Supporting Information

Structure-Activity Relationship of Hetarylpropylguanidines Aiming at the Development of Selective Histamine Receptor Ligands[†]

Steffen Pockes,* David Wifling, Armin Buschauer, and Sigurd Elz

Supporting Information

Contents **Pages**

1. Experimental description of the synthesis and analytical data of compounds 9, 10, 18-22, 24-27, 30-39, 46-55, 62-71, 78-87, 94-109, 111-114, 116-136, 138, 139, 142 and 144

S-Methylisothiourea (9)[1]

Thiourea (25.0 g, 328.43 mmol) and methyl iodide (22.59 mL, 361.27 mmol) in acetonitrile (MeCN) (250 mL) were refluxed for 1h. After evaporation, the crude product was washed three times with diethyl ether (Et_2O) (3x100 mL) and dried under vacuum. The resulting product was obtained as an orange solid (**9** x HI, 70.45 g, 98%): R_f=0.44 (DCM/MeOH 90:10); mp 118.5 °C (HI). ^{1}H NMR (300 MHz, CD_3OD, hydrogen iodide) δ 2.62 (s, 3H). ^{13}C NMR (75 MHz, CD_3OD, hydrogen iodide) δ 171.1, 13.8. HRMS (ESI-MS): m/z [M+H$^+$] calculated for $C_2H_7N_2S^+$: 91.0324, found 91.0325; $C_2H_6N_2S$ x HI (218.06).

N,N'-Di-tert-butoxycarbonyl-S-methylisothiourea (10)[2]

To a solution of **9** (30.0 g, 137.58 mmol) and NEt_3 (19.07 mL, 137.58 mmol) in DCM (150 mL) a solution of Boc_2O (60.05 g, 275.15 mmol) in DCM (100 mL) was added dropwise at room temperature (rt). After stirring over night at rt the mixture was washed with water and brine (each 100 mL), dried with Na_2SO_4 and evaporated under vacuum. The crude product was purified by column chromatography (EtOAc/petroleum ether (PE) 1/9—1/5 v/v) to obtain a colorless solid (10, 34.98 g, 88%): R_f=0.56 (DCM); mp 127 °C. 1H NMR (300 MHz, $CDCl_3$) δ 11.61 (bs, 1H), 2.40 (s, 3H), 1.51 (s, 18H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.07, 165.69, 162.27, 79.91, 78.96, 28.03, 14.44. HRMS (ESI-MS): m/z [M+H$^+$] calculated for $C_{12}H_{23}N_2O_4S^+$: 291.1373, found 291.1377; $C_{12}H_{22}N_2O_4S$ (290.38).

N-(tert-Butoxycarbonyl)-1,4-butanediamine (18)[3]

The reaction was carried out with butane-1,4-diamine (**12**, 4.04 g, 45.87 mmol), Boc_2O (2.0 g, 9.16 mmol) and DCM. The product was obtained as a colorless oil (1.60 g, 93%): R_f=0.45

(DCM/MeOH/NH_3 80:20:0.1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.74 (bs, 1H), 3.11 (q, J = 5.9 Hz, 2H), 2.71 (t, J = 6.6 Hz, 2H), 2.23 (bs, 2H), 1.56 – 1.45 (m, 4H), 1.42 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.07, 79.11, 41.54, 40.36, 30.33, 28.43, 27.43. HRMS (ESI-MS): m/z [M+H^+] calculated for $C_9H_{21}N_2O_2^+$: 189.1598, found 189.1600; $C_9H_{20}N_2O_2$ (188.27).

N-(tert-Butoxycarbonyl)-1,6-hexanediamine (19)[3]

The reaction was carried out with hexane-1,6-diamine (**13**, 5.32 g, 45.87 mmol), Boc_2O (2.0 g, 9.16 mmol) and DCM. The product was obtained as a colorless oil (1.83 g, 92%): R_f=0.50 (DCM/MeOH/NH_3 80:20:0.1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.61 (bs, 1H), 3.07 (q, J = 6.5 Hz, 2H), 2.67 (t, J = 7.0 Hz, 2H), 2.31 (bs, 2H), 1.54 – 1.42 (m, 4H), 1.41 (s, 9H), 1.36 – 1.23 (m, 4H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.03, 79.01, 41.78, 40.45, 33.00, 30.00, 28.42, 26.55, 26.46. HRMS (ESI-MS): m/z [M+H^+] calculated for $C_{11}H_{25}N_2O_2^+$: 217.1911, found 217.1914; $C_{11}H_{24}N_2O_2$ (216.33).

N-(tert-Butoxycarbonyl)-1,8-octanediamine (20)[3]

The reaction was carried out with octane-1,8-diamine (**14**, 6.60 g, 45.87 mmol), Boc_2O (2.0 g, 9.16 mmol) and DCM. The product was obtained as a colorless oil (2.04 g, 91%): R_f=0.55 (DCM/MeOH/NH_3 80:20:0.1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.53 (bs, 1H), 3.09 (q, J = 6.5 Hz, 2H), 2.66 (t, J = 6.9 Hz, 2H), 1.43 (s, 9H), 1.41 – 1.34 (m, 4H), 1.33 – 1.23 (m, 8H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.00, 79.01, 42.22, 40.59, 33.78, 30.06, 29.40, 29.26, 28.43, 26.80, 26.74. HRMS (ESI-MS): m/z [M+H^+] calculated for $C_{13}H_{29}N_2O_2^+$: 245.2224, found 245.2229; $C_{13}H_{28}N_2O_2$ (244.38).

N-(tert-Butoxycarbonyl)-1,10-decanediamine (21)[4]

The reaction was carried out with decane-1,10-diamine (**15**, 7.89 g, 45.87 mmol), Boc_2O (2.0 g, 9.16 mmol) and DCM. The product was obtained as a colorless oil (2.18 g, 87%):

R_f=0.60 (DCM/MeOH/NH_3 80:20:0.1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.52 (bs, 1H), 3.09 (q, J = 6.7 Hz, 2H), 2.67 (t, J = 6.9 Hz, 2H), 1.48 (m, 4H), 1.43 (s, 9H), 1.27 (m, 12H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.99, 79.00, 42.23, 40.63, 33.76, 30.07, 29.53, 29.50, 29.46, 29.28, 28.44, 26.87, 26.80. HRMS (ESI-MS): m/z [M+H^+] calculated for $C_{15}H_{33}N_2O_2^+$: 273.2537, found 273.2542; $C_{15}H_{32}N_2O_2$ (272.43).

N-(tert-Butoxycarbonyl)-1,12-dodecanediamine (22)[3]

The reaction was carried out with dodecane-1,12-diamine (**16**, 9.18 g, 45.87 mmol), Boc_2O (2.0 g, 9.16 mmol) and DCM. The product was obtained as a colorless oil (2.63 g, 96%): R_f=0.66 (DCM/MeOH/NH_3 80:20:0.1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.54 (s, 1H), 3.09 (q, J = 6.5 Hz, 2H), 2.85 (t, J = 7.2 Hz, 2H), 1.65 (t, J = 7.5 Hz, 2H), 1.58 – 1.45 (m, 2H), 1.44 (s, 9H), 1.35 – 1.20 (m, 16H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.97, 82.56, 42.81, 39.78, 33.55, 30.06, 29.53, 29.51, 29.42, 29.29, 29.10, 29.06, 28.44, 26.82, 26.60. HRMS (ESI-MS): m/z [M+H^+] calculated for $C_{17}H_{37}N_2O_2^+$: 301.2850, found 301.2853; $C_{17}H_{36}N_2O_2$ (300.49).

1-(6-Aminohexyl)-2,3-(di-tert-butoxycarbonyl)guanidine (24)[5]

The synthesis was accomplished with **13** (1.80 g, 15.51 mmol) and **10** (1.50 g, 5.17 mmol) according to the general procedure. Column chromatography gave **24** as a yellow oil (1.70 g, 92%): R_f=0.20 (DCM/MeOH/NH_3 95:5:0.1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 11.47 (bs, 1H), 8.29 (t, J = 5.2 Hz, 1H), 3.38 (q, J = 7.3 Hz, 2H), 2.67 (t, J = 6.9 Hz, 2H), 1.97 (bs, 2H), 1.64 – 1.51 (m, 4H), 1.48 (s, 9H), 1.47 (s, 9H), 1.41 – 1.28 (m, 4H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.60, 156.13, 153.32, 83.08, 79.29, 41.92, 40.84, 33.22, 28.91, 28.29, 28.07, 26.67, 26.48. HRMS (ESI-MS): m/z [M+H^+] calculated for $C_{17}H_{35}N_4O_4^+$: 359.2653, found 359.2659; $C_{17}H_{34}N_4O_4$ (358.48).

1-(8-Aminooctyl)-2,3-(di-tert-butoxycarbonyl)guanidine (25)[5]

The synthesis was accomplished with **14** (2.24 g, 15.51 mmol) and **10** (1.50 g, 5.17 mmol) according to the general procedure. Column chromatography gave **25** as a yellow oil (1.93 g, 97%): R_f=0.22 (DCM/MeOH/NH_3 95:5:0.1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 11.46 (bs, 1H), 8.28 (t, J = 5.2 Hz, 1H), 3.36 (q, J = 7.4 Hz, 2H), 2.65 (t, J = 7.0 Hz, 2H), 2.07 (bs, 2H), 1.61 – 1.48 (m, 4H), 1.47 (s, 9H), 1.47 (s, 9H), 1.33 – 1.20 (m, 8H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.59, 156.11, 153.31, 83.05, 79.27, 41.98, 40.95, 33.32, 29.25, 29.19, 28.92, 28.29, 26.77, 26.74. HRMS (ESI-MS): m/z [M+H$^+$] calculated for $C_{19}H_{39}N_4O_4^+$: 387.2966, found 387.2973; $C_{19}H_{38}N_4O_4$ (386.54).

1-(10-Aminodecyl)-2,3-(di-tert-butoxycarbonyl)guanidine (26)

The synthesis was accomplished with **15** (2.67 g, 15.51 mmol) and **10** (1.50 g, 5.17 mmol) according to the general procedure. Column chromatography gave **26** as a yellow oil (1.98 g, 92%): R_f=0.24 (DCM/MeOH/NH_3 95:5:0.1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 11.48 (bs, 1H), 8.28 (t, J = 5.3 Hz, 1H), 3.37 (q, J = 7.3 Hz, 2H), 2.66 (t, J = 7.2 Hz, 2H), 1.72 (bs, 2H), 1.59 – 1.50 (m, 4H), 1.48 (s, 9H), 1.47 (s, 9H), 1.33 – 1.21 (m, 12H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.64, 156.10, 153.33, 83.01, 79.24, 42.17, 40.99, 33.69, 29.52, 29.44, 29.40, 29.24, 28.95, 28.31, 28.07, 26.86, 26.84. HRMS (ESI-MS): m/z [M+H$^+$] calculated for $C_{21}H_{43}N_4O_4^+$: 415.3279, found 415.3290; $C_{21}H_{42}N_4O_4$ (414.59).

1-(12-Aminododecyl)-2,3-(di-tert-butoxycarbonyl)guanidine (27)

The synthesis was accomplished with **16** (3.10 g, 15.51 mmol) and **10** (1.50 g, 5.17 mmol) according to the general procedure. Column chromatography gave **27** as a yellow oil (2.22 g, 92%): R_f=0.26 (DCM/MeOH/NH_3 95:5:0.1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 11.47 (bs, 1H), 8.28 (t, J = 5.2 Hz, 1H), 3.37 (q, J = 7.2 Hz, 2H), 2.66 (t, J = 7.1 Hz, 2H), 2.03 (s, 2H), 1.61 – 1.49 (m, 4H), 1.48 (s, 9H), 1.47 (s, 9H), 1.31 – 1.21 (m, 16H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.61,

156.10, 153.31, 83.02, 79.25, 42.04, 41.00, 33.43, 29.63, 29.60, 29.55, 29.45, 29.39, 29.25, 28.95, 28.30 (+, C(***C***H_3)$_{\boldsymbol{3}}$), 28.06 (+, C(***C***H_3)$_{\boldsymbol{3}}$), 26.93, 26.85. HRMS (ESI-MS): m/z [M+H^+] calculated for $C_{23}H_{47}N_4O_4^+$: 443.3592, found 443.3604; $C_{23}H_{47}N_4O_4$ (442.65).

tert-Butyl [4-(3-benzoylthioureido)butyl]carbamate (30)[6]

The product was developed using **18** (1.60 g, 8.50 mmol) and **28** (1.14 mL, 8.50 mmol) in DCM (30 mL) and the desired compound was isolated as a yellow oil (2.96 g, 99%): R_f=0.18 (DCM); ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.76 (bs, 1H), 9.16 (bs, 1H), 7.86 – 7.74 (m, 2H), 7.64 – 7.54 (m, 1H), 7.51 – 7.42 (m, 2H), 4.69 (bs, 1H), 3.69 (q, J = 7.1 Hz, 2H), 3.15 (q, J = 6.6 Hz, 2H), 1.71 (p, J = 7.2 Hz, 2H), 1.57 (p, J = 7.1 Hz, 2H), 1.40 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 179.96, 167.06, 156.00, 133.54, 131.77, 129.10, 127.51, 79.20, 45.34, 40.07, 28.41, 27.47, 25.55. HRMS (ESI-MS): m/z [M+H^+] calculated for $C_{17}H_{26}N_3O_3S^+$: 352.1689, found 352.1691; $C_{17}H_{25}N_3O_3S$ (351.47).

tert-Butyl [6-(3-benzoylthioureido)hexyl]carbamate (31)

The product was developed using **19** (1.83 g, 8.46 mmol) and **28** (1.14 mL, 8.46 mmol) in DCM (30 mL) and the desired compound was isolated as a yellow oil (2.94 g, 92%): R_f=0.20 (DCM); ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.74 (bs, 1H), 9.18 (bs, 1H), 7.88 – 7.72 (m, 2H), 7.65 – 7.32 (m, 3H), 4.70 (bs, 1H), 3.38 (q, J = 6.7 Hz, 2H), 3.12 – 2.98 (q, J = 6.4, 2H), 1.74 – 1.50 (m, 2H), 1.49 – 1.17 (m, 15H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 179.80, 167.60, 156.19, 134.71, 131.26, 128.44, 126.98, 79.01, 45.71, 40.09, 30.00, 29.45, 28.41, 26.59, 26.19. HRMS (ESI-MS): m/z [M+H^+] calculated for $C_{19}H_{30}N_3O_3S^+$: 380.2002, found 380.2006; $C_{19}H_{29}N_3O_3S$ (379.52).

tert-Butyl [8-(3-benzoylthioureido)octyl]carbamate (32)

The product was developed using **20** (2.04 g, 8.35 mmol) and **28** (1.12 mL, 8.35 mmol) in DCM (30 mL) and the desired compound was isolated as a yellow oil (3.36 g, 99%): R_f=0.22 (DCM); ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.73 (bs, 1H), 9.14 (bs, 1H), 7.89 – 7.76 (m, 2H), 7.67 – 7.54 (m, 1H), 7.53 – 7.40 (m, 2H), 4.58 (bs, 1H), 3.65 (q, J = 7.3 Hz, 2H), 3.07 (q, J = 6.0 Hz, 2H), 1.67 (p, J = 7.2 Hz, 2H), 1.52 – 1.41 (m, 2H), 1.40 (s, 9H), 1.38 – 1.16 (m, 8H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 179.71, 167.02, 155.99, 133.49, 131.83, 129.08, 127.50, 78.97, 45.85, 40.56, 30.01, 29.09, 28.42, 28.14, 28.08, 26.83, 26.68. HRMS (ESI-MS): m/z [M+H$^+$] calculated for $C_{21}H_{34}N_3O_3S^+$: 408.2315, found 408.2321; $C_{21}H_{33}N_3O_3S$ (407.57).

tert-Butyl [10-(3-benzoylthioureido)decyl]carbamate (33)

The product was developed using **21** (2.18 g, 8.00 mmol) and **28** (1.08 mL, 8.00 mmol) in DCM (30 mL) and the desired compound was isolated as a yellow solid (3.22 g, 92%): R_f=0.25 (DCM); mp 105.8 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.73 (bs, 1H), 9.08 (bs, 1H), 7.88 – 7.77 (m, 2H), 7.66 – 7.56 (m, 1H), 7.55 – 7.44 (m, 2H), 4.54 (bs, 1H), 3.67 (q, J = 7.3 Hz, 2H), 3.08 (q, J = 6.5 Hz, 2H), 1.69 (p, J = 7.2 Hz, 2H), 1.52 – 1.42 (m, 2H), 1.41 (s, 9H), 1.38 – 1.19 (m, 12H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 179.68, 166.96, 155.98, 133.52, 131.84, 129.12, 127.46, 78.98, 45.93, 40.62, 30.05, 29.43, 29.36, 29.24, 29.17, 28.43, 28.18, 26.91, 26.78. HRMS (ESI-MS): m/z [M+H$^+$] calculated for $C_{23}H_{38}N_3O_3S^+$: 436.2628, found 436.2630; $C_{23}H_{37}N_3O_3S$ (435.62).

tert-Butyl [12-(3-benzoylthioureido)dodecyl]carbamate (34)

The product was developed using **22** (2.63 g, 8.75 mmol) and **28** (1.18 mL, 8.75 mmol) in DCM (30 mL) and the desired compound was isolated as a yellow oil (3.75 g, 92%): R_f=0.27 (DCM); ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.73 (bs, 1H), 9.18 (bs, 1H), 7.87 – 7.74 (m, 2H), 7.63 – 7.52 (m, 1H), 7.51 – 7.40 (m, 2H), 4.58 (bs, 1H), 3.64 (q, J = 7.1 Hz, 2H), 3.05 (q, J = 6.4 Hz,

2H), 1.67 (p, J = 7.2 Hz, 2H), 1.50 – 1.40 (m, 2H), 1.39 (s, 9H), 1.37 – 1.10 (m, 16H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 179.69, 167.05, 155.99, 133.45, 131.85, 129.05, 127.52, 78.93, 45.90, 40.62, 30.05, 29.52, 29.50, 29.48, 29.42, 29.28, 29.19, 28.42, 28.17, 26.92, 26.79. HRMS (ESI-MS): m/z [M+H$^+$] calculated for $C_{25}H_{42}N_3O_3S^+$: 464.2941, found 464.2947; $C_{25}H_{41}N_3O_3S$ (463.68).

1-(N'-Benzoylthioureidobutyl)-2,3-(di-tert-butoxycarbonyl)guanidine (35)

The product was developed using **23** (1.15 g, 3.48 mmol) and **28** (0.47 mL, 3.48 mmol) in DCM (30 mL) and the desired compound was isolated as a yellow solid (1.46 g, 85%): R_f=0.18 (DCM); mp 137.6 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 11.50 (bs, 1H), 10.75 (t, J = 5.5 Hz, 1H), 8.99 (bs, 1H), 8.36 (t, J = 5.6 Hz, 1H), 7.86 – 7.79 (m, 2H), 7.65 – 7.59 (m, 1H), 7.54 – 7.47 (m, 2H), 3.74 (q, J = 6.9 Hz, 2H), 3.48 (q, J = 6.9 Hz, 2H), 1.83 – 1.63 (m, 4H), 1.49 (s, 9H), 1.48 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 179.96, 166.86, 163.53, 156.18, 153.31, 133.59, 131.78, 129.17, 127.43, 83.19, 79.38, 45.39, 40.40, 28.30, 28.09, 26.61, 25.66. HRMS (ESI-MS): m/z [M+H$^+$] calculated for $C_{23}H_{36}N_5O_5S^+$: 494.2432, found 494.2439; $C_{23}H_{35}N_5O_5S$ (493.62).

1-(N'-Benzoylthioureidohexyl)-2,3-(di-tert-butoxycarbonyl)guanidine (36)

The product was developed using **24** (2.00 g, 5.58 mmol) and **28** (0.75 mL, 5.58 mmol) in DCM (30 mL) and the desired compound was isolated as a colorless foamlike solid (2.59 g, 89%): R_f=0.21 (DCM); ^{1}H NMR (300 MHz, $CDCl_3$) δ 11.49 (bs, 1H), 10.73 (t, J = 5.7 Hz, 1H), 9.01 (bs, 1H), 8.32 (t, J = 5.9 Hz, 1H), 7.89 – 7.76 (m, 2H), 7.68 – 7.56 (m, 1H), 7.54 – 7.43 (m, 2H), 3.68 (q, J = 7.3 Hz, 2H), 3.40 (q, J = 7.2 Hz, 2H), 1.81 – 1.52 (m, 4H), 1.48 (s, 9H), 1.47 (s, 9H), 1.46 – 1.37 (m, 4H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 179.74, 166.88, 163.57, 156.11, 153.32, 133.55, 131.81, 129.14, 127.44, 83.07, 79.29, 45.77, 40.84, 28.88, 28.31, 28.16, 28.09, 26.65, 26.54. HRMS (ESI-MS): m/z [M+H$^+$] calculated for $C_{25}H_{40}N_5O_5S^+$: 522.2745, found 522.2753; $C_{25}H_{39}N_5O_5S$ (521.68).

1-(N'-Benzoylthioureidooctyl)-2,3-(di-tert-butoxycarbonyl)guanidine (37)

The product was developed using **25** (1.89 g, 4.89 mmol) and **28** (0.66 mL, 4.89 mmol) in DCM (30 mL) and the desired compound was isolated as a yellow solid (2.22 g, 83%): R_f=0.23 (DCM); mp 143.4 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 11.49 (bs, 1H), 10.72 (t, J = 5.1 Hz, 1H), 8.99 (bs, 1H), 8.29 (t, J = 5.2 Hz, 1H), 7.90 – 7.76 (m, 2H), 7.70 – 7.56 (m, 1H), 7.55 – 7.46 (m, 2H), 3.68 (q, J = 7.2 Hz, 2H), 3.40 (q, J = 7.3 Hz, 2H), 1.70 (p, J = 6.7 Hz, 2H), 1.54 (p, J = 6.8 Hz, 1H), 1.48 (s, 9H), 1.47 (s, 9H), 1.41 – 1.28 (m, 8H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 179.66, 166.86, 163.61, 156.09, 153.32, 133.54, 131.82, 129.14, 127.43, 83.03, 79.26, 45.91, 40.97, 29.13, 29.07, 28.94, 28.32, 28.17, 28.09, 26.87, 26.78. HRMS (ESI-MS): m/z [M+H$^+$] calculated for $C_{27}H_{44}N_5O_5S^+$: 550.3058, found 550.3063; $C_{27}H_{43}N_5O_5S$ (549.73).

1-(N'-Benzoylthioureidodecyl)-2,3-(di-tert-butoxycarbonyl)guanidine (38)

The product was developed using **26** (1.94 g, 4.68 mmol) and **28** (0.63 mL, 4.68 mmol) in DCM (30 mL) and the desired compound was isolated as a yellow oil (2.31 g, 85%): R_f=0.26 (DCM); ^{1}H NMR (300 MHz, $CDCl_3$) δ 11.50 (bs, 1H), 10.72 (bs, 1H), 8.98 (bs, 1H), 8.30 (bs, 1H), 7.89 – 7.77 (m, 2H), 7.67 – 7.57 (m, 1H), 7.55 – 7.48 (m, 2H), 3.69 (q, J = 7.1 Hz, 2H), 3.40 (q, J = 7.4 Hz, 2H), 1.70 (p, J = 7.4 Hz, 2H), 1.60 – 1.51 (m, 2H), 1.49 (s, 9H), 1.48 (s, 9H), 1.35 – 1.25 (m, 12H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 179.64, 166.84, 163.61, 156.09, 153.33, 133.55, 131.83, 129.16, 127.41, 83.02, 79.27, 45.98, 41.03, 29.39, 29.37, 29.24, 29.20, 28.97, 28.32, 28.21, 28.09, 26.95, 26.86. HRMS (ESI-MS): m/z [M+H$^+$] calculated for $C_{29}H_{48}N_5O_5S^+$: 578.3371, found 578.3388; $C_{29}H_{47}N_5O_5S$ (577.79).

1-(N'-Benzoylthioureidododecyl)-2,3-(di-tert-butoxycarbonyl)guanidine (39)

The product was developed using **27** (2.19 g, 4.95 mmol) and **28** (0.66 mL, 4.95 mmol) in DCM (30 mL) and the desired compound was isolated as a yellow oil (2.54 g, 85%): R_f=0.28 (DCM); ^{1}H NMR (300 MHz, $CDCl_3$) δ 11.50 (bs, 1H), 10.72 (bs, 1H), 8.98 (bs, 1H), 8.29 (t, J =

5.2 Hz, 1H), 7.90 – 7.76 (m, 2H), 7.68 – 7.57 (m, 1H), 7.53 – 7.45 (m, 2H), 3.69 (q, J = 7.3 Hz, 2H), 3.40 (q, J = 7.4 Hz, 2H), 1.71 (p, J = 7.3 Hz, 2H), 1.60 – 1.51 (m, 2H), 1.49 (s, 9H), 1.48 (s, 9H), 1.40 – 1.23 (m, 16H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 179.63, 166.84, 163.67, 156.10, 153.34, 133.56, 131.84, 129.17, 127.41, 83.00, 79.23, 46.01, 41.02, 29.53, 29.51, 29.47, 29.45, 29.28, 29.24, 28.98, 28.32, 28.22, 28.09, 26.97, 26.87. HRMS (ESI-MS): m/z [M+H$^+$] calculated for $C_{31}H_{52}N_5O_5S^+$: 606.3684, found 606.3695; $C_{31}H_{51}N_5O_5S$ (605.84).

tert-Butyl (4-thioureidobutyl)carbamate (46)[6]

46 was made out of **30** (2.90 g, 8.25 mmol) and K_2CO_3 (2.39 g, 17.33 mmol) in 50 ml MeOH/H_2O (7/3 v/v) yielding a yellow oil (1.90 g, 93%): R_f=0.32 (DCM/MeOH 95:5); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40 (bs, 1H,), 6.37 (bs, 1H), 4.94 (bs, 1H), 3.52 + 3.20 (2 bs, 1.1H + 0.9H (thione-thiol tautomerism)), 3.10 (q, J = 6.2 Hz, 2H), 1.75 – 1.43 (m, 4H), 1.39 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 183.32, 156.75, 79.68, 44.90, 40.22, 28.45, 27.71, 26.03. HRMS (ESI-MS): m/z [M+H$^+$] calculated for $C_{10}H_{22}N_3O_2S^+$: 248.1427, found 248.1429; $C_{10}H_{21}N_3O_2S$ (247.36).

tert-Butyl (6-thioureidohexyl)carbamate (47)[7]

47 was made out of **31** (2.90 g, 7.64 mmol) and K_2CO_3 (2.22 g, 16.05 mmol) in 50 ml MeOH/H_2O (7/3 v/v) yielding a yellow solid (1.85 g, 88%): R_f=0.35 (DCM/MeOH 95:5); mp 99.8 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.28 (bs, 1H), 6.34 (bs, 1H), 4.81 (bs, 1H), 3.49 + 3.17 (2 bs, 1.3H + 0.7H (thione-thiol tautomerism)), 3.05 (q, J = 6.6 Hz, 2H), 1.56 (p, J = 7.2 Hz, 2H), 1.50 – 1.42 (m, 2H), 1.40 (s, 9H), 1.35 – 1.24 (m, 4H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 183.35, 156.64, 79.45, 44.85, 40.16, 29.80, 28.45, 26.34, 26.12, 25.91. HRMS (ESI-MS): m/z [M+H$^+$] calculated for $C_{12}H_{26}N_3O_2S^+$: 276.1740, found 276.1741; $C_{12}H_{25}N_3O_2S$ (275.41).

tert-Butyl (8-thioureidooctyl)carbamate (48)

48 was made out of **32** (3.30 g, 8.10 mmol) and K_2CO_3 (2.35 g, 17.00 mmol) in 50 ml MeOH/H_2O (7/3 v/v) yielding a colorless solid (2.30 g, 94%): R_f=0.38 (DCM/MeOH 95:5); mp 96.3 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.29 (bs, 1H), 6.43 (bs, 1H), 4.86 (bs, 1H), 3.39 + 3.06 (2 bs, 1.3H + 0.7H (thione-thiol tautomerism)), 2.96 (q, J = 6.6 Hz, 2H), 1.51 – 1.40 (m, 2H), 1.40 – 1.34 (m, 2H), 1.32 (s, 9H), 1.25 – 1.14 (m, 8H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 183.07, 156.31, 79.19, 45.23, 40.49, 29.82, 29.76, 28.98, 28.94, 28.40, 26.66, 26.50. HRMS (ESI-MS): m/z [M+H$^+$] calculated for $C_{14}H_{30}N_3O_2S^+$: 304.2053, found 304.2055; $C_{14}H_{29}N_3O_2S$ (303.47).

tert-Butyl (10-thioureidodecyl)carbamate (49)

49 was made out of **33** (3.15 g, 7.23 mmol) and K_2CO_3 (2.10 g, 15.19 mmol) in 50 ml MeOH/H_2O (7/3 v/v) yielding a colorless solid (2.20 g, 92%): R_f=0.41 (DCM/MeOH 95:5); mp 98.2 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.25 (bs, 1H), 6.63 (bs, 1H), 4.69 (bs, 1H), 3.56 + 3.12 (2 bs, 1.5H + 0.5H (thione-thiol tautomerism)), 3.03 (q, J = 6.6 Hz, 2H), 1.64 – 1.45 (m, 2H), 1.46 – 1.40 (m, 2H), 1.39 (s, 9H), 1.31 – 1.13 (m, 12H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 183.46, 156.22, 79.18, 45.35, 40.60, 29.93, 29.39, 29.27, 29.19, 29.08, 28.43, 26.96, 26.77, 26.66. HRMS (ESI-MS): m/z [M+H$^+$] calculated for $C_{16}H_{34}N_3O_2S^+$: 332.2366, found 332.2366; $C_{16}H_{33}N_3O_2S$ (331.52).

tert-Butyl (12-thioureidododecyl)carbamate (50)

50 was made out of **34** (3.70 g, 7.98 mmol) and K_2CO_3 (2.32 g, 16.76 mmol) in 50 ml MeOH/H_2O (7/3 v/v) yielding a colorless solid (2.70 g, 94%): R_f=0.45 (DCM/MeOH 95:5); mp 121.2 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.75 (bs, 1H), 5.96 (bs, 1H), 4.56 (bs, 1H), 3.53 + 3.20 (2 bs, 1.0H + 1.0H (thione-thiol tautomerism)), 3.08 (q, J = 6.7 Hz, 2H), 1.58 (p, J = 7.5, 7.0 Hz, 2H), 1.52 – 1.44 (m, 2H), 1.43 (s, 9H), 1.36 – 1.20 (m, 16H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 183.34, 156.79, 79.17, 45.06, 40.63, 29.98, 29.49, 29.44, 29.41, 29.29, 29.15, 29.09, 28.45,

26.76, 26.72, 26.64. HRMS (ESI-MS): m/z [M+H$^+$] calculated for $C_{18}H_{38}N_3O_2S^+$: 360.2679, found 360.2682; $C_{18}H_{37}N_3O_2S$ (359.57).

1,2-(Di-tert-butoxycarbonyl)-3-(thioureidobutyl)guanidine (51)

51 was made out of **35** (1.46 g, 2.96 mmol) and K_2CO_3 (859 mg, 6.22 mmol) in 50 ml MeOH/H_2O (7/3 v/v) yielding a colorless foamlike solid (1.10 g, 95%): R_f=0.41 (DCM/MeOH 95:5); ^{1}H NMR (300 MHz, $CDCl_3$) δ 11.45 (bs, 1H), 8.58 (bs, 1H), 8.24 (bs, 1H), 6.17 (bs, 2H), 3.68 (bs, 2H), 3.39 (q, J = 6.6 Hz, 2H), 1.70 – 1.60 (m, 4H), 1.48 (s, 9H), 1.46 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 183.02, 162.70, 157.13, 153.15, 83.73, 80.66, 46.17, 39.97, 28.56, 28.28, 28.05, 23.12. HRMS (ESI-MS): m/z [M+H$^+$] calculated for $C_{16}H_{32}N_5O_4S^+$: 390.2170, found 390.2176; $C_{16}H_{31}N_5O_4S$ (389.52).

1,2-(Di-tert-butoxycarbonyl)-3-(thioureidohexyl)guanidine (52)

52 was made out of **36** (2.59 g, 4.96 mmol) and K_2CO_3 (1.44 g, 10.42 mmol) in 50 ml MeOH/H_2O (7/3 v/v) yielding a colorless foamlike solid (930 mg, 45%): R_f=0.44 (DCM/MeOH 95:5); ^{1}H NMR (300 MHz, $CDCl_3$) δ 11.34 (bs, 1H), 8.34 (bs, 1H), 7.45 (bs, 1H), 6.31 (bs, 2H), 3.47 + 3.13 (2 bs, 1.5H + 0.5H (thione-thiol tautomerism)), 3.28 (q, J = 7.7 Hz, 2H), 1.57 – 1.48 (m, 4H), 1.44 (s, 9H), 1.42 (s, 9H), 1.36 – 1.27 (m, 4H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 183.19, 163.13, 156.25, 153.17, 83.33, 79.67, 45.15, 40.68, 28.75, 28.65, 28.24, 28.03, 26.36, 26.17. HRMS (ESI-MS): m/z [M+H$^+$] calculated for $C_{18}H_{36}N_5O_4S^+$: 418.2483, found 418.2485; $C_{18}H_{35}N_5O_4S$ (417.57).

1,2-(Di-tert-butoxycarbonyl)-3-(thioureidooctyl)guanidine (53)

53 was made out of **37** (2.22 g, 4.04 mmol) and K_2CO_3 (1.17 g, 8.48 mmol) in 50 ml MeOH/H_2O (7/3 v/v) yielding a colorless foamlike solid (1.70 g, 95%): R_f=0.47 (DCM/MeOH 95:5); ^{1}H NMR (300 MHz, $CDCl_3$) δ 11.46 (bs, 1H), 8.33 (bs, 1H), 6.67 (bs, 1H), 6.07 (bs, 2H),

3.53 + 3.13 (2 bs, 1.1H + 0.9H (thione-thiol tautomerism)), 3.35 (q, J = 6.6 Hz, 2H), 1.61 – 1.51 (m, 4H), 1.48 (s, 9H), 1.48 (s, 9H), 1.36 – 1.29 (m, 8H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 184.89, 163.43, 156.24, 153.28, 83.25, 79.56, 44.45, 40.87, 28.94, 28.82, 28.72, 28.59, 28.30, 28.08, 26.66, 26.50, 26.46. HRMS (ESI-MS): m/z [M+H$^+$] calculated for $C_{20}H_{40}N_5O_4S^+$: 446.2796, found 446.2804; $C_{20}H_{39}N_5O_4S$ (445.62).

1,2-(Di-tert-butoxycarbonyl)-3-(thioureidodecyl)guanidine (54)

54 was made out of **38** (2.31 g, 4.00 mmol) and K_2CO_3 (1.16 g, 8.40 mmol) in 50 ml MeOH/H_2O (7/3 v/v) yielding a colorless foamlike solid (1.90 g, 100%): R_f=0.50 (DCM/MeOH 95:5); ^{1}H NMR (300 MHz, $CDCl_3$) δ 11.48 (bs, 1H), 8.32 (bs, 1H), 6.82 (bs, J = 53.3 Hz, 1H), 5.95 (bs, 2H), 3.53 + 3.11 (2 bs, 0.9H + 1.1H (thione-thiol tautomerism)), 3.37 (q, J = 7.4 Hz, 2H), 1.64 – 1.51 (m, 4H), 1.49 (s, 18H), 1.34 – 1.22 (m, 12H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 183.65, 163.50, 156.20, 153.30, 83.18, 79.47, 44.32, 40.91, 29.18, 29.13, 28.93, 28.82, 28.76, 28.53, 28.31, 28.08, 26.70, 26.68. HRMS (ESI-MS): m/z [M+H$^+$] calculated for $C_{22}H_{44}N_5O_4S^+$: 474.3109, found 474.3113; $C_{22}H_{43}N_5O_4S$ (473.68).

1,2-(Di-tert-butoxycarbonyl)-3-(thioureidododecyl)guanidine (55)

55 was made out of **39** (2.54 g, 4.20 mmol) and K_2CO_3 (1.22 g, 8.82 mmol) in 50 ml MeOH/H_2O (7/3 v/v) yielding a colorless foamlike solid (1.92 g, 91%): R_f=0.53 (DCM/MeOH 95:5); ^{1}H NMR (300 MHz, $CDCl_3$) δ 11.46 (bs, 1H), 8.32 (t, J = 5.1 Hz, 1H), 6.71 (bs, J = 150.7 Hz, 1H), 6.06 (bs, 2H), 3.53 + 3.11 (2 bs, 0.8H + 1.2H (thione-thiol tautomerism)), 3.35 (q, J = 7.3 Hz, 2H), 1.62 – 1.50 (m, 4H), 1.47 (s, 18H), 1.33 – 1.22 (m, 16H). ^{13}C NMR (75 MHz, $CDCl_3$ δ 183.68, 163.48, 156.18, 153.28, 83.16, 79.46, 44.50, 41.00, 29.53, 29.48, 29.37, 29.15, 29.08, 29.06, 28.93, 28.82, 28.30, 28.07, 26.82, 26.76. HRMS (ESI-MS): m/z [M+H$^+$] calculated for $C_{24}H_{48}N_5O_4S^+$: 502.3422, found 502.3429; $C_{24}H_{47}N_5O_4S$ (501.73).

tert-Butyl {4-[(imino(methylthio)methyl)amino]butyl}carbamate (62)

Compound **46** (1.80 g, 7.28 mmol) was dissolved in MeCN (30 mL) and treated with methyl iodide (0.50 mL, 8.00 mmol) resulting a yellow oil (**62** x HI, 2.80 g, 99%): R_f=0.16 (DCM/MeOH 95:5); ^{1}H NMR (300 MHz, $CDCl_3$, hydrogen iodide) δ 3.64 – 3.27 (m, 2H), 3.09 (q, J = 6.4 Hz, 2H), 2.75 (s, 3H), 1.79 – 1.63 (m, 2H), 1.63 – 1.49 (m, 2H), 1.37 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$, hydrogen iodide) δ 170.07, 154.13, 77.71, 42.35, 37.65, 26.35, 25.10, 23.49, 13.82. HRMS (ESI-MS): m/z [M+H$^+$] calculated for $C_{11}H_{24}N_3O_2S^+$: 262.1584, found 262.1589; $C_{11}H_{23}N_3O_2S$ x HI (389.30).

tert-Butyl {6-[(imino(methylthio)methyl)amino]hexyl}carbamate (63)

Compound **47** (1.80 g, 6.54 mmol) was dissolved in MeCN (30 mL) and treated with methyl iodide (0.45 mL, 7.19 mmol) resulting a yellow oil (**63** x HI, 2.70 g, 99%): R_f=0.18 (DCM/MeOH 95:5); ^{1}H NMR (300 MHz, $CDCl_3$, hydrogen iodide) δ 3.63 – 3.20 (m, 2H), 3.05 (t, J = 4.6 Hz, 2H), 2.75 (s, 3H), 1.76 – 1.57 (m, 2H), 1.53 – 1.42 (m, 2H), 1.39 (s, 9H), 1.37 – 1.07 (m, 4H). ^{13}C NMR (75 MHz, $CDCl_3$, hydrogen iodide) δ 170.03, 154.13, 77.13, 42.66, 38.29, 27.67, 26.43, 26.24, 24.24, 24.03, 13.13. [M+H$^+$]. HRMS (ESI-MS): m/z [M+H$^+$] calculated for $C_{13}H_{28}N_3O_2S^+$: 290.1897, found 290.1901; $C_{13}H_{27}N_3O_2S$ x HI (417.35).

tert-Butyl {8-[(imino(methylthio)methyl)amino]octyl}carbamate (64)

Compound **48** (2.20 g, 7.25 mmol) was dissolved in MeCN (30 mL) and treated with methyl iodide (0.50 mL, 7.97 mmol) resulting a yellow oil (**64** x HI, 3.20 g, 99%): R_f=0.20 (DCM/MeOH 95:5); ^{1}H NMR (300 MHz, $CDCl_3$, hydrogen iodide) δ 3.26 (q, J = 6.8 Hz, 2H), 3.03 (q, J = 6.5 Hz, 2H), 2.76 (s, 3H), 1.64 (p, J = 7.2 Hz, 2H), 1.52 – 1.40 (m, 2H), 1.39 (s, 9H), 1.36 – 1.12 (m, 8H). ^{13}C NMR (75 MHz, $CDCl_3$, hydrogen iodide) δ 170.01, 154.03, 77.01, 42.75, 38.50, 27.84, 26.86, 26.73, 26.38, 26.27, 24.53, 24.45, 13.25. HRMS (ESI-MS): m/z [M+H$^+$] calculated for $C_{15}H_{32}N_3O_2S^+$: 318.2210, found 318.2218; $C_{15}H_{31}N_3O_2S$ x HI (445.40).

tert-Butyl {10-[(imino(methylthio)methyl)amino]decyl}carbamate (65)

Compound **49** (2.10 g, 6.33 mmol) was dissolved in MeCN (30 mL) and treated with methyl iodide (0.44 mL, 6.97 mmol) resulting a yellow oil (**65** x HI, 2.90 g, 97%): R_f=0.22 (DCM/MeOH 95:5); ^{1}H NMR (300 MHz, $CDCl_3$, hydrogen iodide) δ 3.40 – 3.16 (m, 2H), 3.00 (q, J = 6.8 Hz, 2H), 2.72 (s, 3H), 1.61 (p, J = 7.2 Hz, 2H), 1.48 – 1.37 (m, 2H), 1.36 (s, 9H), 1.33 – 1.13 (m, 12H). ^{13}C NMR (75 MHz, $CDCl_3$, hydrogen iodide) δ 169.88, 154.02, 76.96, 42.72, 38.51, 27.86, 27.28, 27.22, 27.10, 26.77, 26.34, 24.86, 24.62, 24.50, 13.15 (+, S-***C***H_3). HRMS (ESI-MS): m/z [M+H$^+$] calculated for $C_{17}H_{36}N_3O_2S^+$: 346.2523, found 346.2526; $C_{17}H_{35}N_3O_2S$ x HI (473.46).

tert-Butyl {12-[(imino(methylthio)methyl)amino]dodecyl}carbamate (66)

Compound **50** (2.60 g, 7.23 mmol) was dissolved in MeCN (30 mL) and treated with methyl iodide (0.50 mL, 7.95 mmol) resulting a yellow oil (**66** x HI, 3.60 g, 99%): R_f=0.24 (DCM/MeOH 95:5); ^{1}H NMR (300 MHz, $CDCl_3$, hydrogen iodide) δ 3.24 (q, J = 7.2 Hz, 2H), 3.03 (q, J = 6.6 Hz, 2H), 2.76 (s, 3H), 1.64 (p, J = 7.2 Hz, 2H), 1.50 – 1.39 (m, 2H), 1.38 (s, 9H), 1.21 (m, 16H). ^{13}C NMR (75 MHz, $CDCl_3$, hydrogen iodide) δ 169.95, 154.00, 76.97, 42.79, 38.55, 27.91, 27.39, 27.36, 27.34, 27.22, 27.16, 26.85, 26.36, 25.95, 24.69, 24.55, 13.25. HRMS (ESI-MS): m/z [M+H$^+$] calculated for $C_{19}H_{40}N_3O_2S^+$: 374.2836, found 374.2839; $C_{19}H_{39}N_3O_2S$ x HI (501.51).

1,2-(Di-tert-butoxycarbonyl)-3-(S-methylisothioureidobutyl)guanidine (67)

Compound **51** (1.07 g, 2.75 mmol) was dissolved in MeCN (30 mL) and treated with methyl iodide (0.19 mL, 3.03 mmol) resulting a colorless foamlike solid (**67** x HI, 1.39 g, 95%): R_f=0.25 (DCM/MeOH 95:5); ^{1}H NMR (300 MHz, $CDCl_3$, hydrogen iodide) δ 11.45 (bs, 1H), 9.53 (bs, 1H), 8.62 (bs, 1H), 8.45 (bs, 1H), 3.58 – 3.21 (m, 4H), 2.82 (s, 3H), 1.73 (s, 4H), 1.48 (s, 18H). ^{13}C NMR (75 MHz, $CDCl_3$, hydrogen iodide) δ 172.06, 163.08, 156.59, 153.20, 83.53, 80.12, 44.66, 39.85, 28.34, 28.08, 26.92, 24.97, 15.65. HRMS (ESI-MS): m/z [M+H$^+$] calculated for $C_{17}H_{34}N_5O_4S^+$: 404.2326, found 404.2334; $C_{17}H_{33}N_5O_4S$ x HI (531.45).

1,2-(Di-tert-butoxycarbonyl)-3-(S-methylisothioureidohexyl)guanidine (68)

Compound **52** (930 mg, 2.23 mmol) was dissolved in MeCN (30 mL) and treated with methyl iodide (0.15 mL, 2.45 mmol) resulting a colorless oil (**68** x HI, 1.24 g, 99%): R_f=0.27 (DCM/MeOH 95:5); ^{1}H NMR (300 MHz, $CDCl_3$, hydrogen iodide) δ 11.47 (bs, 1H), 9.12 (bs, 1H), 8.51 (bs, 1H), 8.34 (t, J = 5.3 Hz, 1H), 3.40 (q, J = 7.2 Hz, 2H), 3.30 (q, J = 6.6 Hz, 2H), 2.79 (s, 3H), 1.71 (p, J = 7.0 Hz, 2H), 1.57 (q, J = 7.3 Hz, 2H), 1.49 (s, 9H), 1.49 (s, 9H), 1.46 – 1.35 (m, 4H). ^{13}C NMR (75 MHz, $CDCl_3$, hydrogen iodide) δ 172.11, 163.33, 156.09, 153.28, 83.24, 79.54, 44.72, 40.81, 28.75, 28.32, 28.27, 28.09, 26.32, 26.22, 15.21. HRMS (ESI-MS): m/z [M+H$^+$] calculated for $C_{19}H_{38}N_5O_4S^+$: 432.2639, found 432.2647; $C_{19}H_{37}N_5O_4S$ x HI (559.51).

1,2-(Di-tert-butoxycarbonyl)-3-(S-methylisothioureidooctyl)guanidine (69)

Compound **53** (1.45 g, 3.25 mmol) was dissolved in MeCN (30 mL) and treated with methyl iodide (0.22 mL, 3.58 mmol) resulting a colorless oil (**69** x HI, 1.85 g, 97%): R_f=0.30 (DCM/MeOH 95:5); ^{1}H NMR (300 MHz, $CDCl_3$, hydrogen iodide) δ 11.43 (bs, 1H), 9.12 (bs, 1H), 8.51 (bs, 1H), 8.25 (t, J = 5.2 Hz, 1H), 3.39 – 3.19 (m, 4H), 2.73 (s, 3H), 1.63 (p, J = 7.4 Hz, 2H), 1.49 (p, J = 7.1 Hz, 1H), 1.43 (s, 18H), 1.34 – 1.20 (m, 8H). ^{13}C NMR (75 MHz, $CDCl_3$, hydrogen iodide) δ 171.76, 163.54, 156.13, 153.30, 83.10, 79.34, 44.92, 40.96, 28.96, 28.90, 28.79, 28.58, 28.32, 28.09, 26.72, 26.56, 15.37. HRMS (ESI-MS): m/z [M+H$^+$] calculated for $C_{21}H_{42}N_5O_4S^+$: 460.2952, found 460.2960; $C_{21}H_{41}N_5O_4S$ x HI (587.56).

1,2-(Di-tert-butoxycarbonyl)-3-(S-methylisothioureidodecyl)guanidine (70)

Compound **54** (1.90 g, 4.01 mmol) was dissolved in MeCN (30 mL) and treated with methyl iodide (0.28 mL, 4.41 mmol) resulting a colorless foamlike solid (**70** x HI, 2.40 g, 97%): R_f=0.32 (DCM/MeOH 95:5); ^{1}H NMR (300 MHz, $CDCl_3$, hydrogen iodide) δ 11.48 (bs, 1H), 9.12 (bs, 1H), 8.51 (bs, 1H), 8.29 (t, J = 5.2 Hz, 1H), 3.37 (q, J = 7.4 Hz, 2H), 3.33 – 3.20 (m, 2H), 2.78 (s, 3H), 1.69 (p, J = 7.1 Hz, 2H), 1.55 (p, J = 7.1 Hz, 2H), 1.49 (s, 9H), 1.48 (s, 9H), 1.38 – 1.25 (m,

12H). ^{13}C NMR (75 MHz, $CDCl_3$, hydrogen iodide) δ 171.98, 163.59, 156.12, 153.32, 83.07, 79.32, 44.88, 41.02, 29.28, 29.24, 29.15, 28.95, 28.87, 28.39, 28.33, 28.09, 26.85, 26.61, 15.29. HRMS (ESI-MS): m/z [M+H$^+$] calculated for $C_{23}H_{46}N_5O_4S^+$: 488.3265, found 488.3270; $C_{23}H_{45}N_5O_4S$ x HI (615.62).

1,2-(Di-tert-butoxycarbonyl)-3-(S-methylisothioureidododecyl)guanidine (71)

Compound **55** (1.58 g, 3.15 mmol) was dissolved in MeCN (30 mL) and treated with methyl iodide (0.22 mL, 3.46 mmol) resulting a yellow oil (**71** x HI, 1.95 g, 96%): R_f=0.35 (DCM/MeOH 95:5); ^{1}H NMR (300 MHz, $CDCl_3$, hydrogen iodide) δ 11.48 (bs, 1H), 8.88 (bs, 1H), 8.51 (bs, 1H), 8.29 (t, J = 5.2 Hz, 1H), 3.37 (q, J = 7.3 Hz, 2H), 3.28 (t, J = 7.1 Hz, 2H), 2.78 (s, 3H), 1.69 (p, J = 7.2 Hz, 2H), 1.54 (p, J = 7.0 Hz, 2H), 1.49 (s, 9H), 1.48 (s, 9H), 1.36 – 1.23 (m, 16H). ^{13}C NMR (75 MHz, $CDCl_3$, hydrogen iodide) δ 172.05, 163.61, 156.12, 153.32, 83.05, 79.30, 44.90, 41.03, 29.47, 29.41, 29.38, 29.34, 29.25, 29.18, 28.96, 28.44, 28.33, 28.09, 26.87, 26.66, 15.26. HRMS (ESI-MS): m/z [M+H$^+$] calculated for $C_{25}H_{50}N_5O_4S^+$: 516.3578, found 516.3582; $C_{25}H_{49}N_5O_4S$ x HI (643.67).

tert-Butyl {4-[(((tert-butoxycarbonyl)imino)(methylthio)methyl)amino]butyl}carbamate (78)

The reaction was realized with **62** (2.70 g, 6.94 mmol), NEt_3 (0.96 mL, 6.94 mmol) and Boc_2O (1.51 g, 6.94 mmol). After column chromatography a colorless oil (2.35 g, 94%) was obtained: R_f=0.43 (DCM/MeOH 98:2); ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.79 (bs, 1H), 4.64 (t, J = 6.1 Hz, 1H), 3.29 (t, J = 6.8 Hz, 2H), 3.10 (q, J = 7.0 Hz, 2H), 2.42 (s, 3H), 1.69 – 1.47 (m, 4H), 1.46 (s, 9H), 1.40 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.44, 162.13, 156.01, 79.36, 79.22, 46.27, 39.98, 28.39, 28.21, 27.36, 26.59, 13.56. HRMS (ESI-MS): m/z [M+H$^+$] calculated for $C_{16}H_{32}N_3O_4S^+$: 362.2108, found 362.2115; $C_{16}H_{31}N_3O_4S$ (361.50).

tert-Butyl {6-[(((tert-butoxycarbonyl)imino)(methylthio)methyl)amino]hexyl}carbamate (79)

The reaction was realized with **63** (2.60 g, 6.23 mmol), NEt_3 (0.86 mL, 6.23 mmol) and Boc_2O (1.36 g, 6.23 mmol). After column chromatography a colorless oil (2.30 g, 95%) was obtained: R_f=0.46 (DCM/MeOH 98:2); ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.77 (bs, 1H), 4.56 (bs, 1H), 3.25 (t, J = 7.2 Hz, 2H), 3.06 (q, J = 6.1 Hz, 2H), 2.41 (s, 3H), 1.73 – 1.49 (m, 4H), 1.46 (s, 9H), 1.39 (s, 9H), 1.36 – 1.26 (m, 4H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.32, 162.17, 156.01, 79.20, 79.04, 43.67, 40.37, 30.00, 29.17, 28.41, 28.22, 26.39, 26.27, 13.55. HRMS (ESI-MS): m/z [M+H$^+$] calculated for $C_{18}H_{36}N_3O_4S^+$: 390.2421, found 390.2424; $C_{18}H_{35}N_3O_4S$ (389.56).

tert-Butyl {8-[(((tert-butoxycarbonyl)imino)(methylthio)methyl)amino]octyl}carbamate (80)

The reaction was realized with **64** (3.10 g, 6.96 mmol), NEt_3 (0.96 mL, 6.96 mmol) and Boc_2O (1.52 g, 6.96 mmol). After column chromatography a colorless oil (2.80 g, 96%) was obtained: R_f=0.49 (DCM/MeOH 98:2); ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.68 (t, J = 5.8 Hz, 1H), 4.58 (bs, 1H), 3.24 – 3.11 (m, 2H), 3.03 (q, J = 6.7 Hz, 2H), 2.39 (s, 3H), 1.64 – 1.45 (m, 4H), 1.43 (s, 9H), 1.37 (s, 9H), 1.30 – 1.18 (m, 8H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.35, 163.60, 155.98, 79.08, 78.92, 46.25, 41.01, 29.97, 29.59, 29.07, 29.06, 28.39, 28.26, 26.66, 26.64, 13.50. HRMS (ESI-MS): m/z [M+H$^+$] calculated for $C_{20}H_{40}N_3O_4S^+$: 418.2734, found 418.2735; $C_{20}H_{39}N_3O_4S$ (417.61).

tert-Butyl {10-[(((tert-butoxycarbonyl)imino)(methylthio)methyl)amino]decyl}carbamate (81)

The reaction was realized with **65** (2.80 g, 5.91 mmol), NEt_3 (0.82 mL, 5.91 mmol) and Boc_2O (1.29 g, 5.91 mmol). After column chromatography a colorless oil (2.50 g, 95%) was obtained: R_f=0.52 (DCM/MeOH 98:2); ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.88 (bs, 1H), 4.58 (bs, 1H), 3.46 – 3.16 (m, 2H), 3.06 (q, J = 6.7 Hz, 2H), 2.42 (s, 3H), 1.65 – 1.48 (m, 4H), 1.46 (s, 9H), 1.40 (s,

9H), 1.26 (m, 12H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.21, 163.56, 156.01, 79.13, 78.97, 43.83, 40.08, 30.01, 29.63, 29.40, 29.31, 29.24, 28.42, 28.22, 26.95, 26.74, 26.72, 13.53. MS (LC-MS, ESI): m/z 446.27 [M+H$^+$]. HRMS (ESI-MS): m/z [M+H$^+$] calculated for $C_{22}H_{44}N_3O_4S^+$: 446.3047, found 446.3047; $C_{22}H_{43}N_3O_4S$ (445.66).

tert-Butyl {12-[(((tert-butoxycarbonyl)imino)(methylthio)methyl)amino]dodecyl}carbamate (82)

The reaction was realized with **66** (3.50 g, 6.98 mmol), NEt_3 (0.97 mL, 6.98 mmol) and Boc_2O (1.52 g, 6.98 mmol). After column chromatography a colorless oil (3.20 g, 97%) was obtained: R_f=0.55 (DCM/MeOH 98:2); ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.84 (bs, 1H), 4.64 (bs, 1H), 3.27 – 3.09 (m, 2H), 3.02 (q, J = 6.7 Hz, 2H), 2.38 (s, 3H), 1.63 – 1.46 (m, 4H), 1.44 (s, 9H), 1.36 (s, 9H), 1.27 – 1.13 (m, 16H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.37, 163.50, 155.96, 79.01, 78.86, 43.77, 41.03, 30.01, 29.61, 29.46, 29.40, 29.23, 29.13, 29.07, 28.38, 28.24, 26.75, 26.71, 26.61, 13.46. HRMS (ESI-MS): m/z [M+H$^+$] calculated for $C_{24}H_{48}N_3O_4S^+$: 474.3360, found 474.3355; $C_{24}H_{47}N_3O_4S$ (473.72).

1,2-(Di-tert-butoxycarbonyl)-3-(N'-tert-butoxycarbonyl-S-methylisothioureidobutyl)guanidine (83)

The reaction was realized with **67** (1.36 g, 2.56 mmol), NEt_3 (0.35 mL, 2.56 mmol) and Boc_2O (559 mg, 2.56 mmol). After column chromatography a colorless foamlike solid (1.23 g, 95%) was obtained: R_f=0.15 (DCM); ^{1}H NMR (300 MHz, $CDCl_3$) δ 11.47 (bs, 1H), 9.80 (bs, 1H), 8.32 (t, J = 5.4 Hz, 1H), 3.42 (q, J = 6.3 Hz, 2H), 3.31 (t, J = 7.2 Hz, 2H), 2.42 (s, 3H), 1.63 (m, 4H), 1.46 (m, 27H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.52, 163.55, 162.19, 156.19, 153.29, 83.14, 79.29, 79.23, 43.37, 40.16, 28.27, 28.22, 28.06, 26.67, 26.43, 13.55. HRMS (ESI-MS): m/z [M+H$^+$] calculated for $C_{22}H_{42}N_5O_6S^+$: 504.2850, found 504.2856; $C_{22}H_{41}N_5O_6S$ (503.66).

1,2-(Di-tert-butoxycarbonyl)-3-(N'-tert-butoxycarbonyl-S-methylisothioureidohexyl)guanidine (84)

The reaction was realized with **68** (1.21 g, 2.16 mmol), NEt_3 (0.30 mL, 2.16 mmol) and Boc_2O (472 mg, 2.16 mmol). After column chromatography a colorless foamlike solid (960 mg, 83%) was obtained: R_f=0.19 (DCM); ^{1}H NMR (300 MHz, $CDCl_3$) δ 11.47 (bs, 1H), 9.78 (bs, 1H), 8.28 (t, J = 5.2 Hz, 1H), 3.37 (q, J = 7.4 Hz, 2H), 3.25 (q, J = 7.3 Hz, 2H), 2.42 (s, 3H), 1.63 – 1.51 (m, 4H), 1.49 – 1.45 (m, 27H), 1.39 – 1.31 (m, 4H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.40, 163.62, 162.22, 156.11, 153.31, 83.02, 79.20, 79.13, 43.66, 40.73, 29.19, 28.80, 28.29, 28.23, 28.06, 26.47, 26.40, 13.52. HRMS (ESI-MS): m/z [M+H$^+$] calculated for $C_{24}H_{46}N_5O_6S^+$: 532.3163, found 532.3172; $C_{24}H_{45}N_5O_6S$ (531.71).

1,2-(Di-tert-butoxycarbonyl)-3-(N'-tert-butoxycarbonyl-S-methylisothioureidooctyl)guanidine (85)

The reaction was realized with **69** (1.80 g, 3.06 mmol), NEt_3 (0.42 mL, 3.06 mmol) and Boc_2O (669 mg, 3.06 mmol). After column chromatography a colorless foamlike solid (1.58 g, 92%) was obtained: R_f=0.23 (DCM); ^{1}H NMR (300 MHz, $CDCl_3$) δ 11.38 (s, 1H), 9.65 (s, 1H), 8.12 (t, J = 5.1 Hz, 1H), 3.22 (q, J = 7.2 Hz, 2H), 3.11 (q, J = 6.6 Hz, 2H), 2.26 (s, 3H), 1.47 – 1.37 (m, 4H), 1.34 – 1.27 (m, 27H), 1.21 – 1.12 (m, 8H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.09, 163.44, 162.00, 155.94, 153.10, 82.69, 78.83, 78.72, 43.57, 40.68, 29.11, 28.86, 28.80, 28.75, 28.14, 28.08, 27.90, 26.56, 26.50, 13.33. HRMS (ESI-MS): m/z [M+H$^+$] calculated for $C_{26}H_{50}N_5O_6S^+$: 560.3476, found 560.3483; $C_{26}H_{49}N_5O_6S$ (559.77).

1,2-(Di-tert-butoxycarbonyl)-3-(N'-tert-butoxycarbonyl-S-methylisothioureidodecyl)guanidine (86)

The reaction was realized with **70** (2.38 g, 3.87 mmol), NEt_3 (0.54 mL, 3.87 mmol) and Boc_2O (844 mg, 3.87 mmol). After column chromatography a colorless foamlike solid (2.06 g, 91%)

was obtained: R_f=0.27 (DCM); ^{1}H NMR (300 MHz, $CDCl_3$) δ 11.43 (bs, 1H), 9.72 (bs, 1H), 8.21 (t, J = 5.1 Hz, 1H), 3.30 (q, J = 7.2 Hz, 2H), 3.19 (q, J = 7.2 Hz, 2H), 2.35 (s, 3H), 1.55 – 1.44 (m, 4H), 1.40 (s, 27H), 1.26 – 1.15 (m, 12H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.33, 163.53, 162.10, 156.03, 153.22, 82.86, 79.07, 78.97, 43.74, 40.87, 29.27, 29.25, 29.21, 29.11, 29.02, 28.87, 28.23, 28.16, 27.99, 26.75, 26.67, 13.45. MS (LC-MS, ESI): m/z 588.38 [M+H$^+$]. HRMS (ESI-MS): m/z [M+H$^+$] calculated for $C_{28}H_{54}N_5O_6S^+$: 588.3789, found 588.3799; $C_{28}H_{53}N_5O_6S$ (587.82).

1,2-(Di-tert-butoxycarbonyl)-3-(N'-tert-butoxycarbonyl-S-methylisothioureidododecyl)guanidine (87)

The reaction was realized with **71** (1.91 g, 2.97 mmol), NEt_3 (0.41 mL, 2.97 mmol) and Boc_2O (648 mg, 2.97 mmol). After column chromatography a colorless foamlike solid (1.60 g, 88%) was obtained: R_f=0.31 (DCM); ^{1}H NMR (300 MHz, $CDCl_3$) δ 11.45 (bs, 1H), 9.75 (bs, 1H), 8.24 (t, J = 5.2 Hz, 1H), 3.33 (q, J = 7.4 Hz, 2H), 3.22 (q, J = 7.2 Hz, 2H), 2.38 (s, 3H), 1.60 – 1.47 (m, 4H), 1.45 – 1.40 (m, 27H), 1.28 – 1.17 (m, 16H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.36, 163.56, 162.14, 156.06, 153.25, 82.93, 79.14, 79.05, 43.81, 40.94, 29.45, 29.39, 29.37, 29.25, 29.19, 29.09, 28.91, 28.87, 28.26, 28.19, 28.03, 26.80, 26.71, 13.49. HRMS (ESI-MS): m/z [M+H$^+$] calculated for $C_{30}H_{58}N_5O_6S^+$: 616.4102, found 616.4111; $C_{30}H_{57}N_5O_6S$ (615.88).

2-tert-Butoxycarbonyl-1-(N-tert-butoxycarbonylaminobutanyl)-3-[3-(1-trityl-1*H*-imidazol-4-yl)propyl]guanidine (94)

Compound **94** was prepared from **5** (500 mg, 1.36 mmol), **78** (492 mg, 1.36 mmol), $HgCl_2$ (369 mg, 1.36 mmol) and NEt_3 (0.57 mL, 4.08 mmol) in DCM (20 mL) conforming to the general procedure yielding a yellow foamlike solid (440 mg, 48%): R_f=0.34 (DCM/MeOH/NH_3 98:2:0.1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.09 (bs, 1H), 7.41 – 7.27 (m, 10H), 7.14 – 7.06 (m, 6H), 6.54 (d, J = 0.7 Hz, 1H), 4.78 (bs, 1H), 3.44 – 3.14 (m, 4H), 3.05 (q, J = 6.1 Hz, 2H), 2.56 (t, J = 6.3 Hz,

2H), 1.86 (p, J = 6.6 Hz, 2H), 1.59 – 1.48 (m, 4H), 1.46 (s, 9H), 1.39 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.32, 160.54, 156.06, 142.34, 140.58, 137.98, 129.73, 128.11, 128.09, 118.29, 79.00, 75.23, 75.11, 40.71, 40.59, 39.93, 28.87, 28.54, 28.44, 27.43, 27.32, 26.58. HRMS (ESI-MS): m/z [M+H$^+$] calculated for $C_{40}H_{53}N_6O_4^+$: 681.4123, found 681.4127; $C_{40}H_{52}N_6O_4$ (680.89).

2-tert-Butoxycarbonyl-1-(N-tert-butoxycarbonylaminohexanyl)-3-[3-(1-trityl-1*H*-imidazol-4-yl)propyl]guanidine (95)

Compound **95** was prepared from **5** (500 mg, 1.36 mmol), **79** (530 mg, 1.36 mmol), $HgCl_2$ (369 mg, 1.36 mmol) and NEt_3 (0.57 mL, 4.08 mmol) in DCM (20 mL) conforming to the general procedure yielding a yellow foamlike solid (600 mg, 62%): R_f=0.38 (DCM/MeOH/NH_3 98:2:0.1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.07 (bs, 1H), 7.37 – 7.27 (m, 10H), 7.15 – 7.05 (m, 6H), 6.54 (s, 1H), 4.57 (bs, 1H), 3.45 – 3.12 (m, 4H), 3.03 (q, J = 6.4 Hz, 2H), 2.57 (t, J = 6.3 Hz, 2H), 1.86 (p, J = 6.6 Hz, 2H), 1.56 – 1.48 (m, 2H), 1.46 (s, 9H), 1.41 (s, 9H), 1.40 – 1.34 (m, 2H), 1.29 – 1.20 (m, 4H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.49, 160.67, 156.01, 142.33, 140.59, 137.97, 129.73, 128.11, 128.08, 118.30, 79.01, 75.25, 75.23, 41.21, 40.96, 40.40, 29.87, 29.35, 29.17, 28.74, 28.54, 28.44, 26.55, 26.41. HRMS (ESI-MS): m/z [M+H$^+$] calculated for $C_{42}H_{57}N_6O_4^+$: 709.4436, found 709.4446; $C_{42}H_{56}N_6O_4$ (708.95).

2-tert-Butoxycarbonyl-1-(N-tert-butoxycarbonylaminooctanyl)-3-[3-(1-trityl-1*H*-imidazol-4-yl)propyl]guanidine (96)

Compound **96** was prepared from **5** (500 mg, 1.36 mmol), **80** (568 mg, 1.36 mmol), $HgCl_2$ (369 mg, 1.36 mmol) and NEt_3 (0.57 mL, 4.08 mmol) in DCM (20 mL) conforming to the general procedure yielding a yellow foamlike solid (480 mg, 48%): R_f=0.42 (DCM/MeOH/NH_3 98:2:0.1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.57 (bs, 1H), 7.38 – 7.26 (m, 10H), 7.12 – 7.05 (m, 6H), 6.53 (s, 1H), 4.58 (bs, 1H), 3.40 – 3.17 (m, 4H), 3.04 (q, J = 6.5 Hz, 2H), 2.56 (t, J = 6.3 Hz, 2H), 1.86 (p, J = 6.4 Hz, 2H), 1.58 – 1.46 (m, 4H), 1.45 (s, 9H), 1.40 (s, 9H), 1.27 – 1.14 (m, 8H). ^{13}C

NMR (75 MHz, $CDCl_3$) δ 164.36, 160.40, 156.00, 142.33, 140.59, 137.99, 129.72, 128.07, 128.02, 118.28, 78.94, 75.25, 75.21, 41.39, 40.67, 40.56, 29.99, 29.30, 29.20, 29.11, 28.70, 28.54, 28.44, 26.84, 26.68, 26.60. HRMS (ESI-MS): m/z [$M+H^+$] calculated for $C_{44}H_{61}N_6O_4^+$: 737.4749, found 737.4757; $C_{44}H_{60}N_6O_4$ (736.99).

2-tert-Butoxycarbonyl-1-(N-tert-butoxycarbonylaminodecanyl)-3-[3-(1-trityl-1*H*-imidazol-4-yl)propyl]guanidine (97)

Compound **97** was prepared from **5** (500 mg, 1.36 mmol), **81** (606 mg, 1.36 mmol), $HgCl_2$ (369 mg, 1.36 mmol) and NEt_3 (0.57 mL, 4.08 mmol) in DCM (20 mL) conforming to the general procedure yielding a yellow foamlike solid (590 mg, 57%): R_f=0.46 (DCM/MeOH/NH_3 98:2:0.1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.50 (bs, 1H), 7.43 – 7.27 (m, 10H), 7.13 – 7.07 (m, 6H), 6.54 (s, 1H), 4.54 (bs, 1H), 3.47 – 3.15 (m, 4H), 3.08 (q, J = 6.6 Hz, 2H), 2.57 (t, J = 6.2 Hz, 2H), 1.87 (p, J = 7.2 Hz, 2H), 1.46 (s, 9H), 1.42 (s, 9H), 1.40 – 1.34 (m, 4H), 1.28 – 1.16 (m, 12H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.39, 160.58, 156.00, 142.35, 140.60, 137.99, 129.73, 128.07, 127.99, 118.28, 78.97, 75.27, 75.22, 41.48, 41.19, 40.61, 30.06, 29.44, 29.39, 29.29, 29.27, 29.09, 28.69, 28.53, 28.44, 26.99, 26.92, 26.80. HRMS (ESI-MS): m/z [$M+H^+$] calculated for $C_{46}H_{65}N_6O_4^+$: 765.5062, found 765.5068; $C_{46}H_{64}N_6O_4$ (765.06).

2-tert-Butoxycarbonyl-1-(N-tert-butoxycarbonylaminododecanyl)-3-[3-(1-trityl-1*H*-imidazol-4-yl)propyl]guanidine (98)

Compound **98** was prepared from **5** (500 mg, 1.36 mmol), **82** (644 mg, 1.36 mmol), $HgCl_2$ (369 mg, 1.36 mmol) and NEt_3 (0.57 mL, 4.08 mmol) in DCM (20 mL) conforming to the general procedure yielding a yellow foamlike solid (700 mg, 65%): R_f=0.50 (DCM/MeOH/NH_3 98:2:0.1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.98 (bs, 1H), 7.36 – 7.24 (m, 10H), 7.14 – 7.03 (m, 6H), 6.52 (s, 1H), 4.59 (bs, 1H), 3.53 – 3.12 (m, 4H), 3.06 (q, J = 6.6 Hz, 2H), 2.56 (t, J = 6.2 Hz, 2H), 1.85 (p, J = 6.5 Hz, 2H), 1.60 – 1.46 (m, 4H), 1.45 (s, 9H), 1.40 (s, 9H), 1.28 – 1.13 (m, 16H). ^{13}C

NMR (75 MHz, Chloroform-*d*) δ 164.34, 160.37, 156.00, 142.34, 140.62, 138.00, 129.71, 128.23, 128.05, 118.27, 78.91, 75.23, 75.20, 41.45, 40.81, 40.61, 30.06, 29.68, 29.52, 29.46, 29.33, 29.30, 29.17, 29.11, 28.68, 28.54, 28.44, 26.95, 26.81, 26.72. HRMS (ESI-MS): m/z [M+H$^+$] calculated for $C_{48}H_{69}N_6O_4^+$: 793.5375, found 793.5374; $C_{48}H_{68}N_6O_4$; (793.11).

2-tert-Butoxycarbonyl-1-(N-tert-butoxycarbonylaminododecanyl)-3-[(2-tert-butoxycarbonylamino-4-methylthiazol-5-yl)propyl]guanidine (99)

Compound **99** was prepared from **6** (315 mg, 1.16 mmol), **82** (550 mg, 1.16 mmol), $HgCl_2$ (315 mg, 1.16 mmol) and NEt_3 (0.48 mL, 3.48 mmol) in DCM (20 mL) conforming to the general procedure yielding a yellow foamlike solid (520 mg, 64%): R_f=0.53 (DCM/MeOH/NH_3 98:2:0.1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 11.05 (bs, 1H), 4.67 (bs, 1H), 3.28 – 3.15 (m, 2H), 3.07 – 2.96 (m, 4H), 2.64 (t, J = 7.2 Hz, 2H), 2.16 (s, 3H), 1.79 (p, J = 7.0 Hz, 2H), 1.44 (s, 9H), 1.40 (s, 9H), 1.38 – 1.36 (m, 4H), 1.35 (s, 9H), 1.19 – 1.15 (m, 16H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.17, 159.99, 157.98, 155.98, 152.87, 141.91, 122.84, 82.06, 78.82, 77.85, 41.18, 40.56, 40.07, 30.99, 30.00, 29.61, 29.48, 29.45, 29.38, 29.27, 29.22, 29.20, 28.41, 28.38, 28.22, 26.97, 26.84, 26.74, 14.44. HRMS (ESI-MS): m/z [M+H$^+$] calculated for $C_{35}H_{65}N_6O_6S^+$: 697.4681, found 697.4688; $C_{35}H_{64}N_6O_6S$ (696.99).

2-tert-Butoxycarbonyl-1-(N-tert-butoxycarbonylaminododecanyl)-3-[(2-tert-butoxycarbonylaminothiazol-5-yl)propyl]guanidine (100)

Compound **100** was prepared from **7** (299 mg, 1.16 mmol), **82** (550 mg, 1.16 mmol), $HgCl_2$ (315 mg, 1.16 mmol) and NEt_3 (0.48 mL, 3.48 mmol) in DCM (20 mL) conforming to the general procedure yielding a yellow foamlike solid (500 mg, 63%): R_f=0.52 (DCM/MeOH/NH_3 98:2:0.1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 12.32 (bs, 1H), 6.92 (s, 1H), 4.69 (bs, 1H), 3.29 – 3.15 (m, 2H), 3.10 – 2.91 (m, 4H), 2.70 (t, J = 7.0 Hz, 2H), 1.81 (p, J = 6.7 Hz, 2H), 1.46 (s, 9H), 1.37 (s, 9H), 1.36 – 1.33 (m, 4H), 1.32 (s, 9H), 1.20 – 1.11 (m, 16H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.06,

160.40, 159.95, 155.98, 152.99, 133.09, 130.21, 81.60, 78.76, 77.85, 41.19, 40.53, 40.19, 30.87, 29.97, 29.58, 29.45, 29.43, 29.36, 29.27, 29.23, 29.20, 28.40, 28.36, 28.23, 26.97, 26.82, 26.72. HRMS (ESI-MS): m/z [M+H$^+$] calculated for $C_{34}H_{63}N_6O_6S^+$: 683.4524, found 683.4528; $C_{34}H_{62}N_6O_6S$ (682.97).

2-tert-Butoxycarbonyl-1-(N',N''-di-tert-butoxycarbonylguanidinobutyl)-3-[3-(1-trityl-1*H*-imidazol-4-yl)propyl]guanidine (101)

Compound **101** was prepared from **5** (500 mg, 1.36 mmol), **83** (684 mg, 1.36 mmol), $HgCl_2$ (369 mg, 1.36 mmol) and NEt_3 (0.57 mL, 4.08 mmol) in DCM (20 mL) conforming to the general procedure yielding a yellow oil (560 mg, 50%): R_f=0.28 (DCM/MeOH/NH_3 98:2:0.1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 11.42 (bs, 1H), 9.04 (bs, 1H), 8.17 (t, J = 5.4 Hz, 1H), 7.27 – 7.15 (m, 10H), 7.06 – 6.96 (m, 6H), 6.46 (d, J = 1.3 Hz, 1H), 3.46 – 3.05 (m, 6H), 2.47 (t, J = 6.3 Hz, 2H), 1.78 (p, J = 4.9, 3.8 Hz, 2H), 1.56 – 1.41 (m, 4H), 1.40 – 1.27 (m, 27H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.27, 163.49, 159.54, 156.03, 153.12, 142.22, 140.45, 137.81, 129.62, 128.06, 128.04, 118.24, 82.94, 79.00, 77.56, 75.17, 40.80, 40.44, 40.36, 28.73, 28.62, 28.46, 28.24, 28.01, 26.48, 25.03. HRMS (ESI-MS): m/z [M+H$^+$] calculated for $C_{46}H_{63}N_8O_6^+$: 823.4865, found 823.4872; $C_{46}H_{62}N_8O_6$ (823.05).

2-tert-Butoxycarbonyl-1-(N',N''-di-tert-butoxycarbonylguanidinohexyl)-3-[3-(1-trityl-1*H*-imidazol-4-yl)propyl]guanidine (102)

Compound **102** was prepared from **5** (500 mg, 1.36 mmol), **84** (723 mg, 1.36 mmol), $HgCl_2$ (369 mg, 1.36 mmol) and NEt_3 (0.57 mL, 4.08 mmol) in DCM (20 mL) conforming to the general procedure yielding a yellow oil (690 mg, 60%): R_f=0.32 (DCM/MeOH/NH_3 98:2:0.1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 11.44 (bs, 1H), 8.91 (bs, 1H), 8.21 (t, J = 5.2 Hz, 1H), 7.23 (m, 10H), 7.02 (m, 6H), 6.47 (s, 1H), 3.41 – 3.13 (m, 6H), 2.49 (t, J = 6.3 Hz, 2H), 1.80 (p, J = 6.5 Hz, 2H), 1.59 – 1.41 (m, 4H), 1.37 (m, 27H), 1.27 – 1.16 (m, 4H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.18, 163.55,

159.66, 156.03, 153.21, 142.22, 140.45, 137.84, 129.64, 128.08, 128.04, 118.26, 82.94, 79.05, 77.53, 75.19, 41.35, 40.83, 40.73, 29.09, 29.04, 28.82, 28.69, 28.45, 28.25, 28.02, 26.56, 25.02. HRMS (ESI-MS): m/z [M+H$^+$] calculated for $C_{48}H_{67}N_8O_6^+$: 851.5178, found 851.5188; $C_{48}H_{66}N_8O_6$ (851.11).

2-tert-Butoxycarbonyl-1-(N',N''-di-tert-butoxycarbonylguanidinooctyl)-3-[3-(1-trityl-1*H*-imidazol-4-yl)propyl]guanidine (103)

Compound **103** was prepared from **5** (500 mg, 1.36 mmol), **85** (761 mg, 1.36 mmol), $HgCl_2$ (369 mg, 1.36 mmol) and NEt_3 (0.57 mL, 4.08 mmol) in DCM (20 mL) conforming to the general procedure yielding a yellow oil (370 mg, 31%): R_f=0.36 (DCM/MeOH/NH_3 98:2:0.1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 11.47 (bs, 1H), 9.05 (bs, 1H), 8.24 (t, J = 5.1 Hz, 1H), 7.33 – 7.18 (m, 10H), 7.11 – 6.99 (m, 6H), 6.49 (d, J = 1.3 Hz, 1H), 3.45 – 3.02 (m, 6H), 2.52 (t, J = 6.2 Hz, 2H), 1.84 (p, J = 7.2 Hz, 2H), 1.54 – 1.43 (m, 4H), 1.43 – 1.33 (m, 27H), 1.27 – 1.13 (m, 8H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.45, 163.61, 159.62, 156.06, 153.26, 142.29, 140.55, 137.90, 129.67, 128.08, 128.04, 118.25, 82.94, 79.09, 77.46, 75.18, 41.42, 41.33, 40.88, 29.15, 29.10, 28.90, 28.69, 28.65, 28.63, 28.51, 28.28, 28.04, 26.86, 26.76. HRMS (ESI-MS): m/z [M+H$^+$] calculated for $C_{50}H_{71}N_8O_6^+$: 879.5491, found 879.5505; $C_{50}H_{70}N_8O_6$ (879.16).

2-tert-Butoxycarbonyl-1-(N',N''-di-tert-butoxycarbonylguanidinodecyl)-3-[3-(1-trityl-1*H*-imidazol-4-yl)propyl]guanidine (104)

Compound **104** was prepared from **5** (500 mg, 1.36 mmol), **86** (799 mg, 1.36 mmol), $HgCl_2$ (369 mg, 1.36 mmol) and NEt_3 (0.57 mL, 4.08 mmol) in DCM (20 mL) conforming to the general procedure yielding a yellow oil (550 mg, 45%): R_f=0.40 (DCM/MeOH/NH_3 98:2:0.1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 11.46 (bs, 1H), 8.80 (bs, 1H), 8.22 (t, J = 5.2 Hz, 1H), 7.29 – 7.14 (m, 10H), 7.07 – 6.95 (m, 6H), 6.47 (d, J = 1.3 Hz, 1H), 3.42 – 3.06 (m, 6H), 2.49 (t, J = 6.3 Hz, 2H), 1.79 (p, J = 6.5 Hz, 2H), 1.60 – 1.41 (m, 4H), 1.41 – 1.29 (m, 27H), 1.24 – 1.06 (m, 12H). ^{13}C NMR

(75 MHz, $CDCl_3$) δ 164.18, 163.57, 159.57, 156.04, 153.22, 142.27, 140.51, 137.87, 129.64, 128.04, 128.02, 118.21, 82.87, 79.02, 77.53, 75.15, 41.44, 41.33, 40.87, 29.31, 29.23, 29.16, 29.03, 28.90, 28.63, 28.59, 28.51, 28.48, 28.26, 28.01, 26.86, 26.79. HRMS (ESI-MS): m/z [M+H$^+$] calculated for $C_{52}H_{75}N_8O_6^+$: 907.5804, found 907.5805; $C_{52}H_{74}N_8O_6$ (907.21).

2-tert-Butoxycarbonyl-1-(N',N''-di-tert-butoxycarbonylguanidinododecyl)-3-[3-(1-trityl-1*H*-imidazol-4-yl)propyl]guanidine (105)

Compound **105** was prepared from **5** (500 mg, 1.36 mmol), **87** (837 mg, 1.36 mmol), $HgCl_2$ (369 mg, 1.36 mmol) and NEt_3 (0.57 mL, 4.08 mmol) in DCM (20 mL) conforming to the general procedure yielding a yellow oil (660 mg, 52%): R_f=0.44 (DCM/MeOH/NH_3 98:2:0.1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 11.44 (bs, 1H), 9.03 (bs, 1H), 8.18 (t, J = 5.2 Hz, 1H), 7.23 – 7.12 (m, 10H), 7.05 – 6.90 (m, 6H), 6.42 (s, 1H), 3.31 – 3.00 (m, 6H), 2.44 (t, J = 6.1 Hz, 2H), 1.71 (p, J = 7.4 Hz, 2H), 1.58 – 1.37 (m, 4H), 1.36 (s, 27H), 1.21 – 1.03 (m, 16H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.12, 163.52, 160.37, 156.00, 153.16, 142.24, 140.52, 137.83, 129.59, 128.17, 127.97, 118.15, 82.78, 78.91, 77.63, 75.10, 41.37, 40.90, 40.82, 29.52, 29.41, 29.39, 29.35, 29.23, 29.12, 29.00, 28.98, 28.85, 28.64, 28.46, 28.22, 27.96, 26.84, 26.73. HRMS (ESI-MS): m/z [M+H$^+$] calculated for $C_{54}H_{79}N_8O_6^+$: 935.6117, found 935.6120; $C_{54}H_{78}N_8O_6$ (935.27).

2-tert-Butoxycarbonyl-1-(N',N''-di-tert-butoxycarbonylguanidinooctyl)-3-[(2-tert-butoxycarbonylamino-4-methylthiazol-5-yl)propyl]guanidine (106)

Compound **106** was prepared from **6** (163 mg, 0.60 mmol), **85** (335 mg, 0.60 mmol), $HgCl_2$ (163 mg, 0.60 mmol) and NEt_3 (0.25 mL, 1.80 mmol) in DCM (20 mL) conforming to the general procedure yielding a yellow oil (230 mg, 49%): R_f=0.38 (DCM/MeOH/NH_3 98:2:0.1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 11.48 (bs, 1H), 10.53 (bs, 1H), 8.27 (t, J = 5.1 Hz, 1H), 3.36 (q, J = 4.8 Hz, 4H), 3.27 – 3.11 (m, 2H,), 2.71 (t, J = 7.3 Hz, 2H), 2.20 (s, 3H), 1.86 (p, J = 7.2 Hz, 2H), 1.57 – 1.51 (m, 4H), 1.50 – 1.44 (m, 36H), 1.29 – 1.27 (m, 8H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.63,

160.05, 157.61, 156.09, 153.31, 152.73, 142.16, 122.89, 83.01, 82.28, 79.21, 77.96, 41.20, 41.05, 40.91, 29.65, 29.59, 29.23, 29.10, 29.03, 28.93, 28.46, 28.30, 28.27, 28.07, 26.84, 26.77, 14.54. HRMS (ESI-MS): m/z [M+H$^+$] calculated for $C_{37}H_{67}N_8O_8S^+$: 783.4797, found 783.4796; $C_{37}H_{66}N_8O_8S$ (783.04).

2-tert-Butoxycarbonyl-1-(N',N''-di-tert-butoxycarbonylguanidinooctyl)-3-[(2-tert-butoxycarbonylaminothiazol-5-yl)propyl]guanidine (107)

Compound **107** was prepared from **7** (154 mg, 0.60 mmol), **85** (335 mg, 0.60 mmol), $HgCl_2$ (163 mg, 0.60 mmol) and NEt_3 (0.25 mL, 1.80 mmol) in DCM (20 mL) conforming to the general procedure yielding a yellow oil (300 mg, 65%): R_f=0.36 (DCM/MeOH/NH_3 98:2:0.1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 12.08 (bs, 1H), 11.47 (bs, 1H), 8.26 (t, J = 5.1 Hz, 1H), 7.00 (s, 1H), 3.40 – 3.09 (m, 6H), 2.79 (t, J = 7.3 Hz, 2H), 1.89 (p, J = 7.3 Hz, 2H), 1.53 (s, 9H), 1.52 – 1.48 (m, 4H), 1.47 – 1.43 (m, 27H), 1.30 – 1.24 (m, 8H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.61, 160.30, 160.05, 156.09, 153.30, 152.97, 133.34, 122.53, 83.01, 81.82, 79.21, 77.97, 41.20, 41.05, 40.90, 30.90, 30.77, 29.64, 29.19, 29.09, 28.92, 28.46, 28.29, 28.06, 28.02, 26.84, 26.76. HRMS (ESI-MS): m/z [M+H$^+$] calculated for $C_{36}H_{65}N_8O_8S^+$: 769.4641, found 769.4640; $C_{36}H_{64}N_8O_8S$ (769.02).

2-tert-Butoxycarbonyl-1-(N',N''-di-tert-butoxycarbonylguanidinododecyl)-3-[(2-tert-butoxycarbonylamino-4-methylthiazol-5-yl)propyl]guanidine (108)

Compound **108** was prepared from **6** (157 mg, 0.58 mmol), **87** (355 mg, 0.58 mmol), $HgCl_2$ (157 mg, 0.58 mmol) and NEt_3 (0.24 mL, 1.74 mmol) in DCM (20 mL) conforming to the general procedure yielding a yellow oil (270 mg, 56%): R_f=0.46 (DCM/MeOH/NH_3 98:2:0.1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 11.48 (bs, 1H), 10.39 (bs, 1H), 8.27 (t, J = 5.2 Hz, 1H), 3.43 – 3.06 (m, 6H), 2.71 (t, J = 7.2 Hz, 2H), 2.20 (s, 3H), 1.87 (p, J = 7.1 Hz, 1H), 1.59 – 1.51 (m, 4H), 1.49 (s, 9H), 1.49 – 1.41 (m, 27H), 1.29 – 1.19 (m, 16H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.64, 160.05, 157.54, 156.09, 153.31, 152.70, 142.16, 123.01, 82.99, 82.32, 79.21, 77.98, 41.24, 41.09,

40.99, 29.52, 29.47, 29.45, 29.27, 29.25, 29.20, 29.14, 29.03, 28.96, 28.92, 28.46, 28.30, 28.26, 28.07, 26.92, 26.85, 14.54. HRMS (ESI-MS): m/z [M+H$^+$] calculated for $C_{41}H_{75}N_8O_8S^+$: 839.5423, found 839.5417; $C_{41}H_{74}N_8O_8S$ (839.15).

2-tert-Butoxycarbonyl-1-(N',N''-di-tert-butoxycarbonylguanidinododecyl)-3-[(2-tert-butoxycarbonylaminothiazol-5-yl)propyl]guanidine (109)

Compound **109** was prepared from **7** (148 mg, 0.58 mmol), **87** (355 mg, 0.58 mmol), $HgCl_2$ (157 mg, 0.58 mmol) and NEt_3 (0.24 mL, 1.74 mmol) in DCM (20 mL) conforming to the general procedure yielding a yellow oil (240 mg, 51%): R_f=0.45 (DCM/MeOH/NH_3 98:2:0.1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 11.84 (bs, 1H), 11.49 (bs, 1H), 8.28 (t, J = 5.2 Hz, 1H), 7.02 (s, 1H), 3.42 – 3.04 (m, 6H), 2.80 (t, J = 7.3 Hz, 2H), 1.90 (p, J = 7.2 Hz, 2H), 1.55 (s, 9H), 1.53 – 1.50 (m, 4H), 1.47 (d, J = 2.9 Hz, 27H), 1.28 – 1.18 (m, 16H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.65, 160.22, 160.05, 156.10, 153.32, 152.94, 133.38, 122.20, 82.99, 81.91, 79.22, 78.01, 41.27, 40.99, 40.23, 29.68, 29.53, 29.46, 29.36, 29.26, 29.15, 29.10, 29.03, 28.96, 28.84, 28.47, 28.31, 28.07, 28.03, 26.93, 26.85. HRMS (ESI-MS): m/z [M+H$^+$] calculated for $C_{40}H_{73}N_8O_8S^+$: 825.5267, found 825.5267; $C_{40}H_{72}N_8O_8S$ (825.12).

2-tert-Butoxycarbonyl-1-(N'-tert-butoxycarbonylcarbodiimidobutyl)-3-[3-(1-trityl-1*H*-imidazol-4-yl)propyl]guanidine (111)

Compound **111** was prepared from **5** (1.0 g, 2.72 mmol), **89** (591 mg, 1.36 mmol), $HgCl_2$ (1.48 g, 5.44 mmol) and NEt_3 (1.13 mL, 8.16 mmol) in DCM (20 mL) conforming to the general procedure yielding a yellow oil (480 mg, 50%): R_f=0.48 (DCM/MeOH/NH_3 98:2:0.1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.47 (bs, 1H), 7.31 – 7.21 (m, 10H), 7.10 – 7.04 (m, 6H), 6.49 (s, 1H), 3.43 – 3.01 (m, 6H), 2.65 – 2.43 (m, 2H), 1.88 – 1.71 (m, 2H), 1.67 – 1.47 (m, 4H), 1.49 (s, 9H), 1.45 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.36, 160.75, 158.09, 156.01, 142.31, 140.88, 137.87,

129.69, 128.07, 127.99, 118.29, 85.38, 79.67, 75.21, 53.55, 43.91, 40.44, 28.55, 28.20, 27.20, 26.35, 25.67, 25.30. MS (LC-MS, ESI): m/z 706.41 [M+H$^+$]; $C_{41}H_{51}N_7O_4$ (705.90).

2-tert-Butoxycarbonyl-1-(N'-tert-butoxycarbonylcarbodiimidohexyl)-3-[3-(1-trityl-1*H*-imidazol-4-yl)propyl]guanidine (112)

Compound **112** was prepared from **5** (1.0 g, 2.72 mmol), **90** (629 mg, 1.36 mmol), $HgCl_2$ (1.48 g, 5.44 mmol) and NEt_3 (1.13 mL, 8.16 mmol) in DCM (20 mL) conforming to the general procedure yielding a yellow oil (430 mg, 43%): R_f=0.51 (DCM/MeOH/NH_3 98:2:0.1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.06 (bs, 1H), 7.30 (m, 10H), 7.13 – 7.04 (m, 6H), 6.54 (s, 1H), 3.49 – 2.98 (m, 6H), 2.56 (t, J = 6.5 Hz, 2H), 1.85 (p, J = 6.5 Hz, 2H), 1.64 – 1.54 (m, 2H), 1.49 (s, 9H), 1.45 (s, 9H), 1.35 – 1.16 (m, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.47, 160.50, 157.51, 150.95, 142.34, 140.64, 137.92, 129.73, 128.11, 128.00, 118.31, 85.39, 78.26, 75.21, 53.50, 47.56, 41.09, 29.30, 29.20, 28.56, 27.82, 27.69, 26.56, 26.39, 25.87. MS (LC-MS, ESI): m/z 734.44 [M+H$^+$]; $C_{43}H_{55}N_7O_4$ (733.96).

2-tert-Butoxycarbonyl-1-(N'-tert-butoxycarbonylcarbodiimidooctyl)-3-[3-(1-trityl-1*H*-imidazol-4-yl)propyl]guanidine (113)

Compound **113** was prepared from **5** (1.0 g, 2.72 mmol), **91** (667 mg, 1.36 mmol), $HgCl_2$ (1.48 g, 5.44 mmol) and NEt_3 (1.13 mL, 8.16 mmol) in DCM (20 mL) conforming to the general procedure yielding a yellow oil (380 mg, 37%): R_f=0.54 (DCM/MeOH/NH_3 98:2:0.1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.93 (bs, 1H), 7.31 – 7.23 (m, 10H), 7.11 – 7.02 (m, 6H), 6.51 (s, 1H), 3.45 – 3.08 (m, 6H), 2.54 (t, J = 6.4 Hz, 2H), 1.89 – 1.77 (m, 2H), 1.59 (p, J = 7.3, 6.2 Hz, 2H), 1.47 (s, 9H), 1.43 (s, 9H), 1.34 – 1.06 (m, 10H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.18, 160.57, 157.07, 150.97, 142.33, 140.61, 137.94, 129.70, 128.06, 128.00, 118.27, 85.29, 78.30, 75.19, 53.53, 47.68, 41.37, 29.63, 29.11, 28.88, 28.70, 28.55, 27.81, 27.74, 26.80, 26.02, 25.89. MS (LC-MS, ESI): m/z 762.47 [M+H$^+$]; $C_{45}H_{59}N_7O_4$ (762.01).

2-tert-Butoxycarbonyl-1-(N'-tert-butoxycarbonylcarbodiimidodecyl)-3-[3-(1-trityl-1*H*-imidazol-4-yl)propyl]guanidine (114)

Compound **114** was prepared from **5** (1.0 g, 2.72 mmol), **92** (706 mg, 1.36 mmol), $HgCl_2$ (1.48 g, 5.44 mmol) and NEt_3 (1.13 mL, 8.16 mmol) in DCM (20 mL) conforming to the general procedure yielding a yellow oil (510 mg, 47%): R_f=0.57 (DCM/MeOH/NH_3 98:2:0.1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.43 (bs, 1H), 7.28 – 7.18 (m, 10H), 7.06 (m, 6H), 6.48 (s, 1H), 3.50 – 2.89 (m, 6H), 2.50 (t, J = 6.9 Hz, 2H), 1.94 – 1.68 (m, 2H), 1.66 – 1.48 (m, 2H), 1.45 (s, 9H), 1.33 (s, 9H), 1.29 – 1.04 (m, 14H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.27, 160.47, 156.02, 150.97, 142.49, 140.90, 137.95, 129.68, 127.98, 127.95, 118.24, 85.21, 78.63, 75.16, 53.54, 47.68, 41.37, 29.59, 29.42, 29.28, 29.24, 29.15, 28.95, 28.66, 27.79, 27.75, 26.89, 26.06, 25.69. MS (LC-MS, ESI): m/z 790.50 [M+H$^+$]; $C_{47}H_{63}N_7O_4$ (790.07).

1-(4-Aminobutyl)-3-[3-(1*H*-imidazol-4-yl)propyl]guanidine (116)

The title compound was prepared from **94** (440 mg, 0.65 mmol), TFA (4 mL) and DCM (16 mL) according to the general procedure, yielding a yellow oil (280 mg, 75%): RP-HPLC: 100%, (t_R = 6.35, *k* = 1.47). ^{1}H NMR (300 MHz, CD_3OD, tri-trifluoroacetate) δ 8.81 (d, J = 1.4 Hz, 1H), 7.34 (d, J = 1.0 Hz, 1H), 3.24 (t, J = 7.0 Hz, 4H), 2.96 (t, J = 6.9 Hz, 2H), 2.81 (t, J = 7.4 Hz, 2H), 1.97 (p, J = 7.3 Hz, 2H), 1.78 – 1.60 (m, 4H). ^{13}C NMR (75 MHz, CD_3OD, tri-trifluoroacetate) δ 157.62, 134.92, 134.55, 116.99, 41.98, 41.63, 40.26, 28.80, 26.86, 25.79, 22.55. HRMS (ESI-MS): m/z [M+H$^+$] calculated for $C_{11}H_{23}N_6^+$: 239.1979, found 239.1979; $C_{11}H_{22}N_6$ x 3 TFA. (580.41).

1-(6-Aminohexyl)-3-[3-(1*H*-imidazol-4-yl)propyl]guanidine (117)

The title compound was prepared from **95** (600 mg, 0.85 mmol), TFA (4 mL) and DCM (16 mL) according to the general procedure, yielding a yellow oil (330 mg, 64%): RP-HPLC: 100%, (t_R = 7.00, *k* = 1.72). ^{1}H NMR (300 MHz, CD_3OD, tri-trifluoroacetate) δ 8.80 (d, J = 1.4

Hz, 1H), 7.34 (d, J = 1.3 Hz, 1H), 3.26 (t, J = 7.0 Hz, 2H), 3.19 (t, J = 7.2 Hz, 2H), 2.92 (t, J = 7.7 Hz, 2H), 2.80 (t, J = 7.6 Hz, 2H), 1.96 (p, J = 7.3 Hz, 2H), 1.71 – 1.56 (m, 4H), 1.47 – 1.38 (m, 4H). ^{13}C NMR (75 MHz, CD_3OD, tri-trifluoroacetate) δ 157.57, 134.89, 134.57, 116.98, 42.50, 41.61, 40.62, 29.73, 28.83, 28.49, 28.41, 27.27, 27.12. HRMS (ESI-MS): m/z [M+H$^+$] calculated for $C_{13}H_{27}N_6^+$: 267.2292, found 267.2292; $C_{13}H_{26}N_6$ x 3 TFA. (608.46).

1-(8-Aminooctyl)-3-[3-(1*H*-imidazol-4-yl)propyl]guanidine (118)

The title compound was prepared from **96** (480 mg, 0.65 mmol), TFA (4 mL) and DCM (16 mL) according to the general procedure, yielding a yellow oil (250 mg, 60%): RP-HPLC: 100%, (t_R = 8.56, *k* = 2.33). ^{1}H NMR (300 MHz, CD_3OD, tri-trifluoroacetate) δ 8.80 (d, J = 1.4 Hz, 1H), 7.34 (d, J = 1.3 Hz, 1H), 3.26 (t, J = 7.0 Hz, 2H), 3.18 (t, J = 7.2 Hz, 2H), 2.90 (t, J = 7.1 Hz, 2H), 2.80 (t, J = 7.2 Hz, 2H), 1.96 (p, J = 7.4 Hz, 2H), 1.67 – 1.57 (m, 4H), 1.42 – 1.33 (m, 8H). ^{13}C NMR (75 MHz, CD_3OD, tri-trifluoroacetate) δ 157.57, 134.92, 134.57, 116.98, 42.65, 41.59, 40.73, 30.17, 29.93, 28.84, 28.60, 27.69, 27.44, 26.86, 22.55. HRMS (ESI-MS): m/z [M+H$^+$] calculated for $C_{15}H_{31}N_6^+$: 295.2605, found 295.2606; $C_{15}H_{30}N_6$ x 3 TFA (636.52).

1-(10-Aminodecyl)-3-[3-(1*H*-imidazol-4-yl)propyl]guanidine (119)

The title compound was prepared from **97** (590 mg, 0.77 mmol), TFA (4 mL) and DCM (16 mL) according to the general procedure, yielding a yellow oil (340 mg, 66%): RP-HPLC: 100%, (t_R = 9.89, *k* = 2.85). ^{1}H NMR (300 MHz, CD_3OD, tri-trifluoroacetate) δ 8.80 (d, J = 1.4 Hz, 1H), 7.34 (s, 1H), 3.26 (t, J = 7.0 Hz, 2H), 3.17 (t, J = 7.2 Hz, 2H), 2.90 (t, J = 7.7 Hz, 2H), 2.80 (t, J = 7.8 Hz, 2H), 1.96 (p, J = 7.3 Hz, 2H), 1.65 – 1.57 (m, 4H), 1.38 – 1.32 (m, 12H). ^{13}C NMR (75 MHz, CD_3OD, tri-trifluoroacetate) δ 157.56, 134.90, 134.56, 116.98, 42.67, 41.58, 40.75, 30.59, 30.50, 30.39, 30.26, 29.96, 28.83, 28.62, 27.80, 27.49, 22.55. HRMS (ESI-MS): m/z [M+H$^+$] calculated for $C_{17}H_{35}N_6^+$: 323.2918, found 323.2917; $C_{17}H_{34}N_6$ x 3 TFA (664.57).

1-(12-Aminododecyl)-3-[3-(1*H*-imidazol-4-yl)propyl]guanidine (120)

The title compound was prepared from **98** (700 mg, 0.88 mmol), TFA (4 mL) and DCM (16 mL) according to the general procedure, yielding a yellow oil (430 mg, 70%): RP-HPLC: 97%, (t_R = 11.13, *k* = 3.33). ^{1}H NMR (300 MHz, CD_3OD, tri-trifluoroacetate) δ 8.80 (d, J = 1.4 Hz, 1H), 7.34 (d, J = 1.3 Hz, 1H), 3.26 (t, J = 7.1 Hz, 2H), 3.17 (t, J = 7.2 Hz, 2H), 2.90 (t, J = 7.8 Hz, 2H), 2.80 (t, J = 7.8 Hz, 2H), 1.96 (p, J = 7.3 Hz, 2H), 1.71 – 1.51 (m, 4H), 1.38 – 1.28 (m, 16H). ^{13}C NMR (75 MHz, CD_3OD, tri-trifluoroacetate) δ 157.87, 134.90, 134.57, 116.97, 42.68, 41.59, 40.76, 30.76, 30.73, 30.67, 30.59, 30.45, 30.30, 29.98, 28.83, 28.63, 27.83, 27.51, 22.56. HRMS (ESI-MS): m/z [M+H$^+$] calculated for $C_{19}H_{39}N_6^+$: 351.3231, found 351.3229; $C_{19}H_{38}N_6$ x 3 TFA (692.62).

1-(12-Aminododecyl)-3-[3-(2-amino-4-methylthiazol-5-yl)propyl]guanidine (121)

The title compound was prepared from **99** (520 mg, 0.75 mmol), TFA (4 mL) and DCM (16 mL) according to the general procedure, yielding a yellow oil (290 mg, 53%): RP-HPLC: 98%, (t_R = 11.47, *k* = 3.46). ^{1}H NMR (300 MHz, CD_3OD, tri-trifluoroacetate) δ 3.26 – 3.15 (m, 4H), 2.90 (t, J = 7.3 Hz, 2H), 2.69 (t, J = 7.2 Hz, 2H), 2.18 (s, 3H), 1.84 (p, J = 7.5 Hz, 2H), 1.69 – 1.57 (m, 4H), 1.35 – 1.28 (m, 16H). ^{13}C NMR (75 MHz, CD_3OD, tri-trifluoroacetate) δ 170.39, 162.92 (q, J = 35.3 Hz), 157.65, 157.59, 132.38, 118.50, 42.65, 41.45, 40.78, 30.68, 30.66, 30.57, 30.52, 30.39, 30.25, 29.97, 28.63, 28.58, 27.78, 27.49, 23.51, 11.47. HRMS (ESI-MS): m/z [M+H$^+$] calculated for $C_{20}H_{41}N_6S^+$: 397.3108, found 397.3105; $C_{20}H_{40}N_6S$ x 3 TFA (738.71).

1-(12-Aminododecyl)-3-[3-(2-aminothiazol-5-yl)propyl]guanidine (122)

The title compound was prepared from **100** (500 mg, 0.73 mmol), TFA (4 mL) and DCM (16 mL) according to the general procedure, yielding a yellow oil (380 mg, 72%): RP-HPLC: 100%, (t_R = 10.74, *k* = 3.18). ^{1}H NMR (300 MHz, CD_3OD, tri-trifluoroacetate) δ 6.97 (s, 1H), 3.30 – 3.13 (m, 4H), 2.90 (t, J = 7.2 Hz, 2H), 2.72 (t, J = 7.1 Hz, 2H), 1.89 (p, J = 7.4 Hz, 2H), 1.67 –

1.53 (m, 4H), 1.37 – 1.26 (m, 16H). ^{13}C NMR (75 MHz, CD_3OD, tri-trifluoroacetate) δ 171.84, 162.81 (q, J = 35.6 Hz), 157.61, 157.56, 126.49, 123.06, 42.65, 41.44, 40.78, 30.67, 30.65, 30.51, 30.38, 30.25, 29.95, 28.63, 28.58, 28.15, 27.78, 27.49, 24.85. HRMS (ESI-MS): m/z [M+H$^+$] calculated for $C_{19}H_{39}N_6S^+$: 383.2951, found 383.2951; $C_{19}H_{38}N_6S$ x 3 TFA (724.68).

1-(4-Guanidinobutyl)-3-[3-(1*H*-imidazol-4-yl)propyl]guanidine (123)

The title compound was prepared from **101** (560 mg, 0.68 mmol), TFA (4 mL) and DCM (16 mL) according to the general procedure, yielding a colorless foamlike solid (290 mg, 68%): RP-HPLC: 99%, (t_R = 6.50, *k* = 1.53). ^{1}H NMR (300 MHz, CD_3OD, tri-trifluoroacetate) δ 8.79 (d, J = 1.5 Hz, 1H), 7.35 (d, J = 1.4 Hz, 1H), 3.33 – 3.19 (m, 6H), 2.81 (t, J = 7.7 Hz, 2H), 1.97 (p, J = 7.2 Hz, 2H), 1.65 (p, J = 3.3 Hz, 4H). ^{13}C NMR (75 MHz, CD_3OD, tri-trifluoroacetate) δ 158.75, 157.56, 134.82, 134.57, 117.05, 42.19, 42.05, 41.62, 28.86, 27.10, 22.56. HRMS (ESI-MS): m/z [M+H$^+$] calculated for $C_{12}H_{25}N_8^+$: 281.2197, found 281.2201; $C_{12}H_{25}N_8$ x 3 TFA (622.45).

1-(6-Guanidinohexyl)-3-[3-(1*H*-imidazol-4-yl)propyl]guanidine (124)

The title compound was prepared from **102** (690 mg, 0.81 mmol), TFA (4 mL) and DCM (16 mL) according to the general procedure, yielding a colorless foamlike solid (410 mg, 78%): RP-HPLC: 97%, (t_R = 7.47, *k* = 1.91). ^{1}H NMR (300 MHz, CD_3OD, tri-trifluoroacetate) δ 8.77 (s, 1H), 7.32 (s, 1H), 3.28 – 3.13 (m, 6H), 2.80 (t, J = 7.8 Hz, 2H), 1.95 (p, J = 7.2 Hz, 2H), 1.67 – 1.56 (m, 4H), 1.39 (p, J = 3.5 Hz, 4H). ^{13}C NMR (75 MHz, CD_3OD, tri-trifluoroacetate) δ 158.73, 157.55, 134.82, 134.57, 117.01, 42.52, 42.35, 41.57, 29.78, 29.75, 28.86, 27.33, 27.31, 22.54. HRMS (ESI-MS): m/z [M+H$^+$] calculated for $C_{14}H_{29}N_8^+$: 309.2510, found 309.2507; $C_{14}H_{28}N_8$ x 3 TFA (650.50).

1-(8-Guanidinooctyl)-3-[3-(1*H*-imidazol-4-yl)propyl]guanidine (125)

The title compound was prepared from **103** (370 mg, 0.42 mmol), TFA (4 mL) and DCM (16 mL) according to the general procedure, yielding a colorless foamlike solid (260 mg, 91%): RP-HPLC: 100%, (t_R = 8.93, *k* = 2.47). ^{1}H NMR (300 MHz, CD_3OD, tri-trifluoroacetate) δ 8.77 (s, 1H), 7.32 (s, 1H), 3.25 (t, J = 7.0 Hz, 2H), 3.15 (q, J = 6.8 Hz, 4H), 2.79 (t, J = 7.7 Hz, 2H), 1.95 (p, J = 7.3 Hz, 2H), 1.63 – 1.53 (m, 4H), 1.42 – 1.31 (m, 8H). ^{13}C NMR (75 MHz, CD_3OD, tri-trifluoroacetate) δ 158.73, 157.56, 134.82, 134.58, 116.99, 42.62, 42.44, 41.56, 30.22, 30.20, 29.89, 29.85, 28.86, 27.66, 27.63, 22.. HRMS (ESI-MS): m/z [M+H$^+$] calculated for $C_{16}H_{33}N_8^+$: 337.2823, found 337.2822; $C_{16}H_{32}N_8$ x 3 TFA (678.56).

1-(10-Guanidinodecyl)-3-[3-(1*H*-imidazol-4-yl)propyl]guanidine (126)

The title compound was prepared from **104** (550 mg, 0.61 mmol), TFA (4 mL) and DCM (16 mL) according to the general procedure, yielding a colorless foamlike solid (380 mg, 89%): RP-HPLC: 96%, (t_R = 10.23, *k* = 2.98). ^{1}H NMR (300 MHz, CD_3OD, tri-trifluoroacetate) δ 8.76 (s, 1H), 7.31 (s, 1H), 3.26 (t, J = 7.0 Hz, 2H), 3.16 (q, J = 6.9 Hz, 4H), 2.80 (t, J = 7.8 Hz, 2H), 1.96 (p, J = 7.2 Hz, 2H), 1.66 – 1.50 (m, 4H), 1.34 – 1.27 (m, 12H). ^{13}C NMR (75 MHz, CD_3OD, tri-trifluoroacetate) δ 158.80, 157.56, 134.80, 134.60, 117.02, 42.66, 42.48, 41.57, 30.56, 30.54, 30.31, 30.25, 29.92, 29.89, 28.89, 27.75, 27.71, 22.55. HRMS (ESI-MS): m/z [M+H$^+$] calculated for $C_{18}H_{37}N_8^+$: 365.3136, found 365.3130; $C_{18}H_{36}N_8$ (706.61).

1-(12-Guanidinododecyl)-3-[3-(1*H*-imidazol-4-yl)propyl]guanidine (127)

The title compound was prepared from **105** (660 mg, 0.71 mmol), TFA (4 mL) and DCM (16 mL) according to the general procedure, yielding a colorless foamlike solid (490 mg, 95%): RP-HPLC: 99%, (t_R = 11.50, *k* = 3.47). ^{1}H NMR (300 MHz, CD_3OD, tri-trifluoroacetate) δ 8.76 (s, 1H), 7.31 (s, 1H), 3.26 (t, J = 6.9 Hz, 2H), 3.16 (q, J = 6.8 Hz, 4H), 2.79 (t, J = 7.7 Hz, 2H), 1.96 (p, J = 7.3 Hz, 2H), 1.56 (t, J = 7.1 Hz, 4H), 1.36 – 1.26 (m, 16H). ^{13}C NMR (75 MHz, CD_3OD,

tri-trifluoroacetate) δ 158.75, 157.56, 134.79, 134.60, 117.01, 42.67, 42.49, 41.57, 30.69, 30.67, 30.65, 30.62, 30.36, 30.30, 29.93, 29.91, 28.89, 27.78, 27.74, 22.55. HRMS (ESI-MS): m/z [M+H$^+$] calculated for $C_{20}H_{41}N_8^+$: 393.3449, found 393.3451; $C_{20}H_{40}N_8$ x 3 TFA (734.67).

1-(8-Guanidinooctyl)-3-[3-(2-amino-4-methylthiazol-5-yl)propyl]guanidine (128)

The title compound was prepared from **106** (230 mg, 0.29 mmol), TFA (4 mL) and DCM (16 mL) according to the general procedure, yielding a yellow foamlike solid (160 mg, 75%): RP-HPLC: 98%, (t_R = 9.54, *k* = 2.71). ^{1}H NMR (300 MHz, CD_3OD, tri-trifluoroacetate) δ 3.26 – 3.13 (m, 6H), 2.67 (t, J = 7.6 Hz, 2H), 2.16 (s, 3H), 1.83 (p, J = 7.3 Hz, 2H), 1.61 – 1.55 (m, 4H), 1.39 – 1.34 (m, 8H). ^{13}C NMR (75 MHz, CD_3OD, tri-trifluoroacetate) δ 170.36, 158.71, 157.58, 132.41, 118.54, 42.64, 42.47, 41.46, 30.71, 30.57, 30.25, 29.93, 29.87, 27.70, 27.67, 23.50, 11.45. HRMS (ESI-MS): m/z [M+H$^+$] calculated for $C_{17}H_{35}N_8S^+$: 383.2700, found 383.2700; $C_{17}H_{34}N_8S$ x 3 TFA (724.64).

1-(8-Guanidinooctyl)-3-[3-(2-aminothiazol-5-yl)propyl]guanidine (129)

The title compound was prepared from **107** (300 mg, 0.39 mmol), TFA (4 mL) and DCM (16 mL) according to the general procedure, yielding a yellow foamlike solid (220 mg, 79%): RP-HPLC: 98%, (t_R = 9.64, *k* = 2.75). ^{1}H NMR (300 MHz, CD_3OD, tri-trifluoroacetate) δ 6.97 (s, 1H), 3.28 – 3.12 (m, 6H), 2.73 (t, J = 7.6 Hz, 2H), 1.88 (p, J = 7.3 Hz, 2H), 1.61 – 1.55 (m, 4H), 1.38 – 1.34 (m, 8H). ^{13}C NMR (75 MHz, CD_3OD, tri-trifluoroacetate) δ 171.82, 158.73, 157.55, 126.52, 123.09, 42.64, 42.46, 41.45, 30.31, 30.23, 30.18, 29.91, 29.87, 27.69, 27.65, 24.84. HRMS (ESI-MS): m/z [M+H$^+$] calculated for $C_{16}H_{33}N_8S^+$: 369.2543, found 369.2541; $C_{16}H_{32}N_8S$ x 3 TFA (710.62).

1-(12-Guanidinododecyl)-3-[3-(2-amino-4-methylthiazol-5-yl)propyl]guanidine (130)

The title compound was prepared from **108** (270 mg, 0.32 mmol), TFA (4 mL) and DCM (16 mL) according to the general procedure, yielding a yellow foamlike solid (180 mg, 72%): RP-HPLC: 98%, (t_R = 11.41, *k* = 3.44). ^{1}H NMR (300 MHz, CD_3OD, tri-trifluoroacetate) δ 3.27 – 3.11 (m, 6H), 2.67 (t, J = 7.7 Hz, 2H), 2.17 (s, 3H), 1.83 (p, J = 7.3 Hz, 2H), 1.61 – 1.54 (m, 4H), 1.37 – 1.30 (m, 16H). ^{13}C NMR (75 MHz, CD_3OD, tri-trifluoroacetate) δ 170.33, 158.70, 157.55, 132.38, 118.55, 42.66, 42.49, 41.46, 30.71, 30.69, 30.59, 30.39, 30.38, 30.23, 29.98, 29.92, 29.86, 27.79, 27.75, 23.51, 11.49. HRMS (ESI-MS): m/z [M+H$^+$] calculated for $C_{21}H_{43}N_8S^+$: 439.3326, found 439.3325; $C_{21}H_{42}N_8S$ x 3 TFA (780.75).

1-(12-Guanidinododecyl)-3-[3-(2-aminothiazol-5-yl)propyl]guanidine (131)

The title compound was prepared from **109** (240 mg, 0.29 mmol), TFA (4 mL) and DCM (16 mL) according to the general procedure, yielding a yellow foamlike solid (210 mg, 94%): RP-HPLC: 96%, (t_R = 11.55, *k* = 3.49). ^{1}H NMR (300 MHz, CD_3OD, tri-trifluoroacetate) δ 6.98 (s, 1H), 3.27 – 3.12 (m, 6H), 2.73 (t, J = 7.1 Hz, 2H), 1.88 (p, J = 7.3 Hz, 2H), 1.60 – 1.54 (m, 4H), 1.36 – 1.29 (m, 16H). ^{13}C NMR (75 MHz, CD_3OD, tri-trifluoroacetate) δ 171.81, 158.77, 157.53, 126.50, 123.06, 42.66, 42.49, 41.45, 30.70, 30.68, 30.66, 30.57, 30.51, 30.37, 30.35, 29.96, 29.92, 27.79, 27.75, 24.85. HRMS (ESI-MS): m/z [M+H$^+$] calculated for $C_{20}H_{41}N_8S^+$: 425.3169, found 425.3169; $C_{20}H_{40}N_8S$ x 3 TFA (766.73).

1-{3-[3-(3-(1*H*-Imidazol-4-yl)propyl)guanidino]propyl}urea (132)

The title compound was prepared from **110** (420 mg, 0.61 mmol), TFA (4 mL) and DCM (16 mL) according to the general procedure, yielding a yellow oil (140 mg, 38%): RP-HPLC: 99%, (t_R = 5.09, *k* = 0.98). ^{1}H NMR (300 MHz, CD_3OD, tri-trifluoroacetate) δ 8.79 (s, 1H), 7.35 (s, 1H), 3.50 – 3.38 (m, 4H), 3.36 – 3.12 (m, 2H), 2.86 (t, J = 6.5 Hz, 2H), 2.23 – 2.00 (m, 4H). ^{13}C NMR (75 MHz, CD_3OD, tri-trifluoroacetate) δ 162.92, 157.03, 134.96, 134.22, 117.12, 43.89,

41.53, 39.81, 27.34, 22.73, 21.66. HRMS (ESI-MS): m/z [M+H$^+$] calculated for $C_{11}H_{22}N_7O^+$: 268.1880, found 268.1877; $C_{11}H_{21}N_7O$ x 3 TFA (609.41).

1-{4-[3-(3-(1*H*-Imidazol-4-yl)propyl)guanidino]butyl}urea (133)

The title compound was prepared from **111** (390 mg, 0.55 mmol), TFA (4 mL) and DCM (16 mL) according to the general procedure, yielding a yellow oil (180 mg, 52%): RP-HPLC: 99%, (t_R = 6.45, *k* = 1.51). ^{1}H NMR (300 MHz, CD_3OD, tri-trifluoroacetate) δ 8.77 (s, 1H), 7.32 (s, 1H), 3.33 – 3.07 (m, 6H), 2.84 – 2.75 (t, J = 6.9 Hz, 2H), 1.96 (p, J = 7.6 Hz, 2H), 1.67 – 1.40 (m, 4H). ^{13}C NMR (75 MHz, CD_3OD, tri-trifluoroacetate) δ 162.58, 157.53, 134.83, 134.58, 116.98, 42.23, 41.55, 39.73, 28.81, 27.04, 22.54, 22.37. HRMS (ESI-MS): m/z [M+H$^+$] calculated for $C_{12}H_{24}N_7O^+$: 282.2037, found 282.2037; $C_{12}H_{23}N_7O$ x 3 TFA (623.43).

1-{6-[3-(3-(1*H*-Imidazol-4-yl)propyl)guanidino]hexyl}urea (134)

The title compound was prepared from **112** (420 mg, 0.57 mmol), TFA (4 mL) and DCM (16 mL) according to the general procedure, yielding a yellow oil (160 mg, 43%): RP-HPLC: 99%, (t_R = 7.46, *k* = 1.90). ^{1}H NMR (300 MHz, CD_3OD, tri-trifluoroacetate) δ 8.77 (s, 1H), 7.32 (s, 1H), 3.26 – 3.09 (m, 6H), 2.80 (t, J = 7.7 Hz, 2H), 1.96 (p, J = 7.3 Hz, 2H), 1.57 (p, J = 6.7 Hz, 2H), 1.49 (p, J = 6.6 Hz, 2H), 1.43 – 1.32 (m, 4H). ^{13}C NMR (75 MHz, CD_3OD, tri-trifluoroacetate) δ 162.40, 157.56, 134.83, 134.57, 116.98, 42.52, 41.56, 40.99, 30.89, 29.82, 28.82, 27.39, 27.33, 22.53. HRMS (ESI-MS): m/z [M+H$^+$] calculated for $C_{14}H_{28}N_7O^+$: 310.2350, found 310.2348; $C_{14}H_{27}N_7O$ x 3 TFA (651.49).

1-{8-[3-(3-(1*H*-Imidazol-4-yl)propyl)guanidino]octyl}urea (135)

The title compound was prepared from **113** (380 mg, 0.50 mmol), TFA (4 mL) and DCM (16 mL) according to the general procedure, yielding a yellow oil (210 mg, 62%): RP-HPLC: 98%, (t_R = 9.23, *k* = 2.59). ^{1}H NMR (300 MHz, CD_3OD, tri-trifluoroacetate) δ 8.78 (s, 1H), 7.33

(s, 1H), 3.26 (t, J = 7.1 Hz, 2H), 3.22 – 3.16 (m, 2H), 3.08 (t, J = 6.9 Hz, 2H), 2.80 (t, J = 7.7 Hz, 2H), 1.96 (p, J = 7.3 Hz, 2H), 1.58 (p, J = 6.9 Hz, 2H), 1.47 (p, J = 6.8 Hz, 2H), 1.37 – 1.32 (m, 8H). ^{13}C NMR (75 MHz, CD_3OD, tri-trifluoroacetate) δ 162.42, 157.56, 134.86, 134.57, 116.98, 42.62, 41.57, 41.04, 31.10, 30.28, 30.23, 29.88, 28.84, 27.78, 27.65, 22.54. HRMS (ESI-MS): m/z [M+H$^+$] calculated for $C_{16}H_{32}N_7O^+$: 338.2663, found 338.2662; $C_{16}H_{31}N_7O$ x 3 TFA (679.54).

1-{10-[3-(3-(1*H*-Imidazol-4-yl)propyl)guanidino]decyl}urea (136)

The title compound was prepared from **114** (410 mg, 0.52 mmol), TFA (4 mL) and DCM (16 mL) according to the general procedure, yielding a yellow oil (230 mg, 63%): RP-HPLC: 99%, (t_R = 9.55, *k* = 2.72). ^{1}H NMR (300 MHz, CD_3OD, tri-trifluoroacetate) δ 8.75 (s, 1H), 7.30 (s, 1H), 3.26 (t, J = 6.9 Hz, 2H), 3.16 (t, J = 7.1 Hz, 2H), 3.09 (t, J = 7.0 Hz, 2H), 2.79 (t, J = 7.7 Hz, 2H), 1.94 (p, J = 7.4 Hz, 2H), 1.56 (p, J = 7.0 Hz, 2H), 1.48 (p, J = 6.1 Hz, 2H), 1.39 – 1.22 (m, 12H). ^{13}C NMR (75 MHz, CD_3OD, tri-trifluoroacetate) δ 162.34, 157.56, 134.79, 134.58, 116.98, 42.65, 41.57, 41.41, 30.86, 30.66, 30.56, 30.54, 30.37, 29.91, 28.86, 27.85, 27.72, 22.54. HRMS (ESI-MS): m/z [M+H$^+$] calculated for $C_{18}H_{36}N_7O^+$: 366.2976, found 366.2973; $C_{18}H_{35}N_7O$ x 3 TFA (707.60).

N-{[3-(1-Trityl-1*H*-imidazol-4-yl)propyl]carbamoyl}benzamide (139)

Compound **139** was prepared according to the general procedure described in 4.2.5. using **5** (1.20 g, 3.27 mmol) and **138** (0.40 mL, 3.27 mmol) in 50 mL DCM. After column chromatography (DCM/MeOH 98/2 - 95/5 v/v) the product was obtained as a yellow oil (1.06 g, 63%): R_f=0.14 (DCM/MeOH 98:2); ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.14 (bs, 1H), 8.88 (bs, 1H), 8.07 – 7.90 (m, 2H), 7.55 – 7.46 (m, 1H), 7.46 – 7.39 (m, 2H), 7.37 (s, 1H), 7.32 – 7.27 (m, 9H), 7.13 (m, 6H), 6.57 (s, 1H), 3.40 (q, J = 6.7 Hz, 2H), 2.64 (t, J = 7.6 Hz, 2H), 1.96 (p, J = 7.2 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.39, 154.83, 142.55, 140.74, 138.50, 132.91, 132.52,

129.79, 129.74, 128.62, 128.03, 127.99, 118.00, 75.12, 39.53, 29.20, 25.89. HRMS (ESI-MS): m/z [M+H$^+$] calculated for $C_{33}H_{31}N_4O_2^+$: 515.2442, found 515.2451; $C_{33}H_{30}N_4O_2$ (514.63).

1-[3-(1*H*-Imidazol-4-yl)propyl]thiourea (142)

Compound **142** was prepared according to the general procedure described in 4.2.6. using **141** (160 mg, 0.55 mmol) and K_2CO_3 (153 mg, 1.11 mmol) in 20 mL MeOH/H_2O (7/3 v/v). The crude product was purified by column chromatography (DCM/MeOH/7M NH_3 in MeOH 90/8/2 v/v/v) yielding a colorless solid (80 mg, 78%): R_f=0.16 (DCM/MeOH/NH_3 90:10:0.1); mp 142.2 °C. ^{1}H NMR (300 MHz, CD_3OD) δ 7.63 (s, 1H), 6.84 (s, 1H), 3.50 + 3.16 (2 bs, 1.25H + 0.75H, (thione-thiol tautomerism)), 2.62 (t, J = 7.5 Hz, 2H), 1.87 (p, J = 7.4 Hz, 2H). ^{13}C NMR (75 MHz, CD_3OD) δ 184.79, 137.62, 135.85, 117.85, 45.36, 30.20, 24.82. HRMS (ESI-MS): m/z [M+H$^+$] calculated for $C_7H_{13}N_4S^+$: 185.0855, found 185.0855; $C_7H_{12}N_4S$ (184.26); Anal. calculated for $C_7H_{12}N_4S$ x 0.26 H_2O: C 44.50, H 6.68, N 29.64, found: C 44.91, H 6.58, N 29.24.

N-{[3-(1*H*-Imidazol-4-yl)propyl]carbamoyl}benzamide (144)

The title compound was prepared from **139** (0.98 g, 1.90 mmol), TFA (4 mL) and DCM (16 mL) according to the general procedure (*cf.* 4.2.11). The crude product was purified by column chromatography (DCM/MeOH/7M NH_3 in MeOH 95/3/2 v/v/v) yielding **144** as free base and yellow solid (300 mg, 58%): R_f=0.10 (DCM/MeOH 95:5); mp 170.2 °C. ^{1}H NMR (300 MHz, CD_3OD) δ 7.97 – 7.86 (m, 2H), 7.66 – 7.60 (m, 1H), 7.58 (s, 1H), 7.53 – 7.44 (m, 2H), 6.84 (s, 1H), 3.36 (t, J = 6.9 Hz, 2H), 2.67 (t, J = 7.4 Hz, 2H), 1.92 (p, J = 7.1 Hz, 2H). ^{13}C NMR (75 MHz, CD_3OD) δ 170.45, 156.15, 137.47, 135.93, 134.30, 134.00, 129.79, 129.04, 118.02, 40.11, 30.51, 24.90. HRMS (ESI-MS): m/z [M+H$^+$] calculated for $C_{14}H_{17}N_4O_2^+$: 273.1346, found 273.1352; $C_{14}H_{16}N_4O$ (272.31); Anal. calculated for $C_{14}H_{16}N_4O_2$ x 0.1 H_2O: C 61.35, H 5.96, N 20.44, found: C 61.61, H 6.12, N 20.17.

2. RP-HPLC chromatograms 115-136

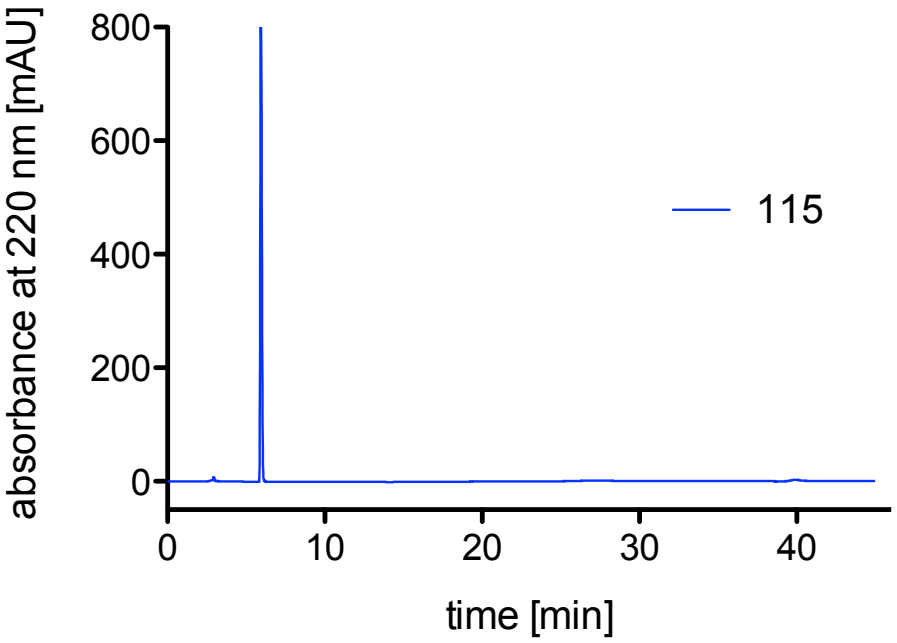

Figure S1. RP-HPLC analysis of compound **115**.

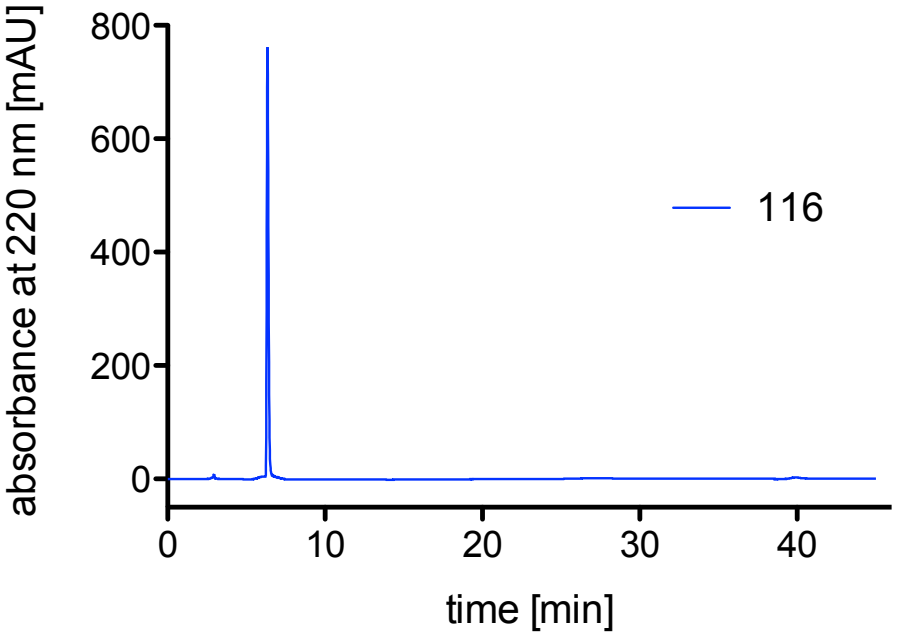

Figure S2. RP-HPLC analysis of compound **116**.

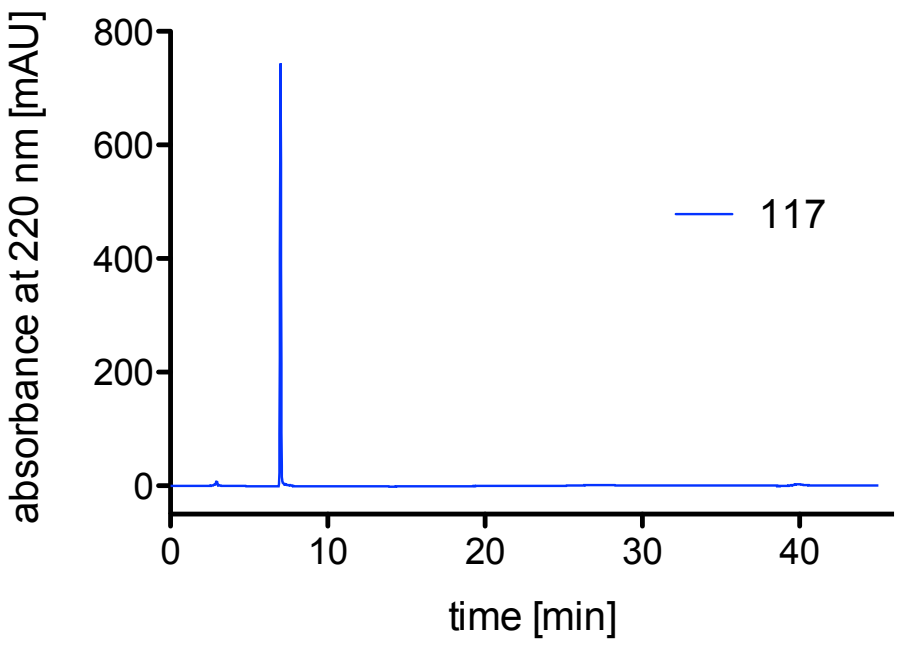

Figure S3. RP-HPLC analysis of compound **117**.

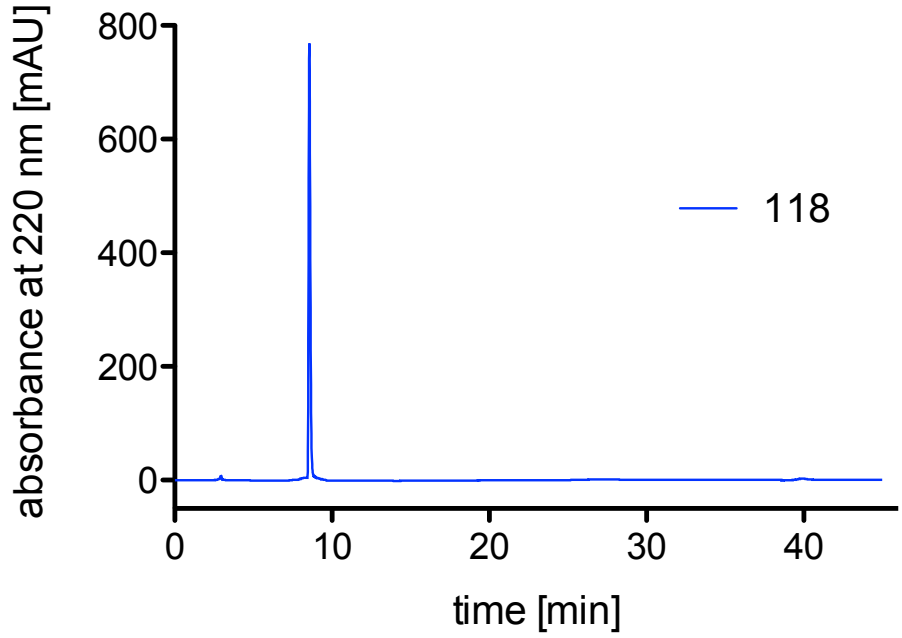

Figure S4. RP-HPLC analysis of compound **118**.

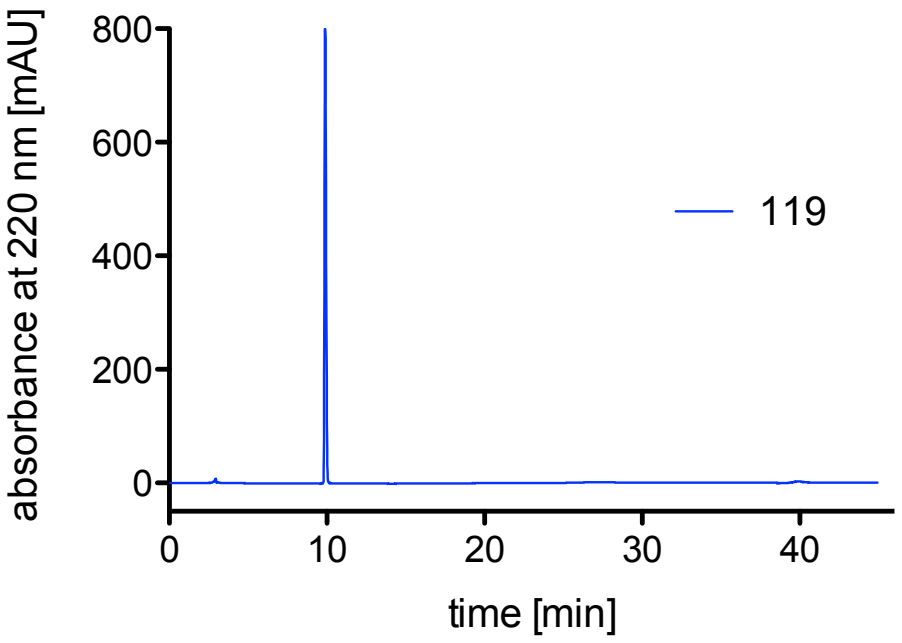

Figure S5. RP-HPLC analysis of compound **119**.

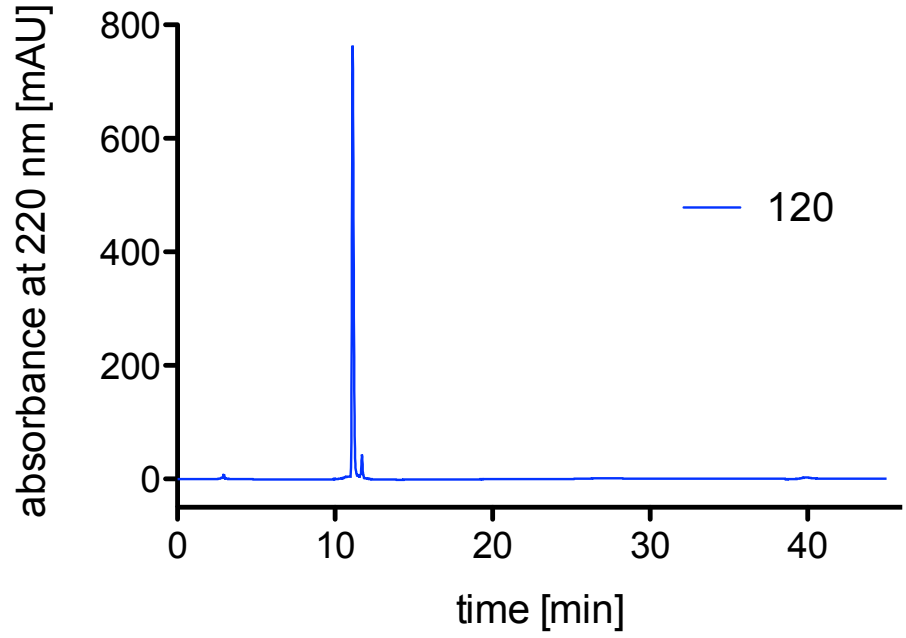

Figure S6. RP-HPLC analysis of compound **120**.

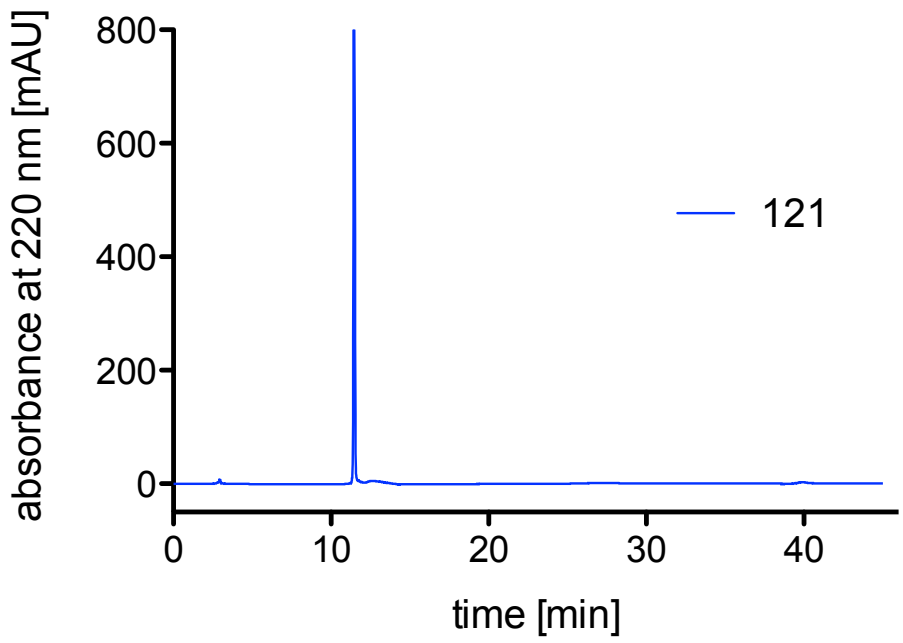

Figure S7. RP-HPLC analysis of compound **121**.

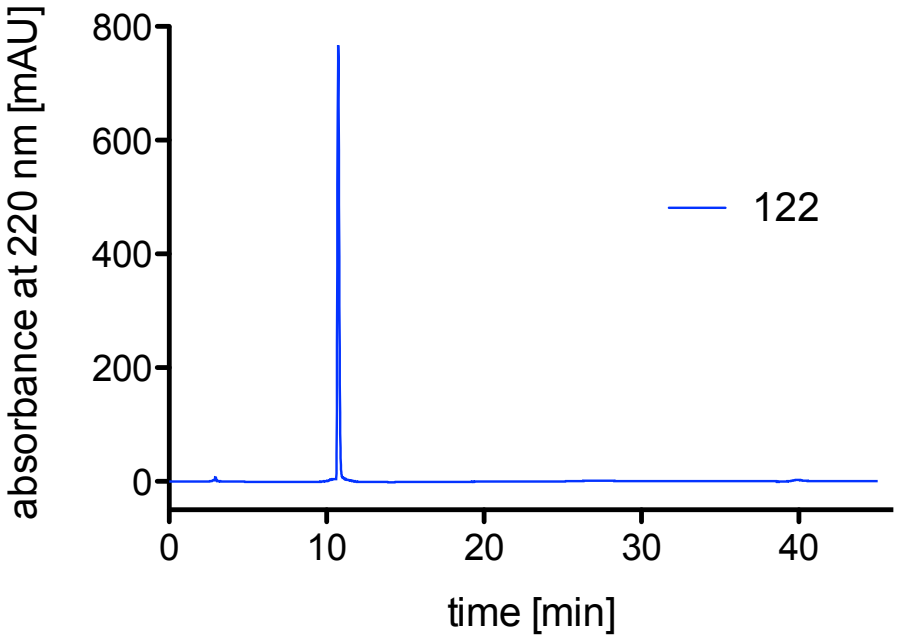

Figure S8. RP-HPLC analysis of compound **122**.

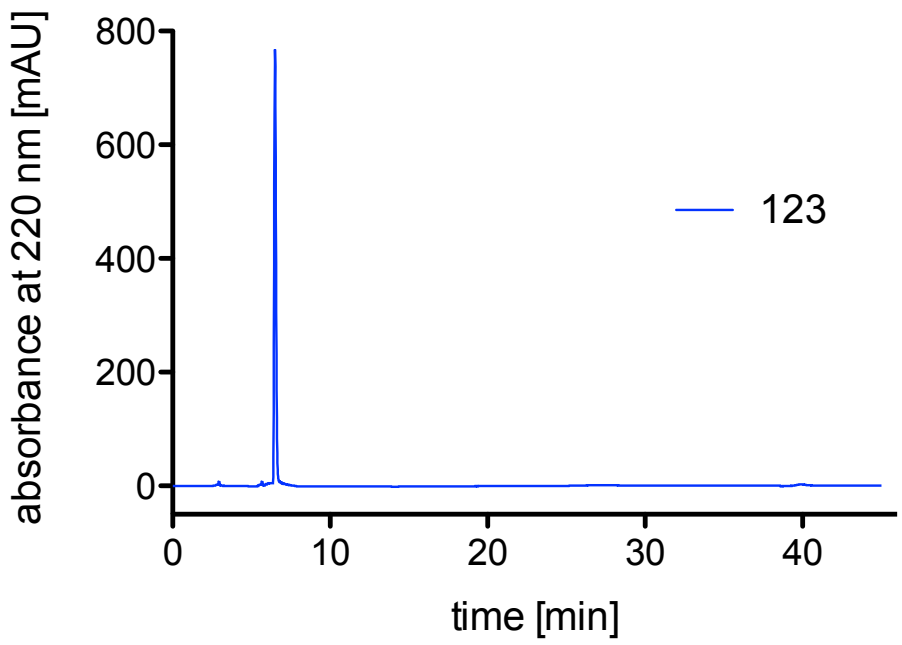

Figure S9. RP-HPLC analysis of compound **123**.

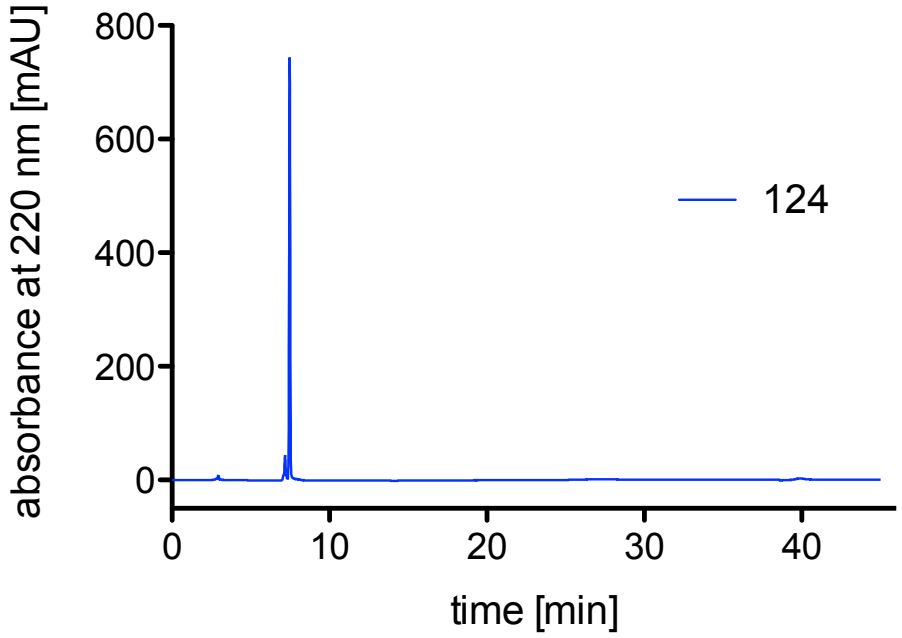

Figure S10. RP-HPLC analysis of compound **124**.

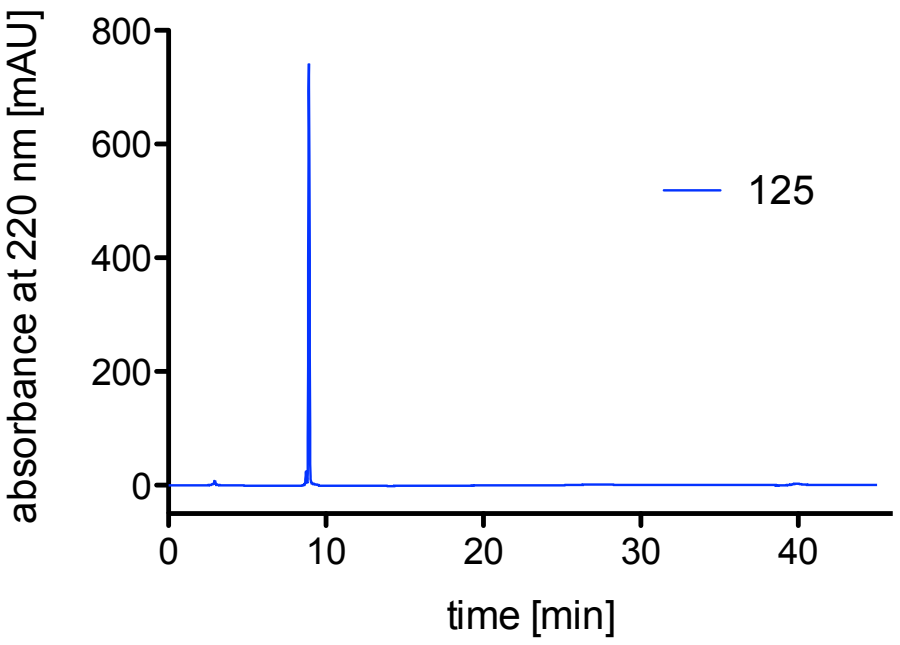

Figure S11. RP-HPLC analysis of compound **125**.

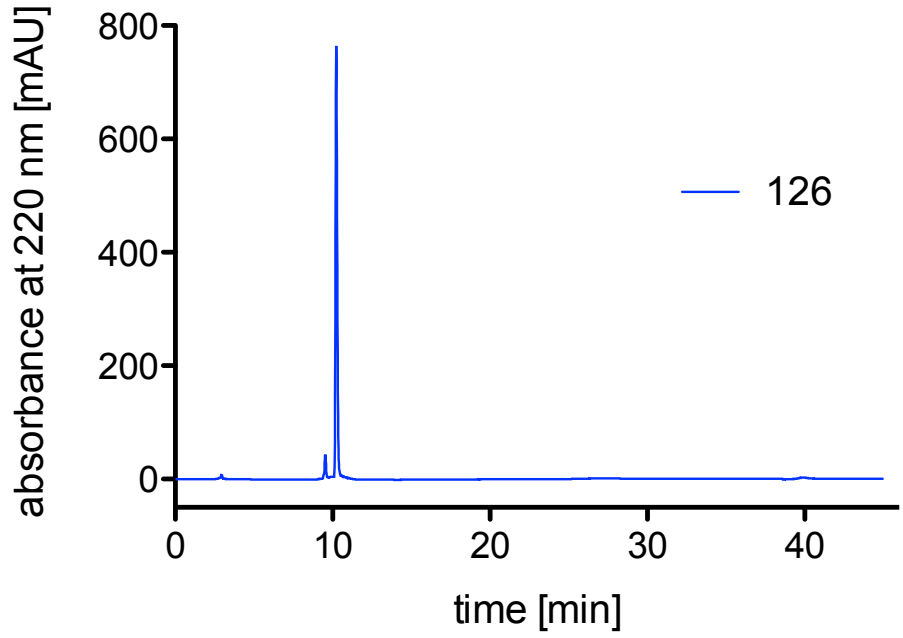

Figure S12. RP-HPLC analysis of compound **126**.

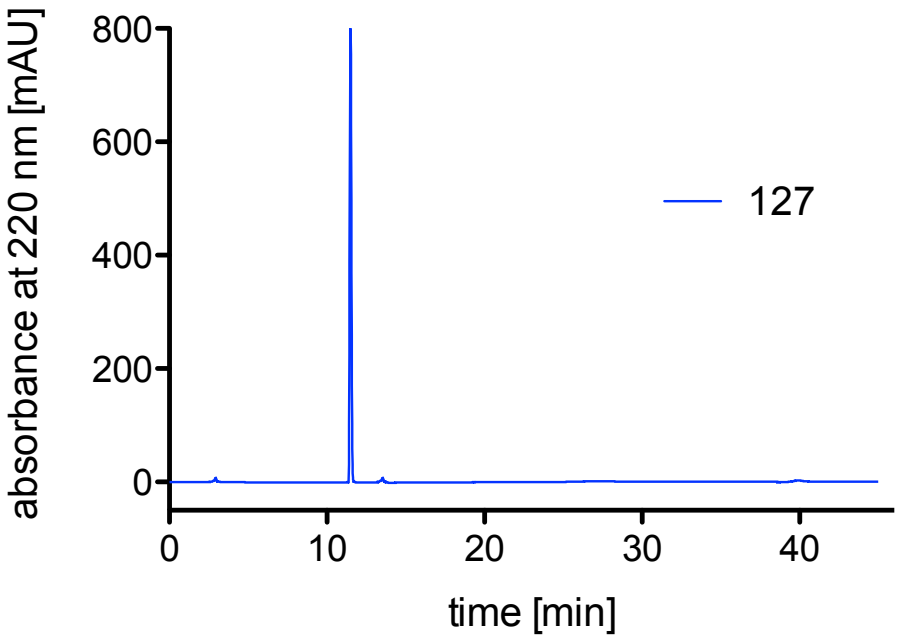

Figure S13. RP-HPLC analysis of compound **127**.

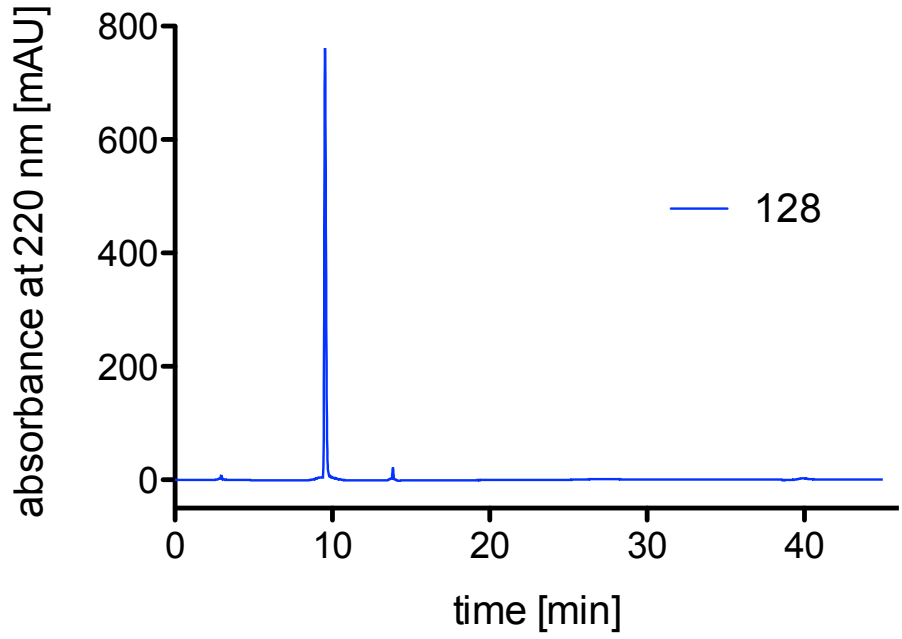

Figure S14. RP-HPLC analysis of compound **128**.

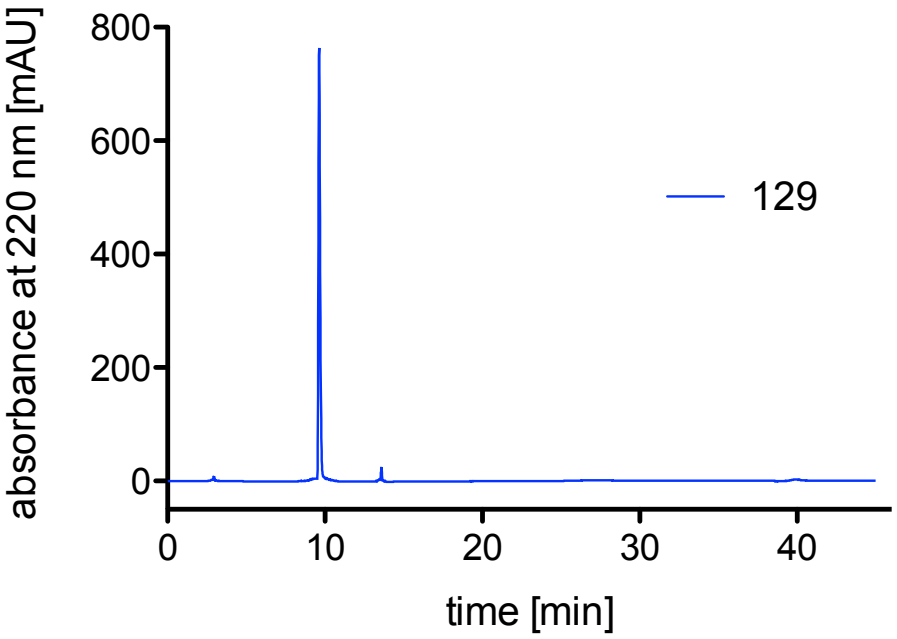

Figure S15. RP-HPLC analysis of compound **129**.

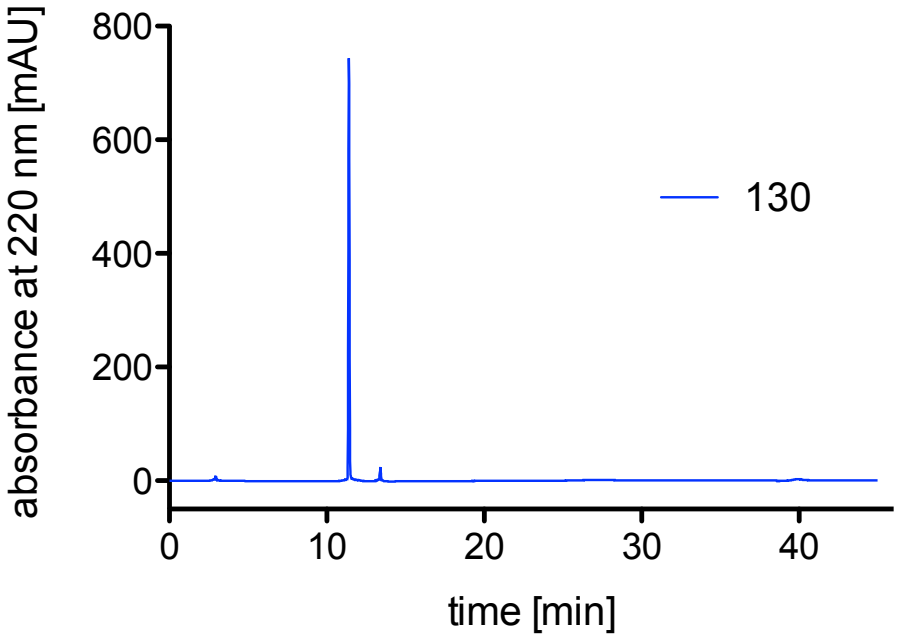

Figure S16. RP-HPLC analysis of compound **130**.

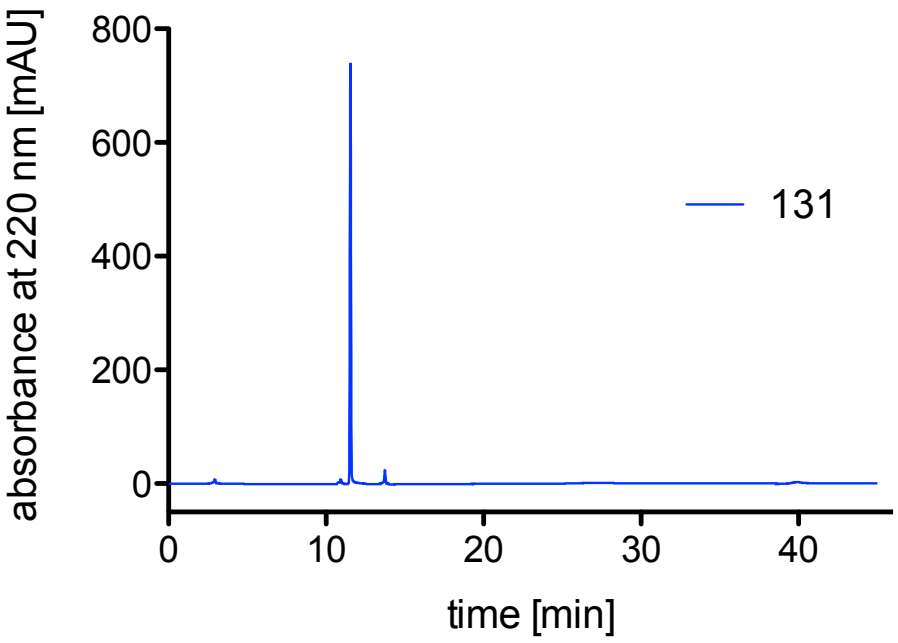

Figure S17. RP-HPLC analysis of compound **131**

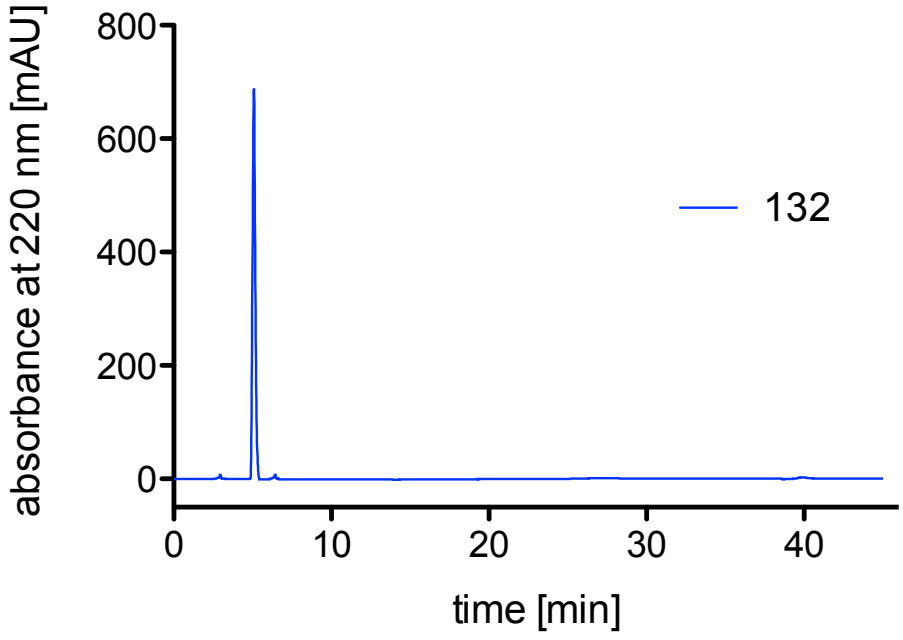

Figure S18. RP-HPLC analysis of compound **132**.

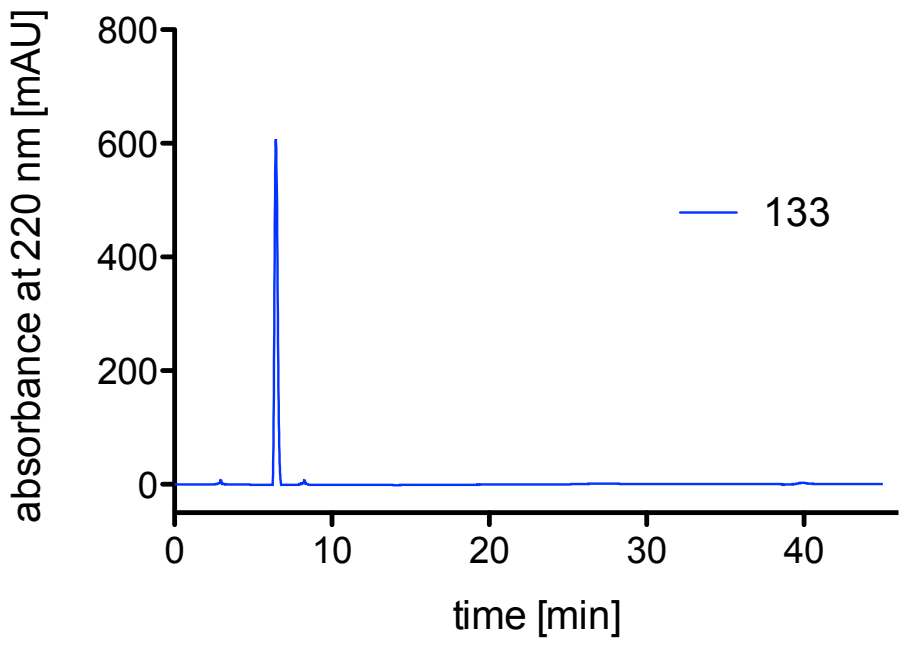

Figure S19. RP-HPLC analysis of compound **133**.

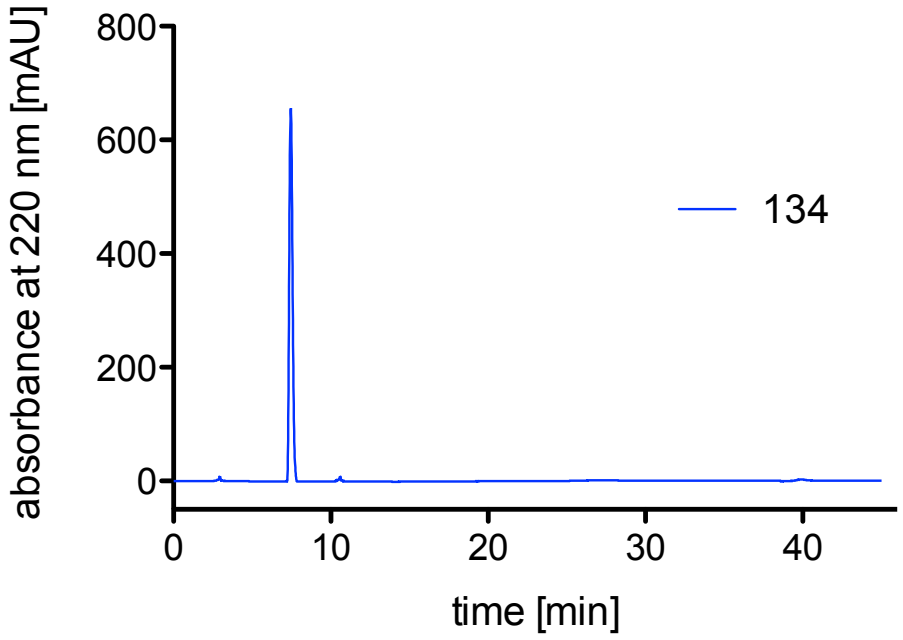

Figure S20. RP-HPLC analysis of compound **134**.

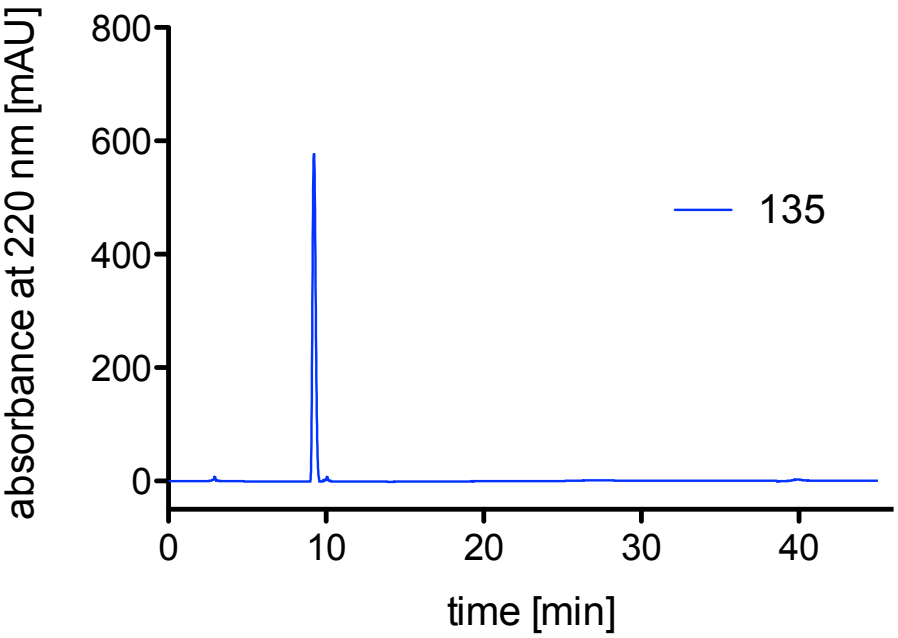

Figure S21. RP-HPLC analysis of compound **135**.

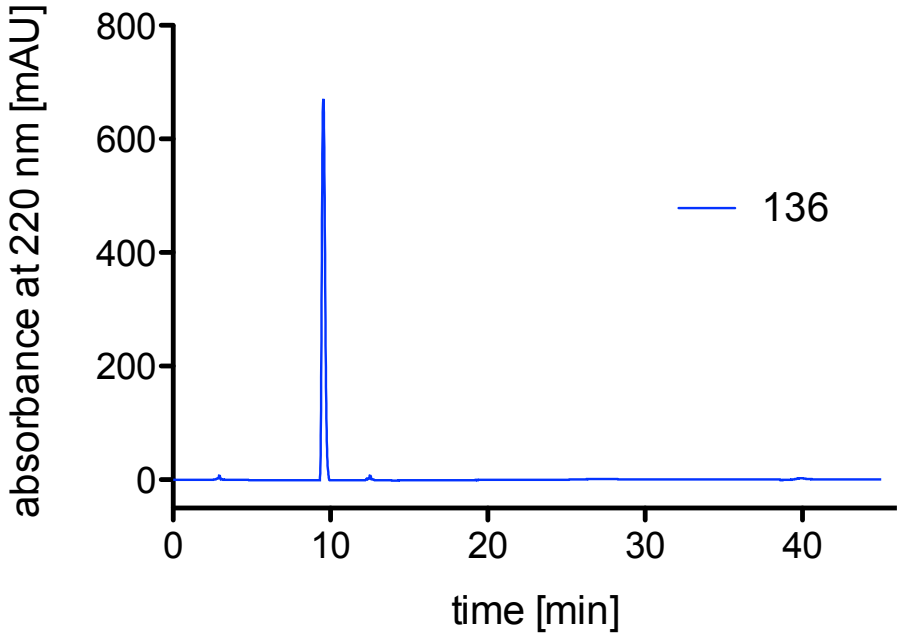

Figure S22. RP-HPLC analysis of compound **136**.

.

3. ^{1}H- and ^{13}C-NMR spectra of 121, 123, 136, 143, 144 and 145

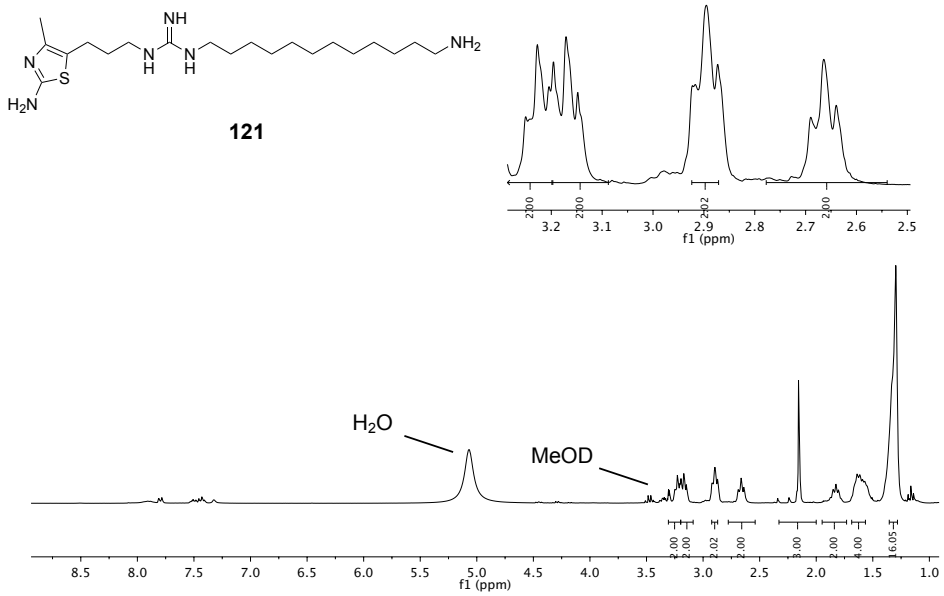

Figure S23. ^{1}H-NMR spectrum (300 MHz, CD_3OD) of compound **121**.

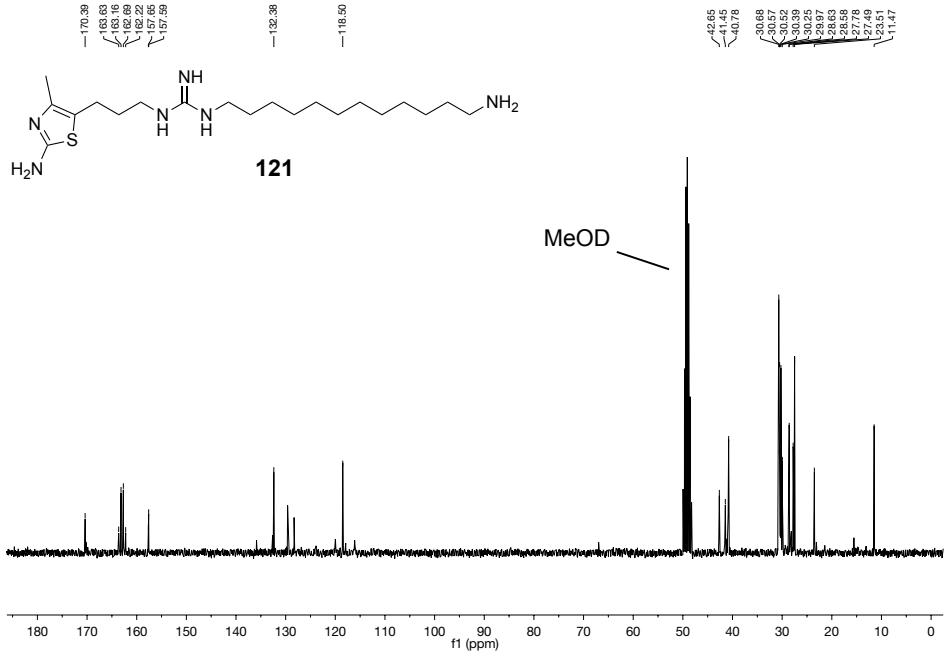

Figure S24. ^{13}C-NMR spectrum (75 MHz, CD_3OD) of compound **121**.

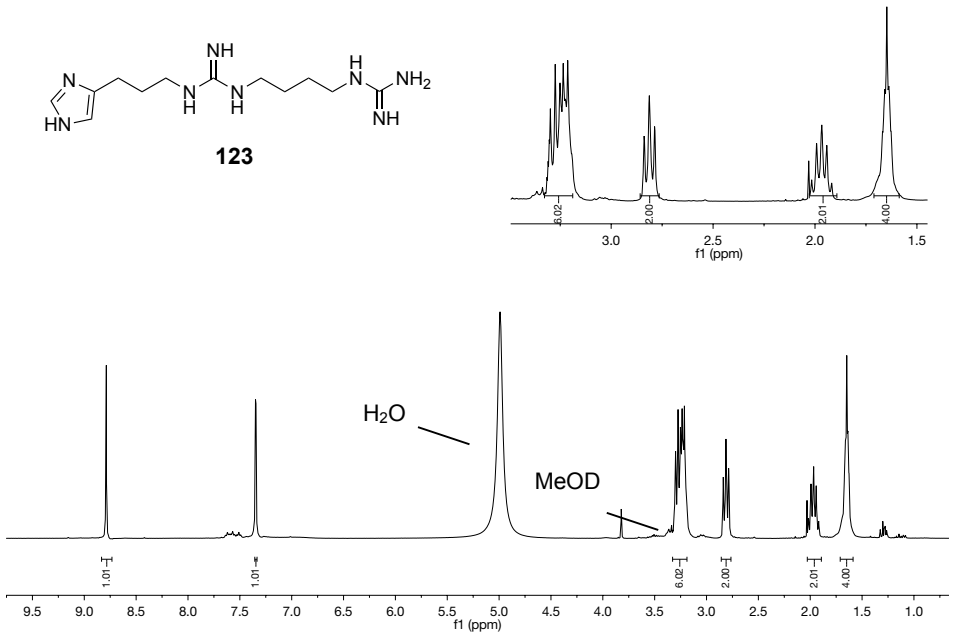

Figure S25. ^{1}H-NMR spectrum (300 MHz, CD_3OD) of compound **123**.

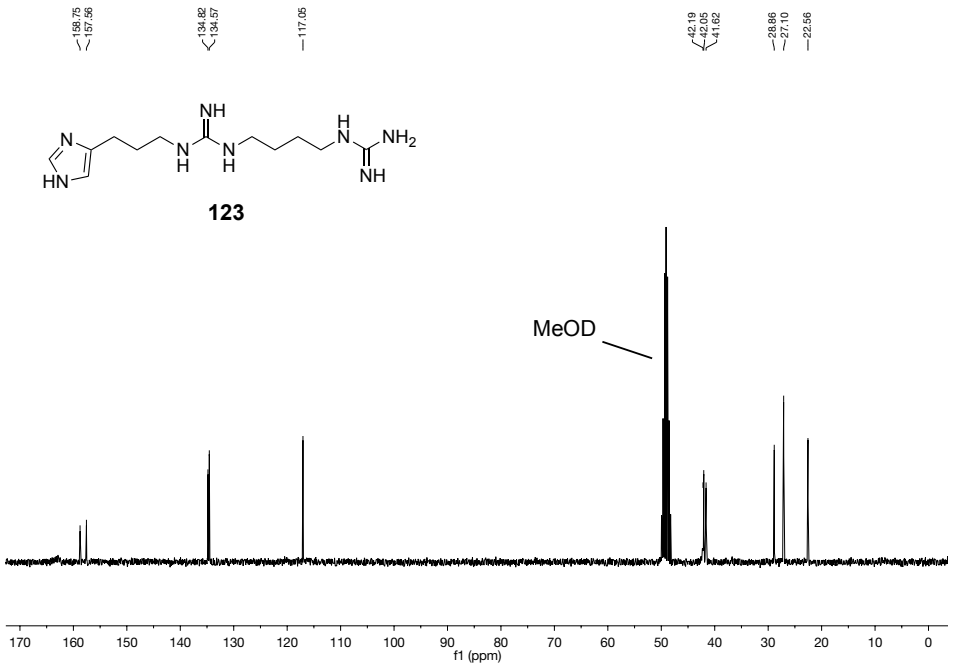

Figure S26. ^{13}C-NMR spectrum (75 MHz, CD_3OD) of compound **123**.

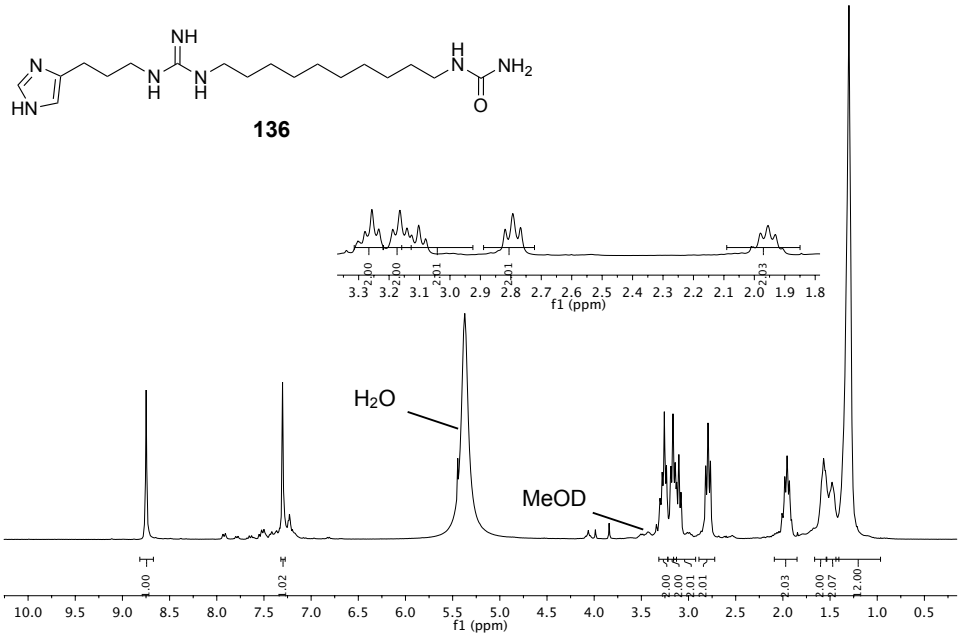

Figure S27. ^{1}H-NMR spectrum (300 MHz, CD_3OD) of compound **136**.

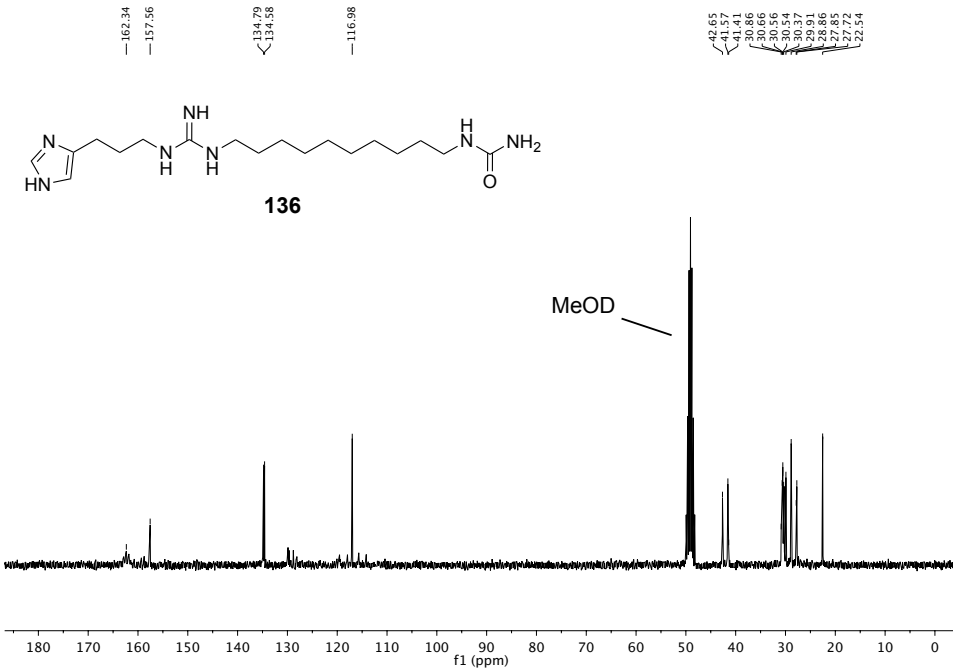

Figure S28. ^{13}C-NMR spectrum (75 MHz, CD_3OD) of compound **136**.

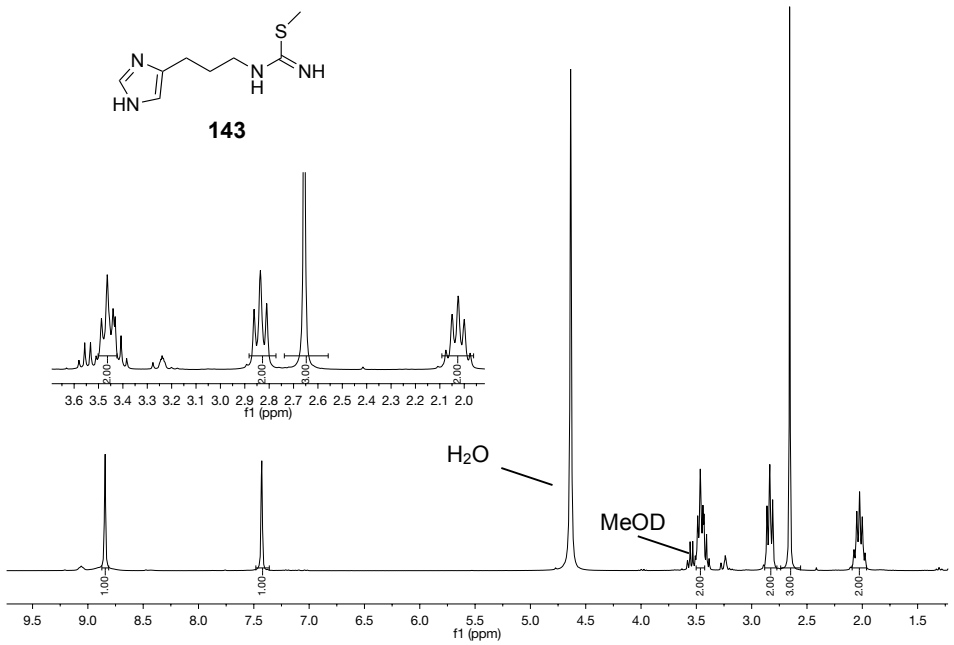

Figure S29. ^{1}H-NMR spectrum (300 MHz, CD_3OD) of compound **143**.

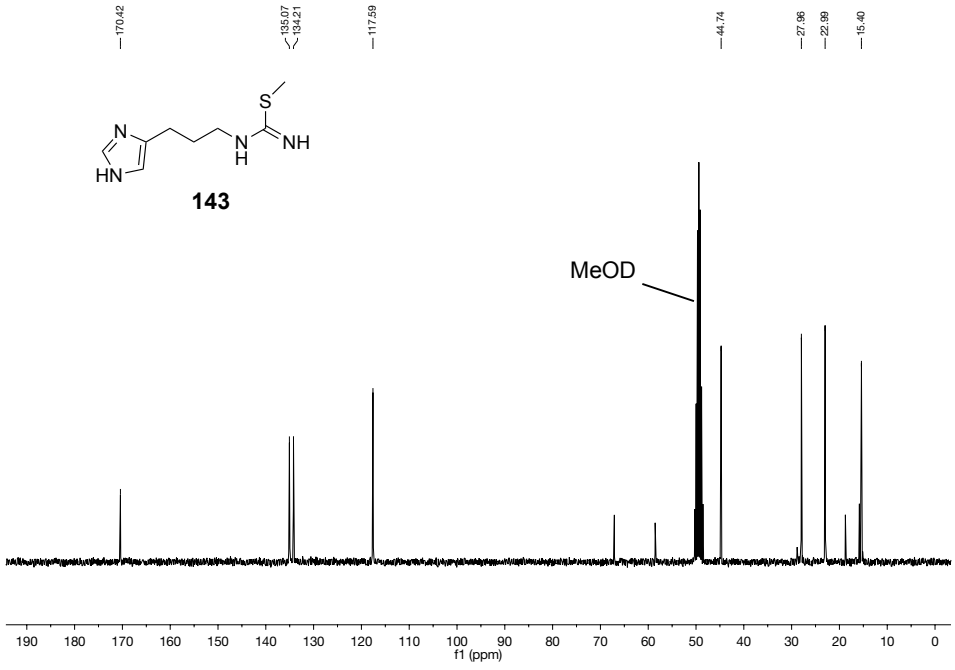

Figure S30. ^{13}C-NMR spectrum (75 MHz, CD_3OD) of compound **143**.

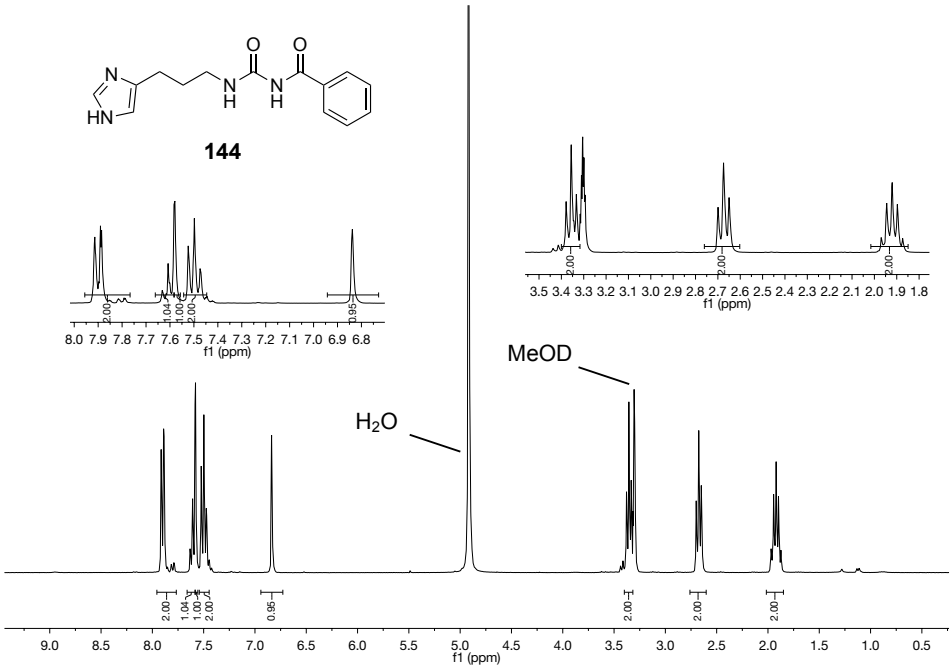

Figure S31. ^{1}H-NMR spectrum (300 MHz, CD_3OD) of compound **144**.

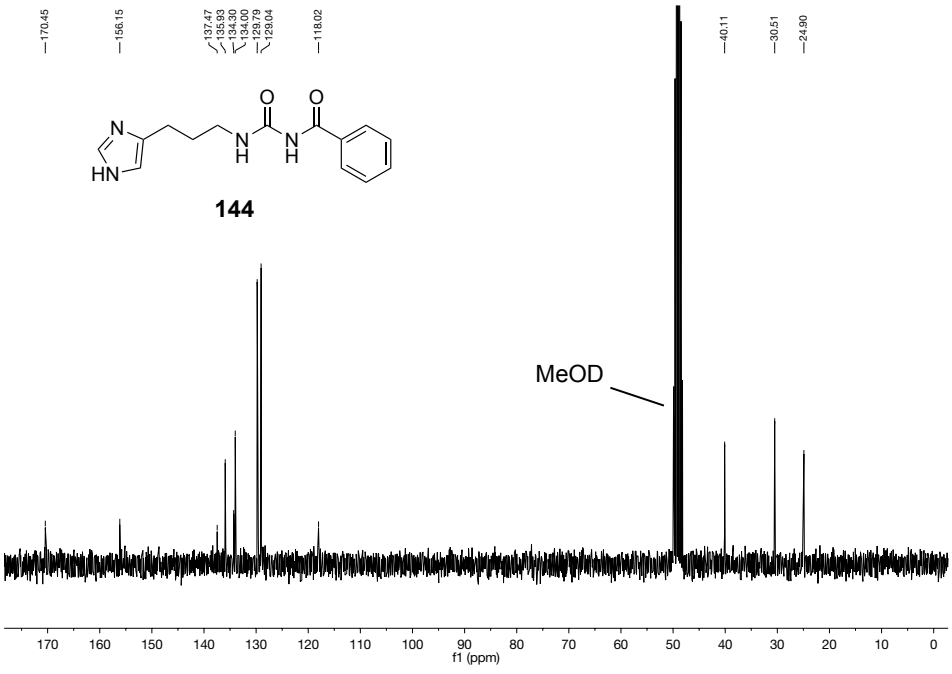

Figure S32. ^{13}C-NMR spectrum (75 MHz, CD_3OD) of compound **144**.

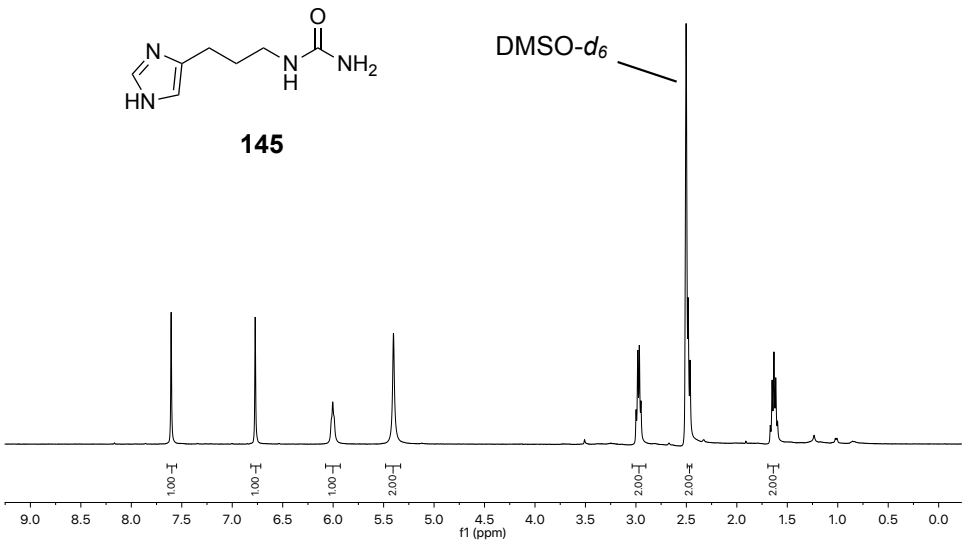

Figure S33. ^{1}H-NMR spectrum (400 MHz, DMSO-d_6) of compound **145**.

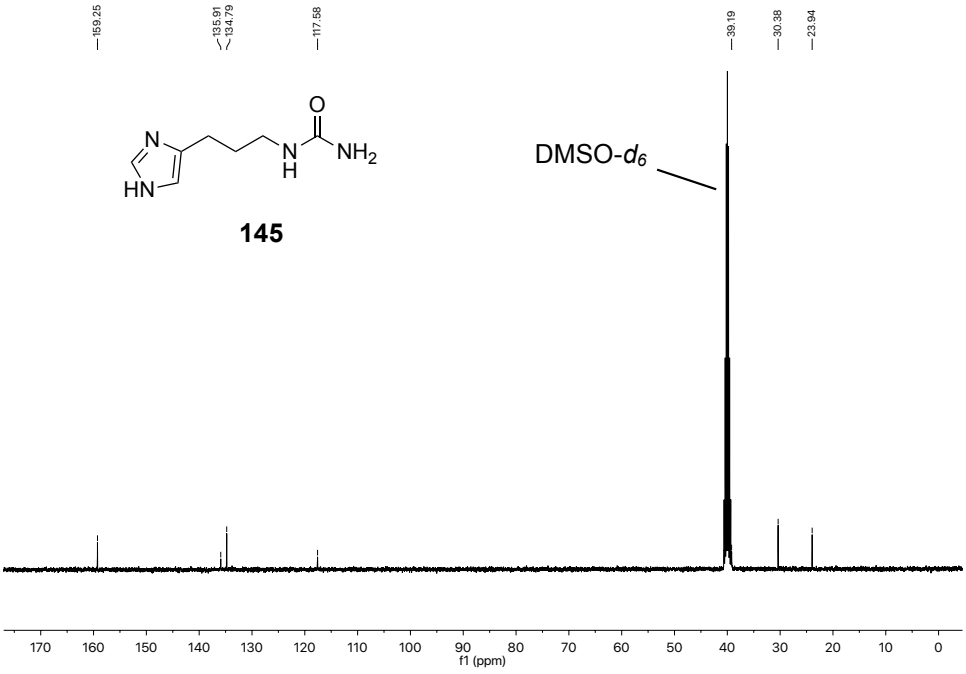

Figure S34. ^{13}C-NMR spectrum (101 MHz, DMSO-d_6) of compound **145**.

4. Guinea-pig right atrium experiments in the presence of cimetidine

Table S2. Experiments for compounds **120, 125** and **135** at the *guinea-pig* right atrium (*gp*H_2R) in the absence (pEC_{50}) and presence ($pEC_{50}(Cim_{pr.})$) of cimetidine (30 µM). The calculated pA_2 values (pA_2(Cim), obtained via *Schild* analysis) for cimetidine are in accordance with literature data (pA_2 = 6.10).[8,9] Data represent mean values ± SEM of three independent experiments.

compound	pEC_{50}	*N*	pEC_{50} ($Cim_{pr.}$)	*N*	pA_2 (Cim)	*N*
120	6.86 ± 0.06	3	5.34 ± 0.02	3	6.00 ± 0.02	3
125	7.69 ± 0.02	3	6.11 ± 0.06	3	6.07 ± 0.07	3
135	6.74 ± 0.09	3	5.20 ± 0.06	3	6.03 ± 0.06	3

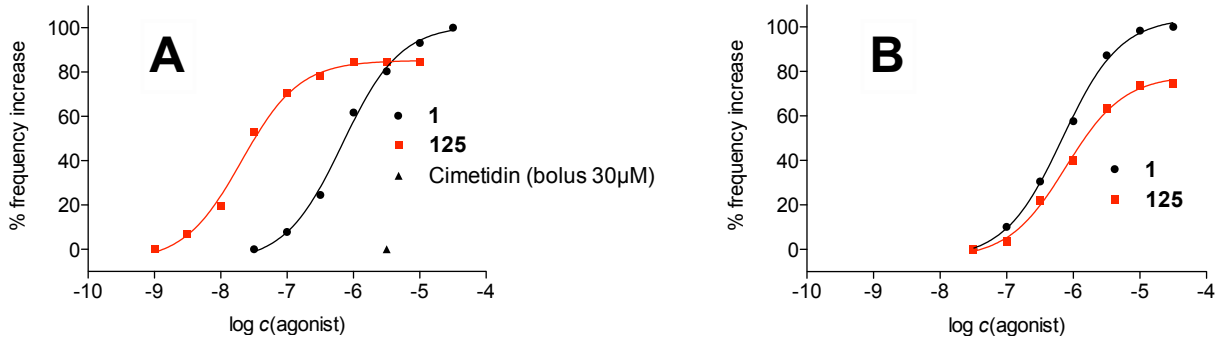

Figure S35. Concentration-response curves of histamine (**1**, reference) and **125** in absence (A) and presence of 30 µM cimetidine (B) at the *gp*H_2R (atrium). Displayed curves are calculated by endpoint determination (*N* = 1).

5. References

[1] A. Kraus, P. Ghorai, T. Birnkammer, D. Schnell, S. Elz, R. Seifert, S. Dove, G. Bernhardt, A. Buschauer, *ChemMedChem* **2009**, *4*, 232–240.

[2] N. Pluym, A. Brennauer, M. Keller, R. Ziemek, N. Pop, G. Bernhardt, A. Buschauer, *ChemMedChem* **2011**, *6*, 1727–1738.

[3] C. Dardonville, C. Fernandez-Fernandez, S.-L. Gibbons, G. J. Ryan, N. Jagerovic, A. M. Gabilondo, J. J. Meana, L. F. Callado, *Bioorg. Med. Chem.* **2006**, *14*, 6570–6580.

[4] M. L. Bolognesi, N. Calonghi, C. Mangano, L. Masotti, C. Melchiorre, *J. Med. Chem.* **2008**, *51*, 5463–5467.

[5] D. Castagnolo, F. Raffi, G. Giorgi, M. Botta, *Eur. J. Org. Chem.* **2009**, *2009*, 334–337.

[6] M. R. Marzabadi, W. C. Wong, T. H. Noble, *Preparation of benzo[2,3]thiepino[4,5-d]thiazol-2-ylaminoalkylsulfonamides and Related Compounds as Selective Neuropeptide Y (Y5) Antagonists*, **2000**, US 6124331 A.

[7] M. R. Marzabadi, W. C. Wong, T. H. Noble, M. N. Desai, *Preparation of Aminothiazoles, Aminotriazines, and Aminobenzothiepinothiazoles as Selective Neuropeptide Y (NPY5) Antagonists.*, **2006**, US 6989379 B1.

[8] R. W. Brimblecombe, W. A. M. Duncan, G. J. Durant, J. C. Emmett, C. R. Ganellin, M. E. Parsons, *J. Int. Med. Res.* **1975**, *3*, 86–92.

[9] R. W. Brimblecombe, W. A. Duncan, G. J. Durant, C. R. Ganellin, M. E. Parsons, J. W. Black, *Br. J. Pharmacol.* **1975**, *53*, 435–436.