Tetrahedron: Asymmetry Vol. 2, No. 12, pp. 1305-1318, 1991
Printed in Great Britain

0957-4166/91 $3.00+.00
Pergamon Press plc

Asymmetric Synthesis of the Hydronaphthalene Moieties of Mevinic Acids

Koichi NARASAKA, Masatoshi SAITOU, and Nobuharu IWASAWA

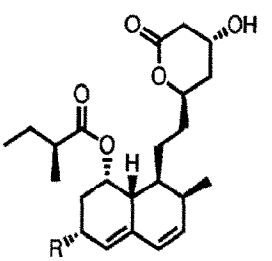
Department of Chemistry, Faculty of Science, The University of Tokyo, Hongo, Bunkyo-ku, Tokyo 113, JAPAN

(*Received* 26 *September* 1991)

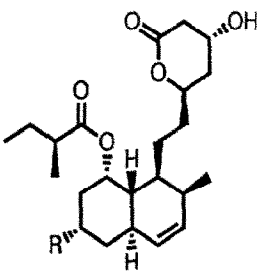
Abstract: The hydronaphthalene moieties of mevinic acids are synthesized enantioselectively by using the asymmetric intramolecular Diels-Alder reaction catalyzed by a chiral titanium reagent.

In 1976, compactin, an inhibitor of 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase, was isolated from the culture broth of the fungus *Penicillium brevicompactum* by Brown and co-workers, and subsequently, three compactin analogues, mevinolin and their dihydro derivatives, were isolated.[1] Each of these four natural products has attracted much attention[2] due to the biological activities not only as an inhibitor of HMG-CoA reductase, the rate-limiting enzyme in cholesterogenesis, but also as an effective hypocholesterolemic agent of atherosclerosis and coronary heart disease.

scheme 1

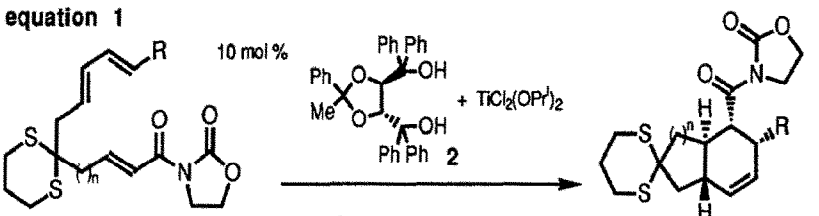


R=H ; compactin
Me ; mevinolin



R=H ; dihydrocompactin
Me ; dihydromevinolin

equation 1



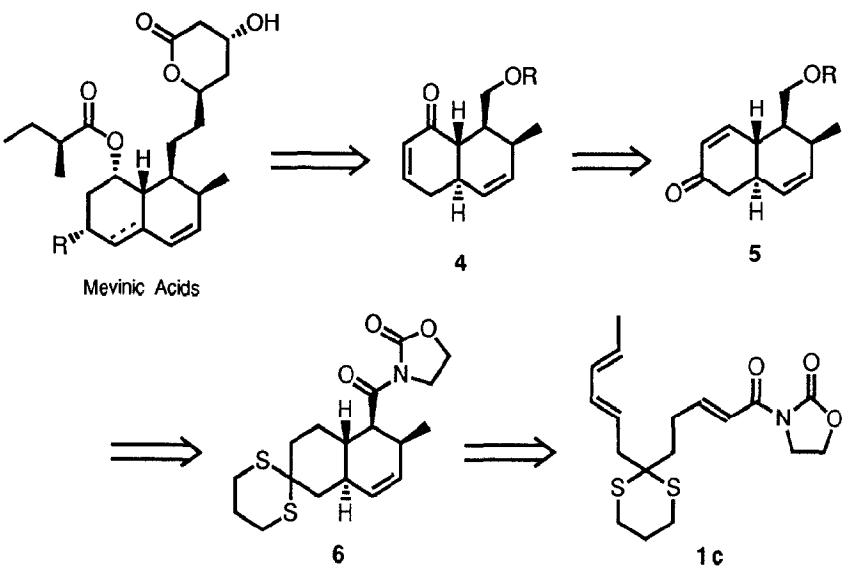
1a ; n=1, R=H
1b ; n=2, R=H
1c ; n=2, R=Me

3a ; 62%, 95% ee
3b ; 64%, 86% ee
3c ; 70%, 87% ee

In the previous paper, we reported that the asymmetric intramolecular Diels-Alder reaction proceeds in a highly enantioselective manner by the use of a catalytic amount of the chiral titanium reagent prepared *in situ* from $TiCl_2(OPr^i)_2$ and the chiral 1,4-diol **2** derived from (+)-tartaric acid, and the cycloadducts having hydronaphthalene or hydroindene skeleton **3a-c** are obtained in high optical purities (equation 1).[3]

As clearly shown from the reaction of dodecatrienoic acid derivative **1c**, the corresponding cycloadduct **3c** satisfies (although absolute stereochemistry is reversed) most of the stereochemistry of the hydronaphthalene moiety of dihydrocompactin or dihydromevinolin, and the stereochemistry of the remaining asymmetric carbons is expected to be controlled efficiently by assuming the α,β-enone **4** as a common intermediate for the synthesis of hydronaphthalene moieties of mevinic acids. Thus, as shown in scheme 2, the optically active cycloadduct **6** would be converted to an unsaturated ketone **5** regioselectively and the successive 1,3-carbonyl transfer would give the common intermediate **4**. In this paper, we would like to report the details of the studies directed toward the enantioselective synthesis of hydronaphthalene moieties of various mevinic acids employing the catalytic asymmetric intramolecular Diels-Alder reaction.

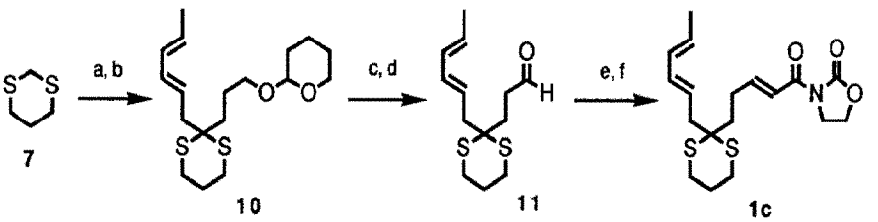
scheme 2



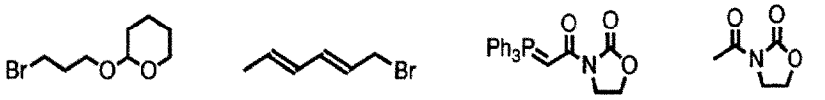
Firstly, the dodecatrienoic acid derivative **1c** was prepared for the intramolecular Diels-Alder reaction as shown in equation 2. Assembly of the basic carbon chain was based on the alkylation reaction of 1,3-dithiane **7** which could be utilized as the key functionality for the manipulation of the cycloadduct after the intramolecular Diels-Alder reaction. Treatment of 1,3-dithiane with Bu^nLi, followed by addition of the 3-bromopropanol derivative **8** gave the monoalkylated product, which was further alkylated using (*E,E*)-2,4-hexadienyl bromide **9** to afford the decadienol derivative **10** in 49% yield (from **7**). Cleavage of the tetrahydropyranyl group and the oxidation of the liberated hydroxyl functionality gave the aldehyde **11** in 83% yield. Attachment of the 3-acetyl-1,3-oxazolidin-2-one moiety was first tried by using the Wittig reagent **12**. However, the reaction of the Wittig reagent **12** with the aldehyde **11** proceeded so slowly even under refluxing CH_2Cl_2 conditions and the partial cycloaddition occurred during the reaction. Then we decided to employ a two-step procedure; the aldol reaction of 3-acetyl-1,3-oxazolidin-2-one **13** with the aldehyde **11** and the dehydration reaction of the obtained aldol product. Treatment of 3-acetyl-1,3-oxazolidin-2-one **13** with $LiN(SiMe_3)_2$ followed by addition of the aldehyde **11** gave the aldol product in 70% yield, and the product was converted to the desired (*E, E, E*)-2,8,10-

dodecatrienoic acid derivative **1c** by converting the aldol product to the corresponding mesylate and the successive treatment with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU).

equation 2

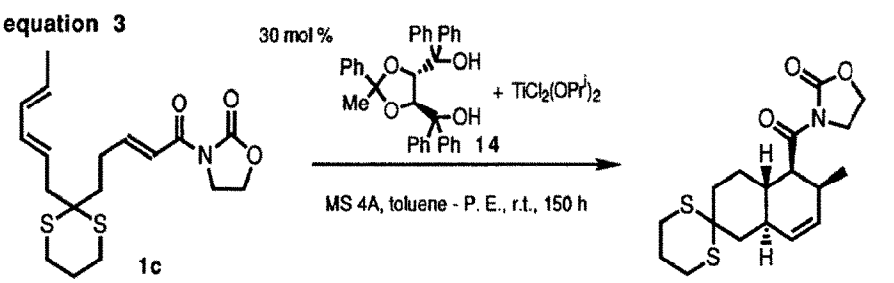


a) Bu^nLi, then **8**, THF, -78~0 °C, 81%. b) Bu^nLi, then **9**, THF, -78 °C, 60%.
c) HCl, MeOH, r.t., 95%. d) SO_3-pyridine complex, Et_3N, DMSO, r.t., 83%.
e) LHMDS - **13**, THF, -78 °C, 70%. f) MsCl, DMAP, Et_3N, CH_2Cl_2, then DBU, 0 °C, 90%.



With the acyclic dodecatrienoic acid derivative **1c** in hand, the enantioselective intramolecular Diels-Alder reaction was examined. In the previous paper, it was reported that treatment of the triene **1c** with 10% amount of the chiral titanium reagent in mesitylene in the presence of Molecular Sieves 4A (MS 4A) at room temperature afforded the Diels-Alder adduct **3c** in 70% yield in 87% optical purity.[3] In order to improve the enantioselectivity, the reaction was investigated under various reaction conditions and it was found that, by carrying out the reaction in a mixed solvent of toluene-petroleum ether (P. E.) (2:1)[4] with 30% amount of the chiral titanium reagent generated from the (-)-1,4-diol **14**, the desired cycloadduct **6** was obtained in 70% yield as a single *endo* isomer and the optical purity was determined to be more than 95%.

equation 3

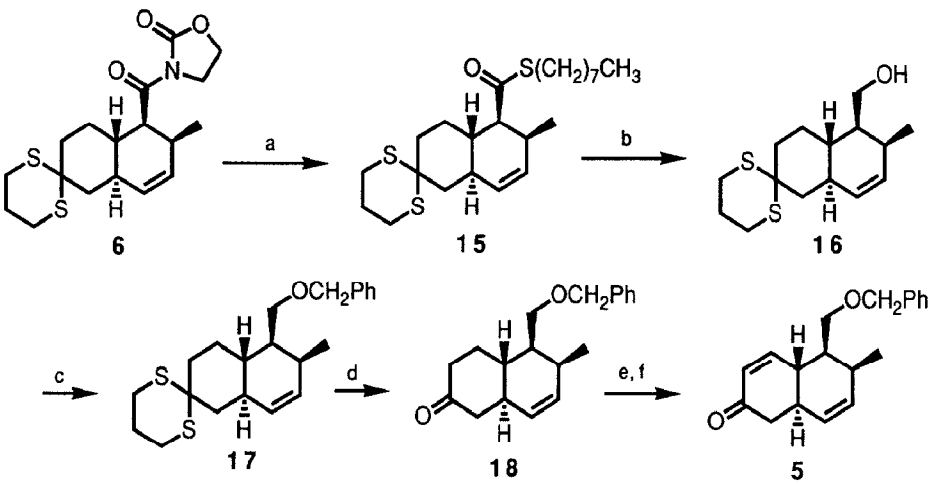


70% yield, >95% ee

Transformation of the cycloadduct **6** into the common synthetic intermediate, the enone **4**, was examined as follows: Firstly the reduction of 3-acyl-1,3-oxazolidin-2-one moiety into hydroxyl group was tried, but the direct reduction of the Diels-Alder adduct **6** with various reducing reagents such as $LiAlH_4$, Bu^i_2AlH, $LiEt_3BH$, and $NaBH_4$-$CeCl_3$ gave the desired alcohol **16** only in moderate yield. Also, treatment of **6** with $Mg(OMe)_2$ gave the corresponding methyl ester in only 21% yield. The side-products were formed by the attack of hydride

or methoxide to the carbonyl group of 1,3-oxazolidin-2-one moiety, which is often observed when the acyl part is bulky. The reduction into the alcohol **16** was finally achieved by a two-step procedure via the thioester **15**. Treatment of the Diels-Alder adduct **6** with $LiS(CH_2)_7CH_3$ afforded the thioester **15** and subsequent reduction with $LiAlH_4$ provided the alcohol **16** in nearly quantitative yield.[5] After the alcohol **16** was protected as the benzyl ether **17**, hydrolysis of 1,3-dithiane part was practiced by the treatment with copper reagents[6] or with silver reagent[7] to afford the ketone **18** in about 80% yield.

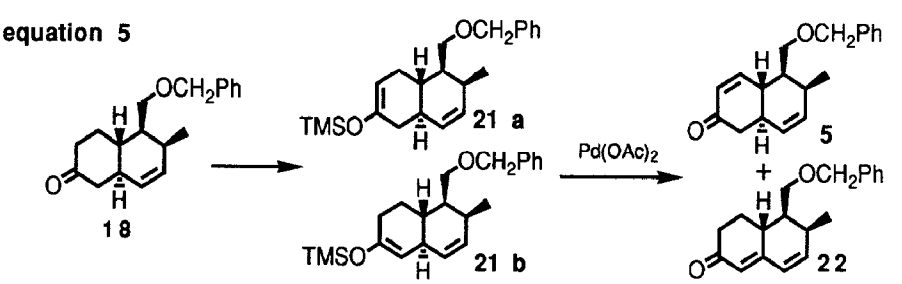
equation 4



a) $LiS(CH_2)_7CH_3$, THF, 0 °C, quant. b) $LiAlH_4$, THF, r.t., 98%.
c) $PhCH_2Br$, NaH, NaI, THF, 0 °C, 97%. d) $CuCl_2$, CuO, acetone-H_2O, reflux, 80%.
e) Et_3N, Me_3SiCl, NaI, MeCN, 40 °C. f) $Pd(OAc)_2$, *p*-benzoquinone, MeCN, r.t., 75%(from **18**)

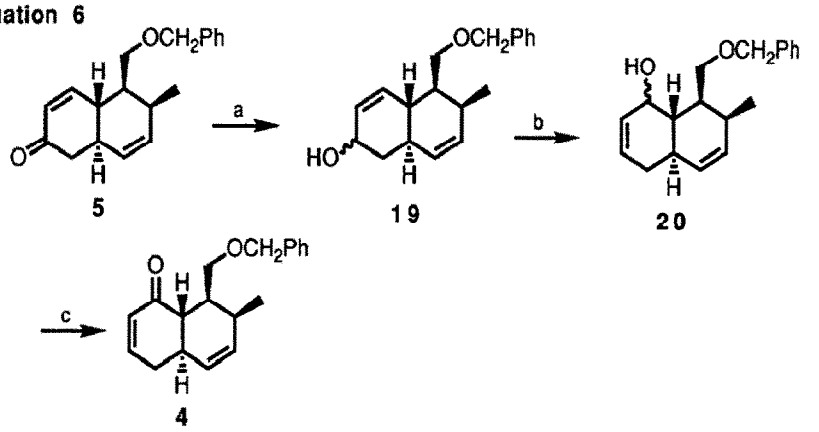
For the transformation of the ketone **18** into the α,β-enone **5**, the regioselective formation of silyl enol ether was investigated under both the kinetic and thermodynamic conditions. Treatment of the ketone **18** with lithium diisopropylamide, followed by addition of Me_3SiCl afforded a 4 : 1 mixture of **21a** and **21b**, while treatment of **18** with Et_3N, Me_3SiCl, NaI gave better results generating the desired silyl enol ether **21a** more selectively (9:1). The mixture of the silyl enol ether **21a** and **21b** was directly treated with $Pd(OAc)_2$ and *p*-benzoquinone[8] to give the enone **5** and the regioisomer **22** in 75% and 8% yield, respectively. These two isomers **5** and **22** were separated easily at this stage.(equation 5)

equation 5



Recently, in our laboratory, 1,3-rearrangement of allylic alcohols has been developed by the catalytic use of $Bu^n_4NReO_4$ and *p*-toluenesulfonic acid,[9] and this rearrangement was applied to the 1,3-carbonyl transfer in the above synthesis. The α,β-unsaturated ketone **5** was converted to the allylic alcohol **19** by 1,2-reduction ($NaBH_4$, $CeCl_3$-$7H_2O$)[10] as a 9 : 1 mixture of stereoisomers. Rearrangement of the allylic alcohol **19** proceeded smoothly by the use of 10% molar amount of $Bu^n_4NReO_4$ in the presence of 5% molar amount of *p*-toluenesulfonic acid in CH_2Cl_2 at room temperature and afforded a mixture of two regioisomeric allylic alcohols **19** and **20**. These isomers were easily separated by column chromatography and the rearranged allylic alcohol **20** was obtained in 81% yield with the recovered allylic alcohol **19** (5%). **19** and **20** were diastereomeric mixtures in about 4 : 1 and 9 : 1 ratio, respectively. One of the reason why the rearranged allylic alcohol **20** was obtained as a major product is attributed to the stabilization by the hydrogen bond formation between the hydrogen of allylic alcohol and the oxygen of benzyl ether [low wave number shift in IR ; cm^{-1}(OH) 3470(**19**), 3340(**20**)]. This allylic alcohol **20** was easily converted to the enone **4** by pyridinium dichromate oxidation, and thus 1,3-carbonyl transfer was achieved effectively via a three-step sequence. (equation 6)

equation 6

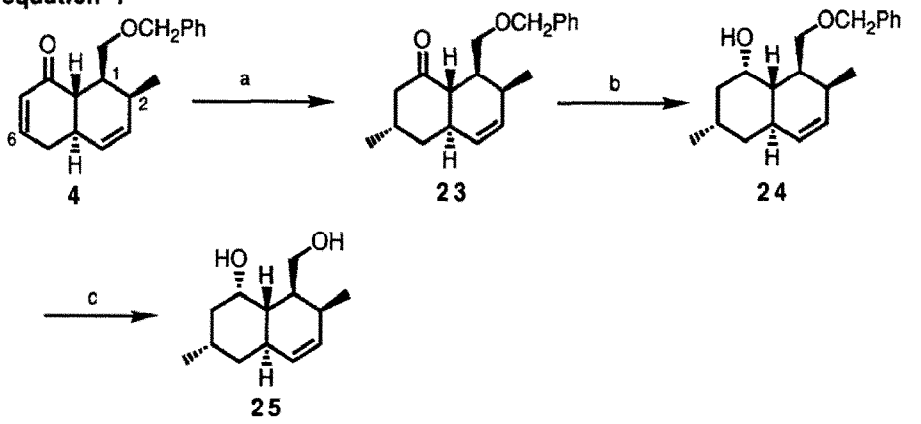


a) $NaBH_4$, $CeCl_3$-$7H_2O$, MeOH, r.t., 100%. b) $Bu^n_4NReO_4$, *p*-TsOH, CH_2Cl_2, r.t., 81%. c) PDC, CH_2Cl_2, r.t., 97%.

The octahydronaphthalene moiety **25** for the synthesis of dihydromevinolin demanded a methylation at C-6 in the enone **4** (equation 7). Conjugate addition of Me_2CuLi yielded the product **23** as a single diastereomer with the methyl group in an axial position. Reduction of **23** with L-selectride afforded the axial alcohol **24** selectively and deprotection by the Birch reduction gave the diol **25**, whose physical properties agreed with those reported by Hanessian[2g] and Davidson.[11]

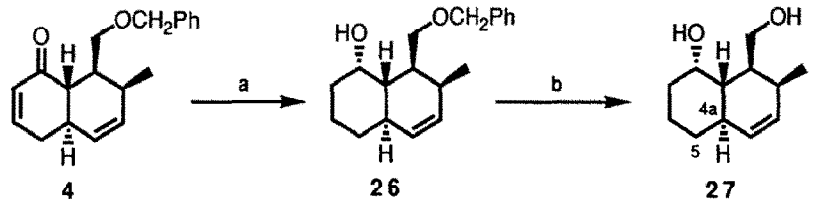
Direct 1,4- and 1,2-reduction of the enone **4** with 3 equivalent of L-selectride gave the axial alcohol **26** selectively and the Birch reduction afforded the diol **27** (equation 8). The diol **27** exhibited indistinguishable chromatographic behavior and spectral data compared with the racemic authentic sample provided by Prof. J. R. Falck.[12]

equation 7



a) Me_2CuLi, Et_2O, -78 °C, quant b) L-selectride, THF, -78 °C, 91%.
c) Li-NH_3, quant.

equation 8



a) L-selectride, THF, -78 °C, 75%. b) Li-NH_3, quant.

As the introduction of double bond between C_{4a} and C_5 from the diol **27** to synthesize compactin intermediate was previously reported by Funk and Zeller,[13] the present synthesis establishes a facile entry into a variety of mevinic acids.

Experimental

General. NMR spectra were recorded on Bruker AM500 spectrometer using tetramethylsilane as the internal standard in $CDCl_3$ as solvent. IR spectra were measured with Horiba FT-300S spectrometer. High mass spectra were obtained with JEOL JMS-D300 mass spectrometer operating at 70 eV. The optical rotations were measured with JASCO DIP-370 digital polarimeter.

Column chromatography was conducted on silica gel (E. Merck, 7734, 70-230 mesh) and Florisil (Wako, 100-200 mesh) and medium pressure column chromatography was performed with the YFLC-254 system of Yamazen Corp. Preparative thin-layer chromatography (TLC) was carried out on silica gel (Wakogel B-5F).

CH_2Cl_2 and CH_3CN was distilled from P_2O_5, then from CaH_2, and dried over MS 4A (Nikkaseiko Co.). Dimethylsulfoxide (DMSO) was distilled from CaH_2 and dried over MS 4A. Toluene and P. E. were distilled and dried over MS 4A. Tetrahydrofuran (THF) and Et_2O were freshly distilled from sodium diphenylketyl. Methanol was distilled from $Mg(OMe)_2$ and dried over MS 4A. Dichlorodiisopropoxytitanium was prepared from titanium(IV) chloride and titanium(IV) isopropoxide according to the literature method.[14] (*E*, *E*)-2,4-

Hexadienyl bromide **9** was prepared according to the literature.[15] All the operations were performed under an argon atmosphere.

2-[4,4-(Trimethylenedithio)butoxy]-3,4,5,6-tetrahydropyran. To a THF solution (80 ml) of 1,3-dithiane **7** (4.80 g, 40 mmol) was added a hexane solution (1.57 M, 28.0 ml) of butyllithium at -78 °C and the mixture was gradually warmed to -23 °C and stirred for 2 h. After the mixture was cooled to -78 °C, 3-bromopropyl 2-tetrahydropyranyl ether **8** (11.1 g, 50 mmol) was added to the mixture, which was gradually warmed to 0 °C and stirred for 12 h. Then the reaction was quenched with pH 7 phosphate buffer and the organic materials were extracted with ethyl acetate. The combined extracts were washed with brine and dried over anhydrous Na_2SO_4. After evaporation of the solvent, the crude product was purified by column chromatography (silica gel, hexane:ethyl acetate=19:1) to afford the title compound (8.45 g, 81%). IR(neat) 2940, 2865, 1425, 1350, 1275, 1195, 1125, 1030, 985, cm^{-1}; ^{1}H-NMR(500MHz) δ=4.58(1H, t, J=3.5Hz), 4.07(1H, t, J=6.8Hz), 3.83-3.88(1H, m), 3.75(1H, dt, J=6.3, 9.8Hz), 3.48-3.52(1H, m), 3.42(1H, dt, J=6.0, 9.8Hz), 2.82-2.91(4H, m), 2.09-2.15(1H, m), 1.78-1.91(6H, m), 1.68-1.73(1H, m), 1.48-1.64(4H, m); Anal. Calcd for $C_{12}H_{22}O_2S_2$: C, 54.92; H, 8.45; S, 24.44%. Found: C, 54.62; H, 8.21; S, 24.44%.

2-[4,4-(Trimethylenedithio)-(*E*,*E*)-6,8-decadienoxy]-3,4,5,6-tetrahydropyran (10). To a THF solution (40 ml) of the above product (10.5 g, 37 mmol) was added a hexane solution (1.62 M, 24.7 ml) of butyllithium at -78 °C and the mixture was gradually warmed to -23 °C and stirred for 2 h. After the mixture was cooled to -78 °C, (*E*,*E*)-2,4-hexadienyl bromide **9** (7.10 g, 44 mmol) was added to the mixture, which was stirred for 12 h. Then the reaction was quenched with pH 7 phosphate buffer and the organic materials were extracted with ethyl acetate. The combined extracts were washed with brine and dried over anhydrous Na_2SO_4. After evaporation of the solvent, the crude product was purified by column chromatography (silica gel, benzene:hexane:Et_2O=20:10:1) to afford **10** (8.23 g, 60%). IR(neat) 3020, 2960, 2920, 2870, 1445, 1350, 1280, 1200, 1120, 1035, 990 cm^{-1}; ^{1}H-NMR(500MHz) δ=6.02-6.11(2H, m), 5.57-5.65(2H, m), 4.59(1H, t, J=3.5Hz), 3.84-3.88(1H, m), 3.71-3.75(1H, m), 3.48-3.51(1H, m), 3.39-3.44(1H, m), 2.78-2.85(4H, m), 2.65(2H, d, J=7.4Hz), 1.91-1.98(4H, m), 1.68-1.84(4H, m), 1.73(3H, d, J=6.9Hz), 1.52-1.61(4H, m); HRMS Found: m/z 342.1696. Calcd for $C_{18}H_{30}O_2S_2$: M, 342.1686.

4,4-(Trimethylenedithio)-(*E*,*E*)-6,8-decadien-1-ol. To a methanol solution (20 ml) of **10** (1.28 g, 3.7 mmol) was added a few drops of hydrochloric acid (2 N) at room temperature. After being stirred for 12 h, the mixture was treated with pH 7 phosphate buffer and the organic materials were extracted with ethyl acetate. The combined extracts were washed with brine and dried over anhydrous Na_2SO_4. After evaporation of the solvent, the crude product was purified by column chromatography (silica gel, hexane:ethyl acetate=3:1) to afford the title compound (0.85 g, 93%). IR(neat) 3380, 3020, 2940,1440, 1425, 1275, 1055, 990, 915 cm^{-1}; ^{1}H-NMR(500MHz) δ=6.03-6.12(2H, m), 5.57-5.67(2H, m), 3.64-3.68(2H, m), 2.82-2.85(4H, m), 2.67(2H, d, J=7.4Hz), 1.93-1.98(4H, m), 1.72-1.77(5H, m), 1.33(1H, t, J=5.3Hz); HRMS Found: m/z 258.1093. Calcd for $C_{13}H_{22}OS_2$: M, 258.1110.

4,4-(Trimethylenedithio)-(*E*,*E*)-6,8-decadienal (11). To a DMSO solution (10 ml) of the above alcohol (785 mg,3.0 mmol) was added triethylamine (5 ml) and a DMSO solution (10 ml) of SO_3-pyridine complex (1.55 g, 9.7 mmol) at room temperature.[16] After being stirred for 1 h, the reaction was quenched with pH 7 phosphate buffer and the organic materials were extracted with Et_2O. The combined extracts were washed with brine and dried over anhydrous Na_2SO_4. After evaporation of the solvent, the crude product was purified by column chromatography (silica gel, hexane:Et_2O=5:1) to afford **11** (665 mg, 85%). IR(neat) 3020, 2910,

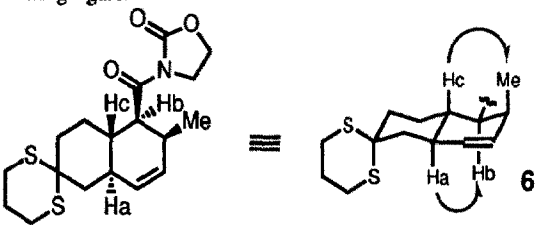
2830, 2720, 1720, 1440, 1420, 1275, 990 cm^{-1}; ^1H-NMR(500MHz) δ=9.74(1H, s), 6,03-6.12(2H, m), 5.56-5.69(2H, m), 2.75-2.88(4H, m), 2.66(2H, t, J=7.9Hz), 2.60(2H, d, J=7.5Hz), 2.25(2H, t, J=7.5Hz), 1.91-2.01(2H, m), 1.74(3H, d, 7.0Hz); HRMS Found: m/z 256.0940. Calcd for $C_{13}H_{20}OS_2$: M, 256.0955.

3-[3-Hydroxy-6,6-(trimethylenedithio)-(*E*,*E*)-8,10-dodecadienoyl]-1,3-oxazolidin-2-one. To a stirred and cooled (0 °C) THF solution (15 ml) of hexamethyldisilazane (2.40 g, 14.9 mmol) was added dropwise a hexane solution (1.55 M, 9.2 ml) of butyllithium. Stirring at 0 °C was continued for 30 min, and the solution was cooled to -78 °C. 3-Acetyl-1,3-oxazolidin-2-one **13** (1.84 g, 14.2 mmol) in THF (40 ml) was added, and the mixture was stirred at -78 °C for 1 h. Then a THF solution (30 ml) of the aldehyde **11** (3.65 g, 14.2 mmol) was added. After being stirred for 30 min at -78 °C, the mixture was quenched with pH 7 phosphate buffer and the organic materials were extracted with ethyl acetate. The combined extracts were washed with brine and dried over anhydrous Na_2SO_4. After evaporation of the solvent, the crude product was purified by column chromatography (silica gel, hexane:ethyl acetate=2:1) to afford the title compound (3.71 g, 70%). IR(neat) 3490, 2920, 1780, 1700, 1390, 1225, 1035, 990 cm^{-1}; ^1H-NMR(500MHz) δ=6.03-6.12(2H, m), 5.56-5.68(2H, m), 4.43(2H, t, J=8.0Hz), 4.00-4.11(3H, m), 3.14(1H, dd, J=3.0, 17.2Hz), 3.05(1H, dd, J=8.6, 17.2Hz), 2.91(1H, d, J=4.3Hz), 2.77-2.88(4H, m), 2.63(2H, d, 7.5Hz), 2.15-2.22(1H, m), 1.88-2.00(3H, m), 1.66-1.75(5H, m).

3-[6,6-(Trimethylenedithio)-(*E*,*E*,*E*)-2,8,10-dodecatrienoyl]-1,3-oxazolidin-2-one (1c). To a CH_2Cl_2 solution (30 ml) of the above product (1.01 g, 2.6 mmol) was added triethylamine (3.65 ml) and dimethylaminopyridine (cat.). After the mixture was cooled to 0 °C, methanesulfonyl chloride (1.50 g, 13 mmol) was added dropwise to the mixture and then DBU (0.40 g, 2.6 mmol) was added. After being stirred for 30 min, the reaction was quenched with pH 7 phosphate buffer and the organic materials were extracted with ethyl acetate. The combined extracts were washed with brine and dried over anhydrous Na_2SO_4. After evaporation of the solvent, the crude product was purified by column chromatography (silica gel, hexane:ethyl acetate=2:1) to afford **1c** (866 mg, 90%). IR(neat) 2910, 1770, 1680, 1640, 1390, 1360, 1225, 1045, 995 cm^{-1}; ^1H-NMR(500MHz) δ=7.27(1H, d, J=16.0Hz), 7.16(1H, dt, J=7.0, 16.0Hz), 6.01-6.12(2H, m), 5.56-5.68(2H, m), 4.42(2H, t, J=8.0Hz), 4.06(2H, t, J=8.0Hz), 2.80-2.83(4H, m), 2.64(2H, d, J=8.0Hz), 2.45-2.50(2H, m), 2.02-2.06(2H, m), 1.93-1.98(2H, m), 1.74(3H, d, J=7.0Hz).

3-[(1*S*,2*S*,4*aR*,8*aS*)-1,2,4a,5,6,7,8,8a-Octahydro-2-methyl-6,6-(trimethylenedithio)-1-naphthalenecarbonyl]-1,3-oxazolidin-2-one (6). Toluene (10 ml) and P. E. (10 ml) were added to dichlorodiisopropoxytitanium (166 mg, 0.70 mmol), the chiral diol **14** (375 mg, 0.71 mmol), and MS 4A (powder, 200 mg) at room temperature and the mixture was stirred for 30 min. Then a toluene solution (10 ml) of **1c** (866 mg, 2.36 mmol) was added to the mixture, which was stirred for 150 h. The reaction was quenched with pH 7 phosphate buffer and inorganic materials were removed by filtration. The organic materials were extracted with ethyl acetate and the extracts were washed with brine and dried over Na_2SO_4. After evaporation of the solvent, the crude product was purified by column chromatography (silica gel, hexane:ethyl acetate=2:1) to afford **6** (606 mg, 70%). mp 90-92 °C; IR(KBr) 2920, 1780, 1745, 1700, 1390, 1245, 1045, 685 cm^{-1}; ^1H-NMR(500MHz) δ=5.58-5.61(1H, m), 5.36(1H, d, J=9.8Hz), 4.40(2H, t, J=8.3Hz), 4.04-4.09(1H, m), 3.95-4.01(1H, m), 3.90(1H, dd, J=6.0, 11.3Hz), 2.82-2.92(2H, m), 2.70-2.77(3H, m), 2.35-2.40(3H, m), 1.97-2.02(2H, m), 1.76-1.82(2H, m), 1.57-1.64(1H, m), 1.52(1H, t, J=13.5Hz), 1.33-1.41(1H, m), 0.87(3H, d, J=7.2Hz); $[\alpha]_D^{21}$ +95 (c 1.07, CH_2Cl_2); HRMS Found: m/z 367.1277. Calcd for $C_{18}H_{25}NO_3S_2$: M, 367.1276.

Assignment of the Stereochemistry of 6. The stereochemistry of **6** was determined by the measurement of 2D NOESY NMR spectrum in C_6D_6. The NOEs were observed between both Ha - Hb and Hc -H_{Me} as shown in the following figure.



S-Octyl=(1*S*,2*S*,4a*R*,8a*S*)-1,2,4a,5,6,7,8,8a-octahydro-2-methyl-6,6-(trimethylenedithio)-1-naphthalenecarbothioate (15). To a THF solution (15 ml) of octanethiol (0.54 g, 3.69 mmol) was added a hexane solution (1.59 M, 2.5 ml) of butyllithium at -23 °C and the mixture was warmed to 0 °C.[5] Then a THF solution (50 ml) of **6** (1.12 g, 3.06 mmol) was added and the mixture was stirred for 1h. The reaction was quenched with pH 7 phosphate buffer and the organic materials were extracted with ethyl acetate. The combined extracts were washed with brine and dried over anhydrous Na_2SO_4. After evaporation of the solvent, the crude product was purified by column chromatography (silica gel, hexane:ethyl acetate=19:1) to afford **15** (1.32 g, quant.). IR(neat) 3020, 2855, 1680, 1250, 855, 745 cm^{-1}; ^{1}H-NMR(500MHz) δ=5.57(1H, ddd, J=2.7, 4.5, 9.8Hz), 5.31(1H, d, J=9.8Hz), 2.80-2.88(4H, m), 2.71-2.73(2H, m), 2.55-2.60(1H, m), 2.50(1H, q, J=7.4Hz), 2.29-2.37(3H, m), 1.95-1.99(2H, m), 1.70-1.75(2H, m), 1.45-1.60(4H, m), 1.25-1.40(11H, m), 0.84-0.90(6H, m); $[\alpha]_D^{24}$ +89 (c 0.93, CH_2Cl_2); HRMS Found: m/z 426.2069. Calcd for $C_{23}H_{38}OS_3$: M, 426,2084.

(1*S*,2*S*,4a*R*,8a*S*)-1,2,4a,5,6,7,8,8a-Octahydro-2-methyl-6,6-(trimethylenedithio)-1-naphthalenemethanol (16). A THF solution (10 ml) of **15** (1.32 g, 3.11 mmol) was added to a THF suspension (20 ml) of $LiAlH_4$ (0.50 g, 13.2 mmol) at room temperature and the mixture was stirred for 12 h. Then saturated aqueous sodium sulfate solution was added dropwise until hydrogen evolution ceased. Inorganic materials were removed by filtration and washed with portions of hot isopropyl alcohol. The filtrate was concentrated in vacuo. The crude product was purified by column chromatography (silica gel, hexane:ethyl acetate=3:1) to give the title compound **16** (0.90 g, 98%). mp 100-101 °C; IR(KBr) 3620, 3050, 2935, 2880, 1435, 1290, 1235, 1015, 790, 695 cm^{-1}; ^{1}H-NMR(500MHz) δ=5.62(1H, ddd, J=2.6, 4.6, 9.8Hz), 5.30(1H, d, J=9.8Hz), 3.80(1H, dd, J=5.5, 10.5Hz), 3.54(1H, dd, J=9.1, 10.5Hz), 2.87(2H, dd, J=4.9, 10.0Hz), 2.72-2.75(2H, m), 2.38-2.44(2H, m), 2.27-2.33(2H, m), 1.95-1.99(2H, m), 1.76-1.82(1H, m), 1.66(1H, dt, J=4.1, 13.2Hz), 1.49-1.59(2H, m), 1.43(1H, t, J=13.2Hz), 1.10-1.17(2H, m), 0.90(3H, d, J=7.1Hz); $[\alpha]_D^{26}$ +63 (c 1.03, CH_2Cl_2); Anal. Calcd for $C_{15}H_{24}OS_2$: C, 63.33; H, 8.50; S, 22.54%. Found: C, 63.04; H, 8.40; S, 22.38%.

Optical Purity of 16. The optical purity of **16** was determined by the ^{1}H NMR (500 MHz) analysis of the (+)-MTPA ester of **16**.[17] Two sets of two double doublet signals of the methylene group adjacent to the (+)-MTPA ester group of the racemate appeared at 4.17 ppm : 4.24 ppm and 4.43 ppm : 4.50 ppm. The corresponding (+)-MTPA ester of the optically active sample **16** showed only one set of signals at 4.24 ppm and 4.43 ppm, respectively. Therefore, the enantiomeric excess of **16** was determined to be >95%.

(4a*S*,5*S*,6*S*,8a*R*)-5-Benzyloxymethyl-1,2,3,4,4a,5,6,8a-octahydro-6-methyl-2,2-(trimethylenedithio)naphthalene(17). To a THF suspension (2 ml) of NaH (60% oil dispersion, 60 mg, 1.5 mmol) was added a THF solution (4 ml) of the alcohol **16** (206.5 mg, 0.73 mmol) at 0 °C. Benzyl bromide (140 mg, 0.82 mmol) and NaI (120 mg, 0.80 mmol) was added, and the mixture was gradually warmed to room temperature and stirred for 12 h. pH 7 Phosphate buffer was added to the mixture and the organic materials were extracted with ethyl acetate. The combined extracts were washed with brine and dried over anhydrous Na_2SO_4. After evaporation of the solvent, the crude product was purified by column chromatography (silica gel, hexane:ethyl acetate=9:1) to afford the benzyl ether **17** (264.3 mg, 97%). IR(neat) 2965, 2935, 2910, 2870, 1455, 1445, 1240, 1105 cm^{-1}; ^{1}H-NMR(500MHz) δ=7.22-7.35(5H, m), 5.61(1H, ddd, J=2.6, 4.7, 9.8Hz), 5.29(1H, d, J=9.8Hz), 4.49(1H, d, J=11.9Hz), 4.43(1H, d, J=11.9Hz), 3.55(1H, dd, J=5.5, 9.2Hz), 3.34(1H, t, J=9.2Hz), 2.82-2.92(2H, m), 2.67-2.78(2H, m), 2.43-2.50(1H, m), 2.26-2.40(3H, m), 1.89-2.00(3H, m), 1.65(1H, dt, J=4.4, 12.9Hz), 1.49-1.54(2H, m), 1.40-1.47(1H, m), 1.14(1H, dq, J=3.9, 10.9Hz), 0.87(3H, d, J=7.1Hz); $[\alpha]_D^{24}$ +59 (c 0.98, CH_2Cl_2); HRMS Found: m/z 374.1747. Calcd for $C_{22}H_{30}OS_2$: M, 374.1737.

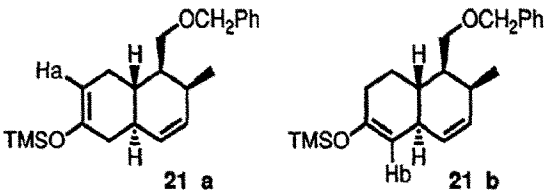
(4a*S*,5*S*,6*S*,8a*R*)-5-Benzyloxymethyl-1,2,3,4,4a,5,6,8a-octahydro-6-methylnaphthalen-2-one (18). To an acetone-H_2O (99:1) suspension (5 ml) of $CuCl_2$ (190 mg, 1.41 mmol) and CuO (225 mg, 2.83 mmol)[6] was added an acetone solution (5 ml) of **17** (264 mg, 0.70 mmol) and the mixture was refluxed for 1 h. After inorganic materials were removed by filtration and washed with ethyl acetate, the filtrate was concentrated in vacuo. The crude product was purified by column chromatography (silica gel, hexane:ethyl acetate=5:1) to give the ketone **18** (160 mg, 80%). mp 74-75 °C; IR(KBr) 3035, 2965, 2875, 1710, 1455, 1415, 1365, 1290, 1105, 740 cm^{-1}; ^{1}H-NMR(500MHz) δ=7.25-7.36(5H, m), 5.69(1H, ddd, J=2.4, 4.8, 9.8Hz), 5.31(1H, d, J=9.8Hz), 4.52(1H, d, J=11.9Hz), 4.47(1H, d, J=11.9Hz), 3.60(1H, dd, J=5.5, 9.3Hz), 3.46(1H, t, J=8.8Hz), 2.39-2.53(3H, m), 2.31(1H, dt, J=6.8, 14.0Hz), 2.04-2.20(3H, m), 1.93-1.99(1H, m), 1.55-1.60(1H, m), 1.42-1.50(1H, m), 0.95(3H, d, J=7.1Hz); $[\alpha]_D^{25}$ +101 (c 0.73, CH_2Cl_2); HRMS Found: m/z 284.1745. Calcd for $C_{19}H_{24}O_2$: M, 284.1775.

(4a*S*,5*S*,6*S*,8a*R*)-5-Benzyloxymethyl-1,2,4a,5,6,8a-hexahydro-6-methylnaphthalen-2-one (5). To an CH_3CN solution (2 ml) of the ketone (270 mg, 0.95 mmol) **18** was added triethylamine (0.35 ml, 2.51 mmol), trimethylsilyl chloride (210 mg, 1.93 mmol), and an CH_3CN solution (2 ml) of NaI(150 mg, 1.00 mmol) at 40 °C. After being stirred for 5 h, the mixture was poured into ice water and the organic materials were extracted with hexane. The combined extracts were washed with brine and dried over anhydrous K_2CO_3. The extracts were concentrated in vacuo to afford the crude products, **21a** and **21b**. IR(neat) 2960, 2890, 1670, 1365, 1255, 1190, 1115, 900, 845, 735 cm^{-1}; ^{1}H-NMR(500MHz) δ=7.32-7.35(4H, m), 7.25-7.29(1H, m), 5.67(1H, ddd, J=2.5, 5.0, 9.8Hz), 5.40(1H, d, J=9.8Hz), 4.84(1H, d, J=5.6Hz), 4.51(1H, d, J=11.8Hz), 4.45(1H, d, J=11.8Hz), 3.58(1H, dd, J=5.2, 9.2Hz), 3.38(1H, t, J=9.4Hz), 2.47-2.50(1H, m), 1.98-2.08(3H, m), 1.89-1.96(1H, m), 1.79-1.84(2H, m), 1.30-1.34(1H, m), 0.90(3H, d, J=7.0Hz), 0.17(9H, s); HRMS Found: m/z 356.2180. Calcd for $C_{22}H_{32}O_2Si$: M, 356.2172.

To an CH_3CN solution (4 ml) of the above crude mixture was added $Pd(OAc)_2$ (100 mg, 0.45 mmol) and *p*-benzoquinone (50 mg, 0.46 mmol) at room temperature.[8] After the mixture was stirred for 24 h, inorganic materials were removed by filtration and washed with ethyl acetate. The filtrate was concentrated in vacuo. The crude product was purified by column chromatography (silica gel, hexane:ethyl acetate=5:1) to give the enone **5** (200 mg, 75%). IR(neat) 2875, 1685, 1455, 1365, 1240, 1120, 1100, 740, 700 cm^{-1}; ^{1}H-NMR(500MHz)

δ=7.26-7.38(6H, m), 6.02(1H, dd, J=2.8, 10.1Hz), 5.65(1H, ddd, J=2.6, 4.6, 9.8Hz), 5.40(1H, d, J=9.8Hz), 4.57(1H, d, J=11.9Hz), 4.53(1H, d, J=11.9Hz), 3.71(1H, dd, J=6.3, 9.6Hz), 3.61(1H, dd, J=5.7, 9.6Hz), 2.58(1H, dd, J=3.4, 16.9Hz), 2.50-2.54(2H, m), 2.31(1H, t, J=10.5Hz), 2.17(1H, dd, J=15.0, 17.2Hz), 2.05-2.12(1H, m), 0.95(3H, d, J=7.1Hz); $[\alpha]_D^{27}$ +121 (c 1.05, CH_2Cl_2); HRMS Found: m/z 282.1611. Calcd for $C_{19}H_{22}O_2$: M, 282.1618.

Assignment of the Regiochemistry of 21a and 21b. The regiochemistry and the ratio of the silyl enol ether **21a** and **21b** were determined by the coupling patterns of the olefinic protons Ha and Hb and their integration. The olefinic proton Ha in **21a** was observed as a doublet (4.84 ppm), while Hb in **21b** was observed as a singlet (4.73 ppm).



(2*RS*,4a*S*,5*S*,6*S*,8a*R*)-5-Benzyloxymethyl-1,2,4a,5,6,8a-hexahydro-6-methyl-2-naphthol (19). To a methanol solution (2 ml) of the enone **5** (44.0 mg, 0.16 mmol) was added $CeCl_3$-$7H_2O$ (58 mg, 0.16 mmol) at room temperature and the mixture was stirred for 30 min. Then $NaBH_4$ (6.0 mg, 0.16 mmol) was added to the mixture, which was stirred for 5 min.[10] The reaction was quenched with pH 7 phosphate buffer and inorganic materials were removed by filtration. The organic materials were extracted with ethyl acetate and the extracts were washed with brine and dried over Na_2SO_4. After evaporation of the solvent, the crude product was purified by column chromatography (silica gel, hexane:ethyl acetate=5:1) to afford **19** (44.0 mg, quant.). IR(neat) 3370, 3340, 3315, 3015, 2925, 2860, 1450, 1365, 1315, 1100, 1055, 740, 700 cm^{-1}; ^{1}H-NMR(500MHz) δ=7.32-7.34(4H, m), 7.25-7.29(1H, m), 5.88(1H, d, J=10.2Hz), 5.64(1H, d, J=10.2Hz), 5.58(1H, ddd, J=2.8, 4.4, 9.7Hz), 5.40(1H, d, J=9.7Hz), 4.52(1H, d, J=11.9Hz), 4.48(1H, d, J=11.9Hz), 4.39(1H, bs), 3.65(1H, dd, J=5.5, 9.4Hz), 3.48(1H, dd, J=7.0, 9.4Hz), 2.46-2.48(1H, m), 2.10-2.16(2H, m), 1.93-2.02(3H, m), 1.28-1.36(1H, m), 0.89(3H, d, 7.0Hz); HRMS Found: m/z 284.1789. Calcd for $C_{19}H_{24}O_2$: M, 284.1777.

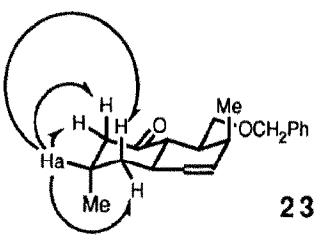
(1*S*,2*S*,4a*R*,8*RS*,8a*S*)-1-Benzyloxymethyl-1,2,4a,5,8,8a-hexahydro-2-methyl-8-naphthol (20). To a CH_2Cl_2 solution (8 ml) of the allyl alcohol **19** (95 mg, 0.33 mmol) was added a CH_2Cl_2 solution (2 ml) of $Bu^n_4NReO_4$[18] (16 mg, 0.03 mmol) and *p*-toluenesulfonic acid (3 mg, 0.015 mmol) at room temperature and the mixture was stirred for 5 min.[9] The reaction was quenched with pH 7 phosphate buffer and the organic materials were extracted with ethyl acetate. The combined extracts were washed with brine and dried over anhydrous Na_2SO_4. After evaporation of the solvent, the crude product was purified by column chromatography (silica gel, hexane:ethyl acetate=5:1) to afford the rearranged allyl alcohol **20** (77 mg, 81%) and the recovered allyl alcohol **19** (5 mg, 5%). IR(neat) 3470, 3020, 2965, 2875, 1455, 1435, 1370, 1290, 1225, 1205, 1090, 1050, 740, 700 cm^{-1}; ^{1}H-NMR(500MHz) δ=7.27-7.35(5H, m), 5.86-5.90(0.2H, m), 5.76(0.8H, ddd, J=2.0, 4.9, 9.8Hz), 5.56-5.64(2H, m), 5.47(0.2H, d, J=9.8Hz), 5.37(0.8H, d, J=9.8Hz), 4.55(2H, s), 4.35(0.8H, bs), 4.19-4.22(1H,bs), 3.86(0.8H, dd, J=8.3, 10.0Hz), 3.64(0.2H, bs), 3.50-3.58(1.2H, m), 2.27-2.41(1H, m), 1.97-2.20(3H, m), 1.74-1.82(0.8H, m), 1.61-1.68(0.2H, m), 1.48(0.8H, q, J=10.0Hz),

1.37(0.2H, dt, J=3.2, 11.1Hz), 0.87(2.4H, d, J=7.1Hz), 0.80(0.6H, d, J=7.0Hz); HRMS Found: m/z 284.1757. Calcd for $C_{19}H_{24}O_2$: M, 284.1775.

(1*S*,2*S*,4a*R*,8a*S*)-1-Benzyloxymethyl-1,2,4a,5,8,8a-hexahydro-2-methylnaphthalen-8-one (4). To a CH_2Cl_2 solution (5 ml) of **20** (77 mg, 0.27 mmol) was added pyridinium dichromate (102 mg, 0.27 mmol) at room temperature. After being stirred for 48 h, the mixture was directly purified by column chromatography (silica gel, hexane:ethyl acetate=5:1) to give the title compound **4** (74 mg, 97%). IR(neat) 3020, 2955, 2910, 2870, 1685, 1455, 1370, 1110, 1090, 740, 700 cm^{-1}; ^{1}H-NMR(500MHz) δ=7.30-7.33(4H, m), 7.23-7.26(1H, m), 6.79(1H, ddd, J=2.1, 5.6, 10.0Hz), 5.92(1H, dd, J=2.8, 10.0Hz), 5.74(1H, ddd, J=2.5, 5.1, 9.8Hz), 5.39(1H, dt, J=1.5, 9.8Hz), 4.55(1H, d, J=11.8Hz), 4.45(1H, d, J=11.8Hz), 4.43(1H, dd, J=3.8, 9.5Hz), 3.53(1H, t, J=9.5Hz), 2.51-2.59(2H, m), 2.41-2.47(1H, m), 2.26-2.37(2H, m), 2.09-2.16(1H, m), 0.95(3H, d, J=7.0Hz); $[\alpha]_D^{25}$ +285 (c 1.33, CH_2Cl_2); HRMS Found: m/z 282.1605. Calcd for $C_{19}H_{22}O_2$: M, 282.1618.

(2*S*,4a*S*,5*S*,6*S*,8a*R*)-5-Benzyloxymethyl-1,2,3,4,4a,5,6,8a-octahydro-2,6-dimethylnaphthalen-4-one (23). To an Et_2O suspension (1 ml) of CuI (114 mg, 0.60 mmol) was added dropwise MeLi (0.86 ml, 1.4 M in Et_2O) at -23 °C. The resulting solution was stirred for 20 min and then cooled to -78 °C. An Et_2O solution (3 ml) of **4** (34.0 mg, 0.12 mmol) was added dropwise at -78 °C. After being stirred for 5 min, the mixture was treated with saturated NH_4Cl and inorganic materials were filtered off. The organic materials were extracted with Et_2O and the extracts were washed with brine and dried over Na_2SO_4. After evaporation of the solvent, the crude product was purified by column chromatography (silica gel, hexane:ethyl acetate=5:1) to give **23** (36.1 mg, quant.). IR(neat) 2960, 2920, 2875, 2855, 1710, 1455, 1365, 1100, 1030, 735, 700 cm^{-1}; ^{1}H-NMR(500MHz) δ=7.24-7.29(5H, m), 5.66(1H, ddd, J=2.6, 5.9, 9.8Hz), 5.35(1H, dd, J=1.6, 9.8Hz), 4.49(1H, d, J=11.8Hz), 4.38(1H, d, J=11.8Hz), 3.97(1H, dd, J=3.1, 9.0Hz), 3.41(1H, t, J=9.0Hz), 2.65(1H, dd, J=6.6, 12.0Hz), 2.48-2.51(2H, m), 2.28-2.37(3H, m), 2.05(1H, dt, J=1.9, 12.0Hz), 1.64-1.70(2H, m), 0.97(3H, d, J=7.2Hz), 0.92(3H, d, J=7.0Hz); $[\alpha]_D^{28}$ +188 (c 0.73, CH_2Cl_2); HRMS Found: m/z 298.1936. Calcd for $C_{20}H_{26}O_2$: M, 298.1933.

Assignment of the Stereochemistry of 23. The stereochemistry of **23** was determined by the measurement of 2D NOESY NMR spectrum. The NOEs were observed between Ha and adjacent four protons as shown in the following figure.



23

(2*S*,4*S*,4a*S*,5*S*,6*S*,8a*R*)-5-Benzyloxymethyl-1,2,3,4,4a,5,6,8a-octahydro-2,6-dimethyl-4-naphthol (24). To a THF solution (3 ml) of **23** (36.1 mg, 0.12 mmol) was added a THF solution (1.0 M, 0.18 ml) of $LiBu^s_3BH$ at -78 °C. After being stirred for 10 min, the mixture was treated with 10% aqueous sodium hydroxide (7 ml) and 30% hydrogenperoxide (5 ml) at 0 °C and was stirred for 12 h. The organic materials were extracted with Et_2O. The combined extracts were washed with saturated Na_2SO_3 and brine, and

dried over anhydrous $MgSO_4$. After evaporation of the solvent, the crude product was purified by column chromatography (silica gel, hexane:ethyl acetate=5:1) to give the title product **24** (33.1 mg, 91%). IR(neat) 3215, 2960, 2910, 2875, 1455, 1360, 1260, 1205, 1095, 1065, 1025, 805, 735, 695 cm^{-1}; ^1H-NMR(500MHz) δ=7.27-7.36(5H, m), 5.53(1H, ddd, J=2.7, 4.8, 9.8Hz), 5.38(1H, d, J=9.8Hz), 4.54(1H, d, J=11.7Hz), 4.50(1H, d, J=11.7Hz), 4.04(1H, d, J=2.7Hz), 3.51(1H, d, J=9.0Hz), 3.48(1H, dd, J=2.8, 9.0Hz), 3.38(1H. bs), 2.50(1H, dd, J=10.7, 12.8Hz), 2.29-2.37(1H, m), 2.04-2.10(1H, m), 1.98-2.02(1H, m), 1.83(1H, dd, J=2.3, 14.4Hz), 1.68(1H, ddd, J=3.9, 5.8, 14.4Hz), 1.55(1H, dd, J=2.8, 12.8Hz), 1.28(1H, dt, J=5.1, 13.1Hz), 1.20(3H, d, J=7.4Hz), 1.15(1H, dd, J=2.1, 10.9Hz), 0.79(3H, d, J=7.0Hz); $[\alpha]_D^{25}$ +76 (c 0.57, CH_2Cl_2); HRMS Found: m/z 282.1956. Calcd for $C_{20}H_{28}O_2$: M-H_2O, 282.1983.

(1*S*,2*S*,4a*R*,6*S*,8*S*,8a*S*)-1,2,4a,5,6,7,8,8a-Octahydro-8-hydroxy-2,6-dimethyl-1-naphthalenemethanol (25). To liquid NH_3 (2 ml) was added lithium (5 mg, 0.72 mmol) at -78 °C. After the color changed to blue, a THF solution (2 ml) of **24** (28.4 mg, 0.095 mmol) was added and the mixture was stirred for 2 h. The reaction was quenched with NH_4Cl. The inorganic materials were filtered off and washed with Et_2O. After evaporation of the filtrate, the crude product was purified by column chromatography (silica gel, hexane:ethyl acetate=5:1) to afford **25** (19.9 mg, quant.). mp 118-120 °C; IR(CH_2Cl_2) 3610, 3490, 2960, 2910, 2885, 1460, 1430, 1330, 1230, 1145, 1105, 10205 cm^{-1}; ^1H-NMR(500MHz) δ=5.52(1H, ddd, J=2.7, 4.7, 9.8Hz), 5.36(1H, d, J=9.8Hz), 4.18(1H, d, 3.0Hz), 3.72(1H, t, J=9.6Hz), 3.63(1H, dd, J=2.6, 10.1Hz), 2.48(1H, t, J=10.5Hz), 2.45(1H, bs), 2.33-2.37(1H, m), 1.94-2.03(2H, m), 1.77-1.81(1H, m), 1.73(1H, ddd, J=3.7, 5.7, 14.6Hz), 1.53-1.57(1H, m), 1.28(2H, dt, J=5.1, 13.0Hz), 1.19(3H, d, J=7.4Hz), 1.15-1.18(1H, m), 0.78(3H, d, J=7.0Hz); $[\alpha]_D^{30}$ +149 (c 1.16, $CHCl_3$), lit.[11] $[\alpha]_D$ +152 (c 0.98, $CHCl_3$); HRMS Found: m/z 192.1504. Calcd for $C_{13}H_{22}O_2$: M-H_2O, 192.1514. NMR spectrum agreed with those reported by Hanessian[2g] and Heathcock.[19]

(4*S*,4a*S*,5*S*,6*S*,8a*R*)-5-Benzyloxymethyl-1,2,3,4,4a,5,6,8a-octahydro-6-methyl-4-naphthol (26). To a THF solution (2 ml) of **4** (10.0 mg, 0.035 mmol) was added a THF solution (1.0 M, 0.11 ml) of $LiBu^s{}_3BH$ at -78 °C. After being stirred for 10 min, the mixture was treated with 10% aqueous sodium hydroxide (7 ml) and 30% hydrogen peroxide (5 ml) at 0°C and stirred for 12 h. The organic materials were extracted with Et_2O. The combined extracts were washed with saturated Na_2SO_3 and brine, and dried over anhydrous $MgSO_4$. After evaporation of the solvent, the crude product was purified by column chromatography (silica gel, hexane:ethyl acetate=5:1) to give **26** (7.6 mg, 75%). IR(neat) 3510, 2925, 2900, 2860, 1450, 1365, 1090, 1070, 1030, 990, 730, 700 cm^{-1}; ^1H-NMR(500MHz) δ=7.26-7.37(5H, m), 5.48(1H, ddd, J=2.6, 4.5, 9.8Hz), 5.40(1H, d, J=9.8Hz), 4.55(1H, d, J=11.6Hz), 4.50(1H, d, J=11.6Hz), 4.02(1H, d, J=1.8Hz), 3.53(1H, t, J=9.1Hz), 3.49(1H, dd, J=2.6, 9.1Hz), 3.32(1H, bs), 2.28-2.36(2H, m), 2.02-2.08(1H, m), 1.95(1H, dd, J=2.4, 15.6Hz), 1.68-1.77(2H, m), 1.42-1.54(2H, m), 1.20(1H, dt, J=1.9, 10.8Hz), 0.96-1.04(1H, m), 0.80(3H, d, J=7.1Hz); $[\alpha]_D^{25}$ +71 (c 1.67, CH_2Cl_2); HRMS Found: m/z 286.1931. Calcd for $C_{19}H_{26}O_2$: M, 286.1933.

(1*S*,2*S*,4a*R*,8*S*,8a*S*)-1,2,4a,5,6,7,8,8a-Octahydro-8-hydroxy-2-methyl-1-naphthalenemethanol (27). To liquid NH_3 (2 ml) was added lithium (5 mg, 0.72 mmol) at -78 °C. After the color changed to blue, a THF solution (2 ml) of **26** (25.0 mg, 0.087 mmol) was added and the mixture was stirred for 2 h. The reaction was quenched with NH_4Cl. The inorganic materials were filtered off and washed with Et_2O. After evaporation of the filtrate, the crude product was purified by column chromatography (silica gel, hexane:ethyl acetate=5:1) to afford **27** (17.1 mg, quant.). mp 110-112 °C; IR(CH_2Cl_2) 3610, 3505, 2960,

2930, 2885, 1450, 1250, 1070, 1035, 1005, 720 cm^{-1}; ^1H-NMR(500MHz) δ=5.51(1H, ddd, J=2.7, 4.6, 9.8HZ), 5.40(1H, d, J=9.8Hz), 4.18(1H, s), 3.76(1H, t, J=9.7Hz), 3.65(1H, dd, J=2.5, 10.1Hz), 3.17(1H, bs), 2.92(1H, bs), 2.35-2.37(1H, m), 2.28(1H, dd, J=10.9, 12.3Hz), 1.92-1.99(2H, m), 1.66-1.76(2H, m), 1.51-1.56(2H, m), 1.19-1.25(1H, m), 1.02(1H, dq, J=3.4, 12.5Hz), 0.81(3H, d, J=7.0Hz); $[\alpha]_D^{25}$ +120 (c 1.00, CH_2Cl_2); HRMS Found: m/z 196.1453. Calcd for $C_{12}H_{20}O_2$: M, 196.1463. Chromatographic behavior and spectral data agreed with the racemic authentic sample provided by Prof. J. R. Falck.[12]

Acknowledgment. We would like to thank Prof. J. R. Falck (University of Texas Southwestern Medical Center) for providing us with the authentic sample and spectral data of **27**. We also would like to thank Sankyo Co. for providing us with a sample of (+)-compactin.

Reference

(1) (a) compactin : Endo, A.; Kuroda, M.; Tsujita, Y. *J. Antibiot.* **1976**, 29, 1346. Brown, A. G.; Smale, T. C.; King, T. J.; Hasenkamp, R.; Thompson, R. H. *J. Chem. Soc., Perkin Trans. I* **1976**, 1165. (b) mevinolin : Endo, A. *J. Antibiot.* **1979**, 32, 852. Alberts, A. W.; Chen, J.; Kuron, G.; Hunt, V.; Huff, J.; Hoffman, C.; Rothrock, J.; Lopez, M.; Joshua, H.; Harris, E.; Patchett, A.; Monaghan, R.; Currie, S.; Stapley, E.; Albers-Schonberg, G.; Hensens, O.; Hirshfield, J.; Hoogsteen, K.; Liesch, J.; Springer, J.; *Proc. Natl. Acad. Sci. U. S. A.* **1980**, 77, 3957. (c) dihydrocompactin : Lam, Y. K. *J. Antibiot.* **1980**, 33, 334. (d) dihydromevinolin : Albers-Schonberg, G.; Joshua, M.; Lopez, M. B.; Hensens, O. D.; Springer, J. P.; Chen, J.; Ostrove, S.; Hoffman, C. H.; Alberts, A. W.; Patchett, A. A. *J. Antibiot.* **1981**, 34, 507.

(2) (a) Rosen, T.; Heathcock, C. H. *Tetrahedron* **1986**, 42, 4909. (b) Grieco, P. A.; Lis, R.; Zelle, R. E.; Finn, J. *J. Am. Chem. Soc.* **1986**, 108, 5908. (c) Keck, G. E.; Kachensky, D. F. *J. Org. Chem.* **1986**, 51, 2487. (d) Kozikowski, A. P.; Li, C.-S. *J. Org. Chem.* **1987**, 52, 3541. (e) Wovkulich, P. M.; Tang, P. C.; Chadha, N. K.; Batcho, A. D.; Barrish, J. C.; Uskokovic, M. R. *J. Am. Chem. Soc.* **1989**, 111, 2596. (f) Danishefsky, S. J.; Simoneau, B. *J. Am. Chem. Soc.* **1989**, 111, 2599. (g) Hanessian, S.; Roy, P. J.; Petrini, M.; Hodges, P. J.; Fabio, R. D.; Carganico, G. *J. Org. Chem.* **1990**, 55, 5766. (h) Clive, D. L. J.; Murthy, K. S. K.; Wee, A. G. H.; Prasad, J. S.; da Silva, G. V. J.; Majewski, M.; Anderson, P. C.; Evans, C. F.; Haugen, R. D.; Heerze, L. D.; Barrie, J. R. *J. Am. Chem. Soc.* **1990**, 112, 3018.

(3) Iwasawa, N.; Sugimori, J.; Kawase, Y.; Narasaka, K. *Chem. Lett.* **1989**, 1947.

(4) Narasaka, K.; Iwasawa, N.; Inoue, M.; Yamada, T.; Nakashima, M.; Sugimori, J. *J. Am. Chem. Soc.* **1989**, 111, 5340.

(5) After we devised this two-step procedure, Damon and Coppola reported the same method for the conversion of 3-acyl-1,3-oxazolidin-2-one moiety into hydroxyl group : Damon, R. E.; Coppola, G. M. *Tetrahedron Lett.* **1990**, 31, 2849.

(6) Narasaka, K.; Sakasita, T.; Mukaiyama, T. *Bull. Chem. Soc. Jpn.* **1972**, 45, 3724.

(7) Corey, E. J.; Erickson, B. W. *J. Org. Chem.* **1971**, 36, 3553.

(8) Ito, Y.; Hirao, T.; Saegusa, T. *J. Org. Chem.* **1978**, 43, 1011.

(9) Narasaka, K.; Kusama, H.; Hayashi, Y. *Chem. Lett.* **1991**, 1413.

(10) Luche, J-L. *J. Am. Chem. Soc.* **1978**, 100, 2226.

(11) Davidson, A. H.; Jones, A. J.; Floyd, C. D.; Lewis, C.; Myers, P. L. *J. Chem. Soc., Chem. Commun.* **1987**, 1786.

(12) Yang, Y-L.; Manna, S.; Falck, J. R. *J. Am. Chem. Soc.* **1984**, 106, 3811.

(13) Funk, R. L.; Zeller, W. E. *J. Org. Chem.* **1982**, 47, 180.

(14) Dijkgraaf, C.; Rousseau, J. P. G. *Spectrochim. Acta, Part A* **1968**, 24, 1213.

(15) Mori, K. *Tetrahedron* **1974**, 30, 3807.

(16) Parikh, J. R.; Doering, W. E. *J. Am. Chem. Soc.* **1967**, 89, 5505.

(17) Dale, J. A; Dull, D. L.; Mosher, H. S. *J. Org. Chem.* **1969**, 34, 2543.

(18) Compton, S. J.; Cox, D. D.; Reed, P. E.; Williams, J. M. *Inorg. Synth.* **1989**, 26, 391.

(19) Hecker, S. J.; Heathcock, C. H. *J. Am. Chem. Soc.* **1986**, 108, 4586.