Novel pyridine-heterocycle hybrids: Synthesis *via* Hantzsch and Biginelli reactions, Docking Simulations, and Anticancer Activity

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Supporting data includes 1H-NMR, 13C-NMR, and IR data

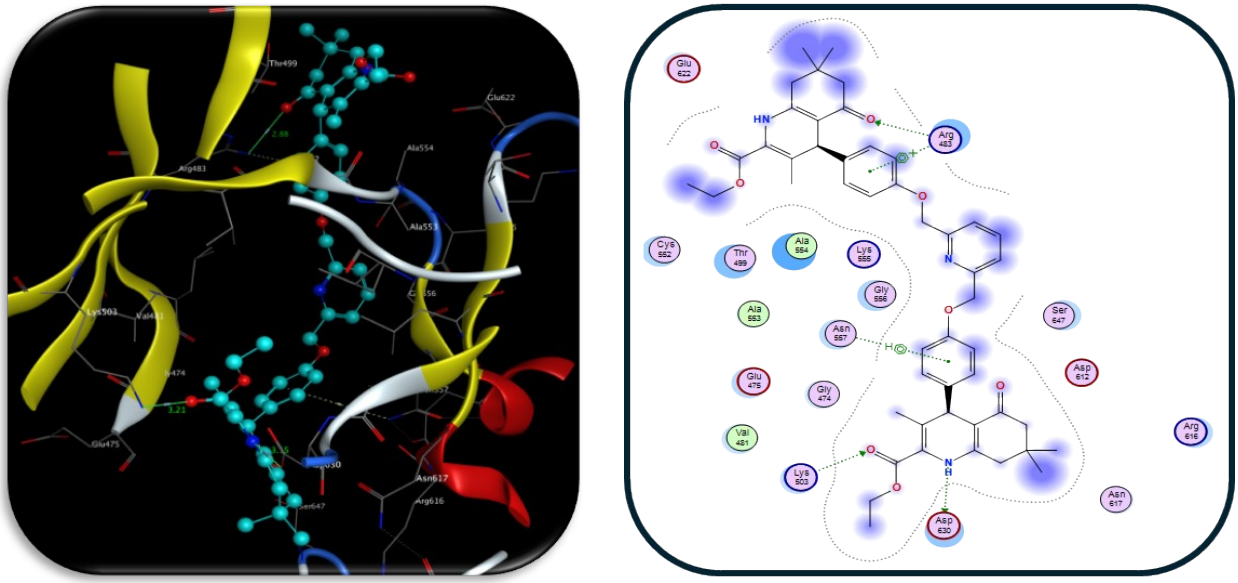


Figure S1. Docked compound **7** interacts with FGFR4 (PDB ID: 4XCU) in 2D (left panel) and 3D (right panel). Carbon atoms are designated turquoise, nitrogen atoms blue, and oxygen atoms red.

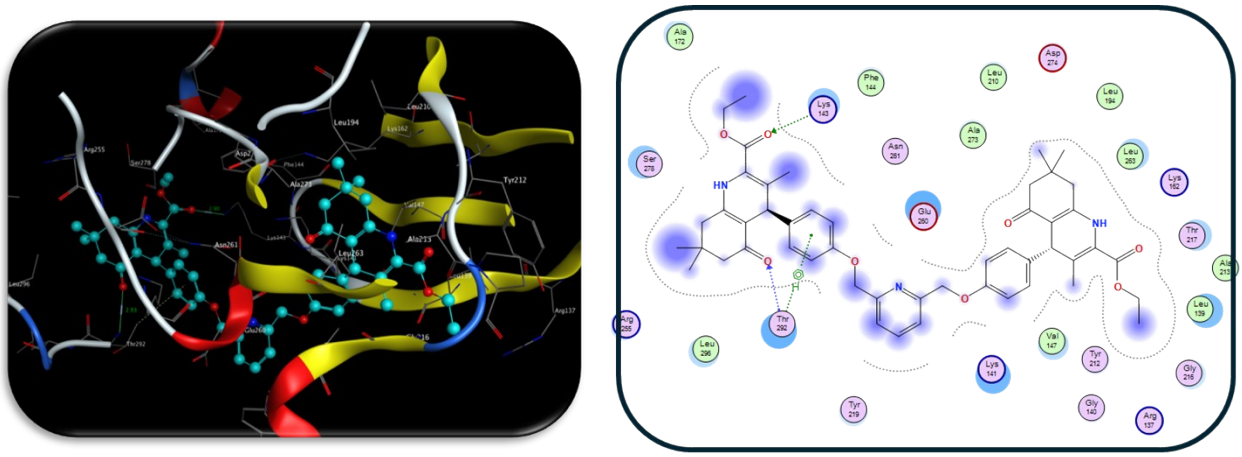


Figure S2. Docked compound **7** interacts with Aurora A (PDB ID: 3H0Z) in 2D (left panel) and 3D (right panel). Carbon atoms are designated turquoise, nitrogen atoms blue, and oxygen atoms red.

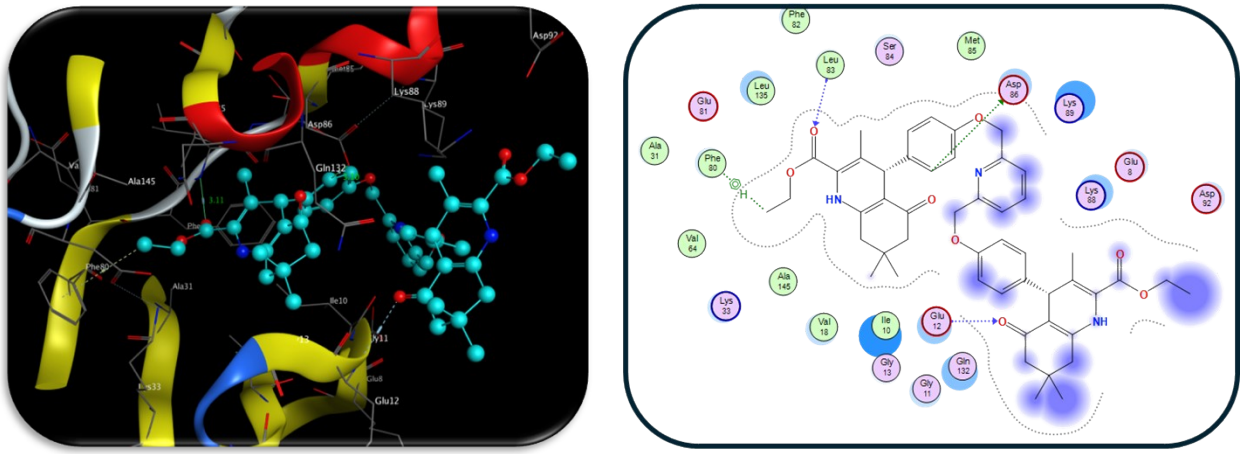


Figure S3. Docked compound **7** interacts with CDK1 (PDB ID: 6GU6) in 2D (left panel) and 3D (right panel). Carbon atoms are designated turquoise, nitrogen atoms blue, and oxygen atoms red.

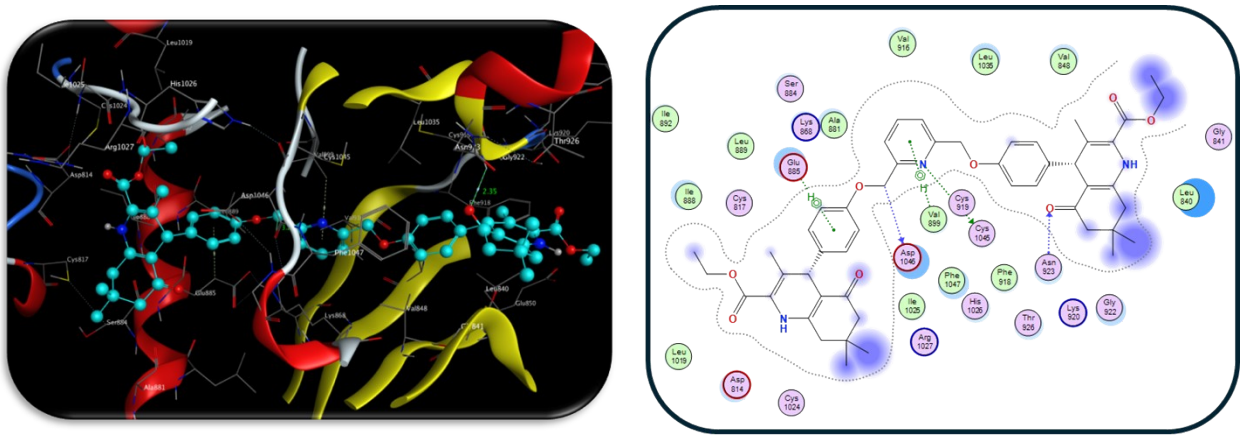


Figure S4. Docked compound **7** interacts with VEGFR2 (PDB ID: 3VHE) in 2D (left panel) and 3D (right panel). Carbon atoms are designated turquoise, nitrogen atoms blue, and oxygen atoms red.

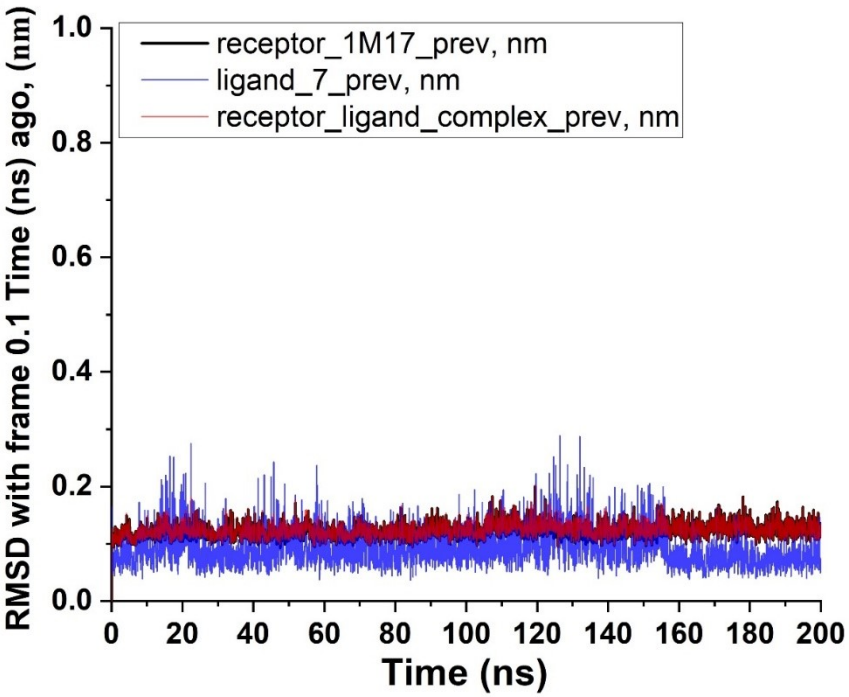


Figure S5. The root mean square deviation (RMSD) vs frame reference 0.1 ns ago of solvated ligand (**7**), receptor, and protein ligand complex (**7-1M17**) during 200 ns MD simulation.

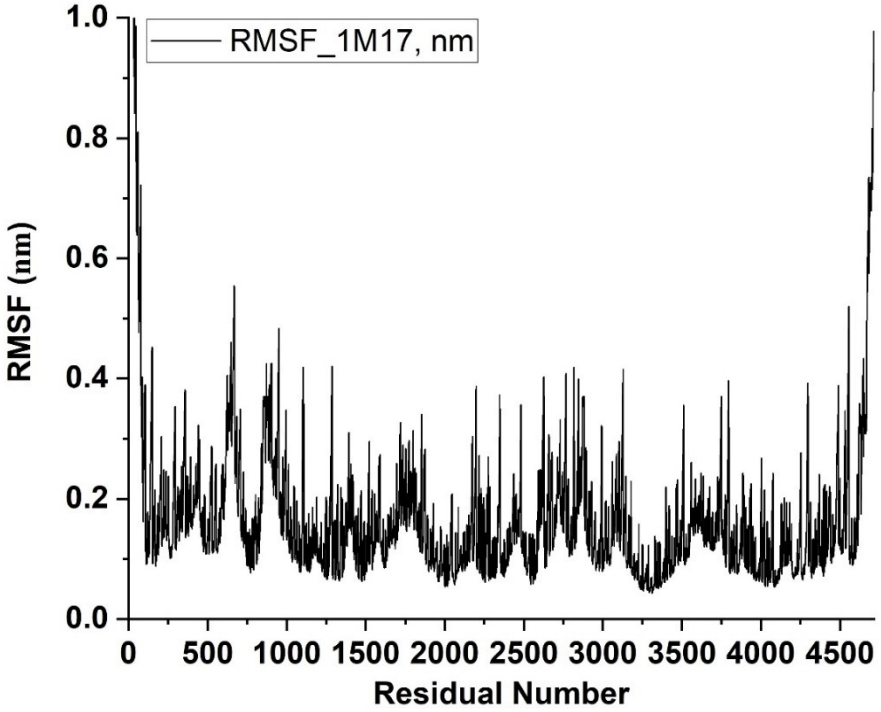


Figure S6. The root means square fluctuation (RMSF) of the solvated receptor complex (**1M17**) during a 200 ns MD simulation time.

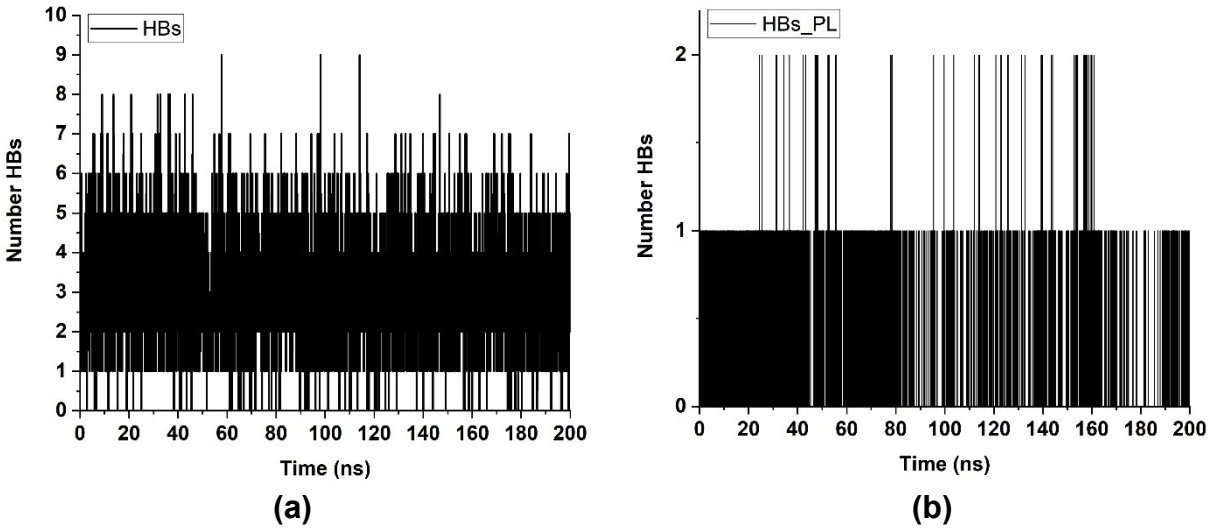


Figure S7. Number of average hydrogen bonding interactions between **(a)** solvated protein receptor and Ligand (**7**); **(b)** protein receptor and Ligand (**7**) only, in solvated protein complex during 200 ns MD simulation time.

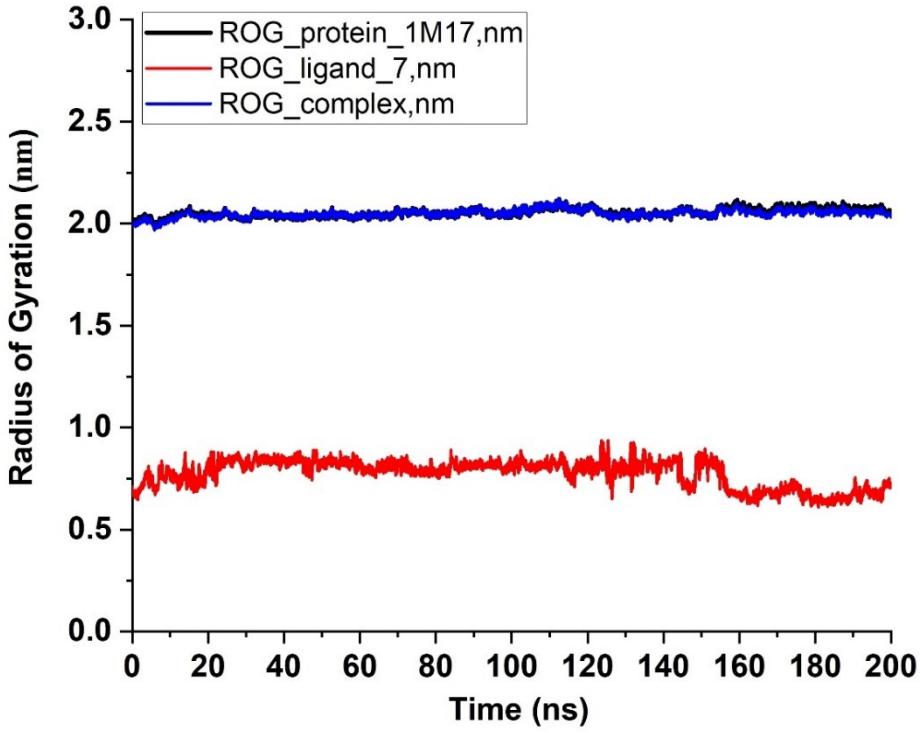


Figure S8. Radius of gyration (Rg) of solvated ligand (**7**), receptor and protein ligand complex (**7-1M17**) during 200 ns MD simulation time.

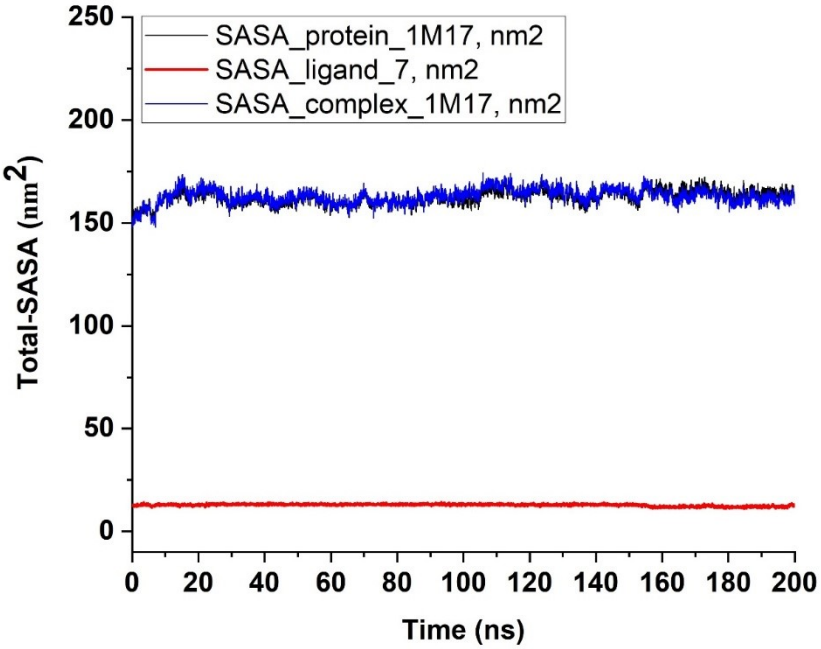


Figure S9. Solvent accessible surface area (SASA) analysis for solvated ligand (**7**), receptor, and protein ligand complex (**7-1M17**) during 200 ns MD simulation time.

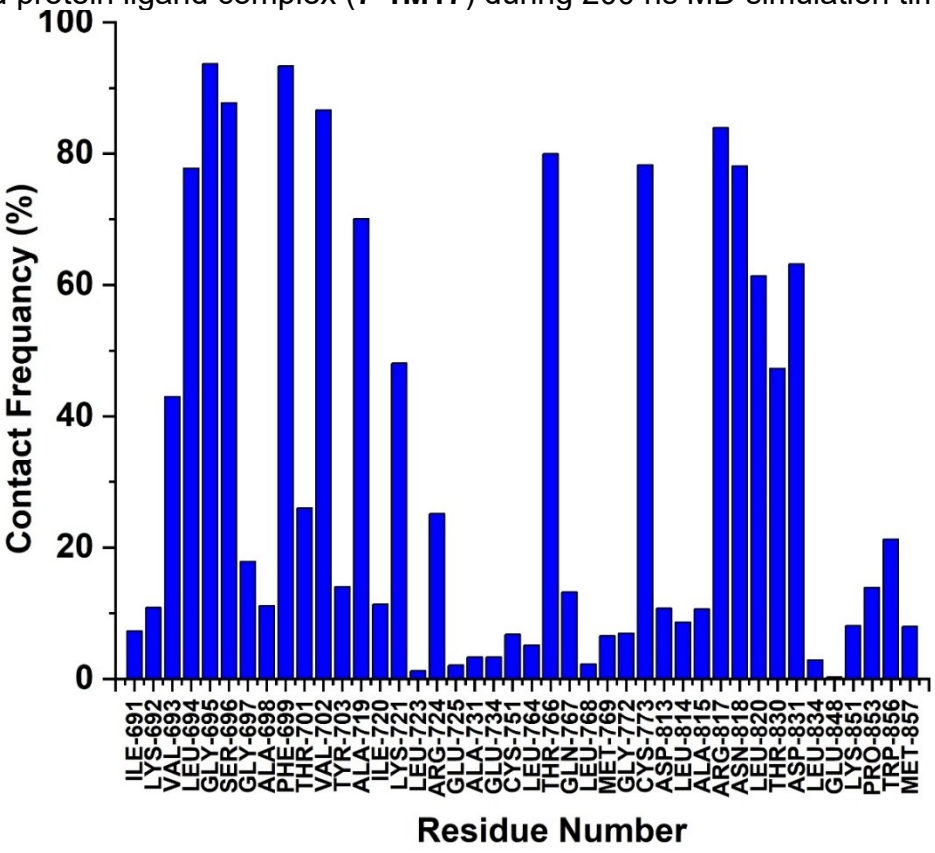
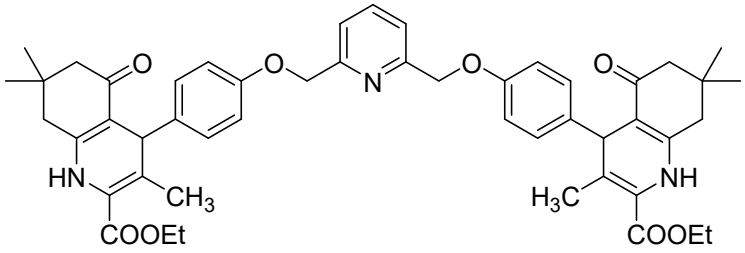


Figure S10. Contact frequency percentage analysis for protein (**1M17**)–ligand (**7)** complex during 200 ns simulation time.



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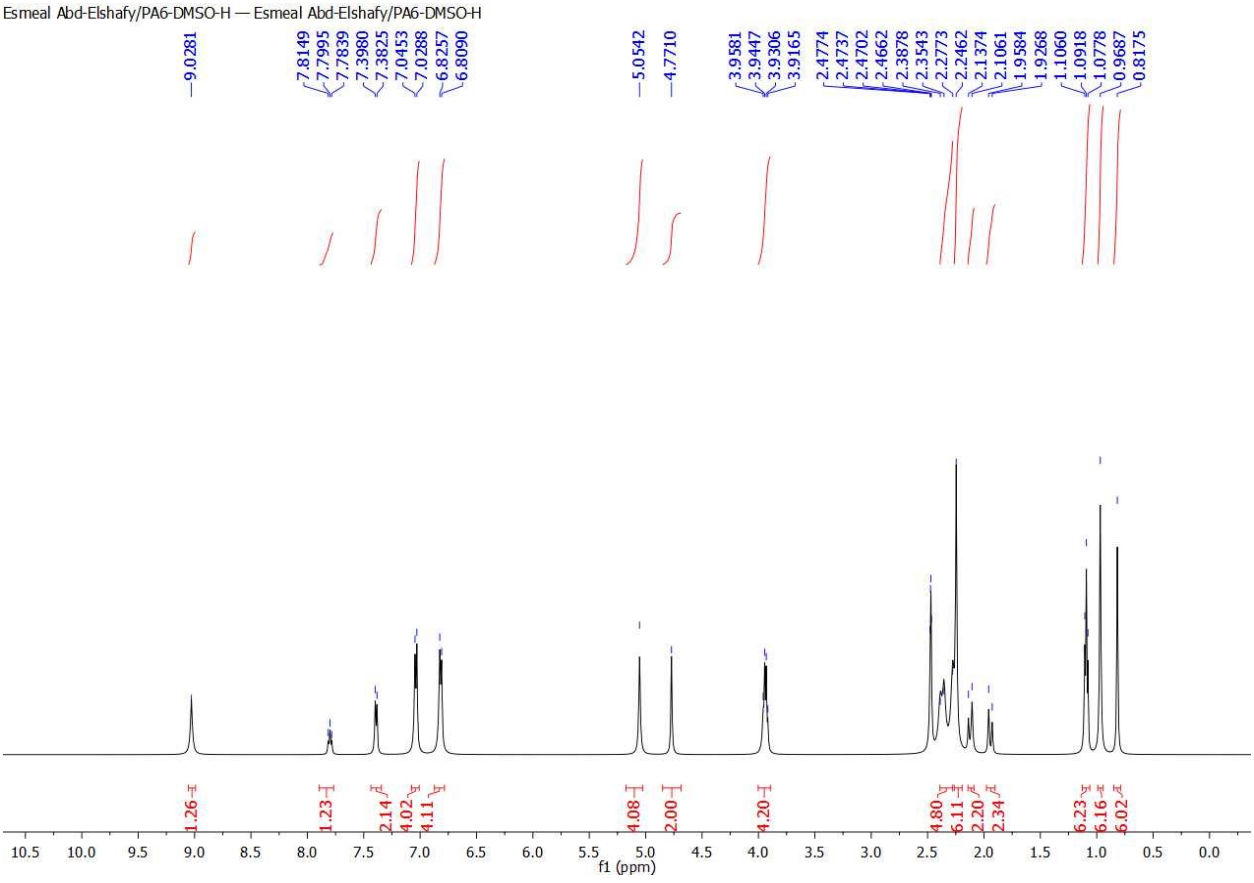
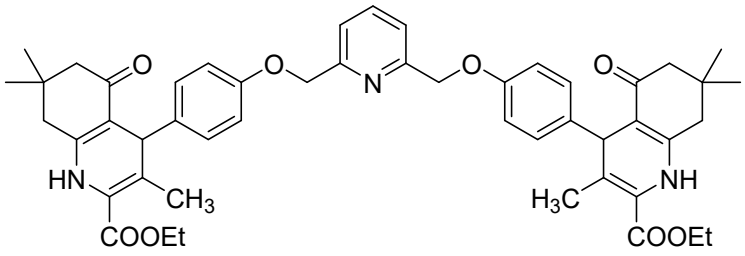


Figure S11. The ^{1}H NMR spectrum of compound **7**



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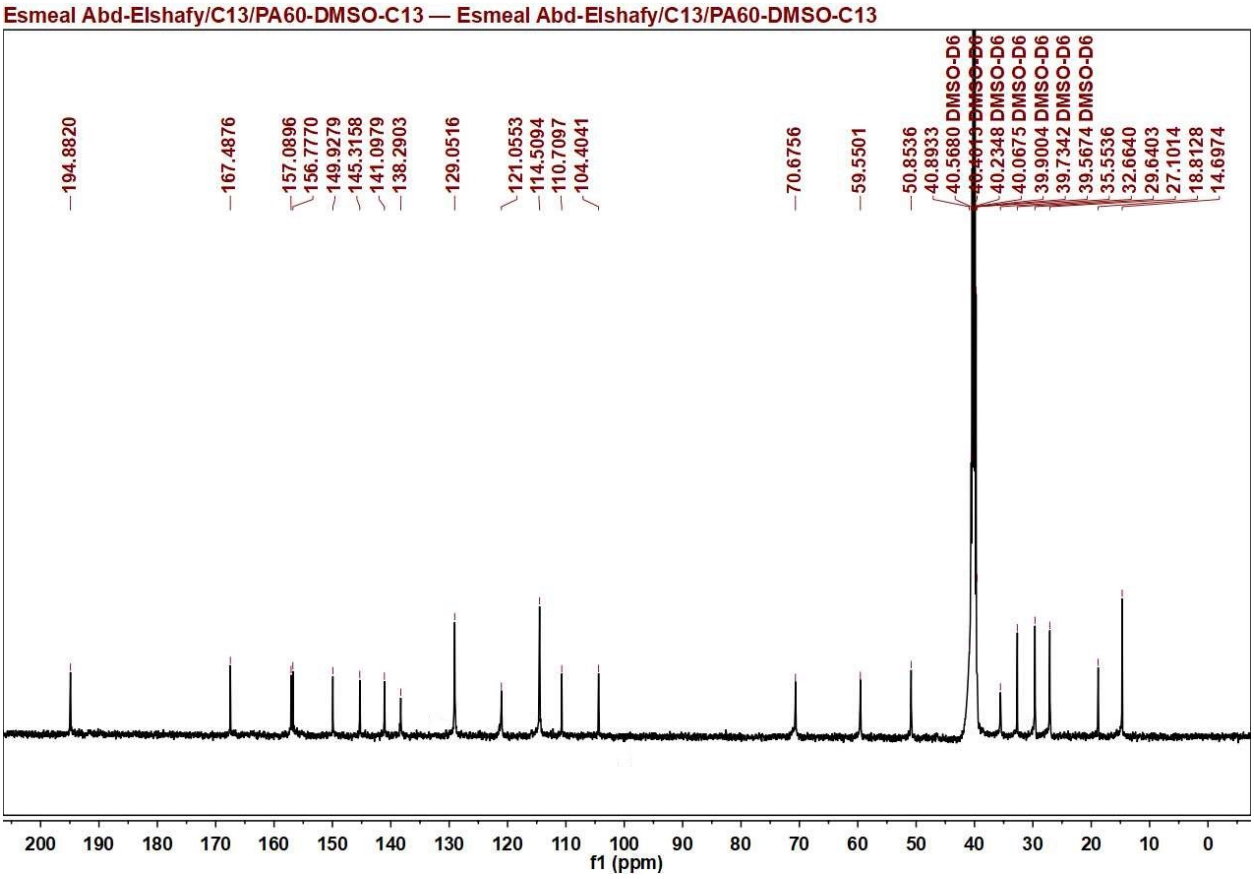
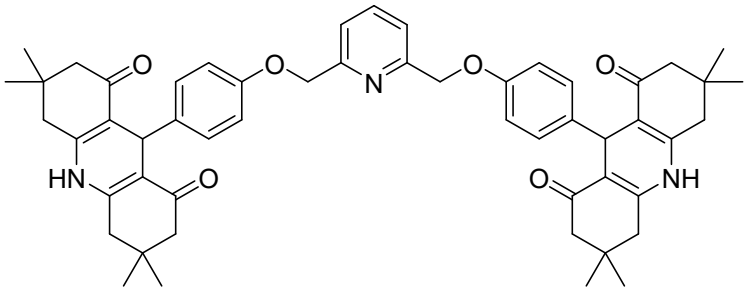


Figure S12. The ^{13}C NMR spectrum of compound **7**



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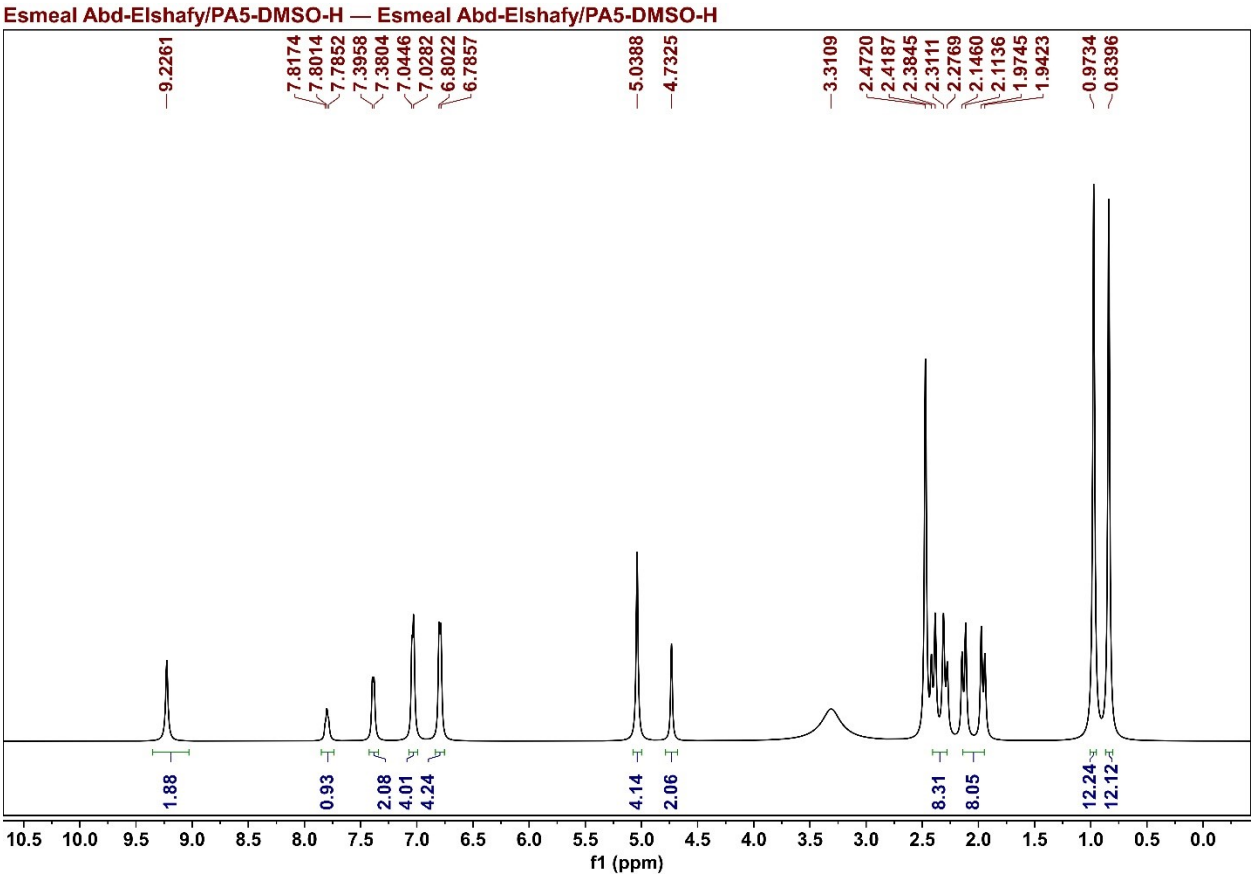
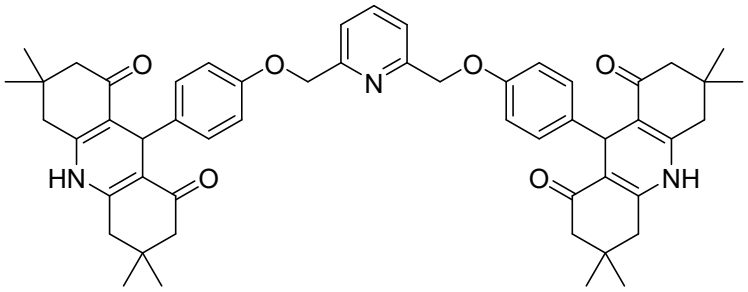


Figure S13. The ^{1}H NMR spectrum of compound **8**



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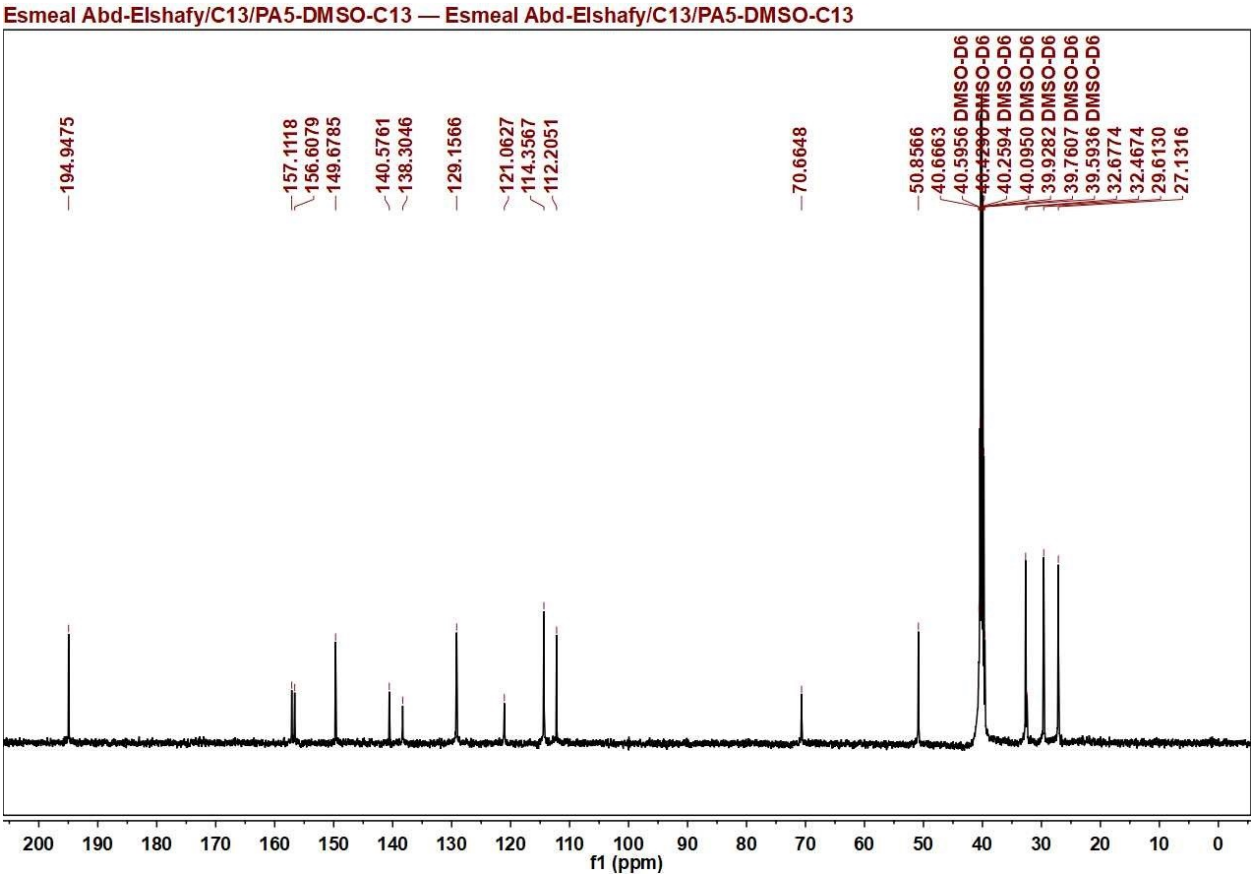
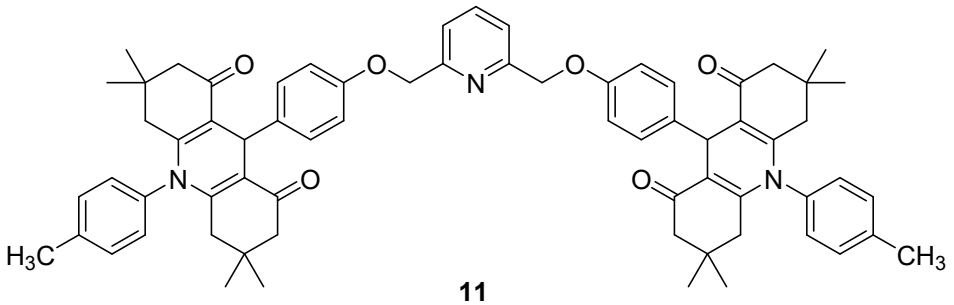


Figure S14. The ^{13}C NMR spectrum of compound **8**



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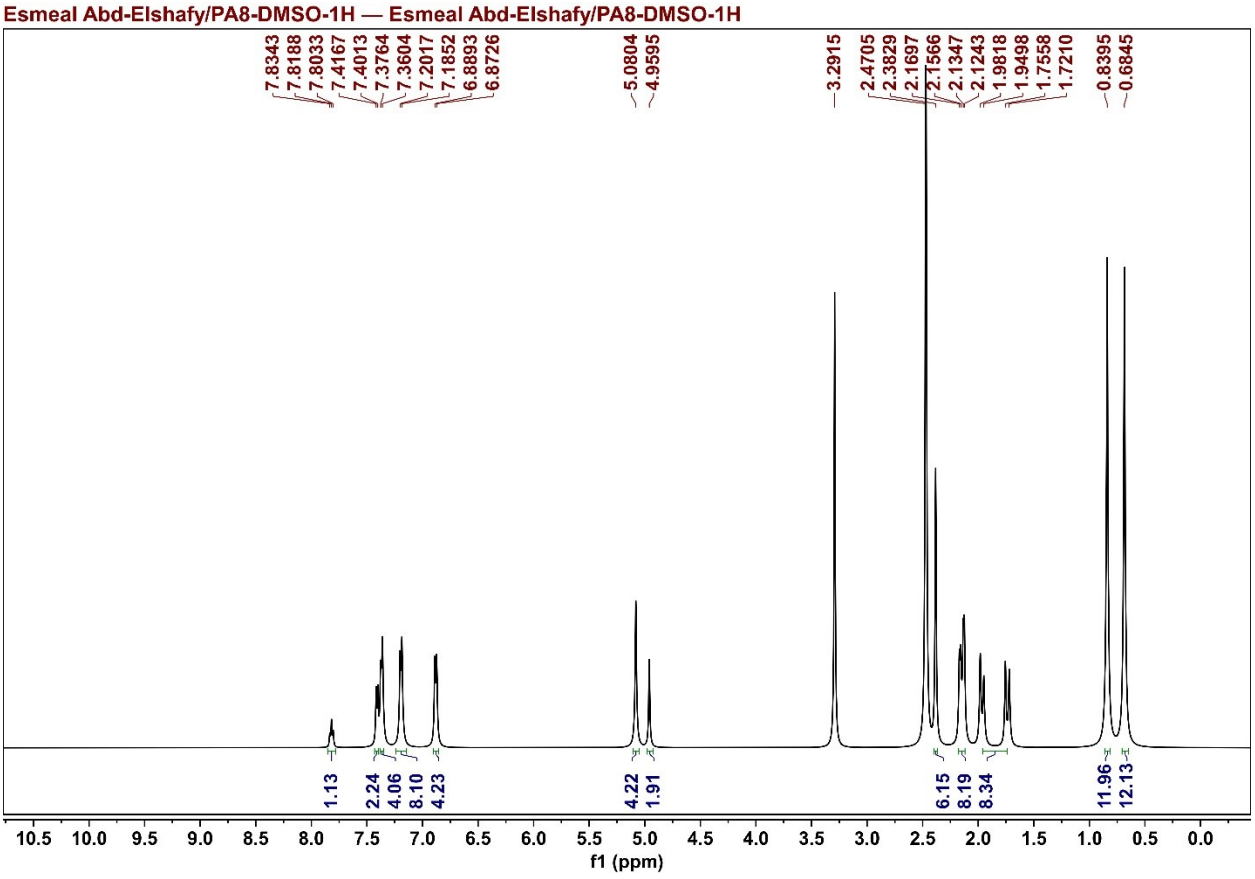
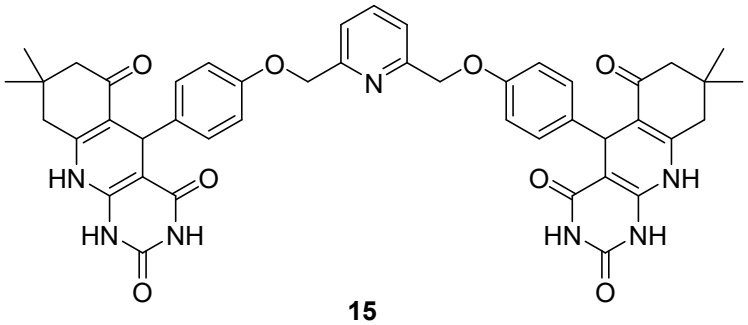


Figure S15. The ^{1}H NMR spectrum of compound **11**



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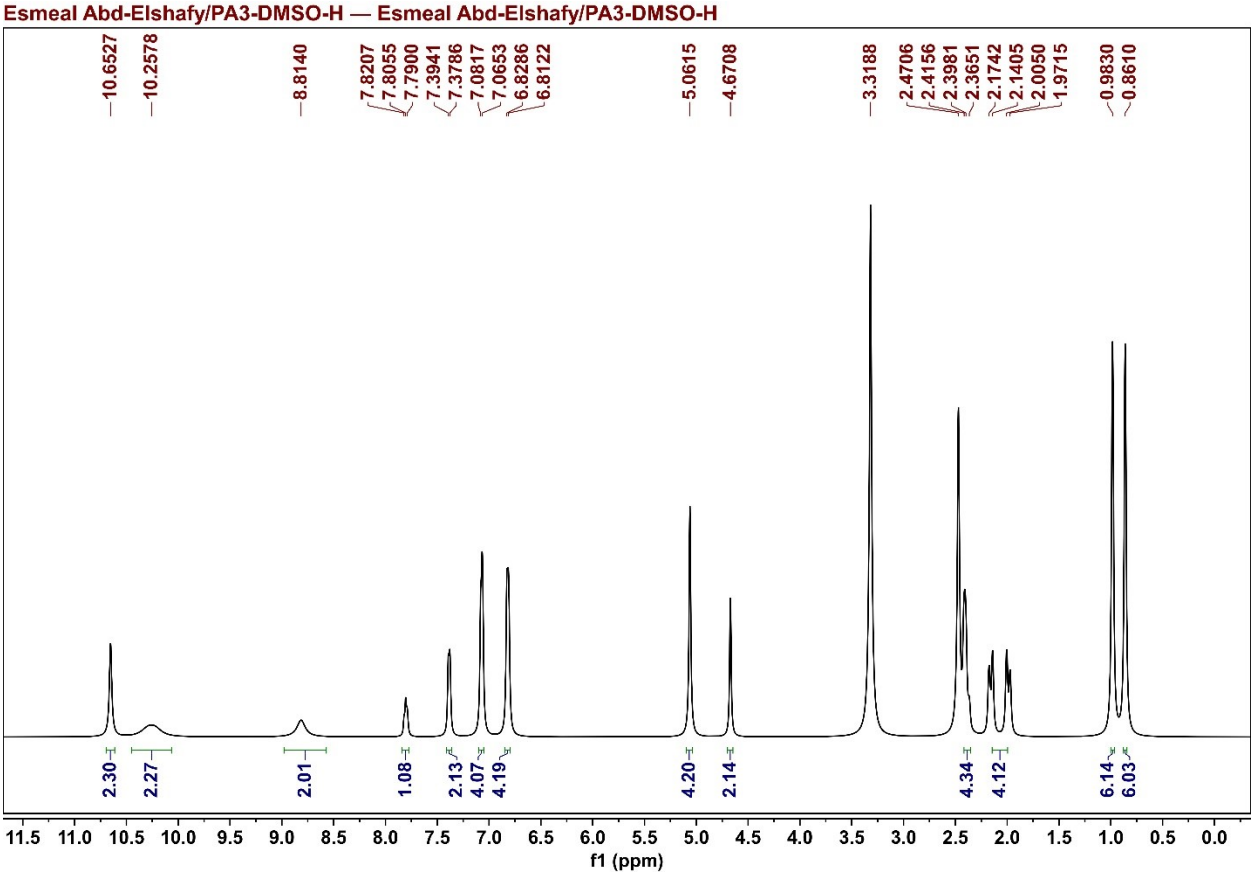
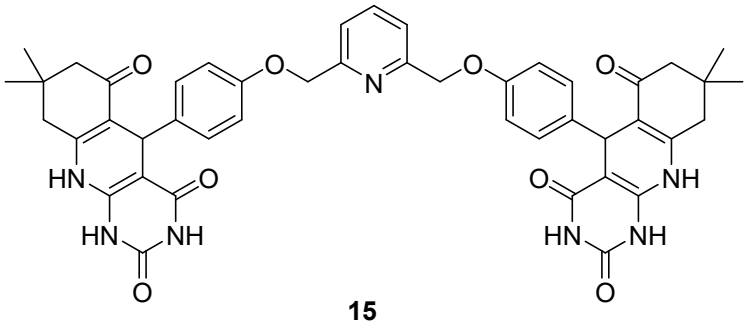


Figure S16. The ^{1}H NMR spectrum of compound **15**



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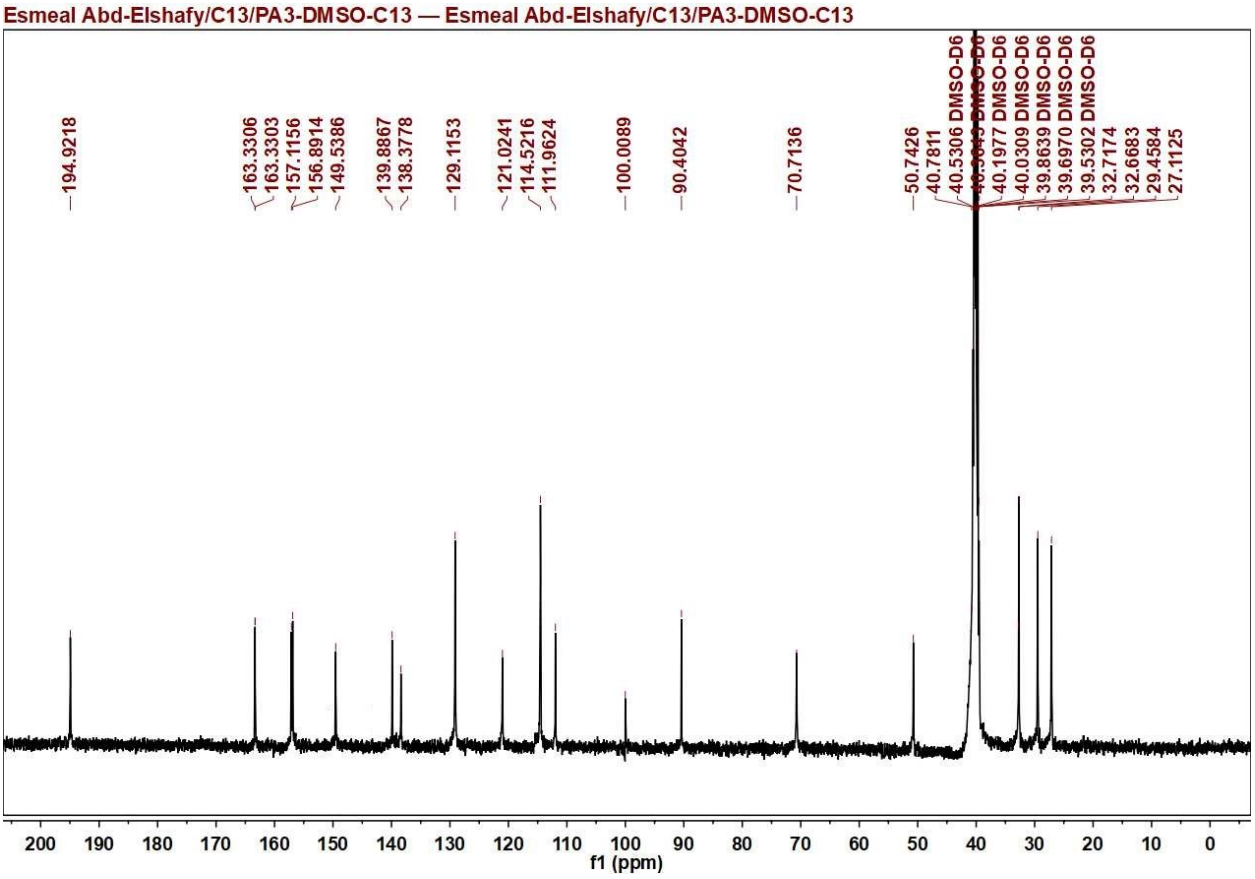


Figure S17. The ^{13}C NMR spectrum of compound **15**

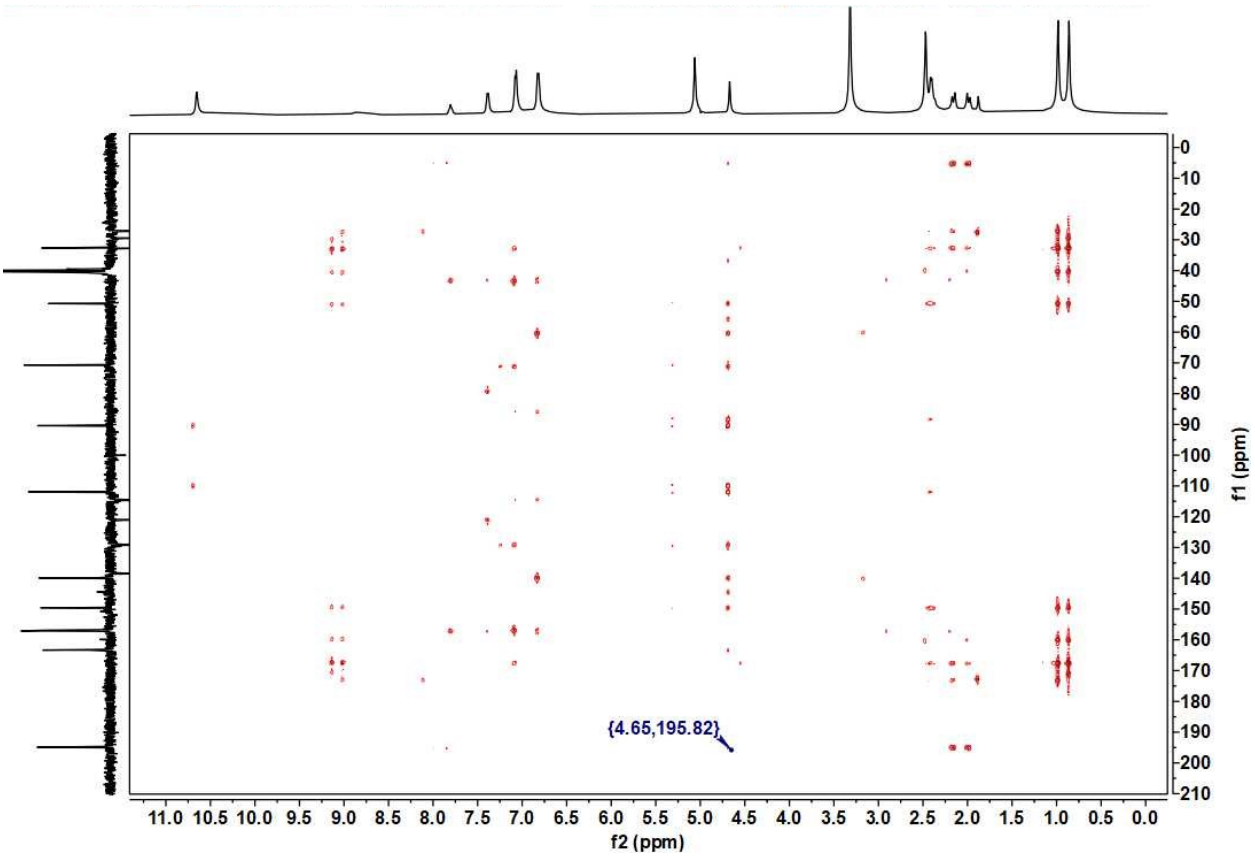
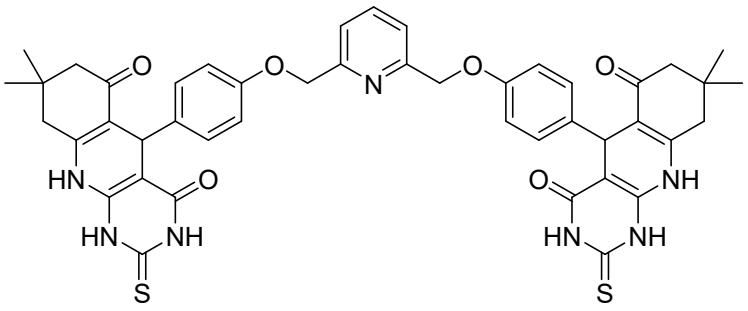


Figure S18: 2D-HMBC NMR spectrum of compound **15**



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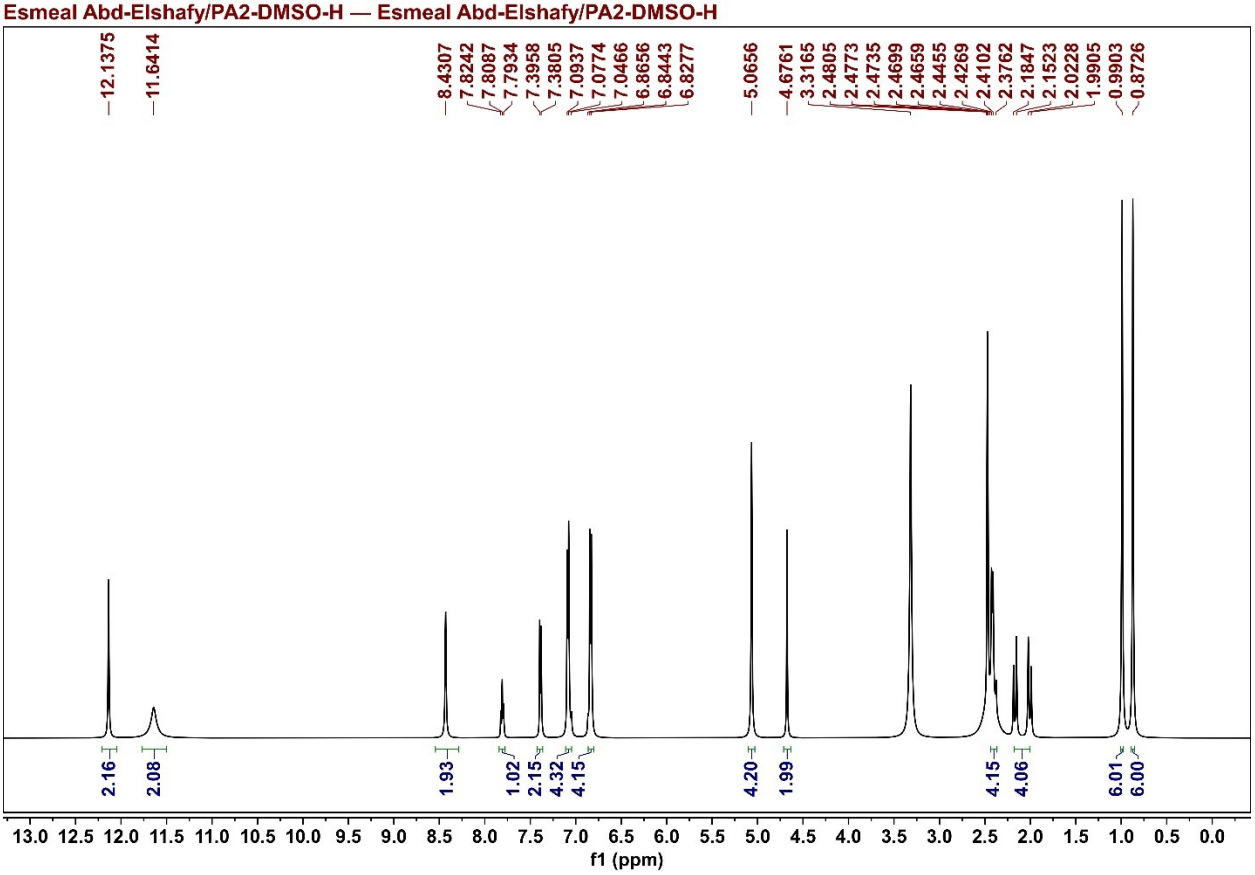
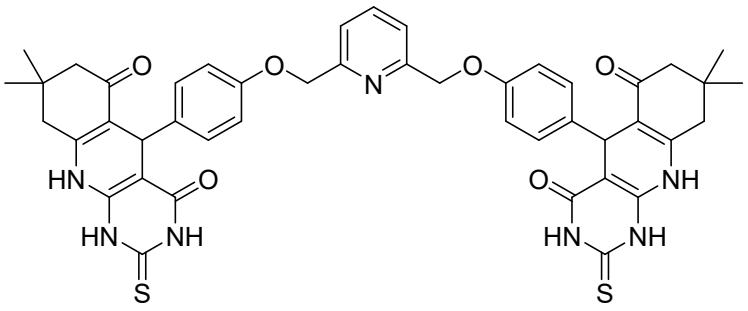


Figure S19. The ^{1}H NMR spectrum of compound **16**



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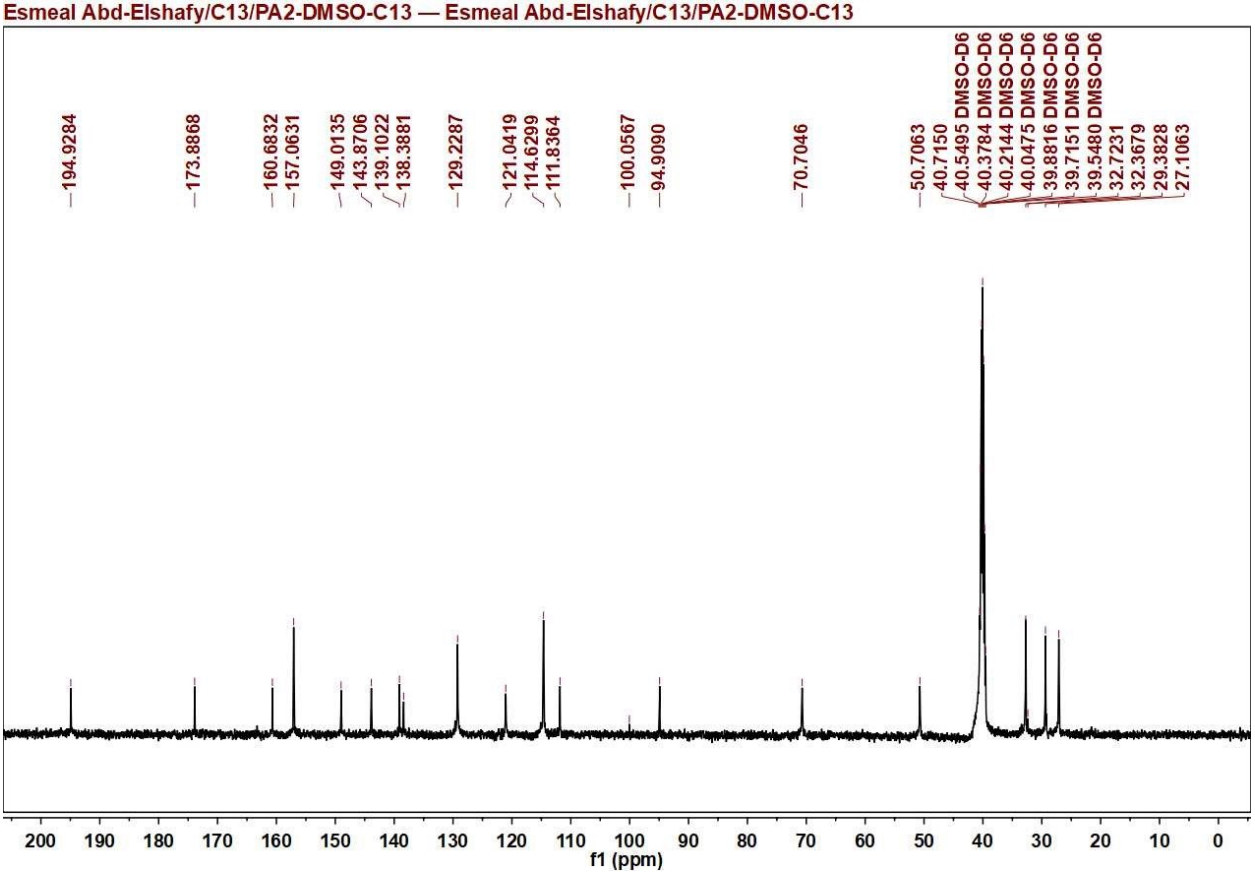
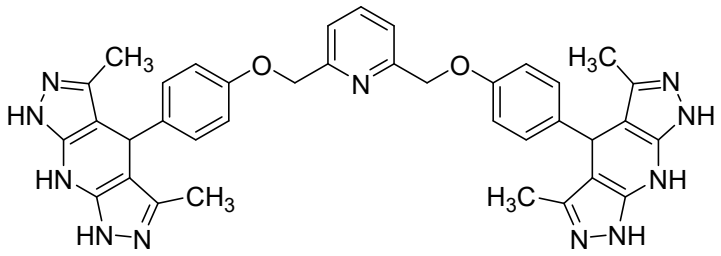


Figure S20. The ^{13}C NMR spectrum of compound **16**



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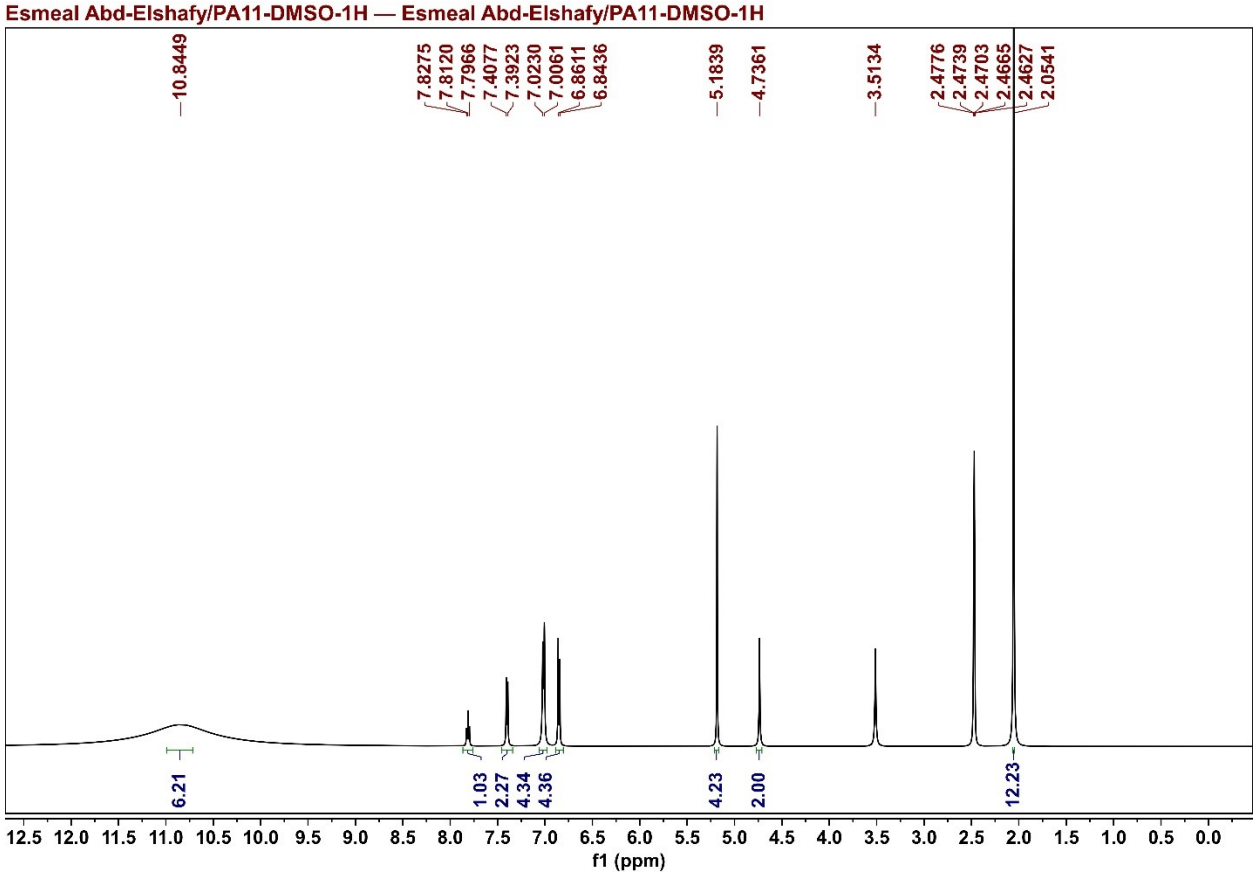
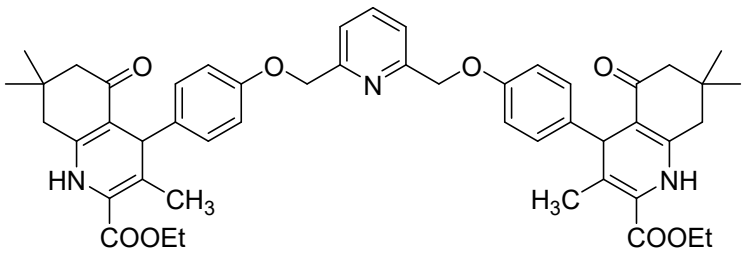


Figure S21. The ^{1}H NMR spectrum of compound **18**

IR Spectra



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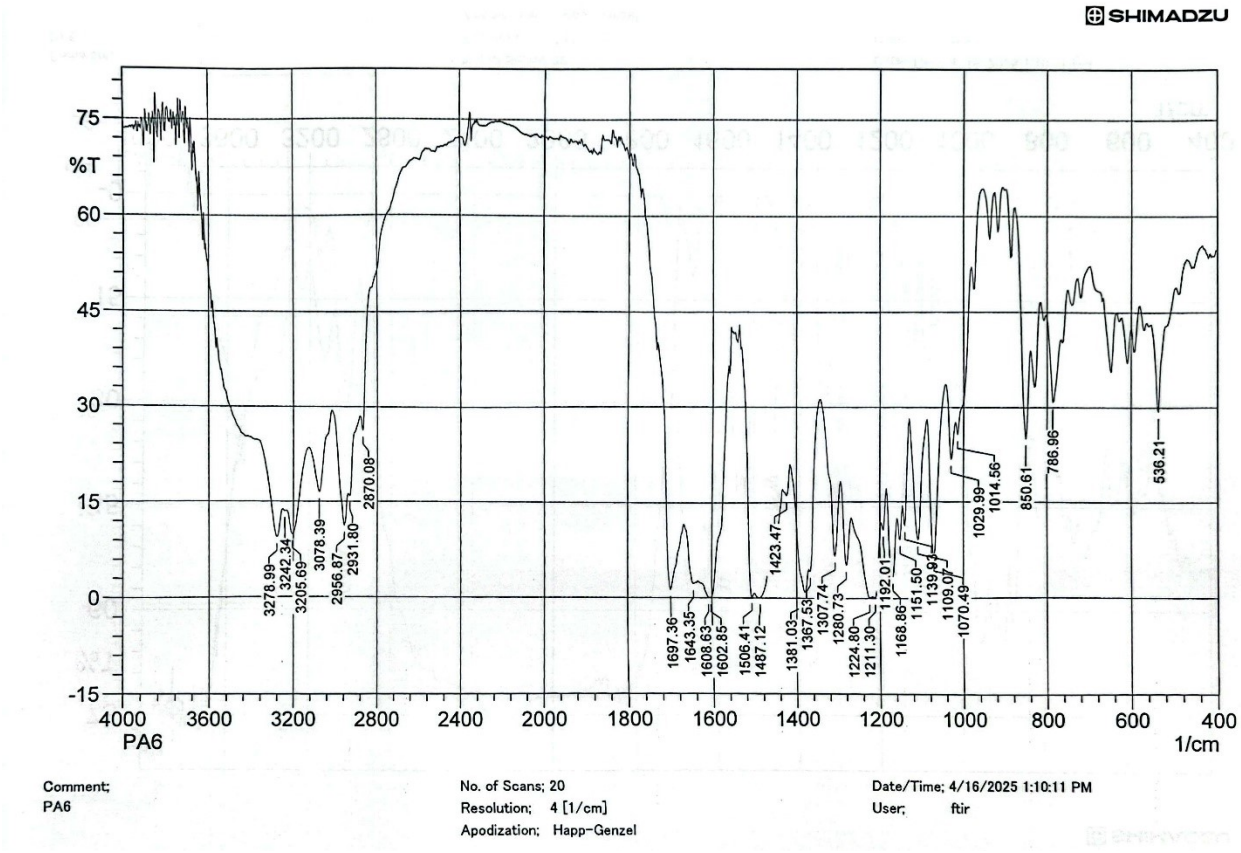
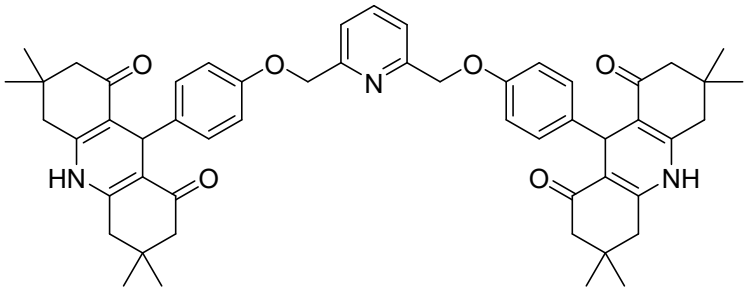


Figure S22. The IR spectrum of compound **7**



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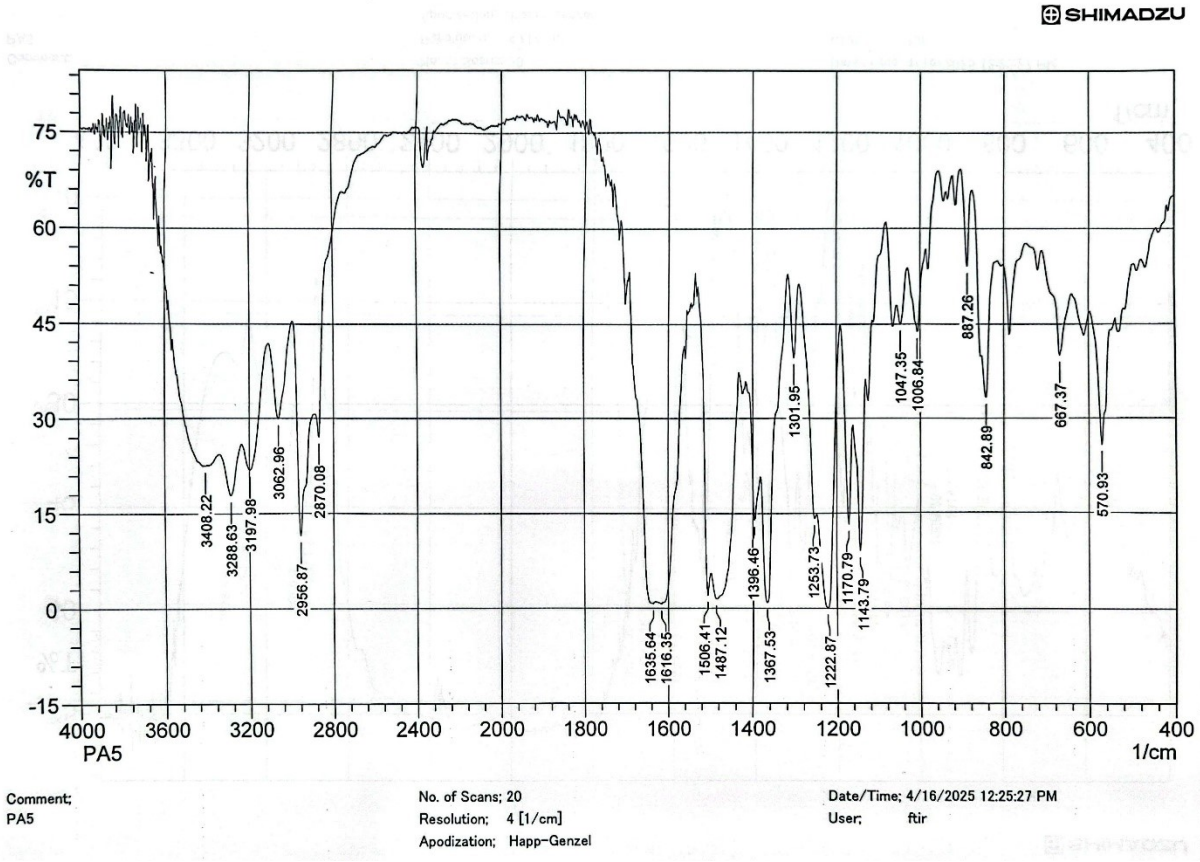
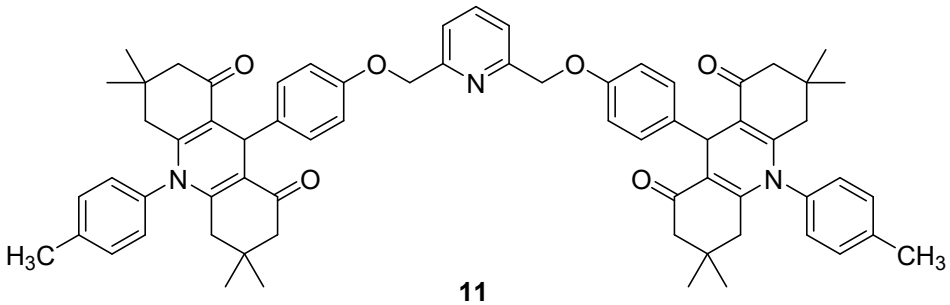


Figure S23. The IR spectrum of compound **8**



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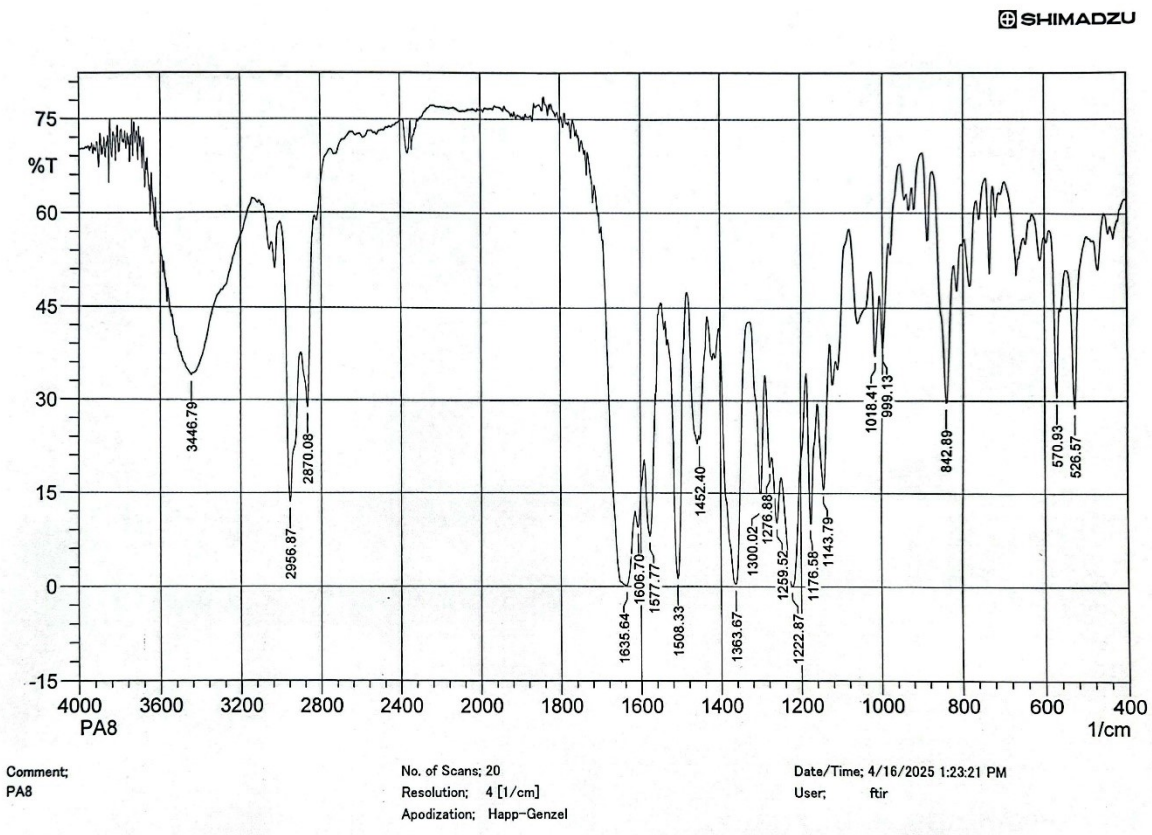
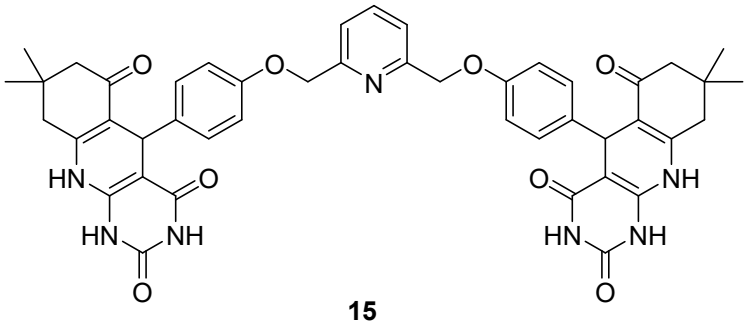


Figure S24. The IR spectrum of compound **11**



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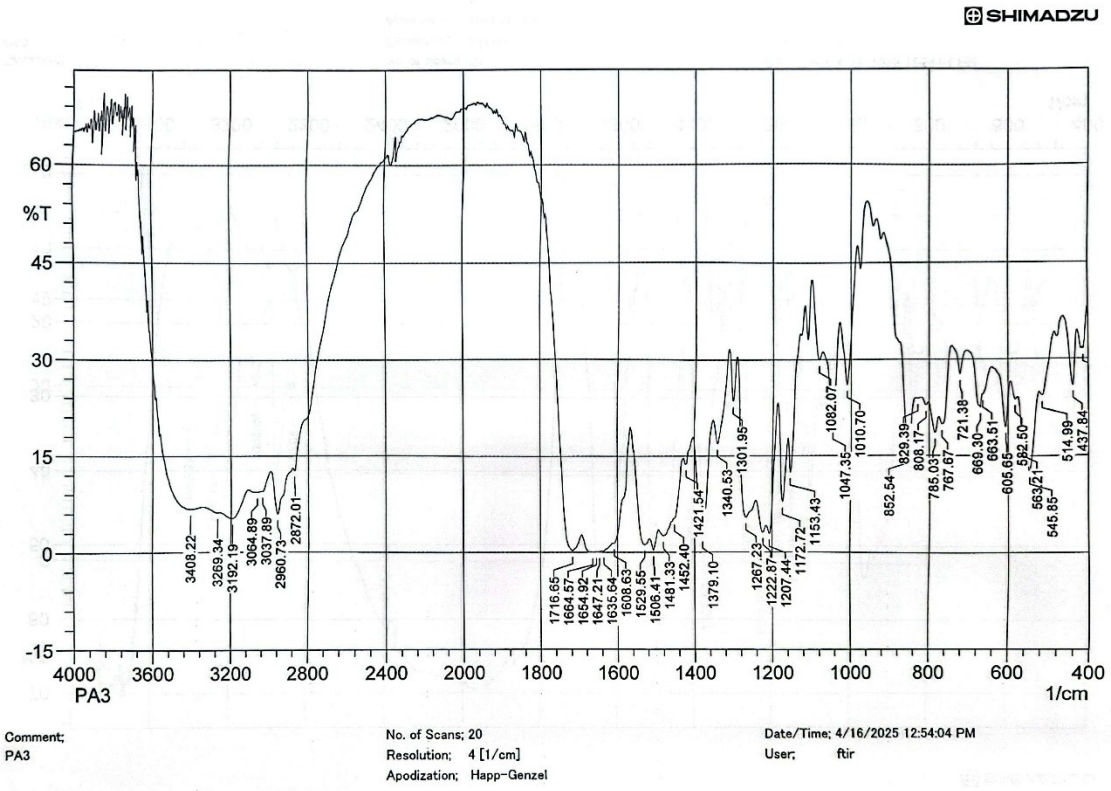
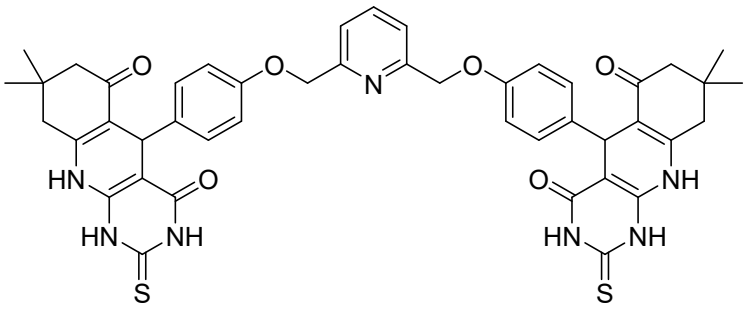


Figure S25. The IR spectrum of compound **15**



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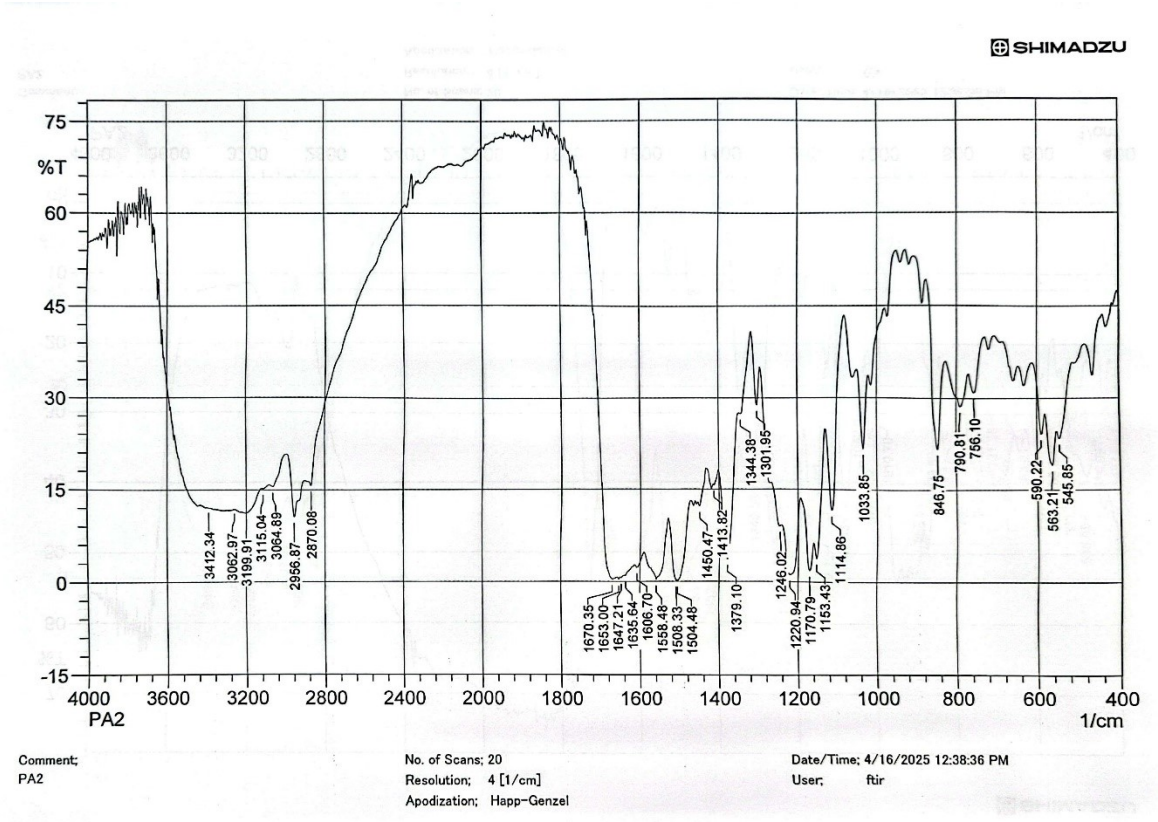
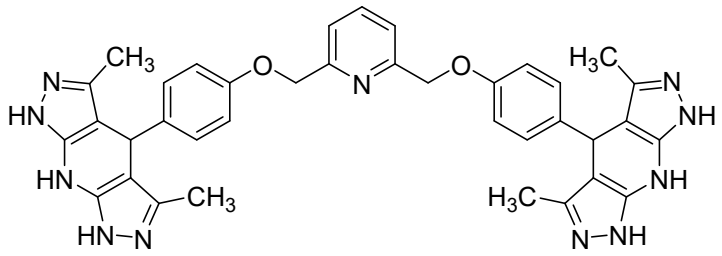


Figure S26. The IR spectrum of compound **16**



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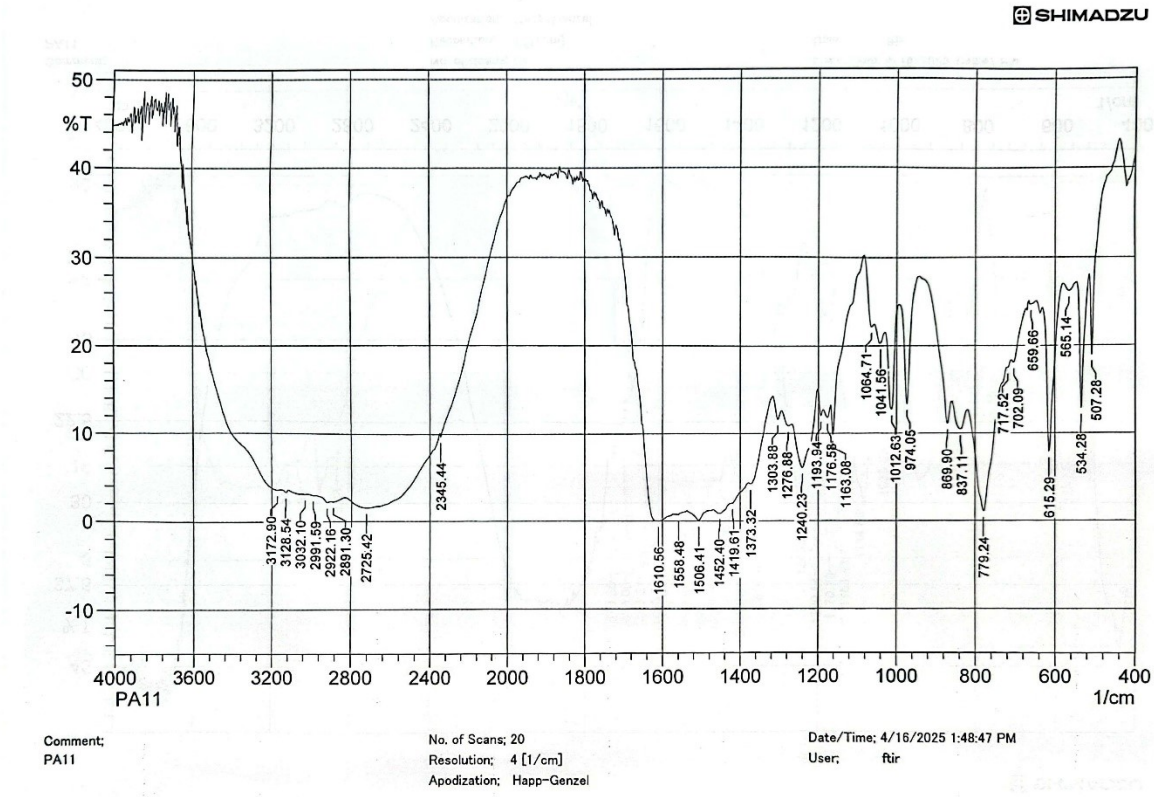

Figure S27. The IR spectrum of compound **18**

Table S1. IC_{50} values (μM) of novel derivatives **(7, 8, 11, 15, 16,** and **18)** toward different human cells, HepG2, A549, MCF7, and HFB4 cells, using MTT assay following 48 h of treatment.

Compound	IC_{50} (μM)[a]				SI[b]		
	HepG2	A549	MCF7	HFB4	HepG2	A549	MCF7
16 (PA2)	46.83 ± 3.86	>118.76	95.84 ± 12.47	> 118.76	>2.53	>1	>1.24
15 (PA3)	81.22 ± 2.31	101.92 ± 8.40	> 123.48	> 123.48	>1.52	>1.21	>1
8 (PA5)	70.91 ± 10.23	53.21 ± 21.39	> 119.89	81.82 ± 5.67	1.15	>1.53	0.68
7 (PA6)	22.20 ± 1.44	17.75 ± 4.58	37.95 ± 8.15	> 122.85	>5.53	>6.92	>3.23
11 (PA8)	72.77 ± 14.68	> 98.59	> 98.59	> 98.59	>1.35	>1	>1
18 (PA11)	83.84 ± 11.16	144.0 ± 5.42	> 150.20	> 150.20	>1.79	>1.04	>1
5-Florouracil	349.40 ± 45.89	369.01 ± 33.21	392.38 ± 88.25	679.05 ± 19.45	1.94	1.84	1.73

[a] The data was expressed as the mean ± SD of three independent experiments.

[b] SI = IC_{50} on HFB4/IC_{50} on cancer cells.