Pergamon

*Tetrahedron*, Vol. 52, No. 12, pp. 4257-4268, 1996

0040-4020/96 $15.00 + 0.00

S0040-4020(96)00086-5

# Synthetic Studies on Aromadendrane-Type Compounds. III.[1] Stereoselective Total Syntheses of (+)-Aromadendrene and (–)-Alloaromadendrene

Tetsuaki Tanaka, Kimiya Maeda, Hidenori Mikamiyama, Yousuke Funakoshi, Kenji Uenaka, and Chuzo Iwata*

Faculty of Pharmaceutical Sciences, Osaka University, 1-6 Yamadaoka, Suita, Osaka 565, Japan.

***Abstract***: The stereoselective total syntheses of (+)-aromadendrene (**5**) and (–)-alloaromadendrene (**6**) were achieved *via* (+)-(1*S*,2*R*,4*R*,7*S*,11*R*)-7-*tert*-butyldimethylsiloxymethyl-3,3,11-trimethyltricyclo[6.3.0.$0^{2,4}$]undec-8-en-10-one (**7**) as a common intermediate.

In the preceding two papers in this series,[1] we described the stereoselective synthesis of a tricyclic enone, (+)-(1*S*,2*R*,4*R*,7*S*)-3,3,7-trimethyltricyclo[6.3.0.$0^{2,4}$]undec-8-en-10-one (**1**), and its conversion into B/C-*trans* and -*cis* compounds (**2** and **3**) corresponding to the aromadendrane and alloaromadendrane skeletons,[1a] and the total synthesis of (+)-1,2-didehydroaromadendrane (**4**) *via* regio- and stereoselective introduction of a methyl group at the C11 position of **1** followed by reductive deoxygenation.[1b] However, among natural products with an aromadendrane skeleton, several functionalities are known at C7, *e.g.*, an *exo*-methylene,[2] a hydroxyl group,[2a,b,3] an isonitrile or an isothiocyanate group,[4] and a sugar moiety.[5]

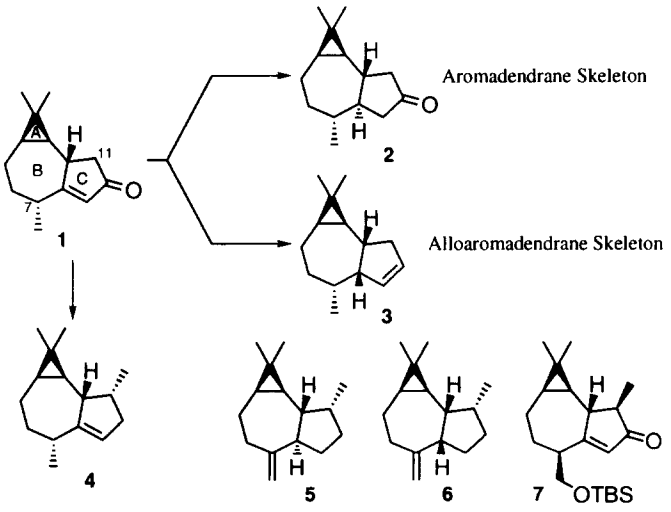
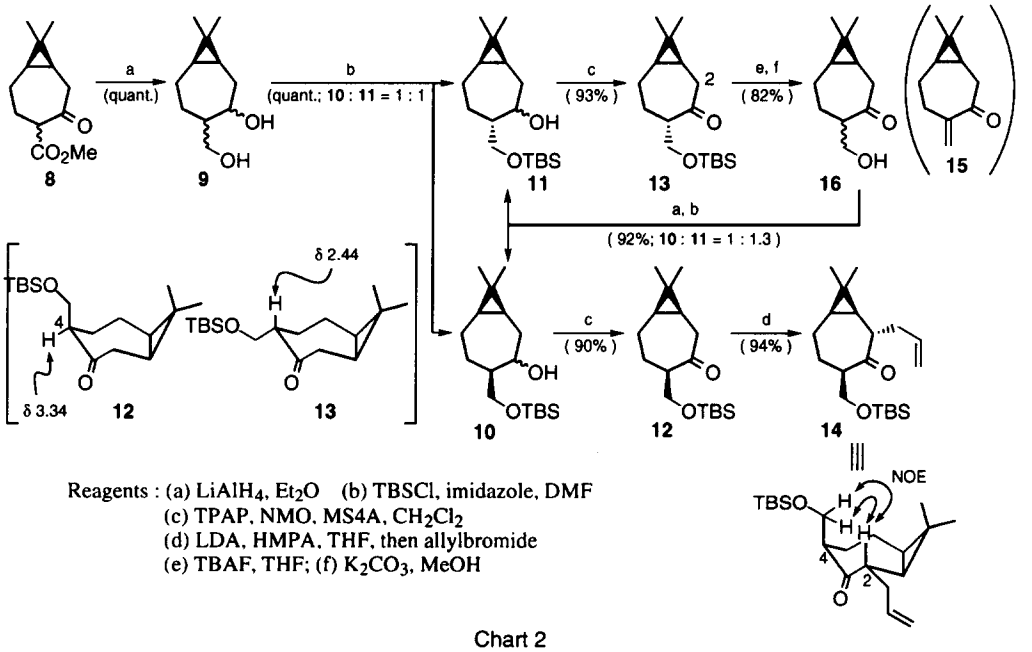



Chart 1

Accordingly, we sought to establish an efficient general synthetic route that could be applied to these

of (+)-aromadendrene (**5**) [2b] and (−)-alloaromadendrene (**6**).[2c] Since the C7 substituent in **1** is a methyl group, functionalization of the C7 position seems difficult. To solve this problem, we used (+)-(1*S*,2*R*,4*R*,7*S*,11*R*)-7-*tert*-butyldimethylsiloxymethyl-3,3,11-trimethyltricyclo[6.3.0.$0^{2,4}$]undec-8-en-10-one (**7**) as a common key intermediate. It has a siloxymethyl group at C7, which simplifies manipulation of the functional group (Chart 1).

Charts 2 and 3 show the preparation of the targeted enone **7** from the previously described 7-membered cyclic β-ketoester **8**.[1a] Exhaustive reduction of **8** using excess lithium aluminum hydride (LAH) in ethyl ether ($Et_2O$) followed by protection of the primary hydroxyl group of diol **9** as a *tert*-butyldimethylsilyl (TBS) ether with TBS chloride and imidazole in *N*,*N*-dimethylformamide (DMF) furnished the alcohols **10** (50 % yield from **8**) and **11** (50 % yield from **8**), which were separated by column chromatography. Compounds **10** and **11** seem to be diastereomers with regard to the hydroxyl group, but their configurations were not determined at this stage. Oxidation of **10** and **11** was carried out separately using Ley's tetrapropylammonium perruthenate (TPAP) / 4-methylmorpholine *N*-oxide (NMO) system [6] to afford the ketones **12** (90 % from **10**) and **13** (93 % from **11**). The configurations at C4 of **12** and **13** were determined to be *R* and *S*, respectively. Chair conformations are presumed for these compounds.[1a] The downfield shift (to δ 3.34) of the C4 proton signal in the $^1$H-NMR spectrum of **12** is ascribed to a deshielding effect arising from its position flush with the carbonyl plane. Since the C4 proton of **13** is located far from the carbonyl plane, its resonance occurs at a higher field (δ 2.44). These data show that the siloxymethyl group of **12** is axial and that of **13** is equatorial, as shown in Chart 2. Allylation at C2 from the less hindered α-side was accomplished by treatment of **12** with lithium diisopropylamide (LDA) followed by addition of hexamethylphosphoric triamide (HMPA) and allyl bromide to provide **14**. The



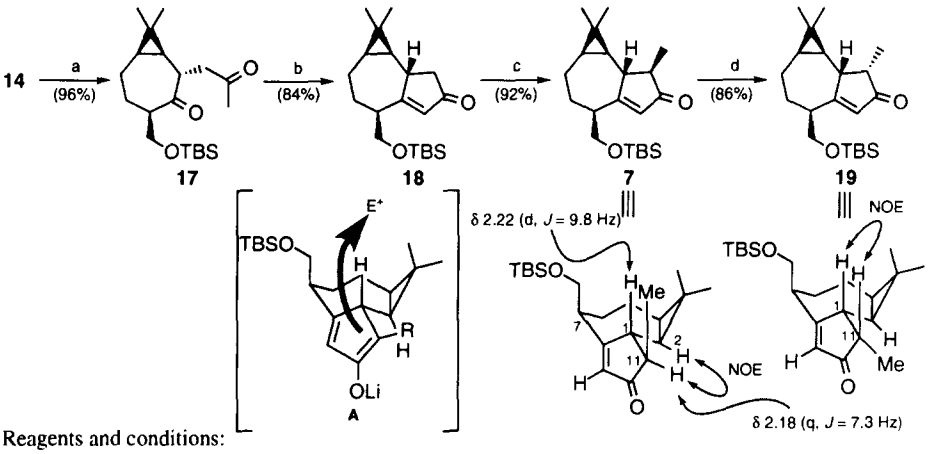

Reagents : (a) $LiAlH_4$, $Et_2O$ (b) TBSCl, imidazole, DMF
(c) TPAP, NMO, MS4A, $CH_2Cl_2$
(d) LDA, HMPA, THF, then allylbromide
(e) TBAF, THF; (f) $K_2CO_3$, MeOH

Chart 2

stereochemistry was determined by the observation of nuclear Overhauser effect (NOE) between the C2 proton and the methylene protons of the siloxymethyl group. However, allylation of **13** did not follow the same course as that of **12**, and a small quantity of **15** was produced along with some recovered starting

material. The different behavior of **12** and **13** can be attributed to the reversed configuration at C4. The C4 proton of **13** is axial, so that it is indistinguishable from the C2 axial proton. Ketone **13** could not be directly isomerized to **12**; however, desilylation of the C4 hydroxyl group of **13** by exposure to tetra-*n*-butylammonium fluoride (TBAF) followed by treatment with potassium carbonate in methanol led to a diastereomeric mixture of keto alcohols **16** (82 % from **13**). LAH reduction of this mixture followed by protection of the primary hydroxyl group of diol as a TBS ether gave the alcohols **10** (40 % yield from **16**) and **11** (52 % yield from **16**). Thus, the recycling of **13** into **10** has been established (Chart 2).

The allyl group of **14** was converted to a methyl ketone by Wacker oxidation [7] to give the diketone **17** in 96 % yield. Aldol condensation of the latter was unexpectedly troublesome. The desired aldol product was not reproducible (27—76 % yield) under previously reported conditions.[1a, 8] After various examinations, we identified effective conditions; namely, **17** was treated with sodium bis(trimethylsilyl)amide (NaHMDS) in tetrahydrofuran (THF) at −78 °C, then warmed to 50 °C to afford the desired enone **18** in 76—84 % yield. Methylation at C11 from the less hindered β-side was accomplished by treatment of **18** with lithium bis(trimethylsilyl)amide (LiHMDS) at −78 °C, followed by alkylation with methyl iodide to provide **7** as a sole product in 92 % yield. The configuration of the newly introduced methyl group was confirmed by analysis of the $^1$H-NMR spectrum, including NOE measurement. The C1 proton signal appeared at δ 2.22 as a doublet ($J$ = 9.8 Hz) coupled only with the C2 cyclopropyl proton. The C11 proton signal appeared at δ 2.18 as a quartet ($J$ = 7.3 Hz) coupled only with the C11 methyl proton. Since vicinal coupling between the C1 and C11 protons was not observed, it is clear that the dihedral angle between them is about 90°. Furthermore, NOE was detected between the C2 and C11 protons. These observations obviously show that the methyl group was introduced stereoselectively from the β-side of the kinetic dienolate (**A**: R=H) (Chart 3).




Reagents and conditions:

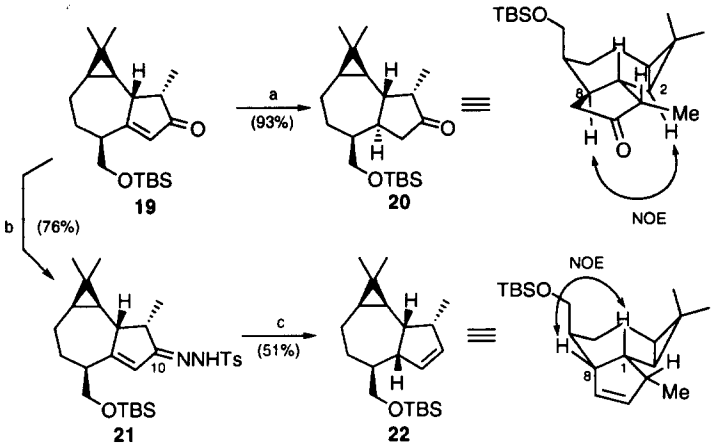
(a) $O_2$, $PdCl_2$, CuCl, $H_2O$, DMF (b) NaHMDS, HMPA, THF, −78°C→50°C

(c) LiHMDS, HMPA, THF, then MeI (d) LiHMDS, HMPA, THF, then satd.$NH_4Cl$ aq.

Chart 3

With the enone **7** in hand, we next focused on the total syntheses of (+)-aromadendrene (**5**) and (−)-alloaromadendrene (**6**), as a part of the development of a general synthetic route to aromadendrane-type compounds. Since **5** and **6** have an α-methyl group at the C11 position, isomerization of the C11 methyl group of **7** is required. We expected that a proton could be introduced from the less hindered β-side by reprotonation of the kinetic dienolate (**A**: R = Me) to give the desired compound **19** bearing an α-oriented methyl group. Although treatment of **7** with LDA did not give a useful result because of the low acidity of

the equatorial C11 proton, treatment with LiHMDS in THF-HMPA at –78 °C followed by warming to 0 °C and quenching with saturated ammonium chloride solution gave **19**. The stereochemistry of **19** was determined by the observation of NOE between the C1 and C11 protons (Chart 3).




Reagents : (a) $H_2$, 5%Pd-C, MeOH (b) $TsNHNH_2$, AcOH (c) $NaBH_4$, AcOH

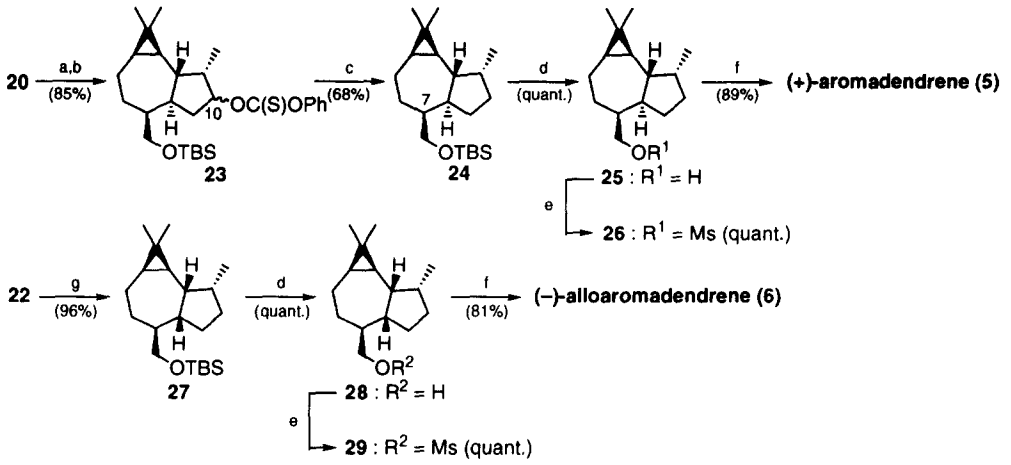
Chart 4

With the enone **19** in hand, we were now ready to attempt the stereoselective construction of the B/C-ring systems for aromadendrane-type and alloaromadendrane-type compounds in accordance with our previously established method.[1a] Catalytic hydrogenation of **19** over Pd/C exclusively afforded the B/C-*trans* compound **20**. The observation of NOE between the C2 and C8 protons supports this result. On the other hand, enone **19** was converted to a tosylhydrazone **21**,[9] which was then treated with sodium borohydride ($NaBH_4$) in acetic acid [10] to provide the desired B/C-*cis* compound **22** as expected. The stereochemistry of **22** was confirmed by the observation of NOE between the C1 and C8 protons (Chart 4).

After securing the B/C-*trans* compound **20** and the *cis* compound **22**, our only remaining task was functional group manipulation. Thus, reduction of the carbonyl group of **20** using $NaBH_4$ followed by treatment with phenyl chlorothionoformate, pyridine and 4-dimethylaminopyridine (DMAP) led to a diastereomeric mixture **23** with respect to the thiocarbonate at C10. Treatment of **23** with tributyltin hydride (*n*-$Bu_3SnH$) in refluxing toluene in the presence of a catalytic amount of 2,2'-azobis(isobutyronitrile) (AIBN) furnished the deoxy derivative **24** in 68 % yield. Desilylation of the C7 hydroxyl group of **24** by exposure to TBAF followed by treatment with methanesulfonyl chloride (MsCl), triethylamine ($Et_3N$) and DMAP led to mesylate **26** in quantitative yield from **24**. Mesylate **26** was treated with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in toluene at 100 °C to afford (+)-aromadendrene (**5**), which was identical to an authentic sample by spectral comparison.[11]

Catalytic hydrogenation of **22** over Pd/C provided **27**, which was converted to (–)-alloaromadendrene (**6**) in the same manner as **24** was converted to (+)-aromadendrene (**5**). Synthetic (–)-alloaromadendrene (**6**) showed spectral data identical to those previously reported,[2b] including the $[\alpha]_D$ value (Chart 5).

Thus, the total syntheses of (+)-aromadendrene (**5**) and (–)-alloaromadendrene (**6**) were achieved *via* a common key intermediate (+)-(1*S*,2*R*,4*R*,7*S*,11*R*)-7-*tert*-butyldimethylsiloxymethyl-3,3,11-trimethyltricyclo[6.3.0.$0^{2,4}$]undec-8-en-10-one (**7**). Further extension of this methodology to other natural products is now underway.




Reagents: (a) $NaBH_4$, MeOH (b) PhOC(S)Cl, pyridine, DMAP, $CH_2Cl_2$ (c) *n*-$Bu_3SnH$, AIBN, toluene (d) TBAF, THF (e) MsCl, $Et_3N$, DMAP, $CH_2Cl_2$ (f) DBU, toluene

Chart 5

## Experimental

Optical rotations were recorded on a JASCO DIP-360 polarimeter. NMR spectra were recorded on a JEOL JNM-GX-500 or a Varian VXR-200 instrument and calibrated using tetramethylsilane (TMS) or residual undeuterated chloroform as an internal standard. IR spectra were recorded on a Hitachi 260-10 spectrometer. Mass spectra (MS) and high resolution mass spectra (HRMS) were obtained on a Shimadzu QP-1000 or a JEOL JMS D-300 mass spectrometer. Merck Kieselgel 60 was used for column chromatography. Preparative thin-layer chromatography (PTLC) separations were carried out on Merck Kieselgel 60 $PF_{254}$. All organic extracts were dried over anhydrous $MgSO_4$ before concentration.

**(−)-(1*S*, 4*R*, 7*R*)- and (+)-(1*S*, 4*S*, 7*R*)-4-*tert*-Butyldimethylsiloxymethyl-8,8-dimethylbicyclo[5.1.0]octan-3-ol (10 and 11 from β-ketoester 8)** ----- A solution of β-ketoester **8** [1a] (91.3 mg, 0.435 mmol) in $Et_2O$ (1 ml) was added dropwise to a stirred suspension of LAH (49.6 mg, 1.30 mmol) in $Et_2O$ (10 ml) and the mixture was stirred at room temperature for 1 h. After successive careful addition of $H_2O$ (0.05 ml), 1N NaOH solution (0.05 ml) and $H_2O$ (0.15 ml), the resulting precipitates were filtered off through a celite pad. The filtrate was dried and concentrated to give the corresponding crude diol **9** which was taken to the next step without further purification. TBSCl (65.5 mg; 0.435 mmol) was added to a solution of the previous diol **9** and imidazole (65.0 mg, 0.957 mmol) in DMF (3 ml) at 0 °C, and the whole was allowed to warm to room temperature under stirring, and the stirring was continued for 12 h. After dilution with $Et_2O$, the reaction mixture was washed with $H_2O$ and brine, dried, concentrated, and purified by column chromatography (*n*-hexane : AcOEt = 50 : 1) to give the alcohols **10** (65.3 mg, 50 %) and **11** (64.2 mg, 50 %), each as a colorless oil. **10**: $[\alpha]^{28}_D$ −0.2 (*c* = 1.85, $CHCl_3$). $^1$H-NMR (500 MHz, $CDCl_3$) δ: 0.08 (6H, s, Si-Me x 2), 0.52—0.59 (2H, m, C1- and C7-H), 0.89 (9H, s, Si-*t*-Bu), 1.00 (6H, s, C8-Me x 2), 1.23—1.36 (2H, m, C6-βH, OH), 1.37—1.52 (2H, m, C5-αH, C6-αH), 1.63—1.70 (2H, m, C2-βH, C5-βH), 2.02 (1H, m, C2-αH), 2.37 (1H, m, C4-H), 3.67 (1H, dd, *J* = 4.2, 9.7 Hz, C3-H), 3.96 (2H, dd, *J* = 9.2, 9.8 Hz, C4-$CH_2$). IR ($CHCl_3$) $cm^{-1}$: 3460 (OH). MS *m/z* (rel. int. %): 298 ($M^+$, 1.8), 149 (100). HRMS Calcd for $C_{17}H_{34}O_2Si$: 298.2326. Found: 298.2321. **11**: $[\alpha]^{28}_D$ +31.6 (*c* = 1.52, $CHCl_3$). $^1$H-NMR (500 MHz, $CDCl_3$) δ: 0.05 (6H, s, Si-Me x 2), 0.62—0.74 (2H, m, C1- and C7-H), 0.89 (9H, s, Si-*t*-Bu), 1.00, 1.03 (each 3H, s, C8-Me x 2), 0.92—1.08 (1H, m, C6-βH), 1.18 (1H, dd, *J* = 10.4, 14.6 Hz, C2-βH), 1.31 (1H, m, C4-H), 1.45 (1H, m, C5-αH), 1.77 (1H, dd, *J* = 12.8, 25.6 Hz, C5-βH), 1.97 (1H, ddd, *J* = 6.1, 6.7, 7.3 Hz, C6-αH), 2.27 (1H, ddd, *J* = 6.7, 14.7, 14.7 Hz, C2-αH), 2.92

(1H, br s, OH), 3.65 (1H, dd, $J$ = 4.9, 9.8 Hz, one of C4-$CH_2$), 3.72 (1H, dd, $J$ = 4.3, 9.8 Hz, one of C4-$CH_2$), 4.23 (1H, d, $J$ = 6.7 Hz, C3-H). IR ($CHCl_3$) $cm^{-1}$: 3450 (OH). MS *m/z* (rel. int. %): 298 ($M^+$, 8.9), 93 (100). HRMS Calcd for $C_{17}H_{34}O_2Si$: 298.2325. Found: 298.2302.

**(+)-(1*S*, 4*R*, 7*R*)-4-*tert*-Butyldimethylsiloxymethyl-8,8-dimethylbicyclo[5.1.0]octan-3-one (12)** ----- A mixture of alcohol **10** (677 mg, 2.27 mmol), NMO (416 mg, 3.55 mmol), and 4Å molecular sieves (1.20 g) in $CH_2Cl_2$ (5 ml) was stirred at room temperature for 10 min. TPAP (44.5 mg, 0.127 mmol) was added, and the whole was stirred at room temperature for 15 min. The reaction mixture was filtered through silica gel. The filtrate was concentrated and the residue was purified by column chromatography (*n*-hexane : AcOEt = 50 : 1) to give the ketone **12** (604 mg, 90 %) as a colorless oil. $[\alpha]^{30}_D$ +113.3 ($c$ = 1.19, $CHCl_3$). $^1$H-NMR (500 MHz, $CDCl_3$) δ: 0.02, 0.03 (each 3H, s, Si-Me x 2), 0.76—0.83 (2H, m, C1- and C7-H), 0.85 (9H, s, Si-*t*-Bu), 0.96, 1.07 (each 3H, s, C8-Me x 2), 1.01—1.19, 1.35 (each 1H, m, C5-αH, C6-βH), 1.84—1.96 (2H, m, C5-βH, C6-αH), 2.15 (1H, dd, $J$ = 7.9, 17.7 Hz, C2-αH), 2.60 (1H, dd, $J$ = 9.2, 17.7 Hz, C2-βH), 3.34 (1H, m, C4-H), 3.51 (1H, dd, $J$ = 7.3, 9.8 Hz, one of C4-$CH_2$), 3.89 (1H, dd, $J$ = 6.1, 9.8 Hz, one of C4-$CH_2$). $^{13}$C-NMR (50.3 MHz, $CDCl_3$) δ: −5.4 (q), −5.3 (q), 15.1 (q), 18.4 (s), 19.8 (d), 20.2 (s), 20.7 (t), 26.0 (q x 3), 26.1 (d), 28.1 (t), 28.7 (q), 39.4 (t), 51.5 (d), 63.6 (t), 214.2 (s). IR ($CHCl_3$) $cm^{-1}$: 1700 (C=O). MS *m/z* (rel. int. %): 296 ($M^+$, 4.0), 239 (100). *Anal.* Calcd for $C_{17}H_{32}O_2Si$: C, 68.86; H, 10.88. Found: C, 69.02; H, 10.68.

**(+)-(1*S*, 4*S*, 7*R*)-4-*tert*-Butyldimethylsiloxymethyl-8,8-dimethylbicyclo[5.1.0]octan-3-one (13)** ----- The alcohol **11** was converted to the ketone **13** in a similar manner to that described for **10**. **13**: A colorless amorphous (93 % yield). $[\alpha]^{27}_D$ +121.8 ($c$ = 0.740, $CHCl_3$). $^1$H-NMR (500 MHz, $CDCl_3$) δ: 0.03, 0.04 (each 3H, s, Si-Me x 2), 0.56 (1H, ddd, $J$ = 6.3, 6.7, 11.3 Hz, C1-H), 0.71 (1H, ddd, $J$ = 6.1, 6.7, 11.0 Hz, C7-H), 0.87 (9H, s, Si-*t*-Bu), 1.04, 1.06 (each 3H, s, C8-Me x 2), 1.01—1.25 (2H, m, C5-αH, C6-βH), 2.09—2.20 (3H, m, C2-αH, C5-βH, C6-αH), 2.44 (1H, m, C4-H), 2.48 (1H, dd, $J$ = 6.7, 11.6 Hz, C2-βH), 3.48 (1H, dd, $J$ = 8.5, 10.4 Hz, one of C4-$CH_2$), 3.94 (1H, dd, $J$ = 4.9, 10.4 Hz, one of C4-$CH_2$). IR ($CHCl_3$) $cm^{-1}$: 1700 (C=O). MS *m/z* (rel. int. %): 296 ($M^+$, 0.3), 239 (100). HRMS Calcd for $C_{17}H_{32}O_2Si$: 296.2172. Found: 296.2173.

**(+)-(1*S*, 2*S*, 4*R*, 7*R*)-4-*tert*-Butyldimethylsiloxymethyl-8,8-dimethyl-2-(2-propenyl)-bicyclo[5.1.0]octan-3-one (14)** ----- *n*-BuLi (0.324 ml of a 1.64 M solution in *n*-hexane, 0.531 mmol) was added to a solution of diisopropylamine (0.071 ml, 0.51 mmol) in THF (2 ml) at −20 °C and the mixture was stirred for 20 min. A solution of ketone **12** (100 mg, 0.337 mmol) in THF (0.5 ml) was added to the above solution at −78 °C and the mixture was stirred for 30 min, after that HMPA (0.25 ml) was added and stirred at −78 °C for 30 min. Allyl bromide (0.035 ml, 0.40 mmol) was added dropwise, and the reaction mixture was allowed to warm to room temperature over the period of 4 h. The reaction was quenched with aqueous $NH_4Cl$ and $H_2O$, and the resulting mixture was extracted with AcOEt. The extracted was washed with $H_2O$ and brine, dried, concentrated, and purified by column chromatography (*n*-hexane : AcOEt = 50 : 1) to give **14** (106 mg, 94 %) as a colorless oil: $[\alpha]^{29}_D$ +109.5 ($c$ = 0.660, $CHCl_3$). $^1$H-NMR (500 MHz, $CDCl_3$) δ: 0.03, 0.04 (each 3H, s, Si-Me x 2), 0.36 (1H, dd, $J$ = 8.6, 9.2, C1-H), 0.74 (1H, m, C7-H), 0.87 (9H, s, Si-*t*-Bu), 0.98, 1.05 (each 3H, s, C8-Me x 2), 0.93—1.20 (1H, m, C6-βH), 1.55 (1H, m, C5-αH), 1.76—1.91 (2H, m, C5-βH, C6-αH), 2.21—2.30 (2H, m, C2- and C1'-H), 2.41 (1H, m, C1'-H), 3.10 (1H, m, C4-H), 3.57 (1H, dd, $J$ = 6.1, 9.8 Hz, one of C4-$CH_2$), 3.86 (1H, dd, $J$ = 7.9, 9.8 Hz, one of C4-$CH_2$), 5.00 (1H, d, $J$ = 9.8 Hz, one of =$CH_2$), 5.04 (1H, d, $J$ = 18.3 Hz, one of =$CH_2$), 5.73 (1H, m, C2'-H). IR ($CHCl_3$) $cm^{-1}$: 1700 (C=O), 1640 (C=C). MS *m/z* (rel. int. %): 336 ($M^+$, 0.03), 279 (100). HRMS Calcd for $C_{20}H_{36}O_2Si$: 336.2483. Found: 336.2483.

**(+)-(1*S*,7*R*)-8,8-Dimethyl-4-methylenebicyclo[5.1.0]octan-3-one (15)** ----- A colorless oil. $[\alpha]^{29}_D$ +125.8 ($c$ = 0.660, $CHCl_3$). $^1$H-NMR (500 MHz, $CDCl_3$) δ: 0.67—0.78 (2H, m, C1- and C7-H), 1.05, 1.06 (each 3H, s, C8-Me x 2), 1.59 (1H, ddd, $J$ = 6.7, 14.7, 14.7 Hz, C6-βH), 2.04 (1H, m, C6-αH), 2.32 (1H, dd, $J$ = 11.0, 14.0 Hz, C2-βH), 2.45 (2H, dd, $J$ = 6.1, 6.7 Hz, C5-H), 2.62 (1H, dd, $J$ = 6.1, 14.0 Hz, C2-αH), 5.13, 5.67 (each 1H, s, =$CH_2$ x 2). IR ($CHCl_3$) $cm^{-1}$: 1700 (C=O), 1605 (C=C).

MS *m/z* (rel. int. %): 164 ($M^+$, 18.0), 69 (100). HRMS Calcd for $C_{11}H_{16}O$: 164.1199. Found: 164.1199.

**(+)-(1*S*,4*R*,7*R*)- and (+)-(1*S*,4*S*,7*R*)-8,8-Dimethyl-4-hydroxymethylbicyclo[5.1.0]octan-3-one (16)** ----- TBAF (5.87 ml of a 1.0 M solution in THF, 5.87 mmol) was added to a solution of ketone **13** (1.16 g, 3.91 mmol) in THF (40 ml), and the whole was stirred at room temperature for 12 h. Then $H_2O$ was added, and resulting mixture was concentrated. After dilution with AcOEt, the organic layer was separated, washed with $H_2O$ and brine, dried, and concentrated to give the corresponding crude keto alcohol which was taken to the next step without further purification. A mixture of the previous keto alcohol and potassium carbonate (1.47 g, 10.6 mmol) in MeOH (18 ml) was stirred at room temperature for 7.5 h. The reaction was quenched with $H_2O$ and 10 % aqueous HCl, and resulting mixture was concentrated. After dilution with AcOEt, the organic layer was separated, washed with $H_2O$ and brine, dried, concentrated, and purified by column chromatography (*n*-hexane : AcOEt = 1 : 1) to give a mixture of keto alcohols **16** (587 mg, 82 %) as a colorless oil: **4*R*-Isomer of 16:** $[\alpha]^{26}_D$ +193.0 (*c* = 0.905, $CHCl_3$). $^1$H-NMR (500 MHz, $CDCl_3$) δ: 0.80—0.88 (2H, m, C1- and C7-H), 0.97, 1.09 (each 3H, s, C8-Me x 2), 0.89—1.16 (1H, m, C6-βH), 1.58 (1H, m, C5-αH), 1.81—1.94 (2H, m, C5-βH, C6-αH), 2.13 (1H, dd, *J* = 7.9, 19.5 Hz, C2-βH), 2.70 (1H, dd, *J* = 7.9, 19.5 Hz, C2-αH), 3.44 (1H, m, C4-H), 3.64 (1H, dd, *J* = 3.7, 11.3 Hz, one of C4-$CH_2$), 3.74 (1H, dd, *J* = 7.3, 11.3 Hz, one of C4-$CH_2$). IR ($CHCl_3$) $cm^{-1}$: 3500 (OH), 1695 (C=O). MS *m/z* (rel. int. %): 182 ($M^+$, 18.9), 81 (100). HRMS Calcd for $C_{11}H_{16}O$: 182.1304. Found: 182.1296. **4*S*-Isomer of 16:** $[\alpha]^{27}_D$ +199.0 (*c* = 0.475, $CHCl_3$). $^1$H-NMR (500 MHz, $CDCl_3$) δ: 0.58 (1H, ddd, *J* = 6.1, 9.2, 11.3 Hz, C1-H), 0.74 (1H, ddd, *J* = 6.1, 9.2, 11.0 Hz, C7-H), 1.06, 1.08 (each 3H, s, C8-Me x 2), 1.26 (1H, m, C6-βH), 1.43 (1H, dd, *J* = 12.2, 25.0 Hz, C5-αH), 1.67 (1H, br s, OH), 1.84 (1H, m, C5-βH), 2.10—2.18 (2H, m, C2-βH, C6-αH), 2.47 (1H, m, C4-H), 2.53 (1H, dd, *J* = 6.1, 11.6 Hz, C2-αH), 3.64 (1H, dd, *J* = 3.1, 11.6 Hz, one of C4-$CH_2$), 3.74 (1H, dd, *J* = 7.3, 11.6 Hz, one of C4-$CH_2$). IR ($CHCl_3$) $cm^{-1}$: 3500 (OH), 1690 (C=O). MS *m/z* (rel. int. %): 182 ($M^+$, 18.9), 81 (100). HRMS Calcd for $C_{11}H_{16}O$: 182.1304. Found: 182.1286.

**(−)-(1*S*,4*R*,7*R*)- and (+)-(1*S*,4*S*,7*R*)-4-*tert*-Butyldimethylsiloxymethyl-8,8-dimethylbicyclo[5.1.0]octan-3-ol (10 and 11 from a mixture of keto alcohols 16)** ----- A solution of a mixture of keto alcohols **16** (587 mg, 3.22 mmol) in $Et_2O$ (5 ml) was added dropwise to a stirred suspension of LAH (124 mg, 3.26 mmol) in $Et_2O$ (30 ml) at 0 °C and the mixture was stirred for 15 min at that temperature. After successive careful addition of $H_2O$ (0.125 ml), 1N NaOH solution (0.125 ml) and $H_2O$ (0.375 ml), the resulting precipitates were filtered off through a celite pad. The filtrate was dried and concentrated to give the corresponding crude diol which was taken to the next step without further purification. TBSCl (532 mg, 3.53 mmol) was added to a solution of the previous diol and imidazole (478 mg, 7.02 mmol) in DMF (16 ml) at 0 °C, and the whole was allowed to warm to room temperature under stirring, and the stirring was continued for 12 h. After dilution with $Et_2O$, the reaction mixture was washed with $H_2O$ and brine, dried, concentrated, and purified by column chromatography (*n*-hexane : AcOEt = 20 : 1) to give the alcohols **10** (385 mg, 40 % from **16**) and **11** (495 mg, 52 % from **16**) each as a colorless oil.

**(+)-(1*S*,2*S*,4*R*,7*R*)-4-*tert*-Butyldimethylsiloxymethyl-8,8-dimethyl-2-(2-oxopropyl)bicyclo[5.1.0]octan-3-one (17)** ----- A suspension of palladium(II) chloride (1.62 g, 9.14 mmol) and copper(I) chloride (3.62 g, 36.6 mmol) in aqueous DMF (DMF : $H_2O$ = 4 : 1, 180 ml) was stirred at room temperature for 3 h under an oxygen atmosphere. A solution of **14** (6.08 g, 18.3 mmol) in DMF (108 ml) was added to the suspension and stirred at room temperature for 4.5 h. After the addition of $H_2O$ (216 ml), the whole was filtered through a celite pad, and the filtrate was extracted with AcOEt. The extract was washed with aqueous $NaHCO_3$, $H_2O$ and brine, dried, concentrated, and purified by column chromatography (*n*-hexane : AcOEt = 4 : 1) to give the diketone **17** (6.08 g, 96 %) as a yellow oil. $[\alpha]^{32}_D$ +153.8 (*c* = 0.835, $CHCl_3$). $^1$H-NMR (500 MHz, $CDCl_3$) δ : 0.05 (6H, s, Si-Me x 2), 0.30 (1H, dd, *J* = 9.2, 9.8 Hz, C1-H), 0.76 (1H, ddd, *J* = 6.1, 9.2, 11.0 Hz, C7-H), 0.88 (9H, s, Si-*t*-Bu), 1.04, 1.04 (each 3H, s, C8-Me x 2), 1.32 (1H, m, C6-βH), 1.76—1.82 (2H, m, C5-H), 1.88 (1H, m, C6-αH), 2.13 (3H, s, C(O)Me),

2.50—2.58 (2H, m, C2-H, one of C1'-H), 2.93—3.02 (2H, m, C4-H, one of C1'-H), 3.69 (1H, dd, $J$ = 7.9, 10.4 Hz, one of C4-$CH_2$), 3.92 (1H, dd, $J$ = 5.5, 10.4 Hz, one of C4-$CH_2$). IR ($CHCl_3$) $cm^{-1}$: 1715, 1700 (C=O). MS *m/z* (rel. int. %): 352 ($M^+$, 0.8), 295 (100). HRMS Calcd for $C_{20}H_{36}O_3Si$: 352.2431. Found: 352.2430.

**(+)-(1*R*, 2*R*, 4*R*, 7*S*)-7-*tert*-Butyldimethylsiloxymethyl-3,3-dimethyltricyclo[6.3.0.$0^{2,4}$]-undec-8-en-10-one (18)** ----- A solution of diketone **17** (2.15 g, 6.10 mmol) in THF (50 ml) was added dropwise to a solution of NaHMDS (6.71 ml of a 1.0 M solution in THF, 6.71 mmol) and HMPA (2.12 ml, 12.2 mmol) in THF (250 ml) and the mixture was stirred at –78 °C for 15 min, at 0° C for 15 min, and at 50 °C for 10 min. The reaction was quenched with aqueous $NH_4Cl$ and $H_2O$, and resulting mixture was concentrated. After dilution with AcOEt, the organic layer was separated, washed with $H_2O$ and brine, dried, concentrated, and purified by column chromatography (*n*-hexane : AcOEt = 15 : 1) to give the enone **18** (1.71 g, 84 %) as a colorless oil. $[\alpha]^{33}_D$ +57.6 ($c$ = 0.725, $CHCl_3$). $^1$H-NMR (500 MHz, $CDCl_3$) δ: 0.01, 0.02 (each 3H, s, Si-Me x 2), 0.29 (1H, dd, $J$ = 9.2, 9.2 Hz, C2-H), 0.70 (1H, ddd, $J$ = 6.1, 9.2, 11.0 Hz, C4-H), 0.86 (9H, s, Si-*t*-Bu), 1.04, 1.09 (each 3H, s, C3-Me x 2), 1.28 (1H, m, C5-βH), 1.71 (1H, m, C6-αH), 1.85 (1H, m, C5-αH), 1.96 (1H, m, C6-βH), 2.20 (1H, d, $J$ = 17.7 Hz, C11-αH), 2.61 (1H, dd, $J$ = 6.7, 17.7 Hz, C11-βH), 2.63 (1H, dd, $J$ = 6.7, 9.2 Hz, C1-H), 3.11 (1H, m, C7-H), 3.64 (2H, dd, $J$ = 1.9, 6.7 Hz, C7-$CH_2$), 5.86 (1H, s, C9-H). $^{13}$C-NMR (50.3 MHz, $CDCl_3$) δ: –5.4 (q x 2), 15.6 (q), 18.3 (s), 19.9 (t), 21.0 (s), 25.9 (q x 3), 28.1 (t), 28.4 (d), 28.7 (q), 32.1 (d), 38.4 (d), 44.6 (d), 44.7 (t), 65.3 (t), 130.3 (d), 186.8 (s), 209.7 (s). IR ($CHCl_3$) $cm^{-1}$: 1690 (C=O), 1615 (C=C). MS *m/z* (rel. int. %): 334 ($M^+$, 0.6), 277 (100). HRMS Calcd for $C_{20}H_{34}O_2Si$: 334.2325. Found: 334.2312.

**(+)-(1*R*, 2*R*, 4*R*, 7*S*, 11*R*)-7-*tert*-Butyldimethylsiloxymethyl-3,3,11-trimethyltricyclo-[6.3.0.$0^{2,4}$]undec-8-en-10-one (7)** ----- *n*-BuLi (3.45 ml of a 1.60 M solution in *n*-hexane, 5.52 mmol) was added to a solution of 1,1,1,3,3,3-hexamethyldisilazane (1.22 ml, 5.49 mmol) in THF (25 ml) at 0 °C and the mixture was stirred for 1 h. HMPA (1.92 ml, 11.0 mmol) was added and the whole was stirred at –78 °C for 15 min, after that a solution of enone **18** (1.23 g, 3.68 mmol) in THF (12 ml) was added dropwise and stirred at –78 °C for 1 h. MeI (0.467 ml, 7.35 mmol) was added dropwise, and the reaction mixture was allowed to warm to room temperature over the period of 2 h. The reaction was quenched with aqueous $NH_4Cl$ and $H_2O$, and resulting mixture was concentrated. After dilution with AcOEt, the organic layer was separated, washed with $H_2O$ and brine, dried, concentrated, and purified by column chromatography (*n*-hexane : AcOEt = 20 : 1) to give **7** (1.18 g, 92 %) as a colorless oil. $[\alpha]^{34}_D$ +58.4 ($c$ = 1.03, $CHCl_3$). $^1$H-NMR (500 MHz, $CDCl_3$) δ: 0.01, 0.02 (each 3H, s, Si-Me x 2), 0.33 (1H, dd, $J$ = 9.2, 9.8 Hz, C2-H), 0.70 (1H, ddd, $J$ = 6.1, 9.2, 11.0 Hz, C4-H), 0.85 (9H, s, Si-*t*-Bu), 1.04, 1.09 (each 3H, s, C3-Me x 2), 1.11 (3H, d, $J$ = 7.3 Hz, C11-Me), 1.30 (1H, m, C5-βH), 1.70—1.95 (3H, m, C5-αH, C6-H), 2.18 (1H, q, $J$ = 9.8 Hz, C11-H), 2.22 (1H, d, $J$ = 9.8 Hz, C1-H), 3.07 (1H, m, C7-H), 3.64 (2H, d, $J$ = 8.6 Hz, C7-$CH_2$), 5.80 (1H, s, C9-H). IR ($CHCl_3$) $cm^{-1}$: 1690 (C=O), 1600 (C=C). MS *m/z* (rel. int. %): 348 ($M^+$, 0.4), 291 (100). HRMS Calcd for $C_{21}H_{36}O_2Si$: 348.2484. Found: 348.2496.

**(+)-(1*R*, 2*R*, 4*R*, 7*S*, 11*S*)-7-*tert*-Butyldimethylsiloxymethyl-3,3,11-trimethyltricyclo-[6.3.0.$0^{2,4}$]undec-8-en-10-one (19)** ----- *n*-BuLi (0.206 ml of a 1.56 M solution in *n*-hexane, 0.321 mmol) was added to a solution of 1,1,1,3,3,3-hexamethyldisilazane (0.0712 ml, 0.321 mmol) in THF (2 ml) at –20 °C and the mixture was stirred for 20 min. To this was added dropwise a solution of **7** (74.4 mg, 0.214 mmol) in THF (0.2 ml), and then HMPA (0.2 ml) at –78 °C. The reaction mixture was allowed to warm to 0 °C over the period of 2 h. The reaction was quenched with aqueous $NH_4Cl$ and $H_2O$ at 0 °C. After dilution with AcOEt, the organic layer was separated, washed with $H_2O$ and brine, dried, concentrated, and purified by column chromatography (*n*-hexane : AcOEt = 15 : 1) to give **19** (63.8 mg, 86 %) as a colorless oil. $[\alpha]^{24}_D$ +41.1 ($c$ = 0.440, $CHCl_3$). $^1$H-NMR (500 MHz, $CDCl_3$) δ : 0.00—0.15 (1H, m, C2-H), 0.01, 0.02 (each 3H, s, Si-Me x 2), 0.69 (1H, ddd, $J$ = 5.5, 9.2, 11.0 Hz, C4-H), 0.86 (9H, s, Si-*t*-Bu), 1.04, 1.07 (each 3H, s, C3-Me x 2), 1.12 (3H, d, $J$ = 7.3 Hz, C11-Me), 0.90—1.40 (1H, m, C5-βH), 1.67 (1H, m, C6-αH), 1.85 (1H, m, C5-αH), 1.98 (1H, m, C6-βH), 2.55 (1H, dq, $J$ = 6.1, 7.3 Hz,

C11-H), 2.68 (1H, dd, $J$ = 6.1, 9.8 Hz, C1-H), 3.11 (1H, m, C7-H), 3.66 (2H, d, $J$ = 7.3 Hz, C7-$CH_2$), 5.83 (1H, s, C9-H). IR ($CHCl_3$) $cm^{-1}$: 1690 (C=O), 1600 (C=C). MS *m/z* (rel. int. %): 348 ($M^+$, 0.4), 291 (100). HRMS Calcd for $C_{21}H_{36}O_2Si$: 348.2485. Found: 348.2491.

**(+)-(1*R*,2*S*,4*R*,7*S*,8*R*,11*S*)-7-*tert*-Butyldimethylsiloxymethyl-3,3,11-trimethyltricyclo-[6.3.0.$0^{2,4}$]undecan-10-one (20)** ----- A suspension of palladium carbon (Pd/C, Pd: 5%, 1.5 mg) in methanol (1 ml) was stirred at room temperature for 20 min under an atmospheric pressure of hydrogen. A solution of **19** (15.7 mg, 0.0451 mmol) in methanol (0.1 ml) was added to the above suspension and the mixture was stirred at room temperature under a hydrogen atmosphere for 2 h. The reaction mixture was filtered, concentrated, and purified by column chromatography (*n*-hexane : AcOEt = 20 : 1) to give the ketone **20** (14.7 mg, 93 %) as a colorless oil. $[\alpha]^{23}_D$ +17.8 ($c$ = 0.510, $CHCl_3$). $^1$H-NMR (500 MHz, $CDCl_3$) δ: 0.03 (6H, s, Si-Me x 2), 0.00—0.12 (1H, m, C2-H), 0.67 (1H, m, C4-H), 0.89 (9H, s, Si-*t*-Bu), 0.98, 1.01 (each 3H, s, C3-Me x 2), 1.02 (3H, d, $J$ = 7.3 Hz, C11-Me), 1.38 (1H, m, C5-βH), 1.53 (1H, m, C6-αH), 1.78—1.88 (2H, m, C5-αH, C6-βH), 1.90—2.00 (2H, m, C7-H, one of C9-H), 2.16—2.22 (2H, m, C1- and C8-H), 2.35 (1H, dq, $J$ = 7.3, 8.6 Hz, C11-H), 2.55 (1H, dd, $J$ = 8.5, 18.9 Hz, one of C9-H), 3.46 (1H, ddd, $J$ = 2.4, 6.1, 9.8 Hz, one of C7-$CH_2$), 3.55 (1H, dd, $J$ = 3.1, 9.8 Hz, one of C7-$CH_2$). IR ($CHCl_3$) $cm^{-1}$: 1730(C=O). MS *m/z* (rel. int. %): 350($M^+$, 0.3), 293 (100). HRMS Calcd for $C_{21}H_{38}O_2Si$: 350.2638. Found: 350.2633.

**(1*R*,2*R*,4*R*,7*S*,11*S*)-7-*tert*-Butyldimethylsiloxymethyl-3,3,11-trimethyltricyclo-[6.3.0.$0^{2,4}$]undec-8-en-10-one Tosylhydrazone (21)** ----- Tosylhydrazine (47.0 mg, 0.253 mmol) was added to a solution of **19** (44.0 mg, 0.126 mmol) in acetic acid (1.5 ml), and the whole was stirred at room temperature for 12 h. The reaction was quenched with $H_2O$, and the resulting mixture was extracted with $CHCl_3$. The extract was washed with $H_2O$ and brine, dried, concentrated, and purified by PTLC (*n*-hexane : AcOEt = 5 : 1) to give **19** (7.0 mg, 16 %) and the tosylhydrazone **21** (41.7 mg, 76 % based on 84 % conversion) as a yellow oil. $^1$H-NMR (200 MHz, $CDCl_3$) δ: –0.01, 0.00 (each 3H, s, Si-Me x 2), 0.11, 0.25 (each 1/2H, dd, $J$ = 9.2, 9.9 Hz, C2-H), 0.45—0.80 (1H, m, C4-H), 0.83 (9H, s, Si-*t*-Bu), 1.00, 1.06 (each 3H, s, C3-Me x 2), 0.80—2.62 (10H, m, C1-, C5-, C6-, C11-H, C11-Me, NH), 2.41 (3H, s, Ar-Me), 2.80—3.00 (1H, m, C7-H), 3.55 (2H, d, $J$ = 6.8 Hz, C7-$CH_2$), 5.78, 5.97 (each 1/2H, s, C9-H), 7.57 (4H, AA'BB', Ar-H). IR ($CHCl_3$) $cm^{-1}$: 1620 (C=C), 1600 (C=N). MS *m/z* (rel. int. %): 516 ($M^+$, 6.7), 187 (100). HRMS Calcd for $C_{28}H_{44}N_2O_3SSi$: 516.2842. Found: 516.2858.

**(+)-(1*R*,2*S*,4*R*,7*S*,8*S*,11*S*)-7-*tert*-Butyldimethylsiloxymethyl-3,3,11-trimethyltricyclo-[6.3.0.$0^{2,4}$]undec-9-ene (22)** ----- $NaBH_4$ (30.7 mg; 0.808 mmol) was carefully added to a solution of tosylhydrazone **21** (41.7 mg, 0.0808 mmol) in acetic acid (0.6 ml) and the mixture was stirred at room temperature for 1 h, and at 70 °C for 4 h. The reaction was quenched with ice-water, made basic (pH = 9) with 1N NaOH solution, and the resulting mixture was extracted with $Et_2O$. The extract was washed with $H_2O$ and brine, dried, concentrated, and purified by column chromatography (*n*-hexane : AcOEt = 100 : 1) to give **22** (13.8 mg, 51 %) as a colorless oil. $[\alpha]^{24}_D$ +42.8 ($c$ = 0.130, $CHCl_3$). $^1$H-NMR (500 MHz, $CDCl_3$) δ: 0.02, 0.04 (each 3H, s, Si-Me x 2), 0.40 (1H, dd, $J$ = 9.2, 9.8 Hz, C2-H), 0.62 (1H, m, C4-H), 0.89 (9H, s, Si-*t*-Bu), 1.01, 1.02 (each 3H, s, C3-Me x 2), 1.04 (3H, d, $J$ = 6.7 Hz, C11-Me), 1.00—2.08 (6H, m, C1-, C5-, C6- and C7-H), 2.60 (1H, m, C11-H), 2.76 (1H, m, C8-H), 3.52 (1H, dd, $J$ = 4.9, 10.4 Hz, one of C7-$CH_2$), 3.61 (1H, dd, $J$ = 5.5, 10.4 Hz, one of C7-$CH_2$), 5.58 (1H, ddd, $J$ = 2.4, 2.4, 5.5 Hz, C9-H), 5.72 (1H, d, $J$ = 5.5 Hz, C10-H). IR ($CHCl_3$) $cm^{-1}$: 1600(C=C). MS *m/z* (rel. int. %): 334 ($M^+$, 1.5), 277 (100). HRMS Calcd for $C_{21}H_{38}OSi$: 334.2692. Found : 334.2693.

**(1*R*,2*S*,4*R*,7*S*,8*R*,11*S*)-7-*tert*-Butyldimethylsiloxymethyl-3,3,11-trimethyltricyclo-[6.3.0.$0^{2,4}$]undecan-10-yl Phenyl Thionocarbonate (23)** ----- $NaBH_4$ (30.7 mg, 0.808 mmol) was added to a solution of ketone **20** (9.8 mg, 0.0280 mmol) in methanol (1 ml), and the whole was stirred at room temperature for 2 h. The reaction was quenched with aqueous $NH_4Cl$. After dilution with water, the reaction mixture was extracted with AcOEt. The extract was washed with $H_2O$ and brine, dried, concentrated to give the corresponding crude alcohol which was taken to the next step without further

purification. Phenyl chlorothionoformate (0.0061 ml, 0.032 mmol) was added to a solution of the previous alcohol, pyridine (0.0080 ml, 0.093 mmol) and DMAP (0.3 mg, 0.003 mmol) in $CH_2Cl_2$ (0.2 ml), and the whole was stirred at room temperature for 6 h. The reaction was quenched with $H_2O$, and the resulting mixture was extracted with AcOEt. The extract was washed with $H_2O$ and brine, dried, concentrated, and purified by column chromatography (*n*-hexane : AcOEt = 100 : 1) to give the thiocarbonate **23** (11.6 mg, 85 %) as a colorless oil. $^1$H-NMR (200 MHz, $CDCl_3$) δ: 0.04, 0.05 (each 3H, s, Si-Me x 2), 0.08—0.75 (2H, m, C2- and C4-H), 0.89 (9H, s, Si-*t*-Bu), 0.80—2.72 (19H, m, C1-, C5-, C6-, C7-, C8-, C9-, C11-H, C3-, C11-Me), 3.28—3.83 (2H, m, C7-$CH_2$), 5.04 (1/4H, m, C10-H), 5.23 (3/4H, m, C10-H), 7.04—7.60 (5H, m, Ar-H). IR ($CHCl_3$) cm$^{-1}$: 1595, 1495(C=C). MS *m/z* (rel. int. %): 334 ($M^+$–PhOC(S)OH, 2.1), 94 (100).

**(−)-(1*R*, 2*S*, 4*R*, 7*S*, 8*R*, 11*R*)-7-*tert*-Butyldimethylsiloxymethyl-3,3,11-trimethyltricyclo-[6.3.0.0$^{2,4}$]undecane (24)** ----- A solution of thiocarbonate **23** , *n*-$Bu_3SnH$ (0.0095 ml, 0.036 mmol) and AIBN (0.8 mg, 0.005 mmol) in degassed toluene (0.35 ml) was stirred at reflux for 3 h, concentrated, and purified by column chromatography (*n*-hexane : AcOEt = 100 : 1) to give **24** (5.4 mg, 68 %) as a colorless oil. $[\alpha]^{28}_D$ −3.6 (*c* = 1.51, $CHCl_3$). $^1$H-NMR (500 MHz, $CDCl_3$) δ: 0.03 (6H, s, Si-Me x 2), 0.45 (1H, dd, *J* = 9.2, 9.2 Hz, C2-H), 0.57 (1H, m, C4-H), 0.89 (9H, s, Si-*t*-Bu), 0.91 (3H, d, *J* = 7.3 Hz, C11-Me), 0.99, 1.00 (each 3H, s, C3-Me x 2), 1.06—2.03 (12H, m, C1-, C5-, C6-, C7-, C8-, C9-, C10- and C11-H), 3.55 (1H, dd, *J* = 9.2, 9.8 Hz, one of C7-$CH_2$), 3.67 (1H, dd, *J* = 6.7, 9.8 Hz, one of C7-$CH_2$). MS *m/z* (rel. int. %): 336 ($M^+$, 27.3), 203 (100). HRMS Calcd for $C_{21}H_{40}OSi$: 336.2848. Found: 336.2853.

**(−)-(1*R*, 2*S*, 4*R*, 7*S*, 8*R*, 11*R*)-3,3,11-Trimethyltricyclo[6.3.0.0$^{2,4}$]undecan-7-ylmethanol (25)** ----- TBAF (0.370 ml of a 1.0 M solution in THF, 0.370 mmol) was added to a solution of **24** (50.0 mg, 0.149 mmol) in THF (2 ml), and the whole was stirred at room temperature for 6 h. Then $H_2O$ was added, and the resulting mixture was extracted with AcOEt. The extract was washed with $H_2O$ and brine, dried, concentrated, and purified by column chromatography (*n*-hexane : AcOEt = 5 : 1) to give the alcohol **25** (33.0 mg, 100 %) as a colorless oil. $[\alpha]^{30}_D$ −7.4 (*c* = 1.03, $CHCl_3$). $^1$H-NMR (500 MHz, $CDCl_3$) δ: 0.47 (1H, dd, *J* = 9.2, 9.2 Hz, C2-H), 0.59 (1H, m, C4-H), 0.89 (3H, d, *J* = 7.3 Hz, C11-Me), 0.98, 1.00 (each 3H, s, C3-Me x 2), 0.84—2.10 (13H, m, C1-, C5-, C6-, C7-, C8-, C9-, C10-, C11-H, OH), 3.58 (1H, dd, *J* = 9.2, 9.8 Hz, one of C7-$CH_2$), 3.72 (1H, dd, *J* = 6.7, 9.8 Hz, one of C7-$CH_2$). IR ($CHCl_3$) cm$^{-1}$: 3600, 3450 (OH). MS *m/z* (rel. int. %): 222 ($M^+$, 21.4), 82 (100). HRMS Calcd for $C_{15}H_{26}O$: 222.1981. Found: 222.1981.

**(+)-(1*R*, 2*S*, 4*R*, 7*S*, 8*R*, 11*R*)-3,3,11-Trimethyltricyclo[6.3.0.0$^{2,4}$]undecan-7-ylmethyl Methanesulfonate (26)** ----- MsCl (0.0207 ml, 0.223 mmol) was added to a solution of alcohol **25** (33.0 mg, 0.149 mmol), $Et_3N$ (0.0447 ml, 0.268 mmol) and DMAP (4.4 mg, 0.030 mmol) in $CH_2Cl_2$ (2 ml), and the whole was stirred at 0 °C for 2 h. The reaction was quenched with $H_2O$, and the resulting mixture was extracted with $Et_2O$. The extract was washed with $H_2O$ and brine, dried, concentrated, and purified by column chromatography (*n*-hexane : AcOEt = 8 : 1) to give the mesylate **26** (44.5 mg, 100 %) as a colorless oil. $[\alpha]^{28}_D$ +5.2 (*c* = 0.905, $CHCl_3$). $^1$H-NMR (500 MHz, $CDCl_3$) δ: 0.49 (1H, dd, *J* = 9.8, 10.4 Hz, C2-H), 0.59 (1H, ddd, *J* = 6.1, 9.8, 11.6 Hz, C4-H), 0.89 (3H, d, *J* = 7.3 Hz, C11-Me), 0.99, 1.00 (each 3H, s, C3-Me x 2), 1.14 (1H, ddd, *J* = 11.6, 12.2, 14.7 Hz, C5-βH), 1.24 (1H, m, one of C10-H), 1.33 (1H, m, one of C9-H), 1.36 (1H, dd, *J* = 9.8, 10.4 Hz, C1-H), 1.48 (1H, ddd, *J* = 3.7, 10.4, 12.2 Hz, C6-αH), 1.64—1.79 (3H, m, C5-αH, one of C9-H, one of C10-H), 1.88—2.11 (3H, m, C6-βH, C8- and C11-H), 2.30 (1H, m, C7-H), 2.99 (3H, s, $SO_2Me$), 4.20 (1H, dd, *J* = 9.2, 9.8 Hz, one of C7-$CH_2$), 4.29 (1H, dd, *J* = 3.7, 9.8 Hz, one of C7-$CH_2$). MS *m/z* (rel. int. %): 300 ($M^+$, 6.6), 161 (100). HRMS Calcd for $C_{16}H_{28}O_3S$: 300.1757. Found: 300.1755.

**(+)-Aromadendrene (3)** ----- A mixture of mesylate **26** (44.5 mg, 0.148 mmol) and DBU (0.115 ml, 0.742 mmol) in toluene (2 ml) was stirred at 100 °C for 18 h. The reaction was quenched with $H_2O$, and the resulting mixture was extracted with *n*-hexane. The extract was concentrated and purified by column

chromatography (*n*-hexane) to give (+)-aromadendrene **3** (27.0 mg, 89 %) as a colorless oil. $[\alpha]^{28}_D$ +8.9 (*c* = 0.390, EtOH). $^1$H-NMR (500 MHz, $CDCl_3$) δ: 0.62 (1H, dd, *J* = 9.8, 11.0 Hz, C2-H), 0.68 (1H, ddd, *J* = 6.1, 9.8, 11.0 Hz, C4-H), 0.97 (3H, d, *J* = 7.3 Hz, C11-Me), 0.90—1.12 (1H, m, C5-βH), 0.98, 1.04 (each 3H, s, C3-Me x 2), 1.18 (1H, m, one of C10-H), 1.38 (1H, ddd, *J* = 10.4, 10.4, 11.0 Hz, C1-H), 1.56 (1H, m, C9-βH), 1.68 (1H, m, C9-αH), 1.85 (1H, m, one of C10-H), 1.96 (1H, ddd, *J* = 4.9, 6.1, 14.3 Hz, C5-αH), 2.06 (1H, dd, *J* = 13.4, 14.0 Hz, C6-αH), 2.10 (1H, m, C11-H), 2.22 (1H, m, C8-H), 2.41 (1H, dd, *J* = 6.1, 13.4 Hz, C6-βH), 4.62 (2H, s, $=CH_2$ x 2). IR ($CHCl_3$) $cm^{-1}$: 1630 (C=C). MS *m/z* (rel. int. %): 204 ($M^+$, 68.9), 161 (100). HRMS Calcd for $C_{15}H_{24}$: 204.1878. Found: 204.1885.

**(+)-(1*R*, 2*S*, 4*R*, 7*S*, 8*S*, 11*R*)-7-*tert*-Butyldimethylsiloxymethyl-3,3,11-trimethyltricyclo-[6.3.0.0$^{2,4}$]undecane (27)** ----- A suspension of Pd/C (Pd : 5%, 1.2 mg) in methanol (1 ml) was stirred at room temperature for 20 min under an atmospheric pressure of hydrogen. A solution of **22** (12.1 mg, 0.0362 mmol) in methanol (0.1 ml) was added to the above suspension and stirred at room temperature under a hydrogen atmosphere for 2 h. The reaction mixture was filtered, concentrated, and purified by column chromatography (*n*-hexane : AcOEt = 100 : 1) to give **27** (11.7 mg, 96 %) as a colorless oil. $[\alpha]^{25}_D$ +4.7 (*c* = 0.433, $CHCl_3$). $^1$H-NMR (500 MHz, $CDCl_3$) δ: 0.03 (6H, s, Si-Me x 2), 0.26 (1H, dd, *J* = 9.2, 11.8 Hz, C2-H), 0.55 (1H, ddd, *J* = 6.1, 9.2, 11.0 Hz, C4-H), 0.89 (9H, s, Si-*t*-Bu), 0.93 (3H, d, *J* = 7.3 Hz, C11-Me), 0.96, 1.02 (each 3H, s, C3-Me x 2), 0.80—2.08 (12H, m, C1-, C5-, C6-, C7-, C8-, C9-, C10- and C11-H), 3.34 (1H, dd, *J* = 6.7, 9.8 Hz, one of C7-$CH_2$), 3.60 (1H, dd, *J* = 3.5, 9.8 Hz, one of C7-$CH_2$). MS *m/z* (rel. int. %): 336 ($M^+$, 6.4), 279 (100). HRMS Calcd for $C_{21}H_{40}OSi$: 336.2847. Found: 336.2847.

**(+)-(1*R*, 2*S*, 4*R*, 7*S*, 8*S*, 11*R*)-3,3,11-Trimethyltricyclo[6.3.0.0$^{2,4}$]undecan-7-ylmethanol (28)** ----- TBAF (0.0720 ml of a 1.0 M solution in THF, 0.0720 mmol) was added to a solution of **27** (11.7 mg, 0.0348 mmol) in THF (0.5 ml), and the whole was stirred at room temperature for 6 h. Then $H_2O$ was added, and the resulting mixture was extracted with AcOEt. The extract was washed with $H_2O$ and brine, dried, concentrated, and purified by column chromatography (*n*-hexane : AcOEt = 5 : 1) to give the alcohol **28** (7.7 mg, 100 %) as a colorless oil. $[\alpha]^{30}_D$ +1.8 (*c* = 0.425, $CHCl_3$). $^1$H-NMR (500 MHz, $CDCl_3$) δ: 0.27 (1H, dd, *J* = 9.2, 11.6 Hz, C2-H), 0.59 (1H, ddd, *J* = 6.1, 9.2, 11.0 Hz, C4-H), 0.94 (3H, d, *J* = 6.7 Hz, C11-Me), 0.97, 1.02 (each 3H, s, C3-Me x 2), 0.80—2.12 (13H, m, C1-, C5-, C6-, C7-, C8-, C9-, C10-, C11-H, OH), 3.42 (1H, dd, *J* = 6.7, 11.0 Hz, one of C7-$CH_2$), 3.67 (1H, dd, *J* = 3.1, 11.0 Hz, one of C7-$CH_2$). IR ($CHCl_3$) $cm^{-1}$: 3600, 3450 (OH). MS *m/z* (rel. int. %): 222 ($M^+$, 27.5), 82 (100). HRMS Calcd for $C_{15}H_{26}O$: 222.1984. Found: 222.2006.

**(+)-(1*R*, 2*S*, 4*R*, 7*S*, 8*S*, 11*R*)-3,3,11-Trimethyltricyclo[6.3.0.0$^{2,4}$]undecan-7-ylmethyl Methanesulfonate (29)** ----- MsCl (0.0032 ml, 0.042 mmol) was added to a solution of alcohol **28** (7.7 mg, 0.035 mmol), $Et_3N$ (0.0087 ml, 0.062 mmol) and DMAP (0.8 mg, 0.007 mmol) in $CH_2Cl_2$ (0.5 ml), and the whole was stirred at 0 °C for 2 h. The reaction was quenched with $H_2O$, and the resulting mixture was extracted with $Et_2O$. The extract was washed with $H_2O$ and brine, dried, concentrated, and purified by column chromatography (*n*-hexane : AcOEt = 8 : 1) to give the mesylate **29** (10.4 mg, 100 %) as a colorless oil. $[\alpha]^{25}_D$ +11.4 (*c* = 0.268, $CHCl_3$). $^1$H-NMR (500 MHz, $CDCl_3$) δ: 0.28 (1H, dd, *J* = 9.2, 11.6 Hz, C2-H), 0.57 (1H, m, C4-H), 0.94 (3H, d, *J* = 7.3 Hz, C11-Me), 0.97, 1.03 (each 3H, s, C3-Me x 2), 0.80—1.95 (10H, m, C1-, C5-, C6-, C8-, C9- and C10-H), 1.98 (1H, m, C11-H), 2.13 (1H, m, C7-H), 2.99 (3H, s, $SO_2Me$), 4.06 (1H, dd, *J* = 6.7, 9.8 Hz, one of C7-$CH_2$), 4.22 (1H, dd, *J* = 3.1, 9.8 Hz, one of C7-$CH_2$). MS *m/z* (rel. int. %): 300 ($M^+$, 0.7), 82 (100). HRMS Calcd for $C_{16}H_{28}O_3S$: 300.1760. Found: 300.1767.

**(−)-Alloaromadendrene (4)** ----- A mixture of mesylate **29** (10.4 mg, 0.0346 mmol) and DBU (0.0240 ml, 0.173 mmol) in toluene (1 ml) was stirred at 100 °C for 18 h. The reaction was quenched with $H_2O$, and the resulting mixture was extracted with *n*-hexane. The extract was concentrated, and purified by column chromatography (*n*-hexane) to give (−)-alloaromadendrene **4** (5.7 mg, 81 %) as a colorless oil. $[\alpha]^{24}_D$ −27.2 (*c* = 1.76, $CHCl_3$). $^1$H-NMR (500 MHz, $CDCl_3$) δ: 0.25 (1H, dd, *J* = 9.2, 11.0 Hz, C2-H), 0.57

(1H, ddd, $J$ = 6.1, 9.2, 11.0 Hz, C4-H), 0.93 (3H, d, $J$ = 6.7 Hz, C11-Me), 0.95, 1.00 (each 3H, s, C3-Me x 2), 1.12—1.40 (2H, m), 1.63—1.97 (5H, m), 2.06 (1H, m), 2.20—2.38 (2H, m), 2.67 (1H, m, C8-H), 4.70, 4.73 (each 1H, s, $=CH_2$ x 2). IR ($CHCl_3$) $cm^{-1}$: 1630 (C=C). MS *m/z* (rel. int. %): 204 ($M^+$, 11.2), 73 (100). HRMS Calcd for $C_{15}H_{24}$: 204.1876. Found: 204.1861.

**References and Notes**


1) a) Part I. Tanaka, T.; Funakoshi, Y.; Uenaka, K.; Maeda, K.; Mikamiyama, H.; Takemoto, Y.; Maezaki, N.; Iwata, C. *Chem. Pharm. Bull.* **1994**, *42*, 300; b) Part II. Tanaka, T.; Funakoshi, Y.; Uenaka, K.; Maeda, K.; Mikamiyama, H.; Iwata, C. *Chem. Pharm. Bull.* **1994**, *42*, 1243.
2) a) Büchi, G.; Chow, S. W.; Matsuura, T.; Popper, T. L.; Rennhard, H. H.; Wittenau, M. S. *Tetrahedron Lett.* **1959**, 14; b) Dolejs L.; Motl, O.; Soucek, M.; Herout, V.; Sorm, F. *Collect. Czech. Chem. Commun.* **1960**, *25*, 1483; Bowyer, R. C.; Jefferies, P. R. *Chem. Ind.* (London) **1963**, 1245. c) Dolejs, L.; Herout, V.; Motl, O.; Sorm, F.; Soucek, M. *Chem. Ind.* (London) **1959**, 566; Braekman, J. C.; Daloze, D.; Ottinger, R.; Tursch, B. *Experientia* **1977**, *33*, 993; Gijsen, H. J. M.; Wijnberg, J. B. P. A.; Stork, G. A.; de Groot, A. *Tetrahedron* **1992**, *48*, 2465.
3) Blumann, A.; Cole, A. R. H.; Thieberg, K. J. L.; White, D. E. *Chem. Ind.* (London) **1954**, 1426; L. Dolejs, L.; Sorm, F. *Collect. Czech. Chem. Commun.* **1960**, *25*, 1483; Beechan, C. M.; Djerassi, C; Eggert, H. *Tetrahedron* **1978**, *34*, 2503; Pakrashi, S. C.; Dastidar, P. P. G.; Chakrabarty, S.; Achari, B. *J. Org. Chem.* **1980**, *45*, 4765; Friedel, von H. D.; Matusch, R. *Helv. Chim. Acta* **1987**, *70*, 1753.
4) Fattorusso, E.; Magno, S.; Mayol, L.; Santacroce, C.; Sica, D. *Tetrahedron* **1974**, *30*, 3911; *Idem, ibid.* **1975**, *31*, 269; Ciminiello, P.; Fattorusso, E.; Magno, S.; Mayol, L. *Can. J. Chem.* **1987**, *65*, 518; Tada, H.; Yasuda, F. *Chem. Pharm. Bull.* **1985**, *33*, 1941; da Silva, C. C.; Almagro, V.; Zukermann-Schpector, J.; Castellano, E. E.; Marsaioli, A. J. *J. Org. Chem.* **1994**, *59*, 2880.
5) Takaoka, D.; Kawahara, H.; Ochi, S.; Hiroi, M.; Nozaki, H.; Nakayama, M.; Ishizaki, K.; Sakata, K.; Ina, K. *Chem. Lett.* **1986**, 1121; Pizza, C.; De Tommasi, N. *Phytochemistry* **1988**, *27*, 2205; de Tommasi, N.; Pizza, C.; Conti, C.; Orsi, N.; Stein, M. L. *J. Nat. Prod.* **1990**, *53*, 830.
6) Griffith, W. P.; Ley, S. V. *Aldrichimica Acta* **1990**, *23*, 13.
7) Magnus, P. D.; Nobbs, M. S. *Synth. Commun.* **1980**, *10*, 273.
8) Treatment with sodium hydride in refluxing benzene in the presence of a catalytic amount of *tert*-amyl alcohol for 10 min.
9) Iida, T.; Tamura, T.; Matsumoto, T.; Chang, F. C. *Synthesis* **1984**, 957.
10) Hutchins, R. O.; Natale N. R. *J. Org. Chem.* **1978**, *43*, 2299.
11) (+)-Aromadendrene was purchased from Fluka.


(*Received in Japan* 1 *December* 1995; *accepted* 17 *January* 1996)