(*S*)-2-((*S*)-3-Benzyloxy-2-*tert*-butoxycarbonylamino-propionylamino)-3-hydroxy-propionic acid methyl ester (13a). Diisopropylethylamine (3.2 mL, 19 mmol) was added portionwise to a stirred suspension of *N*-Boc-*O*-benzyl-L-serine (5.0 g, 17 mmol) and 1-hydroxybenzotriazole (2.5 g, 19 mmol) in dry dichloromethane (130 mL) at 0 °C under a nitrogen atmosphere. 1-[3-(Dimethylamino)propyl]-3-ethylcarbodiimide hydrochloride (3.5 g, 19 mmol) was added and the mixture was then stirred at 0 °C for 15 min. A pre-cooled (0 °C) solution of L-serine methylester hydrochloride (2.9 g, 19 mmol) and diisopropylethylamine (3.2 mL, 19 mmol) in dry *N*,*N*-dimethylformamide (20 mL) was added dropwise over 5 min, and the mixture was then allowed to warm to room temperature overnight. The reaction was quenched with water (80 mL) and the two layers were separated. The organic layer was washed with 10% aqueous citric acid (3 × 80 mL) and the combined aqueous extracts were then extracted with dichloromethane (2 × 50 mL). The combined organic extracts were washed with saturated sodium bicarbonate solution (80 mL), then dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified by chromatography on silica gel using ethyl acetate as eluent to give the *dipeptide* (6.1 g, 90%) as a colourless oil; $[\alpha]_D^{21}$ +29 (*c* = 1.0, $CHCl_3$); $\nu_{max}(CHCl_3)/cm^{-1}$ 3422, 2955, 1745, 1714 and 1681; δ_H(500 MHz, $CDCl_3$) 7.39–7.28 (6H, m, CON*H*, 5 × aryl-H), 5.50 (1H, m, BocN*H*), 4.67–4.62 (1H, m, CONHC*H*), 4.55 (2H, s, OCH_2Ph), 4.37–4.30 (1H, m, BocNHC*H*), 3.93–3.89 (2H, m, CH_2OH), 3.89 (1H, dd, *J* 9.4 and 4.4 Hz, CH_aH$_b$OTBS), 3.75 (3H, s, CO_2CH_3), 3.63 (1H, dd, *J* 9.4 and 5.7 Hz, CH$_a$$H_b$OTBS) and 1.45 (9H, s, OC(CH_3)$_3$) ppm; δ_C(90 MHz, $CDCl_3$) 170.6 (s), 170.5 (s), 155.6 (s), 137.3 (s), 128.4 (d), 127.9 (d), 127.8 (d), 80.4 (s), 73.5 (t), 69.8 (t), 62.8 (t), 54.9 (d), 54.3

(d), 52.6 (q) and 28.2 (q) ppm; *m/z* (ESI) Found: 419.1811, $C_{19}H_{28}N_2O_7Na$ [$(M+Na)^+$] requires 419.1794.

2-((*S*)-2-Benzyloxy-1-*tert*-butoxycarbonylamino-ethyl)-oxazole-4-carboxylic acid methyl ester (15a). (Diethylamino)sulfur trifluoride (2.4 mL, 18 mmol) was added dropwise over 3 min to a stirred solution of the dipeptide **13a** (6.1 g, 15 mmol) in dry dichloromethane (150 mL) at −78 °C under a nitrogen atmosphere. The mixture was stirred at −78 °C for 1.5 h, then allowed to warm to room temperature and stirred for a further 10 min. The mixture was quenched with saturated sodium bicarbonate solution (80 mL) and the separated organic layer was then dried ($MgSO_4$) and concentrated *in vacuo* to leave the crude oxazoline **14a**, which was used immediately without further purification.

Bromotrichloromethane (4.4 mL, 46 mmol) was added to a stirred solution of the crude oxazoline in dry dichloromethane (150 mL) at 0 °C under a nitrogen atmosphere and the mixture was stirred at 0 °C for 5 min. 1,8-Diazabicyclo[5.4.0]undec-7-ene (6.9 mL, 46 mmol) was added dropwise over 5 min and the mixture was allowed to warm to room temperature overnight. The reaction was quenched with 10% aqueous citric acid (80 mL) and the layers were then separated. The aqueous extract was re-extracted with dichloromethane (2 × 80 mL) and the combined organic extracts were evaporated *in vacuo* to leave a brown residue, which was then partitioned between ethyl acetate (100 mL) and 10% aqueous citric acid (80 mL). The separated organic extract was washed with saturated sodium bicarbonate solution (80 mL), dried ($MgSO_4$) and then concentrated *in vacuo*. The residue was purified by chromatography on silica gel using

2:1 petrol–ethyl acetate as eluent to give the *oxazole* (4.3 g, 75%) as a colourless oil; $[\alpha]_D^{22}$ –18 (*c* = 1.0, $CHCl_3$); Found: C, 60.1; H, 6.3; N, 7.1%. $C_{19}H_{24}N_2O_6$ requires C, 60.6; H, 6.4; N, 7.4%; $\nu_{max}(CHCl_3)/cm^{-1}$ 3440, 2980, 2870, 1714 and 1587; δ_H(360 MHz, $CDCl_3$) 8.19 (1H, s, oxazole-H), 7.35–7.19 (5H, m, 5 × aryl-H), 5.54 (1H, d, *J* 8.1 Hz, BocN*H*), 5.16–5.08 (1H, m, BocNHC*H*), 4.53 (1H, d, *J* 12.1 Hz, OCH_aH$_b$Ph), 4.49 (1H, d, *J* 12.1 Hz, OCH$_a$$H_b$Ph), 3.95–3.87 (1H, m, CHCH_aH$_b$OBn), 3.93 (3H, s, CO_2CH_3), 3.81 (1H, dd, *J* 9.6 and 4.4 Hz, CHCH$_a$$H_b$OBn) and 1.46 (9H, s, OC(CH_3)$_3$) ppm; δ_C(90 MHz, $CDCl_3$) 163.5 (s), 161.4 (s), 155.0 (s), 144.1 (d), 137.3 (s), 133.3 (s), 128.3 (d), 127.8 (d), 127.5 (d), 80.2 (s), 73.1 (t), 70.4 (t), 52.1 (q), 49.3 (d) and 28.2 (q) ppm; *m/z* (ESI) Found: 399.1520, $C_{19}H_{24}N_2O_6Na$ [$(M+Na)^+$] requires 399.1532.

2-((*S*)-2-Benzyloxy-1-*tert*-butoxycarbonylamino-ethyl)-oxazole-4-carboxylic acid (16a). A solution of sodium hydroxide (0.64 g, 16 mmol) in water (20 mL) was added in one portion to a stirred solution of the methyl ester **15a** (1.5 g, 4.0 mmol) in tetrahydrofuran (40 mL), and the mixture was stirred at room temperature overnight. The mixture was concentrated *in vacuo* and the residue was then acidified to pH 2 with 10% aqueous citric acid. The aqueous suspension was extracted with dichloromethane (3 × 75 mL) and the combined organic extracts were then dried ($MgSO_4$) and evaporated *in vacuo* to leave the *acid* (1.4 g, 98%) as a colourless foam; $[\alpha]_D^{21}$ –26 (*c* = 1.0, $CHCl_3$); $\nu_{max}(CHCl_3)/cm^{-1}$ 3440, 3169, 2870, 1714 and 1590; δ_H(360 MHz, $CDCl_3$) 8.27 (1H, s, oxazole-H), 7.34–7.20 (5H, m, 5 × aryl-H), 5.89 (1H, d, *J* 8.5 Hz, BocN*H*), 5.32–5.15 (1H, m, BocNHC*H*), 4.54 (1H, d, *J* 12.1 Hz, OCH_aH$_b$Ph), 4.50 (1H, d, *J* 12.1 Hz, OCH$_a$$H_b$Ph), 3.94 (1H, dd, *J* 9.6 and 4.0 Hz, CH_aH$_b$OBn), 3.84 (1H, dd, *J* 9.6 and 4.8 Hz,

CH_aH_bOBn) and 1.45 (9H, s, $OC(CH_3)_3$) ppm; δ_C(90 MHz, $CDCl_3$) 164.3 (s), 164.1 (s), 155.4 (s), 145.0 (d), 137.2 (s), 133.1 (s), 128.4 (d), 127.8 (d), 127.6 (d), 80.4 (s), 73.2 (t), 70.4 (t), 49.3 (d) and 28.2 (q) ppm; *m/z* (ESI) Found: 385.1378, $C_{18}H_{22}N_2O_6Na$ $[(M+Na)^+]$ requires 385.1376.

(*S*)-2-[(*S*)-2-Benzyloxycarbonylamino-3-(*tert*-butyl-dimethyl-silanyloxy)-propionylamino]-3-hydroxy-propionic acid methyl ester (13b). *tert*-Butyldimethylsilyl chloride (9.9 g, 66 mmol) was added to a stirred suspension of *N*-carbobenzyloxy-L-serine (7.4 g, 31 mmol) and imidazole (4.5 g, 66 mmol) in dry dichloromethane (150 mL) at room temperature under a nitrogen atmosphere. The mixture was stirred overnight and was then quenched with water (50 mL). The separated organic layer was evaporated *in vacuo* and the residue was then dissolved in tetrahydrofuran (150 mL). A solution of potassium carbonate (10 g, 72 mmol) in water (100 mL) was added and the mixture was stirred at room temperature for 2 h. The mixture was concentrated *in vacuo* and the residue was then partitioned between dichloromethane (150 mL) and 10% aqueous citric acid (150 mL). The separated organic extract was dried ($MgSO_4$) and then concentrated *in vacuo* to leave a colourless solid. Purification by recrystallisation from ether / petrol gave (*S*)-2-benzyloxycarbonylamino-3-(*tert*-butyl-dimethyl-silanyloxy)-propionic acid (9.6 g, 88%) as a colourless crystalline solid; mp 95–96 °C (from ether / petrol); $[\alpha]_D^{18}$ –20 (*c* = 1.0, $CHCl_3$); Found: C, 57.7; H, 7.7; N, 4.1%. $C_{17}H_{27}NO_5Si$ requires C, 57.8; H, 7.7; N, 4.0%; $\nu_{max}(CHCl_3)/cm^{-1}$ 3444, 2931 and 1719; δ_H(360 MHz, $CDCl_3$) 7.40–7.29 (5H, m, 5 × aryl-H), 5.59 (1H, d, *J* 8.1 Hz, ZN*H*), 5.19–5.10 (2H, m, CO_2CH_2Ph), 4.49–4.43 (1H, m, ZNHC*H*), 4.14 (1H, dd, *J*

10.1 and 2.5 Hz, CH_aH$_b$OTBS), 3.86 (1H, dd, *J* 10.1 and 3.9 Hz, CH$_a$$H_b$OTBS), 0.87 (9H, s, SiC(CH_3)$_3$) and 0.06 (6H, s, Si(CH_3)$_2$) ppm; δ_C(90 MHz, $CDCl_3$) 174.8 (s), 156.0 (s), 136.1 (s), 128.6 (d), 128.2 (d), 128.2 (d), 67.2 (t), 63.3 (t), 55.5 (d), 26.7 (q), 18.2 (s), –5.6 (s) and –5.6 (q) ppm; *m/z* (ESI) Found: 376.1582, $C_{17}H_{27}NO_5SiNa$ [$(M+Na)^+$] requires 376.1556.

4-Methylmorpholine (3.3 mL, 30 mmol) was added to a stirred suspension of the propionic acid (9.6 g, 27 mmol) and 1-hydroxybenzotriazole (4.1 g, 30 mmol) in dry dichloromethane (150 mL) at 0 °C under a nitrogen atmosphere. 1-[3-(Dimethylamino)propyl]-3-ethylcarbodiimide hydrochloride (5.8 g, 30 mmol) was added and the mixture was then stirred at 0 °C for 10 min. A pre-cooled (0 °C) solution of L-serine methylester hydrochloride (4.7 g, 30 mmol) and 4-methylmorpholine (3.3 mL, 30 mmol) in dry dichloromethane (100 mL) was added dropwise over 10 min and the mixture was then allowed to warm to room temperature overnight. The reaction was quenched with water (50 mL) and the separated organic layer was then washed with 10% aqueous citric acid (3 × 50 mL). The combined aqueous extracts were extracted with dichloromethane (2 × 100 mL) and the combined organic extracts were then washed with saturated sodium bicarbonate solution (50 mL), dried ($MgSO_4$) and concentrated *in vacuo* to leave a colourless solid. Purification by recrystallisation from ethyl acetate / petrol gave the *dipeptide* (11.3 g, 92%) as a colourless solid; mp 100 °C (from ethyl acetate / petrol); $[\alpha]_D^{18}$ +35 (*c* = 1.0, $CHCl_3$); Found: C, 55.5; H, 7.5; N, 6.1%. $C_{21}H_{34}N_2O_7Si$ reqires C, 55.5; H, 7.5; N, 6.2%; ν_{max}($CHCl_3$)/cm^{-1} 3419, 2954, 1724 and 1678; δ_H(360 MHz, $CDCl_3$) 7.40–7.29 (6H, m, CON*H*, 5 × aryl-H), 5.66 (1H, m, ZN*H*), 5.14 (2H, s, CO_2CH_2Ph), 4.68–4.62 (1H, m, CONHC*H*), 4.30–4.22 (1H, m, ZNHC*H*), 4.07 (1H, dd, *J*

9.9 and 3.9 Hz, C*H*$_a$H$_b$OH), 4.00–3.89 (2H, m, CH$_a$*H*$_b$OH, C*H*$_a$H$_b$OTBS), 3.79 (3H, s, CO$_2$C*H*$_3$), 3.73 (1H, dd, *J* 9.8 and 6.8 Hz, CH$_a$*H*$_b$OTBS), 2.47 (1H, br s, O*H*), 0.90 (9H, s, SiC(C*H*$_3$)$_3$) and 0.09 (6H, s, Si(C*H*$_3$)$_2$) ppm; δ_C(90 MHz, $CDCl_3$) 170.5 (s), 170.4 (s), 156.2 (s), 136.0 (s), 128.5 (d), 128.2 (d), 128.1 (d), 67.2 (t), 63.2 (t), 63.0 (t), 56.1 (d), 54.9 (d), 52.7 (q), 25.7 (q), 18.2 (s) and –5.6 (q) ppm; *m/z* (ESI) Found: 477.2029, $C_{21}H_{34}N_2O_7SiNa$ [$(M+Na)^+$] requires 477.2033.

2-[(*S*)-1-Benzyloxycarbonylamino-2-(*tert*-butyl-dimethyl-silanyloxy)-ethyl]-oxazole-4-carboxylic acid methyl ester (15b). (Diethylamino)sulfur trifluoride (2.0 mL, 15 mmol) was added dropwise over 5 min to a stirred solution of the dipeptide **13b** (5.7 g, 12.5 mmol) in dry dichloromethane (120 mL) at −78 °C under a nitrogen atmosphere. The mixture was stirred at −78 °C for 2 h and then allowed to warm to room temperature and stirred for a further 15 min. The mixture was quenched with saturated sodium bicarbonate solution (50 mL) and the separated organic layer was then dried ($MgSO_4$) and concentrated *in vacuo* to leave the crude oxazoline**14b**, which was used immediately without further purification.

Bromotrichloromethane (3.7 mL, 38 mmol) was added to a stirred solution of the crude oxazoline in dry dichloromethane (120 mL) at 0 °C under a nitrogen atmosphere and the mixture was stirred at 0 °C for 10 min. 1,8-Diazabicyclo[5.4.0]undec-7-ene (5.7 mL, 38 mmol) was added dropwise over 5 min and the mixture was allowed to warm to room temperature overnight. The reaction was quenched with 10% aqueous citric acid (50 mL) and the organic layer was then concentrated *in vacuo* to leave a brown residue. The

residue was partitioned between ethyl acetate (100 mL) and 10% aqueous citric acid (75 mL) and the separated organic extract was then washed with saturated sodium bicarbonate solution (75 mL), dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified by chromatography on silica gel using 1:1 ether–petrol as eluent to give the *oxazole* (4.1 g, 75%) as a yellow oil; $[\alpha]_D^{23}$ –12 (*c* = 1.5, $CHCl_3$); $\nu_{max}(CHCl_3)/cm^{-1}$ 3435, 2954, 2858, 1722 and 1586; δ_H(360 MHz, $CDCl_3$) 8.22 (1H, s, oxazole-H), 7.42–7.33 (5H, m, 5 × aryl-H), 5.78 (1H, d, *J* 8.5 Hz, ZN*H*), 5.19 (1H, d, *J* 12.2 Hz, $CO_2CH_aH_bPh$), 5.14 (1H, d, *J* 12.2 Hz, $CO_2CH_aH_bPh$), 5.15–5.08 (1H, m, ZNHC*H*), 4.12 (1H, dd, *J* 10.2 and 3.4 Hz, CH_aH_bOTBS), 3.98 (1H, dd, *J* 10.2 and 4.3 Hz, CH_aH_bOTBS), 3.95 (3H, s, CO_2CH_3), 0.82 (9H, s, $SiC(CH_3)_3$), 0.00 (3H, s, $SiCH_3(CH_3)$) and –0.03 (3H, s, $SiCH_3(CH_3)$) ppm; δ_C(90 MHz, $CDCl_3$) 163.4 (s), 161.4 (s), 156.4 (s), 144.1 (d), 136.1 (s), 133.4 (s), 128.5–128.1 (Ar d), 67.2 (t), 64.3 (t), 52.2 (d), 51.6 (q), 25.6 (q), 18.1 (s), –5.6 (q) and –5.7 (q) ppm; *m/z* (ESI) Found: 435.1987, $C_{21}H_{31}N_2O_6Si$ $[(M+H)^+]$ requires 435.1951.

2-((*S*)-1-Amino-2-hydroxy-ethyl)-oxazole-4-carboxylic acid methyl ester (16b). Tetrabutylammonium fluoride (1.3 g, 4.1 mmol) was added to a stirred solution of the silyl ether **15b** (1.5 g, 3.5 mmol) in dry tetrahydrofuran (35 mL) at 0 °C under a nitrogen atmosphere and the mixture was then allowed to warm to room temperature over 2 h. The mixture was quenched with saturated ammonium chloride solution (25 mL) and was then extracted with diethyl ether (3 × 50 mL). The combined organic extracts were dried ($MgSO_4$) and then concentrated *in vacuo* to leave a yellow solid. Purification by recrystallisation from dichloromethane / ether gave the corresponding alcohol (1.1 g,

98%) as a colourless solid; mp 98–100 °C (from dichloromethane / ether); $[\alpha]_D^{24}$ –52 (*c* = 1.0, $CHCl_3$); Found: C, 56.2; H, 5.2; N, 8.7%. $C_{15}H_{16}N_2O_6$ requires C, 56.3; H, 5.0; N, 8.8%; $\nu_{max}(CHCl_3)/cm^{-1}$ 3610, 3432, 2955, 1728 and 1586; δ_H(360 MHz, $CDCl_3$) 8.18 (1H, s, oxazole-H), 7.44–7.25 (5H, m, 5 × aryl-H), 6.30 (1H, d, *J* 8.4 Hz, ZN*H*), 5.20–5.02 (1H, m, ZNHC*H*), 5.16 (1H, d, *J* 12.2 Hz, $CO_2CH_aH_bPh$), 5.10 (1H, d, *J* 12.2 Hz, $CO_2CH_aH_bPh$), 4.17 (1H, dd, *J* 11.4 and 3.2 Hz, CH_aH_bOH), 4.02 (1H, dd, *J* 11.4 and 3.9, CH_aH_bOH), 3.91 (3H, s, CO_2CH_3) and 3.30 (1H, m, O*H*) ppm; δ_C(90 MHz, $CDCl_3$) 163.5 (s), 161.4 (s), 156.1 (s), 144.3 (d), 136.0 (s), 132.8 (s), 128.4 (d), 128.1 (d), 127.9 (d), 67.1 (t), 63.1 (t), 52.2 (q) and 51.3 (d) ppm; *m/z* (ESI) Found: 321.1072, $C_{15}H_{17}N_2O_6$ $[(M+H)^+]$ requires 321.1087.

10% Palladium on carbon (0.1 g) was added to a solution of the above carbamate (1.1 g, 3.4 mmol) in methanol (30 mL) and tetrahydrofuran (10 mL). The mixture was stirred at room temperature under 1 atmosphere pressure of hydrogen for 18 h and the mixture was then filtered through a pad of celite and eluted with methanol (200 mL). The filtrate was concentrated *in vacuo* and the residue was then purified by chromatography on silica gel using 4:1 dichloromethane–methanol as eluent to give the *amine* (0.56 g, 88%) as a colourless solid; mp 93–95 °C; $[\alpha]_D^{22}$ –104 (*c* = 1.0, EtOH); Found: C, 45.3; H, 5.4%. $C_7H_{10}N_2O_4$ requires C, 45.2; H, 5.4%; $\nu_{max}(CHCl_3)/cm^{-1}$ 3610, 3390, 2954, 1738 and 1586; δ_H(360 MHz, $CDCl_3$) 8.20 (1H, s, oxazole-H), 4.19–4.13 (1H, m, NH_2CH), 3.94 (1H, dd, *J* 11.1 and 4.6 Hz, CH_aH_bOH), 3.90 (3H, s, CO_2CH_3), 3.86 (1H, dd, *J* 11.1 and 6.3 Hz, CH_aH_bOH) and 2.44 (1H, br s, NH_2 and O*H*) ppm; δ_C(90 MHz, $CDCl_3$) 166.2 (s), 161.4 (s), 144.2 (d), 133.0 (s), 64.5 (t), 52.2 (q) and 51.5 (d) ppm; *m/z* (CI) Found: 187.0714, $C_7H_{11}N_2O_4$ $[(M+H)^+]$ requires 187.0719.

(2*S*,3*R*)-2-((*S*)-3-Benzyloxy-2-benzyloxycarbonylamino-propionylamino)-3-hydroxy-butyric acid methyl ester (13c). 4-Methylmorpholine (1.4 mL, 12 mmol) was added to a stirred suspension of *N*-carbobenzyloxy-*O*-benzyl-L-serine (1.8 g, 5.6 mmol) and 1-hydroxybenzotriazole (0.8 g, 6.1 mmol) in dry dichloromethane (60 mL) at 0 °C under a nitrogen atmosphere. 1-[3-(Dimethylamino)propyl]-3-ethylcarbodiimide hydrochloride (1.2 g, 6.1 mmol) was added and the mixture was then stirred at 0 °C for 10 min. L-Threonine methylester hydrochloride (0.8 g, 4.7 mmol) was added in one portion, and the mixture was then allowed to warm to room temperature overnight. The reaction was quenched with water (30 mL) and the layers were then separated. The organic layer was washed with 10% aqueous citric acid (3 × 20 mL) and the combined aqueous extracts were then extracted with dichloromethane (1 × 30 mL). The combined organic extracts were washed with saturated sodium bicarbonate solution (30 mL), then dried ($MgSO_4$) and concentrated *in vacuo* to leave a colourless solid. Purification by recrystallisation from ethyl acetate / petrol gave the *dipeptide* (1.75 g, 84%) as a colourless solid; mp 98–99 °C (from ethyl acetate / petrol); $[\alpha]_D^{22}$ +20 (*c* = 1.0, $CHCl_3$); Found: C, 61.8; H, 6.3; N, 6.1%. $C_{23}H_{28}N_2O_7$ requires C, 62.2; H, 6.4; N, 6.3%; $\nu_{max}(CHCl_3)/cm^{-1}$ 3422, 1729 and 1682; δ_H(360 MHz, $CDCl_3$) 7.38–7.27 (11H, m, CON*H*, 10 × aryl-H), 5.81 (1H, d, *J* 7.0 Hz, ZN*H*), 5.12 (2H, s, CO_2CH_2Ph), 4.61 (1H, dd, *J* 9.0 and 2.6 Hz, CONHC*H*), 4.56 (2H, s, CH_2OCH_2Ph), 4.51–4.42 (1H, m, ZNHC*H*), 4.32 (1H, qd, *J* 6.4 and 2.6, NHCHC*H*(CH_3)OH), 3.92 (1H, dd, *J* 9.2 and 4.0 Hz, $CHCH_aH_bOBn$), 3.72 (3H, s, CO_2CH_3), 3.63 (1H, dd, *J* 9.2 and 6.3 Hz, $CHCH_aH_bOBn$), 2.54 (1H, br s, O*H*) and 1.16 (3H, d, *J* 6.4 Hz, CH(CH_3)OH) ppm; δ_C(90 MHz, $CDCl_3$) 171.0 (s), 170.6 (s), 137.2 (s),

136.0 (s), 128.5–127.8 (Ar s and d), 73.5 (t), 69.8 (t), 68.0 (d), 67.2 (t), 57.4 (d), 54.4 (d), 52.5 (q) and 19.8 (q) ppm; *m/z* (ESI) Found: 467.1771, $C_{23}H_{28}N_2O_7Na$ $[(M+Na)^+]$ requires 467.1794.

2-((*S*)-2-Benzyloxy-1-benzyloxycarbonylamino-ethyl)-5-methyl-oxazole-4-carboxylic acid methyl ester (15c). Bis(2-methoxyethyl)aminosulfur trifluoride (2.2 mL, 6.2 mmol) was added dropwise over 2 min to a stirred solution of the dipeptide **13c** (2.3 g, 5.2 mmol) in dry dichloromethane (55 mL) at –20 °C under a nitrogen atmosphere. The mixture was stirred at –20 °C for 2 h and then allowed to warm to room temperature and stirred for a further 10 min. The mixture was quenched with saturated sodium bicarbonate solution (20 mL) and the separated organic layer was then dried ($MgSO_4$) and concentrated *in vacuo* to leave the crude oxazoline **14c**, which was used immediately without further purification.

Bromotrichloromethane (1.5 mL, 15.6 mmol) was added to a stirred solution of the crude oxazoline in dry dichloromethane (55 mL) at 0 °C under a nitrogen atmosphere and the mixture was stirred at 0 °C for 10 min. 1,8-Diazabicyclo[5.4.0]undec-7-ene (2.4 mL, 15.6 mmol) was added dropwise over 5 min and the mixture was allowed to warm to room temperature overnight. The volatile components were removed *in vacuo* and the residue was partitioned between ethyl acetate (50 mL) and a 10% aqueous solution of citric acid (30 mL). The separated organic extract was washed with saturated sodium bicarbonate solution (20 mL), dried ($MgSO_4$) and then concentrated *in vacuo*. The residue was purified by chromatography on silica gel using 2:1 petrol–ethyl acetate as eluent to give the *oxazole* (1.5 g, 68%) as a colourless oil; $[\alpha]_D^{22}$ –14 (*c* = 1.0, $CHCl_3$); $\nu_{max}(CHCl_3)/cm^{-1}$

3431, 2954, 2869, 1723 and 1623; δ_H(360 MHz, $CDCl_3$) 7.35–7.21 (10H, m, 10 × aryl-H), 6.00 (1H, d, *J* 8.6 Hz, ZN*H*), 5.18–5.05 (3H, m, CO_2CH_2Ph, NHC*H*CH_2), 4.53 (1H, d, *J* 12.2 Hz, $CH_2OCH_aH_bPh$), 4.48 (1H, d, *J* 12.2 Hz, $CH_2OCH_aH_bPh$), 3.92 (1H, dd, *J* 9.7 and 5.4 Hz, $CHCH_aH_bOBn$), 3.89 (3H, s, CO_2CH_3), 3.82 (1H, dd, *J* 9.7 and 4.5 Hz, $CHCH_aH_bOBn$) and 2.58 (3H, s, oxazole-CH_3) ppm; δ_C(90 MHz, $CDCl_3$) 162.2 (s), 159.8 (s), 156.5 (s), 155.6 (s), 137.1 (s), 135.9 (s), 128.2 (d), 128.1 (d), 127.9 (d), 127.8 (d), 127.6 (d), 127.4 (d), 127.2 (s), 72.9 (t), 69.8 (t), 66.8 (t), 51.7 (q), 49.4 (d) and 11.7 (q) ppm; *m/z* (ESI) Found: 425.1733, $C_{23}H_{24}N_2O_6$ $[(M+H)^+]$ requires 425.1713.

2-((*S*)-2-Benzyloxy-1-benzyloxycarbonylamino-ethyl)-5-methyl-oxazole-4-carboxylic acid (16c). A solution of sodium hydroxide (0.56 g, 14 mmol) in water (10 mL) was added in one portion to a stirred solution of the methyl ester **15c** (1.1 g, 2.8 mmol) in tetrahydrofuran (30 mL), and the mixture was stirred at room temperature for 18 h. The mixture was concentrated *in vacuo* and the residue was then acidified to pH 2 with 10% aqueous citric acid. The aqueous suspension was extracted with dichloromethane (2 × 50 mL) and the combined organic extracts were dried ($MgSO_4$) and then evaporated *in vacuo* to leave a yellow solid. Purification by recrystallisation from ether / petrol gave the *acid* (0.9 g, 78%) as a colourless solid; mp 157–158 °C (from ether / petrol); $[\alpha]_D^{22}$ –26 (*c* = 1.0, $CHCl_3$); Found: C, 64.3; H, 5.4; N, 6.8%. $C_{22}H_{22}N_2O_6$ requires C, 64.4; H, 5.4; N, 6.8%; $\nu_{max}(CHCl_3)/cm^{-1}$ 3436, 3277, 2955, 2870, 1716 and 1632; δ_H(360 MHz, $CDCl_3$) 7.38–7.22 (10H, m, 10 × aryl-H), 6.73 (1H, d, *J* 8.4 Hz, ZN*H*), 5.23 (1H, m, NHC*H*CH_2), 5.11 (1H, d, *J* 12.2 Hz, $CO_2CH_aH_bPh$), 5.09 (1H, d, *J* 12.2 Hz, $CO_2CH_aH_bPh$), 4.55 (1H, d, *J* 12.2 Hz, $CH_2OCH_aH_bPh$), 4.50 (1H, d, *J* 12.2 Hz, $CH_2OCH_aH_bPh$), 3.92 (1H, dd, *J*

9.6 and 4.4 Hz, CHCH_aH$_b$OBn), 3.83 (1H, dd, *J* 9.6 and 5.1 Hz, CHCH$_a$$H_b$OBn) and 2.53 (3H, s, oxazole-CH_3) ppm; δ_C(90 MHz, $CDCl_3$) 164.6 (s), 161.3 (s), 157.5 (s), 156.2 (s), 137.3 (s), 136.1 (s), 128.2 (d), 128.1 (d), 128.1 (d), 128.0 (d), 127.9 (d), 127.8 (d), 127.6 (s), 73.2 (t), 70.3 (t), 67.1 (t), 49.6 (d) and 11.8 (q) ppm; *m/z* (ESI) Found: 433.1387, $C_{22}H_{22}N_2O_6Na$ [$(M+Na)^+$] requires 433.1370.

2-[(1*S*,2*R*)-1-Benzyloxycarbonylamino-2-(*tert*-butyl-dimethyl-silanyloxy)-propyl]-oxazole-4-carboxylic acid methyl ester (17a). (Diethylamino)sulfur trifluoride (1.8 mL, 13.4 mmol) was added dropwise over 5 min to a stirred solution of (*S*)-2-[(2*S*,3*R*)-2-benzyloxycarbonylamino-3-(*tert*-butyl-dimethyl-silanyloxy)-butyrylamino]-3-hydroxy-propionic acid methyl ester (5.7 g, 12.2 mmol) in dry dichloromethane (120 mL) at −78 °C under a nitrogen atmosphere. The mixture was stirred at −78 °C for 1.5 h and then allowed to warm to room temperature and stirred for a further 10 min. The mixture was quenched with saturated sodium bicarbonate solution (30 mL) and the separated organic layer was then dried ($MgSO_4$) and concentrated *in vacuo* to leave the crude oxazoline, which was used immediately without further purification.

Bromotrichloromethane (3.5 mL, 37 mmol) was added to a stirred solution of the crude oxazoline in dry dichloromethane (120 mL) at 0 °C under a nitrogen atmosphere and the mixture was stirred at 0 °C for 10 min. 1,8-Diazabicyclo[5.4.0]undec-7-ene (5.5 mL, 37 mmol) was added dropwise over 5 min and the mixture was allowed to warm to room temperature overnight. The volatile components were removed *in vacuo* and the residue was partitioned between ethyl acetate (150 mL) and 10% aqueous citric acid (100 mL). The separated organic extract was washed with saturated sodium bicarbonate solution (50

mL), then dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified by chromatography on silica gel using 5:1 petrol–ethyl acetate as eluent to give the *oxazole* (4.3 g, 79%) as a colourless oil; $[\alpha]_D^{22}$ –23 (*c* = 1.5, $CHCl_3$); Found: C, 59.1; H, 7.2; N, 6.2%. $C_{22}H_{32}N_2O_6Si$ requires C, 58.9; H, 7.2; N, 6.2%; $\nu_{max}(CHCl_3)/cm^{-1}$ 3437, 2955, 2930, 2857, 1722 and 1586; δ_H(360 MHz, $CDCl_3$) 8.18 (1H, s, oxazole-H), 7.40–7.30 (5H, m, 5 × aryl-H), 5.69 (1H, d, *J* 9.4 Hz, ZN*H*), 5.17 (1H, d, *J* 12.2 Hz, $CO_2CH_aH_bPh$), 5.13 (1H, d, *J* 12.2 Hz, $CO_2CH_aH_bPh$), 4.94 (1H, dd, *J* 9.4 and 2.1 Hz, NHC*H*CH), 4.44 (1H, qd, *J* 6.2 and 2.1 Hz, CHC*H*(CH_3)OTBS), 3.92 (3H, s, CO_2CH_3), 1.25 (3H, d, *J* 6.2 Hz, CH(CH_3)OTBS), 0.76 (9H, s, SiC(CH_3)$_3$), –0.02 (3H, s, SiCH_3(CH_3)) and –0.22 (3H, s, SiCH_3(CH_3)) ppm; δ_C(90 MHz, $CDCl_3$) 163.9 (s), 161.4 (s), 156.4 (s), 143.8 (d), 136.1 (s), 133.5 (s), 128.5 (d), 128.2 (d), 128.2 (d), 69.8 (d), 67.3 (t), 55.7 (d), 52.2 (q), 25.5 (q), 20.4 (q), 17.7 (s), −4.7 (q) and −5.5 (q) ppm; *m/z* (ESI) Found: 449.2086, $C_{22}H_{33}N_2O_6Si$ [$(M+H)^+$] requires 449.2108.

2-((1*S*,2*R*)-1-Benzyloxycarbonylamino-2-hydroxy-propyl)-oxazole-4-carboxylic acid methyl ester (17b). Tetrabutylammonium fluoride (6.0 g, 19 mmol) was added to a stirred solution of the silyl ether **17a** (4.2 g, 9.3 mmol) in dry tetrahydrofuran (100 mL) at 0 °C under a nitrogen atmosphere and the mixture was then allowed to warm to room temperature overnight. The mixture was quenched with saturated ammonium chloride solution (80 mL) and extracted with diethyl ether (3 × 100 mL). The combined organic extracts were dried ($MgSO_4$) and then concentrated *in vacuo*. The residue was purified by chromatography on silica gel using diethyl ether as eluent to give the *alcohol* (2.6 g, 85%) as a colourless oil; $[\alpha]_D^{22}$ –59 (*c* = 1.0, $CHCl_3$); $\nu_{max}(CHCl_3)/cm^{-1}$ 3430, 2955, 2927,

1723 and 1585; δ_H(360 MHz, $CDCl_3$) 8.14 (1H, s, oxazole-H), 7.39–7.27 (5H, m, 5 × aryl-H), 6.19 (1H, d, *J* 9.3 Hz, ZN*H*), 5.15 (1H, d, *J* 12.3 Hz, $CO_2CH_aH_bPh$), 5.07 (1H, d, *J* 12.3 Hz, $CO_2CH_aH_bPh$), 4.92 (1H, dd, *J* 9.3 and 2.4 Hz, NHC*H*CH), 4.42 (1H, m, CHC*H*(CH_3)OH), 3.87 (3H, s, CO_2CH_3), 3.43 (1H, br s, O*H*) and 1.25 (3H, d, *J* 6.5 Hz, CH(CH_3)OH) ppm; δ_C(90 MHz, $CDCl_3$) 164.0 (s), 161.3 (s), 156.5 (s), 144.2 (d), 136.0 (s), 132.9 (s), 128.5 (d), 128.1 (d), 128.0 (d), 67.9 (d), 67.2 (t), 54.4 (d), 52.2 (q) and 19.2 (q) ppm; *m/z* (ESI) Found: 335.1234, $C_{16}H_{19}N_2O_6$ $[(M+H)^+]$ requires 335.1243.

2-((1*S*,2*R*)-1-Amino-2-hydroxy-propyl)-oxazole-4-carboxylic acid methyl ester (17c). 10% Palladium on carbon (0.5 g) was added to a solution of the carbamate **17b** (2.6 g, 7.7 mmol) in methanol (80 mL) and tetrahydrofuran (20 mL). The mixture was stirred at room temperature under 1 atmosphere pressure of hydrogen for 16 h and the mixture was then filtered through a pad of celite and eluted with methanol (250 mL). The filtrate was concentrated *in vacuo* and the residue was then purified by chromatography on silica gel using 9:1 dichloromethane–methanol as eluent to give the *amine* (1.4 g, 88%) as a yellow solid; mp 89–90 °C; $[\alpha]_D^{22}$ –5.4 (*c* = 1.0, $CHCl_3$); Found: C, 47.7; H, 6.1; N, 13.8%. $C_8H_{12}N_2O_4$ requires C, 48.0; H, 6.0; N, 14.0%; $\nu_{max}(CHCl_3)/cm^{-1}$ 3406, 2978, 2955, 1739 and 1585; δ_H(360 MHz, $CDCl_3$) 8.19 (1H, s, oxazole-H), 3.99 (1H, dq, *J* 6.4 and 6.2 Hz, CHC*H*(CH_3)OH), 3.89 (3H, s, CO_2CH_3), 3.80 (1H, d, *J* 6.4 Hz, NH_2CHCH), 2.48 (3H, br s, NH_2 and O*H*) and 1.17 (3H, d, *J* 6.2 Hz, CH(CH_3)OH) ppm; δ_C(90 MHz, $CDCl_3$) 166.5 (s), 161.4 (s), 143.9 (d), 133.1 (s), 68.9 (d), 55.8 (d), 52.2 (q) and 19.2 (q) ppm; *m/z* (ESI) Found: 201.0863, $C_8H_{13}N_2O_4$ $[(M+H)^+]$ requires 201.0875.

2-[(*S*)-1-Benzyloxycarbonylamino-2-(*tert*-butyl-dimethyl-silanyloxy)-ethyl]-oxazole-4-carboxylic acid (16g). A solution of sodium hydroxide (0.18 g, 4.5 mmol) in water (15 mL) was added in one portion to a stirred solution of the methyl ester **15b** (1.5 g, 3.5 mmol) in tetrahydrofuran (35 mL), and the mixture was stirred at room temperature for 18 h. The mixture was concentrated *in vacuo* and the residue was then acidified to pH 2 with 10% aqueous citric acid. The aqueous suspension was extracted with dichloromethane (2 × 30 mL) and the combined organic extracts were then dried ($MgSO_4$) and evaporated *in vacuo* to leave the *acid* (1.2 g, 82%) as a colourless oil; $[\alpha]_D^{21}$ –25 (*c* = 2.0, $CHCl_3$); $\nu_{max}(CHCl_3)/cm^{-1}$ 3436, 3169, 2930, 2858, 1714 and 1590; δ_H(360 MHz, $CDCl_3$) 8.23 (1H, s, oxazole-H), 7.97 (1H, br s, CO_2H), 7.40–7.26 (5H, m, 5 × aryl-H), 6.57 (1H, d, *J* 9.0 Hz, ZN*H*), 5.23–5.15 (1H, m, ZNHC*H*), 5.15 (1H, d, *J* 12.2 Hz, $CO_2CH_aH_bPh$), 5.10 (1H, d, *J* 12.2 Hz, $CO_2CH_aH_bPh$), 4.10 (1H, dd, *J* 10.0 and 3.7 Hz, CH_aH_bOTBS), 3.98 (1H, dd, *J* 10.0 and 3.7 Hz, CH_aH_bOTBS), 0.80 (9H, s, $SiC(CH_3)_3$), –0.03 (3H, s, $SiCH_3(CH_3)$) and –0.04 (3H, s, $SiCH_3(CH_3)$) ppm; δ_C(90 MHz, $CDCl_3$) 164.6 (s), 163.7 (s), 156.3 (s), 144.8 (d), 136.0 (s), 133.2 (s), 128.4–127.6 (Ar d), 67.2 (t), 64.3 (t), 51.6 (d), 25.5 (q), 18.0 (s), –5.7 (q) and –5.8 (q) ppm; *m/z* (ESI) Found: 421.1763, $C_{20}H_{29}N_2O_6Si$ $[(M+H)^+]$ requires 421.1795.

(2*S*,3*R*)-2-[(*S*)-2-Benzyloxycarbonylamino-3-(*tert*-butyl-dimethyl-silanyloxy)-propionylamino]-3-hydroxy-butyric acid methyl ester (13d). 4-Methylmorpholine (3.3 mL, 30 mmol) was added to a stirred suspension of (*S*)-2-benzyloxycarbonylamino-3-(*tert*-butyl-dimethyl-silanyloxy)-propionic acid (3.5 g, 10 mmol, see preparation of **13b**) and 1-hydroxybenzotriazole (2.7 g, 20 mmol) in dry dichloromethane (100 mL) at 0 °C

under a nitrogen atmosphere. 1-[3-(Dimethylamino)propyl]-3-ethylcarbodiimide hydrochloride (2.1 g, 11 mmol) was added and the mixture was then stirred at 0 °C for 15 min. L-Threonine methylester hydrochloride (1.9 g, 11 mmol) was added in one portion, and the mixture was allowed to warm to room temperature overnight. The reaction was quenched with water (50 mL) and the layers were separated. The organic layer was washed with 10% aqueous citric acid (3 × 30 mL) and saturated sodium bicarbonate solution (30 mL), then dried ($MgSO_4$) and concentrated *in vacuo*. The residue was partially purified by chromatography on silica gel using ethyl acetate–petrol as eluent to give the *amide* (4.0 g, 85%) as a colourless oil; δ_H(360 MHz, $CDCl_3$) 7.35–7.29 (6H, m, 5 × aryl-H, CON*H*), 5.74 (1H, d, *J* 7.0 Hz, ZN*H*), 5.13 (2H, s, CO_2CH_2Ph), 4.62–4.58 (1H, m, CONHC*H*), 4.37–4.27 (2H, m, C*H*(CH_3)OH, ZNHC*H*), 4.06 (1H, dd, *J* 9.8 and 3.9 Hz, CH_aH_bOTBS), 3.78–3.69 (1H, m, CH_aH_bOTBS), 3.74 (3H, s, CO_2CH_3), 2.63 (1H, br s, O*H*), 1.18 (3H, d, *J* 6.0 Hz, CH(CH_3)OH), 0.89 (9H, s, SiC(CH_3)$_3$) and 0.15 (6H, s, Si(CH_3)$_2$) ppm; δ_C(90 MHz, $CDCl_3$) 171.0 (s), 170.7 (s), 156.1 (s), 136.0 (s), 128.5 (d), 128.2 (d), 128.1 (d), 67.8 (d), 67.1 (t), 63.2 (t), 57.4 (d), 56.0 (d), 52.5 (q), 25.7 (q), 19.8 (q), 18.2 (s), –5.6 (q) and –5.6 (q) ppm.

2-[(*S*)-1-Benzyloxycarbonylamino-2-(*tert*-butyl-dimethyl-silanyloxy)-ethyl]-5-methyl-oxazole-4-carboxylic acid methyl ester (15d). Bis(2-methoxyethyl)aminosulfur trifluoride (2.2 mL, 10 mmol) was added dropwise over 5 min to a stirred solution of the dipeptide **13d** (4.0 g, 8.5 mmol) in dry dichloromethane (100 mL) at –20 °C under a nitrogen atmosphere. The mixture was stirred at –20 °C for 2 h and was then allowed to warm to room temperature. The mixture was quenched with saturated sodium bicarbonate

solution (30 mL) and the separated organic layer was then dried ($MgSO_4$) and concentrated *in vacuo* to leave the crude oxazoline, which was used immediately without further purification.

Bromotrichloromethane (2.5 mL, 26 mmol) was added to a stirred solution of the crude oxazoline in dry dichloromethane (100 mL) at 0 °C under a nitrogen atmosphere and the mixture was stirred at 0 °C for 10 min. 1,8-Diazabicyclo[5.4.0]undec-7-ene (4.0 mL, 26 mmol) was added dropwise over 5 min and the mixture was allowed to warm to room temperature overnight. The mixture was concentrated *in vacuo* and the residue was partitioned between ethyl acetate (100 mL) and a 10% aqueous solution of citric acid (100 mL). The separated organic extract was washed with saturated sodium bicarbonate solution (70 mL), then dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified by chromatography on silica gel using 2:1 petrol–ethyl acetate as eluent to give the *oxazole* (1.9 g, 49%) as a colourless oil; $[\alpha]_D^{19}$ –7.8 (c = 1.0, $CHCl_3$); $\nu_{max}(CHCl_3)/cm^{-1}$ 3427, 2929, 1722 and 1623; δ_H(360 MHz, $CDCl_3$) 7.38–7.28 (5H, m, 5 × aryl-H), 5.73 (1H, d, J 8.7 Hz, ZN*H*), 5.15 (1H, d, J 12.3 Hz, $CO_2CH_aH_bPh$), 5.10 (1H, d, J 12.3 Hz, $CO_2CH_aH_bPh$), 5.05–4.98 (NHC*H*CH_2), 4.04 (1H, dd, J 10.1 and 3.7 Hz, CH_aH_bOTBS), 3.92 (1H, dd, J 10.1 and 4.4 Hz, CH_aH_bOTBS), 3.89 (3H, s, CO_2CH_3), 2.59 (3H, s, oxazole-CH_3), 0.80 (9H, s, $SiC(CH_3)_3$), –0.03 (3H, s, $SiCH_3(CH_3)$) and –0.06 (3H, s, $SiCH_3(CH_3)$) ppm; δ_C(90 MHz, $CDCl_3$) 162.5 (s), 160.3 (s), 156.5 (s), 155.7 (s), 136.1 (s), 128.4 (d), 128.1 (d), 128.1 (d), 127.4 (s), 67.1 (t), 64.3 (t), 51.9 (q), 51.4 (d), 25.5 (q), 18.0 (s), 11.8 (q), –5.7 (q) and –5.8 (q) ppm; *m/z* (ESI) Found: 471.1912, $C_{22}H_{32}N_2O_6SiNa$ $[(M+Na)^+]$ requires 471.1927.

2-[(*S*)-1-Benzyloxycarbonylamino-2-(*tert*-butyl-dimethyl-silanyloxy)-ethyl]-5-methyl-oxazole-4-carboxylic acid (16f). A solution of sodium hydroxide (0.34 g, 8.4 mmol) in water (20 mL) was added in one portion to a stirred solution of the methyl ester **15d** (1.9 g, 4.2 mmol) in tetrahydrofuran (40 mL), and the mixture was stirred at room temperature for 18 h. Water 100mL was added and the mixture was concentrated *in vacuo* to approx. 100 mL and then acidified to pH 2 with 10% aqueous citric acid. The aqueous mixture was extracted with dichloromethane (3 × 100 mL) and the combined organic extracts were then dried ($MgSO_4$) and evaporated *in vacuo* to leave the crude *acid* (1.1 g, 60%) as a colourless solid, which was used directly in the next reaction without further purification.

2-((*S*)-1-Benzyloxycarbonylamino-2-hydroxy-ethyl)-oxazole-4-carboxylic acid (16d). Hydrogen chloride (4.0 M solution in dioxane) (3 mL) was added to the corresponding TBS ether **16g** (0.40 g, 0.95 mmol) and the mixture was stirred at room temperature overnight under a nitrogen atmosphere. The mixture was concentrated *in vacuo* to leave a yellow residue, which was then purified by recrystallisation from dichloromethane / methanol to give the *alcohol* (0.23 g, 79%) as a colourless solid; mp 150–151 °C; $[\alpha]_D^{22}$ – 48 (*c* = 1.2, EtOH); $\nu_{max}(CHCl_3)/cm^{-1}$ 3320, 2928, 1725, 1701 and 1602; δ_H(360 MHz, CD_3OD) 8.50 (1H, s, oxazole-H), 7.42–7.23 (5H, m, 5 × aryl-H), 5.21–5.07 (2H, m, OC*H*$_2$Ph), 5.05–4.90 (1H, obs m, ZNHC*H*) and 4.01–3.90 (2H, m, C*H*$_2$OH) ppm; δ_C(90 MHz, CD_3OD) 163.5 (s), 162.4 (s), 156.9 (s), 144.7 (d), 136.5 (s), 133.2 (s), 128.0 (d),

127.6 (d), 127.4 (d), 66.4 (t), 62.0 (t) and 51.6 (d) ppm; *m/z* (ESI) Found: 329.0737, $C_{14}H_{14}N_2O_6Na$ [$(M+Na)^+$] requires 329.0750.

2-[(*S*)-1-Amino-2-(*tert*-butyl-dimethyl-silanyloxy)-ethyl]-oxazole-4-carboxylic acid methyl ester (16e). 10% Palladium on carbon (100 mg) was added to a solution of the carbamate **15b** (2.2 g, 5.1 mmol) in ethyl acetate (50 mL). The mixture was stirred at room temperature under 1 atmosphere pressure of hydrogen for 24 h and the mixture was then filtered through a pad of celite and eluted with 1:1 methanol–ethyl acetate (200 mL). The filtrate was concentrated *in vacuo* and the residue then purified by chromatography on silica gel using ethyl acetate as eluent to give the *amine* (1.1 g, 72%) as a pale yellow oil; $[\alpha]_D^{20}$ –11 (*c* = 1.0, $CHCl_3$); $\nu_{max}(CHCl_3)/cm^{-1}$ 3386, 2954, 1738 and 1589; δ_H(360 MHz, $CDCl_3$) 8.20 (1H, s, oxazole-H), 4.18 (1H, dd, *J* 5.5 and 4.7 Hz, NH_2CH), 3.95–3.93 (2H, m, CH_2OTBS), 3.92 (3H, s, CO_2CH_3), 2.06 (2H, br s, NH_2), 0.83 (9H, s, $SiC(CH_3)_3$), 0.02 (3H, s, $SiCH_3(CH_3)$) and –0.01 (3H, s, $SiCH_3(CH_3)$) ppm; δ_C(90 MHz, $CDCl_3$) 166.4 (s), 161.5 (s), 143.8 (d), 133.0 (s), 65.9 (t), 52.0 (d), 52.0 (q), 25.6 (q), 18.0 (s), –5.7 (q) and –5.7 (q) ppm; *m/z* (ESI) Found: 301.1592, $C_{13}H_{25}N_2O_4Si$ [$(M+H)^+$] requires 301.1584.

2-((1*S*,2*R*)-1-{[2-((*S*)-2-Benzyloxy-1-benzyloxycarbonylamino-ethyl)-5-methyl-oxazole-4-carbonyl]-amino}-2-hydroxy-propyl)-oxazole-4-carboxylic acid methyl ester (21a). 4-Methylmorpholine (0.5 mL, 4.4 mmol) was added to a stirred suspension of the acid **16c** (0.90 g, 2.2 mmol) and 1-hydroxybenzotriazole (0.5 g, 4.4 mmol) in dry dichloromethane (20 mL) at 0 °C under a nitrogen atmosphere. 1-[3-

(Dimethylamino)propyl]-3-ethylcarbodiimide hydrochloride (0.5 g, 2.6 mmol) was added and the mixture was then stirred at 0 °C for 2 min. A solution of the amine **17c** (0.5 g, 2.6 mmol) in dry dichloromethane (10 mL) was added dropwise over 3 min at 0 °C, and the mixture was allowed to warm to room temperature overnight. The reaction was quenched with water (20 mL) and the separated organic layer was then washed with 10% aqueous citric acid (3 × 20 mL). The combined aqueous extracts were extracted with dichloromethane (2 × 40 mL) and the combined organic extracts were then washed with saturated sodium bicarbonate solution (40 mL), dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified by chromatography on silica gel using 9:1 diethyl ether–ethyl acetate as eluent to give the *amide* (0.98 g, 75%) as a colourless solid; mp 56–57 °C (from ether / petrol); $[\alpha]_D^{22}$ –48 (*c* = 1.0, $CHCl_3$); $\nu_{max}(CHCl_3)/cm^{-1}$ 3437, 3401, 2954, 2870, 1725, 1672, 1634 and 1585; δ_H(360 MHz, $CDCl_3$) 8.18 (1H, s, oxazole-H), 7.72 (1H, d, *J* 9.2 Hz, CON*H*), 7.43–7.19 (10H, m, 10 × aryl-H), 5.85 (1H, d, *J* 8.6 Hz, ZN*H*), 5.31 (1H, dd, *J* 9.2 and 2.7 Hz, CONHC*H*CH(CH_3)OH), 5.21–5.05 (3H, m, CO_2CH_2Ph, NHC*H*CH_2OBn), 4.58 (1H, qd, *J* 6.4 and 2.7 Hz, CONHCHC*H*(CH_3)OH), 4.54 (1H, d, *J* 12.2 Hz, $CH_2OCH_aH_b$Ph), 4.47 (1H, d, *J* 12.2 Hz, $CH_2OCH_aH_b$Ph), 3.89 (3H, s, CO_2CH_3), 3.88 (1H, dd, *J* 9.4 and 3.7 Hz, $CHCH_aH_b$OBn), 3.79 (1H, dd, *J* 9.4 and 3.9 Hz, $CHCH_aH_b$OBn), 2.59 (3H, s, oxazole-CH_3) and 1.28 (3H, d, *J* 6.4 Hz, CH(CH_3)OH) ppm; δ_C(90 MHz, $CDCl_3$) 163.6 (s), 162.0 (s), 161.2 (s), 158.9 (s), 155.8 (s), 154.1 (s), 144.1 (d), 137.2 (s), 136.0 (s), 132.9 (s), 128.5–127.5 (Ar s and d), 73.0 (t), 69.9 (t), 67.5 (d), 67.0 (t), 52.1 (q), 51.7 (d), 49.5 (d), 19.2 (q) and 11.6 (q) ppm; *m/z* (ESI) Found: 593.2262, $C_{30}H_{33}N_4O_9$ $[(M+H)^+]$ requires 593.2248.

2′′-((*S*)-2-Benzyloxy-1-benzyloxycarbonylamino-ethyl)-5′,5′′-dimethyl-[2,4′;2′,4′′]teroxazole-4-carboxylic acid methyl ester (22a). Bis(2-methoxyethyl)aminosulfur trifluoride (0.5 mL, 1.1 mmol) was added dropwise over 2 min to a stirred solution of the *bis*-oxazole **21a** (0.52 g, 0.88 mmol) in dry dichloromethane (10 mL) at −20 °C under a nitrogen atmosphere. The mixture was stirred at −20 °C for 2 h and was then allowed to warm to room temperature and stirred for a further 5 min. The mixture was quenched with saturated sodium bicarbonate solution (10 mL) and the separated organic layer was then dried ($MgSO_4$) and concentrated *in vacuo* to leave the crude oxazoline, which was used immediately without further purification.

Bromotrichloromethane (0.26 mL, 2.7 mmol) was added to a stirred solution of the crude oxazoline in dry dichloromethane (10 mL) at 0 °C under a nitrogen atmosphere and the mixture was stirred at 0 °C for 10 min. 1,8-Diazabicyclo[5.4.0]undec-7-ene (0.41 mL, 2.7 mmol) was added dropwise over 5 min and the mixture was allowed to warm to room temperature overnight. The mixture was concentrated *in vacuo* and the residue was partitioned between ethyl acetate (50 mL) and a 10% aqueous solution of citric acid (30 mL). The separated organic extract was washed with saturated sodium bicarbonate solution (20 mL), dried ($MgSO_4$) and then concentrated *in vacuo* to leave a yellow solid. Purification by recrystallisation from ether gave the *tris*-oxazole (0.34 g, 67%) as a colourless solid; mp 165–167 °C (from ether); $[\alpha]_D^{21}$ –24 (*c* = 1.0, $CHCl_3$); Found: C, 62.8; H, 4.9; N, 9.5%. $C_{30}H_{28}N_4O_8$ requires C, 62.9; H, 4.9; N, 9.8%; $\nu_{max}(CHCl_3)/cm^{-1}$ 3435, 2954, 2869, 1723, 1659 and 1582; δ_H(360 MHz, $CDCl_3$) 8.33 (1H, s, oxazole-H), 7.42–

7.20 (10H, m, 10 × aryl-H), 5.81 (1H, d, *J* 8.2 Hz, ZN*H*), 5.22–5.09 (3H, m, CO_2CH_2Ph, NHC*H*CH_2), 4.58 (1H, d, *J* 12.2 Hz, $CH_2OCH_aH_b$Ph), 4.52 (1H, d, *J* 12.2 Hz, $CH_2OCH_aH_b$Ph), 4.00–3.91 (4H, m, CO_2CH_3, $CHCH_aH_bOBn$), 3.87 (1H, dd, *J* 9.7 and 4.2 Hz, $CHCH_aH_bOBn$), 2.84 (3H, s, oxazole-CH_3) and 2.73 (3H, s, oxazole-CH_3) ppm; δ_C(90 MHz, $CDCl_3$) 161.5 (s), 160.8 (s), 156.7 (s), 155.7 (s), 154.7 (s), 150.9 (s), 143.4 (d), 137.3 (s), 136.1 (s), 134.1 (s), 128.4 (d), 128.3 (d), 128.1 (d), 128.0 (d), 127.8 (d), 127.6 (d), 125.4 (s), 124.7 (s), 73.1 (t), 70.1 (t), 67.1 (t), 52.1 (q), 49.7 (d), 11.8 (q) and 11.7 (q) ppm; *m/z* (ESI) Found: 573.2024, $C_{30}H_{29}N_4O_8$ $[(M+H)^+]$ requires 573.1985.

2″-((*S*)-2-Benzyloxy-1-benzyloxycarbonylamino-ethyl)-5′,5″-dimethyl-[2,4′;2′,4″]teroxazole-4-carboxylic acid (23a). A solution of sodium hydroxide (0.20 g, 5.0 mmol) in water (5 mL) was added in one portion to a stirred solution of the methyl ester **22a** (0.29 g, 0.51 mmol) in tetrahydrofuran (10 mL), and the mixture was stirred at room temperature for 18 h. The mixture was concentrated *in vacuo* and the residue was then acidified to pH 2 with 10% aqueous citric acid. The aqueous suspension was extracted with dichloromethane (3 × 30 mL) and the combined organic extracts were then dried ($MgSO_4$) and evaporated *in vacuo* to leave a colourless solid. Purification by recrystallisation from ethyl acetate gave the *carboxylic acid* (0.28 g, 98%) as a colourless solid; mp 195–196 °C (decomp.) (from ethyl acetate); $[\alpha]_D^{21}$ –10 (*c* = 1.0, $CHCl_3$); $\nu_{max}(CHCl_3)/cm^{-1}$ 3436, 3168, 2925, 2868, 1716, 1661 and 1586; δ_H(360 MHz, $CDCl_3$) 8.39 (1H, s, oxazole-H), 7.45–7.20 (10H, m, 10 × aryl-H), 5.90 (1H, d, *J* 8.7 Hz, ZN*H*), 5.90 (1H, br s, CO_2H), 5.26–5.09 (3H, m, CO_2CH_2Ph, NHC*H*CH_2), 4.56 (1H, d, *J* 12.2 Hz, $CH_2OCH_aH_b$Ph), 4.51 (1H, d, *J* 12.2 Hz, $CH_2OCH_aH_b$Ph), 3.95 (1H, dd, *J* 9.6 and 3.5

Hz, CHC*H*$_a$H$_b$OBn), 3.86 (1H, dd, *J* 9.6 and 4.4 Hz, CHCH$_a$*H*$_b$OBn), 2.81 (3H, s, oxazole-C*H*$_3$) and 2.71 (3H, s, oxazole-C*H*$_3$) ppm; δ_C(90 MHz, $CDCl_3$) 164.3 (s), 161.0 (s), 156.8 (s), 155.9 (s), 154.7 (s), 151.1 (s), 151.0 (s), 144.3 (d), 137.2 (s), 136.0 (s), 133.8 (s), 128.5–127.8 (Ar s and d), 125.3 (s), 124.6 (s), 73.2 (t), 70.1 (t), 67.2 (t), 49.7 (d), 11.9 (q) and 11.7 (q) ppm; *m/z* (ESI) Found: 581.1697, $C_{29}H_{26}N_4O_8Na$ [$(M+Na)^+$] requires 581.1648.

(*S*)-2-Benzyloxy-1-(4-methoxycarbonyl-[2,4';2',4'']teroxazol-2''-yl)-ethyl-ammonium; chloride (24b). Hydrogen chloride (4.0 M solution in dioxane) (5 mL) was added to the carbamate **20c** (0.40 g, 0.80 mmol) and the mixture was stirred at room temperature overnight under a nitrogen atmosphere. The volatiles were evaporated to leave the *amine hydrochloride salt* (0.35 g, 98%) as a colourless solid; mp 224 °C (decomp.) (from methanol / ethyl acetate); $[\alpha]_D^{25}$ +21 (*c* = 1.0, EtOH); ν_{max}(solid)/cm^{-1} 1733; δ_H(360 MHz, $CDCl_3$ / CD_3OD (2:1)) 8.32 (2H, s, 2 × oxazole-H), 8.23 (1H, s, oxazole-H), 7.10–6.97 (5H, m, 5 × aryl-H), 5.13 (1H, br s, NH_3CH), 4.42 (1H, d, *J* 12.2 Hz, OC*H*$_a$H$_b$Ph), 4.38 (1H, d, *J* 12.2 Hz, OCH$_a$*H*$_b$Ph), 4.01–3.91 (2H, m, C*H*$_2$OBn) and 3.73 (3H, s, CO_2CH_3) ppm; δ_C(90 MHz, $CDCl_3$ / CD_3OD (2:1)) 160.9 (s), 159.3 (s), 155.6 (s), 154.8 (s), 144.1 (d), 141.1 (d), 139.7 (d), 136.2 (s), 133.4 (s), 129.7 (s), 129.1 (s), 127.9 (d), 127.6 (d), 127.5 (d), 73.1 (t), 66.9 (t), 51.8 (q) and 48.7 (d) ppm; *m/z* (ESI) Found: 411.1298, $C_{20}H_{19}N_4O_6$ [M^+] requires 411.1305.

2''-[(S)-1-{[2''-((S)-1-Amino-2-benzyloxy-ethyl)-5',5''-dimethyl-[2,4';2',4'']teroxazole-4-carbonyl]-amino}-2-(*tert*-butyl-dimethyl-silanyloxy)-ethyl]-

[2,4';2',4'']teroxazole-4-carboxylic acid methyl ester (32a). 10% Palladium on carbon (30 mg) was added to a solution of the carbamate **27** (0.13 g, 0.13 mmol) in methanol (2 mL) and ethyl acetate (4 mL). The mixture was stirred at room temperature under 1 atmosphere pressure of hydrogen for 18 h and the mixture was then filtered through a pad of celite and eluted with methanol–ethyl actetate (1:1) (150 mL). The filtrate was concentrated *in vacuo* to leave the *amine* (0.10 g, 91%) as a colourless solid, which was used directly in the next reaction without further purification.

Sodium; 2''-[(*S*)-1-{[2''-((*S*)-1-amino-2-benzyloxy-ethyl)-5',5''-dimethyl-[2,4';2',4'']teroxazole-4-carbonyl]-amino}-2-(*tert*-butyl-dimethyl-silanyloxy)-ethyl]-[2,4';2',4'']teroxazole-4-carboxylate (32b). A solution of sodium hydroxide (40 mg, 1.0 mmol) in water (1 mL) was added in one portion to a stirred solution of the methyl ester **32a** (0.10 g, 0.12 mmol) in tetrahydrofuran (3 mL), and the mixture was stirred at room temperature for 3.5 h. A solution of sodium bicarbonate (0.34 g, 4.0 mmol) in water (3 mL) was added and the mixture was then evaporated to dryness *in vacuo*. The residue was partitioned between dichloromethane (50 mL), methanol (25 mL) and water (50 mL) and the layers were separated. The aqueous layer was extracted with dichloromethane–methanol (2:1) (3 × 50 mL) and dichloromethane (2 × 50 mL) and the combined organic extracts were then evaporated *in vacuo* to leave the *acid* (90 mg, 88%) as a colourless solid, which was used directly in the next reaction without further purification.

2-[(*S*)-1-({2-[(*S*)-1-Benzyloxycarbonylamino-2-(*tert*-butyl-dimethyl-silanyloxy)-ethyl]-oxazole-4-carbonyl}-amino)-2-hydroxy-ethyl]-oxazole-4-carboxylic acid

methyl ester (18c). 4-Methylmorpholine (0.64 mL, 5.8 mmol) was added to a stirred suspension of the acid **16c** (1.2 g, 2.9 mmol) and 1-hydroxybenzotriazole (0.78 g, 5.8 mmol) in dry dichloromethane (30 mL) at 0 °C under a nitrogen atmosphere. 1-[3-(Dimethylamino)propyl]-3-ethylcarbodiimide hydrochloride (0.84 g, 4.4 mmol) was added and the mixture was then stirred at 0 °C for 2 min. A solution of the amine **16b** (0.54 g, 2.9 mmol) in dry dichloromethane (15 mL) was added dropwise over 3 min at 0 °C, and the mixture was then allowed to warm to room temperature overnight. The reaction was quenched with water (20 mL) and the separated organic layer was then washed with 10% aqueous citric acid (2 × 20 mL). The combined aqueous extracts were extracted with dichloromethane (2 × 20 mL) and the combined organic extracts were then washed with saturated sodium bicarbonate solution (20 mL), dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified by chromatography on silica gel using diethyl ether as eluent to give the *amide* (0.85 g, 50%) as a colourless solid; mp 47–49 °C (from ether / petrol); $[\alpha]_D^{22}$ –30 (*c* = 2.0, $CHCl_3$); $\nu_{max}(CHCl_3)/cm^{-1}$ 3404, 2954, 1723, 1678 and 1599; δ_H(360 MHz, $CDCl_3$) 8.23 (1H, s, oxazole-H), 8.14 (1H, s, oxazole-H), 7.98 (1H, d, *J* 8.6 Hz, CON*H*), 7.43–7.30 (5H, m, 5 × aryl-H), 5.90 (1H, d, *J* 8.7 Hz, ZN*H*), 5.55–5.48 (1H, m, CONHC*H*), 5.20 (1H, d, *J* 12.2 Hz, $CO_2CH_aH_bPh$), 5.15 (1H, d, *J* 12.2 Hz, $CO_2CH_aH_bPh$), 5.08–4.99 (1H, m, ZNHC*H*), 4.33–4.25 (1H, m, CH_aH_bOH), 4.11–3.88 (6H, m, CH_aH_bOH, CH_2OTBS, CO_2CH_3), 3.42–3.34 (1H, m, O*H*), 0.82 (9H, s, $SiC(CH_3)_3$), 0.01 (3H, s, $SiCH_3(CH_3)$) and –0.02 (3H, s, $SiCH_3(CH_3)$) ppm; δ_C(90 MHz, $CDCl_3$) 162.9 (s), 162.4 (s), 161.3 (s), 160.5 (s), 155.8 (s), 144.4 (d), 141.8 (d), 136.0 (s), 135.4 (s), 133.1 (s), 128.5 (d), 128.2 (d), 128.2 (d), 67.2 (t), 63.9 (t), 63.0 (t), 52.3 (q),

51.3 (d), 48.8 (d), 25.6 (q), 18.1 (s), –5.6 (q) and –5.7 (q) ppm; *m/z* (ESI) Found: 589.2295, $C_{27}H_{37}N_4O_9Si$ [$(M+H)^+$] requires 589.2330.

2″-[(*S*)-1-Benzyloxycarbonylamino-2-(*tert*-butyl-dimethyl-silanyloxy)-ethyl]-[2,4′;2′,4″]teroxazole-4-carboxylic acid methyl ester (20c). (Diethylamino)sulfur trifluoride (0.22 mL, 1.7 mmol) was added dropwise over 2 min to a stirred solution of the *bis*-oxazole **18c** (0.85 g, 1.4 mmol) in dry dichloromethane (15 mL) at −78 °C under a nitrogen atmosphere. The mixture was stirred at −78 °C for 2 h and was then allowed to warm to room temperature and stirred for a further 5 min. The mixture was quenched with saturated sodium bicarbonate solution (10 mL) and the separated organic layer was then dried ($MgSO_4$) and concentrated *in vacuo* to leave the crude oxazoline, which was used immediately without further purification.

Bromotrichloromethane (0.40 mL, 4.2 mmol) was added to a stirred solution of the crude oxazoline in dry dichloromethane (15 mL) at 0 °C under a nitrogen atmosphere and the mixture was stirred at 0 °C for 5 min. 1,8-Diazabicyclo[5.4.0]undec-7-ene (0.63 mL, 4.2 mmol) was added dropwise over 2 min and the mixture was then allowed to warm to room temperature overnight. The mixture was concentrated *in vacuo* and the residue was partitioned between ethyl acetate (100 mL) and 10% aqueous citric acid (100 mL). The separated organic extract was washed with saturated sodium bicarbonate solution (100 mL), then dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified by chromatography on silica gel using ethyl acetate as eluent to give the *oxazole* (0.65 g, 82%) as a colourless solid; mp 138 °C (from ether / petrol); $[\alpha]_D^{21}$ –10 (*c* = 1.0, $CHCl_3$);

Found: C, 56.6; H, 5.6; N, 9.6%. $C_{27}H_{32}N_4O_8Si$ requires C, 57.0; H, 5.7; N, 9.9%; $\nu_{max}(CHCl_3)/cm^{-1}$ 3437, 2954, 2869, 1726, 1654 and 1579; δ_H(360 MHz, $CDCl_3$) 8.46 (1H, s, oxazole-H), 8.36 (2H, s, 2 × oxazole-H), 7.47–7.25 (5H, m, 5 × aryl-H), 5.82 (1H, d, *J* 8.5 Hz, ZN*H*), 5.23–5.12 (3H, m, CO_2CH_2Ph, NHC*H*CH_2), 4.17 (1H, dd, *J* 9.9 and 3.3 Hz, CHCH_aH_bOTBS), 4.06–3.96 (4H, m, CO_2CH_3, $CHCH_aH_b$OTBS), 0.82 (9H, s, $SiC(CH_3)_3$), 0.01 (3H, s, $SiCH_3(CH_3)$) and –0.02 (3H, s, $SiCH_3(CH_3)$) ppm; δ_C(90 MHz, $CDCl_3$) 164.0 (s), 161.3 (s), 156.0 (s), 155.4 (s), 143.9 (d), 139.6 (d), 139.3 (d), 136.1 (s), 134.4 (s), 130.8 (s), 129.9 (s), 128.5 (d), 128.2 (d), 128.2 (d), 67.3 (t), 64.3 (t), 52.3 (q), 51.7 (d), 25.6 (q), 18.1 (s), –5.6 (q) and –5.7 (q) ppm; *m/z* (ESI) Found: 591.1880, $C_{27}H_{32}N_4O_8Si$ [$(M+Na)^+$] requires 591.1887.

2′′-[(*S*)-1-Amino-2-(*tert*-butyl-dimethyl-silanyloxy)-ethyl]-[2,4′;2′,4′′]teroxazole-4-carboxylic acid methyl ester (24a). 10% Palladium on carbon (0.1 g) was added to a solution of the carbamate **20c** (0.55 g, 0.97 mmol) in methanol (10 mL) and tetrahydrofuran (5 mL). The mixture was stirred at room temperature under 1 atmosphere pressure of hydrogen for 18 h and the mixture was then filtered through a pad of celite and eluted with methanol–ethyl actetate (1:1) (100 mL). The filtrate was concentrated *in vacuo* to leave the *amine* (0.41 g, 97%) as a colourless solid; mp 190–191 °C (decomp.) (from dichloromethane / ether / petrol); $[\alpha]_D^{21}$ –7.1 (*c* = 1.0, $CHCl_3$); $\nu_{max}(CHCl_3)/cm^{-1}$ 3387, 3170, 2930, 1738, 1654 and 1579; δ_H(360 MHz, $CDCl_3$) 8.42 (1H, s, oxazole-H), 8.32 (2H, s, 2 × oxazole-H), 4.23–4.18 (1H, m, NH_2CH), 3.98–3.92 (5H, m, CO_2CH_3, $CHCH_2$OTBS), 1.99 (2H, br s, NH_2), 0.83 (9H, s, $SiC(CH_3)_3$), 0.02 (3H, s, $SiCH_3(CH_3)$) and –0.01 (3H, s, $SiCH_3(CH_3)$) ppm; δ_C(90 MHz, $CDCl_3$) 167.1 (s), 161.2 (s), 156.2 (s),

155.4 (s), 143.8 (d), 139.4 (d), 139.3 (d), 134.3 (s), 130.7 (s), 129.6 (s), 66.0 (t), 52.3 (q), 52.2 (d), 25.7 (q), 18.1 (s), –5.6 (q) and –5.6 (q) ppm; *m/z* (ESI) Found: 435.1707, $C_{19}H_{27}N_4O_6Si$ [$(M+H)^+$] requires 435.1700.

2-[(1*S*,2*R*)-1-({2-[(*S*)-1-Benzyloxycarbonylamino-2-(*tert*-butyl-dimethyl-silanyloxy)-ethyl]-5-methyl-oxazole-4-carbonyl}-amino)-2-hydroxy-propyl]-oxazole-4-carboxylic acid methyl ester (21b). 4-Methylmorpholine (1.1 mL, 9.6 mmol) was added to a stirred suspension of the acid **16f** (1.1 g, 2.4 mmol) and 1-hydroxybenzotriazole (1.0 g, 7.2 mmol) in dry dichloromethane (25 mL) at 0 °C under a nitrogen atmosphere. 1-[3-(Dimethylamino)propyl]-3-ethylcarbodiimide hydrochloride (0.70 g, 3.6 mmol) was added and the mixture was then stirred at 0 °C for 10 min. The amine **17** (0.70 g, 2.9 mmol) was added in one portion, and the mixture was allowed to warm to room temperature overnight. The reaction was quenched with water (20 mL) and the layers were separated. The organic layer was washed with 10% aqueous citric acid (2 × 20 mL) and saturated sodium bicarbonate solution (20 mL), then dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified by chromatography on silica gel using diethyl ether as eluent to give the *amide* (0.72 g, 48%) as a colourless oil; $[\alpha]_D^{26}$ −51 (*c* = 1.0, $CHCl_3$); $\nu_{max}(CHCl_3)/cm^{-1}$ 3436, 3402, 1723, 1671 and 1634; δ_H(360 MHz, $CDCl_3$) 8.21 (1H, s, oxazole-H), 7.70 (1H, d, *J* 9.3 Hz, CON*H*), 7.42–7.29 (5H, m, 5 × aryl-H), 5.74 (1H, d, *J* 8.7 Hz, ZN*H*), 5.34 (1H, dd, *J* 9.3 and 2.5 Hz, CONHC*H*), 5.19 (1H, d, *J* 12.2 Hz, $CO_2CH_aH_bPh$), 5.14 (1H, d, *J* 12.2 Hz, $CO_2CH_aH_bPh$), 5.02–4.95 (1H, m, ZNHC*H*), 4.61 (1H, qd, *J* 6.4 and 2.5 Hz, CHC*H*(CH_3)OH), 4.04 (1H, dd, *J* 10.1 and 3.3 Hz, $CHCH_aH_bOTBS$), 3.97–3.89 (1H, m, $CHCH_aH_bOTBS$), 3.91 (3H, s, CO_2CH_3), 3.29 (1H,

br s, O*H*), 2.63 (3H, s, oxazole-CH_3), 1.30 (3H, d, *J* 6.4 Hz, CH(CH_3)OH), 0.81 (9H, s, SiC(CH_3)$_3$), 0.00 (3H, s, SiCH_3(CH$_3$)) and –0.04 (3H, s, SiCH$_3$(CH_3)) ppm; δ_C(90 MHz, $CDCl_3$) 163.6 (s), 162.0 (s), 161.2 (s), 159.4 (s), 155.7 (s), 154.1 (s), 144.3 (d), 136.0 (s), 133.1 (s), 128.5 (d), 128.4 (d), 128.2 (d), 67.5 (d), 67.2 (t), 64.1 (t), 52.2 (q), 51.3 (d), 51.2 (d), 25.5 (q), 19.0 (q), 18.0 (s), 11.6 (q), –5.6 (q) and –5.8 (q) ppm; *m/z* (ESI) Found: 617.2613, $C_{29}H_{41}N_4O_9Si$ [$(M+H)^+$] requires 617.2643.

2''-[(*S*)-1-Benzyloxycarbonylamino-2-(*tert*-butyl-dimethyl-silanyloxy)-ethyl]-5',5''-dimethyl-[2,4';2',4'']teroxazole-4-carboxylic acid methyl ester (22b). Bis(2-methoxyethyl)aminosulfur trifluoride (50% solution in tetrahydrofuran) (0.56 mL, 1.3 mmol) was added dropwise over 3 min to a stirred solution of the *bis*-oxazole **21a** (0.66 g, 1.1 mmol) in dry dichloromethane (15 mL) at –30 °C under a nitrogen atmosphere. The mixture was stirred at –20 °C for 1.5 h and then allowed to warm to room temperature. The mixture was quenched with saturated sodium bicarbonate solution (10 mL) and the separated organic layer was then dried ($MgSO_4$) and concentrated *in vacuo* to leave the crude oxazoline, which was used immediately without further purification.

Bromotrichloromethane (0.32 mL, 3.3 mmol) was added to a stirred solution of the crude oxazoline in dry dichloromethane (15 mL) at 0 °C under a nitrogen atmosphere and the mixture was stirred at 0 °C for 10 min. 1,8-Diazabicyclo[5.4.0]undec-7-ene (0.51 mL, 3.3 mmol) was added dropwise over 5 min and the mixture was allowed to warm to room temperature overnight. The reaction was quenched with 10% aqueous citric acid (20 mL) and the separated organic extract was then washed with saturated sodium bicarbonate

solution (20 mL), dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified by chromatography on silica gel using dichloromethane–diethyl ether (4:1) as eluent to give the *amide* (0.42 g, 64%) as a colourless solid; mp 75–77 °C (from dichloromethane / petrol); $[\alpha]_D^{22}$ –17 (*c* = 1.0, $CHCl_3$); $\nu_{max}(CHCl_3)/cm^{-1}$ 3436, 2954, 1723, 1659 and 1582; δ_H(360 MHz, $CDCl_3$) 8.32 (1H, s, oxazole-H), 7.42–7.25 (5H, m, 5 × aryl-H), 5.80 (1H, d, *J* 8.7 Hz, ZN*H*), 5.19 (1H, d, *J* 12.2 Hz, $CO_2CH_aH_bPh$), 5.15 (1H, d, *J* 12.2 Hz, $CO_2CH_aH_bPh$), 5.11–5.05 (1H, m, ZNHC*H*), 4.11 (1H, dd, *J* 10.3 and 3.6 Hz, CH_aH_bOTBS), 3.98 (1H, dd, *J* 10.3 and 4.3 Hz, CH_aH_bOTBS), 3.96 (3H, s, CO_2CH_3), 2.82 (3H, s, oxazole-CH_3), 2.72 (3H, s, oxazole-CH_3), 0.82 (9H, s, $SiC(CH_3)_3$), 0.00 (3H, s, $SiCH_3(CH_3)$) and –0.03 (3H, s, $SiCH_3(CH_3)$) ppm; δ_C(90 MHz, $CDCl_3$) 161.5 (s), 161.2 (s), 156.7 (s), 155.7 (s), 154.7 (s), 150.9 (s), 150.8 (s), 143.3 (d), 136.1 (s), 134.1 (s), 134.1 (s), 128.4 (d), 128.1 (d), 128.1 (d), 125.4 (s), 124.7 (s), 67.1 (t), 64.4 (t), 52.1 (q), 51.5 (d), 25.6 (q), 18.0 (s), 11.8 (q), 11.7 (q), –5.6 (q) and –5.7 (q) ppm; *m/z* (ESI) Found: 619.2144, $C_{29}H_{36}N_4O_8SiNa$ $[(M+Na)^+]$ requires 619.2200.

2''-[(*S*)-1-Benzyloxycarbonylamino-2-(*tert*-butyl-dimethyl-silanyloxy)-ethyl]-5',5''-dimethyl-[2,4';2',4'']teroxazole-4-carboxylic acid (23b). A solution of sodium hydroxide (30 mg, 0.76 mmol) in water (5 mL) was added in one portion to a stirred solution of the methyl ester **22b** (0.41 g, 0.69 mmol) in tetrahydrofuran (20 mL), and the mixture was stirred at room temperature overnight. The mixture was acidified to pH 2 with 10% aqueous citric acid and then extracted with dichloromethane (2 × 70 mL). The combined organic extracts were dried ($MgSO_4$) and evaporated *in vacuo* to leave a colourless solid. Purification by recrystallisation from dichloromethane–petrol gave the

acid (0.38 g, 93%) as a colourless solid; mp 130–133 °C (from dichloromethane / petrol); $[\alpha]_D^{24}$ –21 (*c* = 1.0, $CHCl_3$); $\nu_{max}(CHCl_3)/cm^{-1}$ 3437, 2929, 1716, 1661 and 1587; δ_H(360 MHz, $CDCl_3$) 8.37 (1H, s, oxazole-H), 8.02 (1H, br s, CO_2H), 7.40–7.23 (5H, m, 5 × aryl-H), 5.95 (1H, d, *J* 8.8 Hz, ZN*H*), 5.21–5.05 (3H, m, CO_2CH_2Ph, ZNHC*H*), 4.09 (1H, dd, *J* 10.2 and 3.5 Hz, CH_aH_bOTBS), 3.97 (1H, dd, *J* 10.2 and 4.5 Hz, CH_aH_bOTBS), 2.79 (3H, s, oxazole-CH_3), 2.70 (3H, s, oxazole-CH_3), 0.80 (9H, s, $SiC(CH_3)_3$), –0.02 (3H, s, $SiCH_3(CH_3)$) and –0.04 (3H, s, $SiCH_3(CH_3)$) ppm; δ_C(90 MHz, $CDCl_3$) 164.1 (s), 161.4 (s), 156.7 (s), 155.9 (s), 154.6 (s), 151.1 (s), 150.8 (s), 144.2 (d), 136.0 (s), 133.9 (s), 128.4 (d), 128.1 (d), 128.1 (d), 125.3 (s), 124.5 (s), 67.2 (t), 64.3 (t), 51.5 (d), 25.6 (q), 18.0 (s), 11.8 (q), 11.7 (q), –5.6 (q) and –5.7 (q) ppm; *m/z* (ESI) Found: 605.2022, $C_{28}H_{34}N_4O_8SiNa$ $[(M+Na)^+]$ requires 605.2044.

Sodium; 2''-[(*S*)-1-({2''-[(*S*)-1-amino-2-(*tert*-butyl-dimethyl-silanyloxy)-ethyl]-5',5''-dimethyl-[2,4';2',4'']teroxazole-4-carbonyl}-amino)-2-benzyloxy-ethyl]-[2,4';2',4'']teroxazole-4-carboxylate (36b). 10% Palladium on carbon (0.1 g) was added to a solution of the carbamate **36a** (0.52 g, 0.53 mmol) in methanol (5 mL) and tetrahydrofuran (20 mL). The mixture was stirred at room temperature under 1 atmosphere pressure of hydrogen for 18 h and the mixture was then filtered through a pad of celite and eluted with methanol–ethyl actetate (1:1) (150 mL). The filtrate was concentrated *in vacuo* to leave the *amine* (0.42 g, 94%) as a colourless solid, which was used directly in the next reaction without further purification.

A solution of sodium hydroxide (22 mg, 0.55 mmol) in water (5 mL) was added in one portion to a stirred solution of the amine (0.42 g, 0.50 mmol) in tetrahydrofuran (10 mL)

and the mixture was stirred at room temperature for 8 h. Water (20 mL) was added and the mixture concentrated slowly *in vacuo* to a volume of approx. 20 mL. The aqueous suspension was extracted with dichloromethane–methanol (4:1) (5 × 20 mL) and dichloromethane (3 × 20 mL) and the combined organic extracts were then evaporated *in vacuo* to leave the *acid* (0.33 g, 76%) as a colourless solid, which was used directly in the next reaction without further purification.

Oxazoline macrocycle (34b). 20% $Pd(OH)_2$ on carbon (30 mg) was added to a solution of the benzyl ether **37** (97 mg, 0.12 mmol) in methanol (1 mL) and tetrahydrofuran (4 mL). The mixture was stirred at room temperature under 1 atmosphere pressure of hydrogen for 18 h and the mixture was then filtered through a pad of celite and eluted with 2:1 ethyl acetate–methanol (100 mL). The filtrate was concentrated *in vacuo* and the residue was then partially purified by trituration with ether to give the corresponding alcohol (80 mg, 92%) as a colourless solid, which was used directly in the next reaction without further purification.

(Diethylamino)sulfur trifluoride (73 μL, 0.55 mmol) was added to a stirred solution of the above alcohol (80 mg, 0.11 mmol) in dry dichloromethane (6 mL) at −78 °C under a nitrogen atmosphere. The mixture was stirred at −78 °C for 4 h and then allowed to warm to room temperature. The mixture was quenched with saturated sodium bicarbonate solution (5 mL) and the separated aqueous layer was extracted with dichloromethane (2 × 5 mL). The combined organic extracts were dried ($MgSO_4$) and then concentrated *in vacuo*. The residue was partially purified by trituration with ether to give the impure *oxazoline* (70 mg, 91%) as a colourless solid.

2-[(*S*)-1-{[2-((*S*)-1-Benzyloxycarbonylamino-2-hydroxy-ethyl)-oxazole-4-carbonyl]-amino}-2-(*tert*-butyl-dimethyl-silanyloxy)-ethyl]-oxazole-4-carboxylic acid methyl ester (45a). 4-Methylmorpholine (0.18 mL, 1.6 mmol) was added to a stirred suspension of the acid **16d** (0.22 g, 0.72 mmol) and 1-hydroxybenzotriazole (0.22 g, 1.6 mmol) in dry dichloromethane (5 mL) at 0 °C under a nitrogen atmosphere. 1-[3-(Dimethylamino)propyl]-3-ethylcarbodiimide hydrochloride (0.21 g, 1.1 mmol) was added and the mixture was then stirred at 0 °C for 2 min. A solution of the amine **16e** (0.23 g, 0.78 mmol) in dry dichloromethane (5 mL) was added dropwise over 1 min at 0 °C, and the mixture was allowed to warm to room temperature overnight. The reaction was quenched with water (10 mL) and the separated organic layer was then washed with 10% aqueous citric acid (3 × 10 mL). The combined aqueous extracts were extracted with dichloromethane (2 × 10 mL) and the combined organic extracts were then washed with saturated sodium bicarbonate solution (10 mL), dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified by chromatography on silica gel using diethyl ether as eluent to give the *amide* (0.15 g, 34%) as a colourless oil; $[\alpha]_D^{19}$ –27 (*c* = 1.0, $CHCl_3$); $\nu_{max}(CHCl_3)/cm^{-1}$ 3421, 2930, 1724, 1678 and 1598; δ_H(360 MHz, $CDCl_3$) 8.19 (1H, s, oxazole-H), 8.09 (1H, s, oxazole-H), 7.96 (1H, d, *J* 8.5 Hz, CON*H*), 7.37–7.28 (5H, m, 5 × aryl-H), 6.05 (1H, d, *J* 8.5 Hz, ZN*H*), 5.46–5.39 (1H, m, CONHC*H*), 5.16 (1H, d, *J* 12.2 Hz, OCH_aH$_b$Ph), 5.11 (1H, d, *J* 12.2 Hz, OCH$_a$$H_b$Ph), 5.08–4.99 (1H, m, ZNHC*H*), 4.17 (1H, dd, *J* 10.1 and 4.3 Hz, CH_aH$_b$OTBS), 4.09–3.89 (3H, m, CH$_a$$H_b$OTBS, C$H_2$OH), 3.88 (3H, s, CO_2CH_3), 3.12 (1H, br s, O*H*), 0.81 (9H, s, SiC(CH_3)$_3$), –0.01 (3H, s, SiCH_3(CH$_3$)) and –0.03 (3H, s, SiCH$_3$(CH_3)) ppm; δ_C(90 MHz, $CDCl_3$) 163.5 (s), 162.1

(s), 161.4 (s), 160.0 (s), 156.0 (s), 144.0 (d), 142.0 (d), 135.9 (s), 135.5 (s), 133.3 (s), 128.5 (d), 128.2 (d), 128.1 (d), 67.3 (t), 64.0 (t), 63.1 (t), 52.2 (q), 51.0 (d), 49.2 (d), 25.5 (q), 18.0 (s), −5.6 (q) and −5.7 (q) ppm; *m/z* (FAB) Found: 589.2363, $C_{27}H_{37}N_4O_9Si$ $[(M+H)^+]$ requires 589.2330.

2-[(*S*)-1-{[2-((*S*)-1-Amino-2-hydroxy-ethyl)-oxazole-4-carbonyl]-amino}-2-(*tert*-butyl-dimethyl-silanyloxy)-ethyl]-oxazole-4-carboxylic acid methyl ester (45b). 10% Palladium on carbon (50 mg) was added to a solution of the carbamate **45a** (0.15 g, 0.25 mmol) in ethyl acetate (8 mL) and methanol (2 mL). The mixture was stirred at room temperature under 1 atmosphere pressure of hydrogen for 24 h and the mixture was then filtered through a pad of celite and eluted with 1:1 methanol–ethyl acetate (100 mL). The filtrate was concentrated *in vacuo* and the residue was then purified by chromatography on silica gel using dichloromethane–methanol (9:1) as eluent to give the *amine* (62 mg, 55%) as a colourless oil; $[\alpha]_D^{18}$ +0.1 (*c* = 1.0, $CHCl_3$); $\nu_{max}(CHCl_3)/cm^{-1}$ 3406, 2954, 1738, 1677 and 1599; δ_H(360 MHz, $CDCl_3$) 8.20 (1H, s, oxazole-H), 8.18 (1H, s, oxazole-H), 7.77 (1H, d, *J* 8.7 Hz, CON*H*), 5.48–5.41 (1H, m, CONHC*H*), 4.18 (1H, dd, *J* 10.1 and 4.1 Hz, CH_aH$_b$OTBS), 4.18–4.10 (1H, m, NH_2C*H*), 4.01 (1H, dd, *J* 10.1 and 4.9 Hz, CH$_a$$H_b$OTBS), 3.94 (1H, dd, *J* 11.0 and 4.4 Hz, CH_aH$_b$OH), 3.90 (3H, s, CO_2CH_3), 3.85 (1H, dd, *J* 11.0 and 6.2 Hz, CH$_a$$H_b$OH), 2.31 (3H, br s, N$H_2$, O*H*), 0.83 (9H, s, SiC(CH_3)$_3$), 0.02 (3H, s, SiCH_3(CH$_3$)) and −0.02 (3H, s, SiCH$_3$(CH_3)) ppm; δ_C(90 MHz, $CDCl_3$) 163.1 (s), 161.4 (s), 160.0 (s), 144.1 (d), 141.7 (d), 135.4 (s), 133.4 (s), 64.5 (t), 64.1 (t), 52.2 (q), 51.3 (d), 49.1 (d), 25.6 (q), 18.0 (s), –5.6 (q) and –5.6 (q) ppm; *m/z* (ESI) Found: 477.1781, $C_{19}H_{30}N_4O_7SiNa$ $[(M+Na)^+]$ requires 477.1781.

2-((*S*)-1-{[2-((*S*)-1-{[2''-((*S*)-2-Benzyloxy-1-benzyloxycarbonylamino-ethyl)-5',5''-dimethyl-[2,4';2',4'']teroxazole-4-carbonyl]-amino}-2-hydroxy-ethyl)-oxazole-4-carbonyl]-amino}-2-(*tert*-butyl-dimethyl-silanyloxy)-ethyl)-oxazole-4-carboxylic acid methyl ester (46). 4-Methylmorpholine (30 μL, 0.28 mmol) was added to a stirred suspension of the acid **23** (76 mg, 0.14 mmol) and 1-hydroxybenzotriazole (38 mg, 0.28 mmol) in dry dichloromethane (2 mL) at 0 °C under a nitrogen atmosphere. 1-[3-(Dimethylamino)propyl]-3-ethylcarbodiimide hydrochloride (40 mg, 0.21 mmol) was added and the mixture was then stirred at 0 °C for 2 min. A solution of the amine **45b** (62 mg, 0.14 mmol) in dry dichloromethane (2 mL) was added dropwise over 3 min at 0 °C, and the mixture was allowed to warm to room temperature overnight. The reaction was quenched with water (4 mL) and the separated organic layer was then washed with 10% aqueous citric acid (2 × 5 mL). The combined aqueous extracts were extracted with dichloromethane (2 × 5 mL) and the combined organic extracts were then washed with saturated sodium bicarbonate solution (10 mL), dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified by chromatography on silica gel using ethyl acetate as eluent to give the *amide* (69 mg, 50%) as a colourless solid; mp 85–87 °C (from ethyl acetate / petrol); $[\alpha]_D^{19}$ –5 (*c* = 1.0, $CHCl_3$); $\nu_{max}(CHCl_3)/cm^{-1}$ 3406, 2929, 1724, 1677 and 1596; δ_H(360 MHz, $CDCl_3$) 8.30 (1H, s, oxazole-H), 8.20 (1H, s, oxazole-H), 8.16 (1H, s, oxazole-H), 7.95–7.89 (2H, m, 2 × CON*H*), 7.40–7.17 (10H, m, 10 × aryl-H), 5.87 (1H, d, *J* 8.4 Hz, ZN*H*), 5.53–5.41 (2H, m, 2 × CONHC*H*), 5.20–5.07 (3H, m, CO_2CH_2Ph, ZNHC*H*), 4.54 (1H, d, *J* 12.2 Hz, $CH_2OCH_aH_b$Ph), 4.48 (1H, d, *J* 12.2 Hz, $CH_2OCH_aH_b$Ph), 4.26–3.80 (6H, m, CH_2OTBS, CH_2OBn, CH_2OH), 3.88 (3H, s,

CO_2CH_3), 3.33 (1H, br s, O*H*), 2.74 (3H, s, oxazole-CH_3), 2.68 (3H, s, oxazole-CH_3), 0.80 (9H, s, SiC(CH_3)$_3$), –0.01 (3H, s, SiCH_3(CH$_3$)) and –0.03 (3H, s, SiCH$_3$(CH_3)) ppm; δ_C(90 MHz, $CDCl_3$) 163.3 (s), 161.7 (s), 161.4 (s), 160.9 (s), 160.4 (s), 160.0 (s), 156.0 (s), 155.8 (s), 154.9 (s), 151.0 (s), 150.7 (s), 144.1 (d), 142.1 (d), 141.2 (d), 137.3 (s), 136.3 (s), 136.1 (s), 135.6 (s), 133.3 (s), 128.5 (d), 128.4 (d), 128.4 (d), 128.1 (d), 128.0 (d), 127.8 (d), 127.6 (d), 125.4 (s), 124.7 (s), 73.2 (t), 70.1 (t), 67.1 (t), 64.0 (t), 62.8 (t), 52.1 (q), 49.7 (d), 49.2 (d), 48.6 (d), 25.5 (q), 18.0 (s), 11.8 (q), 11.8 (q), –5.6 (q) and –5.7 (q) ppm; *m/z* (ESI) Found: 1017.3503, $C_{48}H_{54}N_8O_{14}SiNa$ $[(M+Na)^+]$ requires 1017.3426.

2-[(*S*)-1-{[2''''-((*S*)-2-Benzyloxy-1-benzyloxycarbonylamino-ethyl)-5''',5''''-dimethyl-[2,4';2',4'';2'',4''';2''',4'''']quinqueoxazole-4-carbonyl]-amino}-2-(*tert*-butyl-dimethyl-silanyloxy)-ethyl]-oxazole-4-carboxylic acid methyl ester (47a). (Diethylamino)sulfur trifluoride (13 μL, 0.08 mmol) was added dropwise over 1 min to a stirred solution of the amide **46** (69 mg, 0.07 mmol) in dry dichloromethane (2 mL) at −78 °C under a nitrogen atmosphere. The mixture was stirred at −78 °C for 3 h and then allowed to warm to room temperature. The mixture was quenched with saturated sodium bicarbonate solution (2 mL) and the separated organic layer was then dried ($MgSO_4$) and concentrated *in vacuo* to leave the crude oxazoline, which was used immediately without further purification.

Bromotrichloromethane (20 μL, 0.21 mmol) was added to a stirred solution of the crude oxazoline in dry dichloromethane (2 mL) at 0 °C under a nitrogen atmosphere and the

mixture was stirred at 0 °C for 5 min. 1,8-Diazabicyclo[5.4.0]undec-7-ene (30 μL, 0.21 mmol) was added dropwise over 1 min and the mixture was allowed to warm to room temperature overnight. The reaction was quenched with 10% aqueous citric acid (2 mL) and the separated organic extract was then washed with 10% aqueous citric acid (2 mL). The combined aqueous extracts were extracted with dichloromethane (2 × 3 mL) and the combined organic extracts were then washed with saturated sodium bicarbonate solution (10 mL), dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified by chromatography on silica gel using dichloromethane–ethyl acetate (1:1) as eluent to give the oxazole amide (29 mg, 43%) as a colourless solid; mp 172–175 °C (from dichloromethane / petrol); $[\alpha]_D^{18}$ +28 (*c* = 1.0, $CHCl_3$); $\nu_{max}(CHCl_3)/cm^{-1}$ 3410, 2957, 1723, 1677 and 1596; δ_H(360 MHz, $CDCl_3$) 8.47 (1H, s, oxazole-H), 8.36 (1H, s, oxazole-H), 8.31 (1H, s, oxazole-H), 8.21 (1H, s, oxazole-H), 7.83 (1H, d, *J* 8.8 Hz, CON*H*), 7.41–7.19 (10H, m, 10 × aryl-H), 5.81 (1H, d, *J* 8.5 Hz, ZN*H*), 5.56–5.49 (1H, m, CONHC*H*), 5.21–5.09 (3H, m, CO_2CH_2Ph, ZNHC*H*), 4.55 (1H, d, *J* 12.2 Hz, $CH_2OCH_aH_b$Ph), 4.50 (1H, d, *J* 12.2 Hz, $CH_2OCH_aH_b$Ph), 4.20 (1H, dd, *J* 10.1 and 4.4 Hz, CH_aH_bOTBS), 4.06 (1H, dd, *J* 10.1 and 5.0 Hz, CH_aH_bOTBS), 3.98–3.91 (1H, m, CH_aH_bOBn), 3.93 (3H, s, CO_2CH_3), 3.84 (1H, dd, *J* 9.4 and 4.3 Hz, CH_aH_bOBn), 2.85 (3H, s, oxazole-CH_3), 2.72 (3H, s, oxazole-CH_3), 0.85 (9H, s, $SiC(CH_3)_3$), 0.04 (3H, s, $SiCH_3(CH_3)$) and 0.01 (3H, s, $SiCH_3(CH_3)$) ppm; δ_C(90 MHz, $CDCl_3$) 162.9 (s), 161.5 (s), 160.8 (s), 159.9 (s), 157.2 (s), 156.3 (s), 155.8 (s), 154.8 (s), 154.5 (s), 151.0 (s), 144.1 (d), 141.6 (d), 139.1 (d), 139.1 (d), 137.3 (s), 136.7 (s), 136.1 (s), 133.5 (s), 130.9 (s), 130.6 (s), 128.5 (d), 128.4 (d), 128.2 (d), 128.1 (d), 127.8 (d), 127.6 (d), 125.4 (s), 124.7 (s), 73.2 (t), 70.1 (t), 67.2 (t), 64.1 (t), 52.2 (q), 49.7 (d), 49.2 (d), 25.6 (q), 18.1 (s),

11.9 (q), 11.8 (q), –5.6 (q) and –5.6 (q) ppm; *m/z* (ESI) Found: 992.3669, $C_{48}H_{54}N_9O_{13}Si$ $[(M+NH_4)^+]$ requires 992.3610.

Sodium; 2-[(*S*)-1-{[2''''-((*S*)-1-amino-2-benzyloxy-ethyl)-5''',5''''-dimethyl-[2,4';2',4'';2'',4''';2''',4'''']quinqueoxazole-4-carbonyl]-amino}-2-(*tert*-butyl-dimethyl-silanyloxy)-ethyl]-oxazole-4-carboxylate (47b). 10% Palladium on carbon (20 mg) was added to a solution of the carbamate **47a** (29 mg, 0.03 mmol) in methanol (1 mL) and tetrahydrofuran (3 mL). The mixture was stirred at room temperature under 1 atmosphere pressure of hydrogen for 18 h and the mixture was then filtered through a pad of celite and eluted with methanol–tetrahydrofuran (1:1) (50 mL). The filtrate was concentrated *in vacuo* to leave the *amine* (25 mg, 99%) as a colourless solid, which was used directly in the next reaction without further purification.

A solution of sodium hydroxide (1.3 mg, 0.032 mmol) in water (1 mL) was added in one portion to a stirred solution of the amine (25 mg, 0.03 mmol) in tetrahydrofuran (2 mL) and the mixture was stirred at room temperature overnight. Water (10 mL) was added and the mixture was concentrated slowly *in vacuo* to a volume of approx. 10 mL. The aqueous suspension was extracted with dichloromethane–methanol (4:1) (5 × 10 mL) and dichloromethane (3 × 10 mL) and the combined organic extracts were then evaporated *in vacuo* to leave the *acid* (18 mg, 73%) as a colourless solid, which was used directly in the next reaction without further purification.

2-(*tert*-Butoxycarbonylamino-methyl)-oxazole-4-carboxylic acid methyl ester (59a). 4-Methylmorpholine (6.0 mL, 53 mmol) was added to a stirred suspension of Boc-

glycine (3.1 g, 18 mmol) and 1-hydroxybenzotriazole (3.6 g, 27 mmol) in dry dichloromethane (170 mL) at 0 °C under a nitrogen atmosphere. 1-[3-(Dimethylamino)propyl]-3-ethylcarbodiimide hydrochloride (3.7 g, 20 mmol) was added and the mixture was then stirred at 0 °C for 15 min. DL-Serine methylester hydrochloride (3.0 g, 20 mmol) was added in one portion, and the mixture was allowed to warm to room temperature overnight. The reaction was quenched with water (50 mL) and the layers were then separated. The organic layer was washed with 10% aqueous citric acid (3 × 50 mL) and the combined aqueous extracts were then filtered and concentrated *in vacuo* (to approx. 15 mL). The residue was re-extracted with ethyl acetate (4 × 100 mL) and the dichloromethane extract was concentrated *in vacuo* and then combined with the ethyl acetate extracts. The combined organic extracts were washed with saturated sodium bicarbonate solution (15 mL) and the separated basic aqueous extract was then extracted with ethyl acetate (4 × 50 mL). The combined organic extracts were dried ($MgSO_4$) and then concentrated *in vacuo*. The residue was purified by chromatography on silica gel using ethyl acetate as eluent to give 2-(2-*tert*-butoxycarbonylamino-acetylamino)-3-hydroxy-propionic acid methyl ester (4.1 g, 84%) as a colourless oil; $\nu_{max}(CHCl_3)/cm^{-1}$ 3426, 2956, 1743 and 1682; δ_H(360 MHz, $CDCl_3$) 7.14 (1H, d, *J* 7.4 Hz, CON*H*), 5.40 (1H, s, BocN*H*), 4.71–4.62 (1H, m, BocNHC*H*), 4.00–3.91 (2H, m, CH_2OH) 3.85 (2H, d, *J* 5.8 Hz, BocNHCH_2), 3.79 (3H, s, CO_2CH_3) and 1.46 (9H, s, OC(CH_3)$_3$) ppm; δ_C(90 MHz, $CDCl_3$) 170.9 (s), 170.0 (s), 156.4 (s), 80.4 (s), 62.5 (t), 54.7 (d), 52.7 (q), 44.0 (t) and 28.2 (q) ppm; *m/z* (ESI) Found: 299.1208, $C_{11}H_{20}N_2O_6Na$ [$(M+Na)^+$] requires 299.1219.

(Diethylamino)sulfur trifluoride (2.4 mL, 18 mmol) was added dropwise over 5 min to a stirred solution of the above 2-hydroxymethyl-substituted amino ester (4.1 g, 15 mmol) in dry dichloromethane (150 mL) at −78 °C under a nitrogen atmosphere. The mixture was stirred at −78 °C for 1.5 h and then allowed to warm to room temperature and stirred for a further 15 min. The mixture was quenched with saturated sodium bicarbonate solution (50 mL) and the separated organic layer was then dried ($MgSO_4$) and concentrated *in vacuo* to leave the corresponding oxazoline, which was used immediately without further purification.

Bromotrichloromethane (4.3 mL, 44 mmol) was added to a stirred solution of the crude oxazoline in dry dichloromethane (150 mL) at 0°C under a nitrogen atmosphere and the mixture was stirred at 0°C for 10 min. 1,8-Diazabicyclo[5.4.0]undec-7-ene (6.7 mL, 44 mmol) was added dropwise over 5 min and the mixture was allowed to warm to room temperature overnight. The volatile components were removed *in vacuo* and the residue was partitioned between ethyl acetate (200 mL) and 10% aqueous citric acid (100 mL). The separated organic extract was washed with 10% aqueous citric acid (70 mL) and the combined aqueous extracts were then re-extracted with ethyl acetate (2 × 70 mL). The combined organic extracts were washed with saturated sodium bicarbonate solution (100 mL) and the basic aqueous extract was extracted with ethyl acetate (100 mL). The combined organic extracts were dried ($MgSO_4$) and then concentrated *in vacuo*. The residue was purified by chromatography on silica gel using 2:1 petrol–ethyl acetate as eluent to give the *oxazole* (2.4 g, 63%) as a colourless solid; mp 76–77 °C (from ethyl acetate / petrol); Found: C, 51.6; H, 6.3; N, 10.9%. $C_{11}H_{16}N_2O_5$ requires C, 51.6; H, 6.3; N, 10.9%; $\nu_{max}(CHCl_3)/cm^{-1}$ 3452, 2978, 1716 and 1589; δ_H(360 MHz, $CDCl_3$) 8.19 (1H,

s, oxazole-H), 5.35–5.25 (1H, m, BocN*H*), 4.48 (2H, d, *J* 5.9 Hz, BocNHCH_2), 3.90 (3H, s, CO_2CH_3) and 1.43 (9H, s, OC(CH_3)$_3$) ppm; δ_C(90 MHz, $CDCl_3$) 162.3 (s), 161.3 (s), 155.4 (s), 144.1 (d), 133.1 (s), 80.1 (s), 52.0 (q), 37.7 (t) and 28.1 (q) ppm; *m/z* (ESI) Found: 279.0951, $C_{11}H_{16}N_2O_5Na$ [$(M+Na)^+$] requires 279.0957.

2-(*tert*-Butoxycarbonylamino-methyl)-oxazole-4-carboxylic acid (59b). A solution of sodium hydroxide (0.7 g, 16 mmol) in water (30 mL) was added in one portion to a stirred solution of the methyl ester **59a** (2.1 g, 8.2 mmol) in tetrahydrofuran (50 mL), and the mixture was stirred at room temperature for 5 h. The mixture was concentrated *in vacuo* to approx. 20 mL and then acidified to pH 2 by careful addition of citric acid (solid). The aqueous suspension was extracted with dichloromethane (10 × 100 mL) and the combined organic extracts were then dried ($MgSO_4$) and evaporated *in vacuo* to leave a colourless solid. Purification by recrystallisation from ethyl acetate / dichloromethane / petrol gave the carboxylic acid (1.9 g, 96%) as a colourless solid; mp 168–170 °C; Found: C, 49.5; H, 5.8; N, 11.4%. $C_{10}H_{14}N_2O_5$ requires C, 49.6; H, 5.8; N, 11.6%; ν_{max}($CHCl_3$)/cm^{-1} 3452, 3169, 2933, 1714 and 1592; δ_H(500 MHz, DMSO-d_6) 8.69 (1H, s, oxazole-H), 7.52 (1H, t, *J* 6.0 Hz, BocN*H*), 4.28 (2H, d, *J* 6.0 Hz, BocNHCH_2) and 1.40 (9H, s, OC(CH_3)$_3$) ppm; δ_C(125 MHz, DMSO-d_6) 162.6 (s), 162.3 (s), 155.8 (s), 145.5 (d), 133.4 (s), 78.7 (s), 37.5 (t) and 28.4 (q) ppm; *m/z* (ESI) Found: 265.0813, $C_{10}H_{14}N_2O_5Na$ [$(M+Na)^+$] requires 265.0800.

(*S*)-2-Benzyloxy-1-(4-methoxycarbonyl-oxazol-2-yl)-ethyl-ammonium; chloride (60). Hydrogen chloride (4.0 M solution in dioxane) (10 mL) was added to the carbamate **15a**

(2.4 g, 7.7 mmol) and the mixture was stirred at room temperature overnight under a nitrogen atmosphere. The mixture was evaporated to leave the *amine hydrochloride salt* (2.1 g, 100%) as a colourless foaming solid; $[\alpha]_D^{23}$ +1.2 (*c* = 1.0, EtOH); $\nu_{max}(CHCl_3)/cm^{-1}$ 3172, 2872, 1732 and 1588; δ_H(360 MHz, CD_3OD) 8.69 (1H, s, oxazole-H), 7.40–7.28 (5H, m, 5 × aryl-H), 4.69 (1H, d, *J* 12.0 Hz, OCH_aH_bPh), 4.62 (1H, d, *J* 12.0 Hz, OCH_aH_bPh), 4.11–4.04 (2H, m, CH_2OBn) and 3.93 (3H, s, CO_2CH_3) ppm; δ_C(90 MHz, $CDCl_3$) 162.6 (s), 160.1 (s), 147.4 (d), 138.3 (s), 134.5 (s), 129.5 (d), 129.3 (d), 129.1 (d), 74.5 (t), 68.3 (t), 52.8 (q) and 50.1 (d) ppm; *m/z* (ESI) Found: 299.1031, $C_{14}H_{16}N_2O_4Na$ $[(M+Na)^+]$ requires 299.1008.

2-[(*S*)-1-Benzyloxycarbonylamino-2-(*tert*-butyl-dimethyl-silanyloxy)-ethyl]-5-phenyl-oxazole-4-carboxylic acid methyl ester (61a). Bis(2-methoxyethyl)aminosulfur trifluoride (50% solution in tetrahydrofuran) (2.1 mL, 5.0 mmol) was added dropwise over 2 min to a stirred solution of the dipeptide **13e** (2.2 g, 4.1 mmol) in dry dichloromethane (40 mL) at −78 °C under a nitrogen atmosphere. The mixture was stirred at −78 °C for 30 min, at −40 °C for 30 min, and then at −20 °C for a further 30 min before being allowed to warm to room temperature and quenched with saturated sodium bicarbonate solution (20 mL). The separated organic layer was dried ($MgSO_4$) and then concentrated *in vacuo* to leave the crude oxazoline, which was used immediately without further purification.

Bromotrichloromethane (1.2 mL, 12 mmol) was added to a stirred solution of the crude oxazoline in dry dichloromethane (40 mL) at 0 °C under a nitrogen atmosphere and the mixture was stirred at 0 °C for 10 min. 1,8-Diazabicyclo[5.4.0]undec-7-ene (1.9 mL, 12

mmol) was added dropwise over 5 min and the mixture was allowed to warm to room temperature overnight. The reaction was quenched with 10% aqueous citric acid (30 mL) and the layers were separated. The organic layer was washed with saturated sodium bicarbonate solution (30 mL), dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified by chromatography on silica gel using 3:1 petrol–ethyl acetate as eluent to give the *oxazole* (1.0 g, 48%) as a colourless oil; $[\alpha]_D^{24}$ –24 (c = 1.0, $CHCl_3$); $\nu_{max}(CHCl_3)/cm^{-1}$ 3697, 3605, 3437, 2954 and 1723; δ_H(360 MHz, $CDCl_3$) 8.02–7.96 (2H, m, 2 × phenyloxazole-H), 7.50–7.28 (8H, m, 3 × phenyloxazole-H, 5 × aryl-H), 5.81 (1H, d, *J* 8.6 Hz, ZN*H*), 5.02–5.01 (3H, m, CO_2CH_2Ph, ZNHC*H*), 4.14 (1H, dd, *J* 10.2 and 3.4 Hz, CH_aH_bOTBS), 4.00 (1H, dd, *J* 10.2 and 4.3 Hz, CH_aH_bOTBS) 3.94 (3H, s, CO_2CH_3), 0.80 (9H, s, $SiC(CH_3)_3$), –0.01 (3H, s, $SiCH_3(CH_3)$) and –0.04 (3H, s, $SiCH_3(CH_3)$) ppm; δ_C(90 MHz, $CDCl_3$) 162.4 (s), 160.7 (s), 155.8 (s), 136.1 (s), 130.3 (d), 128.5–128.1 (Ar d), 126.7 (s), 126.6 (s), 67.2 (t), 64.5 (t), 52.3 (q), 51.6 (d), 25.6 (q), 18.1 (s), –5.6 (q) and –5.7 (q) ppm; *m/z* (ESI) Found: 511.2224, $C_{27}H_{34}N_2O_6SiNa$ $[(M+Na)^+]$ requires 511.2264.

2-[(*S*)-1-Amino-2-(*tert*-butyl-dimethyl-silanyloxy)-ethyl]-5-phenyl-oxazole-4-carboxylic acid methyl ester (61b). 10% Palladium on carbon (50 mg) was added to a solution of the carbamate **61a** (1.0 g, 2.0 mmol) in methanol (5 mL) and tetrahydrofuran (15 mL). The mixture was stirred at room temperature under 1 atmosphere pressure of hydrogen for 48 h and then the mixture was filtered through a pad of celite and eluted with 1:1 methanol–ethyl acetate (100 mL). The filtrate was concentrated *in vacuo* and the residue was then purified by chromatography on silica gel using ether as eluent to give

the *amine* (0.72 g, 98%) as a colourless oil; $[\alpha]_D^{21}$ –30 (*c* = 1.0, $CHCl_3$); $\nu_{max}(CHCl_3)/cm^{-1}$ 3698, 3388, 2954, 1723 and 1591; δ_H(360 MHz, $CDCl_3$) 8.05–8.00 (2H, m, 2 × phenyloxazole-H), 7.49–7.42 (3H, m, 3 × phenyloxazole-H), 4.22 (1H, t, *J* 5.2 Hz, NH_2CH), 3.98 (2H, d, *J* 5.2 Hz, CH_2OTBS), 3.93 (3H, s, CO_2CH_3), 1.94 (2H, s, NH_2), 0.83 (9H, s, $SiC(CH_3)_3$), 0.02 (3H, s, $SiCH_3(CH_3)$) and 0.00 (3H, s, $SiCH_3(CH_3)$) ppm; δ_C(90 MHz, $CDCl_3$) 163.8 (s), 162.5 (s), 155.6 (s), 130.3 (d), 128.3 (d), 128.3 (d), 126.8 (s), 126.5 (s), 66.1 (t), 52.3 (q), 52.1 (d), 25.7 (q), 18.1 (s), −5.5 (q) and −5.6 (q) ppm; *m/z* (ESI) Found: 399.1715, $C_{19}H_{28}N_2O_4SiNa$ $[(M+Na)^+]$ requires 399.1716.

2-((*S*)-2-Benzyloxy-1-{[2-(*tert*-butoxycarbonylamino-methyl)-oxazole-4-carbonyl]-amino}-ethyl)-oxazole-4-carboxylic acid methyl ester (62a). 4-Methylmorpholine (0.75 mL, 6.8 mmol) was added to a stirred suspension of the acid **59b** (0.41 g, 1.7 mmol) and 1-hydroxybenzotriazole (0.46 g, 3.4 mmol) in dry dichloromethane (25 mL) at 0 °C under a nitrogen atmosphere. 1-[3-(Dimethylamino)propyl]-3-ethylcarbodiimide hydrochloride (0.42 g, 2.2 mmol) was added and the mixture was then stirred at 0 °C for 10 min. The amine **60** (0.53 g, 1.7 mmol) was added in one portion, and the mixture was allowed to warm to room temperature overnight and then quenched with water (20 mL). The separated organic layer was washed with 10% aqueous citric acid (2 × 15 mL) and saturated sodium bicarbonate solution (15 mL), then dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified by chromatography on silica gel using ether as eluent to give the *bis*-oxazole *amide* (0.50 g, 59%) as a colourless solid; mp 43–48 °C (from ether / petrol); $[\alpha]_D^{20}$ +1.4 (*c* = 1.0, $CHCl_3$); $\nu_{max}(CHCl_3)/cm^{-1}$ 3455, 3405, 2980, 1716, 1680 and 1599; δ_H(360 MHz, $CDCl_3$) 8.19 (1H, s, oxazole-H), 8.16 (1H, s, oxazole-H), 7.36 (1H,

d, *J* 8.8 Hz, CON*H*), 7.33–7.23 (5H, m, 5 × aryl-H), 5.62–5.57 (1H, m, CONHC*H*), 5.20 (1H, br s, BocN*H*), 4.58 (1H, d, *J* 12.2 Hz, OC*H*$_a$H$_b$Ph), 4.53 (1H, d, *J* 12.2 Hz, OCH$_a$*H*$_b$Ph), 4.47 (2H, d, *J* 5.6 Hz, BocNHC*H*$_2$) 4.03 (1H, dd, *J* 9.7 and 4.6 Hz, C*H*$_a$H$_b$OBn), 3.92 (3H, s, CO$_2$C*H*$_3$), 3.89 (1H, dd, *J* 9.7 and 4.7 Hz, CH$_a$*H*$_b$OBn) and 1.47 (9H, s, OC(C*H*$_3$)$_3$) ppm; δ_C(90 MHz, $CDCl_3$) 162.5 (s), 161.3 (s), 161.3 (s), 160.1 (s), 155.5 (s), 144.2 (d), 141.8 (d), 137.1 (s), 135.3 (s), 133.3 (s), 128.3 (d), 127.8 (d), 127.6 (d), 80.2 (s), 73.1 (t), 69.7 (t), 52.1 (q), 47.2 (d), 37.7 (t) and 28.2 (q) ppm; *m/z* (ESI) Found: 523.1848, $C_{24}H_{28}N_4O_8Na$ [$(M+Na)^+$] requires 523.1805.

2-((*S*)-1-{[2-(*tert*-Butoxycarbonylamino-methyl)-oxazole-4-carbonyl]-amino}-2-hydroxy-ethyl)-oxazole-4-carboxylic acid methyl ester (62b). 20% $Pd(OH)_2$ on carbon (0.7 g) was added to a solution of the benzyl ether **62a** (2.3 g, 4.6 mmol) in ethanol (50 mL) and ethyl acetate (50 mL). The mixture was stirred at room temperature under 1 atmosphere pressure of hydrogen for 18 h. The mixture was filtered through a pad of celite and eluted with 1:1 methanol–ethyl acetate (200 mL). The filtrate was concentrated *in vacuo* and the residue was then purified by chromatography on silica gel using ethyl acetate as eluent to give the alcohol (1.53 g, 81%) as a colourless solid; mp 73–76 °C (from ethyl acetate / petrol); $[\alpha]_D^{21}$ –25 (*c* = 1.0, $CHCl_3$); $\nu_{max}(CHCl_3)/cm^{-1}$ 3455, 3401, 2954, 1717, 1679 and 1599; δ_H(360 MHz, $CDCl_3$) 8.24 (1H, s, oxazole-H), 8.13 (1H, s, oxazole-H), 8.11 (1H, obs d, *J* 8.5 Hz, CON*H*), 5.58–5.49 (2H, m, BocN*H*, CONHC*H*), 4.50–4.33 (2H, m, BocNHC*H*$_2$), 4.34 (1H, dd, *J* 11.7 and 4.4 Hz, C*H*$_a$H$_b$OH), 4.10 (1H, dd, *J* 11.7 and 4.0 Hz, CH$_a$*H*$_b$OH), 3.93 (3H, s, CO$_2$C*H*$_3$), 2.59 (1H, br s, O*H*) and 1.49 (9H, s, OC(C*H*$_3$)$_3$) ppm; δ_C(90 MHz, $CDCl_3$) 163.1 (s), 161.4 (s), 160.7 (s), 155.6 (s),

144.2 (d), 141.8 (d), 135.3 (s), 133.0 (s), 80.3 (s), 62.7 (t), 52.2 (t), 49.2 (d), 37.7 (t) and 28.3 (q) ppm; *m/z* (ESI) Found: 433.1367, $C_{17}H_{22}N_4O_8Na$ [$(M+Na)^+$] requires 433.1335.

2''-(*tert*-Butoxycarbonylamino-methyl)-[2,4';2',4'']teroxazole-4-carboxylic acid methyl ester (63a). (Diethylamino)sulfur trifluoride (0.55 mL, 4.2 mmol) was added dropwise over 2 min to a stirred solution of the hydroxymethyl amide **62b** (1.43 g, 3.5 mmol) in dry dichloromethane (40 mL) at −78 °C under a nitrogen atmosphere. The mixture was stirred at −78 °C for 2 h and then allowed to warm to room temperature and stirred for a further 5 min. The mixture was quenched with saturated sodium bicarbonate solution (20 mL) and the separated organic layer was then dried ($MgSO_4$) and concentrated *in vacuo* to leave the crude oxazoline, which was used immediately without further purification.

Bromotrichloromethane (1.0 mL, 11 mmol) was added to a stirred solution of the crude oxazoline in dry dichloromethane (40 mL) at 0 °C under a nitrogen atmosphere and the mixture was stirred at 0 °C for 5 min. 1,8-Diazabicyclo[5.4.0]undec-7-ene (1.6 mL, 11 mmol) was added dropwise over 2 min and the mixture was allowed to warm to room temperature overnight. The volatile components were removed *in vacuo* and the brown residue was triturated with methanol to leave the *oxazole* (0.78 g, 57%) as a colourless solid; mp 247–251 °C; $\nu_{max}(CHCl_3)/cm^{-1}$ 3455, 2932 and 1717; δ_H(360 MHz, DMSO-d_6) 9.09 (1H, s, oxazole-H), 9.02 (1H, s, oxazole-H), 8.95 (1H, s, oxazole-H), 7.63 (1H, t, *J* 6.0 Hz, BocN*H*), 4.36 (2H, d, *J* 6.0 Hz, BocNHCH_2), 3.87 (3H, s, CO_2CH_3) and 1.42 (9H, s, $OC(CH_3)_3$) ppm; δ_C(90 MHz, DMSO-d_6) 162.7 (s), 161.2 (s), 155.9 (s), 155.3 (s),

143.8 (d), 139.7 (d), 139.3 (d), 134.3 (s), 130.8 (s), 129.7 (s), 80.4 (s), 52.3 (q), 37.9 (t) and 28.2 (q) ppm; *m/z* (CI) Found: 391.1260, $C_{17}H_{19}N_4O_7$ $[(M+H)^+]$ requires 391.1255.

2''-(*tert*-Butoxycarbonylamino-methyl)-[2,4';2',4'']teroxazole-4-carboxylic acid (63b). A solution of sodium hydroxide (0.70 g, 18 mmol) in water (20 mL) was added in one portion to a stirred suspension of the methyl ester **63a** (0.77 g, 2.0 mmol) in tetrahydrofuran (40 mL), and the mixture was stirred at room temperature for 18 h. The volatile components were removed *in vacuo* and the residue was then acidified to pH 2 with 10% aqueous citric acid. The aqueous suspension was extracted with dichloromethane (6 × 50 mL) and the combined organic extracts were then concentrated *in vacuo* to leave a colourless residue which was triturated with methanol to leave the oxazole carboxylic acid (0.67 g, 88%) as a colourless solid; mp 275 °C (decomp.); Found: C, 51.0; H, 4.3; N, 14.4%. $C_{16}H_{16}N_4O_7$ requires C, 51.1; H, 4.3; N, 14.9%; ν_{max}(solid)/cm^{-1} 3357, 3137, 1693 and 1530; δ_H(360 MHz, $CDCl_3$ / DMSO-d_6 (2:1)) 8.66 (1H, s, oxazole-H), 8.59 (1H, s, oxazole-H), 8.54 (1H, s, oxazole-H), 7.30 (1H, t, *J* 5.9 Hz, BocN*H*), 4.35 (2H, d, *J* 5.9 Hz, BocNHCH_2) and 1.41 (9H, s, OC(CH_3)$_3$) ppm; δ_C(90 MHz, DMSO-d_6) 163.1 (s), 161.8 (s), 155.7 (s), 155.6 (s), 154.8 (d), 144.2 (d), 140.1 (d), 139.6 (d), 134.5 (s), 130.3 (s), 129.1 (s), 78.6 (s), 37.4 (t) and 28.1 (q) ppm; *m/z* (ESI) Found: 399.0926, $C_{16}H_{16}N_4O_7Na$ $[(M+Na)^+]$ requires 399.0917.

2-{(*S*)-1-[(2''-{[(*S*)-1-((2*S*,3*S*)-2-*tert*-Butoxycarbonylamino-3-methyl-pentanoylamino)-2-methyl-propylamino]-methyl}-[2,4';2',4'']teroxazole-4-carbothioyl)-amino]-2-hydroxy-ethyl}-5-phenyl-oxazole-4-carboxylic acid methyl

ester (72). 4-Methylmorpholine (13 μL, 0.12 mmol) was added to a stirred suspension of the acid **71** (17 mg, 0.05 mmol) and 1-hydroxybenzotriazole (16 g, 0.12 mmol) in dry dichloromethane (5 mL) at 0 °C under a nitrogen atmosphere. 1-[3-(Dimethylamino)propyl]-3-ethylcarbodiimide hydrochloride (17 mg, 0.09 mmol) was added and the mixture was then stirred at 0 °C for 15 min. A pre-cooled (0 °C) solution of the amine **70** (20 mg, 0.03 mmol) and 4-methylmorpholine (13 μL, 0.12 mmol) in dry dichloromethane (5 mL) was added dropwise over 5 min and the mixture was then allowed to warm to room temperature overnight. The mixture was concentrated *in vacuo* and the residue was then partially purified by trituratation with methanol to leave the tetraoxazole substituted thioamide (15 mg, 57%) as a cream solid; δ_H(360 MHz, $CDCl_3$ / CD_3OD (1:1)) 10.06 (1H, d, *J* 7.3 Hz, CSN*H*), 8.80 (1H, s, oxazole-H), 8.68 (1H, s, oxazole-H), 8.64 (1H, s, oxazole-H), 7.94–7.32 (7H, m, 2 × phenyloxazole-H, CON*H*CH_2, CON*H*-(val), 3 × phenyloxazole-H), 6.59 (1H, d, *J* 8.7 Hz, BocN*H*), 6.09–5.89 (2H, m, CONHC*H*-(val), CSNHC*H*), 5.47–5.40 (1H, m, BocNHC*H*), 4.48–4.40 (2H, m, gly-CH_2), 4.13–4.00 (2H, m, CH_2OH), 3.80 (3H, s, CO_2CH_3), 2.03–1.87 (1H, m, C*H*), 1.75–1.61 (1H, m, C*H*), 1.36 (9H, s, $OC(CH_3)_3$), 1.16–0.97 (2H, m, CH_2) and 0.88–0.72 (12H, m, 3 × CH_3) ppm.

The Thioamide Cyclopeptide (74). A solution of sodium hydroxide (1.3 mg, 0.034 mmol) in water (2 mL) was added in one portion to a stirred solution of the methyl ester **72** (15 mg, 0.017 mmol) in tetrahydrofuran (4 mL) and the mixture was stirred at room temperature overnight. Water (10 mL) was added and the mixture was concentrated slowly *in vacuo* to a volume of approx. 10 mL. The aqueous suspension was extracted

with dichloromethane–methanol (4:1) (5 × 20 mL) and dichloromethane (3 × 20 mL) and the combined organic extracts were then evaporated *in vacuo* to leave the crude *sodium carboxylate* (12 mg, 80%) as a cream solid, which was used directly in the next reaction without further purification.

Hydrogen chloride (4.0 M solution in dioxane) (3 mL) was added to the crude *sodium carboxylate* (12 mg, 0.014 mmol) and the mixture was stirred at room temperature overnight under a nitrogen atmosphere. The volatiles were evaporated to leave the *co-amino acid hydrochloride salt* **73** (10 mg, 100%) as a cream solid, which was used without further purification.

4-Methylmorpholine (8 μL, 0.073 mmol) was added to a stirred suspension of the ω-amino acid **73** (13 mg, 0.018 mmol) in dry dichloromethane (4 mL) and dry *N*,*N*-dimethylformamide (2 mL) at 0 °C under a nitrogen atmosphere. *O*-(7-Azabenzotriazol-1-yl)-*N*,*N*,*N'*,*N'*-tetramethyluronium hexafluorophosphate (9 mg, 0.024 mmol) was added and the mixture was stirred at 0 °C for 5 min and then allowed to warm to room temperature and stirred for 90 h. The mixture was concentrated *in vacuo* and the residue was then partitioned between dichloromethane (10 mL) and saturated sodium bicarbonate solution (10 mL). The separated aqueous layer was extracted with dichloromethane (2 × 10 mL) and the combined organic extracts were then dried ($MgSO_4$) and concentrated *in vacuo*. The residue was chromatographed on silica gel using dichloromethane–methanol (20:1→10:1) as eluent to give the impure *macrolactam* (10 mg, 77%) as a cream solid; δ_H(360 MHz, DMSO-d_6) 9.80 (1H, d, *J* 7.1 Hz, CSN*H*), 9.07 (1H, s, oxazole-H), 8.96 (1H, s, oxazole-H), 8.92 (1H, s, oxazole-H), 8.55–7.38 (8H, m, 5 × phenyloxazole-H, 3 × CON*H*), 5.90–5.83 (1H, m, CSNHC*H*), 5.33–5.28 (1H, m, CONHC*H*), 4.80–4.15 (5H,

m, CONHC*H*, CH_2OH, gly-CH_2), 2.13–1.98 (1H, m C*H*), 1.83–1.72 (1H, m, C*H*) and 0.97–0.70 (14H, m, CH_2, 3 × CH_3) ppm.

YM-216391 diastereoisomer (76). (Diethylamino)sulfur trifluoride (7 μL, 0.056 mmol) was added to a stirred solution of the thioamide **74** (8 mg, 0.011 mmol) in dry dichloromethane (1 mL) at −78 °C under a nitrogen atmosphere. The mixture was stirred at −78 °C for 1 h, then at −20 °C for 1 h and was then allowed to warm to room temperature. Dichloromethane (20 mL) was added and the mixture was quenched with saturated sodium bicarbonate solution (10 mL). The separated aqueous layer was extracted with dichloromethane (2 × 10 mL) and the combined organic extracts were then dried ($MgSO_4$) and concentrated *in vacuo* to leave the crude thiazoline **75** (4 mg, 50%) as a yellow solid, which was used without further purification.Activated manganese (IV) oxide (10 mg, 0.1 mmol) was added to a stirred solution of the crude thiazoline **75** (4 mg, 0.0057 mmol) in dry dichloromethane (1 mL) at room temperature under a nitrogen atmosphere. The mixture was stirred for 48 h and was then filtered through a pad of celite and eluted with dichloromethane–methanol (1:1) (50 mL). The filtrate was concentrated *in vacuo* to leave a yellow residue, which was partially purified by trituration with ether to give the *thiazole* (1 mg, 27%) as a colourless solid; δ_H(500 MHz, DMSO-d_6) 9.15 (1H, s), 9.05 (1H, s), 8.95 (1H, s), 8.71 (1H, s), 8.58 (1H, d, *J* 8.4 Hz), 8.47 (2H, d, *J* 7.1 Hz), 8.47–8.40 (1H, m), 7.98 (1H, d, *J* 5.6 Hz), 7.62–7.49 (3H, m), 5.13 (1H, dd, *J* 17.2 and 8.9 Hz), 4.68 (1H, dd, *J* 8.4 and 5.5 Hz), 4.20–4.08 (2H, m), 2.18–2.07 (1H, m), 2.06–1.98 (1H, m), 1.68–1.53 (1H, m), 1.29–1.13 (1H, m) and 1.02–0.71 (12H, m) ppm.