Electronic Supplementary Material (ESI) for Polymer Chemistry

Supporting info

Macromolecular platinum-drugs based on statistical and block copolymer structures and their DNA binding ability

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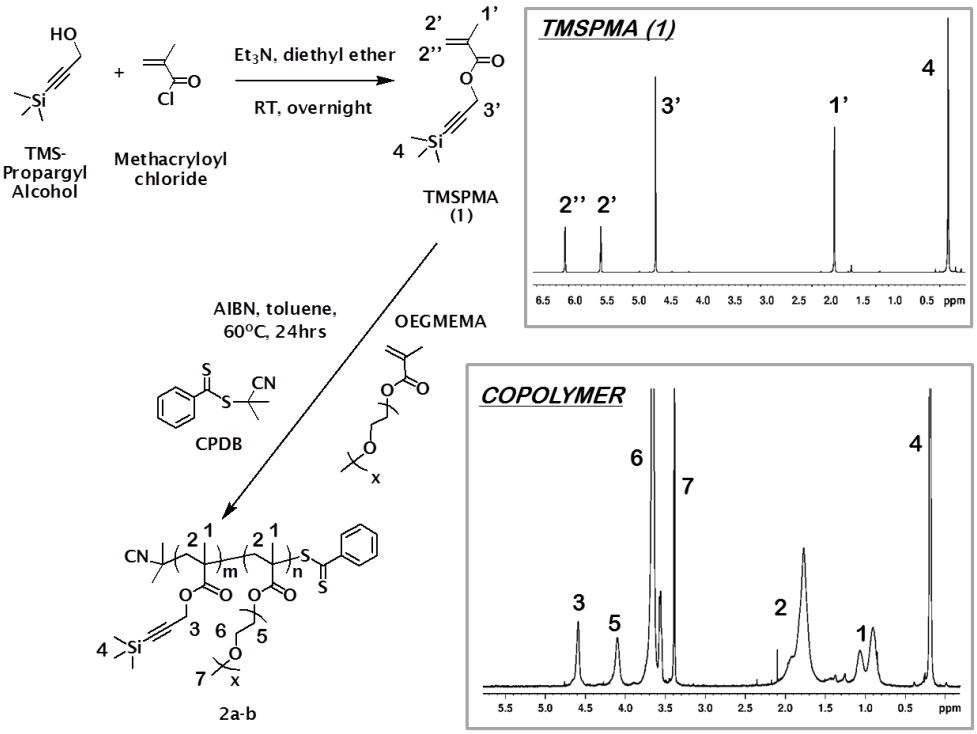


Figure S1 *Synthesis pathway of TMSPMA monomer and its RAFT polymerisation with OEGMEMA for copolymers* ***2a and 2b.*** *^{1}H NMR spectra represent TMSPMA monomer and P(EGMEMA-stat-TMSPMA) copolymer in $CDCl_3$*

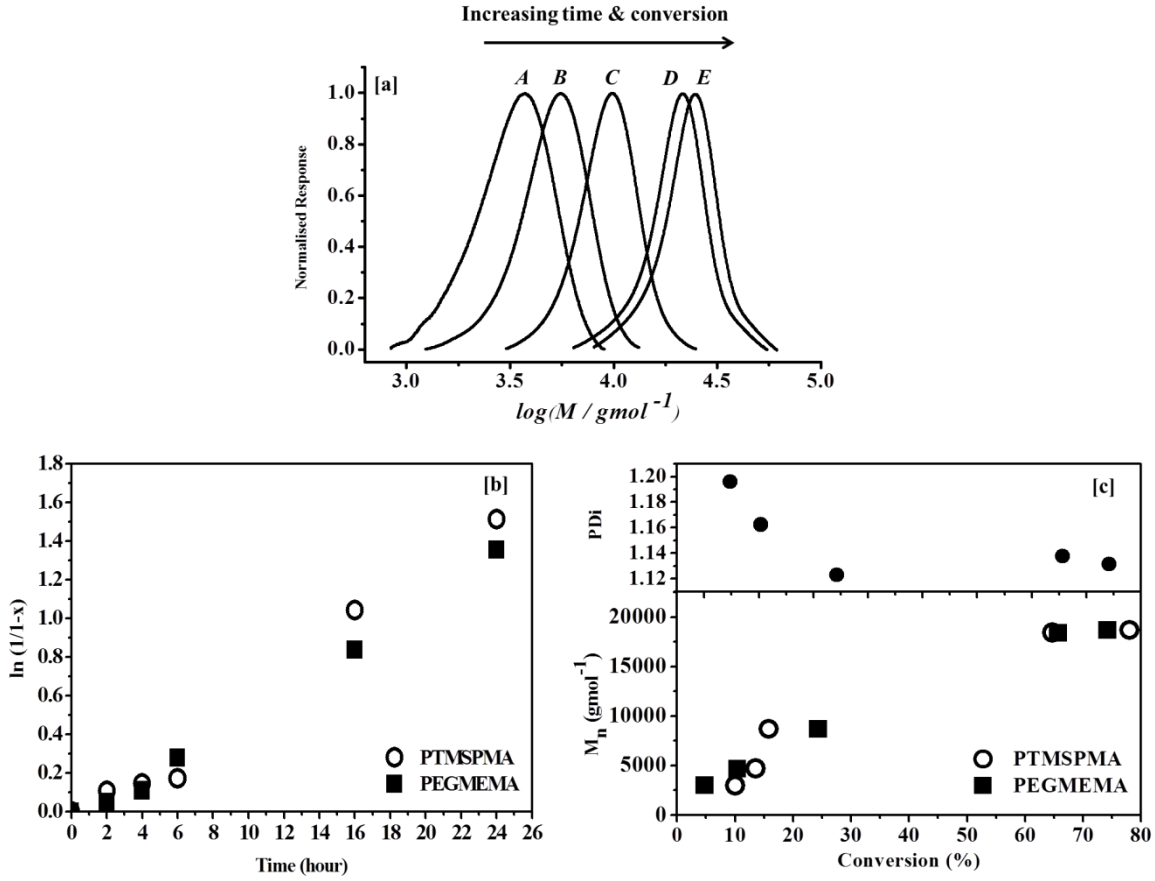


Figure S2 *Kinetics observations of P(OEGMEMA-co-TMSPMA) copolymerisation using CPDB in toluene at 60°C (a) GPC traces of PEGMEMA and PTMSPMA RAFT polymerization at various times (b) ln (1/(1-x)) versus time; and (b) pseudo-first-order kinetic plot of M_n and PDI versus monomer conversion. The RAFT polymerisation was performed at $[M_{OEGMEMA}]:[M_{TMSPMA}]:[RAFT]:[AIBN] = 90:10:1:0.1$. [Monomers] = 0.6 M.*

Table S1 *Kinetics of P(OEGMEMA-co-TMSPMA) copolymer*

GPC trace	Reaction Time (hours)	Conversion (%)		M_n (GPC) ($gmol^{-1}$)	PDI (M_n/M_w)
		OEGMEMA	TMSPMA		
A	2	4.8	10	2997	1.20
B	4	10.4	13.6	4698	1.16
C	6	24.3	15.8	8700	1.12
D	16	64.7	65.7	18406	1.13
E	24	74.2	78	21141	1.13

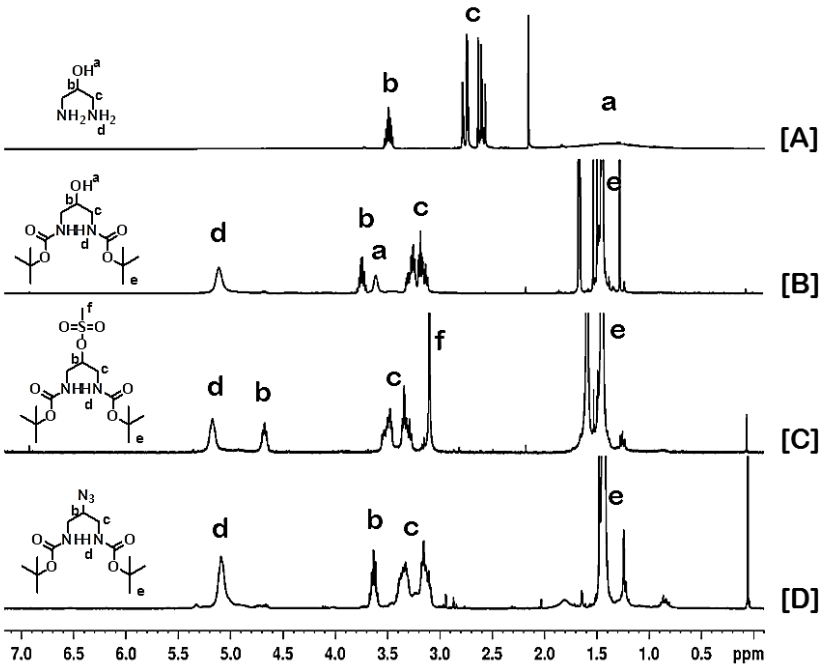


Figure S3 *^{1}H-NMR spectra of DAP modifications into azido-functionality, N_3-DAP-BOC in $CDCl_3$. [A] DAP, [B] DAP-BOC, [C] MS-DAP-BOC and [D] N_3-DAP-BOC*

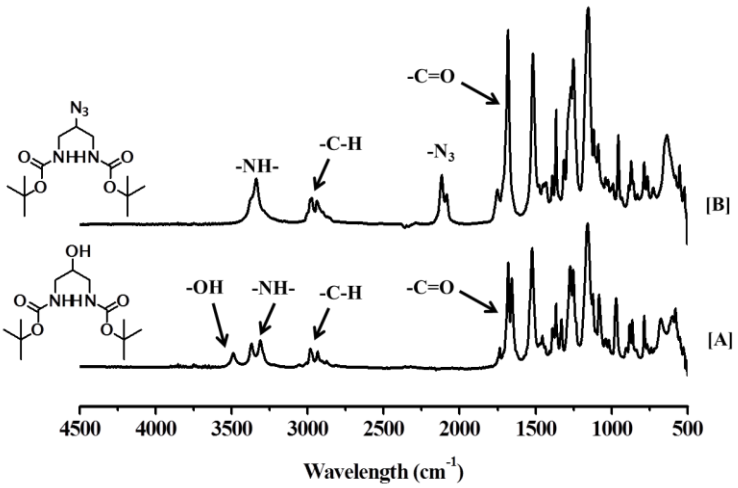


Figure S4 *FT-IR spectrum of modification of hydroxyl functional group of DAP-BOC [A] into azide moiety, N_3-DAP-BOC [B]*

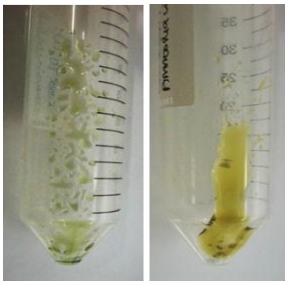
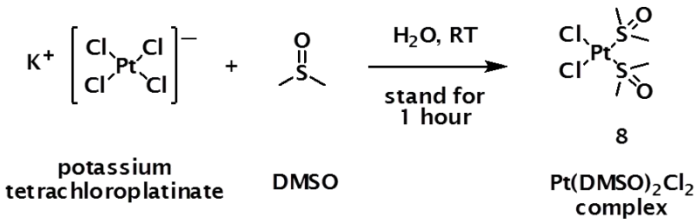


Figure S5 *CuAAC applied copolymers using $CuSO_4$/Na ascorbate after removal of copper. (a) P(OEGMEMA$_{64}$-stat-PMA-DAP-BOC$_8$)and (b) P(OEGMEMA$_{64}$-stat-PMA-DAP-BOC$_{16}$)*



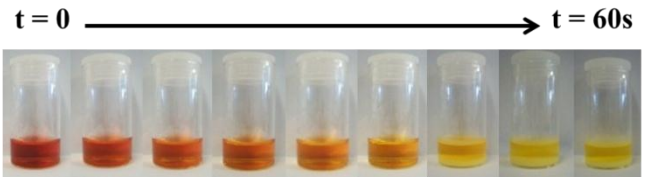


Figure S6 *Synthesis of the $Pt(DMSO)_2Cl_2$ complex and the observed colour change during synthesis*

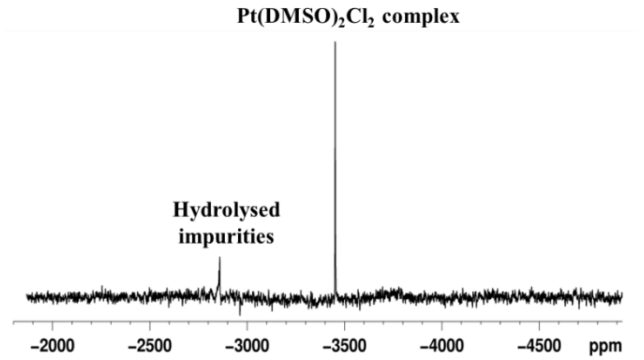


Figure S7 *^{195}Pt NMR of the $Pt(DMSO)_2Cl_2$ complex crystals in DMF/D_2O*

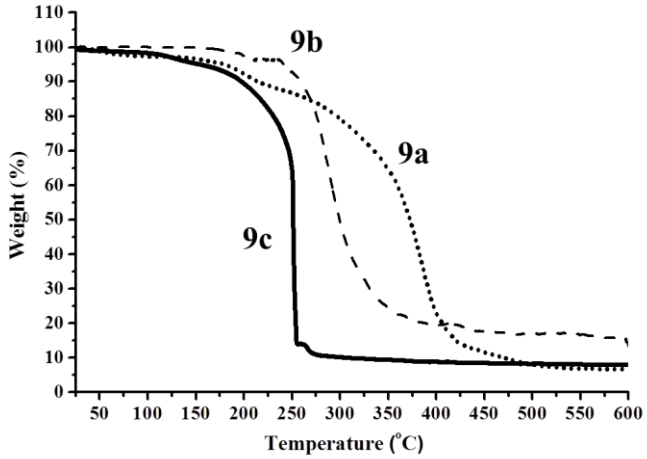


Figure S8 *TGA thermograms of platinum conjugated copolymers 9a, 9b and 9c at 20°C/min in nitrogen*

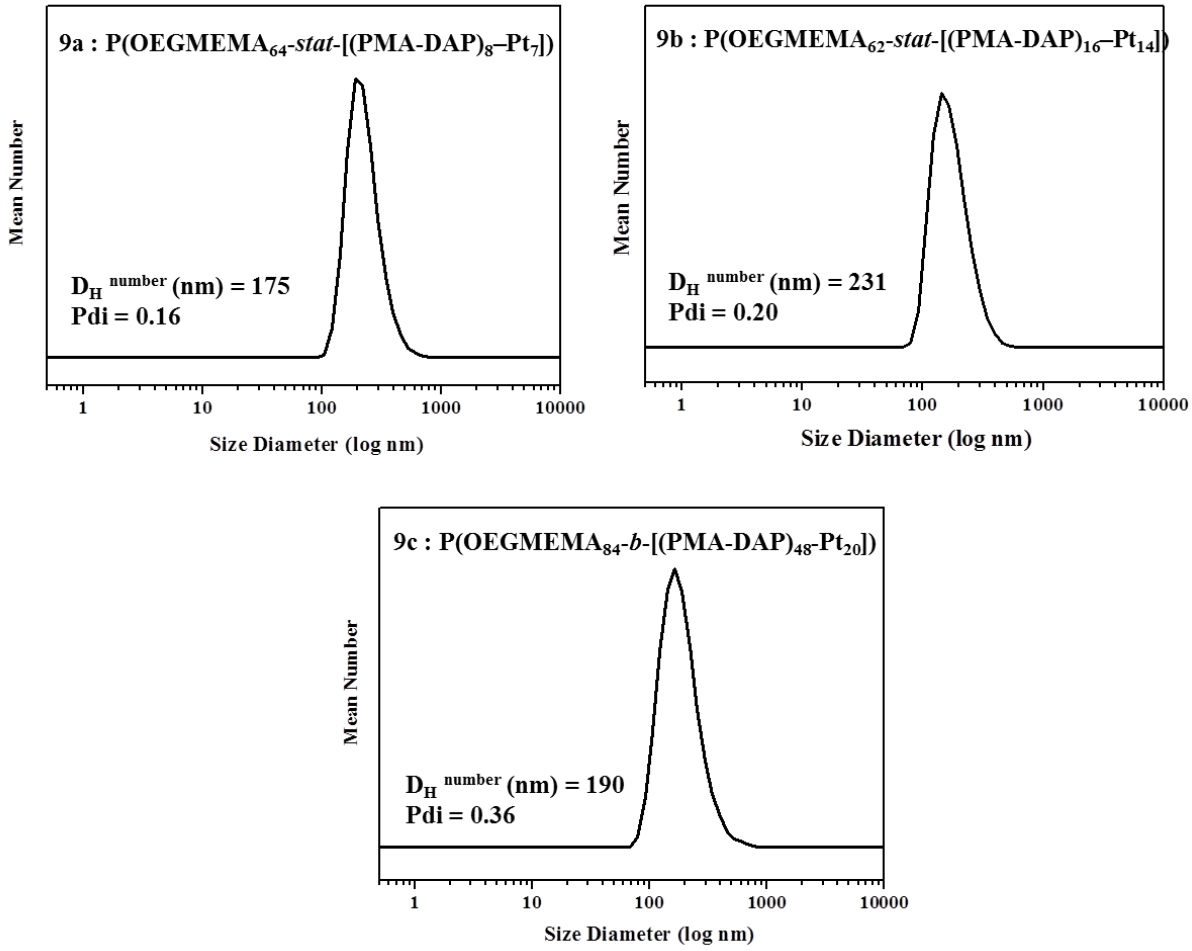


Figure S9. *DLS results of the platinated polymers in water*

Determination of DNA binding

The concentration of CT DNA solution was calculated from Lambert Beer's Law equation expressed as:

$$A = \varepsilon dc$$

where A is the UV absorbance of CT DNA solution at 260 nm, ε is molar absorption coefficient of CT-DNA (6600 M^{-1} cm^{-1}), d is the cuvette path length (1 cm) and c is the molar concentration of CT DNA. The concentration of CT DNA solution was 856 μM.

Using EtBr as the intercalating agent, the optimal wavelengths for fluorescence measurements were fixed to excitation and emission wavelengths of 480 nm and 520 nm respectively (**Figure S10**). Both excitation and emission slit widths were opened to 5 nm. Initially, emission spectra of a blank solution (10 mM $NaClO_4$ buffer only), a CT DNA solution only (26 μM) and an aqueous solution of platinum conjugated copolymer complexes were recorded in the range of 400-800 nm in a 4-sided quartz cuvette. No fluorescence was observed from any of these solutions, thus, confirming no interferences from these solutions took place.

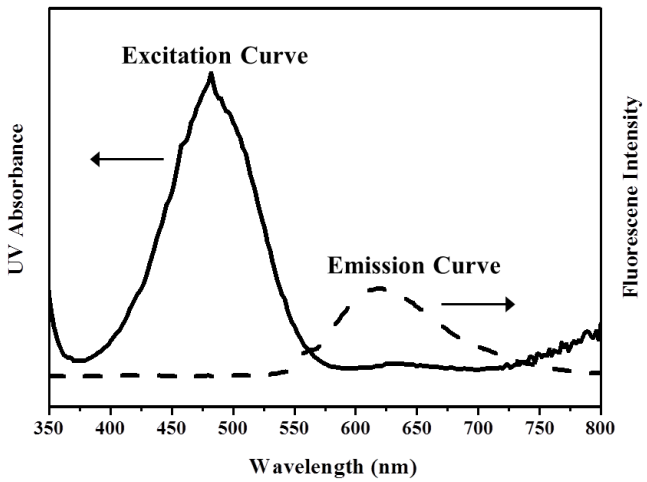


Figure S10 *Excitation and emission spectra of 50 μL EtBr (0.2mg/ml) in 10mM $NaClO_4$ at room temperature. λ_{ex} = 480 nm and λ_{em} = 520 nm*

The EtBr emission intensity is dependent from the CT DNA concentration used. Therefore, a saturation curve was obtained to determine the specific amount of EtBr needed to

fully intercalate a fixed concentration of CT-DNA (26 μM) which was used in this study. Emission spectra were recorded by aliquot titration of EtBr solution into 2 ml of buffer without CT DNA **[A]** and in the presence of 26 μM CT DNA solution **[B]** as shown in **Figure 3.16**. Both emission spectra showed a constant increase of the fluorescence intensity (arbitrary unit, a.u.) with every addition of EtBr. Similarly to previous literature, it was found that the fluorescence intensity increased approximately 10-fold in the presence of CT-DNA **[B]**, indicating formation of complex between intercalating agent and CT DNA [66, 68].

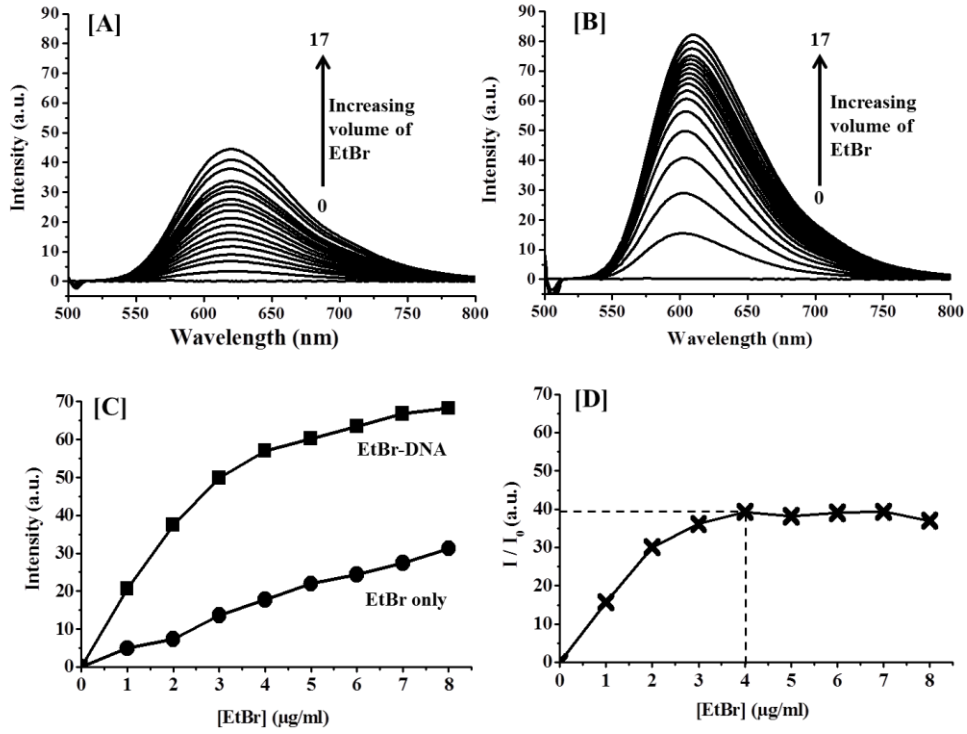


Figure S11 *Emission spectra of EtBr in 10mM $NaClO_4$ buffer in the absence **[A]** and presence of CT DNA **[B]** at 25°C. EtBr (*10 μM*) aliquots addition of 5μL in 2 ml of 10mM $NaClO_4$ from **1-17** and **0** is without EtBr. **[C]** is a summarised emission data plotted in a graph with intensity vs [EtBr]* (represent by ● and ■) *which afforded a **[D]** saturation curve of EtBr-CT DNA.*

In addition , not only was an increase of fluorescence intensity of CT DNA-EtBr mixture observed, but also a blue shift of 5 nm in the emission wavelength from 610nm at 605nm. After a certain concentration of EtBr, the curve plateaus **[B]** due to the saturation of intercalation sites. To estimate the amount of EtBr needed to fully intercalate with the fixed CT DNA concentration, the maximum intensity of every addition of EtBr into the solution without and with CT DNA versus wavelengths was plotted to give a graph **[C]** and used to calculate a saturation curve **[D]** which was plotted as I/I_0 versus concentration of EtBr (✖). I_0 represents the fluorescence intensity of EtBr where I is [(fluorescence intensity of CT DNA-EtBr) – (fluorescence intensity of EtBr)]. Once saturation was reached, the no increase in fluorescence intensity was observed. The levelling-off of this curve **[D]** corresponds to the saturation point of this system, and was determined to be 40 μL of 10 μM EtBr in the 26 μM of CT DNA solution in 2ml of buffer (graph **[D]**). Upon addition of EtBr to CT-DNA solution the colour was seen to change from orange to pink, due to the interaction between ethidium bromide and DNA.

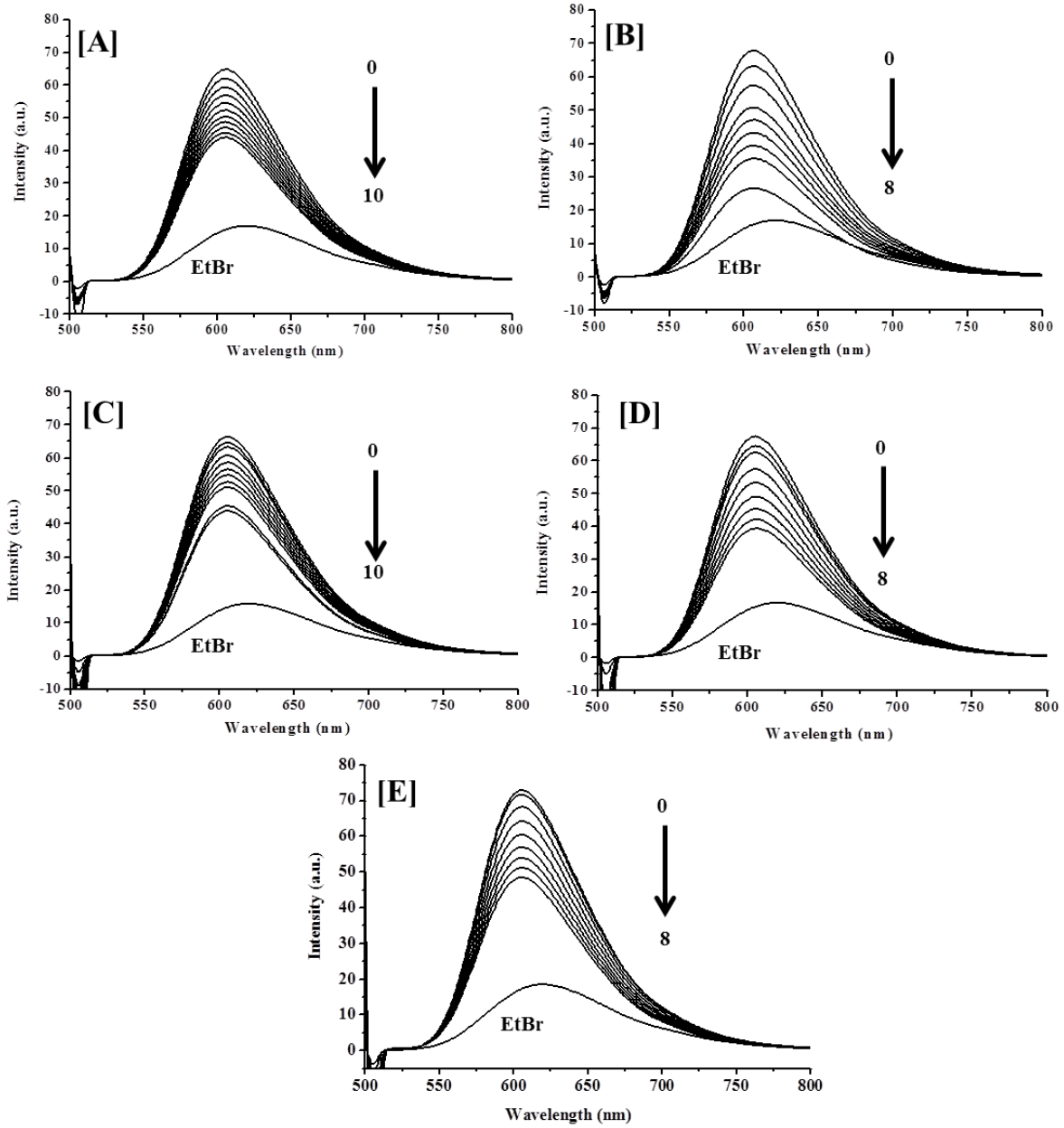


Figure S12 *Emission spectra of CT DNA-EtBr (prepared from the same stock solution) in 10mM $NaClO_4$ buffer in the absence (**0**) and presence (**1-10**) of cisplatin **[A],** $Pt(DMSO)_2Cl_2$ **[B], 9a [C], 9b [D]** and **9c [E]** at ambient temperature**.** Concentrations of cisplatin [A] are : 0μM, **1**: 1.55μM, **2:** 2.58μM, **3** : 5.16μM, **4** : 7.74μM, **5** : 10.3μM, **6 :** 12.9μM, **7** : 15.5μM, **8** : 18.1μM, **9** : 20.6μM, and **10** : 23.2μM.*

Please not note all the concentrations listed in Figure 5 are displayed here