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Total synthesis of the dolabellane marine diterpenoids, claenone, palominol and dolabellatrienone

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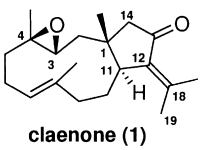
Abstract—The synthesis of marine dolabellane diterpenoids claenone, palominol and dolabellatrienone was conducted from D-mannitol. In each case, formation of the bicyclo[2.2.1]heptane derivative by sequential Michael reaction, preparation of the tetrasubstituted cyclopentane derivative by retro-aldol reaction and cyclization of sulfone were involved as key steps. © 2002 Elsevier Science Ltd. All rights reserved.

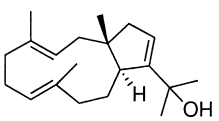
Dolabellane diterpenoid from sea hare was initially isolated by Faulkner et al. in 1976[1] and subsequently, many others were so mainly from marine sources.[2,3] All dolabellane diterpenoids share the unique feature of a *trans*-bicyclo[9.3.0]tetradecane nucleus and most express biological activity.[2,3] Claenone (**1**), isolated by the author's group from the Okinawan marine soft coral, *Clavularia* sp., is a dolabellane diterpenoid (Fig. 1)[4] and has been shown to express ichthyotoxic activity toward killifish *Oryzias latipes* (minimum lethal concentration: 10 μg/mL)[4] and potent cytotoxic activity toward human prostate cancer WMF (GI_{50} 2.42×10^{-7} M) and RB cells (GI_{50} 3.06×10^{-7} M).[5] Palominol (**2**)[6,7a] and 1(*R*), 11(*S*)-dolabella-3(*E*), 7(*E*), 12(18)-trien-13-one (dolabellatrienone, **3**),[6,7] isolated from the gorgonian octocorals *Eunicea calyculata* and *Eunicea laciniata*, are both dolabellane diterpenoids and express week cytotoxic activity toward human colon (HCT 116) cell line (IC_{50} 10 μM, respectively).[6a] These features have prompted research for the total synthesis of dolabellane diterpenoids. Total synthesis[8] of, and synthetic studies[9] on, dolabellane diterpenoid have been reported. The total synthesis of claenone (**1**) appeared in a previous communication of the authors.[8b] The present paper presents the detail of total synthesis of claenone (**1**) together with palominol (**2**) and dolabellatrienone (**3**).

The synthesis of natural products has been conducted at author's laboratory using a bicyclic compound prepared by sequential Michael reaction as chiral building block.[8a,b,10] The synthesis of the objective dolabellane diterpenoids was also attempted in similar methodology. It was considered that synthesis should be conducted via a common synthetic intermediate for the dolabellane diterpenoids (Fig. 2). Diastereoselective sequential Michael reaction of cyclopentenone **F** and chiral α,β-unsaturated ester **G** would provide bicyclo[2.2.1]heptane derivative **E**. Bicyclic compound **E** may possibly be converted to β-hydroxyketone **D** and cleavage of C(14)–C(19) bond in **D** by a retro-aldol reaction may produce tetrasubsutituted cyclopentane segment **C**.[11] It was anticipated that compound **C** would be converted to common synthetic intermediate **B** by elongation of two side chains. Compound **B** may possibly be converted to epoxy sulfone **A** and cyclization of epoxy sulfone **A** would afford claenone (**1**). Cyclization of compound **B** would afford palominol (**2**). Dolabellatrienone (**3**) was considered to be obtained by oxidation of palominol (**2**).[8c]

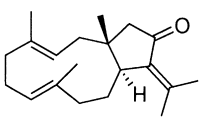
Sequential Michael reaction of enone **4** with chiral α,β-unsaturated ester **5** was carried out. The lithium enolate of enone **4** prepared with LDA was treated with α,β-unsaturated ester **5**[12] from D-mannitol in THF at −78°C to afford bicyclo[2.2.1]heptane derivative **6a** and its diastereomer **6b** (5.3:1) in 82% yield (Scheme 1).



claenone (1)



palominol (2)



dolabellatrienone (3)

Figure 1. Dolabellane diterpenoids claenone (**1**), palominol (**2**) and dolabellatrienone (**3**).

Keywords: antitumour compounds; marine metabolites; terpenes and terpenoids.

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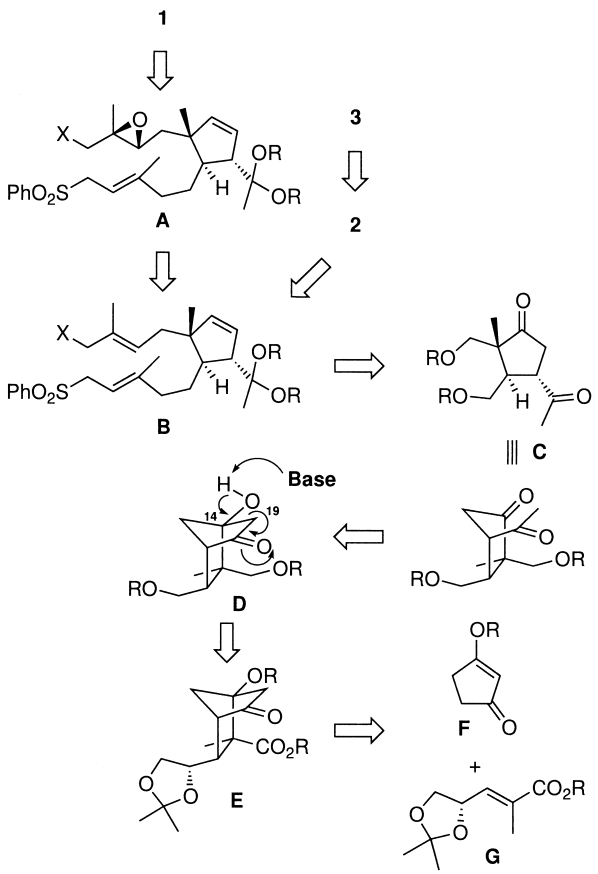
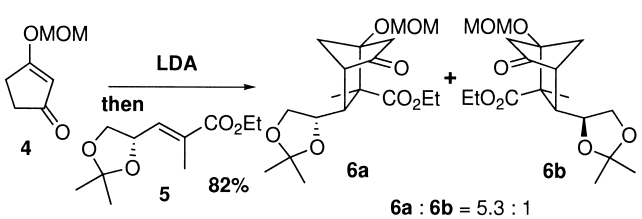


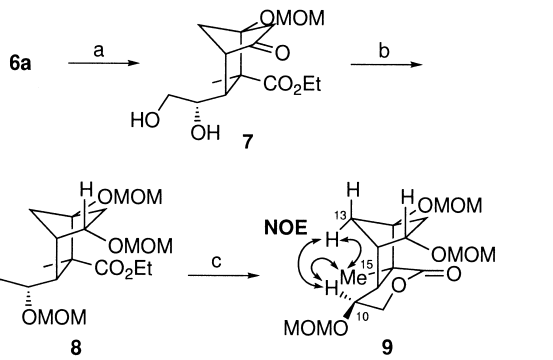
Figure 2. Synthetic strategy for claenone (**1**), palominol (**2**) and dolabellatrienone (**3**).

The relative configuration of bicyclo compound **6a** was determined based on the NOESY spectrum of lactone **9**, obtained from bicyclo compound **6a** via alcohols **7** and **8** (Scheme 2). Acid-catalyzed hydrolysis of acetonide in **6a** gave diol **7**. Protection of the primary hydroxy group in diol **7** as TBS ether, reduction of ketone with $NaBH_4$, protection of two hydroxy groups as MOM ether and removal of TBS group gave alcohol **8**. Hydrolysis of ethyl ester in **8** followed by treatment with bis(2-oxo-3-oxazolidinyl)phosphinic chloride (BOPCl)[13] and Et_3N afforded lactone **9**. NOESY correlations were observed among the methine proton at C-10, one of the methylene protons at C-13 and the methyl protons at C-15.

The stereochemistry of bicyclic compound **6b** was determined by its chemical correlation with compound **6a** (Scheme 3). Diol **7**, obtained from **6a** by hydrolysis of acetonide, was oxidative cleaved by reaction with $NaIO_4$ and subsequent reduction with $NaBH_4$ to give alcohol (−)-**10**, $[\alpha]_D$=−19.8° (*c* 0.55, $CHCl_3$). Acid-



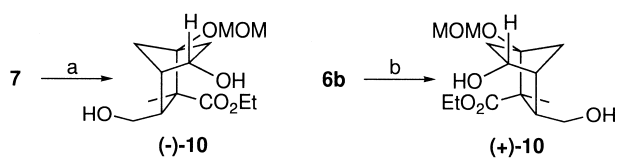
Scheme 1. Sequential Michael reaction of enone **4** with α,β-unsaturated ester **5**.



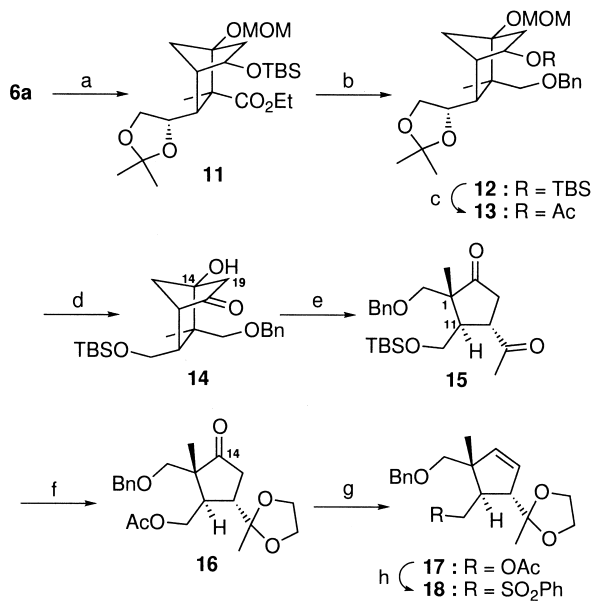
Scheme 2. *Reagents and conditions*: (a) AcOH–H_2O (4:1), 40°C, 83%; (b) (1) TBSCl, imidazole, DMF, rt, 95%, (2) $NaBH_4$, MeOH, 0°C, (3) MOMCl, $^iPr_2NEt$, CH_2ClCH_2Cl, 50°C, (4) TBAF, THF, rt, 60% (three steps); (c) (1) 30% NaOH aq., reflux, (2) BOPCl, Et_3N, CH_2ClCH_2Cl, rt, 38% (two steps).

catalyzed hydrolysis of acetonide in **6b** followed by $NaIO_4$ oxidation-$NaBH_4$ reduction gave alcohol (+)-**10**, $[\alpha]_D$=+19.8° (*c* 0.32, $CHCl_3$), the enantiomer of (−)-**10** from **6a**. In this manner, relative configurations of bicyclic compounds **6a** and **6b** were determined.

The ketone in bicyclic compound **6a** was reduced by treatment with $NaBH_4$ (quantitative yield) followed by protection of the secondary hydroxy group (quantitative yield) to give TBS ether **11** (Scheme 4). The ester in **11** was reduced by $LiAlH_4$ (99% yield) and the primary hydroxy group was protected as Bn ether (94% yield) to give benzyl ether **12**. Deprotection of the TBS group in **12** by treatment with TBAF (quantitative yield) and acetylation of the hydroxy group (99% yield) provided acetate **13**. Acetate **13** was converted to β-hydroxyketone **14**, corresponding to β-hydroxyketone **D** in the synthetic strategy, in the following five steps: (1) acid-catalyzed hydrolysis of acetonide and MOM ether (80% yield), (2) $NaIO_4$ oxidation of 1,2-diol followed by $NaBH_4$ reduction (88% yield), (3) protection of the hydroxy group as TBS ether (96% yield), (4) methanolysis of acetate (quantitative yield) and (5) PCC oxidation of the secondary hydroxy group (90% yield). C(14)–C(19) bond in β-hydroxyketone **14** was cleaved by retro-aldol reaction in the presence of NaH and 15-crown-5 in toluene to produce tetrasubstituted cyclopentane derivative **15**, having the desired chiral centers at C-1 and C-11 corresponding to claenone (**1**), in 86% yield. Selective protection of the less hindered ketone in **15** was done as follows: (1) deprotection of the TBS group by treatment with 80% acetic acid (97% yield), (2) acetylation of the hydroxy group (quantitative yield), and (3) treatment with 1,2-bis(trimethylsilyloxy)ethane in the presence of TMSOTf[14] (97% yield), giving monoketal **16**. Deoxygenation of C-14 position in **16** was carried out by (1) $NaBH_4$ reduction of ketone (98% yield) and (2) dehydration by treatment with *N*-phenylthiosuccinimide and $^nBu_3P$ in



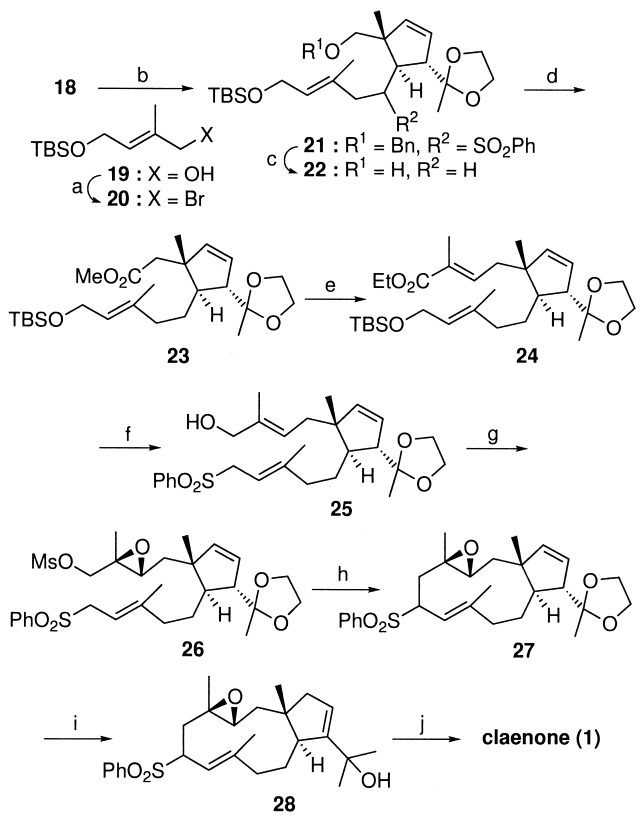
Scheme 3. *Reagents and conditions*: (a) $NaIO_4$, MeOH–H_2O, 0°C, then $NaBH_4$, 0°C, 57%; (b) (1) AcOH–H_2O (4:1), 40°C, 73%, (2) $NaIO_4$, MeOH–H_2O, 0°C, then $NaBH_4$, 0°C, 74%.



Scheme 4. *Reagents and conditions*: (a) (1) $NaBH_4$, MeOH, 0°C, quant., (2) TBSCl, imidazole, DMF, rt, quant.; (b) (1) $LiAlH_4$, Et_2O, 0°C, 99%, (2) BnBr, NaH, DMF, rt, 94%; (c) (1) TBAF, THF, rt, quant., (2) Ac_2O, Py, rt, 99%; (d) (1) AcOH–H_2O (4:1), 65°C, 80%, (2) $NaIO_4$, $(NH_4)_2SO_4$, MeOH–H_2O (1:1), 0°C, then $NaBH_4$, 0°C, 88%, (3) TBSCl, imidazole, DMF, rt, 96%, (4) K_2CO_3, MeOH, rt, quant., (5) PCC, 4 Å MS, CH_2Cl_2, rt, 90%; (e) NaH, 15-crown-5, toluene, rt, 86%; (f) (1) AcOH–H_2O (4:1), rt, 97%, (2) Ac_2O, Py, rt, quant., (3) 1,2-bis(trimethylsilyloxy)ethane, TMSOTf, CH_2Cl_2, −40°C, 90%; (g) (1) $NaBH_4$, MeOH, 0°C, 98%, (2) *N*-phenylthiosuccinimide, $^nBu_3P$, Py, 60°C, 93%; (h) (1) K_2CO_3, MeOH, rt, quant., (2) PhSSPh, $^nBu_3P$, Py, 60°C, (3) OXONE®, THF–MeOH–H_2O (2:2:3), 0°C, 85% (two steps).

pyridine (93% yield) to produce cyclopentene derivative **17**. The acetyl group in **17** was removed by K_2CO_3 in MeOH (quantitative yield) to afford the primary alcohol, whose hydroxy group was converted to phenyl sulfonyl group by PhSSPh and $^nBu_3P$ in pyridine and then OXONE®,[15] affording sulfone **18** in 85% yield (two steps).

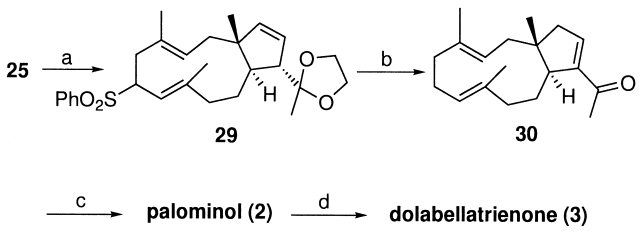
Claenone (**1**) was synthesized from the cyclopentane core **18** by elongation of side chains and macrocyclization (Scheme 5). Allylic alcohol **19**[16] was treated with NBS and Ph_3P to give allylic bromide **20**, corresponding to the C-6–C-9 segment, in 80% yield. Reaction of the lithio derivative of sulfone **18** with allylic bromide **20** at −78°C to −30°C gave the coupling product **21** as a diasereomeric mixture. Treatment of sulfone **21** with Na in liq. NH_3 gave alcohol **22** in 68% yield (two steps). The hydroxy group in **22** was oxidized by PDC to give the aldehyde, which was reacted with Wittig reagent (Ph_3P=CHOMe) to produce methyl enol ether in 80% yield (two steps). Oxidation of the methyl enol ether by PCC–Al_2O_3[17] directly provided methyl ester **23** in 85% yield. Ester **23** was reduced with DIBAH to give the aldehyde, whose reaction with Horner–Emons reagent ($(EtO)_2P(O)CHMeCO_2Et$) gave (*E*)-α,β-unsaturated ester **24** as the sole product in 80% yield (two steps). TBS ether **24** was converted to allylic alcohol **25** in four steps: (1) removal of the TBS group with TBAF (quantitative yield), (2) conversion of the hydroxy group to phenylthio group (92% yield), (3) oxidation of the sulfide to sulfone by OXONE® (90% yield) and (4) DIBAH reduction of the ester to allylic alcohol (98% yield). Allylic alcohol **25** corresponds to the common intermediate **B** in the synthetic



Scheme 5. *Reagents and conditions*: (a) NBS, Ph_3P, CH_2Cl_2, 0°C, 80%; (b) ^nBuLi, THF, ∓78°C, then **20**, −78 to −30°C; (c) Na, liq. NH_3, THF, −78°C, 68% (two steps); (d) (1) PDC, 4 Å MS, CH_2Cl_2, rt, (2) Ph_3P=CHOMe, THF, 0°C, 84% (two steps), (3) PCC–Al_2O_3, benzene, 40°C, 85%; (e) (1) DIBAH, toluene, −78°C, (2) $(EtO)_2P(O)CH(Me)CO_2Et$, NaH, THF, 0°C, 80% (two steps); (f) (1) TBAF, THF, rt, quant., (2) PhSSPh, $^nBu_3P$, Py, 60°C, 92%, (3) OXONE®, THF–MeOH–H_2O (1:1:1), 0°C, 90%, (4) DIBAH, toluene, −78°C, 98%; (g) (1) ^tBuOOH, (−)-DET, $Ti(O^iPr)_4$, 4 Å MS, CH_2Cl_2, −20°C, 95%, (2) MsCl, DMAP, CH_2Cl_2, rt, 97%; (h) KHMDS, THF, 45°C, 60% at 75% conversion; (i) (1) AcOH–H_2O (4:1), 45°C, 93%, (2) K_2CO_3, MeOH, rt, quant., (3) MeLi, THF, −78°C, 86%; (j) (1) Na-Hg, Na_2HPO_4, MeOH–THF (1:1), 0°C, 83%, (2) PCC, 4 Å MS, CH_2Cl_2, rt, 63%.

strategy. Stereoselective epoxidation of allylic alcohol **25** according to Sharpless procedure[18] (95% yield) followed by mesylation of hydroxy group gave mesylate **26** (97% yield) corresponding compound **A** in the synthetic strategy. Regioselective macrocyclization of **26** was carried out by treatment with KHMDS in THF (4.0×10^{-3} M) to give bicyclo[9.3.0]tetradecane derivative **27** as the sole product in 60% yield based on recovery of **26**. Bicyclic compound **27** was converted to allylic alcohol **28** in as follows: (1) acid-catalyzed hydrolysis of acetal to give ketone (93% yield), (2) isomerization of olefin to the enone (quantitative yield) and (3) addition reaction with MeLi (86% yield). The phenylsulfonyl group in **28** was removed by Na-Hg in MeOH (83% yield) and oxidation of the tertiary allylic alcohol with PCC[19] to afford claenone (**1**), $[\alpha]_D$=−49.2° (*c* 0.42, $CHCl_3$), mp 124–125°C, in 63% yield. Spectral data and sign of optical rotation of synthetic claenone (**1**) were identical to those of natural claenone, $[\alpha]_D$=−50.9° (*c* 1.25, $CHCl_3$), mp 124–125°C.[4]

The total synthesis of palominol (**2**) and dolabellatrienone (**3**) was carried out from synthetic intermediate **25** (Scheme 6). Allylic alcohol **25** was treated with MsCl and DMAP in



Scheme 6. *Reagents and conditions*: (a) (1) MsCl, DMAP, CH_2Cl_2, rt, (2) KHMDS, THF, 45°C, 45% (two steps); (b) (1) Na-Hg, Na_2HPO_4, MeOH–THF (1:1), 0°C, 86%, (2) AcOH–H_2O (4:1), 45°C, 93%, (3) K_2CO_3, MeOH, rt, quant.; (c) MeLi, THF, −78°C, 90%; (d) PDC, 4 Å MS, CH_2Cl_2, rt, 63%.

THF to afford allylic chloride. Without purification, macrocyclization of allylic chloride was carried out by KHMDS in THF (4.0×10^{-3} M) to give bicyclo[9.3.0]tetradecane derivative **29** in 45% yield (two steps). Bicyclic compound **29** was converted to enone **30** in three steps: (1) removal of the phenylsulfonyl group with Na-Hg in MeOH (86% yield), (2) acid-catalyzed hydrolysis of acetal to give ketone (93% yield) and (3) isomerization of olefin to the enone (quantitative yield). Enone **30** was treated with MeLi in THF at −78°C to produce palominol (**2**), $[\alpha]_D=-24.7°$ (*c* 0.34, $CHCl_3$) in 90% yield. Spectral data and sign of optical rotation of the synthesized palominol (**2**) were identical to those of natural palminol, $[\alpha]_D=-28°$ (*c* 0.7, $CHCl_3$).[7a] Palominol (**2**) was treated with PDC in CH_2Cl_2 to give dolabellatrienone (**3**), $[\alpha]_D=+29.9°$ (*c* 0.14, $CHCl_3$) in 63% yield. Spectral data and sign of optical rotation of the synthesized dolabellatrienone (**3**) were identical to those of natural dolabellatrienone, $[\alpha]_D=+31.0°$ (*c* 0.88, $CHCl_3$).[7b]

1. Experimental

1.1. General experimental procedures

Melting points were measured on Yazawa BY-2 micro melting point apparatus and uncorrected. Optical rotations were measured with a JASCO DIP-360 automatic polarimeter. IR spectra were recorded with a Perkin–Elmer FT-IR 1710 spectrometer or JASCO FT-IR/620 spectrometer, UV spectra with a JASCO V-550 spectrophotometer and ^1H and ^{13}C NMR spectra with a Varian Gemini-300, a Bruker DPX-400 or a Bruker DRX-500. Chemical shifts are given on a δ (ppm) scale with tetramethylsilane (TMS) as the internal standard (s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad). EIMS was obtained with a Thermo Quest TSQ 700 spectrometer. High resolution EIMS (HREIMS) spectra was obtained with a VG Auto Spec E spectrometer. Column chromatography was carried out on Merck silica gel 60 (70–230 mesh), Merck silica gel 60 (230–400 mesh). Preparative TLC was conducted on a Merck silica gel 60 F_{254} plate.

1.1.1. Ethyl (1*R*,2*S*,3*R*,4*S*)-3-((*S*)-2,2-dimethyl-[1,3]dioxolan-4-yl)-1-methoxymethoxy-2-methyl-5-oxobicyclo[2.2.1]heptane-2-carboxylate (6a) and ethyl (1*S*,2*R*,3*S*,4*R*)-3-((*S*)-2,2-dimethyl-[1,3]dioxolan-4-yl)-1-methoxymethoxy-2-methyl-5-oxobicyclo[2.2.1]heptane-2-carboxylate (6b). To a cold (0°C) solution of $^iPr_2NEt$ (5.20 mL, 51.0 mmol) in THF (200 mL) was added ^{n}BuLi (37.0 mL, 47.0 mmol, 1.27 M in hexane). The mixture was stirred at 0°C for 30 min and was cooled to −78°C. A solution of cyclopentenone **4** (5.60 g, 39.3 mmol) in THF (10 mL) was added and the mixture was stirred at same temperature for 10 min. A solution of α,β-unsaturated ester **5** (10.0 g, 46.7 mmol) in THF (15 mL) was added and the mixture was stirred at same temperature for 2 h. The reaction mixture was diluted with Et_2O, washed with saturated aqueous NH_4Cl, H_2O and saturated aqueous NaCl, dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (eluted with hexane–Et_2O=2:1) to give bicyclo[2.2.1]heptane **6a** (9.60 g, 69%) **6b** (1.80 g, 18%). **6a**: colorless oil; $[\alpha]_D=-14.9°$ (*c* 1.24, $CHCl_3$); IR (neat) 2986, 1755, 1719 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ ppm: 1.25 (3H, t, *J*=7.0 Hz), 1.27 (3H, s), 1.38 (3H, s), 1.42 (3H, s), 1.92 (1H, dt, *J*=10.0, 1.4 Hz), 2.37 (1H, m), 2.43 (2H, m), 2.60 (1H, m), 2.67 (1H, m), 3.39 (3H, s), 3.68 (1H, dd, *J*=7.0, 10.8 Hz), 4.07 (1H, dd, *J*=6.4, 8.2 Hz), 4.12 (1H, dq, *J*=10.8, 7.0 Hz), 4.25 (1H, ddd, *J*=1.2, 6.4, 6.6 Hz), 4.77 (1H, d, *J*=7.3 Hz), 4.83 (1H, d, *J*=7.3 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ ppm: 14.1, 16.9, 25.1, 26.4, 37.4, 45.0, 45.1, 49.5, 54.2, 55.4, 61.1, 68.6, 74.2, 85.1, 93.4, 109.1, 175.1, 211.0; EIMS (*m*/*z*): 356 (M^+, 20), 341 (M^+-CH_3, 100); HREIMS: calcd for $C_{17}H_{25}O_7$ (M^+-CH_3): 341.1600; Found: 341.1588. **6b**: colorless oil; $[\alpha]_D=+25.4°$ (*c* 1.62, $CHCl_3$); IR (neat) 2985, 1756, 1720 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ ppm: 1.26 (3H, t, *J*=7.1 Hz), 1.32 (3H, s), 1.35 (3H, s), 1.55 (3H, s), 1.92 (1H, dt, *J*=10.7, 1.7 Hz), 2.11 (1H, m), 2.25 (1H, ddd, *J*=1.2, 4.2, 10.7 Hz), 2.39 (1H, dd, *J*=4.2, 18.0 Hz), 2.57 (1H, dd, *J*=1.2, 18.0 Hz), 2.67 (1H, m), 3.39 (3H, s), 3.67 (1H, ddd, *J*=4.2, 10.7, 13.7 Hz), 4.09 (2H, m), 4.15 (1H, dq, *J*=11.3, 7.1 Hz), 4.20 (1H, dq, *J*=11.3, 7.1 Hz), 4.75 (1H, d, *J*=7.3 Hz), 4.80 (1H, d, *J*=7.3 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ ppm: 14.1, 16.1, 25.8, 26.5, 37.3, 44.4, 46.3, 50.3, 54.3, 55.5, 61.1, 68.9, 75.4, 85.7, 93.4, 109.5, 174.6, 209.3; EIMS (*m*/*z*): 356 (M^+, 28), 341 (M^+-CH_3, 23), 325 (92); HREIMS: calcd for $C_{17}H_{25}O_7$ (M^+-CH_3): 341.1600; Found: 341.1587.

1.1.2. Ethyl (1*R*,2*S*,3*R*,4*S*)-3-((*S*)-1,2-dihydroxyethyl)-1-methoxymethoxy-2-methyl-5-oxobicyclo[2.2.1]heptane-2-carboxylate (7). A mixture of AcOH and H_2O (4:1) (20.0 mL) was added to keto ester **6a** (2.00 g, 5.60 mmol) and the mixture was stirred at rt for 72 h. The reaction mixture was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (eluted with EtOAc) to give diol **7** (1.47 g, 83%). Colorless oil; $[\alpha]_D=-13.1°$ (*c* 0.65, $CHCl_3$); IR (neat) 3439, 2939, 1748 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ ppm: 1.23 (3H, t, *J*=7.1 Hz), 1.50 (3H, s), 1.90 (1H, br d, *J*=10.4 Hz), 2.24 (1H, br d, *J*=2.8 Hz), 2.35 (1H, dd, *J*=4.4, 18.2 Hz), 2.48 (1H, m), 2.62 (1H, d, *J*=18.2 Hz), 2.68 (1H, br s), 3.30 (2H, br s), 3.37 (3H, s), 3.51 (1H, dd, *J*=7.5, 11.0 Hz), 3.60 (1H, dd, *J*=3.0, 11.0 Hz), 3.91 (1H, m), 4.10 (1H, dq, *J*=10.8, 7.1 Hz), 4.16 (1H, dq, *J*=10.8, 7.1 Hz), 4.76 (1H, d, *J*=7.4 Hz), 4.80 (1H, d, *J*=7.4 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ ppm: 14.1, 16.3, 37.8, 43.3, 45.1, 48.9, 54.9, 55.4, 61.2, 66.1, 66.1, 69.9, 84.9, 93.4, 175.7, 212.5; EIMS (*m*/*z*): 316 (M^+, 9), 298 (16), 285 (100); Anal. calcd for $C_{15}H_{24}O_7$: C, 56.95; H, 7.65. Found: C, 57.14; H, 7.91.

1.1.3. Ethyl (1*R*,2*S*,3*R*,4*S*,5*S*)-3-[(*S*)-2-Hydroxy-1-methoxymethoxyethyl]-1,5-bis(methoxymethoxy)-2-methylbicyclo[2.2.1]heptane-2-carboxylate (8). To a solution of diol **7** (1.00 g, 3.16 mmol) in DMF (6.32 mL) were added imidazole (430 mg, 6.32 mmol) and TBSCl (530 mg, 3.48 mmol). After stirring at rt for 10 min, the reaction mixture was diluted with Et_2O, washed with H_2O and saturated aqueous NaCl, dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (eluted with hexane–EtOAc=3:2) to give TBS ether (1.30 g, 95%). Colorless oil; $[\alpha]_D$=+34.4° (*c* 1.00, $CHCl_3$); IR (neat) 3420, 2929, 1753, 1720 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ ppm: 0.06 (6H, s), 0.88 (9H, s), 1.23 (3H, t, *J*=7.2 Hz), 1.55 (3H, s), 1.89 (1H, br d, *J*=10.2 Hz), 2.21 (1H, br s), 2.38 (1H, dd, *J*=4.4, 18.2 Hz), 2.54 (1H, m), 2.60 (1H, br s), 2.61 (1H, br d, *J*=18.2 Hz), 3.38 (3H, s), 3.44 (1H, t, *J*=9.5 Hz), 3.55 (1H, dd, *J*=3.8, 9.5 Hz), 3.97 (1H, m), 4.10 (1H, dq, *J*=10.9, 7.2 Hz), 4.16 (1H, dq, *J*=10.9, 7.2 Hz), 4.77 (1H, d, *J*=7.3 Hz), 4.82 (1H, d, *J*=7.3 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ ppm: 14.1, 16.5, 18.2, 25.8, 38.3, 43.1, 45.2, 49.1, 55.1, 55.4, 61.0, 66.5, 69.6, 84.8, 93.4, 175.5; EIMS (*m*/*z*): 399 (M^+-OCH_3, 3), 373 (40), 341 (100); HREIMS: calcd for $C_{20}H_{35}O_6Si$ (M^+-OCH_3): 399.2203; Found: 399.2194.

To a cold (0°C) solution of the above ketone (1.30 g, 3.02 mmol) in MeOH (30.0 mL) was added $NaBH_4$ (230 mg, 6.04 mmol) and the mixture was stirred at 0°C for 15 min. The reaction mixture was diluted with Et_2O, washed with H_2O and saturated aqueous NaCl, dried over anhydrous $MgSO_4$ and concentrated under reduced pressure to give crude alcohol. The crude alcohol was used next reaction without purification.

To a solution of the above crude alcohol in CH_2ClCH_2Cl (6.00 mL) were added $^iPr_2NEt$ (1.60 mL, 9.00 mmol) and MOMCl (600 μL, 7.20 mmol). After stirring at 50°C for 5 h, the reaction mixture was diluted with Et_2O, washed with H_2O and saturated aqueous NaCl, dried over anhydrous $MgSO_4$ and concentrated under reduced pressure to give crude MOM ether. The crude MOM ether was used next reaction without purification.

To a solution of the above crude TBS ether in THF (3.00 mL) was added TBAF (3.00 mL, 3.00 mmol, 1.0 M in THF). After stirring at rt for 2 h, the reaction mixture was diluted with Et_2O, washed with H_2O and saturated aqueous NaCl, dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (eluted with EtOAc) to give alcohol **8** (730 mg, 60%, three steps). Colorless oil; $[\alpha]_D$=−1.5° (*c* 0.85, $CHCl_3$); IR (neat) 3442, 2927, 1720 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ ppm: 1.25 (3H, t, *J*=7.2 Hz), 1.36 (3H, s), 1.49 (1H, dt, *J*=14.0, 4.0 Hz), 1.56 (1H, dt, *J*=10.2, 1.5 Hz), 2.08 (1H, ddd, *J*=2.1, 5.5, 10.2 Hz), 2.27 (1H, dd, *J*=10.9, 13.7 Hz), 2.34 (1H, m), 2.95 (1H, dd, *J*=1.4, 4.6 Hz), 3.34 (3H, s), 3.38 (3H, s), 3.62 (1H, m), 3.68 (1H, hept, *J*=4.5 Hz), 3.78 (1H, m), 4.06 (1H, dt, *J*=10.9, 4.8 Hz), 4.15 (1H, dq, *J*=10.8, 7.1 Hz), 4.19 (1H, dq, *J*=10.8, 7.1 Hz), 4.56 (1H, d, *J*=6.6 Hz), 4.61 (1H, d, *J*=6.6 Hz), 4.66 (1H, d, *J*=6.9 Hz), 4.69 (1H, d, *J*=7.2 Hz), 4.74 (1H, d, *J*=6.9 Hz), 4.79 (1H, d, *J*=7.2 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ ppm: 14.2, 16.6, 35.1, 37.3, 37.7, 40.0, 55.3, 55.5, 55.8, 56.4, 60,6, 66.3, 75.5, 83.1, 87.1, 93.3, 95.2, 97.8, 176.1; EIMS (*m*/*z*): 375 (M^+-OCH_3, 25), 343 (35), 126 (100); HREIMS: calcd for $C_{18}H_{31}O_8$ (M^+-OCH_3): 375.2019; Found: 375.2027.

1.1.4. (1*R*,2*S*,6*S*,7*R*,8*S*,9*S*)-1,6,9-Tris(methoxymethoxy)-2-methyl-4-oxatricyclo[6.2.1.0^{2,7}]undecan-3-one (9). An aqueous solution of 30% NaOH (5.00 mL) was added to ester **8** (8.0 mg, 18.7 μmol) and the mixture was refluxed for 14 h. The reaction mixture was diluted with Et_2O, washed with 1N HCl, H_2O and saturated aqueous NaCl, dried over anhydrous $MgSO_4$ and concentrated under reduced pressure to give crude carboxylic acid. The crude carboxylic acid was used next reaction without purification.

To a solution of the above crude carboxylic acid in CH_2Cl_2 (1.80 mL) were added Et_3N (100 μL, 720 μmol) and BOPCl (138 mg, 540 μmol). After stirring at rt for 16 h, the reaction mixture was diluted with Et_2O, washed with H_2O and saturated aqueous NaCl, dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (eluted with EtOAc) to give lactone **9** (2.5 mg, 38%, two steps). Colorless oil; $[\alpha]_D$=−38.4° (*c* 0.83, $CHCl_3$); IR (neat) 2927, 1752 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ ppm: 1.36 (3H, s), 1.57 (1H, d, *J*=11.0 Hz), 1.83 (1H, ddd, *J*=2.9, 5.0, 13.8 Hz), 2.08 (1H, dt, *J*=11.0, 2.8 Hz), 2.29 (1H, s), 2.33 (1H, dd, *J*=10.0, 13.8 Hz), 2.74 (1H, d, *J*=12.3 Hz), 3.36 (3H, s), 3.37 (3H, s), 3.41 (3H, s), 4.13 (1H, m), 4.15 (1H, m), 4.30 (1H, dd, *J*=3.2, 12.9 Hz), 4.59 (1H, d, *J*=6.9 Hz), 4.63 (1H, d, *J*=6.9 Hz), 4.65 (2H, m), 4.74 (1H, dd, *J*=7.0, 12.9 Hz), 4.75 (1H, d, *J*=6.8 Hz), 4.95 (1H, d, *J*=6.8 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ ppm: 13.9, 34.3, 35.8, 38.7, 41.5, 50.1, 56.2, 56.3, 56.3, 73.3, 76.3, 77.9, 86.0, 94.2, 95.2, 96.8, 173.1.

1.1.5. Ethyl (1*R*,2*S*,3*R*,4*S*,5*S*)-5-Hydroxy-3-hydroxymethyl-1-methoxymethoxy-2-methylbicyclo[2.2.1]heptane-2-carboxylate ((−)-10). To a solution of diol 7 (57.3 mg, 181 μmol) in MeOH (1.8 mL) was added a solution of $NaIO_4$ (46.5 mg, 217 μmol) in H_2O (500 μL) at 0°C. After stirring at 0°C for 30 min, $NaBH_4$ (13.7 mg, 362 μmol) was added and stirred at 0°C for 30 min. The reaction mixture was diluted with Et_2O, washed with H_2O and saturated aqueous NaCl, dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (eluted with EtOAc) to give alcohol (−)-**10** (29.7 mg, 57%). Colorless oil; $[\alpha]_D$=−14.1° (*c* 0.30, $CHCl_3$); IR (neat) 3376, 1715 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ ppm: 1.27 (3H, t, *J*=7.1 Hz), 1.31 (3H, s), 1.63 (1H, dt, *J*=10.5, 1.7 Hz), 1.92 (1H, ddd, *J*=1.8, 3.6, 10.5 Hz), 2.08 (1H, m), 2.29 (1H, dd, *J*=10.9, 13.8 Hz), 3.01 (1H, dt, *J*=1.7, 7.4 Hz), 3.35 (3H, s), 3.50 (1H, dd, *J*=7.9, 10.6 Hz), 3.74 (1H, dd, *J*=7.2, 10.6 Hz), 4.20 (3H, m), 4.65 (1H, d, *J*=7.1 Hz), 4.72 (1H, d, *J*=7.1 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ ppm: 14.2, 14.8, 37.5, 37.6, 41.0, 42.1, 54.8, 55.3, 61.3, 62.6, 70.1, 88.1, 93.0, 177.3.

1.1.6. Ethyl (1*S*,2*R*,3*S*,4*R*,5*R*)-5-Hydroxy-3-hydroxymethyl-1-methoxymethoxy-2-methylbicyclo[2.2.1]heptane-2-carboxylate ((+)-10). A mixture of AcOH and H_2O

(4:1) (5.00 mL) was added to keto ester **6b** (116 mg, 362 μmol) and the mixture was stirred at rt for 24 h. The reaction mixture was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (eluted with EtOAc) to give diol (75.4 mg, 73%). Colorless oil; $[\alpha]_D$=+21.1° (*c* 0.80, $CHCl_3$); IR (neat) 3442, 1752, 1715 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ ppm: 1.23 (3H, t, *J*=7.2 Hz), 1.56 (3H, s), 1.88 (1H, br d, *J*=10.6 Hz), 2.20 (1H, dd, *J*=4.1, 10.6 Hz), 2.38 (1H, dd, *J*=5.2, 13.1 Hz), 2.39 (1H, d, *J*=18.0 Hz), 2.59 (1H, d, *J*=18.0 Hz), 3.31 (2H, br s), 3.36 (3H, s), 3.55 (1H, dd, *J*=5.0, 10.9 Hz), 3.65 (1H, m), 3.72 (1H, m), 4.12 (1H, dq, *J*=10.3, 7.2 Hz), 4.17 (1H, dq, *J*=10.3, 7.2 Hz), 4.73 (1H, d, *J*=7.4 Hz), 4.78 (1H, d, *J*=7.4 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ ppm: 14.0, 16.1, 37.1, 44.1, 44.9, 49.4, 54.7, 55.4, 61.4, 65.0, 70.8, 85.1, 93.3, 176.0, 210.7; EIMS (*m*/*z*): 317 (M^++H, 14), 298 (9), 253 (100); HREIMS: calcd for $C_{15}H_{22}O_6$ (M^+-H_2O): 298.1416; Found: 298.1398.

To a solution of the above diol (64.7 mg, 205 μmol) in MeOH (2.0 mL) was added a solution of $NaIO_4$ (54.0 mg, 245 μmol) in H_2O (600 μL) at 0°C. After stirring at 0°C for 30 min, $NaBH_4$ (16.0 mg, 205 μmol) was added and stirred at 0°C for 30 min. The reaction mixture was diluted with Et_2O, washed with H_2O and saturated aqueous NaCl, dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (eluted with EtOAc) to give alcohol (+)-**10** (43.2 mg, 74%). Colorless oil; $[\alpha]_D$=+14.2° (*c* 0.38, $CHCl_3$).

1.1.7. Ethyl (1*R*,2*S*,3*R*,4*S*,5*S*)-5-(*tert*-butyldimethylsilanyloxy)-3-((*S*)-2,2-dimethyl[1,3]dioxolan-4-yl)-1-methoxymethoxy-2-methylbicyclo[2.2.1]heptane-2-carboxylate (11). To a cold (0°C) solution of keto ester **6a** (44.0 g, 124 mmol) in MeOH (600 mL) was added $NaBH_4$ (2.30 g, 61.7 mmol) and the mixture was stirred at 0°C for 15 min. The reaction mixture was diluted with Et_2O, washed with saturated aqueous NH_4Cl, H_2O and saturated aqueous NaCl, dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (eluted with hexane–EtOAc=1:1) to give alcohol (44.2 g, quantitative yield). Colorless oil; $[\alpha]_D$=15.2° (*c* 0.73, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ ppm: 1.28 (3H, t, *J*=7.1 Hz), 1.32 (3H, s), 1.34 (3H, s), 1.40 (3H, s), 1.58 (1H, br d, *J*=2.1 Hz), 1.65 (1H, dd, *J*=11.0, 13.8 Hz), 2.14 (1H, ddd, *J*=1.9, 3.8, 10.2 Hz), 2.28 (1H, br d, *J*=5.0 Hz), 2.31 (1H, dd, *J*=11.0, 13.8 Hz), 2.46 (1H, d, *J*=8.3 Hz), 2.95 (1H, dd, *J*=1.7, 5.5 Hz), 3.37 (3H, s), 3.62 (1H, t, *J*=7.7 Hz), 4.06 (1H, dd, *J*=6.5, 8.0 Hz), 4.15–4.30 (4H, m), 4.69 (1H, d, *J*=7.1 Hz), 4.73 (1H, d, *J*=7.1 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ ppm: 14.1, 16.1, 25.2, 26.5, 38.0, 38.1, 40.2, 42.3, 55.2, 55.3, 61.1, 68.8, 69.9. 75.0. 87.9, 93.1, 108.7, 176.9; EIMS (*m*/*z*): 358 (M^+, 5.1), 327 (M^+−MeO, 5.2), 45 (100); Anal. calcd for $C_{18}H_{30}O_7$: C, 60.32; H, 8.44. Found: C, 60.13; H, 8.39.

To a solution of the above alcohol (49.0 g, 134 mmol) in DMF (134 mL) were added imidazole (14.0 g, 200 mmol) and TBSCl (24.0 g, 160 mmol). After stirring at rt for 10 h, the reaction mixture was diluted with Et_2O, washed with H_2O and saturated aqueous NaCl, dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (eluted with hexane–Et_2O=1:1) to give TBS ether **11** (63.0 g, quantitative yield). Colorless oil; $[\alpha]_D$=−23.0° (*c* 1.24, $CHCl_3$); IR (neat) 2954, 1727 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm: 0.00 (3H, s), 0.02 (3H, s), 0.86 (9H, s), 1.26 (3H, t, *J*=7.1 Hz), 1.32 (3H, s), 1.33 (3H, s), 1.39 (3H, s), 1.41 (1H, dt, *J*=3.5, 13.5 Hz), 1.53 (1H, dt, *J*=1.6, 10.2 Hz), 2.03 (1H, ddd, *J*=2.0, 3.5, 10.2 Hz), 2.13 (1H, br d, *J*=4.7 Hz), 2.22 (1H, dd, *J*=10.4, 13.4 Hz), 3.07 (1H, dd, *J*=1.5, 5.6 Hz), 3.38 (3H, s), 3.68 (1H, t, *J*=7.6 Hz), 4.05 (1H, dd, *J*=6.4, 7.9 Hz), 4.10–4.20 (2H, m), 4.27 (1H, dd, *J*=6.5, 12.8 Hz), 4.70 (1H, d, *J*=7.1 Hz), 4.81 (1H, d, *J*=7.1 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ ppm: −4.9, −4.8, 14.2, 17.5, 17.9, 25.3, 25.7, 26.6, 36.9, 38.4, 40.1, 41.4, 55.2, 55.2, 60.3, 68.8, 70.3, 75.3, 87.4, 93.2, 108.5, 176.1; EIMS (*m*/*z*): 415 ($M^+-{}^t$Bu, 9.5), 45 (100); Anal. calcd for $C_{24}H_{44}O_7Si$: C, 60.98; H, 9.38. Found: C, 60.84; H, 9.19.

1.1.8. [(1*S*,2*S*,4*R*,5*R*,6*R*)-5-Benzyloxymethyl-6-((*S*)-2,2-dimethyl[1,3]dioxolan-4-yl)-4-methoxymethoxy-5-methylbicyclo[2.2.1]hept-2-yloxy]-*tert*-butyldimethylsilane (12). To a cold (0°C) solution of ester **11** (2.20 g, 48.7 mmol) in Et_2O (460 mL) was added $LiAlH_4$ (1.70 g, 48.0 mmol) and the mixture was stirred at 0°C for 10 min. The reaction mixture was diluted with Et_2O and added with saturated aqueous NaCl. After stirring for 20 min, organic layer was dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (eluted with hexane–Et_2O=1:2) to give alcohol (2.07 g, 99%). Colorless oil; $[\alpha]_D$=−9.2° (*c* 0.43, $CHCl_3$); IR (neat) 3495, 2931 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm: 0.03 (3H, s), 0.04 (3H, s), 0.87 (9H, s), 1.15 (3H, s), 1.32 (3H, s), 1.36 (3H, s), 1.54 (1H, br d, *J*=10.1 Hz), 1.61 (1H, dt, *J*=3.5, 13.4 Hz), 2.01 (1H, dd, *J*=0.9, 6.6 Hz), 2.05 (1H, ddd, *J*=2.0, 3.5, 10.1 Hz), 2.12 (1H, dd, *J*=10.5, 13.4 Hz), 2.19 (1H, m), 2.24 (1H, dd, *J*=2.0, 7.9 Hz), 3.36 (3H, s), 3.45 (1H, dd, *J*=8.0, 10.6 Hz), 3.51 (1H, dd, *J*=7.1, 7.7 Hz), 3.90 (1H, br d, *J*=10.6 Hz), 4.05 (1H, dd *J*=6.4, 7.7 Hz), 4.15–4.20 (2H, m), 4.65 (1H, d, *J*=7.1 Hz), 4.71 (1H, d, *J*=7.1 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ ppm: −4.9, −4.8, 16.0, 18.0, 25.2, 25.8, 26.7, 36.6, 36.7, 41.4, 42.7, 46.8, 55.6, 69.1, 69.4, 70.1, 75.2, 89.4, 92.9, 108.4; EIMS (*m*/*z*): 430 (M^+, 3.7), 415 ((M^+−Me, 3.7), 45 (100); Anal. calcd for $C_{22}H_{42}O_6Si$: C, 61.36; H, 9.83. Found: C, 61.34; H, 9.72.

To a cold (0°C) solution of the above alcohol (75.8 g, 176 mmol) in DMF (141 mL) was added NaH (60%, 14.1 g, 350 mmol) and the mixture was stirred at 0 °C for 30 min. BnBr (32.5 mL, 260 mmol) was added to the mixture and the mixture was stirred at rt for 12 h. The reaction mixture was diluted with Et_2O, washed with H_2O and saturated aqueous NaCl, dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (eluted with hexane–Et_2O=2:1) to give Bn ether **12** (86.0 g, 94%). Colorless oil; $[\alpha]_D$=−6.1° (*c* 0.79, $CHCl_3$); IR (neat) 2931 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm: 0.00 (3H, s), 0.02 (3H, s), 0.86 (9H, s), 1.07 (3H, s), 1.32 (3H, s), 1.36 (3H, s), 1.43 (1H, dt, *J*=3.3, 13.3 Hz), 1.48 (1H, br d, *J*=10.1 Hz), 2.00 (1H, dd, *J*=10.6, 13.3 Hz), 2.03 (1H, dt, *J*=3.3, 10.1 Hz), 2.21 (1H, br d, *J*=4.9 Hz), 2.29 (1H, dd, *J*=1.2, 7.6 Hz),

3.34 (3H, s), 3.43 (1H, d, J=8.3 Hz), 3.52 (1H, d, J=8.3 Hz), 3.73 (1H, dd, J=6.8, 7.9 Hz), 4.02 (1H, dd J=6.3, 8.0 Hz), 4.12 (1H, dd, J=6.5, 13.9 Hz), 4.18 (1H, ddd, J=2.7, 4.9, 10.6 Hz), 4.48 (1H, d, J=12.3 Hz), 4.55 (1H, d, J=12.3 Hz), 4.63 (1H, d, J=7.0 Hz), 4.70 (1H, d, J=7.0 Hz), 7.25–7.35 (5H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm: −4.9, 16.3, 18.0, 25.4, 25.9, 26.8, 36.8, 41.2, 44.7, 46.3, 55.3, 69.4, 70.4, 73.6, 75.8, 76.7, 88.5, 93.1, 105.0, 127.3, 127.3, 128.3, 138.9; EIMS (*m*/*z*): 520 (M^+, 1.0), 515 ((M^+−Me, 1.0), 91 (100); Anal. calcd for $C_{29}H_{48}O_6Si$: C, 66.88; H, 9.29. Found: C, 66.78; H, 9.17.

1.1.9. (1*S*,2*S*,4*R*,5*R*,6*R*)-5-Benzyloxymethyl-6-((*S*)-2,2-dimethyl[1,3]dioxolan-4-yl)-4-methoxymethoxy-5-methylbicyclo[2.2.1]hept-2-yl acetate (13). To a solution of TBS ether **12** (83.1 g, 160 mmol) in THF (320 mL) was added TBAF (240 mL, 240 mmol, 1.0 M in THF). After stirring at rt for 2 h, the reaction mixture was diluted with Et_2O, washed with H_2O and saturated aqueous NaCl, dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (eluted with hexane–EtOAc=1:1) to give alcohol (64.5 g, quantitative yield). Colorless oil; $[\alpha]_D$=−6.0° (*c* 1.76, $CHCl_3$); IR (neat) 3460, 2983 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm: 0.97 (3H, s), 1.32 (3H, s), 1.40 (3H, s), 1.52 (1H, dt, J=10.1, 1.4 Hz), 1.66 (1H, dt, J=13.4, 3.3 Hz), 1.72 (1H, br s), 2.04 (1H, ddd, J=1.9, 3.7, 10.1 Hz), 2.10 (1H, dd, J=11.0, 13.5 Hz), 2.29 (1H, br d, J=5.0 Hz), 2.38 (1H, dd, J=1.5, 7.2 Hz), 2.57 (1H, d, J=7.1 Hz), 3.29 (1H, d, J=9.3 Hz), 3.33 (3H, s), 3.64 (1H, d, J=9.3 Hz), 3.66 (1H, dd, J=6.7, 8.0 Hz), 4.04 (1H, dd, J=6.3, 8.0 Hz), 4.16 (1H, dd J=6.6, 13.5 Hz), 4.17 (1H, m), 4.48 (1H, d, J=11.9 Hz), 4.57 (1H, d, J=11.9 Hz), 4.64 (1H, d, J=7.0 Hz), 4.69 (1H, d, J=7.0 Hz), 7.25–7.40 (5H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm: 17.1, 25.3, 26.8, 36.1, 37.0, 41.3, 41.7, 46.6, 55.3, 69.2, 70.1, 73.5, 75.4, 75.6, 88.2, 93.0, 108.3, 127.7, 127.8, 128.4, 137.8; EIMS (*m*/*z*): 406 (M^+, 0.03), 391 ((M^+−Me, 0.1), 91 (100); HREIMS: calcd for $C_{23}H_{34}O_6$ (M^+): 406.2355; Found: 406.2379.

To a solution of the above alcohol (64.5 g, 160 mmol) in pyridine (70.0 mL) was added Ac_2O (20.0 mL). After stirring at rt for 10 h, the reaction mixture was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (eluted with hexane–EtOAc=3:1) to give acetate 13 (71.5 g, 99%). Colorless oil; $[\alpha]_D$=−6.3° (*c* 0.91, $CHCl_3$); IR (neat) 2985, 1736 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm: 1.08 (3H, s), 1.32 (3H, s), 1.37 (3H, s), 1.50–1.60 (2H, m), 1.90 (3H, s), 2.08 (2H, m), 2.16 (1H, dd, J=10.8, 14.1 Hz), 2.47 (1H, br d, J=4.8 Hz), 3.34 (3H, s), 3.36 (1H, d, J=8.4 Hz), 3.47 (1H, d, J=8.4 Hz), 3.85 (1H, dd, J=5.9, 8.0 Hz), 4.03 (1H, d, J=6.3, 8.0 Hz), 4.11 (1H, m), 4.49 (1H, d, J=12.4 Hz), 4.57 (1H, d, J=12.4 Hz), 4.64 (1H, d, J=7.1 Hz), 4.70 (1H, d, J=7.1 Hz), 4.95 (1H, ddd, J=3.3, 4.8, 10.8 Hz), 7.25–7.35 (5H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm: 16.3, 20.6, 25.4, 26.9, 33.5, 36.2, 38.6, 45.1, 46.4, 55.4, 69.0, 72.7, 73.4, 75.5, 76.0, 88.0, 93.2, 108.4, 127.5, 127.5, 128.3, 138.7, 170.5; EIMS (*m*/*z*): 448 (M^+, 0.5), 433 (M^+−Me, 1.5), 91 (100); Anal. calcd for $C_{25}H_{36}O_7$: C, 66.94; H, 8.09. Found: C, 66.98; H, 8.16.

1.1.10. (1*S*,4*R*,5*R*,6*R*)-5-Benzyloxymethyl-6-(*tert*-butyldimethylsilanyloxymethyl)-4-hydroxy-5-methylbicyclo[2.2.1]heptan-2-one (14). A mixture of AcOH and H_2O (4:1) (200 mL) was added to acetate **13** (71.5 g, 160 mmol) and the mixture was stirred at 65°C for 12 h. The reaction mixture was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (eluted with hexane–EtOAc=1:4) to give triol (46.5 g, 80%) and acetate **13** (10.7 g, 15% recovered). Colorless oil; $[\alpha]_D$=−12.6° (*c* 0.73, $CHCl_3$); IR (neat) 3434, 2923, 1730 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm: 1.31 (3H, s), 1.43 (1H, br d, J=4.4 Hz), 1.59 (1H, d, J=4.1 Hz), 1.67 (1H, dt, J=14.0, 3.6 Hz), 1.98 (3H, s), 2.06 (1H, dd, J=10.8, 14.0 Hz), 2.14 (1H, ddd, J=2.0, 3.6, 10.2 Hz), 2.44 (1H, d, J=4.4 Hz), 2.71 (1H, br s), 3.37 (1H, d, J=8.7 Hz), 3.40 (1H, dd, J=8.1, 10.8 Hz), 3.49 (1H, dd, J=3.4, 10.8 Hz), 3.57 (1H, d, J=8.7 Hz), 3.81 (1H, m), 4.48 (1H, d, J=11.9 Hz), 4.52 (1H, d, J=11.9 Hz), 4.99 (1H, ddd, J=3.6, 4.4, 10.8 Hz), 7.25–7.40 (5H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm: 16.2, 21.1, 38.0, 38.6, 39.6, 42.4, 45.6, 66.6, 70.5, 73.7, 74.0, 77.6, 83.9, 127.8, 127.9, 128.5, 137.6, 170.6; EIMS (*m*/*z*): 365 (M^++1, 3.6), 346 (M^+−H_2O, 0.7), 43 (100); HREIMS: calcd for $C_{20}H_{29}O_6$ (M^++H): 365.1964; Found: 365.1962.

To a solution of the above triol (16.0 g, 44.2 mmol) in MeOH (220 mL) was added $(NH_4)_2SO_4$ (17.0 g, 133 mmol). A solution of $NaIO_4$ (9.50 g, 44.2 mmol) in H_2O (220 mL) was added at 0°C and the mixture was stirred for 15 min. $NaBH_4$ (840 mg, 22.0 mmol) was added and the mixture was stirred for 5 min. The reaction mixture was diluted with Et_2O, washed with H_2O and saturated aqueous NaCl, dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (eluted with hexane–EtOAc=1:1) to give diol (13.0 g, 88%). Colorless oil; $[\alpha]_D$=−11.1° (*c* 1.08, $CHCl_3$); IR (neat) 3445, 2927, 1733 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm: 1.21 (3H, s), 1.42 (1H, br d, J=10.4 Hz), 1.67 (1H, dt, J=14.0, 3.5 Hz), 1.91 (2H, m), 2.00 (3H, s), 2.05 (1H, dd, J=10.9, 14.0 Hz), 2.12 (1H, br d, J=4.7 Hz), 2.53 (1H, br s), 3.43 (1H, d, J=8.6 Hz), 3.49 (1H, m), 3.60 (1H, d, J=8.6 Hz), 3.67 (1H, m), 4.51 (2H, s), 5.02 (1H, ddd, J=3.3, 4.7, 10.1 Hz), 7.25–7.40 (5H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm: 15.4, 21.1, 37.9, 38.6, 39.9, 43.8, 44.8, 62.2, 73.5, 73.7, 77.3, 84.3, 127.8, 127.9, 128.5, 137.7, 170.6; EIMS (*m*/*z*): 334 (M^+, 0.2), 243 (M^+−BnO, 2.4), 91 (100); HREIMS: calcd for $C_{19}H_{26}O_5$ (M^+): 334.1780; Found: 334.1764.

To a solution of the above diol (4.13 g, 12.0 mmol) in DMF (25.0 mL) were added imidazole (2.50 g, 36.0 mmol) and TBSCl (2.70 g, 18.0 mmol). After stirring at rt for 5 h, the reaction mixture was diluted with Et_2O, washed with H_2O and saturated aqueous NaCl, dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (eluted with hexane–Et_2O=3:1) to give TBS ether (5.16 g, 96%). Colorless oil; $[\alpha]_D$=−10.8° (*c* 1.05, $CHCl_3$); IR (neat) 3584, 2929, 1738 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm: 0.01 (3H, s), 0.02 (3H, s), 0.86 (9H, s), 1.20 (3H, s), 1.41 (1H, br d, J=10.3 Hz), 1.68 (1H, dt, J=13.8, 3.6 Hz), 1.77 (1H, br t, J=7.7 Hz), 1.92 (1H, ddd, J=2.0, 3.6, 10.3 Hz), 2.00 (3H, s), 2.05 (1H, dd, J=10.9, 13.8 Hz), 2.12 (1H, br d, J=4.6 Hz), 2.70 (1H, br s), 3.42 (1H, d,

J=9.0 Hz), 3.43 (1H, dd, J=7.2, 10.0 Hz), 3.62 (1H, dd, J=7.7, 10.0 Hz), 3.64 (1H, d, J=9.0 Hz), 4.47 (1H, d, J=11.8 Hz), 4.51 (1H, d, J=11.8 Hz), 5.03 (1H, ddd, J=3.4, 4.6, 10.9 Hz), 7.25–7.40 (5H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm: −5.5, −5.4, 15.3, 18.0, 21.1, 25.8, 37.9, 38.4, 39.9, 43.5, 44.6, 62.7, 73.6, 73.7, 77.9, 84.5, 127.8, 127.8, 128.4, 137.8, 170.5; EIMS (*m*/*z*): 449 (M^++1, 1.0), 391 ($M^+-{}^t$Bu, 10), 91 (100); HREIMS: calcd for $C_{25}H_{37}O_5Si$ (M^+−H): 449.2723; Found: 449.2712.

To a solution of the above TBS ether (47.0 g, 105 mmol) in MeOH (200 mL) was added K_2CO_3 (29.0 g, 210 mmol). After stirring at rt for 2 h, the reaction mixture was diluted with Et_2O, washed with H_2O and saturated aqueous NaCl, dried over anhydrous $MgSO_4$ and concentrated under reduced pressure to give diol (42.4 g, quantitative yield). Colorless oil; $[\alpha]_D$=+9.5° (*c* 0.34, $CHCl_3$); IR (neat) 3424, 2954 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm: 0.02 (3H, s), 0.03 (3H, s), 0.88 (9H, s), 1.18 (3H, s), 1.36 (1H, br d, J=9.9 Hz), 1.66 (1H, dt, J=13.3, 3.5 Hz), 1.81 (1H, br s), 1.88 (1H, m), 1.90 (1H, ddd, J=2.0, 3.5, 9.9 Hz), 1.97 (1H, dd, J=10.7, 13.3 Hz), 2.07 (1H, br t, J=7.3 Hz), 2.61 (1H, br s), 3.47 (1H, d, J=9.0 Hz), 3.48 (1H, dd, J=6.7, 9.9 Hz), 3.61 (1H, dd, J=8.0, 9.9 Hz), 3.71 (1H, d, J=9.0 Hz), 4.31 (1H, br d, J=10.7 Hz), 4.46 (1H, d, J=11.8 Hz), 4.53 (1H, d, J=11.8 Hz), 7.25–7.40 (5H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm: −5.4, −5.3, 15.4, 18.2, 25.9, 39.3, 40.6, 41.9, 42.4, 45.0, 63.2, 71.4, 73.6, 77.7, 84.9, 127.7, 127.8, 128.5, 138.0; EIMS (*m*/*z*): 406 (M^+), 257, 223, 91 (100); Anal. calcd for $C_{23}H_{38}O_4Si$: C, 67.94; H, 9.42. Found: C, 67.71; H, 9.41.

To a solution of the above diol (2.18 g, 5.37 mmol) in CH_2Cl_2 (54.0 mL) were added 4 Å molecular sieves (1.70 g) and PCC (1.70 g, 8.05 mmol) at 0°C. After stirring at rt for 2 h, the reaction mixture was diluted with Et_2O, filtered through silica gel column and the filtrate was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (eluted with hexane–EtOAc=1:1) to give keto alcohol **14** (1.97 g, 90%). Colorless oil; $[\alpha]_D$=+13.6° (*c* 0.13, $CHCl_3$); IR (neat) 3451, 2929, 1751 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm: 0.01 (3H, s), 0.02 (3H, s), 0.86 (9H, s), 1.29 (3H, s), 1.35 (1H, br t, J=7.2 Hz), 1.67 (1H, br d, J=10.4 Hz), 2.21 (1H, dd, J=4.3, 10.4 Hz), 2.30 (1H, d, J=18.8 Hz), 2.36 (1H, br s), 2.49 (1H, dd, J=4.4, 17.9 Hz), 2.99 (1H, br s), 3.36 (1H, d, J=9.0 Hz), 3.42 (1H, d, J=9.0 Hz), 3.56 (1H, dd, J=6.3, 10.1 Hz), 3.69 (1H, dd, J=7.9, 10.1 Hz), 4.47 (1H, d, J=11.8 Hz), 4.50 (1H, d, J=11.8 Hz), 7.25–7.40 (5H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm: -5.5, -5.4, 15.4, 18.0, 25.8, 38.7, 44.2, 46.5, 48.1, 51.6, 62.3, 73.7, 78.2, 82.3, 127.8, 128.1, 128.6, 137.4, 212.6; EIMS (*m*/*z*): 347 ($M^+-{}^t$Bu, 0.4), 255, 239, 91 (100); HREIMS: calcd for $C_{19}H_{27}O_4Si$ ($M^+-{}^t$Bu): 347.1678; Found: 347.1677.

1.1.11. (2*R*,3*R*,4*S*)-4-Acetyl-2-benzyloxymethyl-3-(*tert*-butyldimethylsilanyloxymethyl)-2-methylcyclopentanone (15). To a solution of keto alcohol **14** (5.14 g, 12.7 mmol) in toluene (127 mL) were added 15-crown-5 (0.126 mL, 0.635 mmol) and NaH (60%, 0.61 g, 15.3 mmol). After stirring at rt for 1 h, the reaction mixture was diluted with Et_2O, filtered through silica gel column and the filtrate was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (eluted with hexane–Et_2O=3:1) to give diketone **15** (4.42 g, 86%). Colorless oil; $[\alpha]_D$=+47.3° (*c* 0.33, $CHCl_3$); IR (neat) 2930, 1746, 1714 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm: 0.02 (6H, s), 0.87 (9H, s), 0.92 (3H, s), 2.24 (3H, s), 2.48 (1H, dd, J=10.7, 18.3 Hz), 2.54 (1H, dd, J=8.1, 18.3 Hz), 2.92 (1H, m), 2.99 (1H, m), 3.34 (1H, d, J=8.8 Hz), 3.49 (1H, d, J=8.8 Hz), 3.67 (1H, dd, J=5.8, 10.4 Hz), 3.77 (1H, dd, J=5.6, 10.4 Hz), 4.43 (1H, d, J=12.1 Hz), 4.48 (1H, d, J=12.1 Hz), 7.25–7.35 (5H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm: −5.7, −5.7, 14.8, 18.2, 25.8, 29.5, 41.3, 46.3, 48.4, 52.6, 62.4, 73.3, 74.3, 127.4, 127.5, 128.3, 138.1, 209.1, 217.9; EIMS (*m*/*z*): 347 ($M^+-{}^t$Bu, 0.6), 253, 91 (100); HREIMS: calcd for $C_{19}H_{27}O_4Si$ ($M^+-{}^t$Bu): 347.1678; Found: 347.1698.

1.1.12. (1*R*,2*R*,5*S*)-2-Benzyloxymethyl-2-methyl-5-(2-methyl[1,3]dioxolan-2-yl)-3-oxocyclopentylmethyl acetate (16). A mixture of AcOH and H_2O (4:1) (20.0 mL) was added to TBS ether **15** (1.51 g, 3,72 mmol) and the mixture was stirred at rt for 5 h. The reaction mixture was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (eluted with hexane–EtOAc=1:1) to give alcohol (1.05 g, 97%). Colorless oil; $[\alpha]_D$=+83.7° (*c* 0.22, $CHCl_3$); IR (neat) 3403, 2930, 1742, 1709 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm: 0.98 (3H, s), 2.27 (3H, s), 2.40 (1H, dd, J=4.5, 18.4 Hz), 2.65 (1H, dd, J=8.0, 18.4 Hz), 2.75–2.85 (2H, m), 2.92 (1H, dt, J=8.0, 11.2 Hz), 3.45 (1H, d, J=9.1 Hz), 3.48 (1H, d, J=9.1 Hz), 3.61 (1H, m), 3.68 (1H, m), 4.50 (1H, d, J=12.0 Hz), 4.55 (1H, d, J=12.0 Hz), 7.25–7.35 (5H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ ppm: 14.6, 30.1, 41.1, 48.2, 48.3, 53.0, 61.5, 73.6, 74.0, 127.8, 127.9, 128.5, 137.2, 209.3, 216.5; EIMS (*m*/*z*): 272 (M^+-H_2O, 3.0), 166, 123, 91 (100); HREIMS: calcd for $C_{17}H_{22}O_4$ (M^+-H_2O): 290.1518; Found: 290.1506.

To a solution of the above alcohol (1.05 g, 3.59 mmol) in pyridine (5.00 mL) was added Ac_2O (3.00 mL). After stirring at rt for 5 h, the reaction mixture was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (eluted with hexane–Et_2O=1:5) to give acetate (1.19 g, quantitative yield). Colorless oil; $[\alpha]_D$=+47.1° (*c* 0.20, $CHCl_3$); IR (neat) 2863, 1743, 1716 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm: 0.89 (3H, s), 1.98 (3H, s), 2.25 (3H, s), 2.43 (1H, dd, J=11.0, 18.2 Hz), 2.61 (1H, dd, J=7.9, 18.2 Hz), 2.97 (1H, dt, J=7.9, 11.0 Hz), 3.17 (1H, dt, J=6.8, 11.0 Hz), 3.33 (1H, d, J=8.9 Hz), 3.53 (1H, d, J=8.9 Hz), 4.11 (1H, dd, J=7.1, 11.0 Hz), 4.23 (1H, dd, J=6.4, 11.0 Hz), 4.44 (1H, d, J=12.3 Hz), 4.52 (1H, d, J=12.3 Hz), 7.25–7.40 (5H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm: 14.8, 20.7, 29.6, 41.7, 42.5, 48.7, 52.6, 63.8, 73.4, 73.6, 127.6, 127.7, 128.4, 137.9, 170.6, 208.2, 216.5; EIMS (*m*/*z*): 332 (M^+), 314, 200; HREIMS: calcd for $C_{19}H_{24}O_5$ (M^+): 332.1624; Found: 332.1623.

To a solution of the above diketone (4.70 g, 14.2 mmol) in CH_2Cl_2 (70.0 mL) were added TMS–OTf (0.280 mL, 1.45 mmol) and 1,2-bis(trimethylsilyloxy)ethane (3.80 g, 15.6 mmol) at −60°C. After stirring at −40°C for 18 h, pyridine (5.0 mL) was added to the reaction mixture. The mixture was diluted with Et_2O, washed with H_2O and

saturated aqueous NaCl, dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (eluted with hexane–Et_2O=5:1) to give mono acetal **16** (5.00 g, 90%). Colorless oil; $[\alpha]_D$=+34.6° (*c* 0.58, $CHCl_3$); IR (neat) 2981, 1741 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm: 0.90 (3H, s), 1.33 (3H, s), 1.92 (3H, s), 2.20–2.35 (2H, m), 2.51 (1H, dd, *J*=7.8, 17.9 Hz), 2.99 (1H, dt, *J*=4.0, 10.4 Hz), 3.35 (1H, d, *J*=8.8 Hz), 3.59 (1H, d, *J*=8.8 Hz), 3.90–4.05 (5H, m), 4.40 (1H, d, *J*=12.4 Hz), 4.52 (1H, d, *J*=12.4 Hz), 4.69 (1H, dd, *J*=4.0, 11.7 Hz), 7.25–7.40 (5H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ ppm: 14.9, 20.8, 21.7, 39.3, 41.3, 42.7, 53.6, 64.3, 64.4, 65.0, 73.1, 74.1, 110.6, 127.3, 127.4, 128.2, 138.3, 170.6, 218.8; EIMS (*m/z*): 376 (M^+, 0.2), 358, 331, 87 (100); HREIMS: calcd for $C_{21}H_{28}O_6$ (M^+): 376.1886; Found: 376.1899.

1.1.13. (1*R*,2*R*,5*R*)-2-Benzyloxymethyl-2-methyl-5-(2-methyl[1,3]dioxolan-2-yl)cyclopent-3-enylmethyl acetyate (17). To a cold (0°C) solution of ketone **16** (44.0 g, 124 mmol) in MeOH (600 mL) was added $NaBH_4$ (2.30 g, 61.7 mmol) and the mixture was stirred at 0°C for 15 min. The reaction mixture was diluted with Et_2O, washed with saturated aqueous NH_4Cl, H_2O and saturated aqueous NaCl, dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (eluted with hexane–EtOAc=1:1) to give alcohol (44.0 g, 98%). Colorless oil; $[\alpha]_D$=+15.3° (*c* 0.55, $CHCl_3$); IR (neat) 3457, 2969, 1738 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm: 0.95 (3H, s), 1.32 (3H, s), 1.64 (1H, m), 1.91 (3H, s), 2.05–2.15 (2H, m), 2.20 (1H, m), 3.41 (1H, br d, *J*=7.9 Hz), 3.42 (1H, d, *J*=8.8 Hz), 3.66 (1H, d, *J*=8.8 Hz), 3.84 (1H, ddd, *J*=2.5, 5.1, 7.9 Hz), 3.95–4.05 (5H, m), 4.38 (1H, dd, *J*=3.6, 11.1 Hz), 4.48 (1H, d, *J*=12.2 Hz), 4.59 (1H, d, *J*=12.2 Hz), 7.25–7.35 (5H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ ppm: 17.6, 20.9, 22.6, 34.3, 42.2, 46.9, 49.9, 64.7, 65.0, 73.3, 75.0, 79.4, 111.3, 127.4, 127.5, 128.3, 138.6, 170.8; EIMS (*m/z*): 363 (M^+−Me, 0.5), 316, 225, 87 (100); HREIMS: calcd for $C_{20}H_{27}O_6$ (M^+−Me): 363.1808; Found: 363.1800.

To a solution of the above alcohol (100 mg, 263 μmol) in pyridine (420 μL) were added *N*-phenylthiosuccinimide (272 mg, 1.32 mmol) and $^nBu_3P$ (330 μL, 1.32 mmol). After stirring at rt for 6 h, the reaction mixture was diluted with Et_2O, washed with 5% NaOH aqueous solution, H_2O and saturated aqueous NaCl, dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (eluted with hexane–Et_2O=10:1) to give cyclopentene **17** (88.5 mg, 93%). Colorless oil; $[\alpha]_D$=+20.0° (*c* 0.20, $CHCl_3$); IR (neat) 2874, 1738 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm: 1.00 (3H, s), 1.30 (3H, s), 1.93 (3H, s), 2.40 (1H, ddd, *J*=4.5, 8.1, 10.0 Hz), 2.73 (1H, dt, *J*=8.1, 2.1 Hz), 3.31 (1H, d, *J*=8.7 Hz), 3.39 (1H, d, *J*=8.7 Hz), 3.90–4.00 (4H, m), 4.09 (1H, dd, *J*=10.0, 11.0 Hz), 4.42 (1H, dd, *J*=4.5, 11.0 Hz), 4.51 (1H, d, *J*=12.4 Hz), 4.55 (1H, d, *J*=12.4 Hz), 5.56 (1H, dd, *J*=1.9, 5.8 Hz), 5.69 (1H, dd, *J*=2.3, 5.8 Hz), 7.25–7.35 (5H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ ppm: 18.7, 21.0, 21.8, 42.5, 52.1, 55.8, 64.5, 64.9, 65.1, 73.2, 78.0, 111.1, 127.3, 127.4, 128.2, 138.8, 140.0, 171.0; EIMS (*m/z*): 345 (M^+−Me, 0.1), 179, 151, 87 (100); HREIMS: calcd for $C_{20}H_{25}O_5$ (M^+−Me): 345.1702; Found: 345.1692.

1.1.14. 2-((1*S*,4*R*,5*S*)-5-Benzenesulfonylmethyl-4-benzyloxymethyl-4-methylcyclopent-2-enyl)-2-methyl[1,3]-dioxolane (18). To a solution of acetate **17** (16.2 g, 44.8 mmol) in MeOH (200 mL) was added K_2CO_3 (3.00 g, 21 mmol). After stirring at rt for 3 h, the reaction mixture was diluted with Et_2O and filtered through silica gel. The filtrate was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (eluted with hexane–EtOAc=1:1) to give alcohol (14.3 g, quantitative yield). Colorless oil; $[\alpha]_D$=+20.8° (*c* 0.25, $CHCl_3$); IR (neat) 3457, 2875 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm: 1.01 (3H, s), 1.29 (3H, s), 2.18 (1H, dd, *J*=7.1, 15.3 Hz), 2.74 (1H, dt, *J*=8.3, 1.5 Hz), 3.29 (1H, d, *J*=8.6 Hz), 3.39 (1H, d, *J*=8.6 Hz), 3.63 (1H, m), 3.75 (1H, m), 3.82 (1H, br t, *J*=5.1 Hz), 3.90–4.00 (4H, m), 4.56 (1H, d, *J*=12.1 Hz), 4.58 (1H, d, *J*=12.1 Hz), 5.56 (1H, dd, *J*=2.0, 5.8 Hz), 5.58 (1H, dd, *J*=1.4, 5.8 Hz), 7.25–7.35 (5H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ ppm: 18.5, 21.6, 48.8, 52.1, 58.2, 63.0, 64.5, 64.8, 73.4, 77.2, 78.3, 110.9, 127.6, 128.4, 129.4, 137.9, 138.9; EIMS (*m/z*): 318 (M^+, 0.1), 303 (0.1), 197, 87 (100); HREIMS: calcd for $C_{19}H_{26}O_4$ (M^+): 318.1831; Found: 318.1811.

To a solution of the above alcohol (340 mg, 1.06 mmol) in pyridine (2.40 mL) were added PhSSPh (1.20 g, 5.30 mmol) and $^nBu_3P$ (3.80 g, 15.6 mmol) at 60°C. After stirring for 5 h, the reaction mixture was diluted with Et_2O, washed with 5% NaOH aqueous solution, H_2O and saturated aqueous NaCl, dried over anhydrous $MgSO_4$ and concentrated under reduced pressure to give crude sulfide. The crude sulfide was used next reaction without purification.

To a cold (0°C) solution of the above crude sulfide in THF–MeOH (1:1, 255 mL) was added a solution of OXONE® (55.0 g, 89.2 mmol) in H_2O (190 mL). After stirring at rt for 3 h, the reaction mixture was diluted with Et_2O, washed with saturated aqueous $NaHCO_3$, H_2O and saturated aqueous NaCl, dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (eluted with hexane–Et_2O=1:1) to give sulfone **18** (16.8 g, 85%, two steps). Colorless oil; $[\alpha]_D$=+26.5° (*c* 1.30, $CHCl_3$); IR (neat) 2872, 1307, 1149 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm: 1.07 (3H, s), 1.09 (3H, s), 2.66 (1H, dt, *J*=8.9, 2.4 Hz), 2.81 (1H, br t, *J*=8.9 Hz), 3.41 (1H, dd, *J*=10.8, 14.6 Hz), 3.64 (1H, d, *J*=9.1 Hz), 3.65–3.85 (6H, m), 4.58 (1H, d, *J*=12.1 Hz), 4.63 (1H, d, *J*=12.1 Hz), 5.49 (1H, dd, *J*=1.7, 5.9 Hz), 5.72 (1H, dd, *J*=2.4, 5.9 Hz), 7.25–7.40 (5H, m), 7.43 (2H, m), 7.57 (1H, m), 7.90 (2H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ ppm: 19.3, 21.5, 37.0, 51.4, 57.0, 59.0, 64.1, 64.8, 73.0, 76.2, 111.0, 126.9, 127.1, 127.3, 128.1, 128.3, 128.9, 133.3, 139.0, 139.8, 141.3; EIMS (*m/z*): 442 (M^+, 0.1), 351, 300, 87 (100); Anal. calcd for $C_{25}H_{30}O_5S$: C, 67.85; H, 6.83. Found: C, 67.68; H, 6.83.

1.1.15. (4-Bromo-3-methylbut-2-enyloxy)-*tert*-butyldimethylsilane (20). To a cold (0°C) solution of 4-(*tert*-butyldimethylsilanyloxy)-2-methylbut-2-en-1-ol (**19**)[16] (14.4 g, 67.1 mmol) in CH_2Cl_2 (2.40 mL) were added Ph_3P (21.0 g, 80.5 mmol) and NBS (13.0 g, 73.8 mmol) at 0°C. After stirring at 0°C for 2 h, the reaction mixture was diluted with Et_2O and filtered through silica gel. The filtrate was concentrated under reduced pressure. The residue was

purified by distillation under reduce pressure (bp 103°C/3 mmHg) to give allylic bromide **20** (14.9 g, 80%). Colorless oil; IR (neat) 2954, 1474, 1254, 1101 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ ppm: 0.08 (6H, s), 0.91 (9H, s), 1.77 (3H, br s), 3,96 (2H, br s), 4.21 (2H, br d, J=6.2 Hz), 5.71 (1H, br t, J=6.2 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ ppm: 15.2, 18.5, 26.1, 26.1, 40.8, 60.2, 130.5, 132.5; EIMS (m/z): 280 (M^++2, 10), 278 (M^+, 10), 222 (10), 220 (10); HREIMS: calcd for $C_{10}H_{20}OSiBr$ (M^+-CH_3): 263.0467; Found: 263.0454.

1.1.16. (*E*)-{5-Benzenesulfonyl-5-[(1*R*,2*S*,5*R*)-2-benzyloxymethyl-2-methyl-5-(2-methyl-[1,3]dioxolan-2-yl)-3-cyclopentenyl]-(3-methyl-2-pentenyloxy)-*tert*-butyldimethylsilane (21). To a cold (−78°C) solution of sulfone **18** (850 mg, 1.91 mmol) in THF (19.0 mL) was added ^{n}BuLi (1.47 mL, 2.30 mmol, 1.56 M in hexane). After stirring at −78°C for 30 min, a solution of allylic bromide **20** (1.05 g, 3.82 mmol) in THF (2.00 mL) was added and stirred at -30°C for 40 min. The reaction mixture was diluted with Et_2O, washed with saturated aqueous NH_4Cl, H_2O and saturated aqueous NaCl, dried over anhydrous $MgSO_4$ and concentrated under reduced pressure to give crude sulfone **21**. The crude sulfone **21** was used next reaction without purification.

1.1.17. [(1*R*,4*S*,5*R*)-5-[(*E*)-5-(*tert*-Butyldimethylsilanyloxy)-3-methyl-3-pentenyl]-1-methyl-4-(2-methyl[1,3]dioxolan-2-yl)-2-cyclopentenyl]methanol (22). To a cold (−78°C) solution of crude sulfone **21** in THF (20.0 mL) and NH_3 (300 mL) was added Na (1.0 g). After stirring at −78°C for 1 h, NH_4Cl (10 g) was added. After evaporation of NH_3 under atmospheric pressure, the residue was diluted with Et_2O, washed with H_2O and saturated aqueous NaCl, dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (eluted with hexane–EtOAc=2:1) to give alcohol **22** (524 mg, 68%, two steps). Colorless oil; $[\alpha]_D$=+36.7° (c 0.22, $CHCl_3$); IR (neat) 3410, 2930 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm: 0.07 (6H, s), 0.90 (9H, s), 0.97 (3H, s), 1.32 (3H, s), 1.60–1.70 (2H, m), 1.64 (3H, br s), 2.00–2.10 (3H, m), 2.70 (1H, dt, J=6.2, 2.0 Hz), 3.44 (1H, d, J=9.5 Hz), 3.49 (1H, dd, J=2.1, 5.8 Hz), 3.90–4.00 (4H, m), 4.19 (2H, d, J=6.3 Hz), 5.32 (1H, br t, J=6.3 Hz), 5.49 (1H, d, J=12.1 Hz), 5.63 (1H, dd, J=2.1, 5.8 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ ppm: −5.0, 16.4, 18.4, 18.9, 22.6, 26.0, 30.3, 39.1, 41.7, 53.6, 60.3, 61.1, 64.6, 64.7, 70.9, 111.5, 124.2, 129.9, 137.6, 139.6; EIMS (m/z): 410 (M^+, 0.02), 395 (M^+-Me, 0.1), 380, 87 (100); HREIMS: calcd for $C_{22}H_{39}O_4Si$ (M^+-Me): 395.2617; Found: 395.2595.

1.1.18. Methyl [(1*R*,4*S*,5*R*)5-[(*E*)-5-(*tert*-butyldimethylsilanyloxy)-3-methyl-3-pentenyl]-1-methyl-4-(2-methyl-[1,3]dioxolan-2-yl)-2-cyclopentenyl]acetate (23). To a solution of alcohol **22** (4.10 g, 9.98 mmol) in CH_2Cl_2 (100 mL) were added 4 Å molecular sieves (5.6 g) and PDC (5.60 g, 15.0 mmol). After stirring at rt for 5 h, the reaction mixture was diluted with Et_2O, filtered through silica gel column and the filtrate was concentrated under reduced pressure to give crude aldehyde. The crude aldehyde was used next reaction without purification.

To a cold (−78°C) suspension of (methoxymethyl)triphenylphosphonium chloride (15.0 g, 44.0 mmol) in THF (27.0 mL) was added PhLi (34.6 mL, 35.3 mmol, 1.02 M in cyclohexane–Et_2O). The mixture was stirred at 0°C for 30 min. A solution of the above crude aldehyde in THF (5.00 mL) was added and stirred at 0°C for 15 min. The reaction mixture was diluted with Et_2O and saturated aqueous NH_4Cl (10 mL) was added. After stirring at rt for 24 h, organic layer was washed with H_2O and saturated aqueous NaCl, dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (eluted with hexane–Et_2O=10:1) to give the mixture (E/Z=3:2) of methyl enol ether (3.70 g, 84%, two steps). The mixture of geometric isomers was used next reaction.

To a solution of the above enol ether (3.70 g, 8.55 mmol) in benzene (85.5 mL) was added PCC–Al_2O_3 (21.4 g). After stirring at 40°C for 5 h, the reaction mixture was diluted with Et_2O, filtered through silica gel column and the filtrate was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (eluted with hexane–Et_2O=3:1) to give methyl ester **23** (3.25 g, 85%). Colorless oil; $[\alpha]_D$=+30.0° (c 0.28, $CHCl_3$); IR (neat) 2954, 1738 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm: 0.07 (6H, s), 0.90 (9H, s), 1.05 (3H, s), 1.27 (3H, s), 1.50–1.75 (3H, m), 1.64 (3H, s), 1.94 (1H, m), 2.08 (2H, m), 2.40 (1H, d, J=13.7 Hz), 2.52 (1H, d, J=13.7 Hz), 2.63 (1H, dt, J=7.0, 2.1 Hz), 3.64 (3H, s), 3.90–4.00 (4H, m), 4.19 (2H, br d, J=6.3 Hz), 5.32 (1H, br t, J=6.3 Hz), 5.53 (1H, dd, J=2.0, 5.8 Hz), 5.73 (1H, dd, J=2.2, 5.8 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ ppm: −5.0, 16.4, 18.4, 21.5, 22.0, 26.0, 29.6, 38.9, 46.6, 49.7, 51.1, 51.2, 59.9, 60.3, 64.4, 64.7, 111.2, 124.1, 128.3, 137.4, 140.8, 172.4; EIMS (m/z): 452 (M^+, 0.15), 437, 395 (0.1), 87 (100); HREIMS: calcd for $C_{25}H_{44}O_5Si$ (M^+): 452.2958; Found: 452.2957.

1.1.19. Ethyl (*E*)-4-[(1*R*,4*S*,5*R*)-5-[(*E*)-5-(*tert*-butyldimethylsilanyloxy)-3-methyl-3-pentenyl]-1-methyl-4-(2-methyl-[1,3]dioxolan-2-yl)-2-cyclopentenyl]-2-methyl-2-butenoate (24). To a cold (−78°C) solution of ester **23** (4.37 g, 9.67 mmol) in toluene (97.0 mL) was added DIBAH (11.2 mL, 10.6 mmol, 0.95 M in hexane). After stirring at −78°C for 10 min, EtOAc (1.0 mL) was added at −78°C. The reaction mixture was diluted with Et_2O and saturated aqueous NaCl was added. The mixture was stirred at rt for 1 h. Organic layer was dried over anhydrous $MgSO_4$ and concentrated under reduced pressure to give crude aldehyde. The crude aldehyde was used next reaction without purification.

To a cold (0°C) solution of trietyl 2-phosphonopropionate (2.60 mL, 12.0 mmol) in THF (40.0 mL) was added NaH (390 mg, 9.60 mmol, 60%). After stirring at 0°C for 20 min, a solution of the above crude aldehyde in THF (10 mL) was added at 0°C and stirred for 1 h. The reaction mixture was diluted with Et_2O and saturated aqueous NaCl was added. The mixture was stirred at rt for 1 h. The reaction mixture was diluted with Et_2O, was washed with H_2O and saturated aqueous NaCl, dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (eluted with hexane–Et_2O=10:1) to give ethyl ester **24** (3.86 g, 80%, two steps). Colorless oil; $[\alpha]_D$=9.8° (c 0.57, $CHCl_3$); IR (neat) 2930,

1712 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm: 0.06 (6H, s), 0.90 (9H, s), 1.01 (3H, s), 1.26 (3H, s), 1.27 (3H, t, J=7.2 Hz), 1.55–1.65 (2H, m), 1.63 (3H, br s), 1.70–1.85 (2H, m), 1.83 (3H, br s), 1.95–2.15 (2H, m), 2.32 (1H, br d, J=8.0 Hz), 2.63 (1H, d, J=7.4 Hz), 3.85–4.00 (4H, m), 4.10–4.25 (4H, m), 5.30 (1H, br t, J=5.3 Hz), 5.54 (2H, m), 5.81 (1H, br t, J=7.9 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ ppm: −5.0, 12.7, 14.3, 16.4, 18.4, 21.8, 22.1, 26.0, 29.8, 39.3, 41.2, 46.2, 51.3, 60.1, 60.3, 64.4, 64.8, 111.7, 124.1, 128.8, 128.9, 137.5, 139.8, 141.2, 168.1; EIMS (*m*/*z*): 491 (M^+−Me, 0.15), 449 (0.9), 87 (100); HREIMS: calcd for $C_{28}H_{47}O_5Si$ (M^+−Me): 491.3193; Found: 491.3183.

1.1.20. (*E*)-4-[(1*R*,4*S*,5*R*)-5-((*E*)-5-Benzenesulfonyl-3-methyl-3-pentenyl)-1-methyl-4-(2-methyl-[1,3]dioxolan-2-yl)-2-cyclopentenyl]-2-methyl-2-buten-1-ol (25). To a solution of TBS ether **24** (321 mg, 0.634 mmol) in THF (634 μL) was added TBAF (0.770 mL, 770 μmol, 1.0 M in THF). After stirring at rt for 2 h, the reaction mixture was diluted with Et_2O, washed with H_2O and saturated aqueous NaCl, dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (eluted with hexane–Et_2O=1:3) to give alcohol (250 mg, quantitative yield). Colorless oil; $[\alpha]_D$=−4.6° (*c* 0.57, $CHCl_3$); IR (neat) 3402, 2935, 1707, 1647 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm: 1.01 (3H, s), 1.26 (3H, s), 1.27 (3H, t, J=7.1 Hz), 1.55–1.65 (2H, m), 1.69 (3H, br s), 1.75 (1H, m), 1.83 (3H, br s), 1.85 (1H, m), 2.04 (1H, m), 2.12 (1H, m), 2.33 (2H, dd, J=7.5, 0.6 Hz), 2.63 (1H, d, J=7.5 Hz), 3.90–4.00 (4H, m), 4.13–4.23 (4H, m), 5.41 (1H, dt, J=1.3, 6.9 Hz), 5.54 (2H, m), 6.84 (1H, dt, J=1.4, 7.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ ppm: 12.7, 14.3, 16.3, 21.8, 22.2, 29.7, 39.0, 41.1, 45.7, 51.4, 59.4, 60.3, 60.4, 64.4, 64.8, 111.6, 123.3, 128.8, 129.0, 139.7, 140.1, 141.2, 168.1; EIMS (*m*/*z*): 377 (M^+−Me, 0.1), 87 (100); HREIMS: calcd for $C_{22}H_{33}O_5Si$ (M^+−Me): 377.2328; Found: 377.2323.

To a solution of the above alcohol (250 mg, 638 μmol) in pyridine (1.2 mL) were added PhSSPh (700 mg, 3.20 mmol) and ^{n}Bu_3P (800 μL, 3.20 mmol) at 60°C. After stirring for 2 h, the reaction mixture was diluted with Et_2O, washed with 5% NaOH aqueous solution, H_2O and saturated aqueous NaCl, dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (eluted with hexane–Et_2O=10:1) to give sulfide (282 mg, 92%). Colorless oil; $[\alpha]_D$=−10.3° (*c* 0.45, $CHCl_3$); IR (neat) 2937, 1708, 1648 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm: 1.00 (3H, s), 1.26 (3H, s), 1.27 (3H, t, J=7.1 Hz), 1.50–1.60 (2H, m), 1.58 (3H, br s), 1.65–1.85 (2H, m), 1.83 (3H, br s), 1.95–2.15 (2H, m), 2.31 (2H, d, J=7.4 Hz), 2.62 (1H, d, J=7.4 Hz), 3.54 (2H, d, J=7.7 Hz), 3.85–4.00 (4H, m), 4.10–4.20 (2H, m), 5.32 (1H, dt, J=1.1, 7.7 Hz), 5.53 (1H, d, J=6.8 Hz), 5.55 (1H, d, J=6.8 Hz), 6.83 (1H, dt, J=1.4, 7.4 Hz), 7.17 (1H, m), 7.25 (2H, m), 7.33 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm: 12.7, 14.3, 16.1, 21.8, 22.1, 29.9, 32.2, 39.2, 41.2, 46.1, 51.4, 60.2, 60.3, 64.4, 64.8, 111.6, 119.0, 126.0, 128.7, 128.8, 128.9, 129.9, 136.8, 139.7, 140.5, 141.1, 168.1; EIMS (*m*/*z*): 375 (M^+−PhS, 0.8), 357, 87 (100); Anal. calcd for $C_{29}H_{40}O_4S$: C, 71.86; H, 8.32. Found: C,71.86; H, 8.36.

To a cold (0°C) solution of the above sulfide (280 mg, 579 μmol) in THF–MeOH (1:1, 3.00 mL) was added a solution of OXONE® (720 mg, 1.20 mmol) in H_2O (2.50 mL). After stirring at rt for 3 h, the reaction mixture was diluted with Et_2O, washed with saturated aqueous $NaHCO_3$, H_2O and saturated aqueous NaCl, dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (eluted with hexane–EtOAc=1:2) to give sulfone (269 mg, 90%). Colorless oil; $[\alpha]_D$=−9.7° (*c* 0.25, $CHCl_3$); IR (neat) 2937, 1707, 1648, 1307, 1151 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm: 0.93 (3H, s), 1.25 (3H, s), 1.27 (3H, t, J=7.1 Hz), 1.33 (3H, br s), 1.48 (1H, m), 1.63 (1H, m), 1.77 (1H, m), 1.82 (3H, br s), 1.95–2.10 (2H, m), 2.29 (2H, d, J=7.5 Hz), 2.61 (1H, d, J=7.4 Hz), 3.79 (1H, d, J=8.0 Hz), 3.85–4.00 (4H, m), 4.10–4.20 (2H, m), 5.20 (1H, dt, J=1.1, 8.0 Hz), 5.53 (1H, d, J=7.0 Hz), 5.55 (1H, d, J=7.0 Hz), 6.81 (1H, dt, J=1.3, 7.5 Hz), 7.52 (2H, m), 7.63 (1H, m), 7.86 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm: 12.7, 14.3, 16.2, 21.7, 22.1, 29.8, 39.4, 41.1, 46.1, 51.3, 56.1, 60.2, 60.4, 64.4, 64.8, 110.1, 111.5, 128.6, 128.9, 133.5, 138.7, 139.5, 141.1, 147.1, 168.0; EIMS (*m*/*z*): 516 (M^+, 0.8), 501, 87 (100); HREIMS: calcd for $C_{29}H_{40}O_6S$ (M^+): 516.2546; Found: 516.2547.

To a cold (−78°C) solution of the above ester (1.00 g, 1.94 mmol) in toluene (20.0 mL) was added DIBAH (6.00 mL, 5.70 mmol, 0.95 M in hexane). After stirring at −78°C for 15 min, the reaction mixture was diluted with Et_2O and saturated aqueous NaCl was added. The mixture was stirred at rt for 1 h. Organic layer was dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (eluted with hexane–EtOAc=1:1) to give allylic alcohol **25** (900 mg, 98%). Colorless oil; $[\alpha]_D$=+19.4° (*c* 0.29, $CHCl_3$); IR (neat) 3391, 2934, 1306, 1150 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm: 0.96 (3H, s), 1.25 (3H, s), 1.34 (3H, br s), 1.40–1.65 (3H, m), 1.66 (3H, br s), 1.81 (1H, m), 1.95–2.15 (2H, m), 2.15 (2H, d, J=7.5 Hz), 2.60 (1H, br d, J=7.5 Hz), 3.80 (2H, d, J=7.9 Hz), 3.85–4.00 (4H, m), 4.00 (2H, br s), 5.21 (1H, dt, J=1.0, 7.9 Hz), 5.46 (1H, br d, J=7.5 Hz), 5.45–5.55 (2H, m), 7.52 (2H, m), 7.63 (1H, m), 7.86 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm: 14.1, 16.2, 22.0, 22.1, 29.8, 39.5, 39.9, 45.3, 51.5, 56.1, 60.4, 64.4, 64.8, 69.1, 110.0, 111.7, 123.4, 128.1, 128.6, 128.9, 133.5, 136.2, 138.8, 141.7, 147.2; EIMS (*m*/*z*): 459 (M^+−Me, 0.04), 389 (7.3), 87 (100); HREIMS: calcd for $C_{26}H_{35}O_5S$ (M^+−Me): 459.2205; Found: 459.2235.

1.1.21. (2*R*,3*R*)-3-[(1*R*,4*S*,5*R*)-5-((*E*)-5-Benzenesulfonyl-3-methyl-3-pentenyl)-1-methyl-4-(2-methyl-[1,3]dioxolan-2-yl)-2-cyclopentenylmethyl]-2-methyloxiranylmethyl methanesulfonate (26). A mixture of powdered 4 Å molecular sieves (100 mg) and CH_2Cl_2 (2.10 mL) was cooled to −20°C and then to which were added of $Ti(O^iPr)_4$ (6.0 μL, 0.021 mmol) and D-(−)-DET (5.5 μL, 0.032 mmol). After stirring for 30 min, TBHP (140 μL, 0.420 mmol, 3.0 M in CH_2Cl_2) was added, followed by stirring for 30 min and the addition of allylic alcohol **25** (99.0 mg, 0.210 mmol) in CH_2Cl_2 (0.5 mL). Stirring was continued at −20°C for 6 h. The reaction mixture was warmed to 0°C, water (3.0 mL) was added and the mixture

was stirred for 1 h. Aqueous solution of NaOH (30%) in saturated with NaCl (0.10 mL) was added and the mixture was stirred vigorously. After 1 h stirring, the mixture was filtered through celite. The filtrate was diluted with Et_2O, washed with 1N NaOH, H_2O and saturated aqueous NaCl, dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (eluted with hexane–EtOAc=1:2) to give epoxy alcohol (100 mg, 95%). Colorless oil; $[\alpha]_D$=+16.9° (*c* 0.39, $CHCl_3$); IR (neat) 3398, 2932, 1306, 1150 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm: 1.01 (3H, s), 1.28 (3H, s), 1.29 (3H, s), 1.33 (3H, br s), 1.45–1.85 (4H, m), 2.00–2.10 (3H, m), 2.64 (1H, d, *J*=7.6 Hz), 3.11 (1H, dd, *J*=6.8, 4.8 Hz), 3.58 (2H, d, *J*=7.0 Hz), 3.80 (2H, d, *J*=7.9 Hz), 3.85–4.00 (4H, m), 5.21 (1H, br t, *J*=7.9 Hz), 5.56 (2H, m), 7.53 (2H, m), 7.64 (1H, m), 7.86 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm: 14.7, 16.2, 22.1, 22.5, 29.8, 39.4, 40.1, 45.5, 50.3, 56.1, 58.0, 60.0, 60.1, 64.4, 64.7, 66.0, 110.0, 111.5, 128.6, 128.8, 128.9, 133.5, 141.1, 147.1; EIMS (*m*/*z*): 490 (M^+−Me, 0.03), 427 (0.1), 87 (100); HREIMS: calcd for $C_{27}H_{38}O_6S$ (M^+): 490.2389; Found: 490.2382.

To a solution of the above epoxy alcohol (524 mg, 1.49 mmol) in CH_2Cl_2 (15.0 mL) were added DMAP (364 mg, 3.00 mmol) and MsCl (170 μL, 2.20 mmol). After stirring for 1.5 h, the reaction mixture was diluted with Et_2O, washed with H_2O and saturated aqueous NaCl, dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (eluted with Et_2O) to give mesylate **26** (620 mg, 97%). Colorless oil; $[\alpha]_D$=+16.4° (*c* 0.76, $CHCl_3$); IR (neat) 2937, 1357, 1306, 1176, 1151 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm: 1.00 (3H, s), 1.27 (3H, s), 1.33 (3H, br s), 1.35 (3H, br s), 1.40–1.80 (3H, m), 1.82 (1H, dd, *J*=3.8, 14.6 Hz), 1.95–2.10 (3H, m), 2.63 (1H, dt, *J*=7.5, 1.7 Hz), 3.02 (1H, dd, *J*=3.8, 7.4 Hz), 3.04 (3H, s), 3.79 (2H, d, *J*=7.9 Hz), 3.90–4.00 (4H, m), 4.05 (1H, d, *J*=11.3 Hz), 4.23 (1H, d, *J*=11.3 Hz), 5.21 (1H, dt, *J*=1.1, 7.9 Hz), 5.50–5.60 (2H, m), 7.52 (2H, m), 7.63 (1H, m), 7.86 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm: 14.3, 16.2, 22.1, 22.3, 29.7, 37.7, 39.9, 39.9, 45.5, 50.1, 56.1, 57.2, 58.9, 60.0, 64.4, 64.8, 74.0, 110.0, 111.3, 128.5, 128.9, 129.4, 133.5, 138.7, 140.7, 147.0; EIMS (*m*/*z*): 568 (M^+), 553 (0.2), 427 (0.33), 87 (100); HREIMS: calcd for $C_{28}H_{40}O_8S_2$ (M^+): 568.2165; Found: 568.2173.

1.1.22. (1*R*,2*R*,9*R*,10*R*,13*S*)-(*E*)-7-Benzenesulfonyl-1,5,9-trimethyl-13-(2-methyl-[1,3]dioxolan-2-yl)-4-oxatricyclo[10.3.0.0^{3,5}]pentadeca-8,14-diene (27). To a solution of KHMDS (136 μL, 68.0 μmol, 0.5 M in toluene) in THF (7.70 mL) was added a solution of mesylate **26** (16.0 mg, 28.1 μmol) in THF (2.0 mL) at 45°C over 1.5 h. The reaction mixture was diluted with Et_2O, washed with H_2O and saturated aqueous NaCl, dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The residue was purified by silica gel preparative TLC (developed with hexane–Et_2O=3:1) to give sulfone **27** (6.0 mg, 43%) and mesylate **26** (4.0 mg, 25% recovered). Colorless oil; $[\alpha]_D$=+66.8° (*c* 0.61, $CHCl_3$); IR (neat) 3020, 2885, 1357, 1306, 1220, 1146 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm: 1.18 (3H, s), 1.20 (3H, s), 1.35 (3H, br s), 1.36 (3H, br s), 1.41 (1H, dd, *J*=11.0, 14.8 Hz), 1.46 (1H, m), 1.55 (1H, m), 1.61 (1H, m), 1.80 (1H, dd, *J*=1.8, 14.3 Hz), 1.84 (1H, m), 2.15 (1H, m), 2.27 (1H, m), 2.56 (1H, m), 2.60 (1H, dd, *J*=4.3, 12.8 Hz), 2.86 (1H, dd, *J*=1.8, 11.0 Hz), 3.75–4.00 (5H, m), 5.03 (1H, dd, *J*=1.0, 10.4 Hz), 5.35 (1H, dd, *J*=1.9, 5.7 Hz), 5.46 (1H, dd, *J*=2.4, 5.7 Hz), 7.54 (2H, m), 7.64 (1H, m), 7.85 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm: 16.5, 17.0, 21.3, 22.1, 32.4, 35.8, 37.5, 41.0, 50.0, 60.5, 61.9, 62.9, 64.2, 64.4, 66.2, 110.6, 116.9, 120.9, 126.5, 128.9, 129.1, 133.6, 137.6, 143.2, 144.6; EIMS (*m*/*z*): 472 (M^+), 457 (0.1), 331 (0.2), 269, 87 (100); HREIMS: calcd for $C_{27}H_{36}O_5S$ (M^+): 472.2283; Found: 472.2280.

1.1.23. (1*S*,2*S*,9*R*,10*R*)-(*E*)-2-(7-Benzenesulfonyl-1,5,9-trimethyl-4-oxatricyclo[10.3.0.0^{3,5}]pentadeca-8,13-dien-13-yl)-propan-2-ol (28). A mixture of AcOH and H_2O (4:1) (250 μL) was added to acetal **27** (5.0 mg, 10.6 μmol) and the mixture was stirred at 45°C for 30 min. The reaction mixture was concentrated under reduced pressure. The residue was purified by silica gel preparative TLC (developed with hexane–Et_2O=5:1) to give ketone (4.2 mg, 93%). Colorless oil; $[\alpha]_D$=+72.5° (*c* 0.16, $CHCl_3$); IR (neat) 2927, 1711, 1304, 1146 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm: 1.16 (3H, s), 1.19 (1H, m), 1.22 (3H, s), 1.32 (3H, s), 1.37 (1H, m), 1.50–1.65 (2H, m), 1.86 (1H, d, *J*=14.0 Hz), 1.92 (1H, m), 2.12 (3H, s), 2.25 (1H, m), 2.32 (1H, br d, *J*=15.3 Hz), 2.62 (1H, dd, *J*=4.1, 12.9 Hz), 2.85 (1H, dd, *J*=0.9, 9.8 Hz), 3.23 (1H, dt, *J*=2.1, 4.6 Hz), 3.96 (1H, ddd, *J*=4.1, 10.3, 14.3 Hz), 5.07 (1H, br d, *J*=10.3 Hz), 5.49 (1H, dd, *J*=2.2, 5.6 Hz), 5.53 (1H, dd, *J*=2.2, 5.6 Hz), 7.54 (2H, m), 7.64 (1H, m), 7.85 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm: 16.4, 18.9, 20.7, 28.6, 32.0, 34.4, 37.7, 41.2, 41.6, 49.8, 60.7, 61.9, 62.0, 70.3, 116.5, 124.1, 129.0, 129.1, 133.7, 144.3, 144.8, 208.2; EIMS (*m*/*z*): 287 (M^+−$PhSO_2$, 0.4), 245 (0.5), 43 (100); HREIMS: calcd for $C_{19}H_{27}O_2$ (M^+−$PhSO_2$): 287.2011; Found: 287.2003.

A solution of 3% K_2CO_3 in MeOH (300 μL) was added to the above ketone (8.0 mg, 18.7 μmol) and the mixture was stirred at rt for 1 h. The reaction mixture was diluted with Et_2O and filtered through silica gel. The filtrate was concentrated under reduced pressure to give enone (8.0 mg, quantitative yield). Colorless oil; $[\alpha]_D$=+49.2° (*c* 0.42, $CHCl_3$); IR (neat) 2927, 1662, 1618, 1305, 1147 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm: 1.05 (3H, s), 1.25–1.35 (2H, m), 1.33 (3H, s), 1.42 (1H, m), 1.49 (3H, br s), 1.56 (1H, m), 1.70 (1H, dd, *J*=2.3, 13.7 Hz), 2.09 (1H, dd, *J*=5.7, 12.8 Hz), 2.20 (1H, m), 2.22 (3H, s), 2.30 (1H, dt, *J*=5.8, 13.1 Hz), 2.49–2.60 (2H, m), 2.62 (1H, dd, *J*=4.1, 12.8 Hz), 2.92 (1H, dd, *J*=2.7, 11.2 Hz), 4.00 (1H, ddd, *J*=4.3, 10.4, 14.6 Hz), 4.98 (1H, d, *J*=10.4 Hz), 6.58 (1H, br s), 7.54 (2H, m), 7.65 (1H, m), 7.87 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm: 15.4, 16.2, 21.7, 24.7, 26.7, 29.7, 37.5, 37.7, 40.9, 43.3, 43.9, 49.5, 60.4, 62.0, 62.9, 118.6, 128.9, 129.2, 133.7, 137.6, 142.2, 145.6, 148.9, 196.2; EIMS (*m*/*z*): 287 (M^+−$PhSO_2$, 3.6), 229, 171, 43 (100); HREIMS: calcd for $C_{19}H_{27}O_2$ (M^+−$PhSO_2$): 287.2011; Found: 287.2020.

To a cold (−78°C) solution of the above enone (6.8 mg, 15.8 μmol) in THF (200 μL) was added MeLi (23.0 μL,

23.7 μmol, 1.03 M in Et_2O). After stirring at −78°C for 10 min, the reaction mixture was diluted with Et_2O, washed with saturated aqueous NH_4Cl, H_2O and saturated aqueous NaCl, dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The residue was purified by silica gel preparative TLC (developed with hexane–Et_2O=1:1) to give alcohol **28** (6.0 mg, 86%) as a mixture of diastereomers (1:1) at sulfonyl group. Alcohol **27** was used next reaction without separation of diastereomers.

Claenone (1). To a solution of sulfone **28** (6.2 mg, 14.0 μmol) in MeOH–THF (1:1, 300 μL) were added NaH_2PO_4 (50 mg) and 5% Na-Hg (30 mg). After stirring at rt for 1 h, the reaction mixture was diluted with Et_2O, washed with H_2O and saturated aqueous NaCl, dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The residue was purified by silica gel preparative TLC (developed with hexane–Et_2O=1:1) to give alcohol (3.7 mg, 83%). Colorless needs; mp 117–118°C; $[\alpha]_D$=−41.5° (*c* 0.27, $CHCl_3$); IR (KBr) 3443, 2921 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm: 1.21 (3H, s), 1.25 (1H, m), 1.33 (3H, s), 1.34 (3H, s), 1.42 (3H, s), 1.40–1.55 (2H, m), 1.65 (1H, dd, *J*=2.8, 13.7 Hz), 1.73 (3H, br s), 1.95 (1H, dd, *J*=3.2, 16.5 Hz), 2.05–2.20 (4H, m), 2.30–2.45 (3H, m), 2.47 (1H, br d, *J*=11.5 Hz), 2.96 (1H, dd, *J*=2.8, 11.3 Hz), 5.07 (1H, d, *J*=11.4 Hz), 5.42 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm: 15.8, 16.5, 22.7, 24.5, 25.4, 32.2, 32.3, 37.3, 38.9, 41.6, 43.8, 46.9, 49.2, 62.1, 64.0, 71.6, 122.4, 126.5, 134.3, 153.9; EIMS (*m*/*z*): 304 (M^+, 14.6), 286, 152 (100); HREIMS: calcd for $C_{20}H_{32}O_2$ (M^+): 304.2402; Found: 304.2402.

To a solution of the above alcohol (8.0 mg, 26.3 μmol) in CH_2Cl_2 (300 μL) were added 4 Å molecular sieves (15 mg) and PDC (15 mg, 39.5 μmol). After stirring at rt for 5 h, the reaction mixture was diluted with Et_2O, filtered through silica gel column and the filtrate was concentrated under reduced pressure. The residue was purified by ODS preparative TLC (developed with MeOH) to give claenone (**1**)[4] (5.0 mg, 63%). Colorless needs; mp 124–125°C; $[\alpha]_D$=−49.5° (*c* 0.25, $CHCl_3$); IR (KBr) 2936, 1699, 1618 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm: 1.14 (3H, s), 1.27 (1H, m), 1.31 (1H, dd, *J*=11.1, 13.7 Hz), 1.41 (3H, s), 1.49–1.60 (2H, m), 1.68 (1H, m), 1.71 (1H, dd, *J*=2.8, 13.7 Hz), 1.73 (3H, s), 1.84 (3H, s), 2.11 (1H, br d, *J*=18.3 Hz), 2.10–2.30 (2H, m), 2.20 (3H, m), 2.35–2.45 (2H, m), 2.41 (1H, d, *J*=18.3 Hz), 2.94 (1H, br d, *J*=12.0 Hz), 2.98 (1H, dd, *J*=2.9, 11.0 Hz), 5.13 (1H, br d, *J*=11.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm: 15.6, 16.7, 21.4, 23.4, 24.5, 24.6, 27.5, 37.3, 37.7, 38.6, 41.0, 42.5, 55.6, 61.5, 63.9, 128.4, 133.1, 137.3, 148.8, 206.2; EIMS (*m*/*z*): 302 (M^+, 11), 287 (7.3), 150 (100); HREIMS: calcd for $C_{20}H_{30}O_2$ (M^+): 302.2246; Found: 302.2230.

1.1.24. 2-((1*S*,3a*R*,12a*R*)-(5*E*,9*E*)-8-Benzenesulfonyl-3a,6,10-trimethyl-1,3a,4,7,8,11,12,12a-octahydrocyclopentacycloundecen-1-yl)-2-methyl-[1,3]dioxolane (29). To a solution of alcohol **25** (27.0 mg, 57.9 μmol) in CH_2Cl_2 (580 μL) were added DMAP (35.0 mg, 0.290 mmol) and MsCl (9.0 μL, 0.120 mmol). After stirring at rt for 30 min, the reaction mixture was diluted with Et_2O, washed with H_2O and saturated aqueous NaCl, dried over anhydrous $MgSO_4$ and concentrated under reduced pressure to give crude chloride. The crude chloride was used next reaction without purification.

To a solution of the above crude chloride in THF (9.5 mL) was added KHMDS (91.0 μL, 45.4 μmol, 0.5 M in toluene) at 40°C over 1 h. The reaction mixture was diluted with Et_2O, washed with H_2O and saturated aqueous NaCl, dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The residue was purified by silica gel preparative TLC (developed with hexane–Et_2O=10:1) to give sulfone **29** (11.5 mg, 45%, two steps) as a mixture of diastereomers (15:1) at sulfonyl group. Sulfone **29** was used next reaction without separation of diastereomers.

1.1.25. 1-((3a*R*,12a*S*)-(5*E*,9*E*)-3a,6,10-Trimethyl-3,3a,4,7,8,11,12,12a-octahydrocyclopentacycloundecen-1-yl)ethanone (30). To a solution of sulfone **29** (6.0 mg, 13.4 μmol) in MeOH–THF (1:1, 300 μL) were added NaH_2PO_4 (50 mg) and 5% Na-Hg (30 mg) at 0°C. After stirring at 0°C for 1 h, the reaction mixture was diluted with Et_2O, washed with H_2O and saturated aqueous NaCl, dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The residue was purified by silica gel preparative TLC (developed with hexane–Et_2O=10:1) to give acetal (3.6 mg, 86%). Colorless oil; $[\alpha]_D$=+29.3° (*c* 0.27, $CHCl_3$); IR (neat) 2927 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm: 1.06 (3H, s), 1.29 (3H, s), 1.42 (1H, m), 1.54 (3H, br s), 1.54 (3H, br s), 1.63 (3H, br s), 1.70 (1H, m), 1.76 (1H, m), 1.85 (1H, br d, *J*=13.5 Hz), 2.00–2.15 (3H, m), 2.15–2.35 (4H, m), 2.59 (1H, d, *J*=5.1 Hz), 3.90–4.00 (4H, m), 4.94 (1H, br dd, *J*=3.7, 8.3 Hz), 5.04 (1H, br d, *J*=2.6, 11.4 Hz), 5.47 (1H, d, *J*=6.0 Hz), 5.49 (1H, d, *J*=6.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm: 15.6, 17.3, 21.5, 24.1, 29.7, 33.7, 36.0, 37.5, 39.6, 41.1, 41.2, 52.3, 53.0, 64.2, 64.4, 64.8, 111.3, 123.6, 125.5, 127.0, 134.4, 135.1, 143.6; EIMS (*m*/*z*): 316 (M^+, 0.6), 301 (0.7), 235 (5), 87 (100); HREIMS: calcd for $C_{21}H_{32}O_2$ (M^+): 316.2402; Found: 316.2409.

A mixture of AcOH and H_2O (4:1) (200 μL) was added to the above acetal (8.0 mg, 25.3 μmol) and the mixture was stirred at 45°C for 30 min. The reaction mixture was concentrated under reduced pressure. The residue was purified by silica gel preparative TLC (developed with hexane–Et_2O=5:1) to give ketone (6.5 mg, 93%). Colorless oil; $[\alpha]_D$=+73.2°(*c* 0.50, $CHCl_3$); IR (neat) 2921, 1709 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm: 1.01 (3H, s), 1.43 (1H, m), 1.55 (3H, br s), 1.58 (3H, br s), 1.60 (1H, m), 1.74 (1H, m), 1.95 (1H, m), 2.00–2.10 (2H, m), 2.15–2.25 (4H, m), 2.16 (3H, s), 2.32 (1H, m), 3.25 (1H, br dt, *J*=2.1, 6.6 Hz), 4.97 (1H, br d, *J*=10.5 Hz), 5.06 (1H, br dd, *J*=3.9, 11.3 Hz), 5.46 (1H, dd, *J*=2.1, 5.6 Hz), 5.67 (1H, dd, *J*=2.2, 5.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm: 15.5, 19.0, 20.9, 24.3, 27.9, 34.3, 34.9, 39.9, 41.2, 43.2, 52.3, 69.2, 122.4, 124.7, 125.9, 134.5, 135.7, 145.5, 200.7; EIMS (*m*/*z*): 272 (M^+, 3.6), 229 (10), 43 (100); HREIMS: calcd for $C_{19}H_{28}O$ (M^+): 272.2140; Found: 272.2142.

A solution of 3% K_2CO_3 in MeOH (300 μL) was added to the above ketone (6.5 mg, 23.9 μmol) and the mixture was stirred at rt for 2.5 h. The reaction mixture was diluted with Et_2O and filtered through silica gel. The filtrate was concentrated under reduced pressure to give enone **30** (6.5 mg, quantitative yield). Colorless oil; $[\alpha]_D$=−23.5°

(c 0.51, $CHCl_3$); IR (neat) 2914, 1667, 1617 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm: 1.19 (3H, s), 1.31 (1H, m), 1.40 (3H, br s), 1.62 (1H, m), 1.78 (3H, br s), 2.00–2.30 (8H, m), 2.27 (3H, s), 2.41 (1H, m), 2.49 (1H, dt, J=2.3, 18.8 Hz), 2.62 (1H, br d, J=10.8 Hz), 4.80 (1H, br d, J=11.6 Hz), 5.18 (1H, dd, J=3.8, 11.0 Hz), 6.62 (1H, br t, J=2.3 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ ppm: 14.9, 15.4, 21.6, 24.3, 25.7, 26.9, 38.2, 40.3, 40.4, 43.3, 47.0, 48.6, 124.3, 128.3, 134.2, 136.4, 142.6, 149.6, 196.7; EIMS (m/z): 272 (M^+, 60), 229 (35), 123 (100); HREIMS: calcd for $C_{19}H_{28}O$ (M^+): 272.2140; Found: 272.2145.

Palominol (3). To a cold (−78°C) solution of enone **30** (7.1 mg, 26.2 μmol) in THF (500 μL) was added MeLi (30.0 μL, 30.9 μmol, 1.03 M in Et_2O). After stirring at −78°C for 10 min, the reaction mixture was diluted with Et_2O, washed with saturated aqueous NH_4Cl, H_2O and saturated aqueous NaCl, dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The residue was purified by silica gel preparative TLC (developed with hexane–Et_2O=1:3) to give palominol (**3**)[7a] (6.8 mg, 90%). Colorless oil; $[\alpha]_D$=−24.7° (c 0.34, $CHCl_3$); IR (neat) 3364, 2915 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm: 1.17 (3H, br s), 1.25 (1H, m), 1.38 (3H, br s), 1.43 (3H, br s), 1.51 (3H, br s), 1.58 (1H, m), 1.63 (3H, br s), 1.94 (1H, dd, J=3.1, 16.5 Hz), 1.95–2.15 (4H, m), 2.20–2.35 (5H, m), 2.38 (1H, br d, J=10.3 Hz), 4.86 (1H, br d, J=10.6 Hz), 5.22 (1H, br dd, J=4.7, 11.5 Hz), 5.47 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm: 15.5, 16.2, 22.7, 24.4, 26.2, 31.9, 31.9, 38.2, 40.0, 40.7, 46.1, 47.4, 47.9, 71.6, 122.6, 125.4, 128.6, 133.4, 134.6, 154.1; EIMS (m/z): 288 (M^+, 2.7), 270 (28), 133 (100); HREIMS: calcd for $C_{20}H_{32}O$ (M^+): 288.2453; Found: 288.2449.

Dolabellatrienone (2). To a solution of palominol (**3**) (8.0 mg, 26.3 μmol) in CH_2Cl_2 (300 μL) were added 4 Å molecular sieves (15 mg) and PDC (15 mg, 39.5 μmol). After stirring at rt for 5 h, the reaction mixture was diluted with Et_2O, filtered through silica gel column and the filtrate was concentrated under reduced pressure. The residue was purified by silica gel preparative TLC (developed with hexane–Et_2O=1:1) to give dolabellatrienone (**2**)[7b] (5.0 mg, 63%). Colorless oil; $[\alpha]_D$=+29.9°(c 0.14, $CHCl_3$); IR (neat) 2923, 1703 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ ppm: 1.23 (3H, s), 1.45 (3H, s), 1.45–1.50 (1H, m), 1.55–1.65 (2H, m), 1.64 (3H, s), 1.83 (3H, s), 2.05–2.35 (8H, m), 2.22 (3H, s), 2.38 (1H, d, J=18.4 Hz), 2.83 (1H, br d, J=12.2 Hz), 4.93 (1H, br d, J=10.6 Hz), 5.24 (1H, dd, J=5.0, 11.3 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm: 15.6, 16.2, 21.4, 23.2, 24.3, 24.5, 28.0, 38.2, 39.9, 40.2, 41.1, 41.6, 54.9, 124.9, 130.4, 131.8, 135.7, 138.1, 148.3, 207.3; EIMS (m/z): 286 (M^+, 23), 271 (15),150 (100); HREIMS: calcd for $C_{20}H_{30}O$ (M^+): 286.2297; Found: 286.2299.

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