Supporting Information

EFFICIENT SYNTHESIS OF NOVEL SPIRO[INDOLINE-3,5'-PYRANO-[2,3-d]PYRIMIDIN]-2-ONE DERIVATIVES AND ANTITUMOR ACTIVITY EVALUATION

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1. Figure S 1-S 64 Copies of ^{1}H , ^{13}C and ^{19}F NMR spectra data of compounds 2, 3, 4, 5

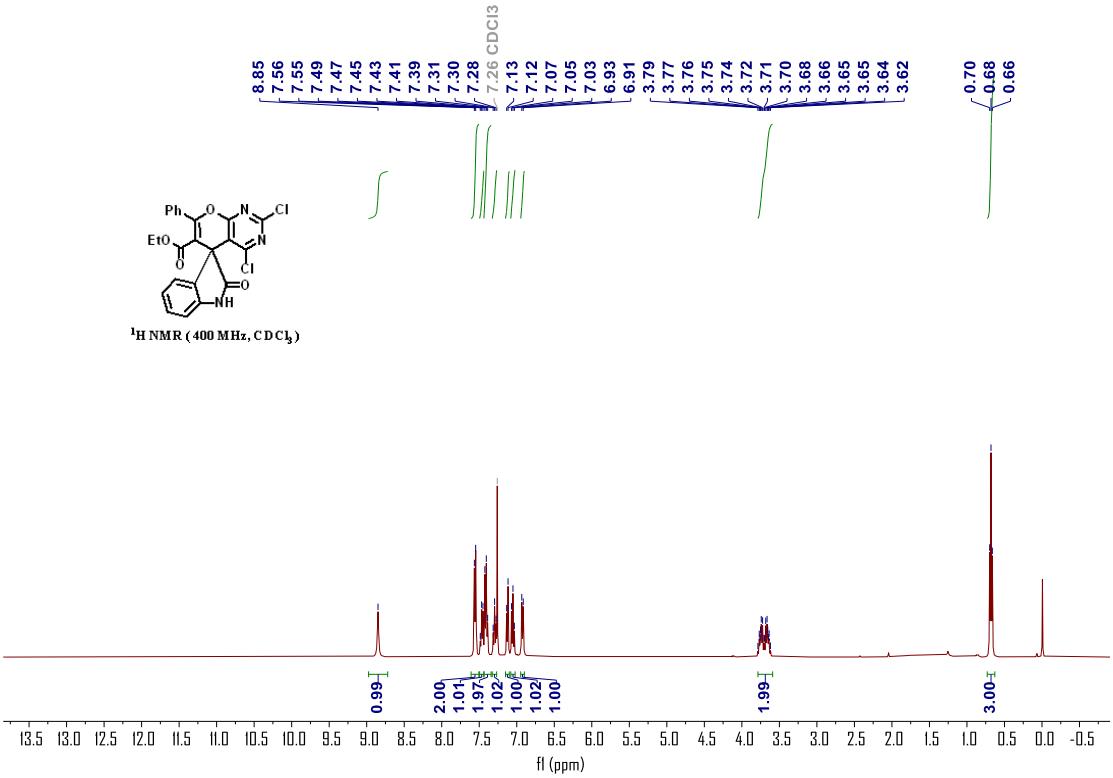


Figure S 1: ^{1}H NMR of **2a**

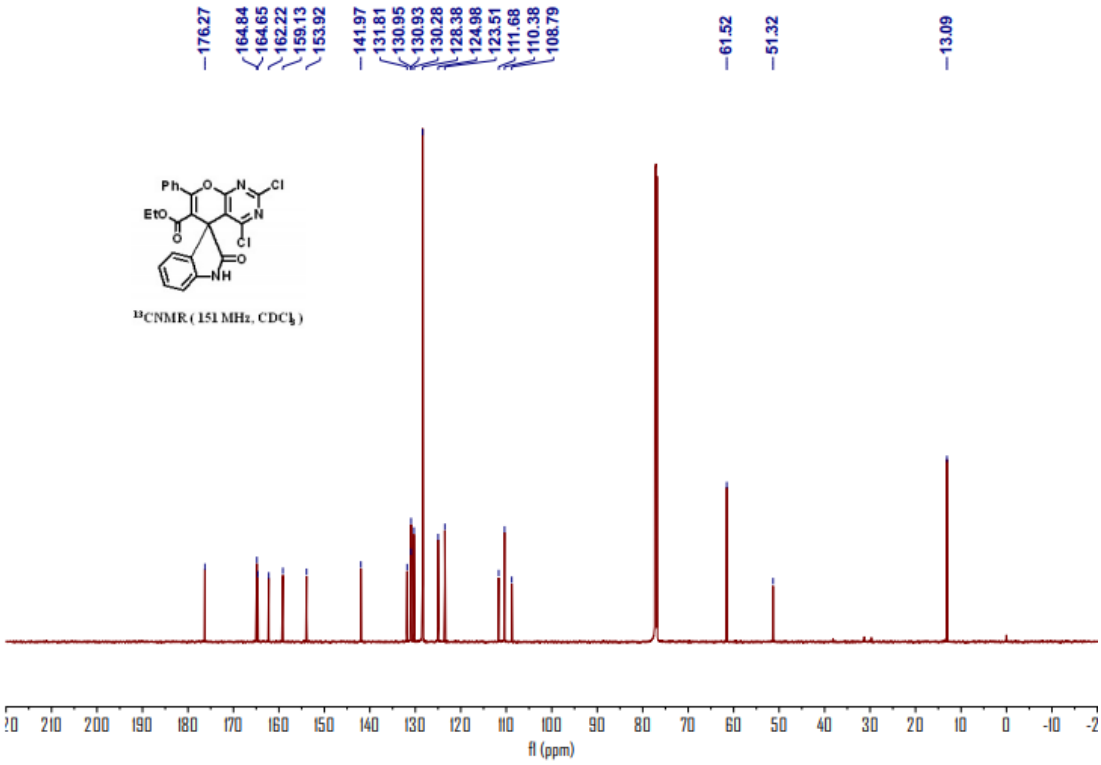


Figure S 2: ^{13}C NMR of **2a**

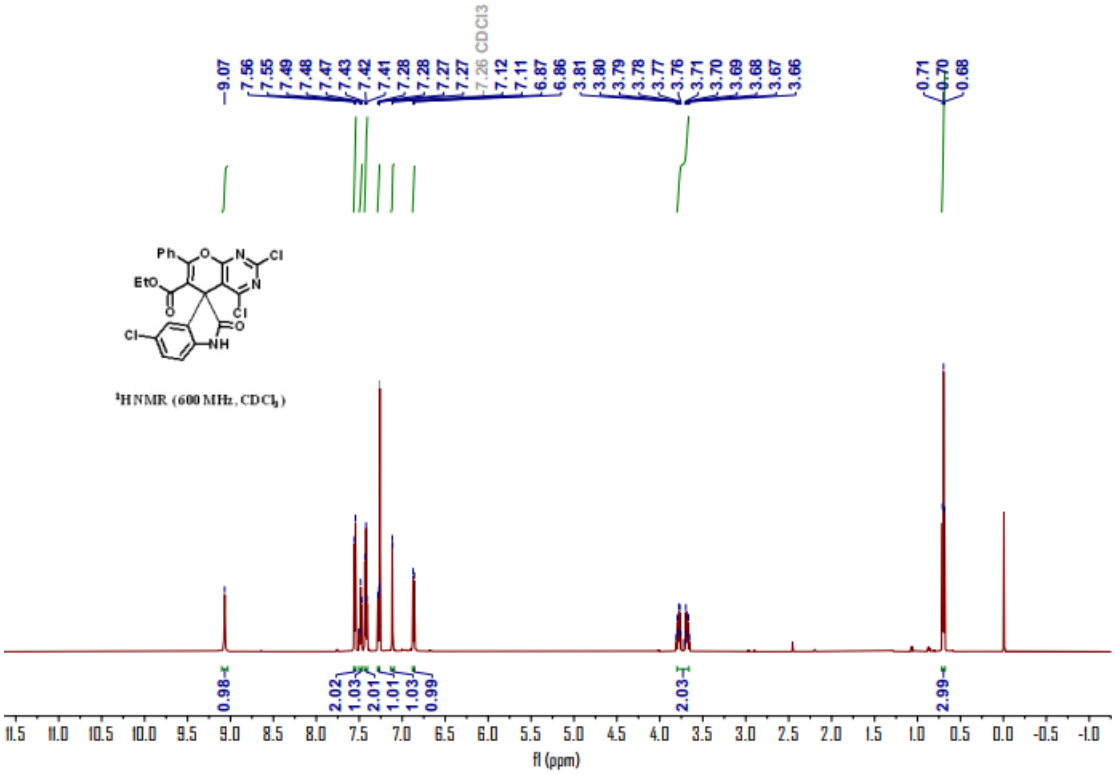


Figure S 3: ^{1}H NMR of **2b**

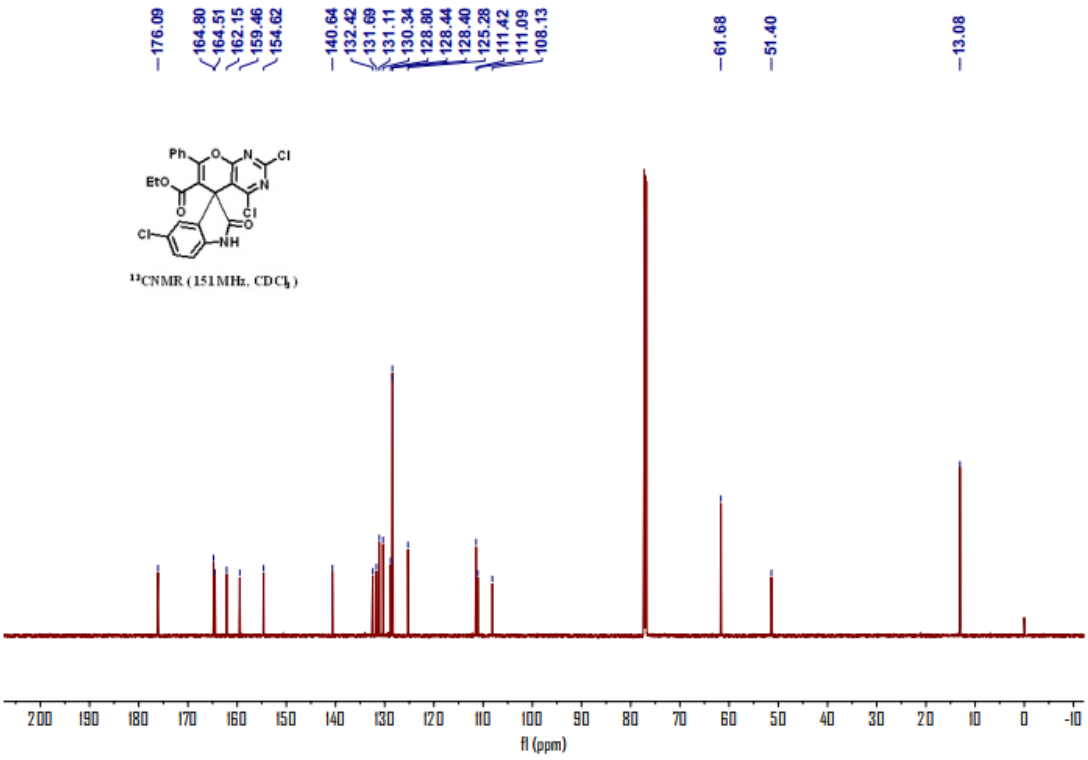


Figure S 4: ^{13}C NMR of **2b**

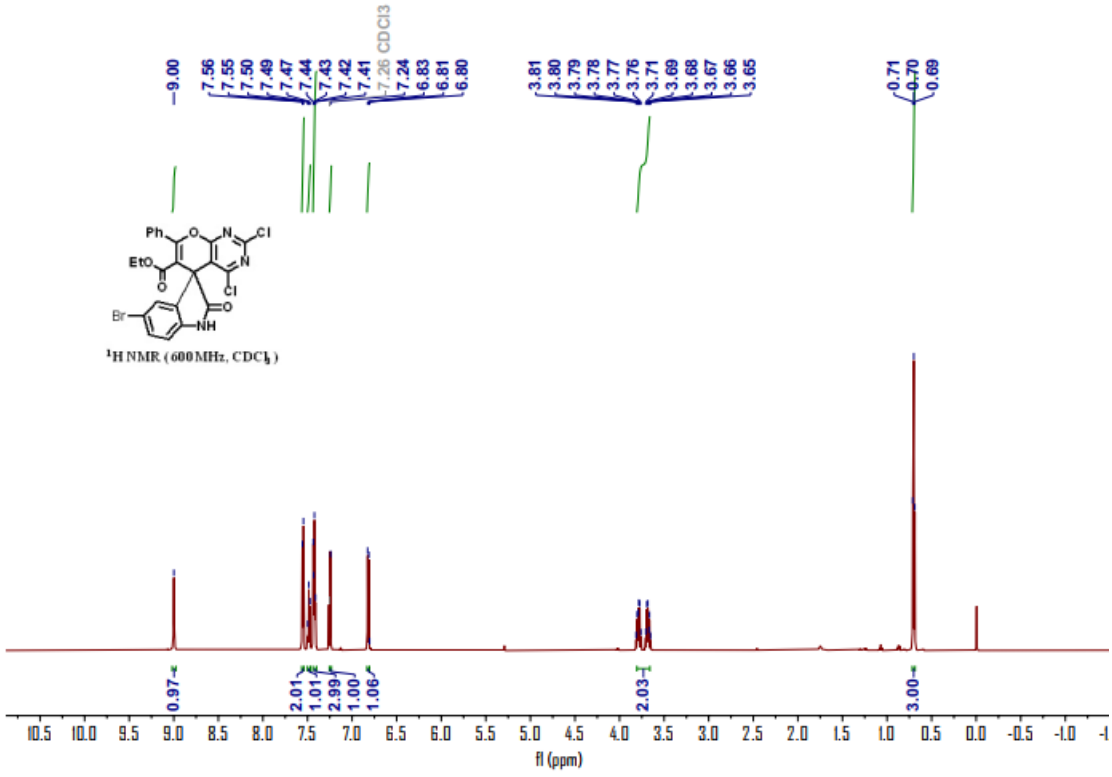


Figure S 5: ^{1}H NMR of **2c**

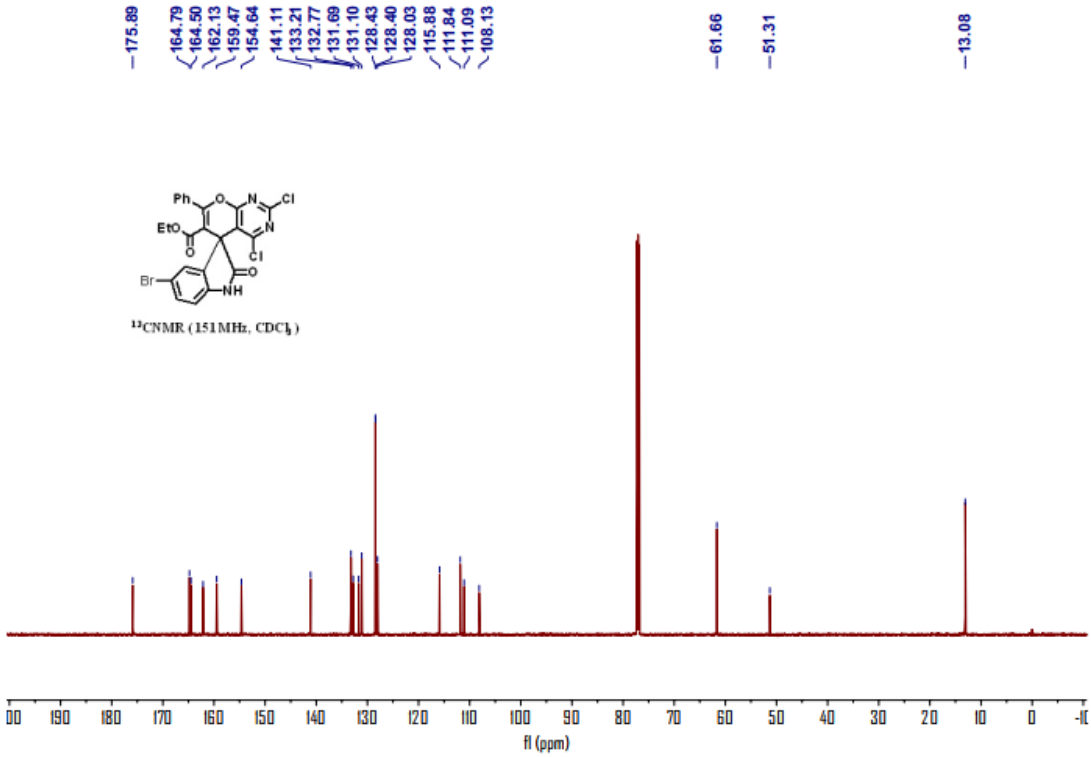


Figure S 6: ^{13}C NMR of **2c**

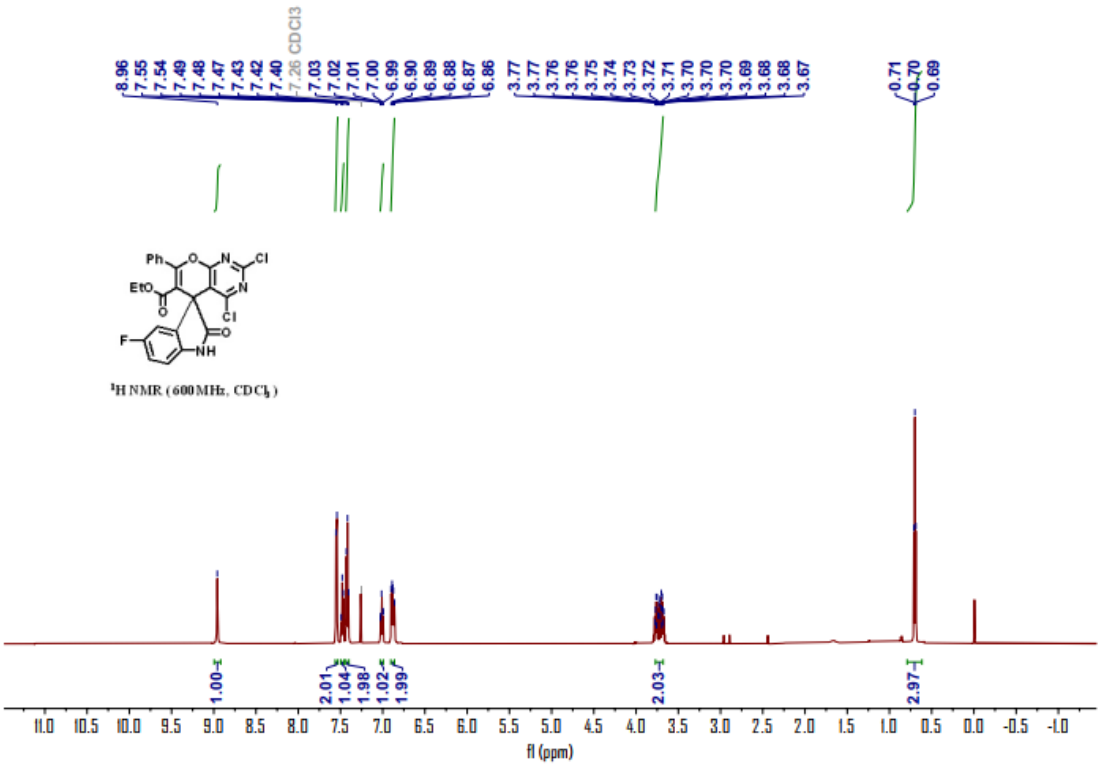


Figure S 7: ^{1}H NMR of **2d**

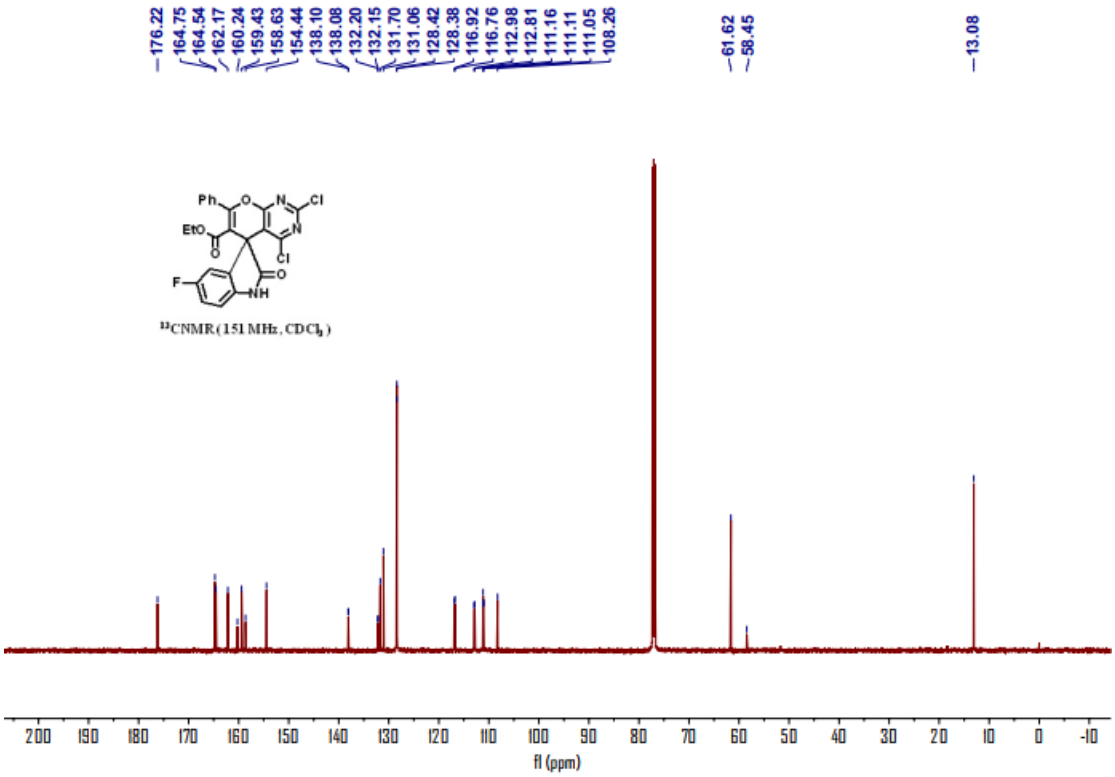


Figure S 8: ^{13}C NMR of **2d**

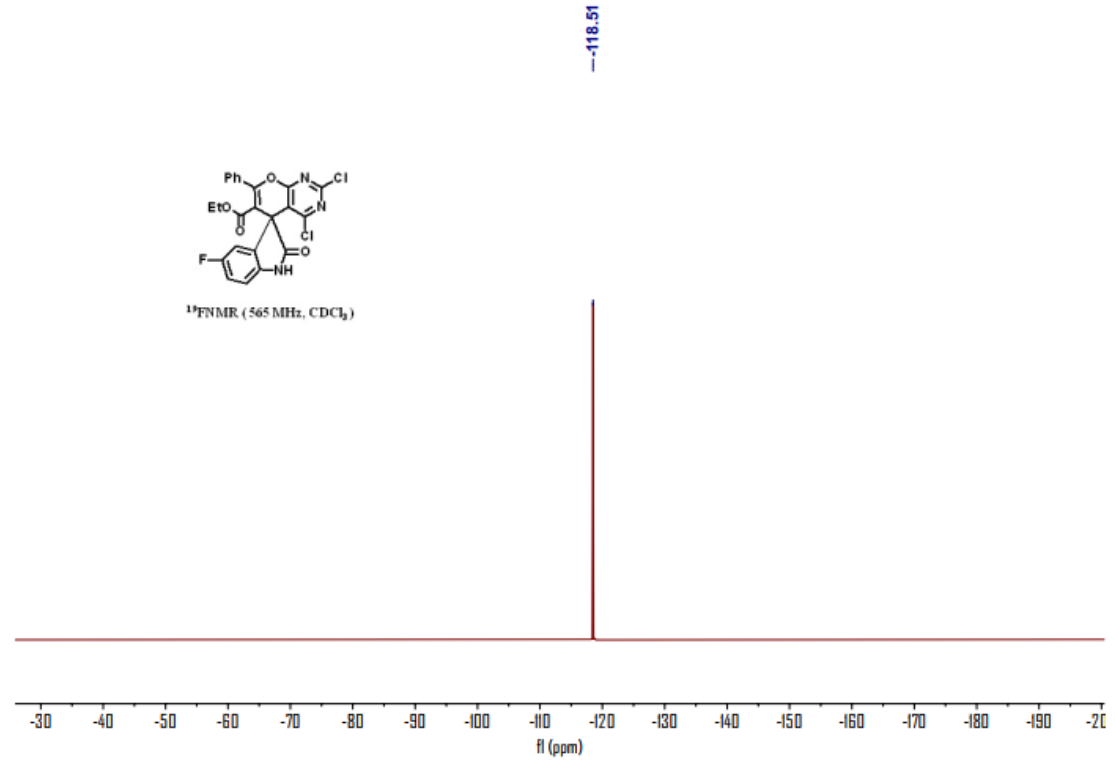


Figure S 9: ^{19}F NMR of **2d**

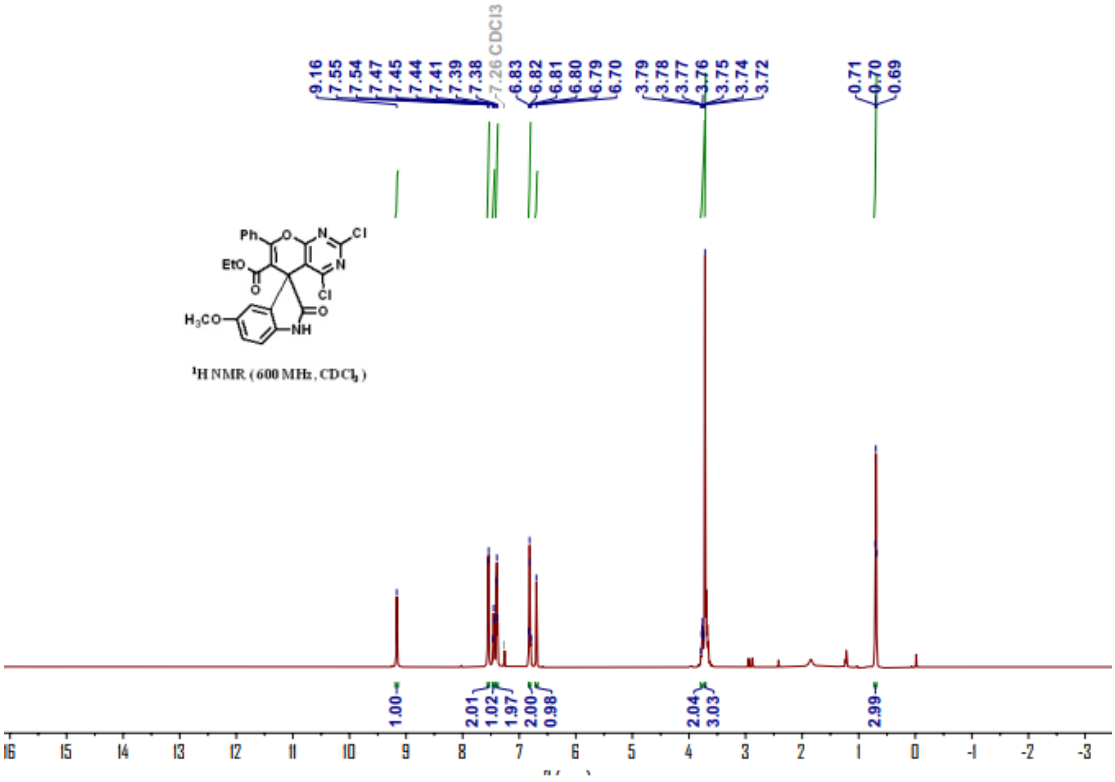


Figure S 10: ^{1}H NMR of **2e**

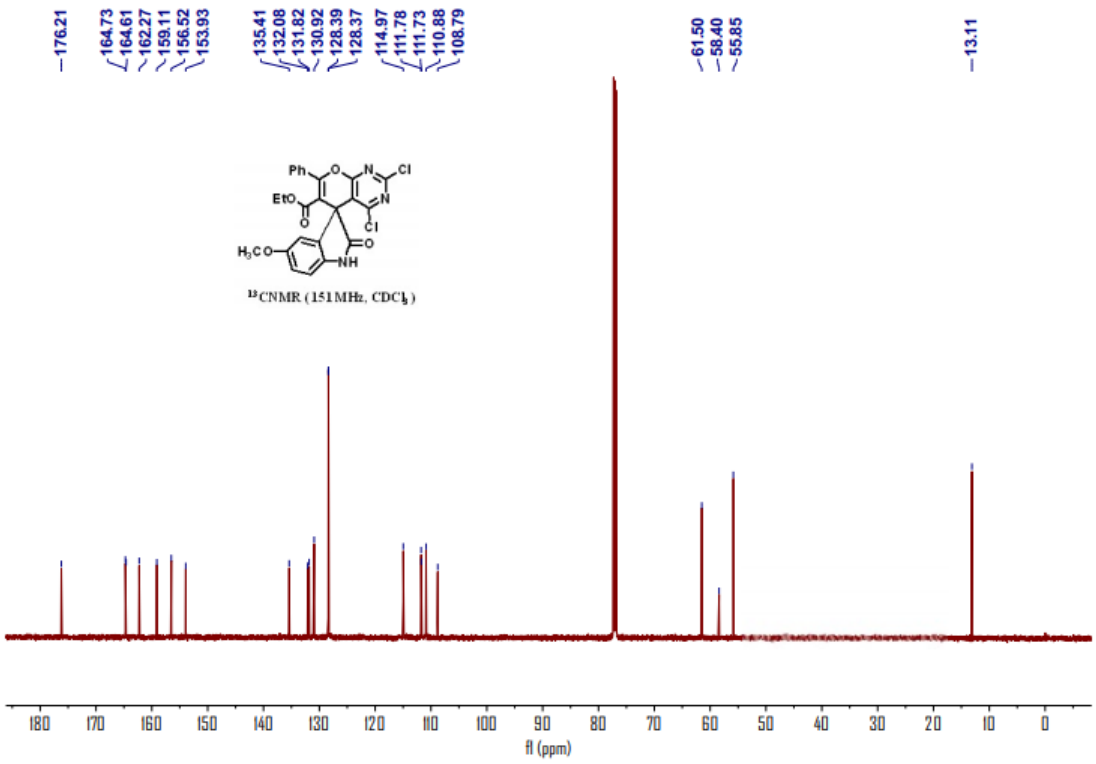


Figure S 11: ^{13}C NMR of **2e**

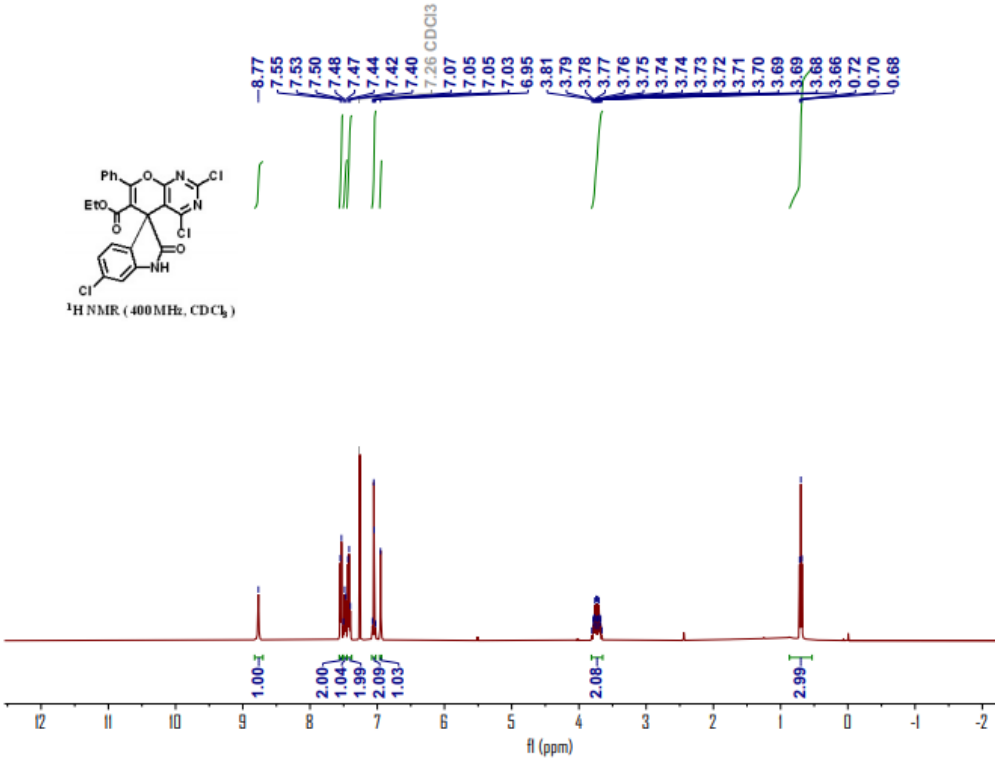


Figure S 12: ^{1}H NMR of **2f**

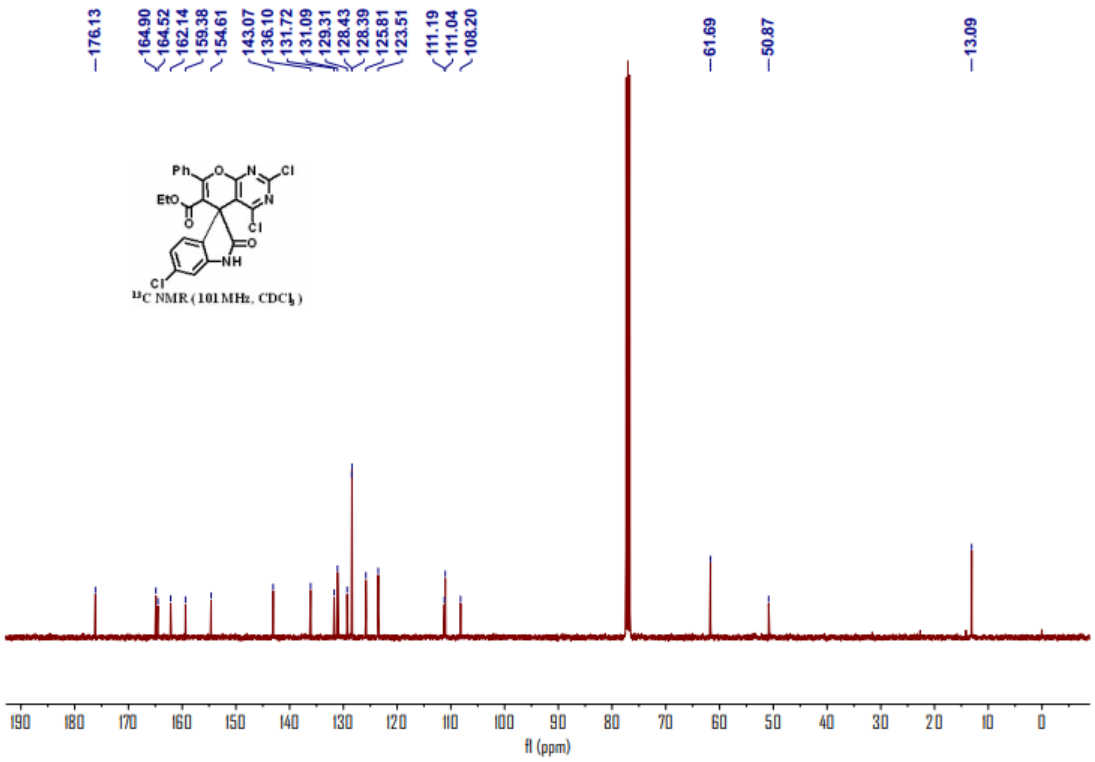


Figure S 13: ^{13}C NMR of **2f**

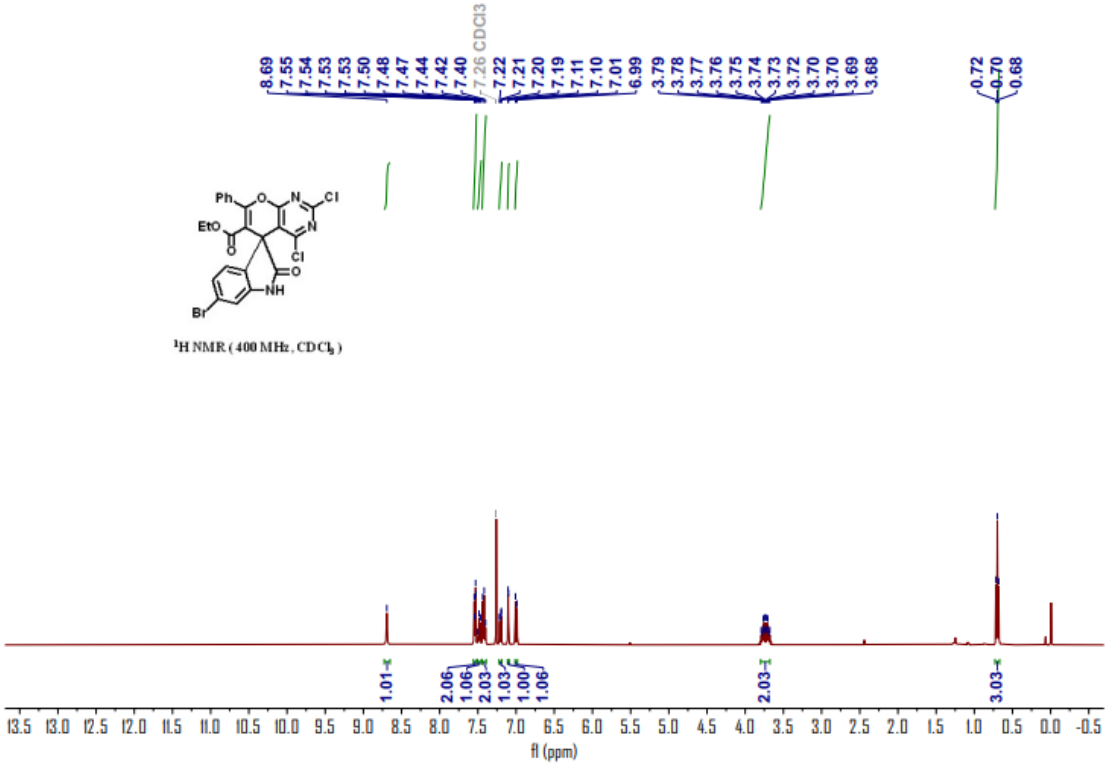


Figure S 14: ^{1}H NMR of **2g**

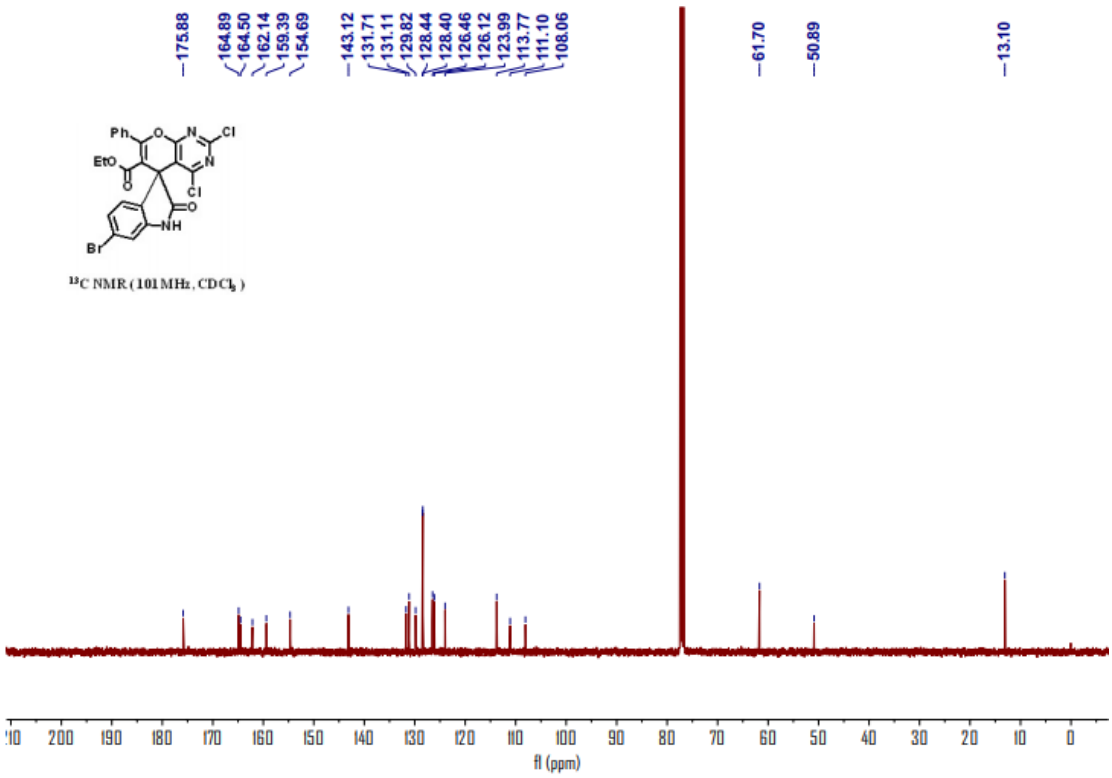


Figure S 15: ^{13}C NMR of **2g**

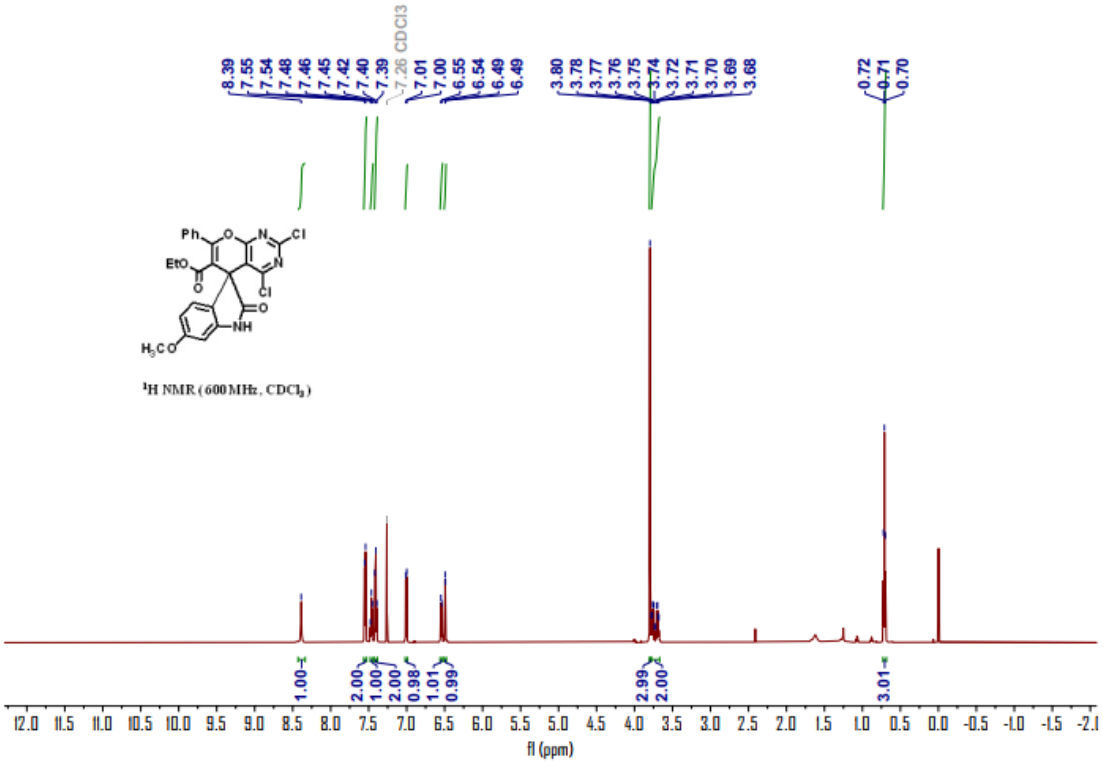


Figure S 16: ^{1}H NMR of **2h**

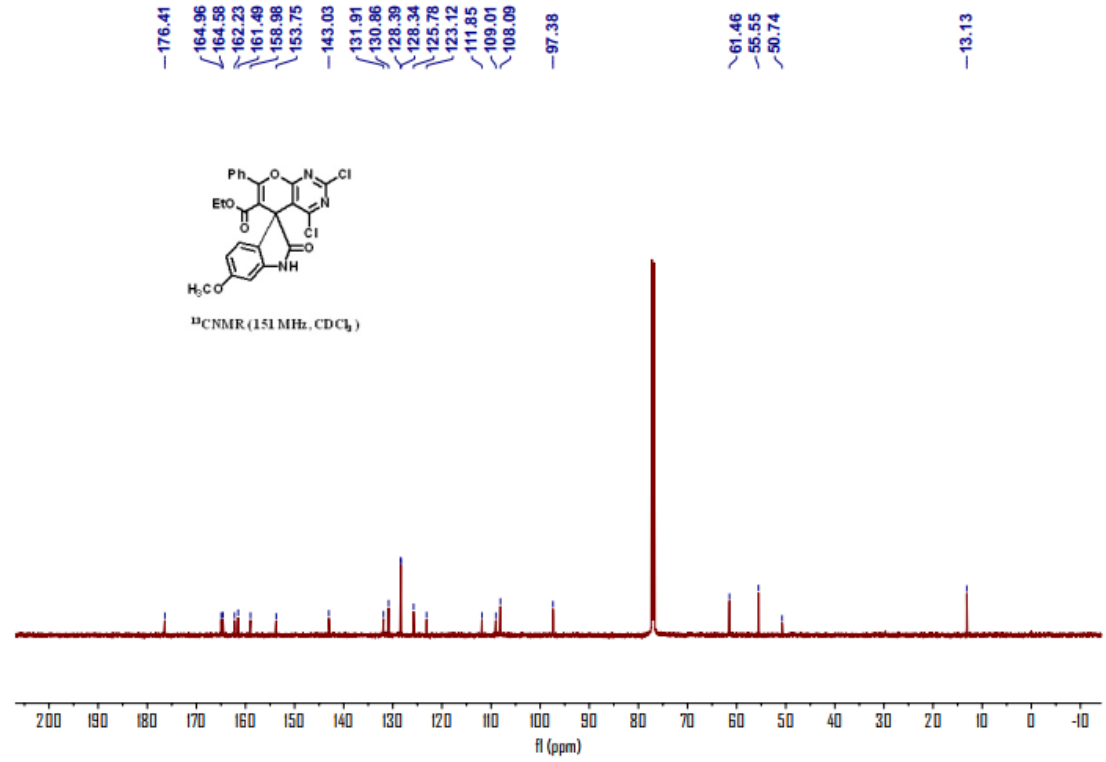


Figure S 17: ^{13}C NMR of **2h**

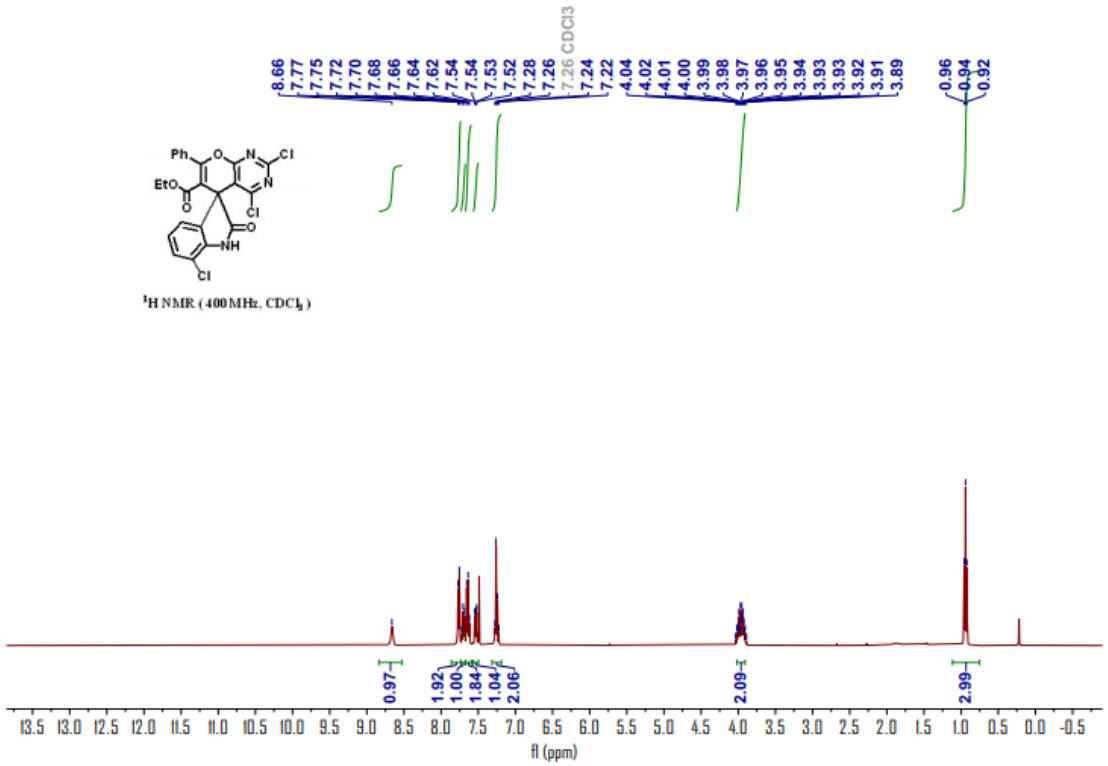


Figure S 18: ^{1}H NMR of **2i**

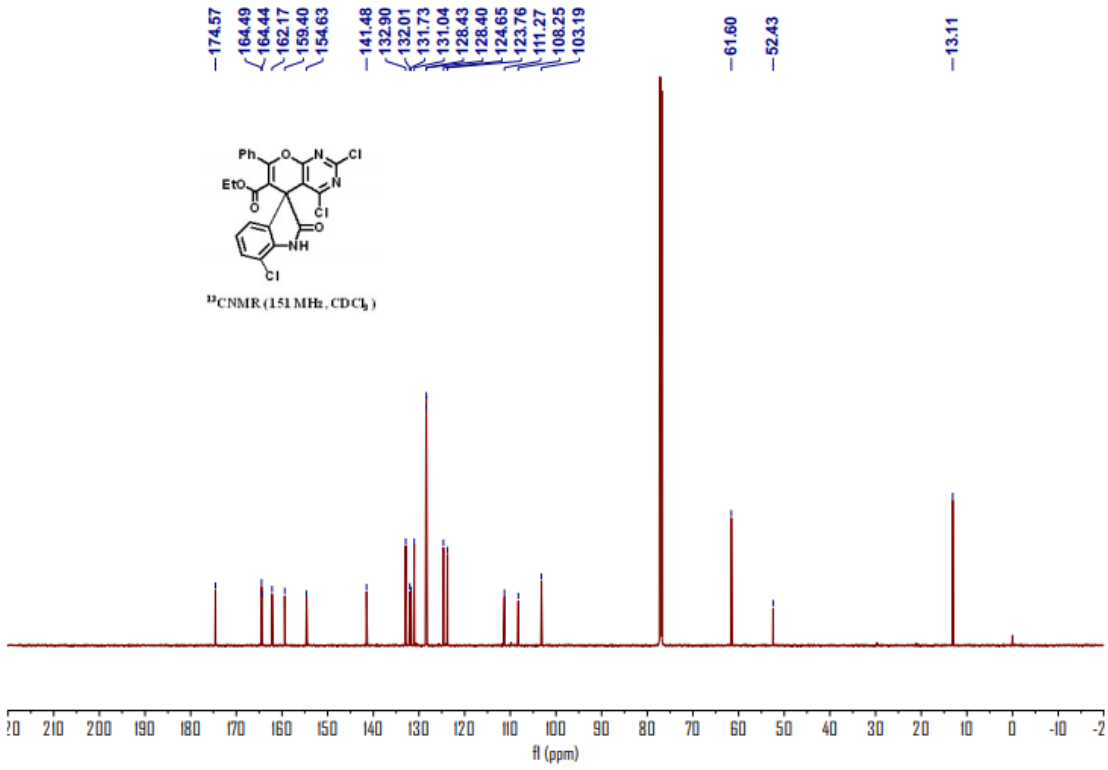


Figure S 19: ^{13}C NMR of **2i**

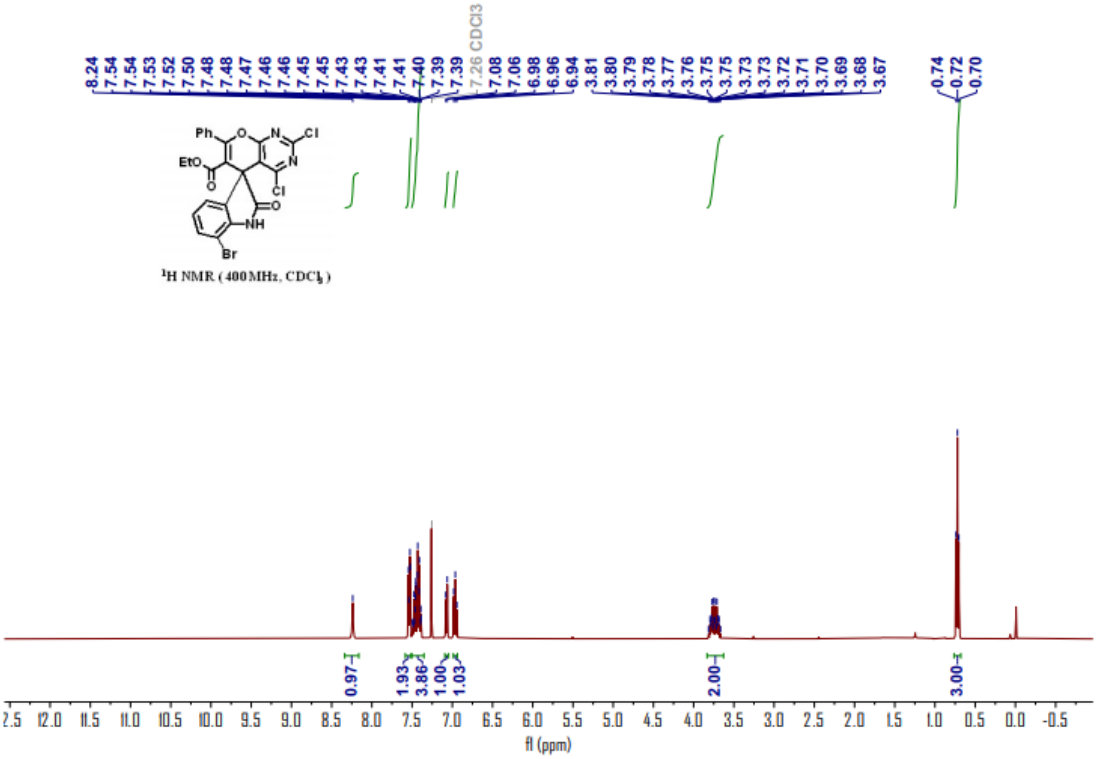


Figure S 20: ^{1}H NMR of **2j**

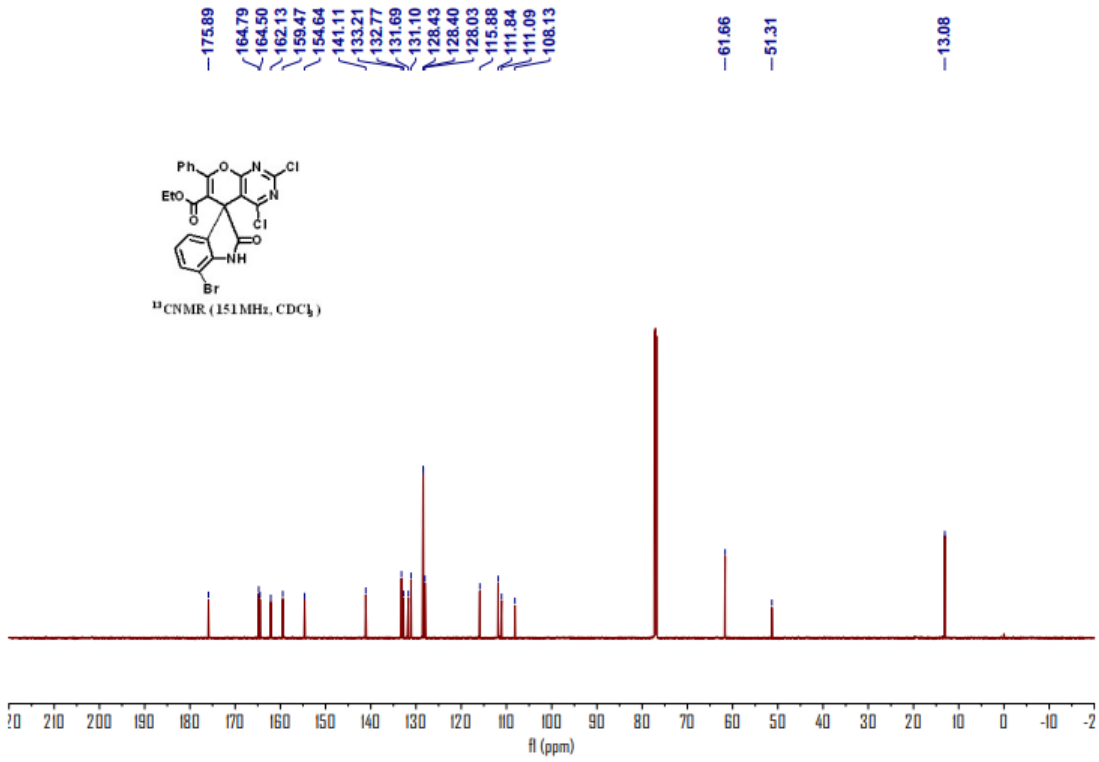


Figure S 21: ^{13}C NMR of **2j**

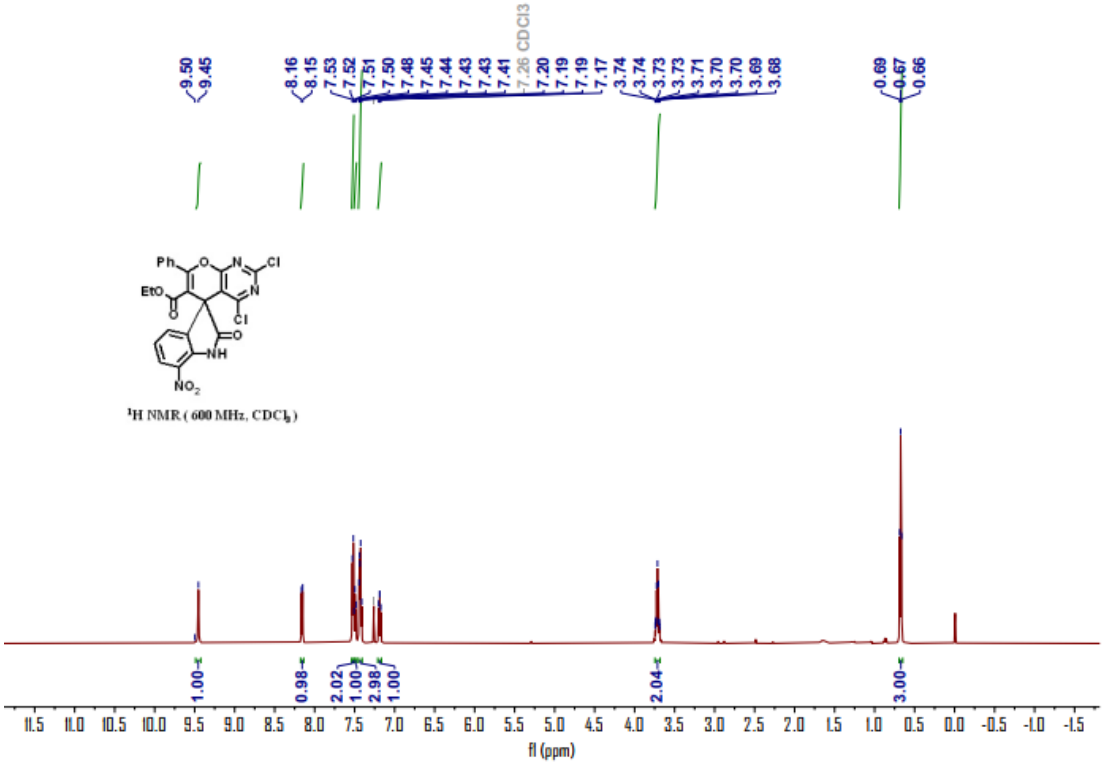


Figure S 22: ^{1}H NMR of **2k**

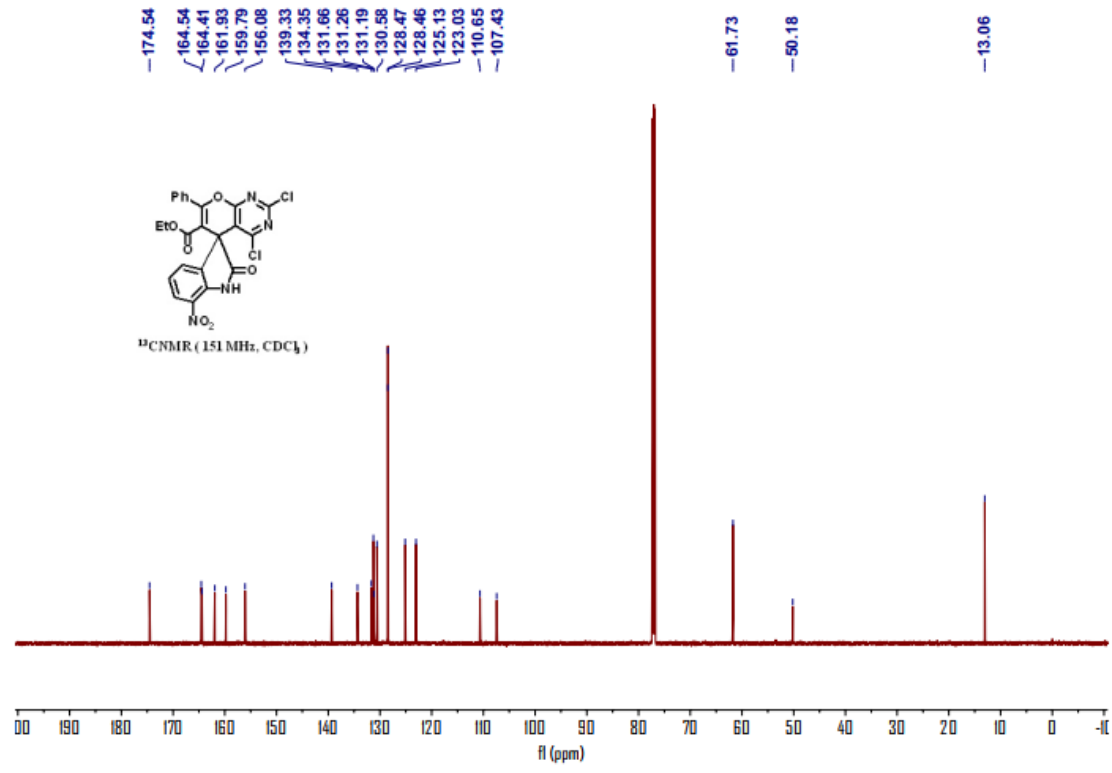


Figure S 23: ^{1}H NMR of **2k**

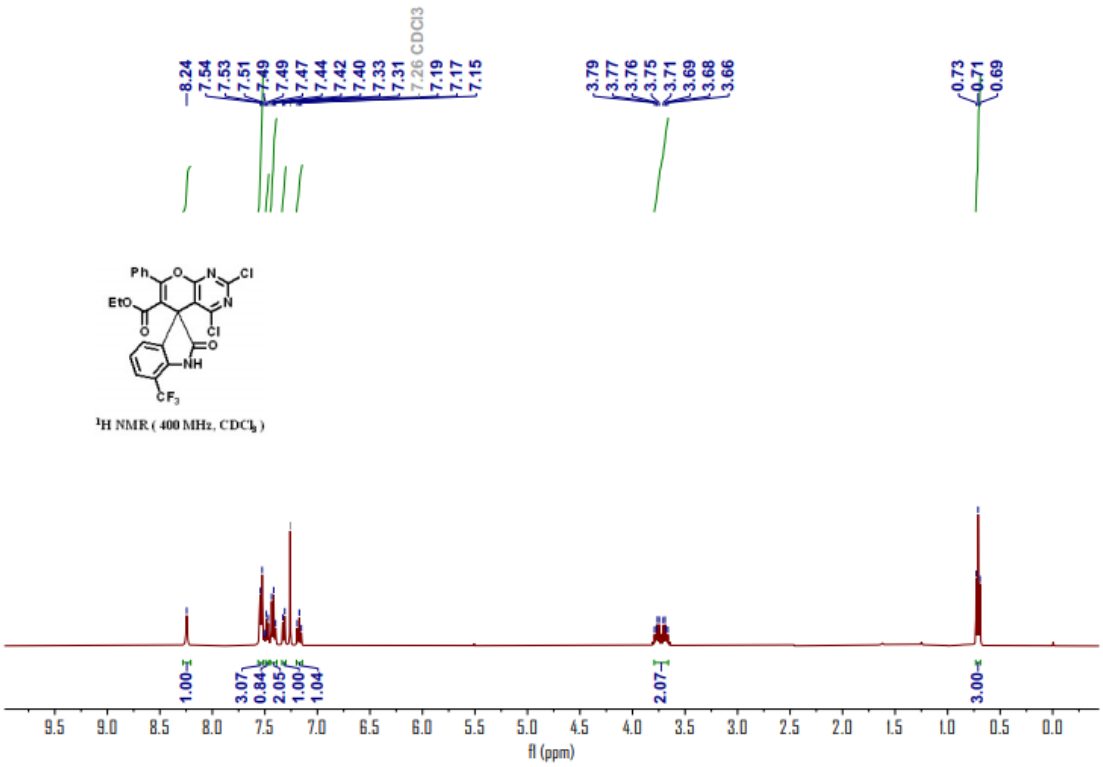


Figure S 24: ^{1}H NMR of **2l**

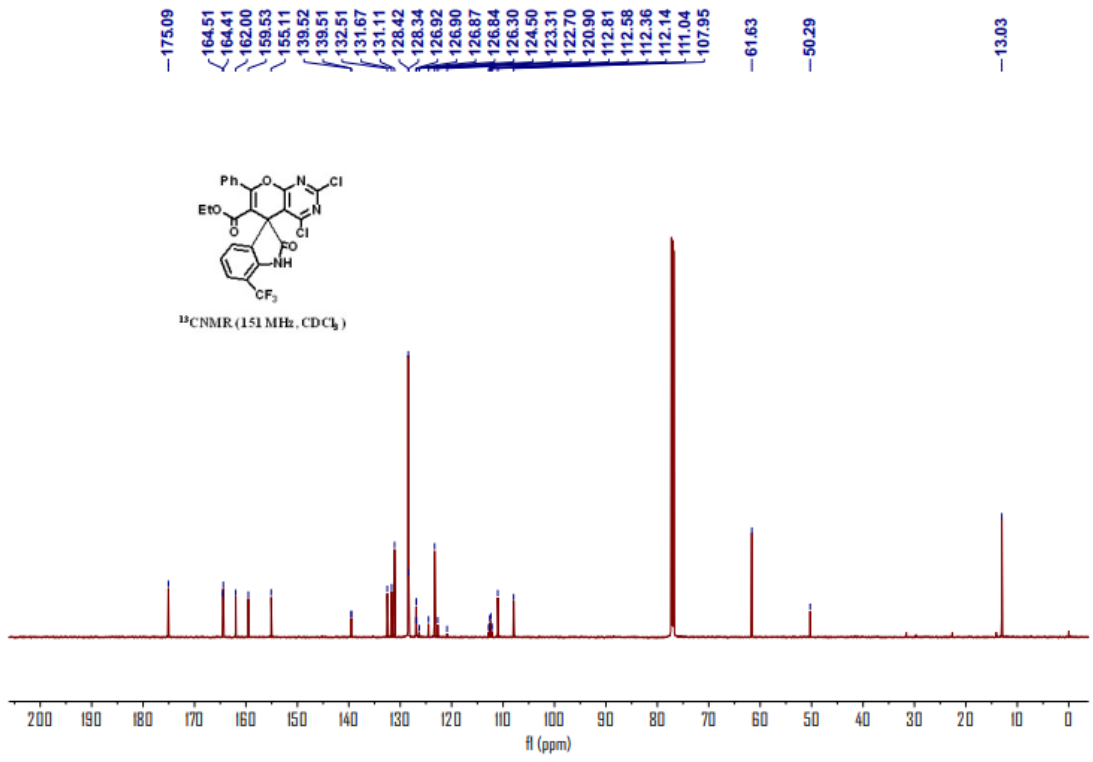


Figure S 25: ^{13}C NMR of **2l**

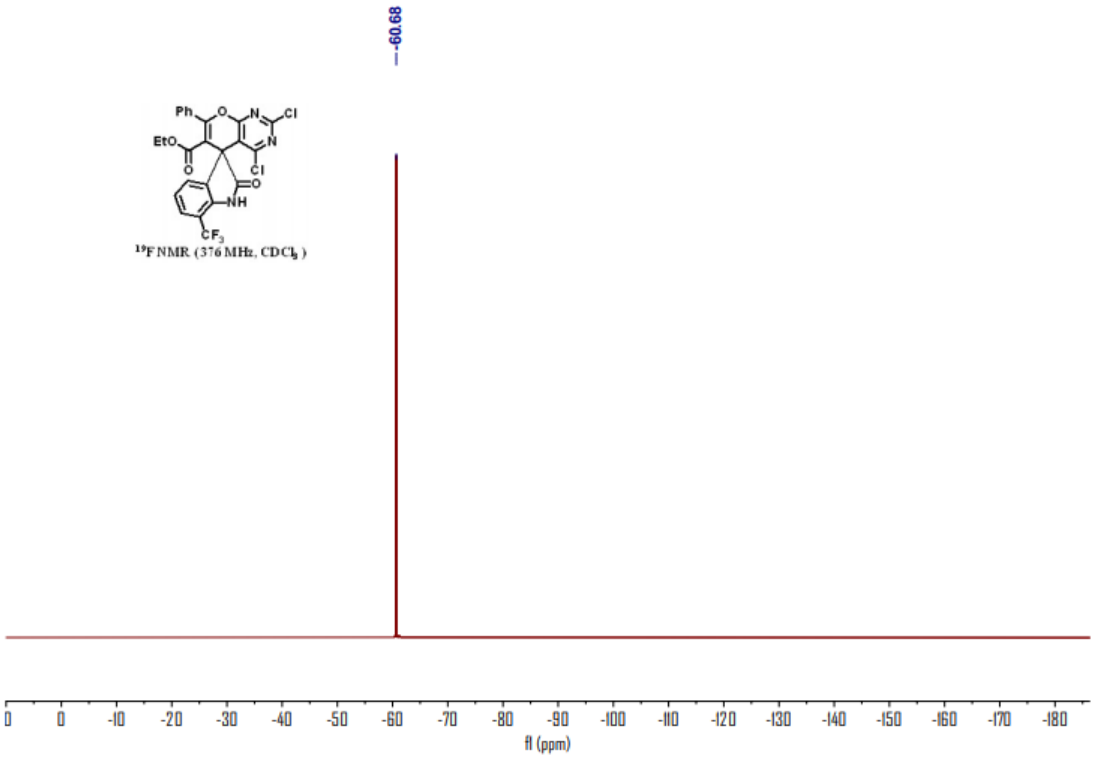


Figure S 26: ^{19}F NMR of **2l**

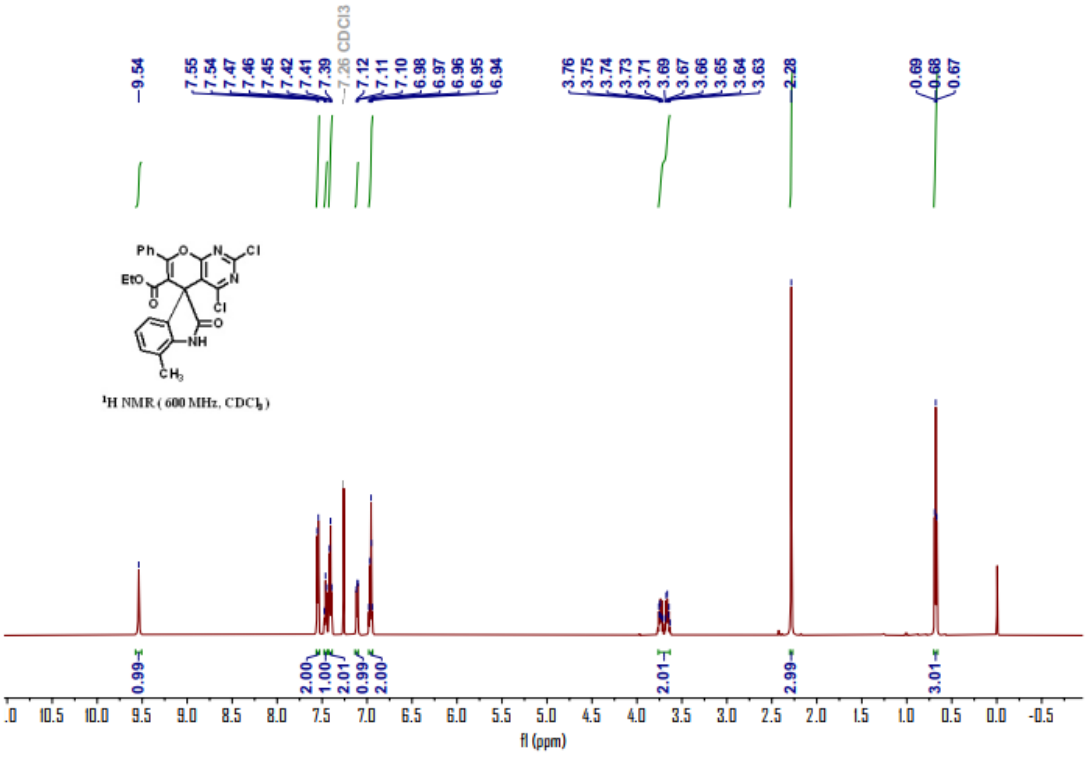


Figure S 27: ^{1}H NMR of **2m**

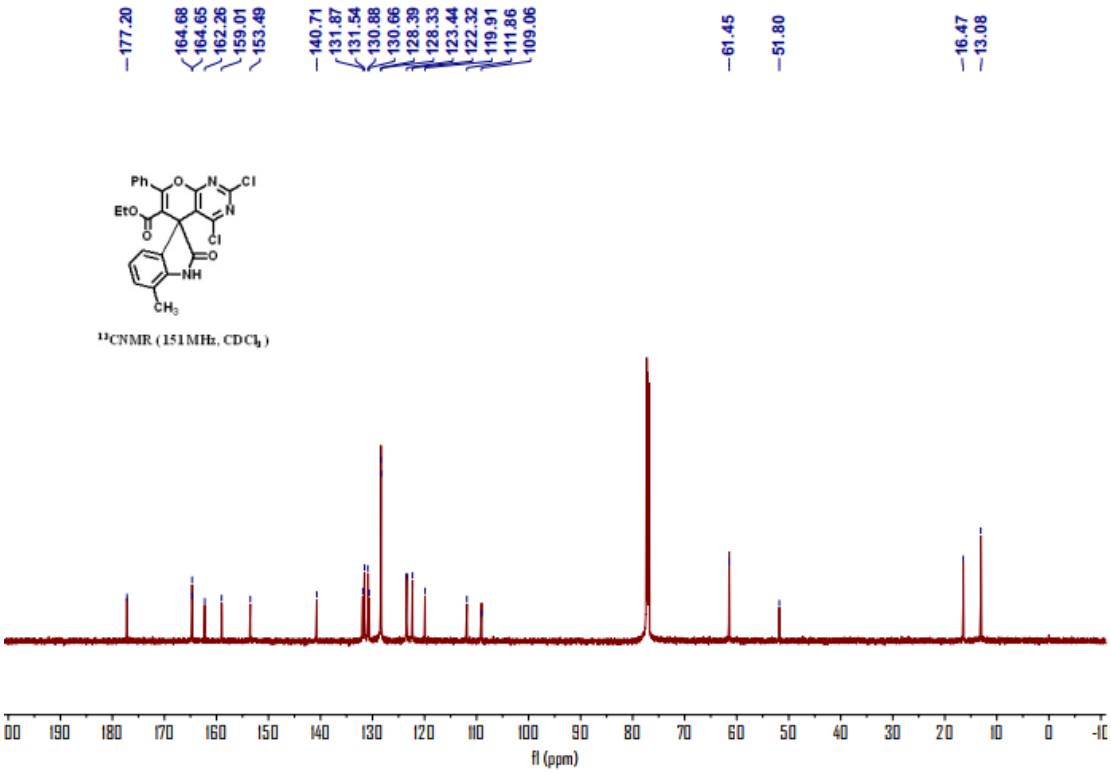


Figure S 28: ^{13}C NMR of **2m**

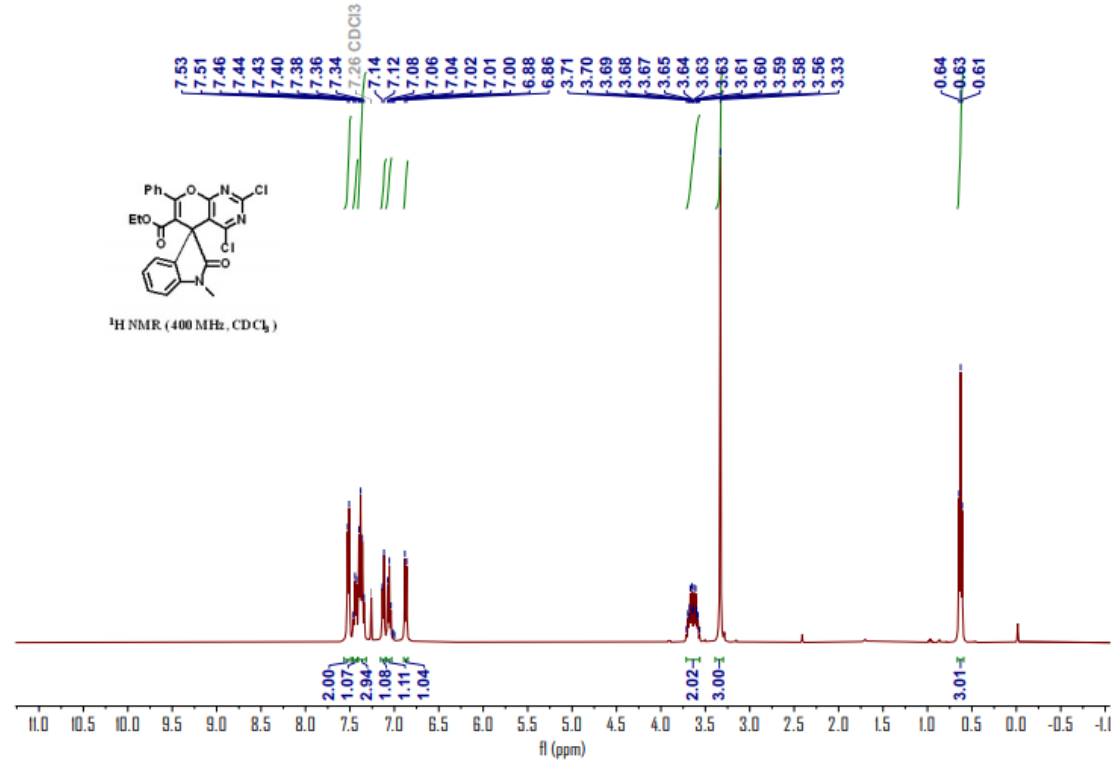


Figure S 29: ^{1}H NMR of **2n**

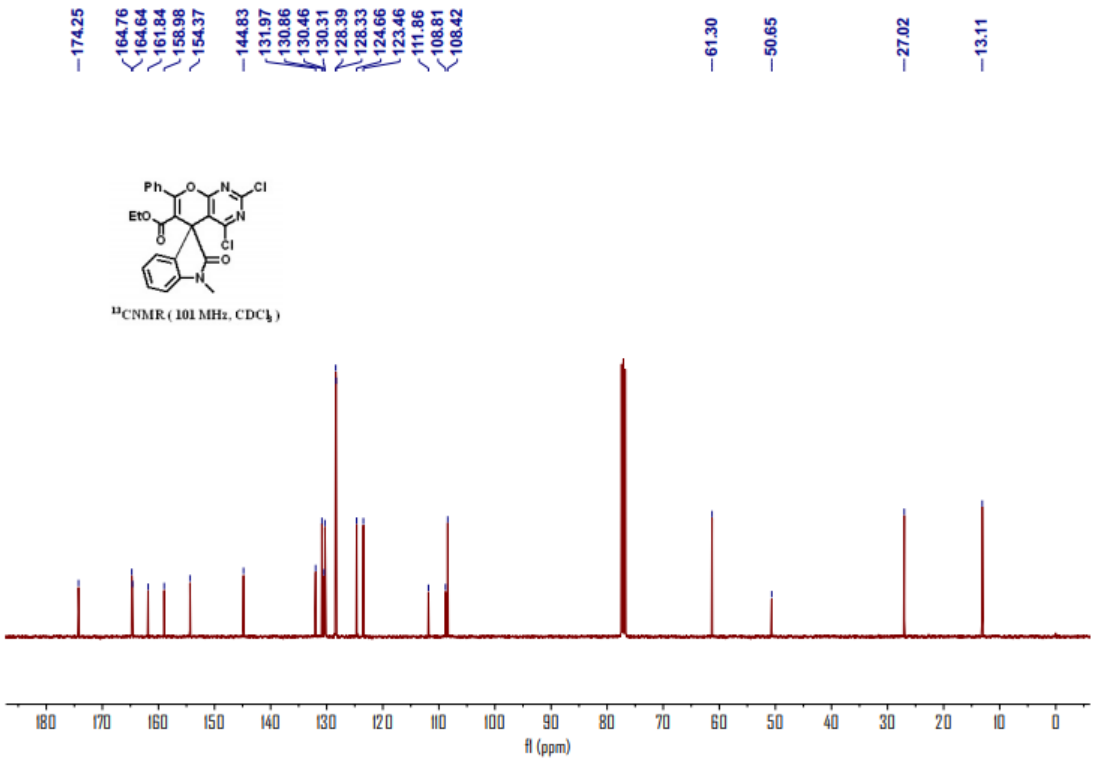


Figure S 30: ^{13}C NMR of **2n**

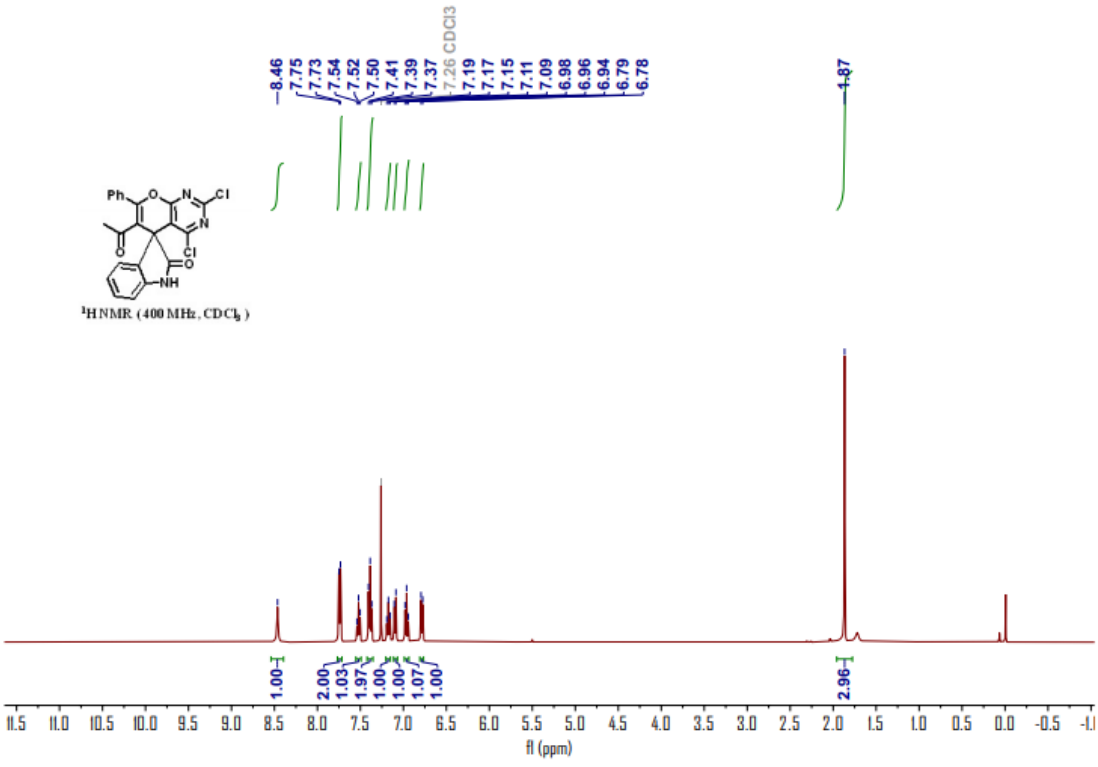


Figure S 31: ^{1}H NMR of **3a**

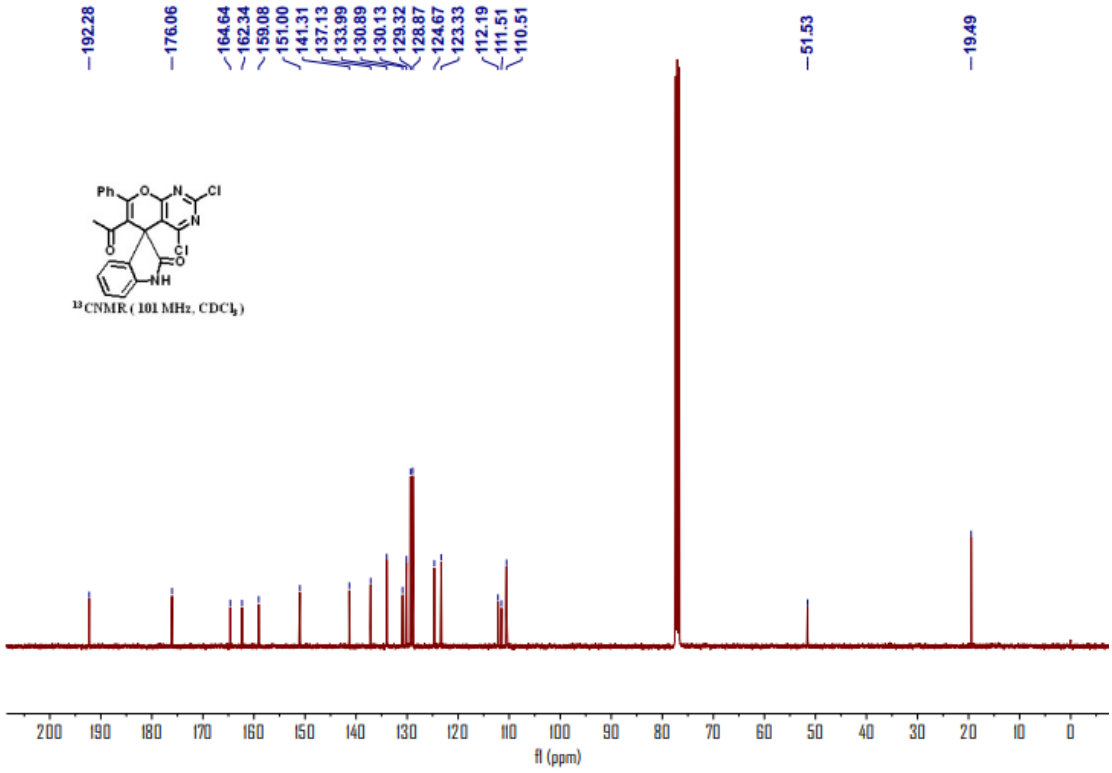


Figure S 32: ^{13}C NMR of **3a**

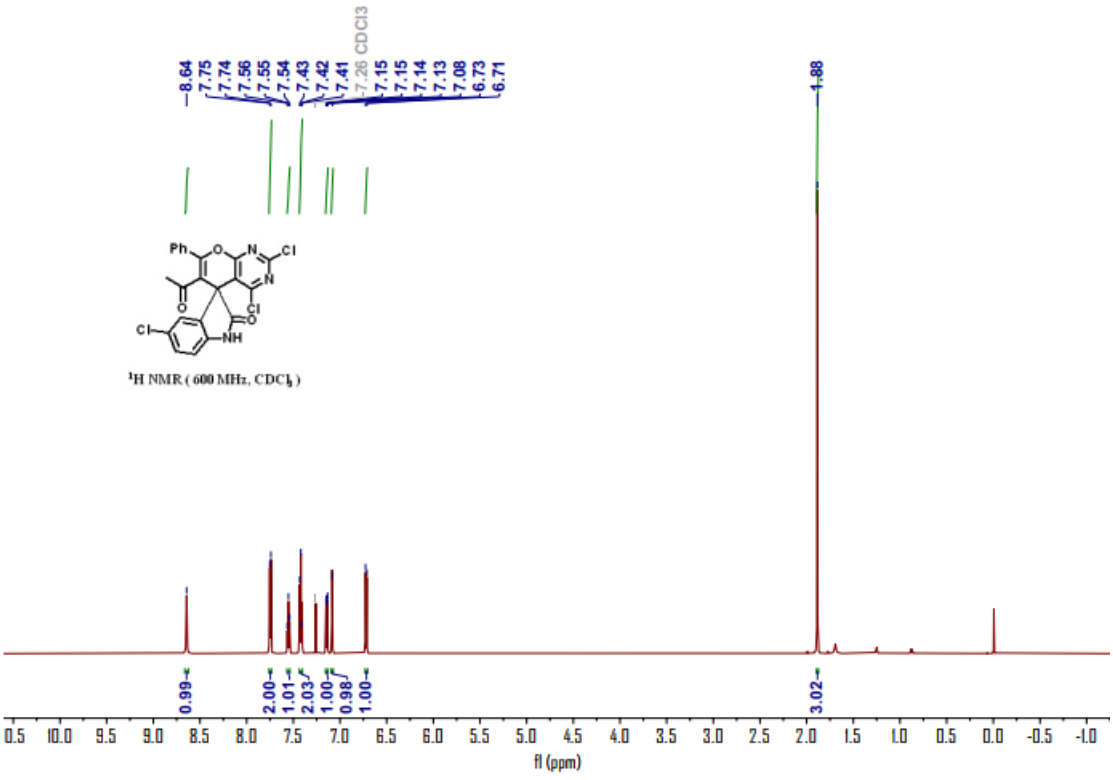


Figure S 33: ^{1}H NMR of **3b**

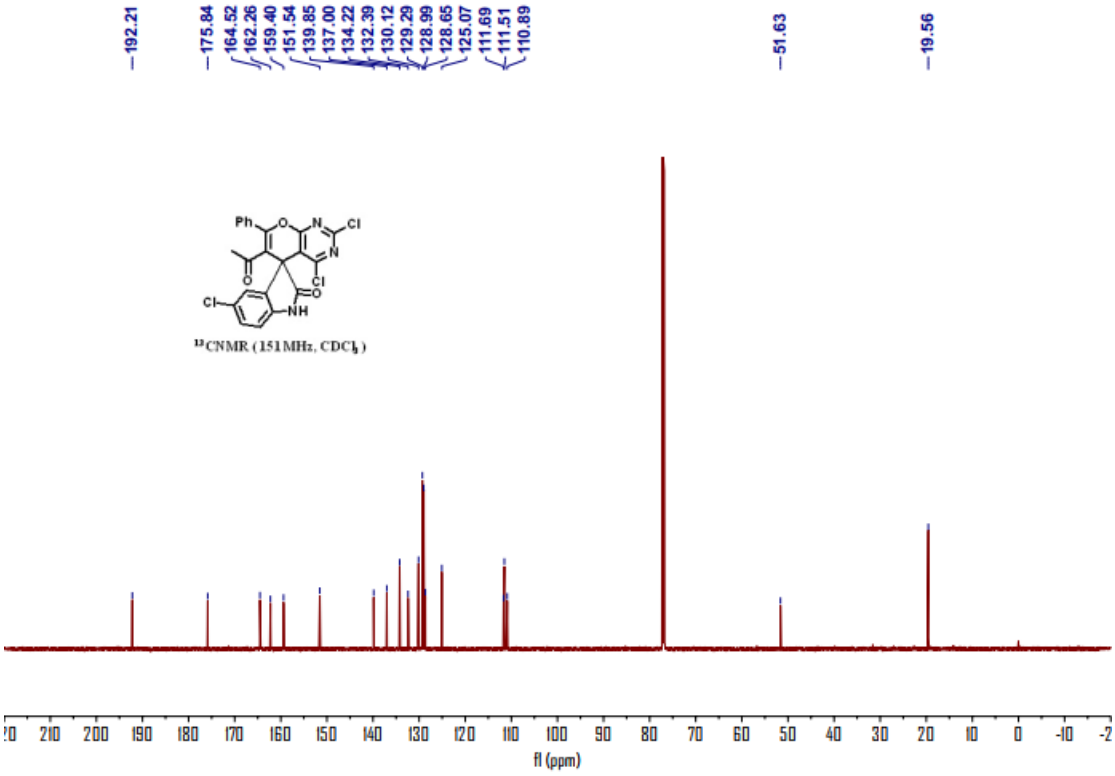


Figure S 34: ^{13}C NMR of **3b**

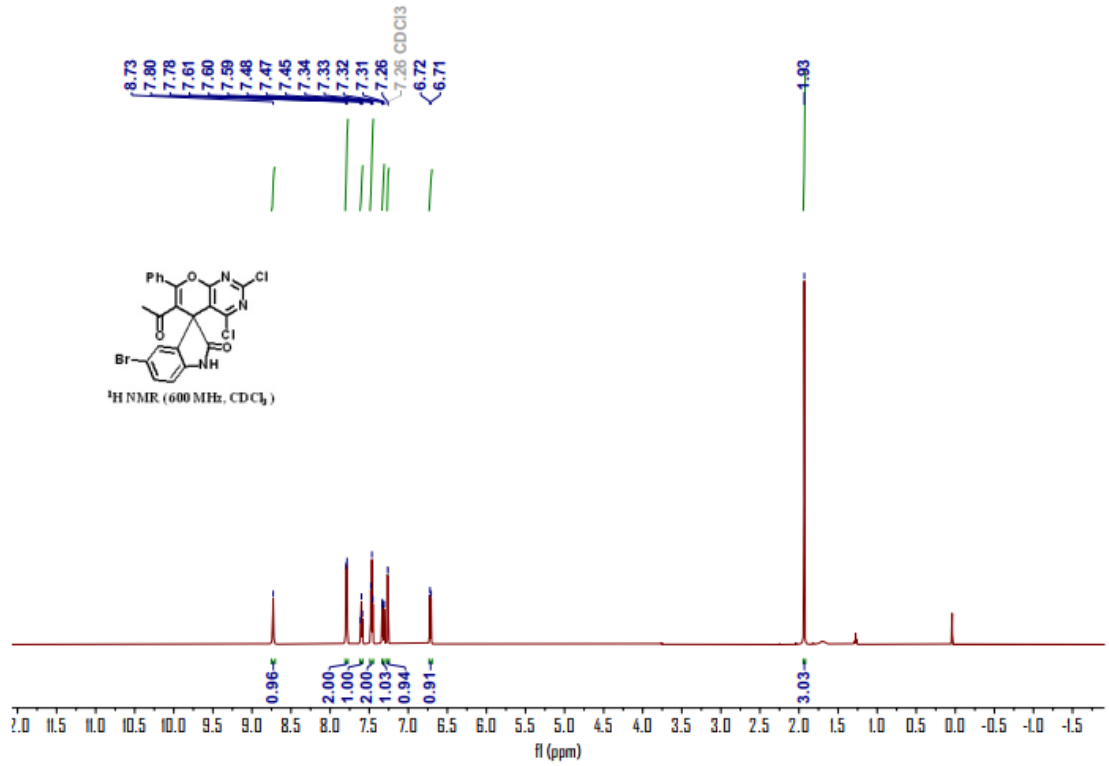


Figure S 35: ^{1}H NMR of **3c**

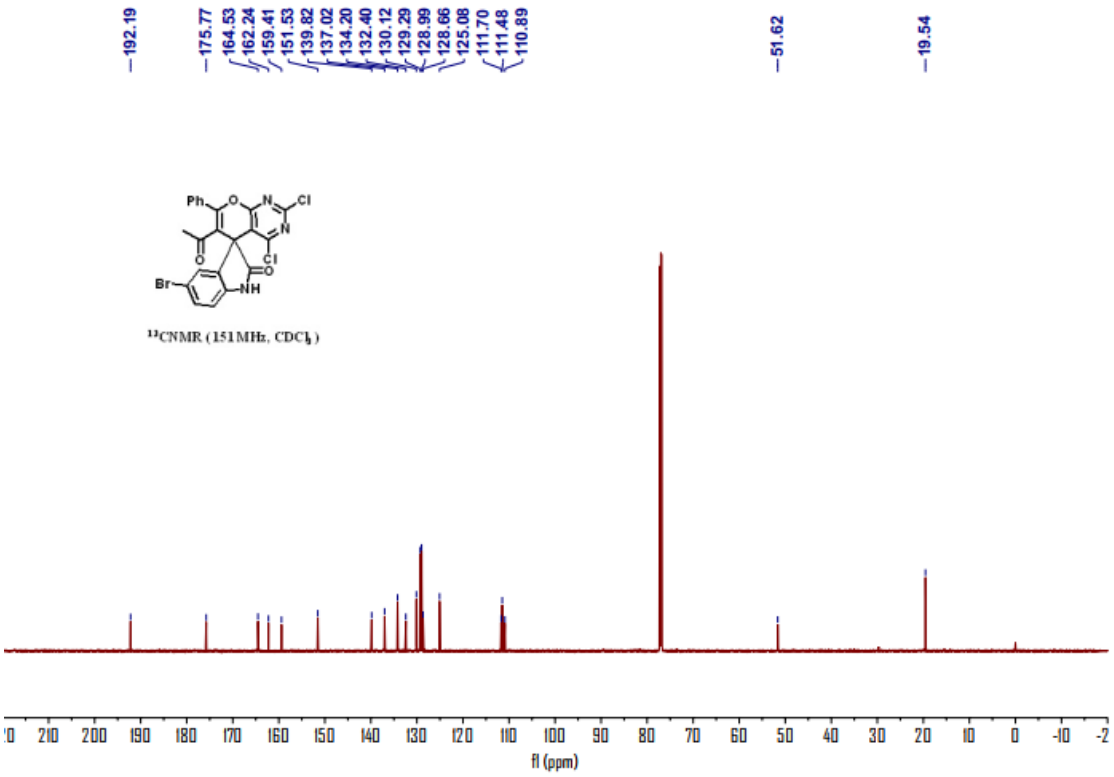


Figure S 36: ^{13}C NMR of **3c**

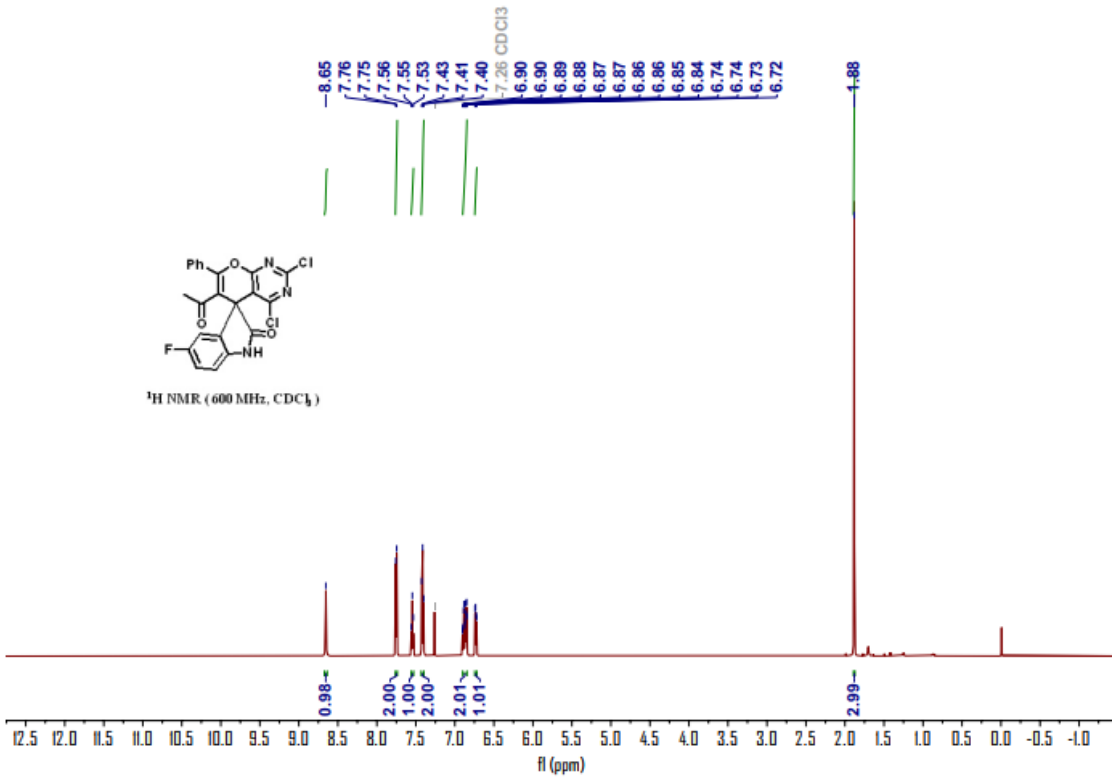


Figure S 37: ^{1}H NMR of **3d**

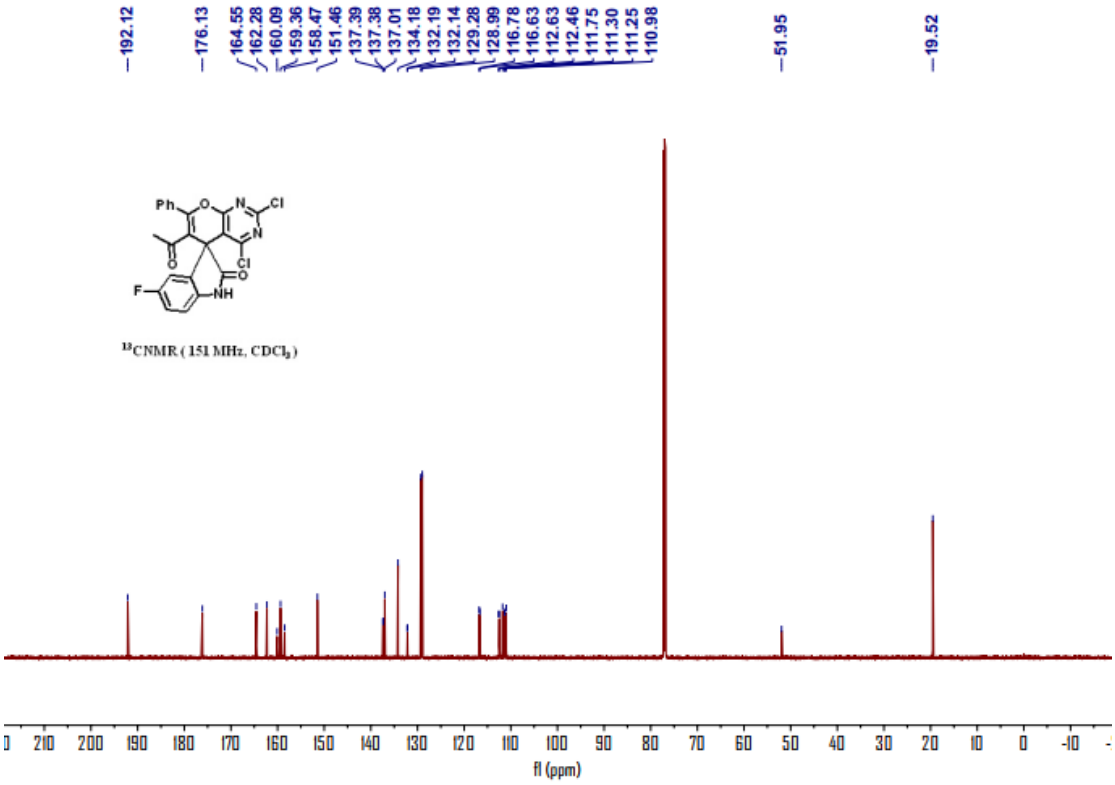


Figure S 38: ^{13}C NMR of **3d**

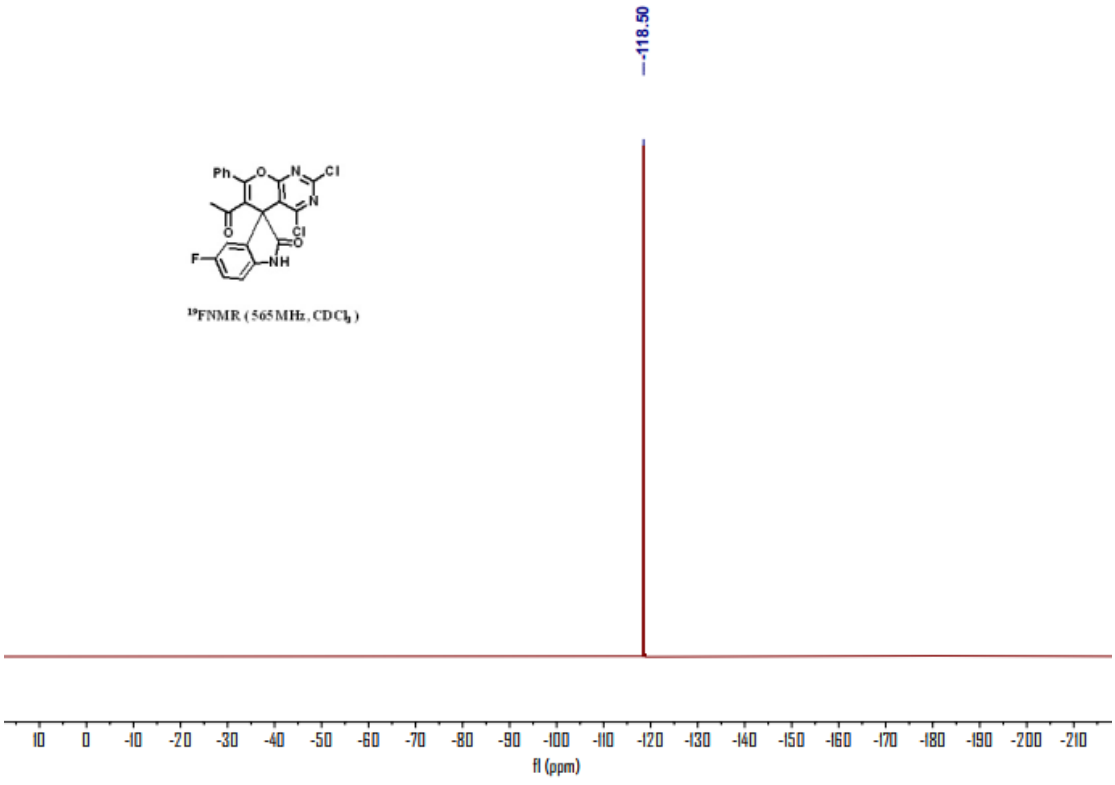


Figure S 39: ^{19}F NMR of **3d**

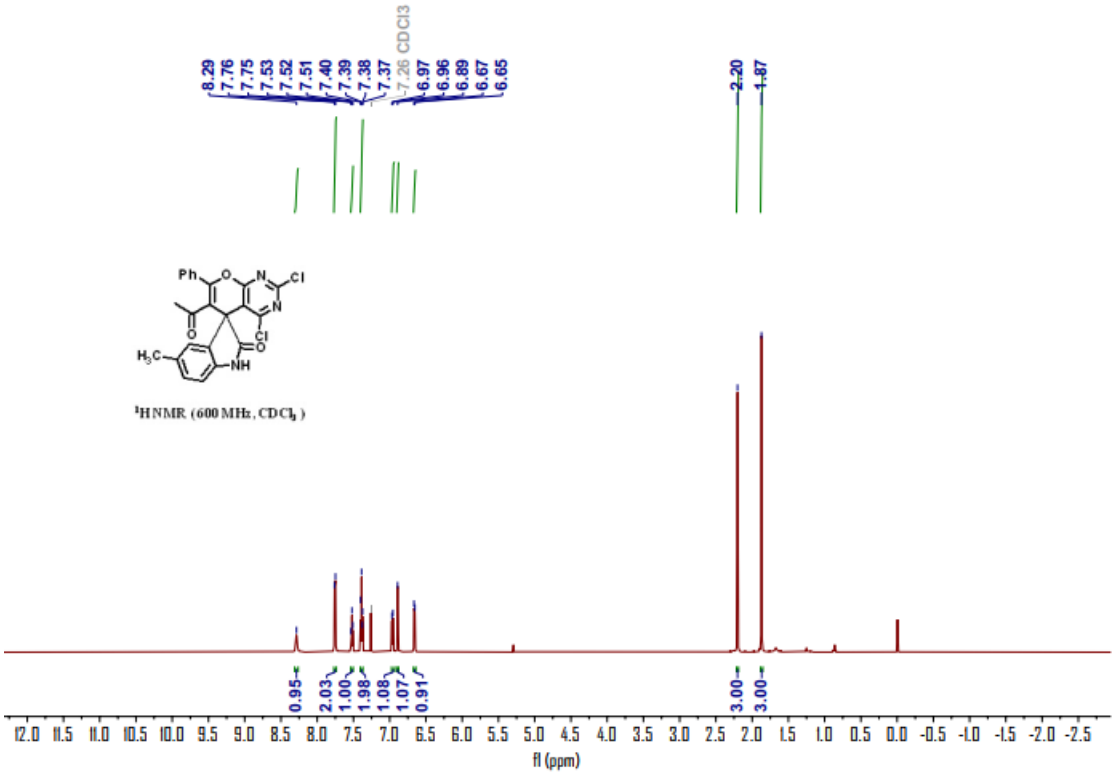


Figure S 40: ^{1}H NMR of **3e**

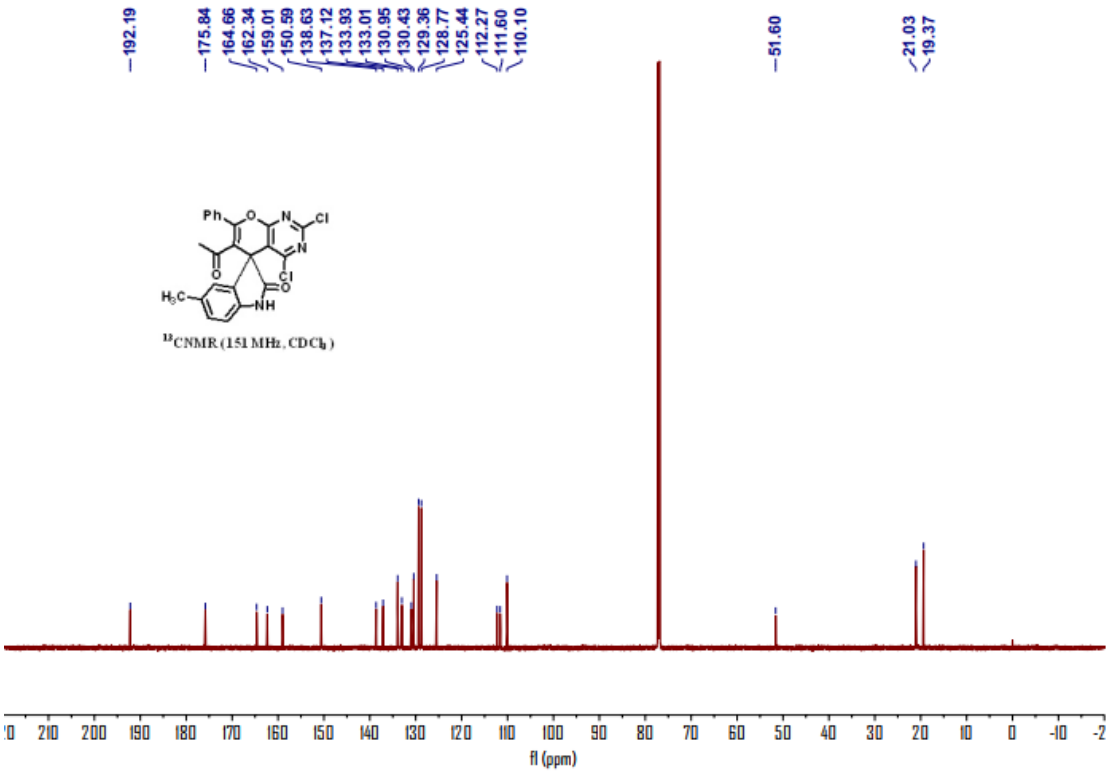


Figure S 41: ^{13}C NMR of **3e**

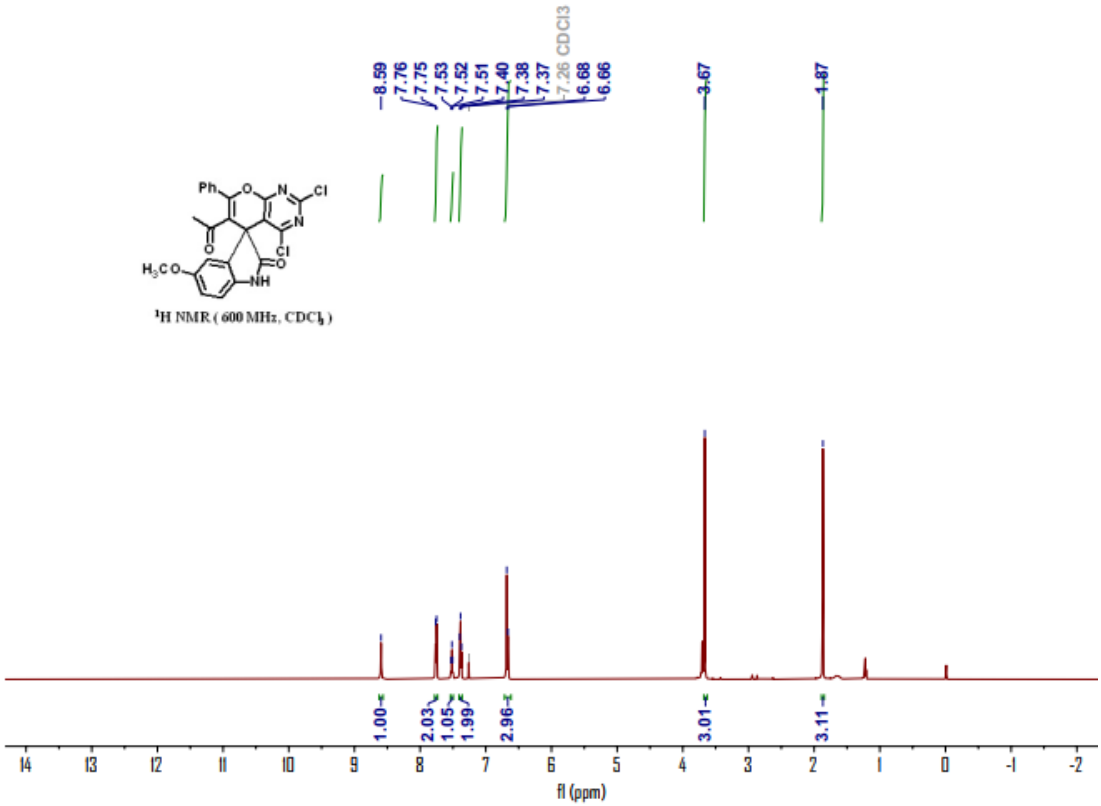


Figure S 42: ^{1}H NMR of **3f**

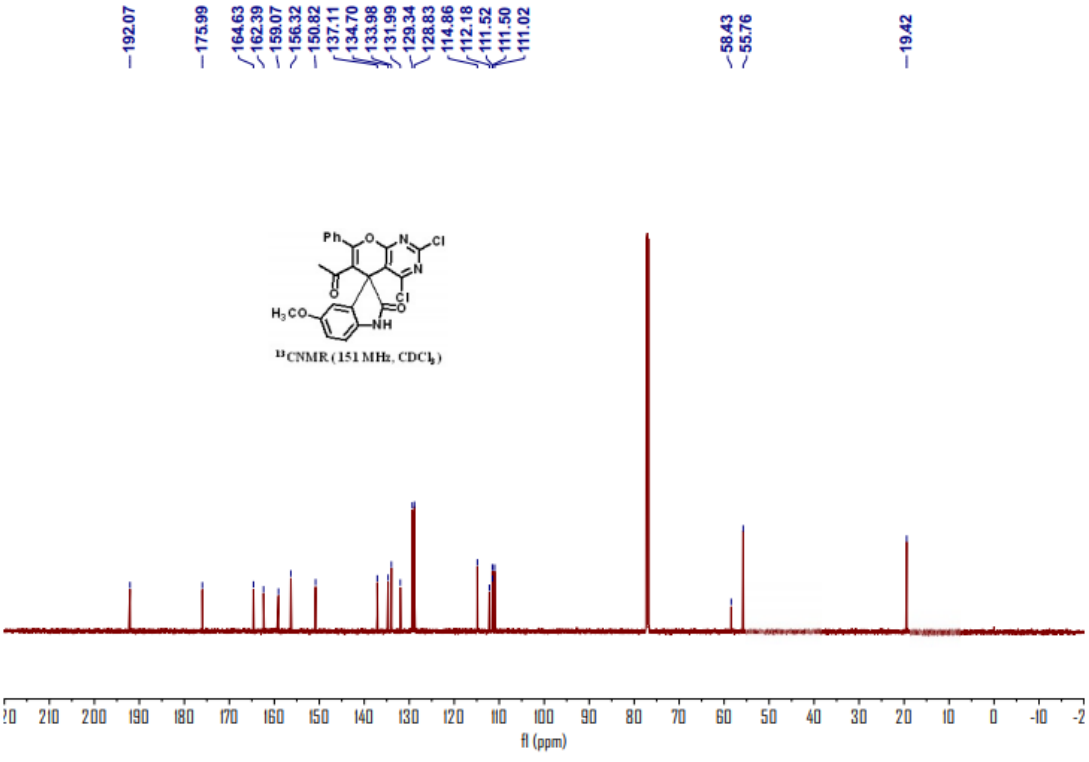


Figure S 43: ^{13}C NMR of **3f**

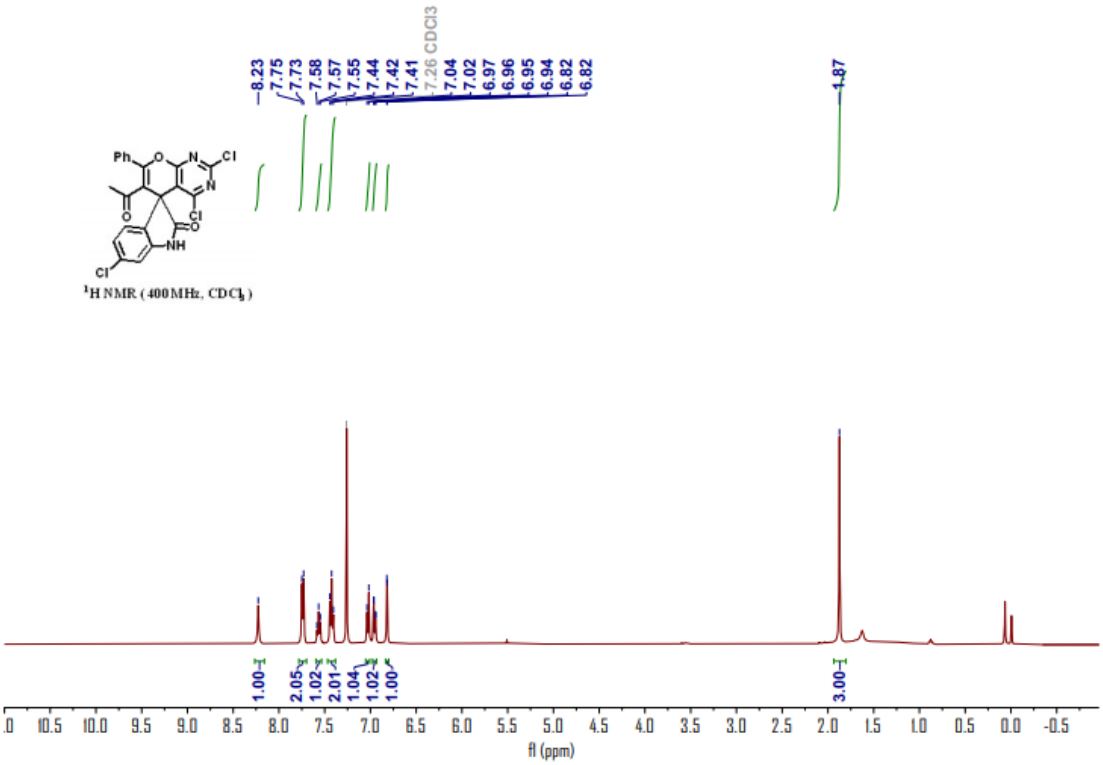


Figure S 44: ^{1}H NMR of **3g**

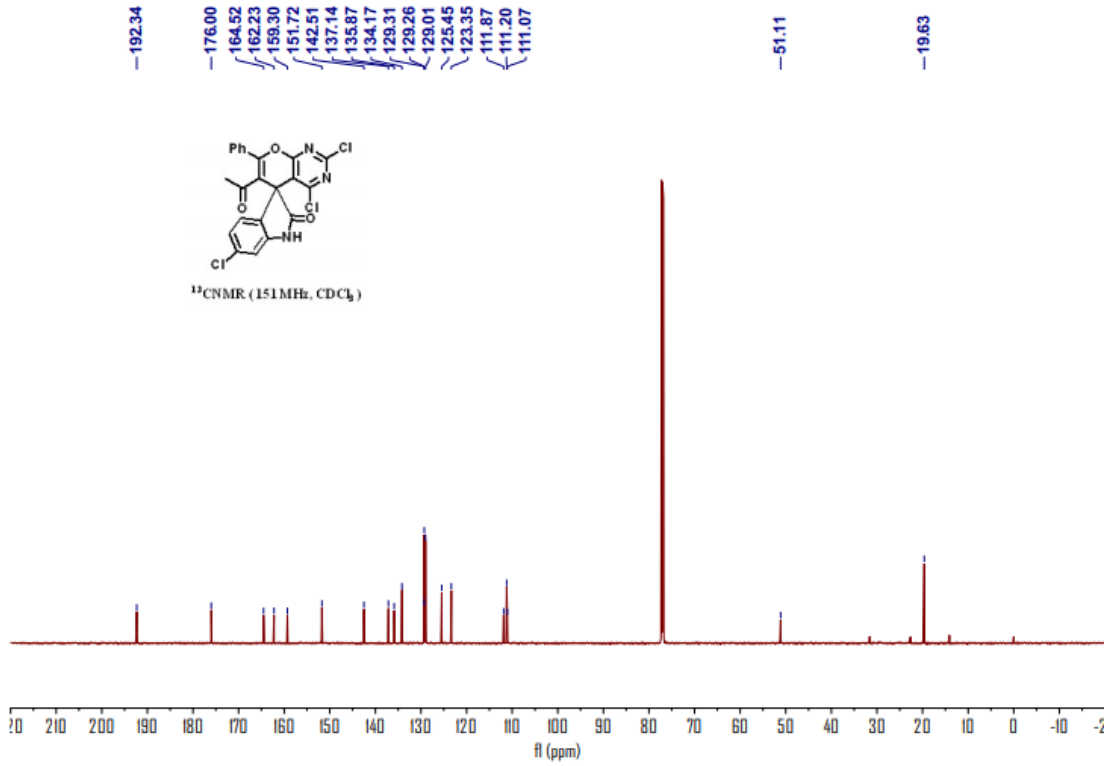


Figure S 45: ^{13}C NMR of **3g**

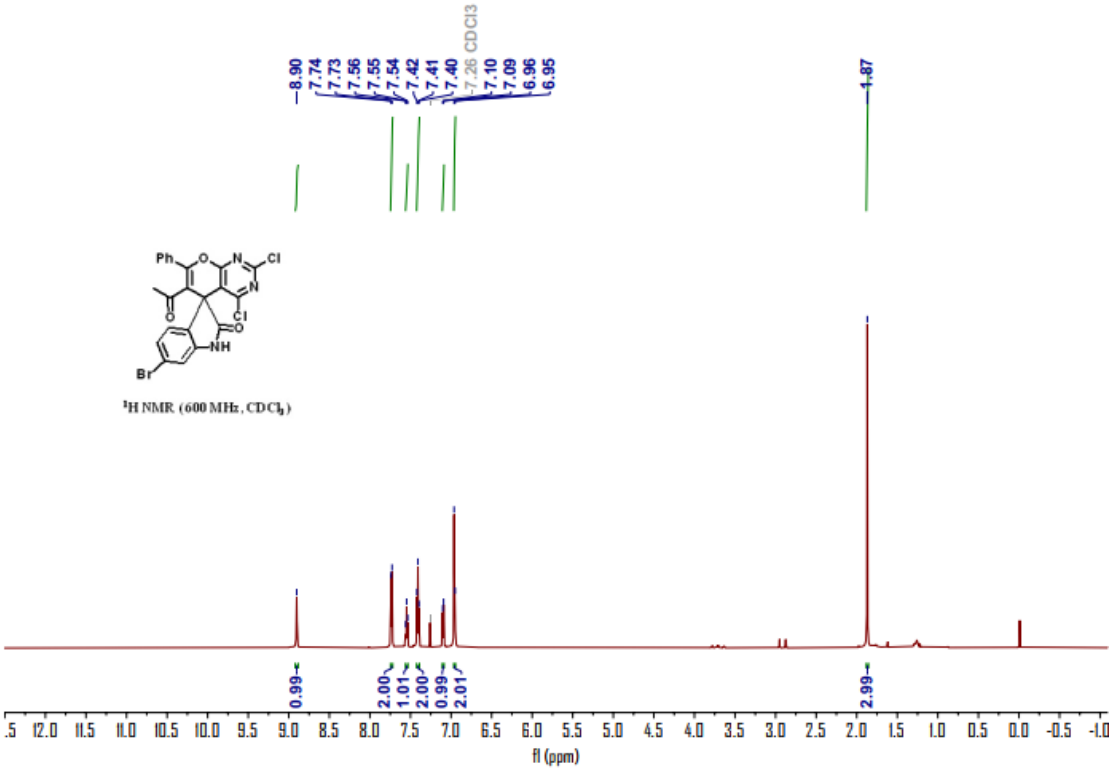


Figure S 46: ^{1}H NMR of **3h**

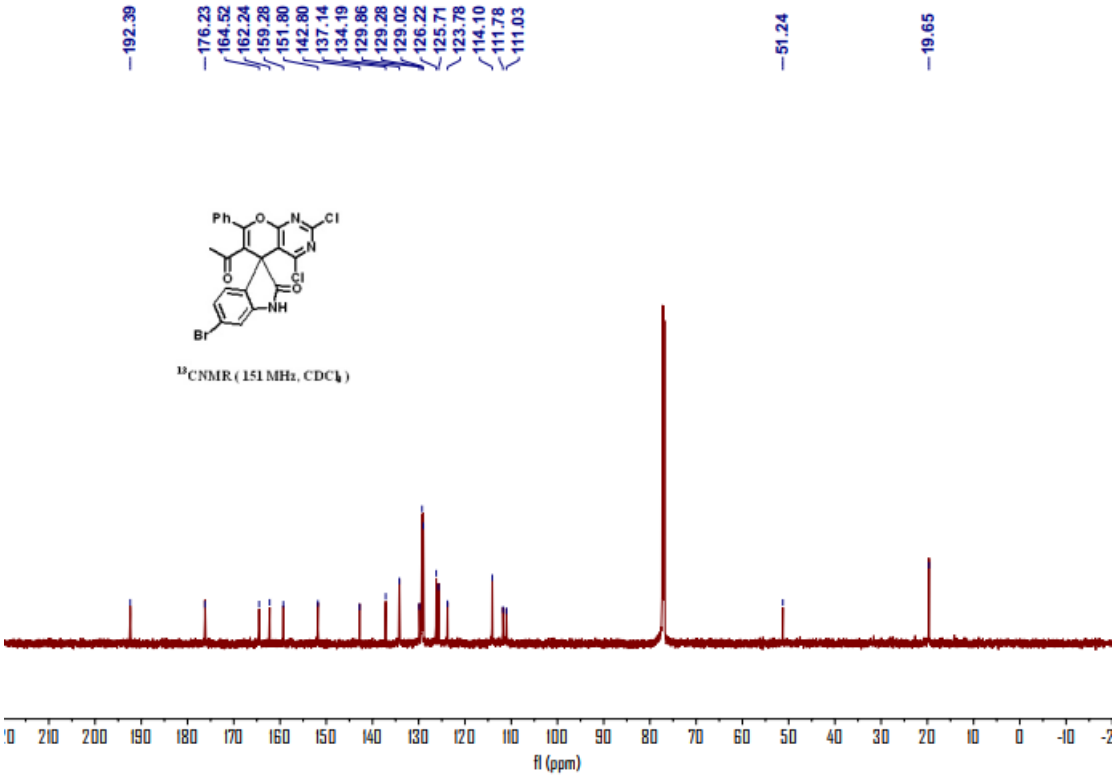


Figure S 47: ^{13}C NMR of **3h**

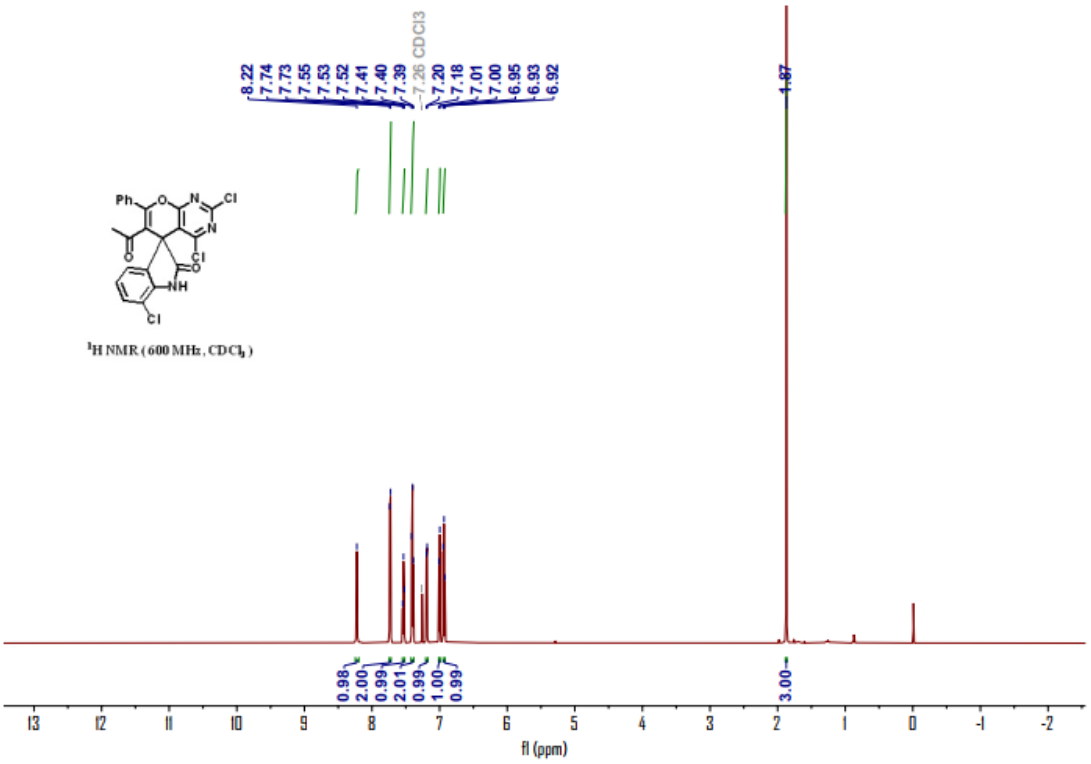


Figure S 48: ^{1}H NMR of **3i**

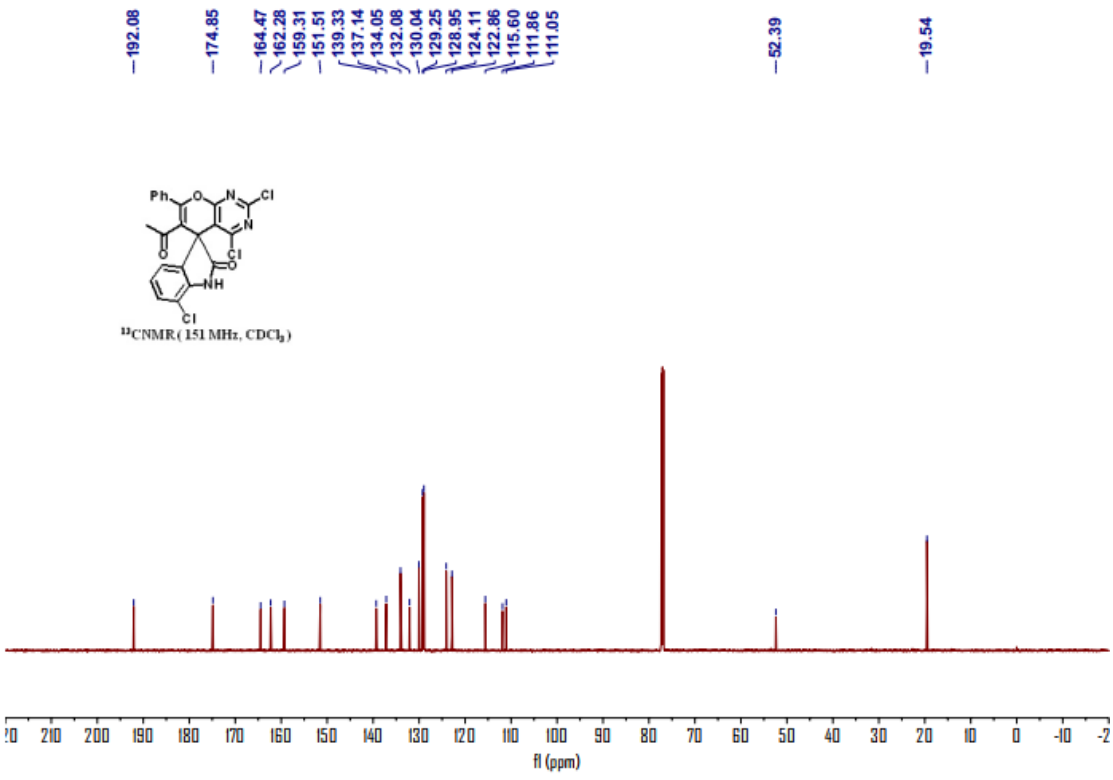


Figure S 49: ^{13}C NMR of **3i**

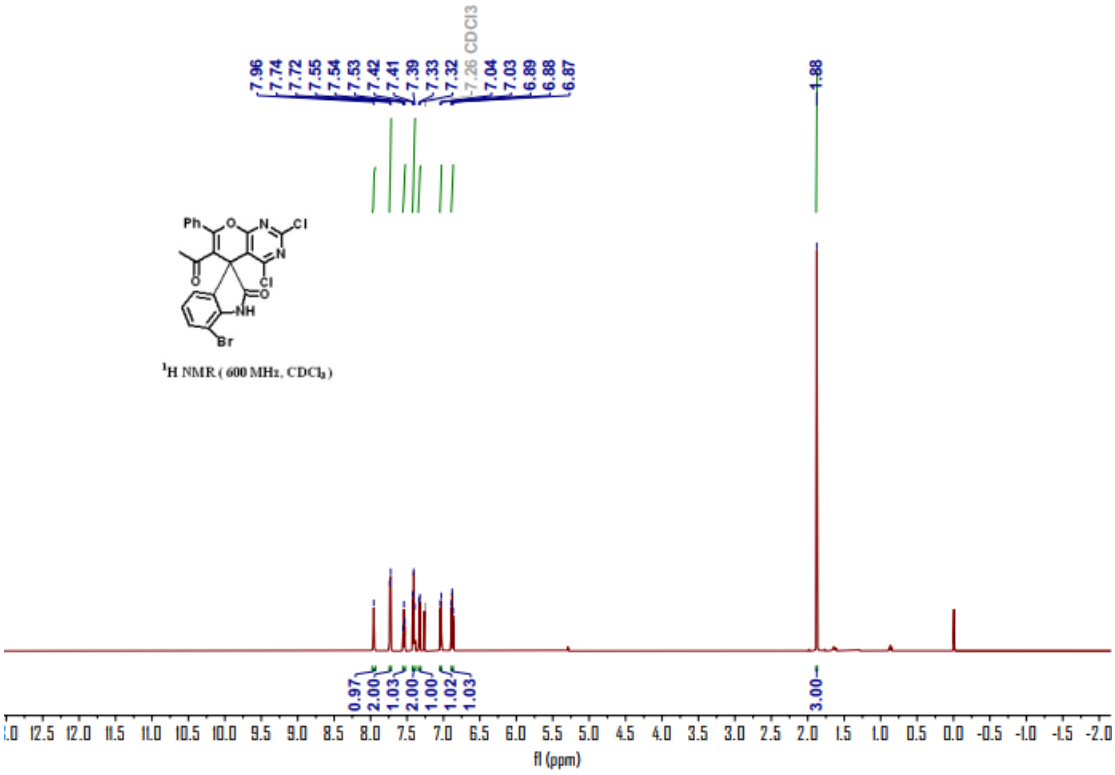


Figure S 50: ^{1}H NMR of **3j**

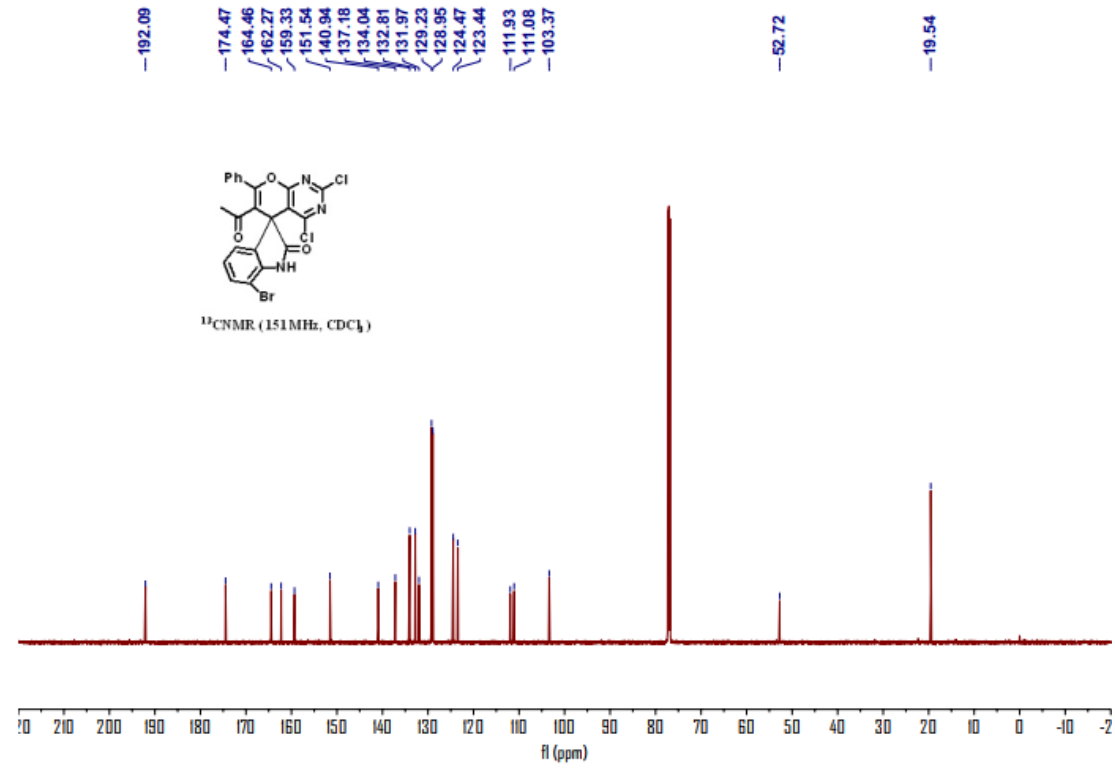
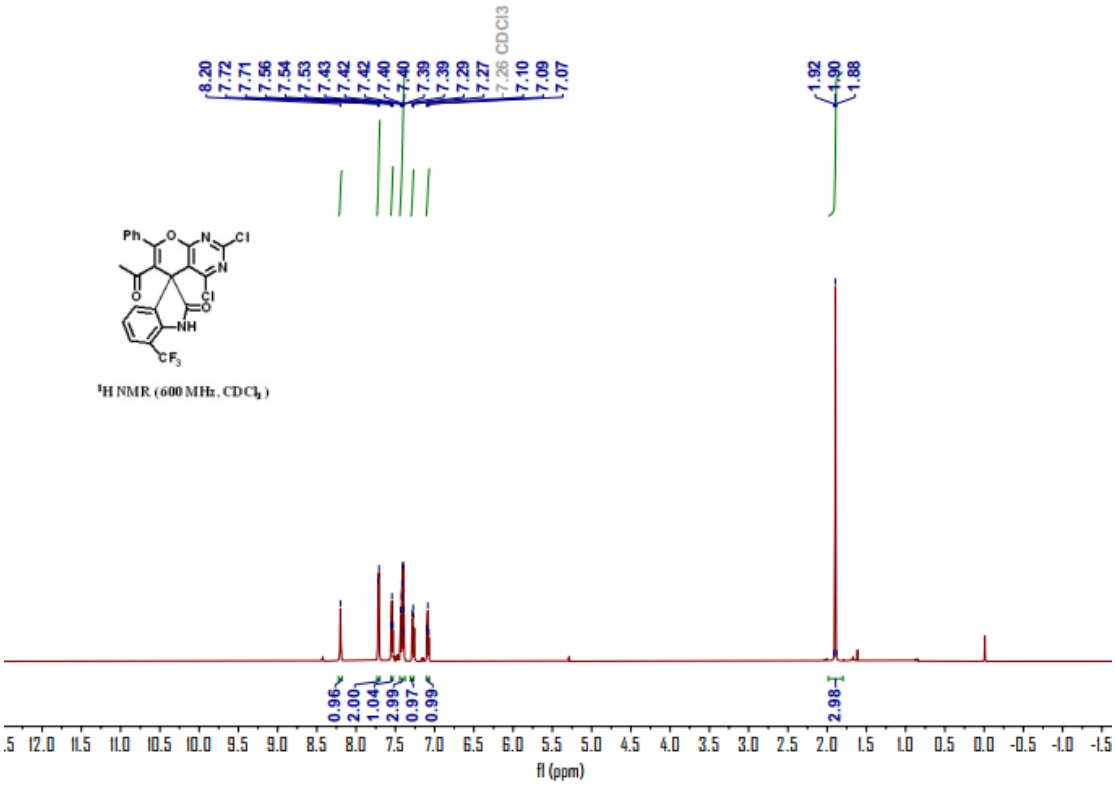
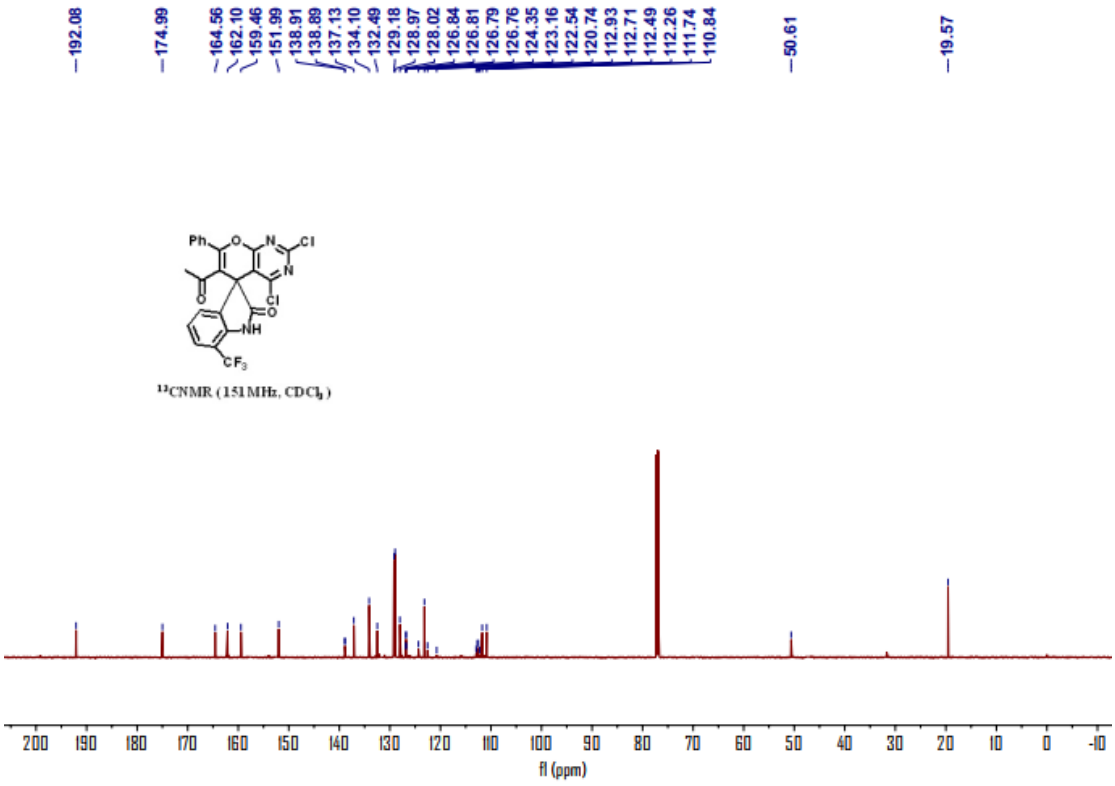


Figure S 51: ^{13}C NMR of **3j**



^{1}H NMR (600 MHz, $CDCl_3$)

Figure S 52: ^{1}H NMR of **3k**



^{13}CNMR (151 MHz, $CDCl_3$)

Figure S 53: ^{13}C NMR of **3k**

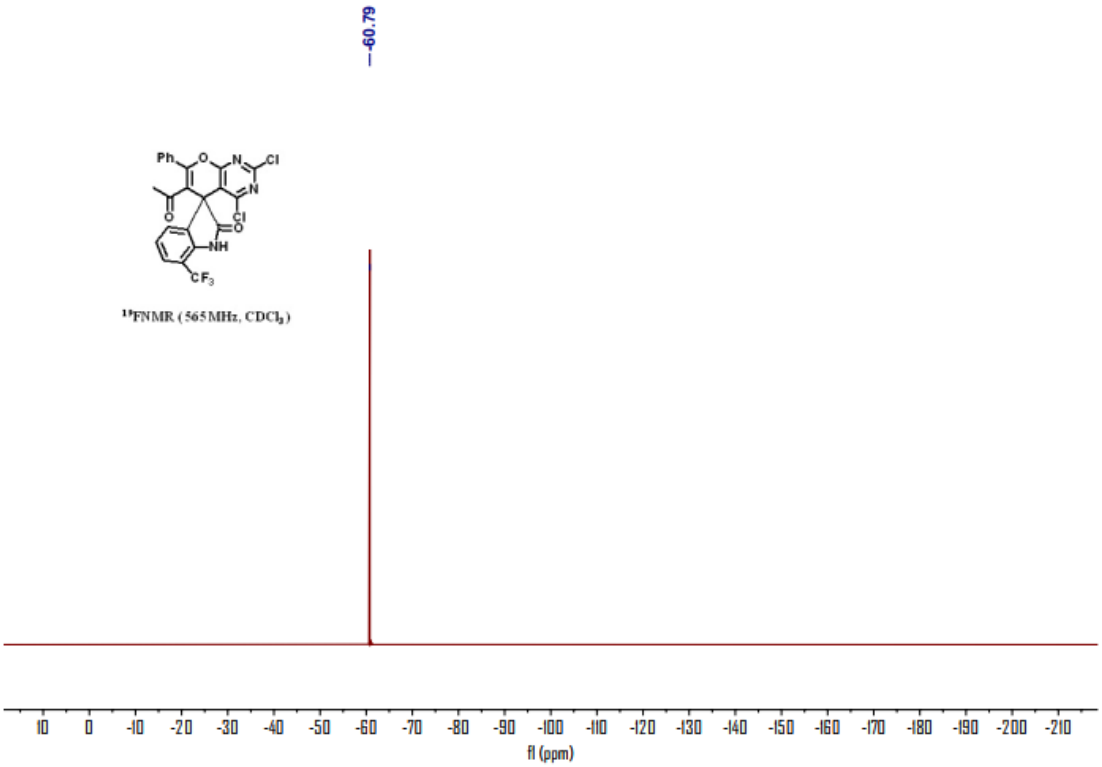


Figure S 54: ^{19}F NMR of **3k**

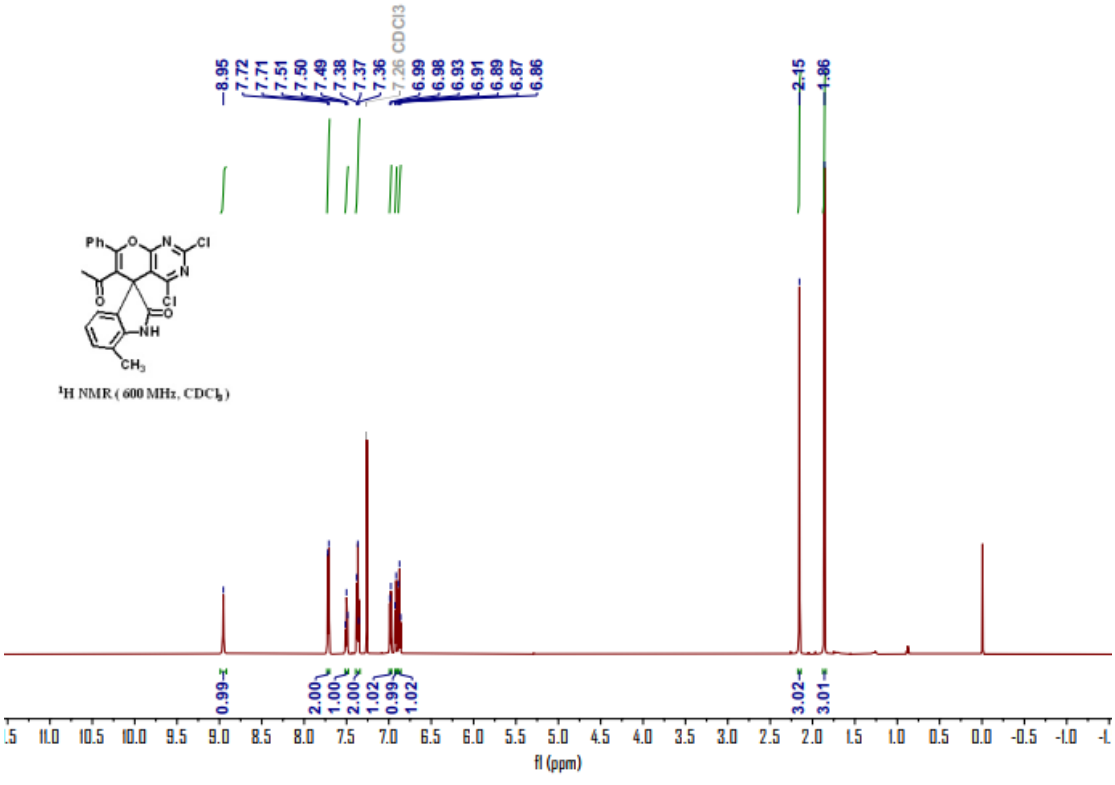


Figure S 55: ^{1}H NMR of **3l**

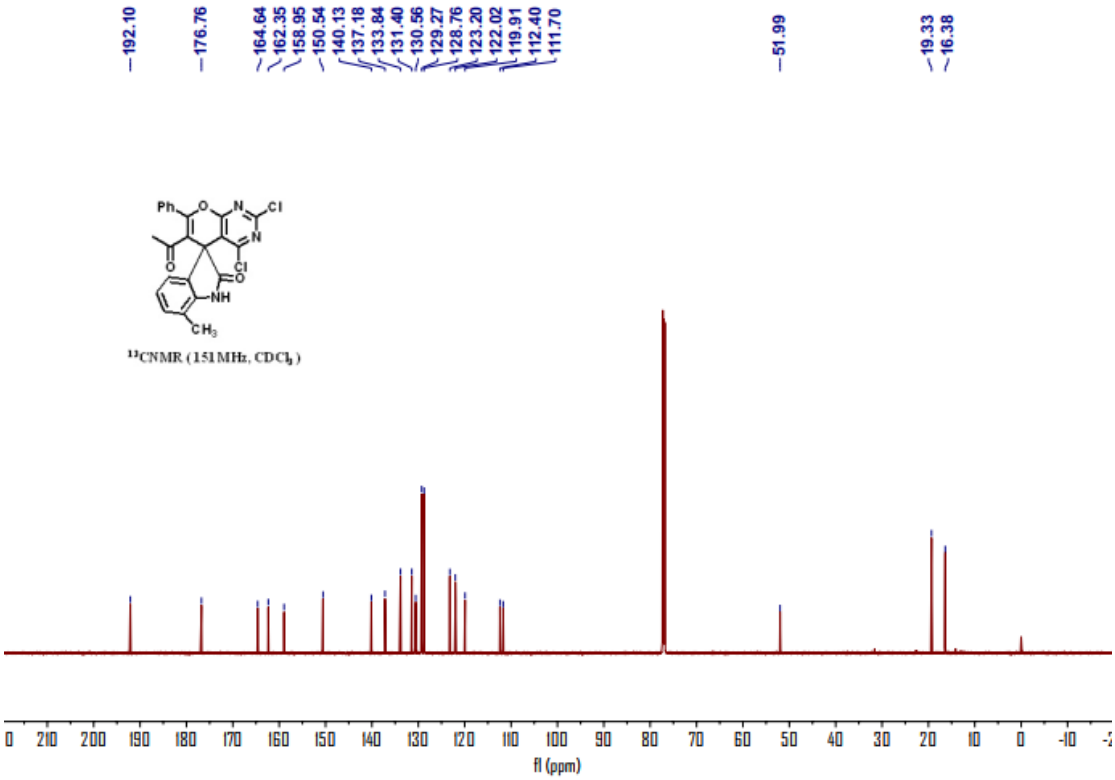


Figure S 56: ^{13}C NMR of **3l**

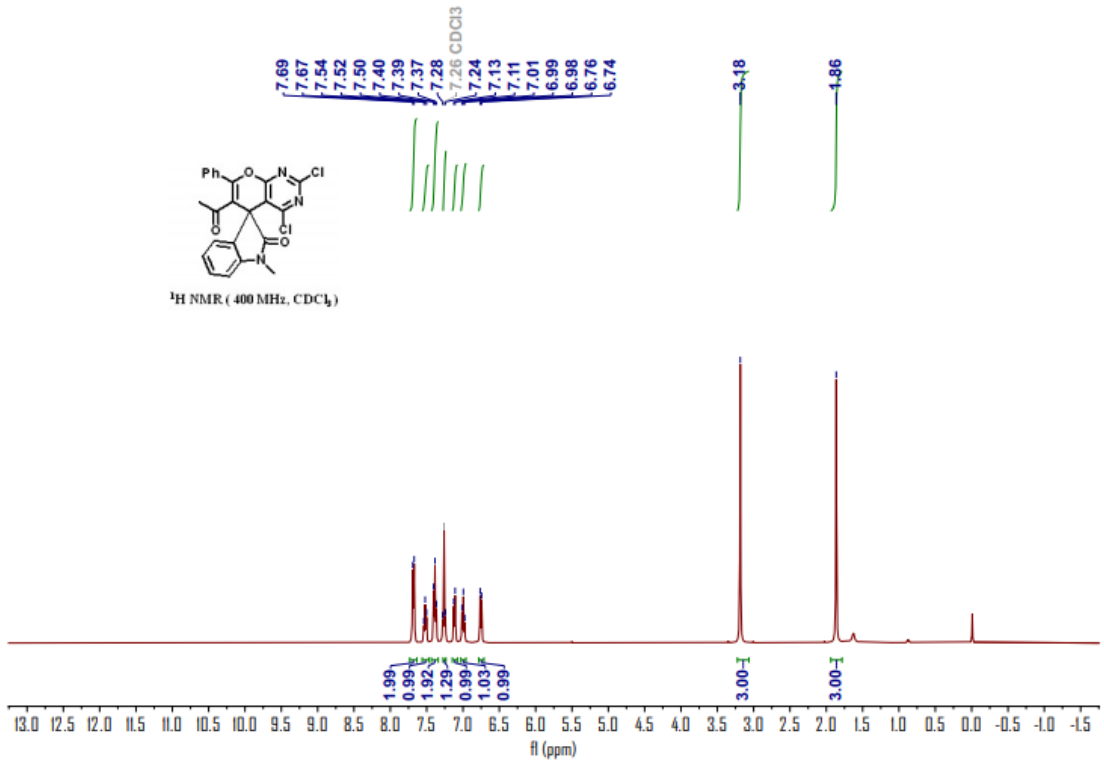


Figure S 57: ^{1}H NMR of **3m**

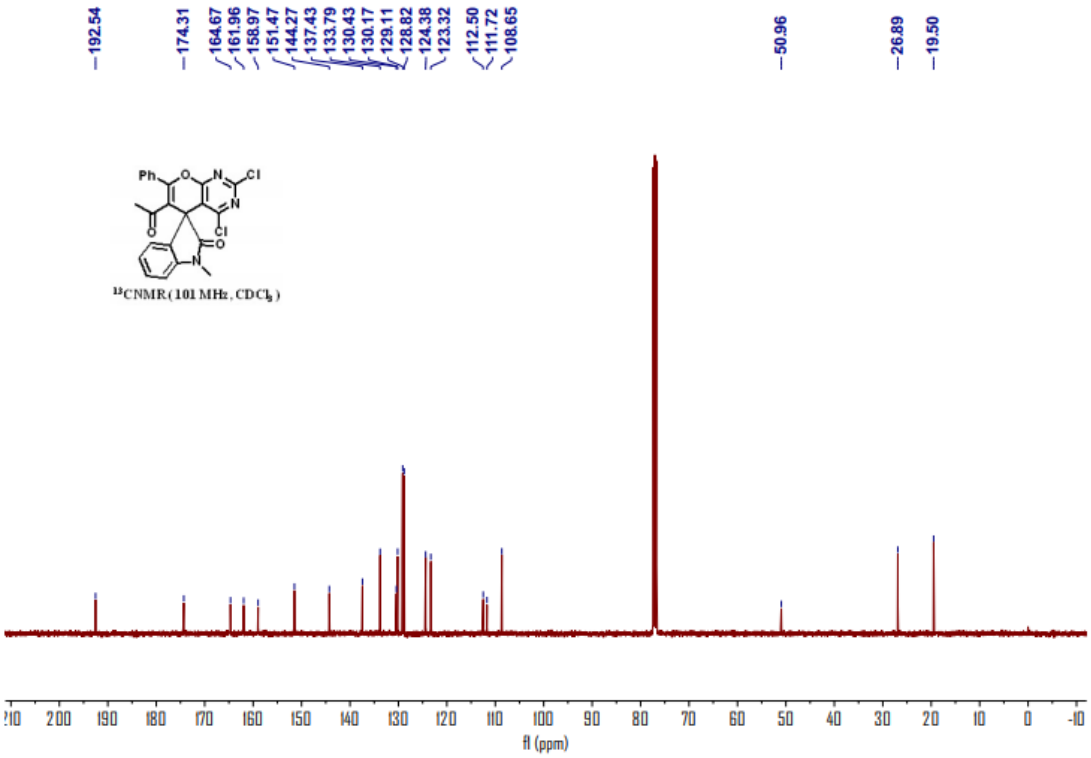


Figure S 58: ^{13}C NMR of **3m**

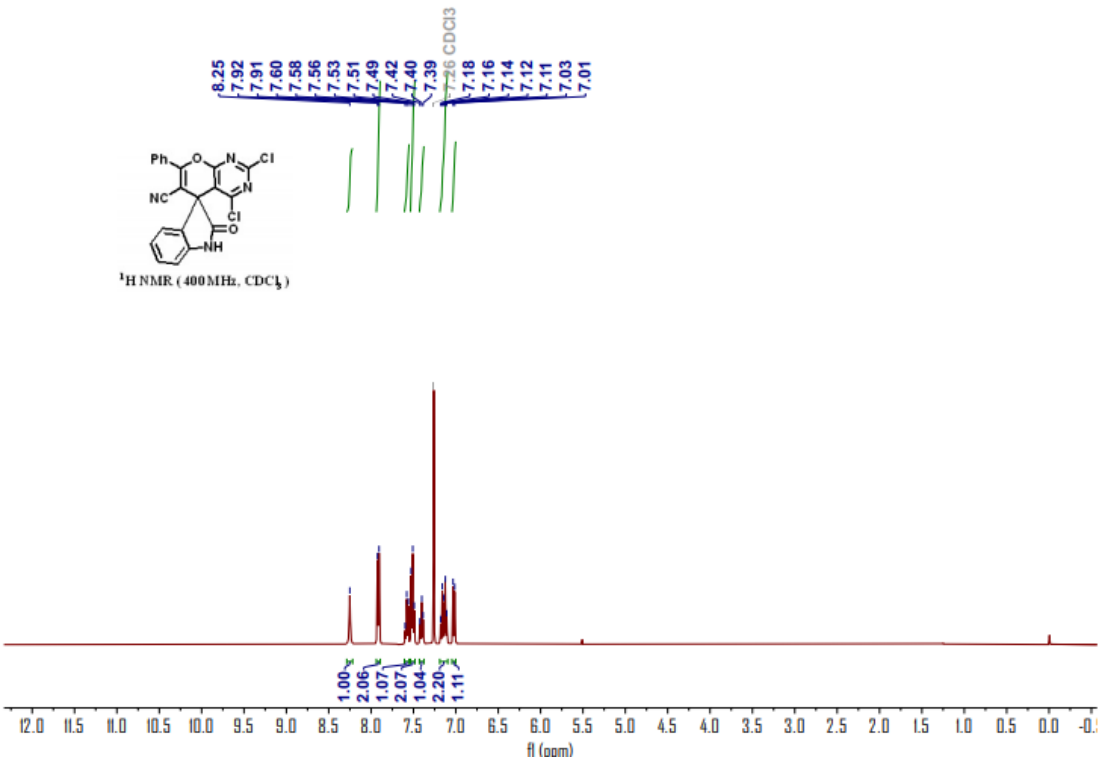


Figure S 59: ^{1}H NMR of **4a**

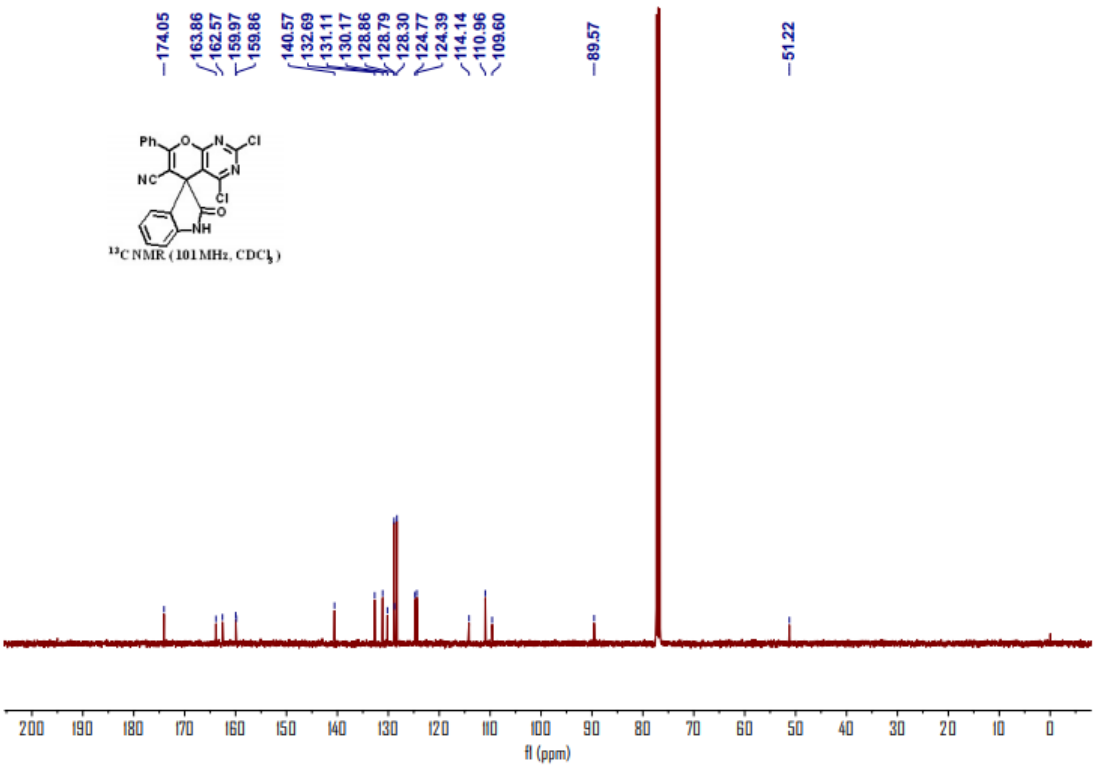


Figure S 60: ^{13}C NMR of **4a**

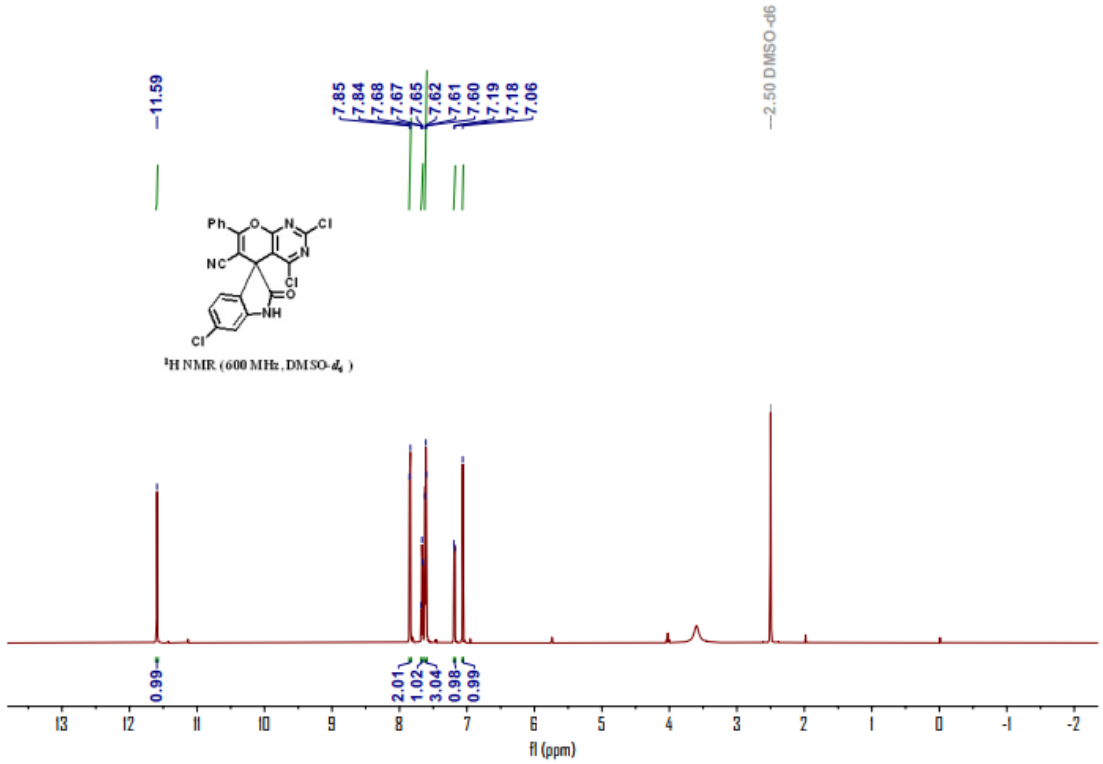


Figure S 61: ^{1}H NMR of **4b**

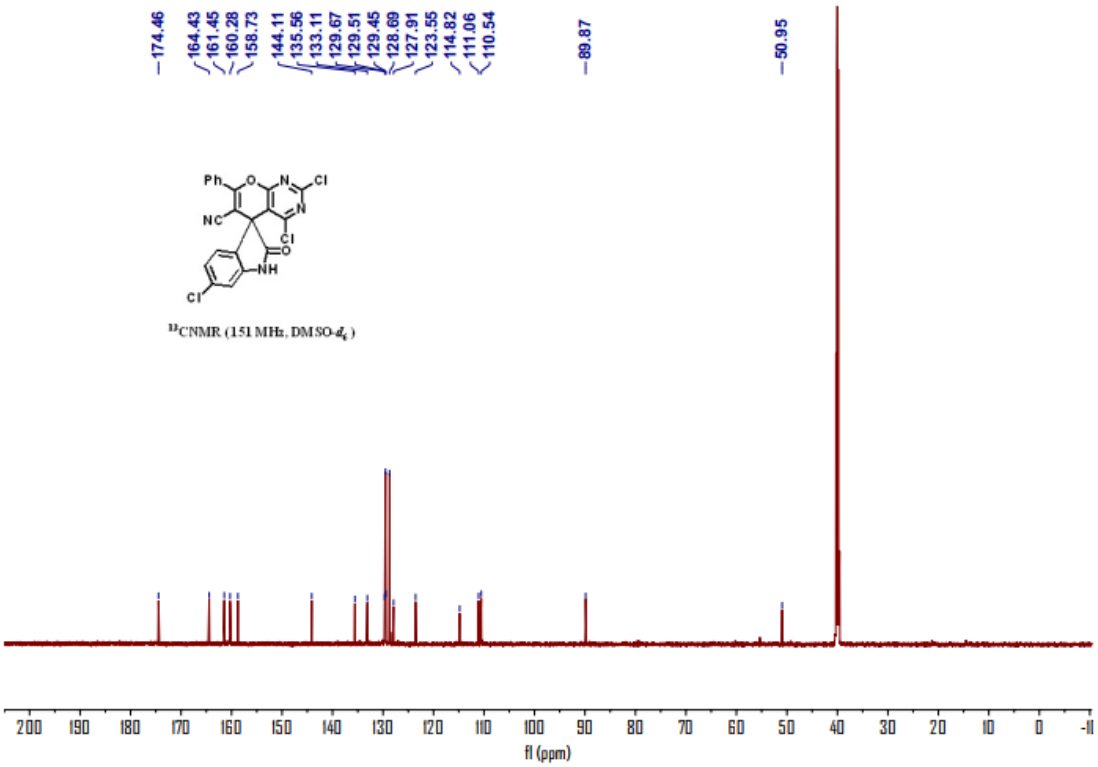


Figure S 62: ^{13}C NMR of **4b**

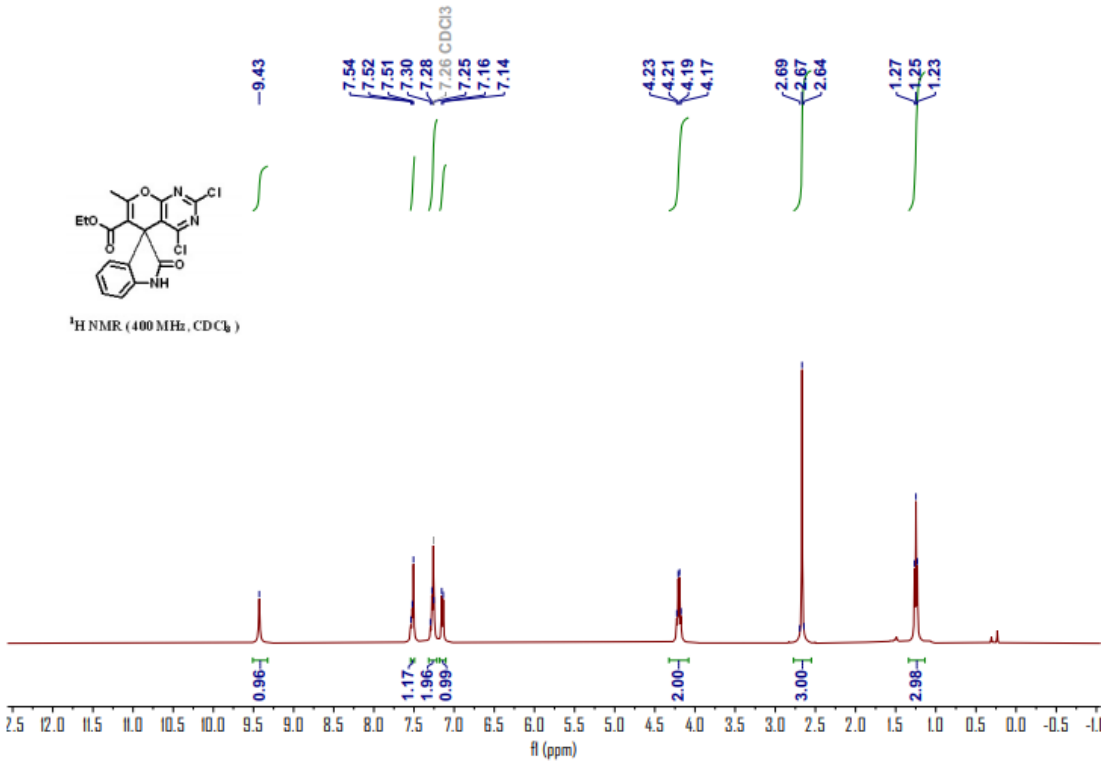


Figure S 63: ^{1}H NMR of **5a**

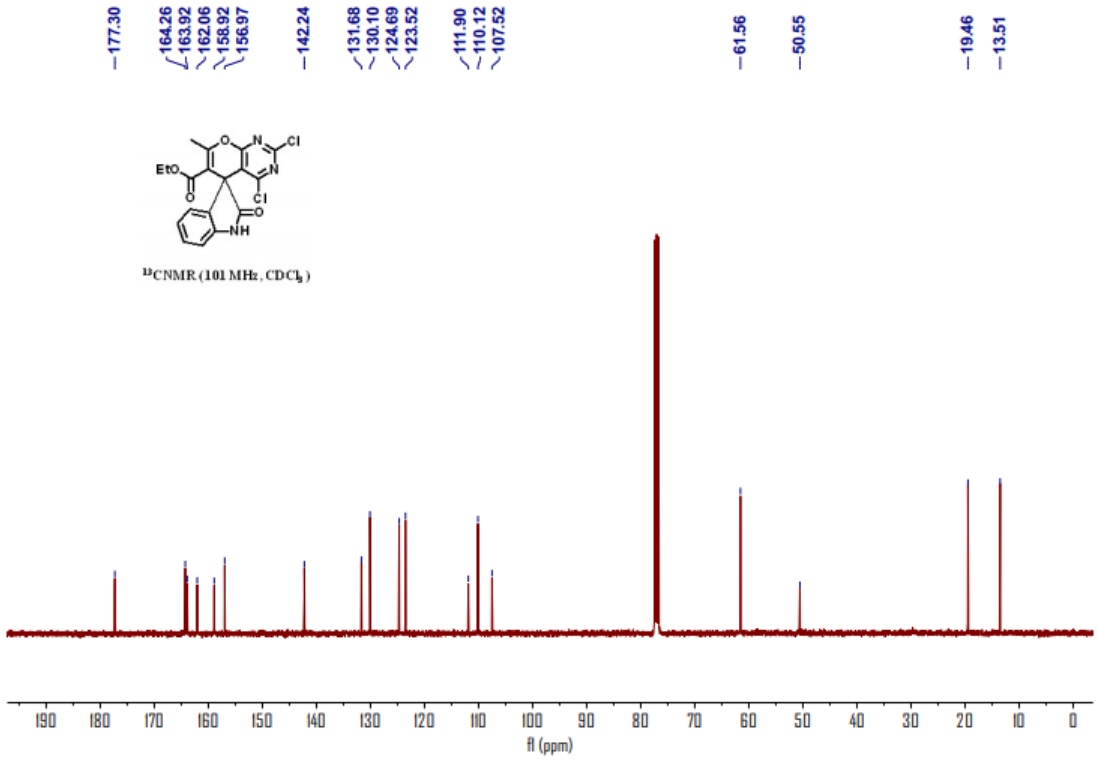


Figure S 64: ^{13}C NMR of **5a**

2. Biological evaluation

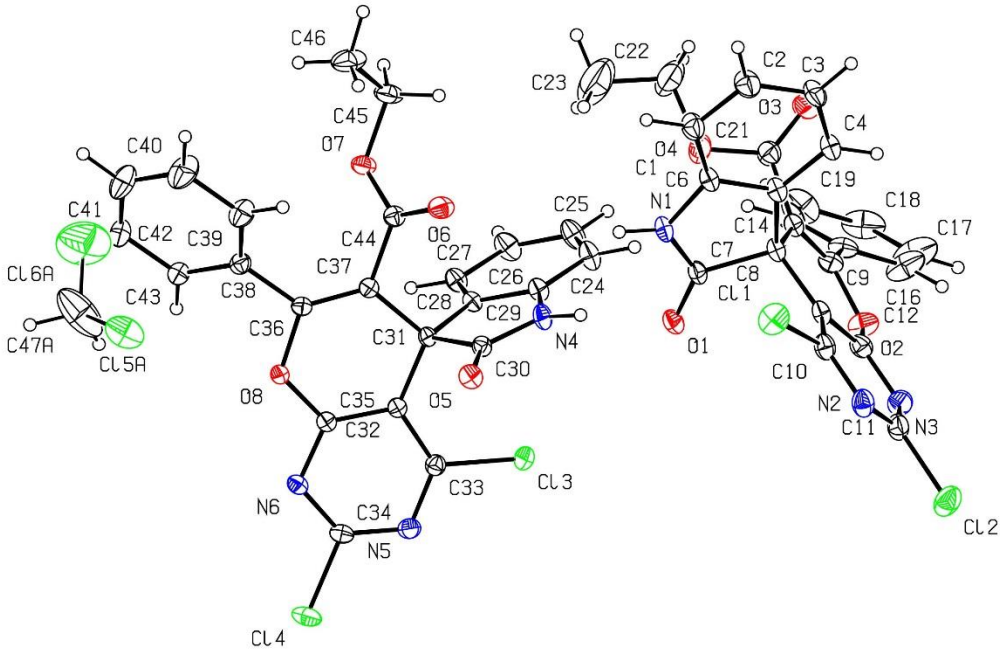
2.1 Experimental reagents

MEM culture medium: NO. 2021110903. DMEM culture medium: NO. 2021110306, PBS (1X) buffer: NO. 2012180208. 0.25% Trypsin: NO. 2004240202 were all produced by zhejiang senrui biotechnology co., LTD. Fetal bovine serum: Zhejiang Tianhang Biotechnology Co., LTD. No. 19110501; CCK8 kit: NO K101819133EF5E, manufactured by Apex BIO Technology LLC, USA. Human lung cancer A549, human liver cancer Hep-G2, human cervical cancer Hela and human breast cancer MCF-7 cell lines: introduced by Shanghai institute of medicine, Chinese Academy of Sciences, preserved in liquid nitrogen in our laboratory; Dimethyl sulfoxide, analytically pure, manufactured by SIGMA Corporation.

2.2 Experimental Instruments

CO_2 water jacket incubator: Model 3111, American Thermoelectric Company; Power Wave XS, Gene Company; HR40-Ⅱ-A2 Medical purification table: Qingdao Haier Special Electric Appliance Co., LTD. 5810R Low-temperature centrifuge: Eppendorf Company; BS210S electronic balance: Manufactured by Sartorius; Ck40-f200 inverted microscope: OLYMPUS Corporation, Japan; Yxq-208sd Electric steam sterilizer: produced by Jiaxing Zhongxin Medical Instrument Co., LTD.

3. The X-ray Crystallography analysis of compound 2a:



A suitable crystal was selected on a **'Bruker APEX-II CCD'** diffractometer. The crystal was kept at 170.0 K during data collection. Using Olex2 [1], the structure was solved with the ShelXT [2] structure solution program using Intrinsic Phasing and refined with the ShelXL [3] refinement package using Least Squares minimization.

Crystal Data for $C_{47}H_{32}Cl_6N_6O_8$ (M =1021.48 g/mol): monoclinic, space group $P2_1/c$ (no. 14), a = 20.9199(9) Å, b = 10.9180(4) Å, c = 20.6550(8) Å, β = 104.6730(10)°, V = 4563.8(3) Å^3, Z = 4, T = 170.0 K, μ(MoKα) = 0.439 mm^{-1}, *Dcalc* = 1.487 g/cm^3, 58022 reflections measured (4.076° ≤ 2Θ ≤ 54.202°), 10047 unique (R_{int} = 0.0595, R_{sigma} = 0.0402) which were used in all calculations. The final R_1 was 0.0517 (I > 2σ (I)) and wR_2 was 0.1409 (all data). CCDC 2132906 contains supplementary crystallographic data for the structure.

4. References:

1. Dolomanov, O.V., Bourhis, L.J., Gildea, R.J, Howard, J.A.K. & Puschmann, H. (2009), J. Appl. Cryst. 42, 339-341.
2. Sheldrick, G.M. (2015). Acta Cryst. A71, 3-8.
3. Sheldrick, G.M. (2015). Acta Cryst. C71, 3-8.