Supporting Information

Microwave-assisted Copper-mediated Tandem Approach for Fused Quinazoline Derivatives

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1. Crystal structure for Compound 3b:

Data collection and Structure solution details: Single crystal X-ray data for KA971 compound were collected at room temperature on a Bruker D8 QUEST equipped with a four-circle kappa diffractometer, Photon 100 detector and an Iμs microfocus Mo source (=0.71073Å) from a multi-mirror monochromatic incident beam. A combination of Phi and Omega scans were used to collect the necessary data and unit cell dimensions were determined using 7473 reflections for KA971. Integration and scaling of intensity data were accomplished using SAINT program.[1] The structures were solved by Direct Methods using SHELXS97[2] and refinement was carried out by full-matrix least-squares technique using SHELXL-2018/3.[2-3] Anisotropic displacement parameters were included for all non-hydrogen atoms. All H atoms were positioned geometrically and treated as riding on their parent C atoms, with C-H distances of 0.93--0.97 Å, and with U_{iso}(H) = 1.2U_{eq} (C) or 1.5U_{eq} for methyl atoms. The N bound H atoms were located from the difference Fourier map. Structures with CCDC deposition number contains the supplementary crystallographic data for this paper which can be obtained free of charge at https://www.ccdc.cam.ac.uk/structures/

Crystal structure determination of KA971:

Datablock: KA971_0m

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Bond precision:  C-C = 0.0032 A          Wavelength=0.71073

Cell:            a=4.954(3)     b=20.606(13)          c=16.56(1)
                 alpha=90       beta=91.728(15)       gamma=90
Temperature:     293 K

                 Calculated                Reported
Volume           1689.7(18)                1689.7(17)
Space group      P 21/n                    P 21/n
Hall group       -P 2yn                    -P 2yn
Moiety formula   C22 H17 N3 O              C22 H17 N3 O
Sum formula      C22 H17 N3 O              C22 H17 N3 O
Mr               339.39                    339.38
Dx,g cm-3        1.334                     1.334
Z                4                         4
Mu (mm-1)        0.084                     0.084
F000             712.0                     712.0
F000'            712.27
h,k,lmax         6,25,20                   6,25,20
Nref             3464                      3445
Tmin,Tmax        0.980,0.985               0.705,0.745
Tmin'            0.978

Correction method= # Reported T Limits: Tmin=0.705 Tmax=0.745
AbsCorr = MULTI-SCAN

Data completeness= 0.995          Theta(max)= 26.397

R(reflections)= 0.0558( 2492)     wR2(reflections)= 0.1559( 3445)

S = 1.055                 Npar= 240
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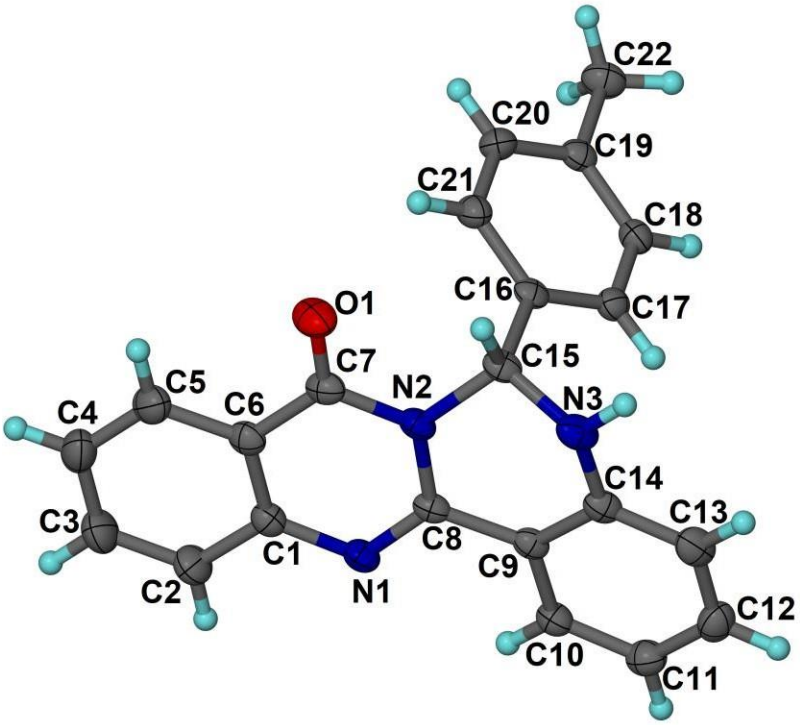
CCDC 2022481 contains the supplementary crystallographic data for this paper which can be obtained free of charge at https://summary.ccdc.cam.ac.uk/structure-summary-form or

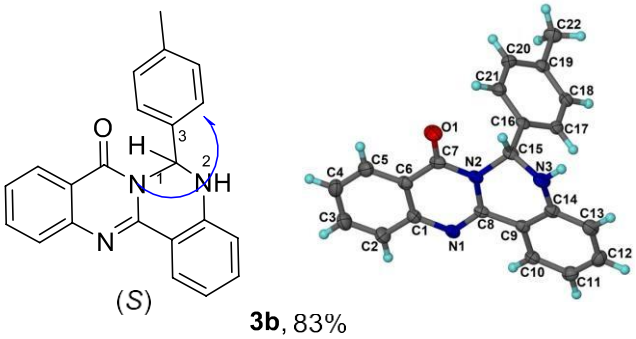
fromthe Cambridge Crystallographic Data Centre (CCDC), 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44(0) 1223 336 033; email: deposit@ccdc.cam.ac.uk.



References:

1. SMART & SAINT. Software Reference manuals. Versions 6.28a & 5.625, Bruker Analytical X-ray Systems Inc., Madison, Wisconsin, U.S.A., 2001.
2. Sheldrick, G. M. SHELXS97 and SHELXL Version 2014/7, http://shelx.uni-ac.gwdg.de/SHELX/index.php
3. Muller, P, Herbst-Imer, R, Spek, A. L, Schneider, T. R, and Sawaya, M. R. Crystal Structure Refinement: A Crystallographer's Guide to SHELXL. Muller, P. Ed. 2006 Oxford University Press: Oxford, New York, pp. 57–91.
4. A. L. Spek, Acta Cryst. 2009, D65, 148-155.

Configuration of 3b



3b, 83%

2. Experimental Section

General information

All reagents and solvents were obtained from commercial suppliers and used without further purification. Analytical thin layer chromatography (TLC) was performed on MERCK precoated silica gel 60-F254 (0.5 mm) aluminum plates. Visualization of the spots on the TLC plates was achieved using UV light. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker 500 MHz spectrometer using tetramethylsilane (TMS) as the internal standard. Chemical shifts for ^{1}H and ^{13}C are reported in parts per million (ppm) downfield from tetramethylsilane. Spin multiplicities are described as s (singlet), bs (broad singlet), d (doublet), dd (double doublet), t (triplet), q (quartet), and m (multiplet). Coupling constant (*J*) values are reported in hertz (Hz). HRMS was performed using an Agilent QTOF 6540 series mass spectrometer. Wherever required, column chromatography was performed using silica gel (60–120 or 100–200) or neutral alumina.

Microwave Irradiation Experiments

Microwave irradiation experiments were performed in a Monowave 300 single-mode microwave reactor. The reaction temperature is monitored by an external infrared (IR) sensor housed in the side walls of the microwave cavity measuring the surface temperature of the reaction vessel. Reaction times refer to hold time at the desired set temperature and not to the total radiation time. Pressure sensing is achieved by a hydraulic sensor integrated in the swivelling cover of the instrument. The reusable 10 mL G10 Pyrex vial is sealed with PEEK snap caps and standard PTFE-coated silicone septa. Reaction cooling is performed by compressed air automatically after the heating period has elapsed. The required force of 6−8

bar is also used to pneumatically seal the vials tightly at the beginning to withstand 30 bar and to ensure smooth release of potentially remaining pressure before the cover is opened.

General procedure for the synthesis of fused quinazoline derivatives 3a-t:

Substituted quinazoline/benzimidazole (1 mmol) and NH_4OAc (1.3 mmol) in microwave vial G10 (10 mL) containing a Teflon-coated stir bar. The vial was sealed and subsequently placed in the microwave cavity and irradiated for 15 min at 120 °C (hold time). After cooling to room temperature, then add Cu_2O (10 mol%) substituted aldehydes (1 mmol) continue the irradiation for 15 min at 120 °C (hold time). After cooling to room temperature, the reaction mixture was extracted with ethyl acetate (3x10 mL), washed with 1:1 mixture of brine. The combined organic extracts were dried over anhydrous sodium sulphate. After removal of the solvent under reduced pressure, the crude product was purified by using column chromatography, EtOAc:Hexane (2:8) as eluent on silica gel to afford the pure products.

2-(3-aminophenyl)quinazolin-4(3H)-one **(Intermediate *III*)**

Off-white solid; yield 70 %; mp:123–127 °C; ^{1}H NMR (500 MHz, DMSO-d_6): δ 12.32 (s, 1H), 8.20–8.10 (m, 1H), 7.87–7.80 (m, 1H), 7.71 (d, J = 7.9 Hz, 1H), 7.55–7.48 (m, 1H), 7.40 (t, J = 1.9 Hz, 1H), 7.28 (d, J = 7.7 Hz, 1H), 7.17 (t, J = 7.8 Hz, 1H), 6.79-6.71 (m, 1H), 5.36 (s, 2H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 162.6, 153.5, 149.4, 149.3, 135.0, 133.9, 129.5, 127.8, 126.8, 126.3, 121.4, 117.4, 115.4, 113.4.

6-phenyl-5,6-dihydro-8H-quinazolino[4,3-b]quinazolin-8-one (3a)

Pale yellow solid; yield 80 %; mp:160–164 °C; FT-IR (cm^{-1}): 3345, 3059, 1683, 1635, 1517, 1330, 1286; ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.20 (d, J = 7.2 Hz, 1H), 8.13 (d, J = 7.1 Hz, 1H), 8.01 (d, J = 3.6 Hz, 1H), 7.91–7.84 (m, 1H), 7.76 (d, J = 8.0 Hz, 1H), 7.56–7.50 (m, 1H), 7.37–7.32 (m, 1H), 7.31–7.21 (m, 4H), 7.19 (d, J = 7.2 Hz, 2H), 6.94 (d, J = 8.0 Hz, 1H), 6.83 (t, J = 7.5 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 160.1, 148.2, 147.7, 145.6, 139.9, 135.5, 134.2, 129.0, 128.6, 127.7, 127.3, 127.1, 126.7, 126.1, 120.4, 119.2, 116.3, 116.0, 62.9; HRMS (ESI): m/z calculated for $C_{21}H_{15}N_3O$ 326.1293 found 326.1320 [M+H]+.

6-(p-tolyl)-5,6-dihydro-8H-quinazolino[4,3-b]quinazolin-8-one (3b)

Pale yellow solid; yield 83 %; mp:161–165 °C; FT-IR (cm^{-1}): 3325, 2923, 1688, 1587, 1372, 1286; ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.20 (d, J = 7.6 Hz, 1H), 8.12 (d, J = 7.8 Hz, 1H), 7.97 (d, J = 3.3 Hz, 1H), 7.88 (t, J = 7.2 Hz, 1H), 7.75 (d, J = 8.1 Hz, 1H), 7.53 (t, J = 7.4 Hz, 1H), 7.34 (t, J = 7.2 Hz, 1H), 7.22 (d, J = 3.3 Hz, 1H), 7.12–7.01 (m, 4H), 6.92 (d, J = 8.1 Hz, 1H), 6.82 (t, J = 7.5 Hz, 1H), 2.24–2.14 (m, 3H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 160.1, 148.2, 147.8, 145.7, 138.0, 136.9, 135.4, 134.1, 129.5, 127.7, 127.3, 127.1, 126.7, 126.1, 120.4, 119.2, 116.3, 116.1, 62.8, 20.9. HRMS (ESI): m/z calculated for $C_{22}H_{17}N_3O$ 340.1450 found 340.1472 [M+H]+.

6-(4-isopropylphenyl)-5,6-dihydro-8H-quinazolino[4,3-b]quinazolin-8-one (3c)

Pale yellow solid; yield 85 %; mp:158–161 °C; FT-IR (cm^{-1}): 3330, 2922, 1684, 1633, 1589, 1514, 1286; ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.20 (d, J = 7.8 Hz, 1H), 8.14 (d, J = 7.8 Hz, 1H), 7.98 (d, J = 2.7 Hz, 1H), 7.87 (t, J = 7.6 Hz, 1H), 7.75 (d, J = 8.1 Hz, 1H), 7.52 (t, J = 7.4 Hz, 1H), 7.34 (t, J = 7.4 Hz, 1H), 7.22 (d, J = 2.6 Hz, 1H), 7.18-7.04 (m, 4H), 6.93 (d, J = 8.0 Hz, 1H), 6.83 (t, J = 7.4 Hz, 1H), 2.77 (dt, J = 13.5, 6.7 Hz, 1H), 1.10-1.00 (m, 6H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 160.1, 148.8, 148.2, 147.7, 145.6, 137.4, 135.4, 134.1, 129.0, 127.7, 127.4, 127.1, 126.9, 126.6, 126.1, 120.4, 119.1, 116.3, 115.9, 62.9, 33.4, 24.1; HRMS (ESI): m/z calculated for $C_{24}H_{21}N_3O$ 368.1763 found 368.1789 [M+H]+.

6-(3,4,5-trimethoxyphenyl)-5,6-dihydro-8H-quinazolino[4,3-b]quinazolin-8-one (3d)

Pale yellow solid; yield 85 %; mp:157–160 °C; FT-IR (cm^{-1}): 3330, 2925, 2855, 1670, 1614, 1508, 1407, 1373, 1282; ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.22 (d, J = 7.3 Hz, 1H), 8.16 (d, J = 7.4 Hz, 1H), 7.92 (d, J = 15.0 Hz, 1H), 7.88 (s, 1H), 7.76 (d, J = 7.8 Hz, 1H), 7.53 (s, 1H), 7.37 (s, 1H), 7.19 (s, 1H), 6.96 (d, J = 7.6 Hz, 1H), 6.86 (s, 1H), 6.50 (s, 2H), 3.56 (s, 9H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 160.1, 153.2, 148.1, 147.6, 145.8, 137.9, 135.7, 135.5, 134.2, 127.7, 127.3, 127.1, 126.8, 120.3, 119.3, 116.2, 116.1, 103.9, 63.1, 60.4, 56.2; HRMS (ESI): m/z calculated for $C_{24}H_{21}N_3O_4$ 416.1610 found 416.1629 [M+H]+.

6-(4-chlorophenyl)-5,6-dihydro-8H-quinazolino[4,3-b]quinazolin-8-one (3e)

Pale yellow solid; yield 78 %; mp:160–164 °C; FT-IR (cm^{-1}): 3341, 2919, 1681, 1622, 1508, 1366, 1334, 1289; ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.21 (d, J = 7.7 Hz, 1H), 8.13 (d, J =

7.8 Hz, 1H), 8.01 (d, *J* = 3.2 Hz, 1H), 7.88 (t, *J* = 7.3 Hz, 1H), 7.76 (d, *J* = 8.1 Hz, 1H), 7.54 (t, *J* = 7.4 Hz, 1H), 7.38-7.30 (m, 3H), 7.26 (d, *J* = 3.2 Hz, 1H), 7.21 (d, *J* = 8.4 Hz, 2H), 6.95 (d, *J* = 8.1 Hz, 1H), 6.85 (t, *J* = 7.5 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 160.1, 148.2, 147.5, 145.3, 138.9, 135.5, 134.2, 133.3, 129.1, 128.1, 127.7, 127.4, 127.1, 126.8, 120.3, 119.4, 116.4, 116.0, 62.5; HRMS (ESI): m/z calculated for $C_{21}H_{14}ClN_3O$ 360.0904 found 360.0936 [M+H]+.

6-(4-bromophenyl)-5,6-dihydro-8H-quinazolino[4,3-b]quinazolin-8-one (3f)

Pale yellow solid; yield 79 %; mp:160–164 °C; FT-IR (cm^{-1}): 3341, 2923, 1682, 1655, 1509, 1334, 1287; ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.32–7.98 (m, 4H), 7.96–7.69 (m, 3H), 7.60-7.50 (m, 4H), 7.40–7.01 (m, 2H), 6.91 (d, *J* = 6.5 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 162.7, 152.7, 149.2, 135.5, 135.1, 133.1, 131.8, 129.0, 128.2, 127.9, 127.4, 127.0, 126.5, 126.3, 125.9, 121.4, 119.4, 116.0, 115.8, 58.9; HRMS (ESI): m/z calculated for $C_{21}H_{14}BrN_3O$ 405.0398 found 405.0381 [M+2]+.

6-(4-fluorophenyl)-5,6-dihydro-8H-quinazolino[4,3-b]quinazolin-8-one (3g)

Pale yellow solid; yield 80 %; mp:159–162 °C; FT-IR (cm−1): 3339, 2925, 1684, 1654, 1638, 1598, 1520, 1345, 1283; ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.21 (d, *J* = 7.7 Hz, 1H), 8.13 (d, *J* = 7.8 Hz, 1H), 8.01 (d, *J* = 3.2 Hz, 1H), 7.88 (t, *J* = 7.3 Hz, 1H), 7.76 (d, *J* = 8.1 Hz, 1H), 7.54 (t, *J* = 7.4 Hz, 1H), 7.35 (d, *J* = 8.4 Hz, 3H), 7.26 (d, *J* = 3.2 Hz, 1H), 7.21 (d, *J* = 8.4 Hz, 2H), 6.95 (d, *J* = 8.1 Hz, 1H), 6.85 (t, *J* = 7.5 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 160.1, 148.2, 147.4, 145.3, 145.1, 135.6, 134.3, 133.1, 127.8, 127.4, 127.3, 127.1, 126.8, 120.3, 119.6, 118.8, 116.5, 116.0, 111.6, 62.7; HRMS (ESI): m/z calculated for $C_{21}H_{14}FN_3O$ 344.1199 found 344.1217 [M+H]+.

4-(8-oxo-5,8-dihydro-6H-quinazolino[4,3-b]quinazolin-6-yl)benzonitrile (3h)

Pale yellow solid; yield 76 %; mp:158–161 °C; FT-IR (cm^{-1}): 3340, 2927, 2245, 1689, 1650, 1597, 1523, 1341, 1327, 1287; ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.26 (d, *J* = 7.2 Hz, 1H), 8.21–8.16 (m, 1H), 8.10 (d, *J* = 7.4 Hz, 1H), 7.88 (d, *J* = 6.8 Hz, 1H), 7.80 (d, *J* = 7.8 Hz, 1H), 7.69 (s, 1H), 7.55 (d, *J* = 7.5 Hz, 2H), 7.43 (s, 1H), 7.31 (s, 1H), 7.14 (t, *J* = 7.0 Hz, 1H), 6.88 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 159.7, 148.1, 148.0, 144.2, 137.2, 135.5,

134.2, 131.8, 130.6, 129.0, 128.2, 128.0, 127.8, 127.3, 126.9, 126.8, 126.2, 120.3, 119.4, 116.6, 115.6, 61.4; HRMS (ESI): m/z calculated for $C_{22}H_{14}N_4O$ 351.1246 found 351.1270 [M+H]+.

6-(4-iodophenyl)-5,6-dihydro-8H-quinazolino[4,3-b]quinazolin-8-one (3i)

Pale yellow solid; yield 79 %; mp:155–159 °C; FT-IR (cm^{-1}): 3332, 2924, 1687, 1658, 1628, 1585, 1533, 1503, 1411, 1380, 1285; ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.25–8.14 (m, 2H), 7.96 (d, J = 3.4 Hz, 1H), 7.90–7.84 (m, 1H), 7.77–7.71 (m, 1H), 7.58-7.50 (m, 1H), 7.50–7.44 (m, 1H), 7.43-7.38 (m, 1H), 7.37–7.30 (m, 1H), 7.18–6.96 (m, 2H), 6.96–6.89 (m, 2H), 6.89–6.77 (m, 1H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 159.6, 148.1, 147.9, 147.1, 145.4, 143.5, 135.5, 134.4, 134.3, 127.7, 127.4, 127.0, 127.0, 126.8, 126.6, 126.4, 120.4, 119.7, 116.6, 115.9, 60.3; HRMS (ESI): m/z calculated for $C_{21}H_{14}IN_3O$ 452.0260 found 452.0284 [M+H]+.

6-(2-chlorophenyl)-5,6-dihydro-8H-quinazolino[4,3-b]quinazolin-8-one (3j)

Pale yellow solid; yield 81 %; mp:154–158 °C; FT-IR (cm^{-1}): 3325, 2928, 1686, 1655, 1634, 1579, 1524, 1334, 1260; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.20–8.14 (m, 1H), 7.75 (t, J = 9.8 Hz, 1H), 7.39 (d, J = 7.9 Hz, 2H), 7.36–7.32 (m, 2H), 7.28-7.20 (m, 1H), 7.19-7.13 (m, 1H), 6.99-6.94 (m, 1H), 6.92 (t, J = 7.5 Hz, 1H), 6.71 (t, J = 10.3 Hz, 1H), 6.60 (s, 1H), 6.48 (t, J = 10.0 Hz, 1H), 5.05 (d, J = 8.1 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 147.7, 144.0, 142.2, 138.5, 133.0, 131.7, 130.0, 129.2, 127.0, 125.6, 122.6, 122.4, 120.0, 119.2, 114.8, 113.0, 110.5, 70.4, 49.4; HRMS (ESI): m/z calculated for $C_{21}H_{14}ClN_3O$ 360.0904 found 360.0930 [M+H]+.

6-(2,5-dichlorophenyl)-5,6-dihydro-8H-quinazolino[4,3-b]quinazolin-8-one (3k)

Pale yellow solid; yield 81 %; mp:158–161 °C; FT-IR (cm^{-1}): 3330, 2852, 1686, 1654, 1598, 1313, 1286, 1230; ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.20-8.04 (m, 4H), 7.86 (s, 1H), 7.77 (s, 1H), 7.59-7.40 (m, 4H), 7.42–6.98 (m, 2H), 6.92 (d, J = 6.7 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 160.5, 152.7, 149.2, 135.4, 135.0, 134.1, 133.2, 131.8, 129.0, 128.2, 127.9, 127.4, 127.0, 126.5, 126.3, 121.4, 119.2, 118.3, 116.0, 115.8, 114.2, 62.4; HRMS (ESI): m/z calculated for $C_{21}H_{13}Cl_2N_3O$ 394.0514 found 394.0544 [M+H]+.

6-(4-bromo-2-fluorophenyl)-5,6-dihydro-8H-quinazolino[4,3-b]quinazolin-8-one (3l)

Pale yellow solid; yield 80 %; mp:160–164 °C; FT-IR (cm^{-1}): 3338, 2921, 1688, 1656, 1621, 1587, 1378, 1367, 1286; ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.24 (d, J = 7.0 Hz, 1H), 8.19 (d, J = 6.7 Hz, 1H), 8.14 (d, J = 7.6 Hz, 1H), 8.05-8.00 (m, 2H), 7.88 (s, 1H), 7.81 (d, J = 5.9 Hz, 1H), 7.75 (d, J = 7.2 Hz, 1H), 7.66 (d, J = 6.5 Hz, 1H), 7.65–7.26 (m, 4H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 163.7, 147.8, 147.7, 135.1, 134.0, 133.0, 132.8, 129.1, 128.1, 127.8, 127.6, 126.3, 121.7, 119.1, 118.8, 117.8, 115.3, 114.9, 114.0, 111.5, 66.0; HRMS (ESI): m/z calculated for $C_{21}H_{13}BrFN_3O$ 423.0304 found 423.0334 [M+H]+.

6-(naphthalen-2-yl)-5,6-dihydro-8H-quinazolino[4,3-b]quinazolin-8-one (3m)

Pale yellow solid; yield 85 %; mp:150–154 °C; FT-IR (cm^{-1}): 3337, 2956, 1688, 1656, 1621, 1587, 1378, 1367, 1286; ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.26 (d, J = 7.5 Hz, 1H), 8.20 (d, J = 7.5 Hz, 1H), 8.10 (d, J = 7.5 Hz, 1H), 7.88 (d, J = 6.9 Hz, 1H), 7.80 (d, J = 7.9 Hz, 1H), 7.70 (s, 1H), 7.59-7.54 (m, 3H), 7.53–7.48 (m, 1H), 7.43 (s, 1H), 7.31 (s, 2H), 7.14 (t, J = 7.2 Hz, 1H), 6.88 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 159.7, 148.1, 148.0, 144.2, 137.2, 135.5, 135.0, 134.2, 131.8, 130.6, 129.0, 128.2, 128.0, 127.8, 127.3, 127.0, 126.9, 126.8, 126.2, 121.4, 120.3, 119.5, 116.6, 115.6, 61.4; HRMS (ESI): m/z calculated for $C_{25}H_{17}N_3O$ 376.1450 found 376.1472 [M+H]+.

6-(anthracen-9-yl)-5,6-dihydro-8H-quinazolino[4,3-b]quinazolin-8-one (3n)

Pale yellow solid; yield 81 %; mp:152–156 °C; FT-IR (cm^{-1}): 3335, 2928, 1715, 1667, 1632, 1524, 1324, 1300, 1250; ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.73 (d, J = 7.4 Hz, 2H), 8.36 (d, J = 8.0 Hz, 1H), 8.30 (d, J = 7.9 Hz, 1H), 8.17 (d, J = 7.5 Hz, 1H), 8.00 (t, J = 5.9 Hz, 2H), 7.95 (d, J = 6.3 Hz, 1H), 7.89 (t, J = 7.2 Hz, 1H), 7.75 (d, J = 7.1 Hz, 1H), 7.57 (t, J = 5.8 Hz, 2H), 7.50 (d, J = 8.3 Hz, 2H), 7.46–7.42 (m, 1H), 7.23–7.18 (m, 1H), 7.14 (t, J = 7.5 Hz, 1H), 7.04 (m, J = 14.7, 7.3 Hz, 2H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 155.4, 154.1, 150.4, 150.2, 149.0, 145.6, 141.4, 137.8, 137.2, 135.1, 134.8, 134.1, 133.4, 132.4, 130.7, 129.1, 127.4, 126.5, 126.3, 125.1, 123.3, 123.1, 122.4, 121.6, 121.0, 119.7, 118.5, 117.7, 115.7; HRMS (ESI): m/z calculated for $C_{29}H_{19}N_3O$ 426.1606 found 426.1632 [M+H]+.

6-(pyridin-2-yl)-5,6-dihydro-8H-quinazolino[4,3-b]quinazolin-8-one (3o)

Pale yellow solid; yield 82 %; mp:155–158 °C; FT-IR (cm^{-1}): 3321, 2916, 1725, 1654, 1627, 1526, 1505, 1382, 1290; ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.43 (d, J = 71.8 Hz, 2H), 8.13 (d, J = 9.2 Hz, 1H), 7.89-7.72 (m, 3H), 7.68-7.52 (m, 3H), 7.30 (d, J = 13.1 Hz, 2H), 6.74 (d, J = 8.8 Hz, 2H), 5.87 (s, 1H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 163.8, 147.9, 145.0, 134.5, 133.9, 131.6, 131.2, 131.0, 130.8, 130.1, 128.1, 127.8, 127.4, 127.2, 126.3, 126.2, 122.3, 122.0, 117.8, 115.3, 114.9, 65.9; HRMS (ESI): m/z calculated for $C_{20}H_{14}N_4O$ 327.1246 found 327.1276 [M+H]+.

6-isobutyl-5,6-dihydro-8H-quinazolino[4,3-b]quinazolin-8-one (3p)

Pale yellow solid; yield 73 %; mp:140–143 °C; FT-IR (cm^{-1}): 3330, 2925, 2855, 1670, 1614, 1508, 1407, 1373, 1282; ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.21–8.12 (m, 2H), 7.85–7.79 (m, 1H), 7.69 (d, J = 8.1 Hz, 1H), 7.50–7.44 (m, 1H), 7.41–7.28 (m, 2H), 6.92–6.83 (m, 2H), 6.19 (dt, J = 9.4, 4.0 Hz, 1H), 1.87–1.79 (m, 1H), 1.72–1.65 (m, 1H), 1.28 (m, 1H), 0.95 (t, J = 6.5 Hz, 3H), 0.85 (t, J = 5.6 Hz, 3H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 159.5, 148.2, 147.4, 145.3, 135.1, 134.0, 127.5, 127.4, 126.8, 126.3, 120.6, 118.9, 116.3, 115.7, 61.0, 41.5, 24.0, 23.6, 21.8.

6-phenyl-5,6-dihydrobenzo[4,5]imidazo[1,2-c]quinazoline (3q)

Pale yellow solid; yield 78 %; mp:156–160 °C; FT-IR (cm^{-1}): 2976, 1721, 1634, 1602, 1515, 1374, 1297; ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.21 (d, J = 7.7 Hz, 1H), 8.13 (d, J = 7.8 Hz, 1H), 8.01 (d, J = 3.2 Hz, 1H), 7.88 (t, J = 7.3 Hz, 1H), 7.76 (d, J = 8.1 Hz, 1H), 7.54 (t, J = 7.4 Hz, 1H), 7.45-7.35 (m, 3H), 7.32–7.21 (m, 2H), 7.21 (d, J = 8.4 Hz, 2H), 6.95 (d, J = 8.1 Hz, 1H), 6.85 (t, J = 7.5 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 159.5, 159.1, 158.3, 150.9, 139.8, 138.8, 135.8, 134.5, 134.2, 133.6, 130.7, 129.4, 128.8, 128.3, 126.3, 123.4, 123.1, 121.0, 114.4; HRMS (ESI): m/z calculated for $C_{20}H_{15}N_3$ 298.1344 found 298.1367 [M+H]+.

6-(4-bromo-2-fluorophenyl)-5,6-dihydrobenzo[4,5]imidazo[1,2-c]quinazoline (3r)

Pale yellow solid; yield 76 %; mp:157–161 °C; FT-IR (cm^{-1}): 3025, 1685, 1659, 1633, 1582, 1527, 1478, 1353, 1310, 1020; ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.56 (s, 1H), 8.08 (d, J = 7.9 Hz, 1H), 8.00-7.89 (m, 3H), 7.53–7.47 (m, 1H), 7.44–7.38 (m, 2H), 7.30 (dd, J = 11.4,

8.2, Hz, 1H), 7.25-7.20 (m, 1H), 7.15–7.08 (m, 1H), 7.05 (d, *J* = 8.5 Hz, 2H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 167.9, 156.2, 154.2, 154.2, 147.6, 134.4, 129.5, 129.0, 126.8, 125.4, 125.2, 124.3, 124.2, 123.9, 123.3, 122.6, 122.5, 116.8, 116.6, 115.6; HRMS (ESI): m/z calculated for $C_{20}H_{13}BrFN_3$ 395.0355 found 395.0348 [M+2]+.

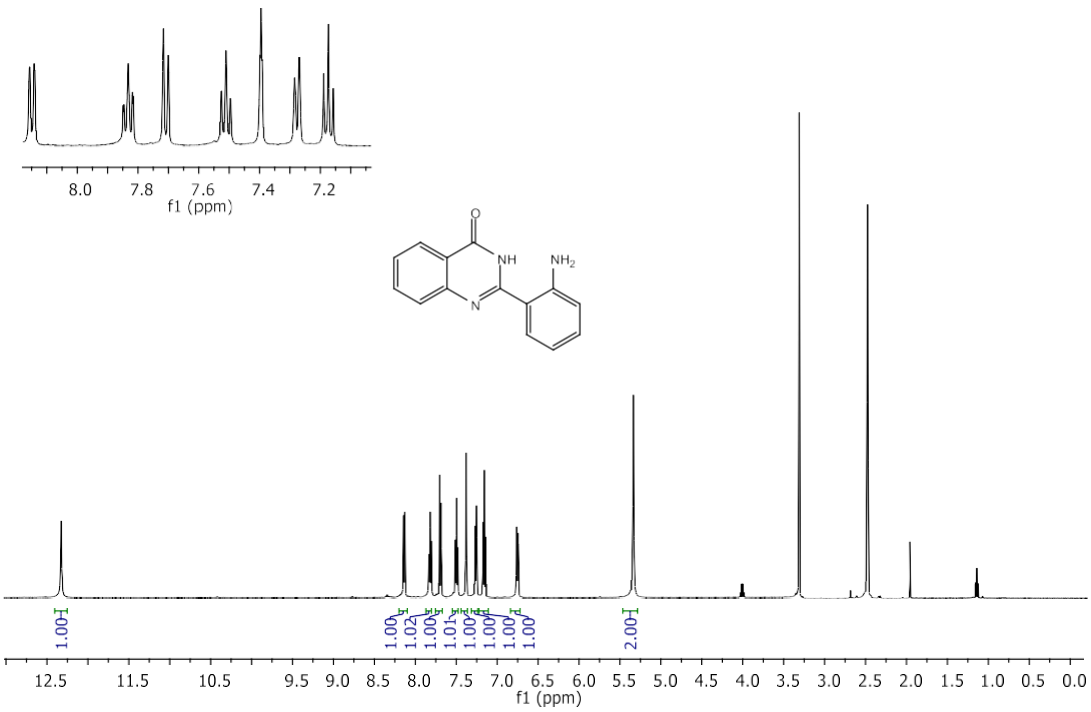
6-(2-chloro-4-methylphenyl)-5,6-dihydrobenzo[4,5]imidazo[1,2-c]quinazoline (3s)

Pale yellow solid; yield 75 %; mp:154–159 °C; FT-IR (cm^{-1}): 2988, 1687, 1857, 1616, 1586, 1511, 1371, 1287; ^{1}H NMR (500 MHz, DMSO-d_6): δ 7.98 (d, *J* = 8.7 Hz, 2H), 7.89 (s, 1H), 7.52 (dd, *J* = 8.8, 6.4 Hz, 2H), 7.31–7.25 (m, 2H), 7.22–7.18 (m, 1H), 7.18-7.12 (m, 2H), 7.08-7.01 (m, 1H), 6.94 (d, *J* = 8.8 Hz, 2H), 2.23 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 163.6, 159.5, 158.3, 150.9, 139.1, 138.8, 135.7, 135.0, 134.2, 133.6, 132.1, 131.9, 130.7, 129.9, 128.9, 128.3, 126.3, 123.1, 120.2, 114.4, 27.3; HRMS (ESI): m/z calculated for $C_{21}H_{16}ClN_3$ 346.1111 found 346.1140 [M+H]+.

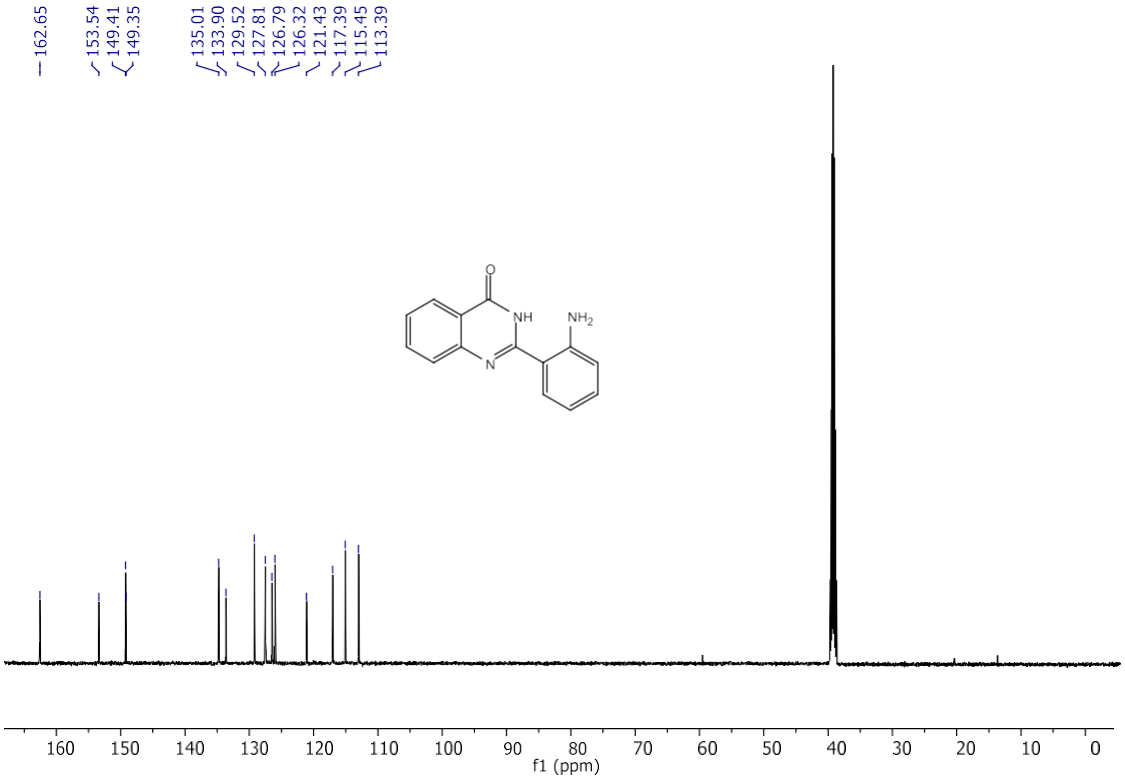
6-(thiophen-2-yl)-5,6-dihydrobenzo[4,5]imidazo[1,2-c]quinazoline (3t)

Pale yellow solid; yield 78 %; mp:152–156 °C; FT-IR (cm^{-1}): 3016, 1686, 1655, 1634, 1579, 1524, 1334, 1260; ^{1}H NMR (500 MHz, DMSO-d_6): δ 9.29-9.24 (m, 1H), 8.31 (d, *J* = 5.5 Hz, 2H), 8.12 (d, *J* = 7.8 Hz, 1H), 8.09–7.98 (m, 3H), 7.57–7.50 (m, 1H), 7.47–7.41 (m, 1H), 7.36 (t, *J* = 9.9 Hz, 2H), 7.09 (t, *J* = 10.2 Hz, 2H); ^{13}C NMR (125 MHz, DMSO-d_6): δ 167.4, 154.2, 150.7, 149.2, 144.3, 134.6, 129.1, 127.0, 126.5, 125.5, 122.9, 122.6, 119.1, 111.0; HRMS (ESI): m/z calculated for $C_{18}H_{13}N_3S$ 304.0908 found 304.0935 [M+H]+.

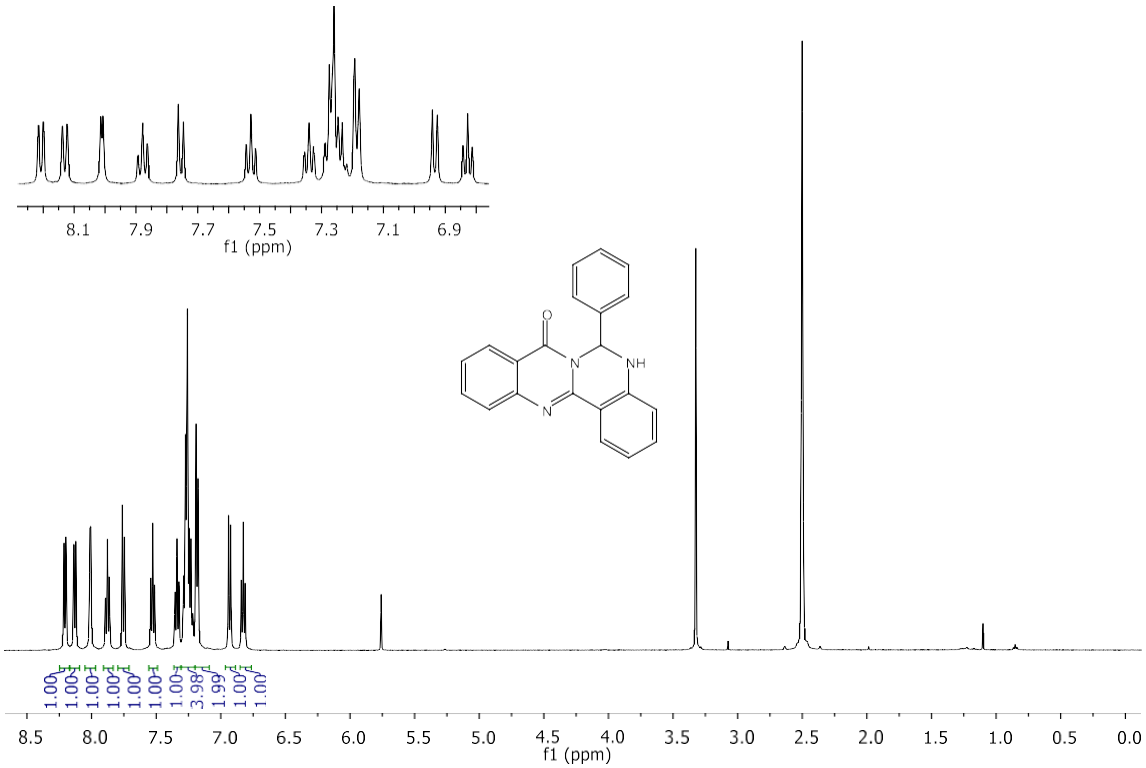
3. Copies of Spectra



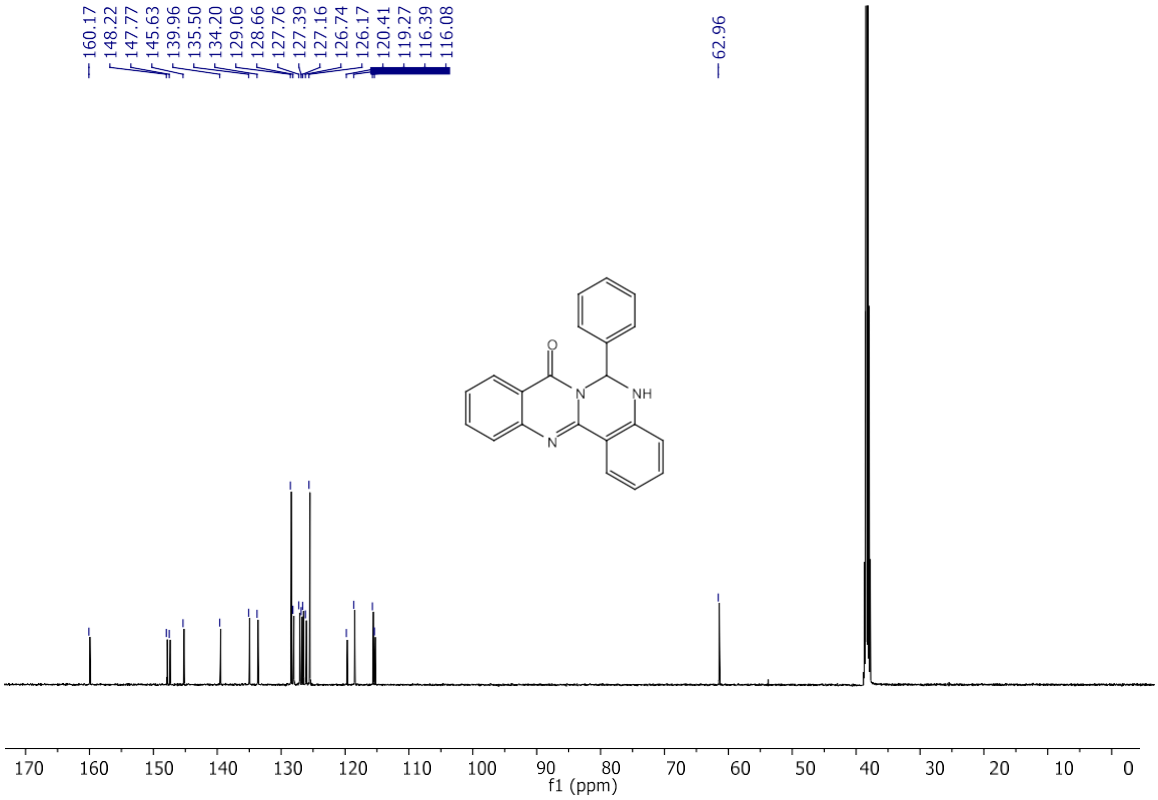
Intermediate **III**: ^{1}H NMR (500 MHz, DMSO-d_6).



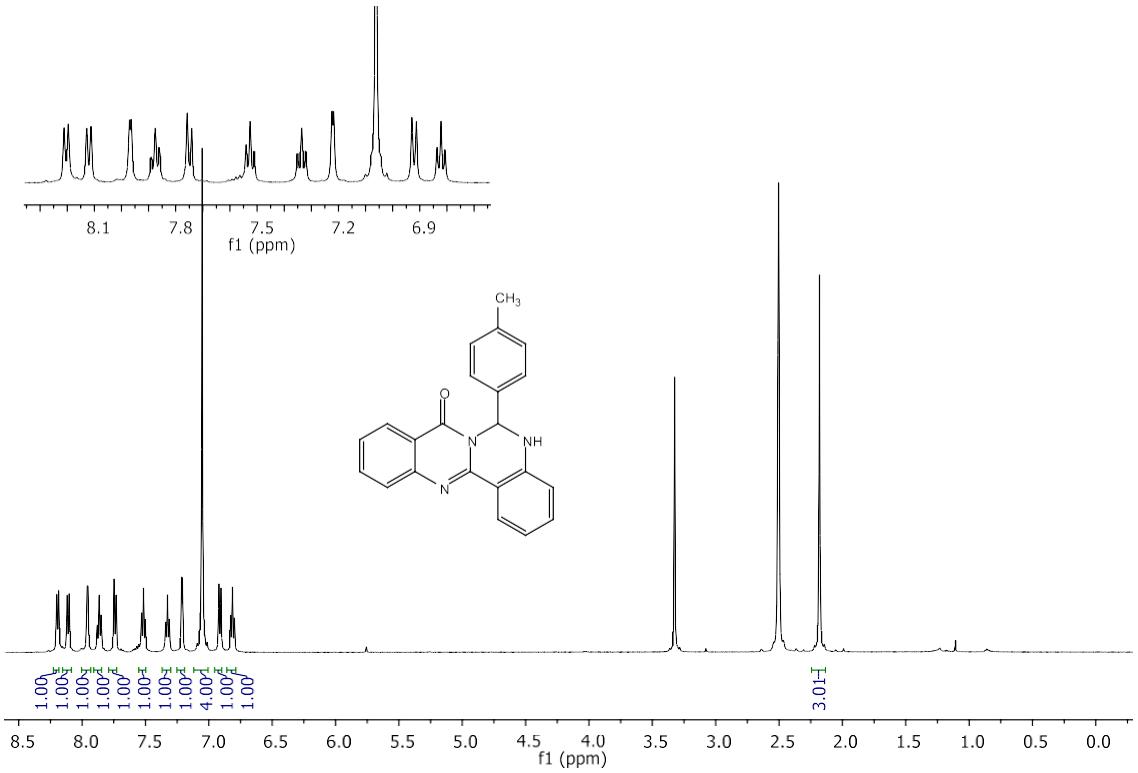
Intermediate **III**: ^{13}C NMR (125 MHz, DMSO-d_6).



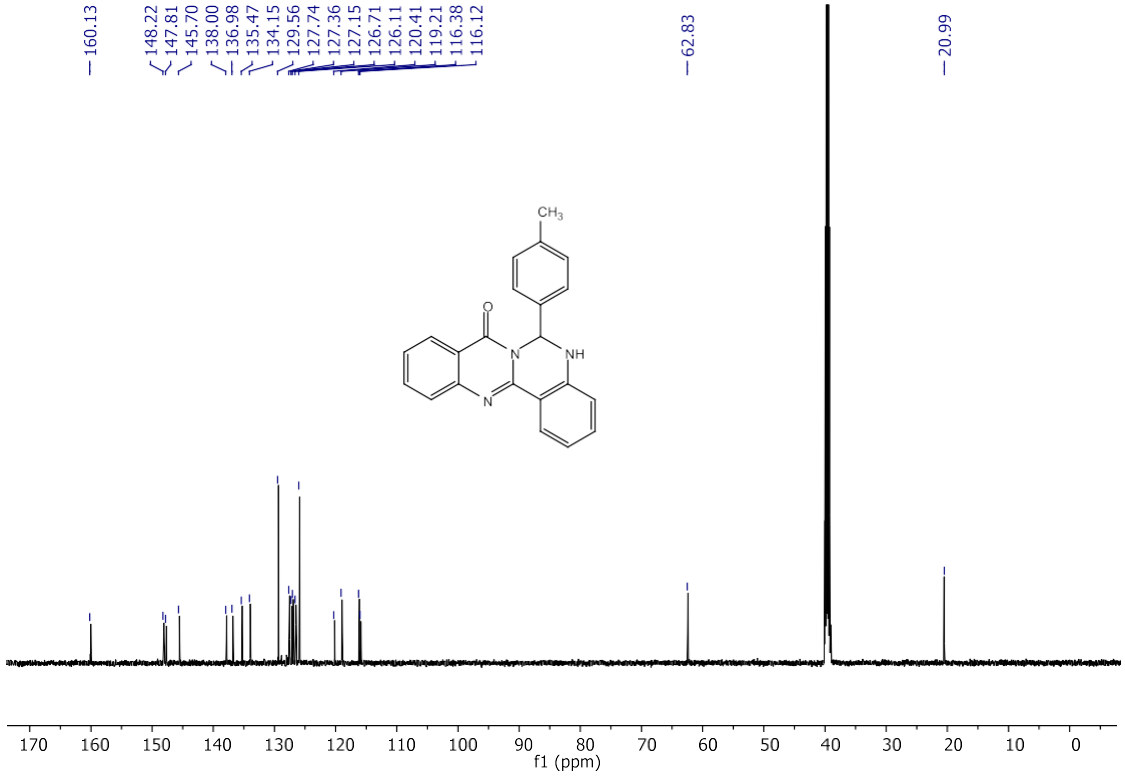
Compound **3a**: ^{1}H NMR (500 MHz, DMSO-d_6).



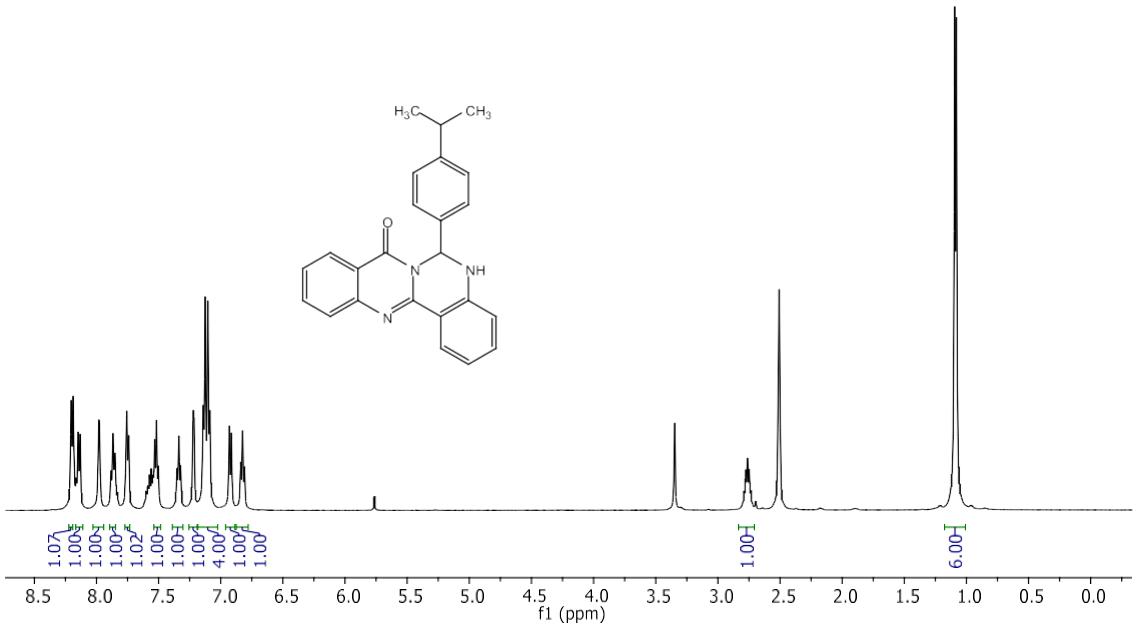
Compound **3a**: ^{13}C NMR (125 MHz, DMSO-d_6).



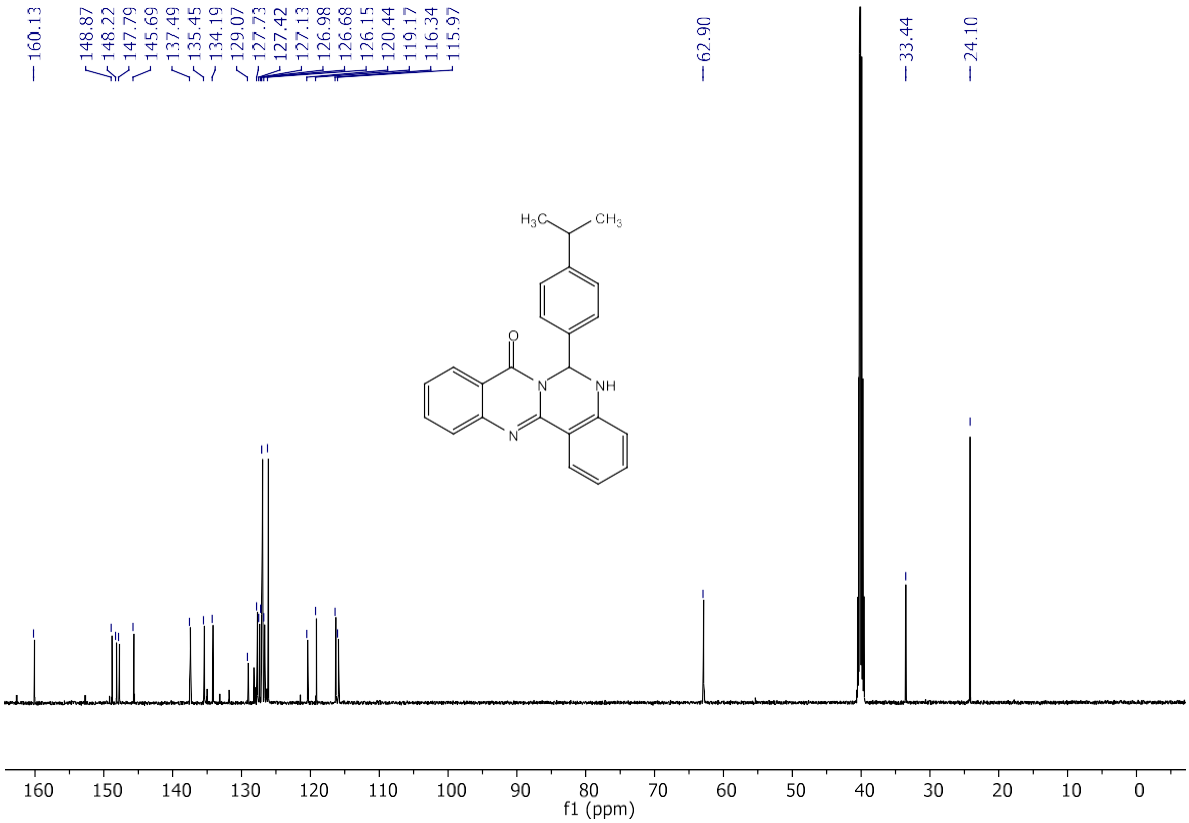
Compound **3b**: ^{1}H NMR (500 MHz, DMSO-d_6).



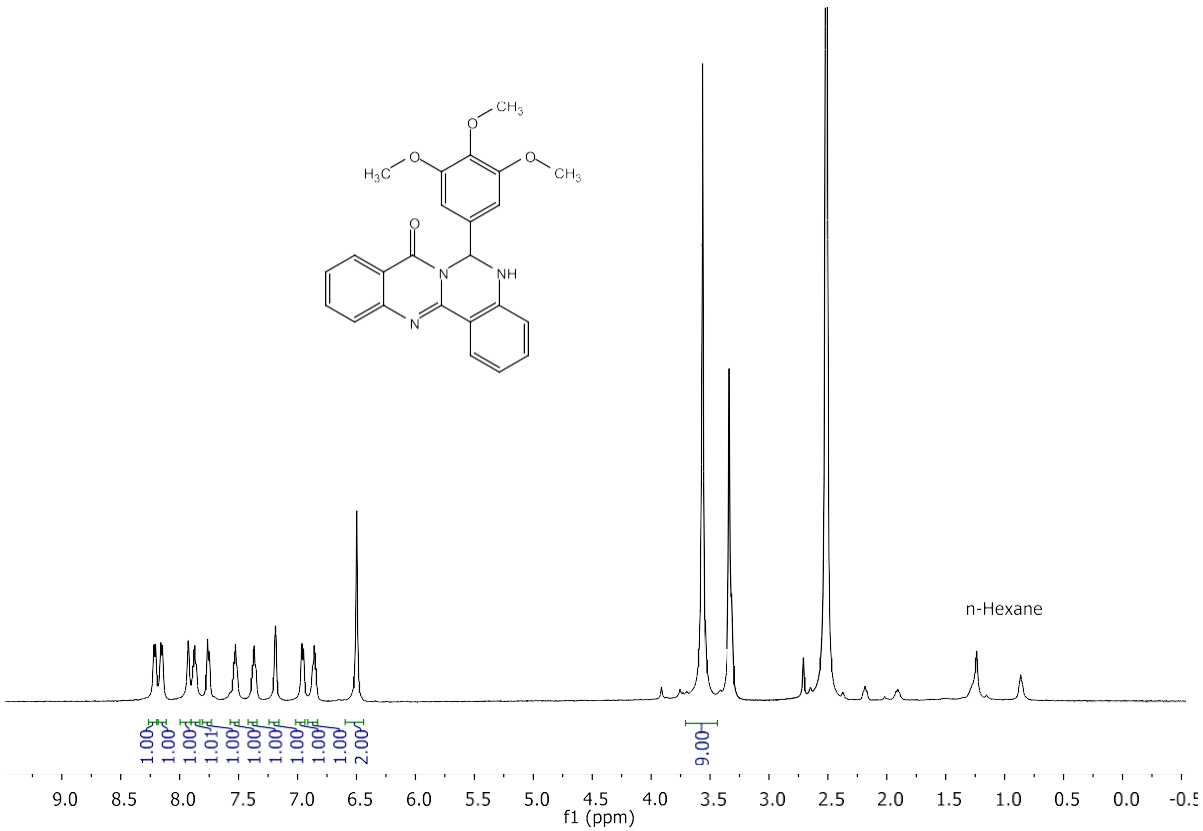
Compound **3b**: ^{13}C NMR (125 MHz, DMSO-d_6).



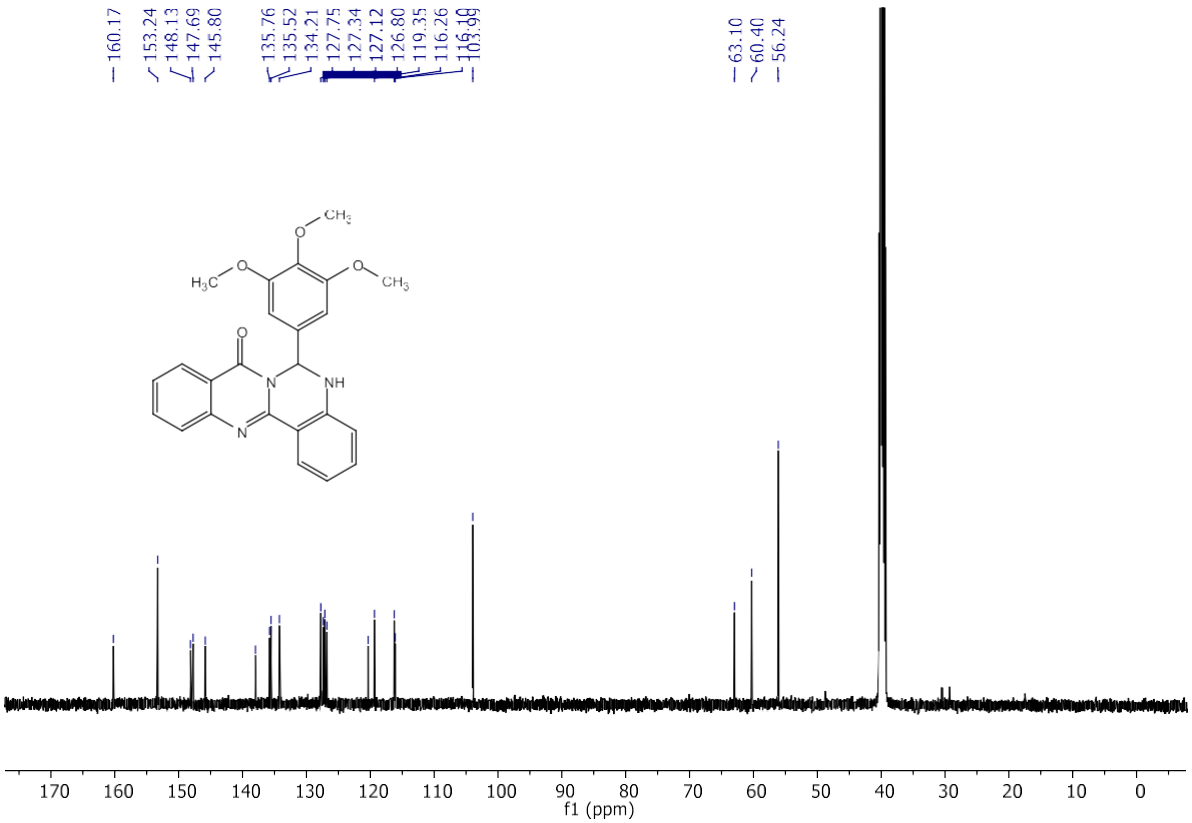
Compound **3c**: ^{1}H NMR (500 MHz, DMSO-d_6).



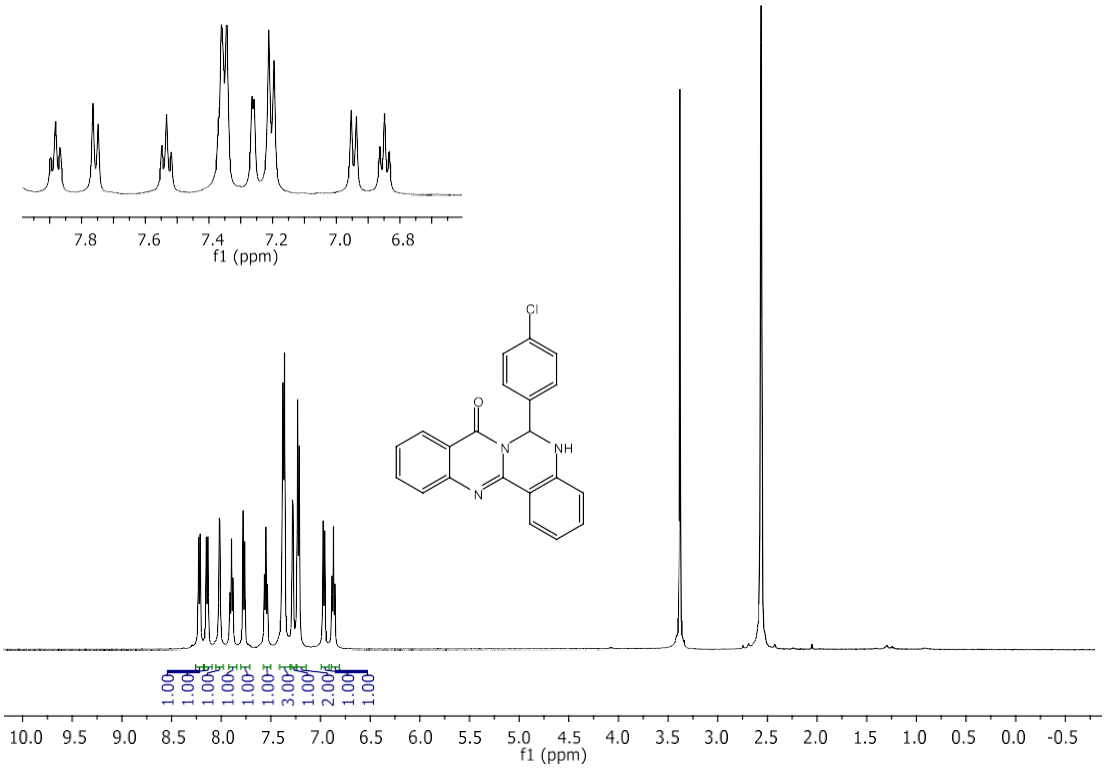
Compound **3c**: ^{13}C NMR (125 MHz, DMSO-d_6).



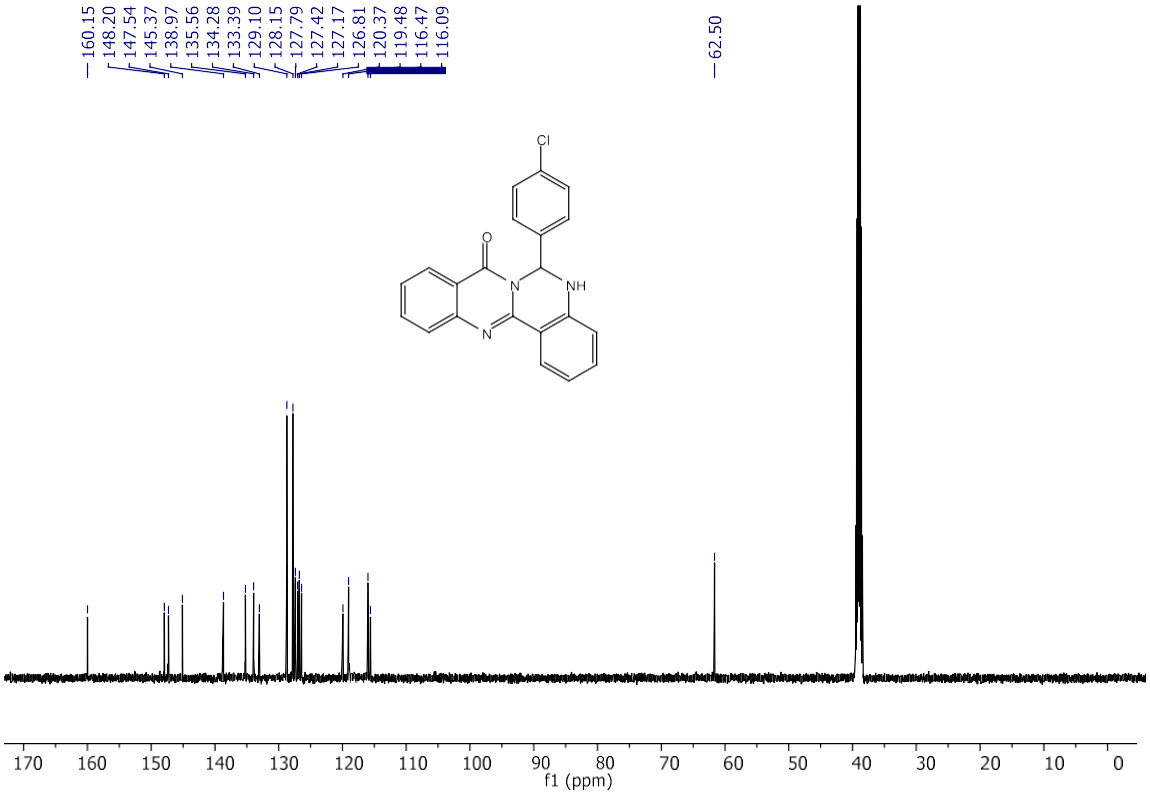
Compound **3d**: ^{1}H NMR (500 MHz, DMSO-d_6).



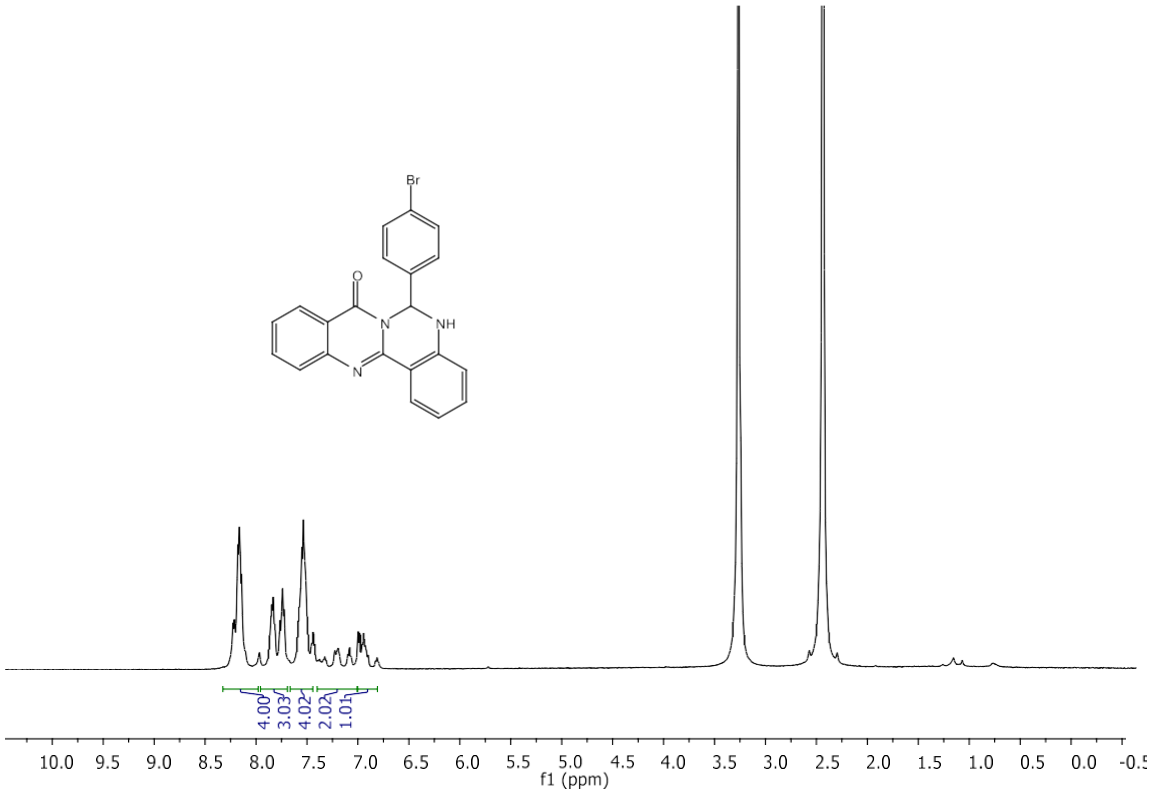
Compound **3d**: ^{13}C NMR (125 MHz, DMSO-d_6).



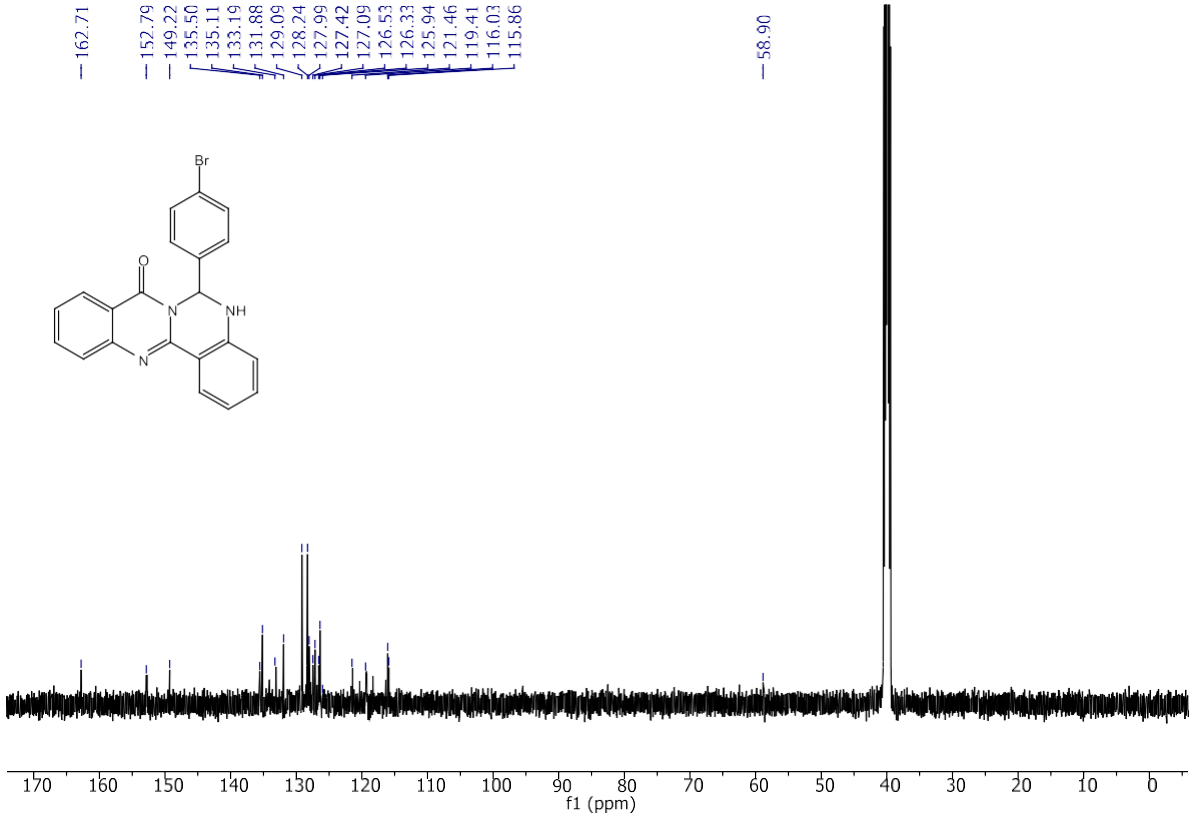
Compound **3e**: ^{1}H NMR (500 MHz, DMSO-d_6).



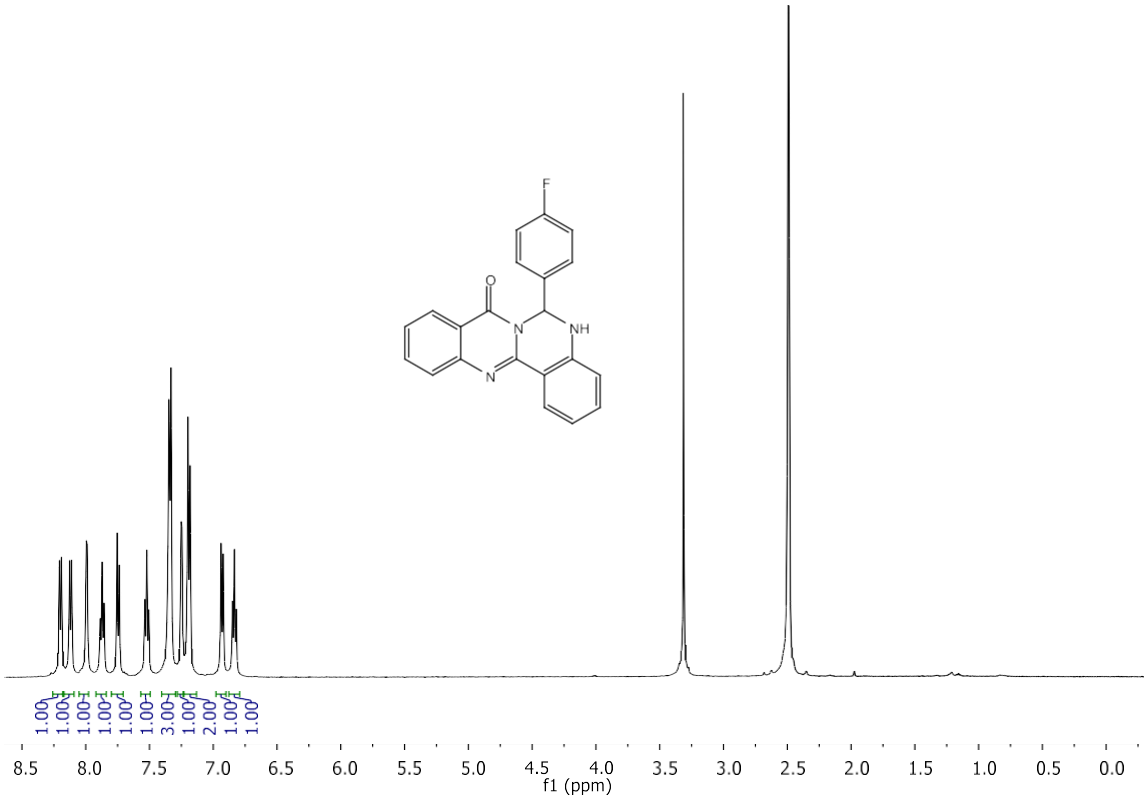
Compound **3e**: ^{13}C NMR (125 MHz, DMSO-d_6).



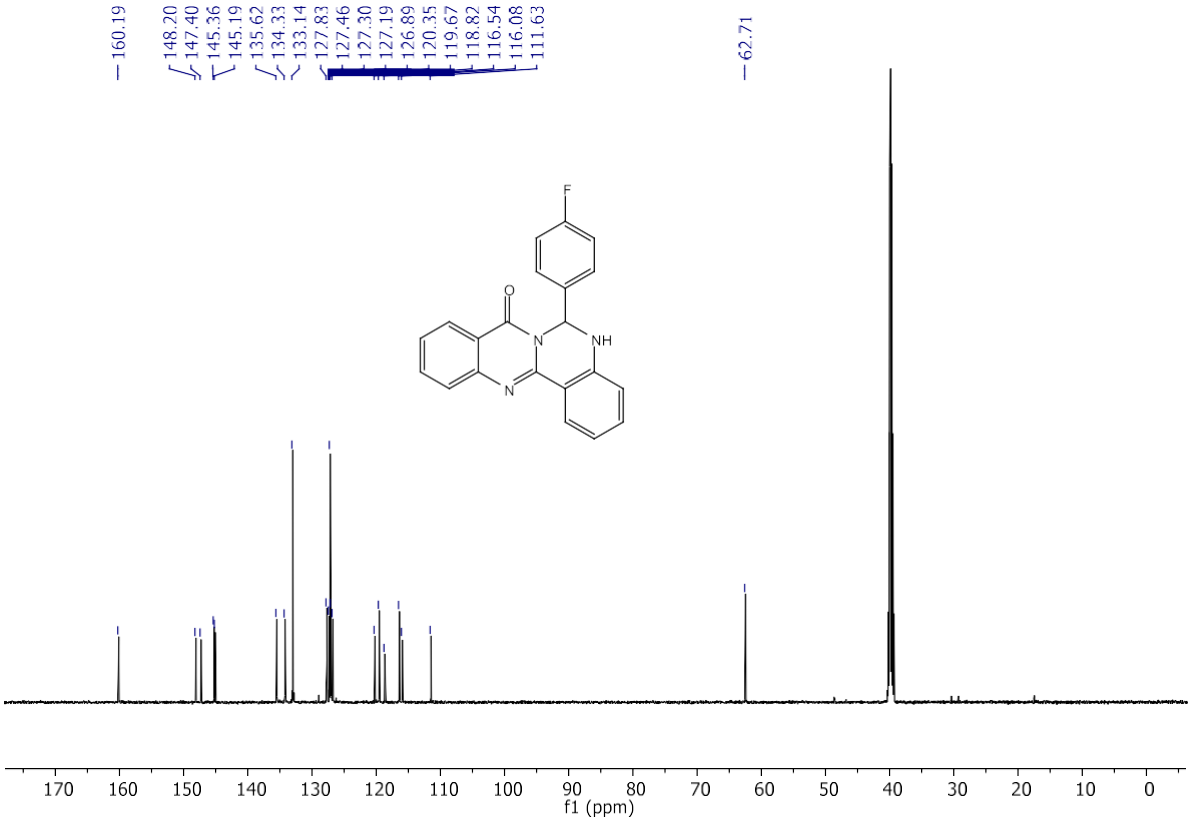
Compound **3f**: ^{1}H NMR (500 MHz, DMSO-d_6).



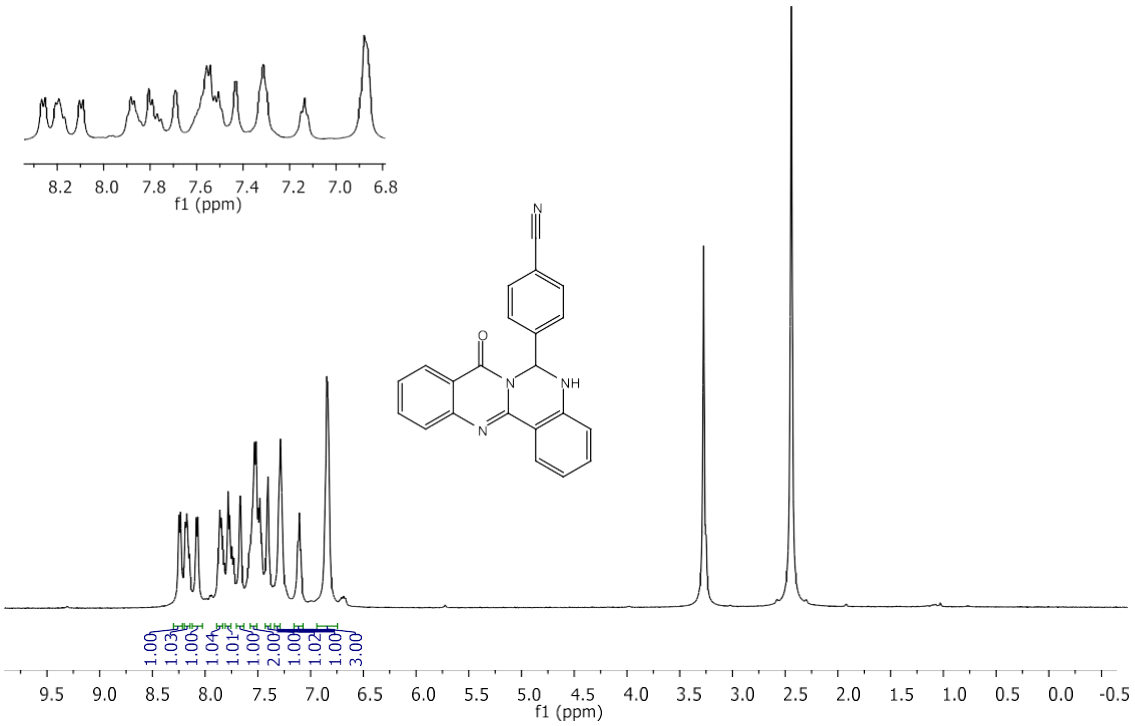
Compound **3f**: ^{13}C NMR (125 MHz, DMSO-d_6).



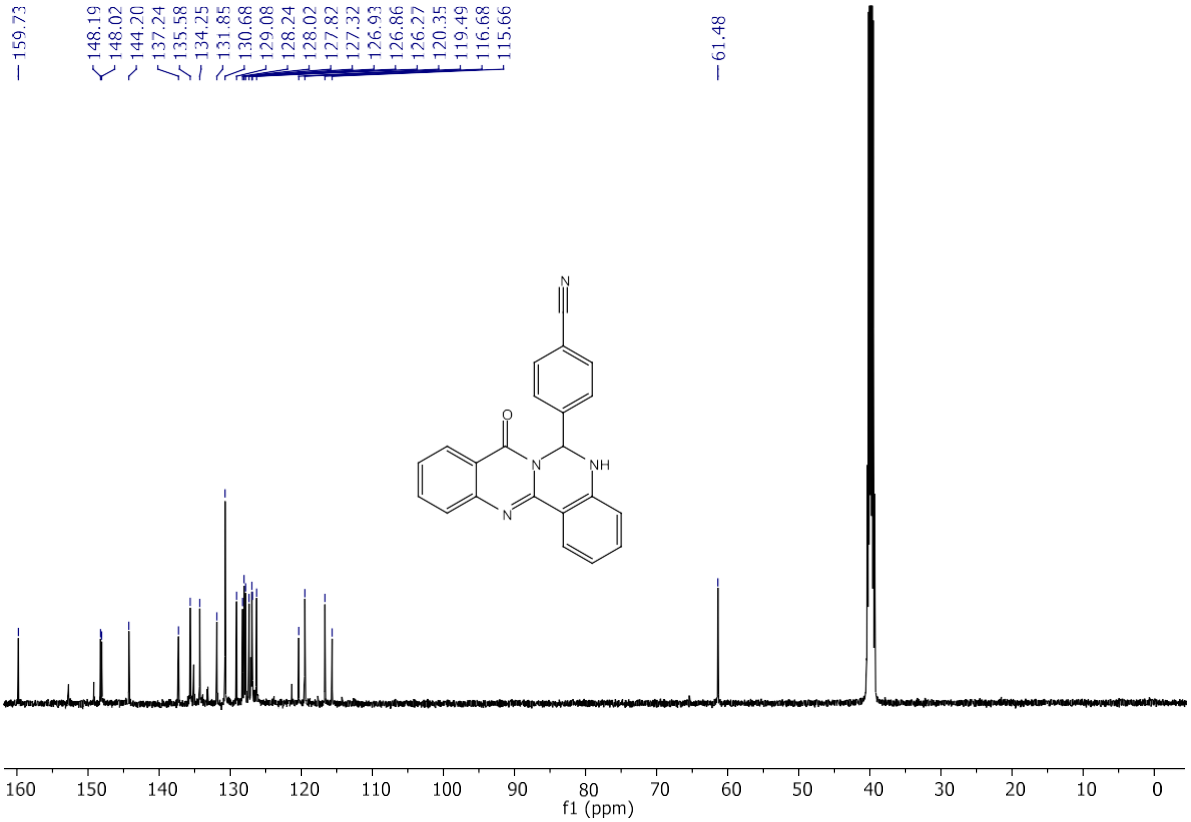
Compound **3g**: ^{1}H NMR (500 MHz, DMSO-d_6).



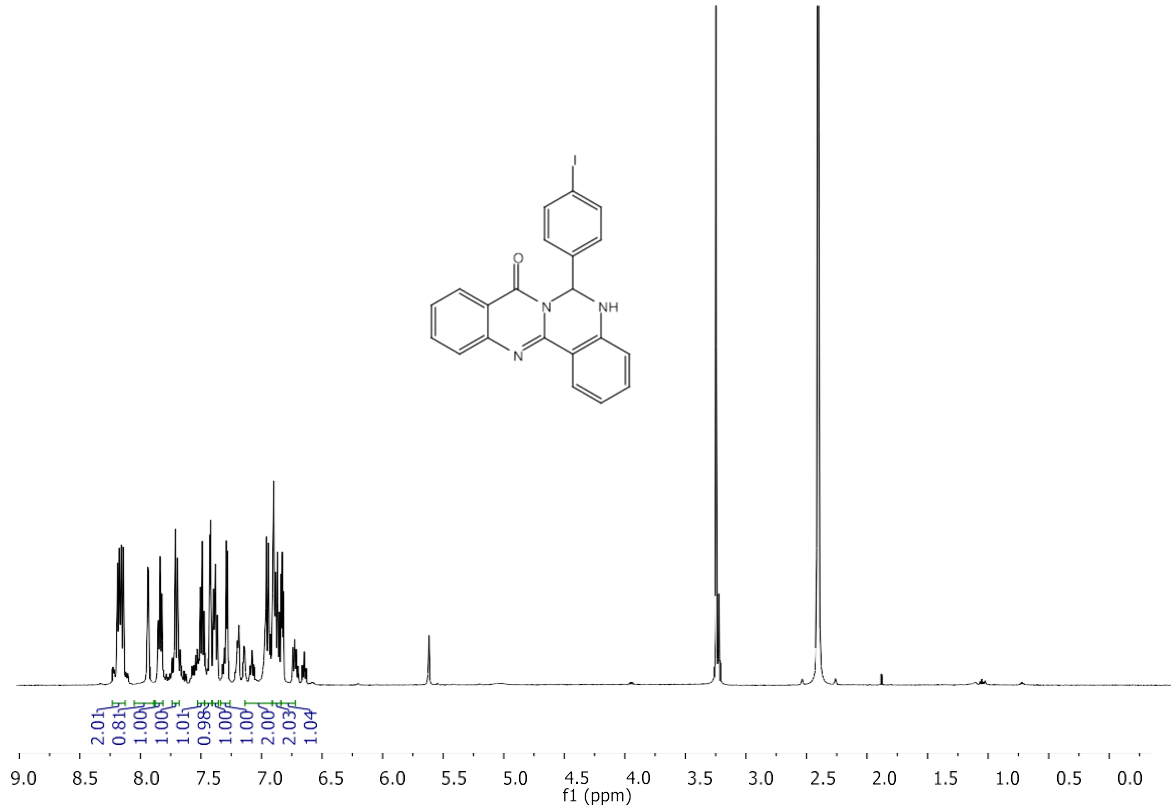
Compound **3g**: ^{13}C NMR (125 MHz, DMSO-d_6).



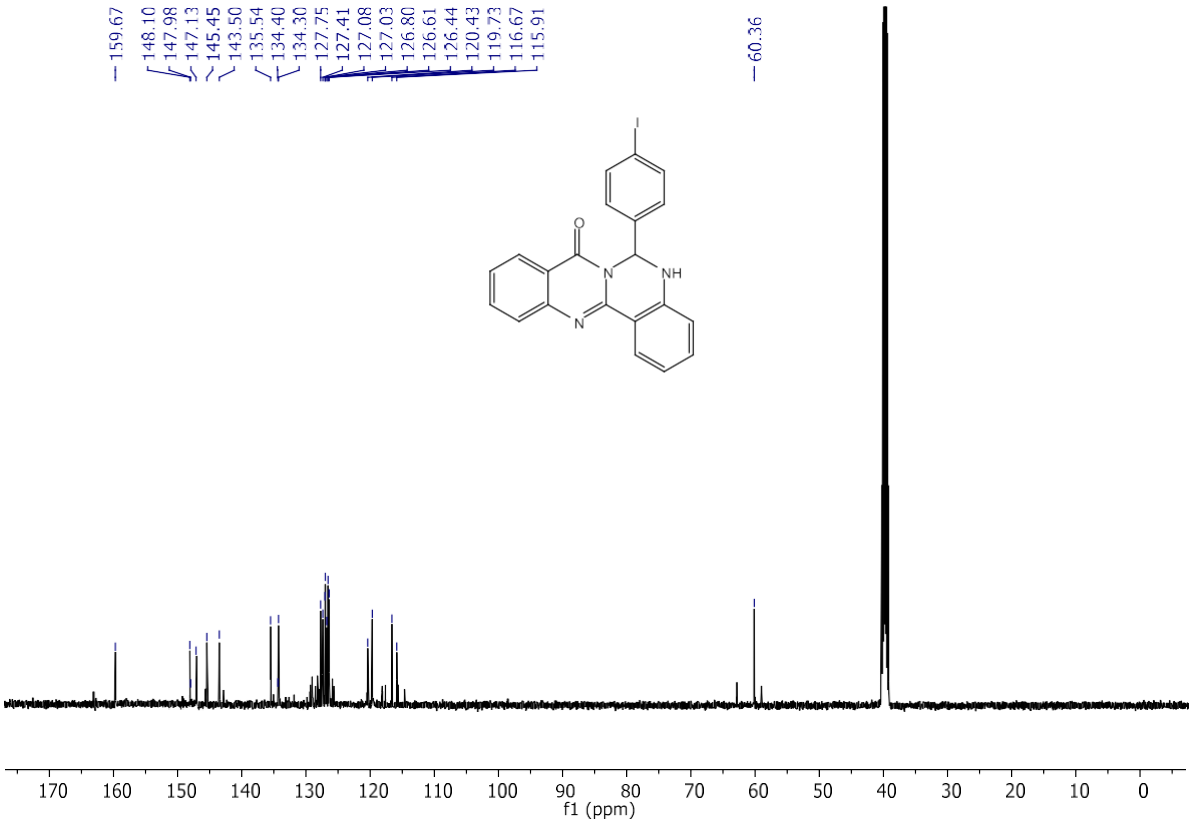
Compound **3h**: ^{1}H NMR (500 MHz, DMSO-d_6).



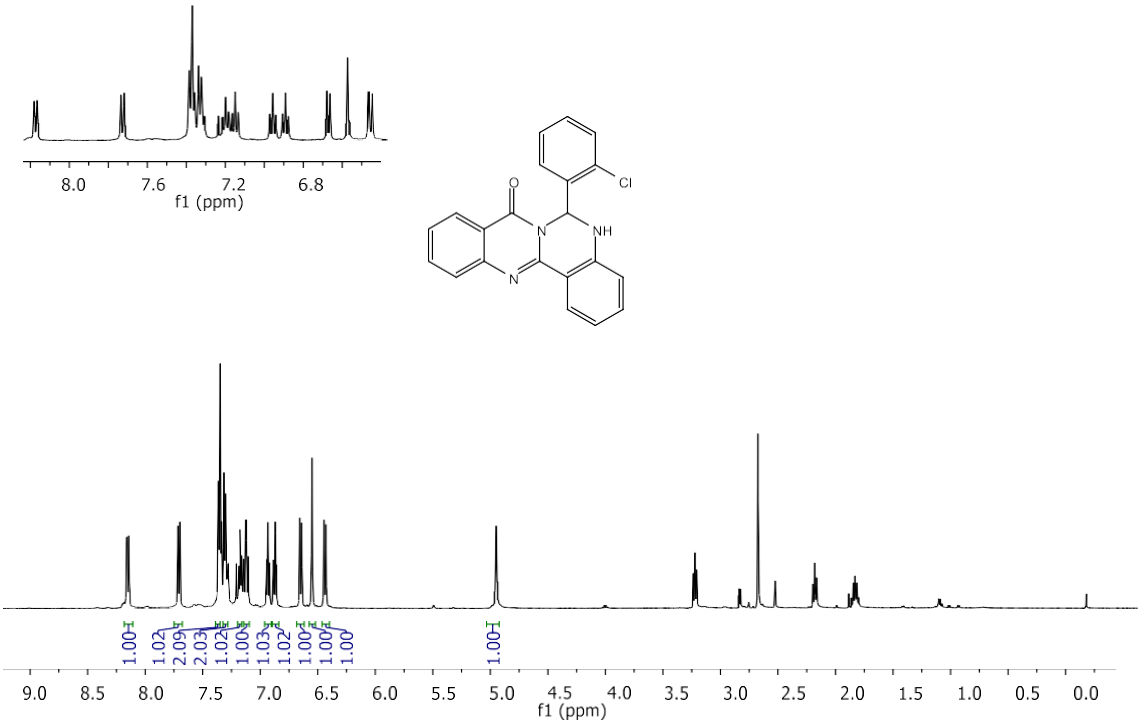
Compound **3h**: ^{13}C NMR (125 MHz, DMSO-d_6).



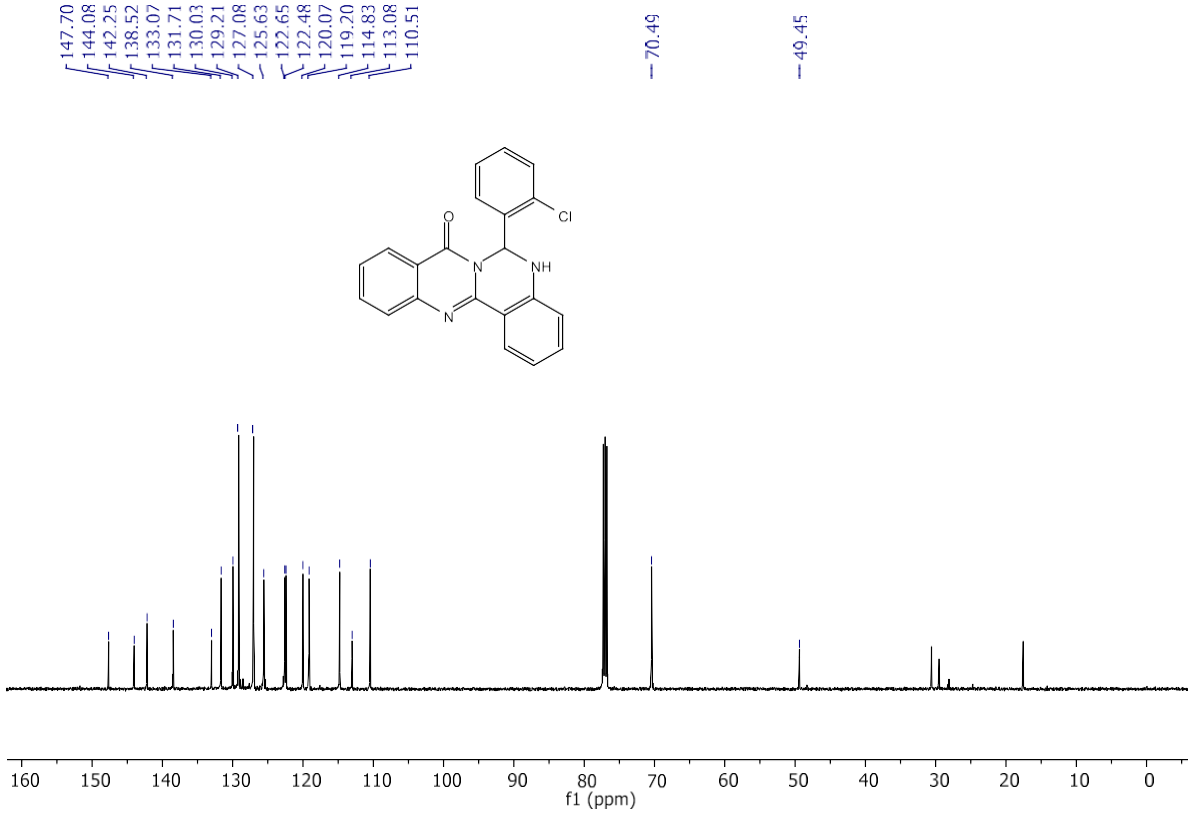
Compound **3i**: ^{1}H NMR (500 MHz, DMSO-d_6).



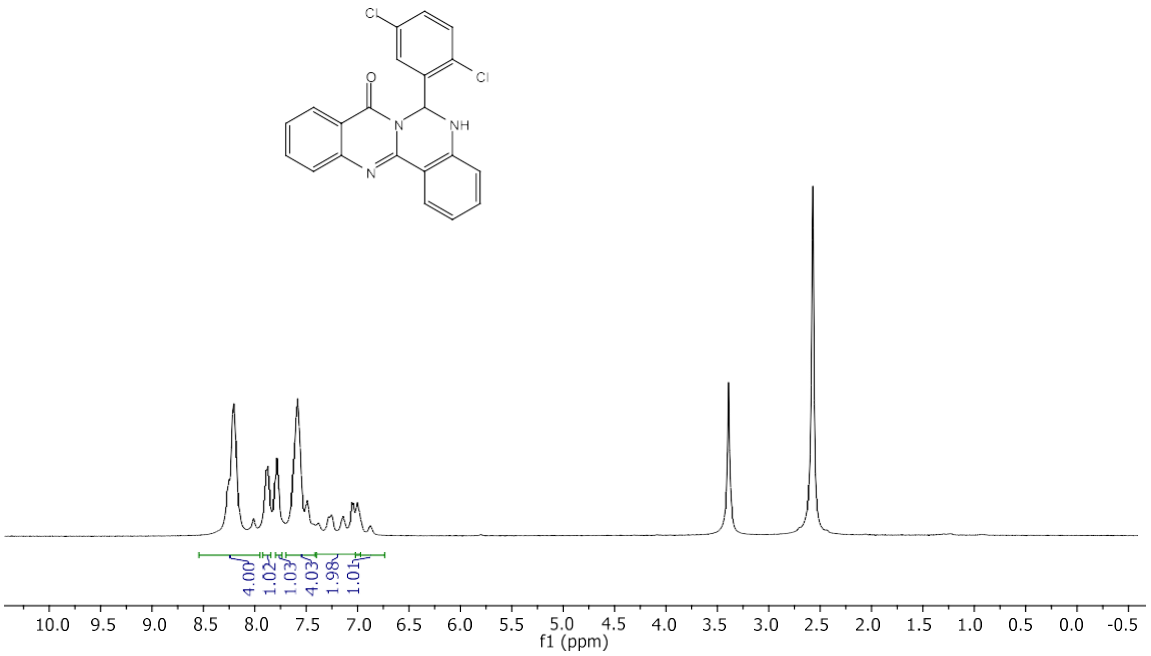
Compound **3i**: ^{13}C NMR (125 MHz, DMSO-d_6).



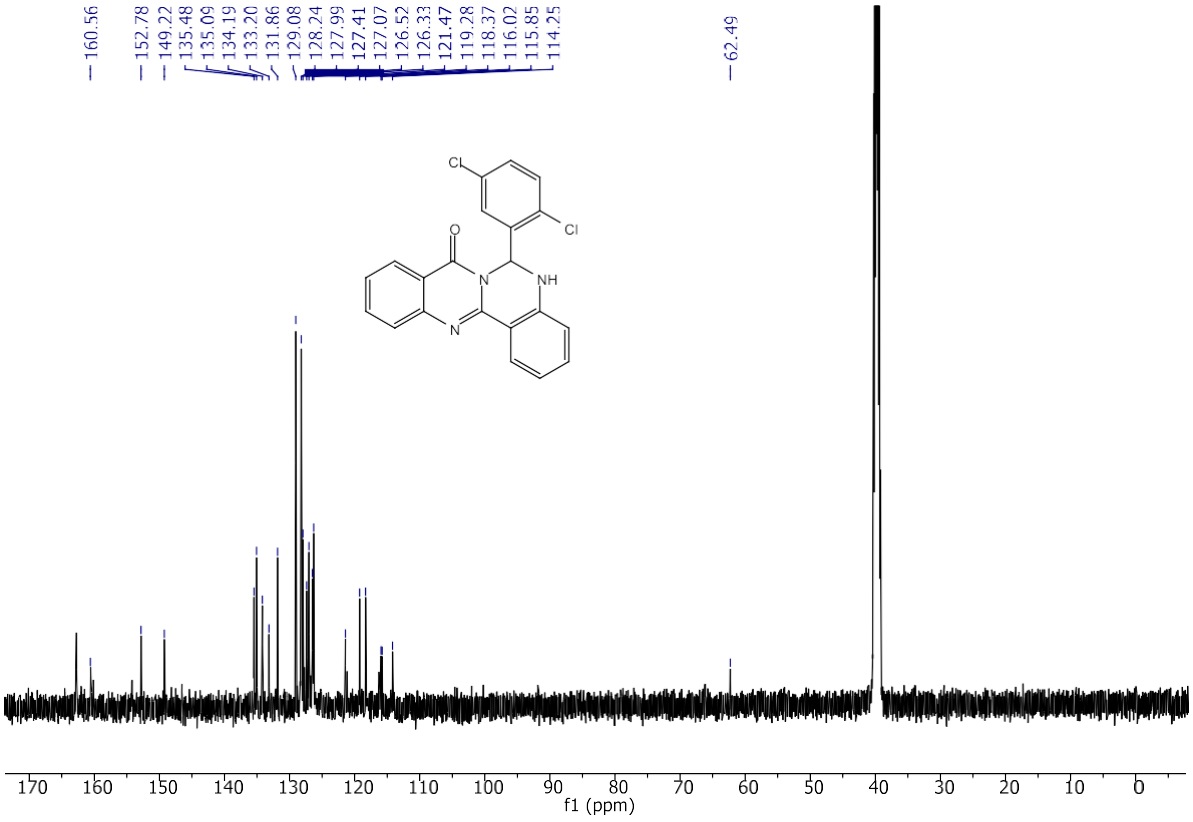
Compound **3j**: ^{1}H NMR (500 MHz, $CDCl_3$).



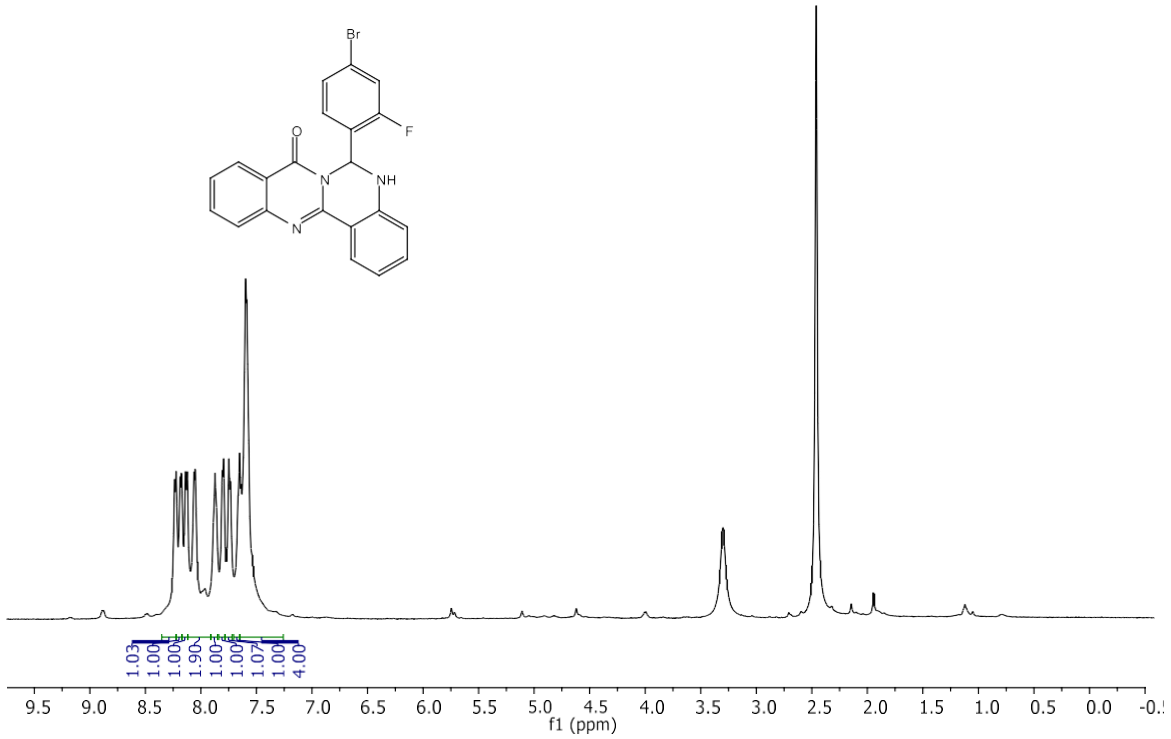
Compound **3j**: ^{13}C NMR (125 MHz, $CDCl_3$).



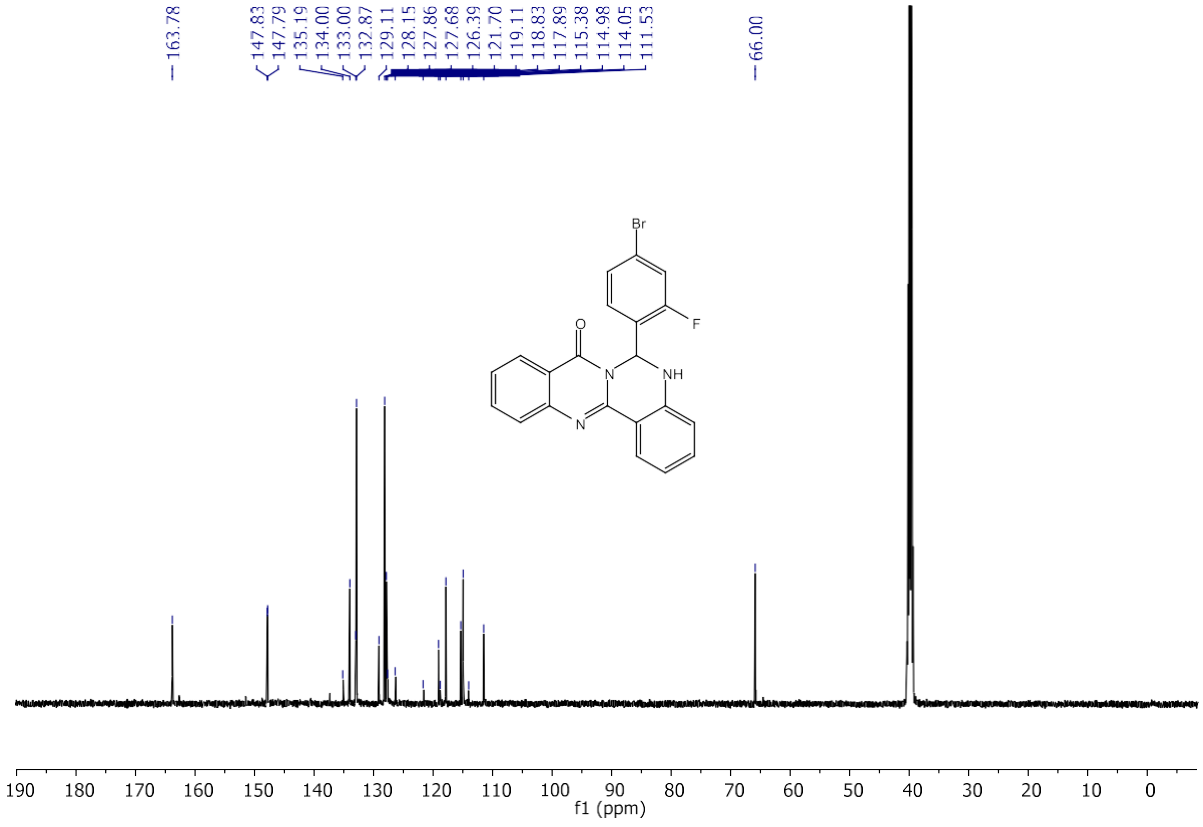
Compound **3k**: ^{1}H NMR (500 MHz, DMSO-d_6).



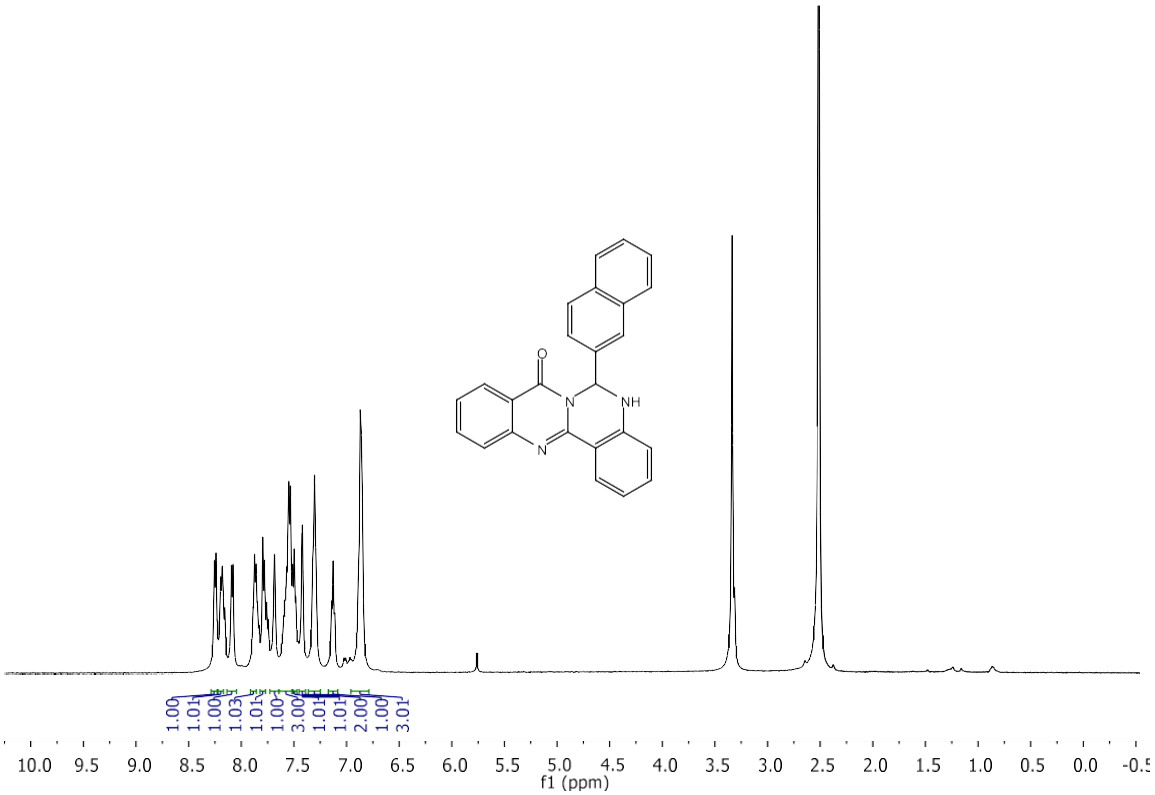
Compound **3k**: ^{13}C NMR (125 MHz, DMSO-d_6).



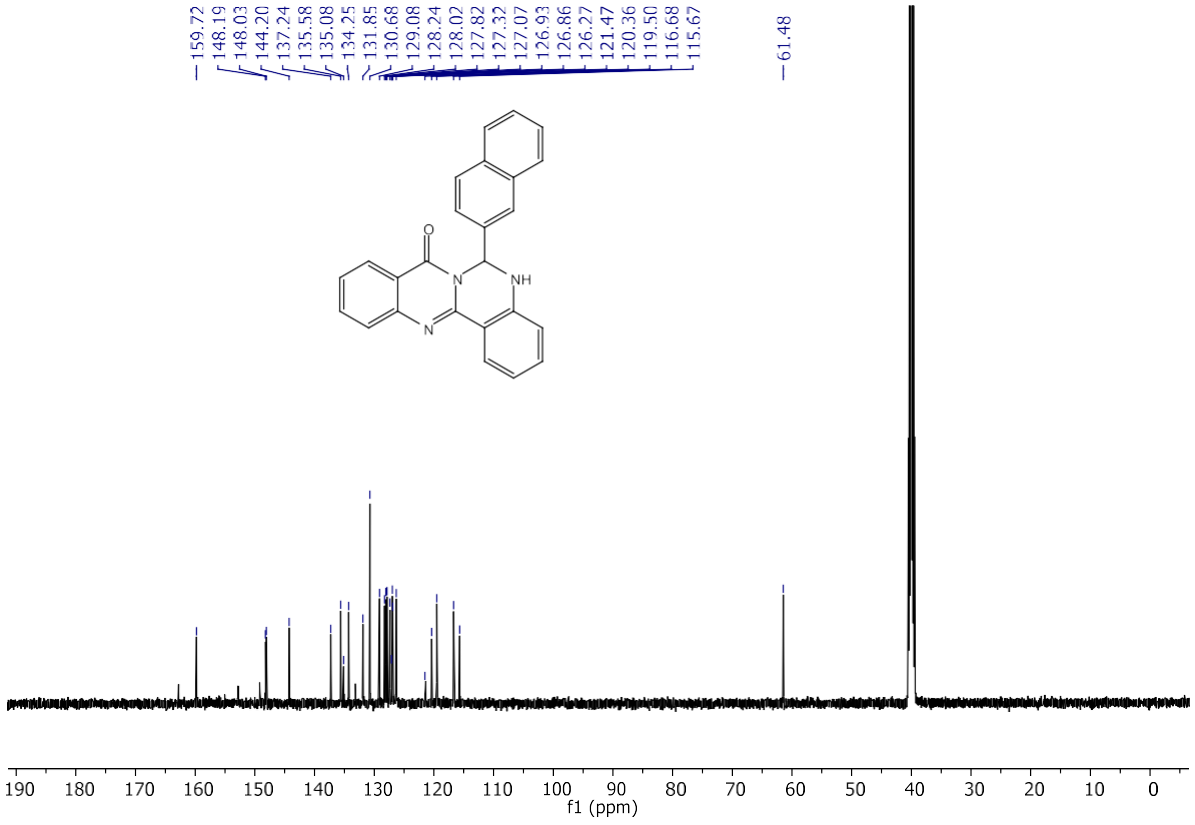
Compound **3l**: ^{1}H NMR (500 MHz, DMSO-d_6).



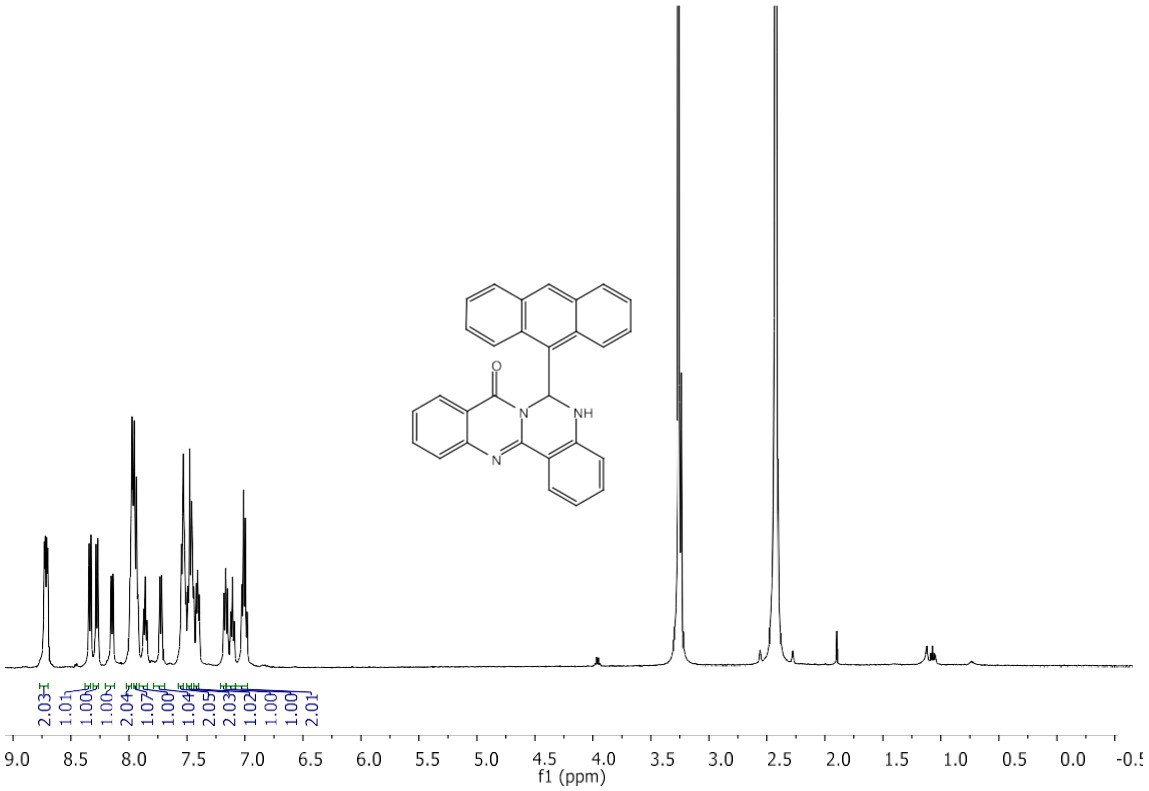
Compound **3l**: ^{13}C NMR (125 MHz, DMSO-d_6).



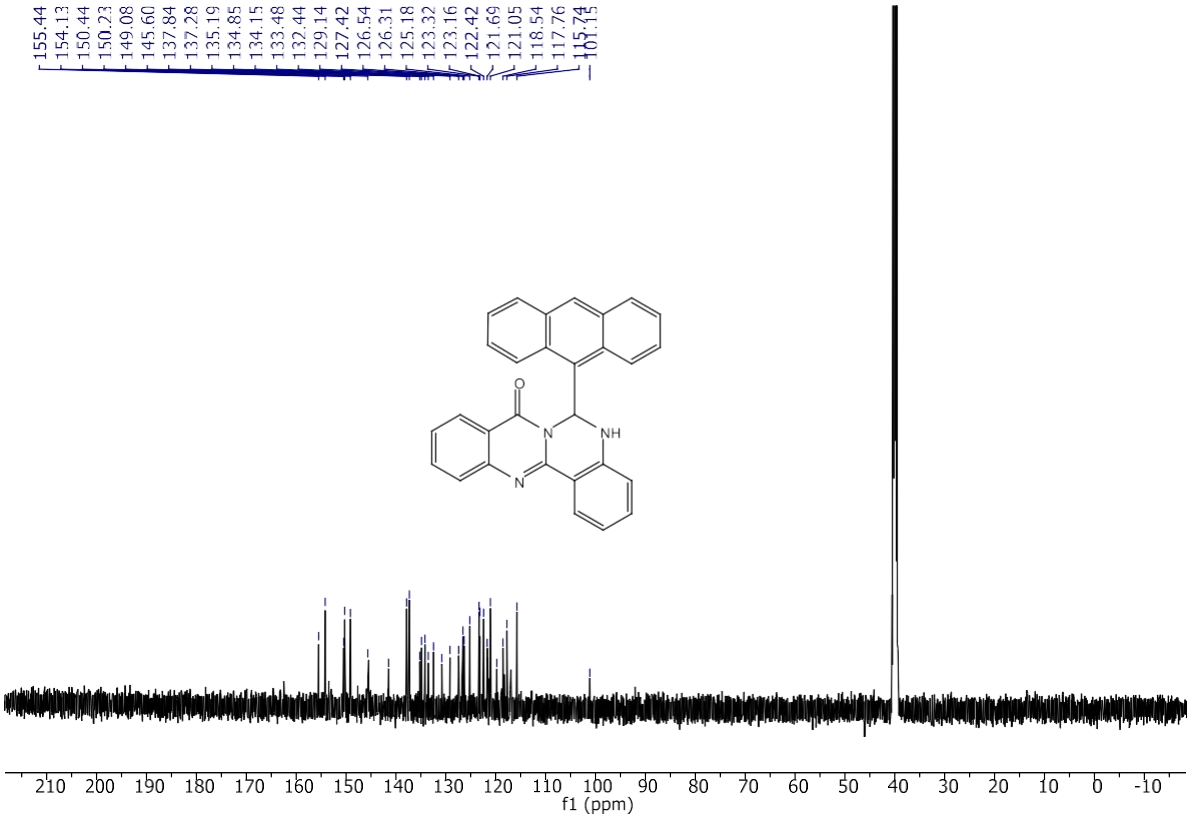
Compound **3m**: ^{1}H NMR (500 MHz, DMSO-d_6).



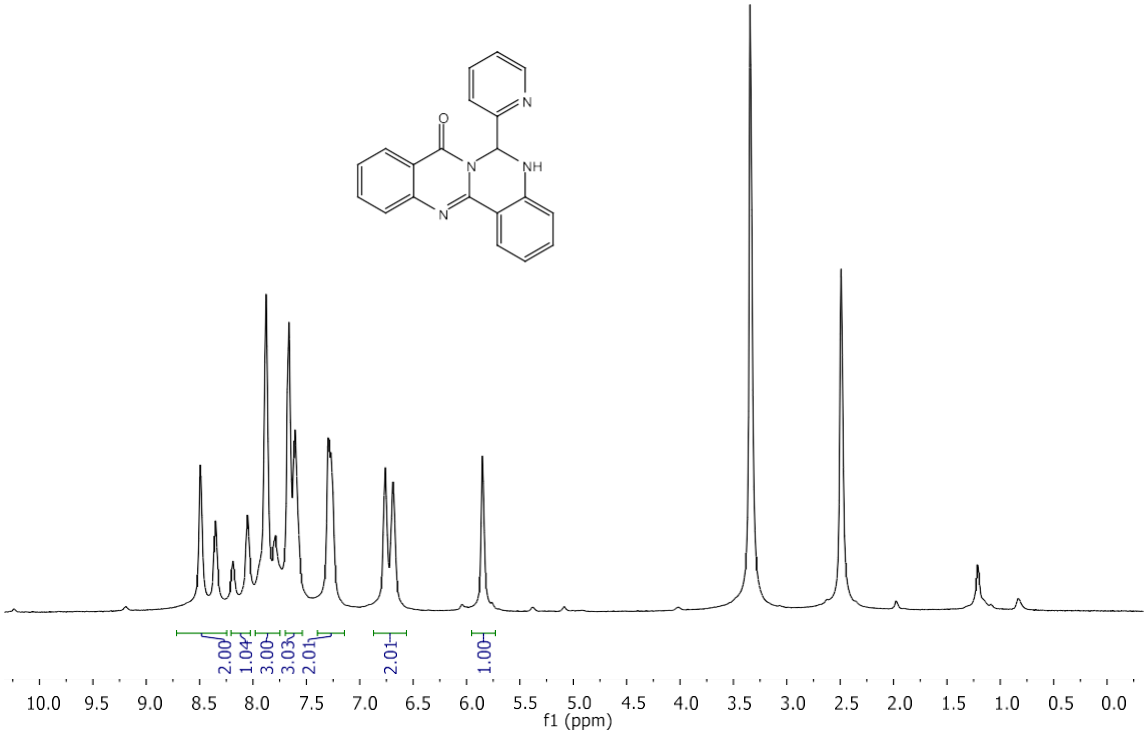
Compound **3m**: ^{13}C NMR (125 MHz, DMSO-d_6).



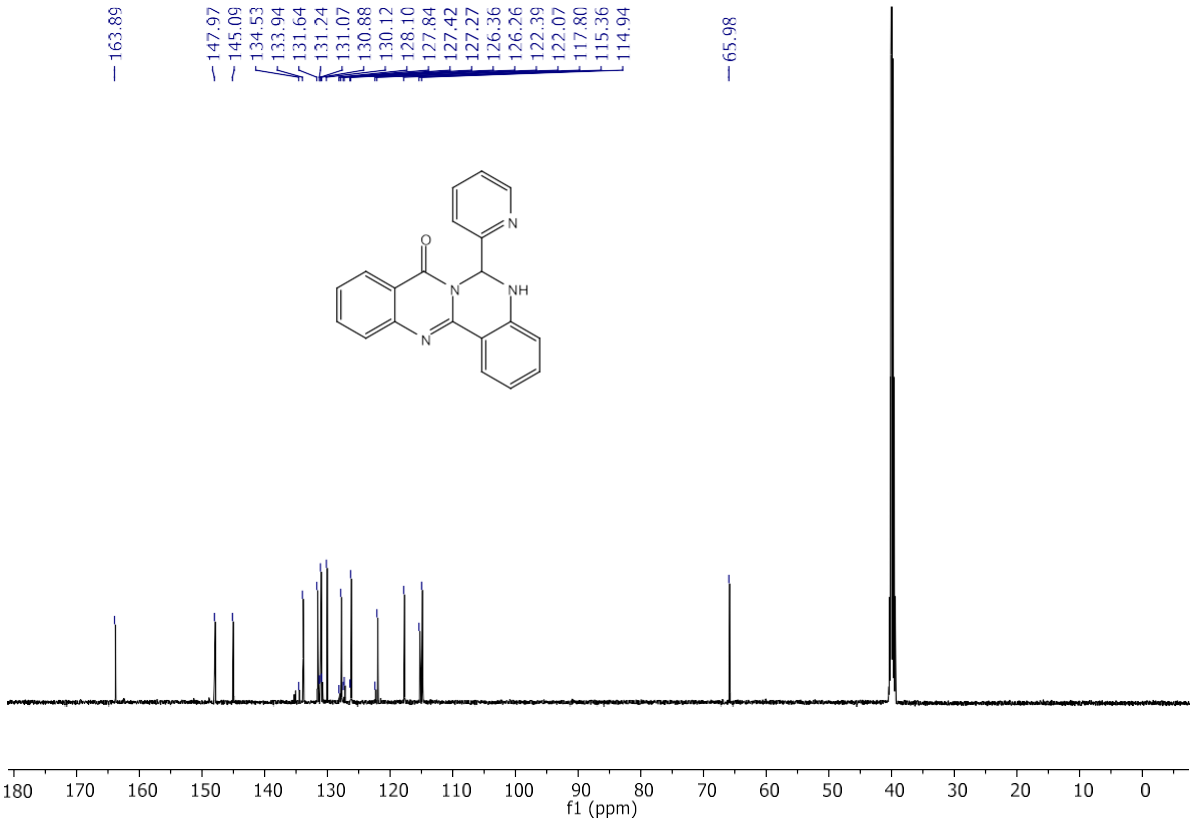
Compound **3n**: ^{1}H NMR (500 MHz, DMSO-d_6).



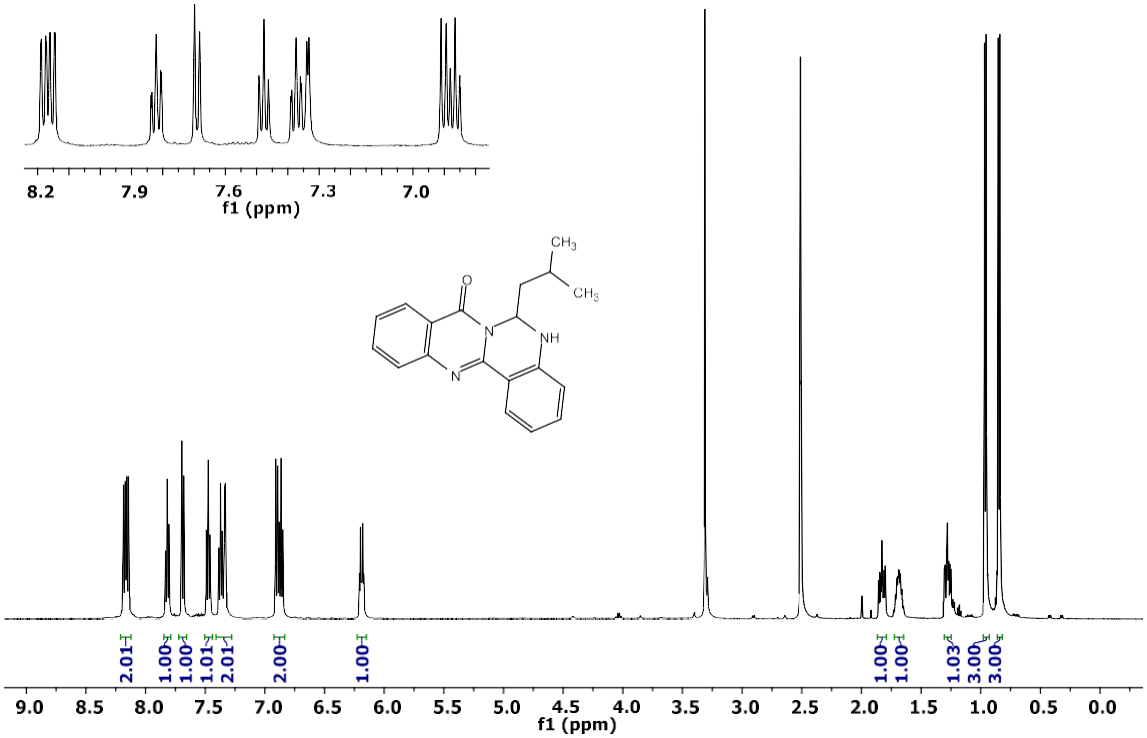
Compound **3n**: ^{13}C NMR (125 MHz, DMSO-d_6).



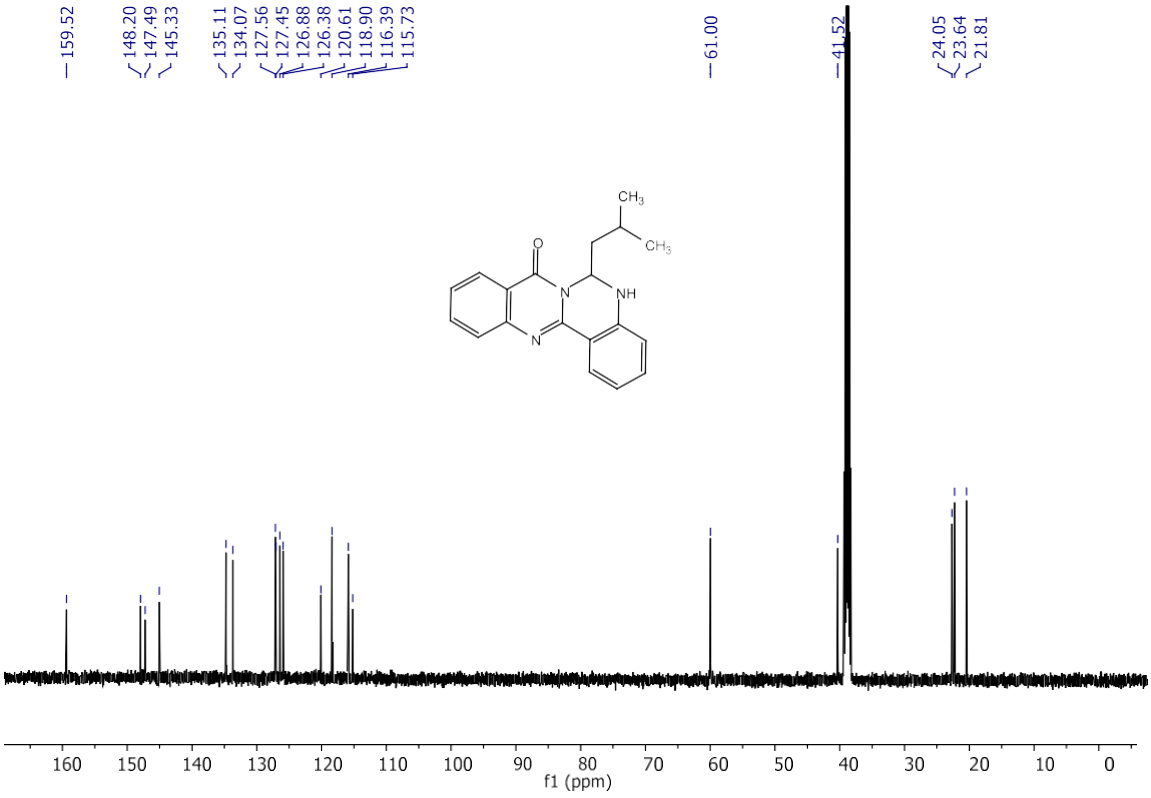
Compound **3o**: ^{1}H NMR (500 MHz, DMSO-d_6).



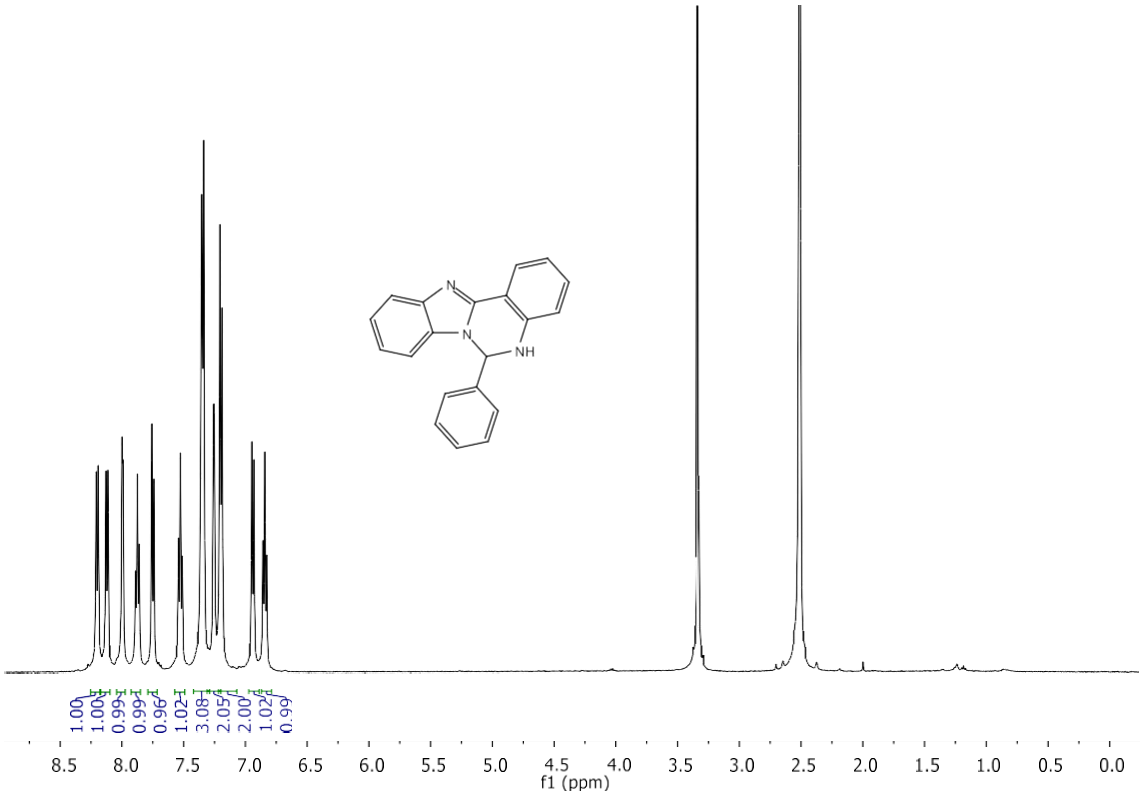
Compound **3o**: ^{13}C NMR (125 MHz, DMSO-d_6).



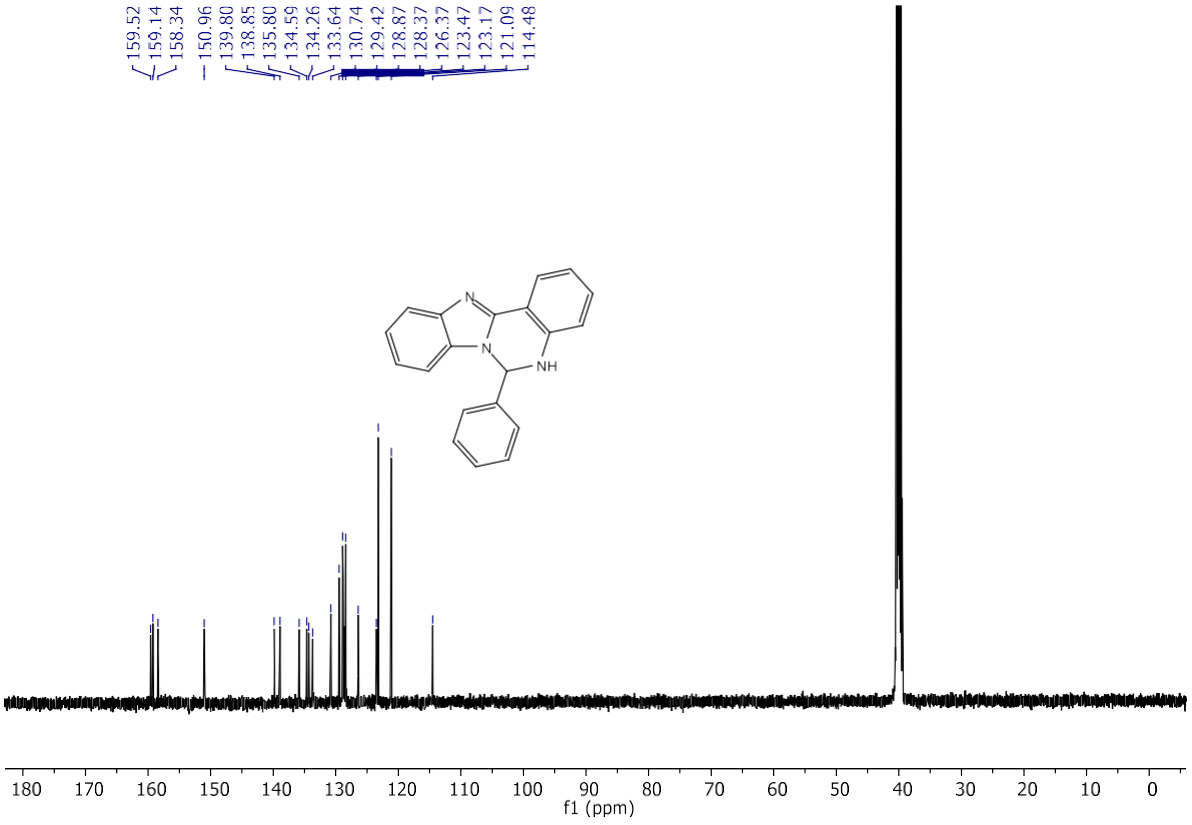
Compound **3p**: ^{1}H NMR (500 MHz, DMSO-d_6).



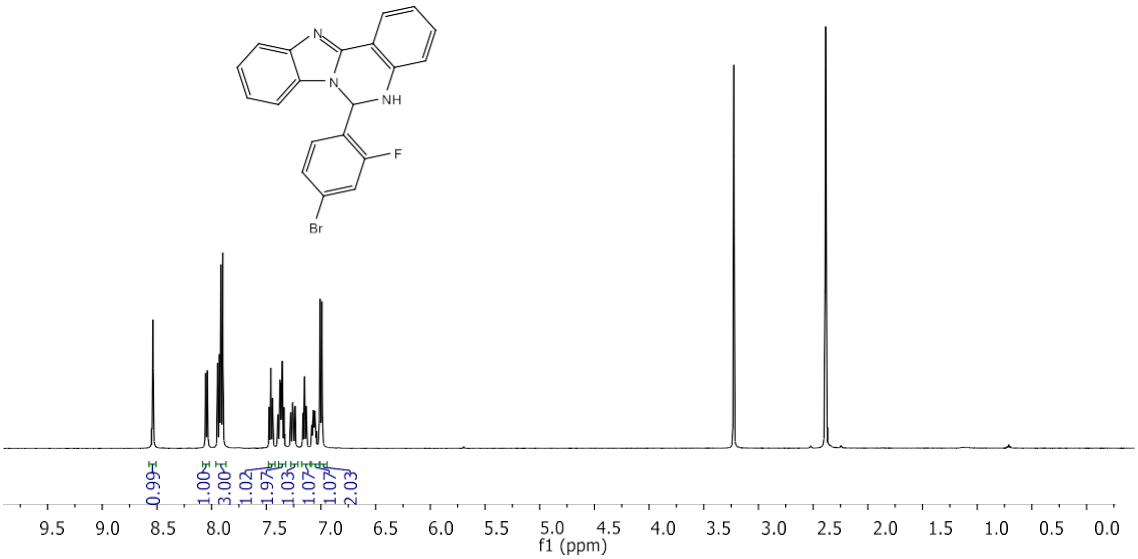
Compound **3p**: ^{13}C NMR (125 MHz, DMSO-d_6).



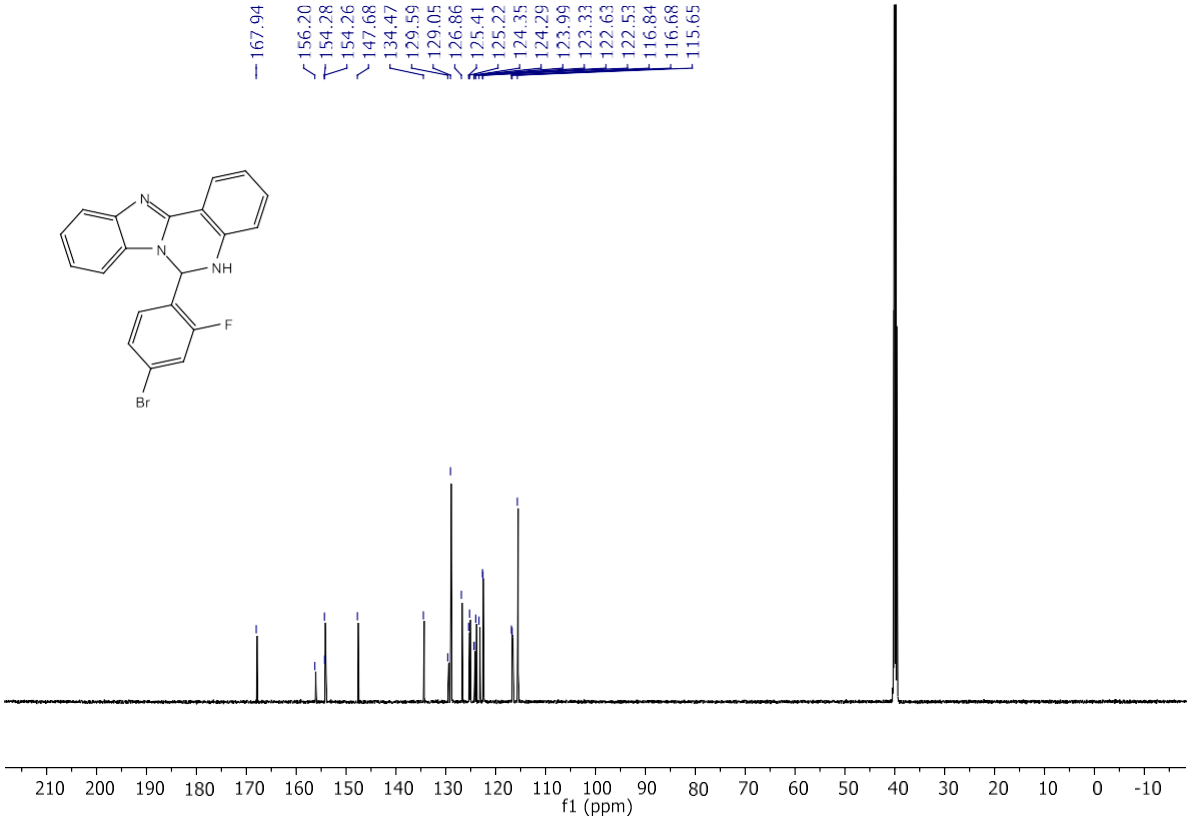
Compound **3q**: ^{1}H NMR (500 MHz, DMSO-d_6).



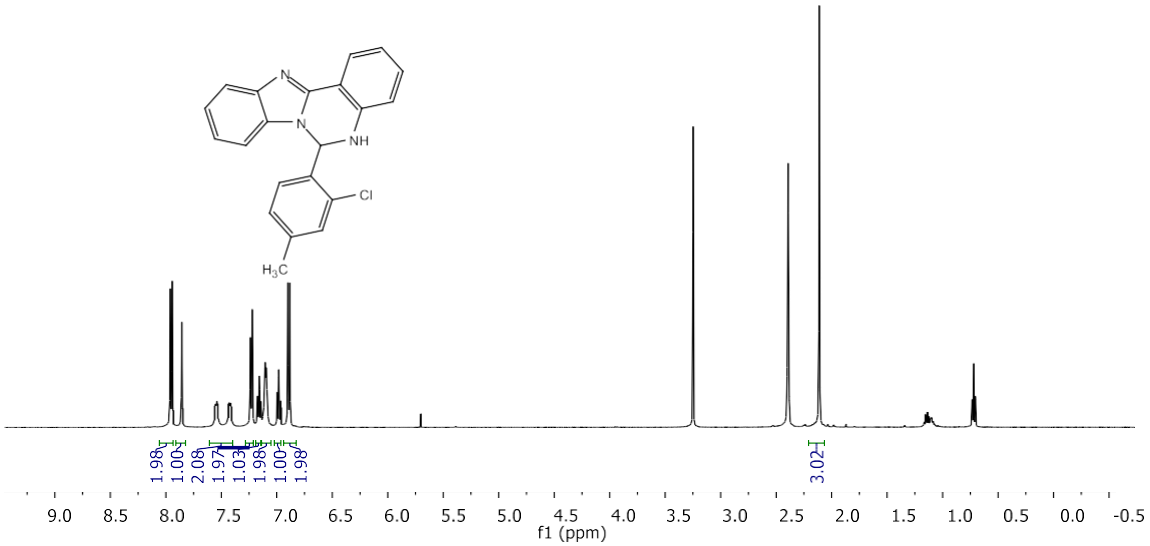
Compound **3q**: ^{13}C NMR (125 MHz, DMSO-d_6).



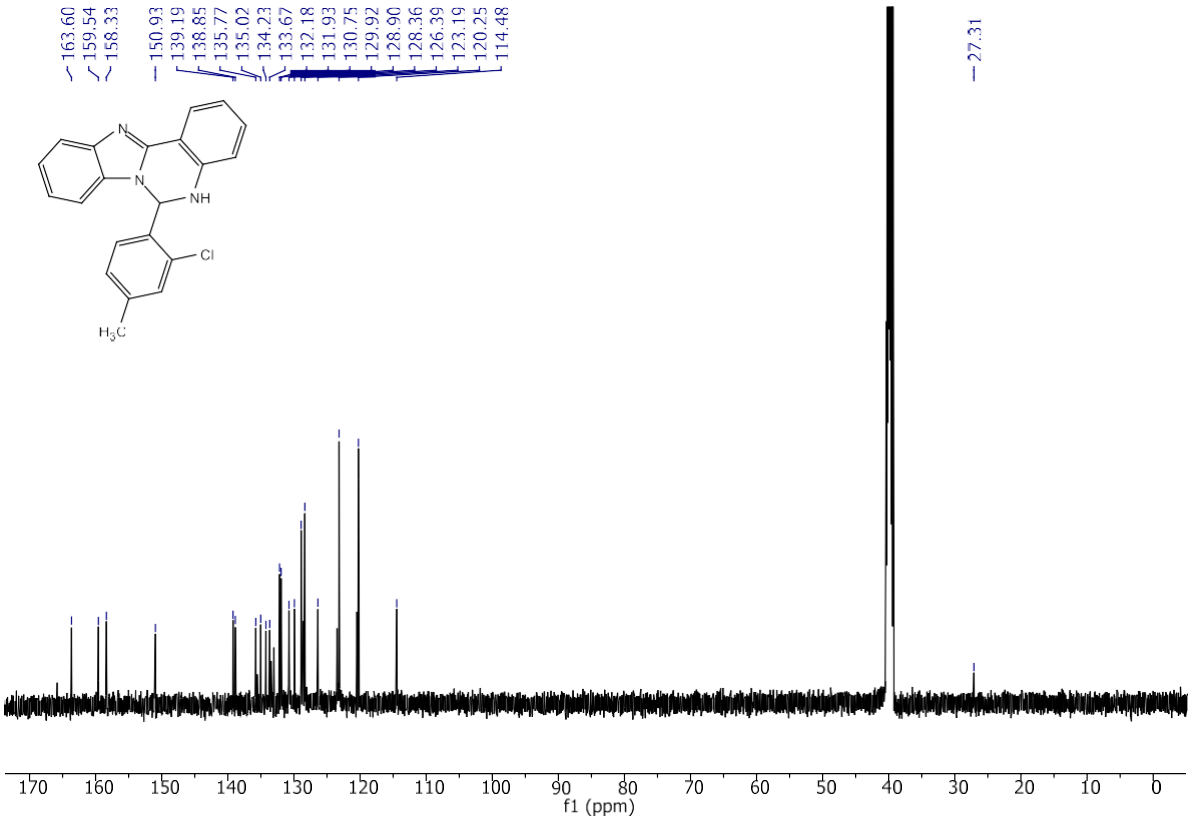
Compound **3r**: ^{1}H NMR (500 MHz, DMSO-d_6).



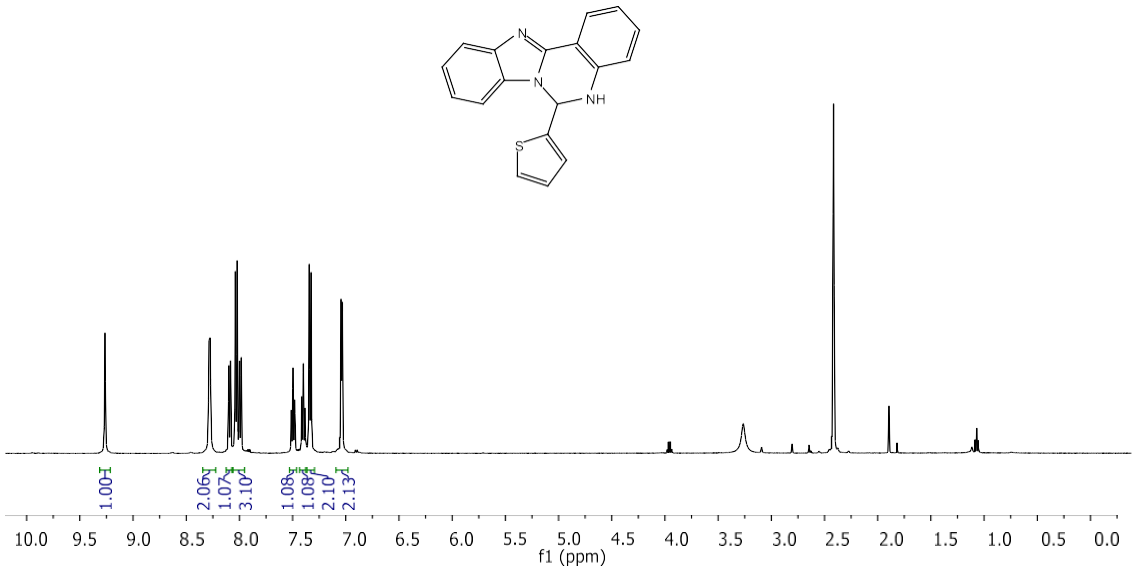
Compound **3r**: ^{13}C NMR (125 MHz, DMSO-d_6).



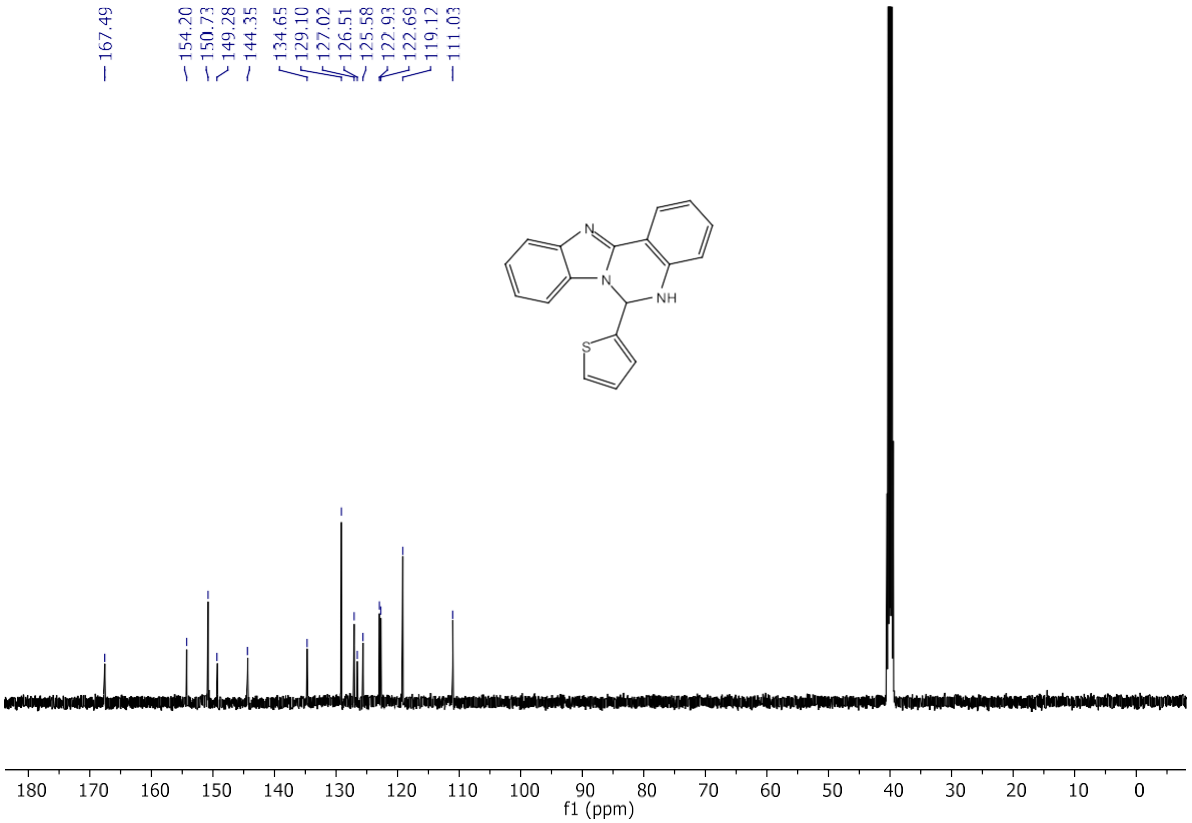
Compound **3s**: ^{1}H NMR (500 MHz, DMSO-d_6).



Compound **3s**: ^{13}C NMR (125 MHz, DMSO-d_6).



Compound **3t**: ^{1}H NMR (500 MHz, DMSO-d_6).



Compound **3t**: ^{13}C NMR (125 MHz, DMSO-d_6).