Electronic Supplementary Information

Syntheses and structural investigation of some alkali metal ion-mediated $LV^{V}O_2^-$ (L^{2-} = Tridentate ONO ligands) species: DNA binding, photo-induced DNA cleavage and cytotoxic activities

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phosphate buffer (pH 7.8) containing 1% DMF] was photo-irradiated with UVA at 350 nm for 3 h. The net DNA cleavage percent was calculated using Eq.2. Inset shows a bar diagram representation of the net DNA cleavage of different complexes at 10 and 100 μM

Fig. S14 Effect of DMF (10%) and ligands on the photo-induced cleavage of SC pUC19 DNA. 300 ng SC pUC19 DNA was photo-irradiated in presence of 10% DMF and various ligands (100 μM) with UVA at 350 nm for 3 h. Lane 1, DNA in presence of 10% DMF; Lane 2, DNA + H_2L^1; Lane 3, DNA + H_2L^2; Lane 4, DNA + H_2L^3;Lane 5, DNA + H_2L^4; Lane 6, DNA + H_2L^5; Lane 7, DNA + H_2L^6.

Fig. S15 Gel diagram depicting cleavage of SC pUC19 DNA by **1**–**8** in presence of various additives in 50 mM Tris-HCl buffer (pH 8.0) containing 10% DMF. SC pUC19 DNA (300 ng) in the presence of various additives was photo-irradiated at 350 nm for 3 h with **1-8** (100 μM). The additive concentrations were: sodium azide (0.5 mM), L-histidine (0.5 mM), KI (0.5 mM) and D-mannitol (0.5 mM). Lane 1, DNA + complex; Lane 2, DNA + complex + sodium azide; Lane 3, DNA + complex + L-histidine; Lane 4, DNA + complex + KI; Lane 5, DNA + complex + D-mannitol

Fig. S16 Cleavage of SC pUC19 DNA by **1**–**4** (a) and **5**–**8** (b) in presence of various additives in 50mM Tris-HCl buffer (pH 8.0) containing 10% DMF. SC pUC19 DNA (300 ng) in the presence of various additives was photo-irradiated at 350 nm for 3 h with **1-8** (100 μM). The additive concentrations were: sodium azide (0.5 mM), L-histidine (0.5 mM), KI (0.5 mM) and D-mannitol (0.5 mM).

Fig. S17 The plot represents the linear fit of log $[(F_0\text{-}F)/F]$ *vs* log [Q] for **6** (a) and **7** (b) and the binding constant (K_{BSA}) was estimated using Eq.4. Here, [Q] stands for [quencher (complexes)].

Fig. S18 SDS-PAGE profile of cleavage of BSA in presence of complexes **1-8** (100 μM) in (a) UVA light of 350 nm (84 W) and (b) dark. Lane 1, Molecular marker; Lane 2, BSA only; Lane 3, BSA + **1** (100 μM); Lane 4, BSA + **2** (100 μM); Lane 5, BSA + **3** (100 μM); Lane 6, BSA + **4** (100 μM); Lane 7, BSA + **5** (100 μM); Lane 8, BSA + **6** (100 μM); Lane 9, BSA + **7** (100 μM); Lane 10, BSA + **8** (100 μM).

Fig. S19 Effect of ligand (H_2L^5) on cell viability and growth: HeLa cells were treated with different concentrations of the test compound for 72 h and then cell viability was measured by MTT assay. Data reported as the mean ± S.D. for $n = 6$ and compared against 10% (v/v) DMF treated control by using a Student's *t*-test. (*significant compared control).

Fig. S20 Study of apoptosis by morphological changes in nuclei of HeLa cells: HeLa cells, from control and treated groups, were fixed with 3.7% formaldehyde for 15 min, permeabilized with 0.1% Triton X-100 and stained with 1 μg/ml DAPI for 5 min at 37 °C. The cells were then washed with PBS and examined by fluorescence microscopy (Olympus IX 71) (200×). HeLa cells were treated with 225 μM of ligand (H_2L^5). Arrows showing the morphological changes in nuclei of HeLa cells were observed on applying ligand (H_2L^5) in comparison to the control group treated with 10% (v/v) DMF.

Fig. S21 ^{1}H NMR spectra of **1** (a), **5** (b), **6** (c) and **7** (d) in DMSO-d_6.

Fig. S22 Electronic absorption spectra of **7** (2.5×10^{-5} M) in DMF.

Fig. S23 FTIR spectra of complex **6**.

Table S1: Summary of intermolecular interactions (A–H…B; Å, º) operating in the crystal structures of **3**, **5**-**7**.[a]

A	H	B	A–H	H…B	A…B	A–H…B	Symmetry operation
3							
O1	H1O	N1	0.84	1.83	2.567(2)	146	*x*, *y*, *z*
O6	H6O	N3	0.84	1.83	2.571(2)	146	*x*, *y*, *z*
O1W	H1W1	O9	0.80	1.93	2.7126(19)	167	*x*, *y*, *z*
O1W	H1W2	O5	0.80	2.01	2.7486(19)	153	*x*, *y*, -1+*z*
O2W	H2W1	O3	0.80	2.09	2.886(2)	173	-1+*x*, *y*, -1+*z*
O2W	H2W2	O8W	0.80	2.04	2.817(2)	165	-1+*x*, *y*, *z*
O3W	H3W1	O7	0.80	2.24	2.972(2)	152	1-*x*, 1-*y*, -*z*
O3W	H3W1	O10	0.80	2.46	3.108(2)	139	1-*x*, 1-*y*, -*z*
O3W	H3W2	O9W	0.80	1.99	2.774(2)	165	*x*, *y*, *z*
O4W	H4W1	O8	0.80	2.06	2.831(2)	163	-1+*x*, *y*, *z*
O4W	H4W2	O7	0.80	2.31	3.088(2)	165	*x*, *y*, *z*
O5W	H5W1	O8W	0.80	1.97	2.736(2)	159	-1+*x*, *y*, *z*
O5W	H5W2	O2	0.80	2.14	2.937(2)	171	1-*x*, -*y*, 1-*z*
O6W	H6W1	O2	0.80	2.06	2.8552(19)	169	*x*, *y*, -1+*z*
O6W	H6W2	O3	0.80	2.39	3.079(2)	145	-1+*x*, *y*, -1+*z*
O6W	H6W2	O4	0.80	2.36	3.0187(19)	140	-1+*x*, *y*, -1+*z*
O7W	H7W1	O4	0.80	1.95	2.744(2)	173	*x*, *y*, -1+*z*
O7W	H7W2	O6W	0.80	2.04	2.825(2)	166	1-*x*, -*y*, -*z*
O8W	H8W1	O8	0.80	2.41	3.073(2)	141	*x*, *y*, *z*
O8W	H8W1	O9	0.80	2.27	2.959(2)	145	*x*, *y*, *z*
O8W	H8W2	O7W	0.80	1.97	2.760(2)	169	*x*, *y*, *z*
O9W	H9W1	O10	0.80	1.97	2.767(2)	178	*x*, *y*, *z*
O9W	H9W2	O2W	0.80	1.99	2.785(2)	171	1+*x*, *y*, *z*

C8	H8	O6	0.95	2.35	3.274(2)	165	1+*x*, *y*, *z*
C22	H22	O1	0.95	2.30	3.240(2)	168	*x*, *y*, *z*
5							
O1W	H1W1	O2	0.84(2)	2.43(3)	3.038(3)	130(2)	*x*, *y*, *z*
O1W	H1W1	O4	0.84(2)	2.48(2)	3.274(3)	159(2)	*x*, *y*, *z*
O1W	H1W2	O4	0.84(3)	1.89(2)	2.723(3)	170(3)	1-*x*, 1-*y*, 1-*z*
O2W	H2W1	O6	0.85(3)	1.96(3)	2.776(3)	160(3)	-*x*, -1-*y*, 1-*z*
O2W	H2W2	O7	0.85(3)	2.15(3)	2.986(3)	171(2)	*x*, -1+*y*, *z*
6							
O1W	H1W1	O1	0.85(3)	2.11(4)	2.931(3)	162(3)	½-*x*, ½+*y*, *z*
O1W	H1W2	N1	0.837(18)	2.01(2)	2.815(3)	162(4)	1-*x*, -*y*, -*z*
C5	H5	O4	0.93	2.54	3.439(3)	164	1-*x*, -*y*, -*z*
C7'	H72	Cg1	0.96	2.56	3.477(3)	159	1½-*x*, - ½+*y*, *z*
O2W	H2W2	O3	0.863(14)	2.44(5)	2.852(4)	110(4)	½-*x*, ½+*y*, *z*

The O2W-water molecule atom lies in a pocket comprising the O3 atom, see above, and the O1W (separation 3.313(2) Å), O3 (3.261(2) Å) and O4 (3.364(2) Å) atoms.

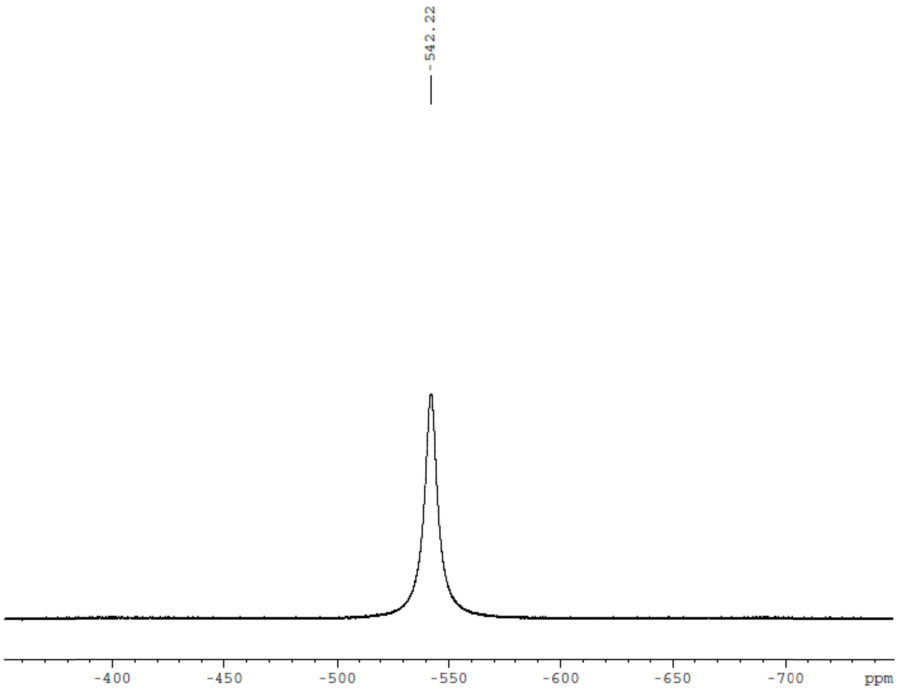
Cg1 is the centroid of the (C8-C13) ring

7							
O1W	H1W1	O1	0.82(3)	2.17(3)	2.975(2)	165(2)	*x*, *y*, *z*
O1W	H1W2	O4W	0.83(3)	1.97(3)	2.787(2)	166(3)	1-*x*, -*y*, 2-*z*
O2W	H2W1	O3	0.84(3)	2.08(3)	2.885(2)	162(3)	-1+*x*, *y*, *z*
O2W	H2W2	O4W	0.83(3)	1.98(3)	2.809(2)	173(3)	*x*, *y*, *z*
O3W	H3W1	O2W	0.83(3)	2.24(3)	3.015(3)	156(3)	-*x*, -*y*, 2-*z*
O3W	H3W2	N2	0.83(3)	2.26(3)	2.991(3)	147(3)	1-*x*, 1-*y*, 2-*z*
O4W	H4W1	N1	0.834(13)	1.982(13)	2.808(2)	171(2)	-1+*x*, -1+*y*, -1+*z*
O4W	H4W2	O2	0.84(2)	2.06(2)	2.876(2)	166(2)	*x*, *y*, *z*

Table S2 Binding Constant (K_b) values for the interaction of CT-DNA with ligands

Complex	Binding Constant (K_b) [a] (M^{-1})
$\mathbf{H_2L^1}$	1.29×10^3
$\mathbf{H_2L^2}$	7.74×10^3
$\mathbf{H_2L^3}$	8.79×10^3
$\mathbf{H_2L^4}$	3.82×10^3
$\mathbf{H_2L^5}$	1.09×10^3
$\mathbf{H_2L^6}$	4.57×10^3

[a]DNA binding constant by UV-vis spectral method.



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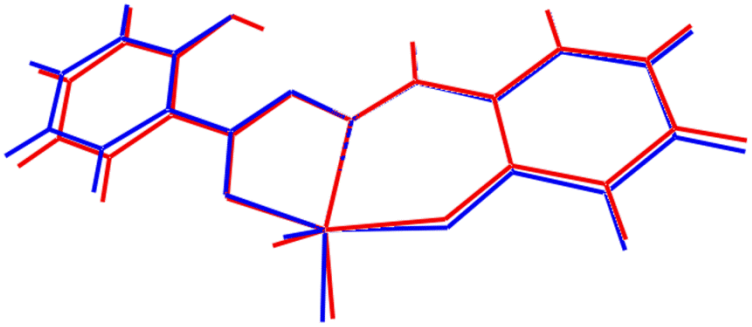

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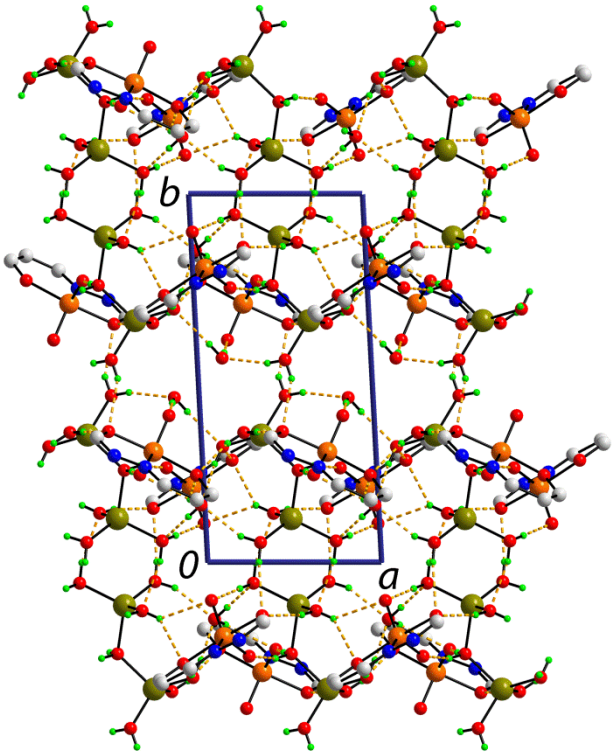

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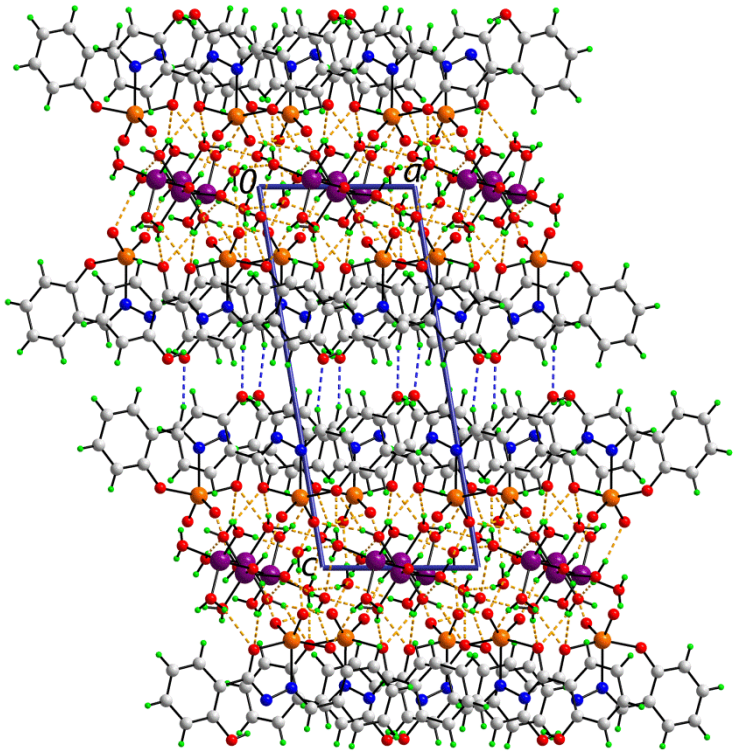

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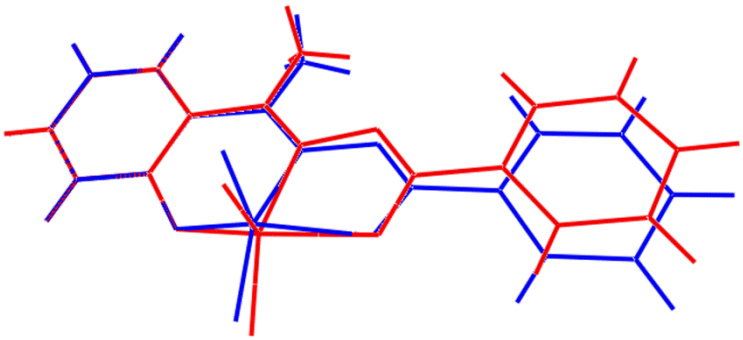
Fig. S3



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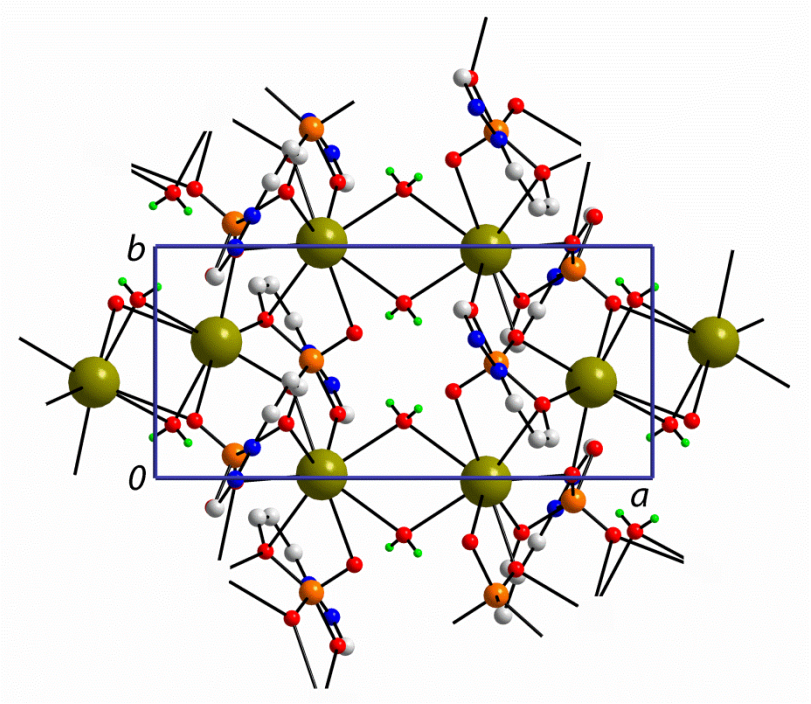

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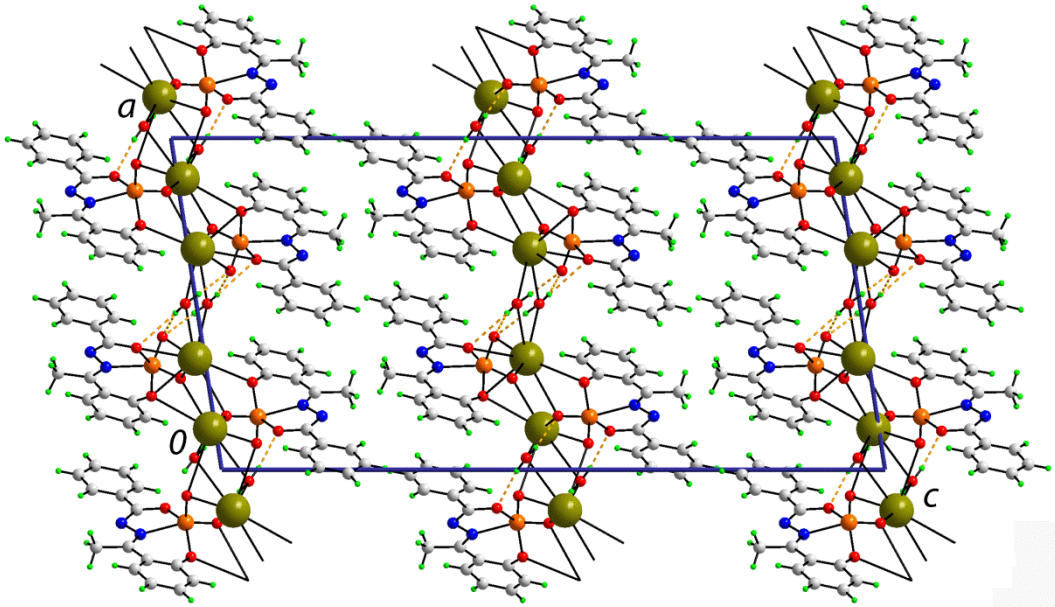

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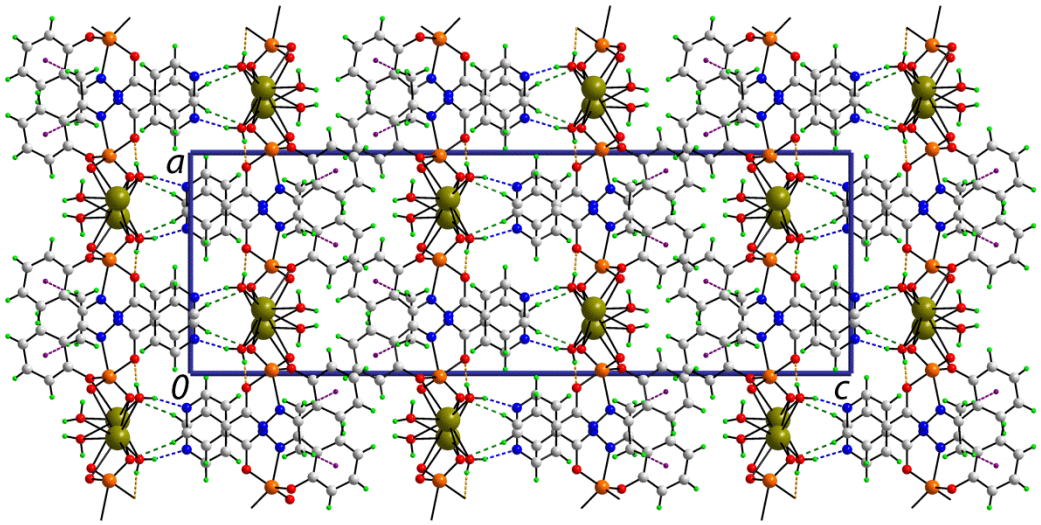

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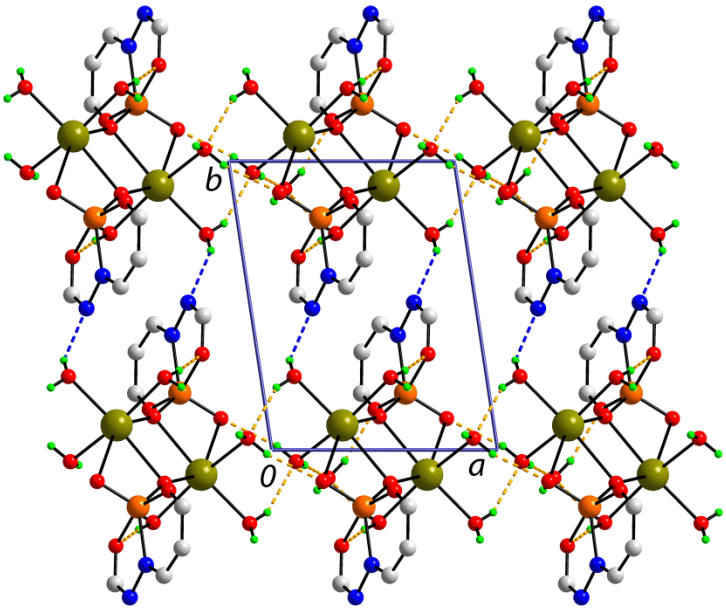

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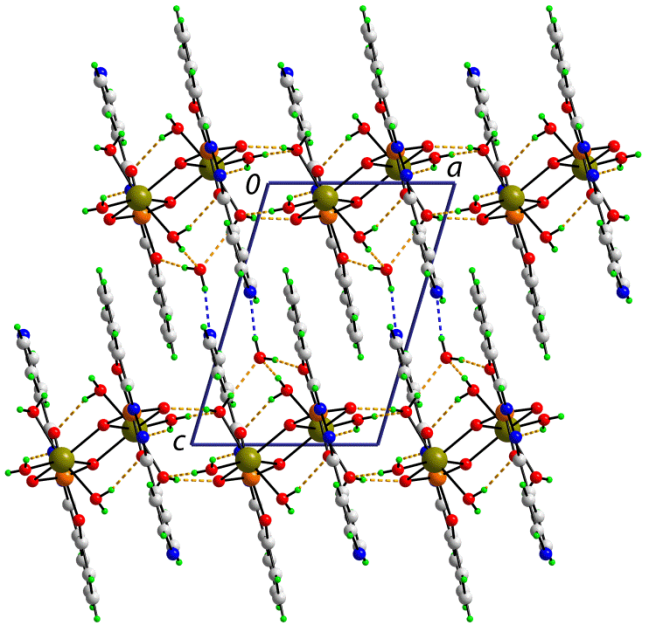

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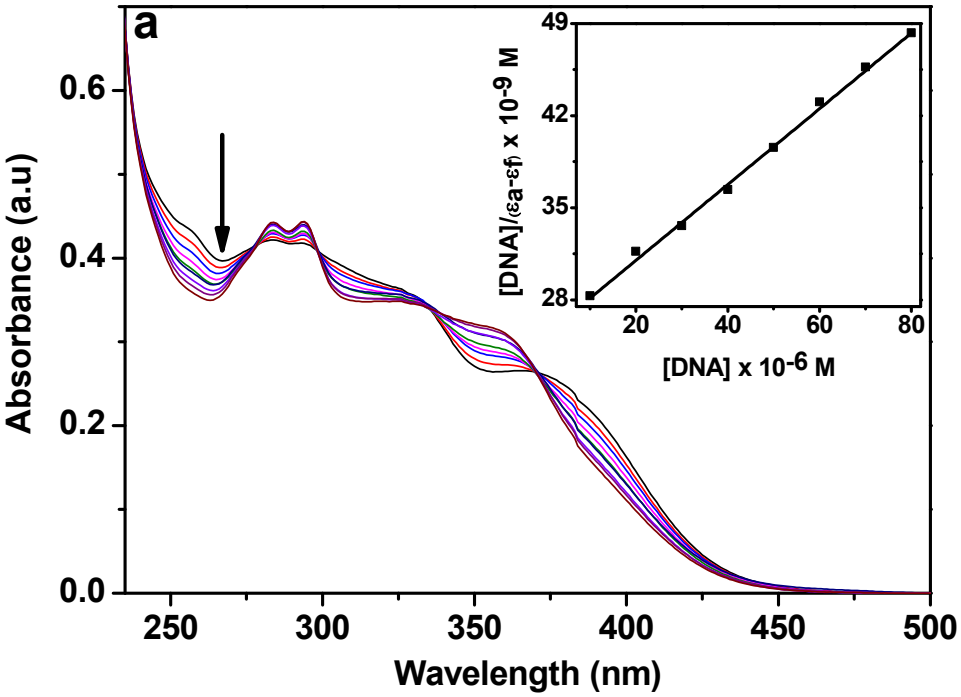
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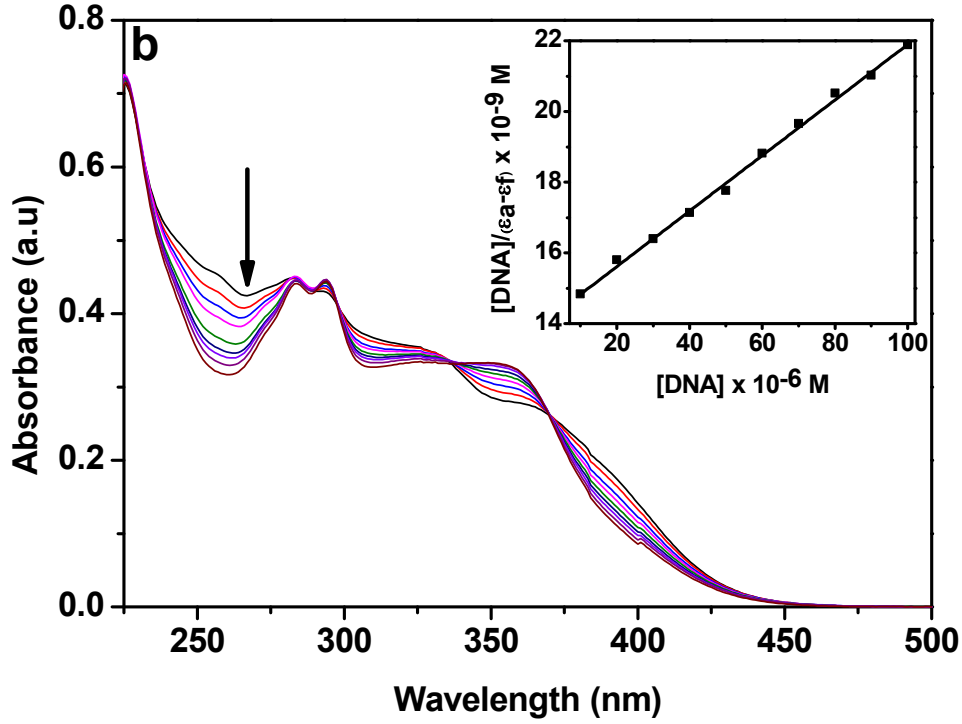
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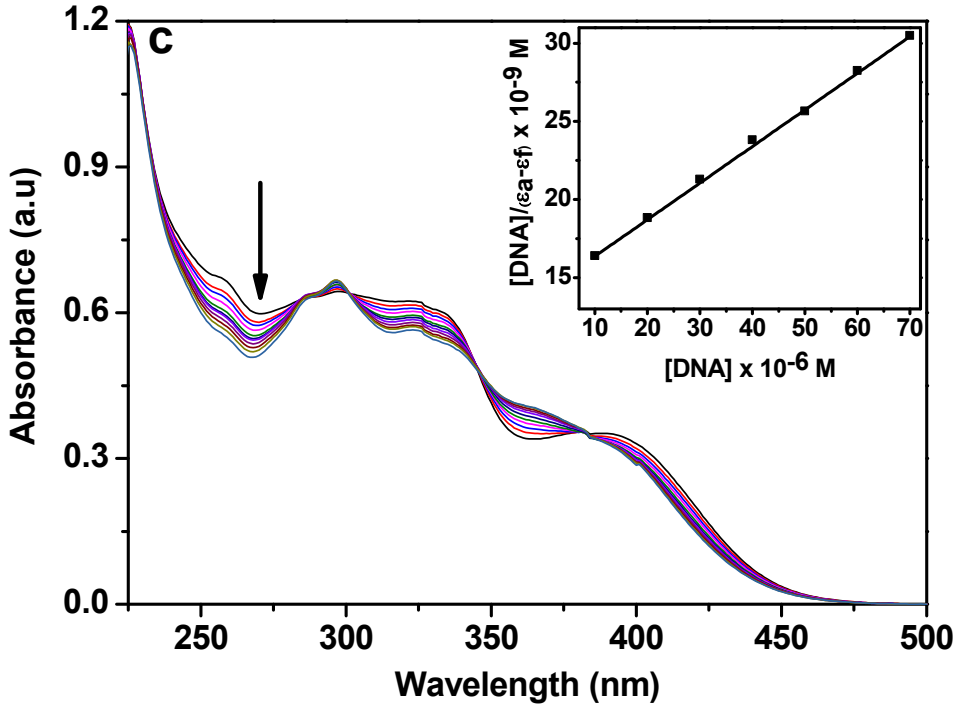
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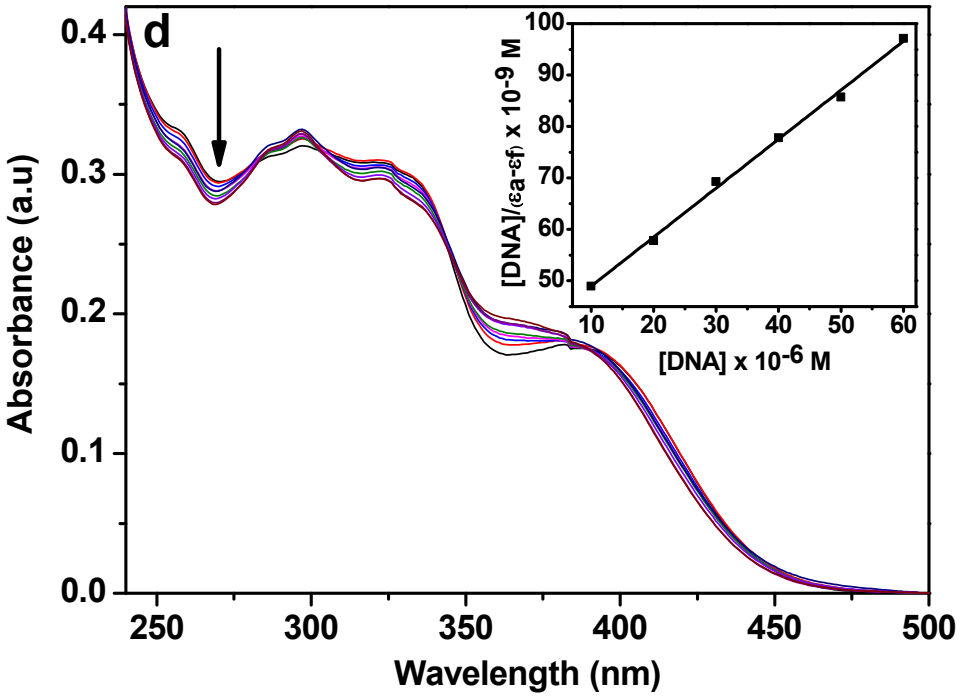
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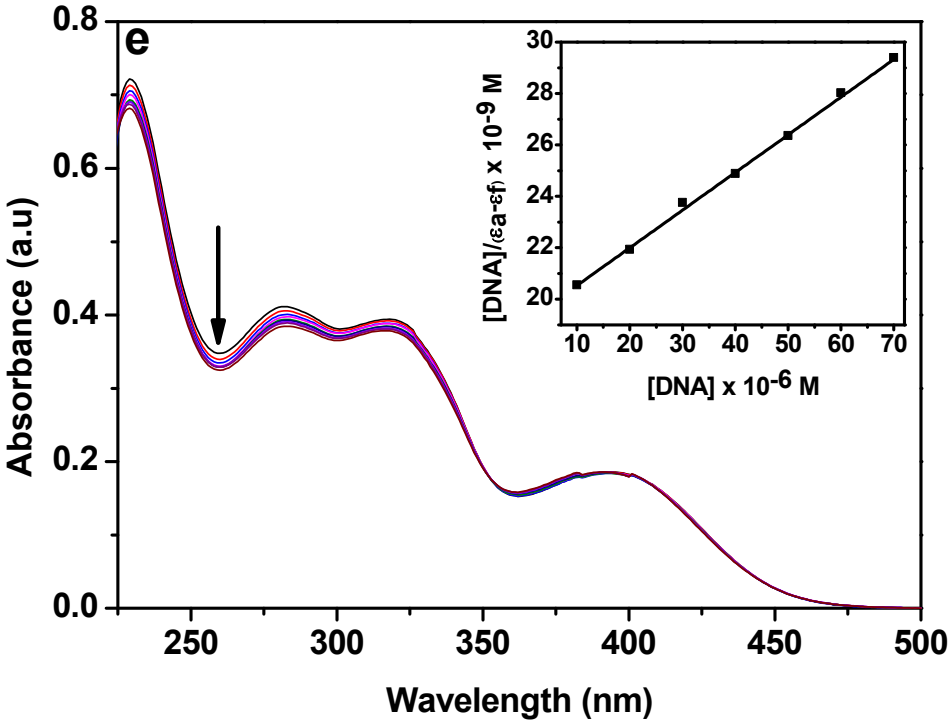
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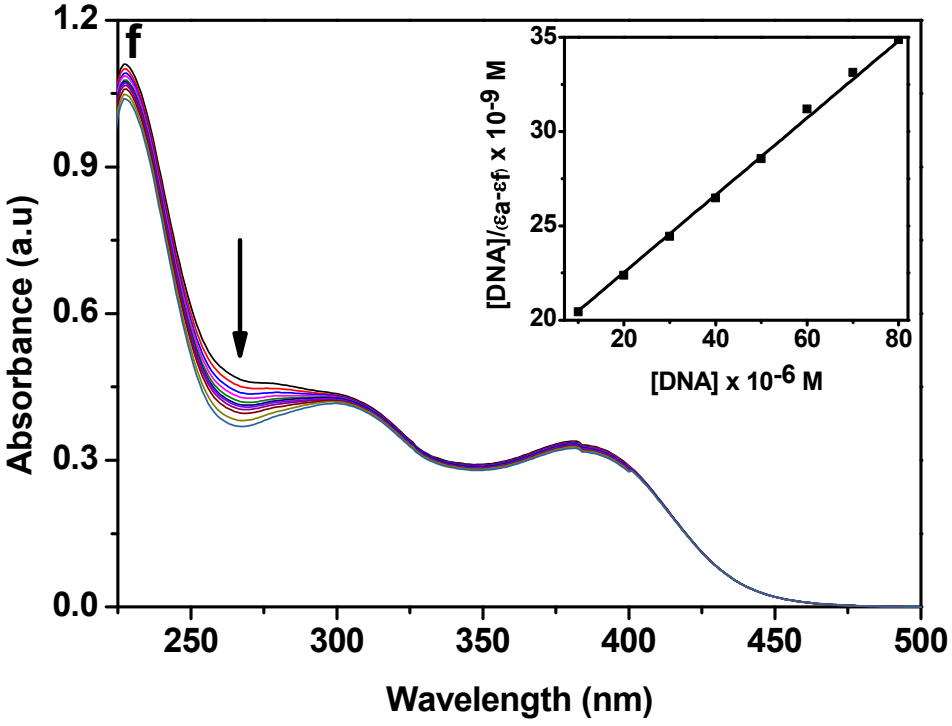
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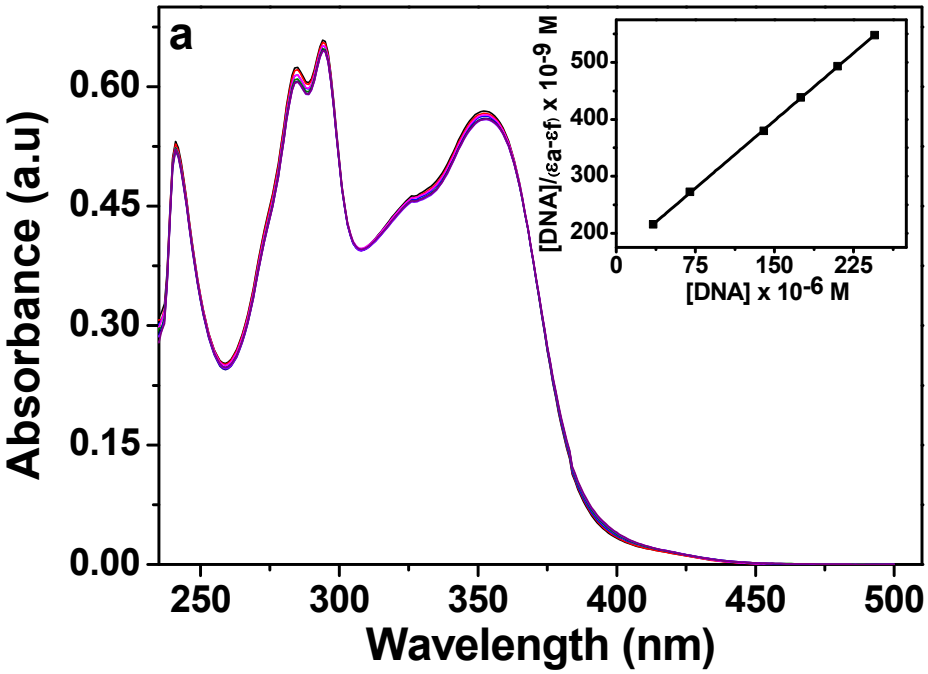
Fig. S8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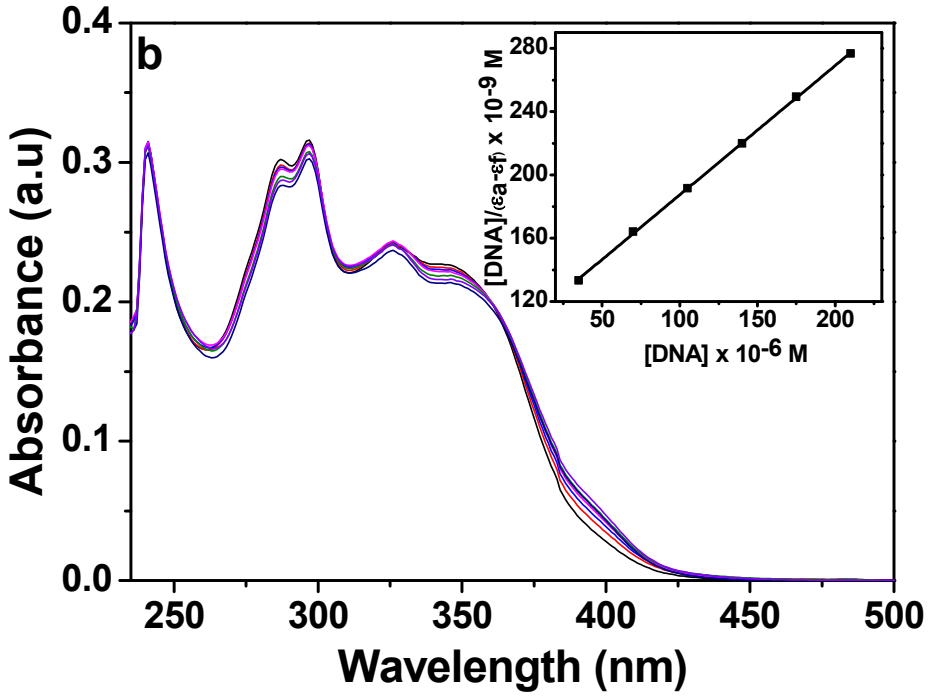
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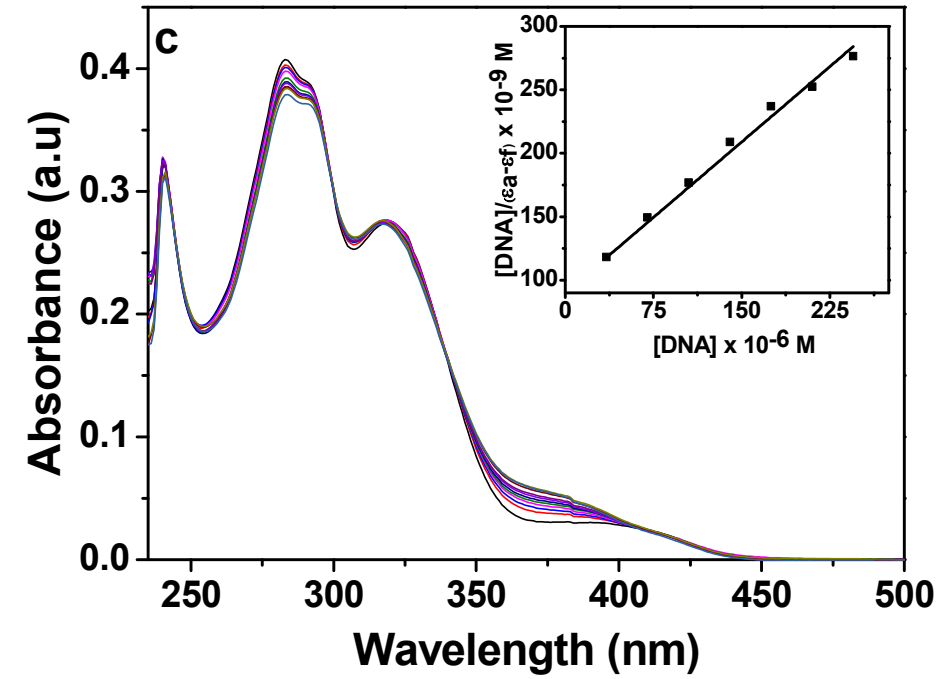
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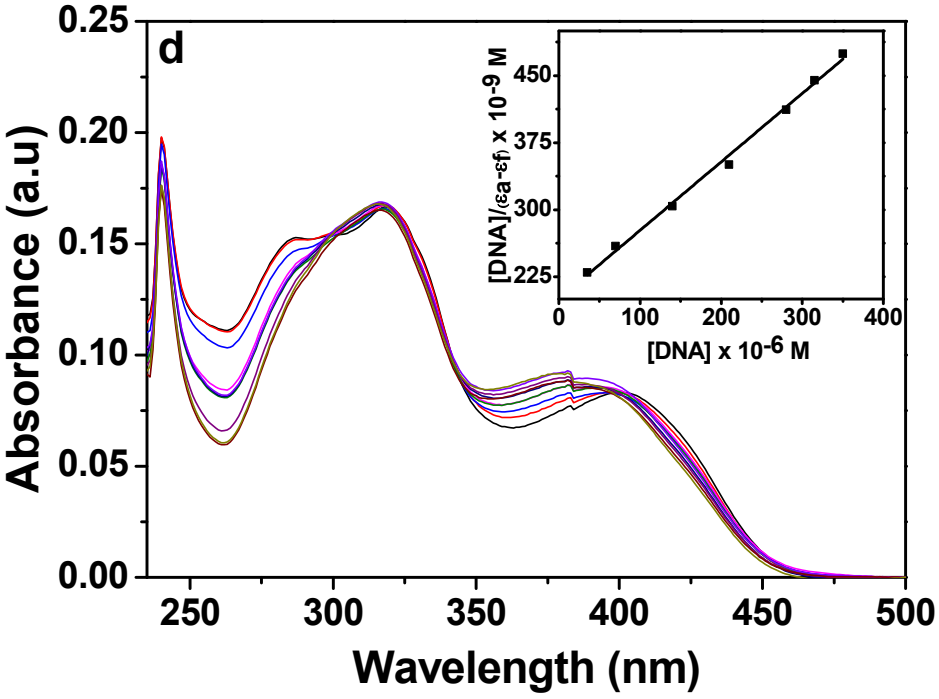
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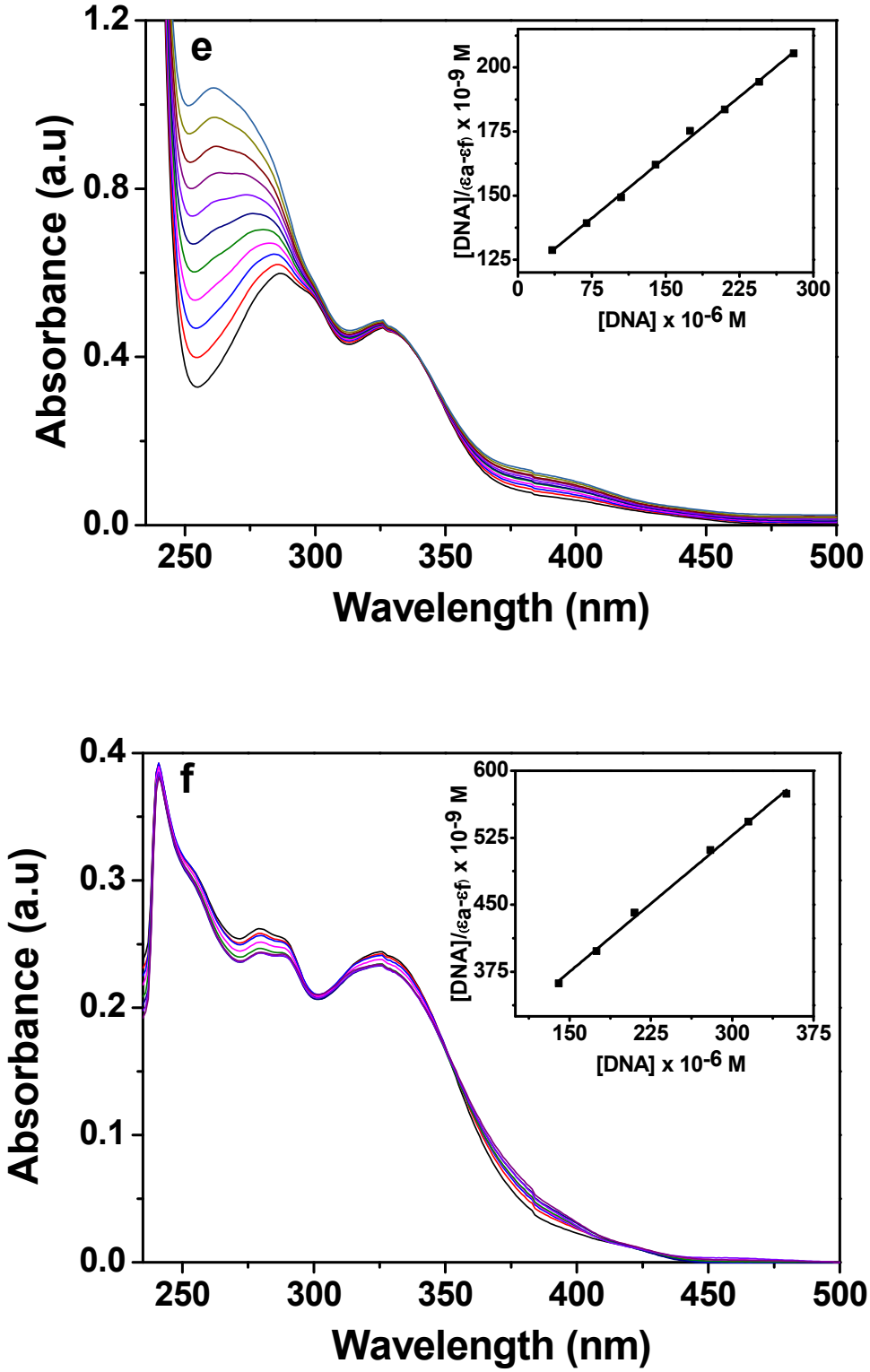
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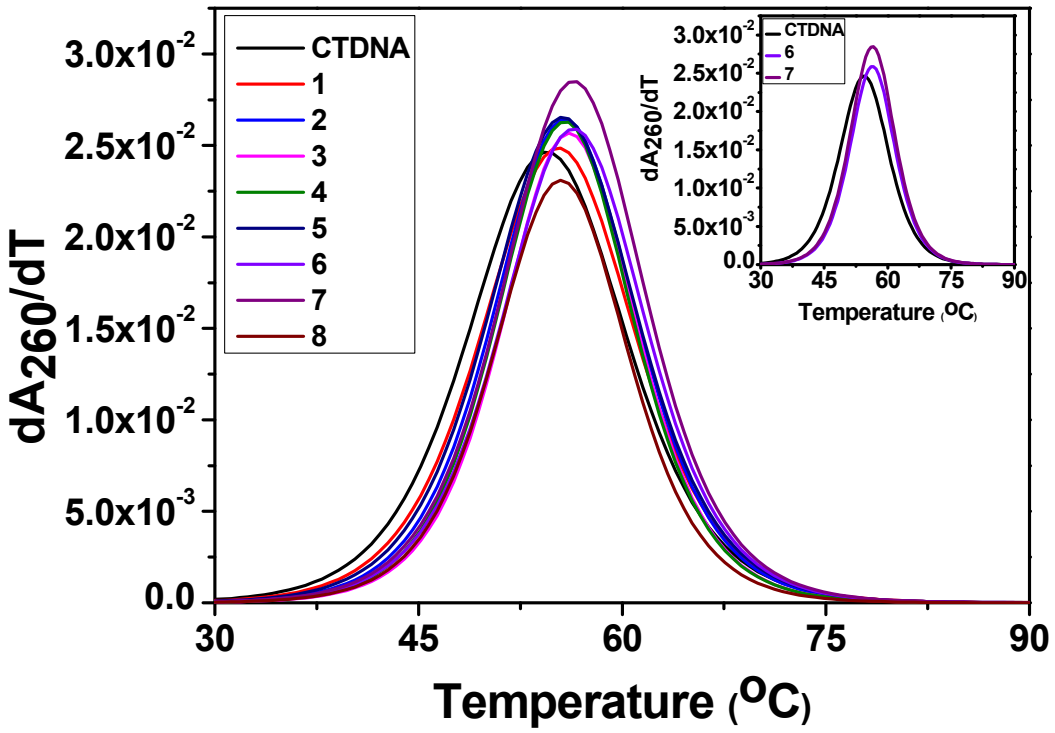
Fig. S9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7
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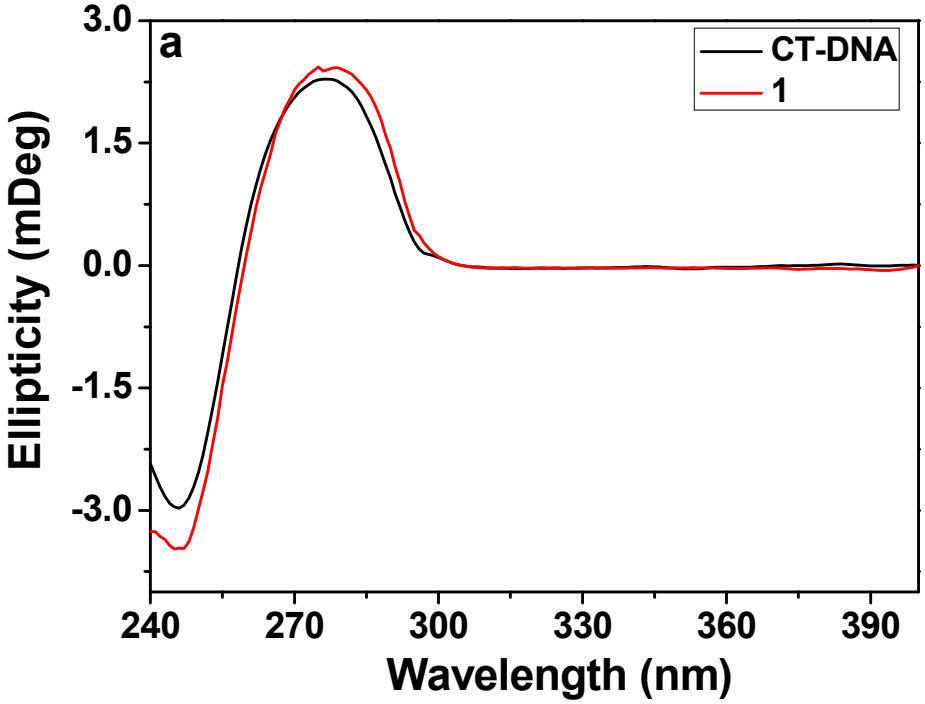
Fig. S10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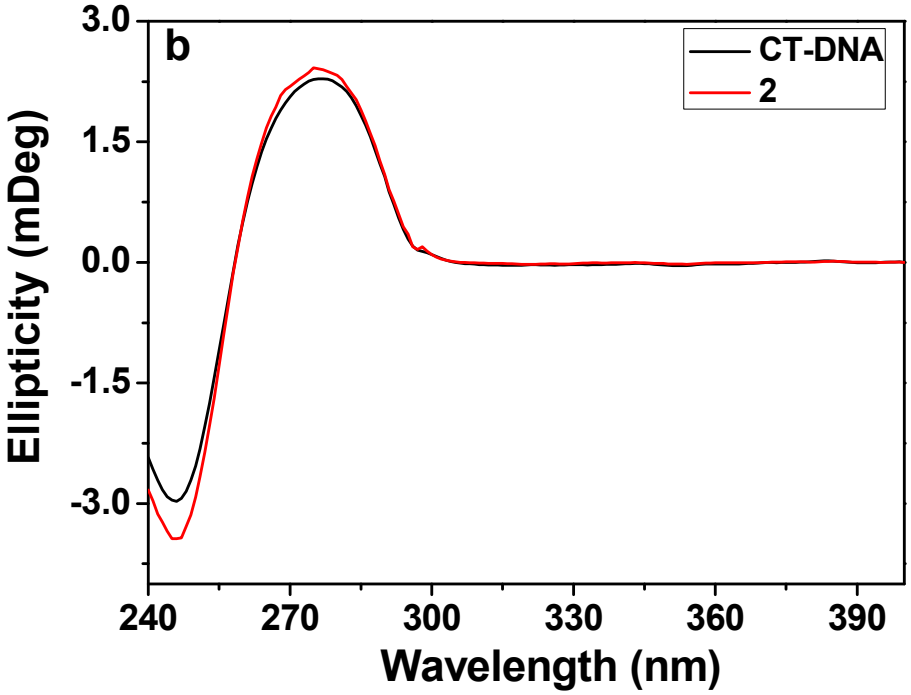
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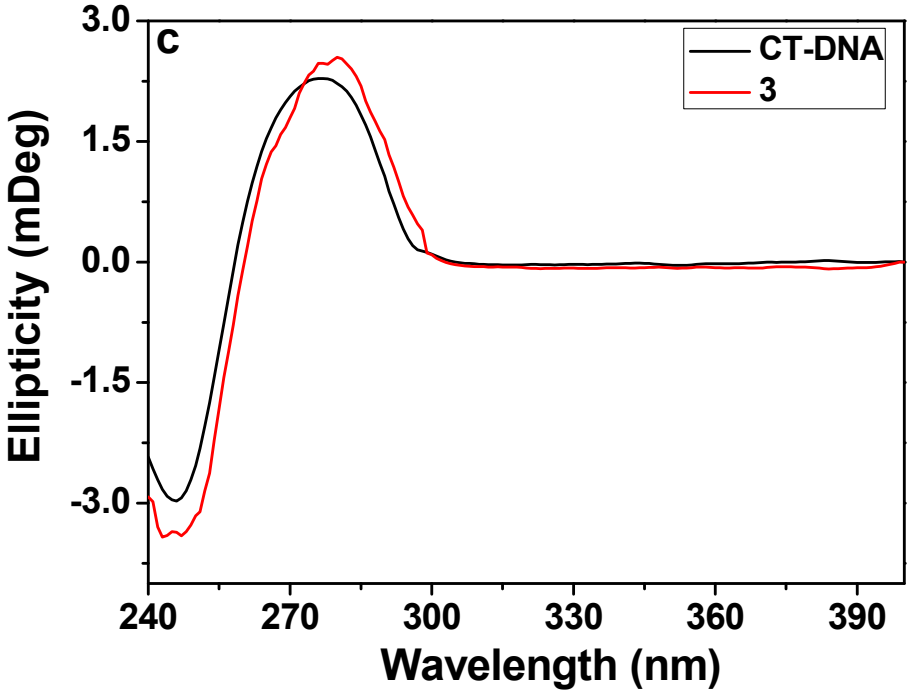
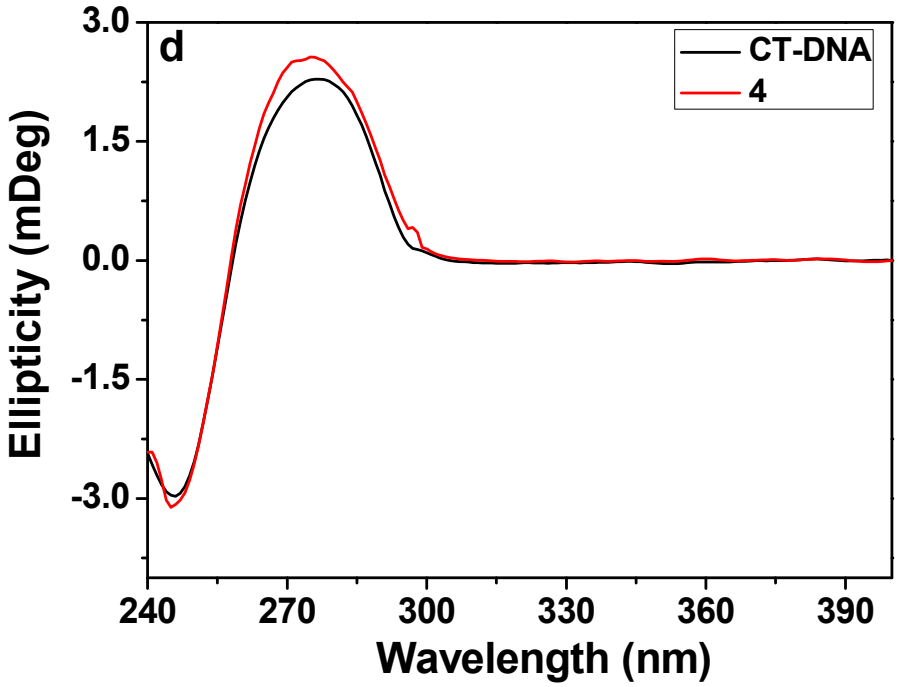
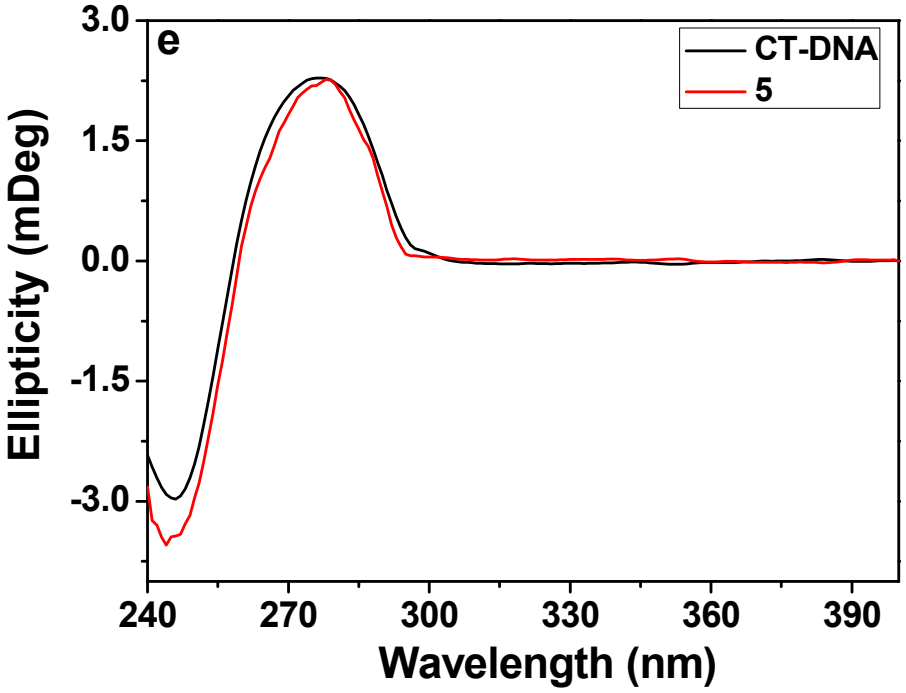
390
Wavelength (nm)


c
CT-DNA
3
Ellipticity (mDeg)
3.0
1.5
0.0
-1.5
-3.0
240
270
300
330
360
390
Wavelength (nm)


d
CT-DNA
4
Ellipticity (mDeg)
3.0
1.5
0.0
-1.5
-3.0
240
270
300
330
360
390
Wavelength (nm)


e
CT-DNA
5
3.0
1.5
0.0
-1.5
-3.0
Ellipticity (mDeg)
240
270
300
330
360
390
Wavelength (nm)

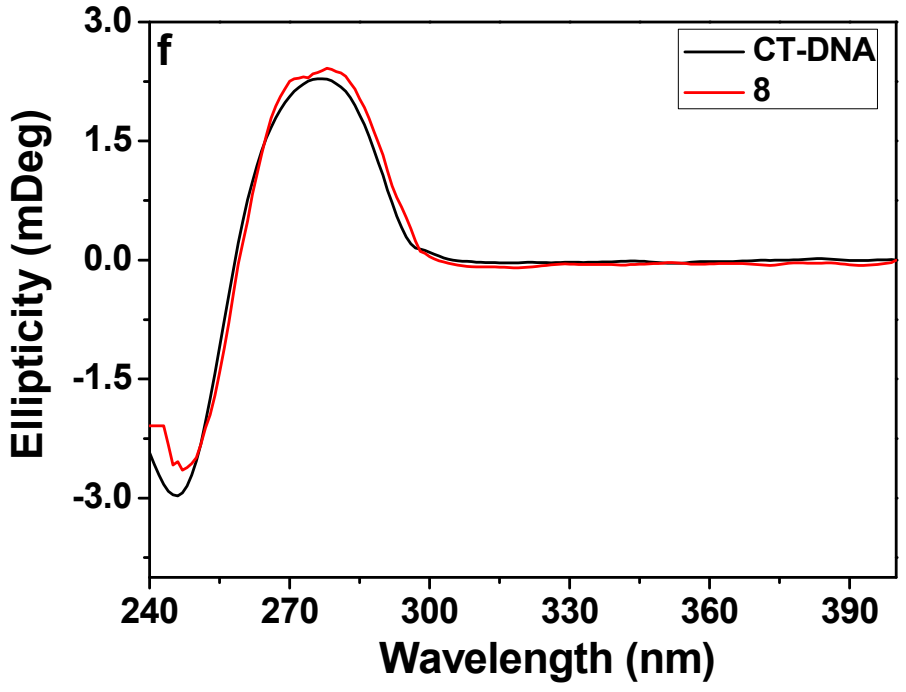
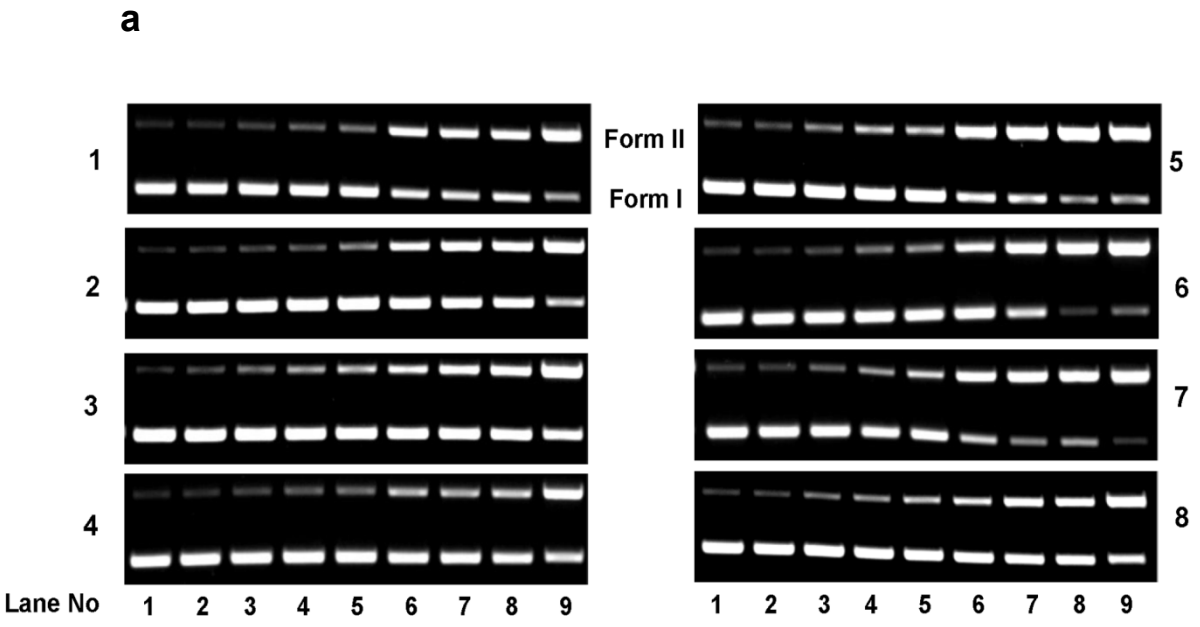

f
CT-DNA
8
3.0
1.5
0.0
-1.5
-3.0
Ellipticity (mDeg)
240
270
300
330
360
390
Wavelength (nm)

Fig. S11


a
Form II
Form I
1
2
3
4
5
6
7
8
Lane No
1 2 3 4 5 6 7 8 9
1 2 3 4 5 6 7 8 9

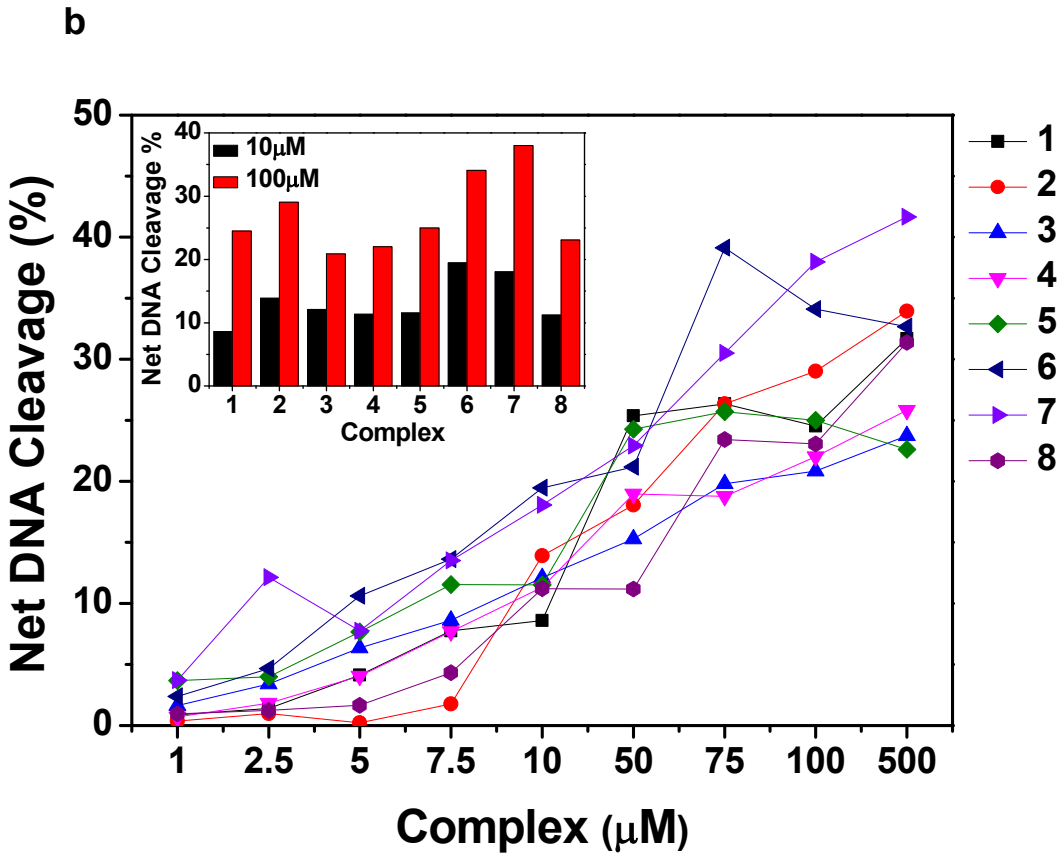

b
Net DNA Cleavage (%)
Complex (μM)
0 10 20 30 40 50
1 2.5 5 7.5 10 50 75 100 500
Net DNA Cleavage %
10μM
100μM
Complex
1 2 3 4 5 6 7 8
1
2
3
4
5
6
7
8

Fig. S12

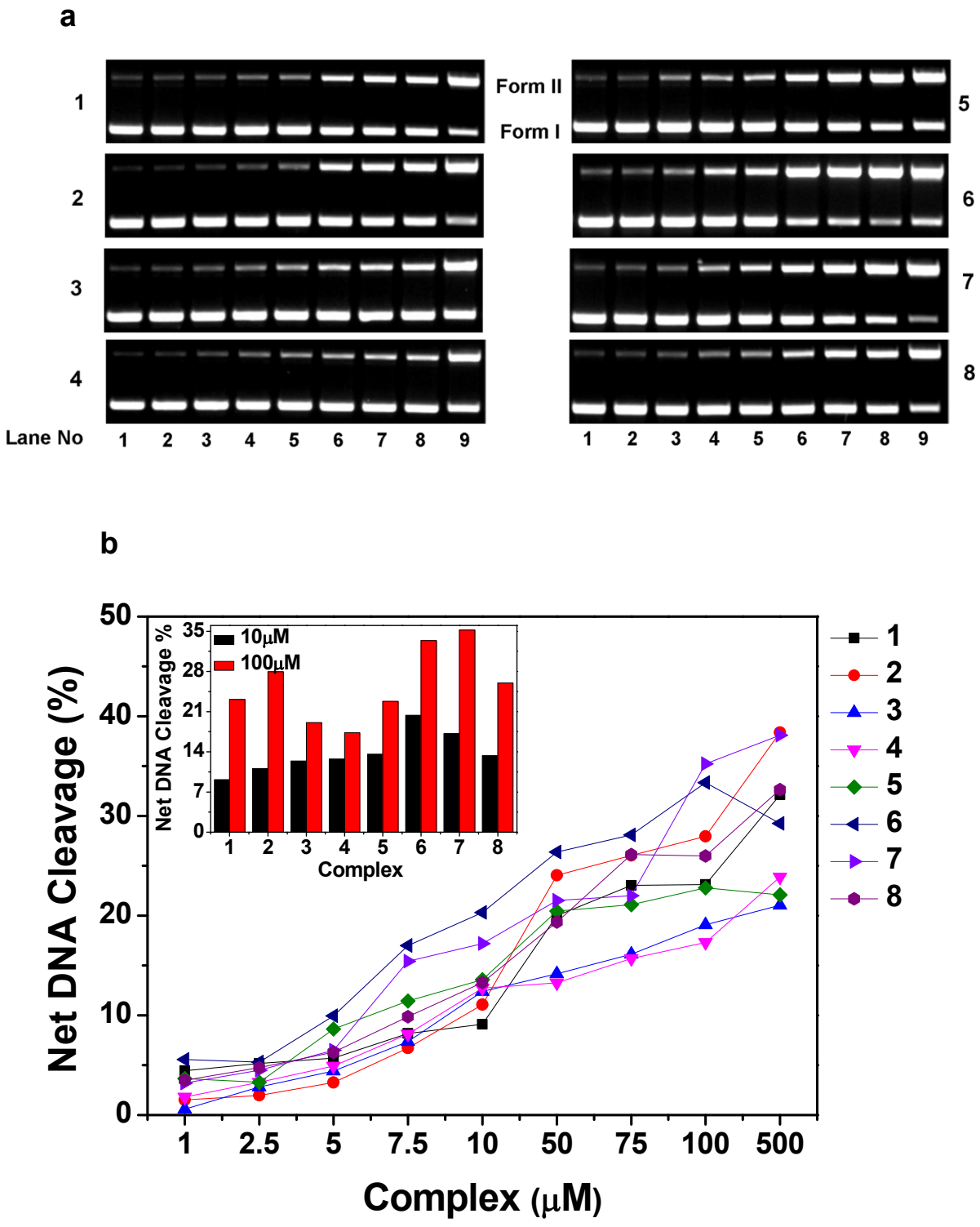

a
1
2
3
4
Form II
Form I
5
6
7
8
Lane No
1 2 3 4 5 6 7 8 9
1 2 3 4 5 6 7 8 9
b
Net DNA Cleavage (%)
Complex (μM)
1 2.5 5 7.5 10 50 75 100 500
0 10 20 30 40 50
Net DNA Cleavage %
10μM
100μM
0 7 14 21 28 35
1 2 3 4 5 6 7 8
Complex
1
2
3
4
5
6
7
8

Fig. S13

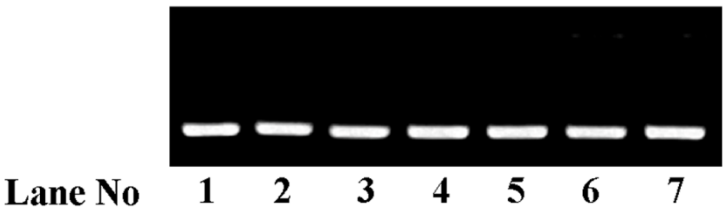


Fig. S14

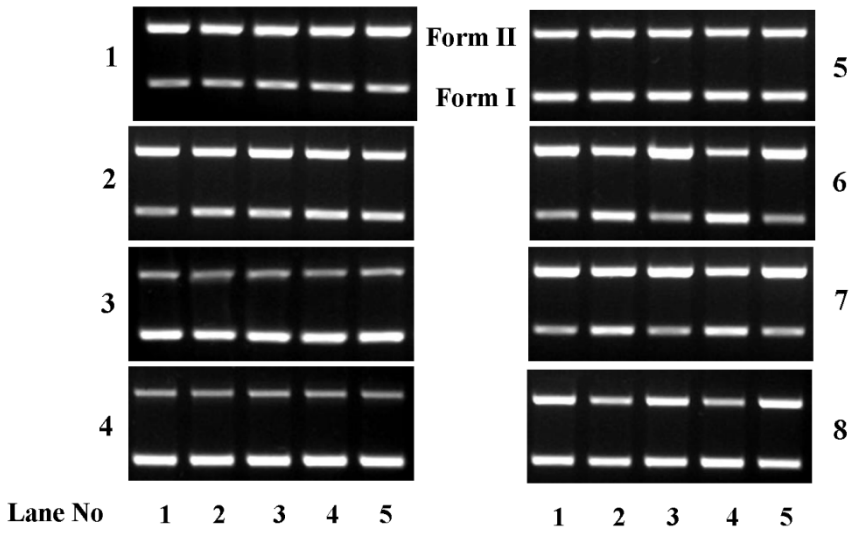


Fig. S15

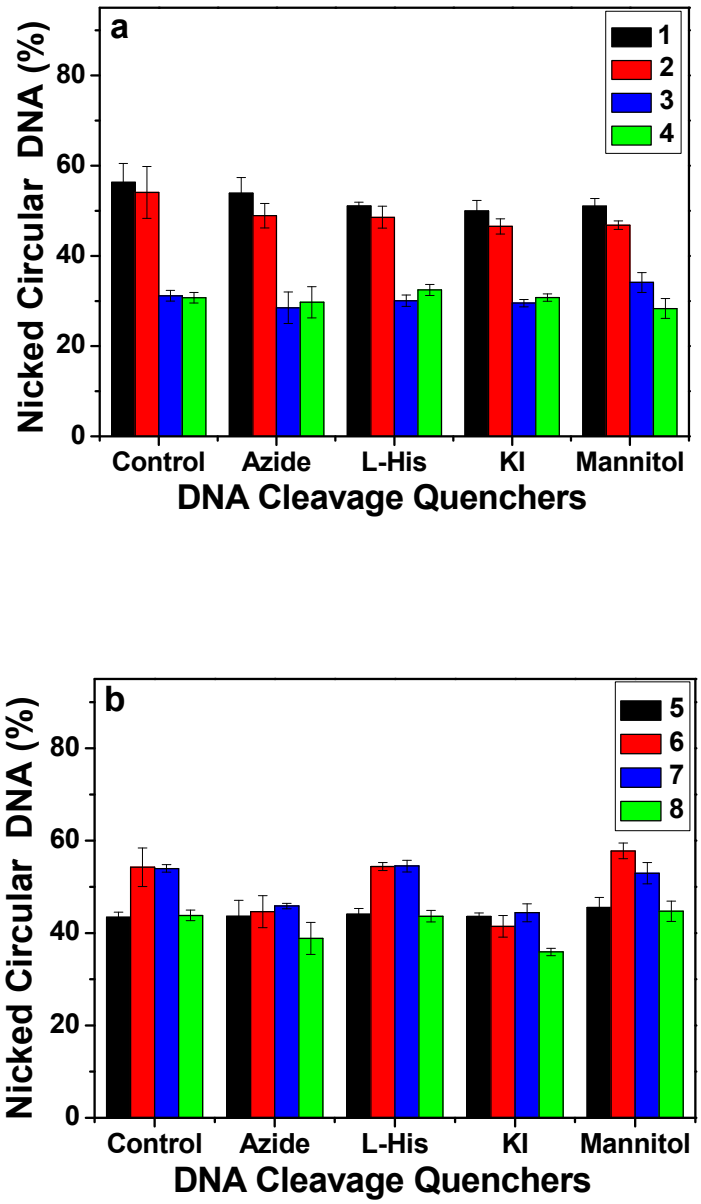
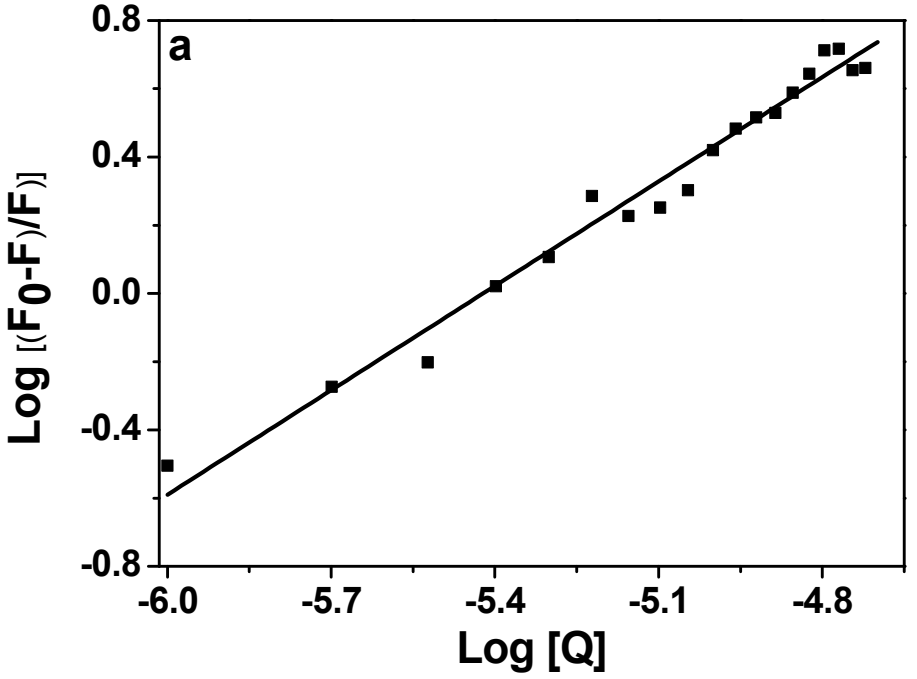

a
1
2
3
4
Nicked Circular DNA (%)
0
20
40
60
80
Control
Azide
L-His
KI
Mannitol
DNA Cleavage Quenchers
b
5
6
7
8
Nicked Circular DNA (%)
0
20
40
60
80
Control
Azide
L-His
KI
Mannitol
DNA Cleavage Quenchers

Fig. S16


a
0.8
0.4
0.0
-0.4
-0.8
-6.0
-5.7
-5.4
-5.1
-4.8
Log [(F0-F)/F)]
Log [Q]

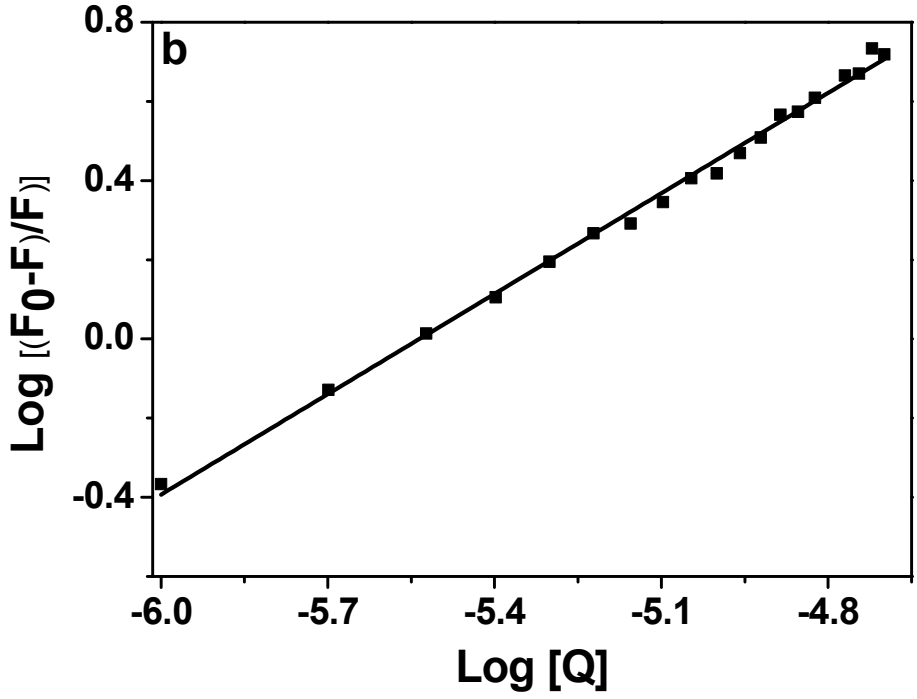

b
0.8
0.4
0.0
-0.4
-6.0
-5.7
-5.4
-5.1
-4.8
Log [(F0-F)/F)]
Log [Q]

Fig. S17

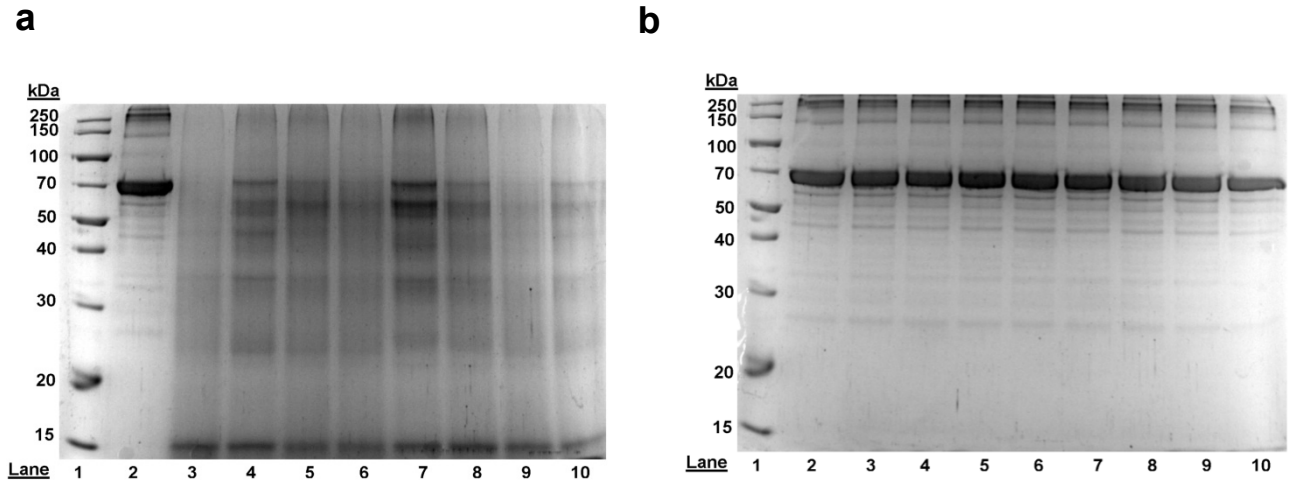

a
kDa
250
150
100
70
50
40
30
20
15
Lane 1 2 3 4 5 6 7 8 9 10
b
kDa
250
150
100
70
50
40
30
20
15
Lane 1 2 3 4 5 6 7 8 9 10

Fig. S18

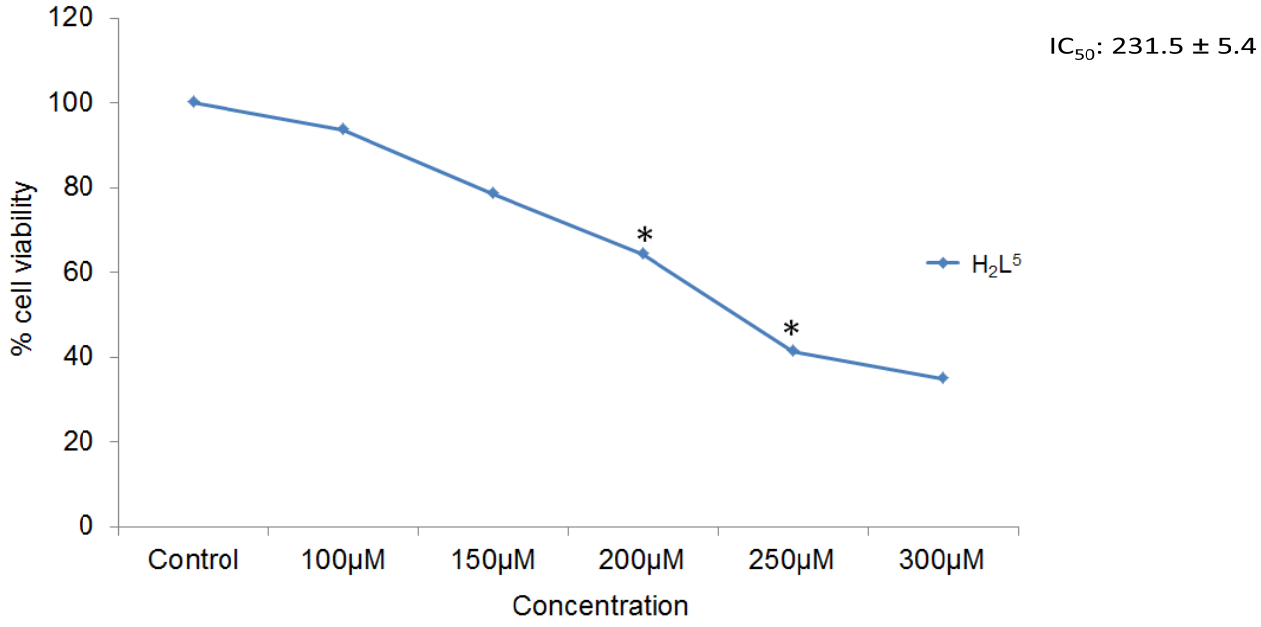

120
100
80
60
40
20
0
% cell viability
Control
100μM
150μM
200μM
250μM
300μM
Concentration
*
*
H2L5
IC50: 231.5 ± 5.4

Fig. S19

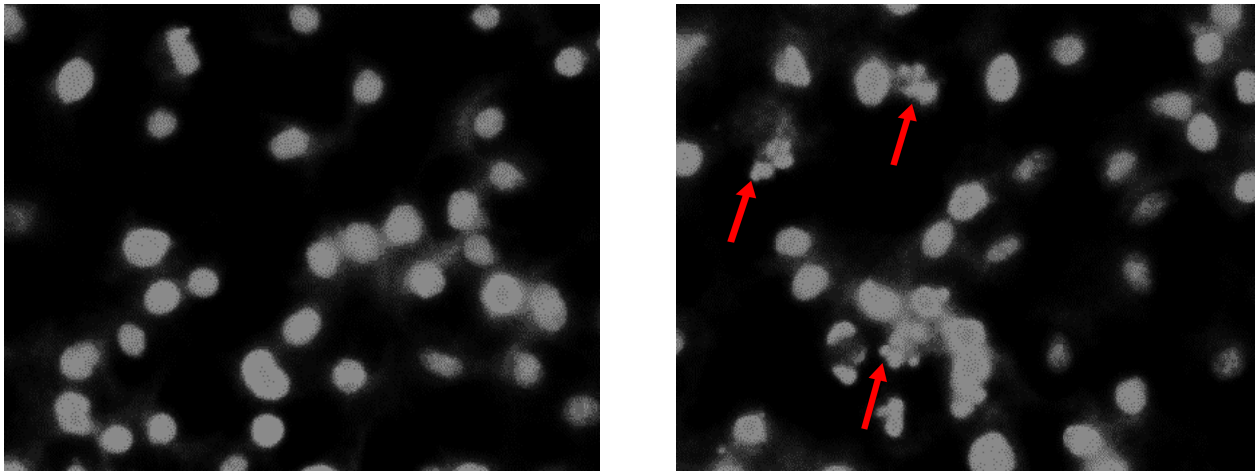
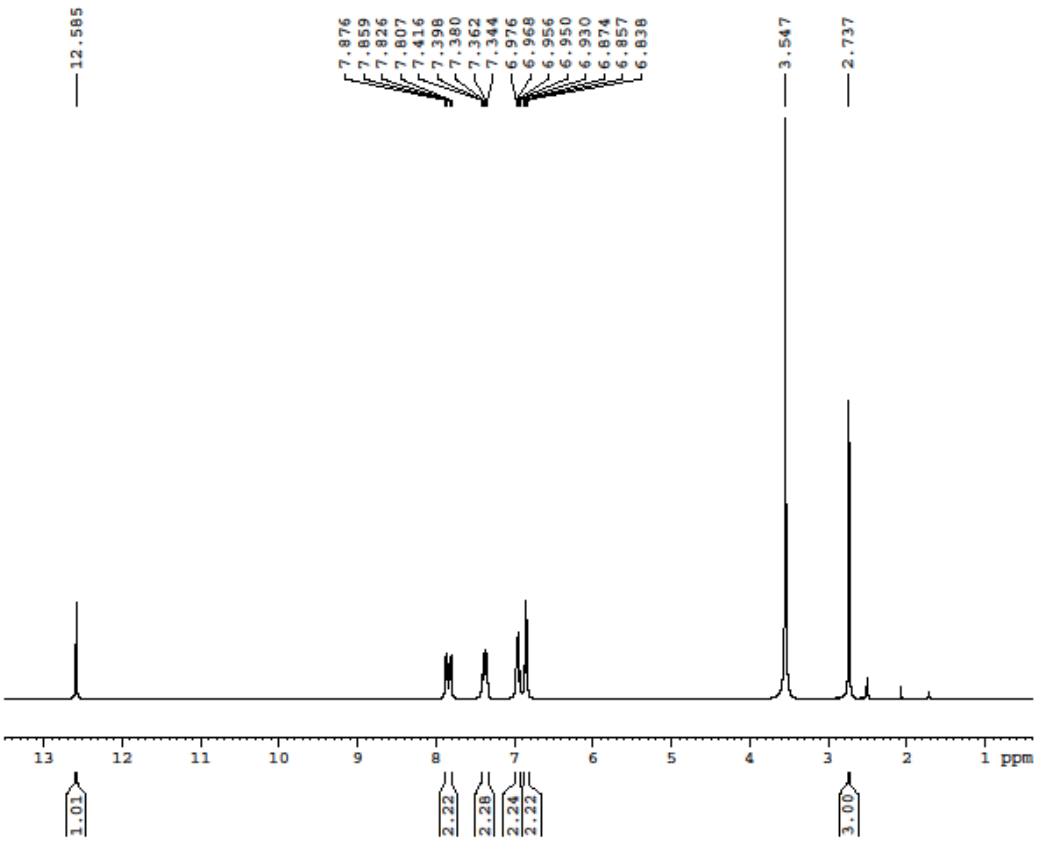
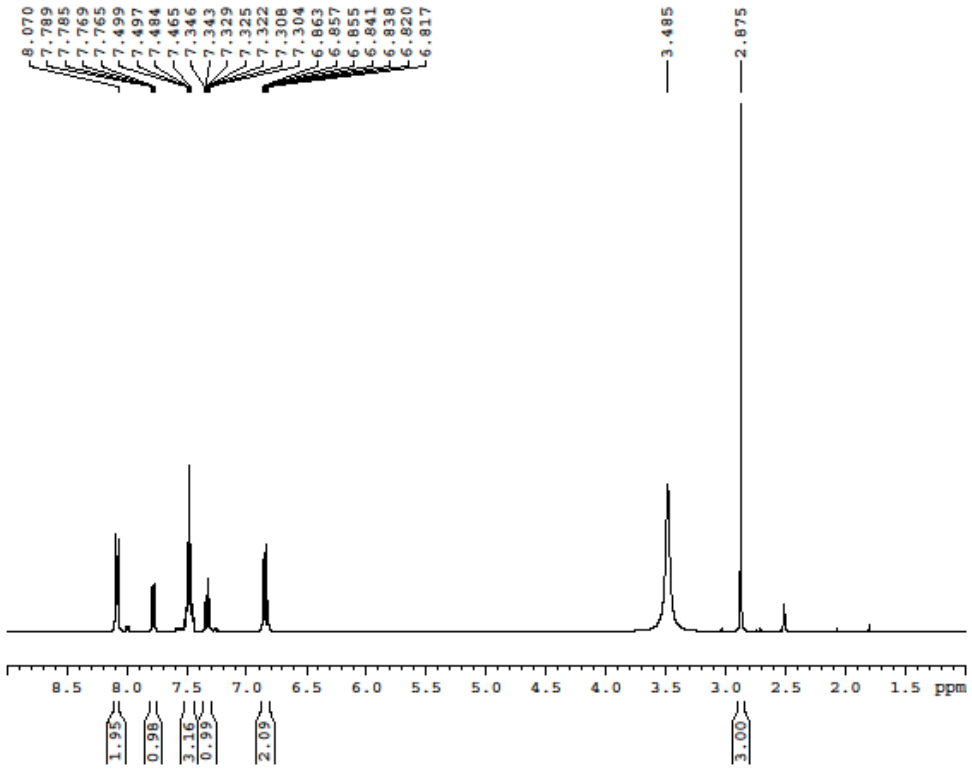


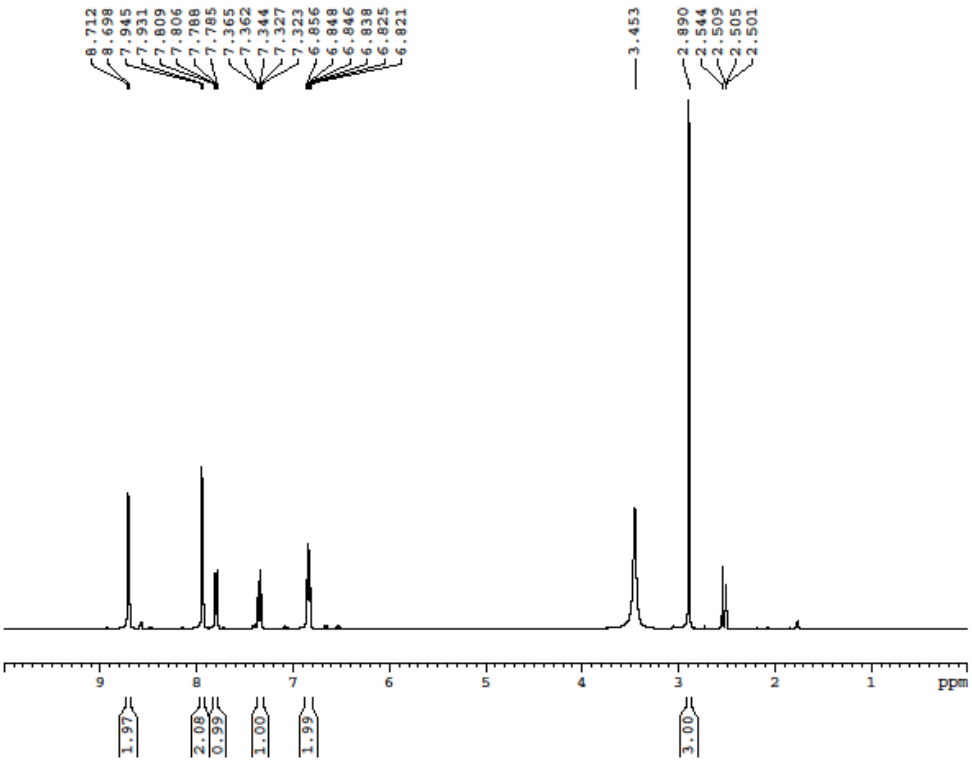
Fig. S20


12.585
7.876
7.859
7.826
7.807
7.416
7.398
7.380
7.362
7.344
6.976
6.968
6.956
6.950
6.930
6.874
6.857
6.838
3.547
2.737
13
12
11
10
9
8
7
6
5
4
3
2
1 ppm
1.01
2.22
2.28
2.24
2.22
3.00

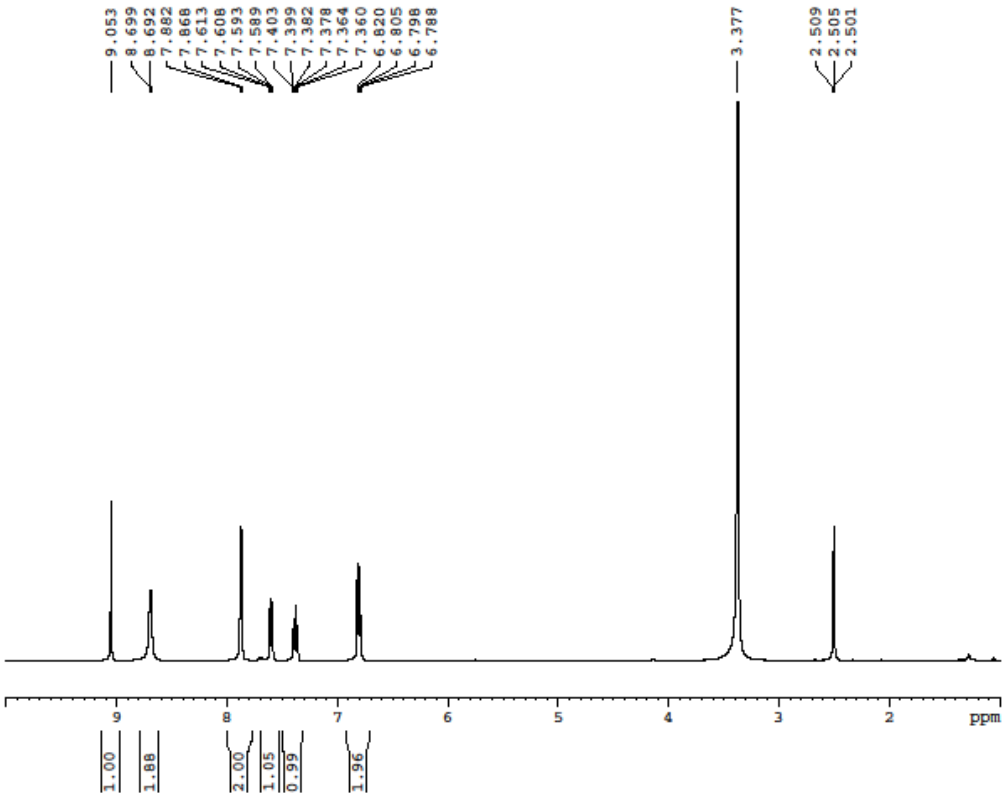
(a)


8.070
7.789
7.785
7.769
7.765
7.499
7.497
7.484
7.465
7.346
7.343
7.329
7.325
7.322
7.308
7.304
6.863
6.857
6.855
6.841
6.838
6.820
6.817
3.485
2.875
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5 ppm
1.95
0.98
3.16
0.99
2.09
3.00

(b)


8.712
8.698
7.945
7.931
7.809
7.806
7.788
7.785
7.365
7.362
7.344
7.327
7.323
6.856
6.848
6.846
6.838
6.825
6.821
3.453
2.890
2.544
2.509
2.505
2.501
9
8
7
6
5
4
3
2
1
ppm
1.97
2.08
0.99
1.00
1.99
3.00

(c)


9.053
8.699
8.692
7.882
7.868
7.613
7.608
7.593
7.589
7.403
7.399
7.382
7.378
7.364
7.360
6.820
6.805
6.798
6.788
3.377
2.509
2.505
2.501
9
8
7
6
5
4
3
2
ppm
1.00
1.88
2.00
1.05
0.99
1.96

(d)

Fig. S21

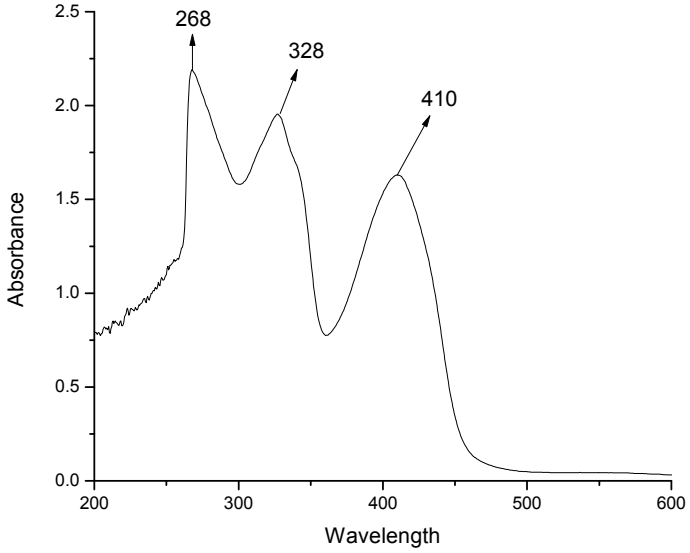


Fig. S22

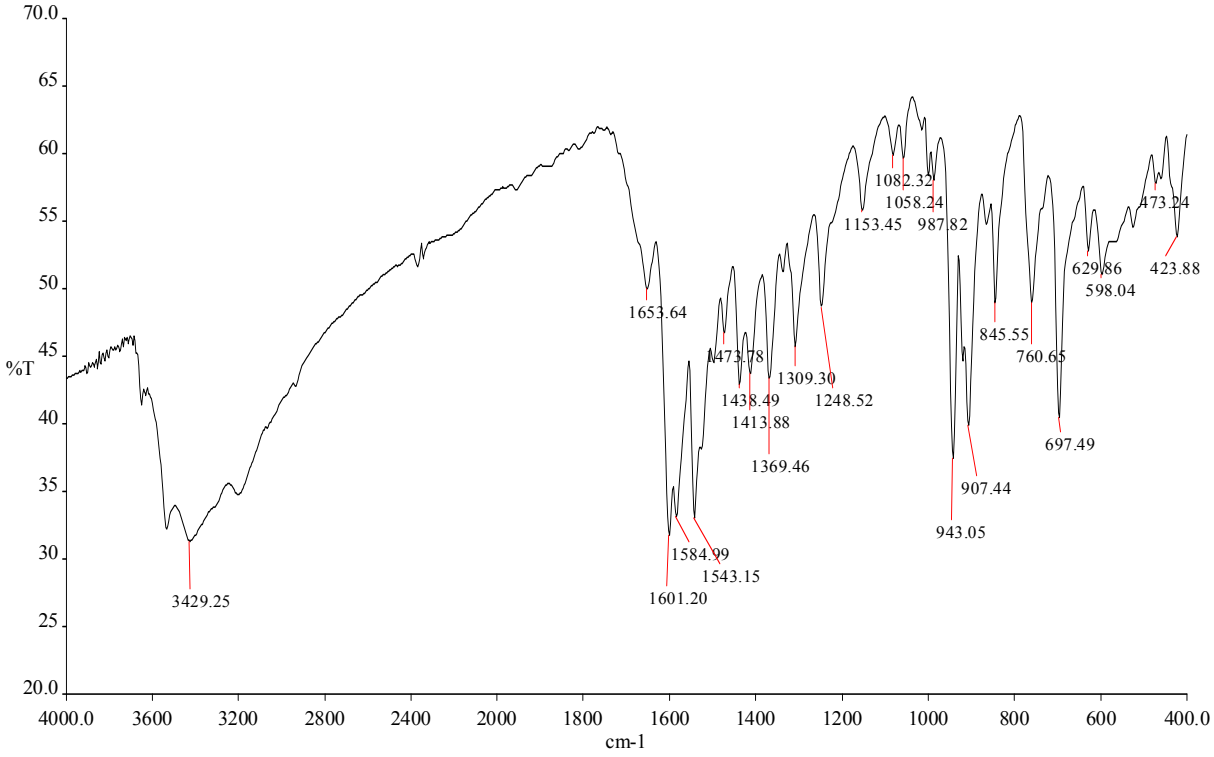


Fig. S23