Stereoselective γ-Lactam Synthesis *via* Palladium-catalysed Intramolecular Allylation

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Experimental procedures and spectroscopic data/physical characteristics of all compounds prepared in this work

N-(Toluene-4-sulfonyl)-L-serine

To a rapidly-stirred solution of L-serine (18.0 g, 171 mol, 1.0 equiv) and TsCl (43.2 g, 227 mol, 1.3 equiv) in EtOAc (400 ml) and H_2O (120 ml) was added NaOH (228 ml of a 2 M aqueous solution, 456 mmol, 2.7 equiv) dropwise over 3 h. After a further 1 h the phases were separated and the aqueous layer acidified with *c*.HCl (25 ml). The resulting white precipitate was filtered and dried azeotropically with toluene to yield *N*-(toluene-4-sulfonyl)-L-serine (26.2 g, 79%) as a colourless solid; mp 236 ºC (EtOAc); R_f 0.32 (50% EtOAc–petrol); δ_H (300 MHz) 7.94 (1H, d, J 8.5 Hz, NH), 7.68 (2H, d, J 8.5 Hz, *ortho* Ts), 7.36 (2H, d, J 8.5 Hz, *meta* Ts), 3.75-3.68 (1H, m, C*H*NHTs), 3.53-3.49 (2H, m, CH_2OH), 2.50 (1H, s, CH_2OH), 2.37 (3H, s, Me of Ts); *m/z* (CI) 277 $[M+NH_4]^+$. *In agreement with published data*.[1]

(+)-(*S*)-3-hydroxy-1-(4-methoxyphenyl)-2-(toluene-4-sulfonamido)propan-1-one

Activated magnesium turnings (15.4 g, 632 mmol, 4.1 equiv) were suspended in THF (400 ml) and 4-bromoanisole (77.2 ml, 616 mmol, 4.0 equiv) added dropwise to maintain a steady reflux. After stirring for 1 h the mixture was transferred to a solution of acid **170** (40.0 g, 154 mmol, 1.0 equiv), and *n*-BuLi (193 ml of a 1.6 M solution in hexanes, 308 mmol, 2.0 equiv) in THF (400 ml) at –78 ºC. The mixture was allowed to warm to rat and after 37 h the reaction mixture was poured into HCl (1 M; 400 ml) and extracted with Teac (3 x 400 ml). The combined organic extracts were washed with saturated aqueous $NaHCO_3$ (600 ml) and dried ($MgSO_4$). Concentration under reduced pressure and recrystallisation (EtOAc–petrol) gave the *ketone* (39.0 g, 73%) as an off-white solid; mp 80–82 ºC (EtOH); R_f 0.25 (10% EtOAc–CH_2Cl_2); $[\alpha]_D^{20}$ +84.0 (*c* 1.0, EtOH); ν_{max} (film) 3489, 3283, 3264, 1680, 1601, 1336, 1308, 1165, 910, 739 cm^{-1}; δ_H (300 MHz), 7.80 (2H, d, J 9.0 Hz, *ortho* ArOMe), 7.73 (2H, d, J 8.0 Hz, *ortho* Ts), 7.21 (2H, d, J 8.0 Hz, *meta* Ts), 6.93 (2H, d, J 9.0 Hz, *meta* ArOMe), 6.11 (1H, d, J 7.5 Hz, N*H*Ts), 4.90-4.85 (1H, m, C*H*NHTs), 4.10-3.90 (1H, m, C*H*HOH), 3.88 (3H, s, ArO*Me*), 3.78-3.73 (1H, m, CH*H*OH), 2.34 (3H, s, Me of Ts); δ_C (75 MHz) 202.2 (C=O), [164.5, 144.0, 136.5 (q Ar)], [131.1, 129.8, 127.1 (ArH)], 126.5 (q Ar), 114.2 (ArH),

64.7 (CH_2OH), 59.6 and 55.7 (*C*HNHTs and OMe of ArOMe), 21.8 (Me of Ts); *m/z* (CI) 367 $[M+NH_4]^+$, 350 $[M+H]^+$ (Found: C, 58.49; H, 5.32; N, 3.92. $C_{17}H_{19}NO_5S$ requires C, 58.44; H, 5.48; N, 4.01%).

(+)-(*R*)-2-(Toluene-4-sulfonamido)-3-(4-methoxyphenyl)propan-1-ol (3)

(+)-(*S*)-3-Hydroxy-1-(4-methoxyphenyl)-2-(toluene-4-sulfonamido)propan-1-one (30.1 g, 85.9 mmol, 1.0 equiv) was dissolved in trifluoroacetic acid (132 ml, 1.72 mol, 20.0 equiv), treated dropwise with triethylsilane (137 ml, 860 mmol, 10.0 equiv) over 3 h and stirred at 40 ºC for 1 d. NaOH (2 M; 1.5 l) was then added and the mixture extracted with EtOAc (3 x 500 ml). The combined organic extracts were concentrated under reduced pressure and the resulting residue stirred with 4% NaOH–MeOH (500 ml) for 1 h. The solution was then diluted with Et_2O (500 ml) and HCl (2 M; 500 ml) and the aqueous phase extracted with Et_2O (2 x 500 ml). The combined organic extracts were washed with H_2O (500 ml), brine (500 ml) and dried ($MgSO_4$). Concentration under reduced pressure and chromatography (60% Et_2O–petrol) gave alcohol **3** (27.0 g, 93%) as a colourless oil; R_f 0.65 (90% CH_2Cl_2–EtOAc); $[\alpha]_D^{20}$ +12.7 (*c* 1.3, $CHCl_3$); ν_{max} (film) 3517, 3289, 1612, 1598, 1440, 1423, 1320, 1247, 1157, 1091, 1037, 813, 665, 549 cm^{-1}; δ_H (300 MHz) 7.59 (2H, d, J 8.0 Hz, *ortho* Ts), 7.22 (2H, d, J 8.0 Hz, *meta* Ts), 6.90 (2H, d, J 9.0 Hz, *meta* ArOMe), 6.72 (2H, d, J 9.0 Hz, *ortho* ArOMe), 4.86 (1H, d, J 7.0 Hz, N*H*Ts), 3.79 (3H, s, OMe of ArOMe), 3.66 (1H, dd, J 15.0, 5.0 Hz, C*H*HOH) 3.55 (1H, dd, J 11.0, 5.0 Hz, CH*H*OH) 3.41-3.39 (1H, m, C*H*NHTs), 2.74 (1H, dd, J 14.0, 7.0 Hz, C*H*HArOMe), 2.62 (1H, dd, J 14.0, 8.0 Hz, CH*H*ArOMe) 2.44 (3H, s, Me of Ts); δ_C (67.5 MHz) 158.3, 143.2, 137.2, 130.2, 129.7, 129.1, 127.0, 114.0, 64.2, 57.2, 55.2, 36.8, 21.6; *m/z* (CI) 353 $[M+NH_4]^+$, 336 $[M+H]^+$, 189 (Found: $[M+H]^+$, 336.1272. $C_{17}H_{21}NO_4S$ requires $[M+H]^+$, 336.1270).

(+)-(*R*)-(*E*)-Ethyl 5-(4-methoxyphenyl)-4-(toluene-4-sulfonamido)pent-2-enoate

To a solution of $(COCl)_2$ (470 μl, 5.40 mmol, 1.2 equiv) in CH_2Cl_2 (8 ml) at –78 ºC was added DMSO (767 μl, 10.8 mmol, 2.4 equiv) in CH_2Cl_2 (8 ml). After 5 min (+)-(*R*)-2-(toluene-4-sulfonamido)-3-(4-methoxyphenyl)propan-1-ol (1.50 g, 4.48 mmol, 1.0 equiv) in CH_2Cl_2 (10 ml) was added and the solution stirred at –78 ºC for 45 min. Et_3N (3.14 ml, 22.5 mmol, 5.0 equiv) in CH_2Cl_2 (5 ml) was then added and the solution warmed to 0 ºC over 30 min and then to rt. After 10 min the mixture was diluted with CH_2Cl_2 (25 ml) and washed with saturated aqueous $NaHCO_3$ (50 ml). The aqueous layer was extracted with CH_2Cl_2 (2 x 50 ml) and the combined organic extracts washed with H_2O (100 ml), brine (100 ml) and dried (Na_2SO_4). Concentration under reduced pressure gave the crude aldehyde as a yellow oil. This was immediately dissolved in CH_2Cl_2 (50 ml) and to it was added Ph_3PCHCO_2Et (7.83 g, 22.5 mmol, 5.0 equiv). After 12 h the reaction was

concentrated under reduced pressure and triturated with Et_2O (250 ml) to precipitate triphenylphosphine oxide. Concentration of the filtrate under reduced pressure and chromatography (50% EtOAc–petrol) gave the *ester* (1.60 g, 86%) as a colourless oil; R_f 0.65 (50% EtOAc–petrol); $[\alpha]_D^{20}$ +29.6 (*c* 0.5, $CHCl_3$); ν_{max} (film) 3274, 2981, 1716, 1658, 1612, 1513, 1444, 1369, 1322, 1303, 1282, 1249, 1178, 1159, 1093, 1035, 973, 813, 667, 580; δ_H (300 MHz) 7.56 (2H, d, J 8.0 Hz, *ortho* Ts), 7.20 (2H, d, J 8.0 Hz, *meta* Ts), 6.88 (2H, d, J 8.5 Hz, *meta* ArOMe), 6.78 (1H, d, 16.0 Hz, C*H*CO_2Et), 6.71 (2H, d, J 9.0 Hz, *ortho* ArOMe), 5.81 (1H, dd, J 16.0, 1.5 Hz, CH=C*H*CHNHTs), 4.44 (1H, d, J 7.0 Hz, N*H*Ts), 4.18-4.07 (3H, m, C*H*NTs and $CO_2CH_2CH_3$), 3.77 (3H, s, OMe of ArOMe), 2.78 (2H, dd, J 14.0, 5.0 Hz, C*H*HArOMe) 2.66 (2H, dd, J 14.0, 7.0 Hz, CH*H*ArOMe), 2.40 (3H, s, Me of Ts), 1.25 (3H, t, J 7.0 Hz, $CO_2CH_2CH_3$); δ_C (67.5 MHz) 165.9 (C=O), 158.5 (q Ar), 146.3 (*C*H=CHCO$_2$Et), [143.5, 137.2, 127.1 (q Ar)], [130.4, 129.7, 127.1, 122.4, 114.2 (ArH and CH=*C*HCO$_2$Et)], 60.6 (OCH_2CH_3), 55.6 (*C*HNHTs), 55.3 (OMe of ArOMe), 40.3 (CH_2Ar), 21.6 (Me of Ts), 14.3 (OCH_2CH_3); *m/z* (CI) 421 $[M+NH_4]^+$, 252, 189 (Found: $[M+NH_4]^+$, 421.1786. $C_{21}H_{25}NO_5S$ requires $[M+NH_4]^+$, 421.1797).

(+)-(*R*)-(*E*)-5-(4-Methoxyphenyl)-4-(toluene-4-sulfonamido)pent-2-enol

To a solution of (+)-(*R*)-(*E*)-ethyl 5-(4-methoxyphenyl)-4-(toluene-4-sulfonamido)pent-2-enoate (685 mg, 1.70 mmol, 1.0 equiv), in CH_2Cl_2 (18 ml) at –78 ºC was added DIBAL-H (6.12 ml of a 1 M solution in CH_2Cl_2, 6.12 mmol, 3.6 equiv). After 1 h MeOH (15 ml) and H_2O (15 ml) were added at -50 ºC and the mixture stirred for 10 min. The reaction mixture was then diluted with EtOAc (100 ml), poured onto $NaHCO_3$ (25 g) and Na_2SO_4 (25 g) and stirred for 30 min. Filtration, concentration under reduced pressure and chromatography (50% EtOAc–petrol) gave the *allylic alcohol* (466 mg, 76%) as a pale yellow oil; R_f 0.37 (50% EtOAc–petrol); $[\alpha]_D^{20}$ +7.5 (*c* 1.0, $CHCl_3$); ν_{max} (film) 3502, 3284, 2924, 1612, 1598, 1511, 1440, 1421, 1320, 1247, 1178, 1157, 1091, 1035, 993, 970, 813; δ_H (300 MHz) 7.60 (2H, d, J 8.0 Hz, *ortho* Ts), 7.24 (2H, d, J 8.0 Hz, *meta* Ts), 6.95 (2H, d, J 8.5 Hz *ortho* ArOMe), 6.77 (2H, d, J 8.5 Hz, *meta* ArOMe), 5.64 (1H, dt, J 16.0, 4.0 Hz, C*H*=CHCHNHTs), 5.52 (1H, dd, J 16.0, 6.0 Hz, CH=C*H*CHNHTs), 4.02-4.00 (3H, m, CH_2OH and C*H*NHTs), 3.81 (3H, s, OMe of ArOMe), 2.76 (2H, dd, J 14.0, 5.0 Hz, C*H*HArOMe), 2.66 (2H, dd, J 14.0, 7.0 Hz, CH*H*ArOMe), 2.40 (3H, s, Me of Ts); δ_C (67.5 MHz) [158.6, 143.3, 137.6 (q Ar)], 131.3, 130.6 (*C*H=*C*HCO$_2$Et), [130.5, 129.5 (ArH)], 128.1 (q Ar), [127.3, 114.0 (ArH)], 62.7 (CH_2OH), 56.4 (*C*HNHTs), 55.3 (OMe of ArOMe), 41.1 (CH_2ArOMe), 21.6 (Me of Ts); *m/z* (CI) 379 $[M+NH_4]^+$, 189, 150, 132 (Found: $[M+NH_4]^+$, 379.1694. $C_{19}H_{23}NO_4S$ requires $[M+NH_4]^+$, 379.1692).

(*R*)-(*E*)-5-(4-Methoxyphenyl)-4-(4-methylbenzylamino)pent-2-enol (4)

To a solution of sodium (823 mg, 35.8 mmol, 6.0 equiv) dissolved in liquid ammonia (*ca*. 65 ml) at –78 ºC was added (+)-(*R*)-(*E*)-5-(4-methoxyphenyl)-4-(toluene-4-sulfonamido)pent-2-en-1-ol (2.00 g, 5.54 mmol, 1.0 equiv). After 30 min MeOH (5 ml) was added dropwise until the colour was discharged. The ammonia was then allowed to evaporate and the remaining residue partitioned between H_2O (100 ml) and CH_2Cl_2 (100 ml) and the aqueous layer was extracted with CH_2Cl_2 (3 x 100 ml). The combined organic extracts were then dried (Na_2SO_4) and the solvent removed under reduced pressure to give (*R*)-(*E*)-4-amino-5-(4-methoxyphenyl)pent-2-en-1-ol (1.1 g, 5.37 mmol) as a brown oil; δ_H (300 MHz) 7.13 (2H, d, J 8.5 Hz, *ortho* ArOMe), 6.87 (2H, d, J 8.5 Hz, *meta* ArOMe), 5.78-5.77 (2H, m, C*H*=C*H*), 4.12-4.11 (2H, m, CH_2OH), 3.80 (3H, s, OMe of ArOMe), 3.63-3.58 (1H, m, C*H*NH_2), 2.83-2.76 (2H, m, C*H*HArOMe), 2.57 (1H, dd, J 13.5, 8.5 Hz, CH*H*ArOMe). 4-Methylbenzaldehyde (2.50 ml, 21.2 mmol, 4.0 equiv), the crude primary amine (1.10 g, 5.3 mmol, 1.0 equiv), MeOH (20 ml), 4 Å MS (2 g), AcOH (10 ml) and THF (20 ml) were stirred together for 1 h at room temperature. $NaCNBH_3$ (1.64 g, 26.5 mmol, 5.0 equiv) was then added in portions over 3 h, after which time the reaction was filtered through celite and concentrated under reduced pressure. The residue was portioned between Et_2O (100 ml) and NaOH (2 M; 100 ml). The organic layer was washed with H_2O (100 ml), brine (100 ml), dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography (MeOH–CH_2Cl_2) yielded the *amine* **4** (1.00 g, 60%) as a colourless oil; R_f 0.10 (90% CH_2Cl_2–Et_2O); $[\alpha]_D^{24}$ +40.0 (*c* 0.1, $CHCl_3$); ν_{max} (film) 3305, 3004, 2919, 2834, 1612, 1511, 1456, 1230, 1248, 1178, 1095, 1036, 808 cm^{-1}; δ_H (300 MHz); 7.13-7.05 (6H, m, ArMe, and *ortho* ArOMe), 6.84 (2H, d, J 9.0 Hz, *meta* ArOMe), 5.69-5.64 (2H, m, C*H*=C*H*), 4.14 (2H, d, J 5.0 Hz, CH_2OH), 3.81 (3H, s, OMe of ArOMe), 3.76 (1H, d, J 14.0 Hz, C*H*HArMe), 3.55 (1H, d, J 14.0 Hz, CH*H*ArMe), 3.31 (1H, q, J 6.0 Hz, C*H*NHArMe), 2.77-2.75 (2H, m, CH_2ArOMe), 2.34 (3H, s, Me of CH_2ArMe); δ_C (75 MHz) 158.6, 136.9, 133.1, 132.6, 130.8, 130.6, 130.5, 129.5, 128.7, 114.5, 63.0, 61.1, 55.7, 51.2, 41.7, 21.5; *m/z* (CI) 312 $[MH]^+$, 294, 190, 122, 105 (Found: $[MH]^+$, 312.1955. $C_{20}H_{25}O_2N$ requires $[MH]^+$, 312.1964) (Found: C, 77.23; H, 8.13; N, 4.45. $C_{20}H_{25}O_2N$ requires C, 77.14; H, 8.10; N, 4.50%).

(+)-(*R*)-(*E*)-5-(4-Methoxyphenyl)-4-{(4-methylbenzyl)[(toluene-4-sulfonyl)acetyl]amino}pent-2-enol

To a solution of amine **4** (250 mg, 0.804 mmol, 1.0 equiv) and tosylacetic acid (342 mg, 1.61 mmol, 2.0 equiv) in CH_2Cl_2 (3 ml) was added DCC (350 mg, 1.77 mmol, 2.1 equiv). The reaction was stirred at rt for 15 h and was then filtered and stirred in 4% NaOH–MeOH for 1 h. The mixture was then concentrated under reduced pressure and the residue partitioned between EtOAc (50 ml) and HCl (2 M; 50 ml). The aqueous phase was then extracted with EtOAc (2 x 50 ml) and the combined

organic extracts washed with saturated aqueous $NaHCO_3$ (100 ml) and dried (Na_2SO_4). Concentration under reduced pressure gave (+)-(*R*)-(*E*)-5-(4-methoxyphenyl)-4-{(4-methylbenzyl)[(toluene-4-sulfonyl)acetyl]amino}pent-2-enol (370 mg, 91%) as a colourless oil; R_f 0.84 (10% MeOH–CH_2Cl_2); $[\alpha]_D^{25}$ +27.2 (*c* 2.5, $CHCl_3$); ν_{max} (film) 3443, 1642, 1318 cm^{-1}; δ_H (400 MHz) 7.71 (1.4H, d, J 8.0 Hz, *ortho* Ts rotamer 1) 7.70 (0.88H, d, J 8.0 Hz, *ortho* Ts rotamer 2), 7.28 (1.12H, d, J 8.0 Hz, *meta* Ts rotamer 1), 7.28 (0.6H, d, J 8.0 Hz, *meta* Ts rotamer 2), 7.26-7.09 (2.88H, m, *ortho* ArMe rotamer 1 and rotamer 2 and *meta* ArOMe rotamer 2), 7.05-7.01 (2H, m, *ortho* ArOMe rotamer 1 and rotamer 2), 6.95 (1.12H, d, J 8.0 Hz, *ortho* ArMe), 6.82 (0.88H, d, J 9.0 Hz, *meta* ArOMe rotamer 2), 6.79 (1.12H, d, J 9.0 Hz, *meta* ArOMe, rotamer 1) 5.85 (0.44H, dt, J 16.0, 4.5 Hz CH=C*H*CH_2OH rotamer 2), 5.74-5.69 (1.56H, m, CH=C*H*CH_2OH rotamer 1 and C*H*=$CHCH_2OH$ rotamer 1 and rotamer 2), 4.95-4.96 (0.56H, CHN rotamer 1), 4.80-4.83 (0.44H, CHN rotamer 2), 4.55-4.66 (1.56H, C*H*$_2$Ts rotamer 1 and C*H*HTs rotamer 2), 4.41 (0.44H, d, J 15.0 Hz, CH*H*Ts rotamer 2), 4.07-3.99 (3.12H, m, C*H*$_2$ArMe rotamer 1 and C*H*$_2$OH), 3.87 (0.44H, d, J 14.0 Hz, C*H*HArMe rotamer 2), 3.78 (3H, s, OMe of ArOMe), 3.71 (0.44H, d, J 14.0 Hz, CH*H*ArMe rotamer 2), 3.00-2.79 (2H, m, C*H*$_2$ArOMe), 2.45 (1.68H, s, Me of Ts rotamer 1), 2.42 (1.32H, s, Me of Ts rotamer 2), 2.33 (1.32H, s, Me of CH_2ArMe rotamer 2), 2.32 (1.68H, s, Me of CH_2ArMe rotamer 1); δ_C (100 MHz); 162.4, 158.7, 158.3, 145.2, 137.5, 136.6, 136.1, 135.2, 133.6, 133.6, 132.9, 130.4, 130.3, 129.7, 129.6, 129.3, 129.1, 128.9, 128.6, 127.8, 126.3, 114.3, 113.9, 62.9, 62.8, 61.6, 60.9, 59.8, 59.5, 55.3, 49.5, 46.1, 37.7, 21.8, 21.1, 21.0; *m/z* (CI) 525 $[M+NH_4]^+$, 508 $[M+H]^+$, 354, 238 (Found: $[M+H]^+$, 508.2152. $C_{29}H_{33}NO_5S$ requires $[M+NH_4]^+$, 508.2158).

(+)-(*R*)-(*E*)-Carbonic acid 5-(4-methoxyphenyl)-4-[(4-methylbenzyl)-2-(toluene-4-sulfonyl)acetylamino]pent-2-enyl ester methyl ester (2)

To a solution of (+)-(*R*)-(*E*)-5-(4-methoxyphenyl)-4-{(4-methylbenzyl)[(toluene-4-sulfonyl)acetyl]amino}pent-2-enol (600 mg, 1.18 mmol, 1.0 equiv) in CH_2Cl_2 (10 ml) at 0 ºC was added pyridine (130 μl, 2.40 mmol, 2.0 equiv), methyl chloroformate (290 μl, 2.40 mmol, 2.0 equiv) and DMAP (14.4 mg, 0.118 mmol, 0.1 equiv). The reaction was brought to rt for 1 h and then quenched with saturated aqueous NH_4Cl (10 ml). The organic phase washed with H_2O (10 ml) brine (10 ml) and dried (Na_2SO_4). Concentration under reduced pressure and chromatography (40% EtOAc–petrol) gave the *carbonate* **2** (650 mg, 96%) as a colourless oil; R_f 0.72 (60% EtOAc–petrol); $[\alpha]_D^{22}$ +24.0 (*c* 0.5, $CHCl_3$); ν_{max} (film) 1747, 1647, 1514, 1443, 1265, 1155, 793 cm^{-1}; δ_H (400 MHz) 7.69 (1.32H, d, J 8.0 Hz, *ortho* Ts rotamer 1), 7.65 (0.68H, d, J 8.0 Hz, *ortho* Ts rotamer 2), 7.29 (1.32H, d, J 8.0 Hz, *meta* Ts rotamer 1), 7.21 (0.68H, d, J 8.0 Hz, *meta* Ts rotamer 2), 7.10 (0.68H, d, J 8.0 Hz, *ortho* CH_2ArMe rotamer 2), 7.05 (2H, m, *meta* CH_2ArMe rotamer 2 and *ortho* CH_2ArMe rotamer 1) 7.00-6.96 (2H, m, *meta* ArOMe rotamer 1 and rotamer 2),

6.91 (1.32H, d, J 8.0 Hz, *meta* CH_2ArMe rotamer 1), 6.78-6.73 (2H, m, *ortho* ArOMe), 5.85-5.76 (1.34H, m, $CH_2CH{=}CH$ and $CH_2CH{=}CH$ rotamer 2), 5.59 (0.66H, dt, J 16.0, 6.0 Hz, $CH_2CH{=}CH$ rotamer 1), 4.82 (1H, m, CHN), 4.61 (0.66H, d, J 18.0 Hz, CHTs rotamer 1), 4.53-4.44 (3H, m, CH_2OCO_2Me, CHTs rotamer 1 and CHTs rotamer 2), 4.39 (0.34H, d, J 15.0 Hz, CHTs rotamer 2), 4.10-4.02 (1.32H, m, CH_2ArMe rotamer 1), 3.87 (0.34H, d, J 14.0 Hz, CHArMe rotamer 2), 3.71-3.64 (6.34H, m, OMe of ArOMe, OCO_2CH_3 and CHArMe rotamer 2), 2.92-2.75 (2H, m, CH_2ArOMe), 2.38 (1.98H, s, Me of Ts rotamer 1), 2.35 (1.02H, s, Me of Ts rotamer 2), 2.29 (1.02H, s, Me of CH_2ArMe rotamer 2), 2.28 (1.98H, s, Me of CH_2ArMe rotamer 1); δ_C (100 MHz) 162.4 (OCO_2Me rotamer 1), 162.3 (OCO_2Me rotamer 2), 158.6 ($NCOCH_2$ rotamer 2), 158.3 ($NCOCH_2$ rotamer 1), [145.1, 145.0, 137.3, 136.4, 136.0, 135.7, 134.9, 133.4, (q Ar)], 132.8 ($CH_2CH{=}CH$ rotamer 2), 132.1 ($CH_2CH{=}CH$ rotamer 1), 130.5, 130.2, 129.7, 129.6, 129.5 (ArH)], 129.4 (q Ar), [128.9, 128.6, 128.4, 127.9 (ArH)], 126.9 ($CH_2CH{=}CH$ rotamer 1), 126.6 ($CH_2CH{=}CH$ rotamer 2), [126.3, 114.1, 113.8 (ArH)], 67.4 (CH_2OCO_2Me rotamer 1), 67.3 (CH_2OCO_2Me rotamer 2), 61.5 (CHN rotamer 1), 60.7 (CH_2ArMe rotamer 1), 59.8 (CHN rotamer 2), 59.6 (CH_2ArMe rotamer 2), [55.1 and 54.8, (OMe of ArOMe and OCO_2CH_3)], 49.8 (CH_2Ts rotamer 1), 46.0 (CH_2Ts rotamer 2), 37.5 (CH_2ArOMe), 21.7 (Me of CH_2ArMe rotamer 1), 21.6 (Me of CH_2ArMe rotamer 2), 21.1 (Me of Ts rotamer 2), 21.0 (Me of Ts rotamer 2); *m/z* (CI) 583 $[M+NH_4]^+$, 566 $[M+H]^+$, 490, 447, 412, 284, 240, 196, 133, 124 (Found: $[M+NH_4]^+$, 583.2479. $C_{31}H_{35}NO_7S$ requires $[M+NH_4]^+$, 583.2478) (Found: C, 65.71; H, 6.32; N, 2.40. $C_{31}H_{35}NO_7S$ requires C, 65.82; H, 6.24; N, 2.48%).

(3*R*, 4*S*,5*R*)-5-(4-Methoxybenzyl)-1-(4-methylbenzyl)-3-(toluene-4-sulfonyl)-4-vinylpyrrolidin-2-one (1) and (3*S*,4*R*,5*R*)-5-(4-methoxybenzyl)-1-(4-methylbenzyl)-3-(toluene-4-sulfonyl)-4-vinylpyrrolidin-2-one (5)

To carbonate **2** (500 mg, 0.890 mmol, 1.0 equiv), $Pd_2(dba)_3$ (42 mg, 0.046 mmol, 5.0 mol%) and tris(2,4,6-trimethoxyphenyl)phosphine (244 mg, 0.458 mmol, 0.5 equiv) was added MeCN (10 ml) and the mixture stirred rapidly at rt. After 30 min the reaction mixture was concentrated under reduced pressure. Chromatography (50% Et_2O–petrol) gave an inseparable 5.6:1 mixture of *γ-lactam* **1** and *γ-lactam* **5** (380 mg, 90%) as a colourless oil; R_f 0.33; ν_{max} (film) 2925, 1697, 1612, 1513, 1439, 1303, 1148, 813, 660 cm^{-1}; δ_H (400 MHz) 7.87 (2H, d, J 8.0 Hz, *ortho* Ts of **5**), 7.84 (2H, d, J 8.0 Hz, *ortho* Ts of **1**), 7.36 (2H, d, J 8.0 Hz, *meta* Ts of **1**), 7.11 (2H, d, J 8.0 Hz, *ortho* CH_2ArMe of **1**), 7.10 (2H, d, J 8.0 Hz, *ortho* ArMe of **5**), 7.05 (2H, d, J 9.0 Hz, *ortho Ar*OMe of **5**), 7.04 (2H, d, J 8.0 Hz, *meta* CH_2ArMe), 6.94 (2H, d, J 8.0 Hz, *ortho* CH_2ArMe of **1**), 6.90 (2H, d, J 9.0 Hz, *meta* ArOMe of **1**), 6.82 (2H, d, J 9.0 Hz, *meta Ar*OMe of **5**), 6.78 (2H, d, J 9.0 Hz, *ortho* ArOMe of **1**), 5.83 (1H, ddd, J 17.0, 10.0, 9.5 Hz, $CH{=}CH_2$ of **1**), 5.41 (1H, ddd, J 17.0, 11.0, 7.0

Hz, C*H*=CH_2 of **5**), 5.26 (1H, d, J 17.0 Hz, *trans* CH_2=CH of **1**), 5.12 (1H, d, J 10.0 Hz, *cis* CH_2=CH of **1**), 4.99 (1H, d, J 15.0 Hz, C*H*HN of **5**), 4.98 (1H, d, J 15.0 Hz, C*H*HN of **1**), 4.86 (1H, d J 17.0, *trans* CH=CH_2 of **5**), 4.72 (1H, d, 10.0 Hz, *cis* CH=CH_2 of **5**), 4.01-4.00 (1H, m, CHN of **1**), 4.01 (1H, d, J 15.0 Hz, CH*H*N of **5**), 3.84 (1H, d, J 4.0 Hz, CHTs of **5**), 3.81 (3H, s, OMe of ArOMe of **5**), 3.80 (1H, d, J 3.5 Hz, CHTs of **1**), 3.77 (3H, s, OMe of ArOMe of **1**), 3.70 (1H, d, J 15.0 Hz, CH*H*N of **1**) 3.53-3.51 (1H, m, C*H*CH=CH_2 of **1**), 3.39-3.33 (2H, m, C*H*CH=CH_2 and CHN of **5**), 3.17 (1H, dd, J 14.0, 5.0 Hz, C*H*HArOMe of **5**), 2.80 (1H, dd, J 14.0, 10.0 Hz, CH*H*ArOMe of **5**), 2.79 (1H, dd, J 14.0, 6.0 Hz CH*H*ArOMe of **1**), 2.72 (1H, dd, J 14.0, 8.0 Hz, C*H*HArOMe of **1**), 2.48 (3H, s, Me of Ts of **5**), 2.45 (3H, s, Me of Ts of **1**), 2.35 (3H, s, Me of CH_2ArMe of **5**), 2.33 (3H, s, Me of CH_2ArMe of **1**); δ_c (75 MHz) 165.6 (C=O, of **5**), 164.7 (C=O, of **1**), [158.5, 158.4, 145.2 (2 signals) (q Ar of **1** and **5**)], [137.6 137.3 (q Ar of **1** and **5**)], 137.0 (*C*H=CH_2 of **5**), 135.0 (2 signals) (q Ar of **1** and **5**), 133.5 (*C*H=CH_2 of **1**), [132.5, 132.2, 130.4, 130.3 (q Ar of **1** and **5**)], [129.7, 129.6, 129.5 (2 signals), 129.4, 129.3, 128.9, 128.2, 128.0, 127.7 (ArH of **1** and **5**)], 119.8 (CH=*C*H_2 of **1**), 116.6 (CH=*C*H_2 of **5**), [114.1, 114.0 (ArH of **1** and **5**)], 70.4 (*C*HTs of **1**), 71.3 (*C*HTs of **5**), 62.4 (CHN of **5**), 59.5 (CHN of **1**), 55.3 (OMe of CH_2ArOMe of **1** and **5**), 44.9 (CH_2N of **1** and **5**), 42.1 (*C*HCH=CH_2 of **1**), 40.3 (*C*HCH=CH_2 of **5**), 38.0 (*C*H_2ArOMe of **5**), 34.2 (*C*H_2ArOMe of **1**), 21.8 (Me of Ts of **1** and **5**), 21.1 (Me of CH_2ArMe of **1** and **5**); *m/z* (CI) 507 $[M+NH_4]^+$, 490 $[M+H]^+$, 436, 353, 336, 59, 53, 35 (Found: $[MH]^+$, 490.2071. $C_{29}H_{31}O_4NS$ requires $[MH]^+$, 490.2052).

(*S*)-2-(Toluene-4-sulfonamido)propionic acid

To a rapidly stirred solution of L-alanine (15.0 g, 170 mmol, 1.0 equiv) and TsCl (42.0 g, 220 mmol, 1.3 equiv) in EtOAc (400 ml) and H_2O (120 ml) was added NaOH (230 ml of a 2 M aqueous solution, 460 mmol, 2.7 equiv) dropwise over 3 h. After a further 1 h the aqueous phase was separated, washed with Et_2O (3 x 250 ml), acidified to pH 1 with concentrated HCl (20 ml) and extracted with EtOAc (3 x 250 ml). The combined organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure to yield (*S*)-2-(toluene-4-sulfonamido)propionic acid (30.0 g, 73%) as a colourless solid; mp 129–131 ºC (EtOAc); δ_H (300 MHz) 7.76 (2H, d, J 8.0 Hz, *ortho* Ts), 7.32 (2H, d, J 8.0 Hz, *meta* Ts), 5.32 (1H, d, J 10.0 Hz, NH), 4.05-4.00 (1H, m, C*H*NHTs), 2.43 (3H, s, Me of Ts), 1.43 (3H, d, J 7.0 Hz, CHCH_3); *m/z* (CI) 303, 261 $[M+NH_4]^+$, 240, 189, 174, 132, 86. *In agreement with published data.*[2]

(*S*)-3-Methyl-2-(toluene-4-sulfonamido)butyric acid

To a rapidly stirred solution of L-valine (15.0 g, 130 mmol, 1.0 equiv) and TsCl (32.0 g, 170 mmol, 1.3 equiv) in EtOAc (276 ml) and H_2O (82 ml) was added NaOH (175 ml of a 2 M aqueous solution,

350 mmol, 2.7 equiv) dropwise over 3 h. After a further 1 h the aqueous phase was separated, washed with Et_2O (3 x 250 ml), acidified to pH 1 with concentrated HCl (20 ml) and extracted with EtOAc (3 x 250 ml). The combined organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure to yield (*S*)-3-methyl-2-(toluene-4-sulfonamido)butyric acid (15.0 g, 38%) as a white solid; mp 149–151 ºC (EtOAc); δ_H (300 MHz) 7.74 (2H, d, J 8.0 Hz, *ortho* Ts), 7.30 (2H, d, J 8.0 Hz, *meta* Ts), 5.14 (1H, d, J 10.0 Hz, NH), 3.81 (1H, dd, C*H*NHTs), 2.43 (3H, s, Me of Ts), 2.15-2.09 (1H, m, C*H*$(CH_3)_2$), 0.98 (3H, d, J 7.0 Hz, CH(C*H*$_3)_2$), 0.89 (3H, d, J 7.0 Hz, CH(C*H*$_3)_2$); *m/z* (CI) 271 $[M+NH_4]^+$, 189, 1174, 118, 106, 72. *In agreement with published data.*[3]

(*S*)-4-Methyl-2-(toluene-4-sulfonamido)pentanoic acid

To a rapidly stirred solution of L-leucine (20.0 g, 150 mmol, 1.0 equiv) and TsCl (36.4 g, 0.19 mol, 1.3 equiv) in EtOAc (300 ml) and H_2O (100 ml) was added NaOH (205 ml of a 2 M aqueous solution, 410 mmol, 2.7 equiv) dropwise over 3 h. After a further 1 h the aqueous phase was separated, washed with Et_2O (3 x 250 ml), acidified to pH 1 with concentrated HCl (20 ml) and extracted with EtOAc (3 x 250 ml). The combined organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure to yield (*S*)-4-methyl-2-(toluene-4-sulfonamido)pentanoic acid (32.0 g, 73%) as an odorous, off-white solid; mp 115–116 ºC (EtOAc); δ_H (300 MHz) 7.75 (2H, d, J 8.0 Hz, *ortho* Ts), 7.31 (2H, d, J 8.0 Hz, *meta* Ts), 5.07 (1H, d, J 10.0 Hz, NH), 3.96-3.91 (1H, m, C*H*NHTs), 2.44 (3H, s, Me of Ts), 1.81-1.74 (1H, m, C*H*$(CH_3)_2$), 1.56-1.51 (2H, m, C*H*$_2{}^i$Pr), 0.92 (3H, d, J 7.0 Hz, CH(C*H*$_3)_2$), 0.85 (3H, d, J 7.0 Hz, CH(C*H*$_3)_2$); *m/z* (CI) 303 $[M+NH_4]^+$, 189, 86. *In agreement with published data.*[4]

2-(Toluene-4-sulfonamido)hexanoic acid

To a rapidly stirred solution of DL-norleucine (15.0 g, 110 mol, 1.0 equiv) and TsCl (27.3 g, 140 mol, 1.3 equiv) in EtOAc (400 ml) and H_2O (120 ml) was added NaOH (230 ml of a 2 M aqueous solution, 460 mmol, 2.7 equiv) dropwise over 3 h. After a further 1 h the aqueous phase was separated, washed with Et_2O, acidified to pH 1 with concentrated HCl (20 ml) and extracted with EtOAc (3 x 250 ml). The combined organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure to yield acid 2-(toluene-4-sulfonamido)hexanoic acid (30.2 g, 73%) as a colourless solid; mp 124 ºC (EtOAc); δ_H (300 MHz DMSO) 12.57 (1H, br s, CO_2H), 8.03 (1H, d, J 9.0 Hz, NH), 7.66 (2H, d, J 8.0 Hz, *ortho* Ts), 7.36 (2H, d, J 8.0 Hz, *meta* Ts), 3.68-3.60 (1H, m, C*H*NHTs), 2.36 (3H, s, Me of Ts), 1.54-1.45 (2H, m, C*H*$_2$CH), 1.13-1.08 (4H, m, (C*H*$_2)_2$Me), 0.75-0.71 (3H, m, Me of *n*Bu); *m/z* (CI) 303 $[M+NH_4]^+$, 206, 149, 103, 86. *In agreement with published data.*[5]

(*S*)-2-(Toluene-4-sulfonamido)propan-1-ol

To a solution of (*S*)-2-(toluene-4-sulfonamido)propionic acid (12.0 g, 49.0 mmol, 1.0 equiv) in THF (192 ml) at 0 ºC was added $LiAlH_4$ (147 ml of a 1 M solution in THF, 147 mmol, 3.0 equiv), the reaction brought slowly to rt and then heated to reflux. After 2 h the reaction was quenched with EtOAc (20 ml), poured into Rochelle's salt (500 ml of a 50% sat. aq. solution) and stirred for 1 h. The solution was extracted with EtOAc (3 x 300 ml) and the combined organic extracts washed with brine (500 ml) and dried ($MgSO_4$). Concentration under reduced pressure yielded (*S*)-2-(toluene-4-sulfonamido)propan-1-ol (10.9 g, 97%) as a colourless solid; mp 128–130 ºC (Et_2O); R_f 0.85 (50% EtOAc–petrol); δ_H (300 MHz) 7.80 (2H, d, J 8.0 Hz, *ortho* Ts), 7.33 (2H, d, J 8.0 Hz, *meta* Ts), 4.92 (1H, d J 6.5 Hz, NH), 3.60-3.36 (3H, m, C*H*$_2$OH and C*H*NHTs), 2.45 (3H, s, Me of Ts), 2.16 (1H, s, OH), 1.05 (3H, d, CHC*H*$_3$); *m/z* (CI) 247 $[M+NH_4]^+$, 230 $[M+H]^+$, 189, 108, 76, 44. *In agreement with published data.*[6]

(*S*)-3-Methyl-2-(toluene-4-sulfonamido)butan-1-ol

To a solution of (*S*)-3-methyl-2-(toluene-4-sulfonamido)butyric acid (12.0 g, 44.0 mmol, 1.0 equiv) in THF (192 ml) at 0 ºC was added $LiAlH_4$ (132 ml of a 1 M solution in THF, 132 mmol, 3.0 equiv), the reaction brought slowly to rt and then heated to reflux. After 2 h the reaction was quenched with EtOAc (20 ml), poured into Rochelle's salt (500 ml of a 50% sat. aq. solution) and stirred for 1 h. The solution was extracted with EtOAc (3 x 300 ml) and the combined organic extracts washed with brine (500 ml) and dried ($MgSO_4$). Concentration under reduced pressure yielded (*S*)-3-methyl-2-(toluene-4-sulfonamido)butan-1-ol (11.5 g, 99%) as a colourless solid; mp 74–75 ºC (Et_2O); R_f 0.70 (50% EtOAc–petrol); δ_H (300 MHz) 7.80 (2H, d, J 8.0 Hz, *ortho* TS), 7.33 (2H, d, J 8.0 Hz, *meta* Ts), 4.81 (1H, d J 8.0 Hz, NH), 3.59-3.58 (2H, m, C*H*$_2$OH), 3.08-3.02 (1H, m, C*H*NHTs), 2.45 (3H, s, Me of Ts), 2.06-2.00 (1H, m, OH), 1.83-1.77 (1H, m, CH C*H*$(CH_3)_2$), 0.81 (3H, d J 3.0 Hz, CH(C*H*$_2$)$_2$), 0.80 (3H, d J 3.0 Hz, CH(C*H*$_3$)$_2$). *m/z* (CI) 275 $[M+NH_4]^+$, 258 $[M+H]^+$, 243. *In agreement with published data.*[7]

(*S*)-4-Methyl-2-(4-methyl benzenesulfonamido)pentan-1-ol

To a solution of (*S*)-4-methyl-2-(toluene-4-sulfonamido)pentanoic acid 12.0 g, 31.0 mmol, 1.0 equiv) in THF (192 ml) at 0 ºC was added $LiAlH_4$ (93 ml of a 1 M solution in THF, 93.0 mmol, 3.0 equiv), the reaction brought slowly to rt and then heated to reflux. After 2 h the reaction was quenched with EtOAc (20 ml), poured into Rochelle's salt (500 ml of a 50% saturated aqueous solution) and stirred for 1 h. The solution was extracted with EtOAc (3 x 300 ml) and the combined organic extracts washed with brine (500 ml) and dried ($MgSO_4$). Concentration under reduced pressure yielded alcohol **214c** (11.0 g, 95%) as a colourless solid; mp 98–100 ºC (Et_2O); R_f 0.74 (50% EtOAc–petrol); δ_H (300 MHz) 7.80 (2H, d, J 8.0 Hz, *ortho* TS), 7.33 (2H, d, J 8.0 Hz, *meta*

Ts), 4.66 (1H, d, J 7.0 Hz, NH), 3.60-3.44 (2H, m, C*H*$_2$OH), 3.32-3.31 (1H, m, C*H*NHTs), 2.45 (3H, s, Me of Ts), 1.62 (1H, s, OH), 1.52-1.44 (1H, m, C*H*(CH$_3$)$_2$), 1.28-1.26 (2H, m, CH$_2$^{i}Pr), 0.80 (3H, d J 6.5 Hz, CH(C*H*$_3$)$_2$), 0.66 (3H, d J 6.5 Hz, CH(C*H*$_3$)$_2$); *m/z* (CI) 289 $[M+NH_4]^+$, 272 $[M+H]^+$, 240, 189, 118, 86. *In agreement with published data.*[7]

2-(Toluene-4-sulfonamido)hexan-1-ol

A solution of 2-(toluene-4-sulfonamido)hexanoic acid (10.0 g, 35.1 mmol, 1.0 equiv) in THF (50 ml) was added to a suspension of $LiAlH_4$ (4.00 g, 105 mmol, 3.0 equiv) in THF (200 ml) at 0 ºC. The resulting solution was warmed slowly to rt and then heated to reflux. After 12 h the reaction was quenched with EtOAc (50 ml) and poured into Rochelle's salt (500 ml of a 50% saturated aqueous solution) and stirred for 1 h. The solution was extracted with EtOAc (3 x 300 ml) and the combined organic extracts washed with brine (500 ml) and dried ($MgSO_4$). Concentration under reduced pressure yielded 2-(toluene-4-sulfonamido)hexan-1-ol (9.50 g, 99%) as a colourless crystalline solid; mp 61–62 ºC (Et_2O–petrol); R_f 0.35 (50% EtOAc–petrol); ν_{max} (film) 3498, 3278, 2954, 2872, 1452, 1323, 1159, 1092, 816, 665 cm^{-1}; δ_H (300 MHz) 7.80 (2H, d, J 8.0 Hz, *ortho* Ts), 7.32 (2H, d, J 8.0 Hz, *meta* Ts), 5.13-5.06 (1H, m, NH), 3.60-3.47 (2H, m, C*H*$_2$OH), 3.24-3.22 (1H, m, C*H*NHTs), 2.44 (4H, br s, Me of Ts and OH), 1.44-1.33 (2H, m, C*H*$_2$(CH$_2$)$_2$CH$_3$), 1.17-1.02 (4H, m, CH$_2$(C*H*$_2$)$_2$CH$_3$), 0.76 (3H, t, J 6.0 Hz, CH$_2$(CH$_2$)$_2$C*H*$_3$); δ_C (75 MHz) 143.6, 137.6, 129.7, 127.2, 64.9, 55.7, 31.4, 27.7, 22.3, 21.6, 13.8; *m/z* (CI) 289 $[M+NH_4]^+$, 272 $[M+H]^+$, 240, 189, 118, 86 (Found: C, 57.52; H, 7.59; N, 5.19. $C_{13}H_{21}NO_3S$ requires C, 57.54; H, 7.80; N, 5.16%).

(–)-(*S*)-(*E*)-Ethyl 4-(toluene-4-sulfonamido)pent-2-enoate

To a solution of oxalyl chloride (4.50 ml, 52.1 mmol, 1.2 equiv) in CH_2Cl_2 (50 ml) at –78 ºC was added DMSO (7.40 ml, 104 mmol, 2.4 equiv) in CH_2Cl_2 (50 ml). After 5 min a solution of (*S*)-2-(toluene-4-sulfonamido)propan-1-ol (10.0 g, 43.4 mmol, 1.0 equiv) in CH_2Cl_2 (75 ml) was added dropwise with stirring. After a further 45 min Et_3N (30.2 ml, 217 mmol, 5.0 equiv) in CH_2Cl_2 (30 ml) was added dropwise and the solution brought slowly to rt. After a further 30 minutes the reaction mixture was diluted with CH_2Cl_2 (500 ml), washed with saturated aqueous $NaHCO_3$ (400 ml) and the aqueous layer re-extracted with CH_2Cl_2 (100 ml). The combined organic extracts were then washed with acetic acid (1 M; 100 ml), H_2O (400 ml), brine (400 ml) and dried (Na_2SO_4). Concentration under reduced pressure gave the crude aldehyde as an orange oil that was immediately dissolved in CH_2Cl_2 (500 ml) and Ph_3PCHCO_2Et (53.9 g, 154.8 mmol, 4 equiv) added at rt with stirring. After 12 h the mixture was concentrated under reduced pressure and triturated with Et_2O (250 ml) to remove triphenylphosphine oxide. Chromatography (30% EtOAc–petrol) gave (–)-(*S*)-(*E*)-ethyl 4-(toluene-4-sulfonamido)pent-2-enoate (8.73 g, 67%) as a colourless oil; R_f 0.33 (30% EtOAc–petrol); $[\alpha]_D^{16}$ –60.0 (*c* 1.0, $CHCl_3$); ν_{max} (film) 1716, 1659, 1369, 1305, 1156, 1093, 977, 815, 666 cm^{-1}; δ_H (300 MHz) 7.76 (2H, d, J 8.0 Hz, *ortho* TS), 7.31 (2H, d, J 8.0 Hz, *meta* Ts), 6.67 (1H, dd, J 16.0, 6.0 Hz, C*H*=CHCO$_2$Et), 5.83 (1H, d, J 16.0 Hz C=C*H*CO$_2$Et), 4.89 (1H, d, J 8.0 Hz, NH), 4.16 (2H, q, J 7.0 Hz, C*H*$_2$CH$_3$), 5.06 (1H, q, J 6.0 Hz, C*H*NHTs), 2.43 (3H, s, Me of Ts), 1.27 (3H, t, J 7.0 Hz, CH$_2$C*H*$_3$) 1.22 (3H, d, J 7.0 Hz, CHC*H*$_3$); δ_C (75 MHz) 172.5,

147.6, 143.7, 137.5, 129.8, 127.2, 121.4, 60.6, 50.2, 21.6, 21.2, 14.2; *m/z* (CI) 315 $[M+NH_4]^+$, 298 $[M+H]^+$, 189, 144 $[MH\text{-}Ts]^+$, 52 (Found: $[M+H]^+$, 298.1118. $C_{14}H_{19}NO_4S$ requires $[M+H]^+$, 298.1113) (Found: C, 56.72; H, 6.31; N, 4.75. $C_{14}H_{19}NO_4S$ requires C, 56.55, 6.44, 4.71%).

(–)-(*S*)-(*E*)-Ethyl 5-methyl-4-(toluene-4-sulfonamido)hex-2-enoate

To a solution of oxalyl chloride (4.10 ml, 46.4 mmol, 1.2 equiv) in CH_2Cl_2 (50 ml) at –78 ºC was added DMSO (6.60 ml, 92.9 mmol, 2.4 equiv) in CH_2Cl_2 (50 ml). After 5 min a solution of (*S*)-3-methyl-2-(toluene-4-sulfonamido)butan-1-ol (10.0 g, 38.7 mmol, 1.0 equiv) in CH_2Cl_2 (75 ml) was added dropwise with stirring. After a further 45 min Et_3N (27.0 ml, 193 mmol, 5.0 equiv) in CH_2Cl_2 (30 ml) was added dropwise and the solution brought slowly to rt. After a further 30 minutes the reaction mixture was diluted with CH_2Cl_2 (500 ml), washed with saturated aqueous $NaHCO_3$ (400 ml) and the aqueous layer re-extracted with CH_2Cl_2 (100 ml). The combined organic extracts were then washed with acetic acid (1 M; 100 ml), H_2O (400 ml), brine (400 ml) and dried (Na_2SO_4). Concentration under reduced pressure gave the crude aldehyde as an orange oil that was immediately dissolved in CH_2Cl_2 (500 ml) and Ph_3PCHCO_2Et (53.9 g, 154 mmol, 4.0 equiv) added at rt with stirring. After 12 h the mixture was concentrated under reduced pressure and triturated with Et_2O (250 ml) to remove triphenylphosphine oxide. Chromatography (30% EtOAc–petrol) gave (–)-(*S*)-(*E*)-ethyl 5-methyl-4-(toluene-4-sulfonamido)hex-2-enoate (11.2 g, 88%) as a colourless crystalline solid; mp 88–90 ºC (Et_2O); R_f 0.50 (30% EtOAc–petrol); $[\alpha]_D^{22}$ –24.1 (*c* 1.0, $CHCl_3$); ν_{max} (film) 3279, 2966, 1719, 1657, 1465, 1326, 1183, 1093, 1039, 984, 667cm^{-1}; δ_H (300 MHz) 7.74 (2H, d, J 8.0 Hz, *ortho* Ts), 7.28 (2H, d, J 8.0 Hz, *meta* Ts), 6.59 (1H, dd, J 16.0, 7.0 Hz, C=C*H*CH), 5.67 (1H, d, J 16.0 Hz =C*H*CO_2Et), 5.14 (1H, d, J 9.0 Hz, NH), 4.13 (2H, q, J 7.0 Hz, C*H*$_2$CH$_3$), 3.75 (1H, q, J 7.0 Hz, C*H*NHTs), 2.40 (3H, s, Me of Ts), 1.84-1.76 (1H, m, C*H*$(CH_3)_2$) 1.26 (3H, t, J 7.0 Hz, CH_2CH_3), 0.86 (6H, t, J 7.0 Hz, $CH(CH_3)_2$); δ_C (75 MHz) 165.7, 145.2, 143.5, 137.7, 129.6, 127.2, 122.8, 60.5, 60.2, 32.7, 21.5, 18.5, 18.1, 14.2; *m/z* (CI) 343 $[M+NH_4]^+$, 189 (Found: C, 59.23; H, 7.25; N, 4.34. $C_{16}H_{23}NO_4S$ requires C, 59.05; H, 7.12; N, 4.30%).

(–)-(*S*)-(*E*)-Ethyl 6-methyl-4-(toluene-4-sulfonamido)hept-2-enoate

To a solution of oxalyl chloride (2.50 ml, 29.0 mmol, 1.2 equiv) in CH_2Cl_2 (31 ml) at –78 ºC was added DMSO (4.10 ml, 58.1 mmol, 2.4 equiv) in CH_2Cl_2 (31 ml). After 5 min a solution of (*S*)-4-methyl-2-(toluene-4-sulfonamido)pentan-1-ol (9.00 g, 24.2 mmol, 1.0 equiv) in CH_2Cl_2 (47 ml) was added dropwise with stirring. After a further 45 min Et_3N (16.9 ml, 121 mmol, 5.0 equiv) in CH_2Cl_2 (19 ml) was added dropwise and the solution brought slowly to rt. After a further 30 minutes the reaction mixture was diluted with CH_2Cl_2 (500 ml), washed with saturated aqueous $NaHCO_3$ (400 ml) and the aqueous layer re-extracted with CH_2Cl_2 (100 ml). The combined organic extracts were

then washed with acetic acid (1 M; 100 ml), H_2O (400 ml), brine (400 ml) and dried (Na_2SO_4). Concentration under reduced pressure gave the crude aldehyde as an orange oil that was immediately dissolved in CH_2Cl_2 (500 ml) and Ph_3PCHCO_2Et (33.7g, 96.8 mmol, 4.0 equiv) added at rt with stirring. After 12 h the mixture was concentrated under reduced pressure and triturated with Et_2O (250 ml) to remove triphenylphosphine oxide. Chromatography (30% EtOAc–petrol) gave (–)-(*S*)-(*E*)-ethyl 6-methyl-4-(toluene-4-sulfonamido)hept-2-enoate (8.40 g, 70 %) as a colourless oil; R_f 0.52 (30% EtOAc–petrol); $[\alpha]_D^{22}$ –44.0 (*c* 1.0, $CHCl_3$); ν_{max} (film) 3279, 2958, 1713, 1659, 1369, 1284, 1094, 813, 666 cm^{-1}; δ_H (300 MHz) 7.73 (2H, d, J 8.0 Hz, *ortho* Ts), 7.27 (2H, d, J 8.0 Hz, *meta* Ts), 6.55 (1H, dd J, 16.0, 7.0 Hz, CH=C*H*CH), 5.71 (1H, d, J 16.0 Hz, C*H*=CHCH), 5.40 (1H, d, J 8.0 Hz, NH), 4.11 (2H, q, J 7.0 Hz, CH_2CH$_3$), 3.91 (1H, quintet, J 7.5 Hz, C*H*NHTs), 2.39 (3H, s, Me of Ts), 1.57 (1H, sextet, J 7.0 Hz, C*H*$(CH_3)_2$) 1.39-1.21 (5H, m, CH_2^{i}Pr and CH$_2$CH_3), 0.80 (3H, d, J 6.5 Hz, CH(CH_3)$_2$), 0.75 (3H, d, J 6.5 Hz, CH(CH_3)$_2$); δ_C (75 MHz) 165.9, 146.9, 143.4, 137.7, 129.6, 127.2, 121.6, 60.4, 53.0, 44.0, 24.2, 22.4, 21.9, 21.5, 14.2; *m/z* (CI) 357 $[M+NH_4]^+$, 340 $[M+H]^+$, 189 (Found: C, 60.22; H, 7.19; N, 4.14. $C_{17}H_{25}NO_4S$ requires C, 60.15; H, 7.42; N, 4.14%).

(*E*)-Ethyl (toluene-4-sulfonamido)oct-2-enoate

To a solution of oxalyl chloride (1.94 ml, 22.2 mmol, 1.2 equiv) in CH_2Cl_2 (25 ml) at –78 ºC was added DMSO (3.15 ml, 44.4 mmol, 2.4 equiv) in CH_2Cl_2 (25 ml). After 5 min a solution of 2-(toluene-4-sulfonamido)hexan-1-ol (5.00 g, 18.5 mmol, 1.0 equiv) in CH_2Cl_2 (35 ml) was added dropwise with stirring. After a further 45 min Et_3N (12.9 ml, 92.5 mmol, 5.0 equiv) in CH_2Cl_2 (15 ml) was added dropwise and the solution brought slowly to rt. After a further 30 minutes the reaction mixture was diluted with CH_2Cl_2 (250 ml), washed with saturated aqueous $NaHCO_3$ (200 ml) and the aqueous layer re-extracted with CH_2Cl_2 (50 ml). The combined organic extracts are then washed with acetic acid (1 M; 50 ml), H_2O (200 ml), brine (200 ml) and dried (Na_2SO_4). Concentration under reduced pressure gave the crude aldehyde as an orange oil that was immediately dissolved in CH_2Cl_2 (250 ml) and Ph_3PCHCO_2Et (25.8 g, 74.0 mmol, 4.0 equiv) added at rt with stirring. After 12 h the mixture was concentrated under reduced pressure and triturated with Et_2O (125 ml) to remove triphenylphosphine oxide. Chromatography (30% EtOAc–petrol) gave (*E*)-ethyl (toluene-4-sulfonamido)oct-2-enoate (5.00 g, 80%) a colourless oil; R_f 0.30 (30% EtOAc–petrol); ν_{max} (film) 2958, 1699, 1657, 1456, 1325, 1159 cm^{-1}; δ_H (300 MHz) 7.71 (2H, d, J 8.0 Hz, *ortho* Ts), 7.23 (2H, d, J 8.0 Hz, *meta* Ts), 6.57 (1H, dd J 16.0, 7.0 Hz, C*H*=CHCO$_2$Et), 5.74-5.67 (2H, m, C=C*H*CO$_2$Et and NH), 4.08 (1H, q J 7.0 Hz, OCH$_2$), 3.83 (1H, t J 7.0 Hz, C*H*NHTs), 2.35 (3H, s, Me of Ts), 1.45-1.43 (2H, m CHCH_2) 1.23-1.12 (7H, m, $(CH_2)_2$ and OCH$_2$CH_3), 0.80-0.73 (3H, m, $(CH_2)_3CH_3$); δ_C (75 MHz) 166.0, 147.0, 143.3, 137.8, 129.6, 128.3,

121.7, 60.4, 54.7, 34.5, 27.3, 22.1, 21.4, 14.2, 13.7; *m/z* (CI) 357 $[M+NH_4]^+$, 206, 189, 86 (Found: $[M+NH_4]^+$, 357.1846. $C_{17}H_{29}N_2O_4S$ requires $[M+H]^+$, 357.1848) (Found: C, 59.96; H, 7.58; N, 4.13. $C_{14}H_{25}N_2O_3S$ requires C, 60.15; H, 7.58; N, 4.13%).

(–)-(*S*)-(*E*)-4-(Toluene-4-sulfonamide)pent-2-en-1-ol

DIBAL-H (91.4 ml of a 1 M solution in CH_2Cl_2, 91.4 mmol, 3.6 equiv) was added dropwise to a solution of (–)-(*S*)-(*E*)-ethyl 4-(toluene-4-sulfonamido)pent-2-enoate (8.00 g, 25.4 mmol, 1.0 equiv) in CH_2Cl_2 (200 ml) at –78 ºC with vigorous stirring. After 15 min the mixture was allowed to warm to rt. After a further 2 h the reaction was quenched with EtOAc (20 ml) and poured into Rochelle's salt (500 ml of a 50% saturated aqueous solution) and the resulting two phase mixture stirred until both layers became clear (1 h). The aqueous layer was extracted with EtOAc (2 x 300 ml) and the combined organic extracts washed with brine (500 ml) and dried (Na_2SO_4). Concentration under reduced pressure gave alcohol (–)-(*S*)-(*E*)-4-(toluene-4-sulfonamido)pent-2-en-ol (6.01 g, 86%) as an off-white crystalline solid; mp 64–65 ºC (Et_2O); R_f 0.25 (50% EtOAc–petrol); $[\alpha]_D^{23}$ –40.0 (*c* 1.0, $CHCl_3$); ν_{max} (film) 3479, 3273, 1450, 1313, 1147, 1093, 974, 816, 665 cm^{-1}; δ_H (300 MHz) 7.77 (2H, d, J 8.0 Hz, *ortho* Ts), 7.31 (2H, d, J 8.0 Hz, *meta* Ts), 5.66 (1H, dt, J 15.5, 5.0 Hz, CH=C*H*CH_2), 5.51 (1H, dd, J 15.5, 6.0 Hz, C*H*=$CHCH_2$), 4.86 (2H, d, J 7.0 Hz, NH), 4.00 (br s, C*H*$_2$OH), 3.91 (1H, q, J 7.0 Hz, C*H*NHTs), 2.44 (3H, s, Me of Ts), 1.18 (3H, d, J 7.0 Hz, $CHCH_3$); δ_C (75 MHz) 143.4, 138.0, 132.1, 130.1, 129.6, 127.3, 62.7, 50.9, 21.7, 21.5; *m/z* (CI) 273 $[M+NH_4]^+$, 189, 52 (Found: $[M+NH_4]^+$, 273.1297. $C_{12}H_{17}NO_3S$ requires $[M+NH_4]^+$, 273.1273) (Found: C, 56.41; H, 6.57; N, 5.47. $C_{12}H_{17}NO_3S$ requires C, 56.45; H, 6.71; N, 5.49%).

(–)-(*S*)-(*E*)-5-Methyl-4-(toluene-4-sulfonamido)hex-2-en-1-ol

DIBAL-H (94.3 ml of a 1 M solution in CH_2Cl_2, 94.3 mmol, 3.6 equiv) was added dropwise to a solution of (–)-(*S*)-(*E*)-ethyl 5-methyl-4-(toluene-4-sulfonamido)hex-2-enoate (8.50 g, 26.2 mmol, 1.0 equiv) in CH_2Cl_2 (200 ml) at –78 ºC with vigorous stirring. After 15 min the mixture was allowed to warm to rt. After a further 2 h the reaction was quenched with EtOAc (20 ml), poured into Rochelle's salt (500 ml of a 50% saturated aqueous solution) and the resulting two phase mixture stirred until both layers became clear (1 h). The aqueous layer was extracted with EtOAc (2 x 300 ml) and the combined organic extracts washed with brine (500 ml) and dried (Na_2SO_4). Concentration under reduced pressure gave alcohol (–)-(*S*)-(*E*)-5-methyl-4-(toluene-4-sulfonamido)hex-2-en-1-ol (6.20 g, 96%) as a colourless oil; R_f 0.30 (50% EtOAc–petrol); $[\alpha]_D^{22}$ –28.0 (*c* 1.0, $CHCl_3$); ν_{max} (film) 3569, 3126, 2964, 2873, 2360, 1452, 1396, 1317, 1153, 1092, 999 cm^{-1}; δ_H (300 MHz) 7.75 (2H, d, J 8.0 Hz, *ortho* Ts), 7.30-7.28 (2H, m, *meta* Ts), 5.49 (1H, dt, J 15.5, 5.0 Hz, C=C*H*CH_2), 5.38 (1H, dd, J 15.5, 7.0 Hz, C*H*=$CHCH_2$), 4.83 (1H, d, J 8.0 Hz, NH),

3.94-3.91 (2H, m, CH_2OH), 3.59 (1H, q, J 7.0 Hz, C*H*NHTs), 2.43 (3H, s, Me of Ts), 1.76-1.70 (1H, m, C*H*(CH_3)$_2$), 0.85 (6H, t, J 7.0 Hz, CH(CH_3)$_2$); δ_C (75 MHz) 143.3, 138.1, 131.8, 129.5, 128.9, 127.4, 62.7, 61.0, 32.8, 21.5, 18.3 (2 signals); *m/z* (CI) 301 $[M+NH_4]^+$, 283, 266, 264, 202, 189, 112, 110, 72 (Found: $[M+NH_4]^+$, 301.1589. $C_{14}H_{25}N_2O_3S$ requires $[M+NH_4]^+$, 301.1588) (Found: C, 59.57; H, 7.36; N, 4.70. $C_{14}H_{25}N_2O_3S$ requires C, 59.34; H, 7.47; N, 4.94%).

(–)-(*S*)-(*E*)-6-Methyl-4-(toluene-4-sulfonamido)hept-2-en-1-ol

DIBAL-H (74.6 ml of a 1 M solution in CH_2Cl_2, 74.6 mmol, 3.6 equiv) was added dropwise to a solution of (–)-(*S*)-(*E*)-ethyl 6-methyl-4-(toluene-4-sulfonamido)hept-2-enoate (7.40 g, 20.7 mmol, 1.0 equiv) in CH_2Cl_2 (200 ml) at –78 ºC with vigorous stirring. After 15 min the mixture was allowed to warm to rt. After a further 2 h the reaction was quenched with EtOAc (20 ml), poured into Rochelle's salt (500 ml of a 50% saturated aqueous solution) and the resulting two phase mixture stirred until both layers became clear (1 h). The aqueous layer was extracted with EtOAc (2 x 300 ml) and the combined organic extracts washed with brine (500 ml) and dried (Na_2SO_4). Concentration under reduced pressure gave (–)-(*S*)-(*E*)-6-methyl-4-(toluene-4-sulfonamido)hept-2-enol (7.3 g, 98%) as a colourless crystalline solid; mp 101–102 ºC (EtOAc); R_f 0.45 (50% EtOAc–petrol); $[\alpha]_D^{22}$ –8.0 (*c* 1.0, $CHCl_3$); ν_{max} (film) 3460, 3180, 2954, 2362, 1319, 1146, 1090 cm^{-1}; δ_H (300 MHz) 7.56 (2H, d, J 8.0 Hz, *ortho* Ts), 7.31 (2H, d, J 8.0 Hz, *meta* Ts), 5.53-5.61 (1H, dt, J 15.0, 5.0 Hz, C=C*H*CH_2); 5.35 (1H, dd, J 15.0, 7.0 Hz, CHC*H*=CH), 4.49 (1H, d, J 8.0 Hz, NH), 3.93-3.89 (2H, m CH_2OH), 3.84 (1H, t, J 8.0 Hz, C*H*NHTs), 2.44 (3H, s, Me of Ts), 1.64-1.56 (1H, m C*H*(CH_3)$_2$), 1.54-1.26 (2H, m, CH_2^{i}Pr), 0.79 (6H, q, J 6.0 Hz, CH(CH_3)$_2$); δ_C (75 MHz); 142.9, 137.9, 131.2, 130.7, 129.2, 127.4, 62.6, 53.9, 44.9, 24.2, 22.6, 22.4, 20.9; *m/z* (CI) 315 $[M+NH_4]^+$, 189, 126, 124, 86 (Found: $[M+NH_4]^+$, 315.1749. $C_{15}H_{23}NO_3S$ requires $[M+NH_4]^+$, 315.1742) (Found: C, 60.58; H, 7.87; N, 4.68. $C_{15}H_{23}NO_3S$ requires C, 60.58; H, 7.79; N, 4.71%).

(*E*)-4-(Toluene-4-sulfonamido)oct-2-en-1-ol

DIBAL-H (39.2 ml of a 1 M in CH_2Cl_2 solution, 39.2 mmol, 3.6 equiv) was added dropwise to a solution of (*E*)-ethyl 4-(toluene-4-sulfonamido)oct-2-enoate (3.70 g, 10.9 mmol, 1.0 equiv) in CH_2Cl_2 (100 ml) at –78 ºC with vigorous stirring. After 15 h the mixture was allowed to warm to rt. After a further 2 h the reaction was quenched with EtOAc (10 ml) and poured into Rochelle's salt (250 ml of a 50% saturated aqueous solution) and the resulting two phase mixture stirred until both layers became clear (1 h). The aqueous layer was extracted with EtOAc (2 x 150 ml) and the combined organic extracts washed with brine (200 ml) and dried (Na_2SO_4). Concentration under reduced pressure gave (*E*)-4-(toluene-4-sulfonamido)oct-2-enol (3.21 g, 99%) as an oil, which upon trituation with Et_2O yielded a white powder; mp 55–59 ºC (Et_2O); R_f 0.20 (50% EtOAc–petrol);

ν_{max} (film) 3055, 1987, 2306, 1421, 1265, 1160, 897, 737 cm^{-1}; δ_H (300 MHz) 7.56 (2H, d, J 8.0 Hz, *ortho* Ts), 7.31 (2H, d, 8.0 Hz, *meta* Ts), 5.58 (1H, dt, J 16.0, 5.0 Hz, CH=C*H*CH_2), 5.39 (1H, dd, J 16.0, 7.0 Hz, C*H*=$CHCH_2$), 4.59 (1H, br s, NH), 3.96 (2H, d, J 5.0 Hz, CH_2OH), 3.77 (1H, t, J 6.0 Hz, C*H*NHTs), 2.44 (3H, s, Me of Ts), 1.48-1.43 (2H, m, OH and $(CH_2)_2$C*H*H), 1.22 (5H, br s, $(CH_2)_2$CH*H*), 0.85-0.83 (3H, m, C$H_3(CH_2)_2$); δ_C (75 MHz) 143.3, 138.2, 131.0, 130.9, 129.5, 127.4, 62.7, 55.5, 35.4, 27.5, 22.3, 21.5, 13.9; *m/z* (CI) 315 $[M+NH_4]^+$, (Found: $[M+NH_4]^+$, 315.1735. $C_{15}H_{23}NO_3S$ requires $[M+NH_4]^+$, 315.1742) (Found: C, 60.60; H, 7.82; N, 4.52. $C_{15}H_{23}NO_3S$ requires C, 60.58; H, 7.82; N, 4.71%).

(+)-(*S*)-(*E*)-4-(4-Methylbenzylamino)pent-2-en-1-ol (6a)

Onto a solution of (–)-(*S*)-(*E*)-4-(toluene-4-sulfonamide)pent-2-en-1-ol (1.77 g, 6.94 mmol, 1.0 equiv), in THF (2 ml) at –78 ºC was condensed NH_3(l) (~50 ml) and freshly-cut sodium metal (1.11 g, 48.3 mmol, 7.0 equiv) added. After the sodium had dissolved (10 min) the reaction was quenched with MeOH (10 ml) until decolourisation was observed. The NH_3(l) was then allowed to evaporate and the residue partitioned between CH_2Cl_2 (50 ml) and $NaHCO_3$(50 ml). The organic layer was washed with H_2O (20 ml) and the aqueous phase extracted with 10:8:1 $CHCl_3$:MeOH:NH_4OH (3 x 10 ml). The combined organic extracts were dried (Na_2SO_4) and concentrated under reduced pressure to give the crude amine (540 mg); δ_H (300 MHz) 5.67-5.55 (2H, m, C*H*=C*H*), 4.04-3.94 (2H, m, CH_2OH), 3.43-3.39 (1H, m, C*H*NH_2), 1.08 (3H, d, J 6.5 Hz, CHCH_3); δ_C (75 MHz) 136.8, 128.6, 62.5, 48.6, 24.8. A portion of the resulting yellow solid (185 mg, 1.83 mmol, 1.0 equiv) was dissolved in MeOH (7 ml) containing activated 4Å MS. Tolualdehyde (240 μl, 2.01 mmol, 1.1 equiv) was then added and the mixture stirred at rt. After 12 h the reaction was cooled to 0 ºC and $NaBH_4$ (84.0 mg, 2.20 mmol, 1.2 equiv) added and the mixture warmed slowly to rt. After a further 1 h, the reaction was filtered and concentrated under reduced pressure. Chromatography (50% MeOH–EtOAc) gave the *amine* **6a** as a pale yellow oil (298 mg, 80%); R_f 0.50 (50% MeOH–EtOAc); $[\alpha]_D^{22}$ +20.0 (*c* 1.0, $CHCl_3$); ν_{max} (film) cm^{-1} 3275, 2970, 2924, 1516, 1452, 1371, 1095, 1014, 974, 804; δ_H (300 MHz) 7.20-7.12 (4H, m, CH_2*Ar*Me), 5.73 (1H, dt, J 15.0, 5.0 Hz, C=C*H*CH_2), 5.61 (1H, dd, J 15.0, 7.0 Hz, CHC*H*=C), 4.10-4.09 (2H, m, CH_2OH,) 3.75 (1H, d, J 13.0 Hz, NC*H*H), 3.65 (1H, d, J 13.0 Hz, NCH*H*), 3.29-3.24 (1H, m, C*H*NH), 2.72 (2H, br, s, NH and OH), 2.34 (3H, s, Me of CH_2ArMe), 1.19 (3H, d, J 6.0 Hz, CHCH_3); δ_C (75 MHz) 136.9, 136.6, 134.7, 130.7, 129.2, 128.2, 62.6, 54.7, 51.0, 21.6, 21.1; *m/z* (CI) 206 $[M+H]^+$, 190, 122, 105 (Found: $[M+NH_4]^+$, 206.1547. $C_{13}H_9NO$ requires $[M+NH_4]^+$, 206.1545). *Elemental analysis failed twice due to the hygroscopic nature of the compound*.

(–)-(*S*)-(*E*)-5-Methyl-4-(4-methylbenzylamino)hex-2-en-1-ol (6b)

Onto a solution of (–)-(*S*)-(*E*)-5-methyl-4-(toluene-4-sulfonamide)hex-2-en-1-ol (3.50 g, 12.3 mmol, 1.0 equiv) in THF (10 ml) at –78 ºC was condensed NH_3(l) (~150 ml) and freshly cut sodium metal (1.70 g, 74.0 mmol, 7.0 equiv) then added. After the sodium had dissolved (10 min) the reaction was quenched with MeOH (50 ml) until the solution decolourised. The NH_3(l) was then allowed to evaporate and the residue partitioned between 2:1 $CHCl_3$:EtOH (20 ml) and H_2O (20 ml). The aqueous phase was further extracted with 2:1 $CHCl_3$:EtOH (5 x 25 ml) and the combined organic extracts washed with brine (50 ml) and dried (Na_2SO_4). After concentration under reduced pressure the resulting residue was passed through a short pad of silica (10:8:1 $CHCl_3$:MeOH:NH_3) and concentrated under reduced pressure to give the crude amine (1.05 g); δ_H (300 MHz) 5.66-5.49 (2H, m, C*H*=C*H*), 3.99 (2H, d, J 5.0 Hz, CH_2OH), 3.00 (1H, t, J 6.0 Hz, C*H*NH_2), 2.65 (2H, br s, NH_2), 1.59-1.49 (1H, m, C*H*$(CH_3)_2$), 0.81 (3H, d, J 7.5 Hz, CH(CH_3)$_2$), 0.79 (3H, d, J 7.5 Hz, CH(CH_3)$_2$); δ_C (75 MHz) 131.1, 130.6, 62.2, 59.0, 33.7, 18.6, 18.5. A portion of this (240 mg, 1.86 mmol, 1.0 equiv) was dissolved in MeOH (7 ml) containing activated 4Å MS. Tolualdehyde (440 μl, 3.70 mmol, 2.0 equiv) was then added and the mixture stirred at rt. After 12 h the reaction was cooled to 0 ºC and $NaBH_4$ (170 mg, 4.50 mmol, 2.4 equiv) added and the mixture warmed slowly to rt. After a further 1 h, the reaction was filtered, NaOH (2 M; 10 ml) added and the mixture extracted with CH_2Cl_2 (2 x 10 ml). The combined organic extracts were washed with brine (20 ml) and dried (Na_2SO_4). Chromatography (5-10% MeOH–CH_2Cl_2) gave the *amine* **6b** (330 mg, 53%); R_f 0.53 (50% MeOH–EtOAc); $[\alpha]_D^{28}$ –32.0 (*c* 0.5, $CHCl_3$); ν_{max} (film) 3307, 2956, 2870, 1513, 1452, 1367, 1088, 976, 806 cm^{-1}; δ_H (300 MHz) 7.21 (2H, d, J 8.0 Hz, *ortho* CH_2ArMe), 7.24 (2H, d, J 8.0 Hz, *meta* CH_2ArMe), 5.72 (1H, dt, J 15.5, 5.0 Hz, C=C*H*CH_2), 5.54 (1H, dd, J 15.5, 8.0 Hz, CHC*H*=C), 4.15 (2H, d, J 5.0 Hz, CH_2OH,) 3.82 (1H, d, J 13.0 Hz, NC*H*H), 3.60 (1H, d, J 13.0 Hz, NCH*H*), 2.85-2.81 (2H, m, C*H*NH and NH), 2.35 (3H, s, Me of CH_2ArMe), 1.77-1.71 (1H, m, C*H*$(CH_3)_2$), 0.93 (3H, d, J 7.0 Hz, CH(CH_3)$_2$), 0.90 (3H, d, J 7.0 Hz, CH(CH_3)$_2$); δ_C (75 MHz) 137.2, 136.5, 132.9 131.8, 129.1, 128.2, 65.5, 62.7, 51.0, 32.2, 21.2, 19.5, 18.5; *m/z* (CI) 234 $[M+H]^+$, 216, 190, 122, 105 (Found: $[M+H]^+$, 234.1860. $C_{15}H_{23}NO$ requires $[M+H]^+$, 234.1858). *Elemental analysis failed twice due to the hygroscopic nature of the compound.*

(+)-(*S*)-(*E*)-6-Methyl-4-(4-methylbenzylamino)hept-2-en-1-ol (6c)

Onto a solution of (–)-(*S*)-(*E*)-6-methyl-4-(toluene-4-sulfonamido)hept-2-en-1-ol (3.00 g, 10.1 mmol, 1.0 equiv) in THF (5 ml) at –78 ºC was condensed NH_3(l) (~75 ml) and freshly cut sodium metal (1.39 g, 60.6 mmol, 7.0 equiv) added. After the sodium had dissolved (10 min) the reaction was quenched with solid NaOAc until the solution decolourised. The NH_3(l) was then allowed to evaporate and the residue partitioned between 2:1 $CHCl_3$:EtOH (20 ml) and H_2O (20 ml). The

aqueous phase was extracted with 2:1 $CHCl_3$:EtOH (5 x 25 ml) and the combined organic extracts washed with brine (50 ml) and dried (Na_2SO_4). After concentration under reduced pressure the resulting residue was passed through a short pad of silica (10:8:1 $CHCl_3$:MeOH:NH_3) and concentrated under reduced pressure to give the crude amine (1.05 g); δ_H (300 MHz) 5.76 (1H, dt, J 15.5, 5.0 Hz, C=C*H*CH_2), 5.64 (1H, dd, J 15.5, 7.0 Hz, C*H*=CHCH_2), 4.15 (2H, d, J 5.0 Hz, C*H*$_2$OH), 3.41 (1H, q, J 7.0 Hz, C*H*NH_2), 1.71-1.62 (4H, m, NH_2 and C*H*$_2$*i*Pr), 1.30 (1H, t, J 7.5 Hz, C*H*$(CH_3)_2$), (6H, d, J 6.5 Hz, CH(C*H*$_3$)$_2$); δ_C (75 MHz) 137.2, 128.3, 63.2, 51.3, 47.1, 24.9, 22.7 (2 signals). A portion of this (250 mg, 1.75 mmol, 1.0 equiv) was dissolved in MeOH (7 ml) containing activated 4Å MS. Tolualdehyde (230 μl, 1.93 mmol, 1.1 equiv) was then added and the mixture stirred at rt. After 12 h the reaction was cooled to 0 ºC and $NaBH_4$ (106 mg, 2.80 mmol, 1.6 equiv) added and the mixture warmed slowly to rt. After a further 1 h, the reaction was filtered, NaOH (1 M; 10 ml) added and the mixture extracted with CH_2Cl_2 (2 x 10 ml). The combined organic extracts were washed with brine (20 ml) and dried (Na_2SO_4). Chromatography (10% MeOH–CH_2Cl_2) gave the *amine* **6c** (453 mg, 72%) as a pale yellow oil; R_f 0.57 (10% MeOH–CH_2Cl_2); $[\alpha]_D^{26}$ +4.0 (*c* 1.0, $CHCl_3$); ν_{max} (film) 3255, 1951, 2912, 1566, 1516, 1254, 1319, 1089, 1025, 972, 804 cm^{-1}; δ_H (300 MHz) 7.19 (2H, d, J 8.0 Hz, *ortho* CH_2ArMe), 7.13 (2H, d, J 8.0 Hz, *meta* CH_2ArMe), 5.73 (1H, dt, J 15.0, 5.0 Hz, C=C*H*CH_2), 5.51 (1H, dd, J 15.0, 8.0 Hz, C*H*=CHCH_2), 4.13 (2H, d, J 5.0 Hz, C*H*$_2$OH), 3.79 (1H, d, J 13.0 Hz, NC*H*H), 3.61 (1H, d, J 13.0 Hz, NCH*H*), 3.14 (1H, td, J 8.0, 8.0 Hz, CHN), 2.34 (3H, s, Me of CH_2ArMe), 1.65-1.58 (1H, m, C*H*$(CH_3)_2$), 1.38-1.33 (2H, m, C*H*$_2$*i*Pr), 0.86 (6H, d, J 6.5 Hz, CH(C*H*$_3$)$_2$); δ_C (75 MHz) 137.0, 136.6, 133.8, 131.8, 129.1, 128.2, 62.7, 57.9, 50.9, 44.9, 24.7, 23.9, 23.1, 21.1; *m/z* (CI) 248 $[M+H]^+$, 190, 122 (Found: $[M+H]^+$, 248.2007. $C_{16}H_{25}NO$ requires $[M+NH]^+$, 248.2014). *Elemental analysis failed twice due to the hygroscopic nature of the compound.*

(*E*)-4-(4-Methylbenzylamino)oct-2-en-1-ol (6d)

Onto a solution of (*E*)-4-(toluene-4-sulfonamido)oct-2-en-1-ol (90.0 mg, 0.231 mmol, 1.0 equiv) in THF (2 ml) at –78 ºC was condensed NH_3(l) (~15 ml) and freshly cut sodium metal (37.0 mg, 1.61 mmol, 7.0 equiv) then added. After the sodium had dissolved (10 min) the reaction was quenched with MeOH (0.5 ml) until the solution decolourised. The NH_3(l) was then allowed to evaporate and the residue extracted with $CHCl_3$ (5 x 5 ml), filtered through celite and dried (Na_2SO_4). Evaporation under reduced pressure gave the crude amine (30.1 mg); δ_H (300 MHz) 5.74-5.67 (2H, m, C*H*=C*H*), 4.14 (2H, d, J 5.0 Hz, C*H*$_2$OH), 3.32 (1H, t, J 6.5 Hz, C*H*NH_2), 1.76-1.53 (2H, m, CHC*H*$_2$), 1.47-1.21 (4H, m, CH(C*H*$_2$)$_2$), 0.91-0.83 (3H, m, $(CH_2)_2$C*H*$_3$); δ_C (75 MHz) 135.6, 127.4, 62.6, 53.7, 35.7, 28.6, 23.0, 14.4. This was then dissolved in MeOH (1 ml) containing activated 4Å MS. Tolualdehyde (30.0 μl, 0.230 mmol, 1.1 equiv) was then added and the mixture stirred at rt. After

12 h the reaction was cooled to 0 ºC and $NaBH_4$ (18.1 mg, 0.460 mmol, 2.0 equiv added and the mixture warmed slowly to rt. After a further 1 h, the reaction was filtered, NaOH (2 M; 5 ml) added and the mixture extracted with CH_2Cl_2 (2 x 5 ml). The combined organic extracts were washed with brine (20 ml) and dried (Na_2SO_4). Chromatography (5-10% MeOH–CH_2Cl_2) gave the *amine* **6d** (40.0 mg, 0.162 mmol, 70%) as a pale yellow oil; R_f 0.50 (50% MeOH–EtOAc); ν_{max} (film) 2954, 2927, 2858, 1514, 1456, 1375, 1090, 974, 806 cm^{-1}; δ_H (300 MHz) 7.21 (2H, d, J 8.0 Hz, *ortho* CH_2ArMe), 7.14 (2H, d, J 8.0 Hz, *meta* CH_2ArMe), 5.74 (1H, dt, J 15.5, 5.0 Hz, C=C*H*CH_2), 5.54 (1H, dd, J 15.5, 8.0 Hz, CHC*H*=C), 4.15 (2H, d, J 5.0 Hz, C*H*$_2$OH,) 3.79 (1H, d, J 13.0 Hz, NC*H*H), 3.63 (1H, d, J 13.0 Hz, NCH*H*), 3.11-3.04 (1H, m, C*H*NH), 2.35 (3H, s, Me of CH_2ArMe), 1.54-1.42 (2H, m, C*H*$_2(CH_2)_2CH_3$), 1.28-1.27 (4H, m, $CH_2(CH_2)_2CH_3$), 0.89 (3H, t, J 6.0 Hz, $CH_2(CH_2)_2CH_3$); δ_C (75 MHz); 137.0, 136.6, 134.0, 131.7, 129.1, 128.5, 63.0, 59.9, 50.9, 35.3, 28.1, 22.7, 21.2, 14.1 *m/z* (CI) 248 $[M+H]^+$, 190, 122, 105, 52 (Found: $[M+H]^+$, 248.2013. $C_{16}H_{25}NO$ requires $[M+H]^+$, 234.2014). *Elemental analysis failed twice due to the hygroscopic nature of the compound.*

(–)-(*S*)-(*E*)-4-{(4-Methylbenzyl)[2-(toluene-4-sulfonyl)acetyl]amino}pent-2-enol

PyBOP (177 mg, 0.340 mmol, 1.0 equiv) was added to a solution of amine **6a** (58.0 mg, 0.280 mmol, 1.0 equiv), $TsCH_2CO_2H$ (72.8 mg, 0.340 mmol, 1.0 equiv) and Hünig's base (16.0 μl, 0.920 mmol, 3.3 equiv) in CH_2Cl_2 (2 ml). After 12 h the reaction was quenched with saturated aqueous NH_4Cl (1 ml) and extracted with CH_2Cl_2 (2 x 5 ml). The combined organic extracts were concentrated under reduced pressure and dissolved in THF (1 ml) and NaOH (2 M; 1 ml). After stirring at rt for 1h the mixture was extracted with CH_2Cl_2 (3 x 5 ml) and dried (Na_2SO_4). Concentration under reduced pressure and chromatography (5% MeOH–CH_2Cl_2) yielded (–)-(*S*)-(*E*)-4-{(4-methylbenzyl)-[2-(toluene-4-sulfonyl)acetyl]amino}pent-2-enol (103 mg, 92%) as a colourless oil; R_f 0.50 (5% MeOH–CH_2Cl_2); $[\alpha]_D^{25}$ –53.3 (*c* 1.0, $CHCl_3$); ν_{max} (film) 3435, 1643, 1439, 1321, 1153, 1001 cm^{-1}; δ_H (300 MHz) 7.83-7.77 (2H, m, *ortho* Ts), 7.37-7.28 (2H, m, *meta* Ts), 7.14 (2H, d, J 8.0 Hz, *ortho* CH_2ArMe), 7.04 (2H, d, J 8.0 Hz, *meta* CH_2ArMe), 5.83-5.63 (2H, m, CH=CH), 5.20 (0.67H, t, J 5.0 Hz, CHN rotamer 1), 4.81-4.79 (0.33 H, m, CHN rotamer 2), 4.69 (0.67 H, d, J 18.0 Hz, C*H*HTs rotamer 1), 4.57 (1H, d, J 18.0 Hz, CH*H*Ts rotamer 1and C*H*HTs rotamer 2), 4.43 (0.33H, d, J 14.0 Hz, C*H*HArMe rotamer 2), 4.50 (0.33H, d, J 15.0 Hz, CH*H*Ts rotamer 2), 4.28 (0.33 H, d, J 14.0 Hz, CH*H*ArMe rotamer 2), 4.01-4.13 (3.34H, C*H*$_2$OH and C*H*$_2$ArMe rotamer 1), 2.45 (3H, s, Me of Ts), 2.34 (3H, s, Me of CH_2Ar), 1.32 (0.99H, d, J 7.0 Hz, CHC*H*$_3$ rotamer 1), 1.22 (2.01H, d, J 7.0 Hz, CHC*H*$_3$ rotamer 1); δ_C (75 MHz) 162.5, 162.1, 145.3, 137.4, 136.5, 136.1, 136.0, 135.2, 134.2, 131.5, 131.2, 130.8, 130.4, 129.8, 129.7, 129.4, 129.0, 128.6, 127.5, 62.9, 62.6, 60.8, 60.4, 51.4, 47.3, 46.1, 44.2, 21.8, 21.2, 19.0, 17.1; *m/z* (CI) 419

$[M+NH_4]^+$, 402 $[M+H]^+$, 190 (Found: $[M+NH_4]^+$, 419.2000. $C_{22}H_{27}NO_4S$ requires $[M+NH_4]^+$, 419.2005) (Found: C, 65.72; H, 6.49; N, 3.22. $C_{22}H_{27}NO_4S$ requires C, 65.81; H, 6.78; N, 3.49%).

(–)-(*S*)-(*E*)-5-Methyl-4-{(4-methylbenzyl)[2-(toluene-4-sulfonyl)acetyl]amino}hex-2-enol

PyBOP (146 mg, 0.274 mmol, 1.2 equiv) was added to a solution of amine **6b** (53.0 mg, 0.228 mmol, 1.0 equiv), $TsCH_2CO_2H$ (58.6 mg, 0.274 mmol, 1.2 equiv) and Hünig's base (131 μl, 0.752 mmol, 3.3 equiv) in CH_2Cl_2 (2 ml). After 12 h the reaction was quenched with saturated aqueous NH_4Cl (4 ml) and extracted with CH_2Cl_2 (3 x 5 ml). The combined organic extracts were concentrated under reduced pressure and dissolved in THF (2 ml) and NaOH (2 M; 2 ml). After stirring at rt for 1h the mixture was extracted with CH_2Cl_2 (3 x 5 ml) and dried (Na_2SO_4). Concentration under reduced pressure and chromatography (80% Et_2O–petrol) yielded (–)-(*S*)-(*E*)-5-methyl-4-{(4-methylbenzyl)[2-(toluene-4-sulfonyl)acetyl]amino}hex-2-enol (75.0 mg, 76%) as a colourless oil; R_f 0.57 (50% EtOAc–petrol); $[\alpha]_D^{24}$ –22.2 (*c* 1.0, $CHCl_3$); ν_{max} (film) 3431, 2960, 1643, 1429, 1321, 1155, 1086, 1018, 974, 800 cm^{-1}; δ_H (300 MHz) 7.73-7.66 (2H, m, *ortho* Ts), 7.19-7.18 (2H, m, *meta* Ts), 7.06-6.93 (4H, m, CH_2ArMe), 5.80 (0.2H, dt, J 16.0 Hz, 4.0 Hz, CH=C*H*CH_2 rotamer 2), 5.68 (0.8H, dt, J 15.0, 5.0 Hz, H-3, CH=C*H*CH_2 rotamer 1), 5.51-5.43 (1H, m, C*H*=$CHCH_2$), 4.82 (0.8H, d, J 18.0 Hz, C*H*HTs rotamer 1), 4.67 (0.2H, d, J 15.0 Hz, C*H*HTs rotamer 2), 4.49 (0.8H, d, J, 18.0 Hz, CH*H*Ts rotamer 1), 4.46-4.39 (0.4H, m, CH*H*Ts rotamer 2 and C*H*HArMe rotamer 2), 4.17 (0.2H, d, J 15.0 Hz, CH*H*ArMe rotamer 2), 4.07 (0.8H, d, J 14.0 Hz, C*H*HArMe rotamer 1), 3.89-3.85 (2.8H, m, CH*H*ArMe rotamer 1 and CHN), 2.36 (3H, s, Me of CH_2ArMe), 2.25 (3H, s, Me of Ts), 2.15-1.90 (2H, m, C*H*$_2$OH), 1.24-1.08 (1H, m, C*H*$(CH_3)_2$), 0.94 (2.4H, d, J 6.0 Hz, CH(C*H*$_3)_2$ rotamer 1), 0.88 (0.6H, d, J 6.0 Hz, CH(C*H*$_3)_2$ rotamer 2), 0.81 (3H, d, J, 6.0 Hz, CH(C*H*$_3)_2$ rotamer 1 and rotamer 2); δ_C (75 MHz) 162.3, 145.1, 137.5, 136.0, 134.4, 134.0, 129.7, 129.5, 128.8, 128.6, 128.5, 128.1, 127.9, 126.3, 64.0, 62.8, 60.9, 48.8, 30.3, 21.7, 21.0, 20.0, 19.4; *m/z* (CI) 447 $[M+NH_4]^+$, 430 $[M+H]^+$, 412, 276, 188, 174 (Found: $[M+NH_4]^+$, 430.2049. $C_{24}H_{31}NO_4S$ requires $[M+NH_4]^+$, 430.2052).

(*E*)-4-{(4-methylbenzyl)[(2-toluene-4-sulfonyl)acetyl]amino}oct-2-enol

PyBOP (146 mg, 0.280 mmol, 2.0 equiv) was added to a solution of amine **6d** (34.0 mg, 0.140 mmol, 1.0 equiv), $TsCH_2CO_2H$ (59.9 mg, 0.280 mmol, 2.0 equiv) and Hünig's base (120 μl, 0.770 mmol, 5.5 equiv) in CH_2Cl_2 (1 ml). After 12 h the reaction was quenched with saturated aqueous NH_4Cl (1 ml) and extracted with CH_2Cl_2 (2 x 5 ml). The combined organic extracts were concentrated under reduced pressure and dissolved in THF (1 ml) and NaOH (2 M; 1 ml). After stirring at rt for 1h the mixture was extracted with CH_2Cl_2 (3 x 5 ml) and dried (Na_2SO_4). Concentration under reduced pressure and chromatography (50% EtOAc–petrol) yielded (*E*)-4-{(4-

methylbenzyl)[(2-toluene-4-sulfonyl)acetyl]amino}oct-2-enol (45.2 mg, 72%) as a colourless oil; R_f 0.25 (50% EtOAc–petrol); ν_{max} (film) 3458, 2953, 2929, 2249, 1641, 1429, 1321, 1155, 1086, 1018, 976, 910, 810, 731 cm^{-1}; δ_H (300 MHz) 7.72 (2H, d, J 8.0 Hz, *ortho* Ts), 7.36-7.34 (2H, m, *meta* Ts), 7.15 (2H, d, J 8.0 Hz, *ortho* ArMe), 7.04 (2H, d, J 8.0 Hz, *meta* ArMe), 5.82-5.77 (1H, m, CH=C*H*CH_2), 5.62 (1H, dd, J 15.0, 7.0 Hz, C*H*=$CHCH_2$), 4.95-4.93 (0.7 H, m, CHN rotamer 1), 4.73 (0.7 H, d, J 18.0 Hz, C*H*HTs rotamer 1), 4.61 (0.7 H, d, J 18.0 Hz, CH*H*Ts rotamer 1), 4.55-4.02 (5H, m, CH_2Ts rotamer 2, 2H CH_2ArMe, 2H CH_2OH and CHN rotamer 2), 2.46 (3H, s, Me of CH_2ArMe), 2.34 (3H, s, Me of Ts), 1.61-0.84 (9H, m, $(CH_2)_3CH_3$); δ_C (75 MHz) 162.4, 145.2, 137.4, 136.6, 136.0, 135.2, 134.1, 132.8, 132.2, 129.6, 129.3, 128.9, 128.6, 126.1, 62.9, 62.7, 60.9, 60.4, 60.1, 56.7, 48.0, 46.3, 32.6, 31.6, 28.6, 28.3, 22.5, 21.8, 21.3, 14.0; *m/z* (CI) 444 $[M+H]^+$, 290 (Found: $[M+H]^+$, 444.2201. $C_{25}H_{33}NO_4S$ requires $[M+H]^+$, 444.2209) (Found: C, 67.55; H, 7.29; N, 3.07. $C_{25}H_{33}NO_4S$ requires C, 67.69; H, 7.50; N, 3.16%).

(–)-(*S*)-(*E*)-Carbonic acid methyl ester 4-{(4-methylbenzyl)-[2-(toluene-4-sulfonyl)-acetyl]amino}pent-2-enyl (7a)

To a solution of (–)-(*S*)-(*E*)-4-{(4-methylbenzyl)[2-(toluene-4-sulfonyl)acetyl]amino}pent-2-enol (87.0 mg, 0.220 mmol, 1.0 equiv) in CH_2Cl_2 (2 ml) at 0 ºC was added pyridine (34.5 μl, 0.660 mmol, 3.0 equiv), methyl chloroformate (50.1 μl, 0.660 mmol, 3.0 equiv) and DMAP (1.3 mg, 0.011 mmol, 0.05 equiv). The reaction mixture was warmed to rt. and after 1 h was diluted with CH_2Cl_2 (5 ml) then quenched by addition of saturated aqueous NH_4Cl (5 ml). The organic layer was washed with brine (5 ml) and dried (Na_2SO_4). Concentration under reduced pressure and chromatography (30% EtOAc–petrol) gave the *carbonate* **7a** (95.4 mg, 95%) as a colourless oil; R_f 0.83 (5% MeOH–CH_2Cl_2); $[\alpha]_D^{22}$ –72.0 (*c* 0.5, $CHCl_3$); ν_{max} (film) 2958, 1750, 1645, 1441, 1265, 1160, 794 cm^{-1}; δ_H (300 MHz) 7.81-7.76 (2H, m, *ortho* Ts), 7.38-7.32 (2H, m, *meta* Ts), 7.17-7.03 (4H, m, CH_2*Ar*Me), 5.77-5.71 (2H, m, CH=CH), 5.22.5.20 (0.86 H, m, CHN rotamer 1), 4.74-4.72 (0.14H, m, CHN rotamer 2), 4.71 (1H, d, J 18.5 Hz, C*H*HTs), 4.59-4.51 (2.86 H, m, CH_2OH and CH*H*Ts rotamer 1), 4.38 (0.14 H, d, J 14.0 Hz, C*H*HArMe rotamer 2), 4.27 (0.14 H, d, J 14.0 Hz, CH*H*ArMe rotamer 2), 4.24 (0.14 H, d, J 15.0 Hz, CH*H*Ts rotamer 2), 4.10 (0.86 H, d, J 14.0 Hz, C*H*HArMe rotamer 1), 4.03 (0.86 H, d, J 14.0 Hz CH*H*ArMe rotamer 1), 3.81 (0.42H, s, OCO_2CH_3 rotamer 2), 3.78 (2.58H, s, OCO_2CH_3 rotamer 1), 2.45 (3H, s, Me of Ts), 2.35 (3H, s, Me of CH_2ArMe), 1.33 (0.42H, d, J 7.0 Hz, $CHCH_3$ rotamer 2), 1.22 (2.58H, d, J 7.0 Hz, $CHCH_3$ rotamer 1); δ_C (75 MHz) 162.5, 162.0, 155.5, 145.2, 137.4, 136.5, 136.0, 135.8, 135.0, 134.6, 134.4, 134.0, 129.8, 129.0, 128.6, 127.4, 125.8, 125.5, 67.6, 67.3, 60.8, 60.4, 55.1, 54.9, 51.3, 45.9, 21.8, 21.1, 18.6, 16.9; *m/z* (CI) 477 $[M+NH_4]^+$, 460 $[M+H]^+$, 384, 306, 230, 174 (Found: $[M+NH_4]^+$, 460.1792.

$C_{24}H_{29}N_1O_6S_1$ requires $[M+NH_4]^+$, 460.1794) (Found: C, 62.80; H, 6.23; N, 3.05. $C_{24}H_{29}N_1O_6S_1$ requires C, 62.73; H, 6.36; N, 3.05%).

(–)-(*S*)-(*E*)-Carbonic acid methyl ester 5-methyl-4-{(4-methylbenzyl)-[2-(toluene-4-sulfonyl)-acetyl]amino}hex-2-enyl ester (7b)

To a solution of (–)-(*S*)-(*E*)-5-methyl-4-{(4-methylbenzyl)[2-(toluene-4-sulfonyl)acetyl]amino}hex-2-enol (50.0 mg, 0.117 mmol, 1.0 equiv) in CH_2Cl_2 (2 ml) at 0 ºC was added pyridine (30.6 μl, 0.585 mmol, 5.0 equiv), methyl chloroformate (36.1 μl, 0.468 mmol, 4.0 equiv) and DMAP (1.4 mg, 0.012 mmol, 0.1 equiv). The reaction mixture was warmed to rt. and after 1 h was diluted with CH_2Cl_2 (5 ml) then quenched by addition of saturated aqueous NH_4Cl (5 ml). The organic layer was washed with brine (5 ml) and dried (Na_2SO_4). Concentration under reduced pressure and chromatography (30% EtOAc–petrol) gave the *carbonate* **7b** (54.1 mg, 95%) as a colourless oil; R_f 0.80 (50% EtOAc–petrol); $[\alpha]_D^{22}$ –3.0 (*c* 4.0, $CHCl_3$); ν_{max} (film) 2958, 1749, 1647, 1443, 1323, 1269, 1155, 1086, 951, 914, 795, 731 cm^{-1}; δ_H (300 MHz) 7.83 (0.24H, d, J 8.0 Hz, *ortho* Ts rotamer 2), 7.76 (1.76H, d, J 8.0 Hz, *ortho* Ts rotamer 1), 7.28-7.40 (2H, *meta* Ts rotamer 1 and rotamer 2), 7.13 (2H, d, J 8.0 Hz, *ortho* CH_2ArMe), 7.02 (2H, d, J 8.0 Hz *meta* CH_2ArMe), 5.90 (0.12H, dt, J 15.0, 6.0 Hz, CH=C*H*CH_2 rotamer 2), 5.72-5.62 (1.88H, m, CH=CH rotamer 1 and C*H*=$CHCH_2$ rotamer 2), 4.89 (0.88H, d, J 18.0 Hz, C*H*HTs rotamer 1), 4.66 (0.12H, d, J 16.0 Hz, C*H*HTs rotamer 2), 4.60 (0.88H, CH*H*Ts rotamer 1), 4.51-4.43 (3.12H, m, C*H*$_2$$OCO_2Me$ CHN and CH*H*Ts rotamer 2), 4.28 (0.12H, d, J 12.0 Hz, C*H*HArMe rotamer 2), 4.23 (0.12H, d, J 12.0 Hz, CH*H*ArMe rotamer 2), 4.14 (0.88H, d, J 14.0 Hz, C*H*HArMe rotamer 1), 3.93 (0.88H. d, J 14.0 Hz, CH*H*ArMe rotamer 1), 3.74 (3H, s, OCO_2OCH_3), 2.45 (3H, s, Me of Ts), 2.34 (3H, s, Me of CH_2ArMe), 2.06-2.01 (1H, m, C*H*$(CH_3)_2$), 1.04 (2.64H, d, J 6.5 Hz, CH(C*H*$_3$)$_2$ rotamer 1), 0.96 (0.36H, d, J 6.5 Hz, CH(C*H*$_3$)$_2$ rotamer 2), 0.88 (3H, d, J 6.5 Hz, CH(C*H*$_3$)$_2$); δ_C (75 MHz) 162.4, 155.4, 145.2, 237.4, 135.9, 135.7, 133.6, 132.2, 131.6, 130.2, 129.9, 129.7, 128.6, 127.8, 126.2, 67.4, 66.7, 64.2, 60.9, 60.8, 54.8, 48.9, 31.0, 29.9, 22.9, 22.2, 20.2, 19.7, 19.4; *m/z* (CI) 505 $[M+NH_4]^+$, 488 $[M+H]^+$, 412, 334, 258, 189 (Found: $[M+NH_4]^+$, 505.2367. $C_{26}H_{33}NO_6S$ requires $[M+NH_4]^+$, 505.2372) (Found: C, 63.84; H, 6.62; N, 2.71. $C_{26}H_{33}NO_6S$ requires C, 64.04; H, 6.82; N, 2.87%).

(–)-(*S*)-(*E*)-Carbonic acid methyl ester 6-methyl-4-{(4-methylbenzyl)[2-(toluene-4-sulfonyl)acetyl]amino}hept-2-enyl ester (7c)

To a solution of $TsCH_2CO_2H$ (501 mg, 2.34 mmol, 2.0 equiv), DCC (532 mg, 2.58 mmol, 2.2 equiv) and HOBt (348 mg, 2.58 mmol, 2.2 equiv) at 0 ºC was added aminoalcohol **6c** (290 mg, 1.17 mmol 1.0 equiv) and the mixture warmed to rt. After 12 h the reaction was concentrated under reduced

pressure and the residue stirred in 10% NaOH:MeOH. After 12 h the mixture was extracted with CH_2Cl_2 (4 x 40 ml), the combined organic extracts washed with H_2O (20 ml), brine (20 ml) and dried (Na_2SO_4). Concentration under reduced pressure gave the crude amide (487 mg). A portion of this (430 mg, 0.970 mmol, 1.0 equiv) was dissolved in CH_2Cl_2 (5 ml) and methylchloroformate (150 μl, 1.94 mmol, 2.0 equiv), pyridine (101 μl, 1.94 mmol, 2.0 equiv) and DMAP (1.2 mg, 0.091 mmol, 0.1 equiv) added. The reaction was warmed to room temperature and after 12 h quenched with saturated aqueous NH_4Cl (10 ml). The mixture was extracted with CH_2Cl_2 (3 x 15 ml) and the combined organic extracts washed with H_2O (20 ml), brine (20 ml) and dried (Na_2SO_4). Evaporation under reduced pressure and chromatography (70% Et_2O–petrol) gave the *carbonate* **7c** (455 mg, 80%) as a colourless oil; R_f 0.32 (30% EtOAc–petrol); $[\alpha]_D^{23}$ −12.0 (*c* 1.0, $CHCl_3$); ν_{max} (film) 2929, 1749, 1649, 1443, 1267, 1155, 1086, 949, 793 cm^{-1}; δ_H (300 MHz) 7.81-7.74 (2H, m, *ortho* Ts), 7.36-7.30 (2H, m, *meta* Ts), 5.75-5.68 (2H, m, CH=CH), 5.03-5.02 (1H, m, CHN), 4.65-4.61 (2H, m, C*H*$_2$Ts), 4.56-4.52 (2H, m, C*H*$_2$ArMe), 4.12-4.02 (2H, m, C*H*$_2$OCO$_2$C*H*$_3$), 3.82-3.73 (3H, m, OCO$_2$C*H*$_3$), 2.44 (3H, s, Me of Ts), 2.33 (3H, s, Me of CH_2ArMe), 1.59-1.43 (3H, m, C*H*$_2$*i*Pr and C*H*(CH$_3$)$_2$), 0.89 (3H, d, J 6.5 Hz, CH(C*H*$_3$)$_2$), 0.84 (3H, d, J 6.5 Hz, CH(C*H*$_3$)$_2$) (75 MHz) 162.4, 162.2, 155.5, 145.2, 137.4, 136.5, 135.9, 135.0, 133.9, 133.4, 133.0, 129.7, 129.6, 129.0, 128.6, 127.6, 127.2, 126.7, 67.6, 67.3, 60.9, 60.4, 58.0 54.8, 48.1, 46.2, 41.8, 40.8, 24.7, 23.2, 22.8, 21.8, 21.0; *m/z* (CI) 519 $[M+NH_4]^+$, 502 $[M+H]^+$, 426, 348, 272 (Found: $[M+NH_4]^+$, 519.2508. $C_{27}H_{35}NO_6S$ requires $[M+NH_4]^+$, 519.2523) (Found: C, 64.83; H, 6.95; N, 2.66. $C_{27}H_{35}NO_6S$ requires C, 64.65; H, 7.03; N, 2.79%).

(*E*)-Carbonic acid methyl ester 4-{(4-methylbenzyl)[2-(toluene-4-sulfonyl)acetyl]amino}oct-2-enyl ester (7d)

To a solution of (*E*)-4-{(4-methylbenzyl)[(2-toluene-4-sulfonyl)acetyl]amino}oct-2-enol (43.0 mg, 0.0971 mmol, 1.0 equiv) in CH_2Cl_2 (1 ml) at 0 ºC was added pyridine (15.2 μl, 0.291 mmol, 3.0 equiv), methyl chloroformate (22.4 μl, 0.291 mmol, 3.0 equiv) and DMAP (1.2 mg, 0.01 mmol, 0.1 equiv). The reaction was warmed to rt and after 1 h was diluted with CH_2Cl_2 and quenched by addition of saturated aqueous NH_4Cl (5 ml). The organic layer was washed with brine (5 ml) and dried (Na_2SO_4). Concentration under reduced pressure and chromatography (30% EtOAc–petrol) gave the *carbonate* **7d** (43.3 mg, 96%) as a colourless oil; R_f 0.80 (50% EtOAc–petrol); ν_{max} (film) 2956, 1749, 1649, 1443, 1267, 1155, 949, 793 cm^{-1}; δ_H (300 MHz) 7.81-7.76 (2H, m, *ortho* Ts) 7.38-7.33 (2H, m, *meta* Ts), 7.17-7.02 (4H, m, CH$_2$*Ar*Me), 5.76-5.75 (2H, m, CH=CH), 4.92-4.91 (0.74 H, m, CHN rotamer 1), 4.74-4.32 (4.26 H, m, C*H*$_2$Ts, C*H*$_2$ArMe rotamer 2 and C*H*$_2$OCO$_2$Me), 4.10 (0.74 H, d, J 14.0 Hz, C*H*HArMe rotamer 1), 4.03 (0.74 H, d, J 14.0 Hz, CH*H*ArMe rotamer 1), 3.81 (0.78 H, s, OCO$_2$C*H*$_3$ rotamer 2), 3.77 (2.22 H, s, OCO$_2$C*H*$_3$ rotamer 1), 2.46 (3H, s, Me of Ts),

2.35-2.33 (3H, m, Me of CH_2ArMe), 1.67-1.60 (2H, m, $CH_2(CH_2)_2CH_3$), 1.45-1.28 (4H, m, $CH_2(CH_2)_2CH_3$), 0.89-0.83 (3H, m, $CH_2(CH_2)_2CH_3$); δ_C (75 MHz) 162.5, 162.3, 155.5, 145.2, 137.4, 136.6, 135.9, 133.8, 133.3, 133.1, 129.7, 128.9, 128.6, 127.9, 126.4, 126.1, 67.6, 67.4, 60.9, 60.4, 60.1, 56.8, 54.9, 48.1, 46.1, 32.5, 31.5, 28.5, 28.3, 22.5, 21.8, 21.1, 14.0, 13.9; *m/z* (CI) 519 $[M+NH_4]^+$, 502 $[M+H]^+$, 376, 365, 348, 272, 225, 289, 174 (Found: $[M+NH_4]^+$, 519.2528. $C_{27}H_{35}NO_6S$ requires $[M+NH_4]^+$, 519.2529) (Found: C, 64.52; H, 7.15; N, 2.76. $C_{27}H_{35}NO_6S$ requires C, 64.65; H, 7.03; N, 2.79%).

(3*S*, 4*R*, 5*S*)-5-Methyl-1-(4-methylbenzyl)-3-(toluene-4-sulfonyl)-4-vinylpyrrolidin-2-one and (3*R*, 4*S*, 5*S*)-5-Methyl-1-(4-methylbenzyl)-3-(toluene-4-sulfonyl)-4-vinylpyrrolidin-2-one (*cis*- and *trans*-8a)

A solution of carbonate **7a** (40.0 mg, 8.72 x 10^{-2} mmol, 1.0 equiv) in MeCN (1 ml) was added to a flask charged with $Pd_2(dba)_3$ (4.1 mg, 0.004 mmol, 5.0 mol%) and TTMPP (23.4 mg, 0.044 mmol, 0.5 equiv) at rt. After stirring for 2 h the reaction was concentrated under reduced pressure. Chromatography (30% EtOAc–petrol) gave an inseparable 86:14 mixture of *cis*- and *trans*- *γ-lactams* **8a** (30.0 mg, 90%) as a colourless oil; R_f 0.43 (30% EtOAc–petrol); ν_{max} (film) 1693, 1431, 1315, 1147, 1086, 1011, 935, 814, 737 cm^{-1}; δ_H (400 MHz) 7.89-7.82 (4H, m, *ortho* Ts of *cis* and *trans*), 7.37 (4H, d, J 8.0 Hz, *meta* Ts of *cis* and *trans*), 7.14 (2H, d, J 8.0 Hz, *ortho* CH_2ArMe of *cis*), 7.10 (2H, d, J 8.0 Hz, *meta* CH_2ArMe of *cis*), 7.09-7.08 (2H, m, *ortho* CH_2ArMe *trans*), 7.05 (2H, d, J 8.0 Hz, *meta* CH_2ArMe *trans*), 5.71 (2H, dt, J 17.0, 10.0 Hz, C*H*=CH_2 of *cis* and *trans*), 5.24 (2H, d, J 17.0 Hz, *trans* CH=C*H*$_2$ of *cis* and *trans*), 5.22 (1H, d, J 10.0 Hz, *cis* CH=C*H*$_2$ of *cis*), 5.16 (1H, d, J 10.0 Hz *cis* CH=C*H*$_2$ *trans*), 4.97 (1H, d, J 15.0 Hz, C*H*HArMe of *cis*), 4.88 (1H, d, J 15.0 Hz, C*H*HArMe *trans*), 3.97 (1H, d, J 15.0 Hz, CH*H*ArMe *trans*), 3.91 (1H, d, J 15.0 Hz, CH*H*ArMe of *cis*), 3.89-3.82 (3H, m, C*H*N of *cis* and C*H*Ts, of *cis* and *trans*), 3.60 (1H, ddd, J 5.0, 7.5, 4.5 Hz, C*H*CH=CH_2 of *cis*), 3.23-3.10 (1H, m, NC*H trans*), 2.46 (6H, s, Me of CH_2ArMe of *cis* and *trans*), 2.34 (3H, s, Me of Ts of *cis*), 2.31 (3H, s, Me of Ts *trans*), 1.27 (3H, d, J 6.5 Hz, NCH*Me trans*), 1.03 (3H, d, J 7.0 Hz, NCH*Me* of *cis*); δ_C (100 MHz)[8] 165.1 (C=O), 145.2 (q Ar), 137.4 (q Ar), 135.0 (q Ar), 133.6 (*C*H=CH_2), 132.3 (q Ar), 129.6 (*meta* Ts), 129.6 (ArH of CH_2ArMe), 129.4 (*ortho* Ts), 127.7 (ArH of CH_2ArMe), 119.4 (CH=*C*H_2), 70.6 (*C*HTs), 54.1 (N*C*HMe), 44.2 (*C*H_2ArMe), 21.8 (Me of CH_2ArMe), 21.1 (Me of Ts), 15.3 (NCH*Me*); *m/z* (CI) 401 $[M+NH_4]^+$, 384 $[M+H]^+$, 230 (Found: $[M+H]^+$, 384.1647. $C_{22}H_{25}NO_3S$ requires $[M+H]^+$, 384.1633)

(3*S*, 4*R*, 5*S*)-5-Isopropyl-1-(4-methylbenzyl)-3-(toluene-4-sulfonyl)-4-vinylpyrrolidin-2-one and (3*R*, 4*S*, 5*S*)-5-isopropyl-1-(4-methylbenzyl)-3-(toluene-4-sulfonyl)-4-vinylpyrrolidin-2-one (*cis*- and *trans*-8b)

A solution of carbonate **7b** (50.0 mg, 0.103 mmol, 1.0 equiv) in MeCN (1 ml) was added to a flask charged with $Pd_2(dba)_3$ (4.6 mg, 0.005 mmol, 5.0 mol%) and TTMPP (26.6 mg, 0.052 mmol, 0.5 equiv) at rt. After stirring for 12 h the reaction was concentrated under reduced pressure. Chromatography (30% EtOAc–petrol) gave an inseparable 67:33 mixture of *cis*- and *trans*- *γ*-*lactams* **8b** (31.9 mg, 78%) as a colourless oil; R_f 0.40 (30% EtOAc–petrol); ν_{max} 1695, 1435, 1319, 1147, 1086, 812 (film) cm^{-1}; δ_H (400 MHz) 7.90 (4H, d, J 8.0 Hz, *ortho* Ts of *cis* and *trans*), 7.38 (4H, d, J 8.0 Hz, *meta* Ts of *cis* and *trans*), 7.10 (2H, d, J 8.0 Hz *ortho* CH_2ArMe of *cis*), 7.09 (2H, d, J 8.0 Hz, *ortho* CH_2ArMe *trans*), 7.05 (2H, d, J 8.0 Hz, *meta* CH_2ArMe *trans*), 6.95 (2H, d, J 8.0 Hz, *meta* CH_2ArMe of *cis*), 5.85 (1H, ddd, J 17.0, 10.0, 9.0 Hz, C*H*=CH_2 of *cis*), 5.72 (1H, ddd, J 17.0, 10.0, 8.0 Hz, C*H*=CH_2 *trans*), 5.27 (2H, d, J 17.0 Hz, *trans* CH=CH_2 of *cis* and *trans*), 5.23 (1H, d, J 10.0 Hz, *cis* CH=CH_2 of *cis*), 5.20 (1H, d, J 15.0 Hz, C*H*HArMe of *cis*), 5.13 (1H, d, J 10.0 Hz *cis* CH=CH_2 *trans*), 5.05 (1H, d, J 15.0 Hz, C*H*HArMe *trans*), 4.03 (1H, d, J 9.0 Hz, CHTs of *cis*), 3.86 (1H, d, J 7.0 Hz, CHTs *trans*), 3.81 (1H, d, J 15.0 Hz, CH*H*ArMe of *cis*), 3.77 (1H, d, J 15.0 Hz, CH*H*ArMe *trans*), 3.59 (1H, ddd, J 8.0, 8.0, 8.0 Hz, C*H*CH=CH_2 of *cis*), 3.49 (1H, dd, J 8.0, 3.0 Hz, C*H*$(CH_3)_2$ of *cis*), 3.40 (1H, ddd, J 7.0, 7.0, 7.0 Hz, C*H*CH=CH_2 *trans*), 3.19-3.17 (1H, m, C*Hi*Pr *trans*), 2.47 (3H, s, Me of Ts of *cis*), 2.45 (3H, s, Me of Ts *trans*), 2.34 (3H, s, Me of CH_2ArMe of *cis*), 2.31 (3H, s, Me of CH_2ArMe *trans*), 2.26-2.21 (1H, m, C*H*$(CH_3)_2$ *trans*), 2.05 (1H, d quintet, J 7.0, 3.0 Hz C*H*$(CH_3)_2$ of *cis*), 0.98 (3H, d, J 7.0 Hz, CH(CH_3)$_2$ of 1), 0.90 (3H, d, J 7.0 Hz, CH(CH_3)$_2$ *trans*), 0.88 (3H, d, J 7.0 Hz, CH(CH_3)$_2$ *trans*), 0.86 (3H, d, J 7.0 Hz, CH(CH_3)$_2$ of *cis*); δ_C (100 MHz) 165.9 (C=O of *cis*), 165.4 (C=O *trans*), 145.1 (*ipso* Ts of *cis* and *trans*), 138.5 (*C*H=CH_2 *trans*), 137.6 (q Ar *trans*), 137.4 (q Ar of *cis*), 135.5 (q Ar *trans*), 134.8 (q Ar of *cis*), 134.0 (*C*H=CH_2 of *cis*), 132.2 (q Ar *trans*), 132.1 (q Ar of *cis*), 129.9 (*ortho* Ts of *cis* and *trans*), 129.6 (*meta* Ts of *cis* and *trans*), 129.4 (*ortho* CH_2ArMe of *cis*), 129.5 (*ortho* CH_2ArMe *trans*), 128.1 (*meta* CH_2ArMe *trans*), 127.7 (*meta* CH_2ArMe of *cis*), 119.8 (CH=*C*H_2 of *cis*), 117.8 (CH=*C*H_2 *trans*), 70.8 (*C*HTs *trans*), 69.7 (*C*HTs of *cis*), 63.6 (*C*H*i*Pr of *cis*), 62.6 (*C*H*i*Pr *trans*), 45.7 (*C*H_2ArMe of *cis*), 44.5 (*C*H_2ArMe *trans*), 42.7 (*C*HCH=CH_2, of *cis*), 36.0 (*C*HCH=CH_2 *trans*), 29.2 (*C*H$(CH_3)_2$ of *cis*), 28.2 (*C*H$(CH_3)_2$ *trans*), 21.8 (Me of Ts of *cis* and *trans*), 21.1 (Me of CH_2ArMe of *cis* and *trans*), 20.5 (CH(*C*H_3)$_2$ of *cis*), 18.5 (CH(*C*H_3)$_2$ *trans*), 17.5 (CH(*C*H_3)$_2$ *trans*), 14.7 (CH(*C*H_3)$_2$ of *cis*); *m/z* (CI) 429 $[M+NH_4]^+$, 412 $[M+H]^+$, 255 $[M-Ts]^+$ (Found: $[M+NH_4]^+$, 412.1942. $C_{24}H_{29}NO_3S$ requires $[M+NH_4]^+$, 412.1940).

(3*S*, 4*R*, 5*S*)-5-Isobutyl-1-(4-methylbenzyl)-3-(toluene-4-sulfonyl)-4-vinylpyrrolidin-2-one and (3*R*, 4*S*, 5*S*)-5-isobutyl-1-(4-methylbenzyl)-3-(toluene-4-sulfonyl)-4-vinylpyrrolidin-2-one (*cis*- and *trans*-8c)

A solution of carbonate **7c** (45.0 mg, 8.98 x 10^{-2} mmol, 1.0 equiv) in MeCN (1 ml) was added to a flask charged with $Pd_2(dba)_3$ (4.6 mg, 0.005 mmol, 5.0 mol%) and TTMPP (26.6 mg, 0.045 mmol, 0.5 equiv) at rt. After stirring for 12 h the reaction was concentrated under reduced pressure. Chromatography (50% EtOAc–petrol) gave a inseparable 90:10 mixture of *cis*- and *trans*- *γ-lactams* **8c** (33.0 mg, 85%) as a colourless oil; R_f 0.40 (50% EtOAc–petrol); ν_{max} (film) 2926, 1697, 1448, 1304, 1149, 1086, 924, 812 cm^{-1}; δ_H (400 MHz) 7.87-7.82 (4H, m, *ortho* Ts of *cis* and *trans*), 7.37-7.35 (4H, m, *meta* Ts of *cis* and *trans*), 7.15-7.04 (8H, m, CH_2*Ar*Me of *cis* and *trans*), 5.72 (1H, dt, J 17.0, 10.0 Hz, C*H*=CH_2 of *cis*), 5.70-5.68 (1H, m, C*H*=CH_2 *trans*), 5.25 (1H, d, J 17.0 Hz, *trans* CH=CH_2 of *cis*), 5.22 (1H, d, J 11.0 Hz, *cis* CH=CH_2 of *cis*), 5.16 (1H, d, J 17.0 Hz, *trans* CH=CH_2 *trans*), 5.09 (1H, d, J 10.0 Hz *cis* CH=CH_2 *trans*), 4.94 (2H, d, J 15.0 Hz, C*H*HArMe of *cis* and *trans*), 3.97 (1H, d, J 15.0 Hz, CH*H*ArMe of *cis*), 3.92 (1H, d, J 15.0 Hz, CH*H*ArMe *trans*), 3.88-3.81 (3H, m, C*H*Ts of *cis* and CHN of *cis* and *trans*), 3.66 (1H, dd, J 10.0, 6.5 Hz, C*H*CH=CH_2 of *cis*), 3.35-3.31 (1H, m, CHTs, *trans*), 3.22-3.18 (1H, m, C*H*CH=CH_2 *trans*), 2.46 (6H, s, Me of Ts of *cis* and *trans*), 2.34 (3H, s, Me of CH_2ArMe of *cis*), 2.31 (3H, s, Me of CH_2ArMe *trans*), 1.75-1.67 (1H, m, C*H*$(CH_3)_2$ *trans*), 1.61-1.52 (3H, m, C*H*$(CH_3)_2$ of *cis* and CH_2*i*Pr *trans*), 1.33 (2H, dd, J 7.0, 7.0 Hz, CH_2*i*Pr of *cis*), 0.94 (3H, d, J 7.0 Hz, CH(CH_3)$_2$ *trans*), 0.80 (3H, d, J 7.0 Hz, CH(CH_3)$_2$ of *cis*), 0.76 (3H, d, J 7.0 Hz, CH(CH_3)$_2$ *trans*), 0.70 (3H, d, J 7.0 Hz, CH(CH_3)$_2$ of *cis*); δ_C (100 MHz)[8] 165.6 (C=O), 145.3 (*ipso* Ts), 137.2 (q Ar), 135.1 (q Ar), 133.6 (*C*H=CH_2), 132.4 (q Ar), 129.6 (*meta* Ts), 129.3 (*ortho* Ts and CH_2ArMe), 127.7 (CH_2ArMe), 119.2 (CH=*C*H_2), 71.5 (*C*HTs), 56.8 (*C*HN), 44.4 (*C*H_2ArMe), 41.8 (*C*HCH=CH_2), 36.9 (*C*H_2*i*Pr), 23.8 (*C*H$(CH_3)_2$), 23.7 (CH(*C*H_3)$_2$), 21.8 (Me of Ts), 21.3 (CH(*C*H_3)$_2$), 21.1 (Me of CH_2ArMe); *m/z* (CI) 443 $[M+NH_4]^+$, 426 $[M+H]^+$, 279, 272 (Found: $[M+NH_4]^+$, 426.2109. $C_{25}H_{31}NO_3S$ requires $[M+NH_4]^+$, 426.2103)

(3*S*, 4*R*, 5*S*)-5-Butyl-1-(4-methylbenzyl)-3-(toluene-4-sulfonyl)-4-vinylpyrrolidin-2-one and (3*R*, 4*S*, 5*S*)-5-butyl-1-(4-methylbenzyl)-3-(toluene-4-sulfonyl)-4-vinylpyrrolidin-2-one (*cis*- and *trans*-8d)

A solution of carbonate **7d** (50.0 mg, 99.8 x 10^{-3} mmol, 1.0 equiv) in MeCN (1 ml) was added to a flask charged with $Pd_2(dba)_3$ (4.61 mg, 5.04 x 10^{-3} mmol, 5.0 mol%) and TTMPP (23.4 mg, 4.40 x 10^{-2} mmol, 0.5 equiv) at rt. After stirring for 6 h the reaction was concentrated under reduced pressure. Chromatography (30% EtOAc–petrol) gave an inseparable 83:17 mixture of *cis*- and *trans*- *γ-lactams* **8d** (30mg, 79%) as a colourless oil; R_f 0.46 (30% EtOAc–petrol); ν_{max} (film) 2929,

1697 (C=O), 1423, 1319 (SO_2), 1149 (SO_2), 1086, 812 cm^{-1}; δ_H (400 MHz) 7.85 (4H, d, J 8.0 Hz *ortho* Ts of *cis* and *trans*), 7.37 (4H, d, J 8.0 Hz, *meta* Ts of *cis* and *trans*), 7.19-7.04 (4H, m, *meta* CH_2ArMe of *cis* and *trans*), 5.75 (1H, dt, J 17.0, 10.0 Hz, C*H*=CH_2 of *cis*), 5.70-5.66 (1H, m, C*H*=CH_2 *trans*), 5.28 (1H, d, J 17.0 Hz, *trans* CH=C*H*$_2$ of *cis*), 5.23 (1H, d, J 10.0 Hz, *cis* CH=C*H*$_2$ of *cis*), 5.19 (1H, d, J 17.0 Hz, *trans* CH=C*H*$_2$ *trans*), 5.12 (1H, d, J 10.0 Hz, *cis* CH=C*H*$_2$ *trans*), 4.95 (2H, d, J 15.0 Hz, C*H*HArMe of *cis*), 4.92 (2H, d, J 15.0 Hz, C*H*HArMe *trans*), 3.97 (2H, d, J 15.0 Hz, CH*H*ArMe of *cis*), 3.91 (2H, d, J 15.0 Hz, CH*H*ArMe *trans*), 3.79-3.74 (3H, m, C*Hn*Bu of *cis* and C*H*Ts of *cis* and *trans*), 3.66-3.65 (1H, m, C*H*CH=CH_2 of *cis*), 3.34-3.30 (1H, m, C*H*CH=CH_2 *trans*), 3.14-3.12 (1H, m, C*Hn*Bu min), 2.45 (6H, s, Me of CH_2ArMe of *cis* and *trans*), 2.33 (3H, s, Me of Ts of *cis*), 2.31 (3H, s, Me of Ts *trans*), 1.77-1.55 (2H, m, C*H*$_2(CH_2)_2CH_3$ *trans*), 1.64-1.51 (2H m, C*H*$_2(CH_2)_2CH_3$ of *cis*), 1.34-1.04 (8H, m, $CH_2(CH_2)_2CH_3$ of *cis* and *trans*), 0.87 (3H, t, J 7.0 Hz, $CH_2(CH_2)_2CH_3$ *trans*), 0.81 (3H, t, J 7.0 Hz, $CH_2(CH_2)_2CH_3$ of *cis*); δ_C (75 MHz) 165.6 (C=O of *cis*), 164.8 (C=O *trans*), 145.2 (q Ar of *cis* and *trans*), 137.3 (*C*H=CH_2 *trans*), 135.1 (q Ar of *cis*), 135.0 (q Ar *trans*), 133.2 (*C*H=CH_2 of *cis*), 132.4 (q Ar of *cis* and *min*), 129.6 (*meta* Ts of *cis*), 129.5 (*meta* Ts *min*), 129.4 (q Ar of *cis* and *trans*), 129.3 (*ortho* Ts and ArMe of *cis* and *trans*) 128.0 (ArMe *trans*) 127.6 (ArMe of *cis*), 119.5 (CH=*C*H$_2$ of *cis*), 117.5 (CH=*C*H$_2$ *trans*), 71.3 (*C*HTs of *cis*), 71.1 (CHTs *trans*), 60.1 (*C*H*n*Bu *trans*), 58.4 (*C*H*n*Bu of *cis*), 44.6 (*C*H_2ArMe *trans*), 44.4 (*C*H_2ArMe of *cis*), 41.6 (*C*HCH=CH_2 of *cis*) 41.0 (*C*HCH=CH_2 *trans*), 31.2 (*C*$H_2(CH_2)_2CH_3$ *trans*), 29.7 (CH_2*C*$H_2CH_2CH_3$ *trans*), 27.7 (*C*$H_2(CH_2)_2CH_3$ of *cis*), 26.4 (CH_2*C*$H_2CH_2CH_3$ of *cis*), 26.1 ($(CH_2)_2$*C*H_2CH_3 *trans*), 22.5 ($(CH_2)_2$*C*H_2CH_3 of *cis*), 21.8 (Me of Ts of *cis* and *trans*), 21.1 (Me of CH_2ArMe of *cis* and *trans*), 13.9 (Me of *n*Bu *trans*), 13.8 (Me of *n*Bu of *cis*); *m/z* (CI) 443 $[M+NH_4]^+$, 426 $[M+H]^+$, 272 (Found: $[M+NH_4]^+$, 426.2106. $C_{25}H_{31}NO_3S$ requires $[M+NH_4]^+$, 426.2103)

(+)-(3*S*, 4*S*, 5*R*)-5-(4-Methoxybenzyl)-1-(4-methylbenzyl)-3-(3-methylbut-2-enyl)-3-(toluene-4-sulfonyl)-4-vinylpyrrolidin-2-one (10)

A solution of lactams *cis*-**1** and *trans*-**1** (5.6:1 mixture; 332 mg, 0.680 mmol, 1.0 equiv) in DMF (5 ml) was added to KH (94.0 mg of a 35% wt dispersion in mineral oil washed with pentane, 0.820 mmol, 1.2 equiv) at 0 ºC under argon. After 15 min prenyl bromide (780 μl, 6.80 mmol, 10 equiv) was added and the mixture warmed to rt. After 20 min the reaction was quenched by dropwise addition of MeOH until the solution decolourised. Saturated aqueous NH_4Cl (5 ml) was then added and the mixture extracted with EtOAc (5 x 10 ml). The combined organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography (20% EtOAc–petrol) gave the *lactam* **10** (265 mg, 70%; 83% from *cis*-**1**) as a colourless oil; R_f 0.60 (30% EtOAc–petrol); $[\alpha]_D^{24}$ +72.0 (*c* 0.5, $CHCl_3$); ν_{max} (film) 1691, 1512, 1441, 1315, 1248, 1140 cm^{-1}; δ_H (400 MHz) 7.72 (2H,

d, J 8.0 Hz, *ortho* Ts), 7.28 (2H, d, J 8.0 Hz, *meta* Ts), 7.06 (2H, d, J 8.5 Hz, *ortho* CH_2ArMe), 6.92 (2H, d, J 8.0 Hz, *ortho* ArOMe), 6.80 (2H, d, J 8.5 Hz, *meta* CH_2ArMe), 6.60 (2H, d, J 8.0 Hz, *meta* ArOMe), 6.50 (1H, dt, J, 17.0, 10.0, Hz, C*H*=CH_2), 5.18 (1H, dd, J 10.0, 2.0 Hz, *trans* CH=C*H*$_2$), 5.00 (1H, dd, J 17.0, 2.0 Hz, *cis* CH=C*H*$_2$), 4.92 (1H, d, J 15.0 Hz, NC*H*H), 4.72 (1H, m, C*H*=C$(Me)_2$), 3.76 (3H, s, OMe of ArOMe), 3.59 (1H, ddd, J 9.0, 9.0, 5.0 Hz, CHN), 3.39 (1H, dd, J 14.0, 9.0 Hz, C*H*HArOMe), 3.22 (1H, m, C*H*CH=CH_2), 3.20 (1H, d, J 15.0 Hz, NCH*H*), 3.11 (1H, dd, J 14.0, 5.0 Hz, CH*H*ArOMe), 2.69 (1H, dd, J 14.0, 11.0 Hz, C*H*HCH=C$(CH_3)_2$), 2.44-2.41 (1H, m, CH*H*CH=C$(CH_3)_2$), 2.38 (3H, s, Me of Ts), 2.21 (3H, s, Me of CH_2ArMe), 1.58 (3H, s, CH_2CH=C(*C*$H_3)_2$) 1.54 (3H, s, CH_2CH=C(*Me*$)_2$); δ_C (100 MHz); 167.7 (C=O), [158.3, 145.1 (q Ar)], 137.7 (*C*$(CH_3)_2$), [137.2, 133.9, 133.0 (q Ar)], 132.7 (*C*H=CH_2), 131.7 (q Ar), 131.1 (*ortho* Ts), 130.4 (*ortho* CH_2ArMe), 129.1 (*meta* Ts), 128.9 (*meta* ArOMe), 128.3 (*ortho* ArOMe), 120.1 (CH=*C*H_2), 117.1 (C*H*=C$(Me)_2$), 114.0 (*meta* CH_2ArMe), 75.8 (CTs), 59.8 (CHN), 55.3 (OMe of CH_2ArOMe), 47.7 (*C*HCH=CH_2), 45.7 (*C*H_2ArMe), 36.4 (*C*H_2ArOMe), 31.2 (*C*H_2CH=$(CMe)_2$), 25.9 (CH_2CH=C(*C*$H_3)_2$), 21.8 (Me of Ts), 21.1 (Me of CH_2ArMe), 18.4 (CH_2CH=C(*C*$H_3)_2$); *m/z* (CI) 558 $[M+H]^+$, 410, 404, 376, 174 (Found: $[M+H]^+$, 558.2682. $C_{34}H_{39}NO_4S$ requires $[M+H]^+$, 558.2678) (Found: C, 73.03; H, 6.78; N, 2.50. $C_{33}H_{39}NO_5S$ requires C, 73.22; H, 7.05; N, 2.51%).

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