Enantioselective Synthesis of Cyclohexenone Derivatives by a Chemicoenzymatic Approach: Stereo- and Regioselective Route to Potential Intermediates of Compactin (ML 236B) and Mevinolin

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As a synthetic application of the chiral monoester 2, prepared by pig liver esterase (PLE)-catalyzed hydrolysis of the corresponding *meso* diester 1, conversion of 2 into various cyclohexenone derivatives was examined. This paper describes the preparation of the isomeric cyclohexenones 6 and 7, potential intermediates for the synthesis of anti-hypercholesmic compactin (ML 236B) and mevinolin, under stereo- and regioselective control.

Keywords pig liver esterase; compactin; ML 236B; mevinolin; cyclohexenone derivative

The chiral monoester **2** is now easily available on a multihundred gram scale by pig liver esterase (PLE)-catalyzed hydrolysis of the *meso* diester **1**.[1] Various functionalizations of this cyclohexane ring are possible by utilizing the carboxyl group, methoxycarbonyl group and carbon–carbon double bond in **2**.

Indeed, we have demonstrated the usefulness of the monoester **2** as a chiral synthon by the successful synthesis of fortamine **3**,[2] the aminocyclitol moiety of the deoxyaminoglycoside antibiotic fortimicin A, and key intermediates **4** and **5** to thienamycin[3] and 1β-methyl carbapenem,[4] respectively. The synthesis of brefeldin A was also reported independently by Gais *et al.*[5]

During the course of our synthetic effort to obtain potential intermediates for biologically interesting compounds, we extensively investigated the conversion of the monoester **2** into various cyclohexenone derivatives. In this context, we first studied the conversion of **2** into the isomeric cyclohexenones **6** and **7**. The cyclohexenone **6** and the trimethylsilyl derivative of **7** in racemic form have already been reported by Heathcock *et al.*[6] and Clive *et al.*,[7] respectively, and these were used for the synthesis of anti-hypercholesmic compactin[8] (ML 236B) and mevinolin.[9] This paper describes the preparation of **6** and **7** under complete stereo- and regiochemical control.

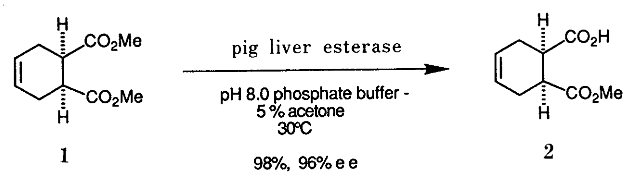

Chart 1

fortamine (3)

4 : R=H
5 : R=Me

Chart 2

Results

Synthetic routes to **6** and **7** from **2** were found rather straightforward. In both cases, the carboxyl and the methoxycarbonyl group in **2** were eventually reduced to hydroxylmethyl and methyl groups, respectively. Since the chiral monoester **2** has a double bond at the γ-position from the carboxylic acid (or ester), the enone group seemed to be most easily accessible by a sequence of reactions involving halolactonization, elimination and oxidation. Therefore, suitable differentiation between the methoxycarbonyl and the carboxyl groups in **2** was most important in the present approach.

Preparation of the Enone 6 For the direct preparation of the chiral cyclohexenone **6**, it was necessary to hydrolyze the methoxycarbonyl group in **2** without disturbing the absolute configuration and to utilize the resulting carboxylate as an internal nucleophile in halolactonization. Two approaches were carefully examined. The first approach is shown in Chart 4, involving protection of the

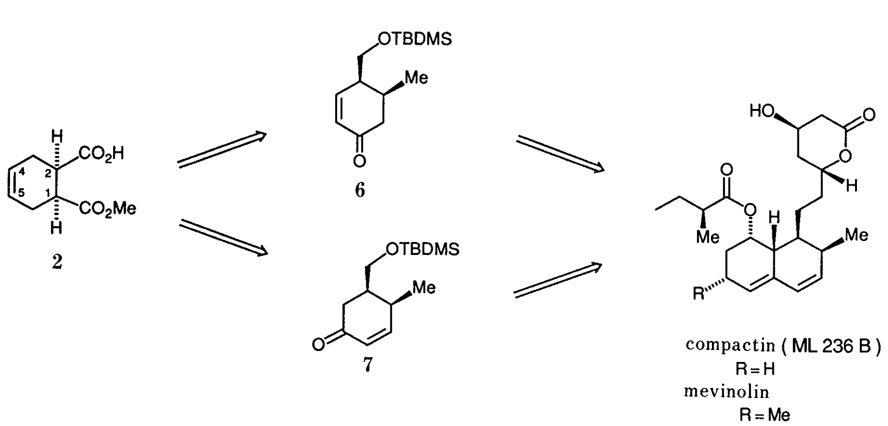

Chart 3

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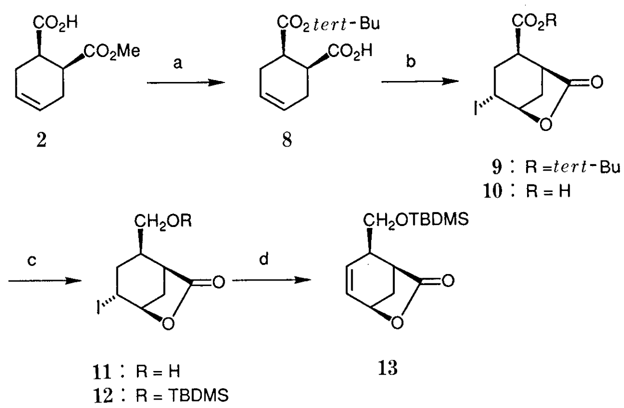
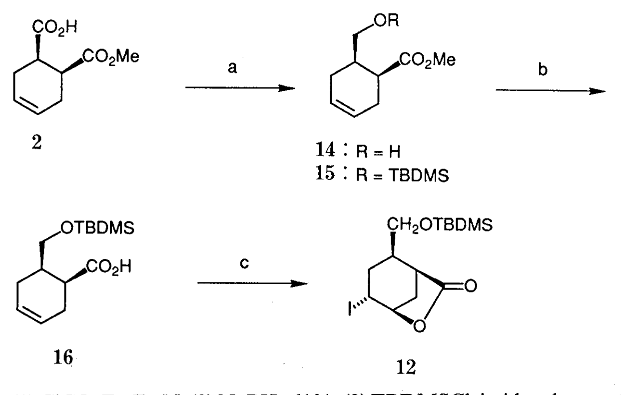
original carboxylate as the *tert*-butyl ester at the beginning. Thus, the chiral monoester **2** was first converted to the *tert*-butyl monoester with isobutene in the presence of concentrated H_2SO_4 followed by basic hydrolysis to afford **8**[1] in excellent yield (2 steps, 94%). Such an ester exchange can be regarded as a formal enantiomer conversion characteristic of the chemicoenzymatic approach. Then, the resulting monoester **8** was subjected to iodolactonization to afford the iodolactone **9**. Treatment of the crude iodolactone with trifluoroacetic acid at 0 °C resulted in the hydrolysis of the *tert*-butyl ester to give the carboxylic acid **10** in 91% overall yield. The acid **10** was reduced to the alcohol **11** *via* the mixed anhydride ((1) $ClCO_2Et$, Et_3N/tetrahydrofuran (THF), −78 °C; (2) $NaBH_4$/THF–H_2O, 0 °C, 82%), and the resulting primary hydroxyl group was protected as the *tert*-butyldimethylsilyl ether (TBDMSCl (*tert*-butyldimethylsilyl chloride), imidazole/dimethylformamide (DMF), 0 °C, quant.) to afford **12** in 82% yield from **10** (7 steps from **2**). Dehydroiodination of **12** proceeded very cleanly by treatment with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) (toluene, reflux), and the olefinic lactone **13** was obtained in 95% yield.

The alternative route to the iodolactone **12** is shown in Chart 5. In this route, the carboxylate was initially reduced



a: (1) isobutene, H^+; (2) OH^- 94% (2 steps)
b: (1) I_2, KI, $NaHCO_3$; (2) CF_3CO_2H 91% (2 steps)
c: (1) $ClCO_2Et$, Et_3N; (2) $NaBH_4$ 82% (2 steps); (3) TBDMSCl, imidazole quant.
d: DBU 95%

Chart 4



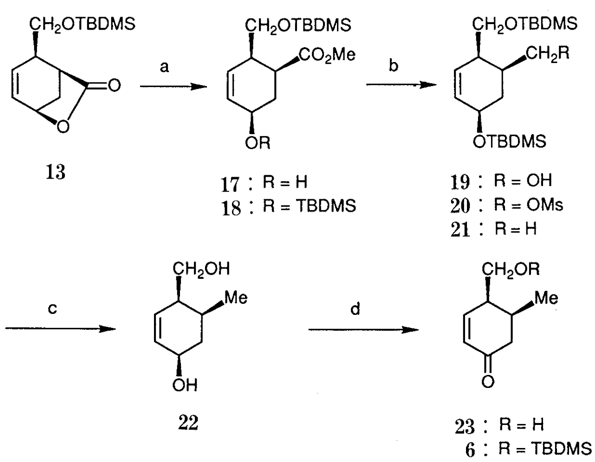
a: (1) $ClCO_2Et$, Et_3N; (2) $NaBH_4$ 61%; (3) TBDMSCl, imidazole quant.
b: NaOH 68%
c: (1) I_2, KI, $NaHCO_3$ 48%

Chart 5

to the corresponding alcohol. Thus, the chiral monoester **2** was converted to the methyl ester **15** in 61% overall yield through the hydroxy ester **14** ((1) $ClCO_2Et$, Et_3N/THF, −78 °C; (2) $NaBH_4$/THF–H_2O, 0 °C; (3) TBDMSCl, imidazole/DMF, 0 °C). After hydrolysis of the methyl ester (NaOH/MeOH–H_2O, room temperature), the resulting olefinic acid **16** was reacted with iodine and potassium iodide under alkaline conditions ($NaHCO_3$/H_2O–CH_2Cl_2) to obtain the iodolactone **12**. Although the yields in the steps were not optimized, the chiral monoester was converted to the iodolactone **12** in only 4 steps.

The remaining transformation from the lactone **13** to the cyclohexenone **6** required the reduction of the lactone carbonyl to a methyl group and oxidation of the lactone hydroxyl group to a ketone. Chart 6 shows the preparation of **6** from **13**. The olefinic lactone **13** was cleaved to the hydroxy ester **17** in quantitative yield (NaOMe/MeOH, 0 °C), and the allylic hydroxyl group was protected as the *tert*-butyldimethylsilyl ether (TBDMSCl, imidazole/DMF, 0 °C) to give **18**. Reduction of the methoxycarbonyl group to the methyl group was carried out through the primary alcohol **19** and the mesylate **20** in 69% overall yield ((1) DIBAL (diisobutylaluminum hydride)/toluene, 0 °C, 80%; (2) MsCl pyridine, 0 °C; (3) $LiBEt_3H$/THF, room temperature, 86% (2 steps)). The *tert*-butyldimethylsilyl ether was deprotected to the diol **22** (40% aqueous HF/CH_3CN, 0 °C, quant.), and the selective oxidation of the allylic hydroxyl group was achieved by 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ) oxidation (dioxane, room temperature) to afford the hydroxy cyclohexenone **23** in 97% yield from **21**. Active MnO_2 oxidation of **22** was unsuccessful due to the formation of by-products. The unchanged primary hydroxyl group was reprotected with *tert*-butyldimethylsilyl ether (TBDMSCl, imidazole/DMF, 0 °C, 83%) to obtain the cyclohexenone **6** ($[\alpha]_D^{20}$ −171° (c=1.11, $CHCl_3$)). The spectral data of **6** (proton and carbon-13 nuclear magnetic resonance (^1H- and ^{13}C-NMR)) were found to be in good accordance with those of racemic **6** reported by Heathcock *et al.*[6]

Preparation of the Enone 7 The synthetic strategy for the cyclohexenone **7** is quite similar to that for **6** described



a: (1) NaOMe quant.; (2) TBDMSCl, imidazole 95%
b: (1) DIBAL 80%; (2) MsCl, pyridine; (3) $LiBEt_3H$ 86% (2 steps)
c: HF quant.
d: (1) DDQ quant.; (2) TBDMSCl, imidazole 82%

Chart 6

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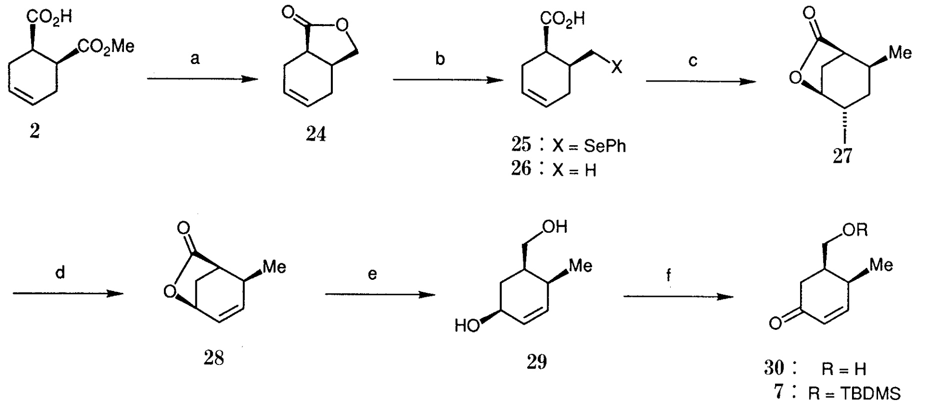

a: (1) $LiAlH_4$; (2) H^+ 53% (2 steps)
b: (1) PhSeSePh, $NaBH_4$ 74%; (2) Raney Ni (W-1) quant.
c: I_2, KI, $NaHCO_3$ 82%
d: DBU 94%
e: $LiAlH_4$ quant.
f: (1) DDQ 48%; (2) TBDMSCl, imidazole 80%

Chart 7

above. In this case, the original carboxyl group in the chiral monoester **2** was utilized in halolactonization. Therefore, it was possible to reduce the methoxycarbonyl group in **2** to the methyl group prior to halolactonization.

The preparation of **7** is shown in Chart 7. Treatment of the chiral monoester **2** with 0.9 mol of lithium aluminum hydride in THF at −78—0 °C resulted in the selective reduction of the methoxycarbonyl group, affording the hydroxy acid, which gave the γ-lactone **24** on treatment with a catalytic amount of *p*-toluenesulfonic acid (toluene, 80 °C) in 53% overall yield from **2**. The relatively low yield may have been due to over-reduction to the corresponding diol. The cleavage of the γ-lactone **24** was cleanly achieved with sodium selenophenolate,[10] prepared *in situ* from diphenyldiselenide and sodium borohydride, in DMF at 140 °C, affording the carboxylic acid **25** in 74% yield. The use of sodium benzenethiolate resulted in epimerization to some extent. The reaction of **24** with trichloromethylsilane and sodium iodide[11] was also examined, but the resulting iodomethyl derivative was found to undergo recyclization to the starting material **24** during work-up. Reductive deselenenylation of **25** was carried out by the use of Raney Ni (W-1) in ethanol at room temperature, and the olefinic acid **26** was obtained in quantitative yield. Racemic **26** was obtained in other laboratories[7,12] by hydrolysis of the corresponding methyl ester separated from another stereoisomer by spinning band distillation. Further, Clive *et al.*[13] recently reported that enantiomerically pure **26** was obtained by epimerization of the corresponding *trans* isomer which had become available by asymmetric Diels–Alder reaction.[14] In contrast to the reported methods, the present method can provide the olefinic acid **26** in a completely stereocontrolled manner.

The olefinic acid **26** was then subjected to iodolactonization (I_2, KI, $NaHCO_3$/CH_2Cl_2–H_2O, room temperature), followed by removal of hydroiodide with DBU (toluene, 110 °C), affording the olefinic lactone **28** in 77% yield from **26**. The lactone **28** was reduced with lithium aluminum hydride (THF, −78—0 °C, quant.), and the selective oxidation of the allylic hydroxyl group in **29** was carried out with DDQ (dioxane, room temperature, 48%) to give the cyclohexenone **30**. The remaining primary hydroxyl group in **30** was silylated (TBDMSCl, imidazole/DMF, 0 °C, quant.) to obtain the cyclohexenone **7** ($[\alpha]_D^{20}$ +90.9° (c= 0.88, $CHCl_3$)) in 80% yield. Spectral data (^1H-, ^{13}C-NMR, infrared (IR), mass (MS)) were fully consistent with the assigned structure.

Although the yield of each step was not optimized, the present study has demonstrated the synthetic usefulness of the chiral monoester **2**.

In addition to the methodologies described herein, stereoselective introduction of substituents at the α-position to the carboxylate or methoxycarbonyl group in **2** is also possible, constructing quaternary chiral center.[15] The combination of these methodologies would further expand the value of the chiral monoester **2** as a potential chiral synthon.

Experimental

General Methods Reagents and solvents were purchased from usual commercial sources, and were used as received or purified by distillation from appropriate drying agents. Reactions requiring anhydrous conditions were run under an atmosphere of dry argon. Silica gel (Wakogel C-200, C-300 or Fujigel BW 200) was used for column chromatography and silica gel (Kiesel gel 60 F_{254}, Merck) for analytical thin layer chromatography. Melting points were measured on a Yanagimoto micro melting point apparatus and are uncorrected. ^1H- and ^{13}C-NMR spectra were recorded on a JEOL FX-100 (100 MHz) spectrometer, and chemical shifts are expressed in ppm downfield from tetramethylsilane (TMS) as an internal reference, unless otherwise stated. Abbreviations are as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad peak. IR spectra were obtained on a JASCO A-102 spectrometer. MS spectra were obtained on a JEOL JMS-01 SG-2 mass spectrometer. Optical rotations were measured with a JASCO DIP-140 digital polarimeter.

(1*S*,2*R*,4*R*,5*R*)-4-Iodo-7-oxo-6-oxabicyclo[3.2.1]octane-2-carboxylic Acid (10) A mixture of **8** (1.221 g, 5.40 mmol), I_2 (4.18 g, 16.5 mmol), KI (5.39 g, 32.5 mmol) in CH_2Cl_2 (10 ml) and H_2O (30 ml) was stirred at room temperature for 1 d, and saturated $Na_2S_2O_3$ solution was added to the reaction mixture. The product was extracted with CH_2Cl_2, and the extract was washed (H_2O, saturated NaCl), dried (Na_2SO_4), and concentrated. The residue was purified by column chromatography on silica gel (eluted with Et_2O : hexane = 1 : 4) to give the iodolactone **9** (1.791 g) as a colorless crystalline solid. A solution of **9** in trifluoroacetic acid (10 ml) was stirred at 0 °C for 2 h, and trifluoroacetic acid was removed under reduced pressure. The residue was crystallized from MeOH–*n*-hexane to give **10** (1.460 g, 91%) as a colorless crystalline solid. **10**: mp 169—170 °C (methanol–hexane). *Anal.* Calcd for $C_8H_9IO_4$: C, 32.46; H, 3.06. Found: C, 32.50; H,

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2.90. MS m/z: 297 ($M^+ +1$), 296 (M^+), 279, 252, 251, 169 $[\alpha]_D^{20}$ +83.4° (c=1.00, acetone). IR (KBr): 3170, 1777, 1714, 1445 cm^{-1}: ^{1}H-NMR ($CDCl_3$) δ: 1.85—2.14 (m, 1H), 2.16—3.16 (m, 6H), 4.52—4.78 (m, 1H), 4.88 (dd, J=5.38, 4.25 Hz, 1H).

(1*S*,2*R*,4*R*,5*R*)-2-Hydroxymethyl-4-iodo-6-oxabicyclo[3.2.1]octan-7-one (11) Triethylamine (2.7 ml, 19 mmol) and ethyl chloroformate (1.7 ml, 18 mmol) were added to a solution of the carboxylic acid **10** (4.701 g, 15.9 mmol) in THF (60 ml) at −78 °C. The mixture was stirred at −78 °C for 1 h, then sodium borohydride (1.230 g, 32.5 mmol) in H_2O (25 ml) was added, and the mixture was stirred at 0 °C for 2 h. The solution was neutralized by adding 1 N HCl, and the product was extracted with Et_2O. The extract was washed (H_2O, saturated NaCl), dried (Na_2SO_4), and concentrated. The residue was purified by column chromatography on silica gel (eluted with Et_2O : hexane = 1 : 4—1, then AcOEt : hexane = 1 : 1) to give **11** (3.69 g, 82%) as a colorless crystalline solid. **11**: mp 79.0 °C (diisopropyl ether). *Anal.* Calcd for $C_8H_{11}IO_3$: C, 34.06; H, 3.93. Found: C, 33.98; H, 3.85. MS m/z: 282 (M^+), 265, 251, 238. $[\alpha]_D^{20}$ +54.9° (c=0.98, $CHCl_3$). IR (KBr): 3485, 2990, 2885, 1762, 1480 cm^{-1}: ^{1}H-NMR ($CDCl_3$) δ: 1.96—2.28 (m, 4H), 2.49 (ddd, J=12.5, 5.8, 1.5 Hz, 1H), 2.64—2.88 (m, 2H), 3.57 (d, J=5.6 Hz, 2H), 4.40—4.60 (m, 1H), 4.83 (dd, J=5.3, 4.5 Hz, 1H).

(1*S*,2*R*,4*R*,5*R*)-2-[(*tert*-Butyldimethylsilyloxy)methyl]-4-iodo-6-oxabicyclo[3.2.1]octan-7-one (12) A mixture of **11** (2.86 g, 10.1 mmol), imidazole (1.40 g, 20.6 mmol) and *tert*-butyldimethylsilyl chloride (2.32 g, 15.4 mmol) in DMF (35 ml) was stirred at 0 °C for 4 h, and poured into Et_2O. A mixture was washed (H_2O, saturated NaCl), dried (Na_2SO_4), and concentrated. The residue was purified by column chromatography on silica gel (eluted with Et_2O : hexane = 1 : 4) to give **12** (4.02 g, quant.) as a colorless crystalline solid. **12**: mp 97.0—98.0 °C (petroleum ether). *Anal.* Calcd for $C_{14}H_{25}IO_3Si$: C, 42.43; H, 6.36. Found: C, 42.24; H, 6.36. MS m/z: 396 (M^+), 381, 366, 351, 339. $[\alpha]_D^{20}$ +52.9° (c=1.08, $CHCl_3$). IR (KBr): 3420, 2965, 2850, 1772 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.08 (s, 6H), 0.90 (s, 9H), 1.84—2.55 (m, 4H), 2.66—2.82 (m, 2H), 3.40 (dd, J=9.8, 5.5 Hz, 1H), 3.55 (dd, J=9.8, 7.3 Hz, 1H), 4.42—4.56 (br, 1H), 4.79 (dd, J=5.0, 4.3 Hz, 1H).

(1*R*,2*R*,5*R*)-2-[(*tert*-Butyldimethylsilyloxy)methyl]-6-oxabicyclo[3.2.1]-oct-3-en-7-one (13) A mixture of **12** (8.683 g, 21.9 mmol) and DBU (15 ml, 100 mmol) in toluene (100 ml) was heated at refluxing temperature for 4 h, and poured into cold 4 N HCl (100 ml). The product was extracted with AcOEt, and the extract was washed (H_2O, saturated NaCl), dried (Na_2SO_4), and concentrated. The residue was purified by column chromatography on silica gel (eluted with Et_2O : hexane = 1 : 4) to give **13** (5.592 g, 95%) as a colorless crystalline solid. **13**: mp 40.0—40.5 °C. MS m/z: 223, 211. $[\alpha]_D^{20}$ +1.96° (c=1.10, $CHCl_3$). IR ($CHCl_3$): 2955, 2930, 2860, 1775 cm^{-1}: ^{1}H-NMR ($CDCl_3$) δ: 0.08 (s, 6H), 0.89 (s, 9H), 2.06 (d, J=11.0 Hz, 1H), 2.40—3.01 (m, 3H), 3.52 (dd, J=9.8, 7.3 Hz, 1H), 3.68 (dd, J=9.8, 7.5 Hz, 1H), 4.66—4.82 (m, 1H), 5.66—5.93 (m, 1H), 6.14—6.35 (m, 1H). ^{13}C-NMR ($CDCl_3$) δ: −5.4 (CH_3), 18.2 (C), 25.9 (CH_3), 36.0 (CH_2), 40.3 (CH), 42.9 (CH), 64.7 (CH_2), 73.3 (CH), 129.5 (CH), 131.9 (CH), 176.7 (C).

(1*S*,6*R*)-Methyl 6-Hydroxymethyl-3-cyclohexene-1-carboxylate (14) Ethyl chloroformate (5.7 ml, 60 mmol) was added to a solution of the monoester **2** (10.03 g, 54.5 mmol) and triethylamine (9.1 ml, 65 mmol) in THF (100 ml) at −78 °C. The mixture was stirred at −40—−20 °C for 1 h, then sodium borohydride (1.99 g, 52.6 mmol) in H_2O (50 ml) was added, and the whole was stirred at 0 °C for 1 h. Then additional sodium borohydride (1.88 g, 50.0 mmol) was added, and the mixture was stirred at 0 °C for 1 h. The mixture was neutralized with 2 N HCl, and the product was extracted with Et_2O. The extract was washed (H_2O, saturated NaCl), dried (Na_2SO_4), and concentrated. The residue was purified by column chromatography on silica gel (eluted with Et_2O : hexane = 1 : 4) to give **14** (5.66 g, 61%) as a colorless oil. **14**: MS m/z: 171 ($M^+ +1$), 170 (M^+), 152, 138. $[\alpha]_D^{20}$ +40.9° (c=1.18, $CHCl_3$). IR ($CHCl_3$): 3430, 3000, 2950, 2840, 1725 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.76—2.56 (m, 6H), 2.84 (dt, J=3.3, 7.4 Hz, 1H), 3.50—3.66 (m, 2H), 3.70 (s, 3H), 5.50—5.78 (br, 2H). ^{13}C-NMR ($CDCl_3$) δ: 24.8 (CH_2), 26.8 (CH_2), 37.0 (CH), 40.0 (CH); 51.7 (CH_3), 63.0 (CH_2), 124.9 (CH), 125.4 (CH), 175.7 (C).

(1*S*,6*R*)-Methyl 6-[(*tert*-Butyldimethylsilyloxy)methyl]-3-cyclohexene-1-carboxylate (15) Imidazole (7.51 g, 110 mmol) and *tert*-butyldimethylsilyl chloride (11.0 g, 73 mmol) were added to a solution of **14** (9.40 g, 55.2 mmol) in DMF (100 ml) at 0 °C, and the mixture was stirred at 0 °C for 10 h then poured into aqueous $NaHCO_3$ solution (55 ml). The product was extracted with Et_2O, and the extract was washed (H_2O, saturated NaCl), dried (Na_2SO_4), and concentrated. The residue was purified by column chromatography on silica gel (eluted with Et_2O : hexane = 1 : 4) to give **15** (15.70 g, quant.) as a colorless oil. **15**: MS m/z: 285 ($M^+ +1$), 284 (M^+), 269, 253, 227. $[\alpha]_D^{20}$ +22.7° (c=1.04, $CHCl_3$). IR ($CHCl_3$): 2945, 2920, 1728 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.04 (s, 6H), 0.88 (s, 9H), 2.02—2.50 (m, 5H), 2.78 (dt, J=3.1, 6.8 Hz, 1H), 3.56 (m, 2H), 3.67 (s, 3H), 5.50—5.76 (br, 2H). ^{13}C-NMR ($CDCl_3$) δ: −5.4 (CH_3), 18.4 (C), 25.0 (CH_2), 26.0 (CH_3), 26.6 (CH_2), 37.0 (CH), 39.7 (CH), 51.3 (CH_3), 63.2 (CH_2), 124.9 (CH), 125.5 (CH), 174.8 (C).

(1*S*,6*R*)-6-[(*tert*-Butyldimethylsilyloxy)methyl]-3-cyclohexene-1-carboxylic Acid (16) A solution of **15** (11.96 g, 42.0 mmol) in 2 N NaOH (50 ml, 100 mmol) and MeOH (80 ml) was stirred at room temperature for 10 h, and neutralized with 2 N HCl. The product was extracted with Et_2O, and the extract was washed (H_2O, saturated NaCl), dried (Na_2SO_4), and concentrated. The residue was purified by column chromatography on silica gel (eluted with Et_2O : hexane = 1 : 2) to give **16** (7.70 g, 68%) as a colorless oil. **16**: MS m/z: 271 ($M^+ +1$), 270 (M^+), 255, 253, 225, 213. $[\alpha]_D^{20}$ +14.2° (c=2.34, $CHCl_3$). IR ($CHCl_3$): 3630, 3450, 2950, 1705 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.04 (s, 6H), 0.88 (s, 9H), 1.70—2.60 (m, 6H), 2.79 (dt, J=3.1, 7.1 Hz, 1H), 3.49—3.75 (m, 2H), 5.48—5.78 (br, 2H). ^{13}C-NMR ($CDCl_3$) δ: −5.6 (CH_3), 18.3 (C), 24.6 (CH_2), 25.9 (CH_3), 26.7 (CH_2), 36.7 (CH), 39.9 (CH), 63.2 (CH_2), 124.9 (CH), 125.5 (CH), 180.9 (C).

(1*S*,2*R*,4*R*,5*R*)-2-[(*tert*-Butyldimethylsilyloxy)methyl]-4-iodo-6-oxabicyclo[3.2.1]octan-7-one (12) from 16 A mixture of **16** (473 mg, 1.75 mmol), $NaHCO_3$ (0.49 g, 5.8 mmol) and iodine (1.30 g, 5.1 mmol) and KI (1.70 g, 10.2 mmol) in CH_2Cl_2 (5 ml) and H_2O (15 ml) was stirred at room temperature for 10 h, then saturated $Na_2S_2O_3$ (10 ml) was added. The product was extracted with CH_2Cl_2, and the extract was washed (H_2O, saturated NaCl), dried (Na_2SO_4), and concentrated. The residue was purified by column chromatography on silica gel (eluted with AcOEt : hexane = 1 : 10) to give **12** (0.335 g, 48%) as a colorless crystalline solid.

(1*S*,2*R*,5*R*)-Methyl [2-(*tert*-Butyldimethylsilyloxy)methyl]-5-hydroxy-3-cyclohexene-1-carboxylate (17) A mixture of **13** (5.59 g, 20.8 mmol) and NaOMe (1.33 g, 24.6 mmol) in MeOH (80 ml) was stirred at 0 °C for 1.5 h, and neutralized with 2 N HCl. After removal of most of the MeOH under reduced pressure, the product was extracted with Et_2O, and the extract was washed (H_2O, saturated NaCl), dried (Na_2SO_4), and concentrated. The residue was purified by column chromatography on silica gel (eluted with Et_2O : hexane = 1 : 4, then 1 : 1) to give **17** (6.25 g, quant.) as a colorless oil. **17**: MS m/z: 243, 225. $[\alpha]_D^{20}$ −58.5° (c=1.16, $CHCl_3$). IR ($CHCl_3$): 3440, 2950, 2925, 2855, 1730 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.04 (s, 6H), 0.88 (s, 9H), 1.93—2.14 (m, 2H), 2.46—2.96 (br, 3H), 3.40—3.70 (m, 5H), 4.04—4.32 (br, 1H), 5.62—5.94 (br, 2H). ^{13}C-NMR ($CDCl_3$) δ: −5.5 (CH_3), 18.3 (C), 25.9 (CH_3), 31.4 (CH_2), 38.6 (CH), 39.7 (CH), 51.6 (CH_3), 63.9 (CH_2), 65.4 (CH), 128.5 (CH), 131.3 (CH), 175.0 (C).

(1*S*,2*R*,5*R*)-Methyl 5-(*tert*-Butyldimethylsilyloxy)-[2-(*tert*-butyldimethylsilyloxy)methyl]-3-cyclohexene-1-carboxylate (18) A mixture of **17** (179 mg, 0.60 mmol), *tert*-butyldimethylsilyl chloride (150 mg, 1.00 mmol) and imidazole (92 mg, 1.35 mmol) in DMF (4 ml) was stirred at 0 °C for 3 h, then poured into saturated $NaHCO_3$ (5 ml). The product was extracted with Et_2O, and the extract was washed (H_2O, saturated NaCl), dried (Na_2SO_4), and concentrated. The residue was purified by column chromatography on silica gel (eluted with Et_2O : hexane = 1 : 10) to give **18** (235 mg, 95%) as a colorless oil. **18**: MS m/z: 414 (M^+), 399, 383, 367, 357. $[\alpha]_D^{20}$ −68.5° (c=1.06, $CHCl_3$). IR ($CHCl_3$): 2955, 2925, 2855, 1732 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.02 (s, 6H), 0.08 (s, 6H), 0.87 (s, 9H), 0.89 (s, 9H), 1.56—2.18 (m, 2H), 2.50—2.86 (m, 2H), 3.42—3.74 (m, 5H), 4.13—4.36 (br, 1H), 5.56—5.80 (br, 2H). ^{13}C-NMR ($CDCl_3$) δ: −5.5 (CH_3), −4.7 (CH_3), 18.2 (C), 25.9 (CH_3), 30.6 (CH_2), 39.4 (CH), 39.9 (CH), 51.4 (CH_3), 63.6 (CH_2), 67.9 (CH), 128.1 (CH), 133.3 (CH), 173.9 (C).

[(1*S*,2*R*,5*R*)-5-(*tert*-Butyldimethylsilyloxy)-[2-(*tert*-butyldimethylsilyloxy)methyl]-3-cyclohexen-1-yl]methanol (19) Diisobutylaluminum hydride (1.0 M toluene solution, 0.64 ml, 0.64 mmol) was added to **18** (120 mg, 0.29 mmol) in toluene (4 ml) at 0 °C, and the mixture was stirred at 0 °C for 2 h. The reaction was quenched with saturated NH_4Cl (4 ml), and insoluble material was filtered off on Celite. The product was extracted with AcOEt, and the extract was washed (H_2O, saturated NaCl), dried (Na_2SO_4), and concentrated. The residue was purified by column chromatography on silica gel (eluted with Et_2O : hexane = 2 : 1) to give **19** (89 mg, 80%) as a colorless oil. **19**: MS m/z: 385 ($M^+ -1$), 371, 357, 355, 329. $[\alpha]_D^{20}$ −16.3° (c=0.92, $CHCl_3$). IR ($CHCl_3$): 3450, 2955, 2925, 2855 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.09 (s, 6H), 0.10 (s, 6H), 0.89 (s, 9H), 0.91 (s, 9H), 1.42—1.80 (m, 2H), 1.90—2.28 (br, 1H), 2.36—2.64 (br, 1H), 3.34—3.82 (m, 5H), 4.15—4.36 (br, 1H), 5.48—5.78 (br, 2H). ^{13}C-NMR ($CDCl_3$) δ: −5.6 (CH_3), −4.7 (CH_3), 18.1 (C), 25.8 (CH_3), 31.8 (CH_2),

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34.7 (CH), 36.7 (CH), 39.3 (CH), 62.9 (CH_2), 64.3 (CH_2), 67.7 (CH), 128.2 (CH), 133.5 (CH).

[(3*S*,4*S*,6*R*)-6-(*tert*-Butyldimethylsilyloxy)-3-[(*tert*-butyldimethylsilyloxy)methyl]-4-methyl-1-cyclohexene (21) A mixture of **19** (256 mg, 0.66 mmol) and methanesulfonyl chloride (0.11 ml, 1.4 mmol) in pyridine (3 ml) was stirred at 0 °C for 1 h, and poured into H_2O. The product was extracted with benzene, and the extract was washed (H_2O, saturated NaCl), dried (Na_2SO_4), and concentrated. The crude mesylate **20** was dissolved in THF (3 ml), and $LiBEt_3H$ (1.0 M THF solution, 1.3 ml, 1.3 mmol) was added to the solution at 0 °C. The mixture was stirred at 0 °C for 30 min, and at room temperature for 10 h. The reaction was quenched with H_2O (2 ml), 1 N NaOH (3 ml), and 30% H_2O_2 (2 ml), and the mixture was stirred at 35 °C for 1 h. The insoluble material was filtered off, and the product was extracted with hexane. The extract was washed (H_2O, saturated NaCl), dried (Na_2SO_4), and concentrated. The residue was purified by column chromatography on silica gel (eluted with Et_2O : hexane = 1 : 4) to give **21** (212 mg, 86%) as a colorless oil. **21**: MS *m/z*: 369 ($M^+ - 1$), 355, 341, 313. $[\alpha]_D^{20}$ −55.6° (*c* = 1.02, $CHCl_3$). IR ($CHCl_3$): 2950, 2925, 2850 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.04 (s, 6H), 0.07 (s, 6H), 0.88 (s, 9H), 0.89 (s, 9H), 0.99 (d, *J* = 7.0 Hz, 3H), 1.36—2.28 (m, 4H), 3.50 (dd, *J* = 6.4, 9.9 Hz, 1H), 3.68 (dd, *J* = 6.1, 9.9 Hz, 1H), 4.12—4.32 (br, 1H), 5.62—5.70 (br, 2H). ^{13}C-NMR ($CDCl_3$) δ: −5.4 (CH_3), −4.5 (CH_3), 18.3 (C), 25.9 (CH_3), 29.1 (CH), 37.5 (CH_2), 41.6 (CH), 63.4 (CH_2), 68.1 (CH), 129.8 (CH), 132.6 (CH).

[(1*S*,4*R*,6*S*)-4-Hydroxy-6-methyl-2-cyclohexen-1-yl]methanol (22) A solution of **21** (107 mg, 0.29 mmol) in CH_3CN (2 ml) was treated with 40% aqueous HF (2 drops) at 0 °C, and the mixture was stirred at 0 °C for 1.5 h. After addition of Et_3N (3 drops), the mixture was concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (eluted with AcOEt : hexane = 1 : 1, then 2 : 1) to give **22** (41 mg, quant.) as a colorless oil. **22**: MS *m/z*: 142 (M^+), 141, 127, 124. $[\alpha]_D^{20}$ −161.8° (*c* = 0.87, $CHCl_3$). IR ($CHCl_3$): 3385, 2955, 2870 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.03 (d, *J* = 6.6 Hz, 3H), 1.17—2.24 (m, 4H), 2.26—2.56 (br, 1H), 2.58—2.86 (br, 1H), 3.68 (d, *J* = 4.6 Hz, 2H), 4.00—4.46 (br, 1H), 5.66—5.92 (m, 2H). ^{13}C-NMR ($CDCl_3$) δ: 18.5 (CH_3), 29.2 (CH), 37.4 (CH_2), 41.0 (CH), 62.5 (CH_2), 67.5 (CH), 130.2 (CH), 133.4 (CH).

(4*S*,5*S*)-4-Hydroxymethyl-5-methyl-2-cyclohexen-1-one (23) A mixture of **22** (49 mg, 0.34 mmol) and DDQ (86 mg, 0.38 mmol) in dioxane (2 ml) was stirred at room temperature for 3 d in the dark. The precipitate was filtered off, and the filtrate was concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (eluted with Et_2O : hexane = 1 : 1) to give **23** (47 mg, 97%) as a pale brown oil. **23**: MS *m/z*: 141 ($M^+ + 1$), 140 (M^+), 125, 122. $[\alpha]_D^{20}$ −213° (*c* = 0.93, $CHCl_3$). IR ($CHCl_3$): 3430, 3000, 2960, 2880, 1670 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.02 (d, *J* = 6.8 Hz, 3H), 2.08—2.84 (m, 5H), 3.80 (d, *J* = 6.6 Hz, 2H), 6.07 (dd, *J* = 10.2, 2.2 Hz, 1H), 6.89 (dd, *J* = 10.2, 3.6 Hz, 1H). ^{13}C-NMR ($CDCl_3$) δ: 15.2 (CH_3), 30.8 (CH), 42.5 (CH), 44.8 (CH_2), 62.1 (CH_2), 129.6 (CH), 150.8 (CH), 200.5 (C).

(4*S*,5*S*)-4-[(*tert*-Butyldimethylsilyloxy)methyl]-5-methyl-2-cyclohexen-1-one (6) A mixture of **23** (44 mg, 0.31 mmol), *tert*-butyldimethylsilyl chloride (71 mg, 0.47 mmol) and imidazole (40 mg, 0.59 mmol) in DMF (2 ml) was stirred at room temperature for 8 h, and poured into saturated $NaHCO_3$ (5 ml). The product was extracted with Et_2O. The organic phase was washed (H_2O, saturated NaCl), dried (Na_2SO_4), and concentrated. The residue was purified by column chromatography on silica gel (eluted with Et_2O : hexane = 1 : 4) to give **6** (66 mg, 83%) as a pale yellow oil. **6**: MS *m/z*: 255 ($M^+ + 1$), 239, 224, 209, 199, 198, 197, 179. $[\alpha]_D^{20}$ −171.3° (*c* = 1.11, $CHCl_3$). IR ($CHCl_3$): 2950, 2925, 2855, 1670, 1470, 1462, 1391, 1252, 1108, 1093, 1042 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.05 and 0.06 (each s, total 6H), 0.89 (s, 9H), 0.98 (d, *J* = 6.6 Hz, 3H), 2.45 (m, 2H), 2.52—2.72 (br, 1H), 3.62—3.80 (m, 2H), 6.05 (dd, *J* = 10.2, 2.1 Hz, 1H), 6.81 (dd, *J* = 10.2, 3.4 Hz, 1H). ^{13}C-NMR ($CDCl_3$) δ: −5.4 (CH_3), 15.3 (CH_3), 18.2 (C), 25.7 (CH_3), 30.7 (CH), 42.4 (CH), 44.7 (CH), 62.3 (CH_2), 129.5 (CH), 150.0 (CH), 199.5 (C).

(3a*S*,7a*R*)-1,3,3a,4,7,7a-Hexahydroisobenzofuran-1-one (24) The monoester **2** (2.15 g, 11.7 mmol) in THF (15 ml) was added to a suspension of lithium aluminum hydride (0.412 g, 10.8 mmol) in THF (15 ml) at −78 °C, and the mixture was gradually warmed to 0 °C with stirring. The reaction mixture was quenched by adding saturated Na_2SO_4, and acidified to pH 3 by adding 2N HCl. Insoluble material was filtered off, and washed with AcOEt. The organic phase was combined, washed (H_2O, saturated NaCl), dried (Na_2SO_4), and concentrated to give the hydroxy acid. A mixture of the crude hydroxy acid and *p*-TsOH (0.1 g) in toluene (30 ml) was heated at 80 °C for 1 h, cooled to room temperature, and poured into cold saturated $NaHCO_3$. The product was extracted with AcOEt, and the extract was washed (H_2O, saturated NaCl), dried (Na_2SO_4), and concentrated. The residue was purified by column chromatography on silica gel (eluted with Et_2O : hexane = 1 : 1) to give **24** (0.85 g, 53%) as a colorless oil. **24**: MS *m/z*: 139 ($M^+ + 1$), 138 (M^+), 123, 93. $[\alpha]_D^{20}$ +51.5° (*c* = 0.92, $CHCl_3$). IR ($CHCl_3$): 3020, 2905, 1770 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.42—3.40 (m, 6H), 4.02 (dd, *J* = 8.9, 2.0 Hz, 1H), 4.34 (dd, *J* = 8.9, 4.8 Hz, 1H), 5.74 (s, 2H). ^{13}C-NMR ($CDCl_3$) δ: 22.0 (CH_2), 24.7 (CH_2), 31.9 (CH), 37.3 (CH), 72.9 (CH_2), 124.9 (CH), 125.1 (CH), 179.4 (C).

(1*R*,6*S*)-6-Phenylselenomethyl-3-cyclohexene-1-carboxylic Acid (25) The lactone **24** (3.49 g, 25.3 mmol) was added to a solution of sodium selenophenolate, prepared *in situ* from diphenyldiselenide (6.0 g, 19 mmol) and sodium borohydride (1.6 g, 42.3 mmol) in DMF (200 ml), and the mixture was stirred at 140 °C for 3 h. After being cooled to 0 °C, the mixture was acidified to pH 3.0 with 2 N HCl, the product was extracted with Et_2O, and the extract was washed (H_2O, saturated NaCl), dried (Na_2SO_4), and concentrated. The residue was purified by column chromatography on silica gel (eluted with Et_2O : hexane = 1 : 4, then 1 : 2) to give **25** (5.52 g, 74%) as a pale yellow crystalline solid. **25**: mp 73.0—73.5 °C (Et_2O–*n*-hexane). *Anal.* Calcd for $C_{14}H_{16}O_2Se$: C, 56.96; H, 5.46. Found: C, 57.04; H, 5.50. MS *m/z*: 296 ($M^+ + 1$), 294, 181, 171, 158, 156, 140, 139. $[\alpha]_D^{20}$ −29.9° (*c* = 0.92, $CHCl_3$). IR ($CHCl_3$): 3075, 3060, 2950, 1705 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 2.02—2.57 (br, 6H), 2.68—3.22 (m, 3H), 5.65 (s, 2H), 7.10—7.30 (m, 3H), 7.34—7.56 (m, 2H). ^{13}C-NMR ($CDCl_3$) δ: 25.0 (CH_2), 29.1 × 2 (CH_2 × 2), 34.8 (CH), 42.1 (CH), 124.7 (CH), 125.4 (CH), 126.7 (CH), 129.0 (CH), 130.2 (C), 132.3 (CH), 180.5 (C).

(1*R*,6*S*)-6-Methyl-3-cyclohexene-1-carboxylic Acid (26) A solution of NaOH (0.50 g, 12.5 mmol) in EtOH (20 ml) and a suspension of Raney nickel W-1 in EtOH (0.5 g/ml, *ca.* 50 ml) were added to a solution of **25** (3.16 g, 10.7 mmol) in EtOH (25 ml), and the mixture was stirred at room temperature for 10 min. Insoluble material was filtered off on a Celite pad, and the filtrate was concentrated *in vacuo*. The residue was acidified with 2 N HCl, and the product was extracted with AcOEt. The extract was washed (H_2O, saturated NaCl), dried (Na_2SO_4), and concentrated. The residue was purified by distillation (Kugelrohr, oven temperature, 180—200 °C/6 mmHg) to give **26** (1.50 g, quant.) as a colorless oil. **26**: MS *m/z*: 140 (M^+), 125, 95. $[\alpha]_D^{20}$ +16.5° (*c* = 0.99, $CHCl_3$). IR ($CHCl_3$): 3020, 2915, 1704 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.97 (d, *J* = 7.5 Hz, 3H), 1.20—2.84 (m, 7H), 5.46—5.96 (br, 2H). ^{13}C-NMR ($CDCl_3$) δ: 15.2 (CH_3), 23.4 (CH_2), 28.4 (CH), 32.3 (CH_2), 42.7 (CH), 124.4 (CH), 125.2 (CH), 181.7 (C).

(1*R*,2*S*,4*S*,5*S*)-4-Iodo-2-methyl-6-oxabicyclo[3.2.1]octan-7-one (27) A mixture of the olefinic acid **26** (1.06 g, 7.56 mmol), iodine (4.80 g, 18.9 mmol), KI (6.20 g, 37.3 mmol) and $NaHCO_3$ (1.60 g, 19.0 mmol) in CH_2Cl_2 (20 ml) and H_2O (30 ml) was stirred at room temperature in the dark for 2 d, and then saturated $Na_2S_2O_3$ was added to the reaction mixture. The product was extracted with CH_2Cl_2, and the extract was washed (H_2O, saturated NaCl), dried (Na_2SO_4), and concentrated. The residue was purified by column chromatography on silica gel (eluted with Et_2O : hexane = 1 : 4) to give **27** (1.65 g, 82%) as a pale yellow crystalline solid. **27**: mp 67.0—68.5 °C (*n*-hexane). *Anal.* Calcd for $C_8H_{11}IO_2$: C, 36.08: H, 4.17. Found: C, 36.15; H, 4.08. MS *m/z*: 266 (M^+), 204, 183. $[\alpha]_D^{20}$ −35.7° (*c* = 0.96, $CHCl_3$). IR ($CHCl_3$): 2965, 1783 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.06 (d, *J* = 6.3 Hz, 3H), 1.88—2.86 (m, 6H), 4.40—4.56 (br, 1H), 4.72—4.86 (m, 1H). ^{13}C-NMR ($CDCl_3$) δ: 18.8 (CH_3), 23.5 (CH), 29.8 (CH), 34.8 (CH_2), 38.2 (CH_2), 44.6 (CH), 79.9 (CH), 176.3 (C).

(1*R*,2*S*,5*S*)-2-Methyl-6-oxabicyclo[3.2.1]oct-3-en-7-one (28) A mixture of **27** (3.337 g, 12.5 mmol) and DBU (5.5 ml, *ca.* 37 mmol) in toluene (90 ml) was heated at refluxing temperature for 4 h, cooled to room temperature, and acidified to pH 2 with 2 N HCl. The product was extracted with AcOEt, and the extract was washed (H_2O, saturated NaCl), dried (Na_2SO_4), and concentrated. The residue was purified by column chromatography on silica gel (eluted with Et_2O : hexane = 1 : 4, then 1 : 3) to give **28** (1.627 g, 94%) as a pale yellow oil. **28**: MS *m/z*: 139 ($M^+ + 1$), 138 (M^+), 109, 94. $[\alpha]_D^{20}$ +20.8° (*c* = 1.07, $CHCl_3$). IR ($CHCl_3$): 3020, 2970, 2880, 1771 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.16 (d, *J* = 7.1 Hz, 3H), 2.06 (d, *J* = 10.9 Hz, 1H), 2.22—2.80 (m, 3H), 4.73 (t, *J* = 5.4 Hz, 1H), 5.63—5.78 (m, 1H), 6.08—6.26 (m, 1H). ^{13}C-NMR ($CDCl_3$) δ: 19.0 (CH_3), 34.6 (CH), 36.3 (CH_2), 44.2 (CH), 73.3 (CH), 128.0 (CH), 136.0 (CH), 177.0 (C).

[(1*R*,2*S*,5*S*)-5-Hydroxy-2-methyl-3-cyclohexen-1-yl]methanol (29) A solution of **28** (0.765 g, 5.54 mmol) in THF (20 ml) was added to a suspension of lithium aluminum hydride (0.33 g, 8.7 mmol) in THF (30 ml) at −78 °C, and the mixture was stirred at −78 °C for 30 min and then at 0 °C for 1.5 h. The reaction mixture was quenched by adding saturated Na_2SO_4, and the insoluble material was filtered off. The filtrate was

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saturated with NaCl, and the product was extracted with AcOEt. The extract was washed (H_2O, saturated NaCl), dried (Na_2SO_4), and concentrated. The residue was purified by column chromatography on silica gel (eluted with AcOEt : hexane = 1 : 1) to give **29** (0.787 g, quant.) as a colorless oil. **29**: MS *m/z*: 142 (M^+), 127, 125, 124. $[\alpha]_D^{20}$ +71.9° (*c* = 1.20, $CHCl_3$). IR ($CHCl_3$): 3415, 3000, 2960, 2925 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.96 (d, J = 7.4 Hz, 3H), 1.22—2.78 (m, 6H), 3.61 (d, J = 6.8 Hz, 2H), 4.12—4.36 (br, 1H), 5.68 (s, 2H). ^{13}C-NMR ($CDCl_3$) δ: 15.1 (CH_3), 30.8 (CH), 31.0 (CH_2), 37.5 (CH), 64.2 (CH_2), 66.5 (CH), 129.5 (CH), 135.1 (CH).

(4*S*,5*R*)-5-Hydroxymethyl-4-methyl-2-cyclohexen-1-one (30) A mixture of **29** (0.168 g, 1.18 mmol) and DDQ (0.280 g, 1.23 mmol) in dioxane (5 ml) was stirred at room temperature for 2 d. Insoluble material was filtered off, and the filtrate was concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (eluted with Et_2O : hexane = 1 : 1) to give **30** (0.080 g, 48%) as a pale yellow oil. **30**: MS *m/z*: 140 (M^+), 110. $[\alpha]_D^{20}$ +98.0° (*c* = 0.61, $CHCl_3$.). IR ($CHCl_3$) 3425, 2995, 2960, 2875, 1670 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.10 (d, J = 7.4 Hz, 3H), 1.78—2.90 (m, 5H), 3.66 (d, J = 5.0 Hz, 2H), 5.97 (d, J = 10.0 Hz, 1H), 6.98 (dd, J = 10.0, 5.1 Hz, 1H). ^{13}C-NMR ($CDCl_3$) δ: 12.5 (CH_3), 31.1 (CH), 36.4 (CH_2), 39.6 (CH), 63.5 (CH_2), 128.2 (CH), 155.9 (CH), 199.6 (C).

(4*S*,5*R*)-5-[*tert*-Butyldimethylsilyloxy)methyl]-4-methyl-2-cyclohexen-1-one (7) A mixture of **30** (0.371 g, 2.65 mmol), TBDMSCl (0.520 g, 3.45 mmol) and imidazole (0.320 g, 4.70 mmol) in DMF (8 ml) was stirred at room temperature for 10 h. Saturated $NaHCO_3$ (15 ml) was added to the reaction mixture, and the product was extracted with Et_2O. The extract was washed (H_2O, saturated NaCl), dried (Na_2SO_4), and concentrated. The residue was purified by column chromatography on silica gel (eluted with Et_2O : hexane = 1 : 1) to give **7** (0.538 g, 80%) as a pale yellow oil. **7**: MS *m/z*: 255 (M^+ + 1), 239, 199, 197. $[\alpha]_D^{20}$ +90.9° (*c* = 0.88, $CHCl_3$). IR ($CHCl_3$): 2955, 2925, 2855, 1672 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.06 (s, 6H), 0.89 (s, 9H), 1.06 (d, J = 7.2 Hz, 3H), 2.14—2.80 (m, 4H), 3.57 (d, J = 5.9 Hz, 2H), 5.95 (dd, J = 10.0, 1.1 Hz, 1H), 6.94 (dd, J = 10.0, 5.4 Hz, 1H). ^{13}C-NMR ($CDCl_3$) δ: −5.4 (CH_3), 12.4 (CH_3), 18.2 (C), 25.9 (CH_3), 31.2 (CH), 36.4 (CH_2), 39.6 (CH), 63.9 (CH_2), 128.2 (CH), 155.6 (CH), 199.3 (C).

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