Supporting Information

Accompanying the manuscript

Copper Phenanthrene Oxidative Chemical Nucleases

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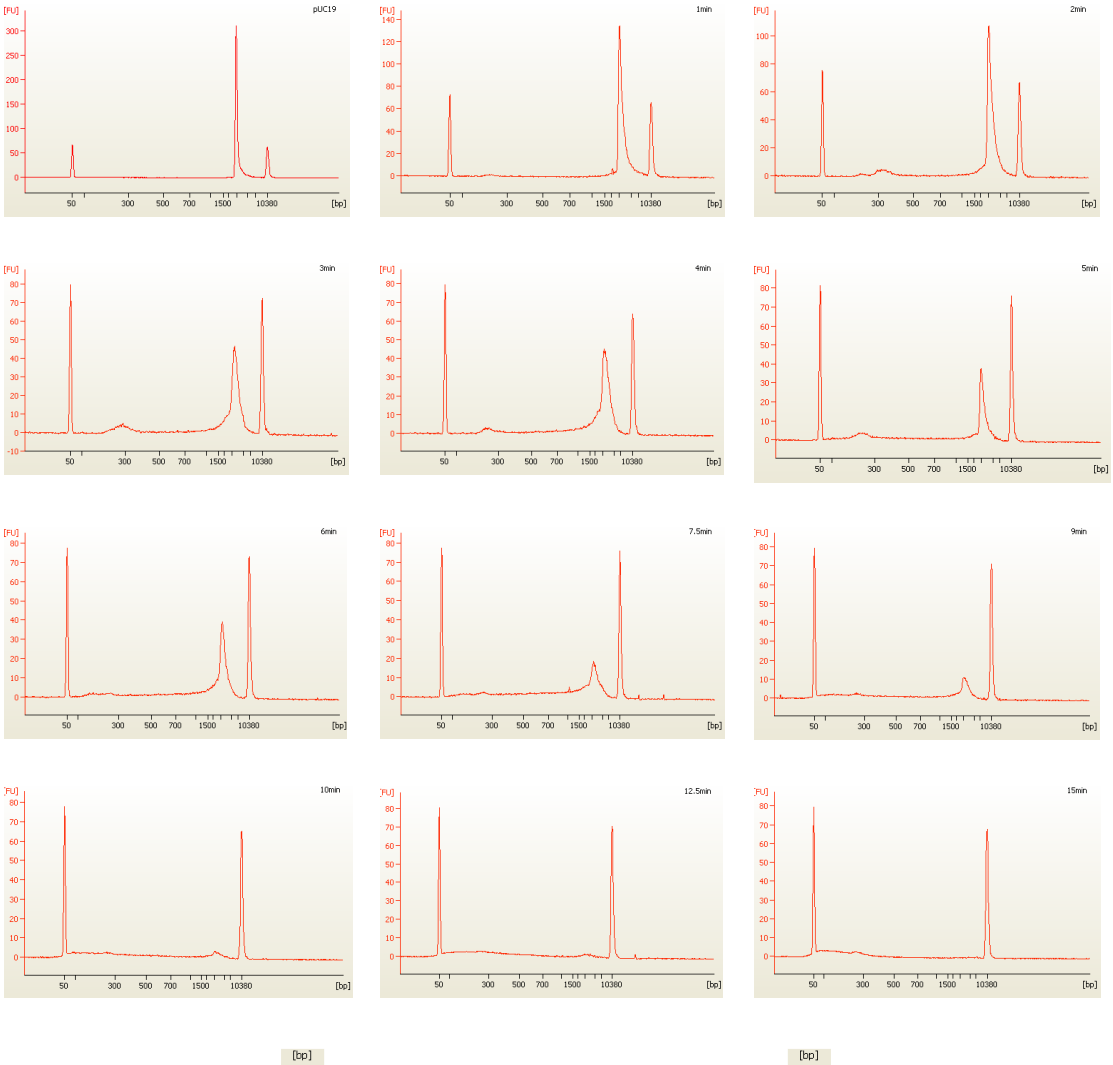
S-1: Electrogram and electropherogram data from the Bioanalyzer 2100



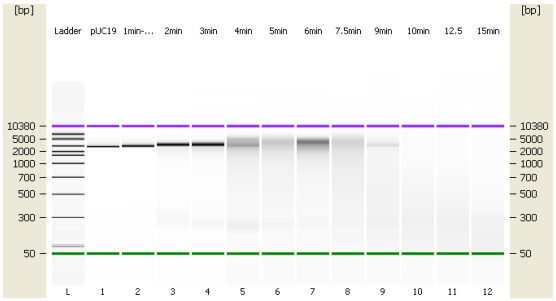


Figure S1. Individual electrograms and electropherogram of linearized pUC19 (400 ng) exposed to **Cu-Phen** (500 nM) in the presence of 1 mM Na-L-ascorbate between 0-15 min generated by a single micofluidic chip. Triplcate microfluidic chips (DNA 7500) were run for each sample.

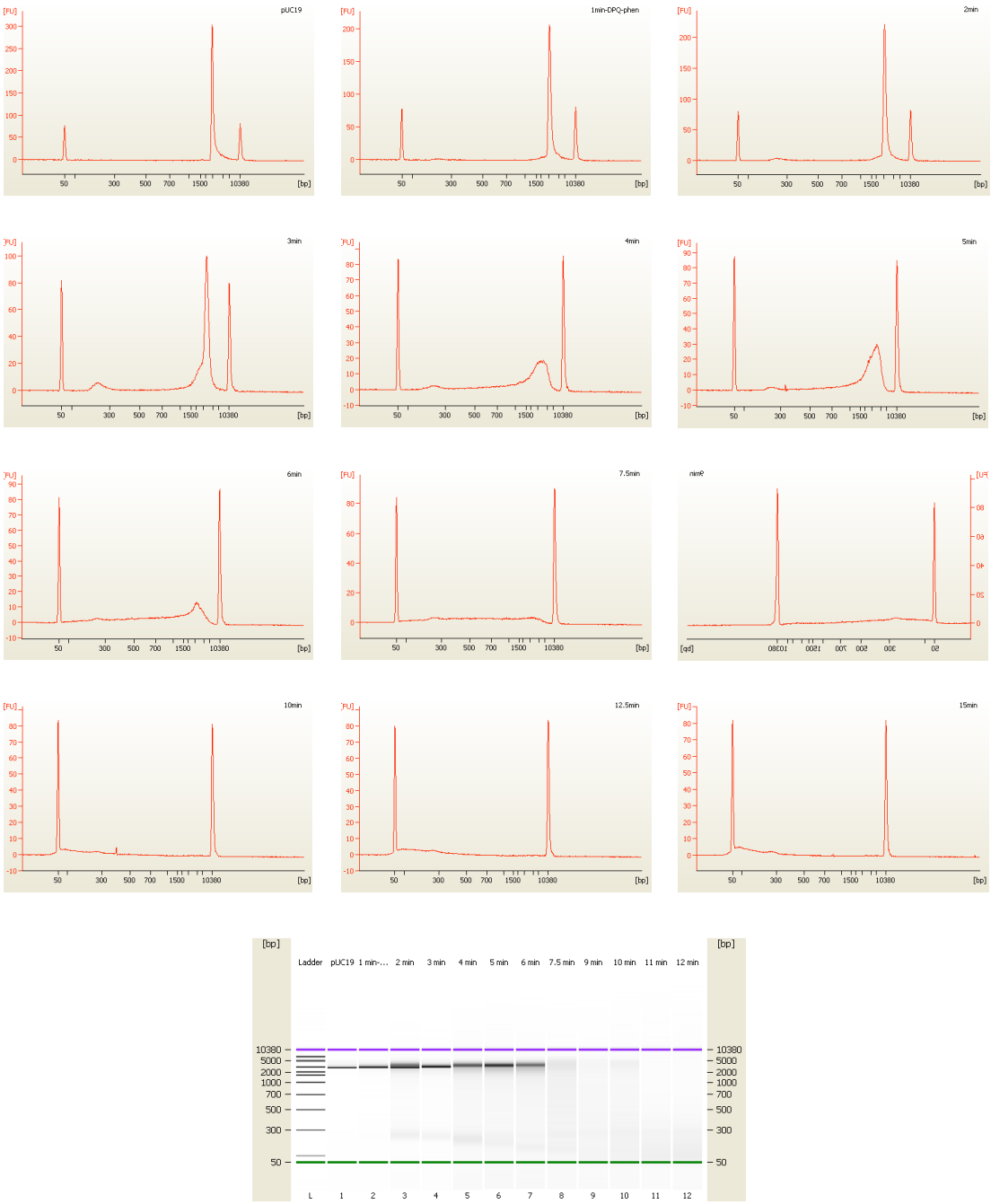


Figure S2. Individual electrograms and electropherogram of linearized pUC19 (400 ng) exposed to **Cu-DPQ-Phen** (500 nM) in the presence of 1 mM Na-L-ascorbate between 0-15 min generated by a single micofluidic chip. Triplcate microfluidic chips (DNA 7500) were run for each sample.

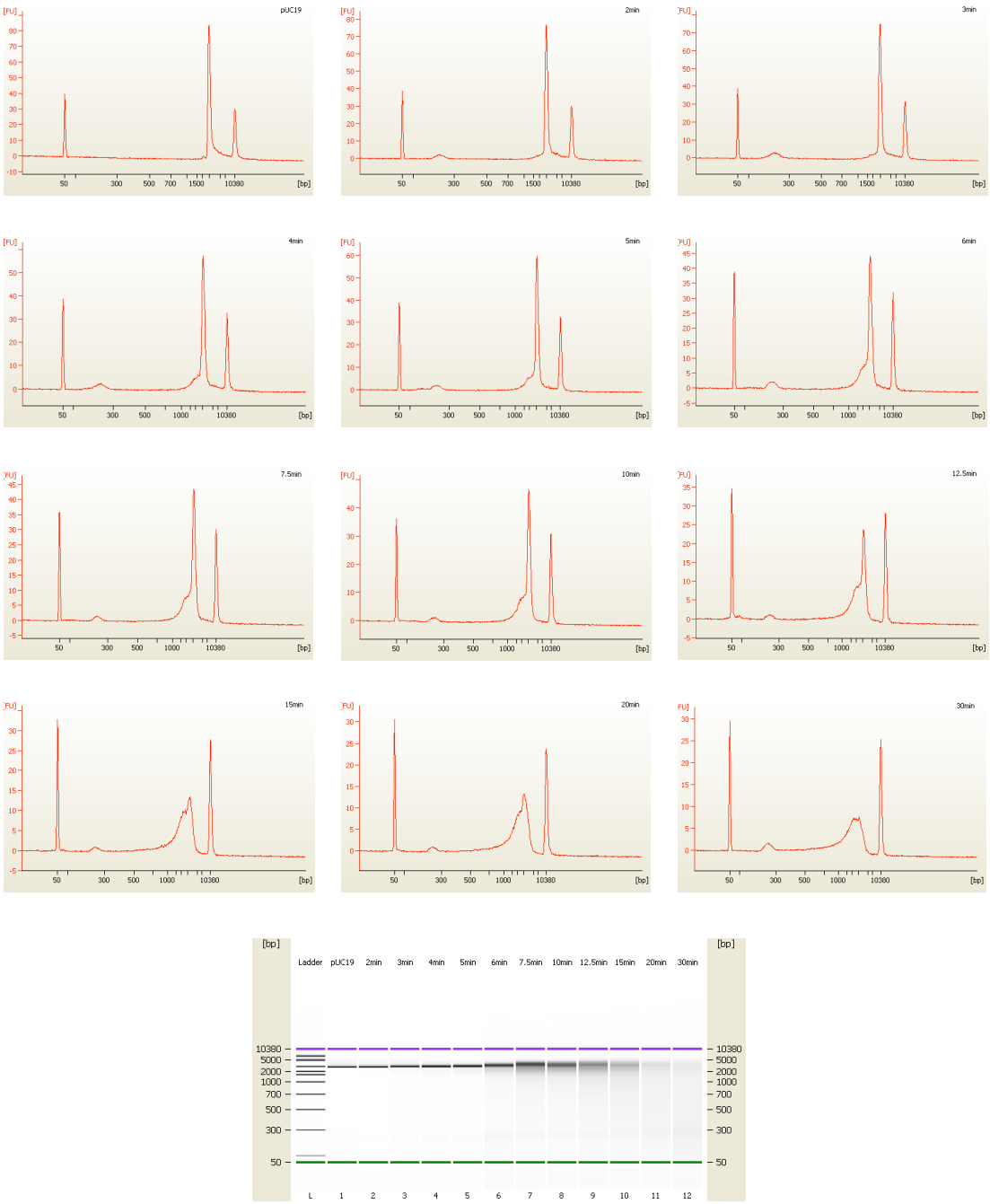


Figure S3. Individual electrograms and electropherogram of linearized pUC19 (400 ng) exposed to **Cu-DPPZ-Phen** (500 nM) in the presence of 1 mM Na-L-ascorbate between 0-30 min generated by a single micofluidic chip. Triplcate microfluidic chips (DNA 7500) were run for each sample.

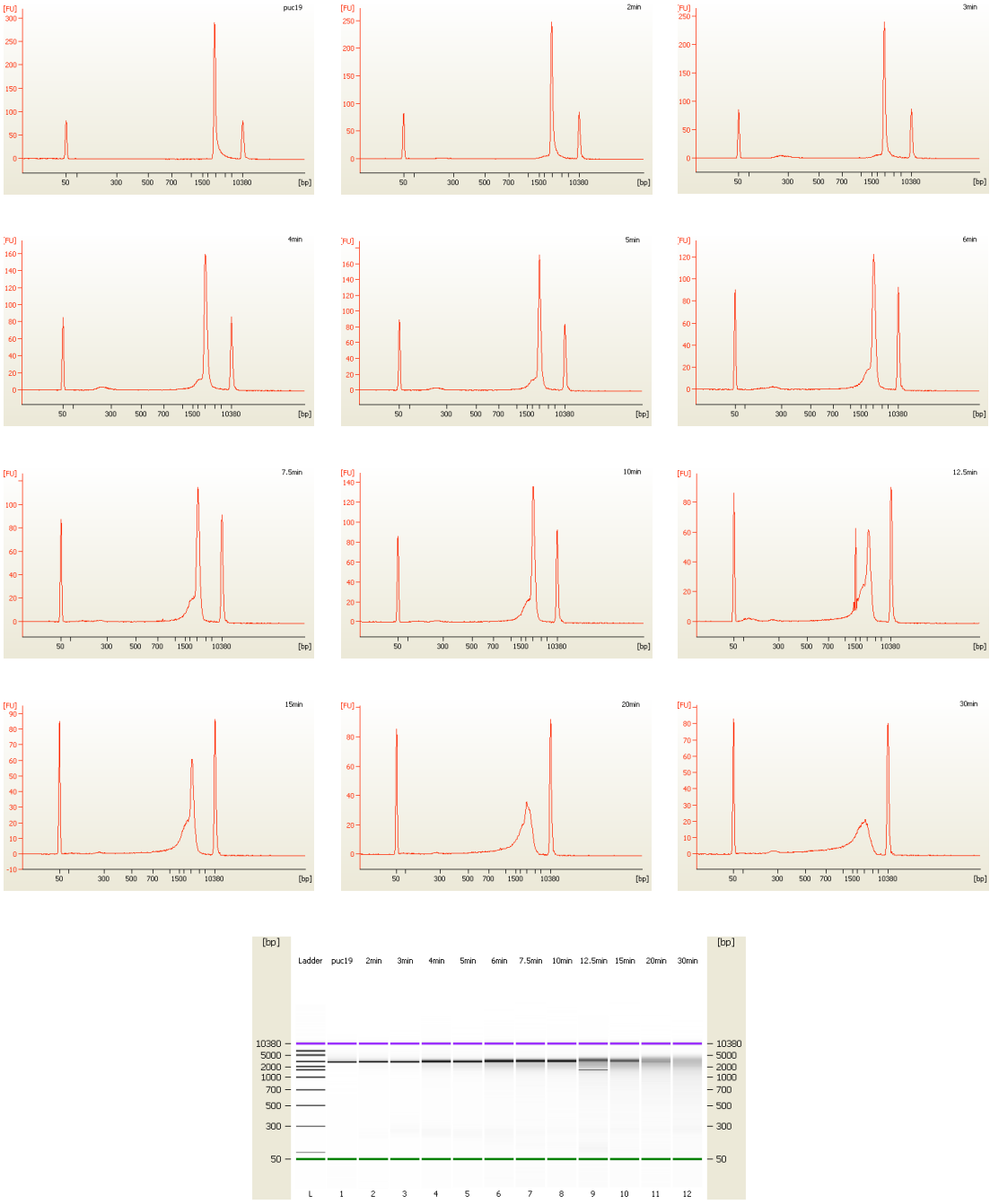


Figure S4. Individual electrograms and electropherogram of linearized pUC19 (400 ng) exposed to **Cu-DPPN-Phen** (500 nM) in the presence of 1 mM Na-L-ascorbate between 0-30 min generated by a single micofluidic chip. Triplcate microfluidic chips (DNA 7500) were run for each sample.

S-2: Optimization of thermal melting on poly[d(A-T)$_2$] and poly[d(G-C)$_2$]

Overview. In order to examine the stabilization effects on poly[d(G-C)$_2$] and poly[d(A-T)$_2$], a series of optimisation experiments were conducted to identify the most suitable pH and ionic buffer strength required (ESI). Previous reports on drug binding effects to G-C polynucleotides, where strands are bound through three hydrogen bonds at each base pair, could not be identified owing to polymer stabilization beyond the limit of detection (>110 °C). In our experiments, suitable conditions for the melting of poly[d(G-C)$_2$] (T_M = 80.74 °C) were found at pH 5.0 in 2.0 mM sodium acetate buffer containing 1.0 mM NaCl. In order to maintain similar experimental conditions for the thermal melting on poly[d(A-T)$_2$], where strands are bound through two hydrogen bonds between each base pair only, pH 5.0 sodium acetate buffered (50 mM) solutions containing 250 mM of NaCl were employed for the thermal melting of this polynucleotide (T_M = 69.32 °C).

poly[d(G-C)$_2$]. It was necessary to carry out experimental optimisation before commencing thermal melting analysis as it was noted in literature previously published, the T_M for poly(dG-dC)•poly(dC-dG) could not be determined as it was beyond the level of detection, in some cases >110 °C.[1,2] Thermal melting analysis was initially investigated in potassium phosphate buffer at pH 7.2 with varying NaCl concentrations of 0.1 mM, 1 mM and 2 mM generating T_M values of 90.60 °C, 89.57 °C and 91.52 °C for the untreated polymer, respectively. It was therefore necessary to identify conditions where the T_M of poly[d(G-C)$_2$] would be lower prior to the addition of any stabilizing test compound. Varying concentrations (2.0 – 5.0 mM) of sodium acetate buffer (NaOAc) at pH 5.0 were then investigated in the presence and absence of added NaCl (Table S1). 2.0 mM NaOAc buffer with 1.0 mM of added NaCl gave a favourable T_M value of 80.74 °C which was used in all thermal denaturation studies.

Table S1. Thermal melting analysis of poly[d(G-C)$_2$] under alternating buffer, pH and ionic strength.

Buffer	Buffer (mM)	Added NaCl (mM)	T_M (°C)
Phosphate (pH 7)	50	0.1	90.60
	50	1.0	89.57
	50	2.0	91.52
NaOAc (pH 5)	2.0	0.0	73.02
	2.0	1.0	80.74
	2.5	0.0	89.02
	5.0	0.0	86.02

poly[d(A-T)$_2$]. The thermal melting was also investigated in both potassium phosphate (pH 7.0) and NaOAc (pH 5.0) buffers with varying ionic strength. At pH 7.0 the T_M of poly[d(A-T)$_2$] in both the presence and absence of additional NaCl was 59 °C and 59.27 °C respectively (Table S2). As experimental conditions for poly[d(G-C)$_2$] were carried out in pH 5.0 sodium acetate buffer, it was necessary to optimise similar conditions for this nucleotide for comparative reasons. The T_M of poly[d(A-T)$_2$] in NaOAc buffer over the concentration range of 100 mM to and 1.0 M NaCl produced an upward trend in T_M, confirming thermal stabilization is directly related to the logarithm of the salt concentration up to ~1 M NaCl.[3,4] poly[d(A-T)$_2$] thermal melting experiments were selected to be carried out in 50 mM NaOAc buffer at pH 5.0 with 250 mM of added NaCl.

Table S2. Thermal melting analysis of poly[d(A-T)$_2$] under alternating buffer, pH and ionic strength.

Buffer	Buffer (mM)	Added NaCl (mM)	T_M (°C)
Phosphate (pH 7)	50	0.0	59.00
	50	2.0	59.27
NaOAc (pH 5)	2.0	0.0	25.52
	50	100	64.01
	50	250	69.32
	50	500	73.02
	50	750	75.22
	50	1000	76.47

S-3: Non-linear regression dose-response curves for cytotoxicity on SKOV3

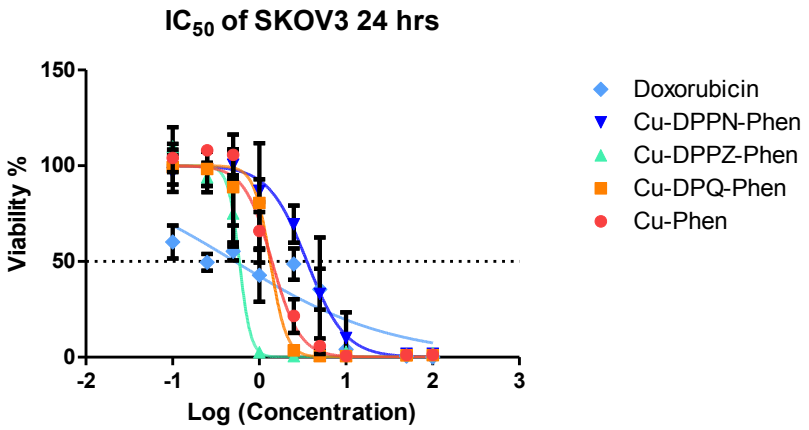


Figure S5. Non-linear regression dose-response curves for **Cu-Phen** (red), **Cu-DPQ-Phen** (orange), **Cu-DPPZ-Phen** (green) and **Cu-DPPN-Phen** (light blue) and doxorubicin (dark blue). IC_{50} values were calculated from log concentrations equivalent to 0.1 - 100 µM.

References:

(1) García, B.; Leal, J. M.; Ruiz, R.; Biver, T.; Secco, F.; Venturini, M. *J. Phys. Chem. B* **2010**, *114*, 8555.

(2) Saha, I.; Hossain, M.; Suresh Kumar, G. *J. Phys. Chem. B* **2010**, *114*, 15278.

(3) Wilson, D.; Tanious, F. A.; Fernandez-Saiz, M.; Rigl, C. T. Evaluation of Drug-Nucleic Acid Interactions by Thermal Melting Curves. In *Methods in Molecular Biology, Vol. 90: Drug-DNA Interaction Protocols*, Fox, K. R., Ed. Humana Press: New Jersey, **1997**; pp. 219–240.

(4) Doktycz, M. J. Nucleic Acids: Thermal Stability and Denaturation. In *eLS*; John Wiley & Sons, Ltd, **2001**.