Supplementary Material (ESI) for Chemical Communications

Total synthesis of viridiofungin A

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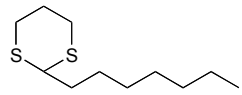
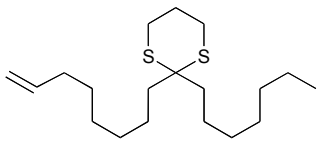
Supporting Information

General Procedure. Where appropriate, reactions were performed in flame-dried glassware under an argon atmosphere. All extracts were dried over $MgSO_4$ and concentrated by rotary evaporation below 30 °C at ca. 25 Torr. Commercial reagents and solvents were used as supplied with the following exceptions. Anhydrous tetrahydrofuran (THF) was purchased from Kanto Chemical Co., Inc. Dichloromethane (CH_2Cl_2), triethylamine, dimethyl sulfoxide (DMSO), and *N*,*N*-dimethyformamide (DMF) were distilled from CaH_2. Toluene was distilled from P_2O_5. Analytical thin-layer chromatography was performed with Merck F-254 TLC plates. Column chromatography was performed employing silica gel 60 (230-630 mesh ASTM, Merk). Recycling preparative HPLC was performed using LC-908 (Japan Analytical Industry Co., LTD). Infrared spectra were measured on a JASCO FTIR-230 spectrometer. Optical rotations were recorded on a JASCO DIP-370 polarimeter at ambient temperature. ^{1}H and ^{13}C NMR spectra were measured on a Varian Gemini 300, JEOL JNM-AL 400, or a Varian Unity plus 500 spectrometer. Tetramethylsilane (TMS) was defined as 0 ppm for ^{1}H NMR spectra and the central line of the triplet of $CDCl_3$ was defined as 77.10 ppm for ^{13}C NMR spectra. EI and FAB Mass spectra were measured on a JEOL JMS-DX303 or a JEOL JMS-700N.

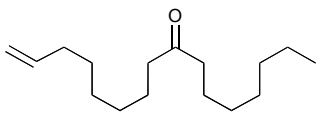


2-Heptyl-1,3-dithiane. To a stirred solution of 1-octanal (15.3 g, 0.119 mol) in CH_2Cl_2 (500 ml) at 0 °C were added 1,3-propanedithiol (15 ml, 0.150 mol) and $BF_3{\cdot}Et_2O$ (13 ml, 0.105 mol). After being stirred at 0 °C for 2 h, the reaction was quenched with saturated $NaHCO_3$ (300 ml). The reaction mixture was extracted with CH_2Cl_2, washed with brine, and concentrated. Purification of the residue by distillation gave 2-heptyl-1,3-dithiane (25.1 g, 97%) as a pale yellow oil: bp 96 °C (0.15 mmHg); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.86 (t, *J* = 6.3 Hz, 3H), 1.26 (m, 8H), 1.48 (quint, *J* = 6.3 Hz, 2H), 1.71 (m, 2H), 1.85 (m, 1H), 2.11 (dquint, *J* = 4.2, 14.1 Hz, 1H), 2.83 (m, 4H), 4.03 (t, *J* = 6.9 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.2, 22.7, 26.1, 26.7, 29.1, 29.3, 30.6, 31.8, 35.5, 47.8; FTIR (neat) 1457, 1421, 1274, 1186 cm^{-1}; MS (EI) m/z 119 (100), 218 (M^+); HRMS (EI) calcd. for $C_{11}H_{22}S_2$ (M^+) 218.1163, found 218.1182.

8-Iodooct-1-ene. To a stirred solution of 7-octene-1-ol (10.0 g, 0.0780 mol), triphenylphosphine (41.0 g, 0.160 mol), and 2,6-lutidine (36 ml, 0.310 mol) in CH_2Cl_2 (500 ml) at 0 °C was added iodine (41.5 g, 0.160 mol). After being stirred at 0 °C for 1 h, the reaction mixture was acidified with 1 M HCl (300 ml) and diluted with hexane (300 ml). The organic layer was washed with H_2O, saturated $Na_2S_2O_3$, and saturated $NaHCO_3$, dried, concentrated, and chromatographed (SiO_2 135 g, hexane) to give 8-iodo-1-ene (17.5 g, 96%) as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.38 (m, 6H), 1.83 (quint., J = 7.1 Hz, 2H), 2.505 (dt, J = 6.9, 6.6 Hz, 2H), 3.19 (t, J = 6.9 Hz, 2H), 4.92 ~ 5.04 (m, 2H), 5.80 (ddt, J = 10.2, 17.1, 5.1 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 7.3, 28.0, 28.7, 30.4, 33.5, 33.7, 114.4, 138.9; FTIR (neat) 1639, 1459, 1201, 1170 cm^{-1}; MS (EI) m/z 41, 55, 69 (100), 111, 238 (M^+); HRMS (EI) calcd. for $C_8H_{15}I$ (M^+) 238.0218, found 238.0224.

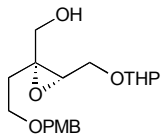


2-Heptyl-2-(oct-7-enyl)-1,3-dithiane. To a stirred solution of 2-heptyl-1,3-dithiane (5.42 g, 24.7 mmol) at –20 °C was added dropwise *n*-butyllithium (1.7 M in hexane, 15 ml, 25.5 mmol) over 10 min, and the mixture was stirred at the same temperature for 2 h. Then, 8-iodo-1-ene (5.41 g, 22.7 mmol) in THF (10 ml) was added dropwise to this mixture at –30 °C over 45 min. After being stirred at –30 °C for 19 h, the reaction was quenched with MeOH (5 ml). The reaction mixture was extracted with Et_2O, washed with brine, dried, and concentrated. Purification of the residue by column chromatography (SiO_2 150 g, hexane/AcOEt = 30/1) gave 2-heptyl-2-(oct-7-enyl)-1,3-dithiane (6.41 g, 86%) as a pale yellow oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.82 (t, J = 6.8 Hz, 3H), 1.23 (m, 14H), 1.32 (m, 4H), 1.78 (m, 2H), 1.88 (m, 2H), 1.97 (dt, J = 6.3, 6.9 Hz, 2H), 2.73 (t, J = 5.4 Hz, 4H), 4.84-4.95 (m, 2H), 5.73 (ddt, J = 10.2, 16.8, 6.6 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.1, 22.6, 24.0, 25.6, 26.0, 28.9, 29.0, 29.2, 29.7, 29.8, 31.8, 33.8, 38.1, 53.3, 114.2, 139.0; FTIR (neat) 1455, 1270 cm^{-1}; MS (EI) m/z 229 (100), 328 (M^+); HRMS (EI) calcd. for $C_{19}H_{36}S_2$ (M^+) 328.2258, found 328.2249.

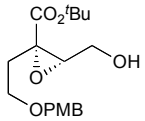


Hexadec-15-en-8-one (6). To a stirred solution of 2-heptyl-2-(oct-7-enyl)-1,3-dithiane (994 mg, 3.03 mmol) in MeOH (16 ml) at room temperature was added *N*-chlorosuccinimide (500 mg, 3.74 mmol). After being stirred at room temperature for 30 min, 1 M HCl (6 ml) was added and the mixture was stirred for 30 min. The reaction mixture was diluted with Et_2O, washed with H_2O and brine, dried, concentrated, and chromatographed (SiO_2 10 g, hexane/AcOEt = 40/1) to give **6** (446 mg, 62%) as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.88 t, J = 6.6 Hz, 3H), 1.27 m, 14H), 1.56 (m, 4H), 2.04 (dt, J = 7.2, 6.9 Hz, 2H), 2.38 (t, J = 7.5 Hz, 4H), 4.91 ~ 5.02 (m, 2H), 5.80 (ddt, J

= 10.5, 17.4, 6.6 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.1, 22.7, 23.9 (2), 28.8, 28.9, 29.1, 29.3, 31.7, 33.8, 42.8, 42.9, 114.3, 139.1, 211.7; FTIR (neat) 1700, 1461 cm^{-1}; MS (EI) m/z 57, 71, 96, 111, 127 (100), 139, 155, 209, 238 (M^+); HRMS (EI) calcd. for $C_{16}H_{30}O$ (M^+) 238.2297, found 238.2274.



(2*R*,3*S*)-2,3-Epoxy-2-[2-(4-methoxybenzyl)oxyethyl]-4-(tetrahydropyran-2-yl)oxybutan-1-ol (8). To a suspension of powdered 4A molecular sieves (4.0 g), prepared by heating overnight at 130 °C under 0.1 mmHg, in CH_2Cl_2 (70 ml) at –40 °C were added (–)-diethyl D-tartrate (0.76 ml, 4.46 mmol) and Ti(O^iPr)$_4$ (1.10 ml, 3.72 mmol) and the mixture was stirred for 30 min at –40 °C. *tert*-Butyl hydroperoxide (3.04 M in CH_2Cl_2, 9.8 ml, 29.7 mmol) and then, 30 min later, a solution of **7**[1] (5.00 g, 14.9 mmol) in CH_2Cl_2 (30 ml) were added to the mixture at –40 °C. After being stirred at –20 °C for 7 h, the mixture was treated with a solution of $FeSO_4 \cdot 7H_2O$ (16.5g, 59.3 mmol) and tartaric acid (11.6 g, 77.3 mmol) in H_2O (90 ml), allowed to warm to room temperature, and stirred overnight. The reaction mixture was diluted with H_2O (100 ml), extracted with CH_2Cl_2, dried, and concentrated. The residue was dissolved into Et_2O (60 ml) and 1 M NaOH (40 ml) was added to the solution at 0 °C. After stirring at room temperature for 1 h, the mixture was extracted with CH_2Cl_2, washed with brine, dried, and concentrated. Purification of the residue by column chromatography (SiO_2 100 g, hexane/AcOEt = 1/3) gave **2** (5.11 g, 98%) as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ1.53-1.82 m, 6H), 1.88-1.98 (m, 1H), 2.01-2.11 (m, 1H), 3.09-3.15 (m, 1H), 3.36 (br t, *J* = 5.4 Hz, 0.5H), 3.38 (br t, *J* = 6.0 Hz, 0.5H), 3.81 s, 3H), 3.49-3.93 (m, 8H), 4.45 (s, 2H), 4.66-4.70 (m, 1H), 6.88 (d, *J* = 8.4 Hz, 2H), 7.27 (d, *J* = 8.7 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ18.9, 19.3, 25.2, 30.2, 30.4, 34.4, 34.5, 55.2, 61.0, 61.5, 61.8, 62.0, 62.3, 62.9 (2), 64.5, 65.8, 66.1, 72.9, 97.8, 99.4, 113.8, 129.4, 129.8, 159.3; FTIR (neat) 3424, 1612, 1513, 1247, 1031 cm^{-1}; MS (EI) m/z 85, 121 (100), 137, 189, 206, 267 [(M–THP)$^+$], 352 (M^+); HRMS (EI) calcd for $C_{19}H_{28}O_6$ (M^+) 352.1886, found 352.1863.



(2*S*,3*S*)-3-(*tert*-Butoxycarbonyl)-2,3-epoxy-5-(4-methoxybenzyl)oxypentan-1-ol (9). To a stirred solution of **8** (5.09 g, 14.44 mmol) in CH_2Cl_2-DMSO (1:1) (86 ml) at room temperature were added triethylamine (60 ml, 427 mmol) and SO_3□pyridine complex (20.7 g, 130 mmol). After being stirred at room temperature for 1 h, the reaction mixture was diluted with H_2O (200 ml), extracted with CH_2Cl_2, washed with brine, dried, and concentrated. Purification of the residue by column chromatography (SiO_2 100 g, hexane/AcOEt = 2/1) afforded the corresponding aldehyde (6.09 g) as a yellow oil: ^{1}H NMR (300 MHz, $CDCl_3$) □1.53-1.90 m, 7H), 2.37-2.47 m, 1H), 3.43-3.60 m, 5H), 3.70 dd, *J* = 2.1, 12.0 Hz, 0.5H), 3.72 dd, *J* = 2.7, 12.0 Hz, 0.5H), 3.79 (s, 3H), 3.93 dd, *J* = 4.8, 12.0 Hz, 0.5H), 3.98 dd, *J* = 3.9, 13.2 Hz, 0.5H), 4.41 (s, 2H), 4.62 (m, 1H), 6.86 (d, *J* = 8.4 Hz, 2H), 7.22 (d, *J* = 8.4 Hz, 2H), 9.45 (s, 0.5H), 9.46 (s, 0.5H); ^{13}C

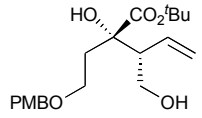
NMR (75 MHz, $CDCl_3$) □ 18.8, 19.0, 25.2, 30.1, 30.2, 31.0, 31.1, 55.2, 61.7, 62.0, 63.3, 63.5, 63.9, 65.1, 72.6, 98.6, 99.0, 113.7, 129.2, 130.1, 159.1, 198.5, 198.6; FTIR (neat) 1724, 1513, 1454, 1247, 1124, 1033 cm^{-1}.

To a stirred solution of the aldehyde (6.09 g) in *tert*-BuOH-H_2O (5:1) (500 ml) at 0 °C were added 2-methyl-2-butene (46 ml, 408 mmol), NaH_2PO_4□$2H_2O$ (7.88 g, 50.5 mmol), and $NaClO_2$ (80% purity, 5.71 g, 50.5 mmol). After being stirred at room temperature for 12 h, the reaction mixture was diluted with brine (200 ml), extracted with AcOEt, dried, and concentrated to give the corresponding carboxylic acid (7.14 g) as a yellow oil, which was used for the next reaction without purification: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.48-1.78 m, 6H), 1.90-2.06 m, 1H), 2.42-2.46 m, 1H), 3.34-3.37 m, 1H), 3.46-3.92 m, 6H), 3.78 (s, 3H), 4.43 (s, 2H), 4.63-4.67 m, 2H), 6.85 (d, J = 8.7 Hz, 2H), 7.23 (d, J = 8.4 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ18.9, 19.0, 25.2, 30.2, 31.1, 55.2, 61.3, 61.6, 61.9, 62.0, 64.7, 65.0, 65.6, 72.6, 98.7, 98.9, 113.5, 129.3, 130.0, 159.1, 160.1; FTIR (neat) 2942, 1793, 1513, 1249, 1112, 1029 cm^{-1}.

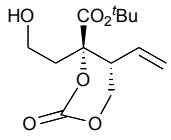
To a solution of the carboxylic acid (7.14 g) in CH_2Cl_2 (50 ml) was added a solution of *N*,*N*'-diisopropyl-*O*-2-*tert*-butylisourea[2] (28.9 g, 144 mmol) in CH_2Cl_2 (22 ml) at 0 °C over 5 min, and the mixture was stirred at room temperature for 12 days. The reaction mixture was filtered through Celite and the filter-pad was washed with Et_2O. The filtrate and washings were concentrated and chromatographed (SiO_2, 150 g, hexane/AcOEt = 4/1) to give the corresponding *tert*-butyl ester (5.35 g, 88% by 3 steps) as a pale yellow oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.43 s, 9H), 1.46-1.82 m, 7H), 2.49 dt, J = 14.4, 6.9 Hz, 1H), 3.26 m, 1H), 3.48-3.61 m, 4H), 3.78 s, 3H), 3.81-3.88 m, 2H), 4.42 (s, 2H), 4.60-4.64 (m, 1H), 6.86 (d, J = 8.4 Hz, 2H), 7.25 (d, J = 8.4 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ19.0, 19.3, 25.3, 27.8, 30.3, 30.4, 33.3, 33.4, 55.1, 60.1, 60.3, 60.8, 61.4, 61.7, 62.2, 64.6, 65.1, 65.5 (2), 82.3, 82.4, 98.5, 99.1, 113.6, 129.3, 130.2, 159.1, 167.8; FTIR (neat) 1735, 1513, 1455, 1361, 1249, 1137, 1031, cm^{-1}; MS (EI) m/z 85 (100), 137, 281, 337 [$(M–THP)^+$], 365 [$(M–^tBu)^+$], 422 (M^+); HRMS (EI) calcd for $C_{23}H_{34}O_7$ (M^+) 422.2304, found 422.2326.

To a solution of the *tert*-butyl ester (1.04g, 2.45 mmol) in MeOH (24 ml) was added pyridinium *p*-toluenesulfonate (185 mg, 0.735 mmol), and the mixture was stirred at room temperature for 39 h. The reaction mixture was diluted with saturated $NaHCO_3$ (10 ml), extracted with CH_2Cl_2, dried, and concentrated. Purification of the residue by column chromatography (SiO_2 13 g, hexane/AcOEt = 4/1 to 1/1) afforded **9** (711 mg, 86%) as a pale yellow oil: $[\alpha]_D^{27}$ –28.5 ° (*c* 1.03, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.42 s, 9H), 1.79-1.85 m, 1H), 2.39 t, J = 6.9 Hz, 1H), 2.41 t, J = 7.2 Hz, 1H), 3.21 dd, J = 4.2, 6.0 Hz, 1H), 3.56 t, J = 5.7 Hz, 2H), 3.64-3.79 m, 2H), 3.79 (s, 3H), 4.42 (s, 2H), 6.86 (d, J = 8.7 Hz, 2H), 7.25 (d, J = 8.1 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ27.8, 33.4, 55.2, 60.4, 61.0, 62.4, 65.4, 72.7, 82.7, 113.7, 129.4, 130.1, 159.2, 168.0; FTIR (neat) 3735, 3511, 2933, 1731, 1511, 1363, 1249, 1139, 1033, 831 cm^{-1}; MS (EI) m/z 41 (100), 122, 138,

145, 233, 281 [(M–^{t}Bu)$^+$], 338 (M$^+$); HRMS (EI) calcd for $C_{18}H_{26}O_6$ (M$^+$) 338.1730, found 338.1748.



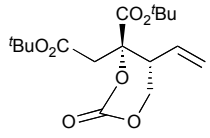
(2*R*,3*S*)-3-(*tert*-Butoxycarbonyl)-5-(4-methoxybenzyl)oxy-2-vinyl-1,3-pentane diol (10). To a suspension of CuI (563 mg, 2.96 mmol) in THF (60 ml) was added a solution of vinylmagnesium bromide (1.14 M in THF, 26 ml, 29.6 mmol) at –26 °C, and the mixture was stirred for 50 min at the same temperature. To the dark blue mixture was added dropwise a solution of **9** (1.00 g, 2.96 mmol) in THF (14 ml) at –26 °C over 5 min. After being stirred for 4 h at –26 °C, the reaction mixture was diluted with saturated NH_4Cl (80 ml), allowed to warm to room temperature, and stirred for 1.5 h. The reaction mixture was filtered through Celite, extracted with CH_2Cl_2, washed with brine, dried, and concentrated. Purification of the residue by column chromatography (SiO_2 40 g, hexane/AcOEt = 4/1 to 2/1) gave **10** (773 mg, 71%) as a pale yellow oil: $[\alpha]_D^{24}$ +14.4 ° (*c* 0.910, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ1.40 s, 9H), 1.99-2.16 m, 2H), 2.44 ddd, *J* = 4.8, 5.1, 9.9 Hz, 1H), 2.68 br s, 1H), 3.50 t, *J* = 6.3 Hz, 2H), 3.77 (s, 3H), 3.74-3.80 (m, 2H), 4.00 (s, 1H), 4.36 (d, *J* = 11.7 Hz, 1H), 4.40 (d, *J* = 11.7 Hz, 1H), 5.18 (dd, *J* = 2.1, 16.2 Hz, 1H), 5.22 (dd, *J* = 1.8, 10.2 Hz, 1H), 5.89 (ddd, *J* = 9.3, 9.6, 16.8 Hz, 1H), 6.85 (d, *J* = 8.7 Hz, 2H), 7.22 (d, *J* = 8.4 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ27.8, 36.6, 53.5, 55.1, 62.3, 65.6, 72.8, 77.8, 82.6, 113.7, 119.1, 129.4, 129.8, 137.7, 159.1, 173.7; FTIR (neat) 3469, 1720, 1612, 1513, 1369, 1249, 1155, 1035 cm^{-1}; MS (EI) m/z 121 (100), 137, 309 [(M–^{t}Bu)$^+$]; HRMS (EI) calcd for $C_{16}H_{21}O_6$ [(M–^{t}Bu)$^+$] 309.1339, found 309.1339.



(4*S*,5*R*)-4-(2-Hydroxyethyl)-4-*tert*-Butoxycarbonyl-5-vinyl-1,3-dioxan-2-one (11). To a stirred solution of **10** (773 mg, 2.11 mmol) and pyridine (1.9 ml, 23.0 mmol) in CH_2Cl_2 (8 ml) at –78 °C was added dropwise a solution of triphosgene (751 mg, 2.53 mmol) in CH_2Cl_2 (4 ml) over 5 min and the mixture was allowed to warm to room temperature. After being stirred at room temperature for 1 h, the reaction mixture was diluted with saturated NH_4Cl (10 ml) and H_2O (30 ml), extracted with CH_2Cl_2, washed with 1 M HCl and saturated $NaHCO_3$, dried, and concentrated. Purification of the residue by column chromatography (SiO_2 20 g, hexane/AcOEt = 5/1) gave the corresponding cyclic carbonate (653 mg, 79%) as a yellow oil: $[\alpha]_D^{25}$ +21.0 ° (*c* 1.09, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ1.45 s, 9H), 2.04 dt, *J* = 14.4, 6.3 Hz, 1H), 2.37 dt, *J* = 14.4, 6.9 Hz, 1H), 2.96 m, 1H), 3.61 m, 2H), 3.79 (s, 3H), 4.12 (dd, *J* = 11.4, 12.3 Hz, 1H), 4.26 (dd, *J* = 5.7, 11.4 Hz, 1H), 4.40 (s, 2H), 5.26-5.36 (m, 2H), 5.62 (m, 1H), 6.86 (d, *J* = 9.0 Hz, 2H), 7.23 (d, *J* = 8.4 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ27.7, 35.5, 43.5, 57.8, 63.6, 68.3, 72.7, 84.4, 113.7, 122.1, 129.2, 129.3, 129.9, 147.6, 159.1, 167.3; FTIR (neat) 1722, 1513, 1249, 1116, 1033 cm^{-1}; MS (EI) m/z 121 (100), 137, 200, 335 [(M–^{t}Bu)$^+$], 392 (M$^+$); HRMS (EI) calcd for

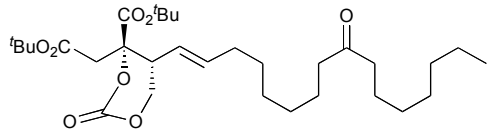
$C_{21}H_{28}O_7$ (M^+) 392.1835, found 392.1852.

To a solution of the cyclic carbonate (653 mg, 1.66 mmol) in CH_2Cl_2-H_2O (20:1) (19 ml) was added DDQ (982 mg, 4.33 mmol) at 0 °C, and the mixture was stirred at room temperature for 1 h. The reaction mixture was diluted with CH_2Cl_2 (150 ml) and filtered through Celite and the filter-pad was washed with CH_2Cl_2. The filtrate and washings were washed with sat. $NaHCO_3$, dried, concentrated, and chromatographed (SiO_2 18 g, hexane/AcOEt = 4/1 to 1.5/1) to give **11** (476 mg, quant.) as a yellow oil: $[\alpha]_D^{25}$ +19.5° (*c* 1.10, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ1.44 (9H, s), 2.05 (dt, *J* = 14.4, 5.7 Hz, 1H), 2.42 (dt, *J* = 14.7, 7.2 Hz, 1H), 2.82 (m, 1H), 2.94 (m, 1H), 3.75 (m, 2H), 4.18 (dd, *J* = 10.8, 12.0 Hz, 1H), 4.36 (dd, *J* = 5.7, 11.1 Hz, 1H), 5.36 (d, *J* = 11.4 Hz, 1H), 5.43 (d, *J* = 5.4 Hz, 1H), 5.55 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ27.7, 38.0, 43.5, 56.6, 68.4, 84.5, 84.9, 122.2, 129.0, 147.8, 167.6; FTIR (neat) 3453, 2979, 1747, 1407, 1371, 1255, 1159 cm^{-1}.



(4*S*,5*R*)-4-(*tert*-Butoxycarbonyl)methyl-4-*tert*-butoxycarbonyl-5-vinyl-1,3-dioxan-2-one (12). To a solution of **11** (50.0 mg, 0.184 mmol) in acetone (5 ml) was added Jones reagent (2.68 M, 175 □l, 0.478 mmol) at –10 °C, and the mixture was stirred for 1 h at the same temperature. After addition of ^{i}PrOH (750 □l), the mixture was allowed to warm to room temperature and stirred for 10 min. The reaction mixture was diluted with AcOEt , washed with brine, dried, and concentrated to give the corresponding carboxylic acid as a pale yellow oil which was used for the next reaction without purification: ^{1}H NMR (300 MHz, $CDCl_3$) δ1.53 s, 9H), 2.77 d, *J* = 17.1 Hz, 1H), 3.05 m, 1H), 3.24 d, *J* = 17.1 Hz 1H), 4.19 dd, *J* = 11.4, 11.7 Hz, 1H), 4.30 (dd, *J* = 6.0, 11.4 Hz, 1H), 5.41 (d, *J* = 8.7 Hz, 1H), 5.41 (d, *J* = 17.4 Hz, 1H), 5.51 (m, 1H).

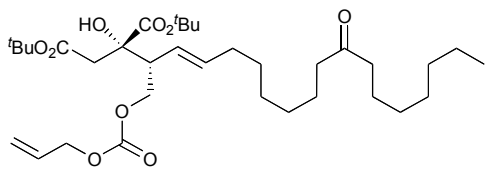
To a solution of the carboxylic acid in CH_2Cl_2 (5 ml) was added a solution of *N*,*N*'-diisopropyl-*O*-2-*tert*-butylisourea[2] (330 mg, 1.650 mmol) in CH_2Cl_2 (2.5 ml) over 2 min at 0 °C, and the mixture was stirred at room temperature for 24 h. The reaction mixture was filtered through Celite and the filter-pad was washed with Et_2O. The filtrate and washings were concentrated and chromatographed (SiO_2, 5 g, hexane/ AdOEt = 4/1) gave **12** as a colorless oil (52.5 mg, 84% by 2 steps): $[\alpha]_D^{27}$ +25.1° (*c* 0.91, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ1.45 s, 9H), 1.53 s, 9H), 2.66 d, *J* = 16.8 Hz, 1H), 3.06 d, *J* = 16.8 Hz, 1H), 3.11 ddd, *J* = 6.0, 8.1, 11.7 Hz 1H), 4.19 dd, *J* = 11.4, 11.7 Hz, 1H), 4.27 (dd, *J* = 6.3, 11.4 Hz, 1H), 5.38 (dd, *J* = 1.5, 9.6 Hz, 1H), 5.39 (dd, *J* = 1.5, 17.4 Hz, 1H), 5.54 (ddd, *J* = 8.1, 9.6, 17.4 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ27.9, 28.0, 41.3, 42.6, 67.9, 81.9, 83.4, 84.7, 123.0, 128.9, 166.8, 167.0; FTIR (neat) 1768, 1367, 1153 cm^{-1}; MS (EI) m/z 57, 124, 186 (100), 213, 230, 269 [(M–O^{t}Bu)$^+$]; HRMS (EI) calcd for $C_{13}H_{17}O_6$ [(M–O^{t}Bu)$^+$] 296.1025, found 269.1030.



(4*S*,5*R*)-4-(*tert*-Butoxycarbonyl)methyl-4-*tert*-butoxycarbonyl-5-[(*E*)-9-oxohexadec-1-enyl]-1,3-dioxan-2-one (15). To a degassed solution of **12** (160 mg, 0.468 mmol) and hexadec-15-en-8-one (**6**) (223 mg, 0.935 mmol) in CH_2Cl_2 (5 ml) was added catalyst **13** (40 mg, 0.047 mmol), and the reaction mixture was refluxed for 42 h. Catalyst **13** (40 mg, 0.047 mmol) was added again, and the mixture was refluxed for 42 h. The reaction mixture was cooled to room temperature and concentrated. The residue was purified by column chromatography (SiO_2 20 g, hexane/AcOEt = 15/1 to 4/1) followed by recycled HPLC (gel permeation, 3.5 ml/min, $CHCl_3$, 3 cycle) to give a 88:12 mixture of **15** and its *Z*-isomer (168 mg, 65%) and recovered **12** (39 mg, 24 %) each as a colorless oil. Pure **15** and its *Z*-isomer were obtained by flash chromatography of the *E*/*Z*-mixture (SiO_2 20 g, hexane/AcOEt = 10/1 to 5/1.

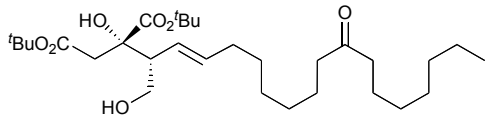
Compound **15**: $[\alpha]_D^{24}$ +20.6 ° (*c* 0.980, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ0.88 (t, *J* = 7.2 Hz, 3H), 1.20-1.40 (m, 18H), 1.46 (s, 9H), 1.54 (s, 9H), 2.05 (m, 2H), 2.38 (t, *J* = 7.8 Hz, 2H), 2.39 (t, *J* = 7.5 Hz, 2H), 2.63 (d, *J* = 16.2 Hz, 1H), 3.02 (m, 1H), 3.04 (d, *J* = 16.5 Hz, 1H), 4.10-4.25 (m, 2H), 5.08 (dd, *J* = 9.2, 15.6 Hz, 1H), 5.79 (dt, *J* = 15.0, 6.9 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ14.0, 22.6, 23.6, 23.8, 27.9, 28.0, 28.6, 28.9, 29.0, 29.1, 29.2, 31.6, 32.6, 41.4, 41.7, 42.6, 42.8, 68.3, 81.8, 83.6, 84.4, 120.2, 139.5, 147.2, 166.9, 167.1, 211.5; FTIR (neat) 1770, 1463, 1369, 1155 cm^{-1}; MS (EI) m/z 299, 334, 356, 378, 423, 440 (100), 552 (M^+); HRMS (EI) calcd for $C_{31}H_{52}O_8$ (M^+) 552.3662, found: 552.3655.

Z-isomer of **15**: ^{1}H NMR (300 MHz, $CDCl_3$) δ0.88 (t, *J* = 6.9 Hz, 3H), 1.27 (m, 18H), 1.45 (s, 9H), 1.54 (s, 9H), 2.11 (m, 2H), 2.39 (t, *J* = 7.4 Hz, 2H), 2.40 (t, *J* = 7.4 Hz, 2H), 2.60 (d, *J* = 16.8 Hz, 1H), 3.03 (d, *J* = 16.8 Hz, 1H), 3.42 (dt, *J* = 10.2, 7.2 Hz, 1H), 4.09 -4.13 (m, 2H), 5.06 (dd, *J* = 9.9, 11.1 Hz, 1H), 5.78 (dt, *J* = 11.1, 7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.1, 22.6, 23.6, 23.9, 27.8, 27.9, 28.0, 29.0, 29.1, 29.2 (2), 31.6, 32.1, 36.4, 41.2, 42.6, 42.8, 67.8, 81.8, 83.7, 84.5, 119.1, 138.6, 167.6, 167.8, 211.2; FT-IR (neat) 2927, 2857, 1770, 1735, 1367, 1153, 1100 cm^{-1}; MS (EI) m/z 57, 356, 423, 440 (100), 496, 552 (M^+); HRMS (EI) calcd for $C_{31}H_{52}O_8$ (M^+) 552.3662, found 552.3642.

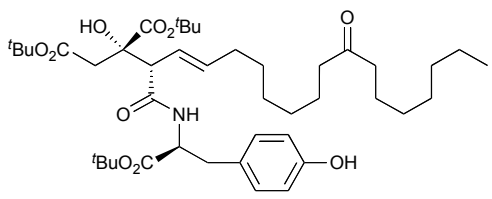


(*S*)-Di-*tert*-Butyl 2-Hydroxy-2-[(*R*,*E*)-1-(allyloxycarbonyl)oxy-11-oxooctadec-3-en-2-yl]succinate (17). To a solution of **15** (121 mg, 0.218 mmol) in allyl alcohol (8 ml) was added K_2CO_3 (90.4 mg, 0.654 mmol) at –20 °C, and the mixture was stirred at that temperature for 5.5 h. The reaction mixture was diluted with saturated NH_4Cl (50 ml) and H_2O (10 ml), extracted with Et_2O,

dried, and concentrated. Purification of the residue by column chromatography (SiO_2 5 g, hexane/AcOEt = 8/1) gave **17** (105 mg, 80%) as a pale yellow oil: $[\alpha]_D^{25}$ +6.9° (*c* 1.06, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ0.87 (t, *J* = 7.2 Hz, 3H), 1.20-1.40 (m, 18H), 1.43 (s, 9H), 1.46 (s, 9H), 1.98 (m, 2H), 2.37 (t, *J* = 7.2 Hz, 4H), 2.60 (ddd, *J* = 5.4, 7.5, 9.3 Hz, 1H), 2.68 (d, *J* = 16.8 Hz, 1H), 2.81 (d, *J* = 16.8 Hz, 1H), 3.83 (s, 1H), 4.16 (dd, *J* = 8.0, 10.8 Hz, 1H), 4.35 (dd, *J* = 5.3, 10.8 Hz, 1H), 4.60 (d, *J* = 5.7 Hz, 2H), 5.23-5.37 (m, 3H), 5.53 (dt, *J* = 6.6, 15.3 Hz, 1H), 5.91 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ14.0, 22.6, 23.6, 23.7, 23.8, 28.0, 28.1, 28.8, 28.9, 29.0, 29.2, 31.6, 32.4, 42.7, 42.8, 43.1, 50.2, 67.0, 68.3, 75.4, 81.3, 82.8, 110.7, 124.8, 131.6, 135.8, 154.8, 169.9, 172.7, 211.6; FTIR (neat) 3492, 1747, 1457, 1392, 1369, 1255, 1155 cm^{-1}; MS (EI) m/z 57, 127, 182, 264 (100), 333, 396, 453, 498, 537 [(M–O^{t}Bu)$^+$]; HRMS (EI) calcd for $C_{30}H_{49}O_8$ [(M–O^{t}Bu)$^+$] 537.3427, found 537.3422.



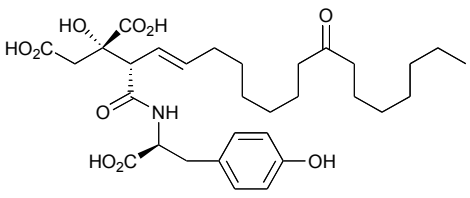
(*S*)-Di-*tert*-Butyl 2-Hydroxy-2-[(*R*,*E*)-1-hydroxy-11-oxooctadec-3-en-2-yl] succinate (18). To a degassed solution of **17** in THF (8 ml) were added $HCOONH_4$ (32.2 mg, 0.513 mmol), triphenylphosphin (13.5 mg, 0.0513 mmol) and $(Ph_3P)_4Pd$ (19.8 mg, 0.0171 mmol), and the mixture was stirred at room temperature for 5 h. The reaction mixture was diluted with H_2O (30 ml), extracted with AcOEt, dried, and concentrated. Purification of the residue by column chromatography (SiO_2 5 g, hexane/AcOEt = 8/1 to 4/1) gave **18** (88.1 mg, 98%): $[\alpha]_D^{25}$ +2.6° (*c* 1.04, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ0.87 (t, *J* = 7.2 Hz, 3H), 1.26-1.55 (m, 18H), 1.43 (s, 9H), 1.46 (s, 9H), 2.01 (m, 2H), 2.35-2.41 (m, 2H), 2.38 (t, *J* = 7.5 Hz, 4H), 2.67 (d, *J* = 16.8 Hz, 1H), 2.81 (d, *J* = 16.8 Hz, 1H), 3.67 (dd, *J* = 6.3, 10.8 Hz, 1H), 3.76 (dd, *J* = 5.1, 10.8 Hz, 1H), 4.01 (s, 1H), 5.45 (dd, *J* = 9.6, 15.6 Hz, 1H), 5.58 (dt, *J* = 15.3, 6.3 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$)δ14.0, 22.6, 23.7, 23.9, 28.0, 28.1, 28.9, 29.0, 29.1 (2), 29.2, 31.6, 32.5, 42.7, 42.8, 43.2, 52.5, 62.7, 76.8, 81.4, 82.6, 125.4, 135.9, 170.2, 172.9, 211.6; FTIR (neat) 3492, 1735, 1369, 1251, 1153 cm^{-1}; MS (EI) m/z 57, 127, 182, 264 (100), 351, 366, 397, 452 [(M–^{t}BuOH)$^+$]; HRMS (EI) calcd for $C_{26}H_{45}O_6$ [(M–O^{t}Bu)$^+$] 453.3216, found 453.3204.



Viridiofungin A Tri-*tert*-butyl Ester (4). To a solution of **18** (62.4 mg, 0.119 mmol) in acetone (5.6 ml) was added Jones reagent (2.68 M solution, 115 μl, 0.308 mmol) at –78 °C, and the mixture was stirred at –10 °C for 1 h. After *i*-PrOH (1 ml) was added, the mixture was allowed to warm to room temperature and stirred for 10 min. The reaction mixture was diluted with brine (10 ml), extracted with AcOEt, dried, and concentrated to give the corresponding carboxylic acid (69.4 mg) as a yellow oil which was used for

the next reaction without purification: ^{1}H NMR (300 MHz, $CDCl_3$) δ0.88 (t, *J* = 6.3 Hz, 3H), 1.26-1.56 (m, 18H), 1.44 (s, 9H), 1.47 (s, 9H), 2.01 (m, 2H), 2.38 (t, *J* = 7.2 Hz, 4H), 2.70 (d, *J* = 16.5 Hz, 1H), 2.90 (d, *J* = 16.5 Hz, 1H), 3.28 (d, *J* = 9.0 Hz, 1H), 4.50 (s, 1H), 5.51 (dd, *J* = 9.0, 15.2 Hz, 1H), 5.69 (dt, *J* = 15.0, 6.6 Hz, 1H); FTIR (neat) 3748, 3667, 3523, 1737, 1369, 1157 cm^{-1}.

To a stirred solution of the carboxylic acid (69.4 mg) and L-tyrosin *tert*-butyl ester[3] (101 mg, 0.425 mmol) in DMF (5.6 ml) at 0 °C were added *N*-methylmorpholin (39 μl, 0.354 mmol), 1-hydroxybenzotriazol (57 mg, 0.425 mmol), and 1-(3-dimethylaminopropyl)-3-ethylcalbodiimide hydrochloride (EDCI) (102 mg, 0.531 mmol). After being stirred at room temperature for 5.5 h, the reaction mixture was diluted with 0.05 M HCl (30 ml), extracted with Et_2O, dried, and concentrated. Purification of the residue by column chromatography (SiO_2 4.5 g, hexane/ AcOEt = 5/1 to 2/1) gave **4** (70.2 mg, 78% by 2 steps) as a yellow oil: $[\alpha]_D^{25}$ –8.3 ° (*c* 1.16, MeOH); ^{1}H NMR (400 MHz, $CDCl_3$) δ0.87 t, *J* = 6.8 Hz, 3H), 1.27 br s, 14H), 1.41 (s, 9H), 1.43 s, 9H), 1.44 (s, 9H), 1.56 m, 4H), 1.97 (m, 2H), 2.41 m, 4H), 2.64 (d, *J* = 16.8 Hz, 1H), 2.75 (d, *J* = 16.8 Hz, 1H), 2.99 (dd, *J* = 6.6, 14.4 Hz, 1H), 3.06 (dd, *J* = 5.6, 14.4 Hz, 1H), 3.09 (d, *J* = 9.6 Hz, 1H), 4.30 (s, 1H), 4.61 (m, 1H), 5.48 (dd, *J* = 9.4, 15.4 Hz, 1H), 5.64 (dt, *J* = 15.2, 6.4 Hz, 1H), 6.21 (br s, 1H), 6.75 (d, *J* = 8.0 Hz, 2H), 6.84 (d, *J* = 8.0 Hz, 1H), 7.03 (d, *J* = 8.4 Hz, 2H); ^{1}H NMR (400 MHz, CD_3OD) δ0.89 t, *J* = 7.0 Hz, 3H), 1.29 brs, 14H), 1.43 (s, 18H), 1.44 s, 9H), 1.52 m, 4H), 1.98 (m, 2H), 2.43 t, *J* = 7.3 Hz, 4H), 2.49 (d, *J* = 16.4 Hz, 1H), 2.76 (d, *J* = 16.4 Hz, 1H), 2.85 (dd, *J* = 8.8, 14.0 Hz, 1H), 3.01 (dd, *J* = 5.6, 14.0 Hz, 1H), 3.12 (d, *J* = 8.8 Hz, 1H), 4.47 (dd, *J* = 5.4, 8.6 Hz, 1H), 5.49 (dd, *J* = 8.8, 15.6 Hz, 1H), 5.57 (dt, *J* = 15.6, 6.4 Hz, 1H), 6.67 (d, *J* = 8.4 Hz, 2H), 7.01 (d, *J* = 8.4 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.0, 22.6, 23.6, 23.9, 27.9, 28.0, 28.6, 29.0, 29.1, 29.2, 31.6, 32.5, 37.1, 42.5, 42.7, 42.9, 54.0, 58.1, 75.6, 81.4, 82.1, 83.0, 115.3, 122.5, 127.5, 130.6, 137.0, 155.4, 169.5, 170.4, 170.5, 171.9, 212.8; FTIR (neat) 3365, 1731, 1652, 1521, 1365, 1253, 1159 cm^{-1}; MS (EI) m/z 57 (100), 136, 171, 379, 428, 546, 686 [(M–O^{t}Bu)$^+$], 759 (M$^+$); HRMS (EI) calcd for $C_{43}H_{69}NO_{10}$ (M$^+$) 759.4922, found 759.4925.



Viridiofungin A (1). A mixture of **4** (32.2 mg, 0.0424 mmol) in HCO_2H (1.5 ml) was stirred at room temperature for 40 min. Most of the HCO_2H was removed by azeotropic distillation with toluene, the residue was purified by column chromatography (ODS 1 g, MeOH/H_2O = 1/1) to afford **1** (18.5 mg, 74%) as a white powder: $[\alpha]_D^{26}$ –15.2 ° (*c* 0.93, MeOH) {lit.[4] $[\alpha]_D^{25}$ –18.2° (*c* 2.37, MeOH)}; ^{1}H NMR (500 MHz, CD_3OD) δ0.88 t, *J* = 7.0 Hz, 3H), 1.28 br s, 14H), 1.53 (m, 4H), 1.97 (m, 2H), 2.42 t, *J* = 7.3 Hz, 3H), 2.43 t, *J* = 7.3 Hz, 3H), 2.62 (d, *J* = 16.3 Hz, 1H), 2.86-2.92 (m, 3H), 3.10 (dd, *J* = 4.6, 14.1 Hz, 1H), 3.21 (d, *J* = 8.0 Hz, 1H), 4.60 (dd, *J* = 4.8, 8.5 Hz, 1H), 5.53 (m, 2H), 6.67 (d, *J* = 8.5 Hz, 2H), 7.02 (d, *J* = 8.5 Hz,

2H); ^{13}C NMR (125 MHz, CD_3OD) δ14.4, 23.7, 24.8, 24.9, 29.8, 29.9, 30.0, 30.2, 30.3, 32.9, 33.5, 37.5, 43.1, 43.5(2), 55.1, 57.7, 80.0, 116.2 (2), 124.5, 128.7, 131.4 (2), 137.6, 157.4, 173.6, 173.9, 174.5, 175.8, 214.6; FTIR (neat) 3748, 3656, 3363, 1712, 1523, 1454, 1232 cm^{-1}; MS (EI) m/z 164 (100), 465, 511 [$(M–2H_2O–CO_2)^+$]; HRMS (EI) calcd for $C_{30}H_{41}NO_6$ [$(M–2H_2O–CO_2)^+$] 511.2934, found 511.2922; HRMS (FAB, NBA) calcd for $C_{31}H_{46}NO_{10}$ [$(M+H)^+$] 592.3121, found 592.3110. These data were identical with those reported.[4]

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