Electronic Supplementary Information (ESI)

Mitochondria and Nucleolus targeted copper (I) complexes with Pyrazole-linked triphenylphosphine moieties for live cell imaging

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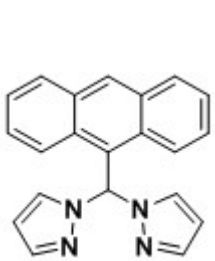
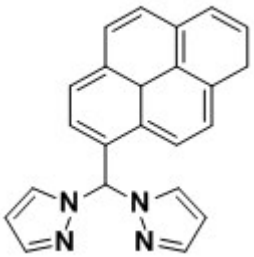
 # Equal Contribution

Table ST1: Structure and characterization data of compounds synthesized during study



(1)



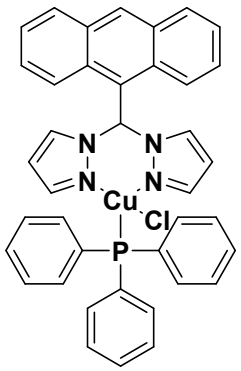
(2)

NMR Characterization Data

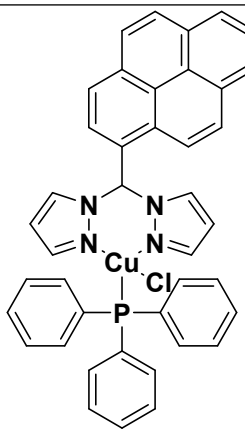
1,1'-(anthracen-9-ylmethylene) bis(1H-pyrazole) (1) MP= 170 ^{o}C,^{1}H NMR (400 MHz, $CDCl_3$) δ 9.04 (s, 1H), 8.61 (s, 1H), 8.08 – 8.01 (m, 2H), 7.81 – 7.73 (m, 2H), 7.66 (d, *J* = 1.8 Hz, 2H), 7.49 – 7.35 (m, 4H), 7.27 (d, *J* = 2.5 Hz, 2H), 6.35 – 6.29 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.27, 141.03, 131.66, 131.63, 130.71, 129.77, 129.57, 127.77, 125.17, 124.62, 122.87, 106.99, 75.01.

1,1'-(pyren-4-ylmethylene) bis(1H-pyrazole) (2) MP= 143 ^{o}C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.73 (s, 1H), 8.26 – 8.07 (m, 5H), 8.07 (s, 1H), 8.09 – 7.92 (m, 4H), 7.74 (d, *J* = 1.8 Hz, 2H), 7.35 – 7.28 (m, 3H), 6.37 – 6.31 (m, 2H).^{13}C NMR (100 MHz, $CDCl_3$ δ 141.27, 132.46, 131.22, 130.45, 129.83, 129.35, 128.71 – 128.30 (m), 127.32, 126.49, 126.15 (d, *J* = 15.4 Hz), 124.92, 124.39 (d, *J* = 10.5 Hz), 121.40, 106.82, 76.40.

Table ST2: Structure and characterization data of compounds synthesized during study



(C1)



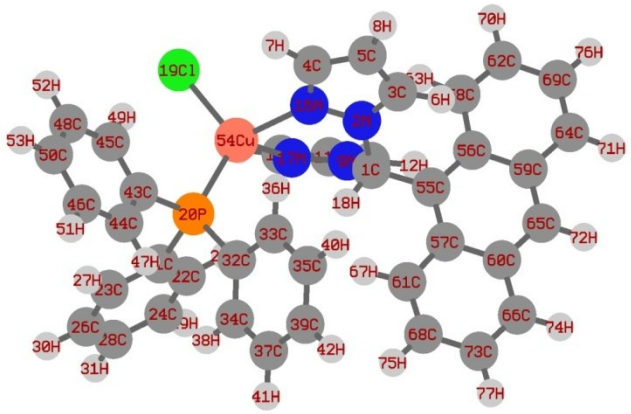
(C2)

Characterization Data

C1: ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.29 – 9.17 (m, 1H), 8.75 (s, 1H), 8.12 (s, 2H), 7.94 (d, J = 9.2 Hz, 2H), 7.63 – 7.23 (m, 23H), 6.43 – 6.31 (m, 2H).^{13}C NMR (101 MHz, DMSO-d_6) δ 140.91, 133.98, 133.83, 133.65, 133.37, 132.45, 131.56, 131.20, 130.68, 130.34, 129.68, 129.07, 128.98, 127.42, 126.12, 125.45, 124.08, 118.23, 106.96, 73.92.Anal.Calcd for $C_{39}H_{31}ClCuN_4P$: C, 68.32; H, 4.56; N, 8.17; Found: C, 69.01; H, 4.51 N, 8.14

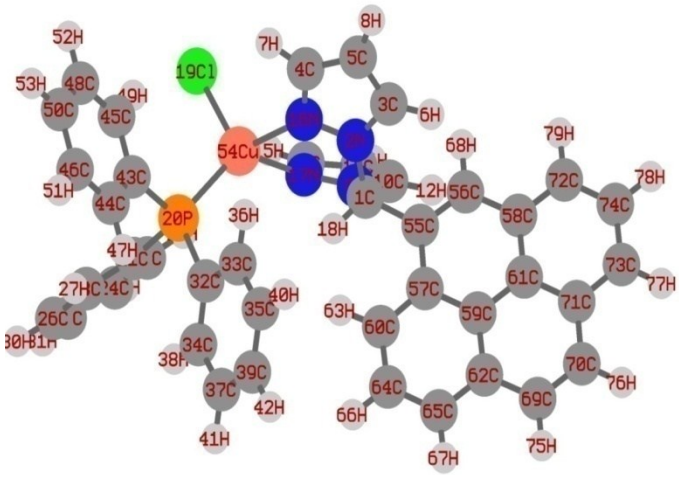
C2: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55 (s, 1H), 7.79 – 7.36 (m, 8H), 7.19 – 6.43 (m, 20H), 5.77 (s, 2H).^{13}C NMR (101 MHz, $CDCl_3$) δ 140.65, 133.41, 133.27, 132.36, 132.05, 131.80, 131.72, 131.57, 131.47, 130.61, 130.12, 129.82, 129.64, 128.70, 128.37, 128.32, 128.24, 128.09, 127.90, 126.90, 126.21, 125.82, 125.61, 124.41, 124.19, 124.08, 123.72, 121.39, 116.66, 106.41, 74.97, Anal.Calcd for $C_{41}H_{31}ClCuN_4P$: C, 69.39; H, 4.40; N, 7.89; Found: C, 69.52; H, 4.36 N, 7.79

Table ST3. Selected bond lengths and bond angles of **C1** as obtained from ground state DFT optimized geometry



Particular Bond	Bond length (A˚)	Particular Angle	Angle Measurement
54Cu – 16N	2.18	20P-54Cu –16N	116.72
54Cu – 17N	2.17	20P - 54Cu –17N	119.46
54Cu – 20P	2.32	20P - 54Cu –19 Cl	115.69
54Cu – 19Cl	2.31	43c – 20P –54Cu	114.15

Table ST4. Selected bond lengths and bond angles of **C2** as obtained from ground state DFT optimized geometry



Particular Bond	Bond length (A˚)	Particular Angle	Angle Measurement
54Cu – 16N	2.22	20P - 54Cu –16N	113.70
54Cu – 17N	2.17	20P - 54Cu –17N	127.90
54Cu – 20P	2.32	20P - 54Cu –19Cl	112.72
54Cu – 19Cl	2.33	43C – 20P –54Cu	112.53

Table ST5. The energy associated with HOMO-LUMO molecular orbitals, as observed from DFT studies

Molecular Orbitals	**Energy (eV)**	
	C1	**C2**
LUMO+3	-0.49	-0.65
LUMO+2	-0.63	-0.87
LUMO+1	-1.01	-1.23
LUMO	-2.43	-2.18
HOMO	-4.68	-4.74
HOMO-1	-4.90	-4.94
HOMO-2	-4.93	-4.96
HOMO-3	-5.60	-5.64

Table ST6. Comparisons of current work with the cell imaging tools already reported in literature.

Sr. No	Concentration used	Time	Mitochondria Tracking	Nucleolus Tracking	Reference
1	10 μM	2 h	Yes	No	[1]
2	25 μM	30 min	Yes	No	[2]
2	25 μM	4 h	No	Yes	[3]
4	20 μM	1 h	Yes	No	[4]
5	5 μM	1 h	Yes	No	[5]
6	10 μM	1h	Yes	No	[6]
8	10 μM	12h	Yes	No	[7]
9	**5 μM**	**30 min**	**Yes**	**Yes**	**Current Work**

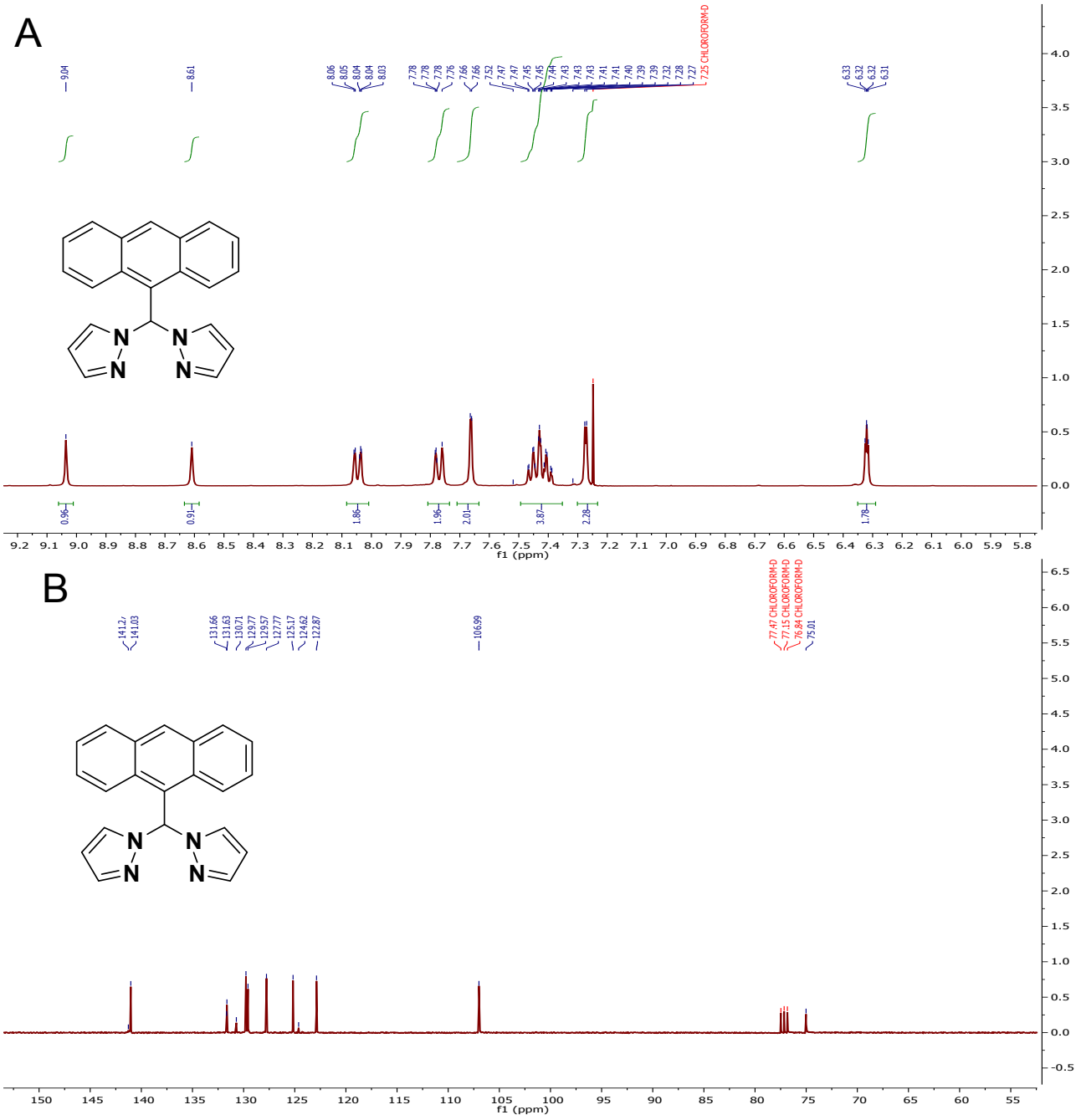


Figure SF1:(A)^{1}H NMR and **(B)**^{13}C NMR of compound (1) used for our study.

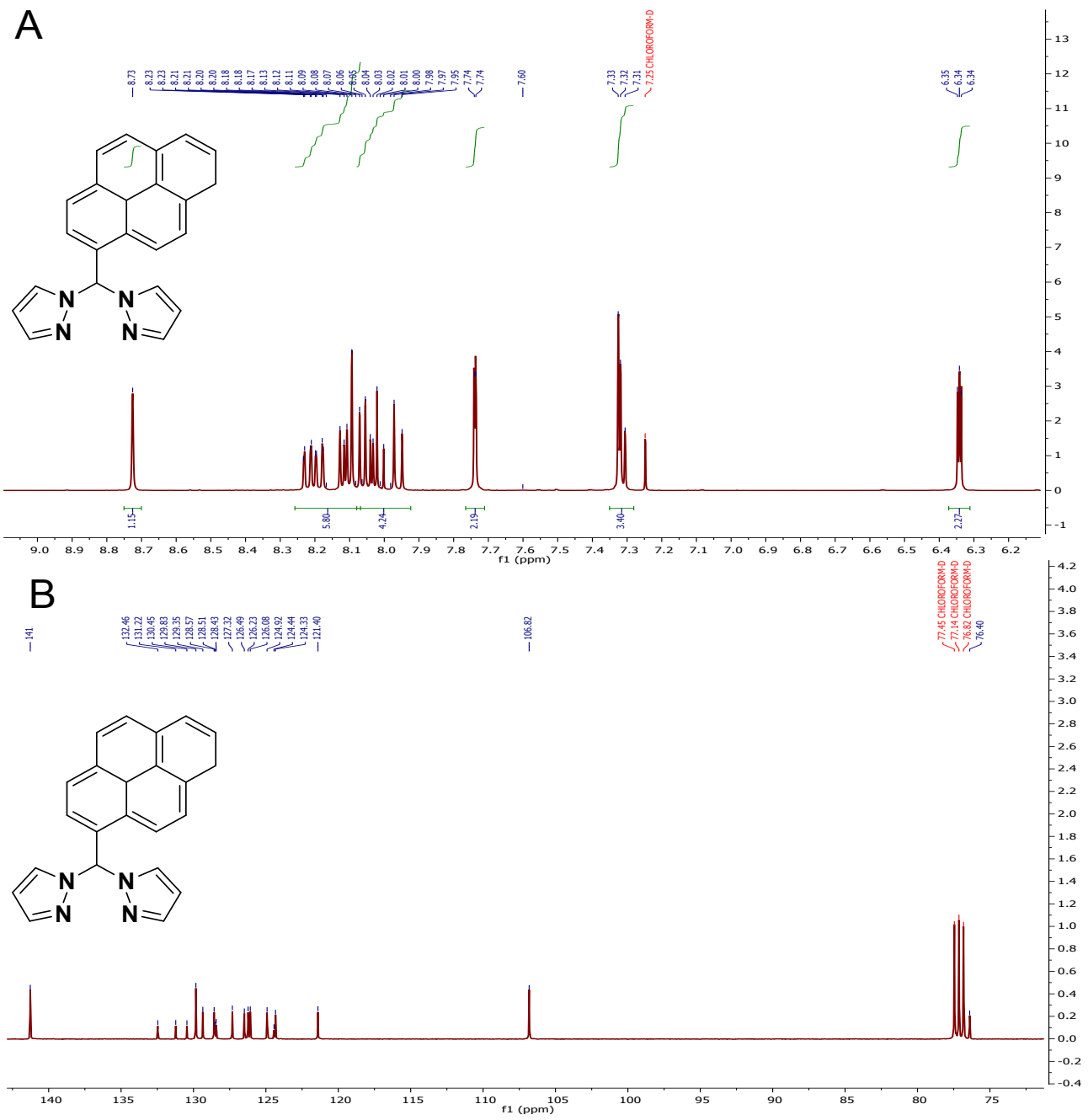


Figure SF2: (A) ^{1}H NMR and **(B)** ^{13}C NMR of compound **(2)** used for our study.

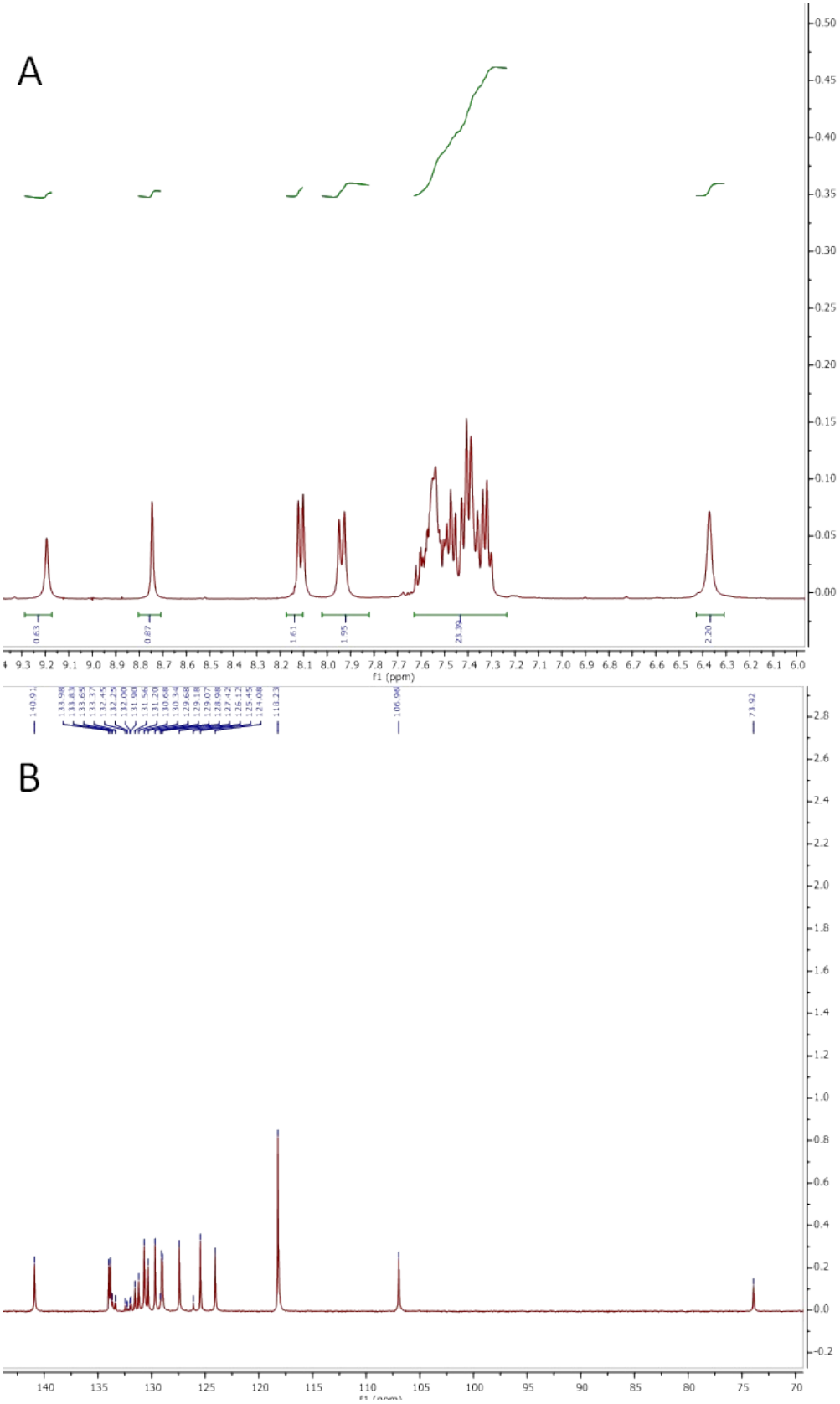


Figure SF3: (A) ^{1}H NMR; and **(B) ^{13}C** NMR of **C1** used for our study

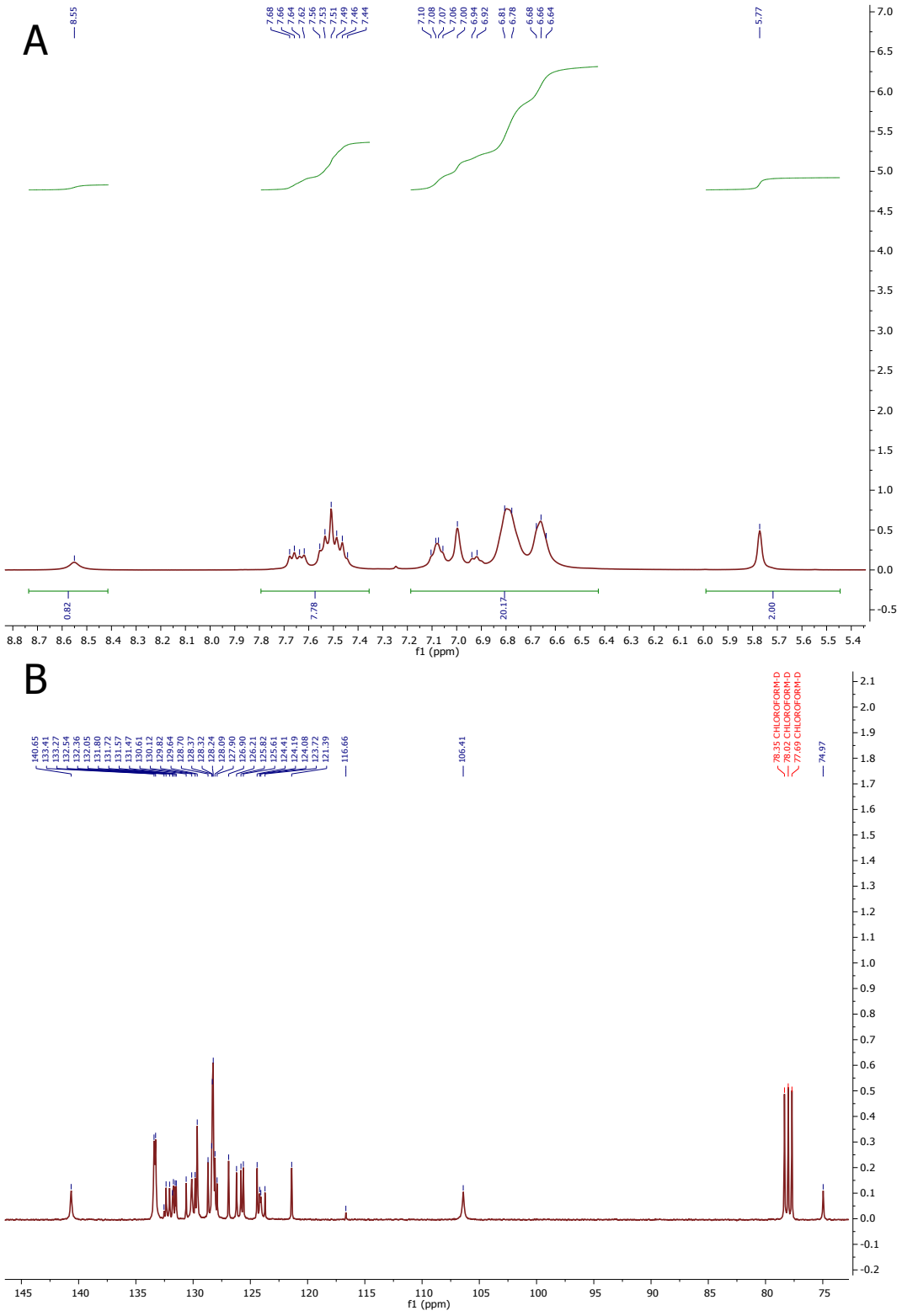


Figure SF4: (A) ^{1}H NMR; and **(B) ^{13}C** NMR of **C2** used for our study.

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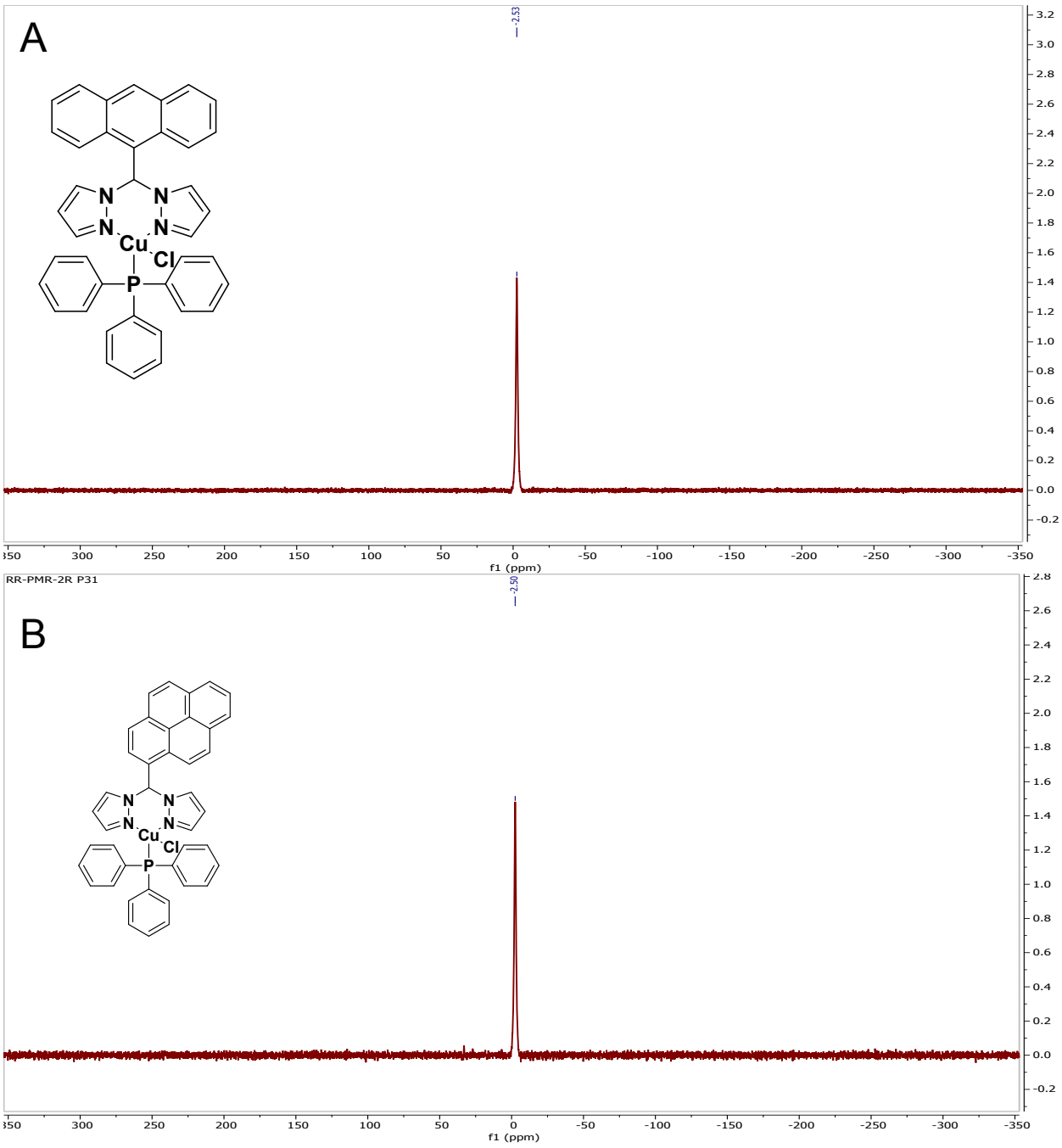

Figure SF5: ^{31}P NMR of (C1) (A) and (C2) (B) used for our study.

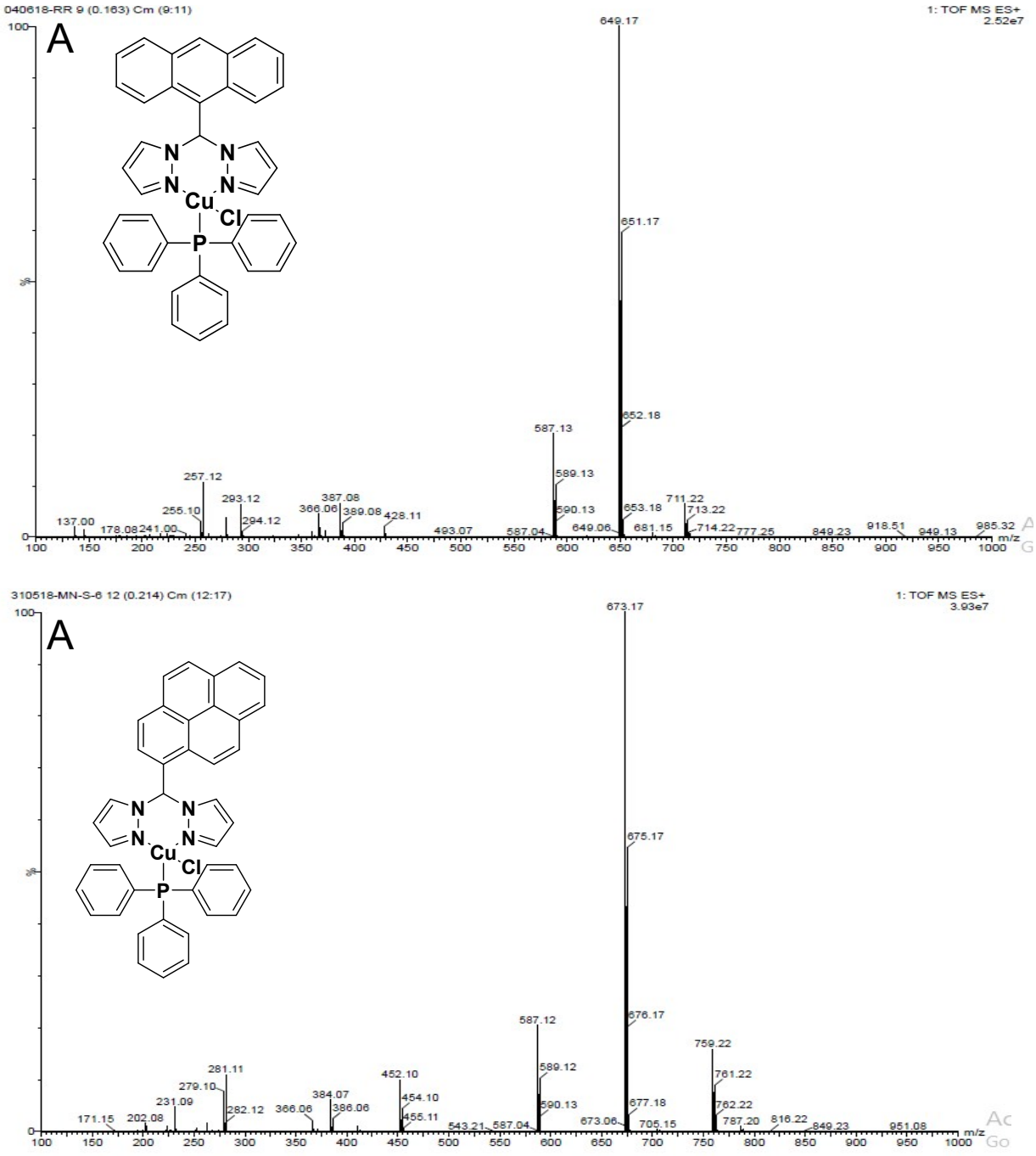

Figure SF6: Mass Spectra of **(C1)** (A) and compound **(C2)** (B) used in the study

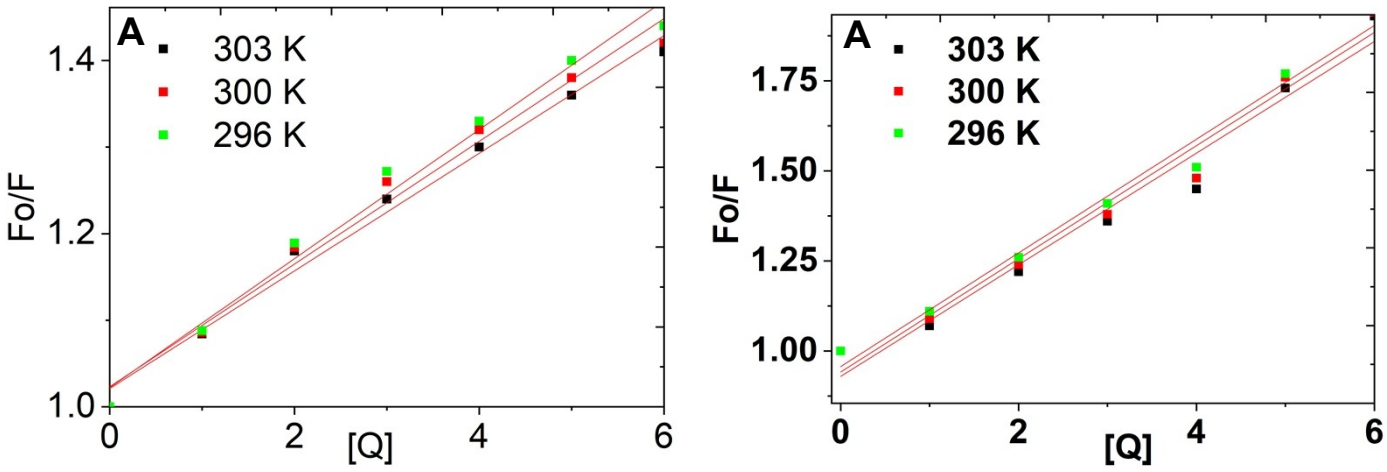

Figure SF7 (A). The Stern–Volmer plots for **DNA-C1** binding and; (B) The Stern–Volmer plots for **DNA-C2** binding; at 296, 300, 303. **[DNA** = 0–6 μM].

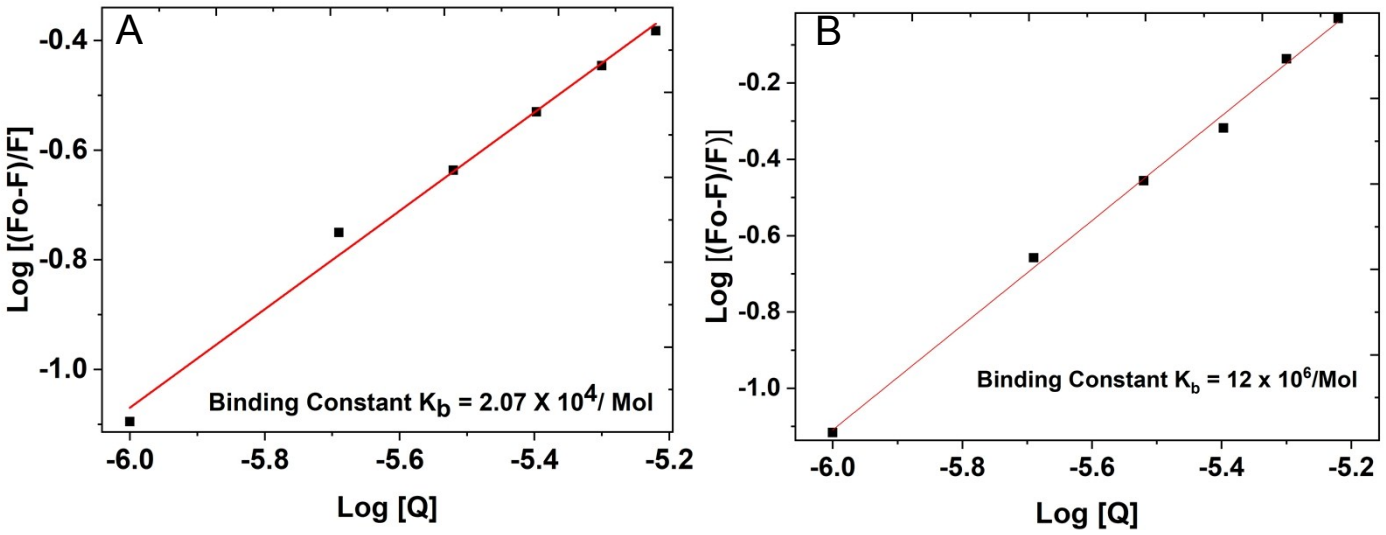

Figure SF8. **(A)**Plot between log[(F_o/F) − 1] and log[Q] for **C1** and (B) Plot between log[(F_o/F) − 1] and log[Q] for **C2;** [DNA = 0–6 μM]. Intercept of the current plot is used to calculate the binding constant in both the cases

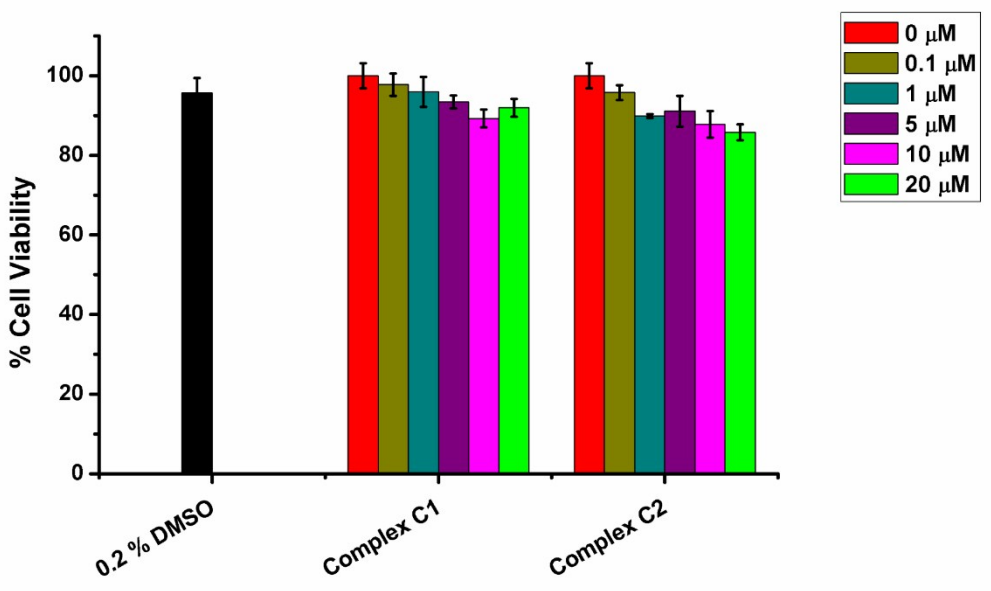

Figure SF9. Cytotoxicity **C1/C2** complexes at various concentration, against living HeLa cells for 12 h as obtained from MTT cytotoxicity assay

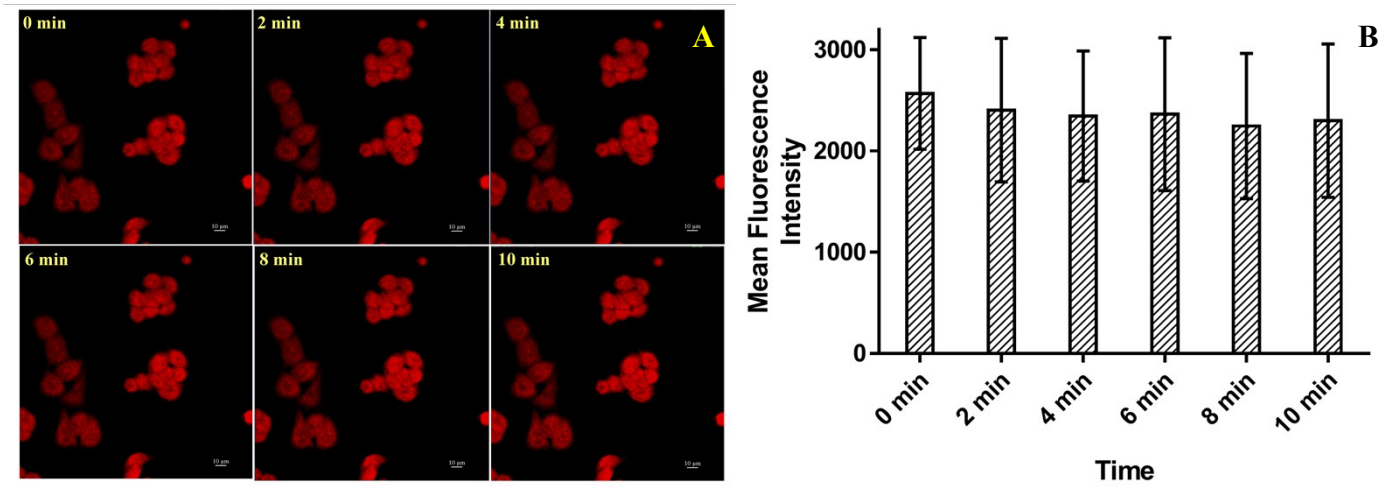

Figure SF 10. Photostability testing of MitoTracker Red, the Hela cells incubated with MitoTracker Red were continuously exposed with 25% of 40mW red laser for 10 mins and images were acquired in an interval of 2 min

References

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