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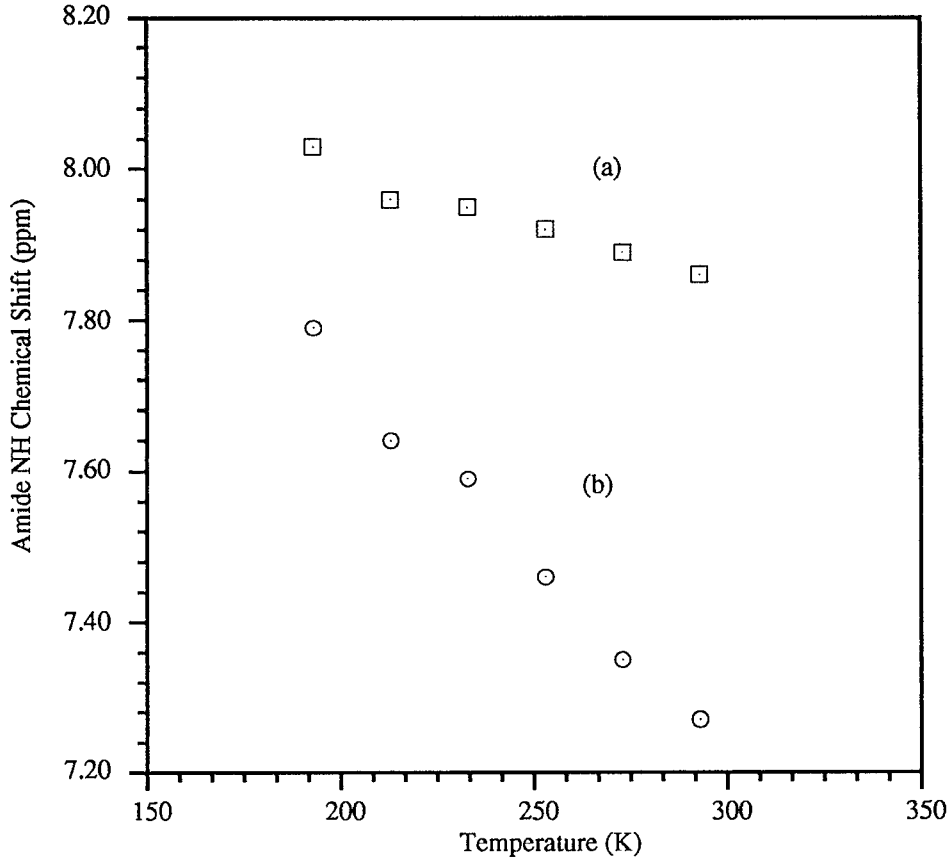
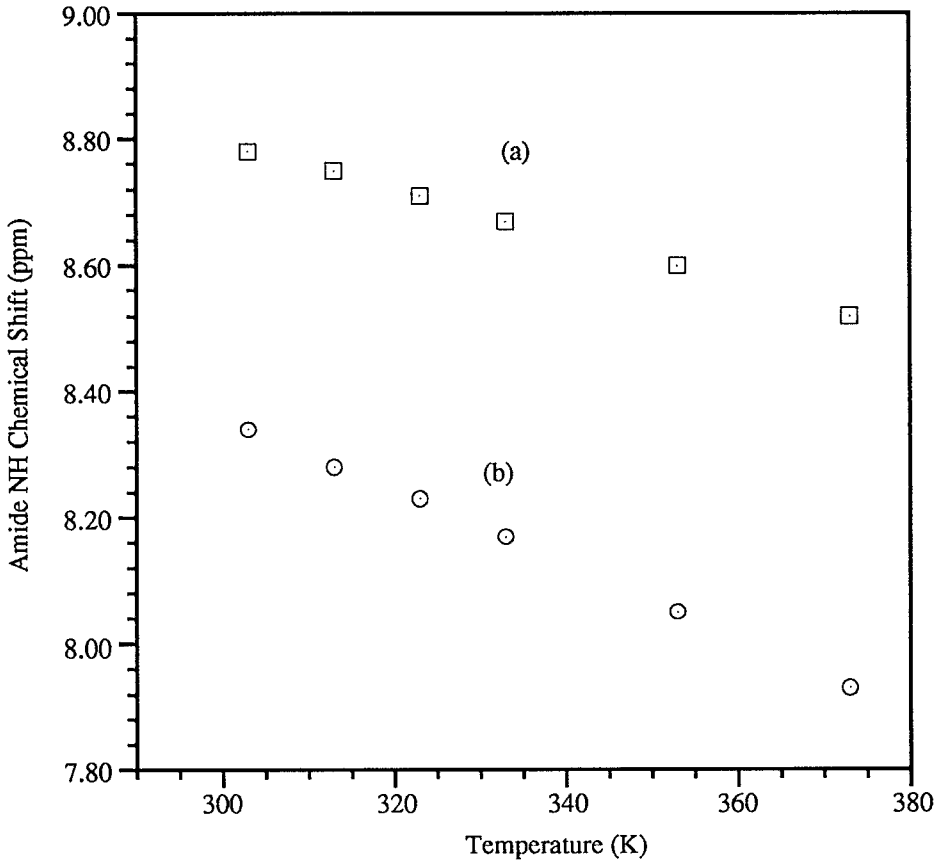
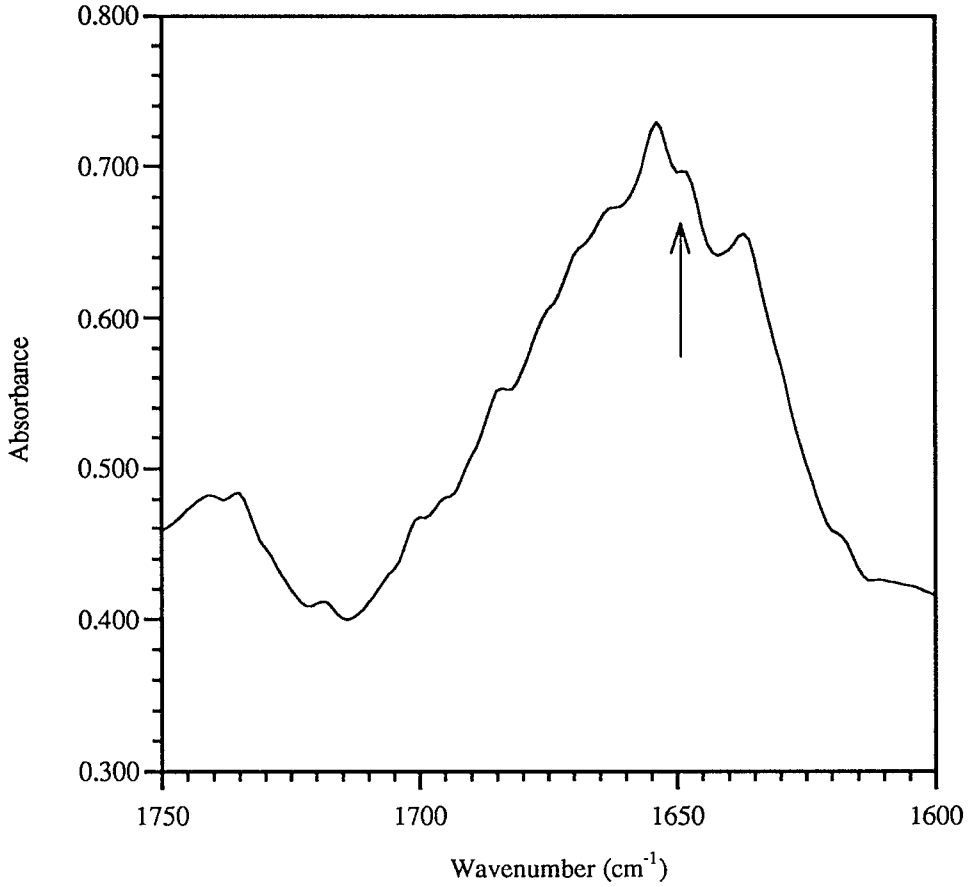
Temperature dependence of amide NH chemical shifts for 13 (0.38 mM) in CD_2Cl_2.
(a) Gly-NH's. (b) Ala-NH's. Reference: $CHDCl_2$ (5.32 ppm).
Instrument: Varian Unity 500 MHz spectrometer



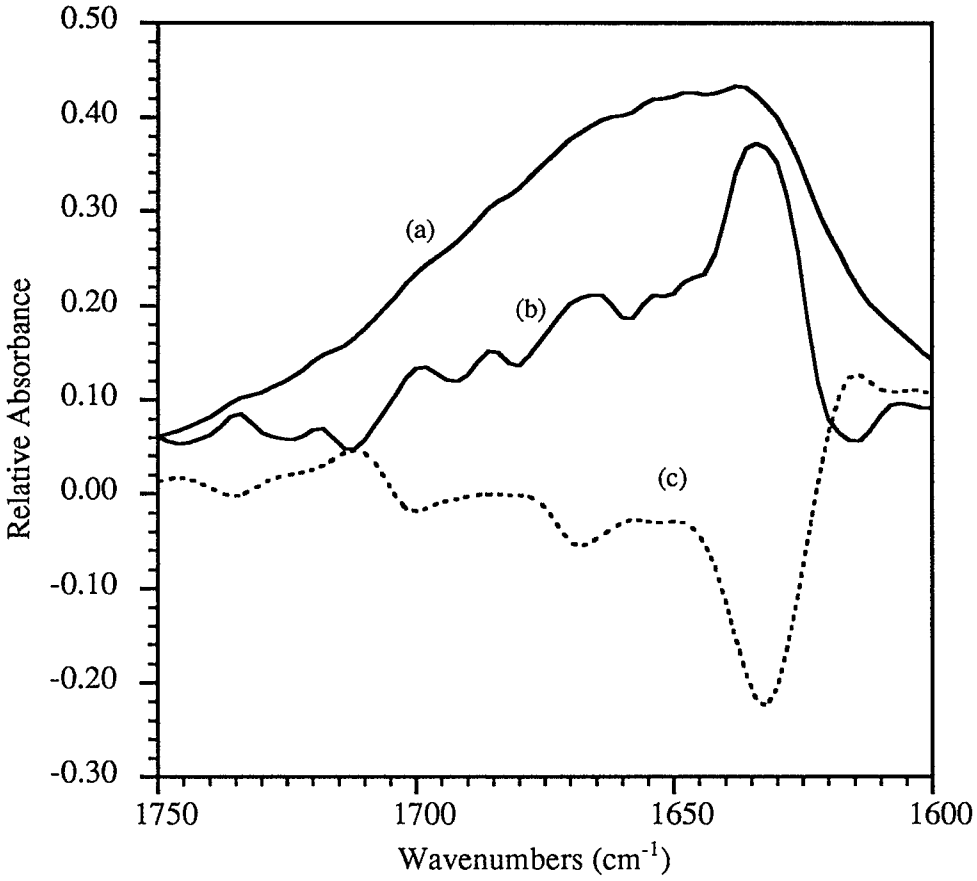
Temperature dependence of amide NH chemical shifts for 13 (1 mM) in DMSO-$_{d6}$.
(a) Gly-NH's. (b) Ala-NH's. Reference: DMSO-$_{d5}$ (2.49 ppm).
Instrument: Varian VXR-S-400 MHz spectrometer



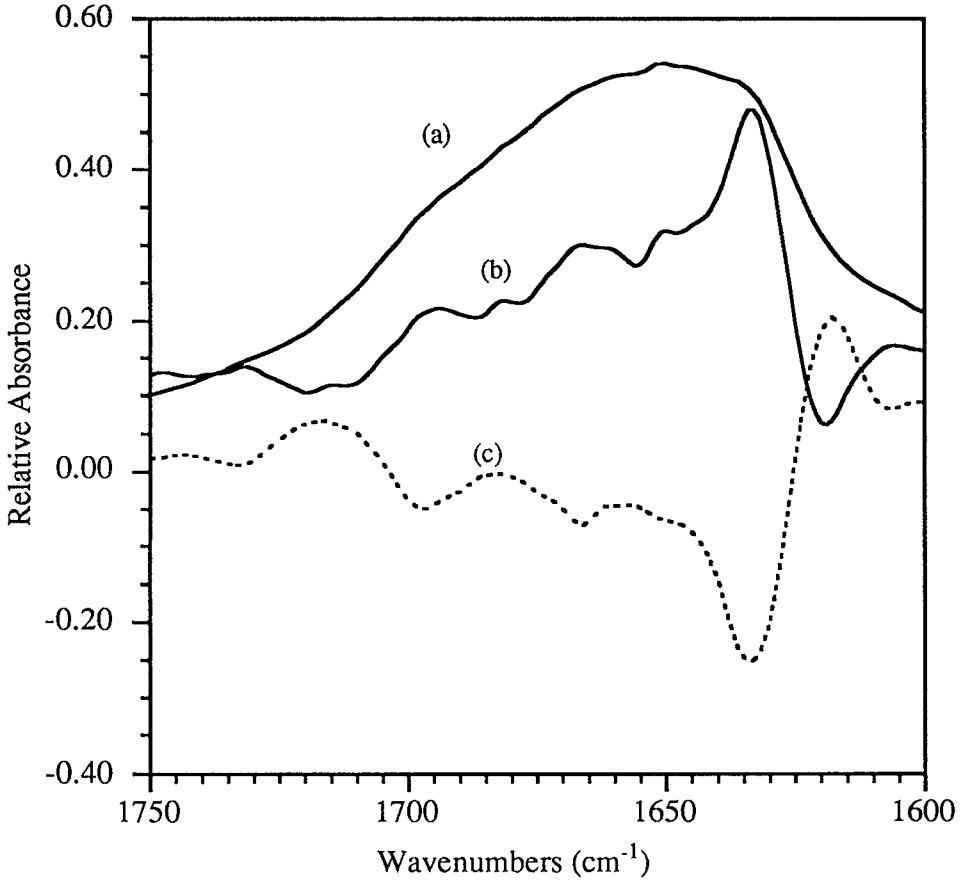
Resolution-enhanced solid state FTIR (KBr, 2.0 cm^{-1} resolution, room temperature) of octapeptide 19. Spectrum was recorded on a Perkin Elmer 16PC FTIR spectrometer.



Raw (a), resolution-enhanced (b) and second derivative solid sate FTIR of polymer P5
(KBr, 4.0 cm-1 resolution, room temperature).
Spectrum was recorded on a Perkin Elmer 16PC FTIR spectrometer



Raw (a), resolution-enhanced (b) and second derivative (c) solid state FTIR spectra of polymer P6. (KBr, 4.0 cm^{-1} resolution, room temperature). Spectrum was recorded on a Perkin Elmer 16PC FTIR spectrometer.



Experimental Procedures, NMR Chemical Shift Assignments and FTIR Peak Listings

2,8-Dimethylphenoxathiin-4,6-dicarboxylic Acid (1). ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.28 (s, 4H, Phen-H), 2.26 (s, 6H, Phen-CH_3). ^{13}C NMR (100 MHz, DMSO-d_6) δ 166.0, 147.3, 134.2, 129.8, 128.9, 123.5, 120.6, 19.8. IR (mineral oil, KBr, cm^{-1}) 1707, 1657, 1253, 1202, 704.

2,8-Dimethylphenoxathiin-4,6-Dicarbonyl Chloride (2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.48 (s, 2H, Phen-H), 7.11 (s, 2H, Phen-H), 2.32 (s, 6H, Phen-CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.494, 147.298, 134.933, 132.126, 130.351, 125.512, 121.673, 20.523. IR ($CHCl_3$, KBr, cm^{-1}): 1777, 1604, 1585, 1568, 1436, 1227, 1132.

2,8-Dimethylphenoxathiin-4-carboxylic acid (3). ^{1}H NMR (400 MHz, DMSO-d_6): δ 13.09 (s, 1H, acid-OH), 7.32 (s, 1H, Phen-H), 7.26 (s, 1H, Phen-H), 7.11 (s, 1H, Phen-H), 7.02 (d, 1H, J = 8.0 Hz, Phen-H), 6.92 (d, 1H, J = 8.0 Hz, Phen-H), 2.24 (s, 3H, Phen-CH_3), 2.23 (s, 3H, Phen-CH_3). ^{13}C NMR (100 MHz, DMSO-d_6) δ 166.3, 149.5, 148.2, 134.6, 133.8, 130.2, 129.1, 128.8, 127.1, 122.5, 121.4, 119.5, 117.6, 20.1, 19.8. IR (solid, KBr, cm^{-1}): 2947 (br), 1694, 1607, 1488, 1451, 1304, 1292, 1268, 1251.

Boc-GlyAlaGlyAla-OBn. To a 250 mL round-bottom flask equipped with a magnetic stirring bar and a rubber septum were added HCl·H_2N-GlyAla-OBn (1.20 g, 4.40 mmol), distilled CH_2Cl_2 (100 mL), DMF (30 mL) and Et_3N (0.62 mL, 4.4 mmol) at 0 °C. The solution was allowed to stir for 20 min under N_2. To the neutralized solution was added BOC-GlyAla-OH (1.08 g, 4.40 mmol) and 1-hydroxybenzotriazole hydrate (HOBT·H_2O, 708 mg, 4.62 mmol). The solution was cooled to 0 °C and DCC (908 mg, 4.40 mmol) was added. The reaction mixture was stirred at 0 °C for 10 min and allowed to stir at room temperature. After stirring overnight

DCU was filtered off and the filtrate was evaporated. The residue was taken up in CH_2Cl_2 and refiltered to remove residual DCU. The crude product was purified via flash chromatography (silica gel, 10% MeOH in CH_2Cl_2) to give a pale yellow solid (1.81 g, 89% yield). R_f 0.52 (10% MeOH in CH_2Cl_2); m.p. 185.8-188.5 °C; $[\alpha]_D^{25}$ = -34.4° (c = 1.29, MeOH). ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.22 (t, 1H, J = 5.8 Hz, Gly-NH), 8.16 (d, 1H, J = 6.7 Hz, Ala-NH), 8.03 (d, 1H, J = 6.4 Hz, Ala-NH), 7.35 (m, 5H, Ar-H), 6.93 (t, 1H, J = 5.8 Hz, Gly-N*H*-BOC), 5.11 (s, 2H, Bn-CH_2), 4.29 (m, 1H, Ala-αH), 4.23 (m, 1H, Ala-αH), 3.70 (m, 2H, Gly-αH), 3.55 (m, 2H, Gly-αH), 1.35 (s, 9H, BOC-CH_3), 1.29 (d, 3H, J = 7.3 Hz, Ala-βH), 1.20 (d, 3H, J = 7.3 Hz, Ala-βH). ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.929, 172.565, 169.508, 168.628, 156.066, 135.265, 128.445, 128.210, 127.884, 79.577, 66.901, 48.968, 48.066, 43.848, 42.915, 28.206, 18.784, 17.768. IR (KBr, cm^{-1}) 3305, 3067, 2981, 2936, 1744, 1715, 1658, 1539, 1456, 1391, 1367, 1249, 1163. FABMS (magic bullet): m/z 465.1 (MH^+).

BOC-Gly-Ala-Gly-Ala-OH. To a 500 mL Parr pressure bottle were added BOC-Gly-Ala-Gly-Ala-OBn (2.10 g, 4.52 mmol) and MeOH (100 mL). To the solution was added 10% dry Pd/C (177 mg) under N_2. The mixture was shaken overnight under an atmosphere of 55 psi H_2. The reaction mixture was filtered through Celite and evaporated to give 1.73 g of a pale yellow foam (100%): R_f 0.0 (10% MeOH in CH_2Cl_2); m.p. 89-98 °C; $[\alpha]_D^{25}$ = -27.4° (c = 1, MeOH); ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.19 (t, 1H, J = 5.8 Hz, Gly-NH), 8.00 (d obscured by Ala-NH, 1H, J = 7.6 Hz, Ala-NH), 7.98 (d obscured by Ala-NH, 1H, J = 8.2 Hz, Ala-NH), 6.93 (t, 1H, J = 5.8 Hz, Gly-N*H*-BOC), 4.23 (collapsed dq, 1H, J = 7.0 Hz, Ala-αH), 4.17 (collapsed dq, 1H, J = 7.0 Hz, Ala-αH), 3.69 (d, 2H, J = 5.8 Hz, Gly-αH), 3.54 (d, 2H, J = 5.8 Hz, Gly-αH), 1.36 (s, 9H, BOC-CH_3), 1.25 (d, 3H, J = 7.3 Hz, Ala-βH), 1.20 (d, 3H, J = 7.0 Hz, Ala-βH). IR (KBr, cm^{-1}): 3318, 3073, 2981, 2938, 2886, 1653, 1540, 1457, 1457, 1368, 1249, 1165.

HCl·H-GlyAlaGlyAla-OBn. Removal of BOC group from BOC-GlyAlaGlyAla-OBn (240 mg, 517 μmol, 10 mL dioxane) was performed using standard procedures (HCl, 3.49 M in dioxane, 10 mL, 35 mmol) to give 184 mg of HCl·H-GlyAlaGlyAla-OBn as an off-white solid

(89%). R_f 0.03 (10% MeOH in CH_2Cl_2); m.p. 190-192.2 °C; $[\alpha]_D^{25}$ = -44.7° (c = 1.39, MeOH). ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.63 (d, 1H, J = 7.3 Hz, Ala-NH), 8.30 (d obscured by Gly-NH, 1H, J = 6.5 Hz, Ala-NH), 8.29 (t obscured by Ala-NH, 1H, J = 5.5 Hz, Gly-NH), 8.06 (bs, 3H, NH_3^+), 7.36 (m, 5H, Ar-H), 5.11 (s, 2H, Bn-CH_2), 4.38 (collapsed dq, 1H, J = 7.0 Hz, Ala-αH), 4.31 (collapsed dq, 1H, J = 7.0 Hz, Ala-αH), 3.74 (d, 2H, J = 5.8 Hz, Gly-αH), 3.56 (d, 2H, J = 5.8 Hz, Gly-αH), 1.30 (d, 3H, J = 7.3 Hz, Ala-βH), 1.23 (d, 3H, J = 7.0 Hz, Ala-βH). IR (KBr, cm^{-1}): 3398, 3283, 3244, 3064, 2992, 2936, 2879, 2623, 1740, 1653, 1558, 1456, 1212, 1157.

Octapeptide 5. ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.45 (t, 2H, J = 5.4 Hz, Phen-CH_2-N*H*), 8.21 (t, 2H, J = 5.4 Hz, Gly-NH), 8.05 (d, 2H, J = 6.8 Hz, Ala-NH), 8.02 (d, 2H, J = 6.9 Hz, Ala-NH), 7.74 (s, 2H, Phen-H), 7.49 (s, 2H, Phen-H), 6.94 (t, 2H, J = 5.9 Hz, Gly-N*H*-BOC), 4.54 (m, 4H, Phen-C*H*$_2$-), 4.29 (collapsed dq, 2H, J = 6.8 Hz, Ala-αH), 4.20 (collapsed dq, 2H, J = 6.8 Hz, Ala-αH), 3.72 (m, 4H, Gly-αH), 3.55 (m, 4H, Gly-αH), 2.39 (s, 6H, Phen-CH_3), 1.35 (s, 18H, BOC-CH_3), 1.27 (d, 6H, J = 7.3 Hz, Ala-βH) , 1.17 (d, 6H, J = 7.3 Hz, Ala-βH). ^{13}C NMR (100 MHz, DMSO-d_6): δ 172.751, 172.721, 169.435, 168.661, 155.854, 146.468, 134.677, 133.630, 129.160, 123.781, 120.571, 78.103, 48.626, 48.557, 43.117, 42.040, 36.872, 28.192, 20.324, 17.979, 17.926. IR (KBr, cm^{-1}): 3300, 3074, 2978, 2933, 1716, 1699, 1683, 1662, 1656, 1636, 1557, 1543, 1527, 1510, 1455, 1367, 1240, 1160, 1113, 1053, 940, 864.

2,2'-(Ethylenedioxy)bis(ethylamine)-containing Octapeptide (7a). ^{1}H NMR (200 MHz, DMSO-d_6): δ 8.17 (t, 2H, J = 5.8 Hz, Gly-NH), 8.02 (d, 2H, J = 7.0 Hz, Ala-NH), 7.88 (t obscured by Ala-NH, 2H, J = 6.1 Hz, -O-CH_2-CH_2-N*H*), 7.86 (d obscured by -O-CH_2-CH_2-N*H*, 2H, J = 8.8 Hz, Ala-NH), 6.92 (t, 2H, J = 6.0 Hz, Gly-N*H*-BOC), 4.22 (collapsed dq, 4H, J = 7.3 Hz, Ala-αH), 3.68 (m, 4H, Gly-αH), 3.55 (m, 4H, Gly-αH), 3.48 (s, 4H, -O-C*H*$_2$-C*H*$_2$-O-), 3.37 (t, 4H, J = 6.1 Hz, -O-C*H*$_2$-CH_2-NH), 3.18 (collapsed dt, 4H, J = 5.7 Hz, -O-CH_2-C*H*$_2$-NH), 1.36 (s, 18H, BOC-CH_3), 1.19 (d, 6H, J = 7.0 Hz, Ala-βH), 1.17 (d, 6H, J =

7.3 Hz, Ala-βH). ^{13}C NMR (100 MHz, DMSO-d_6): δ 172.624, 172.184, 169.316, 168.254, 155.833, 78.102, 69.582, 68.922, 48.421, 48.171, 43.155, 42.032, 38.603, 28.201, 18.360, 18.095. IR (KBr, cm^{-1}): 3276, 3083, 2979, 2934, 1720, 1696, 1683, 1671, 1656, 1630, 1560, 1544, 1526, 1512, 1448, 1367, 1247, 1167, 1052, 939, 865.

Ethylene Diamine-containing Octapeptide (7b). ^1H NMR (400 MHz, DMSO-d_6): δ 8.19 (t, 2H, J = 5.5 Hz, Gly-NH), 8.04 (d, 2H, J = 7.0 Hz, Ala-NH), 7.89 (d, 2H, J = 7.3 Hz, Ala-NH), 7.85 (bs, 2H -CH_2-CH_2-N*H*), 6.94 (t, 2H, J = 6.1 Hz, Gly-N*H*-BOC), 4.24 (collapsed dq, 2H, J = 7.0 Hz, Ala-αH), 4.17 (collapsed dq, 2H, J = 7.0 Hz, Ala-αH), 3.69 (m, 4H, Gly-αH), 3.55 (m, 4H, Gly-αH), 3.08 (bs, 4H, -NH-C*H*$_2$-C*H*$_2$-NH-), 1.36 (s, 18H, BOC-CH_3), 1.20 (d, 6H, J = 7.4 Hz, Ala-βH), 1.18 (d, 6H, J = 7.0 Hz, Ala-βH). ^{13}C NMR (100 MHz, DMSO-d_6): δ 172.656, 172.216, 169.303, 168.331, 155.804, 78.077, 48.409, 48.288, 43.121, 42.013, 38.272, 28.173, 18.165, 18.074. IR (KBr, cm^{-1}): 3293, 3090, 2977, 2933, 1718, 1699, 1686, 1654, 1636, 1559, 1543, 1510, 1250, 1167, 668.

Hexamethylene Diamine-containing Octapeptide (7c). ^1H NMR (400 MHz, DMSO-d_6): δ 8.19 (t, 2H, J = 5.5 Hz, Gly-NH), 8.05 (d, 2H, J = 6.7 Hz, Ala-NH), 7.85 (d, 2H, J = 7.4 Hz, Ala-NH), 7.75 (t, 2H, J = 5.2 Hz, -CH_2-CH_2-N*H*), 6.93 (t, 2H, J = 5.8 Hz, Gly-N*H*-BOC), 4.18 (m, 4H, Ala-αH), 3.68 (m, 4H, Gly-αH), 3.55 (m, 4H, Gly-αH), 3.01 (m, 4H, -CH_2-C*H*$_2$-NH-), 1.35 (m, 22H, -C*H*$_2$-CH_2-NH- and BOC-CH_3), 1.19 (m, 16H, -C*H*$_2$-CH_2-CH_2-NH- and Ala-βH). ^{13}C NMR (100 MHz, DMSO-d_6): δ 172.671, 171.753, 169.348, 168.218, 78.077, 48.470, 48.204, 43.128, 42.081, 38.424, 28.940, 28.166, 25.950, 18.347, 17.983. IR (KBr, cm^{-1}): 3280, 3087, 2980, 2935, 1720, 1698, 1683, 1654, 1630, 1558, 1546, 1510, 1368, 1244, 1167, 668.

1,12-Diaminododecane-containing Octapeptide (7d). ^1H NMR (200 MHz, DMSO-d_6): δ 8.18 (t, 2H, J = 5.6 Hz, Gly-NH), 8.05 (d, 2H, J = 6.7 Hz, Ala-NH), 7.84 (d, 2H, J = 7.3 Hz, Ala-NH), 7.74 (t, 2H, J = 5.1 Hz, -CH_2-CH_2-N*H*), 6.93 (t, 2H, J = 5.6 Hz, Gly-N*H*-

BOC), 4.20 (m, 4H, Ala-αH), 3.67 (d, 4H, J = 5.4 Hz, Gly-αH), 3.55 (d, 4H, J = 5.7 Hz, Gly-αH), 3.00 (m, 4H, -CH_2-CH_2-NH-), 1.35 (m, 22H, -CH_2-CH_2-NH- and BOC-CH_3), 1.22 (m, 22H, -CH_2-CH_2-CH_2- and Ala-βH), 1.18 (d, 6H, J = 6.6 Hz, Ala-βH). ^{13}C NMR (100 MHz, DMSO-d_6): δ 172.73, 171.78, 169.43, 168.26, 155.85, 78.09, 48.56, 48.25, 43.19, 42.16, 38.54, 29.06, 28.79, 28.19, 26.34, 18.36, 17.97. IR (KBr, cm^{-1}): 3495 (sh), 3286, 3079, 2978, 2930, 2857, 1723, 1697, 1684, 1671, 1655, 1630, 1542, 1450, 1390, 1367, 1277 (sh), 1245, 1167, 1050.

2,8-Dimethylphenoxathiin-4,6-dicarboxylic acid monobenzyl ester (8). ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.46-7.24 (m, 9H, Ar-H, Phen-H), 5.34 (s, 2H, Bn-CH_2), 2.25 (s, 3H, Phen-CH_3), 2.24 (s, 3H, Phen-CH_3). ^{13}C NMR (100 MHz, DMSO-d_6): δ 166.32, 165.18, 147.45, 135.81, 134.58, 134.43, 130.09, 130.05, 129.17, 128.43, 128.34, 128.12, 123.26, 122.86, 121.28, 121.14, 66.76, 19.82, 19.79. IR (solid, KBr, cm^{-1}): 3318, 3208, 1724, 1709, 1605, 1592, 1439, 1323, 1305, 1286, 1273, 1246, 1219, 1098.

***N,N'*-(2,8-dimethylphenoxathiin-4,6-diyldicarbonyl)bis(β-alanine) diethyl ester (9).** ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.64 (t, 2H, J = 5.8 Hz, βAla-NH), 7.35 (s, 2H, Phen^3-H, Phen^7-H), 6.95 (s, 2H, Phen^1-H, Phen^9-H), 4.13 (q, 4H, J = 7.0 Hz, ester-CH_2), 3.74 (collapsed dt, 4H, J = 6.1 Hz, J = 6.7 Hz, βAla-βH), 2.67 (t, 4H, J = 6.7 Hz, βAla-αH), 2.25 (s, 6H, Phen-CH_3), 1.23 (t, 6H, J = 7.0 Hz, ester-CH_3). ^{13}C NMR (100 MHz, CD_2Cl_2): δ 172.39, 165.50, 147.46, 134.97, 129.89, 129.39, 124.33, 120.24, 60.89, 36.07, 34.42, 20.44, 14.34; IR (CH_2Cl_2, KBr, cm^{-1}): 3428, 3372, 1728, 1662, 1651 cm^{-1}.

6-(Methoxycarbonylmethylcarbamoyl)-2,8-dimethylphenoxathiin-4-carboxylic acid benzyl ester (10). ^{1}H NMR (400 MHz, CD_2Cl_2): δ 9.33 (bt, 1H, Gly-NH), 7.87 (s, 1H, Phen-H), 7.55 (s, 1H, Phen-H), 7.45-7.34 (m, 5H, Ar-H), 7.15 (s, 1H, Phen-H), 7.06 (s, 1H, Phen-H), 5.28 (s, 2H, Bn-CH_2), 4.18 (d, 2H, J = 6.1 Hz, Gly-αH), 3.72 (s, 3H, ester-CH_3), 2.30 (s, 3H, Phen-CH_3), 2.28 (s, 3H, Phen-CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ

170.66, 165.00, 163.81, 149.34, 147.95, 135.29, 134.64, 134.31, 131.85, 131.69, 130.41, 130.27, 128.73, 128.53, 128.17, 121.79, 120.99, 119.30, 118.93, 67.20, 52.04, 41.91, 20.34, 20.32. IR (2 mM in CH_2Cl_2, KBr, cm^{-1}): 3378, 1753, 1719, 1656.

***N,N'*-(2,8-dimethylphenoxathiin-4,6-diyldicarbonyl)bis(glycine) dimethyl ester (11).** ^1H NMR (400 MHz, $CDCl_3$): δ 7.76 (t, 2H, *J* = 5.5 Hz, Gly-NH), 7.41 (s, 2H, Phen-H), 6.94 (s, 2H, Phen-H), 4.14 (d, 4H, *J* = 5.5 Hz, Gly-αH), 3.75 (s, 6H, OCH_3), 2.23 (s, 6H, Phen-CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.51, 165.92, 147.39, 134.79, 130.20, 129.41, 123.25, 120.05, 52.51, 41.89, 20.56. IR (1.53 mM in CH_2Cl_2, KBr, cm^{-1}): 3428 (sh.), 3407 (sh.), 3375, 1751, 1665, 1655.

***N*-(2,8-dimethylphenoxathiin-4-ylcarbonyl)-β-alanine ethyl ester (12).** ^1H NMR (500 MHz, CD_2Cl_2): δ 8.20 (bt, 1H, βAla-NH), 7.72 (s, 1H, Phen-H), 7.15 (d, 1H, *J* = 8.3 Hz, Phen-H), 7.08 (s, 1H, Phen-H), 7.01 (d, 1H, *J* = 8.3 Hz, Phen-H), 7.00 (s, 1H, Phen-H), 4.17 (q, 2H, *J* = 7.3 Hz, ester-CH_2), 3.76 (collapsed dt, 2H, *J* = 5.8 Hz, *J* = 6.3 Hz, βAla-βH), 2.68 (t, 2H, *J* = 5.9 Hz, βAla-αH), 2.29 (s, 3H, Ar-CH_3), 2.28 (s, 3H, Ar-CH_3), 1.24 (t, 3H, *J* = 7.3 Hz, ester-CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.8, 164.3, 149.5, 148.8, 135.2, 134.1, 130.6, 130.5, 128.4, 127.2, 122.2, 121.2, 120.4, 117.6, 60.8, 35.2, 34.2, 34.2, 20.4, 14.2. IR (22 mM in CH_2Cl_2, KBr, cm^{-1}): 3432, 2926, 1727, 1657, 1603 (w), 1527, 1489, 1445, 1197, 1029.

***N,N'*-(2,8-dimethylphenoxathiin-4,6-diyldicarbonyl)bis(glycyl-L-alanine) dibenzyl ester (13).** ^1H NMR (500 MHz, CD_2Cl_2): δ 7.86 (t, 2H, *J* = 5.0 Hz, Gly-NH), 7.46 (s, 2H, Phen-H), 7.33-7.27 (m, 12H, Ar-H, Phen-H), 7.27 (d, 2H, *J* = 7.0 Hz, Ala-NH), 7.05 (s, 2H, Phen-H), 5.13 (s, 4H, Bn-CH_2), 4.56 (collapsed dq, 2H, *J* = 7.5 Hz, Ala-αH), 4.10 (m, 4H, Gly-αH), 2.30 (s, 6H, Ar-CH_3), 1.41 (d, 6H, *J* = 7.3 Hz, Ala-CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.6, 169.4, 166.0, 147.2, 135.4, 134.7, 130.0, 129.1, 128.5, 128.3, 128.0, 122.9, 119.8, 67.0, 48.4, 44.0, 20.3, 17.8; IR (6.9 mM in CH_2Cl_2, KBr, cm^{-1}): 3408, 3343, 1740, 1712, 1668, 1659.

***N*-(2,8-dimethylphenoxathiin-4-ylcarbonyl)glycyl-L-alanine benzyl ester (14).** ^{1}H NMR (400 MHz, CD_2Cl_2): δ 8.71 (t, 1H, *J* = 4.9 Hz, Gly-NH), 7.75 (s, 1H, Phen-H), 7.39 (d, 1H, *J* = 8.0 Hz, Phen-H), 7.36-7.29 (m, 5H, Ar-H), 7.22 (d, 1H, *J* = 7.3 Hz, Ala-NH), 7.09 (s, 1H, Phen-H), 6.99 (d, 1H, *J* = 8.0 Hz, Phen-H), 6.98 (s, 1H, Phen-H), 5.18 (s, 2H, Bn-CH_2), 4.73 (collapsed dt, 1H, *J* = 7.3 Hz, Ala-αH), 4.33 (d, 2H, *J* = 4.6 Hz, Gly-αH), 2.28 (s, 6H, Ar-CH_3), 1.49 (d, 3H, *J* = 7.3 Hz, Ala-CH_3). ^{13}C NMR (100 MHz, CD_2Cl_2): δ 172.87, 168.78, 164.42, 149.75, 149.31, 136.01, 135.76, 134.58, 131.08, 130.73, 129.01, 128.87, 128.62, 128.31, 127.34, 121.85, 121.77, 120.32, 118.23, 67.36, 48.74, 44.14, 20.70, 20.54, 18.31. IR (13 mM in CH_2Cl_2, KBr, cm^{-1}): 3407, 3343, 1740, 1712, 1668, 1659.

***N,N'*-(1,5-pentanediyldicarbonyl)bis(glycyl-L-alanine) dibenzyl ester (15).** ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.30 (d, 2H, *J* = 7.0 Hz, Ala-NH), 7.99 (t, 2H, *J* = 5.8 Hz, Gly-NH), 7.35 (m, 10H, Ar-H), 5.11 (s, 4H, Bn-CH_2), 4.32 (collapsed dq, 2H, *J* = 7.0 Hz, *J* = 7.3 Hz), 3.71 (m, 4H, Ala-αH), 2.10 (t, 4H, αCH_2), 1.47 (m, 4H, βCH_2), 1.28 (d, 6H, *J* = 7.3 Hz, Ala-CH_3), 1.23 (m, 2H, γCH_2). ^{13}C NMR (100 MHz, DMSO-d_6): δ 172.4 (2), 169.0, 136.0, 128.4, 128.0, 127.7, 65.8, 47.6, 41.5, 35.0, 28.3, 25.0, 17.0. IR (5.1 mM in CH_2Cl_2, KBr, cm^{-1}): 3419, 3332, 2938, 2861, 1742, 1675, 1513, 1455, 1208, 1163.

17. ^{1}H NMR (200 MHz, DMSO-d_6): δ 8.65 (d, 2H, Ala-NH), 8.60 (t, 2H, Phen-CH_2-N*H*), 8.35 (t, 2H, Gly-NH), 8.15 (d, 2H, Ala-NH), 8.05 (bs, 6H, Gly-NH_3^+), 7.75 (s, 2H, Phen-H), 7.50 (s, 2H, Phen-H), 4.55 (d, 4H, Phen-C*H*$_2$-), 4.35 (dq, 2H, Ala-αH), 4.30 (dq, 2H, Ala-αH), 3.75 (m, 4H, Gly-αH), 3.60 (bs, 4H, Gly-αH), 2.40 (s, 6H, Phen-CH_3), 1.30 (d, 6H, Ala-βH), 1.20 (d, 6H, Ala-βH).

2,2'-(Ethylenedioxy)bis(ethylamine) Octapeptide Hydrochloride (18a). ^{1}H NMR (200 MHz, DMSO-d_6): δ 8.65 (d, 2H, *J* = 7.1 Hz, Ala-NH), 8.51 (t, 2H, *J* = 5.6 Hz, -O-CH_2-CH_2-N*H*), 8.05 (bs, 6H, Gly-NH_3^+), 8.00 (t, 2H, *J* = 6.0 Hz, Gly-NH), 7.96 (d, 2H, *J* = 7.5 Hz, Ala-NH), 4.36 (collapsed dq, 2H, *J* = 7.2 Hz, Ala-αH), 4.23 (collapsed dq, 2H, *J* = 7.4 Hz,

Ala-αH), 3.71 (m, 4H, Gly-αH), 3.56 (m, 4H, Gly-αH), 3.49 (s, 4H, -O-C*H*$_2$-C*H*$_2$-O-), 3.39 (t, 4H, *J* = 5.7 Hz, -O-C*H*$_2$-CH$_2$-NH), 3.18 (collapsed dt, 4H, *J* = 5.5 Hz, -O-CH$_2$-C*H*$_2$-NH), 1.24 (d, 6H, *J* = 7.0 Hz, Ala-βH), 1.20 (d, 6H, *J* = 7.0 Hz, Ala-βH).

***N*,*N*'-(2,8-dimethylphenoxathiin-4,6-diyldicarbonyl)bis(glycyl-L-alanyl-glycyl-L-alanine) dibenzyl ester (19).** ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.83 (t, 2H, *J* = 5.8 Hz, Gly-NH), 8.25 (t, 2H, *J* = 5.8 Hz, Gly-NH), 8.23 (d, 2H, *J* = 6.4 Hz, Ala-NH), 8.13 (d, 2H, *J* = 6.7 Hz, Ala-NH), 7.39 (s, 2H, Phen-H), 7.33 (m, 10H, Ar-H), 7.25 (s, 2H, Phen-H), 5.08 (s, 4H, Bn-CH$_2$), 4.25 (collapsed dq, 4H, *J* = 7.0 Hz, Ala-αH), 3.91 (d, 4H, *J* = 5.5 Hz, Gly-αH), 3.72 (m, 4H, Gly-αH), 2.24 (s, 6H, Phen-CH$_3$), 1.24 (d, 6H, *J* = 7.3 Hz, Ala-CH$_3$), 1.23 (d, 6H, *J* = 7.0 Hz, Ala-CH$_3$). ^{13}C NMR (100 MHz, DMSO-d_6): δ 172.563, 172.290, 168.785, 168.671, 164.878, 146.520, 135.968, 134.345, 129.665, 129.437, 128.413, 127.965, 127.616, 123.801, 119.173, 65.792, 48.648, 47.707, 42.526, 41.600, 19.852, 17.826, 16.787. IR (KBr, cm^{-1}): 3308, 3065, 2948, 1741, 1684, 1662, 1654, 1648, 1637, 1558, 1544, 1534, 1528, 1500, 1457, 1436.

Synthesis of BOC-GlyAlaGlyAla-nBu. To a 250 mL round-bottom flask equipped with a magnetic stirring bar and a stopper were added BOC-GAGA-OH (669 mg, 1.79 mmol), HOBT·H$_2$O (329 mg, 2.15 mmol), CH$_2$Cl$_2$ (50 mL) and DMF (5 mL). The stirred mixture was cooled to 0 °C and DCC (406 mg, 1.97 mmol) was added. After 10 min of stirring, n-butylamine (200 μL, 2.02 mmol) was added and the cooling bath was removed. The mixture was allowed to stir for 2 d and evaporated to give a solid. This was purified by flash chromatography (silica gel, 5%-10% MeOH in CH$_2$Cl$_2$) to give the pure product (682 mg, 89% yield). M.p. = 240 °C (dec.). $[\alpha]_D^{25}$ = -14.2° (c = 1.02, DMSO). ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.20 (t, 1H, *J* = 5.4 Hz, NH), 8.06 (d, 1H, *J* = 6.8 Hz, Ala-NH), 7.86 (d, 1H, *J* = 7.8 Hz, Ala-NH), 7.75 (t, 1H, *J* = 5.4 Hz, NH), 6.95 (t, 1H, *J* = 5.9 Hz, Gly-N*H*-BOC), 4.22 (m, 1H, Ala-αH), 4.18 (m, 1H, Ala-αH), 3.68 (m, 2H, Gly-αH), 3.56 (m, 2H, Gly-αH), 3.02 (m, 2H, BA-αH), 1.36 (s, 9H, BOC-CH$_3$), 1.34 (m, 2H, BA-βH), 1.24 (m, 2H, BA-γH), 1.20 (d, 3H, *J* = 6.8 Hz, Ala-CH$_3$), 1.18

(d, 3H, J = 6.8 Hz, Ala-CH_3), 0.84 (t, 3H, J = 7.3 Hz, BA-δH). ^{13}C NMR (100 MHz, DMSO-d_6): δ 172.67, 171.74, 169.33, 168.21, 155.81, 78.07, 48.45, 48.19, 43.13, 42.09, 38.16, 31.12, 28.17, 19.45, 18.36, 18.01, 13.68. IR (KBr, cm^{-1}): 3446, 3282, 3084, 2978, 2934, 2874, 1724, 1702, 1694, 1628, 1544, 1448, 1392, 1366, 1242, 1166, 1052, 1028, 1002.

N,N'-(2,8-dimethylphenoxathiin-4,6-diyldicarbonyl)bis(glycyl-L-alanyl-glycyl-L-alanine)-N-butylamide (20). ^1H NMR (200 MHz, TFA-*d*): δ 7.36 (s, 2H, Ar-H), 7.16 (s, 2H, Ar-H), 4.70 (collapsed dq, 4H, J = 7.1 Hz, Ala-αH), 4.50 (m, 4H, Gly-αH), 4.25 (s, 4H, Gly-αH), 3.39 (t, 4H, J = 6.8 Hz, BA-αH), 2.29 (s, 6H, Ar-CH_3), 1.54 (m, 16H, BA-βH, Ala-CH_3), 1.35 (m, 4H, BA-γH), 0.92 (t, 6H, J = 7.1 Hz, BA-δH). ^{13}C NMR (100 MHz, TFA-*d*): δ 178.31, 177.72, 174.65, 174.34, 173.22, 149.55, 139.06, 134.35, 130.84, 123.93, 122.92, 52.67, 45.81, 45.03, 43.52, 32.40, 21.65, 18.45, 18.19, 17.84, 14.17. IR (KBr, cm^{-1}): 3293, 3069, 2957, 2931, 2871, 1699, 1684, 1666, 1649, 1637, 1546, 1457, 1435, 1397, 1378, 1333, 1306, 1284 (sh), 1252, 1157.