Synthesis and DFT studies of an antitumor active spiro-oxindole

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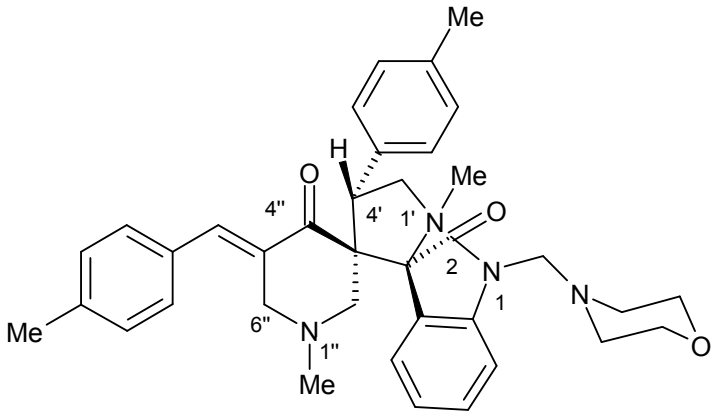

Structure of compound **7**

Table S1. Selected bond lengths (Å) of compound **7** obtained from single crystal X-ray studies and theoretical calculations by AM1, PM3, and DFT methods.

Geometric parameters	Experimental X-ray data	AM1	PM3	DFT
O1—C13	1.248 (4)	1.2382	1.2193	1.2468
O2—C25	1.223 (4)	1.2398	1.2189	1.2460
O3—C2	1.399 (5)	1.4231	1.4148	1.4617
O3—C3	1.400 (5)	1.4228	1.4145	1.4670
N1—C1	1.449 (5)	1.4502	1.4906	1.4859
N1—C4	1.438 (5)	1.4485	1.4905	1.4922
N1—C5	1.486 (5)	1.4584	1.4915	1.4722
N2—C5	1.438 (5)	1.4472	1.4761	1.4753
N2—C6	1.448 (5)	1.4097	1.4357	1.4144
N2—C13	1.383 (5)	1.4078	1.4304	1.3823
N3—C12	1.447 (4)	1.4694	1.5017	1.4778
N3—C14	1.474 (5)	1.4401	1.4717	1.4733
N3—C15	1.499 (5)	1.4576	1.4839	1.4810
N4—C26	1.440 (4)	1.4528	1.4844	1.4767
N4—C27	1.479 (4)	1.4452	1.4787	1.4749
N4—C28	1.452 (4)	1.4554	1.4861	1.4717
C1—C2	1.543 (6)	1.5336	1.5314	1.5350
C3—C4	1.543 (6)	1.5342	1.5310	1.5297
C6—C7	1.416 (5)	1.3945	1.3885	1.3874
C6—C11	1.392 (5)	1.4327	1.4132	1.4073
C7—C8	1.407 (6)	1.4000	1.3955	1.4035
C8—C9	1.369 (6)	1.3900	1.3890	1.3947
C9—C10	1.422 (5)	1.4034	1.3978	1.4046
C10—C11	1.398 (5)	1.3805	1.3836	1.3843
C11—C12	1.567 (5)	1.5243	1.5173	1.5177
C12—C13	1.562 (5)	1.5856	1.5671	1.5626
C12—C17	1.653 (5)	1.5712	1.5737	1.5920
C15—C16	1.515 (5)	1.5417	1.5306	1.5517

C16—C17	1.545 (5)	1.5598	1.5744	1.5866
C16—C18	1.574 (5)	1.4923	1.5030	1.5180
C17—C25	1.543 (5)	1.5286	1.5467	1.5410
C17—C26	1.559 (5)	1.5349	1.5362	1.5352
C18—C19	1.383 (6)	1.4020	1.3980	1.4019
C18—C24	1.435 (6)	1.4011	1.3963	1.4052
C19—C20	1.429 (6)	1.3923	1.3890	1.3956
C20—C22	1.430 (7)	1.3992	1.3957	1.4002
C21—C22	1.568 (7)	1.4805	1.4852	1.5189
C22—C23	1.366 (6)	1.3996	1.3954	1.4017
C23—C24	1.442 (6)	1.3925	1.3886	1.3944
C25—C29	1.472 (4)	1.4841	1.4984	1.4965
C28—C29	1.534 (5)	1.4960	1.4933	1.5147
C29—C30	1.355 (5)	1.3490	1.3448	1.3543
C30—C31	1.449 (5)	1.4535	1.4618	1.4593
C31—C32	1.429 (5)	1.4051	1.3995	1.4135
C31—C37	1.419 (5)	1.4005	1.3960	1.4114
C32—C33	1.370 (5)	1.3904	1.3880	1.3890
C33—C34	1.409 (6)	1.4010	1.3965	1.4027
C34—C35	1.501 (6)	1.4805	1.4852	1.5168
C34—C36	1.420 (6)	1.3988	1.3954	1.4015
C36—C37	1.355 (5)	1.3931	1.3890	1.3924
RMSE		0.032	0.033	0.031
Maximum difference		0.088	0.083	0.067

Table S2. Selected bond angles (°) of compound **7** obtained from single crystal X-ray studies and theoretical calculations by AM1, PM3, and DFT methods.

Geometric parameters	Experimental X-ray data	AM1	PM3	DFT
C2—O3—C3	109.9 (3)	112.11	112.85	109.48
C1—N1—C4	108.0 (3)	114.04	112.00	111.24
C1—N1—C5	111.3 (3)	114.10	112.76	114.94
C4—N1—C5	113.1 (3)	114.65	113.32	113.33
C5—N2—C6	123.5 (3)	125.21	123.35	127.00
C5—N2—C13	122.4 (3)	124.23	125.03	121.68
C6—N2—C13	113.2 (3)	109.69	108.62	111.03
C12—N3—C14	116.0 (3)	115.94	117.37	116.38
C12—N3—C15	105.9 (3)	109.35	107.42	106.98
C14—N3—C15	119.2 (3)	114.49	114.55	115.19
C26—N4—C27	109.7 (3)	112.89	112.39	114.90
C26—N4—C28	109.6 (3)	111.43	111.58	110.58
C27—N4—C28	111.6 (3)	112.20	112.37	112.16
N1—C1—C2	109.0 (4)	112.52	109.88	108.58
C1—C2—O3	111.6 (4)	111.92	112.46	110.78
O3—C3—C4	111.9 (4)	111.66	112.73	110.73
C3—C4—N1	109.9 (4)	112.27	110.07	108.85
N1—C5—N2	111.1 (3)	115.66	109.14	114.43
N2—C6—C7	130.4 (4)	128.87	128.33	129.15
N2—C6—C11	108.6 (3)	110.50	109.98	109.63
C7—C6—C11	121.0 (4)	120.50	121.68	121.14
C6—C7—C8	118.9 (4)	118.19	117.79	118.15
C7—C8—C9	120.9 (4)	121.31	120.98	120.99
C8—C9—C10	119.6 (4)	120.73	120.97	120.30
C9—C10—C11	120.8 (4)	119.03	118.91	118.92
C10—C11—C6	118.7 (4)	120.12	119.61	120.40
C10—C11—C12	132.4 (3)	130.08	129.40	129.88
C6—C11—C12	108.9 (3)	109.65	110.86	109.49

C11—C12—N3	109.6 (3)	110.77	109.40	112.12
C11—C12—C13	102.3 (3)	100.47	100.82	101.40
N3—C12—C13	113.8 (3)	112.15	112.36	111.88
C11—C12—C17	118.4 (3)	115.19	117.51	118.68
N3—C12—C17	103.1 (3)	106.91	104.09	102.44
C13—C12—C17	110.2 (3)	111.43	112.91	110.63
C12—C13—N2	106.8 (3)	109.30	109.22	108.42
C12—C13—O1	126.7 (3)	126.92	129.31	127.50
N2—C13—O1	126.3 (3)	123.50	121.42	123.93
N3—C15—C16	103.0 (3)	108.62	105.08	103.21
C15—C16—C17	102.0 (3)	105.87	106.53	105.10
C15—C16—C18	118.6 (3)	112.13	112.52	113.52
C17—C16—C18	115.8 (3)	115.87	115.19	115.83
C16—C17—C12	104.0 (3)	104.82	104.58	104.06
C16—C17—C25	112.3 (3)	109.19	109.76	108.00
C12—C17—C25	106.6 (3)	109.84	111.13	107.37
C16—C17—C26	110.8 (3)	110.20	109.98	115.99
C12—C17—C26	114.3 (3)	114.21	114.90	111.60
C25—C17—C26	108.6 (3)	108.48	106.48	109.39
C16—C18—C19	119.2 (4)	118.94	119.16	119.65
C16—C18—C24	125.9 (4)	122.28	121.84	122.26
C19—C18—C24	114.9 (4)	118.75	118.99	118.08
C18—C19—C20	121.7 (4)	120.67	120.44	121.16
C19—C20—C22	123.3 (4)	120.48	120.39	120.78
C21—C22—C20	123.2 (5)	120.53	120.32	120.95
C21—C22—C23	121.5 (5)	120.53	120.39	120.92
C20—C22—C23	115.3 (4)	118.94	119.28	118.11
C22—C23—C24	121.8 (5)	120.64	120.30	121.28
C23—C24—C18	122.8 (4)	120.52	120.60	120.59
C17—C25—O2	122.9 (3)	120.93	121.31	120.36
C17—C25—C29	116.0 (3)	118.88	118.91	118.83

O2—C25—C29	121.1 (3)	120.18	119.73	120.81
C17—C26—N4	107.6 (3)	112.35	111.40	106.55
N4—C28—C29	112.3 (3)	114.21	111.82	112.08
C28—C29—C25	117.8 (3)	119.45	118.08	120.12
C28—C29—C30	125.0 (3)	122.22	123.22	124.90
C25—C29—C30	117.1 (3)	118.33	118.64	114.99
C29—C30—C31	124.5 (3)	127.38	127.76	132.05
C30—C31—C32	119.2 (3)	118.60	118.03	117.05
C30—C31—C37	120.9 (3)	122.53	122.71	125.70
C32—C31—C37	120.0 (3)	118.84	119.22	117.25
C31—C32—C33	120.3 (4)	120.53	120.32	121.58
C32—C33—C34	118.9 (4)	120.51	120.36	120.77
C33—C34—C35	119.4 (4)	120.37	120.22	120.90
C33—C34—C36	120.8 (4)	119.03	119.35	118.11
C35—C34—C36	119.8 (4)	120.59	120.43	120.97
C34—C36—C37	120.4 (4)	120.57	120.35	121.39
C31—C37—C36	119.4 (4)	120.51	120.39	120.89
RMSE		6.5	6.0	7.6
Maximum difference		2.49	2.30	2.33

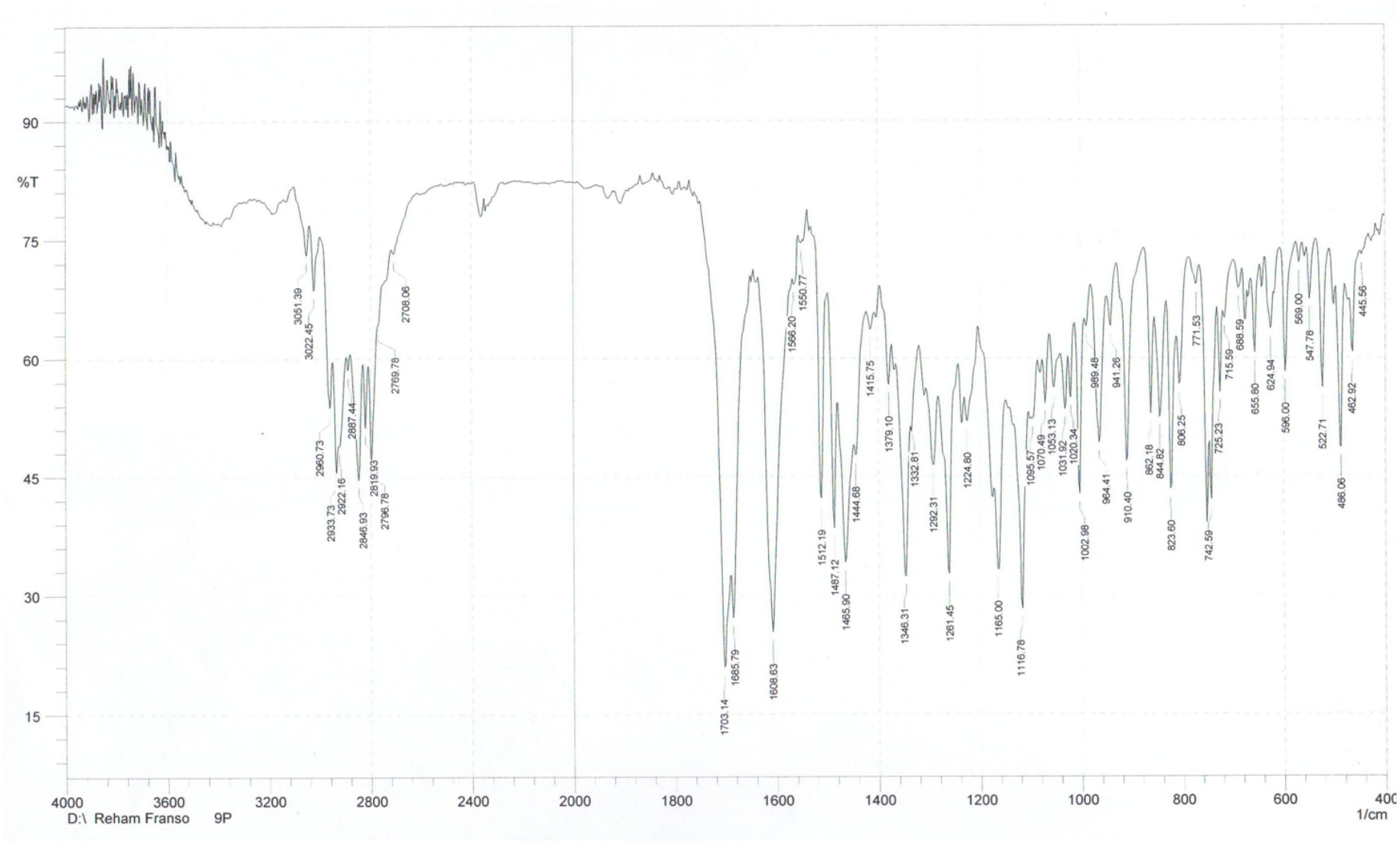

Figure S1. IR spectrum of compound **7** (KBr pellet).

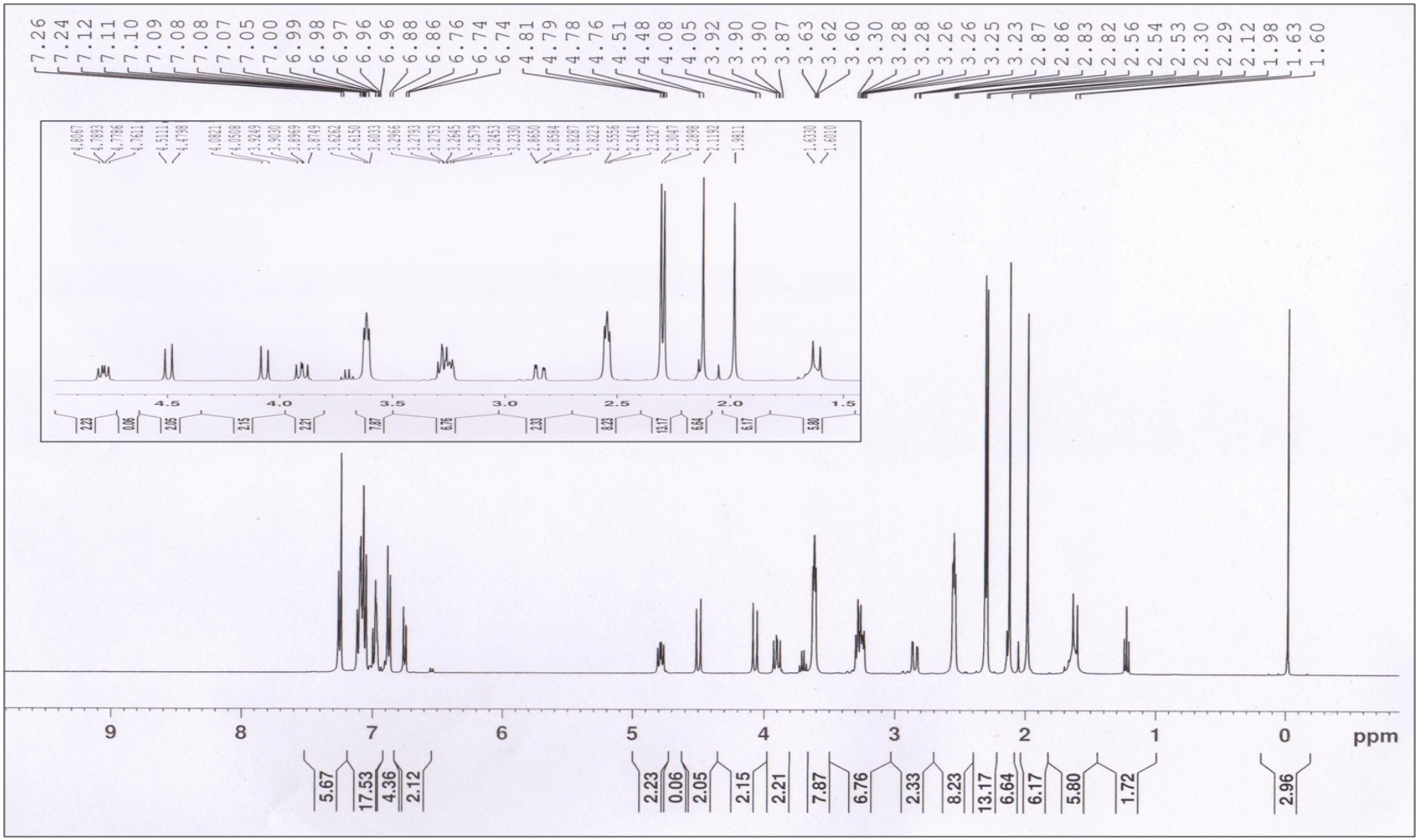

Figure S2. ^{1}H-NMR spectrum of compound **7** in $CDCl_3$ (signals due to trace amount of ethanol "solvent of crystallization" are observed).

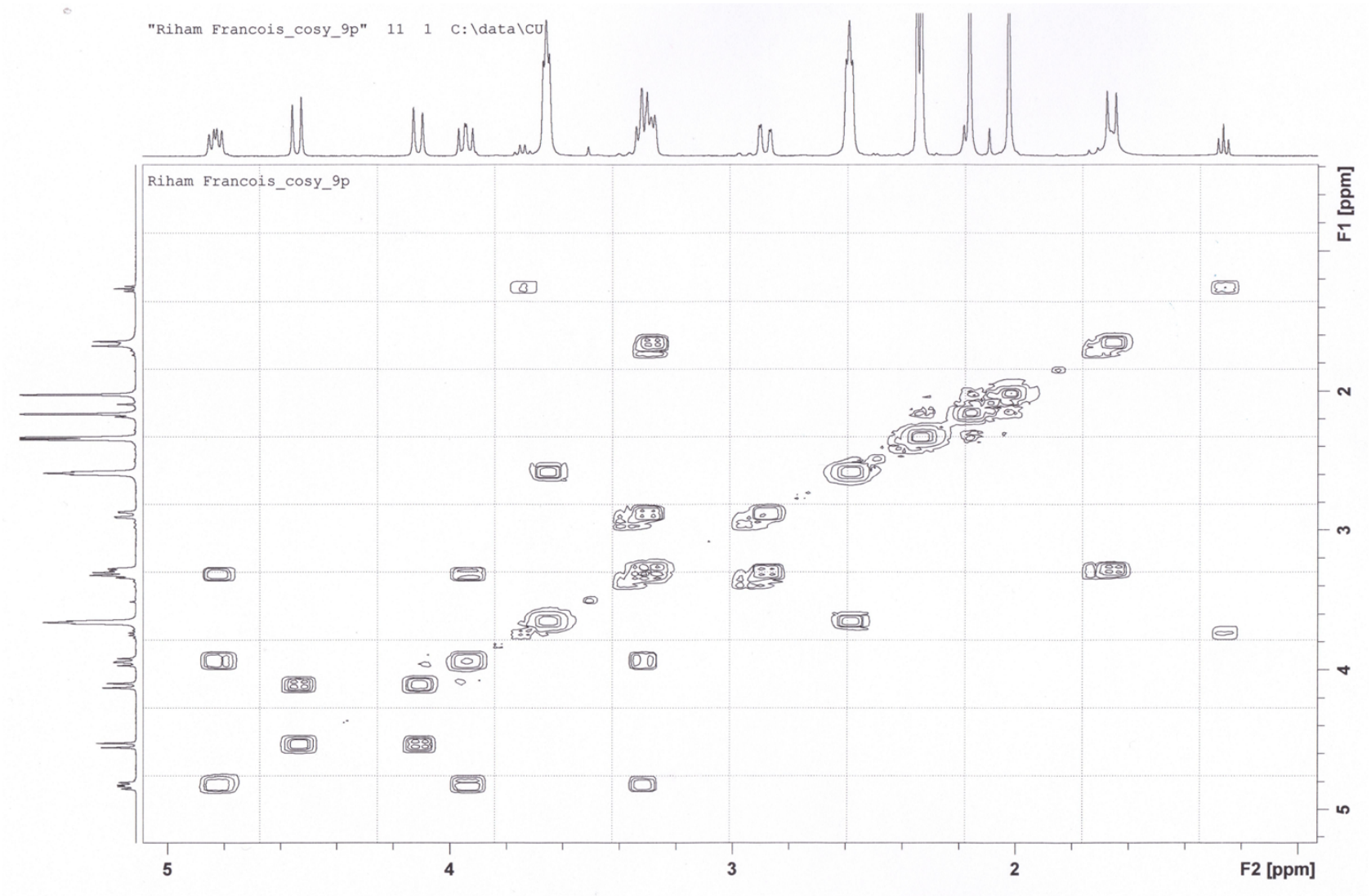

Figure S3. ^{1}H, ^{1}H-COSY spectrum of compound **7** in $CDCl_3$.

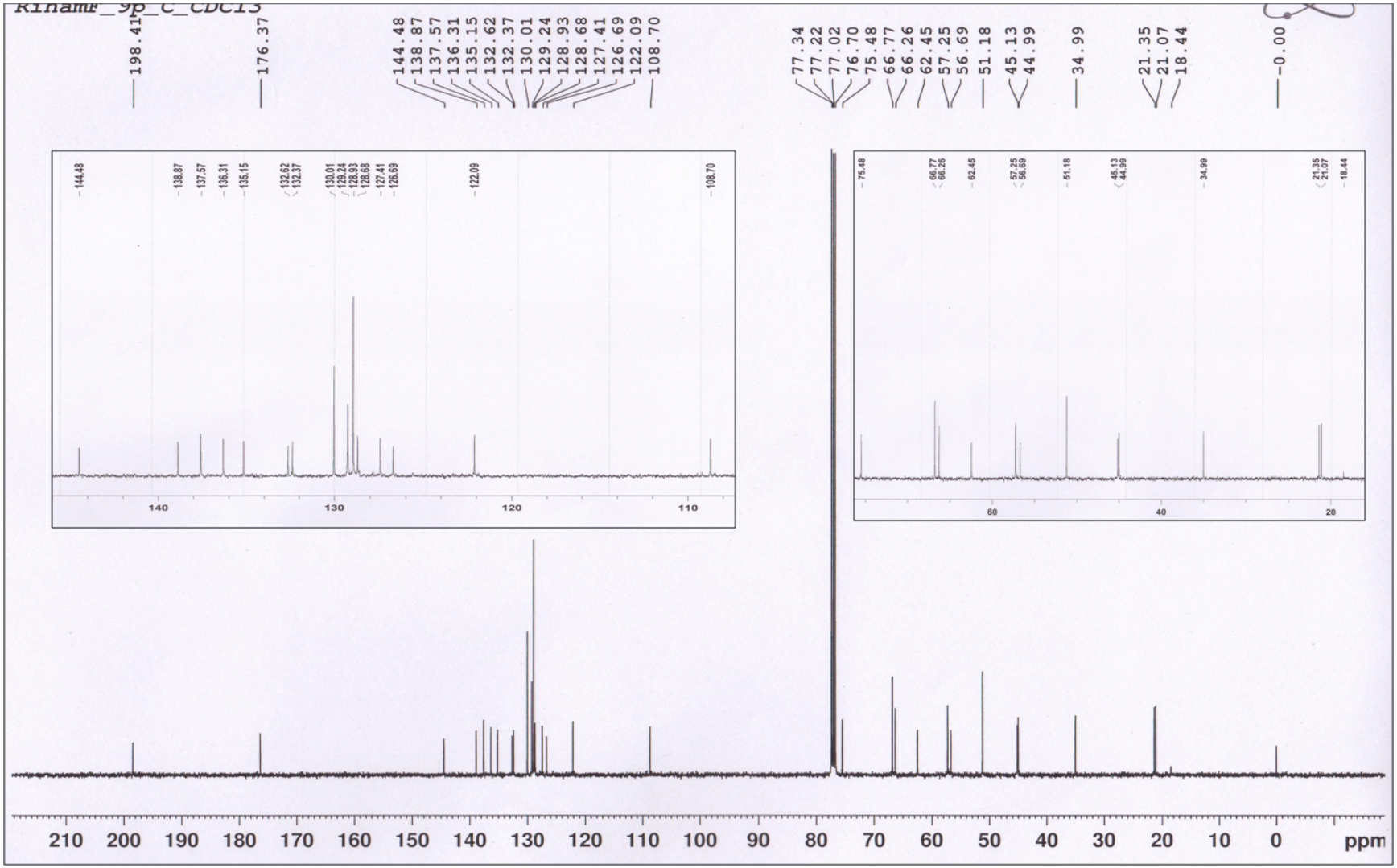

Figure S4. ^{13}C-NMR spectrum of compound **7** in $CDCl_3$.

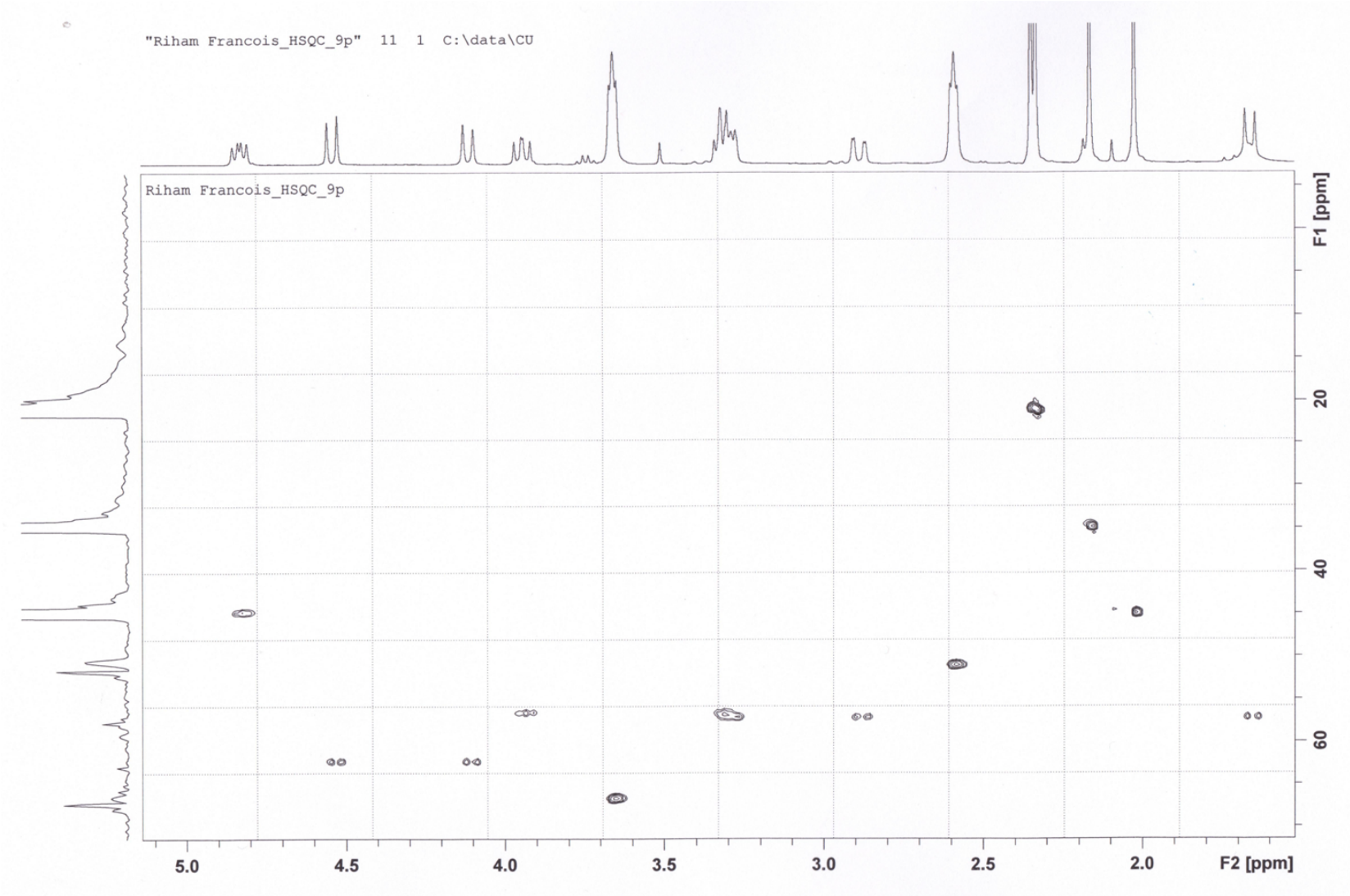

Figure S5. ^{1}H, ^{13}C-Heteronuclear Single Quantum Coherence (HSQC) spectrum of compound **7** in $CDCl_3$.

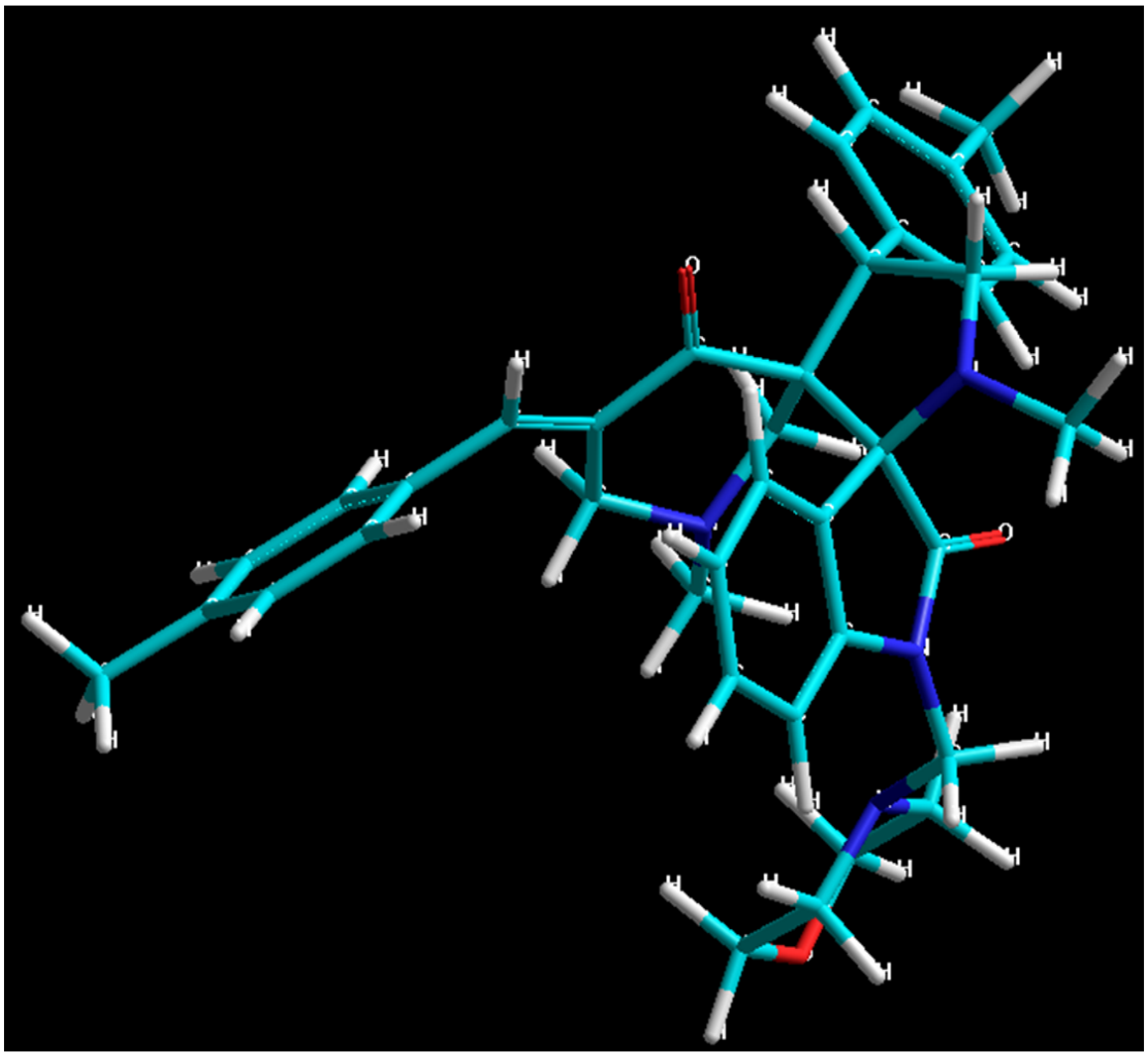

Figure S6. A projection of the optimized structure of compound **7** by semi-empirical AM1.

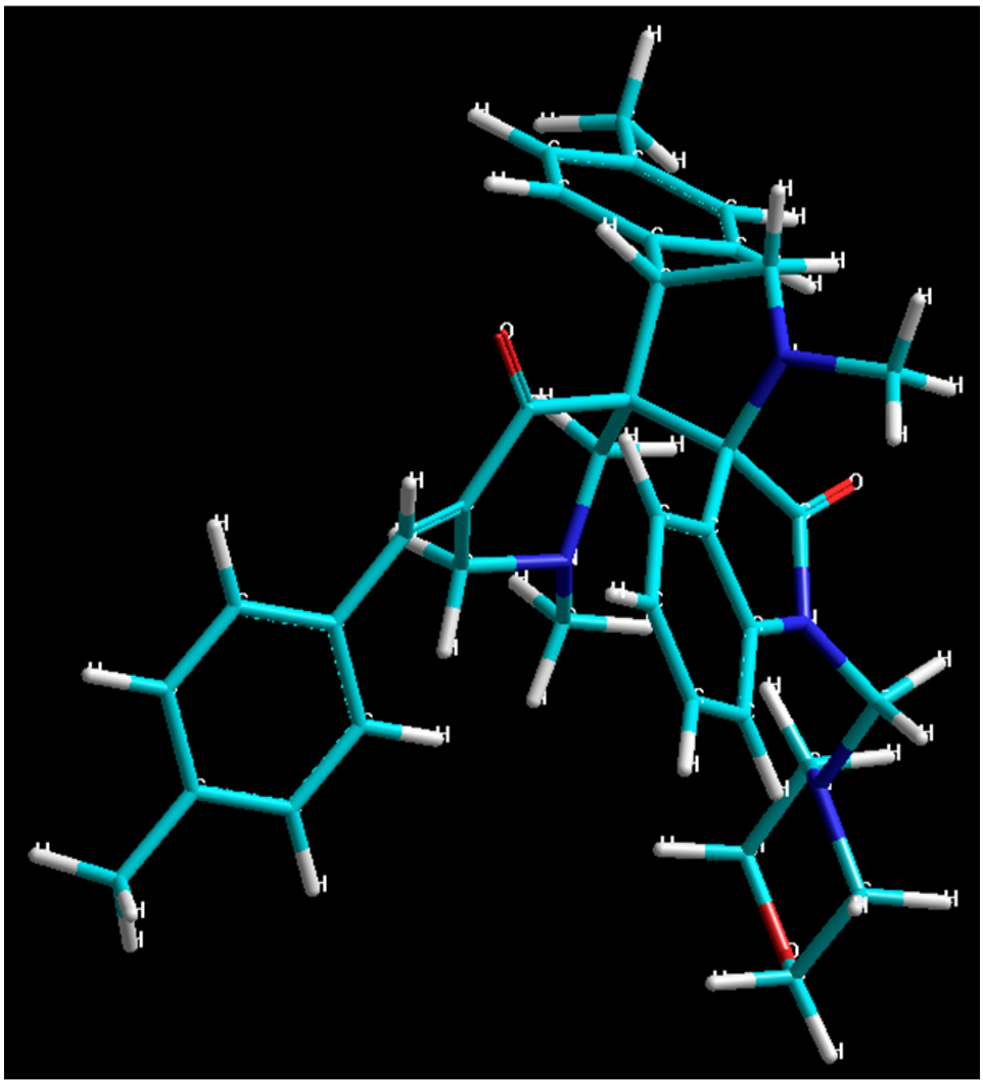

Figure S7. A projection of the optimized structure of compound **7** by semi-empirical PM3.

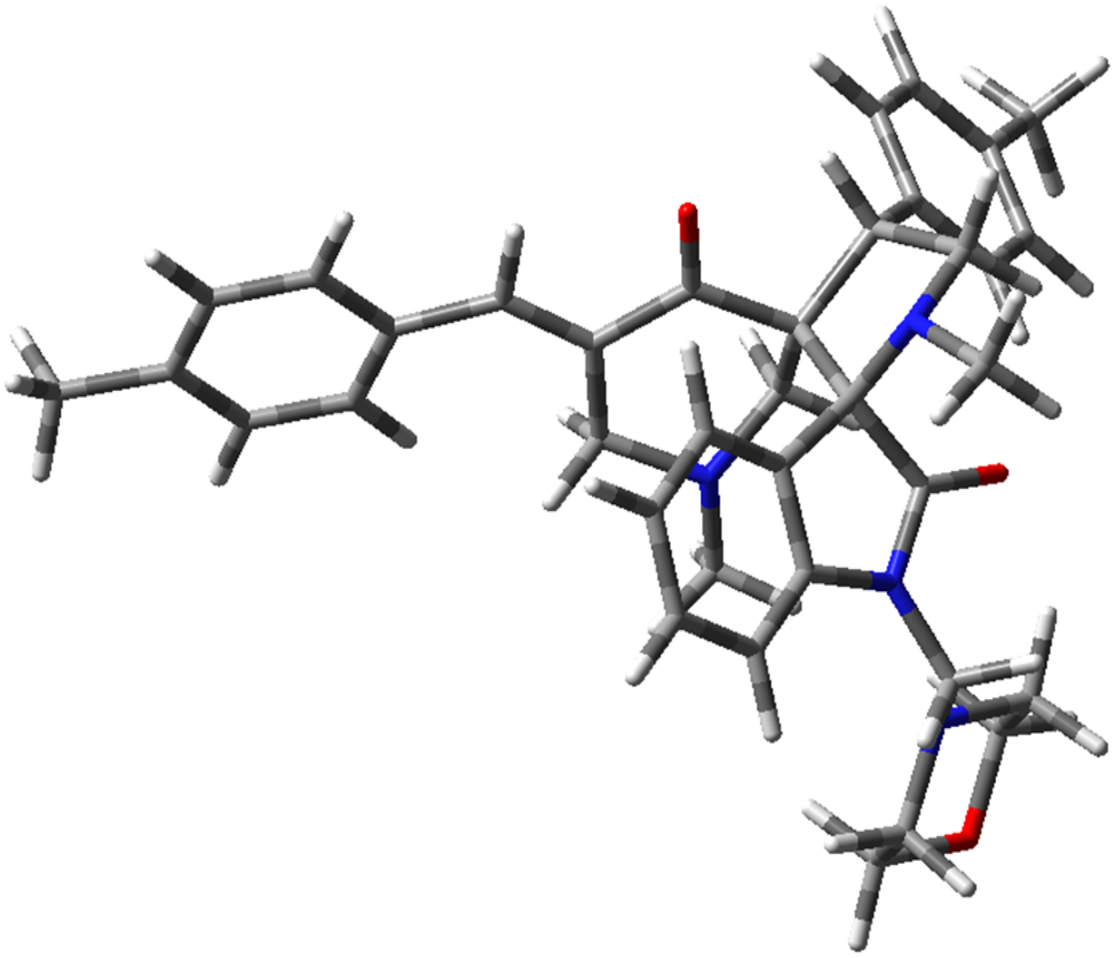

Figure S8. A projection of the optimized structure of compound **7** by DFT/B3LYP method with 3-21G* basis set.

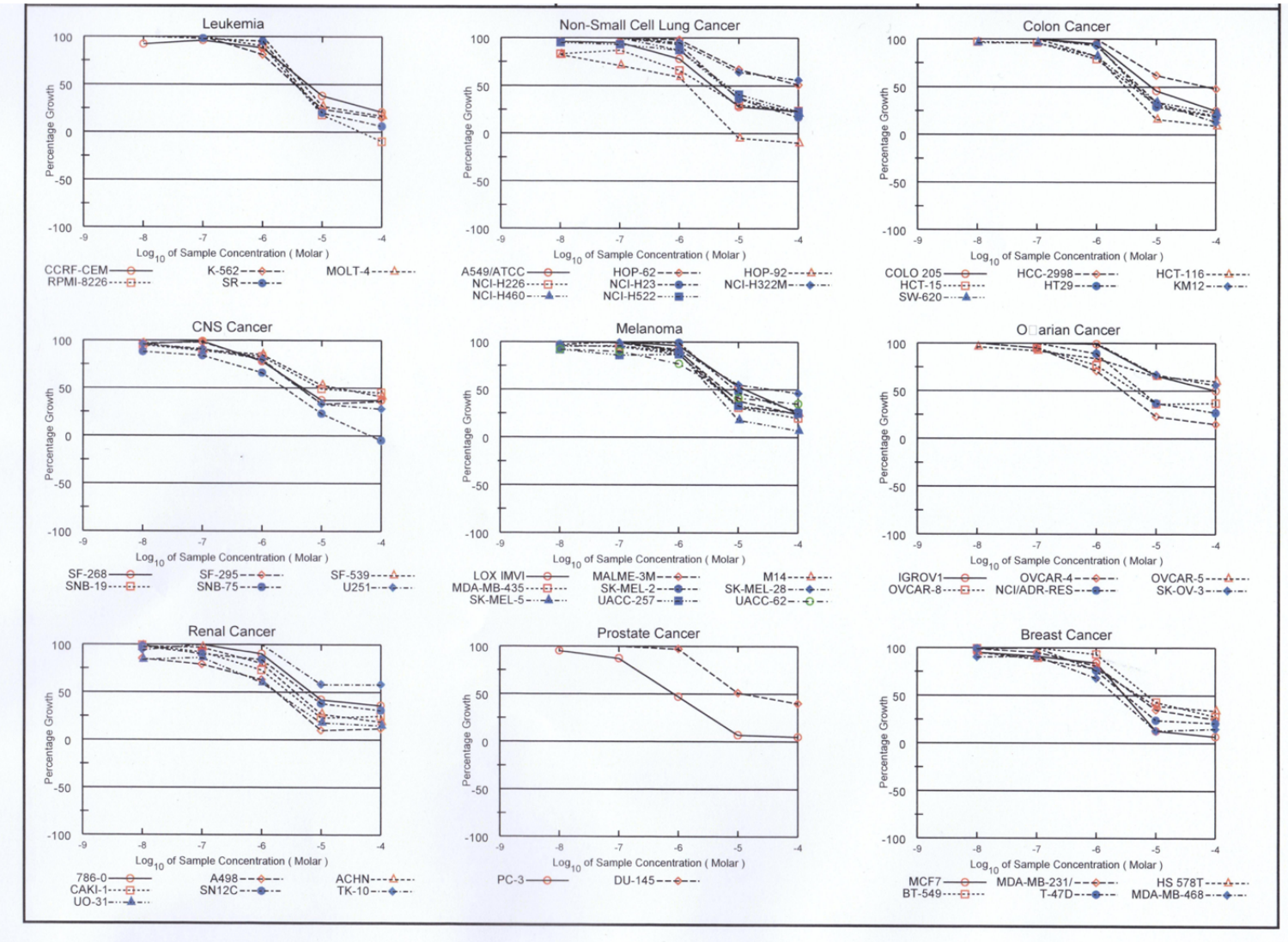

Figure S9. Dose response curves of compound **7** against various human tumor cell lines.

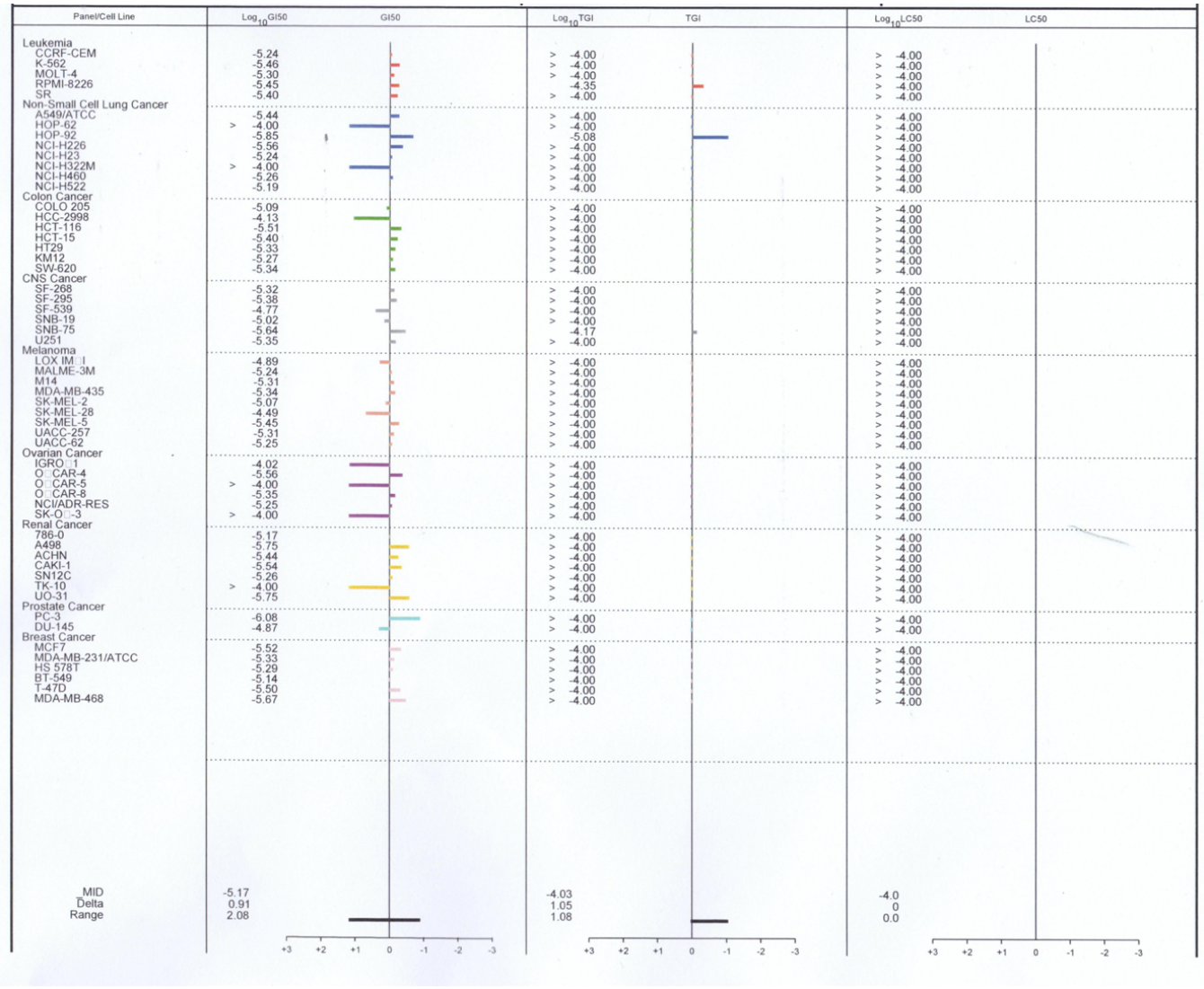

Figure S10. Mean Graphs of bio-assay screening of compound **7** against various human tumor cell lines.