Experimental

For general experimental details see ref. 1.

(2*S*)-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-2*R*-methylpropanoate **15a** (10.0 ml, 90.0 mmol) in dry dichloromethane (106 ml) at 0 ^{o}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 ($MgSO_4$) and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel using 5% ethyl acetate in petroleum ether (40-60 ^{o}C) as eluent to give the *silyl ether* (30.4 g, 95%) as a colourless oil; (Found: C, 71.0, H, 7.9; $C_{21}H_{28}O_3Si$ requires: C, 70.8, H, 7.9%); $[\alpha]_D^{22}$ -11.03 (c 1.15 in $CHCl_3$); ν_{max}/cm^{-1} ($CHCl_3$ solution): 1732, 1461; δ_H (360 MHz, $CDCl_3$) 7.71-7.60 (m, 4H, ArH), 7.47-7.33 (m, 6H, ArH), 3.81 (dd, 1H, *J* 5.7 and 9.6, C*H*HO), 3.72 (dd, 1H, *J* 5.7 and 9.6, CH*H*O), 3.69 (s, 3H, OCH_3), 2.79-2.65 (m, 1H, C*H*CH_3), 1.16 (d, 3H, *J* 6.8, CHC*H*$_3$),

1.03 (s, 9H, $SiC(CH_3)_3$); δ_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)]), $C_{17}H_{19}O_3Si$ 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 ^oC 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_2SO_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 $CHCl_3$); ν_{max}/cm^{-1} ($CHCl_3$ solution): 3626, 3508; δ_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 C*H*$_2$O), 2.68-2.55 (br. s, 1H, OH), 2.10-1.95 (m, 1H, CH_3CH), 1.06 (s, 9H, $SiC(CH_3)_3$),

0.83 (d, 3H, *J* 6.8, C*H*$_3$CH); δ_C (90 MHz, $CDCl_3$) 135.6 (CH), 133.1 (C), 129.7 (CH), 127.7 (CH), 68.6 (CH_2), 67.6 (CH_2), 37.2 (CH), 26.8 (CH_3), 19.1 (C), 13.1 (CH_3); *m/z* (EI) 271.1153 ([M^+-57(t-Bu)]), $C_{16}H_{19}O_2Si$ requires 271.1154.

(2*R*)-3-(*tert*-Butyldiphenylsilyloxy) – 2 – methylpropanal 17a

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 ^{o}C under a nitrogen atmosphere, and the mixture was then stirred at -78 ^{o}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 ^{o}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 ^{o}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 ($MgSO_4$) and concentrated *in vacuo* to leave a yellow oil. Purification by column chromatography on silica gel using petrol ether (40-60 ^{o}C)/diethyl ether = 49:1 as eluent gave the *aldehyde* (2.7 g, 60%) as a colourless waxy solid; m.p. 60-61 ^{o}C; (Found: C, 73.4, H, 8.0, $C_{20}H_{26}O_2Si$ requires C, 73.6, H, 8.0%; $[\alpha]_D^{20}$ -15.7 (c 1.0 in $CHCl_3$) ν_{max}/cm^{-1}($CHCl_3$ solution): 2860, 1722, 1589; δ_H (360 MHz, $CDCl_3$) 9.76 (d, 1H, *J* 1.6, CHC*H*O), 7.70-7.60 (m, 4H, Ar*H*); 7.48-7.33 (m, 6H, Ar*H*); 3.91-3.81 (m, 2H, CHCH_2O), 2.63-2.50 (m, 1H, C*H*CH_3), 1.10 (d, 3H, *J* 7.0, CHCH_3), 1.04 (s, 9H, SiC$(CH_3)_3$, δ_C (90 MHz, $CDCl_3$) 204.5

(CH), 135.5 (CH), 133.1 (C), 129.7 (CH), 127.7 (CH), 64.1 (CH_2), 49.0 (CH), 26.7 (CH_3), 19.2 (C), 10.3 (CH_3); *m/z* (ES) 349.1569 (M^++Na), $C_{20}H_{26}O_2SiNa$ requires 349.1599.

2-(*E*-4-Methyl-pent-2-ene-1-sulfonyl)-benzothiazole 18

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[see ref. 10 in paper] (1.3 g, 13.2 mmol), 2-sulfanylbenzo-thiazole (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 *in vacuo* and the residue was purified by flash column chromatography using 10% diethyl ether in pentane as eluent to give the *2-(E-4-methylpent-2-ene-1-sulfyl)-benzothiazole* (3.1 g, 95%) as a golden yellow oil. (Found: C, 62.4, H, 6.0, N, 5.7, $C_{13}H_{15}NO_2S_2$ requires C, 62.6, H, 6.1, N, 5.6%); δ_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, CHC*H*=CH), 5.55-5.45 (m, 1H, CH**=**C*H*CH_2S), 3.87 (d, 2H, *J* 7.4, CH=CHC*H*$_2$S), 2.25-2.20 (m, 1H, C*H*$(CH_3)_2$), 0.90 (d, 6H, *J* 6.8, CH(*CH$_3$*)$_2$); δ_C (90 MHz, $CDCl_3$) 166.5 (C), 153.0 (C), 142.9 (CH), 137.1 (C), 135.1 (CH), 126.8 (CH),

125.8 (CH), 121.3 (CH), 121.1 (CH), 35.9 (CH_2), 30.6 (CH), 21.9 (CH_3); *m/z* (EI) 249.0656 (M^+), $C_{13}H_{15}NS$ requires 249.0646.

A solution of $(NH_4)_6Mo_7O_{24}.4H_2O$ (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 *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 *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; ν_{max}/cm^{-1} ($CHCl_3$ solution) 1602; δ_H (360 MHz, $CDCl_3$) 8.21-7.55 (m, 4H, ArH), 5.60 (dd, 1H, *J* 6.6 and 15.6, CHC*H*=CH), 5.45-5.5 (m, 1H, CH=C*H*CH_2S), 4.13 (d, 2H, *J* 7.1, CH=CHC*H*$_2$S), 2.25-2.15 (m, 1H, C*H*$(CH_3)_2$), 0.75 (d, 6H, *J* 6.8, CH(*CH*$_3$)$_2$); δ_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^+), $C_{13}H_{15}O_2NS_2$ requires 281.0544.

_E_-3, _E_-5-2,7-Dimethyl-octa-3,5-dien-1-ol 20

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 ^{o}C under a nitrogen atmosphere. The mixture was stirred at -78 ^{o}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 ^{o}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 ($MgSO_4$) 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 ^{1}H n.m.r.) as an oil. $[\alpha]_D^{20}$ +38.5 (c 1.1 in $CHCl_3$); ν_{max}/cm^{-1} ($CHCl_3$ solution): 3694; *m/z* (FAB) 335.1835 (M^+- 57(t-butyl), $[C_{26}H_{36}OSi$-57(t-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 ($MgSO_4$) 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 ^{1}H NMR.); $[\alpha]_D^{21}$ -28.5 (c 1.4 in $CHCl_3$); δ_H (360 MHz, $CDCl_3$) (major *E*-isomer) 6.29 (dd, 1H, *J* 15.1 and 8.1, CH=C*H*CH=CH), 6.11 (dd, 1H, *J* 15.0 and 8.1, CH=CHC*H*=CH), 5.57 (dd, 1H, *J* 15.0 and 8.1, CHC*H*=CHCH=CH), 5.46 (dd, 1H, *J* 15.0 and 8.1, CH=CHCH=C*H*CH), 3.52 (dd, 1H, *J* 10.5 and 5.6, C*H*HOH), 3.50 (dd, 1H, *J* 10.5 and 5.6, CH*H*OH), 2.50-2.25 (m, 2H, C*H*CH_3, and C*H*$(CH_3)_2$), 1.50 (br s, 1H, CH_2OH), 1.01 (d, 3H, *J* 6.8, CHC*H*$_3$), 0.98 (d, *J* 6.8, 6H, CH(C*H*$_3)_2$).

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^{o}C under a nitrogen atmosphere. A solution of 3-(1-ethoxyethoxy)-2*R*-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^{o}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 $CHCl_3$); ν_{max}/cm^{-1} (CCl_4 solution): 2961, 2871; δ_H (360 MHz, $CDCl_3$) 6.28 (dd, 1H, *J* 15.4 and 11.1, : (*Z*) CHC*H*: (*E*) CH), 6.05 (dd, 1H, *J* 14.0 and 10.3, HC: (*E*) C*H*CH: (*E*) CH), 5.96 (dd, 1H, *J* 14.0 and 10.3, HC: (*E*) CHC*H* (*E*) CH), 5.64 (dd, 1H, *J* 16.9 and 6.8, : (*Z*) CHCH: (*E*) C*H*CH), 5.57 (dd, 1H, *J* 14.7 and 6.8, CHC*H*: (*E*) CHCH: (*E*)), 5.53 (dd, 1H, *J* 14.7 and 6.8, : (*E*) CHCH: (*E*) C*H*CH), 5.12 (dd, 1H, *J* 10.0, CHC*H*: (*Z*) CHCH: (*E*)), 4.69 (q, 1H, *J* 5.4, $CH_3CH(O)_2$ (*Z*)), 4.68 (q, 1H, *J* 5.3, $CH_3CH(O)_2$ (*E*)), 3.68-3.21 (m, 4H, OCH_2CH_3 and OCH_2CH), 2.95-2.83 (m, 1H, $CH_2CH(CH_3)CH$: (*Z*)), 2.50-2.25 (m, 2H, :$CHCH(CH_3)_2$ and $CH_2CH(CH_3)CH$: (*E*)), 1.29 (d, 3H, *J* $CH_3CH(O)_2$), 1.19 (t, 3H, *J* 7.1, CH_2CH_3), 1.04 (d, 3H, *J* 4.6, $CHCH_3$ (*Z*)), 1.01 (d, 3H, *J* 7.0, $CHCH_3$ (*E*)), 0.99 (d, 3H, *J* 6.8, $CH(CH_3)_2$); $\square_C$ (90 MHz, $CDCl_3$) 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 (CH_2), 60.6 (CH_2), 36. 9 (CH), 31.2 (CH), 30.9 (CH), 22.4 (CH_3), 19.5 (CH_3), 17.0 (CH_3), 15.2 (CH_3); *m/z* (EI) 137.1110 (M^+), $C_{10}H_{17}$ requires 137.2460 and 89.0279, $C_4H_8O_2$ 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 ws purified by flash column chromatography using 10% EtOAc in petroleum ether (b.p. 40-60 ^{o}C) as eluent to give the *diene alcohol* as a 2:1 mixture of *E-3* and *Z-3* isomers (37.6g, 93%); $[\alpha]_D^{22}$ -15.3 (c 2.0 in $CHCl_3$); ν_{max}/cm^{-1} (CCl_4 solution): 3630, 3590, 3015, 2970, 2935, 2880; δ_H (360 MHz, $CDCl_3$) 6.29 (dd, 1H, *J* 15.0 and 10.9, : (*Z*) CHC*H*: (*E*) CH), 6.11 (ddd, 1H, *J* 14.7 and 10.1 and 1.1, HC: (*E*) C*H*CH: (*E*) CH), 5.98 (ddd, 1H, *J* 14.7 and 10.1 and 1.1, HC: (*E*) CHC*H*: (*E*) CH), 5.68 (dd, 1H, *J* 15.8 and 6.9, : (*Z*) CHCH: (*E*) C*H*CH), 5.62 (dd, 1H, *J* 15.1 and 6.7, CHC*H*: (*E*) CHCH: (*E*)), 5.44 (dd, 1H, *J* 15.1 and 7.9, : (*E*) CHCH: (*E*) C*H*CH), 5.06 (dd, 1H, *J* 10.3, CHC*H*: (*Z*) CHCH: (*E*)), 3.55-3.33 (m, 2H, HOCH_2CH), 2.93-2.80 (m, 1H, $CH_2CH(CH_3)CH$ (*Z*)), 2.43-2.26 (m, 2H, :CHC$H(CH_3)_2$ and $CH_2CH(CH_3)CH$: (*E*)), 1.68 (br. S, OH), 1.01 (d, 3H, *J* 6.8, CHCH_3), 1.00 (d, 3H, *J* 6.8, CH(C$H_3)_2$); δ_C (90 MHz, $CDCl_3$) 143.2 (CH), 140.9 (CH), 133.7 (CH), 131.6 (CH), 130.8 (CH), 127.0 (CH), 122.4 (CH), 67.7 (CH_2),

67.3 (CH_2), 39.6 (CH), 35.2 (CH), 31.3 (CH), 31.0 (CH), 22.3 (CH_3), 17.0 (CH_3), 16.4 (CH_3); *m/z* (EI) 154.1340 (M^+), $C_{10}H_{18}O$ 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 ($MgSO_4$) 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; $[\alpha]_D^{21}$ -15.3 (c 1.4 in $CHCl_3$); ν_{max}/cm^{-1} ($CHCl_3$ solution): 3336, 3020, 2960; δ_H (360 MHz, $CDCl_3$) 6.09 (ddd, 1H, *J* 15.0 and 10.0 and 1.0, CH=C*H*CH=CH), 5.98 (ddd, 1H, *J* 14.5 and 10.0 and 1.0, CH=CHC*H*=CH), 5.61 (dd, 1H, *J* 15.0 and 6.7, CHC*H*=CHCH:), 5.45 (dd, 1H, *J* 14.5 and 7.8, :CHCH=C*H*CH), 3.53-3.33 (m, 2H, HOCH_2CH), 2.45-2.25 (m, 2H, CH_2C*H*(CH_3)CH: and CHC*H*(CH_3)$_2$), 2.08 (br. s, OH), 1.01 (d, 3H, *J* 6.8, CHCH_3), 1.00 (d, 6H, *J* 6.8, CH(CH_3)$_2$); δ_C (90 MHz, $CDCl_3$) 140.9 (CH), 133.7 (CH), 131.6

(CH), 126.9 (CH), 67.4 (CH_2), 39.7 (CH), 30.9 (CH), 22.3 (CH_3), 16.4 (CH); *m/z* (CI) 154.1365 (M^+), $C_{10}H_{18}O$ requires 154.1358.

_E_-2-(4-Methylpentenyl)triphenylphosphonium Bromide 23

A solution of triphenylphosphine (268 g, 1.0 mol) and 1-bromo-4-methyl-2*E*-pentene[2] (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 ^oC (from ether) (C, 67.6, H, 6.3, Br, 18.7 requires C, 67.8, H, 6.2, Br, 18.8%); ν_{max}/cm^{-1} ($CHCl_3$ solution): 2920, 2785, 1590; δ_H (360 MHz, $CDCl_3$) 8.09-7.44 (m, 15H, arylCH), 5.86 (dt, 1H, *J* 14.5 and 7.0, CH_2CH=CH), 5.50-5.12 (m, 1H, CH=C*H*CH), 4.62 (dd, 2H, *J* 14.0 and 7.0, PCH_2CH), 2.44-2.10 (m, 1H, $CH(CH_3)_2$), 0.84 (d, *J* 7.0, CH ($CH_3)_2$).

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

p-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 $NaHCO_3$ (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 ^{o}C/mmHg; (Found: C, 56.9, H, 9.9, $C_9H_{18}O_4$ requires C, 56.8, H, 9.6%); $[\alpha]_D^{22}$ -10.9 (c 1.53 in $CHCl_3$); ν_{max}/cm^{-1} ($CHCl_3$ solution): 1743, 1201, 1136; δ_H (360 MHz, $CDCl_3$) 4.76 (q, 1H, *J* 5.3, $CH_3CH(O)_2$), 3.83-3.66 (m, 4H, OCH_2CH_3 and OCH_2CH), 3.76 (s, 3H, OCH_3), 2.80 (sextet, 1H, *J* 6.3, CH_3CHCH_2), 1.36-1.23 (m, 9H, $CH_3CH(O)_2$), CH_2CH_3 and $CHCH_3$); δ_C (90 MHz, $CDCl_3$) 175.0 (C), 174.9 (C), 99.6 (CH), 99.1 (CH), 66.3 (CH_2), 66.1 (CH_2), 60.5 (CH_2), 60.5 (CH_2), 51.4 (CH_3), 51.2 (CH_3), 39.8 (CH), 39.8 (CH), 19.2 (CH_3), 19.2 (CH_3), 14.9 (CH_3), 14.8 (CH_3), 13.6 (CH_3), 13.0 (CH_3); *m/z*(EI) 175.0963 (M^+), $C_9H_{18}O_4$ 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^{o}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 $CHCl_3$); ν_{max}/cm^{-1} ($CHCl_3$ solution): 3420, 2980; δ_H (360 MHz, $CDCl_3$) 4.61 (q, 1H, *J* 5.3, $CH_3CH(O)_2$), 3.62-3.28 (m, 6H, OCH_2CH_3, OCH_2CH and $CHCH_2OH$), 2.85 (br s, OH), 1.85-1.90 (m, 1H, CH_3CHCH_2), 1.24 (d, 3H, *J* 5.3, $CH_3CH(O)_2$), 1.14 (t, 3H, *J* 7.3, OCH_2CH_3), 0.84 (d, 3H, *J* 6.9, CH_3CHCH_2); δ_C (90 MHz, $CDCl_3$) 99.8 (CH), 99.7 (CH), 69.3 (CH_2), 69.3 (CH_2), 66.8 (CH_2), 66.6 (CH_2), 61.0 (CH_2), 60.8 (CH_2), 35.6 (CH), 35.5 (CH), 19.6 (CH_3), 15.1 (CH_3), 13.6 (CH_3), 13.5 (CH_3); (Found: *m/z* (EI) 162.1256 (M^+), $C_8H_{18}O_3$ 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 $CHCl_3$); ν_{max}/cm^{-1} ($CHCl_3$ solution): 2878, 1741; δ_H (360 MHz, $CDCl_3$) 9.65 (d, 1H, *J* 1.3, CHCHO), 4.63 (q, 1H, *J* 5.6, $CH_3CH(O)_2$), 3.75-3.34 (m, 4H, OCH_2CH_3 and OCH_2CH), 2.56 (m, 1H, $CH_2CH(CH_3)CHO$), 1.23 (d, 3H, *J* 5.6, $CH_3CH(O)_2$), 1.13 (t, 3H, *J* 6.9, OCH_2CH_3), 1.06 (dd, 3H, *J* 7.1 and 0.7, CH_3CHCHO); δ_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 ($MgSO_4$) and evaporated *in vacuo* to leave the *E,E-dienal* (1.3 g) as a pale yellow liquid; ν_{max}/cm^{-1} ($CHCl_3$ solution): 2871, 1727, 991; δ_H (360 MHz, $CDCl_3$) 9.49 (d, 1H, *J* 1.7, CHC*H*O), 6.09 (ddd, 1H, *J* 14.9 and 10.2 and 0.7, HC=C*H*CH=CH), 5.95 (ddd, 1H, *J* 15.1 and 10.2 and 1.0, HC=CHC*H*=CH), 5.62 (dd, 2H, *J* 14.9 and 6.6, CHC*H*=CHCH:), 5.44 (dd, 1H, *J* 15.1 and 7.6, :CHCH=C*H*CH), 3.02 (m, 1H, OHCC*H*(CH_3)CH), 2.25 (m, 1H, :CHC*H*(CH_3)$_2$), 1.14 (d, 3H, *J* 6.9, CHC*H*$_3$), 0.94 (d, 6H, *J* 6.6, CH(C*H*$_3$)$_2$); δ_C (90 MHz, $CDCl_3$) 201.4 (CH), 142.5 (CH), 134.0 (CH), 126.6 (CH), 126.5 (CH), 49.9 (CH), 31.1 (CH), 22.2 (CH_3), 13.4 (CH_3), which was used without further purification.

_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 ^{o}C) as eluent to give the *carboxylic acid* (0.9 g, 61%) as a colourless liquid; $[\alpha]_D^{20}$ -18.1 (c 1.4 in $CHCl_3$); ν_{max}/cm^{-1} ($CHCl_3$ solution): 3523, 3185, 2914, 1715; δ_H (360 MHz, $CDCl_3$) 6.06 (dd, 1H, *J* 15.1 and 10.3, HC=C*H*CH=CH), 5.91 (ddd, 1H, *J* 14.6 and 10.3 and 1.0, HC=CHC*H*=CH), 5.59 (dd, 1H, *J* 15.1 and 8.3, CHC*H*=CHCH:), 5.57 (dd, 1H, *J* 14.6 and 7.6, =CHCH=C*H*CH), 3.22-3.12 (m, 1H, C*H*(CH_3)CH), 2.27 (septet, 1H, *J* 6.6, C*H*(CH_3)$_2$), 1.22 (d, 3H, *J* 7.3, CHC*H*$_3$), 0.93 (d, 6H, *J* 6.6, CH(C*H*$_3$)$_2$); δ_C (90 MHz, $CDCl_3$) 186.1 (s), 142.3 (CH), 132.3 (CH), 129.1 (CH), 125.8 (CH), 42.2 (CH), 31.3 (CH), 21.8 (CH_3), 17.2 (CH_3); *m/z* (CI) 168.1151 (M^+), $C_{10}H_{16}O_2$ 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 *in vacuo* to leave the crude acid chloride as an orange liquid: ν_{max}/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 *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 ^oC) as eluent, gave the *amide* (1.5 g, 74%) as a pale yellow solid. Recrystallization gave prisms, m.p 82-83 ^oC (EtOAc/pentane). $[\alpha]_D^{22}$ +25.6 (c 1.00 in $CHCl_3$); ν_{max}/cm^{-1}($CHCl_3$ solution): 3522, 3047, 2931, 2866, 1691; δ_H (360 MHz, $CDCl_3$) 6.09 (dd, 1H, *J* 15.5 and 10.2, CH=C*H*CH=CH), 5.91 (ddd, 1H, *J* 15.5 and 10.2 and 1.3, HC=CHC*H*=CH), 5.76-5.66 (m, 4H, CHC*H*=CHCH= and =CHCH=C*H*CH and NH_2), 3.10-2.90 (m, 1H, C*H*(CH_3)CH=), 2.28 (septet, 1H, *J* 6.6, C*H*(CH_3)$_2$), 1.22 (d, 3H, *J* 6.9, CHCH_3), 0.94 (d, 6H, *J* 6.6, CH(CH_3)$_2$); δ_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 (CH_3), 17.3 (CH_3); *m/z* (CI) 167.1325 (M^+), $C_{10}H_{17}NO$ requires 167.1310.

E-3, *E*-5-(*S*)-2,7-Dimethyl-octa-3,5-dienethioic acid amide 22

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 ^oC) as eluent, to give the *diene thioamide* (96.0 mg, 87%) as a yellow oil; $[\alpha]_D^{19}$ +32.6 (c 1.23 in $CHCl_3$); ν_{max}/cm^{-1} ($CHCl_3$ solution): 3481, 3359, 3190, 2953, 2867, 1595; δ_H (360 MHz, $CDCl_3$) 8.32 (br. s, 1H, N*H*), 7.31 (br. s, 1H, N*H*), 6.16 (dd, 1H, *J* 15.5 and 10.3, HC=C*H*CH=CH), 5.97 (dd, 1H, *J* 15.2 and 10.3, HC=CHC*H*=CH), 5.69 (dd, 2H, *J* 15.5 and 6.7, CHC*H*=CHCH:), 5.65 (dd, 1H, *J* 15.2 and 7.5, :CHCH=C*H*CH), 3.49-3.42 (m, 1H, C*H*(CH_3)CH), 2.34 (septet, 1H, *J* 6.7, C*H*(CH_3)$_2$), 1.41 (d, 3H, *J* 6.9, CHC*H*$_3$), 1.00 (d, 6H, *J* 6.7, CH(C*H*$_3$)$_2$); δ_C (90 MHz, $CDCl_3$) 212.2 (C), 142.1 (CH), 132.1 (CH), 130.2 (CH), 125.7 (CH), 50.6 (CH), 30.4 (CH_3), 21.5 (CH_3), 19.9 (CH_3); *m/z* (EI) 183.1062 (M^+), $C_{10}H_{17}NS$ requires 183.1082.

2-(1-Trimethylsilanyloxy-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 ^{o}C under a nitrogen atmosphere. The mixture was stirred at 0 ^{o}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 ($MgSO_4$). 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 ^{o}C (EtOAc/hexane); ν_{max}/cm^{-1}($CHCl_3$ solution): 3531, 3412, 1704; δ_H (360 MHz, $CDCl_3$) 8.05 (d, 2H, *J* 8.4, Ar*H*), 7.57 (t, 1H, *J* 7.4, Ar*H*), 7.43 (t, 2H, *J* 7.4, Ar*H*), 6.10 (br. s, 1H, N*H*), 5.90 (br. s, 1H, N*H*), 5.45 (q, 1H, *J* 6.8, C*H*CH_3), 1.60 (d, 3H, *J* 6.8, CHC*H*$_3$); δ_C (90 MHz, $CDCl_3$) 173.1 (C), 165.2 (C), 133.6 (CH), 129.7 (CH), 129.3 (C), 128.6 (CH), 70.7

(CH), 17.7 (CH_3); *m/z* (ES) 216.0639 (M^++Na), $C_{10}H_{11}O_3NNa$ requires 216.0637.

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 ($MgSO_4$). 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 ^oC (EtOH); (Lit.[3] m.p. 104 ^oC) (Found: C, 57.4, H, 5.3, N, 6.5, Calc. for $C_{10}H_{11}O_2NS$: C, 57.4, H, 5.3, 6.7%); ν_{max}/cm^{-1} ($CHCl_3$ solution): 3490, 3373, 3178, 1728, 1592; δ_H (360 MHz, $CDCl_3$) 8.40-8.20 (br. s, 1H, N*H*), 8.05 (d, 2H, *J* 8.4, ArH), 7.80-7.65 (br. s, 1H, N*H*), 7.57 (t, 1H, *J* 7.4, Ar*H*), 7.43 (t, 1H, *J* 7.4, Ar*H*), 5.88 (q, 1H, *J* 6.6, C*H*CH_3), 1.82 (d, 3H, *J* 6.6, CHC*H*$_3$); δ_C (90 MHz, $CDCl_3$) 206.0 (C), 165.4 (C), 134.1 (CH), 130.1 (CH), 129.4 (CH), 76.9 (CH), 21.4 (CH_3); *m/z* (ES) 232.0425 (M^++Na), $C_{10}H_{11}O_2NSNa$ 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^{o}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 ^{o}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 ^{o}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, $C_{15}H_{15}O_4NS$ requires C, 59.0, H, 5.0, N, 4.6%); ν_{max}/cm^{-1} ($CHCl_3$ solution): 3119, 2985, 1728; δ_H (360 MHz, $CDCl_3$) 8.08 (s, 1H, :CH), 8.04-7.36 (m, 5H, ArH), 6.37 (q, 1H, *J* 6.6, C*H*CH_3), 4.35 (q, 2H, *J* 7.3, C$H_2$$CH_3$), 1.77 (d, 3H, *J* 6.6, CHCH_3), 1.32 (t, 3H, *J* 7.3, CH_2CH_3); δ_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 (CH_2), 21.3 (CH_3), 14.5 (CH_3); *m/z* (ES) 328.0621 (M^++Na), $C_{15}H_{15}O_4NSNa$ 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 mmo) 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 ($MgSO_4$) 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 ^oC) as eluent to give methyl 2-(1-hydroxyethl)thiazole-4-carboxylate (6.4 g, 70%) as a colourless solid. Recrystallisation gave colourless prisms m.p. 92-93 ^oC (EtOAc/hexane) (Lit.[see ref. 16 in paper] m.p. 92-93 ^oC). (Found: C, 45.0, H, 4.9, N, 7.5, Calc. for $C_7H_9O_3NS$: C, 44.9, H, 4.9, N, 7.5%); ν_{max}/cm^{-1} ($CHCl_3$ solution): 3356, 3125, 2954, 1732; δ_H (360 MHz, $CDCl_3$) 8.07 (s, 1H, =CH), 5.22 (q, 1H, *J* 6.5, C*H*CH_3), 3.94 (br s, OH), 3.90 (s, 3H, OC*H*$_3$), 1.63 (d, 3H, *J* 6.5, CHC*H*$_3$); δ_C (90MHz, $CDCl_3$) 177.2 (C), 161.9 (C), 146.6 (C), 127.6 (CH), 68.3 (CH), 52.5 (CH_3), 24.2 (q); *m/z* (EI) 187.0305 (M^+), $C_7H_9O_3NS$ 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 ^{o}C (EtOAc/hexane); (Found: C, 46.2, H, 3.9, N, 7.3, $C_7H_7O_3NS$ requires C, 46.4, H, 3.8, N, 7.5%); ν_{max}/cm^{-1} ($CHCl_3$ solution): 1733, 1694, 1602; δ_H (360 MHz, $CDCl_3$) 8.45 (s, 1H, :C*H*), 3.99 (s, 1H, CH_3O), 2.75 (s, 3H, CH_3); δ_C (90 MHz, $CDCl_3$) 177.2 (C), 161.9 (C), 146.6 (C), 133.6 (C), 127.6 (CH), 52.8 (CH_3), 26.1 (CH_3); *m/z* (EI) 185.0150 (M^+), $C_7H_7O_3NS$ 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 ^{o}C, and the solution was stirred at 0 ^{o}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 ($MgSO_4$) 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, $C_{10}H_{15}O_3NSSi$ requires: C, 46.7, H, 5.9, N, 5.5%); ν_{max}/cm^{-1} ($CHCl_3$ solution): 1724, 1616; δ_H (360 MHz, $CDCl_3$) 8.15 (s, 1H, :CH), 5.65 (d, 1H, *J* 2.0, =C*H*H), 4.56 (d, 1H, *J* 2.0, =CH*H*), 3.99 (s, 3H, CH_3O), 1.02 (s, 9H, $SiC(CH_3)_3$), 0.21 (s, 6H, $Si(CH_3)_2$); δ_C (90 MHz, $CDCl_3$) 168.4 (C), 161.9 (C), 148.7 (C), 147.4 (C), 127.7 (CH), 93.2 (CH_2), 52.4 (CH_3), 25.6 (CH_3), 18.1 (C), 4.8 (CH_3); *m/z* (EI) 257.0542 (M^+), $C_{10}H_{15}O_3NSSi$ requires 257.0542.

2-(2-Bromo-acetyl)-thiazole-4-carboxylic acid methyl ester 24b[see ref. 16 in paper]

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 ($MgSO_4$). 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 $C_7H_6O_3BrNS$: C, 31.8, H, 2.3, N, 5.3%); ν_{max}/cm^{-1}($CHCl_3$ solution): 1735, 1710; δ_H (360 MHz, $CDCl_3$) 8.52 (s, 1H, =CH), 4.80 (s, 2H, CH_2Br), 3.99 (s, 3H, CH_3O); δ_C (90 MHz, $CDCl_3$) 184.5 (C), 163.9 (C), 160.8 (C), 148.4 (C), 135.4 (CH), 52.7 (CH_3), 30.9 (CH_2); *m/z* (EI) 264.9211 (M^+), $C_7H_6O_3{}^{81}BrNS$ 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 ^{o}C was stirred vigorously over powdered potassium bicarbonate (5.5 g, 55.1 mmol) for 5 minutes under a nitrogen atmosphere. The α-bromoketone **24b** (2.0 g, 7.5 mmol) was added in one portion, and the mixture was then stirred at -20 ^{o}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 ^{o}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 $CHCl_3$); ν_{max}/cm^{-1} ($CHCl_3$ solution): 1729, 990; δ_H (360 MHz, $CDCl_3$) 8.18 (s, 1H, =CH), 8.03 (s, 1H, =CH), 6.19 (dd, 1H, *J* 15.1 and 10.3, HC=C*H*CH=CH), 6.02 (dd, 1H, *J* 15.0 and 10.3, HC=CHC*H*=CH), 5.79 (dd, 1H, *J* 15.1 and 7.6, CHC*H*=CHCH:), 5.69 (dd, 1H, *J* 15.0 and 6.7, :CHCH=C*H*CH), 3.98 (s, 3H, CH_3O), 3.95-3.91 (m, 1H, C*H*CH_3), 2.35 (septet, 1H, *J* 6.8, C*H*$(CH_3)_2$), 1.55 (d, 3H, *J* 7.0, CHC*H*$_3$), 1.01 (d, 6H, *J* 6.8, CH(C*H*$_3)_2$); δ_C (90 MHz, $CDCl_3$) 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 (CH_3), 40.7 (CH), 30.6 (CH), 21.7 (CH_3), 20.3 (CH_3); *m/z* (EI) 348.0945 (M^+), $C_{17}H_{20}O_2N_2S_2$ 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 di*iso*butylaluminium 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 ($MgSO_4$) 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 ^oC (EtOAc/hexane); $[\alpha]_D^{23}$ -1.99 (c 4.53 in $CHCl_3$); ν_{max}/cm^{-1} ($CHCl_3$ solution): 3352, 2961, 2930, 991; δ_H (360 MHz. $CDCl_3$) 7.83 (s, 1H, =CH), 7.19 (s, 1H, =CH), 6.19 (dd, 1H, *J* 15.1 and 10.3, HC=C*H*CH=CH), 6.03 (dd, 1H, *J* 15.5 and 10.3, HC=CHC*H*=CH), 5.80 (dd, 1H, *J* 15.1 and 7.5, CHC*H*=CHCH:), 5.69 (dd, 1H, *J* 15.5 and 6.8, :CHCH=C*H*CH), 4.81 (s, 2H, CH_2OH), 3.98-3.91 (m, 1H, CHC*H*CH_3), 2.35 (app. octet, 1H, *J* 6.7, C*H*$(CH_3)_2$), 1.55 (d, 1H, *J* 7.0, CHCH_3), 1.01 (d, *J* 6.7, 6H, CH(C$H_3)_2$); δ_C (90 MHz, $CDCl_3$) 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 (CH_2), 40.6 (CH), 30.5 (CH), 21.7 (CH_3), 20.3 (CH_3); *m/z* (ES) 321.1086 (M^++H), $C_{16}H_{21}ON_2S_2$ 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 *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 *Mosher's ester* (33 mg) as a yellow oil; δ_H (360 MHz. $CDCl_3$) 7.80 (s, =C*H*), 7.51-7.23 (m, 6H, Ar*H* and =C*H*), 6.20 (dd, 1H, *J* 15.2 and 10.2, HC=C*H*CH=CH), 6.02 (dd, 1H, *J* 15.2 and 10.2, HC=CHC*H*=CH), 5.80 (dd, 1H, *J* 15.2 and 7.6, CHC*H*=CHCH), 5.69 (dd, 1H, *J* 15.2 and 6.6, :CHCH=C*H*CH), 3.94-3.84 (m, 1H, CH_3C*H*CH), 3.56 (s, 2H, CH_2O), 3.42 (s, 3H, OCH_3), 2.33-2.26 (m, 1H, :CHC*H*(CH_3)$_2$), 1.55 (d, 3H, *J* 6.9, CHCH_3), 1.01 (d, 6H, *J* 6.6, CH(CH_3)$_2$); δ_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 *Mosher's ester*, which showed δ_H (360 MHz. $CDCl_3$) 7.80 (s, =C*H*), 7.51-7.23 (m, 6H, Ar*H* and =C*H*), 6.20 (dd, 1H, *J* 15.2 and 10.2, HC=C*H*CH=CH), 6.02 (dd, 1H, *J* 15.2 and 10.2, HC=CHC*H*=CH), 5.80 (dd, 1H, *J* 15.2 and 7.6, CHC*H*=CHCH), 5.69 (dd, 1H, *J* 15.2 and 6.6, :CHCH=C*H*CH), 3.94-3.80 (m, 1H, CH_3C*H*CH), 3.56 (s, 2H, CH_2O), 3.42 (s, 3H, OCH_3), 2.33-2.20 (m, 1H, :CHC*H*(CH_3)$_2$), 1.55 (d, 3H, *J* 6.9, CHCH_3), 1.01 (d, 6H, *J* 6.6, CH(CH_3)$_2$); δ_F ($CFCl_3$) 2.89 (s).

_E_-2, _E_-4-2'-(1_S_,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 ^{o}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 ^{o}C) as eluent to give a the *iodide* (627 mg, 78%) as an almost colourless solid, m.p. 83-85 ^{o}C (EtOAc/petroleum ether (b.p. 40-60 ^{o}C); $[\alpha]_D^{22}$ +0.36 (c 1.10 in $CHCl_3$); ν_{max}/cm^{-1}($CHCl_3$ solution): 3045, 2974, 1109; δ_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=C*H*CH=CH), 6.02 (ddd, 1H, *J* 15.0 and 10.2 and 1.2, CH=CHC*H*=CH), 5.79 (dd, 1H, *J* 15.0 and 7.5, CHC*H*=CHCH:), 5.69 (dd, *J* 15.0 and 6.7, :CHCH=C*H*CH), 4.55 (d, 2H, *J* 0.4, CH_2I), 4.00-3.88 (m, 1H, CH_3C*H*CH), 2.33 (app. octet, 1H, *J* 6.7, :CHC*H*(CH_3)$_2$), 1.54 (d, 3H, *J* 7.0, CHCH_3), 1.01 (d, 6H, *J* 6.7, CH(CH_3)$_2$); δ_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 (CH_2), 32.5 (CH), 23.6 (CH_3), 22.2 (CH_3); *m/z* (EI) 430.0029 (M^+), $C_{16}H_{19}IN_2S_2$ requires 430.0034.

_E_-2, _E_-4-2'-(1_S_,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; $[\alpha]_D^{22}$ +0.71 (c 1.76 in $CHCl_3$); ν_{max}/cm^{-1}($CHCl_3$ solution): 2949, 2863, 992; δ_H (360 MHz, $CDCl_3$) 8.07 (d, *J* 3.3, =CH), 7.84-7.63 (m, 15H, Ar*H*), 7.28 (s, =CH), 6.17 (dd, 1H, *J* 15.1 and 10.2, CH=C*H*CH=CH), 6.01 (dd, 1H, *J* 15.3 and 10.2, CH=CHC*H*=CH), 5.75 (dd, 1H, *J* 15.1 and 7.6, CHC*H*=CHCH:), 5.69 (dd, 1H, *J* 15.3 and 6.9, :CHCH=C*H*CH), 5.50 (d, 2H, *J* 13.9, CH_2P), 3.88-3.70 (m, 1H, CH_3C*H*CH:), 2.33 (app. octet, 1H, *J* 6.8, C*H*(CH_3)$_2$), 1.51 (d, 3H, *J* 7.0, CHCH_3), 1.01 (d, 6H, *J* 6.8, CH(CH_3)$_2$); δ_C (90 MHz, $CDCl_3$) 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 (CH_2), 22.3 (CH_3), 20.8 (CH_3), which was used without further purification.

5,6-Dihydro-4-methoxy-5α-methyl-6α-*E*-(2-phenylethenyl)-2H-pyran-2-one and 5,6 dihydro-4-methoxy-5α-methyl-6β-*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^{o}C under a nitrogen atmosphere. The solution was stirred at 0^{o}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^{o}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^{o}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; ν_{max}/cm^{-1} ($CHCl_3$ solution): 2930, 2920, 1760, 1730; δ_H (both diastereoisomers) (360 MHz, $CDCl_3$) 7.35 (m, 5H, Ar*H*), 6.78 (dd, 1H, *J* 15.8 and 1.7, CH=C*H*Ph), 6.77 (d, 1H, *J* 15.8, CH=C*H*Ph), 6.19 (dd, 1H, *J* 15.8 and 7.6, CHC*H*=CH), 6.07 (dd, 1H, *J* 15.8 and 6.3, CHC*H*=CH),

5.30 (m, 1H, C*H*(O)CH:), 4.91 (dd, 1H, *J* 9.7 and 7.9, C*H*(O)CH:), 3.64 (d, 1H, *J* 13, C*H*H), 3.59 (d, 1H, *J* 10, C*H*H), 3.49 (d, 1H, *J* 13, CH*H*), 3.47 (d, 1H, *J* 10, CH*H*), 2.95-2.85 (m, 1H, C*H*CH_3), 2.60-2.52 (m, 1H, C*H*CH_3), 1.20 (d, 3H, *J* 7.3, CH_3), 1.19 (d, 3H, *J* 6.9, CH_3); δ_C (90 MHz, $CDCl_3$) 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 (CH_2), 45.6 (CH_2), 11.1 (CH_3), 9.7 (CH_3), 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^{o}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, $C_{15}H_{16}O_3$ requires C,

73.8, H, 6.6%); λ_{max} (EtOH) 242 (19950)nm; ν_{max}/cm^{-1}(CCl_4 solution): 1725, 1630; δ_H (400 MHz, $CDCl_3$) 7.44-7.23 (m, 5H, Ar*H*), 6.82 (d, 1H, *J* 16.0, CH=C*H*Ph), 6.20 (dd, 1H, *J* 16.0 and 6.0, CHC*H*=CH), 5.15 (s, 1H, =CH), 5.10 (ddd, 1H, *J* 6.0, 3.6 and 1.6, CHC*H*(O)CH:), 3.78 (s, 3H, OCH_3), 2.51 (dq, 1H, *J* 7.2 and 3.6, CHC*H*CH_3), 1.17 (d, 3H, *J* 7.2, CHCH_3); δ_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 *anti*-diastereoisomer (eluted second) as a colourless solid, m.p. 112.5-113.5 ºC (from 10 % acetonitrile/dichloromethane), (Found: C, 73.5, H, 6.7, $C_{15}H_{16}O_3$ requires C, 73.8, H, 6.6%); λ_{max} (EtOH) 245 (28200)nm; ν_{max}/cm^{-1}(CCl_4 solution): 1695, 1620; δ_H (400 MHz, $CDCl_3$) 7.40-7.23 (m, 5H, Ar*H*), 6.70 (d, 1H, *J* 15.9, CH=C*H*Ph), 6.22 (dd, 1H, *J* 15.9 and 7.0, CHC*H*=CH), 5.15 (s, 1H, =CH), 4.70 (ddd, 1H, *J* 7.2, 7.0 and 1.1, CHC*H*(O)CH:), 3.75 (s, 3H, OCH_3), 2.64 (dq, 1H, *J* 7.1, CHC*H*CH_3), 1.24 (d, 3H, *J* 7.1, CHCH_3); δ_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.

(±) Methyl (5*SR*)-Hydroxy-3-methoxy-(4*RS*)-methyl-7-phenyl-*E*-2, *E*-6-heptadienoate 32

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; ν_{max}/cm^{-1}($CHCl_3$ solution): 3434, 3025, 1710, 1621; δ_H (360 MHz, $CDCl_3$) 7.38-7.19 (m, 5H, Ar*H*), 6.59 (dd, 1H, *J* 15.9 and 1.0, CH=C*H*Ph), 6.18 (dd, 1H, *J* 15.9 and 6.5, CHCH=CH), 5.09 (s, =CH), 4.45-4.35 (m, 1H, CHC*H*(OH)CH), 4.14 (dq, 1H, *J* 6.9 and 5.6, CH_3C*H*CH), 3.69 (s, OCH_3), 3.63 (s, 3H, CO_2CH_3), 3.07 (d, *J* 2.4, O*H*), 1.16 (d, 3H, *J* 7.5 CH_3CH); δ_C

(90 MHz, $CDCl_3$) 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 (CH_3), 51.1 (CH_3), 40.8 (CH), 13.1 (CH_3); *m/z* (EI) 276.1371 (M^+), $C_{16}H_{20}O_4$ requires 276.1362.

The corresponding 5*RS*-hydroxy ester **33** (5.29 g, 19%) was also separated by chromatography, as a yellow oil, λ_{max}/nm (EtOH) 247 (ε 20, 900 $dm^3.mol^{-1}.cm^{-1}$); ν_{max}/ cm^{-1} (liq film) 3442, 3025, 2977, 2946, 1711, 1620, 1148; δ_H ($CDCl_3$) 7.41-7.20 (m, 5H, Ar*H*), 6.61 (d, 1H, *J* 15.8, CH=C*H*Ph), 6.23 (dd, 1H, *J* 15.8 and 7.1, CHC*H*=CHPh), 5.15 (s, 1H, =C*H*), 4.24 (m, 1H CHC*H*(OH)CH=), 4.06 (dq, 1H, J ~6.6, CH_3CHCH), 3.70 (s, 3H, OCH_3), 3.68 (s, 3H, CO_2CH_3), 2.85 (br, 1H, O*H*), 1.10 (d, 3H, *J* 6.9, CHCH_3); δ_C ($CDCl_3$) 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 (CH_3), 51.1 (CH_3), 41.0 (CH), 14.7 (CH_3); *m/z* (EI) 276.1371 (M^+), $C_{16}H_{20}O_4$ requires 276.1362.

In addition, the major product (9.27 g, 26%) was methyl 3-methoxy-4-methyl-7-phenyl-2*E*, 4*E*, 6*E*-heptatrienoate, λ_{max}/nm (EtOH) 318 (ε 24, 500 $dm^3.mol^{-1}.cm^{-1}$); ν_{max}/ cm^{-1} (liq film) 3036, 2947, 2839, 1718, 1657, 1619, 1602; δ_H ($CDCl_3$) 7.52-6.36 (m, 8H, =C*H*), 5.06 (s, 1H, =C*H*), 3.69 (s, 3H, OCH_3), 3.66 (s, 3H, CO_2CH_3), 2.09 (s, 3H, CH_3C=); *m/z* (EI) 258.1231 (M^+), $C_{16}H_{18}O_3$ requires 258.1256.

(±)-*E*-2, *E*-6-(4RS,5SR)-3,5-Dimethoxy-4-methyl-7-phenyl-hepta-2,6-dienoic acid methylester 34

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; ν_{max}/cm^{-1}($CHCl_3$ solution): 1711, 1622; δ_H (360 MHz, $CDCl_3$) 7.37-7.22 (m, 5H, Ar*H*), 6.47 (d, 1H, *J* 16.0, CH=C*H*Ph), 6.06 (dd, 1H, *J* 16.0 and 6.3, CHC*H*=CH), 4.94 (s, =CH), 4.20 (dq, 1H, *J* 8.6 and 6.9, C*H*(CH_3)CH), 3.74 (app. t, 1H, *J* ~6.5, CHC*H*(OCH_3)CH:), 3.66 (s, 3H, COCH_3), 3.57 (s, 3H, CO_2CH_3), 3.31 (s, 3H, OCH_3), 1.21 (d, 3H, *J* 6.9, CHCH_3); δ_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, $C_{17}H_{22}O_4$ requires 290.1518.

(±) Methyl (3, 5*SR*)-Dimethoxy-(4*RS*)-methyl-6-oxo-2-*E*-hexenoate 30

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^{o}C) as eluent to give the corresponding *vicinal diol* (51 mg, 59%) as a colourless oil; ν_{max}/cm^{-1}($CHCl_3$ solution): 3356, 2981, 1713; δ_H (360 MHz, $CDCl_3$) 7.35-7.22 (m, 5H, Ar*H*), 5.09-5.06 (m, 2H, =C*H* and CH(OH)C*H*(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_2CH_3), 3.56 (s, 3H, OCH_3), 3.54 (s, OH), 3.04 (br s, OH), 1.24 (d, *J* 6.9, 3H, $CHCH_3$); δ_C (90 MHz, $CDCl_3$) 202.1 (CH), 177.3 (C), 167. (C), 141.9 (C), 128.2 (CH), 127.2

(CH), 125.9 (CH), 90.6 (CH), 87.2 (CH), 75.1 (CH), 72.2 (CH), 61.8 (CH_3), 55.8 (CH_3), 51.1 (CH_3), 36.9 (CH_3), 14.3 (CH_3); *m/z* (FAB) 325 (MH^+, 10.3%.

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^{o}C) as eluent to give the (±)-*aldehyde* (22 mg, 65%) as a colourless oil; δ_H (360 MHz, $CDCl_3$) 9.52 (d, 1H, *J* 2.3, CH(OCH_3)C*H*O), 4.99 (s, =CH), 4.42 (app. pentuplet, 1H, *J* 6.9, C*H*CH_3), 3.61 (s, 3H, :COC*H*$_3$), 3.57 (s, 3H, CO_2C*H*$_3$), 3.49 (dd, 1H, *J* 6.9 and 2.3, CHC*H*(OCH_3)CHO), 3.36 (s, 3H, OC*H*$_3$), 1.13 (d, *J* 6.9, 3H, CHC*H*$_3$); δ_C (90 MHz, $CDCl_3$) 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 $CHCl_3$), Lit.[see ref. 7a in paper] $[\alpha]_D^{20}$ +104.7 (c 0.55 in $CHCl_3$), whose spectroscopic data were identical with those of the (±)-material **30**.

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

n-Bu_2BOTf (90 ml, 90.5 mmol), 1M in CH_2Cl_2) 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 ^oC (EtOAc/hexane); Lit.[see ref. 20 in paper] 92-93 ^oC (from EtOAc/hexane), d.e. > 98% as shown by ^1H 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 $CHCl_3$); ν_{max}/cm^{-1} ($CHCl_3$ solution): 3524, 1781, 1690; δ_H (360 MHz, $CDCl_3$) 7.49-7.25 (m, 10H, 10 x Ar*H*); 6.75 (d, 1H, *J* 15.9, PhC*H*=CH), 6.27 (dd, 1H, *J* 15.9 and 5.9, PhCH=C*H*CH), 5.58 (d, 1H, *J* 8.0, PhC*H*CH), 4.80 (app. quintet, 1H, *J* 6.7, CH_3C*H*N), 4.71-4.65 (m, 1H, C*H*OH), 4.06-3.98 (m, 1H, O=CC*H*CH_3), 2.95 (br. d, 1H, *J* 2.91, CHO*H*), 1.33 (d, 3H, *J* 6.7, C*H*$_3$CHN), 0.93 (d, 3H, *J* 6.6, C*H*$_3$CHC=O); δ_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), $C_{22}H_{23}NO_4Na$ requires 388.1525.

(-)(4*R*,5*S*)-3-(*E*-(2*R*,3*S*)-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^{o}C and then methyl trifluoromethanesufonate (0.8 ml, 7.2 mmol) was added dropwise over 5 minutes.[4] 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 ($MgSO_4$), 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; $[\alpha]_D^{24}$ -18.9 (c 0.20 in $CHCl_3$); ν_{max}/cm^{-1} ($CHCl_3$ solution): 1767, 1695, 1599; δ_H (360 MHz, $CDCl_3$) 7.46-7.21 (m, 10H, ArH), 6.63 (d, 1H, *J* 15.9, PhC*H*=CH), 6.26 (dd, 1H, *J* 15.9 and 5.9, PhCH=C*H*CH), 5.33 (d, 1H, *J* 8.0, PhC*H*CH), 4.69 (app. quint, 1H, *J* 6.7, CH_3C*H*N), 4.24 (app. quint, 1H, *J* 6.8, O=CC*H*CH_3), 3.89 (app. t, 1H, *J* 7.6, C*H*OCH_3), 3.29 (s, 3H, CHOC*H*$_3$), 1.29 (d, 3H, *J* 6.8, O=CCHC*H*$_3$), 0.89 (d, 3H, *J* 6.7, (C*H*$_3$CHN); δ_C (90 MHz, $CDCl_3$) 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 (CH_3), 55.1

(CH), 42.9 (CH), 14.4 (CH_3), 13.4 (CH_3); *m/z* (ES) 402.1683 (M^++Na), $C_{23}H_{25}NO_4Na$ requires 402.1681.

(+)-*E*-(2*R*, 3*S*)-3-Methoxy-2-methyl-5-phenyl-pent-4-enoic acid 39

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 ^oC. The mixture was stirred at 0 ^oC 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 ^oC 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. $[\alpha]_D^{24}$ +2.4 (c 1.13 in $CHCl_3$); ν_{max}/cm^{-1} ($CHCl_3$ solution): 3510, 3197, 1753, 1706; δ_H (360 MHz, $CDCl_3$) 7.45-7.25 (m, 5H, ArH); 6.65 (d, 1H, *J* 15.9, PhC*H*=CH), 6.05 (dd, 1H, *J* 15.9 and 5.9, PhCH=C*H*CH), 4.05 (dd, 1H, *J* 8.1 and 5.9, C*H*OCH_3), 3.51 (s, 3H, CHOC*H*$_3$), 2.81-2.75 (m, 1H, O=CC*H*CH_3), 1.22

(d, 3H, *J* 6.7, CHC*H*$_3$); δ_C (90 MHz, $CDCl_3$) 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 (CH_3), 44.6 (CH), 11.9 (CH_3); *m/z* (ES) 243.0994 (M^++Na), $C_{13}H_{16}O_3Na$ requires 243.0997.

(+)-*E*-(4*R*,5*S*)-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 $LiCH_2CO_2Me$ [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 ($MgSO_4$) 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 (c 1.11 in $CHCl_3$); ν_{max}/cm^{-1}($CHCl_3$ solution): 1745, 1713, 1656, 1601; δ_H (360

MHz, $CDCl_3$) 7.42-7.25 (m, 5H, ArH), 7.59 (d, 1H, *J* 15.9, PhC*H*=CH), 6.05 (dd, 1H, *J* 15.9 and 5.8, PhCH=C*H*CH), 3.98 (dd, 1H, *J* 8.1 and 5.8, C*H*OCH_3), 3.73 (s, 3H, $CO_2C\mathit{H}_3$), 3.60 (s, 2H, CH_2), 3.29 (s, 3H, $CHOC\mathit{H}_3$), 3.05-2.90 (m, 1H, C*H*CH_3), 1.19 (d, 3H, *J* 6.7, $CHC\mathit{H}_3$); δ_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.

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

A solution of the *β*-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 ^oC, 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_2O, 5 ml) and H_2O (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-β-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, 5*SR*)-dimethoxy-7-[2'-(1*S*, 6-dimethyl-2*E*, *E*-4-heptadiene)-(2,4'-*bis*-thiazole)]-(4*RS*)-methyl-2-*E* 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_2O in MeOH) to give the *(±)-myxothiazol Z* (3.7 mg, 11%) as a yellow oil; $[\alpha]_D$ +0.41 (c. 0.98 in $CHCl_3$); ν_{max}/cm^{-1}($CHCl_3$ solution): 3034, 2974, 1716, 1599; δ_H (360 MHz, $CDCl_3$) 7.86 (s, =CH), 7.09 (s, =CH), 6.57 (d, 1H, *J* 15.6, CHCH=C*H*), 6.41 (d, 1H, *J* 15.6 and 7.6, CHC*H*=CH), 6.16 (dd, 1H, *J* 15.4 and 10.2, CH=C*H*CH=CH), 6.03 (dd, 1H, *J* 15.4 and 10.2,

CHC*H*=CHCH:), 5.80 (dd, 1H, *J* 15.4 and 7.4, CHCH=C*H*CH=), 5.69 (dd, 1H, *J* 15.4 and 6.9, =CHCH=C*H*CH), 4.96 (s, :CH), 4.17 (app. pentuplet, 1H, *J* ~7.0, $CH_3C\mathit{H}CH(OCH_3)$), 3.95 (app. pentuplet, *J* ~7.0, 1H, $CH_3C\mathit{H}CH$:), 3.81 (br t, *J* ~7.5, 1H, CHC*H*(OCH_3)CH:), 3.67 (s, 3H, =COC*H*$_3$), 3.60 (s, 3H, $CO_2C\mathit{H}_3$), 3.33 (s, 3H, OC*H*$_3$), 2.40-2.30 (m, 1H, C*H*$(CH_3)_2$), 1.55 (d, 3H, *J* 7.0, C*H*$_3$CHCH=), 1.22 (d, 1H, *J* 7.0, C*H*$_3$CHCH(OCH_3)), 1.01 (d, 6H, *J* 7.0, CH$(C\mathit{H}_3)_2$); δ_C (90 MHz, $CDCl_3$) 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 (CH_3), 55.6 (CH_3), 50.9 (CH_3), 41.3 (CH), 39.9 (CH), 31.2 (CH), 22.3 (CH_3), 20.9 (CH_3), 14.2 (CH_3); *m/z* (EI) 359.1238 (M^+-$C_7H_{11}O_3$), $C_{19}H_{23}N_2OS_2$ 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^{o}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^{o}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; $[\alpha]_D$ +118.8 (c 1.44 in $CHCl_3$); whose spectroscopic data were identical to those of the (±)-myxothiazol *Z*; *m/z* 525.1857 (M+Na), $C_{26}H_{34}O_4N_2S_2Na$ 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 CH_2Cl_2 as eluent to give the *amide* (196 mg, 40%) as a yellow oil; ν_{max}/cm^{-1}($CHCl_3$ solution): 3532, 3477, 3416, 3312, 1673, 1652, 1622;

δ_H (360 MHz, $CDCl_3$) 7.41-7.21 (m, 5H, Ar*H*), 6.48 (d, 1H, *J* 15.9, CH=C*H*Ph), 6.09 (dd, 1H, *J* 15.9 and 8.6, CH(OCH_3)C*H*=CHPh), 5.29 (br. s, 2H, NH_2), 4.94 (s, =CH), 4.16 (dd, 1H, *J* 8.0 and 6.9, CH_3C*H*CH), 3.76 (dd, 1H, *J* 8.0 and 8.6, CHC*H*(OCH_3)CH:), 3.56 (s, 3H, :COCH_3), 3.31 (s, 3H, OCH_3), 1.16 (d, 3H, *J* 6.9, CHCH_3); δ_C (90 MHz, $CDCl_3$) 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 (CH_3), 54.9 (CH_3), 39.2 (CH), 14.5 (CH_3); *m/z* (ES) 298.1418 (M^+ + Na), $C_{16}H_{21}O_3N$ 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 CH_2Cl_2, 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 ^oC 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 ($MgSO_4$) and concentrated *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 $CHCl_3$), whose spectroscopic data were identical to those described for **(±)-43**.

(±)-(3, 5*SR*)-Dimethoxy-(4*RS*)-methyl-6-oxo-2-*E*-hexenamide 44

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 eorganic extracts were dried and evaporated *in vacuo* to leave a yellow oil. The oil was purified by flash chromatography using 10% IPA in CH_2Cl_2 as eluent to give the corresponding *vicinal diol* (107 mg, 49%) as a colourless foam; ν_{max}/cm^{-1} ($CHCl_3$ solution): 3532, 3414, 3341, 1668; δ_H (360 MHz, $CDCl_3$) 7.32-7.22 (m, 5H, Ar*H*), 5.89 (br s, 2H, NH_2), 4.98-4.88 (m, 2H, =C*H*), 4.88-4.80 (m, 1H, CHC*H*(OH)Ph), 4.32 (d, 1H, *J* 7.6, O*H*), 4.30-4.20 (m, 1H, *J* 6.9, CH_3C*H*CH(OCH_3)), 3.90 (d, 1H, *J* 4.6, O*H*), 3.61-3.45 (m, 1H, CH(CH_3)C*H*(OCH_3)CH and CH(OCH_3)C*H*(OH)CH), 3.56 (s, 3H, :COCH_3), 3.40 (s, 3H, OCH_3), 1.15 (d, 3H, *J* 7.3, CHCH_3); δ_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 *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;

ν_{max}/cm^{-1}($CHCl_3$ solution): 1731, 1664, 1599; δ_H (360 MHz, $CDCl_3$) 9.59 (d, 1H, *J* 2.4, $CH(OCH_3)CHO$), 5.62 (br s, NH_2), 5.01 (s, =CH), 4.55 (dd, 1H, *J* 7.1 and 6.8, CH_3CHCH), 3.60 (s, 3H, :$COCH_3$), 3.56 (dd, 1H, *J* 6.8 and 2.4, $CHCH(OCH_3)CHO$), 3.44 (s, 3H, OCH_3), 1.20 (d, 3H, *J* 7.1, $CHCH_3$); *m/z* (FAB) 202 (MH^+, 2.6%).

(±)-4-(6-Carbamoyl-(3, 5*SR*)-dimethoxy-(4*RS*)-methyl-*E*-1, *E*-5-hexadienyl)-2'-(1*S*, 6-dimethyl-2-*E*, 4-*E*-heptadienyl-2, 4'-*bis*-thiazole; (±)-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 (±)-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; ν_{max}/cm^{-1} ($CHCl_3$ solution): 3532, 3416, 2944, 2867, 1672, 1653, 1620, 1587; δ_H (360 MHz, $CDCl_3$) 7.85 (s, =CH), 7.13 (s, =CH), 6.56 (d, 1H, *J* 15.8, CH=C*H*), 6.42 (dd, 1H, *J* 15.8 and 8.4, CHC*H*=CH), 6.19 (dd, 1H, *J* 15.2 and 10.8, CH=C*H*CH=CH), 6.02 (dd, 1H, *J* 15.2 and 10.8, CH=CHC*H*=CH), 5.80 (dd, 1H, *J* 15.4 and 7.4, CHCH=C*H*CH:), 5.69 (dd, 1H, *J* 15.4 and 6.8, :CHCH=C*H*CH), 4.98 (s, =CH), 4.20-4.10 (m, 1H, CH_3C*H*CH), 4.0-3.9 (m, 1H, CH_3C*H*CH:), 3.9-3.8 (m, 1H, CHC*H*(OCH_3)CH:), 3.61 (s, 3H, :COC*H*$_3$), 3.37 (s, 3H, OC*H*$_3$), 2.33 (m, 1H, C*H*(CH_3)$_2$), 1.55 (d, 3H, *J* 7.0, C*H*$_3$CHCH:), 1.22 (d, 3H, *J* 6.7, C*H*$_3$CH), 1.01 (d, 3H, *J* 6.8, CH(C*H*$_3$)$_2$); δ_C (90 MHz, $CDCl_3$) 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 (CH_3), 55.0 (CH_3), 41.4 (CH), 39.8 (CH), 31.0

(CH), 22.2 (CH_3), 20.9 (CH_3), 14.6 (CH_3); *m/z* (EI) 487.1906 (M^+), $C_{25}H_{33}N_3O_3S_2$ 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 ^oC (EtOAc/hexane); (Found: C, 60.3, H, 5.4, $C_{16}H_{18}ON_2S_2$ requires C, 60.4, H, 5.7%); $[\alpha]_D^{22}$ -2.08 (c, 0.40 in $CHCl_3$); ν_{max}/cm^{-1} ($CHCl_3$ solution): 2962, 1699, 1602; δ_H (360 MHz, $CDCl_3$) 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=C*H*CH=CH), 6.03 (dd, 1H, *J* 15.5 and 10.3, HC=CHC*H*=CH), 5.80 (dd, 1H, *J* 15.1 and 7.5, CHC*H*=CHCH=CH), 5.68 (dd, 1H, *J* 15.5 and 6.8, =CHCH=C*H*CH), 3.95 (app. pentuplet, 1H, *J* 6.3, C*H*CH_3), 2.35-2.25 (m, 1H, C*H*$(CH_3)_2$), 1.56 (d, 3H, *J* 6.8, CHC*H*$_3$),

1.01 (d, 6H, *J* 6.8, CH(CH_3)$_2$); δ_C (90 MHz, $CDCl_3$) 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 (CH_3), 22.3 (CH_3), 20.8 (CH); *m/z* (ES) 319.0934 (M^++H), $C_{16}H_{19}ON_2S_2$ requires 319.0939.

(+)-*E*--3-[2′-(*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 *in vacuo*. The residue was purified by flash column chromatography on silica gel using 40% diethyl ether in pentane as eluent to give the *α,β-unsaturated aldehyde* (22.0 mg, 72%) as a pale yellow solid, m.p. 75-76 °C (Et_2O/pentane); $[\alpha]_D^{19}$ +0.89 (c 1.12 in $CHCl_3$); ν_{max}/cm^{-1} ($CHCl_3$ solution): 2964, 2869, 1678, 1626; δ_H (360 MHz, $CDCl_3$) 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=C*H*), 7.07 (dd, 1H, *J* 15.2 and 8.0, OHCC*H*=CH), 6.24 (dd, 1H, *J* 15.0 and 8.1, HC=C*H*CH=CH), 6.07 (dd, 1H, *J* 15.1 and 8.1, HC=CHC*H*=CH), 5.83 (dd, 1H, *J* 15.1 and 7.9, CHC*H*=CHCH=CH), 5.77 (dd, 1H, *J* 15.2 and 7.9, CH=CHCH=C*H*CH), 3.98-3.94 (m, 1H, C*H*CH_3),

2.40-2.35 (m, 1H, C*H*(CH_3)$_2$), 1.59 (d, 1H, *J* 6.8, CHC*H*$_3$), 1.03 (d, 6H, *J* 6.8, CH(C*H*$_3$)$_2$); δ_C (90 MHz, $CDCl_3$) 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 (CH_3), 20.8 (CH_3); *m/z* (ES) 345.1093 (M^++H), $C_{18}H_{21}ON_2S_2$ requires 345.1095.

(+)(4*R*,5*S*)-3-{*E*-(2*R*,3*S*)-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-enoyl}-4-methyl-5-phenyl-oxazolidin-2-one 46

Freshly distilled *n*-Bu_2BOTf (1.0 M, 0.80 mmol) in CH_2Cl_2 (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 ^oC under a nitrogen atmophere, and the solution was then stirred at 0 ^oC for 15 minutes. Triethylamine (0.2 ml, 1.1 mmol) was added slowly, such that the internal temperature was maintained below 3 ^oC . The mixture was stirred at 0 ^oC for 2 hours, then cooled to -78 ^oC, 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 ^oC for 1 hour and then allowed to warm up to 0 ^oC 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 ^{o}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 ($MgSO_4$). 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; $[\alpha]_D^{18}$ +20 (c 0.75 in $CHCl_3$); ν_{max}/cm^{-1} ($CHCl_3$ solution): 3691, 2963, 1779, 1684, 1602; δ_H 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=C*H*), 6.63 (d, 1H, *J* 15.5 and 5.1, HOCHC*H*=CH), 6.23 (dd, 1H, *J* 15.0 and 8.1, HC=C*H*CH=CH), 6.07 (dd, 1H, *J* 15.1 and 8.1, HC=CHC*H*=CH), 5.84 (dd, 1H, *J* 15.1 and 7.9, CHC*H*=CHCH=CH), 5.73-5.67 (m, 2H, PhC*H*CH and CH=CHCH=C*H*CH), 4.83-4.76 (m, 2H, CH_3C*H*N and C*H*OH), 4.02-3.95 (m, 2H, CH_3C*H*OH and CH_3C*H*CH=CH), 3.08 (br s, 1H, CHO*H*), 2.36 (m, 1H, C*H*(CH_3)$_2$), 1.57 (d, 3H, *J* 7.1, NCHC*H*$_3$), 1.33 (d, 3H, *J* 6.8, CHC*H*$_3$), 1.04 (d, 6H, *J* 6.8, CH(C*H*$_3$)$_2$), 0.92 (d, 3H, *J* 6.8, CHC*H*$_3$), δ_C (90 MHz, $CDCl_3$) 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 (CH_3), 20.8 (CH_3),

14.4 (CH_3), 10.9 (CH_3); *m/z* (EI) 577.2067 (M^+), $C_{31}H_{35}O_4N_3S_2$ requires 577.2069.

(+)-*E*-(2*R*,3*S*)-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 Et_2O (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 ($MgSO_4$), 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, $[\alpha]_D^{21}$ +7.14 (c 0.56 in $CHCl_3$); ν_{max}/cm^{-1} ($CHCl_3$ solution): 3604, 2962, 1715, 1602; δ_H (360 MHz, $CDCl_3$) 7.98 (s, 1H, =CH), 7.19 (s, 1H, =CH), 6.72 (d, 1H, *J* 15.5, HOCHCH=C*H*), 6.61 (dd, 1H, *J* 5.1 and 15.5, HOCHC*H*=CH), 6.15 (dd, 1H, *J* 15.0 and 8.1, CH=C*H*CH=CH), 6.07 (dd, 1H, *J* 14.9 and 8.1, CH=CHC*H*=CH), 5.84 (dd, 1H, *J* 15.1 and 7.9, CHC*H*=CHCH=CH), 5.73 (dd, 1H, *J* 15.1 and 8.3,

CH=CHCH=C*H*CH), 4.75-4.65 (m, 1H, C*H*OH), 3.95-3.85 (m, 1H, C*H*CH_3), 3.74 (s, 3H, OCH_3), 2.81-2.76 (m, 2H, O=CC*H*CH_3 and CHO*H*), 2.36-2.30 (m, 1H, C*H*$(CH_3)_2$), 1.57 (d, 3H, *J* 6.8, C*H*$_3$CH), 1.26 (d, 3H, *J* 6.9, C*H*$_3$CH), 1.03 (d, 6H, *J* 6.7, $(CH_3)_2$CH); δ_C (90 MHz, $CDCl_3$) 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 (CH_3), 52.0 (CH), 44.5 (CH), 41.2 (CH), 31.1 (CH), 22.2 (CH_3), 20.8 (CH_3), 11.1 (CH_3); *m/z* (ES) 433.1588 (M^++H), $C_{22}H_{29}O_3N_2S_2$ requires 433.1619.

(+)-*E*-(2*R*,3*S*)-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 ^oC, 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 ^oC 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

($MgSO_4$), 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 $CHCl_3$); ν_{max}/cm^{-1}($CHCl_3$ solution): 2928, 1732, 974; δ_H (360 MHz, $CDCl_3$) 8.01 (s, 1H, =CH), 7.13 (s, 1H, =CH), 6.75 (d, 1H, *J* 15.5, MeOCHCH=C*H*), 6.54 (dd, 1H, *J* 5.1 and 15.5, MeOCHC*H*=CH), 6.23 (dd, 1H, *J* 15.0 and 8.3, CH=C*H*CH=CH), 6.07 (dd, 1H, *J* 14.9 and 8.3, CH=CHC*H*=CH), 5.84 (dd, 1H, *J* 15.1 and 8.5, CHC*H*=CHCH=CH), 5.73 (dd, 1H, *J* 15.1 and 8.3, CH=CHCH=C*H*CH), 4.03 (app. t, 1H, *J* 6.4, C*H*OMe), 3.98-3.89 (m, 1H, O=CC*H*CH_3), 3.69 (s, 3H, CO_2CH_3), 3.36 (s, 3H, OCH_3), 2.75 (m, 1H, C*H*CH_3), 2.37 (m, 1H, C*H*$(CH_3)_2$), 1.57 (d, 3H, *J* 7.0, CH_3CH), 1.26 (d, 3H, *J* 6.8, CH_3CH), 1.03 (d, 6H, *J* 6.8, $(CH_3)_2CH$); δ_C (90 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 (CH_3), 57.2 (CH_3), 51.7 (CH), 45.0 (CH), 41.2 (CH), 31.1 (CH), 22.2 (CH_3), 20.8 (CH_3), 12.1 (CH_3); *m/z* (EI) 447.1740 (M^++H), $C_{23}H_{30}O_3N_2S_2$ requires 446.1741.

References

1 I. S. Mitchell, G. Pattenden and J. Stonehouse, *Org. Biomol. Chem.*, 2005, **3**, 4412–4431.

2 E. Vedejs and H. W. Fang, *J. Org. Chem.*, 1984, **49**, 210–212.

3 J. F. Olin and T. B. Johnson, *Recl. Trav. Chim. Pays Bas*, 1931, **50**, 72–76.

4 J. Arnarp, L. Kenne, B. Lindberg and J. Lonngren, *Carbohydr. Res.*, 1975, **44**, C5–C7.