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A Stereocontrolled Synthesis of (4a*S*, 8a*R*)-(+)-7,7-Ethylenedioxy-4,4,8a-trimethyloctahydro-2(1*H*)-naphthalenone

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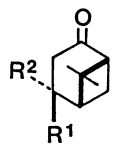
A stereocontrolled synthesis of (4a*S*,8a*R*)-(+)-7,7-ethylenedioxy-4,4,8a-trimethyloctahydro-2(1*H*)- naphthalenone, which will act as a versatile building block for the asymmetric synthesis of natural products possessing a *trans*-1,1,4a-trimethyldecalin unit, was accomplished starting with (1*R*,4*S*,5*R*)-(+)-4,6,6-trimethyl-4-vinylbicyclo[3.1.1]-heptan-2-one, readily accessible from (+)-nopinone.

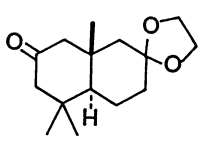
A *trans*-1,1,4a-trimethyldecalin skeleton is found as a structural unit in many classes of natural products,[1] and much attention for the synthesis of natural products possessing this unit has been attracted not only from chemical point of view, but also in inspection of their biological activities at a molecular level.[2] Although a variety of general synthetic routes to this decalin unit and its homologs are known; for examples, the acid-catalyzed cyclization of farnesic acid to give the bicyclofarnesic acid class, and the Robinson annulation with formation of $\Delta^{1,8a}$-4a-methyl-2-octalones followed by introduction of a *gem*-dimethyl grouping,[3] comparatively a few are synthetic ones toward optically active form necessary for the asymmetric synthesis.[4]

We have been studying the asymmetric synthesis using (+)-nopinone (**1**) as a chiral source and recently reported the utility of 4,4-disubstituted nopinones[5] toward natural product synthesis in which the chemical transformation of (1*R*,4*S*,5*R*)-(+)-4,6,6-trimethyl-4-vinylbicyclo[3.1.1]heptan-2-one (**2**) into (+)-β-elemenone and (+)-eleman-8β,12-olide was included.[5] The compound **2** is obtainable in large quantities in four steps and 81% overall yield from **1**. We wish to describe herein that the compound **2** is valuable as a chiral key-intermediate not only for the elemanoid sesquiterpene synthesis, but also for the synthesis of (4a*S*,8a*R*)-(+)-7,7-ethylenedioxy-4,4,8a-trimethyloctahydro-2(1*H*)-naphthalenone (**3**) which will serve as a promising chiral building block for the synthesis of natural products possessing a *trans*-1,1,4a-trimethyldecalin unit. A carbonyl group generally plays an important part for the introduction of a variety of substituents in a molecule. Two kinds of the oxygen functions in **3**; a ketone group in the A ring and an ethylenedioxy group, a protective form of the former, in the B ring are convenient for further chemical manipulation of both rings by a stepwise mode.



1 $R^1 = R^2 = H$

2 $R^1 = Me, R^2 = CH{=}CH_2$



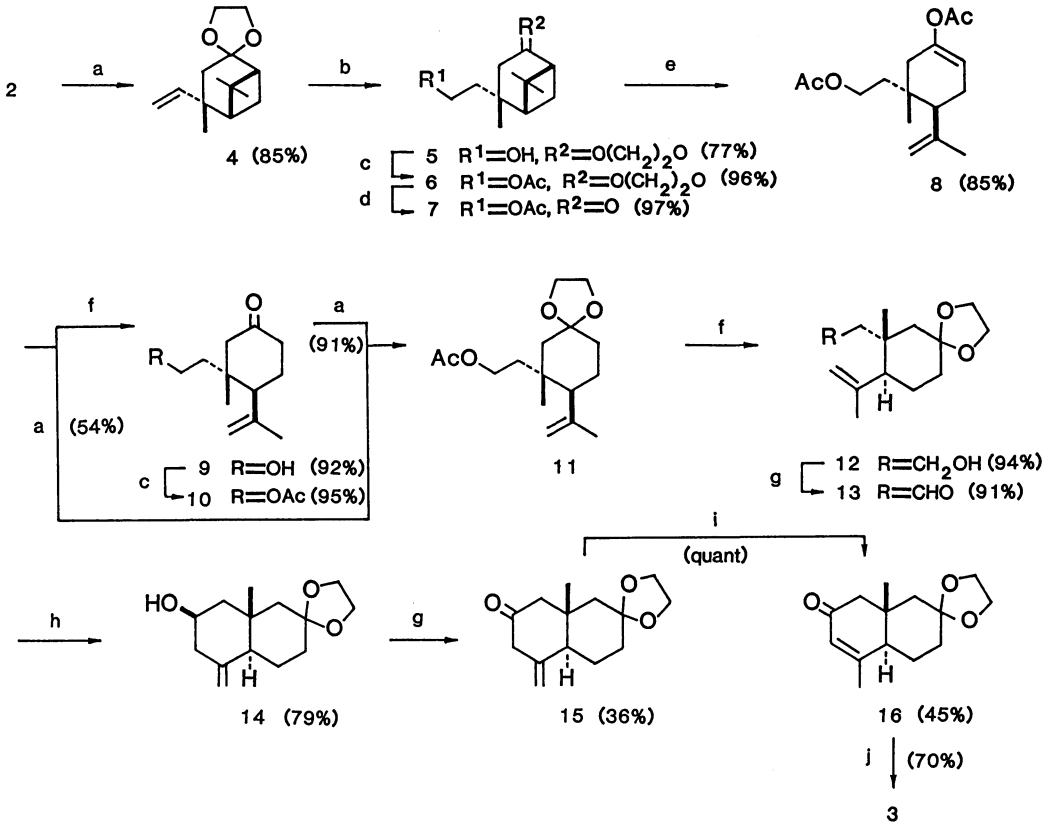
3

Results and Discussion

To prepare 4-(2-acetoxyethyl)-4-methylnopinone (**7**), the compound **2** was subjected to acetalization by the standard procedures, giving the acetal **4**, which was then converted to the acetoxy ketone **7** in good overall yield by a sequence of conventional reactions; (1) hydroboration with 9-borabicyclo[3.3.1]nonane (9-BBN) followed by oxidation with 30% H_2O_2, leading to the alcohol **5**, (2) acetylation of **5**, and (3) acid-catalyzed exchange dioxolanation of the resulting acetate **6** with acetone to afford **7** (Scheme 1). Cyclobutane cleavage of the compound **7** was carried out next. We have confirmed the combined reagent, boron trifluoride etherate ($BF_3 \cdot OEt_2$)/zinc acetate/acetic anhydride,[6] to be suitable for the regioselective cyclobutane-opening of nopinone derivatives with little loss of optical integrity. In fact, BF_3-promoted cyclobutane cleavage of **7** proceeded smoothly in regio- and diastereoselective fashion to give the expected enol acetate **8**, $[\alpha]_D^{20}$ −17.3° ($CHCl_3$), in 85% yield.

To transform the compound **8** into the known aldehyde **13**,[7] **8** was first converted to the acetoxy ketone **10** by hydrolysis followed by acetylation of the resulting alcohol **9**. Subsequent acetalization of **10** gave acetoxy acetal **11** in 80% overall yield from **8**. Attempted direct transformation of **8** to **11** by treatment with ethylene glycol and *p*-toluenesulfonic acid in refluxing benzene resulted in disappointing 54% yield. Hydrolysis of the acetoxy group in **11** followed by Swern oxidation of the resulting alcohol **12** provided the aldehyde **13**[7] in 88 and 42% overall yield from **11** and **2**, respectively.

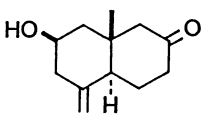
On the way to the synthesis of (+)-ivalin, Koga and co-workers reported that the stereoselective ene reaction of the aldehyde **13** with tin(IV) chloride resulted in



Scheme 1. (a) ethylene glycol, *p*-TsOH, PhH; (b) 9-BBN, THF, then 30% H_2O_2, 3 M NaOH; (c) Ac_2O, Py; (d) *p*-TsOH, acetone; (e) $BF_3 \cdot OEt_2$, $Zn(OAc)_2$, Ac_2O, r.t., 4 d; (f) K_2CO_3, MeOH; (g) $(COCl)_2$, DMSO, CH_2Cl_2, then Et_3N; (h) Et_3AlCl, CH_2Cl_2, 0 °C; (i) DBU, CH_2Cl_2; (j) Me_2CuLi, THF, 0 °C.

concomitant deprotection of the acetal function to give the hydroxy ketone **17** in 61% yield.[7] After trials to establish the optimum conditions wherein the acetal group remains unchanged, it was found that exposure of **13** upon diethylaluminium chloride in CH_2Cl_2 underwent the ene reaction smoothly and cleanly to afford 79% yield of hydroxy acetal **14**, $[\alpha]_D^{20}$ +42.4° ($CHCl_3$), as the sole product. It can be assumed that this ene reaction proceeds predominantly via the six-membered transition state with chair conformation to give the *trans*-decalin with an axially oriented hydroxyl group. In fact, the ^1H NMR spectrum of **14** shows an absorption due to the C-2 proton at δ=4.18 as a multiplet with half band width (11 Hz), indicating our consideration correct.

Mild acid-catalyzed exchange dioxolanation of **14** with acetone afforded the hydroxy ketone **17** whose optical rotation, $[\alpha]_D^{15}$ −9.4° ($CHCl_3$), is almost identical with that, $[\alpha]_D^{20}$ −10.0° ($CHCl_3$), of the reported **17**.[7,8]



17

Swern oxidation of the compound **14** provided a mixture of the deconjugated enone **15**, $[\alpha]_D^{16}$ +109.6° ($CHCl_3$), and conjugated enone **16**, $[\alpha]_D^{16}$ +97.3° ($CHCl_3$), in 81% yield (a 1 : 1.3 ratio), which is separable by column chromatography on silica gel. Double bond isomerization of the former was attained by treatment with DBU in CH_2Cl_2, providing the latter quantitatively. Finally, conjugate addition of **16** with lithium dimethylcuprate in ether gave our target molecule (+)-**3** as crystals, $[\alpha]_D^{20}$ +43.1° ($CHCl_3$), in 52 and 23% overall yield from **13** and **2**, respectively.

Although the overall yield of the target molecule seems not necessarily desirable, the synthetic methodology employed here is practically useful for the laboratory scale preparation of not only (+)-enantiomer **3**, but also (−)-enantiomer **3** which may be obtainable when this synthesis begins with (−)-enantiomer **2**. The preparation of (−)-enantiomer **2** from (+)-nopinone (**1**) via (1*S*)-(−)-verbenone will be published in due course. In addition, the compounds, alcohol **14** and conjugated enone **16** obtained in 41 and 33% overall yields from **2**, respectively, are also utilizable as the chiral key-intermediates for the synthesis of natural products possessing *trans*-4a-methyl-1-methylenedecalin and *trans*-1,4a-dimethyldecalin units, respectively.

Experimental

Melting points are uncorrected. IR spectra were obtained with a JASCO IR/FT-8300 spectrophotometer. ^{1}H NMR spectra were recorded on a JEOL FX90Q spectrometer. All reactions were carried out under N_2 or Ar atmosphere with use of standard procedures for exclusion of moisture. Extracts obtained on aqueous workup of the reaction mixtures were washed successively with water and brine, and dried over $MgSO_4$, unless otherwise stated. Column chromatography was performed by using silica gel (Merck, Kieselgel 60, 70—230 mesh). Solvents for elution are shown in parentheses.

(1*R*,4*S*,5*R*)-(+)-4,6,6-Trimethyl-4-vinylbicyclo[3.1.1]heptan-2-one (2).[5] This ketone was prepared according to our synthetic procedures, starting from (+)-nopinone of 92% ee.

(1*R*,4*S*,5*R*)-4,6,6-Trimethyl-4-vinylbicyclo[3.1.1]heptan-2-one Ethylene Acetal (4). A solution of (+)-**2**[5] (751 mg, 4.21 mmol), ethylene glycol (2.4 ml, 42.1 mmol), and *p*-toluenesulfonic acid (10 mg) in benzene (30 ml) was refluxed azeotropically for 13 h, cooled to room temperature, and washed successively with aqueous $NaHCO_3$, water and brine, and dried. Evaporation followed by chromatography of an oily residue on silica gel (hexane–AcOEt, 15 : 1) gave **4** (796 mg, 85%) as an oil: $[\alpha]_D^{22}$ +39.2° (*c* 1.64, $CHCl_3$); IR ($CHCl_3$) 3080(vw), 1640(w), 1100, and 920 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.10, 1.17 and 1.27 (3 H, s each, 3 CH_3), 1.38—2.30 (4H, m), 2.01 and 2.32 (2 H in total, d each, *J*=15.5 Hz, $OCC\underline{H}_2CCH_3$), 3.86 (4 H, m, OCH_2CH_2O), 4.83—5.05 (2 H, m, $CH{=}C\underline{H}_2$), and 5.72 (1 H, dd, *J*=18.0 and 10.8 Hz, $C\underline{H}{=}CH_2$).

Found: C, 75.38; H, 10.03%. Calcd for $C_{14}H_{22}O_2$: C, 75.63; H, 9.98%.

(1*R*,4*R*,5*R*)-4-(2-Hydroxyethyl)-4,6,6-trimethylbicyclo[3.1.1]heptan-2-one Ethylene Acetal (5). To a stirred solution of **4** (1.08 g, 4.85 mmol) in THF (15 ml) was added dropwise at 0 °C a solution of 0.5 M 9-BBN (1 M=1 mol dm^{-3}) in THF (2.91 ml, 14.56 mmol). After stirring for 30 min, stirring was continued for an additional 17 h at room temperature, and the reaction mixture was recooled to 0 °C. Water (2 ml) was added dropwise with stirring, and then 3 M NaOH (5 ml) and 30% H_2O_2 (5 ml) were added successively. After stirring for 30 min, the reaction mixture was stirred at room temperature for an additional 6 h. The product was extracted with a mixed solvent (ether–CH_2Cl_2, 3 : 1), and an oily residue obtained by evaporation of the extract was chromatographed on silica gel (hexane–AcOEt, 2 : 1) to give **5** (896 mg, 77%) as an oil: $[\alpha]_D^{20}$ −4.9° (*c* 0.71, $CHCl_3$); IR ($CHCl_3$) 3600, 3450(br), and 1100 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.05, 1.10, and 1.28 (3 H, s each, 3 CH_3), 1.40—2.42 (9 H, m), 3.63 (2 H, t, *J*=7.6 Hz, $C\underline{H}_2OH$), and 3.92 (4 H, m, OCH_2CH_2O).

Found: *m/z* 240.1726. Calcd for $C_{14}H_{24}O_3$: M, 240.1724.

(1*R*,4*R*,5*R*)-4-(2-Acetoxyethyl)-4,6,6-trimethylbicyclo[3.1.1]heptan-2-one Ethylene Acetal (6). A mixture of **5** (1.00 g, 4.16 mmol), acetic anhydride (4 ml), and pyridine (4 ml) was stirred at room temperature for 10 h. To the reaction mixture was added at 0 °C methanol (4 ml) and stirring was continued for an additional 1 h at room temperature. Water was added and the product was extracted with a mixed solvent (ether–CH_2Cl_2, 3 : 1). Evaporation of the extract followed by purification of an oily residue by column chromatography on silica gel (hexane–AcOEt 4 : 1) gave **6** (1.13 g, 96%) as an oil: $[\alpha]_D^{19}$ +2.5° (*c* 1.01, $CHCl_3$); IR ($CHCl_3$) 1730, 1260, and 1100 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.07, 1.12, and 1.28 (3 H, s each, 3 CH_3), 1.4—2.4 (8 H, m), 2.02 (3 H, s, $COCH_3$), 3.85 (4 H, m, OCH_2CH_2O), and 4.03 (2 H, t, *J*=7.2 Hz, CH_2O).

Found: *m/z* 282.1826. Calcd for $C_{16}H_{26}O_4$: M, 282.1830.

(1*R*,4*R*,5*R*)-4-(2-Acetoxyethyl)-4,6,6-trimethylbicyclo[3.1.1]heptan-2-one (7). A mixture of **6** (51 mg, 0.18 mmol), *p*-toluenesulfonic acid (5 mg), and acetone (2 ml) was stirred at room temperature for 4 h and diluted with water. Extraction with ether followed by evaporation left an oily residue, which was chromatographed on silica gel (hexane–AcOEt, 4 : 1) to give **7** (40 mg, 93%) as crystals: Mp 43—44 °C (ether–hexane); $[\alpha]_D^{17}$ +39.5° (*c* 1.63, $CHCl_3$); IR ($CHCl_3$) 1740, 1700, and 1200 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.01, 1.20, and 1.38 (3 H, s each, 3 CH_3), 1.5—2.1 (4 H, m), 2.03 (3 H, s, $COCH_3$), 2.38—2.63 (4 H, m), and 4.12 (2 H, t, *J*=7.2 Hz, CH_2O).

Found: C, 70.47; H, 9.28%. Calcd for $C_{14}H_{22}O_3$: C, 70.55; H, 9.31%.

(4*S*,5*R*)-1-Acetoxy-5-(2-acetoxyethyl)-4-isopropenyl-5-methyl-1-cyclohexene (8). A mixture of **7** (445 mg, 1.86 mmol), freshly distilled $BF_3 \cdot OEt_2$ (96 μl, 0.78 mmol), zinc acetate (343 mg, 1.86 mmol), and acetic anhydride (11 ml) was stirred at room temperature for 4 d. Methanol (10 ml) was added and stirring was continued at room temperature for an additional 2 h. Water was added and the product was extracted with ether. The combined extracts were washed successively with aqueous $NaHCO_3$, water, and brine, and dried. Evaporation of the extract left an oily residue, which was chromatographed on silica gel (hexane–AcOEt, 6 : 1) to give the unreacted **7** (32 mg) and **8** (412 mg, 79%; 85% based on consumed **7**) as an oil: $[\alpha]_D^{20}$ −17.3° (*c* 1.12, $CHCl_3$); IR ($CHCl_3$) 1740, 1640(w), 1235, 1015, and 900 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.01 (3 H, s, CH_3), 1.77 (3 H, br s, $=CCH_3$), 2.03 and 2.12 (3 H, s each, 2 $COCH_3$), 1.6—2.3 (7 H, m), 4.17 (2 H, t, *J*=7.2 Hz, OCH_2), 4.88 (2 H, br m, $=CH_2$), and 5.38 (1 H, br s, $=CH-$).

Found: C, 68.54; H, 8.76%. Calcd for $C_{16}H_{24}O_4$: C, 68.54; H, 8.63%.

(3*R*,4*S*)-3-(2-Hydroxyethyl)-4-isopropenyl-3-methylcyclohexanone (9). A mixture of **8** (907 mg, 3.23 mmol), K_2CO_3 (1.07 g, 7.77 mmol), and methanol (15 ml) was stirred at 0 °C for 1 h, and then at room temperature for an additional 1 h. The solvent was mostly removed under reduced pressure, water was added, and the product was extracted with ether. Evaporation followed by purification by chromatography on silica gel (hexane–AcOEt; 1 : 1) gave **9** (583 mg, 93%) as an oil: $[\alpha]_D^{20}$ −8.1° (*c* 0.66, $CHCl_3$); IR ($CHCl_3$) 3600(w), 3500(br), 1710, 1640(w), 1230, and 910 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=0.97 (3 H, s, CH_3), 1.25 (1 H, br s, OH), 1.6—2.58 (9 H, m), 1.80 (3 H, br s, $=CCH_3$), 3.75 (2 H, m, CH_2O), and 4.80 and 4.98 (1 H, br s each, $=CH_2$).

Found: *m/z* 196.1444. Calcd for $C_{12}H_{20}O_2$: M, 196.1462.

(3*R*,4*S*)-3-(2-Acetoxyethyl)-4-isopropenyl-3-methylcyclohexanone (10). A mixture of **9** (583 mg, 2.97 mmol), acetic anhydride (1 ml), and pyridine (2 ml) was stirred at room temperature for 12 h and diluted with water. The product was extracted with a mixed solvent (ether–CH_2Cl_2, 3 : 1) and the combined extracts were washed successively with aqueous $NaHCO_3$, aqueous $CuSO_4$, water and brine, and dried. Removal of the solvent left an oily residue, which was chromatographed on silica gel (hexane–AcOEt, 4 : 1) to give **10** (669 mg, 95%) as an oil: $[\alpha]_D^{17}$ −3.1° (*c* 0.56, $CHCl_3$); IR ($CHCl_3$) 3070(vw), 1730, 1710, 1640, 1250, 1135, and 900 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=0.98 (3 H, s, CH_3), 1.80 (3 H, br s,

=CCH_3), 1.6—2.58 (9 H, m), 2.02 (3 H, s, $COCH_3$), 4.16 (2 H, t, J=7.2 Hz, CH_2O), and 4.80 and 4.97 (1 H, br s each, =CH_2).

Found: m/z 238.1577. Calcd for $C_{14}H_{22}O_3$: M, 238.1568.

(3*R*,4*S*)-3-(2-Acetoxyethyl)-4-isopropenyl-3-methylcyclohexanone Ethylene Acetal (11). According to the procedure for the preparation of **4**, treatment of **10** (273 mg, 1.14 mmol) with ethylene glycol (711 mg, 11.4 mmol) and a catalytic amount of *p*-toluenesulfonic acid in benzene provided **11** (294 mg, 91%) as an oil: $[\alpha]_D^{17}$ −5.30° (*c* 0.50, $CHCl_3$); IR ($CHCl_3$) 3080(vw), 1730, 1640(w), and 1250 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.05 (3 H, s, CH_3), 1.76 (3 H, br s, =CCH_3), 1.4—2.1 (9 H, m), 2.03 (3 H, s, $COCH_3$), 3.93 (4 H, m, OCH_2CH_2O), 4.14 (2 H, t, J=7.2 Hz, CH_2O), and 4.71 and 4.90 (1 H, br s each, =CH_2).

Found: m/z 282.1821. Calcd for $C_{16}H_{26}O_4$: M, 282.1830.

(3*R*,4*S*)-4-Isopropenyl-3-(2-hydroxyethyl)-3-methylcyclohexanone Ethylene Acetal (12). According to the procedure described for the preparation of **9**, treatment of **11** (294 mg, 1.05 mmol) with K_2CO_3 (288 mg, 2.07 mmol) in methanol (10 ml) gave **12** (234 mg, 84%) as an oil: $[\alpha]_D^{20}$ −3.8° (*c* 0.56, $CHCl_3$); IR ($CHCl_3$) 3600(w) , 2450(br), 1650(w), 1100, and 900 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.02 (3 H, s, CH_3), 1.75 (3 H, s with fine splittings, =CCH_3), 1.2—2.0 (10 H, m), 3.75 (2 H, m, CH_2O), 3.92 (4 H, m, OCH_2CH_2O), and 4.71 and 4.85 (1 H, br s each, =CH_2).

Found: m/z 240.1792. Calcd for $C_{14}H_{24}O_3$: M, 240.1724.

(1*R*,2*S*)-3,3-Ethylenedioxy-6-isopropenyl-1-methylcyclohexeneacetaldehyde (13). To a stirred solution of oxalyl dichloride (0.28 ml, 2.88 mmol) in CH_2Cl_2 (8 ml) was added at −78 °C a solution of dimethyl sulfoxide (0.41 ml, 5.76 mmol) in CH_2Cl_2 (9 ml). After stirring for 10 min, a solution of **12** (346 mg, 1.44 mmol) in CH_2Cl_2 (8 ml) was added dropwise and the resulting mixture was stirred at −78 °C for 45 min. Triethylamine (1.0 ml, 7.2 mmol) was added, and stirring was continued for 10 min, and then at room temperature for 1 h. The reaction mixture was diluted with a mixed solvent (hexane–ether, 1 : 1) and washed successively with water and brine, and dried. Evaporation followed by purification by chromatography on silica gel (hexane–AcOEt, 1 : 1) gave **13** (313 mg, 91%) as an oil: IR ($CHCl_3$) 3080(vw), 1707, and 1100 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.20 (3 H, s, CH_3), 1.75 (3 H, br s, =CCH_3), 1.4—2.4 (7 H, m), 2.23 and 2.48 (2 H in total, dd, J=15.0 and 3.5 Hz, $C\underline{H}_2CHO$), 3.94 (4 H, m, OCH_2CH_2O), 4.75 and 4.93 (1 H, br s each, =CH_2), and 9.85 (1 H, t, J=3.5 Hz, CHO).

The compound **13** was used for the next reaction without further purification because of instability on heating.

(2*R*,4a*S*,8a*R*)-7,7-Ethylenedioxy-8a-methyl-4-methylenedecahydro-2-naphthol (14). To a stirred solution of **13** (313 mg, 1.31 mmol) in CH_2Cl_2 (14 ml) was added dropwise at 0 °C over a period of 13 min, a solution of 1.0 M diethylaluminium chloride in toluene (1.31 ml, 1.31 mmol) and stirring was continued for an additional 20 min. The reaction mixture was quenched by addition of aqueous NH_4Cl and the product was extracted with ether. Evaporation followed by purification of an oily residue by chromatography on silica gel (hexane–AcOEt, 1 : 1) gave **14** (248 mg, 79%) as crystals: Mp 93—94 °C (ether–hexane); $[\alpha]_D^{20}$ +42.4° (*c* 0.89, $CHCl_3$); IR ($CHCl_3$) 3600, 3450(br), 3080(vw), 1650(vw), and 1100 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.10 (3 H, s, CH_3), 1.2—2.1 (10 H, m), 2.39 (2 H, br s, CH_2CO), 3.90 (4 H, m, OCH_2CH_2O), 4.18 (1 H, m, half band width; 11 Hz, $C\underline{H}OH$), and 4.68 and 4.91 (1 H, br s each, =CH_2).

Found: C, 70.47; H, 9.43%. Calcd for $C_{14}H_{22}O_3$: C, 70.55; H, 9.31%.

(4a*S*,7*R*,8a*R*)-7-Hydroxy-8a-methyl-5-methyleneoctahydro-2(1*H*)-naphthalenone (17).[7] According to the procedure for the preparation of **7**, exchange dioxolanation of **14** (120 mg, 0.5 mmol) with acetone gave **17** (96 mg, quant) as crystals: Mp 95—96 °C (ether–hexane) (lit,[7] mp 100—103 °C); $[\alpha]_D^{15}$ −9.4° (*c* 1.00, $CHCl_3$) (lit,[7] $[\alpha]_D^{20}$ −10.0°, $CHCl_3$); IR ($CHCl_3$) 3610, 3470, 3080(vw), 1705, 1651, 1027, and 902 cm^{-1}; ^1H NMR ($CDCl_3$) δ=0.92 (3 H, s), 1.54 (1 H, br s, OH), 1.65—2.55 (11 H, m), 4.20 (1 H, m, half band width, 11 Hz), and 4.78 and 5.01 (1 H, br s each).

(4a*S*,8a*R*)-7,7-Ethylenedioxy-8a-methyl-4-methyleneoctahydro-2(1*H*)-naphthalenone (15) and (4a*R*,8a*R*)-7,7-Ethylenedioxy-4,8a-dimethyl-4a,5,6,7,8,8a-hexahydro-2(1*H*)-naphthalenone (16). According to the procedure described for the preparation of **13**, **14** (303 mg, 1.27 mmol) was treated with oxalyl dichloride (0.24 ml, 2.54 mmol) and dimethyl sulfoxide (0.36 ml, 5.08 mmol) in CH_2Cl_2 (13 ml) followed by triethylamine (0.89 ml, 6.36 mmol) to give a mixture of **15** (109 mg, 36%) and **16** (134 mg, 45%) which was separable by chromatography on silica gel (hexane–AcOEt, 1 : 1). Analytically pure samples were obtained by use of preparative medium pressure-LC (Kusano Kagaku KHLC-201-32 system packed with silica gel) (hexane–AcOEt, 1 : 1).

15: An oil; $[\alpha]_D^{16}$ +109.6° (*c* 0.91, $CHCl_3$); IR ($CHCl_3$) 3080(vw), 1710, 1650(w), 1230, 1080, and 900 cm^{-1}; ^1H NMR ($CDCl_3$) δ=0.82 (3 H, s, CH_3), 1.5—2.05 (7 H, m), 2.24 (2 H, br s, CH_2CO), 3.10 (2 H, br s, =CH_2CO), 3.93 (4 H, m, OCH_2CH_2O), and 4.07 and 4.85 (1 H, s with fine splittings, =CH_2).

Found: C, 71.18; H, 8.52%. Calcd for $C_{14}H_{20}O_3$: C, 71.16; H, 8.53%.

16: Crystals; mp 83—84 °C (ether–hexane); $[\alpha]_D^{16}$ +97.3° (*c* 0.66, $CHCl_3$), IR ($CHCl_3$) 1660, 1620, and 1090 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.04 (3 H, s, CH_3), 1.93 (3 H, s with fine splittings, =CCH_3), 1.4—2.1 (9 H, m), 2.23 (2 H, br s, CH_2CO), 3.93 (4 H, m, OCH_2CH_2O), and 5.90 (1 H, br s, =CH).

Found: C, 71.45; H, 8.67%. Calcd for $C_{14}H_{20}O_3$: C, 71.16; H, 8.53%.

Isomerization of 15. A mixture of **15** (31 mg, 0.13 mmol) and DBU (32 mg, 0.21 mmol) in CH_2Cl_2 (1 ml) was stirred at room temperature for 2 h. Workup followed by filtration of an oily residue through a short silica-gel column (hexane–AcOEt, 1 : 1) gave **16** (30 mg, quant) whose IR and ^1H NMR spectra were identical with those of the authentic sample.

(4a*S*,8a*R*)-7,7-Ethylenedioxy-4,4,8a-trimethyloctahydro-2(1*H*)-naphthalenone (3). To a stirred mixture of copper(I) iodide (670 mg, 4.48 mmol) in ether (10 ml) was added dropwise at −30 °C a solution of 1.1 M MeLi in ether (8.1 ml, 8.96 mmol), and the resulting mixture was stirred at 0 °C for 1 h. To this solution was added a solution of **16** (264 mg, 1.12 mmol) in ether (5 ml) and stirring was continued at 0 °C for an additional 3 h. The reaction mixture was quenched by addition of aqueous NH_4Cl and the product was extracted with ether. Evaporation of the extract followed by purification of a residue on silica gel (hexane–AcOEt, 1 : 1) gave **3** (196 mg, 70%) as crystals: Mp 108—109 °C (ether–hexane); $[\alpha]_D^{20}$ +43.1° (*c* 0.34, $CHCl_3$); IR ($CHCl_3$) 1705 and 1100 cm^{-1}; ^1H NMR ($CDCl_3$) δ=0.88, 1.04, and 1.08 (3 H, s each, 3 CH_3), 1.4—2.1 (7 H, m), 2.18—2.28 (4 H, m, CH_2COCH_2), and 3.90 (4 H, m, OCH_2CH_2O).

Found: C, 71.32; H, 9.73%. Calcd for $C_{15}H_{24}O_3$: C, 71.39; H, 9.59%.

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8) The optical purity of the reported **17** is presumed to be in 95% ee. See Ref. 7.