(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 (MgSO₄) 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; [α]₂¹ +29 (c = 1.0, CHCl₃); ν_{max}(CHCl₃)/cm⁻¹ 3422, 2955, 1745, 1714 and 1681; δ_{H}(500 MHz, CDCl₃) 7.39–7.28 (6H, m, CONH, 5 × aryl-H), 5.50 (1H, m, BocNH), 4.67–4.62 (1H, m, CONHCH), 4.55 (2H, s, OCH₂Ph), 4.37–4.30 (1H, m, BocNHCH), 3.93–3.89 (2H, m, CH₂OH), 3.89 (1H, dd, J 9.4 and 4.4 Hz, CH₃H₂OTBS), 3.75 (3H, s, CO₂CH₃), 3.63 (1H, dd, J 9.4 and 5.7 Hz, CH₂H₂OTBS) and 1.45 (9H, s, OC(CH₃)₃) ppm; δ_{C}(90 MHz, CDCl₃) 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_{2}O_{7}Na [(M+Na)^+] requires 419.1794.

2-((S)-2-Benzylxyloxy-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; $[\alpha]_D^{22} -18 \ (c = 1.0, \text{CHCl}_3)$; Found: C, 60.1; H, 6.3; N, 7.1%. C$_{19}$H$_{24}$N$_2$O$_6$ requires C, 60.6; H, 6.4; N, 7.4%; $\nu_{\text{max}}$(CHCl$_3$/cm$^{-1}$) 3440, 2980, 2870, 1714 and 1587; $\delta_{\text{H}}$(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, BocNH), 5.16–5.08 (1H, m, BocNHCH), 4.53 (1H, d, J 12.1 Hz, OCH$_2$H$_5$Ph), 4.49 (1H, d, J 12.1 Hz, OCH$_2$H$_5$Ph), 3.95–3.87 (1H, m, CHCH$_a$H$_b$OBn), 3.93 (3H, s, CO$_2$C$_3$H$_3$), 3.81 (1H, dd, J 9.6 and 4.4 Hz, CHCH$_a$H$_b$OBn) and 1.46 (9H, s, OC(C$_3$H$_3$)$_3$) ppm; $\delta_{\text{C}}$(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$_2$O$_6$Na$^+$ requires 399.1532.

2-((S)-2-Benzylxy-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; $[\alpha]_D^{21} -26 \ (c = 1.0, \text{CHCl}_3)$; $\nu_{\text{max}}$(CHCl$_3$/cm$^{-1}$) 3440, 3169, 2870, 1714 and 1590; $\delta_{\text{H}}$(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, BocNH), 5.32–5.15 (1H, m, BocNHCH), 4.54 (1H, d, J 12.1 Hz, OCH$_2$H$_5$Ph), 4.50 (1H, d, J 12.1 Hz, OCH$_2$H$_5$Ph), 3.94 (1H, dd, J 9.6 and 4.0 Hz, CH$_2$H$_5$OBn), 3.84 (1H, dd, J 9.6 and 4.8 Hz,
CH₄H₂OBn) and 1.45 (9H, s, OC(CH₃)₃) ppm; δc(90 MHz, CDCl₃) 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, C₁₈H₂₂N₂O₆Na [(M+Na)+] requires 385.1376.

(S)-2-[(S)-2-Benzoylcarnobalamino-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 (MgSO₄) and then concentrated in vacuo to leave a colourless solid. Purification by recrystallisation from ether / petrol gave (S)-2-benzoylcarnobalamino-3-(tert-butyl-dimethyl-silanyloxy)-propionic acid (9.6 g, 88%) as a colourless crystalline solid; mp 95–96 °C (from ether / petrol); [α]D¹⁰ −20 (c = 1.0, CHCl₃); Found: C, 57.7; H, 7.7; N, 4.1%. C₁₇H₂₇NO₅Si requires C, 57.8; H, 7.7; N, 4.0%; νmax(CHCl₃)/cm⁻¹ 3444, 2931 and 1719; δH(360 MHz, CDCl₃) 7.40–7.29 (5H, m, 5 × aryl-H), 5.59 (1H, d, J₈.₁ Hz, ZNH), 5.19–5.10 (2H, m, CO₂CH₂Ph), 4.49–4.43 (1H, m, ZNHCH₃), 4.14 (1H, dd, J

\( \text{H}_2\text{OBn} \) and 1.45 (9H, s, OC(CH₃)₃) ppm; δc(90 MHz, CDCl₃) 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, C₁₈H₂₂N₂O₆Na [(M+Na)+] requires 385.1376.

(S)-2-[(S)-2-Benzoylcarnobalamino-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 (MgSO₄) and then concentrated in vacuo to leave a colourless solid. Purification by recrystallisation from ether / petrol gave (S)-2-benzoylcarnobalamino-3-(tert-butyl-dimethyl-silanyloxy)-propionic acid (9.6 g, 88%) as a colourless crystalline solid; mp 95–96 °C (from ether / petrol); [α]D¹⁰ −20 (c = 1.0, CHCl₃); Found: C, 57.7; H, 7.7; N, 4.1%. C₁₇H₂₇NO₅Si requires C, 57.8; H, 7.7; N, 4.0%; νmax(CHCl₃)/cm⁻¹ 3444, 2931 and 1719; δH(360 MHz, CDCl₃) 7.40–7.29 (5H, m, 5 × aryl-H), 5.59 (1H, d, J₈.₁ Hz, ZNH), 5.19–5.10 (2H, m, CO₂CH₂Ph), 4.49–4.43 (1H, m, ZNHCH₃), 4.14 (1H, dd, J
10.1 and 2.5 Hz, CH$_3$H$_2$OTBS), 3.86 (1H, dd, $J$ 10.1 and 3.9 Hz, CH$_3$H$_2$OTBS), 0.87 (9H, s, Si(CH$_3$)$_3$) and 0.06 (6H, s, Si(CH$_3$)$_2$) ppm; $\delta$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$_5$SiNa [(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$_2$O$_5$Si requires C, 55.5; H, 7.5; N, 6.2%; $\nu_{\text{max}}$(CHCl$_3$)/cm$^{-1}$ 3419, 2954, 1724 and 1678; $\delta$H(360 MHz, CDCl$_3$) 7.40–7.29 (6H, m, CONH$_2$aryl-H), 5.66 (1H, m, ZNH$_2$), 5.14 (2H, s, CO$_2$CH$_2$Ph), 4.68–4.62 (1H, m, CONHCH$_2$), 4.30–4.22 (1H, m, ZNHCH$_2$), 4.07 (1H, dd, $J$
9.9 and 3.9 Hz, CH$_2$H$_2$OH), 4.00–3.89 (2H, m, CH$_2$H$_2$OH, \(\text{CH}_2\text{H}_2\text{OTBS}\)), 3.79 (3H, s, CO$_2$CH$_3$), 3.73 (1H, dd, \(J\) 9.8 and 6.8 Hz, CH$_2$H$_2$OTBS), 2.47 (1H, br s, OH), 0.90 (9H, s, SiC(CH$_3$)$_3$) and 0.09 (6H, s, Si(CH$_3$)$_2$) ppm; \(\delta_C(90 \text{ MHz, CDCl}_3)\) 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$_2$O$_7$SiNa \([\text{M+Na}^+]\) requires 477.2033.

2-[(S)-1-Benzzyloxy carbonylamino-2-(\text{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 \textit{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 \textit{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 (MgSO₄) 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; [α]²³D –12 (c = 1.5, CHCl₃); νmax(CHCl₃)/cm⁻¹ 3435, 2954, 2858, 1722 and 1586; δH(360 MHz, CDCl₃) 8.22 (1H, s, oxazole-H), 7.42–7.33 (5H, m, 5 × aryl-H), 5.78 (1H, d, J 8.5 Hz, ZNH), 5.19 (1H, d, J 12.2 Hz, CO₂CH₆H₄Ph), 5.14 (1H, d, J 12.2 Hz, CO₂CH₆H₄Ph), 5.15–5.08 (1H, m, ZNHC₆H₄OTBS), 4.12 (1H, dd, J 10.2 and 3.4 Hz, CH₆H₄OTBS), 3.98 (1H, dd, J 10.2 and 4.3 Hz, CH₆H₄OTBS), 3.95 (3H, s, CO₂CH₃), 0.82 (9H, s, SiC(CH₃)₃), 0.00 (3H, s, SiCH₃(CH₃)) and –0.03 (3H, s, SiCH₃(CH₃)) ppm; δC(90 MHz, CDCl₃) 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, C₂₁H₃₁N₂O₆Si [(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 (MgSO₄) 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$_2$O$_6$ requires C, 56.3; H, 5.0; N, 8.8%; $\nu_{\text{max}}$(CHCl$_3$)/cm$^{-1}$ 3610, 3432, 2955, 1728 and 1586; $\delta_{\text{H}}$(360 MHz, CDCl$_3$) 8.18 (1H, s, oxazole-H), 7.44–7.25 (5H, m, 5 x aryl-H), 6.30 (1H, d, J 8.4 Hz, ZNH), 5.20–5.02 (1H, m, ZNHCH), 5.16 (1H, d, J 12.2 Hz, CO$_2$CH$_3$H$_3$Ph), 5.10 (1H, d, J 12.2 Hz, CO$_2$CH$_3$H$_3$Ph), 4.17 (1H, dd, J 11.4 and 3.2 Hz, CH$_3$H$_3$OH), 4.02 (1H, dd, J 11.4 and 3.9, CH$_3$H$_3$OH), 3.91 (3H, s, CO$_2$CH$_3$) and 3.30 (1H, m, OH) ppm; $\delta_{\text{C}}$(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$_2$O$_6$ [(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$_7$H$_{10}$N$_2$O$_4$ requires C, 45.2; H, 5.4%; $\nu_{\text{max}}$(CHCl$_3$)/cm$^{-1}$ 3610, 3390, 2954, 1738 and 1586; $\delta_{\text{H}}$(360 MHz, CDCl$_3$) 8.20 (1H, s, oxazole-H), 4.19–4.13 (1H, m, NH$_2$CH), 3.94 (1H, dd, J 11.1 and 4.6 Hz, CH$_3$H$_3$OH), 3.90 (3H, s, CO$_2$CH$_3$), 3.86 (1H, dd, J 11.1 and 6.3 Hz, CH$_3$H$_3$OH) and 2.44 (1H, br s, NH$_2$ and OH) ppm; $\delta_{\text{C}}$(90 MHz, CDCl$_3$) 166.2 (s), 161.4 (s), 144.2 (d), 133.0 (s), 64.5 (t), 52.2 (q) and 51.3 (d) ppm; m/z (CI) Found: 187.0714, C$_7$H$_{11}$N$_2$O$_4$ [(M+H)$^+$] requires 187.0719.
(2S,3R)-2-((S)-3-Benzylxoy-2-benzyloxycarbonylamino-propionylamino)-3-hydroxybutyric acid methyl ester (13c). 4-Methylmorpholine (1.4 mL, 12 mmol) was added to a stirred suspension of N-carbobenzylxoy-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 (MgSO₄) 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); [α]₂²° +20 (c = 1.0, CHCl₃); Found: C, 61.8; H, 6.3; N, 6.1%. C₂₃H₂₈N₂O₇ requires C, 62.2; H, 6.4; N, 6.3%; νmax(CHCl₃)/cm⁻¹ 3422, 1729 and 1682; δh(360 MHz, CDCl₃) 7.38–7.27 (11H, m, CONH), 5.81 (1H, d, J 7.0 Hz, ZNH), 5.12 (2H, s, CO₂CH₂Ph), 4.61 (1H, dd, J 9.0 and 2.6 Hz, CONHCH), 4.56 (2H, s, CH₂OCH₂Ph), 4.51–4.42 (1H, m, ZNHCH), 4.32 (1H, qd, J 6.4 and 2.6, NHCHCH(CH₃)OH), 3.92 (1H, dd, J 9.2 and 4.0 Hz, CHCH₃H₅OBn), 3.72 (3H, s, CO₂CH₂), 3.63 (1H, dd, J 9.2 and 6.3 Hz, CHCH₃H₅OBn), 2.54 (1H, br s, OH) and 1.16 (3H, d, J 6.4 Hz, CH(CH₃)OH) ppm; δc(90 MHz, CDCl₃) 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, \( \text{C}_{23}\text{H}_{28}\text{N}_{2}\text{O}_{7}\text{Na} \) \([\text{M}+\text{Na}]^+\) requires 467.1794.

\[ 2-((S)-2-\text{Benzyloxy}-1-\text{benzyloxycarbonylamino-ethyl})-5-\text{methyl-oxazole-4-carboxylic acid methyl ester (15c).} \]

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 \(-20^\circ\text{C}\) under a nitrogen atmosphere. The mixture was stirred at \(-20^\circ\text{C}\) 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 (\(\text{MgSO}_4\)) and concentrated \textit{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 \(^\circ\text{C}\) under a nitrogen atmosphere and the mixture was stirred at 0 \(^\circ\text{C}\) 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 \textit{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 (\(\text{MgSO}_4\)) and then concentrated \textit{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; \([\alpha]_D^{22} -14 \) \((c = 1.0, \text{CHCl}_3)\); \( \nu_\text{max} (\text{CHCl}_3)/\text{cm}^{-1} \)
δ_H(360 MHz, CDCl_3) 7.35–7.21 (10H, m, 10 × aryl-H), 6.00 (1H, d, J 8.6 Hz, ZNH), 5.18–5.05 (3H, m, CO_2CH_2Ph, NHCHCH_2), 4.53 (1H, d, J 12.2 Hz, CH_2OCH_2H_3Ph), 4.48 (1H, d, J 12.2 Hz, CH_2OCH_2H_3Ph), 3.92 (1H, dd, J 9.7 and 5.4 Hz, CHCH_2H_3OBn), 3.89 (3H, s, CO_2CH_3), 3.82 (1H, dd, J 9.7 and 4.5 Hz, CHCH_2H_3OBn) 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); [α]_D^25 –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%; ν_{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, ZNH), 5.23 (1H, m, NHCHCH_2), 5.11 (1H, d, J 12.2 Hz, CO_2CH_2H_3Ph), 5.09 (1H, d, J 12.2 Hz, CO_2CH_2H_3Ph), 4.55 (1H, d, J 12.2 Hz, CH_2OCH_2H_3Ph), 4.50 (1H, d, J 12.2 Hz, CH_2OCH_2H_3Ph), 3.92 (1H, dd, J
9.6 and 4.4 Hz, CHCH$_2$OBn), 3.83 (1H, dd, $J$ 9.6 and 5.1 Hz, CHCH$_2$OBn) and 2.53 (3H, s, oxazole-CH$_3$) ppm; $\delta$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-[(1S,2R)-1-Benzoxycarbonylamino-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-[(2S,3R)-2-benzoxycarbonylamino-3-(tert-butyl-dimethyl-silanyloxy)-butyrylamino]-3-hydroxy-propionic acid methyl ester (5.7 g, 12.2 mmol) in dry dichloromethane (120 mL) at $-78^\circ$C under a nitrogen atmosphere. The mixture was stirred at $-78^\circ$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 (MgSO₄) 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; \([\alpha]_{D}^{22} \text{D} -23 \) (c = 1.5, CHCl₃); Found: C, 59.1; H, 7.2; N, 6.2%. C₂₂H₃₂N₂O₆Si requires C, 58.9; H, 7.2; N, 6.2%; \(\nu_{\text{max}}\text{(CHCl₃)/cm}^{-1} 3437, 2955, 2930, 2857, 1722 \text{ and } 1586\); \(\delta_{\text{H}}\text{(360 MHz, CDCl₃) 8.18 (1H, s, oxazole-H), 7.40–7.30 (5H, m, 5 × aryl-H), 5.69 (1H, d, } J 9.4 \text{ Hz, ZNH), 5.17 (1H, d, } J 12.2 \text{ Hz, CO₂CH₃H₃Ph), 5.13 (1H, d, } J 12.2 \text{ Hz, CO₂CH₃H₃Ph), 4.94 (1H, dd, } J 9.4 \text{ and 2.1 Hz, NHCHCH), 4.44 (1H, qd, } J 6.2 \text{ Hz, CH(CH₃)OTBS), 3.92 (3H, s, CO₂CH₃), 1.25 (3H, d, } J 6.2 \text{ Hz, CH(CH₃)OTBS), 0.76 (9H, s, SiC(CH₃)₃), -0.02 (3H, s, SiCH₃(CH₃)) and -0.22 (3H, s, SiCH₃(CH₃)) ppm; } \delta_{C}(90 MHz, CDCl₃) 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; \text{m/z (ESI) Found: 449.2086, C}_{22}H_{33}N_{2}O_{6}Si [(M+H)⁺] requires 449.2108.}

2-((1S,2R)-1-Benzylxycarbonylamino-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 (MgSO₄) 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, CHCl₃); \(\nu_{\text{max}}\text{(CHCl₃)/cm}^{-1} 3430, 2955, 2927,
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1723 and 1585; $\delta_H(360$ 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, ZNH), 5.15 (1H, d, $J$ 12.3 Hz, CO$_2$CH$_2$H$_5$Ph), 5.07 (1H, d, $J$ 12.3 Hz, CO$_2$CH$_4$H$_5$Ph), 4.92 (1H, dd, $J$ 9.3 and 2.4 Hz, NHCCH), 4.42 (1H, m, CHCH(CH$_3$)OH), 3.87 (3H, s, CO$_2$CH$_3$), 3.43 (1H, br s, OH) and 1.25 (3H, d, $J$ 6.5 Hz, CH(CH$_3$)OH) ppm; $\delta_C (90$ 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$_2$O$_6$ [(M+H)$^+$] requires 335.1243.

2-((1S,2R)-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; [α]$_D^{22}$ –5.4 (c = 1.0, CHCl$_3$); Found: C, 47.7; H, 6.1; N, 13.8%. C$_8$H$_{12}$N$_2$O$_4$ requires C, 48.0; H, 6.0; N, 14.0%; $\nu_{max}$(CHCl$_3$)/cm$^{-1}$ 3406, 2978, 2955, 1739 and 1585; $\delta_H(360$ MHz, CDCl$_3$) 8.19 (1H, s, oxazole-H), 3.99 (1H, dq, $J$ 6.4 and 6.2 Hz, CHCH(CH$_3$)OH), 3.89 (3H, s, CO$_2$CH$_3$), 3.80 (1H, d, $J$ 6.4 Hz, NH$_2$CHCH), 2.48 (3H, br s, NH$_2$ and OH) and 1.17 (3H, d, $J$ 6.2 Hz, CH(CH$_3$)OH) ppm; $\delta_C (90$ 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$_{8}$H$_{13}$N$_2$O$_4$ [(M+H)$^+$] requires 201.0875.
2-[(S)-1-Benzoxycarbonylamino-2-( tert-butyl-dimethyl-silyloxy)-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 (MgSO₄) and evaporated in vacuo to leave the acid (1.2 g, 82%) as a colourless oil; [α]_D

–25 (c = 2.0, CHCl₃); ν_{max} (CHCl₃)/cm⁻¹ 3436, 3169, 2930, 2858, 1714 and 1590; δ_H(360 MHz, CDCl₃) 8.23 (1H, s, oxazole-H), 7.97 (1H, br s, CO₂H), 7.40–7.26 (5H, m, 5 × aryl-H), 6.57 (1H, d, J 9.0 Hz, ZN₃H), 5.23–5.15 (1H, m, ZNHC₃H), 5.15 (1H, d, J 12.2 Hz, CO₂CH₃H₅Ph), 5.10 (1H, d, J 12.2 Hz, CO₂CH₃H₅Ph), 4.10 (1H, dd, J 10.0 and 3.7 Hz, CH₃H₅OTBS), 3.98 (1H, dd, J 10.0 and 3.7 Hz, CH₃H₅OTBS), 0.80 (9H, s, SiC(CH₃)₃), –0.03 (3H, s, SiCH₃(CH₃)) and –0.04 (3H, s, SiCH₃(CH₃)) ppm; δ_C(90 MHz, CDCl₃) 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, C₂₀H₂₉N₂O₆Si [(M+H)⁺] requires 421.1795.

(2S,3R)-2-[(S)-2-Benzoxycarbonylamino-3-( tert-butyl-dimethyl-silyloxy)-propionylamino]-3-hydroxy-butryic acid methyl ester (13d). 4-Methylmorpholine (3.3 mL, 30 mmol) was added to a stirred suspension of (S)-2-benzoxycarbonylamino-3-( tert-butyl-dimethyl-silyloxy)-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 (MgSO₄) 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, CDCl₃) 7.35–7.29 (6H, m, 5 × aryl-H, CONH), 5.74 (1H, d, J 7.0 Hz, ZNH), 5.13 (2H, s, CO₂CH₂Ph), 4.62–4.58 (1H, m, CONHCH), 4.37–4.27 (2H, m, CH(CH₃)OH, ZNHCH), 4.06 (1H, dd, J 9.8 and 3.9 Hz, CH₃CH₂OTBS), 3.78–3.69 (1H, m, CH₂H₂OTBS), 3.74 (3H, s, CO₂CH₃), 2.63 (1H, br s, OCH), 1.18 (3H, d, J 6.0 Hz, CH(CH₃)OH), 0.89 (9H, s, SiCH(CH₃)₃) and 0.15 (6H, s, Si(CH₃)₂ ppm; δ_C(90 MHz, CDCl₃) 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-Benzoxycarbonylamino-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 (MgSO₄) 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 (MgSO₄) 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; [α]$_D^{19}$ $-$7.8 ($c$ = 1.0, CHCl$_3$); $\nu_{\text{max}}$(CHCl$_3$)/cm$^{-1}$ 3427, 2929, 1722 and 1623; $\delta_{1H}$(360 MHz, CDCl$_3$) 7.38–7.28 (5H, m, 5 $\times$ aryl-H), 5.73 (1H, d, $J$ 8.7 Hz, ZNH), 5.15 (1H, d, $J$ 12.3 Hz, CO$_2$CH$_3$H$_6$Ph), 5.10 (1H, d, $J$ 12.3 Hz, CO$_2$CH$_3$H$_6$Ph), 5.05–4.98 (NHCH$_2$CH$_2$), 4.04 (1H, dd, $J$ 10.1 and 3.7 Hz, CH$_2$H$_6$OTBS), 3.92 (1H, dd, $J$ 10.1 and 4.4 Hz, CH$_2$H$_6$OTBS), 3.89 (3H, s, CO$_2$CH$_3$), 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; $\delta_{1C}$(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$_2$O$_6$SiNa [(M+Na)$^+$] requires 471.1927.
2-[(S)-1-Benzylxycarbonylamino-2-(tert-butyl-dimethyl-silyloxy)-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 100 mL 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-Benzylxycarbonylamino-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); $\nu_{\text{max}}$(CHCl$_3$)/cm$^{-1}$ 3320, 2928, 1725, 1701 and 1602; $\delta_H$(360 MHz, CD$_3$OD) 8.50 (1H, s, oxazole-H), 7.42–7.23 (5H, m, 5 × aryl-H), 5.21–5.07 (2H, m, OCH$_2$Ph), 5.05–4.90 (1H, obs m, ZNHCH) and 4.01–3.90 (2H, m, CH$_2$OH) ppm; $\delta_C$(90 MHz, CD$_3$OD) 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_{2}O_{6}Na [\text{[(M+Na)^+]}] requires 329.0750.

2-[(S)-1-Amino-2-(tert-butyl-dimethyl-silyloxy)-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_{\text{max}}(\text{CHCl}_{3})/\text{cm}^{-1} 3386, 2954, 1738 and 1589; \delta_{H}(360 MHz, CDCl_{3}) 8.20 (1H, s, oxazole-H), 4.18 (1H, dd, J 5.5 and 4.7 Hz, NH \text{C H}), 3.95–3.93 (2H, m, CH_{2}OTBS), 3.92 (3H, s, CO_{2}CH_{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; \delta_{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_{2}O_{4}Si [\text{[(M+H)^+]}] requires 301.1584.

2-(((S,2R)-1-{[(2-((S)-2-Benzzyloxy-1-benzzyloxy carbonylamino-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 (MgSO₄) 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); [α]D 22 ±48 (c = 1.0, CHCl₃); νmax(CHCl₃)/cm⁻¹ 3437, 3401, 2954, 2870, 1725, 1672, 1634 and 1585; δH(360 MHz, CDCl₃) 8.18 (1H, s, oxazole-H), 7.72 (1H, d, J 9.2 Hz, CONH), 7.43–7.19 (10H, m, 10 × aryl-H), 5.85 (1H, d, J 8.6 Hz, ZNH), 5.31 (1H, dd, J 9.2 and 2.7 Hz, CONHCCH(CH₃)OH), 5.21–5.05 (3H, m, CO₂CH₂Ph, NHCH₂CH₂OBn), 4.58 (1H, qd, J 6.4 and 2.7 Hz, CONHCHCH(CH₃)OH), 4.54 (1H, d, J 12.2 Hz, CH₂OCH₂H₆Ph), 4.47 (1H, d, J 12.2 Hz, CH₂OCH₂H₆Ph), 3.89 (3H, s, CO₂CH₃), 3.88 (1H, dd, J 9.4 and 3.7 Hz, CHCH₃H₆OBn), 3.79 (1H, dd, J 9.4 and 3.9 Hz, CHCH₃H₆OBn), 2.59 (3H, s, oxazole-CH₃) and 1.28 (3H, d, J 6.4 Hz, CH(CH₃)OH) ppm; δC(90 MHz, CDCl₃) 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, C₃₀H₃₃N₄O₉ [(M+H)+] requires 593.2248.
2’’-((S)-2-Benzylxy-1-benzylxoycarbonylamino-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 (MgSO₄) 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 (MgSO₄) 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); [α]D21 –24 (c = 1.0, CHCl₃); Found: C, 62.8;
H, 4.9; N, 9.5%. C₃₀H₂₈N₄O₈ requires C, 62.9; H, 4.9; N, 9.8%; νmax(CHCl₃)/cm⁻¹ 3435,
2954, 2869, 1723, 1659 and 1582; δH(360 MHz, CDCl₃) 8.33 (1H, s, oxazole-H), 7.42–
7.20 (10H, m, 10 × aryl-H), 5.81 (1H, d, J 8.2 Hz, ZNH), 5.22–5.09 (3H, m, CO₂CH₂Ph, NHCHCH₂), 4.58 (1H, d, J 12.2 Hz, CH₂OCH₃H₅Ph), 4.52 (1H, d, J 12.2 Hz, CH₂OCH₃H₅Ph), 4.00–3.91 (4H, m, CO₂CH₃, CHCH₃H₅OBn), 3.87 (1H, dd, J 9.7 and 4.2 Hz, CHCH₃H₅OBn), 2.84 (3H, s, oxazole-CH₃) and 2.73 (3H, s, oxazole-CH₃) ppm; δC(90 MHz, CDCl₃) 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, C₃₀H₂₉N₄O₈ [(M+H)+] requires 573.1985.

2′′-((S)-2-Benzoyloxy-1-benzzyloxycarbonylamino-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 (MgSO₄) 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); [α]D²⁻¹⁰ (c = 1.0, CHCl₃); νmax(CHCl₃)/cm⁻¹ 3436, 3168, 2925, 2868, 1716, 1661 and 1586; δH(360 MHz, CDCl₃) 8.39 (1H, s, oxazole-H), 7.45–7.20 (10H, m, 10 × aryl-H), 5.90 (1H, d, J 8.7 Hz, ZNH), 5.90 (1H, br s, CO₂H), 5.26–5.09 (3H, m, CO₂CH₂Ph, NHCHCH₂), 4.56 (1H, d, J 12.2 Hz, CH₂OCH₃H₅Ph), 4.51 (1H, d, J 12.2 Hz, CH₂OCH₃H₅Ph), 3.95 (1H, dd, J 9.6 and 3.5
Hz, CHCH$_3$H$_8$OBn), 3.86 (1H, dd, $J$ 9.6 and 4.4 Hz, CHCH$_3$H$_8$OBn), 2.81 (3H, s, oxazole-CH$_3$) and 2.71 (3H, s, oxazole-CH$_3$) ppm; $\delta$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$_4$O$_8$Na $[(M+Na)^+]$ requires 581.1648.

(S)-2-Benzylxy-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); [$\alpha$]$^\text{D}_{25}$ +21 ($c$ = 1.0, EtOH); $\nu_{\text{max}}$(solid)/cm$^{-1}$ 1733; $\delta$(360 MHz, CDCl$_3$ / CD$_3$OD (2:1)) 8.32 (2H, s, 2 $\times$ oxazole-H), 8.23 (1H, s, oxazole-H), 7.10–6.97 (5H, m, 5 $\times$ aryl-H), 5.13 (1H, br s, NH$_3$CH$_3$), 4.42 (1H, d, $J$ 12.2 Hz, OCH$_3$H$_8$Ph), 4.38 (1H, d, $J$ 12.2 Hz, OCH$_3$H$_8$Ph), 4.01–3.91 (2H, m, CH$_2$OBn) and 3.73 (3H, s, CO$_2$CH$_3$) ppm; $\delta$C(90 MHz, CDCl$_3$ / CD$_3$OD (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$_4$O$_6$ [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-silyloxy)-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 acetate (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-Benzylxocarbonylamino-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 (MgSO₄) 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); [α]D²⁻⁻ –30 (c = 2.0, CHCl₃); νmax(CHCl₃)/cm⁻¹ 3404, 2954, 1723, 1678 and 1599; δH(360 MHz, CDCl₃) 8.23 (1H, s, oxazole-H), 8.14 (1H, s, oxazole-H), 7.98 (1H, d, J 8.6 Hz, CONH), 7.43–7.30 (5H, m, 5 × aryl-H), 5.90 (1H, d, J 8.7 Hz, ZNH), 5.55–5.48 (1H, m, CONHCH), 5.20 (1H, d, J 12.2 Hz, CO₂CH₃H₆Ph), 5.15 (1H, d, J 12.2 Hz, CO₂CH₃H₆Ph), 5.08–4.99 (1H, m, ZNHCH), 4.33–4.25 (1H, m, CH₂H₆OH), 4.11–3.88 (6H, m, CH₂H₆OH, CH₂OTBS, CO₂CH₃), 3.42–3.34 (1H, m, OH), 0.82 (9H, s, SiC(CH₃)₃), 0.01 (3H, s, SiCH₃(CH₃)) and –0.02 (3H, s, SiCH₃(CH₃)) ppm; δC(90 MHz, CDCl₃) 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$_{4}$O$_{9}$Si [(M+H)$^+$] requires 589.2330.

2′′-[(S)-1-Benzylcarboxyldiamino-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); $[\alpha]_D^{19}$ −10 (c = 1.0, CHCl$_3$);
Found: C, 56.6; H, 5.6; N, 9.6%. C$_{27}$H$_{32}$N$_4$O$_8$Si requires C, 57.0; H, 5.7; N, 9.9%;

$\nu_{\text{max}}$(CHCl$_3$/cm$^{-1}$) 3437, 2954, 2869, 1726, 1654 and 1579; $\delta_{\text{H}}$(360 MHz, CDCl$_3$) 8.46 (1H, s, oxazole-H), 8.36 (2H, s, 2 $\times$ oxazole-H), 7.47–7.25 (5H, m, 5 $\times$ aryl-H), 5.82 (1H, d, $J$ 8.5 Hz, ZNH), 5.23–5.12 (3H, m, CO$_2$CH$_2$Ph, NHCHCH$_2$), 4.17 (1H, dd, $J$ 9.9 and 3.3 Hz, CHCH$_3$H$_6$OTBS), 4.06–3.96 (4H, m, CO$_2$CH$_3$, CHCH$_3$H$_6$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; $\delta_{\text{C}}$(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$_4$O$_8$Si [(M+Na)$^+$] requires 591.1887.

2''-[(S)-1-Amino-2-(tert-butyl-dimethyl-silanyloxy)-ethyl]-[2',4',2'';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 acetate (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); [$\alpha$]$^\text{D}$ $\text{H} = –7.1$ ($c = 1.0$, CHCl$_3$); $\nu_{\text{max}}$(CHCl$_3$/cm$^{-1}$) 3387, 3170, 2930, 1738, 1654 and 1579; $\delta_{\text{H}}$(360 MHz, CDCl$_3$) 8.42 (1H, s, oxazole-H), 8.32 (2H, s, 2 $\times$ oxazole-H), 4.23–4.18 (1H, m, NH$_2$CH), 3.98–3.92 (5H, m, CO$_2$CH$_3$, 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; $\delta_{\text{C}}$(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_{4}O_{6}Si [(M+H)^+] requires 435.1700.

2-[(1S,2R)-1-((2-[{(S)}-1-Benzyl oxy carbamyl amino]-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 (MgSO₄) 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; [α]₀²⁶° = -51 (c = 1.0, CHCl₃); ν_{max} (CHCl₃)/cm⁻¹ 3436, 3402, 1723, 1671 and 1634; δ_{H}(360 MHz, CDCl₃) 8.21 (1H, s, oxazole-H), 7.70 (1H, d, J 9.3 Hz, CONH), 7.42–7.29 (5H, m, 5 × aryl-H), 5.74 (1H, d, J 8.7 Hz, ZNH), 5.34 (1H, dd, J 9.3 and 2.5 Hz, CONHCH), 5.19 (1H, d, J 12.2 Hz, CO₂CH₃H₆Ph), 5.14 (1H, d, J 12.2 Hz, CO₂CH₃H₆Ph), 5.02–4.95 (1H, m, ZNHCH), 4.61 (1H, qd, J 6.4 and 2.5 Hz, CHCH(CH₃)OH), 4.04 (1H, dd, J 10.1 and 3.3 Hz, CHCH₃H₆OTBS), 3.97–3.89 (1H, m, CHCH₃H₆OTBS), 3.91 (3H, s, CO₂CH₃), 3.29 (1H,
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br s, O\text{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; $\delta$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$_4$O$_9$Si [(M+H)$^+$] requires 617.2643.

2''-[(S)-1-Benzoylcarbonylamino-2-(\textit{tert}-butyl-dimethyl-silanyloxy)-ethyl]-5',5''-dimethyl-[2,4';2',4'']teroxazole-4-carboxylic acid methyl ester (22b). Bis(2-methoxyethyl)amino sulfor 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 \textit{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 (MgSO₄) 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); $[α]_{D}^{22} -17 (c = 1.0, \text{CHCl}_3)$; $ν_{\text{max}}(\text{CHCl}_3)/\text{cm}^{-1}$ 3436, 2954, 1723, 1659 and 1582; δH(360 MHz, CDCl₃) 8.32 (1H, s, oxazole-H), 7.42–7.25 (5H, m, 5 × aryl-H), 5.80 (1H, d, $J$ 8.7 Hz, ZNH), 5.19 (1H, d, $J$ 12.2 Hz, CO₂CH₃H₅Ph), 5.15 (1H, d, $J$ 12.2 Hz, CO₂CH₃H₆Ph), 5.11–5.05 (1H, m, ZNHCH), 4.11 (1H, dd, $J$ 10.3 and 3.6 Hz, CH₃H₅OTBS), 3.98 (1H, dd, $J$ 10.3 and 4.3 Hz, CH₂H₆OTBS), 3.96 (3H, s, CO₂CH₃), 2.82 (3H, s, oxazole-CH₃), 2.72 (3H, s, oxazole-CH₃), 0.82 (9H, s, SiC(CH₃)₃), 0.00 (3H, s, SiCH₃(CH₃)) and –0.03 (3H, s, SiCH₃(CH₃)) ppm; δC(90 MHz, CDCl₃) 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, C₁₀H₁₀N₂O₈SiNa [(M+Na)+] requires 619.2200.

2''-[(S)-1-Benzylxycarbonylamino-2-(tern-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 (MgSO₄) 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); 
\([\alpha]_{D}^\text{24}\)  –21 (c = 1.0, CHCl₃); \(\nu_{\text{max}}(\text{CHCl}_3)/\text{cm}^{-1}\) 3437, 2929, 1716, 1661 and 1587; \(\delta_{\text{H}}(360\text{ MHz, CDCl}_3)\) 8.37 (1H, s, oxazole-H), 8.02 (1H, br s, CO₂H), 7.40–7.23 (5H, m, 5 × aryl-H), 5.95 (1H, d, \(J = 8.8 \text{ Hz, ZNH}\)), 5.21–5.05 (3H, m, CO₂CH₂Ph, ZNHC₃H), 4.09 (1H, dd, \(J = 10.2\) and 3.5 Hz, \(CH_3H_2OTBS\)), 3.97 (1H, dd, \(J = 10.2\) and 4.5 Hz, \(CH_3H_2OTBS\)), 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, SiCH₃(CH₃)) and –0.04 (3H, s, SiCH₃(CH₃)) ppm; \(\delta_{\text{C}}(90\text{ MHz, CDCl}_3)\) 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, \(C_{28}H_{34}N_{4}O_{8}SiNa [(M+Na)^+]\) 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 acetate (1:1) (150 mL). The filtrate was concentrated \textit{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-Benzzyloxycarbonylamino-2-hydroxy-ethyl)-oxazole-4-carbonyl]-amino}-2-\(\text{tert}\)-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; \([\alpha]_D^{19} -27 \ \text{(c = 1.0, CHCl}_3\); \(\nu\)\(_{\text{max}}\)(CHCl\(_3\))/cm\(^{-1}\) 3421, 2930, 1724, 1678 and 1598; \(\delta\)\(_{\text{H}}\)(360 MHz, CDCl\(_3\)) 8.19 (1H, s, oxazole-H), 8.09 (1H, s, oxazole-H), 7.96 (1H, d, \(J\) 8.5 Hz, CONH), 7.37–7.28 (5H, m, 5 × aryl-H), 6.05 (1H, d, \(J\) 8.5 Hz, ZNH), 5.46–5.39 (1H, m, CONHC), 5.16 (1H, d, \(J\) 12.2 Hz, OCH\(_3\)H\(_3\)Ph), 5.11 (1H, d, \(J\) 12.2 Hz, OCH\(_3\)H\(_3\)Ph), 5.08–4.99 (1H, m, ZNHCH), 4.17 (1H, dd, \(J\) 10.1 and 4.3 Hz, CH\(_3\)H\(_3\)OTBS), 4.09–3.89 (3H, m, CH\(_3\)H\(_3\)OTBS, CH\(_2\)OH), 3.88 (3H, s, CO\(_2\)CH\(_3\)), 3.12 (1H, br s, OH), 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; \(\delta\)\(_{\text{C}}\)(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_{4}O_{9}Si [(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; [α]_{D}^{18} +0.1 (c = 1.0, CHCl_{3}); ν_{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, CONH), 5.48–5.41 (1H, m, CONHCH), 4.18 (1H, dd, J 10.1 and 4.1 Hz, CH\textsubscript{a}H\textsubscript{b}OTBS), 4.18–4.10 (1H, m, NH\textsubscript{2}CH), 4.01 (1H, dd, J 10.1 and 4.9 Hz, CH\textsubscript{a}H\textsubscript{b}OTBS), 3.94 (1H, dd, J 11.0 and 4.4 Hz, CH\textsubscript{a}H\textsubscript{b}OH), 3.90 (3H, s, CO\textsubscript{2}CH\textsubscript{3}), 3.85 (1H, dd, J 11.0 and 6.2 Hz, CH\textsubscript{a}H\textsubscript{b}OH), 2.31 (3H, br s, NH\textsubscript{2}, OH), 0.83 (9H, s, SiC(CH\textsubscript{3})\textsubscript{3}), 0.02 (3H, s, SiCH\textsubscript{3}(CH\textsubscript{3})) and −0.02 (3H, s, SiCH\textsubscript{3}(CH\textsubscript{3})) ppm; δ_{C}(90 MHz, CDCl\textsubscript{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\textsubscript{19}H\textsubscript{30}N\textsubscript{4}O\textsubscript{7}SiNa [(M+Na)^{+}] requires 477.1781.
2-((S)-1-[[2-((S)-1-[[2''-(S)-2-Benzoxyl-1-benzyloxycarbonylamino-ethyl]-5',5''-dimethyl-[2',4',2″]-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 (MgSO₄) 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); [α]₀°ₐ –5 (c = 1.0, CHCl₃); νₛ макс(CHCl₃)/cm⁻¹ 3406, 2929, 1724, 1677 and 1596; δ₁₇(360 MHz, CDCl₃) 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 × CONH), 7.40–7.17 (10H, m, 10 × aryl-H), 5.87 (1H, d, J 8.4 Hz, ZNH, 5.53–5.41 (2H, m, 2 × CONHCH), 5.20–5.07 (3H, m, CO₂CH₂Ph, ZNHCH), 4.54 (1H, d, J 12.2 Hz, CH₂OCH₂H₂Ph), 4.48 (1H, d, J 12.2 Hz, CH₂OCH₃H₂Ph), 4.26–3.80 (6H, m, CH₂OTBS, CH₂OBn, CH₂OH), 3.88 (3H, s,
CO\textsubscript{2}CH\textsubscript{3}), 3.33 (1H, br s, OH), 2.74 (3H, s, oxazole-CH\textsubscript{3}), 2.68 (3H, s, oxazole-CH\textsubscript{3}), 0.80 (9H, s, SiC(CH\textsubscript{3})\textsubscript{3}), –0.01 (3H, s, SiCH\textsubscript{3}(CH\textsubscript{3})) and –0.03 (3H, s, SiCH\textsubscript{3}) ppm; δ\textsubscript{C}(90 MHz, CDCl\textsubscript{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\textsubscript{48}H\textsubscript{54}N\textsubscript{8}O\textsubscript{14}SiNa [(M+Na\textsuperscript{+})] requires 1017.3426.

2-[(S)-1-{{[2''''-(S)-2-Benzylxy-1-benzylxocarbonylamino-ethyl]-5''',5''''-dimethyl-[2,4'':2'',4''';2'',4'''';2'',4''''']quinqueoxazole-4-carbonyl]-amino}-2-(tert-butyl-dimethyl-silylxyloxy)-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\textsubscript{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 (MgSO₄) 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); [α]D° +28 (c = 1.0, CHCl₃); νmax(CHCl₃)/cm⁻¹ 3410, 2957, 1723, 1677 and 1596; δH(360 MHz, CDCl₃) 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, CONH), 7.41–7.19 (10H, m, 10 × aryl-H), 5.81 (1H, d, J 8.5 Hz, ZNH), 5.56–5.49 (1H, m, CONHCH), 5.21–5.09 (3H, m, CO₂CH₂Ph, ZNHCH), 4.55 (1H, d, J 12.2 Hz, CH₂OCH₃H₅Ph), 4.50 (1H, d, J 12.2 Hz, CH₂OCH₃H₅Ph), 4.20 (1H, dd, J 10.1 and 4.4 Hz, CH₃H₂OTBS), 4.06 (1H, dd, J 10.1 and 5.0 Hz, CH₃H₂OTBS), 3.98–3.91 (1H, m, CH₃H₂OBn), 3.93 (3H, s, CO₂CH₃), 3.84 (1H, dd, J 9.4 and 4.3 Hz, CH₃H₂OBn), 2.85 (3H, s, oxazole-CH₂), 2.72 (3H, s, oxazole-CH₃), 0.85 (9H, s, SiC(CH₃)₃), 0.04 (3H, s, SiCH₃(CH₃)) and 0.01 (3H, s, SiCH₃(CH₃)) ppm; δC(90 MHz, CDCl₃) 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_{9}O_{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 (MgSO₄) 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; ν<sub>max</sub>(CHCl₃)/cm⁻¹
3426, 2956, 1743 and 1682; δ<sub>H</sub>(360 MHz, CDCl₃) 7.14 (1H, d, J 7.4 Hz, CONH), 5.40
(1H, s, BocNH), 4.71–4.62 (1H, m, BocNHCH), 4.00–3.91 (2H, m, CH₂OH) 3.85 (2H, d,
J 5.8 Hz, BocNHCH₂), 3.79 (3H, s, CO₂CH₃) and 1.46 (9H, s, OC(CH₃)₃) ppm; δ<sub>C</sub>(90
MHz, CDCl₃) 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, C₁₁H₂₀N₂O₆Na [(M+Na)<sup>+</sup>] 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 (MgSO₄) 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 (MgSO₄) 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%. C₁₁H₁₆N₂O₅ requires C, 51.6; H, 6.3; N, 10.9%; ν_max(CHCl₃)/cm⁻¹ 3452, 2978, 1716 and 1589; δ_H(360 MHz, CDCl₃) 8.19 (1H,
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 (MgSO₄) 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%. C₁₀H₁₄N₂O₅ requires C, 49.6; H, 5.8; N, 11.6%; νmax(CHCl₃)/cm⁻¹ 3452, 3169, 2933, 1714 and 1592; δH(500 MHz, DMSO-d₆) 8.69 (1H, s, oxazole-H), 7.52 (1H, t, J 6.0 Hz, BocNH), 4.28 (2H, d, J 6.0 Hz, BocNHCH₂) and 1.40 (9H, s, OC(CH₃)₃) ppm; δC(125 MHz, DMSO-d₆) 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, C₁₀H₁₄N₂O₅Na [(M+Na)⁺] requires 265.0800.

(S)-2-Benzoyloxy-1-(4-methoxycarbonyloxazol-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); \(v_{\text{max}}(\text{CHCl}_3)/\text{cm}^{-1} 3172, 2872, 1732\) and 1588; \(\delta_{\text{H}}(360 \text{ MHz, CD}_{3}\text{OD}) 8.69\) (1H, s, oxazole-H), 7.40–7.28 (5H, m, 5 \times \text{aryl-H}), 4.69 (1H, d, \(J 12.0\) Hz, OCH\(_2\)Ph), 4.62 (1H, d, \(J 12.0\) Hz, OCH\(_3\)Ph), 4.11–4.04 (2H, m, CH\(_2\)OBn) and 3.93 (3H, s, CO\(_2\)C\(_3\)H\(_3\)) ppm; \(\delta_{\text{C}}(90 \text{ MHz, CDCl}_3) 162.6\) (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\(_2\)O\(_4\)Na \([\text{M+Na}^+]\) requires 299.1008.

2-[(\(S\)-1-Benzoxycarbonylamino-2-\((\text{tert-butyl-dimethyl-silanyloxy})\)-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 \textit{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\textsubscript{4}) and concentrated \textit{in vacuo}. The residue was purified by chromatography on silica gel using 3:1 petrol–ethyl acetate as eluent to give the \textit{oxazole} (1.0 g, 48%) as a colourless oil; $[\alpha]_{D}^{24} = -24$ ($c = 1.0$, CHCl\textsubscript{3}); $\nu_{\text{max}}$(CHCl\textsubscript{3})/cm\textsuperscript{-1} 3697, 3605, 3437, 2954 and 1723; $\delta_{H}$(360 MHz, CDCl\textsubscript{3}) 8.02–7.96 (2H, m, 2 $\times$ phenyloxazole-H), 7.50–7.28 (8H, m, 3 $\times$ phenyloxazole-H, 5 $\times$ aryl-H), 5.81 (1H, d, J 8.6 Hz, ZNH), 5.02–5.01 (3H, m, CO\textsubscript{2}CH\textsubscript{2}Ph, ZNHCH), 4.14 (1H, dd, J 10.2 and 3.4 Hz, CH\textsubscript{2}H\textsubscript{3}OTBS), 4.00 (1H, dd, J 10.2 and 4.3 Hz, CH\textsubscript{2}H\textsubscript{3}OTBS) 3.94 (3H, s, CO\textsubscript{2}CH\textsubscript{3}), 0.80 (9H, s, SiC(CH\textsubscript{3})\textsubscript{3}), –0.01 (3H, s, SiCH\textsubscript{3}(CH\textsubscript{3})) and –0.04 (3H, s, SiCH\textsubscript{3}(CH\textsubscript{3})) ppm; $\delta_{C}$(90 MHz, CDCl\textsubscript{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\textsubscript{27}H\textsubscript{34}N\textsubscript{2}O\textsubscript{6}SiNa [(M+Na)$^{+}$] requires 511.2264.

\textbf{2-[(S)-1-Amino-2-(\textit{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 \textbf{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 \textit{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; $[\alpha]_D^{11} = -30$ (c = 1.0, CHCl$_3$); $\nu_{\text{max}}$(CHCl$_3$)/cm$^{-1}$ 3698, 3388, 2954, 1723 and 1591; $\delta_{\text{H}}$(360 MHz, CDCl$_3$) 8.05–8.00 (2H, m, 2 $\times$ phenyloxazole-H), 7.49–7.42 (3H, m, 3 $\times$ phenyloxazole-H), 4.22 (1H, t, $J$ 5.2 Hz, NH$_2$C$_2$H), 3.98 (2H, d, $J$ 5.2 Hz, CH$_2$OTBS), 3.93 (3H, s, CO$_2$C$_3$H$_3$), 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; $\delta_{\text{C}}$(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$_2$O$_4$SiNa [(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 $\times$ 15 mL) and saturated sodium bicarbonate solution (15 mL), then dried (MgSO$_4$) and concentrated $\textit{in vacuo}$. 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); $[\alpha]_D^{10} +1.4$ (c = 1.0, CHCl$_3$); $\nu_{\text{max}}$(CHCl$_3$)/cm$^{-1}$ 3455, 3405, 2980, 1716, 1680 and 1599; $\delta_{\text{H}}$(360 MHz, CDCl$_3$) 8.19 (1H, s, oxazole-H), 8.16 (1H, s, oxazole-H), 7.36 (1H,
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$_3$); $\nu_{\text{max}}$(CHCl$_3$)/cm$^{-1}$ 3455, 3401, 2954, 1717, 1679 and 1599; $\delta$$_H$(360 MHz, CDCl$_3$) 8.24 (1H, s, oxazole-H), 8.13 (1H, s, oxazole-H), 8.11 (1H, obs d, J 8.5 Hz, CONH$_2$), 5.58–5.49 (2H, m, BocNH$_2$, CONHC$_2$H$_2$), 4.50–4.33 (2H, m, BocNHCH$_2$), 4.34 (1H, dd, J 11.7 and 4.4 Hz, CH$_2$H$_2$OH), 4.10 (1H, dd, J 11.7 and 4.0 Hz, CH$_2$H$_2$OH), 3.93 (3H, s, CO$_2$CH$_3$), 2.59 (1H, br s, OH) and 1.49 (9H, s, OC(CH$_3$)$_3$) ppm; $\delta$$_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 \textit{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 \textit{in vacuo} and the brown residue was triturated with methanol to leave the \textit{oxazole} (0.78 g, 57%) as a colourless solid; mp 247–251 °C; \( \nu_{\text{max}}(\text{CHCl}_3)/\text{cm}^{-1} \) 3455, 2932 and 1717; \( \delta_H(360 \text{ MHz, DMSO-}d_6) \) 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, BocNH), 4.36 (2H, d, \( J \) 6.0 Hz, BocNHCH\(_2\)), 3.87 (3H, s, CO\(_2\)CH\(_3\)) and 1.42 (9H, s, OC(CH\(_3\))\(_3\)) ppm; \( \delta_C(90 \text{ MHz, DMSO-}d_6) \) 162.7 (s), 161.2 (s), 155.9 (s), 155.3 (s),
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_{4}O_{7} requires C, 51.1; H, 4.3; N, 14.9%; ν_{max}(solid)/cm^{-1} 3357, 3137, 1693 and 1530; δH(360 MHz, CDCl₃ / DMSO-d₆ (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, BocNH), 4.35 (2H, d, J 5.9 Hz, BocNH₂) and 1.41 (9H, s, OC(C₃H₇)₃) ppm; δC(90 MHz, DMSO-d₆) 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_{4}O_{7}Na [(M+Na)^+] requires 399.0917.
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; δH(360 MHz, CDCl₃ / CD₃OD (1:1)) 10.06 (1H, d, J 7.3 Hz, CSNH), 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, CONHCH₂, CONH-(val), 3 × phenyloxazole-H), 6.59 (1H, d, J 8.7 Hz, BocNH), 6.09–5.89 (2H, m, CONHCH-(val), CSNHCH), 5.47–5.40 (1H, m, BocNHCH), 4.48–4.40 (2H, m, gly-CH₂), 4.13–4.00 (2H, m, CH₂OH), 3.80 (3H, s, CO₂CH₃), 2.03–1.87 (1H, m, CH), 1.75–1.61 (1H, m, CH), 1.36 (9H, s, OC(CH₃)₃), 1.16–0.97 (2H, m, CH₂) and 0.88–0.72 (12H, m, 3 × CH₃) 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 (MgSO₄) 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;
δH(360 MHz, DMSO-d₆) 9.80 (1H, d, J 7.1 Hz, CSNH), 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 ×
CONH), 5.90–5.83 (1H, m, CSNHCH), 5.33–5.28 (1H, m, CONHCH), 4.80–4.15 (5H,
m, CONHCH, CH₂OH, gly-CH₂), 2.13–1.98 (1H, m CH), 1.83–1.72 (1H, m, CH) and 0.97–0.70 (14H, m, CH₂, 3 × CH₃) 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 (MgSO₄) 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; δH(500 MHz, DMSO-d₆) 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.