Supporting Information

for

Novel Total Synthesis of the Anti-Cancer Natural Product Dysidiolide

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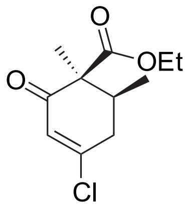
Contents: Experimental procedures and characterization data for all chemical transformations described in the text.

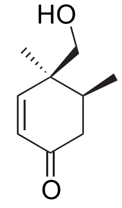
General: Unless noted otherwise, all oxygen and moisture-sensitive reactions were executed in oven-dried glassware sealed under a positive pressure of dry argon or nitrogen and moisture-sensitive solutions and anhydrous solvents were transferred via standard syringe and cannula techniques.

Unless stated otherwise, all commercial reagents, were used as received. All solvents were dried under nitrogen atmosphere: THF and Et_2O were distilled over Na-benzophenone; CH_2Cl_2, Et_3N, and pyridine were distilled from CaH_2. Flash chromatography was performed using Baker Flash silica gel 60 (40 ❍M); analytical TLC was performed using 0.25 mm EM silica gel 60 F_{254} plates that were visualized by irradiation (254 nm) or by staining (450 mL of 95% EtOH, 25 mL conc. H_2SO_4, 15 mL acetic acid, and 25 mL anisaldehyde). Optical rotations were obtained using a JASCO DIP-370 digital polarimeter. IR spectra were recorded using a Perkin-Elmer 683 infrared spectrophotometer. NMR spectra were obtained using INOVA 500 and 300 MHz Varian instruments. High resolution mass spectrometric data were obtained using a VG Analytical Sector-Field mass spectrometer.



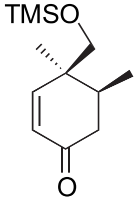
(±)-2a

4-Chloro-1,6-dimethyl-2-oxo-cyclohex-3-ene-carboxylic acid [(±)-2a]. Dry NaH (95 %, 3.39 g, 134 mmol) was added to a stirred solution of **4-Chloro-6-methyl-2-oxo-cyclohex-3-enecarboxylic acid ethyl ester [(±)-2]** (24.12 g, 111.6 mmol) in THF (372 mL) at 0 ºC. When the evolution of gas ceased, HMPA (38 mL, 218 mmol) followed by CH_3I (8.35 mL, 134 mmol) were added and the solution allowed to warm to rt and stir for 6 h. The solvent was removed *in vacuo* and the residue was suspended in Et_2O (1000 mL) and washed with saturated aqueous NH_4Cl (100 mL) then brine (100 mL). After drying over Na_2SO_4, the solution was filtered and concentrated *in vacuo* and the residue was chromatographed over silica gel (hexanes - ethyl acetate, 8:1, v/v) to give **2a** (21.9 g, 94.9 mmol, 85 %) as a colorless oil. R_f (hexanes - ethyl acetate, 3:1, v/v) **2** : 0.59, **2a** : 0.70; IR (film) υ_{max} 2983, 2939, 1736, 1676, 1623,1454, 1375, 1357, 1307, 1277, 1247, 1231, 1193, 1133, 1108 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 6.27 (d, J = 2.4 Hz, 1H), 4.14 (m, 2H), 2.80 (ddd, J = 2.4, 11.1, 18.6 Hz, 1H), 2.56 (dd, J = 4.8, 18.6 Hz, 1H), 2.23 (m, 1H), 1.41 (s, 3H), 1.23 (t, J = 7.2 Hz, 3H), 1.13 (d, J = 6.9 Hz, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 194.5, 169.9, 157.5, 127.1, 61.2, 56.0, 40.1, 38.6, 18.3, 16.0, 14.1; HRMS (CI, NH_3) *m/z* calcd for $[C_{11}H_{15}ClO_3+NH_4]^+$, 248.1052; found, 248.1066.



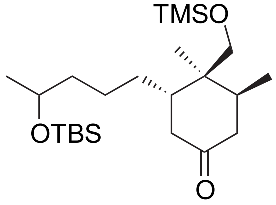
2b

4-Hydroxymethyl-4,5-dimethyl-cyclohex-2-enone [(±)-2b]. Dry NaH (95 %, 2.88 g, 114 mmol) was added in small portions to a solution of **2a** (21.89 g, 94.89 mmol) in absolute ethanol (500 mL) at 0 ºC. After 30 min the solvent was evaporated *in vacuo* and replaced with Et_2O (500 mL) containing Et_3N (30 mL). Vacuum filtration through a thin layer of silica gel and concentration *in vacuo* quantitatively produced the presumed vinologous ester intermediate (22.84 g crude), which was dissolved in dry Et_2O (250 mL) and added drop wise to a suspension of $LiAlH_4$ (3.6 g, 95 mmol) in Et_2O (750 mL) at rt. After stirring for an additional 1h, the solution was cooled to 0 ºC and H_2O (5 mL) followed by 2 M HCl (250 mL) were carefully added and the solution stirred at rt for 30 min. The aqueous layer was removed and the organic phase washed with saturated aqueous $NaHCO_3$ (100 mL), H_2O (100 mL), brine (100 mL), and dried over Na_2SO_4. The solution was filtered and concentrated *in vacuo* and the residual oil was chromatographed over silica gel (hexanes - ethyl acetate, 1:1, v/v) to give **2b** (13.20 g, 86 mmol, 90 %) as a colorless oil. R_f 0.25 (hexanes - ethyl acetate, 1:1, v/v); IR (film) υ_{max} 3444, 2964, 2879, 1669, 1457, 1377, 1285, 1257, 1049 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 6.60 (d, J = 10.2 Hz, 1H), 5.91 (d, J = 10.2 Hz, 1H), 3.67 (d, J = 10.8 Hz, 1H), 3.44 (d, J = 11.1 Hz, 1H), 3.29 (s, 1H), 2.50 (dd, J = 11.7, 17.4 Hz, 1H), 2.26 (dd, J = 4.8, 17.1 Hz, 1H), 2.01 (sept, J = 6.9 Hz, 1H), 1.04 (s, 3H), 0.98 (d, J = 6.9 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 201.3, 157.4, 128.8, 66.2, 42.9, 40.9, 37.1, 22.7, 15.6; HRMS (CI, NH_3) *m/z* calcd for $[C_9H_{14}O_2+NH_4]^+$, 172.1338; found, 172.1327.



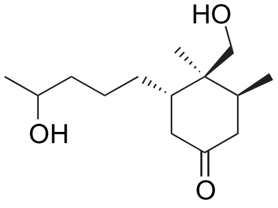
3

4,5-Dimethyl-4-trimethylsilanyloxymethyl-cyclohex-2-enone [(±)-3]. TMSCl (1.31 mL, 10.3 mmol) was added drop wise to a stirred solution of **2b** (1.06 g, 6.9 mmol), imidazole (2.34 g, 35.0 mmol) and DMAP (0.12 g, 1.0 mmol) in CH_2Cl_2 (35 mL) at 0 ºC. The solution was allowed to warm to room temperature and stir for 1 h before it was diluted with EtOAc (150 mL), washed with H_2O (25 mL), brine (25 mL) then dried over Na_2SO_4. The solvent was removed *in vacuo* and the residue chromatographed over silica gel (hexanes - ethyl acetate, 8:1, v/v, 0.5% Et_3N) to give **3** (1.45 g, 6.4 mmol, 93 %) as a colorless oil. R_f 0.52 (hexanes - ethyl acetate, 5:1, v/v); IR (film) υ_{max} 2961, 2878, 1681, 1454, 1378, 1252, 1092 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHZ) δ 6.58 (d, *J* = 10.2 Hz, 1H), 6.00 (d, *J* = 10.2, 1H), 3.69 (d, *J* = 9.6 Hz, 1H), 3.41 (d, *J* = 10.5 Hz, 1H), 2.58 (dd, *J* = 11.7, 16.8 Hz, 1H), 2.33 (dd, *J* = 5.1, 17.1 Hz, 1H), 2.6 (sept, *J* = 4.8 Hz, 1H), 1.08 (s, 3H), 1.04 (d, *J* = 6.9 Hz, 3H), 0.07 (s, 9H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 200.6, 156.7, 128.7, 66.3, 43.0, 40.6, 37.1, 22.8, 15.5, -0.728; HRMS (CI, NH_3) *m/z* calcd for $[C_{12}H_{22}O_2Si+NH_4]^+$, 244.1733; found, 244.1715.



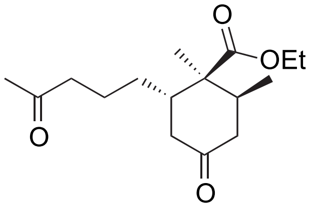
4

3-[4-(*tert*-Butyl-dimethyl-silanyloxy)-pentyl]-4,5-dimethyl-4-trimethylsilanyloxy-methyl-cyclohexanone [(±)-4]. To a stirred –78 ºC solution of bromide **7** (8.95 g, 32 mmol) in Et_2O (70 mL), *t*-BuLi (37.5 mL of 1.7 M in pentane, 64 mmol) was added drop wise and the solution allowed to stir for 20 min before CuCN (1.40 g, 16 mmol) was added *via* a solid addition funnel. After gradual warming to homogeneity (–10 ºC), the solution was re-cooled to –78 ºC and a solution of enone **3** (2.97 g, 13 mmol) in Et_2O (10 mL) was added drop wise. After stirring for 2 h, the solution was gradually warmed to –30 ºC, quenched with 10% NH_4OH/ saturated aqueous NH_4Cl solution (10 mL) and warmed to rt. After dilution with Et_2O (400 mL), the solution was washed with water (100 mL), brine (100 mL) and dried over Na_2SO_4. The solution was concentrated *in vacuo* and the residue chromatographed over silica gel (hexanes - ethyl acetate, 20:1, v/v, 0.5% Et_3N) to give **4** (4.6 g, 11 mmol, 82 %) as a colorless oil. R_f 0.61 (hexanes - ethyl acetate, 5:1, v/v); IR (film) υ_{max} 2958, 2929, 2857, 1716, 1462, 1376, 1251, 1091 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 3.74 (sex, *J* = 6.0 Hz, 1H), 3.56 (d, *J* = 9.5 Hz, 1H), 3.43 (d, *J* = 9.5 Hz, 1H), 2.46 - 2.41 (m, 2H), 2.20 - 2.14 (m, 1H), 2.12 - 2.03 (m, 2H), 1.96 - 1.90 (m, 1H), 1.44 - 0.83 (m, 6H), 1.09 (d, *J* = 6.5 Hz, 3H), 1.00 (d, *J* = 3.0 Hz, 3H), 0.91 (dd, *J* = 2.0, 7.0 Hz, 3H), 0.87 (s, 9H), 0.10 (s, 9H), 0.05 (s, 6H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 213.0, 68.5, 42.2, 39.9, 39.2, 38.5, 37.5, 29.9, 25.9, 23.9, 18.7, 18.1, 15.5, -0.7, -4.4, -4.7; HRMS (FAB) *m/z* calcd for $[C_{23}H_{48}O_3Si_2+H]^+$, 429.3220; found, 429.3191.



8

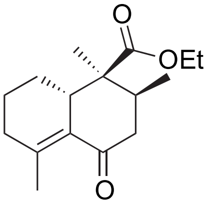
4-Hydroxymethyl-3-(4-hydroxy-pentyl)-4,5-dimethyl-cyclohexanone [(±)-8]. To a stirred solution of **4** (3.77 g, 8.8 mmol) in methanol (50 mL) and CH_2Cl_2 (50 mL) *p*-TsOH·H_2O (0.17 g, 0.9 mmol) was added. After stirring for 2 h $NaHCO_3$ (70 mg) was added and the solution concentrated *in vacuo*. The residue was chromatographed over silica gel with ethyl acetate to give **8** (2.00 g, 8.3 mmol, 94 %) as a colorless oil. R_f 0.32 (hexanes - ethyl acetate, 1:1, v/v); IR (film) υ_{max} 3432, 2959, 2932, 2860, 1456, 1373, 1348, 1328, 1177, 1110 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 3.91 (d, *J* = 15 Hz, 1H), 3.73 (q, *J* = 7.5 Hz, 1H), 3.34 (dd, *J* = 3.0, 15.0 Hz, 1H), 3.25 (s (br), 2H), 2.17 - 2.02 (m, 1H), 2.02 (s (br), 1H), 1.91 - 1.74 (m, 2H), 1.63 - 1.57 (m, 1H), 1.49 - 0.98 (m, 7H), 1.22 (d, *J* = 10.5 Hz, 3H), 0.91 (d, *J* = 11.5, 3H), 0.62 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 98.6, 72.4, 67.9, 49.2, 42.3, 39.4, 36.9, 33.8, 30.7, 28.2, 23.6, 23.3, 17.6, 16.7; HRMS (CI, NH_3)) *m/z* calcd for $[C_{14}H_{26}O_3+NH_4]^+$, 260.2226; found, 260.2215.



9

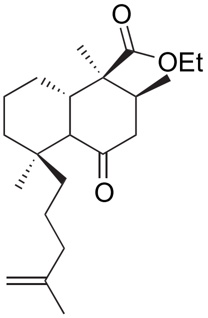
1,2-Dimethyl-4-oxo-6-(4-oxo-pentyl)-cyclohexanecarboxylic acid ethyl ester [(±)-9]. To a stirred solution of **8** (2.20 g, 9.1 mmol) in acetone (50 mL) excess Jones reagent was added until a red solution persisted. The red solution was allowed to stir for 30 min before it was titrated with 2-propanol. After removal of the solvent *in vacuo* and addition of water (20 mL), the mixture was extracted with ether (4 x 50 mL). The extract was washed with brine (20 mL), dried over Na_2SO_4 and concentrated *in vacuo*. The residue was dissolved in acetone (50 mL) then K_2CO_3 (6.27g, 45.4 mmol) and EtI (2.18 mL, 27.2 mmol) were added. The solution was refluxed for 1hr then filtered through a pad of celite and concentrated *in vacuo*. The residue was suspended in EtOAc (200 mL), washed with H_2O (40 mL), brine (40 mL), dried over Na_2SO_4. After concentration *in vacuo*, the remaining oil was chromatographed over silica gel (hexanes - ethyl acetate, 3:1, v/v) to provide **9** (2.08g, 7.4 mmol, 81%) as a colorless oil. R_f 0.54 (hexanes - ethyl acetate, 1:1, v/v); IR (film) υ_{max} 2961, 1716, 1457, 1419, 1364, 1273, 1212, 1163, 1118 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ

4.14 (t, *J* = 7.5 Hz, 2H), 2.52 (dd, *J* = 5.1, 14.7 Hz, 1H), 2.45 - 2.36 (m, 4H), 2.27 (ddd, *J* = 1.5, 5.5, 14.5 Hz, 1H), 2.14 - 2.01 (m, 2H), 2.10 (s, 3H), 1.68 - 1.59 (m, 1H), 1.48 - 1.36 (m, 2H), 1.29 (s, 3H), 1.25 (t, *J* = 6.5 Hz, 3H), 1.08 - 1.00 (m, 1H), 0.88 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 210.6, 208.5, 175.6, 60.5, 48.4, 44.4, 43.3, 42.2, 39.3, 38.1, 31.3, 29.9, 21.5, 18.1, 16.7, 14.2; HRMS (CI, NH_3) *m/z* calcd for $[C_{16}H_{26}O_4 + NH_4]^+$, 300.2149; found, 300.2175.



5

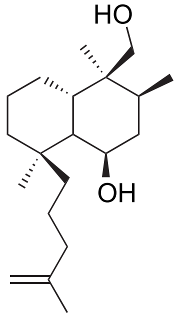
1,2,5-Trimethyl-4-oxo-1,2,3,4,6,7,8,8a-octahydro-naphthalene-1-carboxylic acid ethyl ester [(±)-5]. To a stirred solution of **9** (1.52 g, 5.38 mmol) in absolute ethanol (100 mL), *t*-BuOK (0.67 g, 5.5 mmol) was added and the solution refluxed for 30 min. The heating source was removed and the NH_4Cl (0.3 g, 5.5 mmol) was added. After removing most of the ethanol *in vacuo*, EtOAc (300 ml) was added and the solution was washed with H_2O (50 mL), brine (50 mL) and dried over Na_2SO_4. The solution was concentrated *in vacuo* and the residue was chromatographed over silica gel (hexanes - ethyl acetate, 10:1, v/v) to give **5** (1.03 g, 3.89 mmol, 72 %) as a colorless oil. R_f 0.49 (hexanes - ethyl acetate, 5:1, v/v); IR (film) υ_{max} 2936, 1725, 1683, 1608, 1456, 1423, 1377, 1252, 1220, 1174, 1134, 1100 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 4.65 (t, *J* = 7.5 Hz, 2H), 3.12 - 3.11 (m, 1H), 2.67 (dd, *J* = 5.0, 15.5 Hz, 1H), 2.31 (dd, *J* = 4.0, 15.5 Hz, 1H), 2.16 - 2.13 (m, 3H), 1.95 (d, *J* = 2.5, 3H), 1.90 - 1.87 (m, 1H), 1.75 - 1.73 (m, 1H), 1.56 - 1.52 (m, 1H), 1.33 - 1.27 (m, 4H), 1.28 (t, *J* = 2.5 Hz, 3H), 0.96 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 202.5, 175.7, 148.5, 130.7, 60.4, 48.6, 45.0, 38.7, 38.5, 34.2, 24.7, 22.7, 21.4, 19.6, 19.8, 14.2; HRMS (CI, NH_3) *m/z* calcd for $[C_{16}H_{24}O_3 + NH_4]^+$, 282.2069; found, 282.2069.



5a

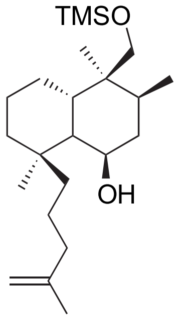
1,2,5-Trimethyl-5-(4-methyl-pent-4-enyl)-4-oxo-decahydro-naphthalene-1-carboxylic acid ethyl ester [(±)-5a]. To a stirred solution of 5-bromo-2-methyl-1-pentene

(**10**, 1.30 g, 8.0 mmol) in ether (53 mL) at –78 ºC, *t*-BuLi (9.4 mL, 1.7 M in pentane, 16.0 mmol) was added drop wise. After 30 min, a solution of CuI (0.73 g, 4.0 mmol) and PBu_3 (2.5 mL, 10 mmol) in THF (21 mL) was added. The mixture was stirred for an additional 20 min before a solution of enone **5** (0.51 g, 1.9 mmol) in THF (6 mL) was added drop wise followed by $BF_3 \cdot OEt_2$ (1.0 mL, 8.0 mmol). After 4 hr, saturated aqueous NH_4Cl (10 mL) was added and the solution warmed to rt. The solution was diluted with Et_2O (100 mL), washed with H_2O (20 mL) then stirred with aqueous H_2O_2 (2 mL) for 15 min. The resulting brown solution was filtered through a plug of silica gel and concentrated *in vacuo*. The residue was chromatographed over silica gel (hexanes - ethyl acetate, 15:1, v/v) to give **5a** (0.58 g, 1.66 mmol, 86 %) as a colorless oil. R_f 0.56 (hexanes - ethyl acetate, 5:1, v/v); FTIR (film) _$_{max}$ 3072, 2936, 2870, 1712, 1648, 1463, 1388, 1375, 1268, 1246, 1215, 1179, 1148, 1110 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 4.65, (m, 2H), 4.14 (q, *J* = 6 Hz, 2H), 2.65 - 2.60 (m, 2H), 2.10 - 2.04 (m, 2H), 1.97 - 0.82 (m, 13H), 1.71 (s, 3H), 1.37 (s, 3H), 1.25 (t, *J*= 11.0 Hz, 3H), 1.10 (s, 3H), 0.83, (d, *J* = 12 Hz, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 210.4, 175.6, 146.3, 109.4, 60.3, 58.7, 48.5, 45.6, 40.7, 38.7, 37.6, 35.7, 29.9, 27.4, 22.3, 21.4, 18.9, 16.5, 14.1; HRMS (FAB) *m/z* calcd for $[C_{22}H_{36}O_3+H]^+$, 349.2743; found, 341.2721.



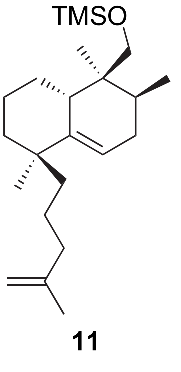
5b

4-Hydroxy-3,4,8-trimethyl-8-(4-methyl-pent-4-enyl)-decahydro-naphthalene-1-ol [(±)-5b]. To a suspension of $LiAlH_4$ (0.01 g, 0.27 mmol) in Et_2O (3 mL) at 0 ºC, a solution of **5a** (0.10 g, 0.28 mmol) in Et_2O (1 mL) was added dropwise. The solution was allowed to warm to rt and stir for 1h. The solution was cooled to 0 ºC and H_2O (1 mL) was added, followed by saturated sodium potassium tartrate solution (1 mL). This solution was extracted with Et_20 (3 x 10 mL) and the combined extract washed with brine (5 mL). After drying over Na_2SO_4, the solvent was removed *in vacuo* and the residue was chromatographed over silica gel (hexanes - ethyl acetate, 4:1, v/v) to give **5b** (0.08 g, 0.25 mmol, 91 %) as a colorless oil. R_f 0.15 (hexanes - ethyl acetate, 5:1, v/v); IR (film) υ_{max} 3446, 2931, 1647, 1458, 1375, 1018 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 4.67(d, *J* = 7.5 Hz, 2H), 4.28 (d, *J* = 3.0 Hz, 1H), 3.54 (d, *J* = 3.5 Hz, 2H), 1.99 – 0.80 (m, 19H), 1.71 (s, 3H), 1.20 (d, *J* = 7.0 Hz, 3H), 0.98 (s, 3H), 0.97 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 146.6, 109.4, 70.0, 68.1, 50.3, 40.7, 39.0, 37.7, 37.4, 36.4, 34.4, 33.4, 29.7, 27.5, 26.6, 22.6, 21.9, 20.9, 18.7, 18.3; HRMS (CI, NH_3) *m/z* calcd for $[C_{20}H_{36}O_2+ H]^+$, 309.2794; found, 309.2791.



5c

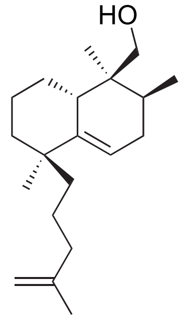
3,4,8-Trimethyl-8-(4-methyl-pent-4-enyl)-4-trimethylsilanyloxymethyl-decahydro-naphthalen-1-ol [(±)-5c]. To a stirred 0 ºC solution of **5b** (0.25 g, 0.81 mmol) and DMAP (0.01 g, 0.09 mmol) in CH_2Cl_2 (5 mL) was added TMSCl (0.11 mL, 0.86 mmol) followed by Et_3N (0.6, 4.3 mmol). After the solution was warmed to rt and stirred for 1h, EtOAc (20 mL) was added and the solution was washed with H_2O (5 mL), brine (5 mL), then dried over Na_2SO_4. The solvent was removed *in vacuo* and the residue chromatographed over silica gel (hexanes - ethyl acetate, 10:1, v/v, Et_3N 0.5%) to give **5c** (0.27 g, 0.70 mmol, 86 %) as a colorless oil. R_f 0.68 (hexanes - ethyl acetate, 5:1, v/v); IR (film) 2931, 1652, 1458, 1375, 1250, 1088, 1072 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 4.68 (d, *J* = 6.0, 2H), 4.25 (s, 1H), 3.42 (s, 2H), 1.99 (t, *J* = 7.5 Hz, 2H), 1.95 - 1.86 (m, 2H), 1.76 - 1.67 (m, 2H), 1.72 (s, 3H), 1.63 - 1.57 (m, 2H), 1.50 (dt, *J* = 2.5, 14.4 Hz, 1H), 1.46 - 1.41 (m, 1H), 1.34 - 1.28 (m, 4H), 1.14 (d, *J* = 8 Hz, 3H), 1.13 - 1.06 (m, 3H), 0.98 (s, 3H), 0.92 (s, 3H), 0.87 - 0.83 (m, 1H), 0.08 (s, 9H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 146.7, 109.4, 69.2, 68.3, 50.5, 40.5, 39.1, 37.7, 37.5, 36.4, 34.0, 33.6, 29.8, 27.5, 26.7, 22.6, 21.9, 21.0, 18.8, 17.9, -0.5; HRMS (CI) *m/z* calcd for $[C_{23}H_{44}O_2Si+H]^+$, 381.3189; found, 381.3176.



11

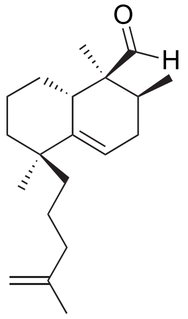
Trimethyl-[1,2,5-trimethyl-5-(4-methyl-pent-4-enyl)-1,2,3,5,6,7,8,8a-ocahydro-naphthalen-1-ylmethoxy]-silane [(±)-11]. To a stirred solution of **5c** (0.12 g, 0.32 mmol) in pyridine (5 mL) at 0 ºC, $SOCl_2$ (0.12 mL, 1.64 mmol) was added drop wise and the solution was stirred for 30 min. The solution diluted with wet Et_2O (200 mL) and washed with 1N

HCl (70 mL), saturated $NaHCO_3$ (20 mL), H_20 (20 mL), brine (20 mL) then dried over Na_2SO_4. After concentration *in vacuo*, the residue was chromatographed over silica gel (hexanes - ethyl acetate, 20:1, v/v, Et_3N 0.5%) to give **11** (0.10 g, 0.28 mmol, 89 %) as a colorless oil. R_f 0.74 (streaky) (hexanes - ethyl acetate, 15:1, v/v); IR (film) 2953, 1652, 1456, 1374, 1250, 1093, 881, 839 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 5.29 (t, *J* = 2.8 Hz, 1H), 4.69 (s, 1H), 4.66 (s, 1H), 3.46 (d, *J* = 9.5 Hz, 1H), 3.34 (d, *J* = 9.5 Hz, 1H), 2.00 - 1.95 (m, 4H), 1.77 - 1.62 (m, 4H), 1.71 (s, 3H), 1.59 - 1.55 (m, 1H), 1.52 - 1.49 (br, 1H), 1.30 - 1.26 (m, 1H), 1.20 - 1.00 (m, 5H), 0.98 (s, 3H), 0.88 (s, 3H), 0.86 (s, 3H), 0.07 (s, 9H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 146.2, 145.5, 116.7, 109.6, 66.0, 41.9, 40.0, 39.8, 38.7, 38.3, 37.1, 31.7, 31.6, 29.3, 26.2, 22.5, 22.4, 22.0, 20.9, 15.4, -0.54; HRMS (CI, NH_3) *m/z* calcd for $[C_{23}H_{42}OSi+H]^+$, 363.3083; found, 363.3058.



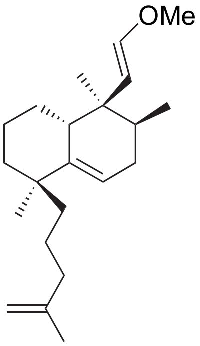
11a

[1,2,5-Trimethyl-5-(4-methyl-pent-4-enyl)-1,2,3,5,6,7,8,8a-ocahydro-naphthalen-1-yl]-methanol [(±)-11a]. To a stirred 0 °C solution of **11** (61.5 mg, 0.17 mmol) in THF (2 mL), TBAF (0.2 mL of 1.0 M in THF, 0.20 mmol) was added. After stirring for 30 min, the solution was diluted with Et_2O (10 mL) washed with water (2 mL), brine (2 mL) and dried over Na_2SO_4. The solvent was removed *in vacuo* and the residue chromatographed over silica gel (hexanes - ethyl acetate, 8:1, v/v) to give **11a** (43.3 mg, 0.15 mmol, 88 %) as a colorless oil. R_f 0.48 (hexanes - ethyl acetate, 5:1, v/v); IR (film) 3412, 2937, 1648, 1456, 1374, 1020, 887 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 5.31 (s, 1H), 4.68 (s, 1H), 4.66 (s, 1H), 3.51 (m, 2H), 2.04 (br, 1H), 2.02 (br, 1H), 1.97 (t, *J* = 7.5, 2H), 1.76 - 1.50 (m, 7H), 1.70 (s, 3H), 1.30 (m, 1H), 1.20 - 1.05 (m, 5H),0.98 (s, 3H), 0.94 (s, 3H), 0.88 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR ($CDCl_3$, 125 MHZ) δ 146.6, 145.3, 116.9, 109.6, 66.5, 41.9, 40.0, 39.9, 38.7, 38.6, 38.4, 37.1, 31.7, 31.6, 29.3, 26.14, 22.40, 22.36, 20.5, 15.3; HRMS (CI, NH_3) *m/z* calcd for $[C_{20}H_{34}O+H]^+$, 291.2688; found, 291.2699.



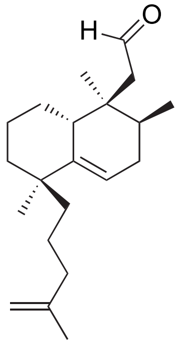
11b

1,2,5-Trimethyl-5-(4-methyl-pent-4-enyl)-1,2,3,5,6,7,8,8a-ocahydro-naphthalen-1-carbaldehyde [(±)-11b]. To a stirred solution of **11a** (0.16 g, 0.54 mmol) in CH_2Cl_2 (5 mL) at rt, silica gel (0.16 g) and PCC (0.15 g, 0.71 mmol) were added. After 1h, the solution was filtered through a plug of silica gel and the solvent was removed *in vacuo*. The residue was chromatographed over silica gel (hexanes - ethyl acetate, 10:1, v/v) to give **11b** (0.14 g, 0.49 mmol, 91 %) as a colorless oil. R_f 0.70 (hexanes - ethyl acetate, 5:1, v/v); IR (film) υ_{max} 2937, 2706, 1721, 1649, 1453, 1376, 886, 812 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 9.57 (s, 1H), 5.36 (s, 1H), 4.67 (s, 1H), 4.64 (s, 1H), 2.35 (d, J = 11.5 Hz, 1H), 2.26 (d, J = 18.0 Hz, 1H), 1.95 (t, J = 7.5 Hz, 2H), 1.89 - 1.85 (m, 1H), 1.82 (sex, J = 6.0 Hz, 1H), 1.71 - 1.66 (m, 3H), 1.68 (s, 3H), 1.60 - 1.53 (m, 2H), 1.31 - 1.06 (m, 5H), 1.00 (s, 3H), 0.99 (s, 3H), 0.90 (d, J = 6.5 Hz, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 207.2, 146.1, 144.3, 116.9, 109.8, 49.9, 41.3, 39.7, 38.58, 37.2, 36.6, 31.7, 31.1, 29.1, 26.1, 22.4, 22.3, 21.9, 17.7, 15.5; HRMS (CI, NH_3) *m/z* calcd for $[C_{20}H_{32}O+NH_4]^+$, 306.2797; found, 306.2785.



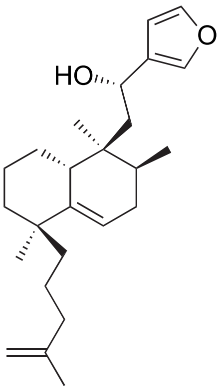
6a

5-(2-Methoxy-vinyl)-1,5,6-trimethyl-1-(4-methyl-pent-4-enyl)-1,2,3,4,4a,5,6,7-octahydro-naphthalene [(±)-6a]. To a suspension of methoxymethyltriphenyl-phosphonium chloride (0.25 g, 0.73 mmol) in THF (1 mL) at –78 ºC, 15% KHMDS (1.10 mL, 0.73 mmol) in toluene was added drop wise and the solution stirred for 30 min. A solution of **11b** (88.1 mg, 0.31 mmol) in THF (1 mL) was added drop wise and the solution stirred for 1 h. The solution was gradually warmed to rt. After cooling to 0 ºC and dilution with wet Et_2O (20 mL), the solution was washed with H_2O (5 mL), brine (5 mL) then dried over Na_2SO_4. After concentration *in vacuo*, the residue was chromatographed over silica gel (hexanes) to give **6a** as a colorless oil (71.1 mg, 0.22 mmol, 71 %). R_f 0.73 (hexanes - ethyl acetate, 10:1, v/v); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 6.26 (d, *J* = 13.0 Hz, 1H), 5.32 (dd, *J* = 1.0, 5.0 Hz, 1H), 4.89 (d, *J* = 13.0 Hz, 1H), 4.66 (s, 1H), 4.64 (s, 1H), 3.44 (s, 3H), 2.03 - 2.00 (m, 1H), 1.95 (t, *J* = 7.5 Hz, 2H), 1.83 - 1.50 (m, 8H), 1.69 (s, 3H), 1.33 - 0.95 (m, 5H), 0.99 (s, 3H), 0.95 (s, 3H), 0.76 (d, *J* = 7.0 Hz, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 146.6, 146.3, 117.1, 109.6, 55.6, 42.3, 39.9, 39.5, 38.6, 37.6, 37.0, 34.8, 26.1, 22.5, 22.4, 22.2, 20.0, 15.5, 15.0. HRMS (CI, NH_3) *m/z* calcd for $[C_{22}H_{36}O+H]^+$, 317.2844; found, 317.2857.

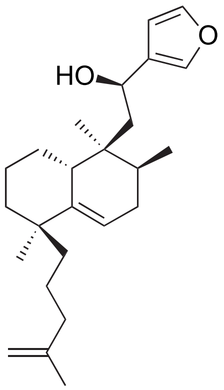


6

[1,2,5-Trimethyl-5-(4-methyl-pent-4-enyl)-1,2,3,5,6,7,8,8a-octahydro-naphthalen-1-yl]-acetaldehyde [(±)-6]. To a solution **6a** (71.1 mg, 0.22 mmol) in dioxane (12 mL) at rt, 1N HCl (12 drops) was added. After 20 min Et_2O (50 mL) was added and the solution washed with H_2O (10 mL), brine (10 mL) then dried over Na_2SO_4. The solvent was removed *in vacuo* and the residue chromatographed over silica gel (hexanes - ethyl acetate, 30:1, v:v) to give **6** (61.4 mg, 0.20 mmol, 91 %) as a colorless oil. R_f 0.56 (hexanes - ethyl acetate, 10:1, v/v); IR (film) υ_{max} 2936, 2724, 1719, 1649, 1445, 1374, 885, 812 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 9.90 (t, *J* = 3.0 Hz, 1H), 5.33 (t, *J* = 3.0 Hz, 1H), 4.67 (s, 1H), 4.64 (s, 1H), 2.33 (dd, *J* = 2.5, 15.0 Hz, 1H), 2.24 (dd, 3.0, 14.5 Hz, 1H), 2.08 - 1.93 (m, 4H), 1.80 (m, 1H), 1.73 - 1.51 (m, 6H), 1.68 (s, 3H), 1.31 - 1.28 (m, 1H), 1.20 - 1.09 (m, 4H), 1.07 (s, 3H), 0.99 (s, 3H), 0.84 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 204.6,146.3, 128.6, 128.2, 117.12, 109.7, 42.0, 40.0, 38.6, 37.6, 37.0, 33.0, 31.6, 29.4, 26.0, 23.0, 22.5, 22.4, 22.3, 15.0; HRMS (CI, NH_3) *m/z* calcd for $[C_{21}H_{34}O+H]^+$, 303.2688; found 303.2685.

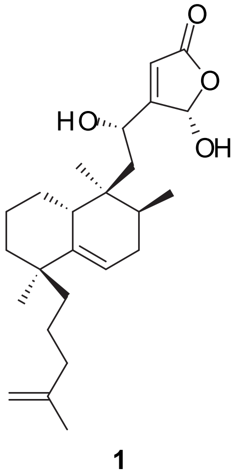


12



4-epi-**12**

1-Furan-3-yl-2-[1,2,5-trimethyl5-(4-methyl-pent-4-enyl)-1,2,3,5,6,7,8,8a-octahydro-naphthalen-1-yl]-ethanol [(±)-12]. To a solution of 3-bromofuran (31 μL, 0.34 mmol) in THF (5 mL) at –78 ºC, 2.5 M BuLi (0.14 mL, 0.34 mmol) was added and the solution stirred for 30 min. To the solution **5** (34.6 mg, 0.114 mmol) in THF (2 mL) was added drop wise and the solution stirred for 30 min. After adding saturated aqueous NH_4Cl (1 mL), the mixture warmed to rt and diluted with Et_2O (50 mL). The solution was washed with H_2O (10 mL), brine (10 mL), dried over Na_2SO_4 and concentrated *in vacuo*. The residue was chromatographed to yield the alcohol diastereomers (15.7 mg, 0.042 mmoles (**12**) and 19.1 mg, 0.051 mmoles (4-*epi*-**12**) 82 %). Characterization data for **12**; R_f 0.30 (hexanes - ethyl acetate, 8:1, v/v); IR (film) υ_{max} 3388, 2937, 1650, 1503, 1445, 1374, 1161, 1025, 874; ^1H NMR ($CDCl_3$, 500 MHz) δ 7.33 (d, *J* = 8.5 Hz, 2H), 6.38 (s, 1H), 5.32 (s, 1H), 4.85 (t, *J* = 6.0 Hz, 1H), 4.66 (s, 1H), 4.59 (s, 1H), 1.90 - 1.03 (m, 21 H), 1.65 (s, 3H), 0.97 (s, 3H), 0.88 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 145.9, 143.2, 142.0, 138.4, 131.1, 117.2, 113.9, 109.7, 108.7, 64.0, 41.5, 39.8, 38.5, 36.9, 36.2, 33.4, 31.8, 31.6, 29.7, 26.1, 22.5, 22.4, 22.1, 21.9, 15.0 cm^{-1}; HRMS (FAB) *m/z* calcd for $[C_{25}H_{38}O_2+Na]^+$, 393.2769; found 393.2786. R_f 4-*epi*-**12** 0.45 (hexanes - ethyl acetate, 8:1, v/v); IR (film) υ_{max} 3454, 2936, 1649, 1502, 1444, 1374, 1160, 1056, 1024, 873; ^1H NMR ($CDCl_3$, 500 MHz) δ 7.36 (s, 2H), 6.39 (s, 1H), 5.34 (s, 1H), 4.85 (s, 1H), 4.65 (s, 1H), 4.64 (s, 1H), 1.97 - 0.97 (m, 18 H), 1.68 (s, 3H), 1.00 (s, 3H), 0.97 (s, 3H) 0.77 (d, *J* = 6.0 Hz, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 146.6, 143.2, 142.0, 138.5, 131.3, 117.1, 113.8, 109.6, 108.6, 64.9, 42.9, 42.3, 40.1, 38.7, 38.6, 38.2, 37.2, 35.9, 33.2, 33.0, 31.8, 29.8, 26.2, 22.5, 14.9; HRMS (FAB) *m/z* calcd for $[C_{25}H_{38}O_2+Na]^+$, 393.2769; found 393.2780.



1

5-Hydroxy-4-{1-hydroxy-2-[1,2,5-trimethyl-5-(4-methyl-pent-4-enyl)-1,2,3,5,6,7,8,8a-octahydro-naphthalen-1-yl]-ethyl}-5*H*-furan-2-one[(±)-1] Dysidiolide. To diisopropylethylamine (10 μL, 0.06 mmol) and Rose Bengal (0.2 mg) in CH_2Cl_2 (3 mL) at rt, a solution of **12** (1.3 mg, 3.5 μmol) in CH_2Cl_2 (1 mL) was transferred via cannula. The solution was cooled to –78 ºC and irradiated with a 28 W fluorescent lamp while anhydrous O_2 was bubbled through it for 20 min. The irradiation was continued for 2 h after removal of the oxygen line. Then Ar was bubbled through the solution for 10 min and the solution warmed to rt. Saturated aqueous oxalic acid (0.3 mL) was added and the solution stirred until a colorless solution resulted. The organic layer was removed and the remaining aqueous phase washed with CH_2Cl_2 (2 x 10 mL). The combined CH_2Cl_2 layers were dried over $MgSO_4$, concentrated *in vacuo* and chromatographed over silica gel (2% MeOH - CH_2Cl_2) to provide dysidiolide (**1**) as a white solid (1.1 mg, 2.8 μmol, 78%). R_f 0.51 (hexanes: ethyl acetate 1:1, v/v); HPLC (C_{18} 5μm, 100 Å, 250 mm x 4.6 mm ID column): t_R = 17.01 min (85% MeOH-15% H_2O, flow rate = 0.75 mL / min); co-eluted with a sample of naturally occurring **1**. ^{1}H NMR (DMSO, 500 MHZ) δ 7.84 (d (br), *J* = 6.5 Hz, 1H), 6.09 (s (br), 1H), 5.92 (s (br), 1H), 5.28 - 5.25 (br, 2H), 5.12 (s, 1H), 4.63 (s, 1H), 4.60 (s, 1H), 4.50 (s, 1H), 4.38 (br, 1H), 2.24 (br, 1H), 1.98 - 0.78 (m, 15H), 1.61 (s, 3H), 1.47 (s (br), 3H), 0.93 (s, 3H), 0.81 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 176.2, 170.9, 145.9, 142.3, 116.4, 116.0, 110.54, 98.5, 98.2, 64.9, 40.5, 38.4, 36.9, 33.6, 29.9, 29.5, 26.4, 23.2, 22.6, 22.1, 20.4, 15.4; HRMS (FAB) *m/z* calcd for $[C_{21}H_{34}O+H]^+$, 403.2848; found 403.2825.