, s, 3H), 2.33 (dd, J = 17.4, 13.8 Hz, 1H), 2.46 (dd, J = 17.4, 3.9 Hz, 1H), 5.77 (d, J = 9.8 Hz, 1H), 6.64 (d, J = 9.8 Hz, 1H); HRMS Calcd. for $C_{13}H_{20}O$ 192.1514, Found 192.1501.

(1*S*,4a*S*,7*R*,8a*S*)-(-)-7-(Methoxymethoxy)-1,4a-dimethyl-1,4,4a,5,6,7,8,8a-octahydronaphthalene [(-)-17]: To a stirred solution of (-)-**14** (354 mg, 1.49 mmol) in EtOAc (20 mL) was added 5% Rh-C (100 mg), and the resulting suspension was hydrogenated at 4 atm for 5 h. The catalyst was removed by filtration through celite pad, and the catalyst was washed with CH_2Cl_2. The filtrate and washings were combined and evaporated to give the essentially pure ketone (345 mg, 96%) as a colorless oil, which was used directly in the next step. An analytical sample was obtained by column chromatography on SiO_2 as a colorless oil.

IR (neat): 2935, 1710, 1452, 1378, 1149, 1103, 1045 cm^{-1}; ^1H NMR δ 0.99 (3H, d, J = 6.6 Hz), 1.05-2.00 (12H, m, including δ 1.14, 3H, s), 2.20-2.39 (2H, m), 2.54 (1H, dt, J = 14.4, 6.4 Hz), 3.38 (3H, s), 3.48 (1H, br m), 4.70 (2H, s); ^{13}C NMR δ 11.19 (u), 16.20 (u), 27.76 (d), 32.19 (d), 33.17 (s), 37.79 (d), 38.60 (d), 40.64 (d), 45.09 (u), 49.15 (u), 55.12 (u), 75.85 (u), 94.62 (d), 212.34 (s); HRMS Calcd. for $C_{14}H_{24}O_3$ 240.1726, Found 240.1732; $[\alpha]^{26}_D$ -6.6 (*c* 1.10, $CHCl_3$).

To a stirred solution of the oil obtained above in benzene (3.5 mL) were added $TsNHNH_2$ (310 mg, 1.62 mmol) and catalytic amounts of BF_3•Et_2O (2 drops), and the resulting solution was stirred at room temperature for 1 h. The reaction mixture was diluted with CH_2Cl_2 (10 mL), and the organic layer was washed with satd. aqueous $NaHCO_3$ (3 mL x 1). The aqueous layer was extracted with CH_2Cl_2 (6 mL x 3), and the organic extracts were combined, dried, and evaporated to give a colorless oil, which was used directly in the next step. To a stirred solution of the oil obtained above in THF (7 mL) was added MeLi (1.14 M in Et_2O, 7.1 mL, 8.1 mmol) at 0 ℃, and the resulting solution was stirred at room temperature for 1 h. The reaction was quenched with satd. aqueous NaCl (5 mL), and the aqueous layer was extracted with Et_2O (15 mL x 3). The combined Et_2O layer was dried over $MgSO_4$ and evaporated to give a pale yellow oil, which was chromatographed on SiO_2 (12 g, hexane:acetone=50:1) to afford (-)-**17** (259 mg, 86% in 2 steps) as a colorless oil.

IR (neat): 3015, 2935, 1654, 1148, 1107, 1041 cm^{-1}; ^1H NMR δ 0.86 (3H, s), 0.90-1.20 (6H, m, including δ 0.97, 3H, d, J = 6.6 Hz), 1.44-1.56 (2H, m), 1.70-1.90 (4H, br m), 2.01-2.12 (1H, m), 3.38 (3H, s), 3.43-3.53 (1H, m), 4.70 (2H, s), 5.43 (1H, d-like, J = 10.0 Hz), 5.53 (1H, dd-like, J = 10.0, 2.4 Hz); ^{13}C NMR δ 17.06 (u), 19.25 (u), 28.52 (d), 31.83 (s), 32.16 (d), 33.37 (u), 39.26 (d), 41.31 (d), 45.81 (u), 55.12 (u), 76.29 (u), 94.50 (d), 124.24 (u), 132.68 (u); HRMS Calcd. for $C_{14}H_{24}O_2$ 224.1776, Found 224.1797; *Anal.* Calcd. for $C_{14}H_{24}O_2$ C, 74.95; H, 10.78, Found C, 75.13; H, 11.12; $[\alpha]^{26}_D$ -27.6 (*c* 1.93, $CHCl_3$).

(4a*S*,8*S*,8a*S*)-(-)-4a,8-Dimethyl-1,2,3,4,4a,5,8,8a-octahydronaphthalen-2-one [(-)-18]: To a stirred solution of (-)-**17** (259 mg, 1.15 mmol) in MeOH (3 mL) was added a catalytic amount of c. HCl (1 drop), and the resulting solution was refluxed for 1 h. After cooling, satd. aqueous $NaHCO_3$ (6 drops) was added to the mixture, and the volatiles were removed. The residue was extracted with $CHCl_3$ (2 mL x 6), and the $CHCl_3$ layer was combined, dried over $MgSO_4$, and evaporated to give a colorless oil, which was used directly in the next step. To a stirred solution of the oil obtained above in CH_2Cl_2 (2 mL) was added PCC (349 mg, 1.62 mmol), and the resulting suspension was stirred at room temperature for 20 h. Direct column chromatography of the reaction mixture (SiO_2, 6 g, hexane:acetone=50:1) afforded (-)-**18** (179 mg, 90% in 2 steps) as a colorless oil.

IR (neat): 3017, 2961, 2924, 1715, 1458, 1380, 1179 cm^{-1}; ^1H NMR δ 0.90-1.15 (7H, br m, including at δ 0.96, 3H, d, J = 6.6 Hz and δ 1.07, 3H, s), 1.41 (1H, tt-like, J = 14.0, 3.5 Hz), 1.54 (1H, dd, J = 14.0, 4.5 Hz), 1.76-1.95 (3H, br m), 2.06 (1H, t-like, J = 15.0 Hz), 2.29 (1H, d of quintet, J = 15.0, 2.2 Hz), 2.50 (2H, tm, J = 15.0 Hz), 5.46 (1H, dd, J = 10.0, 1.2 Hz), 5.58 (1H, dd-like, J = 10.0, 2.5 Hz); ^{13}C NMR δ 16.31 (u), 18.64 (u), 31.66 (s), 34.27 (u), 37.95 (d), 40.30 (d), 40.37 (d), 41.85 (d), 47.67 (u), 123.92 (u), 131.86 (u), 211.14 (s); HRMS Calcd. for $C_{12}H_{18}O$ 178.1358, Found 178.1399; $[\alpha]^{26}_D$ -52.0 (*c* 2.20, $CHCl_3$).

(1*S*,4a*S*,7*R*,8a*S*)-(-)-7-Acetyl-1,4a-dimethyl-1,4,4a,5,6,7,8,8a-octahydronaphthalene [(-)-19]: To a stirred suspension of $Ph_3P^+CH_2OMeCl^-$ (677 mg, 1.98 mmol) in THF (6 mL) was added *n*-BuLi (10% solution in hexane, 1.1 mL, 1.73 mmol) at 0 ℃, and the resulting orange solution was stirred at 0 ℃ for 15 min. A solution of ketone (-)-**18** (88 mg, 0.49 mmol) in THF (2 mL) was added to the solution at 0 ℃, and the resulting suspension was stirred at room temperature for 1 h. The reaction was quenched with H_2O (5 mL), and the aqueous layer was extracted with Et_2O (10 mL x 3). The combined Et_2O layer was dried over $MgSO_4$ and evaporated to give a pale yellow oil, which was chromatographed on SiO_2 (12 g, hexane:acetone=80:1) to afford an enol ether (76 mg, 75%) as a colorless oil, as a mixture of *Z* and *E* isomers. To a stirred solution of the enol ether obtained above (76 mg, 0.37 mmol) in CH_2Cl_2 (2 mL) was added a catalytic amount of c. HCl (1 drop), and the solution was stirred at room temperature for 1 h. The reaction was quenched with satd. aqueous $NaHCO_3$ (2 mL), and the volatiles were removed. The residue was extracted with CH_2Cl_2 (6 mL x 3), and the combined CH_2Cl_2 layer was dried over $MgSO_4$, and evaporated to give a colorless oil, which was used directly in the next step. To a stirred solution of the oil obtained above in THF (5 mL) was added MeMgBr (0.96 M in THF, 0.46 mL, 0.44 mmol) at 0 ℃, and the solution was stirred at room temperature for 1 h. The reaction was quenched with satd. aqueous NH_4Cl (5 mL), and the aqueous layer was extracted with CH_2Cl_2 (10 mL x 3). The combined CH_2Cl_2 layer was dried over $MgSO_4$ and evaporated to give a colorless oil, which was used directly in the next step. To a stirred solution of the oil obtained above in CH_2Cl_2 (1 mL) was added PCC (119 mg, 0.56 mmol), and the resulting suspension was stirred at room temperature for 13 h. Direct column chromatography of the reaction mixture (SiO_2, 10 g, hexane:acetone=40:1) afforded the ketone (46 mg, 60% in 3 steps) as a colorless oil, as a mixture of the epimers. To a stirred solution of the ketone obtained above (46 mg, 0.22 mmol) in MeOH (1 mL) was added K_2CO_3 (304 mg, 2.2 mmol), and the resulting suspension was stirred at room temperature for 26 h. The reaction was quenched with 10% aqueous acetic acid, and the volatiles were removed. The residue was extracted with $CHCl_3$ (2 mL x 6), and the $CHCl_3$ layer was combined, dried over $MgSO_4$, and evaporated to

give a colorless oil, which was chromatographed on SiO_2 (10 g, hexane:acetone=40:1) to afford (-)-**19** (40.5 mg, 88%) as a colorless oil.

IR (neat): 3015, 2934, 1709, 1654, 1458, 1378, 1157 cm^{-1}; ^1H NMR δ 0.83 (3H, s), 0.90-1.30 (6H, br m, including δ 0.97, 3H, d, J = 6.8 Hz), 1.47-1.62 (2H, m), 1.76 (3H, br), 1.89 (1H, d-like, J = 11.2 Hz), 2.15 (3H, s), 2.30-2.42 (1H, m), 5.42 (1H, d-like, J = 10.0 Hz), 5.52 (1H, dm, J = 10.0 Hz); ^{13}C NMR δ 17.00 (u), 19.23 (u), 24.00 (d), 27.17 (d), 27.93 (d), 32.03 (s), 33.14 (u), 40.53 (d), 41.55 (d), 46.85 (u), 51.92 (u), 124.11 (u), 132.78 (u), 211.94 (s); HRMS Calcd. for $C_{14}H_{22}O$ 206.1669, Found 206.1661; $[\alpha]^{26}_D$ -52.2 (*c* 1.65, $CHCl_3$).

(2*R*,4a*S*,8*S*,8a*S*)-(-)-α,α,4a,8-Tetramethyl-1,4,4a,5,6,7,8,8a-octahydronaphthalene-2-methanol [(-)-20]: To a stirred solution of (-)-**19** (61 mg, 0.30 mmol) in THF (3 mL) was added MeMgBr (0.96 M in THF, 0.35 mL, 0.44 mmol) at 0 ℃, and the resulting solution was stirred at room temperature for 1 h. The reaction was quenched with satd. aqueous NH_4Cl (3 mL), and the aqueous layer was extracted with CH_2Cl_2 (10 mL x 3). The combined CH_2Cl_2 layer was dried and evaporated to give a colorless oil, which was chromatographed on SiO_2 (6 g, hexane:acetone=50:1) to afford (-)-**20** (50 mg, 76%) as a colorless solid (mp 56~59 ℃, lit.[9] mp 47~48 ℃).

IR ($CHCl_3$): 3620, 3463, 2910, 1653, 1460, 1374, 1206 cm^{-1}; ^1H NMR δ 0.80-1.09 (7H, m, including δ 0.82, 3H, s, and δ 0.98, 3H, d, J = 6.9 Hz), 1.10-1.92 (17H, br m, including δ 1.189 & 1.194, each 3H, each s), 5.43 (1H, d, J = 9.8 Hz), 5.54 (1H, dm, J = 9.8 Hz); ^{13}C NMR δ 17.16 (u), 19.36 (u), 22.73 (d), 26.20 (d), 26.79 & 27.30 (each u, due to rotamers), 32.06 (s), 33.52 (u), 41.34 (d), 41.72 (d), 47.44 (u), 49.28 (u), 72.88 (s), 124.26 (u), 133.05 (u); HRMS Calcd. for $C_{15}H_{26}O$ 222.1982, Found 222.1937; $[\alpha]^{26}_D$ -37.7 (*c* 1.39, $CHCl_3$), lit.[9] $[\alpha]_D$ -35.5 (*c* 0.945, $CHCl_3$).

Ethyl (2*S*,4a*S*,7*R*,8a*R*)-(-)-2-Acetoxy-7-[(1,1-dimethylethyl)dimethylsiloxy]decahydronaphthalene-4a-carboxylate: To a stirred solution of (-)-**6** (191 mg, 0.67 mmol) in CH_2Cl_2 (5 mL) were added TBSCl (183 mg, 1.21 mmol), Et_3N (0.28 mL, 2.01 mmol), and DMAP (10 mg, 0.08 mmol) at 0 ℃, and the resulting mixture was stirred at room temperature for 24 h. The reaction was quenched with H_2O (5 mL), and the organic layer was separated. The aqueous layer was extracted with CH_2Cl_2 (10 mL x 3), and the organic layer and extracts were combined, dried over $MgSO_4$, and evaporated to give a pale yellow oil, which was chromatographed on SiO_2 (10 g, hexane:acetone=50:1) to afford silyl ether (225 mg, 84%) as a colorless oil.

IR (neat): 2934, 1731, 1248, 1199, 1098 cm^{-1}; ^1H NMR δ 0.02 (6H, s), 0.89 (9H, s), 1.05-1.29 (8H, br m, including δ 1.25, 3H, t, J = 7.1 Hz), 1.62-2.18 (8H, br m), 2.03 (3H, s), 3.45-3.65 (1H, br m), 4.12 (2H, q, J = 7.1 Hz), 4.63-4.77 (1H, m); HRMS Calcd. for $C_{21}H_{38}O_5Si$ 398.2486, Found 398.2497; *Anal.* Calcd. for $C_{21}H_{38}O_5Si$ C, 63.28; H, 9.61, Found C, 63.25; H, 9.76; $[\alpha]^{26}_D$ -8.9 (*c* 1.24, $CHCl_3$).

Ethyl (2*R*,4a*S*,7*S*,8a*R*)-(-)-2-[(1,1-Dimethylethyl)dimethylsiloxy]-7-(methoxymethoxy)-decahydronaphthalene-4a-carboxylate [(-)-3]: To a stirred solution of the silyl ether obtained above (192 mg, 0.48 mmol) in MeOH (5 mL) was added K_2CO_3 (35 mg, 0.50 mmol) at 0 ℃, and the resulting suspension was stirred at room temperature for 2 h. The reaction was quenched with 10% aqueous acetic acid, and the volatiles were removed. The residue was extracted with hot $CHCl_3$ (6 mL x 5), and the $CHCl_3$ layer was combined, dried over $MgSO_4$, and evaporated to give a colorless oil, which was used directly in the next step. To a stirred solution of the oil obtained above in CH_2Cl_2 (5 mL) were added MOMCl (0.072 mL,

0.94 mmol) and Hünig base (0.18 mL, 1.03 mmol) at 0 ℃, and the reaction mixture was stirred at room temperature for 20 h. The reaction was quenched with H_2O (5 mL), and the organic layer was separated. The aqueous layer was extracted with CH_2Cl_2 (10 mL x 3), and the organic layer and extracts were combined, dried over $MgSO_4$, and evaporated to give a pale yellow oil, which was chromatographed on SiO_2 (10 g, hexane:acetone=50:1) to afford (-)-**3** (161 mg, 85% in 2 steps) as a colorless oil. The spectral data (IR, ^1H NMR, ^{13}C NMR, and Mass) for (-)-**3** were in good accordance with those for (+)-**3**.
$[\alpha]^{26}_D$ -1.19 (*c* 1.03, $CHCl_3$).

Acknowledgment We acknowledge partial financial support from the Ministry of Education, Sciences and Culture, a Grant-in-Aid for Encouragement of Young Scientists (No. 06772065).

References

1. Merritt, A. T.; Ley, S. V. *Nat. Prod. Rep.* **1992**, 243-287.
2. Ho, T.-L. Carbocycle Construction in Terpene Synthesis, VCH, New York, 1988; An, J.; Wiemer, D. F. *J. Org. Chem.* **1996**, *61*, 8775-8779 and references cited therein.
3. Tamai, Y.; Mizutani, Y.; Hagiwara, H.; Uda, H.; Harada, N. *J. Chem. Res.* **1985**, (S) 148-149; (M) 1746-1787; Hagiwara, H.; Uda, H. *J. Chem. Soc., Chem. Commun.* **1987**, 1351-1353; Idem *J. Chem. Soc., Perkin Trans. 1* **1990**, 1901-1908; Hanselmann, R.; Benn, M. *Synth. Commun.* **1996**, *26*, 945-961 and references cited therein.
4. For preliminary accounts, see: Toyooka, N.; Nishino, A.; Momose, T. *Tetrahedron Lett.* **1993**, *34*, 4539-4540.
5. Jones, J. B.; Dodds, D. R. *Can. J. Chem.* **1987**, *65*, 2397-2404.
6. Bianch, D.; Cesti, P.; Battistel, E. *J. Org. Chem.* **1988**, *53*, 5531-5534.
7. Jansen, B. J. M.; Kreuger, J. A.; Groot, A. D. *Tetrahedron* **1989**, *45*, 1447-1452.
8. Ito, Y.; Hirao, T.; Saegusa, T. *J. Org. Chem.* **1978**, *43*, 1011-1013.
9. Wenkert, E.; Strike, D. P. *J. Am. Chem. Soc.* **1964**, *86*, 2044-2050.
10. Kim, D.; Lim, J. I.; Shin, K. J.; Kim, H. S. *Tetrahedron Lett.* **1993**, *34*, 6557-6558 and references cited therein.
11. Kutney, J. P.; Singh, A. K. *Can. J. Chem.* **1983**, *61*, 1111-1114.

(*Received in Japan* 16 *January* 1997; *accepted* 21 *March* 1997)