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Synthesis and structural revision of marine eicosanoid agardhilactone

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Abstract—Synthesis of the marine eicosanoid agardhilactone has been achieved. The relative and absolute configuration of agardhilactone was successfully determined.

Marine eicosanoids are of interest given their unique structures, peculiar biosynthetic pathways, and biological activities.[1] Agardhilactone, first isolated from the marine red algae *Agardhiella subulata* by Gerwick et al., is a novel tricyclic eicosanoid containing δ-lactone, cyclopentane, and epoxide rings (Fig. 1).[2] Initial structural reports were based on the NMR analysis of agardhilactone acetate, derived from agardhilactone. However, the complete structure of agardhilactone was not determined since agardhilactone is a particle constituent. The relative configuration (C-6, C-8, C-9, and C-10) of the cyclopentane ring system was determined to be 6*S**, 8*R**, 9*S**, and 10*R**, based on coupling constants and the NOESY analysis of agardhilactone acetate. To date, 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 methoxycarbonyl derivative. Although the precise biological function of agardhilactone has not been reported, given its structural characteristics the eicosanoid might be an inhibitor of phospholipase A_2.[1]

Numerous attempts have been made to synthesize carbocyclic eicosanoids, prompted by their unique structural features and potential biological significance.[1] The authors previously reported on the synthesis of the carbocyclic eicosanoids, constanolactone[3] and bacillariolide.[4] To date, the total synthesis of agardhilactone has not been reported. The synthesis of agardhilactone was therefore conducted in the present study so as to clarify its structure.

The authors began by synthesizing the model compounds **1**–**4** of agardhilactone in an effort to determine the relative configuration at C-5 and to confirm the relative configuration at C-6, C-8, C-9, and C-10 (Fig. 1). The model compounds **1**–**4** correspond to four diastereomers of 16,17-dihydro-18-dehydroxyagardhilactone.

The model compounds **1**–**4** were, respectively, synthesized from 4-vinyldihydrofuran-2-one (**5**).[5] The lactone **5** was treated with LDA and then 3-iodopropene to give *trans*-lactone **6** as a single compound (Scheme 1). The relative configuration of *trans*-lactone **6** was determined by NOESY. *trans*-Configuration of two side chains was

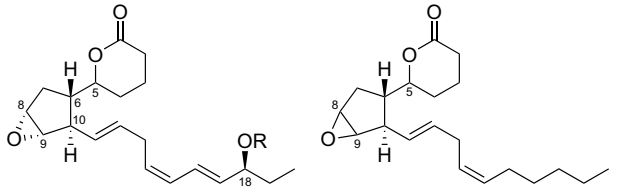

Figure 1. Proposed structure of agardhilactone and structure of model compounds.

Keywords: Agardhilactone; Marine eicosanoid; Structural revision.
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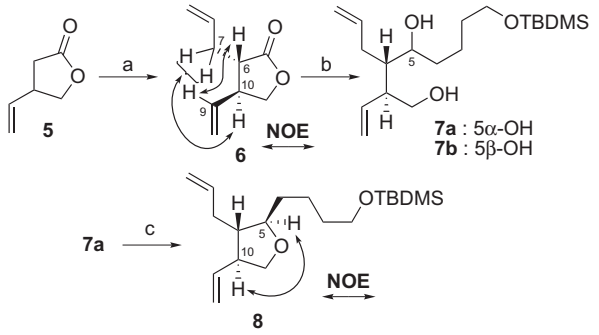
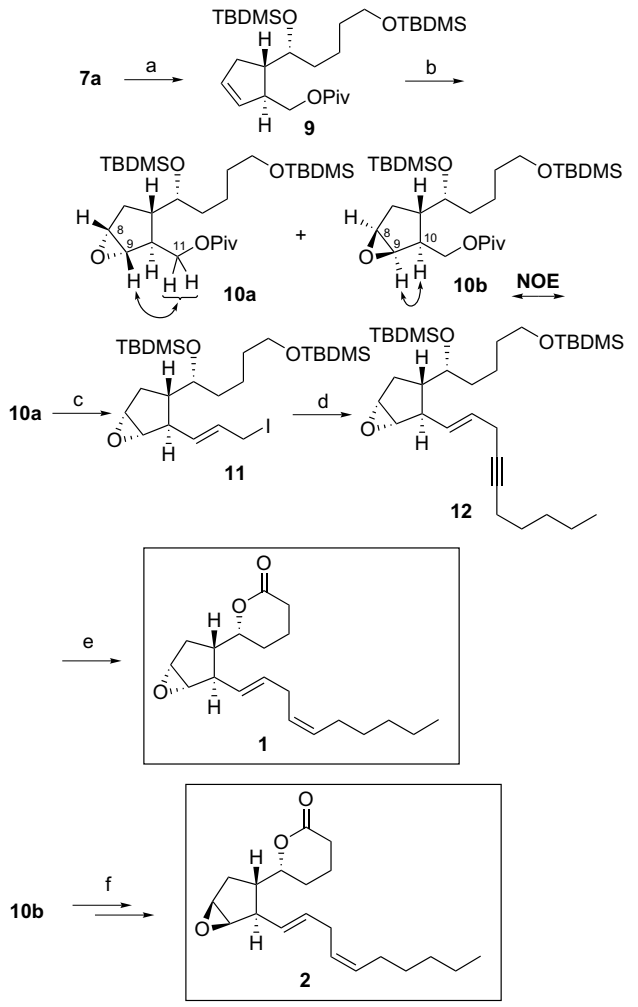


Scheme 1. Reagents and conditions: (a) LDA, 3-iodopropene, THF, −78 °C to rt, 74%; (b) (i) DIBALH, CH_2Cl_2, −78 °C, 98%, (ii) $TBDMSOCH_2CH_2CH_2CH_2MgI$, DME, 0 °C, 73% (**7a**), 25% (**7b**); (c) TsCl, DABCO, AcOEt, 0 °C, 71%.

indicated by the NOE correlation between H-6 and H-9 and between H-7 and H-10. Lactone **6** was reduced to hemiacetal with DIBALH and the hemiacetal was then treated with Grignard reagent ($TBDMSOCH_2CH_2CH_2CH_2MgI$)[6] in DME to afford a mixture of α-alcohol **7a** and β-alcohol **7b** (**7a**/**7b** = 3:1), which were readily separated by silica gel chromatography. 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 toluenesulfonyl chloride (TsCl) and 1,4-diazabicyclo[2.2.2]octane (DABCO) in AcOEt to give tetrahydrofuran **8**. The NOE correlation between H-5 and H-10 in tetrahydrofuran **8** indicated the relative configuration at C-5 and C-10 to be that as shown in Scheme 1. An α-configuration of the hydroxy group at C-5 was found for **7a**, while a β-configuration of the hydroxy group at C-5 was found for **7b**, a diastereomer of **7a**.

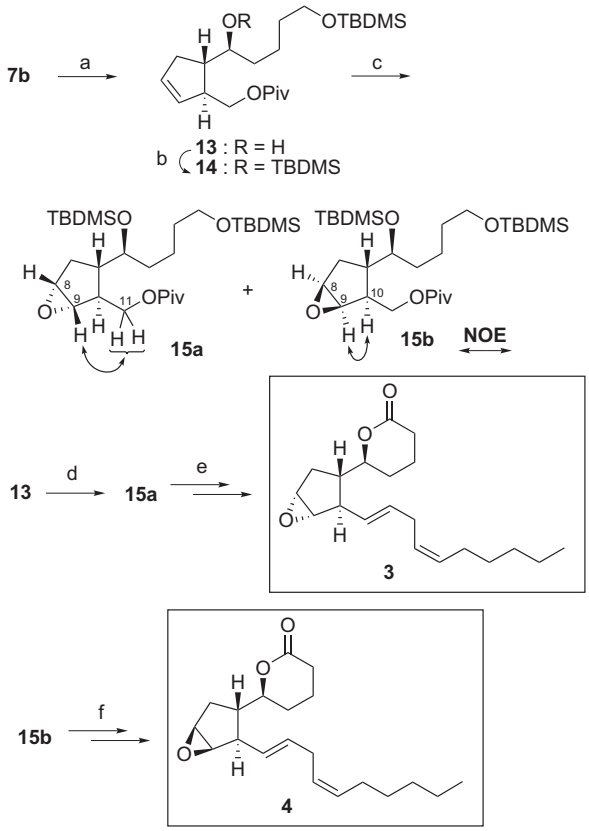
The ring-closing metathesis (RCM) reaction of α-alcohol **7a** with 1st generation Grubbs' catalyst[7] in CH_2Cl_2 afforded the cyclopentene derivative (Scheme 2). The primary hydroxy group of the cyclopentene derivative was protected as the pivalate, while the secondary hydroxy group was protected as the TBDMS ether to give cyclopentene **9**. Epoxidation of cyclopentene **9** with *m*-chloroperbenzoic acid (*m*CPBA) 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[8] 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 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



Scheme 2. Reagents and conditions: (a) (i) Grubbs' catalyst 1st generation, CH_2Cl_2, rt, 99%, (ii) PivCl, pyridine, CH_2ClCH_2Cl, 0 °C to rt, 82%, (iii) TBDMSCl, imidazole, DMF, 45 °C, 99%; (b) *m*CPBA, Na_2HPO_4, CH_2Cl_2, 0 °C to rt, 23% (**10a**), 77% (**10b**); (c) (i) DIBALH, CH_2Cl_2, −78 °C, 87%, (ii) Dess–Martin periodinane, $NaHCO_3$, CH_2Cl_2, rt, then $Ph_3P{=}CHCO_2Me$, reflux, 61%, (iii) DIBALH, CH_2Cl_2, −78 °C, 79%, (iv) Ts_2O, pyridine, CH_2Cl_2, rt, then NaI, acetone, rt, 72%; (d) hept-1-yne, CuI, NaI, K_2CO_3, DMF, rt, 63%; (e) (i) TBAF, DMF, 40 °C, 73%, (ii) TPAP, NMO, MS 4 Å, CH_2ClCH_2Cl, rt, 60%, (iii) H_2, 5% Pd on $BaSO_4$, quinoline, MeOH, rt, 79%; (f) (i) DIBALH, CH_2Cl_2, −78 °C, 90%, (ii) Dess–Martin periodinane, $NaHCO_3$, CH_2Cl_2, rt, then $Ph_3P{=}CHCO_2Me$, reflux, 86%, (iii) DIBALH, CH_2Cl_2, −78 °C, 77%, (iv) Ts_2O, pyridine, CH_2Cl_2, rt, then NaI, acetone, rt, 64%, (v) hept-1-yne, CuI, NaI, K_2CO_3, DMF, rt, 79%, (vi) TBAF, DMF, 40 °C, 69%, (vii) TPAP, NMO, MS 4 Å, CH_2ClCH_2Cl, rt, 70%, (viii) H_2, 5% Pd on $BaSO_4$, quinoline, MeOH, rt, 71%.

and gave enyne **12**.[9] The protective groups of the two hydroxy groups were removed by treatment with tetrabutylammonium fluoride (TBAF) to give the diol. The diol was treated with tetrapropylammonium perruthenate (TPAP) and 4-methylmorpholine *N*-oxide (NMO) to give the δ-lactone.[10] Finally, alkyne hydrogenation with 5% Pd on $BaSO_4$ in the presence of quinoline afforded model compound **1**.[11] Model compound **2** was synthesized from β-epoxide **10b** in a similar manner as described above.

Model compounds **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**. Epoxidation of cyclopentene **14** using *m*CPBA afforded predominantly β-epoxide **15b** (α-epoxide **15a**/**15b** = 1:15). The mixture of the two diastereomers was separated by silica gel chromatography. 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. The epoxide of **15b** was determined to be in the β-configuration from the NOE



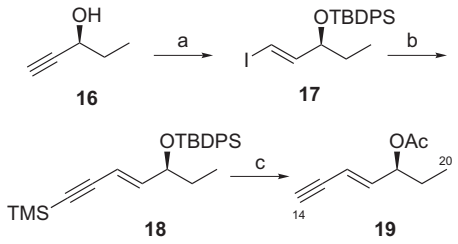
Scheme 3. Reagents and conditions: (a) (i) Grubbs' catalyst 1st generation, CH_2Cl_2, rt, 82%, (ii) PivCl, pyridine, CH_2ClCH_2Cl, 0 °C to rt, 86%; (b) TBDMSCl, imidazole, DMF, 45 °C, 94%; (c) *m*CPBA, Na_2HPO_4, CH_2Cl_2, 0 °C to rt, 6% (**15a**), 91% (**15b**); (d) (i) TBHP, $VO(acac)_2$, CH_2Cl_2, rt, 83%, (ii) TBDMSOTf, 2,6-lutidine, CH_2Cl_2, −78 °C, 88%; (e) (i) DIBALH, CH_2Cl_2, −78 °C, 84%, (ii) Dess–Martin periodinane, $NaHCO_3$, CH_2Cl_2, rt, then $Ph_3P{=}CHCO_2Me$, reflux, 83%, (iii) DIBALH, CH_2Cl_2, −78 °C, 90%, (iv) Ts_2O, pyridine, CH_2Cl_2, rt, then NaI, acetone, rt, 73%, (v) hept-1-yne, CuI, NaI, K_2CO_3, DMF, rt, 84%, (vi) TBAF, DMF, 40 °C, 40%, (vii) TPAP, NMO, MS 4 Å, CH_2ClCH_2Cl, rt, 64%, (viii) H_2, 5% Pd on $BaSO_4$, quinoline, MeOH, rt, 88%; (f) (i) DIBALH, CH_2Cl_2, −78 °C, 96%, (ii) Dess–Martin periodinane, $NaHCO_3$, CH_2Cl_2, rt, then $Ph_3P{=}CHCO_2Me$, reflux, 78%, (iii) DIBALH, CH_2Cl_2, −78 °C, 94%, (iv) Ts_2O, pyridine, CH_2Cl_2, rt, then NaI, acetone, rt, 62%, (v) hept-1-yne, CuI, NaI, K_2CO_3, DMF, rt, 60%, (vi) TBAF, DMF, 40 °C, 69%, (vii) TPAP, NMO, MS 4 Å, CH_2ClCH_2Cl, rt, 40%, (viii) H_2, 5% Pd on $BaSO_4$, quinoline, MeOH, rt, 80%.

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 $VO(acac)_2$[12] to give the α-epoxide as the sole product. The hydroxy group in the α-epoxide was protected as the TBDMS ether to afford α-epoxide **15a**. α-Epoxide **15a** and β-epoxide **15b** were converted to model compounds **3** and **4**, respectively, according to the aforementioned established method.

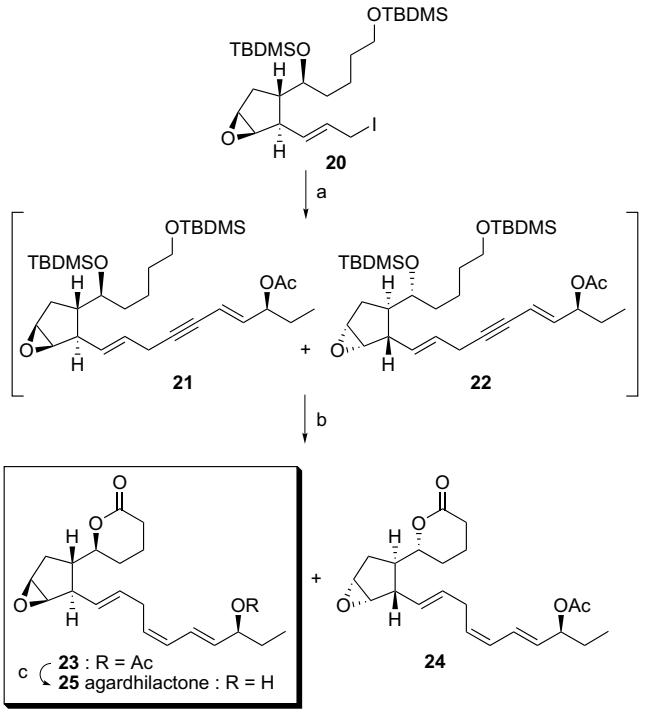
The NMR spectra of synthesized model compounds **1**–**4**[13] were compared with those of agardhilactone acetate.[2] The NMR spectrum of **4** most closely resembled that of agardhilactone acetate.[2] Therefore, the relative configuration of agardhilactone was estimated to be 5*S**, 6*S**, 8*S**, 9*R**, and 10*R**. On the basis of this result, the authors examined the synthesis of natural agardhilactone.

The 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**. The coupling reaction of *E*-iodoalkene **17** and (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 acetylated to afford acetate **19**.

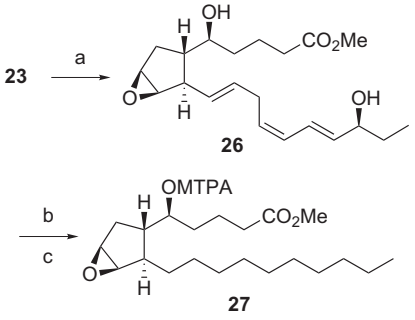
The coupling reaction of enyne **19** and allylic iodide **20**, which was a synthetic intermediate of model compound **4**, was achieved by treatment with CuI, NaI, and K_2CO_3 and gave a mixture of dienynes **21** and **22** (Scheme 5). Without purifying the mixture, the two TBDMS groups in dienynes **21** and **22** were removed by treatment with TBAF to give the corresponding diols. The diols were treated with TPAP and NMO to give the δ-lactones. Partial hydrogenation of the alkynes with 5% Pd on $BaSO_4$ in the presence of quinoline afforded the diastereomeric mixture of *E*,*Z*,*E*-trienes **23** and **24**. Separation of the diastereomeric mixture using a chiral HPLC column gave acetates **23** and **24**.[18] The spectral data of acetate **23** were identical to those of agardhilactone acetate.[2] The absolute configuration of acetate **23** was determined using a modified Mosher method[19] for



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



Scheme 5. Reagents and conditions: (a) **19**, CuI, NaI, K_2CO_3, DMF, rt, 90% (**21** and **22**); (b) (i) TBAF, DMF, 60 °C, 56%, (ii) TPAP, NMO, MS 4 Å, CH_2ClCH_2Cl, rt, 67%, (iii) H_2, 5% Pd on $BaSO_4$, quinoline, MeOH, rt, then separation by HPLC, 19% (**23**), 17% (**24**); (c) (i) NaOH aq, THF, rt, (ii) DCC, DMAP, CH_2Cl_2, rt, 90% (two steps).



Scheme 6. Reagents and conditions: (a) K_2CO_3, MeOH, rt, 60%; (b) (i) (*S*)-MTPACl, DMAP, CH_2ClCH_2Cl, rt, (ii) H_2, 10% Pd on C, MeOH, rt, 25% (two steps); (c) (i) (*R*)-MTPACl, DMAP, CH_2ClCH_2Cl, rt, (ii) H_2, 10% Pd on C, MeOH, rt, 64% (two steps).

MTPA **27**, which was derived from **23** via diol **26** (Scheme 6). Saponification of acetate **23** followed by lactonization of the resulting dihydroxycarboxylic acid yielded lactone **25**.[20] The spectral data of **25** were identical to those of agardhilactone.[2] Therefore, the absolute configuration of agardhilactone was determined to be 5*S*, 6*S*, 8*S*, 9*R*, 10*R*, and 18*S*.

Acknowledgments

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13. Compound **1**: A colorless oil; IR (neat) cm^{-1}: 2926, 1737; ^1H 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).
Compound **2**: A colorless oil; IR (neat) cm^{-1}: 2925, 1738; ^1H 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).
Compound **3**: A colorless oil; IR (neat) cm^{-1}: 2925, 1737; ^1H 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).
Compound **4**: A colorless oil; IR (neat) cm^{-1}: 2925, 1739; ^1H 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).
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18. A mixture of triene **23** and **24** was separated by HPLC (CHIRALPAK AS-H, 0.46 cm×25 cm, hexane–isopropanol = 82:18, flow rate: 2.0 mL/min) to give triene **23** ($t_R = 20.2$ min) and triene **24** ($t_R = 28.2$ min).
Compound **23**: $[\alpha]_D^{20}$ −179.6 (*c* 0.52, $CHCl_3$); IR (neat) cm^{-1}: 2924, 1734; ^1H 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).
Compound **24**: $[\alpha]_D^{24}$ +165.2 (*c* 0.50, $CHCl_3$); IR (neat) cm^{-1}: 2925, 1733; ^1H 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).
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20. Agardhilactone (**25**): $[\alpha]_D^{31}$ −104.4 (*c* 0.09, $CHCl_3$); IR (neat) cm^{-1}: 3442, 2958, 1733; ^1H 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).