Design, synthesis, theoretical study, antioxidant, and anticholinesterase activities of new Pyrazolo-fused phenanthrolines.

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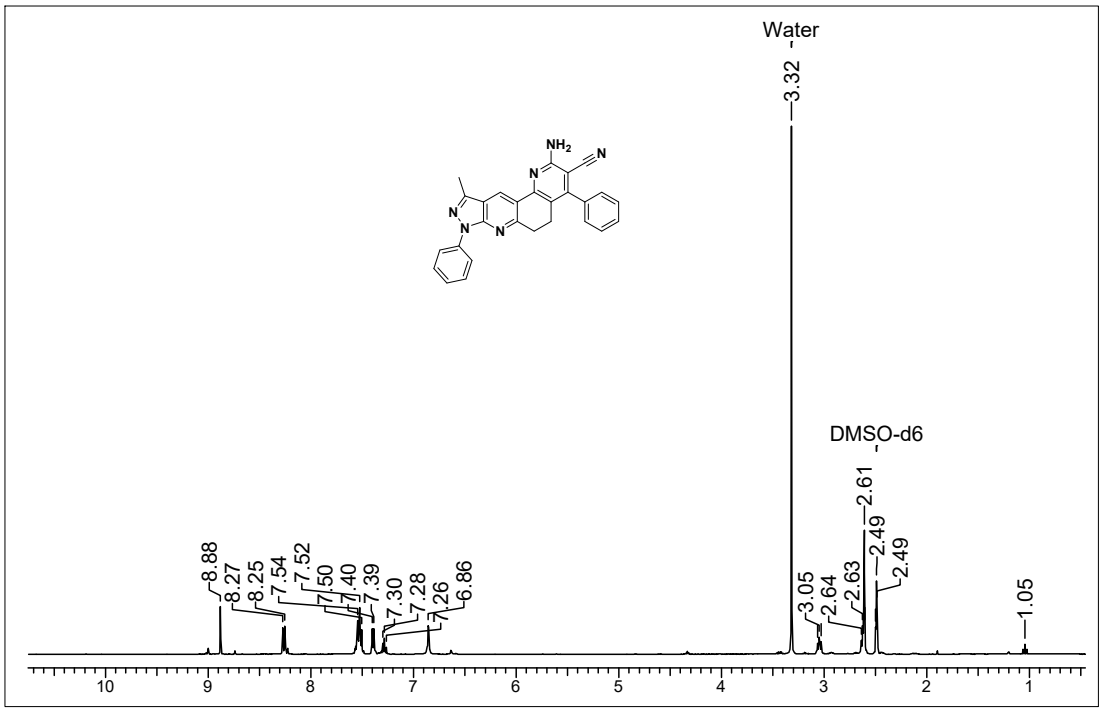

Fig S1. [1]H NMR for 2-amino-10-methyl-4,8-diphenyl-6,8-dihydro-5*H*-pyrazolo[3,4-*j*][1,7]phenanthroline-3-carbonitrile (**5a**)

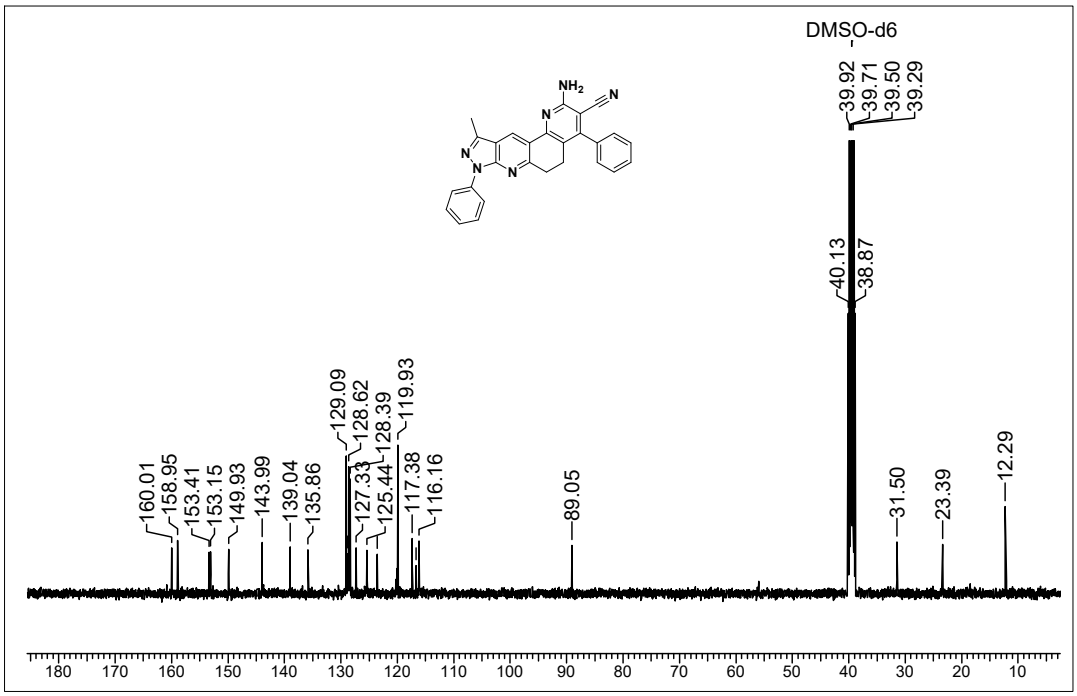

Fig S2. [13]C NMR for 2-amino-10-methyl-4,8-diphenyl-6,8-dihydro-5*H*-pyrazolo[3,4-*j*][1,7]phenanthroline-3-carbonitri-le (**5a**)

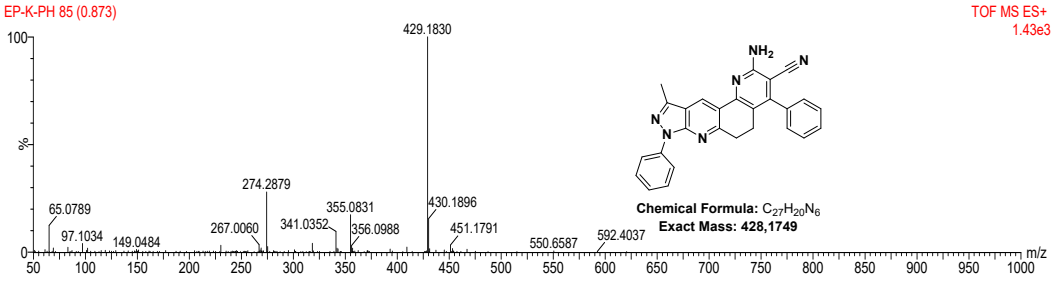

Fig S3. HRMS for 2-amino-10-methyl-4,8-diphenyl-6,8-dihydro-5*H*-pyrazolo[3,4-*j*][1,7]phenanthroline-3-carbonitrile (**5a**)

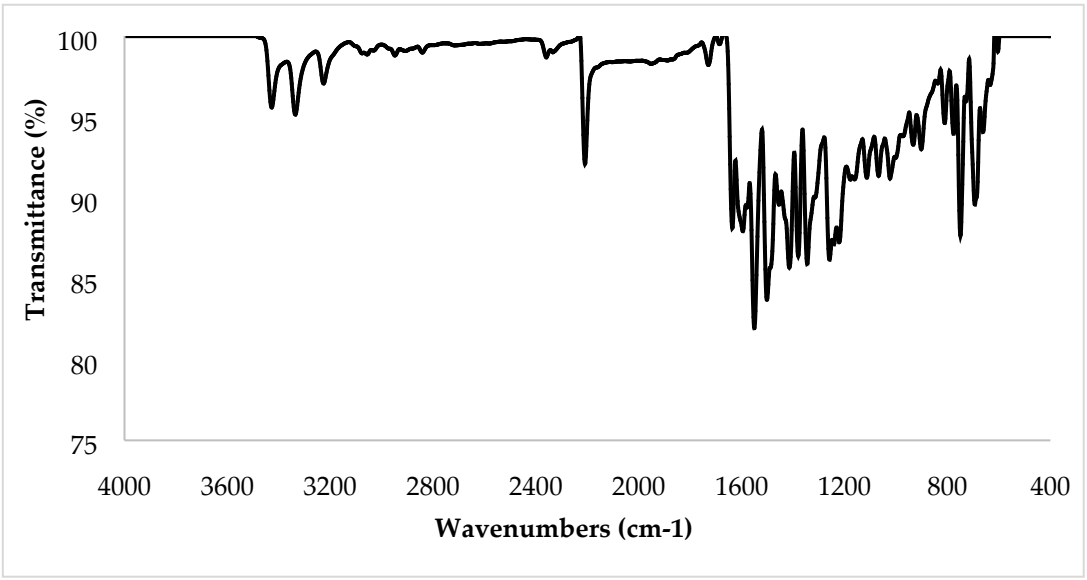

Fig S4. IR spectrum for 2-amino-10-methyl-4,8-diphenyl-6,8-dihydro-5*H*-pyrazolo[3,4-*j*][1,7]phenanthroline-3-carbonitrile (**5a**)

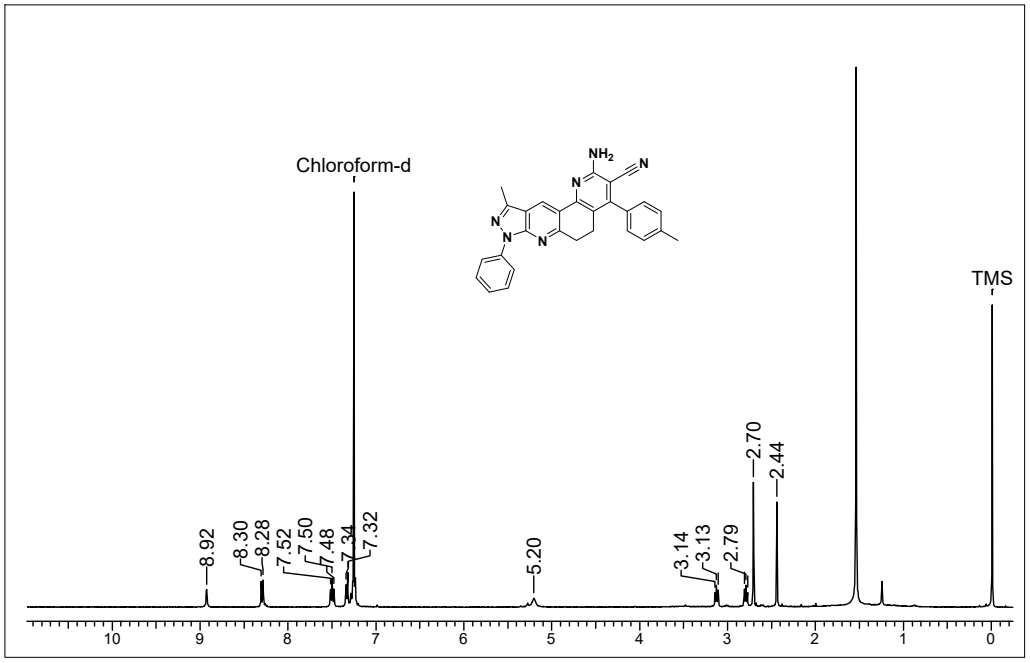

Fig S5. [1]H NMR for 2-amino-10-methyl-8-phenyl-4-(p-tolyl)-6,8-dihydro-5*H*-pyrazolo[3,4-*j*][1,7]phenanthroline-3-carbonitrile (**5b**)

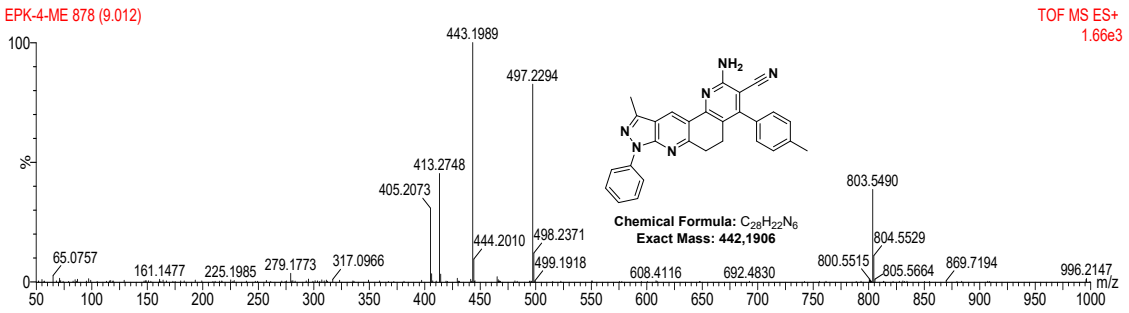

Fig S6. HRMS for 2-amino-10-methyl-8-phenyl-4-(p-tolyl)-6,8-dihydro-5*H*-pyrazolo[3,4-*j*][1,7]phenanthroline-3-carbonitrile (**5b**)

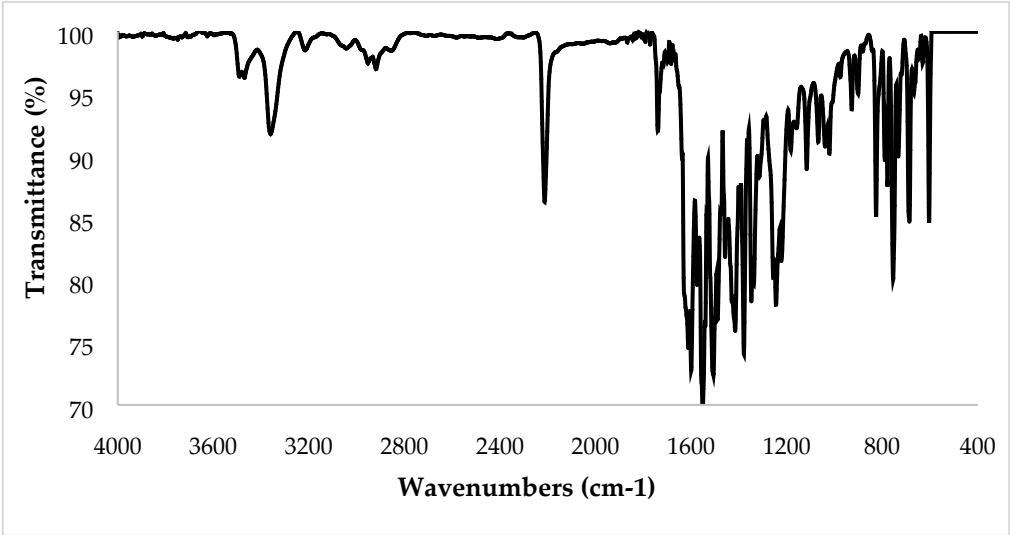

Fig S7. IR spectrum for 2-amino-10-methyl-8-phenyl-4-(p-tolyl)-6,8-dihydro-5*H*-pyrazolo[3,4-*j*][1,7]phenanthroline-3-carbonitrile (**5b**)

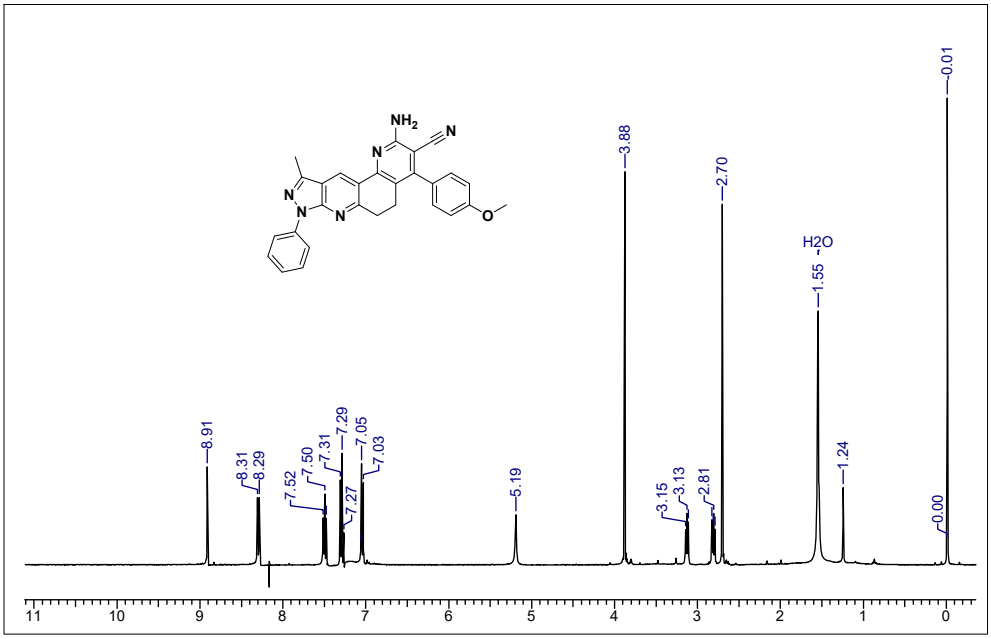

Fig S8. [1]HNMR for 2-amino-4-(4-methoxyphenyl)-10-methyl-8-phenyl-6,8-dihydro-5*H*-pyrazolo[3,4-*j*][1,7]phenanthroline-3-carbonitrile (**5c**)

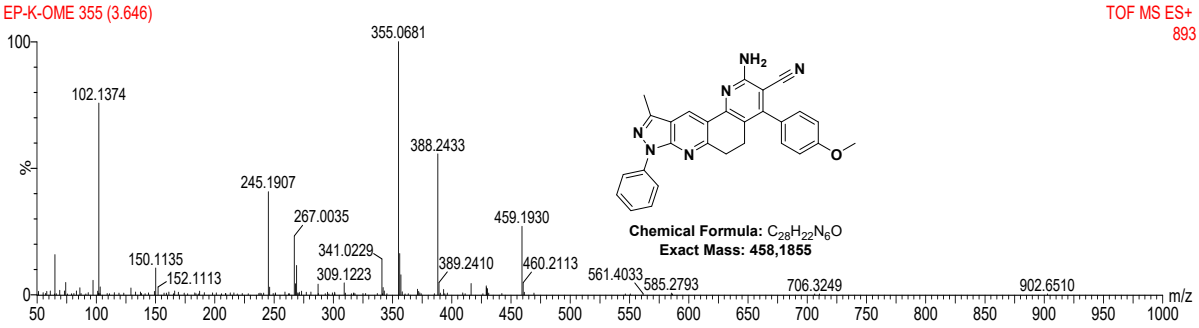

Fig S9. HRMS for 2-amino-4-(4-methoxyphenyl)-10-methyl-8-phenyl-6,8-dihydro-5*H*-pyrazolo[3,4-*j*][1,7]phenanthroline-3-carbonitrile (**5c**)

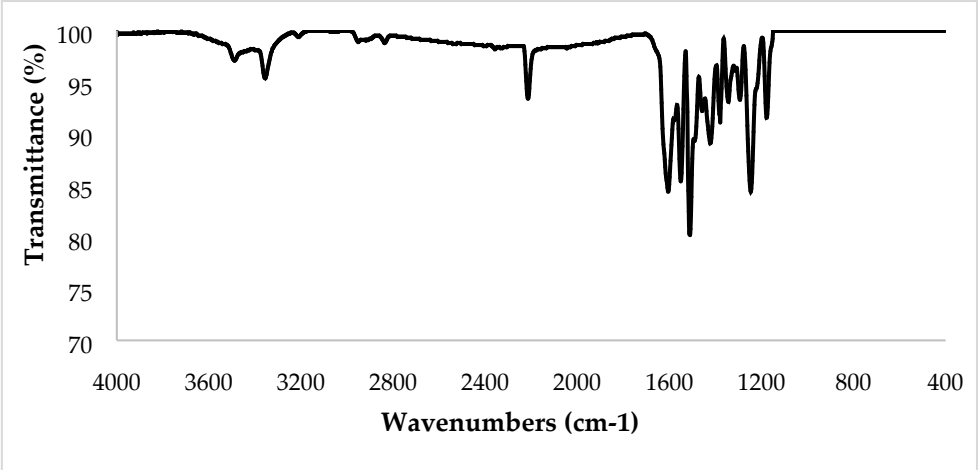

Fig S10. IR spectrum for 2-amino-4-(4-methoxyphenyl)-10-methyl-8-phenyl-6,8-dihydro-5*H*-pyrazolo[3,4-*j*][1,7]phenanthroline-3-carbonitrile (**5c**)

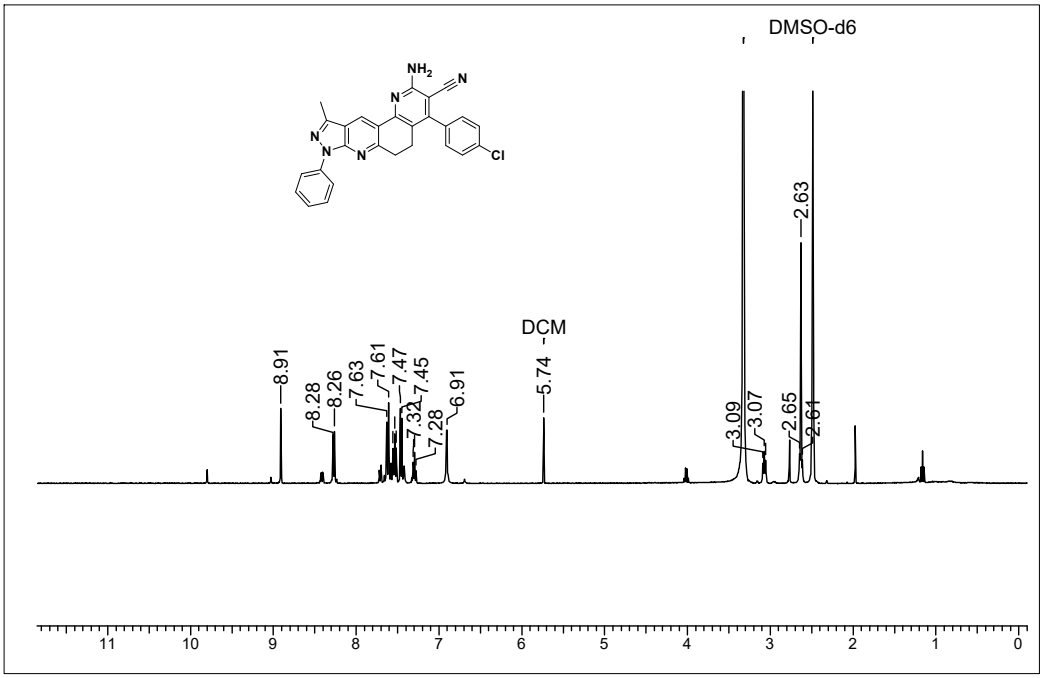

Fig S11. ^{1}H NMR for 2-amino-4-(4-chlorophenyl)-10-methyl-8-phenyl-6,8-dihydro-5*H*-pyrazolo[3,4-*j*][1,7]phenanthroline-3-carbonitrile (**5d**)

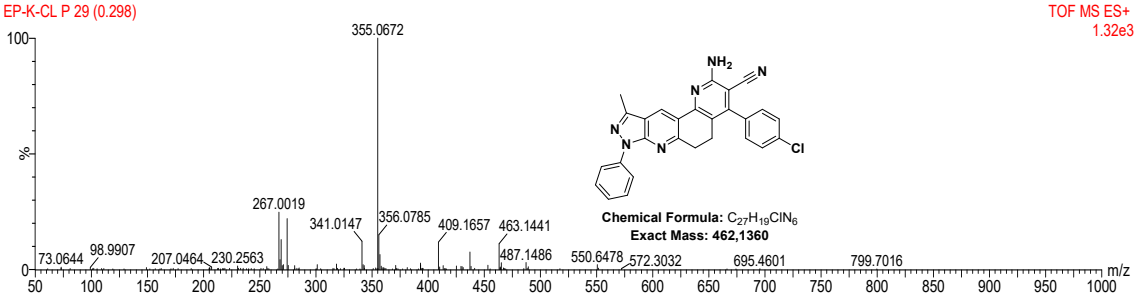

Fig S12. HRMS for 2-amino-4-(4-chlorophenyl)-10-methyl-8-phenyl-6,8-dihydro-5*H*-pyrazolo[3,4-*j*][1,7]phenanthroline-3-carbonitrile (**5d**)

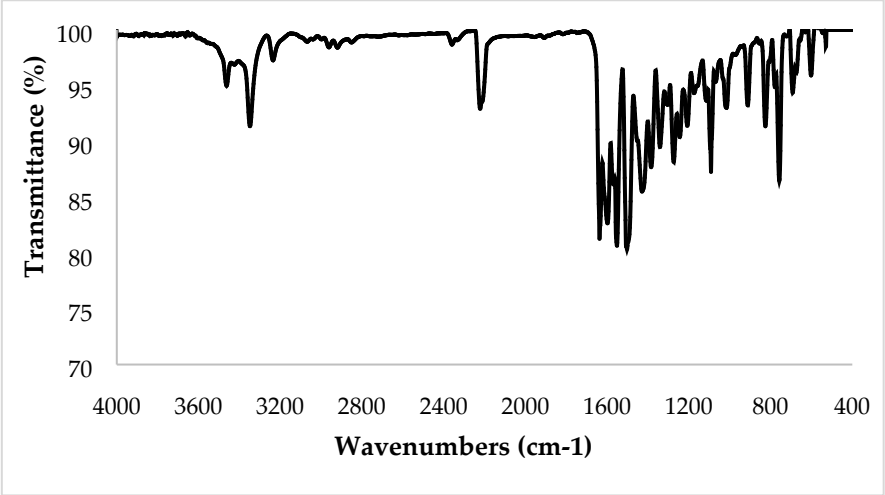

Fig S13. IR spectrum for 2-amino-4-(4-chlorophenyl)-10-methyl-8-phenyl-6,8-dihydro-5*H*-pyrazolo[3,4-*j*][1,7]phenanthroline-3-carbonitrile (**5d**)

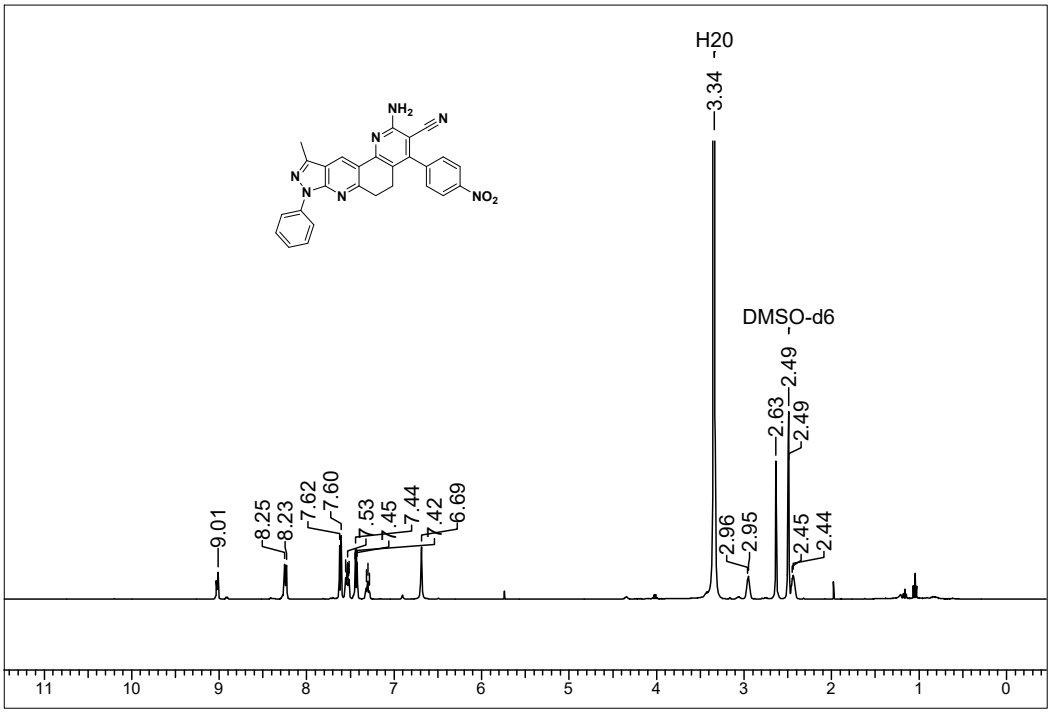

Fig S14. ^{1}H NMR for 2-amino-10-methyl-4-(4-nitrophenyl)-8-phenyl-6,8-dihydro-5*H*-pyrazolo[3,4-*j*][1,7]phenanthroline-3-carbonitrile (**5e**)

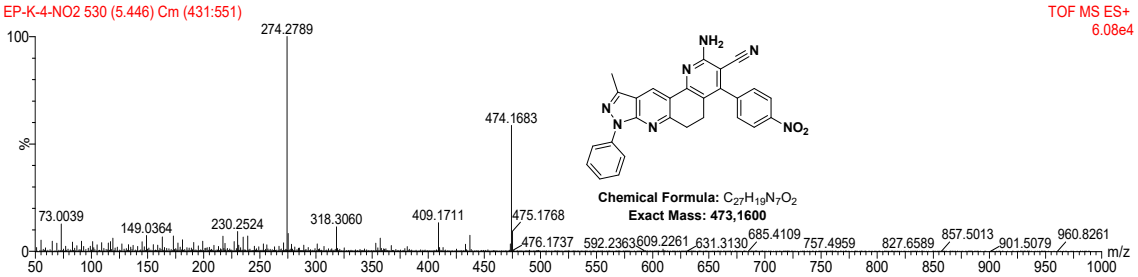

Fig S15. HRMS for 2-amino-10-methyl-4-(4-nitrophenyl)-8-phenyl-6,8-dihydro-5*H*-pyrazolo[3,4-*j*][1,7]phenanthroline-3-carbonitrile (**5e**)

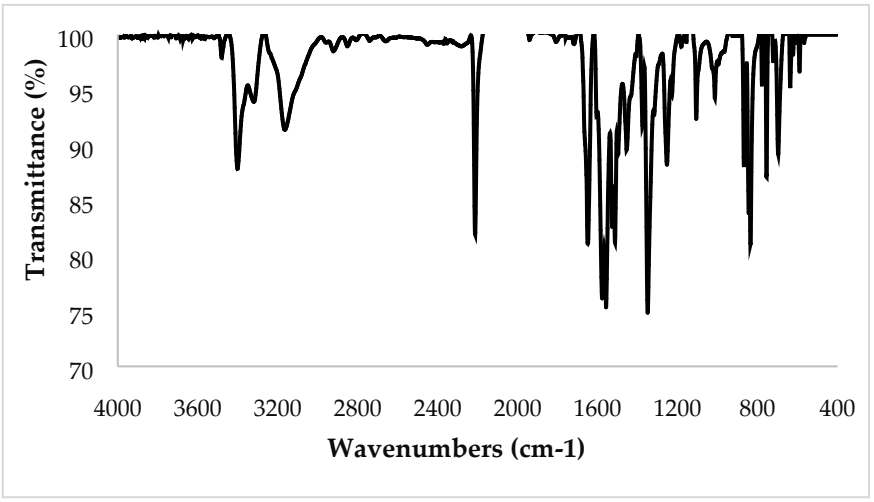

Fig S16. IR spectrum for 2-amino-10-methyl-4-(4-nitrophenyl)-8-phenyl-6,8-dihydro-5*H*-pyrazolo[3,4-*j*][1,7]phenanthroline-3-carbonitrile (**5e**)

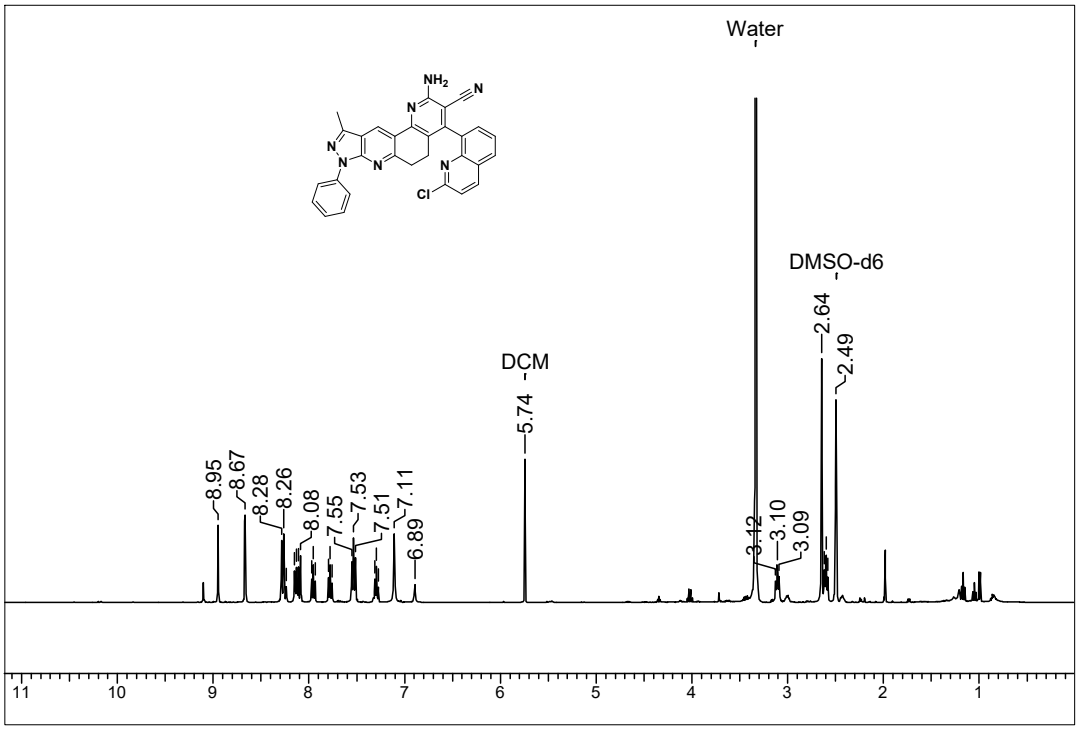

Fig S17. ^{1}H NMR for 2-amino-4-(2-chloroquinolin-3-yl)-10-methyl-8-phenyl-6,8-dihydro-5*H*-pyrazolo[3,4-*j*][1,7]phenanthroline-3-carbonitrile (**5f**)

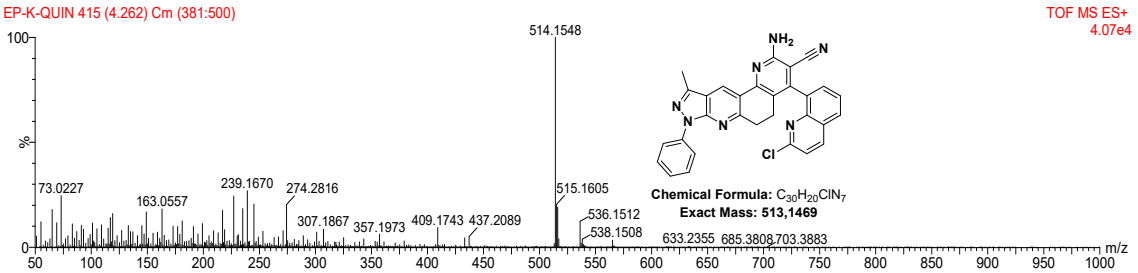

Fig S18. HRMS for 2-amino-4-(2-chloroquinolin-3-yl)-10-methyl-8-phenyl-6,8-dihydro-5*H*-pyrazolo[3,4-*j*][1,7]phenanthroline-3-carbonitrile (**5f**)

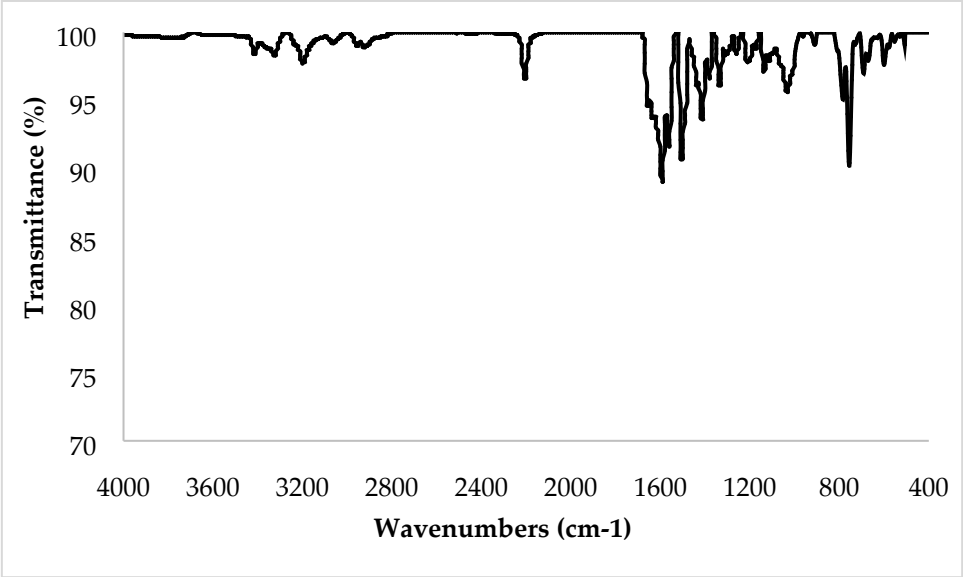

Fig S19. IR spectrum for 2-amino-4-(2-chloroquinolin-3-yl)-10-methyl-8-phenyl-6,8-dihydro-5*H*-pyrazolo[3,4-*j*][1,7]phenanthroline-3-carbonitrile (**5f**)

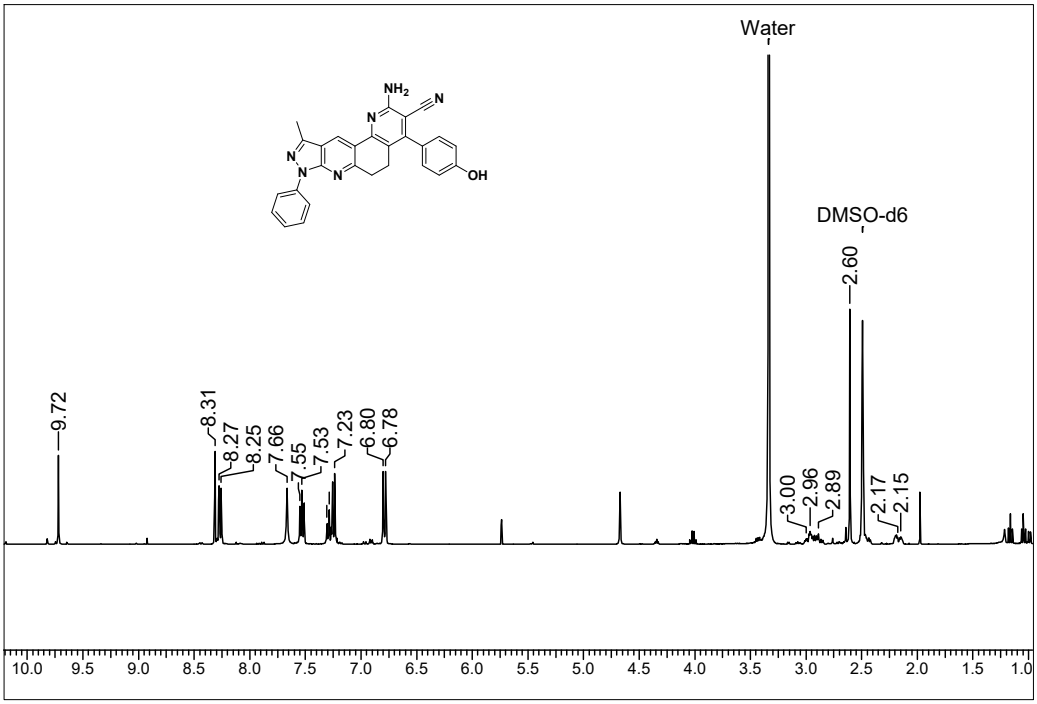

Fig S20. ^{1}H NMR for 2-amino-4-(4-hydroxyphenyl)-10-methyl-8-phenyl-6,8-dihydro-5*H*-pyrazolo[3,4-*j*][1,7]phenanthroline-3-carbonitrile (**5g**)

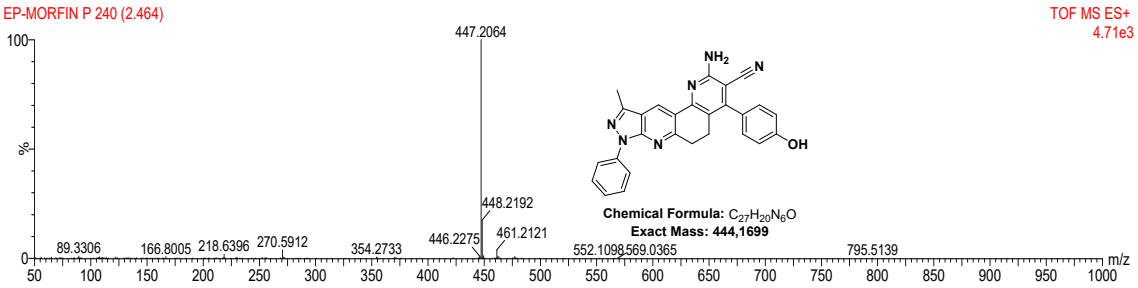

Fig S21. HRMS for 2-amino-4-(4-hydroxyphenyl)-10-methyl-8-phenyl-6,8-dihydro-5*H*-pyrazolo[3,4-*j*][1,7]phenanthroline-3-carbonitrile (**5g**)

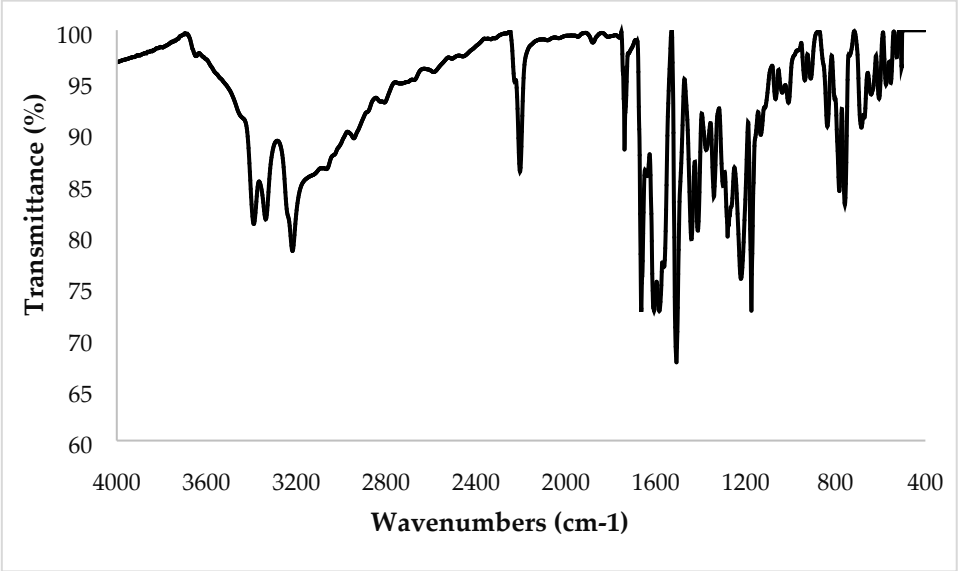

Fig S22. IR spectrum for 2-amino-4-(4-hydroxyphenyl)-10-methyl-8-phenyl-6,8-dihydro-5*H*-pyrazolo[3,4-*j*][1,7]phenanthroline-3-carbonitrile (**5g**)

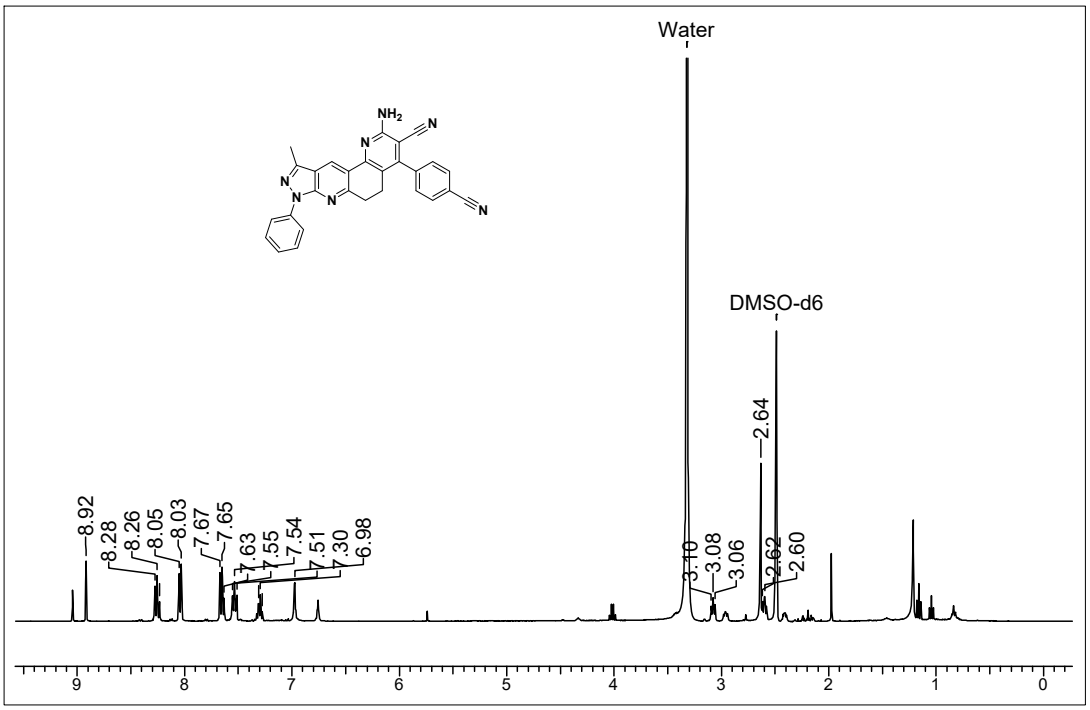

Fig S23. ^{1}H NMR for 2-amino-4-(4-cyanophenyl)-10-methyl-8-phenyl-6,8-dihydro-5*H*-pyrazolo[3,4-*j*][1,7]phenanthroline-3-carbonitrile (**5h**)

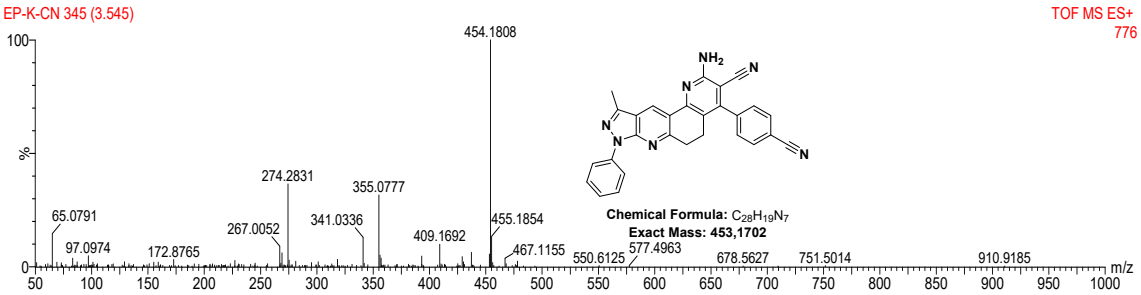

Fig S24. HRMS for 2-amino-4-(4-cyanophenyl)-10-methyl-8-phenyl-6,8-dihydro-5*H*-pyrazolo[3,4-*j*][1,7]phenanthroline-3-carbonitrile (**5h**)

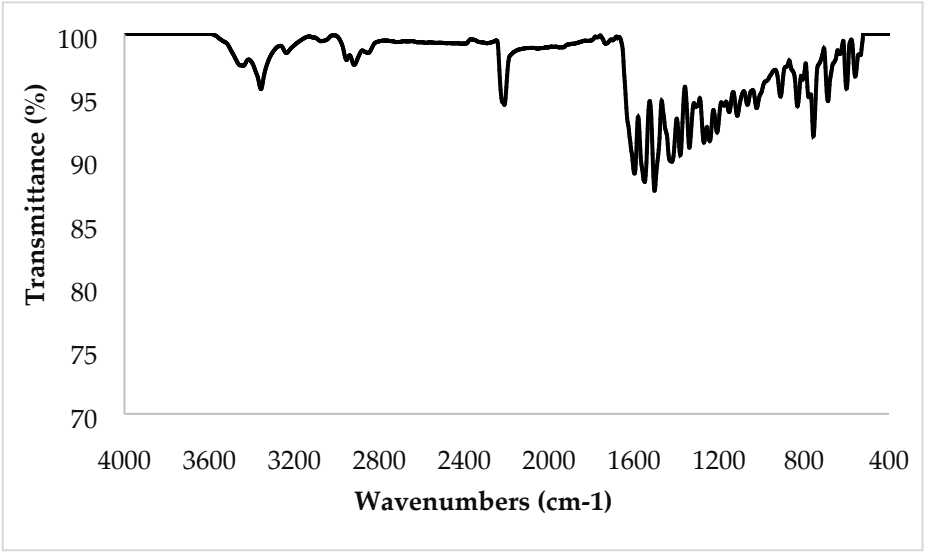

Fig S25. IR spectrum for 2-amino-4-(4-cyanophenyl)-10-methyl-8-phenyl-6,8-dihydro-5*H*-pyrazolo[3,4-*j*][1,7]phenanthroline-3-carbonitrile (**5h**)

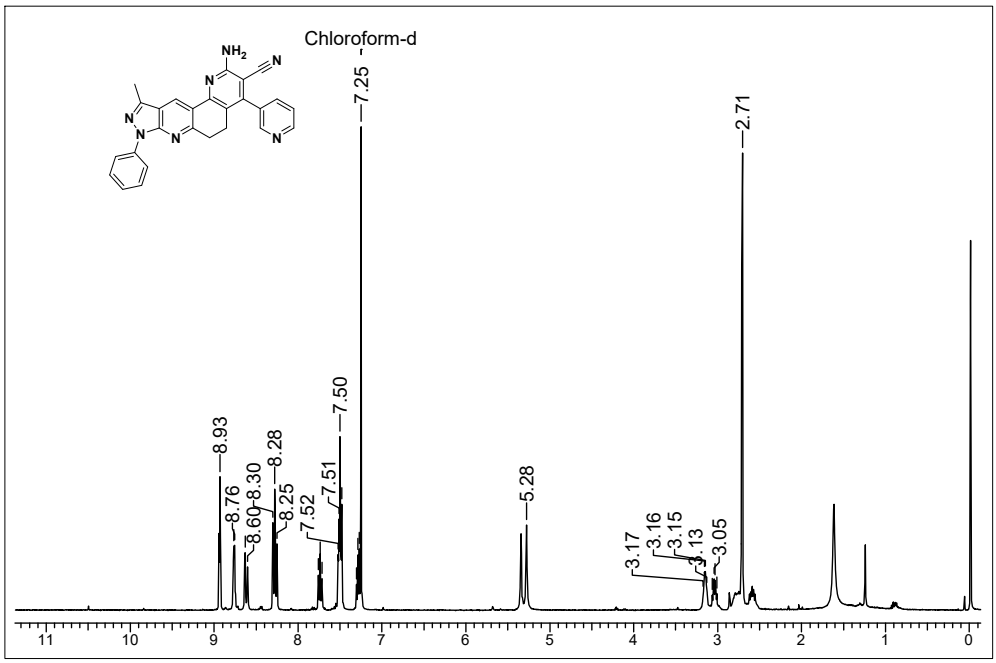

Fig S26. [1]H NMR for 2-amino-10-methyl-8-phenyl-4-(pyridin-3-yl)-6,8-dihydro-5*H*-pyrazolo[3,4-*j*][1,7]phenanthroline-3-carbonitrile (**5i**)

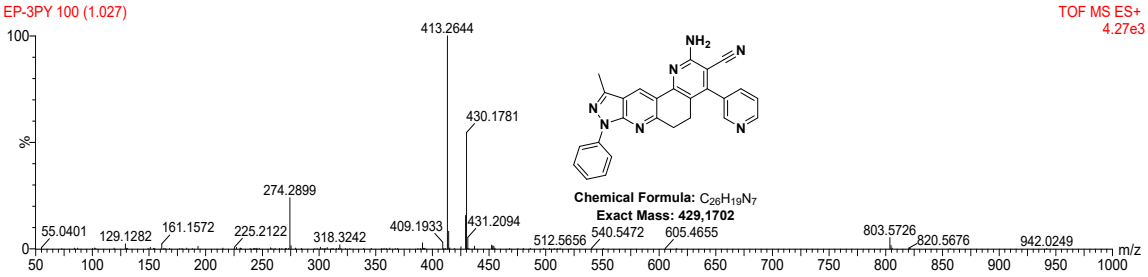

Fig S27. HRMS for 2-amino-10-methyl-8-phenyl-4-(pyridin-3-yl)-6,8-dihydro-5*H*-pyrazolo[3,4-*j*][1,7]phenanthroline-3-carbonitrile (**5i**)

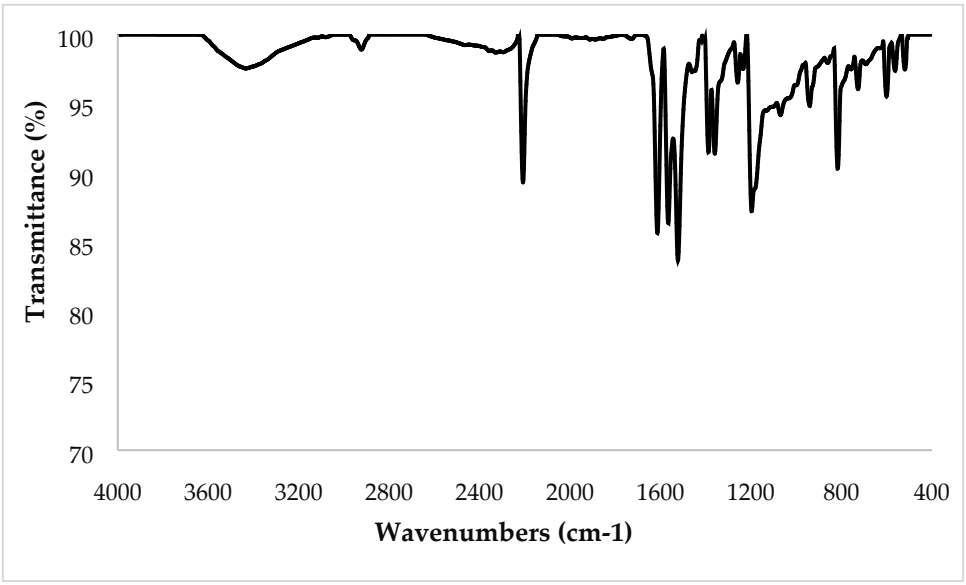

Fig S28. IR spectrum for 2-amino-10-methyl-8-phenyl-4-(pyridin-3-yl)-6,8-dihydro-5*H*-pyrazolo[3,4-*j*][1,7]phenanthroline-3-carbonitrile (**5i**)

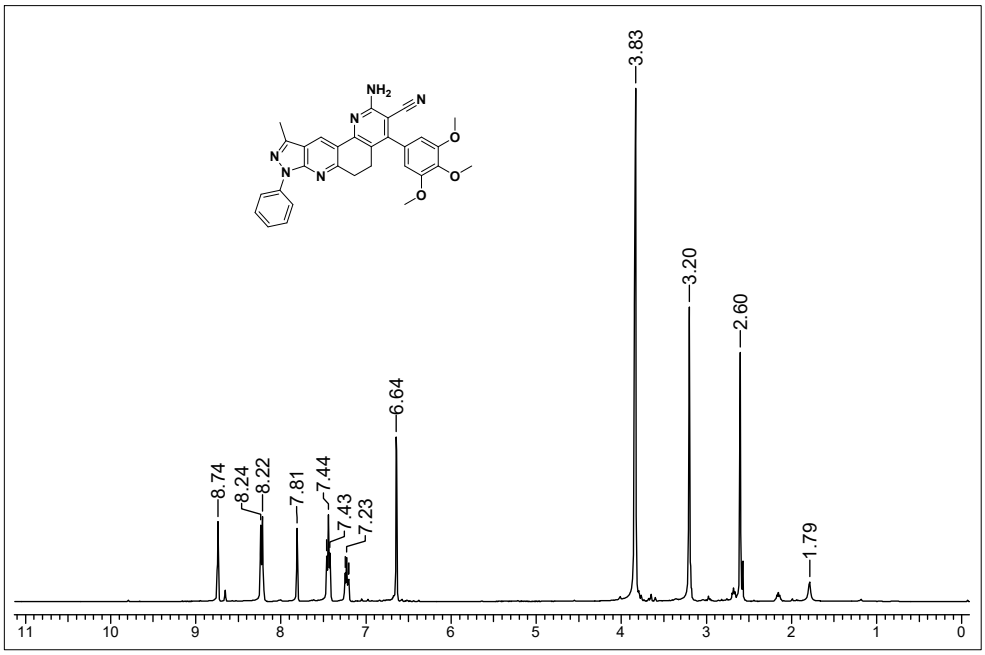

Fig S29. ^{1}H NMR for 2-amino-10-methyl-8-phenyl-4-(3,4,5-trimethoxyphenyl)-6,8-dihydro-5*H*-pyrazolo[3,4-*j*][1,7]phenanthroline-3-carbonitrile **(5j)**

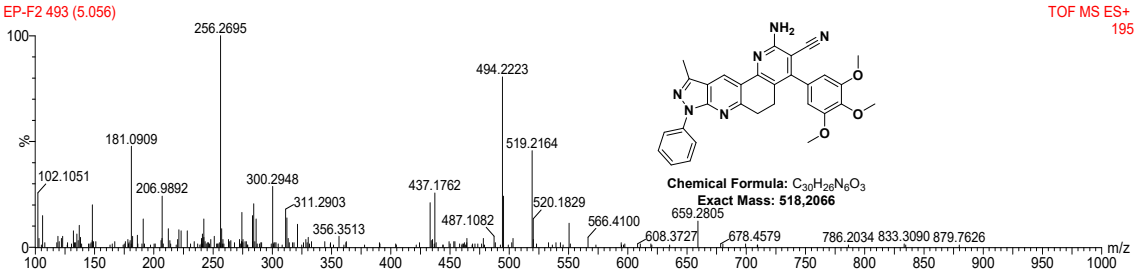

Fig S30. HRMS for 2-amino-10-methyl-8-phenyl-4-(3,4,5-trimethoxyphenyl)-6,8-dihydro-5*H*-pyrazolo[3,4-*j*][1,7]phenanthroline-3-carbonitrile **(5j)**

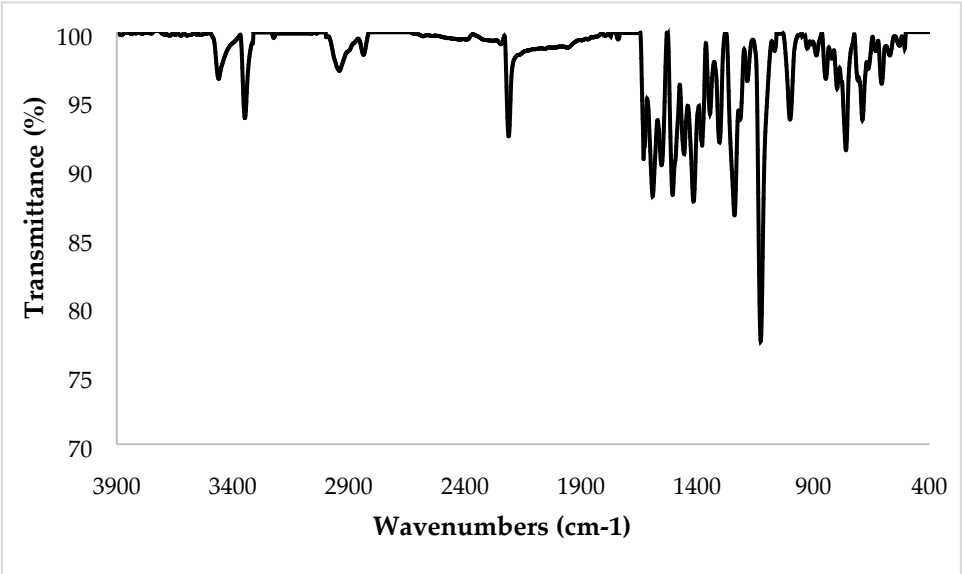

Fig S31. IR spectrum for 2-amino-10-methyl-8-phenyl-4-(3,4,5-trimethoxyphenyl)-6,8-dihydro-5*H*-pyrazolo[3,4-*j*][1,7]phenanthroline-3-carbonitrile **(5j)**

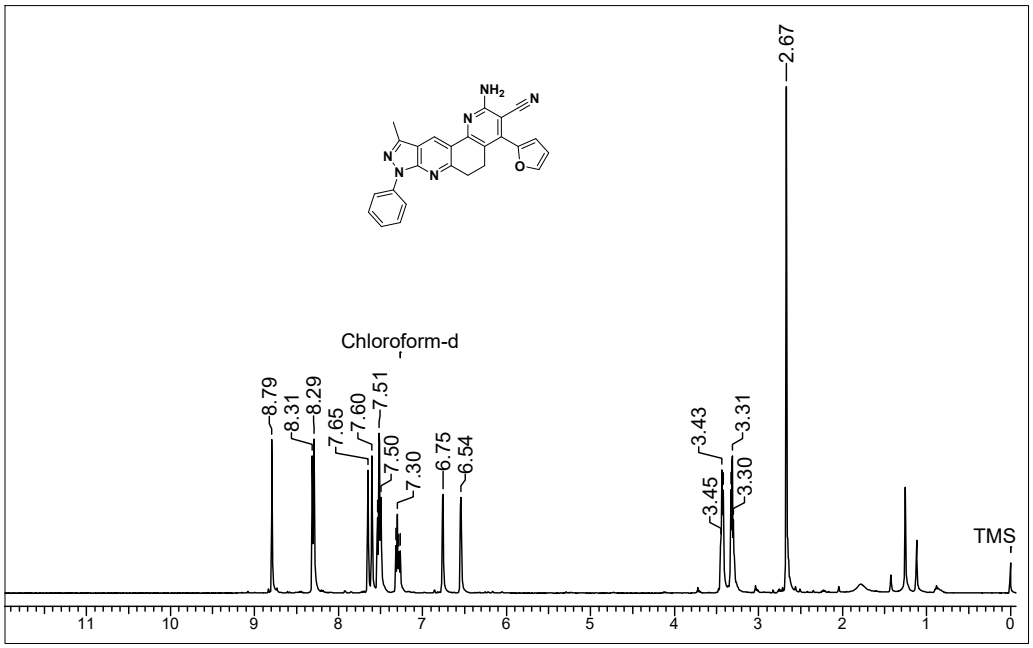

Fig S32. ^{1}H NMR for 2-amino-4-(furan-2-yl)-10-methyl-8-phenyl-6,8-dihydro-5*H*-pyrazolo[3,4-*j*][1,7]phenanthroline-3-carbonitrile(**5k**)

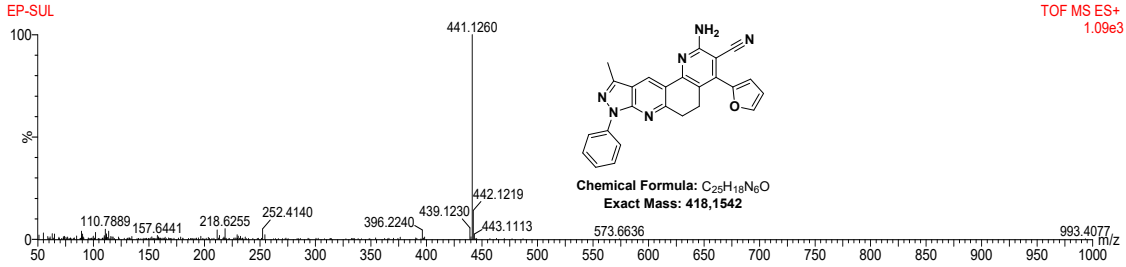

Fig S33. HRMS for 2-amino-4-(furan-2-yl)-10-methyl-8-phenyl-6,8-dihydro-5*H*-pyrazolo[3,4-*j*][1,7]phenanthroline-3-carbonitrile(**5k**)

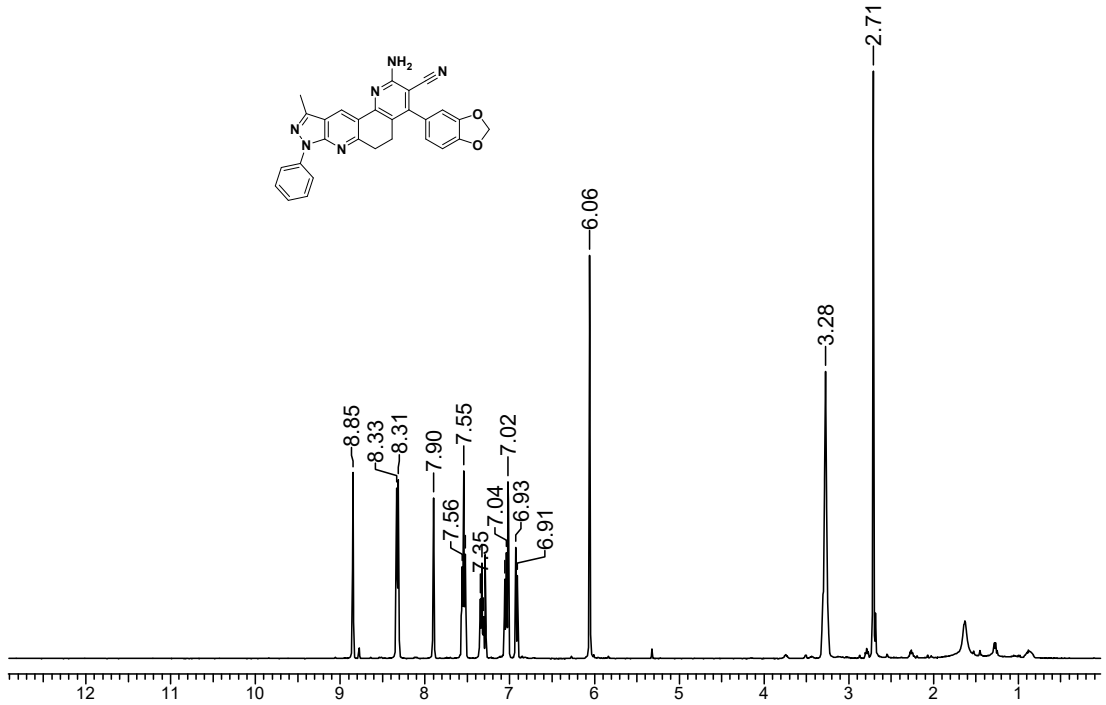

Fig S34. [1]HNMR 2-amino-4-(benzo[d][1,3]dioxol-5-yl)-10-methyl-8-phenyl-6,8-dihydro-5*H*-pyrazolo[3,4-*j*][1,7]phenanthroline-3-carbonitrile **(5l)**

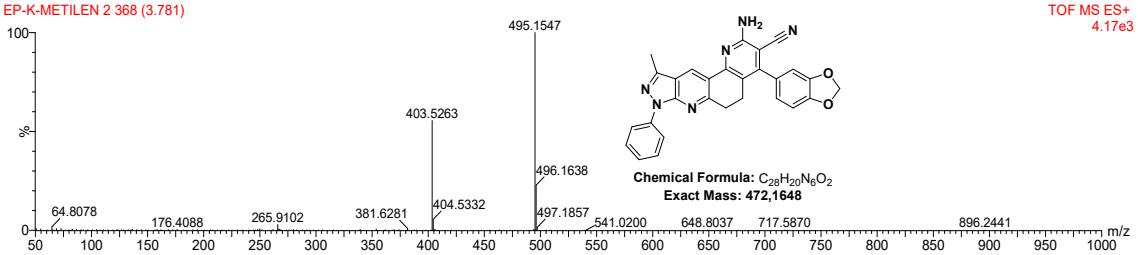

Fig S35. HRMS for 2-amino-4-(benzo[d][1,3]dioxol-5-yl)-10-methyl-8-phenyl-6,8-dihydro-5*H*-pyrazolo[3,4-*j*][1,7]phenanthroline-3-carbonitrile **(5l)**

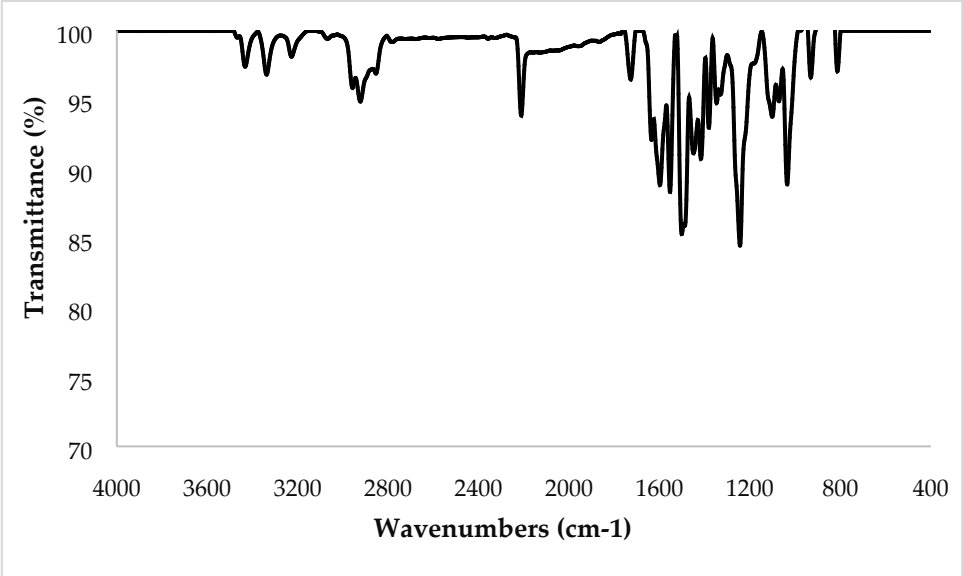

Fig S36. IR spectrum for 2-amino-4-(benzo[d][1,3]dioxol-5-yl)-10-methyl-8-phenyl-6,8-dihydro-5*H*-pyrazolo[3,4-*j*][1,7]phenanthroline-3-carbonitrile **(5l)**

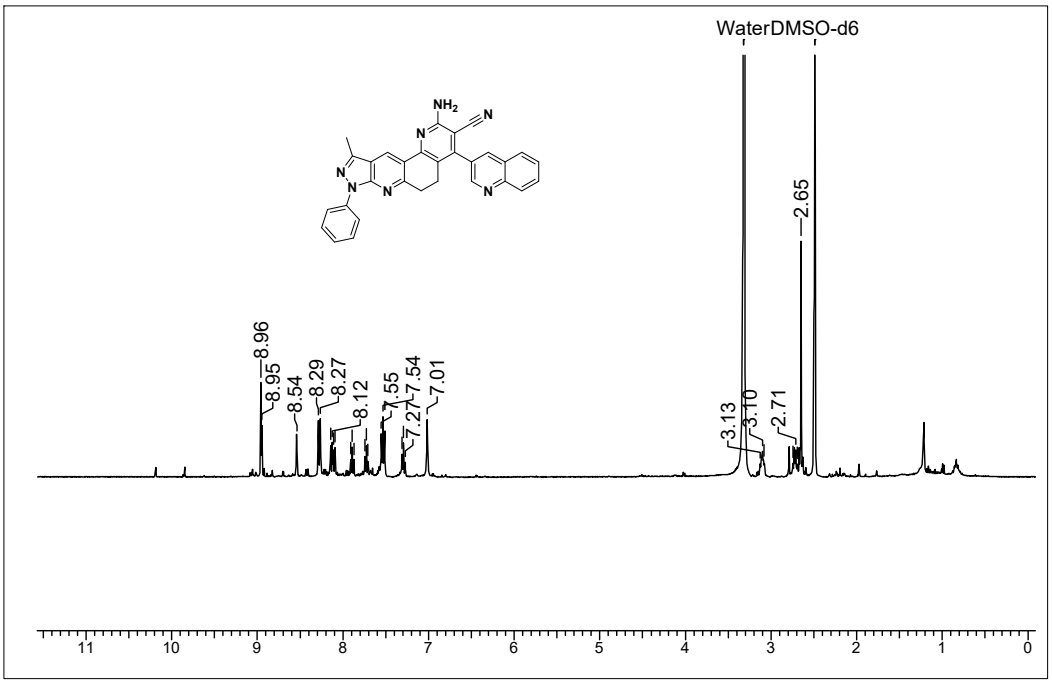

Fig S37. ^{1}H NMR for 2-amino-10-methyl-8-phenyl-4-(quinolin-3-yl)-6,8-dihydro-5*H*-pyrazolo[3,4-*j*][1,7]phenanthroline-3-carbonitrile (**5m**)

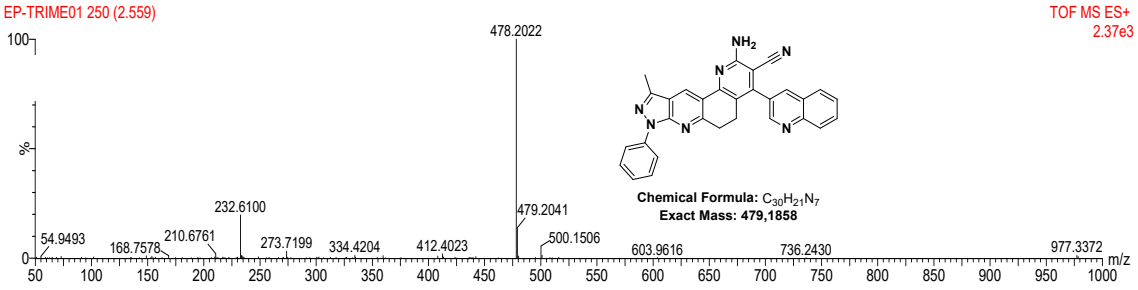

Fig S38. HRMS for 2-amino-10-methyl-8-phenyl-4-(quinolin-3-yl)-6,8-dihydro-5*H*-pyrazolo[3,4-*j*][1,7]phenanthroline-3-carbonitrile (**5m**)

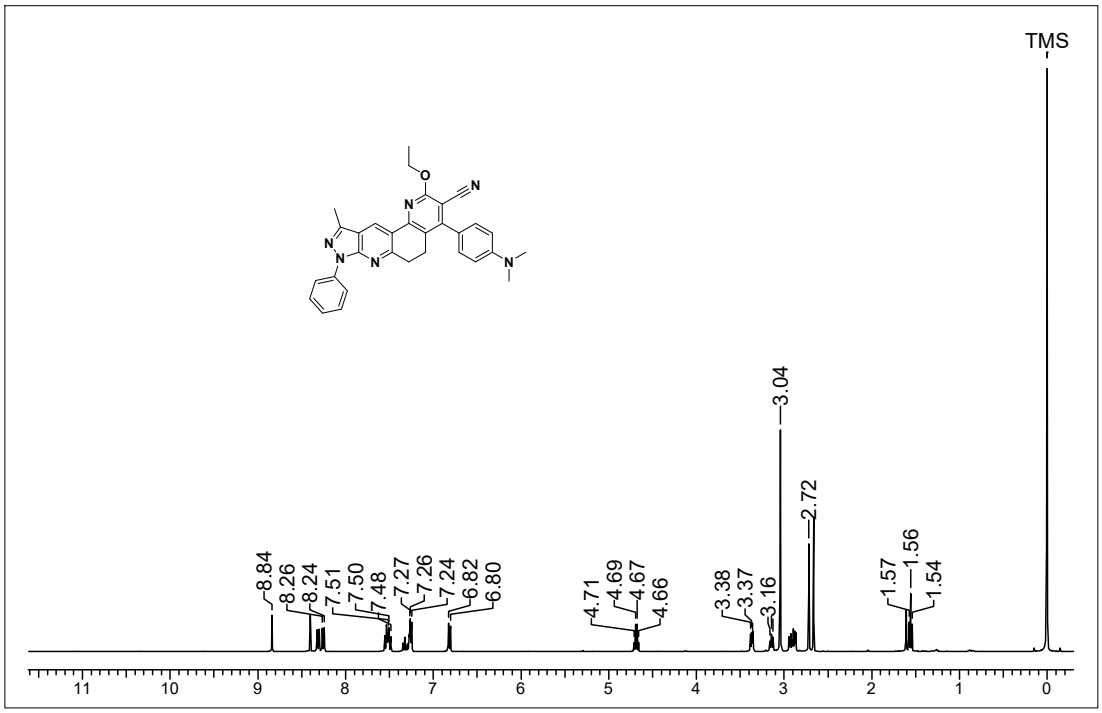

Fig S39. ^{1}H NMR for 4-(4-(dimethylamino)phenyl)-2-ethoxy-10-methyl-8-phenyl-6,8-dihydro-5*H*-pyrazolo[3,4-*j*][1,7]phenanthroline-3-carbonitrile (**5n**)

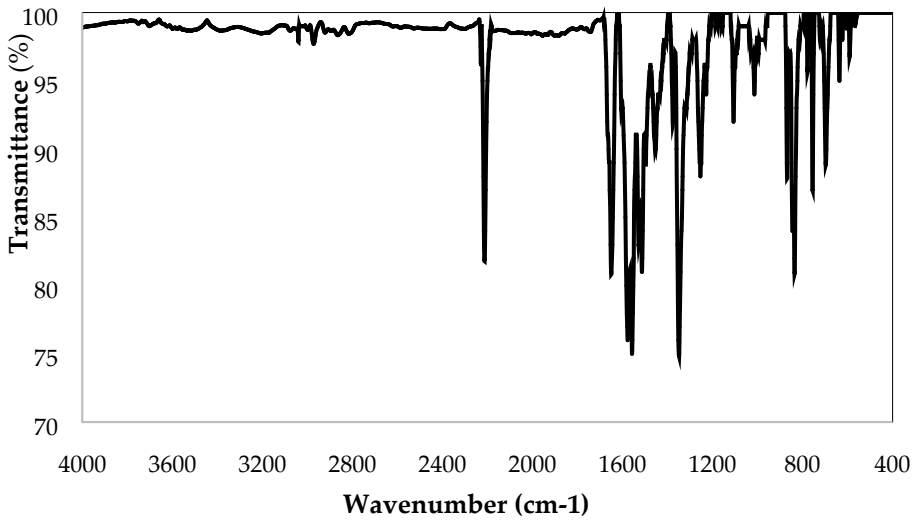

Fig S40. IR spectrum for 4-(4-(dimethylamino)phenyl)-2-ethoxy-10-methyl-8-phenyl-6,8-dihydro-5*H*-pyrazolo[3,4-*j*][1,7]phenanthroline-3-carbonitrile (**5n**)

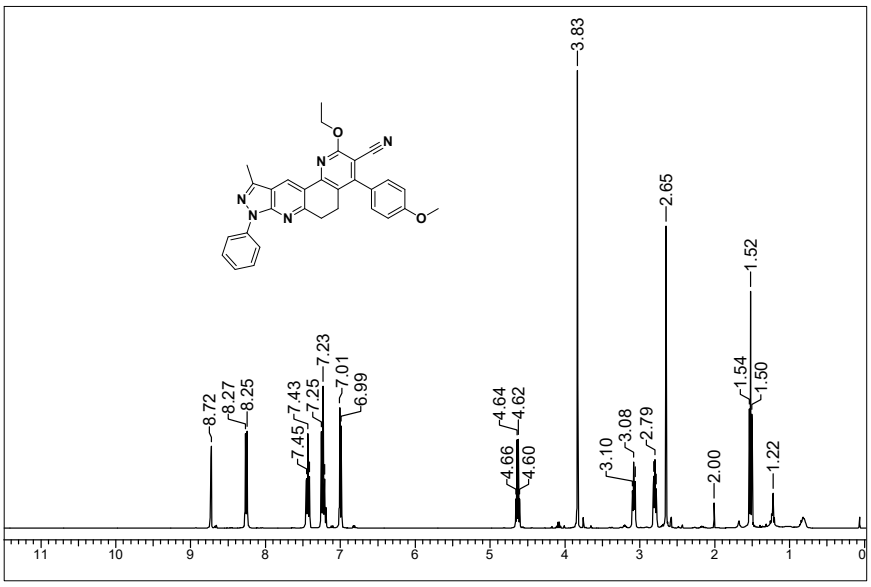

Fig S41. ^{1}H NMR for 2-ethoxy-4-(4-methoxyphenyl)-10-methyl-8-phenyl-6,8-dihydro-5*H*-pyrazolo[3,4-*j*][1,7]phenanthroline-3-carbonitrile (**5o**)

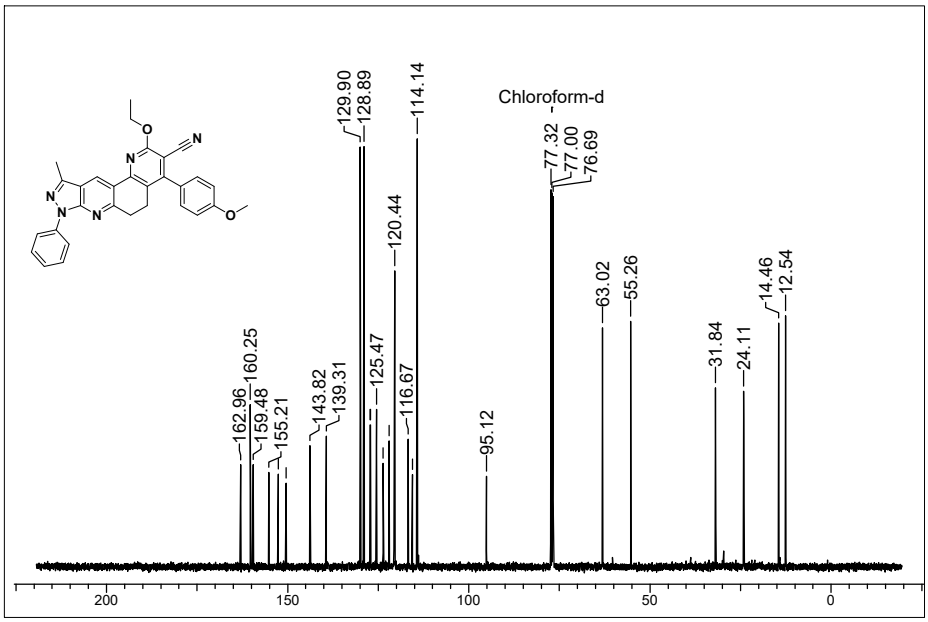

Fig S42. ^{13}C NMR for 2-ethoxy-4-(4-methoxyphenyl)-10-methyl-8-phenyl-6,8-dihydro-5*H*-pyrazolo[3,4-*j*][1,7]phenanthroline-3-carbonitrile (**5o**)

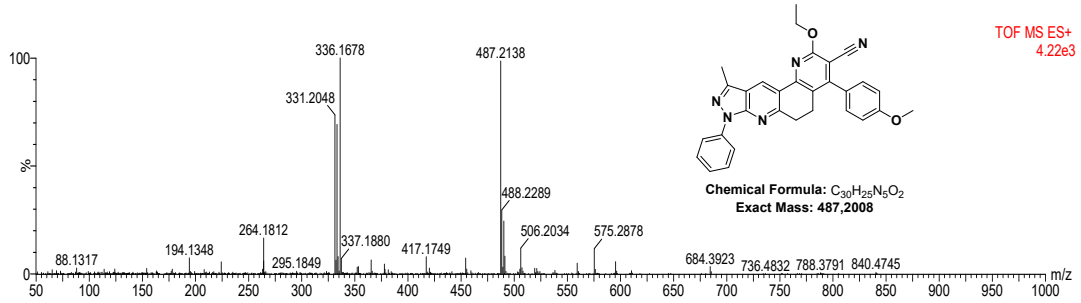

Fig S43. HRMS for 2-ethoxy-4-(4-methoxyphenyl)-10-methyl-8-phenyl-6,8-dihydro-5*H*-pyrazolo[3,4-*j*][1,7]phenanthroline-3-carbonitrile (**5o**)

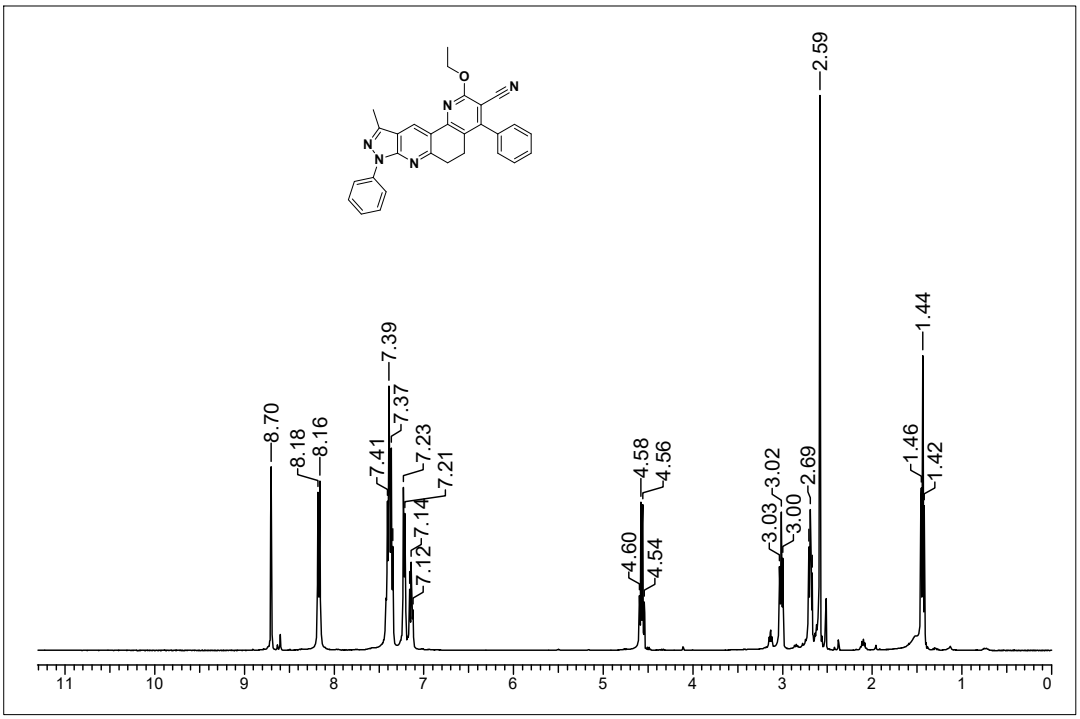

Fig S44. [1]H NMR for 2-ethoxy-10-methyl-4,8-diphenyl-6,8-dihydro-5*H*-pyrazolo[3,4-*j*][1,7]phenanthroline-3-carbonitrile (**5p**)

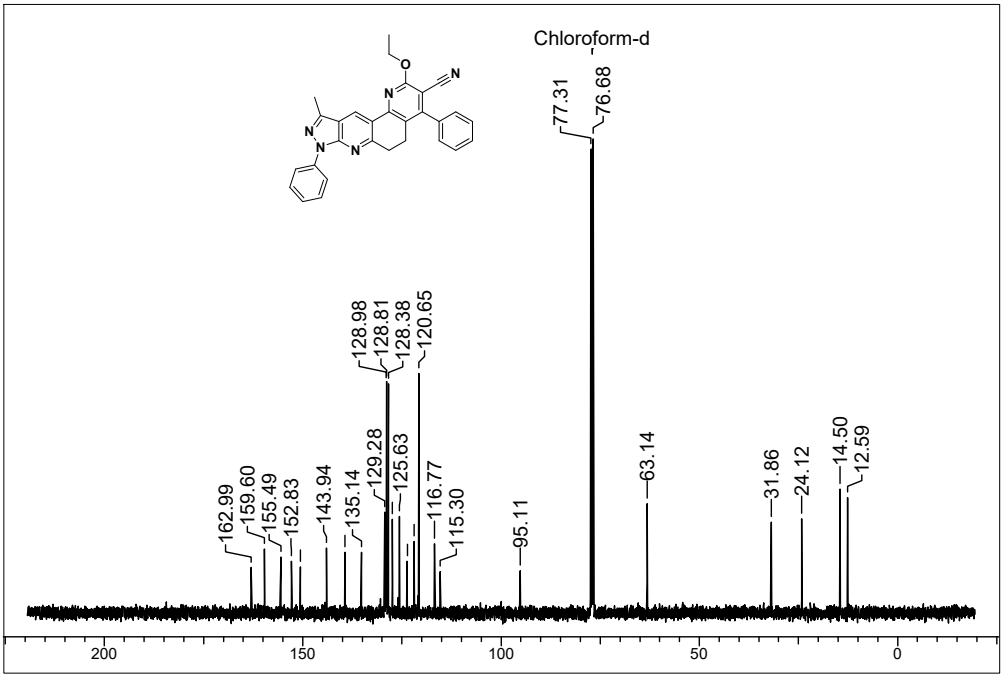

Fig S45. [13]C NMR for 2-ethoxy-10-methyl-4,8-diphenyl-6,8-dihydro-5*H*-pyrazolo[3,4-*j*][1,7]phenanthroline-3-carbonitrile (**5p**)

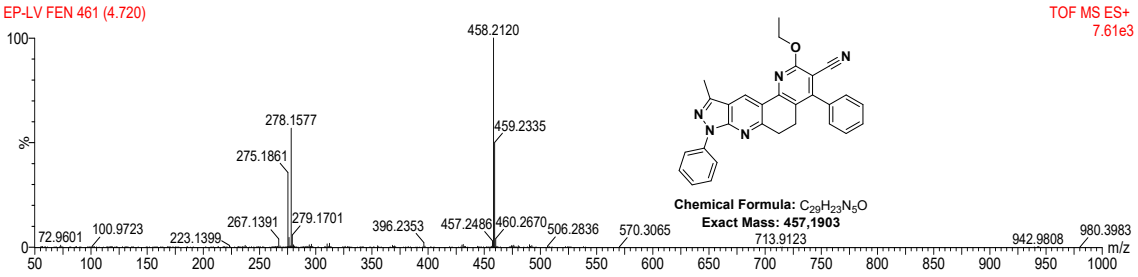

Fig S46. HRMS for 2-ethoxy-10-methyl-4,8-diphenyl-6,8-dihydro-5*H*-pyrazolo[3,4-*j*][1,7]phenanthroline-3-carbonitrile (**5p**)

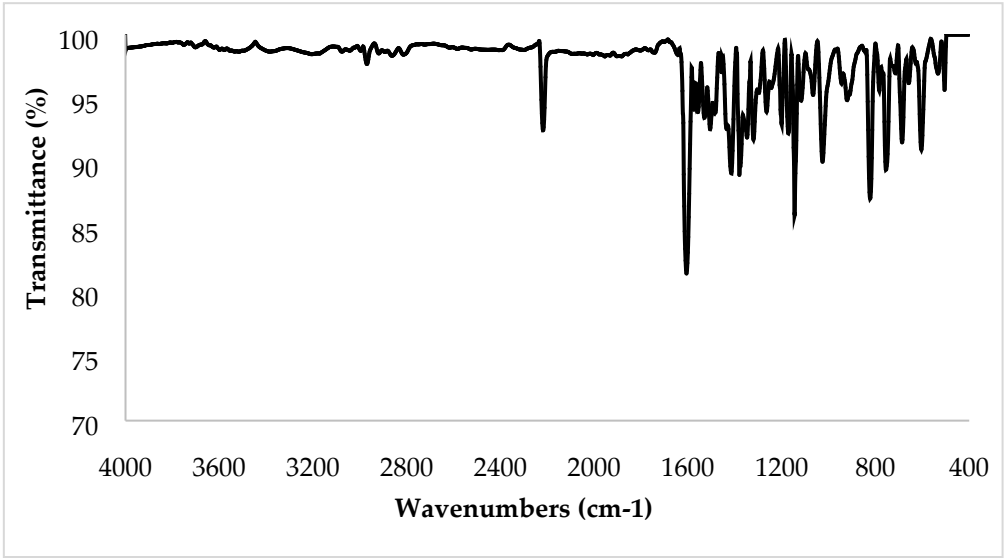

Fig S47. IR spectrum for 2-ethoxy-10-methyl-4,8-diphenyl-6,8-dihydro-5*H*-pyrazolo[3,4-*j*][1,7]phenanthroline-3-carbonitrile (**5p**)

Table S1. Main descriptors for the series (**5a-p**) calculated with SwissADME

Entry	MW (g/mol)	Acceptor HB[a]	Donor HB[b]	PSA (Å²)[c]	log P (o/w) [d]	log S[e]	GI absorption [f]	BBB entry[g]	Rule 5[h]
5a	428,49	4	1	9341	3,54	-6,35	High	No	0
5b	442,53	4	1	9341	3,75	-6,65	High	No	0
5c	458,51	5	1	10264	3,88	-6,42	High	No	0
5d	462,95	4	1	9341	3,93	-6,94	High	No	0
5e	473,49	6	1	13923	3,10	-6,40	Low	No	0
5f	513,98	5	1	10630	3,89	-7,65	Low	No	1
5g	444,49	5	2	11364	3,13	-6,21	High	No	0
5h	453,50	5	1	11720	3,39	-6,29	Low	No	0
5i	429,48	5	1	10630	3,22	-5,68	High	No	0
5j	518,57	7	1	12110	4,28	-6,56	Low	No	1
5k	472,50	6	1	11187	3,82	-6,46	High	No	0
5l	418,45	5	1	10655	3,37	-5,71	High	No	0
5m	479,53	5	1	10630	3,60	-6,85	Low	No	0
5n	500,59	5	0	7986	4,79	-6,89	High	No	1
5o	487,55	6	0	8585	4,69	-6,73	High	No	0
5p	457,53	5	0	7662	4,51	-6,66	High	No	0

[a]Estimated number of H bonds that are accepted by the solute of water molecules in an aqueous solution. [b] Estimated number of H bonds donated by the solute to water molecules in an aqueous

solution. [c] Van der Waals polar surface area for nitrogen and oxygen atoms. [d] log P for octanol / water (-2.0 to -6.5). [e] Predicted aqueous solubility, log S, S in mol/dm^3 (-6.5 to 0.5). [f] Gastrointestinal absorption according to BOILED-Egg diagram. [g] Permeability of the blood-brain barrier (BBB). [h] Number of violations of Lipinski's rule of five. The rules are: PM <500, log P o/w <5, donor HB ≤ 5, accept HB ≤ 10. Compounds that meet these rules are considered drugs. (The "five" refers to the limits, which are multiples of 5.)

Table S2. Frontier molecular orbitals energies (E_{HOMO} and E_{LUMO}), electronegativity (χ), chemical hardness (η), chemical softness (S) and electron affinity (EA).

Entry	E_{HOMO} (eV)	E_{LUMO} (eV)	ΔE (eV)	χ (eV)	η (eV)	S (eV)$^{-1}$	EA (eV)
5a	-5,66	-1,92	3,74	3,79	1,87	0,53	1,92
5b	-5,64	-1,89	3,75	3,76	1,88	0,53	1,89
5c	-5,63	-1,86	3,77	3,74	1,88	0,53	1,86
5d	-5,73	-2,03	3,7	3,88	1,85	0,54	2,03
5e	-5,83	-2,64	3,19	4,24	1,6	0,63	2,64
5f	-5,68	-2,04	3,64	3,86	1,82	0,55	2,04
5g	-5,6	-1,87	3,73	3,74	1,87	0,54	1,87
5h	-5,82	-2,22	3,6	4,02	1,8	0,56	2,22
5i	-5,61	-1,66	3,95	3,64	1,98	0,51	1,66
5j	-5,32	-1,75	3,57	3,53	1,78	0,56	1,75
5k	-5,64	-1,90	3,74	3,77	1,87	0,53	1,9
5l	-5,69	-2,04	3,64	3,86	1,82	0,55	2,04
5m	-5,63	-2,08	3,55	3,86	1,78	0,56	2,08
5n	-5,61	-1,88	3,73	3,74	1,87	0,54	1,88
5o	-5,73	-2,04	3,69	3,88	1,84	0,54	2,04
5p	-5,7	-1,99	3,71	3,84	1,86	0,54	1,99
5q	-5,27	-1,86	3,41	3,57	1,7	0,59	1,86

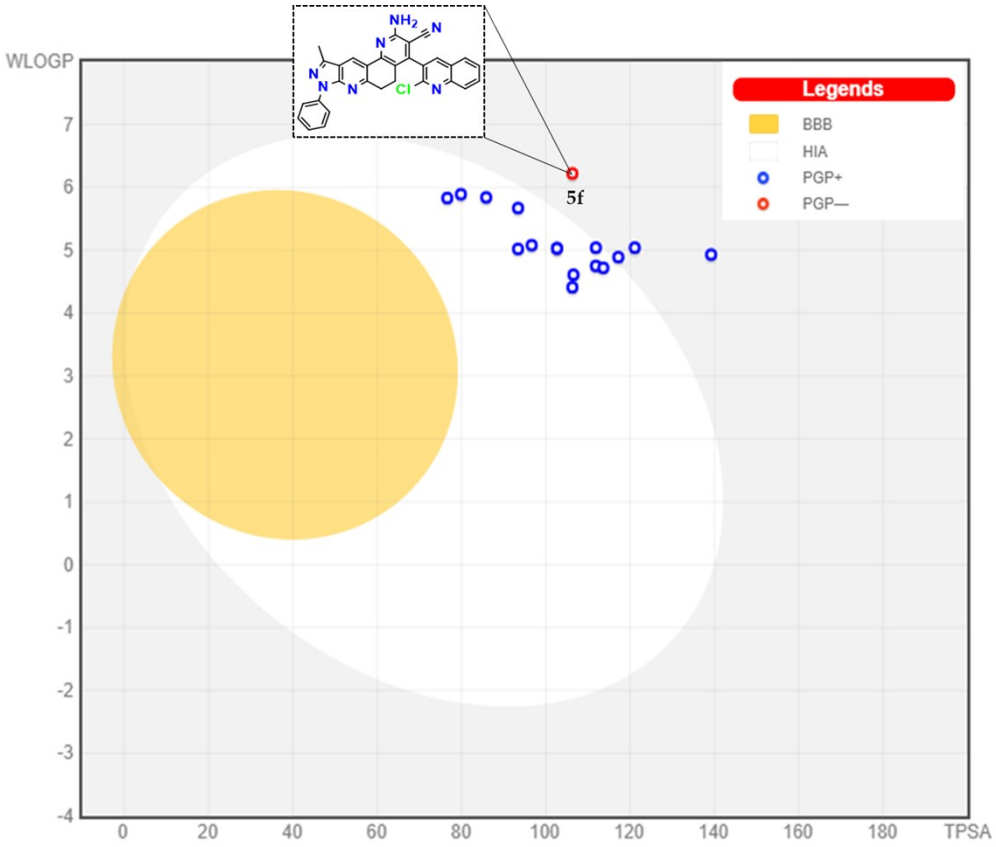

Fig S48. Pharmacokinetic profile of the compounds **5a-p**. BOILED-Egg diagram of synthesized compounds. White region: high probability of passive absorption by the gastrointestinal tract; yellow region (yolk): high probability of brain penetration. Yolk and the white region are not mutually exclusive. Bluepoint: P-gp substrate. Redpoint: No P-gp substrate.