

## Supplementary Materials: Potent in vitro and in vivo anticancer activity of new bipyridine and bipyrimidine gold(III)-dithiocarbamate derivatives

Muhammad Altaf, Naike Casagrande, Elena Mariotto, Nadeem Baig, Abdel-Nasser Kawde, Giuseppe Corona, Roberto Larcher, Cinzia Borghese, Claudia Pavan, Adam A. Seliman, Donatella Aldinucci and Anvarhusein A. Isab

### Supplementary Materials and Methods

#### Reagents

Sodium tetrachloroaurate(III) dihydrate, sodium dimethyldithiocarbamate hydrate, sodium diethyldithiocarbamate trihydrate, sodium dibenzylthiocarbamate hydrate, 2,2'-bipyrimidine, 2,2'-bipyridine-3,3'-diol, disodium hydrogen phosphate, sodium dihydrogen phosphate, tryptophan, lysozyme, 98% guanine, and 99.8% ethanol were obtained from Sigma-Aldrich. Anhydrous 99.8% dichloromethane were purchased from Merck and used without further purification. Double distilled water used only for electrochemical measurements was from an Aquatron A4000D water still (Stuart). All reactions were carried out at ambient room temperature.

#### Synthesis of gold(III) compounds (C1-C8)

**[Au(BPYH)(Cl)<sub>2</sub>]Cl (C1)** was synthesized by combining 0.5 mM Na[AuCl<sub>4</sub>].2H<sub>2</sub>O (200 mg in 3 mL H<sub>2</sub>O) and 0.5 mM 2,2'-bipyridine-3,3'-diol (94 mg in 15 mL of ethanol:dichloromethane (3:1)) and stirred for 3 h. The solution was filtered and kept in an undisturbed area for 3 days. Black cubic crystals appeared. The black precipitate was collected by filtration, washed with distilled water (3 × 10 mL) and dried under vacuum.

**[Au(BPYH)(DMDTC)]Cl<sub>2</sub> (C2)** was synthesized stepwise. First, 0.5 mM Na[AuCl<sub>4</sub>].2H<sub>2</sub>O (200 mg in 3 mL distilled water) and 0.5 mM 2,2'-bipyridine-3,3'-diol (94.0 mg in 15 mL ethanol:dichloromethane (3:1)) were added simultaneously to 20 mL of 99.8% ethanol, and the mixture was stirred for 3 h, generating a pale yellow, turbid solution. Second, 0.5 mM sodium dimethyldithiocarbamate hydrate (71.6 mg in 10 mL distilled water) was added dropwise and the mixture was stirred for an additional 1 h. The product light-yellow precipitate was collected by filtration, washed with distilled water (3 × 10 mL), and dried under vacuum.

**[Au(BPYH)(DEDTC)]Cl<sub>2</sub> (C3)** was synthesized stepwise. First, 0.5 mM Na[AuCl<sub>4</sub>].2H<sub>2</sub>O (200 mg in 3 mL H<sub>2</sub>O) and 0.5 mM 2,2'-bipyridine-3,3'-diol (94.0 mg in 15 mL ethanol:dichloromethane (3:1)) were added simultaneously to 20 mL of 99.8% ethanol, and the mixture was stirred for 3 h, generating a yellow turbid solution. Second, 0.5 mM sodium diethyldithiocarbamate trihydrate (112.6 mg in 10 mL distilled water) was added dropwise and the mixture was stirred for an additional 1 h. The obtained yellow precipitate was collected by filtration, washed with distilled water (3 × 10 mL) and dried under vacuum. The final product was a yellow crystalline powder.

**[Au(BPYH)(DBDTC)]Cl<sub>2</sub> (C4)** was synthesized stepwise. First, 0.5 mM 2,2'-bipyridine-3,3'-diol (94.0 mg in 15 mL ethanol:dichloromethane (3:1)) was combined with 0.5 mM Na[AuCl<sub>4</sub>].2H<sub>2</sub>O (200 mg in 3 mL distilled water) and the mixture was stirred for 3 h, generating an orange turbid solution. Second, 0.5 mM sodium dibenzylthiocarbamate hydrate (148 mg in 10 mL 99.8% ethanol) was added dropwise and the mixture was stirred for an additional 1 h. The orange precipitate was collected by filtration, washed with distilled water (3 × 10 mL) and dried under vacuum. The final product was an orange crystalline powder.

**[Au<sub>2</sub>(BPM)(Cl)<sub>4</sub>]Cl<sub>2</sub> (C5)** was synthesized by combining 0.5 mM 2,2'-bipyrimidine (79 mg in 20 mL 99.8% ethanol) and 1.0 mM Na[AuCl<sub>4</sub>].2H<sub>2</sub>O (397.8 mg in 10 mL distilled water). The mixture was stirred for 3 h. The yellow precipitate was collected by filtration, washed with distilled water (3 × 10 mL), and dried under vacuum.

**[Au<sub>2</sub>(BPM)(DMDTC)<sub>2</sub>]Cl<sub>4</sub> (C6)** was synthesized stepwise. First, 0.5 mM 2,2'-bipyrimidine (79 mg in 20 mL 99.8% ethanol) was combined with 1.0 mM Na[AuCl<sub>4</sub>].2H<sub>2</sub>O (397.8 mg in 3 mL distilled water). The mixture was stirred for 3 h, generating a bright yellow, turbid solution. Then, 1.0 mM sodium

dimethyldithiocarbamate hydrate (143.2 mg in 20 mL distilled water) was slowly added, and the reaction mixture was stirred for 1 h. The product appeared as a pale yellow precipitate. The precipitate was collected by filtration, washed with distilled water ( $3 \times 10$  mL) and dried under vacuum.

[Au<sub>2</sub>(BPM)(DEDTC)<sub>2</sub>]Cl<sub>4</sub> (C7) was synthesized stepwise. First, 0.5 mM 2,2'-bipyrimidine (79 mg in 20 mL 99.8% ethanol) was combined with 1.0 mM Na[AuCl<sub>4</sub>].2H<sub>2</sub>O (397.8 mg in 3.0 mL distilled water). The mixture was stirred for 3 h, generating a bright yellow, turbid solution. Then, 1.0 mM sodium diethyldithiocarbamate hydrate (226 mg in 20 mL distilled water) was slowly added, and the reaction mixture was stirred for 1 h. The product appeared as a dark yellow precipitate; it was collected by filtration, washed with distilled water ( $3 \times 10$  mL), and dried under vacuum for 72 hours.

[Au<sub>2</sub>(BPM)(DBDTC)<sub>2</sub>]Cl<sub>4</sub> (C8) was synthesized stepwise. First, 0.5 mM 2,2'-bipyrimidine (79 mg in 20 mL 99.8% ethanol) was combined with 1.0 mM Na[AuCl<sub>4</sub>].2H<sub>2</sub>O (397.8 mg in 3 mL distilled water). The mixture was stirred for 3 h, generating a yellow, turbid solution. Then, 1.0 mM sodium diethyldithiocarbamate hydrate (295.4 mg in 20 mL distilled water) was slowly added, and the reaction mixture was stirred for 1 h. The product appeared as a yellowish green precipitate; it was collected by filtration, washed with distilled water ( $3 \times 10$  mL), and dried under vacuum for 72 h.

#### *Chemical characterization of gold(III) compounds*

Due to the poor solubility of the gold(III) compounds in water, they were dissolved in 99.8% ethanol. The pH of buffers was monitored on a Accumet XL50 pH meter. A GR-2000 electrical balance was used to weigh the various chemicals. Electrochemical measurements for cyclic voltammetry and square wave voltammetry were performed using Autolab instruments (Metrohm; Netherlands). The electrochemical workstation had three electrodes (from CH Instruments): a glassy carbon electrode (GCE) as the working electrode, platinum as the counter electrode, and Ag/AgCl as the reference electrode (in saturated KCl). The GCE was polished as a mirror-like surface with alumina slurry on a synthetic cloth before every electrochemical analysis. Square wave voltammetry and cyclic voltammetry were scanned from 0 to 1.3 V for the various analyses. Elemental analyses of gold(III) compounds (C1-C8) were performed on PerkinElmer Series 11 (CHNS/O), Analyzer 2400.

The solid state FTIR spectra of sodium dimethyldithiocarbamate hydrate, sodium diethyldithiocarbamate trihydrate, and sodium dibenzoyldithiocarbamate hydrate (free ligands) and their corresponding gold(III) complexes were recorded on a PerkinElmer FTIR 180 spectrophotometer or NICOLET 6700 FTIR using potassium bromide (KBr) pellets over the range 4000–400 cm<sup>-1</sup>. <sup>1</sup>H and <sup>13</sup>C NMR spectra were recorded on a LAMBDA 500 spectrophotometer operating at 500.01 and 125.65 MHz respectively, corresponding to a magnetic field of 11.74 T. Tetramethylsilane was used as an internal standard for <sup>1</sup>H and <sup>13</sup>C. The <sup>13</sup>C NMR spectra were obtained with <sup>1</sup>H broadband decoupling, and the spectral conditions were: 32 k data points, 0.967 s acquisition time, 1.00 s pulse delay and 45 g pulse angle.

#### *Gold (III) compound interactions with lysozyme, tryptophan and guanine*

The electrochemical investigation of the interactions between the gold(III) compounds (C1-C8) and lysozyme, tryptophan and guanine was performed using the Autolab instrument described above, with a three-electrode system (CH Instruments): platinum wire counter electrode (CHI115), Ag/AgCl reference electrode (in 3 M KCl, CHI111) and glassy carbon working electrode (CHI112) inserted into a 5.0 ml glass cell. Solutions of 1 mM lysozyme, 5 mM tryptophan and 5 mM guanine were prepared in double distilled water, and the experiment was performed in 0.1 M phosphate buffer at pH 6.8.

#### *Cellular uptake of gold (III) compounds*

PC3 cells ( $1 \times 10^6$  cells seeded in  $100 \times 20$  culture dishes) were treated for 2 h in duplicate with 3 μM C4, C5, C6 or C7 in complete culture medium. After treatment, monolayers were washed with ice-cold PBS four times, and the cells were detached with trypsin-EDTA and washed three times with ice-cold PBS by centrifugation. The cell pellet was solubilized in 700 μL of HNO<sub>3</sub>-HCl solution (1:3 molar ratio) for 2 h at 100 °C, and then diluted with 4 mL water. Samples were analyzed for gold on an Agilent 7500 inductively

coupled plasma mass spectrometer (ICP-MS). Results were expressed as ng gold/10<sup>6</sup> cells. The experiment was performed a total of two times and the results were expressed as mean and SD.

#### *Growth inhibition curves for C6 in adipose-derived stromal cells*

Human adipose-derived stromal cells (ADSCs) were from Lonza (Verviers, Belgium). ADSCs were maintained in MSGM bullet kit (Lonza) and experiments were performed in DMEM (Cambrex Bio Science, Milan, Italy) supplemented with 10 % FBS. To evaluate effects of C6, ADSCs were seeded in 96-well flat-bottomed microplates (5.0 × 10<sup>3</sup> cells in 100 µL per well) and incubated for 24 h (to allow cell adhesion) before drug testing. The medium was removed and replaced with fresh medium containing C6 at increasing concentrations (from 0.1 to 1 µM). Cells were incubated at 37 °C for 72 h. Each treatment was performed in triplicate. Cell growth was measured using the MTT assay.

## Supplementary Results

#### *Analytical data of gold(III) compounds*

**[Au(BPYH)(Cl)<sub>2</sub>]<sub>2</sub>Cl (C1).** Yield: 83.09% (219.98 mg). FT-IR (KBr,  $\nu_{\max}$ , cm<sup>-1</sup>): 3470 (b), 3071 (w), 1647 (m), 1584 (s), 1459 (s), 1269 (m), 1134 (s), 1012 (m), 916 (w), 790 (s), 565 (m), 508 (m). <sup>1</sup>H NMR (500 MHz, DMSO-d<sub>6</sub>):  $\delta$  = 7.57, 8.25 and 8.77 (3H, 2 × CH, BPYH). <sup>13</sup>C NMR (125.65 MHz, DMSO-d<sub>6</sub>):  $\delta$  = 125.81, 128.31, 136.68, 138.63 and 155.31 (BPYH). Anal. calc. for C<sub>10</sub>H<sub>7</sub>Cl<sub>2</sub>N<sub>2</sub>O<sub>2</sub>Au (456); C, 26.38; H, 1.55; N, 6.16; Found: C, 26.42; H, 1.53; N, 6.18%.

**[Au(BPYH)(DMDTC)]Cl<sub>2</sub> (C2).** Yield: 83.09% (219.98 mg). FT-IR (KBr,  $\nu_{\max}$ , cm<sup>-1</sup>): 3437 (b), 3055 (w), 2921 (w); 1576 (s), 1484 (s), 1299 (m), 1111 (w), 1060 (m), 989 (w), 795 (s), 580 (m). <sup>1</sup>H NMR (500 MHz, DMSO-d<sub>6</sub>):  $\delta$  = 2.49 (6H, 2 × CH<sub>3</sub>), 7.51, 8.18 and 8.63 (2H, 2 × CH, BPYH). <sup>13</sup>C NMR (125.65 MHz, DMSO-d<sub>6</sub>):  $\delta$  = 39.38 (CH<sub>3</sub>), 126.20, 128.30, 135.49, 138.74 and 155.33 (2,2'-BPYH), 193.84 (NC = S). Anal. calc. for C<sub>13</sub>H<sub>13</sub>Cl<sub>2</sub>N<sub>3</sub>O<sub>2</sub>S<sub>2</sub>Au (539.81): C, 28.92; H, 2.43; N, 7.79; S, 11.88%. Found: C, 28.97; H, 2.39; N, 7.81; S, 11.91%.

**[Au(BPYH)(DEDTC)]Cl<sub>2</sub> (C3).** Yield: 86.87% (166.87 mg). FT-IR (KBr,  $\nu_{\max}$ , cm<sup>-1</sup>): 3443 (b), 3047 (w), 2928 (w), 1572 (s), 1490 (s), 1235 (m), 1155 (w), 1063 (m), 876 (m), 796 (s), 548 (m). <sup>1</sup>H NMR (500 MHz, DMSO-d<sub>6</sub>):  $\delta$  = 2.49 (6H, 2 × CH<sub>3</sub>), 3.75 (4H, 2 × CH<sub>2</sub>), 7.49, 8.18 and 8.62 (2H, 2 × CH, BPYH). <sup>13</sup>C NMR (125.65 MHz, DMSO-d<sub>6</sub>):  $\delta$  = 12.11 (CH<sub>3</sub>), 46.52 (CH<sub>2</sub>), 125.78, 128.21, 136.74, 138.79 and 155.33 (2,2'-BPYH), 195.11 (NC = S). Anal. calc. for C<sub>15</sub>H<sub>17</sub>Cl<sub>2</sub>N<sub>3</sub>O<sub>2</sub>S<sub>2</sub>Au (567.86): C, 31.73; H, 3.02; N, 7.40; S, 11.29%. Found: C, 31.76; H, 2.99; N, 7.43; S, 11.31%.

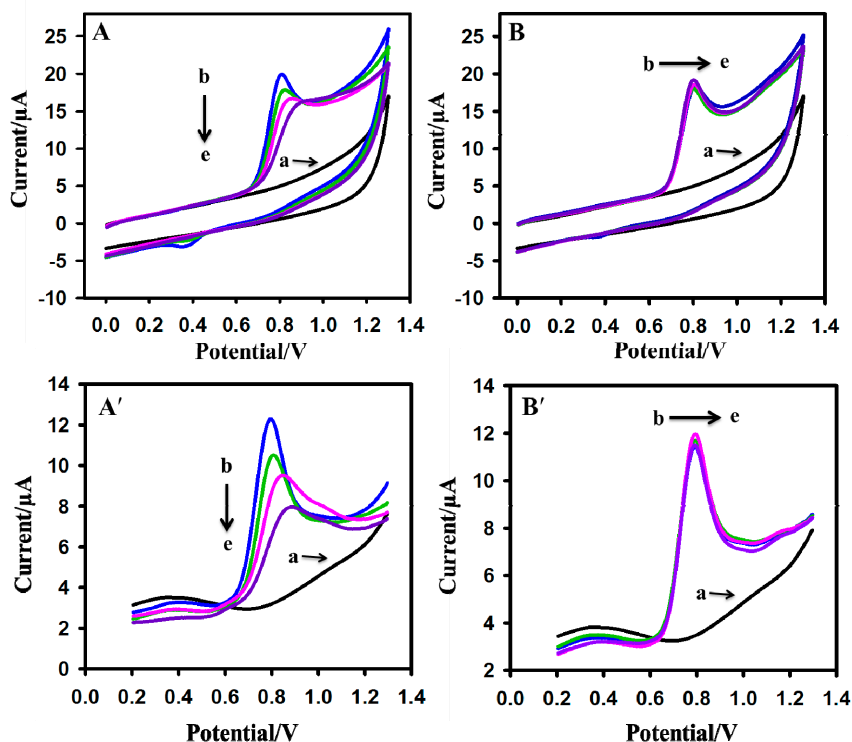
**[Au(BPYH)(DBDTC)]Cl<sub>2</sub> (C4).** Yield: 85.55% (226.13 mg). FT-IR (KBr,  $\nu_{\max}$ , cm<sup>-1</sup>): 3444 (b), 3021 (w), 2925 (w); 1532 (s), 1434 (s), 1223 (s), 1117 (m), 1068 (m), 982 (m), 796 (s), 549 (m). <sup>1</sup>H NMR (500 MHz, DMSO-d<sub>6</sub>):  $\delta$  = 5.78 (4H, 2 × CH<sub>2</sub>), 8.10 (10H, 2 × C<sub>6</sub>H<sub>5</sub>), 8.18, 8.27 and 8.93 (2H, 2 × CH, BPYH). <sup>13</sup>C NMR (125.65 MHz, DMSO-d<sub>6</sub>):  $\delta$  = 55.01 (CH<sub>2</sub>), 125.67, 128.93, 138.78 and 155.35 (BPYH), 128.21–132.49 (C<sub>6</sub>H<sub>5</sub>), 199.10 (NC = S). Anal. calc. for C<sub>25</sub>H<sub>21</sub>Cl<sub>2</sub>N<sub>3</sub>O<sub>2</sub>S<sub>2</sub>Au (692.00): C, 43.39; H, 3.06; N, 6.07; S, 9.27%. Found: C, 43.41; H, 3.05; N, 6.09; S, 9.31%.

**[Au<sub>2</sub>(BPM)(Cl)<sub>4</sub>]<sub>2</sub>Cl<sub>2</sub> (C5).** Yield: 80.09% (187.27 mg). FT-IR (KBr,  $\nu_{\max}$ , cm<sup>-1</sup>): 3073 (m), 1577 (s), 1406 (s), 1226 (m), 1113 (m), 1023 (m), 821 (m), 570 (m). <sup>1</sup>H NMR (500 MHz, DMSO-d<sub>6</sub>):  $\delta$  = 7.35 and 8.72 (4H, 4 × CH and 2H, 2 × CH, BPM). <sup>13</sup>C NMR (125.65 MHz, DMSO-d<sub>6</sub>):  $\delta$  = 121.99, 157.89 and 161.84 (BPM). Anal. calc. for C<sub>8</sub>H<sub>6</sub>Cl<sub>6</sub>N<sub>4</sub>Au<sub>2</sub> (764.81): C, 12.56; H, 0.79; N, 7.33%. Found: C, 12.59; H, 0.78; N, 7.35%.

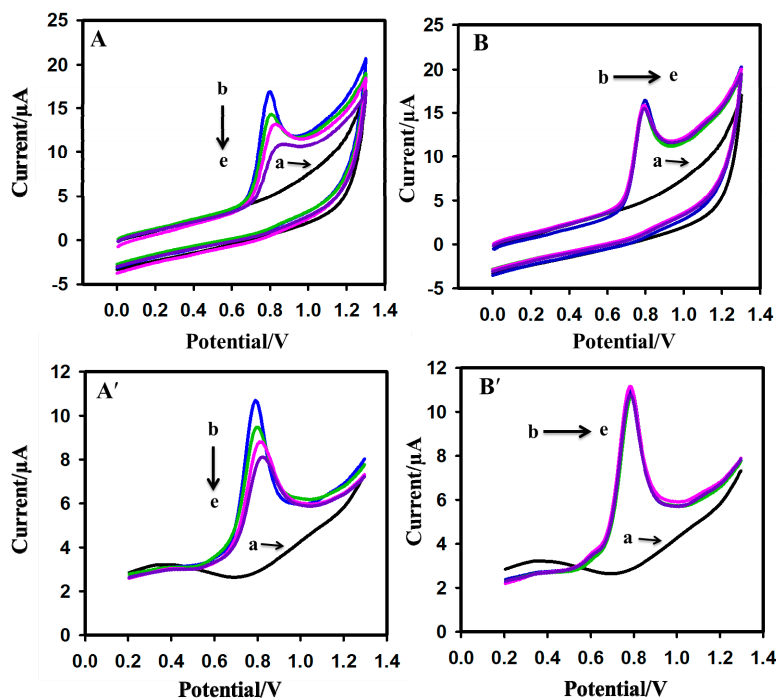
**[Au<sub>2</sub>(BPM)(DMDTC)<sub>2</sub>]<sub>2</sub>Cl<sub>4</sub> (C6).** Yield: 80.09% (187.27 mg). FT-IR (KBr,  $\nu_{\max}$ , cm<sup>-1</sup>): 3057 (w), 2925 (w), 1578 (s), 1402 (s), 1238 (m), 1163 (m), 1046 (m), 967 (w), 876 (w), 559 (m). <sup>1</sup>H NMR (500 MHz, DMSO-d<sub>6</sub>):  $\delta$  = 2.35 (6H, 2 × CH<sub>3</sub>), 7.35 and 8.70 (4H, 4 × CH and 2H, 2 × CH, BPM). <sup>13</sup>C NMR (125.65 MHz, DMSO-d<sub>6</sub>):  $\delta$  = 40.29 (CH<sub>3</sub>), 121.28, 135.33, 140.27 and 147.80 (2,2'-BPM), 193.87 (NC = S). Anal. calc. for C<sub>14</sub>H<sub>18</sub>Cl<sub>4</sub>N<sub>6</sub>S<sub>4</sub>Au<sub>2</sub> (934.34): C, 18.00; H, 1.94; N, 8.99; S, 13.73%. Found: C, 18.05; H, 1.91; N, 9.03; S, 13.77%.

**[Au<sub>2</sub>(BPM)(DEDTC)<sub>2</sub>]<sub>2</sub>Cl<sub>4</sub> (C7).** Yield: 88.51% (343.9 mg). FT-IR (KBr,  $\nu_{\max}$ , cm<sup>-1</sup>): 3055 (w), 2978 (w), 2930 (w), 1552 (s), 1463 (s), 1351 (m), 1286 (s), 1195 (m), 1089 (m), 994 (m), 846 (m), 584 (m). <sup>1</sup>H NMR (500 MHz, DMSO-d<sub>6</sub>):  $\delta$  = 2.43 (6H, 2 × CH<sub>3</sub>), 3.85 (4H, 2 × CH<sub>2</sub>),  $\delta$  = 7.33 and 8.71 (4H, 4 × CH and 2H, 2 × CH, BPM). <sup>13</sup>C NMR (125.65 MHz, DMSO-d<sub>6</sub>):  $\delta$  = 12.13 (CH<sub>3</sub>), 46.58 (CH<sub>2</sub>), 120.55, 156.63 and 161.75 (BPM), 193.89 (NC = S). Anal. calc. for C<sub>18</sub>H<sub>26</sub>Cl<sub>4</sub>N<sub>6</sub>S<sub>4</sub>Au<sub>2</sub> (990.44): C, 21.83; H, 2.65; N, 8.49; S, 12.95%. Found: C, 21.88; H, 2.61; N, 8.55; S, 13.07%.

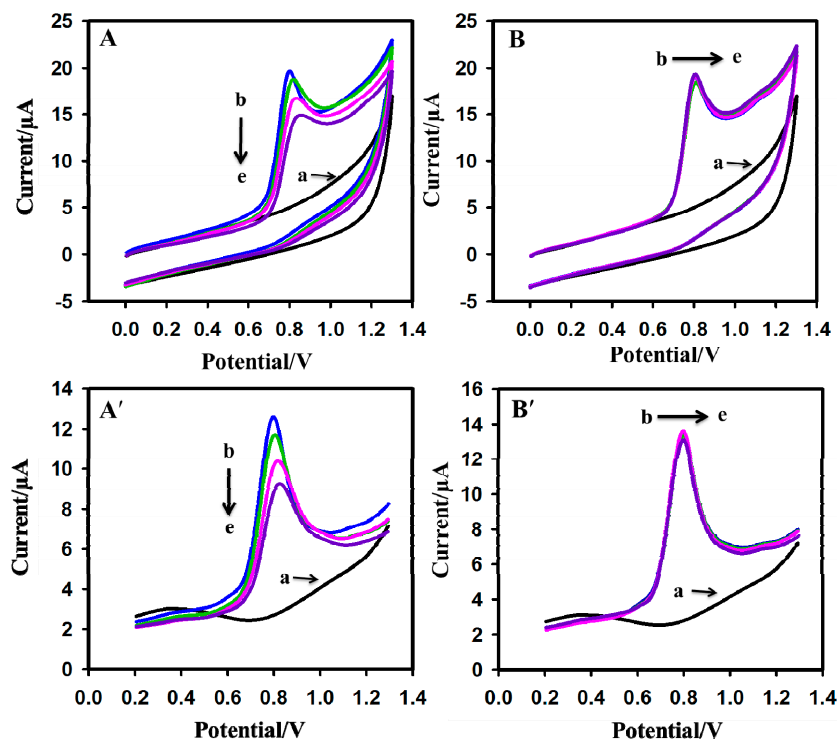
**[Au<sub>2</sub>(BPM)(DBDTC)<sub>2</sub>]Cl<sub>4</sub> (C8)**. Yield: 78.01% (256.6 mg). FT-IR (KBr,  $\nu_{\max}$ , cm<sup>-1</sup>): 3051 (w), 2972 (w), 2922 (m), 1573 (s), 1471 (s), 1355 (m), 1234 (s), 1133 (m), 1047 (m), 980 (s), 553 (m). <sup>1</sup>H NMR (500 MHz, DMSO-d<sub>6</sub>):  $\delta$  = 5.02 (4H, 2 × CH<sub>2</sub>), 7.37 (10H, 2 × C<sub>6</sub>H<sub>5</sub>), 7.33 and 8.75 (4H, 4 × CH and 2H, 2 × CH, BPM). <sup>13</sup>C NMR (125.65 MHz, DMSO-d<sub>6</sub>):  $\delta$  = 55.37 (CH<sub>2</sub>), 120.81, 156.23 and 161.90 (BPM), 128.17–132.50 (C<sub>6</sub>H<sub>5</sub>), 199.14 (NC = S). Anal. calc. for C<sub>38</sub>H<sub>34</sub>Cl<sub>4</sub>N<sub>6</sub>S<sub>4</sub>Au<sub>2</sub> (1238.72): C, 36.85; H, 2.77; N, 6.78; S, 10.35%. Found: C, 36.88; H, 2.73; N, 6.80; S, 10.37%.



**Figure S1.** Voltammograms for the interaction of **C1** with lysozyme in 0.1 M phosphate buffer (pH 6.8). **(A)** Cyclic voltammetry of 100  $\mu$ M **C1** with varying concentrations of lysozyme: (a) buffer blank; (b) **C1** alone; (c) **C1** and 1  $\mu$ M lysozyme; (d) **C1** and 4  $\mu$ M lysozyme; and (e) **C1** and 10  $\mu$ M lysozyme. **(A')** Square-wave voltammetry of 100  $\mu$ M **C1** with various concentrations of lysozyme as in **(A)**. **(B)** Cyclic voltammetry of 100  $\mu$ M **C1** in control experiments with varying volumes of double-distilled water: (a) buffer blank; (b) 0  $\mu$ L; (c) 3  $\mu$ L; (d) 12  $\mu$ L; and (e) 30  $\mu$ L. **(B')** Square-wave voltammetry of 100  $\mu$ M **C1** in control experiments with varying volumes of double-distilled water as in **(B)**.

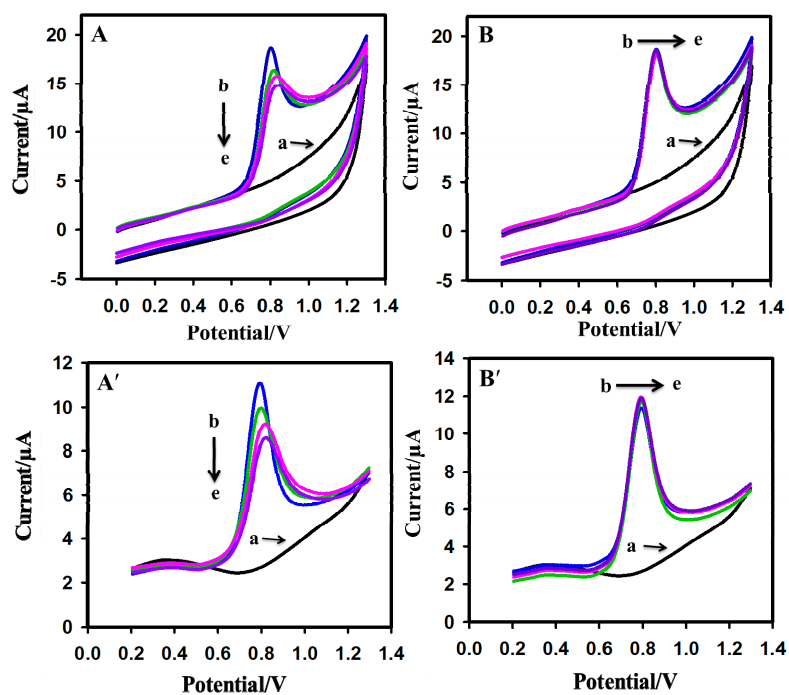


**Figure S2.** Voltammograms for the interaction of C2 with lysozyme in 0.1 M phosphate buffer (pH 6.8). (A) Cyclic voltammetry of 100  $\mu\text{M}$  C2 with varying concentrations of lysozyme: (a) buffer blank; (b) C2 alone; (c) C2 and 1  $\mu\text{M}$  lysozyme; (d) C2 and 4  $\mu\text{M}$  lysozyme; and (e) C2 and 10  $\mu\text{M}$  lysozyme. (A') Square-wave voltammetry of 100  $\mu\text{M}$  C2 with various concentrations of lysozyme as in (A). (B) Cyclic voltammetry of 100  $\mu\text{M}$  C2 in control experiments with varying volumes of double-distilled water: (a) buffer blank; (b) 0  $\mu\text{L}$ ; (c) 3  $\mu\text{L}$ ; (d) 12  $\mu\text{L}$ ; and (e) 30  $\mu\text{L}$ . (B') Square-wave voltammetry of 100  $\mu\text{M}$  C2 in control experiments with varying volumes of double-distilled water as in (B).

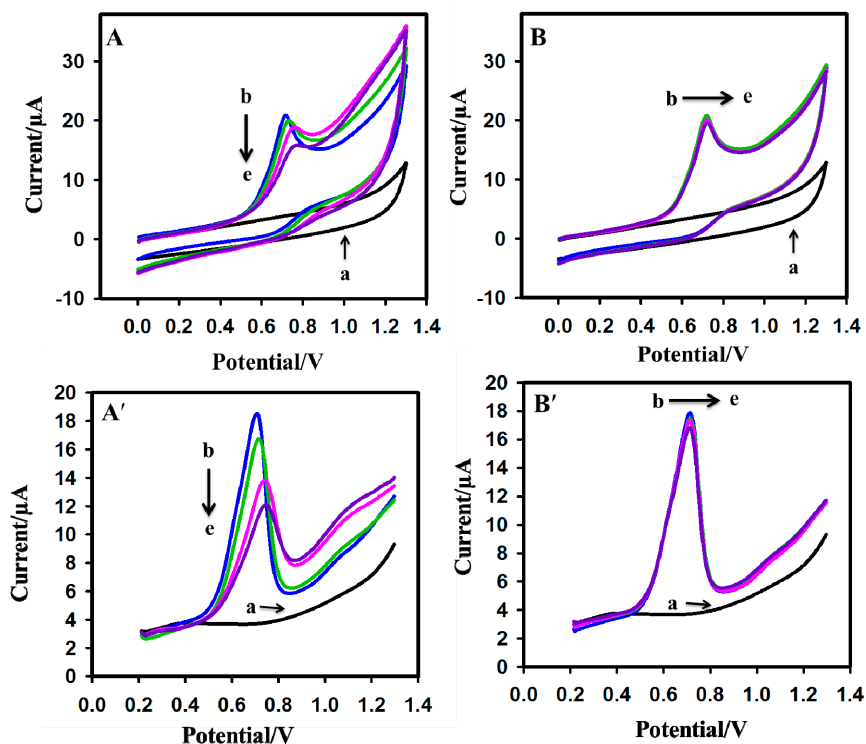


**Figure S3.** Voltammograms for the interaction of C3 with lysozyme in 0.1 M phosphate buffer (pH 6.8). (A) Cyclic voltammetry of 100  $\mu\text{M}$  C3 with varying concentrations of lysozyme: (a) buffer blank; (b) C3 alone; (c)

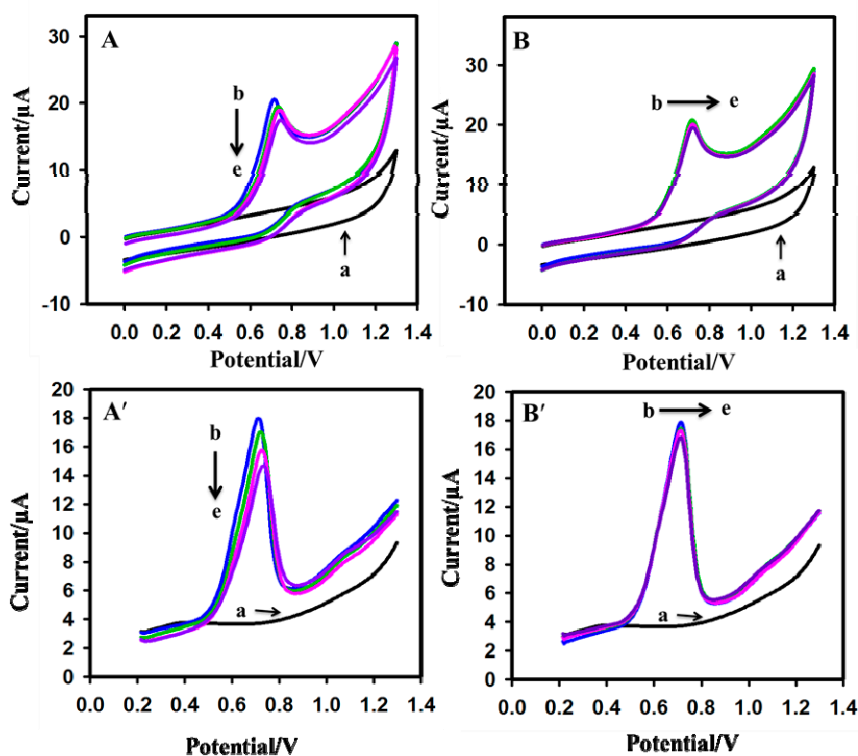
C3 and 1  $\mu\text{M}$  lysozyme; (d) C3 and 4  $\mu\text{M}$  lysozyme; and (e) C3 and 10  $\mu\text{M}$  lysozyme. (A') Square-wave voltammetry of 100  $\mu\text{M}$  C3 with various concentrations of lysozyme as in (A). (B) Cyclic voltammetry of 100  $\mu\text{M}$  C3 in control experiments with varying volumes of double-distilled water: (a) buffer blank; (b) 0  $\mu\text{L}$ ; (c) 3  $\mu\text{L}$ ; (d) 12  $\mu\text{L}$ ; and (e) 30  $\mu\text{L}$ . (B') Square-wave voltammetry of 100  $\mu\text{M}$  C3 in control experiments with varying volumes of double-distilled water as in (B).



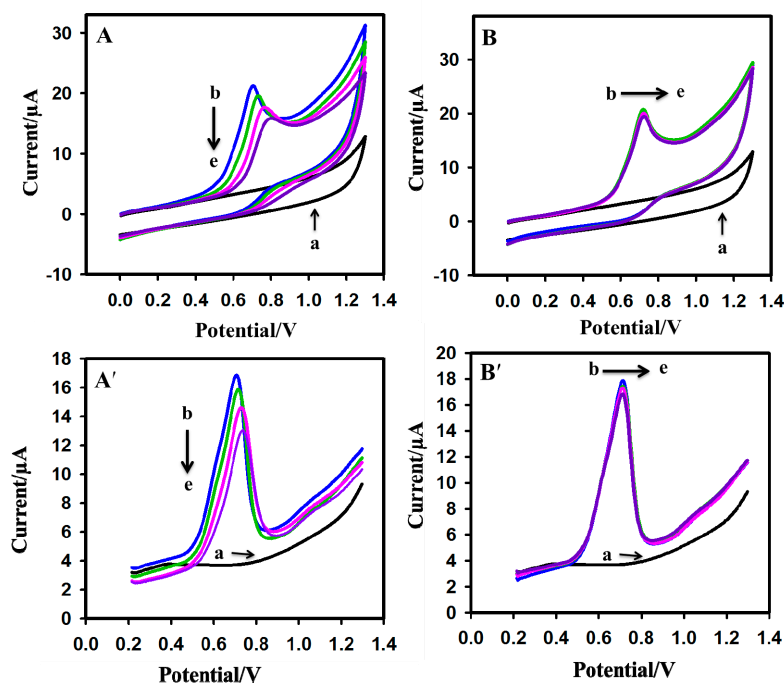
**Figure S4.** Voltammograms for the interaction of compound C4 with lysozyme in 0.1 M phosphate buffer (pH 6.8). (A) Cyclic voltammetry of 100  $\mu\text{M}$  C4 with varying concentrations of lysozyme: (a) buffer blank; (b) C4 alone; (c) C4 and 1  $\mu\text{M}$  lysozyme; (d) C4 and 4  $\mu\text{M}$  lysozyme; and (e) C4 and 10  $\mu\text{M}$  lysozyme. (A') Square-wave voltammetry of 100  $\mu\text{M}$  C4 with various concentrations of lysozyme as in (A). (B) Cyclic voltammetry of 100  $\mu\text{M}$  C4 in control experiments with varying volumes of double-distilled water: (a) buffer blank; (b) 0  $\mu\text{L}$ ; (c) 3  $\mu\text{L}$ ; (d) 12  $\mu\text{L}$ ; and (e) 30  $\mu\text{L}$ . (B') Square-wave voltammetry of 100  $\mu\text{M}$  C4 in control experiments with varying volumes of double-distilled water as in (B).



**Figure S5.** Voltammograms for the interaction of compound C5 with 0.5 mM tryptophan in 0.1 M phosphate buffer (pH 6.8). (A) Cyclic voltammetry of 0.5 mM tryptophan with varying concentrations of C5: (a) buffer blank; (b) tryptophan alone; (c) tryptophan and 10  $\mu\text{M}$  C5; (d) tryptophan and 40  $\mu\text{M}$  C5; and (e) tryptophan and 100  $\mu\text{M}$  C5. (A') Square-wave voltammetry of 0.5 mM tryptophan with varying concentrations of C5 as in (A). (B) Cyclic voltammetry of 0.5 mM tryptophan in control experiments with varying volumes of ethanol: (a) buffer blank; (b) 0  $\mu\text{L}$ ; (c) 15  $\mu\text{L}$ ; (d) 60  $\mu\text{L}$ ; and (e) 150  $\mu\text{L}$ . (B') Square-wave voltammetry of 100  $\mu\text{M}$  C5 in control experiments with varying volumes of ethanol as in (B).

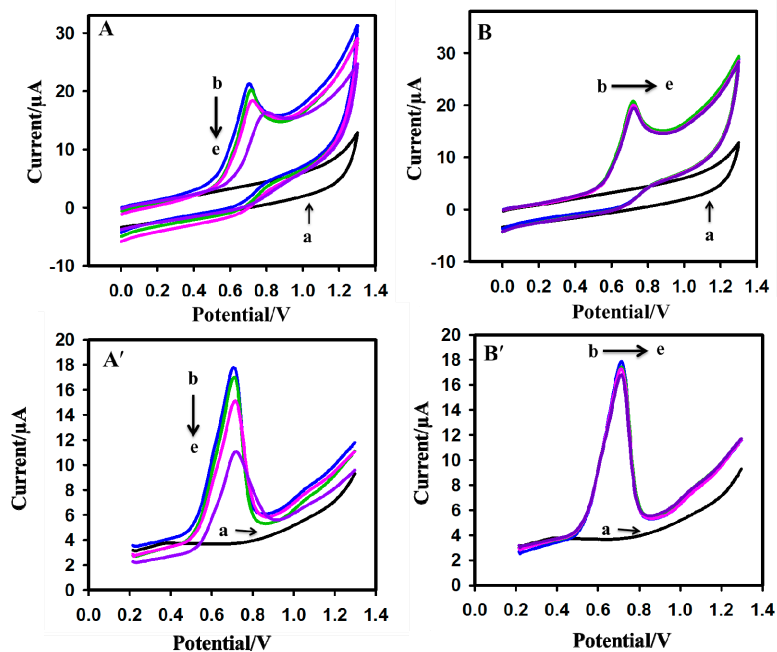


**Figure S6.** Voltammograms for the interaction of compound **C6** with 0.5 mM tryptophan in 0.1 M phosphate buffer (pH 6.8). (A) Cyclic voltammetry of 0.5 mM tryptophan with varying concentrations of **C6**: (a) buffer blank; (b) tryptophan alone; (c) tryptophan and 10  $\mu\text{M}$  **C6**; (d) tryptophan and 40  $\mu\text{M}$  **C6**; and (e) tryptophan and 100  $\mu\text{M}$  **C6**. (A') Square-wave voltammetry of 0.5 mM tryptophan with varying concentrations of **C6** as in (A). (B) Cyclic voltammetry of 0.5 mM tryptophan in control experiments with varying volumes of ethanol: (a) buffer blank; (b) 0  $\mu\text{L}$ ; (c) 15  $\mu\text{L}$ ; (d) 60  $\mu\text{L}$ ; and (e) 150  $\mu\text{L}$ . (B') Square-wave voltammetry of 100  $\mu\text{M}$  **C6** in control experiments with varying volumes of ethanol as in (B).

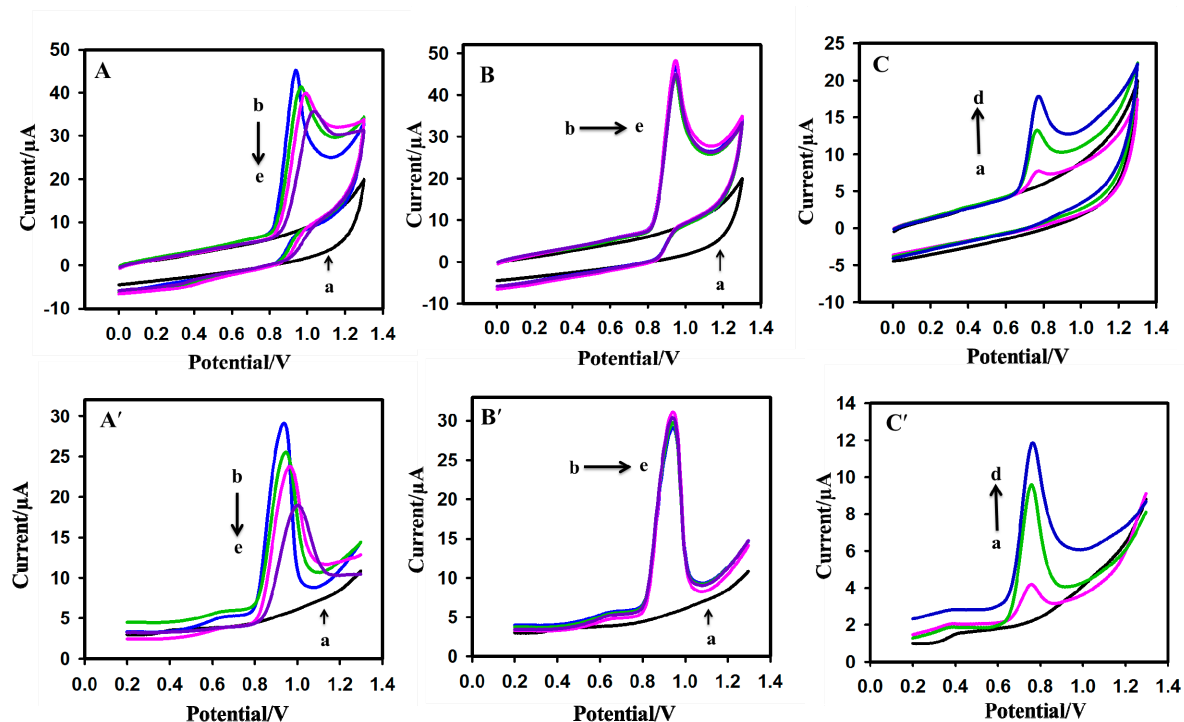


**Figure S7.** Voltammograms for the interaction of compound **C7** with 0.5 mM tryptophan in 0.1 M phosphate buffer (pH 6.8). (A) Cyclic voltammetry of 0.5 mM tryptophan with varying concentrations of **C7**: (a) buffer blank; (b) tryptophan alone; (c) tryptophan and 10  $\mu\text{M}$  **C7**; (d) tryptophan and 40  $\mu\text{M}$  **C7**; and (e) tryptophan and 100  $\mu\text{M}$  **C7**. (A') Square-wave voltammetry of 0.5 mM tryptophan with varying concentrations of **C7** as in (A). (B) Cyclic voltammetry of 0.5 mM tryptophan in control experiments with varying volumes of ethanol: (a) buffer blank; (b) 0  $\mu\text{L}$ ; (c) 15  $\mu\text{L}$ ; (d) 60  $\mu\text{L}$ ; and (e) 150  $\mu\text{L}$ . (B') Square-wave voltammetry of 100  $\mu\text{M}$  **C7** in control experiments with varying volumes of ethanol as in (B).



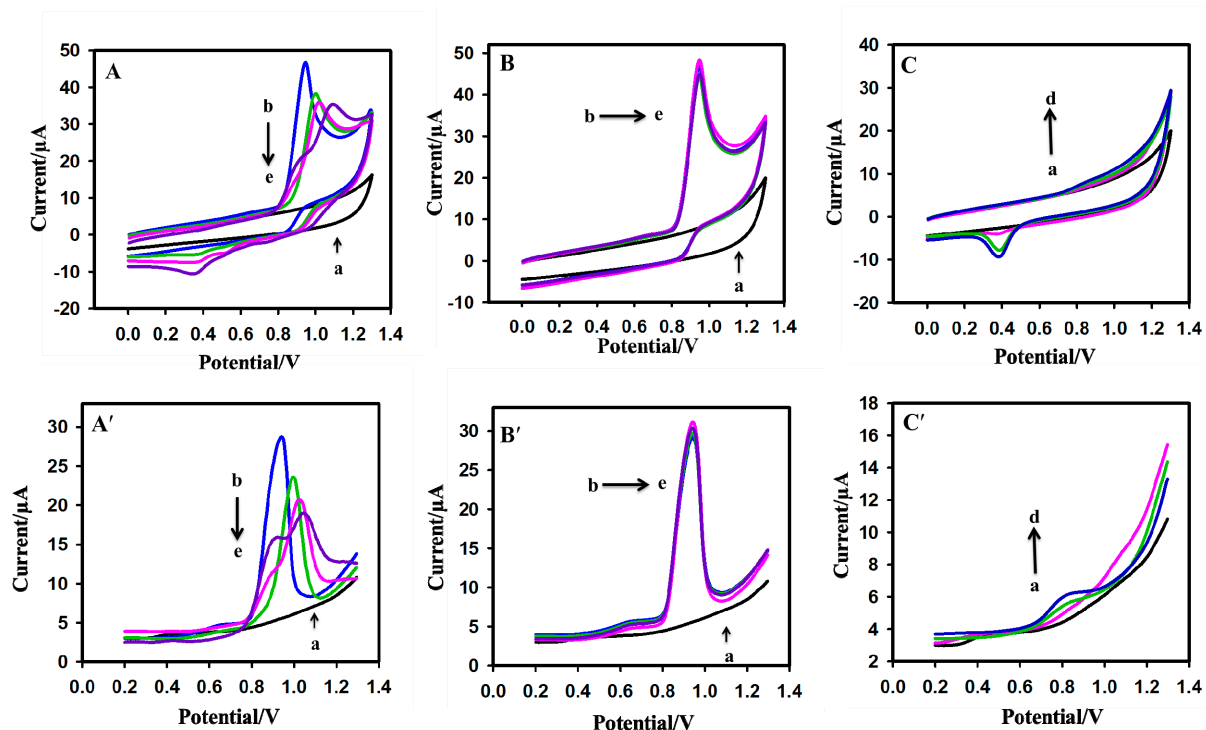


**Figure S8.** Voltammograms for the interaction of compound C8 with 0.5 mM tryptophan in 0.1 M phosphate buffer (pH 6.8). (A) Cyclic voltammetry of 0.5 mM tryptophan with varying concentrations of C8: (a) buffer blank; (b) tryptophan alone; (c) tryptophan and 10  $\mu\text{M}$  C8; (d) tryptophan and 40  $\mu\text{M}$  C8; and (e) tryptophan and 100  $\mu\text{M}$  C8. (A') Square-wave voltammetry of 0.5 mM tryptophan with varying concentrations of C8 as in (A). (B) Cyclic voltammetry of 0.5 mM tryptophan in control experiments with varying volumes of ethanol: (a) buffer blank; (b) 0  $\mu\text{L}$ ; (c) 15  $\mu\text{L}$ ; (d) 60  $\mu\text{L}$ ; and (e) 150  $\mu\text{L}$ . (B') Square-wave voltammetry of 100  $\mu\text{M}$  C5 in control experiments with varying volumes of ethanol as in (B).

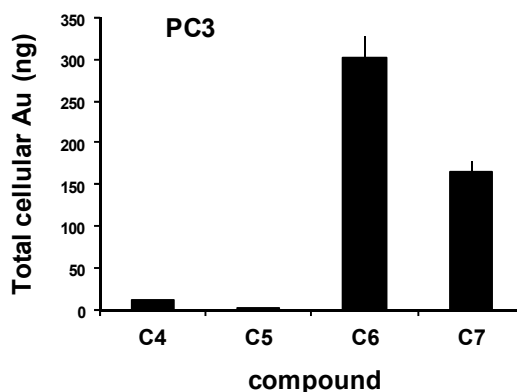


**Figure S9.** Voltammograms for the interaction of compound C1 with 0.5 mM guanine in 0.1 M phosphate buffer (pH 6.8). (A) Cyclic voltammetry of 0.5 mM guanine with varying concentrations of C1: (a) buffer blank; (b) guanine alone; (c) guanine and 10  $\mu\text{M}$  C1; (d) guanine and 40  $\mu\text{M}$  C1; and (e) guanine and 100  $\mu\text{M}$  C1. (A') Square-wave voltammetry of 0.5 mM guanine with varying concentrations of C1 as in (A). (B) Cyclic

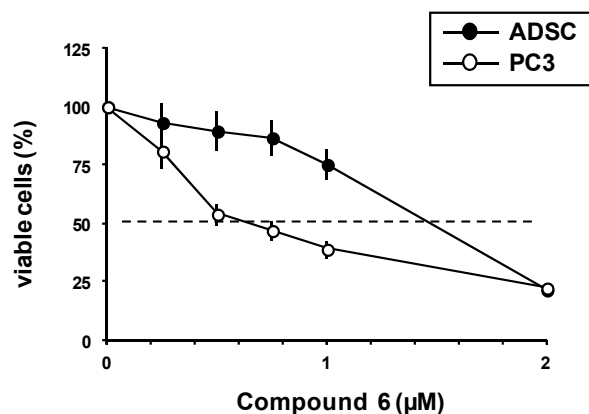
voltammetry of 0.5 mM guanine in control experiments with varying volumes of ethanol: (a) buffer blank; (b) 0  $\mu\text{L}$ ; (c) 15  $\mu\text{L}$ ; (d) 60  $\mu\text{L}$ ; and (e) 150  $\mu\text{L}$ . (**B'**) Square-wave voltammetry of 0.5 mM guanine in control experiments with varying volumes of ethanol: (a) buffer blank; (b) 0  $\mu\text{L}$ ; (c) 15  $\mu\text{L}$ ; (d) 60  $\mu\text{L}$ ; and (e) 150  $\mu\text{L}$ . (**C**) Cyclic voltammetry of **C1** alone at: (a) 0  $\mu\text{M}$ ; (b) 10  $\mu\text{M}$ ; (c) 40  $\mu\text{M}$ ; and (d) 100  $\mu\text{M}$ . (**C'**) Square-wave voltammetry of **C1** alone at: (a) 0  $\mu\text{M}$ ; (b) 10  $\mu\text{M}$ ; (c) 40  $\mu\text{M}$ ; and (d) 100  $\mu\text{M}$ .



**Figure S10.** Voltammograms for the interaction of compound **C5** with 0.5 mM guanine in 0.1 M phosphate buffer (pH 6.8). (**A**) Cyclic voltammetry of 0.5 mM guanine with varying concentrations of **C5**: (a) buffer blank; (b) guanine alone; (c) guanine and 10  $\mu\text{M}$  **C5**; (d) guanine and 40  $\mu\text{M}$  **C5**; and (e) guanine and 100  $\mu\text{M}$  **C5**. (**A'**) Square-wave voltammetry of 0.5 mM guanine with varying concentrations of **C5** as in (**A**). (**B**) Cyclic voltammetry of 0.5 mM guanine in control experiments with varying volumes of ethanol: (a) buffer blank; (b) 0  $\mu\text{L}$ ; (c) 15  $\mu\text{L}$ ; (d) 60  $\mu\text{L}$ ; and (e) 150  $\mu\text{L}$ . (**B'**) Square-wave voltammetry of 0.5 mM guanine in control experiments with varying volumes of ethanol: (a) buffer blank; (b) 0  $\mu\text{L}$ ; (c) 15  $\mu\text{L}$ ; (d) 60  $\mu\text{L}$ ; and (e) 150  $\mu\text{L}$ . (**C**) Cyclic voltammetry of **C5** alone at: (a) 0  $\mu\text{M}$ ; (b) 10  $\mu\text{M}$ ; (c) 40  $\mu\text{M}$ ; and (d) 100  $\mu\text{M}$ . (**C'**) Square-wave voltammetry of **C5** alone at: (a) 0  $\mu\text{M}$ ; (b) 10  $\mu\text{M}$ ; (c) 40  $\mu\text{M}$ ; and (d) 100  $\mu\text{M}$ .



**Figure S11.** Uptake of selected gold(III) compounds by PC3 cells. PC3 cells ( $1 \times 10^6$  cells/dish) were treated for 2 h with 3  $\mu\text{M}$  **C4**, **C5**, **C6** or **C7**, and internalized gold was determined by ICP mass spectrometry. Results are means and SD of three independent experiments.



**Figure S12.** Growth inhibition curves for C6 in PC3 prostate cancer cells and adipose-derived stromal cells (ADSCs). Cell viability was determined with the MTT assay after 72 h drug treatment. Results are means and SD for three replicate wells from three independent experiments.

**Table S1.** Voltammetry peak potential (mV) of 100 μM compounds (C1–C4) with 1–10 μM lysozyme.

Compound	Technique	Lysozyme			
		0 μM	1 μM	4 μM	10 μM
C1	CV	0.73898	0.81421	0.83191	0.87616
C1	SWV	0.79338	0.80345	0.8387	0.86388
C2	CV	0.79208	0.80093	0.81863	0.83191
C2	SWV	0.78835	0.79338	0.80849	0.81352
C3	CV	0.79651	0.80978	0.82306	0.83633
C3	SWV	0.79338	0.80345	0.81352	0.82359
C4	CV	0.79651	0.80978	0.81863	0.82748
C4	SWV	0.78835	0.79338	0.80849	0.81352

CV, cyclic voltammetry; SWV, square-wave voltammetry.

**Table S2.** Voltammetry peak potential (mV) of 0.5 mM tryptophan with 10–100 μM compounds (C5–C8).

Compound	Technique	Compound			
		0 μM	10 μM	40 μM	100 μM
C5	CV	0.71243	0.72571	0.74341	0.74783
C5	SWV	0.70862	0.71365	0.73883	0.7489
C6	CV	0.71243	0.73013	0.73898	0.74341
C6	SWV	0.70862	0.71869	0.72372	0.72876
C7	CV	0.71243	0.72571	0.75668	0.78323
C7	SWV	0.70862	0.71365	0.72876	0.7338
C8	CV	0.71243	0.71686	0.72128	0.78323
C8	SWV	0.70862	0.70862	0.71365	0.71869

CV, cyclic voltammetry; SWV, square-wave voltammetry.

**Table S3.** Voltammetry peak potential (mV) of 0.5 mM guanine with 10–100 μM compounds C1 and C5.

Compound	Technique	Compound			
		0 μM	10 μM	40 μM	100 μM
C1	CV	0.93811	0.96024	0.98236	1.0222
C1	SWV	0.93437	0.94444	0.95955	0.9948
C5	CV	0.93811	0.99564	1.0133	1.0753
C5	SWV	0.93437	0.9948	1.025	1.0502

CV, cyclic voltammetry; SWV, square-wave voltammetry.



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