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Supplementary Data

The Discovery of Allyltyrosine Based Tripeptides as Selective Inhibitors of the HIV-1 Integrase Strand-Transfer Reaction

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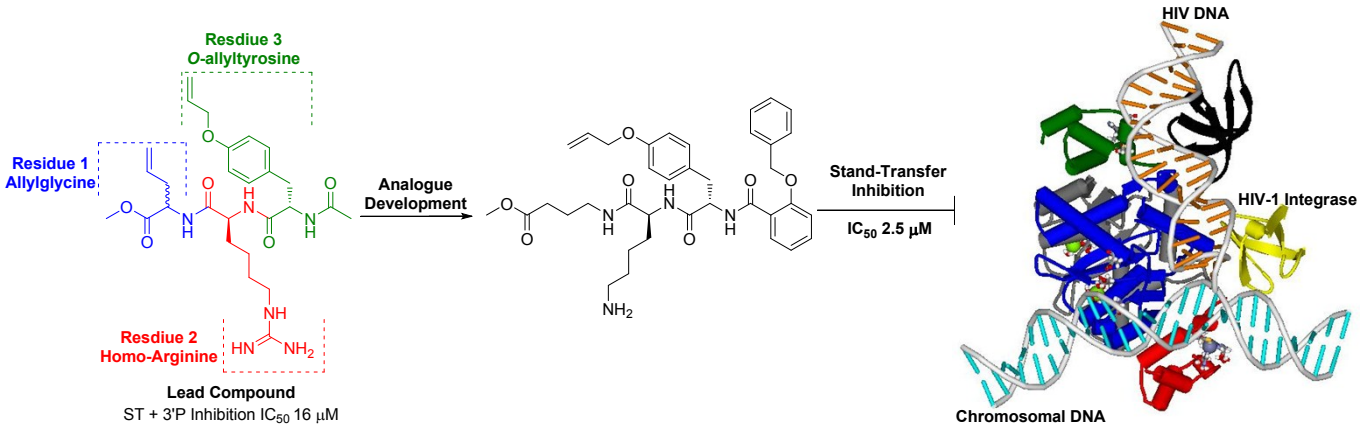


Compound Characterisation

Nomenclature - New compounds were named according to the following order of precedence acid > ester > amide; due to the frequent use of several carbamate protecting groups in the synthesis, for simplicity, this functionality was excluded from the naming hierarchy. The aza/oxo substitution method was then used, where the longest chain of the highest priority was found and the remaining functional groups named as substituents of that chain.

Methyl (*2S*,5*S*,8*S*)-2-allyl-8-(4-allyloxybenzyl)-3,6,9-triaza-5-(4-guanidinobutyl)-4,7,10-trioxoundecanoate hydrochloride (6)

Compound **17** (50 mg, 0.07 mmol) was converted to the uncharacterised *N*-Boc deprotected trifluoroacetate salt *via* procedure E and the resulting solid was then converted immediately, *via* procedure H to the hydrochloride salt **6** (35 mg, 0.06 mmol, 86%) as a hygroscopic light brown amorphous solid. MS (ESI$^+$), *m/z* 545 (100%) [MH$^+$], 446 (30), 273 (20). HRMS (ESI$^+$) calcd for $C_{27}H_{40}N_6O_6$ + H: 545.3088; found 545.3085. $[\alpha]_D^{25}$ +62.9 (*c*. 0.12, EtOH). ^{1}H NMR (300 MHz, CD_3OD): δ 8.25 (d, *J* = 7.8 Hz, 1H, NH); 8.14 (d, *J* = 6.9 Hz, 1H, NH); 7.15 (d, *J* = 8.7 Hz, 2H, 2′-CH and 6′-CH); 7.08 (d, *J* = 7.8 Hz, 1H, NH); 6.96 (d, *J* = 7.7 Hz, 1H, NH); 6.83 (d, *J* = 8.7 Hz, 2H, 3′-CH and 5′-CH); 6.04 (tdd, *J* = 17.3, 10.4, 5.2 Hz, 1H, $OCH_2C\underline{H}=CH_2$); 5.78 (tdd, *J* = 17.1, 10.1, 6.9 Hz, 1H, C-2$CH_2C\underline{H}=CH_2$); 5.38 (dd, *J* = 17.3, 1.7 Hz, 1H, $OCH_2CH=C\underline{H}H$ *trans*); 5.23 (dd, *J* = 10.6, 1.6 Hz, 1H, $OCH_2CH=CH\underline{H}$ *cis*); 5.14 (dd, *J* = 17.3, 1.5 Hz, 1H, $CHCH_2CH=C\underline{H}H$ *trans*); 5.09 (dd, *J* = 10.5, 1.5 Hz, 1H, $CHCH_2CH=CH\underline{H}$ *cis*); 4.55-4.45 (m, 3H, $OC\underline{H}_2CH=CH_2$ and 8-CH); 4.42-4.38 (m, 2H, 2-CH and 5-CH); 3.70 (s, 3H, OCH_3); 3.16 (t, *J* = 6.9 Hz, 2H, 4′′-CH_2); 3.03 (dd, *J* = 13.9, 5.8 Hz, 1H, 8-$CHC\underline{H}_aH_b$); 2.82 (dd, *J* = 13.9, 9.1 Hz, 1H, 8-$CHCH_a\underline{H}_b$); 2.55-2.47 (m, 2H, $CHC\underline{H}_2CH=CH_2$); 1.92 (s, 3H, 11-$CH_3$); 1.84-1.77 (m, 1H, 1′′-$C\underline{H}_aH_b$); 1.70-1.64 (m, 1H, 1′′-$CH_a\underline{H}_b$); 1.62-1.54 (m, 2H, 3′′-CH_2); 1.45-1.42 (m, 2H, 2′′-CH_2). ^{13}C NMR (75 MHz, CD_3OD): δ 172.7 (C-7); 172.6 (C-1); 172.3 (C-4); 172.2 (C-10); 157.8 (C-4′); 157.4 (C=N); 133.8 ($CHCH_2\underline{C}H=CH_2$); 133.0 ($OCH_2\underline{C}H=CH_2$); 130.0 (C-1′); 129.2 (C-2′ and C-6′); 117.7 ($OCH_2CH=\underline{C}H_2$); 116.2 ($CHCH_2CH=\underline{C}H_2$); 114.6 (C-3′ and C-5′); 68.6 ($O\underline{C}H_2CH=CH_2$); 55.5 (C-8); 52.7 (C-5); 52.5 (C-2); 51.5 (OCH_3); 41.1 (C-4′′); 36.6 (8-$CH\underline{C}H_2$); 35.5 ($CH\underline{C}H_2CH=CH_2$); 31.5 (C-1′′); 28.0 (C-3′′); 22.4 (C-11); 21.2 (C-2′′).

Ethyl (*S*)-2-(4-allyloxybenzyl)-3-aza-4-oxopentanoate (7)[1, 2]

Using procedure A and the commercially available (*S*)-*N*-acetyltyrosine ethyl ester monohydrate (2.60 g, 10.35 mmol), anhydrous potassium carbonate (3.20 g, 23.15 mmol), allyl bromide (3.0g, 24.80 mmol) and DMF (15 mL) as solvent, the ester **7** (2.74 g, 9.38 mmol, 97%) was obtained as a white solid, mp. 69-71°C. MS (CI + ve) *m/z* 292 (100%) [MH$^+$]. HRMS (ESI$^+$) calcd for $C_{16}H_{21}NO_4$ + H: 292.1543, found 292.1531. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.00 (d, *J* = 8.7 Hz, 2H, 2′-CH and 6′-CH); 6.83 (d, *J* = 8.7 Hz, 2H, 3′-CH and 5′-CH); 6.04 (tdd, *J* = 17.3, 10.5, 5.3 Hz, 1H, $OCH_2C\underline{H}=CH_2$); 5.91 (bs, 1H, 3-NH); 5.40 (dd, *J* = 17.3, 1.6 Hz, 1H, $OCH_2CH=C\underline{H}H$ *trans*); 5.28 (dd, *J* = 10.5, 1.4 Hz, 1H, $OCH_2CH=CH\underline{H}$ *cis*); 4.82 (td, *J* = 7.6, 5.6 Hz, 1H, 2-CH); 4.51 (d, *J* = 5.3 Hz, 2H, $OC\underline{H}_2CH=CH_2$); 4.17 (q, *J* = 7.1 Hz, 2H, $OC\underline{H}_2CH_3$); 3.06 (d, *J* = 5.4 Hz, 2H, 2-$CHC\underline{H}_2$); 1.99 (s, 3H, 5-CH_3); 1.25 (t, *J* = 7.1 Hz, 3H, $OCH_2C\underline{H}_3$). ^{13}C NMR (75 MHz, $CDCl_3$): δ 172.0 (C-1); 169.9 (C-4); 157.9 (C-4′); 133.5 ($OCH_2\underline{C}H=CH_2$); 130.5 (C-2′ and C-6′); 128.3 (C-1′); 117.9 ($OCH_2CH=\underline{C}H_2$); 115.7 (C-3′ and C-6′); 69.0 ($O\underline{C}H_2CH=CH_2$); 61.7 ($O\underline{C}H_2CH_3$); 53.5 (C-2); 37.3 (2-$CH\underline{C}H_2$); 23.3 (C-5); 14.4 ($OCH_2\underline{C}H_3$).

(*S*)-2-(4-Allyloxybenzyl)-3-aza-4-oxopentanoic acid (10)[1, 2]

This compound was synthesised using procedure C, from the ester **7** (2.71 g, 9.31 mmol) in THF/water 3:1 (80mL) with $LiOH.H_2O$ (837 mg, 19.35 mmol) to yield **10** (2.07 g, 7.86 mmol, 84%) as white granular crystals, mp.175-178°C. MS (ESI$^-$), *m/z* 261 (20%) [M - H$^+$], 114 (25), 112 (100). HRMS (ESI$^-$) calcd for $C_{14}H_{17}NO_4$ - H: 262.1085; found 262.1078. ^{1}H NMR (300 MHz, $(CD_3)_2CO$): δ 7.25 (bs, 1H, 3-NH); 7.03 (d, *J* = 8.7 Hz, 2H, 2′-CH and 6′-CH); 6.81 (d, *J* = 8.7 Hz, 2H, 3′-CH and 5′-CH); 6.01 (tdd, *J* = 17.3, 10.6, 5.3 Hz, 1H, $OCH_2C\underline{H}=CH_2$); 5.37 (dd, *J* = 17.3, 1.6 Hz, 1H, $OCH_2CH=C\underline{H}H$ *trans*); 5.25 (dd, *J* = 10.5, 1.4 Hz, 1H, $OCH_2CH=CH\underline{H}$ *cis*); 4.75-4.70 (m, 1H, 2-CH); 4.47 (ddd, *J* = 5.3, 1.5, 1.5 Hz, 2H, $OC\underline{H}_2CH=CH_2$); 3.11 (dd, *J* = 14.1, 5.6 Hz, 1H, 2-$CHC\underline{H}_aH_b$); 3.01 (dd, *J* = 14.1, 5.9 Hz, 1H, 2-$CHCH_a\underline{H}_b$); 1.95 (s, 3H, 5-CH_3). ^{13}C NMR (75 MHz, $(CD_3)_2CO$): δ 172.5 (C-1); 169.7 (C-4); 157.8 (C-4′); 134.2 ($OCH_2\underline{C}H=CH_2$); 130.5 (C-2′ and C-6′); 129.6 (C-1′); 116.6 ($OCH_2CH=\underline{C}H_2$); 114.6 (C-3′ and C-6′); 68.5 ($O\underline{C}H_2CH=CH_2$); 53.9 (C-2); 36.7 (2-$CH\underline{C}H_2$); 22.0 (C-5).

Methyl (2*S*,5*S*)-5-(4-allyloxybenzyl)-3,6-diaza-2-[4-(*tert*-butoxycarbonyl)aminobutyl]-4,7-dioxooctanoate (12)

The ester was synthesised using procedure D from the acid **10** (330 mg, 1.25 mmol), the commercially available methyl (*S*)-2-amino-6-(*tert*-butoxycarbonylamino)hexanoate hydrochloride **11** (330 mg, 1.12 mmol), EDCI (240 mg, 1.26 mmol), HOBt (170 mg, 1.26 mmol), DIPEA (0.20 mL, 1.15 mmol) and DMF (3 mL) as the solvent. The reaction mixture was allowed to stir for 14 h before being quenched to yield **12** (530 mg, 1.05 mmol, 94%) as an off-white powder, mp. 102-105°C. MS (ESI$^+$), *m/z* 506 (100%) [MH$^+$], 528 (40) [M + Na$^+$], 450 (20), 406 (55). HRMS (ESI$^+$) calcd for $C_{26}H_{39}N_3O_7$ + Na: 528.2686; found: 528.2690. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.11 (d, *J* = 8.5 Hz, 2H, 2′-CH and 6′-CH); 6.82 (d, *J* = 8.5 Hz, 2H, 3′-CH and 5′-CH); 6.59 (d, *J* = 6.7 Hz, 1H, 3-NH); 6.04 (tdd, *J* = 16.9, 10.5, 5.3 Hz, 1H, $OCH_2C\underline{H}=CH_2$); 5.40 (dd *J* = 17.3, 1.5 Hz, 1H, $OCH_2CH=C\underline{H}H$ *trans*); 5.27 (dd, *J* = 10.5, 1.3 Hz, 1H, $OCH_2CH=CH\underline{H}$ *cis*); 4.95 (bs, 1H, 5-CH); 4.76-4.68 (m, 1H, 2-CH); 4.50 (bd, *J* = 5.3 Hz, 2H, $OC\underline{H}_2CH=CH_2$); 3.70 (s, 3H, OCH_3); 3.10-2.90 (m, 6H, 5-$CHC\underline{H}_2$, 4′′-CH_2, 6-NH and 4′′-$CH_2N\underline{H}$); 1.96 (s, 3H, 8-CH_3); 1.86-1.71 (m, 1H, 1′′-$C\underline{H}_aH_b$); 1.67-1.58 (m, 1H, 1′′-$CH_a\underline{H}_b$); 1.49-1.37 (m, 11H, $OC(C\underline{H}_3)_3$ and 3′′-CH_2); 1.27 (m, 2H, 2′′-CH_2). ^{13}C NMR (75 MHz, $CDCl_3$): δ 172.4 (C-4); 171.5 (C-1); 170.5 (C-7); 157.8 (C-4′); 156.3 ($NH\underline{C}OOC(CH_3)_3$); 133.5 ($OCH_2\underline{C}H=CH_2$); 130.5 (C-1′); 128.9 (C-2′ and C-6′); 117.8 ($OCH_2CH=\underline{C}H_2$); 115.0 (C-3′ and C-5′); 79.3 ($COO\underline{C}(CH_3)_3$); 69.0 ($O\underline{C}H_2CH=CH_2$); 54.7 (C-5); 52.5 (C-2); 52.4 (OCH_3); 40.3 (C-4′′); 37.6 (5-$CH\underline{C}H_2$); 32.0 (C-1′′); 29.6 (C-3′′); 28.7 ($OC(\underline{C}H_3)_3$); 23.2 (C-8); 22.7 (C-2′′).

(2*S*,5*S*)-5-(4-Allyloxybenzyl)-3,6-diaza-2-[4-(*tert*-butoxycarbonyl)aminobutyl]-4,7-dioxooctanoic acid (13)

The acid **58** was synthesised using procedure C from the ester **12** (1.54 g, 3.05 mmol), $LiOH.H_2O$ (256 mg, 6.1 mmol) and THF/water 3:1 (80 mL). The reaction was stirred for 14 h before being quenched with water (25 mL). Unreacted starting

materials were extracted using CH_2Cl_2 (30 mL) then EtOAc (30 mL). After the aqueous solution was acidified the product was extracted with CH_2Cl_2 (2 x 30 mL) and EtOAc (2 x 30 mL), the combined organic fractions were dried and evaporated to yield the acid **13** (1.29 g, 2.63 mmol, 86%) as white crystals, mp. 62-66°C. MS (ESI^+), *m/z* 492 (100%) [MH^+], 436 [MH^+ - $OCH_2CH=CH_2$] (25), 392 [MH^+ - Boc] (70). HRMS (ESI^+) calcd for $C_{25}H_{37}N_3O_7$ + H: 492.2704; found 492.2715. ^{1}H NMR (300 MHz, $(CD_3)_2CO$): δ 7.15 (d, *J* = 8.7 Hz, 2H, 2′-CH and 6′-CH); 6.81 (d, *J* = 8.7 Hz, 2H, 3′-CH and 5′-CH); 6.01 (tdd, *J* = 17.2, 10.5, 5.2 Hz, 1H, $OCH_2C\underline{H}=CH_2$); 5.36 (dd, *J* = 17.3, 1.7 Hz, 1H, $OCH_2CH=C\underline{H}H$ *trans*); 5.19 (dd, *J* = 10.6, 1.5 Hz, 1H, $OCH_2CH=CH\underline{H}$ *cis*); 4.61 (dd, *J* = 8.9, 5.2 Hz, 1H, 5-CH); 4.48 (d, *J* = 5.2, Hz, 2H, $OC\underline{H}_2CH=CH_2$); 4.41-4.33 (m, 1H, 2-CH); 3.07 (dd, *J* = 14.1, 5.1 Hz, 1H, 5-$CHC\underline{H}_aH_b$); 3.01 (t, *J* = 6.8 Hz, 2H, 4′′-CH_2); 2.78 (dd, *J* = 14.0, 8.9 Hz, 1H, 5-$CHCH_a\underline{H}_b$); 1.86 (s, 3H, 8-CH_3); 1.83-1.79 (m, 1H, 1′′-$C\underline{H}_aH_b$); 1.72-1.68 (m, 1H, 1′′-$CH_a\underline{H}_b$); 1.43-1.31 (m, 13H, $OC(CH_3)_3$, 3′′-CH_2 and 2′′-CH_2). ^{13}C NMR (75 MHz, $(CD_3)_2CO$): δ 175.3 (C-1); 174.1 (C-4); 174.0 (C-7); 159.6 (C-4′); 157.8 ($NH\underline{C}OOC(CH_3)_3$); 135.9 ($OCH_2\underline{C}H=CH_2$); 132.2 (C-1′), 131.4 (C-2′ and C-6′), 118.2 ($OCH_2CH=\underline{C}H_2$); 116.4 (C-3′ and C-5′); 80.2 ($COO\underline{C}(CH_3)_3$); 70.4 ($O\underline{C}H_2CH=CH_2$); 56.7 (C-5); 54.2 (C-2); 41.9 (C-4′′); 38.8 (5-$CH\underline{C}H_2$); 33.3 (C-1′′); 31.3 (C-3′′); 29.6 ($OC(\underline{C}H_3)_3$); 24.8 (C-8); 23.4 (C-2′′).

Methyl (*S*)-2-amino-4-pentenoate hydrochloride (14)[3, 4]

Using procedure B, the commercially available (*S*)-allylglycine (**15**) (600 mg, 5.21 mmol) and $SOCl_2$ (1.25 mL, 17.21 mmol), the salt **14** (850 mg, 5.13 mmol, 98%) was obtained as an off-white solid. MS (ESI^+), *m/z* 130 (100%) [MH^+]. HRMS (ESI^+) calcd for $C_6H_{11}NO_2$ + H: 130.0863; found 130.0867. ^{1}H NMR (300 MHz, CD_3OD): δ 5.95-5.79 (m, 1H, $CH_2C\underline{H}=CH_2$); 5.32 (bd, *J* = 16.8 Hz, 1H, $CH_2CH=C\underline{H}H$ *trans*); 5.25 (bd, *J* = 9.9 Hz, 1H, $CH_2CH=CH\underline{H}$ *cis*); 4.30 (bs, 1H, 2-CH); 3.81 (s, 3H, OCH_3); 2.86 (bs, 2H, $CHC\underline{H}_2CH=CH_2$). ^{13}C NMR (75 MHz, CD_3OD): δ 171.6 (C-1); 132.4 ($CH_2\underline{C}H=CH_2$); 119.5 ($CH_2CH=\underline{C}H_2$); 52.7 (C-2); 52.1 (OCH_3); 36.4 ($CH\underline{C}H_2CH=CH_2$).

Methyl (2*S*,5*S*,8*S*)-2-allyl-8-(4-allyloxybenzyl)-3,6,9-triaza-5-[4-(tert-butoxycarbonyl)aminobutyl]-4,7,10-trioxoundecanoate (16)[1]

The ester **16** was synthesised using procedure D from the acid **13** (200 mg, 0.41 mmol), the amine hydrochloride (14) (87 mg, 0.53 mmol), EDCI (116 mg, 0.61 mmol), HOBt (62 mg, 0.46 mmol), DIPEA (0.10 mL, 0.57 mmol) and DMF (3 mL) as the solvent, to yield **16** (129 mg, 0.21 mmol, 51%) as an off-white powder, mp. 148-151°C. MS (ESI^+), *m/z* 603 (100%) [MH^+]. HRMS (ESI^+) calcd for $C_{31}H_{46}N_4O_8$ + H: 603.3388; found 603.3400. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.07 (d, *J* = 8.6 Hz, 2H, 2′-CH and 6′-CH); 6.97 (d, *J* = 6.4 Hz, 1H, 3-NH); 6.80 (d, *J* = 8.6 Hz, 2H, 3′-CH and 5′-CH); 6.60 (d, *J* = 7.2 Hz, 1H, 9-NH); 6.03 (tdd, *J* = 17.1, 10.6, 5.3 Hz, 1H, $OCH_2C\underline{H}=CH_2$); 5.69 (tdd, *J* = 14.5, 9.7, 7.1 Hz, 1H, $CHCH_2C\underline{H}=CH_2$); 5.39 (dd, *J* = 17.3, 1.5 Hz, 1H, $OCH_2CH=C\underline{H}H$ *trans*); 5.26 (dd, *J* = 10.5, 1.4 Hz, 1H, $OCH_2CH=CH\underline{H}$ *cis*); 5.18-4.98 (m, 2H, $CHCH_2CH=C\underline{H}_2$); 4.93 (bs, 1H, 4′′-$CH_2N\underline{H}$); 4.78-4.72 (m, 1H, 8-CH); 4.61-4.58 (m, 1H, 2-CH); 4.55-4.45 (m, 2H, $OC\underline{H}_2CH=CH_2$, 5-NH and 5-CH); 3.74 (s, 3H, OCH_3); 3.08-2.88 (m, 4H, 4′′-CH_2 and 8-$CHC\underline{H}_2$); 2.62-2.42 (m, 2H, $CHC\underline{H}_2CH=CH_2$); 1.98 (s, 3H, 11-$CH_3$); 1.82-1.77 (m, 1H, 1′′-$C\underline{H}_aH_b$); 1.63-1.58 (m, 1H, 1′′-$CH_a\underline{H}_b$); 1.46-1.40 (m, 11H, $OC(CH_3)_3$ and 3′′-CH_2); 1.33-1.27 (m, 2H, 2′′-CH_2). ^{13}C NMR (75 MHz, $CDCl_3$): δ 171.9 (C-7), 171.2 (C-1), 171.1 (C-4), 170.0 (C-10); 157.8 (C-4′); 156.1 ($NH\underline{C}OOC(CH_3)_3$); 133.5 (C-2$CH_2\underline{C}H=CH_2$); 132.4 ($OCH_2\underline{C}H=CH_2$); 130.4 (C-2′ and C-6′); 128.7 (C-1′); 119.5 ($CHCH_2CH=\underline{C}H_2$); 117.9 ($OCH_2CH=\underline{C}H_2$); 115.0 (C-3′ and C-5′); 79.3 ($COO\underline{C}(CH_3)_3$); 69.0 ($O\underline{C}H_2CH=CH_2$); 54.6 (C-8); 52.7 (C-2); 52.6 (C-5); 52.1 (OCH_3); 40.3 (C-4′′); 37.6 (8-$CH\underline{C}H_2$); 36.4 ($CH\underline{C}H_2CH=CH_2$); 32.4 (C-1′′); 29.7 (C-3′′); 28.7 ($OC(\underline{C}H_3)_3$); 23.3 (C-11); 22.5 (C-2′′).

Methyl (2*S*,5*S*,8*S*)-2-allyl-8-(4-allyloxybenzyl)-3,6,9-triaza-5-[4-(*N*,*N*-di-tert-butoxycarbonyl)guanidinobutyl]-4,7,10-trioxoundecanoate (17)[1]

Starting with the ester **16** (106 mg, 0.18 mmol), procedure E was used to obtain the *N*-Boc deprotected trifluoroacetate salt. The salt was then carried forward (assuming 100% yield) for use in procedure G, along with $(BocNH)_2C=NSO_2CF_3$ (82 mg, 0.21 mmol) and NEt_3 (0.10 mL, 0.72 mmol) to yield **17** (80 mg, 0.11 mmol, 61%) as a white powder, mp. 112-115°C. MS (ESI^+), *m/z* 745 (100%) [MH^+]. HRMS (ESI^+) calcd for $C_{37}H_{56}N_6O_{10}$ + H: 745.4131; found 745.4142. ^{1}H NMR (300 MHz, $CDCl_3$): δ 11.45 (bs, 1H, $N\underline{H}COOC(CH_3)_3$); 8.26 (bs, 1H, 4′′-$CH_2N\underline{H}$); 7.07 (d, *J* = 8.6 Hz, 2H, 2′-CH and 6′-CH); 7.01 (d, *J* = 7.9 Hz, 1H, 5-NH); 6.85 (d, *J* = 8.4 Hz, 1H, 3-NH); 6.81 (d, *J* = 6.7 Hz, 2H, 3′-CH and 5′-CH); 6.59 (d, *J* = 7.8 Hz, 1H, 9-NH); 6.04 (tdd, *J* = 17.2, 10.5, 5.3 Hz, 1H, $OCH_2C\underline{H}=CH_2$); 5.79-5.69 (m, 1H, $CHCH_2C\underline{H}=CH_2$); 5.40 (dd, *J* = 17.2, 1.5 Hz, 1H, $OCH_2CH=C\underline{H}H$ *trans*); 5.27 (dd, *J* = 10.5, 1.2 Hz, 1H, $OCH_2CH=CH\underline{H}$ *cis*); 5.15-5.13 (m, 1H, $CHCH_2CH=C\underline{H}H$ *trans*); 5.11-5.09 (m, 1H, $CHCH_2CH=CH\underline{H}$ *cis*); 4.73-4.69 (m, 1H, 8-CH); 4.59-4.55 (m, 1H, 2-CH); 4.49 (d, *J* = 5.3 Hz, 2H, $OC\underline{H}_2CH=CH_2$); 4.47-4.43 (m, 1H, 5-CH); 3.74 (s, 3H, OCH_3); 3.33 (bs, 2H, 4′′-CH_2); 3.03-2.94 (m, 2H, 8-$CHC\underline{H}_2$); 2.55-2.49 (m, 2H, $CHC\underline{H}_2CH=CH_2$); 1.98 (s, 3H, 11-$CH_3$); 1.86-1.78 (m, 1H, 1′′-$C\underline{H}_aH_b$); 1.68-1.62 (m, 1H, 1′′-$CH_a\underline{H}_b$); 1.58-1.54 (m, 2H, 3′′-CH_2); 1.49 (s, 18H, $NHCOOC(C\underline{H}_3)_3$ and $C=NCOOC(C\underline{H}_3)_3$); 1.37-1.33 (m, 2H, 2′′-CH_2). ^{13}C NMR (75 MHz, $CDCl_3$): δ 172.2 (C-4); 171.5 (C-1); 171.2 (C-10); 171.0 (C-7); 163.5 (N=C); 157.8 (C-4′); 156.4 ($NH\underline{C}OOC(CH_3)_3$); 153.5 ($N\underline{C}OOC(CH_3)_3$); 133.6 (C-2$CH_2\underline{C}H=CH_2$); 132.5 ($OCH_2\underline{C}H=CH_2$); 130.2 (C-2′ and C-6′); 128.6 (C-1′); 119.3 ($CHCH_2CH=\underline{C}H_2$); 117.8 ($OCH_2CH=\underline{C}H_2$); 115.0 (C-3′ and C-5′); 83.5 ($NCOO\underline{C}(CH_3)_3$); 79.8 ($NHCOO\underline{C}(CH_3)_3$); 69.0 ($O\underline{C}H_2CH=CH_2$); 54.7 (C-8); 52.5 (C-2 and C-5); 52.3 (OCH_3); 40.6 (C-4′′); 37.4 (8-$CH\underline{C}H_2$); 36.2 ($CH\underline{C}H_2CH=CH_2$); 32.0 (C-1′′); 29.2 (C-3′′); 28.5 ($NHCOOC(\underline{C}H_3)_3$[a]); 28.4 ($NCOOC(\underline{C}H_3)_3$[a]); 23.3 (C-11); 22.7 (C-2′′).

Methyl (2*S*,5*S*)-5-(4-allyloxybenzyl)-3,6-diaza-2-(4-guanidinobutyl)-4,7-dioxooctanoate hydrochloride (18)

Compound **26** (137 mg, 0.21 mmol) was converted to the *N*-Boc deprotected trifluoroacetate salt *via* procedure E, and the resulting solid was then converted, *via* procedure H, to the hydrochloride salt **18** (80 mg, 0.17 mmol, 81%) as a hygroscopic brown amorphous solid. MS (ESI^+), *m/z* 448 (100%) [MH^+], HRMS (ESI^+) calcd for $C_{22}H_{33}N_5O_5$ + H: 448.2560; found 448.2558. $[\alpha]_D^{25}$ +19.2 (*c*. 0.08, EtOH). ^{1}H NMR (300 MHz, CD_3OD): δ 7.18 (d, *J* = 8.5 Hz, 2H, 2′-CH and 6′-CH); 6.84 (d, *J* = 8.5 Hz, 2H, 3′-CH and 5′-CH); 6.04 (tdd, *J* = 17.2, 10.4, 5.1 Hz, 1H, $OCH_2C\underline{H}=CH_2$); 5.38 (dd, *J* = 17.3, 1.6 Hz, 1H, $OCH_2CH=C\underline{H}H$ *trans*); 5.22 (dd, *J* = 10.6, 1.5 Hz, 1H, $OCH_2CH=CH\underline{H}$ *cis*); 4.60 (dd, *J* = 9.1, 5.7 Hz, 1H, 5-CH); 4.50 (bd, *J* = 5.1 Hz, 2H, $OC\underline{H}_2CH=CH_2$); 4.41 (dd, *J* = 9.2,

4.7 Hz, 1H, 2-CH); 3.68 (s, 3H, OCH_3); 3.17 (t, *J* = 6.7 Hz, 2H, 4''-CH_2); 3.08 (dd, *J* = 14.0, 5.6 Hz, 1H, 5-CHCH_aH_b); 2.84 (dd, *J* = 13.9, 9.2 Hz, 1H, 5-CHCH_aH_b); 1.98 (s, 3H, 8-CH_3); 1.91-1.79 (m, 1H, 1''-CH_aH_b); 1.79-1.67 (m, 1H, 1''-CH_aH_b); 1.59 (bs, 2H, 3''-CH_2); 1.45 (bs, 2H, 2''-CH_2). ^{13}C NMR (75 MHz, CD_3OD): δ 172.7 (C-1); 172.5 (C-4 and C -7); 157.8 (C-4'); 157.5 (C=N); 133.9 ($OCH_2CH=CH_2$); 130.2 (C-2' and C-6'); 129.2 (C-1'); 116.3 ($OCH_2CH=CH_2$); 114.6 (C-3' and C-5'); 68.6 ($OCH_2CH=CH_2$); 55.5 (C-5); 52.2 (C-2); 51.7 (OCH_3); 41.1 (C-4''); 36.8 (5-CHCH_2); 30.9 (C-1''); 28.0 (C-3''); 22.6 (C-8); 21.2 (C-2'').

***N*-{(1*S*,4*S*)-1-(4-Allyloxybenzyl)-4-[*N*-(4-amidino)piperazinyl]carbonyl-3-aza-8-guanidino-2-oxooctyl}acetamide dihydrochloride (19)**

Compound **36** (100 mg, 0.11 mmol) was converted to the *N*-Boc deprotected trifluoroacetate salt *via* procedure E, and the resulting solid was then converted *via* procedure H to give the hydrochloride salt **19** (58 mg, 0.09 mmol, 86%) as a hygroscopic light brown amorphous solid. MS (ESI^+), *m/z* 544 (5%) [MH^+], 520 (10), 519 (25), 460 (5), 459 (10), 273 (100). HRMS (ESI^+) calcd for $C_{26}H_{41}N_9O_4$ + H: 544.3360; found 544.3350. $[\alpha]_D^{25}$ -73.0 (*c*. 0.11, EtOH). ^{1}H NMR (300 MHz, CD_3OD): δ 7.17 (d, *J* = 8.2 Hz, 2H, 2'-CH and 6'-CH); 6.84 (d, *J* = 8.2 Hz, 2H, 3'-CH and 5'-CH); 6.04 (tdd, *J* = 15.5, 10.2, 5.0 Hz, 1H, $OCH_2CH=CH_2$); 5.38 (dd, *J* = 17.2, 1.1 Hz, 1H, $OCH_2CH=CHH$ *trans*); 5.23 (dd, *J* = 10.4, 0.8 Hz, 1H, $OCH_2CH=CHH$ *cis*); 4.77 (bs, 1H, 1-CH); 4.54 (bs, 1H, 4-CH); 4.50 (d, *J* = 4.9 Hz, 2H, $OCH_2CH=CH_2$); 3.80-3.39 (m, 8H, 2''-CH_2, 3''-CH_2, 5''-CH_2 and 6''-CH_2); 3.17 (bs, 2H, 8-CH_2); 3.03 (dd, *J* = 13.6, 5.7 Hz, 1H, 1-CHCH_aH_b); 2.84 (dd, *J* = 14.0, 9.0 Hz, 1H, 1-CHCH_aH_b); 1.93 (s, 3H, $COCH_3$); 1.70 (bs, 1H, 5-CH_2); 1.60 (bs, 2H, 7-CH_2); 1.43 (bs, 2H, 6-CH_2). ^{13}C NMR (75 MHz, CD_3OD): δ 172.6 (C-2); 172.2 ($COCH_3$); 170.9 (4-CHCO); 157.8 (C-4'); 157.4 (NHC=NH); 157.1 (NC=NH); 133.8 ($OCH_2CH=CH_2$); 130.1 (C-2' and C-6'); 129.3 (C-1'); 116.3 ($OCH_2CH=CH_2$); 114.5 (C-3' and C-5'); 68.6 ($OCH_2CH=CH_2$); 55.4 (C-1); 49.1 (C-4); 45.3 (C-3'' and C-5''); 44.2 (C-2'' and C-6''); 41.1 (C-8); 36.6 (1-CHCH_2); 31.2 (C-5); 28.2 (C-7); 22.4 (COCH_3); 21.3 (C-6).

***N*-{(1*S*,4*S*)-1-(4-Allyloxybenzyl)-3-aza-8-guanidino-4-[*N*-(4-guanidino)piperidinyl]carbonyl-2-oxooctyl}acetamide dihydrochloride (20)**

Compound **37** (100 mg, 0.10 mmol) was converted to the *N*-Boc deprotected trifluoroacetate salt *via* procedure E, and the resulting solid was then transformed *via* procedure H to the hydrochloride salt **20** (49 mg, 0.08 mmol, 78%) as a hygroscopic brown amorphous solid. MS (ESI^+), *m/z* 558 (5%) [MH^+], 467 (10), 466 (17), 280 (100). HRMS (ESI^+) calcd for $C_{27}H_{43}N_9O_4$ + H: 558.3516; found 558.3519. $[\alpha]_D^{25}$ +16.4 (*c*. 0.12, EtOH). ^{1}H NMR (300 MHz, CD_3OD): δ 7.17 (d, *J* = 7.6 Hz, 2H, 2'-CH and 6'-CH); 6.84 (d, *J* = 5.2 Hz, 2H, 3'-CH and 5'-CH); 6.08-5.94 (m, 1H, $OCH_2CH=CH_2$); 5.37 (bd, *J* = 17.3 Hz, 1H, $OCH_2CH=CHH$ *trans*); 5.22 (bd, *J* = 10.3 Hz, 1H, $OCH_2CH=CHH$ *cis*); 4.50 (bd, *J* = 4.4 Hz, 2H, $OCH_2CH=CH_2$); 4.42 (d, *J* = 13.5 Hz, 1H, 1-CH); 4.31 (d, *J* = 13.5 Hz, 1H, 1H, 4-CH); 4.13-3.89 (m, 2H, 2''-CH_aH_b and 6''-CH_aH_b); 3.77-3.57 (m, 1H, 4''-CH); 3.17 (m, 4H, 1-CHCH_2 and 8-CH_2); 3.11- 2.77 (m, 2H, 2''-CH_aH_b and 6''-CH_aH_b); 1.98-1.89 (m, 7H, $COCH_3$, 3''-CH_2 and 5''-CH_2); 1.75-1.49 (m, 4H, 5-CH_2 and 7-CH_2); 1.41 (m, 2H, 6-CH_2). ^{13}C NMR (75 MHz, CD_3OD): δ 172.5 (4-CHCO); 172.4 (C-2); 170.5 ($COCH_3$); 157.8 (C-4'); 157.4 (8-CH_2NHC=NH); 156.6 (4''-CH_2NHC=NH); 133.9 ($OCH_2CH=CH_2$); 130.1 (C-2' and C-6'); 129.4 (C-1'); 116.3 ($OCH_2CH=CH_2$); 114.6 (C-3' and C-5'); 68.6 ($OCH_2CH=CH_2$); 55.5 (C-1); 49.0 (C-4); 44.3 (C-4''); 43.9 (C-2'' and C-6''); 41.1 (C-8); 36.7 (1-CHCH_2); 32.1 (C-3'' and C-5''); 31.4 (C-5); 28.3 (C-7); 22.5 (COCH_3); 21.4 (C-5).

Methyl (5*S*,8*S*)-8-(4-allyloxybenzyl)-3,6,9-triaza-5-(4-guanidinobutyl)-4,7,10-trioxoundecanoate hydrochloride (21)

Compound **38** (98 mg, 0.14 mmol) was converted to the uncharacterised *N*-Boc deprotected trifluoroacetate salt *via* procedure E and the resulting solid was then converted, *via* procedure H to the hydrochloride salt **21** (62 mg, 0.12 mmol, 83%) as a hygroscopic light brown amorphous solid. MS (ESI^+), *m/z* 505 (100%) [MH^+], 506 (50). HRMS (ESI^+) calcd for $C_{24}H_{36}N_6O_6$ + H: 505.2775; found 505.2763. $[\alpha]_D^{25}$ +22.6 (*c*. 0.10, EtOH). ^{1}H NMR (300 MHz, CD_3OD): δ 7.17 (d, *J* = 8.6 Hz, 2H, 2'-CH and 6'-CH); 6.84 (d, *J* = 8.6 Hz, 2H, 3'-CH and 5'-CH); 6.04 (tdd, *J* = 17.2, 10.4, 5.2 Hz, 1H, $OCH_2CH=CH_2$); 5.38 (dd, *J* = 17.3, 1.6 Hz, 1H, $OCH_2CH=CHH$ *trans*); 5.23 (dd, *J* = 10.6, 1.3 Hz, 1H, $OCH_2CH=CHH$ *cis*); 4.52-4.45 (m, 3H, $OCH_2CH=CH_2$ and 8-CH); 4.37 (dd, *J* = 9.1, 5.0 Hz, 1H, 5-CH); 3.88 (d, *J* = 1.7 Hz, 2H, 2-CH_2); 3.71 (s, 3H, OCH_3); 3.16 (t, *J* = 6.7 Hz, 2H, 4''-CH_2); 3.03 (dd, *J* = 13.8, 6.6 Hz, 1H, 8-CHCH_aH_b); 2.87 (dd, *J* = 13.9, 8.6 Hz, 1H, 8-CHCH_aH_b); 1.93 (s, 3H, 11-CH_3); 1.90-1.78 (m, 1H, 1''-CH_aH_b) 1.73-1.51 (m, 3H, 1''-CH_aH_b and 3''-CH_2); 1.49-1.35 (m, 2H, 2''-CH_2). ^{13}C NMR (75 MHz, CD_3OD): δ 173.1 (C-7); 172.9 (C-4); 172.4 (C-10); 170.4 (C-1); 157.8 (C-4'); 157.4 (C=N); 133.8 ($OCH_2CH=CH_2$); 130.2 (C-2' and C-6'); 129.2 (C-1'); 116.3 ($OCH_2CH=CH_2$); 114.6 (C-3' and C-5'); 68.6 ($OCH_2CH=CH_2$); 55.6 (C-8); 52.8 (C-5); 51.5 (OCH_3); 41.1 (C-4''); 40.6 (C-2); 36.6 (8-CHCH_2); 31.3 (C-1''); 28.0 (C-3''); 22.4 (C-11); 21.3 (C-2'').

Methyl (2*R*,5*S*,8*S*)-8-(4-allyloxybenzyl)-3,6,9-triaza-2-benzyl-5-(4-guanidinobutyl)-4,7,10-trioxoundecanoate hydrochloride (22)

Compound **39** (80 mg, 0.10 mmol) was converted to the *N*-Boc deprotected trifluoroacetate salt *via* procedure E, and the resulting solid then converted, *via* procedure H, to afford the hydrochloride salt **22** (50 mg, 0.08 mmol, 79%) as a hygroscopic light brown amorphous solid. MS (ESI^+), *m/z* 595 (100%) [MH^+], 596 (35) [MD^+]. HRMS (ESI^+) calcd for $C_{31}H_{42}N_6O_6$ + H: 595.3244; found 595.3245. $[\alpha]_D^{25}$ -51.4 (*c*. 0.10, EtOH). ^{1}H NMR (300 MHz, CD_3OD): δ 7.30-7.17 (m, 5H, 2''-CH, 3''-CH, 4''-CH, 5''-CH and 6''-CH); 7.13 (d, *J* = 8.5 Hz, 2H, 2'-CH and 6'-CH); 6.82 (d, *J* = 8.5 Hz, 2H, 3'-CH and 5'-CH); 6.03 (tdd, *J* = 17.2, 10.4, 5.1 Hz, 1H, $OCH_2CH=CH_2$); 5.38 (dd, *J* = 17.3, 1.6 Hz, 1H, $OCH_2CH=CHH$ *trans*); 5.22 (dd, *J* = 10.6, 1.4 Hz, 1H, $OCH_2CH=CHH$ *cis*); 4.69-4.65 (m, 1H, 8-CH); 4.50-4.48 (m, 2H, $OCH_2CH=CH_2$); 4.47-4.43 (m, 1H, 2-CH); 4.33 (dd, *J* = 8.6, 4.8 Hz, 1H, 5-CH); 3.71 (s, 3H, OCH_3); 3.18 (dd, *J* = 13.9, 5.3 Hz, 1H, 2-CHCH_aH_b); 3.08 (t, *J* = 6.7 Hz, 2H, 4'''-CH_2); 2.98 (dd, *J* = 15.5, 7.6 Hz, 1H, 8-CHCH_aH_b); 2.94 (dd, *J* = 15.4, 7.7 Hz, 1H, 2-CHCH_aH_b); 2.79 (dd, *J* = 14.1, 9.1 Hz, 1H, 8-CHCH_aH_b); 1.91 (s, 3H, 11-CH_3); 1.66-1.54 (m, 1H, 1''-CH_aH_b); 1.54-1.38 (m, 3H, 1''-CH_aH_b and 3'''-CH_2); 1.26-1.14 (m, 2H, 2''-CH_2). ^{13}C NMR (75 MHz, CD_3OD): δ 173.4 (C-7); 172.8 (C-4); 172.2 (C-10); 170.1 (C-1); 157.9 (C-4'); 157.3 (C=NH); 136.2 (C-1''); 133.7 ($OCH_2CH=CH_2$); 130.1 (C-2' and C-6'); 129.6 (C-3'' and C-5''); 129.2 (C-1'); 128.7 (C-2'' and C-6''); 127.2 (C-4''); 116.9 ($OCH_2CH=CH_2$); 114.9 (C-3' and C-5'); 68.9 ($OCH_2CH=CH_2$); 55.6 (C-8); 52.9 (C-5); 51.2 (OCH_3); 41.1 (C-4''); 40.2 (C-2); 36.1 (8-CHCH_2); 31.5 (C-1''); 28.1 (C-3''); 22.5 (C-11); 21.4 (C-2'').

Methyl (6*S*,9*S*)-9-(4-allyloxybenzyl)-4,7,10-triaza-6-(4-guanidinobutyl)-5,8,11-trioxododecanoate hydrochloride (23)

Compound **40** (118 mg, 0.16 mmol) was converted to the *N*-Boc deprotected trifluoroacetate salt *via* procedure E, and the resulting solid was then directly converted, *via* procedure H to the hydrochloride salt **23** (65 mg, 0.12 mmol, 75%) as a hygroscopic, brown amorphous solid. MS (ESI$^+$), *m/z* 519 (100%) [MH$^+$], 520 (30). HRMS (ESI$^+$) calcd for $C_{25}H_{38}N_6O_6$ + H: 519.2931; found 519.2920. $[\alpha]_D^{25}$ -76.4 (*c*. 0.16, EtOH). ^{1}H NMR (300 MHz, CD_3OD): δ 7.19 (d, *J* = 8.6 Hz, 2H, 2′-CH and 6′-CH); 6.86 (d, *J* = 8.6 Hz, 2H, 3′-CH and 5′-CH); 6.04 (tdd, *J* = 17.2, 10.4, 5.2 Hz, 1H, $OCH_2C\underline{H}=CH_2$); 5.38 (dd, *J* = 17.3, 1.6 Hz, 1H, $OCH_2CH=C\underline{H}H$ *trans*); 5.23 (dd, *J* = 10.6, 1.5 Hz, 1H, $OCH_2CH=CH\underline{H}$ *cis*); 4.52-4.49 (m, 3H, $OC\underline{H}_2CH=CH_2$ and 9-CH); 4.25 (dd, *J* = 9.3, 4.8 Hz, 1H, 6-CH); 3.66 (s, 3H, OCH_3); 3.40 (t, *J* = 6.7 Hz, 2H, 3-CH_2); 3.17 (t, *J* = 6.8 Hz, 2H, 4′′-CH_2); 3.05 (dd, *J* = 13.9, 6.2 Hz, 1H, 9-$CHC\underline{H}_aH_b$); 2.88 (dd, *J* = 13.9, 8.8 Hz, 1H, 9-$CHCH_a\underline{H}_b$); 2.52 (t, *J* = 6.7 Hz, 2H, 2-CH_2); 1.95 (s, 3H, 12-CH_3); 1.85-1.72 (m, 1H, 1′′-$C\underline{H}_aH_b$); 1.71-1.51 (m, 3H, 1′′-$CH_a\underline{H}_b$ and 3′′-CH_2); 1.46-1.35 (m, 2H, 2′′-CH_2). ^{13}C NMR (75 MHz, CD_3OD): δ 172.9 (C-1); 172.8 (C-5 and C-8); 172.6 (C-11); 157.8 (C-4′); 157.4 (C=NH); 133.8 ($OCH_2\underline{C}H=CH_2$); 130.2 (C-2′ and C-6′); 129.2 (C-1′); 116.3 ($OCH_2CH=\underline{C}H_2$); 114.6 (C-3′ and C-5′); 68.6 ($O\underline{C}H_2CH=CH_2$); 55.8 (C-9); 53.4 (C-6); 51.2 (OCH_3); 41.1 (C-4′′); 36.5 (9-$CH\underline{C}H_2$); 35.2 (C-3); 33.4 (C-2); 31.2 (C-1′′); 28.0 (C-3′′); 22.7 (C-12); 21.4 (C-2′′).

Methyl (7*S*,10*S*)-10-(4-allyloxybenzyl)-5,8,11-triaza-7-(4-guanidinobutyl)-6,9,12-trioxotridecanoate hydrochloride (24)

Compound **41** (99 mg, 0.14 mmol) was converted to the *N*-Boc deprotected trifluoroacetate salt *via* procedure E, the resulting solid was then converted, *via* procedure H to give hydrochloride salt **24** (64 mg, 0.11 mmol, 83%) as a hygroscopic light brown amorphous solid. MS (ESI$^+$), *m/z* 533 (100%) [MH$^+$], 534 (35). HRMS (ESI$^+$) calcd for $C_{26}H_{40}N_6O_6$ + H: 533.3088; found 533.3072. $[\alpha]_D^{25}$ +89.7 (*c*. 0.13, EtOH). ^{1}H NMR (300 MHz, CD_3OD): δ 7.70 (bs, 1H, NH); 7.62 (bs, 1H, NH); 7.17 (d, *J* = 8.4 Hz, 2H, 2′-CH and 6′-CH); 7.09 (d, *J* = 7.8, 1H, NH); 7.07 (bs, 1H, NH); 6.85 (d, *J* = 8.5 Hz, 2H, 3′-CH and 5′-CH); 6.12-5.94 (m, 1H, $OCH_2C\underline{H}=CH_2$); 5.38 (dd, *J* = 17.3, 1.6 Hz, 1H, $OCH_2CH=C\underline{H}H$ *trans*); 5.22 (dd, *J* = 10.6, 1.5 Hz, 1H, $OCH_2CH=CH\underline{H}$ *cis*); 4.55-4.45 (m, 3H, $OC\underline{H}_2CH=CH_2$ and 10-CH); 4.24 (dd, *J* = 9.4, 4.6 Hz, 1H, 7-CH); 3.64 (s, 3H, OCH_3); 3.20-3.11 (m, 4H, 4′′-CH_2 and 4-CH_2); 3.03 (dd, *J* = 13.9, 6.4 Hz, 1H, 10-$CHC\underline{H}_aH_b$); 2.86 (dd, *J* = 13.7, 8.5 Hz, 1H, 10-$CHCH_a\underline{H}_b$); 2.33 (t, *J* = 7.4 Hz, 2H, 2-CH_2); 1.93 (s, 3H, 13-CH_3); 1.86-1.69 (m, 3H, 1′′-$C\underline{H}_aH_b$ and C-3H_2); 1.66-1.51 (m, 3H, 1′′-$CH_a\underline{H}_b$ and 3′′-CH_2); 1.47-1.25 (m, 2H, 2′′-CH_2). ^{13}C NMR (75 MHz, CD_3OD): δ 174.1 (C-1); 172.9 (C-6); 172.8 (C-9 and C-12); 157.8 (C-4′); 157.4 (C=NH); 133.8 ($OCH_2\underline{C}H=CH_2$); 130.2 (C-2′ and C-6′); 129.2 (C-1′); 116.3 ($OCH_2CH=\underline{C}H_2$); 114.6 (C-3′ and C-5′); 68.7 ($O\underline{C}H_2CH=CH_2$), 55.8 (C-10); 53.5 (C-7); 51.1 (OCH_3); 41.2 (C-4′′); 38.6 (C-4); 36.5 (10-$CH\underline{C}H_2$); 31.3 (C-1′′); 30.9 (C-13); 28.1 (C-3′′); 24.5 (C-3); 22.8 (C-13); 21.5 (C-2′′).

Methyl (6*S*,9*S*)-9-(4-allyloxybenzyl)-4,7,10-triaza-6-(4-guanidinobutyl)-3-methoxycarbonylmethyl-5,8,11-trioxododecanoate hydrochloride (25)

Compound **42** (116 mg, 0.15 mmol) was converted to the *N*-Boc deprotected trifluoroacetate salt *via* procedure E, the resulting solid was then converted directly, *via* procedure H, to the hydrochloride salt **25** (90 mg, 0.14 mmol, 98%) as a hygroscopic light brown amorphous solid. MS (ESI$^+$), *m/z* 591 (100%) [MH$^+$], 592 (40) [MD$^+$]. HRMS (ESI$^+$) calcd for $C_{28}H_{42}N_6O_8$ + H: 591.3142; found 591.3148. $[\alpha]_D^{25}$ -33.9 (*c*. 0.09, EtOH). ^{1}H NMR (300 MHz, CD_3OD): δ 7.16 (d, *J* = 7.6 Hz, 2H, 2′-CH and 6′-CH); 6.85 (d, *J* = 7.1 Hz, 1H, 3′-CH and 5′-CH); 6.12-5.95 (m, 1H, $OCH_2C\underline{H}=CH_2$); 5.36 (bd, *J* = 17.7 Hz, 1H, $OCH_2CH=C\underline{H}H$ *trans*); 5.21 (bd, *J* = 10.3 Hz, 1H, $OCH_2CH=CH\underline{H}$ *cis*); 4.55-4.45 (m, 4H, $OC\underline{H}_2CH=CH_2$, 9-CH and 3-CH); 4.29-4.18 (m, 1H, 6-CH); 3.65 (s, 3H, OCH_3); 3.25-3.12 (m, 2H, 4′′-CH_2); 3.11-2.97 (m, 1H, 9-$CHC\underline{H}_aH_b$); 2.95-2.79 (m, 1H, 9-$CHCH_a\underline{H}_b$); 2.61 (s, 4H, 2-CH_2 and 3-$CHC\underline{H}_2$); 1.92 (s, 3H, 12-CH_3); 1.84-1.72 (m, 1H, 1′′-$C\underline{H}_aH_b$); 1.70-1.50 (m, 3H, 1′′-$CH_a\underline{H}_b$ and 3′′-CH_2); 1.47-1.22 (m, 2H, 2′′-CH_2). ^{13}C NMR (75 MHz, CD_3OD): δ 172.7 (C-1 and 3-$CHCH_2\underline{C}OOCH_3$); 172.1 (C-8); 171.7 (C-5); 171.6 (C-11); 157.8 (C-4′); 157.4 (C=NH); 133.9 ($OCH_2\underline{C}H=CH_2$); 130.2 (C-2′ and C-6′); 129.4 (C-1′); 116.4 ($OCH_2CH=\underline{C}H_2$); 114.7 (C-3′ and C-5′); 68.8 ($O\underline{C}H_2CH=CH_2$); 55.7 (C-9); 53.4 (C-6); 51.6 (1-$COO\underline{C}H_3$ and 3-$CHCH_2COO\underline{C}H_3$); 43.9 (C-2 and 3-$CH\underline{C}H_2$); 41.3 (C-4′′); 38.1 (C-3); 36.7 (9-$CH\underline{C}H_2$); 31.5 (C-1′′); 28.2 (C-3′′); 22.7 (C-12); 21.7 (C-2′′).

Methyl (2*S*,5*S*)-5-(4-allyloxybenzyl)-3,6-diaza-2-[4-(*N,N*-di-*tert*-butoxycarbonyl)guanidinobutyl]-4,7-dioxooctanoate (26)

Procedure E was used to convert the ester **12** (350 mg, 0.70 mmol) to the uncharacterised *N*-Boc deprotected trifluoroacetate salt. This salt was then carried forward (assuming 100% yield) for use in procedure G, along with $(BocNH)_2C=NSO_2CF_3$ (250 mg, 0.64 mmol), NEt_3 (0.10 mL, 0.72 mmol) and CH_2Cl_2 (4 mL) as the solvent to yield **26** (415 mg, 0.64 mmol, 92%) as a cream solid, mp. 95-98°C. MS (ESI$^+$), *m/z* 648 (100%) [MH$^+$]. HRMS (ESI$^+$) calcd for $C_{32}H_{49}N_5O_9$ + H: 648.3603; found 648.4201. ^{1}H NMR (300 MHz, $CDCl_3$): δ 11.47 (s, 1H, $N\underline{H}COOC(CH_3)_3$); 8.34 (s, 1H, 4′′-$CH_2N\underline{H}$); 7.10 (d, *J* = 8.6, Hz, 2H, 2′-CH and 6′-CH); 6.83 (d, *J* = 8.6 Hz, 2H, 3′-CH and 5′-CH); 6.69 (d, *J* = 7.8 Hz, 1H, 3-NH); 6.55 (d, *J* = 7.9 Hz, 1H, 5-NH); 6.04 (tdd, *J* = 17.2, 10.5, 5.3 Hz, 1H, $OCH_2C\underline{H}=CH_2$); 5.40 (dd, *J* = 17.2, 1.5 Hz, 1H, $OCH_2CH=C\underline{H}H$ *trans*); 5.28 (dd, *J* = 10.5, 1.3 Hz, 1H, $OCH_2CH=CH\underline{H}$ *cis*); 4.67-4.62 (m, 1H, 5-CH); 4.50 (d, *J* = 5.2 Hz, 2H, $OC\underline{H}_2CH=CH_2$); 4.47-4.43 (m, 1H, 2-CH); 3.70 (s, 3H, OCH_3); 3.35 (t, *J* = 6.7 Hz, 2H, 4′′-CH_2); 3.00 (dd, *J* = 14.3, 7.4 Hz, 1H, 5-$CHC\underline{H}_aH_b$); 2.93 (dd, *J* = 14.3, 7.6 Hz, 1H, 5-$CHCH_a\underline{H}_b$); 1.97 (s, 3H, 8-CH_3); 1.83-1.77 (m, 1H, 1′′-$C\underline{H}_aH_b$); 1.65-1.60 (m, 3H, 1′′-$CH_a\underline{H}_b$ and 3′′-CH_2); 1.49 (s, 18H, $NHCOOC(C\underline{H}_3)_3$ and $C=NCOOC(C\underline{H}_3)_3$); 1.35-1.28 (m, 2H, 2′′-CH_2). ^{13}C NMR (75 MHz, $CDCl_3$): δ 172.2 (C-4); 171.5 (C-1); 171.0 (C-7); 163.5 (N=C); 157.8 (C-4′); 156.4 ($NH\underline{C}OOC(CH_3)_3$); 153.5 ($N\underline{C}OOC(CH_3)_3$); 133.4 ($OCH_2\underline{C}H=CH_2$); 130.4 (C-2′ and C-6′); 128.5 (C-1′); 117.9 ($OCH_2CH=\underline{C}H_2$); 115.0 (C-3′ and C-5′); 83.5 ($NCOO\underline{C}(CH_3)_3$); 79.8 ($NHCOO\underline{C}(CH_3)_3$); 69.0 ($O\underline{C}H_2CH=CH_2$); 54.9 (C-5); 52.7 (C-2); 52.4 (OCH_3); 40.8 (C-4′′); 37.5 (5-$CH\underline{C}H_2$); 32.0 (C-1′′); 28.7 (C-3′′); 28.4 ($NCOOC(\underline{C}H_3)_3$[a]); 28.3 ($NHCOOC(\underline{C}H_3)_3$[a]); 23.1 (C-8); 22.8 (C-2′′).

Methyl 4-aminobutanoate hydrochloride (27)[5, 6]

Using procedure B, γ-aminobutyric acid (100 mg, 0.97 mmol) and $SOCl_2$ (0.7 mL, 9.6 mmol), gave **27** (140 mg, 0.92 mmol, 95%) as an off-white solid, mp. 164-166°C. MS (ESI$^+$), *m/z* 118 (100%) [MH$^+$]. HRMS (ESI$^+$) calcd for $C_5H_{11}NO_2$ + H: 118.0863; found

118.0872. ^{1}H NMR (300 MHz, CD_3OD): δ 3.69 (s, 3H, OCH_3); 2.99 (t, *J* = 7.5 Hz, 2H, 4-CH_2); 2.49 (t, *J* = 7.2 Hz, 2H, 2-CH_2); 2.01-1.89 (m, 2H, 3-CH_2). ^{13}C NMR (75 MHz, CD_3OD): δ 173.0 (C-1); 51.6 (OCH_3); 39.5 (C-4); 30.5 (C-2); 28.4 (C-3).

Dimethyl 3-aminopentanedioate hydrochloride (28)[7]

Using procedure B, the commercially available β-glutamic acid (300 mg, 2.04 mmol) and $SOCl_2$ (0.7 mL, 9.6 mmol), **28** (332 mg, 1.90 mmol, 93%) was obtained as an off-white solid, mp. 172-174°C. MS (ESI$^+$), *m/z* 176 (100%) [MH$^+$]. HRMS (ESI$^+$) calcd for $C_7H_{13}NO_4$ + H: 176.0917; found 176.0924. ^{1}H NMR (300 MHz, CD_3OD): δ 3.92 (m, 1H, 3-CH); 3.66 (s, 6H, OCH_3); 2.51 (d, *J* = 5.8 Hz, 4H, 2-CH_2 and 4-CH_2). ^{13}C NMR (75 MHz, CD_3OD): δ 173.2 (C-1 and C-5); 52.1 (OCH_3); 43.6 (C-2 and C-4); 41.3 (C-3).

***N*-{(1*S*,4*S*)-1-(4-Allyloxybenzyl)-3-aza-8-(*tert*-butoxycarbonyl)amino-4-{*N*-[4-(*tert*-butoxy)carbonyl]piperazinyl}carbonyl-2-oxooctyl}acetamide (29)**

The amide was synthesised using procedure D from the acid **13** (211 mg, 0.43 mmol), the commercially available 1-(*tert*-butoxycarbonyl)piperazine (108 mg, 0.58 mmol), EDCI (120 mg, 0.63 mmol), HOBt (82 mg, 0.61 mmol) and DMF (3 mL) as the solvent, to yield the amide **29** (185 mg, 0.28 mmol, 65%) as an off-white powder, mp. 117-120°C. MS (ESI$^+$), *m/z* 660 (100%). HRMS (ESI$^+$) calcd for $C_{32}H_{53}N_5O_8$ + H: 660.3967; found 660.3960. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.34 (d, *J* = 8.1 Hz, 1H, 3-NH); 7.06 (d, *J* = 8.5 Hz, 2H, 2′-CH and 6′-CH); 6.79 (d, *J* = 8.6 Hz, 2H, 3′-CH and 5′-CH); 6.71 (d, *J* = 7.0 Hz, 1H, N<u>H</u>$COCH_3$); 6.03 (tdd, *J* = 17.2, 10.5, 5.3 Hz, 1H, $OCH_2C\underline{H}=CH_2$); 5.39 (dd, *J* = 17.2, 1.5 Hz, 1H, $OCH_2CH=C\underline{H}H$ *trans*); 5.27 (dd, *J* = 10.5, 1.4 Hz, 1H, $OCH_2CH=CH\underline{H}$ *cis*); 5.06 (bs, 1H, 8-$CH_2N\underline{H}$); 4.86-4.80 (m, 1H, 4-CH); 4.73-4.68 (m, 1H, 1-CH); 4.48 (d, *J* = 5.2 Hz, 2H, $OC\underline{H}_2CH=CH_2$); 3.64 (bs, 2H, 2′′-$C\underline{H}_aH_b$ and 6′′-$C\underline{H}_aH_b$); 3.45 (bs, 2H, 2′′-$CH_a\underline{H}_b$ and 6′′-$CH_a\underline{H}_b$); 3.07-3.01 (m, 2H, 8-CH_2); 2.99-2.93 (m, 2H, 1-$CHC\underline{H}_2$); 2.79 (bs, 2H, 3′′-$C\underline{H}_aH_b$ and 5′′-$C\underline{H}_aH_b$); 2.61 (bs, 2H, 3′′-$CH_a\underline{H}_b$ and 5′′-$CH_a\underline{H}_b$); 1.96 (s, 3H, $COCH_3$); 1.72-1.66 (m, 1H, 5-$C\underline{H}_aH_b$); 1.59-1.53 (m, 1H, 5-$CH_a\underline{H}_b$); 1.48 (s, 9H, (4′′-NCOOC($C\underline{H}_3$)$_3$[a]); 1.46-1.39 (m, 11H, $CH_2NHCOOC(C\underline{H}_3)_3$[a] and 7-$CH_2$); 1.32-1.26 (m, 2H, 6-$CH_2$). ^{13}C NMR (75 MHz, $CDCl_3$): δ 171.2 (4-CH<u>C</u>O); 170.6 (C-2); 170.2 (<u>C</u>OCH_3); 157.7 (C-4′); 156.4 (8-$CH_2NHC\underline{O}OOC(CH_3)_3$); 154.6 (4′′-N<u>C</u>$OOC(CH_3)_3$); 133.4 ($OCH_2\underline{C}H=CH_2$); 130.4 (C-2′ and C-6′); 128.7 (C-1′); 117.8 ($OCH_2CH=\underline{C}H_2$); 114.9 (C-3′ and C-5′); 80.7 (4′′-NCOO<u>C</u>$(CH_3)_3$); 79.3 (8-$CH_2NHCOO\underline{C}(CH_3)_3$); 68.9 ($O\underline{C}H_2CH=CH_2$); 54.7 (C-1); 50.6 (C-4); 48.8 (C-3′′ and C-6′′); 45.6 (C-2′′ and C-5′′); 40.2 (C-8); 37.5 (1-$CH\underline{C}H_2$); 32.5 (C-5); 29.7 (C-7); 28.6 (4′′-NCOOC($\underline{C}H_3$)$_3$); 28.5 ($CH_2NHCOOC(\underline{C}H_3)_3$); 23.2 ($CO\underline{C}H_3$); 22.4 (C-6).

***N*-{(1*S*,4*S*)-1-(4-Allyloxybenzyl)-3-aza-8-(*tert*-butoxycarbonyl)amino-4-{*N*-[4-(*tert*-butoxycarbonyl)amino] piperidinyl}carbonyl-2-oxooctyl}acetamide (30)**

The amide was synthesised using procedure D from the acid **13** (192 mg, 0.40 mmol), the commercially available 4-(*tert*-butoxycarbonylamino)piperidine (110 mg, 0.47 mmol), EDCI (99 mg, 0.52 mmol), HOBt (78 mg, 0.58 mmol), DIPEA (0.10 mL, 0.57 mmol) and DMF (3 mL) as the solvent, to yield **30** (200 mg, 0.30 mmol, 75%) as an off-white powder, mp. 118-120°C. MS (ESI$^+$), *m/z* 674 (100%) [MH$^+$]. HRMS (ESI$^+$) calcd for $C_{35}H_{55}N_5O_8$ + H: 674.4123; found 674.4125. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.33-7.19 (m, 1H, N<u>H</u>$COCH_3$); 7.07 (d, *J* = 8.8 Hz, 2H, 2′-CH and 6′-CH); 6.80 (d, *J* = 5.8 Hz, 2H, 3′-CH and 5′-CH); 6.69-6.51 (m, 1H, 3-NH); 6.04 (tdd, *J* = 15.9, 10.5, 5.2 Hz, 1H, $OCH_2C\underline{H}=CH_2$); 5.39 (dd, *J* = 17.3, 1.3 Hz, 1H, $OCH_2CH=C\underline{H}H$ *trans*); 5.27 (dd, *J* = 10.5, 1.3 Hz, 1H, $OCH_2CH=CH\underline{H}$ *cis*); 5.07-4.91 (m, 1H, 1-CH); 4.89-4.78 (m, 2H, 8-$CH_2N\underline{H}COOC(CH_3)_3$ and 4′′-CHN<u>H</u>$COOC(CH_3)_3$); 4.77-4.70 (m, 1H, 4-CH); 4.51-4.46 (m, 2H, $OC\underline{H}_2CH=CH_2$); 3.94-3.80 (m, 1H, 4′′-CH); 3.15-2.92 (m, 8H, 1-$CHC\underline{H}_2$, 2′′-CH_2, 6′′-CH_2 and 8-CH_2); 2.03-1.85 (m, 7H, $COCH_3$, 3′′-CH_2 and 5′′-CH_2); 1.78-1.62 (m, 1H, 5-$C\underline{H}_aH_b$); 1.53-1.36 (m, 19H, 8-$CH_2NHCOOC(C\underline{H}_3)_3$, 4′′-$CHNHCOOC(C\underline{H}_3)_3$ and 5-$CH_a\underline{H}_b$); 1.34-1.21 (m, 4H, 6-CH_2 and 7-CH_2). ^{13}C NMR (75 MHz, $CDCl_3$): δ 171.1 (4-CH<u>C</u>O); 170.3 (C-2); 170.2 (<u>C</u>OCH_3); 157.7 (C-4′); 156.3 ($CH_2NH\underline{C}OOC(CH_3)_3$); 155.4 ($CHNH\underline{C}OOC(CH_3)_3$); 133.5 ($OCH_2\underline{C}H=CH_2$); 130.5 (C-2′ and C-6′); 129.0 (C-1′); 118.0 ($OCH_2CH=\underline{C}H_2$); 115.0 (C-3′ and C-5′); 79.7 ($CH_2NHCOO\underline{C}(CH_3)_3$); 79.3 ($CHNHCOO\underline{C}(CH_3)_3$); 68.9 ($O\underline{C}H_2CH=CH_2$); 54.7 (C-1); 48.8 (C-4); 44.6 (C-4′′); 41.5 (C-2′′ and C-6′′); 40.3 (C-8); 37.7 (1-$CH\underline{C}H_2$); 33.2 (C-3′′ and C-5′′); 32.6 (C-5); 29.8 (C-7); 28.6 ($CHNHCOOC(\underline{C}H_3)_3$ and $CH_2NHCOOC(\underline{C}H_3)_3$); 23.3 ($CO\underline{C}H_3$); 22.4 (C-6).

Methyl (5*S*,8*S*)-8-(4-allyloxybenzyl)-3,6,9-triaza-5-[4-(*tert*-butoxycarbonyl)aminobutyl]-4,7,10-trioxoundecanoate (31)

The ester was synthesised using procedure D from the acid **13** (110 mg, 0.22 mmol), the commercially available glycine methyl ester hydrochloride (45 mg, 0.36 mmol), EDCI (50 mg, 0.26 mmol), HOBt (50 mg, 0.37 mmol), DIPEA (0.04 mL, 0.23 mmol) and DMF (10 mL) as the solvent, to yield **31** (60 mg, 0.11 mmol, 48%) as an off-white powder, mp. 120-124°C. MS (ESI$^+$), *m/z* 563 (100%) [MH$^+$]. HRMS (ESI$^+$) calcd for $C_{28}H_{42}N_4O_8$ + H: 563.3075; found 563.3064. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.08 (d, *J* = 8.5 Hz, 2H, 2′-CH and 6′-CH); 7.00 (d, *J* = 7.9 Hz, 1H, 6-NH); 6.93 (bs, 1H, 3-NH); 6.80 (d, *J* = 8.5 Hz, 2H, 3′-CH and 5′-CH); 6.69 (d, *J* = 7.2 Hz, 1H, 9-NH); 6.03 (tdd, *J* = 16.8, 10.4, 5.3 Hz, 1H, $OCH_2C\underline{H}=CH_2$); 5.40 (dd, *J* = 17.3, 1.4 Hz, 1H, $OCH_2CH=C\underline{H}H$ *trans*); 5.28 (dd, *J* = 10.5, 0.9 Hz, 1H, $OCH_2CH=CH\underline{H}$ *cis*); 4.95 (bs, 1H, 4′′-$CH_2N\underline{H}$); 4.76-4.72 (m, 1H, 8-CH); 4.53-4.49 (m, 1H, 5-CH); 4.47 (d, *J* = 5.3 Hz, 2H, $OC\underline{H}_2CH=CH_2$); 3.95 (d, *J* = 5.4 Hz, 2H, 2-CH_2); 3.74 (s, 3H, OCH_3); 3.08-3.04 (m, 2H, 4′′-CH_2); 2.99 (m, 2H, 8-$CHC\underline{H}_2$); 1.99 (s, 3H, 11-CH_3); 1.90-1.80 (m, 1H 1′′-$C\underline{H}_aH_b$); 1.66-1.55 (m, 1H, 1′′-$CH_a\underline{H}_b$); 1.46-1.40 (m, 11H, $OC(C\underline{H}_3)_3$ and 3′′-CH_2); 1.36-1.30 (m, 2H, 2′′-CH_2). ^{13}C NMR (75 MHz, $CDCl_3$): δ 171.8 (C-7); 171.4 (C-4); 170.8 (C-10); 170.4 (C-1); 157.8 (C-4′); 156.4 ($NH\underline{C}OOC(CH_3)_3$); 133.4 ($OCH_2\underline{C}H=CH_2$); 130.5 (C-2′ and C-6′); 128.7 (C-1′); 117.9 ($OCH_2CH=\underline{C}H_2$); 115.0 (C-3′ and C-5′); 79.3 ($COO\underline{C}(CH_3)_3$); 69.0 ($O\underline{C}H_2CH=CH_2$); 54.9 (C-8); 53.0 (C-5); 52.6 (OCH_3); 41.3 (C-4′′); 40.4 (C-2); 37.7 (8-$CH\underline{C}H_2$); 32.1 (C-1′′); 29.6 (C-3′′); 28.7 ($OC(\underline{C}H_3)_3$); 23.3 (C-11); 22.7 (C-2′′).

Methyl (2*R*,5*S*,8*S*)-8-(4-allyloxybenzyl)-3,6,9-triaza-2-benzyl-5-[4-(*tert*-butoxycarbonyl)aminobutyl]-4,7,10-trioxoundecanoate (32)

The ester was synthesised using procedure D from acid **13** (100 mg, 0.20 mmol), the commercially available (*R*)-phenylalanine methyl ester (44 mg, 0.20 mmol), EDCI (107 mg, 0.56 mmol), HOBt (53 mg, 0.39 mmol) and DIPEA (0.04 mL, 0.23 mmol), to yield **32** (123 mg, 0.19 mmol, 93%) as a white powder, mp. 122-126°C. MS (ESI$^+$), *m/z* 653 (50%) [MH$^+$], 675 (100), 316 (32). HRMS (ESI$^+$) calcd for $C_{35}H_{48}N_4O_8$ + H: 653.3550; found 653.3562. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.30-7.19 (m, 4H, 3′′-CH, 5′′-CH, 3-NH and 6-NH); 7.15-7.09 (m, 3H, 2′′-CH, 4′′-CH and 6′′-CH); 7.05 (d, *J* = 8.5 Hz, 2H, 2′-CH and 6′-CH); 6.79 (d, *J* = 8.6 Hz, 2H, 3′-CH and 5′-

CH); 6.40 (d, *J* = 6.0 Hz, 1H, 9-NH); 6.02 (tdd, *J* = 15.8, 10.6, 5.3 Hz, 1H, $OCH_2C\underline{H}=CH_2$); 5.38 (dd, *J* = 17.3, 1.4 Hz, 1H, $OCH_2CH=C\underline{H}H$ *trans*); 5.26 (dd, *J* = 10.5, 1.0 Hz, 1H, $OCH_2CH=CH\underline{H}$ *cis*); 4.87-4.71 (m, 2H, 4'''-$CH_2N\underline{H}$ and 8-CH); 4.66-4.54 (m, 1H, 2-CH); 4.47 (d, *J* = 4.9, Hz, 2H, $OC\underline{H}_2CH=CH_2$); 4.41-4.30 (m, 1H, 5-CH); 3.70 (s, 3H, OCH_3); 3.15 (dd, *J* = 13.9, 5.7 Hz, 1H, 8-$CHC\underline{H}_aH_b$); 3.04-2.90 (m, 5H, 2-$CHC\underline{H}_2$, 4'''-CH_2 and 8-$CHCH_a\underline{H}_b$); 1.95 (s, 3H, 11-CH_3); 1.78-1.62 (m, 1H, 1'''-$C\underline{H}_aH_b$); 1.59-1.43 (m, 10H, 1'''-$CH_a\underline{H}_b$ and $OC(CH_3)_3$); 1.40-1.30 (m, 2H, 3'''-CH_2); 1.22-1.09 (m, 2H, 2'''-CH_2). ^{13}C NMR (75 MHz, $CDCl_3$): δ 172.1 (C-7); 171.5 (C-1); 171.1 (C-4), 170.7 (C-10); 157.9 ($NHCOOC(CH_3)_3$); 157.8 (C-4'); 136.2 (C-1''); 133.5 ($OCH_2CH=CH_2$); 130.4 (C-2' and C-6'); 129.4 (C-3'' and C-5''); 128.8 (C-2'' and C-6''); 127.3 (C-1'); 127.2 (C-4''); 117.8 ($OCH_2CH=CH_2$); 115.1 (C-3' and C-5'); 79.3 ($COOC(CH_3)_3$); 69.0 ($OCH_2CH=CH_2$); 54.9 (C-8); 53.5 (C-5); 53.0 (C-2); 52.6 (OCH_3); 45.7 (C-4'''); 38.1 (2-$CHCH_2$); 37.3 (8-$CHCH_2$); 32.0 (C-1'''); 29.6 (C-3'''); 28.7 ($OC(CH_3)_3$); 23.2 (C-11); 22.5 (C-2''').

Methyl (6*S*,9*S*)-9-(4-allyloxybenzyl)-4,7,10-triaza-6-[4-(*tert*-butoxycarbonyl)aminobutyl]-5,8,11-trioxododecanoate (33)

The ester **33** was synthesised using procedure D from the acid **13** (217 mg, 0.15 mmol, β-alanine methyl ester hydrochloride (25 mg, 0.18 mmol), EDCI (103 mg, 0.54 mmol), HOBt (89 mg, 0.66 mmol), DIPEA (0.10 mL, 0.57 mmol) and DMF (3 mL) as the solvent to yield **33** (80 mg, 0.14 mmol, 93%) as an off-white powder, mp. 126-129°C. MS (ESI^+), *m/z* 577 (100%) [MH^+]. HRMS (ESI^+) calcd for $C_{29}H_{44}N_4O_8$ + H: 577.3232; found 577.3244. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.48 (d, *J* = 8.1 Hz, 1H, 7-NH); 7.35 (bs, 1H, 4-NH); 7.16 (d, *J* = 7.8 Hz, 1H, 10-NH); 7.06 (d, *J* = 8.5 Hz, 2H, 2'-CH and 6'-CH); 6.79 (d, *J* = 8.5 Hz, 2H, 3'-CH and 5'-CH); 6.03 (tdd, *J* = 15.8, 10.5, 5.3 Hz, 1H, $OCH_2C\underline{H}=CH_2$); 5.39 (dd, *J* = 17.3, 1.4 Hz, 1H, $OCH_2CH=C\underline{H}H$ *trans*); 5.26 (dd, *J* = 10.5, 1.2 Hz, 1H, $OCH_2CH=CH\underline{H}$ *cis*); 5.04 (bs, 1H, 4''-$CH_2N\underline{H}$); 4.88-4.83 (m, 1H, 9-CH); 4.52-4.42 (m, 3H, $OC\underline{H}_2CH=CH_2$ and 6-CH); 3.68 (s, 3H, OCH_3); 3.56-3.54 (m, 1H, 3-$C\underline{H}_aH_b$); 3.41-3.37 (m, 1H, 3-$CH_a\underline{H}_b$); 2.95-2.81 (m, 4H, 4''-CH_2 and 9-$CHCH_2$); 2.54 (t, *J* = 6.3 Hz, 2H, 2-CH_2); 2.00 (s, 3H, 12-CH_3); 1.80-1.74 (m, 1H, 1''-$C\underline{H}_aH_b$); 1.62-1.56 (m, 1H, 1''-$CH_a\underline{H}_b$); 1.48-1.36 (m, 11H, $OC(C\underline{H}_3)_3$ and 3''-CH_2); 1.29 (m, 2H, 2''-CH_2). ^{13}C NMR (75 MHz, $CDCl_3$): δ 172.8 (C-1); 171.7 (C-5 and C-8); 170.7 (C-11); 157.7 (C-4'); 156.4 ($NHCOOC(CH_3)_3$); 133.5 ($OCH_2CH=CH_2$); 130.5 (C-2' and C-6'); 128.9 (C-1'); 117.8 ($OCH_2CH=CH_2$); 114.9 (C-3' and C-5'); 79.2 ($COOC(CH_3)_3$); 68.9 ($OCH_2CH=CH_2$); 54.7 (C-9); 53.2 (C-6); 52.1 (OCH_3); 40.4 (C-4''); 38.0 (9-$CHCH_2$); 35.4 (C-3); 34.0 (C-2); 32.6 (C-1''); 29.7 (C-3''); 28.7 ($OC(CH_3)_3$); 23.2 (C-12); 22.9 (C-2'').

Methyl (7*S*,10*S*)-10-(4-allyloxybenzyl)-5,8,11-triaza-7-[4-(*tert*-butoxycarbonyl)aminobutyl]-6,9,12-trioxotridecanoate (34)

The ester was synthesised using procedure D from the acid **13** (204 mg, 0.42 mmol), the prepared amine hydrochloride **27** (95 mg, 0.63 mmol), EDCI (97 mg, 0.51 mmol), HOBt (86 mg, 0.64 mmol) and DIPEA (0.15 mL, 0.86 mmol). The ester **34** (143 mg, 0.24 mmol, 58%) was obtained as a white powder, mp. 149-151°C. MS (ESI^+), *m/z* 591 (30%) [MH^+], 316 (50), 288 (40), 132 (100). HRMS (ESI^+) calcd for $C_{30}H_{46}N_4O_8$ + H: 591.3394; found 591.3379. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.08 (d, *J* = 8.5 Hz, 2H, 2'-CH and 6'-CH); 6.99 (d, *J* = 7.0 Hz, 1H, 8-NH); 6.81 (d, *J* = 8.6 Hz, 2H, 3'-CH and 5'-CH); 6.72-6.66 (m, 2H, 5-NH and 11-NH); 6.02 (tdd, *J* = 16.9, 10.4, 5.3 Hz, 1H, $OCH_2C\underline{H}=CH_2$); 5.38 (dd, *J* = 17.2, 1.4 Hz, 1H, $OCH_2CH=C\underline{H}H$ *trans*); 5.26 (dd, *J* = 10.5, 1.2 Hz, 1H, $OCH_2CH=CH\underline{H}$ *cis*); 5.04 (bs, 1H, 4''-$CHN\underline{H}$); 4.72-4.66 (m, 1H, 10-CH); 4.48 (d, *J* = 5.2 Hz, 2H, $OC\underline{H}_2CH=CH_2$); 4.38-4.32 (m, 1H, 7-CH); 3.66 (s, 3H, OCH_3); 3.27-3.12 (m, 2H, 4-CH_2); 3.08-2.89 (m, 4H, 4''-CH_2 and 10-$CHC\underline{H}_2$); 2.34 (t, *J* = 7.3 Hz, 2H, 2-CH_2); 1.98 (s, 3H, 13-CH_3); 1.83-1.78 (m, 3H, 1''-$C\underline{H}_aH_b$ and 3-CH_2); 1.64-1.52 (m, 1H, 1''-$CH_a\underline{H}_b$); 1.48-1.36 (m, 11H, $OC(C\underline{H}_3)_3$ and 3''-CH_2); 1.33-1.24 (m, 2H, 2''-CH_2). ^{13}C NMR (75 MHz, $CDCl_3$): δ 173.6 (C-1); 171.5 (C-6); 171.4 (C-9); 170.8 (C-12); 157.7 (C-4'); 156.4 ($NHCOOC(CH_3)_3$); 133.4 ($OCH_2CH=CH_2$); 130.5 (C-2' and C-6'); 128.8 (C-1'); 117.8 ($OCH_2CH=CH_2$); 114.9 (C-3' and C-5'); 79.3 ($COOC(CH_3)_3$); 68.9 ($OCH_2CH=CH_2$); 54.8 (C-10); 53.3 (C-7); 51.9 (OCH_3); 40.4 (C-4''); 39.0 (C-4); 37.8 (10-$CHC\underline{H}_2$); 32.4 (C-1''); 31.6 (C-2); 29.7 (C-3''); 28.7 ($OC(C\underline{H}_3)_3$); 24.8 (C-3); 23.2 (C-13); 23.0 (C-2'').

Methyl (6*S*,9*S*)-9-(4-allyloxybenzyl)-4,7,10-triaza-6-[4-(*tert*-butoxycarbonyl)aminobutyl]-3-methoxycarbonylmethyl-5,8,11-trioxododecanoate (35)

The ester was synthesised using procedure D from the acid **13** (187 mg, 0.38 mmol), the prepared amine hydrochloride **28** (80 mg, 0.45 mmol), EDCI (138 mg, 0.72 mmol), HOBt (86 mg, 0.64 mmol) and DIPEA (0.2 mL, 1.15 mmol), to yield **35** (185 mg, 0.29 mmol, 75%) as a white powder, mp. 162-165°C. MS (ESI^+), *m/z* 649 (100%) [MH^+]. HRMS (ESI^+) calcd for $C_{32}H_{48}N_4O_{10}$ + H: 649.3443; found 649.3434. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.13-6.92 (m, 3H, 2'-CH and 6'-CH and 4-NH); 6.91 (d, *J* = 6.2 Hz, 1H, 7-NH); 6.81 (d, *J* = 8.6 Hz, 2H, 3'-CH and 5'-CH); 6.50 (s, 1H, 10-NH); 6.03 (tdd, *J* = 17.1, 10.5, 5.3 Hz, 1H, $OCH_2C\underline{H}=CH_2$); 5.38 (dd, *J* = 17.3, 1.5 Hz, 1H, $OCH_2CH=C\underline{H}H$ *trans*); 5.26 (dd, *J* = 10.5, 1.4 Hz, 1H, $OCH_2CH=CH\underline{H}$ *cis*); 4.90 (bs, 1H, 4''-CNH); 4.68-4.60 (m, 1H, 9-CH); 4.57-4.52 (m, 1H, 3-CH); 4.48 (d, *J* = 5.3 Hz, 1H, $OC\underline{H}_2CH=CH_2$); 4.34-4.29 (m, 1H, 6-CH); 3.66 (s, 6H, 1-$COOCH_3$ and 3-$CHCH_2COOC\underline{H}_3$); 3.08-3.00 (m, 3H, 4''-CH_2 and 9-$CHC\underline{H}_aH_b$); 2.94 (dd, *J* = 13.9, 7.4 Hz, 1H, 9-$CHCH_a\underline{H}_b$); 2.63 (d, *J* = 5.8 Hz, 4H, 2-CH_2 and 3-$CHC\underline{H}_2$); 1.96 (s, 3H, 12-CH_3); 1.85-1.69 (m, 1H, 1''-$C\underline{H}_aH_b$); 1.65-1.50 (m, 1H, 1''-$CH_a\underline{H}_b$); 1.41 (s, 9H, $OC(C\underline{H}_3)_3$); 1.33-1.16 (m, 2H, 3''-CH_2); 1.15-0.98 (m, 1H, 2''-CH_2). ^{13}C NMR (75 MHz, $CDCl_3$): δ 171.7 (C-1 and 3-$CHCH_2\underline{C}OOCH_3$); 171.6 (C-8); 170.8 (C-5); 170.7 (C-11); 163.0 ($NHCOOC(CH_3)_3$); 157.8 (C-4'); 133.5 ($OCH_2CH=CH_2$); 130.4 (C-2' and C-6'); 128.8 (C-1'); 117.8 ($OCH_2CH=CH_2$); 115.1 (C-3' and C-5'); 79.0 ($COOC(CH_3)_3$); 69.0 ($OCH_2CH=CH_2$); 55.0 (C-9); 53.3 (C-96; 52.1 (OCH_3); 43.5 (C-4''); 37.8 (9-$CHCH_2$); 37.2 (C-2 and 3-$CHCH_2$); 32.1 (C-3); 31.6 (C-1''); 29.7 (C-3''); 28.7 ($OC(C\underline{H}_3)_3$); 23.3 (C-12); 22.6 (C-2'').

***N*-{(1*S*,4*S*)-1-(4-Allyloxybenzyl)-3-aza-4-{*N*-[4-(*N*,*N*'-di-*tert*-butoxycarbonyl)diaminomethyl]piperazinyl}carbonyl-8-(*N*,*N*'-di-*tert*-butoxycarbonyl)guanidino-2-oxooctyl}acetamide (36)**

Staring with the amide **29** (158 mg, 0.24 mmol) procedure E was used to obtain the uncharacterised *N*-Boc deprotected trifluoroacetate salt. The salt was then carried forward (assuming 100% yield) for use in procedure G, along with $(BocNH)_2C=NSO_2CF_3$ (202 mg, 0.52 mmol), NEt_3 (0.10 mL, 0.72 mmol) and CH_2Cl_2 (4 mL) as solvent to yield **36** (181 mg, 0.19 mmol, 80%) as a white powder, mp. 122-127°C. MS (ESI^+), *m/z* 946 (100%) [MH^+]. HRMS (ESI^+) calcd for $C_{46}H_{75}N_9O_{12}$ + H: 946.5608; found 946.5616. ^{1}H NMR (300 MHz, $CDCl_3/CD_3OD$): δ 7.08 (d, *J* = 8.5 Hz, 2H, 2'-CH and 6'-CH); 6.91 (d, *J* = 8.1 Hz, 1H,

4''-NCH); 6.81 (d, *J* = 8.5 Hz, 2H, 3'-CH and 5'-CH); 6.04 (tdd, *J* = 17.1, 10.5, 5.3 Hz, 1H, $OCH_2C\underline{H}=CH_2$); 5.39 (dd, *J* = 17.3, 1.4 Hz, 1H; $OCH_2CH=C\underline{H}H$ *trans*); 5.27 (dd, *J* = 10.5, 1.2 Hz, 1H, $OCH_2CH=CH\underline{H}$ *cis*); 4.83-4.78 (m, 1H, 4-CH); 4.69-4.63 (m, 1H, 1-CH); 4.49 (d, *J* = 5.1, Hz, 2H, $OC\underline{H}_2CH=CH_2$); 3.89-3.36 (m, 10H, 2''-CH_2, 3''-CH_2, 5''-CH_2, 6''-CH_2 and 8-CH_2); 3.07-2.91 (m, 2H, 1-$CHCH_2$); 1.99 (s, 3H, $COCH_3$); 1.98-1.89 (m, 1H, 5-$C\underline{H}_aH_b$); 1.79-1.54 (m, 3H, 5-$CH_a\underline{H}_b$ and 7-CH_2); 1.52-1.47 (m, 36H, $N=C(NHCOOC(C\underline{H}_3)_3)_2$ and $CH(NHCOOC(C\underline{H}_3)_3)_2$); 1.30 (m, 2H, 6-$CH_2$). ^{13}C NMR (75 MHz, $CDCl_3/CD_3OD$): δ 171.0 (C-2); 170.5 ($\underline{C}OCH_3$); 169.9 (4-CH$\underline{C}$O); 161.3 (N=C); 157.8 (C-4'); 155.6 (4''-NCH($NH\underline{C}OOC(CH_3)_3)_2$); 153.2 ($N=C(NH\underline{C}OOC(CH_3)_3)_2$); 133.5 ($OCH_2\underline{C}H=CH_2$); 130.4 (C-2' and C-6'); 128.8 (C-1'); 117.8 ($OCH_2CH=\underline{C}H_2$); 115.0 (C-3' and C-5'); 84.4 (4''-NCH); 81.9 ($CH(NHCOO\underline{C}(CH_3)_3)_2$); 81.4 ($N=C(NHCOO\underline{C}(CH_3)_3)_2$); 69.0 ($O\underline{C}H_2CH=CH_2$); 54.8 (C-1); 48.6 (C-4); 45.0 (C-2'' and C-5''); 41.7 (C-3'' and C-6''); 41.5 (C-8); 37.4 (1-$CH\underline{C}H_2$); 32.5 (C-5); 28.8 (C-7); 28.3 ($OC(\underline{C}H_3)_3$); 23.3 ($CO\underline{C}H_3$); 22.4 (C-6).

_N_-{(1*S*,4*S*)-1-(4-Allyloxybenzyl)-3-aza-8-(*N*,*N*'-di-tert-butoxycarbonyl)guanidino-4-{*N*-[4-(*N*,*N*'-di-tert-butoxycarbonyl)guanidino]piperidinyl}carbonyl-2-oxooctyl}acetamide (37)

Staring with the amide **30** (160 mg, 0.24 mmol) procedure E was used to obtain the uncharacterised *N*-Boc deprotected trifluoroacetate salt. This salt was then carried forward for use in procedure G, along with $(BocNH)_2C=NSO_2CF_3$ (180 mg, 0.46 mmol), NEt_3 (0.20 mL, 1.4 mmol) and CH_2Cl_2 (4 mL) as solvent to yield **37** (182 mg, 0.19 mmol, 81%) as a white powder, mp.126-129°C. MS (ESI^+), *m/z* 958 (100%) [MH^+]. HRMS (ESI^+) calcd for $C_{47}H_{75}N_9O_{12}$ + H: 958.5608; found 958.5618. ^{1}H NMR (300 MHz, $CDCl_3/CD_3OD$): δ 7.08 (d, *J* = 8.5 Hz, 2H, 2'-CH and 6'-CH); 6.83 (d, *J* = 6.6 Hz, 2H, 3'-CH and 5'-CH); 6.11-5.96 (m, 1H, 1H, $OCH_2C\underline{H}=CH_2$); 5.39 (bd, *J* = 17.2 Hz, 1H, $OCH_2CH=C\underline{H}H$ *trans*); 5.26 (bd, *J* = 10.4 Hz, 1H, $OCH_2CH=CH\underline{H}$ *cis*); 4.86-4.77 (m, 1H, 1-CH); 4.70 (dd, *J* = 13.8, 6.9 Hz, 1H, 4-CH); 4.52-4.48 (m, 2H, $OC\underline{H}_2CH=CH_2$); 4.40-4.21 (m, 2H, 2''-$C\underline{H}_aH_b$ and 6''-$C\underline{H}_aH_b$); 3.87-3.72 (m, 1H, 4''-CH); 3.42-3.30 (m, 2H, 2''-$CH_a\underline{H}_b$ and 6''-$CH_a\underline{H}_b$); 3.26-3.15 (m, 1H, 1-$CHC\underline{H}_aH_b$); 3.04-2.79 (m, 3H, 1-$CHCH_a\underline{H}_b$ and 8-CH_2); 2.12-1.90 (m, 7H, $COCH_3$, 3''-CH_2 and 5''-CH_2); 1.75-1.64 (m, 1H, 5-$C\underline{H}_aH_b$); 1.59-1.42 (m, 37H, 4''-$CHNHCNHCOOC(C\underline{H}_3)_3$, 4''-$CHNHC=NCOOC(C\underline{H}_3)_3$, 8-$CH_2NHCNHCOOC(C\underline{H}_3)_3$, 8-$CH_2NHC=NCOOC(C\underline{H}_3)_3$ and 5-$CH_a\underline{H}_b$); 1.36-1.24 (m, 4H, 6-CH_2 and 7-CH_2). ^{13}C NMR (75 MHz, $CDCl_3/CD_3OD$): δ 170.9 (4-CH$\underline{C}$O); 170.1 (C-2); 169.5 ($\underline{C}OCH_3$); 163.8 (8-$CH_2NH\underline{C}$=N and 4''-CHNH$\underline{C}$=N); 157.8 (C-4'); 156.3 (8-$CH_2NHCNH\underline{C}OOC(CH_3)_3$); 155.7 (4''-$CHNHCNH\underline{C}OOC(CH_3)_3$); 153.5 (8-$CH_2NHC=N\underline{C}OOC(CH_3)_3$); 153.4 (4''-$CHNHC=N\underline{C}OOC(CH_3)_3$); 133.5 ($OCH_2\underline{C}H=CH_2$); 130.4 (C-1', C-2' and C-6'); 117.8 ($OCH_2CH=\underline{C}H_2$); 115.0 (C-3' and C-5'); 83.5 (8-$CH_2NHC=NCOO\underline{C}(CH_3)_3$); 83.3 (4''-$CHNHC=NCOO\underline{C}(CH_3)_3$); 79.6 (8-$CH_2NHCNHCOO\underline{C}(CH_3)_3$ and 4''-$CHNHCNHCOO\underline{C}(CH_3)_3$); 68.9 ($O\underline{C}H_2CH=CH_2$); 54.6 (C-1); 48.8 (C-4); 44.4 (C-4''); 41.2 (C-2'' and C-6''); 40.8 (C-8); 37.6 (1-$CH\underline{C}H_2$); 32.7 (C-3'' and C-5''); 31.6 (C-5); 28.9 (C-7); 28.5 (4''-$CHNHCNHCOOC(\underline{C}H_3)_3$[a] and 8-$CH_2NHCNHCOOC(\underline{C}H_3)_3$[a]); 28.3 (4''-$CHNHC=NCOOC(\underline{C}H_3)_3$[a] and 8-$CH_2NHC=NCOOC(\underline{C}H_3)_3$[a]); 23.4 ($CO\underline{C}H_3$); 22.5 (C-6).

Methyl (5*S*,8*S*)-8-(4-allyloxybenzyl)-3,6,9-triaza-5-[4-(*N*,*N*-di-*tert*-butoxycarbonyl)guanidinobutyl]-4,7,10-trioxoundecanoate (38)

Starting with the ester **31** (145 mg, 0.28 mmol), procedure E was used to obtain the uncharacterised *N*-Boc deprotected trifluoroacetate salt. This salt was then used directly (assuming 100% yield) in procedure G, along with $(BocNH)_2C=NSO_2CF_3$ (123 mg, 0.31 mmol), NEt_3 (0.20 mL, 1.43 mmol) and CH_2Cl_2 4 (mL) as solvent, to yield **38** (180 mg, 0.26 mmol, 93%) as a white powder, mp. 114-117°C. MS (ESI^+), *m/z* 705 (100%) [MH^+]. HRMS (ESI^+) calcd for $C_{34}H_{52}N_6O_{10}$ + H: 705.3818; found 705.3825. ^{1}H NMR (300 MHz, $CDCl_3$): δ 11.47 (bs, 1H, $N\underline{H}COOC(CH_3)_3$); 8.28 (bs, 1H, 4''-$CH_2N\underline{H}$); 7.10-7.04 (m, 3H, 2'-CH and 6'-CH and 6-NH); 7.01 (t, *J* = 5.4 Hz, 1H, 3-NH); 6.79 (d, *J* = 8.7 Hz, 2H, 3'-CH and 5'-CH); 6.74 (d, *J* = 7.8 Hz, 1H, 9-NH); 6.03 (tdd, *J* = 17.5, 10.5, 5.3 Hz, 1H, $OCH_2C\underline{H}=CH_2$); 5.39 (dd, *J* = 17.3, 1.6 Hz, 1H, $OCH_2CH=C\underline{H}H$ *trans*); 5.27 (dd, *J* = 10.5, 1.3 Hz, 1H, $OCH_2CH=CH\underline{H}$ *cis*); 4.80-4.74 (m, 1H, 8-CH); 4.58-4.49 (m, 1H, 5-CH); 4.47 (d, *J* = 5.3 Hz, 2H, $OC\underline{H}_2CH=CH_2$); 3.96 (d, *J* = 5.6 Hz, 2H, 2-CH_2); 3.74 (s, 3H, OCH_3); 3.38-3.32 (m, 2H, 4''-CH_2); 2.98 (d, *J* = 7.3 Hz, 2H, 8-$CHC\underline{H}_2$); 2.01 (s, 3H, 11-CH_3); 1.90-1.80 (m, 1H, 1''-$C\underline{H}_aH_b$); 1.70-1.59 (m, 1H, 1''-$CH_a\underline{H}_b$); 1.59-1.52 (m, 2H, 3''-CH_2); 1.49 (s, 9H, $NCOOC(CH_3)_3$[a]); 1.48 (s, 9H, $NHCOOC(CH_3)_3$[a]); 1.41-1.30 (m, 2H, 2''-CH_2). ^{13}C NMR (75 MHz, $CDCl_3$): δ 171.6 (C-7); 171.4 (C-4); 170.7 (C-10); 170.3 (C-1); 163.7 (N=C); 157.8 (C-4'); 156.3 ($N\underline{H}COOC(CH_3)_3$); 153.4 ($N\underline{C}OOC(CH_3)_3$); 133.4 ($OCH_2\underline{C}H=CH_2$); 130.5 (C-2' and C-6'); 128.7 (C-1'); 117.9 ($OCH_2CH=\underline{C}H_2$); 115.0 (C-3' and C-5'); 83.3 ($NCOO\underline{C}(CH_3)_3$); 79.5 ($NHCOO\underline{C}(CH_3)_3$); 68.9 ($O\underline{C}H_2CH=CH_2$); 54.8 (C-8); 52.9 (C-5); 52.5 (OCH_3); 41.3 (C-4''); 40.9 (C-2); 37.8 (8-$CH\underline{C}H_2$); 32.2 (C-1''); 28.8 (C-3''); 28.5 ($NCOOC(\underline{C}H_3)_3$[a]); 28.3 ($NHCOOC(\underline{C}H_3)_3$[a]); 23.3 (C-11); 22.9 (C-2'').

Methyl (2*R*,5*S*,8*S*)-8-(4-allyloxybenzyl)-3,6,9-triaza-2-benzyl-5-[4-(*N*,*N*-di-*tert*-butoxycarbonyl)guanidinobutyl]-4,7,10-trioxoundecanoate (39)

Using procedure E, ester **32** (106 mg, 0.16 mmol), was deprotected to the *N*-Boc trifluoroacetate salt, which was then subjected to procedure G, with $(BocNH)_2C=NSO_2CF_3$ (74 mg, 0.19 mmol), NEt_3 (0.10 mL, 0.72 mmol) to yield **39** (123 mg, 0.15 mmol, 95%) as a white powder, mp. 187-189°C. MS (ESI^+), *m/z* 795 (100%) [MH^+], 796 (40), 755 (10). HRMS (ESI^+) calcd for $C_{41}H_{58}N_6O_{10}$ + H: 795.4287; found 795.4301. ^{1}H NMR (300 MHz, $CDCl_3$): δ 11.42 (s, 1H, $N\underline{H}COOC(CH_3)_3$); 8.33 (s, 1H, 4'''-$CH_2N\underline{H}$); 7.31-7.19 (m, 2H, 3''-CH and 5''-CH); 7.12 (s, 1H, 4''-CH); 7.11 (d, *J* = 6.3 Hz, 1H, 2H, 2''-CH and 6''-CH); 7.02 (d, *J* = 8.6 Hz, 2H, 2'-CH and 6'-CH); 6.84 (d, *J* = 2.1 Hz, 1H, 3-NH); 6.81 (d, *J* = 2.9 Hz, 1H, 6-NH); 6.78 (d, *J* = 8.7 Hz, 2H, 3'-CH and 5'-CH); 6.51 (d, *J* = 7.7 Hz, 1H, 9-NH); 6.01 (tdd, *J* = 17.2, 10.5, 5.3 Hz, 1H, $OCH_2C\underline{H}=CH_2$); 5.37 (dd, *J* = 17.3, 1.6 Hz, 1H, $OCH_2CH=C\underline{H}H$ *trans*); 5.25 (dd, *J* = 10.5, 1.4 Hz, 1H, $OCH_2CH=CH\underline{H}$ *cis*); 4.80-4.76 (m, 1H, 8-CH); 4.66-4.58 (m, 1H, 2-CH); 4.46 (d, *J* = 5.4, Hz, 2H, $OC\underline{H}_2CH=CH_2$); 4.38-4.33 (m, 1H, 5-CH); 3.70 (s, 3H, OCH_3); 3.27 (t, *J* = 6.9 Hz, 2H, 4'''-CH_2); 3.14 (dd, *J* = 13.8, 5.5 Hz, 1H, 8-$CHC\underline{H}_aH_b$), 3.02-2.91 (m, 2H, 8-$CHCH_a\underline{H}_b$ and 2-$CHC\underline{H}_aH_b$); 2.90-2.77 (m, 1H, 2-$CHCH_a\underline{H}_b$); 1.93 (s, 3H, 11-CH_3); 1.74-1.58 (m, 2H, 1'''-CH_2); 1.55-1.40 (m, 20H, $NHCOOC(C\underline{H}_3)_3$, $C=NCOOC(\underline{C}H_3)_3$ and 3'''-CH_2); 1.22-1.11 (m, 2H, 2'''-CH_2). ^{13}C NMR (75 MHz, $CDCl_3$): δ 172.2 (C-7); 171.7 (C-1); 171.1 (C-4); 171.0 (C-10); 163.5 (N=C); 157.8 (C-4'); 156.3 ($NH\underline{C}OOC(CH_3)_3$); 153.5 ($N\underline{C}OOC(CH_3)_3$); 136.1 (C-1''); 133.5 ($OCH_2\underline{C}H=CH_2$); 130.4 (C-2' and C-6'); 129.4 (C-3'' and C-5''); 128.8 (C-2'' and C-6''); 128.6 (C-1'); 127.4 (C-4''); 117.8 ($OCH_2CH=\underline{C}H_2$); 115.1 (C-3' and C-5'); 83.5 ($NCOO\underline{C}(CH_3)_3$); 79.8 ($NHCOO\underline{C}(CH_3)_3$); 69.0 ($O\underline{C}H_2CH=CH_2$); 54.9 (C-8); 53.6 (C-5); 53.1

(C-2); 52.7 (OCH_3); 40.9 (C-4'''); 38.0 (2-$CH\underline{C}H_2$); 37.4 (8-$CH\underline{C}H_2$); 32.0 (C-1'''); 28.8 (C-3'''); 28.4 ($NCOOC(\underline{C}H_3)_3$[a]); 28.3 ($NHCOOC(\underline{C}H_3)_3$[a]); 23.1 (C-11); 22.7 (C-2''').

Methyl (6*S*,9*S*)-9-(4-allyloxybenzyl)-4,7,10-triaza-6-[4-(*N,N*-di-*tert*-butoxycarbonyl)guanidinobutyl]-5,8,11-trioxododecanoate (40)

Starting with the ester **33** (104 mg, 0.18 mmol) procedure E was used to access the *N*-Boc deprotected trifluoroacetate salt. This salt was then carried forward (assuming 100% yield) for use in procedure G, along with $(BocNH)_2C{=}NSO_2CF_3$ (75 mg, 0.19 mmol) and NEt_3 (0.11 mL, 0.79 mmol) to yield **40** (118 mg, 0.16 mmol, 88%) as a white powder, mp. 122-126°C. MS (ESI^+), *m/z* 719 (100%). HRMS (ESI^+) calcd for $C_{35}H_{54}N_6O_{10}$ + H: 719.3974; found 719.3980. ^1H NMR (300 MHz, $CDCl_3$): δ 11.42 (s, 1H, $N\underline{H}COOC(CH_3)_3$); 8.33 (s, 1H, 4''-$CH_2N\underline{H}$); 7.14 (bs, 1H, 7-NH); 7.07 (d, *J* = 8.6 Hz, 2H, 2'-CH and 6'-CH); 6.89 (t, *J* = 5.91 Hz, 1H, 4-NH); 6.81 (d, *J* = 8.45 Hz, 2H, 3'-CH and 5'-CH); 6.78 (s, 1H, 10-NH); 6.03 (tdd, *J* = 17.1, 10.5, 5.3 Hz, 1H, $OCH_2C\underline{H}{=}CH_2$); 5.39 (dd, *J* = 17.3, 1.5 1H, $OCH_2CH{=}C\underline{H}H$ *trans*); 5.27 (dd, *J* = 10.5, 1.3 Hz, 1H, $OCH_2CH{=}CH\underline{H}$ *cis*); 4.77-4.71 (m, 1H, 9-CH); 4.49 (bd, *J* = 5.28 Hz, 2H, $OC\underline{H}_2CH{=}CH_2$); 4.39-4.33 (m, 1H, 6-CH); 3.68 (s, 3H, OCH_3); 3.57-3.36 (m, 2H, 3-CH_2); 3.32 (bs, 2H, 4''-CH_2); 3.00 (dd, *J* = 13.8, 6.8 Hz, 1H, 9-$CHC\underline{H}_aH_b$); 2.92 (dd, *J* = 13.9, 7.3 Hz, 1H, 9-$CHCH_a\underline{H}_b$); 2.52 (t, *J* = 6.3 Hz, 2H, 2-CH_2); 1.98 (s, 3H, 12-CH_3); 1.82-1.76 (m, 1H, 1''-$C\underline{H}_aH_b$); 1.58-1.52 (m, 1H, 1''-$CH_a\underline{H}_b$); 1.53-143 (m, 20H, $NHCOOC(C\underline{H}_3)_3$, $C{=}NCOOC(C\underline{H}_3)_3$ and 3''-CH_2); 1.37-1.25 (m, 2H, 2''-CH_2). ^{13}C NMR (75 MHz, $CDCl_3$): δ 172.9 (C-1); 171.7 (C-5); 171.4 (C-8); 171.1 (C-11); 163.5 (C=N); 157.8 (C-4'); 156.4 ($NH\underline{C}OOC(CH_3)_3$); 153.5 ($N\underline{C}OOC(CH_3)_3$); 133.4 ($OCH_2\underline{C}H{=}CH_2$); 130.4 (C-2' and C-6'); 128.5 (C-1'); 117.9 ($OCH_2CH{=}\underline{C}H_2$); 115.1 (C-3' and C-5'); 83.5 ($NCOO\underline{C}(CH_3)_3$); 79.8 ($NHCOO\underline{C}(CH_3)_3$); 69.0 ($O\underline{C}H_2CH{=}CH_2$); 54.9 (C-9); 53.3 (C-6); 52.1 (OCH_3); 40.9 (C-4''); 37.5 (9-$CH\underline{C}H_2$); 35.3 (C-3); 33.8 (C-2); 32.1 (C-1''); 28.7 (C-3''); 28.4 ($NHCOOC(\underline{C}H_3)_3$[a]); 28.3 ($NCOOC(\underline{C}H_3)_3$[a]); 23.2 (C-12); 23.0 (C-2'').

Methyl (7*S*,10*S*)-10-(4-allyloxybenzyl)-5,8,11-triaza-7-[4-(*N,N*-di-*tert*-butoxycarbonyl)guanidinobutyl]-6,9,12-trioxotridecanoate (41)

Using procedure E, the ester **34** (135 mg, 0.23 mmol) gave the uncharacterised *N*-Boc deprotected trifluoroacetate salt, which was carried forward (assuming 100% yield) using procedure G, with $(BocNH)_2C{=}NSO_2CF_3$ (101 mg, 0.26 mmol), NEt_3 (0.20 mL, 1.44 mmol) and CH_2Cl_2 (4 mL) to yield **41** (122 mg, 0.17 mmol, 73%) as a white powder, mp. 145-147°C. MS (ESI^+), *m/z* 733 (100%) [MH^+]. HRMS (ESI^+) calcd for $C_{36}H_{56}N_6O_{10}$ + H: 733.4131; found 733.4133. ^1H NMR (300 MHz, $CDCl_3$): δ 11.45 (bs, 1H, $N\underline{H}COOC(CH_3)_3$); 8.27 (bs, 1H, 4''-$CH_2N\underline{H}$); 7.07 (d, *J* = 8.7 Hz, 2H, 2'-CH and 6'-CH); 6.81 (d, *J* = 8.7 Hz, 2H, 3'-CH and 5'-CH); 6.77 (d, *J* = 8.2 Hz, 1H, 8-NH); 6.56 (t, *J* = 5.6 Hz, 1H, 5-NH); 6.47 (d, *J* = 7.5 Hz, 1H, 11-NH); 6.02 (tdd, *J* = 17.3, 10.5, 5.3 Hz, 1H, $OCH_2C\underline{H}{=}CH_2$); 5.38 (dd, *J* = 17.3, 1.6 Hz, 1H, $OCH_2CH{=}C\underline{H}H$ *trans*); 5.26 (dd, *J* = 10.5, 1.4 Hz, 1H, $OCH_2CH{=}CH\underline{H}$ *cis*); 4.70-4.66 (m, 1H, 7-CH); 4.48 (d, *J* = 5.3 Hz, 2H, $OC\underline{H}_2CH{=}CH_2$); 4.36-4.31 (m, 1H, 10-CH); 3.66 (s, 3H, OCH_3); 3.32 (m, 2H, 4''-CH_2); 3.22 (m, 2H, 4-CH_2); 3.06-2.88 (m, 2H, 10-$CHC\underline{H}_2$); 2.34 (t, *J* = 7.3 Hz, 2H, 2-CH_2); 1.99 (s, 3H, 13-CH_3); 1.89-1.73 (m, 3H, 1''-$C\underline{H}_aH_b$ and 3-CH_2); 1.64-1.50 (m, 3H, 1''-$CH_a\underline{H}_b$ and 3''-CH_2); 1.47 (s, 18H, $NHCOOC(C\underline{H}_3)_3$ and $C{=}NCOOC(C\underline{H}_3)_3$); 1.33-1.23 (m, 2H, 2''-CH_2). ^{13}C NMR (75 MHz, $CDCl_3$): δ 173.9 (C-1); 171.3 (C-9); 171.2 (C-6); 170.7 (C-12); 163.7 (N=C); 157.9 (C-4'); 156.3 ($NH\underline{C}OOC(CH_3)_3$); 153.5 ($N\underline{C}OOC(CH_3)_3$); 133.5 ($OCH_2\underline{C}H{=}CH_2$); 130.4 (C-2' and C-6'); 128.6 (C-1'); 117.8 ($OCH_2CH{=}\underline{C}H_2$); 115.1 (C-3' and C-5'); 83.3 ($NCOO\underline{C}(CH_3)_3$); 79.5 ($NHCOO\underline{C}(CH_3)_3$); 69.0 ($O\underline{C}H_2CH{=}CH_2$); 54.9 (C-10); 53.2 (C-7); 51.9 (OCH_3); 40.9 (C-4''); 39.1 (C-4); 37.5 (10-$CH\underline{C}H_2$); 32.1 (C-1''); 31.6 (C-2); 28.8 (C-3''); 28.5 ($NCOOC(\underline{C}H_3)_3$[a]); 28.3 ($NHCOOC(\underline{C}H_3)_3$[a]); 24.7 (C-3); 23.3 (C-13); 23.1 (C-2'').

Methyl (6*S*,9*S*)-9-(4-allyloxybenzyl)-4,7,10-triaza-6-[4-(*N,N*-di-*tert*-butoxycarbonyl)guanidinobutyl]-3-methoxycarbonylmethyl-5,8,11-trioxododecanoate (42)

Starting with the ester **35** (150 mg, 0.23 mmol) procedure E was used to obtain the corresponding *N*-Boc deprotected trifluoroacetate salt. The salt was then used directly (assuming 100% yield) in procedure G, together with $(BocNH)_2C{=}NSO_2CF_3$ (106 mg, 0.27 mmol), NEt_3 (0.1 mL, 0.72 mmol) and CH_2Cl_2 (4 mL) as solvent to yield **42** (123 mg, 0.16 mmol, 67%) as a white powder, mp. 161-163°C. MS (ESI^+), *m/z* 791 (100%) [MH^+]. HRMS (ESI^+) calcd for $C_{38}H_{58}N_6O_{12}$ + H: 791.4185; found 791.4190. ^1H NMR (300 MHz, $CDCl_3$): δ 11.46 (bs, 1H, $N\underline{H}COOC(CH_3)_3$); 8.36 (bs, 1H, 4''-$CH_2N\underline{H}$); 7.09 (d, *J* = 8.6 Hz, 2H, 2'-CH and 6'-CH); 6.96 (d, *J* = 8.5 Hz, 1H, 4-NH); 6.82 (d, *J* = 8.6 Hz, 2H, 3'-CH and 5'-CH); 6.73 (d, *J* = 7.9 Hz, 1H, 7-NH); 6.35 (d, *J* = 7.5 Hz, 1H, 10-NH); 6.02 (tdd, *J* = 17.2, 10.5, 5.3 Hz, 1H, $OCH_2C\underline{H}{=}CH_2$); 5.38 (dd, *J* = 17.3, 1.5 Hz, 1H, $OCH_2CH{=}C\underline{H}H$ *trans*); 5.25 (dd, *J* = 10.5, 1.3 Hz, 1H, $OCH_2CH{=}CH\underline{H}$ *cis*); 4.63-4.58 (m, 1H, 9-CH); 4.57-4.51 (m, 1H, 3-CH); 4.48 (d, *J* = 5.3 Hz, 2H, $OC\underline{H}_2CH{=}CH_2$); 4.32-4.28 (m, 1H, 6-CH); 3.66 (s, 6H, 1-$COOCH_3$ and 3-$CHCH_2COOC\underline{H}_3$); 3.36 (m, 2H, 4''-$CH_2$); 3.05 (dd, *J* = 14.0, 6.6 Hz, 1H, 9-$CHC\underline{H}_aH_b$); 2.94 (dd, *J* = 14.2, 7.2 Hz, 1H, 9-$CHCH_a\underline{H}_b$); 2.66-2.60 (m, 4H, 2-CH_2 and 3-CCH_2); 1.97 (s, 3H, 12-CH_3); 1.87-1.75 (m, 1H, 1''-$C\underline{H}_aH_b$); 1.64-1.51 (m, 1H, 1''-$CH_a\underline{H}_b$); 1.52-1.42 (m, 20H, $NHCOOC(C\underline{H}_3)_3$, $C{=}NCOOC(C\underline{H}_3)_3$ and 3''-CH_2); 1.34-1.22 (m, 2H, 2''-CH_2). ^{13}C NMR (75 MHz, $CDCl_3$): δ 171.6 (C-1 and 3-$CHCH_2\underline{C}OOCH_3$); 171.3 (C-8); 170.7 (C-5 and C-11); 163.5 (N=C); 157.8 (C-4'); 156.4 ($NH\underline{C}OOC(CH_3)_3$); 153.4 ($N\underline{C}OOC(CH_3)_3$); 133.5 ($OCH_2\underline{C}H{=}CH_2$); 130.4 (C-2' and C-6'); 128.8 (C-1'); 117.8 ($OCH_2CH{=}\underline{C}H_2$); 115.1 (C-3' and C-5'); 83.4 ($NCOO\underline{C}(CH_3)_3$); 79.6 ($NHCOO\underline{C}(CH_3)_3$); 69.0 ($O\underline{C}H_2CH{=}CH_2$); 55.1 (C-9); 53.2 (C-6); 52.1 (OCH_3); 41.0 (C-4''); 37.8 (9-$CH\underline{C}H_2$); 37.1 (C-2 and 3-$CH\underline{C}H_2$); 32.1 (C-3); 31.6 (C-1''); 28.8 (C-3''); 28.4 ($NCOOC(\underline{C}H_3)_3$[a]); 28.2 ($NHCOOC(\underline{C}H_3)_3$[a]); 23.3 (C-11); 22.9 (C-2'').

Methyl (6*S*,9*S*)-9-(4-allyloxybenzyl)-6-(4-aminobutyl)-4,7,10-triaza-5,8,11-trioxododecanoate hydrochloride (43)

Compound **33** (106 mg, 0.18 mmol) was converted to the *N*-Boc deprotected trifluoroacetate salt *via* procedure E. The resulting solid was then converted, *via* procedure H, to the hydrochloride salt **43** (80 mg, 0.16 mmol, 85%) obtained as a hygroscopic light brown amorphous solid. MS (ESI^+), *m/z* 477 (100%), 480 (55). HRMS (ESI^+) calcd for $C_{24}H_{36}N_4O_6$ + H: 477.2713; found 477.2709. $[\alpha]_D^{25}$ +6.6 (*c*. 0.21, EtOH). ^1H NMR (300 MHz, CD_3OD): δ 7.17 (d, *J* = 7.5 Hz, 2H, 2'-CH and 6'-CH); 6.85 (d, *J* = 6.2 Hz, 2H, 3'-CH and 5'-CH); 6.11-5.96 (m, 1H, $OCH_2C\underline{H}{=}CH_2$); 5.36 (bd, *J* = 17.0 Hz, 1H, $OCH_2CH{=}C\underline{H}H$ *trans*); 5.21 (bd, *J* = 10.3 Hz, 1H, $OCH_2CH{=}CH\underline{H}$ *cis*); 4.55-4.45 (m, 3H, $OC\underline{H}_2CH{=}CH_2$ and 9-CH); 4.30-4.22 (m, 1H, 6-CH); 3.66 (s, 3H, OCH_3); 3.39 (bs, 2H, 3-CH_2); 3.13-3.00 (m, 1H, 9-$CHC\underline{H}_aH_b$); 2.99-2.82 (m, 3H, 9-$CHCH_a\underline{H}_b$ and 4''-CH_2); 2.50 (s, 2H, 2-CH_2), 1.97 (s, 3H, 12-CH_3); 1.87-1.75 (m, 1H, 1''-$C\underline{H}_aH_b$); 1.74-1.57 (m, 3H, 1''-$CH_a\underline{H}_b$ and 3''-CH_2); 1.50-1.33 (m, 2H, 2''-CH_2). ^{13}C NMR (75 MHz, CD_3OD): δ 173.4 (C-1); 172.8 (C-5); 172.6 (C-8); 172.0 (C-11); 158.7 (C-4'); 134.8 ($OCH_2\underline{C}H{=}CH_2$); 131.2 (C-2' and C-6'); 130.1 (C-1'); 117.4 ($OCH_2CH{=}\underline{C}H_2$); 115.6 (C-3' and C-

5′); 69.8 (O<u>C</u>H$_2$CH=CH$_2$); 56.7 (C-9); 54.2 (C-6); 51.4 (OCH$_3$); 40.8 (C-4′′); 37.6 (9-CH<u>C</u>H$_2$); 36.3 (C-3); 34.5 (C-2); 32.3 (C-1′′); 27.8 (C-3′′); 23.6 (C-12); 22.7 (C-2′′).

Methyl (7*S*,10*S*)-10-(4-allyloxybenzyl)-7-(4-aminobutyl)-5,8,11-triaza-6,9,12-trioxotridecanoate hydrochloride (44)

Compound **34** (27 mg, 0.05 mmol) was converted to the *N*-Boc deprotected trifluoroacetate salt *via* procedure E, and the resulting solid was then converted immediately, *via* procedure H to the hydrochloride salt **44** (18 mg, 0.03 mmol, 73%) which was obtained as a hygroscopic brown amorphous solid. MS (ESI$^+$), *m/z* 491 (100%) [MH$^+$], 451 (34), 246 (5). HRMS (ESI$^+$) calcd for $C_{25}H_{38}N_4O_6$ + H: 491.2864; found 491.2872. $[\alpha]_D^{25}$ +61.3 (*c*. 0.13, EtOH). ^{1}H NMR (300 MHz, CD$_3$OD): δ 7.17 (d, *J* = 7.9 Hz, 2H, 2′-CH and 6′-CH); 6.86 (d, *J* = 8.3 Hz, 2H, 3′-CH and 5′-CH); 6.13-5.94 (m, 1H, OCH$_2$C<u>H</u>=CH$_2$); 5.38 (bd, *J* = 16.7 Hz, 1H, OCH$_2$CH=C<u>H</u>H *trans*); 5.23 (bd, *J* = 10.2 Hz, 1H, OCH$_2$CH=CH<u>H</u> *cis*); 4.57-4.39 (m, 3H, 10-CH and O<u>C</u>H$_2$CH=CH$_2$); 4.29-4.20 (m, 1H, 7-CH); 3.64 (s, 3H, OCH$_3$); 3.31-3.07 (m, 2H, 4-CH$_2$); 3.03-2.77 (m, 4H, 4′′-CH$_2$ and 10-CHC<u>H</u>$_2$); 2.32 (t, *J* = 6.7 Hz, 2H, 2-CH$_2$); 1.93 (s, 3H, 13-CH$_3$); 1.79-1.58 (m, 4H, 1′′-CH$_2$ and 3-CH$_2$); 1.47-1.30 (m, 4H, 2′′-CH$_2$ and 3′′-CH$_2$). ^{13}C NMR (75 MHz, CD$_3$OD): δ 175.1 (C-1); 174.9 (C-6); 174.5 (C-9); 174.0 (C-12); 158.9 (C-4′); 134.6 (OCH$_2$<u>C</u>H=CH$_2$); 131.1 (C-2′ and C-6′); 130.5 (C-1′); 117.6 (OCH$_2$CH=<u>C</u>H$_2$); 115.3 (C-3′ and C-5′); 70.1 (O<u>C</u>H$_2$CH=CH$_2$); 57.5 (C-10); 54.4 (C-7); 52.4 (OCH$_3$); 40.8 (C-4′′); 39.8 (C-4); 37.9 (10-CH<u>C</u>H$_2$); 32.2 (C-1′′); 31.8 (C-2); 28.1 (C-3′′); 25.3 (C-3); 23.7 (C-13); 22.4 (C-2′′).

Methyl (7*S*,10*S*)-10-(4-allyloxybenzyl)-7-(3-aminopropyl)-5,8,11-triaza-6,9,12-trioxotridecanoate hydrochloride (45)

Compound **49** (121 mg, 0.21 mmol) was converted to the uncharacterised *N*-Boc deprotected trifluoroacetate salt *via* procedure E, and the resulting solid was then converted, *via* procedure H, to the hydrochloride salt **45** (86 mg, 0.17 mmol, 80%), obtained as a hygroscopic brown amorphous solid. MS (ESI$^+$), *m/z* 477 (100%) [MH$^+$], 478 (50). HRMS (ESI$^+$) calcd for $C_{24}H_{36}N_4O_6$ + H: 477.2713; found 477.2711. $[\alpha]_D^{25}$ -41.8 (*c*. 0.15, EtOH). ^{1}H NMR (300 MHz, CD$_3$OD): δ 7.16 (bs, 2H, 2′-CH and 6′-CH); 6.82 (bs, 2H, 3′-CH and 5′-CH); 6.09-5.92 (m, 1H, OCH$_2$C<u>H</u>=CH$_2$); 5.34 (bd, *J* = 15.8 Hz, 1H, OCH$_2$CH=C<u>H</u>H *trans*); 5.19 (bd, *J* = 7.4 Hz, 1H, OCH$_2$CH=CH<u>H</u> *cis*); 4.50-4.44 (m, 3H, 7-CH and O<u>C</u>H$_2$CH=CH$_2$); 4.34-4.23 (m, 1H, 10-CH); 3.60 (s, 3H, OCH$_3$); 3.23-2.75 (m, 6H, 3′′-CH$_2$, 4-CH$_2$ and 10-CHC<u>H</u>$_2$); 2.30 (bs, 2H, 2-CH$_2$); 1.99-1.85 (m, 4H, 1′′-C<u>H</u>$_a$H$_b$ and 13-CH$_3$); 1.81-1.60 (m, 5H, 1′′-CH$_a$<u>H</u>$_b$, 2′′-CH$_2$ and 3-CH$_2$). ^{13}C NMR (75 MHz, CD$_3$OD): δ 174.9 (C-1); 172.6 (C-6); 171.5 (C-9 and C-12); 158.6 (C-4′); 134.7 (OCH$_2$<u>C</u>H=CH$_2$); 131.1 (C-2′ and C-6′); 130.0 (C-1′); 117.3 (OCH$_2$CH=<u>C</u>H$_2$); 115.5 (C-3′ and C-5′); 69.7 (O<u>C</u>H$_2$CH=CH$_2$); 56.8 (C-10); 53.8 (C-7); 52.3 (OCH$_3$); 40.3 (C-3′′); 39.6 (C-4), 37.4 (10-CH<u>C</u>H$_2$); 31.9 (C-2); 29.7 (C-1′′); 25.4 (C-2′′); 24.8 (C-3); 22.7 (C-13).

Methyl (2*S*,5*S*)-5-(4-allyloxybenzyl)-3,6-diaza-2-[3-(*tert*-butoxycarbonyl)aminopropyl]-4,7-dioxooctanoate (47)

Using procedure D, ester **47** was synthesised from the acid **10** (320 mg, 1.22 mmol), (2*S*)-2-amino-5-[(*tert*-butoxycarbonyl) amino]pentanoic acid methyl ester hydrochloride **46** (370 mg, 1.31 mmol), EDCI (270 mg, 1.41 mmol), HOBt (162 mg, 1.20 mmol) and DIPEA (0.25 mL, 1.44 mmol), to yield **47** (484 mg, 0.98 mmol, 81%) as an off-white powder, mp. 92-96°C. MS (ESI$^+$), *m/z* 492 (100%) [MH$^+$], 436 (20), 392 (70). HRMS (ESI$^+$) calcd for $C_{25}H_{37}N_3O_7$ + H: 492.2704; found 492.2711. ^{1}H NMR (500 MHz, CDCl$_3$): δ 7.08 (d, *J* = 7.9 Hz, 2H, 3′-CH and 5′-CH); 6.99 (d, *J* = 6.30 Hz, 1H, 3-NH); 6.80 (d, *J* = 8.5 Hz, 2H, 2′-CH and 6′-CH); 6.57 (d, *J* = 7.8 Hz, 1H, 6-NH); 6.06-5.97 (m, 1H, OCH$_2$C<u>H</u>=CH$_2$); 5.40-5.35 (m, 1H, OCH$_2$CH=C<u>H</u>H *trans*); 5.27-5.23 (m, 1H, OCH$_2$CH=CH<u>H</u> *cis*); 4.85 (bs, 1H, 3′′-CH$_2$N<u>H</u>); 4.73-4.68 (m, 1H, 5-CH); 4.48-4.46 (m, 3H, 2-CH and O<u>C</u>H$_2$CH=CH$_2$); 3.68 (s, 3H, OCH$_3$); 3.08-2.97 (m, 3H, 3′′-CH$_2$ and 5-CHC<u>H</u>$_a$H$_b$); 2.94 (dd, *J* = 13.8, 7.1 Hz, 1H, 5-CHCH$_a$<u>H</u>$_b$); 1.94 (s, 3H, 8-CH$_3$); 1.85-1.76 (m, 1H, 1′′-C<u>H</u>$_a$H$_b$); 1.67-1.62 (m, 1H, 1′′-CH$_a$<u>H</u>$_b$); 1.45-1.36 (m, 11H, OC(C<u>H</u>$_3$)$_3$ and 2′′-CH$_2$). ^{13}C NMR (126 MHz, CDCl$_3$): δ 172.2 (C-4); 171.5 (C-1); 170.5 (C-7); 157.8 (C-4′); 156.4 (NH<u>C</u>OOC(CH$_3$)$_3$); 133.5 (OCH$_2$<u>C</u>H=CH$_2$); 130.5 (C-2′ and C-6′); 128.9 (C-1′); 117.8 (OCH$_2$CH=<u>C</u>H$_2$); 115.0 (C-3′ and C-5′); 79.4 (COO<u>C</u>(CH$_3$)$_3$); 67.0 (O<u>C</u>H$_2$CH=CH$_2$); 54.7 (C-5); 52.6 (C-2); 52.4 (OCH$_3$); 40.1 (C-3′′); 37.7 (5-CH<u>C</u>H$_2$); 29.1 (C-1′′); 28.6 (OC(<u>C</u>H$_3$)$_3$); 26.3 (C-2′′); 23.3 (C-8).

(2*S*,5*S*)-5-(4-Allyloxybenzyl)-3,6-diaza-2-[3-(*tert*-butoxycarbonyl)aminopropyl]-4,7-dioxooctanoic acid (48)

The acid was synthesised using procedure C from the ester **47** (400 mg, 0.81 mmol), LiOH.H$_2$O (95 mg, 2.26 mmol) and THF/water 3:1 (60 mL), to yield **48** (358 mg, 0.75 mmol, 92%) as white crystals, mp. 78-79°C. MS (ESI$^-$), *m/z* 476 (70%) [M - H$^+$], 477 (95), 379 (100). HRMS (ESI$^-$) calcd for $C_{24}H_{35}N_3O_6$ - H: 476.2402; found 476.2411. ^{1}H NMR (500 MHz, CDCl$_3$/CD$_3$OD): δ 7.12 (d, *J* = 8.58 Hz, 2H, 3′-CH and 5′-CH); 6.83 (d, *J* = 8.6 Hz, 2H, 2′-CH and 6′-CH); 6.04 (tdd, *J* = 17.2, 10.5, 5.3 Hz, 1H, OCH$_2$C<u>H</u>=CH$_2$); 5.40 (dd, *J* = 17.3, 1.5 Hz, 1H, OCH$_2$CH=C<u>H</u>H *trans*); 5.27 (dd, *J* = 10.5, 1.4 Hz, 1H, OCH$_2$CH=CH<u>H</u> *cis*); 4.61 (dd, *J* = 8.1, 6.0 Hz, 1H, 5-CH); 4.51-4.49 (m, 2H, O<u>C</u>H$_2$CH=CH$_2$); 4.45-4.41 (m, 1H, 2-CH); 3.09-3.04 (m, 3H, 3′′-CH$_2$ and 5-CHC<u>H</u>$_a$H$_b$); 2.86 (dd, *J* = 14.1, 8.2 Hz, 1H, 5-CHCH$_a$<u>H</u>$_b$); 1.94 (s, 3H, 8-CH$_3$); 1.92-1.84 (m, 1H, 1′′-C<u>H</u>$_a$H$_b$); 1.74-1.65 (m, 1H, 1′′-CH$_a$<u>H</u>$_b$); 1.53-1.47 (m, 2H, 2′′-CH$_2$); 1.44 (s, 9H, OC(C<u>H</u>$_3$)$_3$). ^{13}C NMR (126 MHz, CDCl$_3$/CD$_3$OD): δ 173.3 (C-1); 171.6 (C-4); 171.1 (C-7); 157.2 (C-4′); 156.6 (NH<u>C</u>OOC(CH$_3$)$_3$); 133.0 (OCH$_2$<u>C</u>H=CH$_2$); 129.9 (C-2′ and C-6′); 128.6 (C-1′); 117.1 (OCH$_2$CH=<u>C</u>H$_2$); 114.4 (C-3′ and C-5′); 79.0 (COO<u>C</u>(CH$_3$)$_3$); 68.6 (O<u>C</u>H$_2$CH=CH$_2$); 54.3 (C-5); 51.7 (C-2); 39.5 (C-3′′); 36.7 (5-CH<u>C</u>H$_2$); 28.7 (C-1′′); 28.0 (OC(<u>C</u>H$_3$)$_3$); 25.4 (C-2′′); 22.0 (C-8).

Methyl (7*S*,10*S*)-10-(4-allyloxybenzyl)-5,8,11-triaza-7-[3-(*tert*-butoxycarbonyl)aminopropyl]-6,9,12-trioxotridecanoate (49)

Using procedure D, ester **49** was m from the acid **48** (161 mg, 0.34 mmol), the amine hydrochloride **27** (57 mg, 0.37 mmol), EDCI (107 mg, 0.56 mmol), HOBt (62 mg, 0.46 mmol) and DIPEA (0.07 mL, 0.40 mmol), to yield **49** (156 mg, 0.27 mmol, 80%) as a white powder, mp. 132-135°C. MS (ESI$^+$), *m/z* 577 (60%) [MH$^+$], 542 (20), 255 (100). HRMS (ESI$^+$) calcd for $C_{29}H_{44}N_4O_8$ + H: 577.3237; found 577.3248. ^{1}H NMR (300 MHz, CDCl$_3$): δ 7.29 (d, *J* = 8.2 Hz, 1H, 8-NH); 7.05 (d, *J* = 8.5 Hz, 2H, 2′-CH and 6′-CH); 6.89 (t, *J* = 5.8 Hz, 1H, 5-NH); 6.78 (d, *J* = 8.5 Hz, 2H, 3′-CH and 5′-CH); 6.70 (d, *J* = 7.3 Hz, 1H, 11-NH); 6.00 (tdd, *J* = 15.8, 10.5, 5.3 Hz, 1H, OCH$_2$C<u>H</u>=CH$_2$); 5.36 (dd, *J* = 17.3, 1.4 Hz, 1H, OCH$_2$CH=C<u>H</u>H *trans*); 5.23 (dd, *J* = 10.5, 1.1 Hz, 1H, OCH$_2$CH=CH<u>H</u> *cis*); 4.74-4.68 (m, 1H, 10-CH); 4.50-4.40 (m, 4H, 3′′-CHN<u>H</u>, 7-CH and O<u>C</u>H$_2$CH=CH$_2$); 3.63 (s, 3H, OCH$_3$); 3.27-3.12 (m, 2H, 4-CH$_2$); 3.05-2.87 (m, 4H, 3′′-CH$_2$ and 10-CHC<u>H</u>$_2$); 2.31 (t, *J* = 7.4 Hz, 2H, 2-CH$_2$); 1.94 (s, 3H, 13-CH$_3$); 1.83-1.71 (m, 5H, 1′′-C<u>H</u>$_a$H$_b$, 2′′-CH$_2$ and 3-CH$_2$); 1.61-1.49 (m, 1H, 1′′-CH$_a$<u>H</u>$_b$); 1.39 (m, 9H, OC(C<u>H</u>$_3$)$_3$). ^{13}C NMR (75 MHz, CDCl$_3$): δ 173.6 (C-1); 171.39 (C-6[a]); 171.37 (C-9[a]); 170.5

(C-12); 157.8 (C-4'); 156.9 (NH<u>C</u>OOC$(CH_3)_3$); 133.4 ($OCH_2\underline{C}H=CH_2$); 130.4 (C-2' and C-6'); 128.7 (C-1'); 117.8 ($OCH_2CH=\underline{C}H_2$); 115.0 (C-3' and C-5'); 79.6 (COO<u>C</u>$(CH_3)_3$); 69.0 ($O\underline{C}H_2CH=CH_2$); 54.9 (C-10); 52.8 (C-5); 51.9 (OCH_3); 39.9 (C-3''); 39.0 (C-4); 37.6 (10-CH<u>C</u>H_2); 31.5 (C-2); 29.5 (C-1''); 28.6 (OC(<u>C</u>$H_3)_3$); 26.7 (C-2''); 24.8 (C-3); 23.3 (C-13).

Methyl (*2S*,5*S*,8*S*)-8-(4-allyloxybenzyl)-5-(4-aminobutyl)-2-(3-aminopropyl)-3,6,9-triaza-4,7,10-trioxoundecanoate dihydrochloride (50)

Compound **68** (110 mg, 0.15 mmol) was deprotected to the uncharacterised *N*-Boc trifluoroacetate salt *via* procedure E, and then converted, *via* procedure H to the hydrochloride salt **50** (59 mg, 0.10 mmol, 65%) giving a hygroscopic brown amorphous solid. MS (ESI^+), *m/z* 520 (100%) [MH^+], 521 (40) [MD^+], 420 (37). HRMS (ESI^+) calcd for $C_{26}H_{41}N_5O_6$ + H: 520.3135; found 520.3136. $[\alpha]_D^{25}$ +26.9 (*c*. 0.1, EtOH). ^{1}H NMR (500 MHz, CD_3OD): δ 7.18 (d, *J* = 5.7 Hz, 2H, 3'-CH and 5'-CH); 6.85 (d, *J* = 6.0 Hz, 2H, 2'-CH and 6'-CH); 6.13-5.97 (m, 1H, $OCH_2C\underline{H}=CH_2$); 5.38 (bd, *J* = 17.5 Hz, 1H, $OCH_2CH=C\underline{H}H$ *trans*); 5.23 (bd, *J* = 9.8 Hz, 1H, $OCH_2CH=CH\underline{H}$ *cis*); 4.90-4.85 (m, 1H, 8-CH); 4.56-4.42 (m, 4H, 2-CH and $OC\underline{H}_2CH=CH_2$); 4.37-4.31 (m, 1H, 5-CH); 3.73 (s, 3H, OCH_3); 3.11-2.79 (m, 6H, 3'''-CH_2, 4''-CH_2, and 8-$CHC\underline{H}_2$); 2.00-1.88 (m, 5H, 1''-$C\underline{H}_aH_b$, 1'''-$C\underline{H}_aH_b$ and 11-CH_3); 1.81-1.65 (m, 6H, 1''-$CH_a\underline{H}_b$, 1'''-$CH_a\underline{H}_b$, 2'''-CH_2 and 3''-CH_2); 1.55-1.41 (m, 2H, 2''-CH_2). ^{13}C NMR (126 MHz, CD_3OD): δ 174.0 (C-7); 173.9 (C-1); 173.1 (C-4); 173.0 C-10); 158.6 (C-4'); 134.8 ($OCH_2\underline{C}H=CH_2$); 131.1 (C-2' and C-6'); 130.2 (C-1'); 117.4 ($OCH_2CH=\underline{C}H_2$); 115.6 (C-3' and C-5'); 69.9 ($O\underline{C}H_2CH=CH_2$); 56.6 (C-8); 54.2 (C-2 and C-5); 52.8 (OCH_3); 41.0 (C-4''); 40.7 (C-3'''); 37.6 (8-CH<u>C</u>H_2); 32.1 (C-1''); 29.2 (C-3''); 28.0 (C-1'''); 25.0 (C-2'''); 23.6 (C-11); 22.9 (C-2'').

***N*-{(1*S*,4*S*)-1-(4-Allyloxybenzyl)-11-amino-4-(4-aminobutyl)-3,6-diaza-2,5-dioxoundecyl}acetamide dihydrochloride (51)**

Using procedure E, **69** (80 mg, 0.12 mmol) was deprotected to the *N*-Boc trifluoroacetate salt, and the resulting solid converted, *via* procedure H to the hydrochloride salt **51** (44 mg, 0.08 mmol, 68%) giving a hygroscopic brown amorphous solid. MS (ESI^+), *m/z* 476 (10%) [MH^+], 259 (17), 239 (100). HRMS (ESI^+) calcd for $C_{25}H_{41}N_5O_4$ + H: 476.3237; found 476.3229. $[\alpha]_D^{25}$ +11.8 (*c*. 0.10, EtOH). ^{1}H NMR (300 MHz, CD_3OD): δ 7.21 (bs, 2H, 2'-CH and 6'-CH); 6.86 (d, *J* = 6.5 Hz, 2H, 3'-CH and 5'-CH); 6.13-5.97 (m, 1H, $OCH_2C\underline{H}=CH_2$); 5.39 (bd, *J* = 17.3 Hz, 1H, $OCH_2CH=C\underline{H}H$ *trans*); 5.23 (bd, *J* = 10.5 Hz, 1H, $OCH_2CH=CH\underline{H}$ *cis*); 4.55-4.47 (m, 3H, $O\underline{C}H_2CH=CH_2$ and 1-CH); 4.31-4.21 (m, 1H, 3-CH); 3.33-3.28 (m, 2H, 7-CH_2); 3.20-3.11 (m, 1H, 1-$CHC\underline{H}_aH_b$); 2.98-2.86 (m, 5H, 1-$CHCH_a\underline{H}_b$, 4''-CH_2 and 11-CH_2); 2.00-1.85 (m, 4H, $COCH_3$ and 1''-CH_2); 1.75-1.62 (m, 5H, 18-CH_2, 10-CH_2 and 3''-CH_2); 1.57-1.35 (m, 4H, 2''-CH_2 and 9-CH_2). ^{13}C NMR (75 MHz, CD_3OD): δ 174.2 (C-8); 173.8 ($\underline{C}OCH_3$); 173.7 C-2); 159.0 (C-4'); 135.0 ($OCH_2\underline{C}H=CH_2$); 130.4 (C-2' and C-6'); 129.7 (C-1'); 117.5 ($OCH_2CH=\underline{C}H_2$); 115.8 (C-3' and C-5'); 69.8 ($O\underline{C}H_2CH=CH_2$); 57.1 (C-1); 54.7 (C-4); 40.7 (C-4'' and C-14); 40.1 (C-7); 37.6 (1-CH<u>C</u>H_2); 32.4 (C-1''); 29.7 (C-3''); 28.1 (C-10); 28.0 (C-8); 24.7 (C-9); 23.9 (CO<u>C</u>H_3); 22.7 (C-2'').

(6*S*,9*S*)-9-(4-Allyloxybenzyl)-6-(4-aminobutyl)-4,7,10-triaza-5,8,11-trioxododecanamide hydrochloride (52)

Compound **70** (100 mg, 0.18 mmol) was converted to the *N*-Boc deprotected trifluoroacetate salt *via* procedure E, and the resulting solid was then converted, *via* procedure H, to give the hydrochloride salt **52** (67 mg, 0.14 mmol, 76%) as a hygroscopic light brown amorphous solid. MS (ESI^+), *m/z* 462 (100%) [MH^+], 463 (85), 422 (40), 174 (75). HRMS (ESI^+) calcd for $C_{23}H_{35}N_5O_5$ + H: 462.2716; found 462.2714. $[\alpha]_D^{25}$ +86.0 (*c*. 0.17, EtOH). ^{1}H NMR (300 MHz, CD_3OD): δ 7.17 (d, *J* = 8.4 Hz, 2H, 2'-CH and 6'-CH); 6.86 (d, *J* = 8.5 Hz, 2H, 3'-CH and 5'-CH); 6.04 (tdd, *J* = 17.3, 10.6, 5.2 Hz, 1H, $OCH_2C\underline{H}=CH_2$); 5.38 (dd, *J* = 17.3, 1.6 Hz, 1H, $OCH_2CH=C\underline{H}H$ *trans*); 5.23 (dd, *J* = 10.7, 1.3 Hz, 1H, $OCH_2CH=CH\underline{H}$ *cis*); 4.51 (d, *J* = 5.1 Hz, 2H, $OC\underline{H}_2CH=CH_2$); 4.48-4.39 (m, 1H, 9-CH); 4.30-4.19 (m, 1H, 6-CH); 3.38 (t, *J* = 6.0 Hz, 1H, 3-CH_2); 2.96-2.80 (m, 4H, 4''-CH_2 and 9-$CHC\underline{H}_2$); 2.45-2.34 (m, 2H, 2-CH_2); 1.93 (s, 3H, 12-CH_3); 1.89-1.74 (m, 2H, 1''-$C\underline{H}_aH_b$); 1.72-1.54 (m, 3H, 1''-$CH_a\underline{H}_b$ and 3''-CH_2); 1.48-1.30 (m, 2H, 2''-CH_2). ^{13}C NMR (75 MHz, CD_3OD): δ 173.8 (C-1); 173.7 (C-5); 173.5 (C-8); 173.0 (C-11); 159.0 (C-4'); 135.0 ($OCH_2\underline{C}H=CH_2$); 131.4 (C-2' and C-6'); 129.1 (C-1'); 117.5 ($OCH_2CH=\underline{C}H_2$); 115.8 (C-3' and C-5'); 69.8 ($O\underline{C}H_2CH=CH_2$); 57.0 (C-9); 54.4 (C-6); 40.6 (C-4''); 37.7 (9-CH<u>C</u>H_2); 36.9 (C-3); 36.4 (C-2); 32.4 (C-1''); 28.0 (C-3''); 23.6 (C-12); 22.5 (C-2'').

Methyl (8*S*,11*S*)-11-(4-allyloxybenzyl)-8-(4-aminobutyl)-3,6,9,12-tetraaza-4,7,10,13-tetraoxotetradecanoate hydrochloride (53)

Compound **71** (71 mg, 0.11 mmol) was converted to the uncharacterised *N*-Boc deprotected trifluoroacetate salt *via* procedure E, and the resulting solid was then converted, *via* procedure H to give the hydrochloride salt **53** (47 mg, 0.08 mmol, 73%) as a hygroscopic white amorphous solid. MS (ESI^+), *m/z* 520 (100%) [MH^+], 521 (30), 506 (20). HRMS (ESI^+) calcd for $C_{25}H_{37}N_5O_7$ + H: 520.2771; found 520.2776. $[\alpha]_D^{25}$ +46.1 (*c*. 0.12, EtOH). ^{1}H NMR (300 MHz, CD_3OD): δ 7.19 (bs, 2H, 2'-CH and 6'-CH); 6.85 (bs, 2H, 3'-CH and 5'-CH); 6.13-5.94 (m, 1H, $OCH_2C\underline{H}=CH_2$); 5.37 (bd, *J* = 15.1 Hz, 1H, $OCH_2CH=C\underline{H}H$ *trans*); 5.22 (bd, *J* = 5.3 Hz, 1H, $OCH_2CH=CH\underline{H}$ *cis*); 4.62-4.43 (m, 3H, 11-CH and $OC\underline{H}_2CH=CH_2$); 4.36-4.24 (m, 1H, 8-CH); 4.01-3.83 (m, 4H, 2-CH_2 and 5-CH_2); 3.69 (s, 3H, OCH_3); 3.12-2.78 (m, 4H, 4''-CH_2 and 11-$CHC\underline{H}_2$); 2.03-1.85 (m, 3H, 14-CH_3); 1.78-1.61 (m, 4H, 1''-CH_2 and 3''-CH_2); 1.54-1.38 (m, 2H, 2''-CH_2). ^{13}C NMR (75 MHz, CD_3OD): δ 174.4 (C-10); 174.0 (C-7); 173.6 (C-4); 171.7 (C-13); 171.3 (C-1); 158.6 (C-4'); 134.8 ($OCH_2\underline{C}H=CH_2$); 131.3 (C-2' and C-6'); 130.1 (C-1'); 117.5 ($OCH_2CH=\underline{C}H_2$); 115.6 (C-3' and C-5'); 69.7 ($O\underline{C}H_2CH=CH_2$); 56.6 (C-11); 54.6 (C-8); 53.0 (OCH_3); 43.3 (C-5); 41.9 (C-4''); 40.7 (C-2); 37.6 (10-CH<u>C</u>H_2); 31.7 (C-3''); 27.8 (C-1''); 23.5 (C-14); 22.6 (C-2'').

***N*-{(1*S*,4*S*)-1-(4-Allyloxybenzyl)-8-amino-3-aza-4-{*N*-[4-(2-pyridinyl)methyl]piperazinyl}carbonyl-2-oxooctyl}acetamide hydrochloride (54)**

Using procedure E, **72** (90 mg, 0.14 mmol) was converted to the *N*-Boc trifluoroacetate salt. The resulting solid was then converted, *via* procedure H, to the hydrochloride salt **54** (67 mg, 0.11 mmol, 82%) giving a hygroscopic brown amorphous solid. MS (ESI^+), *m/z* 551 (100%) [MH^+], 552 (37), 331 (42). HRMS (ESI^+) calcd for $C_{30}H_{42}N_6O_4$ + H: 551.3346; found 551.3354. $[\alpha]_D^{25}$ +41.8 (*c*. 0.11, EtOH). ^{1}H NMR (300 MHz, CD_3OD): δ 8.83-8.75 (m, 1H, 6'''-CH); 8.23-8.10 (m, 1H, 4'''-CH); 7.87-7.78 (m, 1H, 3'''-CH); 7.72-7.64 (m, H, 5'''-CH); 7.17 (d, *J* = 7.6 Hz, 2H, 2'-CH and 6'-CH); 6.86 (d, *J* = 7.4 Hz, 2H, 3'-CH and 5'-CH); 6.11-5.98 (m, 1H, $OCH_2C\underline{H}=CH_2$); 5.38 (bd, *J* = 17.3 Hz, 1H, $OCH_2CH=C\underline{H}H$ *trans*); 5.23 (bd, *J* = 10.4 Hz, 1H, $OCH_2CH=CH\underline{H}$ *cis*); 4.83-4.75 (m, 1H, 1-CH); 4.67-4.58 (m, 1H, 4-CH); 4.51 (d, *J* = 4.7 Hz, 1H, $OC\underline{H}_2CH=CH_2$); 4.02-3.91 (m, 2H, 4''-NCH_2); 3.50-3.21 (m, 6H, 2''-$C\underline{H}_2$, 6''-CH_2 and 8-CH_2); 3.07-2.79 (m, 6H, 3''-CH_2, 1-$CHC\underline{H}_2$ and 5''-CH_2); 1.93 (s, 3H, $COCH_3$); 1.79-1.62 (m, 4H, 5-CH_2 and 7-CH_2); 1.53-1.38 (m, 2H, 6-CH_2). ^{13}C NMR (75 MHz, CD_3OD): δ 173.5 (C-2); 171.7 ($\underline{C}OCH_3$); 158.8 (C-4'); 158.3 (C-2'''); 147.6 (C-6'''); 147.1 (C-4'''');

145.2 (C-3‴); 134.9 ($OCH_2\underline{C}H=CH_2$); 131.3 (C-2′ and C-6′); 130.3 (C-5‴); 128.4 (C-1′); 117.5 ($OCH_2CH=\underline{C}H_2$); 115.7 (C-3′ and C-5′); 69.9 ($O\underline{C}H_2CH=CH_2$); 59.4 (4′′-$NHCH_2$); 56.6 (C-1); 54.2 (C-4); 48.6 (C-3′′ and C-5′′); 44.3 (C-2′′ and C-6′′); 41.0 (C-8); 37.8 (1-$CH\underline{C}H_2$); 32.2 (C-5); 28.3 (C-7); 23.6 ($CO\underline{C}H_3$); 22.7 (C-6).

_N_-{(1*S*,4*S*)-1-(4-Allyloxybenzyl)-8-amino-3-aza-4-[3-(methoxycarbonylmethyl)phenylcarbamoyl]-2-oxooctyl}acetamide hydrochloride (55)

Using procedure E, **73** (79 mg, 0.12 mmol) was deprotected to the *N*-Boc deprotected trifluoroacetate salt, and the resulting solid reacted *via* procedure H giving the hydrochloride salt **55** (46 mg, 0.08 mmol, 64%) as a hygroscopic brown amorphous solid. MS (ESI^+), *m/z* 539 (100%) [MH^+], 540 (33), 406 (70). HRMS (ESI^+) calcd for $C_{29}H_{38}N_4O_6$ + H: 539.2870; found 539.2876. $[\alpha]_D^{25}$ -25.8 (*c*. 0.14, EtOH). ^{1}H NMR (300 MHz, CD_3OD): δ 7.59-7.50 (m, 2H, 2′′-CH and 6′′-CH); 7.30-7.15 (m, 2H, 2′-CH and 6′-CH); 7.07-7.01 (m, 1H, 5′′-CH); 6.92-6.82 (m, 2H, 3′-CH and 5′-CH); 6.80-6.71 (m, 1H, 4′′-CH); 6.19-5.86 (m, 1H, $OCH_2C\underline{H}=CH_2$); 5.39 (bd, *J* = 17.5 Hz, 1H, $OCH_2CH=C\underline{H}H$ *trans*); 5.20 (bd, *J* = 10.0 Hz, 1H, $OCH_2CH=CH\underline{H}$ *cis*); 4.61-4.46 (m, 3H, $OC\underline{H}_2CH=CH_2$ and 1-CH); 4.38-4.27 (m, 1H, 4-CH); 3.67 (s, 3H, OCH_3); 3.37 (s, 2H, 3′′-CCH_2); 3.12-2.81 (m, 4H, 8-CH_2 and 1-$CHC\underline{H}_2$); 2.03-1.89 (m, 4H, 5-$C\underline{H}_aH_b$ and $COCH_3$); 1.79-1.61 (m, 3H, 5-$CH_a\underline{H}_b$ and 7-CH_2); 1.56-1.40 (m, 2H, 6-CH_2). ^{13}C NMR (75 MHz, CD_3OD): δ 173.6 (4-$CH\underline{C}$=O); 173.3 (C-5); 172.9 (3′′-$CCH_2\underline{C}$=O); 171.7 ($\underline{C}OCH_3$); 158.8 (C-4′); 139.4 (C-1′′); 136.2 (C-3′′); 134.9 ($OCH_2\underline{C}H=CH_2$); 131.4 (C-1′); 131.2 (C-2′ and C-6′); 129.9 (C-5′′); 126.3 (C-4′′); 122.1 (C-2′′); 120.0 (C-6′′); 117.3 ($OCH_2CH=\underline{C}H_2$); 115.6 (C-3′ and C-5′); 69.6 ($O\underline{C}H_2CH=CH_2$); 56.9 (C-1); 55.0 (C-4); 52.6 (OCH_3); 41.7 (3′′-$C\underline{C}H_2$); 40.6 (C-8); 37.7 (1-$CH\underline{C}H_2$); 32.4 (C-5); 28.0 (C-7); 23.7 ($CO\underline{C}H_3$); 22.7 (C-6).

_N_-{(1*S*,4*S*)-8-Amino-1-(4-allyloxybenzyl)-3-aza-4-[3-(methoxycarbonyl)benzyl]carbamoyl-2-oxooctyl}acetamide hydrochloride (56)

Compound **74** (88 mg, 0.14 mmol) was deprotected to the uncharacterised *N*-Boc trifluoroacetate salt *via* procedure E, and then converted, *via* procedure H, to the hydrochloride salt **56** (70 mg, 0.12 mmol, 89%), giving a hygroscopic brown amorphous solid. MS (ESI^+), *m/z* 539 (100%) [MH^+], 540 (40) [MD^+]. HRMS (ESI^+) calcd for $C_{29}H_{38}N_4O_6$ + H: 539.2870; found 539.2869. $[\alpha]_D^{25}$ +100.6 (*c*. 0.16, EtOH). ^{1}H NMR (300 MHz, CD_3OD): δ 7.95-7.90 (m, 2H, 2′′-CH and 4′′-CH); 7.53-7.45 (m, 2H, 5′′-CH and 6′′-CH); 7.20-7.13 (m, 2H, 2′-CH and 6′-CH); 7.10-7.03 (m, 2H, 3′-CH and 5′-CH); 6.28-6.13 (m, 1H, $OCH_2C\underline{H}=CH_2$); 5.49 (bd, *J* = 16.7 Hz, 1H, $OCH_2CH=C\underline{H}H$ *trans*); 5.36 (bd, *J* = 9.7 Hz, 1H, $OCH_2CH=CH\underline{H}$ *cis*); 4.87-4.82 (m, 3H, $NHC\underline{H}_2Ar$ and 1-CH); 4.79-4.73 (m, 2H, $OC\underline{H}_2CH=CH$); 4.63-4.54 (m, 1H, 4-CH); 3.63 (s, 3H, OCH_3); 3.37-3.22 (m, 2H, 8-CH_2); 2.96-2.89 (m, 1H, 1-$CHC\underline{H}_2$); 1.99-1.66 (m, 7H, $COCH_3$, 5-CH_2 and 7-CH_2); 1.54-1.43 (m, 2H, 6-CH_2). ^{13}C NMR (75 MHz, CD_3OD): δ 176.8 (C-2); 175.3 (4-$CH\underline{C}$=O); 174.0 ($\underline{C}OCH_3$); 167.6 ($\underline{C}OOCH_3$); 158.2 (C-4′); 134.5 (C-1′′); 134.1 ($OCH_2\underline{C}H=CH_2$); 132.2 (C-2′ and C-6′); 130.1 (C-6′′); 129.2 (C-1′); 128.5 (C-3′′); 122.7 (C-2′′ and C-5′′); 122.3 (C-4′′); 119.7 ($OCH_2CH=\underline{C}H_2$); 114.5 (C-3′ and C-5′); 71.4 ($O\underline{C}H_2CH=CH_2$); 54.9 (C-1 and C-4); 52.3 (OCH_3); 40.7 (C-8); 39.7 (1-$CH\underline{C}H_2$); 32.1 (C-5); 28.2 (C-7); 25.7 ($CO\underline{C}H_3$); 23.8 (C-6).

_N_-{(1*S*,4*S*)-1-(4-Allyloxybenzyl)-8-amino-3-aza-4-(3-methoxycarbonyl)phenylcarbamoyl-2-oxooctyl}acetamide hydrochloride (57)

Using procedure E, **75** (55 mg, 0.09 mmol) was deprotected to the *N*-Boc deprotected trifluoroacetate salt, and the resulting solid reacted *via* procedure H giving the hydrochloride salt **57** (40 mg, 0.07 mmol, 81%) as a hygroscopic light brown amorphous solid. MS (ESI^+), *m/z* 525 (100%) [MH^+], 526 (30), 406 (15). HRMS (ESI^+) calcd for $C_{28}H_{36}N_4O_6$ + H: 525.2713; found 525.2705. $[\alpha]_D^{25}$ -56.9 (*c*. 0.09, EtOH). ^{1}H NMR (300 MHz, CD_3OD): δ 8.26 (s, 1H, 2′′-CH); 7.79-7.70 (m, 2H, 4′′-CH and 6′′-CH); 7.41 (dd, *J* = 6.8, 6.8 Hz, 1H, 5′′-CH); 7.12 (d, *J* = 7.4 Hz, 2H, 2′-CH and 6′-CH); 6.70 (d, *J* = 6.6 Hz, 2H, 3′-CH and 5′-CH); 6.00-5.85 (m, 1H, $OCH_2C\underline{H}=CH_2$); 5.28 (bd, *J* = 17.1 Hz, 1H, $OCH_2CH=C\underline{H}H$ *trans*); 5.16 (bd, *J* = 10.4 Hz, 1H, $OCH_2CH=CH\underline{H}$ *cis*); 4.53-4.48 (m, 2H, 1-CH and 4-CH); 4.29 (bs, 2H, $OC\underline{H}_2CH=CH_2$); 3.88 (s, 3H, OCH_3); 3.28 (bs, 2H, 8-CH_2); 3.07-2.81 (m, 2H, 1-$CHC\underline{H}_2$); 2.01-1.88 (m, 4H, $COCH_3$ and 5-$C\underline{H}_aH_b$); 1.74-1.62 (m, 3H, 5-$CH_a\underline{H}_b$ and 7-CH_2); 1.46 (bs, 2H, 6-CH_2). ^{13}C NMR (75 MHz, CD_3OD): δ 173.9 (4-$CH\underline{C}$O); 172.8 (C-2); 172.1 ($\underline{C}OCH_3$); 168.1 ($\underline{C}OOCH_3$); 158.8 (C-4′); 139.8 (C-1′′); 134.9 ($OCH_2\underline{C}H=CH_2$); 131.9 (C-2′ and C-6′); 131.2 (C-3′′); 130.1 (C-1′); 130.0 (C-5′′); 126.2 (C-4′′); 125.7 (C-6′′); 122.1 (C-2′′); 117.2 ($OCH_2CH=\underline{C}H_2$); 115.6 (C-3′ and C-5′); 69.6 ($O\underline{C}H_2CH=CH_2$); 56.9 (C-1); 54.9 (C-4); 52.8 (OCH_3); 40.6 (C-8); 37.8 (1-$CH\underline{C}H_2$); 32.3 (C-5); 28.0 (C-7); 23.6 ($CO\underline{C}H_3$); 22.5 (C-6).

Methyl (8*S*,11*S*)-11-(4-allyloxybenzyl)-8-(4-aminobutyl)-6,9,12-triaza-7,10,13-trioxotetradecanoate hydrochloride (58)

Compound **76** (70 mg, 0.12 mmol) was converted to the *N*-Boc deprotected trifluoroacetate salt *via* procedure E, and the resulting solid was then converted, *via* procedure H, to give the hydrochloride salt **58** (53 mg, 0.10 mmol, 84%) as a hygroscopic brown amorphous solid. MS (ESI^+), *m/z* 505 (100%) [MH^+], 508 (80), 509 (23). HRMS (ESI^+) calcd for $C_{26}H_{40}N_4O_6$ + H: 505.3026; found 505.3035. $[\alpha]_D^{25}$ +53.5 (*c*. 0.22, EtOH). ^{1}H NMR (300 MHz, CD_3OD): δ 8.22 (bs, 1H, NH); 8.10 (bs, 1H, NH); 7.50 (bs, 1H, NH); 7.16 (d, *J* = 8.0 Hz, 2H, 2′-CH and 6′-CH); 6.86 (d, *J* = 7.9 Hz, 2H, 3′-CH and 5′-CH); 6.11-5.97 (m, 1H, $OCH_2C\underline{H}=CH_2$); 5.38 (bd, *J* = 17.3 Hz, 1H, $OCH_2CH=C\underline{H}H$ *trans*); 5.23 (bd, *J* = 10.5 Hz, 1H, $OCH_2CH=CH\underline{H}$ *cis*); 4.56-4.41 (m, 3H, $OC\underline{H}_2CH=CH_2$ and 11-CH); 4.30-4.21 (m, 1H, 8-CH); 3.63 (s, 3H, OCH_3); 3.15-3.06 (m, 2H, 5-CH_2); 3.04-2.81 (m, 4H, 4′′-CH_2 and 11-$CHC\underline{H}_2$); 2.33 (t, *J* = 7.1 Hz, 2H, 2-CH_2); 1.93 (s, 3H, 14-CH_3); 1.78-1.25 (m, 10H, 1′′-$C\underline{H}_aH_b$, 1′′-$CH_a\underline{H}_b$, 3-CH_2, 4-CH_2, 2′′-CH_2 and 3′′-CH_2). ^{13}C NMR (126 MHz, CD_3OD): δ 175.2 (C-1); 173.7 (C-10); 173.4 (C-7); 173.3 (C-13); 158.5 (C-4′); 134.7 ($OCH_2\underline{C}H=CH_2$); 131.1 (C-2′ and C-6′); 129.9 (C-1′); 117.3 ($OCH_2CH=\underline{C}H_2$); 115.5 (C-3′ and C-5′); 69.8 ($O\underline{C}H_2CH=CH_2$); 56.6 (C-11); 54.2 (C-8); 52.3 (OCH_3); 40.9 (C-4′′); 39.8 (C-5); 37.4 (11-$CH\underline{C}H_2$); 34.2 (C-2); 32.3 (C-2′′); 29.5 (C-3′′); 27.8 (C-4); 23.6 (C-14); 23.0 (C-2′′); 22.8 (C-3).

Methyl 5-amino-3-aza-4-oxopentanoate hydrochloride (62)[8]

Using procedure B, 2-(aminoacetamido)acetic acid (212 mg, 1.60 mmol) and $SOCl_2$ (1.25 mL, 17.21 mmol), **62** (278 mg, 1.52 mmol, 95%) was obtained as an off-white solid. MS (ESI^+), *m/z* 147 (100%) [MH^+]. HRMS (ESI^+) calcd for $C_5H_{10}N_2O_3$ + H: 147.0764; found 147.0768. ^{1}H NMR (500 MHz, CD_3OD): δ 4.05 (s, 2H, 2-CH_2); 3.82 (s, 2H, 5-CH_2); 3.77 (s, 3H, OCH_3). ^{13}C NMR (126 MHz, CD_3OD): δ 170.8 (C-4); 167.0 (C-1); 52.8 (OCH); 41.5 (C-5); 41.2 (C-2).

Methyl 3-aminophenylacetate hydrochloride (64)[9]

Using procedure B, the commercially available 3-aminophenylacetic acid (220 mg, 1.33 mmol) and $SOCl_2$ (1.25 mL, 17.21 mmol), **64** (258 mg, 1.28 mmol, 96%) was obtained as an off-white solid. MS (ESI^+), *m/z* 166 (100%) [MH^+]. HRMS (ESI^+) calcd for $C_9H_{11}NO_2$ + H: 166.0863; found 166.0859. ^1H NMR (500 MHz, CD_3OD): δ 7.45 (dd, *J* = 7.6, 7.6 Hz, 1H, 5'-CH); 7.40-7.34 (m, 3H, 2'-CH, 4'-CH and 6'-CH); 3.73-3.71 (m, 5H, OCH_3 and 2-CH_2). ^{13}C NMR (126 MHz, CD_3OD): δ 172.2 (C-1); 136.7 (C-3'); 131.0 (C-1'); 130.6 (C-5'); 130.5 (C-6'); 124.5 (C-2'); 122.3 (C-4'); 52.6 (OCH_3); 40.8 (C-2).

Methyl 3-(aminomethyl)benzoate hydrochloride (65)[10]

Using procedure B, the commercially available 3-(aminomethyl)benzoic acid hydrochloride (200 mg, 1.01 mmol) and $SOCl_2$ (1.25 mL, 17.21 mmol), **65** (196 mg, 0.97 mmol, 91%) was obtained as an off-white solid. MS (ESI^+), *m/z* 166 (100%) [MH^+]. HRMS (ESI^+) calcd for $C_9H_{11}NO_2$ + H: 166.0863; found 166.0857. ^1H NMR (300 MHz, CD_3OD): δ 8.17 (s, 1H, 2-CH); 8.05 (d, *J* = 7.5 Hz, 1H, 6-CH); 7.77 (d, *J* = 7.1 Hz, 1H, 4-CH); 7.58 (dd, *J* = 7.4, 7.4 Hz, 1H, 5-CH); 4.23 (s, 2H, CH_2); 3.92 (s, 3H, OCH_3). ^{13}C NMR (75 MHz, CD_3OD): δ 167.8 (C=O); 135.1 (C-3); 134.9 (C-4); 132.2 (C-1); 131.10 (C-5); 131.07 (C-2); 130.5 (C-6); 52.9 (OCH_3); 44.0 (CH_2).

Methyl 5-aminopentanoate hydrochloride (67)[11]

Using procedure B, 5-aminopentanoic acid (1.0 g, 8.54 mmol) and $SOCl_2$ (1.25 mL, 17.21 mmol), the hydrochloride salt **67** (1.36 g, 8.11 mmol, 95%) was obtained as an off-white solid. MS (ESI^+), *m/z* 132 (100%) [MH^+]. HRMS (ESI^+) calcd for $C_6H_{13}NO_2$ + H: 132.1019; found 132.1023. ^1H NMR (300 MHz, CD_3OD): δ 3.66 (s, 3H, OCH_3); 2.94 (bs, 2H, 5-CH_2); 2.40 (t, *J* = 6.20 Hz, 2H, 2-CH_2); 1.75-1.65 (m, 4H, 3-CH_2 and 4-CH_2). ^{13}C NMR (75 MHz, CD_3OD): δ 175.2 (C-1); 52.2 (OCH_3); 40.5 (C-5); 34.0 (C-2); 27.9 (C-4); 22.8 (C-3).

Methyl (*2S*,5*S*,8*S*)-8-(4-allyloxybenzyl)-3,6,9-triaza-5-[4-(*tert*-butoxycarbonyl)aminobutyl]-2-[3-(*tert*-butoxycarbonyl)aminopropyl]-4,7,10-trioxoundecanoate (68)

Using procedure D, and the acid **13** (121 mg, 0.25 mmol), (2*S*)-2-amino-5-[(*tert*-butoxycarbonyl)amino]pentanoic acid methyl ester hydrochloride **59** (76 mg, 0.27 mmol), EDCI (57 mg, 0.30 mmol), HOBt (100 mg, 0.74 mmol) and DIPEA (0.05 mL, 0.29 mmol), to yield **68** (149 mg, 0.21 mmol, 84%) as a cream powder, mp. 137-139°C. MS (ESI^+), *m/z* 720 (100%) [MH^+], 620 (30). HRMS (ESI^+) calcd for $C_{36}H_{57}N_5O_{10}$ + H: 720.4178; found 720.4186. ^1H NMR (500 MHz, $CDCl_3$): δ 7.68 (bs, 1H, 3-NH); 7.51 (bs, 1H, 6-NH); 7.13 (bs, 1H, 9-NH); 7.02 (bs, 2H, 3'-CH and 5'-CH); 6.73 (d, *J* = 8.5 Hz, 2H, 2'-CH and 6'-CH); 6.02-5.93 (m, 1H, $OCH_2C\underline{H}=CH_2$); 5.34 (dd, *J* = 17.3, 1.4 Hz, 1H, $OCH_2CH=C\underline{H}H$ *trans*); 5.21 (dd, *J* = 10.5, 1.3 Hz, 1H, $OCH_2CH=CH\underline{H}$ *cis*); 5.09 (bs, 2H, 4''-$CH_2N\underline{H}$ and 8-CH); 4.81-4.74 (m, 1H, 2-CH); 4.53 (bs, 1H, 3'''-$CH_2N\underline{H}$); 4.44-4.40 (m, 3H, $OC\underline{H}_2CH=CH_2$ and 5-CH); 3.67 (s, 3H, OCH_3); 3.08-2.95 (m, 6H, 3'''-CH_2, 4''-CH_2, and 8-$CHC\underline{H}_2$); 1.91 (s, 3H, 11-CH_3); 1.84-1.70 (m, 2H, 1''-$C\underline{H}_aH_b$ and 1'''-$C\underline{H}_aH_b$); 1.69-1.54 (m, 2H, 1''-$CH_a\underline{H}_b$ and 1'''-$CH_a\underline{H}_b$); 1.52-1.24 (m, 24H, 2''-CH_2, 2'''-CH_2, 3''-CH_2, 3'''-$CH_2NHCOOC(C\underline{H}_3)_3$ and 4''-$CH_2NHCOOC(C\underline{H}_3)_3$). ^{13}C NMR (126 MHz, $CDCl_3$): δ 172.0 (C-7); 171.21C-1); 171.19 (C-4); 170.2 (C-10); 157.7 (C-4'); 156.5 (3'''-$CH_2NH\underline{C}OOC(CH_3)_3$ and 4''-$CH_2NH\underline{C}OOC(CH_3)_3$); 133.5 ($OCH_2\underline{C}H=CH_2$); 130.5 (C-2' and C-6'); 129.0 (C-1'); 117.8 ($OCH_2CH=\underline{C}H_2$); 114.9 (C-3' and C-5'); 79.3 (4''-$CH_2NHCOO\underline{C}(CH_3)_3$[a]); 79.1 (3'''-$CH_2NHCOO\underline{C}(CH_3)_3$[a]); 69.0 ($O\underline{C}H_2CH=CH_2$); 54.7 (C-8); 53.1 (C-2 and C-5); 52.5 (OCH_3); 40.4 (C-4''); 40.1 (C-3'''); 37.8 (8-$CH\underline{C}H_2$); 32.4 (C-1''); 29.6 (C-3''); 28.9 (C-1'''); 28.6 (3'''-$CH_2NHCOOC(\underline{C}H_3)_3$ and 4''-$CH_2NHCOOC(\underline{C}H_3)_3$); 26.5 (C-2'''); 23.1 (C-11); 22.6 (C-2'').

***N*-{(1*S*,4*S*)-1-(4-Allyloxybenzyl)-3,6,12-triaza-13-(*tert*-butoxy)-4-[4-(*tert*-butoxycarbonyl)aminobutyl]-2,5,13-trioxotridecyl}acetamide (69)**

The amide was synthesised using procedure D from the acid **13** (87 mg, 0.18 mmol), the commercially available *N*-(*tert*-butoxy carbonyl)-1,5-diaminopentane hydrochloride **60** (50 mg, 0.21 mmol), EDCI (84 mg, 0.44 mmol), HOBt (45 mg, 0.33 mmol) and DIPEA (0.05 mL, 0.29 mmol), to yield (69) (112 mg, 0.17 mmol, 94%) as a cream powder, mp. 123-125°C. MS (ESI^+), *m/z* 676 (20%) [MH^+], 576 (45), 476 (20), 129 (100). HRMS (ESI^+) calcd for $C_{35}H_{57}N_5O_8$ + H: 676.4280; found 676.4284. ^1H NMR (300 MHz, $CDCl_3$): δ 7.03 (d, *J* = 8.5 Hz, 2H, 2'-CH and 6'-CH); 6.91-6.82 (m, 1H, 3-NH); 6.75 (d, *J* = 8.5 Hz, 2H, 3'-CH and 5'-CH); 6.50-6.34 (m, 2H, $N\underline{H}COCH_3$ and 6-NH); 5.97 (tdd, *J* = 17.3, 10.5, 5.3 Hz, 1H, $OCH_2C\underline{H}=CH_2$); 5.33 (dd, *J* = 17.3, 1.6 Hz, 1H, $OCH_2CH=C\underline{H}H$ *trans*); 5.21 (dd, *J* = 10.5, 1.4 Hz, 1H, $OCH_2CH=CH\underline{H}$ *cis*); 4.88-4.77 (m, 1H, 12-NH); 4.76-4.65 (m, 1H, 1-CH); 4.64-4.53 (m, 1H, 4''-CHN$\underline{H}$); 4.42 (d, *J* = 5.3 Hz, 2H, $OC\underline{H}_2CH=CH_2$); 4.30-4.18 (m, 1H, 4-CH); 3.14-2.83 (m, 8H, 1-$CHC\underline{H}_2$, 4''-CH_2, 7-CH_2 and 11-CH_2); 1.91 (s, 3H, $COCH_3$); 1.82-1.70 (m, 1H, 1''-$C\underline{H}_aH_b$); 1.60-1.50 (m, 1H, 1''-$CH_a\underline{H}_b$); 1.46-1.31 (m, 24H, 4''-$CH_2NHCOOC(C\underline{H}_3)_3$, 13-$COOC(C\underline{H}_3)_3$, 8-$CH_2$, 10-$CH_2$ and 3''-CH_2); 1.32-1.12 (m, 4H, 2''-CH_2 and 9-CH_2). ^{13}C NMR (75 MHz, $CDCl_3$): δ 171.6 (C-2); 171.4 (C-5); 170.8 ($\underline{C}OCH_3$); 157.5 (C-4'); 156.4 ($NH\underline{C}OOC(CH_3)_3$); 133.5 ($OCH_2\underline{C}H=CH_2$); 130.5 (C-2' and C-6'); 129.5 (C-1'); 117.9 ($OCH_2CH=\underline{C}H_2$); 115.0 (C-3' and C-5'); 79.3 ($NHCOO\underline{C}(CH_3)_3$ and 13-$COO\underline{C}(CH_3)_3$); 69.0 ($O\underline{C}H_2CH=CH_2$); 56.1 (C-1); 55.1 (C-4); 40.6 (C-4'' and C-11); 39.5 (C-7); 37.5 (1-$CH\underline{C}H_2$); 31.9 (C-1''); 29.7 (C-8 and C-10); 29.1 (C-3''); 28.7 ($NHCOOC(\underline{C}H_3)_3$ and 13-$COOC(\underline{C}H_3)_3$); 24.3 (C-9); 23.2 ($CO\underline{C}H_3$and C-2'').

(6*S*,9*S*)-9-(4-Allyloxybenzyl)-7,10-triaza-6-[4-(*tert*-butoxycarbonyl)aminobutyl]-5,8,11-trioxododecanamide (70)

This compound was synthesised using procedure D from the acid **13** (199 mg, 0.40 mmol), the commercially available amine β-alanine amide hydrochloride **61** (68 mg, 0.55 mmol), EDCI (131 mg, 0.67 mmol), HOBt (94 mg, 0.70 mmol) and DIPEA (0.15 mL, 0.86 mmol) to yield the amide **70** (200 mg, 0.36 mmol, 88%) as an off-white powder, mp. 154-156°C. MS (ESI^+), *m/z* 584 (100%), 562 (25) [MH^+], 174 (40). HRMS (ESI^+) calcd for $C_{28}H_{43}N_5O_7$ + H: 562.3241; found 562.3257. ^1H NMR (300 MHz, CD_3OD): δ 7.15 (d, *J* = 8.6 Hz, 2H, 2'-CH and 6'-CH); 6.85 (d, *J* = 8.7 Hz, 2H, 3'-CH and 5'-CH); 6.04 (tdd, *J* = 17.2, 10.5, 5.2 Hz, 1H, $OCH_2C\underline{H}=CH_2$); 5.38 (dd, *J* = 17.3, 1.7 Hz, 1H, $OCH_2CH=C\underline{H}H$ *trans*); 5.22 (dd, *J* = 10.6, 1.5 Hz, 1H, $OCH_2CH=CH\underline{H}$ *cis*); 4.58-4.52 (m, 1H, 9-CH); 4.51 (d, *J* = 5.2 Hz, 2H, $OC\underline{H}_2CH=CH_2$); 4.27-4.18 (m, 1H, 6-CH); 3.43.38 (m, 2H, 3-CH_2); 3.09-2.97 (m, 3H, 4''-CH_2 and 9-$CHC\underline{H}_aH_b$); 2.83 (dd, *J* = 14.0, 8.7 Hz, 1H, 9-$CHCH_a\underline{H}_b$); 2.39 (t, *J* = 6.8 Hz, 2H, 2-CH_2); 1.92 (s, 3H, 12-CH_3); 1.82-1.74 (m, 1H, 1''-$C\underline{H}_aH_b$); 1.69-1.53 (m, 1H, 1''-$CH_a\underline{H}_b$); 1.42 (s, 9H, $OC(C\underline{H}_3)_3$); 1.37-1.23 (m, 4H, 3''CH_2 and 2''-CH_2). ^{13}C NMR (75 MHz, CD_3OD): δ 175.2 (C-1); 172.8 (C-8);

172.6 (C-5); 172.1 (C-11); 157.8 (C-4′); 156.5 (NH<u>C</u>OOC(CH_3)$_3$); 133.8 (OCH$_2$<u>C</u>H=CH$_2$); 130.1 (C-2′ and C-6′); 129.3 (C-1′); 116.3 (OCH$_2$CH=<u>C</u>H$_2$); 114.5 (C-3′ and C-5′); 68.6 (COO<u>C</u>(CH_3)$_3$ and O<u>C</u>H$_2$CH=CH$_2$); 55.3 (C-9); 53.5 (C-6); 40.0 (C-4′′); 36.7 (9-CH<u>C</u>H$_2$); 35.8 (C-3); 34.7 (C-2); 31.6 (C-1′′); 29.3 (C-3′′); 27.6 (OC(<u>C</u>H$_3$)$_3$); 22.9 (C-12); 21.3 (C-2′′).

Methyl (8*S*,11*S*)-11-(4-allyloxybenzyl)-3,6,9,12-tetraaza-8-[4-(*tert*-butoxycarbonyl)aminobutyl]-4,7,10,13-tetraoxotetradecanoate (71)

The ester was synthesised using procedure D from the acid **13** (156 mg, 0.32 mmol), the prepared amine hydrochloride **62** (66 mg, 0.36 mmol), EDCI (116 mg, 0.61 mmol), HOBt (67 mg, 0.50 mmol) and DIPEA (0.07 mL, 0.40 mmol), to yield the ester (**71**) (171 mg, 0.28 mmol, 87%) as a cream powder, mp. 119-121°C. MS (ESI$^+$), *m/z* 620 (40%) [MH$^+$], 520 (100), 174 (50), 129 (75). HRMS (ESI$^+$) calcd for $C_{30}H_{45}N_5O_9$ + H: 620.3290; found 620.3287. ^{1}H NMR (300 MHz, $CDCl_3$/CD_3OD): δ 7.02 (d, *J* = 8.6 Hz, 2H, 2′-CH and 6′-CH); 6.73 (d, *J* = 8.6 Hz, 2H, 3′-CH and 5′-CH); 5.94 (tdd, *J* = 17.2, 10.5, 5.3 Hz, 1H, OCH$_2$<u>C</u>H=CH$_2$); 5.30 (dd, *J* = 17.3, 1.5 Hz, 1H, OCH$_2$CH=C<u>H</u>H *trans*); 5.18 (dd, *J* = 10.5, 1.4 Hz, 1H, OCH$_2$CH=CH<u>H</u> *cis*); 4.84-4.72 (m, 1H, 11-CH); 4.41-4.27 (m, 5H, OC<u>H</u$_2$CH=CH$_2$, 2-CH$_2$ and 8-CH); 4.05-3.96 (m, 2H, 5-CH$_2$); 3.72 (s, 3H, OCH$_3$); 3.06-2.86 (m, 4H, 4′′-CH$_2$ and 11-CHC<u>H</u$_2$); 2.01 (s, 3H, 14-CH$_3$); 1.85-1.73 (m, 1H, 1′′-C<u>H</u$_a$H$_b$); 1.72-1.57 (m, 1H, 1′′-CH$_a$<u>H</u$_b$); 1.51-1.35 (m, 11H, OC(C<u>H</u$_3$)$_3$ and 3′′-CH$_2$); 1.35-1.23 (m, 2H, 2′′-CH$_2$). ^{13}C NMR (75 MHz, $CDCl_3$/CD_3OD): δ 172.1 (C-10); 171.7 (C-7); 170.7 (C-4); 170.3 (C-13); 169.7 (C-1); 157.6 (C-4′); 156.4 (NH<u>C</u>OOC(CH_3)$_3$); 133.5 (OCH$_2$<u>C</u>H=CH$_2$); 130.7 (C-2′ and C-6′); 129.1 (C-1′); 117.7 (OCH$_2$CH=<u>C</u>H$_2$); 114.6 (C-3′ and C-5′); 79.0 (COO<u>C</u>(CH_3)$_3$); 68.9 (O<u>C</u>H$_2$CH=CH$_2$); 54.4 (C-11); 53.2 (C-8); 52.5 (OCH$_3$); 43.1 (C-5); 41.5 (C-4′′); 40.7 (C-2); 38.9 (10-CH<u>C</u>H$_2$); 30.0 (C-1′′ and C-3′′); 28.7 (OC(<u>C</u>H$_3$)$_3$); 23.2 (C-14); 22.9 (C-2′′).

***N*-{(1*S*,4*S*)-1-(4-Allyloxybenzyl)-3-aza-8-(*tert*-butoxycarbonyl)amino-4-{*N*-[4-(2-pyridinyl)methyl]piperazinyl}carbonyl-2-oxooctyl}acetamide (72)**

The amide was synthesised using procedure D from the acid **13** (110 mg, 0.22 mmol), the commercially available 1-(2-pyridinylmethyl) piperazine **63** (61 mg, 0.34 mmol), EDCI (61 mg, 0.32 mmol) and HOBt (77 mg, 0.57 mmol), to yield (72) (108 mg, 0.17 mmol, 74%) as a white powder, mp. 118-120°C. MS (ESI$^+$), *m/z* 651 (100%) [MH$^+$]. HRMS (ESI$^+$) calcd for $C_{35}H_{50}N_6O_6$ + H: 651.3865; found 651.3877. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.52 (d, *J* = 3.86 Hz, 1H, 6′′′-CH); 7.63 (dd, *J* = 7.60, 1.55 Hz, 1H, 4′′′-CH); 7.35 (d, *J* = 7.73 Hz, 1H, 3′′′-CH); 7.16-7.11 (m, 2H, 5′′′-CH and 6-NH); 7.00 (d, *J* = 8.6 Hz, 2H, 2′-CH and 6′-CH); 6.74 (d, *J* = 8.6 Hz, 2H, 3′-CH and 5′-CH); 6.52 (d, *J* = 7.18 Hz, 1H, 3-NH); 5.97 (tdd, *J* = 17.1, 10.5, 5.3, Hz, 1H, OCH$_2$C<u>H</u>=CH$_2$); 5.33 (dd, *J* = 17.3, 1.6 Hz, 1H, OCH$_2$CH=C<u>H</u>H *trans*); 5.20 (dd, *J* = 10.5, 1.4 Hz, 1H, OCH$_2$CH=CH<u>H</u> *cis*); 4.95 (s, 1H, 8-CH$_2$N<u>H</u>); 4.80-4.75 (m, 1H, 1-CH); 4.69-4.62 (m, 1H, 4-CH); 4.43 (d, *J* = 5.2, Hz, 1H, O<u>C</u>H$_2$CH=CH$_2$); 3.64 (s, 2H, 4′′-NCH$_2$); 3.61-3.54 (m, 2H, 2′′-C<u>H</u$_a$H$_b$ and 6′′-C<u>H</u$_a$H$_b$); 3.48 (bs, 2H, 2′′-CH$_a$<u>H</u$_b$ and 6′′-CH$_a$<u>H</u$_b$); 3.03-2.92 (m, 3H, 8-CH$_2$ and 1-CHC<u>H</u$_a$H$_b$); 2.91-2.84 (m, 1H, 1-CHCH$_a$<u>H</u$_b$); 2.45 (bs, 4H, 3′′-CH$_2$ and 5′′-CH$_2$); 1.90 (s, 3H, COCH$_3$); 1.68-1.59 (m, 1H, 5-C<u>H</u$_a$H$_b$); 1.53-1.44 (m, 1H, 5-CH$_a$<u>H</u$_b$); 1.43-1.30 (m, 11H, OC(C<u>H</u$_3$)$_3$ and 7-CH$_2$); 1.25-1.18 (m, 2H, 6-CH$_2$). ^{13}C NMR (75 MHz, $CDCl_3$): δ 171.0 (C-2); 170.3 (<u>C</u>OCH$_3$); 169.7 (4-CH<u>C</u>=O); 157.7 (C-2′′′ and C-4′); 156.4 (NH<u>C</u>OOC(CH_3)$_3$); 149.6 (C-6′′′); 136.8 (C-4′′′); 133.5 (OCH$_2$<u>C</u>H=CH$_2$); 130.4 (C-2′ and C-6′); 128.8 (C-1′); 123.5 (C-3′′′); 122.6 (C-5′′′); 117.7 (OCH$_2$CH=<u>C</u>H$_2$); 114.9 (C-3′ and C-5′); 79.1 (COO<u>C</u>(CH_3)$_3$); 68.9 (O<u>C</u>H$_2$CH=CH$_2$); 64.4 (4′′-NHCH$_2$); 54.7 (C-1); 53.0 (C-4); 48.6 (C-3′′ and C-5′′); 45.6 (C-2′′ and C-6′′); 40.3 (C-8); 37.5 (1-CH<u>C</u>H$_2$); 32.6 (C-5); 29.7 (C-7); 28.7 (OC(<u>C</u>H$_3$)$_3$); 23.2 (CO<u>C</u>H$_3$); 22.4 (C-6).

***N*-{(1*S*,4*S*)-1-(4-Allyloxybenzyl)-3-aza-8-(*tert*-butoxycarbonyl)amino-4-[3-(methoxycarbonylmethyl)phenyl]carbamoyl-2-oxooctyl}acetamide (73)**

The amide was synthesised using procedure D from the acid **13** (150 mg, 0.31 mmol), and the prepared amine hydrochloride **64** (63 mg, 0.31 mmol), EDCI (63 mg, 0.54 mmol), HOBt (94 mg, 0.70 mmol) and DIPEA (0.07 mL, 0.40 mmol), to yield the crude product. The crude product was purified by pTLC (silica gel) using 15:1 CH_2Cl_2/MeOH as the developing solvent to yield **73** (88 mg, 0.14 mmol, 45%) as a cream powder, mp. 132-134°C. MS (ESI$^+$), *m/z* 639 (100%) [MH$^+$]. HRMS (ESI$^+$) calcd for $C_{34}H_{46}N_4O_8$ + H: 639.3388; found 639.3395. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.49 (s, 1H, 2′′-CH); 7.45 (d, *J* = 8.1 Hz, 1H, 6′′-CH); 7.08-7.00 (m, 4H, 2′-CH, 4′′-CH, 5′′-CH and 6′-CH); 6.71 (d, *J* = 8.3 Hz, 2H, 3′-CH and 5′-CH); 6.02-5.94 (m, 1H, OCH$_2$C<u>H</u>=CH$_2$); 5.35 (bd, *J* = 17.3 Hz, 1H, OCH$_2$CH=C<u>H</u>H *trans*); 5.24 (bd, *J* = 10.5 Hz, 1H, OCH$_2$CH=CH<u>H</u> *cis*); 4.69 (dd, *J* = 13.8, 6.8 Hz, 1H, 1-CH); 4.51 (dd, *J* = 13.2, 7.2 Hz, 1H, 4-CH); 4.36 (d, *J* = 4.2 Hz, 2H, O<u>C</u>H$_2$CH=CH$_2$); 3.68 (s, 3H, OCH$_3$); 3.60 (s, 2H, 3′′-CCH$_2$); 3.12-3.01 (m, 3H, 8-CH$_2$ and 1-CHC<u>H</u$_a$H$_b$); 2.96 (dd, *J* = 14.4, 7.3 Hz, 1H, 1-CHCH$_a$<u>H</u$_b$); 2.04-1.86 (m, 4H, COCH$_3$and 5-C<u>H</u$_a$H$_b$); 1.70-1.61 (m, 1H, 5-CH$_a$<u>H</u$_b$); 1.53-1.44 (m, 2H, 7-CH$_2$); 1.43 (s, 9H, OC(C<u>H</u$_3$)$_3$); 1.39-1.31 (m, 2H, 6-CH$_2$). ^{13}C NMR (75 MHz, $CDCl_3$): δ 171.8 (4-CH<u>C</u>=O); 171.7 (C-2); 170.7 (3′′-CCH$_2$<u>C</u>=O); 170.2 (<u>C</u>OCH$_3$); 157.5 (C-4′); 156.9 (NH<u>C</u>OOC(CH_3)$_3$); 138.3 (C-1′′); 135.0 (C-3′′); 133.5 (OCH$_2$<u>C</u>H=CH$_2$); 130.4 (C-2′ and C-6′); 129.8 (C-1′); 129.3 (C-5′′); 125.5 (C-4′′); 121.1 (C-2′′); 119.1 (C-6′′); 117.7 (OCH$_2$CH=<u>C</u>H$_2$); 115.1 (C-3′ and C-5′); 68.9 (O<u>C</u>H$_2$CH=CH$_2$); 54.2 (C-1); 53.2 (C-4); 52.3 (OCH$_3$); 45.7 (3′′-C<u>C</u>H$_2$); 41.3 (C-8); 37.6 (1-CH<u>C</u>H$_2$); 31.5 (C-5); 29.9 (C-7); 28.7 (OC(<u>C</u>H$_3$)$_3$); 23.2 (CO<u>C</u>H$_3$); 22.9 (C-6).

***N*-(1*S*,4*S*)-1-(4-Allyloxybenzyl)-3-aza-8-(*tert*-butoxycarbonyl)amino-4-[3-(methoxycarbonyl)benzyl]carbamoyl-2-oxooctyl}acetamide (74)**

The amide was synthesised using procedure D from the acid **13** (204 mg, 0.41 mmol), the prepared amine hydrochloride **65** (86 mg, 0.43 mmol), EDCI (94 mg, 0.49 mmol), HOBt (71 mg, 0.53 mmol) and DIPEA (0.08 mL, 0.46 mmol), to yield **74** (149 mg, 0.21 mmol, 84%) as a white powder, mp. 141-143°C. MS (ESI$^+$), *m/z* 661 (100%) [M + Na+], 639 (60) [MH$^+$], 539 (30). HRMS (ESI$^+$) calcd for $C_{34}H_{46}N_4O_8$ + H: 639.3394; found 639.3387. ^{1}H NMR (300 MHz, $CDCl_3$/CD_3OD): δ 7.86-7.72 (m, 2H, 2′′-CH and 4′′-CH); 7.35-7.20 (m, 2H, 5′′-CH and 6′′-CH); 6.93 (d, *J* = 8.0 Hz, 2H, 2′-CH and 6′-CH); 6.62 (d, *J* = 7.9 Hz, 2H, 3′-CH and 5′-CH); 5.97-5.84 (m, 1H, OCH$_2$C<u>H</u>=CH$_2$); 5.27 (bd, *J* = 17.1 Hz, 1H, OCH$_2$CH=C<u>H</u>H *trans*); 5.15 (bd, *J* = 10.4 Hz, 1H, OCH$_2$CH=CH<u>H</u> *cis*); 4.93-4.81 (m, 1H, 1-CH); 4.61-4.50 (m, 1H, 4-CH); 4.40-4.27 (m, 4H, NHC<u>H</u$_2$Ar and O<u>C</u>H$_2$CH=CH$_2$); 3.77 (s, 3H, OCH$_3$); 2.99-2.72 (m, 4H, 1-CHC<u>H</u$_2$ and 8-CH$_2$); 1.82 (s, 3H, COCH$_3$); 1.78-1.67 (m, 1H, 5-C<u>H</u$_a$H$_b$); 1.62-1.45 (m, 1H, 5-CH$_a$<u>H</u$_b$); 1.41-1.16 (m, 13H, OC(C<u>H</u$_3$)$_3$, 6-CH$_2$ and 7-CH$_2$). ^{13}C NMR (75 MHz, $CDCl_3$/CD_3OD): δ 171.6 (C-2); 171.5 (4-CH<u>C</u>=O); 170.6 (<u>C</u>OCH$_3$); 166.7 (3′′-CH<u>C</u>=O); 157.3 (C-4′); 156.1 (NH<u>C</u>OOC(CH_3)$_3$); 138.7 (C-1′′); 133.2 (OCH$_2$<u>C</u>H=CH$_2$); 131.8 (C-6′′); 130.22 (C-2′ and C-6′); 130.17 (C-3′′); 129.2 (C-1′); 128.7 (C-5′′);

128.5 (C-2''); 128.4 (C-4''); 117.4 ($OCH_2CH=\underline{C}H_2$); 114.5 (C-3' and C-5'); 78.9 ($COO\underline{C}(CH_3)_3$); 68.6 ($O\underline{C}H_2CH=CH_2$); 54.4 (C-1); 52.9 (C-4); 52.0 (OCH_3); 42.7 ($NH\underline{C}H_2Ar$); 40.3 (C-8); 37.9 (1-$CH\underline{C}H_2$); 32.3 (C-5); 29.4 (C-7); 28.3 ($OC(\underline{C}H_3)_3$); 22.8 ($CO\underline{C}H_3$); 22.6 (C-6).

_N_-{(1*S*,4*S*)-1-(4-Allyloxybenzyl)-3-aza-8-(*tert*-butoxycarbonyl)amino-4-(3-methoxycarbonyl)phenylcarbamoyl-2-oxooctyl}acetamide (75)

The amide was synthesised using procedure D from the acid **13** (97 mg, 0.20 mmol), and the commercially available methyl 3-amino benzoate **66** (42 mg, 0.28 mmol), EDCI (46 mg, 0.24 mmol) and HOBt (97 mg, 0.72 mmol), to yield the crude product. The crude product was then purified by pTLC (silica gel) using 15:1 CH_2Cl_2/MeOH as the developing solvent to yield **75** (64 mg, 0.10 mmol, 52%) as white powder, mp. 140-142°C. MS (ESI^+), *m/z* 647 (100%) [M + Na^+], 625 (50) [MH^+]. HRMS (ESI^+) calcd for $C_{33}H_{44}N_4O_8$ + Na^+: 647.3057; found 647.3061. ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.51 (s, 1H, 1''-CNH); 8.15 (s, 1H, 2''-CH); 7.91 (d, *J* = 7.4 Hz, 1H, 4''-CH); 7.70 (d, *J* = 7.8 Hz, 1H, 6''-CH); 7.60 (bs, 1H, 3-NH); 7.30 (dd, *J* = 8.0, 8.0 Hz, 1H, 5''-CH); 7.28-7.23 (m, 1H, $N\underline{H}COCH_3$); 6.96 (d, *J* = 8.5 Hz, 2H, 2'-CH and 6'-CH); 6.59 (d, *J* = 8.6 Hz, 2H, 3'-CH and 5'-CH); 5.84 (tdd, *J* = 15.8, 10.5, 5.3 Hz, 1H, $OCH_2C\underline{H}=CH_2$); 5.22 (dd, *J* = 17.2, 1.5 Hz, 1H, $OCH_2CH=CH\underline{H}$ *trans*); 5.13 (dd, *J* = 10.5, 1.3 Hz, 1H, $OCH_2CH=CH\underline{H}$ *cis*); 4.90-4.82 (m, 2H, 8-$CH_2N\underline{H}$ and 1-CH); 4.75-4.67 (m, 1H, 4-CH); 4.23-4.14 (m, 2H, $OC\underline{H}_2CH=CH_2$); 3.82 (s, 3H, OCH_3); 2.99-2.91 (m, 3H, 8-CH_2 and 1-$CHC\underline{H}_aCH_b$); 2.87 (dd, *J* = 12.8, 6.5 Hz, 1H, 1-$CHCH_aC\underline{H}_b$); 1.98 (s, 3H, $COCH_3$); 1.90-1.80 (m, 1H, 5-$C\underline{H}_aH_b$); 1.71-1.58 (m, 1H, 5-$CH_a\underline{H}_b$); 1.40-1.30 (s, 11H, $OC(C\underline{H}_3)_3$ and 7-CH_2); 1.25-1.16 (m, 2H, 6-CH_2). ^{13}C NMR (126 MHz, $CDCl_3$): δ 171.9 (4-$CH\underline{C}O$); 170.8 (C-2); 170.1 ($\underline{C}OCH_3$); 166.8 (3''-$C\underline{C}O$); 157.5 (C-4'); 156.1 ($NH\underline{C}OOC(CH_3)_3$); 138.4 (C-1''); 133.2 ($OCH_2\underline{C}H=CH_2$); 130.6 (C-2' and C-6'); 130.1 (C-3''); 129.0 (C-1'); 128.3 (C-5''); 125.2 (C-4''); 124.3 (C-6''); 120.9 (C-2''); 117.3 ($OCH_2CH=\underline{C}H_2$); 114.6 (C-3' and C-5'); 79.0 ($COO\underline{C}(CH_3)_3$); 68.5 ($O\underline{C}H_2CH=CH_2$); 54.9 (C-1); 53.7 (C-4); 52.2 (OCH_3); 40.0 (C-8); 37.9 (1-$CH\underline{C}H_2$); 32.4 (C-5); 29.5 (C-7); 28.4 ($OC(\underline{C}H_3)_3$); 22.9 ($CO\underline{C}H_3$); 22.7 (C-6).

Methyl (8*S*,11*S*)-11-(4-allyloxybenzyl)-6,9,12-triaza-8-[4-(*tert*-butoxycarbonyl)aminobutyl]-7,10,13-trioxotetradecanoate (76)

The ester was synthesised using procedure D from the acid **13** (106 mg, 0.22 mmol), the prepared amine hydrochloride (67) (46 mg, 0.27 mmol), EDCI (98 mg, 0.51 mmol), HOBt (77 mg, 0.57 mmol) and DIPEA (0.04 mL, 0.23 mmol), to yield **76** (90 mg, 0.15 mmol, 69%) as a white powder, mp. 134-136°C. MS (ESI^+), *m/z* 627 (100%) [M + Na^+], 605 (70) [MH^+]. HRMS (ESI^+) calcd for $C_{31}H_{48}N_4O_8$ + H: 605.3550; found 605.3556. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.46 (d, *J* = 8.3 Hz, 1H, 9-NH); 7.13 (bs, 1H, 12-NH); 7.09-6.90 (m, 3H, 2'-CH, 6'-CH and 6-NH); 6.70 (d, *J* = 8.6 Hz, 2H, 3'-CH and 5'-CH); 5.95 (tdd, *J* = 17.2, 10.5, 5.3 Hz, 1H, $OCH_2C\underline{H}=CH_2$); 5.31 (dd, *J* = 17.3, 1.6 Hz, 1H, $OCH_2CH=CH\underline{H}$ *trans*); 5.18 (dd, *J* = 10.5, 1.4 Hz, 1H, $OCH_2CH=CH\underline{H}$ *cis*); 4.95 (bs, 1H, 4''-$CH_2N\underline{H}$); 4.82-4.76 (m, 1H, 11-CH); 4.50-4.30 (m, 3H, $OC\underline{H}_2CH=CH_2$ and 8-CH); 3.58 (s, 3H, OCH_3); 3.18 (dd, *J* = 13.2, 6.4 Hz, 1H, 5-$C\underline{H}_aH_b$); 3.07 (dd, *J* = 13.0, 6.1 Hz, 1H, 5-$CH_a\underline{H}_b$); 3.01-2.92 (m, 2H, 4''-CH_2); 2.92-2.84 (m, 2H, 11-$CHC\underline{H}_2$); 2.26 (t, *J* = 7.2 Hz, 2H, 2-CH_2); 1.91 (s, 3H, 14-CH_3); 1.79-1.67 (m, 1H, 1''-$C\underline{H}_aH_b$); 1.63-1.51 (m, 3H, 1''-$CH_a\underline{H}_b$ and 3-CH_2); 1.50-1.40 (m, 4H, 4-CH_2 and 3''-CH_2); 1.35 (s, 9H, $OC(C\underline{H}_3)_3$); 1.29-1.14 (m, 2H, 2''-CH_2). ^{13}C NMR (75 MHz, $CDCl_3$): δ 174.1 (C-1); 171.7 (C-10); 171.5 (C-7); 170.7 (C-13); 157.7 (C-4'); 156.4 ($NH\underline{C}OOC(CH_3)_3$); 133.5 ($OCH_2\underline{C}H=CH_2$); 130.5 (C-2' and C-6'); 129.0 (C-1'); 117.8 ($OCH_2CH=\underline{C}H_2$); 114.9 (C-3' and C-5'); 79.2 ($COO\underline{C}(CH_3)_3$); 68.9 ($O\underline{C}H_2CH=CH_2$); 54.7 (C-11); 53.3 (C-8); 51.8 (OCH_3); 40.4 (C-4''); 39.2 (C-5); 38.0 (11-$CH\underline{C}H_2$); 33.7 (C-2); 32.5 (C-1''); 29.6 (C-3''); 29.0 (C-4); 28.7 ($OC(\underline{C}H_3)_3$); 23.2 (C-14); 23.0 (C-2''); 22.3 (C-3).

Methyl (7*S*,10*S*)-5,8,11-triaza-7-(4-aminobutyl)-10-benzyl-6,9,12-trioxotridecanoate hydrochloride (77)

Compound **83** (60 mg, 0.11 mmol) was converted to the uncharacterised *N*-Boc deprotected trifluoroacetate salt *via* procedure E, and the resulting solid was then converted, *via* procedure H to obtain the hydrochloride salt **77** (47 mg, 0.10 mmol, 89%) as a hygroscopic light brown amorphous solid. MS (ESI^+), *m/z* 435 (100%) [MH^+], 436 (25). HRMS (ESI^+) calcd for $C_{22}H_{34}N_4O_5$ + H: 435.2607; found 435.2620. $[\alpha]_D^{25}$ +42.4 (*c*. 0.10, EtOH). ^{1}H NMR (300 MHz, CD_3OD): δ 7.40-7.14 (m, 5H, 2''-CH, 3''-CH, 4''-CH, 5''-CH and 6''-CH); 4.59-4.45 (m, 1H, 10-CH); 4.31-4.21 (m, 1H, 7-CH); 3.65 (s, 3H, OCH_3); 3.23-3.07 (m, 3H, 4-CH_2 and 10-$CHC\underline{H}_aH_b$); 2.99-2.83 (m, 3H, 4'-CH_2 and 10-$CHCH_a\underline{H}_b$); 2.36-2.30 (m, 2H, 2-CH_2); 1.92 (s, 3H, 13-CH_3); 1.82-1.59 (m, 6H, 1'-CH_2, 3-CH_2 and 3'-CH_2); 1.52-1.31 (m, 2H, 2'-CH_2). ^{13}C NMR (75 MHz, CD_3OD): δ 175.0 (C-1); 174.2 (C-9); 173.8 (C-6); 173.4 (C-12); 138.0 (C-1''); 130.2 (C-3'' and C-5''); 129.4 (C-2'' and C-6''); 127.8 (C-4''); 56.5 (C-10); 54.3 (C-7); 52.4 (OCH_3); 41.0 (C-4'); 39.6 (C-4); 38.3 (10-$CH\underline{C}H_2$); 32.4 (C-1'); 32.0 (C-2); 28.0 (C-3'); 25.6 (C-3); 23.7 (C-13); 22.8 (C-2').

Methyl (7*S*,10*S*)-7-(4-aminobutyl)-5,8,11-triaza-6,9,12-trioxo-10-(4-hydroxyphenyl)methyltridecanoate hydrochloride (78)

Compound **84** (56 mg, 0.10 mmol) was converted to the uncharacterised *N*-Boc deprotected trifluoroacetate salt *via* procedure E, and the resulting solid was then converted, *via* procedure H to give the hydrochloride salt **78** (39 mg, 0.08 mmol, 78%) as a hygroscopic brown amorphous solid. MS (ESI^+), *m/z* 451 (100%) [MH^+], 452 (30) [MD^+]. HRMS (ESI^+) calcd for $C_{22}H_{34}N_4O_6$ + H: 451.2557; found 451.2560. $[\alpha]_D^{25}$ +98.8 (*c*. 0.35, EtOH). ^{1}H NMR (300 MHz, CD_3OD): δ 7.08 (d, *J* = 8.3 Hz, 2H, 2''-CH and 6''-CH); 6.71 (d, *J* = 8.2 Hz, 2H, 3''-CH and 5''-CH); 4.45-4.39 (m, 1H, 10-CH); 4.23 (dd, *J* = 9.1, 4.2 Hz, 1H, 7-CH); 3.65 (s, 3H, OCH_3); 3.22-3.05 (m, 2H, 4-CH_2); 3.00-2.82 (m, 4H, 4'-CH_2 and 10-$CHCH_2$); 2.32 (t, *J* = 7.4 Hz, 2H, 2-CH_2); 1.94 (s, 3H, 13-CH_3); 1.87-1.71 (m, 4H, 1'-CH_2 and 3-CH_2); 1.67-1.57 (m, 2H, 3'-CH_2); 1.50-1.27 (m, 2H, 2H, 2'-CH_2). ^{13}C NMR (75 MHz, CD_3OD): δ 175.2 (C-1); 174.6 (C-6); 174.4 (C-9); 174.2 (C-12); 157.2 (C-4''); 131.3 (C-2'' and C-6''); 128.6 (C-1''); 116.2 (C-3'' and C-5''); 57.0 (C-10); 54.4 (C-7); 52.1 (OCH_3); 40.8 (C-4'); 39.6 (C-4); 37.6 (10-$CH\underline{C}H_2$); 32.3 (C-1'); 32.0 (C-2); 27.9 (C-3'); 25.6 (C-3); 23.7 (C-13); 22.6 (C-2').

Methyl (7*S*,10*S*)-7-(4-aminobutyl)-5,8,11-triaza-10-[4-(methoxycarbonyl)methoxy]benzyl-6,9,12-trioxotridecanoate hydrochloride (79)

Compound **90** (120 mg, 0.15 mmol) was converted to the uncharacterised *N*-Fmoc deprotected amine **91** *via* procedure F, using 1% piperidine in a solution of 9:1 acetonitrile/DMF (10 mL). The resulting solid was then further converted to the uncharacterised *N*-Boc deprotected trifluoroacetate salt *via* procedure E, the product of which was then converted, *via* procedure H, to give the hydrochloride salt **79** (63 mg, 0.11 mmol, 74%) as a hygroscopic light brown amorphous solid. MS (ESI^+), *m/z* 523 (100%) [MH^+]. HRMS (ESI^+) calcd for $C_{25}H_{38}N_4O_8$ + H: 523.2768; found 523.2772. $[\alpha]_D^{25}$ +77.5 (*c*. 0.18, EtOH). ^{1}H NMR (300 MHz, CD_3OD): δ 7.26-7.16 (m, 2H, 2''-CH and 6''-CH); 6.92-6.83 (m, 2H, 3''-CH and 5''-CH); 5.02-4.85 (m, 2H, 10-CH and

$OCH_2C=O$); 4.74-4.65 (m, 1H, 7-CH); 3.78 (s, 6H, 1-COOC$\underline{H}_3$ and $OCH_2COOC\underline{H}_3$); 3.40-3.30 (m, 2H, 4-CH_2); 3.26-3.15 (m, 2H, 4''-CH_2); 3.04-2.81 (m, 2H, 10-CHC$\underline{H}_2$); 2.44-2.22 (m, 2H, 2-CH_2); 2.03-1.68 (m, 9H, 1''-CH_2, 3-CH_2, 3''-CH_2 and 13-CH_3); 1.45-1.31 (m, 2H, 2''-CH_2). ^{13}C NMR (75 MHz, CD_3OD): δ 175.2 (C-1); 172.0 (C-9); 171.5 (C-6); 171.2 (C-12); 169.8 ($OCH_2\underline{C}$=O); 158.1 (C-4''); 131.4 (C-2'' and C-6''); 131.2 (C-1''); 115.6 (C-3'' and C-5''); 66.1 ($O\underline{C}H_2C$=O); 55.4 (C-10); 54.4 (C-7); 52.8 (OCH_3); 40.7 (C-4'); 39.6 (C-4); 37.5 (10-CH$\underline{C}H_2$); 32.3 (C-1'); 32.0 (C-2); 28.0 (C-3'); 25.6 (C-3); 23.7 (C-2' and C-13).

Methyl (2*S*,5*S*)-3,6-diaza-5-benzyl-2-[4-(*tert*-butoxycarbonyl)aminobutyl]-4,7-dioxooctanoate (81)

The ester was synthesised using procedure D from the commercially available *N*-acetyl-(*S*)-phenylalanine (329 mg, 1.59 mmol), the commercially available methyl (*S*)-2-amino-6-(*tert*-butoxycarbonylamino)hexanoate hydrochloride (483 mg, 1.63 mmol), EDCI (320 mg, 1.64 mmol), HOBt (248 mg, 1.84 mmol) and DIPEA (0.30 mL, 1.72 mmol), to yield **81** (551 mg, 1.23 mmol, 77%) as white powder, mp. 94-97°C. MS (ESI$^+$), *m/z* 450 (100%) [MH$^+$], 350 (60). HRMS (ESI$^+$) calcd for $C_{23}H_{35}N_3O_6$ + H: 450.2599; found 450.2607. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.28-7.13 (m, 5H, 2'-CH, 3'-CH, 4'-CH, 5'-CH and 6'-CH); 7.02 (d, *J* = 6.5 Hz, 1H, 3-NH); 6.79 (d, *J* = 6.7 Hz, 1H, 6-NH); 5.02 (bs, 1H, 4''-CHN$\underline{H}$); 4.82-4.74 (m, 1H, 5-CH); 4.48-4.42 (m, 1H, 2-CH); 3.66 (s, 3H, OCH_3); 3.12-2.91 (m, 4H, 5-CHC$\underline{H}_2$ and 4''-CH_2); 1.91 (s, 3H, 8-CH_3); 1.82-1.66 (m, 1H, 1''-C$\underline{H}_a$H$_b$); 1.65-1.58 (m, 1H, 1''-CH$_a\underline{H}_b$); 1.49-1.35 (m, 11H, OC(C$\underline{H}_3$)$_3$ and 3''-CH_2); 1.29-1.18 (m, 2H, 2''-CH_2). ^{13}C NMR (75 MHz, $CDCl_3$): δ 172.4 (C-4); 171.6 (C-1); 170.7 (C-7); 156.4 (NH$\underline{C}$OOC(CH$_3$)$_3$); 136.8 (C-1'); 129.5 (C-3' and C-5'); 128.7 (C-2' and C-6'); 127.1 (C-4'); 79.3 (COO$\underline{C}$(CH$_3$)$_3$); 54.6 (C-5); 52.6 (C-2); 52.4 (OCH_3); 40.3 (C-4''); 38.5 (5-CH$\underline{C}H_2$); 31.9 (C-1''); 29.6 (C-3''); 28.7 (OC($\underline{C}$H$_3$)$_3$); 23.2 (C-8); 22.7 (C-2'').

(2*S*,5*S*)-3,6-Diaza-5-benzyl-2-[4-(*tert*-butoxycarbonyl)aminobutyl]-4,7-dioxooctanoic acid (82)

The acid was synthesised using procedure C from the ester **81** (1.20 g, 2.40 mmol), $LiOH.H_2O$ (250 mg, 5.96 mmol) and THF/water 3:1 (60 mL), to yield **82** (949 mg, 2.17 mmol, 91%) as white crystals, mp. 61-65°C. MS (ESI$^+$), *m/z* 436 (100%) [MH$^+$]. HRMS (ESI$^+$) calcd for $C_{22}H_{33}N_3O_6$ + H: 436.2442; found 436.2437. ^{1}H NMR (500 MHz, $(CD_3)_2CO$): δ 7.25 (s, 2H, 3'-CH and 5'-CH); 7.24 (s, 2H, 2'-CH and 6'-CH); 7.22-7.16 (m, 1H, 4'-CH); 4.66 (dd, *J* = 9.4, 5.2 Hz, 1H, 5-CH); 4.37 (dd, *J* = 8.7, 4.9 Hz, 1H, 2-CH); 3.15 (dd, *J* = 14.0, 5.1 Hz, 1H, 5-CHC$\underline{H}_a$H$_b$); 3.02 (t, *J* = 6.9 Hz, 2H, 4''-CH_2); 2.85 (dd, *J* = 14.2, 9.3 Hz, 1H, 5-CHCH$_a\underline{H}_b$); 1.88 (s, 3H, 8-CH_3); 1.86-1.82 (m, 1H, 1''-C$\underline{H}_a$H$_b$); 1.75-1.64 (m, 1H, 1''-CH$_a\underline{H}_b$); 1.52-1.43 (m, 2H, 3''-CH_2); 1.41 (s, 9H, OC(C$\underline{H}_3$)$_3$); 1.39-1.34 (m, 2H, 2''-CH_2). ^{13}C NMR (126 MHz, $(CD_3)_2CO$): δ 175.0 (C-1); 173.7 (C-4); 173.0 (C-7); 158.5 (NH$\underline{C}$OOC(CH$_3$)$_3$); 138.5 (C-1'); 130.3 (C-3' and C-5'); 129.3 (C-2' and C-6'); 127.7 (C-4'); 79.8 (COO$\underline{C}$(CH$_3$)$_3$); 55.9 (C-5); 53.5 (C-2); 41.1 (C-4''); 38.8 (5-CH$\underline{C}H_2$); 32.4 (C-1''); 30.4 (C-3''); 28.8 (OC($\underline{C}$H$_3$)$_3$); 24.1 (C-8); 22.4 (C-2'').

Methyl (7*S*,10*S*)-5,8,11-triaza-10-benzyl-7-[4-(*tert*-butoxycarbonyl)aminobutyl]-6,9,12-trioxotridecanoate (83)

The ester was synthesised using procedure D from the acid **82** (204 mg, 0.47 mmol), the prepared amine hydrochloride **27** (81 mg, 0.53 mmol), EDCI (135 mg, 0.71 mmol), HOBt (125 mg, 0.93 mmol) and DIPEA (0.08 mL, 0.46 mmol), to yield **83** (75 mg, 0.14 mmol, 30%) as a white powder, mp. 133-136°C. MS (ESI$^+$), *m/z* 535 (100%) [MH$^+$], 479 (10), 435 (20). HRMS (ESI$^+$) calcd for $C_{27}H_{42}N_4O_7$ + H: 535.3126; found 535.3137. **^{1}**H NMR (300 MHz, $CDCl_3$): δ 7.66-7.41 (m, 1H, 8-NH); 7.22-7.08 (m, 7H, 2'-CH, 3'-CH, 4'-CH, 5'-CH, 6'-CH, 5-NH and 11-NH); 5.07 (bs, 1H, 4''-CHN$\underline{H}$); 4.82-4.73 (m, 1H, 10-CH); 4.38-4.32 (m, 1H, 7-CH); 3.59 (s, 3H, OCH_3); 3.19-3.08 (m, 2H, 4-CH_2); 3.01-2.88 (m, 4H, 4''-CH_2 and 10-CHC$\underline{H}_2$); 2.27 (t, *J* = 7.4, Hz, 2H, 2-CH_2); 1.90 (s, 3H, 13-CH_3); 1.78-1.67 (m, 3H, 1''-C$\underline{H}_a$H$_b$ and 3-CH_2); 1.58-1.45 (m, 1H, 1''-CH$_a\underline{H}_b$); 1.40-1.31 (m, 11H, OC(C$\underline{H}_3$)$_3$ and 3''-CH_2); 1.28-1.16 (m, 2H, 2''-CH_2). ^{13}C NMR (75 MHz, $CDCl_3$): δ 173.3 (C-1); 171.3 (C-9); 171.2 (C-6); 170.4 (C-12); 155.9 (NH$\underline{C}$OOC(CH$_3$)$_3$); 136.5 (C-1'); 129.0 (C-3' and C-5'); 128.1 (C-2' and C-6'); 126.5 (C-4'); 78.6 (COO$\underline{C}$(CH$_3$)$_3$); 54.3 (C-10); 52.8 (C-17); 51.4 (OCH_3); 40.0 (C-4''); 38.5 (C-4); 38.1 (10-CH$\underline{C}H_2$); 31.8 (C-1''); 31.2 (C-2); 29.2 (C-3''); 28.2 (OC($\underline{C}$H$_3$)$_3$); 24.3 (C-3); 22.7 (C-13); 22.5 (C-2'').

Methyl (7*S*,10*S*)-5,8,11-triaza-7-[4-(*tert*-butoxycarbonyl)amino butyl]-6,9,12-trioxo-10-(4-hydroxyphenyl)methyltridecanoate (84)

To the ester **34** (443 mg, 0.75 mmol) and $Pd(PPh_3)_4$ (94 mg, 0.08 mmol) sealed in a flask flushed with N_2 was added THF (6 mL) at rt and the solution stirred at rt for 10 min. Morpholine (0.7 mL, 8.1 mmol) was added to the mixture, which was allowed to stir for 3 h. The solvent was then removed *in vacuo* to yield the crude product, which was purified by silica gel pTLC (silica gel; 15:1 CH_2Cl_2/MeOH) to yield the product **84** (289 mg, 0.52 mmol, 70%) as a white powder, mp. 155-159°C. MS (ESI$^+$), *m/z* 551 (100%) [MH$^+$]. HRMS (ESI$^+$) calcd for $C_{27}H_{42}N_4O_8$ + H: 551.3081; found 551.3083. ^{1}H NMR (300 MHz, $CDCl_3$/CD_3OD): δ 7.05 (d, *J* = 8.3 Hz, 2H, 2''-CH and 6''-CH); 6.74 (d, *J* = 8.4 Hz, 2H, 3''-CH and 5''-CH); 4.52 (dd, *J* = 7.3, 7.3 Hz, 1H, 10-CH); 4.22 (dd, *J* = 8.7, 5.2 Hz, 1H, 7-CH); 3.68 (s, 3H, OCH_3); 3.24-3.09 (m, 2H, 4-CH_2); 3.07-2.94 (m, 3H, 4'-CH_2 and 10-CHC$\underline{H}_a$H$_b$); 2.86 (dd, *J* = 14.0, 7.6 Hz, 1H, 10-CHCH$_a\underline{H}_b$); 2.34 (t, *J* = 7.4, Hz, 2H, 2-CH_2); 1.96 (s, 3H, 13-CH_3); 1.82-1.71 (m, 3H, 1'-C$\underline{H}_a$H$_b$ and 3-CH_2); 1.64-1.52 (m, 1H, 1'-CH$_a\underline{H}_b$); 1.48-1.40 (m, 11H, OC(C$\underline{H}_3$)$_3$ and 3'-CH_2); 1.35-1.23 (m, 2H, 2'-CH_2). **^{13}**C NMR (75 MHz, $CDCl_3$/CD_3OD): δ 174.4 (C-1); 172.4 (C-6); 172.3 (C-9); 172.0 (C-12); 157.2 (C-4''); 156.0 (NH$\underline{C}$OOC(CH$_3$)$_3$ 130.3 (C-2'' and C-6''); 127.5 (C-1''); 115.4 (C-3'' and C-5''); 79.2 (COO$\underline{C}$(CH$_3$)$_3$); 55.3 (C-10); 53.4 (C-7); 51.6 (OCH_3); 40.1 (C-4'); 38.7 (C-4); 36.9 (10-CH$\underline{C}H_2$); 31.6 (C-1'); 31.2 (C-2); 29.3 (C-3'); 28.2 (OC($\underline{C}$H$_3$)$_3$); 24.6 (C-3); 22.9 (C-13); 22.1 (C-2').

Ethyl (*S*)-3-aza-2-[4-(*tert*-butoxycarbonyl)methoxy]benzyl-4-oxopentanoate (87)

Using procedure A and (*S*)-*N*-acetyltyrosine ethyl ester monohydrate **85** (2.0 g, 7.43 mmol), anhydrous potassium carbonate (2.11 g, 15.26 mmol), *tert*-butyl bromoacetate **86** (2.19 mL, 14.80 mmol) and DMF (10 mL) as solvent the ester **87** (2.50 g, 6.83 mmol, 92%) was obtained as a white solid, mp. 72-75°C. MS (ESI$^+$), *m/z* 366 (100%) [MH$^+$], 310 (70). HRMS (ESI$^+$) calcd for $C_{19}H_{27}NO_6$ + H: 366.1911; found 366.1914. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.00 (d, *J* = 8.5 Hz, 2H, 2'-CH and 6'-CH); 6.78 (d, *J* = 8.6 Hz, 2H, 3'-CH and 5'-CH); 6.09 (d, *J* = 7.7 Hz, 1H, NH); 4.80-4.76 (m, 1H, 2-CH); 4.45 (s, 2H, OCH_2C=O); 4.13 (q, *J* = 7.0, Hz, 2H, OC$\underline{H}_2$CH$_3$); 3.07-2.98 (m, 2H, 2-CHC$\underline{H}_2$); 1.95 (s, 3H, 5-CH_3); 1.45 (s, 9H, OC(C$\underline{H}_3$)$_3$); 1.21 (t, *J* = 7.1 Hz, 3H, $OCH_2C\underline{H}_3$). ^{13}C NMR (126 MHz, $CDCl_3$): δ 171.9 (C-1); 170.0 (C-4); 168.2 ($OCH_2\underline{C}$=O); 157.3 (C-4'); 130.5 (C-2' and C-6'); 129.0 (C-1'); 114.9 (C-3' and C-5'); 82.6 (COO$\underline{C}$(CH$_3$)$_3$); 66.0 ($O\underline{C}H_2C$=O); 61.7 ($O\underline{C}H_2CH_3$); 53.5 (C-2); 37.2 (2-CH$\underline{C}H_2$); 28.2 (OC($\underline{C}$H$_3$)$_3$); 23.3 (C-5); 14.3 ($OCH_2\underline{C}H_3$).

(*S*)-3-Aza-2-[4-(*tert*-butoxycarbonyl)methoxy]benzyl-4-oxopentanoic acid (88)

Using procedure C, the ester **87** (100 mg, 0.27 mmol) in THF/water 3:1 (6 mL) was reacted with $LiOH.H_2O$ (25 mg, 0.60 mmol). The reaction was monitored by TLC analysis, and quenched when the starting material disappeared, yielding **88** (77 mg, 0.23 mmol, 83%) as white granular crystals, mp. 65-68°C. MS (ESI^-), *m/z* 336 (100%) [M - H^+], 280 (10). HRMS (ESI^-) calcd for $C_{17}H_{23}NO_6$ - H: 336.1453; found 336.1446. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.07 (d, *J* = 8.6 Hz, 2H, 2′-CH and 6′-CH); 6.80 (d, *J* = 8.6 Hz, 2H, 3′-CH and 5′-CH); 6.19 (d, *J* = 7.6 Hz, 1H, NH); 4.82-4.78 (m, 1H, 2-CH); 4.48 (s, 2H, OCH_2C=O); 3.15 (dd, *J* = 14.2, 5.6 Hz, 1H, 2-CHC$H_a$$H_b$); 3.06 (dd, *J* = 14.2, 6.0 Hz, 1H, 2-CHC$H_a$$H_b$); 1.98 (s, 3H, 5-$CH_3$); 1.48 (s, 9H, OC($CH_3$)$_3$). ^{13}C NMR (75 MHz, $CDCl_3$): δ 173.9 (C-1); 171.6 (C-4); 168.6 (OCH_2C=O); 157.4 (C-4′); 130.7 (C-2′ and C-6′); 129.0 (C-1′); 115.0 (C-3′ and C-5′); 82.9 (COOC(CH_3)$_3$); 66.0 (OCH_2C=O); 53.8 (C-2); 36.6 (2-CH_2); 28.3 (OC(CH_3)$_3$); 23.1 (C-5).

Methyl (*S*)-7-amino-5-aza-11-[9-(9*H*)-fluorenyl]methoxycarbonylamino]-6-oxoundecanoate hydrochloride (89)

Compound **103** (2.20 g, 3.88 mmol) was converted to the uncharacterised *N*-Boc deprotected trifluoroacetate salt *via* procedure E, using 1:1 CH_2Cl_2/TFA (8 mL). The resulting solid was then converted, *via* procedure H, to the hydrochloride salt **89** (1.91 g, 3.80 mmol, 98%) as a hygroscopic white amorphous solid, mp. 135-140°C. MS (ESI^+), *m/z* 468 (100%) [MH^+], 469 (25) [MD^+], 248 (15). HRMS (ESI^+) calcd for $C_{26}H_{33}N_3O_5$ + H: 468.2498; found 468.2501. ^{1}H NMR (300 MHz, CD_3OD): δ 7.79 (d, *J* = 7.5 Hz, 2H, 4′-CH and 5′-CH); 7.64 (d, *J* = 7.3 Hz, 2H, 1′-CH and 8′-CH); 7.39 (dd, *J* = 7.3, 7.3 Hz, 2H, 3′-CH and 6′-CH); 7.31 (dd, *J* = 7.4, 7.4 Hz, 2H, 2′-CH and 7′-CH); 4.35 (d, *J* = 6.4 Hz, 2H, 9′-CHCH_2); 4.19 (t, *J* = 6.6 Hz, 1H, 9′-CH); 3.81 (t, *J* = 6.3 Hz, 1H, 7-CH); 3.63 (s, 3H, OCH_3); 3.25 (t, *J* = 6.8 Hz, 2H, 4-CH_2); 3.11 (bs, 2H. 11-CH_2); 2.35 (t, *J* = 7.4 Hz, 2H, 2-CH_2); 1.91-1.73 (m, 4H, 3-CH_2 and 8-CH_2); 1.59-1.46 (m, 2H, 10-CH_2); 1.46-1.30 (m, 2H, 9-CH_2). ^{13}C NMR (126 MHz, CD_3OD): δ 173.7 (C-1); 168.7 (C-6); 143.9 (C-9a′ and C-8a′); 141.2 (C-4a′ and C-4b′); 127.4 (C-3′ and C-6′); 126.7 (C-2′ and C-7′); 124.7 (C-1′ and C-8′); 119.5 (C-4′ and C-5′); 66.3 (9′-CHCH_2); 53.1 (C-7); 51.1 (OCH_3); 48.7 (C-9′); 39.8 (C-11); 38.4 (C-4); 30.9 (C-8); 30.5 (C-2); 29.1 (C-10); 24.2 (C-3); 21.6 (C-9).

Methyl (7*S*,10*S*)-5,8,11-triaza-10-[4-(*tert*-butoxycarbonyl)methoxy]benzyl-7-{4-[9-(9*H*) fluorenyl]methoxycarbonylamino}butyl-6,9,12-trioxotridecanoate (90)

The ester was synthesised using procedure D from **88** (134 mg, 0.40 mmol), **89** (197 mg, 0.39 mmol), EDCI (94 mg, 0.49 mmol), HOBt (77 mg, 0.57 mmol) and DIPEA (0.07 mL, 4.00 mmol), to yield **90** (249 mg, 0.32 mmol, 81%) as a white powder, mp. 164-167°C. MS (ESI^+), *m/z* 787 (45%) [MH^+], 373 (80), 143 (100). HRMS (ESI^+) calcd for $C_{43}H_{54}N_4O_{10}$ + H: 787.3918; found 787.3908. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.69 (d, *J* = 7.5 Hz, 2H, 4‴-CH and 5‴-CH); 7.52 (d, *J* = 7.3 Hz, 2H, 1‴-CH and 8‴-CH); 7.32 (dd, *J* = 7.4, 7.4 Hz, 2H, 3‴-CH and 6‴-CH); 7.23 (dd, *J* = 7.4, 7.4 Hz, 2H, 2‴-CH and 7‴-CH); 7.03 (d, *J* = 8.1 Hz, 2H, 2′-CH and 6′-CH); 6.72 (d, *J* = 8.2 Hz, 2H, 3′-CH and 5′-CH); 4.61-4.52 (m, 1H, 10-CH); 4.39 (s, 2H, OCH_2C=O); 4.3-4.21 (m, 3H, 7-CH and 9‴-CHCH_2); 4.13 (t, *J* = 7.0 Hz, 1H, 9‴-CH); 3.58 (s, 3H, OCH_3); 3.21-3.11 (m, 2H, 4-CH_2); 3.11-3.03 (m, 2H, 4″-CH_2); 2.98-2.86 (m, 2H, 10-CHCH_2); 2.27 (t, *J* = 7.1 Hz, 2H, 2-CH_2); 1.89 (s, 3H, 13-CH_3); 1.79-1.68 (m, 3H, 1″-C$H_a$$H_b$ and 3-CH_2); 1.63-1.48 (m, 1H, 1″-C$H_a$$H_b$); 1.49-1.33 (m, 11H, 3″-CH_2 and OC(CH_3)$_3$); 1.31-1.17 (m, 2H, 2″-CH_2). ^{13}C NMR (75 MHz, $CDCl_3$): δ 174.0 (C-1); 172.0 (C-9); 171.7 (C-6); 170.1 (C-12); 168.2 (OCH_2C=O); 157.5 (C-4′); 156.3 (NHCOOCH_2); 144.0 (C-9a‴ and C-8a‴); 141.3 (C-4a‴ and C-4b‴); 130.6 (C-2′ and C-6′); 129.1 (C-1′); 127.8 (C-3‴ and C-6‴); 127.4 (C-2‴ and C-7‴); 125.4 (C-1‴ and C-8‴); 120.1 (C-4‴ and C-5‴); 114.8 (C-3′ and C-5′); 82.7 (COOC(CH_3)$_3$); 66.9 (9‴-CHCH_2); 66.1 (OCH_2C=O); 53.4 (C-10); 53.0 (C-7); 51.7 (OCH_3); 47.3 (C-9‴); 40.5 (C-4″); 39.3 (C-4); 37.2 (10-CHCH_2); 31.3 (C-1″ and C-2); 29.5 (C-3″); 28.3 (OC(CH_3)$_3$); 24.5 (C-3); 23.5 (C-13); 22.7 (C-2″).

Methyl (7*S*,10*S*)-11-(4-allyloxyphenyl)-10-amino-7-(4-aminobutyl)-5,8-diaza-6,9-dioxoundecanoate dihydrochloride (92)

Compound **100** (72 mg, 0.11 mmol) was converted to the *N*-Boc deprotected trifluoroacetate salt *via* procedure E, and the resulting solid was then converted, *via* procedure H to give the hydrochloride salt **92** (41 mg, 0.08 mmol, 71%) as a cream, hygroscopic amorphous solid. MS (ESI^+), *m/z* 449 (30%) [MH^+], 246 (100), 225 (20). HRMS (ESI^+) calcd for $C_{23}H_{36}N_4O_5$ + H: 449.2764; found 449.2767. $[\alpha]_D^{25}$ +26.1 (*c*. 0.09, EtOH). ^{1}H NMR (300 MHz, CD_3OD): δ 7.21 (d, *J* = 8.3 Hz, 2H, 2′-CH and 6′-CH); 6.92 (d, *J* = 8.3 Hz, 2H, 3′-CH and 5′-CH); 6.05 (tdd, *J* = 17.2, 10.5, 5.2 Hz, 1H, OCH_2CH=CH_2); 5.39 (dd, *J* = 17.3, 1.6 Hz, 1H, OCH_2CH=CHH *trans*); 5.24 (dd, *J* = 10.6, 1.4 Hz, 1H, OCH_2CH=CHH *cis*); 4.54 (d, *J* = 5.0 Hz, 2H, OCH_2CH=CH_2); 4.29 (t, *J* = 7.1 Hz, 1H, 7-CH); 4.15 (t, *J* = 6.3 Hz, 1H, 10-CH); 3.65 (s, 3H, OCH_3); 3.24-3.17 (m, 2H, 4-CH_2); 3.05-2.88 (m, 4H, 4″-CH_2 and 10-CH_2); 2.37 (t, *J* = 7.4 Hz, 2H, 2-CH_2); 1.86-1.74 (m, 4H, 1″-CH_2 and 3-CH_2); 1.72-1.65 (m, 4H, 2″-CH_2 and 3″-CH_2). ^{13}C NMR (75 MHz, CD_3OD): δ 175.2 (C-1); 173.4 (C-9); 171.0 (C-6); 159.6 (C-4′); 134.8 (OCH_2CH=CH_2); 131.8 (C-2′ and C-6′); 128.9 (C-1′); 117.5 (OCH_2CH=CH_2); 116.3 (C-3′ and C-5′); 69.8 (OCH_2CH=CH_2); 55.7 (C-10); 54.9 (C-7); 52.3 (OCH_3); 40.8 (C-4″); 39.7 (C-4); 37.7 (C-11); 32.8 (C-1″); 32.1 (C-2); 28.2 (C-3″); 25.7 (C-3); 23.9 (C-2″).

Methyl (7*S*,10*S*)-10-(4-allyloxybenzyl)-7-(4-aminobutyl)-5,8,11-triaza-6,9,12-trioxo-12-(2-pyridinyl)dodecanoate hydrochloride (93)

Compound **106** (230 mg, 0.30 mmol) was converted to the uncharacterised *N*-Fmoc deprotected amine *via* procedure F, using 1% piperidine in a solution of 9:1 acetonitrile/DMF (10 mL). The resulting solid was then converted, *via* procedure H to give the hydrochloride salt **93** (140 mg, 0.24 mmol, 80%) as a hygroscopic light brown amorphous solid. MS (ESI^+), *m/z* 554 (100%) [MH^+], 555 (35) [MD^+], 540 (40). HRMS (ESI^+) calcd for $C_{29}H_{39}N_5O_6$ + H: 554.2979; found 554.2969. $[\alpha]_D^{25}$ +152.2 (*c*. 0.13, EtOH). ^{1}H NMR (300 MHz, CD_3OD): δ 8.86-8.74 (m, 1H, 6‴-CH); 8.48-8.34 (m, 2H, 3‴-CH and 4‴-CH); 8.00-7.89 (m, 1H, 5‴-CH); 7.27-7.18 (m, 2H, 2′-CH and 6′-CH); 6.88-6.81 (m, 2H, 3′-CH and 5′-CH); 6.09-5.95 (m, 1H, OCH_2CH=CH_2); 5.36 (bd, *J* = 17.5 Hz, 1H, OCH_2CH=CHH *trans*); 5.21 (bd, *J* = 10.1 Hz, 1H, OCH_2CH=CHH *cis*); 4.83-4.76 (m, 1H, 10-CH); 4.53-4.45 (m, 2H, OCH_2CH=CH_2); 4.36-4.26 (m, 1H, 7-CH); 3.64 (s, 3H, OCH_3); 3.24-3.16 (m, 4H, 4-CH_2 and 10-CHCH_2); 3.00-2.86 (m, 2H, 4″-CH_2); 2.41-2.28 (m, 2H, 2-CH_2); 1.83-1.64 (m, 6H, 1″-CH_2, 3-CH_2 and 3″-CH_2); 1.52-1.41 (m, 2H, 2″-CH_2). ^{13}C NMR (75 MHz, CD_3OD): δ 174.7 (C-1); 173.4 (C-9); 172.5 (C-6); 161.5 (C-12); 158.4 (C-4′); 146.7 (C-2‴); 145.0 (C-6‴); 138.4 (C-4‴); 134.6 (OCH_2CH=CH_2); 131.3 (C-2′ and C-6′); 129.7 (C-1′);

125.6 (C-3‴); 125.3 (C-5‴); 117.5 ($OCH_2CH=\underline{C}H_2$); 115.6 (C-3′ and C-5′); 69.8 ($O\underline{C}H_2CH=CH$); 57.0 (C-10); 54.6 (C-7); 54.4 (OCH_3); 40.8 (C-4″); 39.6 (C-4); 37.6 (10-$CH\underline{C}H_2$); 32.2 (C-1″); 32.0 (C-2); 27.7 (C-3″); 25.4 (C-3); 23.6 (C-2″).

Methyl (7*S*,10*S*)-10-(4-allyloxybenzyl)-7-(4-aminobutyl)-5,8,11-triaza-12-[2-(benzyloxy)phenyl]-6,9,12-trioxododecanoate hydrochloride (94)

Compound **110** (48 mg, 0.05 mmol) was converted to the uncharacterised *N*-Fmoc deprotected amine *via* procedure F, using 1% piperidine in a solution of 9:1 acetonitrile/DMF (10 mL). The resulting solid was then converted, *via* procedure H to give the hydrochloride salt **94** (33 mg, 0.05 mmol, 87%) as a hygroscopic light brown amorphous solid. MS (ESI^+), *m/z* 659 (20%) [MH^+], 152 (32), 150 (100). HRMS (ESI^+) calcd for $C_{37}H_{46}N_4O_7$ + H: 659.3445; found 659.3438. $[\alpha]_D^{25}$ +48.6 (*c*. 0.13, EtOH). ^{1}H NMR (300 MHz, CD_3OD): δ 7.50 (d, *J* = 7.4 Hz, 1H, 6‴-CH); 7.38-7.23 (m, 8H, 2‴′-CH, 3‴-CH, 3‴′-CH, 4‴-CH, 4‴′-CH, 5‴-CH, 5‴′-CH and 6‴′-CH); 7.14 (d, *J* = 7.8 Hz, 2H, 2′-CH and 6′-CH); 6.88 (d, *J* = 8.0 Hz, 2H, 3′-CH and 5′-CH); 6.11-5.91 (m, 1H, $OCH_2C\underline{H}=CH_2$); 5.40 (bd, *J* = 16.5 Hz, 1H, $OCH_2CH=C\underline{H}H$ *trans*); 5.20 (bd, *J* = 10.0 Hz, 1H, $OCH_2CH=CH\underline{H}$ *cis*); 5.14-5.00 (m, 2H, $OC\underline{H}_2Ar$); 4.56-4.40 (m, 3H, 10-CH and $OC\underline{H}_2CH=CH_2$); 4.30-4.21 (m, 1H, 7-CH); 3.67 (s, 3H, OCH_3); 3.30-3.10 (m, 2H, 4-CH_2); 3.00-2.78 (m, 4H, 4″-CH_2 and 10-$CHC\underline{H}_2$); 2.35 (t, *J* = 6.6 Hz, 2H, 2-CH_2); 1.80-1.9 (m, 4H, 1″-CH_2 and 3-CH_2); 1.45-1.28 (m, 4H, 2″-CH_2 and 3″-CH_2). ^{13}C NMR (75 MHz, CD_3OD): δ 175.1 (C-1); 174.8 (C-9); 174.7 (C-6); 174.2 (C-12); 158.9 (C-4′); 157.0 (C-2‴); 141.2 (C-1‴′); 135.3 (C-4‴); 134.5 ($OCH_2\underline{C}H=CH_2$); 133.6 (C-6‴); 132.3 (C-4‴′); 131.0 (C-2′ and C-6′); 130.4 (C-1′); 128.8 (C-3‴′ and C-5‴′); 127.7 (C-2‴′ and C-6‴′); 121.4 (C-5‴); 120.4 (C-1‴); 117.5 ($OCH_2CH=\underline{C}H_2$); 115.2 (C-3′ and C-5′); 112.6 (C-3‴); 71.4 ($O\underline{C}H_2Ar$); 70.2 ($O\underline{C}H_2CH=CH_2$); 57.5 (C-10); 54.5 (C-7); 52.3 (OCH_3); 40.7 (C-4″); 39.7 (C-4); 38.0 (10-$CH\underline{C}H_2$); 32.0 (C-1″); 31.6 (C-2); 28.0 (C-3″); 25.6 (C-3); 22.3 (C-2″).

Methyl (7*S*,10*S*)-10-(4-allyloxybenzyl)-7-(4-aminobutyl)-5,8,11-triaza-6,9,12-trioxo-12-(2-hydroxyphenyl)dodecanoate hydrochloride (95)

A solution of **110** (107 mg, 0.12 mmol) and thioanisole (0.7 mL, 5.96 mmol) in TFA (2 mL), under N_2 was stirred at rt for 3 h. The solvent was removed under reduced pressure and the residue subjected to column chromatography (silica gel; 15:1 CH_2Cl_2/MeOH) to yield the free hydroxyl intermediate. This was then was converted to the uncharacterised *N*-Fmoc deprotected amine *via* procedure F, using 1% piperidine in a solution of 9:1 acetonitrile/DMF (10 mL). The resulting solid was then converted, *via* procedure H to the hydrochloride salt **95** (47 mg, 0.08 mmol, 64%), as a hygroscopic cream amorphous solid. MS (ESI^+), *m/z* 569 (32%) [MH^+], 152 (30), 150 (100). HRMS (ESI^+) calcd for $C_{30}H_{40}N_4O_7$ + H: 569.2975; found 569.2966. $[\alpha]_D^{25}$ -69.8 (*c*. 0.13, EtOH). ^{1}H NMR (300 MHz, CD_3OD): δ 8.26 (d, *J* = 8.9 Hz, 1H, 6‴-CH); 7.83 (dd, *J* = 8.1, 8.1 Hz, 1H, 4‴-CH); 7.36 (dd, *J* = 7.5, 7.5 Hz, 1H, 5‴-CH); 7.21 (d, *J* = 8.4 Hz, 2H, 2′-CH and 6′-CH); 6.93-6.85 (m, 3H, 2′-CH, 3‴CH and 6′-CH); 6.04 (tdd, *J* = 17.3, 10.5, 5.0 Hz, 1H, $OCH_2C\underline{H}=CH_2$); 5.40 (bs, 1H, $OCH_2CH=C\underline{H}H$ *trans*); 5.34 (bs, $OCH_2CH=CH\underline{H}$ *cis*); 5.25-5.18 (m, 1H, 10-CH); 4.50 (d, *J* = 5.6 Hz, 2H, $OC\underline{H}_2CH=CH_2$); 4.36-4.26 (m, 1H, 7-CH); 3.65 (s, 3H, OCH_3); 3.31-3.29 (m, 2H, 4-CH_2); 3.25-3.12 (m, 2H, 10-$CHC\underline{H}_2$); 2.90 (t, *J* = 7.3Hz, 2H, 4″-CH_2); 2.35 (t, *J* = 7.3 Hz, 2H, 2-CH_2); 1.84-1.59 (m, 2H, 3-CH_2); 1.38-1.27 (m, 6H, 1″-CH_2, 2″-CH_2 and 3″-CH_2). ^{13}C NMR (75 MHz, CD_3OD): δ 175.3 (C-1); 174.1 (C-9); 173.8 (C-6); 170.0 (C-12); 159.9 (C-4′); 159.2 (C-2″); 135.0 (C-4″); 134.9 (C-6″); 131.5 ($OCH_2\underline{C}H=CH_2$); 130.4 (C-2′ and C-6′); 130.1 (C-1′); 120.5 (C-5″); 118.1 (C-1″); 117.8 (C-3″); 117.5 ($OCH_2CH=\underline{C}H_2$); 115.9 (C-3′ and C-5′); 69.8 ($O\underline{C}H_2CH=CH$); 57.1 (C-10); 53.7 (C-7); 52.2 (OCH); 40.6 (C-4″); 39.7 (C-4); 37.8 (10-$CH\underline{C}H_2$); 32.4 (C-1″); 32.0 (C-2); 28.0 (C-3″); 25.7 (C-3); 23.8 (C-2″).

Methyl (7*S*,10*S*)-10-(4-allyloxybenzyl)-7-(4-aminobutyl)-5,8,11-triaza-12-benzyloxy-6,9,12-trioxododecanoate hydrochloride (96)

Compound **114** (264 mg, 0.33 mmol) was converted to the uncharacterised *N*-Fmoc deprotected amine *via* procedure F, using 1% piperidine in 9:1 acetonitrile/DMF (10 mL). This was then converted, *via* procedure H to the hydrochloride salt **96** (142 mg, 0.23 mmol, 70%) as a hygroscopic brown amorphous solid. MS (ESI^+), *m/z* 583 (100%) [MH^+], 584 (35) [MD^+]. HRMS (ESI^+) calcd for $C_{31}H_{42}N_4O_7$ + H: 583.3132; found 583.3135. $[\alpha]_D^{25}$ +176.9 (*c*. 0.1, EtOH). ^{1}H NMR (300 MHz, CD_3OD): δ 8.08 (bs, 1H, NH); 7.56 (bs, 1H, NH); 7.34-7.25 (m, 5H, 2‴-CH, 3‴-CH, 4‴-CH, 5‴-CH, 6‴-CH,); 7.15 (d, *J* = 7.0 Hz, 2H, 2′-CH and 6′-CH); 6.84 (d, *J* = 7.0 Hz, 2H, 3′-CH and 5′-CH); 6.14-5.96 (m, 1H, $OCH_2C\underline{H}=CH_2$); 5.38 (bd, *J* = 17.2 Hz, 1H, $OCH_2CH=C\underline{H}H$ *trans*); 5.23 (bd, *J* = 10.2 Hz, 1H, $OCH_2CH=CH\underline{H}$ *cis*); 5.09-4.97 (m, 2H, 12-$COOCH_2$); 4.50 (d, *J* = 4.0 Hz, 2H, $OC\underline{H}_2CH=CH_2$); 4.34-4.24 (m, 2H, 7-CH, 10-CH); 3.64 (s, 3H, OCH_3); 3.23-3.11 (m, 2H, 4-CH_2); 3.04-2.95 (m, 2H, 4″-CH_2); 2.91-2.82 (m, 2H, 10-$CHCH_2$); 2.36-2.29 (m, 2H, 2-CH_2); 1.84-1.60 (m, 6H, 1″-CH_2, 3-CH_2 and 3″-CH_2); 1.44-1.30 (m, 2H, 2″-CH_2). ^{13}C NMR (75 MHz, CD_3OD): δ 174.2 (C-1); 173.5 (C-9); 173.0 (C-6); 157.9 (C-4′); 157.3 (C-12); 137.1 (C-1‴); 134.3 ($OCH_2\underline{C}H=CH_2$); 130.8 (C-2′ and C-6′); 129.4 (C-1′); 129.0 (C-3‴ and C-5‴); 128.4 (C-4‴); 128.0 (C-2‴ and C-6‴); 117.3 ($OCH_2CH=\underline{C}H_2$); 115.2 (C-3′ and C-5′); 69.7 ($O\underline{C}H_2CH=CH$); 67.4 (12-$COO\underline{C}H_2$); 57.4 (C-10); 53.8 (C-7); 52.9 (OCH_3); 41.5 (C-4″); 39.5 (C-4); 37.4 (10-$CH\underline{C}H_2$); 32.1 (C-1″); 31.9 (C-2); 27.8 (C-3″); 25.3 (C-3); 23.6 (C-2″).

Methyl (2*S*,5*S*)-5-(4-allyloxybenzyl)-3,6-diaza-7-*tert*-butoxy-2-[4-(*tert*-butoxycarbonyl)aminobutyl]-4,7-dioxoheptanoate (98)

The ester was synthesised using procedure D from the commercially available *N*-*tert*-butoxycarbonyl-*O*-allyltyrosine **97** (501 mg, 1.56 mmol), methyl (*S*)-2-amino-6-(*tert*-butoxycarbonylamino)hexanoate hydrochloride **11** (464 mg, 1.56 mmol), EDCI (540 mg, 2.83 mmol), HOBt (275 mg, 2.04 mmol) and DIPEA (0.32 mL, 1.84 mmol), to yield **98** (703 mg, 1.25 mmol, 80%) as a cream powder, mp. 107-110°C. MS (ESI^+), *m/z* 564 (50%) [MH^+], 408 (100). HRMS (ESI^+) calcd for $C_{29}H_{45}N_3O_8$ + H: 564.3279; found 564.3286. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.09 (d, *J* = 8.5 Hz, 2H, 2′-CH and 6′-CH); 6.81 (d, *J* = 8.7 Hz, 2H, 3′-CH and 5′-CH); 6.60-6.51 (bs, 1H, 3-NH); 6.06-5.97 (m, 1H, $OCH_2C\underline{H}=CH_2$); 5.38 (dd, *J* = 17.3, 1.5 Hz, 1H, $OCH_2CH=C\underline{H}H$ *trans*); 5.25 (dd, *J* = 10.5, 1.3 Hz, 1H, $OCH_2CH=CH\underline{H}$ *cis*); 5.16-5.03 (bs, 1H, 6-NH); 4.77-4.69 (bs, 1H, 4″-$CH_2N\underline{H}$); 4.50-4.47 (m, 3H, 2-CH and $OC\underline{H}_2CH=CH_2$); 4.35-4.26 (m, 1H, 5-CH); 3.68 (s, 3H, OCH_3); 3.08-3.01 (m, 2H, 4″-CH_2); 2.99-2.96 (m, 2H, 5-$CHC\underline{H}_2$); 1.81-1.72 (m, 1H, 1″-$C\underline{H}_aH_b$); 1.65-1.56 (m, 1H, 1″-$CH_a\underline{H}_b$); 1.47-1.34 (m, 22H, 4″-CH_2NH $COOC(C\underline{H}_3)_3$, 7-$COOC(C\underline{H}_3)_3$ and 3″-CH_2); 1.28-1.16 (m, 2H, 2″-CH_2). ^{13}C NMR (126 MHz, $CDCl_3$): δ 172.5 (C-4); 171.5 (C-1); 157.8 (C-4′); 156.2 (4″-$CH_2NH\underline{C}OOC(CH_3)_3$[a]); 155.7 (C-7[a]); 133.5 ($OCH_2\underline{C}H=CH_2$); 130.5 (C-2′ and C-6′); 128.9 (C-1′); 117.8 ($OCH_2CH=\underline{C}H_2$); 115.1 (C-3′ and C-5′); 80.4 (4″-$CH_2NHCOO\underline{C}(CH_3)_3$[b]); 79.3 (7-$COO\underline{C}(CH_3)_3$[b]); 69.0

($O\underline{C}H_2CH=CH_2$); 56.0 (C-5); 52.5 (OCH_3); 52.2 (C-2); 40.4 (C-4''); 37.5 (5-CH$\underline{C}H_2$); 32.2 (C-1''); 29.6 (C-3''); 28.6 (4''-$CH_2NHCOOC(\underline{C}H_3)_3$[c]); 28.5 (7-$COOC(\underline{C}H_3)_3$[c]); 22.5 (C-2'').

(2*S*,5*S*)-5-(4-Allyloxybenzyl)-3,6-diaza-7-*tert*-butoxy-2-[4-(*tert*-butoxycarbonyl)aminobutyl]- 4,7-dioxoheptanoic acid (99)

The acid was synthesised using procedure C from the ester **98** (680 mg, 1.21 mmol), $LiOH.H_2O$ (121 mg, 2.88 mmol) and THF/water 3:1 (60 mL). Unreacted starting materials were extracted using CH_2Cl_2 (2 x 30 mL). After the aqueous solution was acidified the product was extracted with CH_2Cl_2 (3 x 30 mL) and EtOAc (3 x 30 mL), and the combined organic fractions were dried and evaporated to yield **99** (603 mg, 1.10 mmol, 91%) as white crystals, mp. 72-75°C. MS (ESI^-), *m/z* 548 (100%) [M - H^+], 474 (80), 265 (20). HRMS (ESI^-) calcd for $C_{28}H_{43}N_3O_8$ - H: 548.2977; found 548.2988. ^{1}H NMR (300 MHz, $CDCl_3/CD_3OD$): δ 7.07 (d, *J* = 8.4 Hz, 2H, 2'-CH and 6'-CH); 6.78 (d, *J* = 8.5 Hz, 2H, 3'-CH and 5'-CH); 6.01 (tdd, *J* = 17.2, 10.5, 5.3 Hz, 1H, $OCH_2C\underline{H}=CH_2$); 5.37 (dd, *J* = 17.3, 1.6 Hz, 1H, $OCH_2CH=CH\underline{H}$ *trans*); 5.24 (dd, *J* = 10.5, 1.3 Hz, 1H, $OCH_2CH=CH\underline{H}$ *cis*); 4.45 (d, *J* = 5.2 Hz, 2H, $OC\underline{H}_2CH=CH_2$); 4.41-4.28 (m, 2H, 2-CH and 5-CH); 3.09-2.79 (m, 4H, 4''-CH_2 and 5-$CHCH_2$); 1.89-1.71 (m, 1H, 1''-$C\underline{H}_aH_b$); 1.70-1.53 (m, 1H, 1''-$CH_a\underline{H}_b$); 1.42-1.39 (m, 11H, 3''-$CH_2NHCOOC(C\underline{H}_3)_3$[a] and 3''-$CH_2$); 1.30-1.23 (m, 11H, 2''-CH_2 and 7-$COOC(C\underline{H}_3)_3$[a]). ^{13}C NMR (75 MHz, $CDCl_3/CD_3OD$): δ 173.5 (C-1); 172.5 (C-4); 157.7 (C-4'); 156.7 ($NH\underline{C}OOC(CH_3)_3$[a]); 156.0 (C-7[a]); 133.6 ($OCH_2\underline{C}H=CH_2$); 130.6 (C-2' and C-6'); 128.6 (C-1'); 117.8 ($OCH_2CH=\underline{C}H_2$); 114.9 (C-3' and C-5'); 80.1 ($NHCOO\underline{C}(CH_3)_3$[b]); 79.5 (7-$COO\underline{C}(CH_3)_3$[b]); 69.0 ($O\underline{C}H_2CH=CH_2$); 55.8 (C-5); 52.4 (C-2); 40.1 (C-4''); 37.7 (5-CH$\underline{C}H_2$); 32.0 (C-1''); 29.7 (C-3''); 28.7 ($NHCOOC(\underline{C}H_3)_3$[c]); 28.5 (7-$COOC(\underline{C}H_3)_3$[c]); 22.4 (C-2'').

Methyl (7*S*,10*S*)-10-(4-allyloxybenzyl)-5,8,11-triaza-12-*tert*-butoxy-7-[4-(*tert*-butoxycarbonyl)aminobutyl]-6,9,12-trioxododecanoate (100)

The ester was synthesised using procedure D from the acid **99** (101 mg, 0.18 mmol), the prepared amine hydrochloride **27** (39 mg, 0.25 mmol), EDCI (75 mg, 0.27 mmol), HOBt (61 mg, 0.32 mmol) and DIPEA (0.04 mL, 0.23 mmol), to yield **100** (105 mg, 0.16 mmol, 88%) as an off-white powder, mp. 118-120°C. MS (ESI^+), *m/z* 649 (15%) [MH^+], 549 (10), 520 (15), 449 (20), 142 (100). HRMS (ESI^+) calcd for $C_{33}H_{52}N_4O_9$ + H: 649.3807; found 649.3812. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.10 (d, *J* = 8.4 Hz, 2H, 2'-CH and 6'-CH); 6.91 (d, *J* = 7.1 Hz, 1H, 8-NH); 6.82 (d, *J* = 8.6 Hz, 2H, 3'-CH and 5'-CH); 6.71-6.64 (m, 2H, 5-NH and 11-NH); 6.02 (tdd, *J* = 16.8, 10.5, 5.1 Hz, 1H, $OCH_2C\underline{H}=CH_2$); 5.38 (dd, *J* = 17.3, 1.3 Hz, 1H, $OCH_2CH=CH\underline{H}$ *trans*); 5.24 (dd, *J* = 10.3, 1.3 Hz, 1H, $OCH_2CH=CH\underline{H}$ *cis*); 5.01 (bs, 1H, 4''-CHN$\underline{H}$); 4.72-4.67 (m, 1H, 10-CH); 4.48 (d, *J* = 5.2 Hz, 2H, $OC\underline{H}_2CH=CH_2$); 4.40-4.37 (m, 1H, 7-CH); 3.63 (s, 3H, OCH_3); 3.24-3.12 (m, 2H, 4-CH_2); 3.09-2.90 (m, 4H, 4''-CH_2 and 10-$CHC\underline{H}_2$); 2.34 (t, *J* = 7.4 Hz, 2H, 2-CH_2); 1.84-1.78 (m, 3H, 1''-$C\underline{H}_aH_b$ and 3-CH_2); 1.63-1.51 (m, 1H, 1''-$CH_a\underline{H}_b$); 1.47-1.37 (m, 20H, 4''-$CH_2NHCOOC(C\underline{H}_3)_3$, 12-$COOC(C\underline{H}_3)_3$ and 3''-CH_2); 1.33-1.24 (m, 2H, 2''-CH_2). ^{13}C NMR (75 MHz, $CDCl_3$): δ 173.9 (C-1); 172.2 (C-9); 171.8 (C-6); 157.9 (C-4'); 156.5 ($NH\underline{C}OOC(CH_3)_3$ and C-12); 133.4 ($OCH_2\underline{C}H=CH_2$); 130.5 (C-2' and C-6'); 128.6 (C-1'); 117.9 ($OCH_2CH=\underline{C}H_2$); 115.2 (C-3' and C-5'); 80.8 ($NHCOO\underline{C}(CH_3)_3$[a]); 79.4 (12-$COO\underline{C}(CH_3)_3$[a]); 69.0 ($O\underline{C}H_2CH=CH_2$); 53.3 (C-10); 52.1 (C-10); 51.9 (OCH_3); 40.1 (C-4''); 39.1 (C-4); 37.2 (10-CH$\underline{C}H_2$); 31.6 (C-1''); 29.9 (C-2); 29.7 (C-3''); 28.7 ($NHCOOC(\underline{C}H_3)_3$[b]); 28.5 (12-$COOC(\underline{C}H_3)_3$[b]); 24.8 (C-3); 22.9 (C-2'').

Methyl (7*S*,10*S*)-11-(4-allyloxyphenyl)-10-amino-5,8-diaza-7-{4-[9-(9*H*)-fluorenyl]methoxycarbonylamino}butyl-6,9-dioxoundecanoate hydrochloride (101)

Compound **105** (1.51 g, 1.96 mmol) was converted to the *N*-Boc deprotected trifluoroacetate salt *via* procedure E, using 1:1 TFA/CH_2Cl_2 (6 mL). The resulting solid was then converted, *via* procedure H, to give the hydrochloride salt **101** (1.26 g, 1.78 mmol, 91%) as a white amorphous solid. MS (ESI^+), *m/z* 671 (100%) [MH^+], 555 (7). HRMS (ESI^+) calcd for $C_{38}H_{46}N_4O_7$ + H: 671.3439; found 671.3447. ^{1}H NMR (300 MHz, CD_3OD): δ 7.80 (d, *J* = 7.3 Hz, 2H, 4'''-CH and 5'''-CH); 7.64 (d, *J* = 7.1 Hz, 2H, 1'''-CH and 8'''-CH); 7.39 (dd, *J* = 7.3, 7.3 Hz, 2H, 3'''-CH and 6'''-CH); 7.30 (dd, *J* = 7.3, 7.3 Hz, 2H, 2'''-CH and 7'''-CH); 7.19 (d, *J* = 7.7 Hz, 2H, 2'-CH and 6'-CH); 6.91 (d, *J* = 7.7 Hz, H, 3'-CH and 5'-CH); 6.12-5.98 (m, 1H, $OCH_2C\underline{H}=CH_2$); 5.39 (bd, *J* = 17.2 Hz, 1H, $OCH_2CH=CH\underline{H}$ *trans*); 5.24 (bd, *J* = 10.4 Hz, 1H, $OCH_2CH=CH\underline{H}$ *cis*); 4.53 (d, *J* = 4.3 Hz, 2H, $OC\underline{H}_2CH=CH_2$); 4.37-4.23 (m, 3H, 10-CH and 9'-$CHC\underline{H}_2$); 4.23-4.15 (m, 1H, 9'-CH); 4.13-4.05 (m, 1H, 7-CH); 3.63 (s, 3H, OCH_3); 3.24-3.15 (m, 3H, 4-$C\underline{H}_aH_b$ and 4''-CH_2); 3.13-3.05 (m, 2H, 4-$CH_a\underline{H}_b$ and 11-$C\underline{H}_aH_b$); 3.03-2.91 (m, 1H, 11-$CH_a\underline{H}_b$); 2.34 (t, *J* = 7.0 Hz, 2H, 2-CH_2); 1.85-1.61 (m, 4H, 3-CH_2 and 1''-CH_2); 1.60-1.45 (m, 2H, 3''-CH_2); 1.44-1.29 (m, 2H, 2''-CH_2). ^{13}C NMR (75 MHz, CD_3OD): δ 173.7 (C-1); 172.3 (C-9); 171.6 (C-6); 157.9 (C-4'); 156.1 ($NH\underline{C}OOCH_2$); 144.3 (C-9a''' and C-8a'''); 141.4 (C-4a''' and C-4b'''); 133.3 ($OCH_2\underline{C}H=CH_2$); 130.4 (C-2' and C-6'); 128.5 (C-1'); 128.0 (C-3''' and C-6'''); 127.4 (C-2''' and C-7'''); 125.2 (C-1''' and C-8'''); 120.4 (C-4''' and C-5'''); 118.1 ($OCH_2CH=\underline{C}H_2$); 115.2 (C-3' and C-5'); 69.1 ($O\underline{C}H_2CH=CH$); 66.7 (9'''-$CH\underline{C}H_2$); 53.8 (C-10); 53.3 (C-7); 51.9 (OCH_3); 47.4 (C-9'''); 40.3 (C-4''); 39.1 (C-4); 37.5 (11-CH_2); 31.4 (C-1'' and C-2); 29.6 (C-3''); 24.9 (C-3); 22.4 (C-2'').

Methyl (*S*)-7-(*tert*-butoxycarbonyl)amino-11-[9-(9*H*)-fluorenyl]methoxycarbonylamino-5-aza-6-oxoundecanoate (103)

The ester was synthesised using procedure D from (*S*)-2-(*tert*-butoxycarbonyl)amino-6-[9-(9*H*)-fluorenyl]methoxycarbonyl aminohexanoic acid **102** (2.31 g, 4.93 mmol), the prepared amine hydrochloride **27** (750 mg, 4.90 mmol), EDCI (1.24 g, 6.49 mmol), HOBt (850 mg, 6.30 mmol) and DIPEA (0.90 mL, 5.17 mmol), to yield **103** (2.34 g, 4.12 mmol, 84%) as a white powder, mp. 123-126°C. MS (ESI^+), *m/z* 568 (100%) [MH^+]. HRMS (ESI^+) calcd for $C_{31}H_{41}N_3O_7$ + H: 568.3017; found 568.3025. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.75 (d, *J* = 7.5 Hz, 2H, 4'-CH and 5'-CH); 7.58 (d, *J* = 7.5 Hz, 2H, 1'-CH and 8'-CH); 7.38 (dd, *J* = 7.4, 7.4 Hz, 2H, 3'-CH and 6'-CH); 7.29 (dd, *J* = 7.1, 7.1 Hz, 2H, 2'-CH and 7'-CH); 6.67 (bs, 1H, 5-NH); 5.26 (s, 1H, 7-CHN$\underline{H}$); 5.10 (bs, 1H, 11-$CH_2N\underline{H}$); 4.39 (d, *J* = 6.8 Hz, 2H, 9'-$CHC\underline{H}_2$); 4.19 (t, *J* = 6.6, Hz, 1H, 9'-CH); 4.04-3.97 (m, 1H, 7-CH); 3.64 (s, 3H, OCH_3); 3.29-3.26 (m, 2H, 4-CH_2); 3.16 (bs, 2H, 11-CH_2); 2.33 (t, *J* = 7.3, Hz, 2H, 2-CH_2); 1.84-1.78 (m, 3H, 3-CH_2 and 8-$C\underline{H}_aH_b$); 1.64-1.56 (m, 1H, 8-$CH_a\underline{H}_b$); 1.54-1.46 (m, 2H, 10-CH_2); 1.44-1.39 (m, 9H, $OC(C\underline{H}_3)_3$); 1.38-1.33 (m, 2H, 9-CH_2). ^{13}C NMR (126 MHz, $CDCl_3$): δ 173.9 (C-1); 172.0 (C-6); 156.9 ($NH\underline{C}OOC(CH_3)_3$ and $NH\underline{C}OOCH_2$); 144.2 (C-9a' and C-8a'); 141.5 (C-4a' and C-4b'); 127.9 (C-3' and C-6'); 127.2 (C-2' and C-

7′); 125.2 (C-1′ and C-8′); 120.2 (C-4′ and C-5′); 79.4 (O<u>C</u>(CH$_3$)$_3$); 66.8 (9′-CH<u>C</u>H$_2$); 51.9 (OCH$_3$); 50.9 (C-7); 47.5 (C-9′); 39.0 (C-11 and C-4); 32.2 (C-8); 31.5 (C-2); 29.7 (C-10); 28.5 (OC(<u>C</u>H$_3$)$_3$); 24.8 (C-3); 22.8 (C-9).

Methyl (7*S*,10*S*)-10-(4-allyloxybenzyl)-5,8,11-triaza-12-*tert*-butoxy-7-{4-[9-(9*H*)-fluorenyl]methoxycarbonylamino}butyl-6,9,12-trioxododecanoate (105)

The ester was synthesised using procedure D from the commercially available *N*-*tert*-butoxycarbonyl-*O*-allyltyrosine (913 mg, 2.84 mmol), the prepared amine hydrochloride **89** (1.37 g, 2.72 mmol), EDCI (627 mg, 3.28 mmol), HOBt (515 mg, 3.81 mmol) and DIPEA (0.50 mL, 2.87 mmol), to yield the crude product. The crude product was purified by silica gel column chromatography using 15:1 CH_2Cl_2/MeOH as the developing solvent to yield **105** (1.61 g, 2.09 mmol, 77%) as a white powder, mp. 175-177°C. MS (ESI$^+$), *m/z* 771 (37%) [MH$^+$], 671 (100), 463 (40), 409 (55). HRMS (ESI$^+$) calcd for $C_{43}H_{54}N_4O_9$ + H: 771.3964; found 771.3972. ^{1}H NMR (500 MHz, $CDCl_3$/CD_3OD): δ 7.75 (d, *J* = 7.5 Hz, 2H, 4‴-CH and 5‴-CH); 7.58 (d, *J* = 7.2 Hz, 2H, 1‴-CH and 8‴-CH); 7.38 (dd, *J* = 7.4, 7.4 Hz, 2H, 3‴-CH and 6‴-CH); 7.29 (dd, *J* = 7.4, 7.4 Hz, 2H, 2‴-CH and 7‴-CH); 7.07 (d, *J* = 8.3 Hz, 2H, 2′-CH and 6′-CH); 6.80 (d, *J* = 8.4 Hz, 2H, 3′-CH and 5′-CH); 6.01 (tdd, *J* = 17.1, 10.5, 5.3 Hz, 1H, OCH$_2$C<u>H</u>=CH$_2$); 5.38 (dd, *J* = 17.3, 1.4 Hz, 1H, OCH$_2$CH=C<u>H</u>H *trans*); 5.25 (dd, *J* = 10.5, 1.2 Hz, 1H, OCH$_2$CH=CH<u>H</u> *cis*); 4.46 (d, *J* = 5.2 Hz, 2H, OC<u>H</u>$_2$CH=CH$_2$); 4.41-4.28 (m, 4H, 7-CH, 10-CH and 9‴-CHC<u>H</u>$_2$); 4.23-4.16 (m, 1H, 9‴-CH); 3.64 (s, 3H, OCH$_3$); 3.29-3.24 (m, 1H, 4-C<u>H</u>$_a$H$_b$); 3.21-3.10 (m, 3H, 4-CH$_a$<u>H</u>$_b$ and 4″-CH$_2$); 3.03 (dd, *J* = 14.0, 6.0 Hz, 1H, 10-CHC<u>H</u>$_a$H$_b$); 2.93 (dd, *J* = 13.8, 7.5 Hz, 1H, 10-CHCH$_a$<u>H</u>$_b$); 2.32 (t, *J* = 7.3 Hz, 2H, 2-CH$_2$); 1.81-1.77 (m, 3H, 1″-C<u>H</u>$_a$H$_b$ and 3-CH$_2$); 1.67-1.56 (m, 1H, 1″-CH$_a$<u>H</u>$_b$); 1.53-1.45 (m, 2H 3″-CH$_2$); 1.42-1.34 (m, 9H, OC(C<u>H</u>$_3$)$_3$); 1.32-1.24 (m, 2H, 2″-CH$_2$). ^{13}C NMR (75 MHz, $CDCl_3$/CD_3OD): δ 173.9 (C-1); 172.1 (C-9); 171.5 (C-6); 157.9 (C-4′); 156.9 (C-12); 156.1 (NH<u>C</u>OOCH$_2$); 144.2 (C-9a‴ and C-8a‴); 141.5 (C-4a‴ and C-4b‴); 133.4 (OCH$_2$<u>C</u>H=CH$_2$); 130.4 (C-2′ and C-6′); 128.6 (C-1′); 127.9 (C-3‴ and C-6‴); 127.3 (C-2‴ and C-7‴); 125.3 (C-1‴ and C-8‴); 120.2 (C-4‴ and C-5‴); 117.9 (OCH$_2$CH=<u>C</u>H$_2$); 115.2 (C-3′ and C-5′); 80.8 (COO<u>C</u>(CH$_3$)$_3$); 69.0 (O<u>C</u>H$_2$CH=CH); 66.8 (9‴-CH<u>C</u>H$_2$); 53.4 (C-7 and C-10); 51.9 (OCH$_3$); 47.5 (C-9‴); 40.6 (C-4″); 39.1 (C-4); 37.3 (10-CH<u>C</u>H$_2$); 31.5 (C-1″ and C-2); 29.6 (C-3″); 28.5 (OC(<u>C</u>H$_3$)$_3$); 24.7 (C-3); 22.6 (C-2″).

Methyl (7*S*,10*S*)-10-(4-allyloxybenzyl)-5,8,11-triaza-7-{4-[9-(9*H*)-fluorenyl]methoxycarbonylamino}butyl-6,9,12-trioxo-12-(2-pyridinyl)dodecanoate (106)

Using procedure D, ester **106** was synthesised from 2-pyridinecarboxylic acid (132 mg, 1.07 mmol), the prepared amine hydrochloride **101** (500 mg, 0.71 mmol), EDCI (193 mg, 1.01 mmol), HOBt (240 mg, 1.78 mmol) and DIPEA (0.15 mL, 0.86 mmol), to yield **106** (374 mg, 0.48 mmol, 68%) as a white powder, mp. 158-161°C. MS (ESI$^+$), *m/z* 776 (30%) [MH$^+$], 146 (80), 100 (100). HRMS (ESI$^+$) calcd for $C_{44}H_{49}N_4O_8$ + H: 776.3654; found 776.3660. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.50 (d, *J* = 7.0 Hz, 1H, 11-NH); 8.44 (d, *J* = 4.3 Hz, 1H, 6‴-CH); 8.07 (d, *J* = 7.8 Hz, 1H, 3‴-CH); 7.74 (dd, *J* = 7.5, 7.5 Hz, 1H, 4‴-CH); 7.67 (d, *J* = 7.5 Hz, 2H, 4‴-CH and 5‴-CH); 7.50 (dd, *J* = 7.1, 3.1 Hz, 2H, 1‴-CH and 8‴-CH); 7.36 (dd, *J* = 5.0 Hz, 1H, 5‴-CH); 7.30 (dd, *J* = 7.2, 7.2 Hz, 2H, 3‴-CH and 6‴-CH); 7.20 (dd, *J* = 7.1, 7.1 Hz, 2H, 2‴-CH and 7‴-CH); 7.10 (d, *J* = 8.6 Hz, 2H, 2′-CH and 6′-CH); 6.75 (d, *J* = 8.6 Hz, 2H, 3′-CH and 5′-CH); 6.60 (d, *J* = 7.9 Hz, 1H, 8-NH); 6.46 (t, *J* = 5.6 Hz, 1H, 5-NH); 5.94 (tdd, *J* = 17.2, 10.5, 5.3 Hz, 1H, OCH$_2$C<u>H</u>=CH$_2$); 5.30 (dd, *J* = 17.3, 1.6 Hz, 1H, OCH$_2$CH=C<u>H</u>H *trans*); 5.20-5.12 (m, 2H, 4″-CH$_2$N<u>H</u> and OCH$_2$CH=CH<u>H</u> *cis*); 4.72-4.68 (m, 1H, 10-CH); 4.39 (d, *J* = 5.3 Hz, 2H, OC<u>H</u>$_2$CH=CH$_2$); 4.32-4.23 (m, 3H, 7-CH and 9‴-CHC<u>H</u>$_2$); 4.11 (t, *J* = 6.8 Hz, 1H, 9‴-CH); 3.57 (s, 3H, OCH$_3$); 3.19-3.08 (m, 4H, 4-CH$_2$ and 10-CHC<u>H</u>$_2$); 3.07-2.98 (m, 2H, 4″-CH$_2$); 2.26 (t, *J* = 7.3 Hz, 2H, 2-CH$_2$); 1.84-1.67 (m, 3H, 1″-C<u>H</u>$_a$H$_b$ and 3-CH$_2$); 1.55-1.43 (m, 1H, 1″-CH$_a$<u>H</u>$_b$); 1.42-1.31 (m, 2H, 3″-CH$_2$); 1.26-1.12 (m, 2H, 2″-CH$_2$). ^{13}C NMR (75 MHz, $CDCl_3$): δ 173.7 (C-1); 171.1 (C-9); 171.0 (C-6); 157.6 (C-4′); 156.6 (NH<u>C</u>OOCH$_2$); 148.5 (C-12); 147.7 (C-2‴′); 144.0 (C-6‴′); 143.9 (C-9a‴ and C-8a‴′); 141.2 (C-4a‴ and C-4b‴′); 138.2 (C-4‴′); 133.1 (OCH$_2$<u>C</u>H=CH$_2$); 130.3 (C-2′ and C-6′); 128.4 (C-1′); 127.6 (C-3‴ and C-6‴′); 127.0 (C-2‴ and C-7‴′); 126.8 (C-5‴′); 125.1 (C-1‴ and C-8‴′); 122.8 (C-3‴′); 119.9 (C-4‴ and C-5‴′); 117.6 (OCH$_2$CH=<u>C</u>H$_2$); 114.9 (C-3′ and C-5′); 68.7 (O<u>C</u>H$_2$CH=CH); 66.5 (9‴-CH<u>C</u>H$_2$); 55.7 (C-10); 53.3 (C-7); 51.7 (OCH$_3$); 47.2 (C-9‴′); 40.3 (C-4″); 38.9 (C-4); 36.8 (10-CH<u>C</u>H$_2$); 31.4 (C-1″); 31.1 (C-2); 29.2 (C-3″); 24.5 (C-3); 22.5 (C-2″).

2-Benzyloxybenzoic acid (107)[12, 13]

This compound was synthesised (procedure C) from the ester **109** (1.20 g, 4.95 mmol) in MeOH/water 3:1 (80 mL) with potassium hydroxide (863 mg, 15.38 mmol) to yield **107** (984 mg, 4.31 mmol, 87%) as a yellow amorphous solid, mp. 73-75°C. MS (ESI$^-$), *m/z* 227 (100%) [M - H$^+$]. HRMS (ESI$^-$) calcd for $C_{14}H_{12}O_3$ - H: 227.0714; found 227.0708. ^{1}H NMR (300 MHz, $(CD_3)_2CO$): δ 7.97 (d, *J* = 7.8 Hz, 1H, 6-CH); 7.51-7.28 (m, 6H, 4-CH, 2′-CH, 3′-CH, 4′-CH, 5′-CH and 6′-CH); 7.10-7.00 (m, 2H, 3-CH and 5-CH); 5.21 (s, 2H, OCH$_2$Ar). ^{13}C NMR (75 MHz, $(CD_3)_2CO$): δ 169.7 (C=O); 157.6 (C-2); 136.5 (C-1′); 133.1 (C-4); 131.9 (C-6); 128.8 (C-3′ and C-5′); 128.0 (C-4′); 126.6 (C-2′ and C-6′); 121.1 (C-5); 120.7 (C-1); 113.8 (C-3); 70.5 (O<u>C</u>H$_2$Ar).

Methyl 2-benzyloxybenzoate (109)[12, 14, 15]

Using procedure A, methyl salicylate (1.18 g, 7.75 mmol), anhydrous potassium carbonate (2.18 g, 15.77 mmol), benzyl bromide (1.84 mL, 15.49 mmol) in DMF (10 mL), gave ester **109** (1.60 g, 6.59 mmol, 85%) as a yellow oil. MS (ESI$^+$), *m/z* 243 (100%) [MH$^+$]. HRMS (ESI$^+$) calcd for $C_{15}H_{14}O_3$ + H: 243.1016; found 243.1021. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.84 (d, *J* = 7.6 Hz, 1H, 6-CH); 7.52-7.25 (m, 6H, 4-CH, 2′-CH, 3′-CH, 4′-CH, 5′-CH and 6′-CH); 7.04-6.98 (m, 2H, 3-CH and 5-CH); 5.19 (s, 2H, OCH$_2$Ar); 3.91 (s, 3H, OCH$_3$). ^{13}C NMR (75 MHz, $CDCl_3$): δ 166.7 (C=O); 158.0 (C-2); 136.7 (C-1′); 133.3 (C-4); 131.7 (C-6); 128.5 (C-3′ and C-5′); 127.7 (C-4′); 126.7 (C-2′ and C-6′); 120.7 (C-5); 120.5 (C-1); 113.8 (C-3); 70.5 (O<u>C</u>H$_2$Ar); 51.9 (OCH$_3$).

Methyl (7*S*,10*S*)-10-(4-allyloxybenzyl)-5,8,11-triaza-12-[2-(benzyloxy)phenyl]-7-{4-[9-(9*H*)-fluorenyl]methoxycarbonyl amino}butyl-6,9,12-trioxododecanoate (110)

The ester was synthesised (procedure D) from **107** (85 mg, 0.37 mmol), the amine hydrochloride **101** (250 mg, 0.36 mmol), EDCI (99 mg, 0.52 mmol), HOBt (75 mg, 0.56 mmol) and DIPEA (0.15 mL, 0.86 mmol), to yield **110** (236 mg, 0.27 mmol, 72%) as a white powder, mp. 161-165°C. MS (ESI$^+$), *m/z* 881 (20%) [MH$^+$], 563 (45), 547 (50), 526 (70), 426 (100). HRMS (ESI$^+$) calcd for

$C_{52}H_{56}N_4O_9$ + H: 881.4120; found 881.4128. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.33 (d, *J* = 5.6 Hz, 1H, 11-NH); 8.08 (d, *J* = 7.8 Hz, 2H, 1''''-CH and 8''''-CH); 7.66 (d, *J* = 7.5 Hz, 2H, 4''''-CH and 5''''-CH); 7.49 (d, *J* = 7.4 Hz, 1H, 6''-CH); 7.37-7.26 (m, 8H, 4''-CH, 2'''-CH, 3'''-CH, 4'''-CH, 5'''-CH, 6'''-CH, 3''''-CH and 6''''-CH); 7.21-7.15 (m, 1H, 5''-CH); 6.95 (dd, *J* = 7.5, 7.5 Hz, 2H, 2'''-CH and 7'''-CH); 6.88 (d, *J* = 8.3 Hz, 1H, 3''-CH); 6.79 (d, *J* = 8.5 Hz, 2H, 2'-CH and 6'-CH); 6.68-6.57 (m, 3H, 5-NH, 3'-CH and 5'-CH); 5.89 (tdd, *J* = 17.3, 10.5, 5.3 Hz, 1H, $OCH_2C\underline{H}=CH_2$); 5.26 (dd, *J* = 17.3, 1.5 Hz, 1H, $OCH_2CH=C\underline{H}H$ *trans*); 5.17-5.12 (m, 2H, 8-NH and $OCH_2CH=CH\underline{H}$ *cis*); 5.11-4.98 (m, 2H, $OC\underline{H}_2Ar$); 4.67-4.56 (m, 1H, 10-CH); 4.31-4.22 (m, 5H, $OC\underline{H}_2CH=CH_2$, 7-CH and 9''''-$CHC\underline{H}_2$); 4.08 (t, *J* = 6.9 Hz, 1H, 9''''-CH); 3.55 (s, 3H, OCH_3); 3.15 (td, *J* = 12.3, 6.4 Hz, 2H, 4-CH_2); 3.05-2.87 (m, 4H, 4''''-CH_2, 4''''-$CH_2N\underline{H}$ and 10-$CHC\underline{H}_aH_b$); 2.70 (dd, *J* = 14.1, 8.1 Hz, 1H, 10-$CHCH_a\underline{H}_b$); 2.25 (t, *J* = 7.3 Hz, 2H, 2-CH_2); 1.88-1.67 (m, 3H, 1''''-$C\underline{H}_aH_b$ and 3-CH_2); 1.54-1.32 (m, 3H, 1''''-$CH_a\underline{H}_b$ and 3''''-CH_2); 1.26-1.10 (m, 2H, 2''''-CH_2). ^{13}C NMR (75 MHz, $CDCl_3$): δ 173.6 (C-1); 171.5 (C-9); 171.3 (C-6); 166.2 (C-12); 157.5 (C-4'); 156.9 (C-2''); 156.5 ($NH\underline{C}OOCH_2$); 144.0 (C-9a'''' and C-8a''''); 141.2 (C-1''', C-4a'''' and C-4b''''); 135.4 (C-4''); 133.5 (C-6''); 133.1 ($OCH_2\underline{C}H=CH_2$); 132.3 (C-4'''); 130.0 (C-2' and C-6'); 128.9 (C-3''' and C-5'''); 128.4 (C-1'); 127.7 (C-2''' and C-6'''); 127.6 (C-3'''' and C-6''''); 127.0 (C-2'''' and C-7''''); 125.1 (C-1'''' and C-8''''); 121.6 (C-5''); 120.4 (C-1''); 119.8 (C-4'''' and C-5''''); 117.6 ($OCH_2CH=\underline{C}H_2$); 114.7 (C-3' and C-5'); 112.8 (C-3''); 71.2 ($O\underline{C}H_2Ar$); 68.6 ($O\underline{C}H_2CH=CH$); 66.5 (9''''-$CH\underline{C}H_2$); 56.2 (C-10); 53.2 (C-7); 51.6 (OCH_3); 47.2 (C-9''''); 40.4 (C-4'''); 38.9 (C-4); 36.2 (10-$CH\underline{C}H_2$); 31.3 (C-1''''); 31.0 (C-2); 29.2 (C-3''''); 24.5 (C-3); 22.6 (C-2'''').

Methyl (*S*)-2-(4-allyloxybenzyl)-3-aza-4-benzyloxy-4-oxobutanoate (112)

Using procedure A and the commercially available *N*-(benzyloxycarbonyl)tyrosine methyl ester **111** (510 mg, 1.55 mmol), anhydrous potassium carbonate (420 mg, 3.04 mmol), allyl bromide (0.30, 3.47 mmol) and DMF (10 mL) as solvent, the ester (515 mg, 1.39 mmol, 90%) was obtained as a white solid, mp. 135-137°C. MS (ESI^+), *m/z* 370 (85%) [MH^+], 326 (100). HRMS (ESI^+) calcd for $C_{21}H_{23}NO_5$ + H: 370.1649; found 370.1660. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.25-7.18 (m, 5H, 2''-CH, 3''-CH, 4''-CH, 5''-CH and 6''-CH); 6.90 (d, *J* = 8.7 Hz, 2H, 3'-CH and 5'-CH); 6.71 (d, *J* = 8.7 Hz, 2H, 2'-CH and 6'-CH); 5.93 (tdd, *J* = 17.2, 10.5, 5.3 Hz, 1H, $OCH_2C\underline{H}=CH_2$); 5.29 (dd, *J* = 17.3, 1.6 Hz, 1H, $OCH_2CH=C\underline{H}H$ *trans*); 5.16 (dd, *J* = 10.5, 1.4 Hz, 1H, $OCH_2CH=CH\underline{H}$ *cis*); 4.98 (d, *J* = 4.1 Hz, 2H, OCH_2Ar); 4.51 (dd, *J* = 14.0, 6.0 Hz, 1H, 2-CH); 4.38 (d, *J* = 5.3 Hz, 2H, $OC\underline{H}_2CH=CH_2$); 3.59 (s, 3H, OCH_3); 2.97 (dd, *J* = 14.1, 5.8 Hz, 1H, 2-$CHC\underline{H}_aH_b$); 2.89 (dd, *J* = 14.1, 6.2 Hz, 1H, 2-$CHCH_a\underline{H}_b$). ^{13}C NMR (75 MHz, $CDCl_3$): δ 171.9 (C-1); 157.6 (C-4'); 155.5 (C-4); 136.1 (C-1''); 133.1 ($OCH_2\underline{C}H=CH_2$); 130.1 (C-2' and C-6'); 128.3 (C-1'); 128.0 (C-3'' and C-5''); 127.9 (C-4''); 127.7 (C-2'' and C-6''); 117.4 ($OCH_2CH=\underline{C}H_2$); 114.6 (C-3' and C-5'); 68.6 ($O\underline{C}H_2CH=CH_2$); 66.7 ($O\underline{C}H_2Ar$); 54.8 (C-2); 52.1 (OCH_3); 37.1 (2-$CH\underline{C}H_2$).

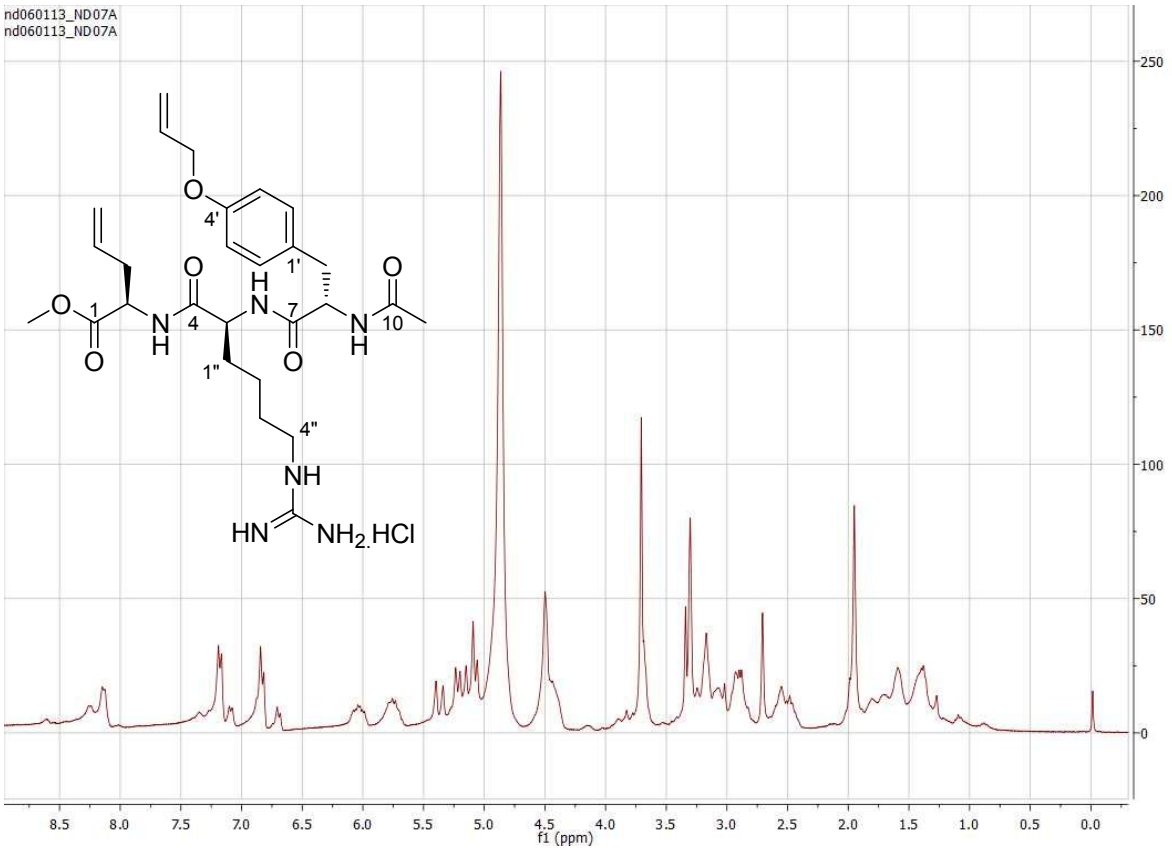
(*S*)-2-(4-Allyloxybenzyl)-3-aza-4-benzyloxy-4-oxobutanoic acid (113)

The acid was synthesised using procedure C from the ester **112** (600 mg, 1.63 mmol), $LiOH.H_2O$ (180 mg, 4.29 mmol) and THF/water 3:1 (60 mL). Unreacted starting materials were extracted using CH_2Cl_2 (2 x 30 mL). After the aqueous solution was acidified the product was extracted with CH_2Cl_2 (3 x 30 mL) and EtOAc (3 x 30 mL), and the combined organic fractions were dried and evaporated to yield **113** (664 mg, 1.87 mmol, 87%) as white crystals, mp. 140-142°C. MS (ESI^-), *m/z* 354 (100%) [M - H^+], 316 (55). HRMS (ESI^-) calcd for $C_{20}H_{21}NO_5$ - H: 354.1341; found 354.1340. ^{1}H NMR (300 MHz, $(CD_3)_2CO$): δ 7.38-7.31 (m, 5H, 2''-CH, 3''-CH, 4''-CH, 5''-CH and 6''-CH); 7.07 (d, *J* = 8.4 Hz, 2H, 3'-CH and 5'-CH); 6.84 (d, *J* = 8.3 Hz, 2H, 2'-CH and 6'-CH); 6.03 (tdd, *J* = 17.2, 10.5, 5.2 Hz, 1H, $OCH_2C\underline{H}=CH_2$); 5.37 (dd, *J* = 17.3, 1.7 Hz, 1H, $OCH_2CH=C\underline{H}H$ *trans*); 5.22 (dd, *J* = 10.6, 1.6 Hz, 1H, $OCH_2CH=CH\underline{H}$ *cis*); 5.01 (d, *J* = 6.3 Hz, 2H, OCH_2Ar); 4.47 (d, *J* = 5.1 Hz, 2H, $OC\underline{H}_2CH=CH_2$); 4.42-4.36 (m, 2H, 2-CH and 3-NH); 3.12 (dd, *J* = 14.0, 4.9 Hz, 1H, 2-$CHC\underline{H}_aH_b$); 2.86 (dd, *J* = 13.9, 9.2 Hz, 1H, 2-$CHCH_a\underline{H}_b$). ^{13}C NMR (75 MHz, $(CD_3)_2CO$): δ 172.2 (C-1); 157.8 (C-4'); 155.6 (C-4); 136.1 (C-1''); 134.1 ($OCH_2\underline{C}H=CH_2$); 130.4 (C-2' and C-6'); 129.5 (C-1'); 128.1 (C-3'' and C-5''); 127.9 (C-4''); 127.7 (C-2'' and C-6''); 116.9 ($OCH_2CH=\underline{C}H_2$); 114.6 (C-3' and C-5'); 68.6 ($O\underline{C}H_2CH=CH_2$); 66.6 ($O\underline{C}H_2Ar$); 54.1 (C-2); 36.8 (2-$CH\underline{C}H_2$).

Methyl (7*S*,10*S*)-10-(4-allyloxybenzyl)-5,8,11-triaza-12-benzyloxy-7-{4-[9-(9*H*)-fluorenyl]methoxycarbonylamino}butyl-6,9,12-trioxododecanoate (114)

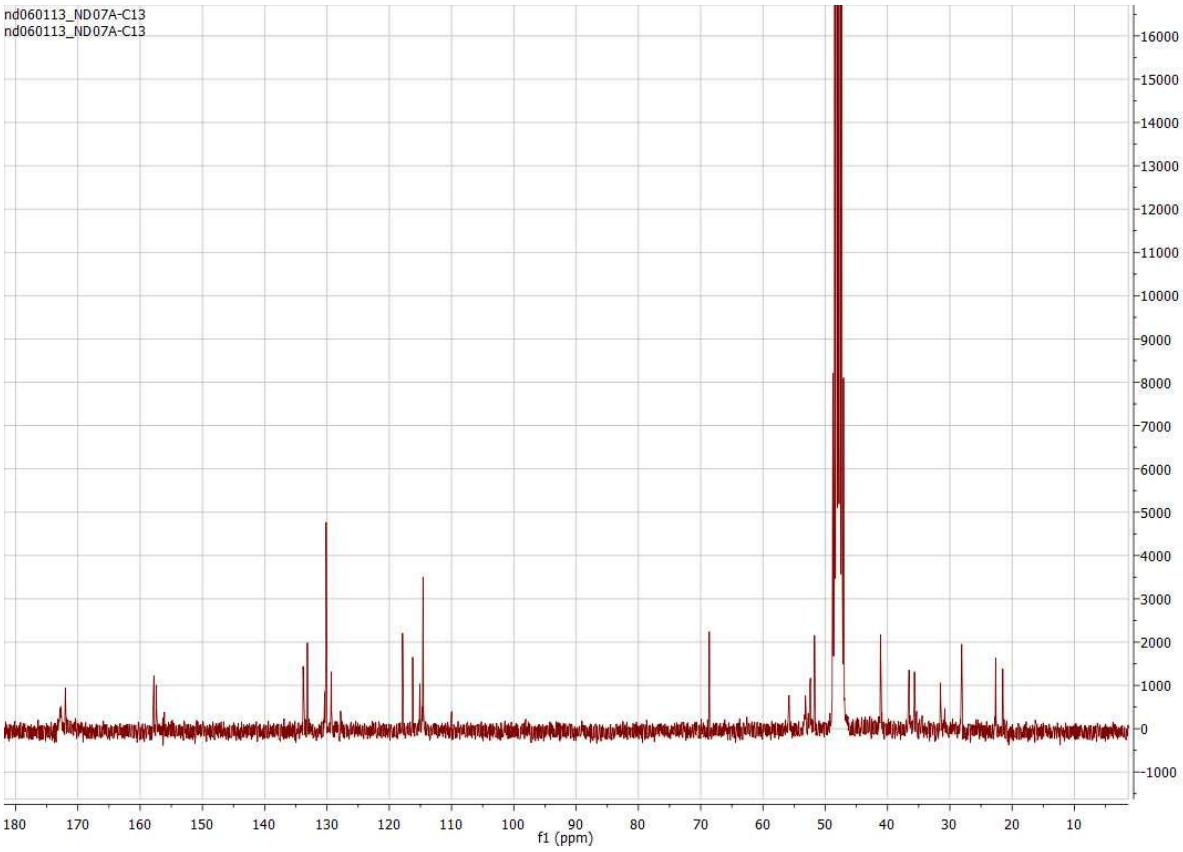
The ester was synthesised using procedure D from the acid **113** (200 mg, 0.56 mmol), the amine hydrochloride **89** (307 mg, 0.61 mmol), EDCI (191 mg, 1.04 mmol), HOBt (140 mg, 1.04 mmol) and DIPEA (0.16 mL, 0.92 mmol), to yield **114** (403 mg, 0.50 mmol, 89%) as an off-white powder, mp. 180-183°C. MS (ESI^+), *m/z* 805 (100%) [MH^+], 689 (30), 468 (60). HRMS (ESI^+) calcd for $C_{46}H_{52}N_4O_9$ + H: 805.3734; found 805.3745. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.69 (d, *J* = 7.5 Hz, 2H, 4''''-CH and 5''''-CH); 7.50 (d, *J* = 7.2 Hz, 2H, 1''''-CH and 8''''-CH); 7.32 (dd, *J* = 7.4, 7.4 Hz, 2H, 3''''-CH and 6''''-CH); 7.26-7.18 (m, 7H, 2''-CH, 3''-CH, 4''-CH, 5''-CH, 6''-CH, 2''''-CH and 7''''-CH); 6.99 (d, *J* = 8.3 Hz, 2H, 2'-CH and 6'-CH); 6.72 (d, *J* = 8.3 Hz, 2H, 3'-CH and 5'-CH); 6.52-6.44 (m, 1H, 5-NH); 6.39-6.31 (m, 1H, 8-NH); 5.95 (tdd, *J* = 17.2, 10.6, 5.3 Hz, 1H, $OCH_2C\underline{H}=CH_2$); 5.36-5.25 (m, 2H, 11-NH and $OCH_2CH=C\underline{H}H$ *trans*); 5.19 (dd, *J* = 10.4, 1.3 Hz, 1H, $OCH_2CH=CH\underline{H}$ *cis*); 5.04-4.95 (m, 3H, 12-$COOCH_2$ and 4'''-$CH_2N\underline{H}$); 4.39 (d, *J* = 5.4 Hz, 2H, $OC\underline{H}_2CH=CH_2$); 4.33-4.20 (m, 4H, 7-CH, 10-CH and 9''''-$CHC\underline{H}_2$); 4.14-4.05 (m, 1H, 9''''-CH); 3.57 (s, 3H, OCH_3); 3.19-3.09 (m, 2H, 4-CH_2); 3.09-3.00 (m, 2H, 4'''-CH_2); 2.97-2.88 (m, 2H, 10-$CHCH_2$); 2.25 (t, *J* = 7.2 Hz, 2H, 2-CH_2); 1.79-1.63 (m, 3H, 1'''-$C\underline{H}_aH_b$ and 3-CH_2); 1.58-1.46 (m, 1H, 1'''-$CH_a\underline{H}_b$); 1.45-1.32 (m, 2H, 3'''-CH_2); 1.23-1.09 (m, 2H, 2'''-CH_2). ^{13}C NMR (75 MHz, $CDCl_3$): δ 173.8 (C-1); 172.0 (C-9); 171.4 (C-6); 157.8 (C-4'); 156.7 (C-12 and 4'''-$CH_2NH\underline{C}OOCH_2$); 144.1 (C-9a'''' and C-8a''''); 144.0 (C-1''); 141.3 (C-4a''' and C-4b''') 133.1 ($OCH_2\underline{C}H=CH_2$); 130.2 (C-2' and C-6'); 128.5 (C-3'' and C-5''); 128.3 (C-1'); 128.1 (C-4''); 128.0 (C-2'' and C-6''); 127.7 (C-3'''' and C-6''''); 127.0 (C-2''' and C-7'''); 125.0 (C-1''' and C-8'''); 119.9 (C-4'''' and C-5''''); 117.7 ($OCH_2CH=\underline{C}H_2$); 115.0 (C-3' and C-5'); 68.8 ($O\underline{C}H_2CH=CH$); 67.2 (12-$COO\underline{C}H_2$); 66.5 (9''''-$CH\underline{C}H_2$); 55.7 (C-10); 53.2 (C-10); 51.7 (OCH_3); 47.2 (C-9'''') 40.2 (C-4'''); 38.9 (C-4); 37.0 (10-$CH\underline{C}H_2$); 31.3 (C-1''' and C-2); 29.3 (C-3'''); 24.5 (C-3); 22.2 (C-2''').

^{1}H NMR spectrum of compound **6**

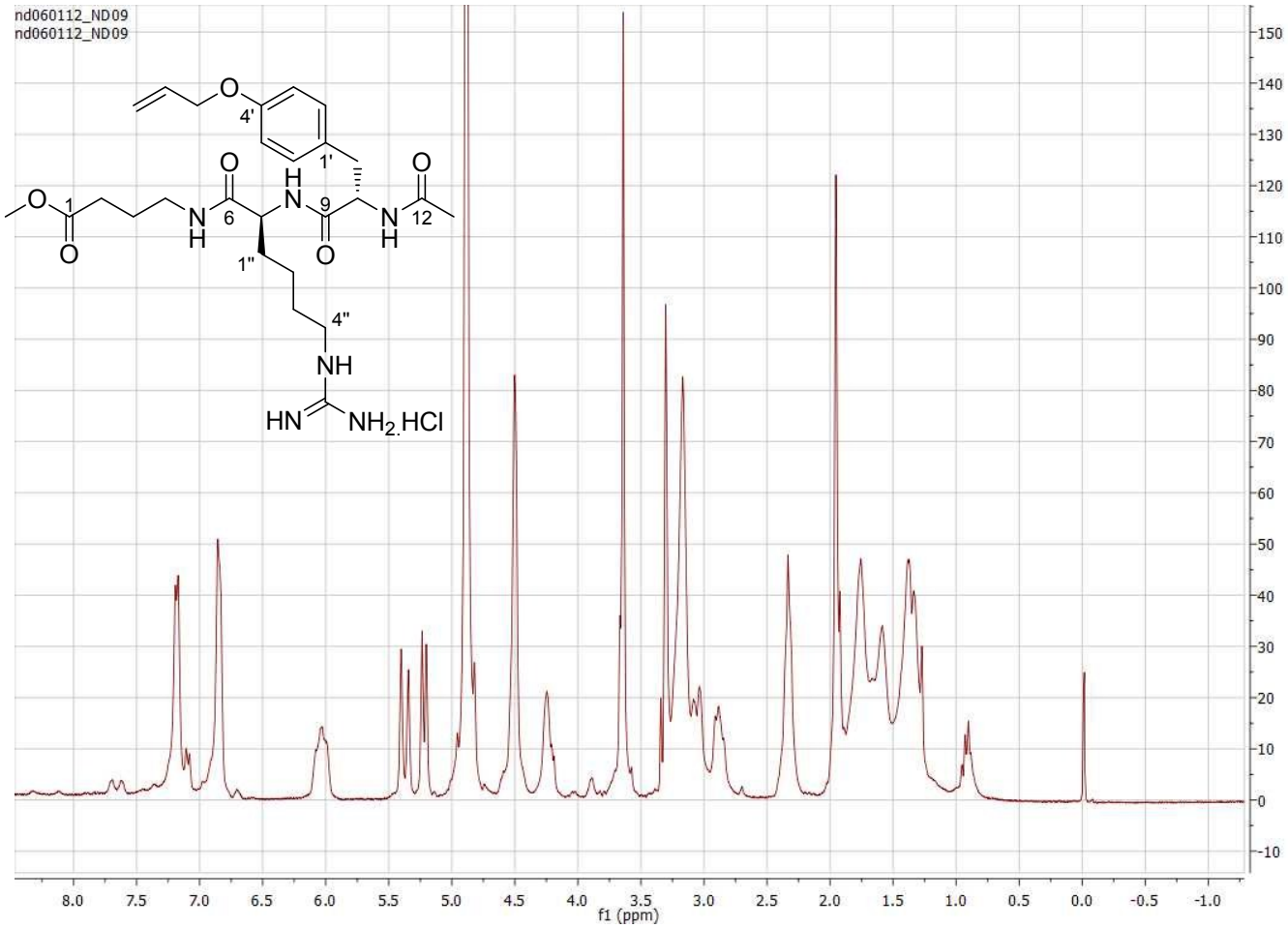


^{1}H NMR (300 MHz, CD_3OD): δ 8.11 (d, J = 6.4, 1H, NH); 7.16 (d, *J* = 8.6 Hz, 2H, 2′-CH and 6′-CH); 6.83 (d, *J* = 8.6 Hz, 2H, 3′-CH and 5′-CH); 6.04 (tdd, *J* = 17.2, 10.4, 5.1 Hz, 1H, $OCH_2C\underline{H}=CH_2$); 5.83-5.65 (m, 1H, $CHCH_2C\underline{H}=CH_2$); 5.37 (dd, *J* = 17.3, 1.7 Hz, 1H, $OCH_2CH=C\underline{H}H$ *trans*); 5.22 (dd, *J* = 10.5, 1.4 Hz, 1H, $OCH_2CH=CH\underline{H}$ *cis*); 5.16-5.04 (m, 2H, $CHCH_2CH=C\underline{H}_2$); 4.54-4.47 (m, 3H, $OC\underline{H}_2CH=CH_2$ and 8-CH); 4.47-4.36 (m, 2H, 2-CH and 5-CH); 3.71 (s, 3H, OCH_3); 3.20-3.11 (m, 2H, 4″-CH_2); 2.96-2.79 (m, 2H, 8-$CHC\underline{H}_2$); 2.64-2.38 (m, 2H, $CHC\underline{H}_2CH=CH_2$); 1.93 (s, 3H, 11-$CH_3$); 1.86-1.74 (m, 1H, 1″-$C\underline{H}_aH_b$); 1.72-1.52 (m, 3H, 3″-$CH_2$ and 1″-$CH_a\underline{H}_b$); 1.46-1.32 (m, 2H, 2″-CH_2).

^{13}C NMR spectrum of compound **6**

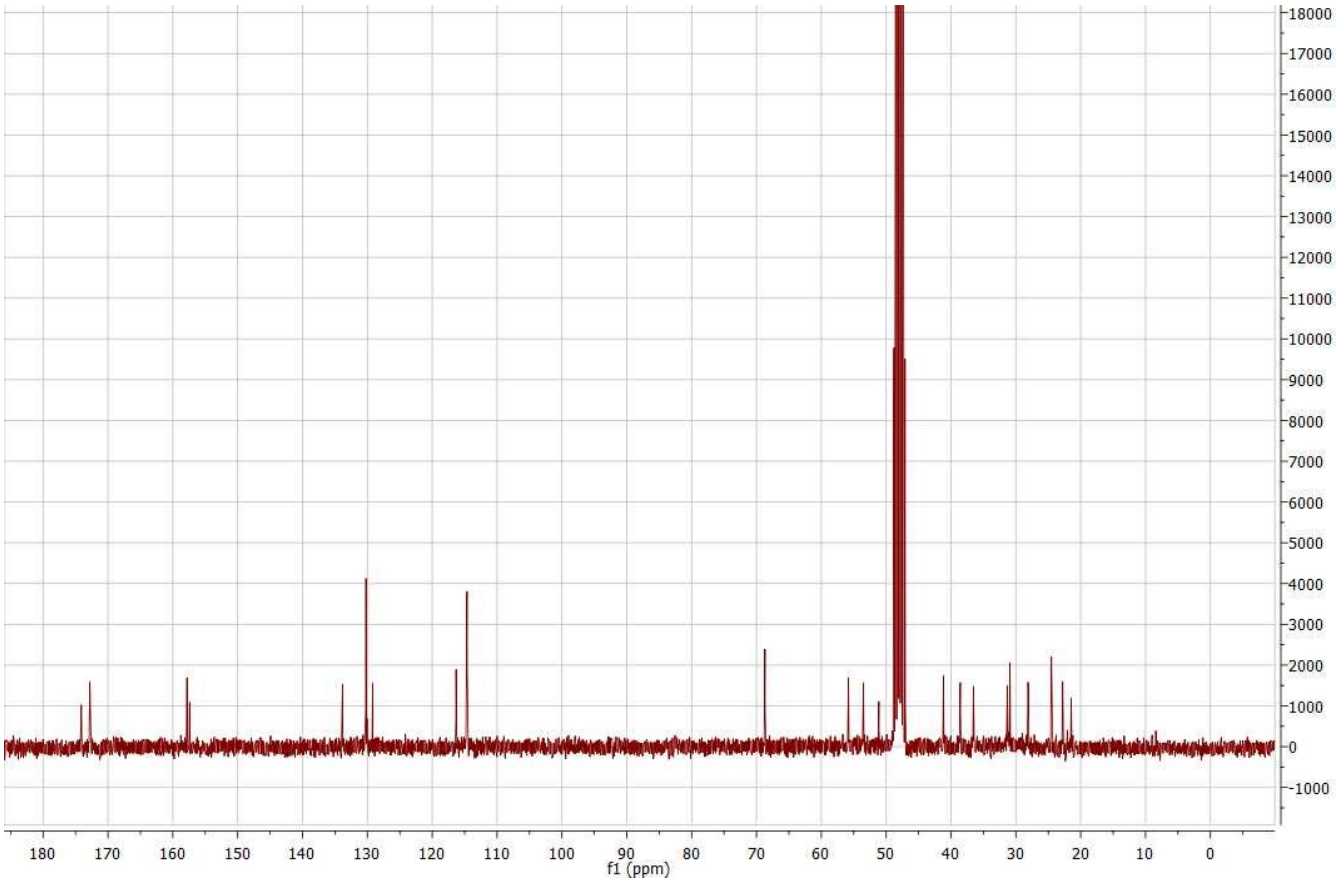


^{1}H NMR spectrum of compound **24**

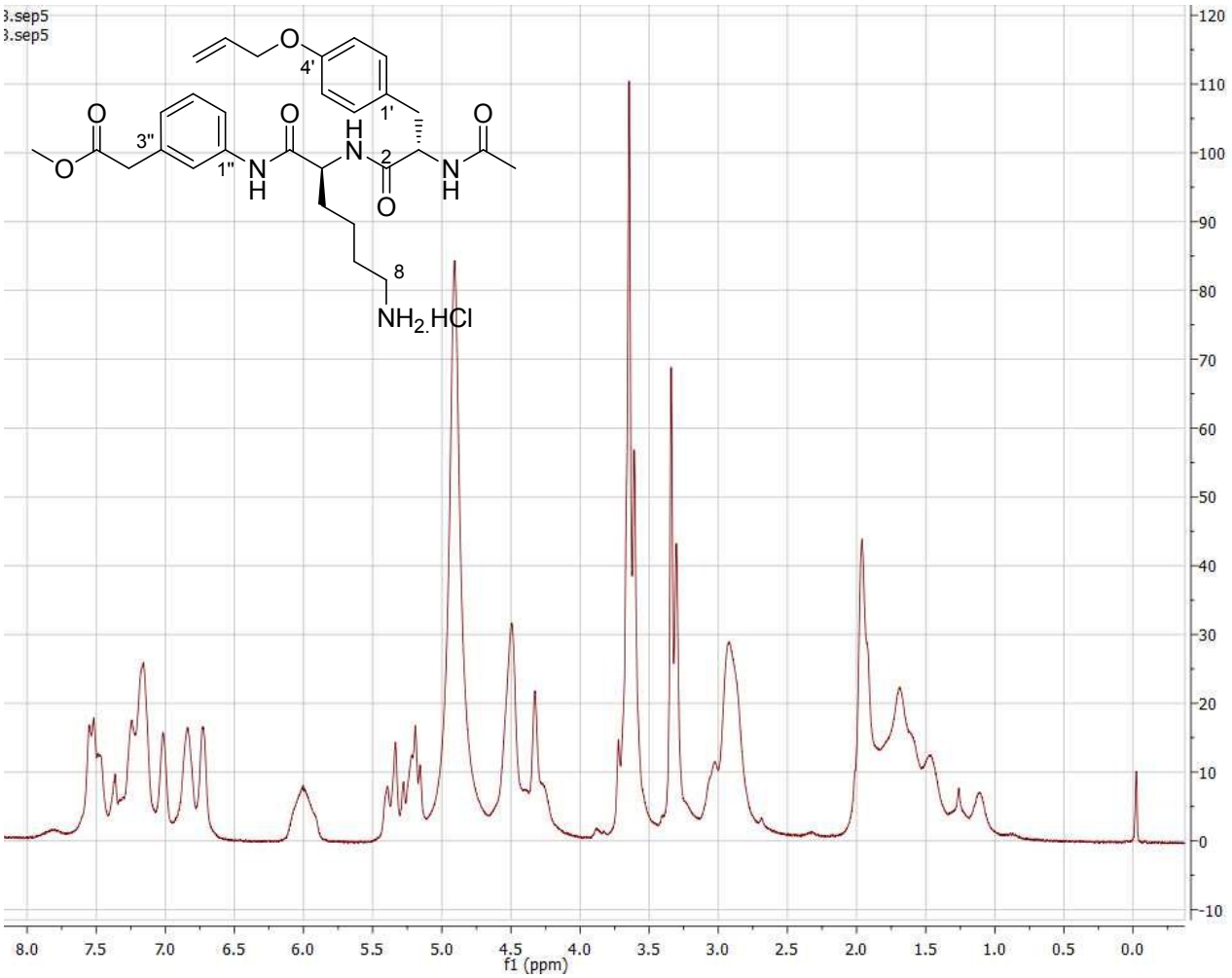


^{1}H NMR (300 MHz, CD_3OD): δ 7.70 (bs, 1H, NH); 7.62 (bs, 1H, NH); 7.17 (d, *J* = 8.4 Hz, 2H, 2′-CH and 6′-CH); 7.09 (d, *J* = 7.8, 1H, NH); 7.07 (bs, 1H, NH); 6.85 (d, *J* = 8.5 Hz, 2H, 3′-CH and 5′-CH); 6.12-5.94 (m, 1H, $OCH_2C\underline{H}=CH_2$); 5.38 (dd, *J* = 17.3, 1.6 Hz, 1H, $OCH_2CH=C\underline{H}H$ *trans*); 5.22 (dd, *J* = 10.6, 1.5 Hz, 1H, $OCH_2CH=CH\underline{H}$ *cis*); 4.55-4.45 (m, 3H, $OC\underline{H}_2CH=CH_2$ and 10-CH); 4.24 (dd, *J* = 9.4, 4.6 Hz, 1H, 7-CH); 3.64 (s, 3H, OCH_3); 3.20-3.11 (m, 4H, 4″-CH_2 and 4-CH_2); 3.03 (dd, *J* = 13.9, 6.4 Hz, 1H, 10-$CHC\underline{H}_aH_b$); 2.86 (dd, *J* = 13.7, 8.5 Hz, 1H, 10-$CHCH_a\underline{H}_b$); 2.33 (t, *J* = 7.4 Hz, 2H, 2-CH_2); 1.93 (s, 3H, 13-CH_3); 1.86-1.69 (m, 3H, 1″-$C\underline{H}_aH_b$ and C-3H_2); 1.66-1.51 (m, 3H, 1″-$CH_a\underline{H}_b$ and 3″-CH_2); 1.47-1.25 (m, 2H, 2″-CH_2).

^{13}C NMR spectrum of compound **24**

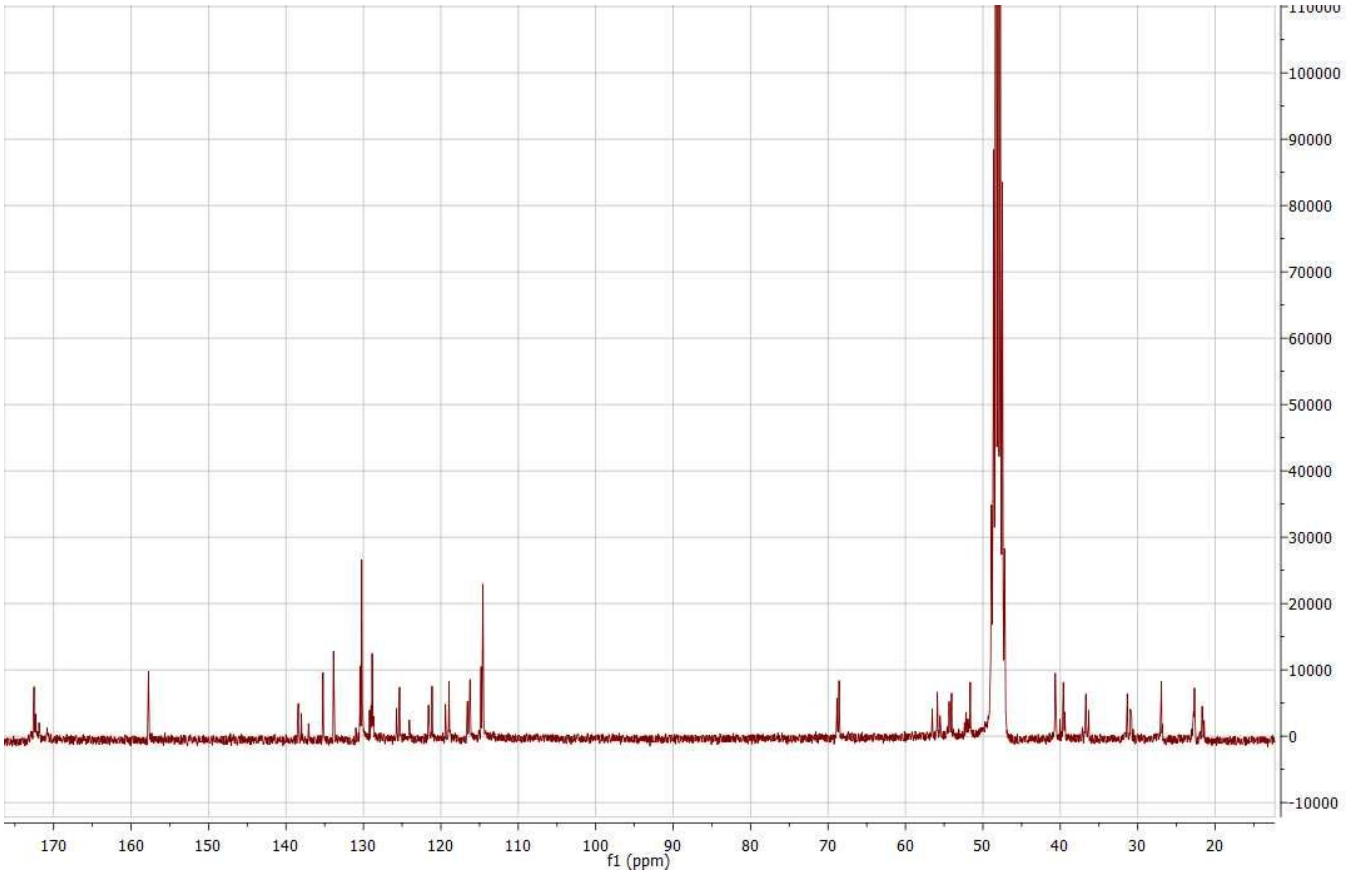


^{1}H NMR spectrum of compound **55**

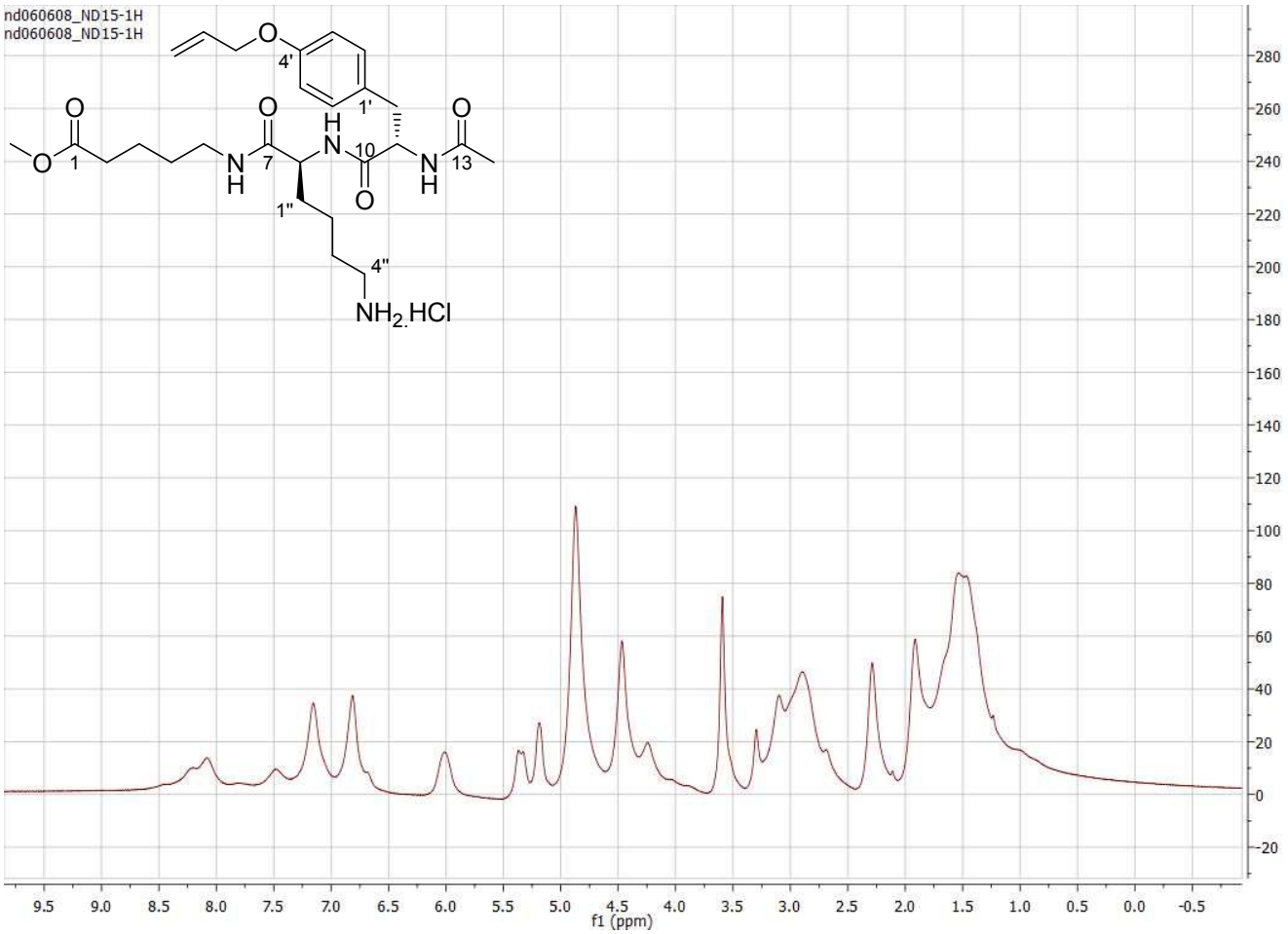


^{1}H NMR (300 MHz, CD_3OD): δ 7.59-7.50 (m, 2H, 2″-CH and 6″-CH); 7.30-7.15 (m, 2H, 2′-CH and 6′-CH); 7.07-7.01 (m, 1H, 5″-CH); 6.92-6.82 (m, 2H, 3′-CH and 5′-CH); 6.80-6.71 (m, 1H, 4″-CH); 6.19-5.86 (m, 1H, $OCH_2C\underline{H}=CH_2$); 5.39 (bd, *J* = 17.5 Hz, 1H, $OCH_2CH=C\underline{H}H$ *trans*); 5.20 (bd, *J* = 10.0 Hz, 1H, $OCH_2CH=CH\underline{H}$ *cis*); 4.61-4.46 (m, 3H, $OC\underline{H}_2CH=CH_2$ and 1-CH); 4.38-4.27 (m, 1H, 4-CH); 3.67 (s, 3H, OCH_3); 3.37 (s, 2H, 3″-CCH_2); 3.12-2.81 (m, 4H, 8-CH_2 and 1-$CHC\underline{H}_2$); 2.03-1.89 (m, 4H, 5-$C\underline{H}_aH_b$ and $COCH_3$); 1.79-1.61 (m, 3H, 5-$CH_a\underline{H}_b$ and 7-CH_2); 1.56-1.40 (m, 2H, 6-CH_2).

^{13}C NMR spectrum of compound **55**

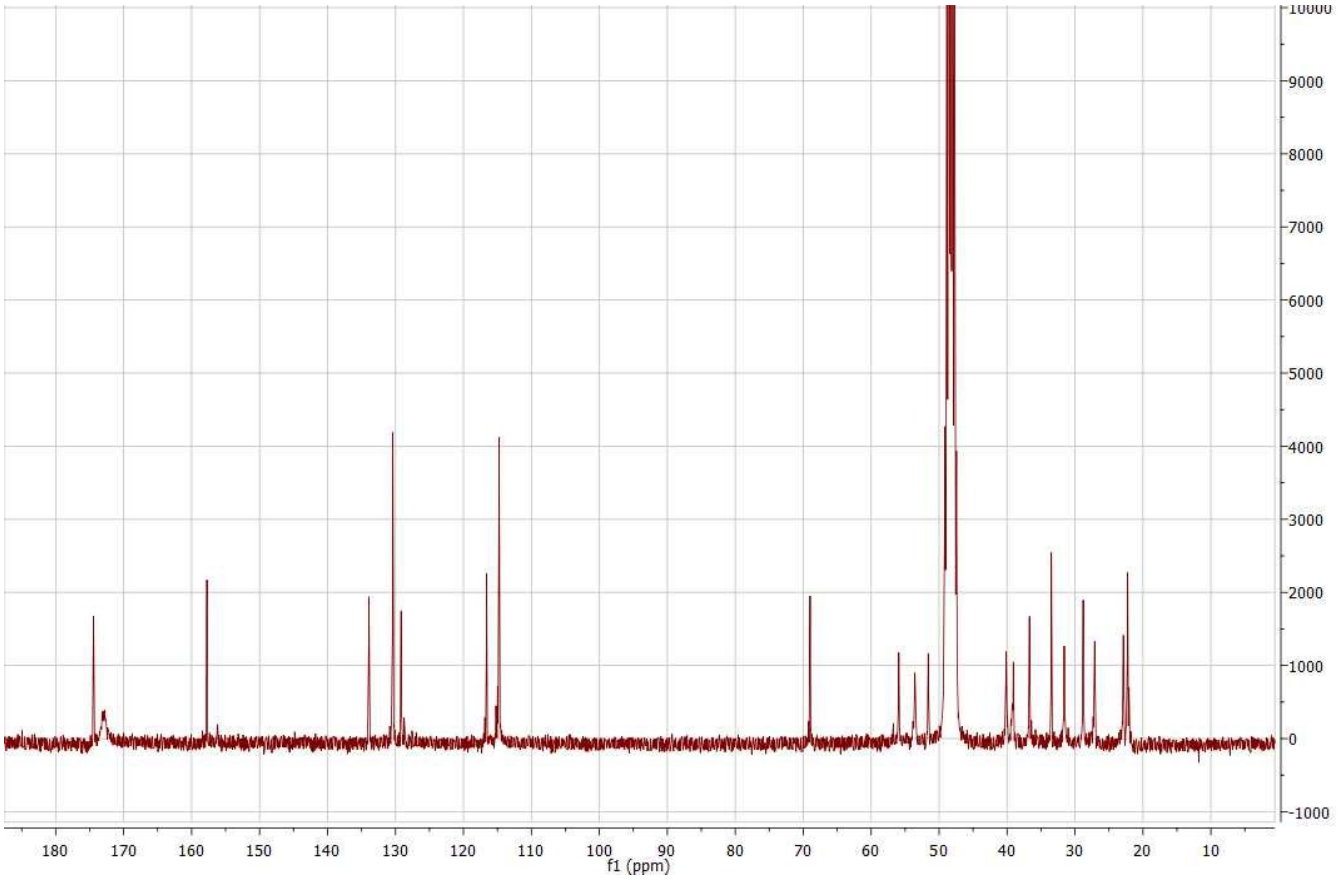


^{1}H NMR spectrum of compound **58**

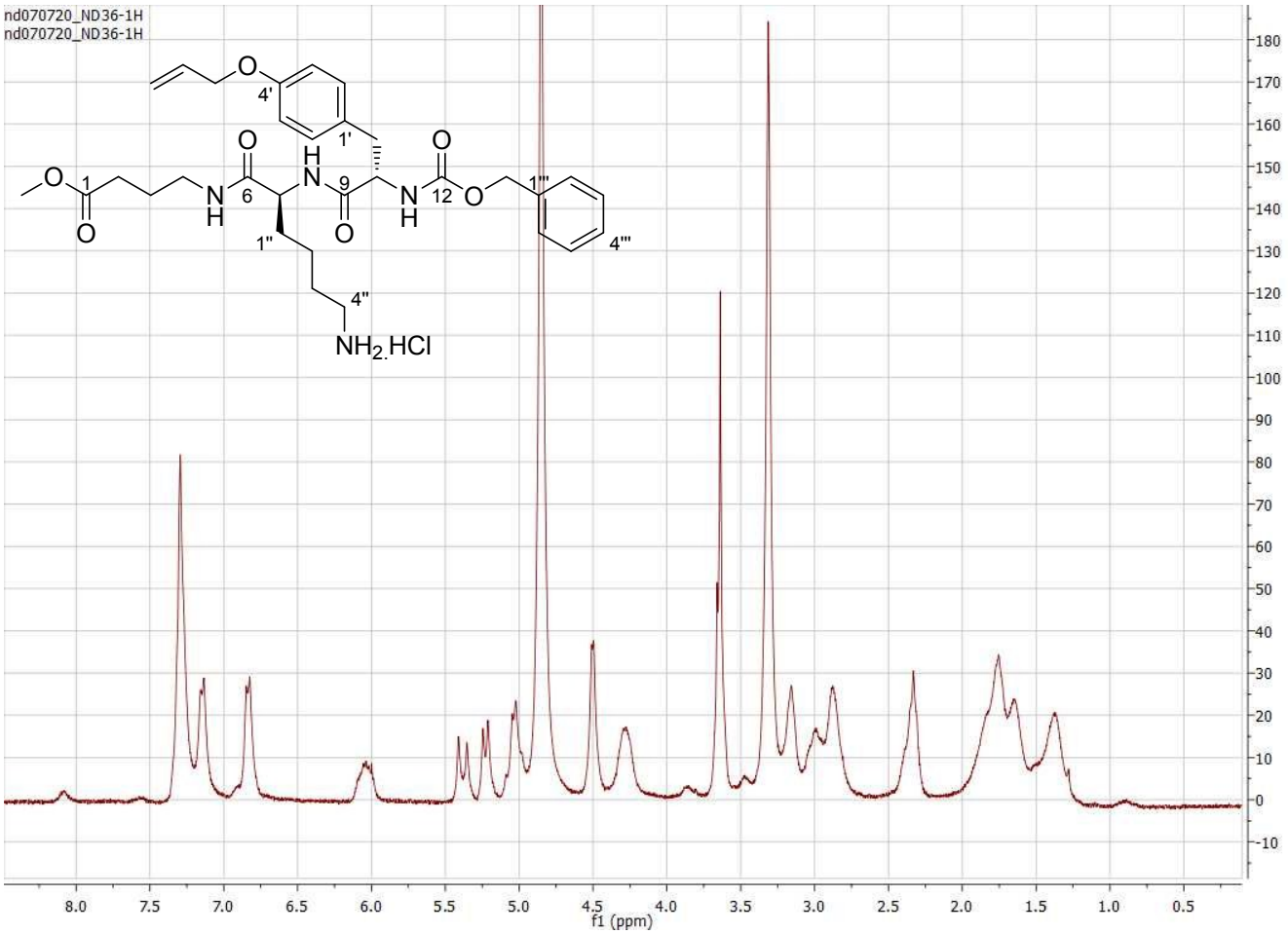


^{1}H NMR (300 MHz, CD_3OD): δ 8.22 (bs, 1H, NH); 8.10 (bs, 1H, NH); 7.50 (bs, 1H, NH); 7.16 (d, *J* = 8.0 Hz, 2H, 2′-CH and 6′-CH); 6.86 (d, *J* = 7.9 Hz, 2H, 3′-CH and 5′-CH); 6.11-5.97 (m, 1H, $OCH_2C\underline{H}=CH_2$); 5.38 (bd, *J* = 17.3 Hz, 1H, $OCH_2CH=C\underline{H}H$ *trans*); 5.23 (bd, *J* = 10.5 Hz, 1H, $OCH_2CH=CH\underline{H}$ *cis*); 4.56-4.41 (m, 3H, $OC\underline{H}_2CH=CH_2$ and 11-CH); 4.30-4.21 (m, 1H, 8-CH); 3.63 (s, 3H, OCH_3); 3.15-3.06 (m, 2H, 5-CH_2); 3.04-2.81 (m, 4H, 4″-CH_2 and 11-CHC$\underline{H}_2$); 2.33 (t, *J* = 7.1 Hz, 2H, 2-CH_2); 1.93 (s, 3H, 14-CH_3); 1.78-1.25 (m, 10H, 1″-C$\underline{H}_a\underline{H}_b$, 1″-$CH_a\underline{H}_b$, 3-$CH_2$, 4-$CH_2$, 2″-$CH_2$ and 3″-CH_2).

^{13}C NMR spectrum of compound **58**

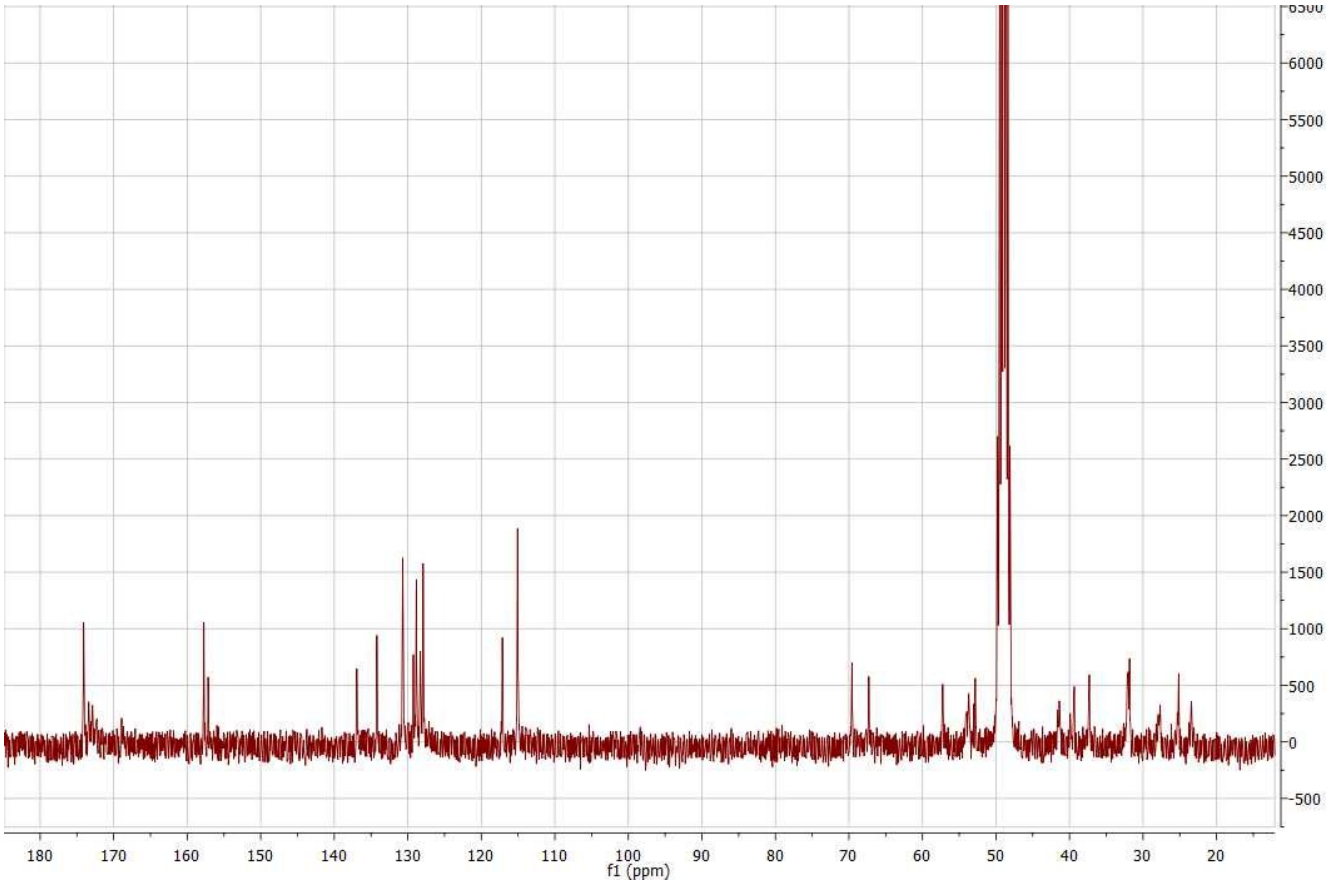


^{1}H NMR spectrum of compound **96**



^{1}H NMR (300 MHz, CD_3OD): δ 8.08 (bs, 1H, NH); 7.56 (bs, 1H, NH); 7.34-7.25 (m, 5H, 2‴-CH, 3‴-CH, 4‴-CH, 5‴-CH, 6‴-CH,); 7.15 (d, *J* = 7.0 Hz, 2H, 2′-CH and 6′-CH); 6.84 (d, *J* = 7.0 Hz, 2H, 3′-CH and 5′-CH); 6.14-5.96 (m, 1H, $OCH_2C\underline{H}=CH_2$); 5.38 (bd, *J* = 17.2 Hz, 1H, $OCH_2CH=C\underline{H}H$ *trans*); 5.23 (bd, *J* = 10.2 Hz, 1H, $OCH_2CH=CH\underline{H}$ *cis*); 5.09-4.97 (m, 2H, 12-$COOCH_2$); 4.50 (d, *J* = 4.0 Hz, 2H, $OC\underline{H}_2CH=CH_2$); 4.34-4.24 (m, 2H, 7-CH, 10-CH); 3.64 (s, 3H, OCH_3); 3.23-3.11 (m, 2H, 4-CH_2); 3.04-2.95 (m, 2H, 4″-CH_2); 2.91-2.82 (m, 2H, 10-$CHCH_2$); 2.36-2.29 (m, 2H, 2-CH_2); 1.84-1.60 (m, 6H, 1″-CH_2, 3-CH_2 and 3″-CH_2); 1.44-1.30 (m, 2H, 2″-CH_2).

^{13}C NMR spectrum of compound **96**



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