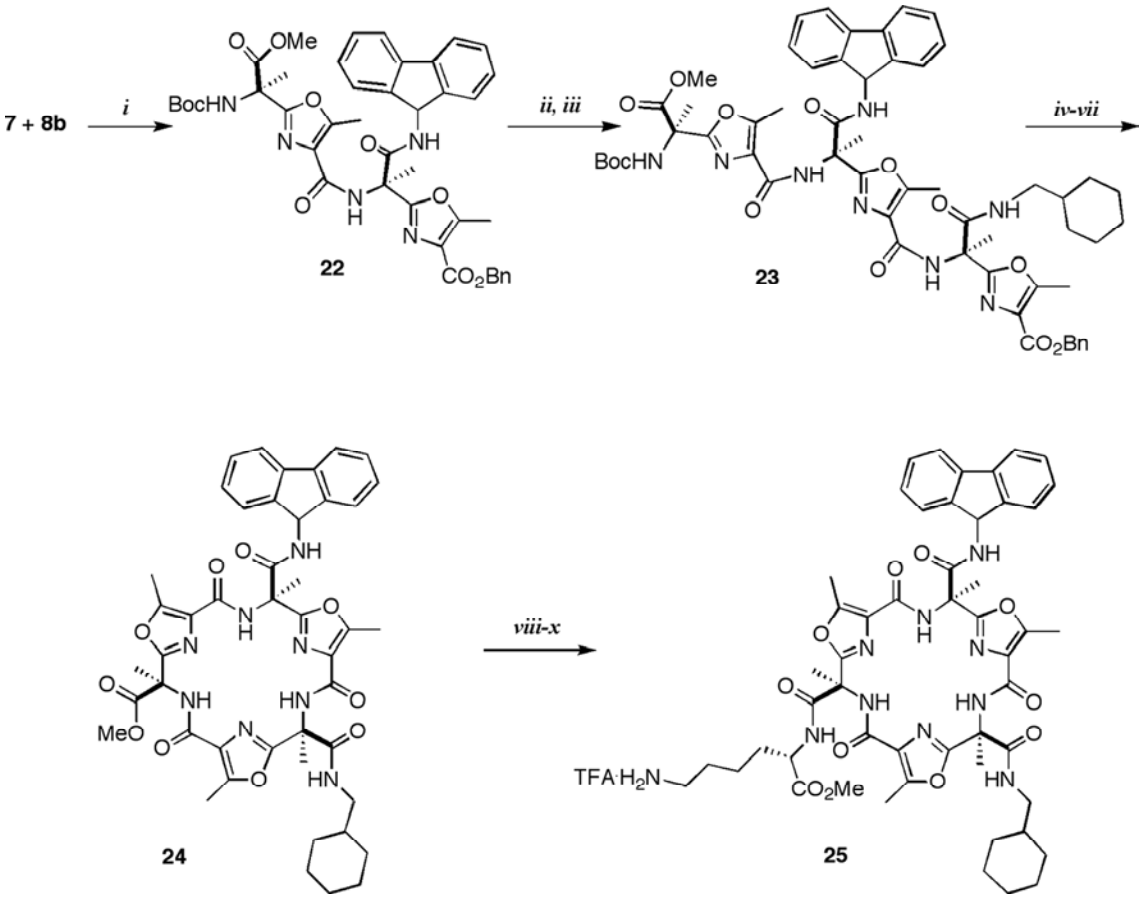
Supporting Text

Synthesis of the Cyclodiasteromer 25



Reagents and Conditions. (*i*) EDCI, HOBt, DIEA, DMF (65%); (*ii*) H_2/Pd-C(10%); (*iii*) **8a**, EDCI, HOBt, DIEA, DMF (54%, two steps); (*iv*) H_2/Pd-C(10%); (*v*) C_6F_5OH, DCC; (*vi*) TFA, DCM, RT, 3 h; (*vii*) DMAP, toluene, 95°C (71%, four steps); (*viii*) LiOH.H_2O, acetone, RT, 30 min. (71%); (*ix*) ε-*t*-Boc-*L*-lysine, EDCI, HOBt, DMF, DIEA (82%); (*x*) TFA, DCM, RT., 3 h (quantitative).

Synthesis of the Dimer 22. Following general procedure *i* the dimer **22** was obtained in a 65% yield (0.55 g) as a colorless foam. ^{1}H-NMR ($CDCl_3$): 8.48 (s, NH, 1H); 7.68 (d, J = 7.8 Hz, H-ar, 1H); 7.66 (d, J = 7.8 Hz, H-ar, 1H); 7.50 (d, J = 7.5Hz, H-ar, 1H); 7.28-7.39 (m, H-ar, 9H); 7.19 (t, J = 8.7 Hz, H-ar, 1H); 6.93 (d, J = 8.5 Hz, NH, 1H); 6.16 (d, J =

8.7 Hz, CH, 1H); 6.11 (s, NH, 1H); 5.25 (s, CH_2, 2H); 3.79 (s, CH_3, 3H); 2.55 (s, CH_3, 3H); 2.13 (s, CH_3, 3H); 2.09 (s, CH_3, 3H); 2.02 (s, CH_3, 3H); 1.44 [s, $(CH_3)_3$, 9H]. ^{13}C-NMR ($CDCl_3$): 171.19; 170.07; 169.49; 161.72; 161.03; 160.95; 157.39; 143.64; 143.53; 140.76; 140.70; 138.96; 138.65; 138.39; 135.71; 128.91; 128.37; 127.87; 127.79; 124.99; 124.83; 120.20; 120.15; 80.57; 66.60; 60.46; 58.97; 58.75; 55.52; 55.23; 53.77; 53.64; 28.31; 23.87; 21.10; 14.30; 12.43; 11.90. MALDI-FTMS [M+Na]+: expected, 800.2902; observed, 800.2909.

Synthesis of the Trimer 23: The benzyl ester of the dimer **22** (0.55 g) was deprotected following general procedure *v* to give the corresponding acid that was coupled with **8a** (0.29 g) following general procedure *i* (EDCI). The trimer **23** was obtained in 54% yield (0.4 g) as a colorless foam. ^{1}H NMR ($CDCl_3$): 8.61 (s, NH, 1H); 8.35 (s, NH, 1H); 7.68 (t, J = 7.5 Hz, 1H); 7.67 (d, J = 7.5 Hz, 1H); 7.45 (t, J = 7.5 Hz, 1H); 7.41-7.27 (m, 6H); 7.22 (t, J = 7.5 Hz, 1H); 6.69 (broad s, 1H); 6.50 (d, J = 8.6 Hz, 2H); 6.19 (d, J = 8.6 Hz, 2H); 5.32 (s, 2H); 3.79 (s, 3H); 3.05 (m, 2H); 2.57 (s, 3H); 2.54 (s, 3H); 2.47 (s, 3H); 2.14 (s, 3H); 2.02 (s, 3H); 1.99 (s, 3H); 1.66-1.53 (m, 7H); 1.43 [s, $(CH_3)_3$, 9H]; 1.15-1.11 (m, 2H). ^{13}C NMR ($CDCl_3$): 170.154; 169.47; 168.06; 161.89; 161.53; 161.48; 161.03; 160.50; 157.37; 155.87143.63; 143.54; 140.78; 140.60; 135.80; 129.17; 129.00; 128.95; 128.93; 128.73; 128.71; 128.55; 128.52; 128.06; 127.87; 127.77; 125.00; 124.78; 120.28; 120.24; 66.73; 59.01; 58.87; 58.23; 55.50; 55.26; 53.83; 46.44; 37.75; 30.70; 30.63; 29.60; 28.34; 26.43; 25.84; 25.83; 24.03; 23.24; 22.75; 18.95; 12.50; 11.99; 11.95. MALDI-FTMS $[M+Na]^+$: expected, 1091.4485; observed, 1091.4474.

Synthesis of the Cyclic Product 24: The benzyl ester of the trimer **23** (0.40 g) was deprotected following general procedure *v* to give the corresponding acid that was coupled with pentafluorophenol following general procedure *vi*. Deprotection of the Boc group following general procedure *iv* afforded the linear trimer that was transformed into the cyclic product **24** following general procedure *vii*. **24** was obtained as a colorless foam in 70% yield (0.23 g). ^{1}H NMR-300 ($CDCl_3$): 8.99 (s, NH, 1H); 8.92 (s, NH, 1H); 7.66 (d, J = 7.5 Hz, 2H); 7.58 (d, J = 7.5 Hz, 1H); 7.36 (m, 3H); 7.29-7.19 (m, 3H); 6.70 (d, J = 9 Hz, 1H); 6.59 (pseudo t, J = 6 Hz, 1H); 6.24 (d, J = 9 Hz, 1H); 3.76 (s, 3H); 3.15

(m, 1H); 2.98 (m, 1H); 2.75 (s, 3H); 2.68 (s, 3H); 2.66 (s, 3H); 2.19 (s, 3H); 2.10 (s, 3H); 2.03 (s, 3H); 1.70-1.40 (m, 7H); 1.22-1.08 (m, 2H); 0.92-0.76 (m, 2H). ^{13}C NMR-75 (routine + DEPT, $CDCl_3$): 168.36; 168.25; 167.53; 160.29; 160.23; 160.09; 160.03; 159.15; 156.26; 156.04; 155.76; 143.95; 143.79; 140.84; 140.79; 128.94 (CH); 128.89 (CH); 128.44; 128.20; 127.79 (CH); 127.77 (CH); 125.45 (CH); 124.91 (CH); 120.23 (CH); 120.16 (CH); 60.68; 60.55; 59.03; 55.53 (CH); 53.98 (CH_3); 46.53 (CH_2); 38.08 (CH); 30.93 (CH_2); 26.74 (CH_2); 26.13 (CH_2); 26.12 (CH_2); 22.90 (CH_3); 21.88 (CH_3); 21.76 (CH_3); 12.25 (CH_3); 12.21 (CH_3); 12.15 (CH_3). MALDI-FTMS $[M+Na]^+$: expected, 883.3385; observed, 883.3385.

Synthesis of 25. The methyl ester **24** (200 mg) was hydrolyzed following general procedure *ii* (method b) to give the corresponding acid in 71% yield (140 mg). ^{1}H NMR-300 ($CDCl_3$): 8.90 (s, NH, 1H); 8.84 (s, NH, 1H); 8.81 (s, NH, 1H); 7.53 (d, J = 7.2 Hz, 1H); 7.51 (d, J = 7.2 Hz, 1H); 7.46 (d, J = 7.2 Hz, 1H); 7.28-7.07 (m, 5H); 6.69 (d, J = 9 Hz, 1H); 6.52 (t, J = 6 Hz, 1H); 6.23 (d, J = 9 Hz, 1H); 6.23 (s broad, 1H), 6.10 (d, J = 9 Hz, 1H); 3.01 (m, 1H); 2.85 (m, 1H); 2.63 (s, 3H); 2.58 (s, 3H); 2.56 (s, 3H); 2.08 (s, 3H); 1.98 (s, 3H); 1.96 (s, 3H); 1.60-1.20 (m, 6H); 1.15-0.90 (m, 3H); 0.80-0.55 (m, 2H). ^{13}C NMR-75 (routine + DEPT, $CDCl_3$): 170.16; 168.17; 167.21; 160.50; 160.00; 159.96; 159.91; 159.87; 158.58; 156.06; 155.91; 155.88; 143.49; 143.36; 140.40; 128.60 (CH); 128.55 (CH); 128.17; 127.82; 127.78; 127.53 (CH); 125.05 (CH; 124.63 (CH); 119.85 (CH); 119.79 (CH); 60.32; 60.27; 55.22 (CH); 46.27 (CH_2); 37.66 (CH); 30.56 (CH_2); 26.38 (CH_2); 25.74 (CH_2); 22.22 (CH_3); 21.83 (CH_3); 21.42 (CH_3); 11.99 (CH_3); 11.94 (CH_3); 11.86 (CH_3). MALDI-FTMS $[M+H]^+$: expected: 847.3409; observed: 847.3405. The acid (100 mg) was coupled with ε-*t*-Boc-L-lysine following general procedure *i* to yield the corresponding amide (105 mg, 82%). ^{1}H NMR-300 ($CDCl_3$): 8.94 (s, NH, 1H); 8.92 (s, NH, 1H); 8.87 (s, NH, 1H); 7.65 (d, J = 7.8 Hz, 2H); 7.57 (d, J = 7.5 Hz, 1H); 7.40-7.18 (m, 5H); 7.07 (d, J = 7.5 Hz, 1H); 6.93 (d, J = 8.1 Hz, 1H); 6.76 (t, 1H); 6.21 (d, J = 9 Hz, 1H); 4.78 (m broad, 1H); 4.54 (m, 1H); 3.61 (s, 3H); 3.18-2.95 (m, 2H); 2.76 (s, 3H); 2.67 (s, 6H); 2.19 (s, 3H); 2.11 (s, 3H); 2.10 (s, 3H); 1.75-1.04 (m, 13H); 1.43 (s, 9H); 1.20-1.00 (m, 2H); 0.94-0.76 (m, 2H). ^{13}C NMR-75 (routine + DEPT, $CDCl_3$): 172.19; 168.70; 167.71; 167.49; 160.55; 160.50; 160.40; 160.25; 159.73;

156.35; 156.23; 156.16; 144.06; 143.74; 140.82; 128.95 (CH); 128.84 (CH); 128.36; 128.30; 128.11; 127.93 (CH); 127.78 (CH); 125.34 (CH); 125.02 (CH); 120.18 (CH); 120.16 (CH); 60.86; 60.76; 60.55; 55.58 (CH); 52.89 (CH); 52.64 (CH_3); 46.56 (CH_2); 40.63; 38.07 (CH); 32.02 (CH_2); 30.96 (CH_2); 29.67 (CH_2); 28.79 (CH_3); 26.73 (CH_2); 26.11 (CH_2); 22.74 (CH_2); 22.05 (CH_3); 21.88 (CH_3); 21.87 (CH_3) 12.33 (CH_3); 12.28 (CH_3); 12.21 (CH_3). MALDI-FTMS $[M+Na]^+$: expected, 1111.4859; observed, 1111.4831. The Boc group was deprotected following general procedure *iv* to produce **25** quantitatively (106 mg). ^{1}H NMR-300 ($CDCl_3$): 9.01 (s, NH, 1H); 8.94 (s, NH, 1H); 8.89 (s, NH, 1H); 7.97 (s broad, 3H); 7.65 (d, J = 7.5 Hz, 2H); 7.55 (d, J = 7.2 Hz, 1H); 7.42-7.19 (m, 5H); 6.87 (t, J = 5.4 Hz, 1H); 6.15 (d, J = 8.4 Hz, 1H); 4.55 (m broad, 1H); 3.61 (s, 3H); 3.38 (s broad, 1H); 3.12 (m, 1H); 2.90 (m, 3H); 2.70 (s, 3H); 2.65 (s, 6H); 2.19 (s, 3H); 2.09 (s, 3H); 2.04 (s, 3H); 2.00-1.28 (m, 14H); 1.20-1.04 (m, 3H); 0.92-0.76 (m, 2H). ^{13}C NMR-75 (routine + DEPT, $CDCl_3$): 171.61; 168.81; 167.39; 160.44; 160.41; 160.11; 159.97; 159.17; 156.09; 156.03; 155.91; 143.62; 143.39; 140.50; 140.43; 128.67 (CH); 128.58 (CH); 127.85 (CH); 127.65 (CH); 124.97 (CH); 124.72 (CH); 119.87 (CH); 60.68; 60.45; 59.90; 55.34 (CH); 52.46 (CH_3); 52.16 (CH); 46.27 (CH_2); 39.55 (CH_2); 37.74 (CH); 30.63 (CH_2); 26.43 (CH_2); 26.23 (CH_2); 25.80 (CH_2); 21.69 (CH_3); 21.50 (CH_3); 21.44 (CH_3); 11.89 (3 CH_3). MALDI-FTMS $[M+H]^+$: expected, 989.4510; observed, 989.4508.