Synthesis, DNA interaction and anticancer activity of 2-anthryl substituted benzimidazole derivatives

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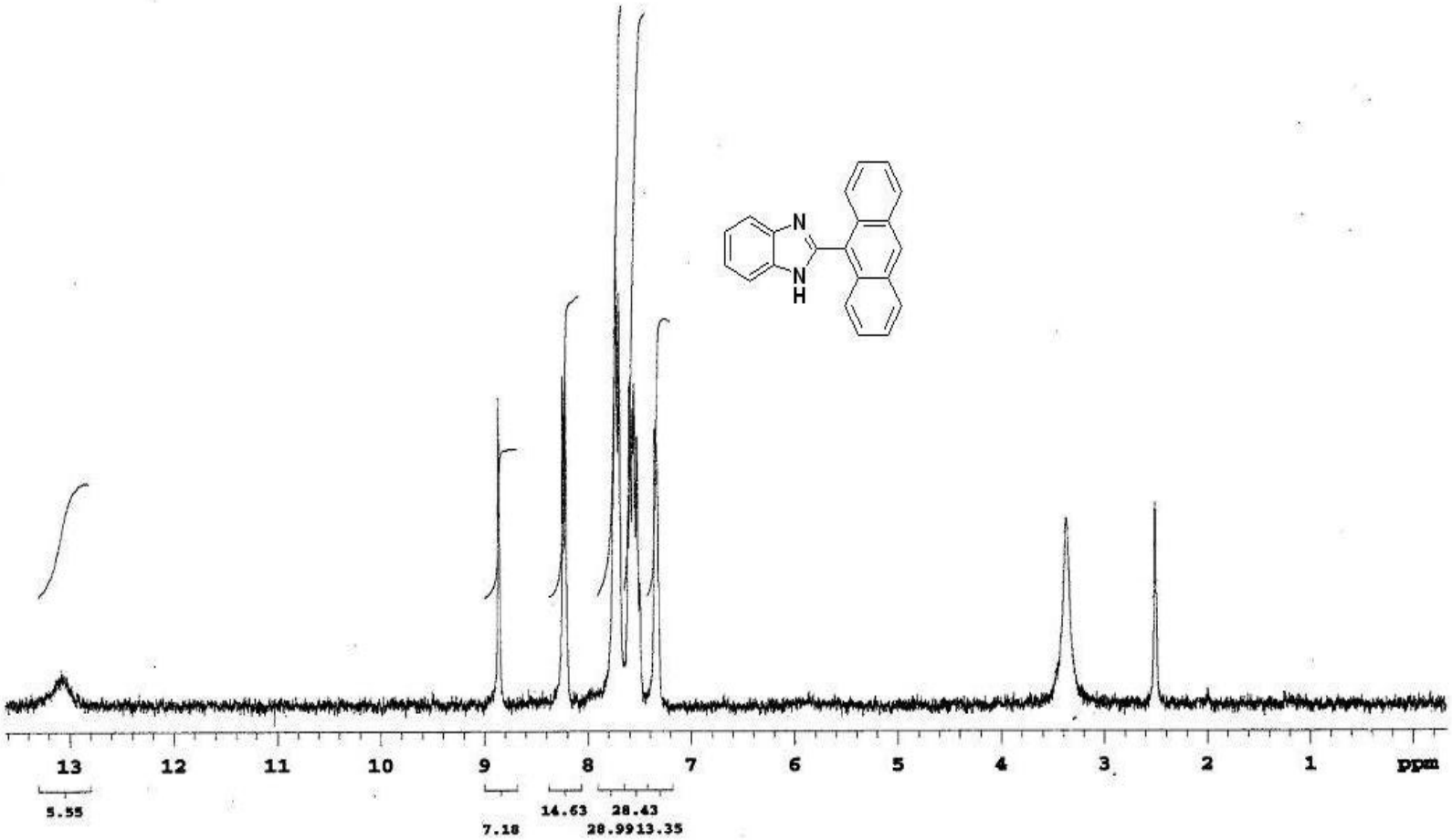

Figure 1S: 1HNMR (300MHz, DMSO-d6) Spectrum of compound 5

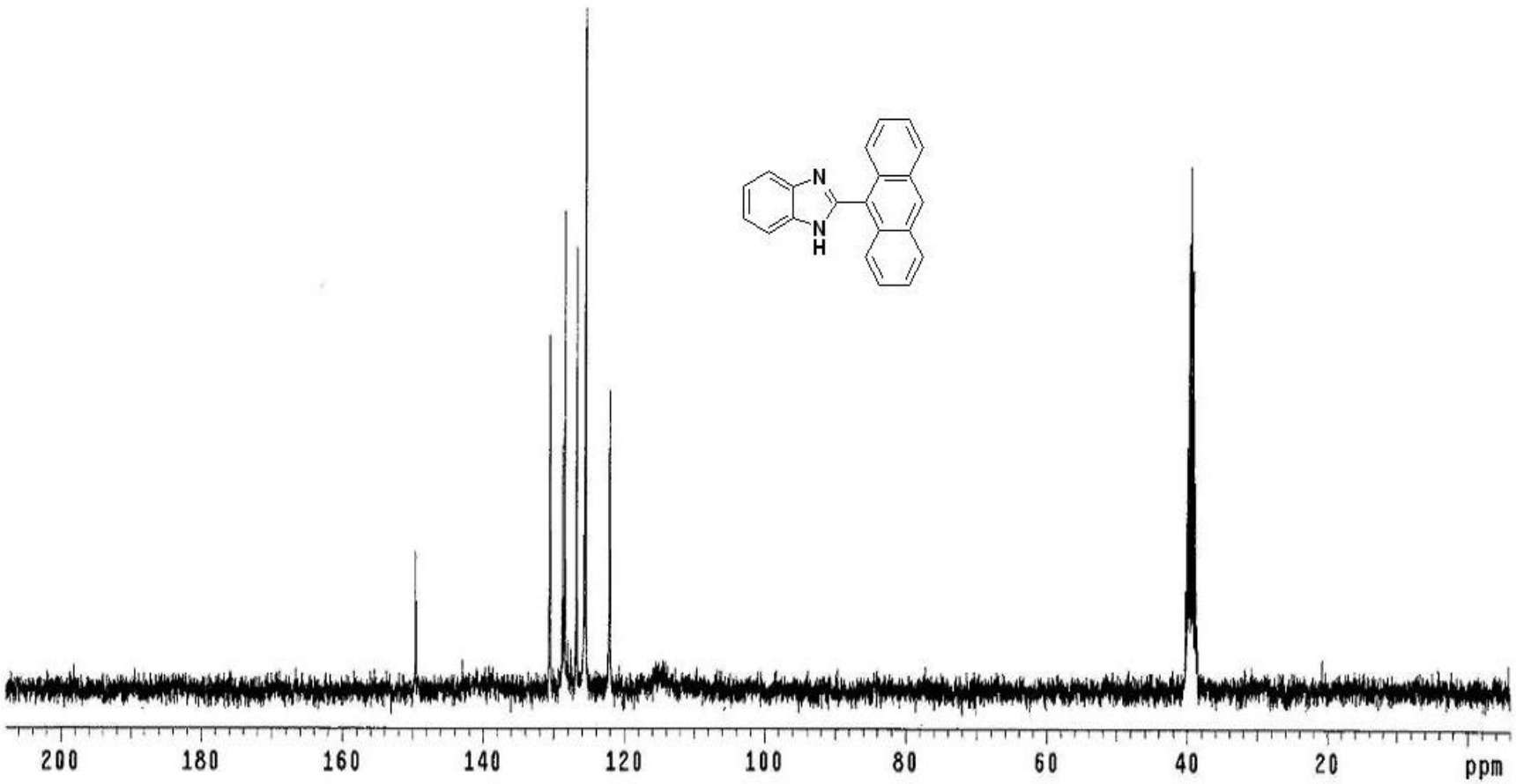

Figure 2S: 13C NMR (300MHz, DMSO-*d*6) Spectrum of compound 5

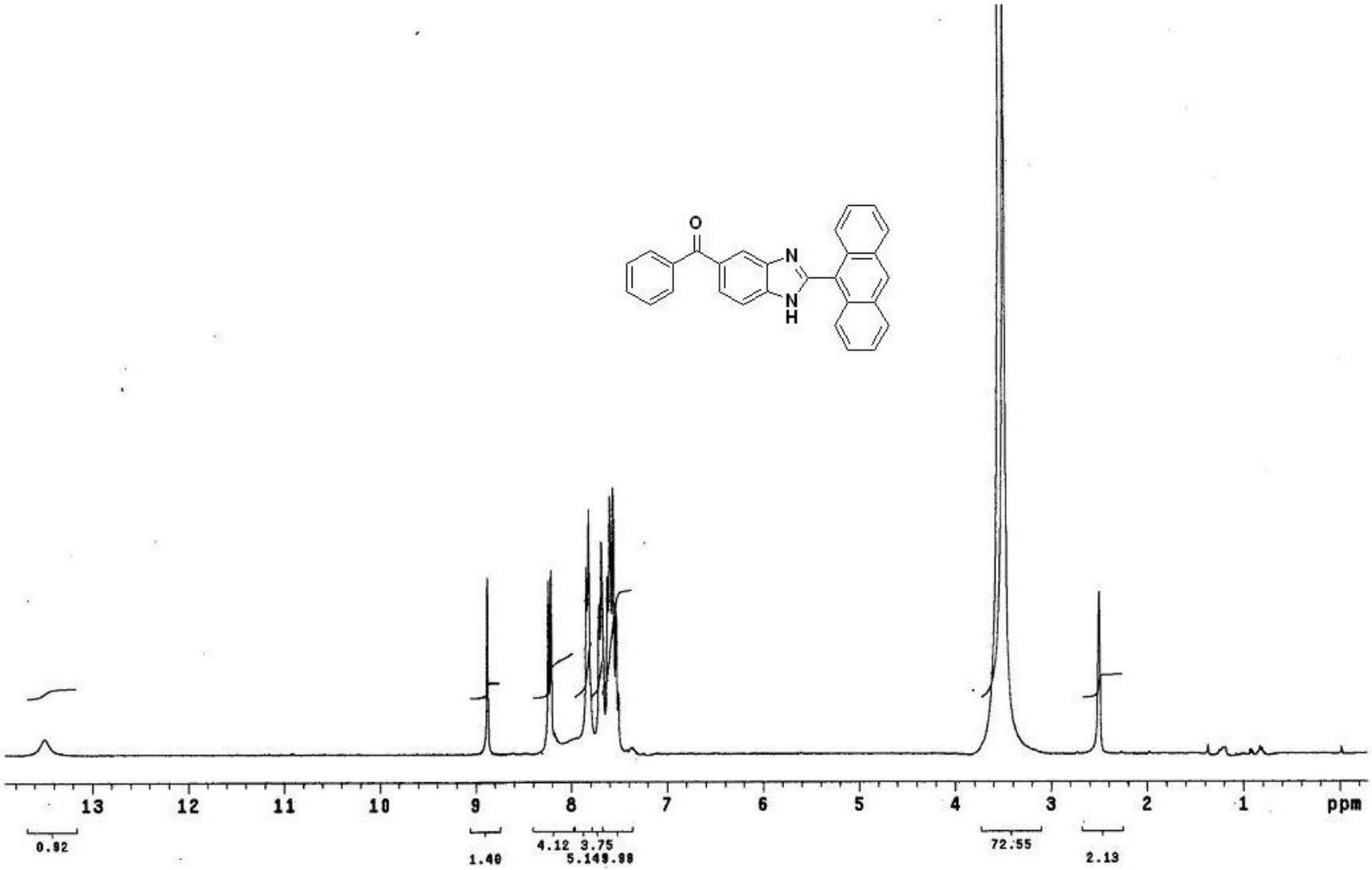

Figure 3S: 1HNMR (300 MHz, DMSO-d6) Spectrum of Compound 6

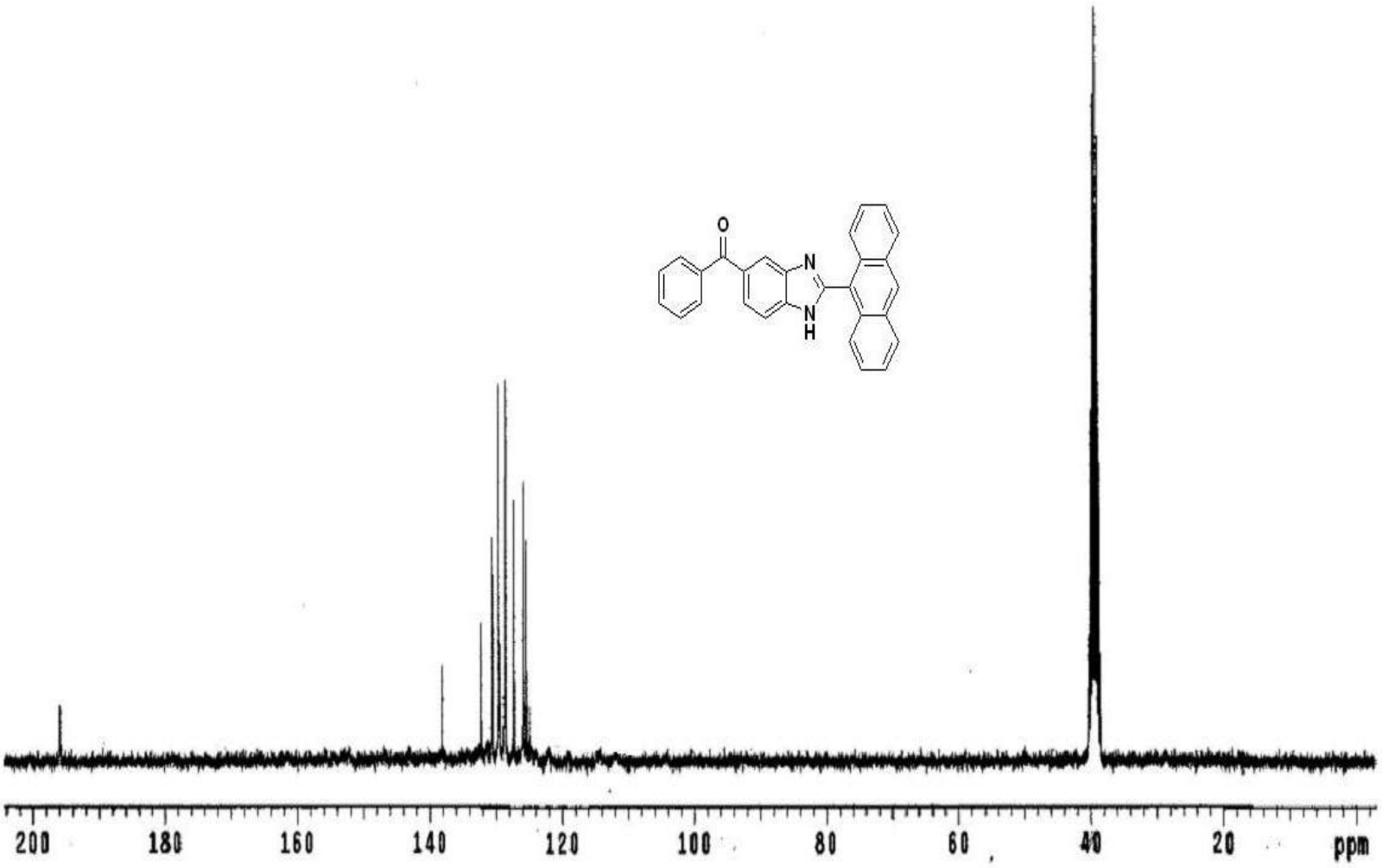

Figure 4S: 13C NMR (300 MHz, DMSO-d*6*) Spectrum of compound **6**

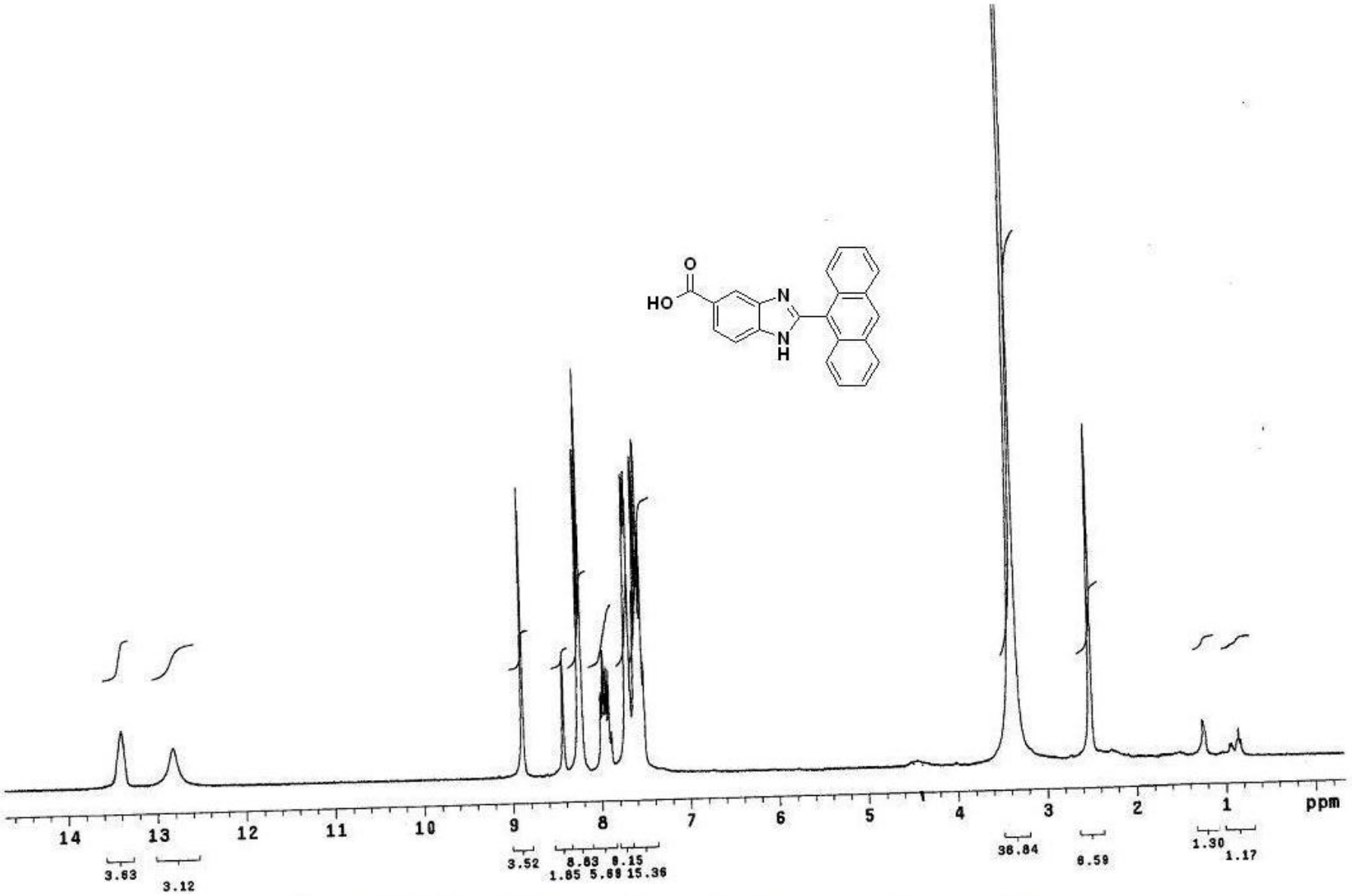

Figure 5S: 1H NMR (300MHz, DMSO-*d*6) Spectrum of compound **7**

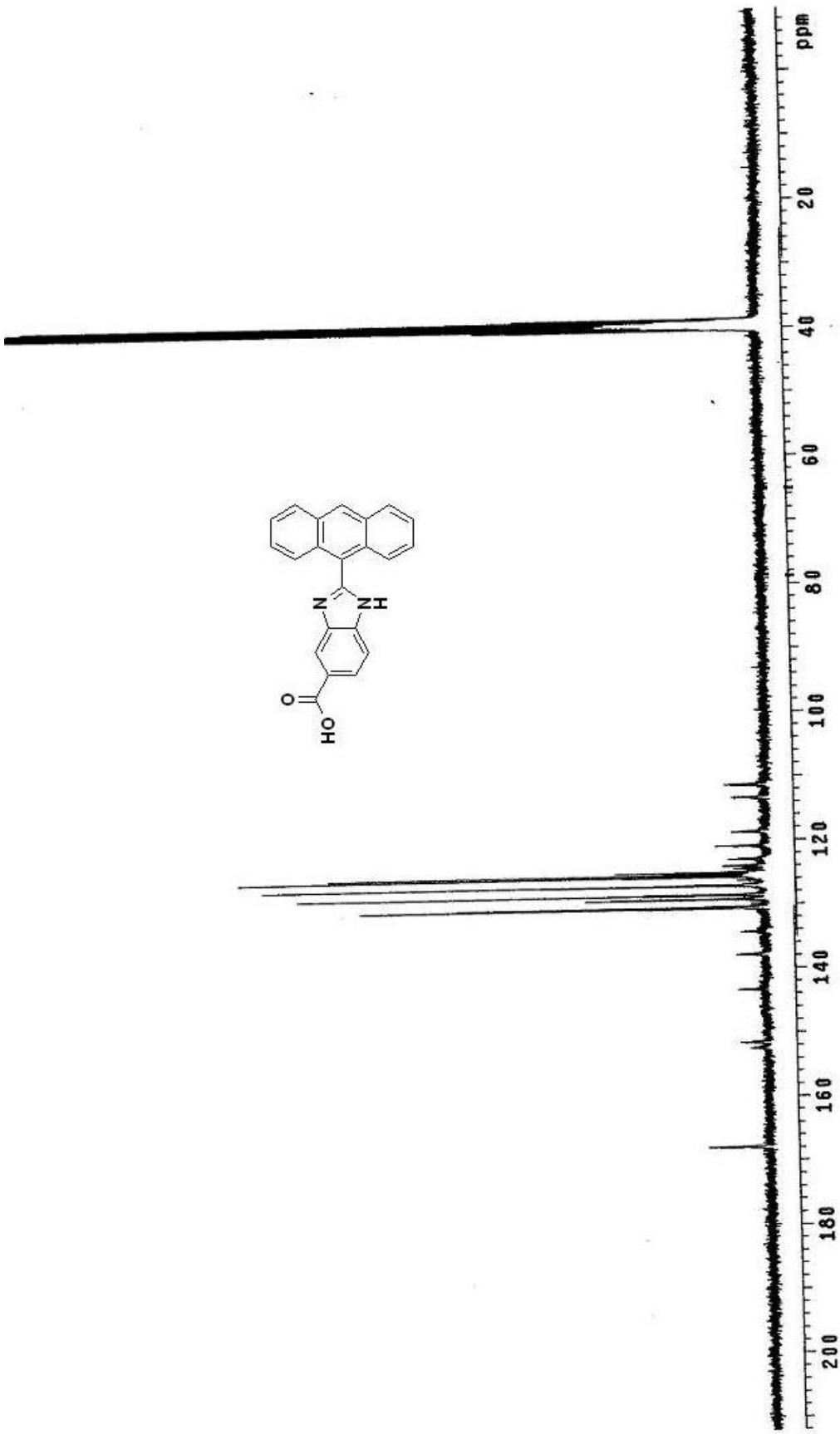

Figure 6S: 13C NMR (300MHz, DMMSO-d6) Spectrum of compound 7

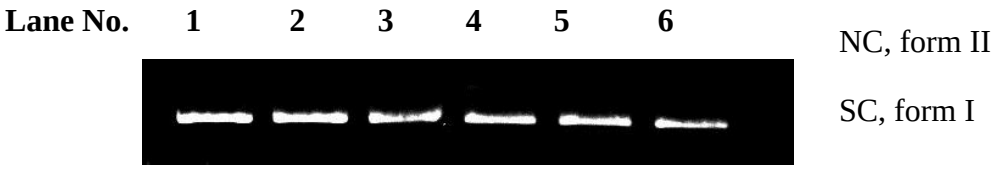

Fig. 10S Photograph of 1% Agarose gel showing cleavage of plasmid pBR322 DNA by **5** on incubation for 20 min and 30 min irradiation (365 nm). [DNA] = 200ng, Lane 1 = DNA Control, Lane 2-6= DNA + **5** 25, 50,100,150, 200 μM.

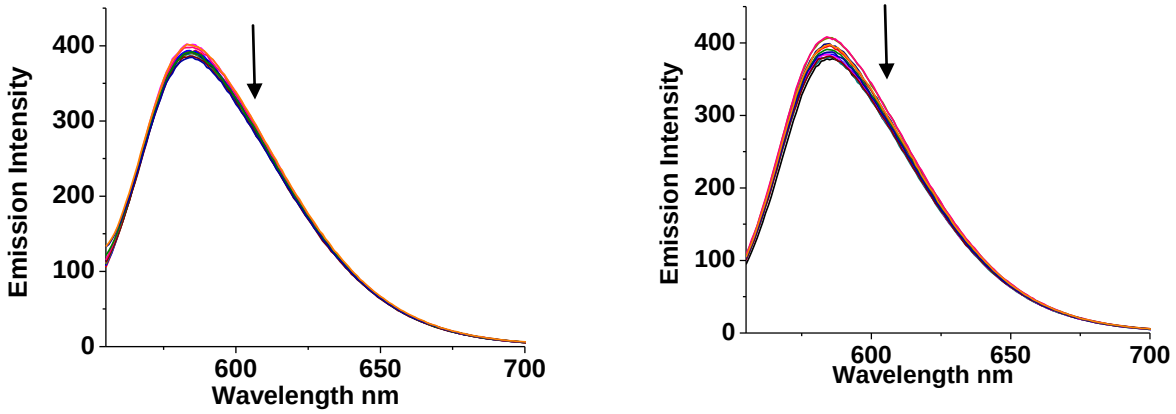

Fig. 11S Effect of addition of (**A**) **5** and (**B**) **6** on the emission intensity of the CT-DNA-bound ethidium bromide (20 μM) at different concentrations (0-100 μM) in 10% DMSO phosphate buffer (pH 7.2).

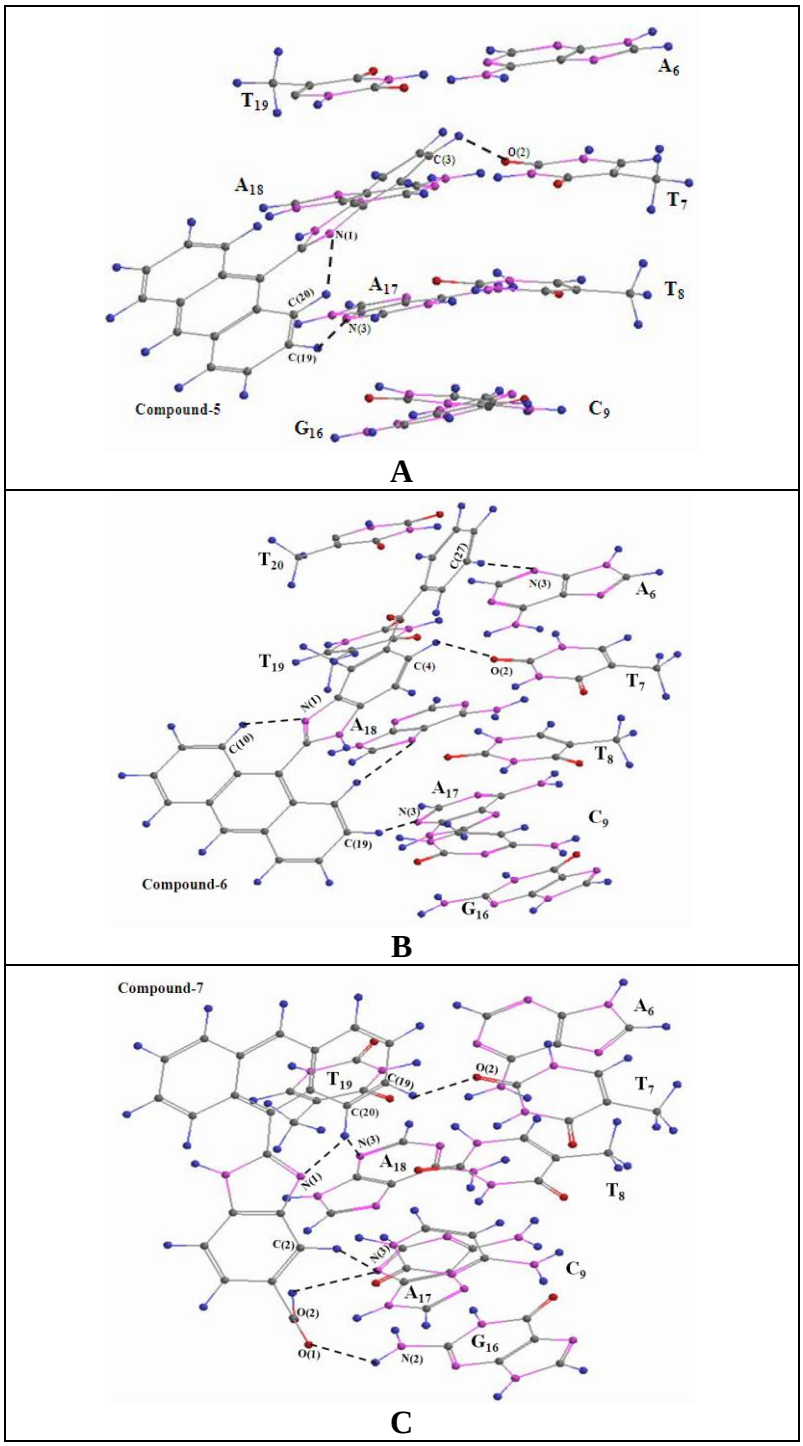

Fig. 12S H-bond interactions of (A) **5**, (B) **6**, (C) **7** with DNA

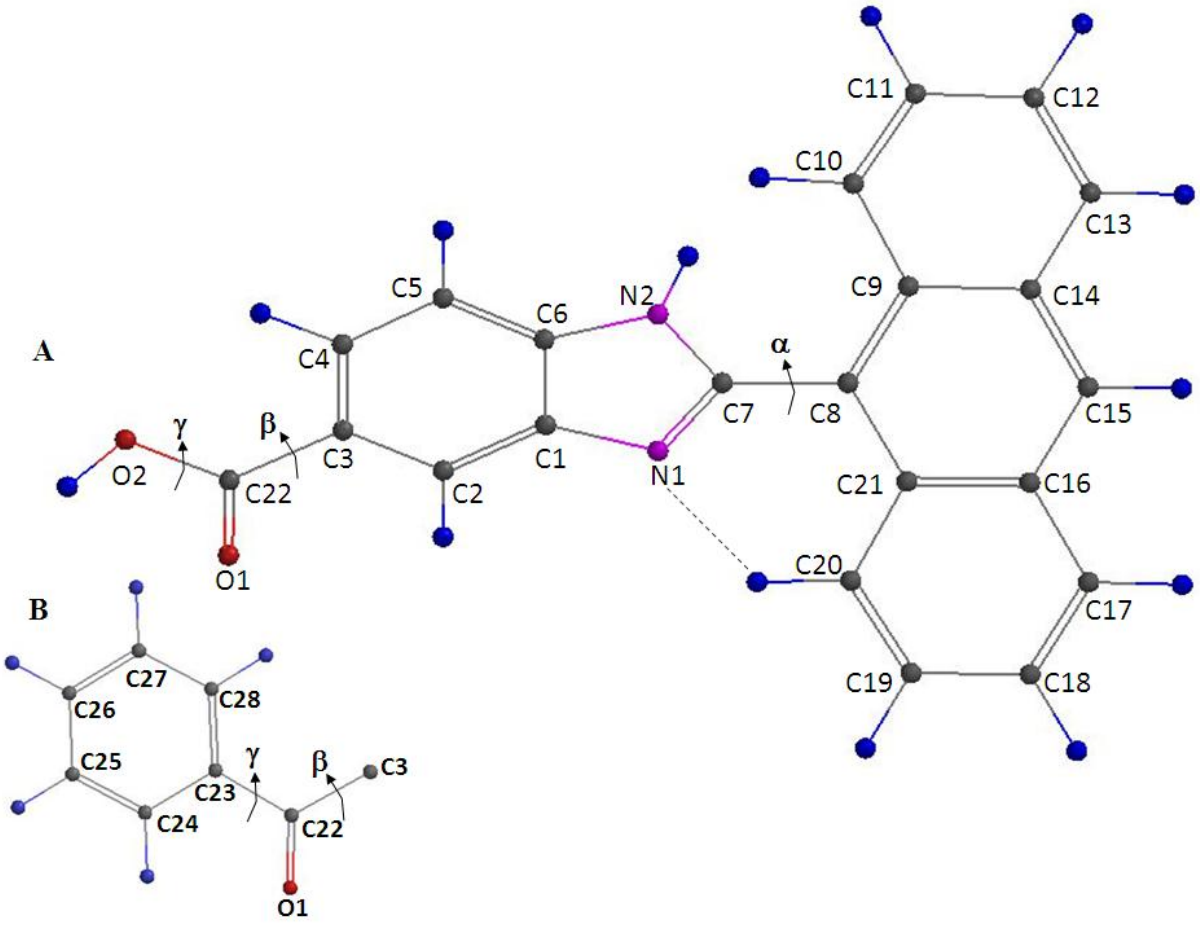

Figure 13S Depicts nomenclature and conventional numbering system for 2-anthryl substituted benzimidazole derivatives describing torsion angles α, β and γ.

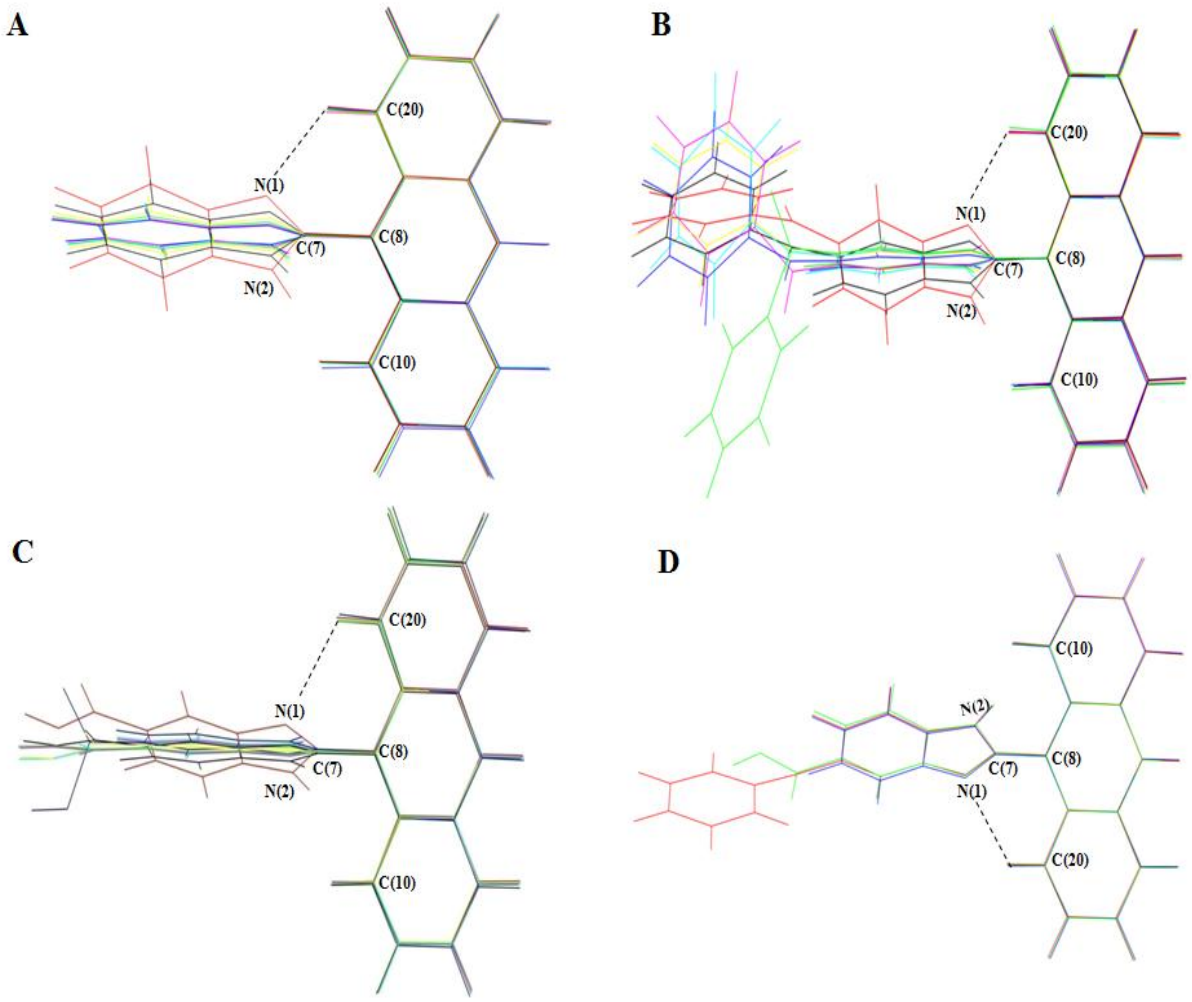

Figure 14S Depicts automated complete geometry optimizations performed using DFT, HF and semi-empirical methods such as RM1, PM6, PM3, MNDO and AM1 on A) 5 compound, B) 6 compound, C) 7 compound, D) DFT optimizations over 5-7 compounds.

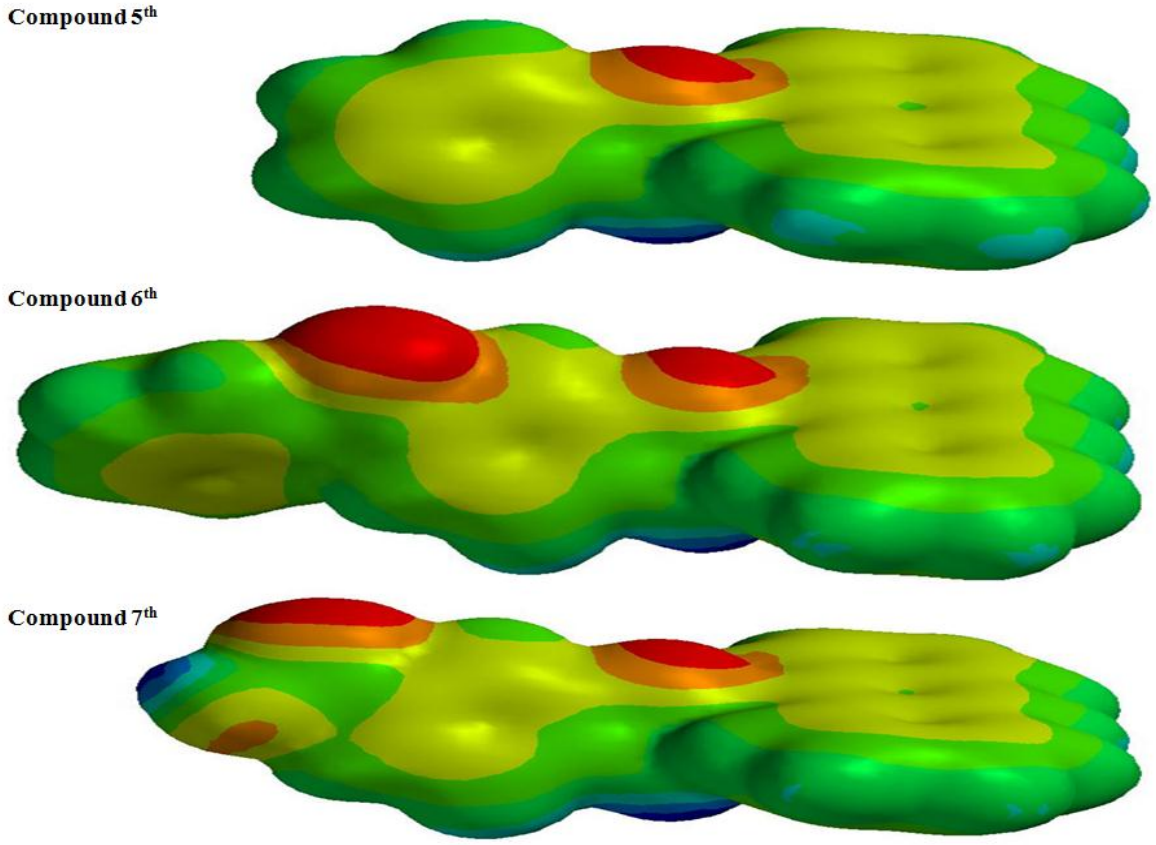

Figure 15S Depicts molecular electrostatic potentials (MEPs) calculated on 2-anthryl substituted benzimidazole derivatives (compounds 5, 6 and 7) by DFT method.

Table 1S Crystal structure data for **5**

Parameters	**Values for 5**
Empirical formula	$C_{21}H_{14}N_2$
Mol. Wt.	294.34
Wavelength (Å)	0.71073
T	296(2)K
Crystal system	Monoclinic
Space group	$P2_1/C$
a(Å)	12.8102(3)
b(Å)	12.3291(3)
c(Å)	10.2865(2)
α(deg)	90^o
β(deg)	112.067(1)
γ(deg)	90^o
V(Å^3)	1506.26(6)
Z	4
μ (mm^{-1})	0.077
F(000)	616
$D_{calcd.}$(g/cm^3)	1.298
total reelections	9838
$R_{int.}$	0.0984
No. of parameters refined	208
Final R (I>2σ)	0.1088
WR_2 (I>2σ)	0.2479

Table 2S Geometrical parameters for torsion angles and hydrogen bonding interactions after automated complete geometry optimizations by semi-empirical, HF and DFT methods.

Compound Name	**Methods**	**Torsion angles In (degree)**	Atoms involved 1-2-3	**Distance 1-2**	**Angle 1-2-3**	**Energy Kcal/mol**
5	Crystal structure	α=120.24°	N(1)...H-C(20)	2.502	114.44	0.0
5	DFT	α=123.33°	N(1)...H-C(20)	2.463	120.38	0.0
	HF-SCF	α=103.41°	N(1)...H-C(20)	2.763	115.54	0.011
	RM1	α=97.62°	N(1)...H-C(20)	2.813	114.80	102.523
	MNDO	α=89.79°	N(1)...H-C(20)	3.052	111.58	111.619
	PM6	α=93.72°	N(1)...H-C(20)	2.891	115.93	113.216
	PM3	α=91.27°	N(1)...H-C(20)	2.934	114.38	115.363
	AM1	α=90.95°	N(1)...H-C(20)	2.927	114.58	139.014
6	DFT	α=122.50°, β=152.61°, γ=151.85°	N(1)...H-C(20) O(1)...H-C(2) O(1)...H-C(28)	2.474 2.561 2.550	115.76 92.62 93.56	0.0
	HF-SCF	α=103.56°, β=151.17°, γ=148.33°	N(1)...H-C(20) O(1)...H-C(2) O(1)...H-C(28)	2.763 2.556 2.565	115.62 92.00 92.49	0.013
	RM1	α=74.05°, β=142.93°, γ=144.93°	N(1)...H-C(10) O(1)...H-C(2) O(1)...H-C(28)	2.689 - 2.658	115.76 - 90.25	92.552
	MNDO	α=89.47°, β=266.25°, γ=264.00°	O(1)...H-C(2) O(1)...H-C(28) N(1)...H-C(10)	- - 3.047	- - 111.67	106.974
	PM6	α=85.97°, β=156.16°, γ=133.02°	O(1)...H-C(2) O(1)...H-C(28) N(1)...H-C(10)	2.568 - 2.880	91.63 - 116.10	108.434
	PM3	α=90.92°, β=147.74°, γ=111.62°	O(1)...H-C(2) O(1)...H-C(28) N(1)...H-C(20)	- - 2.939	- - 114.42	109.805
	AM1	α=89.00°, β=148.54°, γ=147.82°	O(1)...H-C(2) O(1)...H-C(28) N(1)...H-C(10)	2.614 2.617 2.926	91.20 91.94 114.63	137.995
	DFT	α=122.51°, β=180.00°, γ=180.00°	O(1)...H-C(2) O(2)...H-C(4) N(1)...H-C(20)	2.545 2.395 2.479	94.69 97.73 120.30	0.0
	HF-SCF	α=104.10°, β=180.20°, γ=180.00°	O(1)...H-C(2) O(2)...H-C(4) N(1)...H-C(20)	2.529 2.398 2.756	94.31 97.26 115.67	0.011
	RM1	α=95.72°, β=194.25°,	O(1)...H-C(2) O(2)...H-C(4)	2.598 2.444	92.12 95.58	11.388

		γ=180.00°	N(1)...H-C(20)	2.842	114.59	
7	MNDO	α=89.58°, β=272.05°, γ=179.29°	O(1)...H-C(2) O(2)...H-C(4) N(1)...H-C(20)	- - 3.051	- - 111.57	20.906
	PM6	α=92.26°, β=180.56°, γ=180.12°	O(1)...H-C(2) O(2)...H-C(4) N(1)...H-C(20)	2.650 2.301 2.915	92.36 99.28 115.70	24.543
	PM3	α=89.92°, β=192.68°, γ=180.00°	O(1)...H-C(2) O(2)...H-C(4) N(1)...H-C(20)	2.663 2.481 2.950	92.16 96.55 114.36	25.988
	AM1	α=90.26°, β=181.48°, γ=180.34°	O(1)...H-C(2) O(2)...H-C(4) N(1)...H-C(10)	2.618 2.379 2.940	93.76 98.30 114.42	49.138

Table 3S Intra and Intermolecular hydrogen bonding interactions between compounds **5**/**6**/**7**-DNA complexes.

Name of DNA-Drug Complex	**Atoms involved 1-2-3**	**Distance in A° 1-2**	**Angle in Degree 1-2-3**
5	$N(3)A_{17}$..H-$C(19)_5$	2.209	143.18
	$O(2)C_6$….H-$C(19)_5$	2.256	105.36
	$N(1)_5$…H-C(4')T_{19}	2.636	106.18
	$O(2)T_7$….H-$C(3)_5$	2.423	124.05
	$N(3)A_{18}$…H-$C(2)_5$	2.395	133.12
	$N(1)_5$…H-$C(20)_5$	2.101	122.57
6	$N(3)A_{17}$..H-$C(19)_6$	2.207	144.35
	$O(2)C_6$….H-$C(19)_6$	2.284	105.28
	N(3)A18…H-$N(2)_6$	2.634	124.50
	$N(1)_6$…..H-C(4')T_{19}	2.232	158.31
	$N(1)_6$….H-C(4')C_6	2.424	125.09
	$N(1)_6$….H-C(5')C_6	2.550	111.45
	$O(1)_6$….H-C(4')T_7	2.306	136.52
	$N(3)A_5$…..H-$C(27)_6$	2.393	157.99
	$O(2)T_{19}$…..H-$C(24)_6$	2.720	127.23
	$O(2)T_6$……H-$C(4)_6$	2.279	129.97
	$N(1)_6$…H-$C(10)_6$	2.038	125.82
7	$N(3)A_{17}$..H-$O(2)_7$	2.552	102.89
	$N(3)A_{17}$..H-$C(2)_7$	2.396	135.40
	O(1')A_{18}..H-$O(2)_7$	2.061	165.65
	$O(1)_7$….H-N(2)G_{16}	2.125	111.56
	$O(2)_7$….H-C(1')A_{17}	1.970	133.88
	$O(2)_7$….H-C(1')A_{18}	1.873	149.99
	N(3)A18…H-$C(21)_6$	2.571	124.08
	$O(2)T_7$…..H-$C(19)_7$	1.970	131.09
	$O(2)T_8$…..H-$C(20)_7$	2.547	105.88
	$O(2)T_7$…..H-$C(18)_7$	2.668	103.96
	$N(1)_7$….H-C(4')C_9	2.639	108.93
	$N(1)_7$…H-$C(20)_7$	2.001	125.00