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SYNTHESIS OF MARINE OXYLIPIN AGARDHILACTONE AND ITS ANALOGUES: A STRUCTURAL REVISION

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Abstract – Synthesis of four analogues of the marine oxylipin agardhilactone was carried out. The relative configuration of agardhilactone was determined by comparison with agardhilactone acetate and four analogues. Furthermore, synthesis of agardhilactone was achieved. The absolute configuration of agardhilactone was successfully determined by this synthesis.

INTRODUCTION

Marine organisms, and especially marine algae, are an extremely rich source of novel oxylipins. Many of the oxylipins are of interest given their unique structures, peculiar biosynthetic pathways and biological activities.[1] Agardhilactone is a structurally unique oxylipin which was first isolated from the marine red alga *Agardhiella subulata*, obtained off Massachusetts, by Gerwick et al in 1996.[2] Agardhilactone is a novel tricyclic oxylipin containing δ-lactone, cyclopentane and epoxide rings and a conjugated diene moiety. The structure was determined based on the NMR analysis of agardhilactone acetate and GC-MS analysis of the (-)-menthoxycarbonyl derivative. However, the complete structure of agardhilactone was not determined since agardhilactone is a particle constituent. The relative configuration of the cyclopentane ring system (C-6, C-8, C-9 and C-10) was determined to be 6*S**, 8*R**, 9*S** and 10*R**, respectively, based on the NOESY analysis combined with ^{1}H-^{1}H coupling constants of agardhilactone acetate. However, the relative configuration at C-5 remains unknown. The absolute configuration of the secondary hydroxy group at C-18 was determined as being in the *S* configuration by converting agardhilactone to the known (-)-menthoxycarbonyl derivative. Although the biological activity of agardhilactone has not been reported, it is anticipated that agardhilactone possesses biological activity

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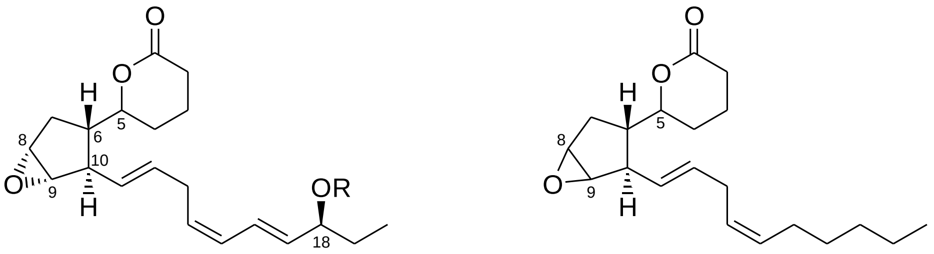
This paper is dedicated to Professor Emeritus Keiichiro Fukumoto on the occasion of his 75th birthday.

since oxylipins generally possess a broad range of biological activities including inhibitory activity against phospholipase A_2.[1]

Many syntheses of carbocyclic oxylipins have been performed given their unique structural features and potential biological significance.[1] The authors previously synthesized the carbocyclic oxylipins constanolactone[3] and bacillariolide,[4] and recently reported the total synthesis and structural revision of agardhilactone.[5] In this paper, the authors wish to report the detailed synthesis and structural revision of agardhilactone.

As mentioned above, given that the relative configuration at C-5 of agardhilactone had not been determined, the authors began by synthesizing analogues **1** - **4** of agardhilactone in an effort to determine the relative configuration at C-5 and to confirm the relative configurations at C-6, C-8, C-9 and C-10. Analogues **1** - **4** correspond to four diastereomers of 16,17-dihydro-18-dehydroxyagardhilactone.



agardhilactone : R = H
agardhilactone acetate : R = Ac
(Gerwick's structures)

1 : 5*R**, 8*R**, 9*S**
2 : 5*R**, 8*S**, 9*R**
3 : 5*S**, 8*R**, 9*S**
4 : 5*S**, 8*S**, 9*R**

Figure 1. Proposed structure of agardhilactone and analogues **1** - **4**.

RESULTS AND DISCUSSION

Analogues **1** - **4** were respectively synthesized from (±)-4-vinyldihydrofuran-2-one (**5**)[6] *via* ring-closing metathesis (RCM) and allylic halide-alkyne coupling reactions. Lactone **5** was treated with LDA in THF at -78 °C and then with 3-iodopropene to give *trans*-lactone **6** as a single compound (Scheme 1). The relative configuration of *trans*-lactone **6** was determined by its NOESY. The *trans*-configuration of the allyl and vinyl groups was indicated by the NOE correlation between H-6 and H-9 and between H-7 and H-10, as shown in Figure 2. Lactone **6** was reduced to the hemiacetal with DIBALH, and the hemiacetal was then treated with Grignard reagent ($TBDMSOCH_2CH_2CH_2CH_2MgI$)[7] in DME at 0 °C to afford a mixture of α-alcohol **7a** and β-alcohol **7b** (**7a**/**7b** = 3:1), which were readily separated by silica gel chromatography. In this reaction, when Et_2O was used as the solvent, α-alcohol **7a** was predominantly obtained (**7a**/**7b** = 5:1).

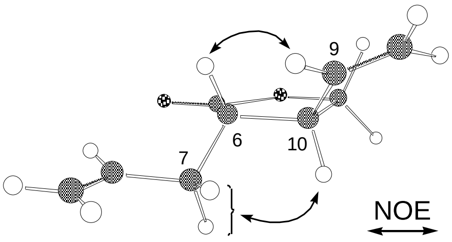


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Figure 2. Selected NOE correlations of **6**.

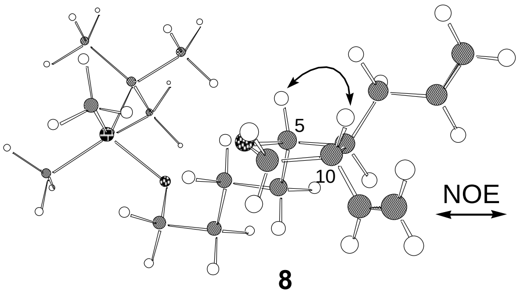

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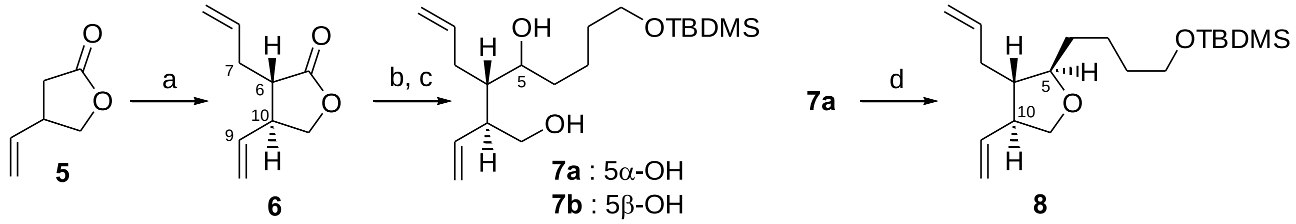
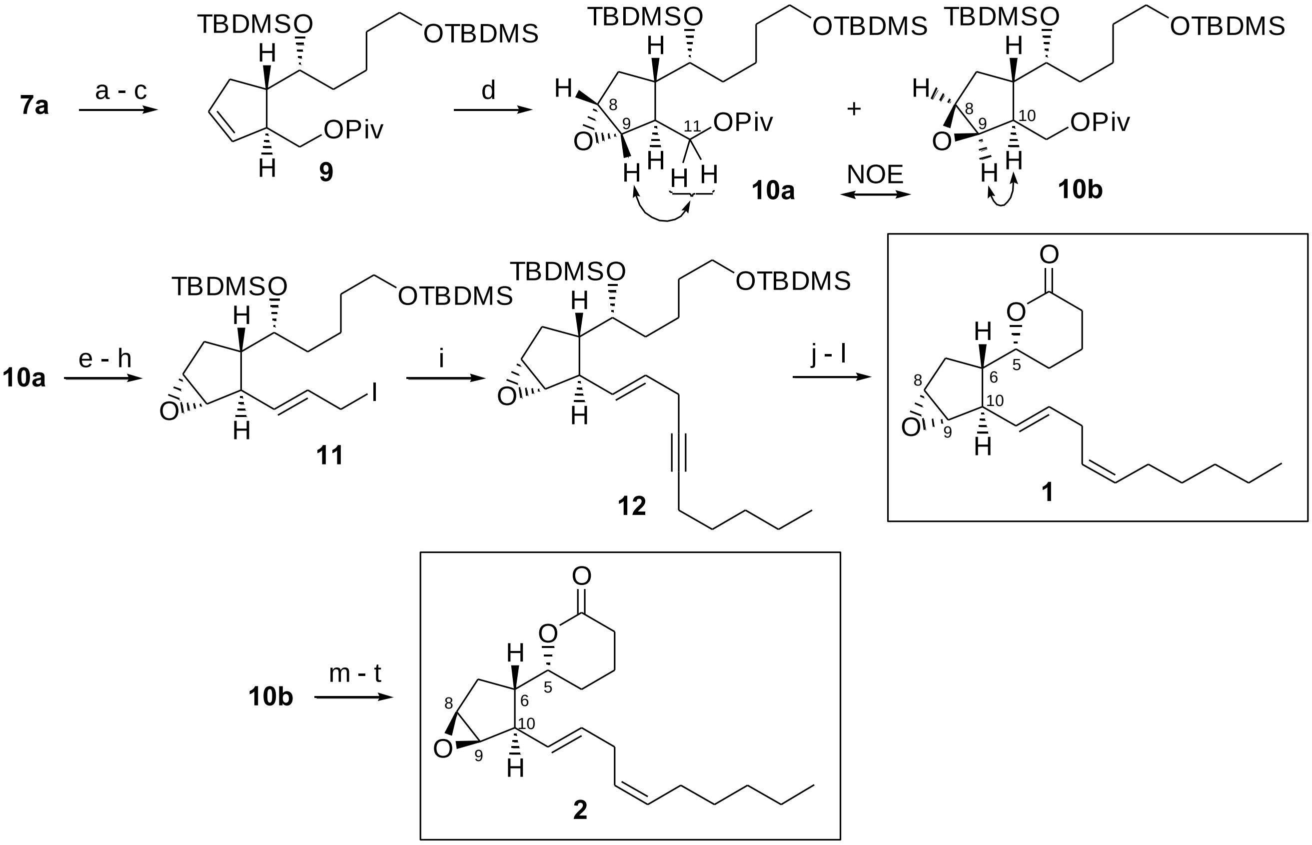
Figure 3. Selected NOE correlations of **8**.

The relative configuration of the hydroxy group at C-5 was determined by the NOESY of tetrahydrofuran **8** derived from α-alcohol **7a**. α-Alcohol **7a** was treated with TsCl and DABCO in AcOEt at 0 °C to give tetrahydrofuran **8**. The NOE correlation between H-5 and H-10 in tetrahydrofuran **8** indicated that C-5 and C-10 adopt a *cis*-configuration, as shown in Figure 3. Therefore, the configuration of the hydroxy group at C-5 of **7a** was determined as being in the α-configuration, and that of the hydroxy group at C-5 of **7b**, which is a diastereomer of **7a**, to be in the β-configuration.



Scheme 1. Reagents and conditions: (a) LDA, 3-iodopropene, THF, -78 °C to rt, 74%; (b) DIBALH, CH_2Cl_2, -78 °C, 98%; (c) $TBDMSOCH_2CH_2CH_2CH_2MgI$, DME, 0 °C, 73% (**7a**), 25% (**7b**); (d) TsCl, DABCO, AcOEt, 0 °C, 71%.

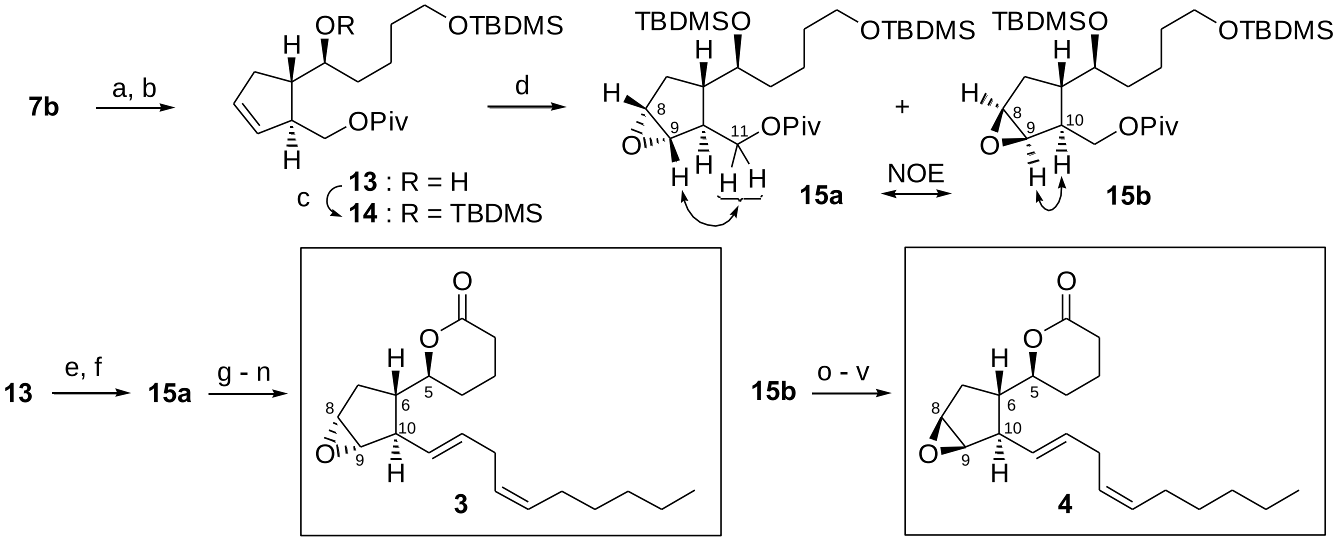
The RCM reaction of α-alcohol **7a** with 1st generation Grubbs' catalyst[8] in CH_2Cl_2 afforded the cyclopentene derivative in 99% yield (Scheme 2). The primary hydroxy group of the cyclopentene derivative was protected as the pivalate, while the secondary hydroxy group was protected as the TBDMS ether to give cyclopentene **9**. Epoxidation of cyclopentene **9** with *m*-CPBA in the presence of Na_2HPO_4 in CH_2Cl_2 afforded a mixture of α-epoxide **10a** and β-epoxide **10b** (**10a**/**10b** = 1:3). The diastereomeric mixture was separated by silica gel chromatography. The relative configuration of epoxides **10a** and **10b** was determined by NOESY. The epoxide of **10a** was determined to be in the α-configuration from the NOE correlation between H-9 and H-11, while the epoxide of **10b** was determined to be in the β-configuration from the NOE correlation between H-9 and H-10. α-Epoxide **10a** was converted to allylic iodide **11** in four steps consisting of (1) reductive removal of the pivaloyl group with DIBALH, (2) oxidation of the hydroxy group with Dess-Martin periodinane[9] to give the aldehyde, followed by a Wittig reaction with $Ph_3P=CHCO_2Me$, (3) reduction of the α,β-unsaturated ester with DIBALH, and finally (4) tosylation of the hydroxy group with Ts_2O and pyridine, followed by treatment with NaI. The coupling reaction of allylic iodide **11** with hept-1-yne was achieved by treatment with CuI, NaI and K_2CO_3 to give enyne **12**.[10] The two TBDMS groups of enyne **12** were removed by treatment with tetrabutylammonium fluoride (TBAF) in DMF at 40 °C to give the diol. The diol was treated with tetrapropylammonium perruthenate (TPAP) and 4-methylmorpholine *N*-oxide (NMO) to directly give the δ-lactone.[11] Finally, alkyne hydrogenation with 5% Pd on $BaSO_4$ in the presence of quinoline[12] afforded analogue **1**, whose relative configuration is 5*R**, 6*S**, 8*R**, 9*S** and 10*R**. Analogue **2**, whose relative configuration is 5*R**, 6*S**, 8*S**, 9*R** and 10*R**, was synthesized from β-epoxide **10b** in a similar manner as described above.



Scheme 2. Reagents and conditions: (a) Grubbs' catalyst 1st generation, CH_2Cl_2, rt, 99%; (b) PivCl, pyridine, CH_2ClCH_2Cl, 0 °C to rt, 82%; (c) TBDMSCl, imidazole, DMF, 45 °C, 99%; (d) *m*-CPBA, Na_2HPO_4, CH_2Cl_2, 0 °C to rt, 23% (**10a**), 77% (**10b**); (e) DIBALH, CH_2Cl_2, -78 °C, 87%; (f) Dess-Martin periodinane, $NaHCO_3$, CH_2Cl_2, rt, then $Ph_3P{=}CHCO_2Me$, reflux, 61%; (g) DIBALH, CH_2Cl_2, -78 °C, 79%; (h) Ts_2O, pyridine, CH_2Cl_2, rt, then NaI, acetone, rt, 72%; (i) hept-1-yne, CuI, NaI, K_2CO_3, DMF, rt, 63%; (j) TBAF, DMF, 40 °C, 73%; (k) TPAP, NMO, MS 4A, CH_2ClCH_2Cl, rt, 60%; (l) H_2, 5% Pd on $BaSO_4$, quinoline, MeOH, rt, 79%; (m) DIBALH, CH_2Cl_2, -78 °C, 90%; (n) Dess-Martin periodinane, $NaHCO_3$, CH_2Cl_2, rt, then $Ph_3P{=}CHCO_2Me$, reflux, 86%; (o) DIBALH, CH_2Cl_2, -78 °C, 77%; (p) Ts_2O, pyridine, CH_2Cl_2, rt, then NaI, acetone, rt, 64%; (q) hept-1-yne, CuI, NaI, K_2CO_3, DMF, rt, 79%; (r) TBAF, DMF, 40 °C, 69%; (s) TPAP, NMO, MS 4A, CH_2ClCH_2Cl, rt, 70%; (t) H_2, 5% Pd on $BaSO_4$, quinoline, MeOH, rt, 71%.

Analogues **3** and **4** were synthesized from β-alcohol **7b** (Scheme 3). The RCM reaction of β-alcohol **7b** with 1st generation Grubbs' catalyst in CH_2Cl_2 afforded the cyclopentene derivative. The primary hydroxy group of the cyclopentene derivative was protected as the pivalate to give cyclopentene **13**. Protection of the secondary hydroxy group in **13** as the TBDMS ether gave cyclopentene **14**. Diastereoselective epoxidation of cyclopentene **14** with *m*-CPBA was carried out and predominantly afforded β-epoxide **15b** (α-epoxide **15a**/**15b** = 1:15). Cyclopentene **14** reacted with *m*-CPBA at the less hindered side and principally gave β-epoxide **15b**. The mixture of the two diastereomers was separated by silica gel chromatography and the relative configuration of epoxides **15a** and **15b** was determined by

NOESY. The epoxide of **15a** was determined to be in the α-configuration from the NOE correlation between H-9 and H-11, and the epoxide of **15b** was determined to be in the β-configuration from the NOE correlation between H-9 and H-10. α-Epoxide **15a** was obtained stereoselectively by the epoxidation of β-alcohol **13** followed by protection of the secondary hydroxy group. β-Alcohol **13** was treated with TBHP in the presence of $VO(acac)_2$[13] to give the α-epoxide as the sole product. The stereochemical outcome of this epoxidation may be accounted for by invoking a process involving coordination of the hydroxy group at C-5 to the reagent. The hydroxy group in the α-epoxide was protected as the TBDMS ether to afford α-epoxide **15a**. α-Epoxide **15a** was converted to analogue **3**, whose relative configuration is 5*S**, 6*S**, 8*R**, 9*S** and 10*R**, according to the aforementioned established method. β-Epoxide **15b** was also converted to analogue **4**, whose relative configuration is 5*S**, 6*S**, 8*S**, 9*R** and 10*R**, according to the aforementioned established method.



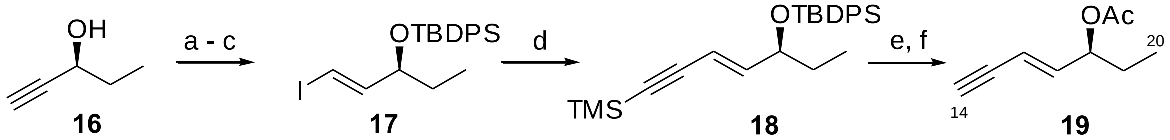
Scheme 3. Reagents and conditions: (a) Grubbs' catalyst 1st generation, CH_2Cl_2, rt, 82%; (b) PivCl, pyridine, CH_2ClCH_2Cl, 0 °C to rt, 86%; (c) TBDMSCl, imidazole, DMF, 45 °C, 94%; (d) *m*-CPBA, Na_2HPO_4, CH_2Cl_2, 0 °C to rt, 6% (**15a**), 91% (**15b**); (e) TBHP, $VO(acac)_2$, CH_2Cl_2, rt, 83%; (f) TBDMSOTf, 2,6-lutidine, CH_2Cl_2, -78 °C, 88%; (g) DIBALH, CH_2Cl_2, -78 °C, 84%; (h) Dess-Martin periodinane, $NaHCO_3$, CH_2Cl_2, rt, then $Ph_3P{=}CHCO_2Me$, reflux, 83%; (i) DIBALH, CH_2Cl_2, -78 °C, 90%; (j) Ts_2O, pyridine, CH_2Cl_2, rt, then NaI, acetone, rt, 73%; (k) hept-1-yne, CuI, NaI, K_2CO_3, DMF, rt, 84%; (l) TBAF, DMF, 40 °C, 40%; (m) TPAP, NMO, MS 4A, CH_2ClCH_2Cl, rt, 64%; (n) H_2, 5% Pd on $BaSO_4$, quinoline, MeOH, rt, 88%; (o) DIBALH, CH_2Cl_2, -78 °C, 96%; (p) Dess-Martin periodinane, $NaHCO_3$, CH_2Cl_2, rt, then $Ph_3P{=}CHCO_2Me$, reflux, 78%; (q) DIBALH, CH_2Cl_2, -78 °C, 94%; (r) Ts_2O, pyridine, CH_2Cl_2, rt, then NaI, acetone, rt, 62%; (s) hept-1-yne, CuI, NaI, K_2CO_3, DMF, rt, 60%; (t) TBAF, DMF, 40 °C, 69%; (u) TPAP, NMO, MS 4A, CH_2ClCH_2Cl, rt, 40%; (v) H_2, 5% Pd on $BaSO_4$, quinoline, MeOH, rt, 80%.

The NMR spectra of synthesized analogues **1** - **4** were compared with that of agardhilactone acetate.[2] The characteristic ^1H- and ^{13}C-NMR data are shown in Table 1. When the NMR of the four analogues **1** - **4** was compared, the chemical shift and coupling constant of **4** were remarkably similar to that of agardhilactone acetate.[2] Therefore, the relative configuration of agardhilactone was estimated to be 5*S**, 6*S**, 8*S**, 9*R** and 10*R**. On the basis of this result, the authors examined the synthesis of natural agardhilactone.

Table 1. Selected NMR data of agardhilactone acetate and analogues **1 - 4**.

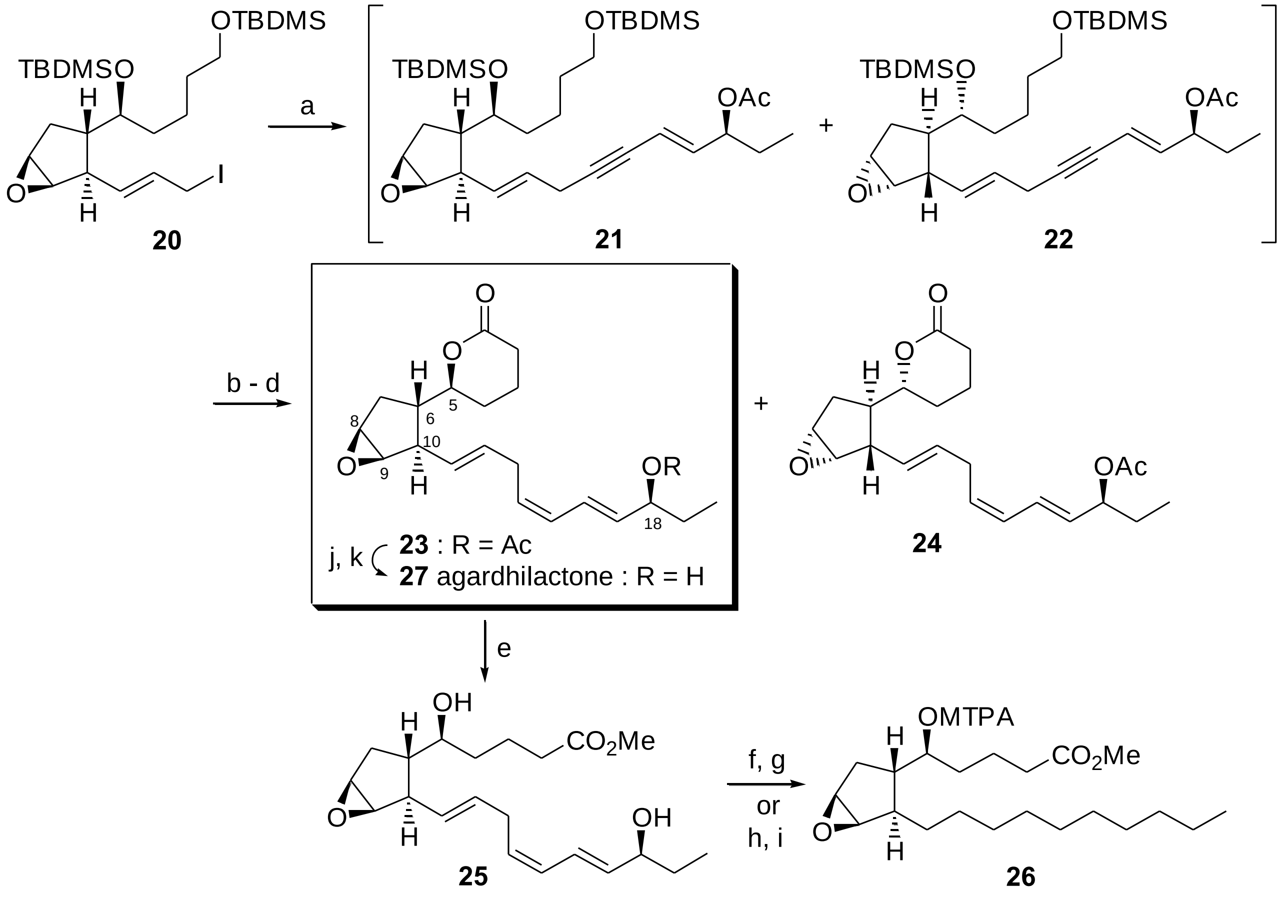
agardhilactone acetate			**1** (5*R**, 8*R**, 9*S**)			**2** (5*R**, 8*S**, 9*R**)		
No.	^{1}H (*J* in Hz)	^{13}C	No.	^{1}H (*J* in Hz)	^{13}C	No.	^{1}H (*J* in Hz)	^{13}C
5	4.24 ddd, 11.7, 2.4, 2.4	78.5	5	4.18 ddd, 11.1, 9.5, 2.6	83.6	5	4.30 ddd, 9.8, 3.5, 3.5	81.1
8	3.46 br d, 7.5	55.7	8	3.52 d, 2.2	57.5	8	3.45 d, 2.6	55.8
9	3.40 dd, 2.7, 1.4	60.2	9	3.37 d, 2.6	61.1	9	3.37 dd, 2.5, 1.7	61.3
10	2.71 br dd, 9.0, 9.0	44.7	10	3.18 d, 7.8	43.3	10	2.63 m	42.7
			3 (5*S**, 8*R**, 9*S**)			**4** (5*S**, 8*S**, 9*R**)		
			No.	^{1}H (*J* in Hz)	^{13}C	No.	^{1}H (*J* in Hz)	^{13}C
			5	4.13 ddd, 10.5, 10.4, 3.0	83.6	5	4.23 ddd, 11.7, 2.6, 2.6	78.5
			8	3.56 br s	58.5	8	3.45 br s	55.6
			9	3.32 d, 2.5	61.1	9	3.39 dd, 2.5, 1.2	60.2
			10	2.66 d, 8.2	44.6	10	2.70 dd, 9.0, 8.9	44.7

The authors designed the synthesis of natural agardhilactone *via* the separation route of the two diastereomers, which were obtained by a coupling reaction of a racemic synthetic intermediate of analogue **4** with a chiral side-chain segment. The chiral side-chain segment **19** (C14-C20) was synthesized from (*S*)-3-hydroxypent-1-yne (**16**)[14] (Scheme 4). The hydroxy group in **16** was protected as the TBDPS ether and subsequently treated with catecholborane[15] and then iodine[16] to give *E*-iodoalkene **17** as the sole product. The coupling reaction of *E*-iodoalkene **17** with (trimethylsilyl)acetylene was achieved by treatment with $(Ph_3P)_4Pd$, CuI and $PrNH_2$ in benzene to give enyne **18**.[17] Removal of the TMS and TBDPS groups in enyne **18** was carried out by treatment with TBAF to give the alcohol. The hydroxy group was then acetylated to afford acetate **19**, $[\alpha]_D^{24}$ -104.1° (*c* 0.63, $CHCl_3$), which is the chiral side-chain segment (C14-C20).



Scheme 4. Reagents and conditions: (a) TBDPSCl, imidazole, DMF, rt, 83%; (b) catecholborane, 80 °C; (c) I_2, NaOH aq., Et_2O, 0 °C, 75% (two steps); (d) (trimethylsilyl)acetylene, $(Ph_3P)_4Pd$, CuI, $PrNH_2$, benzene, rt, 63%; (e) TBAF, THF, rt, 90%; (f) AcCl, DMAP, CH_2Cl_2, 0 °C, 86%.

The coupling reaction of enyne **19** and allylic iodide **20**, a racemic synthetic intermediate of analogue **4**, was achieved by treatment with CuI, NaI and K_2CO_3 and gave a diastereomeric mixture of dienynes **21** and **22** (Scheme 5). Without separation of the mixture, the two TBDMS groups in dienynes **21** and **22** were removed by treatment with TBAF in DMF at 60 °C to give the corresponding diols. The diols were treated with TPAP and NMO to directly give the δ-lactones. Partial hydrogenation of the alkynes with 5% Pd on $BaSO_4$ in the presence of quinoline afforded a diastereomeric mixture of *E*,*Z*,*E*-trienes **23** and **24**. Separation of the diastereomeric mixture using a chiral HPLC column gave acetates **23**, $[\alpha]_D^{20}$ -179.6° (*c* 0.52, $CHCl_3$), and **24**, $[\alpha]_D^{24}$ +165.2° (*c* 0.50, $CHCl_3$). The spectral data of acetate **23** was identical to that of agardhilactone acetate.[2] The absolute configuration of acetate **23** was determined by application of a modified Mosher's method.[18] Agardhilactone acetate (**23**) was treated with K_2CO_3 in MeOH to give diol **25**. Diol **25** was converted to (*S*)-α-methoxy-α-(trifluoromethyl)phenylacetyl (MTPA) ester (*S*)-**26** and (*R*)-MTPA ester (*R*)-**26**. The absolute configuration at C-5 was determined to be in the *S* configuration by comparison of the ^{1}H-NMR of the (*S*)- and (*R*)-MTPA esters. Therefore, the absolute configurations of agardhilactone and agardhilactone acetate (**23**) were determined to be 5*S*, 6*S*, 8*S*, 9*R*, 10*R* and 18*S*. Saponification of acetate **23** followed by lactonization of the resulting dihydroxycarboxylic acid gave lactone **27**, $[\alpha]_D^{31}$ -104.4° (c 0.09, $CHCl_3$). The spectral data of **27** were identical to that of agardhilactone.[2]



Scheme 5. Reagents and conditions: (a) **19**, CuI, NaI, K_2CO_3, DMF, rt, 90% (**21** and **22**); (b) TBAF, DMF, 60 °C, 56%; (c) TPAP, NMO, MS 4A, CH_2ClCH_2Cl, rt, 67%; (d) H_2, 5% Pd on $BaSO_4$, quinoline, MeOH, rt, then separation by HPLC, 19% (**23**), 17% (**24**); (e) K_2CO_3, MeOH, rt, 60%; (f) (*S*)-MTPACl, DMAP, CH_2ClCH_2Cl, rt; (g) H_2, 10% Pd on C, MeOH, rt, 25% (two steps); (h) (*R*)-MTPACl, DMAP, CH_2ClCH_2Cl, rt; (i) H_2, 10% Pd on C, MeOH, rt, 64% (two steps); (j) NaOH aq., THF, rt; (k) DCC, DMAP, CH_2Cl_2, rt, 90% (two steps).

In conclusion, the total synthesis of agardhilactone has been achieved in 17 steps from lactone **5**. The absolute configuration of agardhilactone was successfully determined by this total synthesis. The synthesis is flexible and potentially allows for introduction of a variety of unnatural substitutions. The preparation of such analogues and evaluation of the bioactivity of agardhilactone is currently underway.

EXPERIMENTAL

Optical rotations were measured using a Jasco P-1030 polarimeter or a Jasco DIP-360 polarimeter. IR spectra were recorded using a Jasco FT-IR/620 spectrometer. UV spectra were recorded using a Jasco V-550 spectrophotometer. ^{1}H- and ^{13}C-NMR spectra were recorded on a Varian Mercury-300 spectrometer, a Bruker DRX-400 spectrometer or a Bruker DRX-500 spectrometer. Chemical shifts are given on the δ (ppm) scale using TMS as the internal standard (s, singlet; d, doublet; t, triplet; m, multiplet; br, broad). EIMS spectra were obtained using a Thermo Quest TSQ 700 spectrometer. High resolution EIMS (HREIMS) spectra were obtained using a VG Auto Spec E spectrometer. ESIMS and high resolution ESIMS (HRESIMS) spectra were obtained using a Micromass LCT spectrometer. Elemental analysis data were obtained using an Elemental Vavio EL. Flash column chromatography was performed using Kanto Chemical Silica Gel 60N (spherical, neutral) 40-50 μm.

(3*S,4*S**)-3-Allyl-4-vinyldihydrofuran-2-one (6).** A solution of BuLi (1.58 M in hexane, 8.10 mL, 12.8 mmol) was added to a cold (0 °C) solution of diisopropylamine (1.90 mL, 13.9 mmol) in THF (26.0 mL) under an argon atmosphere. The mixture was stirred for 30 min at 0 °C and cooled to -78 °C. A solution of 4-vinyldihydrofuran-2-one (**5**)[5] (1.20 g, 10.7 mmol) in THF (1.00 mL) was added to the mixture and stirred for 30 min at -78 °C. 3-Iodopropene (1.50 mL, 16.1 mmol) was added to this mixture at -78 °C. The reaction mixture was warmed to rt for 5 h and diluted with Et_2O, washed with saturated aqueous NH_4Cl, water and saturated aqueous NaCl, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane : acetone = 8 : 1) to give *trans*-lactone **6** (1.20 g, 74% yield) as a colorless oil: IR (neat) cm^{-1}: 2907, 1780; ^{1}H-NMR (500 MHz, $CDCl_3$) δ : 5.78 (1H, m), 5.69 (1H, ddd, J = 17.8, 10.0, 8.2 Hz), 5.19 (2H, m), 5.11 (2H, m), 4.35 (1H, dd, J = 8.7, 8.4 Hz), 3.90 (1H, dd, J = 9.5, 9.4 Hz), 2.98 (1H, m), 2.46 (3H, m); ^{13}C-NMR (125 MHz, $CDCl_3$) δ : 177.6, 135.1, 133.8, 118.7, 118.4, 70.0, 44.9, 44.6, 32.1; EIMS *m/z*: 152 (M$^+$, 28), 54 (100); *Anal*. Calcd for $C_9H_{12}O_2$: C, 71.03; H, 7.95. Found: C, 70.78; H, 7.99.

(2*S,3*S**,4*S**)-3-Allyl-8-*tert*-butyldimethylsiloxy-4-vinyloctane-1,4-diol (7a) and (2*S**,3*S**,4*R**)-3-Allyl-8-*tert*-butyldimethylsiloxy-4-vinyloctane-1,4-diol (7b)**. To a cold (-78 °C) solution of lactone **6** (1.87 g, 12.3 mmol) in CH_2Cl_2 (41.0 mL), was added DIBALH (0.90 M in hexane, 17.8 mL, 14.8 mmol) under an argon atmosphere. The mixture was stirred for 20 min at -78 °C, added MeOH, diluted with

Et_2O and added saturated aqueous NaCl. The mixture was stirred for 3 h, dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane : AcOEt = 4 : 1) to give anomeric mixture (1 : 1) of hemiacetal (1.85 g, 98% yield) as a colorless oil: IR (neat) cm^{-1}: 3416, 2934, 1642; ^1H-NMR (400 MHz, $CDCl_3$) δ : 5.81 (1.5H, m), 5.61 (0.5H, ddd, *J* = 17.0, 9.7, 9.1 Hz), 5.40 (0.5H, m), 5.14 (0.5H, m), 5.06 (4H, m), 4.12 (0.5H, t, *J* = 8.5 Hz), 3.99 (0.5H, t, *J* = 8.0 Hz), 3.81 (0.5H, t, *J* = 9.0 Hz), 3.59 (0.5H, t, *J* = 8.7 Hz), 3.05 (0.5H, br s), 2.88 (0.5H, br s), 2.76 (0.5H, m), 2.53 (0.5H, m), 2.23 (2H, m), 1.93 (1H, m); ^{13}C-NMR (100 MHz, $CDCl_3$) δ : 137.7, 137.6, 136.8, 135.9, 117.4, 116.7, 116.6, 115.8, 103.2, 98.6, 71.9, 71.3, 52.2, 49.8, 49.7, 46.8, 35.4, 31.2; EIMS *m/z*: 136 (M^+-H_2O, 10), 83 (100); HREIMS *m/z*: 136.0918 (Calcd for $C_9H_{12}O$: M^+-H_2O, 136.0888).

To a solution of the above hemiacetal (33.0 mg, 214 μmol) in DME (1.10 mL), was added 4-*tert*-butyldimethylsiloxybutyl magnesium iodide[6] (642 μL, 642 μmol) at 0 °C, followed by stirring for 30 min. The reaction mixture was diluted with Et_2O, washed with saturated aqueous NH_4Cl, water and saturated aqueous NaCl, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane : Et_2O = 1 : 2) to give α-alcohol **7a** (53.5 mg, 73% yield) and β-alcohol **7b** (18.5 mg, 25% yield) as each colorless oil. **7a**: IR (neat) cm^{-1}: 3349, 2928; ^1H-NMR (400 MHz, $CDCl_3$) δ : 5.86 (1H, m), 5.79 (1H, m), 5.20 (1H, s), 5.17 (1H, m), 5.05 (2H, m), 3.60 (5H, m), 2.59 (1H, m), 2.20 (1H, m), 1.88 (2H, br s), 1.77 (2H, m). 1.54 (5H, m), 1.37 (1H, m), 0.88 (9H, s), 0.04 (6H, s); ^{13}C-NMR (100 MHz, $CDCl_3$) δ : 138.7, 137.7, 118.0, 116.4, 73.4, 64.0, 63.1, 46.8, 44.4, 35.1, 32.7, 32.5, 26.0, 22.5, 18.4, -5.3; EIMS *m/z*: 343 (M^++H, 100); HREIMS *m/z*: 343.2649 (Calcd for $C_{19}H_{39}O_3Si$: M^++H, 343.2668). **7b**: IR (neat) cm^{-1}: 3290, 2857; ^1H-NMR (400 MHz, $CDCl_3$) δ : 5.83 (2H, m), 5.10 (4H, m), 3.70 (5H, m), 2.42 (1H, m), 2.22 (1H, m), 1.72-1.20 (7H, m), 0.89 (9H, s), 0.05 (6H, s); ^{13}C-NMR (100 MHz, $CDCl_3$) δ : 139.0, 138.2, 117.1, 116.1, 71.6, 63.1, 63.0, 46.6, 45.2, 34.3, 32.5, 31.2, 26.0, 22.8, 18.4, -5.3; ESIMS *m/z*: 365 (M^++Na, 100); HRESIMS *m/z*: 365.2472 (Calcd for $C_{19}H_{38}O_3NaSi$: M^++Na, 365.2488).

4-[(2*R,3*S**,4*S**)-3-Allyl-4-vinyltetrahydrofuran-2-yl]butoxy-*tert*-butyldimethylsilane (8)**. To a solution of α-alcohol **7a** (16.6 mg, 48.5 μmol) in AcOEt (1.00 mL) were added DABCO (11.1 mg, 58.2 μmol) and TsCl (8.1 mg, 72.8 μmol) at 0 °C, followed by stirring for 20 h. The reaction mixture was diluted with Et_2O, washed with saturated aqueous $NaHCO_3$, water and saturated aqueous NaCl, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane : AcOEt = 5 : 1) to give tetrahydrofuran **8** (11.0 mg, 71% yield) as a colorless oil: IR (neat) cm^{-1}: 2929; ^1H-NMR (400 MHz, $CDCl_3$) δ : 5.71 (2H, m), 5.06 (1H, m), 5.00 (3H, m), 3.89 (1H, dd, *J* = 8.3, 8.0 Hz), 3.57 (4H, m), 2.55 (1H, m), 2.22 (1H, m), 2.15 (1H, m), 1.64-1.36 (7H, m), 0.89 (9H, s), 0.04 (6H, s); ^{13}C-NMR (100 MHz, $CDCl_3$) δ : 138.8, 136.2, 116.5, 115.9, 84.2, 71.5, 63.1, 50.5, 50.1, 35.5, 34.7, 32.9, 25.9, 22.6, 18.4, -5.3; ESIMS *m/z*: 347 (M^++Na, 100); HRESIMS *m/z*: 347.2408 (Calcd for $C_{19}H_{36}O_2NaSi$: M^++Na, 347.2382).

(1*S,5*S**)-5-[(1*R**)-1,5-Bis(*tert*-butyldimethylsiloxy)pentyl]cyclopent-2-enylmethyl 2,2-dimethylpropionate (9)**. To a solution of α-alcohol **7a** (55.0 mg, 160 μmol) in CH_2Cl_2 (16.0 mL), was added (benzylidene)bis(tricyclohexylphosphine)ruthenium(IV) dichloride[7] (13.0 mg, 15.9 μmol) and stirred at rt for 3 h. The reaction mixture was diluted with Et_2O, filtered through silica gel and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane : AcOEt = 3 : 1) to give cyclopentene (50.1 mg, 99% yield) as a colorless oil: IR (neat) cm^{-1}: 3302, 2929; ^1H-NMR (400 MHz, $CDCl_3$) δ : 5.71 (1H, m), 5.46 (1H, m), 3.84 (1H, dd, *J* = 10.0, 3.7 Hz), 3.79 (2H, br s), 3.64 (2H, m), 3.49 (1H, m), 3.32 (1H, dd, *J* = 10.0, 9.9 Hz), 2.85 (1H, m), 2.50 (1H, m), 2.05 (2H, m), 1.57 (4H, m),1.43 (2H, m), 0.89 (9H, s), 0.05 (6H, s); ^{13}C-NMR (100 MHz, $CDCl_3$) δ : 130.8, 130.7, 75.4, 67.1, 63.2, 53.5, 50.9, 36.9, 35.5, 32.5, 25.9, 21.7, 18.4, -5.3; EIMS *m/z*: 315 (M^++H, 100); HREIMS *m/z*: 315.2345 (Calcd for $C_{17}H_{35}O_3Si$: M^++H, 315.2355).

To a cold (0 °C) solution of the above cyclopentene (989 mg, 3.14 mmol) in CH_2ClCH_2Cl (32.0 mL), were added pyridine (380 μL, 4.71 mmol) and pivaloyl chloride (454 μL, 3.77 mmol) and stirred at rt for 14 h. The reaction mixture was diluted with Et_2O, washed with saturated aqueous $NaHCO_3$, water and saturated aqueous NaCl, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane : AcOEt = 6 : 1) to give alcohol (1.02 g, 82% yield) as a colorless oil: IR (neat) cm^{-1}: 3481, 2930, 1730; ^1H-NMR (400 MHz, $CDCl_3$) δ : 5.73 (1H, m), 5.59 (1H, m), 4.17 (1H, dd, *J* = 10.6, 5.7 Hz), 3.96 (1H, dd, *J* = 10.6, 6.6 Hz), 3.62 (2H, t, *J* = 6.0 Hz), 3.53 (1H, br s), 2.97 (1H, m), 2.49 (1H, m), 2.07 (2H, m), 1.84 (1H, d, *J* = 4.4 Hz), 1.60-1.48 (4H, m), 1.41 (2H, m), 1.20 (9H, s), 0.89 (9H, s), 0.05 (6H, s); ^{13}C-NMR (100 MHz, $CDCl_3$) δ : 178.6, 131.2, 130.9, 75.6, 67.9, 63.1, 48.2, 46.6, 38.8, 36.0, 35.1, 32.7, 27.2, 25.9, 22.1, 18.4, -5.3; ESIMS *m/z*: 421 (M^++Na, 100); HRESIMS *m/z*: 421.2719 (Calcd for $C_{22}H_{42}O_4NaSi$: M^++Na, 421.2750).

To a solution of the above alcohol (510 mg, 1.28 mmol) in DMF (1.30 mL), were added imidazole (172 mg, 2.56 mmol) and TBDMSCl (289 mg, 1.92 mmol) and stirred at 45 °C for 12 h. The reaction mixture was diluted with Et_2O, washed with saturated aqueous $NaHCO_3$, water and saturated aqueous NaCl, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane : AcOEt = 10 : 1) to give TBDMS ether **9** (647 mg, 99% yield) as a colorless oil: IR (neat) cm^{-1}: 2955, 1732; ^1H-NMR (400 MHz, $CDCl_3$) δ : 5.70 (1H, m), 5.55 (1H, m), 4.12 (1H, dd, *J* = 10.5, 5.4 Hz), 3.88 (1H, dd, *J* = 10.5, 7.0 Hz), 3.64 (1H, m), 3.60 (2H, t, *J* = 6.4 Hz), 2.83 (1H, m), 2.42 (1H, m), 2.18 (2H, m), 1.53-1.31 (6H, m), 1.19 (9H, s), 0.89 (9H, s), 0.86 (9H, s), 0.04 (12H, m); ^{13}C-NMR (100 MHz, $CDCl_3$) δ : 178.5, 131.5, 130.7, 75.4, 67.8, 63.2, 47.9, 44.9, 38.8, 34.9, 33.8, 33.2, 27.2, 26.0, 21.3, 18.3, 18.1, -4.2, -4.5, -5.3; ESIMS *m/z*: 535 (M^++Na, 100); HRESIMS *m/z*: 535.3602

(Calcd for $C_{28}H_{56}O_4NaSi_2$: M^++Na, 535.3615).

(1*S,2*S**,3*S**,5*R**)-3-[(1*R**)-1,5-Bis(*tert*-butyldimethylsiloxy)pentyl]-6-oxabicyclo[3.1.0]hex-2-ylmethyl 2,2-dimethylpropionate (10a) and (1*R**,2*S**,3*S**,5*S**)-3-[(1*R**)-1,5-bis(*tert*-butyldimethylsiloxy)pentyl]-6-oxabicyclo[3.1.0]hex-2-ylmethyl 2,2-dimethylpropionate (10b)**. To a cold (0 °C) solution of cyclopentene **9** (607 mg, 1.18 mmol) in CH_2Cl_2 (12.0 mL), were added Na_2HPO_4 (670 mg, 4.72 mmol) and 65% *m*-CPBA (467 mg, 1.77 mmol). After stirring for 5 h at rt, saturated aqueous $Na_2S_2O_3$ was added and stirred for 30 min. The mixture was diluted with Et_2O, washed with saturated aqueous $NaHCO_3$, water and saturated aqueous NaCl, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography ($CHCl_3$: acetone = 100 : 1) to give α-epoxide **10a** (160 mg, 23% yield) and β-epoxide **10b** (542 mg, 77% yield) as each colorless oil. **10a**: IR (neat) cm^{-1}: 2929, 1734; ^{1}H-NMR (400 MHz, $CDCl_3$) δ : 4.11 (1H, dd, *J* = 11.0, 4.6 Hz), 3.92 (1H, dd, *J* = 11.0, 7.6 Hz), 3.59 (2H, m), 3.54 (1H, ddd, *J* = 9.3, 3.8, 3.5 Hz), 3.46 (1H, m), 3.38 (1H, d, *J* = 2.5 Hz), 2.57 (1H, m), 1.96 (1H, m), 1.89 (1H, m), 1.74 (1H, dd, *J* = 14.4, 2.1 Hz), 1.51-1.24 (6H, m), 1.20 (9H, s), 0.89 (9H, s), 0.87 (9H, s), 0.05 (12H, m); ^{13}C-NMR (125 MHz, $CDCl_3$) δ : 178.4, 75.5, 65.5, 63.1, 60.6, 58.8, 45.4, 42.0, 38.8, 34.3, 33.4, 29.5, 27.2, 26.0, 19.3, 18.3, 18.1, -4.0, -4.6, -5.3; ESIMS *m/z*: 551 (M^++Na, 100); HRESIMS *m/z*: 551.3602 (Calcd for $C_{28}H_{56}O_5NaSi_2$: M^++Na, 551.3564). **10b**: IR (neat) cm^{-1}: 2929, 1732; ^{1}H-NMR (400 MHz, $CDCl_3$) δ : 4.35 (1H, dd, *J* = 10.6, 4.3 Hz), 4.01 (1H, t, *J* = 10.3 Hz), 3.59 (3H, m), 3.50 (1H, m), 3.48 (1H, m), 2.16 (1H, m), 2.11 (1H, dd, *J* = 13.8, 7.6 Hz), 1.62 (1H, m), 1.55-1.38 (5H, m), 1.34 (2H, m), 1.22 (9H, s), 0.89 (9H, s), 0.87 (9H, s), 0.04 (12H, m); ^{13}C-NMR (125 MHz, $CDCl_3$) δ : 178.1, 74.6, 64.9, 63.1, 58.8, 57.0, 42.4, 40.3, 38.7, 34.7, 33.2, 31.2, 27.2, 26.0, 20.6, 18.3, 18.1, -4.2, -4.6, -5.3; ESIMS *m/z*: 551 (M^++Na, 100); HRESIMS *m/z*: 551.3544 (Calcd for $C_{28}H_{56}O_5NaSi_2$: M^++Na, 551.3564).

(1*S,2*S**,3*S**,5*R**)-3-[(1*R**)-1,5-Bis(*tert*-butyldimethylsiloxy)pentyl]-2-[(1*E*)-3-iodopropenyl]-6-oxabicyclo[3.1.0]hexane (11)**. To a cold (-78 °C) solution of α-epoxide **10a** (966 mg, 1.82 mmol) in CH_2Cl_2 (18.0 mL), was added DIBALH (0.93 M in hexane, 2.93 mL, 2.73 mmol) under an argon atmosphere. The mixture was stirred for 30 min at -78 °C, added MeOH, diluted with Et_2O and added saturated aqueous NaCl. The mixture was stirred for 3 h, dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane : AcOEt = 3 : 1) to give alcohol (701 mg, 87% yield) as a colorless oil: IR (neat) cm^{-1}: 3453, 2929; ^{1}H-NMR (400 MHz, $CDCl_3$) δ : 3.59 (4H, m), 3.52 (1H, ddd, *J* = 9.9, 3.5, 3.4 Hz), 3.47 (1H, m), 3.41 (1H, d, *J* = 2.5 Hz), 2.39 (1H, dt, *J* = 2.9, 6.9 Hz), 2.05 (1H, m), 1.91 (1H, ddd, *J* = 14.8, 10.4, 1.9 Hz), 1.72 (2H, m), 1.53-1.37 (5H, m), 1.27 (1H, m), 0.89 (18H, s), 0.05 (12H, m); ^{13}C-NMR (100 MHz, $CDCl_3$) δ : 75.8, 64.0, 63.2, 61.0, 59.0, 46.0, 45.7, 34.2, 33.4, 29.7, 26.0, 19.1, 18.3, 18.1, -4.1, -4.4, -5.3; ESIMS *m/z*: 467 (M^++Na, 100); HRESIMS *m/z*: 467.3011 (Calcd for $C_{23}H_{48}O_4NaSi_2$: M^++Na, 467.2989).

To a solution of the above alcohol (685 mg, 1.54 mmol) in CH_2Cl_2 (15.0 mL), were added $NaHCO_3$ (1.29 g, 15.4 mmol) and Dess-Martin periodinane[8] (1.96 g, 4.62 mmol), stirred for 1 h at rt and added excess $Na_2S_2O_3$. After stirring for 10 min, methyl (triphenylphosphoranylidene)acetate (2.57 g, 7.70 mmol) was added and stirred under reflux for 14 h. The reaction mixture was diluted with Et_2O and filtered through silica gel and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane : AcOEt = 6 : 1) to give α,β-unsaturated ester (468 mg, 61% yield) as a colorless oil: IR (neat) cm^{-1}: 2929, 1730; ^{1}H-NMR (400 MHz, $CDCl_3$) δ : 6.86 (1H, dd, J = 15.9, 8.0 Hz), 5.86 (1H, dd, J = 15.9, 1.2 Hz), 3.74 (3H, s), 3.60 (3H, m), 3.51 (1H, br s), 3.38 (1H, d, J = 2.5 Hz), 3.11 (1H, d, J = 8.0 Hz), 2.01 (1H, m), 1.88 (1H, ddd, J = 14.9, 9.4, 1.3 Hz), 1.79 (1H, dd, J = 14.9, 2.0 Hz), 1.52-1.18 (6H, m), 0.89 (9H, s), 0.88 (9H, s), 0.05 (12H, m); ^{13}C-NMR (100 MHz, $CDCl_3$) δ : 166.9, 148.5, 121.0, 75.0, 63.1, 60.5, 58.2, 51.6, 47.7, 43.8, 34.3, 33.4, 28.7, 26.0, 19.1, 18.3, 18.1, -4.0, -4.4, -5.3; ESIMS *m/z*: 521 (M^++Na, 100); HRESIMS *m/z*: 521.3119 (Calcd for $C_{26}H_{50}O_5NaSi_2$: M^++Na, 521.3095).

To a cold (-78 °C) solution of α,β-unsaturated ester (468 mg, 934 μmol) in CH_2Cl_2 (9.40 mL), was added DIBALH (0.93 M in hexane, 2.12 mL, 1.96 mmol) under an argon atmosphere. The mixture was stirred for 20 min at –78 °C, added MeOH, diluted with Et_2O and added saturated aqueous NaCl. The mixture was stirred for 3 h, dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane : AcOEt = 3 : 1) to give allylic alcohol (351 mg, 79% yield) as a colorless oil: IR (neat) cm^{-1}: 3389, 2929; ^{1}H-NMR (400 MHz, $CDCl_3$) δ : 5.71 (1H, ddt, J = 15.7, 0.5, 5.2 Hz), 5.60 (1H, dd, J = 15.7, 7.7 Hz), 4.12 (2H, br s), 3.59 (3H, m), 3.48 (1H, br s), 3.33 (1H, d, J = 2.5 Hz), 2.96 (1H, d, J = 7.5 Hz), 1.95 (1H, m), 1.86 (1H, ddd, J = 14.7, 9.4, 1.4 Hz), 1.76 (1H, dd, J = 14.7, 2.0 Hz), 1.52-1.19 (7H, m), 0.89 (9H, s), 0.88 (9H, s), 0.06 (12H, m); ^{13}C-NMR (100 MHz, $CDCl_3$) δ : 132.5, 129.5, 75.1, 63.6, 63.2, 61.4, 58.2, 48.3, 43.7, 33.4, 28.8, 26.0, 18.3, 18.1, -4.0, -4.4, -5.3; ESIMS *m/z*: 493 (M^++Na, 100); HRESIMS *m/z*: 493.3173 (Calcd for $C_{25}H_{50}O_4NaSi_2$: M^++Na, 493.3145).

To a solution of the above allylic alcohol (160 mg, 340 μmol) in CH_2Cl_2 (17.0 mL), were added pyridine (550 μL, 6.80 mmol) and *p*-toluenesulfonic anhydride (444 mg, 1.36 mmol). After stirring at rt for 10 min, acetone (11.0 mL) and NaI (1.50 g, 10.2 mmol) were added and stirred for 30 min. The reaction mixture was diluted with Et_2O and filtered through celite and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane : AcOEt = 10 : 1) to give allylic iodide **11** (142 mg, 72% yield) as a colorless oil: IR (neat) cm^{-1}: 2929; ^{1}H-NMR (400 MHz, $CDCl_3$) δ : 5.78 (1H, ddt, J = 15.3, 0.7, 7.8 Hz), 5.60 (1H, dd, J = 15.3, 8.0 Hz), 3.86 (2H, d, J = 7.9 Hz), 3.58 (3H, m), 3.48 (1H, br s), 3.32 (1H, d, J = 2.5 Hz), 2.92 (1H, d, J = 7.9 Hz), 1.84 (3H, m), 1.52-1.21 (6H, m), 0.89 (9H, s), 0.88 (9H, s), 0.05 (12H, m); ^{13}C-NMR (100 MHz, $CDCl_3$) δ : 134.4, 128.5, 75.1, 63.2, 61.0, 58.2, 48.2, 43.6, 34.3, 33.4, 28.8, 26.0, 19.4, 18.3, 18.1, 5.8, -3.9, -4.4, -5.3; ESIMS *m/z*: 603 (M^++Na, 100);

HRESIMS *m/z*: 603.2156 (Calcd for $C_{25}H_{49}IO_3NaSi_2$: M^++Na, 603.2163).

(1*S,2*S**,3*S**,5*R**)-3-[(1*R**)-1,5-Bis(*tert*-butyldimethylsiloxy)pentyl]-2-[(1*E*)-dec-1-en-4-ynyl]-6-oxa-bicyclo[3.1.0]hexane (12).** To a solution of K_2CO_3 (230 mg, 1.66 mmol), NaI (249 mg, 1.66 mmol) and CuI (158 mg, 831 μmol) in DMF (2.80 mL), were added hept-1-yne (109 μL, 831 μmol) and allylic iodide **11** (161 mg, 277 μmol). After stirring at rt for 3 h, the reaction mixture was diluted with Et_2O, washed with saturated aqueous NH_4Cl, water and saturated aqueous NaCl, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane : Et_2O = 20 : 1) to give eneyne **12** (95.8 mg, 63% yield) as a colorless oil: IR (neat) cm^{-1}: 2930; ^{1}H-NMR (400 MHz, $CDCl_3$) δ : 5.59 (1H, ddt, *J* = 15.4, 7.8, 1.4 Hz), 5.48 (1H, ddt, *J* = 15.4, 0.5, 5.0 Hz), 3.59 (3H, m), 3.47 (1H, br s), 3.33 (1H, d, *J* = 2.5 Hz), 2.91 (3H, m), 2.18 (2H, m), 1.95 (1H, m), 1.85 (1H, ddd, *J* = 14.7, 9.5, 1.3 Hz), 1.75 (1H, dd, *J* = 14.6, 1.8 Hz), 1.56-1.21 (12H, m), 0.89 (21H, m), 0.06 (12H, m); ^{13}C-NMR (100 MHz, $CDCl_3$) δ : 131.3, 125.6, 82.7, 75.2, 63.3, 61.6, 58.3, 48.4, 43.9, 34.4, 33.5, 31.1, 28.8, 28.7, 26.0, 22.2, 22.1, 19.5, 18.8, 18.3, 18.1, 14.0, -3.9, -4.4, -5.3; ESIMS *m/z*: 571 (M^++Na, 100); HRESIMS *m/z*: 571.4033 (Calcd for $C_{32}H_{60}O_3NaSi_2$: M^++Na, 571.3979).

(6*R)-6-{(1*S**,2*S**,3*S**,5*R**)-2-[(1*E*,4*Z*)-Deca-1,4-dienyl]-6-oxabicyclo[3.1.0]hex-3-yl}tetrahydro-pyran-2-one (1)**. To a solution of enyne **12** (95.0 mg, 173 μmol) in DMF (1.70 mL), was added TBAF (1.0 M in THF, 865 μL, 865 μmol). After stirring at 40 °C for 12 h, the reaction mixture was diluted with AcOEt, washed with saturated aqueous NH_4Cl, water and saturated aqueous NaCl, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane : acetone = 2 : 1) to give diol (40.7 mg, 73% yield) as a colorless oil: IR (neat) cm^{-1}: 3387, 2930; ^{1}H-NMR (400 MHz, $CDCl_3$) δ : 5.62 (1H, m), 5.55 (1H, dt, *J* = 15.4, 4.7 Hz), 3.64 (2H, t, *J* = 6.5 Hz), 3.59 (1H, m), 3.46 (1H, m), 3.39 (1H, d, *J* = 2.6 Hz), 3.08 (1H, d, *J* = 7.4 Hz), 2.92 (2H, m), 2.18 (4H, m), 1.99 (1H, m), 1.61-1.27 (14H, m), 0.89 (3H, t, *J* = 7.1 Hz); ^{13}C-NMR (100 MHz, $CDCl_3$) δ : 130.2, 126.6, 83.0, 76.6, 73.9, 62.8, 62.3, 59.2, 47.9, 42.1, 36.3, 32.7, 32.6, 31.1, 28.7, 22.2, 22.0, 18.7, 14.0; ESIMS *m/z*: 343 (M^++Na, 100); HRESIMS *m/z*: 343.2261 (Calcd for $C_{20}H_{32}O_3Na$: M^++Na, 343.2249).

To a solution of the above diol (10.0 mg, 31.2 μmol) in CH_2ClCH_2Cl (1.70 mL), were added MS 4A (15.5 mg), NMO (18.2 mg, 156 μmol) and TPAP (0.54 mg, 1.6 μmol). After stirring at rt for 12 h, the reaction mixture was diluted with Et_2O, filtered through silica gel and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane : AcOEt = 3 : 2) to give lactone (5.9 mg, 60% yield) as a colorless oil: IR (neat) cm^{-1}: 2927, 1733; ^{1}H-NMR (400 MHz, $CDCl_3$) δ : 5.60 (2H, m), 4.19 (1H, m), 3.54 (1H, d, *J* = 2.2 Hz), 3.40 (1H, d, *J* = 2.5 Hz), 3.23 (1H, d, *J* = 5.4 Hz), 2.90 (2H, d, *J* = 2.3 Hz), 2.55 (1H, ddd, *J* = 17.3, 7.0, 6.7 Hz), 2.41 (1H, ddd, *J* = 17.3, 7.7, 7.3 Hz), 2.17 (2H, m), 2.05-1.77 (6H, m), 1.50 (1H, m), 1.40-1.26 (5H, m), 0.90 (3H, t, *J* = 7.0 Hz); ^{13}C-NMR (100 MHz, $CDCl_3$) δ : 172.0, 129.6, 126.9, 83.5, 82.9, 76.6, 60.9, 57.7, 47.9, 43.0, 31.1, 29.4, 28.7, 28.3, 26.3, 22.2, 22.0, 18.7, 18.1, 14.0; ESIMS *m/z*: 339 (M^++Na, 100); HRESIMS *m/z*: 339.1918 (Calcd for $C_{20}H_{28}O_3Na$: M^++Na, 339.1936).

A solution of the above lactone (14.0 mg, 44.2 μmol) in MeOH (1.40 mL) in the presence of 5% Pd on $BaSO_4$ (6.6 mg) and quinoline (8.8 μL) was stirred at rt for 2 h under a hydrogen atmosphere. The reaction mixture was diluted with Et_2O and filtered through silica gel and the filtrate was concentrated under reduced pressure. The residue was purified by silica gel column chromatography ($CHCl_3$: AcOEt = 9 : 1) to give analogue **1** (11.1 mg, 79% yield) as a colorless oil: IR (neat) cm^{-1}: 2926, 1737; ^{1}H-NMR (400 MHz, $CDCl_3$) δ : 5.57 (1H, m), 5.43 (1H, m), 5.33 (2H, m), 4.18 (1H, m), 3.52 (1H, d, *J* = 2.2 Hz), 3.37 (1H, d, *J* = 2.6 Hz), 3.18 (1H, d, *J* = 7.8 Hz), 2.74 (2H, t, *J* = 6.7 Hz), 2.55 (1H, dt, *J* = 17.3, 6.9 Hz), 2.41 (1H, dt, *J* = 17.3, 7.6 Hz), 2.06-1.78 (8H, m), 1.39-1.22 (7H, m), 0.89 (3H, t, *J* = 6.8 Hz); ^{13}C-NMR (100 MHz, $CDCl_3$) δ : 172.0, 131.2, 130.5, 128.7, 126.7, 83.6, 61.1, 57.7, 48.1, 43.3, 31.5, 30.4, 29.4, 29.3, 28.3, 27.1, 26.3, 22.5, 18.1, 14.0; ESIMS *m/z*: 341 (M^++Na, 100); HRESIMS *m/z*: 341.2088 (Calcd for $C_{20}H_{30}O_3Na$: M^++Na, 341.2093).

(6*R)-6-{(1*R**,2*S**,3*S**,5*S**)-2-[(1*E*,4*Z*)-Deca-1,4-dienyl]-6-oxabicyclo[3.1.0]hex-3-yl}tetrahydropyran-2-one (2).** Analogue **2** was synthesized from β-epoxide **10b** according to the above synthetic method of analogue **1** from α-epoxide **10a**. **2**: a colorless oil; IR (neat) cm^{-1}: 2925, 1738; ^{1}H-NMR (400 MHz, $CDCl_3$) δ : 5.58 (2H, m), 5.39 (2H, m), 4.30 (1H, m), 3.45 (1H, d, *J* = 2.6 Hz), 3.37 (1H, m), 2.78 (2H, t, *J* = 6.3 Hz), 2.63 (1H, m), 2.57 (1H, m), 2.42 (1H, m), 2.14 (1H, m), 2.02 (2H, m), 1.91-1.66 (6H, m), 1.36-1.25 (6H, m), 0.88 (3H, t, *J* = 6.7 Hz); ^{13}C-NMR (100 MHz, $CDCl_3$) δ : 171.7, 131.1, 131.0, 130.1, 126.8, 81.1, 61.3, 55.8, 44.0, 42.7, 31.5, 30.6, 30.5, 29.5, 29.3, 27.1, 26.2, 22.5, 18.8, 14.0; ESIMS *m/z*: 341 (M^++Na, 78), 195 (100); HRESIMS *m/z*: 341.2110 (Calcd for $C_{20}H_{30}O_3Na$: M^++Na, 341.2093).

(1*S,5*S**)-5-[(1*S**)-5-*tert*-Butyldimethylsiloxy-1-hydroxypentyl]cyclopent-2-enylmethyl 2,2-dimethylpropionate (13).** To a solution of β-alcohol **7b** (54.5 mg, 159 μmol) in CH_2Cl_2 (16.0 mL), was added (benzylidene)bis(tricyclohexylphosphine)ruthenium(IV) dichloride (13.0 mg, 15.9 μmol) and stirred at rt for 3 h. The reaction mixture was diluted with Et_2O, filtered through silica gel and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane : AcOEt = 3 : 1) to give cyclopentene (41.0 mg, 82% yield) as a colorless oil: IR (neat) cm^{-1}: 3348, 2929; ^{1}H-NMR (400 MHz, $CDCl_3$) δ : 5.76 (1H, m), 5.54 (1H, m), 3.68 (2H, m), 3.65 (2H, m), 3.47 (1H, dd, *J* = 10.2, 7.2 Hz), 2.85 (1H, m), 2.48 (1H, m), 2.23 (2H, m), 1.60-1.36 (6H, m), 0.89 (9H, s), 0.04 (6H, s); ^{13}C-NMR (100 MHz, $CDCl_3$) δ : 131.8, 130.5, 73.2, 66.4, 63.2, 50.3, 47.5, 34.4, 33.6, 32.6, 25.9, 22.7, 18.4, -5.3; EIMS *m/z*: 315 (M^++H, 8), 147 (100); HREIMS *m/z*: 314.2258 (Calcd for $C_{17}H_{34}O_3Si$: M^+, 314.2277).

To a cold (0 °C) solution of the above cyclopentene (252 mg, 801 μmol) in CH_2ClCH_2Cl (8.00 mL), were added pyridine (129 μL, 1.60 mmol) and pivaloyl chloride (148 μL, 1.20 mmol) and stirred at rt for 12 h. The reaction mixture was diluted with Et_2O, washed with saturated aqueous $NaHCO_3$, water and saturated aqueous NaCl, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane : AcOEt = 6 : 1) to give alcohol **13** (276 mg, 86% yield) as a colorless oil: IR (neat) cm^{-1}: 3484, 2931, 1731; ^{1}H-NMR (400 MHz, $CDCl_3$) δ : 5.76 (1H, m), 5.58 (1H, m), 4.07 (1H, dd, *J* = 10.7, 6.4 Hz), 3.96 (1H, dd, *J* = 10.7, 6.3 Hz), 3.62 (3H, m), 2.91 (1H, m), 2.40 (2H, m), 2.08 (1H, m), 1.59-1.35 (7H, m), 1.19 (9H, s), 0.89 (9H, s), 0.04 (6H, s); ^{13}C-NMR (100 MHz, $CDCl_3$) δ : 178.5, 131.8, 130.3 73.5, 67.4, 63.1, 47.9, 46.2, 38.8, 35.1, 32.9, 32.7, 27.2, 25.9, 22.5, 18.3, -5.3; ESIMS *m/z*: 421 (M^++Na, 100); HRESIMS *m/z*: 421.2761 (Calcd for $C_{22}H_{42}O_4NaSi$: M^++Na, 421.2750).

(1*S,5*S**)-5-[(1*S**)-1,5-Bis(*tert*-butyldimethylsiloxy)pentyl]cyclopent-2-enylmethyl 2,2-dimethylpropionate (14)**. To a solution of alcohol **13** (243 mg, 609 μmol) in DMF (600 μL), were added imidazole (83.0 mg, 1.21 mmol) and TBDMSCl (138 mg, 914 μmol) and stirred at 45 °C for 17 h. The reaction mixture was diluted with Et_2O, washed with saturated aqueous $NaHCO_3$, water and saturated aqueous NaCl, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane : AcOEt = 10 : 1) to give TBDMS ether **14** (295 mg, 94% yield) as a colorless oil: IR (neat) cm^{-1}: 2930, 1732; ^{1}H-NMR (400 MHz, $CDCl_3$) δ : 5.71 (1H, m), 5.52 (1H, m), 4.09 (1H, dd, *J* = 10.6, 6.0 Hz), 3.94 (1H, dd, *J* = 10.6, 6.4 Hz), 3.72 (1H, m), 3.60 (2H, t, *J* = 6.5 Hz), 2.89 (1H, m), 2.34 (2H, m), 2.13 (1H, m), 1.55-1.26 (6H, m), 1.19 (9H, s), 0.89 (9H, s), 0.86 (9H, s), 0.04 (12H, m); ^{13}C-NMR (100 MHz, $CDCl_3$) δ : 178.5, 131.6, 130.4, 73.5, 67.7, 63.0, 47.5, 45.6, 38.8, 35.3, 33.1, 32.8, 27.2, 26.0, 22.2, 18.3, 18.1, -3.9, -4.4, -5.3; ESIMS *m/z*: 535 (M^++Na, 100); HRESIMS *m/z*: 535.3618 (Calcd for $C_{28}H_{56}O_4NaSi_2$: M^++Na, 535.3615).

(1*S,2*S**,3*S**,5*R**)-3-[(1*S**)-1,5-Bis(*tert*-butyldimethylsiloxy)pentyl]-6-oxabicyclo[3.1.0]hex-2-ylmethyl 2,2-dimethylpropionate (15a) and (1*R**,2*S**,3*S**,5*S**)-3-[(1*S**)-1,5-bis(*tert*-butyldimethylsiloxy)pentyl]-6-oxabicyclo[3.1.0]hex-2-ylmethyl 2,2-dimethylpropionate (15b)**. To a cold (0 °C) solution of cyclopentene **14** (261 mg, 508 μmol) in CH_2Cl_2 (5.10 mL), were added Na_2HPO_4 (288 mg, 2.03 mmol) and 65% *m*-CPBA (202 mg, 762 μmol). After stirring for 1 h at rt, saturated aqueous $Na_2S_2O_3$ was added and stirred for 30 min. The mixture was diluted with Et_2O, washed with saturated aqueous $NaHCO_3$, water and saturated aqueous NaCl, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane : Et_2O = 9 : 1) to give α-epoxide **15a** (16.2 mg, 6% yield) and β-epoxide **15b** (244 mg, 91% yield) as each colorless oil. **15a**: IR (neat) cm^{-1}: 2931, 1733; ^{1}H-NMR (400 MHz, $CDCl_3$) δ : 4.11 (1H, dd, *J* = 11.1, 5.0 Hz), 3.93 (1H, dd, *J* = 11.1, 7.5 Hz), 3.68 (2H, t, *J* = 6.4 Hz), 3.52 (1H, m), 3.47 (1H, m), 3.36 (1H, d, *J* = 2.5 Hz), 2.31 (1H, m), 2.12 (1H, dd, *J* = 14.9, 2.3 Hz), 1.97 (1H, m), 1.79 (1H, ddd, *J* = 14.9, 9.8, 1.6 Hz), 1.52-1.30 (6H, m), 1.21

(9H, s), 0.89 (9H, s), 0.88 (9H, s), 0.05 (12H, m); ^{13}C-NMR (100 MHz, $CDCl_3$) δ : 178.4, 75.0, 65.1, 63.2, 60.0, 58.8, 45.6, 41.7, 38.8, 34.7, 33.4, 29.1, 27.2, 26.0, 20.4, 18.3, 18.1, -3.9, -4.2, -5.3; ESIMS *m/z*: 551 (M^++Na, 100); HRESIMS *m/z*: 551.3563 (Calcd for $C_{28}H_{56}O_5NaSi_2$: M^++Na, 551.3564). **15b**: IR (neat) cm^{-1}: 2931, 1732; ^{1}H-NMR (400 MHz, $CDCl_3$) δ : 4.24 (1H, dd, *J* = 10.8, 4.7 Hz), 4.02 (1H, dd, *J* = 10.7, 9.4 Hz), 3.67 (1H, m), 3.57 (1H, t, *J* = 6.4 Hz), 3.48 (2H, br s), 2.23 (1H, dt, *J* = 4.8, 9.1 Hz), 1.97 (1H, dd, *J* = 13.7, 7.8 Hz), 1.84 (1H, dd, *J* = 13.7, 9.2 Hz), 1.56-1.23 (7H, m), 1.22 (9H, s), 0.89 (9H, s), 0.87 (9H, s), 0.04 (12H, m); ^{13}C-NMR (100 MHz, $CDCl_3$) δ : 178.3, 70.8, 63.8, 62.9, 58.1, 56.5, 41.1, 39.8, 38.8, 36.2, 33.0, 27.2, 26.8, 26.0, 22.1, 18.3, 18.1, -3.9, -4.7, -5.3; ESIMS *m/z*: 551 (M^++Na, 100); HRESIMS *m/z*: 551.3591 (Calcd for $C_{28}H_{56}O_5NaSi_2$: M^++Na, 551.3564).

(1*S,2*S**,3*S**,5*R**)-3-[(1*S**)-1,5-Bis(*tert*-butyldimethylsiloxy)pentyl]-6-oxabicyclo[3.1.0]hex-2-ylmethyl 2,2-dimethylpropiolate (15a)**. To a solution of alcohol **13** (93.0 mg, 233 μmol) in CH_2Cl_2 (2.30 mL), VO(acac)$_2$ (6.2 mg, 23.3 μmol) and TBHP (3.68 M in CH_2Cl_2, 127 μL, 466 μmol) under argon atmosphere. After stirring the mixture at rt for 3 h, excess of Me_2S was added and stirring for 3 h. The reaction mixture was diluted with Et_2O and filtered through silica gel and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane : AcOEt = 4 : 1) to give α-epoxide (80.6 mg, 83% yield) as a colorless oil: IR (neat) cm^{-1}: 3437, 2932, 1732; ^{1}H-NMR (400 MHz, $CDCl_3$) δ : 4.12 (1H, dd, *J* = 11.1, 5.7 Hz), 4.01 (1H, dd, *J* = 11.1, 6.9 Hz), 3.59 (2H, t, *J* = 6.5 Hz), 3.56 (1H, br s), 3.47 (2H, s), 3.44 (1H, d, *J* = 2.6 Hz), 2.53 (1H, m), 2.20 (1H, dd, *J* = 14.9, 1.7 Hz), 2.06 (1H, dd, *J* = 10.5, 2.0 Hz), 1.92 (1H, ddd, *J* = 14.9, 10.5, 1.6 Hz), 1.56-1.28 (6H, m), 1.20 (9H, s), 0.88 (9H, s), 0.03 (6H, s); ^{13}C-NMR (100 MHz, $CDCl_3$) δ : 178.3, 73.4, 64.7, 63.0, 60.3, 59.5, 45.3, 44.8, 38.8, 36.5, 32.8, 27.2, 26.8, 26.0, 22.3, 18.3, -5.3; ESIMS *m/z*: 437 (M^++Na, 100); HRESIMS *m/z*: 437.2727 (Calcd for $C_{22}H_{42}O_5NaSi$: M^++Na, 437.2699).

To a cold (-78 °C) solution of the above α-epoxide (1.26 g, 3.04 mmol) in CH_2Cl_2 (31.0 mL), were added 2,6-lutidine (3.54 mL, 30.4 mmol) and TBDMSOTf (768 mL, 3.34 mmol). After stirring for 10 min, Et_3N (1.00 mL) and saturated aqueous $NaHCO_3$ were added and stirred for 20 min. The mixture was diluted with Et_2O, washed with water and saturated aqueous NaCl, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane : Et_2O = 7 : 1) to give TBDMS ether **15a** (1.41 g, 88% yield) as a colorless oil.

(6*S)-6-{(1*S**,2*S**,3*S**,5*R**)-2-[(1*E*,4*Z*)-Deca-1,4-dienyl]-6-oxabicyclo[3.1.0]hex-3-yl}tetrahydropyran-2-one (3)**. Analogue **3** was synthesized from α-epoxide **15a** according to the above synthetic method of analogue **1** from α-epoxide **10a**. **3**: a colorless oil; IR (neat) cm^{-1}: 2925, 1737; ^{1}H-NMR (400 MHz, $CDCl_3$) δ : 5.54 (1H, ddt, *J* = 15.3, 0.5, 6.2 Hz), 5.46 (1H, m), 5.33 (2H, m), 4.14 (1H, dt, *J* = 3.0, 10.4 Hz), 3.56 (1H, br s), 3.32 (1H, d, *J* = 2.5 Hz), 2.76 (2H, t, *J* = 6.7 Hz), 2.66 (1H, d, *J* = 8.2 Hz), 2.55 (1H, ddd, *J* = 17.2, 7.0, 6.7 Hz), 2.42 (2H, m), 2.12-1.78 (7H, m), 1.41-1.25 (7H, m), 0.89 (3H, t, *J* = 6.7

Hz); ^{13}C-NMR (100 MHz, $CDCl_3$) δ : 172.0, 131.4, 130.7, 128.4, 126.4, 83.6, 61.1, 58.5, 48.6, 44.6, 31.5, 30.3, 29.4, 29.2, 28.4, 27.1, 26.5, 22.5, 18.1, 14.0; ESIMS *m/z*: 341 (M^++Na, 100); HRESIMS *m/z*: 341.2068 (Calcd for $C_{20}H_{30}O_3Na$: M^++Na, 341.2093).

(6*S)-6-{(1*R**,2*S**,3*S**,5*S**)-2-[(1*E*,4*Z*)-Deca-1,4-dienyl]-6-oxabicyclo[3.1.0]hex-3-yl}tetrahydropyran-2-one (4)**. Analogue **4** was synthesized from β-epoxide **15b** according to the above synthetic method of analogue **1** from α-epoxide **10a**. **4**: a colorless oil; IR (neat) cm^{-1}: 2925, 1739; ^{1}H-NMR (400 MHz, $CDCl_3$) δ : 5.61 (1H, dt, *J* = 15.4, 6.2 Hz), 5.44 (3H, m), 4.23 (1H, dt, *J* = 11.7, 2.6 Hz), 3.45 (1H, br s), 3.39 (1H, m), 2.78 (2H, t, *J* = 6.5 Hz), 2.70 (1H, t, *J* = 9.0 Hz), 2.60 (1H, m), 2.41 (1H, ddd, *J* = 17.7, 9.3, 7.4 Hz), 2.11 (1H, dd, *J* = 13.5, 7.5 Hz), 2.02 (2H, m), 1.95-1.70 (4H, m), 1.64-1.46 (2H, m), 1.36-1.25 (7H, m), 0.88 (3H, t, *J* = 6.6 Hz); ^{13}C-NMR (100 MHz, $CDCl_3$) δ : 171.8, 132.2, 131.1, 128.2, 126.8, 78.5, 60.2, 55.6, 44.7, 43.2, 31.5, 30.4, 29.5, 29.3, 27.5, 27.2, 27.1, 22.5, 18.8, 14.0; ESIMS *m/z*: 341 (M^++Na, 100); HRESIMS *m/z*: 341.2111 (Calcd for $C_{20}H_{30}O_3Na$: M^++Na, 341.2093).

***tert*-Butyl{(1*S*,2*E*)-1-ethyl-3-iodoallyloxy}diphenylsilane (17)**. To a solution of (*S*)-pent-1-yn-3-ol (**16**) (2.90 g, 34.4 mmol) in DMF (34.0 mL), were added imidazole (5.85 g, 86.0 mmol) and TBDPSCl (17.9 mL, 68.8 mmol) and stirred at rt for 12 h. The reaction mixture was diluted with Et_2O, washed with saturated aqueous $NaHCO_3$, water and saturated aqueous NaCl, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane : AcOEt = 25 : 1) to give TBDPS ether (9.20 g, 83% yield) as a colorless oil: $[\alpha]_D^{24}$ -64.3° (*c* 1.20, $CHCl_3$); IR (neat) cm^{-1}: 3306, 2932; ^{1}H-NMR (400 MHz, $CDCl_3$) δ : 7.77 (2H, m), 7.70 (2H, m), 7.38 (6H, m), 4.32 (1H, ddd, *J* = 7.0, 5.4, 2.1 Hz), 2.31 (1H, d, *J* = 2.1 Hz), 1.68 (2H, m), 1.09 (9H, s), 0.96 (3H, t, *J* = 7.4 Hz); ^{13}C-NMR (100 MHz, $CDCl_3$) δ : 136.0, 133.6, 129.7, 127.6, 84.9, 72.5, 64.9, 31.3, 26.9, 19.3, 9.0; EIMS *m/z*: 265 (M^+-^{t}Bu, 100); HREIMS *m/z*: 265.1044 (Calcd for $C_{17}H_{17}OSi$: M^+-^{t}Bu, 265.1049).

To the above TBDPS ether (11.2 g, 34.7 mmol), was added catecholborane (5.55 mL, 52.1 mmol) at 80 °C. After stirring for 6 h, 10% aqueous solution of K_2CO_3 was added and stirred at rt for 3 h. The mixture was diluted with Et_2O, washed with water and saturated aqueous NaCl, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was used next reaction without purification.

To a solution of the above crude product in Et_2O (70.0 mL), were added NaOH (3 M in H_2O, 34.7 mL, 104 mmol) and I_2 (26.4 g, 104 mmol) at 0 °C. After stirring for 12 h, saturated aqueous $Na_2S_2O_3$ was added and stirred for 1 h. The mixture was diluted with Et_2O, washed with water and saturated aqueous NaCl, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane : AcOEt = 50 : 1) to give iodoalkene **17** (11.8 g, 75% yield (two steps)) as a colorless oil: $[\alpha]_D^{19}$ -97.7° (*c* 1.50, $CHCl_3$); IR (neat) cm^{-1}: 2931; ^{1}H-NMR (400 MHz, $CDCl_3$) δ : 7.65 (4H, m), 7.38 (6H, m), 6.43 (1H, dd, *J* = 14.4, 6.8 Hz), 5.95 (1H, d, *J* = 14.4 Hz), 4.04 (1H, m), 1.49 (2H, m), 1.07 (9H, s), 0.80 (3H, t, *J* = 7.5 Hz); ^{13}C-NMR (100 MHz, $CDCl_3$) δ : 148.0, 135.8, 134.0, 133.7, 129.7, 127.5, 29.9, 27.0, 19.4, 8.7; EIMS *m/z*: 393 (M^+-^{t}Bu, 100); HREIMS *m/z*: 393.0162 (Calcd for $C_{17}H_{18}IOSi$: M^+-^{t}Bu, 393.0172).

***tert*-Butyl[(1*S*,2*E*)-1-ethyl-5-trimethylsilylpent-2-en-4-ynyloxy]diphenylsilane (18)**. To a solution of iodoalkene **17** (10.7 mg, 23.7 μmol) in benzene (0.12 mL), were added $PrNH_2$ (2.9 μL, 35.5 μmol) and $(Ph_3P)_4Pd$ (2.7 mg, 2.40 μmol) at rt. After stirring for 30 min, (trimethylsilyl)acetylene (5.0 μL, 35.5 μmol) and CuI (0.2 mg, 1.20 μmol) were added and stirred for 3 h. The reaction mixture was diluted with Et_2O, washed with saturated aqueous NH_4Cl, water and saturated aqueous NaCl, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane : AcOEt = 20 : 1) to give enyne **18** (6.3 mg, 63% yield) as a colorless oil: $[\alpha]_D^{25}$ -73.5° (*c* 1.11, $CHCl_3$); IR (neat) cm^{-1}: 2932, 2133; ^{1}H-NMR (400 MHz, $CDCl_3$) δ : 7.65 (4H, m), 7.39 (6H, m), 6.15 (1H, dd, *J* = 15.9, 5.5 Hz), 5.64 (1H, dd, *J* = 15.9, 1.3 Hz), 4.20 (1H, m), 1.44 (2H, m), 1.08 (9H, s), 0.76 (3H, t, *J* = 7.4 Hz), 0.20 (9H, s); ^{13}C-NMR (100 MHz, $CDCl_3$) δ : 146.6, 135.8, 134.2, 133.8, 129.6, 127.5, 109.4, 103.7, 94.3, 74.2, 29.9, 27.0, 19.4, 8.4, 0.0; EIMS *m/z*: 421 (M^+, 14), 363 (M^+-^{t}Bu, 100); HREIMS *m/z*: 363.1609 (Calcd for $C_{22}H_{27}OSi_2$: M^+-^{t}Bu, 363.1600).

(1*S*,2*E*)-1-Ethylpent-2-en-4-ynyl acetate (19). To a solution of enyne **18** (1.09 g, 2.59 mmol) in THF (13.0 mL), was added TBAF (1.0 M in THF, 7.77 mL, 7.77 mmol) and stirred at rt for 2 h. The reaction mixture was diluted with Et_2O, washed with saturated aqueous NH_4Cl, water and saturated aqueous NaCl, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane : Et_2O = 2 : 1) to give alcohol (253 mg, 90% yield) as a colorless oil: $[\alpha]_D^{24}$ +6.9° (*c* 1.16, $CHCl_3$); IR (neat) cm^{-1}: 3290, 2935, 2103; ^{1}H-NMR (500 MHz, $CDCl_3$) δ : 6.24 (1H, dd, *J* = 16.0, 5.8 Hz), 5.69 (1H, ddd, *J* = 16.0, 2.0, 1.7 Hz), 4.10 (1H, m), 2.88 (1H, d, *J* = 2.1 Hz), 1.69 (1H, br s), 1.57 (2H, m), 0.93 (3H, t, *J* = 7.5 Hz); ^{13}C-NMR (125 MHz, $CDCl_3$) δ : 147.3, 108.8, 81.6, 77.8, 73.3, 29.7, 9.4; EIMS *m/z*: 109 (M^+-H, 31), 53 (100).

To a cold (0 °C) solution of the above alcohol (1.30 g, 11.8 mmol) in CH_2Cl_2 (59.0 mL), were added DMAP (4.32 g, 35.4 mmol) and AcCl (1.68 mL, 23.6 mmol) stirred for 2 h. The reaction mixture was diluted with Et_2O, filtered through silica gel, washed with water and saturated aqueous NaCl, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane : Et_2O = 3 : 1) to give acetate **19** (1.53 g, 86% yield) as a colorless oil: $[\alpha]_D^{24}$ -104.1° (*c* 0.63, $CHCl_3$); IR (neat) cm^{-1}: 3294, 2939, 2106, 1737; ^{1}H-NMR (400 MHz, $CDCl_3$) δ : 6.13 (1H, dd, *J* = 16.0, 6.5 Hz), 5.67 (1H, ddd, *J* = 16.0, 2.1, 1.4 Hz), 5.21 (1H, m), 2.90 (1H, d, *J* = 2.2 Hz), 2.06 (3H, s), 1.65 (2H, m), 0.90 (3H, t, *J* = 7.4 Hz); ^{13}C-NMR (100 MHz, $CDCl_3$) δ : 170.1, 142.6, 110.9, 81.2, 78.4, 74.6, 27.1, 21.1, 9.2; EIMS *m/z*: 152 (M^+, 15), 43 (100).

(1*S*,2*E*,7*E*)-8-(1*R*,2*S*,3*S*,5*S*)-{3-[(*S*)-1,5-Bis(*tert*-butyldimethylsiloxy)pentyl]-6-oxabicyclo[3.1.0]hex-2-yl}-1-ethylocta-2,7-dien-4-ynyl acetate (21) and (1*S*,2*E*,7*E*)-8-(1*S*,2*R*,3*R*,5*R*)-{3-[(*R*)-1,5-bis(*tert*-

butyldimethylsiloxy)pentyl]-6-oxabicyclo[3.1.0]hex-2-yl}-1-ethylocta-2,7-dien-4-ynyl acetate (22). To a solution of enyne **19** (213 mg, 1.40 mmol) in DMF (4.70 mL), were added K_2CO_3 (517 mg, 3.74 mmol), NaI (561 mg, 3.74 mmol), CuI (356 mg, 1.87 mmol) and allylic iodide **20** (543 mg, 935 μmol). After stirring at rt for 4 h, the reaction mixture was diluted with Et_2O, washed with saturated aqueous NH_4Cl, water and saturated aqueous NaCl, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane : Et_2O = 4 : 1) to give a diastereomeric mixture of dienynes **21** and **22** (543 mg, 90% yield) as colorless oil. The mixture was used next reaction without separation: IR (neat) cm^{-1}: 2928, 1739; ^1H-NMR (500 MHz, $CDCl_3$) δ : 5.96 (1H, dd, *J* = 15.8, 6.9 Hz), 5.70 (2H, m), 5.57 (1H, dt, *J* = 15.5, 5.5 Hz), 5.19 (1H, dt, *J* = 6.4, 6.3 Hz), 3.59 (1H, m), 3.57 (2H, t, *J* = 6.6 Hz), 3.44 (1H, m), 3.39 (1H, m), 3.08 (2H, d, *J* = 5.4 Hz), 2.50 (1H, t, *J* = 8.8 Hz), 2.05 (3H, s), 1.97 (1H, dd, *J* = 13.8, 7.6 Hz), 1.80 (1H, ddd, *J* = 13.8, 9.5, 1.0 Hz), 1.64 (2H, m), 1.57 (1H, m), 1.46 (3H, m), 1.36 (1H, m), 1.23 (2H, m), 0.90 (3H, t, *J* = 7.4 Hz), 0.89 (9H, s), 0.87 (9H, s), 0.04 (3H, s), 0.04 (9H, s); ^{13}C-NMR (125 MHz, $CDCl_3$) δ : 170.2, 139.6, 131.1, 125.9, 112.6, 88.7, 79.9, 75.0, 70.1, 63.0, 60.3, 56.0, 44.9, 42.6, 36.4, 33.0, 27.2, 26.8, 26.0, 22.8, 21.8, 21.1, 18.3, 18.1, 9.3, -3.7, -4.4, -5.3; ESIMS *m/z*: 627 (M^++Na, 100); HRESIMS *m/z*: 627.3896 (Calcd for $C_{34}H_{60}O_5NaSi_2$: M^++Na, 627.3877).

(1*S*,2*E*,4*Z*,7*E*)-1-Ethyl-8-{(1*R*,2*S*,3*S*,5*S*)-3-[(*S*)-6-oxotetrahydropyran-2-yl]-6-oxabicyclo[3.1.0]hex-2-yl}octa-2,4,7-trienyl acetate (23) and (1*S*,2*E*,4*Z*,7*E*)-1-Ethyl-8-{(1*S*,2*R*,3*R*,5*R*)-3-[(*R*)-6-oxotetrahydropyran-2-yl]-6-oxabicyclo[3.1.0]hex-2-yl}octa-2,4,7-trienyl acetate (24). To a solution of the mixture of dienynes **21** and **22** (208 mg, 342 μmol) in DMF (1.70 mL), were added TBAF (1.0 M in THF, 1.71 mL, 1.71 mmol) and acetic acid (97.9 μL, 1.71 μmol). After stirring for 37 h at 60 °C, the reaction mixture was diluted with AcOEt, washed with saturated aqueous NH_4Cl, water and saturated aqueous NaCl, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane : acetone = 1 : 1) to give a mixture of diols (72.9 mg, 56% yield) and a mixture of mono TBDMS ethers (55.0 mg, 33% yield): **diols**: IR (neat) cm^{-1}: 3418, 2935, 1734; ^1H-NMR (400 MHz, $CDCl_3$) δ : 5.94 (1H, dd, *J* = 15.9, 6.8 Hz), 5.69 (2H, m), 5.57 (1H, dt, *J* = 15.3, 5.4 Hz), 5.15 (1H, m), 3.59 (2H, t, *J* = 6.2 Hz), 3.54 (1H, m), 3.43 (1H, m), 3.38 (1H, m), 3.05 (2H, d, *J* = 5.3 Hz), 2.57 (1H, t, *J* = 8.9 Hz), 2.22 (2H, br s), 2.03 (3H, s), 2.01 (1H, dd, *J* = 13.9, 7.6 Hz), 1.69 (1H, m), 1.62 (2H, m), 1.56-1.30 (7H, m), 0.87 (3H, t, *J* = 7.4 Hz); ^{13}C-NMR (100 MHz, $CDCl_3$) δ : 170.3, 139.5, 130.7, 126.2, 112.5, 88.6, 79.9, 75.1, 69.4, 62.4, 60.2, 55.9, 45.1, 43.6, 35.9, 32.3, 27.1, 26.9, 22.6, 22.3, 21.1, 9.3; ESIMS *m/z*: 399 (M^++Na, 40), 254 (100); HRESIMS *m/z*: 399.2139 (Calcd for $C_{22}H_{32}O_5Na$: M^++Na, 399.2147); **TBDMS ethers**: IR (neat) cm^{-1}: 3446, 2931, 1739; ^1H-NMR (400 MHz, $CDCl_3$) δ : 5.95 (1H, dd, *J* = 15.9, 6.9 Hz), 5.70 (2H, m), 5.56 (1H, dt, *J* = 15.4, 5.4 Hz), 5.17 (1H, m), 3.59 (3H, m), 3.43 (1H, m), 3.37 (1H, m), 3.06 (2H, d, *J* = 5.3 Hz), 2.48 (1H, t, *J* = 8.7 Hz), 2.04 (3H, s), 1.96 (1H, dd, *J* = 13.8, 7.5 Hz), 1.78 (1H, m), 1.68-1.42 (7H, m), 1.40-1.21 (3H, m), 0.89 (3H, t, *J* = 7.4 Hz), 0.86 (9H, s), 0.03 (3H, s), 0.03 (3H, s); ^{13}C-NMR (100 MHz, $CDCl_3$) δ : 170.3, 139.5, 131.1, 125.9, 112.6, 88.7, 79.9, 75.1, 70.0, 62.7, 60.3, 56.0, 44.9, 42.4, 36.3, 32.8, 27.2, 26.9, 25.9, 22.8, 21.7, 21.1, 18.1, 9.3, -3.8, -4.5; ESIMS *m/z*: 513 (M^++Na, 100); HRESIMS *m/z*: 513.3025 (Calcd for $C_{28}H_{46}O_5NaSi$: M^++Na, 513.3012).

To a solution of the above diols (72.9 mg, 192 μmol) in CH_2ClCH_2Cl (9.60 mL), were added MS 4A (96 mg), NMO (110 mg, 960 μmol) and TPAP (6.7 mg, 19.2 μmol). After stirring at rt for 30 min, the reaction mixture was diluted with Et_2O, filtered through silica gel and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane : AcOEt = 1 : 1) to give a mixture of lactones (48.4 mg, 67% yield) as colorless oil: IR (neat) cm^{-1}: 2930, 2880, 1736; ^{1}H-NMR (400 MHz, $CDCl_3$) δ : 5.97 (1H, dd, *J* = 16.0, 6.8 Hz), 5.71 (2H, m), 5.63 (1H, dt, *J* = 15.3, 5.0 Hz), 5.18 (1H, m), 4.24 (1H, dt, *J* = 11.7, 2.5 Hz), 3.46 (1H, m), 3.40 (1H, m), 3.08 (2H, d, *J* = 4.9 Hz), 2.76 (1H, dt, *J* = 0.9, 9.1 Hz), 2.60 (1H, m), 2.42 (1H, ddd, *J* = 17.8, 9.2, 7.4 Hz), 2.12 (1H, dd, *J* = 13.4, 7.4 Hz), 2.05 (3H, s), 1.93-1.72 (4H, m), 1.64 (3H, m), 1.52 (1H, m), 0.89 (3H, t, *J* = 7.4 Hz); ^{13}C-NMR (100 MHz, $CDCl_3$) δ : 171.7, 170.2, 139.8, 129.9, 127.3, 112.5, 88.2, 80.2, 78.3, 75.0, 59.9, 55.6, 44.4, 43.0, 29.4, 27.3, 27.2, 27.1, 22.6, 21.1, 18.7, 9.3; ESIMS *m/z*: 395 (M^++Na, 82), 327 (100); HRESIMS *m/z*: 395.1834 (Calcd for $C_{22}H_{28}O_4Na$: M^++Na, 395.1834).

A solution of the above lactones (28.2 mg, 75.3 μmol) in EtOH (1.50 mL) in the presence of 5% Pd on $BaSO_4$ (11.3 mg) and quinoline (14.1 μL) was stirred at rt for 16 h under a hydrogen atmosphere. The reaction mixture was diluted with Et_2O and filtered through silica gel and the filtrate was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane : acetone = 3 : 1) to give mixture of trienes. Trienens were separation by HPLC (CHIRALPAK AS-H, 0.46 cm x 25 cm, hexane : isopropanol = 82 : 18, flow rate: 2.0 mL/min) to give triene **23** (t_R = 20.2 min, 5.4 mg, 19% yield) and triene **24** (t_R = 28.2 min, 5.0 mg, 17% yield); **23**: $[\alpha]_D^{20}$ -179.6° (*c* 0.52, $CHCl_3$); IR (neat) cm^{-1}: 2924, 1734; ^{1}H-NMR (400 MHz, $CDCl_3$) δ : 6.49 (1H, dd, *J* = 15.2, 11.0 Hz), 6.01 (1H, t, *J* = 11.0 Hz), 5.63 (1H, dt, *J* = 15.4, 6.2 Hz), 5.60 (1H, dd, *J* = 15.5, 7.0 Hz), 5.48 (2H, m), 5.22 (1H, q, *J* = 6.8 Hz), 4.24 (1H, dt, *J* = 11.7, 2.6 Hz), 3.46 (1H, br s), 3.40 (1H, dd, *J* = 2.6, 1.4 Hz), 2.94 (2H, dd, *J* = 6.9, 6.8 Hz), 2.71 (1H, t, *J* = 8.9 Hz), 2.61 (1H, m), 2.42 (1H, ddd, *J* = 17.7, 9.2, 7.4 Hz), 2.12 (1H, dd, *J* = 13.5, 7.5 Hz), 2.06 (3H, s), 1.95-1.49 (7H, m), 0.90 (3H, t, *J* = 7.4 Hz); ^{13}C-NMR (100 MHz, $CDCl_3$) δ : 171.8, 170.4, 131.6, 131.2, 130.3, 129.0, 128.4, 127.7, 78.5, 75.9, 60.1, 55.6, 44.7, 43.2, 30.9, 29.5, 27.5, 27.5, 27.2, 21.3, 18.8, 9.5; ESIMS *m/z*: 397 (M^++Na, 88), 315 (100); HRESIMS *m/z*: 397.1966 (Calcd for $C_{22}H_{30}O_5Na$: M^++Na, 397.1991). **24**: $[\alpha]_D^{24}$ +165.2° (*c* 0.50, $CHCl_3$); IR (neat) cm^{-1}: 2925, 1733; ^{1}H-NMR (400 MHz, $CDCl_3$) δ : 6.49 (1H, dd, *J* = 15.3, 11.1 Hz), 6.01 (1H, t, *J* = 10.8 Hz), 5.64 (1H, dt, *J* = 15.4, 6.1 Hz), 5.60 (1H, dd, *J* = 14.8, 7.4 Hz), 5.48 (2H, m), 5.21 (1H, q, *J* = 6.8 Hz), 4.24 (1H, dt, *J* = 11.7, 2.6 Hz), 3.46 (1H, br s), 3.40 (1H, dd, *J* = 2.6, 1.4 Hz), 2.94 (2H, dd, *J* = 7.5, 6.2 Hz), 2.72 (1H, t, *J*

= 9.1 Hz), 2.61 (1H, m), 2.42 (1H, ddd, *J* = 17.8, 9.3, 7.8 Hz), 2.12 (1H, dd, *J* = 13.6, 7.5 Hz), 2.06 (3H, s), 1.94-1.48 (7H, m), 0.90 (3H, t, *J* = 7.4 Hz); ^{13}C-NMR (100 MHz, $CDCl_3$) δ : 171.8, 170.4, 131.6, 131.2, 130.3, 129.0, 128.4, 127.7, 78.5, 75.8, 60.1, 55.6, 44.7, 43.1, 30.8, 29.5, 27.5, 27.5, 27.1, 21.3, 18.8, 9.5; ESIMS *m/z*: 397 (M^++Na, 100); HRESIMS *m/z*: 397.1980 (Calcd for $C_{22}H_{30}O_5Na$: M^++Na, 397.1991).

Methyl (*S*)-5-hydroxy-5-{(1*S*,2*R*,3*S*,5*S*)-2-[(1*E*,4*Z*,6*E*,8*S*)-8-hydroxydeca-1,4,6-trienyl]-6-oxabicyclo-[3.1.0]hex-3-yl}pentanoate (25). To a solution of lactone **23** (2.9 mg, 7.8 μmol) in MeOH (100 μL), was added K_2CO_3 (3.2 mg, 23.4 μmol). After stirring at rt for 1 h, the reaction mixture was diluted with Et_2O, washed with saturated aqueous NH_4Cl, water and saturated aqueous NaCl, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography ($CHCl_3$: MeOH = 25 : 1) to give ester **25** (1.7 mg, 60% yield) as colorless oil: $[\alpha]_D^{20}$ -75.5° (*c* 0.02, $CHCl_3$); IR (neat) cm^{-1}: 3419, 2923, 1732; ^{1}H-NMR (400 MHz, $CDCl_3$) δ : 7.45 (2H, m), 7.40 (3H, m), 5.15 (1H, m), 3.67 (3H, s), 3.54 (3H, s), 3.35 (1H, d, *J* = 2.6 Hz), 3.30 (1H, d, *J* = 2.8 Hz), 2.31 (2H, t, *J* = 2.8 Hz), 2.03 (1H, dd, *J* = 12.3, 6.0 Hz), 1.71 (1H, m), 1.59 (2H, m), 1.57 (1H, m), 1.54 (1H, m), 1.53 (1H, m), 1.42 (2H, m), 1.39 (1H, m), 1.26 (16H, m), 0.89 (3H, t, *J* = 7.0 Hz).

Methyl 5-[(1*R*,2*R*,3*S*,5*S*)-2-decyl-6-oxa-bicyclo[3.1.0]hex-3-yl]-5-[(*S*)-(3,3,3-trifluoro-2-methoxy-2-phenylpropionyloxy]pentanoate ((*S*)-26). To a solution of alcohol **25** (1.7 mg, 4.7 μmol) in CH_2ClCH_2Cl (800 μL), were added DMAP (34.0 mg, 282 μmol) and (*S*)-(+)-MTPA-Cl (26.2 μL, 141 μmol). After stirring at rt for 30 min, the reaction mixture was diluted with Et_2O, washed with water and saturated aqueous NaCl, dried over $MgSO_4$, and concentrated under reduced pressure. The crude product was used next reaction without purification.

A solution of the above crude ester in MeOH (200 μL) in the presence of 10% Pd on C (0.5 mg) was stirred at rt for 2 h under a hydrogen atmosphere. The reaction mixture was diluted with Et_2O and filtered through silica gel and the filtrate was concentrated under reduced presser. The residue was purified by silica gel thin layer chromatography (hexane : AcOEt = 3 : 1) to give (*S*)-MTPA ester (*S*)-**26** (0.7 mg, 25% yield, two steps) as a colorless oil: $[\alpha]_D^{31}$ -26.2° (*c* 0.45, $CHCl_3$); IR (neat) cm^{-1}: 2925, 2854, 1742; ^{1}H-NMR (400 MHz, $CDCl_3$) δ : 7.52 (2H, m), 7.40 (3H, m), 5.17 (1H, m), 3.66 (3H, s), 3.49 (3H, s), 3.39 (1H, d, *J* = 2.1 Hz), 3.35 (1H, d, *J* = 2.6 Hz), 2.28 (2H, t, *J* = 7.0 Hz), 2.06 (1H, dd, *J* = 13.1, 6.8 Hz), 1.65 (1H, m), 1.60 (1H, dd, *J* = 16.9, 7.5 Hz), 1.57 (1H, m), 1.54 (1H, m), 1.49 (1H, m), 1.45 (2H, m), 1.27 (18H, m), 0.88 (3H, t, *J* = 6.7 Hz); ^{13}C-NMR (100 MHz, $CDCl_3$) δ : 173.3, 166.2, 132.0, 129.6, 128.5, 127.5, 75.5, 58.6, 55.6, 55.3, 51.6, 42.4, 41.6, 33.4, 32.5, 31.9, 29.8, 29.6, 29.5, 29.3, 28.2, 27.9, 22.7, 20.9, 14.1; ESIMS *m/z*: 593 (M^++Na, 88), 315 (10), 319 (100); HRESIMS *m/z*: 593.3068 (Calcd for $C_{31}H_{45}O_6F_3Na$: M^++Na, 593.3066).

Methyl 5-[(1*R*,2*R*,3*S*,5*S*)-2-decyl-6-oxa-bicyclo[3.1.0]hex-3-yl]-5-[(*R*)-(3,3,3-trifluoro-2-methoxy-2-

phenylpropionyloxy]pentanoate ((*R*)-26). To a solution of alcohol **25** (0.9 mg, 2.5 μmol) in CH_2ClCH_2Cl (400 μL), were added DMAP (18.1 mg, 148 μmol) and (*R*)-(-)-MTPA-Cl (14.0 μL, 74.1 μmol). After stirring at rt for 30 min, the reaction mixture was diluted with Et_2O, washed with water and saturated aqueous NaCl, dried over $MgSO_4$, and concentrated under reduced pressure. The crude product was used next reaction without purification.

A solution of the above crude ester in MeOH (100 μL) in the presence of 10% Pd on C (0.3 mg) was stirred at rt for 2 h under a hydrogen atmosphere. The reaction mixture was diluted with Et_2O and filtered through silica gel and the filtrate was concentrated under reduced pressure. The residue was purified by silica gel thin layer chromatography (hexane : AcOEt = 3 : 1) to give (*R*)-MTPA ester (*R*)-**26** (0.9 mg, 64% yield, two steps) as a colorless oil: $[\alpha]_D^{31}$ -61.1° (*c* 0.45, $CHCl_3$); IR (neat) cm^{-1}: 2925, 2854, 1743; ^{1}H-NMR (400 MHz, $CDCl_3$) δ : 7.54 (2H, m), 7.40 (3H, m), 5.17 (1H, m), 3.67 (3H, s), 3.54 (3H, s), 3.35 (1H, d, *J* = 2.6 Hz), 3.30 (1H, d, *J* = 2.8 Hz), 2.31 (2H, t, *J* = 2.8 Hz), 2.03 (1H, dd, *J* = 12.3, 6.0 Hz), 1.71 (1H, m), 1.59 (2H, m), 1.57 (1H, m), 1.54 (1H, m), 1.53 (1H, m), 1.42 (2H, m), 1.39 (1H, m), 1.26 (16H, m), 0.89 (3H, t, *J* = 6.7 Hz); ^{13}C-NMR (100 MHz, $CDCl_3$) δ : 173.3, 166.2, 132.2, 129.6, 128.4, 127.3, 75.3, 58.6, 55.7, 55.4, 51.6, 42.2, 41.4, 33.4, 32.6, 31.9, 29.9, 29.6, 29.6, 29.5, 29.4, 28.2, 27.6, 22.7, 21.1, 14.1; ESIMS *m/z*: 571 (M^++H, 30), 319 (100); HRESIMS *m/z*: 571.3237 (Calcd for $C_{31}H_{46}O_6F_3$: M^++H, 571.3246).

(*S*)-6-{(1*S*,2*S*,3*R*,5*S*)-2-[(1*E*,4*Z*,6*E*,8*S*)-8-Hydroxydeca-1,4,6-trienyl]-6-oxabicyclo[3.1.0]hex-3-yl}-tetrahydropyran-2-one (agadhilactone) (27). To a solution of lactone **23** (7.0 mg, 18.7 μmol) in THF (400 μL), was added NaOH (1 M aqueous solution, 187 μL, 187 μmol). After stirring at rt for 4 h, saturated aqueous NH_4Cl was added. The reaction mixture was diluted with AcOEt, washed with water and saturated aqueous NaCl, dried over $MgSO_4$, and concentrated under reduced pressure. The crude carboxylic acid was used next reaction without purification.

To a solution of the above crude carboxylic acid in CH_2Cl_2 (900 μL), were added DMAP (0.5 mg, 4.09 μmol) and DCC (4.6 mg, 22.3 μmol). After stirring at rt for 30 min, the reaction mixture was diluted with Et_2O, filtered through silica gel and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane : AcOEt = 2 : 3) to give agardhilactone (**27**) (5.0 mg, 90% yield, two steps) as colorless oil: $[\alpha]_D^{31}$ -104.4° (c 0.09, $CHCl_3$); IR (neat) cm^{-1}: 3442, 2958, 1733; ^{1}H-NMR (400 MHz, $CDCl_3$) δ : 6.49 (1H, m), 6.05 (1H, t, *J* = 11.0 Hz), 5.70 (1H, dd, *J* = 15.1, 6.8 Hz), 5.64 (1H, m), 5.42 (2H, m), 4.24 (1H, dt, *J* = 11.7, 2.8 Hz), 4.10 (1H, m), 3.46 (1H, br s), 3.40 (1H, m), 2.94 (2H, dd, *J* = 7.4, 6.3 Hz), 2.72 (1H, t, *J* = 8.9 Hz), 2.61 (1H, m), 2.42 (1H, ddd, *J* = 17.7, 9.2, 7.3 Hz), 2.12 (1H, dd, *J* = 13.5, 7.5 Hz), 1.94-1.70 (4H, m), 1.65-1.49 (5H, m), 0.94 (3H, t, *J* = 7.4 Hz); ^{13}C-NMR (100 MHz, $CDCl_3$) δ : 171.8, 136.4, 131.3, 129.3, 129.0, 128.7, 125.5, 78.5, 74.0, 60.2, 55.7, 44.6, 43.2, 30.9, 30.2, 29.5, 27.5, 27.2, 18.8, 9.7; ESIMS *m/z*: 355 (M^++Na, 100); HRESIMS *m/z*: 355.1877 (Calcd for $C_{20}H_{28}O_4Na$: M^++Na, 355.1885).

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