

## Copper(II) complexes of salicylaldehydes and 2-hydroxyphenones: Synthesis, Structure, Thermal decomposition study and Interaction with calf-thymus DNA and albumins

Ariadne Zianna, George Psomas, Antonios G. Hatzidimitriou, Maria Lalia-Kantouri \*

Department of General and Inorganic Chemistry, Faculty of Chemistry, Aristotle University of  
Thessaloniki, GR-54124 Thessaloniki, Greece

### Supplementary material

#### S1. Interaction with CT DNA

The binding constant,  $K_b$ , can be obtained by monitoring the changes in the absorbance at the corresponding  $\lambda_{\max}$  with increasing concentrations of CT DNA and it is given by the ratio of slope to the y intercept in plots  $\frac{[\text{DNA}]}{(\epsilon_A - \epsilon_f)}$  versus  $[\text{DNA}]$ , according to the Wolfe-Shimer equation

[1]:

$$\frac{[\text{DNA}]}{(\epsilon_A - \epsilon_f)} = \frac{[\text{DNA}]}{(\epsilon_b - \epsilon_f)} + \frac{1}{K_b(\epsilon_b - \epsilon_f)} \quad (\text{eq. S1})$$

where  $[\text{DNA}]$  is the concentration of DNA in base pairs,  $\epsilon_A = A_{\text{obsd}}/[\text{compound}]$ ,  $\epsilon_f$  = the extinction coefficient for the free compound and  $\epsilon_b$  = the extinction coefficient for the compound in the fully bound form.

#### S2. Competitive studies with EB

The Stern-Volmer constant  $K_{SV}$  is used to evaluate the quenching efficiency for each compound according to the Stern-Volmer equation:

$$\frac{I_0}{I} = 1 + K_{SV}[Q] \quad (\text{eq. S2})$$

where  $I_0$  and  $I$  are the emission intensities in the absence and the presence of the quencher, respectively,  $[Q]$  is the concentration of the quencher (i.e. complexes **1-6**);  $K_{SV}$  is obtained from the Stern-Volmer plots by the slope of the diagram  $\frac{I_0}{I}$  vs  $[Q]$ .

---

\* Corresponding author: Tel./fax: +30 2310 997844, E-mail address: lalia@chem.auth.gr (M. Lalia-Kantouri)

### S3. Interaction with serum albumins

The extent of the inner-filter effect can be roughly estimated with the following formula:

$$I_{\text{corr}} = I_{\text{meas}} \times 10^{\frac{\varepsilon(\lambda_{\text{exc}})cd}{2}} \times 10^{\frac{\varepsilon(\lambda_{\text{em}})cd}{2}} \quad (\text{eq. S3})$$

where  $I_{\text{corr}}$  = corrected intensity,  $I_{\text{meas}}$  = the measured intensity,  $c$  = the concentration of the quencher,  $d$  = the cuvette (1 cm),  $\varepsilon(\lambda_{\text{exc}})$  and  $\varepsilon(\lambda_{\text{em}})$  = the  $\varepsilon$  of the quencher at the excitation and the emission wavelength, respectively, as calculated from the UV-Vis spectra of the complexes [2].

The Stern-Volmer and Scatchard graphs are used in order to study the interaction of a quencher with serum albumins. According to Stern-Volmer quenching equation [3]:

$$\frac{I_0}{I} = 1 + k_q \tau_0 [Q] = 1 + K_{\text{SV}} [Q] \quad (\text{eq. S4}),$$

where  $I_0$  = the initial tryptophan fluorescence intensity of SA,  $I$  = the tryptophan fluorescence intensity of SA after the addition of the quencher,  $k_q$  = the quenching rate constants of SA,  $K_{\text{SV}}$  = the dynamic quenching constant,  $\tau_0$  = the average lifetime of SA without the quencher,  $[Q]$  = the concentration of the quencher, the dynamic quenching constant ( $K_{\text{SV}}, \text{M}^{-1}$ ) can be obtained by the slope of the diagram  $\frac{I_0}{I}$  vs  $[Q]$ . From the equation:

$$K_{\text{SV}} = k_q \tau_0 \quad (\text{eq. S5})$$

and taking  $\tau_0 = 10^{-8}$  s as fluorescence lifetime of tryptophan in SA, the approximate quenching constant ( $k_q, \text{M}^{-1}\text{s}^{-1}$ ) is calculated.

From the Scatchard equation [3]:

$$\frac{\Delta I / I_0}{[Q]} = nK - K \frac{\Delta I}{I_0} \quad (\text{eq. S6})$$

where  $n$  is the number of binding sites per albumin and  $K$  is the association binding constant,  $K$  (in  $\text{M}^{-1}$ ) is calculated from the slope in plots  $\frac{\Delta I / I_0}{[Q]}$  versus  $\frac{\Delta I}{I_0}$  and  $n$  is given by the ratio of y intercept to the slope [3].

### References

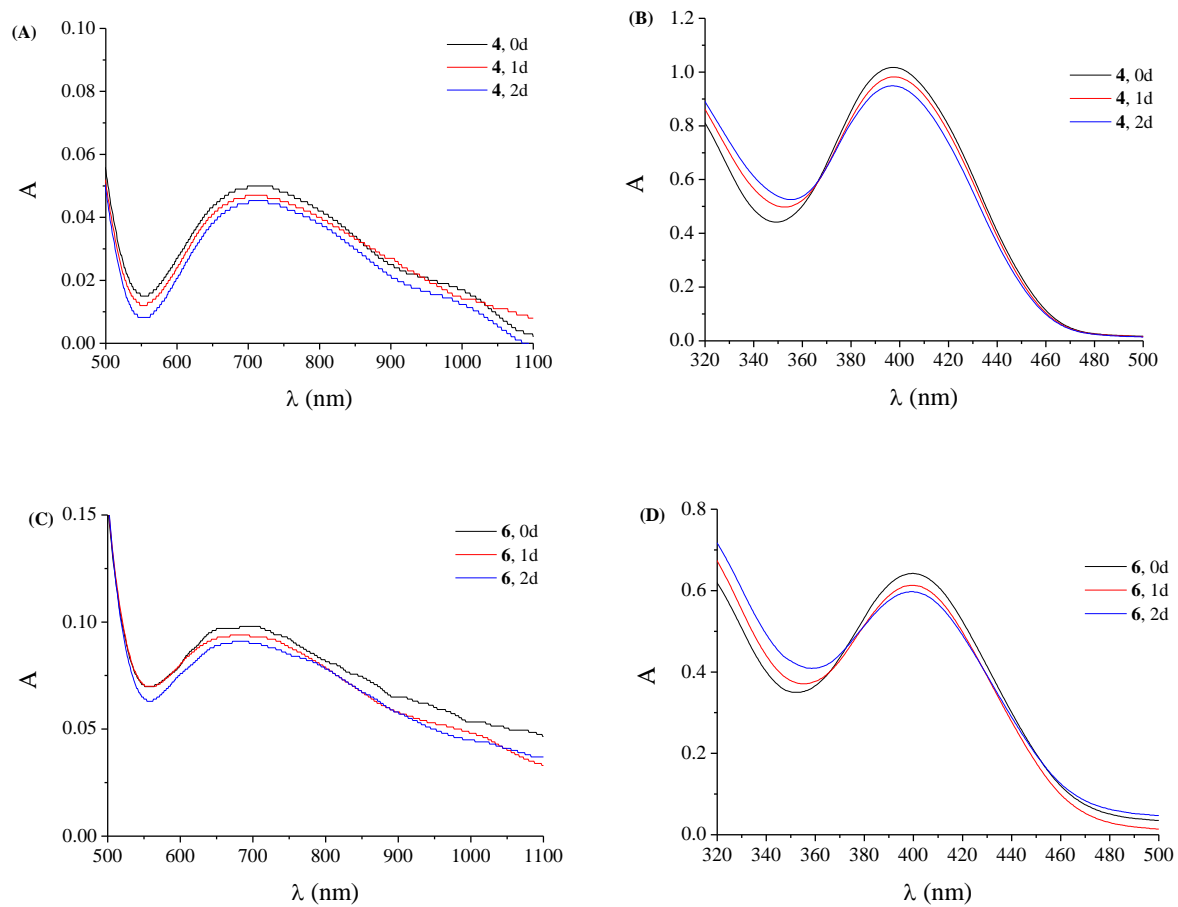
- [1] A. Wolfe, G. Shimer and T. Meehan, *Biochemistry*, 1987, **26**, 6392–6396.
- [2] L. Stella, A.L. Capodilupo and M. Bietti, *Chem. Commun.*, 2008, 4744–4746.
- [3] Y. Wang, H. Zhang, G. Zhang, W. Tao and S. Tang, *J. Luminescence*, 2007, **126**, 211–218.

**Table S1.** The HSA constants derived for the free saloH and ketoH and their complexes **1–7**.

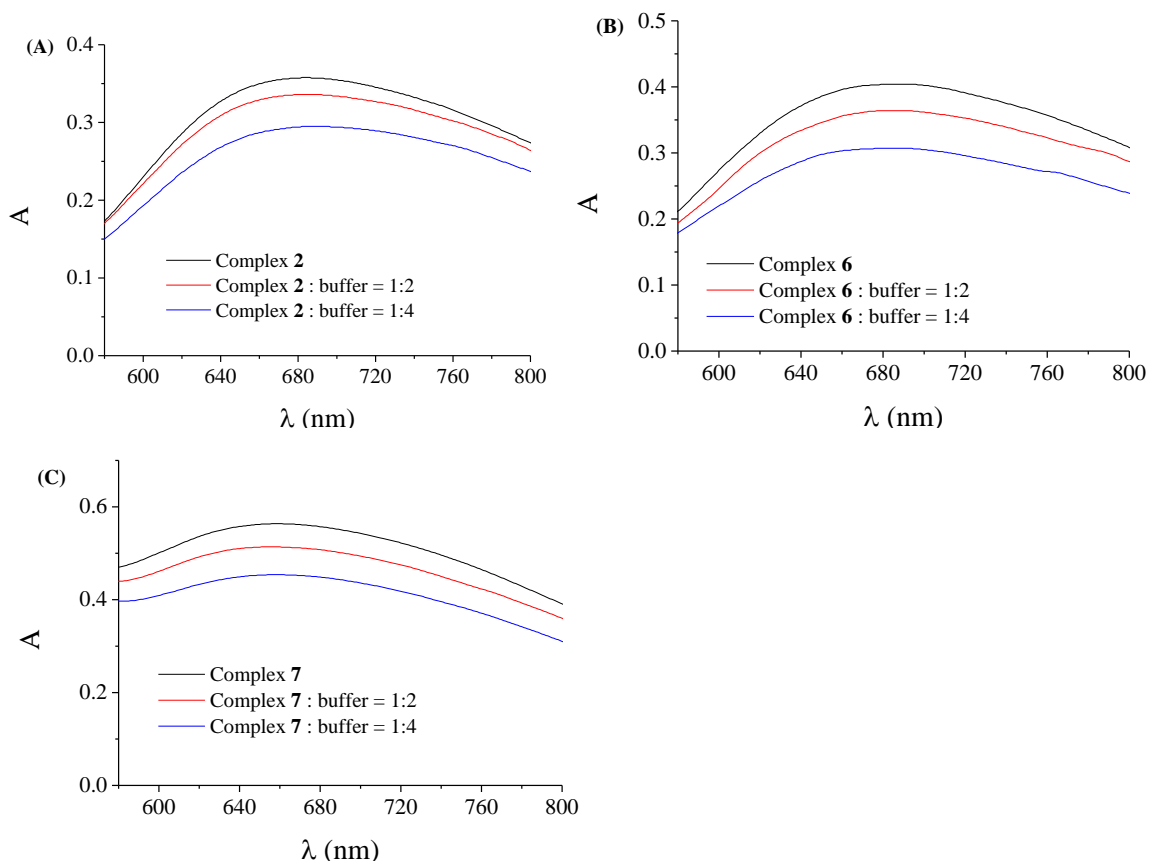
Compound	$K_{sv} (M^{-1})$	$K_q (M^{-1} s^{-1})$	$K (M^{-1})$	<b>n</b>
o–vanH	$2.52(\pm 0.23) \times 10^3$	$2.52(\pm 0.23) \times 10^{11}$	$1.56(\pm 0.17) \times 10^5$	0.10
5–Me–salOH	$2.00(\pm 0.15) \times 10^4$	$2.00(\pm 0.15) \times 10^{12}$	$8.71(\pm 0.12) \times 10^5$	0.41
5–NO <sub>2</sub> –salOH	$5.00(\pm 0.46) \times 10^4$	$5.00(\pm 0.46) \times 10^{12}$	$2.41(\pm 0.09) \times 10^5$	0.45
5–Cl–salOH	$5.64(\pm 0.40) \times 10^3$	$5.64(\pm 0.40) \times 10^{11}$	$2.19(\pm 0.10) \times 10^5$	0.10
5–Br–salOH	$2.31(\pm 0.32) \times 10^3$	$2.31(\pm 0.32) \times 10^{11}$	$1.43(\pm 0.09) \times 10^6$	0.22
bpoH	$3.05(\pm 0.19) \times 10^3$	$3.05(\pm 0.19) \times 10^{11}$	$8.33(\pm 0.12) \times 10^5$	0.17
mpoH	$7.67(\pm 0.46) \times 10^3$	$7.67(\pm 0.46) \times 10^{11}$	$4.26(\pm 0.41) \times 10^4$	0.26
[Cu(o–van) <sub>2</sub> H <sub>2</sub> O]·0.25H <sub>2</sub> O, <b>1</b> ·0.25H <sub>2</sub> O	$1.49(\pm 0.25) \times 10^4$	$1.49(\pm 0.25) \times 10^{12}$	$4.39(\pm 0.22) \times 10^5$	0.18
[Cu(5–CH <sub>3</sub> –salO) <sub>2</sub> ], <b>2</b>	$2.81(\pm 0.54) \times 10^4$	$2.81(\pm 0.54) \times 10^{12}$	$6.32(\pm 0.48) \times 10^5$	0.18
[Cu(5–NO <sub>2</sub> –salO) <sub>2</sub> (CH <sub>3</sub> OH) <sub>2</sub> ], <b>3</b>	$6.09(\pm 0.27) \times 10^4$	$6.09(\pm 0.27) \times 10^{12}$	$1.23(\pm 0.11) \times 10^5$	0.76
[Cu(5–Cl–salO) <sub>2</sub> ], <b>4</b>	$4.50(\pm 0.60) \times 10^3$	$4.50(\pm 0.60) \times 10^{11}$	$5.74(\pm 0.43) \times 10^5$	0.10
[Cu(5–Br–salO) <sub>2</sub> ], <b>5</b>	$1.38(\pm 0.07) \times 10^6$	$1.38(\pm 0.07) \times 10^{14}$	$8.61(\pm 0.36) \times 10^5$	1.02
[Cu(bpo) <sub>2</sub> ], <b>6</b>	$5.61(\pm 0.64) \times 10^4$	$5.61(\pm 0.64) \times 10^{12}$	$3.12(\pm 0.12) \times 10^5$	0.47
[Cu(mpo) <sub>2</sub> ]·2H <sub>2</sub> O, <b>7</b> ·2H <sub>2</sub> O	$3.79(\pm 0.18) \times 10^3$	$3.79(\pm 0.18) \times 10^{11}$	$4.57(\pm 0.68) \times 10^4$	0.12

**Table S2.** The **BSA** constants derived for the free saloH and ketoH and their complexes **1–7**.

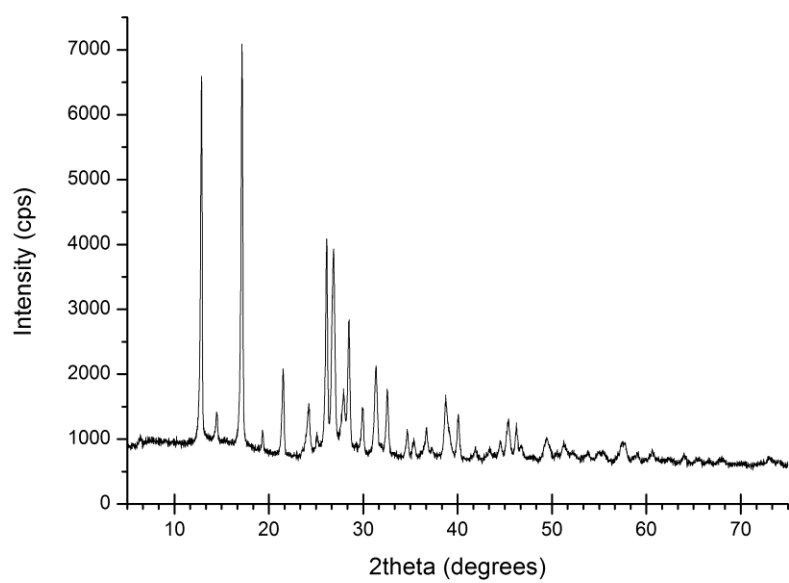
Compound	$K_{SV} (M^{-1})$	$k_q (M^{-1} s^{-1})$	$K (M^{-1})$	<b>n</b>
o-vanH	$2.37(\pm 0.13) \times 10^4$	$2.37(\pm 0.13) \times 10^{12}$	$2.15(\pm 0.10) \times 10^5$	0.41
5-Me-saloH	$6.15(\pm 0.58) \times 10^3$	$6.15(\pm 0.58) \times 10^{11}$	$2.35(\pm 0.27) \times 10^6$	0.32
5-NO <sub>2</sub> -saloH	$6.55(\pm 0.17) \times 10^4$	$6.55(\pm 0.17) \times 10^{12}$	$1.25(\pm 0.07) \times 10^5$	0.76
5-Cl-saloH	$1.46(\pm 0.06) \times 10^4$	$1.46(\pm 0.06) \times 10^{12}$	$3.11(\pm 0.20) \times 10^4$	0.59
5-Br-saloH	$4.63(\pm 0.31) \times 10^4$	$4.63(\pm 0.31) \times 10^{12}$	$1.43(\pm 0.08) \times 10^5$	0.66
bpoH	$9.43(\pm 0.36) \times 10^3$	$9.43(\pm 0.36) \times 10^{11}$	$3.18(\pm 0.23) \times 10^5$	0.31
mpoH	$7.41(\pm 0.46) \times 10^3$	$7.41(\pm 0.46) \times 10^{11}$	$7.02(\pm 0.17) \times 10^4$	0.17
[Cu(o-van) <sub>2</sub> H <sub>2</sub> O]·0.25H <sub>2</sub> O, <b>1</b> ·0.25H <sub>2</sub> O	$3.33(\pm 0.23) \times 10^4$	$3.33(\pm 0.23) \times 10^{12}$	$9.69(\pm 0.98) \times 10^4$	0.54
[Cu(5-CH <sub>3</sub> -salo) <sub>2</sub> ], <b>2</b>	$8.55(\pm 0.51) \times 10^3$	$8.55(\pm 0.51) \times 10^{11}$	$1.00(\pm 0.13) \times 10^5$	0.19
[Cu(5-NO <sub>2</sub> -salo) <sub>2</sub> (CH <sub>3</sub> OH) <sub>2</sub> ], <b>3</b>	$7.11(\pm 0.43) \times 10^4$	$7.11(\pm 0.43) \times 10^{12}$	$3.03(\pm 0.20) \times 10^5$	0.65
[Cu(5-Cl-salo) <sub>2</sub> ], <b>4</b>	$1.52(\pm 0.09) \times 10^4$	$1.52(\pm 0.09) \times 10^{12}$	$7.36(\pm 0.81) \times 10^4$	0.34
[Cu(5-Br-salo) <sub>2</sub> ], <b>5</b>	$6.42(\pm 0.29) \times 10^4$	$6.42(\pm 0.29) \times 10^{12}$	$1.69(\pm 0.06) \times 10^5$	0.72
[Cu(bpo) <sub>2</sub> ], <b>6</b>	$6.56(\pm 0.35) \times 10^4$	$6.56(\pm 0.35) \times 10^{12}$	$1.93(\pm 0.10) \times 10^5$	0.73
[Cu(mpo) <sub>2</sub> ]·2H <sub>2</sub> O, <b>7</b> ·2H <sub>2</sub> O	$2.88(\pm 0.14) \times 10^4$	$2.88(\pm 0.14) \times 10^{12}$	$2.14(\pm 0.23) \times 10^3$	0.95



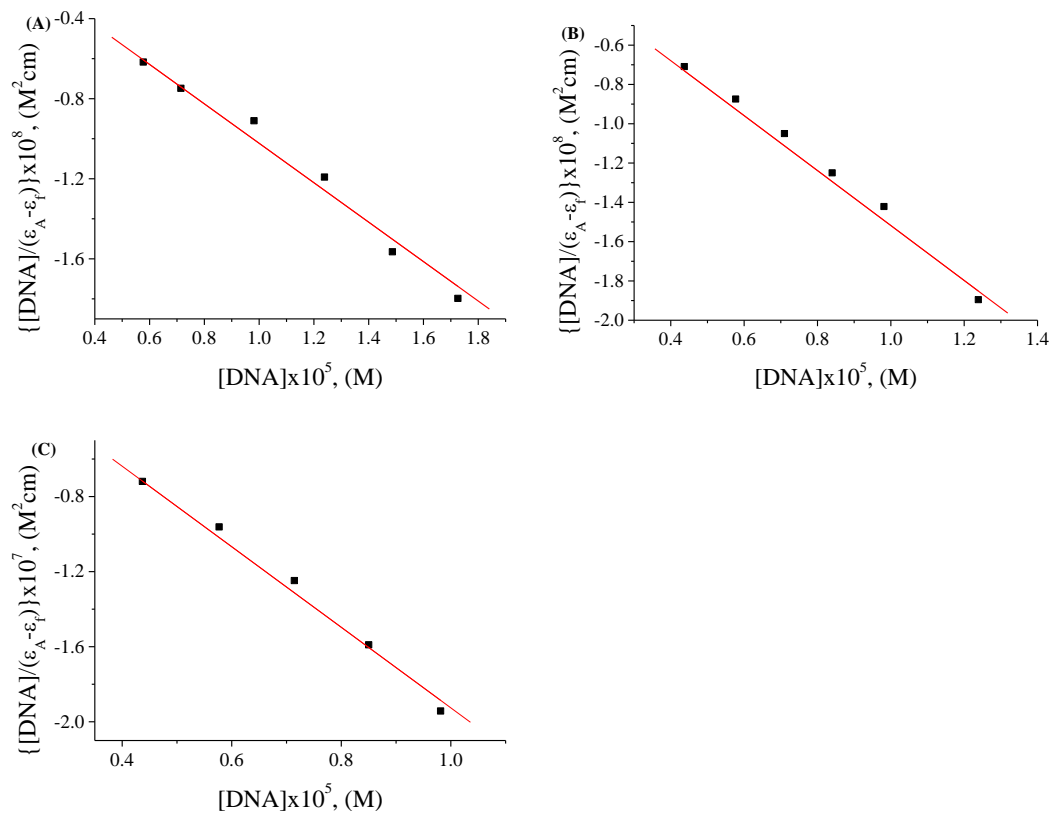
**Figure S1.** UV spectra of a DMSO solution of complexes (A) **4** ( $10^{-3}$  M), (B) **4** ( $2 \times 10^{-4}$  M), (C) **6** ( $10^{-3}$  M) and (D) **6** ( $2 \times 10^{-4}$  M) during time (0 h, 24 h and 48 h).



**Figure S2.** Visible spectra of  $10^{-3}$  M DMSO solution of complex (A) **2**, (B) **6** and (C) **7** upon addition of buffer solution (150 mM NaCl and 15 mM trisodium citrate at pH 7.0) at diverse ratios.

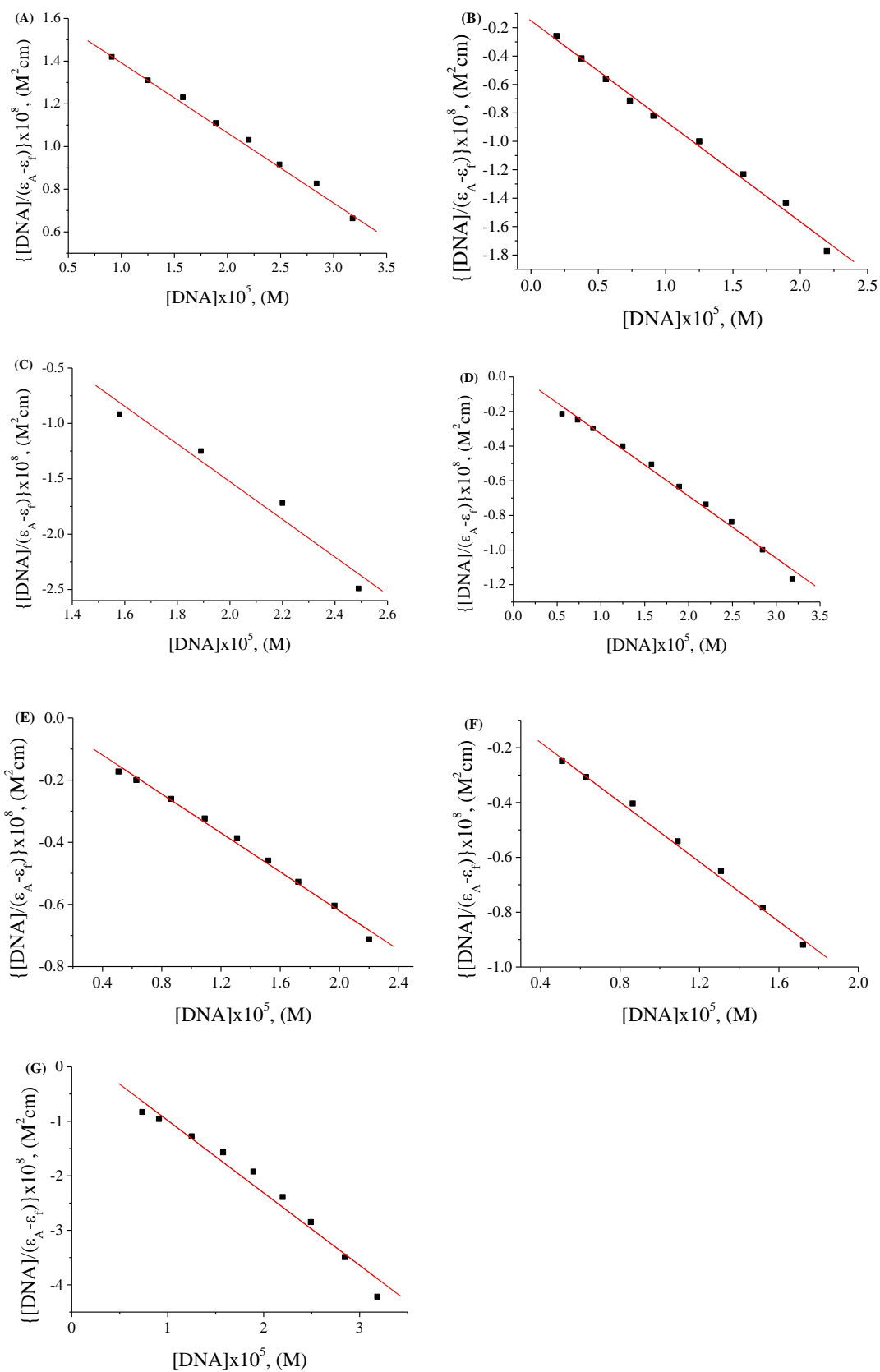


**Figure S3.** PXRD of complex **5**.

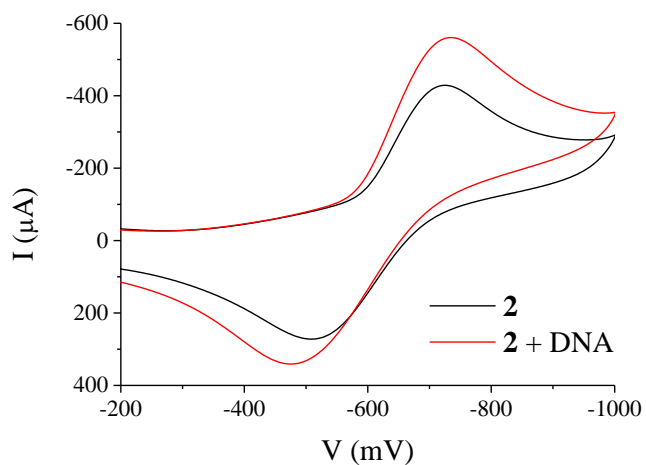


**Figure S4.** Plot of  $\frac{[\text{DNA}]}{(\epsilon_A - \epsilon_f)}$  vs [DNA] for (A) o-vanH, (B) 5-Me-saloH and (C) mpoH.

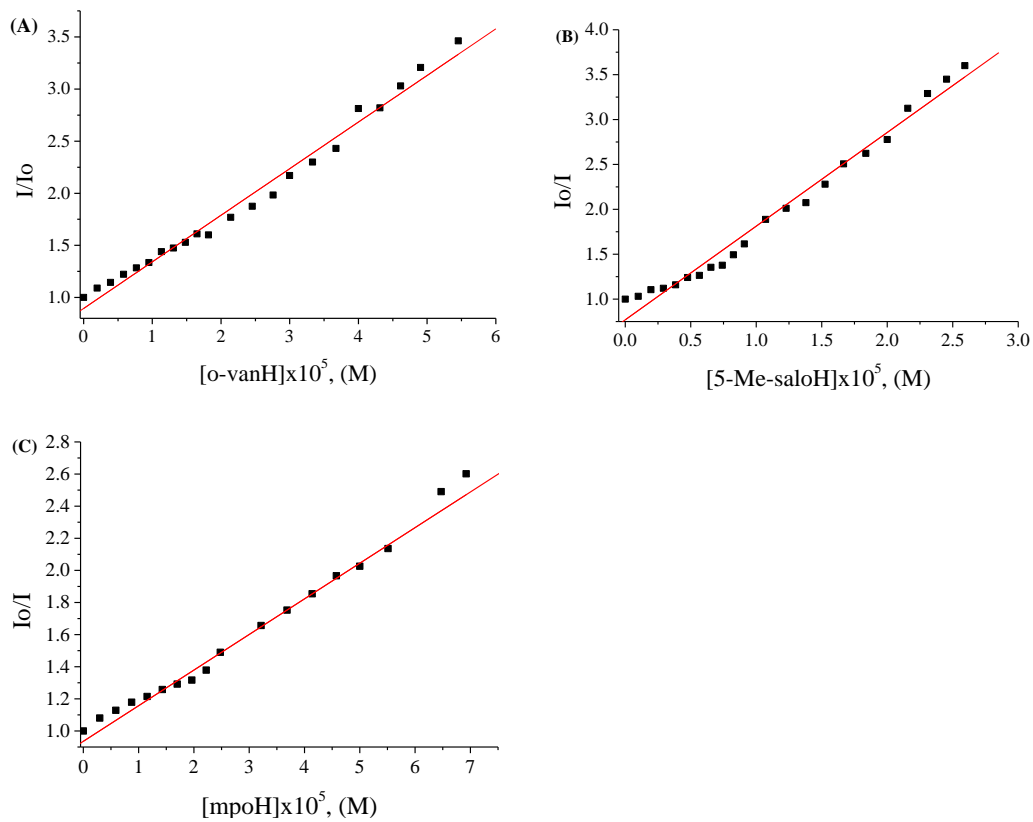




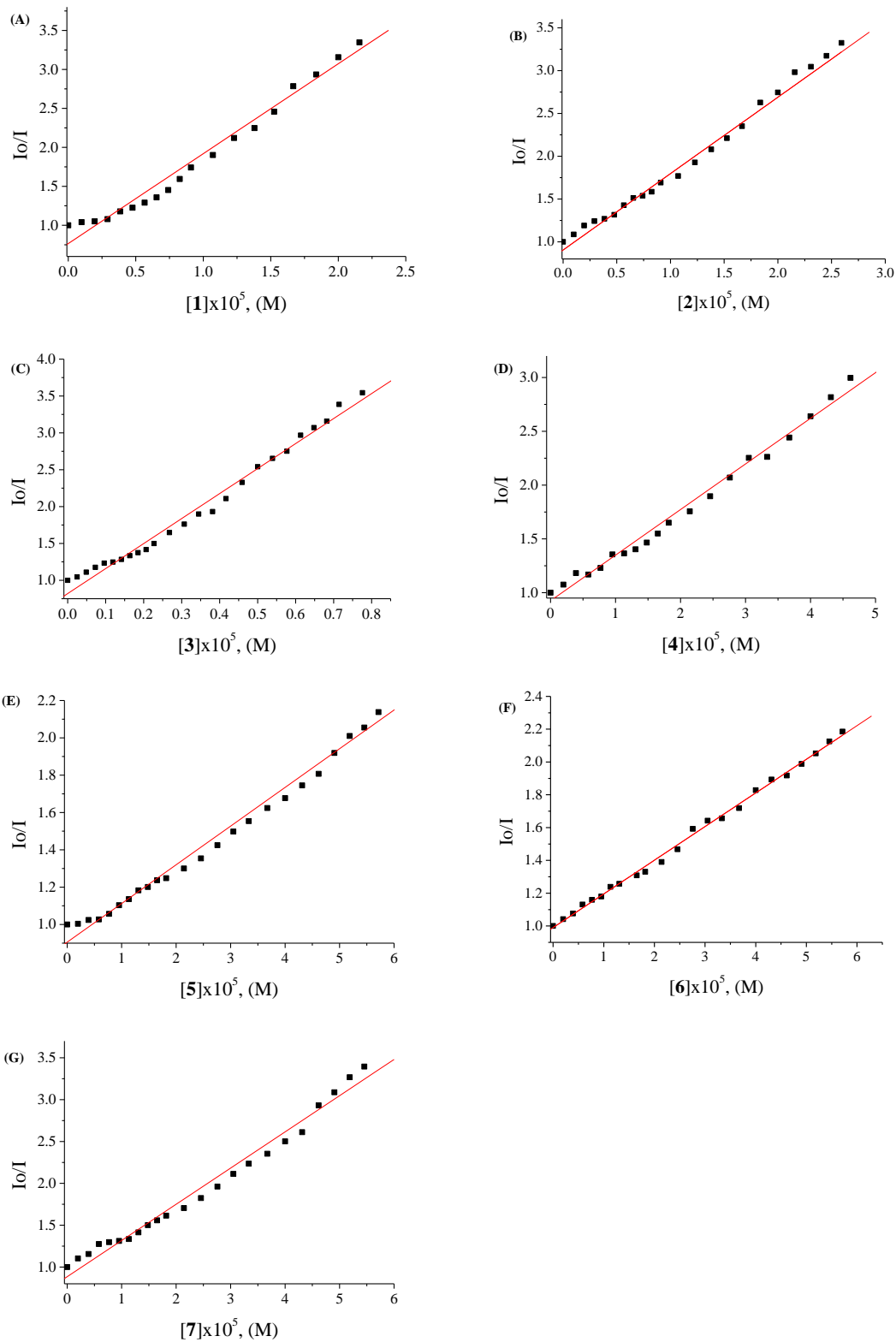
**Figure S5.** (A)–(G) Plot of  $\frac{[DNA]}{(\epsilon_A - \epsilon_f)}$  vs  $[DNA]$  for complexes 1–7, respectively.



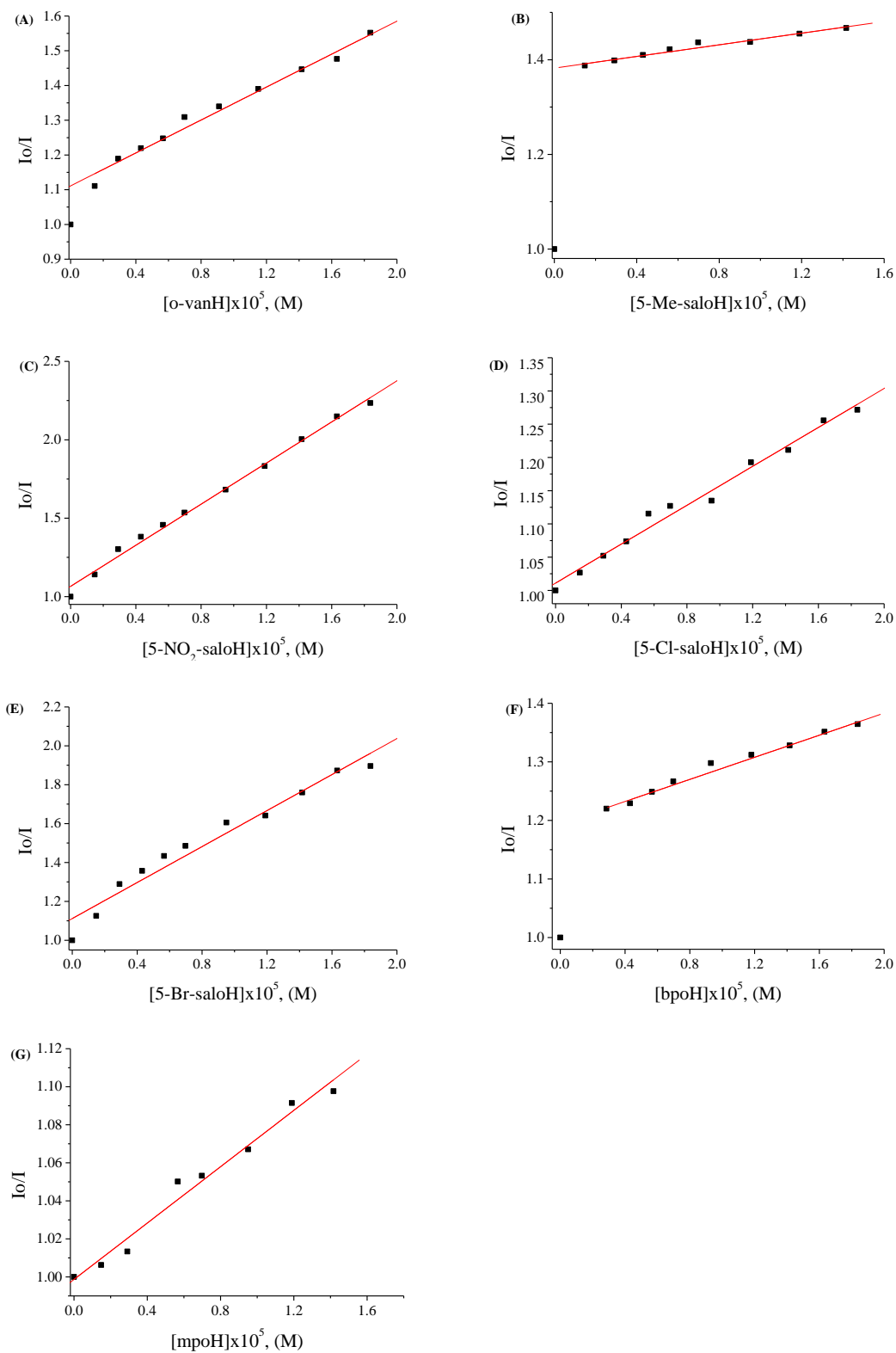
**Figure S6.** Cyclic voltammogram of 0.4 mM 1/2 dmsso/buffer (containing 150 mM NaCl and 15 mM trisodium citrate at pH 7.0) solution of  $[\text{Cu}(5\text{-Me-salo})_2]$ , **2** in the absence or presence of CT DNA. Scan rate =  $100 \text{ mV s}^{-1}$ . Supporting electrolyte = buffer solution.



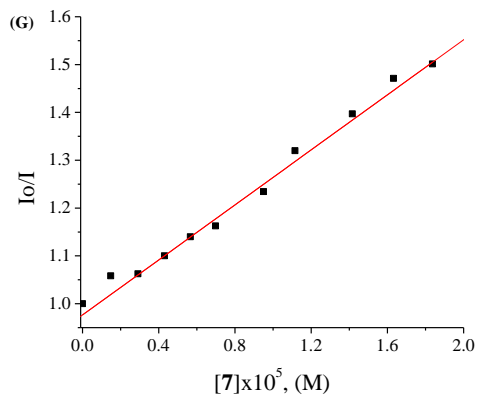
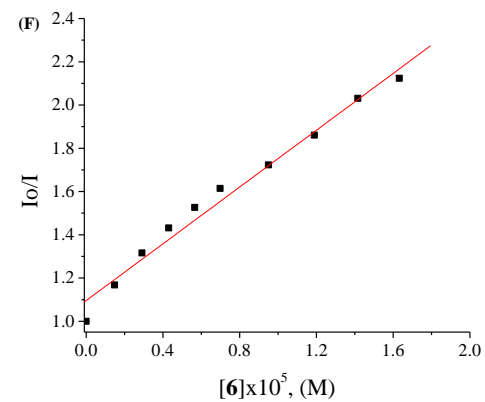
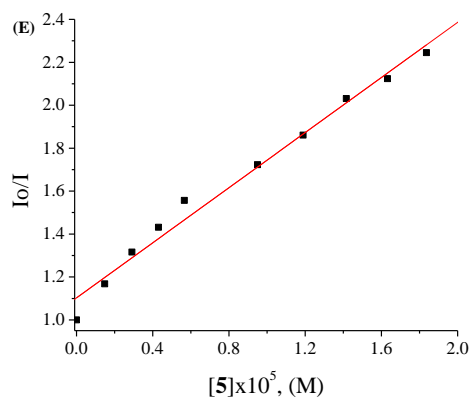
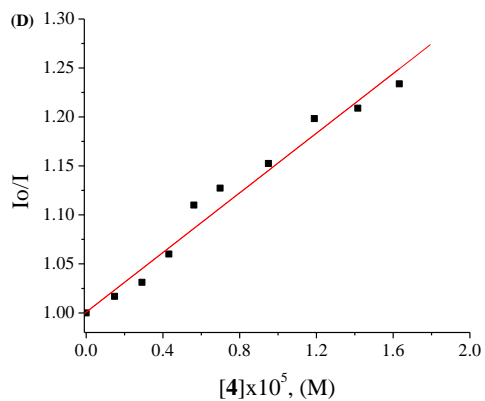
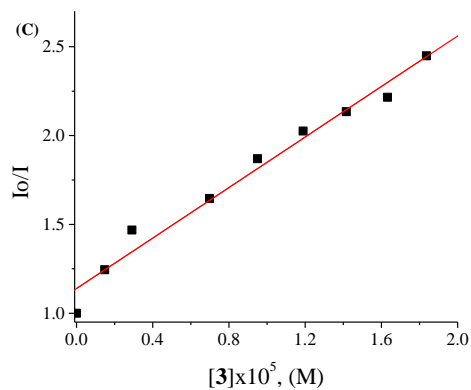
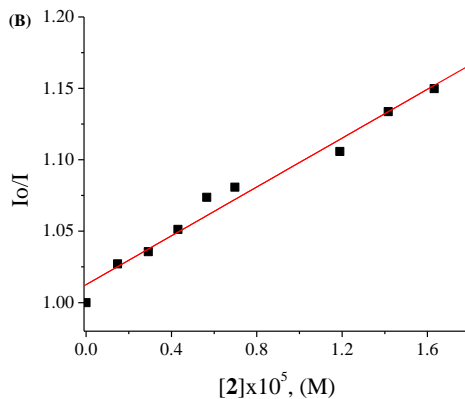
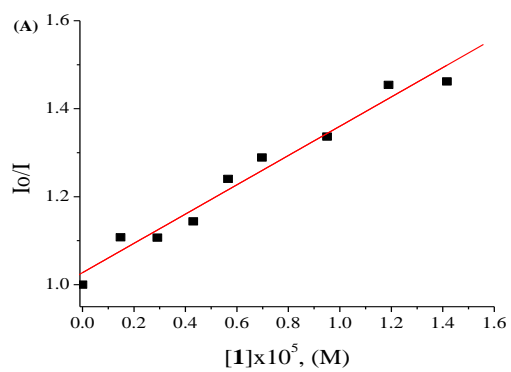
**Figure S7.** Stern–Volmer quenching plot of EB bound to CT DNA for (A) *o*-vanH, (B) 5-Me-saloH and (C) mpoH.



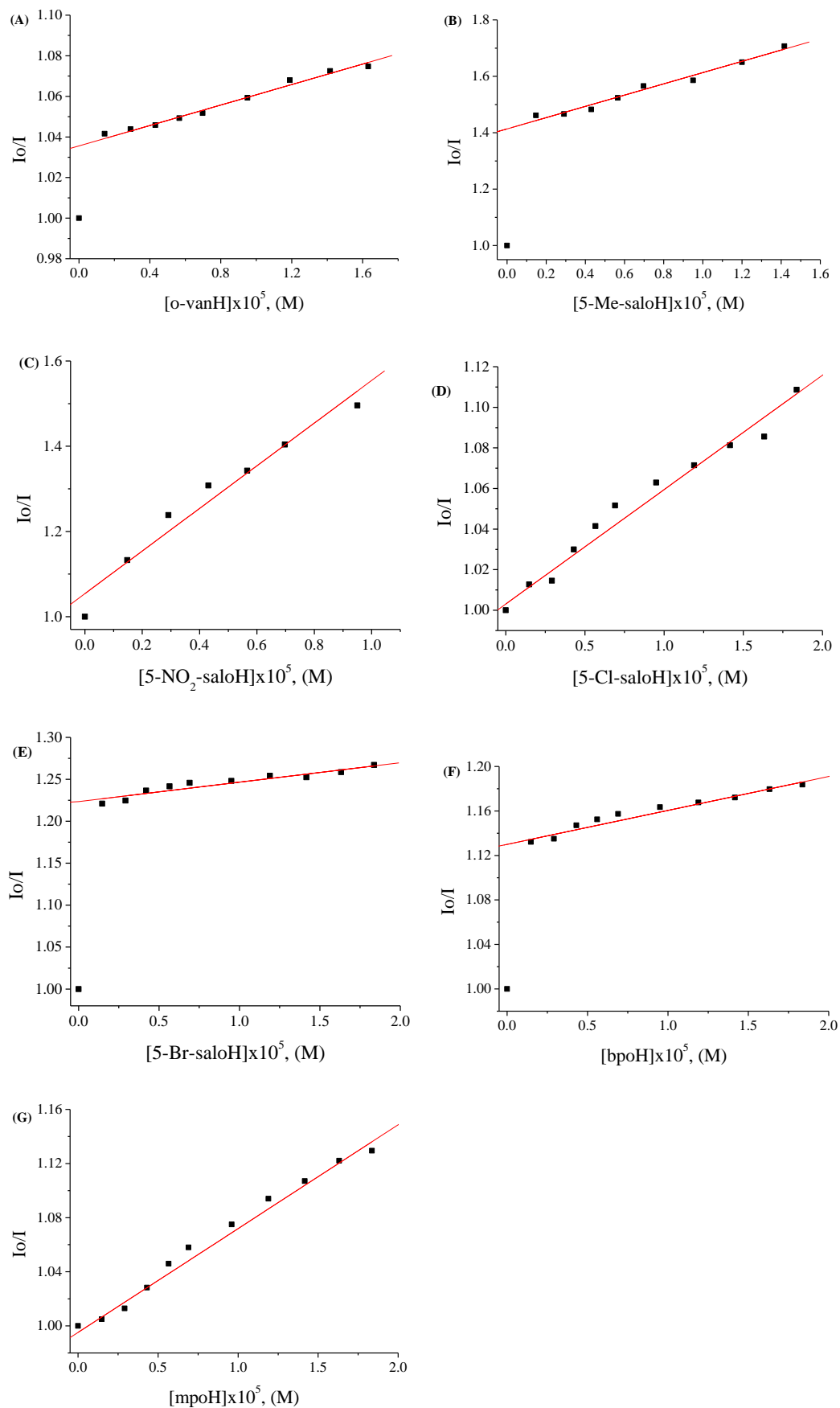
**Figure S8.** (A)–(G) Stern–Volmer quenching plot of EB bound to CT DNA for complexes 1–7, respectively.



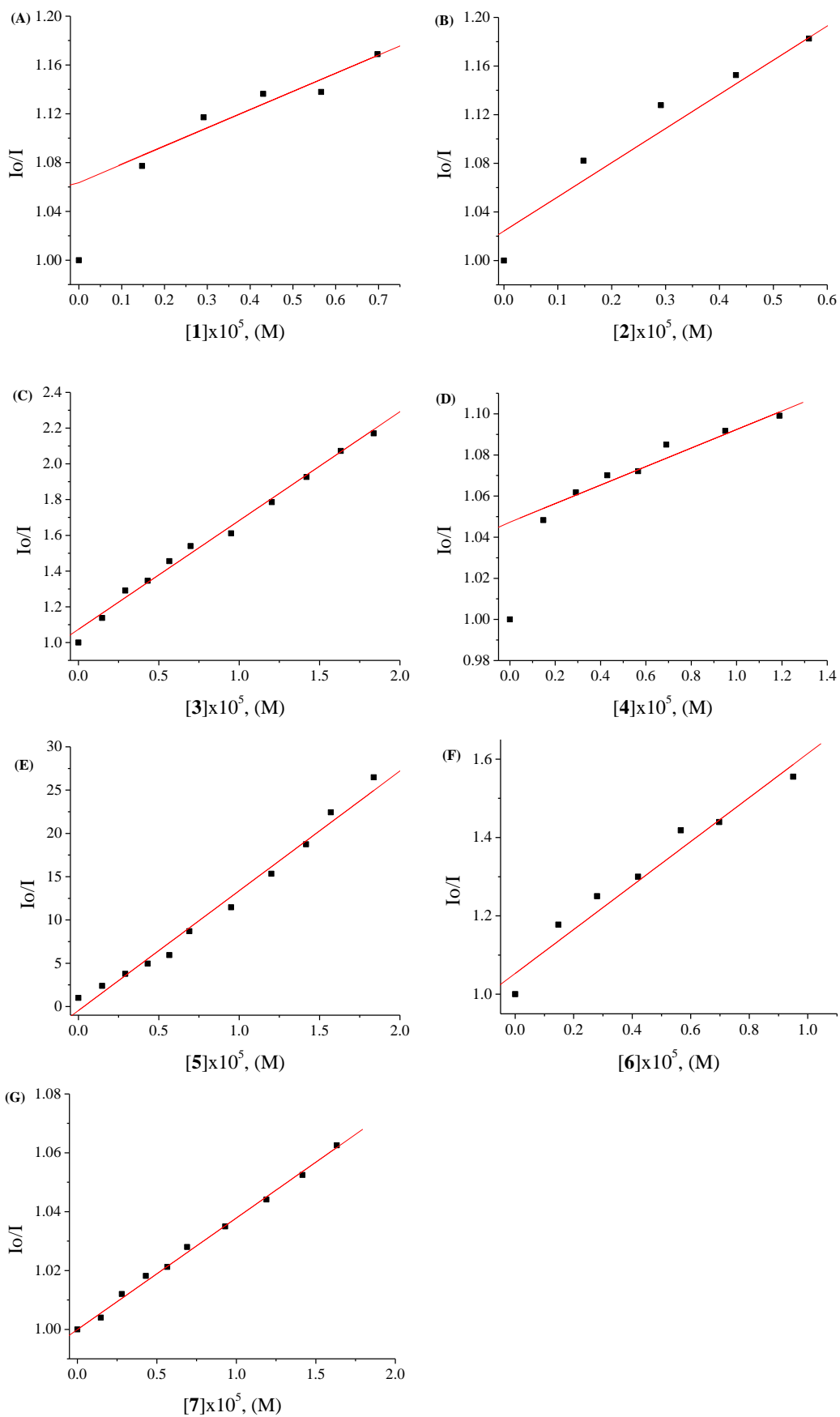
**Figure S9.** Stern–Volmer quenching plot of BSA for (A) o–vanH, (B) 5–Me–saloH, (C) 5–NO<sub>2</sub>–saloH, (D) 5–Cl–saloH, (E) 5–Br–saloH, (F) bpoH and (G) mpoH.



**Figure S10.** (A)–(G) Stern–Volmer quenching plot of BSA for complexes 1–7, respectively.

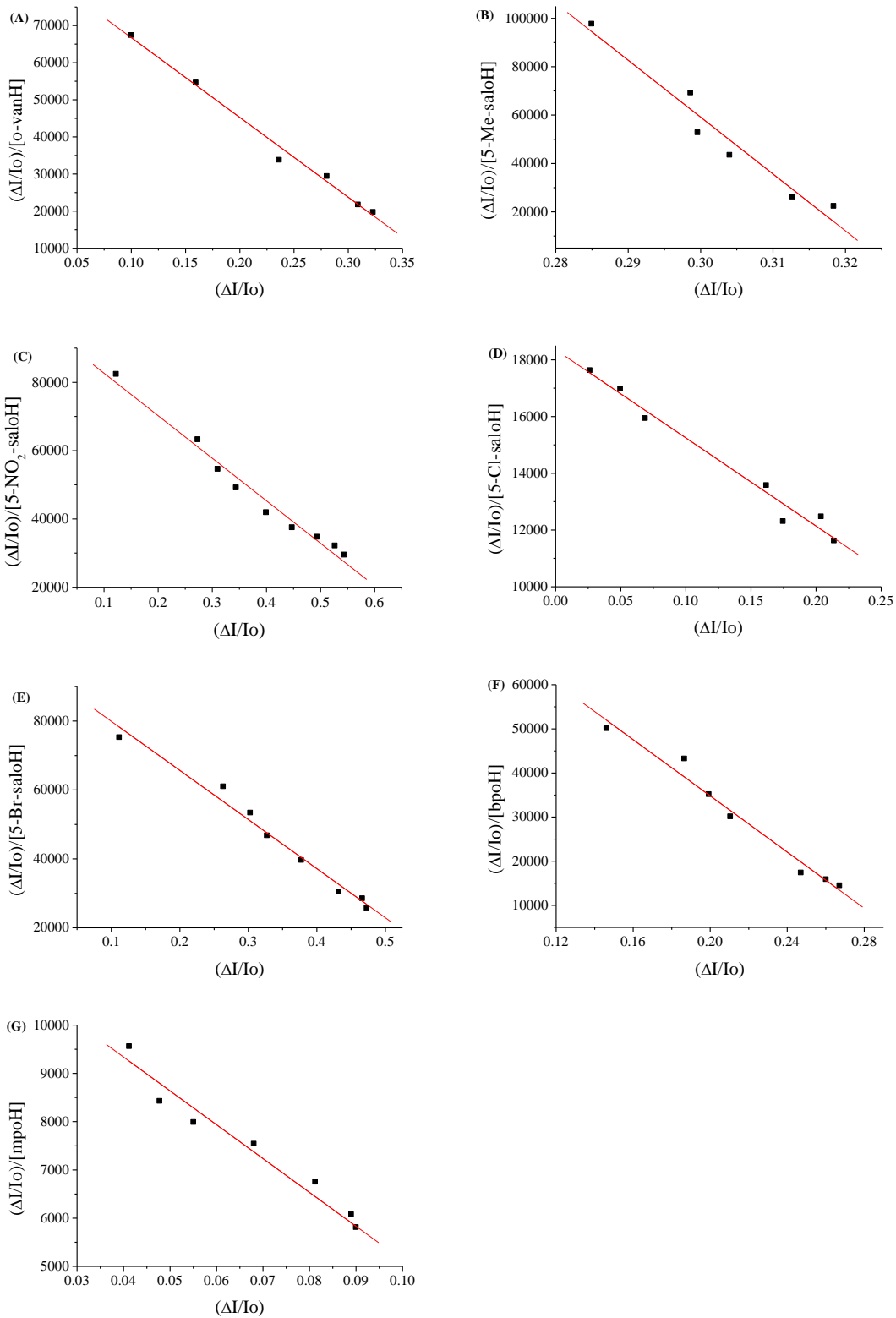


**Figure S11.** Stern–Volmer quenching plot of HSA for (A) *o*-vanH, (B) 5-Me-saloH, (C) 5-NO<sub>2</sub>-saloH, (D) 5-Cl-saloH, (E) 5-Br-saloH, (F) bpoH and (G) mpoH.

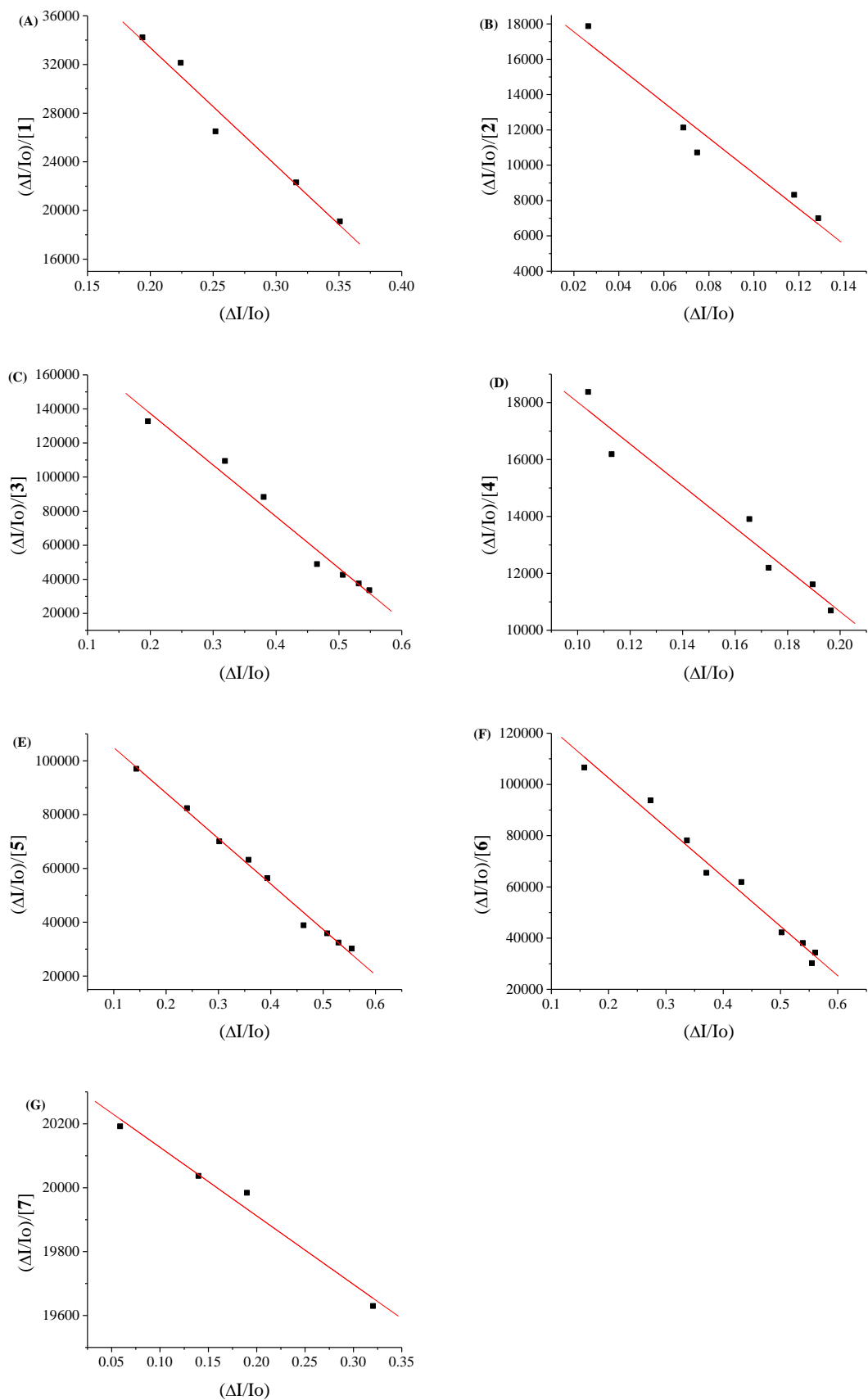


**Figure S12.** (A)–(G) Stern–Volmer quenching plot of HSA for complexes 1–7, respectively.

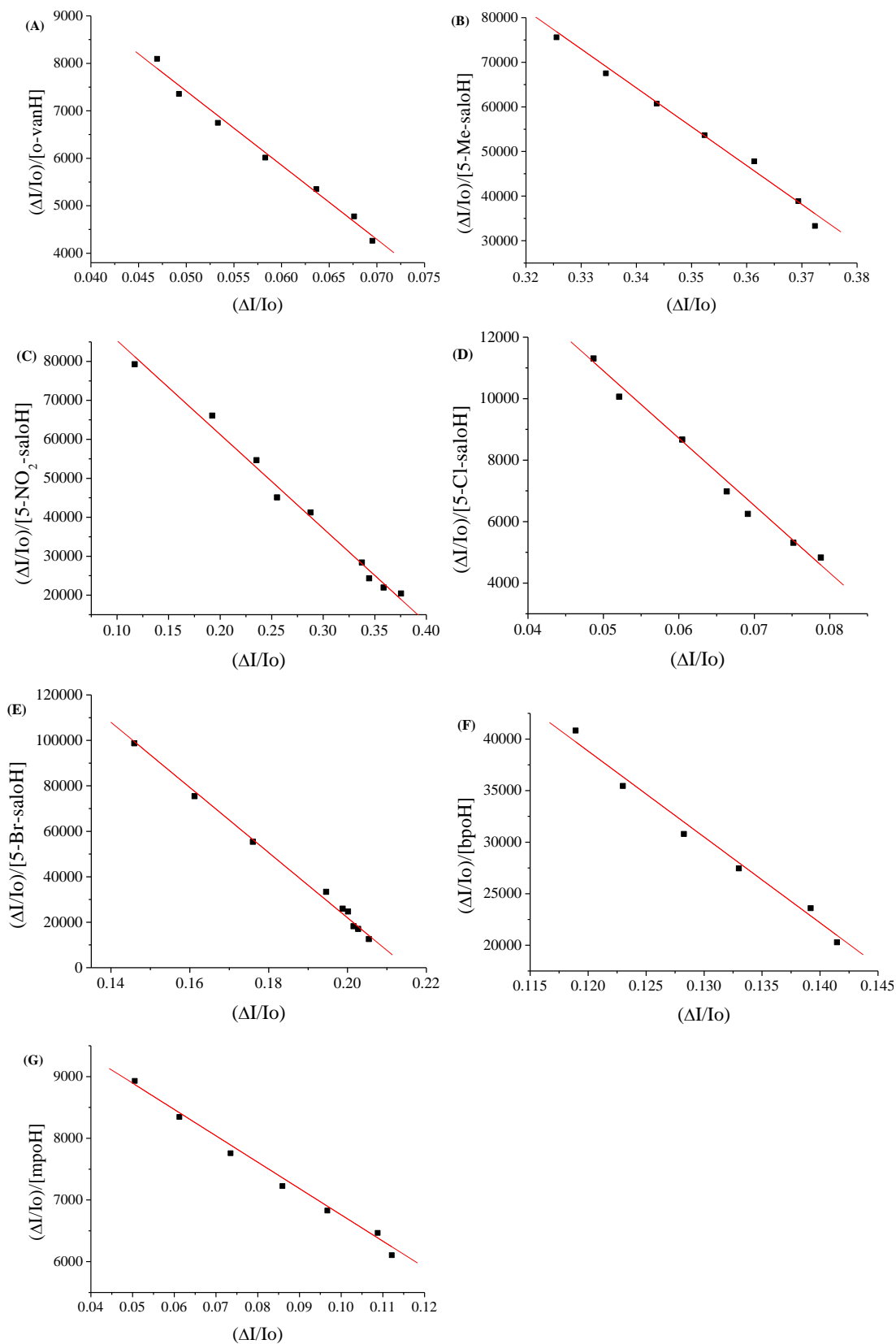




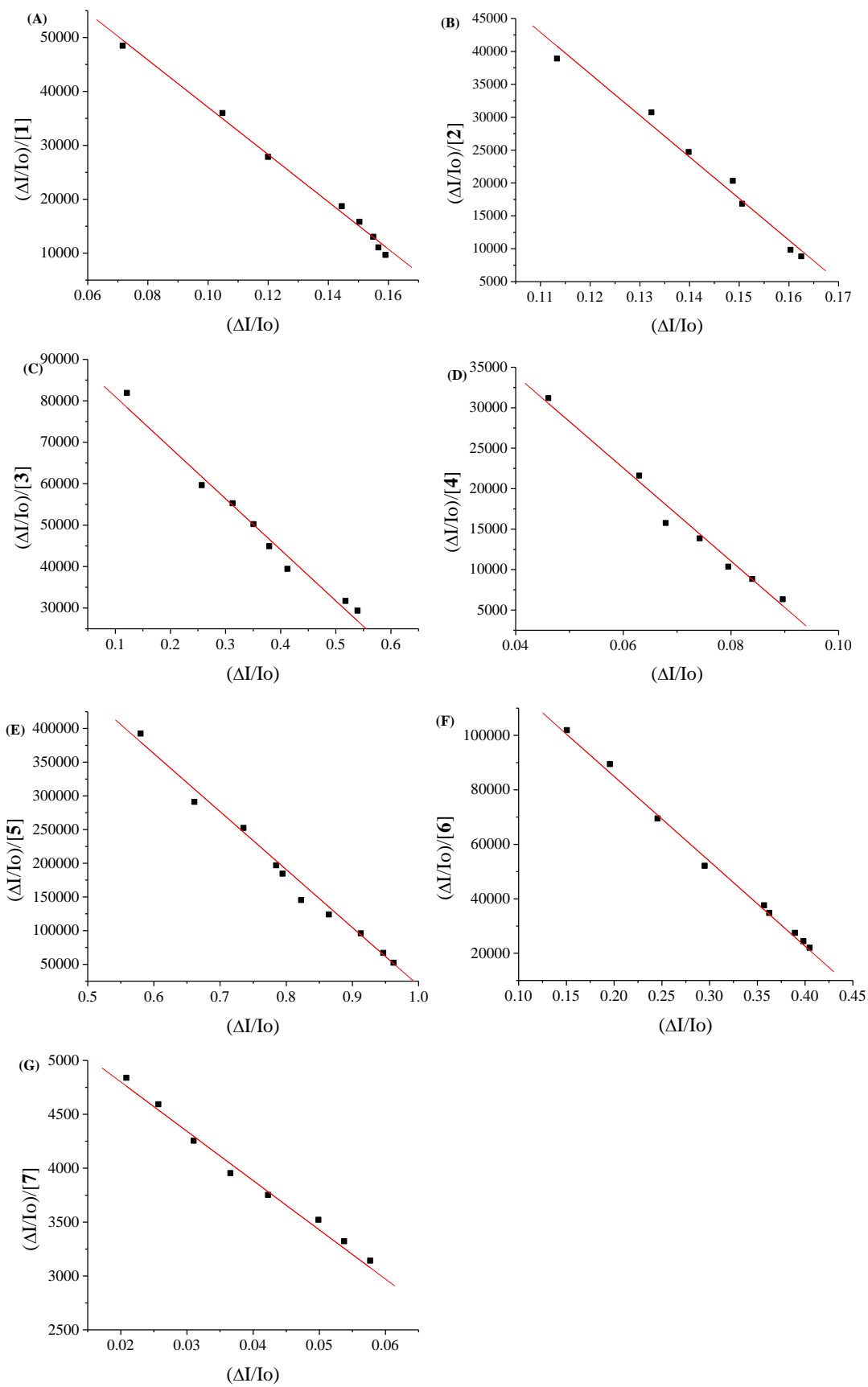
**Figure S13.** Scatchard plot of BSA for (A) *o*-vanH, (B) 5-Me-saloH, (C) 5-NO<sub>2</sub>-saloH, (D) 5-Cl-saloH, (E) 5-Br-saloH, (F) bpoH and (G) mpoH.



**Figure S14.** (A)–(G) Scatchard plot of BSA for complexes 1–7, respectively.



**Figure S15.** Scatchard plot of HSA for (A) o-vanH, (B) 5-Me-saloH, (C) 5-NO<sub>2</sub>-saloH, (D) 5-Cl-saloH, (E) 5-Br-saloH, (F) bpoH and (G) mpoH.



**Figure S16.** (A)–(G) Scatchard plot of HSA for complexes 1–7, respectively.