Supplementary Information for OBC b708139a

(*E*)-5-[*N*-(3-Methylbut-2-enyl)-*N*-(toluene-4-sulfonyl)amino]pent-2-enoic acid methyl ester (2)
Methyl triphenylphosphoranylideneacetate (0.67 g, 2.00 mmol) was added to a solution of aldehyde **1** (0.59 g, 2.00 mmol) in CH_2Cl_2 (15 cm^3) and the reaction mixture was stirred at ambient temperature overnight. Removal of the CH_2Cl_2 *in vacuo* followed by flash column chromatography (silica; eluent 3:2 petrol:ethyl acetate) gave ester **2** as a white crystalline solid (0.46 g, 65%); (R_f = 0.40); mp = 32-34 °C (from petrol/ethyl acetate); (Found: C, 61.72; H, 7.22; N, 4.17; S, 9.23. $C_{18}H_{25}NO_4S$ requires C, 61.51; H, 7.17; N, 3.99; S, 9.12%); ν_{max}(nujol)/cm^{-1} 2926 (CH), 2869 (CH), 1723 (C=O), 1659 (C=C), 1598 (ArC=C), 1340 (SO_2), 1159 (SO_2); δ_H(300 MHz) 1.61 (3 H, s, C*H*$_3$), 1.66 (3 H, s, C*H*$_3$), 2.42 (3 H, s, C*H*$_3$), 2.42-2.48 (2 H, m, C*H*$_2$CH$_2$N), 3.17 (2 H, t, *J* 7.5, CH$_2$C*H*$_2$N), 3.72 (3 H, s, OC*H*$_3$), 3.77 (2 H, d, *J* 7.1, CHC*H*$_2$N), 4.98 (1 H, t, *J* 7.1, C*H*CH$_2$N), 5.81 (1 H, d, *J* 15.8, C*H*CO$_2$CH$_3$), 6.79-6.89 (1 H, m, C*H*=CHCO$_2$CH$_3$), 7.29 (2 H, d, *J* 8.1, Ar C*H*), 7.67 (2 H, d, *J* 8.1, Ar C*H*); δ_C(75 MHz) 17.8 (CH_3), 25.8 (CH_3), 21.6 (CH_3), 32.1 (CH_2, *C*H$_2$CH$_2$N), 45.8 (CH_2, CH$_2$*C*H$_2$N), 46.0 (CH_2, CH*C*H$_2$N), 51.6 (CH_3), 118.9 (CH, *C*HCH$_2$N), 122.9 (CH, *C*H=CHCO$_2$CH$_3$), 127.2 (CH, Ar), 129.7 (CH, Ar), 136.8 (C^4), 137.3 (C^4), 143.3 (C^4), 145.3 (CH, *C*HCO$_2$CH$_3$), 166.6 (C^4, *C*O$_2$CH$_3$); *m/z* (ES) 374 ($[M+Na]^+$, 100%).

(3*R,4*S**)-4-[(Carbomethoxy)methyl]-3-isopropenyl-1-(toluene-4-sulfonyl)piperidine (3) and (3*S**,4*S**)-4-[(carbomethoxy)methyl]-3-isopropenyl-1-(toluene-4-sulfonyl)piperidine (4)**
Ester **2** (50 mg, 0.14 mmol) and diphenylether (2 g) were heated under reflux for 7 h. Removal of the solvent by kugelrohr distillation followed by flash column chromatography (silica; eluent 3:2 petrol:ethyl acetate) gave an inseparable mixture of diastereomeric piperidines **3** and **4** as a colourless oil (60:40 **3**:**4**, 31 mg, 62%); (R_f = 0.40); data were recorded on the mixture; ν_{max}(neat)/cm^{-1} 2947 (CH), 2928 (CH), 1736 (C=O), 1643 (C=C), 1597 (ArC=C), 1342 (SO_2), 1157 (SO_2); due to the complexity of the ^{1}H NMR spectrum, only selected resonances are reported; δ_H(500 MHz) 1.62 (3 H, s, C*H*$_3$ major isomer), 1.75 (3 H, s, C*H*$_3$ minor isomer), 2.44 (3 H, s, C*H*$_3$ major isomer), 2.45 (3 H, s, C*H*$_3$ minor isomer), 3.61 (6 H, s, OC*H*$_3$ major and minor isomers), 4.51 (1 H, s, C=C*H*H, minor isomer), 4.77 (1 H, s, C=C*H*H, major isomer), 4.86 (1 H, s, C=CH*H*, minor isomer), 4.88 (1 H, s, C=CH*H*, major isomer); δ_C(125 MHz) 20.4 (CH_3, major isomer), 21.5 (CH_3, major and minor isomers), 23.0 (CH_3, minor isomer), 30.7 (CH_2, major isomer), 31.7 (CH_2, minor isomer), 35.0 (CH, major and minor isomers), 37.8 (CH_2, major and minor isomers), 42.0 (CH_2, minor isomer), 44.1 (CH, minor isomer), 45.6 (CH_2, minor isomer), 46.3 (CH_2, major isomer), 48.9 (CH, major isomer), 50.6 (CH_2, major isomer), 51.5 (CH_3, major isomer), 51.6 (CH_3, minor isomer), 111.8 (CH_2, minor isomer), 114.2 (CH_2, major isomer), 127.6 (CH, minor isomer), 127.7 (CH, major isomer), 129.6 (CH, major isomer), 129.7 (CH, minor isomer), 133.3 (C^4, major

isomer), 133.4 (C^4, minor isomer), 143.5 (C^4, major and minor isomers), 143.6 (C^4, major isomer), 144.5 (C^4, minor isomer), 172.9 (C^4, major isomer), 173.1 (C^4, minor isomer); HRMS (ES) 374.1413 ($[M+Na]^+$, $C_{18}H_{25}NO_4NaS$ requires 374.1402); *m/z* (EI) 351 (M^+, 8%), 336 (6), 320 (9), 296 (2), 278 (11), 260 (7), 236 (3), 212 (4), 196 (100), 184 (16), 155 (92), 136 (30), 122 (61), 105 (79), 91 (98), 77 (64), 55 (54), 42 (94), 32 (52).

(*E*)-5-(Toluene-4-sulfonylamino)pent-2-enoic acid methyl ester (5)

Iron (III) chloride (23 mg, 0.14 mmol) or scandium (III) triflate (70 mg, 0.14 mmol) was added to a solution of ester **2** (100 mg, 0.28 mmol) in CH_2Cl_2 (10 cm^3). The resulting mixture was stirred at ambient temperature for 7 h after which it was quenched by careful addition of water (10 cm^3). The aqueous phase was extracted with diethyl ether (4 x 10 cm^3) and the combined organic phases were washed with brine (10 cm^3), dried over $MgSO_4$ and evaporated *in vacuo* to give the fragmented ester **5** as a yellow oil (62 mg, 78%); (R_f = 0.25, 3:2 petrol:ethyl acetate); ν_{max}(chloroform)/cm^{-1} 1720 (C=O), 1661 (C=C), 1599 (ArC=C), 1332 (SO_2), 1152 (SO_2); δ_H(300 MHz) 2.32-2.37 (2 H, m, C*H*$_2$CH$_2$N), 2.41 (3 H, s, C*H*$_3$), 3.02-3.09 (2 H, m, C*H*$_2$N), 3.69 (3 H, s, C*H*$_3$), 5.05 (1 H, t, *J* 6.3, N*H*), 5.78 (1 H, d, *J* 15.8, C*H*CO$_2$CH$_3$), 6.77 (1 H, dt, *J* 15.8 and 7.1, C*H*=CHCO$_2$CH$_3$), 7.29 (2 H, d, *J* 8.3, Ar C*H*), 7.72 (2 H, d, *J* 8.3, Ar C*H*); δ_C(75 MHz) 21.6 (CH_3), 32.3 (CH_2, *C*H$_2$CH$_2$N), 41.5 (CH_2, *C*H$_2$N), 51.6 (CH_3, O*C*H$_3$), 123.5 (CH, *C*H=CHCO$_2$CH$_3$), 127.1 (CH, Ar), 129.8 (CH, Ar), 136.7 (C^4), 143.6 (C^4), 144.5 (CH, *C*HCO$_2$CH$_3$), 166.5 (C^4, *C*O$_2$CH$_3$); HRMS (ES) 306.0782 ($[M+Na]^+$, $C_{13}H_{17}NO_4NaS$ requires 306.0776); *m/z* (CI) 301 ($[M+NH_4]^+$, 30%), 284 (54), 252 (77), 201 (12), 184 (90), 155 (88), 139 (10), 108 (25), 100 (7), 91 (100), 65 (34).

(*E*)-5-Aza-8-methyl-5-(*p*-toluenesulfonyl)-1-(1,3-oxazolidin-2-onyl)dec-1,7-dien-1-one (7)

A solution of phosphine **6** (4.09 g, 10.50 mmol) in CH_2Cl_2 (20 mL) was added dropwise to a solution of aldehyde **1** (2.07 g, 7.01 mmol) in CH_2Cl_2 (20 mL) at ambient temperature. The reaction was stirred for 36 h before concentration *in vacuo* followed by flash column chromatography (silica; eluent 1:1 hexane/ethyl acetate) afforded first the (*Z*)-isomer (R_f = 0.53) as a colourless oil (0.09 g, 3%), followed by **7** (R_f = 0.30) as a colourless oil (2.14 g, 75%).

Data for (*Z*)-isomer:

δ_H (500 MHz) 1.60 (3 H, s, CH_3), 1.62 (3 H, s, CH_3), 2.41 (3 H, s, CH_3), 2.85 (2 H, apparent q, *J* 7.2, C*H*$_2$CH$_2$N), 3.23 (2 H, t, *J* 7.0, CH$_2$C*H*$_2$N), 3.79 (2 H, d, *J* 7.0, NC*H*$_2$CH), 4.03 (2 H, t, *J* 8.1, C*H*$_2$CH$_2$O), 4.41 (2 H, t, *J* 8.1, CH$_2$O), 4.95 (1 H, t, *J* 7.0, NCH$_2$C*H*), 6.33 (1 H, dt, *J* 11.8, 7.2, C*H*CH$_2$CH$_2$N), 7.06 (1 H, d, *J* 11.8, C*H*=CHCH$_2$CH$_2$N), 7.27 (2 H, d, *J* 8.2, Ar CH), 7.67 (2 H, d, *J* 8.2, Ar CH); δ_C (125 MHz) 18.1 (CH_3), 21.8 (CH_3), 26.1 (CH_3), 29.4 (*C*H$_2$CH$_2$N), 42.8

(CH$_2$CH$_2$O), 45.9 (CH$_2$$CH_2$N), 46.4 (N$CH_2$CH), 62.3 (CH$_2$O), 119.3 (NCH$_2$$C$H), 120.9 ($C$H=CHCH$_2CH_2$N), 127.6 (CH, Ar), 129.9 (CH, Ar), 137.2 (C^4), 137.5 (C^4), 143.4 (C^4), 147.5 (CHCH$_2$CH$_2$N), 153.6 (C=O), 165.1 (C=O); *m/z* (ES$^+$) 429 (100%, [M+Na]$^+$).

Data for **7**:

Found: C 59.53, H 6.38, N 6.93; Required for $C_{20}H_{26}N_2O_5S$: C 59.09, H 6.45, N 6.89; ν_{max} (film)/cm^{-1} 3022 (CH), 2976 (CH), 2924 (CH), 1777 (C=O), 1685 (C=O), 1638 (C=C), 1598 (Ar C=C), 1387 (C-N), 1361 (SO_2), 1159 (SO_2); δ_H (500 MHz) 1.62 (3 H, s, CH_3), 1.67 (3 H, s, CH_3), 2.42 (3 H, s, CH_3), 2.52 (2 H, apparent q, *J* 7.1, CH_2CH$_2$N), 3.22 (2 H, t, *J* 7.5, CH$_2$CH_2N), 3.79 (2 H, d, *J* 6.9, NCH_2CH), 4.05 (2 H, t, *J* 8.0, CH_2CH$_2$O), 4.42 (2 H, t, *J* 8.0, CH$_2$O), 4.98-5.04 (1 H, t, *J* 7.2, NCH$_2$C*H*), 7.03 (1 H, dt, *J* 15.4, 7.1, C*H*CH$_2$CH$_2$N), 7.21 (1 H, d, *J* 15.4, C*H*=CHCH$_2$CH$_2$N), 7.30 (2 H, d, *J* 8.2, Ar CH), 7.68 (2 H, d, *J* 8.2, Ar CH); δ_C (125 MHz) 18.0 (CH_3), 21.7 (CH_3), 25.9 (CH_3), 32.5 (CH$_2$CH$_2$N), 42.9 (CH$_2$CH$_2$O), 46.0 (CH$_2$$CH_2$N), 46.0 (N$CH_2$CH), 62.4 (CH$_2$O), 119.0 (NCH$_2$$C$H), 122.0 ($C$H=CHCH$_2CH_2$N), 127.3 (CH, Ar), 129.9 (CH, Ar), 137.1 (C^4), 137.5 (C^4), 143.4 (C^4), 147.0 (CHCH$_2$CH$_2$N), 153.7 (C=O), 164.8 (C=O); *m/z* (ES$^+$) 445.2 (15%, [M+K]$^+$), 430.1 (25%), 429.1 (100%, [M+Na]$^+$); HRMS (ES$^+$) Found: 429.1450, required for $C_{20}H_{26}N_2O_5SNa$: 429.1460.

(3*S,4*S**)-4-[(1,3-Oxazolidin-2-onyl)-3-acetyl]-3-isopropenyl-1-(*p*-toluenesulfonyl)piperidine (8), (3*R**,4*S**)-4-[(1,3-oxazolidin-2-onyl)-3-acetyl]-3-isopropenyl-1-(*p*-toluenesulfonyl)piperidine (9) and (1*R**,6*S**)-8-aza-5,5-dimethyl-4-oxa-8-(*p*-toluenesulfonyl)bicyclo[4.4.0]decan-3-one (10)**

MeAlCl$_2$ (1 M solution in hexanes, 185 μL, 0.19 mmol) was added dropwise to a solution of oxazolidinone **7** (75 mg, 0.18 mmol), in CH$_2$Cl$_2$ (10 mL) at ambient temperature. The reaction was stirred for 18 h before pouring into water (10 mL). The aqueous phase was extracted with CH$_2$Cl$_2$ (4 × 10 mL) and the organic extracts washed with brine (10 mL), dried over MgSO$_4$ and concentrated *in vacuo* to give a colourless oil which was purified by flash column chromatography (silica; eluent 1:1 hexane/ethyl acetate) to afford a colourless oil (60 mg) containing an inseparable 2:4:1 mixture of *trans* and *cis* piperidines **8** and **9** and lactone **10** (R_f = 0.46) respectively. Further purification of a sample of this mixture by semi-preparative HPLC (water/acetonitrile gradient; 100% water to 100% acetonitrile over 100 min) allowed separation of the three components.

Data for **10**:

Analytical HPLC (1:1 water/acetonitrile over 40 min); t_r = 9.00 min; mp 180-182 °C (from hexane/ethyl acetate); Found: C 60.50, H 7.03, N 4.11; Required for $C_{17}H_{23}NO_4S$: C 60.51, H 6.87,

N 4.15; ν_{max} (film)/cm^{-1} 3022 (CH), 2985 (CH), 2930 (CH), 1725 (C=O), 1598 (Ar C=C), 1463 (Ar C=C), 1342 (SO_2), 1162 (SO_2), 1115 (C-O); δ_H (400 MHz) 1.19 (3 H, s, CH_3), 1.32-1.45 (1 H, m, C*H*HCH$_2$N), 1.47 (3 H, s, CH_3), 1.62-1.87 (3 H, env, CH*H*CH$_2$N, C*H*CH$_2$CH$_2$N, NCH$_2$C*H*), 1.98-2.13 (2 H, env, NC*H*HCH and C*H*H(CO)O), 2.67 (1 H, td, *J* 12.3, 2.6, CH$_2$C*H*HN), 2.44 (3 H, s, CH_3), 2.66 (1 H, dd B of ABX *J* 18.1, 5.4, CH*H*(CO)O), 3.82-3.91 (2 H, env, CH$_2$CH*H*N and NCH*H*CH), 7.34 (2 H, d, *J* 8.2, Ar CH), 7.64 (2 H, d, *J* 8.2, Ar CH); δ_C (100 MHz) 21.9 (CH_3), 24.0 (CH_3), 28.9 (CH_3), 30.9 (*C*HCH$_2$CH$_2$N), 31.9 (*C*H$_2$CH$_2$N), 36.2 (*C*H$_2$(CO)O), 45.9 (NCH$_2$*C*H) 46.2 (CH$_2$*C*H$_2$N), 47.4 (N*C*H$_2$CH), 83.6 (C^4), 127.9 (CH, Ar), 130.2 (CH, Ar), 133.7 (C^4), 144.3 (C^4), 169.6 (C=O); *m/z* (ES$^+$) 392.1 (40%, [M+Na+MeOH]$^+$), 360.0 (100%, [M+Na]$^+$); HRMS (ES$^+$) Found: 360.1249, required for $C_{17}H_{23}NO_4SNa$: 360.1245.

Data for **9**:

Analytical HPLC (1:1 water/acetonitrile over 40 min); t_r = 17.76 min; mp 86-89 °C (from hexane/ethyl acetate); ν_{max} (film)/cm^{-1} 2922 (CH), 2852 (CH), 1778 (C=O), 1697 (C=O), 1598 (Ar C=C), 1443 (Ar C=C), 1389 (C-N), 1339 (SO_2), 1224 (C-O), 1162 (SO_2); δ_H (400 MHz) 1.68-1.79 (4 H, env including 1.76 (3 H, s, CH_3) and C*H*HCH$_2$N), 1.82-1.93 (1 H, m, CH*H*CH$_2$N), 2.41-2.50 (4 H, env including 2.44 (3 H, s, CH_3) and NCH$_2$C*H*), 2.55-2.77 (4 H, env, C*H*CH$_2$CH$_2$N, CH$_2$HC*H*HN, NC*H*HCH and C*H*H(CO)N), 2.80 (1 H, dd B of ABX, *J* 16.7, 4.0, CH*H*(CO)N), 3.34-3.42 (1 H, m, CH$_2$C*H*HN, 3.43-3.50 (1 H, m, NCH*H*CH), 3.89-4.02 (2 H, m, C*H*$_2$CH$_2$O), 4.37 (2 H, t, *J* 8.1, CH$_2$O), 4.55 (1 H, s, C=C*H*H), 4.86 (1 H, s, C=CH*H*), 7.33 (2 H, d, *J* 8.1, Ar CH), 7.65 (2 H, d, *J* 8.1, Ar CH); δ_C (100 MHz) 21.9 (CH_3), 23.5 (CH_3), 29.2 (*C*H$_2$CH$_2$N), 30.1 (*C*HCH$_2$CH$_2$N), 32.9 (*C*H$_2$(CO)N), 42.7 (CH$_2$*C*H$_2$N), 42.9 (*C*H$_2$CH$_2$O), 44.7 (NCH$_2$*C*H), 46.3 (N*C*H$_2$CH), 62.3 (CH$_2$O), 112.2 (C=*C*H$_2$), 127.9 (CH, Ar), 130.1 (CH, Ar), 134.0 (C^4), 143.9 (C^4), 145.1 (C^4), 153.7 (C=O), 172.7 (C=O); *m/z* (ES$^+$) 430.1 (29%), 429.0 (100%, [M+Na]$^+$); HRMS (ES$^+$) Found: 429.1450, required for $C_{20}H_{26}N_2O_5SNa$: 429.1460.

Data for the **8**:

Analytical HPLC (1:1 water/acetonitrile over 40 min); t_r = 19.11 min; mp 147-149 °C (from hexane/ethyl acetate); Found: C 59.21, H 6.46, N 6.61; Required for $C_{20}H_{26}N_2O_5S$: C 59.09, H 6.45, N 6.89; ν_{max} (film)/cm^{-1} 3021 (CH), 2923 (CH), 2852 (CH), 1781 (C=O), 1699 (C=O), 1646 (C=C), 1599 (Ar C=C), 1480 (Ar C=C), 1389 (C-N), 1340 (SO_2), 1216 (C-O), 1163 (SO_2); δ_H (400 MHz) 1.31-1.45 (1 H, m, C*H*HCH$_2$N), 1.64 (3 H, s, CH_3), 1.85-1.98 (2 H, env, CH*H*CH$_2$N and CHCH$_2$CH$_2$N), 2.07-2.19 (2 H, env, NCH$_2$C*H* and NC*H*HCH), 2.27 (1 H, td, *J* 12.0, 2.1, CH$_2$C*H*HN), 2.44 (3 H, s, CH_3), 2.69 (1 H, dd A of ABX, *J* 17.6, 9.4, C*H*H(CO)N), 2.97 (1 H, dd B of ABX, *J* 17.6, 3.2, CH*H*(CO)N), 3.72 (1 H, dd, *J* 7.5, 1.8, NCH*H*CH), 3.75-3.83 (1 H, m, CH$_2$CH*H*N), 3.89-4.02 (2 H, m, C*H*$_2$CH$_2$O), 4.37 (2 H, t, *J* 8.1, CH$_2$O), 4.79 (1 H, s, C=C*H*H), 4.87

(1 H, s, C=CH*H*), 7.32 (2 H, d, *J* 7.9, Ar CH), 7.62 (2 H, d, *J* 7.9, Ar CH); δ_C (100 MHz) 20.9 (CH_3), 21.9 (CH_3), 31.2 (*C*H_2CH_2N), 34.4 (*C*HCH_2CH_2N), 38.9 (*C*H_2(CO)N), 42.8 (*C*H_2CH_2O), 46.6 (CH_2*C*H_2N), 49.2 (NCH_2*C*H), 51.0 (N*C*H_2CH), 62.3 (CH_2O), 114.5 (C=*C*H_2), 128.0 (CH, Ar), 130.0 (CH, Ar), 133.6 (C^4), 143.8 (C^4), 144.1 (C^4), 153.7 (C=O), 172.5 (C=O); *m/z* (ES^+) 430.1 (25%), 429.1 (100%, $[M+Na]^+$); HRMS (ES^+) Found: 429.1452, required for $C_{20}H_{26}N_2O_5SNa$: 429.1460.

(1*E*,7*E*)-5-aza-5-(*p*-toluenesulfonyl)-1-(1,3-oxazolidin-2-onyl)dec-1,7-dien-1-one 11)
Oxazolidinone **11** was prepared as for **7** from a 5:1 mixture of (*E*) and (*Z*) crotyl aldehydes **15** and **16** (0.96 g, 3.42 mmol) and Wittig reagent **6** (2.00 g, 5.14 mmol). Aqueous work up followed by flash column chromatography (silica; eluent 2:1 hexane/ethyl acetate) afforded the *title compound* (R_f = 0.31) as a colourless crystalline solid containing a 3:1 inseparable mixture of (*E*) and (*Z*) crotyl isomers (0.82 g, 62%).

Data for a 3:1 mixture of **11** and **13**:
mp 85-88 °C (from hexane/ethyl acetate); Found: C 58.11, H 5.96, N 6.92; Required for $C_{19}H_{24}N_2O_5S$: C 58.15, H 6.16, N 7.14; ν_{max} (film)/cm^{-1} 3024 (CH), 2922 (CH), 2858 (CH), 1777 (C=O), 1684 (C=O), 1638 (C=C), 1598 (Ar C=C), 1479 (Ar C=C), 1451 (Ar C=C), 1387 (C-N), 1361 (SO_2), 1160 (SO_2); δ_H (300 MHz) 1.56-1.71 (3 H major isomer and 3 H minor isomer, env including 1.63 (3 H, d, *J* 6.3, CH_3, major isomer) and CH_3 minor isomer), 2.41 (3 H major isomer and 3 H minor isomer, s, CH_3, major and minor isomers), 2.44-2.58 (2 H major isomer and 2 H minor isomer, env, C*H*$_2$$CH_2N$, major and minor isomers), 3.22 (2 H major isomer and 2 H minor isomer, t, *J* 7.4, CH_2C*H*$_2$N, major and minor isomers), 3.71 (2 H, d, *J* 6.8, NC*H*$_2$CH, major isomer), 3.84 (2 H, d, *J* 6.8, NC*H*$_2$CH, minor isomer), 4.04 (2 H major isomer and 2 H minor isomer, t, *J* 7.9, C*H*$_2$$CH_2O$, major and minor isomers), 4.41 (2 H major isomer and 2 H minor isomer, t, *J* 7.9, CH_2O, major and minor isomers), 5.14-5.34 (1 H major isomer and 1 H minor isomer, m, C*H*CH_3, major and minor isomers), 5.50-5.69 (1 H major isomer and 1 H minor isomer, m, NCH_2C*H*, major and minor isomers), 6.93-7.10 (1 H major isomer and 1 H minor isomer, m, C*H*CH_2CH_2N, major and minor isomers), 7.15-7.37 (3 H major isomer and 3 H minor isomer, env including 7.28 (2 H major isomer and 2 H minor isomer, d, *J* 8.1, Ar CH, major and minor isomers) and C*H*=CHCH_2CH_2N, major and minor isomers), 7.66 (2 H major isomer and 2 H minor isomer, d, *J* 8.1, Ar CH, major and minor isomers); δ_C (75 MHz) 13.2 (CH_3, minor isomer), 17.9 (CH_3, major isomer), 21.8 (CH_3, major and minor isomers), 32.3 (C*H*$_2$$CH_2N$, major and minor isomers), 42.9 (*C*H_2CH_2O, major and minor isomers), 44.8 (CH_2, major isomer), 45.7 (CH_2, minor isomer), 46.1 (CH_2, minor isomer), 50.6 (CH_2, major isomer), 62.4 (CH_2O, major and minor isomers), 122.0

(C*H*=CHCH$_2$CH$_2$N, major isomer), 122.1 (C*H*=CHCH$_2$CH$_2$N, minor isomer), 124.9 (CH, minor isomer), 125.7 (CH, major isomer), 127.4 (CH, Ar, major and minor isomers), 129.2 (CH, minor isomer), 130.0 (CH, Ar, major and minor isomers), 131.1 (CH, major isomer), 137.0 (C^4, major and minor isomers), 143.6 (C^4, major and minor isomers), 147.0 (C*H*CH$_2$CH$_2$N, minor isomer), 147.2 (C*H*CH$_2$CH$_2$N, major isomer), 153.7 (C=O, major and minor isomers), 164.9 (C=O, major and minor isomers); *m/z* (ES^+) 415.1 (100%, $[M+Na]^+$); HRMS (ES^+) Found: 415.1296, required for $C_{19}H_{24}N_2O_5SNa$: 415.1304.

(1*E*,7*Z*)-5-Aza-5-(*p*-toluenesulfonyl)-1-(1,3-oxazolidin-2-onyl)dec-1,7-dien-1-one 13)
Oxazolidinone **13** was prepared as for **7** from a 1:6 mixture of (*E*) and (*Z*) crotyl aldehydes **15** and **16** (0.42 g, 1.49 mmol) and phosphine **6** (0.87 g, 2.23 mmol). Aqueous work up followed by flash column chromatography (silica; eluent 2:1 hexane/ethyl acetate) afforded the *title compound* (R_f = 0.33) as a colourless oil (0.42 g, 72%) containing a 1:7 mixture of (*E*) and (*Z*) crotyl isomers; Found: C 58.05, H 6.32, N 7.13; Required for $C_{19}H_{24}N_2O_5S$: C 58.15, H 6.16, N 7.14; ν_{max} (film)/cm^{-1} 3020 (CH), 2983 (CH), 1778 (C=O), 1686 (C=O), 1638 (C=C), 1593 (Ar C=C), 1483 (Ar C=C), 1438 (Ar C=C), 1387 (C-N), 1362 (SO_2), 1216 (C-O), 1160 (SO_2); δ_H (300 MHz) 1.53-1.69 (3 H major isomer and 3 H minor isomer, env including 1.62 (3 H, d, *J* 6.6, CH_3 major isomer) and CH_3 minor isomer), 2.42 (3 H major isomer and 3 H minor isomer, s, CH_3, major and minor isomers), 2.53 (2 H major isomer and 2 H minor isomer, apparent q, *J* 7.1, C*H*$_2$CH$_2$N, major and minor isomers), 3.23 (2 H major isomer and 2 H minor isomer, t, *J* 7.4, CH$_2$C*H*$_2$N, major and minor isomers), 3.72 (2 H, d, *J* 6.8, NC*H*$_2$CH, minor isomer), 3.85 (2 H, d, *J* 6.8, NC*H*$_2$CH, minor isomer), 4.05 (2 H major isomer and 2 H minor isomer, t, *J* 7.9, C*H*$_2$CH$_2$O, major and minor isomers), 4.42 (2 H major isomer and 2 H minor isomer, t, *J* 7.9, CH$_2$O, major and minor isomers), 5.17-5.33 (1 H major isomer and 1 H minor isomer, m, C*H*CH$_3$, major and minor isomers), 5.52-5.71 (1 H major isomer and 1 H minor isomer, m, NCH$_2$C*H*, major and minor isomers), 6.95-7.11 (1 H major isomer and 1 H minor isomer, C*H*CH$_2$CH$_2$N, major and minor isomers), 7.16-7.38 (3 H major isomer and 3 H minor isomer, env including 7.29 (2 H major isomer and 2 H minor isomer, d, *J* 8.1, Ar CH, major and minor isomers) and C*H*=CHCH$_2$CH$_2$N, major and minor isomers), 7.69 (2 H major isomer and 2 H minor isomer, d, *J* 8.1, Ar CH, major and minor isomers); δ_C (75 MHz) 13.2 (CH_3, major isomer), 18.0 (CH_3, minor isomer), 21.9 (CH_3, major and minor isomers), 32.6 (C*H*$_2$CH$_2$N, major and minor isomers), 43.0 (*C*H$_2$CH$_2$O, major and minor isomers), 44.9 (CH_2, major isomer), 45.8 (CH_2, minor isomer), 46.1 (CH_2, major isomer), 50.7 (CH_2, minor isomer), 62.4 (CH_2O, major and minor isomers), 122.0 (C*H*=CHCH$_2$CH$_2$N, minor isomer), 122.1 (C*H*=CHCH$_2$CH$_2$N, major isomer), 125.0 (CH, major isomer), 125.8 (CH, minor isomer), 127.5 (CH, Ar, major and minor isomers), 129.3 (CH, major isomer), 130.1 (CH, Ar, major and minor), 131.1 (CH, minor isomer), 137.1 (C^4, major and minor isomers), 143.7 (C^4, major and minor

isomers), 147.2 (C*H*CH_2CH_2N, major and minor isomers), 153.8 (C=O, major and minor isomers), 165.0 (C=O, major and minor isomers); *m/z* (ES^+) 415.1 (100%, $[M+Na]^+$); HRMS (ES^+) Found: 415.1315, required for $C_{19}H_{24}N_2O_5SNa$: 415.1304.

(3*S,4*S**)-4-[(1,3-Oxazolidin-2-onyl)-3-acetyl]-3-vinyl-1-(*p*-toluenesulfonyl)piperidine (12), (3*R**,4*S**)-4-[(1,3-oxazolidin-2-onyl)-3-acetyl]-3-vinyl-1-(*p*-toluenesulfonyl)piperidine (14), (1*R**,5*R**,6*S**)-8-aza-5-methyl-4-oxa-8-(*p*-toluenesulfonyl)bicyclo[4.4.0]decan-3-one (17) and (1*R**,5*S**,6*S**)-8-aza-5-methyl-4-oxa-8-(*p*-toluenesulfonyl)bicyclo[4.4.0]decan-3-one (18)**

Lewis acid-catalysed cyclisation of a 3:1 mixture of **11** and **13**:

$MeAlCl_2$ (1 M solution in hexanes, 255 μL, 0.255 mmol) was added dropwise to a solution of a 3:1 mixture of (*E*) and (*Z*) oxazolidinones **11** and **13** (100 mg, 2.55 mmol) in CH_2Cl_2 (10 mL) in an Ace tube under argon at ambient temperature. The Ace tube was sealed and heated to 60 °C for 18 h. The reaction mixture was allowed to cool before pouring into a saturated solution of Rochelle's salt (20 mL). The aqueous phase was extracted with CH_2Cl_2 (4 × 20 mL) and the combined organic extracts washed with brine (20 mL), dried over $MgSO_4$ and concentrated *in vacuo* before purification by flash column chromatography (silica; eluent 1:1 hexane/ethyl acetate) afforded a pale yellow oil (76 mg) containing a complex mixture of products (R_f = 0.25) from which small amounts of a 1:2 inseparable mixture of *trans* and *cis* piperidines **12** and **14** and a 10:1 inseparable mixture of lactones **17** and **18** were isolated *via* semi-preparative HPLC (7:3 water/acetonitrile over 190 min).

Lewis acid-catalysed cyclisation of a 1:7 mixture of **11** and **13:**

The cyclisation of a 1:7 mixture of (*E*) and (*Z*) crotyl oxazolidinones **11** and **13** (147 mg, 0.375 mmol) was performed as for the 6:1 (*E*):(*Z*) mixture with $MeAlCl_2$ (1 M solution in hexanes, 375 μL, 0.375 mmol). Aqueous work-up followed by flash column chromatography afforded a complex mixture of products (11 mg). Analytical HPLC (7:3 water/acetonitrile over 180 min) indicated a 2:4:3 mixture of *trans* and *cis* piperidines **12** and **14**, and a mixture of Diels-Alder products **17** and **18** in an undetermined ratio.

Data recorded on a 1:2 mixture of piperidines **12** and **14**:

Analytical HPLC (7:3 water/acetonitrile over 180 min); t_r = 123.33 min, 136.47 min; Found: C 58.16, H 6.32, N 6.93; Required for $C_{19}H_{24}N_2O_5S$: C 58.15, H 6.16, N 7.14; ν_{max} (film)/cm^{-1} 2961 (CH), 2920 (CH), 2851 (CH), 1778 (C=O), 1696 (C=O), 1671 (C=C), 1598 (Ar C=C), 1443 (Ar C=C), 1388 (SO_2), 1162 (SO_2); δ_H (500 MHz) 1.40 (1 H, m, C*H*HCH_2N, minor isomer), 1.57-1.67 (2 H, m, CH_2CH_2N, major isomer), 1.69-1.79 (1 H, m, C*H*CH_2CH_2N, minor isomer), 1.83-1.89 (1

H, m, CH*H*CH_2N, minor isomer), 1.99-2.08 (1 H major isomer and 1 H minor isomer, env including 2.04 (1 H, t, A of ABX, *J* 11.2, NC*H*HCH, minor isomer) and C*H*CH_2CH_2N, major isomer), 2.11-2.20 (1 H, m, NCH_2C*H*, minor isomer), 2.26 (1 H, td, *J* 12.0, 2.2, CH_2C*H*HN, minor isomer), 2.37-2.47 (4 H major isomer and 3 H minor isomer, env including 2.43 (6 H major isomer and 6 H minor isomer, s, CH_3, major and minor isomers) and CH_2C*H*HN major isomer), 2.48-2.53 (1 H, m, NCH_2C*H*, major isomer), 2.56 (1 H, dd, *J* 11.4, 2.9, NC*H*HCH, major isomer), 2.61-2.71 (1 H major isomer and 1 H minor isomer, env, C*H*H(CO)N, major isomer and minor isomers), 2.91 (1 H, dd B of ABX, *J* 17.2, 6.6, CH*H*(CO)N, major isomer), 3.11 (1 H, dd B of ABX, *J* 17.3, 3.6, CH*H*(CO)N, minor isomer), 3.57-3.62 (1 H, m, NCH*H*CH, major isomer), 3.66-3.73 (1 H major isomer and 1 H minor isomer, env, CH_2CH*H*N, major isomer and NCH*H*CH, minor isomer), 3.75-3.81 (1 H, CH_2CH*H*N, minor isomer), 3.96 (2 H major isomer and 2 H minor isomer, t, *J* 8.1, C*H*$_2CH_2$O, major and minor isomers), 4.38 (2 H major isomer and 2 H minor isomer, t, *J* 8.1, CH_2O, major and minor isomers), 5.09-5.22 (2 H major isomer and 2 H minor isomer, env, CH=C*H*$_2$, major and minor isomers), 5.43 (1 H, dt, *J* 16.7, 9.5, C*H*=CH_2, minor isomer), 6.01 (1 H, dt, *J* 17.1, 9.6, C*H*=CH_2, major isomer), 7.32 (2 H major isomer and 2 H minor isomer, d, *J* 8.1, Ar CH, major and minor isomers), 7.62 (2 H major and 2 H minor, d, *J* 8.1, Ar CH, major and minor isomers); δ_C (125 MHz) 21.9 (CH_3, major and minor isomers), 27.4 (*C*H_2CH_2N, major isomer), 30.9 (*C*H_2CH_2N, minor isomer), 34.5 (*C*HCH_2CH_2N, major isomer), 35.9 (*C*HCH_2CH_2N, minor isomer), 38.4 (*C*H_2(CO)N major isomer), 39.1 (*C*H_2(CO)N, minor isomer), 42.0 (NCH_2*C*H, major isomer), 42.8 (*C*H_2CH_2O, major isomer), 42.9 (*C*H_2CH_2O, minor isomer), 46.46 (NCH_2*C*H, minor isomer), 46.52 (CH_2*C*H_2N, major isomer), 46.53 (CH_2*C*H_2N, minor isomer), 51.0 (N*C*H_2CH, major isomer), 51.2 (N*C*H_2CH, minor isomer), 62.3 (CH_2O, major and minor isomers), 118.7 (C=*C*H_2, major isomer), 119.0 (C=*C*H_2, minor isomer), 128.0 (CH, Ar, major and minor isomers), 130.0 (CH, Ar, major and minor isomers), 133.4 (C^4, major and minor isomers), 135.3 (*C*H=CH_2, major isomer), 137.7 (*C*H=CH_2, minor isomer), 143.8 (C^4, major isomer), 143.9 (C^4, minor isomer), 153.7 (C=O, major and minor isomers), 172.3 (C=O, major isomer), 172.5 (C=O, minor isomer); *m/z* (ES^+) 415.3 (100%, $[M+Na]^+$); HRMS (ES^+) Found: 415.1293, required for $C_{19}H_{24}N_2O_5SNa$: 415.1304.

Data recorded on a 10:1 mixture of lactones **17** and **18**:
Analytical HPLC (7:3 water/acetonitrile over 180 min); t_r = 36.23 min; mp 176-179 °C (from hexane/ethyl acetate); ν_{max} (film)/cm^{-1} 2982 (CH), 2931 (CH), 2862 (CH), 1727 (C=O), 1598 (Ar C=C), 1451 (Ar C=C), 1330 (SO_2), 1158 (SO_2), 1116 (CO); NMR data reported for major isomer only: δ_H (300 MHz) 1.30-1.64 (5 H, env including 1.38 (3 H, d, *J* 6.3, C*H*$_3$CH), NCH_2C*H* and C*H*HCH_2N), 1.66-1.86 (2 H, m, C*H*CH_2CH_2N and C*H*HCH_2N), 1.90 (1 H, t, *J*, 11.0, NC*H*HCH), 2.12 (1 H, dd A of ABX, *J* 18.0, 11.4, C*H*H(CO)O), 2.23 (1 H, td, *J* 12.1, 2.6, CH_2C*H*HN), 2.43 (3

H, s, CH_3), 2.69 (1 H, dd B of ABX, *J* 18.0, 4.4, C*H*H(CO)O), 3.82-3.94 (2 H, m, CH_2CH*H*N and NCH*H*CH), 3.96-4.09 (1 H, m, NCH_2CHC*H*), 7.33 (2 H, d, *J* 8.1, Ar CH), 7.63 (2 H, d, *J* 8.1, Ar CH); δ_C (75 MHz) 20.5 (CH_3), 21.9 (CH_3), 31.1 (*C*H_2CH_2N), 34.7 (*C*HCH_2CH_2N), 36.4 (*C*H_2(CO)O), 43.0 (NCH_2*C*H), 46.1 (CH_2*C*H_2N), 47.5 (N*C*H_2CH), 79.1 (NCH_2CH*C*H), 127.9 (CH, Ar), 130.2 (CH, Ar), 133.4 (C^4), 144.3 (C^4), 169.5 (C=O); *m/z* (ES^+) 346.2 (100%, $[M+Na]^+$); HRMS (ES^+) Found: 346.1090, required for $C_{16}H_{21}NO_4SNa$: 346.1089.

{3-[*N*-(3-Methylbut-2-enyl)-*N*-(toluene-4-sulfonyl)amino]propyl}-triphenylphosphonium bromide (24)

Triphenylphosphine (0.87 g, 3.33 mmol) was added to a solution of bromide **23** (1.0 g, 2.78 mmol) in acetonitrile (20 cm^3). The resulting mixture was heated under reflux for 48 h using a condenser fitted with a $CaCl_2$ drying tube. Removal of the solvent *in vacuo* gave a viscous colourless oil that was triturated with diethyl ether (5 x 20 cm^3) and dried under high vacuum to give phosphonium bromide salt **24** as a white crystalline solid that was not further purified (1.52 g, 87%); the product decomposed on heating above 150 °C so an accurate melting point could not be determined; δ_H(300 MHz; DMSO) 1.45 (3 H, s, C*H*$_3$), 1.52 (3 H, s, C*H*$_3$), 1.58-1.74 (2 H, m, C*H*$_2CH_2N$), 2.38 (3 H, s, C*H*$_3$), 3.13-3.22 (2 H, m, CH_2C*H*$_2N$), 3.49-3.59 (2 H, m, C*H*$_2CH_2CH_2N$), 3.65-3.72 (2 H, m, CHC*H*$_2N$), 4.86-4.94 (1 H, m, C*H*CH_2N), 7.38 (2 H, d, *J* 7.7, Ar C*H*), 7.62 (2 H, d, *J* 7.7, Ar C*H*), 7.73-7.85 (12 H, m, Ar C*H*), 7.88-7.97 (3 H, m, Ar C*H*); δ_C(75 MHz; DMSO) 17.9 (CH_3), 18.5 (CH_2, d, $^1J_{C\text{-}P}$ 51.9, *C*$H_2CH_2CH_2N$), 21.4 (CH_3), 21.9 (CH_2, d, $^2J_{C\text{-}P}$, 3.0, *C*H_2CH_2N), 25.8 (CH_3), 46.1 (CH_2, CH*C*H_2N), 47.5 (CH_2, d, $^3J_{C\text{-}P}$ 21.0, CH_2*C*H_2N), 118.6 (C^4, d, $^1J_{C\text{-}P}$ 86.2), 119.3 (CH, *C*HCH_2N), 127.2 (CH, Ar), 130.2 (CH, Ar), 130.7 (CH, d, $^3J_{C\text{-}P}$ 12.4, Ar), 133.9 (CH, d, $^2J_{C\text{-}P}$ 10.3, Ar), 135.4 (CH, d, $^4J_{C\text{-}P}$ 3.1, Ar), 136.8 (C^4), 136.9 (C^4), 143.6 (C^4); δ_P(121 MHz; DMSO) 25.37 (P^4, s); HRMS (ES) 542.2274 (M^+, $C_{33}H_{37}NO_2PS$ requires 542.2283); *m/z* (ES) 542 (M^+, 100%).

2-{3-[*N*-(3-Methylbut-2-enyl)-*N*-(toluene-4-sulfonyl)amino]propylidene}malonic acid diethyl ester (25) and 2,5-*bis*-ethoxycarbonyl-5-hydroxy-4-{[*N*-(3-methylbut-2-enyl)-*N*-(toluene-4-sulfonyl)amino]methyl}hex-2-enedioic acid diethyl ester (26)

NaHMDS (1 M soln. in THF, 0.32 cm^3, 0.32 mmol) was added dropwise to a solution of phosphonium bromide **24** (200 mg, 0.32 mmol) in THF (15 cm^3) at -78 °C. The reaction mixture was warmed to 0 °C and stirred for 2 h before being cooled back to -78 °C. Diethylketomalonate (49 µl, 0.32 mmol) was added and the reaction mixture was stirred for 2 h at -78 °C and then warmed to ambient temperature and stirred for a further 2 h. The THF was evaporated *in vacuo* and the residue purified by flash column chromatography (silica; eluent 3:1 petrol:ethyl acetate) to give diester **25** as a colourless oil (55 mg, 39%); (R_f = 0.42); ν_{max}(neat)/cm^{-1} 2982 (CH), 2932 (CH),

1720 (C=O), 1651 (C=C), 1597 (ArC=C), 1339 (SO_2), 1157 (SO_2); δ_H(300 MHz) 1.25-1.34 (6 H, env, 2 x CH_2CH_3), 1.61 (3 H, s, CH_3), 1.66 (3 H, s, CH_3), 2.42 (3 H, s, CH_3), 2.54-2.62 (2 H, m, CH_2CH_2N), 3.19 (2 H, t, *J* 7.2, CH_2CH_2N), 3.76 (2 H, d, *J* 7.0, $CHCH_2N$), 4.23 (2 H, q, *J* 7.1, CH_2CH_3), 4.29 (2 H, q, *J* 7.1, CH_2CH_3), 4.95-5.01 (1 H, m, $CHCH_2N$), 6.93 (1 H, t, *J* 7.7, $CH=C(CO_2Et)_2$), 7.29 (2 H, d, *J* 8.1, Ar C*H*), 7.68 (2 H, d, *J* 8.1, Ar C*H*); δ_C(75 MHz) 14.1 (CH_3, 2 x CH_2CH_3), 17.8 (CH_3), 21.5 (CH_3), 25.8 (CH_3), 29.7 (CH_2, CH_2CH_2N), 45.6 (CH_2), 46.0 (CH_2), 61.4 (CH_2, 2 x CH_2CH_3), 118.7 (CH, $CHCH_2N$), 127.3 (CH, Ar), 129.7 (CH, Ar), 130.3 (C^4), 136.6 (C^4), 137.5 (C^4), 143.3 (C^4), 145.2 (CH, $CHCH_2CH_2N$), 163.7 (C^4), 165.1 (C^4); HRMS (ES) 460.1759 ($[M+Na]^+$, $C_{22}H_{31}NO_6NaS$ requires 460.1770); *m/z* (ES) 460 ($[M+Na]^+$, 100%). Further elution afforded **26** as a colourless oil (39 mg, 20%); (R_f = 0.27); ν_{max}(neat)/cm^{-1} 2984 (CH), 2932 (CH), 1730 (C=O), 1651 (C=C), 1597 (ArC=C), 1339 (SO_2), 1157 (SO_2); δ_H(300 MHz) 1.20-1.42 (12 H, env, 4 x CH_2CH_3), 1.52 (3 H, s, CH_3), 1.59 (3 H, s, CH_3), 1.71 (1 H, s, O*H*), 2.40 (3 H, s, CH_3), 3.08-3.17 (1 H, A of ABX spin system, $CHHCHCOH(CO_2Et)_2$), 3.21-3.30 (1 H, B of ABX spin system, $CHHCHCOH(CO_2Et)_2$), 3.72-3.84 (2 H, m, $CH_2CH=C(CH_3)_2$), 4.11-4.45 (9 H, env, $CHCOH(CO_2Et)_2$ and 4 x CH_2CH_3), 4.56-4.62 (1 H, m, $CH=C(CH_3)_2$), 6.81 (1 H, d, *J* 11.4, $CH=C(CO_2Et)_2$), 7.25 (2 H, d, *J* 8.1, Ar C*H*), 7.65 (2 H, d, *J* 8.1, Ar C*H*); δ_C(75 MHz) 13.8 (CH_3, 2 x CH_2CH_3), 14.1 (CH_3, 2 x CH_2CH_3), 17.8 (CH_3), 21.5 (CH_3), 25.8 (CH_3), 44.6 (CH), 45.9 (CH_2), 46.9 (CH_2), 61.5 (CH_2), 61.7 (CH_2), 63.2 (CH_2, 2 x CH_2CH_3), 79.0 (C^4), 117.5 (CH), 127.6 (CH, Ar), 129.5 (CH, Ar), 132.1 (C^4), 136.5 (C^4), 137.5 (C^4), 142.7 (CH), 143.3 (C^4), 163.5 (C^4), 164.6 (C^4), 168.9 (2 x C^4); HRMS (ES) 634.2309 ($[M+Na]^+$, $C_{29}H_{41}NO_{11}NaS$ requires 634.2298); *m/z* (FAB) 634 ($[M+Na]^+$, 100%), 544 (12), 498 (8), 456 (10), 309 (6), 221 (7), 184 (14).

(3*R,4*S**)-4-[*Bis*(carboethoxy)methyl]-3-isopropenyl-1-(toluene-4-sulfonyl)piperidine**

Methyl aluminium dichloride (1 M soln. in hexanes, 0.12 cm^3, 0.12 mmol) was added to a solution of diester **103** (53 mg, 0.12 mmol) in CH_2Cl_2 (10 cm^3) at -78 °C. The resulting mixture was stirred at -78 °C for 5 h, after which it was quenched by addition of water (10 cm^3). The aqueous phase was extracted with CH_2Cl_2 (4 x 10 cm^3) and the combined organic phases washed with brine (10 cm^3), dried over Na_2SO_4 and evaporated *in vacuo* to leave a colourless oil, which was purified by flash column chromatography (silica; eluent 3:1 petrol:ethyl acetate) to give the *title compound* as a white crystalline solid (35 mg, 67%); (R_f = 0.39); mp = 84-86 °C (from petrol/ethyl acetate); (Found: C, 60.41; H, 7.31; N, 3.09; S, 7.33. $C_{22}H_{31}NO_6S$ requires C, 60.39; H, 7.14; N, 3.20; S, 7.33%); ν_{max}(neat)/cm^{-1} 2982 (CH), 2928 (CH), 1724 (C=O), 1643 (C=C), 1597 (ArC=C), 1342 (SO_2), 1157 (SO_2); δ_H(400 MHz) 1.21 (3 H, t, *J* 7.1, CH_2CH_3), 1.26 (3 H, t, *J* 7.1, CH_2CH_3), 1.62-1.73 (4 H, env, CH_3 and $CHHCH_2N$), 1.92-2.01 (2 H, env, $CHHCH_2N$ and $CHCH_2CH_2N$), 2.09 (1 H, apparent t, *J* 11.2, $CHCHHN$), 2.22-2.28 (1 H, m, CH_2CHHN), 2.37 (1 H, dt, *J* 4.1 and 11.2,

C*H*CH_2N), 2.43 (3 H, s, C*H*$_3$), 3.52 (1 H, d, *J* 2.9, C*H*$(CO_2Et)_2$), 3.71-3.76 (1 H, m, CHCH*H*N), 3.79-3.85 (1 H, m, CH_2CH*H*N), 4.08-4.19 (4 H, m, 2 x C*H*$_2CH_3$), 4.78 (1 H, br s, C=C*H*H), 4.93 (1 H, t, *J* 1.5, C=CH*H*), 7.31 (2 H, d, *J* 8.1, Ar C*H*), 7.62 (2 H, d, *J* 8.1, Ar C*H*); δ_C(100 MHz) 14.0 (CH_3), 14.1 (CH_3), 20.7 (CH_3), 21.5 (CH_3), 26.8 (CH_2, *C*H_2CH_2N), 38.3 (CH, *C*HCH_2CH_2N), 46.4 (CH, *C*HCH_2N), 46.5 (CH_2, CH_2*C*H_2N), 51.0 (CH_2, CH*C*H_2N), 52.0 (CH, *C*H$(CO_2Et)_2$), 61.2 (CH_2, *C*H_2CH_3), 61.3 (CH_2, *C*H_2CH_3), 114.6 (CH_2, C=*C*H_2), 127.6 (CH, Ar), 129.6 (CH, Ar), 133.1 (C^4), 143.3 (C^4, C=*C*H_2), 143.5 (C^4), 167.8 (C^4, *C*O_2Et), 168.9 (C^4, *C*O_2Et); *m/z* (EI) 437 (M^+, 4%), 392 (5), 346 (4), 282 (100), 278 (9), 241 (17), 210 (4), 184 (5), 155 (19), 122 (48), 107 (5), 96 (55), 91 (68), 65 (12), 42 (38).

(5*S,9*R**,10*S**)-5-Isopropenyl-3-oxo-7-(toluene-4-sulfonyl)-1,1,4-[*tris*(ethoxycarbonyl)methyl]octahydropyrano[3,4-c]pyridine (30) and 3-[*bis*(carbomethoxy)hydroxymethyl]-4-[*bis*(carboethoxy)methyl]-5-isopropenyl-1-(toluene-4-sulfonyl)piperidine (31)**

Methyl aluminium dichloride (1 M soln. in hexanes, 0.13 cm^3, 0.13 mmol) was added to a solution of diester **26** (39 mg, 0.06 mmol) in CH_2Cl_2 (10 cm^3) at ambient temperature. The resulting mixture was stirred for 25 h, after which it was quenched by addition of water (10 cm^3). The aqueous phase was extracted with CH_2Cl_2 (4 x 10 cm^3) and the combined organic phases washed with brine (10 cm^3), dried over Na_2SO_4 and evaporated *in vacuo* to leave a colourless oil, which was purified by flash column chromatography (silica; eluent 2:1 petrol:ethyl acetate) to give an inseparable mixture of piperidines **30** and **31** as a white crystalline solid (25 mg); (R_f = 0.41); data were recorded on the mixture; ν_{max}(neat)/cm^{-1} 2986 (CH), 2932 (CH), 1736 (C=O), 1643 (C=C), 1597 (ArC=C), 1335 (SO_2), 1157 (SO_2); resonances from the major lactone product were clearly distinguishable. NMR data for lactone; δ_H(500 MHz) 1.20-1.39 (9 H, env, 3 x CH_2C*H*$_3$), 1.56 (3 H, s, C*H*$_3$), 2.12-2.20 (1 H, m, C*H*C=CH_2), 2.21-2.33 (2 H, env, C*H*CH_2N and C=CCHC*H*HN), 2.39-2.51 (4 H, env, C*H*$_3$ and C*H*C$(CO_2Et)_2$O), 2.59 (1 H, t, *J* 11.6, C*H*HN), 3.24 (1 H, d, *J* 9.8, C*H*$(CO_2)_2$), 3.72-3.77 (1 H, m, C=CCHCH*H*N), 4.12 (2 H, q, *J* 7.1, C*H*$_2CH_3$), 4.19-4.25 (1 H, m, CH*H*N), 4.26-4.39 (4 H, env, 2 x C*H*$_2CH_3$), 4.81 (1 H, s, C=C*H*H), 4.87 (1 H, s, C=CH*H*), 7.34 (2 H, d, *J* 8.2, Ar C*H*), 7.67 (2 H, d, *J* 8.2, Ar C*H*); δ_C(125 MHz) 13.8 (CH_3, 2 x CH_2*C*H_3), 13.9 (CH_3, CH_2*C*H_3), 19.8 (CH_3), 21.6 (CH_3), 36.5 (CH, *C*HCHCH_2N), 40.0 (CH, *C*HC$(CO_2Et)_2$O), 46.4 (CH_2, *C*H_2N), 49.8 (CH_2, *C*H_2N), 50.7 (CH, *C*HC=C), 52.4 (CH, *C*H$(CO_2)_2$), 62.1 (CH_2, *C*H_2CH_3), 63.4 (CH_2, *C*H_2CH_3), 63.5 (CH_2, *C*H_2CH_3), 85.0 (C^4, *C*$(CO_2Et)_2$O), 117.0 (CH_2, C=*C*H_2), 127.5 (CH, Ar), 129.9 (CH, Ar), 133.9 (C^4), 140.8 (C^4, *C*=CH_2), 143.9 (C^4), 163.5 (C^4), 163.8 (C^4), 165.8 (C^4), 167.4 (C^4); HRMS (ES) 588.1887 ([M(**30**)+Na]$^+$, $C_{27}H_{35}NO_{10}NaS$ requires 588.1879); *m/z* (ES) 634

([M(**31**)+Na]$^+$, 6%), 588 ([M(**30**)+Na]$^+$, 100). Further elution afforded alcohol **31** as a colourless oil (4 mg, 10%); (R_f = 0.34); *m/z* (ES) 634 ([M+Na]$^+$, 100%).

(*E*)-4-Aza-1-bromo-4-(*p*-toluenesulfonyl)hept-6-ene

The bromide were prepared as for **23** from a 5:1 mixture of alcohols **32** and **33** (1.51 g, 5.33 mmol), triphenylphosphine (1.80 g, 6.86 mmol) and carbon tetrabromide (2.29 g, 6.88 mmol). Concentration *in vacuo* followed by flash column chromatography (silica; eluent 3:1 hexane/ethyl acetate) afforded the *title compound* as a colourless oil (1.78 g, 97%); (R_f = 0.44) containing a 5:1 mixture of (*E*) and (*Z*) crotyl isomers; ν_{max} (film)/cm^{-1} 2923 (CH), 2863 (CH), 1668 (C=C), 1598 (Ar C=C), 1447 (Ar C=C), 1339 (SO_2), 1159 (SO_2); δ_H (300 MHz) 1.54-1.66 (3 H major isomer and 3 H minor isomer, env, including 1.62 (3 H, d, *J* 5.9, CH_3 major isomer) and CH_3, minor isomer), 2.12 (2 H major isomer and 2 H minor isomer, p, *J* 6.7, C*H*$_2$CH$_2$N, major and minor isomers), 2.42 (3 H major isomer and 3 H minor isomer, s, CH_3, major and minor isomers), 3.20 (2 H major isomer and 2 H minor isomer, t, *J* 6.7, CH$_2$C*H*$_2$N, major and minor isomers), 3.42 (2 H major isomer and 2 H minor isomer, t, *J* 6.7, CH_2Br, major and minor isomers), 3.69 (2 H, d, *J* 6.6, NC*H*$_2$CH, major isomer), 3.84 (2 H, d, *J* 6.6, NC*H*$_2$CH, minor isomer), 5.15-5.31 (1 H major isomer and 1 H minor isomer, m, C*H*CH$_3$, major and minor isomers), 5.55-5.69 (1 H major isomer and 1 H minor isomer, m, NCH$_2$C*H*, major and minor isomers), 7.30 (2 H major isomer and 2 H minor isomer, d, *J* 8.1, Ar CH, major and minor isomers), 7.69 (2 H major isomer and 2 H minor isomer, d, *J* 8.1, Ar CH, major and minor isomers); δ_C (75 MHz) 13.2 (CH_3, minor isomer), 17.9 (CH_3, major isomer), 21.9 (CH_3, major and minor isomers), 30.8 (CH_2, minor isomer), 30.8 (CH_2, major isomer), 32.1 (CH_2, major isomer), 32.4 (CH_2, minor isomer), 45.4 (CH_2, minor isomer), 45.9 (CH_2, major isomer), 46.6 (CH_2 minor isomer), 51.1 (CH_2CH major isomer), 125.0 (CH, minor isomer), 125.6 (CH, major isomer), 127.5 (CH, Ar, major and minor isomers), 129.2 (CH, minor isomer), 129.9 (CH, Ar, major), 130.0 (CH, Ar minor), 131.2 (CH, major isomer), 137.0 (C^4, major and minor isomers), 143.6 (C^4, major and minor isomers); *m/z* (ES$^+$) 370.0 (95%, [M(^{81}Br)+Na]$^+$), 368.0 (100%, [M(^{79}Br)+Na]$^+$), 266.2 (13%, [M-Br]$^+$); HRMS (ES$^+$) Found: 368.0309, required for $C_{14}H_{20}NO_2S^{79}BrNa$: 368.0296.

(*Z*)-4-Aza-1-bromo-4-(*p*-toluenesulfonyl)hept-6-ene

The bromide was prepared as for **23** from alcohol **33** (0.95 g, 3.35 mmol), triphenylphosphine (1.14 g, 4.35 mmol) and carbon tetrabromide (1.45 g, 4.36 mmol). Concentration *in vacuo* followed by flash column chromatography (silica; eluent 3:1 hexane/ethyl acetate) afforded the *title compound* as a colourless crystalline solid containing traces of the (*E*) isomer as a inseparable impurity (1.13 g, 97%); (R_f = 0.43); mp 50-52 °C (from hexane/ethyl acetate); ν_{max} (film)/cm^{-1} 2923 (CH), 2863

(CH), 1669 (C=C), 1598 (Ar C=C), 1447 (Ar C=C), 1339 (SO_2), 1158 (SO_2); NMR data reported for major isomer only: δ_H (300 MHz) 1.62 (3 H, d, *J* 6.6, CH_3), 2.12 (2 H, p, *J* 6.7, C*H*$_2$CH$_2$N), 2.42 (3 H, s, CH_3), 3.20 (2 H, t, *J* 6.7, CH$_2$C*H*$_2$N), 3.42 (2 H, t, *J* 6.7, C*H*$_2$Br), 3.84 (2 H, d, *J* 6.6, NC*H*$_2$CH), 5.15-5.31 (1 H, m, C*H*CH$_3$), 5.55-5.69 (1 H, m, NCH$_2$C*H*), 7.30 (2 H, d, *J* 8.1, Ar CH), 7.69 (2 H, d, *J* 8.1, Ar CH); δ_C (75 MHz) 13.2 (CH_3), 21.9 (CH_3), 30.8 (CH_2), 32.4 (CH_2), 45.4 (CH_2), 46.6 (CH_2), 125.0 (CH), 127.5 (CH, Ar), 129.2 (CH), 130.0 (CH, Ar), 137.0 (C^4), 143.6 (C^4); *m/z* (ES^+) 370.2 (100%, $[M(^{81}Br)+Na]^+$), 368.2 (98%, $[M(^{79}Br)+Na]^+$); HRMS (ES^+) Found: 368.0307, required for $C_{14}H_{20}NO_2S^{79}BrNa$: 368.0296.

(*E*)-2-[4-Aza-4-(*p*-toluenesulfonyl)oct-6-enyl]malonic acid dimethyl ester

The diester was prepared as for 2-[4-aza-7-methyl-4-(*p*-toluenesulfonyl)oct-6-enyl]malonic acid dimethyl ester from a 5:1 *E:Z* mixture of 4-aza-1-bromo-4-(*p*-toluenesulfonyl)hept-6-ene (1.53 g, 4.42 mmol), NaHMDS (4.45 mL, 4.45 mmol) and dimethyl malonate (0.51 mL, 0.59 g, 4.46 mmol). Concentration *in vacuo* followed by flash column chromatography (silica; eluent 3:1 hexane/ethyl acetate) afforded the *title compound* as a colourless oil (1.24 g, 71%) containing a mixture of (*E*) and (*Z*) isomers; (R_f = 0.38); ν_{max} (film)/cm^{-1} 2954 (CH), 2871 (CH), 1736.1 (C=O), 1735.9 (C=O), 1598 (Ar C=C), 1437 (Ar C=C), 1339 (SO_2), 1160 (SO_2); δ_H (300 MHz) 1.46-1.64 (5 H major isomer and 5 H minor isomer, env including 1.62 (3 H major isomer and 3 H minor isomer, d, *J* 5.5, CH_3, major and minor isomers and CH_2, major and minor isomers), 1.80-1.92 (2 H major isomer and 2 H minor isomer, m, CH_2, major and minor isomers), 2.40 (3 H major isomer and 3 H minor isomer, s, CH_3, major and minor isomers), 3.07 (2 H major isomer and 2 H minor isomer, t, *J* 7.2, CH$_2$C*H*$_2$N, major and minor isomers), 3.34 (1 H, t, *J* 7.4, C*H*(CO$_2$CH$_3$)$_2$), major isomer), 3.37 (1 H, t, *J* 7.4, C*H*(CO$_2$CH$_3$)$_2$, minor isomer), 3.63-3.83 (8 H major isomer and 6 H minor isomer, env including 3.72 (6 H major isomer and 6 H minor isomer, s, 2 × CO$_2$CH$_3$, major and minor isomers) and NC*H*$_2$CH, major isomer), 3.83 (2 H, d, *J* 7.0, NC*H*$_2$CH minor isomer), 5.10-5.27 (1 H major isomer and 1 H minor isomer, m, C*H*CH$_3$, major and minor isomers), 5.47-5.63 (1 H major isomer and 1 H minor isomer, m, NCH$_2$C*H*, major and minor isomers), 7.27 (2 H major isomer and 2 H minor isomer, d, *J* 8.1, Ar CH, major and minor isomers), 7.65 (2 H major isomer and 2 H minor isomer, d, *J* 8.1, Ar CH, major and minor isomers); δ_C (75 MHz) 13.2 (CH_3, minor isomer), 17.9 (CH_3, major isomer), 21.9 (CH_3, major and minor isomers), 26.1 (CH_2, major and minor isomers), 26.4 (CH_2, major and minor isomers), 44.5 (CH_2, minor isomer), 46.6 (CH_2, major isomer), 47.0 (CH_2, minor isomer), 50.3 (CH_2, major isomer), 51.4 (*C*H(CO$_2$*C*H$_3$)$_2$, major and minor isomer), 52.9 (2 × CO$_2$*C*H$_3$, major and minor isomers), 125.1 (CH, minor isomer), 125.8 (CH, major isomer), 127.5 (CH, Ar, major and minor isomers), 128.9 (CH, minor isomer), 130.0 (CH, Ar, major and minor isomers), 130.8 (CH, major isomer), 137.2 (C^4, major and minor isomers), 143.4

(C^4, major and minor isomers), 169.9 (C=O, major and minor isomers); *m/z* (ES^+) 420.5 (100%, $[M+Na]^+$); HRMS (ES^+) Found: 420.1461, required for $C_{19}H_{27}NO_6NaS$: 420.1457.

(*Z*)-2-[4-Aza-4-(*p*-toluenesulfonyl)oct-6-enyl]malonic acid dimethyl ester

The diester was prepared as for 2-[4-aza-7-methyl-4-(*p*-toluenesulfonyl)oct-6-enyl]malonic acid dimethyl ester from bromide (*Z*)-4-aza-1-bromo-4-(*p*-toluenesulfonyl)hept-6-ene (1.03 g, 2.97 mmol), NaHMDS (3.00 mL, 3.00 mmol) and dimethyl malonate (0.34 mL, 0.39 g, 2.97 mmol). Concentration *in vacuo* followed by flash column chromatography (silica; eluent 3:1 hexane/ethyl acetate) afforded the *title compound* as a colourless oil (0.74 g, 63%) containing small traces of the (*E*) isomer as an inseparable impurity; (R_f = 0.40); ν_{max} (film)/cm^{-1} 2955 (CH), 1740 (C=O), 1736 (C=O), 1598 (Ar C=C), 1494 (Ar C=C), 1436 (Ar C=C), 1341 (SO_2), 1159 (SO_2); NMR data reported for major isomer only: δ_H (300 MHz) 1.49-1.59 (5 H, env including 1.60 (3 H, d, *J* 5.9, CH_3) and CH_2), 1.83-1.94 (2 H, m, CH_2), 2.41 (3 H, s, CH_3), 3.09 (2 H, t, *J* 7.4, CH_2CH_2N), 3.37 (2 H, t, *J* 7.4, $CH(CO_2CH_3)_2$), 3.72 (6 H, s, 2 × CO_2CH_3), 3.83 (2 H, d, *J* 7.0, NCH_2CH), 5.12-5.25 (1 H, m, $CHCH_3$), 5.51-5.65 (1 H, m, NCH_2CH), 7.28 (2 H, d, *J* 8.1, Ar CH), 7.67 (2 H, d, *J* 8.1, Ar CH); δ_C (75 MHz) 13.2 (CH_3), 21.9 (CH_3), 26.1 (CH_2), 26.4 (CH_2), 44.5 (CH_2), 47.0 (CH_2), 51.4 ($CH(CO_2CH_3)_2$), 52.9 (2 × CO_2CH_3), 125.1 (CH), 127.5 (CH, Ar), 128.9 (CH), 130.0 (CH, Ar), 137.2 (C^4), 143.4 (C^4), 169.9 (C=O); *m/z* (ES^+) 420.0 (100%, $[M+Na]^+$); HRMS (ES^+) Found: 420.1456, required for $C_{19}H_{27}NO_6SNa$: 420.1457.

(*E*)-2-[4-Aza-4-(*p*-toluenesulfonyl)oct-6-enylidine]malonic acid dimethyl ester (34)

Diester **34** was prepared as for **19** from 2-[4-aza-4-(*p*-toluenesulfonyl)oct-6-enyl]malonic acid dimethyl ester (1.23 g, 3.09 mmol), *n*-BuLi (2.1 M solution in hexanes, 1.65 mL, 3.47 mmol), diisopropylamine (0.55 mL, 3.90 mmol) and PhSeCl (0.91 g, 4.73 mmol) to give, after flash column chromatography (silica; eluent 15:1 toluene/diethyl ether), the (*E*) and (*Z*) selenides as a yellow oil (1.54 g, 90%); (R_f = 0.55); δ_H (300 MHz) 1.59-1.73 (5 H major isomer and 5 H minor isomer, env including 1.63 (3 H, d, *J* 6.3, CH_3, major isomer), CH_3, minor isomer and CH_2, major and minor isomers), 1.75-1.88 (2 H, m, CH_2, major and minor isomers), 2.41 (3 H major isomer and 3 H minor isomer, s, CH_3, major and minor isomers), 3.04 (2 H major isomer and 2 H minor isomer, t, *J* 7.2, CH_2CH_2N, major and minor isomers), 3.66-3.79 (8 H major isomer and 6 H minor isomer, env including 3.71 (6 H major isomer and 6 H minor isomer, s, 2 × CO_2CH_3, major and minor isomers and NCH_2CH, major isomer), 3.80-3.88 (2 H, m, NCH_2CH, minor isomer), 5.14-5.27 (1 H major isomer and 1 H minor isomer, m, $CHCH_3$, major and minor isomers), 5.49-5.64 (1 H major isomer and 1 H minor isomer, m, NCH_2CH, major and minor isomers), 7.11-7.37 (4 H major isomer and 4 H minor isomer, env, Ar CH, major and minor isomers), 7.37-7.46 (1 H major isomer and 1 H

minor isomer, m, Ar CH, major and minor isomers), 7.53 (1 H major isomer and 1 H minor isomer, d, *J* 8.1, Ar CH, major and minor isomers), 7.66 (1 H major isomer and 1 H minor isomer, d, *J* 8.1, Ar CH, major and minor isomers).

The (*E*) and (*Z*) selenides (1.32 g, 2.39 mmol) were immediately treated with H_2O_2 (0.54 mL, 30% aqueous solution, 4.76 mmol). Aqueous work-up and concentration *in vacuo* followed by flash column chromatography (silica; eluent 15:1 toluene/diethyl ether) afforded diester **34** as a colourless oil (0.73 g, 77%) containing a 5:1 mixture of (*E*) and (*Z*) isomers; (R_f = 0.45); Found: C 57.50, H 6.36, N 3.24; Required for $C_{19}H_{25}NO_6S$: C 57.70, H 6.37, N 3.54; ν_{max} (film)/cm^{-1} 2954 (CH), 1735 (C=O), 1729 (C=O), 1649 (C=C), 1598 (Ar C=C), 1494 (Ar C=C), 1437 (Ar C=C), 1339 (SO_2), 1160 (SO_2); δ_H (300 MHz) 1.55-1.63 (3 H major isomer and 3 H minor isomer, env including 1.60 (3 H, d, *J* 6.3, CH_3, major isomer) and CH_3 minor isomer), 2.42 (3 H major isomer and 3 H minor isomer, s, CH_3, major and minor isomers), 2.56 (2 H major isomer and 2 H minor isomer, apparent q, *J* 7.4, C*H*$_2$CH$_2$N, major and minor isomers), 3.20 (2 H major isomer and 2 H minor isomer, t, *J* 7.4, CH$_2$C*H*$_2$N, major and minor isomers), 3.68 (2 H, d, *J* 7.4, NC*H*$_2$CH, major isomer), 3.75 (3 H major isomer and 3 H minor isomer, s, CO_2CH_3, major and minor isomers), 3.77-3.83 (3 H major isomer and 5 H minor isomer, env including 3.79 (3 H major isomer and 3 H minor isomer, s, CO_2CH_3, major and minor isomers) and NC*H*$_2$CH, minor isomer), 5.13-5.27 (1 H major isomer and 1 H minor isomer, m, C*H*CH$_3$, major and minor isomers), 5.51-5.69 (1 H major isomer and 1 H minor isomer, m, NCH$_2$C*H*, major and minor isomers), 6.94 (1 H, t, *J* 7.9, C*H*CH$_2$CH$_2$N, major isomer), 6.98 (1 H, t, *J* 7.9, C*H*CH$_2$CH$_2$N, minor isomer), 7.28 (2 H major isomer and 2 H minor isomer, d, *J* 8.1, Ar CH, major and minor isomers), 7.66 (2 H major isomer and 2 H minor isomer, d, *J* 8.1, Ar CH, major and minor isomers); δ_C (75 MHz) 13.1 (CH_3, minor isomer), 17.9 (CH_3, major isomer), 21.8 (CH_3, major and minor isomers), 29.7 (*C*H$_2$CH$_2$N, major and minor isomers), 44.8 (CH_2, minor isomer), 45.5 (CH_2, major isomer), 45.9 (CH_2, minor isomer), 50.7 (CH_2, major isomer), 52.5 (CO_2CH_3, major and minor isomers), 52.6 (CO_2CH_3, major and minor isomers), 124.8 (CH, minor isomer), 125.6 (CH, major isomer), 127.4 (CH, Ar, major and minor isomers), 129.3 (CH, minor isomer), 129.8 (C^4, minor and major isomers), 129.9 (CH, Ar, major and minor isomers), 131.3 (CH, major isomer), 136.8 (C^4, major and minor isomers), 143.8 (C^4, major and minor isomers), 146.5 (*C*HCH$_2$CH$_2$N, major and minor isomers), 164.3 (C=O, major and minor isomers), 165.6 (C=O, major and minor isomers); *m/z* (ES^+) 418.0 (100%, $[M+Na]^+$); HRMS (ES^+) Found: 418.1296, required for $C_{19}H_{25}NO_6SNa$: 418.1300.

(*Z*)-2-[4-Aza-4-(*p*-toluenesulfonyl)oct-6-enylidine]malonic acid dimethyl ester (35)

Diester **35** was prepared as for **19** from (*Z*)-2-[4-aza-4-(*p*-toluenesulfonyl)oct-6-enyl]malonic acid dimethyl ester (0.97 g, 2.44 mmol), *n*-BuLi (2.1 M solution in hexanes, 1.28 mL, 2.69 mmol), diisopropylamine (0.42 mL, 2.98 mmol), PhSeCl (0.71 g, 3.69 mmol) to give, after flash column

chromatography (silica; eluent 15:1 toluene/diethyl ether), the selenide as a yellow oil (1.12 g, 83%); (R_f = 0.56); δ_H (300 MHz) 1.51-1.74 (5 H major isomer and 5 H minor isomer, env including 1.55 (3 H, d, *J* 8.8, CH_3, major isomer), CH_3, minor isomer and CH_2, major and minor isomers), 1.77-1.89 (2 H major isomer and 2 H minor isomer, m, CH_2, major and minor isomers), 2.41 (3 H major isomer and 3 H minor isomer, s, CH_3, major and minor isomers), 3.04 (2 H major isomer and 2 H minor isomer, t, *J* 7.4, CH_2CH_2N, major and minor isomers), 3.67-3.75 (6 H major isomer and 8 H minor isomer, env including 3.71 (6 H major isomer and 6 H minor isomer, s, $2 \times CO_2CH_3$, major and minor isomers and NCH_2CH, minor isomer), 3.84 (2 H, d, *J* 6.6, NCH_2CH, major isomer), 5.12-5.26 (1 H major isomer and 1 H minor isomer, m, $CHCH_3$, major and minor isomers), 5.50-5.67 (1 H major isomer and 1 H minor isomer, m, NCH_2CH, major and minor isomers), 7.14-7.37 (4 H major isomer and 4 H minor isomer, env, Ar CH, major and minor isomers), 7.38-7.46 (1 H major isomer and 1 H minor isomer, m, Ar CH, major and minor isomers), 7.53 (1 H major isomer and 1 H minor isomer, d, *J* 8.1, Ar CH, major and minor isomers), 7.67 (1 H major isomer and 1 H minor isomer, d, *J* 8.1, Ar CH, major and minor isomers).

The selenide (0.94 g, 1.70 mmol) was treated with H_2O_2 (0.39 mL, 30% aqueous solution, 3.44 mmol). Aqueous work-up, concentration *in vacuo* followed by flash column chromatography (silica; eluent 15:1 toluene/diethyl ether) afforded the diester **35** as a colourless oil (0.54 g, 80%) containing a 5:1 mixture of (*Z*) and (*E*) isomers; (R_f = 0.47); ν_{max} (film)/cm^{-1} 2955 (CH), 1739 (C=O), 1731 (C=O), 1649 (C=C), 1598 (Ar C=C), 1438 (Ar C=C), 1339 (SO_2), 1160 (SO_2); NMR signals for major isomer reported only: δ_H (300 MHz) 1.61 (3 H, d, *J* 8.5, CH_3), 2.42 (3 H, s, CH_3), 2.56 (2 H, apparent q, *J* 7.4, CH_2CH_2N), 3.20 (2 H, t, *J* 7.4, CH_2CH_2N), 3.75 (3 H, s, CO_2CH_3), 3.77-3.89 (5 H, env including (3 H, s, CO_2CH_3) and NCH_2CH), 5.13-5.30 (1 H, m, $CHCH_3$), 5.51-5.69 (1 H, m, NCH_2CH), 6.98 (1 H, t, *J* 7.9, $CHCH_2CH_2N$), 7.28 (2 H, d, *J* 8.1, Ar CH), 7.66 (2 H, d, *J* 8.1, Ar CH); δ_C (75 MHz) 13.1 (CH_3), 21.8 (CH_3), 29.7 (CH_2CH_2N), 44.8 (CH_2), 45.9 (CH_2), 52.5 (CO_2CH_3), 52.6 (CO_2CH_3), 125.2 (CH), 127.9 (CH, Ar), 129.7 (CH), 130.3 (C^4), 130.4 (CH, Ar), 137.3 (C^4), 143.8 (C^4), 146.9 ($CHCH_2CH_2N$), 164.9 (C=O), 166.3 (C=O); *m/z* (ES^+) 418.2 (100%, $[M+Na]^+$; HRMS (ES^+) Found: 418.1308, required for $C_{19}H_{25}NO_6SNa$: 418.1300.

(3*S,4*S**)-4-[Bis(carbomethoxy)methyl]-3-vinyl-1-(*p*-toluenesulfonyl) piperidine (36), (3*R**,4*S**)-4-[bis(carbomethoxy)methyl]-3-vinyl-1-(*p*-toluene sulfonyl)piperidine (37), *N*-(*p*-toluenesulfonyl)but-2-en-1-amine (38)**

Lewis acid-catalysed cyclisation of a 5:1 mixture of **34** and **35**: $MeAlCl_2$ (1 M solution in hexanes, 255 μL, 0.255 mmol) was added dropwise to a solution of a 5:1 mixture of (*E*) and (*Z*) diesters **34** and **35** (100 mg, 0.252 mmol), in CH_2Cl_2 (20 mL) under argon at ambient temperature. The reaction was stirred for 24 h before pouring into water (20 mL). The aqueous phase was extracted with

CH_2Cl_2 (4 × 20 mL) and the organic extracts washed with brine (20 mL), dried over $MgSO_4$ and concentrated *in vacuo* to give a colourless oil which was purified by flash column chromatography (silica; eluent 3:1 hexane/ethyl acetate) to afford first the cleavage product **38** (R_f = 0.42) as a colourless oil (13 mg, 20%) containing a 7:1 inseparable mixture of (*E*) and (*Z*) isomers, followed by piperidines **36** and **37** (R_f = 0.24) as a colourless oil (60 mg, 60%) containing a 20:1 inseparable mixture of *trans* and *cis* isomers.

Lewis acid-catalysed cyclisation of a 1:5 mixture of **34** and **35**:

Cyclisation of a 1:5 mixture of (*E*) and (*Z*) diesters **34** and **25** (100 mg, 0.252 mmol) was performed as for the 5:1 mixture of (*E*) and (*Z*) isomers with $MeAlCl_2$ (1 M solution in hexanes, 255 μL, 0.255 mmol). Aqueous work-up followed by flash column chromatography afforded a complex mixture of products (67 mg) from which small amounts of the *trans* piperidine **36** were isolated *via* semi-preparative HPLC (1:1 water/acetonitrile over 110 min).

Data for **38** recorded on a 7:1 *E:Z* mixture: δ_H (300 MHz) 1.54 (3 H, d, *J* 7.0, CH_3, minor isomer), 1.60 (3 H, d, *J* 6.3, CH_3, major isomer), 2.42 (3 H major isomer and 3 H minor isomer, s, CH_3, major and minor isomers), 3.49 (2 H, t, *J* 5.7, CH_2, major isomer), 3.60 (2 H, t, *J* 6.1, CH_2, minor isomer), 4.35-4.47 (1 H major isomer and 1 H minor isomer, m, NH, major and minor isomers), 5.25-5.39 (1 H major isomer and 1 H minor isomer, m, C*H*CH_3, major and minor isomers), 5.49-5.64 (1 H major isomer and 1 H minor isomer, m, NCH_2CH, major and minor isomers), 7.30 (2 H major isomer and 2 H minor isomer, d, *J* 8.1, Ar CH, major and minor isomers), 7.70-7.79 (2 H major isomer and 2 H minor isomer, env including 7.74 (2 H, d, *J* 8.1, Ar CH, major isomer) and Ar CH, minor isomer); ^{13}C NMR Signals reported for major isomer only: δ_C (75 MHz) 17.9 (CH_3), 21.9 (CH_3), 45.7 (CH_2), 125.9 (CH), 127.5 (CH, Ar), 130.0 (CH, Ar), 130.2 (CH), 137.3 (C^4), 143.7 (C^4); *m/z* (ES^+) 280.0 (100%, $[M+Na+MeOH]^+$), 248.0 (50%, $[M+Na]^+$); HRMS (ES^+) Found: 248.0711, required for $C_{11}H_{15}NO_2SNa$: 248.0721.

Data for **36** and **37** recorded on a 20:1 mixture:

Analytical HPLC (1:1 water/acetonitrile over 60 min); t_r = 22.61 min; ν_{max} (film)/cm^{-1} 2954 (CH), 1739 (C=O), 1733 (C=O), 1646 (C=C), 1598 (Ar C=C), 1437 (Ar C=C), 1341 (SO_2), 1165 (SO_2); NMR data reported for major isomer only: δ_H (300 MHz) 1.51-1.71 (2 H, m, C*H*HCH_2N), 1.76-1.91 (2 H, env, C*H*CH_2CH_2N and CH*H*CH_2N), 2.03 (1 H, t, *J* 11.4, NC*H*HCH), 2.23 (1 H, td, *J* 11.8, 2.3, CH_2CHHN), 2.30-2.48 (4 H, env including 2.43 (3 H, s, CH_3) and NCH_2CH), 3.54 (1 H, d, *J* 4.0, C*H*$(CO_2CH_3)_2$), 3.60-3.75 (8 H, env including 3.66 (3 H, s, CO_2CH_3), 3.71 (3 H, s, CO_2CH_3) and NCH*H*CH), 3.76-3.87 (1 H, m, CH_2CHHN), 5.12-5.23 (2 H, env, $CH=CH_2$), 5.38 (1 H, dt, *J* 16.9, 9.6, C*H*=CH_2), 7.32 (2 H, d, *J* 8.1, Ar CH), 7.62 (2 H, d, *J* 8.1, Ar CH); δ_C (75 MHz) 21.9 (CH_3), 27.3 (CH_2CH_2N), 40.1 ($CHCH_2CH_2N$), 44.6 (NCH_2CH), 46.6 (CH_2CH_2N), 51.3 (NCH_2CH), 52.7 ($CH(CO_2CH_3)_2$), 52.8 (CO_2CH_3), 53.1 (CO_2CH_3), 119.8 ($CH=CH_2$), 128.0 (CH, Ar), 130.0

(CH, Ar), 133.2 (C^4), 136.9 (*C*H=CH_2), 144.0 (C^4), 168.7 (C=O), 169.5 (C=O); *m/z* (ES^+) 418.0 (100%, $[M+Na]^+$); HRMS (ES^+) Found: 418.1316, required for $C_{19}H_{25}NO_6SNa$: 418.1300.

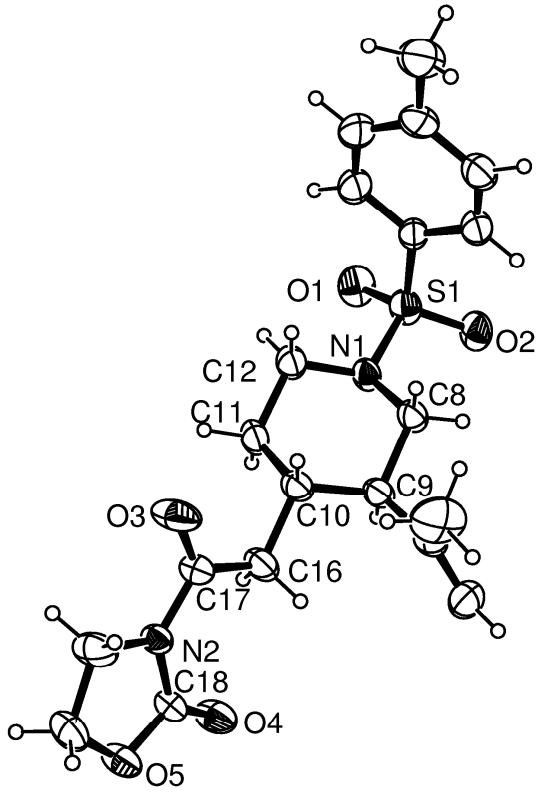

Figure S1. ORTEP plot of 8. Ellipsoids drawn at 30% probability.

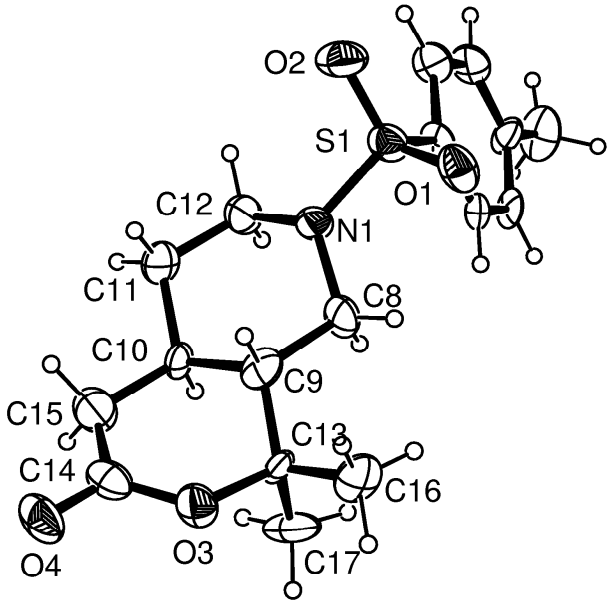

Figure S2. ORTEP plot of 10. Ellipsoids drawn at 30% probability.

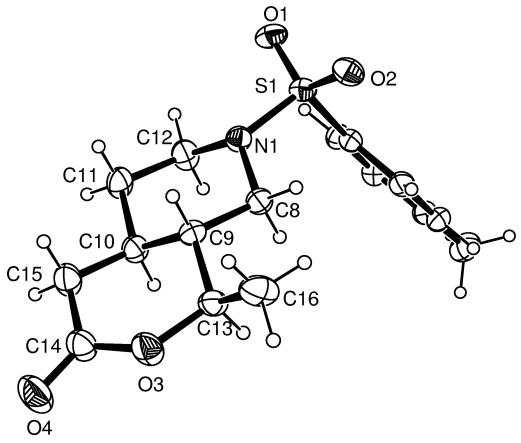

Figure S3. ORTEP plot of 17. Ellipsoids drawn at 30% probability.

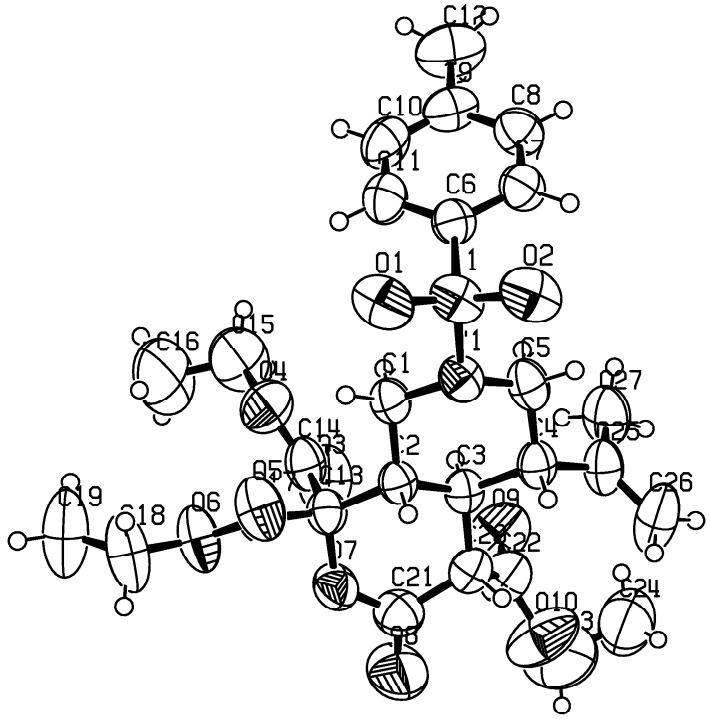

Figure S4. ORTEP plot of 30. Ellipsoids drawn at 30% probability.