Experimental

For general experimental details see ref. 1.

**(2S)-3-(**tert***-Butyldiphenylsilyloxy)-2-methylpropionate  15b**

Imidazole (9.2 g, 135.4 mmol) and **tert***-butyldiphenylsilyl chloride (26.1 g, 95.2 mmol, 25.0 ml) were added to a stirred solution of commercially available methyl 3-hydroxy-2R-methylpropanoate  **15a** (10.0 ml, 90.0 mmol) in dry dichloromethane (106 ml) at 0 °C under a nitrogen atmosphere. The solution was stirred at room temperature for 1 hour then quenched with saturated ammonium chloride solution (100 ml). The separated aqueous phase was extracted with diethyl ether (3 x 50 ml) and the combined organic extracts were washed with saturated ammonium chloride solution (3 x 100 ml) and brine (3 x 100 ml), then dried (MgSO₄) and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel using 5% ethyl acetate in petroleum ether (40-60 °C) as eluent to give the **silyl ether** (30.4 g, 95%) as a colourless oil; (Found: C, 71.0, H, 7.9; C₂₁H₂₈O₃Si requires: C, 70.8, H, 7.9%); [α]D²²  -11.03 (c 1.15 in CHCl₃); νmax/cm⁻¹ (CHCl₃ solution): 1732, 1461; δH (360 MHz, CDCl₃)  7.71-7.60 (m, 4H, ArH), 7.47-7.33 (m, 6H, ArH), 3.81 (dd, 1H, J 5.7 and 9.6, CHHO), 3.72 (dd, 1H, J 5.7 and 9.6, CHHO), 3.69 (s, 3H, OCH₃), 2.79-2.65 (m, 1H, CHCH₃), 1.16 (d, 3H, J 6.8, CHCH₃),
1.03 (s, 9H, SiC(CH$_3$)$_3$); $\delta_C$ (90 MHz, CDCl$_3$) 175.3 (C), 135.5 (C), 133.4 (C), 129.6 (CH), 127.6 (CH), 65.9 (CH$_2$), 51.5 (CH$_3$), 42.4 (CH), 26.7 (CH$_3$), 19.2 (C), 13.4 (CH$_3$); $m/z$ (EI) 299.1110 ([M$^+$ - 57(t-Bu)]), C$_{17}$H$_{19}$O$_3$Si requires 299.1103.

(2S)-3-(tert-Butyldiphenylsilyloxy)-2-methylpropan-1-ol  16a

Lithium borohydride (3.7 g, 169.1 mmol) was added in one portion to a stirred solution of the ester 15b (30.0 g, 84.5 mmol) in dry THF (300 ml) at room temperature under a nitrogen atmosphere, and the mixture was then stirred at room temperature for 5 days. The mixture was cooled to 0 °C and then quenched with saturated ammonium chloride solution (100 ml). The separated aqueous layer was extracted with ether (3 x 50 ml) and the combined organic extracts were washed with saturated aqueous ammonium chloride (3 x 100 ml) and brine (3 x 100 ml), then dried (Mg$_2$SO$_4$) and concentrated in vacuo to leave a colourless oily residue. The residue was purified by flash column chromatography on silica gel eluting with 20% diethyl ether in pentane as eluent to give the alcohol (21.5 g, 85%) as a colourless oil. $[\alpha]_D^{20}$ -4.3 (c 1.15 in CHCl$_3$); $\nu_{max}$/cm$^{-1}$ (CHCl$_3$ solution): 3626, 3508; $\delta_H$ (360 MHz, CDCl$_3$) 7.73-7.60 (m, 4H, ArH), 7.49-7.33 (m, 6H, ArH), 3.80-3.55 (m, 4H, 2 x CH$_2$O), 2.68-2.55 (br. s, 1H, OH), 2.10-1.95 (m, 1H, CH$_3$CH), 1.06 (s, 9H, SiC(CH$_3$)$_3$).
0.83 (d, 3H, J 6.8, CH₃CH );  δC (90 MHz, CDCl₃)  135.6 (CH), 133.1 (C),
129.7 (CH), 127.7 (CH), 68.6 (CH₂), 67.6 (CH₂), 37.2 (CH), 26.8 (CH₃),
19.1 (C), 13.1 (CH₃);  m/z (EI) 271.1153 ([M⁺-57(t-Bu)]), C₁₆H₁₉O₂Si
requires 271.1154.
A solution of dimethylsulfoxide (6.0 ml, 89.0 mmol) in dichloromethane (5 ml) was added dropwise over 10 minutes to a stirred solution of oxalyl chloride (44.6 mmol, 4 ml) in dichloromethane (60 ml) at -78 °C under a nitrogen atmosphere, and the mixture was then stirred at -78 °C for 15 minutes. A solution of the alcohol 16a (4.9g, 14.9 mmol) in dichloromethane (60 ml) was added dropwise over 20 minutes, and the mixture was again stirred at -78 °C for 30 minutes. Triethylamine (113.0 mmol, 16 ml) was added dropwise over 15 mins, and the mixture was allowed to warm to -55 °C over 2 hours, and then quenched with saturated aqueous ammonium chloride solution (50 ml). The mixture was extracted with diethyl ether (3 x 50 ml), and the separated organic extracts were dried (MgSO₄) and concentrated in vacuo to leave a yellow oil. Purification by column chromatography on silica gel using petrol ether (40-60 °C)/diethyl ether = 49:1 as eluent gave the aldehyde (2.7 g, 60%) as a colourless waxy solid; m.p. 60-61 °C; (Found: C, 73.4, H, 8.0, C₂₀H₂₆O₂Si requires C, 73.6, H, 8.0%; [α]D²⁰ -15.7 (c 1.0 in CHCl₃) νmax/cm⁻¹(CHCl₃ solution): 2860, 1722, 1589; δH (360 MHz, CDCl₃) 9.76 (d, 1H, J 1.6, CHCHO), 7.70-7.60 (m, 4H, ArH); 7.48-7.33 (m, 6H, ArH); 3.91-3.81 (m, 2H, CHCH₂O), 2.63-2.50 (m, 1H, CHCH₃), 1.10 (d, 3H, J 7.0, CHCH₃), 1.04 (s, 9H, SiC(CH₃)₃), δC (90 MHz, CDCl₃) 204.5
A solution of diisopropyl azodicarboxylate (4.0 g, 20.1 mmol) in dry THF (22 ml) was added slowly over 20 minutes to a stirred solution of \(E\)-4-methyl-pent-2-en-1-ol \(^{19}\) in paper (1.3 g, 13.2 mmol), 2-sulfanylbenzothiazole (3.3 g, 20.1 mmol) and triphenylphosphine (5.6 g, 21.5 mmol) in dry THF (72 ml) under a nitrogen atmosphere at 0 °C. The mixture was stirred at 0 °C for 1 hr, then allowed to warm to room temperature where it was stirred for a further 24 hours. The solvent was removed \textit{in vacuo} and the residue was purified by flash column chromatography using 10% diethyl ether in pentane as eluent to give the \(2-(E\text{-}4\text{-methylpent-2-ene-1-sulfyl})\text{-benzothiazole}\) (3.1 g, 95%) as a golden yellow oil. (Found: C, 62.4, H, 6.0, N, 5.7, \(C_{13}H_{15}NO_{2}S_{2}\) requires C, 62.6, H, 6.1, N, 5.6%); \(\delta\) \(^{1}H\) (360 MHz, CDCl\(_3\)) 7.81 (d, 1H, \(J\ 8.2\), ArH), 7.69 (d, \(J\ 9.1\), 1H, ArH), 7.35-7.15 (m, 3H, ArH), 5.75-5.65 (dd, 1H, \(J\ 6.6\) and 15.6, \(CHCH=CH\)), 5.55-5.45 (m, 1H, \(CH=CHCH_{2}S\)), 3.87 (d, 2H, \(J\ 7.4\), \(CH=CHCH_{2}S\)), 2.25-2.20 (m, 1H, \(CH(CH_{3})_{2}\)), 0.90 (d, 6H, \(J\ 6.8\), \(CH(CH_{3})_{2}\)); \(\delta\) \(^{13}C\) (90 MHz, CDCl\(_3\)) 166.5 (C), 153.0 (C), 142.9 (CH), 137.1 (C), 135.1 (CH), 126.8 (CH),...
A solution of \((\text{NH}_4)_6\text{Mo}_7\text{O}_{24}.4\text{H}_2\text{O}\) (2.0 g, 1.6 mmol) in hydrogen peroxide (30 wt % solution in water, 6.6 ml, 58.4 mmol) was added dropwise over 10 minutes to a stirred solution of the above thioether (1.6 g, 6.5 mmol) in ethanol (40 ml) at 0 °C. The mixture was stirred at room temperature for 16 hours, then water (50 ml) was added and the ethanol was removed \textit{in vacuo}. The remaining aqueous suspension was extracted with diethyl ether (4 x 40 ml), and the combined organic extracts were then dried (MgSO\(_4\)) and concentrated \textit{in vacuo}. The residue was purified by flash column chromatography using 30% diethyl ether in pentane as eluent to give the corresponding sulfone (1.7 g, 91%) as a colourless waxy solid; \(\nu_{\text{max}}/\text{cm}^{-1}\) (CHCl\(_3\) solution) 1602; \(\delta_{\text{H}}\) (360 MHz, CDCl\(_3\)) 8.21-7.55 (m, 4H, ArH), 5.60 (dd, 1H, \(J\) 6.6 and 15.6, CHCH=CH), 5.45-5.5 (m, 1H, CH=CHCH\(_2\)S), 4.13 (d, 2H, \(J\) 7.1, CH=CHCH\(_2\)S), 2.25-2.15 (m, 1H, CH(CH\(_3\))\(_2\)), 0.75 (d, 6H, \(J\) 6.8, CH(CH\(_3\))\(_2\)); \(\delta_{\text{C}}\) (90 MHz, CDCl\(_3\)) 165.1 (C), 152.6 (C), 150.1 (CH), 136.7 (C), 127.9 (CH), 127.5 (CH), 125.4 (CH), 122.2 (CH), 111.6 (CH), 58.6 (CH\(_2\)), 31.2 (CH), 21.6 (CH\(_3\)); \(m/z\) (EI) 281.0542 (M\(^+\)), \(C_{13}H_{15}O_{2}NS_2\) requires 281.0544.
**Method A.** A solution of sodium bis(trimethylsilyl)amide (2M) in THF (4.4 ml) was added dropwise over 2 mins to a stirred solution of the sulfone 18 (2.4 g, 8.5 mmol) in dry THF (30 ml) at -78 °C under a nitrogen atmosphere. The mixture was stirred at -78 °C for 30 minutes, and then a solution of the aldehyde 17 (2.6 g, 8.1 mmol) in THF (20 ml) was added slowly via cannula over 15 minutes. The mixture was stirred at -78 °C for 3 hours, and then at room temperature for 1 hour. The reaction was quenched with saturated aqueous ammonium chloride solution (30 ml) and the separated aqueous layer was then extracted with diethyl ether (3 x 20 ml). The combined organic extracts were dried (MgSO₄) and concentrated *in vacuo*. The residue was purified by flash column chromatography, using pentane as eluent, to give a 3:1 mixture of E-3 and Z-3 isomers of the diene silyl ether 19a (2.3g, 75%)(as determined by ¹H n.m.r.) as an oil. \([\alpha]_D^{20} +38.5\) (c 1.1 in CHCl₃); \(\nu_{\text{max}}/\text{cm}^{-1}\) (CHCl₃ solution): 3694; \(m/z\) (FAB) 335.1835 (M⁺- 57(t-butyl)), \([C_{26}H_{36}OSi-57(t-\text{butyl})]\) requires 335.1831.

Solid n-tetrabutyl ammonium fluoride (3.0 g, 9.1 mmol) was added in one portion to a stirred solution of the above silyl ether (1.9 g, 4.8 mmol) in dry THF (20 ml) at room temperature. The mixture was stirred at room temperature for 4 hours, and then quenched with saturated aqueous ammonium chloride (20 ml). The mixture was extracted with diethyl ether (4 x 20 ml) and the combined organic
extracts were then washed with brine (2 x 20 ml), dried (MgSO₄) and concentrated in vacuo to leave a yellow oil. The residue was purified by flash column chromatography, using 20% diethyl ether in pentane as eluent to give the corresponding diene alcohol (0.7 g, 94%) as a 4:1 mixture of E-3 and Z-3 isomers (as determined by ¹H NMR.); [α]D²¹ - 28.5 (c 1.4 in CHCl₃); δH (360 MHz, CDCl₃) (major E-isomer) 6.29 (dd, 1H, J 15.1 and 8.1, CH=CHCH=CH), 6.11 (dd, 1H, J 15.0 and 8.1, CH=CHCH=CH), 5.57 (dd, 1H, J 15.0 and 8.1, CHCH=CHCH=CH), 5.46 (dd, 1H, J 15.0 and 8.1, CH=CHCH=CHCH), 3.52 (dd, 1H, J 10.5 and 5.6, CH(OH)), 3.50 (dd, 1H, J 10.5 and 5.6, CHHOH), 2.50-2.25 (m, 2H, CH(CH₃), and CH(CH₃)₂); 1.50 (br s, 1H, CH₂OH), 1.01 (d, 3H, J 6.8, CH(CH₃)), 0.98 (d, J 6.8, 6H, CH(CH₃)₂).

Method B. A solution of n-butyllithium (1.6 M, 0.44 mol) in hexane (2730 ml) was added dropwise to a vigorously stirred (overhead stirrer) suspension of the phosphonium bromide 23 (204 g, 0.48 mol) in dry ether (1000 ml) at -10°C under a nitrogen atmosphere. A solution of 3-(1-ethoxyethoxy)-2R-methyl-1-propanal 17b (70.0 g, 0.44 mol) in dry ether (700 ml) was next added to the resulting deep red solution over 30 min at -10°C. The orange slurry, thus formed, was stirred at room temperature for 1hr and then filtered through Kieselguhr. The residue was washed with ether (150 ml) and the combined filtrate and washings were
evaporated in vacuo. The residue was purified by flash column chromatography using 5% EtOAc in petroleum ether (b.p. 40-60°C) as eluent to give the 1,3-diene 19c (59.9 g, 42%) as a 2:1 mixture of E-3 and Z-3 isomers (by GC); (Found: C, 74.2, H, 11.3, C_{14}H_{26}O_{2} requires C, 74.3, H, 11.6%); [\alpha]_D^{22} +8.1 (c. 1.57 in CHCl₃); \nu_{\text{max}}/\text{cm}^{-1} (CCl₄ solution): 2961, 2871; \delta_{\text{H}} (360 MHz, CDCl₃) 6.28 (dd, 1H, J 15.4 and 11.1, : (Z) CHCH: (E) CH), 6.05 (dd, 1H, J 14.0 and 10.3, HC: (E) CHCH: (E) CH), 5.96 (dd, 1H, J 14.0 and 10.3, HC: (E) CHCH (E) CH), 5.64 (dd, 1H, J 16.9 and 6.8, : (Z) CHCH: (E) CHCH), 5.57 (dd, 1H, J 14.7 and 6.8, CHCH: (E) CHCH: (E)), 5.35 (dd, 1H, J 14.7 and 6.8, : (E) CHCH: (E) CHCH), 5.12 (dd, 1H, J 10.0, CHCH: (Z) CHCH: (E)), 4.69 (q, 1H, J 5.4, CH₃CH(O)₂ (Z)), 4.68 (q, 1H, J 5.3, CH₃CH(O)₂ (E)), 3.68-3.21 (m, 4H, OCH₂CH₃ and OCH₂CH), 2.95-2.83 (m, 1H, CH₂CH(CH₃)CH: (Z)), 2.50-2.25 (m, 2H, :CHCH(CH₃)₂ and CH₂CH(CH₃)CH: (E)), 1.29 (d, 3H, J CH₃CH(O)₂), 1.19 (t, 3H, J 7.1, CH₂CH₃), 1.04 (d, 3H, J 4.6, CHCH₃ (Z)), 1.01 (d, 3H, J 7.0, CHCH₃ (E)), 0.99 (d, 3H, J 6.8, CH(CH₃)₂); C (90 MHz, CDCl₃) 142.2 (CH), 140.0 (CH), 134.3 (CH), 132.1 (CH), 129.9 (CH), 129.0 (CH), 127.2 (CH), 122.6 (CH), 99.4 (CH), 69.7 (CH₂), 60.6 (CH₂), 36.9 (CH), 31.2 (CH), 30.9 (CH), 22.4 (CH₃), 19.5 (CH₃), 17.0 (CH₃), 15.2 (CH₃); m/z (EI) 137.1110 (M⁺), C_{16}H_{17} requires 137.2460 and 89.0279, C₄H₈O₂ requires 89.1148.
A mixture of hydrochloric acid (0.5 M, 630 ml, 0.31 mol) and the ethoxyethoxy ether 19c (59.3 g, 0.26 mol) in THF (1000 ml) was stirred at room temperature for 3 hr. The resulting turbid solution was partitioned between water (1000 ml) and ether (1000 ml), and the two phases were then separated. The aqueous phase was extracted with ether (3x500 ml) and the combined ether extracts were washed with brine (500 ml), dried and evaporated in vacuo. The residue was purified by flash column chromatography using 10% EtOAc in petroleum ether (b.p. 40-60 °C) as eluent to give the diene alcohol as a 2:1 mixture of E-3 and Z-3 isomers (37.6 g, 93%); \([\alpha]_D^{22} -15.3 \) (c 2.0 in CHCl₃); \(\nu_{\text{max}}/\text{cm}^{-1}\) (CCl₄ solution): 3630, 3590, 3015, 2970, 2935, 2880; \(\delta_H\) (360 MHz, CDCl₃) 6.29 (dd, 1H, J 15.0 and 10.9, : (Z) CHCH: (E) CH), 6.11 (ddd, 1H, J 14.7 and 10.1 and 1.1, HC: (E) CHCH: (E) CH), 5.98 (ddd, 1H, J 14.7 and 10.1 and 1.1, HC: (E) CHCH: (E) CH), 5.68 (dd, 1H, J 15.8 and 6.9, : (Z) CHCH: (E) CHCH), 5.62 (dd, 1H, J 15.1 and 6.7, CHCH: (E) CHCH: (E)), 5.44 (dd, 1H, J 15.1 and 7.9, : (E) CHCH: (E) CHCH), 5.06 (dd, 1H, J 10.3, CHCH: (Z) CHCH: (E)), 3.55-3.33 (m, 2H, HOCH₂CH₂), 2.93-2.26 (m, 2H, CH₂CH₃CH₃CH: (E)), 2.43-2.26 (m, 2H, :CHCH(CH₃)₂ and CH₂CH(CH₃)CH: (E)), 1.68 (br. S, OH), 1.01 (d, 3H, J 6.8, CHCH₃), 1.00 (d, 3H, J 6.8, CH(CH₃)₂); \(\delta_C\) (90 MHz, CDCl₃) 143.2 (CH), 140.9 (CH), 133.7 (CH), 131.6 (CH), 130.8 (CH), 127.0 (CH), 122.4 (CH), 67.7 (CH₂),
67.3 (CH₂), 39.6 (CH), 35.2 (CH), 31.3 (CH), 31.0 (CH), 22.3 (CH₃), 17.0 (CH₃), 16.4 (CH₃); m/z (EI) 154.1340 (M⁺), C₁₀H₁₈O requires 154.1358.

Iodine (9.0 mg, 0.04 mmol) was added to a solution of the 4:1 mixture of E-3 and Z-3 isomers of the 3,5-diene alcohol 19b (553.0 mg, 3.6 mmol) in dry diethyl ether (16 ml), and the solution was heated under reflux and irradiated with U.V. light from a 40W bulb for 75 minutes. The solution was cooled to room temperature and then washed with 0.1 M aqueous solution of sodium thiosulphate (3 x 20 ml). The separated aqueous phase was extracted with diethyl ether (3 x 20 ml) and the combined organic extracts were then washed with brine (2 x 20 ml), dried (MgSO₄) and concentrated in vacuo to leave a yellow oil. The residue was purified by flash column chromatography using 20% diethyl ether in pentane as eluent to give the E-3,E-5-diene alcohol (405 mg, 74%) (ee > 98% by Moshers’ ester analysis) as a colourless liquid; [α]D²¹ -15.3 (c 1.4 in CHCl₃); νmax/cm⁻¹ (CHCl₃ solution): 3336, 3020, 2960; δH (360 MHz, CDCl₃) 6.09 (ddd, 1H, J 15.0 and 10.0 and 1.0, CH=CHCH=CH), 5.98 (ddd, 1H, J 14.5 and 10.0 and 1.0, CH=CHCH=CH), 5.61 (dd, 1H, J 15.0 and 6.7, CHCH=CHCH:), 5.45 (dd, 1H, J 14.5 and 7.8, :CHCH=CHCH), 3.53-3.33 (m, 2H, HOCH₂CH), 2.45-2.25 (m, 2H, CH₂CH(CH₃)CH: and CHCH(CH₃)₂), 2.08 (br. s, OH), 1.01 (d, 3H, J 6.8, CHCH₃), 1.00 (d, 6H, J 6.8, CH(CH₃)₂); δC (90 MHz, CDCl₃) 140.9 (CH), 133.7 (CH), 131.6
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(CH), 126.9 (CH), 67.4 (CH₂), 39.7 (CH), 30.9 (CH), 22.3 (CH₃), 16.4 (CH); m/z (CI) 154.1365 (M⁺), C₁₀H₁₈O requires 154.1358.

**E-2-(4-Methylpentenyl)triphenylphosphonium Bromide** 23

A solution of triphenylphosphine (268 g, 1.0 mol) and 1-bromo-4-methyl-2E-pentene² (83.5 g, 0.51 mol) in dry toluene (1000 ml) was stirred vigorously (overhead stirrer) and heated under reflux for 6 hours. The mixture was cooled to room temperature and the resulting white precipitate was then filtered off and washed with ether to give the phosphonium salt (201.5 g, 93%) as a colourless solid. Recrystallisation gave needles m.p. 201-202.5 °C (from ether) (C, 67.6, H, 6.3, Br, 18.7 requires C, 67.8, H, 6.2, Br, 18.8%); \( \nu_{\max} / \text{cm}^{-1} \) (CHCl₃ solution): 2920, 2785, 1590; \( \delta_H \) (360 MHz, CDCl₃) 8.09-7.44 (m, 15H, arylCH), 5.86 (dt, 1H, J 14.5 and 7.0, CH₂CH=CH), 5.50-5.12 (m, 1H, CH=CHCH), 4.62 (dd, 2H, J 14.0 and 7.0, PCH₂CH), 2.44-2.10 (m, 1H, CH(CH₃)₂), 0.84 (d, J 7.0, CH (CH₃)₂).

**Methyl 3-(1-Ethoxyethoxy)-(2R)-methylpropanoate** 15c

\( \rho \)-Toluenesulphonic acid (20 mg) was added to a stirred solution of the alcohol 15a (75 g, 0.635 mol) in ether (700 ml) and ethyl vinyl ether (500 ml) at room temperature. The mixture came to a spontaneous reflux
and was then stirred at room temperature for 2 hr. The yellow solution was then washed with saturated aqueous NaHCO₃ (2x500 ml) and brine (500 ml), then dried, filtered and evaporated in vacuo to leave an orange liquid. Distillation gave the ester (112.6 g, 93%) as a colourless liquid, b.p. 87-89 °C/mmHg; (Found: C, 56.9, H, 9.9, C₉H₁₈O₄ requires C, 56.8, H, 9.6%); [α]₀²² -10.9 (c 1.53 in CHCl₃); νₘₐₓ/cm⁻¹ (CHCl₃ solution): 1743, 1201, 1136; δ_H (360 MHz, CDCl₃) 4.76 (q, 1H, J 5.3, CH₃C(H)₂), 3.83-3.66 (m, 4H, OCH₂CH₃ and OCH₂CH), 3.76 (s, 3H, OCH₃), 2.80 (sextet, 1H, J 6.3, CH₃CH₂CH₂), 1.36-1.23 (m, 9H, CH₃CH(O)₂), CH₂CH₃ and CHCH₃; δ_C (90 MHz, CDCl₃) 175.0 (C), 174.9 (C), 99.6 (CH), 99.1 (CH), 66.3 (CH₂), 66.1 (CH₂), 60.5 (CH₂), 60.5 (CH₂), 51.4 (CH₃), 51.2 (CH₃), 39.8 (CH), 39.8 (CH), 19.2 (CH₃), 19.2 (CH₃), 14.9 (CH₃), 14.8 (CH₃), 13.6 (CH₃), 13.0 (CH₃); m/z(EI) 175.0963 (M⁺), C₉H₁₈O₄ requires 175.0963.

**3-(1-Ethoxyethoxy)-(2R)-methylpropan-1-ol 16b**

A solution of the ester 15c (225.2 g, 1.18 mol) in dry ether (300 ml) was added dropwise over 90 min to a stirred solution of lithium hydride (1.0 M, 1.18 mol) in ether (944 ml) at 0°C under nitrogen. The mixture was stirred for 17 hr at ambient temperature, after which time it was cooled to
0°C and then ethyl acetate (100 ml) was added over 30 min. Water (60 ml), aqueous potassium hydroxide (15%, 60 ml) and then more water (180 ml) were added sequentially and the resulting fine granular precipitate was filtered through a pad of Kieselguhr. The residue was washed thoroughly with ethyl acetate (3x150 ml) and the combined filtrate and washings were then dried and evaporated in vacuo to leave a pale yellow liquid. Distillation gave the alcohol (131.1 g, 68%) as a colourless liquid, b.p. 68-71°C/10mmHg; $[\alpha]_D^{22}$ -8.2 (c 1.25 in CHCl₃); $\nu_{\text{max}}/\text{cm}^{-1}$ (CHCl₃ solution): 3420, 2980; $\delta_H$ (360 MHz, CDCl₃) 4.61 (q, 1H, 2H, J 5.3, CH₂CH(O)₂), 3.62-3.28 (m, 6H, OCH₂CH₃, OCH₂CH and CHCH₂OH), 2.85 (br s, OH), 1.85-1.90 (m, 1H, CH₃CHCH₂), 1.24 (d, 3H, J 5.3, CH₃CH(O)₂), 1.14 (t, 3H, J 7.3, OCH₂CH₃), 0.84 (d, 3H, J 6.9, CH₃CHCH₂); $\delta_C$ (90 MHz, CDCl₃) 99.8 (CH), 99.7 (CH), 69.3 (CH₂), 66.8 (CH₂), 66.6 (CH₂), 61.0 (CH₂), 60.8 (CH₂), 35.6 (CH), 35.5 (CH), 19.6 (CH₃), 15.1 (CH₃), 13.6 (CH₃), 13.5 (CH₃); (Found: m/z (EI) 162.1256 (M⁺), C₈H₁₈O₃ requires 162.1256.

3-(1-Ethoxyethoxy)-(2R)-methylpropanal 17b

A solution of the alcohol 16b (60.9 g, 0.38 mol) in dry dichloromethane (200 ml) was added over 30 min to a stirred suspension of Dess-Martin
periodinane (175.2 g, 0.41 mol) in dry dichloromethane (500 ml) at room
temperature. The mixture came to a spontaneous reflux and after cooling
it was then stirred at room temperature for 90 min. The mixture was
diluted with ether (1000 ml) and poured onto a stirred solution of sodium
thiosulphate (160 g) in saturated aqueous sodium hydrogen carbonate
(2500 ml). The two phases were separated and the aqueous phase was
then extracted with ethyl acetate (3x250 ml). The combined organic
extracts were dried and evaporated in vacuo to leave the aldehyde (50.6
g) as a colourless liquid; $[\alpha]_D^{22} -31.1$ (c 1.31 in CHCl$_3$); $\nu_{\text{max}}$/cm$^{-1}$ (CHCl$_3$
solution): 2878, 1741; $\delta_H$ (360 MHz, CDCl$_3$) 9.65 (d, 1H, $J$ 1.3, CHCHO),
4.63 (q, 1H, $J$ 5.6, CH$_2$CH(O)$_2$), 3.75-3.34 (m, 4H, OCH$_2$CH$_3$ and
OCH$_2$CH), 2.56 (m, 1H, CH$_2$CH(CH$_3$)CHO), 1.23 (d, 3H, $J$ 5.6, CH$_3$CH(O)$_2$),
1.13 (t, 3H, $J$ 6.9, OCH$_2$CH$_3$), 1.06 (dd, 3H, $J$ 7.1 and 0.7, CH$_3$CHCHO);
$\delta_C$ (90 MHz, CDCl$_3$) 203.1 (C), 99.7 (CH), 99.6 (CH), 64.7 (CH$_2$), 64.6
(CH$_2$), 60.9 (CH$_2$), 60.6 (CH$_2$), 46.6 (CH), 19.5 (CH$_3$), 15.2 (CH$_3$), 15.2
(CH$_3$), 10.7 (CH$_3$); which was used without further purification.

**E-3, E-5-(S)-2,7-Dimethyl-octa-3,5-dienal 21a**

Solid potassium bicarbonate (1.5 g) was added in one portion to a stirred
solution of the $E,E$-dienol 20 (1.4 g, 9.0 mmol) in dry dichloromethane (7
ml) followed by one portion of Dess-Martin periodinane (4.6 g, 11.0
mmol) at room temperature. The mixture was stirred at room
temperature for 2 hours under an atmosphere of nitrogen, and then
diluted with diethyl ether (25 ml). The mixture was poured onto a stirred
solution of sodium thiosulphate (4.2 g) in saturated aqueous sodium
bicarbonate solution (25 ml) and stirred at room temperature 20 minutes.
More ether (8 ml) was added, and the separated aqueous phase was
extracted with diethyl ether (3 x 15 ml). The combined ether extracts
were washed with saturated aqueous sodium bicarbonate (3 x 20 ml),
dried (MgSO₄) and evaporated in vacuo to leave the \textit{E,E}-dienal (1.3 g) as
a pale yellow liquid; \( \nu_{\text{max}}/\text{cm}^{-1} \) (CHCl₃ solution): 2871, 1727, 991; \( \delta \text{H} \) (360
MHz, CDCl₃) 9.49 (d, 1H, \( J \) 1.7, CHCHO), 6.09 (ddd, 1H, \( J \) 14.9 and 10.2
and 0.7, HC=CHCH=CH), 5.95 (ddd, 1H, \( J \) 15.1 and 10.2 and 1.0,
HC=CHCH=CH), 5.62 (dd, 2H, \( J \) 14.9 and 6.6, CHCH=CHCH::), 5.44 (dd,
1H, \( J \) 15.1 and 7.6, :CHCH=CHCH), 3.02 (m, 1H, OHCH(CH₃)CH), 2.25
(m, 1H, :CHCH(CH₃)₂), 1.14 (d, 3H, \( J \) 6.9, CHCH₃), 0.94 (d, 6H, \( J \) 6.6,
CH(CH₃)₂); \( \delta \text{C} \) (90 MHz, CDCl₃) 201.4 (CH), 142.5 (CH), 134.0 (CH),
126.6 (CH), 126.5 (CH), 49.9 (CH), 31.1 (CH), 22.2 (CH₃), 13.4 (CH₃),
which was used without further purification.

\textit{E-3, E-5-(S)-2,7-Dimethyl-octa-3,5-dienoic acid} 21b
A solution of sodium chlorite (7.9 g, 87.0 mmol) and sodium dihydrogen orthophosphate dihydrate (7.8 g, 50.0 mmol) in water (45 ml) was added dropwise over 45 min to a solution of the dienal 21a (1.4 g, 9.0 mmol) in tert-butanol (75 ml) and 2-methyl-2-butene (38 ml) at room temperature. The mixture was stirred at room temperature for 90 min and the separated aqueous phase was then extracted with ethyl acetate (4 x 50 ml). The combined organic extracts were dried and concentrated in vacuo to leave a residue which was purified by flash column chromatography using 30% ethyl acetate in petroleum ether (b.p 40-60 °C) as eluent to give the carboxylic acid (0.9 g, 61%) as a colourless liquid; [α]D20 -18.1 (c 1.4 in CHCl3); νmax/cm-1 (CHCl3 solution): 3523, 3185, 2914, 1715; δH (360 MHz, CDCl3) 6.06 (dd, 1H, J 15.1 and 10.3, HC=CHCH=CH), 5.91 (ddd, 1H, J 14.6 and 10.3 and 1.0, HC=CHCH=CH), 5.59 (dd, 1H, J 15.1 and 8.3, CHCH=CHCH:), 5.57 (dd, 1H, J 14.6 and 7.6, =CHCH=CHCH), 3.22-3.12 (m, 1H, CH(CH3)CH), 2.27 (septet, 1H, J 6.6, CH(CH3)2), 1.22 (d, 3H, J 7.3, CHCH3), 0.93 (d, 6H, J 6.6, CH(CH3)2); δC (90 MHz, CDCl3) 186.1 (s), 142.3 (CH), 132.3 (CH), 129.1 (CH), 125.8 (CH), 42.2 (CH), 31.3 (CH), 21.8 (CH3), 17.2 (CH3); m/z (Cl) 168.1151 (M+), C10H16O2 requires 168.1150.

**E-3, E-5-(S)-2,7-Dimethyl-octa-3,5-dienoic acid amide**  21c
Dry DMF (3 drops) was added to a stirred solution of the \(E,E\)-dienoic acid \(21b\) (2.1 g, 12.3 mmol) and oxalyl chloride (7.8 g, 62.0 mmol) in dry dichloromethane (50 ml) at room temperature under a nitrogen atmosphere. The mixture was stirred at room temperature for 3 hours, and the solvent was then removed \textit{in vacuo} to leave the crude acid chloride as an orange liquid: \(\nu_{\text{max}}/\text{cm}^{-1}\) (CHCl\(_3\) solution): 2962, 2870, 1786, 1654, 1458, 1251, 989, 937. This was immediately taken up in dry ether (50 ml), and the resulting solution treated with ammonia gas for 30 min. The mixture resulting mixture was purged with nitrogen gas and then filtered through a pad of Kieselguhr. The residue was washed with ethyl acetate (3 x 50 ml) and the filtrate was concentrated \textit{in vacuo} to leave an orange-brown solid. Purification by flash column chromatography on silica gel, using 50% ethyl acetate in petroleum ether (40-60 \(^\circ\)C) as eluent, gave the amide (1.5 g, 74%) as a pale yellow solid. Recrystallization gave prisms, m.p 82-83 \(^\circ\)C (EtOAc/pentane). \([\alpha]_D^{22} +25.6\) (c 1.00 in CHCl\(_3\)); \(\nu_{\text{max}}/\text{cm}^{-1}\)(CHCl\(_3\) solution): 3522, 3047, 2931, 2866, 1691; \(\delta_H\) (360 MHz, CDCl\(_3\)) 6.09 (dd, 1H, \(J_{15.5}\) and \(J_{10.2}\), CH=CHCH=CH), 5.91 (ddd, 1H, \(J_{15.5}\) and \(J_{10.2}\) and \(J_{1.3}\), HC=CHCH=CH), 5.76-5.66 (m, 4H, CHCH=CHCH= and =CHCH=CHCH and \(NH_2\)), 3.10-2.90 (m, 1H, CH(CH\(_3\))CH=), 2.28 (septet, 1H, \(J_{6.6}\), CH(CH\(_3\))\(_2\)), 1.22 (d, 3H, \(J_{6.9}\), CHCH\(_3\)), 0.94 (d, 6H, \(J_{6.6}\), CH(CH\(_3\))\(_2\)); \(\delta_C\) (90 MHz, CDCl\(_3\)) 177.8 (C), 142.2 (CH), 132.6 (CH), 130.4 (CH), 126.4 (CH), 43.9 (CH), 31.0
(CH), 22.2 (CH₃), 17.3 (CH₃); m/z (CI) 167.1325 (M⁺), C₁₀H₁₇NO requires 167.1310.

**E-3, E-5-(S)-2,7-Dimethyl-octa-3,5-dienethioic acid amide**  

Lawesson’s reagent (121.0 mg, 0.3 mmol) was added in one portion to a stirred solution of the amide 21c (100.0 mg, 0.6 mmol) in dry THF (4ml) at room temperature under a nitrogen atmosphere. The mixture was heated under reflux for 10 minutes, then cooled to room temperature when the solvent was evaporated *in vacuo*. The residue was purified by flash column chromatography, using 20% ethyl acetate in petroleum ether (40-60 °C) as eluent, to give the diene thioamide (96.0 mg, 87%) as a yellow oil; [α]Dₙ° +32.6 (c 1.23 in CHCl₃); νₚₑₜₐₚₑₚₑₑₚₑₑₑₚₑₚₑ in CHCl₃ solution:
3481, 3359, 3190, 2953, 2867, 1595; δₑ (360 MHz, CDCl₃) 8.32 (br. s, 1H, NH), 7.31 (br. s, 1H, NH), 6.16 (dd, 1H, J 15.5 and 10.3, HC=CHCH=CH), 5.97 (dd, 1H, J 15.2 and 10.3, HC=CHCH=CH), 5.69 (dd, 2H, J 15.5 and 6.7, CHCH=CHCH=:), 5.65 (dd, 1H, J 15.2 and 7.5, :CHCH=CHCH), 3.49-3.42 (m, 1H, CH(CH₃)CH), 2.34 (septet, 1H, J 6.7, CH(CH₃)₂), 1.41 (d, 3H, J 6.9, CHCH₃), 1.00 (d, 6H, J 6.7, CH(CH₃)₂); δₑ (90 MHz, CDCl₃) 212.2 (C), 142.1 (CH), 132.1 (CH), 130.2 (CH), 125.7 (CH), 50.6 (CH), 30.4 (CH₃), 21.5 (CH₃), 19.9 (CH₃); m/z (EI) 183.1062 (M⁺), C₁₀H₁₇NS requires 183.1082.
2-(1-Trimethylsilyloxy-vinyl)-thiazole-4-carboxylic acid methyl ester 26

Freshly distilled benzoyl chloride (31.0 ml, 269.0 mmol) was added dropwise over 15 minutes to a stirred solution of 2-hydroxypropionamide (20.1 g, 225.0 mmol) and pyridine (36 ml, 449.0 mmol) in dry dichloromethane (200 ml) at 0 °C under a nitrogen atmosphere. The mixture was stirred at 0 °C for 3 hours, and then quenched with distilled water (50 ml). The separated aqueous layer was extracted with dichloromethane (4 x 30 ml) and the combined organic extracts were washed successfully with 2M aqueous hydrochloric acid (4 x 40 ml), distilled water (2 x 40 ml), saturated aqueous sodium bicarbonate solution (3 x 40 ml) and brine (3 x 40 ml), and then dried (MgSO₄). The solvent was removed in vacuo to leave benzyloxypropionamide as a solid (41.2 g, 95%) which crystallized as colourless crystals, m.p. 86-87 °C (EtOAc/hexane); ν_{max}/cm⁻¹(CHCl₃ solution): 3531, 3412, 1704; δ_H (360 MHz, CDCl₃) 8.05 (d, 2H, J 8.4, ArH), 7.57 (t, 1H, J 7.4, ArH), 7.43 (t, 2H, J 7.4, ArH), 6.10 (br. s, 1H, NH), 5.90 (br. s, 1H, NH), 5.45 (q, 1H, J 6.8, CHCH₃), 1.60 (d, 3H, J 6.8, CHCH₃); δ_C (90 MHz, CDCl₃) 173.1 (C), 165.2 (C), 133.6 (CH), 129.7 (CH), 129.3 (C), 128.6 (CH), 70.7
Lawesson’s reagent (8.1 g, 20.5 mmol) was added in one portion to a stirred solution of 2-benzyloxythiopropionamide (7.7 g, 40.4 mmol) in dry dimethoxyethane (100 ml) at room temperature under a nitrogen atmosphere. The mixture was stirred at room temperature for 8 hours and then the solvent was removed in vacuo. The residue was dissolved in ethyl acetate and the solution was washed with 2M aqueous sodium hydroxide solution (4 x 40 ml) and brine (4 x 40 ml) and then dried (MgSO₄). The solvent was removed in vacuo to leave a yellow oil which was purified by flash column chromatography on silica gel using 50% diethyl ether in pentane as eluent to give the benzyloxythiopropionamide (7.2 g, 85%) as a colourless solid. Recrystallisation gave prisms, m.p. 103-104 °C (EtOH); (Lit.³ m.p. 104 °C) (Found: C, 57.4, H, 5.3, N, 6.5, Calc. for C₁₀H₁₁O₂NS: C, 57.4, H, 5.3, 6.7%); νmax/cm⁻¹ (CHCl₃ solution): 3490, 3373, 3178, 1728, 1592; δH (360 MHz, CDCl₃) 8.40-8.20 (br. s, 1H, NH), 8.05 (d, 2H, J 8.4, ArH), 7.80-7.65 (br. s, 1H, NH), 7.57 (t, 1H, J 7.4, ArH), 7.43 (t, 1H, J 7.4, ArH), 5.88 (q, 1H, J 6.6, CHCH₃), 1.82 (d, 3H, J 6.6, CH₂CH₃); δC (90 MHz, CDCl₃) 206.0 (C), 165.4 (C), 134.1 (CH), 130.1 (CH), 129.4 (CH), 76.9 (CH), 21.4 (CH₃); m/z (ES) 232.0425 (M⁺+Na), C₁₀H₁₁O₂NSNa requires 232.0408.
A mixture of the above thioamide (9.8 g, 47.0 mmol) and powdered potassium bicarbonate (38.0 g, 375.0 mmol) in dimethoxyethane (70 ml) was stirred vigorously at room temperature for 10 minutes under a nitrogen atmosphere. Ethyl 3-bromopyruvate (18 ml, 141.0 mmol) was added, in one portion, and the suspension was then cooled to 0°C. A solution of triluoroacetic anhydride (27 ml, 187.0 mmol) and pyridine (32 ml, 398.0 mmol) in dimethoxyethane (50 ml), pre-cooled to 0 °C, was added dropwise over 20 minutes via cannula, and the mixture was then allowed to reach room temperature where it was stirred for a further 30 min. The solvent was evaporated in vacuo. The residue was taken up in chloroform (300 ml) and the solution was stirred vigorously with water (150 ml) until effervescence had ceased. The separated organic phase was dried and evaporated in vacuo to leave a brown oily residue. The residue was purified by flash chromatography on silica gel, using 30% EtOAc in petroleum ether (40-60 °C), as eluent to give ethyl 2-(1-benzyloxy-ethyl)-thiazole-4-carboxylate (13.9 g, 97%) as an orange oil; (Found: C, 59.1, H, 4.9, N, 4.5, C_{15}H_{15}O_{4}NS requires C, 59.0, H, 5.0, N, 4.6%); $\nu_{\text{max}}$ cm$^{-1}$ (CHCl$_3$ solution): 3119, 2985, 1728; $\delta_{\text{H}}$ (360 MHz, CDCl$_3$) 8.08 (s, 1H, :CH), 8.04-7.36 (m, 5H, ArH), 6.37 (q, 1H, $J_{6.6}$, CH$_3$), 4.35 (q, 2H, $J_{7.3}$, CH$_2$CH$_3$), 1.77 (d, 3H, $J_{6.6}$, CHCH$_3$), 1.32 (t, 3H, $J_{7.3}$, CH$_2$CH$_3$); $\delta_{\text{C}}$ (90 MHz, CDCl$_3$) 171.7 (C), 165.2 (C), 161.2 (C), 147.3 (C), 133.7 (CH), 129.9 (CH), 129.5 (C),
128.7 (CH), 127.9 (CH), 70.7 (CH), 61.5 (CH2), 21.3 (CH3), 14.5 (CH3); 
m/z (ES) 328.0621 (M+Na), C15H15O4NSNa requires 328.0620.

Sodium methoxide (2.5 g, 46.1 mmol) was added in one portion to a stirred solution of the benzoate ester from above (14.2 g, 46.1 mmol) in dry methanol (140 ml) at room temperature under a nitrogen atmosphere. The orange solution was stirred at room temperature for 24 hours and then neutralized carefully with a few drops of 2M aqueous hydrochloric acid until the solution slightly just acidic. The solution was extracted with ethyl acetate (5 x 50 ml), and the combined organic extracts were dried (MgSO4) and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel using 50% ethyl acetate in petroleum ether (b.p. 40-60 °C) as eluent to give methyl 2-(1-hydroxyethyl)thiazole-4-carboxylate (6.4 g, 70%) as a colourless solid. Recrystallisation gave colourless prisms m.p. 92-93 °C (EtOAc/hexane) (Lit. see ref. 16 in paper m.p. 92-93 °C). (Found: C, 45.0, H, 4.9, N, 7.5, Calc. for C7H9O3NS: C, 44.9, H, 4.9, N, 7.5%); νmax/cm−1 (CHCl3 solution): 3356, 3125, 2954, 1732; δH (360 MHz, CDCl3) 8.07 (s, 1H, =CH), 5.22 (q, 1H, J 6.5, CH3), 3.94 (br s, OH), 3.90 (s, 3H, OCH3), 1.63 (d, 3H, J 6.5, CH3); δC (90MHz, CDCl3) 177.2 (C), 161.9 (C), 146.6 (C), 127.6 (CH), 68.3 (CH), 52.5 (CH3), 24.2 (q); m/z (EI) 187.0305 (M+), C7H9O3NS requires 187.0303.
Activated manganese dioxide (8.1 g, 93.0 mmol) was added in one portion to a stirred solution of the above secondary alcohol (0.6 g, 3.1 mmol) in dry dichloromethane (15 ml) at room temperature, and the suspension was then stirred at room temperature for 24 hours. The suspension was filtered through celite and the residue was washed with ethyl acetate (5 x 50 ml). The filtrate was concentrated in vacuo to leave the corresponding methyl ketone 24a (0.46 g, 80%) as a solid which recrystallised as yellow crystals m.p. 84-85 °C (EtOAc/hexane); (Found: C, 46.2, H, 3.9, N, 7.3, C7H7O3NS requires C, 46.4, H, 3.8, N, 7.5%); νmax/cm⁻¹ (CHCl₃ solution): 1733, 1694, 1602; δH (360 MHz, CDCl₃) 8.45 (s, 1H, :C₇H₇), 3.99 (s, 1H, CH₃O), 2.75 (s, 3H, CH₃); δC (90 MHz, CDCl₃) 177.2 (C), 161.9 (C), 146.6 (C), 133.6 (C), 127.6 (CH), 52.8 (CH₃), 26.1 (CH₃); m/z (EI) 185.0150 (M⁺), C₇H₇O₃NS requires 185.0147.

Freshly distilled triethylamine (0.23 ml, 1.6 mmol) was added by syringe to a stirred solution of the methyl ketone 24a (100.0 mg, 0.5 mmol) in dry dichloromethane (3 ml) at room temperature under a nitrogen atmosphere. tert-Butyldimethylsilyl trifluoromethane sulfonate (0.25 ml, 1.1 mmol) was added dropwise over 2 mins at 0 °C, and the solution was stirred at 0 °C for 2.5 hours. Water (5 ml) was added and the mixture was stirred vigorously for 5 mins. The separated aqueous phase was extracted with dichloromethane (3 x 10 ml) and the combined organic
extracts were dried then (MgSO₄) and concentrated in vacuo to leave an oil. Purification by flash column chromatography on silica gel using 50% diethyl ether in pentane as eluent gave the silyl enol ether (198.0 mg, 0.6 mmol, 100%) as a yellow oil; (Found: C, 46.7, H, 5.9, N, 5.5, C₁₀H₁₅O₃NSSi requires: C, 46.7, H, 5.9, N, 5.5%); νmax/cm⁻¹ (CHCl₃ solution): 1724, 1616; δH (360 MHz, CDCl₃) 8.15 (s, 1H, :CH), 5.65 (d, 1H, J 2.0, =CHH), 4.56 (d, 1H, J 2.0, =CHH), 3.99 (s, 3H, CH₃O), 1.02 (s, 9H, SiC(CH₃)₃), 0.21 (s, 6H, Si(CH₃)₂); δC (90 MHz, CDCl₃) 168.4 (C), 161.9 (C), 148.7 (C), 147.4 (C), 127.7 (CH), 93.2 (CH₂), 52.4 (CH₃), 25.6 (CH₃), 18.1 (C), 4.8 (CH₃); m/z (EI) 257.0542 (M⁺), C₁₀H₁₅O₃NSSi requires 257.0542.
2-(2-Bromo-acetyl)-thiazole-4-carboxylic acid methyl ester

**Method A.** N-Bromosuccinimide (106.0 mg, 0.6 mmol) was added in one portion to a stirred solution of the silyl enol ether 26 (198.0 mg, 0.6 mmol) in dry THF (6 ml) at 0°C under a nitrogen atmosphere, and the solution was then stirred at 0°C for 1 hour. Water (5 ml) was added and the organic phase was separated and dried (MgSO₄). The solvent was removed *in vacuo* to leave a yellow solid. Purification by flash column chromatography on silica gel using 50 % diethyl ether in pentane as eluant gave the α-bromoketone (81.0 mg, 54%) as a solid which recrystallised as colourless crystals, m.p. 83-85°C (EtOAc/hexane);

(Found: C, 31.9, H, 2.3, N, 5.2; Calc. for C₇H₆O₃BrNS: C, 31.8, H, 2.3, N, 5.3%); $\nu_{\text{max}}$ cm⁻¹(CHCl₃ solution): 1735, 1710; $\delta_{\text{H}}$ (360 MHz, CDCl₃) 8.52 (s, 1H, =CH), 4.80 (s, 2H, CH₂Br), 3.99 (s, 3H, CH₃O); $\delta_{\text{C}}$ (90 MHz, CDCl₃) 184.5 (C), 163.9 (C), 160.8 (C), 148.4 (C), 135.4 (CH), 52.7 (CH₃), 30.9 (CH₂); m/z (EI) 264.9211 (M⁺), C₇H₆O₃⁸¹BrNS requires 264.9231.

**Method B.** N-Bromosuccinimide (15.5 g, 87.4 mmol) was added to a stirred suspension of methyl 2-(1-hydroxyethyl)thiazole-4-carboxylate 16 (8.18 g, 43.7 mmol) in carbon tetrachloride (250 ml). The flask was fitted
with a reflux condenser which was in turn connected to an HBr trap via a
calcium chloride drying tube. The mixture was heated under reflux for 5
hr. It was then cooled to room temperature and filtered. The filtrate was
washed with water (3x50 ml), was dried and evaporated in vacuo to leave
a solid. Recrystallisation gave the bromoketone (5.90 g, 54%) as
colourless crystals.

\[ E-2,\ E-4-2-(S)-1,6-Dimethyl-hepta-2,4-dieny)-[2,4']bithiazolyl-4-\]
carboxylic acid methyl ester \[ 25 \]

A solution of the diene thioamide \[ 22 \] (1.3 g, 6.8 mmol) in dry THF (30 ml)
at -20 °C was stirred vigorously over powdered potassium bicarbonate
(5.5 g, 55.1 mmol) for 5 minutes under a nitrogen atmosphere. The \[ \alpha \]-
bromoketone \[ 24b \] (2.0 g, 7.5 mmol) was added in one portion, and the
mixture was then stirred at -20 °C for 5 minutes. A solution of
trifluoroacetic anhydride (5.8 g, 27.6 mmol) and pyridine (4.6 g, 58.6
mmol) in dry THF (20 ml), pre-cooled to -20 °C, was added slowly over
20 minutes, and the mixture was then warmed to room temperature for 5
minutes. The mixture was evaporated in vacuo and the residue was then
taken up in chloroform (100 ml) and the solution was stirred vigorously
with water (50 ml) until effervescence had ceased. The separated organic
phase was dried and evaporated in vacuo to leave a brown oil which was
purified by flash column chromatography on silica gel, using 25% ethyl
acetate in pentane as eluent to give the *bis-thiazole methyl ester* (1.41 g, 59%) as a pale yellow solid. Recrystallisation gave prisms, m.p. 90-91°C (ether); \([\alpha]_D^{25} +1.96\) (c 1.5 in CHCl₃); \(\nu_{\text{max}}/\text{cm}^{-1}\) (CHCl₃ solution): 1729, 990; \(\delta_H\) (360 MHz, CDCl₃) 8.18 (s, 1H, =CH), 8.03 (s, 1H, =CH), 6.19 (dd, 1H, J 15.1 and 10.3, HC=CH=CH), 6.02 (dd, 1H, J 15.0 and 10.3, HC=CHCH=CH), 5.79 (dd, 1H, J 15.1 and 7.6, CHCH=CHCH), 5.69 (dd, 1H, J 15.0 and 6.7, :CHCH=CHCH), 3.98 (s, 3H, CH₃O), 3.95-3.91 (m, 1H, CHCH₃), 2.35 (septet, 1H, J 6.8, CH(CH₃)₂), 1.55 (d, 3H, J 7.0, CHCH₃), 1.01 (d, 6H, J 6.8, CH(CH₃)₂); \(\delta_C\) (90 MHz, CDCl₃) 175.5 (C), 163.3 (C), 161.4 (C), 147.4 (C), 146.9 (C), 141.9 (CH), 131.8 (CH), 131.5 (CH), 127.4 (CH), 125.9 (CH), 116.4 (CH), 52.0 (CH₃), 40.7 (CH), 30.6 (CH), 21.7 (CH₃), 20.3 (CH₃); \(m/z\) (EI) 348.0945 (M⁺), \(C_{17}H_{20}O_{2}N_{2}S_{2}\) requires 348.0966.

**E-2, E-4-2’-(S)-1,6-Dimethyl-hepta-2,4-dienyl)-[2,4’]bithiazolyl-4-yl] methanol 27a**

A solution of diisobutylaluminium hydride (1.0 M) in hexanes (23 ml) was added dropwise over 20 minutes to a stirred solution of the methyl ester 25 (2.0 g, 7.7 mmol) in dry THF (60 ml) at -78 °C under a nitrogen atmosphere. The mixture was stirred at -78 °C for 1 hour and then at 0 °C for 1 hour. Methanol (5 ml) was added over 5 minutes and the mixture
was diluted with dichloromethane (60 ml). A saturated solution of aqueous sodium potassium tartrate (60 ml) was added, and the mixture was stirred vigorously for 24 hours. The separated aqueous layer was extracted with dichloromethane (3 x 40 ml) and the combined organic extracts were then washed with brine (2 x 40 ml), dried (MgSO₄) and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel using 50% ethyl acetate in pentane as eluent to give the alcohol (1.3 g, 56%) as a pale yellow solid, m.p. 84-85 °C (EtOAc/hexane); [α]D²³ -1.99 (c 4.53 in CHCl₃); νmax/cm⁻¹ (CHCl₃ solution): 3352, 2961, 2930, 991; δH (360 MHz, CDCl₃) 7.83 (s, 1H, =CH), 7.19 (s, 1H, =CH), 6.19 (dd, 1H, J 15.1 and 10.3, HC=CHCH=CH), 6.03 (dd, 1H, J 15.5 and 10.3, HC=CHCH=CH), 5.80 (dd, 1H, J 15.1 and 7.5, CHCH=CHCH:) 5.69 (dd, 1H, J 15.5 and 6.8, :CHCH=CHCH), 4.81 (s, 2H, CH₂OH), 3.98-3.91 (m, 1H, CHCHCH₃), 2.35 (app. octet, 1H, J 6.7, CH(CH₃)₂), 1.55 (d, 1H, J 7.0, CHCH₃), 1.01 (d, J 6.7, 6H, CH(CH₃)₂); δC (90 MHz, CDCl₃) 175.8 (C), 163.2 (C), 156.6 (C), 147.9 (C), 146.9 (C), 141.9 (CH), 131.9 (CH), 131.3 (CH), 115.3 (CH), 114.9 (CH), 60.1 (CH₂), 40.6 (CH), 30.5 (CH), 21.7 (CH₃), 20.3 (CH₃); m/z (ES) 321.1086 (M⁺+H), C₁₆H₂₁ON₂S₂ requires 321.1095.

The alcohol (13 mg, 0.04 mmol) was added to a stirred solution of 4-dimethylaminopyridine (5.0 mg, 0.04 mmol) and triethylamine (21 mg, 0.21 mmol) in dry dichloromethane (1 ml), and
after 30 seconds at room temperature a solution of $R$-$(+)$-α-methoxy-α-trifluoromethylphenylacetyl chloride (95 mg, 0.38 mmol) in dry dichloromethane (0.5 ml) was added. The mixture was stirred at room temperature for 30 min, and then evaporated \textit{in vacuo}. The residue was filtered through a short pad of silica using 30\% EtOAc in petroleum ether (b.p. 40-60 °C) as eluent to give the corresponding \textit{Mosher’s ester} (33 mg) as a yellow oil; $\delta_H$ (360 MHz. CDCl$_3$) 7.80 (s, =CH), 7.51-7.23 (m, 6H, ArH and =CH), 6.20 (dd, 1H, $J$ 15.2 and 10.2, HC=CHCH=CH), 6.02 (dd, 1H, $J$ 15.2 and 10.2, HC=CHCH=CH), 5.80 (dd, 1H, $J$ 15.2 and 7.6, CHCH=CHCH), 5.69 (dd, 1H, $J$ 15.2 and 6.6, :CHCH=CHCH), 3.94-3.84 (m, 1H, CH$_3$CHCH), 3.56 (s, 2H, CH$_2$O), 3.42 (s, 3H, OCH$_3$), 2.33-2.26 (m, 1H, :CHCH(CH$_3$)$_2$), 1.55 (d, 3H, $J$ 6.9, CHCH$_3$), 1.01 (d, 6H, $J$ 6.6, CH(CH$_3$)$_2$); $\delta_F$ (CFCl$_3$) 4.30 (s).

In a similar manner the alcohol was treated with $S$-$(−)$-α-methoxy-α-trifluoromethylphenylacetyl chloride to give the corresponding \textit{Mosher’s ester}, which showed $\delta_H$ (360 MHz. CDCl$_3$) 7.80 (s, =CH), 7.51-7.23 (m, 6H, ArH and =CH), 6.20 (dd, 1H, $J$ 15.2 and 10.2, HC=CHCH=CH), 6.02 (dd, 1H, $J$ 15.2 and 10.2, HC=CHCH=CH), 5.80 (dd, 1H, $J$ 15.2 and 7.6, CHCH=CHCH), 5.69 (dd, 1H, $J$ 15.2 and 6.6, :CHCH=CHCH), 3.94-3.80 (m, 1H, CH$_3$CHCH), 3.56 (s, 2H, CH$_2$O), 3.42 (s, 3H, OCH$_3$), 2.33-2.20 (m, 1H, :CHCH(CH$_3$)$_2$), 1.55 (d, 3H, $J$ 6.9, CHCH$_3$), 1.01 (d, 6H, $J$ 6.6, CH(CH$_3$)$_2$); $\delta_F$ (CFCl$_3$) 2.89 (s).
**E-2, E-4-2′-(1S,6-Dimethylheptadiene)-(2,4′-bis-thiazole)-4-methyl iodide 27b**

Iodine (658 mg, 2.60 mmol) was added in portions over 20 min to a stirred solution of the *bis*-thiazole methanol 27a (603 mg, 1.88 mmol), triphenylphosphine (740 mg, 2.82 mmol) and imidazole (192 mg, 2.82 mmol) in dry ether (10 ml) and acetonitrile (2 ml) at 0 °C under a nitrogen atmosphere. The mixture was then stirred at room temperature for 15 min. The solvent was evaporated *in vacuo* to leave a yellow solid which was purified by flash column chromatography using 10% EtOAc in petroleum ether (b.p. 40-60 °C) as eluent to give a the *iodide* (627 mg, 78%) as an almost colourless solid, m.p. 83-85 °C (EtOAc/petroleum ether (b.p. 40-60 °C); [α]$_D^{22}$ +0.36 (c 1.10 in CHCl$_3$); $\nu_{\text{max}}$/cm$^{-1}$(CHCl$_3$ solution): 3045, 2974, 1109; $\delta_{\text{H}}$ (360 MHz, CDCl$_3$) 7.87 (s, =CH), 7.25 (s, =CH), 6.19 (ddd, 1H, J 15.0 and 10.2 and 0.9, CH=CHCH=CH), 6.02 (ddd, 1H, J 15.0 and 10.2 and 1.2, CH=CHCH=CH), 5.79 (dd, 1H, J 15.0 and 7.5, CHCH=CHCH:], 5.69 (dd, J 15.0 and 6.7, :CHCH=CHCH), 4.55 (d, 2H, J 0.4, CH$_2$I), 4.00-3.88 (m, 1H, CH$_3$CHCH), 2.33 (app. octet, 1H, J 6.7, :CHCH(CH$_3$)$_2$), 1.54 (d, 3H, J 7.0, CHCH$_3$), 1.01 (d, 6H, J 6.7, CH(CH$_3$)$_2$); $\delta_{\text{C}}$ (90 MHz, CDCl$_3$) 177.5 (C), 164.4 (C), 155.3 (C), 149.7 (C), 143.8 (CH), 133.8 (CH), 127.9 (CH), 118.1 (CH), 117.3 (CH), 42.6
(CH), 42.5 (CH₂), 32.5 (CH), 23.6 (CH₃), 22.2 (CH₃); m/z (EI) 430.0029 (M⁺), C₁₆H₁₉IN₂S₂ requires 430.0034.

**E-2, E-4-2'-(1S,6-Dimethylheptadiene)-(2,4'-bis-thiazole)-4-methyltriphenylphosphonium iodide 27c**

A solution of the iodide 27b (627 mg, 1.46 mmol) and triphenylphosphine (746 mg, 2.91 mmol) in dry benzene (10 ml) was stirred for 120 hr at room temperature under a nitrogen atmosphere. The mixture was then filtered and the solid was washed with hexane (3x2 ml) to give the *phosphonium iodide salt* (790 mg, 80%) as a colourless powder, m.p. 164.5-166 °C; [α]D 22 +0.71 (c 1.76 in CHCl₃); ν max/cm⁻¹(CHCl₃ solution): 2949, 2863, 992; δH (360 MHz, CDCl₃) 8.07 (d, J 3.3, =CH), 7.84-7.63 (m, 15H, ArH), 7.28 (s, =CH), 6.17 (dd, 1H, J 15.1 and 10.2, CH=CHCH=CH), 6.01 (dd, 1H, J 15.3 and 10.2, CH=CHCH=CH), 5.75 (dd, 1H, J 15.1 and 7.6, CHCH=CHCH:), 5.69 (dd, 1H, J 15.3 and 6.9, :CHCH=CHCH), 5.50 (d, 2H, J 13.9, CH₂P), 3.88-3.70 (m, 1H, CH₃CHCH:), 2.33 (app. octet, 1H, J 6.8, CH(CH₃)₂), 1.51 (d, 3H, J 7.0, CHCH₃), 1.01 (d, 6H, J 6.8, CH(CH₃)₂); δC (90 MHz, CDCl₃) 176.6 (C), 162.7 (C), 148.4 (C), 142.8 (C), 142.7 (C), 142.5 (CH), 132.3 (CH), 132.0 (CH), 130.1 (CH), 130.0 (CH), 126.5 (CH), 123.0 (CH), 118.2 (C), 115.3 (CH), 41.3 (CH), 31.1 (CH), 27.7 (CH₂), 22.3 (CH₃), 20.8 (CH₃), which was used without further purification.
5,6-Dihydro-4-methoxy-5\(\alpha\)-methyl-6\(\alpha\)E-(2-phenylethenyl)-2H-pyran-2-one and 5,6 dihydro-4-methoxy-5\(\alpha\)-methyl-6\(\beta\)E-(2-phenylethenyl)-2H-pyran-2-one 31b

Methyl 3-oxopentanoate (17.9 g, 138 mmol) was added over 20 min to a stirred slurry of sodium hydride (6.61 g, 138 mmol) in dry THF (250 ml) at 0°C under a nitrogen atmosphere. The solution was stirred at 0°C for 10 min and then a solution of \(n\)-butyllithium (1.6 M, 138 mmol) in hexanes (86 ml) was added via cannula over 10 min. The solution was stirred at 0°C for 10 min before the addition of cinnamaldehyde (9.11 g, 69 mmol) over 10 min. The resulting orange solution was stirred at 0°C for 30 min and was poured onto ice-water (2000 ml). The strongly alkaline solution was stirred at room temperature overnight, after which time it was extracted with ether (3x100 ml). The aqueous solution was acidified to pH=1 (36% HCl) with simultaneous addition of ice, and the mixture was then extracted with dichloromethane (3x100 ml). The combined organic extracts were washed with brine (2x100 ml), then dried, and the solvent evaporated in vacuo to leave the pyrone 31a (19.5 g) as a pale yellow solid; \(\nu_{\text{max}}/\text{cm}^{-1}\) (CHCl\(_3\) solution): 2930, 2920, 1760, 1730; \(\delta_{H}\) (both diastereoisomers) (360 MHz, CDCl\(_3\)) 7.35 (m, 5H, Ar\(H\)), 6.78 (dd, 1H, \(J = 15.8\) and \(1.7\), CH=CHPh), 6.77 (d, 1H, \(J = 15.8\), CH=CHPh), 6.19 (dd, 1H, \(J = 15.8\) and 7.6, CHCH=CH), 6.07 (dd, 1H, \(J = 15.8\) and 6.3, CHCH=CH),
5.30 (m, 1H, CH(O)CH:), 4.91 (dd, 1H, J 9.7 and 7.9, CH(O)CH:), 3.64 (d, 1H, J 13, CHH), 3.59 (d, 1H, J 10, CHH), 3.49 (d, 1H, J 13, CHH), 3.47 (d, 1H, J 10, CHH), 2.95-2.85 (m, 1H, CHCH₃), 2.60-2.52 (m, 1H, CHCH₃), 1.20 (d, 3H, J 7.3, CH₃), 1.19 (d, 3H, J 6.9, CH₃); δC (90 MHz, CDCl₃) 202.3 (C), 202.1 (C), 167.4 (C), 167.0 (C), 135.2 (C), 136.0 (CH), 135.5 (CH), 128.8 (CH), 126.9 (CH), 126.8 (CH), 123.4 (CH), 121.2 (CH), 81.5 (CH), 79.1 (CH), 47.1 (CH), 46.6 (CH), 46.0 (CH₂), 45.6 (CH₂), 11.1 (CH₃), 9.7 (CH₃), which was used without further purification.

Freshly distilled dimethyl sulphate (21.4 g, 0.17 mol) was added dropwise over 15 min to a vigorously stirred solution of the pyrone 31a (40.2 g, 0.17 mol) over anhydrous potassium carbonate (48.3 g, 0.35 mol) in dry acetone (500 ml) at room temperature under a nitrogen atmosphere. The mixture was heated under gentle reflux for 2 hr, then cooled to room temperature, poured onto water (750 ml) and extracted with ether (2x200 ml). The combined ether extracts were dried and evaporated in vacuo to leave a crude oily residue which was purified by flash column chromatography using 30% EtOAc in petroleum ether (b.p. 40-60°C) as eluent to give the pyranone O-methyl ether as a mixture of diastereoisomers (21.9 g, 65% from cinnamaldehyde). The diastereomers were separated by HPLC on DuPont Zorbax SIL, using 10% acetonitrile in dichloromethane as eluent, to give (i) the syn-diastereoisomer (eluted first) as a pale yellow oil, (Found: C, 73.6, H, 6.7, C₁₅H₁₆O₃ requires C,
73.8, H, 6.6%); \( \lambda_{\text{max}} \) (EtOH) 242 (19950)nm; \( \nu_{\text{max}}/\text{cm}^{-1}(\text{CCl}_4 \text{ solution}) : \)
1725, 1630; \( \delta_{\text{H}} \) (400 MHz, CDCl\(_3\)) 7.44-7.23 (m, 5H, ArH), 6.82 (d, 1H, J 16.0, CH=CHPh), 6.20 (dd, 1H, J 16.0 and 6.0, CHCH=CH), 5.15 (s, 1H, =CH), 5.10 (ddd, 1H, J 6.0, 3.6 and 1.6, CHCH(O)CH:), 3.78 (s, 3H, OCH\(_3\)), 2.51 (dq, 1H, J 7.2 and 3.6, CHCHCH\(_3\)), 1.17 (d, 3H, J 7.2, CHCH\(_3\)); \( \delta_{\text{C}} \) (100.61 MHz, CDCl\(_3\)) 178.3 (C), 166.8 (C), 136.0 (C), 133.2 (CH), 128.7 (CH), 128.2 (CH), 126.7 (CH), 123.4 (CH), 89.3 (CH), 78.8 (CH), 56.3 (CH), 37.4 (CH), 11.5 (CH\(_3\)); \( m/z \) (EI) 244.1097 (M\(^+\)), C\(_{15}\)H\(_{16}\)O\(_3\) requires 244.1099; and (ii), the \textit{anti}-diastereoisomer (eluted second) as a colourless solid, m.p. 112.5-113.5 °C (from 10 % acetonitrile/dichloromethane), (Found: C, 73.5, H, 6.7, C\(_{15}\)H\(_{16}\)O\(_3\) requires C, 73.8, H, 6.6%); \( \lambda_{\text{max}} \) (EtOH) 245 (28200)nm; \( \nu_{\text{max}}/\text{cm}^{-1}(\text{CCl}_4 \text{ solution}) : \)
1695, 1620; \( \delta_{\text{H}} \) (400 MHz, CDCl\(_3\)) 7.40-7.23 (m, 5H, ArH), 6.70 (d, 1H, J 15.9, CH=CHPh), 6.22 (dd, 1H, J 15.9 and 7.0, CHCH=CH), 5.15 (s, 1H, =CH), 4.70 (ddd, 1H, J 7.2, 7.0 and 1.1, CHCH(O)CH:), 3.75 (s, 3H, OCH\(_3\)), 2.64 (dq, 1H, J 7.1, CHCHCH\(_3\)), 1.24 (d, 3H, J 7.1, CHCH\(_3\)); \( \delta_{\text{C}} \) (100.61 MHz, CDCl\(_3\)) 175.3 (C), 166.2 (C), 135.8 (C), 134.5 (C), 128.7 (CH), 128.4 (CH), 126.8 (CH), 125.3 (CH), 89.8 (CH), 82.0 (CH), 56.2 (CH), 37.1 (CH), 13.9 (CH\(_3\)); \( m/z \) (EI) 244.1097 (M\(^+\)), C\(_{15}\)H\(_{16}\)O\(_3\) requires 244.1099.
A vigorously stirred mixture of diastereoisomers of 5,6-dihydro-4-methoxy-5-methyl-6-(2-phenylethenyl)-2H-pyran-2-one 31b (24.14 g, 0.10 mol) and potassium hydroxide (6.10 g, 0.11 mol) in water (250 ml) was heated under reflux for 90 min. The turbid mixture was cooled to 0°C and then was acidified to pH=1 (36% HCl) to produce a gummy precipitate. The precipitate was extracted with ethyl acetate (3 x 150 ml) and the combined organic extracts were then dried and evaporated in vacuo. The residue was taken up in ether (250 ml) and then treated with an ethereal solution of diazomethane at 0°C. The mixture was left to stand overnight and the excess diazomethane was then destroyed by dropwise addition of glacial acetic acid at 0°C. The solvent was evaporated in vacuo to leave an oily residue which was purified by flash column chromatography using 10%-40% EtOAc in petroleum ether (b.p. 40-60°C) as eluent to give the 5SR-hydroxy ester (2.49 g, 9%) as a yellow oil; νmax/cm⁻¹(CHCl₃ solution): 3434, 3025, 1710, 1621; δH (360 MHz, CDCl₃) 7.38-7.19 (m, 5H, ArH), 6.59 (dd, 1H, J 15.9 and 1.0, CH=CHPh), 6.18 (dd, 1H, J 15.9 and 6.5, CHCH=CH), 5.09 (s, =CH), 4.45-4.35 (m, 1H, CHCH(OH)CH), 4.14 (dq, 1H, J 6.9 and 5.6, CH₂CHCH), 3.69 (s, OCH₃), 3.63 (s, 3H, CO₂CH₃), 3.07 (d, J 2.4, OH), 1.16 (d, 3H, J 7.5 CH₃CH); δC
(90 MHz, CDCl₃) 176.7 (C), 168.9 (C), 137.1 (C), 130.7 (CH), 129.9 (CH), 128.5 (CH), 127.4 (CH), 126.5 (CH), 91.7 (CH), 75.6 (CH), 55.6 (CH₃), 51.1 (CH₃), 40.8 (CH), 13.1 (CH₃); m/z (EI) 276.1371 (M⁺), C₁₆H₂₀O₄ requires 276.1362.

The corresponding 5RS-hydroxy ester 33 (5.29 g, 19%) was also separated by chromatography, as a yellow oil, λₘₐₓ/nm (EtOH) 247 (ε 20, 900 dm³.mol⁻¹.cm⁻¹); νₘₐₓ/ cm⁻¹ (liq film) 3442, 3025, 2977, 2946, 1711, 1620, 1148; δₗ (CDCl₃) 7.41-7.20 (m, 5H, ArH), 6.61 (d, 1H, J 15.8, CH=CHPh), 6.23 (dd, 1H, J 15.8 and 7.1, CHC=CHPh), 5.15 (s, 1H, =CH), 4.24 (m, 1H CHCH(OH)CH=), 4.06 (dq, 1H, J ~6.6, CH₃CHCH), 3.70 (s, 3H, OCH₃), 3.68 (s, 3H, CO₂CH₃), 2.85 (br, 1H, OH), 1.10 (d, 3H, J 6.9, CHCH₃); δₗ (CDCl₃) 176.8 (C), 169.1 (C), 136.8 (C), 131.6 (CH), 131.0 (CH), 128.5 (CH), 127.6 (CH), 126.5 (CH), 92.1 (CH), 75.5 (CH), 55.7 (CH₃), 51.1 (CH₃), 41.0 (CH), 14.7 (CH₃); m/z (EI) 276.1371 (M⁺), C₁₆H₂₀O₄ requires 276.1362.

In addition, the major product (9.27 g, 26%) was methyl 3-methoxy-4-methyl-7-phenyl-2E, 4E, 6E-heptatrienoate, λₘₐₓ/nm (EtOH) 318 (ε 24,500 dm³.mol⁻¹.cm⁻¹); νₘₐₓ/ cm⁻¹ (liq film) 3036, 2947, 2839, 1718, 1657, 1619, 1602; δₗ (CDCl₃) 7.52-6.36 (m, 8H, =CH), 5.06 (s, 1H, =CH), 3.69 (s, 3H, OCH₃), 3.66 (s, 3H, CO₂CH₃), 2.09 (s, 3H, CH₃C=); m/z (EI) 258.1231 (M⁺), C₁₆H₁₈O₃ requires 258.1256.
Methyl iodide (7.70 g, 54.3 mmol) was added to a vigorously stirred solution of the alcohol 32 (500 mg, 1.81 mmol) over freshly prepared silver (I) oxide (1.26 g, 5.43 mmol) in dry ether (30 ml) at room temperature. The mixture was stirred in the dark for 60 hr, after which time it was filtered through Kieselguhr. The residue was washed with ether (3x50 ml), and the combined filtrate and washings were then evaporated in vacuo to leave a yellow oil. The oil was purified by flash column chromatography using 10 to 40% EtOAc in petroleum ether (b.p. 40-60°C) as eluent to give the methyl ether (144 mg, 55%) as a colourless oil; \( \nu_{\text{max}}/\text{cm}^{-1} (\text{CHCl}_3 \text{ solution}) \): 1711, 1622; \( \delta_H \) (360 MHz, CDCl\(_3\)) 7.37-7.22 (m, 5H, ArH), 6.47 (d, 1H, J 16.0, CH=CHPh), 6.06 (dd, 1H, J 16.0 and 6.3, CHCH=CH), 4.94 (s, =CH), 4.20 (dq, 1H, J 8.6 and 6.9, CH(CH\(_3\))CH), 3.74 (app. t, 1H, J~6.5, CHCH(OCH\(_3\))CH\(_2\)), 3.66 (s, 3H, COCH\(_3\)), 3.57 (s, 3H, CO\(_2\)CH\(_3\)), 3.31 (s, 3H, OCH\(_3\)), 1.21 (d, 3H, J 6.9, CHCH\(_3\)); \( \delta_C \) (90 MHz, CDCl\(_3\)) 176.6 (C), 167.9 (C), 136.9 (C), 132.8 (CH), 129.0 (CH), 128.6 (CH), 127.7 (CH), 126.6 (CH), 91.3 (CH), 85.0 (CH), 55.8 (CH\(_3\)), 55.6 (CH\(_3\)), 50.9 (CH\(_3\)), 39.9 (CH), 14.5 (CH\(_3\)); m/z (EI) (M\(^+\)) 290.1527, \( \text{C}_{17}\text{H}_{22}\text{O}_4 \) requires 290.1518.
Osmium tetraoxide (10 mg) was added to a stirred solution of the substituted styrene (±)-34 (77 mg, 0.27 mmol) and 4-methylmorpholine-N-oxide (62 mg, 0.53 mmol) in acetone/water (9:1, 5 ml) at room temperature. The solution was stirred for 3 hr at room temperature under a nitrogen atmosphere. Saturated aqueous sodium metabisulphite (1.5 ml) was then added and the resulting red solution was stirred for 10 min at room temperature. The two phases were separated and the aqueous phase was extracted with ethyl acetate (3x2 ml). The combined organic extracts were dried and evaporated in vacuo to leave a pale yellow oil. The oil was purified by flash column chromatography using 30 to 50% EtOAc in petroleum ether (b.p. 40-60°C) as eluent to give the corresponding vicinal diol (51 mg, 59%) as a colourless oil; $\nu_{\text{max}}/\text{cm}^{-1}$

$^{1}$CHCl$_3$ solution): 3356, 2981, 1713; $\delta_{\text{H}}$ (360 MHz, CDCl$_3$) 7.35-7.22 (m, 5H, ArH), 5.09-5.06 (m, 2H, =CH and CH(OH)CH(OH)Ph), 4.29 (d, 1H, $J$ 7.3, CH(CH$_3$)CH(OH)), 3.68 (s, 3H, :COCH$_3$), 3.65 (m, 1H, CH(CH$_3$)CH(OCH$_3$)CH(OH)), 3.64 (s, 3H, CO$_2$CH$_3$), 3.56 (s, 3H, OCH$_3$), 3.54 (s, OH), 3.04 (br s, OH), 1.24 (d, $J$ 6.9, 3H, CHCH$_3$); $\delta_{\text{C}}$ (90 MHz, CDCl$_3$) 202.1 (CH), 177.3 (C), 167. (C), 141.9 (C), 128.2 (CH), 127.2
Sodium periodate (34 mg, 0.16 mmol) was added in one portion to a stirred solution of the vicinal diol (51 mg, 0.16 mmol) in THF/water (1:3, 3 ml) at room temperature. The mixture was stirred for 3 hr at room temperature under a nitrogen atmosphere. Ether (2 ml) was then added and the two phases were separated. The aqueous phase was extracted with ether (3x1 ml) and the combined ether extracts were dried and evaporated in vacuo to leave a pale yellow oil. The oil was purified by flash column chromatography using 10 to 20% EtOAc in petroleum ether (b.p. 40-60°C) as eluent to give the (±)-aldehyde (22 mg, 65%) as a colourless oil; δ<br>\( ^1H \) (360 MHz, CDCl3) 9.52 (d, 1H, \( J = 2.3 \), CH(OCH\(_3\)C\(\text{H}_3\)OH), 4.99 (s, =CH), 4.42 (app. pentuplet, 1H, \( J = 6.9 \), CHCH\(_3\)), 3.61 (s, 3H, :COCH\(_3\)), 3.57 (s, 3H, CO\(_2\)CH\(_3\)), 3.49 (dd, 1H, \( J = 6.9 \) and 2.3, CHCH(OCH\(_3\))CHO), 3.36 (s, 3H, OCH\(_3\)), 1.13 (d, \( J = 6.9 \), 3H, CHCH\(_3\)); δ<br>\( ^13C \) (90 MHz, CDCl3) 202.1 (CH), 174.3 (C), 167.5 (C), 91.8 (CH), 87.3 (CH), 58.6 (CH\(_3\)), 55.6 (CH\(_3\)), 51.0 (CH\(_3\)), 36.5 (CH\(_3\)), 13.8 (CH\(_3\)); m/z (FAB) 217 (MH\(^+\), 8.4% 187 (54.9%).

Treatment of the enantiopure (+)-34 with OsO\(_4\)-NMMO followed by NaIO\(_4\), as described for the (±)-heptadienoate, gave (+)-30 (~55%) as a colourless
oil, \([\alpha]_D^{22} +105\) (c 0.55 in CHCl₃), Lit. see ref. 7a in paper \([\alpha]_D^{20} +104.7\) (c 0.55 in CHCl₃), whose spectroscopic data were identical with those of the \((\pm)\)-material 30.

\((-)(4R,5S)-3-(E-(2R,3S)-3-Hydroxy-2-methyl-5-phenyl-pent-4-enoyl)-4-methyl-5-phenyl-oxazolidin-2-one\) 38a

\(n\)-Bu₂BOTf (90 ml, 90.5 mmol), 1M in CH₂Cl₂) was added dropwise over 30 minutes to a stirred solution of the oxazolidin-2-one 37 (19.2 g, 82.3 mmol) in dichloromethane (165 ml) at 0 °C under an atmosphere of nitrogen. see ref. 20 in paper After 10 minutes triethylamine (10.8 g, 107.2 mmol, 15 ml) was added dropwise over 45 minutes whilst maintaining the temperature below 10 °C. The solution was stirred at 0 °C for 1 hour (for complete enolisation) and then cooled to -78 °C. A solution of E-cinnamaldehyde (11.4 g, 82.5 mmol, 10 ml), in dichloromethane (10 ml) was added dropwise, and the mixture was then stirred at this temperature for 50 minutes. The mixture was warmed to 0 °C and stirred at this temperature for 1.5 hours before being quenched by the addition of a 1:1 mixture of pH 7 phosphate buffer/MeOH (200 ml). A 2:3 mixture of 30% aqueous hydrogen peroxide/MeOH (400 ml) was added over 60 minutes whilst maintaining the internal temperature below 10 °C. The separated aqueous layer was extracted with dichloromethane (4 x 100 ml)
and the combined organic extracts were next washed with a saturated aqueous solution of sodium bicarbonate (3 x 100 ml), brine (2 x 100 ml), then dried (MgSO$_4$) and concentrated in vacuo. The residue was purified by flash column chromatography using 20% ethyl acetate in pentane as eluent to give the alcohol (26.6 g, 90%) as a colourless solid. Recrystallization gave crystals m.p. 91-92 °C (EtOAc/hexane); Lit. see ref. 20 in paper 92-93 °C (from EtOAc/hexane), d.e. > 98% as shown by $^1$H nmr. (Found: C, 72.2, H, 6.3, N, 3.8; Calc. for C$_{22}$H$_{23}$NO$_4$: C, 72.3, H, 6.3, N, 3.9%); $[\alpha]_{D}^{24}$ - 5.3 (c 1.15 in CHCl$_3$); $\nu_{\max}$/cm$^{-1}$ (CHCl$_3$ solution): 3524, 1781, 1690; $\delta$$_H$ (360 MHz, CDCl$_3$) 7.49-7.25 (m, 10H, 10 x Ar $H$); 6.75 (d, 1H, $J$ 15.9, PhCH=CH), 6.27 (dd, 1H, $J$ 15.9 and 5.9, PhCH=CHCH), 5.58 (d, 1H, $J$ 8.0, PhCHCH), 4.80 (app. quintet, 1H, $J$ 6.7, CH$_3$CHN), 4.71-4.65 (m, 1H, CHO), 4.06-3.98 (m, 1H, O=CC$_2$H$_5$), 2.95 (br. d, 1H, $J$ 2.91, CHO), 1.33 (d, 3H, $J$ 6.7, CH$_3$CHN), 0.93 (d, 3H, $J$ 6.6, CH$_3$CHC=O); $\delta$$_C$ (90 MHz, CDCl$_3$) 176.4 (C), 152.7 (s), 136.5 (C), 133.1 (C), 131.4 (CH), 128.8 (CH), 128.7 (CH), 128.6 (CH), 128.5 (CH), 127.7 (CH), 126.5 (CH), 125.6 (CH), 78.9 (CH), 72.8 (CH), 54.8 (CH), 43.0 (CH), 14.4 (CH$_3$), 11.2 (CH$_3$); m/z (ES) 388.1515 (M$^+$+Na), C$_{22}$H$_{23}$NO$_4$Na requires 388.1525.

(-)-(4$R,5S$)-3-(E-(2$R,3S$)-3-Hydroxy-2-methyl-5-phenyl-pent-4-enoyl)-4-methyl-5-phenyl-oxazolidin-2-one 38b
2,6-Di-tert-butylpyridine (0.8 g, 4.2 mmol) was added via syringe over 10 minutes to a stirred solution of the alcohol **38a** (0.5 g, 1.5 mmol) in dry dichloromethane (7 ml) at room temperature. The solution was cooled to 0°C and then methyl trifluoromethanesulfonate (0.8 ml, 7.2 mmol) was added dropwise over 5 minutes. The mixture was stirred at room temperature for 40 hours and then poured into a saturated aqueous solution of sodium bicarbonate (30 ml). The separated aqueous phase was extracted with dichloromethane (3 x 15 ml) and the combined organic extracts were then washed with brine (3 x 20 ml), dried (MgSO₄), and concentrated in vacuo to leave a colourless oil. The oil was purified by flash column chromatography using 15% EtOAc in pentane as eluent to give the **methyl ether** (380 mg, 72%) as a colourless oil; |α|_D^24 -18.9 (c 0.20 in CHCl₃); ν max/cm⁻¹ (CHCl₃ solution): 1767, 1695, 1599; δH (360 MHz, CDCl₃) 7.46-7.21 (m, 10H, ArH), 6.63 (d, 1H, J 15.9, PhCH=CH), 6.26 (dd, 1H, J 15.9 and 5.9, PhCH=CHCH), 5.33 (d, 1H, J 8.0, PhCHCH), 4.69 (app. quint, 1H, J 6.7, CH₂CHN), 4.24 (app. quint, 1H, J 6.8, O=CCHCH₃), 3.89 (app. t, 1H, J 7.6, CHOCH₃), 3.29 (s, 3H, CHOC₃H₃), 1.29 (d, 3H, J 6.8, O=CCHCH₃), 0.89 (d, 3H, J 6.7, (CH₃CHN); δC (90 MHz, CDCl₃) 174.3 (C), 152.9 (C), 136.2 (C), 133.8 (CH), 133.2 (CH), 128.7 (CH), 128.6 (CH), 127.9 (CH), 127.6 (CH), 126.5 (CH), 125.6 (CH), 84.2 (CH), 78.8 (CH), 77.2 (CH), 56.9 (CH₃), 55.1
(CH), 42.9 (CH), 14.4 (CH₃), 13.4 (CH₃); m/z (ES) 402.1683 (M^+Na),
C₂₃H₂₅NO₄Na requires 402.1681.

(+)-E-(2R, 3S)-3-Methoxy-2-methyl-5-phenyl-pent-4-enoic acid

30% Hydrogen peroxide (4 ml, 31.0 mmol) was added dropwise over 10
minutes, followed by a solution of LiOH (0.6 g, 14.3 mmol) in water (15
ml), to a stirred solution of the imide 38b (3.3 g, 8.5 mmol) in THF/water
4:1 (40 ml) at 0 °C. The mixture was stirred at 0 °C for 4 hours and then
a solution of sodium sulfite (4.3 g, 34.4 mmol) in water (23 ml) was
added. The mixture was allowed to warm to room temperature where it
was stirred for 12 hours. The THF was removed in vacuo and the aqueous
residue was washed with dichloromethane (4 x 80 ml). The aqueous
residue was next cooled to 0 °C and acidified to pH 3 with 1M
hydrochloric acid, and then extracted with ethyl acetate (5 x 80 ml). The
combined organic extracts were evaporated to leave the acid (1.5 g, 80%)
as a colourless oil which was not purified further. [α]D²⁴  +2.4  (c 1.13 in
CHCl₃); νmax/cm⁻¹ (CHCl₃ solution): 3510, 3197, 1753, 1706; δH   (360
MHz, CDCl₃)    7.45-7.25 (m, 5H, ArH); 6.65 (d, 1H, J 15.9, PhCH=CH),
6.05 (dd, 1H, J 15.9 and 5.9, PhCH=CHCH), 4.05 (dd, 1H, J 8.1 and 5.9,
CHOCH₃), 3.51 (s, 3H, CHOCH₃), 2.81-2.75 (m, 1H, O=CCHCH₃), 1.22
(d, 3H, J 6.7, CHCH3); δC (90 MHz, CDCl3) 178.3 (C), 135.9 (C), 134.8 (CH), 128.6 (CH), 128.1 (CH), 126.7 (CH), 125.8 (CH), 83.1 (CH), 56.8 (CH3), 44.6 (CH), 11.9 (CH3); m/z (ES) 243.0994 (M+Na), C13H16O3Na requires 243.0997.

(+)-E-(4R,5S)-5-Methoxy-4-methyl-3-oxo-7-phenyl-hept-6-enoic-acid methyl ester  40

*N,N*-Carbonyldiimidazole (1.6 g, 10.0 mmol) was added in one portion to a stirred solution of the carboxylic acid 39 (2.1 g, 10.2 mmol) in dry THF (40 ml) at 0 °C. The mixture was stirred at room temperature for 2 hours and then added via cannula to a solution of LiCH2CO2Me [which had been prepared from MeOAc (2.3 g, 30.5 mmol) and LDA (3.4 g, 33.2 mmol) in anhydrous THF (13 ml) at -78 °C]. The mixture was stirred at -78 °C for 2 hours and then at 0 °C for 1 hour. The mixture was quenched with aqueous 1M hydrochloric acid (30 ml), and then acidified to pH 3 with aqueous 1M hydrochloric acid. The mixture was extracted with EtOAc (3 x 50 ml) and the combined organic extracts were then dried (MgSO4) and concentrated in vacuo. The residue was purified by flash column chromatography using 10% ethyl acetate in pentane as eluent to give the β-keto ester (1.8 g, 85%) as a colourless oil. \([\alpha]_D^{21} +10.2 \text{ (c 1.11 in CHCl}_3\); \(\nu_{\max}/\text{cm}^{-1}(\text{CHCl}_3 \text{ solution}): 1745, 1713, 1656, 1601\); \(\delta_H \text{ (360})
MHz, CDCl$_3$) 7.42-7.25 (m, 5H, ArH), 7.59 (d, 1H, $J$ 15.9, PhCH=CH), 6.05 (dd, 1H, $J$ 15.9 and 5.8, PhCH=CHCH), 3.98 (dd, 1H, $J$ 8.1 and 5.8, CHOCH$_3$), 3.73 (s, 3H, CO$_2$CH$_3$), 3.60 (s, 2H, CH$_2$), 3.29 (s, 3H, CHOCH$_3$), 3.05-2.90 (m, 1H, CHCH$_3$), 1.19 (d, 3H, $J$ 6.7, CHCH$_3$); $\delta$C (90 MHz, CDCl$_3$) 204 (C), 167.4 (C), 136.0 (C), 134.3 (CH), 128.6 (CH), 127.9 (CH), 126.6 (CH), 126.1 (CH), 89.5 (CH$_3$), 56.6 (CH$_3$), 52.2 (CH$_3$), 51.1 (CH), 49.5 (CH$_2$), 12.0 (CH); m/z (ES) 299.1260 (M$^+$+ Na), $C_{16}H_{19}O_4Na$ requires 299.1259.

(+)\textit{-E-2, E-6-(4R,5S)-3,5-Dimethoxy-4-methyl-7-phenyl-hepta-2,6-dienoic acid methylester} 34

A solution of the $\beta$-ketoester 40 (174.0 g, 6.3 mmol) in DMPU (6 ml) was added to a suspension of sodium hydride (60% dispersion in mineral oil, 169.0 mg, 7.1 mmol) in DMPU (7 ml) at 0 °C, and the mixture was then stirred until gas evolution ceased. Dimethyl sulfate (1.6 g, 13.0 mmol, 1.2 ml) was added over 10 minutes, and the mixture was stirred at room temperature for 24 hours. The mixture was diluted with diethyl ether (10 ml), and then quenched with dimethylamine (2 N in H$_2$O, 5 ml) and H$_2$O (5 ml). The separated aqueous layer was extracted with diethyl ether (2 x 10 ml) and the combined organic extracts were then dried (MgSO$_4$) and
concentrated in vacuo to leave the methyl enol ether as a 10:1 mixture of E and Z isomers (by $^1$H NMR). Purification by column chromatography on silica gel using 4%-7%-10% diethyl ether in pentane as eluent gave the $E$-$\beta$-methoxy acrylate isomer (700 mg, 66%) as a colourless oil, $[\alpha]_D^{24} +130$ (c 1.0 in CHCl$_3$), whose spectroscopic data were identical to those described for (±)-34.

(±)-Methyl (3, 5SR)-dimethoxy-7-|2'-(1S, 6-dimethyl-2E, E-4-heptadiene)-(2,4'-bis-thiazole)|-(4RS)-methyl-2-|6-E-heptadienoate; (±)-Myxothiazol Z (1b)

Sodium methoxide (3.6 mg, 0.07 mmol) was added to a stirred mixture of the (±)-aldehyde 30 (15.7 mg, 0.07 mmol) and the phosphonium iodide 27c (51.7 mg, 0.08 mmol) in dry THF (3 ml) at 0°C under an argon atmosphere. The solution was stirred at 0°C for 1 hr. The solvent was then evaporated in vacuo to leave a brown oil which was purified first by flash chromatography using 12% EtOAc in petroleum ether (b.p. 40-60 °C) as eluent and then by HPLC (Whatman 76 x 5.6 mm ODS, 17% H$_2$O in MeOH) to give the (±)-myxothiazol Z (3.7 mg, 11%) as a yellow oil; $[\alpha]_D^{19} +0.41$ (c. 0.98 in CHCl$_3$); $\nu_{\text{max}}$/cm$^{-1}$(CHCl$_3$ solution): 3034, 2974, 1716, 1599; $\delta_H$ (360 MHz, CDCl$_3$) 7.86 (s, =CH), 7.09 (s, =CH), 6.57 (d, 1H, $J$ 15.6, CHCH=CH), 6.41 (d, 1H, $J$ 15.4 and 7.6, CHCH=CH), 6.16 (dd, 1H, $J$ 15.4 and 10.2, CH=CHCH=CH), 6.03 (dd, 1H, $J$ 15.4 and 10.2,
CHCH=CHCH:), 5.80 (dd, 1H, J 15.4 and 7.4, CHCH=CHCH=), 5.69 (dd, 1H, J 15.4 and 6.9, =CHCH=CHCH), 4.96 (s, =CH), 4.17 (app. pentuplet, 1H, J ~7.0, CH3CHCH(OCH3)), 3.95 (app. pentuplet, J ~7.0, 1H, CH3CHCH:), 3.81 (br t, J ~7.5, 1H, CHCH(OCH3)CH:), 3.67 (s, 3H, =COCH3), 3.60 (s, 3H, CO2CH3), 3.33 (s, 3H, OCH3), 2.40-2.30 (m, 1H, CH(CH3)2), 1.55 (d, 3H, J 7.0, CH2CHCH=), 1.22 (d, 1H, J 7.0, CH3CHCH(OCH3)), 1.01 (d, 6H, J 7.0, CH(CH3)2); δC (90 MHz, CDCl3) 176.8 (C), 176.3 (C), 167.8 (C), 162.7 (C), 154.5 (C), 149.1 (C), 142.5 (CH), 132.6 (CH), 131.9 (CH), 131.7 (CH), 126.6 (CH), 125.7 (CH), 115.6 (CH), 115.1 (CH), 91.2 (CH), 84.5 (CH), 57.1 (CH3), 55.6 (CH3), 50.9 (CH3), 41.3 (CH), 39.9 (CH), 31.2 (CH), 22.3 (CH3), 20.9 (CH3), 14.2 (CH3); m/z (EI) 359.1238 (M+-C7H11O3), C19H23N2OS2 requires 359.1252.

(+)-Myxothiazol Z (1b) (with W.B. Goldring)

A solution of lithium hexamethyldisilylamide (1.0M) in THF (0.2 ml) was added to a stirred solution of the phosphonium salt 27c (75 mg) in THF (3 ml) at 0°C for further 15 mins. A solution of the (+)-aldehyde 30 (40 mg) in THF (2 ml) was added dropwise over 5 mins to the stirred solution at 0°C, and then the mixture was stirred and allowed to warm to room temperature over 20 mins. Water was added and the mixture was extracted with ethyl acetate. The solvent was evaporated in vacuo and the
residue was purified by flash column chromatography using 12% EtOAc in petroleum ether (40-60 °C) as eluent to give (+)-myxothiazol Z (40 mg, 74%) as a colourless oil. Further purification by HPLC (10 x 25 mm silica dynax) using 20% EtOAc in petroleum ether (40-60 °C) as eluent gave a colourless oil; [α]D +118.8 (c 1.44 in CHCl₃); whose spectroscopic data were identical to those of the (±)-myxothiazol Z; m/z 525.1857 (M+Na), C₂₆H₃₄O₄N₂S₂Na requires 525.1858.

(±)-E-2, E-6-(4RS,5SR)-3,5-Dimethoxy-4-methyl-7-phenyl-hepta-2,6-dienoic acid amide 43

A solution of dimethylaluminium amide (0.67 M, 8.9 mmol) in dichloromethane (13.3 ml) was added dropwise over 10 min to a stirred solution of the ester 34 (490 mg, 1.78 mmol) at room temperature under a nitrogen atmosphere. The mixture was heated under reflux for 18 hr. It was then cooled to 0°C and aqueous hydrochloric acid (1.0 M, 20 ml) was added over 10 min. The two phases were separated and the aqueous phase was extracted with dichloromethane (3x10 ml). The combined organic extracts were dried and evaporated in vacuo to leave a yellow oil. The oil was purified by flash column chromatography using 1 to 6% IPA in CH₂Cl₂ as eluent to give the amide (196 mg, 40%) as a yellow oil; νmax/cm⁻¹(CHCl₃ solution): 3532, 3477, 3416, 3312, 1673, 1652, 1622;
δ_H (360 MHz, CDCl₃) 7.41-7.21 (m, 5H, ArH), 6.48 (d, 1H, J 15.9, CH=CHPh), 6.09 (dd, 1H, J 15.9 and 8.6, CH(OCH₃)CH=CHPh), 5.29 (br. s, 2H, NH₂), 4.94 (s, =CH), 4.16 (dd, 1H, J 8.0 and 6.9, CH₃CHCH), 3.76 (dd, 1H, J 8.0 and 8.6, CHCH(OCH₃)CH:), 3.56 (s, 3H, :COCH₃), 3.31 (s, 3H, OCH₃), 1.16 (d, 3H, J 6.9, CHCH₃); δ_C (90 MHz, CDCl₃) 171.5 (C), 169.3 (C), 136.7 (C), 133.0 (CH), 128.5 (CH), 128.3 (CH), 127.5 (CH), 126.5 (CH), 94.3 (CH), 85.5 (CH), 56.3 (CH₃), 54.9 (CH₃), 39.2 (CH), 14.5 (CH₃); m/z (ES) 298.1418 (M^+ + Na), C₁₆H₂₁O₃N requires 298.1419.

(+)E-2, E-6-(4R,5S)-3,5-Dimethoxy-4-methyl-7-phenyl-hepta-2,6-dienoic acid amide 43

Trimethylaluminium (0.67 M solution in CH₂Cl₂, 20.0 ml, 10.0 mmol) was added slowly over 10 minutes to a stirred suspension of anhydrous ammonium chloride solid (1.1 g, 20 mmol) in dry dichloromethane (30 ml) at room temperature under a nitrogen atmosphere. The mixture was stirred at room temperature for 20 minutes and then a solution of the (+)-methyl ester 34 (566.0 mg, 2.0 mmol) in dry dichloromethane (5 ml) was added dropwise over 4 minutes. The mixture was heated under reflux at 40 °C under a nitrogen atmosphere for 6 hours (monitored by TLC) and then cooled to room temperature. The mixture was carefully quenched with dilute hydrochloric acid and then extracted with
dichloromethane (3 x 20 ml). The combined organic extracts were dried (MgSO₄) and concentrated \textit{in vacuo}. The residue was purified by flash column chromatography on silica gel using 80\% EtOAc in pentane as eluent to give the (+)-amide (450.0 mg, 84\%) as a viscous yellow oil, $[\alpha]_{D}^{21}+80.4$ (c 0.51 in CHCl₃), whose spectroscopic data were identical to those described for (±)-43.
Osmium tetraoxide (catalytic amount) was added to a stirred solution of the substituted styrene 43 (195 mg, 1.42 mmol) in acetone (4.5 ml) and water (0.5 ml) at room temperature. The mixture was stirred for 3 hr at room temperature under a nitrogen atmosphere. Saturated aqueous sodium metabisulphite (2 ml) was then added and the mixture was stirred for a further 20 min at room temperature. The two phases were separated and the aqueous phase was extracted with ethyl acetate (3x2 ml). The combined organic extracts were dried and evaporated in vacuo to leave a yellow oil. The oil was purified by flash chromatography using 10% IPA in CH$_2$Cl$_2$ as eluent to give the corresponding vicinal diol (107 mg, 49%) as a colourless foam; $\nu_{\text{max}}$/cm$^{-1}$ (CHCl$_3$ solution): 3532, 3414, 3341, 1668; $\delta$$_H$ (360 MHz, CDCl$_3$) 7.32-7.22 (m, 5H, ArH), 5.89 (br s, 2H, NH$_2$), 4.98-4.88 (m, 2H, =$CH$), 4.88-4.80 (m, 1H, CHCH(OH)Ph), 4.32 (d, 1H, J 7.6, OH), 4.30-4.20 (m, 1H, J 6.9, CH$_3$CHCH(OCH$_3$)), 3.90 (d, 1H, J 4.6, OH), 3.61-3.45 (m, 1H, CH(CH$_3$)CH(OCH$_3$)CH and CH(OCH$_3$)CH(OH)CH), 3.56 (s, 3H, :COCH$_3$), 3.40 (s, 3H, OCH$_3$), 1.15 (d, 3H, J 7.3, CHCH$_3$); $\delta$$_C$ (90 MHz, CDCl$_3$) 174.8 (C), 169.7 (C), 142.1 (C), 128.1 (CH), 127.1 (CH), 126.2 (CH), 92.0 (CH), 85.5 (CH), 75.7 (CH), 72.5 (CH), 60.4 (CH$_3$), 55.3 (CH$_3$), 36.2 (CH$_3$), 13.5 (CH$_3$); m/z (FAB) 310 (MH$^+$, 11.6%).
Sodium periodate (73 mg, 0.34 mmol) was added in one portion to a stirred solution of the above diol (105 mg, 0.34 mmol) in water/THF (3:1, 3 ml) at room temperature. The mixture was stirred at room temperature for 90 min under a nitrogen atmosphere and then partitioned between water (2 ml) and ethyl acetate (2 ml). The two phases were separated and the aqueous phase was extracted with ethyl acetate (3x2 ml). The combined organic extracts were dried and evaporated \textit{in vacuo} to leave a yellow oil. The oil was purified by flash column chromatography using EtOAc as eluent to give the aldehyde (22 mg, 32%) as a colourless oil;

\[ \nu_{\text{max}}/\text{cm}^{-1}(\text{CHCl}_3 \text{ solution}) : 1731, 1664, 1599; \ \delta_{\text{H}} (360 \text{ MHz, CDCl}_3) \]

9.59 (d, 1H, J 2.4, CH(OCH₃)CHO), 5.62 (br s, NH₂), 5.01 (s, =CH), 4.55 (dd, 1H, J 7.1 and 6.8, CH₃CHCH), 3.60 (s, 3H, :COCH₃), 3.56 (dd, 1H, J 6.8 and 2.4, CHCH(OCH₃)CHO), 3.44 (s, 3H, OCH₃), 1.20 (d, 3H, J 7.1, CHCH₃); \ m/z (FAB) 202 (MH⁺, 2.6%).

\((\pm)-4\text{-}(6\text{-Carbamoyl-(3, 5SR)-dimethoxy-(4RS)-methyl-E-1, E-5-hexadienyl})-2\text{-}(1S, 6\text{-dimethyl-2-E, 4-E-heptadienyl-2, 4\text{-bis-thiazole; (}\pm\text{-Myxothiazol A}}) (1a)\)

A solution of lithium bis-(trimethylsilyl)amide (1.0 M, 0.08 mmol) in THF (84 µl) was added dropwise over 10 min to a stirred mixture of the \((\pm)-\)aldehyde 44 (22 mg, 0.11 mmol) and the phosphonium iodide 27c (57
mg, 0.08 mmol) in dry THF (3 ml) at 0°C under a nitrogen atmosphere. The mixture was stirred at 0°C for 10 min and then warmed to room temperature. Saturated aqueous ammonium chloride (2 ml) was added over 5 min and the mixture was then partitioned between ethyl acetate (2 ml) and water (2 ml). The two phases were separated and the aqueous phase was extracted with ethyl acetate (3x2 ml). The combined organic extracts were dried and evaporated in vacuo to leave a brown oil. The oil was purified by flash column chromatography using EtOAc as eluent to leave the (+) myxothiazol A (9.0 mg, 22%) as a yellow oil; \( \nu_{\text{max}}/\text{cm}^{-1} \) (CHCl3 solution): 3532, 3416, 2944, 2867, 1672, 1653, 1620, 1587; \( \delta_{\text{H}} \) (360 MHz, CDCl3) 7.85 (s, =CH), 7.13 (s, =CH), 6.56 (d, 1H, J 15.8, CH=CH), 6.42 (dd, 1H, J 15.8 and 8.4, CHCH=CH), 6.19 (dd, 1H, J 15.2 and 10.8, CH=CHCH=CH), 6.02 (dd, 1H, J 15.2 and 10.8, CH=CHCH=CH), 5.80 (dd, 1H, J 15.4 and 7.4, CHCH=CHCH:), 5.69 (dd, 1H, J 15.4 and 6.8, CHCH=CHCH:), 4.98 (s, =CH), 4.20-4.10 (m, 1H, CH3CHCH), 4.0-3.9 (m, 1H, CH3CHCH:), 3.9-3.8 (m, 1H, CHCH(OCH3)CH:), 3.61 (s, 3H, :COCH3), 3.37 (s, 3H, OCH3), 2.33 (m, 1H, CH(CH3)2), 1.55 (d, 3H, J 7.0, CH3CHCH:), 1.22 (d, 3H, J 6.7, CH3CH), 1.01 (d, 3H, J 6.8, CH(CH3)2); \( \delta_{\text{C}} \) (90 MHz, CDCl3) 176.4 (C), 171.9 (C), 169.7 (C), 162.3 (C), 154.5 (C), 148.9 (C), 142.6 (CH), 132.7 (CH), 132.1 (CH), 131.4 (CH), 126.8 (CH), 126.0 (CH), 116.1 (CH), 115.3 (CH), 94.4 (CH), 85.2 (CH), 56.7 (CH3), 55.0 (CH3), 41.4 (CH), 39.8 (CH), 31.0
(CH), 22.2 (CH₃), 20.9 (CH₃), 14.6 (CH₃); m/z (EI) 487.1906 (M⁺), C₂₅H₃₃N₃O₃S₂ requires 487.1963.

(-)2′-(E-2, E-4-(S)-1,6-Dimethyl-hepta-2,4-dienyl)-[2,4]bithiazolyl-4-carbaldehyde 45a

Pyridinium dichromate (3.4 g, 9.0 mmol) was added in one portion to a stirred solution of the alcohol 27a (1.3 g, 4.1 mmol) in dry dichloromethane (30 ml) at room temperature and the suspension was then stirred at room temperature for 12 hours. The mixture was filtered over a pad of celite and the residue was washed with dichloromethane (40 x 50 ml). The filtrate was concentrated in vacuo to leave a brown oily residue. The oil was purified by flash column chromatography on silica gel, using 20% diethyl ether in pentane as eluent to give the aldehyde (0.6 g, 58%) as a pale yellow solid, m.p.77-78 °C (EtOAc/hexane); (Found: C, 60.3, H, 5.4, C₁₆H₁₈ON₂S₂ requires C, 60.4, H, 5.7%); [α]D²² -2.08 (c, 0.40 in CHCl₃); νmax/cm⁻¹ (CHCl₃ solution): 2962, 1699, 1602; δH (360 MHz, CDCl₃) 10.10 (s, 1H, CHO), 8.18 (s, 1H, =CH), 8.05 (s, 1H, =CH), 6.19 (dd, 1H, J 15.1 and 10.3, HC=CHCH=CH), 6.03 (dd, 1H, J 15.5 and 10.3, HC=CHCH=CH), 5.80 (dd, 1H, J 15.1 and 7.5, CHCH=CHCH=CH), 5.68 (dd, 1H, J 15.5 and 6.8, =CHCH=CHCH), 3.95 (app. pentuplet, 1H, J 6.3, CHCH₃), 2.35-2.25 (m, 1H, CH(CH₃)₂), 1.56 (d, 3H, J 6.8, CHCH₃),
1.01 (d, 6H, J 6.8, CH(CH₃)₂); \( \delta_C \) (90 MHz, CDCl₃) 184.8 (CH), 175.8 (C), 163.2 (C), 156.6 (C), 147.9 (C), 142.6 (CH), 132.3 (CH), 132.1 (CH), 128.3 (CH), 126.5 (CH), 117.7 (CH), 41.3 (CH), 31.1 (CH₃), 22.3 (CH₃), 20.8 (CH); \( m/z \) (ES) 319.0934 (M⁺+H), \( C_{16}H_{19}ON_{2}S_{2} \) requires 319.0939.

\((-)\)-\( E-3\)′-[\( E-2, \ E-4-(S)-1,6\)-Dimethyl-hepta-2,4-dienyl]-[\( 2,4\)′]-bithiazolyl-4-yl]-propenal 45b

(Formylmethylene)triphenylphosphorane (30 mg, 0.1 mmol) was added in one portion to a stirred solution of the aldehyde 45a (28.0 mg, 0.1 mmol) in dry benzene (1 ml) at room temperature under a nitrogen atmosphere, and the mixture was then heated under reflux for 1 hour. The mixture was cooled to room temperature and the solvent was then removed \textit{in vacuo}. The residue was purified by flash column chromatography on silica gel using 40% diethyl ether in pentane as eluent to give the \( \alpha,\beta\)-unsaturated aldehyde (22.0 mg, 72%) as a pale yellow solid, m.p. 75-76 °C (Et₂O/pentane); \([\alpha]_D^{19} +0.89 \) (c 1.12 in CHCl₃); \( \nu_{\max} \)/cm⁻¹ (CHCl₃ solution): 2964, 2869, 1678, 1626; \( \delta_H \) (360 MHz, CDCl₃) 9.75 (d, 1H, J 8.0, CHO), 7.98 (s, 1H, =CH), 7.19 (s, 1H, =CH), 7.47 (d, 1H, J 15.2, OHCCH=CH), 7.07 (dd, 1H, J 15.2 and 8.0, OHCCH=CH), 6.24 (dd, 1H, J 15.0 and 8.1, HC=CHCH=CH), 6.07 (dd, 1H, J 15.1 and 8.1, HC=CHCH=CH), 5.83 (dd, 1H, J 15.1 and 7.9, CHCH=CHCH=CH), 5.77 (dd, 1H, J 15.2 and 7.9, CH=CHCH=CHCH), 3.98-3.94 (m, 1H, CHCH₃).
2.40-2.35 (m, 1H, CH(CH₃)₂), 1.59 (d, 1H, J 6.8, CHCH₃), 1.03 (d, 6H, J 6.8, CH(CH₃)₂); δₑ (90 MHz, CDCl₃) 193.6 (CH), 176.6 (C), 163.9 (C), 152.2 (C), 148.2 (C), 143.6 (CH), 142.5 (CH), 132.3 (CH), 132.0 (CH), 130.5 (CH), 126.4 (CH), 123.5 (CH), 116.6 (CH), 41.2 (CH), 31.1 (CH), 22.2 (CH₃), 20.8 (CH₃); m/z (ES) 345.1093 (M⁺+H), C₁₈H₂₁ON₂S₂ requires 345.1095.

(+)(4R,5S)-3-{E-(2R,3S)-5-{2′-(E-2, E-4-(S)-1,6-Dimethyl-heptadienyl)-[2,4′]bithiazolyl-4-yl]-3-hydroxy-2-methyl-pent-4-enoyl}4-methyl-5-phenyl-oxazolidin-2-one 46

Freshly distilled n-Bu₂BOTf (1.0 M, 0.80 mmol) in CH₂Cl₂ (0.8 ml) was added slowly over 3 minutes to a stirred solution of the oxazolidinone 37 (162.0 mg, 0.7 mmol) in dry dichloromethane (5 ml) at 0 °C under a nitrogen atmosphere, and the solution was then stirred at 0 °C for 15 minutes. Triethylamine (0.2 ml, 1.1 mmol) was added slowly, such that the internal temperature was maintained below 3 °C. The mixture was stirred at 0 °C for 2 hours, then cooled to -78 °C, and a solution of the α,β-unsaturated aldehyde 45b (200.0 mg, 0.6 mmol) in dry dichloromethane (5 ml) was added slowly over 3 minutes. The mixture was stirred at -78 °C for 1 hour and then allowed to warm up to 0 °C over 10 hours, where it was stirred for an additional 6 hours. The mixture was quenched with 2:1 MeOH/aqueous pH 7 phosphate buffer (3 ml), followed by careful addition
of 2:1 MeOH/ 30% hydrogen peroxide (3 ml). The mixture was stirred at
0 °C for 1 hour and then evaporated in vacuo. The residue was diluted
with ethyl acetate (20 ml) and the solution was washed with saturated
aqueous sodium bicarbonate solution (3 x 20 ml). The separated aqueous
layer was re-extracted with ethyl acetate (3 x 20 ml) and the combined
organic extracts were then dried (MgSO₄). Purification by flash column
chromatography on silica gel using 30% ethyl acetate in pentane as eluent
gave the alcohol (310 mg, 93%) as a yellow foam; [α]D ¹⁸ +20 (c 0.75 in
CHCl₃); νmax/cm⁻¹ (CHCl₃ solution): 3691, 2963, 1779, 1684, 1602; δH
7.98 (s, 1H, =CH), 7.43-7.27 (m, 5H, ArH), 7.19 (s, 1H, =CH), 6.75
(d, 1H, J 15.5, HOCHCH=CH), 6.63 (d, 1H, J 15.5 and 5.1,
HOCHCH=CH), 6.23 (dd, 1H, J 15.0 and 8.1, HC=CHCH=CH), 6.07 (dd,
1H, J 15.1 and 8.1, HC=CHCH=CH), 5.84 (dd, 1H, J 15.1 and 7.9,
CHCH=CHCH=CH), 5.73-5.67 (m, 2H, PhCHCH and CH=CHCH=CHCH),
4.83-4.76 (m, 2H, CH₂CHN and CHOCH), 4.02-3.95 (m, 2H, CH₃CHOH and
CH₂CHCH=CH), 3.08 (br s, 1H, CHOCH), 2.36 (m, 1H, CH(CH₃)₂), 1.57 (d,
3H, J 7.1, NCHCH₃), 1.33 (d, 3H, J 6.8, CHCH₃), 1.04 (d, 6H, J 6.8,
CH(CH₃)₂), 0.92 (d, 3H, J 6.8, CHCH₃), δC (90 MHz, CDCl₃) 176.6 (C),
176.2 (C), 162.8 (C), 154.1 (C), 152.6 (C), 148.9 (C), 142.3 (CH), 133.1
(C), 132.5 (CH), 131.8 (CH), 131.7 (CH), 128.8 (CH), 128.7 (CH), 126.5
(CH), 125.6 (CH), 124.2 (CH), 115.9 (CH), 115.7 (CH), 78.9 (CH), 72.0
(CH), 54.8 (CH), 43.2 (CH), 41.2 (CH), 31.0 (CH), 22.2 (CH₃), 20.8 (CH₃),
14.4 (CH₃), 10.9 (CH₃); m/z (EI) 577.2067 (M⁺), C₃₁H₃₅O₄N₃S₂ requires 577.2069.

(+) - E-(2R,3S)-5-[2′-(E-2, E-4-(S)-1,6-Dimethyl-hepta-2,4-dienyl)-[2,4]bithiazolyl-4-yl]-3-hydroxy-2-methyl-pent-4-enoic acid methyl ester 47a

A solution of methylmagnesium bromide (3.0 M) in Et₂O (0.5 ml) was added to methanol (3 ml) at 0 °C, and the suspension was stirred at 0 °C for 5 min. A solution of the substituted oxazolidinone 46 (150.0 mg, 0.3 mmol) in methanol (2 ml) was added, and the mixture was stirred at 0 °C for 3 hours. The mixture was quenched with aqueous saturated ammonium chloride solution (5 ml) and the separated aqueous phase was then extracted with dichloromethane (2 x 15 ml). The combined organic extracts were dried (MgSO₄), and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel, using 30% EtOAc in pentane as eluent to give the β-hydroxy ester (30.0 mg, 27%) as a viscous pale yellow oil, [α]D²¹ +7.14 (c 0.56 in CHCl₃); νmax/cm⁻¹ (CHCl₃ solution): 3604, 2962, 1715, 1602; δH (360 MHz, CDCl₃) 7.98 (s, 1H, =CH), 7.19 (s, 1H, =CH), 6.72 (d, 1H, J 15.5, HOCHCH=CH), 6.61 (dd, 1H, J 5.1 and 15.5, HOCHCH=CH), 6.15 (dd, 1H, J 15.0 and 8.1, CH=CHCH=CH), 6.07 (dd, 1H, J 14.9 and 8.1, CH=CHCH=CH), 5.84 (dd, 1H, J 15.1 and 7.9, CHCH=CHCH=CH), 5.73 (dd, 1H, J 15.1 and 8.3,
CH=CHCH=CHCH), 4.75-4.65 (m, 1H, CHO(OH), 3.95-3.85 (m, 1H, CHCH₃), 3.74 (s, 3H, OCH₃), 2.81-2.76 (m, 2H, O=CCCH₃ and CHO(OH), 2.36-2.30 (m, 1H, CH(CH₃)₂), 1.57 (d, 3H, J 6.8, C₃(CH₃), 1.26 (d, 3H, J 6.9, CH₃CH), 1.03 (d, 6H, J 6.7, (CH₃)₂CH); δc (90 MHz, CDCl₃) 176.3 (C), 175.9 (C), 162.8 (C), 154.1 (C), 148.2 (C), 142.4 (CH), 132.5 (CH), 131.9 (CH), 131.5 (CH), 126.5 (CH), 124.3 (CH), 116.0 (CH), 115.7 (CH), 72.2 (CH₃), 52.0 (CH), 44.5 (CH), 41.2 (CH), 31.1 (CH), 22.2 (CH₃), 20.8 (CH₃), 11.1 (CH₃); m/z (ES) 433.1588 (M⁺+H), C₂₂H₂₉O₃N₂S₂ requires 433.1619.

(±)-E-(2R,3S)-5-[2'-(E-2, E-4-(S)-1,6-Dimethyl-hepta-2,4-dienyl)•[2,4]bithiazolyl-4-yl]-3-methoxy-2-methyl-pent-4-enoic acid methyl ester 47b

Methyl iodide (1.2 ml, 19.9 mmol) was added via syringe in one portion to a solution of the secondary alcohol 47a (26 mg, 0.06 mmol) in DMSO/THF (2:1) (5.1 ml) at room temperature. The mixture was cooled to 0 °C, and then sodium hydroxide (79 mg, 2 mmol, powdered by mortar and pestle) was added in small portions, and the mixture was stirred at 0 °C for 30 minutes. The mixture was diluted with dichloromethane (10 ml) and then acidified to pH 3 using 2M aqueous hydrochloric acid. The separated aqueous phase was extracted with dichloromethane (2 x 10 ml) and the combined organic extracts were washed with brine (15 ml), dried
(MgSO₄), and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel using 10% EtOAc in pentane as eluent to give the methyl ether (11.5 mg, 45%) as a viscous oil; \([\alpha]_D^{22}\) +1.67 (c 0.2 in CHCl₃); \(\nu_{max}/cm^{-1}(\text{CHCl}_3 \text{ solution})\): 2928, 1732, 974; \(\delta_H (360 \text{ MHz, CDCl}_3)\) 8.01 (s, 1H, =CH), 7.13 (s, 1H, =CH), 6.75 (d, 1H, J 15.5, MeOCH=CH), 6.54 (dd, 1H, J 5.1 and 15.5, MeOCHCH=CH), 6.23 (dd, 1H, J 15.0 and 8.3, CH=CHCH=CH), 6.07 (dd, 1H, J 14.9 and 8.3, CH=CHCH=CH), 5.84 (dd, 1H, J 15.1 and 8.5, CHCH=CHCH=CH), 5.73 (dd, 1H, J 15.1 and 8.3, CH=CHCH=CHCH), 4.03 (app. t, 1H, J 6.4, CHOMe), 3.98-3.89 (m, 1H, O=CC=CHCH₃), 3.69 (s, 3H, CO₂CH₃), 3.36 (s, 3H, OCH₃), 2.75 (m, 1H, CHCH₃), 2.37 (m, 1H, CH(CH₃)₂), 1.57 (d, 3H, J 7.0, CH₃CH), 1.26 (d, 3H, J 6.8, CH₃CH), 1.03 (d, 6H, J 6.8, (CH₃)₂CH); \(\delta_C (90 \text{ MHz, CDCl}_3)\) 176.2 (C), 174.6 (C), 162.8 (C), 153.9 (C), 148.9 (C), 142.4 (CH), 132.5 (CH), 131.9 (CH), 130.3 (CH), 126.5 (CH), 126.2 (CH), 115.9 (CH), 115.7 (CH), 82.8 (CH₃), 57.2 (CH₃), 51.7 (CH), 45.0 (CH), 41.2 (CH), 31.1 (CH), 22.2 (CH₃), 20.8 (CH₃), 12.1 (CH₃); \(m/z\) (EI) 447.1740 (M⁺+H), \(C_{23}H_{30}O_3N_2S_2\) requires 446.1741.
References


