Supporting Information

Cu(II)-TACN complexes selectively induced antitumor activities in HepG-2 cells by DNA damage and mitochondrial-ROS-mediated apoptosis

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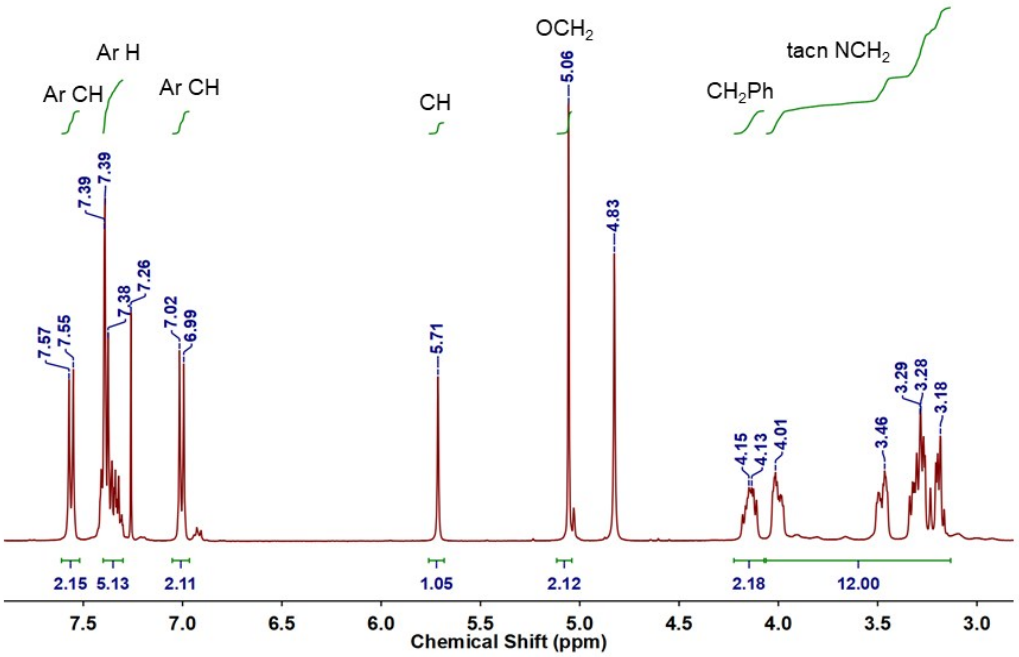
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Ar CH
CH
OCH2
tacn NCH2
CH2Ph
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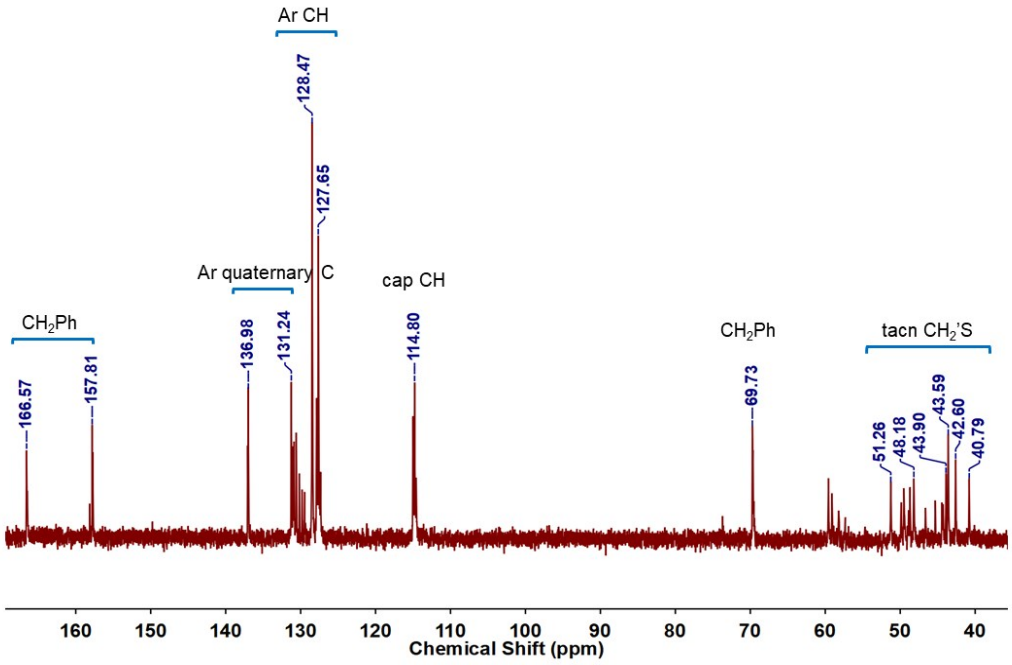
7.55
7.39
7.39
7.38
7.26
7.02
6.99
5.71
5.06
4.83
4.15
4.13
4.01
3.46
3.29
3.28
3.18
2.15
5.13
2.11
1.05
2.12
2.18
12.00
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
Chemical Shift (ppm)

A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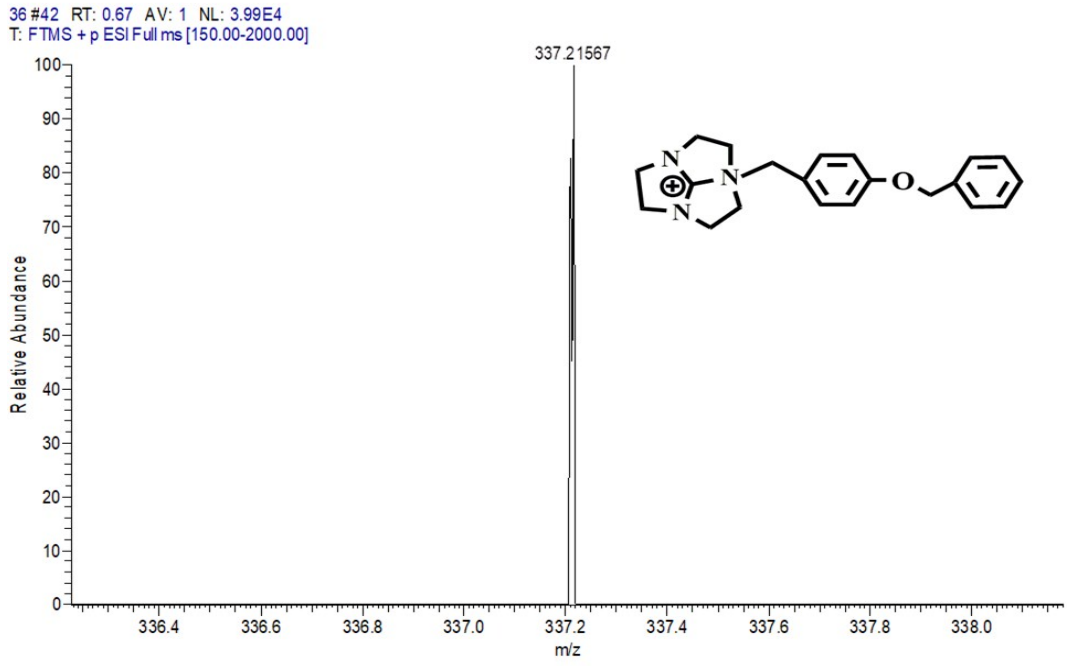
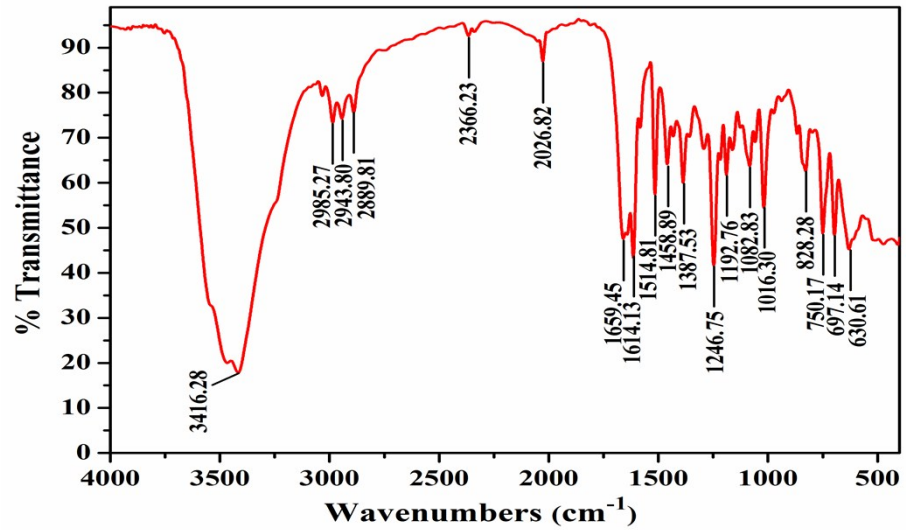
127.65
Ar quaternary C
cap CH
CH2Ph
136.98
131.24
114.80
166.57
157.81
CH2Ph
69.73
tacn CH2'S
51.26
48.18
43.90
43.59
42.60
40.79
160
150
140
130
120
110
100
90
80
70
60
50
40
Chemical Shift (ppm)

B

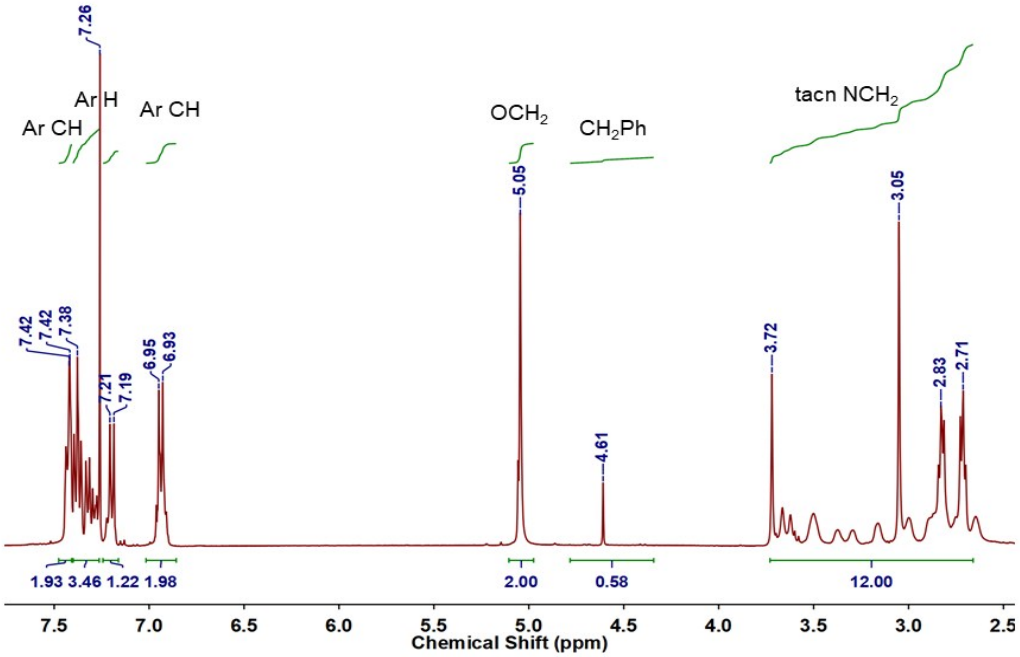


C



D

Fig. S1. Synthesis of 4-benzyloxy-benzyl-tricyclo[5.2.1.0$^{4.10}$]decane chloride: (A) 400 MHz ^{1}HNMR ($CDCl_3$, 298 K); (B) 100 MHz ^{13}CNMR (D_2O, 305 K); (C) ESI-mass spectrum.Attributions:337.22; (D)FTIR patterns.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Ar CH
OCH2
CH2Ph
tacn NCH2
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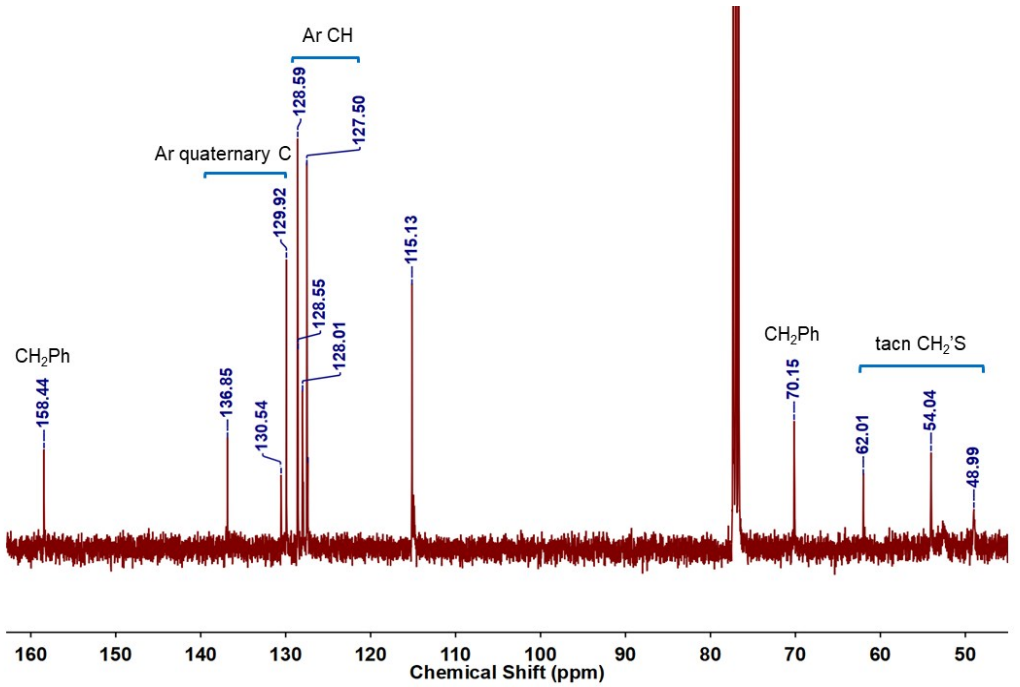
3.05
7.42
7.42
7.38
6.95
6.93
7.21
7.19
4.61
3.72
2.83
2.71
1.93 3.46 1.22 1.98
2.00
0.58
12.00
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5
Chemical Shift (ppm)

A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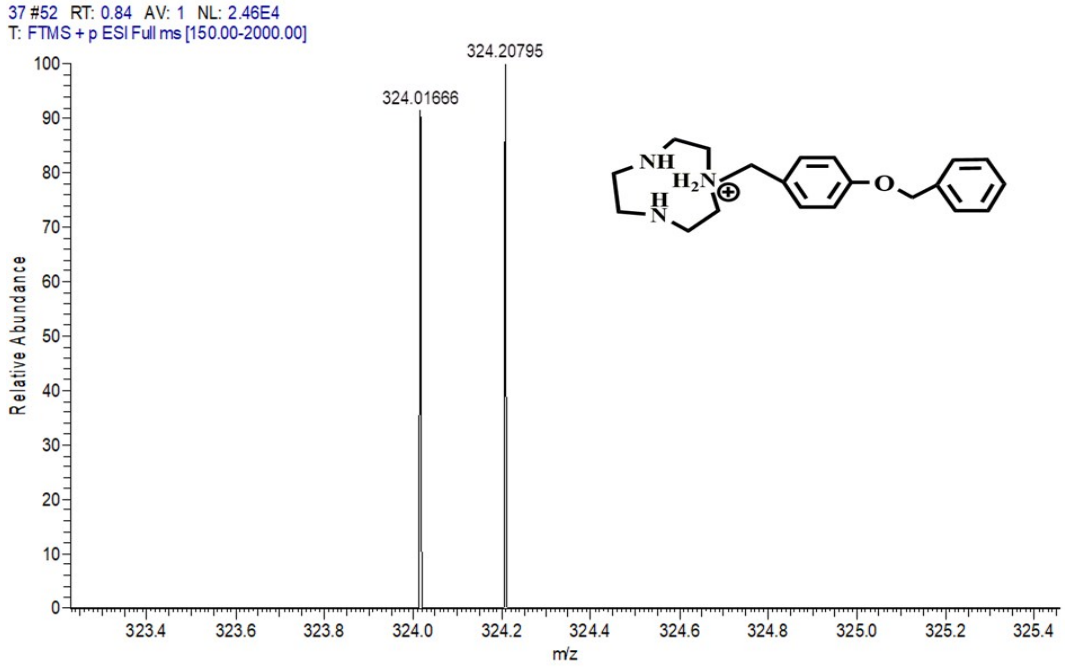
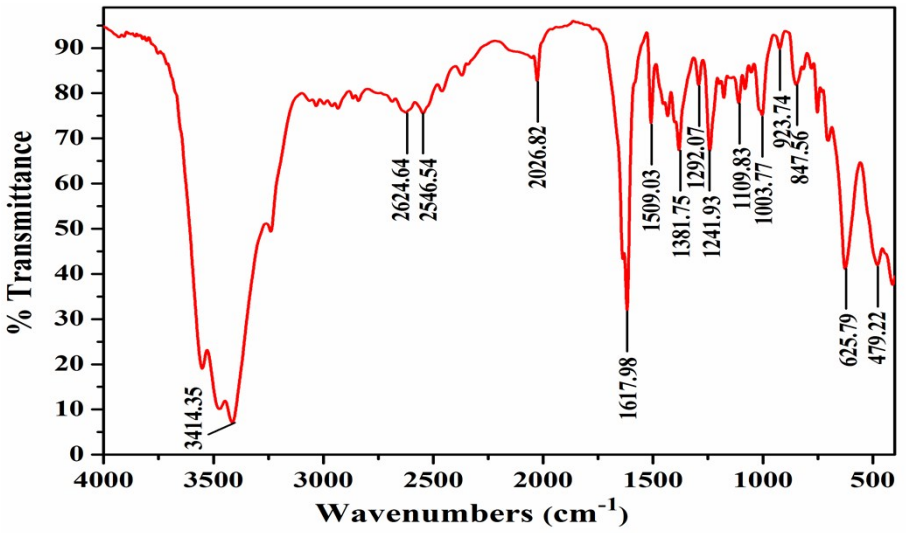
127.50
Ar quaternary C
129.92
115.13
128.55
128.01
CH2Ph
158.44
136.85
130.54
CH2Ph
tacn CH2'S
70.15
62.01
54.04
48.99
160 150 140 130 120 110 100 90 80 70 60 50
Chemical Shift (ppm)

B



C



D

Fig. S2. Synthesis of btacn: (A) 400 MHz ^{1}HNMR ($CDCl_3$, 298 K); (B) 100 MHz ^{13}CNMR ($CDCl_3$, 305 K); (C) ESI-mass spectrum.Attributions:324.21, $[M+H^+]^+$; (D)FTIR patterns.

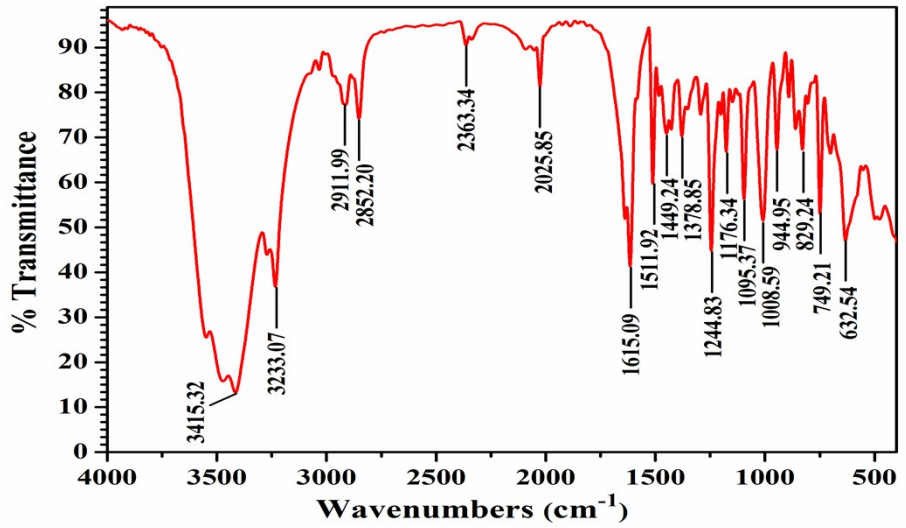
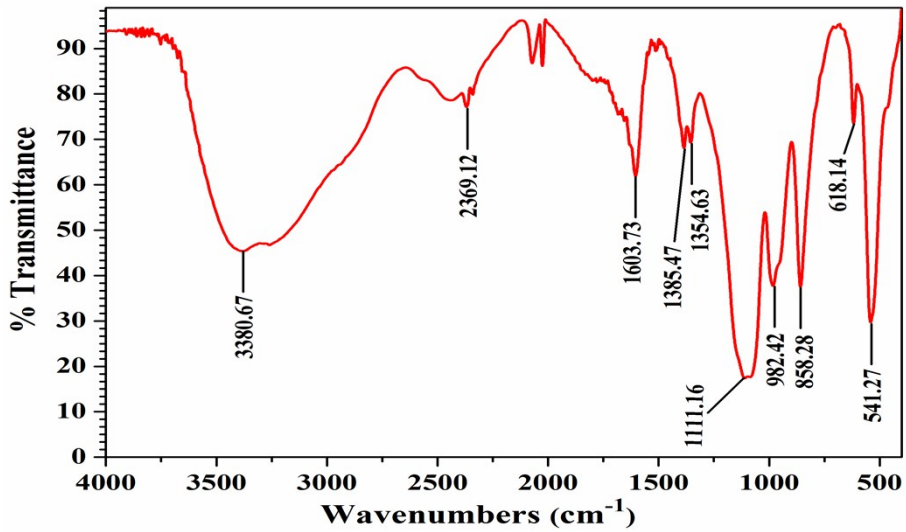
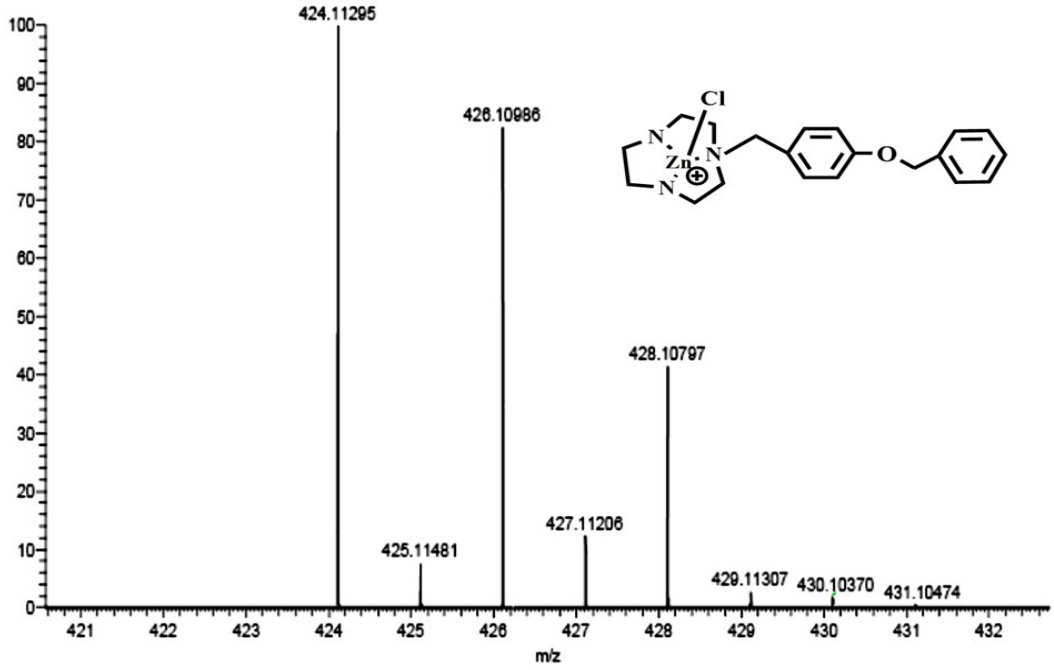


Fig. S3.FTIR patterns for Cu(btacn)Cl_2.

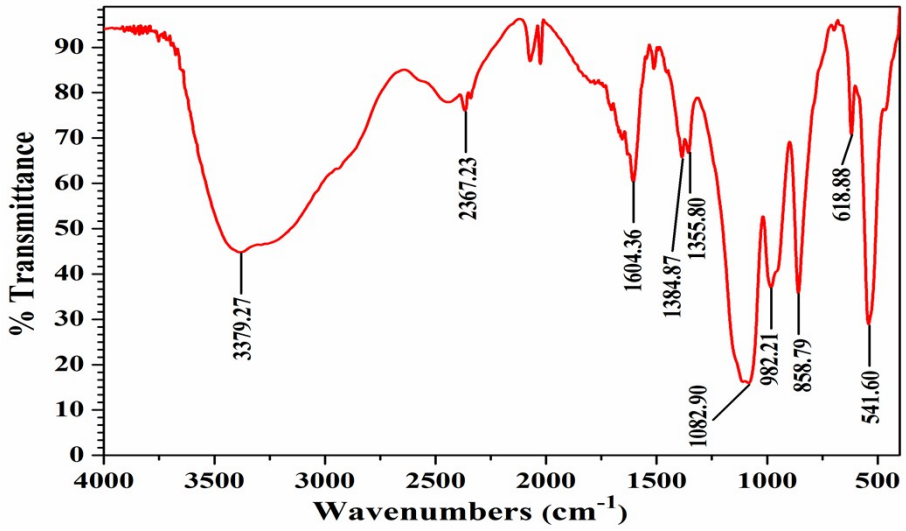


A

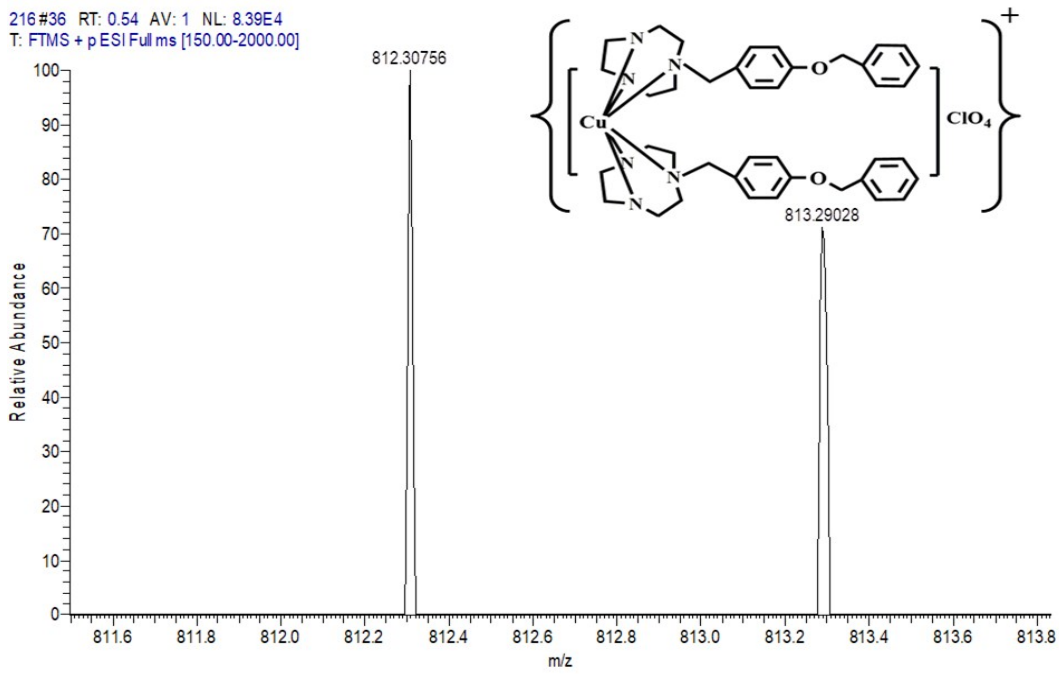


B

Fig. S4.(A) FTIR patterns for Zn(btacn)Cl_2. (B) Electrospray mass spectra and the isotope distribution patterns for Zn(btacn)Cl_2. Attributions: 426.113, $[M-Cl^-]^+$.



A



B

Fig. S5.(A)FTIR patterns for $[Cu(btacn)_2]\cdot(ClO_4)_2$. (B) Electrospray mass spectra and the isotope distribution patterns for $[Cu(btacn)_2]\cdot(ClO_4)_2$. Attributions:813.3, $[M-ClO_4^-]^+$.

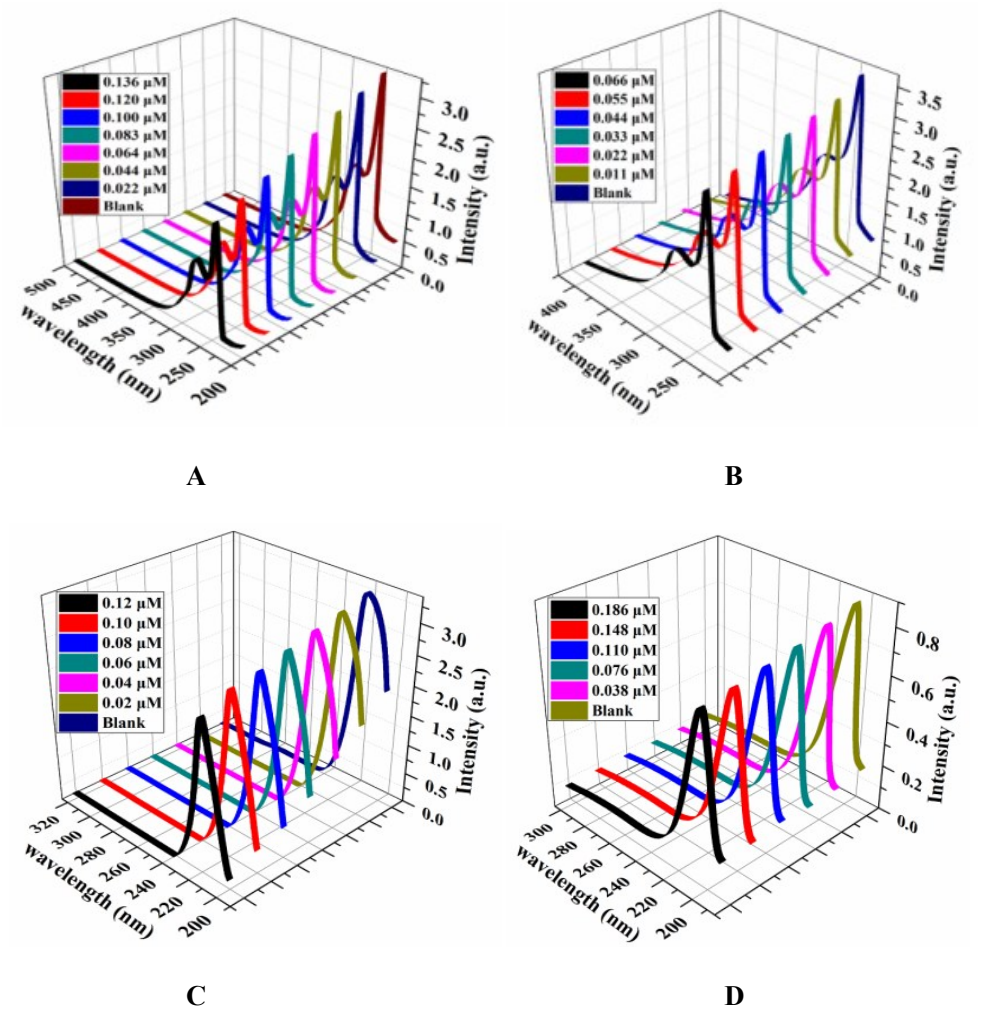


Fig. S6. Absorption spectra of the compounds in the absence and presence of increasing amounts of CT-DNA at room temperature in 5 mMTris-HCl/NaCl buffer (pH 7.4), the dashed lines indicate the free compound. (A) $[Cu(btacn)_2]\cdot(ClO_4)_2$($4.63 \times 10^{-4}$M), CT-DNA (0.0, 2.2×10^{-5} M, 4.4×10^{-5} M, 6.4×10^{-5} M, 8.3×10^{-5} M, 1.0×10^{-4} M, 1.2×10^{-4} M, 1.36×10^{-4} M). (B) $Cu(btacn)Cl_2$ (2.0×10^{-4}M), CT-DNA (0.0, 1.1×10^{-5}M, 2.2×10^{-5} M, 3.3×10^{-5}M, 4.4×10^{-5}M, 5.5×10^{-5}M, 6.6×10^{-5}M). (C) $Zn(btacn)Cl_2$ (1.6×10^{-4}M), CT-DNA (0.0, 2.0×10^{-5}M, 4.0×10^{-5}M, 6.0×10^{-5}M, 8.0×10^{-5}M, 1.0×10^{-4}M, 1.2×10^{-4}M). (D) btacn (1.0×10^{-5}M), CT-DNA (0.0, 3.8×10^{-5}M, 7.6×10^{-5}M, 1.1×10^{-4}M, 1.48×10^{-4}M, 1.86×10^{-4}M).

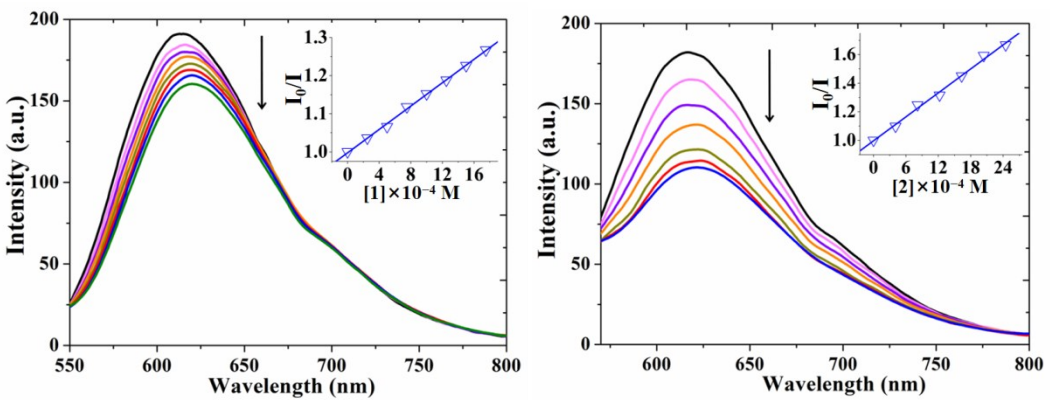


Fig. S7. Fluorescence quenching curves of the complexes to EB-DNA, [DNA] = 6.0 μM, [EB] = 4.0 μM and Stern–Volmer plots of the fluorescence titrations (Insert figure): (1) [Cu(btacn)Cl_2] = 0–175 μM; (2) [[Cu(btacn)$_2$]·(ClO_4)$_2$] = 0–245μM.

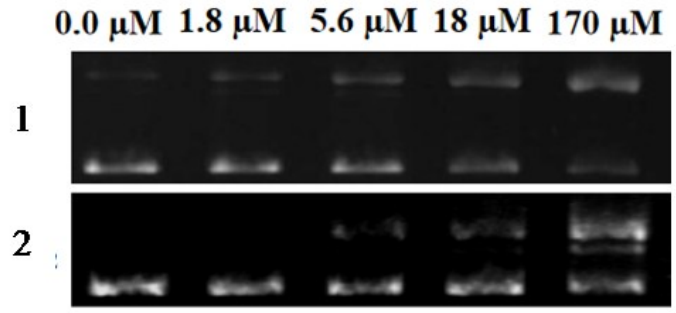


Fig. S8. Various amounts of (1) Cu(btacn)Cl_2 and (2) [Cu(btacn)$_2$]·(ClO_4)$_2$ were reacted with a constant concentration of DNA for 3 h at 37 ◦C in pH 7.4 Tris−HCl/NaCl buffer analyzed by agarosegel electrophoresis.

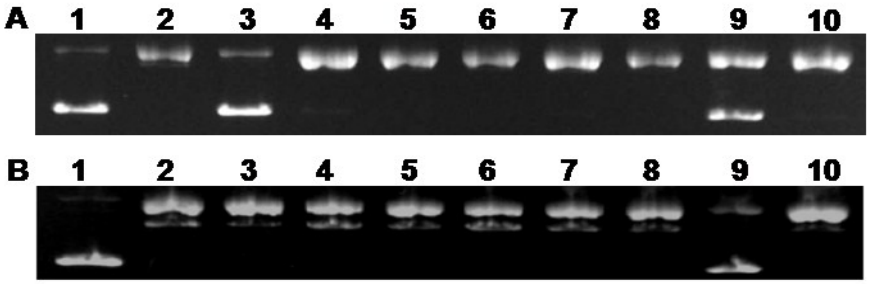


Fig.S9. Gel electrophoresis diagram showing the cleavage of pBR322 DNA in the presence of different additives at pH 7.4 and 37 ◦C for 24 h under aerobic condition: Lane 1: DNA control; Lane 2: DNA +2.0 mMCu(btacn)Cl_2 (A){0.5 mM$[Cu(btacn)_2]\cdot(ClO_4)_2$(B)}; Lane 3−10: DNA + complex+ 1 mM DMSO; 200 Unit/ml SOD; 25 mM L-histidine; 200 Unit/ml catalase; 0.05 mM methyl green; 10 Unit/mL SYBR Green; 50 mM KI; 25 M NaN_3.

Table S1

Selected bond lengths (Å) and angles (°) for Cu(btacn)Cl_2.

Cu(1)-N(1)	2.264(18)	Cu(1)-Cl(1)	2.267(6)
Cu(1)-N(2)	2.039(19)	Cu(1)-Cl(2)	2.277(7)
Cu(1)-N(3)	2.038(18)		
N(1)-Cu(1)-Cl(1)	100.71(5)	Cl(1)-Cu(1)-Cl(2)	95.59(3)
N(1)-Cu(1)-Cl(2)	107.57(5)	N(3)-Cu(1)-Cl(1)	172.16(6)
N(2)-Cu(1)-Cl(1)	90.86(6)	N(3)-Cu(1)-Cl(2)	89.96(6)
N(2)-Cu(1)-N(1)	83.33(7)	N(3)-Cu(1)-N(2)	82.55(8)
N(2)-Cu(1)-Cl(2)	165.97(6)	N(3)-Cu(1)-N(1)	82.81(7)

Table S2

Crystal data and structure refinement for $Cu(btacn)Cl_2$.

complex	$Cu(btacn)Cl_2$
CCDC number	1557714
Empirical formula	$C_{20}H_{27}Cl_2CuN_3O$
Formula weight	459.88
Crystal system	orthorhombic
Space group	P_{bca}
Temperature(K)	154.4(2)
a (Å)	8.1762(3)
b (Å)	12.4060(4)
c (Å)	40.2745(12)
α(°)	90
β(°)	90
γ(°)	90
Z	8
Calculated density (mg/m^3)	1.495
Absorption coefficient (mm^{-1})	1.346
F(000)	1912.0
Crystal size (mm^3)	0.25 × 0.18 × 0.17
Limiting indices	$-9 \le h \le 9$, $-14 \le k \le 12$, $-46 \le l \le 47$
Reflections collected	36032
Independent reflections	3601 [R_{int} = 0.0475, R_{sigma} = 0.0236]
Data / restraints / parameters	3601/0/244
Goodness-of-fit on F^2	1.051
Final R indices [I>2σ(I)]	R_1 = 0.0301, wR_2 = 0.0686
R indices (all data)	R_1 = 0.0349, wR_2 = 0.0718

Table S3

Electronic absorption spectral data between CT-DNA with synthesized compounds in Tris-HCl buffer solution.

Compounds		$[Cu(btacn)_2]\cdot(ClO_4)_2$	$Cu(btacn)Cl_2$	$Zn(btacn)Cl_2$	btacn
Band position (π—π*)λmax (nm)	Free	240	237	217.2	201
	Bound	242	237.2	219.4	203
Red shift Δλ		2	0.2	2.2	2
Chromism effect (%)		34.8	19.4	24.2	16.0
Band position (n—π)λmax (nm)	Free	270	269	–	–
	Bound	272	269.8	–	–
Red shift Δλ		2	0.8	–	–
Chromism effect (%)		18.8	23.8	–	–