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Synthetic Studies on the Cornexistins: Synthesis of (±)-5-*epi*-Hydroxycornexistin

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Supplementary Information

General

Unless otherwise stated, all solvents were dried prior to use: THF was distilled from sodium / benzophenone ketyl; dichloromethane and toluene was distilled from calcium hydride. Other solvents and reagents were used as supplied unless otherwise stated. All reactions were performed under nitrogen or argon.

Column chromatography was performed with silica gel (Merck 7734 grade) or using an Isco Combiflash Companion using prepacked Redisep® cartridges. Petroleum ether used for column chromatography was the fraction boiling at 40–60 ºC.

Melting points were determined using a Mel-Temp II melting point apparatus. IR spectra were recorded using a Perkin-Elmer 1600 FT-IR instrument or Bruker Tensor 27 at ambient temperature. ^{1}H NMR spectra were recorded on a Bruker DRX500 (500 MHz) or a Bruker AM400 (400 MHz) spectrometer at ambient temperature. ^{13}C NMR spectra were recorded on a Bruker DRX500 (125

MHz) or a Bruker AM400 (100 MHz) spectrometer at ambient temperature. Mass spectra and accurate mass measurements (HRMS) were obtained using a VG 70E, VG AutoSpec, Micromass LCT or Bruker MicroTof using electrospray ionisation (ESI), electron impact (EI) or chemical ionisation (CI). Elemental analyses were performed by the microanalysis section of the School of Chemistry, University of Nottingham.

4-Pyrrolidin-1-ylfuran-2(5*H*)-one 21

Pyrrolidine (50 mL, 0.60 mol) was added to tetronic acid (10 g, 0.10 mol) and the mixture was stirred for 1 min. The excess pyrrolidine was removed under reduced pressure and the mixture was heated repeatedly under reduced pressure until solid formed on cooling. The vinylogous carbamate **21** (14.8 g, 97%) was obtained as a pale brown solid which could be used directly in the next step of the synthesis. Alternatively, the product could be purified by flash column chromatography on silica gel (petroleum ether-ethyl acetate, 1:4) to give product **21** as a colourless solid: mp 120–123 °C; (Found: C, 62.51; H, 7.23; N, 8.92; $C_8H_{11}O_2N$ requires: C, 62.73; H, 7.24; N, 9.14%); R_f: = 0.21 (petroleum ether-ethyl acetate, 1:4); ν_{max} ($CHCl_3$)/cm^{-1} 2870, 1729, 1620, 1058; δ_H (500 MHz, $CDCl_3$) 4.67 (2H, s, OC*H₂*), 4.52 (1H, s, C*H*=C), 3.29–3.25 (4H, m, 2 × NCH_2), 2.04–2.01 (4H, m, 2 × NCH$_2$CH_2); δ_C (100 MHz, $CDCl_3$) 175.6 (C), 166.1 (C), 80.7 (CH), 67.0 (CH_2), 49.3 (CH_2), 47.3 (CH_2), 25.8 (CH_2), 24.9 (CH_2); *m/z* (EI) 153.0784 $[M]^+$, $C_8H_{11}O_2N$ requires 153.0790.

5-Allyl-4-pyrrolidin-1-ylfuran-2(5*H*)-one 22

A solution of the vinylogous carbamate **21** (14.8 g, 96.7 mmol) in THF (650 mL) was cooled to –78 °C and *tert*-butyllithium (85 mL of a 1.7 M solution in pentane, 0.15 mol) was added slowly over 1 h. The mixture was stirred at –78 °C for 1 h and then allyl bromide (83 mL, 0.96 mol) was added slowly to the solution of the anion. The mixture was allowed to warm slowly to room temperature and then stirred for a further 16 h. The mixture was then cooled to 0 °C and the reaction was quenched by the addition of a saturated aqueous solution of ammonium chloride (200 mL) followed by the addition of water (100 mL). Most of the THF was removed under reduced pressure and ethyl acetate (300 mL) was added. The phases were separated and the aqueous phase was extracted with further ethyl acetate (2 × 150 mL). The combined organic extracts were then washed with brine (300 mL) and dried ($MgSO_4$). The solvent was removed under reduced pressure and the residue was purified by flash column chromatography on silica gel (petroleum ether-ethyl acetate, 3:7) to give the alkylated product **22** (14.1 g, 76%) as a pale yellow oil: (Found: C, 68.23; H, 7.88; N, 7.62; $C_{11}H_{15}O_2N$ requires: C, 68.37; H, 7.82; N, 7.25%); R_f: = 0.33 (petroleum ether-ethyl acetate, 3:7); ν_{max} ($CHCl_3$)/cm^{-1} 2980, 2953, 2927, 2871, 1722, 1614; δ_H (400 MHz, $CDCl_3$) 5.80 (1H, dddd, *J* = 17.1, 10.2, 7.0, 6.8 Hz, C*H*=CH_2), 5.18–5.11 (2H, m, CH=C*H*$_2$), 4.91 (1H, dd, *J* = 6.8, 3.1 Hz, C*H*CH_2CH=CH_2), 4.50 (1H, s, COC*H*=C), 3.42–3.15 (4H, m, 2 × NC*H*$_2$), 2.74 (1H, ddddd, *J* = 15.0, 7.0, 3.1, 1.4, 1.4 Hz, C*H*$_2$CH=CH_2), 2.42 (1H, ddddd, *J* = 15.0, 6.8, 6.8, 1.2, 1.2 Hz, C*H*$_2$CH=CH_2), 2.09–1.88 (4H, m, 2 × NCH_2C*H*$_2$); δ_C (100 MHz, $CDCl_3$) 174.3 (C), 168.3 (C), 131.4 (CH), 118.9 (CH_2), 82.4 (CH), 76.8 (CH), 49.9 (CH_2), 48.5 (CH_2), 36.4 (CH_2), 26.2 (CH_2), 24.7 (CH_2); *m*/*z* (EI) 193.1105 $[M]^+$, $C_{11}H_{15}O_2N$ requires 193.1103.

5-Allyl-4-hydroxyfuran-2(5*H*)-one 23

The alkylated product **22** was added to 0.5 M aqueous hydrochloric acid (280 mL) and the mixture heated to 70 °C for 6 h. The mixture was then cooled to room temperature and water (250 mL) was added followed by ethyl acetate (250 mL). The phases were separated and the aqueous phase was extracted with ethyl acetate (2 × 250 mL). The combined organic extracts were washed with brine (250 mL) and dried ($MgSO_4$). The solvent was removed under reduced pressure and the residue was purified by flash column chromatography on silica gel (petroleum ether-ethyl acetate, 3:7) to give a tautomeric mixture of the allylated tetronic acid **23** (8.7 g, 89%) as a colourless solid: mp 73–76 °C; (Found: C, 59.78; H, 5.68; $C_7H_8O_3$ requires: C, 60.00; H, 5.75%); R_f: = 0.22 (petroleum ether-ethyl acetate, 3:7); ν_{max} ($CHCl_3$)/cm^{-1} 2926, 1807, 1764, 1626; δ_H (400 MHz, $CDCl_3$) 5.76 (1H, dddd, *J* = 17.3, 10.1, 7.1, 7.1 Hz, C*H*=CH_2), 5.27–5.17 (2H, m, CH=C*H*$_2$), 5.06 (0.5H, s, COC*H*=C), 4.91–

4.83 (1H, m, OC*H*CH_2), 3.22–3.07 (1.5H, m, $COCH_2CO$), 2.79–2.69 (1H, m, C*H*$_2$CH=CH_2), 2.61–2.45 (1H, m, C*H*$_2$CH=CH_2); δ_C (100 MHz, $CDCl_3$) 205.1 (C), 183.0 (C), 177.0 (C), 169.8 (C), 130.3 (CH), 129.7 (CH), 121.3 (CH_2), 119.9 (CH_2), 89.6 (CH), 85.6 (CH), 79.9 (CH), 37.9 (CH_2), 35.3 (CH_2), 35.2 (CH_2); *m*/*z* (EI) 140.0469 $[M]^+$, $C_7H_8O_3$ requires 140.0474.

2-Allyl-5-oxo-2,5-dihydrofuran-3-yl trifluoromethanesulfonate 24

The allylated tetronic acid **23** (671 mg, 4.79 mmol) was dissolved in dichloromethane (50 mL) and the solution was cooled to –78 °C. Diisopropylethylamine (1.0 mL, 5.7 mmol) was added to the solution followed by triflic anhydride (0.94 mL, 5.7 mmol) and the mixture was stirred at –78 °C for 1 h. The mixture was diluted with dichloromethane (50 mL) and then warmed to room temperature. Water (50 mL) was then added and the phases were separated. The organic phase was washed with brine (50 mL) and dried ($MgSO_4$). The solvent was removed under reduced pressure and the residue was then purified by flash column chromatography on silica gel (petroleum ether-diethyl ether, 7:3) to give the triflate **24** (1.16 g, 89%) as a pale yellow oil: (Found: C, 35.34; H, 2.47; $C_8H_7O_5SF_3$ requires: C, 35.30; H, 2.59%); R_f: = 0.46 (petroleum ether-diethyl ether, 7:3); ν_{max} ($CHCl_3$)/cm^{-1} 3146, 1774, 1647, 990; δ_H (400 MHz, $CDCl_3$) 6.02 (1H, d, *J* = 1.5 Hz, COC*H*=C), 5.70 (1H, dddd, *J* = 17.2, 10.7, 7.2, 6.9 Hz, C*H*=CH_2), 5.25 (1H, dddd, *J* = 17.2, 1.3, 1.2, 1.2 Hz, CH=C*H*$_2$), 5.24 (1H, dddd, *J* = 10.7, 1.3, 1.2, 1.2 Hz, CH=C*H*$_2$), 5.06 (1H, ddd, *J* = 6.1, 4.4, 1.5 Hz, OC*H*C=CH), 2.78 (1H, ddddd, *J* = 14.9, 6.9, 4.4, 1.2, 1.2 Hz, C*H*$_2$CH=CH_2), 2.49 (1H, ddddd, *J* = 14.9, 7.2, 6.1, 1.2, 1.2 Hz, C*H*$_2$CH=CH_2); δ_C (100 MHz, $CDCl_3$) 168.3 (C), 168.2 (C), 128.7 (CH), 121.3 (CH_2), 118.5 (CF_3, q, *J* = 320 Hz), 104.1 (CH), 78.1 (CH), 35.0 (CH_2); *m*/*z* (EI) 271.9965 $[M]^+$, $C_8H_7O_5SF_3$ requires 271.9966.

5-Allyl-4-(tributylstannyl)furan-2(5*H*)-one 25

The triflate **24** (6.82 g, 25.1 mmol) was dissolved in THF (250 mL) and hexabutylditin (15.2 mL, 30.1 mmol) was added followed by dry lithium chloride (6.4 g, 0.15 mol) and $Pd(PPh_3)_4$ (0.87 g, 0.75 mmol). The mixture was heated to 60 °C and stirred at this temperature for 3 h. The mixture was cooled to room temperature and the reaction was quenched by the addition of a saturated aqueous solution of sodium bicarbonate (150 mL) followed by water (150 mL). Ethyl acetate (250 mL) was added and the phases were separated. The aqueous phase was extracted with ethyl acetate (2 × 250 mL) and the combined organic extracts were washed with brine and dried ($MgSO_4$). The solvent was removed under reduced pressure and the residue was then purified by flash column chromatography on silica gel (petroleum ether-diethyl ether, 100:0 → 7:3) to give the stannane **25** (5.54 g, 54%) as a pale yellow oil: (Found: C, 55.21; H, 8.10; $C_{19}H_{34}O_2Sn$ requires: C, 55.23; H, 8.29%); R_f: = 0.63 (petroleum ether-diethyl ether, 7:3); ν_{max} ($CHCl_3$)/cm^{-1} 2917, 2872, 2833, 1746, 867; δ_H (400 MHz, $CDCl_3$) 6.16 (1H, d, J = 2.0 Hz, COC*H*=C), 5.74 (1H, dddd, J = 17.1, 10.2, 6.9, 6.8 Hz, C*H*=CH_2), 5.20–5.13 (3H, m, CH=CH_2, C*H*CH_2CH=CH_2), 2.64 (1H, ddddd, J = 14.8, 7.2, 4.1, 1.1, 1.1 Hz, CH_2CH=CH_2) 2.29 (1H, dddd, J = 14.8, 7.1, 6.9, 1.3 Hz, CH_2CH=CH_2), 1.56–1.48 (6H, m, 3 × C$H_2$$CH_3$), 1.38–1.28 (6H, m, 3 × SnCH_2CH_2), 1.16–1.09 (6H, m, 3 × SnCH_2), 0.91 (9H, t, J = 7.3 Hz, 3 × CH_2CH_3); δ_C (125 MHz, $CDCl_3$) 177.4 (C), 172.9 (C), 131.9 (CH), 130.5 (CH), 119.0 (CH_2), 88.9 (CH), 37.8 (CH_2), 28.9 (CH_2), 27.3 (CH_2), 13.6 (CH_3), 10.2 (CH_2); *m*/*z* (CI, CH_4) 415.1674 $[M+H]^+$, $C_{19}H_{35}O_2{}^{120}Sn$ requires 415.1659.

Furan-3,4-diyldimethanol

Lithium aluminium hydride (4.95 g, 130 mmol) was cooled to –78 °C under argon and THF (250 mL) was added. A solution of diester **26** (12 g, 65 mmol) in THF (250mL) was added slowly and the mixture was allowed to warm to room temperature. The mixture was stirred at room temperature for 16 h and then cooled to 0 °C. Ethyl acetate (10 mL) was added slowly, followed by a saturated aqueous solution of ammonium chloride (10 mL). The mixture was dried by addition of $MgSO_4$ to the thick white suspension and then filtered. The resulting solution was concentrated under reduced pressure to yield the diol (7.34 g, 88% yield) as a pale yellow oil. This product was of sufficient purity to be used in the next reaction. Alternatively, purification could be performed by flash column chromatography on silica gel (petroleum ether-ethyl acetate, 1:1) to give diol as a colourless oil: (Found: C, 55.91; H, 6.27; $C_6H_8O_3$ requires: C, 56.25; H, 6.29%); R_f: = 0.27 (ethyl acetate-dichloromethane, 1:1); ν_{max} ($CHCl_3$)/cm^{-1} 3605, 3465, 2950, 2880, 1731, 873, 602; δ_H (400 MHz, $CDCl_3$) 7.34 (2H, s, 2 × Fur-*H*), 4.49 (4H, s, 2 × C*H₂*OH) 4.05 (2H, br, 2 × O*H*); δ_C (100 MHz, $CDCl_3$) 140.9 (CH), 124.3 (C) 54.9 (CH_2); *m/z* (EI) 128.0476 $[M]^+$, $C_6H_8O_3$ requires 128.0473.

4-Hydroxymethyl-3-furaldehyde 27

Activated manganese dioxide (37 g, 0.43 mol) was added to a solution of furan-3,4-diyldimethanol (9.2 g, 72 mmol) in CH_2Cl_2 (600 mL) and the mixture was stirred at room temperature for 3 h. Further portions of manganese dioxide (5.0 g, 57 mmol) were added after 3 h and 4 h. After stirring for a total of 5 h, the mixture was then filtered through Celite® and then concentrated under reduced pressure. The aldehyde **27** (8.15 g, 90% yield) was obtained as a pale yellow oil which was of sufficient purity to be used in the next reaction. Alternatively, purification could be performed by flash column chromatography on silica gel (petroleum ether-ethyl acetate, 80:20 then 65:35), to give aldehyde **27** as a colourless oil that solidifies on standing: mp 46–48 °C; (Found: C, 57.07; H, 4.73; $C_6H_6O_3$ requires: C, 57.13; H, 4.80%); R_f: = 0.59 (ethyl acetate-dichloromethane, 1:1); ν_{max} ($CHCl_3$)/cm^{-1} 3484, 2841, 1672, 876; δ_H (400 MHz, $CDCl_3$) 9.98 (lH, s, C*H*O), 8.12 (lH, s, Fur-*H*), 7.48 (lH, s, Fur-*H*), 4.61 (2H, d, *J* = 6.1 Hz, C*H₂*OH), 3.71 (lH, t, *J* = 6.1 Hz, O*H*); δ_C (100 MHz, $CDCl_3$) 186.5 (CH) 154.4 (CH), 141.8 (CH), 127.9 (C), 124.1 (C), 55.2 (CH_2); *m/z* (EI) 126.0314 $[M]^+$, $C_6H_6O_3$ requires 126.0317.

4-({[*tert*-Butyl(dimethyl)silyl]oxy}methyl)-3-furaldehyde

Imidazole (4.6 g, 67 mmol), DMAP (0.78 g, 6.4 mmol) and *t*-butydimethylsilyl chloride (10.2 g, 67.5 mmol) were added successively to a solution of aldehyde **27** (8.1 g, 64 mmol) in CH_2Cl_2 (650 mL). The mixture was stirred at room temperature for 6 h and water (400 mL) was then added. After separation of the phases, the organic phase was washed with brine (300 mL) and dried

($MgSO_4$). The solvent was removed under reduced pressure and the residue was purified by flash column chromatography on silica gel (petroleum ether-dichloromethane, 1:4) to give the silyl ether (13.1 g, 84% yield) as a colourless oil: (Found: C, 60.03; H, 8.32; $C_{12}H_{20}O_3Si$ requires: C, 59.96; H, 8.39%); R_f: = 0.72 (petroleum ether-ethyl acetate, 70:30); ν_{max} ($CHCl_3$)/cm^{-1} 2954, 2930, 2857, 1689, 1356, 1143, 1091, 1046; δ_H (400 MHz, $CDCl_3$) 9.94 (lH, s, C*H*O) 8.02 (lH, s, Fur-*H*), 7.43 (lH, s, Fur-*H*), 4.86 (2H, s, CH_2O) 0.93 (9H, s, C{CH_3}$_3$) 0.11 (6H, s, Si{CH_3}$_2$); δ_C (100 MHz, $CDCl_3$) 185.2 (C*H*O) 152.8 (CH), 142.1 (CH), 126.5 (C), 125.8 (C), 57.9 (CH_2), 25.9 (CH_3) 18.4 (C), –5.4 (CH_3).

Methyl (2*E*)-3-[4-({[*tert*-butyl(dimethyl)silyl]oxy}methyl)-3-furyl]acrylate 28

(Methoxycarbonylethylene)triphenylphosphorane (27 g, 81 mmol) was added to a solution of 4-({[*tert*-Butyl(dimethyl)silyl]oxy}methyl)-3-furaldehyde (12.9 g, 53.8 mmol) in THF (450 ml). The mixture was stirred at room temperature for 16 h and the reaction was then quenched by addition of water (300 mL). Diethyl ether (100 mL) was added and the phases were separated. The aqueous phase was extracted with diethyl ether (2 × 300 mL) and the combined organic extracts were washed with brine (300 mL) and dried ($MgSO_4$). The solvent was removed under reduced pressure and the residue was purified by flash column chromatography on silica gel (petroleum ether-dichloromethane, 1:4) to give the ester **28** (14.2 g, 89% yield) as a pale yellow oil: (Found: C, 60.73; H, 8.14; $C_{15}H_{24}O_4Si$ requires: C, 60.78; H, 8.16%); R_f: = 0.74 (petroleum ether-ethyl acetate, 7:3); ν_{max} ($CHCl_3$)/cm^{-1} 2952, 2930, 2885, 2858, 1704, 1644; δ_H (400 MHz, $CDCl_3$) 7.64 (lH, d, *J* = 1.7 Hz, Fur-*H*), 7.58 (lH, d, *J* = 16.0 Hz, C*H*=CHCO$_2$), 7.37 (lH, s, Fur-*H*), 6.27 (lH, d, *J* = 16.0 Hz, CH=C*H*CO$_2$), 4.67 (2H, d, *J* = 1.7, OCH_2), 3.78 (3H, s, OCH_3), 0.91 (9H, s, C{CH_3}$_3$) 0.01 (6H, s, Si{CH_3}$_2$); δ_C (100 MHz, $CDCl_3$) 167.7 (C), 145.6 (CH), 142.0 (CH), 134.7 (CH), 124.4 (C), 121.6 (C), 118.4 (CH), 56.7 (CH_2), 51.6 (CH_3), 25.9 (CH_3), 18.3 (C), –5.3 (CH_3).

(2*E*)-3-[4-({[*tert*-Butyl(dimethyl)silyl]oxy}methyl)-3-furyl]prop-2-en-1-ol

A solution of lithium aluminium hydride (47 mL of a 1M in diethyl ether, 47 mmol) was added slowly to a solution of ester **28** (13.8 g, 46.6 mmol) in THF (450 mL) at –78 °C. The mixture was warmed to –30 °C over 3 h and then stirred at that temperature for 20 min. The reaction was quenched by addition of ethyl acetate (10 mL) and a saturated aqueous solution of ammonium chloride (10 mL). The mixture was warmed to room temperature and further saturated aqueous ammonium chloride (250 mL) was added. The THF was removed under reduced pressure and the aqueous mixture was extracted with diethyl ether (3 × 250 mL). The combined organic extracts were then washed with brine (250 mL), dried ($MgSO_4$). The solvent was removed under reduced pressure and the residue was purified by flash column chromatography on silica gel (ethyl acetate-dichloromethane, 0:100 then 5:95) to give the product alcohol (10.4 g, 84% yield) as a pale yellow oil: R_f: = 0.33 (petroleum ether-ethyl acetate, 7:3); ν_{max} ($CHCl_3$)/cm^{-1} 3609, 2953, 2929, 2857; δ_H (400 MHz, $CDCl_3$) 7.44 (lH, d, *J* = 1.4 Hz, Fur-*H*), 7.32 (lH, d, *J* = 0.9 Hz, Fur-*H*), 6.45 (lH, d, *J* = 16.0 Hz, C*H*=CHCH$_2$), 6.14 (lH, dt, *J* = 16.0, 5.8 Hz, CH=C*H*CH$_2$), 4.66 (2H, d, *J* = 0.9 Hz, C*H$_2$*OSi), 4.25 (2H, dd, *J* = 5.8, 1.4 Hz, C*H$_2$*OH), 1.50 (lH, br, O*H*), 0.92 (9H, s, C{C*H$_3$*}$_3$) 0.09 (6H, Si{CH$_3$}$_2$); δ_C (100 MHz, $CDCl_3$) 141.5 (CH), 141.2 (CH), 129.3 (CH), 124.3 (C), 122.6 (C), 121.0 (CH), 64.1 (CH_2), 57.1 (CH_2), 25.9 (CH_3), 18.4 (C), –5.2 (CH_3); *m*/*z* (CI, NH_3) 267.1417 [M–H]$^+$, $C_{14}H_{23}O_3Si$ requires 267.1417.

(2*E*)-3-[4-({[*tert*-Butyl(dimethyl)silyl]oxy}methyl)-3-furyl]prop-2-en-1-yl diethyl phosphate 29

(2*E*)-3-[4-({[*tert*-Butyl(dimethyl)silyl]oxy}methyl)-3-furyl]prop-2-en-1-ol (10.2 g, 381 mmol) was dissolved in dichloromethane (115 mL) at 0 °C and DMAP (0.46 g, 3.8 mmol), pyridine (11 mL, 0.14 mol) and diethylchlorophosphate (11 mL, 76 mmol) were added successively. The mixture was stirred at 0 °C for 30 min. and the mixture was then warmed to room temperature and stirred for a further 2 h. The reaction was quenched by addition of water (200 mL) and diethyl ether (250 mL). After separation of the phases, the aqueous phase was extracted with diethyl ether (2 × 250 mL), and the combined organic extracts were washed with brine (250 mL) and dried ($MgSO_4$). The solvent was removed under reduced pressure to give a mixture (1:1) of the allylic phosphate **29** and diethylchlorophosphate (15.3 g) as a yellow oil. The phosphate **29** proved to be unstable on silica gel when purification was attempted by flash column chromatography and so the material was used crude in the next reaction.

***tert*-Butyl(dimethyl){[4-(1-vinylbutyl)-3-furyl]methoxy}silane 30**

The crude allylic phosphate **29** (15.3 g, ~38.1 mmol) was dissolved in THF (400 mL). Lithium chloride (484 mg, 11.4 mmol) and copper(I) cyanide (340 mg, 3.81 mmol) – both flame-dried prior to use – were added at room temperature. The mixture was cooled to –78 °C and propylmagnesium chloride (38 mL of a 2M solution in diethyl ether, 76 mmol) was added over 20 min. The mixture was allowed to warm slowly to room temperature and was stirred for a further 16 h. The reaction mixture was cooled to 0 °C and a saturated aqueous solution of ammonium chloride (150 mL) was added, followed by water (150 mL) and diethyl ether (200 mL). After separation of the phases, the aqueous phase was extracted with diethyl ether (2 × 200 mL) and the combined organic extracts were washed with brine (150 mL) and dried ($MgSO_4$). The solvent was removed under reduced pressure and the residue was purified by flash column chromatography on silica gel (petroleum ether-diethyl ether, 100:0 then 98:2) to give the olefin **30** (7.15 g, 64% yield over 2 steps) as a pale yellow oil: (Found: C, 69.32; H, 10.12; $C_{17}H_{30}O_2Si$ requires: C, 69.33; H, 10.27%); R_f: = 0.41 (petroleum ether-diethyl ether, 98:2); ν_{max} ($CHCl_3$)/cm^{-1} 2953, 2929, 2857, 1462, 1050; δ_H (500 MHz, $CDCl_3$) 7.31 (lH, t, *J* = 0.8 Hz, Fur-*H*), 7.17 (lH, d, *J* = 0.8 Hz, Fur-*H*), 5.80 (lH, dddd, *J* = 17.5, 9.6, 7.8, 0.8 Hz, CH=C*H*CH_2), 5.03–4.97 (2H, m, CH=CHCH_2), 4.55 (2H, d, *J* = 0.8 Hz, CH_2OSi), 3.22 (1H, dt, *J* = 7.8, 7.2 Hz, C*H*CH_2CH_2), 1.61–1.57 (2H, m, CHC$H_2$$CH_2$), 1.41–1.36 (2H, m, C$H_2$$CH_3$), 0.94–0.92 (12H, m, C{CH_3}$_3$, CH_2CH_3) 0.08 (6H, s, Si{CH_3}$_2$); δ_C (125 MHz, $CDCl_3$) 141.4 (CH), 140.4 (CH), 139.4 (CH), 126.6 (C), 125.3 (C), 114.2 (CH_2), 56.9 (CH_2), 39.4 (CH), 36.0 (CH_2), 26.0 (CH_3), 20.6 (CH_2), 18.4 (C), 14.1 (CH_3), –5.3 (CH_3).

[4-(1-Vinylbutyl)-3-furyl]methanol

A solution of TBAF (28 mL of 1M in THF, 28 mmol) was added to a solution of alkene **30** (6.9 g, 23 mmol) in THF (115 mL) at 0 °C and the mixture was stirred at this temperature for 5 h. The reaction was quenched by addition of water (200 mL) and diethyl ether (200 mL). After separation of the phases, the aqueous phase was extracted with diethyl ether (2 × 200 mL), and the combined organic extracts were washed with brine (200 mL) and dried ($MgSO_4$). Removal of the solvent under reduced pressure gave a residue which was purified by flash chromatography on silica gel (petroleum ether-diethyl ether, 4:1 → 3:2) to give the product alcohol (4.04 g, 96% yield) as a pale yellow oil: (Found: C, 72.93; H, 8.90; $C_{11}H_{16}O_2$ requires: C, 73.30; H, 8.95%); R_f: = 0.48 (petroleum ether-diethyl ether, 3:2); ν_{max} ($CHCl_3$)/cm^{-1} 3610, 2958, 2931, 2873, 995; δ_H (400 MHz, $CDCl_3$) 7.38 (lH, d, *J* = 0.6 Hz, Fur-*H*), 7.20 (lH, d, *J* = 0.6 Hz, Fur-*H*), 5.82 (lH, ddd, *J* = 17.6, 10.0, 7.6 Hz, C*H*=CH_2), 5.05 (lH, d, *J* = 10.0 Hz, CH=CH_2), 5.04 (lH, d, *J* = 17.6 Hz, CH=CH_2), 4.49 (2H, s, CH_2O), 3.26 (lH, dt, *J* = 7.6, 7.3 Hz, C*H*CH_2CH_2), 2.10 (lH, br, O*H*), 1.65–1.60 (2H, m, CHC$H_2$$CH_2$) 1.41–1.35 (2H, m, C$H_2$$CH_3$), 0.92 (3H, t, *J* = 7.4 Hz, CH_3); δ_C (100 MHz, $CDCl_3$) 142.2 (CH), 141.1(CH), 139.7 (CH), 126.8 (C), 124.8 (C), 114.5 (CH_2), 55.6 (CH_2), 39.4 (CH), 36.3 (CH_2), 20.5 (CH_2), 14.0 (CH_3); *m/z* (EI) 180.1154 $[M]^+$, $C_{11}H_{16}O_2$ requires 180.1150.

3-(Chloromethyl)-4-(1-vinylbutyl)furan 31

[4-(1-Vinylbutyl)-3-furyl]methanol (7.6 g, 42 mmol) and collidine (11 mL, 84 mmol) were dissolved in DMF (90 mL) at room temperature. Flame-dried lithium chloride (3.6 g, 84 mmol) was added and the mixture was cooled to 0 °C. Methanesulfonyl chloride (4.9 mL, 63 mmol) was added slowly and the resulting mixture was stirred at 0 °C for 1 h before being warmed to room temperature and stirred for a further 4 h. The reaction was then quenched by addition of water (300 mL) and diethyl ether (300 mL). After separation of the phases, the aqueous phase was extracted with diethyl ether (2 × 150 mL) and the combined organic extracts were washed sequentially with a saturated aqueous solution of copper sulfate (3 × 250 mL), water (250 mL) and brine (250 mL). The organic extracts were dried ($MgSO_4$) and the solvent was removed under reduced pressure. The residue was purified by flash column chromatography on silica gel (petroleum ether-diethyl ether, 98:2) to give the volatile chloride **31** (6.46 g, 77% yield) as a pale yellow oil: (Found: C, 66.59; H, 7.66; $C_{11}H_{15}ClO$ requires: C, 66.50; H, 7.61%); R_f: = 0.84 (petroleum ether-diethyl ether, 19:1); ν_{max} (CH_2Cl_2)/cm^{-1} 2956, 2930, 2872, 1637, 995, 913, 868; δ_H (500 MHz, $CDCl_3$) 7.44 (1H, s, Fur-*H*), 7.21 (1H, s, Fur-*H*), 5.78 (1H, ddd, *J* = 17.5, 9.7, 7.6 Hz, C*H*=CH$_2$), 5.08 (1H, d, *J* = 17.5 Hz, CH=C*H*$_2$), 5.05 (1H, d, *J* = 9.7 Hz, CH=C*H*$_2$), 4.49 (1H, d, *J* = 12.1 Hz, C*H*$_2$Cl), 4.45 (1H, d, *J* = 12.1 Hz, C*H*$_2$Cl), 3.31 (1H, ddd, *J* = 7.6, 7.5, 7.3 Hz, C*H*CH$_2$CH$_2$), 1.68–1.62 (2H, m, C*H*$_2$CH$_2$CH$_3$), 1.40–1.35 (2H, m, C*H*$_2$CH$_3$), 0.94 (3H, t, *J* = 7.3 Hz, C*H*$_3$); δ_C (125 MHz, $CDCl_3$) 142.1 (CH), 141.1 (CH), 140.1 (CH), 126.9 (C), 122.0 (C), 114.6 (CH_2), 39.1 (CH), 36.5 (CH_2), 36.4 (CH_2), 20.5 (CH_2), 14.0 (CH_3); *m/z* (EI) 200.0787 [M]$^+$, $C_{11}H_{15}{}^{37}ClO$ requires 200.0782.

5-Allyl-4-{[4-(1-vinylbutyl)-3-furyl]methyl}furan-2(5*H*)-one 32

The chloride **31** (672 mg, 3.38 mmol) was dissolved in THF (35 mL) and triphenylarsine (83 mg, 0.27 mmol) and $Pd_2(dba)_3$ (62 mg, 0.068 mmol) were added at room temperature. After strirring for 10 min, the stannane **25** (1.39 g, 3.38 mmol) was added and the mixture was heated to 60 °C. The reaction mixture was stirred at this temperature for 11 h and then cooled to room temperature. The reaction was then quenched by the addition of water (100 mL) and diethyl ether (150 mL). The phases were separated and the aqueous phase was extracted with diethyl ether (2 × 100 mL). The combined organic extracts were washed with brine (100 mL) and then dried ($MgSO_4$). The solvent was removed under reduced pressure to give a residue which was purified by flash column chromatography on silica gel (petroleum ether-diethyl ether, 100:0, 98:2, 9:1 then 7:3) to give an inseparable diastereoisomeric mixture (1:1) of the diene **32** (790 mg, 82%) as a pale yellow oil: (Found: C, 75.25; H, 8.12; $C_{18}H_{22}O_3$ requires: C, 75.50; H, 7.74%); R_f: = 0.64 (petroleum ether-diethyl ether, 1:1); ν_{max} (CH_2Cl_2)/cm^{-1} 2959, 2931, 2873, 1749, 1641, 984, 915, 878; δ_H (500 MHz,

$CDCl_3$) 7.26–7.23 (2H, m, 2 × Ar-*H*), 5.77–5.67 (3H, m, $O_2CCH=C$, C*H*=CH_2, C*H*=CH_2), 5.24–5.16 (2H, m, $CH_2CH=CH_2$), 5.03–4.89 (3H, m, CHCH=C*H*$_2$, CH=CC*H*O), 3.50–3.42 (1H, m, CC*H*$_2$C), 3.29–3.37 (1H, m, CC*H*$_2$C), 3.00 (1H, ddd, *J* = 7.2, 7.5, 7.5 Hz, C*H*CH=CH_2), 2.76–2.68 (1H, m, C*H*$_2$CH=CH_2), 2.42–2.34 (1H, m, C*H*$_2$CH=CH_2), 1.64–1.53 (2H, m, CHC*H*$_2$$CH_2$), 1.43–1.26 (2H, m, C*H*$_2$$CH_3$), 0.90 (3H, t, *J* = 7.3 Hz, C*H*$_3$); δ_C (125 MHz, $CDCl_3$) 172.5 (C), 170.7 (C), 141.3 (CH), 141.2 (CH), 140.9 (CH), 140.1 (CH), 140.0 (CH), 130.7 (CH), 130.7 (CH), 126.9 (C), 126.8 (C), 119.6 (CH_2), 119.1 (CH_2), 119.0 (C), 117.9 (CH), 117.8 (CH), 114.7 (CH_2), 114.6 (CH_2), 82.6 (CH), 82.6 (CH), 39.3 (CH), 36.7 (CH_2), 36.5 (CH_2), 36.1 (CH_2), 36.1 (CH_2), 23.2 (CH_2), 23.1 (CH_2), 20.6 (CH_2), 14.0 (CH_3); *m/z* (CI, NH_3) 286.1569 $[M]^+$, $C_{18}H_{22}O_3$ requires 286.1578.