Supplementary Material

2-(Butylamino)-6-chloro-4-[3-(7-chloro-4-quinolylamino)propylamino]-1,3,5-triazine

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NMR spectrometry

Figure S1. ^{1}H NMR spectrum ($CDCl_3$, 150 MHz) of compound **2**.

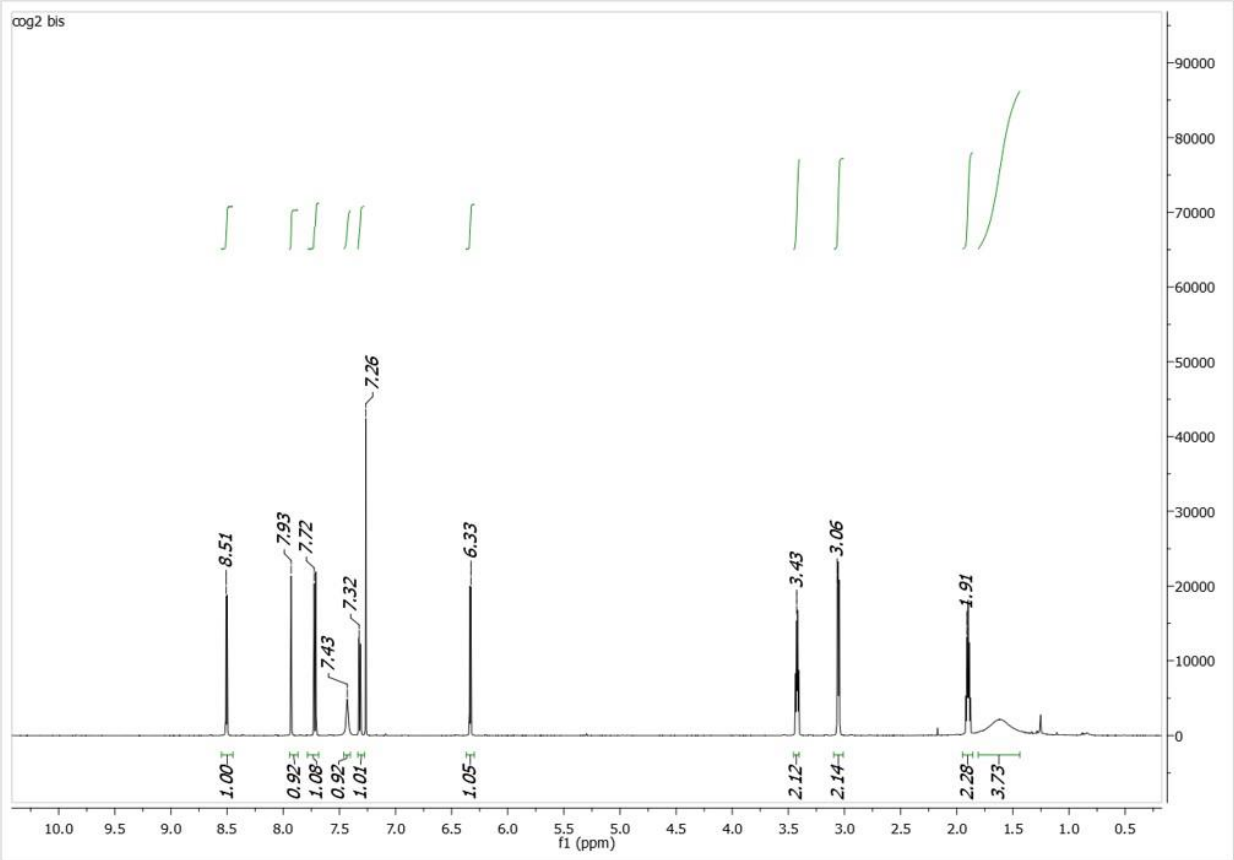


Figure S2. ^{13}C spectrum ($CDCl_3$, 150 MHz) of compound **2**.

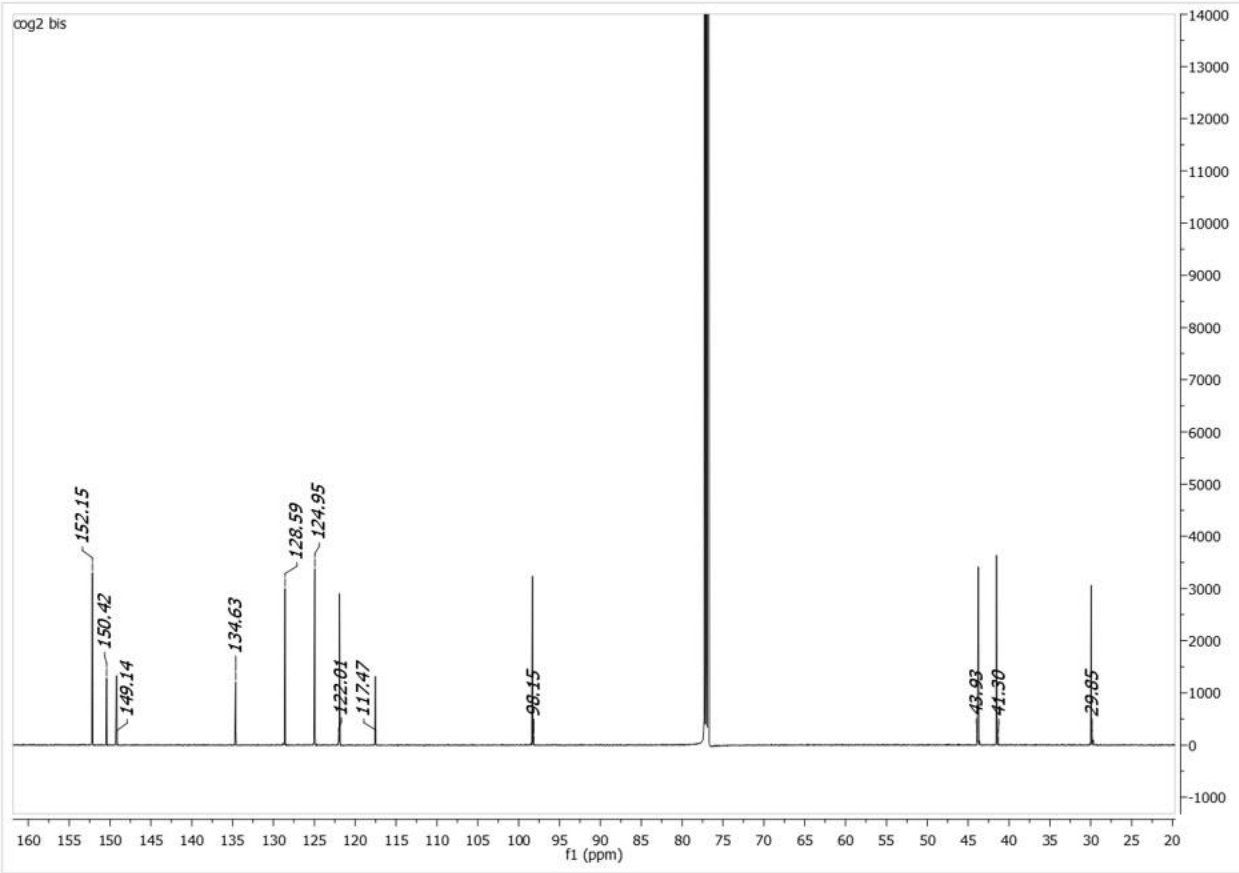


Figure S3. ^{1}H NMR spectrum (CDCl3, 600 MHz) of **4**.

Traces : water at 1.6

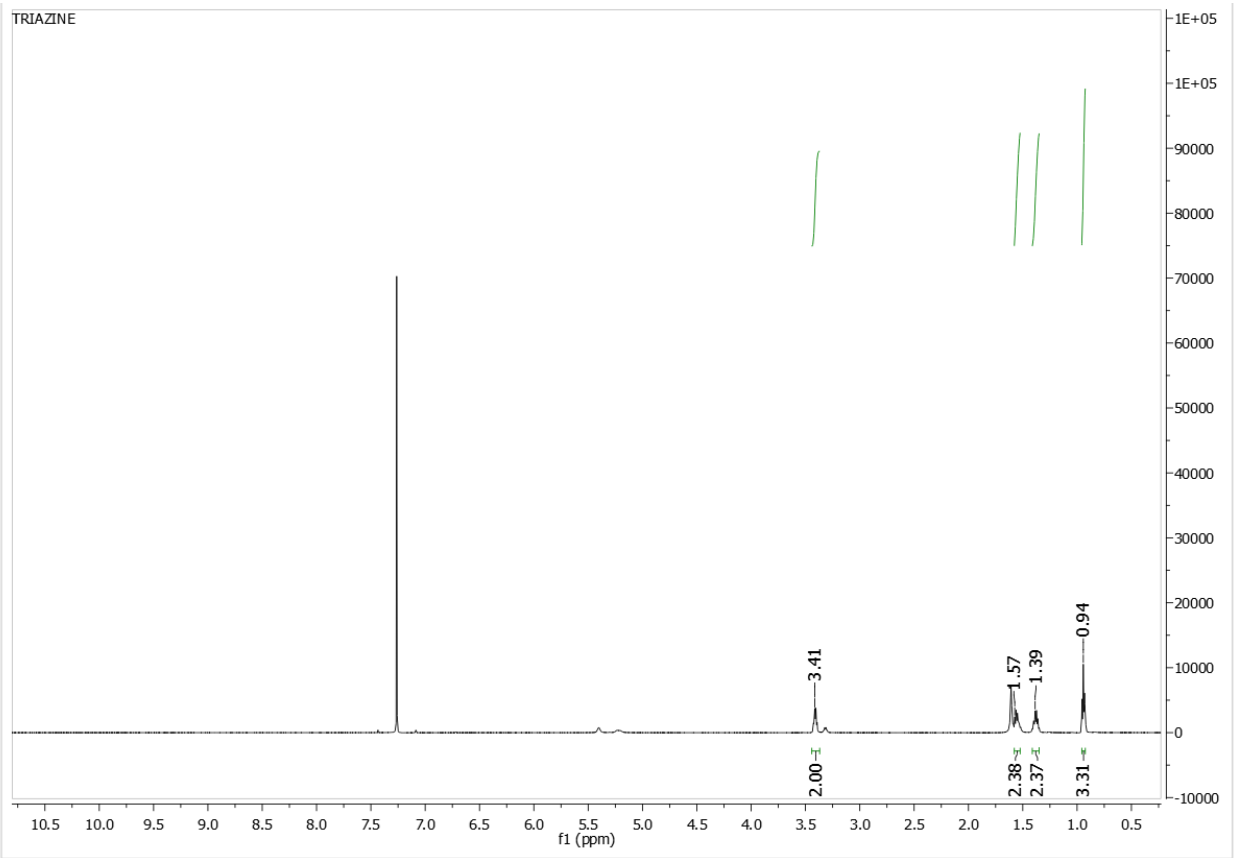
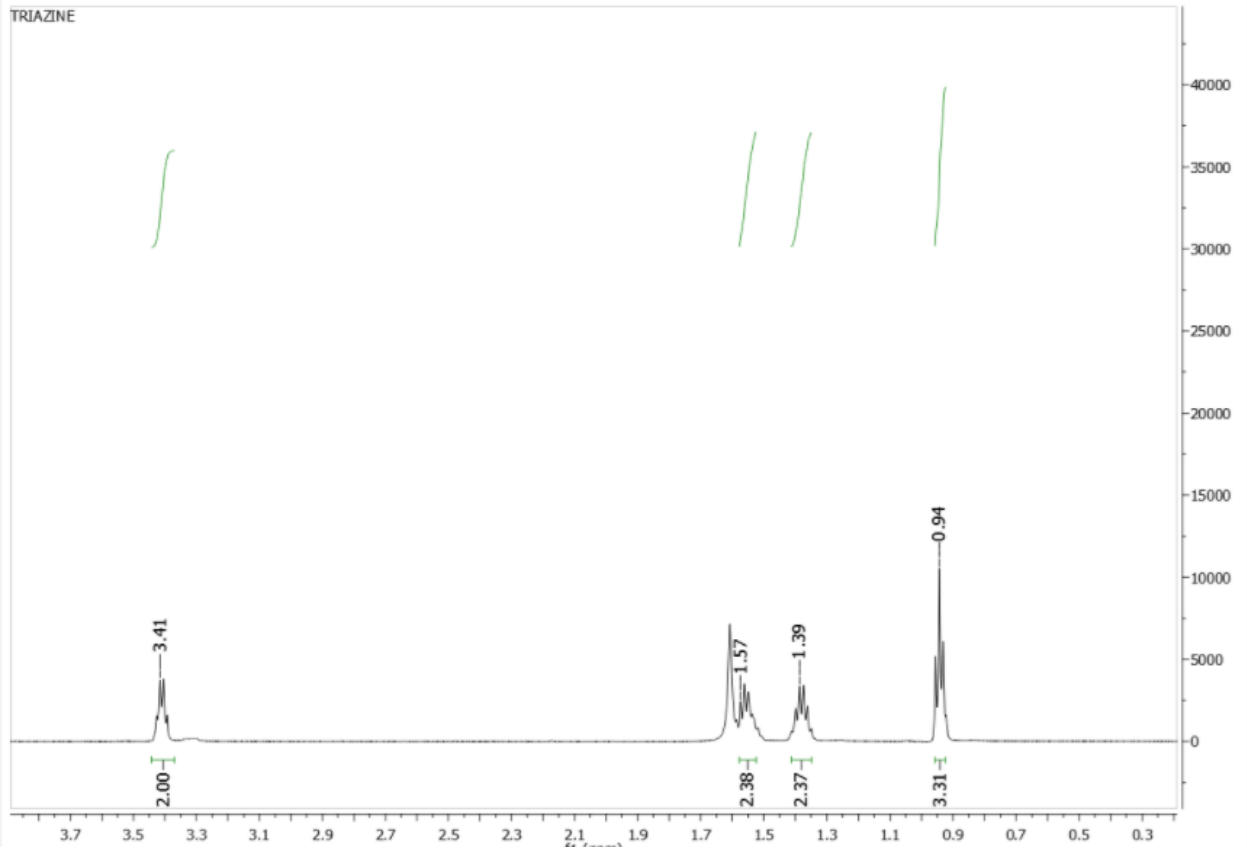


Figure S4. An expanded view of ^{1}H NMR spectrum (CDCl3, 150 MHz) of **4**.



Traces: water at 1.6

Figure S5. ^{13}C NMR spectrum ($CDCl_3$, 150 MHz) of compound **4**.

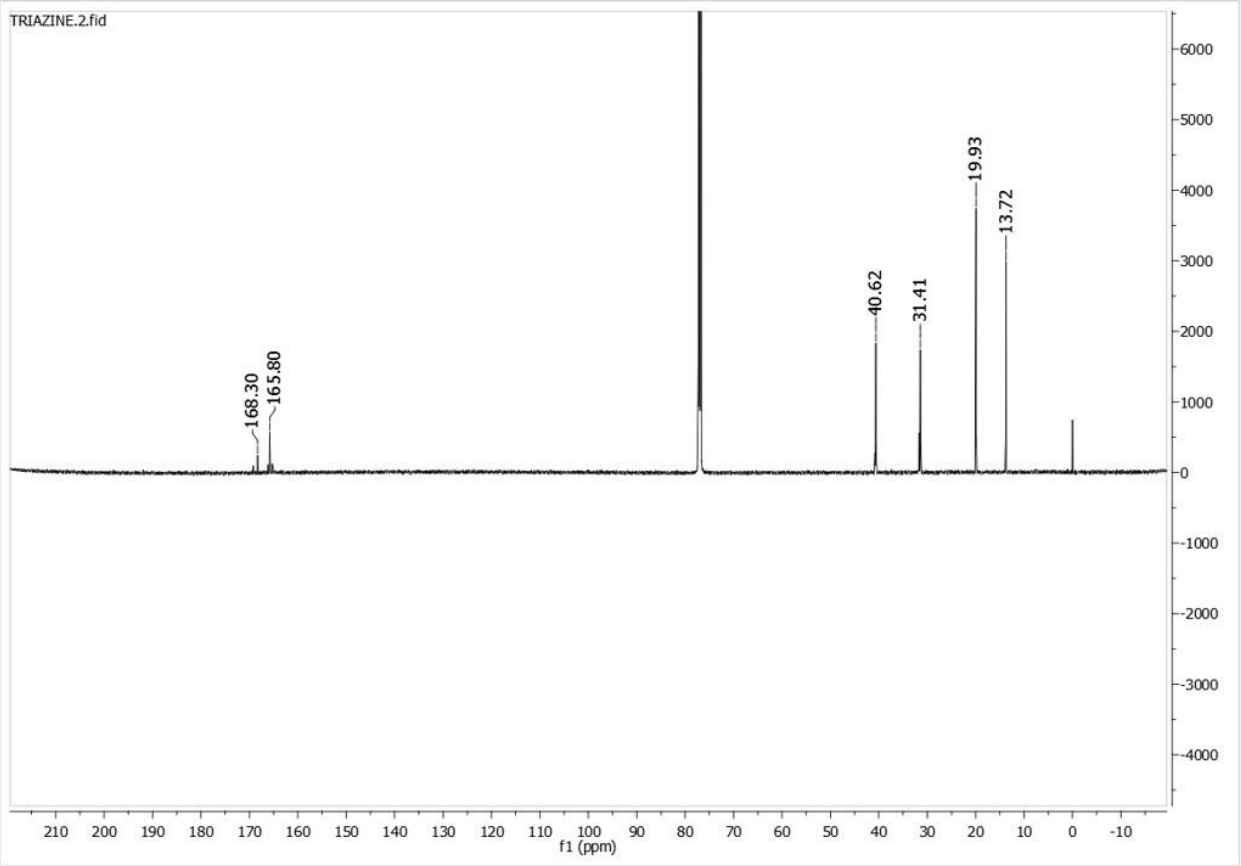


Figure S6. DEPT -135 NMR spectrum ($CDCl_3$, 600 MHz) of compound **4**.

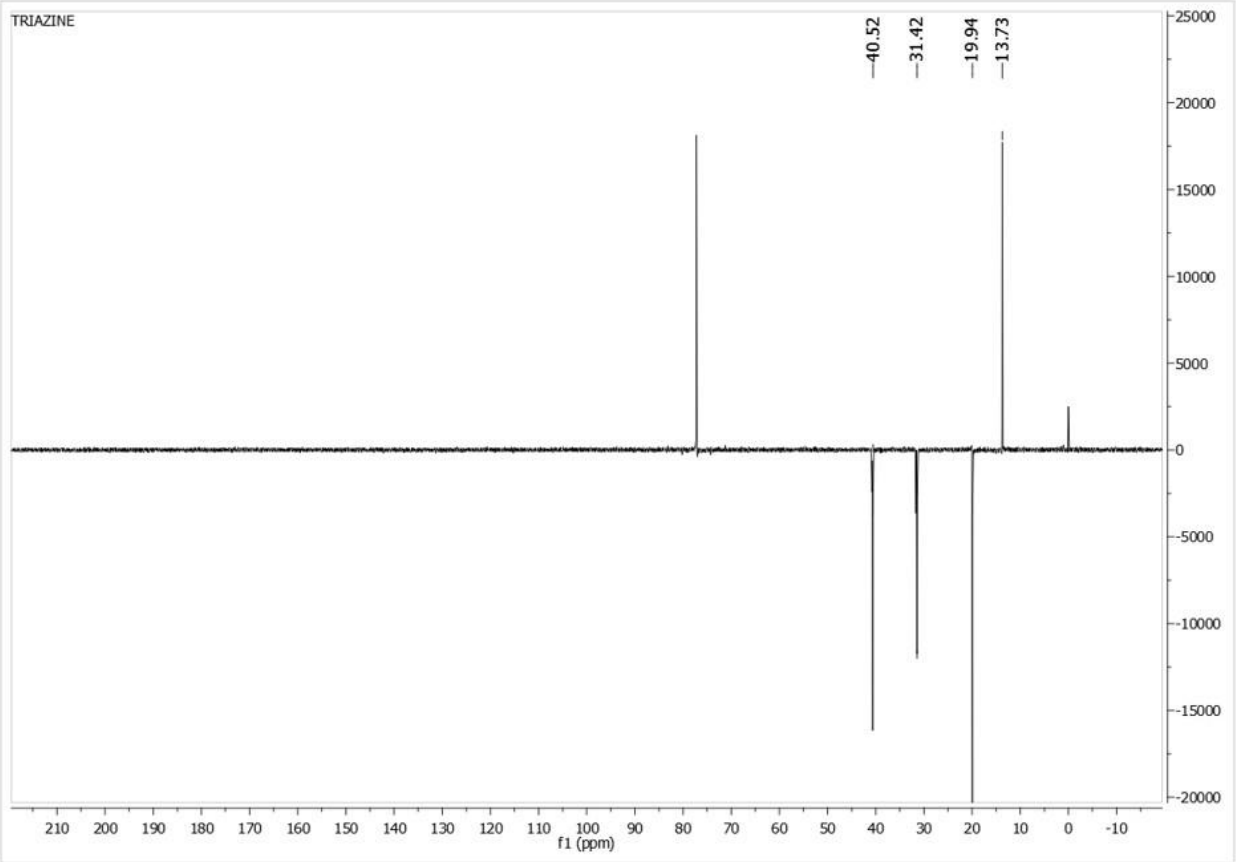


Figure S7. HSQC spectrum ($CDCl_3$, 600 MHz) of compound **4**.

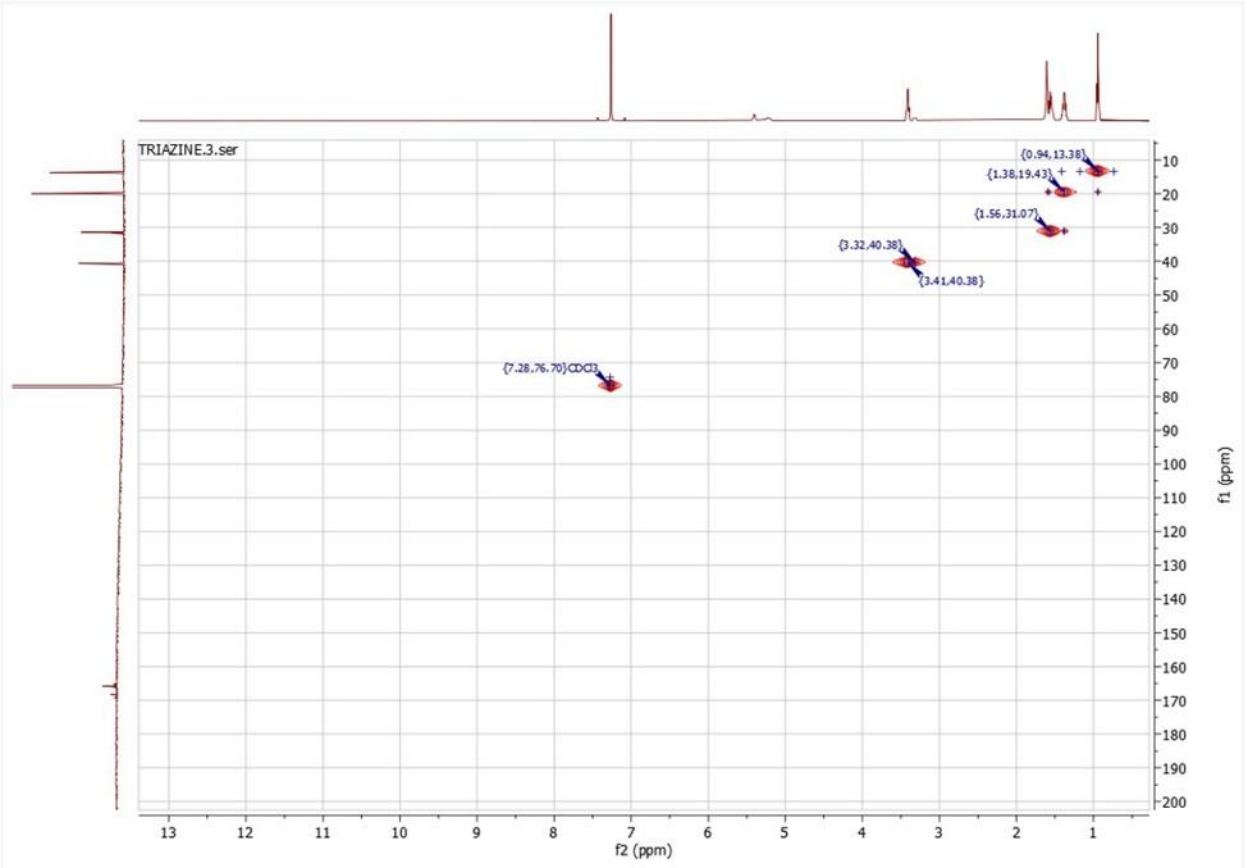
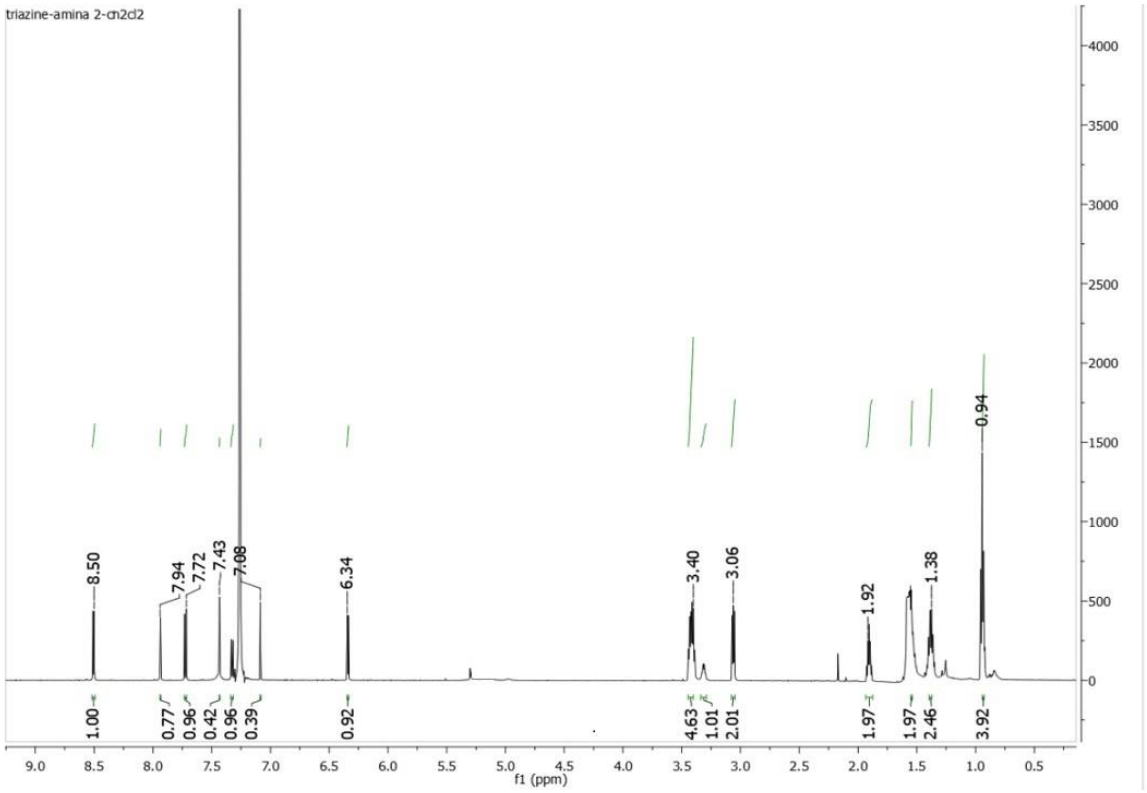


Figure S8. ^{1}H NMR spectrum ($CDCl_3$, 600 MHz) of compound **5**.



Traces : water at 1.6 (overlay with peaks at H-3’’’)

Dichloromethane at 5.2

Figure S9. An expanded view of ^{1}H NMR spectrum ($CDCl_3$, 150 MHz) of compound **5**.

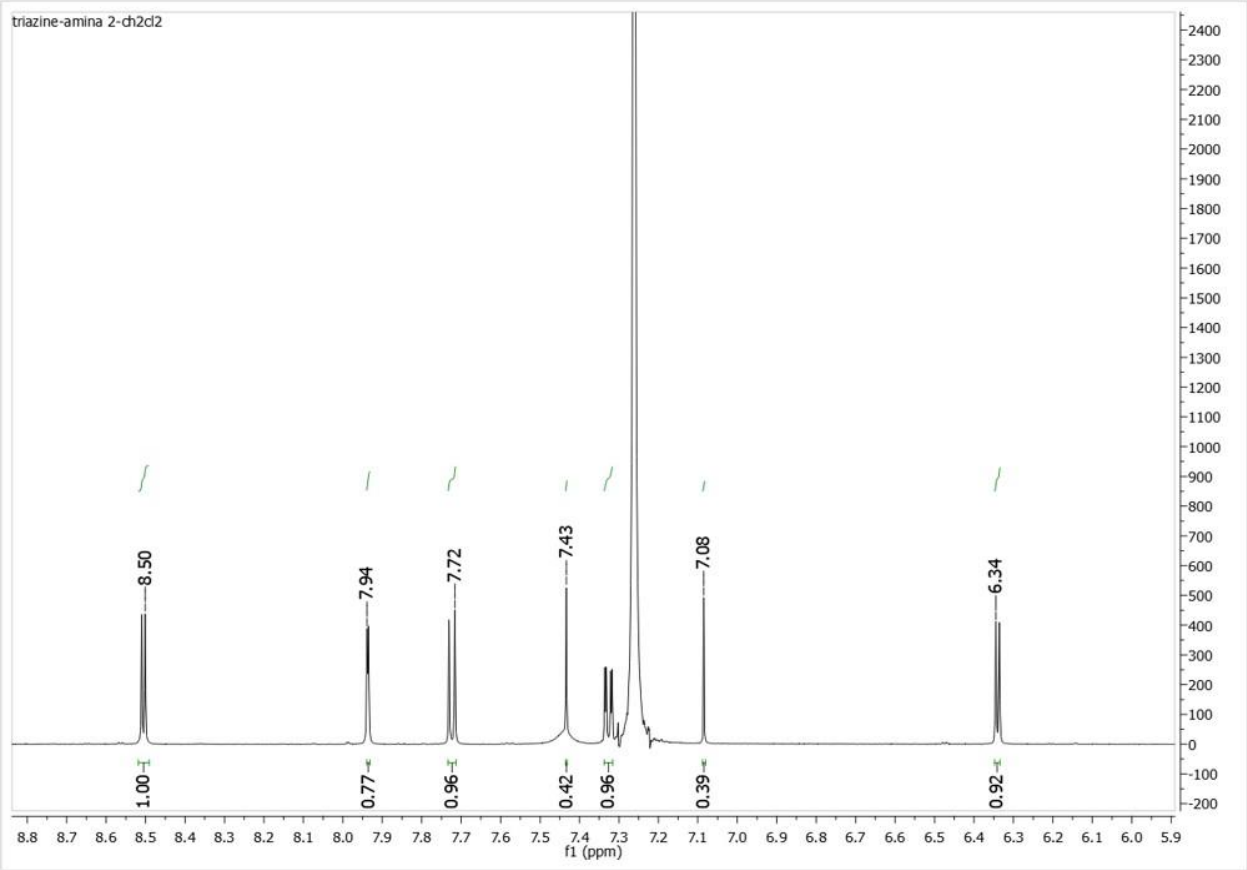


Figure S10. ^{13}C NMR spectrum ($CDCl_3$, 150 MHz) of compound **5**.

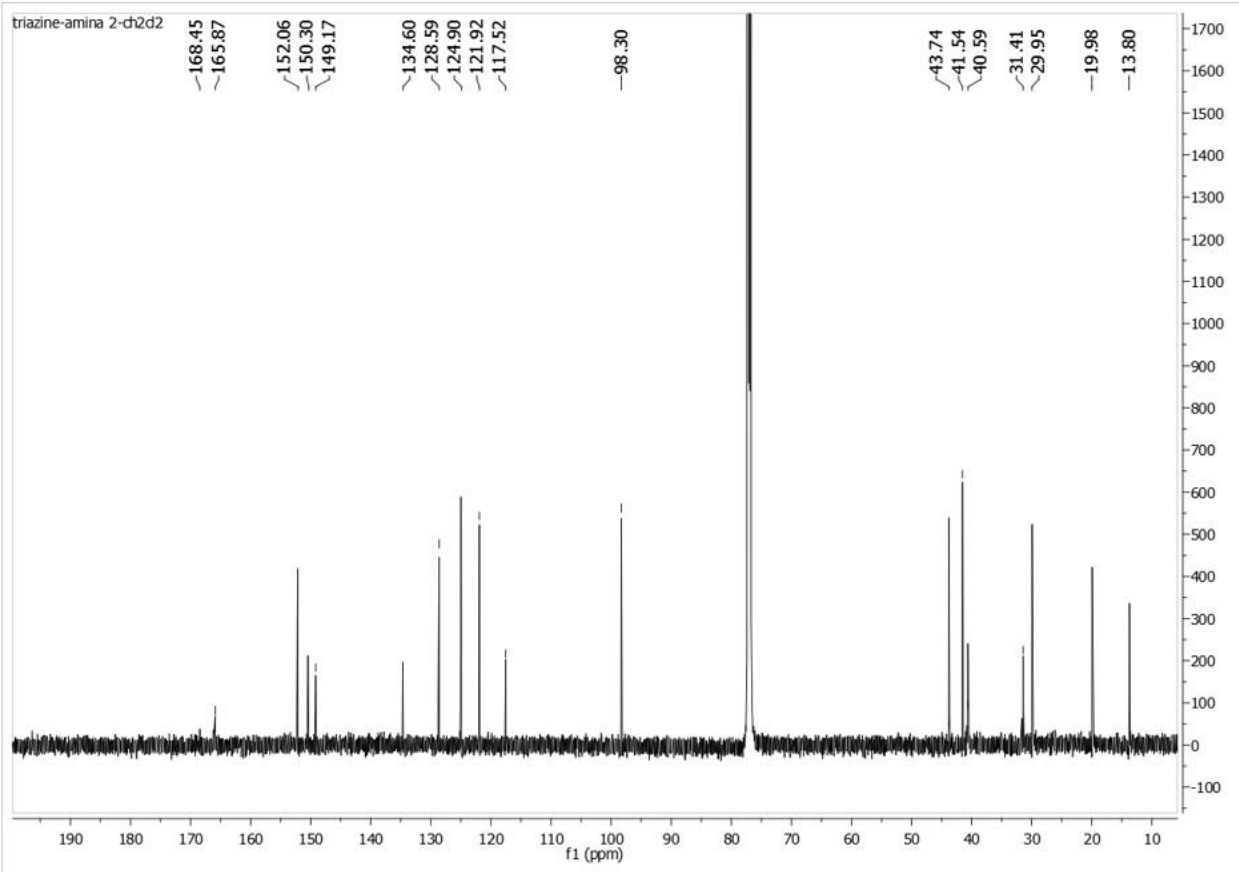


Figure S11. An expanded view of ^{1}C NMR spectrum ($CDCl_3$, 150 MHz) of compound **5**.

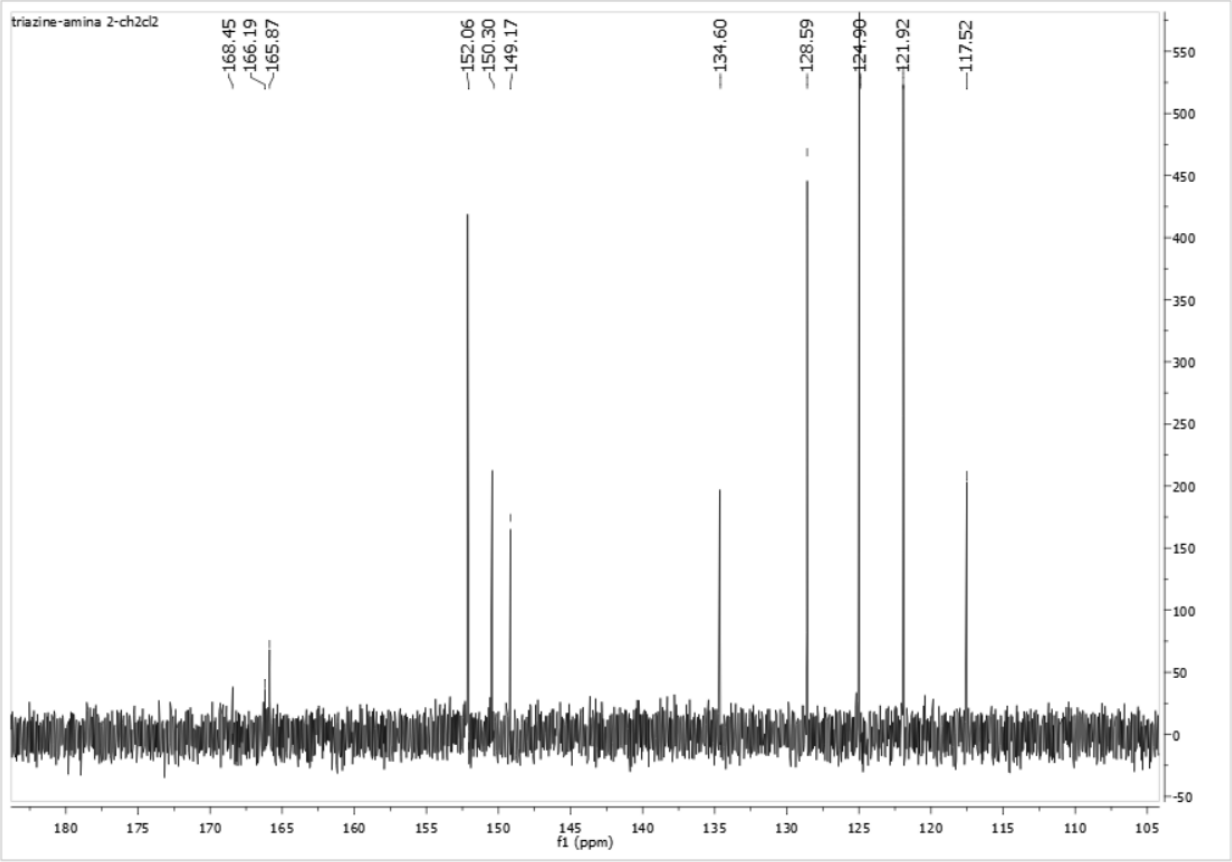
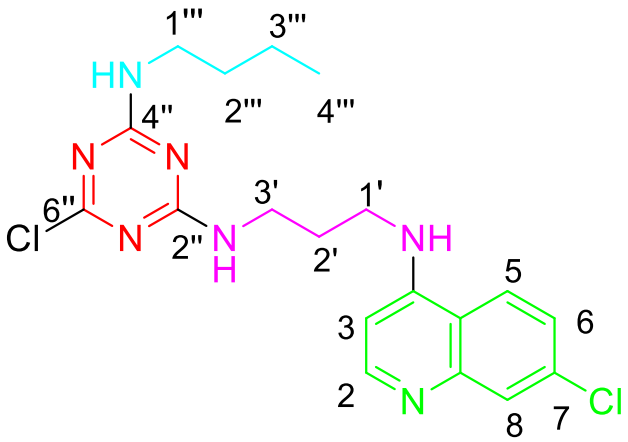


Table S1. ^{1}H and ^{13}C-nuclear magnetic spectroscopy (NMR) chemical shifts and the structure of **5**.



Chemical Formula: $C_{19}H_{23}Cl_2N_7$

^{1}H Chemical Shift	^{13}C Chemical Shift	**Assignment**
0.94	13.8	C-4''' (CH_3)
1.38	19.9	C-3''' (CH_2)
1.55	31.4	C-2''' (CH_2)
1.92	29.9	C-2' (CH_2)
3.06	40.8	C-1''' (CH_2)
3.20	---	NH
3.41-3.44	40.5-43.7	C-1', C-3' (CH_2 + CH_2)
6.34	98.3	C-3 ($_{aromat}$)
---	117.5	C-4a
7.08	---	NH
7.34	124.9	C-6 ($_{aromat}$)
7.43	---	NH
7.72	121.4	C-5 ($_{aromat}$)
7.94	128.5	C-8 ($_{aromat}$)
---	134.5	C-7
---	149.1	C-8a
---	150.3	C-4
8.51	152.0	C-2 ($_{aromat}$)
---	165.8	C-4''
---	166.2	C-2''
---	168.4	C-6''

Figure S12. DEPT-135 spectrum (CDCl3, 600 MHz) of compound **5**.

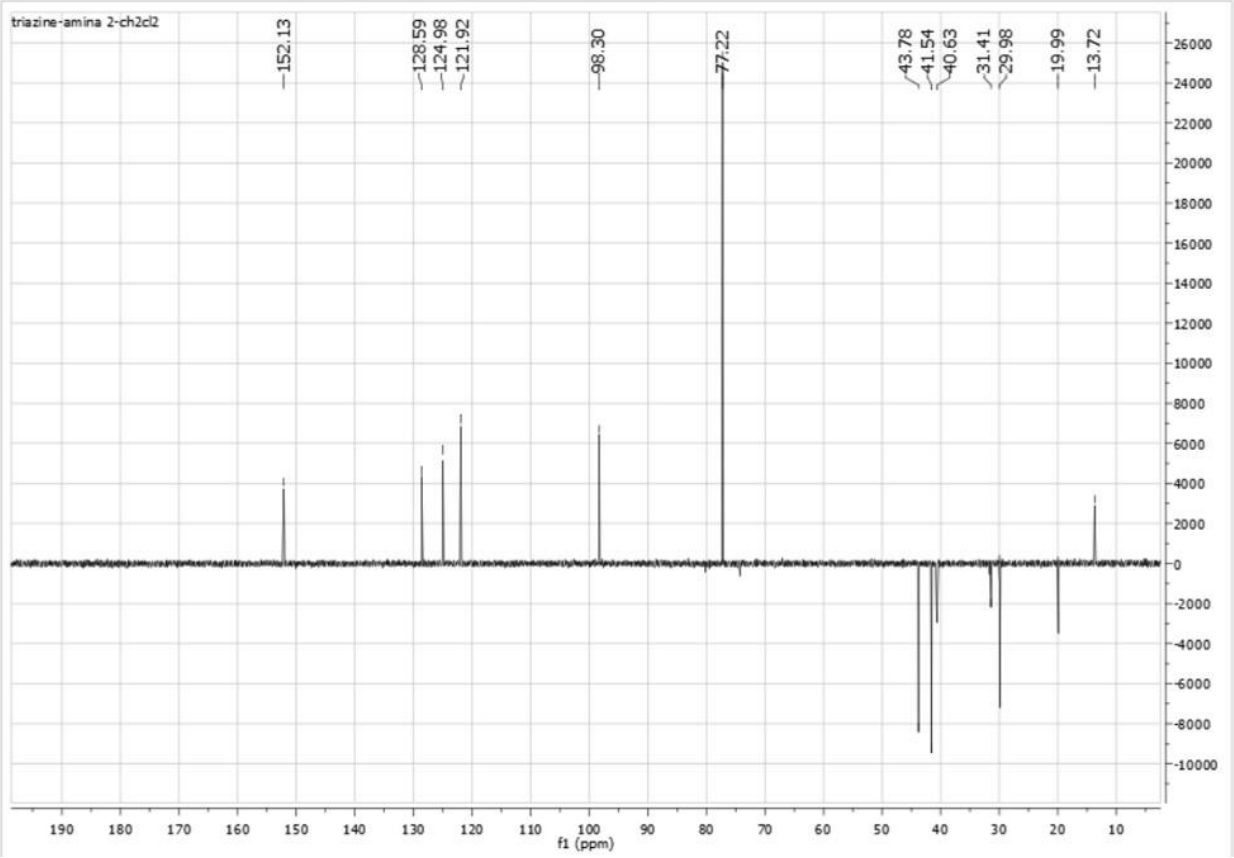
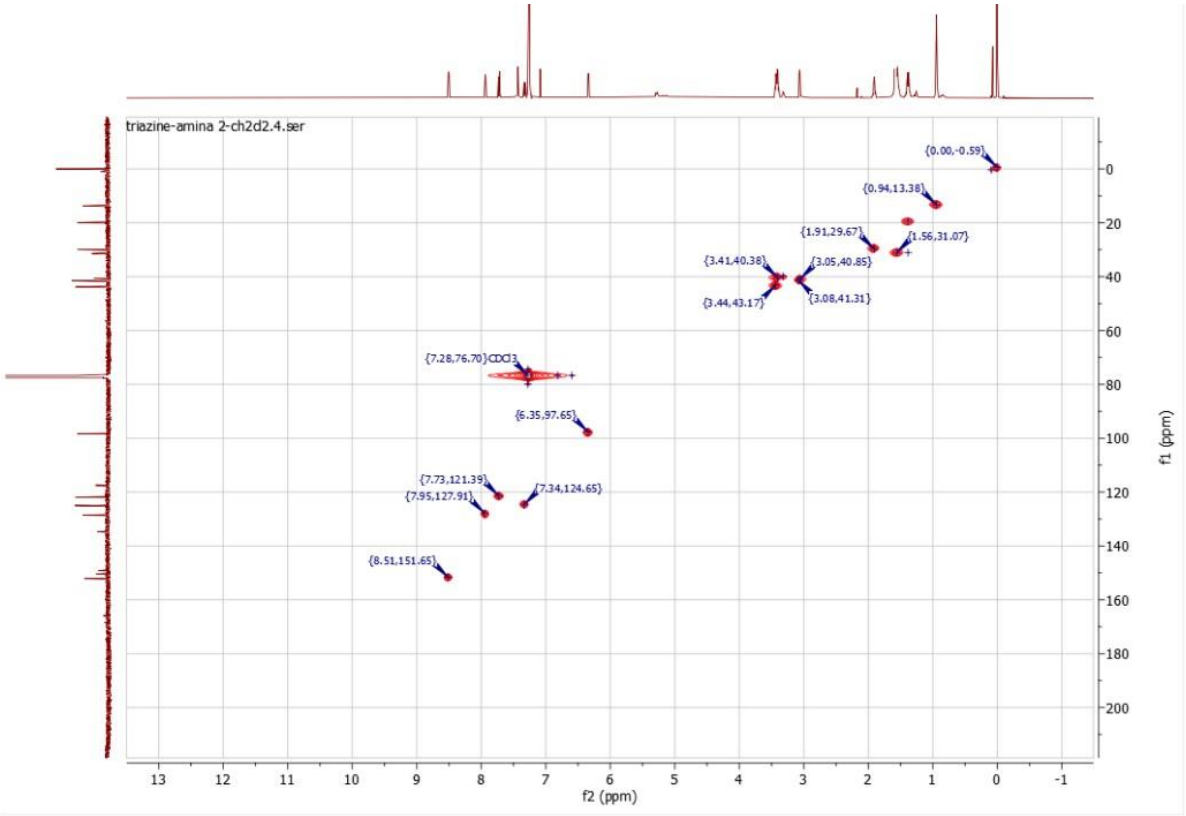


Figure S13. HSQC spectrum ($CDCl_3$, 600 MHz) of compound **5**.



Traces : acetone at 2.1

Figure S14. An expanded view of HSQC spectrum ($CDCl_3$, 600 MHz) of compound **5**.

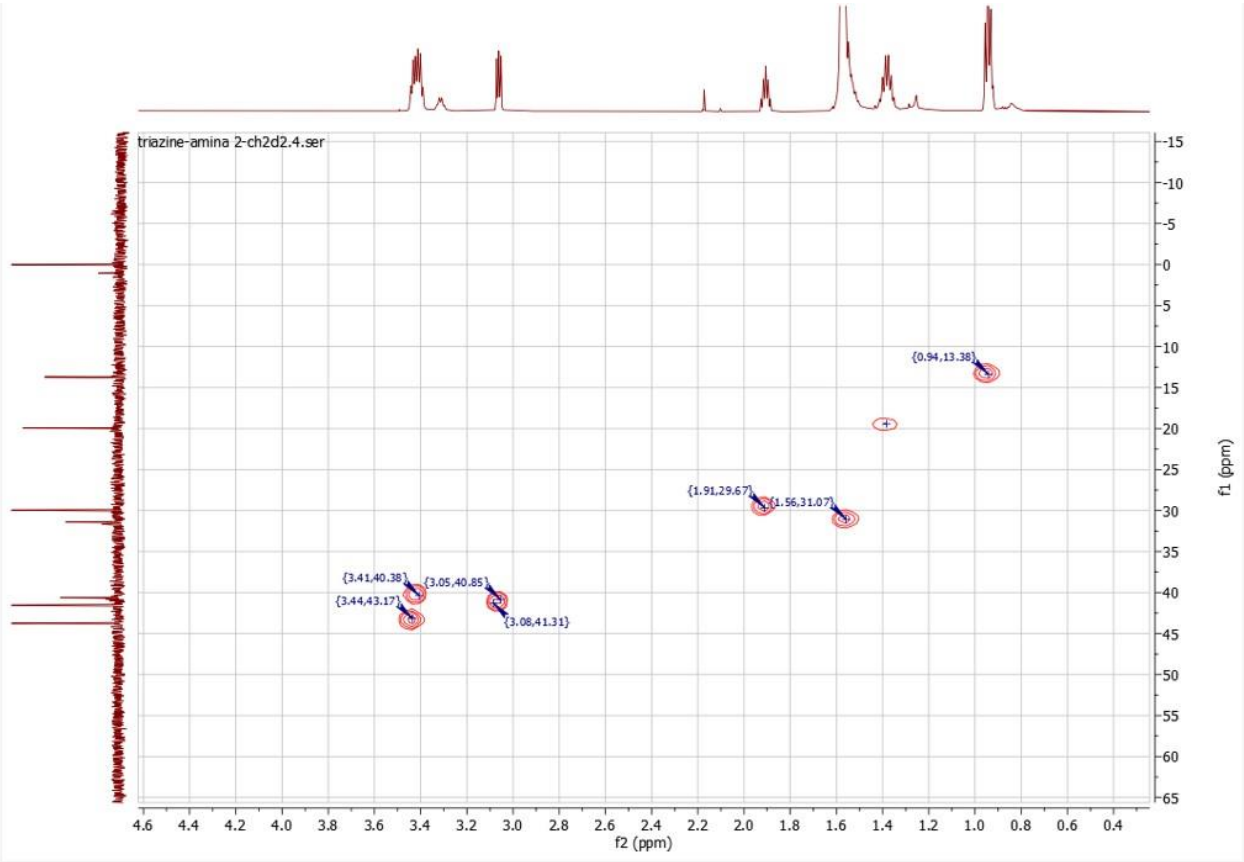


Figure S15. 1H-1H COSY spectrum ($CDCl_3$, 600 MHz) of compound **5**.

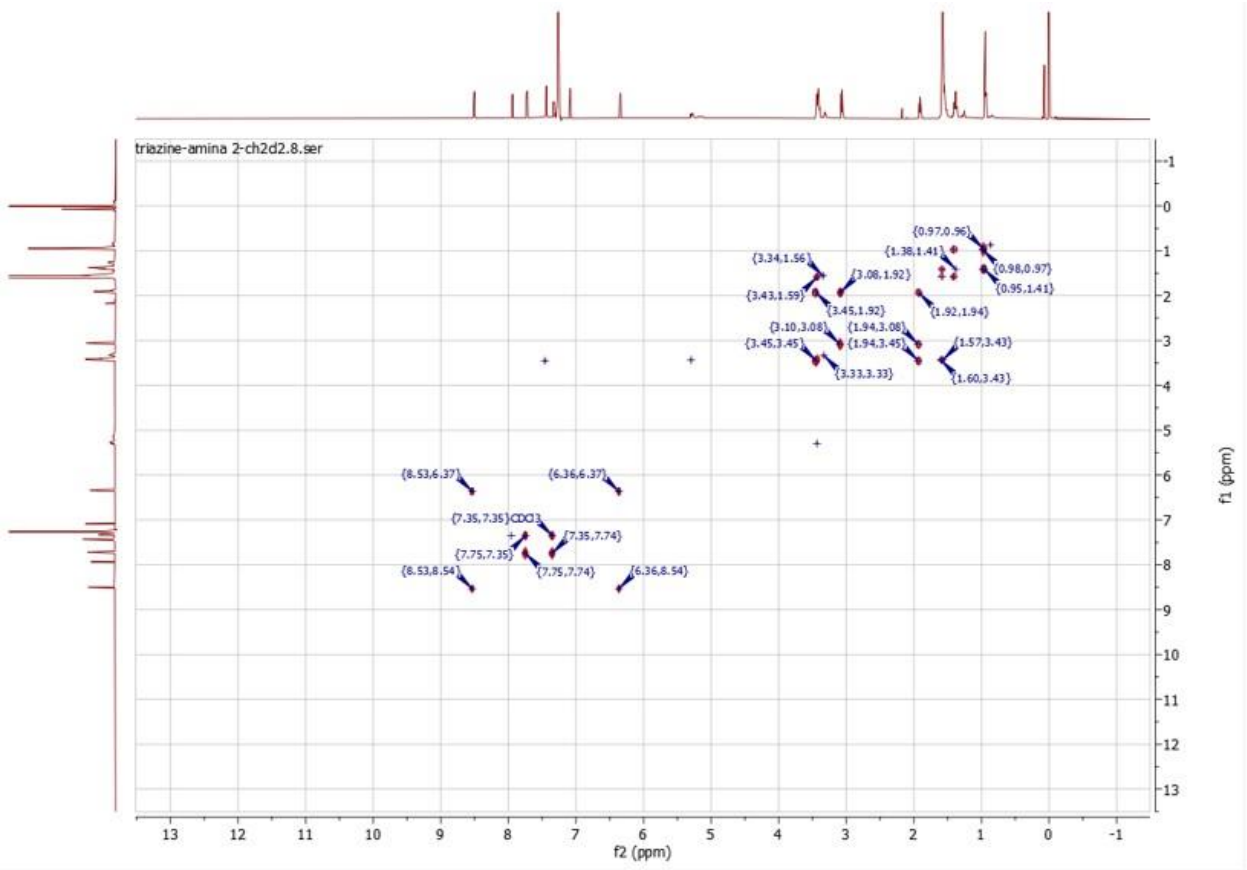
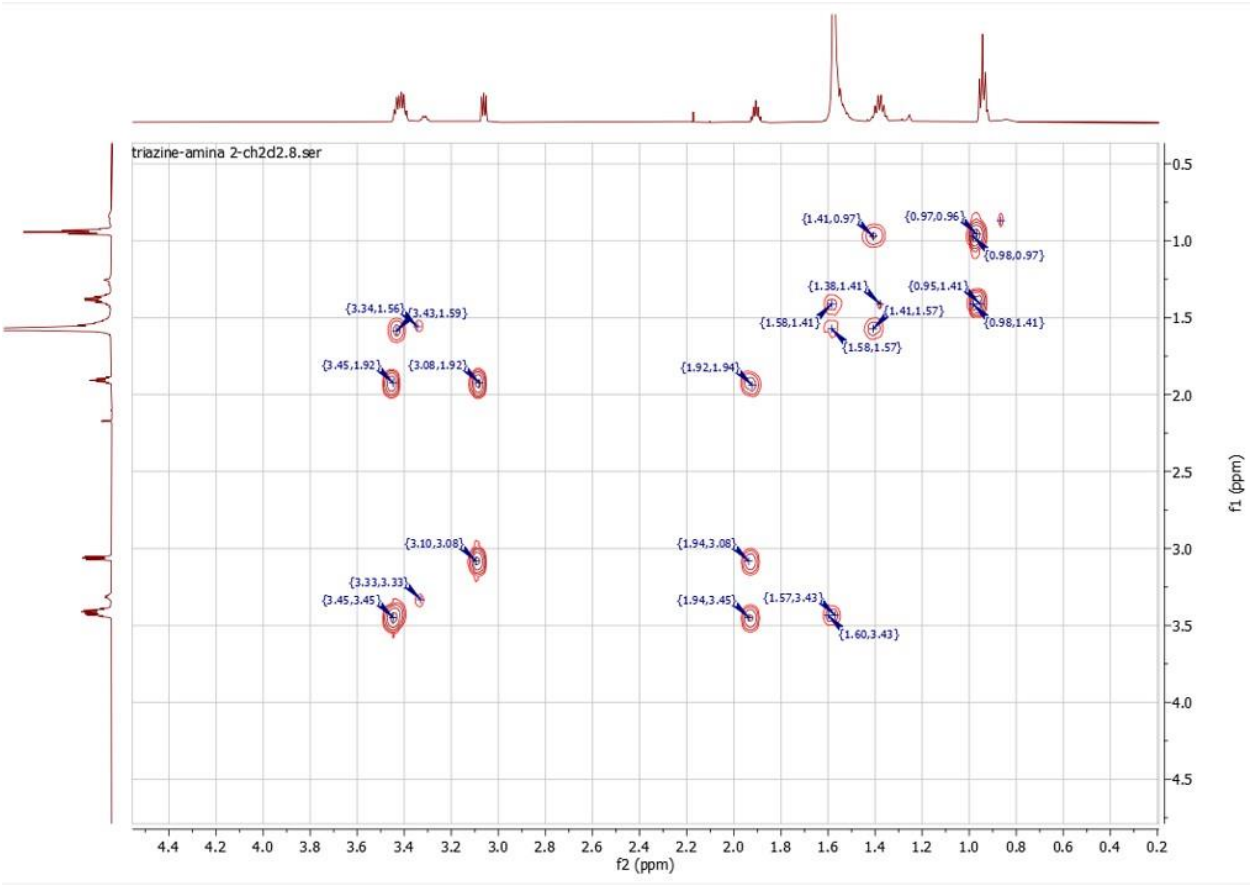


Figure S16. An expanded view of 1H-1H COSY spectrum ($CDCl_3$, 600 MHz) of compound **5**.



IR spectrometry

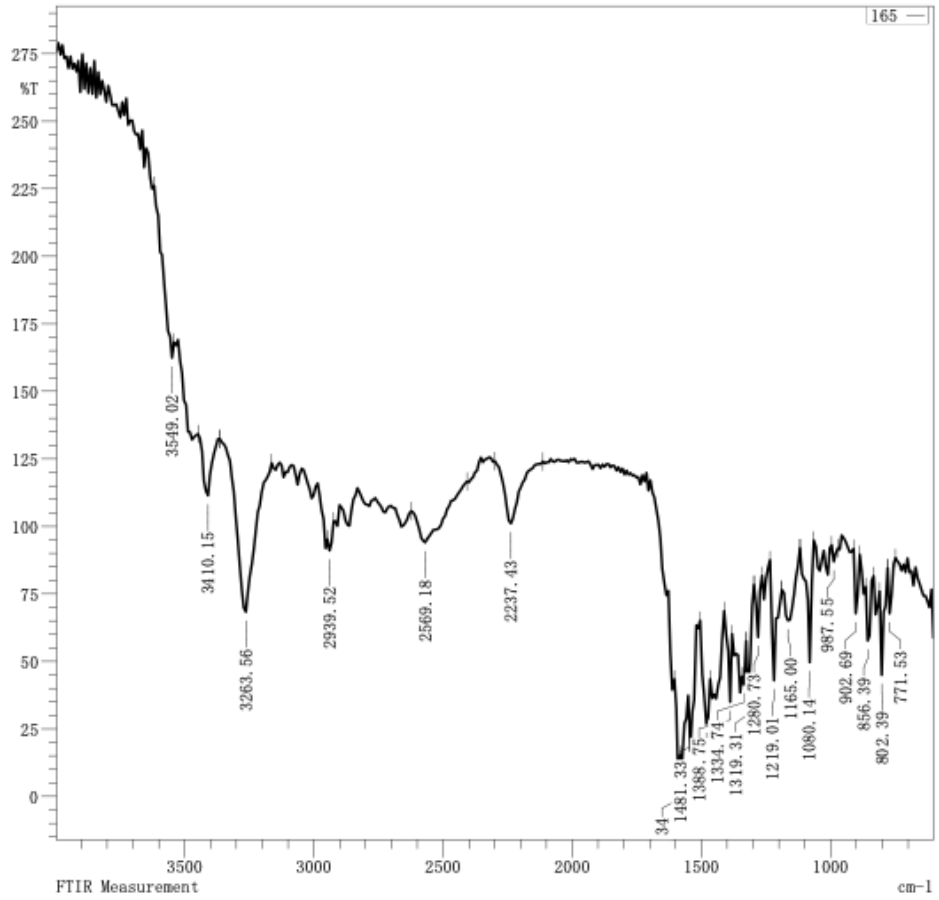


Figure S17. IR spectrum (KBr) of compound **5**.

UV-VIS spectrometry

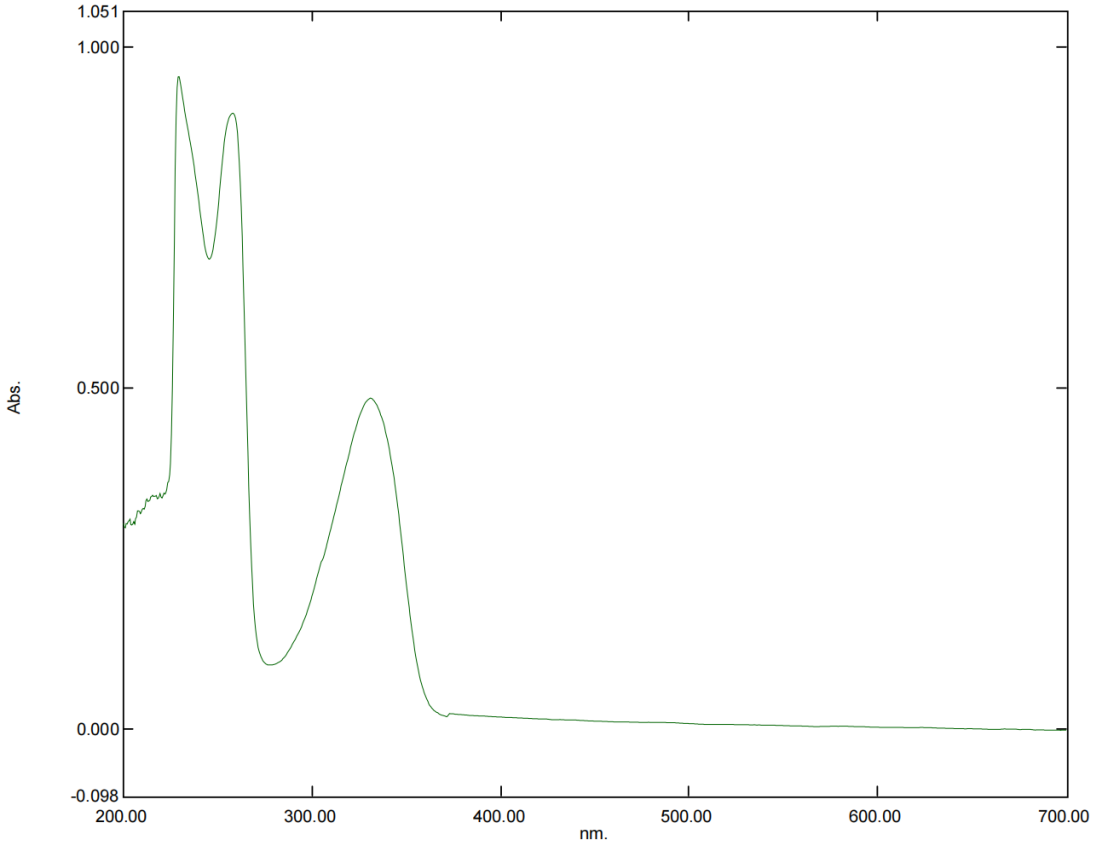


Figure S18. UV spectrum of compound **5** (range 200-700nm in CH_2Cl_2)

Mass spectrometry of **5**

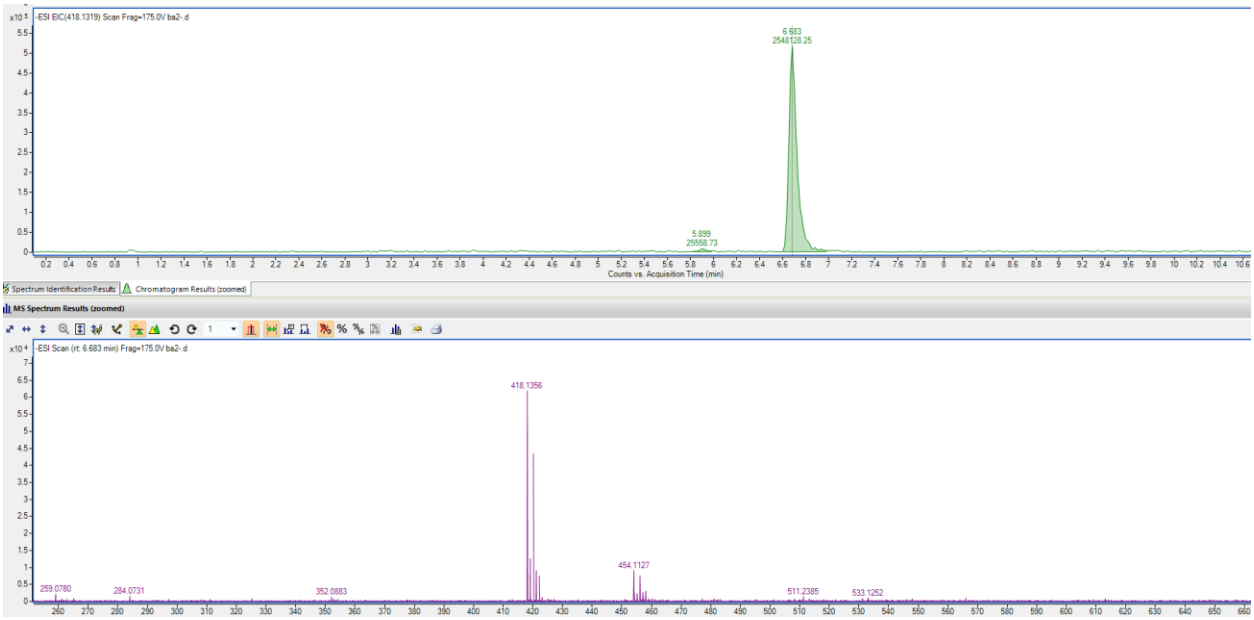


Figure S19

Figure S19. Mass spectrum and UPLC-UV chromatogram (254 nm) of compound **5**. The spectrum was recorded in negative ionization mode (ESI). Analysis was performed using a solvent mixture containing acetonitrile/water at a flow rate of 0.5 mL/min. The mobile phase was isocratic (water + 0.01% TFA; CH_3CN).

Figure S20

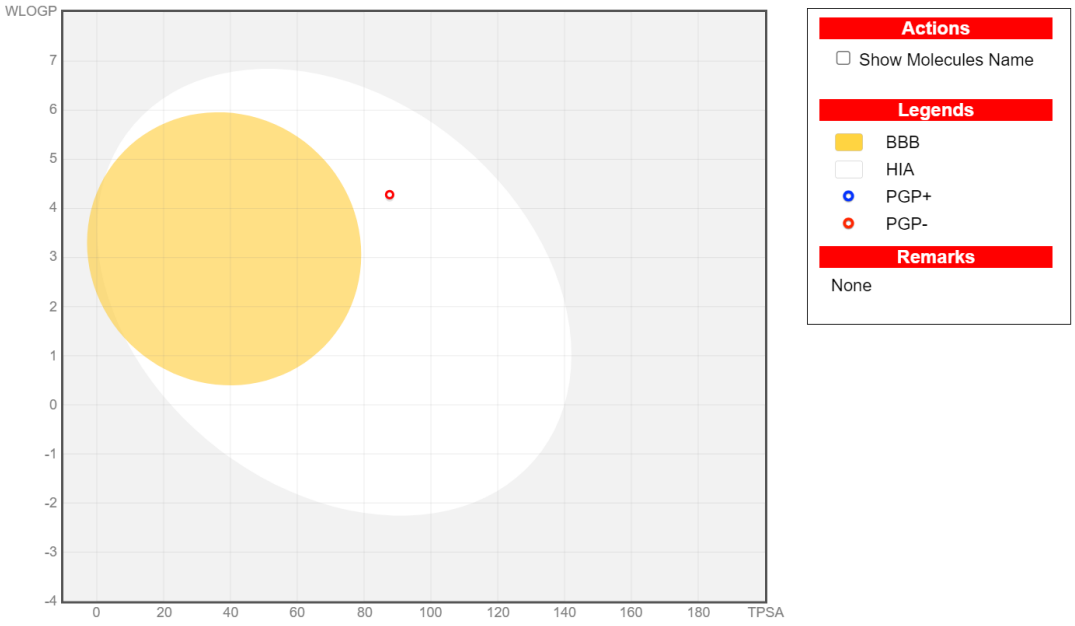


Figure S20. BOILED-Egg graph resuming the predicted properties for the compound 5. The overall predicted pharmacokinetic properties were resumed in the BOILED-Egg graph4 as reported in Figure S20. The white area indicated the molecules with high probability to be absorbed by the GI tract, while the yellow area indicated the molecules with high probability to passively permeate through the blood-brain barrier. The red dot represented the molecule which was predicted to be not effluated from the CNS by P-glycoprotein.

Table S2. Physicochemical properties of compound **5** calculated by SwissADME[1]

Compound	MW	HBA	HBD	tPSA	nRtB
5	420	4	3	87.65A^2	10

MW: Molecular weight. nRtB: Number of rotatable bond. HBA: Number of hydrogen-bond acceptor. HBD: Number of hydrogen-bond donor. tPSA: Topological surface area^3

Figure S21

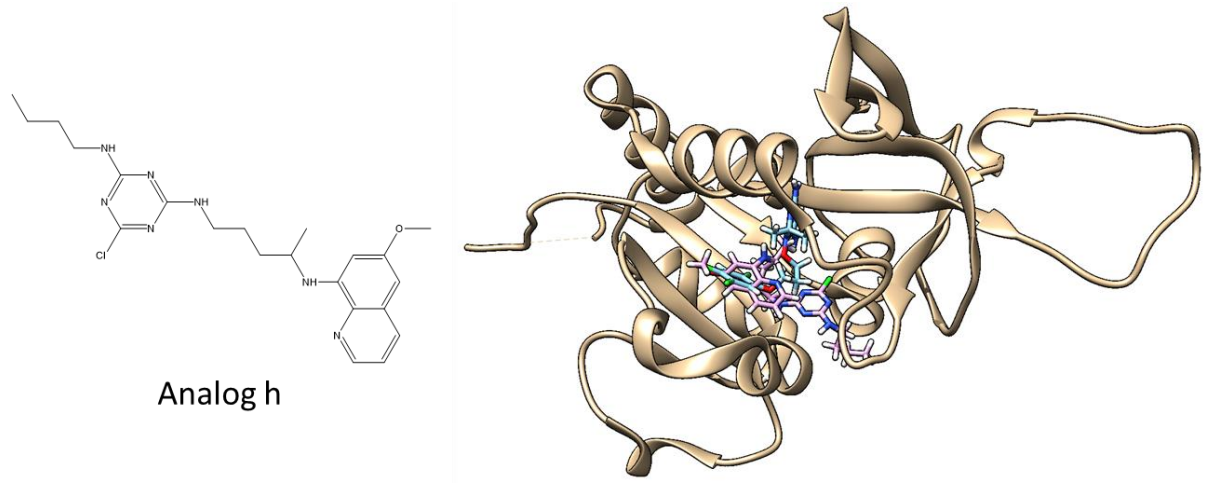


Figure S21. Molecular modeling for analog H (pink) in comparison with compound **5** (cyan).

References

1. Daina, A.; Zoete, V. A BOILED-Egg To Predict Gastrointestinal Absorption and Brain Penetration of Small Molecules. *ChemMedChem* **2016**, *11*, 1117-1121, doi:10.1002/cmdc.201600182.