

Supporting Information

Regioselective House–Meinwald Rearrangement in Oxindoles: Access to Substituted Quinolinones

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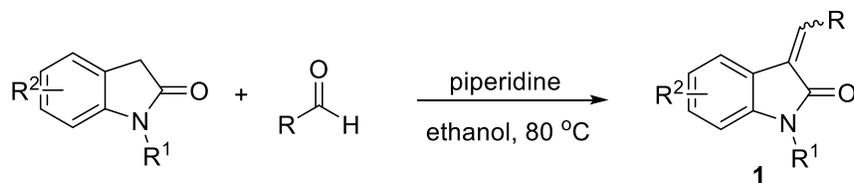
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1. General information

All the chemicals and solvents were commercially purchased from Sigma-Aldrich and used without further purification. Column chromatography was performed using silica gel (100-200 mesh), and a mixture of hexane-ethyl acetate was used for elution. NMR spectra were recorded at 500 (^1H) and 125 (^{13}C) MHz on a Bruker ASCENDTM spectrometer by using CDCl_3 as a solvent and tetramethylsilane (TMS) as an internal standard. Chemical shifts (δ) for ^1H NMR spectra are represented in parts per million (ppm) downfield from TMS (δ 0.0) and relative to the signal of chloroform-d (δ 7.26, singlet), DMSO-d_6 (δ 2.50, quintet), and acetone- d_6 (δ 2.05, quintet). Coupling constants (J) are given in Hertz (Hz), and multiplicities were represented as s, d, t, q, m, and dd for singlet, doublet, triplet, quartet, multiplet, and doublet of a doublet, respectively. Chemical shifts (δ) for ^{13}C NMR are represented in parts per million (ppm) downfield from TMS (δ 0.0) and relative to the signal of chloroform-d (δ 77.16, triplet), DMSO-d_6 (39.52, septet), and Acetone- d_6 (206.26 singlet and 29.84 septet). Infrared spectra were recorded with a Bruker Alpha-T FT-IR spectrometer. Mass spectra were recorded under HRMS (ESI) using a Thermo Scientific Exactive mass spectrometer. Melting points were determined on a Stuart melting point apparatus, SMP30 and are uncorrected. All substrates were synthesized by following reported procedures.^{1,2}

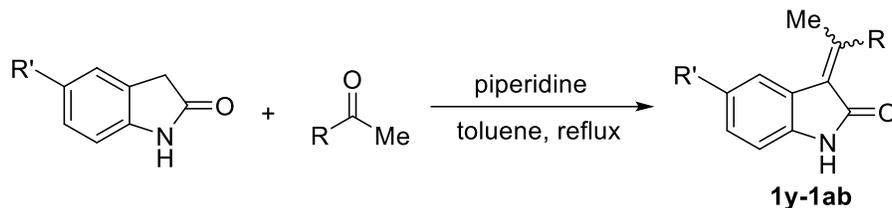
2. General procedures for the synthesis of substrates and reagent EBHP

2.1 General procedure for the synthesis of substrates **1**¹



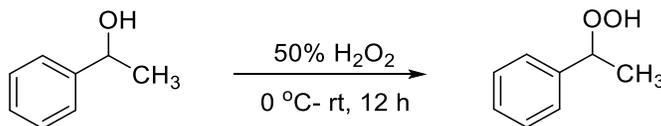
Aldehyde (1.1 equiv) and piperidine (2 equiv) were added to a suspension of oxindole (1 equiv) in ethanol. The solution was heated at $80\text{ }^\circ\text{C}$ for 1.5h. The reaction was cooled to room temperature. The precipitate was filtered, washed with ethanol and dried to afford the product as a coloured solid.

2.2 General procedure for the synthesis of substrates 1y-1ab²



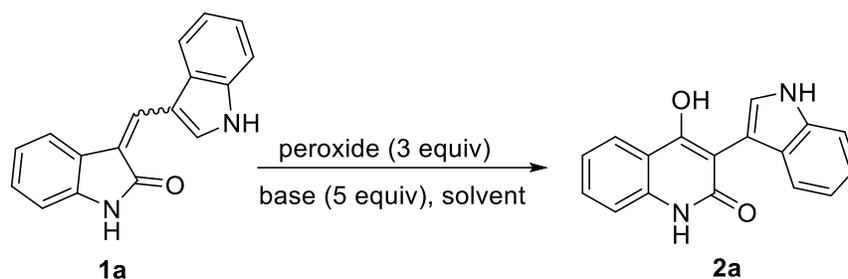
A suitable ketone (1.126 mmol) and piperidine (0.225 mmol) were added to a suspension of oxindole (0.751 mmol) in toluene (2 mL). The solution was heated at 110 °C for 4 hours. The reaction was cooled to room temperature, concentrated, and the residue was purified by flash chromatography on silica gel to afford the products (1y-1ab) as a yellow solid.

2.3 Procedure for the synthesis of ethylbenzene hydroperoxides (EBHP)³



At 0 °C, 5 g of MgSO₄ was added to 8 mL of 50% H₂O₂ over 30 min. To this mixture, 1-Phenylethanol (8 mmol) was added dropwise and stirred at 0 °C for 2h. The solution was then stirred at room temperature for a further 12h and then quenched with NaHCO₃. The crude product was extracted with diethyl ether (3x15 mL) and the combined organic extracts dried over MgSO₄. The solvent was removed in *vacuo*, and the product purified by column chromatography.

3. Table S1: Optimization of reaction conditions^a

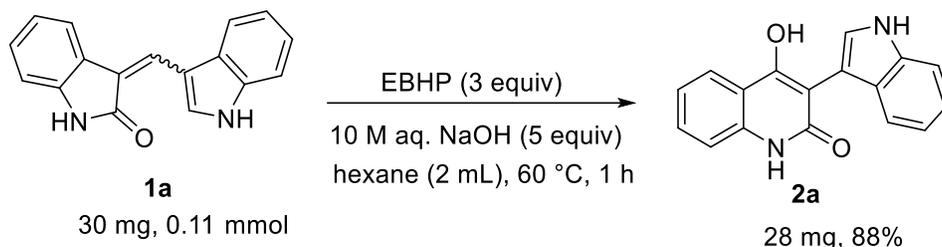


entry	Peroxide	base	temp (°C)	time (h)	solvent	yield (%) ^b
1 ^c	EBHP	10 M NaOH	rt	24	xylene	06
2 ^d	EBHP	10 M NaOH	70	24	xylene	13
3 ^e	EBHP	10 M NaOH	90	24	xylene	27
4 ^f	EBHP	10 M NaOH	110	24	xylene	26
5	EBHP	10 M NaOH	90	1	xylene	75
6	-	10 M NaOH	90	1	xylene	-
7	70% TBHP	10 M NaOH	90	1	xylene	47
8	30% H ₂ O ₂	10 M NaOH	90	1	xylene	-
9 ^g	EBHP	10 M NaOH	90	1	xylene	56
10 ^h	EBHP	10 M NaOH	90	1	xylene	38
11 ⁱ	EBHP	10 M NaOH	90	1	xylene	70
12	EBHP	10 M KOH	90	1	xylene	70
13	EBHP	10 M LiOH	90	1	xylene	35
14	EBHP	10 M NaOH	90	1	<i>p</i> -xylene	60
15	EBHP	10 M NaOH	90	1	<i>o</i> -xylene	57
16	EBHP	10 M NaOH	70	1	ethanol	76
17	EBHP	10 M NaOH	60	1	hexane	88
18	EBHP	10 M NaOH	60	3	hexane	79
19	EBHP	1.0 M NaOH	60	1	hexane	-
20	EBHP	2.5 M NaOH	60	1	hexane	trace
21	EBHP	5.0 M NaOH	60	1	hexane	70
22	EBHP	7.5 M NaOH	60	1	hexane	79

^aReaction condition: Substrate **1a** (30 mg, 0.11 mmol), peroxide (3 equiv), base (5 equiv), solvent (2 mL). ^bIsolated yield. ^{c,d,e,f}3 equiv NaOH was used. ^g2 equiv EBHP was used. ^h1 equiv EBHP was used. ⁱ7 equiv NaOH was used. EBHP = ethylbenzene hydroperoxide, TBHP = *tert*-butyl hydroperoxide.

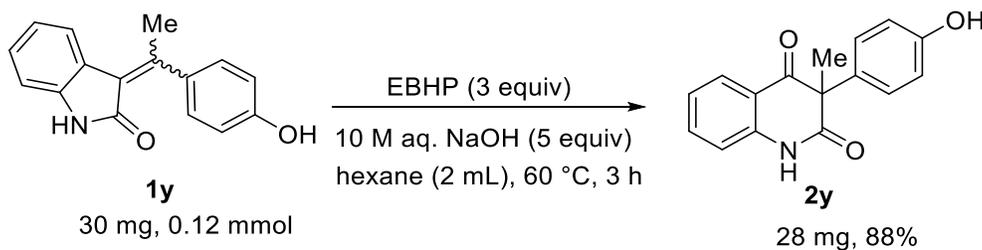
4. Representative protocols for the synthesis of 4-hydroxy-3-(1*H*-indol-3-yl)quinolin-2(1*H*)-one (2a) and 3-(4-hydroxyphenyl)-3-methylquinoline-2,4(1*H*,3*H*)-dione (2y)

4.1. Representative protocol for the synthesis of 4-hydroxy-3-(1*H*-indol-3-yl)quinolin-2(1*H*)-one (2a)



Substrate **1a** (30 mg, 0.11 mmol, 1 equiv.) was taken in a 10 mL RB flask, 2 mL hexane was added, followed by EBHP (0.33 mmol, 3 equiv) and a 10 M aqueous solution of NaOH (0.55 mmol, 5 equiv) at room temperature. The reaction mixture was stirred at 60° C for an hour. The reaction was cooled to room temperature, water was added and then acidified with dilute HCl. The crude product was extracted with ethyl acetate (3x15 mL). The combined organic layer was dried over anhydrous Na₂SO₄, and the solvent was removed in *vacuo*. The product was purified by silica gel chromatography using hexane/ethyl acetate (40/60) as an eluent to give the desired product as a white solid (28 mg, 88%).

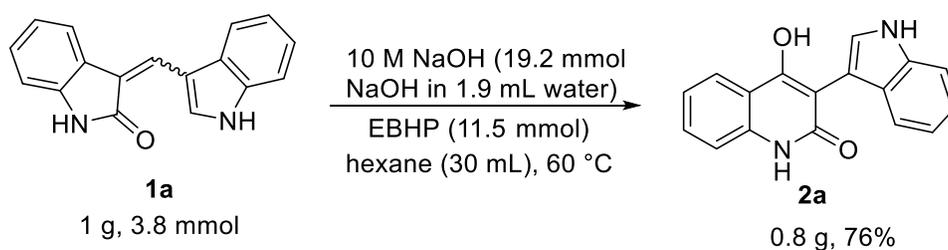
4.2. Representative protocol for the synthesis of 3-(4-hydroxyphenyl)-3-methylquinoline-2,4(1*H*,3*H*)-dione (2y)



Substrate **1y** (30 mg, 0.12 mmol, 1 equiv) was taken in a 10 mL RB flask, 2 mL hexane was added, followed by EBHP (0.33 mmol, 3 equiv) and a 10 M aqueous solution of NaOH (0.55 mmol, 5

equiv) at room temperature. The reaction mixture was stirred at 60° C for 3 hours. The reaction was cooled to room temperature, water was added and then acidified with dilute HCl. The crude product was extracted with ethyl acetate (3x15 mL). The combined organic layer was dried over anhydrous Na₂SO₄, and the solvent was removed in *vacuo*. The product was purified by silica gel chromatography using hexane/ethyl acetate (70/30) as an eluent to give the desired product as a white solid (28 mg, 88%).

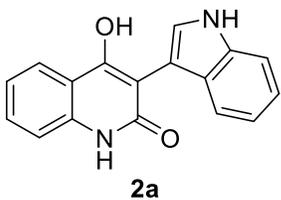
5. Gram scale demonstration of the protocol



30 mL of hexane was added to the 100 mL RB flask containing substrate **1a** (1 g, 3.8 mmol). To the reaction mixture, EBHP (11.5 mmol, 1.4 mL) was added, followed by slow addition of a 10 M aqueous solution of NaOH (19.2 mmol NaOH in 1.9 mL water) at room temperature. The reaction mixture was stirred at 60 °C for an hour. The reaction was cooled to room temperature, water was added and then acidified with dilute HCl. The product was extracted with EtOAc (3 x 30 mL). The combined organic layer was dried over anhydrous Na₂SO₄, and the solvent was removed in *vacuo*. The product was purified by silica gel chromatography using hexane/ethyl acetate (40/60) as an eluent and obtained compound **2a** in 76% (0.806 g) yield as a white solid.

6. Characterization data of 2a-2af

4-hydroxy-3-(1*H*-indol-3-yl)quinolin-2(1*H*)-one (2a)



The title compound was obtained as a white solid (28 mg, 88% yield) *via* column chromatography on a silica gel (hexane/ethyl acetate = 2:3, v/v); mp: 269 °C (decomposition).

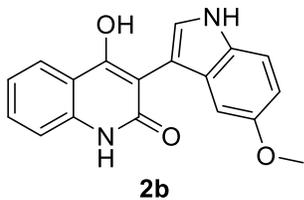
IR (neat, cm⁻¹): 3438, 3320, 3010, 2921, 2628, 1637, 1603, 1542, 1496, 1400, 1243, 1160, 1100, 910, 756.

¹H NMR (500 MHz, Acetone-d₆): δ 11.08 (br s, 1H), 10.52 (s, 1H), 8.53 (br s, 1H), 7.99 (d, *J* = 8.0 Hz, 1H), 7.52 - 7.38 (m, 5H), 7.22 (t, *J* = 7.5 Hz, 1H), 7.14 (t, *J* = 7.5 Hz, 1H), 7.02 (t, *J* = 7.5 Hz, 1H).

¹³C NMR (125 MHz, Acetone-d₆): δ 164.0, 158.8, 139.2, 137.6, 131.1, 128.4, 127.5, 124.0, 122.2, 122.1, 121.0, 119.9, 116.3, 115.7, 112.3, 106.7, 106.5.

HRMS (ESI-Orbitrap) m/z: [M+H]⁺ calcd. for C₁₇H₁₃N₂O₂ 277.0977, found 277.0982.

4-hydroxy-3-(5-methoxy-1*H*-indol-3-yl)quinolin-2(1*H*)-one (2b)



The title compound was obtained as a white solid (25 mg, 80% yield) *via* column chromatography on a silica gel (hexane/ethyl acetate = 2:3, v/v); mp: 214 °C (decomposition).

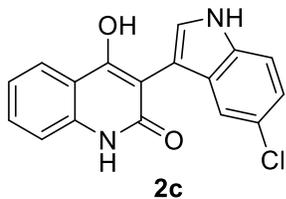
IR (neat, cm⁻¹): 3619, 3317, 3125, 2925, 2855, 1638, 1604, 1488, 1397, 1280, 1215, 1107, 1032, 757.

¹H NMR (500 MHz, Acetone-d₆): δ 10.79 (br s, 1H), 10.36 (s, 1H), 8.43 (br s, 1H), 7.99 (d, *J* = 8.0 Hz, 1H), 7.52 (t, *J* = 7.5 Hz, 1H), 7.45 (s, 1H), 7.41 (d, *J* = 8.5 Hz, 1H), 7.34 (d, *J* = 8.5 Hz, 1H), 7.22 (t, *J* = 7.5 Hz, 1H), 6.90 (s, 1H), 6.79 (d, *J* = 9.0 Hz, 1H), 3.73 (s, 3H).

¹³C NMR (125 MHz, Acetone-d₆): δ 163.8, 158.6, 155.0, 139.1, 132.6, 131.0, 128.9, 128.0, 124.0, 122.0, 116.3, 115.6, 112.8, 112.5, 106.8, 106.2, 102.7, 55.8.

HRMS (ESI-Orbitrap) m/z: [M+H]⁺ calcd. for C₁₈H₁₅N₂O₃ 307.1082, found 307.1075.

3-(5-chloro-1H-indol-3-yl)-4-hydroxyquinolin-2(1H)-one (2c)



The title compound was obtained as a white solid (22 mg, 70% yield) *via* column chromatography on a silica gel (hexane/ethyl acetate = 2:3, v/v); mp: 283 - 285 °C.

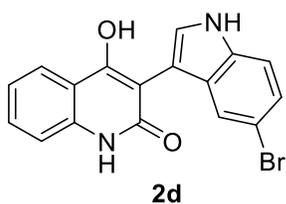
IR (neat, cm⁻¹): 3526, 3288, 2928, 2862, 2360, 1641, 1601, 1465, 1358, 1286, 1103, 1039, 742.

¹H NMR (500 MHz, DMSO-d₆): δ 11.44 (s, 1H), 11.42 (s, 1H), 9.85 (br s, 1H), 7.94 (d, *J* = 7.5 Hz, 1H), 7.54 (d, *J* = 2.5 Hz, 1H), 7.50 (t, *J* = 7.5 Hz, 1H), 7.44 (d, *J* = 8.5 Hz, 1H), 7.32 (d, *J* = 8.0 Hz, 1H), 7.28 (d, *J* = 2.0 Hz, 1H), 7.19 (t, *J* = 7.5 Hz, 1H), 7.10 (dd, *J* = 8.5, 2.0 Hz, 1H).

¹³C NMR (125 MHz, DMSO-d₆): δ 162.8, 157.5, 137.8, 134.6, 130.2, 128.7, 128.5, 123.1, 122.9, 121.1, 120.5, 119.6, 115.4, 114.8, 112.9, 105.9, 105.7.

HRMS (ESI-Orbitrap) m/z: [M+H]⁺ calcd. for C₁₇H₁₂ClN₂O₂ 311.0587, found 311.0587.

3-(5-bromo-1H-indol-3-yl)-4-hydroxyquinolin-2(1H)-one (2d)



The title compound was obtained as a white solid (24 mg, 77% yield) *via* column chromatography on a silica gel (hexane/ethyl acetate = 2:3, v/v); mp: 209 - 211 °C.

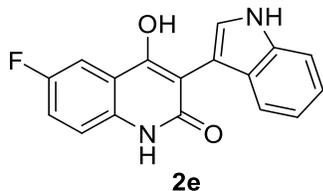
IR (neat, cm⁻¹): 3574, 3372, 3282, 2925, 2854, 1641, 1604, 1463, 1287, 1235, 1091, 966, 757.

¹H NMR (500 MHz, DMSO-d₆): δ 11.45 (s, 1H), 11.42 (s, 1H), 9.85 (br s, 1H), 7.94 (d, *J* = 7.5 Hz, 1H), 7.52-7.49 (m, 2H), 7.42 - 7.39 (m, 2H), 7.32 (d, *J* = 8.5 Hz, 1H), 7.22 - 7.17 (m, 2H).

¹³C NMR (125 MHz, DMSO-d₆): δ 162.8, 157.5, 137.8, 134.8, 130.1, 129.2, 128.5, 123.0, 122.9, 122.5, 121.1, 115.4, 114.8, 113.4, 111.1, 105.8, 105.6.

HRMS (ESI-Orbitrap) m/z: [M+H]⁺ calcd. for C₁₇H₁₂BrN₂O₂ 355.0082, found 355.0100.

3-(5-fluoro-1H-indol-3-yl)-4-hydroxyquinolin-2(1H)-one (2e)



The title compound was obtained as a white solid (25 mg, 79% yield) *via* column chromatography on a silica gel (hexane/ethyl acetate = 2:3, v/v); mp: 291 - 293 °C.

IR (neat, cm⁻¹): 3534, 3277, 2969, 2931, 2555, 2368, 2254, 1607, 1500, 1443, 1370, 1255, 1180, 1095, 818, 730.

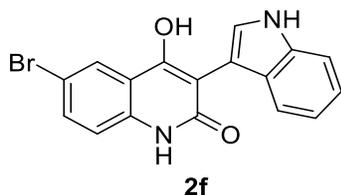
¹H NMR (500 MHz, DMSO-d₆): δ 11.48 (s, 1H), 11.28 (s, 1H), 9.85 (s, 1H), 7.63 (d, *J* = 9.5 Hz, 1H), 7.47 - 7.29 (m, 5H), 7.09 (t, *J* = 7.0 Hz, 1H), 6.97 (t, *J* = 7.0 Hz, 1H).

¹³C NMR (125 MHz, DMSO-d₆): δ 162.6, 156.8 (d, ¹*J*_{C-F} = 235.1 Hz), 156.3, 136.0, 134.4, 127.1, 127.0, 120.6, 120.4, 118.4, 117.9 (d, ²*J*_{C-F} = 24.2 Hz), 116.6 (d, ³*J*_{C-F} = 8.2 Hz), 116.4 (d, ³*J*_{C-F} = 8.2 Hz), 111.4, 107.9 (d, ²*J*_{C-F} = 23.7 Hz), 107.4, 105.6.

¹⁹F NMR (371 MHz, DMSO-d₆): δ 121.4

HRMS (ESI-Orbitrap) m/z: [M+H]⁺ calcd. for C₁₇H₁₂FN₂O₂ 295.0882, found 295.0888.

6-bromo-4-hydroxy-3-(1H-indol-3-yl)quinolin-2(1H)-one (2f)



The title compound was obtained as a pale yellow solid (27 mg, 85% yield) *via* column chromatography on a silica gel (hexane/ethyl acetate = 2:3, v/v); mp: 293 - 295 °C.

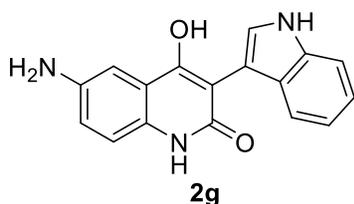
IR (neat, cm⁻¹): 3558, 3310, 3251, 2967, 2523, 2165, 1629, 1592, 1358, 1234, 1118, 865, 730.

¹H NMR (500 MHz, DMSO-d₆): δ 11.54 (s, 1H), 11.27 (s, 1H), 9.92 (br s, 1H), 8.02 (s, 1H), 7.64 (d, *J* = 7.0 Hz, 1H), 7.47 - 7.42 (m, 2H), 7.30 - 7.26 (m, 2H), 7.12 - 7.09 (m, 1H), 6.99 - 6.98 (m, 1H).

¹³C NMR (125 MHz, DMSO-d₆): δ 162.7, 156.0, 136.7, 136.1, 132.5, 127.1, 127.0, 125.0, 120.7, 120.4, 118.5, 117.4, 117.0, 112.8, 111.4, 107.5, 105.5.

HRMS (ESI-Orbitrap) m/z: [M+H]⁺ calcd. for C₁₇H₁₂BrN₂O₂ 355.0082, found 355.0076.

6-amino-4-hydroxy-3-(1H-indol-3-yl)quinolin-2(1H)-one (2g)



The title compound was obtained as a pale brown solid (27 mg, 85% yield) *via* filtration; mp: 330 - 332 °C.

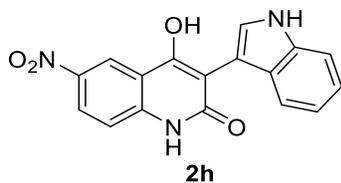
IR (neat, cm⁻¹): 3409, 3356, 3263, 2959, 2922, 1630, 1597, 1564, 1465, 1262, 1098, 1036, 805, 749.

¹H NMR (500 MHz, DMSO-d₆): δ 11.29 (s, 1H), 10.99 (s, 1H), 9.21 (br s, 1H), 7.41 - 7.38 (m, 2H), 7.26 (d, *J* = 7.5 Hz, 1H), 7.08 - 7.03 (m, 3H), 6.94 (t, *J* = 7.0 Hz, 1H), 6.82 (d, *J* = 8.5 Hz, 1H), 4.95 (br s, 2H).

¹³C NMR (125 MHz, DMSO-d₆): δ 162.1, 156.9, 142.8, 136.1, 129.6, 127.4, 126.7, 120.5, 120.3, 118.9, 118.3, 116.2, 115.3, 111.3, 106.1, 105.7, 105.3.

HRMS (ESI-Orbitrap) m/z: [M+H]⁺ calcd. for C₁₇H₁₄N₃O₂ 292.1086, found 292.1088.

4-hydroxy-3-(1H-indol-3-yl)-6-nitroquinolin-2(1H)-one (2h)



The title compound was obtained as a pale orange coloured solid (19 mg, 60% yield) *via* column chromatography on a silica gel (hexane/ethyl acetate = 2:3, v/v); mp: 299 - 301 °C.

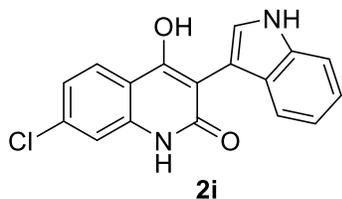
IR (neat, cm⁻¹): 3434, 3386, 2921, 1662, 1616, 1582, 1516, 1478, 1337, 1293, 1114, 1071, 827, 734.

¹H NMR (500 MHz, DMSO-d₆): δ 12.02 (s, 1H), 11.32 (s, 1H), 10.39 (br s, 1H), 8.77 (d, *J* = 2.5 Hz, 1H), 8.34 (dd, *J* = 9.0, 2.5 Hz, 1H), 7.51 - 7.44 (m, 3H), 7.32 (d, *J* = 8.0 Hz, 1H), 7.12 (t, *J* = 7.0 Hz, 1H), 7.00 (t, *J* = 7.5 Hz, 1H).

¹³C NMR (125 MHz, DMSO-d₆): δ 163.1, 156.6, 142.0, 141.2, 136.1, 127.2, 127.0, 124.8, 120.8, 120.3, 119.6, 118.6, 115.7, 115.5, 111.5, 108.1, 105.0.

HRMS (ESI-Orbitrap) m/z: [M+H]⁺ calcd. for C₁₇H₁₂N₃O₄ 322.0827, found 322.0827.

7-chloro-4-hydroxy-3-(1H-indol-3-yl)quinolin-2(1H)-one (2i)



The title compound was obtained as a pale brown solid (26 mg, 82% yield) *via* column chromatography on a silica gel (hexane/ethyl acetate = 2:3, v/v); mp: 291 - 293 °C.

IR (neat, cm⁻¹): 3439, 3315, 3280, 2923, 2629, 1685, 1619, 1426, 1377, 1213, 1107, 755.

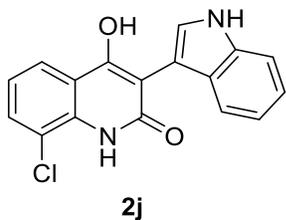
¹H NMR (500 MHz, DMSO-d₆): δ 11.49 (s, 1H), 11.26 (s, 1H), 9.86 (br s, 1H), 7.90 (d, *J* = 8.5 Hz, 1H), 7.45-7.42 (m, 2H), 7.34 (s, 1H),

7.29 (d, *J* = 7.5 Hz, 1H), 7.22 (d, *J* = 8.5 Hz, 1H), 7.10 (t, *J* = 7.0 Hz, 1H), 6.98 (t, *J* = 7.5 Hz, 1H).

¹³C NMR (125 MHz, DMSO-d₆): δ 162.9, 156.8, 138.6, 136.1, 134.3, 127.2, 126.9, 124.9, 121.2, 120.7, 120.3, 118.5, 114.5, 113.9, 111.4, 106.6, 105.4.

HRMS (ESI-Orbitrap) m/z: [M+H]⁺ calcd. for C₁₇H₁₂ClN₂O₂ 311.0587, found 311.0586.

8-chloro-4-hydroxy-3-(1H-indol-3-yl)quinolin-2(1H)-one (2j)



The title compound was obtained as a white solid (28 mg, 90% yield) *via* column chromatography on a silica gel (hexane/ethyl acetate = 2:3, v/v); mp: 280 °C (decomposition).

IR (neat, cm⁻¹): 3561, 3343, 3294, 2927, 1638, 1524, 1397, 1264, 1102, 1029, 803, 746.

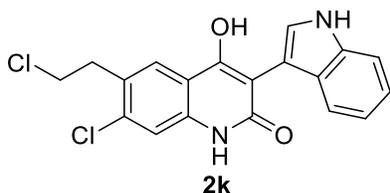
¹H NMR (500 MHz, DMSO-d₆): δ 11.29 (s, 1H), 10.49 (s, 1H), 9.99 (br s, 1H), 7.92 (d, *J* = 7.5 Hz, 1H), 7.66 (d, *J* = 7.5 Hz, 1H), 7.48 - 7.44

(m, 2H), 7.30 (d, *J* = 7.5 Hz, 1H), 7.22 (t, *J* = 7.5 Hz, 1H), 7.12 (t, *J* = 7.0 Hz, 1H), 6.99 (t, *J* = 7.0 Hz, 1H).

¹³C NMR (125 MHz, DMSO-d₆): δ 162.7, 157.1, 136.1, 134.0, 130.1, 127.2, 127.0, 122.3, 121.8, 120.8, 120.2, 118.6, 118.0, 117.6, 111.5, 107.0, 105.3.

HRMS (ESI-Orbitrap) m/z: [M+H]⁺ calcd. for C₁₇H₁₂ClN₂O₂ 311.0587, found 311.0594.

7-chloro-6-(2-chloroethyl)-4-hydroxy-3-(1*H*-indol-3-yl)quinolin-2(1*H*)-one (2k)



The title compound was obtained as a pale yellow solid (25 mg, 80% yield) *via* column chromatography on a silica gel (hexane/ethyl acetate =1:1, v/v); mp: 302 - 304 °C

IR (neat, cm⁻¹): 3437, 3314, 3282, 2924, 2627, 1684, 1617, 1425, 1374, 1215, 1108, 754.

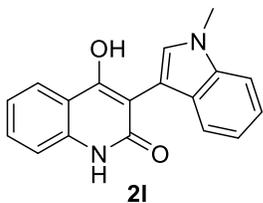
¹H NMR (500 MHz, DMSO-d₆): δ 11.45 (s, 1H), 11.27 (s, 1H), 9.85 (br s, 1H), 7.91 (s, 1H), 7.44 - 7.42 (m, 2H), 7.36 (s, 1H),

7.28 (d, *J* = 8.0 Hz, 1H), 7.10 (t, *J* = 7.5 Hz, 1H), 6.97 (t, *J* = 7.5 Hz, 1H), 3.87 (t, *J* = 7.0 Hz, 2H), 3.21 (t, *J* = 7.0 Hz, 2H).

¹³C NMR (125 MHz, DMSO-d₆): δ 162.8, 156.6, 137.4, 136.1, 134.6, 127.8, 127.1, 127.0, 125.6, 120.7, 120.2, 118.5, 114.8, 114.7, 111.4, 106.7, 105.4, 43.9, 35.4.

HRMS (ESI-Orbitrap) m/z: [M+H]⁺ calcd. for C₁₉H₁₅Cl₂N₂O₂ 373.0511, found 373.0523.

4-hydroxy-3-(1-methyl-1*H*-indol-3-yl)quinolin-2(1*H*)-one (2l)



The title compound was obtained as a white solid (12 mg, 38% yield) *via* column chromatography on a silica gel (hexane/ethyl acetate = 3:2, v/v); mp: 279 - 281 °C.

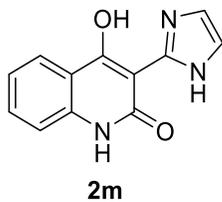
IR (neat, cm⁻¹): 3547, 3360, 2918, 1634, 1594, 1469, 1400, 1206, 1161, 886, 729.

¹H NMR (500 MHz, DMSO-d₆): δ 11.40 (s, 1H), 9.71 (br s, 1H), 7.91 (d, *J* = 7.5 Hz, 1H), 7.50 - 7.45 (m, 3H), 7.31 (d, *J* = 8.5 Hz, 1H), 7.18 (t, *J* = 7.5 Hz, 1H), 7.02 (t, *J* = 7.5 Hz, 1H), 3.85 (s, 3H).

¹³C NMR (125 MHz, DMSO-d₆): δ 162.9, 157.3, 137.8, 136.6, 131.1, 130.0, 127.6, 122.9, 121.0, 120.8, 120.5, 118.6, 115.5, 114.7, 109.5, 105.8, 105.0, 32.5.

HRMS (ESI-Orbitrap) m/z: [M+H]⁺ calcd. for C₁₈H₁₅N₂O₂ 291.1133, found 291.1141.

4-hydroxy-3-(1H-imidazol-2-yl)quinolin-2(1H)-one (2m)



The title compound was obtained as a white solid (31 mg, 97 % yield) *via* filtration; mp: 335 - 337 °C.

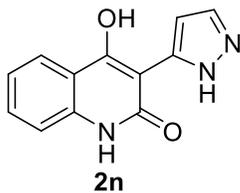
IR (neat, cm⁻¹): 3492, 3385, 3314, 3273, 2968, 2357, 1633, 1598, 1526, 1357, 1262, 1028, 850, 750.

¹H NMR (500 MHz, DMSO-d₆): δ 13.03 (br s, 2H), 10.74 (s, 1H), 8.01 (d, *J* = 7.5 Hz, 1H), 7.46 (t, *J* = 7.0 Hz, 1H), 7.24 - 7.21 (m, 3H), 7.11 (t, *J* = 7.5 Hz, 1H).

¹³C NMR (125 MHz, DMSO-d₆): δ 174.7, 163.8, 145.6, 139.3, 132.1, 125.4, 121.6, 120.7, 116.0, 115.6, 91.1.

HRMS (ESI-Orbitrap) m/z: [M+H]⁺ calcd. for C₁₂H₁₀N₃O₂ 228.0773, found 228.0773.

4-hydroxy-3-(1H-pyrazol-5-yl)quinolin-2(1H)-one (2n)



The title compound was obtained as a white solid (30 mg, 95 % yield) *via* filtration; mp: 316 - 318 °C.

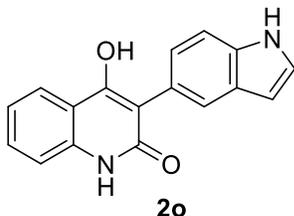
IR (neat, cm⁻¹): 3480, 3380, 3277, 2960, 2931, 2374, 1644, 1604, 1455, 1388, 1047, 820, 785.

¹H NMR (500 MHz, DMSO-d₆): δ 13.86 (br s, 1H), 13.46 (br s, 1H), 11.53 (s, 1H), 7.96 - 7.94 (m, 2H), 7.52 (t, *J* = 7.5 Hz, 1H), 7.34 - 7.31 (m, 2H), 7.20 (t, *J* = 7.0 Hz, 1H).

¹³C NMR (125 MHz, DMSO-d₆): δ 161.4, 160.3, 147.9, 137.6, 131.0, 129.0, 123.0, 121.4, 115.0, 114.5, 105.0, 100.7

HRMS (ESI-Orbitrap) m/z: [M+H]⁺ calcd. for C₁₂H₁₀N₃O₂ 228.0773, found 228.0773.

4-hydroxy-3-(1*H*-indol-5-yl)quinolin-2(1*H*)-one (2o)



The title compound was obtained as a white solid (24 mg, 75% yield) *via* column chromatography on a silica gel (hexane/ethyl acetate = 2:3, v/v); mp: 292 - 294 °C.

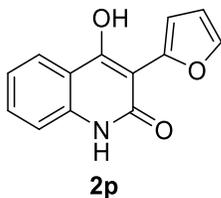
IR (neat, cm⁻¹): 3451, 3370, 3264, 2924, 1640, 1601, 1464, 1261, 1098, 1029, 799.

¹H NMR (500 MHz, DMSO-*d*₆): δ 11.40 (s, 1H), 11.07 (s, 1H), 9.68 (s, 1H), 7.90 (d, *J* = 8.0 Hz, 1H), 7.50 - 7.47 (m, 2H), 7.41 (d, *J* = 8.0 Hz, 1H), 7.34 (s, 1H), 7.29 (d, *J* = 8.0 Hz, 1H), 7.16 (t, *J* = 7.5 Hz, 1H), 7.05 (d, *J* = 8.0 Hz, 1H), 6.44 (s, 1H).

¹³C NMR (125 MHz, DMSO-*d*₆): δ 163.2, 156.8, 137.8, 135.2, 130.1, 127.6, 125.1, 124.5, 123.1, 123.0, 122.7, 121.0, 115.6, 114.7, 113.7, 110.8, 101.2.

HRMS (ESI-Orbitrap) m/z: [M+H]⁺ calcd. for C₁₇H₁₃N₂O₂ 277.0977, found 277.0976.

3-(furan-2-yl)-4-hydroxyquinolin-2(1*H*)-one (2p)



The title compound was obtained as a white solid (16 mg, 48% yield) *via* column chromatography on a silica gel (hexane/ethyl acetate = 1:1, v/v); mp: 195 °C (decomposition).

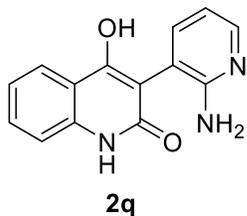
IR (neat, cm⁻¹): 3444, 3354, 2921, 2876, 1653, 1613, 1481, 1423, 1301, 1152, 814, 748.

¹H NMR (500 MHz, DMSO-*d*₆): δ 11.56 (s, 1H), 10.36 (br s, 1H), 7.96 (d, *J* = 8.0 Hz, 1H), 7.72 (s, 1H), 7.52 (t, *J* = 7.5 Hz, 1H), 7.30 (d, *J* = 8.0 Hz, 1H), 7.20 (t, *J* = 7.5 Hz, 1H), 6.96 (d, *J* = 3.0 Hz, 1H), 6.59 (s, 1H).

¹³C NMR (125 MHz, DMSO-*d*₆): δ 160.8, 157.4, 147.4, 141.5, 137.6, 131.0, 123.2, 121.4, 114.9, 111.0, 102.4.

HRMS (ESI-Orbitrap) m/z: [M+H]⁺ calcd. for C₁₃H₁₀NO₃ 228.0660, found 228.0661.

3-(2-aminopyridin-3-yl)-4-hydroxyquinolin-2(1H)-one (2q)



The title compound was obtained as a white solid (23 mg, 72% yield) *via* column chromatography on a silica gel (chloroform/methanol = 3:1, v/v); mp: 396 - 398 °C.

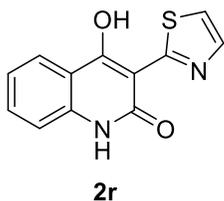
IR (neat, cm⁻¹): 3418, 3410, 3348, 3026, 2927, 2632, 1635, 1567, 1544, 1472, 1428, 1246, 1178, 1124, 893, 757.

¹H NMR (500 MHz, DMSO-d₆): δ 11.24 (s, 1H), 7.97 – 7.92 (m, 2H), 7.50 - 7.45 (m, 2H), 7.28 (d, *J* = 8.0 Hz, 1H), 7.12 (t, *J* = 7.5 Hz, 1H), 6.70 (t, *J* = 6.0 Hz, 1H).

¹³C NMR (125 MHz, DMSO-d₆): δ 162.6, 160.2, 157.0, 144.1, 141.2, 138.5, 130.4, 123.5, 120.8, 116.3, 115.1, 114.8, 112.3, 107.2.

HRMS (ESI-Orbitrap) m/z: [M+H]⁺ calcd. for C₁₄H₁₂N₃O₂ 254.0930, found 254.0932.

4-hydroxy-3-(thiazol-2-yl)quinolin-2(1H)-one (2r)



The title compound was obtained as a pale yellow solid (12 mg, 36% yield) *via* column chromatography on a silica gel (hexane/ethyl acetate = 4:1, v/v); mp: 198 - 200 °C.

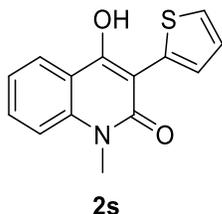
IR (neat, cm⁻¹): 3486, 3387, 3275, 2964, 2353, 1632, 1594, 1525, 1354, 1260, 1024, 856, 756.

¹H NMR (500 MHz, DMSO-d₆): δ 12.89 (br s, 1H), 12.55 (s, 1H), 8.10 - 8.09 (m, 2H), 7.97 (d, *J* = 2.5 Hz, 1H), 7.56 (d, *J* = 8.0 Hz, 1H), 7.27 (t, *J* = 7.5 Hz, 1H) 7.20 (t, *J* = 7.5 Hz, 1H).

¹³C NMR (125 MHz, DMSO-d₆): δ 166.3, 156.8, 142.3, 135.7, 135.6, 126.9, 123.9, 123.7, 122.0, 121.7, 112.4, 104.9.

HRMS (ESI-Orbitrap) m/z: [M+Na]⁺ calcd. for C₁₂H₈N₂NaO₂S 267.0204, found 267.0207.

4-hydroxy-1-methyl-3-(thiophen-2-yl)quinolin-2(1H)-one (2s)



The title compound was obtained as a white solid (10 mg, 31% yield) *via* column chromatography on a silica gel (hexane/ethyl acetate = 7:3, v/v); mp: 190 - 192 °C.

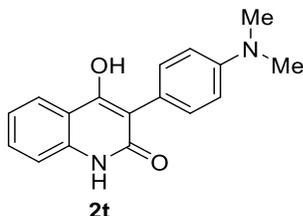
IR (neat, cm⁻¹): 3461, 2946, 1608, 1576, 1506, 1462, 1394, 1240, 1157, 961, 848, 751.

¹H NMR (500 MHz, CDCl₃): δ 8.03 (d, *J* = 8.0 Hz, 1H), 7.58 (t, *J* = 8.0 Hz, 1H), 7.49 (d, *J* = 5.5 Hz, 1H), 7.34 (d, *J* = 8.5 Hz, 1H), 7.25 - 7.22 (m, 2H), 7.12 (t, *J* = 4.0 Hz, 1H), 6.82 (br s, 1H), 3.70 (s, 3H).

¹³C NMR (125 MHz, CDCl₃): δ 162.0, 156.5, 139.3, 133.3, 131.7, 128.4, 127.4, 126.9, 124.4, 122.1, 115.2, 114.1, 105.5, 29.9.

HRMS (ESI-Orbitrap) m/z: [M+H]⁺ calcd. for C₁₄H₁₂NO₂S 258.0588, found 258.0594.

3-(4-(dimethylamino)phenyl)-4-hydroxyquinolin-2(1H)-one (2t)



The title compound was obtained as a white solid (29 mg, 92% yield) *via* filtration; mp: 323 - 325 °C.

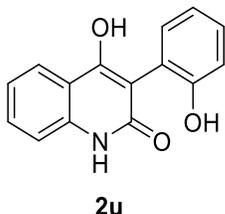
IR (neat, cm⁻¹): 3504, 3320, 2956, 2923, 1640, 1596, 1525, 1363, 1217, 1144, 1105, 865, 800, 757.

¹H NMR (500 MHz, DMSO-d₆): δ 11.32 (s, 1H), 7.89 (d, *J* = 7.5 Hz, 1H), 7.45 (t, *J* = 7.5 Hz, 1H), 7.26 - 7.21 (m, 3H), 7.14 (t, *J* = 7.5 Hz, 1H), 6.76 (d, *J* = 8.5 Hz, 2H), 2.92 (s, 6H).

¹³C NMR (125 MHz, DMSO-d₆): δ 163.0, 157.0, 149.4, 137.7, 131.7, 130.0, 123.0, 120.9, 120.7, 115.8, 114.7, 112.4, 111.8, 40.2.

HRMS (ESI-Orbitrap) m/z: [M+H]⁺ calcd. for C₁₇H₁₇N₂O₂ 281.1290, found 281.1323.

4-hydroxy-3-(2-hydroxyphenyl)quinolin-2(1H)-one (2u)



The title compound was obtained as a white solid (19 mg, 59% yield) *via* column chromatography on a silica gel (hexane/ethyl acetate = 3:2, v/v); mp: 294 - 296 °C.

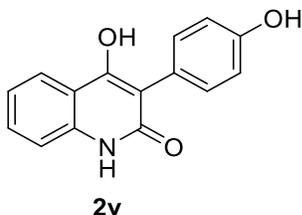
IR (neat, cm⁻¹): 3602, 3507, 3346, 3212, 2924, 2852, 1715, 1621, 1458, 1368, 1262, 1079, 845, 742.

¹H NMR (500 MHz, DMSO-d₆): δ 11.44 (s, 1H), 9.50 (br s, 2H), 7.90 (d, *J* = 8.0 Hz, 1H), 7.50 (t, *J* = 7.5 Hz, 1H), 7.30 (d, *J* = 8.5 Hz, 1H), 7.18 (t, *J* = 7.5 Hz, 2H), 7.12 (d, *J* = 7.0 Hz, 1H), 6.89 (d, *J* = 8.0 Hz, 1H), 6.83 (t, *J* = 7.5 Hz, 1H).

¹³C NMR (125 MHz, DMSO-d₆): δ 162.9, 157.9, 155.8, 138.1, 132.8, 130.4, 128.6, 123.1, 121.1, 120.2, 118.7, 116.0, 115.5, 114.8, 109.6.

HRMS (ESI-Orbitrap) m/z: [M+H]⁺ calcd. for C₁₅H₁₂NO₃ 254.0817, found 254.0819.

4-hydroxy-3-(4-hydroxyphenyl)quinolin-2(1H)-one (2v)



The title compound was obtained as a white solid (29 mg, 92% yield) *via* column chromatography on a silica gel (hexane/ethyl acetate = 2:3, v/v); mp: 290 - 292 °C.

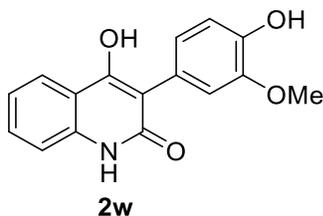
IR (neat, cm⁻¹): 3605, 3509, 3332, 3207, 2928, 2857, 1718, 1612, 1467, 1371, 1267, 1083, 849, 744.

¹H NMR (500 MHz, DMSO-d₆): δ 11.39 (s, 1H), 9.82 (br s, 1H), 9.40 (s, 1H), 7.91 (d, *J* = 8.0 Hz, 1H), 7.48 (t, *J* = 8.0 Hz, 1H), 7.28 (d, *J* = 8.0 Hz, 1H), 7.18 - 7.14 (m, 3H), 6.80 (d, *J* = 8.0 Hz, 2H).

¹³C NMR (125 MHz, DMSO-d₆): δ 162.9, 156.9, 156.3, 137.8, 132.2, 130.2, 123.3, 123.0, 121.0, 115.5, 114.8, 114.7, 112.5.

HRMS (ESI-Orbitrap) m/z: [M+H]⁺ calcd. for C₁₅H₁₂NO₃ 254.0817, found 254.0821.

4-hydroxy-3-(4-hydroxy-3-methoxyphenyl)quinolin-2(1H)-one (2w)



The title compound was obtained as a white solid (27 mg, 85% yield) *via* column chromatography on a silica gel (hexane/ethyl acetate = 2:3, v/v); mp: 310 - 312 °C.

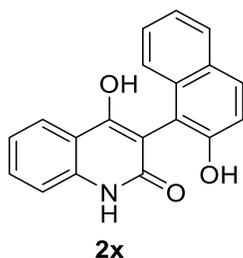
IR (neat, cm⁻¹): 3585, 3457, 3329, 2956, 2923, 2327, 1635, 1564, 1496, 1376, 1240, 1115, 920, 760.

¹H NMR (500 MHz, DMSO-d₆): δ 11.38 (s, 1H), 9.79 (br s, 1H), 8.96 (s, 1H), 7.90 (d, *J* = 8.0 Hz, 1H), 7.48 (t, *J* = 7.5 Hz, 1H), 7.28 (d, *J* = 8.0 Hz, 1H), 7.16 (t, *J* = 7.5 Hz, 1H), 6.89 (s, 1H), 6.82 - 6.76 (m, 2H), 3.76 (s, 3H).

¹³C NMR (125 MHz, DMSO-d₆): δ 162.8, 156.9, 147.0, 145.7, 137.8, 130.3, 123.9, 123.7, 123.0, 121.0, 115.4, 115.4, 115.1, 114.7, 112.5, 55.6.

HRMS (ESI-Orbitrap) m/z: [M+Na]⁺ calcd. for C₁₆H₁₃NNaO₄ 306.0742, found 306.0736.

4-hydroxy-3-(2-hydroxynaphthalen-1-yl)quinolin-2(1H)-one (2x)



The title compound was obtained as a white solid (10 mg, 32% yield) *via* column chromatography on a silica gel (hexane/ethyl acetate = 2:3, v/v); mp: 287 - 289 °C.

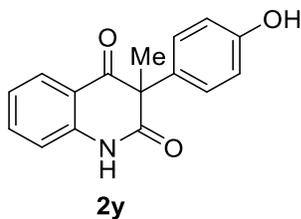
IR (neat, cm⁻¹): 3496, 3341, 2958, 2923, 2361, 1638, 1601, 1433, 1349, 1230, 1106, 816, 750.

¹H NMR (500 MHz, DMSO-d₆): δ 11.39 (s, 1H), 9.66 (s, 1H), 9.27 (s, 1H), 7.90 (d, *J* = 8.0 Hz, 1H), 7.82 - 7.78 (m, 2H), 7.53 (t, *J* = 7.5 Hz, 1H), 7.34 - 7.17 (m, 6H).

¹³C NMR (125 MHz, DMSO-d₆): δ 162.7, 158.7, 153.8, 138.6, 134.3, 130.3, 128.9, 128.2, 127.8, 125.8, 124.1, 123.0, 122.1, 120.9, 118.7, 115.4, 114.8, 112.2, 106.5.

HRMS (ESI-Orbitrap) m/z: [M+Na]⁺ calcd. for C₁₉H₁₃NNaO₃ 326.0793, found 326.0801.

3-(4-hydroxyphenyl)-3-methylquinoline-2,4(1H,3H)-dione (2y)



The title compound was obtained as a white solid (28 mg, 88% yield) *via* column chromatography on a silica gel (hexane/ethyl acetate = 7:3, v/v); mp: 239 - 240 °C.

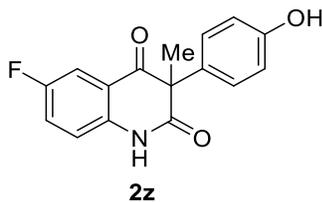
IR (neat, cm⁻¹): 3574, 3325, 3264, 2926, 2858, 1699, 1659, 1608, 1513, 1373, 1265, 1100, 809.

¹H NMR (500 MHz, DMSO-d₆): δ 10.94 (s, 1H), 9.77 (s, 1H), 7.69 (d, *J* = 7.5 Hz, 1H), 7.54 (t, *J* = 7.5 Hz, 1H), 7.09 - 7.04 (m, 2H), 6.98 (d, *J* = 9.0 Hz, 2H), 6.67 (d, *J* = 9.0 Hz, 2H), 1.58 (s, 3H).

¹³C NMR (125 MHz, DMSO-d₆): δ 196.2, 173.3, 157.2, 141.7, 136.6, 130.0, 127.7, 127.6, 123.4, 119.5, 116.7, 116.2, 60.8, 21.0.

HRMS (ESI-Orbitrap) m/z: [M+Na]⁺ calcd. for C₁₆H₁₃NNaO₃ 290.0793, found 290.0797.

6-fluoro-3-(4-Hydroxyphenyl)-3-methylquinoline-2,4(1H,3H)-dione (2z)



The title compound was obtained as a white solid (27 mg, 86% yield) *via* column chromatography on a silica gel (hexane/ethyl acetate = 7:3, v/v); mp: 271 - 273 °C.

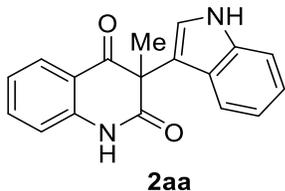
IR (neat, cm⁻¹): 3520, 3273, 2924, 2856, 1730, 1662, 1610, 1494, 1457, 1374, 1273, 1190, 1027, 826.

¹H NMR (500 MHz, DMSO-d₆): δ 11.00 (s, 1H), 9.52 (s, 1H), 7.46 - 7.42 (m, 2H), 7.10 - 7.08 (m, 1H), 6.99 (d, *J* = 8.0 Hz, 2H), 6.68 (d, *J* = 8.5 Hz, 2H), 1.59 (s, 3H).

¹³C NMR (125 MHz, DMSO-d₆): δ 194.7, 172.1, 157.4 (d, ¹*J*_{C-F} = 239.1 Hz), 156.9, 138.1, 129.0, 127.2, 123.0 (d, ²*J*_{C-F} = 23.6 Hz), 120.0 (d, ³*J*_{C-F} = 6.0 Hz), 118.2 (d, ³*J*_{C-F} = 7.5 Hz), 115.6, 112.1 (d, ²*J*_{C-F} = 22.8 Hz), 60.0, 20.4.

HRMS (ESI-Orbitrap) m/z: [M+H]⁺ calcd. for C₁₆H₁₃FNO₃ 286.0879, found 286.0876.

3-(1*H*-indol-3-yl)-3-methylquinoline-2,4(1*H*,3*H*)-dione (2aa)



The title compound was obtained as a white solid (27 mg, 85% yield) *via* column chromatography on silica gel (hexane/ethyl acetate = 3:1, v/v); mp: 224 - 226 °C.

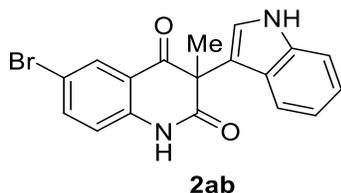
IR (neat, cm⁻¹): 3437, 3325, 3262, 2927, 2529, 2168, 1697, 1658, 1609, 1543, 1497, 1402, 1352, 1237, 1114, 912, 754.

¹H NMR (500 MHz, DMSO-*d*₆): δ 11.09 (s, 1H), 10.98 (s, 1H), 7.73 (d, *J* = 7.5 Hz, 1H), 7.55 (t, *J* = 7.5 Hz, 1H), 7.43 (d, *J* = 7.5 Hz, 1H), 7.34 (d, *J* = 8.0 Hz, 1H), 7.10 - 7.04 (m, 4H), 6.92 (t, *J* = 7.5 Hz, 1H), 1.77 (s, 3H).

¹³C NMR (125 MHz, DMSO-*d*₆): δ 194.9, 172.3, 141.4, 136.5, 135.6, 127.0, 124.7, 123.7, 122.5, 121.3, 119.07, 119.02, 116.1, 112.9, 111.9, 56.4, 19.8.

HRMS (ESI-Orbitrap) m/z: [M+H]⁺ calcd. for C₁₈H₁₄N₂O₂ 291.1134, found 291.1140.

6-bromo-3-(1*H*-indol-3-yl)-3-methylquinoline-2,4(1*H*,3*H*)-dione (2ab)



The title compound was obtained as a white solid (26 mg, 83% yield) *via* column chromatography on silica gel (hexane/ethyl acetate = 3:1, v/v); mp: 285 - 287 °C.

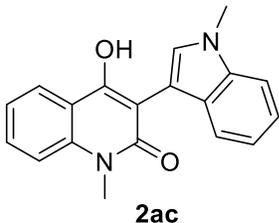
IR (neat, cm⁻¹): 3432, 3324, 3264, 2926, 2524, 2162, 1698, 1657, 1607, 1594, 1356, 1237, 1114, 862, 735.

¹H NMR (500 MHz, DMSO-*d*₆): δ 11.11 (s, 1H), 11.08 (s, 1H), 7.78 (s, 1H), 7.71 (d, *J* = 8.5 Hz, 1H), 7.47 (d, *J* = 8.0 Hz, 1H), 7.34 (d, *J* = 8.5 Hz, 1H), 7.07 - 7.03 (m, 3H), 6.95 (t, *J* = 7.0 Hz, 1H), 1.76 (s, 3H).

¹³C NMR (125 MHz, DMSO-*d*₆): δ 193.5, 172.0, 140.6, 137.8, 136.5, 128.9, 124.6, 123.7, 121.4, 120.8, 119.1, 119.0, 118.4, 113.9, 112.2, 112.0, 56.5, 19.3.

HRMS (ESI-Orbitrap) m/z: [M+H]⁺ calcd. for C₁₈H₁₃BrN₂O₂ 369.0239, found 369.0246.

4-hydroxy-1-methyl-3-(1-methyl-1*H*-indol-3-yl)quinolin-2(1*H*)-one (2ac)



The title compound was obtained as a white solid (8 mg, 25% yield) *via* column chromatography on a silica gel (hexane/ethyl acetate = 3:2, v/v); mp: 277 - 279 °C.

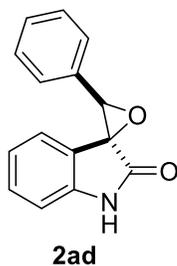
IR (neat, cm⁻¹): 3518, 3437, 3324, 2928, 1622, 1572, 1466, 1377, 1332, 1245, 1158, 739.

¹H NMR (500 MHz, DMSO-*d*₆): δ 9.69 (s, 1H), 8.02 (d, *J* = 8.0 Hz, 1H), 7.63 (t, *J* = 8.0 Hz, 1H), 7.53 (d, *J* = 8.5 Hz, 1H), 7.48 (d, *J* = 8.5 Hz, 1H), 7.43 (s, 1H), 7.30 - 7.26 (m, 2H), 7.17 (t, *J* = 7.5 Hz, 1H), 7.01 (t, *J* = 7.0 Hz, 1H), 3.85 (s, 3H), 3.64 (s, 3H).

¹³C NMR (125 MHz, DMSO-*d*₆): δ 162.1, 156.3, 138.7, 136.6, 131.0, 130.5, 127.7, 123.3, 121.3, 120.8, 120.4, 118.5, 116.2, 114.2, 109.6, 105.4, 105.3, 32.5, 29.3.

HRMS (ESI-Orbitrap) m/z: [M+H]⁺ calcd. for C₁₉H₁₇N₂O₂ 305.1290, found 305.1295.

3'-phenylspiro[indoline-3,2'-oxiran]-2-one (2ad)



The title compound was obtained as a white solid (27 mg, 85%) *via* column chromatography on a silica gel (hexane/ethyl acetate = 7:3, v/v); mp: 157 - 159 °C.

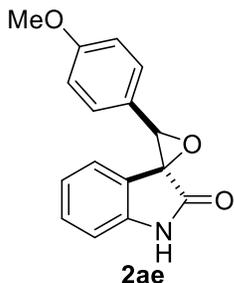
IR (neat, cm⁻¹): 3208, 2981, 1716, 1625, 1607, 1516, 1468, 1345, 1245, 1222, 1016, 926, 839, 786.

¹H NMR (500 MHz, CDCl₃): δ 8.84 (br s, 1H), 7.47 - 7.46 (m, 2H), 7.43 - 7.38 (m, 3H), 7.22 (t, *J* = 7.5 Hz, 1H), 6.94 (d, *J* = 8.0 Hz, 1H), 6.75 (t, *J* = 7.5 Hz, 1H), 6.46 (d, *J* = 7.5 Hz, 1H), 4.82 (s, 1H).

¹³C NMR (125 MHz, CDCl₃): δ 174.1, 142.4, 133.1, 130.3, 128.9, 128.6, 126.8, 124.1, 122.7, 121.3, 110.9, 65.2, 62.0.

HRMS (ESI-Orbitrap) m/z: [M+H]⁺ calcd. for C₁₅H₁₂NO₂ 238.0868, found 238.0871.

3'-(4-methoxyphenyl)spiro[indoline-3,2'-oxiran]-2-one (2ae)



The title compound was obtained as a white solid (26 mg, 82%) *via* column chromatography on a silica gel (hexane/ethyl acetate =7:3, v/v); mp: 174 - 176 °C.

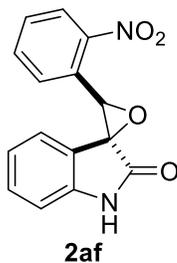
IR (neat, cm⁻¹): 3142, 3075, 3023, 2957, 2834, 1723, 1614, 1514, 1464, 1394, 1304, 1219, 1033, 894, 792.

¹H NMR (500 MHz, CDCl₃): δ 8.64 (br s, 1H), 7.38 (d, *J* = 8.5 Hz, 2H), 7.22 (t, *J* = 7.5 Hz, 1H), 6.95 - 6.93 (m, 3H), 6.77 (t, *J* = 8.0 Hz, 1H), 6.50 (d, *J* = 7.5 Hz, 1H), 4.77 (s, 1H), 3.83 (s, 3H).

¹³C NMR (125 MHz, CDCl₃): δ 174.1, 159.9, 142.3, 130.2, 128.1, 125.0, 124.2, 122.7, 121.5, 114.0, 110.8, 65.2, 62.1, 55.4.

HRMS (ESI-Orbitrap) m/z: [M+H]⁺ calcd. for C₁₆H₁₄NO₃ 268.0974 found, 268.0974.

3'-(2-nitrophenyl)spiro[indoline-3,2'-oxiran]-2-one (2af)



The title compound was obtained as a white solid (20 mg, 62%) *via* column chromatography on a silica gel (hexane/ethyl acetate =7:3, v/v); mp: 176 - 178 °C.

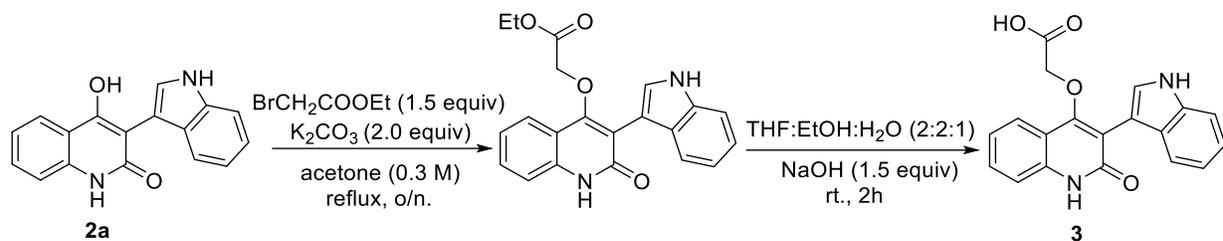
IR (neat, cm⁻¹): 3232, 3098, 2925, 2856, 1729, 1622, 1577, 1523, 1468, 1411, 1342, 1217, 1202, 1161, 1081, 914, 855, 791.

¹H NMR (500 MHz, CDCl₃): δ 8.35 (br s, 1H), 8.21 (d, *J* = 8.5 Hz, 1H), 8.04 (d, *J* = 7.5 Hz, 1H), 7.86 (t, *J* = 7.5 Hz, 1H), 7.63 (t, *J* = 7.5 Hz, 1H), 7.20 (t, *J* = 8.0 Hz, 1H), 6.90 (d, *J* = 8.0 Hz, 1H), 6.66 (t, *J* = 7.5 Hz, 1H), 6.02 (d, *J* = 7.5 Hz, 1H), 5.15 (s, 1H).

¹³C NMR (125 MHz, CDCl₃): δ 172.8, 147.0, 142.5, 134.5, 130.7, 130.0, 129.7, 125.1, 122.8, 122.5, 120.5, 111.1, 64.5, 62.1.

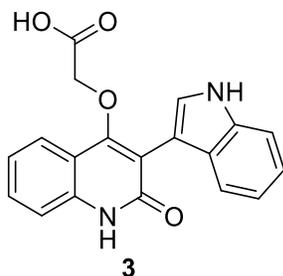
HRMS (ESI-Orbitrap) m/z: [M+ Na]⁺ calcd. for C₁₅H₁₀N₂NaO₄ 305.0538 found, 305.0544.

7. Chemical transformation of 2a and 2v



To a solution of **2a** (1.0 equiv) in acetone (0.3 M) was added potassium carbonate (2.0 equiv) and ethyl bromoacetate (1.5 equiv). The mixture was heated to reflux overnight and concentrated under reduced pressure. H₂O was added to the residue, and the resulting mixture was extracted with EtOAc. The organic layers were combined and washed with 1 M aqueous HCl, saturated aqueous NaHCO₃ and brine. The organic layer was dried over MgSO₄, filtered and concentrated under reduced pressure to give the crude product as a light brown oil that was used immediately in the next step. To a solution of the crude product obtained from the previous step (1.0 equiv) in THF: EtOH: H₂O mixed solvent system (2:2:1) was added NaOH (1.5 equiv). The resulting mixture was stirred at room temperature overnight. Then the mixture was acidified with 1 M aqueous HCl and extracted with EtOAc. The combined organic layer was dried over anhydrous Na₂SO₄, and the solvent was removed in *vacuo*. The product was purified by silica gel chromatography.

2-((3-(1H-indol-3-yl)-2-oxo-1,2-dihydroquinolin-4-yl)oxy)acetic acid (**3**)



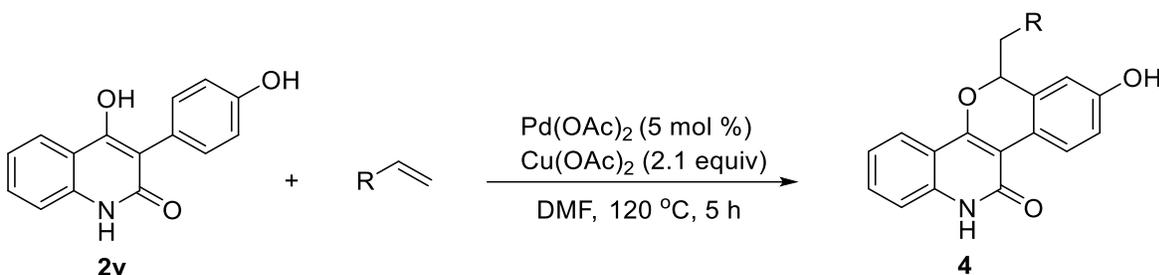
The title compound was obtained as a white solid (23 mg, 62% yield) *via* column chromatography on silica gel (chloroform/methanol = 4:1, v/v); mp: 275 - 277 °C.

IR (neat, cm⁻¹): 3320, 3270, 3012, 2924, 2627, 1712, 1634, 1548, 1498, 1403, 1312, 1248, 1165, 1106, 912, 755.

¹H NMR (500 MHz, DMSO-*d*₆): δ 12.75 (br s, 1H), 11.74 (s, 1H), 11.45 (s, 1H), 8.12 (d, *J* = 8.0 Hz, 1H), 7.63 (s, 1H), 7.51 (t, *J* = 7.0 Hz, 1H), 7.47 (d, *J* = 8.0 Hz, 1H), 7.38 (d, *J* = 7.5 Hz, 1H), 7.34 (d, *J* = 8.0 Hz, 1H), 7.23 (t, *J* = 7.5 Hz, 1H), 7.14 (t, *J* = 7.0 Hz, 1H), 7.03 (t, *J* = 7.0 Hz, 1H), 4.05 (s, 2H).

¹³C NMR (125 MHz, DMSO-*d*₆): δ 169.6, 162.9, 158.5, 137.1, 135.6, 130.0, 127.6, 126.5, 123.5, 121.4, 121.1, 119.9, 119.2, 117.2, 114.5, 112.5, 111.6, 105.6, 67.1.

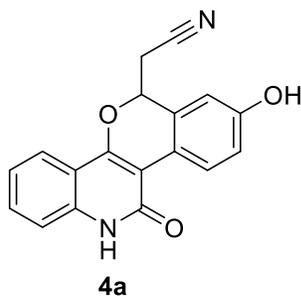
HRMS (ESI-Orbitrap) *m/z*: [M+H]⁺ calcd. for C₁₉H₁₅N₂O₄ 335.1032, found 335.1035.



A solution of substrate **2v** (30 mg, 0.12 mmol), Cu(OAc)₂ (46 mg, 0.25 mmol), Pd(OAc)₂ (1.3 mg, 0.006 mmol) and the appropriate alkene (0.18 mmol) in DMF (1.0 mL) was stirred at 120 °C for 5 hours. The reaction was cooled to room temperature and filtered through a plug of silica gel using Et₂O (2 x 20 mL) as eluent. The mixture was washed with brine (3 x 20 mL), dried (MgSO₄), filtered, and concentrated in *vacuo*. Purification of the residue by column chromatography gave the benzopyran.

2-(8-hydroxy-11-oxo-11,12-dihydro-6H-isochromeno[4,3-c]quinolin-6-yl)acetonitrile (**4a**)

The title compound was obtained as a white solid (13 mg, 36% yield) *via* column chromatography on a silica gel (hexane/ethyl acetate = 7:3, v/v); mp: 390 - 392 °C.



IR (neat, cm⁻¹): 3571, 3321, 3268, 2934, 2854, 2254, 1625, 1581, 1460, 1392, 1151, 892, 758, 743.

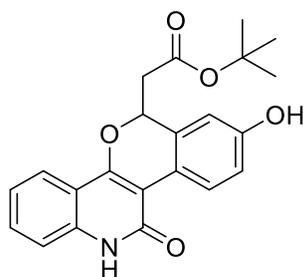
¹H NMR (500 MHz, DMSO-*d*₆): δ 11.73 (s, 1H), 9.86 (s, 1H), 8.70 (d, *J* = 8.5 Hz, 1H), 7.87 (d, *J* = 8.0 Hz, 1H), 7.54 (t, *J* = 7.0 Hz, 1H),

7.34 (d, $J = 8.0$ Hz, 1H), 7.24 (t, $J = 7.0$ Hz, 1H), 6.83 (d, $J = 8.5$ Hz, 1H), 6.76 (s, 1H), 5.85 (br s, 1H), 3.25 (dd, $J = 17.0, 8.0$ Hz, 1H), 3.15 (d, $J = 17.0$ Hz, 1H).

^{13}C NMR (125 MHz, DMSO- d_6): δ 160.9, 157.3, 153.3, 137.4, 131.2, 130.8, 126.8, 122.0, 121.7, 117.7, 117.6, 115.4, 114.9, 114.1, 111.5, 106.8, 73.1, 22.7.

HRMS (ESI-Orbitrap) m/z : $[\text{M}+\text{H}]^+$ calcd. for $\text{C}_{18}\text{H}_{13}\text{N}_2\text{O}_3$ 305.0926, found 305.0932.

***tert*-butyl 2-(8-hydroxy-11-oxo-11,12-dihydro-6H-isochromeno[4,3-*c*]quinolin-6-yl)acetate (4b)**



4b

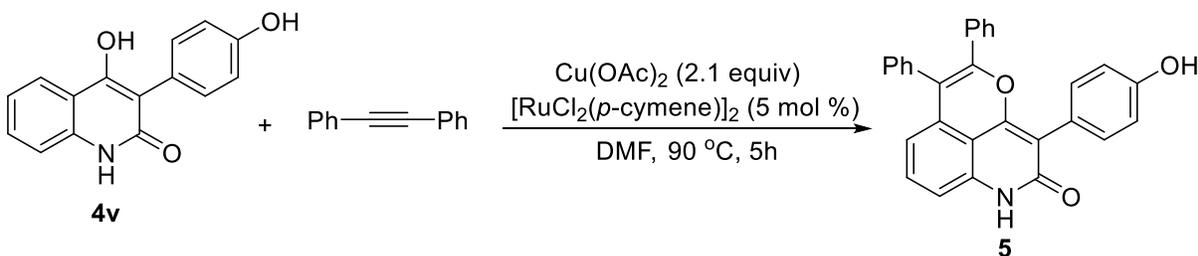
The title compound was obtained as a white solid (10 mg, 23% yield) *via* column chromatography on a silica gel (hexane/ethyl acetate =7:3, v/v); mp: 151 - 153 °C.

IR (neat, cm^{-1}): 3567, 3342, 3258, 2924, 2855, 1738, 1632, 1590, 1467, 1371, 1308, 1165, 1114, 786, 757, 732.

^1H NMR (500 MHz, DMSO- d_6): δ 11.69 (s, 1H), 9.78 (s, 1H), 8.65 (d, $J = 8.0$ Hz, 1H), 7.73 (d, $J = 7.5$ Hz, 1H), 7.51 (t, $J = 7.0$ Hz, 1H), 7.32 (d, $J = 8.0$ Hz, 1H), 7.18 (t, $J = 7.0$ Hz, 1H), 6.79 (d, $J = 8.0$ Hz, 1H), 6.68 (s, 1H), 5.78 (br s, 1H), 2.75 - 2.70 (m, 2H), 1.39 (s, 9H).

^{13}C NMR (125 MHz, DMSO- d_6): δ 168.5, 160.9, 157.3, 153.8, 137.4, 132.4, 130.7, 126.6, 122.1, 121.5, 117.8, 114.9, 114.3, 111.2, 106.7, 80.6, 75.0, 40.5, 27.7.

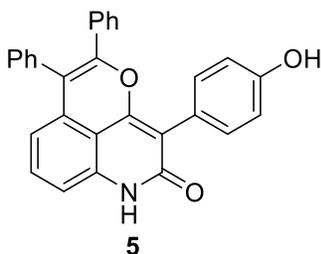
HRMS (ESI-Orbitrap) m/z : $[\text{M}+\text{H}]^+$ calcd. for $\text{C}_{22}\text{H}_{22}\text{NO}_5$ 380.1498, found 380.1500.



A solution of substrate **4j** (30 mg, 0.12 mmol), $\text{Cu}(\text{OAc})_2$ (46 mg, 0.25 mmol), $[\text{RuCl}_2(p\text{-cymene})]_2$ (3.6 mg, 0.006 mmol), and diphenylethyne (0.18 mmol) in DMF (1.0 mL) was stirred at 90 °C for 5 hours. The reaction was cooled to room temperature and diluted with Et_2O (20 mL). The

mixture was washed with brine (3 x 20 mL), dried (MgSO₄), filtered, and concentrated in *vacuo*. Purification of the residue by column chromatography gave the oxidative annulation product.

3-(4-hydroxyphenyl)-5,6-diphenylpyrano[2,3,4-*de*]quinolin-2(1*H*)-one (5)



The title compound was obtained as a white solid (27 mg, 54% yield) *via* column chromatography on a silica gel (hexane/ethyl acetate =6:4, v/v); mp: 335 - 337 °C.

IR (neat, cm⁻¹): 3540, 3372, 2924, 2840, 1628, 1572, 1495, 1453, 1362, 1217, 932, 768, 695.

¹H NMR (500 MHz, DMSO-*d*₆): δ 11.62 (s, 1H), 9.41 (s, 1H), 7.43 - 7.36 (m, 6H), 7.26 (d, *J* = 7.0 Hz, 2H), 7.23 - 7.18 (m, 1H), 7.16 - 7.15 (m, 4H), 7.09 (d, *J* = 8.5 Hz, 1H), 6.77 (d, *J* = 8.5 Hz, 2H), 6.33 (d, *J* = 8.0 Hz, 1H).

¹³C NMR (125 MHz, DMSO-*d*₆): δ 162.4, 156.3, 154.8, 148.9, 137.6, 134.1, 132.8, 132.0, 131.6, 131.1, 130.7, 129.1, 128.9, 128.7, 128.0, 127.7, 122.2, 116.2, 114.5, 114.2, 112.8, 109.4, 108.9

HRMS (ESI-Orbitrap) *m/z*: [M+H]⁺ calcd. for C₂₉H₂₀NO₃ 430.1443, found 430.1449.

8. References:

1. A. Nagarsenkar, S. K. Prajapati, S. D. Guggilapu, S. Birineni, S. Sravanti Kotapalli, R. Ummanni and B. N. Babu, *Medchemcomm*, 2016, **7**, 646–653.
2. X. P. Chen, J. X. Liu, H. Y. Li, Y. C. Xiao and F. E. Chen, *Adv. Synth. Catal.*, 2022, **364**, 2067–2071.
3. K. Zilbeyaz, H. Kilic, M. Sisecioglu, H. Ozdemir and A. A. Güngör, *Tetrahedron Asymmetry*, 2012, **23**, 594–601.

9. X-ray crystal structure and data for compound 2v
CCDC 2168144

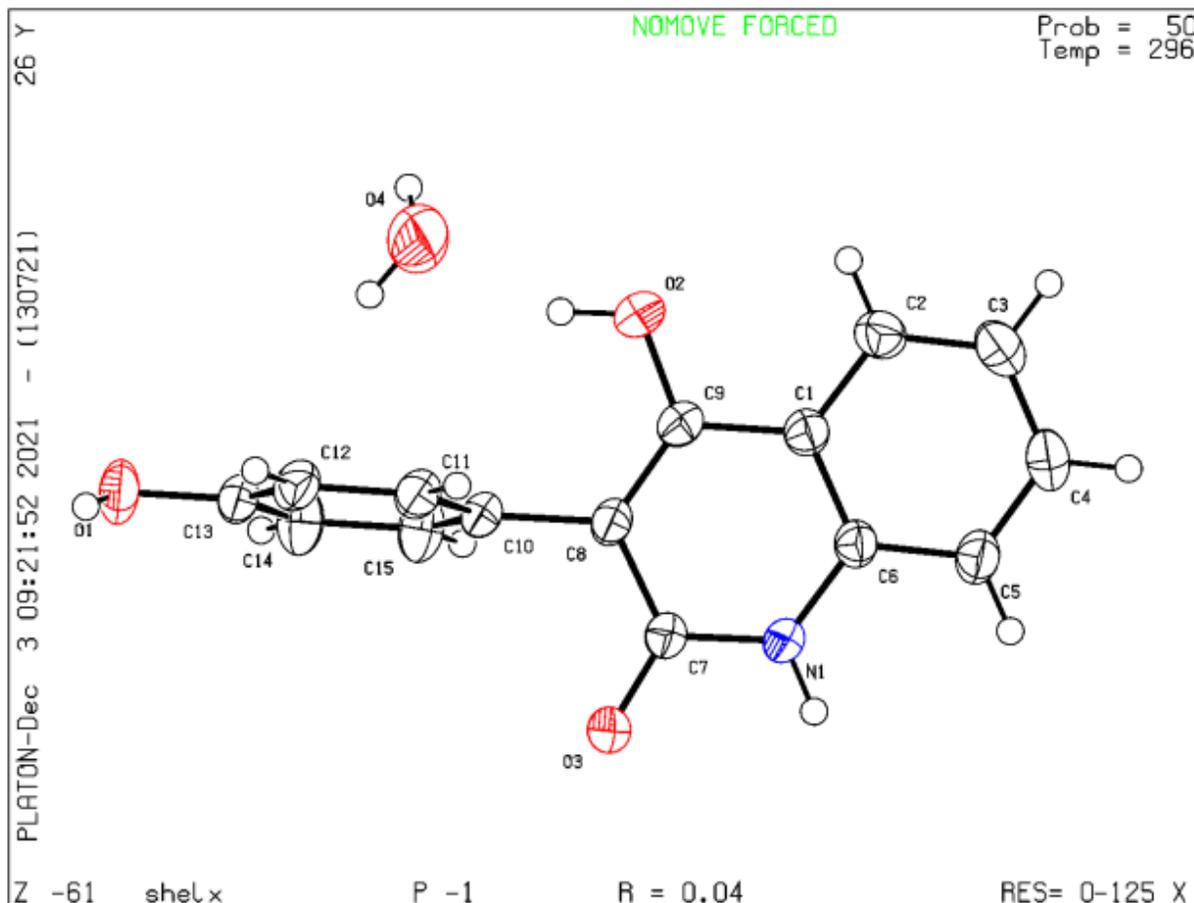


Fig S1. ORTEP diagram of compound **2v**

Table S2. Crystal data and structure refinement for mb132.

Identification code	shelx	
Empirical formula	C15 H13 N O4	
Formula weight	271.26	
Temperature	296(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P -1	
Unit cell dimensions	a = 7.2227(3) Å	a = 68.4130(10)°.
	b = 9.2625(4) Å	b = 86.8380(10)°.
	c = 11.1958(4) Å	g = 67.7030(10)°.

Volume	641.28(5) Å ³
Z	2
Density (calculated)	1.405 Mg/m ³
Absorption coefficient	0.103 mm ⁻¹
F(000)	284
Crystal size	0.200 x 0.150 x 0.100 mm ³
Theta range for data collection	3.338 to 28.000°.
Index ranges	-9<=h<=9, -12<=k<=12, -14<=l<=14
Reflections collected	27762
Independent reflections	3099 [R(int) = 0.0397]
Completeness to theta = 25.242°	99.7 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.985 and 0.973
Refinement method	Full-matrix least-squares on F ²
Data / restraints / parameters	3099 / 3 / 199
Goodness-of-fit on F ²	1.064
Final R indices [I>2sigma(I)]	R1 = 0.0422, wR2 = 0.1163
R indices (all data)	R1 = 0.0496, wR2 = 0.1289
Extinction coefficient	n/a
Largest diff. peak and hole	0.341 and -0.336 e.Å ⁻³

Table S3. Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for mb132. $U(\text{eq})$ is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	$U(\text{eq})$
C(1)	6213(2)	2504(2)	4817(1)	30(1)
C(2)	8239(2)	1920(2)	5273(1)	37(1)
C(3)	8737(2)	1942(2)	6436(1)	40(1)
C(4)	7225(2)	2542(2)	7167(1)	40(1)
C(5)	5232(2)	3136(2)	6736(1)	36(1)
C(6)	4711(2)	3134(2)	5547(1)	29(1)
C(7)	2097(2)	3880(2)	3918(1)	29(1)
C(8)	3595(2)	3149(2)	3177(1)	29(1)
C(9)	5586(2)	2489(2)	3619(1)	32(1)
C(10)	2919(2)	3104(2)	1962(1)	30(1)
C(11)	2989(2)	4249(2)	755(1)	32(1)
C(12)	2387(2)	4166(2)	-371(1)	34(1)
C(13)	1686(2)	2936(2)	-288(1)	33(1)
C(14)	1590(3)	1797(2)	909(1)	43(1)
C(15)	2201(2)	1887(2)	2022(1)	42(1)
N(1)	2721(2)	3778(1)	5078(1)	31(1)
O(1)	1067(2)	2772(1)	-1349(1)	44(1)
O(2)	7100(2)	1796(2)	3003(1)	51(1)
O(3)	245(1)	4607(1)	3539(1)	36(1)
O(4)	6915(3)	718(2)	1065(2)	89(1)

Table S4. Bond lengths [Å] and angles [°] for mb132.

C(1)-C(6)	1.3996(17)
C(1)-C(2)	1.4044(17)
C(1)-C(9)	1.4460(17)
C(2)-C(3)	1.3790(19)
C(2)-H(2)	0.9300
C(3)-C(4)	1.395(2)
C(3)-H(3)	0.9300
C(4)-C(5)	1.3743(19)
C(4)-H(4)	0.9300
C(5)-C(6)	1.4042(16)
C(5)-H(5)	0.9300
C(6)-N(1)	1.3786(15)
C(7)-O(3)	1.2617(15)
C(7)-N(1)	1.3560(15)
C(7)-C(8)	1.4411(16)
C(8)-C(9)	1.3687(17)
C(8)-C(10)	1.4904(15)
C(9)-O(2)	1.3390(15)
C(10)-C(15)	1.3889(18)
C(10)-C(11)	1.3902(17)
C(11)-C(12)	1.3930(17)
C(11)-H(11)	0.9300
C(12)-C(13)	1.3842(19)
C(12)-H(12)	0.9300
C(13)-O(1)	1.3713(15)
C(13)-C(14)	1.3846(19)
C(14)-C(15)	1.3855(19)
C(14)-H(14)	0.9300
C(15)-H(15)	0.9300
N(1)-H(1)	0.878(19)
O(1)-H(1A)	0.87(2)
O(2)-H(2A)	0.92(3)
O(4)-H(4B)	0.874(17)
O(4)-H(4A)	0.860(16)

C(6)-C(1)-C(2)	119.10(11)
C(6)-C(1)-C(9)	117.69(11)
C(2)-C(1)-C(9)	123.21(12)
C(3)-C(2)-C(1)	120.32(13)
C(3)-C(2)-H(2)	119.8
C(1)-C(2)-H(2)	119.8
C(2)-C(3)-C(4)	119.98(12)
C(2)-C(3)-H(3)	120.0
C(4)-C(3)-H(3)	120.0
C(5)-C(4)-C(3)	120.87(12)
C(5)-C(4)-H(4)	119.6
C(3)-C(4)-H(4)	119.6
C(4)-C(5)-C(6)	119.52(12)
C(4)-C(5)-H(5)	120.2
C(6)-C(5)-H(5)	120.2
N(1)-C(6)-C(1)	119.40(11)
N(1)-C(6)-C(5)	120.40(11)
C(1)-C(6)-C(5)	120.18(11)
O(3)-C(7)-N(1)	118.84(11)
O(3)-C(7)-C(8)	123.16(11)
N(1)-C(7)-C(8)	118.01(11)
C(9)-C(8)-C(7)	119.35(11)
C(9)-C(8)-C(10)	122.00(11)
C(7)-C(8)-C(10)	118.64(10)
O(2)-C(9)-C(8)	124.35(11)
O(2)-C(9)-C(1)	114.36(11)
C(8)-C(9)-C(1)	121.28(11)
C(15)-C(10)-C(11)	118.32(11)
C(15)-C(10)-C(8)	119.74(11)
C(11)-C(10)-C(8)	121.94(11)
C(10)-C(11)-C(12)	121.10(12)
C(10)-C(11)-H(11)	119.4
C(12)-C(11)-H(11)	119.4
C(13)-C(12)-C(11)	119.52(11)
C(13)-C(12)-H(12)	120.2

C(11)-C(12)-H(12)	120.2
O(1)-C(13)-C(12)	123.04(12)
O(1)-C(13)-C(14)	116.91(12)
C(12)-C(13)-C(14)	120.05(12)
C(13)-C(14)-C(15)	119.92(13)
C(13)-C(14)-H(14)	120.0
C(15)-C(14)-H(14)	120.0
C(14)-C(15)-C(10)	121.08(12)
C(14)-C(15)-H(15)	119.5
C(10)-C(15)-H(15)	119.5
C(7)-N(1)-C(6)	124.01(10)
C(7)-N(1)-H(1)	115.3(11)
C(6)-N(1)-H(1)	120.3(11)
C(13)-O(1)-H(1A)	110.7(15)
C(9)-O(2)-H(2A)	111.8(15)
H(4B)-O(4)-H(4A)	106(2)

Symmetry transformations used to generate equivalent atoms:

Table S5. Anisotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for mb132. The anisotropic displacement factor exponent takes the form: $-2p^2 [h^2 a^* 2U_{11} + \dots + 2 h k a^* b^* U_{12}]$

	U ₁₁	U ₂₂	U ₃₃	U ₂₃	U ₁₃	U ₁₂
C(1)	30(1)	29(1)	31(1)	-13(1)	0(1)	-8(1)
C(2)	31(1)	35(1)	43(1)	-17(1)	0(1)	-8(1)
C(3)	35(1)	38(1)	45(1)	-14(1)	-9(1)	-11(1)
C(4)	47(1)	40(1)	33(1)	-13(1)	-8(1)	-16(1)
C(5)	41(1)	40(1)	27(1)	-14(1)	1(1)	-14(1)
C(6)	31(1)	29(1)	26(1)	-10(1)	-1(1)	-9(1)
C(7)	30(1)	32(1)	24(1)	-12(1)	2(1)	-10(1)
C(8)	33(1)	32(1)	25(1)	-14(1)	3(1)	-11(1)
C(9)	32(1)	33(1)	32(1)	-18(1)	5(1)	-9(1)
C(10)	31(1)	33(1)	26(1)	-16(1)	3(1)	-9(1)
C(11)	35(1)	37(1)	31(1)	-17(1)	7(1)	-16(1)
C(12)	39(1)	38(1)	24(1)	-12(1)	6(1)	-13(1)

C(13)	34(1)	37(1)	28(1)	-17(1)	-1(1)	-7(1)
C(14)	62(1)	41(1)	34(1)	-14(1)	-1(1)	-27(1)
C(15)	62(1)	40(1)	27(1)	-10(1)	1(1)	-26(1)
N(1)	29(1)	39(1)	25(1)	-16(1)	3(1)	-8(1)
O(1)	57(1)	47(1)	31(1)	-19(1)	-8(1)	-15(1)
O(2)	34(1)	71(1)	53(1)	-44(1)	6(1)	-7(1)
O(3)	29(1)	49(1)	29(1)	-18(1)	1(1)	-9(1)
O(4)	70(1)	93(1)	100(1)	-73(1)	-20(1)	11(1)

Table S6. Hydrogen coordinates ($\times 10^4$) and isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for mb132.

	x	y	z	U(eq)
H(2)	9249	1516	4789	44
H(3)	10080	1557	6733	48
H(4)	7571	2539	7955	48
H(5)	4235	3538	7229	43
H(11)	3445	5083	697	39
H(12)	2456	4932	-1173	41
H(14)	1117	973	965	52
H(15)	2130	1119	2822	50
H(1)	1770(30)	4270(20)	5489(17)	40(4)
H(1A)	710(30)	3720(30)	-2010(20)	66(6)
H(2A)	6650(40)	1600(30)	2350(20)	77(7)
H(4B)	7610(40)	-340(20)	1200(30)	106
H(4A)	5710(30)	920(30)	810(30)	106

Table S7. Torsion angles [°] for mb132.

C(6)-C(1)-C(2)-C(3)	1.06(19)
C(9)-C(1)-C(2)-C(3)	-178.86(12)
C(1)-C(2)-C(3)-C(4)	0.2(2)
C(2)-C(3)-C(4)-C(5)	-0.9(2)
C(3)-C(4)-C(5)-C(6)	0.2(2)
C(2)-C(1)-C(6)-N(1)	177.13(11)
C(9)-C(1)-C(6)-N(1)	-2.95(18)
C(2)-C(1)-C(6)-C(5)	-1.67(19)
C(9)-C(1)-C(6)-C(5)	178.25(11)
C(4)-C(5)-C(6)-N(1)	-177.75(12)
C(4)-C(5)-C(6)-C(1)	1.03(19)
O(3)-C(7)-C(8)-C(9)	175.42(12)
N(1)-C(7)-C(8)-C(9)	-4.50(18)
O(3)-C(7)-C(8)-C(10)	-5.86(18)
N(1)-C(7)-C(8)-C(10)	174.21(11)
C(7)-C(8)-C(9)-O(2)	-179.31(12)
C(10)-C(8)-C(9)-O(2)	2.0(2)
C(7)-C(8)-C(9)-C(1)	0.28(19)
C(10)-C(8)-C(9)-C(1)	-178.39(11)
C(6)-C(1)-C(9)-O(2)	-176.93(12)
C(2)-C(1)-C(9)-O(2)	2.99(19)
C(6)-C(1)-C(9)-C(8)	3.44(19)
C(2)-C(1)-C(9)-C(8)	-176.63(12)
C(9)-C(8)-C(10)-C(15)	100.14(16)
C(7)-C(8)-C(10)-C(15)	-78.54(16)
C(9)-C(8)-C(10)-C(11)	-79.60(16)
C(7)-C(8)-C(10)-C(11)	101.72(14)
C(15)-C(10)-C(11)-C(12)	-1.02(19)
C(8)-C(10)-C(11)-C(12)	178.72(11)
C(10)-C(11)-C(12)-C(13)	0.73(19)
C(11)-C(12)-C(13)-O(1)	180.00(12)
C(11)-C(12)-C(13)-C(14)	-0.1(2)
O(1)-C(13)-C(14)-C(15)	179.73(13)
C(12)-C(13)-C(14)-C(15)	-0.1(2)

C(13)-C(14)-C(15)-C(10)	-0.2(2)
C(11)-C(10)-C(15)-C(14)	0.7(2)
C(8)-C(10)-C(15)-C(14)	-179.01(13)
O(3)-C(7)-N(1)-C(6)	-174.74(11)
C(8)-C(7)-N(1)-C(6)	5.19(18)
C(1)-C(6)-N(1)-C(7)	-1.41(19)
C(5)-C(6)-N(1)-C(7)	177.39(12)

Symmetry transformations used to generate equivalent atoms:

Table S8. Hydrogen bonds for mb132 [\AA and $^\circ$].

D-H...A	d(D-H)	d(H...A)	d(D...A)	\angle (DHA)
N(1)-H(1)...O(3)#1	0.878(19)	1.975(19)	2.8519(14)	176.4(16)
O(1)-H(1A)...O(3)#2	0.87(2)	1.78(2)	2.6326(15)	166(2)
O(2)-H(2A)...O(4)	0.92(3)	1.87(3)	2.7295(18)	156(2)
O(4)-H(4B)...O(1)#3	0.874(17)	2.029(18)	2.8976(19)	172(3)

Symmetry transformations used to generate equivalent atoms:

#1 -x,-y+1,-z+1 #2 -x,-y+1,-z #3 -x+1,-y,-z

10. Associated information of DFT calculations

To optimize reactants, intermediates, transition states, and products, DFT at the B3LYP-D3/6-31G(d,p) level was used. Frequency calculations were conducted for each structure to confirm results. Using water as the solvent, the implicit involvement of the solvent was assessed through optimization calculations with the PCM model.

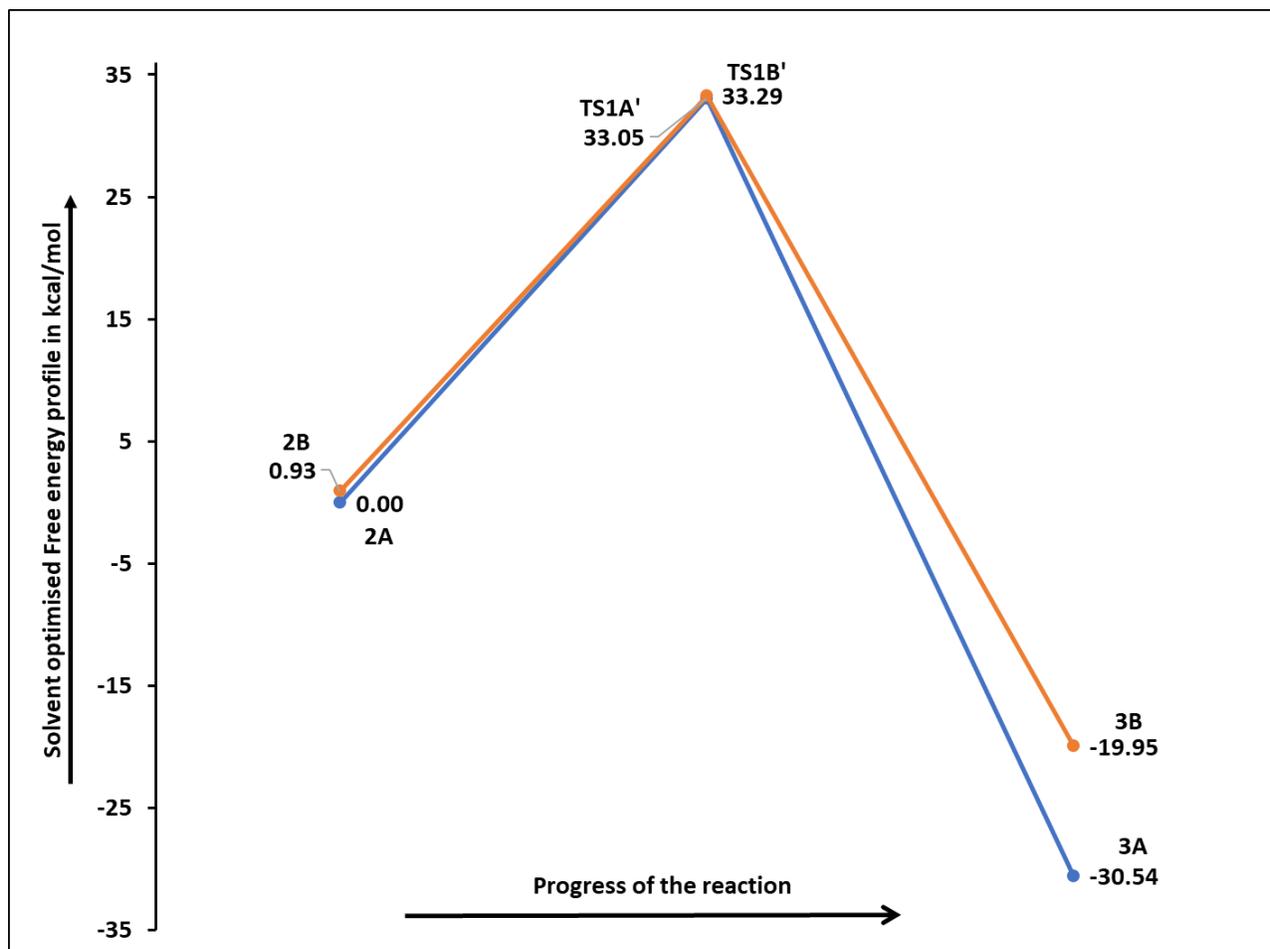


Fig S2. Solvent optimized free energy profile of the reaction mechanism for the formation of **3A** and **3B** via neutral intermediates.

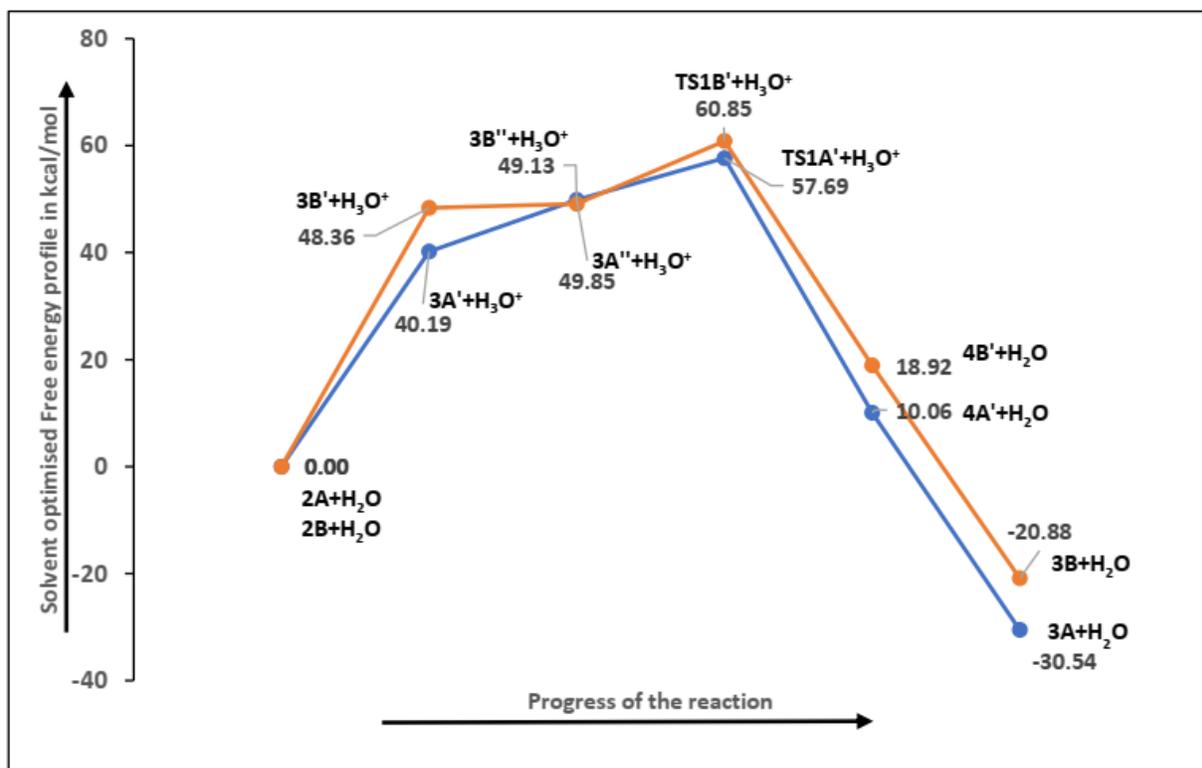


Fig S3. Solvent optimized free energy profile of the reaction mechanism for the formation of **3A** and **3B** via acidic conditions.

For 2A

6	-3.278258000	0.303164000	0.978769000
1	-3.769758000	0.778087000	1.823320000
6	-3.871508000	0.356136000	-0.287496000
8	-5.063626000	0.997639000	-0.517186000
6	1.451568000	0.470326000	0.298377000
6	0.751861000	1.599645000	0.703913000
1	-0.197550000	1.507604000	1.217379000
6	1.302506000	2.862136000	0.441950000

6	2.530965000	2.980875000	-0.213908000
1	2.942820000	3.966113000	-0.409756000
6	3.250352000	1.848737000	-0.620615000
1	4.207572000	1.934886000	-1.123761000
6	2.693387000	0.607728000	-0.349738000
6	2.415235000	-1.666264000	-0.189783000
6	-0.136441000	-1.690238000	0.209875000
6	1.172228000	-0.985255000	0.368304000
6	-1.431328000	-0.975553000	0.060371000
6	-2.064273000	-0.360437000	1.145659000
1	-1.603088000	-0.402884000	2.126570000
6	-3.251934000	-0.264035000	-1.380204000
1	-3.727410000	-0.219278000	-2.354475000
6	-2.042815000	-0.927963000	-1.200480000
1	-1.565803000	-1.412322000	-2.048039000
7	3.224774000	-0.663563000	-0.639516000
8	0.532470000	-1.636056000	1.477281000
8	2.624348000	-2.875375000	-0.243651000
1	4.130032000	-0.824968000	-1.062829000
1	-0.068196000	-2.663430000	-0.279199000
1	0.768861000	3.754156000	0.753606000
1	-5.385716000	1.383313000	0.312288000

For 3A'

6	-3.381006000	-0.313216000	-1.341092000
1	-3.892406000	-0.368498000	-2.299843000
6	-4.003521000	0.458158000	-0.298683000
8	-5.123220000	1.076685000	-0.467780000
6	1.452822000	0.461115000	0.301833000
6	0.795222000	1.619998000	0.696283000
1	-0.148749000	1.567353000	1.224470000
6	1.379696000	2.860145000	0.400908000
6	2.599320000	2.930371000	-0.278073000
1	3.037022000	3.898957000	-0.499531000
6	3.275562000	1.768887000	-0.676696000
1	4.225120000	1.815826000	-1.199408000
6	2.686971000	0.550677000	-0.371246000
6	2.339160000	-1.708571000	-0.161336000
6	-0.217278000	-1.645256000	0.231787000
6	1.127657000	-0.981805000	0.392628000
6	-1.496602000	-0.921571000	0.078657000
6	-2.179175000	-0.978486000	-1.151042000
1	-1.750096000	-1.556771000	-1.968159000
6	-3.289322000	0.477896000	0.948745000
1	-3.731525000	1.033829000	1.772897000
6	-2.083425000	-0.185887000	1.123291000
1	-1.581509000	-0.151749000	2.086922000

7	3.173046000	-0.740540000	-0.647231000
8	0.459371000	-1.604048000	1.499093000
8	2.514816000	-2.925648000	-0.197042000
1	4.063542000	-0.938569000	-1.085829000
1	-0.155440000	-2.620725000	-0.255920000
1	0.878500000	3.773484000	0.705067000

For 3A''

6	-4.031789000	-0.751173000	-0.106110000
1	-4.963139000	-1.310437000	-0.090540000
6	-4.119925000	0.687214000	-0.295689000
8	-5.226387000	1.280178000	-0.431574000
6	1.586168000	0.348941000	0.369007000
6	1.327843000	1.533044000	1.043834000
1	0.544516000	1.571155000	1.794783000
6	2.082360000	2.674442000	0.733645000
6	3.100934000	2.608236000	-0.221858000
1	3.678117000	3.497746000	-0.456026000
6	3.408146000	1.404605000	-0.872002000
1	4.221182000	1.339373000	-1.587926000
6	2.646283000	0.289845000	-0.545843000
6	1.972150000	-1.892850000	-0.337080000
6	-0.408644000	-1.393298000	0.164608000
6	1.000094000	-1.041125000	0.546667000

6	-1.578971000	-0.657329000	0.031651000
6	-2.830093000	-1.376727000	0.044039000
1	-2.795258000	-2.454384000	0.187437000
6	-2.852676000	1.400857000	-0.333437000
1	-2.895050000	2.472767000	-0.506606000
6	-1.655940000	0.765738000	-0.175427000
1	-0.740369000	1.338348000	-0.238393000
7	2.813734000	-1.036534000	-0.988319000
8	0.820731000	-1.485549000	1.846919000
8	1.960783000	-3.118488000	-0.446789000
1	3.569669000	-1.346596000	-1.586784000
1	-0.511795000	-2.475206000	0.134869000
1	1.879348000	3.611330000	1.242938000

For TS1A

6	3.714184000	0.548567000	0.012843000
1	4.665080000	1.051851000	-0.139616000
6	3.695066000	-0.896258000	-0.114509000
8	4.732550000	-1.564373000	-0.398004000
6	-1.776418000	-0.131860000	0.498977000
6	-2.232163000	-1.120178000	1.363089000
1	-2.218960000	-0.943668000	2.434507000
6	-2.688732000	-2.338391000	0.842338000
6	-2.697492000	-2.549459000	-0.539107000

1	-3.051156000	-3.494581000	-0.939727000
6	-2.265447000	-1.552064000	-1.422003000
1	-2.286888000	-1.703495000	-2.496675000
6	-1.815422000	-0.351144000	-0.884786000
6	-1.069323000	1.859150000	-0.895780000
6	0.214841000	1.438132000	0.826760000
6	-1.238792000	1.220224000	0.916200000
6	1.311553000	0.616885000	0.525761000
6	2.583660000	1.254083000	0.313522000
1	2.630803000	2.337618000	0.398124000
6	2.408606000	-1.531192000	0.114422000
1	2.373351000	-2.615238000	0.045817000
6	1.283724000	-0.816353000	0.416101000
1	0.355315000	-1.344968000	0.592010000
7	-1.379287000	0.758900000	-1.631384000
8	-1.965242000	1.976856000	1.667462000
8	-0.920033000	2.999328000	-1.296503000
1	-1.563926000	0.835033000	-2.628252000
1	0.446651000	2.486416000	1.014582000
1	-3.040538000	-3.116614000	1.512315000

For 4A'

6	2.574029000	-0.762619000	-1.432859000
1	2.562695000	-1.184414000	-2.435780000

6	3.786386000	-0.886379000	-0.671757000
8	4.843767000	-1.467023000	-1.134750000
6	-1.854272000	-0.430095000	0.554355000
6	-2.577366000	-1.612577000	0.777422000
1	-2.270028000	-2.254441000	1.596460000
6	-3.651592000	-1.950813000	-0.033913000
6	-4.020833000	-1.090411000	-1.078088000
1	-4.861395000	-1.343307000	-1.716859000
6	-3.325323000	0.091792000	-1.311547000
1	-3.617829000	0.759308000	-2.116215000
6	-2.235763000	0.426910000	-0.498524000
6	-0.438017000	2.045676000	-0.054161000
6	0.173525000	1.078930000	0.944817000
6	-0.730492000	-0.052416000	1.425159000
6	1.431734000	0.434819000	0.355477000
6	1.442740000	-0.132434000	-0.931559000
1	0.550114000	-0.076036000	-1.551550000
6	3.732491000	-0.310806000	0.643670000
1	4.627114000	-0.375936000	1.259741000
6	2.595741000	0.319763000	1.132763000
1	2.605229000	0.739645000	2.136748000
7	-1.553511000	1.626767000	-0.721529000
8	-0.472007000	-0.644996000	2.474815000
8	0.068219000	3.145878000	-0.287457000

1	-1.917275000	2.260883000	-1.425671000
1	0.459898000	1.669996000	1.818710000
1	-4.201709000	-2.869982000	0.136719000

For 3A

6	3.771134000	-0.189869000	0.640445000
1	4.684917000	-0.190299000	1.228325000
6	3.771918000	-0.743108000	-0.644253000
8	4.894227000	-1.297361000	-1.209426000
6	-1.954112000	-0.463932000	0.510263000
6	-2.728190000	-1.625757000	0.667521000
1	-2.430946000	-2.339527000	1.428465000
6	-3.837680000	-1.852047000	-0.133663000
6	-4.189691000	-0.900918000	-1.102810000
1	-5.057600000	-1.067018000	-1.733345000
6	-3.442748000	0.260421000	-1.271550000
1	-3.722141000	0.996625000	-2.018702000
6	-2.318269000	0.484984000	-0.467679000
6	-0.444567000	1.992050000	0.047629000
6	0.132081000	0.946377000	0.991274000
6	-0.786471000	-0.219481000	1.364755000
6	1.420577000	0.372284000	0.401453000
6	2.597904000	0.361107000	1.155164000
1	2.602479000	0.790061000	2.152560000

6	2.597720000	-0.745447000	-1.406965000
1	2.611602000	-1.180197000	-2.401017000
6	1.433198000	-0.193917000	-0.882027000
1	0.525512000	-0.205411000	-1.478690000
7	-1.582326000	1.662742000	-0.628394000
8	-0.497723000	-0.929765000	2.327781000
8	0.111875000	3.078520000	-0.121921000
1	-1.926975000	2.355880000	-1.285245000
1	0.379003000	1.471116000	1.918214000
1	-4.428020000	-2.753905000	-0.012916000
1	5.634601000	-1.224160000	-0.587699000

For 3A.H₂O

6	-2.320333000	-1.862958000	-0.757140000
1	-2.226234000	-2.840732000	-1.217997000
6	-3.588713000	-1.282607000	-0.635122000
8	-4.659327000	-1.995563000	-1.115401000
1	-5.471842000	-1.485381000	-0.975388000
6	2.051235000	0.323545000	-0.478992000
6	2.847073000	0.399755000	-1.635651000
1	2.532276000	1.066428000	-2.431283000
6	3.997365000	-0.364819000	-1.753912000
6	4.369390000	-1.213132000	-0.699624000
1	5.269623000	-1.814105000	-0.781846000

6	3.602691000	-1.298960000	0.457546000
1	3.898601000	-1.952116000	1.272366000
6	2.436158000	-0.533027000	0.574758000
6	0.508191000	0.051367000	1.981915000
6	-0.094658000	0.833043000	0.822476000
6	0.838775000	1.130985000	-0.347655000
6	-1.326417000	0.083239000	0.306159000
6	-1.201668000	-1.181737000	-0.288071000
1	-0.222048000	-1.640472000	-0.387803000
6	-3.727727000	-0.023537000	-0.042111000
1	-4.714070000	0.422186000	0.052680000
6	-2.599158000	0.650333000	0.423809000
1	-2.710680000	1.629105000	0.877423000
7	1.681072000	-0.605551000	1.747054000
8	0.534169000	2.007169000	-1.164815000
8	-0.060748000	-0.018297000	3.072001000
1	2.040220000	-1.166143000	2.513599000
1	-0.850916000	3.143667000	-0.643283000
1	4.604350000	-0.309428000	-2.650961000
1	-0.422756000	1.793736000	1.226754000
8	-1.549999000	3.733184000	-0.296739000
1	-2.360004000	3.311218000	-0.614318000

For TS2A

6	3.459769000	-1.042481000	-1.132207000
1	3.863384000	-1.783014000	-1.815765000
6	4.339126000	-0.265545000	-0.370587000
8	5.689423000	-0.489322000	-0.527717000
1	6.178169000	0.110522000	0.055998000
6	-2.262008000	-0.570791000	-0.135912000
6	-3.190891000	-1.624792000	-0.136349000
1	-2.811645000	-2.637546000	-0.050539000
6	-4.552160000	-1.377066000	-0.242379000
6	-5.008317000	-0.051952000	-0.345735000
1	-6.072025000	0.150444000	-0.428449000
6	-4.112281000	1.008283000	-0.342099000
1	-4.460063000	2.034327000	-0.419307000
6	-2.733297000	0.753312000	-0.238430000
6	-0.445044000	1.650237000	-0.176596000
6	0.070158000	0.302217000	-0.013411000
6	-0.812550000	-0.833353000	-0.023258000
6	1.546272000	0.104868000	-0.134733000
6	2.085662000	-0.853627000	-1.011484000
1	1.415873000	-1.464818000	-1.606142000
6	3.831472000	0.693404000	0.510715000
1	4.514247000	1.293944000	1.106069000
6	2.452442000	0.866280000	0.623571000

1	2.069401000	1.610691000	1.313816000
7	-1.823546000	1.792180000	-0.225815000
8	-0.402997000	-2.021270000	0.161267000
8	0.252500000	2.686838000	-0.258830000
1	-2.160302000	2.742292000	-0.329314000
1	0.321852000	-1.491301000	2.293624000
1	-5.260663000	-2.199204000	-0.243394000
1	0.072698000	-0.024610000	1.741177000
8	0.213859000	-0.569837000	2.619796000
1	1.061509000	-0.292222000	3.020164000

For 4A.H₂O

6	3.390583000	-0.435545000	-1.254958000
1	3.857813000	-0.947392000	-2.089927000
6	4.195277000	0.095102000	-0.239891000
8	5.553435000	-0.072315000	-0.353051000
1	5.988577000	0.339807000	0.408963000
6	-2.335948000	-0.530844000	-0.036823000
6	-3.196857000	-1.646483000	-0.062474000
1	-2.765344000	-2.640490000	-0.064685000
6	-4.571870000	-1.475683000	-0.086006000
6	-5.117378000	-0.179529000	-0.078635000
1	-6.194454000	-0.045019000	-0.096619000
6	-4.292665000	0.934551000	-0.045759000

1	-4.705599000	1.938697000	-0.035676000
6	-2.897830000	0.764928000	-0.023666000
6	-0.672973000	1.795531000	0.030820000
6	-0.081300000	0.466714000	-0.019156000
6	-0.891865000	-0.650737000	-0.013520000
6	1.397237000	0.366510000	-0.101318000
6	2.006899000	-0.294615000	-1.180590000
1	1.385848000	-0.715358000	-1.965418000
6	3.609526000	0.771299000	0.837006000
1	4.239844000	1.186193000	1.618777000
6	2.223393000	0.904836000	0.897536000
1	1.774483000	1.426750000	1.736182000
7	-2.052982000	1.854277000	0.022796000
8	-0.433096000	-1.918567000	0.004028000
8	-0.017707000	2.857839000	0.071990000
1	-2.453487000	2.785938000	0.045924000
1	0.507102000	-1.999704000	0.322257000
1	-5.226722000	-2.340566000	-0.108172000
1	2.214577000	-1.697397000	1.563943000
8	1.969922000	-2.503669000	1.082010000
1	2.582424000	-2.493906000	0.329658000

For 2v

6	-3.547530000	-1.042980000	0.875732000
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1	-4.012233000	-1.755816000	1.548960000
6	-4.349307000	-0.298711000	0.005609000
8	-5.703891000	-0.519930000	0.043737000
1	-6.141261000	0.067523000	-0.591557000
6	2.220974000	-0.600192000	-0.091698000
6	3.138442000	-1.662037000	-0.226173000
1	2.761478000	-2.668181000	-0.368108000
6	4.502069000	-1.422239000	-0.174743000
6	4.977825000	-0.111534000	0.010396000
1	6.046390000	0.075439000	0.050651000
6	4.095833000	0.950043000	0.142347000
1	4.455031000	1.964822000	0.283538000
6	2.712210000	0.711344000	0.092034000
6	0.434615000	1.621906000	0.189038000
6	-0.087050000	0.272347000	0.016255000
6	0.788671000	-0.781020000	-0.134417000
6	-1.558331000	0.078086000	0.012311000
6	-2.168115000	-0.848105000	0.878187000
1	-1.555959000	-1.412401000	1.576042000
6	-3.764387000	0.634891000	-0.859870000
1	-4.394599000	1.208942000	-1.533861000
6	-2.385028000	0.815666000	-0.852855000
1	-1.939059000	1.540376000	-1.525265000
7	1.809769000	1.746927000	0.215487000

8	0.385569000	-2.059798000	-0.344510000
8	-0.273568000	2.640950000	0.316968000
1	2.161147000	2.690164000	0.341723000
1	-0.582010000	-2.089397000	-0.436060000
1	5.202449000	-2.244538000	-0.276950000

For 2B

6	3.518597000	-1.067212000	-1.196966000
1	3.949339000	-1.573815000	-2.054362000
6	4.306907000	-0.171546000	-0.463965000
8	5.600374000	0.020010000	-0.884183000
6	-2.283754000	-0.308117000	0.254612000
6	-3.041128000	-1.447485000	0.483248000
1	-2.635116000	-2.270919000	1.062816000
6	-4.340322000	-1.500759000	-0.041148000
6	-4.849588000	-0.430024000	-0.783379000
1	-5.856561000	-0.487822000	-1.185071000
6	-4.088962000	0.723991000	-1.020152000
1	-4.484293000	1.556429000	-1.592516000
6	-2.808864000	0.762392000	-0.486212000
6	-0.717383000	1.493800000	0.145304000
6	0.240218000	-0.925393000	0.667671000
6	-0.892666000	0.055251000	0.617795000
6	1.649477000	-0.636603000	0.294572000

6	2.202401000	-1.299481000	-0.810636000
1	1.595778000	-2.003498000	-1.373903000
6	3.771928000	0.482908000	0.652466000
1	4.392863000	1.169096000	1.221799000
6	2.449753000	0.251198000	1.022810000
1	2.032135000	0.762338000	1.881969000
7	-1.853398000	1.793003000	-0.558365000
8	-0.298556000	-0.340630000	1.861916000
8	0.235043000	2.241957000	0.343157000
1	-2.019807000	2.704266000	-0.966539000
1	-0.078205000	-1.956064000	0.502338000
1	-4.954729000	-2.378695000	0.129922000
1	6.037821000	0.659453000	-0.301127000

For 3B'

6	3.646861000	-1.274548000	-1.000109000
1	4.104827000	-1.966368000	-1.704621000
6	4.472344000	-0.200329000	-0.492897000
8	5.685589000	-0.034612000	-0.841877000
6	-2.243560000	-0.289055000	0.286313000
6	-2.960798000	-1.439839000	0.580774000
1	-2.535182000	-2.201936000	1.226852000
6	-4.246660000	-1.587042000	0.040724000
6	-4.786556000	-0.593845000	-0.782776000

1	-5.782201000	-0.722605000	-1.196367000
6	-4.070273000	0.573810000	-1.084578000
1	-4.493357000	1.346404000	-1.718138000
6	-2.801973000	0.707101000	-0.534653000
6	-0.751127000	1.563929000	0.105675000
6	0.307201000	-0.819927000	0.683003000
6	-0.870455000	0.144970000	0.632734000
6	1.706106000	-0.570760000	0.304374000
6	2.330489000	-1.447018000	-0.608395000
1	1.758012000	-2.282456000	-1.012815000
6	3.799937000	0.664747000	0.452891000
1	4.381758000	1.482390000	0.875244000
6	2.479691000	0.486771000	0.826467000
1	2.013232000	1.167367000	1.530874000
7	-1.889125000	1.766079000	-0.653807000
8	-0.248214000	-0.220995000	1.865354000
8	0.143655000	2.377955000	0.280541000
1	-2.084824000	2.648678000	-1.104776000
1	-0.027044000	-1.849936000	0.527085000
1	-4.826957000	-2.476659000	0.263880000

For 3B''

6	3.839660000	-1.418659000	0.071835000
1	4.556102000	-2.220972000	0.222878000

6	4.294125000	-0.247376000	-0.666837000
8	5.464130000	-0.155145000	-1.116554000
6	-2.087740000	-0.359856000	0.296497000
6	-2.717015000	-1.591712000	0.388977000
1	-2.374172000	-2.329080000	1.109877000
6	-3.805172000	-1.864541000	-0.455276000
6	-4.243021000	-0.905525000	-1.373357000
1	-5.085064000	-1.126910000	-2.022405000
6	-3.618096000	0.346991000	-1.471264000
1	-3.961396000	1.096345000	-2.177340000
6	-2.546805000	0.592169000	-0.622607000
6	-0.844065000	1.660801000	0.494057000
6	0.323202000	-0.656577000	0.841207000
6	-0.894839000	0.208166000	1.072245000
6	1.596020000	-0.445524000	0.358517000
6	2.571379000	-1.502959000	0.550248000
1	2.255028000	-2.387077000	1.098581000
6	3.308407000	0.809827000	-0.864229000
1	3.629546000	1.681217000	-1.427759000
6	2.041456000	0.718205000	-0.380050000
1	1.348444000	1.526939000	-0.566575000
7	-1.775801000	1.763671000	-0.501616000
8	-0.955758000	0.214420000	2.448406000
8	-0.142984000	2.586385000	0.904699000

1	-1.995684000	2.640309000	-0.958799000
1	0.142040000	-1.629813000	1.293970000
1	-4.312311000	-2.822497000	-0.393307000

For TS1B

6	3.095749000	-1.286244000	0.760295000
1	3.621137000	-2.162089000	1.132207000
6	3.736741000	-0.519943000	-0.288312000
8	4.866861000	-0.847460000	-0.773025000
6	-1.628596000	-0.308532000	0.420789000
6	-2.142899000	-1.412666000	1.099592000
1	-2.124716000	-1.445315000	2.184847000
6	-2.652050000	-2.486143000	0.363212000
6	-2.650038000	-2.444298000	-1.036362000
1	-3.038290000	-3.286701000	-1.600276000
6	-2.177684000	-1.321822000	-1.727057000
1	-2.218188000	-1.266959000	-2.810374000
6	-1.680318000	-0.258047000	-0.983115000
6	-1.104993000	1.935792000	-0.513646000
6	-0.119346000	0.487542000	1.357058000
6	-1.242167000	1.328225000	0.914848000
6	1.159646000	0.212865000	0.795545000
6	1.875231000	-0.928153000	1.271696000
1	1.417795000	-1.531831000	2.052987000

6	3.014039000	0.652511000	-0.732867000
1	3.489319000	1.274196000	-1.487271000
6	1.786373000	0.993744000	-0.221156000
1	1.310862000	1.905230000	-0.565235000
7	-1.282499000	0.985969000	-1.479305000
8	-2.034857000	1.946375000	1.725632000
8	-0.888847000	3.126543000	-0.726998000
1	-1.291192000	1.221749000	-2.465317000
1	-0.307669000	0.073864000	2.346696000
1	-3.044959000	-3.356584000	0.878871000

For 4B'

6	3.492059000	-0.211661000	0.709607000
1	4.408510000	0.046681000	1.236005000
6	3.612183000	-0.970987000	-0.507327000
8	4.751442000	-1.346917000	-0.979968000
6	-1.480377000	-0.416406000	0.661022000
6	-1.909947000	-1.591087000	1.280944000
1	-1.388924000	-1.931034000	2.171459000
6	-2.981018000	-2.324910000	0.768712000
6	-3.631332000	-1.883997000	-0.386859000
1	-4.463153000	-2.448085000	-0.796822000
6	-3.219678000	-0.712569000	-1.019472000
1	-3.720364000	-0.358352000	-1.915697000

6	-2.148428000	0.017554000	-0.494243000
6	-0.843176000	2.104048000	-0.656955000
6	-0.274516000	0.339323000	1.162903000
6	-0.286742000	1.788780000	0.742494000
6	1.058023000	-0.157181000	0.569730000
6	2.263785000	0.182950000	1.214191000
1	2.222315000	0.767513000	2.131505000
6	2.365688000	-1.279370000	-1.151527000
1	2.404449000	-1.852955000	-2.075224000
6	1.141489000	-0.879688000	-0.634024000
1	0.231965000	-1.151211000	-1.163438000
7	-1.734633000	1.201594000	-1.141354000
8	0.185414000	2.705265000	1.400871000
8	-0.538167000	3.140409000	-1.250946000
1	-2.163283000	1.431807000	-2.033126000
1	-0.223440000	0.300142000	2.254719000
1	-3.303248000	-3.234521000	1.265275000

For 3B

6	2.446917000	-1.070006000	-1.216715000
1	2.540490000	-1.578479000	-2.170732000
6	3.602041000	-0.760646000	-0.491072000
8	4.809226000	-1.127622000	-1.033215000
6	-1.436793000	-0.506329000	0.630064000

6	-1.677990000	-1.756688000	1.203999000
1	-1.045310000	-2.084251000	2.023997000
6	-2.703424000	-2.577793000	0.735328000
6	-3.501319000	-2.148390000	-0.328975000
1	-4.300760000	-2.779609000	-0.703816000
6	-3.279159000	-0.903931000	-0.913535000
1	-3.895352000	-0.556421000	-1.737640000
6	-2.249825000	-0.087315000	-0.432710000
6	-1.201434000	2.140709000	-0.587077000
6	-0.285084000	0.352045000	1.100196000
6	-0.437749000	1.810536000	0.708274000
6	1.077490000	-0.079816000	0.528329000
6	1.196357000	-0.726534000	-0.708339000
1	0.308162000	-0.978462000	-1.278463000
6	3.499298000	-0.103044000	0.741016000
1	4.398456000	0.133025000	1.303464000
6	2.243549000	0.236713000	1.237468000
1	2.167932000	0.753378000	2.189596000
7	-2.034245000	1.170225000	-1.035235000
8	0.067336000	2.726794000	1.331477000
8	-1.068689000	3.234819000	-1.137601000
1	-2.580895000	1.400642000	-1.860276000
1	-0.218321000	0.324236000	2.191596000
1	-2.877680000	-3.544914000	1.195637000

1 5.522747000 -0.869708000 -0.429524000

For 3B.H₂O

6 2.171205000 -1.916640000 -0.936480000

1 2.159350000 -2.782630000 -1.590215000

6 3.395033000 -1.439932000 -0.454950000

8 4.531120000 -2.108071000 -0.839406000

6 -1.512516000 -0.303527000 0.669335000

6 -1.779689000 -1.163815000 1.736521000

1 -1.108514000 -1.158836000 2.590630000

6 -2.879725000 -2.020861000 1.710498000

6 -3.727243000 -2.024645000 0.599065000

1 -4.585049000 -2.688811000 0.566618000

6 -3.479948000 -1.171960000 -0.474066000

1 -4.134396000 -1.163540000 -1.340584000

6 -2.375047000 -0.314749000 -0.435998000

6 -1.212403000 1.533763000 -1.583505000

6 -0.284494000 0.577225000 0.675614000

6 -0.392710000 1.733375000 -0.297181000

6 1.005841000 -0.167197000 0.280317000

6 0.988110000 -1.278876000 -0.571684000

1 0.045222000 -1.663297000 -0.946358000

6 3.427757000 -0.322292000 0.388031000

1 4.380487000 0.042884000 0.761806000

6	2.239151000	0.309366000	0.744601000
1	2.267731000	1.181916000	1.389736000
7	-2.132409000	0.540945000	-1.531988000
8	0.182167000	2.800324000	-0.147767000
8	-1.045646000	2.266521000	-2.559015000
1	-2.717677000	0.434627000	-2.355893000
1	-3.073551000	-2.681087000	2.549529000
1	5.304815000	-1.678440000	-0.443734000
1	1.014253000	3.106491000	1.563650000
1	-0.137396000	1.008299000	1.669701000
8	1.456260000	3.229583000	2.424022000
1	1.020443000	2.573542000	2.985641000

For TS2B

6	-3.413696000	-0.421412000	-1.200981000
1	-4.004939000	-0.786579000	-2.034918000
6	-4.049046000	0.279305000	-0.169691000
8	-5.408472000	0.468659000	-0.273452000
6	1.126257000	0.770114000	-0.170048000
6	0.696455000	2.113225000	-0.195047000
1	-0.365656000	2.325123000	-0.155793000
6	1.601399000	3.166652000	-0.277901000
6	2.978498000	2.915769000	-0.333017000
1	3.687487000	3.735261000	-0.394621000

6	3.435919000	1.602815000	-0.317467000
1	4.497926000	1.378869000	-0.371398000
6	2.521623000	0.545530000	-0.241935000
6	2.217390000	-1.894175000	-0.284261000
6	0.219759000	-0.379122000	-0.042234000
6	0.709354000	-1.701178000	-0.275532000
6	-1.262490000	-0.160010000	-0.076411000
6	-2.038832000	-0.632501000	-1.148921000
1	-1.555262000	-1.175994000	-1.953766000
6	-3.302131000	0.756851000	0.911322000
1	-3.798047000	1.296996000	1.713409000
6	-1.925788000	0.532329000	0.949683000
1	-1.355579000	0.909831000	1.794079000
7	2.986703000	-0.770074000	-0.249363000
8	0.013153000	-2.745467000	-0.375079000
8	2.727751000	-3.024940000	-0.332387000
1	3.990264000	-0.924577000	-0.277595000
1	1.233022000	4.187848000	-0.301534000
1	-5.717193000	0.973867000	0.493805000
1	-0.194460000	-1.115914000	2.978634000
1	0.505260000	-0.638809000	1.542507000
8	0.635753000	-0.740188000	2.627496000
1	1.336738000	-1.405059000	2.774746000

For 4B.H₂O

6	-3.106351000	-0.362754000	1.277930000
1	-3.701270000	-0.221540000	2.174245000
6	-3.700402000	-0.931634000	0.144649000
8	-5.024161000	-1.279831000	0.231158000
6	1.492729000	-0.729555000	0.015676000
6	1.259226000	-2.122367000	0.018129000
1	0.237465000	-2.483618000	0.042446000
6	2.311607000	-3.025205000	-0.008531000
6	3.638356000	-2.563828000	-0.034255000
1	4.461828000	-3.270652000	-0.056347000
6	3.902787000	-1.202208000	-0.026820000
1	4.922243000	-0.827864000	-0.040141000
6	2.837731000	-0.288974000	0.001528000
6	2.136755000	2.061061000	0.049148000
6	0.429634000	0.258288000	0.043819000
6	0.742748000	1.593705000	0.042824000
6	-0.994641000	-0.175832000	0.080838000
6	-1.764643000	0.010415000	1.238957000
1	-1.308407000	0.459138000	2.115893000
6	-2.946324000	-1.129903000	-1.018350000
1	-3.412290000	-1.574040000	-1.893501000
6	-1.603343000	-0.756129000	-1.041841000
1	-1.022406000	-0.909833000	-1.945929000

7	3.085874000	1.073080000	0.024493000
8	-0.140351000	2.623124000	0.040074000
8	2.455928000	3.263756000	0.068990000
1	4.049428000	1.392790000	0.019690000
1	2.107645000	-4.091230000	-0.007271000
1	-5.307028000	-1.670213000	-0.610021000
1	-1.064196000	2.351944000	-0.200744000
1	-3.166014000	2.022017000	0.050098000
8	-2.726059000	2.377996000	-0.737536000
1	-2.736185000	1.620712000	-1.343565000

For 2v'

6	3.382877000	0.413494000	-1.041464000
1	4.003429000	0.797221000	-1.844472000
6	3.974850000	-0.324121000	-0.011000000
8	5.330503000	-0.522487000	-0.072366000
6	-1.220806000	-0.700593000	-0.046975000
6	-0.848981000	-2.058263000	-0.160927000
1	0.203081000	-2.314026000	-0.208029000
6	-1.805462000	-3.060319000	-0.219319000
6	-3.171956000	-2.737232000	-0.170221000
1	-3.920016000	-3.522466000	-0.214514000
6	-3.572048000	-1.413134000	-0.072927000
1	-4.623946000	-1.144242000	-0.043799000

6	-2.604090000	-0.398075000	-0.016209000
6	-2.150884000	2.009446000	0.110601000
6	-0.265106000	0.390744000	0.016521000
6	-0.724629000	1.679598000	0.087943000
6	1.201291000	0.132869000	0.007514000
6	2.008644000	0.636524000	-1.027422000
1	1.551055000	1.199761000	-1.835410000
6	3.188424000	-0.830746000	1.031484000
1	3.656564000	-1.397568000	1.831445000
6	1.815774000	-0.600645000	1.035684000
1	1.210948000	-0.993833000	1.846716000
7	-2.992186000	0.928958000	0.061757000
8	0.067090000	2.790301000	0.172200000
8	-2.586582000	3.172850000	0.177634000
1	-3.983565000	1.146998000	0.082117000
1	0.997103000	2.511419000	0.210914000
1	-1.495500000	-4.096709000	-0.306705000
1	5.610674000	-1.051859000	0.689993000

For TS1A'

6	-3.764643000	-0.690572000	0.163675000
1	-4.725065000	-1.195899000	0.182999000
6	-3.705419000	0.675604000	-0.194075000
8	-4.792621000	1.379816000	-0.522261000

6	1.736132000	0.198501000	0.522311000
6	1.888686000	1.188573000	1.480412000
1	1.667660000	0.976958000	2.522205000
6	2.318640000	2.461673000	1.076930000
6	2.594583000	2.718977000	-0.269176000
1	2.924099000	3.708331000	-0.571622000
6	2.462194000	1.717551000	-1.241861000
1	2.685013000	1.910375000	-2.286225000
6	2.038523000	0.465124000	-0.817195000
6	1.497217000	-1.776651000	-0.856661000
6	-0.205400000	-1.466626000	0.728813000
6	1.276130000	-1.245206000	0.714432000
6	-1.326356000	-0.688220000	0.438510000
6	-2.600663000	-1.349911000	0.468880000
1	-2.633312000	-2.401113000	0.736836000
6	-2.469423000	1.365670000	-0.219330000
1	-2.467665000	2.415668000	-0.488987000
6	-1.309537000	0.705012000	0.091609000
1	-0.375459000	1.247050000	0.070867000
7	1.846578000	-0.689274000	-1.599320000
8	1.951723000	-1.980873000	1.602099000
8	1.442746000	-2.937295000	-1.234058000
1	2.162225000	-0.774366000	-2.559580000
1	-0.411044000	-2.508676000	0.973753000

1	2.440633000	3.249785000	1.813341000
1	-5.591888000	0.826619000	-0.488226000

For TS1B'

6	3.263661000	-1.150310000	0.889939000
1	3.881190000	-1.908515000	1.358056000
6	3.730637000	-0.513844000	-0.279407000
8	4.930397000	-0.898434000	-0.744933000
6	-1.823882000	-0.226399000	0.401072000
6	-2.298475000	-1.327549000	1.109266000
1	-2.258577000	-1.339093000	2.194098000
6	-2.826645000	-2.407606000	0.395180000
6	-2.871019000	-2.374131000	-1.004470000
1	-3.280548000	-3.220704000	-1.546865000
6	-2.412436000	-1.264044000	-1.726239000
1	-2.473508000	-1.228293000	-2.808937000
6	-1.889827000	-0.199763000	-1.003264000
6	-1.129831000	1.907744000	-0.478605000
6	-0.027445000	0.475804000	1.360223000
6	-1.270526000	1.182846000	0.907935000
6	1.224759000	0.197421000	0.776071000
6	2.041543000	-0.791706000	1.406670000
1	1.671171000	-1.278121000	2.303578000
6	2.964869000	0.492161000	-0.906809000

1	3.361472000	0.993291000	-1.784235000
6	1.737141000	0.840257000	-0.390046000
1	1.190073000	1.646785000	-0.857539000
7	-1.442241000	1.033283000	-1.485829000
8	-1.958381000	1.860124000	1.817655000
8	-0.814416000	3.083244000	-0.632394000
1	-1.501278000	1.316127000	-2.457486000
1	-0.187375000	0.058665000	2.354490000
1	-3.205387000	-3.274680000	0.926415000
1	5.162512000	-0.403209000	-1.548505000

11. ¹H NMR and ¹³C NMR spectra of products

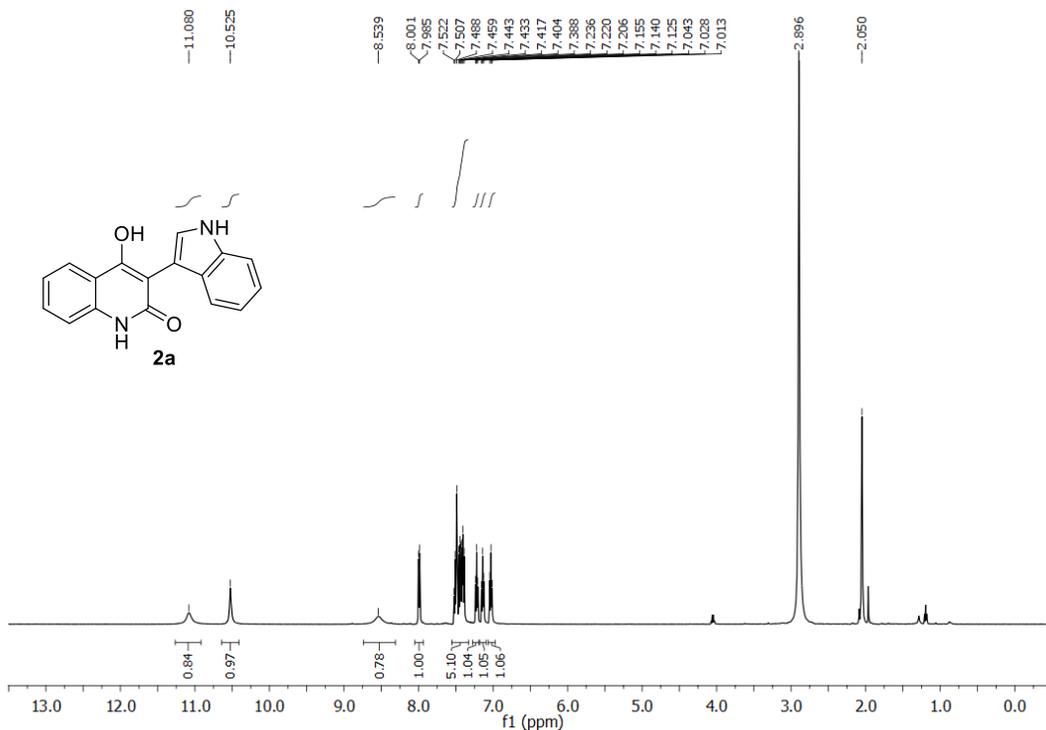


Fig S4. ¹H NMR (500 MHz, Acetone d₆) of 2a

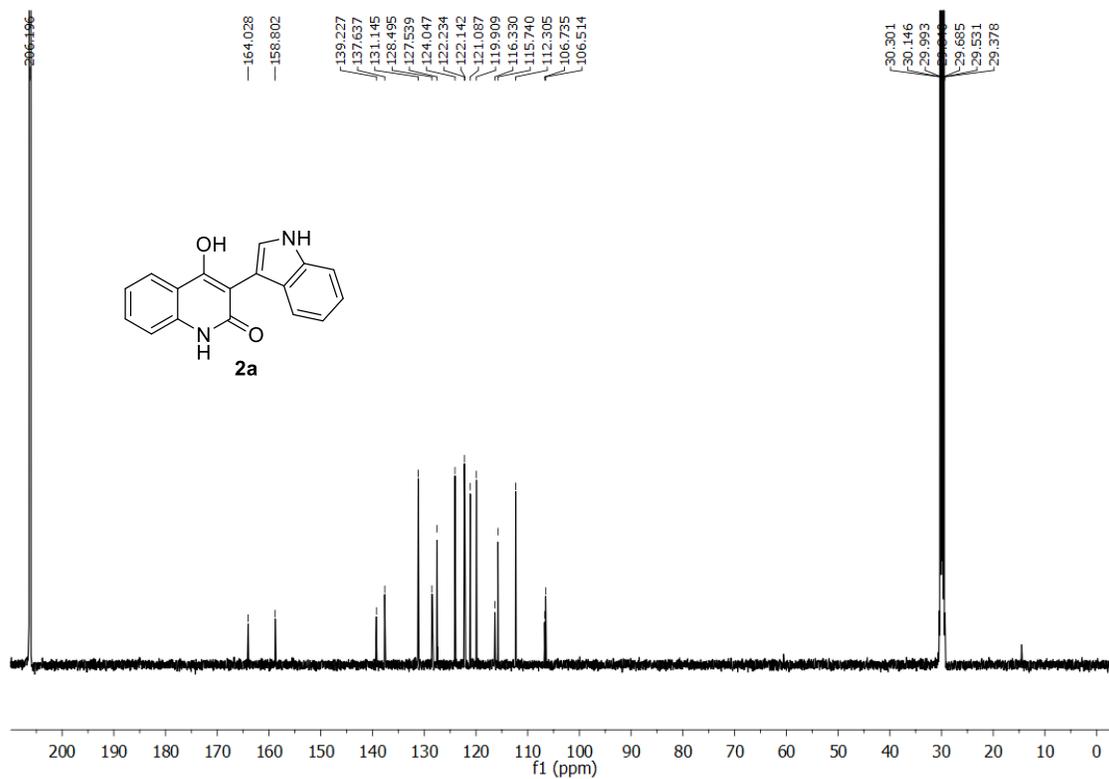


Fig S5. ¹³C NMR (125 MHz, Acetone d₆) of 2a

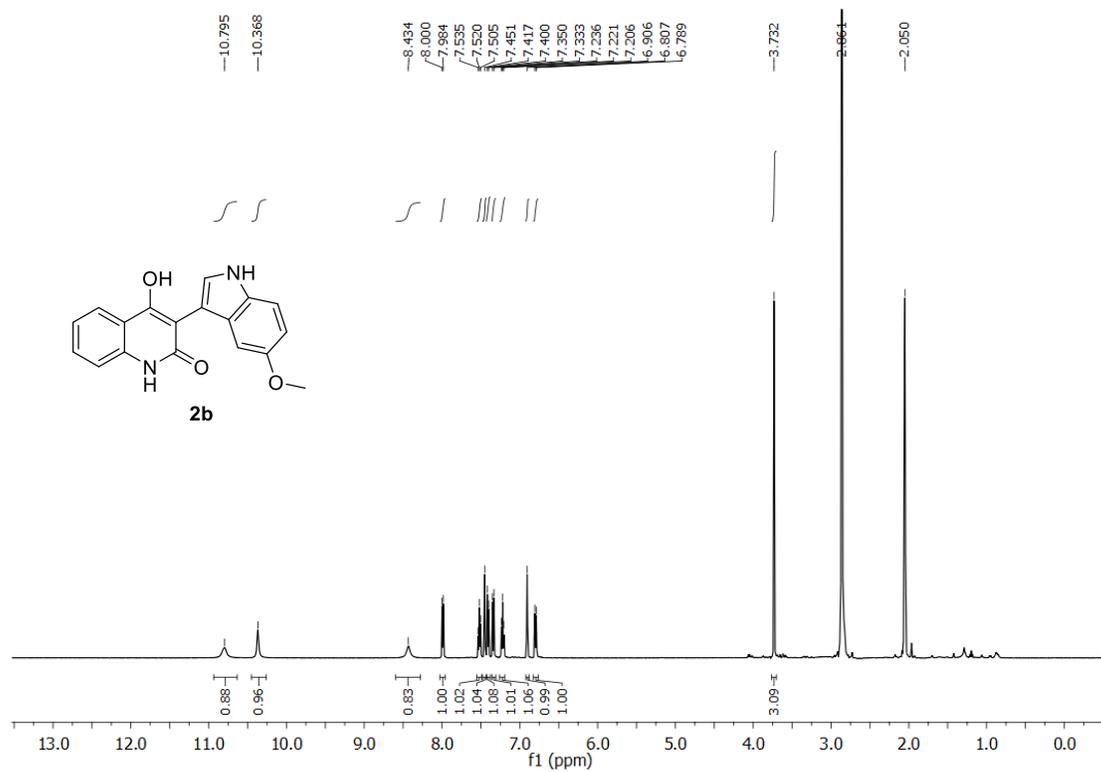


Fig S6. ¹H NMR (500 MHz, Acetone d₆) of **2b**

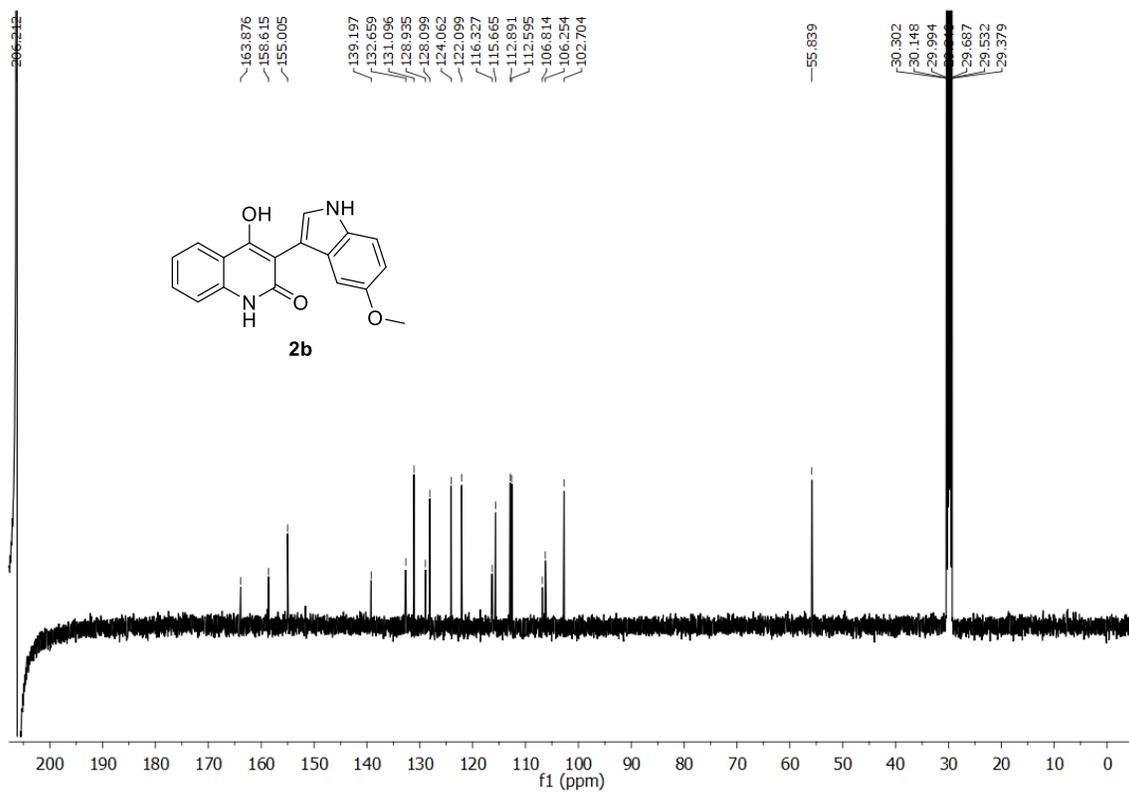


Fig S7. ¹³C NMR (125 MHz, Acetone d₆) of **2b**

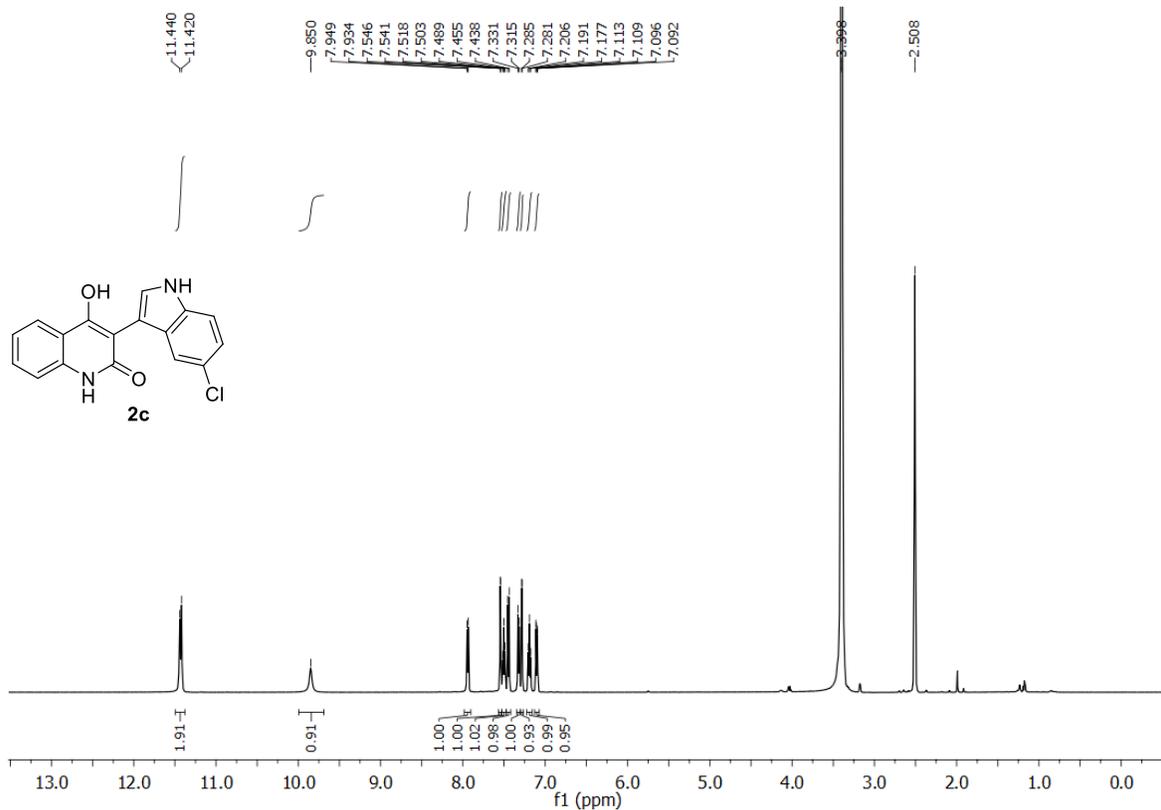


Fig S8. ¹H NMR (500 MHz, DMSO d₆) of **2c**

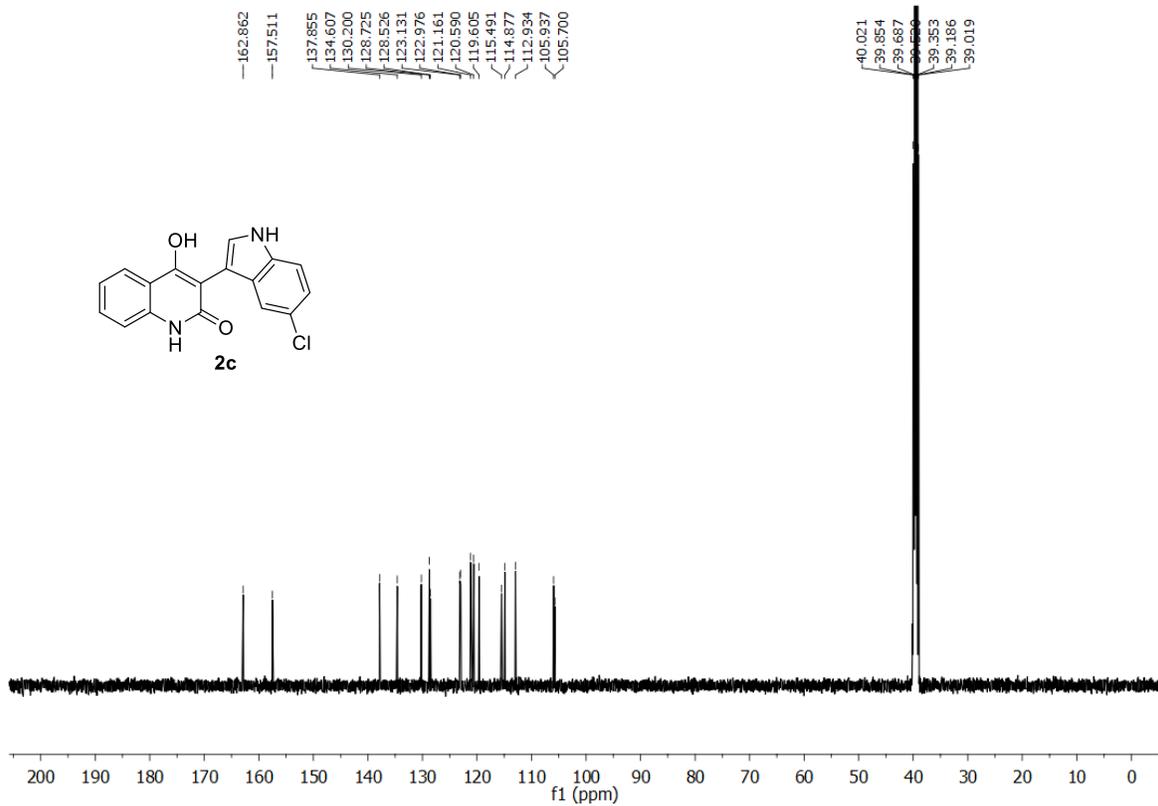


Fig S9. ¹³C NMR (125 MHz, DMSO d₆) of **2c**

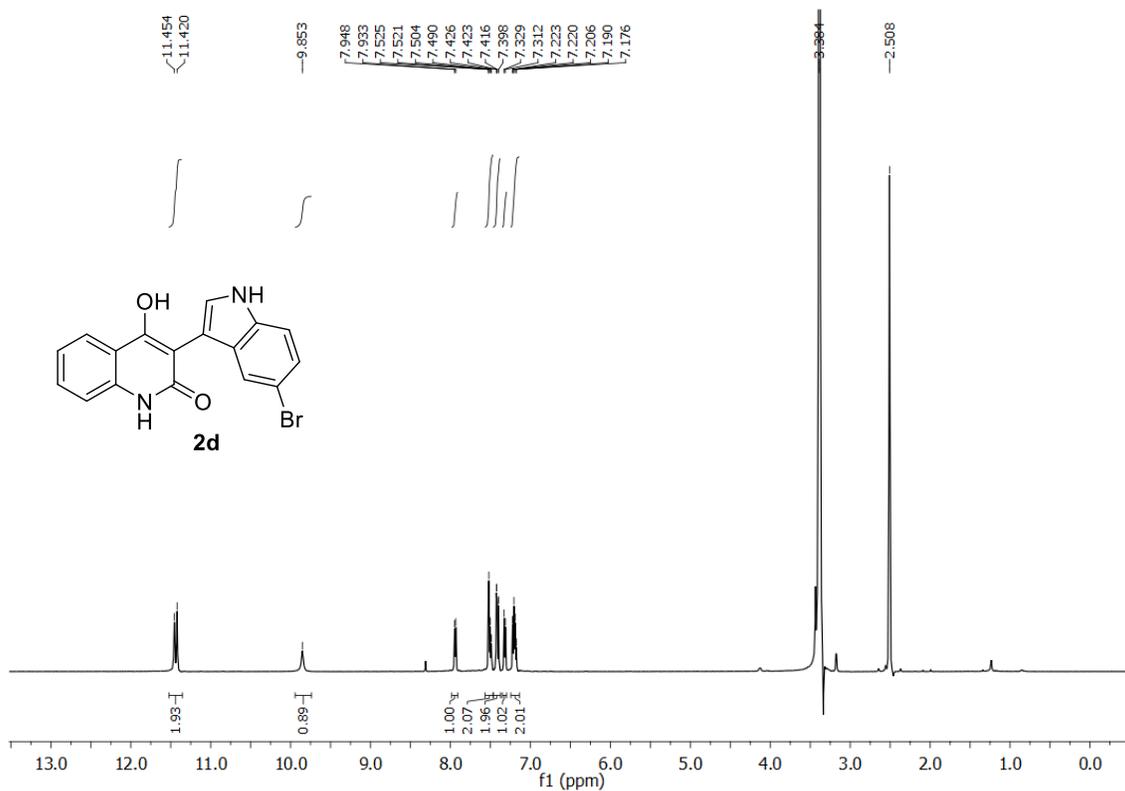


Fig S10. ¹H NMR (500 MHz, DMSO d₆) of **2d**

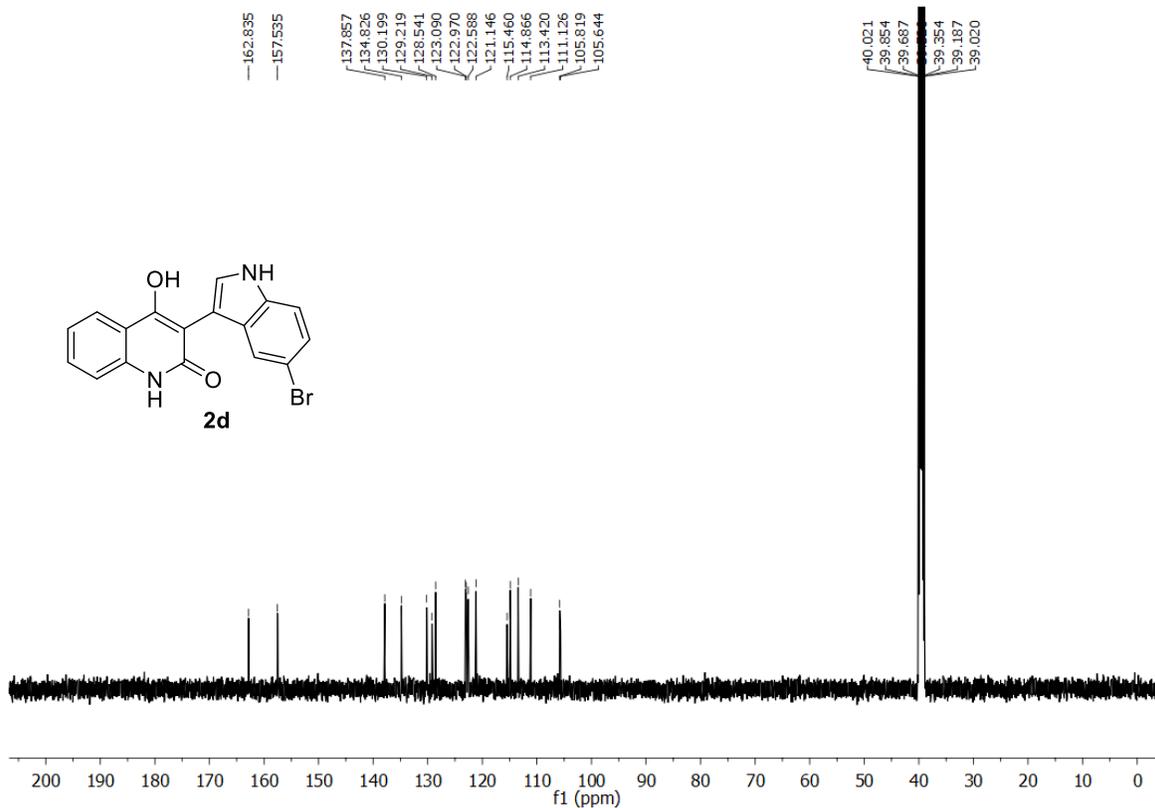


Fig S11. ¹³C NMR (125 MHz, DMSO d₆) of **2d**

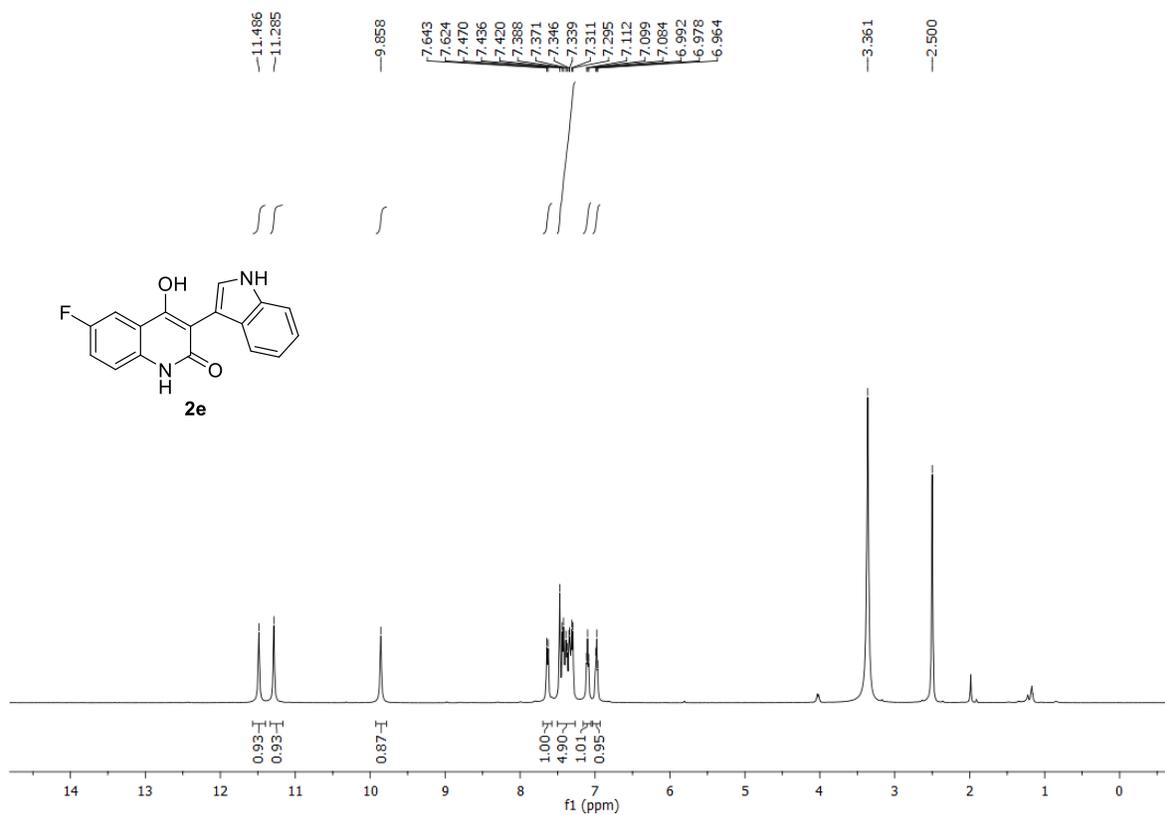


Fig S12. ¹H NMR (500 MHz, DMSO d₆) of **2e**

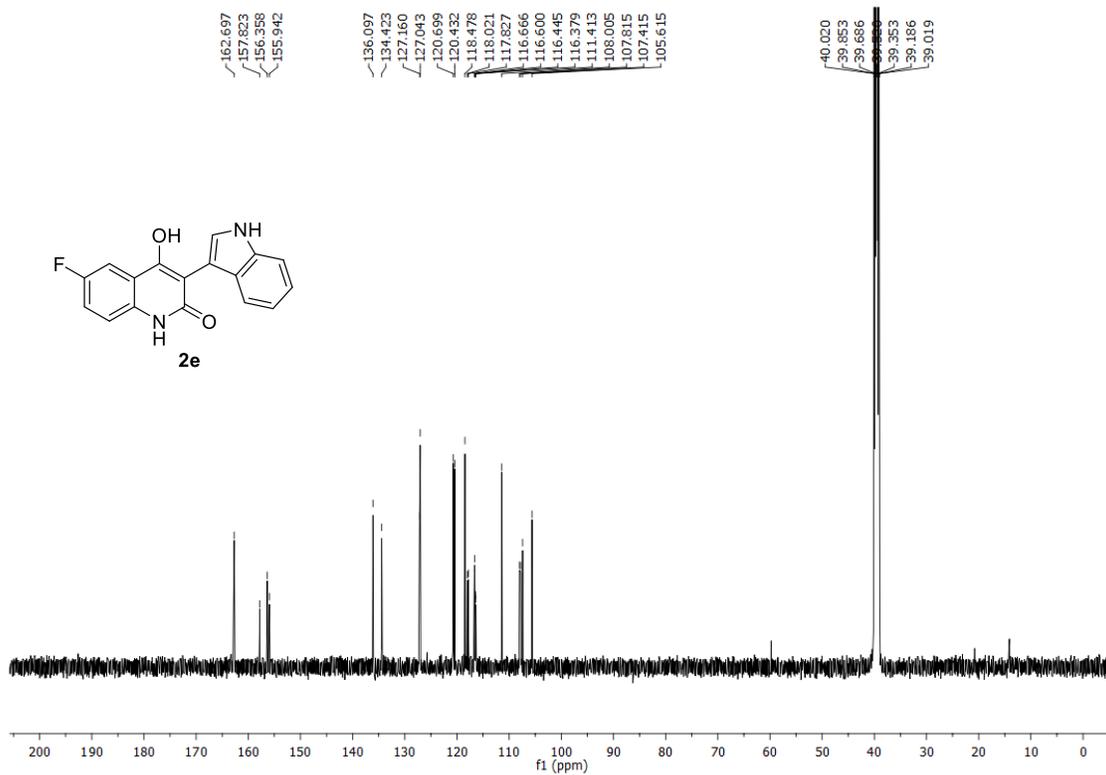


Fig S13. ¹³C NMR (125 MHz, DMSO d₆) of **2e**

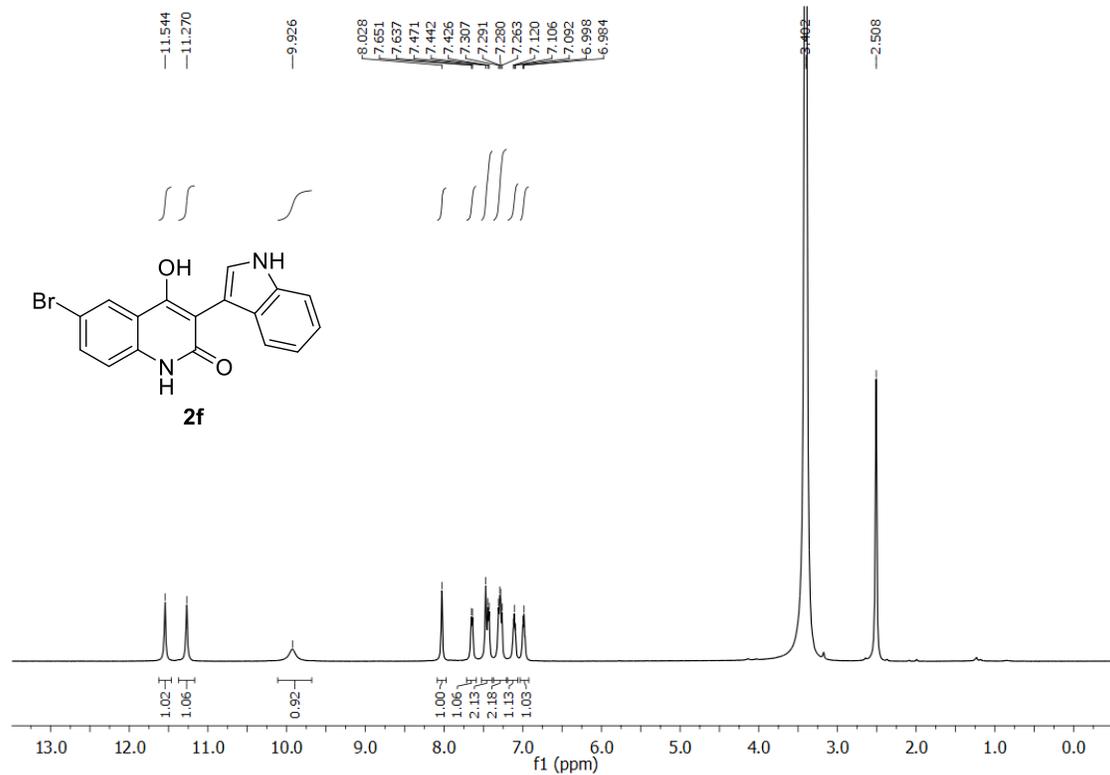


Fig S14. ¹H NMR (500 MHz, DMSO d₆) of **2f**

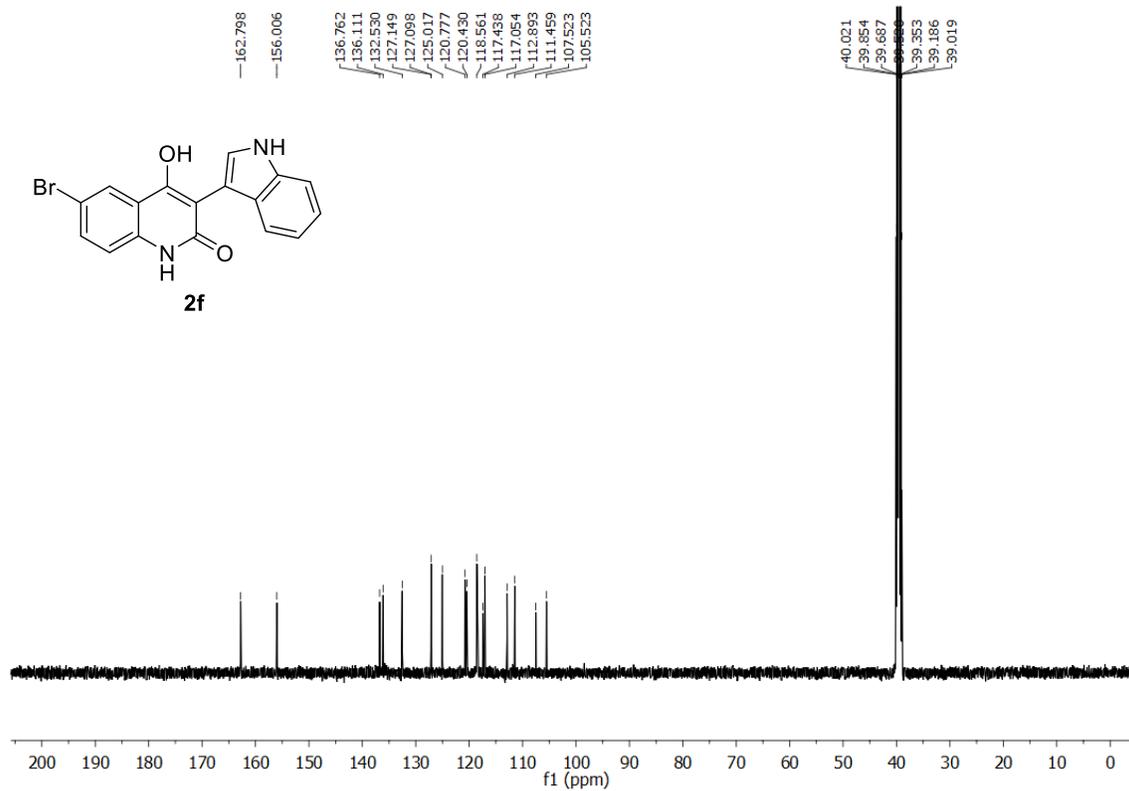


Fig S15. ¹³C NMR (125 MHz, DMSO d₆) of **2f**

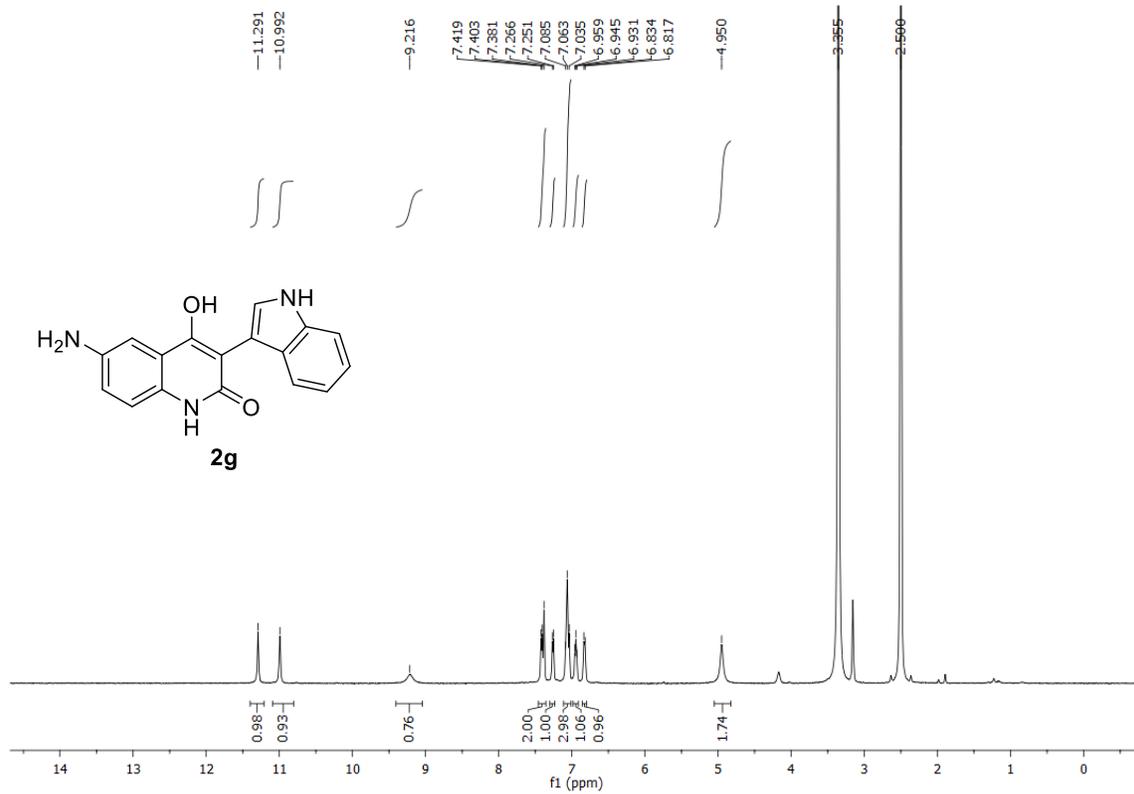


Fig S16. ¹H NMR (500 MHz, DMSO d₆) of **2g**

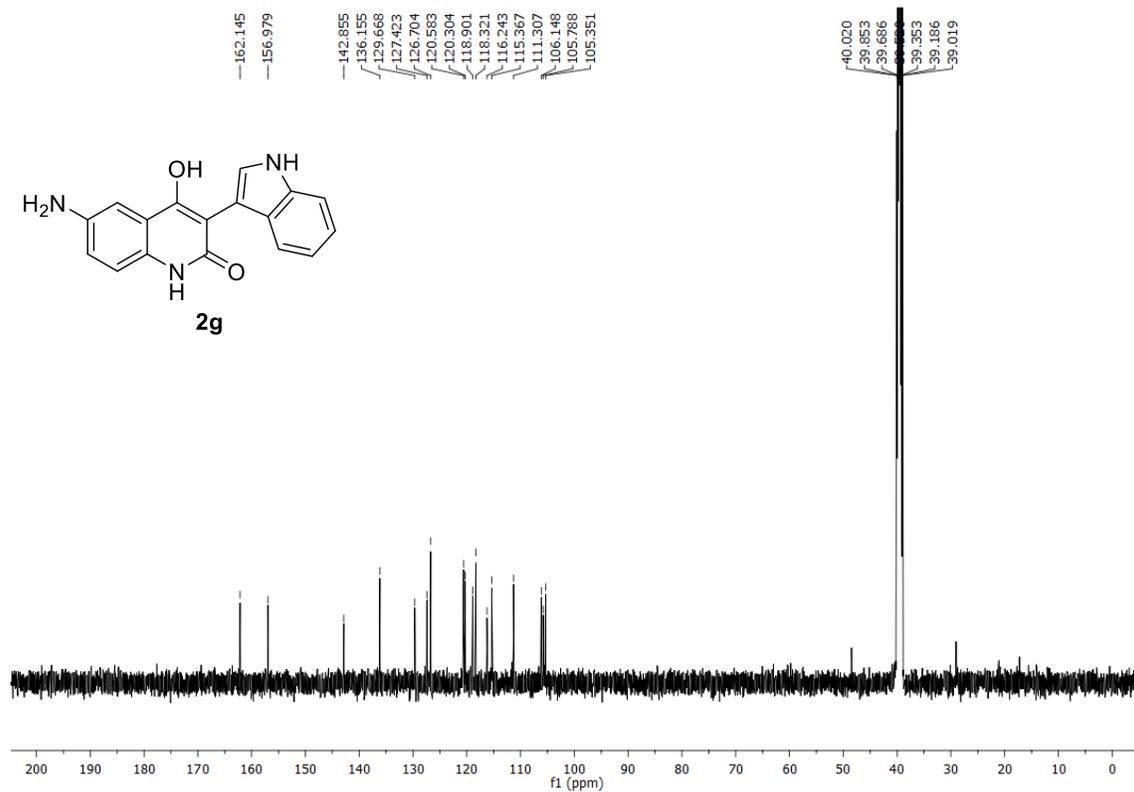


Fig S17. ¹³C NMR (125 MHz, DMSO d₆) of **2g**

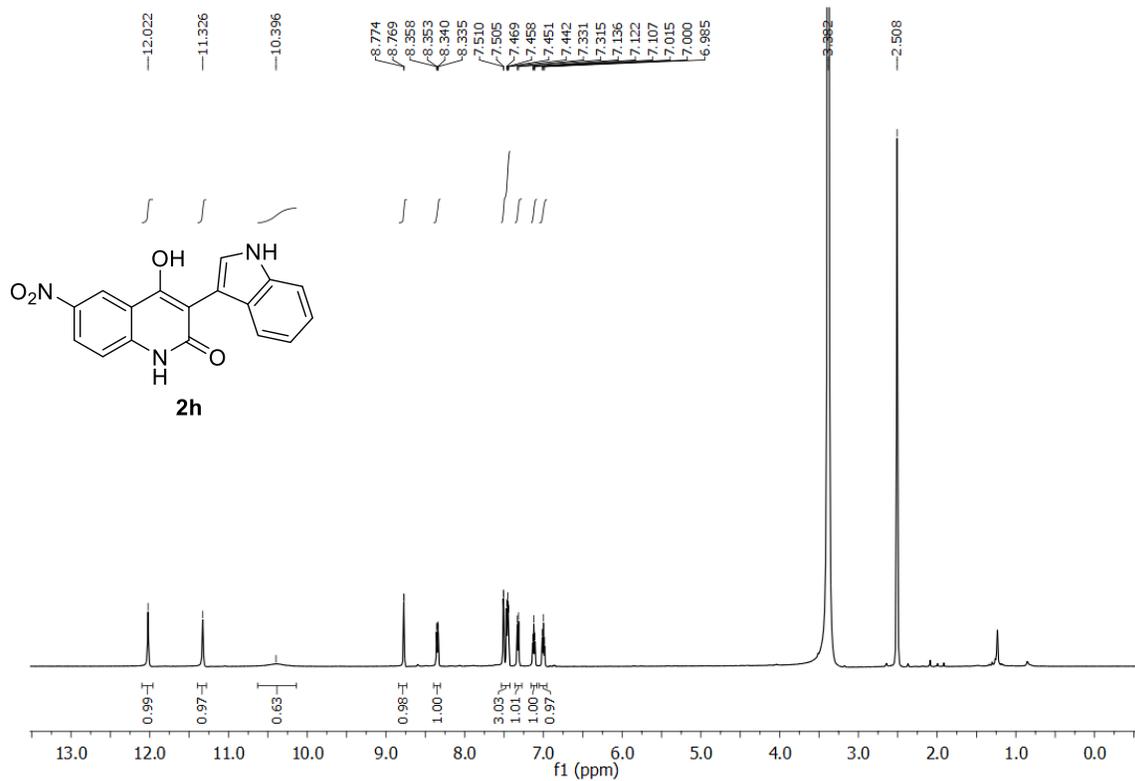


Fig S18. ¹H NMR (500 MHz, DMSO d₆) of **2h**

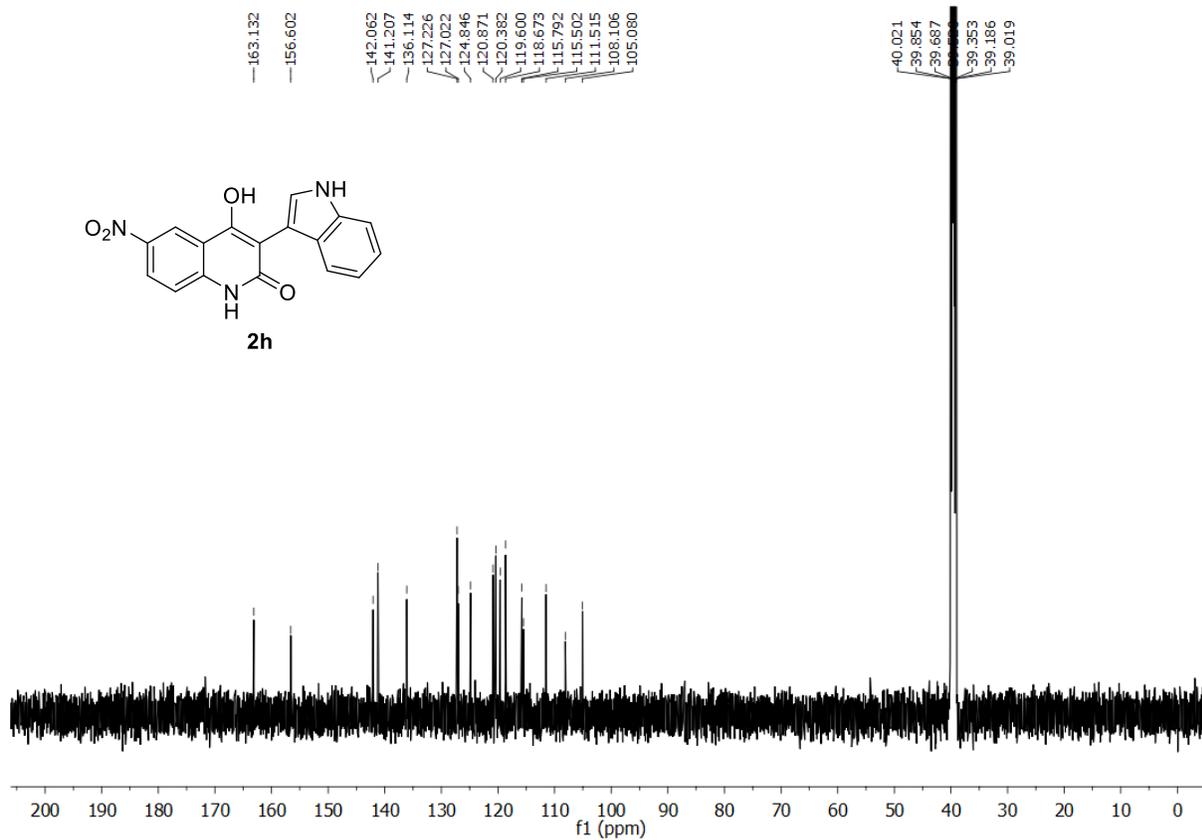


Fig S19. ¹³C NMR (125 MHz, DMSO d₆) of **2h**

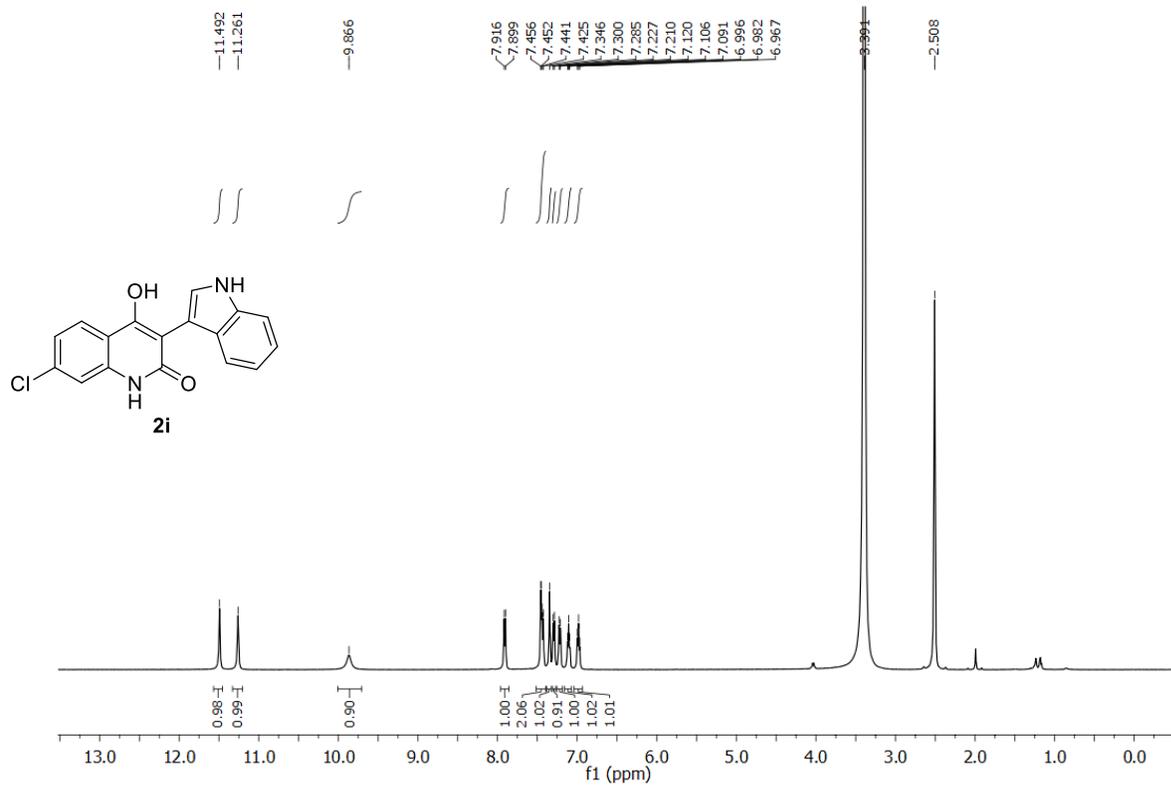


Fig S20. ¹H NMR (500 MHz, DMSO d₆) of **2i**

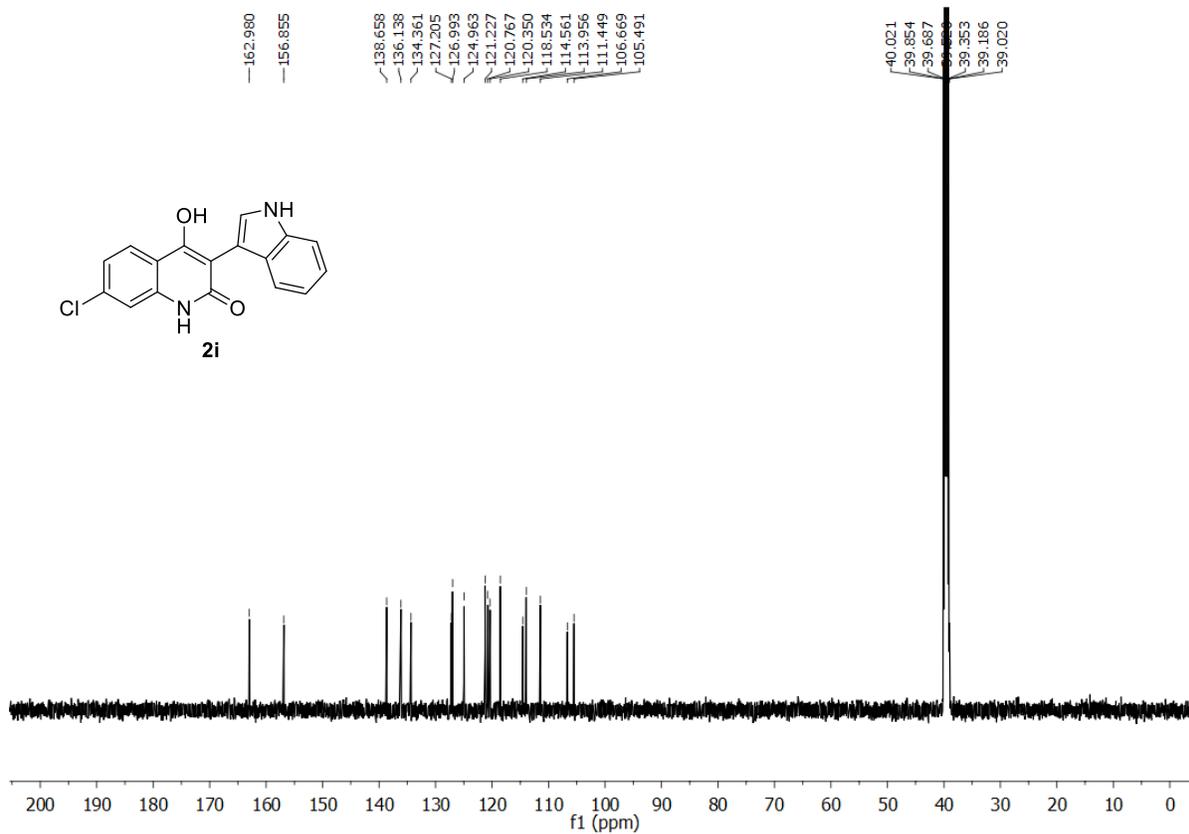


Fig S21. ¹³C NMR (125 MHz, DMSO d₆) of **2i**

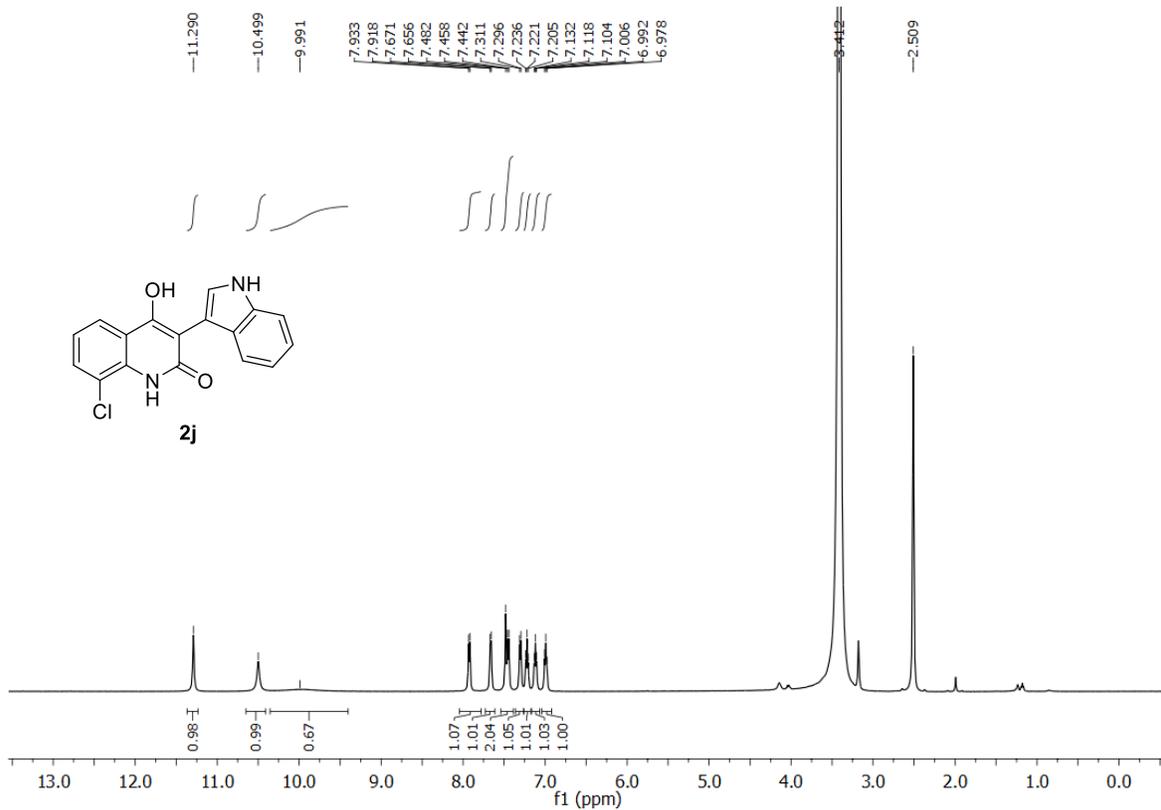


Fig S22. ¹H NMR (500 MHz, DMSO d₆) of **2j**

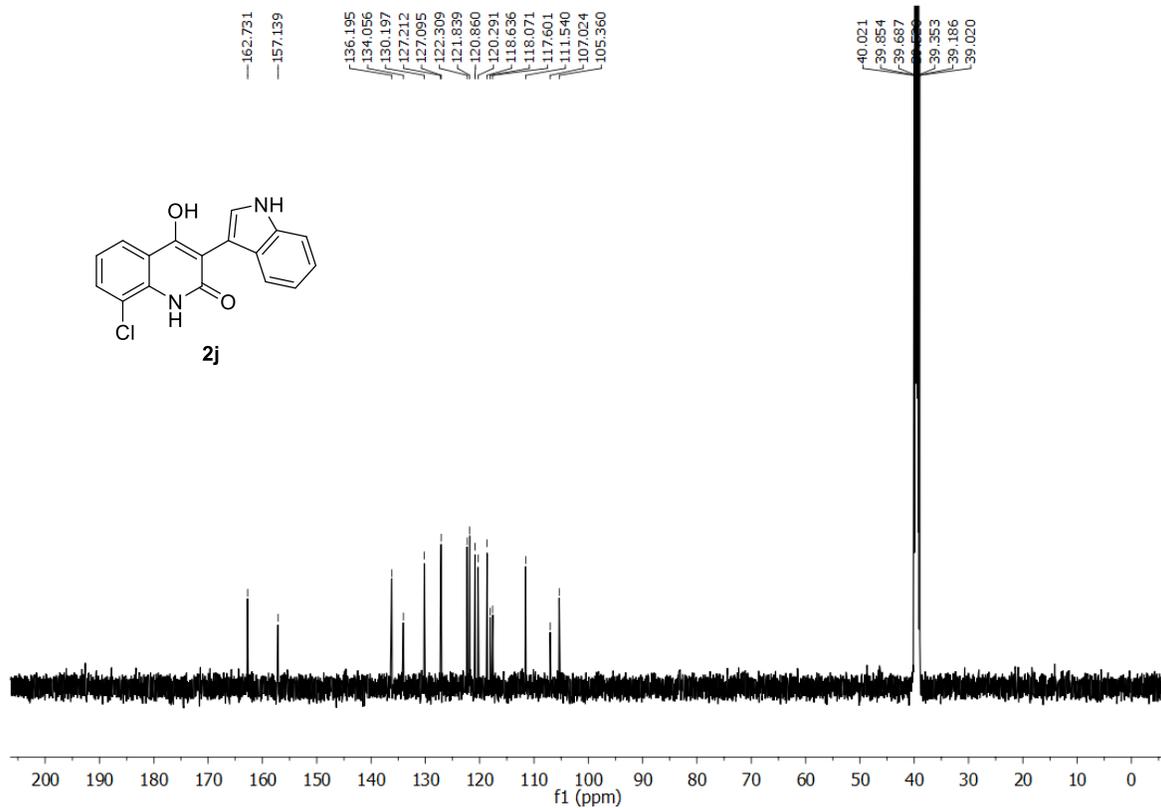


Fig S23. ¹³C NMR (125 MHz, DMSO d₆) of **2j**

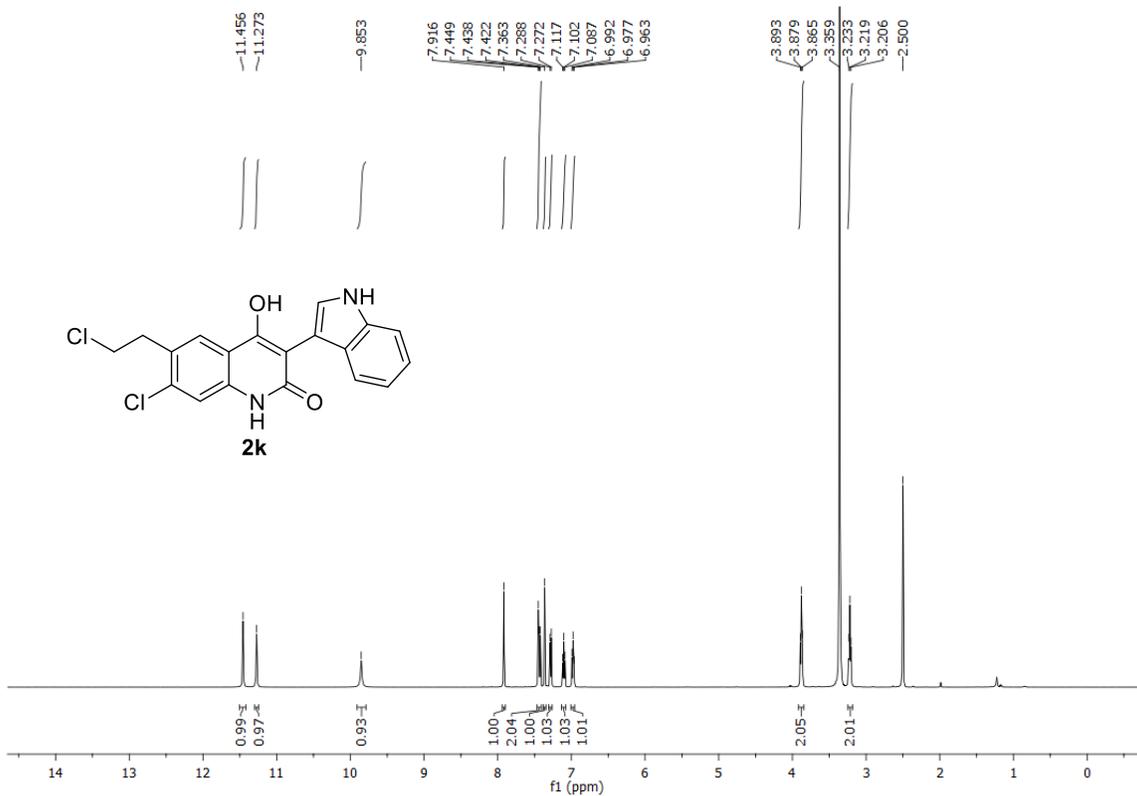


Fig S24. ¹H NMR (500 MHz, DMSO d₆) of **2k**

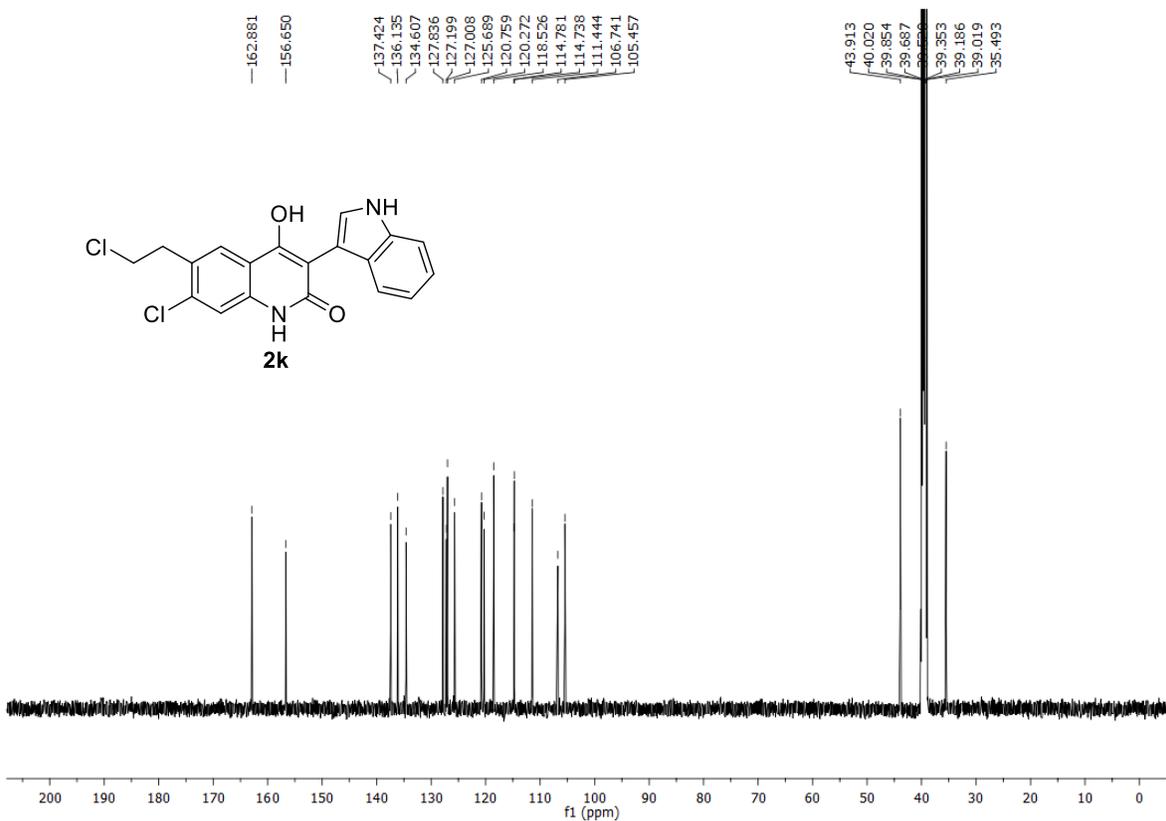


Fig S25. ¹³C NMR (125 MHz, DMSO d₆) of **2k**

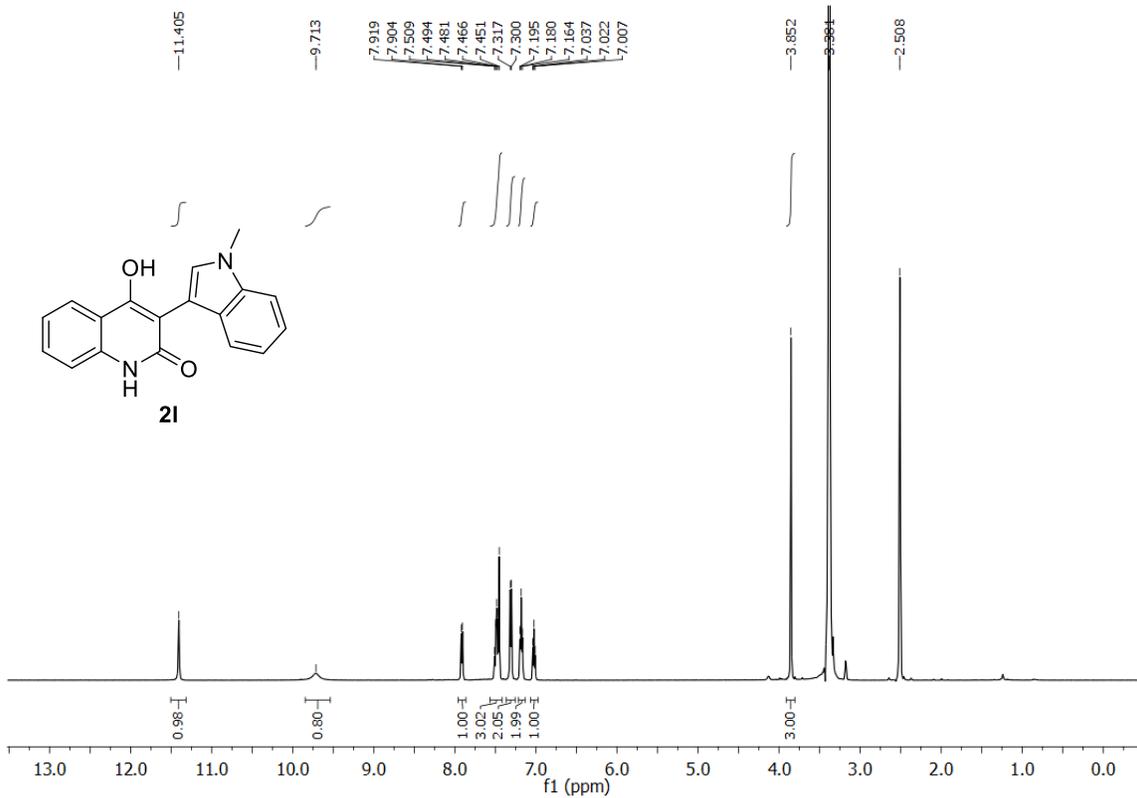


Fig S26. ¹H NMR (500 MHz, DMSO d₆) of **2I**

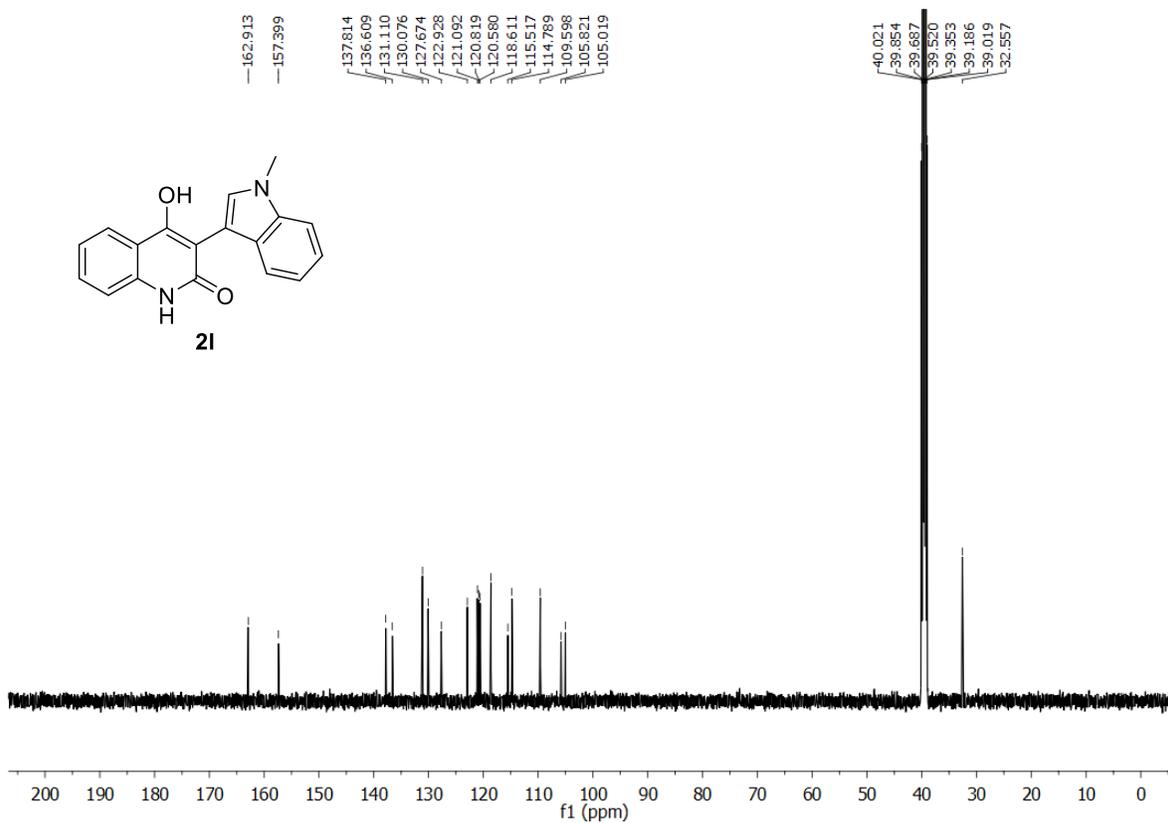


Fig S27. ¹³C NMR (125 MHz, DMSO d₆) of **2I**

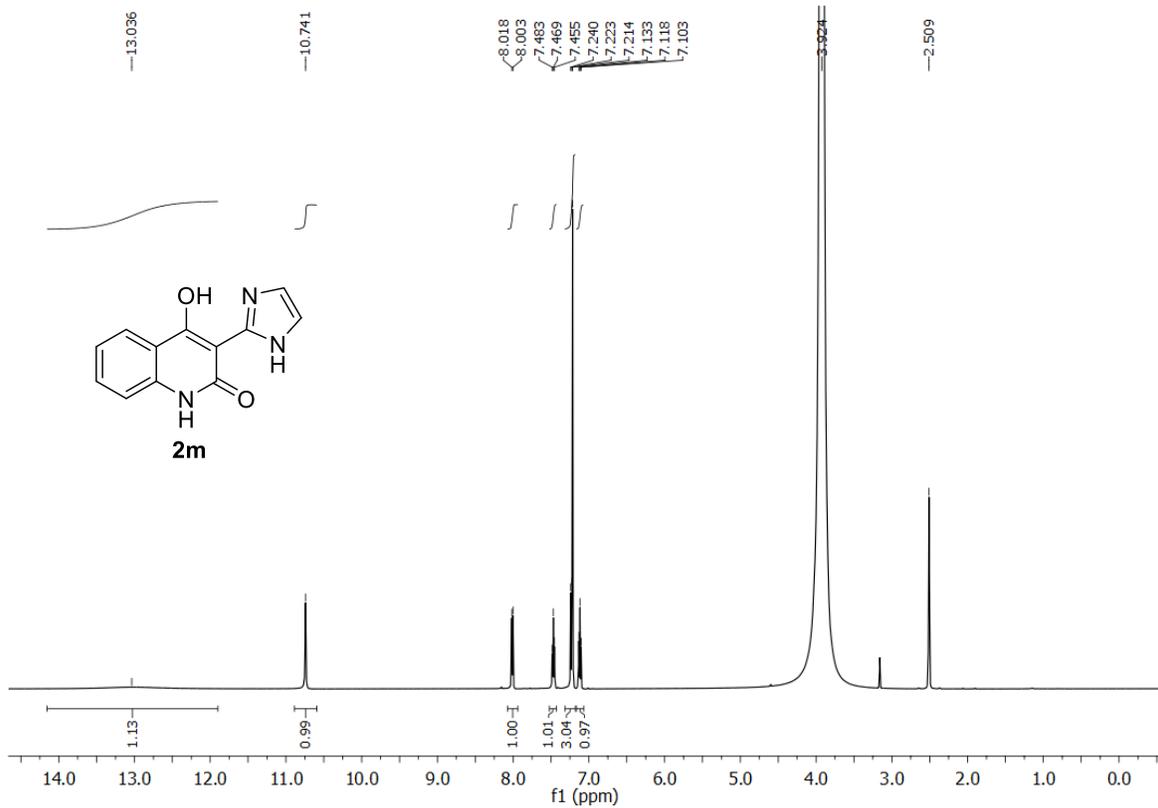


Fig S28. ¹H NMR (500 MHz, DMSO d₆) of **2m**

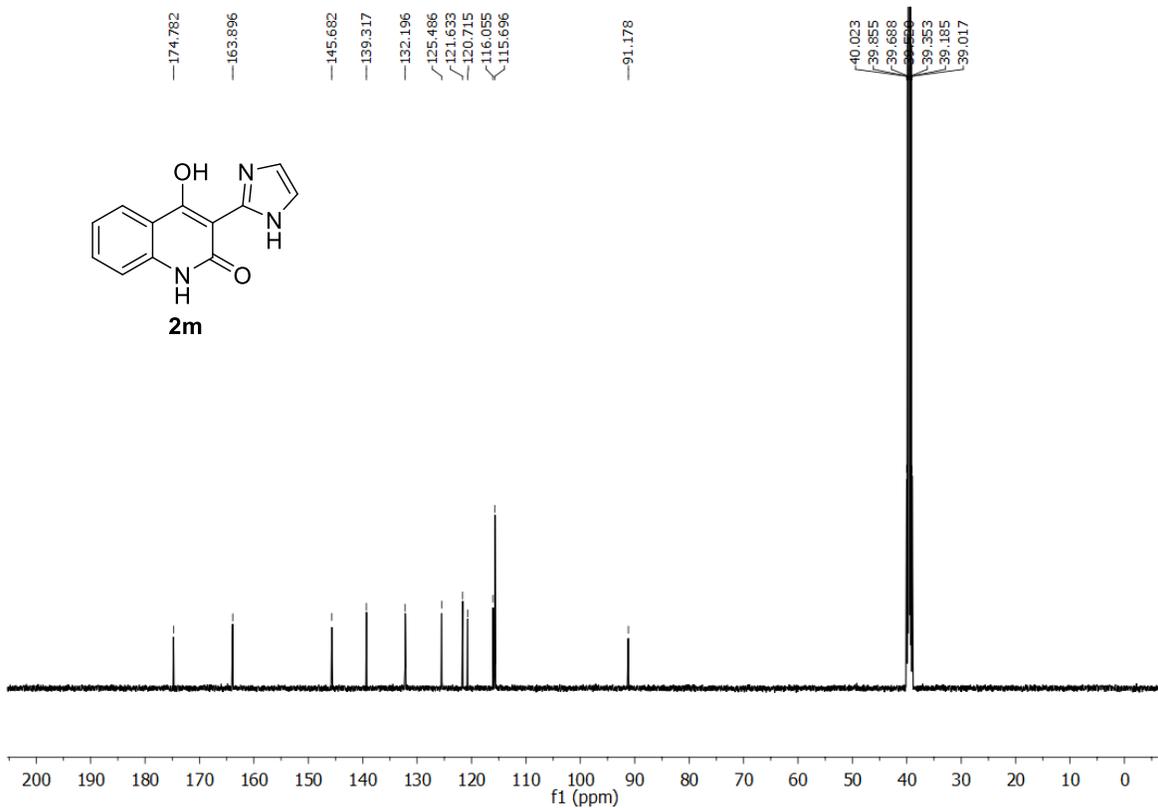


Fig S29. ¹³C NMR (125 MHz, DMSO d₆) of **2m**

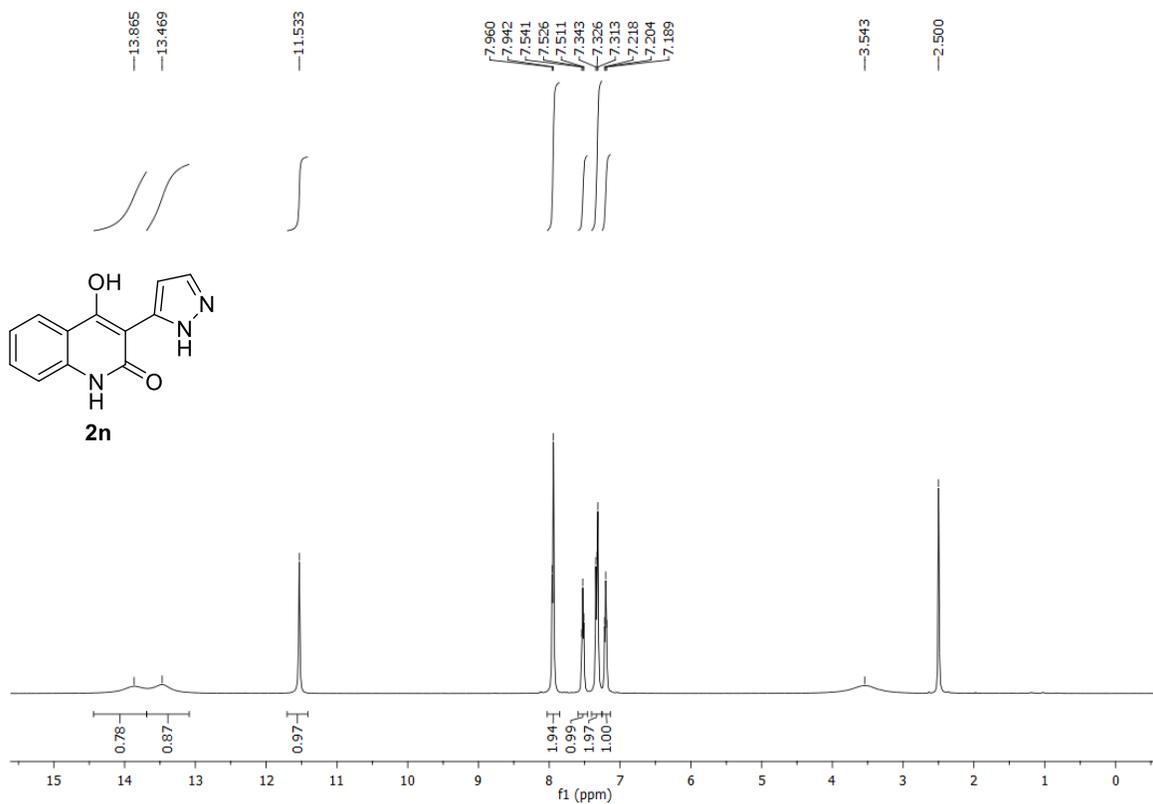


Fig S30. ^1H NMR (500 MHz, DMSO d_6) of **2n**

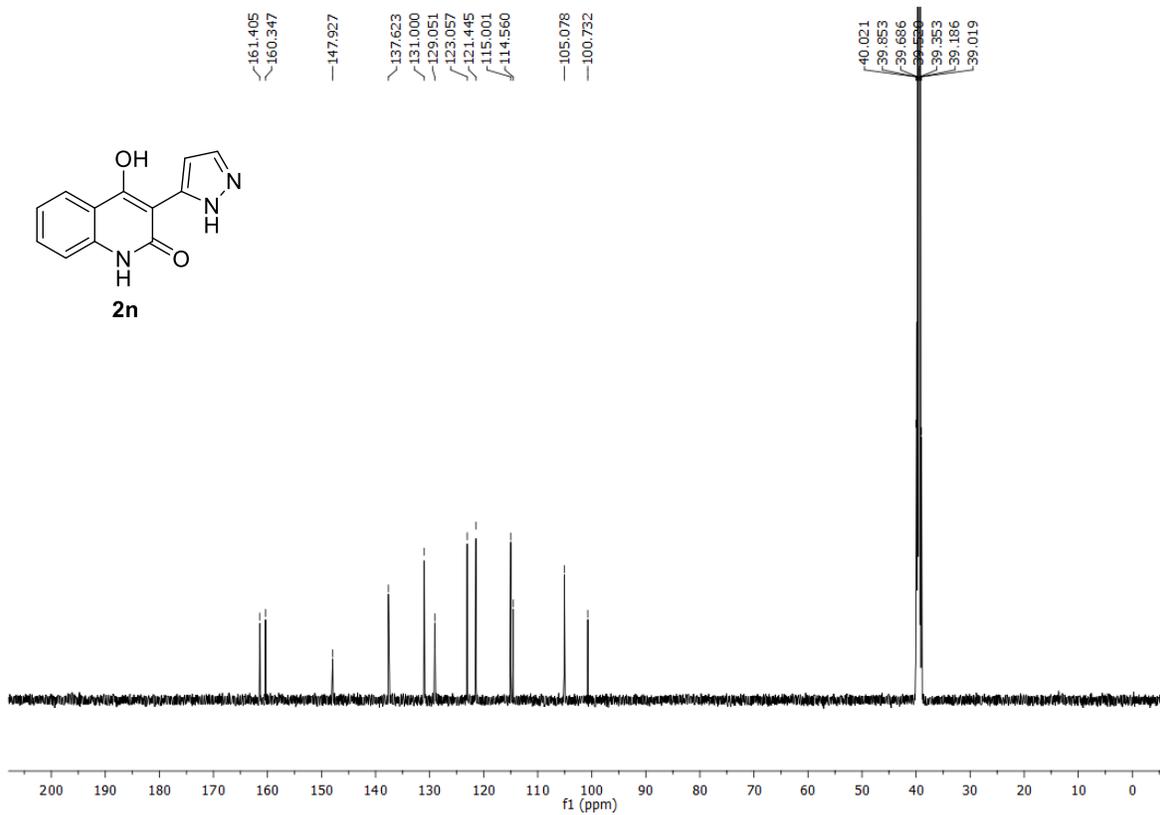


Fig S31. ^{13}C NMR (125 MHz, DMSO d_6) of **2n**

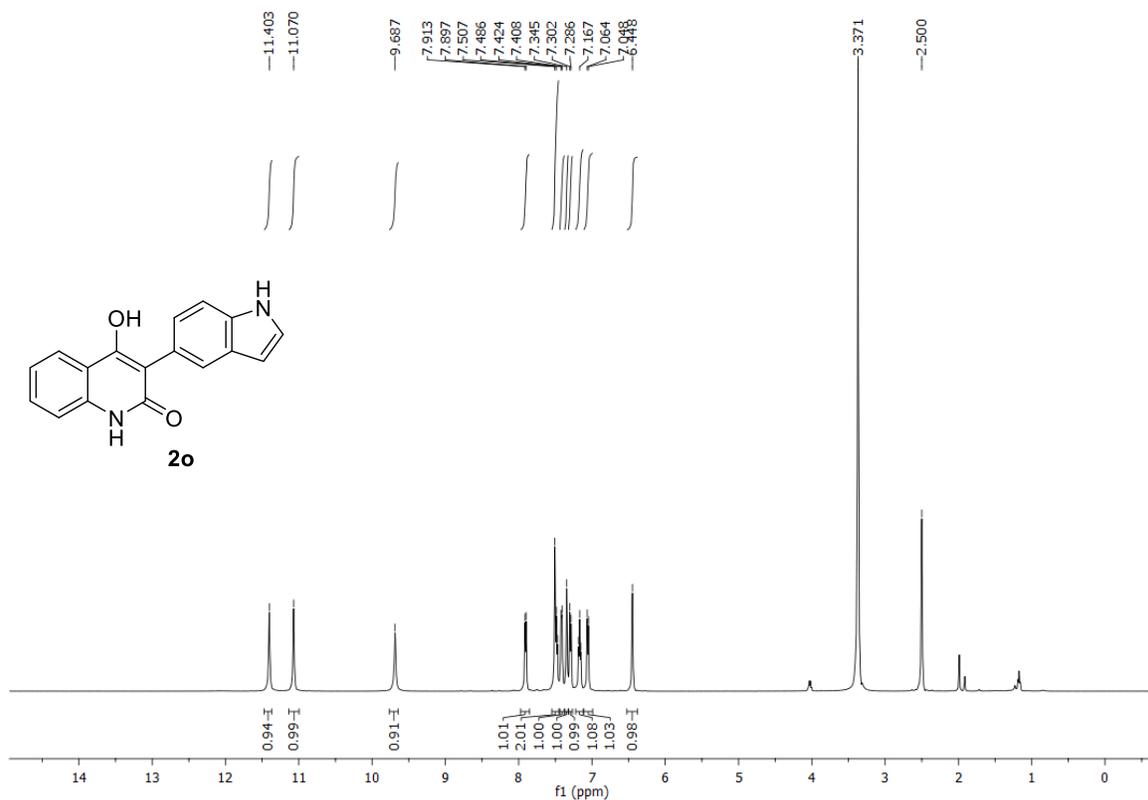


Fig S32. ¹H NMR (500 MHz, DMSO d₆) of **2o**

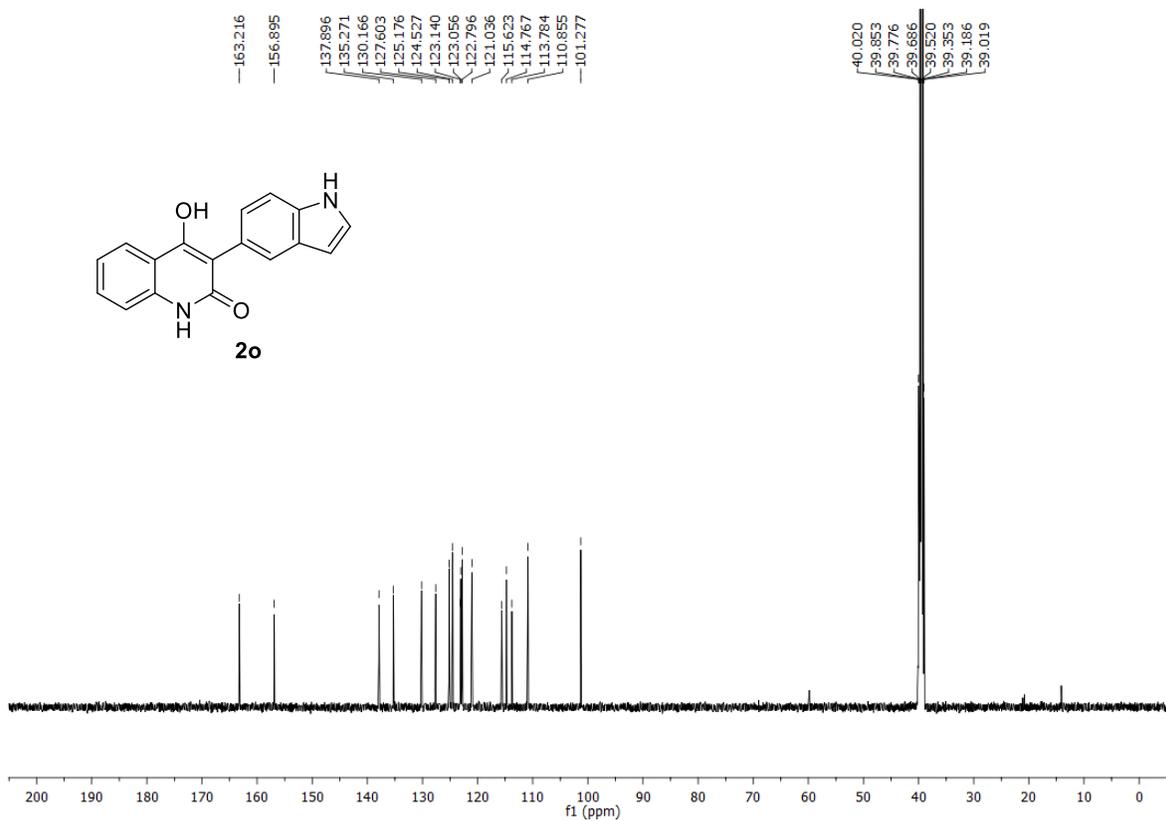


Fig S33. ¹³C NMR (125 MHz, DMSO d₆) of **2o**

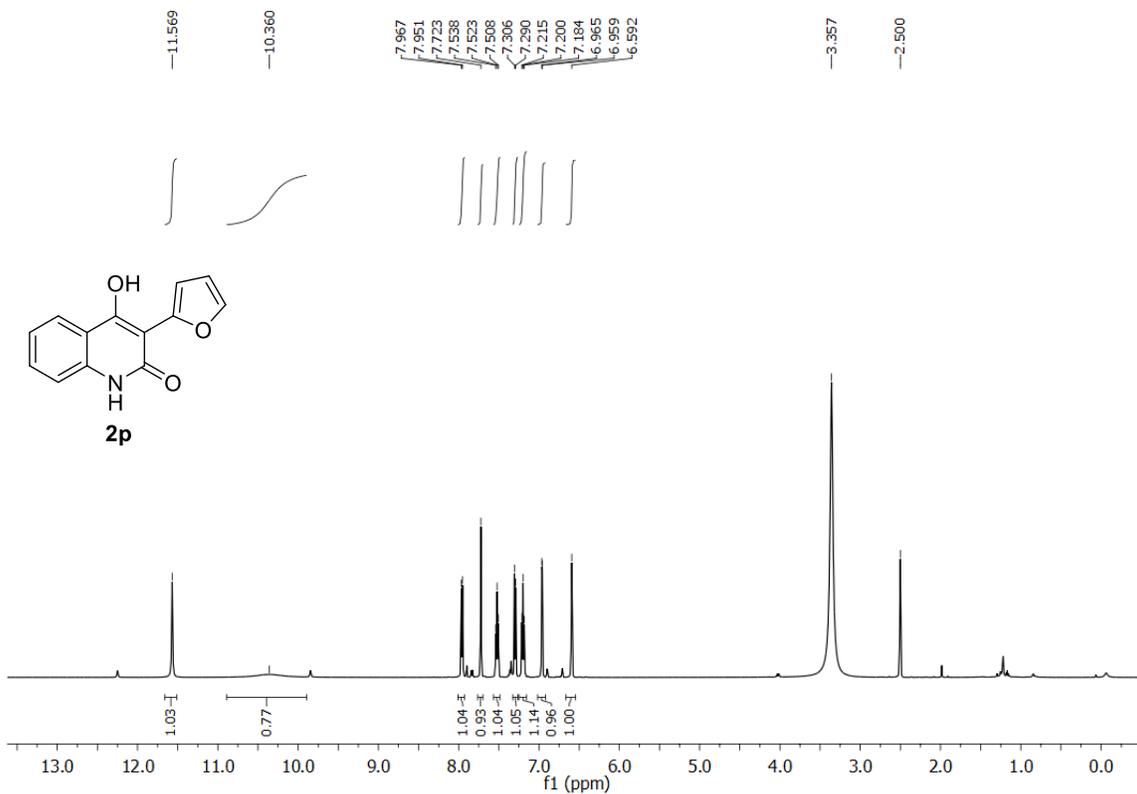


Fig S34. ¹H NMR (500 MHz, DMSO d₆) of **2p**

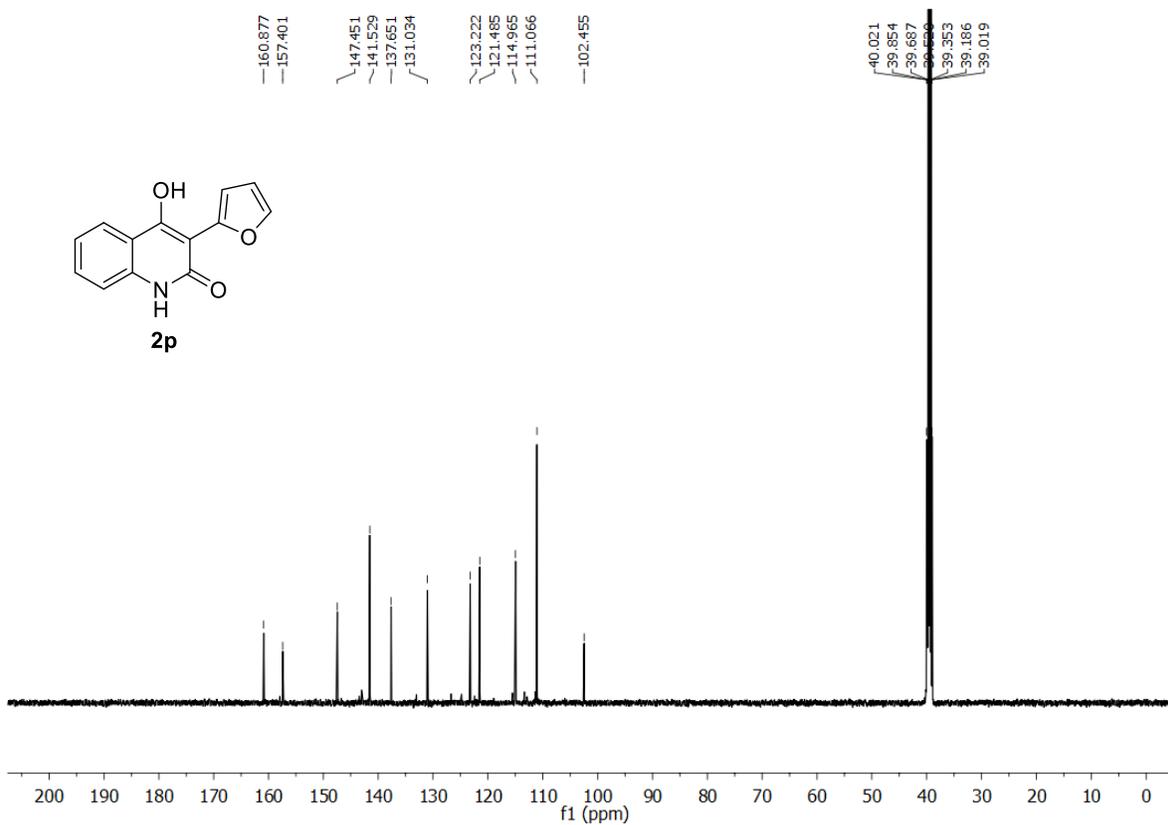


Fig S35. ¹³C NMR (125 MHz, DMSO d₆) of **2p**

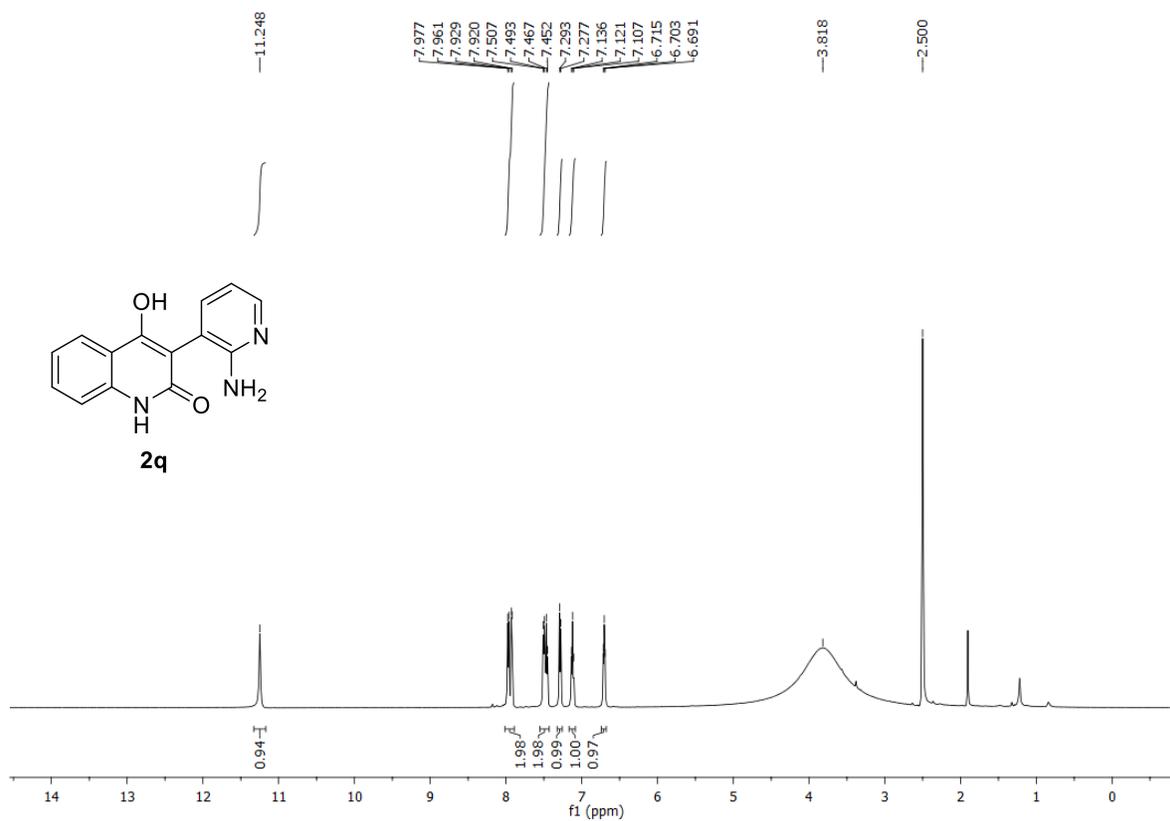


Fig S36. ¹H NMR (500 MHz, DMSO d₆) of **2q**

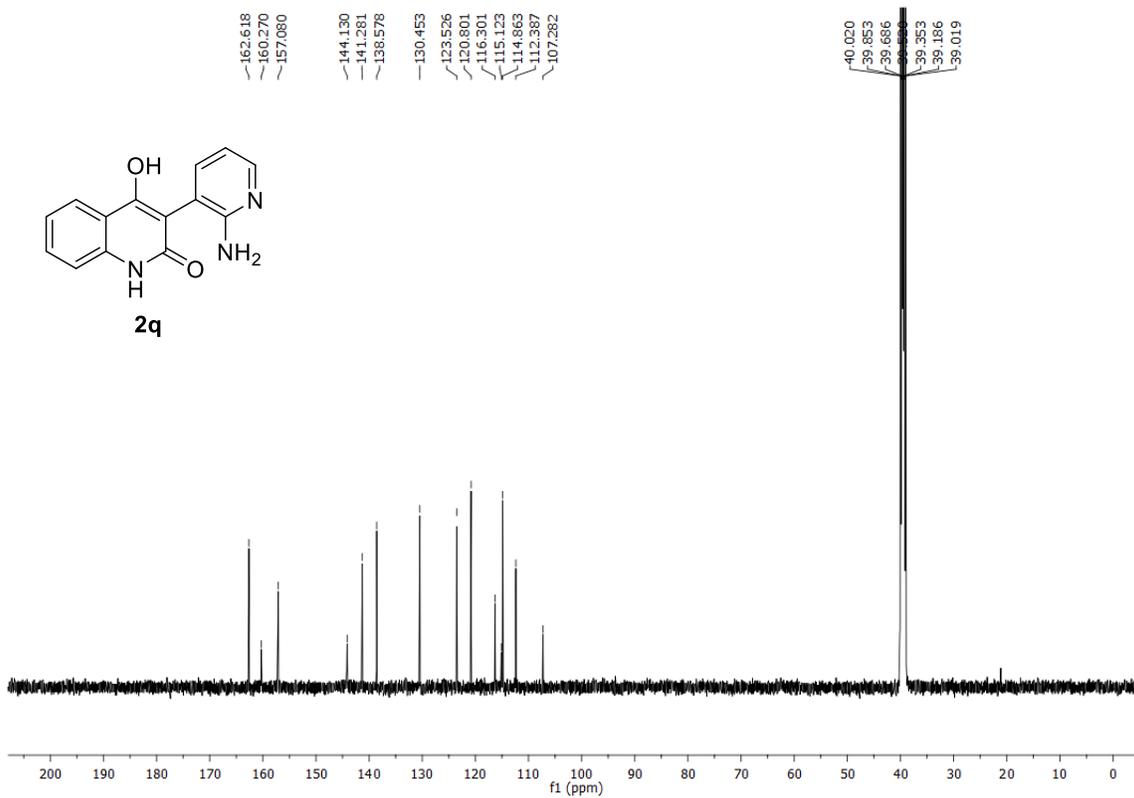


Fig S37. ¹³C NMR (125 MHz, DMSO d₆) of **2q**

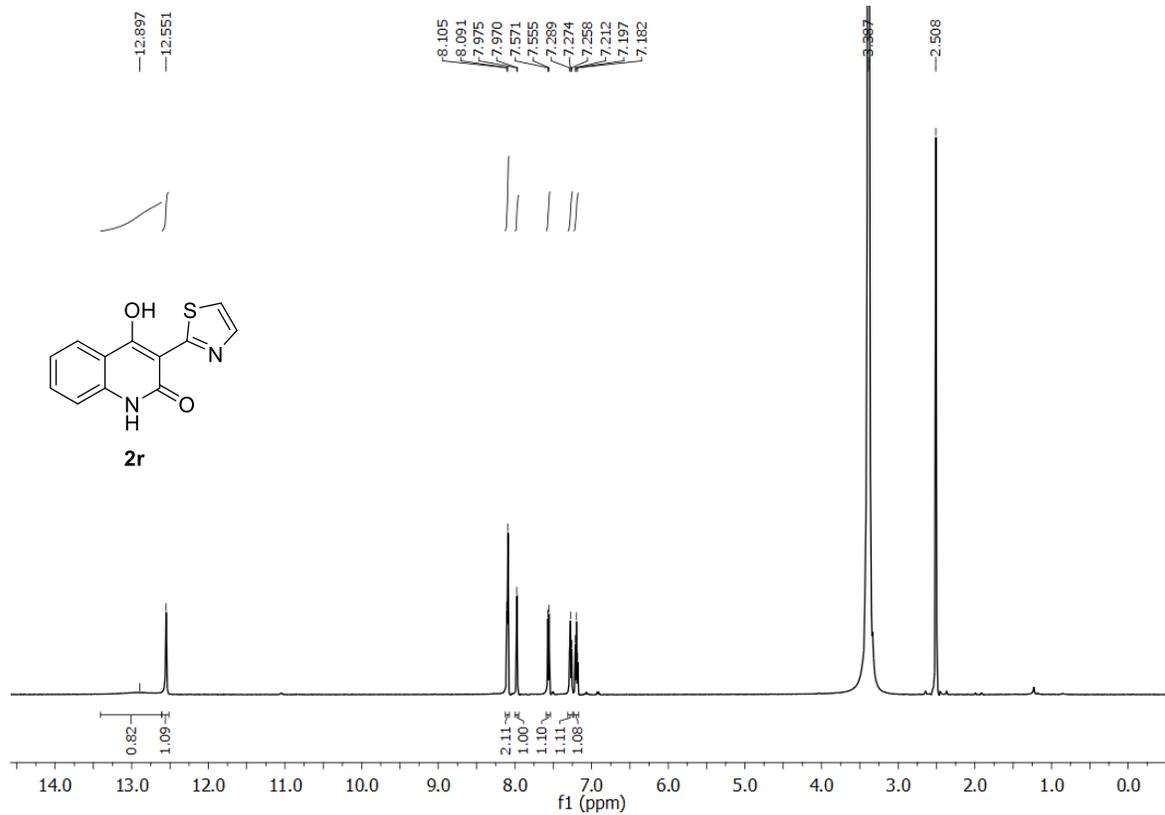


Fig S38. ¹H NMR (500 MHz, DMSO d₆) of **2r**

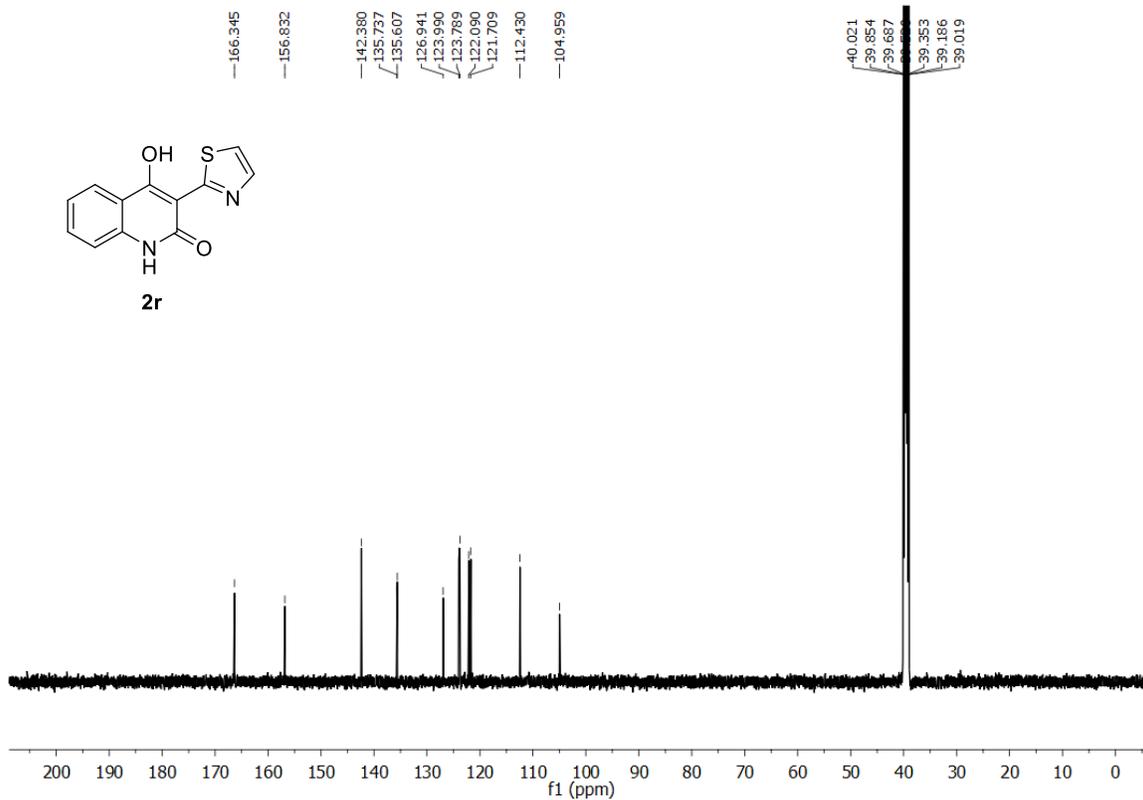


Fig S39. ¹³C NMR (125 MHz, DMSO d₆) of **2r**

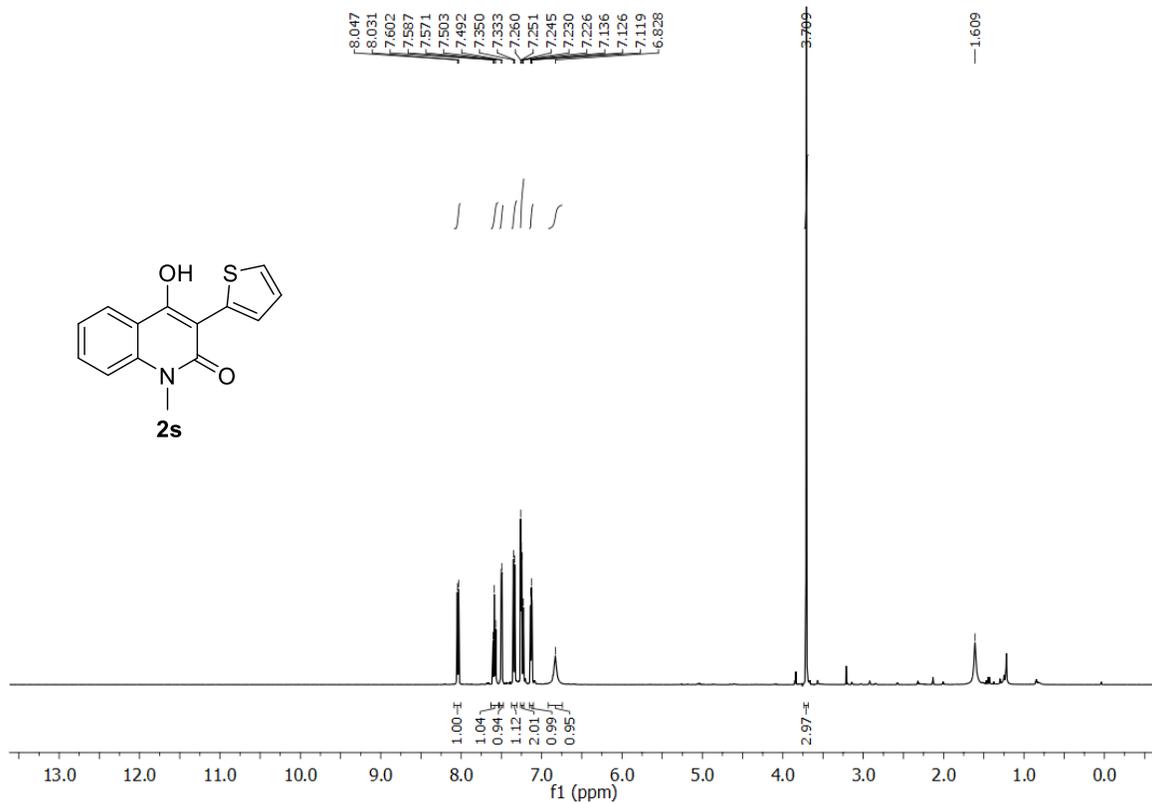


Fig S40. ¹H NMR (500 MHz, CDCl₃) of **2s**

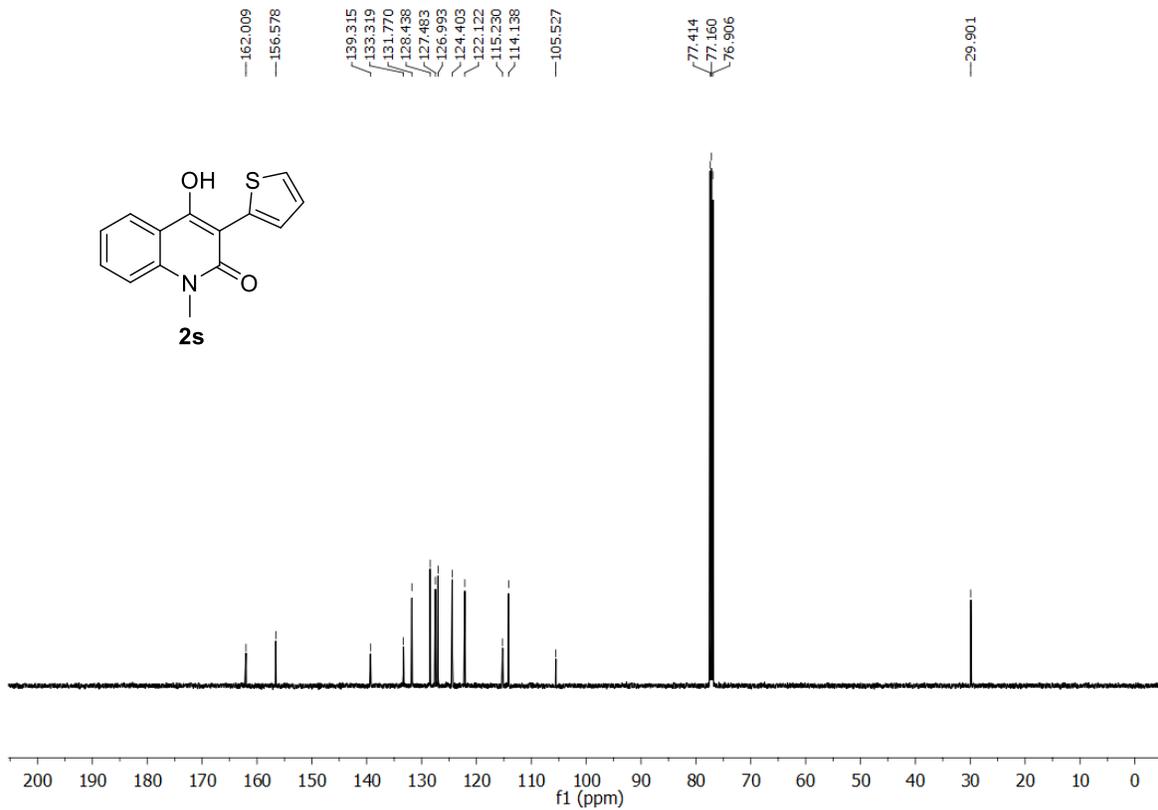


Fig S41. ¹³C NMR (125 MHz, CDCl₃) of **2s**

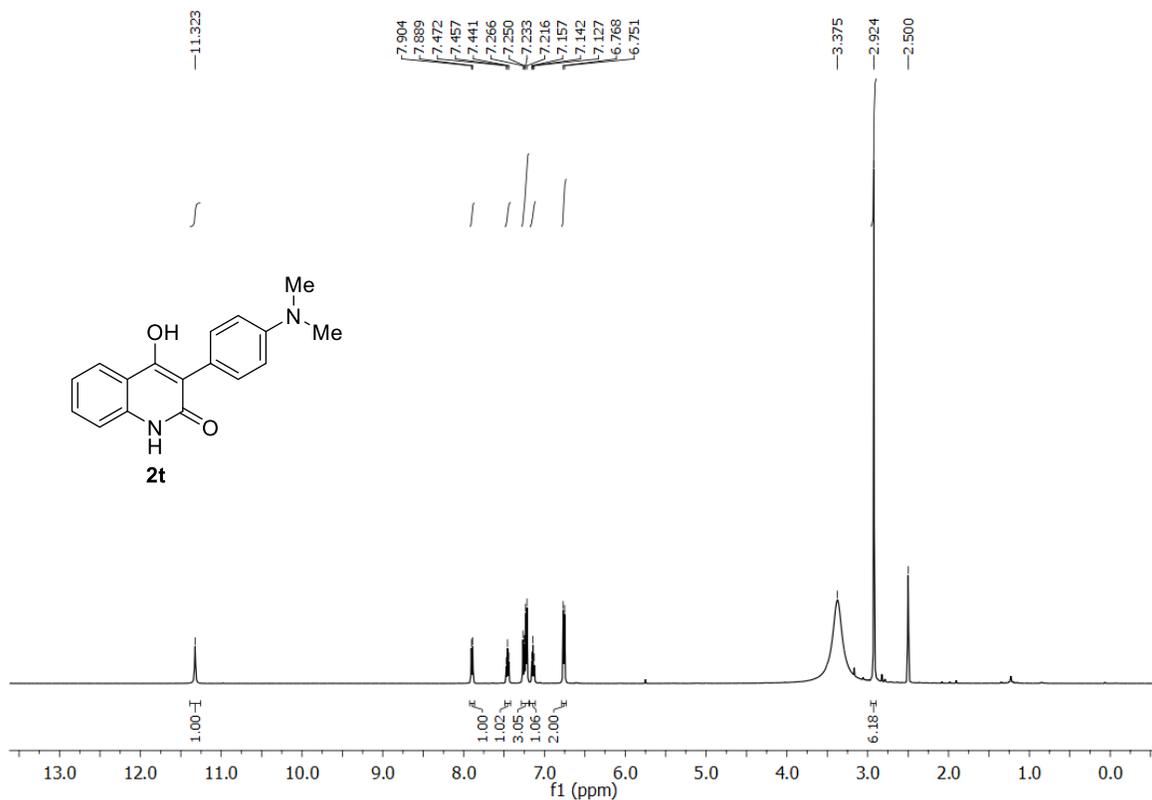


Fig S42. ¹H NMR (500 MHz, DMSO d₆) of **2t**

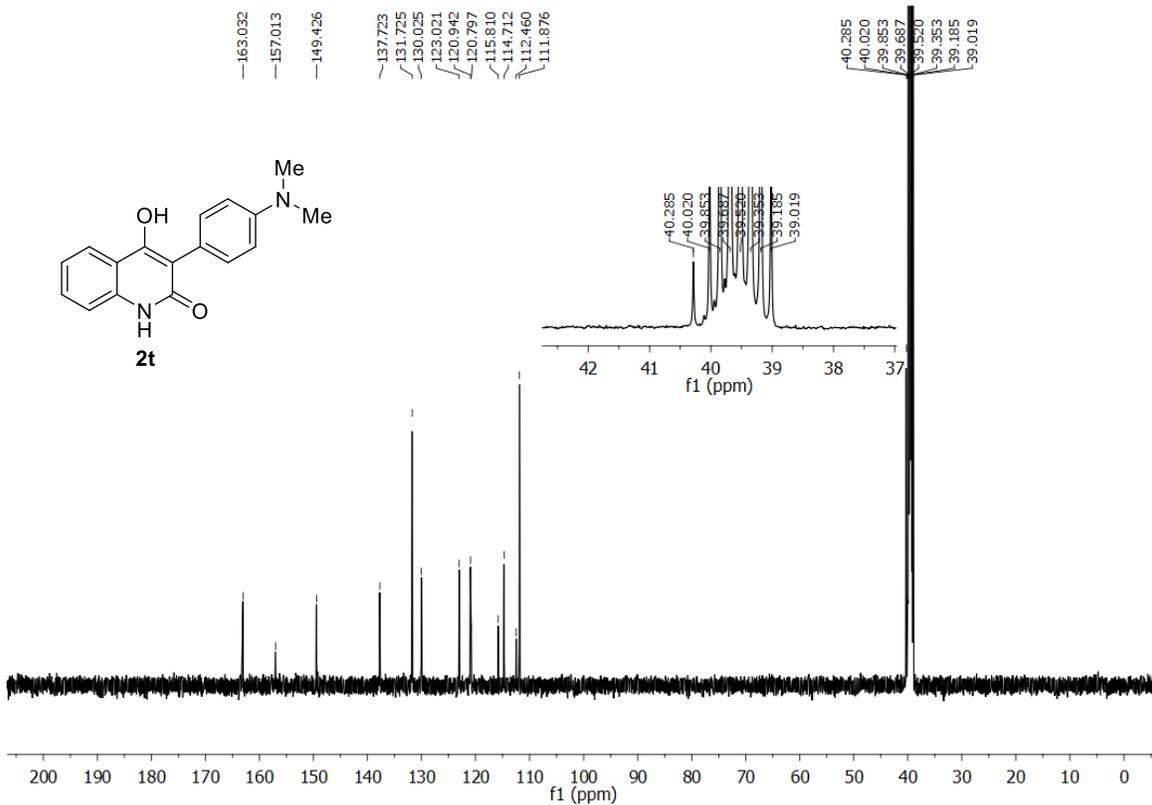


Fig S43. ¹³C NMR (125 MHz, DMSO d₆) of **2t**

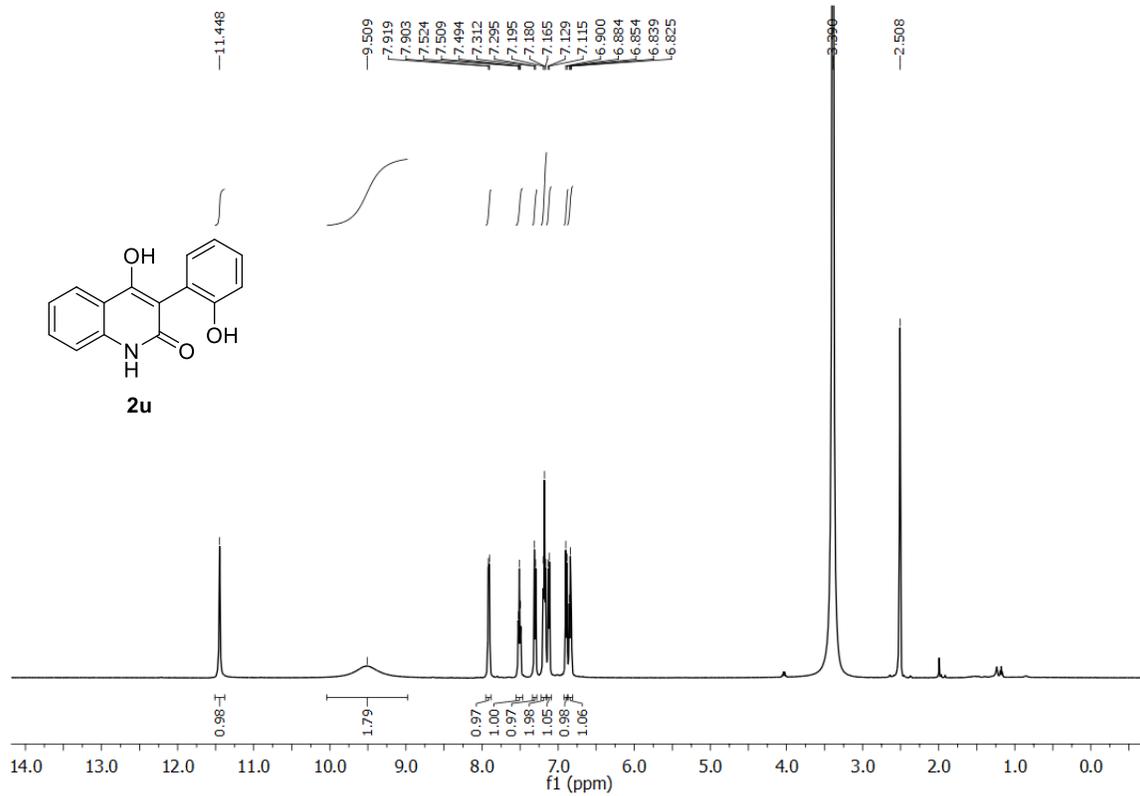


Fig S44. ¹H NMR (500 MHz, DMSO d₆) of **2u**

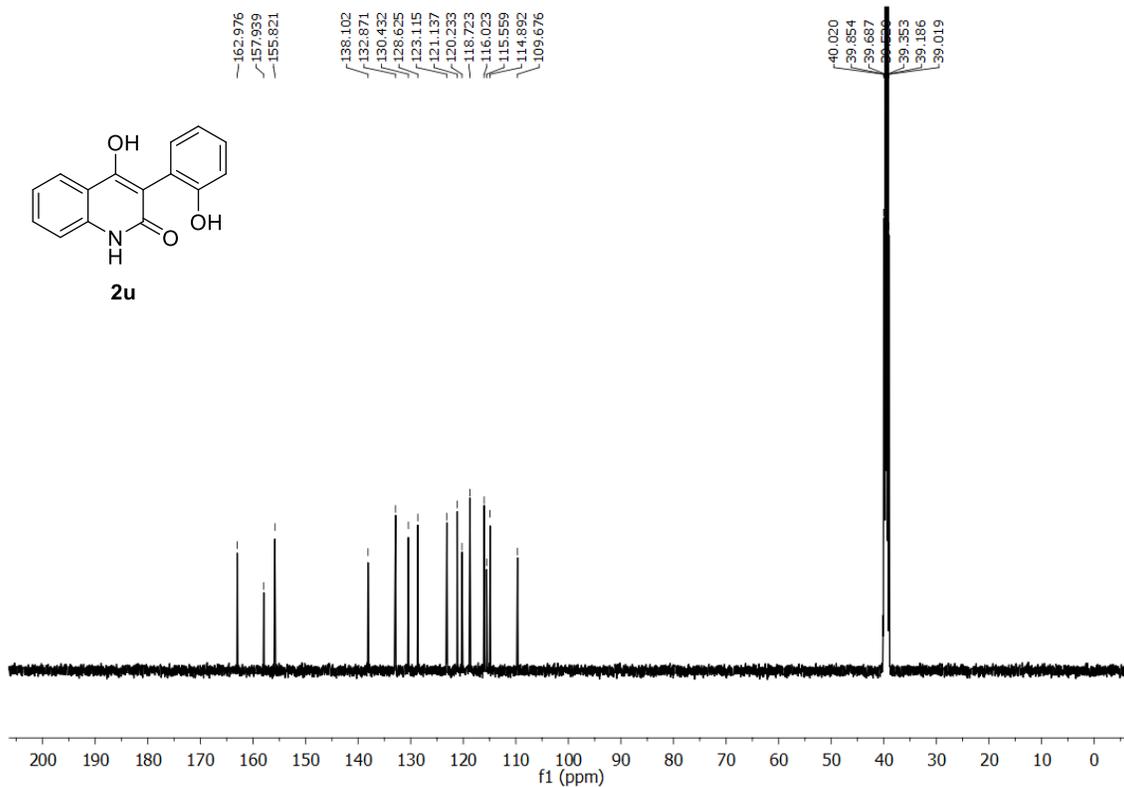


Fig S45. ¹³C NMR (125 MHz, DMSO d₆) of **2u**

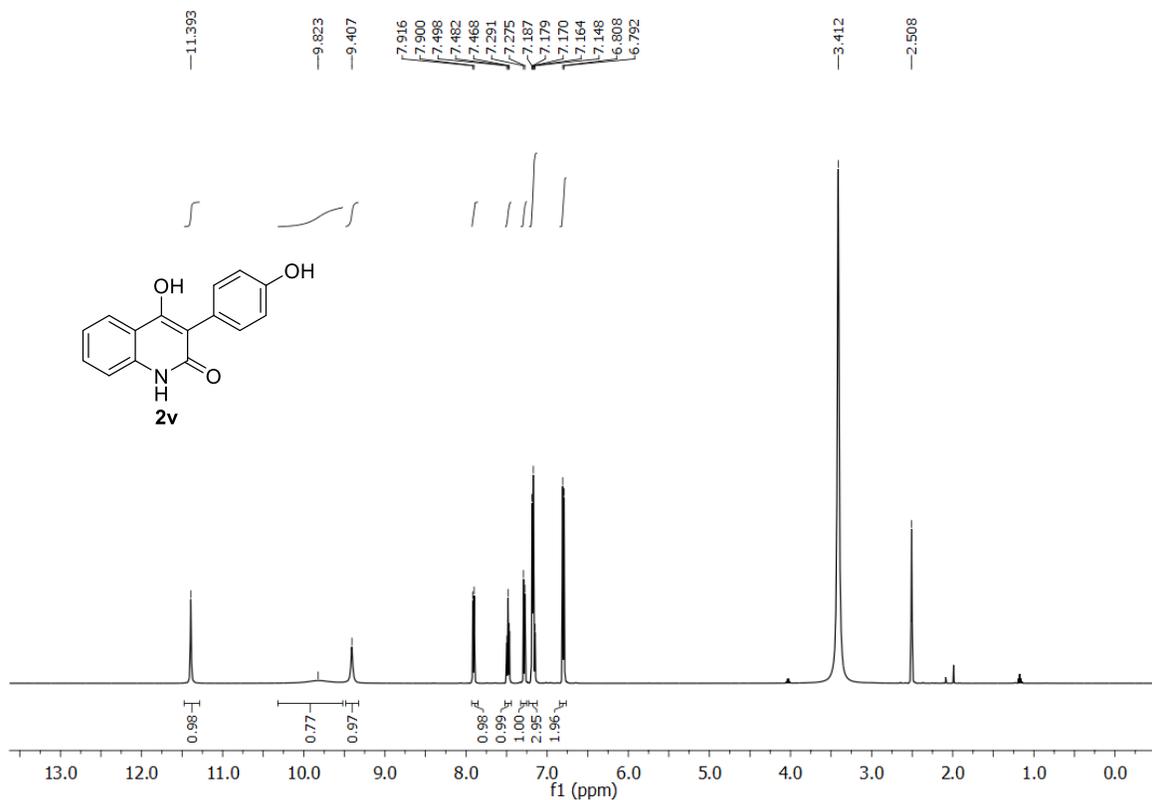


Fig S46. ¹H NMR (500 MHz, DMSO d₆) of **2v**

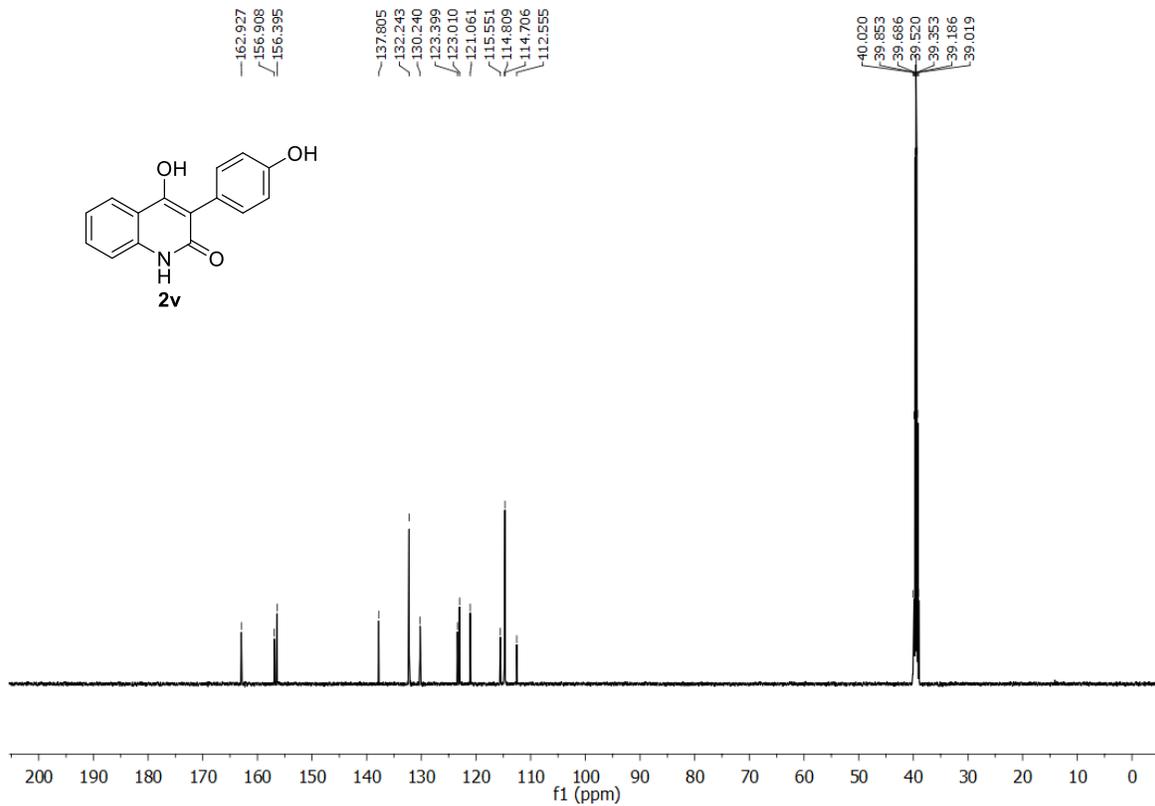


Fig S47. ¹³C NMR (125 MHz, DMSO d₆) of **2v**

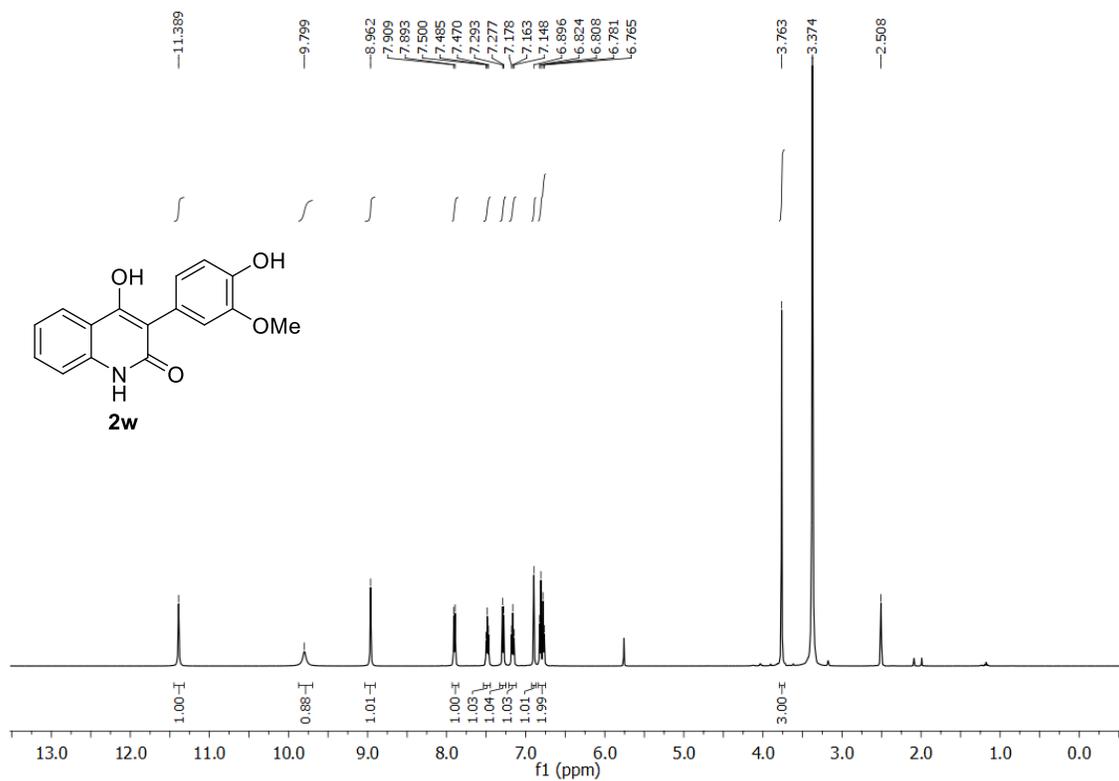


Fig S48. ¹H NMR (500 MHz, DMSO d₆) of **2w**

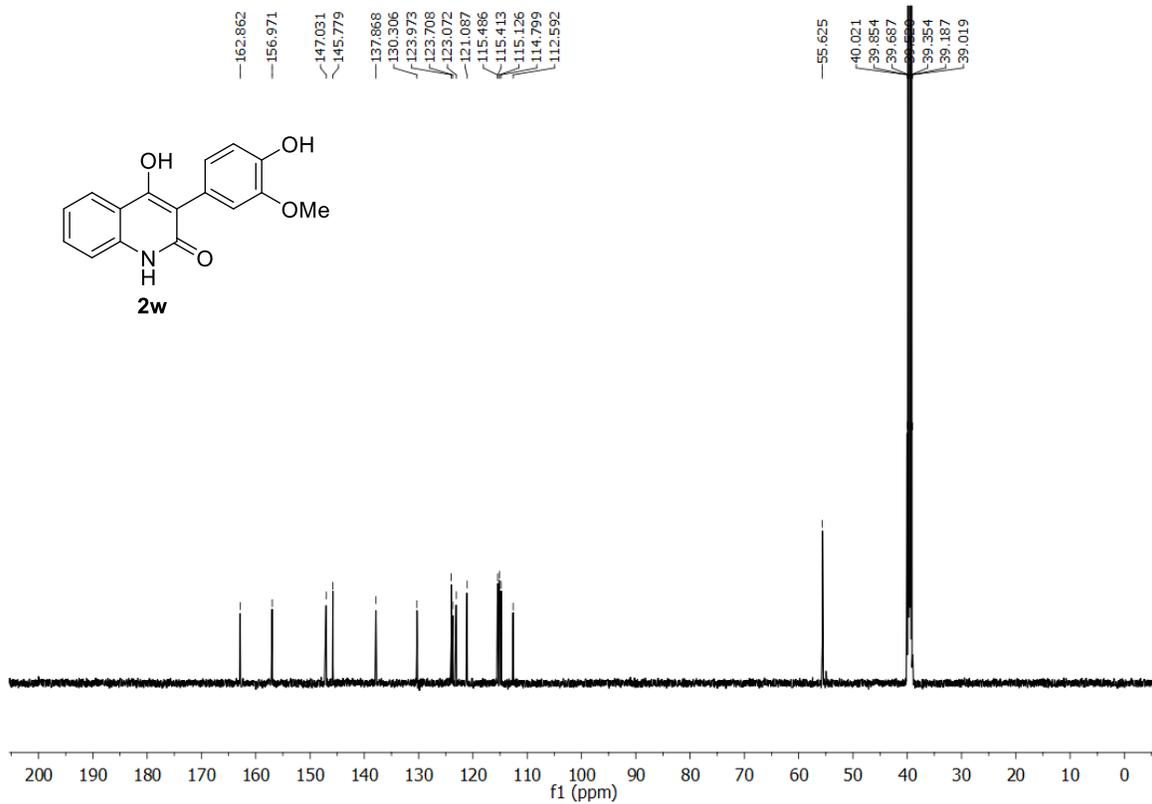


Fig S49. ¹³C NMR (125 MHz, DMSO d₆) of **2w**

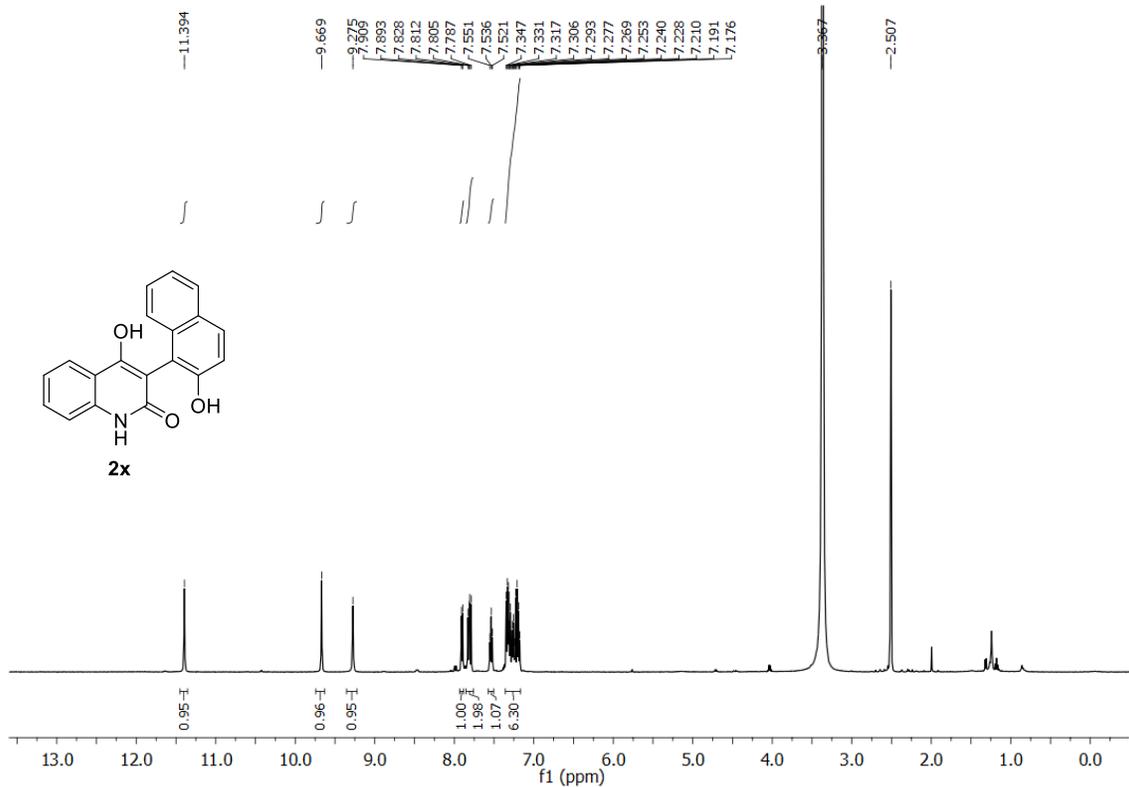


Fig S50. ¹H NMR (500 MHz, DMSO d₆) of **2x**

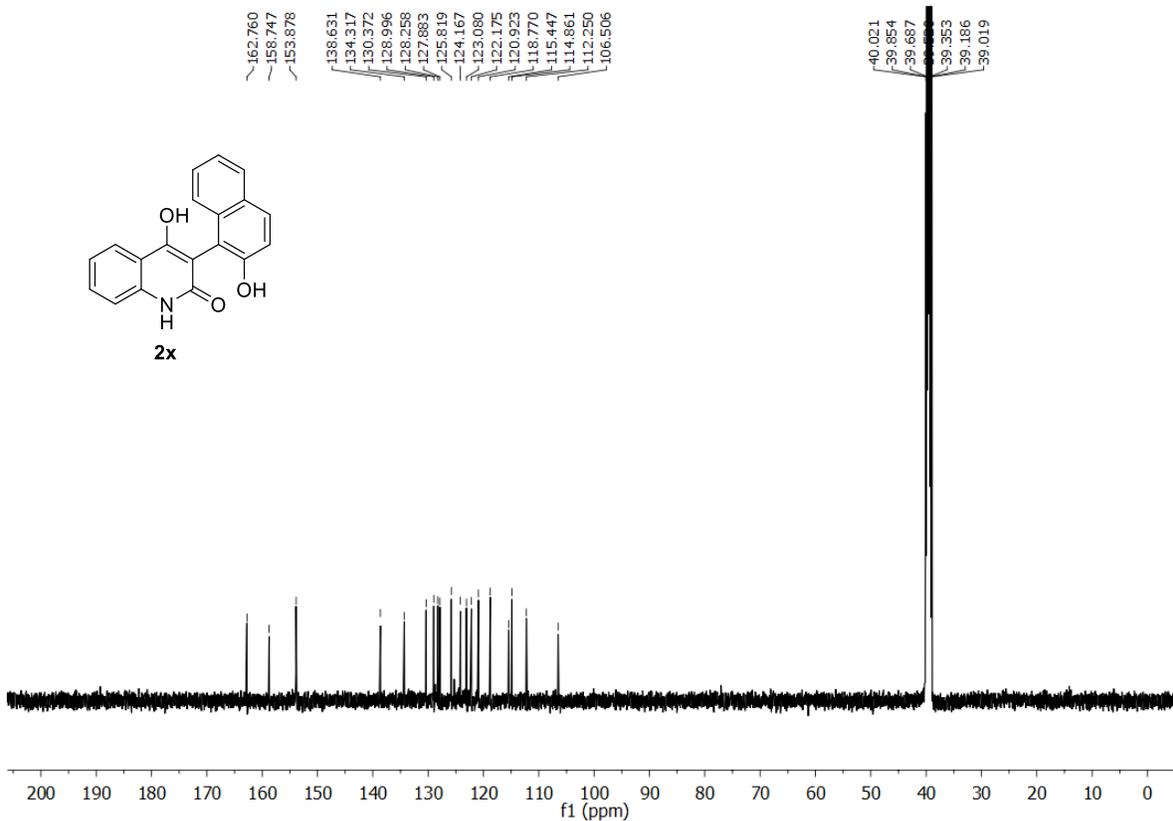


Fig S51. ¹³C NMR (125 MHz, DMSO d₆) of **2x**

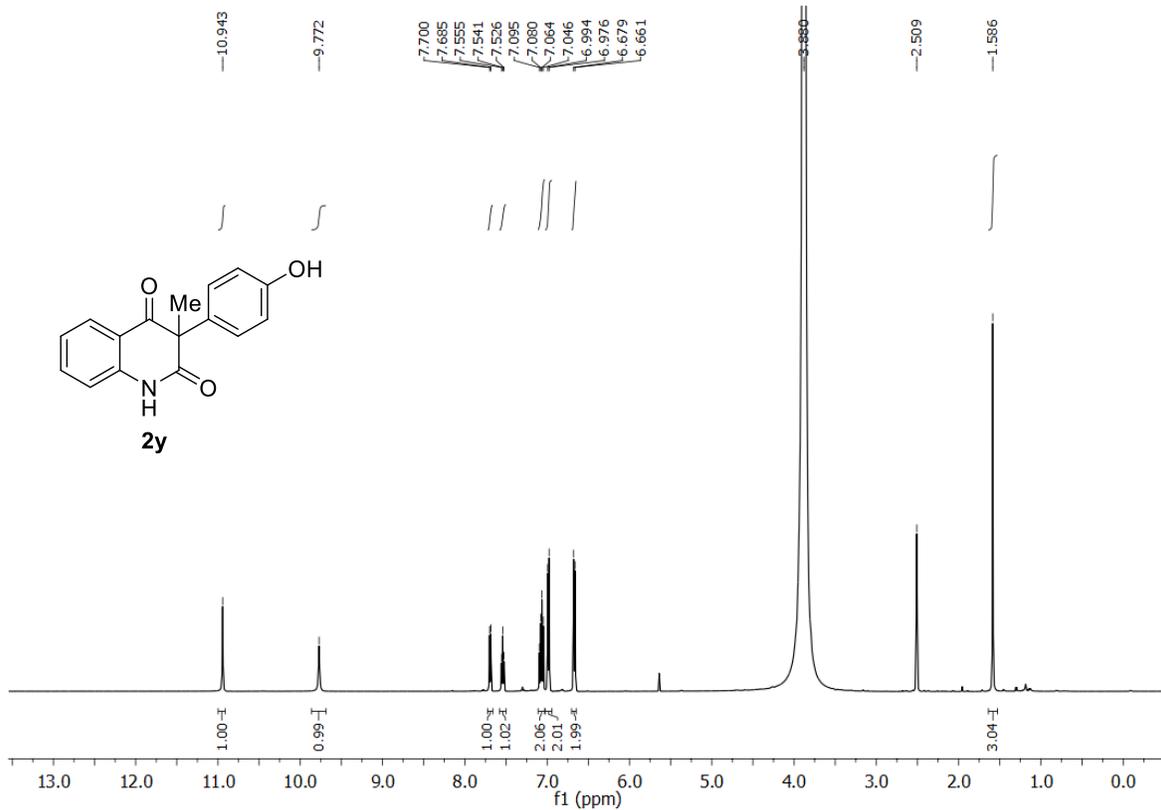


Fig S52. ¹H NMR (500 MHz, DMSO d₆) of **2y**

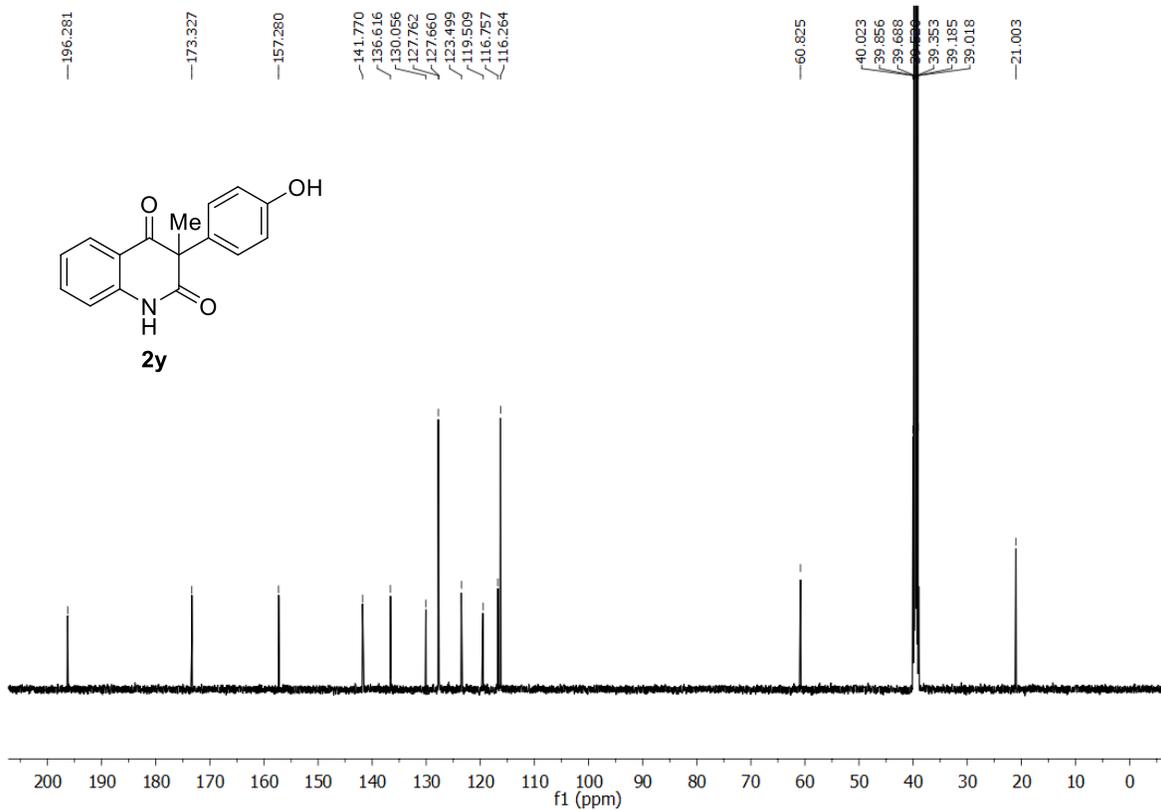


Fig S53. ¹³C NMR (125 MHz, DMSO d₆) of **2y**

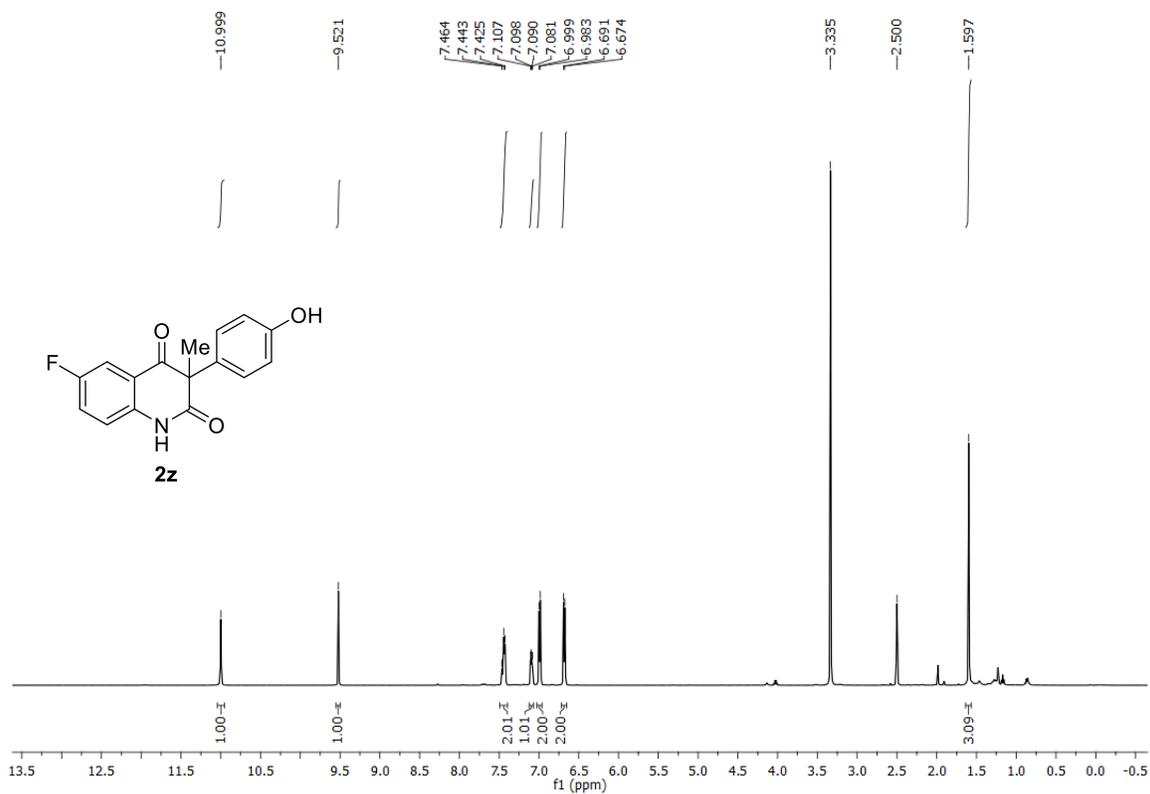


Fig S54. ¹H NMR (500 MHz, DMSO d₆) of **2z**

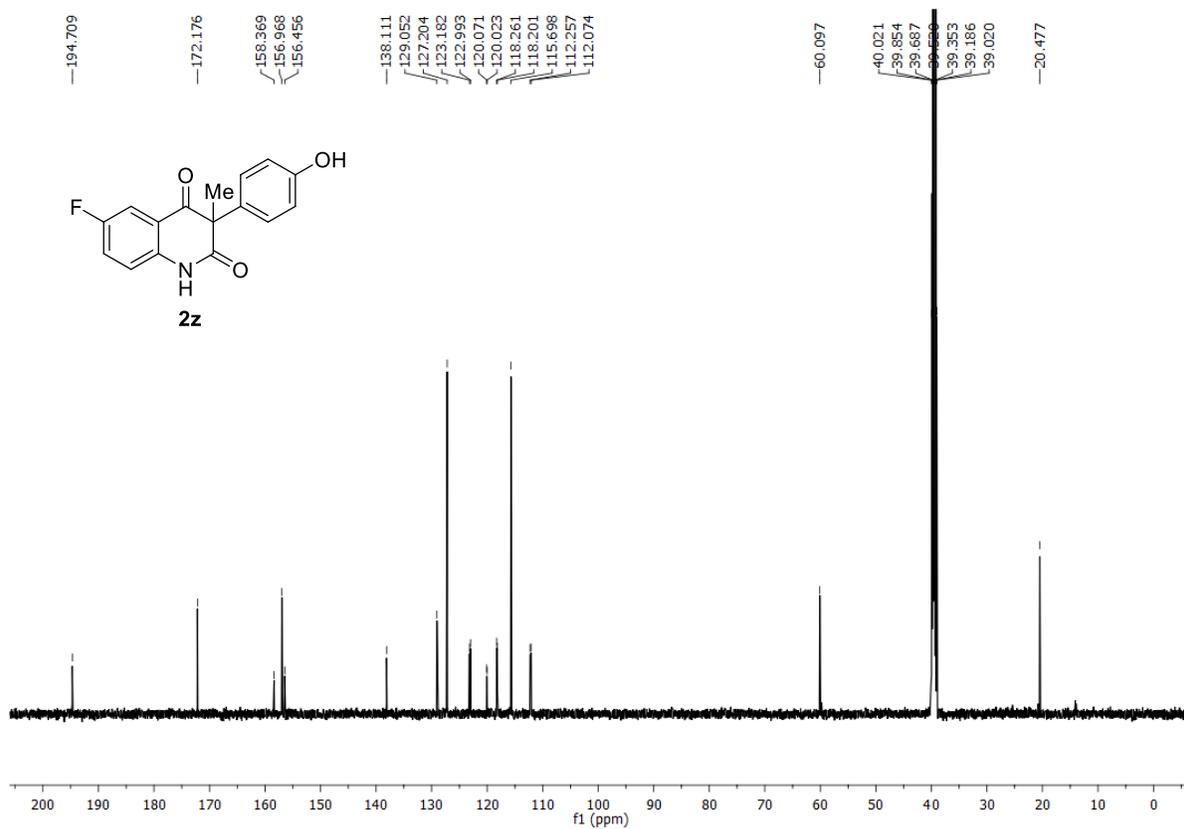


Fig S55. ¹³C NMR (125 MHz, DMSO d₆) of **2z**

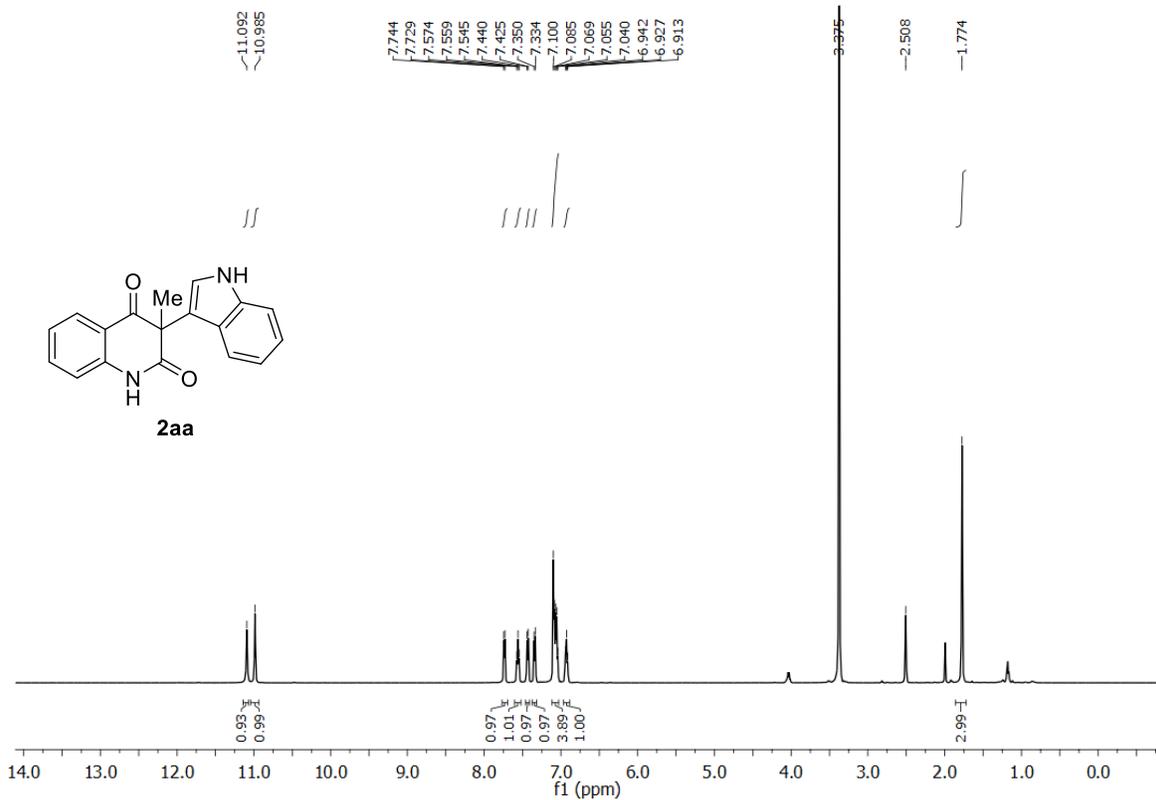


Fig S56. ¹H NMR (500 MHz, DMSO d₆) of **2aa**

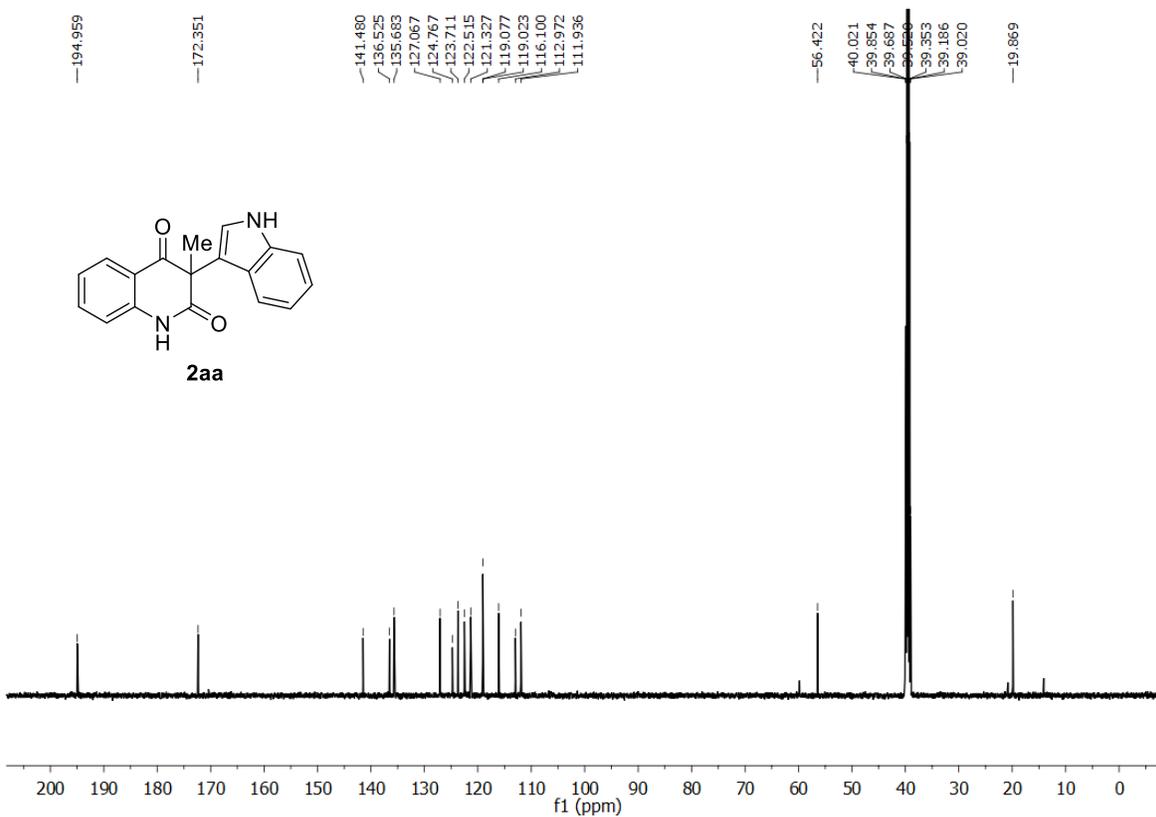


Fig S57. ¹³C NMR (125 MHz, DMSO d₆) of **2aa**

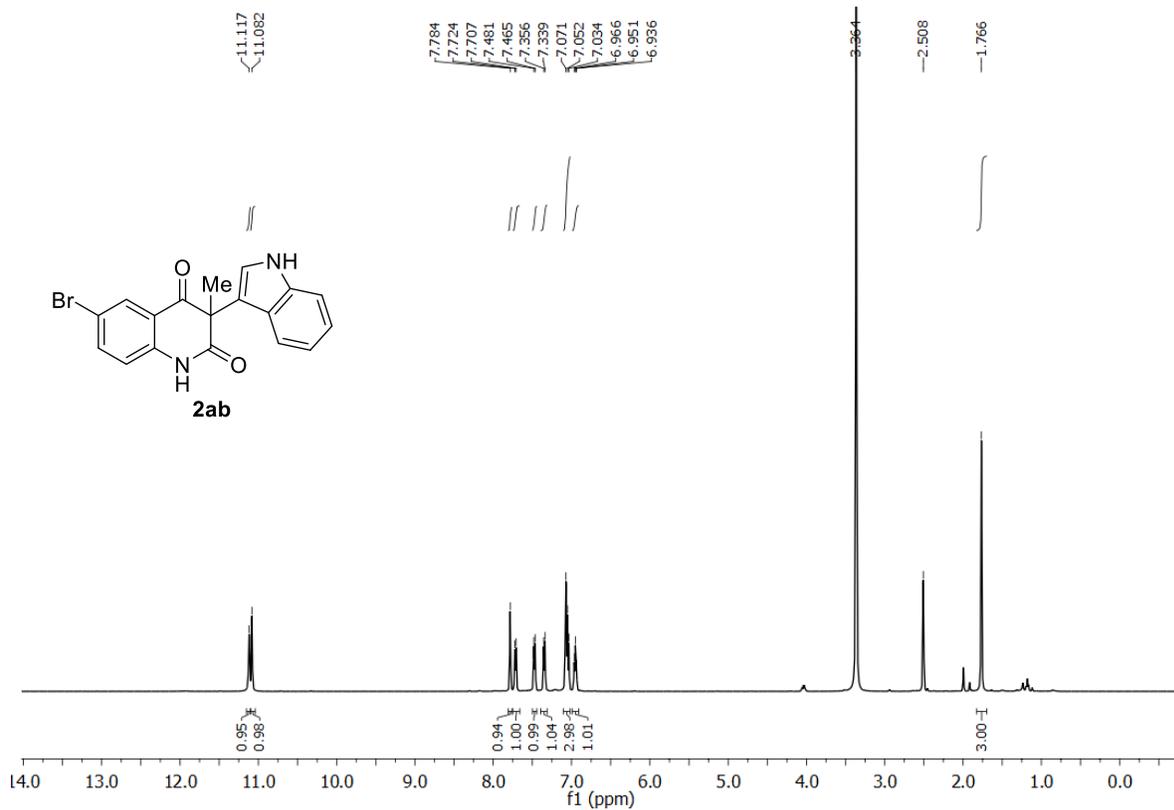


Fig S58. ¹H NMR (500 MHz, DMSO d₆) of 2ab

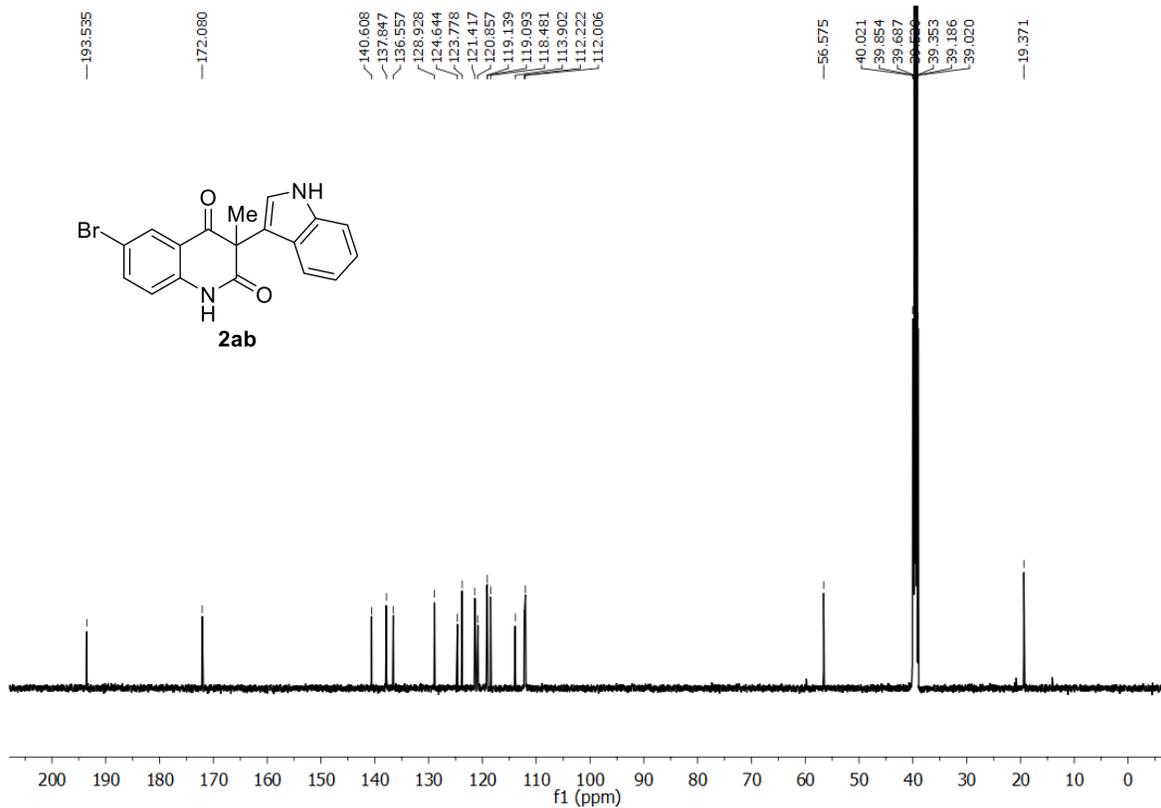


Fig S59. ¹³C NMR (125 MHz, DMSO d₆) of 2ab

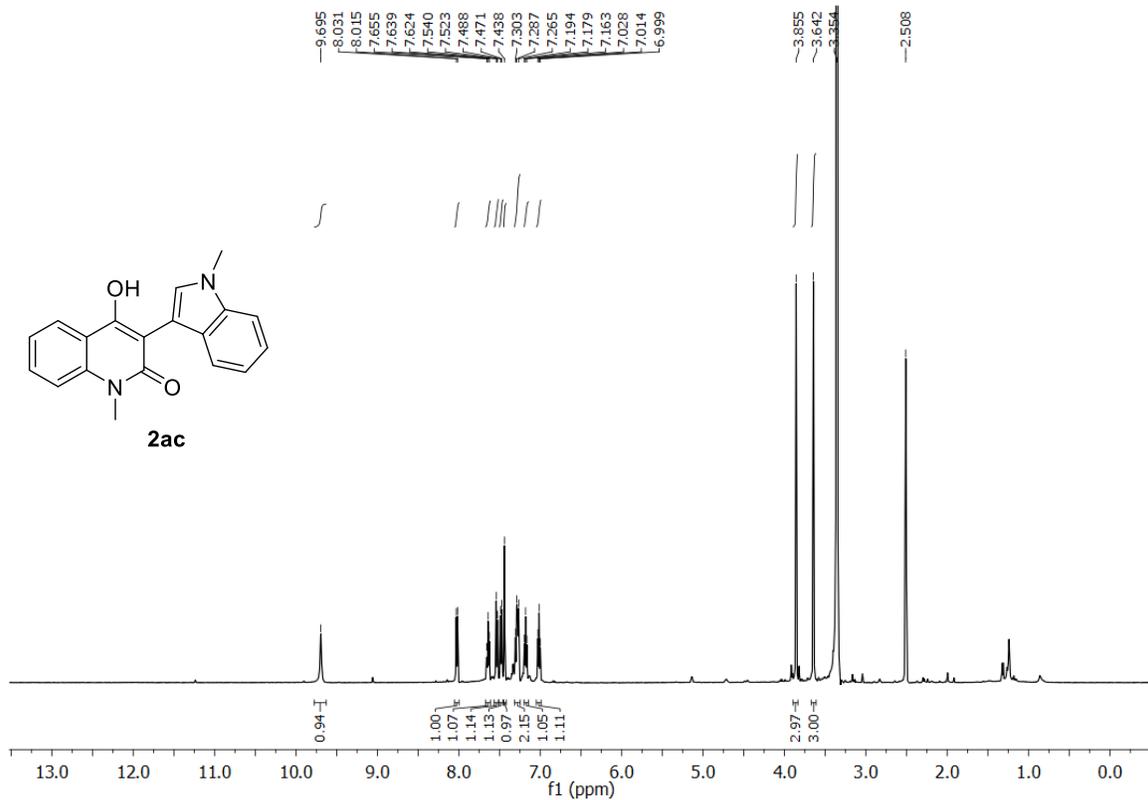


Fig S60. ¹H NMR (500 MHz, DMSO d₆) of **2ac**

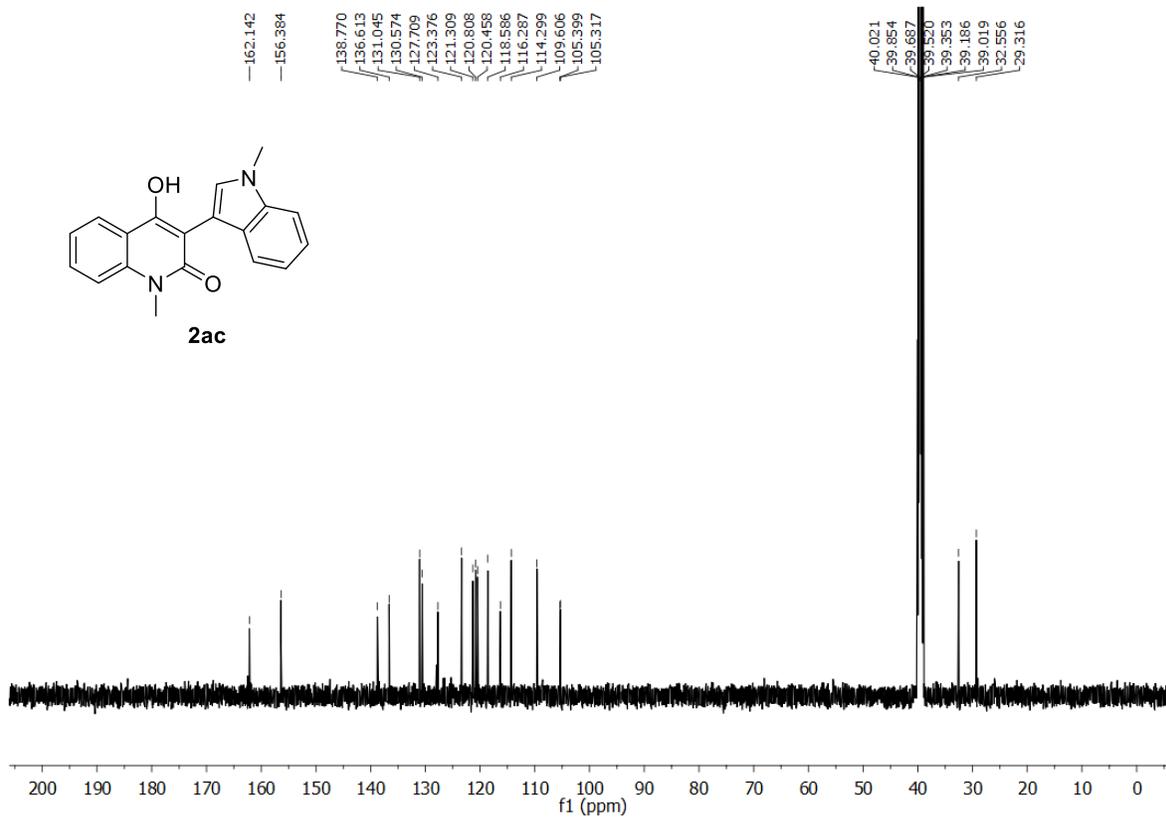


Fig S61. ¹³C NMR (125 MHz, DMSO d₆) of **2ac**

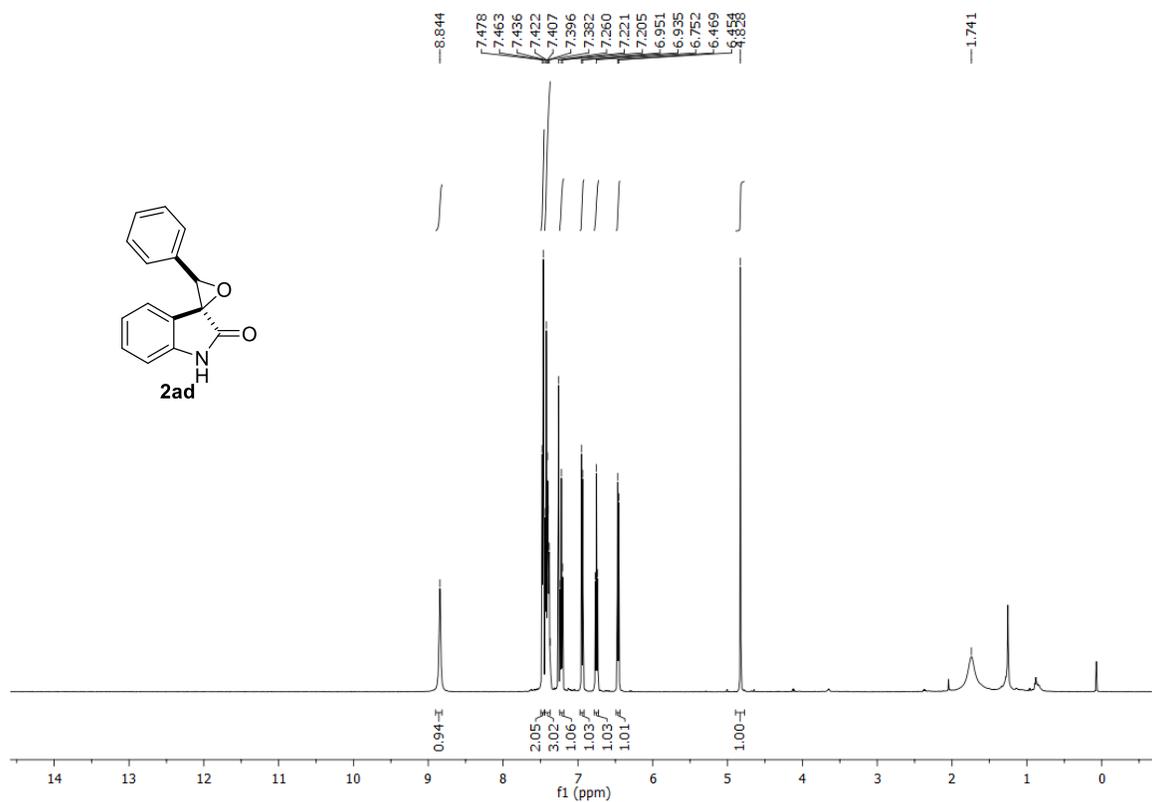


Fig S62. ¹H NMR (500 MHz, CDCl₃) of **2ad**

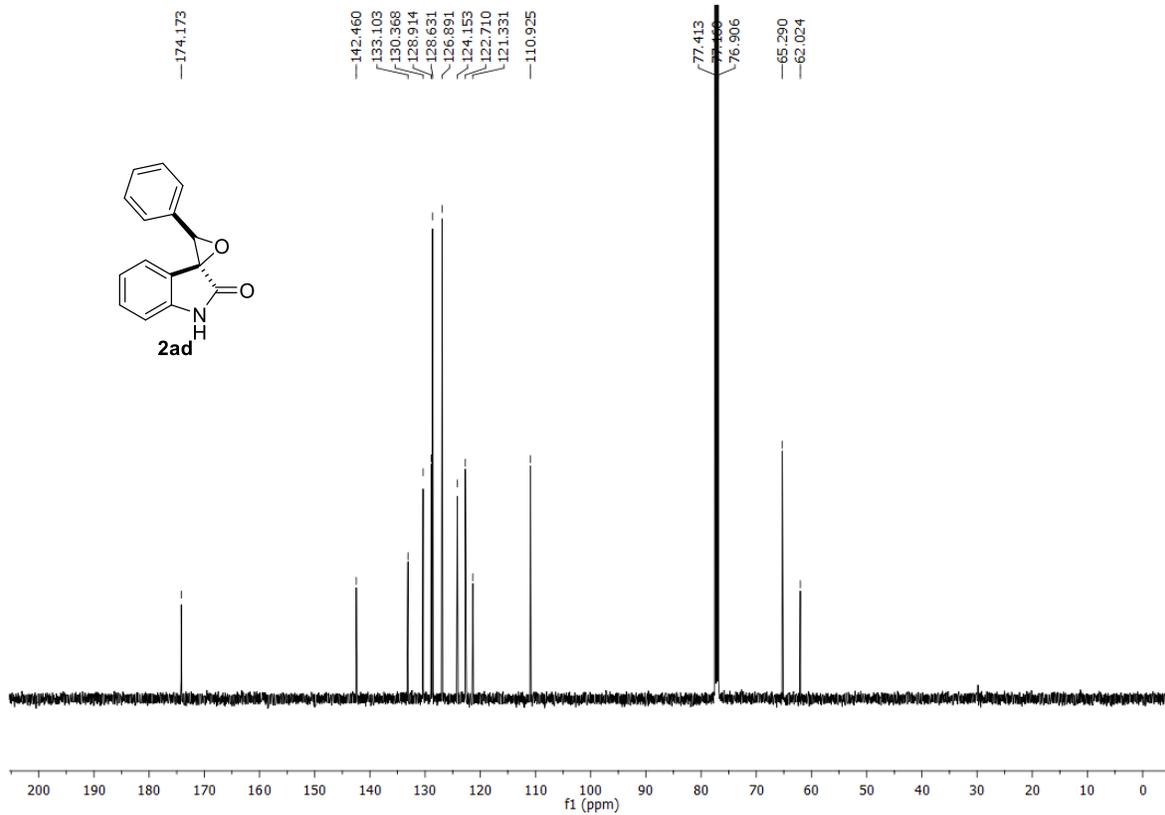


Fig S63. ¹³C NMR (125 MHz, CDCl₃) of **2ad**

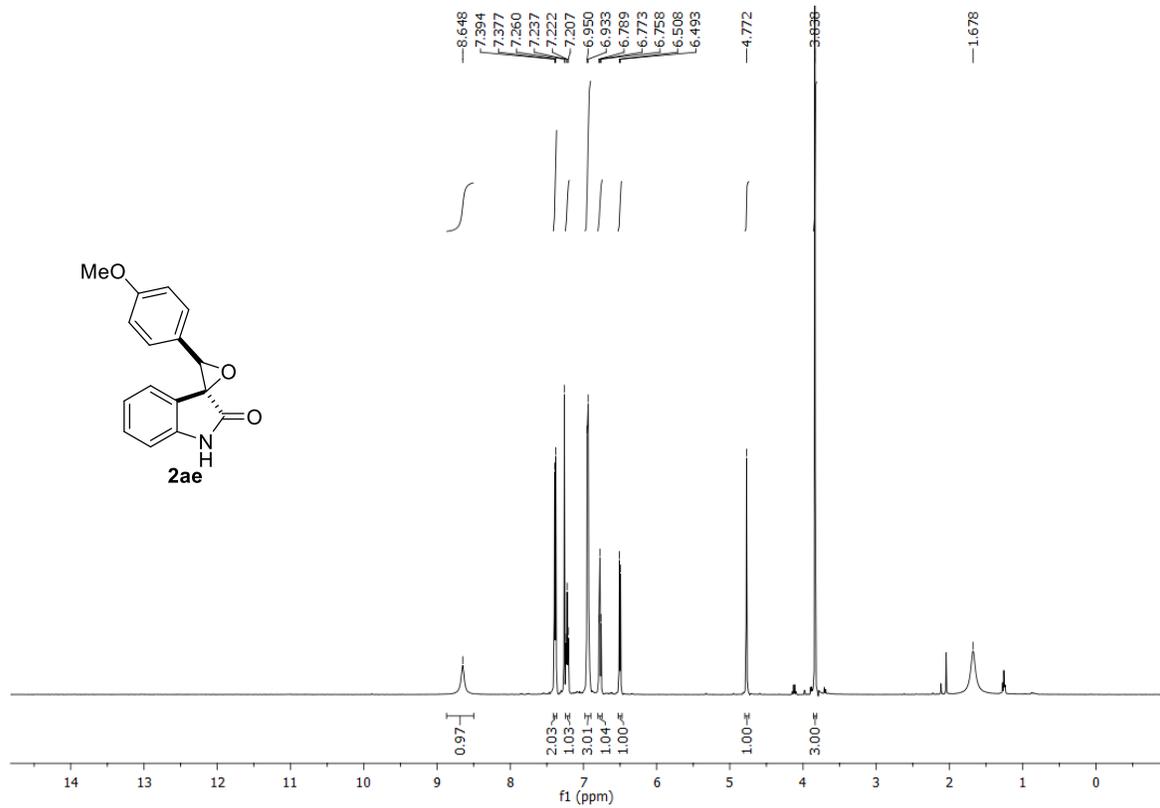


Fig S64. ¹H NMR (500 MHz, CDCl₃) of **2ae**

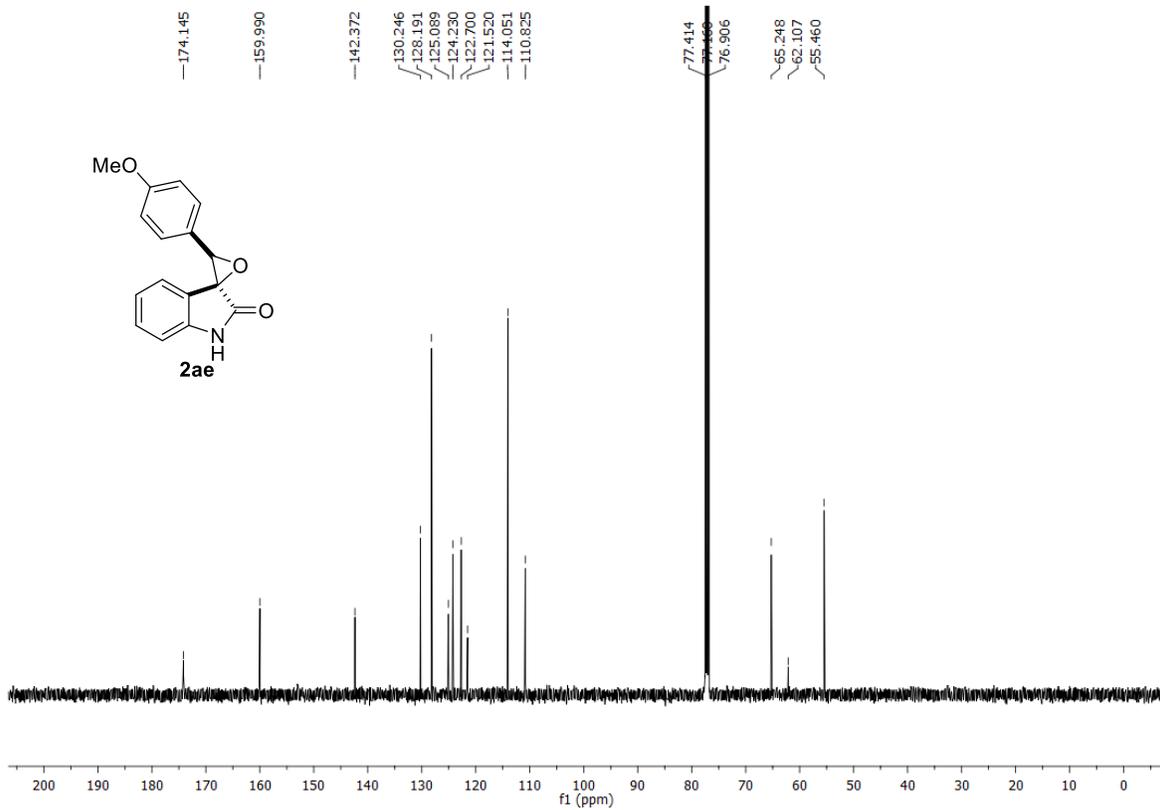


Fig S65. ¹³C NMR (125 MHz, CDCl₃) of **2ae**

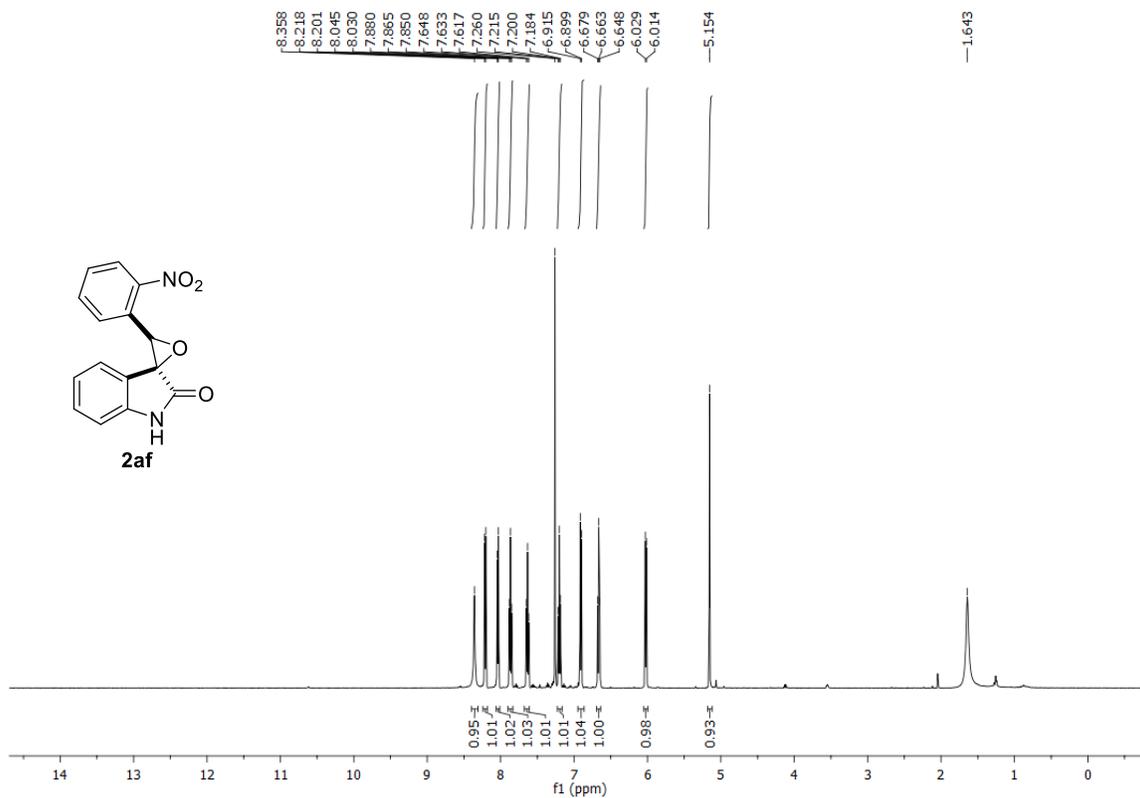


Fig S66. ¹H NMR (500 MHz, CDCl₃) of **2af**

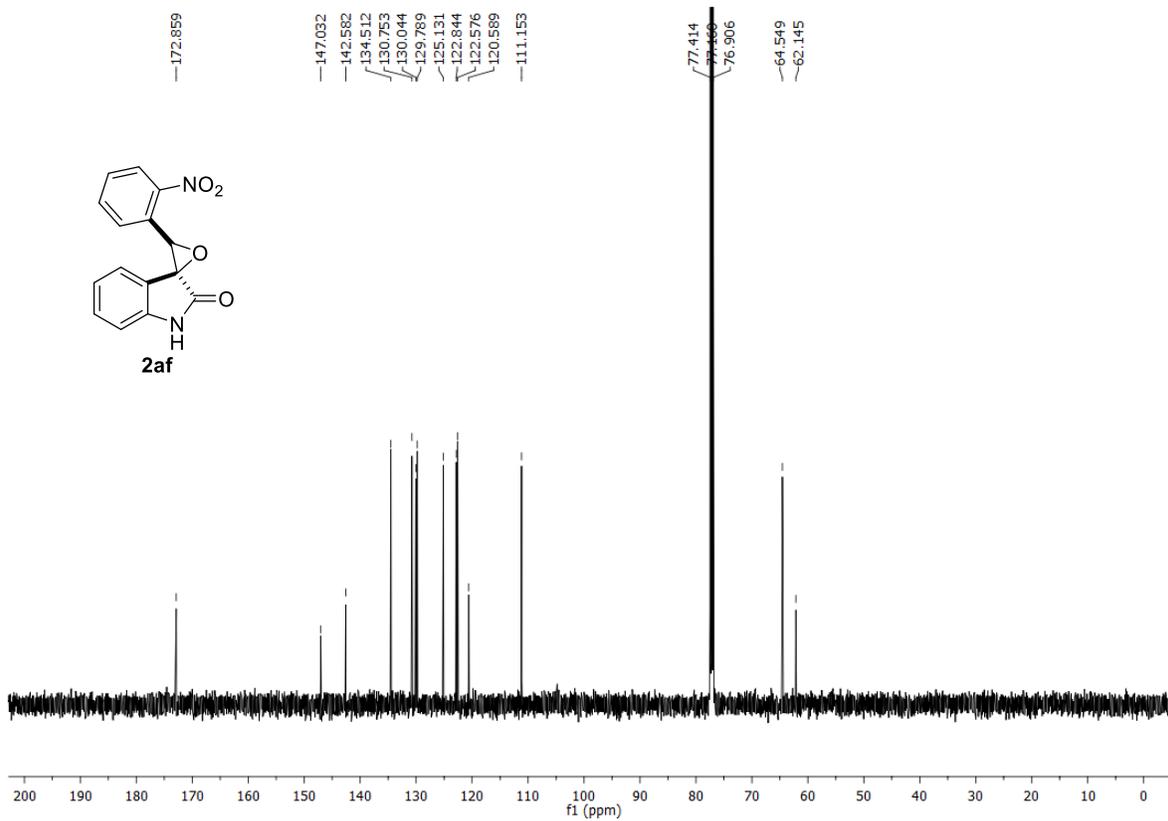


Fig S67. ¹³C NMR (125 MHz, CDCl₃) of **2af**

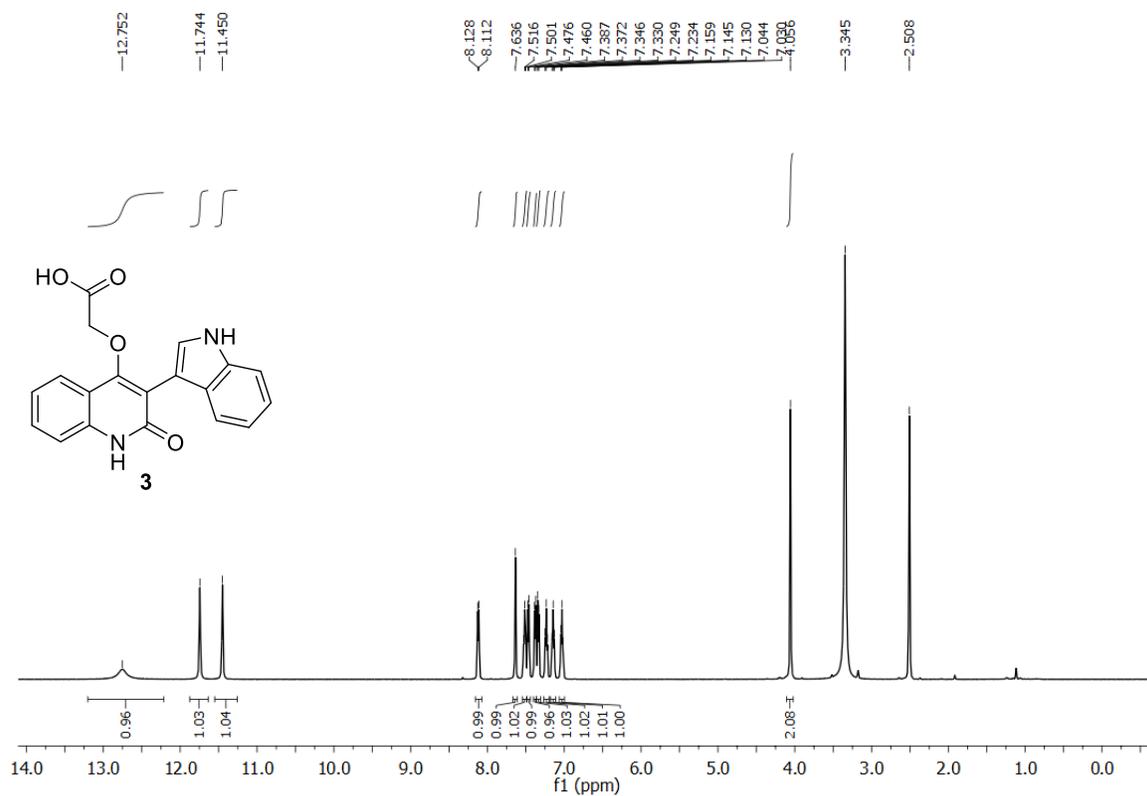


Fig S68. ¹H NMR (500 MHz, DMSO d₆) of **3**

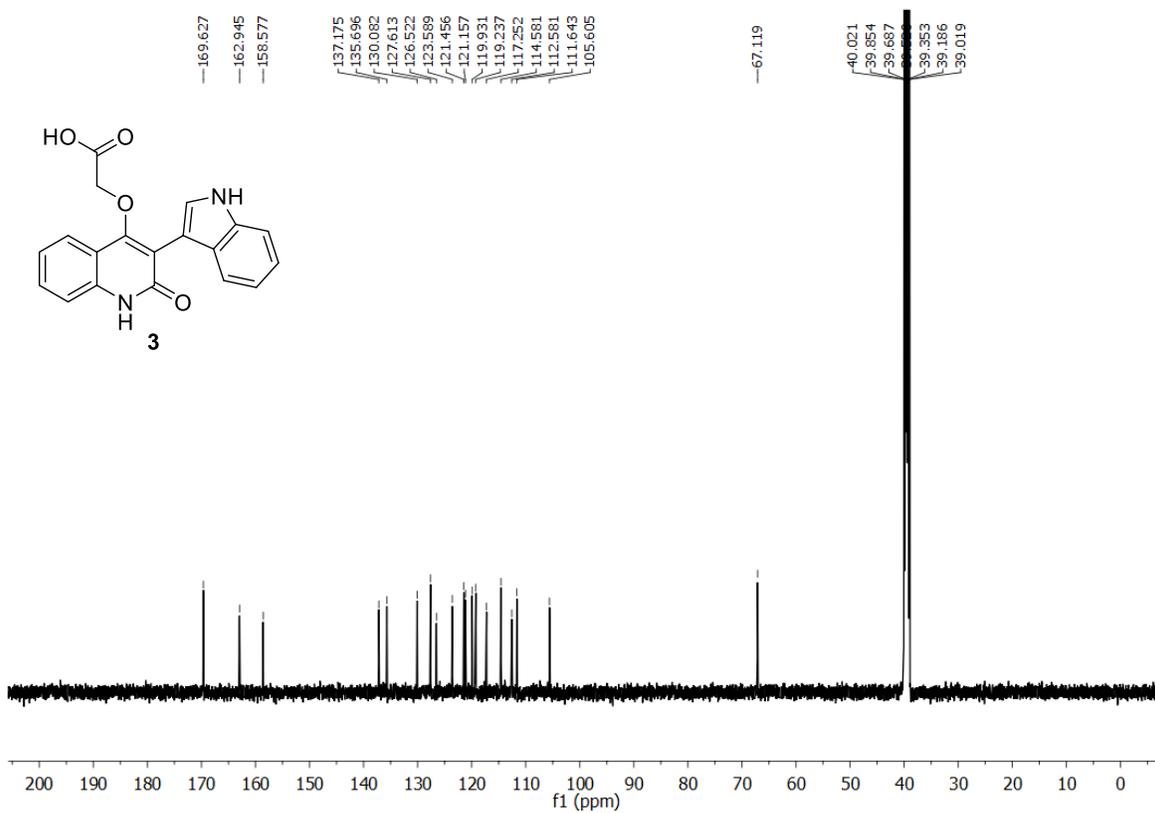


Fig S69. ¹³C NMR (125 MHz, DMSO d₆) of **3**

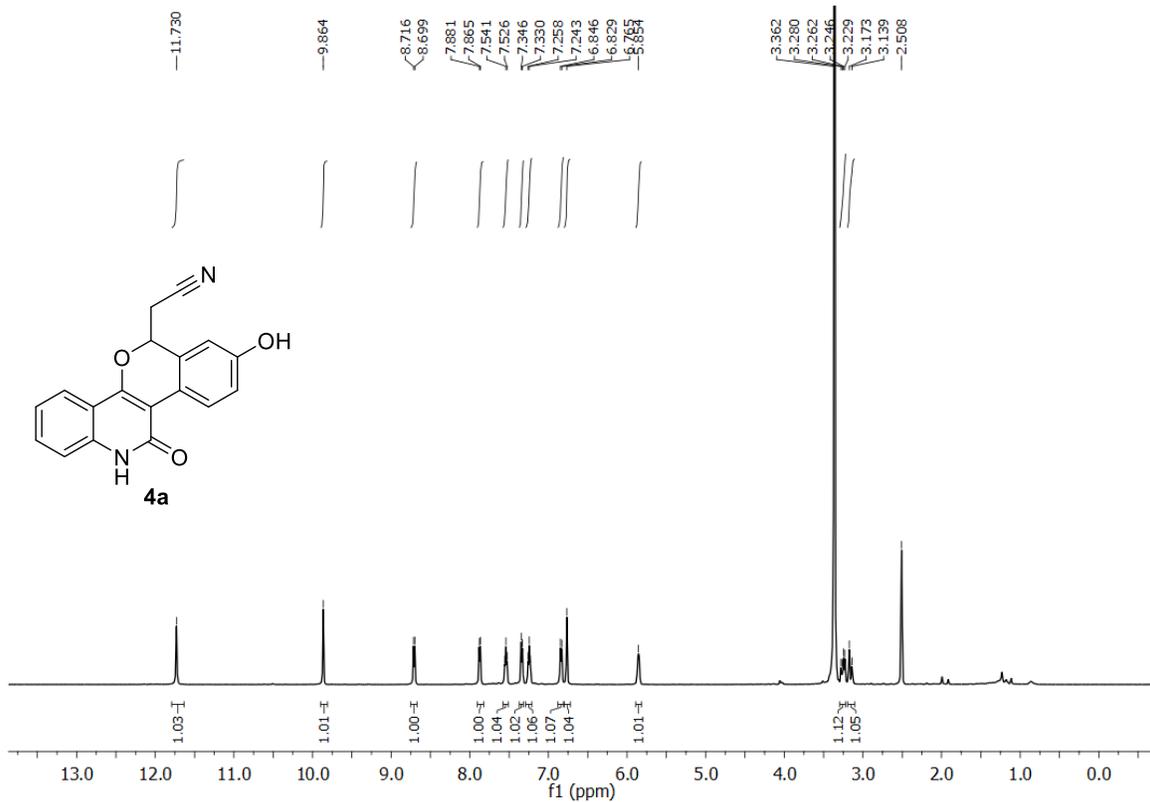
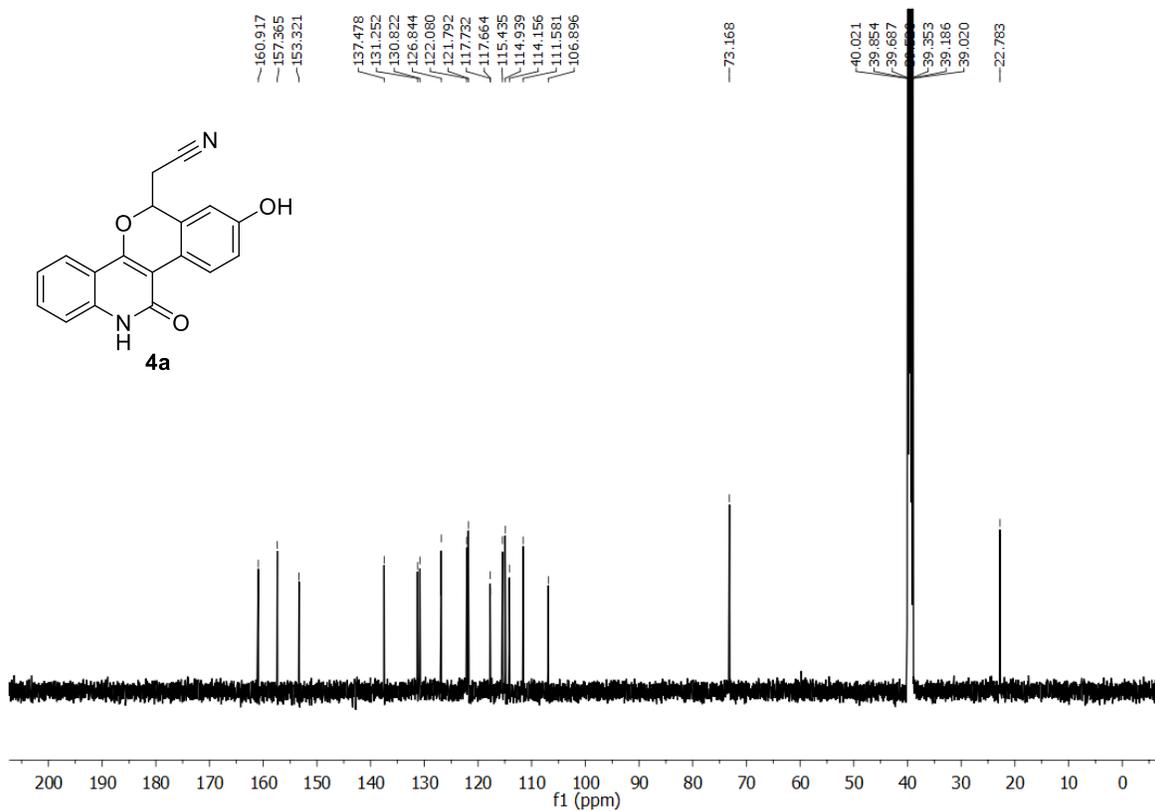


Fig S70. ¹H NMR (500 MHz, DMSO d₆) of **4a**



S71. ¹³C NMR (125 MHz, DMSO d₆) of **4a**

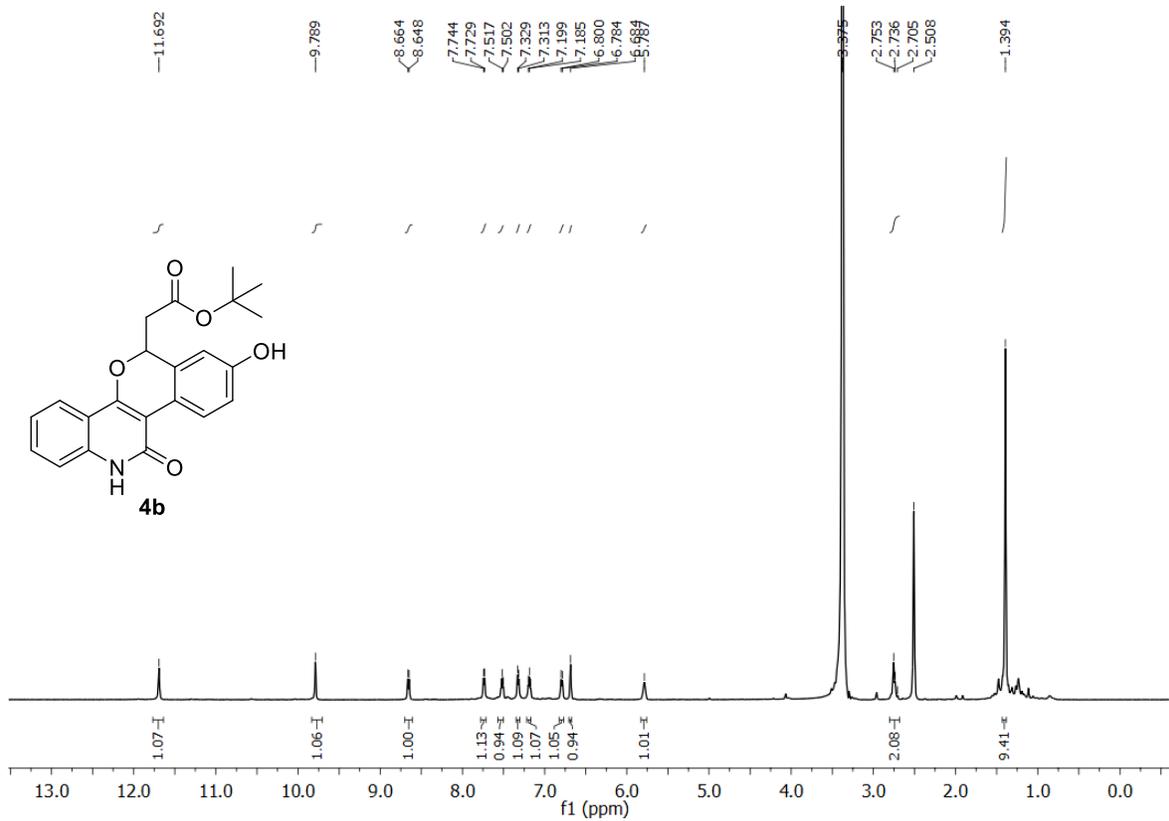
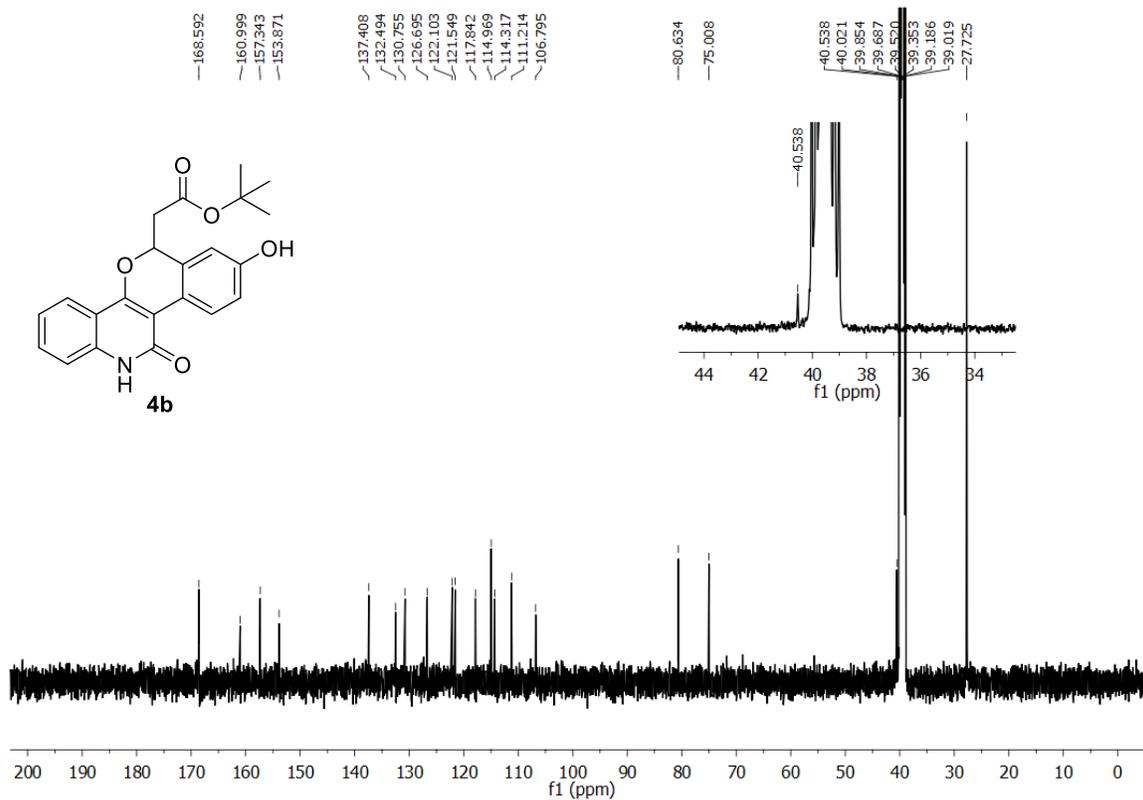
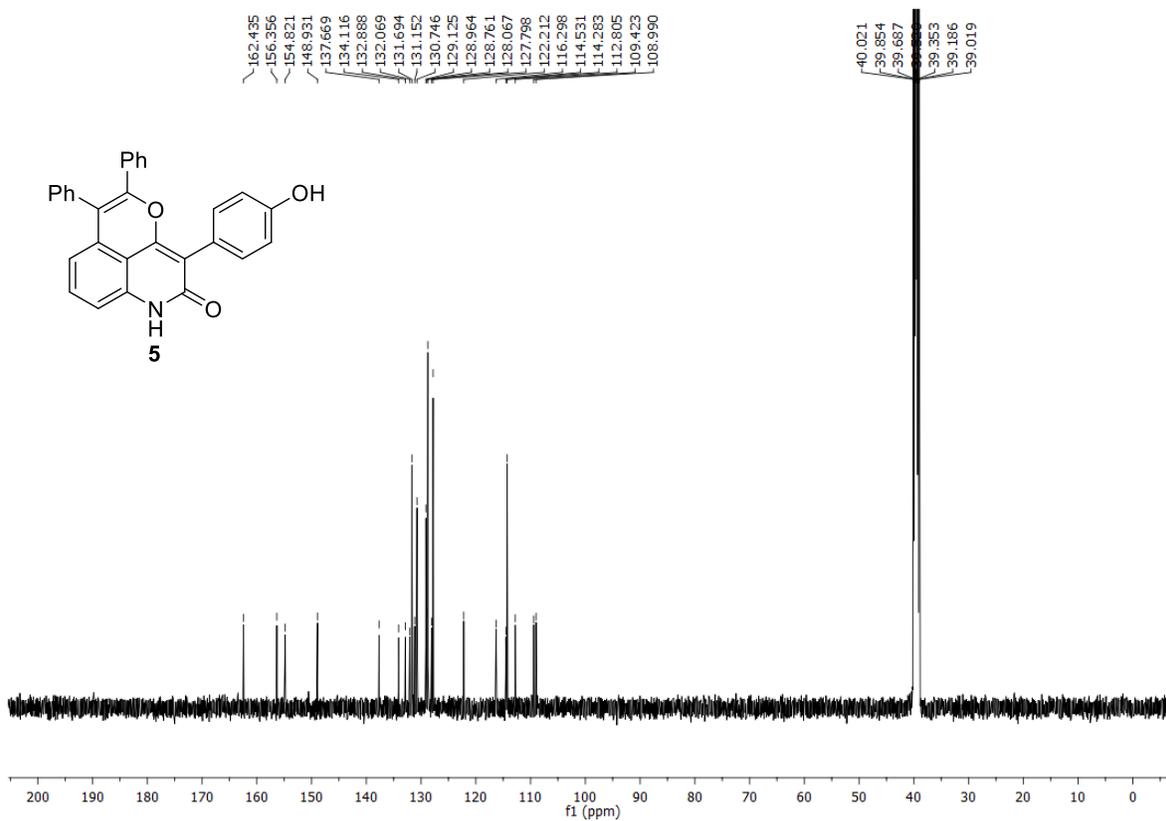
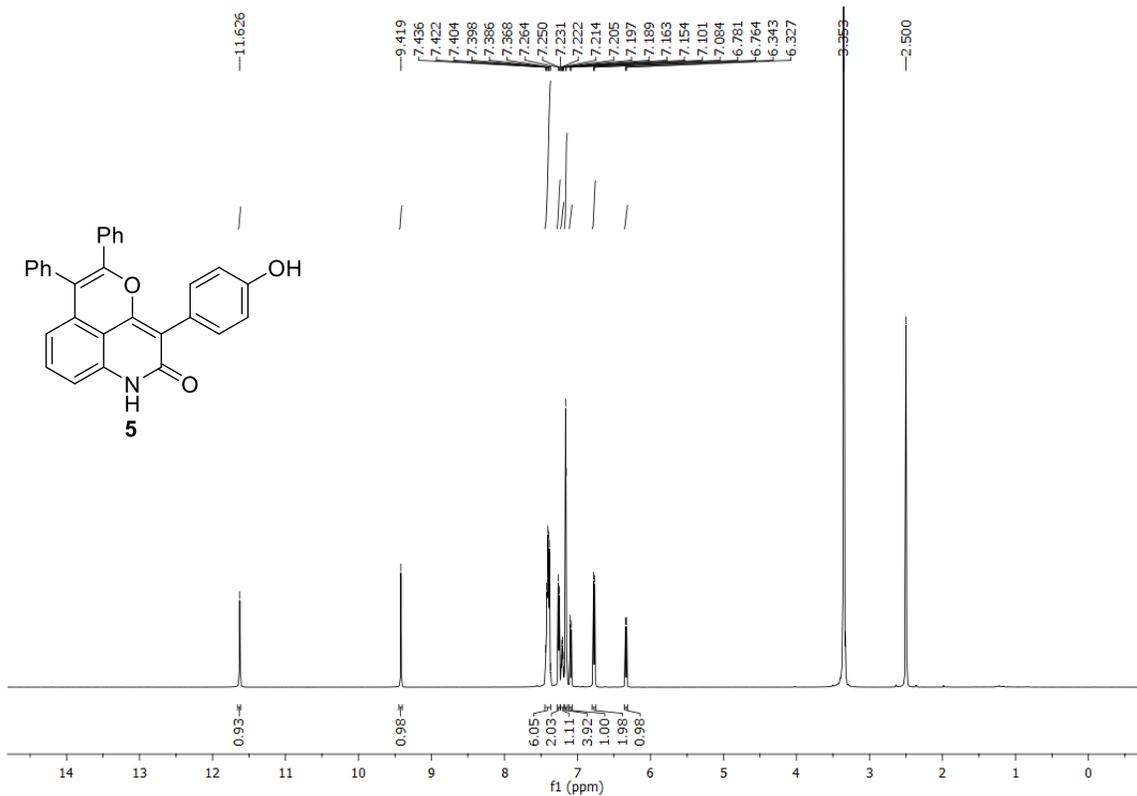


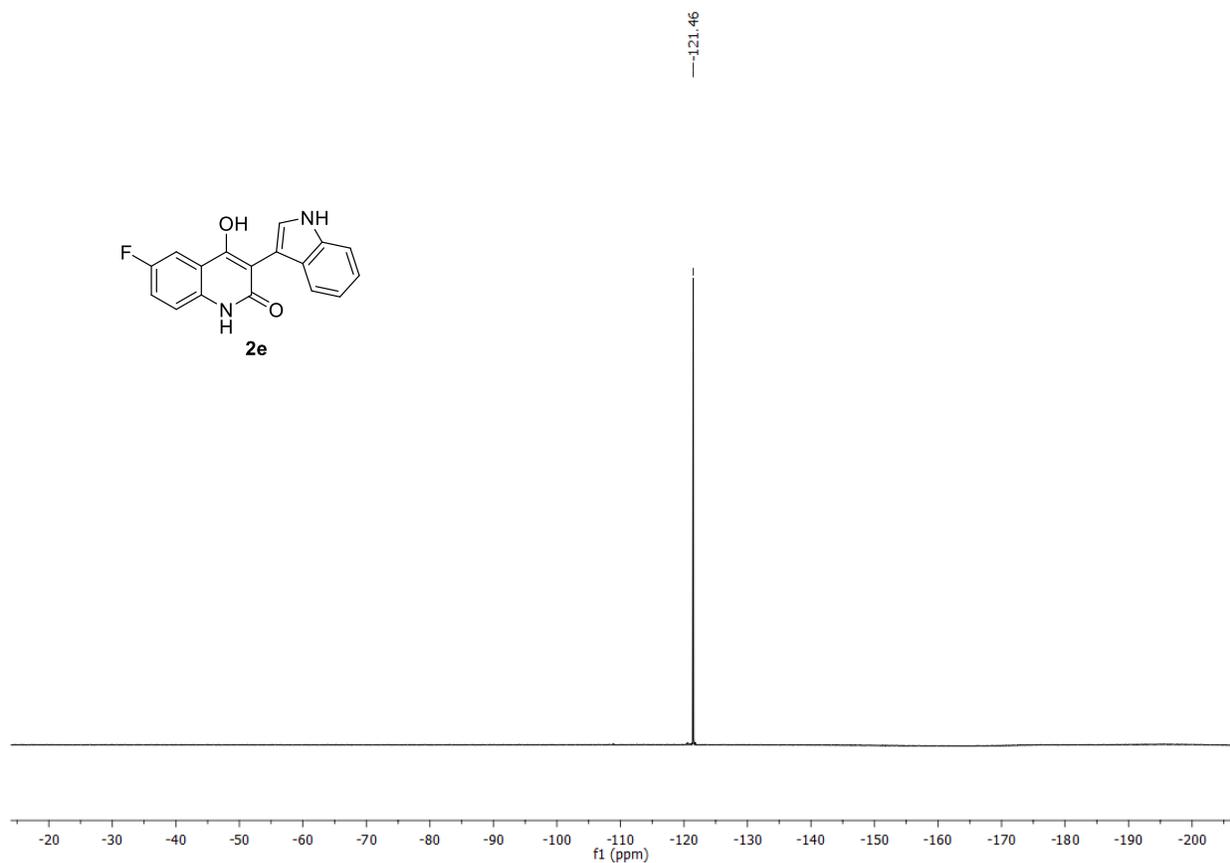
Fig S72. ^1H NMR (500 MHz, $\text{DMSO-}d_6$) of **4b**



S73. ^{13}C NMR (125 MHz, $\text{DMSO-}d_6$) of **4b**



12. ^{19}F NMR spectrum of compound 2e



S76. ^{19}F NMR (125 MHz, DMSO d_6) of 2e