Supporting Information

TOPOMIMETICS OF AMPHIPATHIC β-SHEET AND HELIX-FORMING BACTERICIDAL PEPTIDES NEUTRALIZE LIPOPOLYSACCHARIDE ENDOTOXINS

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Full spectroscopic characterization data of calixarene derivatives **2**– **4**, **6**–**12**, **15**, **19**–**23**.

Tetra-amide 2: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.67 (br t, *J* = 6.0 Hz, 4H), 6.77 (s, 8H), 4.52 (s, 8H), 4.49 (d, *J* = 13.0, 4H), 3.45 (br dt, *J* = 6.5, 6.0 Hz, 8H), 3.23 (d, *J* = 13.0 Hz, 4H), 2.47 (t, *J* = 6.5 Hz, 8H), 2.23 (s, 24 H), 1.07 (s, 36 H); ^{13}C NMR (125 MHz) δ 170.0 (4C), 153.2 (4C), 145.8 (4C), 132.9 (8C), 125.9 (8C), 74.8 (4C), 67.6 (4C), 58.3 (4C), 45.5 (8C), 37.3 (4C), 34.1 (4C), 31.5 (12C); HRMS (ESI) *m/z* calcd for $C_{68}H_{105}N_8Na_1O_8$ $(M+H+Na)^{2+}$ 592.3977, found 592.3992.

Tetra-amine 3: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.58 (br t, *J* = 6.4 Hz, 4H), 6.42 (s, 8H), 4.46 (s, 8H), 4.41 (d, *J* = 13.8 Hz, 4H), 3.42 (dt, *J* = 6.9, 6.4 Hz, 8H), 3.15 (d, *J* = 13.8 Hz, 4H), 2.44 (t, *J* = 6.9 Hz, 8H), 2.24 (t, *J* = 7.4 Hz, 8H), 2.20 (s, 24 H), 1.44 (app sextet, *J* ≈ 7 Hz, 8H), 0.84 (t, *J* = 7.2 Hz, 12H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.8 (4C), 153.8 (4C), 137.0 (4C), 133.6 (8C), 128.8 (8C), 74.4 (4C), 58.2 (4C), 45.5 (8C), 37.4 (4C), 37.2 (4C), 31.3 (4C), 24.6 (4C), 13.8 (4C); HRMS (ESI) *m/z* calcd for $C_{64}H_{97}N_8O_8$ $(M+H)^+$ 1105.7424, found 1105.7471.

Tetra-amine 4: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42 (t, *J* = 5.7 Hz, 2H), 7.05 (s, 2H), 6.94 (s, 2H), 6.70 (t, *J* =5.6 Hz, 1H), 6.66 (d, *J* = 2.0 Hz, 2H), 6.40 (d, *J* = 2.0 Hz, 2H), 5.31 (t, *J* = 5.9 Hz, 1H), 4.36 (d, *J* = 14.1 Hz, 2H), 4.24 (d, *J* = 13.2 Hz, 2H), 4.11^+ (s, 2H), 4.11^- (d, *J* = 14.1 Hz, 2H), 4.08 (s, 2H), 3.82 (d, *J* = 15.1 Hz, 2H), 3.62 (d, *J* = 15.1 Hz, 2H), 3.52 (ddt, *J* = 13.3, 6.6, 6.6 Hz, 2H), 3.37 (ddt, *J* = 13.3, 6.5, 5.3 Hz, 2H), 3.18 (d, *J* = 13.2, 2H), 3.09 (dt, *J* = 6.4, 5.8 Hz, 2H), 2.97 (dt, *J* = 7.7, 6.0 Hz, 2H), 2.58 (t, *J* = 8.8 Hz, 2H), 2.56 (t, *J* = 8.5 Hz, 2H), 2.49 (t, *J* = 6.7 Hz, 4H), 2.30-2.10 (m, 8H), 2.26 (s, 6H), 2.24 (s, 12H), 2.15 (s, 6H), 1.66 (m, 4H), 1.40 (app sextet, *J* = 7 Hz, 4H), 0.99 (t, *J* = 7.2 Hz, 3H), 0.96 (t, *J* = 7.2 Hz, 3H), 0.83 (t, *J* = 7.4 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.8 (1C), 169.0 (2C), 168.6 (1C), 153.2 (2C), 152.7 (1C), 152.0 (1C), 138.1 (1C), 137.9 (1C), 137.4 (2C), 135.3 (2C), 133.5 (2C), 132.9 (2C), 131.7 (2C), 130.3 (2C), 129.6 (2C), 129.0 (2C), 128.9 (2C), 73.6 (2C), 72.0 (1C), 69.8 (1C), 58.3 (2C), 58.3 (1C), 58.2 (1C), 45.9 (2C), 45.6 (4C), 45.4 (2C), 37.9 (1C), 37.8 (2C), 37.6^+ (1C), 37.6^- (2C), 37.3 (2C), 37.1 (1C), 37.0 (1C), 31.6 (2C), 24.8^+ (2C), 24.8^- (1C), 24.8^- (1C), 14.4 (1C), 14.1(2C), 14.0 (1C); HRMS (ESI) *m/z* calcd for $C_{64}H_{97}N_8O_8$ $(M+H)^+$ 1105.7424, found 1105.7514.

Tetra-amine 6: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.94 (br t, *J* = 6.5 Hz, 2H), 7.33 (br t, *J* = 6.5 Hz, 2H), 6.73 (s, 4H), 6.17 (s, 4H), 5.65 (ddt, *J* = 17.1, 10.5, 6.8 Hz, 2H), 4.91 (dd, *J* = 10.5, 1.4 Hz, 2H), 4.85 (dd, *J* = 17.1, 1.4 Hz, 2H), 4.80 (s, 2H), 4.65 (s, 2H), 4.61 (s, 4H), 4.45 (d, *J* = 13.5 Hz, 4H), 4.33 (s, 4H), 3.50 (dt, *J* ≈ 6, 6 Hz, 4H), 3.37 (dt, *J* ≈ 6, 6 Hz, 4H), 3.17 (d, *J* = 14.7 Hz, 4H), 3.16 (s, 4H), 2.86 (d, *J* =6.8 Hz, 4H), 2.52 (t, *J* = 6.4 Hz, 4H), 2.40 (t, *J* = 6.4 Hz, 4H), 2.24 (s,

12H), 2.19 (s, 12H), 1.68 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.2 (2C), 169.5 (2C), 154.9 (2C), 153.4 (2C), 145.9 (2C), 137.8 (2C), 134.9 (4C), 134.4 (2C), 134.3 (2C), 132.9 (4C), 130.1 (4C), 128.5 (4C), 115.4 (2C), 111.6 (2C), 74.7 (2C), 74.2 (2C), 58.3 (2C), 58.1 (2C), 45.5 (4C), 45.4 (4C), 44.1 (2C), 39.6 (2C), 37.1 (2C), 37.1 (2C), 31.3 (4C), 22.3 (2C); HRMS (ESI) *m/z* calcd for $C_{66}H_{93}N_8O_8$ $(M+H)^+$ 1125.7116, found 1125.7213.

Tetra-amine 7: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.87 (t, *J* = 6.0 Hz, 2H), 7.36 (t, *J* = 5.9 Hz, 2H), 6.63 (s, 4H), 6.20 (s, 4H), 4.58 (s, 4H), 4.43 (d, *J* =13.9 Hz, 4H), 4.36 (s, 4H), 3.48 (td, *J* ≈ 7, 6 Hz, 4H), 3.38 (td, *J* ≈ 6, 6 Hz, 4H), 3.15 (d, *J* = 13.9 Hz, 4H), 2.49 (t, *J* = 6.6 Hz, 4H), 2.39 (t, *J* = 6.2 Hz, 4H), 2.28 (d, *J* = 2.7 Hz, 4H), 2.23 (s, 12H), 2.18 (s, 12H), 2.06 (t, *J* = 7.0 Hz, 4H), 1.78 (m, 2H), 1.30 (tq, *J* = 7.5, 7.0 Hz, 4H), 0.87 (d, *J* = 6.8 Hz, 12H), 0.78 (t, *J* = 7.5 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.3 (2C), 169.7 (2C), 154.4 (2C), 153.1 (2C), 137.1 (2C), 136.2 (2C), 134.4 (4C), 132.7 (4C), 130.1 (4C), 128.4 (4C), 74.7 (2C), 74.2 (2C), 58.3 (2C), 58.1 (2C), 45.4 (4C), 45.4 (4C), 44.9 (2C), 37.4 (2C), 37.1 (2C), 37.1 (2C), 31.3 (4C), 30.7 (2C), 24.5 (2C), 22.4 (4C), 14.0 (2C); HRMS (ESI) *m/z* calcd for $C_{66}H_{101}N_8O_8$ $(M+H)^+$ 1133.7742, found 1133.7813.

Tetra-amide 8: ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.56 (t, *J* = 5.5 Hz, 4H), 6.45 (s, 8H), 4.35 (d, *J* =13.2 Hz, 4H), 3.87 (t, *J* = 7.2 Hz, 8H), 3.32 (td, *J* = 6, 6 Hz, 8H), 3.40 (d, *J* = 13.2 Hz, 4H), 5.27 (br t, *J* = 7.8 Hz, 8H), 2.41 (t, *J* = 6.1 Hz, 8H), 2.27 (br t, *J* = 7.8 Hz, 8H), 2.22 (s, 24H), 1.79 (m, 12H), 0.95 (d, *J* = 7.0 Hz, 24H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.0 (4C), 154.9 (4C), 134.9 (8C), 134.3 (4C), 128.0 (8C), 73.8 (4C), 58.3 (4C), 45.4 (8C), 39.1 (4C), 38.8 (4C), 37.2 (4C), 31.3 (4C), 31.2 (4C), 25.6 (4C), 23.0 (8C); HRMS (ESI) *m/z* calcd for $C_{76}H_{122}N_8O_8$ $(M+2H)^{2+}$ 637.4693, found 637.4686.

Di-amide 9: ^{1}H NMR (500 MHz, CD_3OD) δ 7.14 (d, *J* = 7.5 Hz, 4H), 6.93 (d, *J* = 7.5 Hz, 4H), 6.73 (t, *J* = 7.5 Hz, 4H), 4.62 (s, 4H), 4.23 (d, *J* = 13.0 Hz, 4H), 3.61 (t, *J* = 6.6 Hz, 4H), 3.51 (d, *J* = 13.0 Hz, 4H), 2.65 (t, *J* = 6.6 Hz, 4H), 2.29 (s, 12H); ^{13}C NMR (75 MHz, CD_3OD) δ 170.6 (2C), 153.2 (2C), 152.4 (2C), 134.3 (4C), 130.6 (4C), 130.1 (4C), 128.9 (4C), 127.4 (2C), 121.4 (2C), 75.4 (2C), 59.2 (2C), 45.5 (4C), 37.7 (2C), 32.3 (4C); HRMS (ESI) *m/z* calcd for $C_{40}H_{49}N_4O_6$ $(M+H)^+$ 681.3652, found 681.3628.

5,11,17,23-Tetra-*tert*-butyl-25,27-bis(2-guanidinoethoxy)-26,28-dihydroxy calix[4]arene trifluoroacetic acid salt (10): ^{1}H NMR (500 MHz, CD_3OD) δ 7.19 (s, 4H), 7.02 (s, 4H), 4.26 (d, *J* = 13.2 Hz, 4H), 4.22 (t, *J* = 5.2 Hz, 4H), 3.81 (t, *J* = 5.2 Hz, 4H), 3.48 (d, *J* = 13.2 Hz, 4H), 1.27 (s, 18H), 1.03 (s, 18H); ^{13}C NMR (125 MHz, $CDCl_3$ and CD_3OD) δ 157.6 (2C), 148.9 (2C), 148.4 (2C), 148.1 (2C), 143.9 (2C), 132.5 (4C), 127.9 (4C), 126.1 (4C), 125.5 (4C), 74.0 (2C), 41.5 (2C), 34.1 (2C), 33.8 (2C), 31.5 (4C), 31.3 (6C), 30.8 (6C); HRMS (ESI) *m/z* calcd for $C_{50}H_{72}N_6O_4$ $(M+2H)^{2+}$ 410.2808, found 410.2787.

25,27-bis(2-guanidinoethoxy)-26,28-dihydroxy calix[4]arene trifluoroacetic acid salt (11): ^{1}H NMR (300 MHz, CD_3OD) δ 7.14 (d, *J* = 7.3 Hz, 4H), 6.79 (d, *J* = 7.3 Hz, 4H), 6.74 (t, *J* = 7.3 Hz, 2H), 6.60 (t, *J* = 7.3 Hz, 2H), 4.28 (d, *J* = 12.0 Hz, 4H), 4.18 (t, *J* = 4.9 Hz, 4H), 3.81 (t, *J* = 4.9 Hz, 4H), 3.47 (d, *J* = 13.0 Hz, 4H); ^{13}C NMR (75 MHz, CD_3OD) δ 159.4 (2C), 153.8 (2C), 152.8 (2C), 134.3 (4C), 130.5 (4C), 130.1 (4C), 129.6 (4C), 126.7 (2C), 121.1 (2C), 75.6 (2C), 42.9 (2C), 32.0 (4C); HRMS (ESI) *m/z* calcd for $C_{34}H_{39}N_6O_4$ $(M+H)^{+}$ 595.3033, found 595.2967.

5,11,17,23-Tetra-*tert*-butyl-25-(2-aminoethoxy)-27-(2-guanidinoethoxy)-26,28-dihydroxy Calix[4]arene trifluoroacetic acid salt (12): ^{1}H NMR (500 MHz, CD_3OD) δ 7.21 (s, 4H), 6.98 (m, 4H), 4.26 (m, 4H), 4.22 (d, *J* = 13.2 Hz, 2H), 4.18 (d, *J* = 13.2 Hz, 2H), 3.80 (m, 2H), 3.61 (m, 2H), 3.50 (d, *J* = 13.2 Hz, 2H), 3.49 (d, *J* = 13.2 Hz, 2H), 1.29 (s, 18H), 1.00 (m, 18H); HRMS (ESI) *m/z* calcd for $C_{49}H_{70}N_4O_4$ $(M+2H)^{2+}$ 389.2698, found 389.2686.

Tetra-triazole 15: ^{1}H NMR (300 MHz, CD_3OD, 55 °C) δ 8.44 (s, 4H), 7.94 (s, 4H), 7.04 (s, 8H), 4.59 (s, 8H), 4.57 (d, *J* = 12.0, 4H), 4.23 (t, *J* = 7.0, 8H), 3.37 (d, *J* = 13.0 Hz, 4H), 3.31 (t, *J* = 6.6, 8H), 2.10 (tt, *J* ≈ 7, 7, 8H), 1.13 (s, 36H); HRMS (ESI) *m/z* calcd for $C_{72}H_{96}N_{16}Na_2O_8$ $(M+2Na)^{2+}$ 679.3696, found 679.3747.

Tetra-amide 19: ^{1}H NMR (300 MHz, CD_3OD, 55 °C) δ 6.95 (br s, 8H), 4.59 (s, 8H), 4.50 (d, *J* = 12.9 Hz, 4 H), 3.64 (t, *J* = 5.9 Hz, 8H), 3.33 (d, *J* = 12.9 Hz, 4H), 3.19 (t, *J* = 6.0 Hz, 8H), 1.13 (s, 36H); HRMS (ESI) *m/z* calcd for $C_{60}H_{90}N_8O_8$ $(M+2H)^{2+}$ 525.3441, found 525.3446.

Diamide 20: ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.00 (br t, *J* = 4.8 Hz, 2H), 8.16 (s, 2H), 7.10 (d, *J* = 7.5 Hz, 4H), 6.97 (d, *J* = 7.5 Hz, 4H), 6.83 (t, *J* = 7.5 Hz, 2H), 6.75 (t, *J* = 7.5 Hz, 2H), 4.60 (s, 4H), 4.18 (d, *J* = 13.2 Hz, 4H), 3.48 (m, 8H), 2.93 (t, *J* = 6.0 Hz, 4H), 1.82 (br s, 4H); ^{13}C NMR

(75 MHz, $CDCl_3$) δ 168.7 (2C), 152.0 (2C), 151.2 (2C), 133.0 (4C), 129.9 (4C), 129.2 (4C), 127.8 (4C), 126.9 (2C), 120.9 (2C), 75.2 (2C), 42.7 (2C), 41.8 (2C), 31.8 (4C); HRMS (ESI) *m/z* calcd for $C_{36}H_{41}N_4O_6$ $(M+H)^+$ 625.3026, found 625.2997.

5,17-Di-(hydroxycabonyl)ethyl-25,27-di-(3-methylbutoxy)-26,28-dihydroxycalix[4]arene (21): ^1H NMR (300 MHz, CD_3OD) δ 6.96 (d, *J* = 7.2 Hz, 4H), 6.95 (s, 4H), 6.75 (t, *J* = 7.2 Hz, 2H), 4.27 (d, *J* = 13.0 Hz, 4H), 4.01 (t, *J* = 6.7 Hz, 4H), 3.37 (d, *J* = 13.0, 4H), 2.77 (t, *J* = 7.6 Hz, 4H), 2.52 (t, *J* = 7.6 Hz, 4H), 2.18 (tqq, *J* ≈ 7, 7, 7 Hz, 2H), 1.97 (dt, *J* ≈ 7, 7 Hz, 4H), 1.11 (d, *J* = 6.6 Hz, 12H); ^{13}C NMR (125 MHz, CD_3OD) δ 177.3 (2C), 153.6 (2C), 152.7 (2C), 135.1 (4C), 132.7 (2C), 130.1 (4C), 129.6 (4C), 129.5 (4C), 126.3 (2C), 76.5 (2C), 40.3 (2C), 37.5 (2C), 32.3 (4C), 31.5 (2C), 26.1 (2C), 23.4 (4C); HRMS (ESI) *m/z* calcd for $C_{44}H_{51}O_8$ $(M-H)^-$ 707.3589, found 707.3568.

Di-phosphonic acid 22: ^1H NMR (500 MHz, CD_3OD) δ 6.96 (d, *J* = 7.8 Hz, 4H), 6.93 (s, 4H), 6.76 (t, *J* = 7.8 Hz, 2H), 4.29 (d, *J* = 12.6 Hz, 4H), 4.03 (t, *J* = 6.9 Hz, 4H), 3.38 (d, *J* = 12.6 Hz, 4H), 2.57 (t, *J* = 7.0 Hz, 4H), 2.19 (tqq, *J* ≈ 7, 6, 6 Hz, 2H), 1.98 (dt, *J* ≈7, 7 Hz, 4H), 1.84 (nfom, 4H), 1.61 (nfom including J_{PH} = 18.0 Hz, 4H), 1.12 (d, *J* = 6.5 Hz, 12H); ^{13}C NMR (125 MHz, CD_3OD) δ 153.4 (2C), 152.4 (2C), 135.0 (4C), 133.1 (2C), 129.9 (4C), 129.6 (4C), 129.4 (4C), 126.2 (2C), 76.4 (2C), 40.1 (2C), 36.6 (d, J_{CP} = 17.1 Hz, 2C), 32.2 (6C), 27.3 (d, J_{CP} = 137.9 Hz, 2C), 26.0 (2C), 23.4 (4C); ^{31}P (121 MHz, CD_3OD) δ 31.0; HRMS (ESI) *m/z* calcd for $C_{44}H_{56}O_{10}P_2$ $(M-2H)^{2-}$ 403.1680, found 403.1682.

Bis-sulfate 23: ^1H NMR (500 MHz, CD_3OD) δ 6.96 (d, *J* = 7.5 Hz, 4H), 6.95 (s, 4H), 6.76 (t, *J* = 7.5 Hz, 2H), 4.27 (d, *J* = 12.8 Hz, 4H), 4.02 (t, *J* = 6.8 Hz, 4H), 3.98 (t, *J* = 6.4 Hz, 4H), 3.36 (d, *J* = 12.8 Hz, 4H), 2.58 (t, *J* = 7.6 Hz, 4H), 2.18 (tqq, *J* ≈ 7, 6, 6 Hz, 2H), 1.97 (td, *J* ≈ 7, 7 Hz, 4H), 1.89 (tt, *J* ≈ 7, 6 Hz, 4H), 1.11 (d, *J* = 6.2 Hz, 12H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.6 (2C), 152.5 (2C), 135.2 (4C), 133.4 (2C), 130.1 (4C), 129.8 (4C), 129.5 (4C), 126.3 (2C), 76.4 (2C), 68.5 (2C), 40.4 (2C), 32.8 (2C), 32.3 (4C), 32.2 (2C), 26.1 (2C), 23.5 (4C); HRMS (ESI) *m/z* calcd for $C_{44}H_{54}O_{12}S_2$ $(M-2Na)^{2-}$ 419.1534, found 419.1524.