

## Supplementary material

### Evaluation of cytotoxic potential of structurally well-characterized RNA targeted Ionic Non-steroidal anti-inflammatory (NSAID) Cu(II) & Zn(II) DACH-mefenamato drug conjugates against human cancer cell lines.

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**Table S1**

Selected bond lengths for **1**

Atom	Atom	Length/Å	Atom	Atom	Length/Å
Cu1	N3	2.018 (3)	C37	C36	1.389 (6)
Cu1	N1	2.019 (3)	C37	C38	1.376 (7)
Cu1	N4	2.019 (3)	C24	C23	1.393 (7)
Cu1	N2	2.005 (3)	C24	C27	1.506 (7)
O2	C13	1.266 (5)	C18	C17	1.378 (6)
N3	C7	1.483 (6)	C16	C17	1.382 (7)
O1	C13	1.260 (5)	C41	C40	1.513 (6)
C29	C34	1.414 (6)	C22	C23	1.380 (7)
C29	C30	1.396 (6)	C31	C32	1.388 (6)
C29	C28	1.508 (6)	C35	C36	1.382 (6)
N5	C19	1.387 (6)	C35	C40	1.397 (6)
N5	C20	1.417 (5)	C33	C32	1.379 (6)
N1	C1	1.475 (6)	C11	C10	1.534 (6)
N4	C12	1.495 (6)	C11	C12	1.496 (6)
N6	C34	1.376 (5)	C38	C39	1.388 (7)
N6	C35	1.426 (5)	C39	C42	1.506 (6)
N2	C6	1.462 (6)	C39	C40	1.403 (6)
C14	C19	1.420 (6)	C8	C9	1.540 (7)
C14	C15	1.391 (6)	C8	C7	1.541 (6)
C14	C13	1.510 (6)	C9	C10	1.464 (7)
C19	C18	1.397 (6)	C5	C6	1.507 (6)
C25	C20	1.403 (6)	C5	C4	1.505 (7)
C25	C24	1.404 (6)	C12	C7	1.465 (7)

C25	C26	1.504 (6)	C2	C3	1.526 (8)
C34	C33	1.405 (6)	C2	C1	1.515 (7)
C15	C16	1.378 (6)	C3	C4	1.301 (9)
C30	C31	1.377 (6)	C6	C1	1.303 (9)
C20	C21	1.399 (6)	O5	C28	1.258 (5)
C21	C22	1.384 (6)	O6	C28	1.265 (5)

**Table S2**

**Bond Angles for Complex 1**

<b>Atom Atom Atom</b>	<b>Angle/°</b>	<b>Atom Atom Atom</b>	<b>Angle/°</b>
N1 Cu1 N3	93.53 (13)	C36 C35 N6	119.0 (4)
N4 Cu1 N3	85.13 (13)	C40 C35 N6	120.3 (4)
N4 Cu1 N1	175.91 (15)	C40 C35 C36	120.7 (4)
N2 Cu1 N3	176.69 (14)	C35 C36 C37	120.2 (4)
N2 Cu1 N1	83.99 (13)	C32 C33 C34	121.2 (4)
N2 Cu1 N4	97.19 (13)	C12 C11 C10	111.4 (4)
C7 N3 Cu1	106.8 (3)	C22 C23 C24	121.3 (4)
C30 C29 C34	118.1 (4)	C39 C38 C37	121.6 (4)
C28 C29 C34	122.8 (4)	C42 C39 C38	120.4 (4)
C28 C29 C30	119.1 (4)	C40 C39 C38	119.2 (4)
C20 N5 C19	126.7 (4)	C40 C39 C42	120.5 (4)
C1 N1 Cu1	108.7 (3)	O1 C13 O2	124.2 (4)
C12 N4 Cu1	107.7 (3)	C14 C13 O2	119.4 (4)
C35 N6 C34	122.8 (4)	C14 C13 O1	116.5 (4)
C6 N2 Cu1	108.9 (3)	C33 C32 C31	120.4 (4)
C15 C14 C19	119.0 (4)	C35 C40 C41	121.0 (4)
C13 C14 C19	123.1 (4)	C39 C40 C41	120.0 (4)
C13 C14 C15	117.8 (4)	C39 C40 C35	119.0 (4)
C14 C19 N5	119.9 (4)	C16 C17 C18	120.9 (4)
C18 C19 N5	121.8 (4)	C7 C8 C9	108.5 (4)
C18 C19 C14	118.3 (4)	C10 C9 C8	110.6 (5)
C24 C25 C20	118.9 (4)	C4 C5 C6	111.9 (4)
C26 C25 C20	119.2 (4)	C9 C10 C11	112.5 (4)
C26 C25 C24	121.8 (4)	C11 C12 N4	114.3 (4)
N6 C34 C29	120.9 (4)	C7 C12 N4	108.0 (4)
C33 C34 C29	118.8 (4)	C7 C12 C11	114.7 (4)
C33 C34 N6	120.2 (4)	C1 C2 C3	110.5 (5)
C16 C15 C14	121.8 (4)	C8 C7 N3	112.8 (4)
C31 C30 C29	122.8 (4)	C12 C7 N3	108.8 (4)
C25 C20 N5	118.4 (4)	C12 C7 C8	112.6 (4)

C21	C20	N5	120.9 (4)	C4	C3	C2	121.0 (6)
C21	C20	C25	120.6 (4)	C5	C6	N2	116.5 (4)
C22	C21	C20	119.7 (4)	C1	C6	N2	117.2 (6)
C38	C37	C36	119.3 (4)	C1	C6	C5	119.8 (6)
C23	C24	C25	119.4 (4)	C2	C1	N1	114.7 (5)
C27	C24	C25	121.3 (4)	C6	C1	N1	116.1 (5)
C27	C24	C23	119.3 (4)	C6	C1	C2	120.9 (6)
C17	C18	C19	120.9 (4)	C3	C4	C5	121.3 (6)
C17	C16	C15	118.9 (4)	O5	C28	C29	120.1 (3)
C23	C22	C21	120.0 (4)	O6	C28	C29	116.8 (4)
C32	C31	C30	118.8 (4)	O6	C28	O5	123.1 (4)

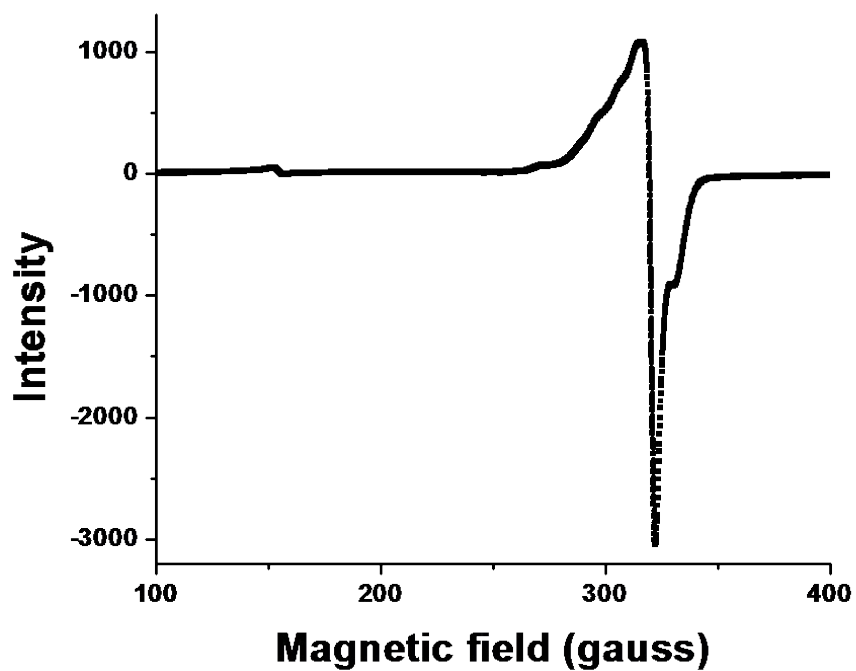


Fig. S1 EPR spectrum of complex 1

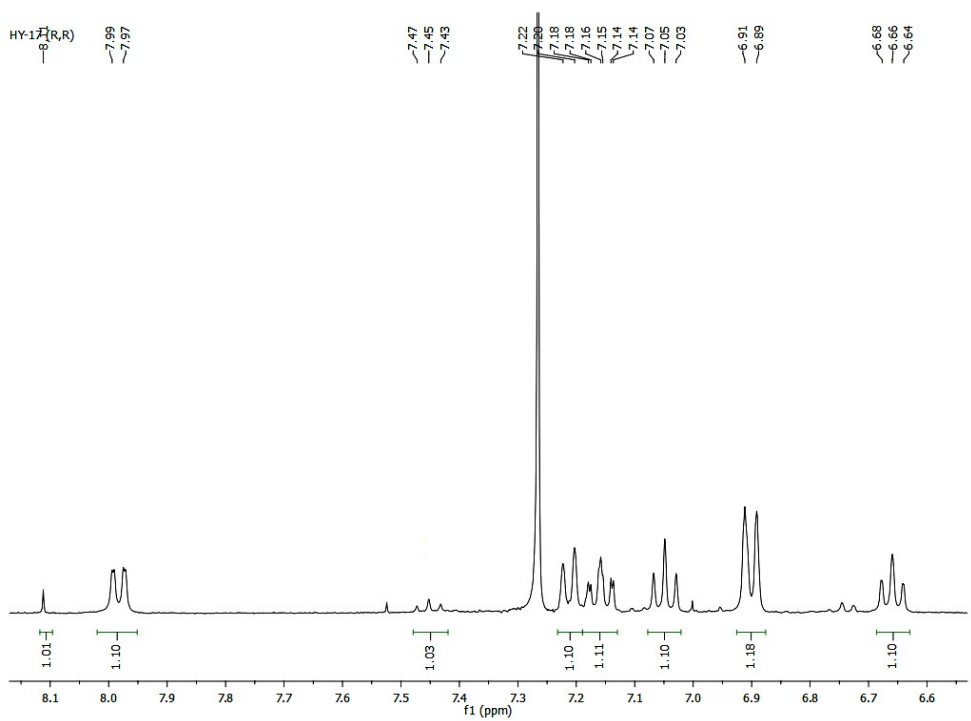
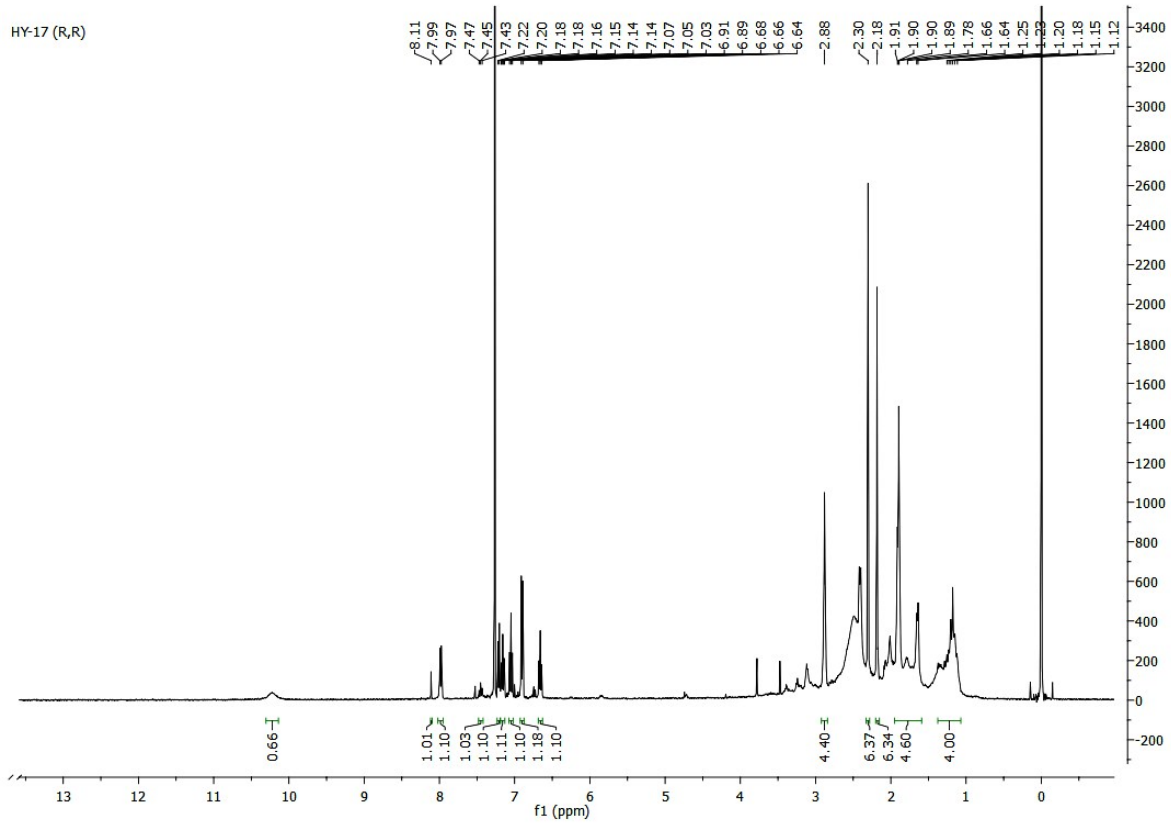
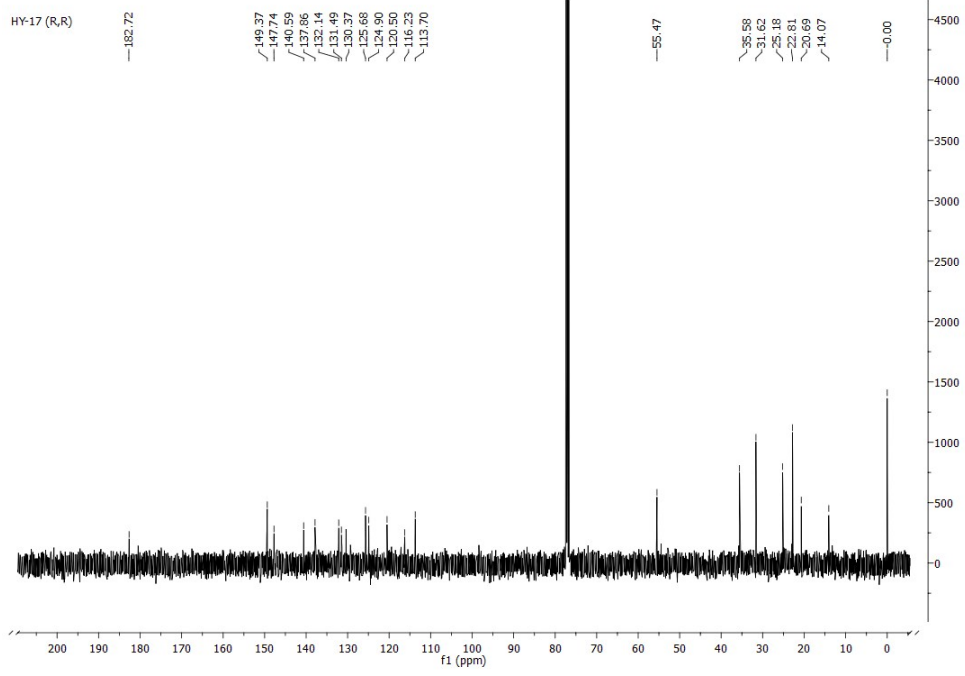
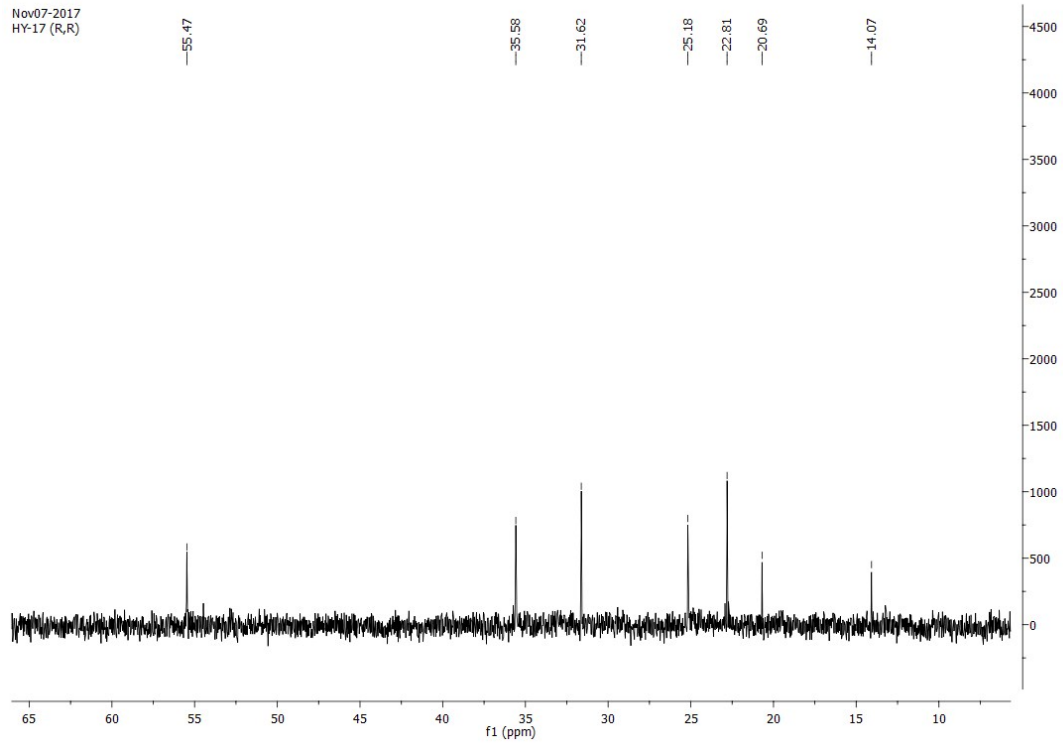


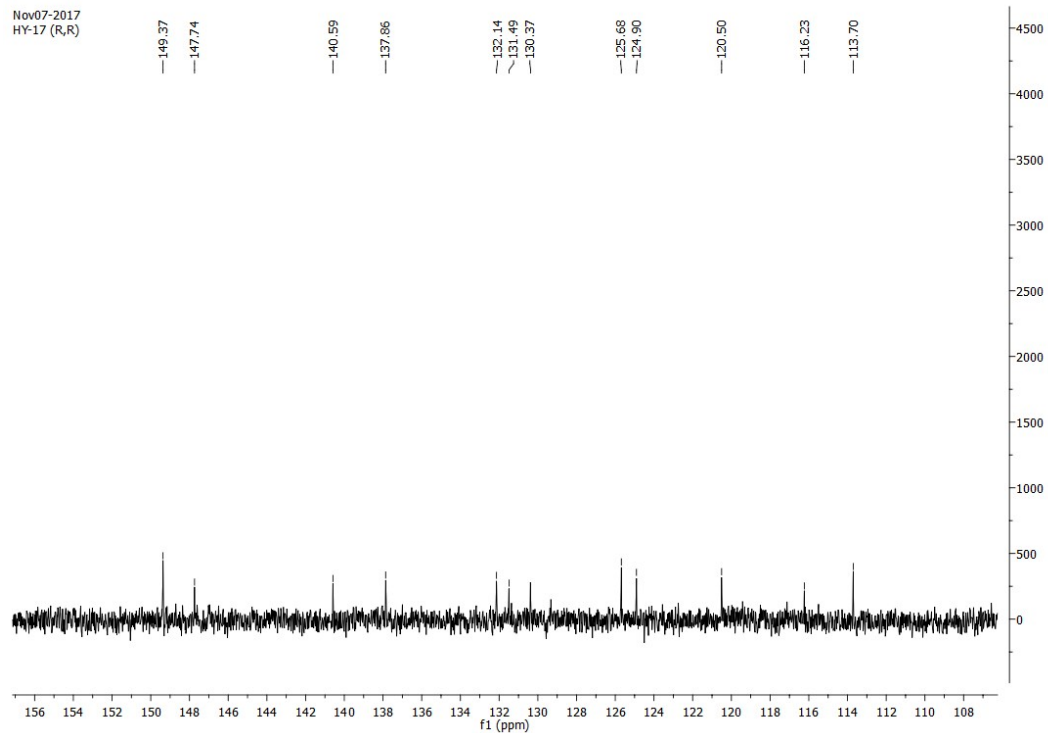
Fig. S2  $^1\text{H}$  NMR spectrum of complex **2**

HY-17 (R,R)

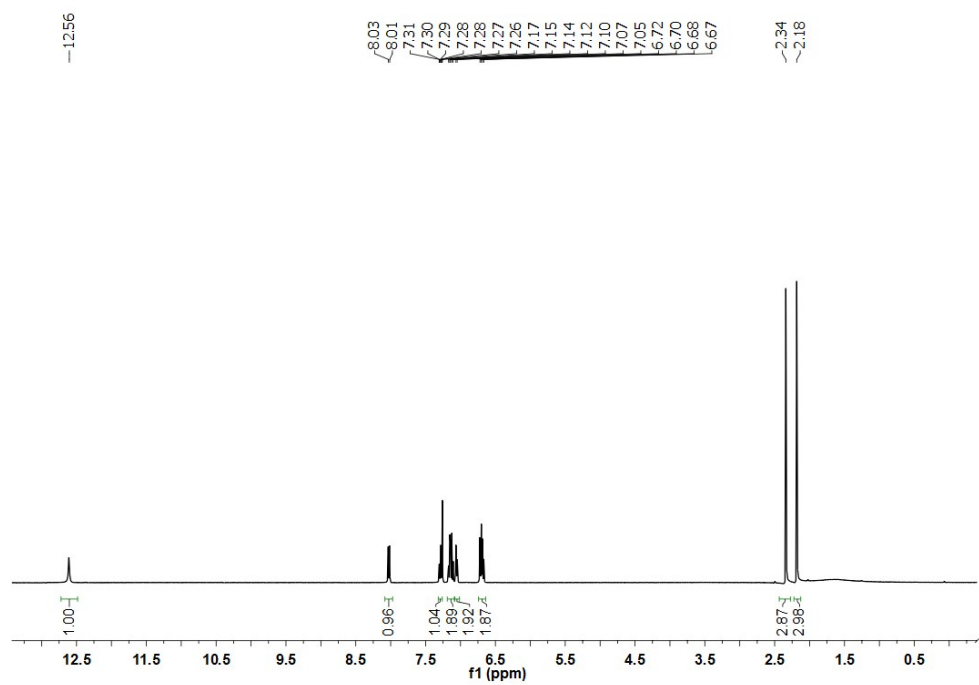


Nov07-2017  
HY-17 (R,R)





**Fig. S3**  $^{13}\text{C}$  NMR spectrum of complex 2



**Fig. S4**  $^1\text{H}$ NMR spectrum of Mefenamic acid

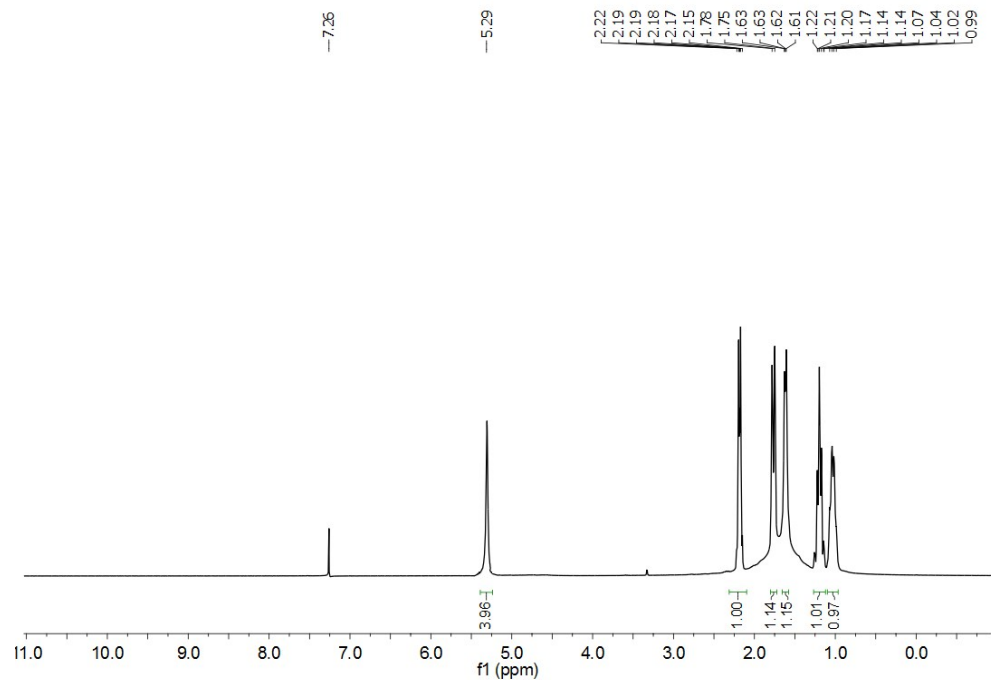


Fig. S5 (a)  $^1\text{H}$ NMR spectrum of DACH

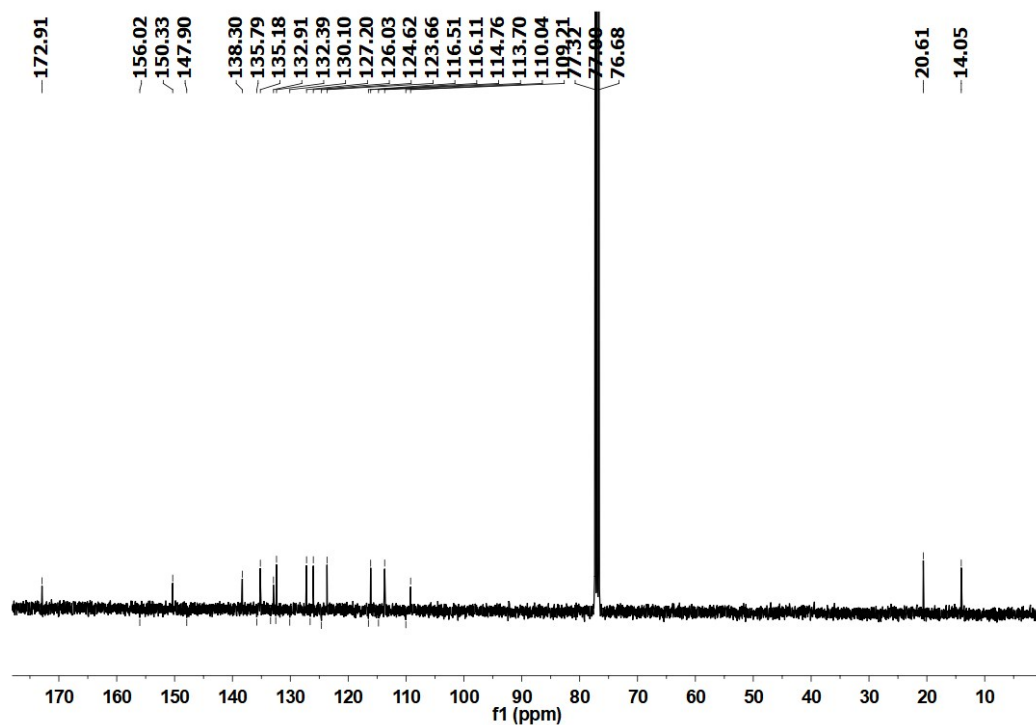


Fig. S5 (b)  $^{13}\text{C}$  NMR spectrum of free mefenamic acid

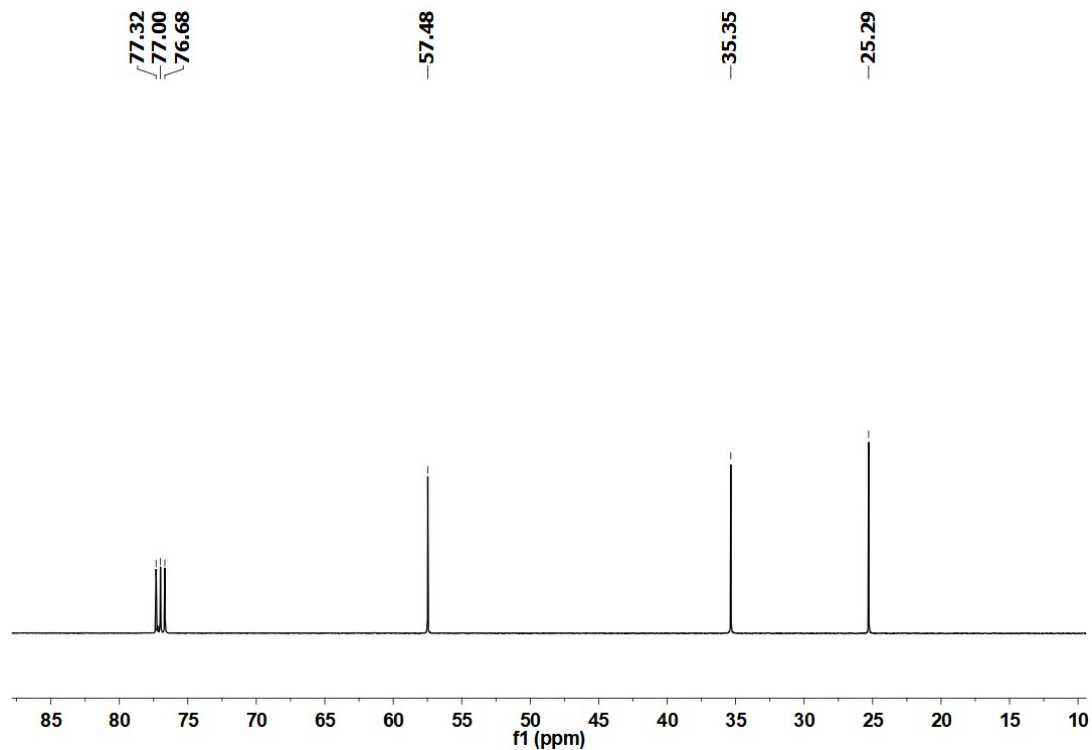


Fig. S5 (c)  $^{13}\text{C}$  NMR spectrum of free DACH

Sample Name	HY-16	Position	Vial 1	Instrument Name	QTOF	User Name	
Inj Vol	-1	InjPosition		SampleType	Sample	IRM Calibration Status	Success
Data Filename	HY-16.d	ACQ Method		Comment		Acquired Time	6/7/2018 11:00:02 AM

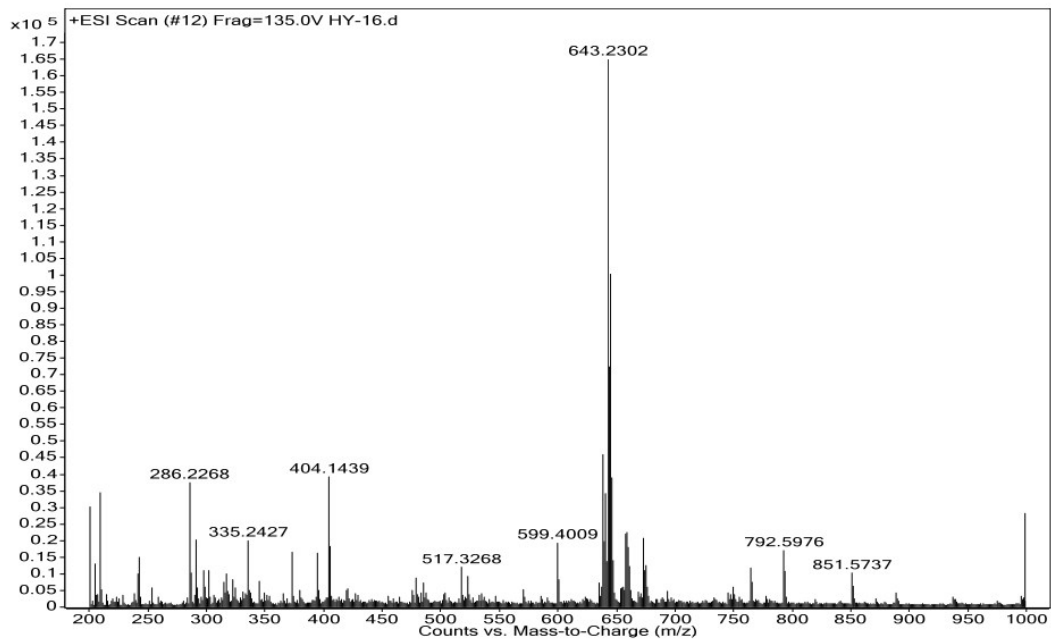


Fig. S6 ESI-MS spectrum of complex 1.



Sample Name	HY-17	Position	Vial 1	Instrument Name	QTOF	User Name	
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Data Filename	HY-17.d	ACQ Method		Comment		Acquired Time	6/7/2018 11:01:59 AM

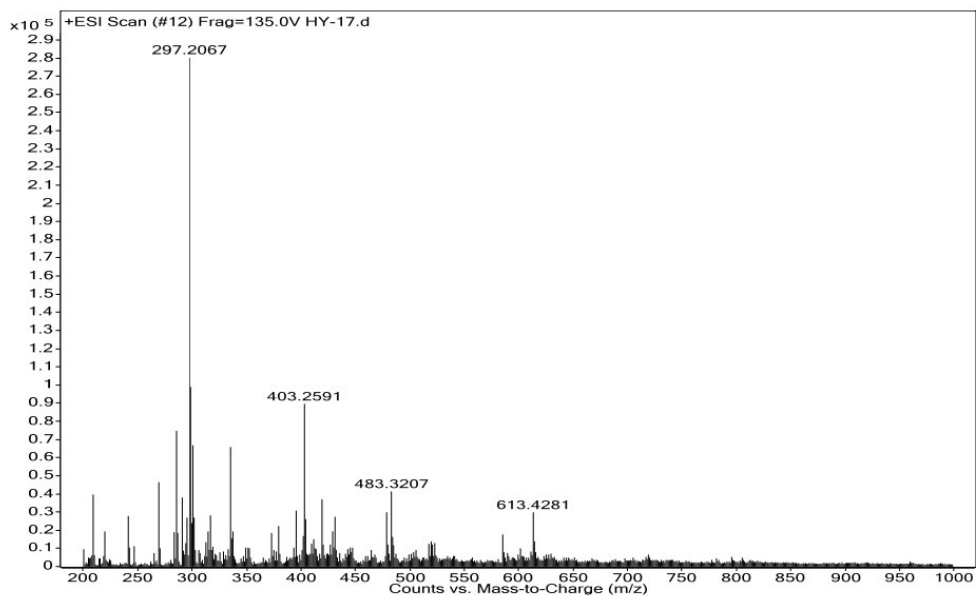
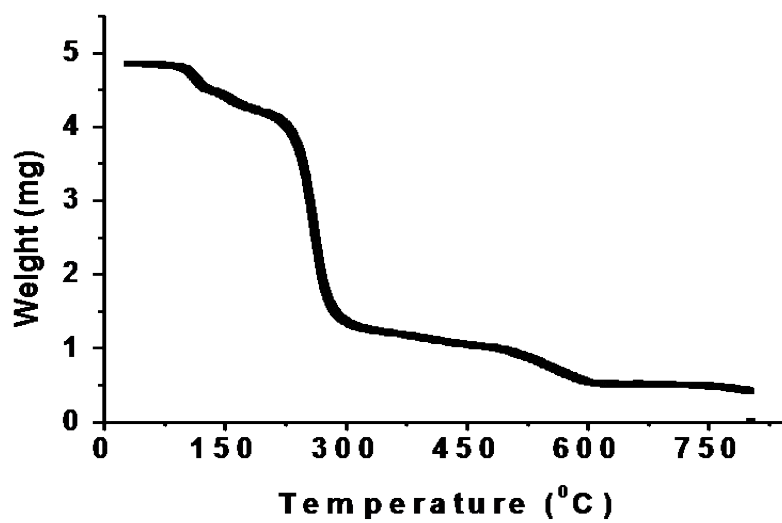
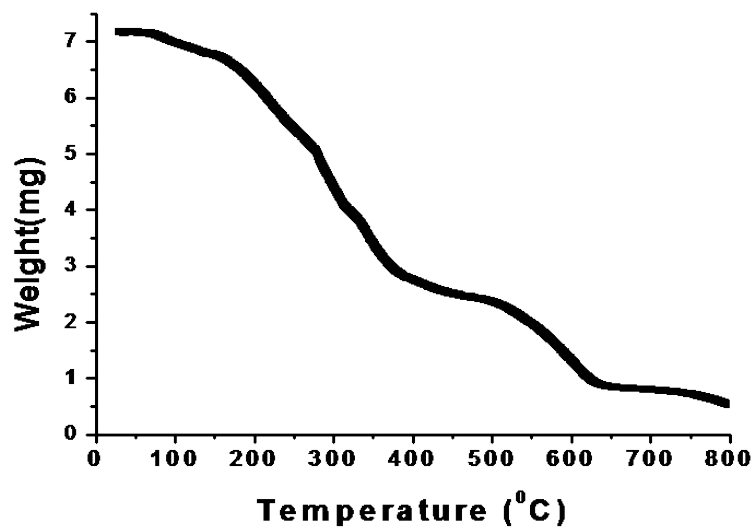


Fig. S7 ESI-MS spectrum of complex 2.

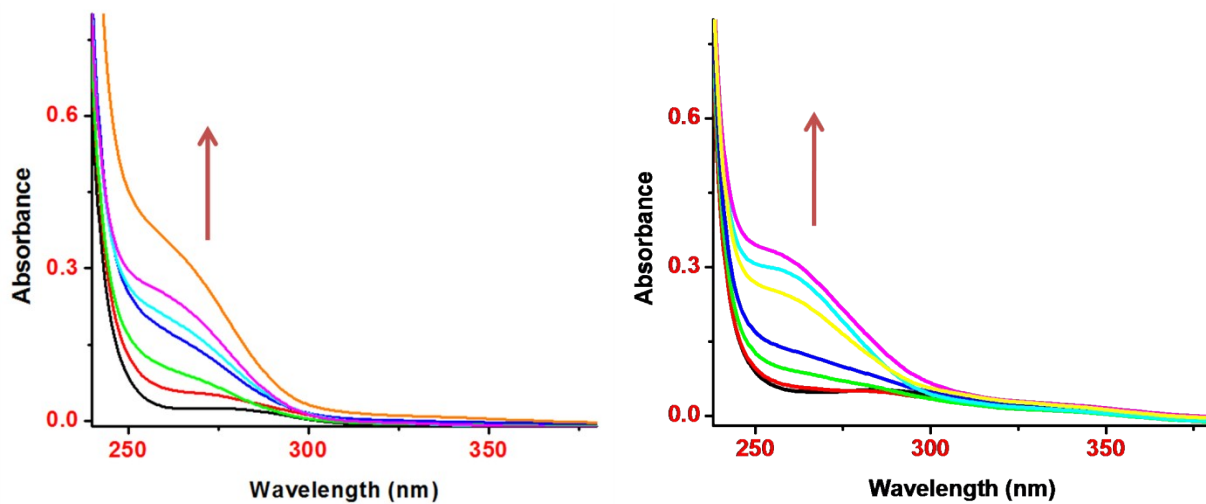


(a)



(b)

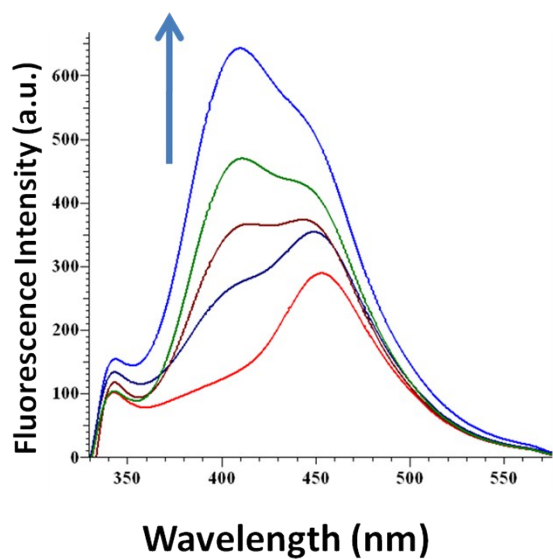
Fig. S8 TGA plot of (a) 1 and (b) 2



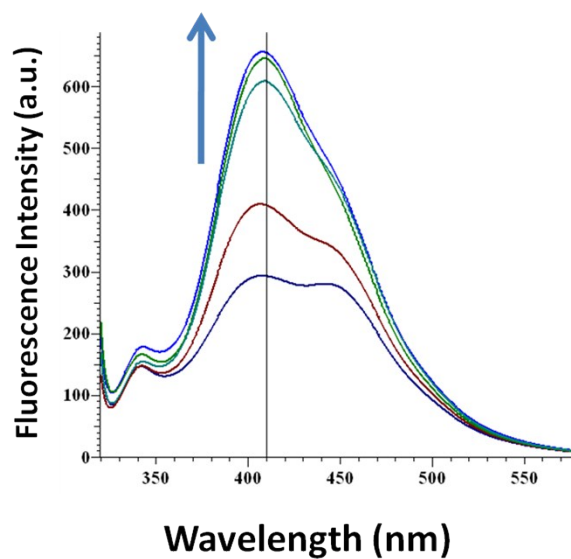
(a)

(b)

Fig. S9 Absorption spectra of complexes 1 (a) and 2 (b) in the presence of increasing ctDNA concentration.

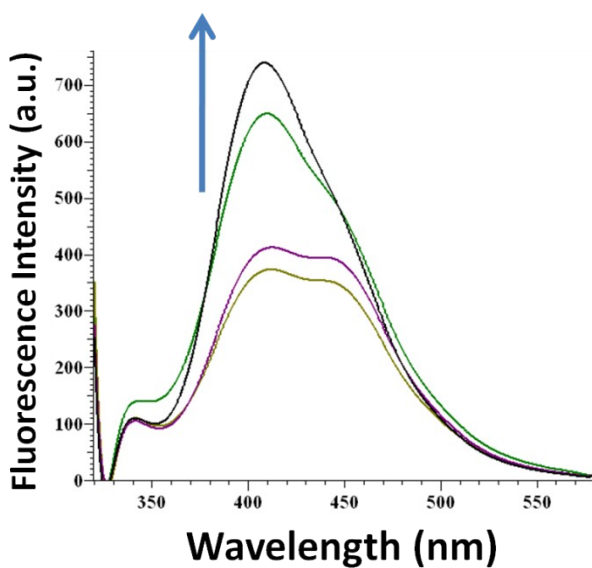


(a)

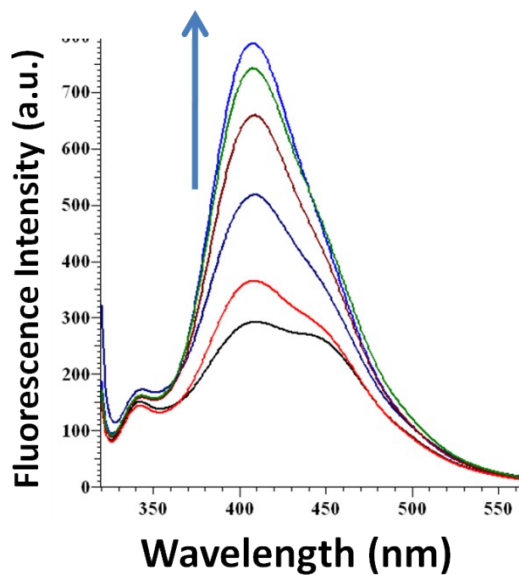


(b)

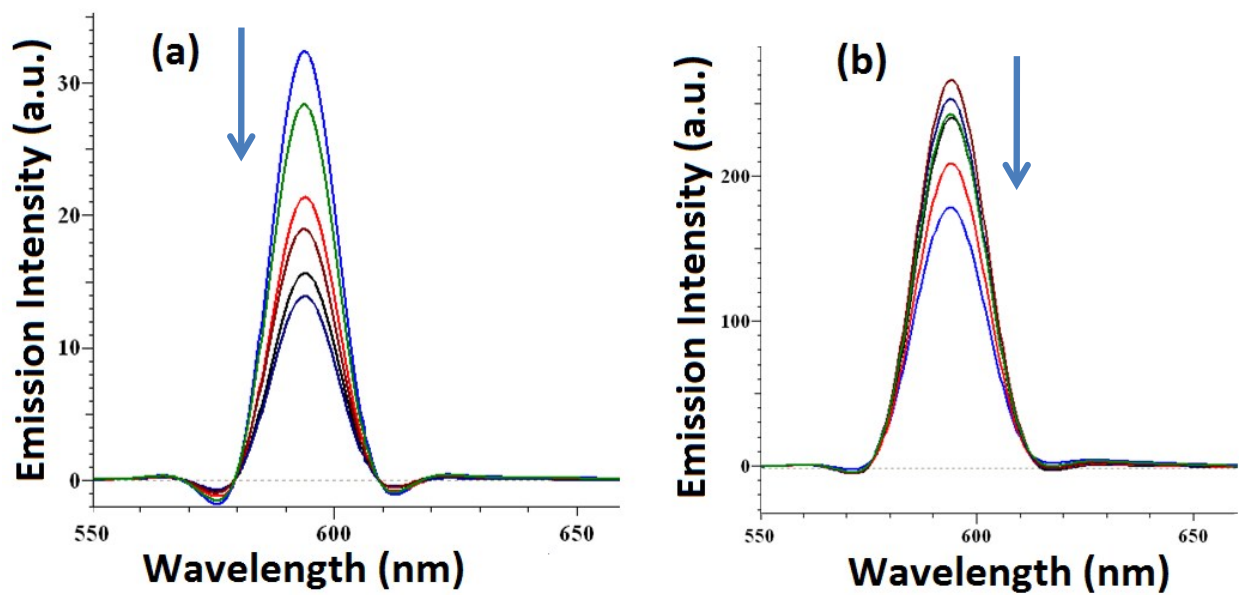
**Fig. S10** Emission spectra of (a) complex 1 and (b) complex 2 in TrisHCl buffer at pH 7.2 upon addition of ctDNA. Arrow indicates changes in intensity with increasing concentration of ctDNA.



(a)



**Fig. S11** Emission spectra of **(a)** complex 1 and **(b)** complex 2 in Tris HCl buffer at pH 7.2 upon addition of tRNA. Arrow indicates changes in intensity with increasing concentration of tRNA.



**Fig. S12** Emission titration spectra of the EB-tRNA system of complexes 1 and 2.

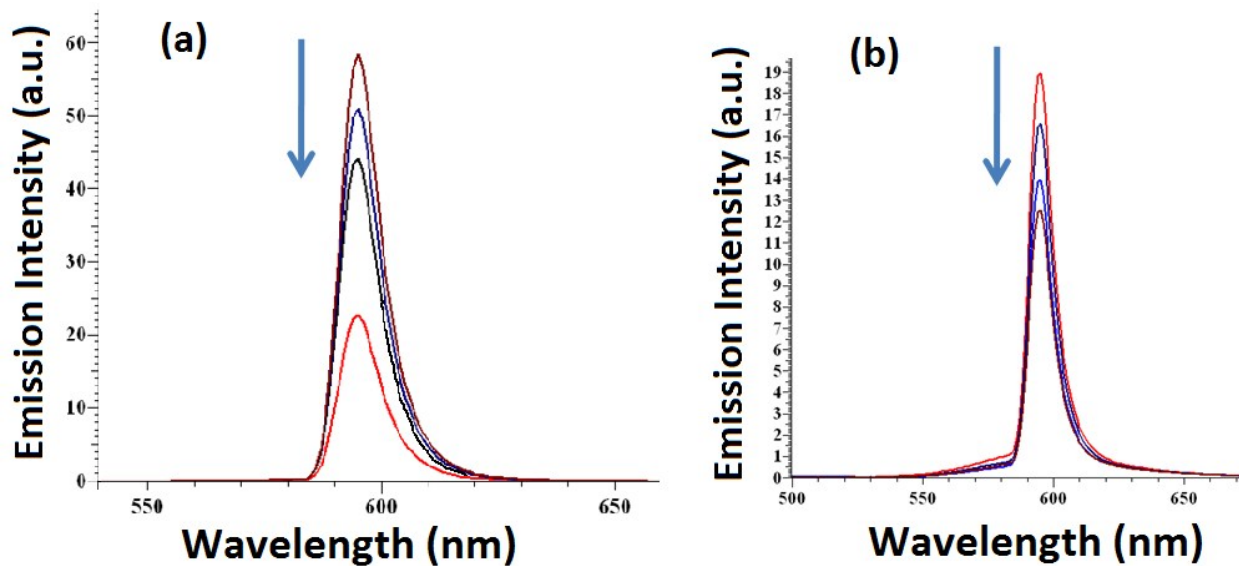


Fig. S13 Emission titration spectra of the EB–ctDNA system of complexes 1 and 2.

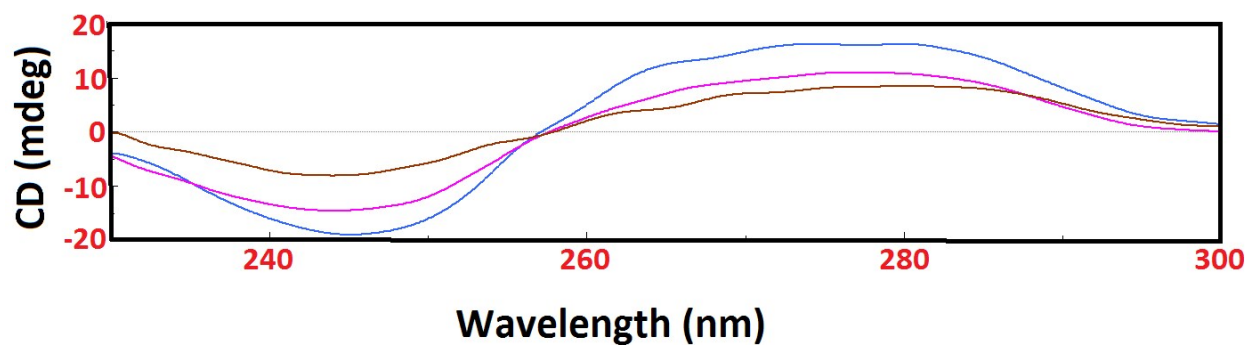
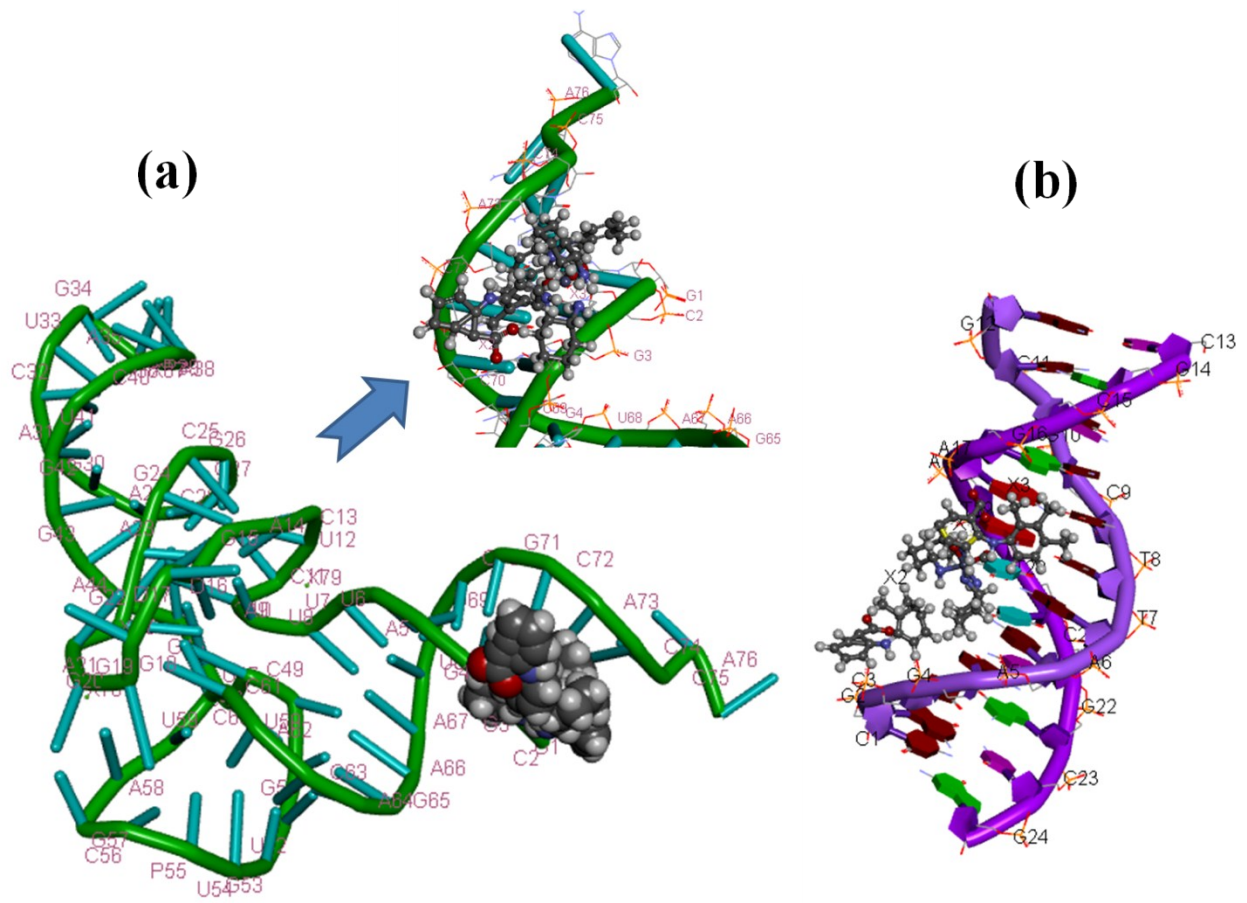
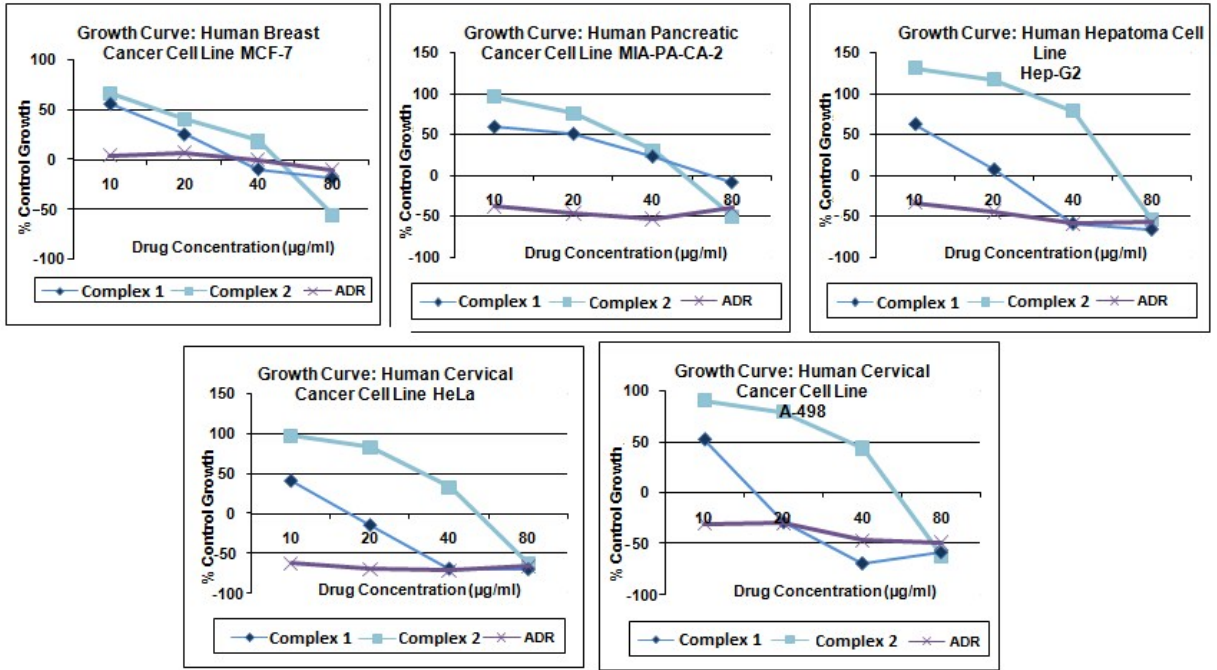


Fig. S14 CD spectra of ctDNA alone (pink), ctDNA + complex 1 (blue) and ctDNA + complex 2 (brown).



**Fig. S15** Molecular docked model of complex 2 with **(a)** tRNA **(b)** ctDNA



**Fig. S16** Growth curve showing % control growth versus drug concentration ( $\mu\text{g/ml}$ ) of 1 and 2 against different human carcinoma cell lines