Supporting Information

A total synthesis of galbonolide B.

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General information and instrumentation

All reactions were conducted under an atmosphere of nitrogen unless otherwise stated. Solvents were purified under nitrogen as follows: dichloromethane and ^{t}butyl methyl ether from calcium hydride: diethyl ether, THF and dimethoxyethane from sodium wire/benzophenone: distilled petrol ether 40-60ºC.

Thin layer chromatography was performed on glass plates pre-coated with silica gel 60 F_{254}. Visualisation was achieved with U.V. florescence (254nm) or by staining with a potassium permanganate dip. Flash column was carried out using silica gel 60 (40-63µm).

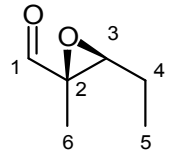
Infrared spectra were recorded as either an evaporated film or liquid film on sodium chloride plates. Absorption maxima are reported in wave numbers (cm^{-1}).

Mass spectrometry data (EI) were recorded double focussing spectrometers. Only molecular ions, fractions from molecular ions and other major peaks are reported as mass/charge (m/z) ratios.

Proton nuclear magnetic resonance spectra were recorded at 300MHz (at ambient probe temperature). Using residual isotopic solvent ($CHCl_3$, δ_H = 7.27ppm) as an internal reference. Chemical shifts are quoted in parts per million (ppm). Coupling constants (J) are recorded in Hertz (Hz). Carbon nuclear magnetic

resonance spectra were recorded at 75MHz and are proton decoupled. Using residual isotopic solvent ($CHCl_3$, δ_C = 77.00ppm) as an internal reference. Carbon spectra assignments are supported by DEPT editing. Chemical shifts (δ_C) are quoted in ppm.

(2*R*,3*S*)-3-Ethyl-2-methyl-oxirane-2-carbaldehyde **(6)**



To solution of ((2*S*,3*S*)-3-ethyl-2-methyl-oxiranyl)-methanol (29 g, 0.25 mol) in CH_2Cl_2 (180 mL) at 0°C was added dimethyl sulfoxide (177 mL, 2.50 mol) and triethylamine (174 mL, 1.25 mol). Sulfur trioxide pyridine complex (198 g, 1.25 mol) was added in portions to the reaction mixture at 0°C over 1 hour. After the addition the brown reaction mixture was stirred for a further 30 minutes where it was then diluted with diethyl ether (250 mL) and H_2O (250 mL). The phases were separated and the aqueous phase was extracted with diethyl ether (3 x 300 mL). The combined organic extracts were washed with saturated aqueous sodium hydrogen carbonate (200 mL), brine (200 mL), dried over magnesium sulfate then filtered and partially concentrated under reduced pressure. The crude product was absorbed onto flash silica gel and was purified by flash column chromatography eluting with 20% diethyl ether / pentane. The solvent was partially removed under reduced pressure to afford the title compounds **(6)** in a pale yellow solution (24.5 g, 8:2 product:diethyl ether, therefore 19.5 g, 68%).

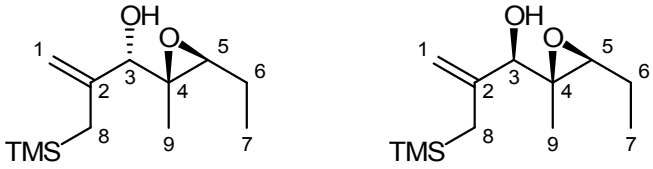
TLC, (50% diethyl ether / petrol) R_f = 0.59; $[\alpha]^{22}_D$ +89 (*c* 2.15 in $CHCl_3$); ν_{max} (film/cm^{-1}) 3411 (s), 2969 (m), 2924 (m), 1728 (m), 1647 (w), 1459 (w), 1382 (w), 1316 (w), 1253 (w), 1074 (s), 958 (w), 879 (w), 823 (w); δ_H (300 MHz, $CDCl_3$) 8.86 (1H, s), 3.11 (1H, t, *J*=6.2 Hz), 1.80-1.56 (2H, m), 1.40 (3H, s), 1.08 (3H, t, *J*=7.5 Hz); δ_C (75.5 MHz, $CDCl_3$) 200.4, 62.5, 61.1, 21.5, 14.4, 10.5.

(*S*)-1-((2*S*,3*S*)-3-Ethyl-2-methyl-oxiranyl)-2-trimethylsilanylmethyl-prop-2-en-1-ol

(6a)

(*R*)-1-((2*S*,3*S*)-3-Ethyl-2-methyl-oxiranyl)-2-trimethylsilanylmethyl-prop-2-en-1-ol

(6a')



To a solution of *tert*-butyllithium (250 mL, 0.376 mol, 1.5 M in pentane) at -78°C was slowly added a solution of (2-bromo-allyl)-trimethyl-silane (36.3 g, 0.188 mol) in diethyl ether (200 mL). After stirring for 1 hour at -78°C a solution of aldehyde **(6)** (19.5 g, 0.171 mol) in diethyl ether (150 mL) was added dropwise. The reaction mixture was stirred for 3 hours over which time it was allowed to warm to -40°C. The reaction was quenched with a solution of acetic acid (6 mL) in diethyl ether (60 mL) at -78°C then allowed to warm and a solution of saturated aqueous sodium hydrogen carbonate (300 mL) was added. The phases were separated and the aqueous phase was extracted with diethyl ether (3 x 200 mL). The combined organic extracts were washed brine (100 mL) then dried over magnesium sulfate, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography, eluting with a gradient of 5% diethyl ether / petrol to 20% diethyl ether / petrol, to afford the title compounds **(6a)** as a pale yellow oil (10.4 g, 27%) and **(6a')** as a pale yellow oil (12.5 g, 32%).

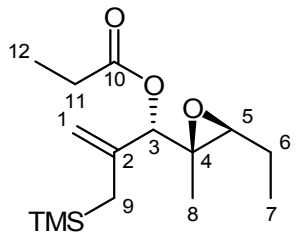
(6a)

TLC, (20% diethyl ether / petrol) R_f = 0.22; $[\alpha]^{23}_D$ +53 (*c* 1.10 in $CHCl_3$); ν_{max} (film/cm^{-1}) 3465 (br), 2956 (s), 2895 (m), 2878 (m), 1714 (w), 1637 (m), 1459 (m), 1419 (m), 1383 (m), 1248 (s), 1163 (m), 1059 (m), 971 (w), 938 (w), 888 (s), 850 (s), 770 (w), 715 (m), 693 (m); δ_H (300 MHz, $CDCl_3$) 4.93 (1H, s), 4.78 (1H, s), 3.90 (1H, s), 3.07 (1H, t, *J*=6.4 Hz), 2.21 (1H, t, *J*=1.9 Hz), 1.71-1.49 (4H, m), 1.23 (3H, s), 1.03 (3H, t, *J*=7.5 Hz), 0.03 (9H, s); δ_C (75.5 MHz, $CDCl_3$) 145.7, 110.5, 77.2, 62.2, 61.0, 23.1, 21.5, 14.2, 10.5, -1.2; *m/z* (EI) 170 (11%), 155 (M^+-TMS, 23), 141 (17), 127 (23), 75 (57), 73 (TMS^+, 100), 43 (27); HRMS (ESI): calcd. for $C_{12}H_{24}O_2SiNa$ $[M + Na]^+$ 251.1438, found 251.1425;

(6a')

TLC, (20% diethyl ether / petrol) R_f = 0.19; $[\alpha]^{23}_D$ +20 (*c* 1.13 in $CHCl_3$); ν_{max} (film/cm^{-1}) 3459 (br), 2956 (s), 2896 (m), 2878 (m), 1715 (w), 1638 (m), 1459 (m), 1419 (m), 1384 (m), 1248 (s), 1160 (m), 1043 (s), 971 (w), 920 (m), 889 (s), 848 (s), 783 (w), 716 (m), 693 (m), 663 (w); δ_H (300 MHz, $CDCl_3$) 5.06 (1H, s), 4.75 (1H, s), 3.59 (1H, d, *J*=2.3 Hz), 2.91 (1H, t, *J*=6.4 Hz), 1.82-1.38 (4H, m), 1.18 (3H, s), 1.02 (3H, t, *J*=7.4 Hz), 0.00 (9H, s); δ_C (75.5 MHz, $CDCl_3$) 144.7, 108.9, 79.1, 63.9, 63.3, 23.0, 21.4, 11.2, 10.4, -1.3; *m/z* (EI) 170 (13%), 155 (M^+-TMS, 36), 127 (31), 75 (75), 73 (TMS^+, 100), 43 (51); HRMS (ESI): calcd. for $C_{12}H_{24}O_2SiNa$ $[M + Na]^+$ 251.1438, found 251.1423.

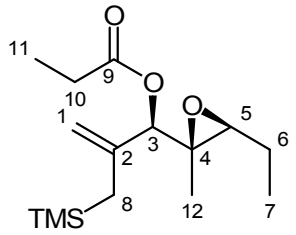
Propionic acid (*S*)-1-((2*R*,3*S*)-3-ethyl-2-methyl-oxiranyl)-2-trimethylsilanylmethyl-allyl ester **(7)**



To a solution of alcohol **(6a)** (19.4 g, 84.9 mmol) in CH_2Cl_2 (350 mL) was added pyridine (13.7 mL, 169.9 mmol) and 4-dimethylaminopyridine (0.5 g , 4.2 mmol) followed by the dropwise addition of propionyl chloride (14.8 mL, 169.9 mmol). The reaction mixture was stirred at room temperature for 6 hours where it was then quenched with saturated aqueous sodium hydrogen carbonate (100 mL) and the phases separated. The aqueous phase was extracted with CH_2Cl_2 (3 x 100 mL) and the combined organic extracts were washed brine (100 mL). The organic phase was then dried over magnesium sulfate, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography, eluting with a gradient of 5% diethyl ether / petrol to 10% diethyl ether / petrol, to afford the title compound **(7)** as a colourless oil (17.8 g, 74%).

TLC, (10% diethyl ether / petrol) R_f = 0.48; $[\alpha]^{25}_D$ -72 (*c* 1.05 in $CHCl_3$); ν_{max} (film/cm^{-1}) 3464 (br), 2970 (s), 2955 (s), 2892 (m), 2880 (m), 1746 (s), 1638 (m), 1462 (m), 1422 (m), 1384 (m), 1365 (m), 1249 (s), 1180 (s), 1082 (m), 1031 (m), 1019 (m), 985 (w), 928 (w), 887 (s), 850 (s), 772 (w), 717 (w), 695 (w), 659 (w); δ_H (300 MHz, $CDCl_3$) 4.89 (1H, bs), 4.85 (1H, bs), 4.77 (1, bs), 2.84 (1H, t, *J*=6.4 Hz), 2.37 (2H, q, *J*=7.5 Hz), 1.66-1.48 (4H, m), 1.22 (3H, s), 1.16 (3H, t, *J*=7.6 Hz), 1.01 (3H, t, *J*=7.5 Hz), 0.04 (9H, s); δ_C (75.5 MHz, $CDCl_3$) 172.8, 142.7, 109.6, 79.0, 62.3, 60.1, 27.7, 23.3, 21.6, 12.7, 10.3, 9.2, -1.3; HRMS (ESI): calcd. for $C_{15}H_{28}O_3SiNa$ $[M + Na]^+$ 307.1700, found 307.1693.

Propionic acid (*R*)-1-((2*R*,3*S*)-3-ethyl-2-methyl-oxiranyl)-2-trimethylsilanylmethyl-allyl ester **(8)**



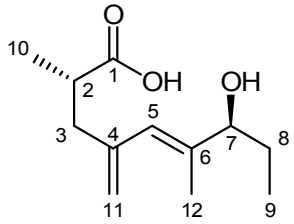
To a solution of alcohol **(6a')** (30.0 g, 131.3 mmol) in CH_2Cl_2 (500 mL) was added pyridine (21.2 mL, 262.7 mmol) and 4-dimethylaminopyridine (0.8 g , 6.6 mmol) followed by the dropwise addition of propionyl chloride (22.8 mL, 262.7 mmol). The reaction mixture was stirred at room temperature for 6 hours where it was then quenched with saturated aqueous sodium hydrogen carbonate (200 mL) and the phases separated. The aqueous phase was extracted with CH_2Cl_2 (3 x 200 mL) and the combined organic extracts were washed brine (200 mL). The organic phase wash then dried over magnesium sulfate, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography, eluting with gradient of 5% diethyl ether / petrol to 10% diethyl ether / petrol, to afford the title compound **(8)** as a colourless oil (33.1 g, 89%).

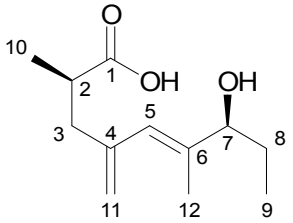
TLC, (10% diethyl ether / petrol) R_f = 0.39; $[\alpha]^{26}_D$ +89 (*c* 0.99 in $CHCl_3$); ν_{max} (film/cm^{-1}) 3464 (br), 2970 (s), 2955 (s), 2892 (m), 2880 (m), 1746 (s), 1638 (m), 1462 (m), 1422 (m), 1384 (m), 1365 (m), 1249 (s), 1180 (s), 1082 (m), 1031 (m), 1019 (m), 985 (w), 928 (w), 887 (s), 850 (s), 772 (w), 717 (w), 695 (w), 659 (w); δ_H

(300 MHz, $CDCl_3$) 4.86 (1H, bs), 4.78 (1H, bs), 4.72 (1H, bs), 2.89 (1H, t, *J*=6.4 Hz), 2.42 (2H, q, *J*=7.6 Hz), 1.72-1.48 (4H, m), 1.25 (3H, s), 1.17 (3H, t, *J*=7.6 Hz), 1.05 (3H, t, *J*=7.5 Hz), 0.06 (9H, s); δ_C (75.5 MHz, $CDCl_3$) 173.0, 142.4, 108.9, 80.5, 63.6, 60.7, 27.7, 23.6, 21.3, 12.2, 10.4, 9.1, -1.3; HRMS (ESI): calcd. for $C_{15}H_{28}O_3SiNa$ $[M + Na]^+$ 307.1700, found 307.1674.

(*E*)-(2*S*,7*S*)-7-Hydroxy-2,6-dimethyl-4-methylene-non-5-enoic acid **(9)**

(*E*)-(2*R*,7*S*)-7-Hydroxy-2,6-dimethyl-4-methylene-non-5-enoic acid **(10)**



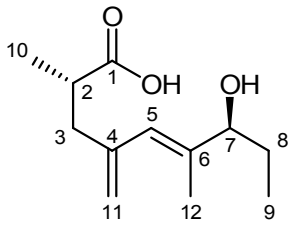


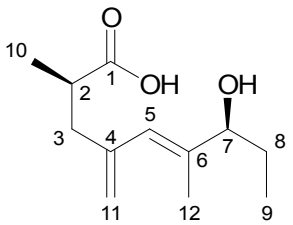
To a solution of di-*iso*-propylamine (0.19 mL, 2.2 mmol) in THF (4 mL) at 0°C was added *n*-butyllithium (0.80 mL, 2.0 mmol, 2.5 M in hexanes) and stirred for 10 minutes. The yellow solution was cooled to -78°C where ester **(7)** (284 mg, 1.0 mmol) in THF (2 mL) was added slowly. After stirring for 1 hour at -78°C a solution of *tert*-butyldimethylsilyl chloride (753 mg, 5.0 mmol) in THF (1 mL) was added. The pale yellow reaction mixture was allowed to warm to room temperature where it was then refluxed for 8 hours. After this time the dark yellow solution was cooled to room temperature, quenched with a saturated aqueous solution of ammonium chloride (5 mL) and stirred for 1 hour. The aqueous phase was extracted with CH_2Cl_2 (3 x 5 mL) and the combined organic extracts were then dried over magnesium sulfate, filtered and concentrated under reduced pressure. The residue was dissolved in THF (5 mL) and 2 M HCl (5 mL), stirred vigorously for 1 hour and then H_2O (10 mL) was added. The phases were separated and the aqueous phase extracted with CH_2Cl_2 (3 x 5 mL). The combined organic extracts were washed with 1 M sodium hydroxide (3 x 5 mL). The basic extracts were washed with CH_2Cl_2 (3 mL) and then acidified to pH 3 with conc. HCl to give a milky suspension. The suspension was extracted with CH_2Cl_2 (4 x 5 mL) and the combined organic extracts washed with brine (2 mL), dried over magnesium sulfate, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography,

eluting with a gradient of 70% diethyl ether / petrol to 100% diethyl ether, to afford the title compound **(9 + 10)** as a yellow gum (146 mg, 51%).

TLC, (90% diethyl ether / petrol) R_f = 0.20; ν_{max} (film/cm^{-1}) 3405 (br), 2967 (s), 2936 (s), 2877 (m), 1708 (s), 1632 (m), 1459 (m), 1379 (w), 1337 (w), 1248 (m), 1194 (m), 1092 (w), 1050 (w), 992 (m), 963 (w), 901 (m), 854 (m); δ_H (300 MHz, $CDCl_3$) **(9)** 6.20 (1H, bs), 5.76 (1H, bs), 5.07 (1H, bs), 4.89 (1H, bs), 3.95 (1H, t, *J*=6.7 Hz), 2.59-2.46 (2H, m), 2.24-2.14 (1H, m), 1.73 (3H, s), 1.65-1.53 (3H, m), 1.13 (3H, d, *J*=6.6 Hz), 0.86 (3H, t, *J*=7.4 Hz); **(10)** 6.20 (1H, bs), 5.76 (1H, bs), 5.07 (1H, bs), 4.89 (1H, bs), 3.95 (1H, t, *J*=6.7 Hz), 2.59-2.46 (2H, m), 2.24-2.14 (1H, m), 1.73 (3H, s), 1.65-1.53 (3H, m), 1.13 (3H, d, *J*=6.6 Hz), 0.86 (3H, t, *J*=7.4 Hz); δ_C (75.5 MHz, $CDCl_3$) **(9)** 181.7, 142.4, 140.5, 126.2, 116.0, 79.3, 41.5, 38.5, 27.6, 16.6, 13.0, 10.0; **(10)** 181.6, 142.2, 140.5, 126.1, 116.0, 79.3, 41.4, 38.2, 27.6, 16.3, 13.1, 10.0; *m/z* (EI) 3405 (br), 2967 (s), 2936 (s), 2877 (m), 1708 (s), 1632 (m), 1459 (m), 1379 (w), 1337 (w), 1248 (m), 1194 (m), 1092 (w), 1050 (w), 992 (m), 963 (w), 901 (m), 854 (m).

(*E*)-(2*S*,7*S*)-7-Hydroxy-2,6-dimethyl-4-methylene-non-5-enoic acid **(9)**
(*E*)-(2*R*,7*S*)-7-Hydroxy-2,6-dimethyl-4-methylene-non-5-enoic acid **(10)**





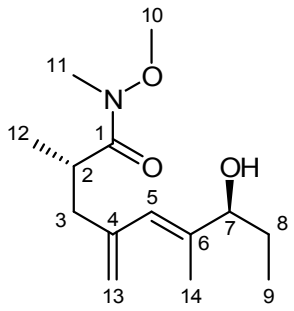
To a solution of di-*iso*-propylamine (3.3 mL, 38.7 mmol) in THF (85 mL) at 0°C was added *n*-butyllithium (22 mL, 35.1 mmol, 1.60 M in hexanes) and stirred for 10 minutes. The yellow solution was cooled to -78°C and DMPU (70 mL) was added. Ester **(8)** (5.0 g, 17.5 mmol) in THF (10 mL) was added slowly and the reaction mixture was stirred for 1 hour at -78°C. To this was added a solution of *tert*-butyldimethylsilyl chloride (13.2 g, 87.9 mmol) in THF (10 mL). The pale yellow solution was allowed to warm to room temperature where it was then refluxed for 8 hours. After this time the reaction mixture was cooled to room temperature,

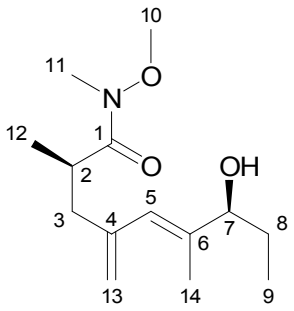
quenched with a saturated aqueous solution of ammonium chloride (50 mL) and stirred for 1 hour. The aqueous phase was extracted with CH_2Cl_2 (3 x 50 mL) and the combined organic extracts were then dried over magnesium sulfate, filtered and concentrated under reduced pressure. The residue was dissolved in THF (50 mL) and 2 M HCl (50 mL), stirred vigorously for 1 hour and then H_2O (100 mL) was added. The phases were separated and the aqueous phase extracted with CH_2Cl_2 (3 x 50 mL). The combined organic extracts were washed with 1 M sodium hydroxide (3 x 50 mL). The basic extracts were washed with CH_2Cl_2 (25 mL) and then acidified to pH 3 with conc. HCl to give a milky suspension. The suspension was extracted with CH_2Cl_2 (4 x 50 mL) and the combined organic extracts washed with brine (20 mL), dried over magnesium sulfate, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography, eluting with a gradient of 70% diethyl ether / petrol to 100% diethyl ether, to afford the title compound **(9 + 10)** as a yellow gum (3.58 g, 72%).

Spectroscopic data as above **(9)** and **(10).**

(*E*)-(2*S*,7*S*)-7-Hydroxy-2,6-dimethyl-4-methylene-non-5-enoic acid methoxy-methyl-amide **(9a)**

(*E*)-(2*R*,7*S*)-7-Hydroxy-2,6-dimethyl-4-methylene-non-5-enoic acid methoxy-methyl-amide **(10a)**





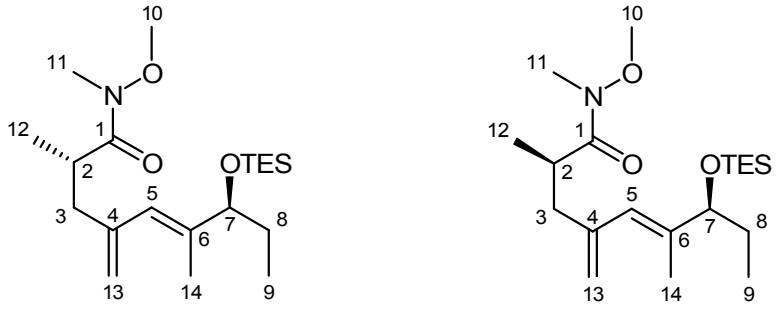
To a solution of acids **(9 + 10)** (5.5 g, 25.9 mmol) in CH_2Cl_2 (55 mL) at room temperature was added 1,1'-carbonyldiimidazole (4.2 g, 25.9 mmol) portionwise. After 20 minutes the effervescence had ceased and *N,O*-dimethylhydroxylamine hydrochloride (2.5 g, 25.9 mmol) was added. The resultant yellow solution stirred for 18 hours after which time a white precipitate had formed. The reaction mixture

was diluted with CH_2Cl_2 (50 mL) and washed with 0.25 M HCl (2 x 10 mL), saturated aqueous sodium hydrogen carbonate (2 x 10 mL) and then brine (10 mL). The organic phase was then dried over magnesium sulfate, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography, eluting with a gradient of 80% diethyl ether / petrol to 90% diethyl ether / petrol, to afford the title compounds **(9a + 10a)** as a pale yellow oil (5.5 g, 83%).

TLC, (90% diethyl ether / petrol) R_f = 0.31; δ_H (400 MHz, $CDCl_3$) **(9a)** 5.80 (1H, d, *J*=0.8 Hz), 5.08 (1H, bs), 4.88 (1H, s), 3.96 (1H, t, *J*=6.5 Hz), 3.66 (3H, s), 3.16 (3H, s), 3.07-2.92 (1H, m), 2.52 (1H, dd, J_{ABX}=13.9, 6.7 Hz), 2.11 (1H, dd, J_{ABX}=13.9, 7.3 Hz), 1.75 (3H, d, *J*=1.4 Hz), 1.60 (2H, dq, *J*=6.5, 7.4 Hz), 1.09 (3H, d, *J*=6.9 Hz), 0.89 (3H, t, *J*=7.4 Hz); **(10a)** 5.79 (1H, d, *J*=0.8 Hz), 5.08 (1H, bs), 4.88 (1H, s), 3.95 (1H, t, *J*=6.4 Hz), 3.66 (3H, s), 3.16 (3H, s), 3.07-2.92 (1H, m), 2.52 (1H, dd, J_{ABX}=13.9, 6.7 Hz), 2.11 (1H, dd, J_{ABX}=13.9, 7.3 Hz), 1.74 (3H, d, *J*=1.6 Hz), 1.60 (2H, dq, *J*=6.4, 7.4 Hz), 1.09 (3H, d, *J*=6.9 Hz), 0.88 (3H, t, *J*=7.4 Hz); δ_C (75.5 MHz, $CDCl_3$) **(9a)** 177.3, 142.8, 140.2, 126.1, 115.4, 78.8, 61.3, 41.4, 34.0, 32.1, 27.7, 17.0, 13.2, 9.9; **(10a)** 177.3, 142.6, 140.2, 126.3, 115.5, 79.2, 61.3, 41.4, 33.9, 32.1, 27.5, 17.0, 12.9, 10.0.

(*E*)-(2*S*,7*S*)-2,6-Dimethyl-4-methylene-7-triethylsilanyloxy-non-5-enoic acid methoxy-methyl-amide **(9b)**

(*E*)-(2*R*,7*S*)-2,6-Dimethyl-4-methylene-7-triethylsilanyloxy-non-5-enoic acid methoxy-methyl-amide **(10b)**



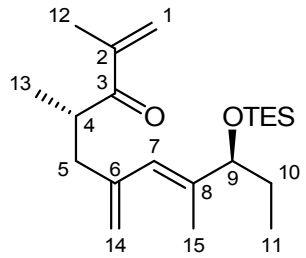
To a solution of alcohols **(9a + 10a)** (5.5 g, 21.5 mmol), triethylamine (6.0 mL, 43.1 mmol) and 4-dimethylaminopyridine (132 mg, 1.1 mmol) in CH_2Cl_2 (55 mL) was

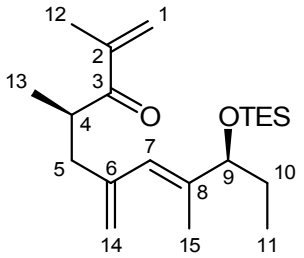
added triethylsilyl chloride (4.3 mL, 25.8 mmol). The reaction mixture was stirred at room temperature for 3 hours and then quenched with saturated aqueous ammonium chloride (50 mL). The phases were separated, the aqueous phase was extracted with CH_2Cl_2 (3 x 50 mL) and the combined organic extracts were washed brine (50 mL). The organic phase was then dried over magnesium sulfate, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography, eluting with 30% diethyl ether / petrol, to afford the title compounds **(9b + 10b)** as a colourless oil (7.6 g, 95%).

TLC, (30% diethyl ether / petrol) R_f = 0.34; δ_H (400 MHz, $CDCl_3$) **(9b)** 5.73 (1H, bs), 5.06 (1H, d, *J*=0.9 Hz), 4.88 (1H, bs), 3.92 (1H, t, *J*=6.3 Hz), 3.66 (3H, s,), 3.17 (3H, s), 3.06-2.92 (1H, m), 2.51 (1H, dd, J_{ABX}=13.6, 6.4 Hz), 2.09 (1H, dd, J_{ABX}=13.6, 8.2 Hz), 1.73 (3H, d, *J*=1.3 Hz), 1.53 (2H, dq, *J*=6.3, 7.4 Hz), 1.07 (3H, d, *J*=6.9 Hz), 0.94 (9H, t, *J*=8.0 Hz), 0.83 (3H, t, *J*=7.4 Hz), 0.58 (6H, q, *J*=8.0 Hz); **(10b)** 5.73 (1H, bs), 5.06 (1H, d, *J*=0.9 Hz), 4.88 (1H, bs), 3.91 (1H, t, *J*=6.3 Hz), 3.66 (3H, s), 3.17 (3H, s), 3.06-2.92 (1H, m), 2.51 (1H, dd, J_{ABX}=13.6, 6.4 Hz), 2.09 (1H, dd, J_{ABX}=13.6, 8.2 Hz), 1.72 (3H, d, *J*=1.4 Hz), 1.53 (2H, dq, *J*=6.3, 7.4 Hz), 1.08 (3H, d, *J*=6.9 Hz), 0.95 (9H, t, *J*=8.0 Hz), 0.82 (3H, t, *J*=7.4 Hz), 0.58 (6H, q, *J*=8.0 Hz); δ_C (75.5 MHz, $CDCl_3$) **(9b)** 177.4, 142.8, 141.0, 125.3, 115.5, 79.6, 61.3, 41.5, 33.9, 32.2, 29.1, 16.6, 13.2, 10.0, 6.8, 4.8 **(10b)** 177.4, 142.9, 140.6, 125.7, 115.4, 79.9, 61.3, 41.5, 33.9, 32.2, 28.9, 16.8, 13.0, 10.1, 6.8, 4.8.

(*E*)-(4*S*,9*S*)-2,4,8-Trimethyl-6-methylene-9-triethylsilanyloxy-undeca-1,7-dien-3-one **(11)**

(*E*)-(4*R*,9*S*)-2,4,8-Trimethyl-6-methylene-9-triethylsilanyloxy-undeca-1,7-dien-3-one **(11')**





Isopropenylmagnesium bromide (131 mL, 65.7 mmol, 0.5 m in THF) was added slowly to a solution of amides **(9b + 10b)** (8.1 g, 21.9 mmol) in THF (80 mL) at -20°C. The reaction mixture was allowed to warm to room temperature where it was stirred for 5 hours and then quenched with a solution of saturated aqueous ammonium chloride (100 mL). The phases were separated, the aqueous phase was extracted with diethyl ether (3 x 50 mL) and the combined organic extracts were washed brine (50 mL). The organic phase was then dried over magnesium sulfate, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography, eluting with a gradient of 100% petrol to 10% diethyl ether / petrol, to afford the title compounds **(11 + 11')** as a colourless oil (7.6 g, 99%).

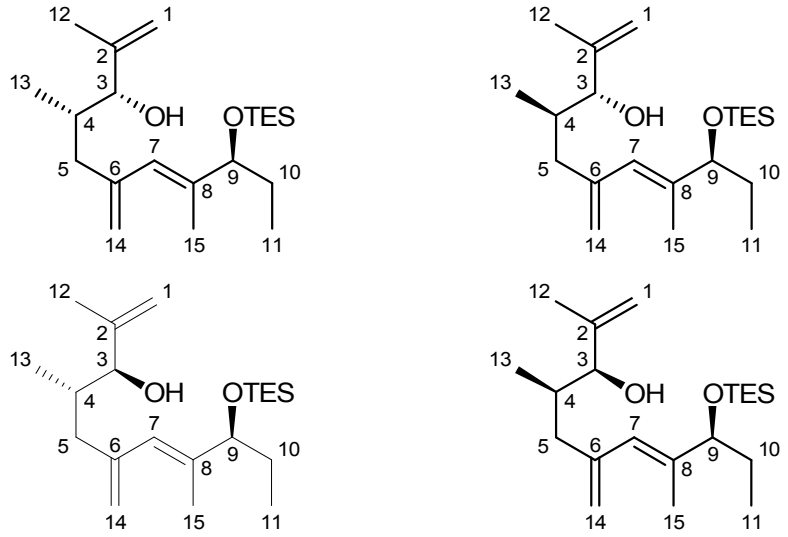
TLC, (10% diethyl ether / petrol) R_f = 0.63; δ_H (400 MHz, $CDCl_3$) **(11)** 5.89 (1H, s), 5.74 (1H, s), 5.71 (1H, s), 5.00 (1H, s), 4.85 (1H, s), 3.92 (1H, t, *J*=6.4 Hz), 3.31 (1H, ddq, *J*=6.0, 6.8, 8.0 Hz), 2.48 (1H, dd, J_{ABX}=13.8, 6.0 Hz), 2.05 (1H, dd, J_{ABX}=13.8, 8.0 Hz), 1.87 (3H, s), 1.70 (3H, d, *J*=1.3 Hz), 1.58-1.49 (2H, m), 1.04 (3H, d, *J*=6.8 Hz), 0.95 (9H, t, *J*=7.8 Hz,), 0.83 (3H, t, *J*=7.4 Hz), 0.58 (6H, q, *J*=7.8 Hz); **(11')** 5.89 (1H, s), 5.74 (1H, s), 5.71 (1H, s), 4.99 (1H, s), 4.84 (1H, s), 3.92 (1H, t, *J*=6.6 Hz), 3.31 (1H, ddq, *J*=6.0, 6.9, 8.1 Hz), 2.48 (1H, dd, J_{ABX}=13.8, 6.0 Hz), 2.05 (1H, dd, J_{ABX}=13.8, 8.1 Hz), 1.85 (3H, s), 1.69 (3H, d, *J*=1.3 Hz), 1.58-1.49 (2H, m), 1.05 (3H, d, *J*=6.9 Hz), 0.94 (9H, t, *J*=7.8 Hz), 0.82 (3H, t, *J*=7.5 Hz), 0.58 (6H, q, *J*=7.8 Hz); δ_C (100 MHz, $CDCl_3$) **(11)** 205.6, 144.1, 143.0, 141.3, 125.3, 123.8, 115.5, 79.6, 41.9, 38.3, 29.2, 17.9, 17.1, 13.2, 10.0, 6.9, 4.9; **(11')** 205.6, 144.1, 143.1, 141.0, 125.5, 123.8, 115.3, 79.7, 41.7, 38.4, 29.1, 17.9, 17.3, 13.2, 10.0, 6.9, 5.0; HRMS (ESI): calcd. for $C_{21}H_{38}O_2SiNa$ $[M + Na]^+$ 373.2533, found 373.2524.

(*E*)-(3*R*,4*S*,9*S*)-2,4,8-Trimethyl-6-methylene-9-triethylsilanyloxy-undeca-1,7-dien-3-ol **(12)**

(*E*)-(3*R*,4*R*,9*S*)-2,4,8-Trimethyl-6-methylene-9-triethylsilanyloxy-undeca-1,7-dien-3-ol **(12')**

(*E*)-(3*S*,4*S*,9*S*)-2,4,8-Trimethyl-6-methylene-9-triethylsilanyloxy-undeca-1,7-dien-3-ol **(12'')**

(*E*)-(3*S*,4*R*,9*S*)-2,4,8-Trimethyl-6-methylene-9-triethylsilanyloxy-undeca-1,7-dien-3-ol **(12''')**

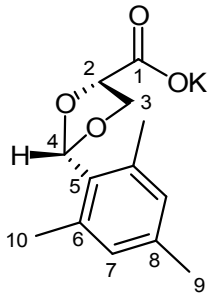


Trimethylboroxine (0.94 mL, 7.5 mmol) was added to a solution of (*R*)-(+)-2-amino-1,1,2-triphenylethanol (3.23 g , 11.18 mmol) in toluene (20 mL) and the mixture stirred for 1 hour at room temperature. The reaction mixture was concentrate under reduced pressure and the residue dissolved in toluene (20 mL). This was concentrated under reduced pressure and again the residue was dissolved in toluene (20 mL). This was concentrated under reduced pressure a final time and the residue dissolved in THF (33 mL). To this solution was added borane dimethylsulfide complex (1.17 mL, 12.30 mmol) at 0°C and the reaction mixture was then stirred for 10 minutes. Ketones **(11 + 11')** (3.91 g, 11.18 mmol) in THF (15 mL) were then added over 45 minutes by syringe pump to the reaction flask. The reaction was monitored by TLC and quenched with saturated aqueous ammonium chloride (30 mL). The phases were separated, the aqueous phase was extracted with diethyl ether

(3 x 50 mL) and the combined organic extracts were washed brine (30 mL). The organic phase was then dried over magnesium sulfate, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography, eluting with a gradient of 5% diethyl ether / petrol to 15% diethyl ether / petrol, to afford the title compounds **(12, 12', 12''** and **12''')** as a yellow oil (3.2 g, 81%).

TLC, (10% diethyl ether / petrol) R_f = 0.23; δ_H (500 MHz, $CDCl_3$) **(12)** 5.71 (1H, s), 5.03 (1H, s), 4.95 (1H, s), 4.89 (1H, s), 4.87 (1H, s), 3.91 (1H, t, *J*=6.6 Hz), 3.88 (1H, d, *J*=4.9 Hz), 2.22 (1H, dd, J_{ABX}=13.3, 6.6 Hz), 1.93 (1H, dd, J_{ABX}=13.3, 9.0 Hz), 1.80-1.73 (1H, m), 1.73 (3H, d, *J*=1.4 Hz), 1.67 (3H, s), 1.57-1.47 (2H, m), 0.94 (9H, t, *J*=7.8 Hz), 0.82 (3H, t, *J*=7.4 Hz), 0.81 (3H, d, *J*=5.1 Hz), 0.58 (6H, q, *J*=7.8 Hz); **(12')** 5.70 (1H, s), 5.03 (1H, s), 4.92 (1H, s), 4.87 (2H, s), 3.91 (1H, t, *J*=6.6 Hz), 3.88 (1H, d, *J*=4.9 Hz), 2.21 (1H, dd, J_{ABX}=13.1, 6.7 Hz), 1.92 (1H, dd, J_{ABX}= 3.1, 9.35 Hz), 1.81-1.74 (1H, m), 1.74 (3H, d, *J*=1.4 Hz), 1.67 (3H, s), 1.57-1.47 (2H, m), 0.93 (9H, t, *J*=7.8 Hz), 0.82 (3H, t, *J*=7.4 Hz), 0.76 (3H, d, *J*=6.6 Hz), 0.58 (6H, q, *J*=7.8 Hz); **(12'')** 5.70 (1H, s), 5.03 (1H, s), 4.92 (1H, s), 4.87 (2H, bs), 3.91 (1H, t, *J*=6.5 Hz), 3.78 (1H, d, *J*=6.7 Hz), 2.53 (1H, bt, J_{AX}=11.8 Hz), 1.82-1.71 (2H, m), 1.75 (3H, d, *J*=1.4 Hz), 1.70 (3H, dd, *J*=1.3, 0.9 Hz), 1.57-1.47 (2H, m), 0.94 (9H, t, *J*=7.8 Hz), 0.82 (3H, t, *J*=7.4 Hz), 0.76 (3H, d, *J*=6.6 Hz), 0.58 (6H, q, *J*=7.8 Hz); **(12''')** 5.69 (1H, s), 5.03 (1H, s), 4.95 (1H, s), 4.89 (1H, s), 4.87 (1H, s), 3.91 (1H, t, *J*=6.5 Hz), 3.78 (1H, d, *J* = 6.7 Hz), 2.53 (1H, bt, J_{AX}=11.8 Hz), 1.82-1.71 (2H, m), 1.74 (3H, d, *J*=1.4 Hz), 1.69 (3H, dd, *J*=1.3, 0.9 Hz), 1.57-1.47 (2H, m), 0.93 (9H, t, *J*=7.8 Hz), 0.82 (3H, t, *J*=7.4 Hz), 0.77 (3H, d, *J*=6.6 Hz), 0.58 (6H, q, *J*=7.8 Hz); δ_C (125 MHz, $CDCl_3$) **(12)** 146.7, 144.0, 140.8, 125.7, 115.0, 111.0, 79.8, 78.2, 42.5, 34.1, 29.2, 18.6, 13.1, 13.0, 10.1, 6.8, 4.9; **(12')** 146.4, 144.0, 140.5, 125.8, 115.0, 112.3, 79.8, 78.3, 42.3, 34.7, 29.1, 18.6, 13.0, 12.9, 10.0, 6.8, 4.9; **(12'')** 146.4, 144.4, 140.8, 125.9, 114.9, 112.4, 81.0, 79.9, 40.6, 34.7, 29.3, 17.4, 15.9, 13.1, 10.1, 6.8, 4.9; **(12''')** 146.7, 144.5, 140.3, 126.1, 114.8, 111.1, 80.9, 80.0, 40.3, 34.1, 29.0, 17.5, 16.0, 12.9, 10.0, 6.8, 4.9; HRMS (ESI): calcd. for $C_{21}H_{40}O_2SiNa$ $[M + Na]^+$ 375.2690, found 375.2680.

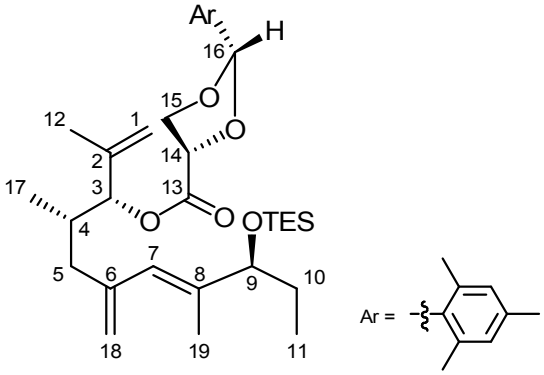
(2*S*,4*S*)-2-(2,4,6-Trimethyl-phenyl)-1,3-dioxolane-4-carboxylic acid potassium salt **(13)**



To a solution of (2*S*,4*S*)-2-(2,4,6-trimethyl-phenyl)-1,3-dioxolane-4-carboxylic acid methyl ester (2.0 g, 7.99 mmol) in MeOH (10 mL) was added a solution of potassium hydroxide (448 mg, 7.99 mmol) in water (10 mL). The reaction mixture was stirred at room temperature for 24 hours before being concentrated under reduced pressure. Benzene (20 mL) was added and removed under reduced pressure to afford the title compound **(13)** as a white solid (2.20 g, 100%).

M.P. 250°C decomposed; $[\alpha]^{32}_{D}$ -15.1 (*c* 0.53 in MeOH); δ_H (300 MHz, $(CD_3)_2SO$) 6.78 (2H, s), 6.01 (1H, s), 4.27 (1H, app t, J_{ABC}=8.3 Hz), 4.03 (1H, app t, J_{ABC}=7.6 Hz), 3.79 (1H, app t, J_{ABC}=7.6Hz), 2.34 (6H, s), 2.20 (3H, s); δ_C (75.5 MHz, $(CD_3)_2SO$) δ_C 171.2, 137.6, 137.5, 129.4, 129.3, 101.0, 77.6, 67.6, 20.5, 19.8.

(2*S*,4*S*)-2-(2,4,6-Trimethyl-phenyl)-1,3-dioxolane-4-carboxylic acid (*E*)-(1*R*,2*S*,7*S*)-1-isopropenyl-2,6-dimethyl-4-methylene-7-triethylsilanyloxy-non-5-enyl ester **(14)**



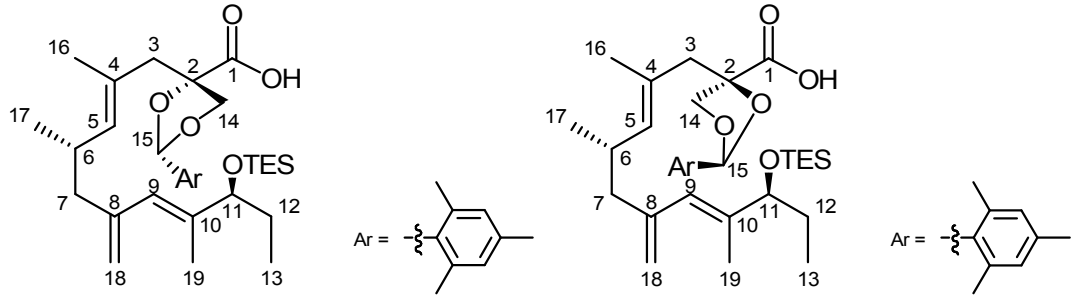
To a stirred suspension of dioxolane **(13)** (1.82 g, 6.60 mmol) in THF (200 mL) was added triethylamine (0.92 mL, 6.60 mmol) followed by pivaloyl chloride (0.81 mL,

6.60 mmol). After 3 hours alcohol **(12)** (2.20 g, 6.28 mmol) in THF (20 mL) and 4-dimethylaminopyridine (38 mg, 0.31 mmol) were added. The reaction mixture was stirred for a further 3 hours before being quenched with a saturated aqueous solution of sodium hydrogen carbonate (100 mL). The phases were separated, the aqueous phase was extracted with diethyl ether (3 x 100 mL) and the combined organic extracts were washed brine (20 mL). The organic phase was then dried over magnesium sulfate, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography, eluting with a gradient of 5% diethyl ether / petrol to 10% diethyl ether / petrol, to afford the title compound **(14)** as a pale yellow oil (2.23 g, 63%).

TLC, (10% diethyl ether / petrol) R_f = 0.34; δ_H (300 MHz, C_6D_6) 6.67 (2H, s), 6.05 (1H, s), 5.69 (1H, s), 5.28 (1H, d, *J*=5.4 Hz), 5.03 (2H, s), 4.94 (1H, s), 4.87 (1H, s), 4.38-4.28 (1H, m), 4.28-4.18 (1H, m), 3.89 (1H, t, *J*=6.0 Hz), 3.85-3.74 (1H, m), 2.45 (6H, s), 2.26-2.14 (1H, m), 2.06 (3H, s), 1.98-1.91 (1H, m), 1.90-1.81 (1H, m), 1.77 (3H, s), 1.61 (3H, s), 1.56-1.44 (2H, m), 0.98 (9H, t, *J*=7.7 Hz), 0.92 (3H, d, *J*=6.6 Hz), 0.84 (3H, t, *J*=7.2 Hz), 0.59 (6H, q, *J*=7.7 Hz); δ_C (75.5 MHz, C_6D_6) 168.7, 143.5, 142.1, 141.6, 138.9, 138.7, 130.4, 125.7, 116.0, 113.7, 103.9, 80.9, 79.9, 74.7, 67.4, 42.3, 33.6, 29.6, 21.0, 20.4, 18.9, 14.3, 13.4, 10.3, 7.2, 5.3.

(2*S*,4*S*)-4-((2*E*,7*E*)-(4*S*,9*S*)-2,4,8-Trimethyl-6-methylene-9-triethylsilanyloxy-undeca-2,7-dienyl)-2-(2,4,6-trimethyl-phenyl)-1,3-dioxolane-4-carboxylic acid **(15)**

(2*S*,4*R*)-4-((2*E*,7*E*)-(4*S*,9*S*)-2,4,8-Trimethyl-6-methylene-9-triethylsilanyloxy-undeca-2,7-dienyl)-2-(2,4,6-trimethyl-phenyl)-1,3-dioxolane-4-carboxylic acid **(15')**

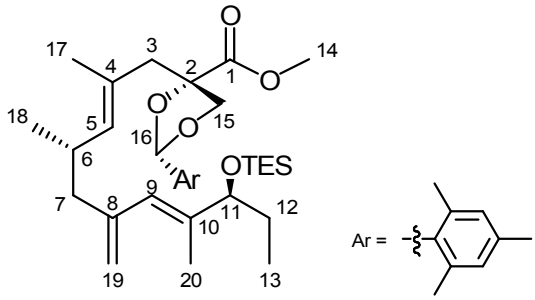


To a solution of di-*iso*-propylamine (230 µL, 2.70 mmol) in THF (9 mL) at 0°C was added *n*-butyllithium (1.15 mL, 2.70 mmol, 2.35 M in hexanes) and stirred for 10 minutes. The yellow solution was cooled to -100°C and HMPA (2 mL) was added. A mixture of trimethylsilyl chloride (454 µL, 3.59 mmol) and triethylamine (250 µL, 1.80 mmol) in THF (1 mL) was filtered and added to the reaction mixture at -100°C quickly followed by the dropwise addition of ester **(14)** (530 mg, 0.90 mmol) in THF (6 mL). The resultant pale yellow solution was stirred for 1 hour at -100°C then allowed to warm slowly to room temperature before being warmed to 40°C for 10 hours. The reaction mixture was cooled to room temperature, quenched with a saturated aqueous solution of ammonium chloride (20 mL) and phases separated.The aqueous phase was extracted with CH_2Cl_2 (3 x 50 mL) and the combined organic extracts were washed brine (20 mL). The organic phase was then dried over magnesium sulfate, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography, eluting with a gradient of 60% diethyl ether / petrol to 100% diethyl ether, to afford the title compound **(15)** as a yellow gum (209 mg, 39%) and **(15')** as a yellow gum (190 mg, 36%).

TLC, (90% diethyl ether / petrol) **(15)** R_f = 0.53; **(15')** R_f = 0.38; ν_{max} (film/cm^{-1}) 2956 (s), 2876 (s), 1725 (m), 1613 (w), 1454 (m), 1376 (w), 1249 (m), 1067 (s), 1006 (m), 965 (w), 848 (s), 743 (m); δ_H (300 MHz, C_6D_6) **(15)** 7.25 (1H, bs), 6.68 (2H, s), 6.21 (1H, s), 5.81 (1H, s), 5.17 (1H, d, *J*=9.1 Hz), 5.07 (1H, s), 4.97 (1H, s), 4.64 (1H, d, J_{AX}=8.7 Hz), 3.93 (1H, t, *J*=6.2 Hz), 3.69 (1H, d, *J*=8.7 Hz), 2.71-2.47 (3H, m), 2.45 (6H, s), 2.23-2.13 (1H, m), 2.07-1.99 (1H, m), 2.06 (3H, s), 1.80 (3H, s), 1.78 (3H, s), 1.65-1.54 (2H, m), 1.01 (9H, t, *J*=7.9 Hz), 0.97 (3H, d, *J*=9.1 Hz), 0.88 (3H, t, *J*=7.2 Hz), 0.62 (6H, q, *J*=7.9 Hz); **(15')** 10.11 (1H, bs), 6.68 (2H, s), 6.45 (1H, s), 5.79 (1H, s), 5.24 (1H, d, *J*=8.8 Hz), 5.04 (1H, s), 4.93 (1H, s), 4.35 (1H, d, J_{AX}=8.3 Hz), 3.92 (1H, t, *J*=6.2 Hz), 3.85 (1H, d, J_{AX}=8.3 Hz), 2.71 (1H, d, J_{AB}=13.8 Hz), 2.65-2.54 (1H, m), 2.54-2.48 (1H, m), 2.46 (6H, s), 2.24-2.14 (1H, m), 2.10-2.00 (1H, m), 2.06 (3H, s), 1.82 (3H, s), 1.79 (3H, s), 1.62-1.50 (2H, m), 1.01 (3H, d, *J*=5.8 Hz), 0.99 (9H, t, *J*=6.7 Hz), 0.86 (3H, t, *J*=7.6 Hz), 0.61 (6H, q, *J*=6.7 Hz); δ_C (75.5 MHz, C_6D_6) **(15)** 175.7, 144.1, 140.9, 139.1, 138.5, 137.3, 130.5, 130.4, 126.4, 115.5, 103.4, 84.3, 80.2, 73.7, 46.1, 45.6, 31.7, 29.7, 20.9, 20.4,

20.3, 17.6, 13.4, 10.3, 7.2, 5.3; **(15')** 178.8, 144.2, 140.9, 138.9, 138.5, 136.5, 130.4, 129.4, 126.5, 115.2, 103.9, 85.4, 80.2, 73.4, 46.1, 46.1, 31.6, 30.2, 20.9, 20.6, 20.4, 17.4, 13.3, 10.4, 7.2, 5.3; *m/z* (EI) 571 (MH+, 1%), 542 (2), 447 (27), 350 (14), 254 (54), 147 (100), 121 (36), 103 (56), 87 (68), 41 (55); HRMS (ESI): calcd. for $C_{34}H_{54}O_5SiNa$ $[M + Na]^+$ 593.3633, found 593.3625.

(2*S*,4*S*)-4-((2*E*,7*E*)-(4*S*,9*S*)-2,4,8-Trimethyl-6-methylene-9-triethylsilanyloxy-undeca-2,7-dienyl)-2-(2,4,6-trimethyl-phenyl)-1,3-dioxolane-4-carboxylic acid methyl ester **(15a)**



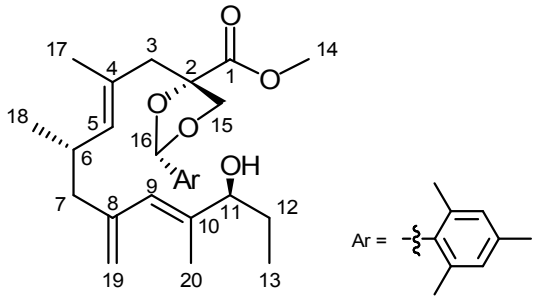
A solution of acid **(15)** (80 mg, 0.140 mmol) in benzene (6 mL) and MeOH (1.5 mL) had (trimethylsilyl)diazomethane (91 μL, 0.182 mmol, 2.0 M in Et_2O) added at room temperature. The yellow solution was stirred for 1 hour before being concentrated under reduced pressure. The residue was purified by flash column chromatography, eluting with 10% diethyl ether / hexanes, to afford the title compound **(15a)** as a pale yellow oil (56 mg, 68%).

TLC, (10% diethyl ether / petrol) $R_f = 0.50$; ν_{max} (film/cm^{-1}) 2955 (s), 2875 (s), 1762 (m), 1737 (s), 1689 (w), 1613 (m), 1454 (s), 1221 (m), 1094 (m), 1067 (s), 1006 (m), 849 (m), 743 (m); δ_H (300 MHz, C_6D_6) 6.69 (2H, s), 6.27 (1H, s), 5.80 (1H. s), 5.06 (1H, d, *J*=10.5 Hz), 5.04 (1H, s), 4.96 (1H, s), 4.76 (1H, d, J_{AX}=8.8 Hz), 3.93 (1H, t, *J*=6.0 Hz), 3.71 (1H, d, *J*=8.8 Hz), 3.39 (3H, s), 2.68-2.49 (3H, m), 2.47 (6H, s), 2.19-2.11 (1H, m), 2.06 (3H, s), 2.03-1.97 (1H, m), 1.81 (3H, s), 1.74 (3H, s), 1.64-1.50 (2H, m), 1.01 (9H, t, *J*=7.8 Hz), 0.94 (3H, d, *J*=6.9 Hz), 0.88 (3H, t, *J*=*7.5* Hz), 0.62 (6H, q, *J*=7.3 Hz); δ_C (75.5 MHz, C_6D_6) 172.0, 144.1, 141.0, 138.8, 138.6, 136.7, 130.4, 129.0, 126.3, 115.3, 103.0, 84.4, 80.1, 73.6, 51.6, 46.3, 46.2, 31.5, 29.7, 20.9, 20.4, 20.3, 17.4, 13.3, 10.3, 7.2, 5.3; *m/z* (EI) 584 (M^+, 17%), 555

(19), 446 (52), 407 (27), 293 (32), 253 (100), 249 (67), 147 (92), 115 (51), 87 (79); HRMS (ESI): calcd. for $C_{35}H_{56}O_5SiNa$ $[M + Na]^+$ 607.3789, found 607.3615.

(2*S*,4*S*)-4-((2*E*,7*E*)-(4*S*,9*S*)-9-Hydroxy-2,4,8-trimethyl-6-methylene-undeca-2,7-dienyl)-2-(2,4,6-trimethyl-phenyl)-1,3-dioxolane-4-carboxylic acid methyl ester

(15b)

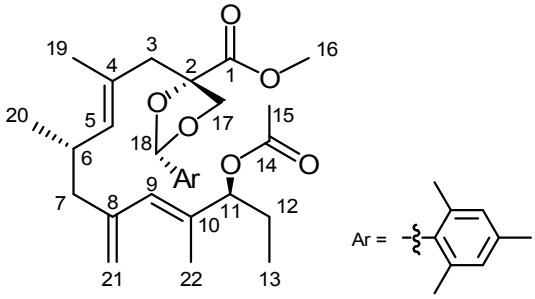


A solution of ester **(15a)** (54 mg, 0.096 mmol) in THF (5 mL) at 0°C was reacted with tetrabutylammonium fluoride (105 μL, 0.105 mmol, 1.0 M in THF with 5% H_2O) and was stirred for 3 hours. The reaction was quenched with a solution of saturated aqueous sodium hydrogen carbonate (5 mL) and the phases separated. The aqueous phase was extracted with diethyl ether (3 x 10 mL) and the combined organic extracts were washed brine (20 mL). The organic phase wash then dried over magnesium sulfate, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography, eluting with 35% diethyl ether / hexanes, to afford the title compound **(15b)** as a pale yellow oil (41 mg, 94%).

TLC, (30% diethyl ether / petrol) R_f = 0.20; δ_H (300 MHz, C_6D_6) 6.69 (2H, s), 6.27 (1H, s), 5.79 (1H, s), 5.12-4.97 (1H, m), 5.03 (1H, s), 4.94 (1H, s), 4.75 (1H, d, J_{AX}=8.8 Hz), 3.70 (1H, d, J_{AX}=8.8 Hz), 3.69 (1H, t, J=6.5 Hz), 3.38 (3H, s), 2.63 (1H, d, J_{AB}=14.6 Hz), 2.59-2.48 (2H, m), 2.47 (6H, s), 2.09-1.94 (2H, m), 2.06 (3H, s), 1.72 (3H, s), 1.67 (3H, s), 1.53-1.43 (2H, m), 0.90 (3H, d, J=7.0 Hz), 0.83 (3H, t, J=7.5 Hz); δ_C (75.5 MHz, C_6D_6) 172.13, 144.3, 140.8, 138.9, 138.6, 136.5, 130.4, 129.0, 126.2, 115.1, 103.0, 84.4, 78.8, 73.6, 51.6, 46.3, 46.0, 31.7, 28.3, 20.9, 20.7, 20.3, 17.4, 13.7, 10.2; *m/z* (EI) 471 (MH^+, 2%), 337 (M^+-Ar, 21), 249 (82), 219 (30),

149 (92), 133 (100), 101 (50); HRMS (ESI): calcd. for $C_{29}H_{42}O_5Na$ $[M + Na]^+$ 493.2713, found 493.2832.

(2*S*,4*S*)-4-((2*E*,7*E*)-(4*S*,9*S*)-9-Acetoxy-2,4,8-trimethyl-6-methylene-undeca-2,7-dienyl)-2-(2,4,6-trimethyl-phenyl)-1,3-dioxolane-4-carboxylic acid methyl ester **(16)**

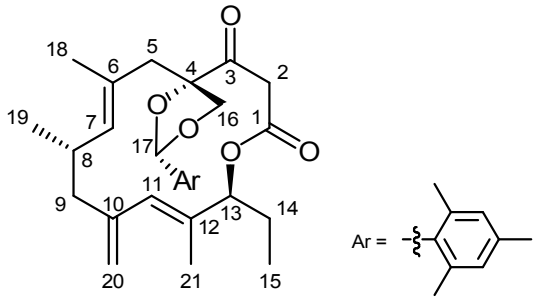


To a solution of alcohol **(15b)** (42 mg, 0.089 mmol) in toluene (5 mL) was added pyridine (43 µL, 0.536 mmol) and acetyl chloride (27 µL, 0.357 mmol) at 0°C. The reaction mixture was allowed to warm to room temperature where it was stirred for 4 hours. The reaction was quenched with a solution of saturated aqueous sodium hydrogen carbonate (5 mL) and the phases separated. The aqueous phase was extracted with diethyl ether (3 x 10 mL) and the combined organic extracts were washed brine (10 mL). The organic phase wash then dried over magnesium sulfate, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography, eluting with 25% diethyl ether / hexanes, to afford the title compound **(16)** as a yellow oil (33 mg, 72%).

TLC, (30% diethyl ether / petrol) $R_f = 0.43$; ν_{max} (film/cm^{-1}) 2954 (s), 2925 (s), 1753 (s), 1736 (s), 1613 (s), 1451 (w), 1369 (m), 1238 (s), 1204 (m), 1070 (s), 965 (m), 850 (w); δ_H (300 MHz, C_6D_6) 6.69 (2H, s), 6.26 (1H, s), 5.89 (1H, s), 5.21 (1H, t, *J*=6.9 Hz), 5.02 (1H, d, *J*=8.6 Hz), 5.01 (1H, s), 4.90 (1H, s), 4.76 (1H, d, J_{AX}=8.7 Hz), 3.71 (1H, d, J_{AX}=8.7 Hz), 3.38 (3H, s), 2.63 (1H, d, J_{AB}=13.6 Hz), 2.57-2.48 (2H, m), 2.45 (6H, s), 2.06 (3H, s), 2.04-1.93 (2H, m,), 1.74 (3H, s), 1.69 (3H, s), 1.68 (3H, s), 1.62-1.56 (1H, m), 1.54-1.48 (1H, m), 0.88 (3H, d, *J*=6.7 Hz), 0.75 (3H, d, *J*=7.3 Hz); δ_C (75.5 MHz, C_6D_6) 172.0, 169.4, 144.0, 138.8, 138.6, 136.5, 136.1, 130.4, 129.1, 129.1, 115.5, 103.0, 84.4, 80.5, 73.5, 51.6, 46.3, 45.9, 31.5,

26.1, 20.9, 20.9, 20.8, 20.3, 17.4, 13.8, 10.0; *m/z* (EI) 368 (9), 244 (8), 207 (15), 147 (9), 111 (10), 83 (27), 57, (49), 31 (100); HRMS (ESI): calcd. for $C_{31}H_{44}O_6Na$ $[M + Na]^+$ 535.3030, found 535.3044.

(11*E*,16*E*)-(2*S*,5*S*,10*S*,15*S*)-10-Ethyl-11,15,17-trimethyl-13-methylene-2-(2,4,6-trimethyl-phenyl)-1,3,9-trioxa-spiro[4.13]octadeca-11,16-diene-6,8-dione **(17)**



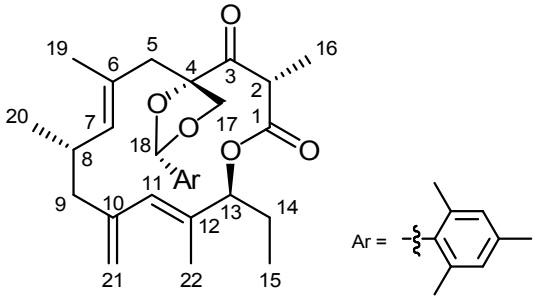
To a solution of ester **(16)** (280 mg, 0.547 mmol) in THF (280 mL) at 0°C was added LHMDS (3.3 mL, 3.28 mmol, 1.0 M solution in THF). This mixture was added over 1 hour to flask containing THF (280 mL) under reflux. After the addition was completed the reaction mixture was refluxed for a further 1 hour and then concentrated under reduced pressure. The residue was taken into CH_2Cl_2 and washed with a saturated aqueous ammonium chloride solution. The organic phase was dried over magnesium sulfate, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography, eluting with a gradient of hexanes to 15% diethyl ether / hexanes, to afford the title compound **(17)** as pale yellow foam (62.1 mg, 32%).

TLC, (10% diethyl ether / petrol) $R_f = 0.25$; ν_{max} (film/cm^{-1}) 2956 (s), 2926 (s), 2864 (m), 1751 (s), 1719 (s), 1655 (m), 1614 (m), 1452 (s), 1272 (m), 1220 (s), 1071 (s), 1035 (s), 965 (s), 851 (m), 665 (s); δ_H (300 MHz, C_6D_6) 6.68 (2H, s), 6.11 (1H, s), 5.94 (1H, s), 5.31-5.24 (1H, m), 5.14 (1H, d, *J*=9.2 Hz), 5.00 (1H, s), 4.82 (1H, s), 4.39 (1H, d, J_{AX}=8.9 Hz), 4.04 (1H, d, J_{AX}=15.9 Hz), 3.44 (1H, d, J_{AX}=8.9 Hz), 3.21 (1H, d, J_{AX}=15.9 Hz), 2.47-2.35 (3H, m, 5-CH_2), 2.30 (6H, s), 2.17-2.05 (2H, m), 2.07 (3H, s), 1.60 (3H, s), 1.56 (3H, s), 1.48-1.30 (2H, m) 0.89 (3H, d, *J*=6.2 Hz), 0.80-0.72 (3H, m); δ_C (75.5 MHz, C_6D_6) 201.8, 165.7, 145.4, 139.0, 138.2, 136.4, 134.5, 130.5, 130.4, 127.9, 126.2, 114.7, 102.4, 88.2, 78.1, 72.8, 45.8, 45.4, 44.6,

33.9, 26.1, 22.3, 20.9, 20.5, 17.7, 15.8, 9.2; *m/z* (EI) 480 (M^+, 9%), 436 (M^+-CO_2, 8), 202 (30), 162 (79), 147 (97), 122 (60), 107 (68), 93 (100), 55 (57); HRMS (ESI): calcd. for $C_{30}H_{40}O_5Na$ [M + Na]$^+$ 503.2767, found 503.2780.

(11*E*,16E)-(2*S*,5*S*,7*S*,10*S*,15*S*)-10-Ethyl-7,11,15,17-tetramethyl-13-methylene-2-(2,4,6-trimethyl-phenyl)-1,3,9-trioxa-spiro[4.13]octadeca-11,16-diene-6,8-dione

(17a)

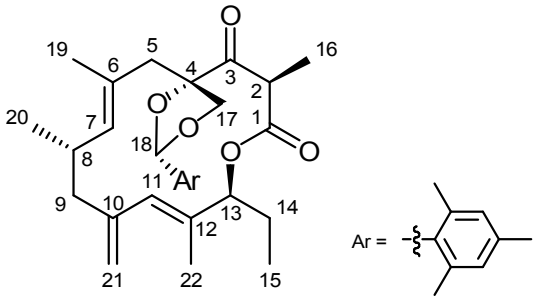


A solution of macrocycle **(17)** (123 mg, 0.246 mmol) in THF (10 mL) at 0°C had potassium *tert*-butoxide (0.29 mL, 0.295 mmol, 1.0 M solution in THF) added. The yellow solution was stirred for 10 minutes at 0°C before methyl iodide (79 μL, 1.281 mmol). The pale yellow mixture was then stirred for 1 hour at 0°C and then concentrated under reduced pressure. The residue was purified by flash column chromatography, eluting with a gradient of 3% diethyl ether / hexanes to 15% diethyl ether / hexanes, to afford the title compound **(17a)** as colourless foam (62.1 mg, 49%).

TLC, (10% diethyl ether / petrol) R_f = 0.40; δ_H (300 MHz, C_6D_6) 6.69 (2H, s), 6.14 (1H, s), 5.93 (1H, s), 5.20 (1H, t, *J*=6.1 Hz), 5.10 (1H, d, *J*=9.5 Hz), 5.00 (1H, s), 4.78 (1H, s), 4.74 (1H, d, J_{AX}=9.1 Hz), 4.21 (1H, q, *J*=6.9 Hz), 3.58 (1H, d, J_{AX}=9.1 Hz), 2.77 (1H, d, J_{AB}=16.0 Hz), 2.54 (1H, d, J_{AB}=16.0 Hz), 2.42-2.35 (1H, m), 2.39 (6H, s), 2.10-2.01 (1H, m), 2.06 (3H, s), 1.90-1.80 (1H, m), 1.58 (3H, s), 1.52 (3H, s), 1.48-1.32 (2H, m), 1.42 (3H, d, *J*=6.9 Hz), 0.88 (3H, d, *J*=6.7 Hz), 0.68 (3H, t, *J*=7.3 Hz); δ_C (75.5 MHz, C_6D_6) 205.3, 169.5, 145.8, 138.8, 137.9, 135.3, 134.4, 130.6, 130.5, 129.1, 127.2, 114.7, 102.9, 87.7, 79.7, 72.0, 47.4, 45.6, 43.7, 35.4, 25.9, 22.4, 20.9, 20.9, 18.7, 15.7, 15.1, 9.5; HRMS (ESI): calcd. for $C_{31}H_{42}O_5Na$ [M + Na]$^+$ 517.2924, found 517.2921.

(11*E*,16*E*)-(2*S*,5*S*,7*R*,10*S*,15*S*)-10-Ethyl-7,11,15,17-tetramethyl-13-methylene-2-(2,4,5-trimethyl-phenyl)-1,3,9-trioxa-spiro[4.13]octadeca-11,16-diene-6,8-dione

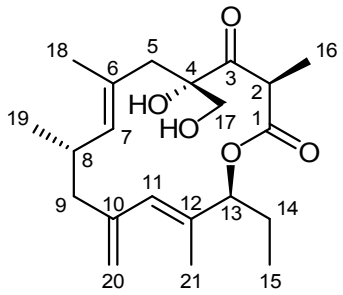
(18)



A solution of macrocycle **(17a)** (58.0 mg, 0.117 mmol) in THF (10 mL) at 0°C had potassium *tert*-butoxide (176 µL, 0.176 mmol, 1.0 M solution in THF) added. The yellow solution was stirred at 0°C for 10 minutes. Glacial acetic acid was added (47 µL, 0.822 mmol) and the mixture was concentrated under reduced pressure. The residue was purified by flash column chromatography, eluting with a gradient of 5% diethyl ether / hexanes to 15% diethyl ether / hexanes, to afford the title compound **(18)** as colourless foam (27.2 mg, 47%)

TLC, (10% diethyl ether / petrol) $R_f = 0.18$; ν_{max} (film/cm^{-1}) 2961 (s), 2962 (s), 2875 (m), 1739 (m), 1781 (s), 1641 (m), 1450 (m), 1245 (s), 1071 (s), 665 (s); δ_H (300 MHz, C_6D_6) 6.68 (2H, s), 6.32 (1H, s), 5.99 (1H, s), 5.19 (1H, d, *J*=9.2 Hz), 5.00 (1H, s), 4.95 (1H, t, *J*=7.0 Hz), 4.83 (1H, s), 4.34 (1H, d, J_{AX}=9.1 Hz), 3.65 (1H, q, *J*= 6.7 Hz), 3.59 (1H, d, J_{AX}=9.1 Hz), 2.76 (1H, d, J_{AB}=14.4 Hz), 2.56-2.46 (1H, m), 2.53 (1H, d, J_{AB}=14.4 Hz), 2.40 (6H, s), 2.38-3.32 (1H, m), 2.08-2.04 (1H, m), 2.06 (3H, s), 1.76 (3H, s), 1.71 (3H, s), 1.56-1.49 (2H, m), 1.32 (3H, d, *J*=6.7 Hz), 0.89 (3H, d, *J*=6.8 Hz), 0.84 (3H, t, *J*=7.3 Hz); δ_C (75.5 MHz, C_6D_6) 199.4, 167.9, 144.5, 138.9, 138.4, 135.4, 135.0, 130.5, 130.4, 129.3, 126.8, 116.5, 102.6, 89.3 80.2, 72.7, 50.9, 45.6 43.4, 32.7, 26.6, 20.9, 20.4, 19.8, 18.6, 16.4, 15.7, 10.0; *m/z* (EI) 289 (7%), 247 (8), 190 (18), 162 (24), 147 (100), 123 (36), 107, (51), 93 (99), 69 (72), 41 (98); HRMS (ESI): calcd. for $C_{31}H_{42}O_5Na$ $[M + Na]^+$ 517.2924, found 517.2922.

Galbonolide B **(1)**



The macrocycle **(18)** (21.3 mg, 0.0431 mmol) was dissolved in glacial acetic acid (1 mL) and water (0.5 mL). The mixture was stirred at room temperature for 30 minutes and then concentrated under reduced pressure. The residue was purified by flash column chromatography, eluting with a gradient of 40% diethyl ether / hexanes to 60% diethyl ether / hexanes, to afford the title compound **(1)** as pale yellow soild (14.3 mg, 91%).

TLC, (50% diethyl ether / petrol) $R_f = 0.36$; ν_{max} (thin film) /cm^{-1} 3478 (b), 2950 (s), 2925 (s), 2878 (m), 1709 (s), 1620 (w), 1454 (m), 1380 (m), 1302 (m), 1244 (s), 1078 (m), 1018 (m), 665 (m); δ_H (300 MHz, CD_3OD) 5.68 (1H, d, *J*=0.9 Hz), 5.05 (1H, bd, *J*=1.4 Hz), 5.00 (1H, dd, *J*=9.5, 1.2 Hz), 4.91-4.85 (1H, m), 4.80 (1H, d, *J*=1.1 Hz), 4.65 (2H, bs), 4.02 (1H, q, *J*=6.9 Hz), 3.96 (1H, d, J_{AB}=11.8 Hz), 3.61 (1H, d, J_{AB}=11.8 Hz), 2.71 (1H, d, J_{AX}=14.0 Hz), 2.62-2.46 (1H, m), 2.25 (1H, dd, J_{ABX}=12.8, 1.5 Hz), 2.15 (1H, dd, J_{ABX}=13.1, 7.5 Hz), 2.06 (1H, d, J_{AX}=14.0 Hz), 1.82 (3H, d, *J*=1.4 Hz), 1.80-1.69 (2H, m), 1.68 (3H, d, *J*=1.2 Hz), 1.46 (3H, d, *J*=6.9 Hz), 0.97 (3H, t, *J*=7.4 Hz), 0.77 (3H, d, *J*=6.9 Hz); δ_C (75.5 MHz, CD_3OD) 210.0, 170.5, 145.3, 137.7, 136.2, 129.6, 128.2, 117.2, 85.7, 82.0, 69.0, 51.1, 46.5, 42.6, 33.9, 27.5, 19.6, 19.2, 16.4, 15.8, 10.4; *m/z* (EI) 244 (8%), 209 (18), 151 (8), 108 (7), 94 (29), 81 (21), 67 (25), 55 (45), 41 (100), 28 (44); HRMS (ESI): calcd. for $C_{21}H_{32}O_5Na$ $[M + Na]^+$ 387.2141, found 387.2145.