Supporting Information

From Biomass to Bioactivity: *Butea monosperma* Bark-Derived Carbon Quantum Dots for Benzopyran Synthesis and their *In Silico* Studies

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1. Yield and concentration of BM-CQDs:

The yield and concentration were calculated using the following equations:

$$\textbf{Yield (\%)} = \frac{\textbf{Mass of dried BM-CQDs (g)}}{\textbf{Mass of biomass used (g)}} \times \mathbf{100}$$

Mass of dried BM-CQDs = Final beaker weight – Initial beaker weight

= 49.285 – 48.303

= 0.982 g or 982 mg

Yield = 0.982 g /4.000 g × 100

= **24.55%**

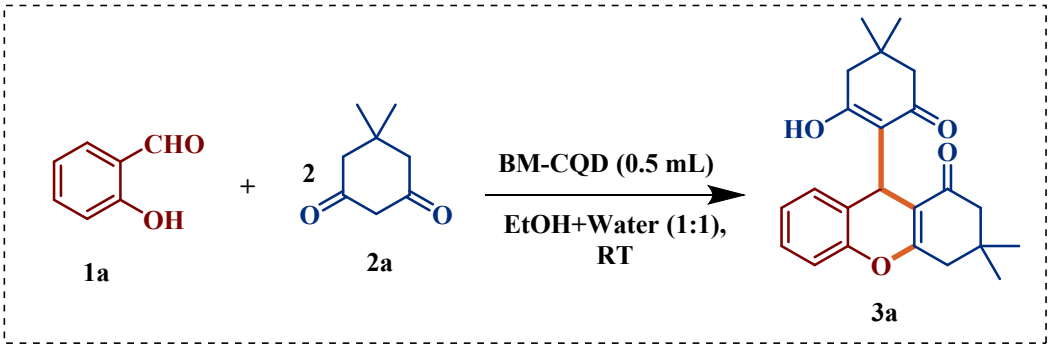
$$\textbf{Concentration (mg/mL)} = \frac{\textbf{Mass of dried BM-CQDs (mg)}}{\textbf{Volume of BM-CQD solution (mL)}}$$

Concentration = 982 mg/ 62 mL

= **15.84 mg/mL**

2. Green chemistry metrics

The green chemistry matrix serves as a comprehensive framework for quantitatively assessing and improving the environmental, health, and safety aspects of chemical processes[1]. Green matrix calculations for all synthesized derivatives are performed using following parameters[2] and detailed in **Table S1.**



Scheme 1. Reaction for green chemistry matrix calculations.

Compound	1a	2a	3a
M.W. (gm/mol)	122.12	140.18	366.46
In present work used mass (mg/mmol)	61.06	140.18	183.23 (required)

Total mass of the reactants (mg) used in the present work = 201.24

Total MW of the reactants (mg) = 402.48

Obtained wt. of the product (mg) = 177.20

- **Environmental factor (E-factor):**

E-factor = Mass of waste ÷ Mass of product

Where; mass of waste = total mass of raw materials - total mass of the product

= 201.24 – 177.20

= 24.04

E-factor = 24.04 ÷ 177.20

= **0.135**

Ideal value of E-factor = 0

- **Atom-economy (AE):**

AE = MW of product ÷ Σ (MW of all reactants) × 100

AE = 366.46 ÷ 402.48 × 100

AE = **90.99 %** (Ideal value of AE = 100%)

- **Reaction mass efficiency (RME):**

RME = Mass of product / Σ (Mass of all reactants) × 100

= 177.20 / 201.24 × 100

= **88.06**

Higher RME value means cleanness of the reaction.

- **Process mass intensity (PMI):**

PMI = Σ (Mass of all reactants + solvent) / Mass of product

= 204.82 / 177.20

= **1.16**

- **Eco-score (E-score):**

An ideal Eco-score value is 100, with the Eco-scale ranging from 0 to 100, categorized as follows: > 75, excellent; > 50, acceptable; and < 50, inadequate.

E-score has been calculated for the reaction by evaluating the following six parameters.

S. No.	Parameter	Values	Penalty points
1	Yield	(100-96.72)/ 2	1.64
2	Price of the reaction components	Inexpensive	0

3	Safety (Reactant)*	5+5 = 10	10
4	Technical setup	Common setup	0
5	Temperature/ Time	Room temp./ < 1h	0
6	Workup and purification	Column chromatography	0
	Total penalty points		11.64
***Based on the hazard warning symbols.**			

***Eco-Score = 100 – the sum of individual penalties**

= 100 – 11.64

= **88.36**

Table S1. The green chemistry matric calculation for all synthesized benzopyran derivatives.

S. No.	Compound code	Yield (%)	E factor	AE (%)	RME (%)	PMI	Eco-Score
1	3a	96.72	0.136	90.99	88.06	1.156	88.36
2	3b	95.14	0.143	91.95	87.48	1.161	87.57
3	3c	90.79	0.184	93.02	84.45	1.201	85.40
4	3d	92.63	0.182	91.35	84.62	1.202	86.32
5	3e	90.62	0.207	91.43	82.86	1.227	85.31
6	3f	94.23	0.153	92.04	86.73	1.171	87.12
7	3g	96.13	0.161	89.60	86.13	1.185	88.07
8	3h	88.82	0.245	90.43	80.32	1.269	84.41
9	3i	87.13	0.269	90.48	78.83	1.293	83.57
10	3j	84.57	0.296	91.27	77.19	1.318	82.29
11	3k	94.63	0.151	91.81	86.88	1.169	87.32
12	3l	87.02	0.230	93.46	81.33	1.245	83.51
13	3m	87.08	0.235	93.01	80.99	1.252	83.54
14	3n	82.74	0.305	92.63	76.64	1.324	81.37
15	3o	94.35	0.143	92.74	87.50	1.159	87.18

16	3p	90.57	0.186	93.13	84.35	1.202	85.29
17	3q	89.77	0.171	95.14	85.41	1.182	84.89

Our pyran synthesis protocol using BM-CQD showcased remarkable results, including low E-factor (0.136-0.305), excellent reaction mass efficiency (88.06 - 76.64 %), high atom economy (95.14-89.60%), and high eco-score (88.36-81.37%). These metrics firmly establish the eco-friendliness of the developed BM-CQDs assisted process.

3. Synthesis of benzopyrans

3.1. Materials and methods

All chemicals used in this study were procured from reliable commercial suppliers, including Avra, BLD-Pharma, Sigma-Aldrich, SRL and Merck and were employed without further purification. TECHINSTRO Teflon-lined hydrothermal autoclave (capacity-150 mL) was used for hydrothermal process. Filtration of the catalyst was performed using a Merck MCE 0.45 µm, 47 mm diameter filter membrane. Reaction progress was monitored using thin-layer chromatography (TLC) performed on silica gel 60 RP-18 F254S plates and visualized under a 3 NOS UV cabinet. HRTEM and SAED analyses were conducted using a Jeol Model (JEM 2100 plus) operated at 200 kV with CCD detector. XRD analysis of was performed using a Rigaku Ultima IV diffractometer with CuKα radiation (λ = 0.1541 nm). FT-IR spectra were recorded on a Bruker FT-IR spectrometer. EDX analysis was carried out using a Hitachi SU8010 system (Japan). UV-Visible spectrum was obtained using a JASCO V-750 spectrophotometer, while fluorescence emission spectrum was recorded on a JASCO FP-8850 fluorometer. Melting points of the synthesized compounds were determined using a digital melting point apparatus and are reported without correction. ^{1}H,^{13}C, and ^{19}F NMR spectra were acquired on a JEOL JNM-ECZ400S/L1 spectrometer operating at 400, 100, and 376 MHz, respectively, using DMSO-d_6 as the solvent and tetramethylsilane (TMS) as the internal reference. HRMS analyses were performed using a Xevo G2-XS QToF mass spectrometer (LC-MS/MS) coupled with an Acquity H-Class PLUS UPLC system.

3.2. General synthetic procedure

A mixture of the appropriate salicylaldehyde derivative (1.0 equivalent, 0.5 mmol) and the corresponding C-H activated compound (1.0 equivalent, 0.5 mmol / 2.0 equivalents, 1.0 mmol /

3.0 equivalents, 1.5 mmol, as required) was taken in a reaction vessel containing BM-CQDs (0.5 mL) as the catalyst and an ethanol-water solvent system (4 mL). The reaction mixture was stirred at RT for the appropriate time. The progress of the reaction was monitored by TLC using hexane/ethyl acetate (7:3) as the eluent. Upon completion of the reaction, the desired benzopyran product precipitated out of the reaction mixture and isolated by simple filtration, washed thoroughly with water and then dried to afford the pure product. The collected filtrate, containing the BM-CQD catalyst, was directly reused in subsequent reaction cycles without any further treatment**,** demonstrating the excellent recyclability of the catalyst.

4. Spectral data of synthesized compounds

1. **9-(2-hydroxy-4,4-dimethyl-6-oxocyclohex-1-en-1-yl)-3,3-dimethyl-2,3,4,9-tetrahydro-1*H*-xanthen-1-one (3a):**

Off white solid; yield 97%, m.p. 196-198 ^{o}C[3, 4], ^{1}H NMR (400 MHz, $CDCl_3$); δ 10.49 (s, 1H, OH), 7.16 - 7.12 (m, 1H, Ar-H), 7.02 – 6.98 (m, 3H, Ar-H), 4.65 (s, 1H, CH), 2.61 – 2.44 (m, 2H, CH_2), 2.36 – 2.31 (m, 4H, CH_2), 2.00 – 1.89 (m, 2H, CH_2), 1.11 (s, 3H, CH_3), 1.01 (s, 3H, CH_3), 0.97 (s, 6H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$); δ 201.08, 196.73, 170.82, 169.30, 151.10, 128.07, 127.63, 124.68, 124.38, 118.40, 115.82, 111.11, 50.65, 49.98, 43.23, 41.60, 32.41, 31.03, 30.01, 29.25, 27.84, 27.31, 26.51. ESI-MS (m/z) for $C_{23}H_{26}O_4$; 366.1831[M^+].

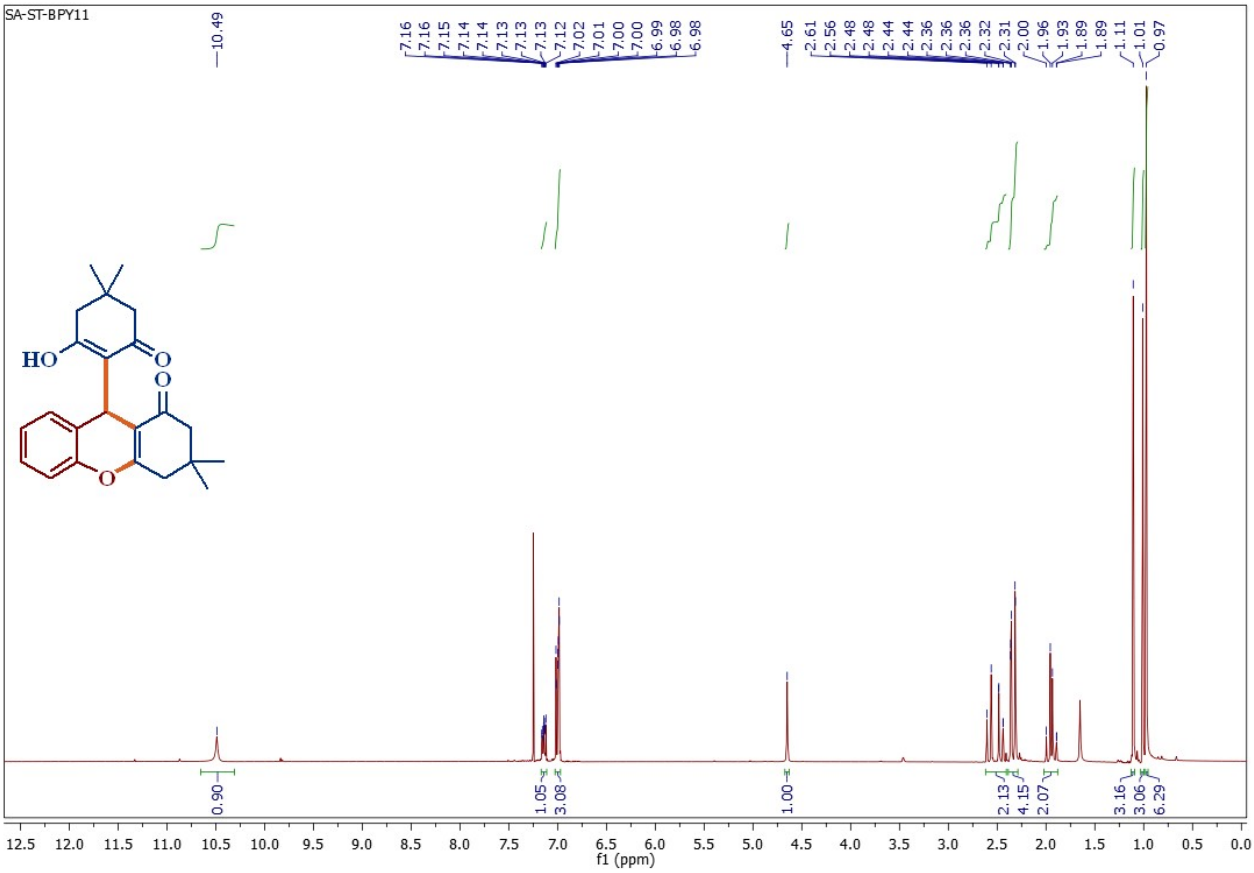


Figure S1: ^{1}H NMR of compound 3a.

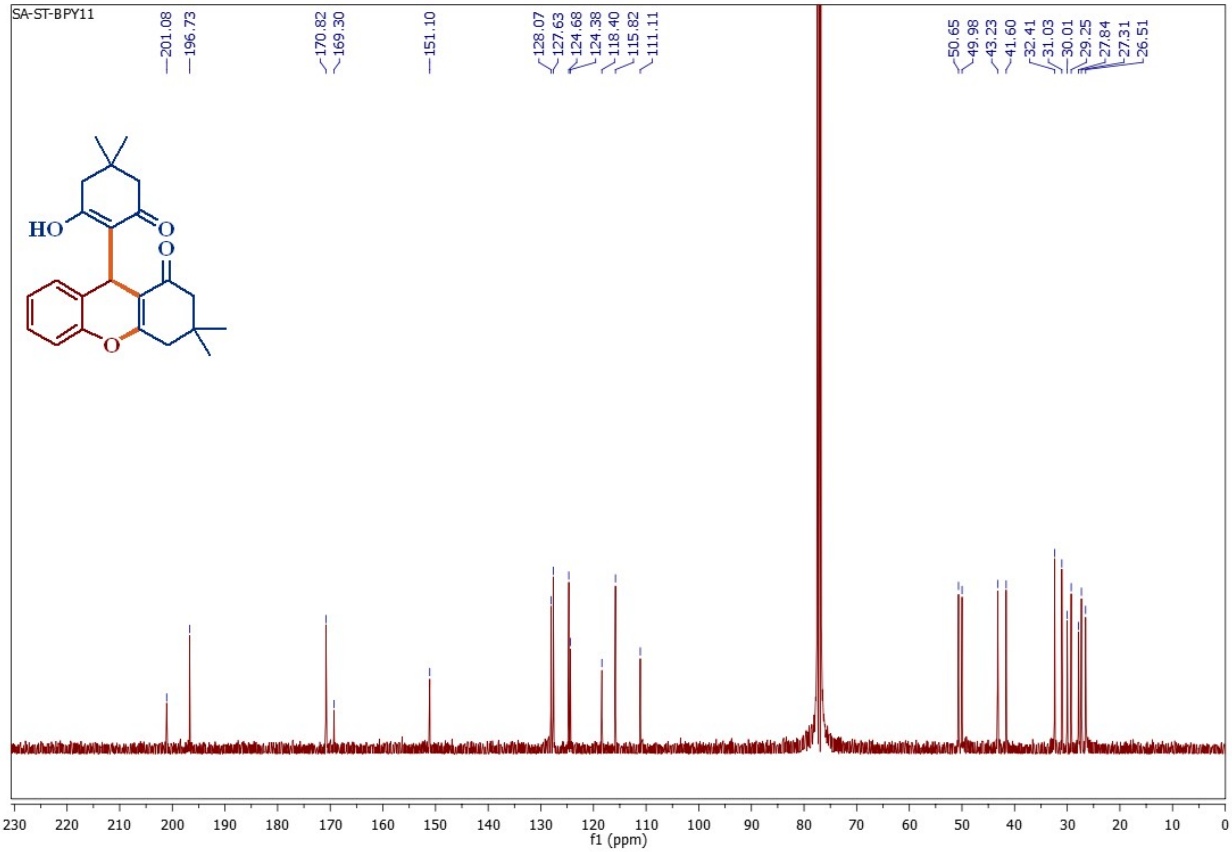


Figure S2: ^{13}C NMR of compound 3a.

2. **9-(2-hydroxy-4,4-dimethyl-6-oxocyclohex-1-en-1-yl)-3,3-dimethyl-7-nitro-2,3,4,9-tetrahydro-1*H*-xanthen-1-one (3b):**

White powder, yield 95%, m.p. 192 - 195 ^{o}C[5], ^{1}H NMR (400 MHz, $CDCl_3$); δ 10.33 (s, 1H, OH), 8.03 (dd, *J* = 8.9, 2.7 Hz, 1H, Ar-H), 7.92 (d, *J* = 2.5 Hz, 1H, Ar-H), 7.10 (d, *J* = 8.9 Hz, 1H, Ar-H), 4.67 (s, 1H, CH), 2.62 – 2.33 (m, 6H, CH_2), 1.96 (q, *J* = 16.6 Hz, 2H, CH_2), 1.13 (s, 3H, CH_3), 0.99 (d, *J* = 14.8 Hz, 9H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$); δ 200.98, 196.98, 172.09, 167.99, 155.49, 144.32, 126.00, 123.84, 123.69, 117.71, 116.51, 110.99, 50.59, 49.95, 43.22, 41.25, 32.44, 31.25, 29.73, 29.27, 27.93, 27.13, 26.74. ESI-MS (m/z) calculated for $C_{23}H_{25}NO_6$[M+1]: 412.1682 and found 412.1763.

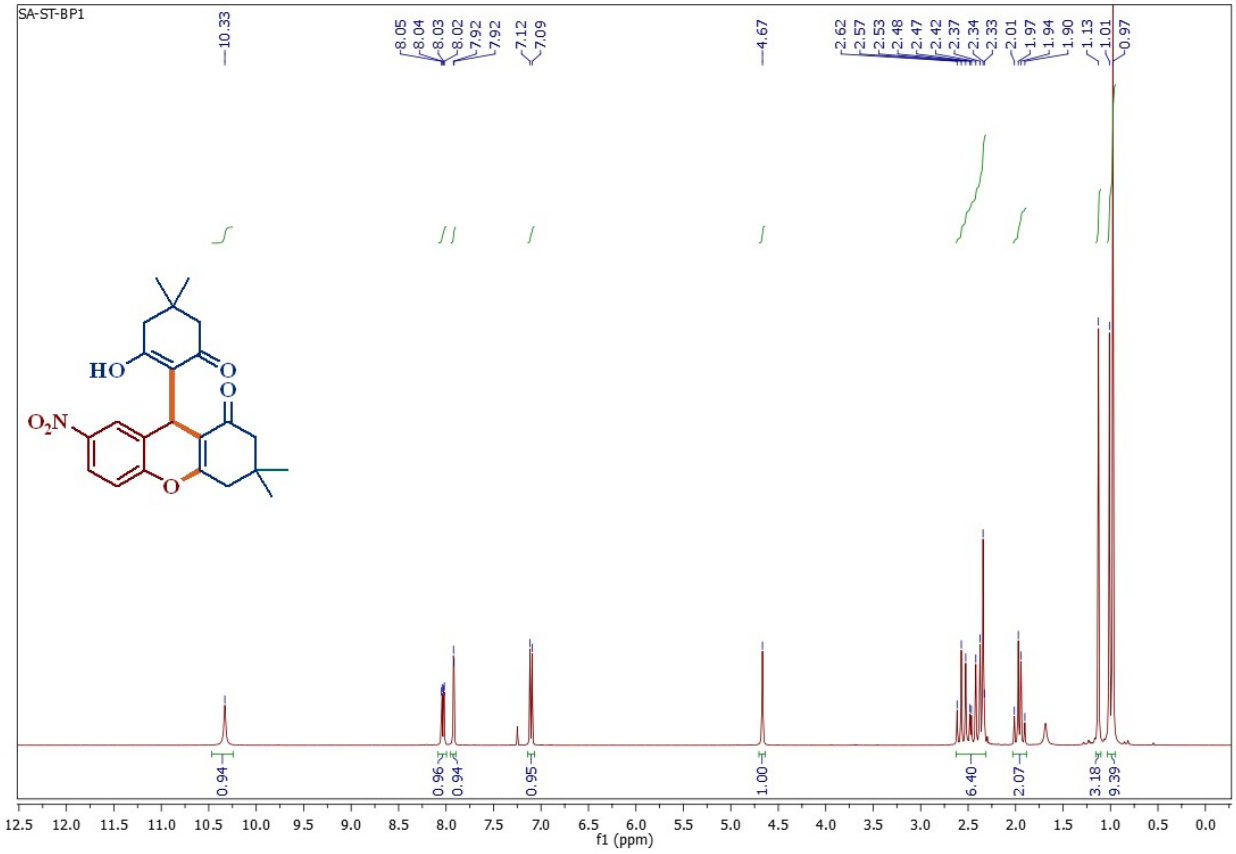


Figure S3: ^{1}H NMR of compound 3b.

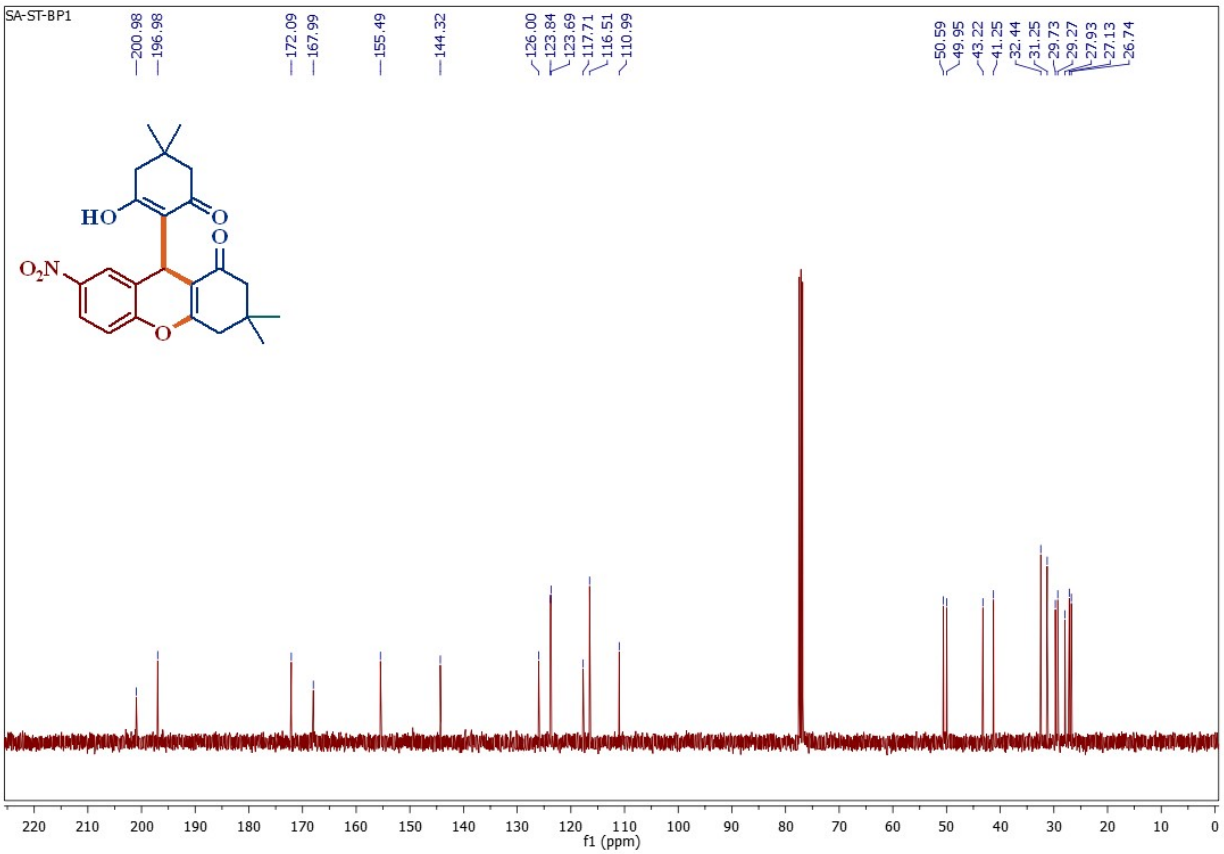


Figure S4: ^{13}C NMR of compound 3b.

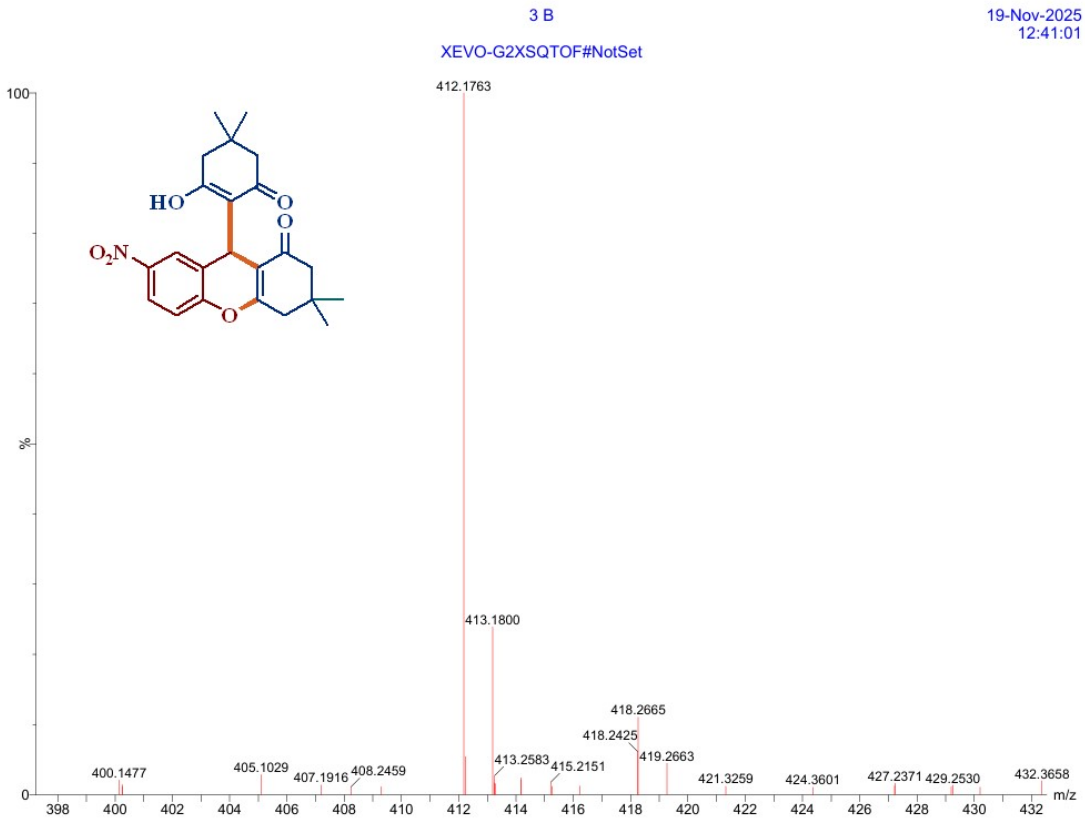


Figure S5: HRMS of compound 3b.

3. **5-bromo-7-chloro-9-(2-hydroxy-4,4-dimethyl-6-oxocyclohex-1-en-1-yl)-3,3-dimethyl-2,3,4,9-tetrahydro-1*H*-xanthen-1-one (3c)**

Fluffy white, yield 91%, m.p. 236 - 238 ^{o}C[6], ^{1}H NMR (400 MHz, DMSO-d_6); δ 10.76 (s, 1H, OH), 7.51 (d, J = 2.5 Hz, 1H, Ar-H), 6.84 (d, J = 2.1 Hz, 1H, Ar-H), 5.01 (s, 1H, CH), 2.57 – 2.50 (m, 1H, CH_2), 2.35 – 1.98 (m, 7H, CH_2), 1.01 (s, 3H, CH_3), 0.92 (s, 3H, CH_3), 0.84 (s, 6H, CH_3). ^{13}C NMR (101 MHz, DMSO-d_6); δ 197.61, 196.19, 164.85, 164.68, 146.14, 130.25, 129.69, 128.37, 127.66, 120.59, 111.21, 110.49, 50.82, 50.35, 43.28, 40.79, 32.24, 32.15, 29.64, 29.04, 28.12, 27.05, 26.49. ESI-MS (m/z) for $C_{23}H_{24}BrClO_4$: 478.0546 [M^+].

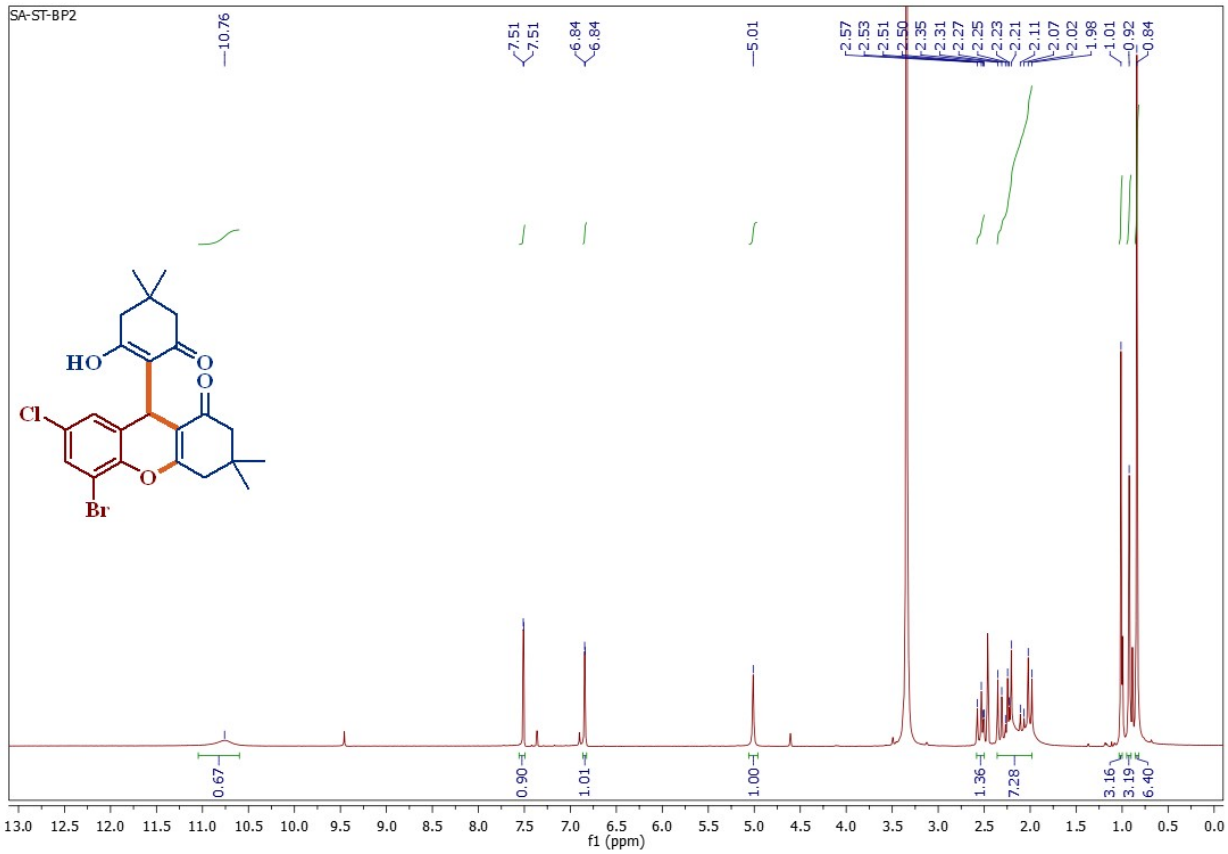


Figure S6: ^{1}H NMR of compound 3c.

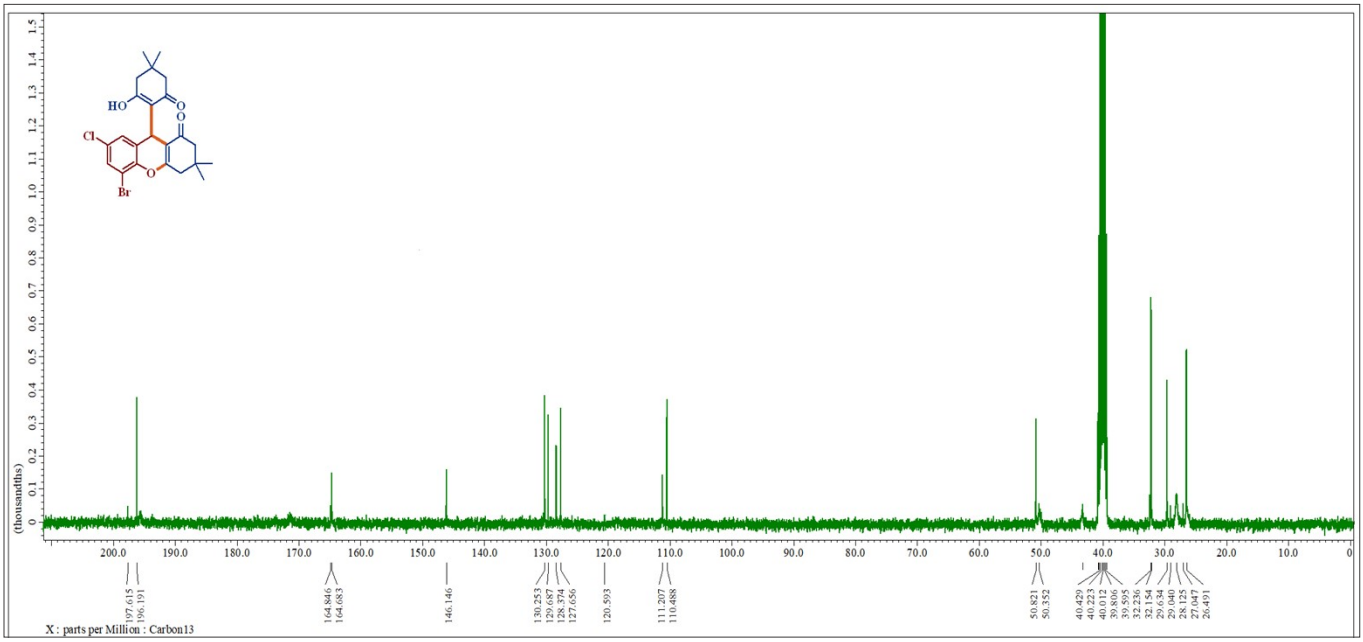


Figure S7: ^{13}C NMR of compound 3c.

4. **9-(2-hydroxy-4,4-dimethyl-6-oxocyclohex-1-en-1-yl)-3,3,6-trimethyl-2,3,4,9-tetrahydro-1*H*-xanthen-1-one (3d)**

Off white powder, yield 93%, m.p. 202 - 204 ^{o}C[7], ^{1}H NMR (400 MHz, $CDCl_3$); δ 10.48 (s, 1H, OH), 6.87 - 6.80 (m, 3H, Ar-H), 4.62 (s, 1H, CH), 2.55 - 2.31 (m, 6H, CH_2), 2.28 (s, 3H, CH_3), 1.95 (q, J = 16.5 Hz, 2H, CH_2), 1.10 (s, 3H, CH_3), 0.99 (d, J = 14.1 Hz, 9H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$); δ 201.03, 196.79, 170.73, 169.34, 150.86, 137.60, 127.76, 125.58, 121.26, 118.43, 116.34, 111.22, 50.71, 50.00, 43.23, 41.64, 32.41, 31.03, 30.01, 29.20, 27.54, 27.38, 26.52, 21.23. ESI-MS (m/z) for $C_{24}H_{28}O_4$: 380.1988 [M^+].

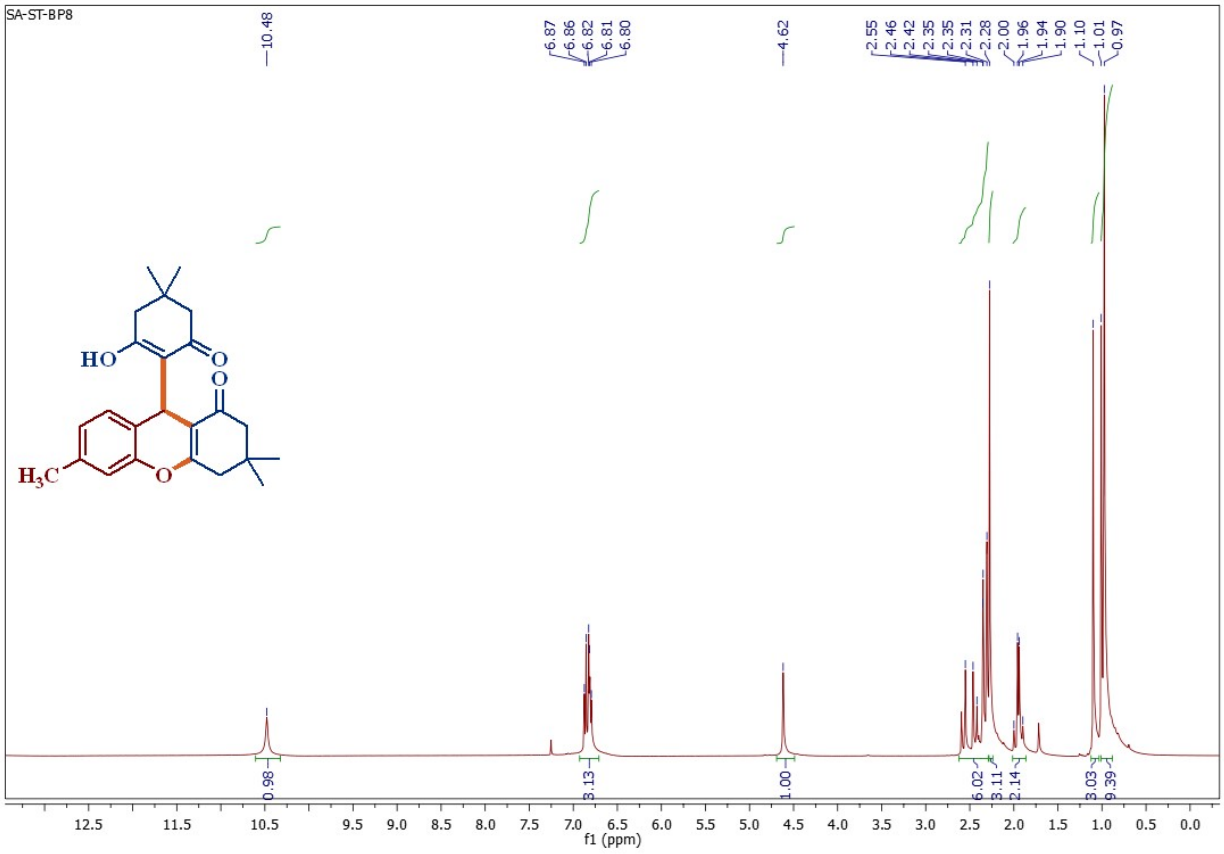


Figure S8: ^{1}H NMR of compound 3d.

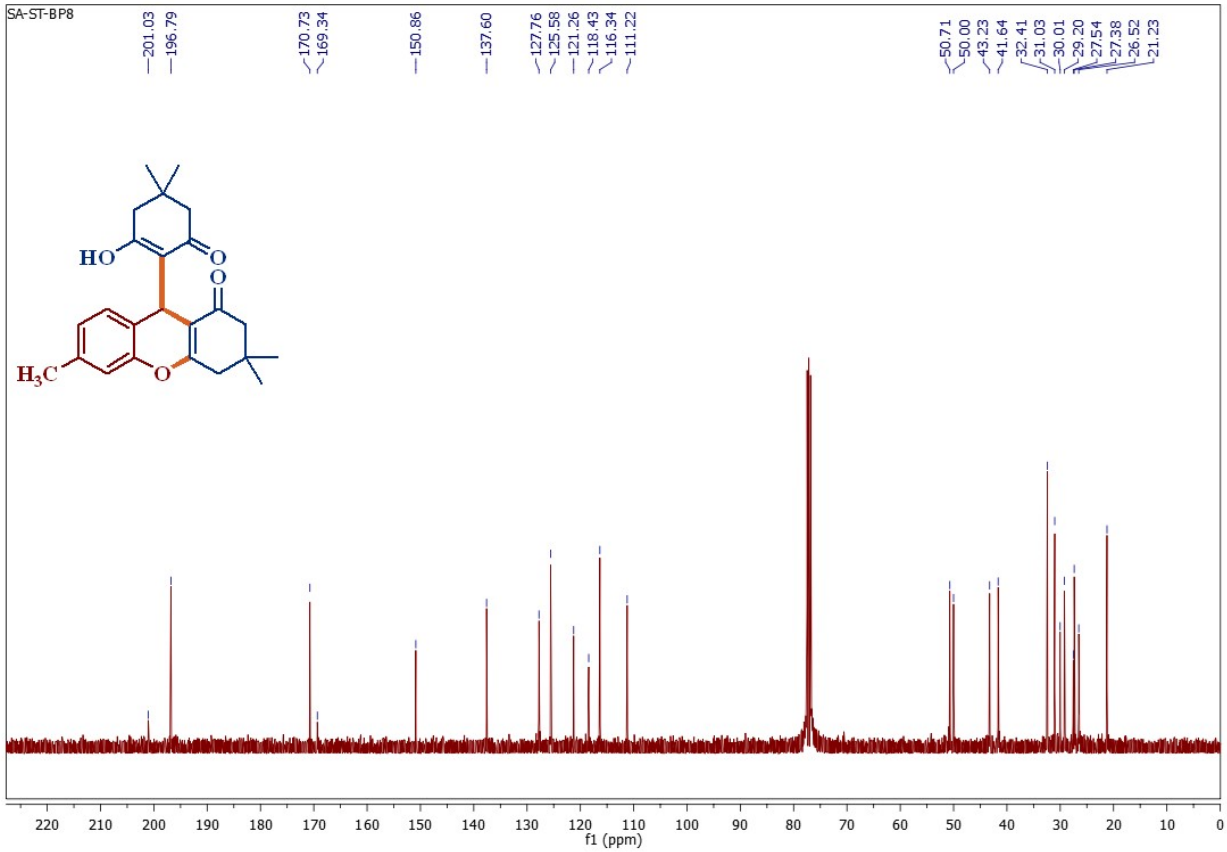


Figure S9: ^{13}C NMR of compound 3d.

5. **7-fluoro-9-(2-hydroxy-4,4-dimethyl-6-oxocyclohex-1-en-1-yl)-3,3-dimethyl-2,3,4,9-tetrahydro-1*H*-xanthen-1-one (3e):**

White solid, yield 91%, m.p. 198 - 201 ^{o}C[7], ^{1}H NMR (400 MHz, $CDCl_3$); δ 10.48 (s, 1H, OH), 6.98 -6.95 (m, 1H, Ar-H), 6.85 -6.80 (m, 1H, Ar-H), 6.69 (dd, *J* = 8.6, 2.9 Hz, 1H, Ar-H), 4.62 (s, 1H, CH), 2.59 – 2.31 (m, 6H, CH_2), 2.01 – 1.92 (m, 2H, CH_2), 1.11 (s, 3H, CH_3), 1.00 – 0.98 (m, 9H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$); δ 200.98, 196.79, 171.34, 169.17, 159.43 (d, *J* = 242.7 Hz, C-F), 147.23 (d, *J* = 2.9 Hz), 126.19 (d, *J* = 7.9 Hz), 117.89, 116.94 (d, *J* = 8.9 Hz), 114.39 (d, *J* = 7.5 Hz), 114.15 (d, *J* = 7.5 Hz), 110.27, 50.67, 49.97, 43.26, 41.54, 32.37, 31.08, 29.90, 29.29, 28.21, 27.19, 26.65. ^{19}F NMR (376 MHz, $CDCl_3$); δ -118.33 (s). ESI-MS (m/z) for $C_{23}H_{25}FO_4$: 384.1737 [M^+].

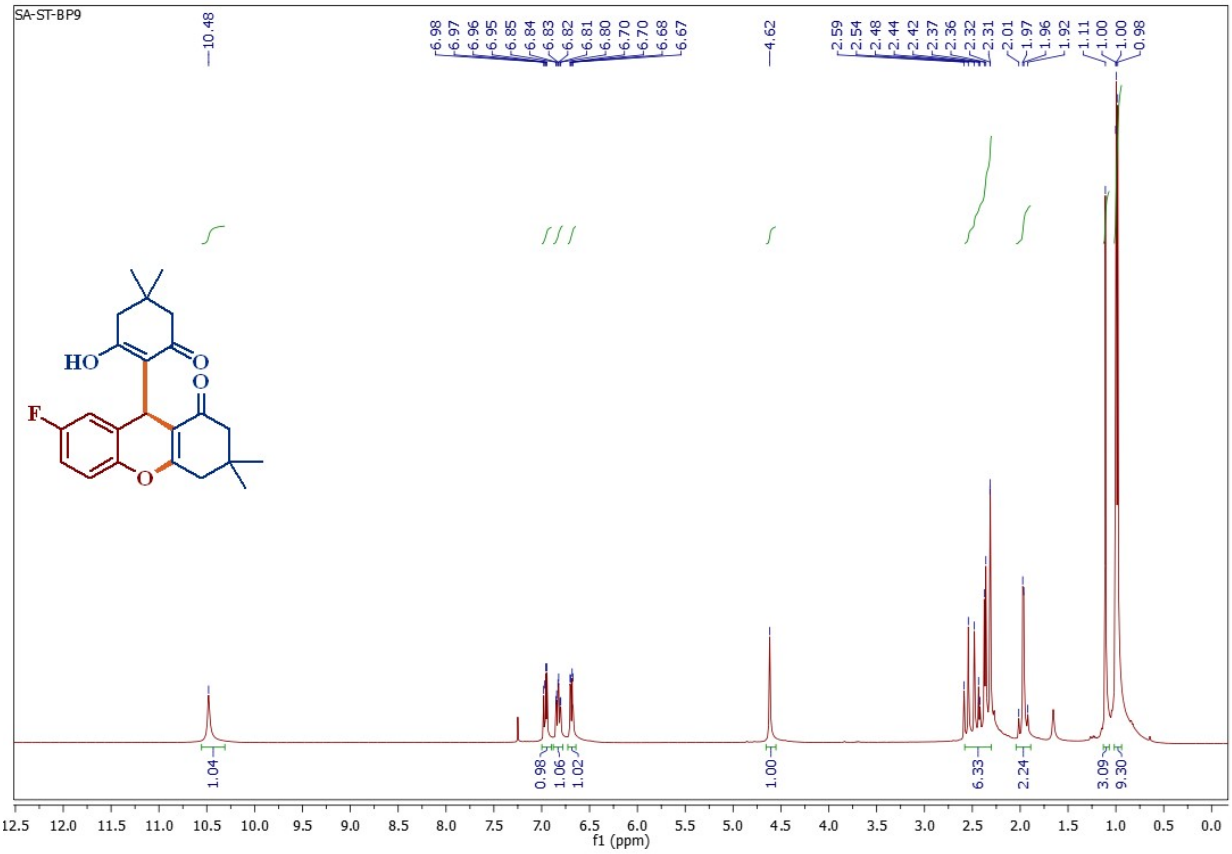


Figure S10: ^{1}H NMR of compound 3e.

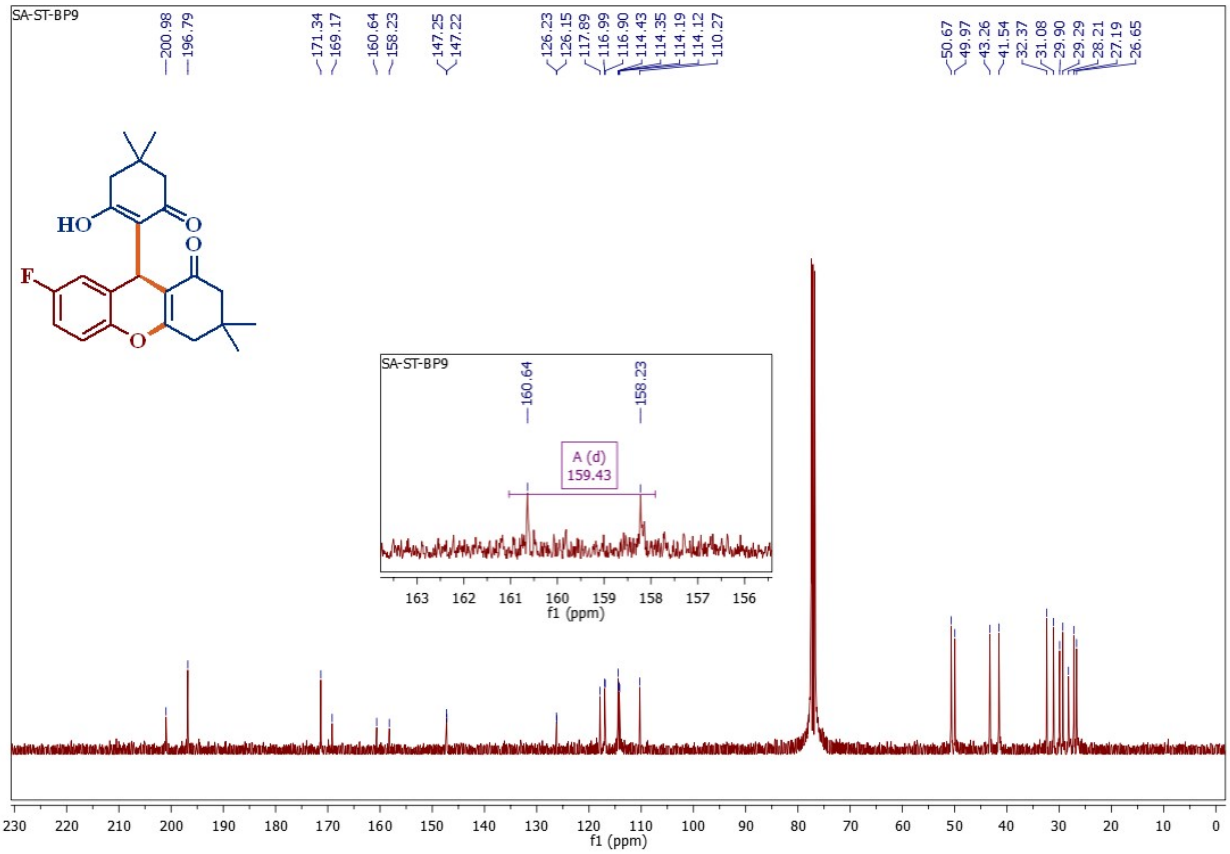


Figure S11: ^{13}C NMR of compound 3e.

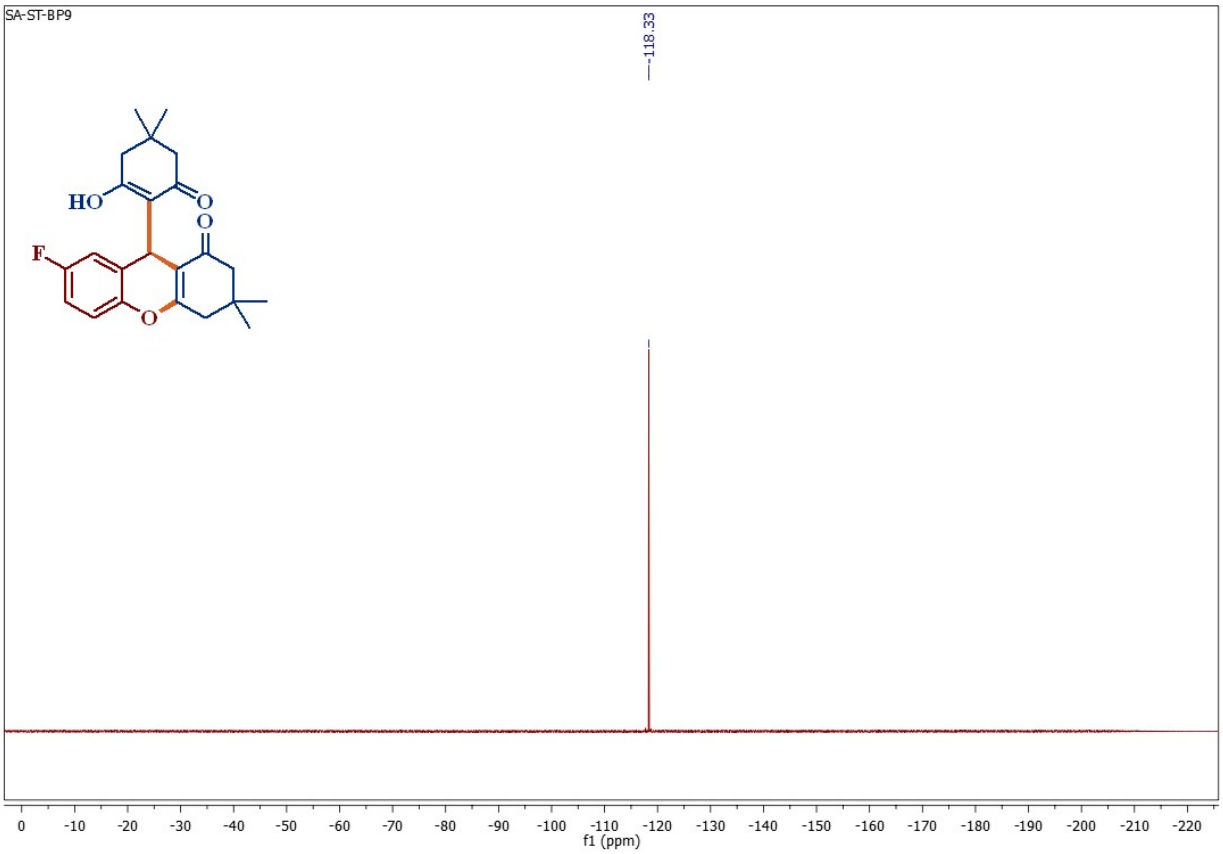


Figure S12: ^{19}F NMR of compound 3e.

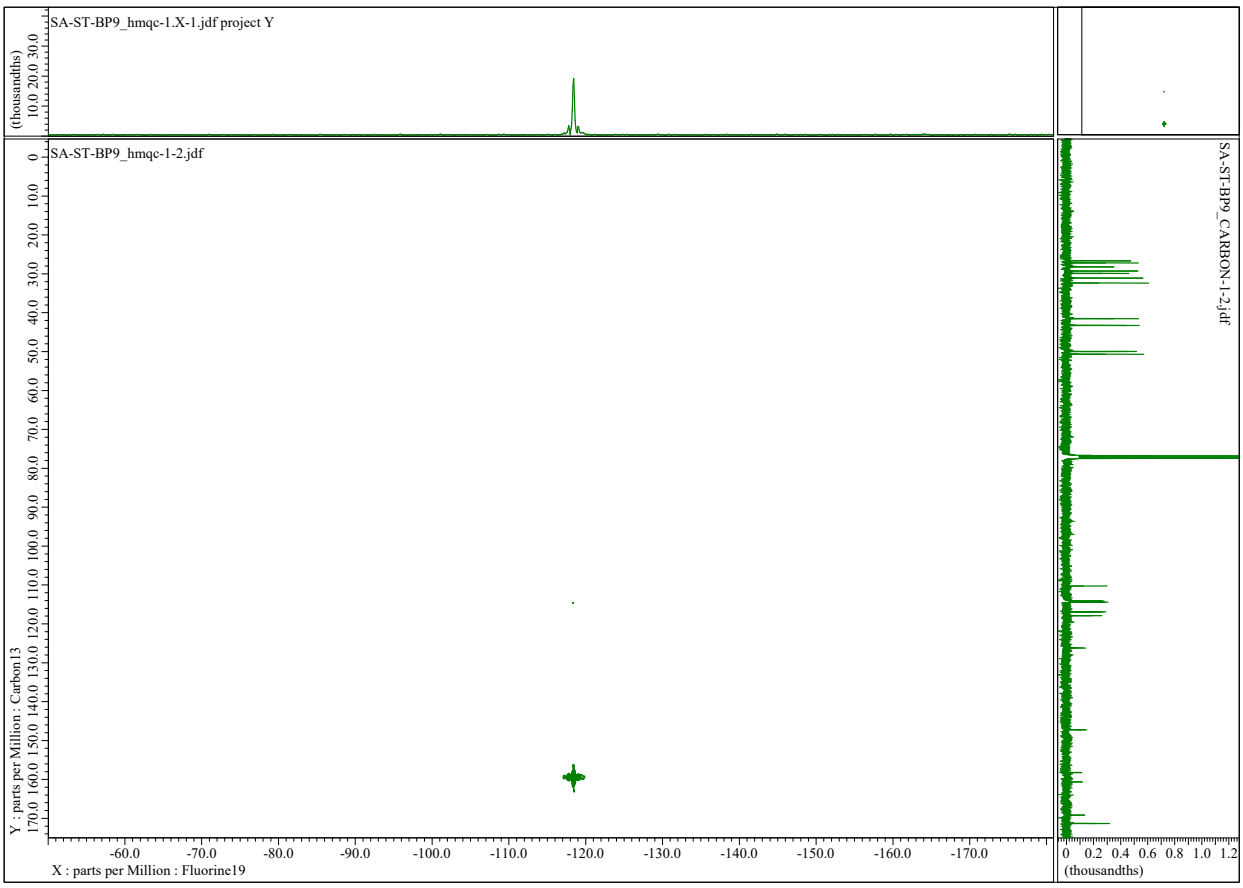


Figure S13. ^{19}F- HMQC of compound 3e.

6. **12-(2-hydroxy-4,4-dimethyl-6-oxocyclohex-1-en-1-yl)-9,9-dimethyl-8,9,10,12-tetrahydro-11*H*-benzo[a]xanthen-11-one (3f):**

White powder, yield 94%, m.p. 238 - 240 ^{o}C[5], ^{1}H NMR (400 MHz, $CDCl_3$); δ 10.68 (s, 1H, OH), 7.76 – 7.68 (m, 3H, Ar-H), 7.46 – 7.23 (m, 3H, Ar-H), 5.24 (s, 1H, CH), 2.67 – 2.52 (m, 2H, CH_2), 2.43 – 2.33 (m, 4H, CH_2), 1.96 – 1.71 (m, 2H, CH_2), 1.14 (s, 3H, CH_3), 1.04 (s, 3H, CH_3), 0.92 (s, 3H, CH_3), 0.69 (s, 3H, CH_3).^{13}C NMR (101 MHz, $CDCl_3$); δ 201.17, 196.96, 170.34, 169.16, 148.96, 131.34, 131.05, 128.63, 128.57, 126.79, 124.73, 122.96, 117.75, 116.67, 116.22, 111.15, 50.78, 50.05, 43.27, 41.44, 32.49, 30.72, 30.00, 29.44, 27.15, 26.47, 25.46. ESI-MS (m/z) for $C_{27}H_{28}O_4$: 416.1988 [M^+].

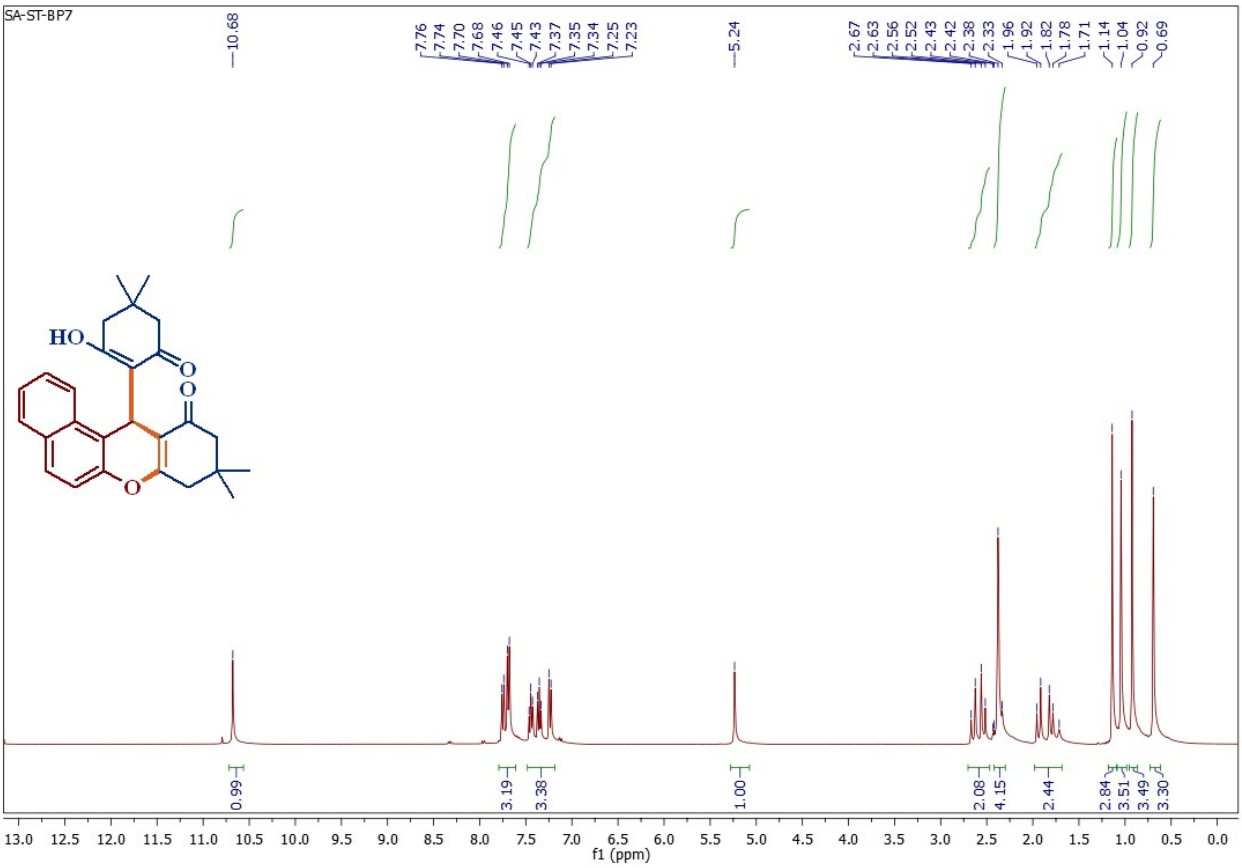


Figure S14: ^{1}H NMR of compound 3f.

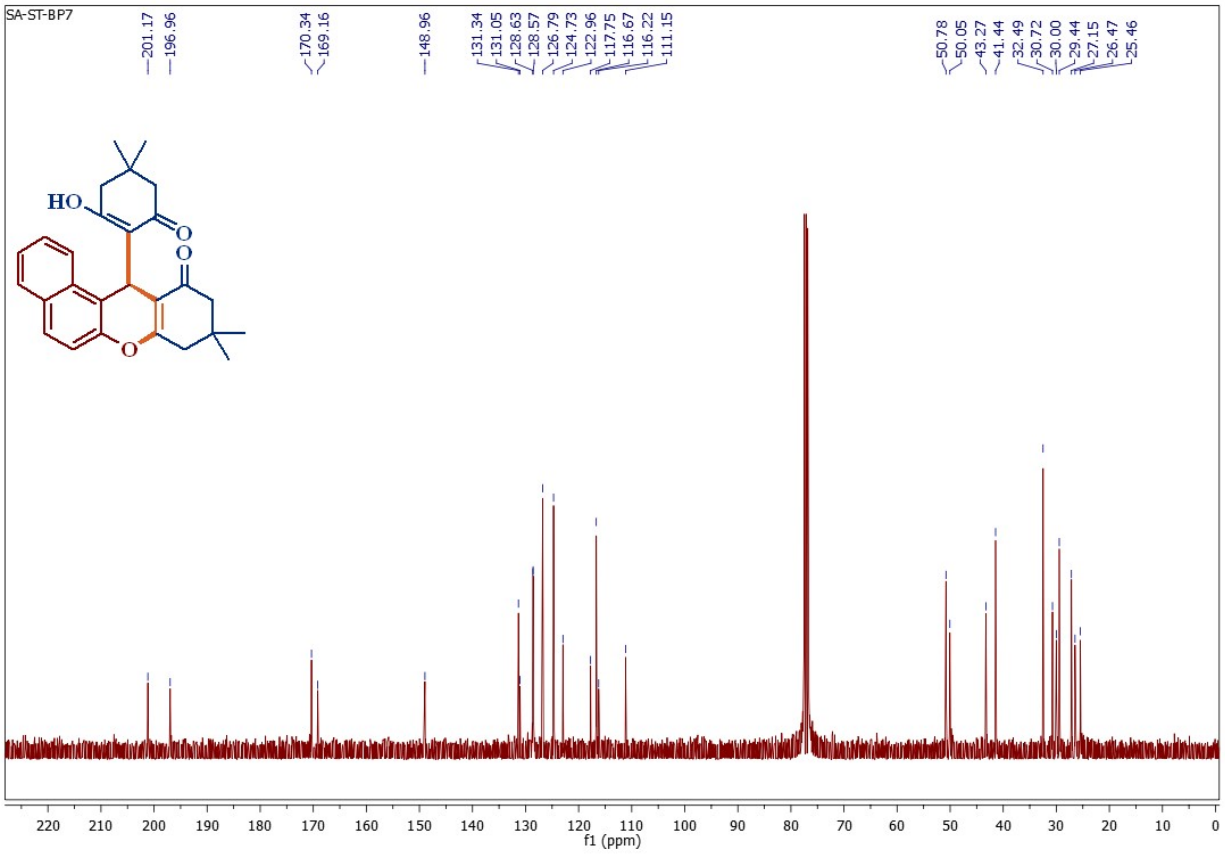


Figure S15: ^{13}C NMR of compound 3f.

7. **9-(2-hydroxy-6-oxocyclohex-1-en-1-yl)-2,3,4,9-tetrahydro-1*H*-xanthen-1-one (3g):**

White solid, yield 96%, m.p. 220 - 222 ^{o}C[7], ^{1}H NMR (400 MHz, $CDCl_3$); δ 10.84 (s, 1H, OH), 7.17 – 7.12 (m, 1H, Ar-H), 7.02 – 6.99 (m, 3H, Ar-H), 4.62 (s, 1H, CH), 2.78 – 2.71 (m, 1H, CH_2), 2.62 – 2.49 (m, 3H, CH_2), 2.45 – 2.35 (m, 2H, CH_2), 2.16 – 1.70 (m, 6H, CH_2). ^{13}C NMR (101 MHz, $CDCl_3$); δ 201.65, 197.24, 172.99, 171.30, 150.94, 128.15, 127.62, 124.74, 127.68, 119.92, 115.62, 112.37, 37.06, 36.09, 29.81, 28.09, 28.08, 19.98, 19.70. ESI-MS (m/z) for $C_{19}H_{18}O_4$: 310.1205 [M^+].

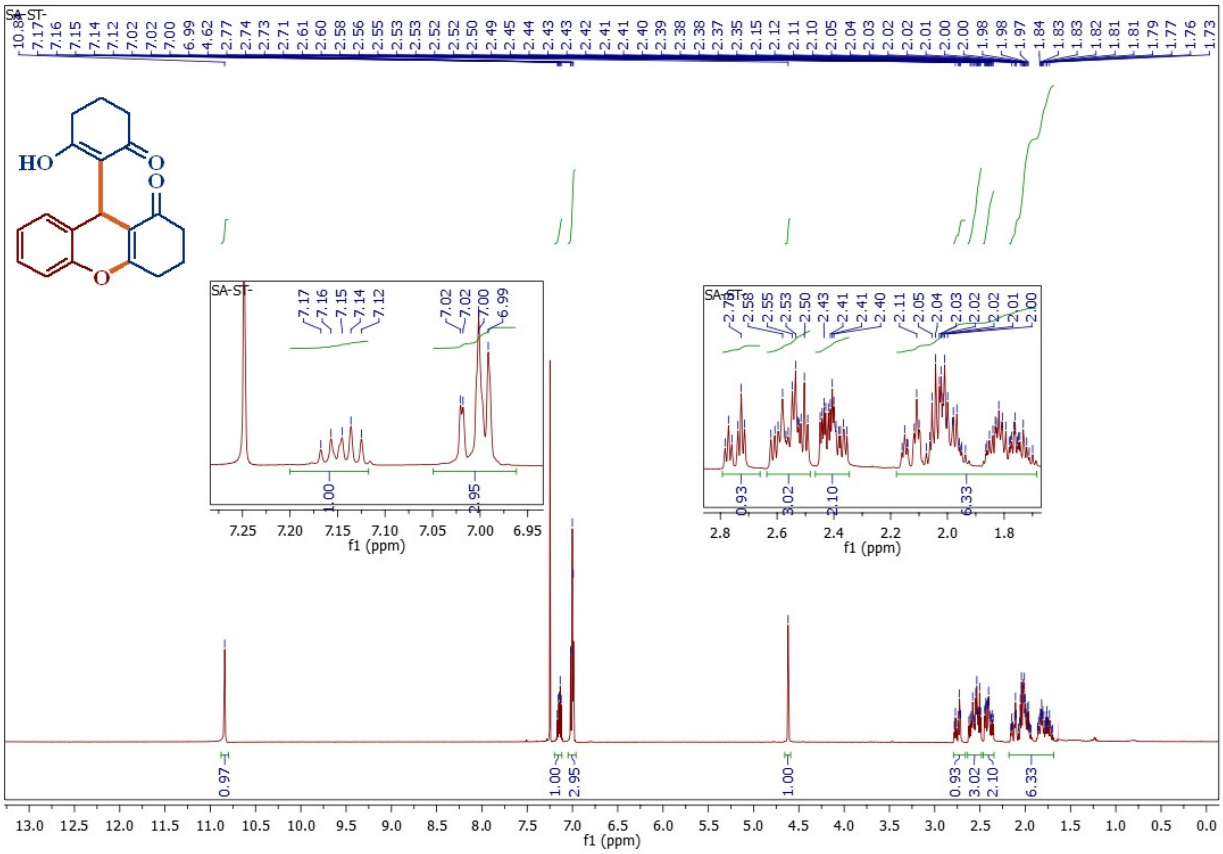


Figure S16: ^{1}H NMR of compound 3g.

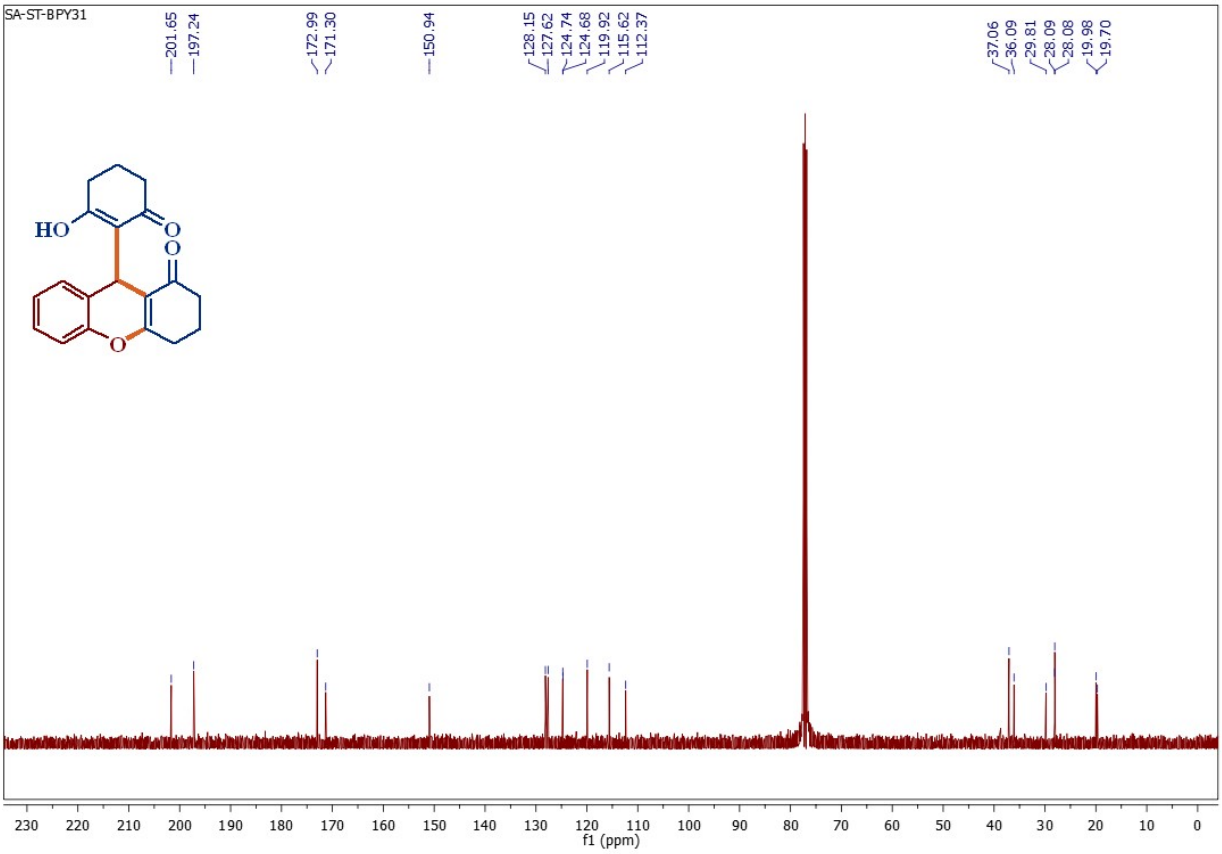


Figure S17: ^{13}C NMR of compound 3g.

8. 9-(2-hydroxy-6-oxocyclohex-1-en-1-yl)-5-methoxy-2,3,4,9-tetrahydro-1*H*-xanthen-1-one (3h)

Fluffy white solid, yield 89%, m.p. 232 - 235 ^{o}C[5], ^{1}H NMR (400 MHz, DMSO-d_6); δ 10.45 (s, 1H, OH), 6.88 – 6.84 (m, 1H, Ar-H), 6.78 – 6.71 (m, 1H, Ar-H), 6.52 – 6.50 (m, 1H, Ar-H), 5.02 (s, 1H, CH), 3.73 (s, 3H, OCH_3), 2.52 – 2.48 (m, 1H, CH_2), 2.22 – 2.16 (m, 6H, CH_2), 1.90 – 1.63 (m, 5H, CH_2). ^{13}C NMR (101 MHz, DMSO-d_6); δ 204.71, 196.58, 167.01, 147.13, 139.54, 126.85, 124.39, 120.21, 112.27, 110.05, 101.50, 101.09, 55.97 (OCH_3), 37.18, 36.33, 27.81, 25.82, 24.01, 23.95, 20.83. ESI-MS (m/z) for $C_{20}H_{20}O_5$: 340.1311 [M^+].

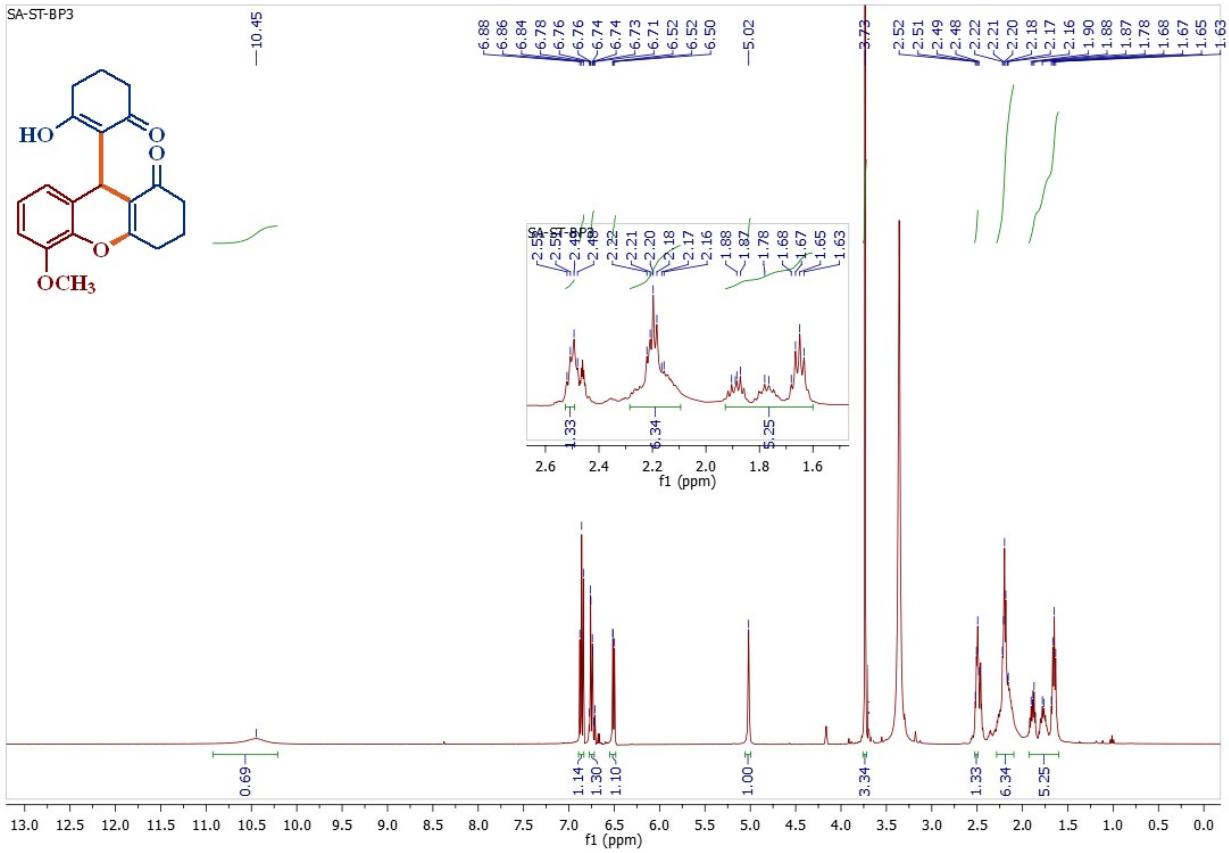


Figure S18: ^{1}H NMR of compound 3h.

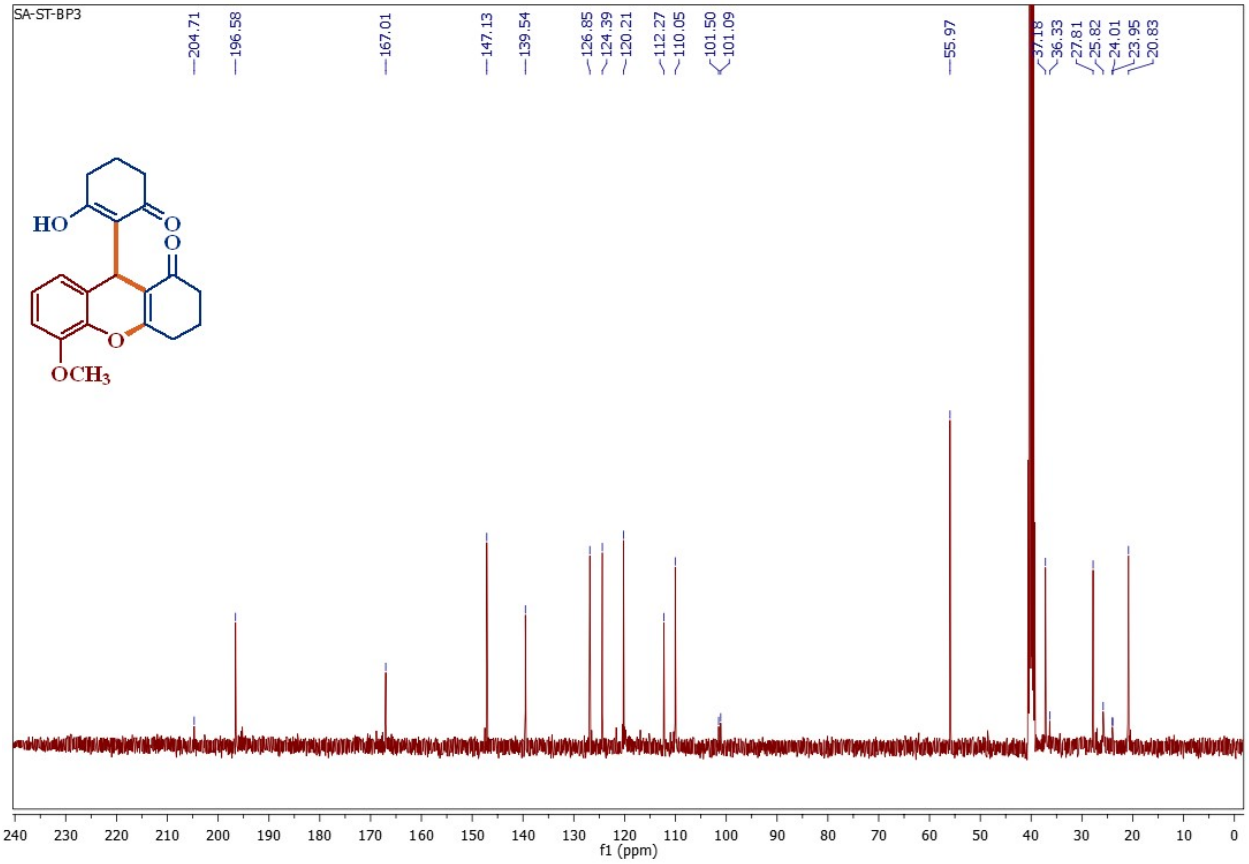


Figure S19: ^{13}C NMR of compound 3h.

9. 5-(2,4-dioxo-1,3,4,5-tetrahydro-2*H*-chromeno[2,3-*d*]pyrimidin-5-yl)pyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (3i)

Off white powder, yield 87%, m.p. 218 - 220 ^{o}C[3, 4], ^{1}H NMR (400 MHz, DMSO-d_6); δ 11.96 (s, 1H, NH), 11.28 (s, 1H, NH), 11.16 (s, 1H, NH), 10.97 (s, 1H, NH), 7.32 – 7.28 (m, 1H, Ar-H), 7.19 – 7.15 (m, 1H, Ar-H), 7.10 – 7.04 (m, 2H, Ar-H), 4.67 (d, J = 2.3 Hz, 1H, CH), 3.80 (d, J = 2.4 Hz, 1H, CH). ^{13}C NMR (101 MHz, DMSO-d_6); δ 170.17, 169.50, 164.04, 155.91, 151.10, 150.08, 149.61, 131.14, 129.77, 128.56, 126.13, 117.01, 85.71, 54.40, 34.12. ESI-MS (m/z) for $C_{15}H_{10}N_4O_6$: 342.0600 [M^+].

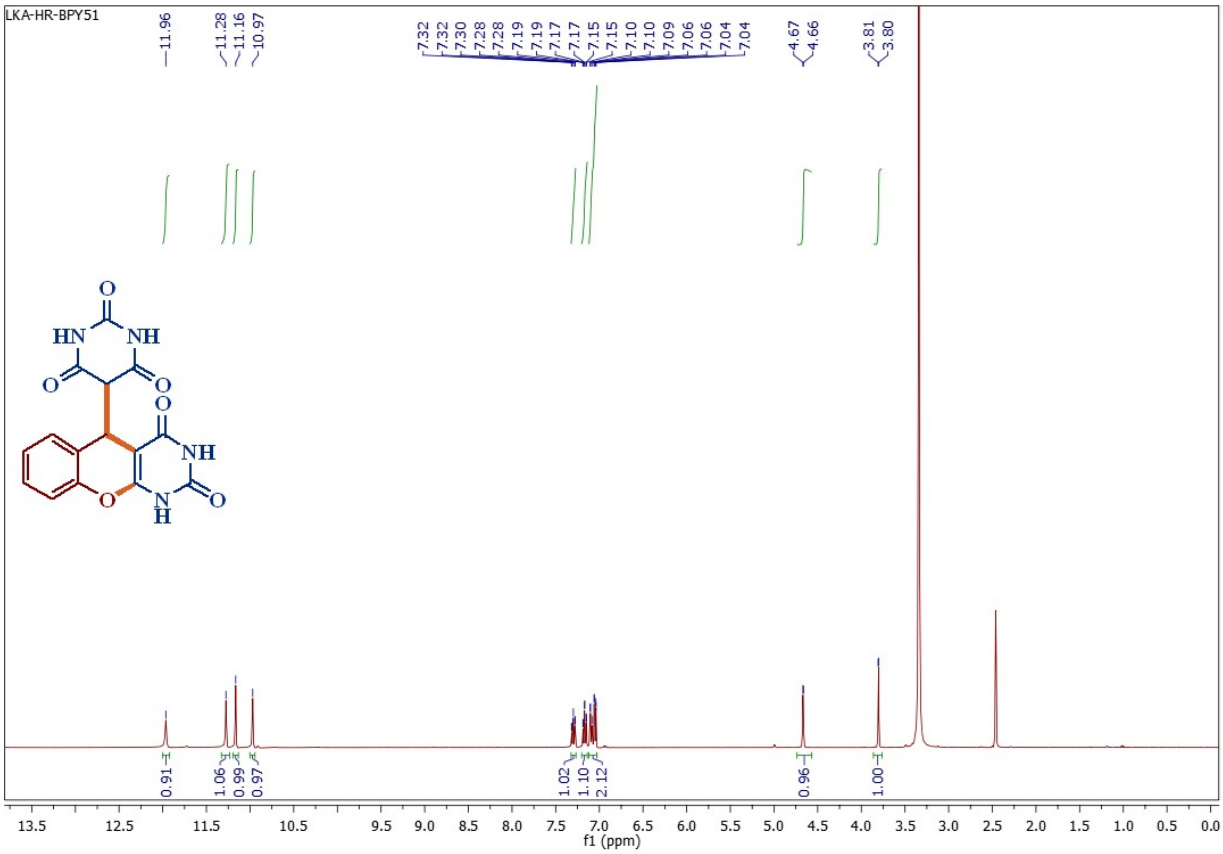


Figure S20: ^{1}H NMR of compound 3i.

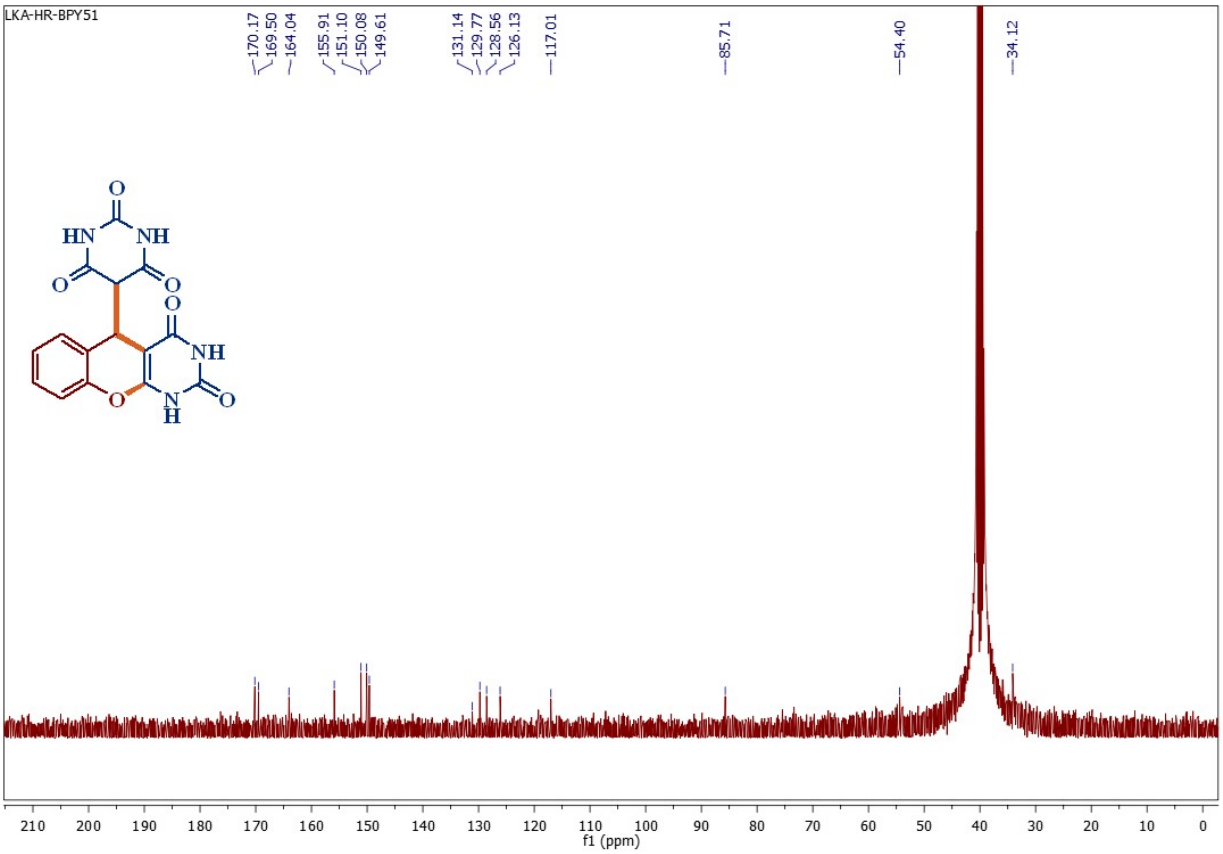


Figure S21: ^{13}C NMR of compound 3i.

10. 5-(8-chloro-2,4-dioxo-1,3,4,5-tetrahydro-2*H*-chromeno[2,3-*d*]pyrimidin-5-yl)pyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (3j)

Off white solid, yield 85%, m.p. 290 -292 $^{o}C^{new}$, ^{1}H NMR (400 MHz, DMSO-d_6); δ 12.07 (s, 1H, NH), 11.31 (s, 1H, NH), 11.21 (s, 1H, NH), 11.04 (s, 1H, NH), 7.29 – 7.03 (m, 3H, Ar-H), 4.67 (d, J = 1.6 Hz, 1H, CH), 3.85 (d, J = 2.1 Hz, 1H, CH). ^{13}C NMR (101 MHz, DMSO-d_6); δ 169.96, 169.37, 163.94, 155.59, 151.08, 150.20 149.99, 133.44, 130.14, 126.23, 120.92, 116.96, 85.72, 53.92, 33.34. ESI-MS (m/z) calculated for $C_{15}H_9ClN_4O_6$: 377.0211[M+1] and found 377.0289.

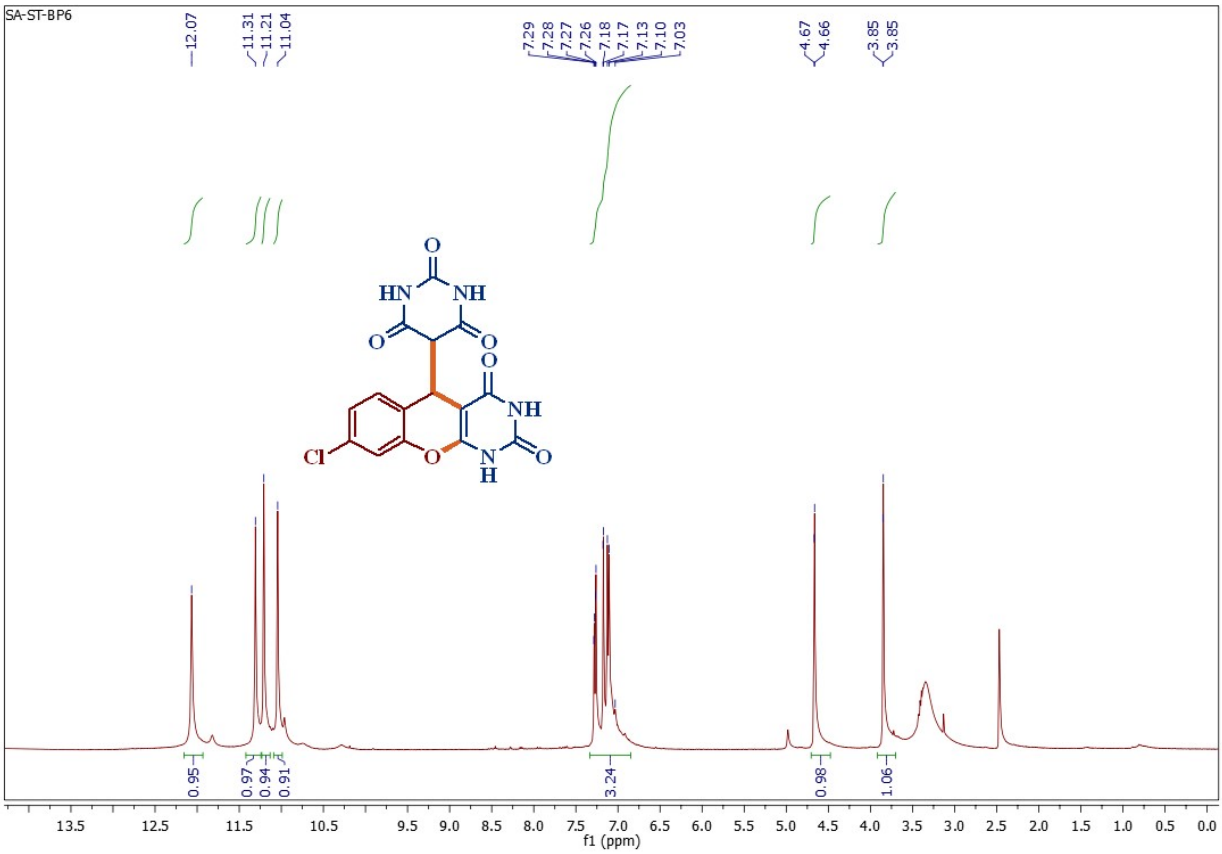


Figure S22: ^{1}H NMR of compound 3j.

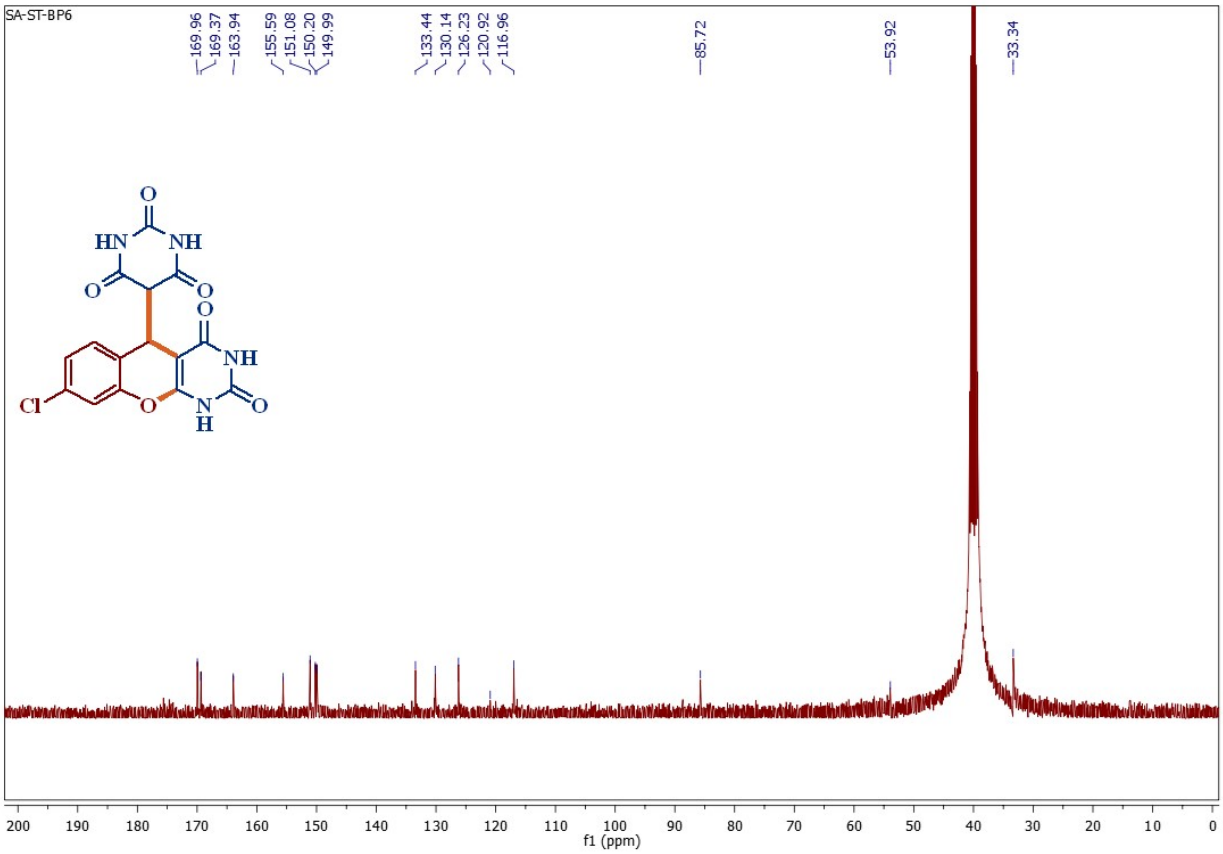


Figure S23: ^{13}C NMR of compound 3j.

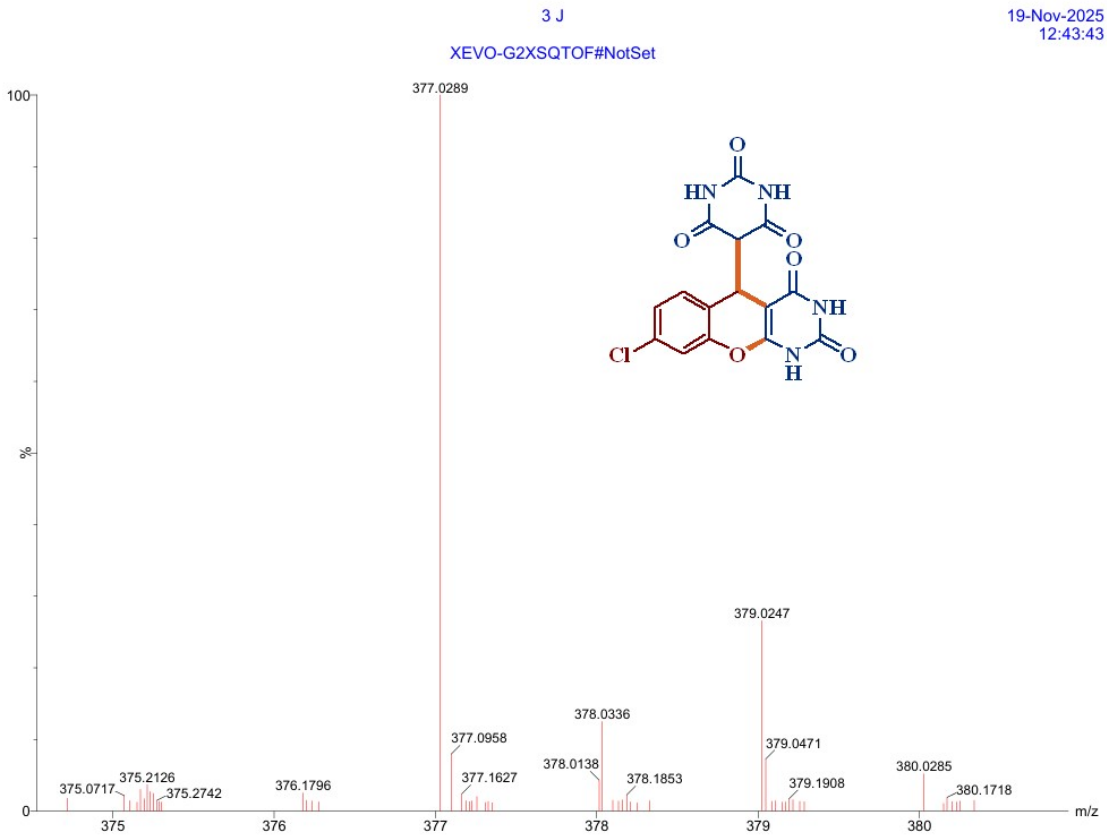


Figure S24: HRMS of compound 3j.

11. 7-(4-hydroxy-2-oxo-2*H*-chromen-3-yl)-6*H*,7*H*-chromeno[4,3-*b*]chromen-6-one (3k)

White powder, yield 95%, m.p. 237 - 239 ^{o}C[8], ^{1}H NMR (400 MHz, $CDCl_3$); δ 10.41 (s, 1H, OH), 8.14 (dd, *J* = 8.0, 1.6 Hz, 1H, Ar-H), 8.02 (dd, *J* = 8.0, 1.6 Hz, 1H, Ar-H), 7.64 – 7.60 (m, 1H, Ar-H), 7.50 – 7.39 (m, 3H, Ar-H), 7.33 – 7.27 (m, 3H, Ar-H), 7.19 – 7.17 (m, 1H, Ar-H), 7.13 – 7.08 (m, 2H, Ar-H), 5.36 (s, 1H, CH). ^{13}C NMR (101 MHz, $CDCl_3$); δ 166.26, 161.53, 161.33, 158.89, 153.11, 152.14, 151.01, 132.90, 132.07, 128.84, 128.64, 125.66, 125.13, 124.44, 123.98, 123.50, 121.44, 117.07, 116.89, 116.42, 116.36, 114.65, 108.71, 100.24, 30.01. ESI-MS (m/z) for $C_{25}H_{14}O_6$: 410.0790[M^+].

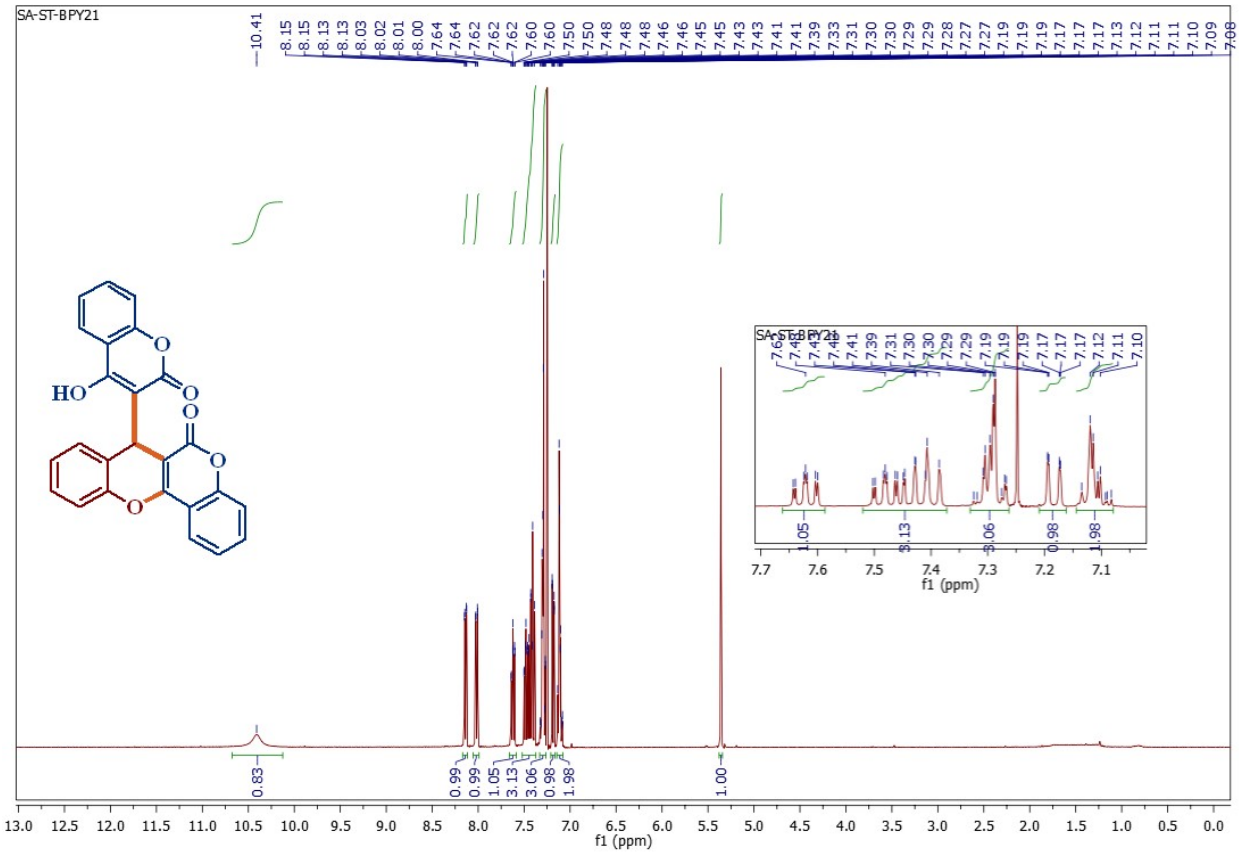


Figure S25: ^{1}H NMR of compound 3k.

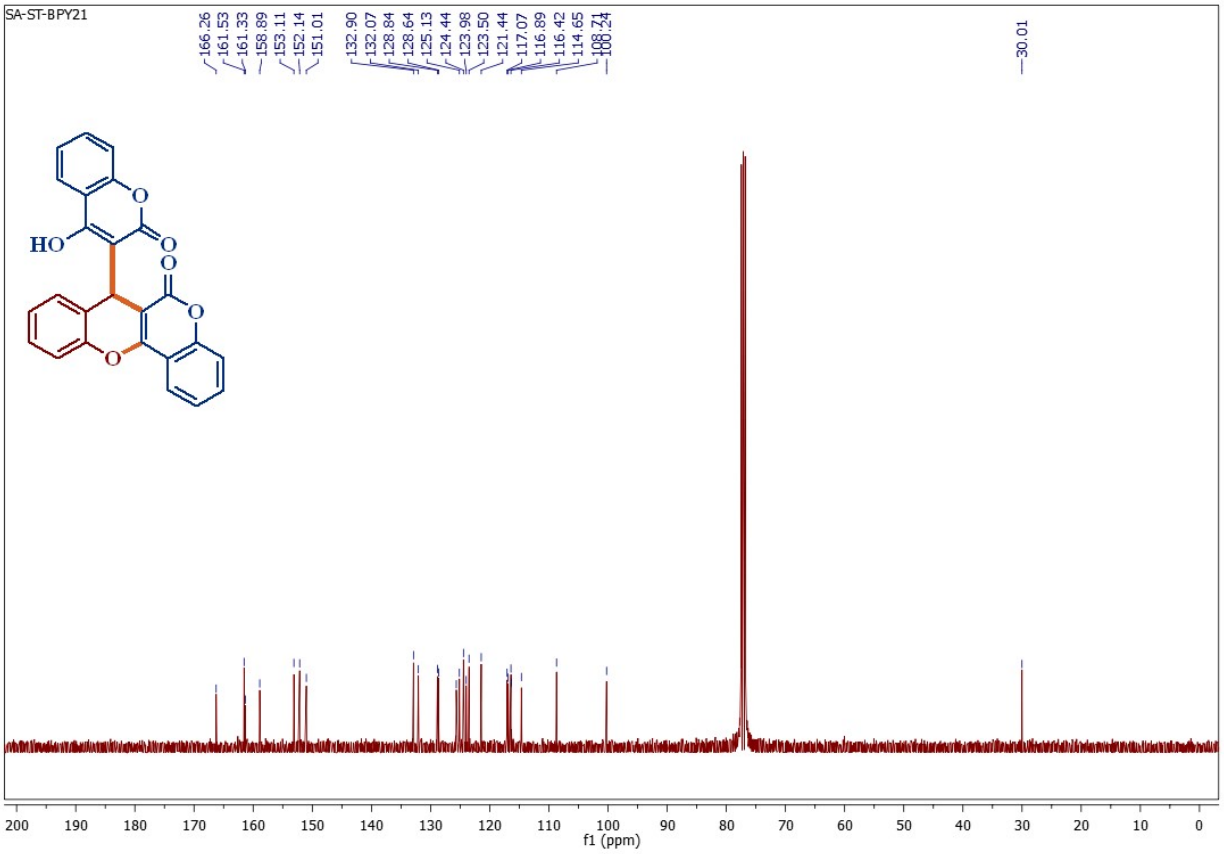


Figure S26: ^{13}C NMR of compound 3k.

12. 11-bromo-9-chloro-7-(4-hydroxy-2-oxo-2*H*-chromen-3-yl)-6*H*,7*H*-chromeno[4,3-b]chromen-6-one (3l)

Off white, yield 87%, m.p. 203 - 205 ^{o}C[9], ^{1}H NMR (400 MHz, DMSO-d_6); δ 10.80 (s, 1H, OH), 8.08 - 7.96 (m, 2H, Ar-H), 7.71 – 7.68 (m, 2H, Ar-H), 7.57 (s, 1H, Ar-H), 7.48 – 7.41 (m, 2H, Ar-H), 7.31 (s, 2H, Ar-H), 7.22 – 7.15 (m, 1H, Ar-H), 5.68 (s, 1H, CH). ^{13}C NMR (101 MHz, DMSO-d_6); δ 164.44, 161.97, 160.47, 156.08, 152.81, 152.45, 151.21, 133.41, 133.04, 131.65, 129.65, 128.09, 126.31, 125.38, 124.62, 124.53, 122.75, 120.14, 117.18, 116.88, 116.54, 113.83, 111.31, 107.36, 29.74. ESI-MS (m/z) for $C_{25}H_{12}BrClO_6$: 521.9506 [M^+].

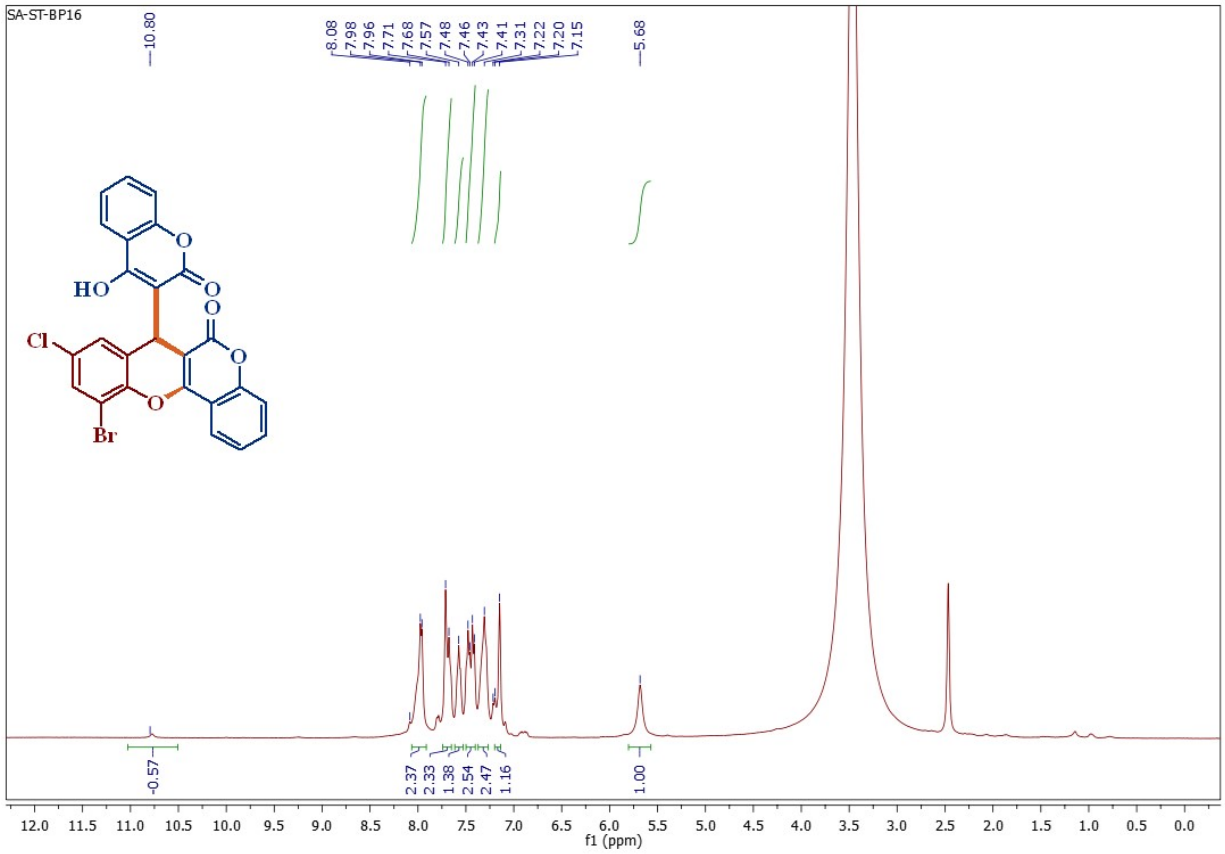


Figure S27: ^{1}H NMR of compound 3l.

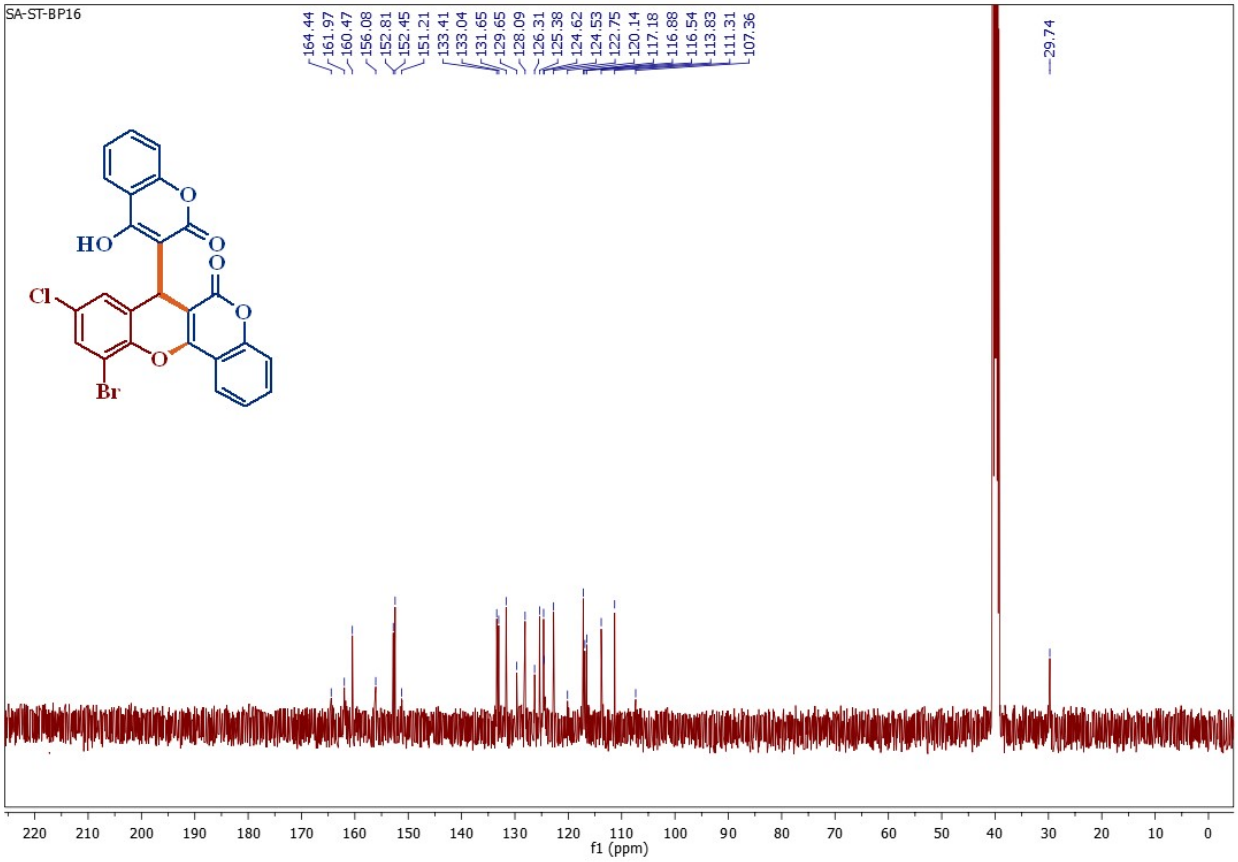


Figure S28: ^{13}C NMR of compound 3l.

13. 3-methyl-4-(3-methyl-6-nitro-1-phenyl-1,4-dihydrochromeno[2,3-*c*]pyrazol-4-yl)-1-phenyl-1*H*-pyrazol-5-ol (3m)

Light yellow powder, yield 87%, m.p. 228 - 230 ^{o}C[10], ^{1}H NMR (400 MHz, DMSO-d_6); 11.33 (s, 1H, OH), 8.48 (s, 1H, Ar-H), 7.98 (d, J = 7.6 Hz, 1H, Ar-H), 7.68 – 7.66 (m, 4H, Ar-H), 7.41 (s, 4H, Ar-H), 7.22 (s, 2H, Ar-H), 6.92 (d, J = 8.6 Hz, 1H, Ar-H), 5.12 (s, 1H, CH), 2.28 (s, 6H, CH_3). ^{13}C NMR (101 MHz, DMSO-d_6); δ 161.38, 146.78, 139.79, 130.42, 129.51, 126.27, 125.28, 124.51, 121.24, 115.76, 28.19, 12.18. ESI-MS (m/z) calculated for $C_{27}H_{21}N_5O_4$: 479.1594 [M+1] and found 480.1667.

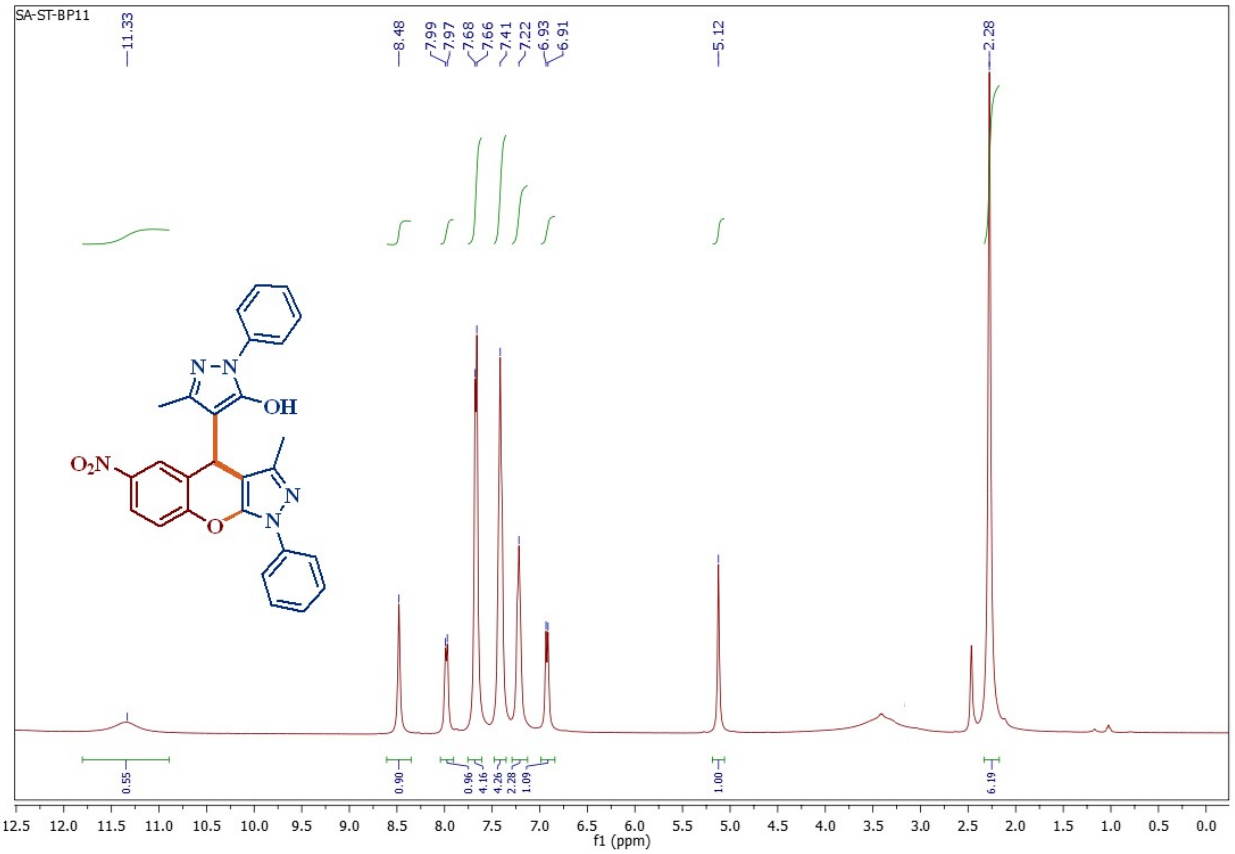


Figure S29: ^{1}H NMR of compound 3m.

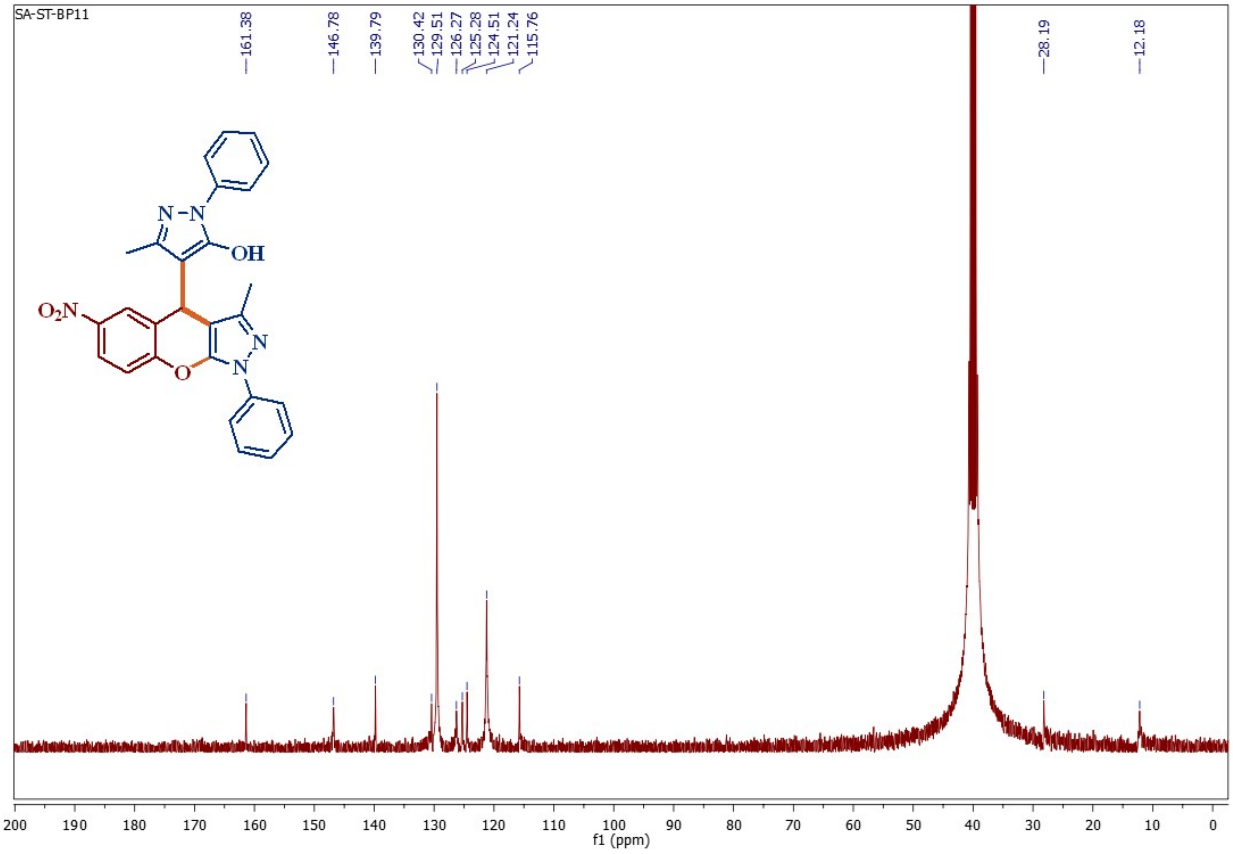


Figure S30: ^{13}C NMR of compound 3m.

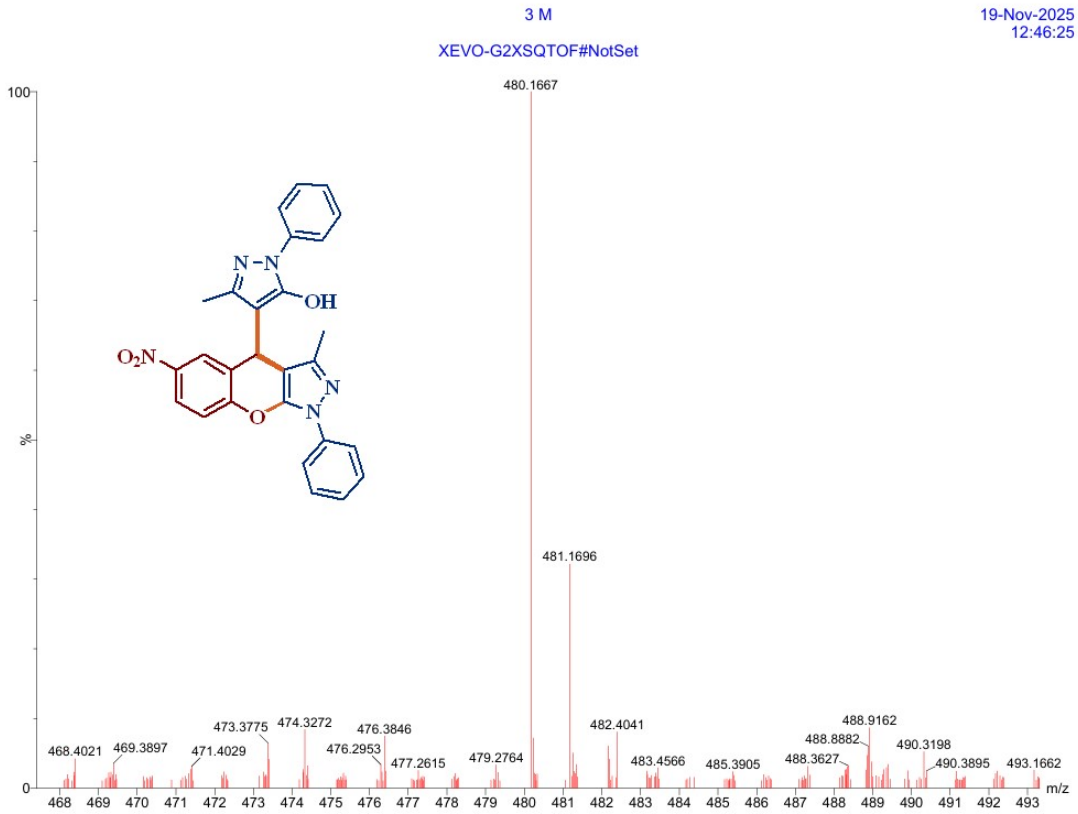


Figure S31: HRMS of compound 3m.

14. 4-(6-fluoro-3-methyl-1-phenyl-1,4-dihydrochromeno[2,3-c]pyrazol-4-yl)-3-methyl-1-phenyl-1*H*-pyrazol-5-ol (3n)

Off white powder, yield 83%, m.p. 204 – 206 $^{o}C^{new}$, ^{1}H NMR (400 MHz, DMSO-d_6); δ 7.67 (d, J = 7.4 Hz, 4H, Ar-H), 7.42 – 7.31 (m, 5H, Ar-H), 7.22 (d, J = 6.2 Hz, 2H, Ar-H), 6.81 – 6.72 (m, 2H, Ar-H), 5.13 (s, 1H, CH), 2.27 (s, 6H, CH_3). ^{13}C NMR (101 MHz, DMSO-d_6); δ 155.68 (d, J = 232.9 Hz, C-F), 150.68, 146.79, 131.45, 129.47, 126.17 (d, J = 5.4 Hz), 121.28, 115.96 (d, J = 9.5 Hz), 115.60 (d, J = 23.8 Hz), 113.55 (d, J = 22.7 Hz), 113.28, 28.04, 12.27. ^{19}F NMR (376 MHz, DMSO-d_6); δ -125.30 (s). ESI-MS (m/z) calculated for $C_{27}H_{21}FN_4O_2$: 453.1649 [M+1] and found 453.1736.

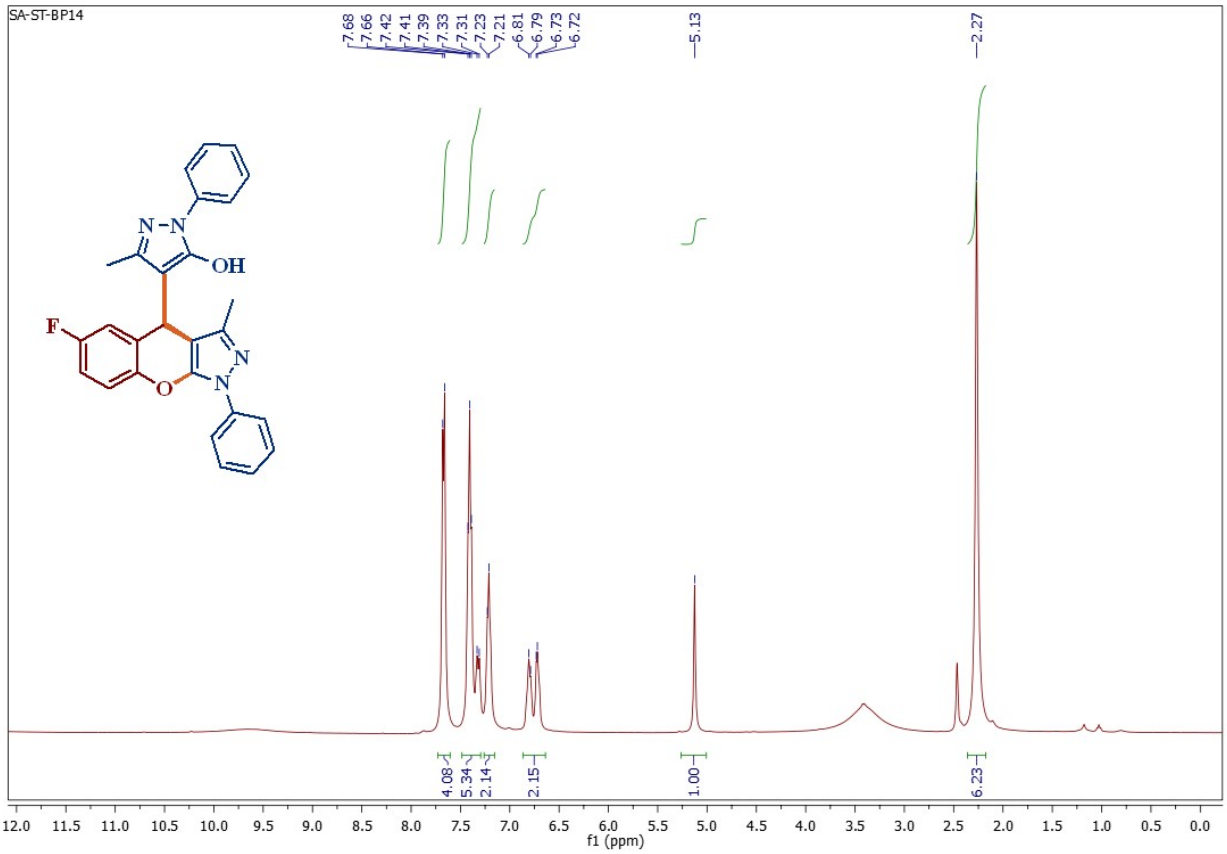


Figure S32: ^{1}H NMR of compound 3n.

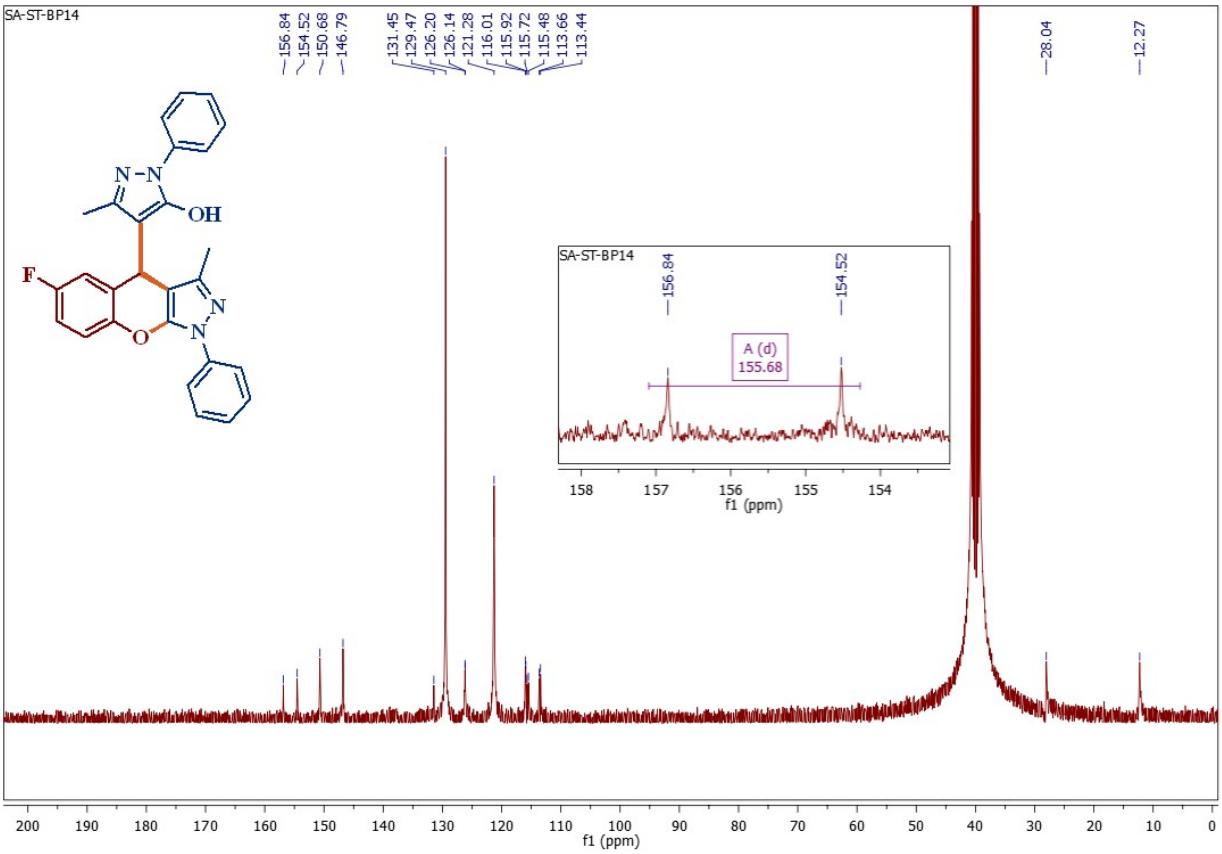


Figure S33: ^{13}C NMR of compound 3n.

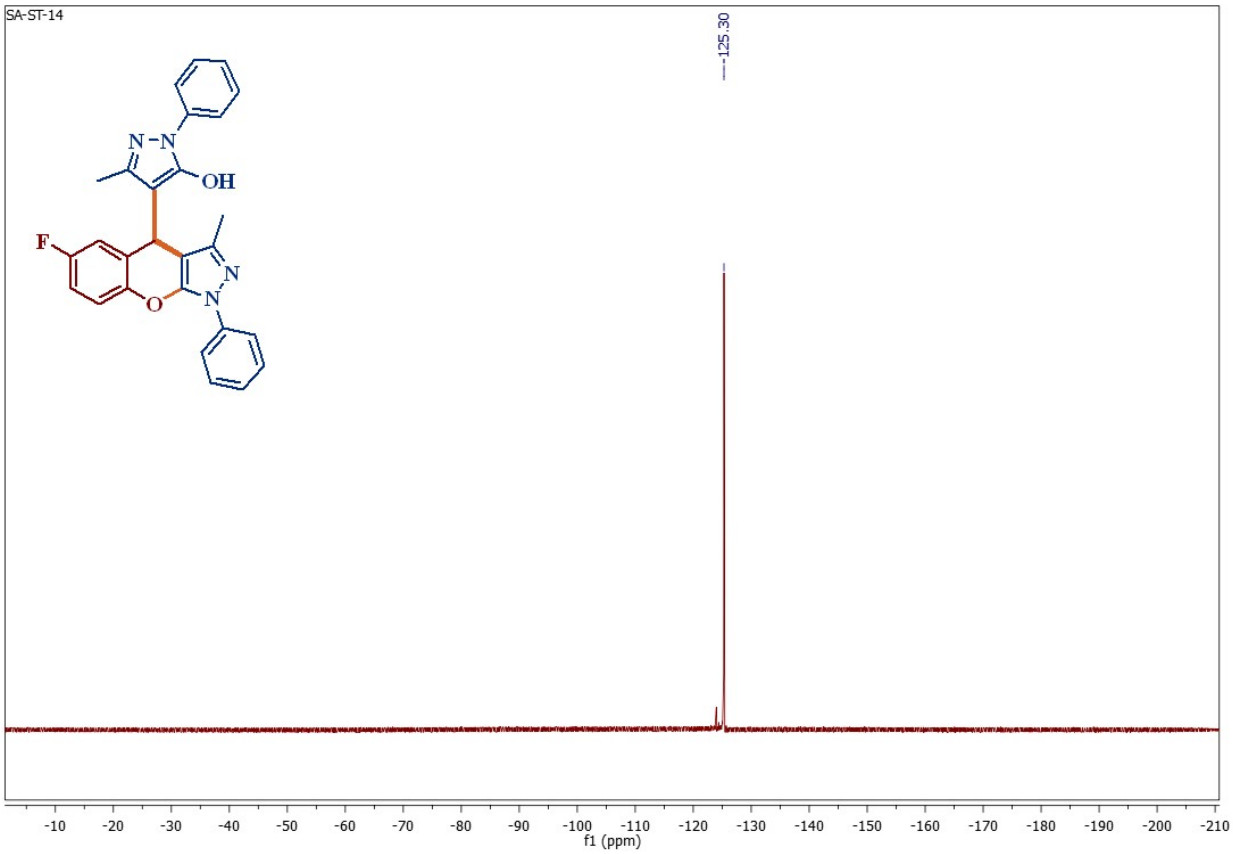


Figure S34: ^{19}F NMR of compound 3n.

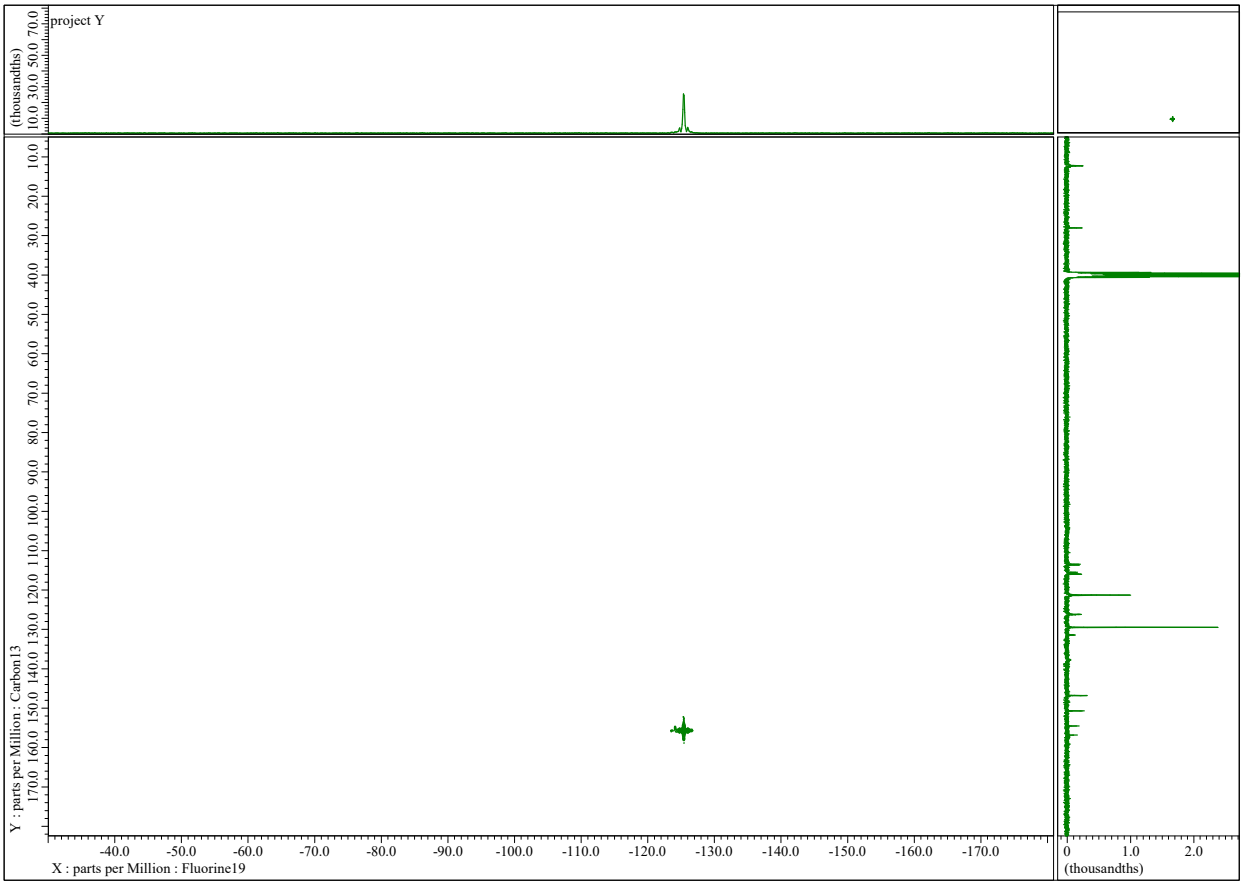


Figure S35. ^{19}F HMQC of compound 3n.

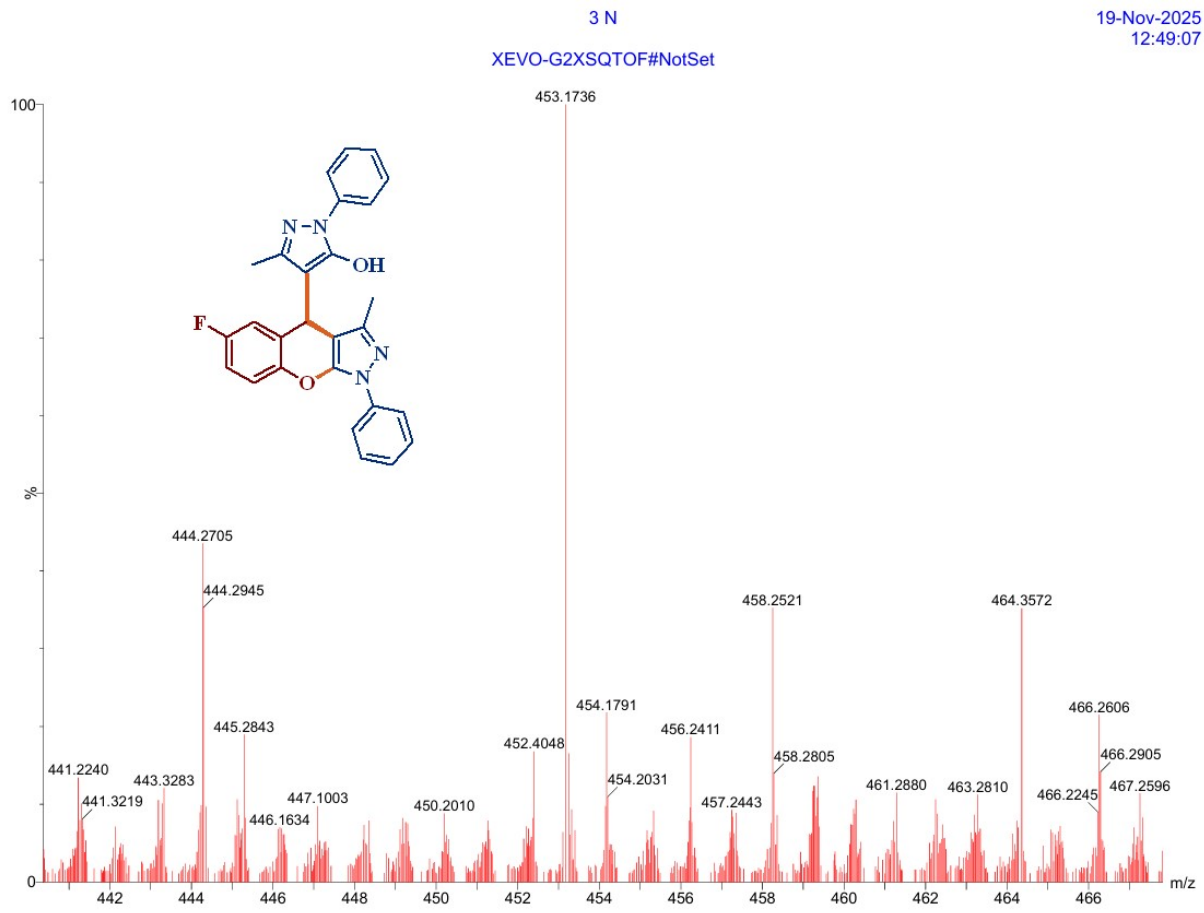


Figure S36: HRMS of compound 3n.

15. 3-(1-hydroxy-3-oxobut-1-en-1-yl)-2H-chromen-2-one (3o)

Pale yellow solid, yield 94%, m.p. 134 – 136 ^{o}C[11], ^{1}H NMR (400 MHz, $CDCl_3$); δ 8.65 (s, 1H, CH), 7.65 – 7.61 (m, 2H, Ar-H), 7.397 – 7.32 (m, 2H, Ar-H), 7.02 (s, 1H, Ar-H of pyrone ring), 2.26 (s, 3H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$); δ 200.01, 171.95, 158.20, 154.47, 145.61, 134.11, 129.66, 125.08, 120.66, 118.61, 116.69, 101.74, 27.74. ESI-MS (m/z) calculated for $C_{13}H_{10}O_4$: 231.0579 [M+1] and found 231.0659.

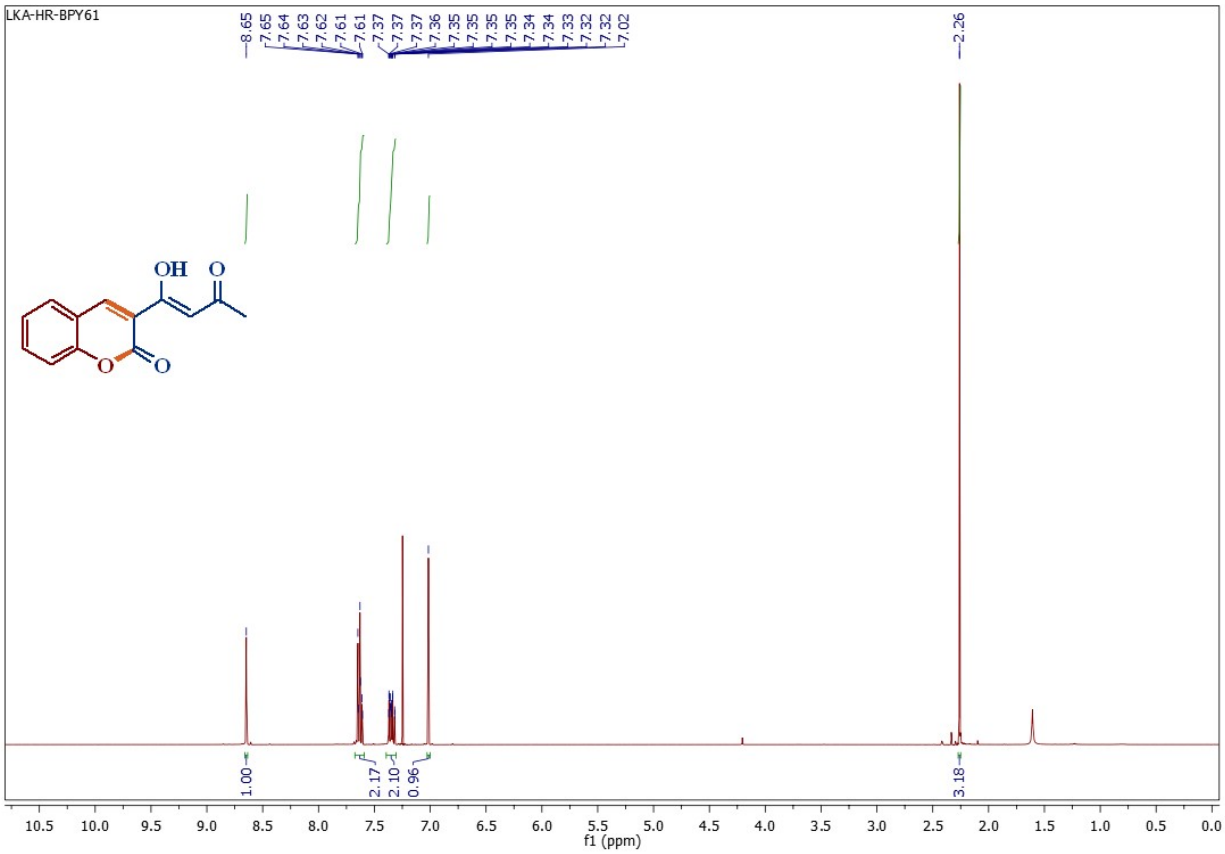


Figure S37: ^{1}H NMR of compound 3o.

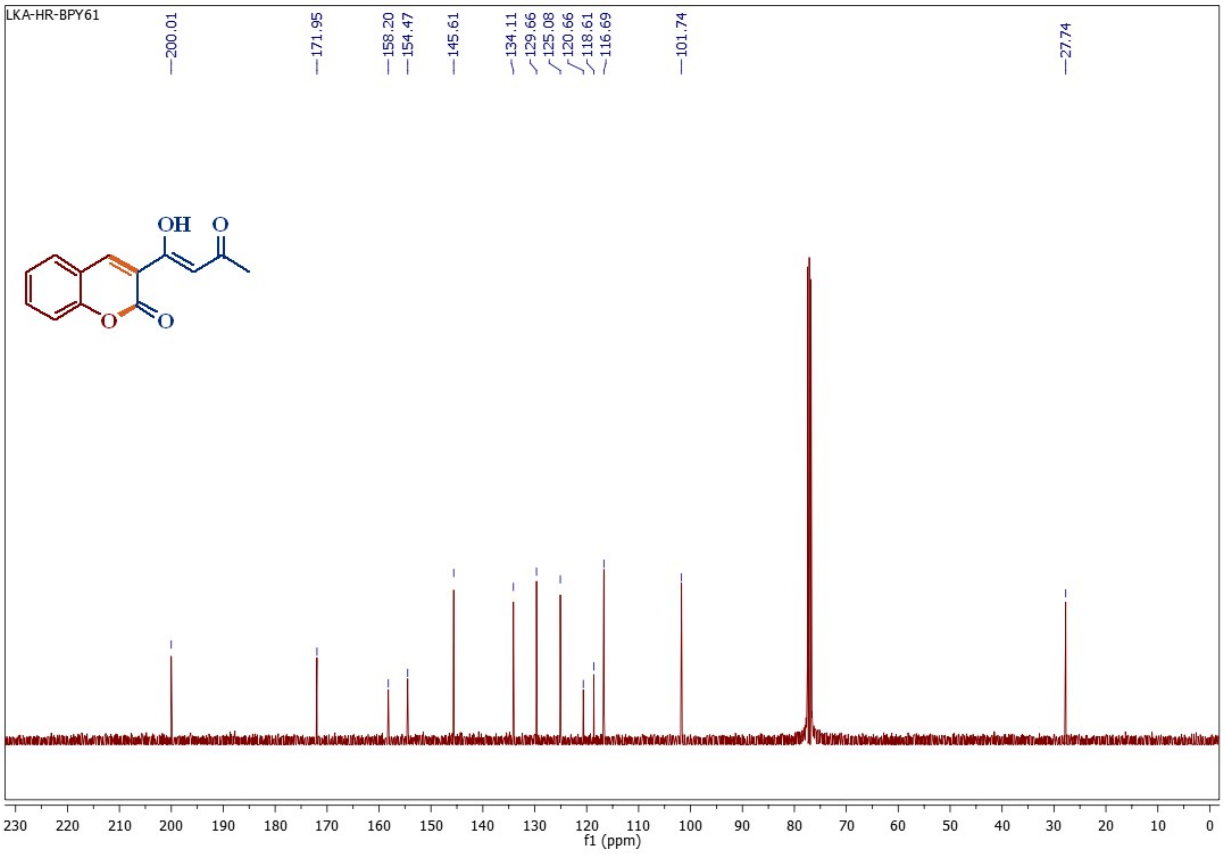


Figure S38: ^{13}C NMR of compound 3o.

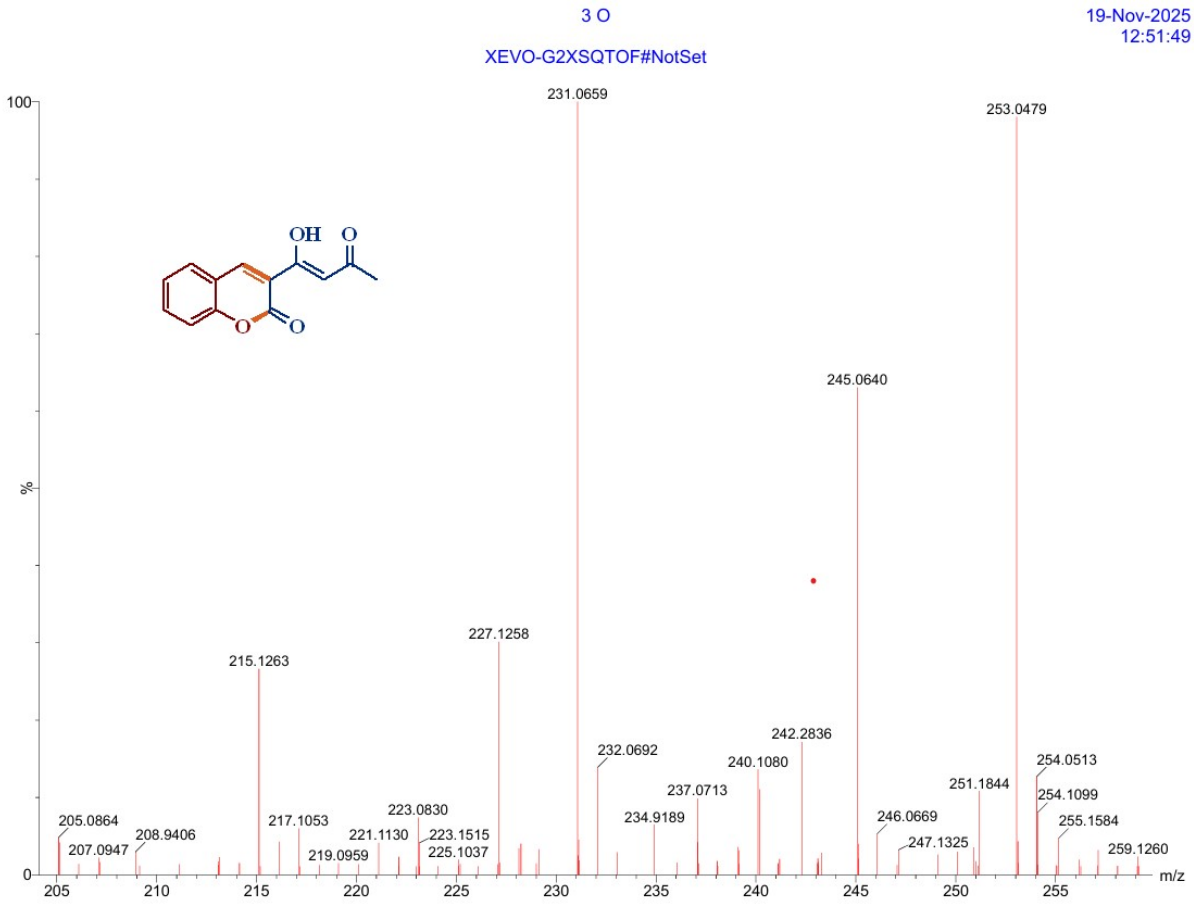


Figure S39: HRMS of compound 3o.

16. 3-(1-hydroxy-3-oxobut-1-en-1-yl)-7-methyl-2*H*-chromen-2-one (3p)

Light yellow powder, yield 91%, m.p. 137 – 140 $^{o}C^{new}$, ^{1}H NMR (400 MHz, $CDCl_3$); δ 8.59 (s, 1H, CH), 7.52 – 7.48 (m, 1H, Ar-H), 7.14 – 7.12 (m, 2H, Ar-H), 6.99 (s, 1H, Ar-H of pyrone ring), 2.46 (s, 3H, CH_3), 2.24 (s, 3H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$); δ 199.54, 172.60, 158.41, 154.67, 146.08, 145.63, 129.36, 126.40, 119.37, 116.79, 116.30, 101.44, 27.57, 22.26. ESI-MS (m/z) calculated for $C_{14}H_{12}O_4$: 245.0736 [M+1] and found 245.0824.

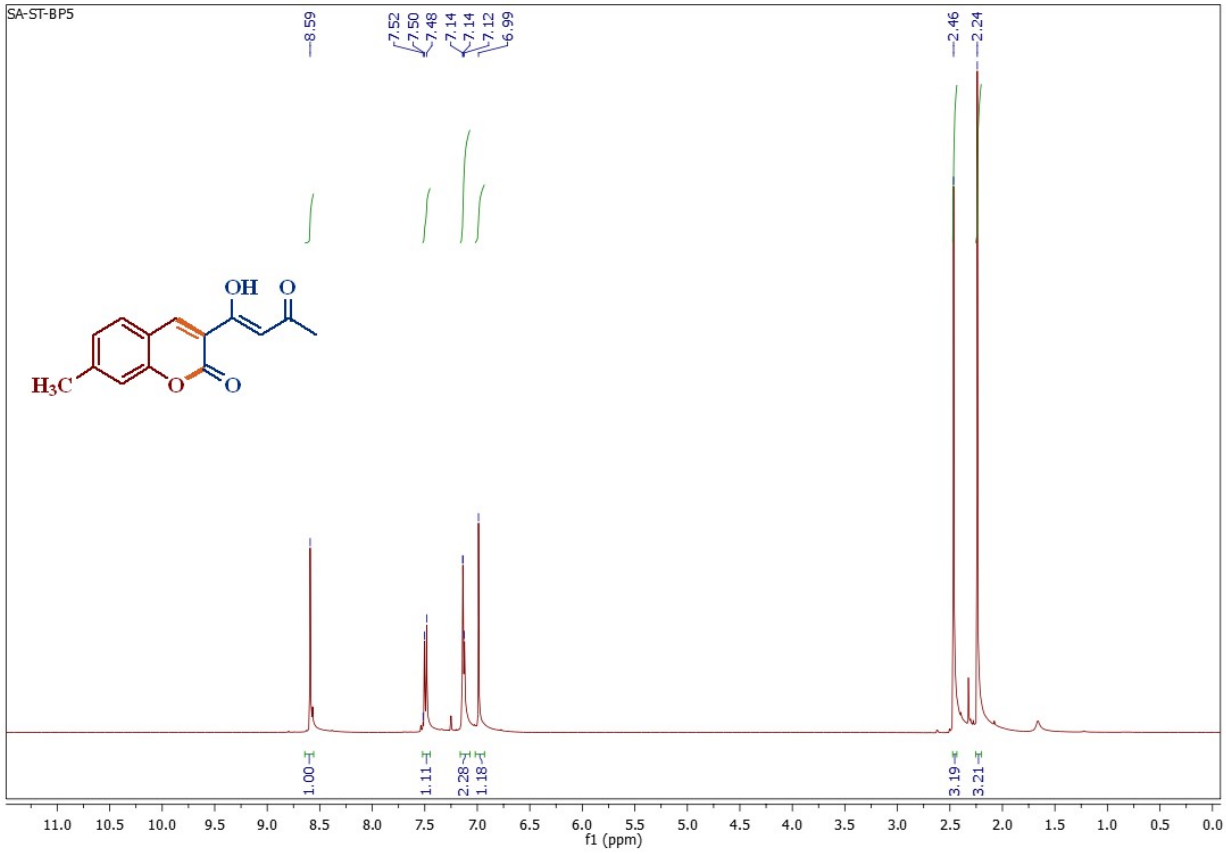


Figure S40: ^{1}H NMR of compound 3p.

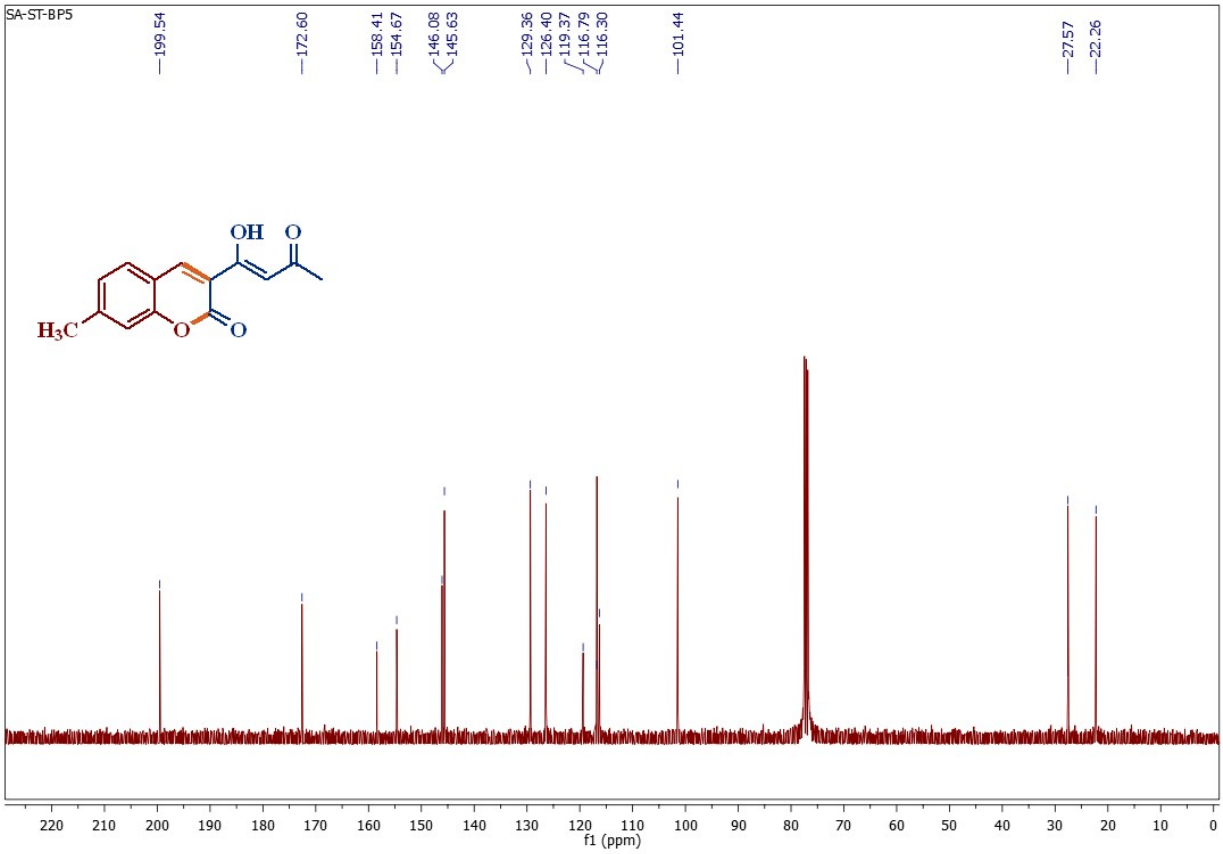


Figure S41: ^{13}C NMR of compound 3p.

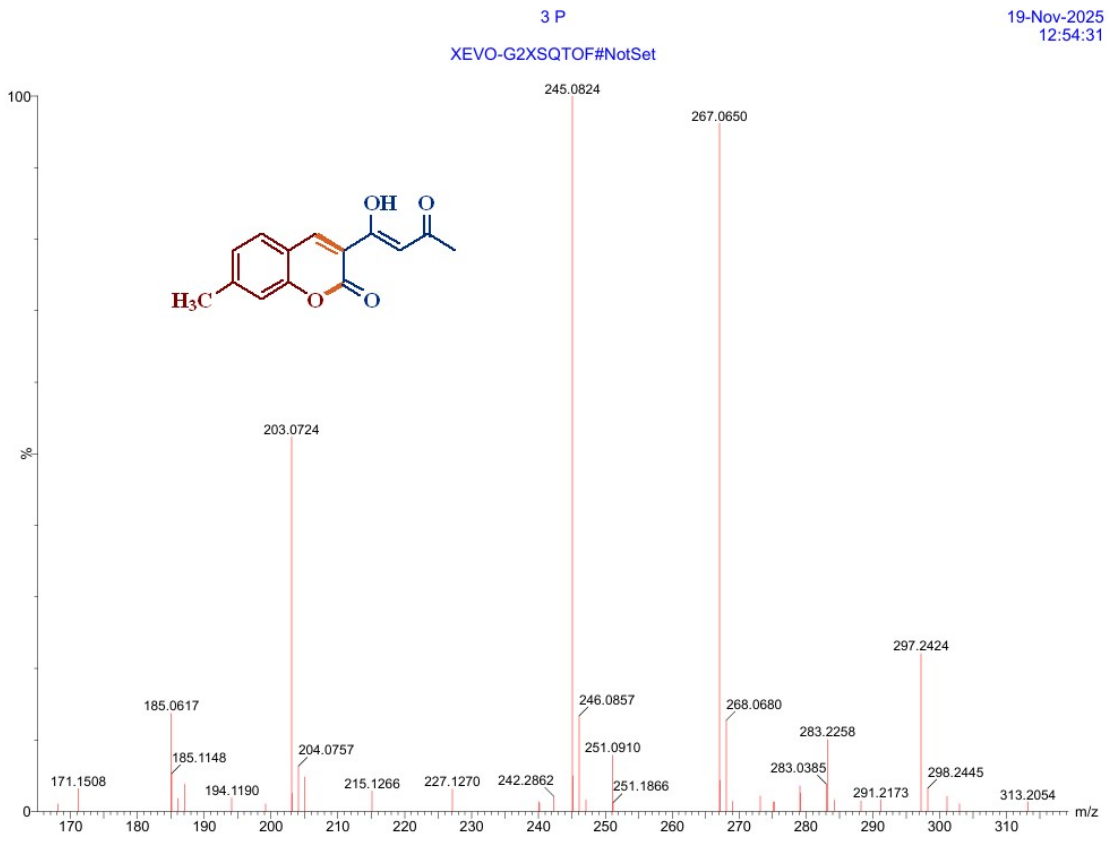


Figure S42: HRMS of compound 3p.

17. 2-(9,11-diamino-10-cyano-12*H*-benzo[5,6]chromeno[2,3-*b*]pyridin-12-yl)malononitrile (3q)

Yellow solid, yield 90%, m.p. >300 ^{o}C[12], ^{1}H NMR (400 MHz, DMSO-d_6); δ 8.38 (d, J = 8.6 Hz, 1H, Ar-H), 7.99 - 7.93 (m, 2H, Ar-H), 7.64 - 7.38 (m, 3H, Ar-H), 7.23 (s, 2H, NH_2), 6.76 (s, 2H, NH_2), 5.92 (d, J = 4.5 Hz, 1H, CH), 5.01 (d, J = 4.6 Hz, 1H, CH).^{13}C NMR (101 MHz, DMSO-d_6); δ 161.40 (N-C-O), 161.01 (C-NH_2), 157.76 (N=C-NH_2), 151.01 (C-O), 131.23, 131.08, 130.85, 129.08, 127.56, 125.75, 123.99, 118.07, 116.96, 113.86 and 113.73 ($(CN)_2$), 112.19 (Ali-C-CN), 85.05 (C-CH), 71.21 (C-CN), 31.01 (CH-$(CN)_2$), 30.25 (CH); ESI-MS (m/z) for $C_{20}H_{12}N_6O$: 352.1073 [M^+].

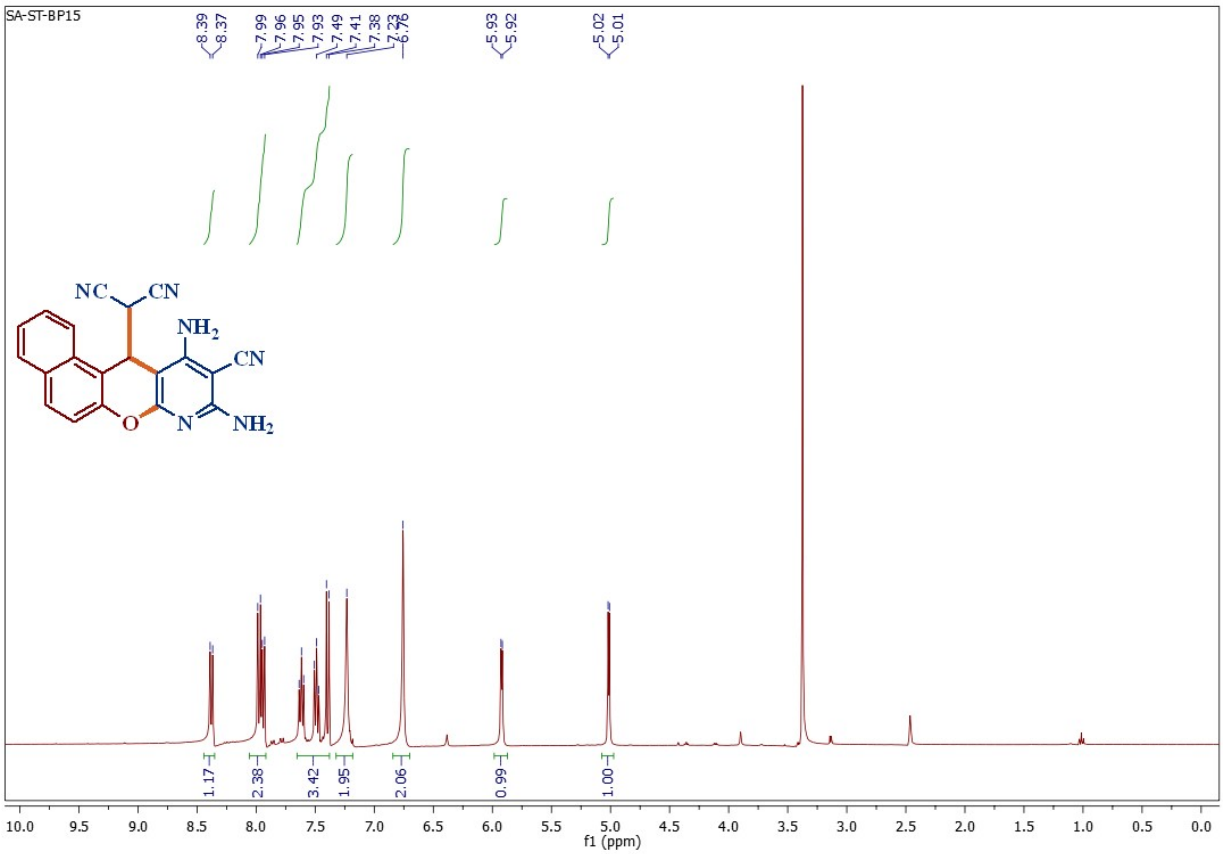


Figure S43: ^{1}H NMR of compound 3q.

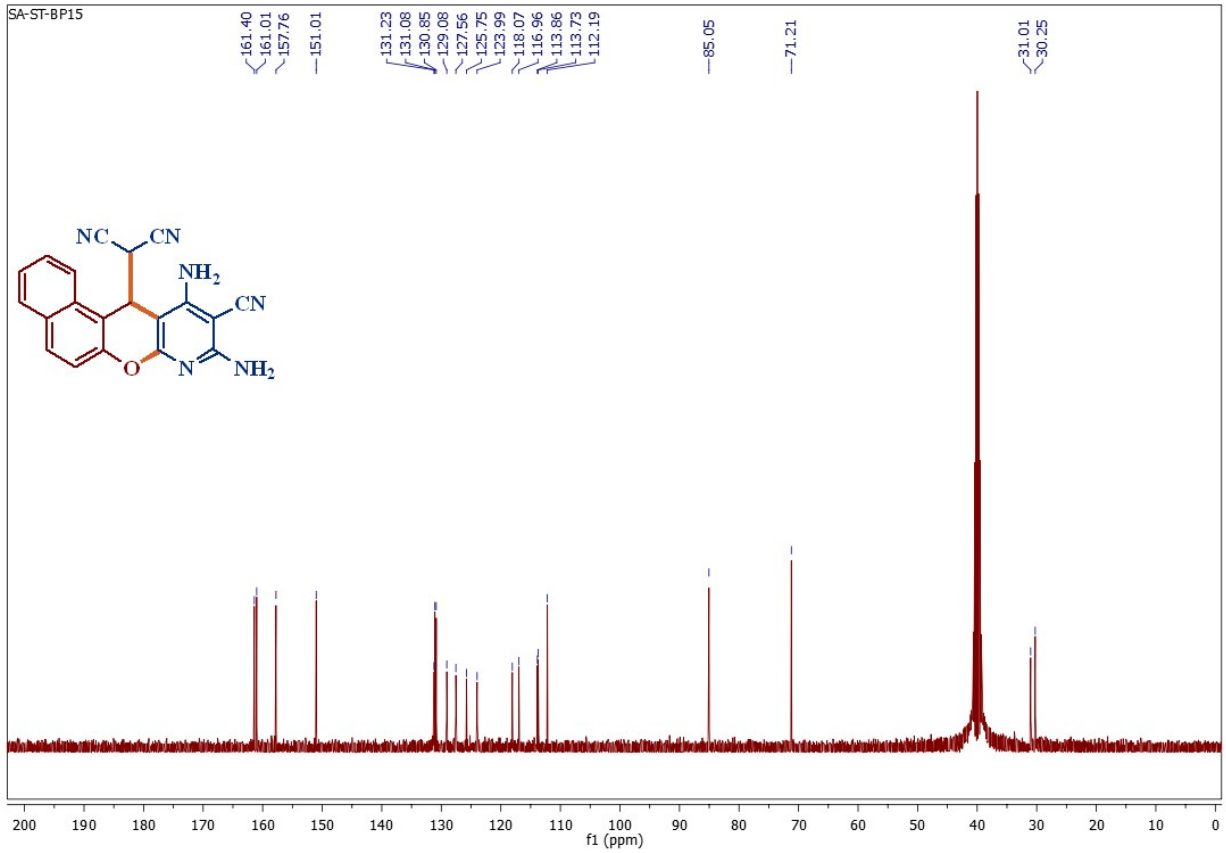


Figure S44: ^{13}C NMR of compound 3q.

5. Gram scale synthesis

Figure S45: Progress of gram scale reaction (a) to (b) and final dried product (c).

6. Molecular docking

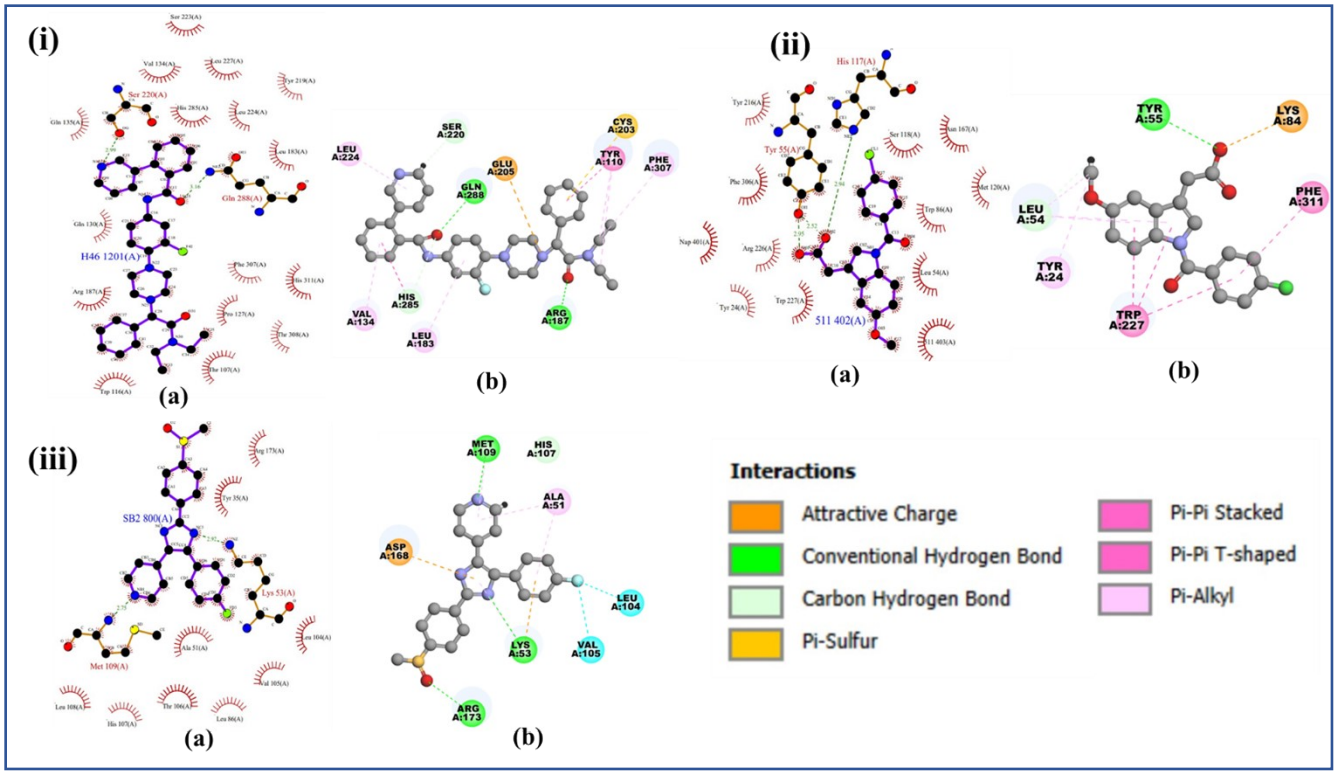


Figure S46: 2D interaction plot of the experimentally co-crystallised pose and redocked pose of **(i)** H46 (7DDZ), **(ii)** 511 (4DBW) and **(iii)** SB2 (1A9U), where '**(a)**' represents the plot of the co-crystalized pose and '**(b)**' represents the redocked pose.

Table S2: List of the redocking and docking score of co-crystallised and seventeen synthesized benzopyran derivatives in selected PDBs 7DDZ, 4DBW and 1A9U.

Molecules	**7DDZ**	**4DBW**	**1A9U**
	Docking Score (kcal/mol)		
H46	**-15.00**	**--**	**--**
511	**--**	**-17.33**	**--**
SB2	**--**	**--**	**-08.70**
3a	-15.42*	-12.85	-06.49
3b	-13.63	-19.37*	-13.13*
3c	-15.49*	01.55	-07.33
3d	-15.33*	-11.37	-11.14*
3e	-14.95	-10.90	-10.40*
3f	-17.69*	**--**	-10.63*
3g	-13.74	-10.22	-09.52*
3h	-15.11*	-04.47	-09.14*
3i#	-16.34*	-17.35*	-14.35*
3j#	-18.91*	-18.67*	-12.49*
3k#	-15.99*	-19.38*	-09.44*
3l	-15.33*	-06.13	-09.89*
3m	-12.20	-18.86*	-15.19*
3n#	-15.01*	-19.63*	-11.47*
3o#	-16.30*	-17.94*	-09.20*
3p	-12.38	-16.96	-08.77*
3q#	-16.33*	-19.49*	-08.89*

*Showed highest docking score than the respective redocked reference

#commonly docked candidates

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