Supporting information

Leveraging in Situ N-tosylhydrazones as Diazo Surrogates for Efficient Access to Pyrazolo-[1,5-c]quinazolinone Derivatives

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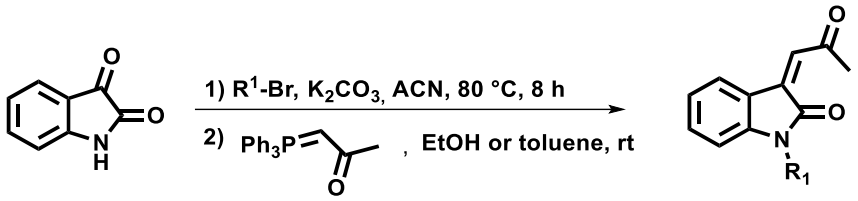
Contents

General information

All reactions were carried out in sealed tubes under argon atmosphere with magnetic stirring. All solvents and reagents were used as obtained from suppliers, unless otherwise noted. ^{1}H, ^{13}C and ^{19}F NMR spectra were recorded in $CDCl_3$, CD_3OD or $(CD_3)_2SO$ on Bruker Avance 200 and 300. Solvent peaks were used as reference values, with $CDCl_3$ at δ = 7.26 ppm for ^{1}H NMR and δ = 77.16 ppm for ^{13}C NMR, with CD_3OD at δ = 3.31 ppm for ^{1}H NMR and δ = 39.00 ppm for ^{13}C NMR, and with $(CD_3)_2SO$ at δ = 2.50 ppm for ^{1}H NMR and δ = 39.52 ppm for ^{13}C NMR. Chemical shifts δ are given in ppm, with the following abbreviations: singlet (s), doublet (d), doublet of doublet (dd), triplet (t), multiplet (m) and broad singlet (bs). Reaction courses and product mixtures were routinely monitored by TLC on silica gel, and compounds were visualized with under a UVP Mineralight UVGL-58 lamp (254 nm). Flash chromatography was performed using silica gel 60 (40–63 mm, 230–400 mesh) at medium pressure (200 mbar). Melting points (mp) were recorded on a Büchi B-450 apparatus and were uncorrected. High-resolution mass spectra were recorded on Microtof Q. All products reported showed ^{1}H and ^{13}C NMR spectra in agreement with the assigned structures.

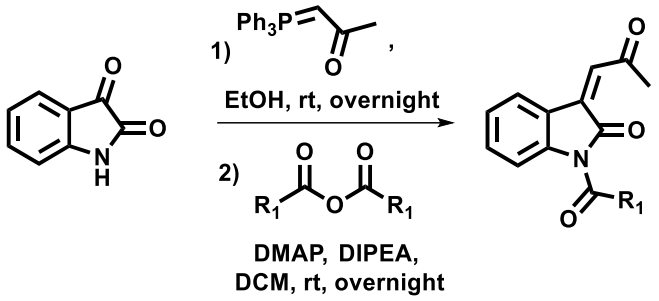
General experimental procedures for enones synthesis

General procedure A for enones



To a mixture of bromomethyl compound (1.2 equiv.) and K_2CO_3 (2.0 equiv.) in ACN (15 mL), isatin (1.0 equiv.) was added. The reaction mixture was stirred at reflux for 8 h. Then, the reaction crude was concentrated under reduced pressure, and purified by column chromatography on silica gel (Petroleum ether/EtOAc = 5/1) to afford the *N*-substituted isatins. To a solution of N-protected isatin (1.0 equiv.) in toluene or EtOH (12 mL), 1-(triphenylphosphoranylidene)-2-propanone (1.2 equiv.) was added, and the mixture was stirred until the *N*-protected isatin was consumed (monitored by TLC) at room temperature. The mixture was then concentrated under reduced pressure, and directly purified by flash chromatography on silica gel (Petroleum ether/EtOAc = 8/1) to afford desired enones.

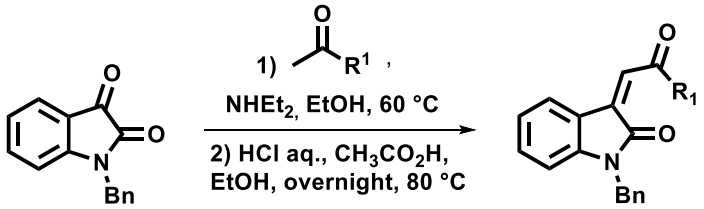
General procedure B for enones



A solution of isatin (1.0 equiv.) and 1-(triphenylphosphoranylidene)-2-propanone (1.0 equiv.) in EtOH (15 mL) was stirred at room temperature overnight. Then the solvent was evaporated under vacuum, and the crude mixture was purified by column chromatography on silica gel (Petroleum ether/EtOAc = 3/1) to give desired enones as a red solid.

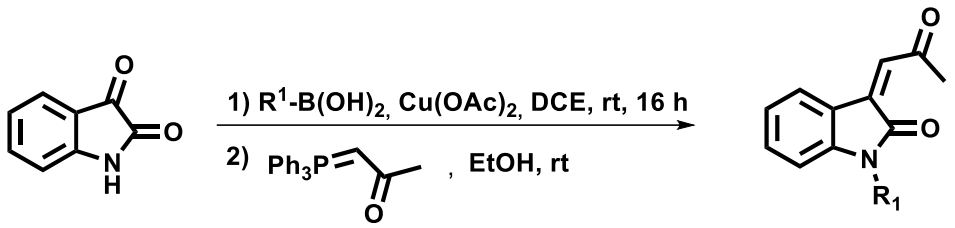
DMAP (0.1 equiv.) and DIPEA (1.0 equiv.) were added to a solution of enones in DCM (10 mL), then the anhydride compound (1.5 equiv.) was dropped slowly into the mixture. Then the reaction was stirred overnight. The solvent was removed under reduced pressure and the residue was purified by column chromatography on silica gel (Petroleum ether/EtOAc = 5/1) to give the *N*-substituted enones.

General procedure C for enones



To a solution of *N*-benzylisatin (1.0 equiv.) and ketone (1.0 equiv.) in EtOH (10 mL), diethylamine (1.1 equiv.) was added, and the mixture was stirred at 60 ˚C until *N*-benzylisatine was consumed (monitored by TLC). After being cooled to room temperature, CH_3COOH (1.2 equiv.) was added to the mixture, and the mixture was concentrated under vacuum. To the reaction mixture, water was added, and extracted three times with EtOAc. The organic layers were combined, washed with brine, dried over Na_2SO_4, filtered, and concentrated to give corresponding aldol product. This crude product was directly dissolved in EtOH (3 mL), and CH_3COOH (3 mL) and aqueous HCl solution (35%, 1 mL) were added at 80 °C overnight. The reaction mixture was cooled to room temperature and quenched with a saturated aqueous solution of $NaHCO_3$. The reaction mixture was extracted three times with EtOAc, and the combined extracts were dried over Na_2SO_4. The organic layers were directly purified by flash column chromatography on silica gel (Petroleum ether/EtOAc = 10/1) to afford desired enones.

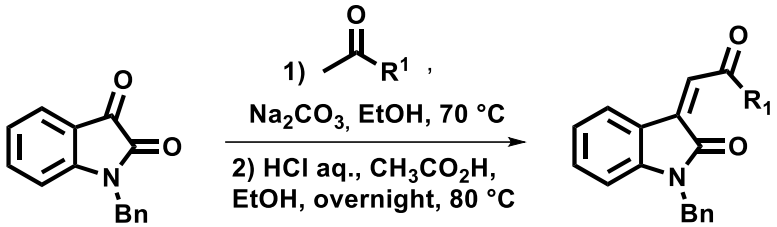
General procedure D for enones



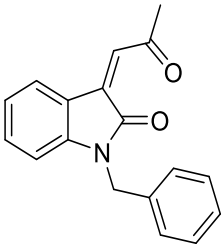
A mixture of isatin (1.0 equiv.), phenylboronic acid (2.0 equiv.), anhydrous $Cu(OAc)_2$ (2 equiv.), in 25 mL DCE was stirred at room temperature for 16 h at room temperature. The reaction mixture was poured into water and extracted with DCM then volatiles were removed, and the resulting residue was purified by column chromatography (Petroleum ether/EtOAc = 5/1) to afford the *N*-substituted isatins.

To a solution of N-protected isatin (1.0 equiv.) in EtOH (12 mL), 1-(triphenylphosphoranylidene)-2-propanone (1.2 equiv.) was added, and the mixture was stirred until the *N*-protected isatin was consumed (monitored by TLC) at room temperature. The mixture was then concentrated under reduced pressure, and directly purified by flash chromatography on silica gel (Petroleum ether/EtOAc = 8/1) to afford desired enones.

General procedure E for enones

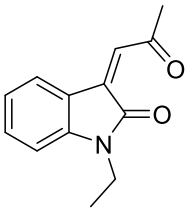


To a solution of *N*-benzylisatin (1.0 equiv.) and ketone (1.0 equiv.) in EtOH (10 mL), Na_2CO_3 (1.1 equiv.) was added, and the mixture was stirred at 70 °C until *N*-benzylisatine was consumed (monitored by TLC). After being cooled to room temperature, water was added, and extracted three times with EtOAc. The organic layers were combined, washed with brine, dried over Na_2SO_4, filtered, and concentrated to give corresponding aldol product. This crude product was directly dissolved in EtOH (3 mL), and CH_3COOH (3 mL) and aqueous HCl solution (35%, 1 mL) were added at 80 °C overnight. The reaction mixture was cooled to room temperature and quenched with a saturated aqueous solution of $NaHCO_3$. The reaction mixture was extracted three times with EtOAc, and the combined extracts were dried over Na_2SO_4. The organic layers were directly purified by flash column chromatography on silica gel (Petroleum ether/EtOAc = 10/1) to afford desired enones.



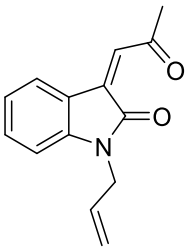
1-Benzyl-3-(2-oxopropylidene)indolin-2-one (1a)[1]

Was prepared according to the general method **A** in EtOH. 1.0 g of the desired compound was obtained in 61% yield, as a red solid. TLC: Rf = 0.4 (Cyclohexane/Ethyl acetate = 5/1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.54 (d, J = 7.6 Hz, 1H), 7.32 - 7.26 (m, 7H), 7.03 (t, J = 7.5 Hz, 1H), 6.70 (d, J = 7.7 Hz, 1H), 4.96 (s, 2H), 2.51 (s, 3H). HRMS (ESI) m/z: $(M + H)^+$ calcd. for $C_{18}H_{16}NO_2$ 278.1176, found 278.1179.
Data are consistent with the literature.



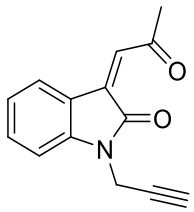
1-Ethyl-3-(2-oxopropylidene)indolin-2-one (1b)[2]

Was prepared according to the general method **A** in EtOH. 600 mg of the desired compound was obtained in 42% yield, as a yellow solid. TLC: Rf = 0.3 (Cyclohexane/Ethyl acetate = 4/1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.49 (d, J = 7.7 Hz, 1H), 7.35 (t, J = 7.7 Hz, 1H), 7.17 (s, 1H), 7.01 (t, J = 7.7 Hz, 1H), 6.78 (d, J = 7.7 Hz, 1H), 3.76 (q, J = 7.2 Hz, 2H), 2.46 (s, 3H), 1.26 (t, J = 7.2 Hz, 3H). HRMS (ESI) m/z: $(M + H)^+$ calcd. for $C_{13}H_{14}NO_2$ 216.1021, found 216.1019.
Data are consistent with the literature.



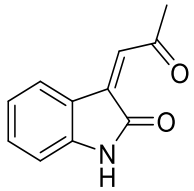
1-Allyl-3-(2-oxopropylidene)indolin-2-one (1c)

Was prepared according to the general method **A** in EtOH. 700 mg of the desired compound was obtained in 50% yield, as a yellow solid. TLC: Rf = 0.4 (Cyclohexane/Ethyl acetate = 4/1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.50 (d, J = 7.7 Hz, 1H), 7.33 (t, J = 7.7 Hz, 1H), 7.19 (s, 1H), 7.02 (t, J = 7.7 Hz, 1H), 6.77 (d, J = 7.8 Hz, 1H), 5.89 – 5.84 (m, 1H), 5.24 (d, J = 6.1 Hz, 1H), 5.20 (s, 1H), 4.35 (d, J = 5.1 Hz, 2H), 2.47 (s, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 198.6, 168.0, 145.5, 135.2, 132.9, 131.2, 128.3, 127.9, 123.0, 120.3, 117.8, 109.1, 42.5, 32.3. IR (film, cm^{-1}): 1010, 1037, 1099, 1136, 1182, 1332, 1384, 1421, 1442, 1469, 1597, 1625, 1707. Melting point: 66-69 °C. HRMS (ESI) m/z: $(M + H)^+$ calcd. for $C_{14}H_{14}NO_2$ 228.1019, found 228.1021.



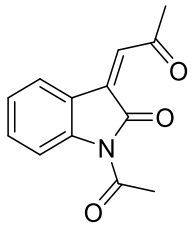
3-(2-Oxopropylidene)-1-(prop-2-yn-1-yl)indolin-2-one (1d)

Was prepared according to the general method **A** in EtOH. 500 mg of the desired compound was obtained in 33% yield, as a yellow solid. TLC: Rf = 0.5 (Cyclohexane/Ethyl acetate = 4/1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.51 (d, J = 7.7 Hz, 1H), 7.40 (t, J = 7.7 Hz, 1H), 7.19 (s, 1H), 7.07 (t, J = 7.7 Hz, 1H), 6.99 (d, J = 7.7 Hz, 1H), 4.51 (d, J = 2.5 Hz, 2H), 2.46 (s, 3H), 2.24 (t, J = 2.5 Hz, 1H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 198.4, 167.4, 144.3, 134.9, 133.0, 128.4, 128.3, 123.4, 120.3, 109.2, 76.7, 72.6, 32.3, 29.5. IR (film, cm^{-1}): 1014, 1153, 1201, 1421, 1600, 1622, 1676, 1720, 2117, 3211. Melting point: 62-65 °C. HRMS (ESI) m/z: $(M + H)^+$ calcd. for $C_{14}H_{12}NO_2$ 226.0863, found 226.0863.



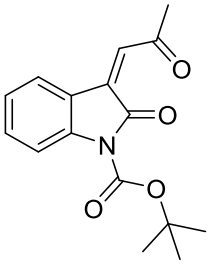
3-(2-Oxopropylidene)indolin-2-one (1e)[3]

Was prepared according to the general method **B** without acetylation. 520 mg of the desired compound was obtained in 70% yield, as a red solid. TLC: Rf = 0.4 (Cyclohexane/Ethyl acetate = 3/1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.50 (d, J = 7.8 Hz, 2H), 7.33 (t, J = 7.8 Hz, 1H), 7.16 (s, 1H), 7.03 (t, J = 7.8 Hz, 1H), 6.85 (d, J = 7.8 Hz, 1H), 2.48 (s, 3H). HRMS (ESI) m/z: $(M + H)^+$ calcd. for $C_{11}H_{10}NO_2$ 188.0706, found 188.0706.
Data are consistent with the literature.



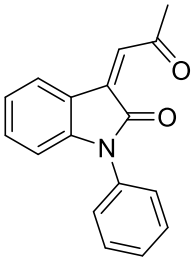
1-Acetyl-3-(2-oxopropylidene)indolin-2-one (1f)

Was prepared according to the general method **B**. 250 mg of the desired compound was obtained in 36% yield, as a yellow solid. TLC: Rf = 0.5 (Cyclohexane/Ethyl acetate = 6/1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.60 (d, J = 7.9 Hz, 1H), 8.27 (d, J = 8.8 Hz, 1H), 7.45 (t, J = 7.9 Hz, 1H), 7.23 - 7.18 (m, 1H), 7.18 (s, 1H), 2.71 (s, 3H), 2.49 (s, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 198.1, 170.4, 168.7, 142.4, 133.9, 133.5, 128.7, 127.6, 125.5, 120.8, 116.5, 32.4, 26.9. IR (film, cm^{-1}): 1008, 1037, 1062, 1168, 1211, 1276, 1305, 1417, 1456, 1612, 1714. Melting point: 129-132 °C. HRMS (ESI) m/z: $(M + H)^+$ calcd. for $C_{13}H_{12}NO_3$ 230.0812, found 230.0812.



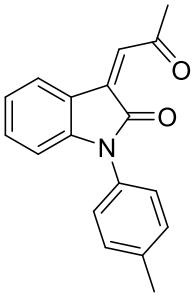
tert-Butyl-2-oxo-3-(2-oxopropylidene)indoline-1-carboxylate (1g)[4]

Was prepared according to the general method **B**. 220 mg of the desired compound was obtained in 26% yield, as a yellow solid. TLC: Rf = 0.5 (Cyclohexane/Ethyl acetate = 6/1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.60 (d, J = 7.9 Hz, 1H), 7.88 (d, J = 8.7 Hz, 1H), 7.43 (t, J = 7.9 Hz, 1H), 7.19 - 7.14 (m, 2H), 2.47 (s, 3H), 1.65 (s, 9H). HRMS (ESI) m/z: $(M + Na)^+$ calcd. for $C_{16}H_{17}NO_4Na$ 310.1050, found 310.1052.
Data are consistent with the literature.



3-(2-oxopropylidene)-1-phenylindolin-2-one np-10 (1h)[5]

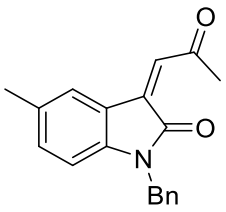
Was prepared according to the general method **D**. 0.11 g of the desired compound was obtained in 10% yield, as a red solid. TLC: Rf = 0.4 (Cyclohexane/Ethyl acetate = 4/1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.57 (d, J = 8.4 Hz, 1H), 7.54 – 7.42 (m, 2H), 7.43 – 7.37 (m, 3H), 7.31 – 7.24 (m, 2H), 7.06 (td, J = 7.7, 1.0 Hz, 1H), 6.75 (d, J = 7.9 Hz, 1H), 2.49 (s, 3H). HRMS (ESI) m/z: $(M + H)^+$ calcd. for $C_{17}H_{14}NO_2$ 264.1019, found 264.1014.
Data are consistent with the literature.



3-(2-oxopropylidene)-1-(p-tolyl)indolin-2-one (1i)

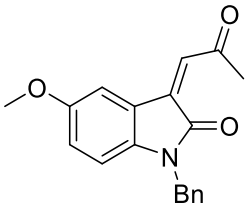
Was prepared according to the general method **D**. 100 mg of the desired compound was obtained in 15% yield, as a red solid. TLC: Rf = 0.5 (Cyclohexane/Ethyl acetate = 4/1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.52 (d, J = 7.7 Hz, 1H), 7.29 – 7.20 (m, 6H), 7.01 (t, J = 7.7 Hz, 1H), 6.68 (d, J = 7.9 Hz, 1H), 2.44 (s, 3H), 2.36 (s, 3H). ^{13}C{1H} NMR (75 MHz, $CDCl_3$) δ 198.6, 167.8, 146.5, 138.5, 135.3, 132.9, 131.5, 130.5 (2 C), 128.4, 128.3, 126.6 (2 C), 123.3, 120.3, 109.6, 32.4, 21.4. IR (film, cm^{-1}): 1020, 1045, 1085, 1176, 1296, 1315, 1365, 1462, 1516,

16018, 1681, 1718. Melting point: 84-87 °C. HRMS (ESI) m/z: $(M + H)^+$ calcd. for $C_{18}H_{16}NO_2$ 278.1176, found 278.1170.



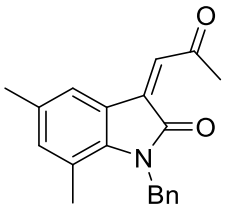
1-Benzyl-5-methyl-3-(2-oxopropylidene)indolin-2-one (1j)[6]

Was prepared according to the general method **A** in EtOH. 400 mg of the desired compound was obtained in 45% yield, as a red solid. TLC: Rf = 0.5 (Cyclohexane/Ethyl acetate = 3/1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.33 (s, 1H), 7.34 – 7.24 (q, J = 6.1, 5.3 Hz, 6H), 7.07 (d, J = 8.0 Hz, 1H), 6.57 (d, J = 8.0 Hz, 1H), 4.92 (s, 2H), 2.49 (s, 3H), 2.31 (s, 3H). HRMS (ESI) m/z: $(M + H)^+$ calcd. for $C_{19}H_{18}NO_2$ 292.1332, found 292.1337.
Data are consistent with the literature.



1-Benzyl-5-methoxy-3-(2-oxopropylidene)indolin-2-one (1k)

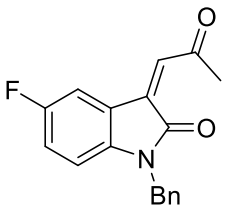
Was prepared according to the general method **A** in EtOH. 250 mg of the desired compound was obtained in 36% yield, as a red solid. TLC: Rf = 0.5 (Cyclohexane/Ethyl acetate = 6/1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.24 (d, J = 2.7 Hz, 1H), 7.34 - 7.23 (m, 6H), 6.83 (dd, J = 8.5, 2.7 Hz, 1H), 6.56 (d, J = 8.5 Hz, 1H), 4.90 (s, 2H), 3.81 (s, 3H), 2.49 (s, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 198.7, 156.0, 139.3, 139.1, 136.0, 135.7, 129.0 (2 C), 128.2, 127.9, 127.3, 121.0, 119.3, 113.9, 109.8, 77.6, 56.0, 44.1, 32.4. IR (film, cm^{-1}): 1085, 1112, 1217, 1319, 1363, 1435, 1479, 1589, 1602, 1680, 1707. Melting point: 90-93 °C. HRMS (ESI) m/z: $(M + H)^+$ calcd. for $C_{19}H_{18}NO_2$ 308.1281, found 308.1287.



1-Benzyl-5,7-dimethyl-3-(2-oxopropylidene)indolin-2-one (1l)

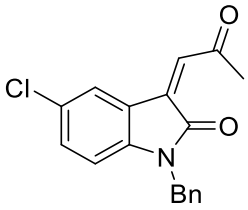
Was prepared according to the general method **A** in toluene. 300 mg of the desired compound was obtained in 25% yield, as a red solid. TLC: Rf = 0.4 (Cyclohexane/Ethyl acetate = 4/1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.30 (s, 1H), 7.35 - 7.25 (m, 4H), 7.17 (d, J = 7.0 Hz, 2H), 6.88 (s, 1H), 5.22 (s, 2H), 2.51 (s, 3H), 2.30 (s, 3H), 2.22 (s, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 198.9, 169.6, 141.0, 137.8, 137.4, 135.0, 132.5, 129.0 (2 C), 127.8, 127.3, 126.6, 125.7 (2 C), 121.2, 119.6, 45.4, 32.4, 20.8, 18.8. IR (film, cm$^{-1)}$: 1099, 1190, 1344, 1448, 1481, 1618, 1678,

1678, 1701. Melting point: 133-138 °C. HRMS (ESI) m/z: $(M + H)^+$ calcd. for $C_{20}H_{20}NO_2$ 306.1489, found 306.1489.



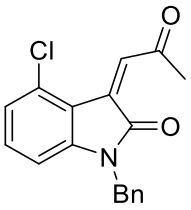
1-Benzyl-5-fluoro-3-(2-oxopropylidene)indolin-2-one (1m)[1]

Was prepared according to the general method **A** in EtOH. 300 mg of the desired compound was obtained in 33% yield, as a red solid. TLC: Rf = 0.5 (Cyclohexane/Ethyl acetate = 4/1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.27 (dd, J = 9.2, 2.6 Hz, 1H), 7.29 – 7.18 (m, 6H), 6.91 (td, J = 8.6, 2.6 Hz, 1H), 6.53 (dd, J = 8.6, 4.2 Hz, 1H), 4.87 (s, 2H), 2.44 (s, 3H). HRMS (ESI) m/z: $(M + H)^+$ calcd. for $C_{18}H_{15}FNO_2$ 296.1081, found 296.1081.
Data are consistent with the literature.



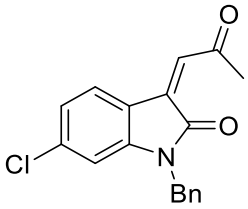
1-Benzyl-5-chloro-3-(2-oxopropylidene)indolin-2-one (1n)

Was prepared according to the general method **A** in EtOH. 350 mg of the desired compound was obtained in 38% yield, as a yellow solid. TLC: Rf = 0.5 (Cyclohexane/Ethyl acetate = 5/1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.57 (s, 1H), 7.37 - 7.22 (m, 7H), 6.61 (d, J = 8.4 Hz, 1H), 4.94 (s, 2H), 2.52 (s, 3H). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 198.4, 168.0, 143.8, 135.1, 134.4, 132.5, 129.4, 129.1 (2 C), 128.5, 128.4, 128.1, 127.3 (2 C), 121.5, 110.2, 44.1, 32.4. IR (film, cm^{-1}): 1085, 1116, 1159, 1259, 1365, 1444, 1595, 1622, 1683, 1714. Melting point: 160-164 °C. HRMS (ESI) m/z: $(M + H)^+$ calcd. for $C_{18}H_{15}ClNO_2$ 312.0786, found 312.0786.



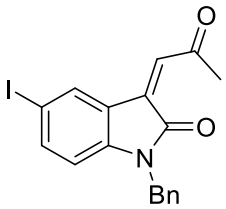
1-Benzyl-4-chloro-3-(2-oxopropylidene)indolin-2-one (1o)[1]

Was prepared according to the general method **A** in toluene. 320 mg of the desired compound was obtained in 34% yield, as a yellow solid. TLC: Rf = 0.5 (Cyclohexane/Ethyl acetate = 5/1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.60 (s, 1H), 7.33 – 7.25 (m, 5H), 7.13 (t, J = 7.9 Hz, 1H), 6.98 (d, J = 7.9 Hz, 1H), 6.63 (dd, J = 7.9, 2.4 Hz, 1H), 4.90 (s, 2H), 2.59 (s, 3H). HRMS (ESI) m/z: $(M + H)^+$ calcd. for $C_{18}H_{15}ClNO_2$ 312.0786, found 312.0787.
Data are consistent with the literature.



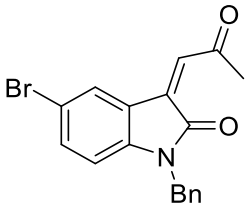
1-Benzyl-6-chloro-3-(2-oxopropylidene)indolin-2-one (1p)

Was prepared according to the general method **A** in EtOH. 400 mg of the desired compound was obtained in 41% yield, as a yellow solid. TLC: Rf = 0.5 (Cyclohexane/Ethyl acetate = 4/1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.50 (d, J = 8.3 Hz, 1H), 7.34 - 7.25 (m, 6H), 6.98 (dd, J = 8.3, 1.9 Hz, 1H), 6.68 (d, J = 1.9 Hz, 1H), 4.91 (s, 2H), 2.49 (s, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 198.4, 168.5, 138.9, 135.1, 134.3, 129.5, 129.1 (2 C), 128.2, 128.1, 127.3 (2 C), 123.0, 118.9, 109.9, 44.1, 32.4. IR (film, cm^{-1}): 1080, 1103, 1157, 1186, 1348, 1436, 1477, 1598, 1620, 1680, 1718. Melting point: 135-140 °C. HRMS (ESI) m/z: $(M + H)^+$ calcd. for $C_{18}H_{15}ClNO_2$ 312.0786, found 312.0790.



1-Benzyl-5-iodo-3-(2-oxopropylidene)indolin-2-one (1q)

Was prepared according to the general method **A** in EtOH. 120 mg of the desired compound was obtained in 10% yield, as a red solid. TLC: Rf = 0.4 (Cyclohexane/Ethyl acetate = 5/1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.87 (d, J = 1.7 Hz, 1H), 7.59 (dd, J = 8.2, 1.7 Hz, 1H), 7.34 - 7.28 (m, 6H), 6.48 (d, J = 8.2 Hz, 1H), 4.93 (s, 2H), 2.52 (s, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 198.4, 167.7, 144.9, 141.4, 136.7, 135.1, 129.3 (2 C), 129.1, 128.1, 127.3 (2 C), 122.3, 111.3, 102.4, 85.7, 44.1, 32.4. IR (film, cm^{-1}): 1075, 1103, 1178, 1226, 1335, 1444, 1489, 1555, 1622, 1683, 1795. Melting point: 144-148 °C. HRMS (ESI) m/z: $(M + H)^+$ calcd. for $C_{18}H_{15}INO_2$ 404.0142, found 404.0143.



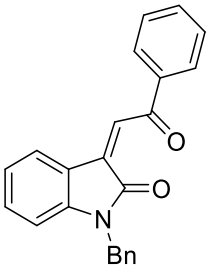
1-Benzyl-5-bromo-3-(2-oxopropylidene)indolin-2-one (1r)[1]

Was prepared according to the general method **A** in EtOH. 300 mg of the desired compound was obtained in 29% yield, as a red solid.

Gram-scale reaction: The reaction was realized with 2 g (9 mmol, 1.0 equiv.) of 5-bromoindoline-2,3-dione afford 1.1 g of **1r** in 34% yield.

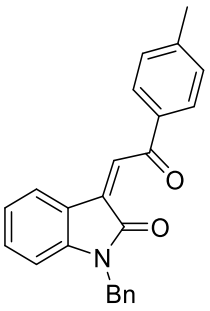
TLC: Rf = 0.4 (Cyclohexane/Ethyl acetate = 4/1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.70 (d, J = 2.0 Hz, 1H), 7.40 (dd, J = 8.3, 2.0 Hz, 1H), 7.34 - 7.25 (m, 6H), 6.57 (d, J = 8.3 Hz, 1H), 4.94

(s, 2H), 2.52 (s, 3H). HRMS (ESI) m/z: $(M + H)^+$ calcd. for $C_{18}H_{15}BrNO_2$ 356.0281, found 356.0280.
Data are consistent with the literature.



1-Benzyl-3-(2-oxo-2-phenylethylidene)indolin-2-one (1s)[1]

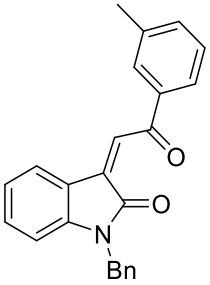
Was prepared according to the general method **C**. 400 mg of the desired compound was obtained in 39% yield, as a red solid. TLC: Rf = 0.6 (Cyclohexane/Ethyl acetate = 6/1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.34 (d, J = 7.7 Hz, 1H), 8.14 (d, J = 7.3 Hz, 2H), 7.98 (s, 1H), 7.64 (t, J = 7.3 Hz, 1H), 7.54 (t, J = 7.7 Hz, 2H), 7.35 – 7.23 (m, 6H), 7.00 (t, J = 7.7 Hz, 1H), 6.72 (d, J = 7.7 Hz, 1H), 4.99 (s, 2H). HRMS (ESI) m/z: $(M + H)^+$ calcd. for $C_{23}H_{18}NO_2$ 340.1332, found 340.1333.
Data are consistent with the literature.



1-benzyl-3-(2-oxo-2-(p-tolyl)ethylidene)indolin-2-one (1t)[7]

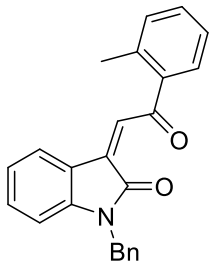
0.45 g of the desired compound was obtained in 42% yield with GPC, as a red solid. TLC: Rf = 0.6 (Cyclohexane/Ethyl acetate = 4/1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.31 (d, J = 7.7 Hz, 1H), 8.05 (d, J = 8.4 Hz, 2H), 7.97 (s, 1H), 7.36 - 7.23 (m, 8H), 7.00 (t, J = 7.7 Hz, 1H), 6.72 (d, J = 7.9 Hz, 1H), 5.00 (s, 2H), 2.47 (s, 3H). HRMS (ESI) $(M + H)^+$ calcd for $C_{24}H_{20}NO_2$, m/z 354.1489, found 354.1490.

Data are consistent with the literature.



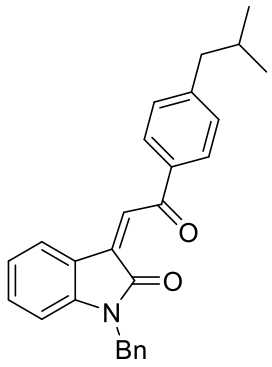
1-Benzyl-3-(2-oxo-2-(m-tolyl)ethylidene)indolin-2-one (1u)

Was prepared according to the general method **C**. 340 mg of the desired compound was obtained in 32% yield, as a red solid. TLC: Rf = 0.5 (Cyclohexane/Ethyl acetate = 6/1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.34 (d, J = 7.7 Hz, 1H), 7.98 – 7.93 (m, 3H), 7.48 – 7.41 (m, 2H), 7.36 – 7.23 (m, 6H), 7.00 (t, J = 7.7 Hz, 1H), 6.72 (d, J = 7.7 Hz, 1H), 4.99 (s, 2H), 2.47 (s, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 191.4, 168.2, 145.2, 138.9, 137.7, 136.2, 135.6, 134.7, 132.5, 129.4, 128.9, 128.9 (2 C), 127.8, 127.8, 127.4 (2 C), 127.1, 126.2, 122.9, 120.4, 109.3, 44.0, 21.4. IR (film, cm^{-1}): 1017, 1056, 1121, 1188, 1245, 1379, 1421, 1477, 1612, 1666, 1708. Melting point: 108-111 °C. HRMS (ESI) m/z: $(M + H)^+$ calcd. for $C_{24}H_{20}NO_2$ 354.1489, found 354.1494.



1-Benzyl-3-(2-oxo-2-(o-tolyl)ethylidene)indolin-2-one (1v)

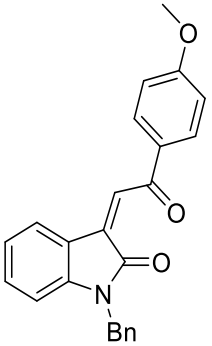
Was prepared according to the general method **C**. 270 mg of the desired compound was obtained in 25% yield, as a red solid. TLC: Rf = 0.6 (Cyclohexane/Ethyl acetate = 4/1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.32 (d, J = 7.5 Hz, 1H), 7.81 (d, J = 7.5 Hz, 1H), 7.76 (s, 1H), 7.45 (t, J = 7.5 Hz, 1H), 7.36 – 7.23 (m, 8H), 7.00 (t, J = 7.7 Hz, 1H), 6.72 (d, J = 7.8 Hz, 1H), 4.98 (s, 2H), 2.65 (s, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 194.6, 168.2, 145.2, 139.1, 137.8, 135.6, 135.6, 132.5, 132.4, 132.2, 130.1, 129.6, 128.9 (2 C), 127.8, 127.7, 127.4 (2 C), 126.0, 122.9, 120.4, 109.3, 44.0, 21.3. IR (film, cm^{-1}): 1008, 1025, 1112, 1195, 1225, 1266, 1301, 1435, 1499, 1623, 1708. Melting point: 100-105 °C. HRMS (ESI) m/z: $(M + H)^+$ calcd. for $C_{24}H_{20}NO_2$ 354.1489, found 354.1490.



1-Benzyl-3-(2-(4-isobutylphenyl)-2-oxoethylidene)indolin-2-one (1w)

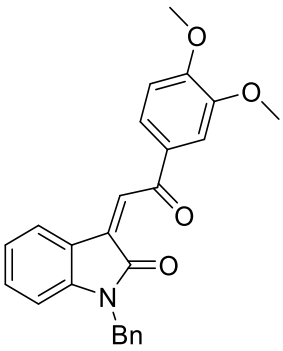
Was prepared according to the general method **C**. 370 mg of the desired compound was obtained in 31% yield, as a red solid. TLC: Rf = 0.4 (Cyclohexane/Ethyl acetate = 6/1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.23 (d, J = 7.7 Hz, 1H), 7.98 (d, J = 8.4 Hz, 2H), 7.89 (s, 1H), 7.26 - 7.13 (m, 8H), 6.90 (td, J = 7.7, 1.0 Hz, 1H), 6.63 (d, J = 7.7 Hz, 1H), 4.90 (s, 2H), 2.50 (d, J = 7.2 Hz, 2H), 1.86 (hept, J = 6.7 Hz, 1H), 0.86 (d, J = 6.7 Hz, 6H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 191.0, 168.2, 148.7, 145.2, 136.0, 135.7, 135.5, 132.4, 129.8 (2 C), 129.0 (2 C), 128.9

(2 C), 127.8, 127.7, 127.4 (2 C), 127.3, 122.9, 120.4, 109.3, 45.6, 44.0, 30.2, 22.4 (2 C). IR (film, cm^{-1}): 1009, 1155, 1161, 1211, 1258, 1365, 1416, 1512, 1556, 1605, 1678, 1758. Melting point: 113-117 °C. HRMS (ESI) m/z: $(M + H)^+$ calcd. for $C_{27}H_{26}NO_2$ 396.1958, found 396.1959.



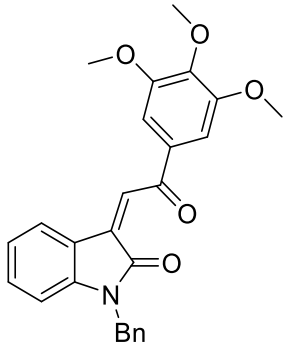
1-Benzyl-3-(2-(4-methoxyphenyl)-2-oxoethylidene)indolin-2-one (1x)[8]

Was prepared according to the general method **C**. 370 mg of the desired compound was obtained in 42% yield, as a red solid. TLC: Rf = 0.6 (Cyclohexane/Ethyl acetate = 5/1). ^1H NMR (300 MHz, $CDCl_3$) δ 8.25 - 8.09 (m, 3H), 7.93 (s, 1H), 7.34 - 7.21 (m, 6H), 7.03 – 6.95 (m, 3H), 6.70 (d, J = 7.8 Hz, 1H), 4.98 (s, 2H), 3.90 (s, 3H). HRMS (ESI) m/z: $(M + H)^+$ calcd. for $C_{24}H_{20}NO_3$ 370.1438, found 370.1441.
Data are consistent with the literature.



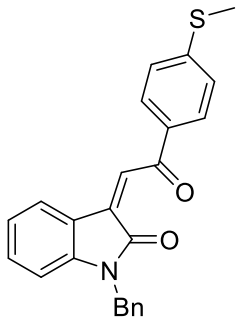
1-Benzyl-3-(2-(3,4-dimethoxyphenyl)-2-oxoethylidene)indolin-2-one (1y)

Was prepared according to the general method **C**. 400 mg of the desired compound was obtained in 33% yield, as a red solid. TLC: Rf = 0.5 (Cyclohexane/Ethyl acetate = 3/1). ^1H NMR (300 MHz, $CDCl_3$) δ 8.26 (d, J = 7.6 Hz, 1H), 7.94 (s, 1H), 7.78 (dd, J = 8.4, 2.0 Hz, 1H), 7.67 (d, J = 2.0 Hz, 1H), 7.33 – 7.20 (m, 6H), 7.00 – 6.91 (m, 2H), 6.70 (d, J = 7.8 Hz, 1H), 4.97 (s, 2H), 3.98 (s, 3H), 3.96 (s, 3H). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 189.6, 168.2, 154.2, 149.6, 145.0, 135.6, 135.5, 132.2, 130.9, 128.8 (2 C), 127.7, 127.6, 127.3, 127.1 (2 C), 124.3, 122.8, 120.3, 110.4, 110.2, 109.2, 56.2, 56.1, 43.9. IR (film, cm^{-1}): 1022, 1099, 1143, 1163, 1205, 1350, 1419, 1460, 1510, 1598, 1647, 1705. Melting point: 142-145 °C. HRMS (ESI) m/z: $(M + H)^+$ calcd. for $C_{25}H_{22}NO_4$ 400.1543, found 400.1552.



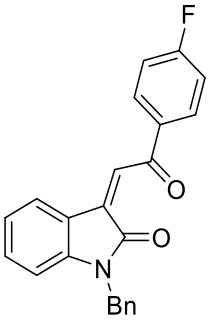
1-Benzyl-3-(2-oxo-2-(3,4,5-trimethoxyphenyl)ethylidene)indolin-2-one (1z)

Was prepared according to the general method **C**. 380 mg of the desired compound was obtained in 30% yield, as a red solid. TLC: Rf = 0.5 (Cyclohexane/Ethyl acetate = 3/1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.28 (d, J = 8.1 Hz, 1H), 7.91 (s, 1H), 7.38 (s, 2H), 7.35 – 7.32 (m, 4H), 7.29 – 7.25 (m, 2H), 6.99 (td, J = 7.7, 1.0 Hz, 1H), 6.71 (d, J = 7.7 Hz, 1H), 4.97 (s, 2H), 3.96 (s, 3H), 3.95 (s, 6H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 190.0, 168.2, 153.5, 145.2, 143.7, 136.4, 135.6, 132.9, 132.6, 129.0 (2 C), 127.9, 127.8, 127.4 (2 C), 126.7, 123.0, 120.4, 109.4, 106.5 (2 C), 61.1, 56.6 (2 C), 44.1. IR (film, cm^{-1}): 1072, 1085, 1099, 1130, 1163, 1192, 1228, 1317, 1352, 1381, 1413, 1504, 1600, 1654, 1716. Melting point: 130-135 °C. HRMS (ESI) m/z: $(M + H)^+$ calcd. for $C_{26}H_{24}NO_5$ 430.1649, found 430.1658.



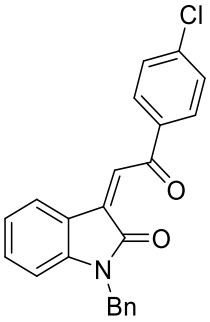
1-benzyl-3-(2-(4-(methylthio)phenyl)-2-oxoethylidene)indolin-2-one (1aa)

Was prepared according to the general method **E**. 400 mg of the desired compound was obtained in 35% yield, as a red solid. TLC: Rf = 0.4 (Cyclohexane/Ethyl acetate = 4/1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.30 (d, J = 7.7 Hz, 1H), 8.04 (d, J = 8.7 Hz, 2H), 7.92 (s, 1H), 7.34 – 7.21 (m, 8H), 6.98 (td, J = 7.7, 1.0 Hz, 1H), 6.70 (d, J = 7.8 Hz, 1H), 4.98 (s, 2H), 2.54 (s, 3H). ^{13}C{1H} NMR (75 MHz, $CDCl_3$) δ 190.1, 168.3, 147.5, 145.2, 136.2, 135.6, 134.1, 132.5, 129.4 (2 C), 129.0 (2 C), 127.9 (2 C), 127.4 (2 C), 126.9, 125.3 (2 C), 123.0, 120.4, 109.3, 44.1, 14.8. IR (film, cm^{-1}): 1020, 1111, 1185, 1264, 1374, 1485, 1521, 1621, 1698, 1756. Melting point: 120-124 °C. HRMS (ESI) m/z: $(M + H)^+$ calcd. for $C_{24}H_{20}NSO_2$ 386.1209, found 386.1204.



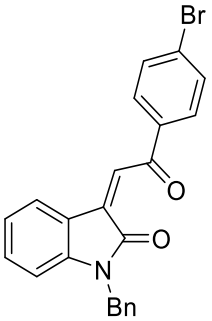
1-Benzyl-3-(2-(4-fluorophenyl)-2-oxoethylidene)indolin-2-one (1ab)

Was prepared according to the general method **C**. 200 mg of the desired compound was obtained in 19% yield, as a red solid. TLC: Rf = 0.4 (Cyclohexane/Ethyl acetate = 5/1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.31 (d, J = 7.7 Hz, 1H), 8.19 - 8.13 (m, 2H), 7.91 (s, 1H), 7.34 - 7.17 (m, 8H), 6.99 (t, J = 7.2 Hz, 1H), 6.71 (d, J = 7.7 Hz, 1H), 4.98 (s, 2H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 189.7, 168.1, 168.0, 166.3 (d, J = 256.3 Hz), 145.4, 136.7, 135.6, 134.2 (d, J = 3.0 Hz), 132.8, 131.7 (d, J = 9.4 Hz), 129.0 (2 C), 127.9 (2 C), 127.4 (2 C), 126.2, 123.0, 120.3 (2 C), 116.2 (d, J = 22.0 Hz), 109.4, 44.1. ^{19}F NMR (188 MHz, $CDCl_3$) δ -103.52. IR (film, cm^{-1}): 1014, 1049, 1153, 1201, 1421, 1467, 1622, 1676, 1720, 2117. Melting point: 160-164 °C. HRMS (ESI) m/z: $(M + H)^+$ calcd. for $C_{23}H_{17}FNO_2$ 358.1238, found 358.1237.



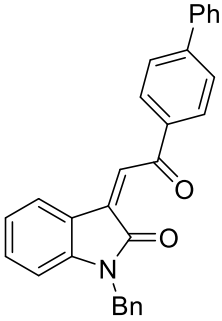
1-Benzyl-3-(2-(4-chlorophenyl)-2-oxoethylidene)indolin-2-one (1ac)

Was prepared according to the general method **C**. 250 mg of the desired compound was obtained in 22% yield, as a red solid. TLC: Rf = 0.4 (Cyclohexane/Ethyl acetate = 6/1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.26 (d, J = 7.8 Hz, 1H), 8.01 – 7.97 (m, 2H), 7.82 (s, 1H), 7.45 - 7.41 (m, 2H), 7.26 - 7.16 (m, 6H), 6.92 (t, J = 7.8 Hz, 1H), 6.63 (d, J = 7.8 Hz, 1H), 4.90 (s, 2H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 189.9, 168.1, 145.5, 140.5, 137.0, 136.2, 135.6, 132.9, 130.3 (2 C), 129.4 (2 C), 129.0 (2 C), 128.0, 127.9, 127.4 (2 C), 125.8, 123.0, 120.3, 109.4, 44.1. IR (film, cm^{-1}): 1006, 1066, 1091, 1147, 1292, 1313, 1344, 1371, 1404, 1465, 1618, 1654, 1714. Melting point: 130-135 °C. HRMS (ESI) m/z: $(M + H)^+$ calcd. for $C_{23}H_{17}ClNO_2$ 374.0942, found 374.0944.



1-Benzyl-3-(2-(4-bromophenyl)-2-oxoethylidene)indolin-2-one (1ad)

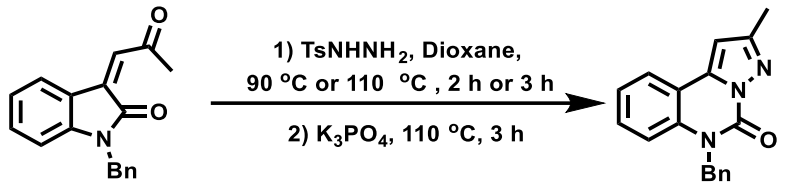
Was prepared according to the general method **C**. 280 mg of the desired compound was obtained in 21% yield, as a red solid. TLC: Rf = 0.3 (Cyclohexane/Ethyl acetate = 6/1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.38 (d, J = 7.7 Hz, 1H), 8.01 (d, J = 8.4 Hz, 2H), 7.91 (s, 1H), 7.69 (d, J = 8.4 Hz, 2H), 7.37 - 7.28 (m, 6H), 7.02 (t, J = 7.7 Hz, 1H), 6.73 (d, J = 7.7 Hz, 1H), 4.99 (s, 2H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 190.0, 168.1, 145.5, 137.1, 136.5, 135.5, 132.9, 132.4 (2 C), 130.4 (2 C), 129.3, 129.0 (2 C), 128.0, 127.9, 127.4 (2 C), 125.7, 123.0, 120.3, 109.4, 44.1. IR (film, cm^{-1}): 1019, 1055, 1111, 1201, 1330, 1406, 1485, 1569, 1600, 1666, 1708. Melting point: 123-126 °C. HRMS (ESI) m/z: $(M + H)^+$ calcd. for $C_{23}H_{17}BrNO_2$ 418.0437, found 418.0433.



3-(2-([1,1'-Biphenyl]-4-yl)-2-oxoethylidene)-1-benzylindolin-2-one (1ae)

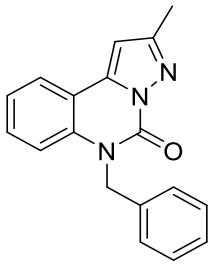
Was prepared according to the general method **C**. 150 mg of the desired compound was obtained in 15% yield, as a red solid. TLC: Rf = 0.6 (Cyclohexane/Ethyl acetate = 6/1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.28 (d, J = 7.2 Hz, 1H), 8.16 - 8.12 (m, 2H), 7.93 (s, 1H), 7.69 (d, J = 8.6 Hz, 2H), 7.61 - 7.57 (m, 2H), 7.45 - 7.33 (m, 3H), 7.27 - 7.16 (m, 6H), 6.93 (td, J = 7.7, 1.0 Hz, 1H), 6.65 (d, J = 7.8 Hz, 1H), 4.92 (s, 2H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 190.8, 168.3, 146.7, 145.3, 139.9, 136.5, 136.5, 135.7, 132.7, 129.6 (2 C), 129.2 (2 C), 129.0 (2 C), 128.6, 127.9 (2 C), 127.7 (2 C), 127.5 (2 C), 127.4 (2 C), 126.9, 123.0, 120.5, 109.4, 44.1. IR (film, cm^{-1}): 1006, 1018, 1049, 1101, 1147, 1238, 1301, 1369, 1408, 1465, 1496, 1600, 1651, 1707. Melting point: 165-170 °C. HRMS (ESI) m/z: $(M + H)^+$ calcd. for $C_{29}H_{22}NO_2$ 416.1645, found 416.1646.

General procedure for cyclization reactions



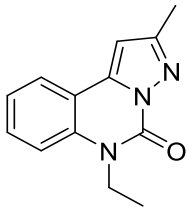
General procedure F: In an oven-dried 10 mL tube, enones (0.20 mmol, 1.0 equiv.), and *p*-toluenesulfonyl hydrazide (0.24 mmol, 1.2 equiv.) were dissolved in dioxane (2 mL). The reaction was heated in an oil bath at 90 °C and stirred for 2 h. Then tripotassium phosphate (0.40 mmol, 2.0 equiv.) was added in the reaction mixture, which was stirred at 110 °C for 3 h. The reaction mixture was concentrated under reduced pressure, and the residue was purified by flash chromatography with cyclohexane to afford the desired product.

General procedure G: In an oven-dried 10 mL tube, enones (0.20 mmol, 1.0 equiv.), and *p*-toluenesulfonyl hydrazide (0.24 mmol, 1.2 equiv.) were dissolved in dioxane (2 mL). The reaction was heated in an oil bath at 110 °C and stirred for 3 h. Then tripotassium phosphate (0.40 mmol, 2.0 equiv.) was added in the reaction mixture, which was stirred at 110 °C for 3 h. The reaction mixture was concentrated under reduced pressure, and the residue was purified by flash chromatography with cyclohexane to afford the desired product.



6-Benzyl-2-methylpyrazolo[1,5-*c*]quinazolin-5(6*H*)-one (2a)

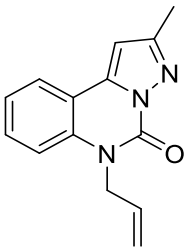
53 mg of the desired compound were obtained with procedure F in 92% yield as a white solid. TLC: Rf = 0.5 (Cyclohexane/Ethyl acetate = 2/1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.75 (d, J = 7.8 Hz, 1H), 7.35 - 7.29 (m, 1H), 7.26 - 7.15 (m, 7H), 6.64 (s, 1H), 5.51 (s, 2H), 2.48 (s, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 155.0, 146.2, 140.4, 135.8, 135.2, 130.2, 128.9 (2 C), 127.7, 126.7 (2 C), 124.5, 123.6, 115.7, 113.7, 101.1, 47.5, 14.2. IR (film, cm^{-1}): 1011, 1095, 1126, 1179, 1277, 1333, 1355, 1422, 1456, 1616, 1695, 1725. Melting point: 178-181 °C. HRMS (ESI) m/z: $(M + H)^+$ calcd. for $C_{18}H_{16}N_3O$ 290.1288, found 290.1292.



6-Ethyl-2-methylpyrazolo[1,5-*c*]quinazolin-5(6*H*)-one (2b)

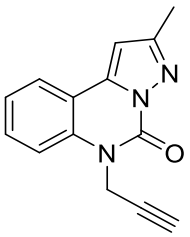
25 mg of the desired compound were obtained with procedure F in 54% yield as a white solid. TLC: Rf = 0.4 (Cyclohexane/Ethyl acetate = 2/1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.77 (dd, J =

7.8, 1.4 Hz, 1H), 7.48 (ddd, *J* = 8.7, 7.3, 1.4 Hz, 1H), 7.29 – 7.23 (m, 2H), 6.60 (s, 1H), 4.35 (q, *J* = 7.1 Hz, 2H), 2.45 (s, 3H), 1.37 (t, *J* = 7.1 Hz, 3H). $^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) δ 154.7, 145.3, 140.2, 130.3 (2 C), 124.7, 123.3, 114.6, 113.8, 100.7, 38.9, 14.2, 12.8. IR (film, cm^{-1}): 1022, 1056, 1136, 1185, 1297, 1312, 1333, 1395, 1456, 1502, 1568, 1668, 1702. Melting point: 147-151 °C. HRMS (ESI) m/z: $(M + H)^+$ calcd. for $C_{13}H_{14}N_3O$ 228.1131, found 228.1138.



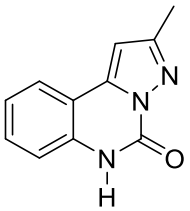
6-Ethyl-2-methylpyrazolo[1,5-*c*]quinazolin-5(6*H*)-one (2c)

36 mg of the desired compound were obtained with procedure F in 75% yield as a white solid. TLC: Rf = 0.4 (Cyclohexane/Ethyl acetate = 3/1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.77 (d, *J* = 6.7 Hz, 1H), 7.47 - 7.41 (m, 1H), 7.26 - 7.21 (m, 2H), 6.62 (s, 1H), 6.00 – 5.87 (m, 1H), 5.24 - 5.15 (m, 2H), 4.94 - 4.91 (m, 2H), 2.46 (s, 3H). $^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) δ 154.9, 145.6, 140.4, 135.1, 131.5, 130.2, 124.5, 123.5, 117.8, 115.5, 113.6, 101.0, 46.0, 14.2. IR (film, cm^{-1}): 1010, 1037, 1099, 1136, 1155, 1182, 1332, 1384, 1421, 1444, 1469, 1625, 1707. Melting point: 128-131 °C. HRMS (ESI) m/z: $(M + H)^+$ calcd. for $C_{14}H_{14}N_3O$ 240.1131, found 240.1136.



2-Methyl-6-(prop-2-yn-1-yl)pyrazolo[1,5-c]quinazolin-5(6H)-one (2d)

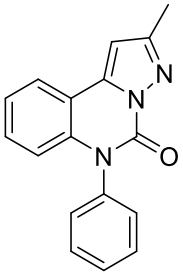
38 mg of the desired compound were obtained with procedure F in 80% yield as a white solid. TLC: Rf = 0.3 (Cyclohexane/Ethyl acetate = 3/1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.79 (dd, *J* = 7.8, 1.3 Hz, 1H), 7.57 - 7.44 (m, 2H), 7.32 – 7.27 (m, 1H), 6.64 (s, 1H), 5.10 (d, *J* = 2.5 Hz, 2H), 2.47 (s, 3H), 2.29 (t, *J* = 2.5 Hz, 1H). $^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) δ 155.1, 145.2, 140.3, 134.4, 130.3, 124.5, 123.9, 115.4, 113.7, 101.3, 77.4, 73.6, 33.4, 14.2. IR (film, cm^{-1}): 1014, 1049, 1101, 1201, 1421, 1467, 1600, 1676, 1720, 2117, 3233. Melting point: 197- 201 °C. HRMS (ESI) m/z: $(M + Na)^+$ calcd. for $C_{14}H_{11}N_3ONa$ 260.0794, found 260.0798.



2-Methylpyrazolo[1,5-*c*]quinazolin-5(6*H*)-one (2e)

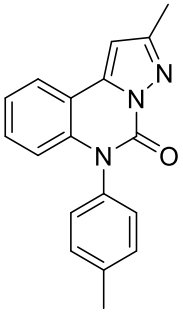
29 mg of the desired compound were obtained with procedure F in 72% yield as a white solid. TLC: Rf = 0.3 (Cyclohexane/Ethyl acetate = 1/1). ^{1}H NMR (300 MHz, CD_3OD) δ 7.76 (dd, *J*

= 8.1, 1.5 Hz, 1H), 7.43 - 7.38 (m, 1H), 7.22 - 7.16 (m, 2H), 6.75 (s, 1H), 2.41 (s, 3H). $^{13}C\{^{1}H\}$ NMR (75 MHz, CD_3OD) δ 155.8, 148.9, 142.8, 135.6, 131.4, 124.9, 124.6, 116.6, 113.6, 102.1, 13.8. IR (film, cm^{-1}): 1024, 1093, 1168, 1211, 1305, 1417, 1456, 1591, 1612, 1685, 1714, 1745. Melting point: 224-228 °C. HRMS (ESI) m/z: $(M + H)^+$ calcd. for $C_{11}H_{10}N_3O$ 200.0818, found 200.0822.



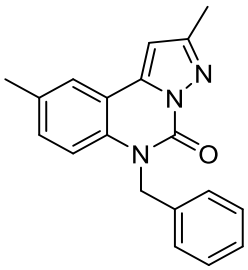
2-methyl-6-phenylpyrazolo[1,5-c]quinazolin-5(6H)-one (2h)

46 mg of the desired compound were obtained with procedure F in 83% yield as a white solid. TLC: Rf = 0.5 (Cyclohexane/Ethyl acetate = 3/1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.85 – 7.82 (m, 1H), 7.62 – 7.51 (m, 3H), 7.37 - 7.35 (m, 2H), 7.28 - 7.24 (m, 2H), 6.73 (s, 1H), 6.64 – 6.54 (m, 1H), 2.52 (s, 3H). $^{13}C\{1H\}$ NMR (75 MHz, $CDCl_3$) δ 155.0, 145.3, 140.7, 137.3, 136.7, 130.4 (2 C), 129.9, 129.5, 129.4 (2 C), 124.1, 123.7, 116.6, 113.2, 101.3, 14.3. IR (film, cm^{-1}): 1016, 1072, 1143, 1294, 1311, 1342, 1452, 1591, 1616, 1714. Melting point: 142-143 °C. HRMS (ESI) m/z: $(M + H)^+$ calcd. for $C_{17}H_{14}N_3O$ 276.1131, found 276.1135.



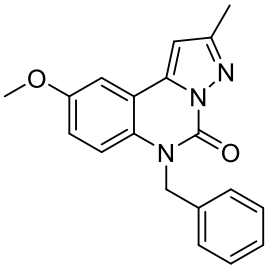
2-methyl-6-(p-tolyl)pyrazolo[1,5-c]quinazolin-5(6H)-one (2i)

49 mg of the desired compound were obtained with procedure F in 84% yield as a white solid. TLC: Rf = 0.5 (Cyclohexane/Ethyl acetate = 3/1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.88 – 7.85 (m, 1H), 7.43 (d, J = 8.4 Hz, 2H), 7.35 – 7.26 (m, 4H), 6.76 (s, 1H), 6.69 – 6.66 (m, 1H), 2.56 (s, 3H), 2.50 (s, 3H). $^{13}C\{1H\}$ NMR (75 MHz, $CDCl_3$) δ 154.9, 145.4, 140.7, 139.5, 137.5, 134.0, 131.1 (2 C), 129.8, 129.0 (2 C), 124.1, 123.6, 116.7, 113.2, 101.2, 21.4, 14.3. IR (film, cm^{-1}):1178, 1249, 1290, 1315, 1340, 1452, 1477, 1510, 1593, 1714. Melting point: 162-166 °C. HRMS (ESI) m/z: $(M + H)^+$ calcd. for $C_{18}H_{16}N_3O$ 290.1288, found 290.1292.



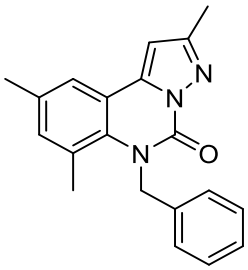
6-Benzyl-2,9-dimethylpyrazolo[1,5-*c*]quinazolin-5(6*H*)-one (2j)

52 mg of the desired compound were obtained with procedure F in 86% yield as a white solid. TLC: Rf = 0.4 (Cyclohexane/Ethyl acetate = 3/1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.56 (s, 1H), 7.29 – 7.05 (m, 7H), 6.63 (s, 1H), 5.50 (s, 2H), 2.49 (s, 3H), 2.35 (s, 3H). $^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) δ 154.9, 146.2, 140.5, 135.9, 133.3, 133.0, 131.3, 128.9 (2 C), 127.6, 126.7 (2 C), 124.4, 115.6, 113.5, 100.8, 47.4, 20.7, 14.2. IR (film, cm^{-1}): 1002, 1032, 1056, 1215, 1256, 1385, 1410, 1466, 1612, 1689. Melting point: 85-90 °C. HRMS (ESI) m/z: $(M + H)^+$ calcd. for $C_{19}H_{18}N_3O$ 304.1444, found 304.1450.



6-Benzyl-9-methoxy-2-methylpyrazolo[1,5-*c*]quinazolin-5(6*H*)-one (2k)

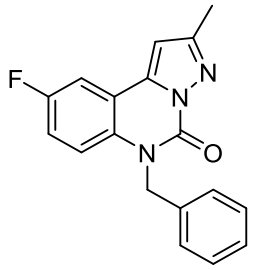
55 mg of the desired compound were obtained with procedure F in 85% yield as a white solid. TLC: Rf = 0.4 (Cyclohexane/Ethyl acetate = 2/1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.27 – 7.19 (m, 6H), 7.09 (d, J = 9.2 Hz, 1H), 6.91 (dd, J = 9.2, 2.8 Hz, 1H), 6.63 (s, 1H), 5.49 (s, 2H), 3.80 (s, 3H), 2.49 (s, 3H). $^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) δ 155.7, 154.8, 146.0, 140.2, 135.9, 129.2, 128.9 (2 C), 127.6, 126.7 (2 C), 117.6, 117.1, 114.4, 107.6, 101.1, 55.8, 47.5, 14.2. IR (film, cm^{-1}): 1002, 1022, 1236, 1290, 1317, 1342, 1500, 1604, 1691. Melting point: 90-93 °C. HRMS (ESI) m/z: $(M + Na)^+$ calcd. for $C_{19}H_{17}N_3O_2Na$ 342.1213, found 342.1218.



6-Benzyl-2,7,9-trimethylpyrazolo[1,5-*c*]quinazolin-5(6*H*)-one (2l)

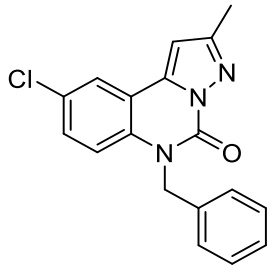
58 mg of the desired compound were obtained with procedure F in 90% yield as a white solid. TLC: Rf = 0.4 (Cyclohexane/Ethyl acetate = 4/1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.47 (s, 1H), 7.27 - 7.19 (m, 3H), 7.10 - 7.01 (m, 3H), 6.61 (s, 1H), 5.64 (s, 2H), 2.48 (s, 3H), 2.47 (s, 3H), 2.34 (s, 3H). $^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) δ 155.0, 147.5, 140.7, 137.6, 136.3, 133.8, 133.6, 128.6 (2 C), 127.0, 125.9 (2 C), 125.8, 122.9, 115.4, 100.9, 51.2, 23.4, 20.3, 14.1. IR (film, cm^{-}

[1]): 1141, 1172, 1201, 1238, 1278, 1344, 1404, 1494, 1564, 1598, 1695. Melting point: 92-97 °C. HRMS (ESI) m/z: $(M + H)^+$ calcd. for $C_{20}H_{20}N_3O$ 318.1601, found 318.1608.



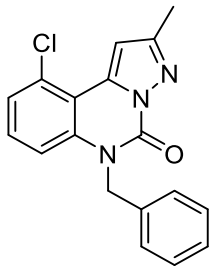
6-Benzyl-9-fluoro-2-methylpyrazolo[1,5-*c*]quinazolin-5(6*H*)-one (2m)

43 mg of the desired compound were obtained with procedure F in 72% yield as a white solid. TLC: Rf = 0.3 (Cyclohexane/Ethyl acetate = 3/1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.39 (dd, J = 8.1, 2.8 Hz, 1H), 7.24 - 7.17 (m, 5H), 7.11 (dd, J = 9.3, 4.4 Hz, 1H), 7.04 - 6.97 (m, 1H), 6.60 (s, 1H), 5.48 (s, 2H), 2.45 (s, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 158.6 (d, J = 245.0 Hz), 155.1, 145.9, 139.5 (d, J = 3.0 Hz), 135.5, 131.6, 129.1 (2 C), 127.8, 126.7 (2 C), 117.8, 117.6 (d, J = 13.5 Hz), 114.9 (d, J = 9.0 Hz), 110.33 (d, J = 24.3 Hz), 101.8, 47.8, 14.2. ^{19}F NMR (188 MHz, $CDCl_3$) δ -118.55. IR (film, cm^{-1}): 1118, 1168, 1240, 1273, 1311, 1496, 1577, 1598, 1697. Melting point: 157-161 °C. HRMS (ESI) m/z: $(M + H)^+$ calcd. for $C_{18}H_{15}FN_3O$ 308.1194, found 308.1196.



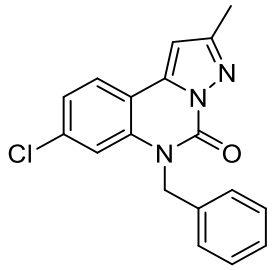
6-Benzyl-9-chloro-2-methylpyrazolo[1,5-*c*]quinazolin-5(6*H*)-one (2n)

41 mg of the desired compound were obtained with procedure F in 65% yield as a white solid. TLC: Rf = 0.3 (Cyclohexane/Ethyl acetate = 2/1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.86 (d, J = 2.3 Hz, 1H), 7.40 (dd, J = 9.0, 2.3 Hz, 1H), 7.29 – 7.20 (m, 5H), 7.04 (d, J = 9.0 Hz, 1H), 6.64 (s, 1H), 5.49 (s, 2H), 2.48 (s, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 155.3, 145.9, 139.1, 135.4, 134.2, 133.0, 129.1 (2 C), 127.9, 127.0 (2 C), 126.7, 117.5, 116.5, 115.4, 101.8, 47.7, 14.3. IR (film, cm^{-1}): 1058, 1115, 1189, 1223, 1296, 1306, 1411, 1469, 1559, 1597, 1621, 1748. Melting point: 145-149 °C. HRMS (ESI) m/z: $(M + H)^+$ calcd. for $C_{18}H_{15}ClN_3O$ 324.0898, found 324.0891.



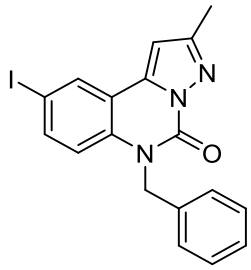
6-Benzyl-10-chloro-2-methylpyrazolo[1,5-*c*]quinazolin-5(6*H*)-one (2o)

46 mg of the desired compound were obtained with procedure F in 71% yield as a white solid. TLC: Rf = 0.2 (Cyclohexane/Ethyl acetate = 3/1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.34 (s, 1H), 7.30 - 7.19 (m, 7H), 7.12 (dd, *J* = 7.8, 1.8 Hz, 1H), 5.54 (s, 2H), 2.51 (s, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 155.0, 145.9, 137.4, 136.9, 135.4, 131.5, 129.6, 129.1 (2 C), 127.8, 126.6 (2 C), 125.6, 114.4, 112.8, 107.5, 48.2, 14.2. IR (film, cm^{-1}): 1028, 1053, 1213, 1247, 1327, 1361, 1438, 1469, 1581, 1597, 1701. Melting point: 109-113 °C. HRMS (ESI) m/z: $(M + H)^+$ calcd. for $C_{18}H_{15}ClN_3O$ 324.0898, found 324.0902.



6-Benzyl-8-chloro-2-methylpyrazolo[1,5-*c*]quinazolin-5(6*H*)-one (2p)

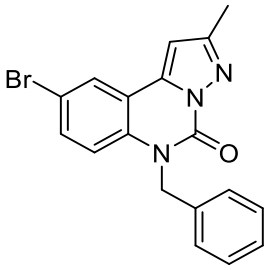
46 mg of the desired compound were obtained with procedure F in 72% yield as a white solid. TLC: Rf = 0.4 (Cyclohexane/Ethyl acetate = 3/1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.66 (dd, *J* = 8.3, 0.5 Hz, 1H), 7.29 – 7.13 (m, 7H), 6.64 – 6.57 (m, 1H), 5.47 (s, 2H), 2.46 (s, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 155.3, 145.9, 139.7, 136.1, 136.0, 135.2, 129.1 (2 C), 128.0, 126.8 (2 C), 125.5, 124.0, 115.8, 112.2, 101.4, 47.6, 14.2. IR (film, cm^{-1}): 1082, 1103, 1116, 1184, 1240, 1344, 1369, 1427, 1494, 1598, 1614, 1693. Melting point: 130-135 °C. HRMS (ESI) m/z: $(M + H)^+$ calcd. for $C_{18}H_{15}ClN_3O$ 324.0898, found 324.0903.



6-Benzyl-9-iodo-2-methylpyrazolo[1,5-*c*]quinazolin-5(6*H*)-one (2q)

46 mg of the desired compound were obtained with procedure F in 55% yield as a white solid. TLC: Rf = 0.2 (Cyclohexane/Ethyl acetate = 3/1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.04 (d, *J* = 2.0 Hz, 1H), 7.57 (dd, *J* = 8.9, 2.0 Hz, 1H), 7.27 – 7.20 (m, 5H), 6.91 (d, *J* = 8.9 Hz, 1H), 6.64 (s, 1H), 5.48 (s, 2H), 2.48 (s, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 155.3, 145.9, 138.9, 138.8, 135.4, 134.8, 132.9, 129.1 (2 C), 127.9, 126.7 (2 C), 117.7, 115.8, 101.7, 86.6, 47.6, 14.3. IR

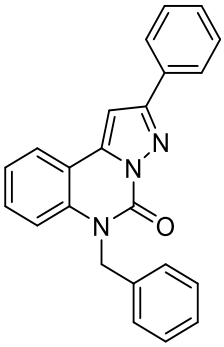
(film, cm^{-1}): 1001, 1130, 1192, 1215, 1238, 1300, 1338, 1490, 1598, 1691. Melting point: 148-152 °C. HRMS (ESI) m/z: $(M + H)^+$ calcd. for $C_{18}H_{15}IN_3O$ 416.0524, found 416.0530.



6-Benzyl-9-bromo-2-methylpyrazolo[1,5-*c*]quinazolin-5(6*H*)-one (2r)

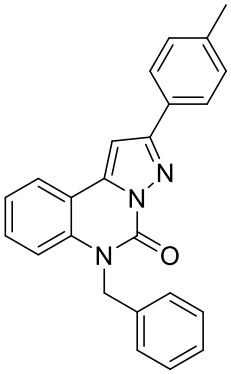
49 mg of the desired compound were obtained with procedure F in 67% yield as a white solid.

Gram-scale reaction: In an oven-dried 10 mL tube, enones (5 mmol, 1.0 equiv.), and *p*-toluenesulfonyl hydrazide (6 mmol, 1.2 equiv.) were dissolved in dioxane (10 mL). The reaction was heated in an oil bath at 90 °C and stirred for 2 h. Then tripotassium phosphate (10 mmol, 2.0 equiv.) was added in the reaction mixture, which was stirred at 110 °C for 3 h. The reaction mixture was concentrated under reduced pressure, and the residue was purified by flash chromatography with cyclohexane to afford the desired product **2r** in a 68% yield (1250 mg) as a white solid.
TLC: Rf = 0.2 (Cyclohexane/Ethyl acetate = 2/1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.73 (d, J = 2.4 Hz, 1H), 7.31 - 7.23 (m, 6H), 7.13 (d, J = 9.0 Hz, 1H), 6.67 (s, 1H), 5.52 (s, 2H), 2.52 (s, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 155.1, 145.8, 139.1, 135.3 (2 C), 133.5, 130.1, 129.0 (2 C), 128.9, 127.8, 126.6 (2 C), 123.8, 117.1, 101.7, 47.6, 14.1. IR (film, cm^{-1}): 1002, 1082, 1130, 1159, 1188, 1205, 1273, 1342, 1375, 1444, 1560, 1612, 1710. Melting point: 155-160 °C. HRMS (ESI) m/z: $(M + H)^+$ calcd. for $C_{18}H_{15}BrN_3O$ 368.0393, found 368.0393.



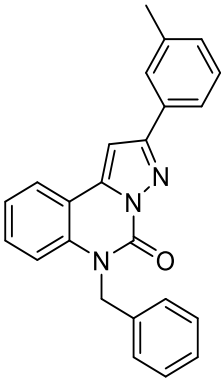
6-Benzyl-2-phenylpyrazolo[1,5-*c*]quinazolin-5(6*H*)-one (2s)

58 mg of the desired compound were obtained with procedure G in 82% yield as a white solid.
TLC: Rf = 0.5 (Cyclohexane/Ethyl acetate = 4/1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.03 – 7.99 (m, 2H), 7.82 (d, J = 7.8 Hz, 1H), 7.44 – 7.17 (m, 11H), 7.12 (s, 1H), 5.51 (s, 2H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 156.5, 146.4, 141.1, 135.8, 135.3, 131.9, 130.5, 129.4, 129.0 (2 C), 128.8 (2 C), 127.8, 127.0 (2 C), 126.9 (2 C), 124.6, 123.8, 115.8, 113.8, 98.2, 47.7. IR (film, cm^{-1}): 1014, 1174, 1228, 1259, 1336, 1367, 1440, 1485, 1568, 1618, 1705, 2233. Melting point: 185-191 °C. HRMS (ESI) m/z: $(M + H)^+$ calcd. for $C_{23}H_{18}N_3O$ 352.1444, found 352.1448.



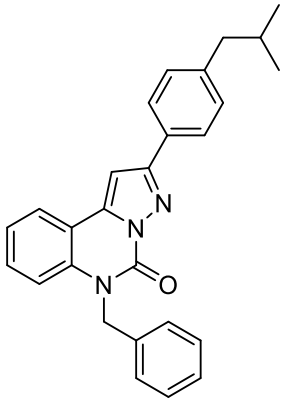
6-benzyl-2-(*p*-tolyl)pyrazolo[1,5-c]quinazolin-5(6H)-one (2t)

59 mg of the desired compound were obtained with procedure G in 81% yield as a white solid. TLC: Rf = 0.3 (Cyclohexane/Ethyl acetate = 3/1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.91 (d, J = 8.1 Hz, 2H), 7.82 – 7.79 (m, 1H), 7.34 – 7.16 (m, 10H), 7.08 (s, 1H), 5.50 (s, 2H), 2.33 (s, 3H). ^{13}C{1H} NMR (75 MHz, $CDCl_3$) δ 156.5, 146.4, 141.0, 139.4, 135.8 (2C), 135.2, 130.4, 129.5 (2C), 129.1, 129.0 (2C), 127.8, 126.9 (4C), 124.6, 123.7, 115.8, 113.8, 98.0, 47.7, 21.5. IR (film, cm^{-1}):1104, 1158, 1222, 1285, 1326, 1357, 1429, 1493, 1585, 1658, 1736. Melting point: 136-140 °C. HRMS (ESI) m/z: $(M + H)^+$ calcd. for $C_{24}H_{20}N_3O$ 366.1601, found 366.1607.



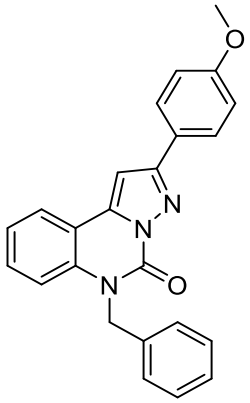
6-Benzyl-2-(*m*-tolyl)pyrazolo[1,5-*c*]quinazolin-5(6*H*)-one (2u)

55 mg of the desired compound were obtained with procedure G in 75% yield as a white solid. TLC: Rf = 0.5 (Cyclohexane/Ethyl acetate = 5/1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.98 (s, 1H), 7.91 (d, *J* = 7.8 Hz, 1H), 7.85 (d, *J* = 7.6 Hz, 1H), 7.39 – 7.19 (m, 11H), 5.60 (s, 2H), 2.44 (s, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 156.7, 146.5, 141.0, 138.6, 135.8, 135.3, 131.8, 130.5, 130.2, 129.1 (2 C), 128.7, 127.8, 127.7, 126.9 (2 C), 124.6, 124.1, 123.7, 115.8, 113.9, 98.2, 47.8, 21.5. IR (film, cm^{-1}): 1078, 1190, 1207, 1255, 1311, 1330, 1363, 1444, 1483, 1566, 1616, 1697. Melting point: 182-187 °C. HRMS (ESI) m/z: $(M + H)^+$ calcd. for $C_{24}H_{20}N_3O$ 366.1601, found 366.1606.



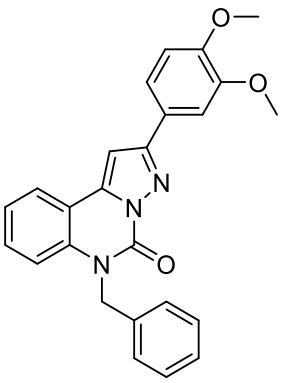
6-Benzyl-2-(4-isobutylphenyl)pyrazolo[1,5-*c*]quinazolin-5(6*H*)-one (2w)

50 mg of the desired compound were obtained with procedure G in 50% yield as a white solid. TLC: Rf = 0.5 (Cyclohexane/Ethyl acetate = 5/1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.95 (d, J = 8.2 Hz, 2H), 7.84 (dd, J = 8.2, 1.4 Hz, 1H), 7.36 – 7.18 (m, 10H), 7.11 (s, 1H), 5.53 (s, 2H), 2.49 (d, J = 7.2 Hz, 2H), 1.87 (dq, J = 13.6, 6.8 Hz, 1H), 0.91 (s, 3H), 0.88 (s, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 156.6, 146.4, 143.3, 141.0, 135.8, 135.3, 130.4, 129.6 (2 C), 129.4, 129.0 (2 C), 127.8, 126.9 (2 C), 126.8 (2 C), 124.6, 123.7, 115.8, 113.8, 98.1, 47.7, 45.4, 30.3, 22.5 (2 C). IR (film, cm^{-1}): 1026, 1056, 1120, 1174, 1230, 1307, 1336, 1363, 1442, 1485, 1566, 1597, 1616, 1705. Melting point: 203-208 °C. HRMS (ESI) m/z: $(M + H)^+$ calcd. for $C_{27}H_{26}N_3O$ 408.2070, found 408.2077.



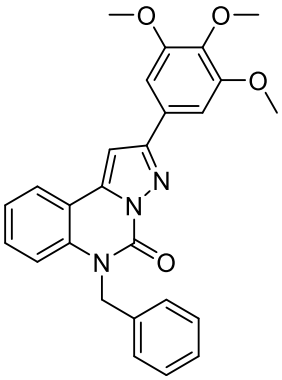
6-Benzyl-2-(4-methoxyphenyl)pyrazolo[1,5-*c*]quinazolin-5(6*H*)-one (2x)

56 mg of the desired compound were obtained with procedure G in 73% yield as a white solid. TLC: Rf = 0.5 (Cyclohexane/Ethyl acetate = 5/1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.05 – 8.00 (m, 2H), 7.89 (d, J = 7.8 Hz, 1H), 7.42 - 7.25 (m, 8H), 7.12 (s, 1H), 7.02 – 6.97 (m, 2H), 5.59 (s, 2H), 3.86 (s, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 160.8, 156.3, 146.5, 141.0, 135.9 (2 C), 135.3, 130.4, 129.0 (2 C), 128.4 (2 C), 127.8, 126.9 (2 C), 124.6, 123.7, 115.8, 114.2 (2 C), 113.8, 97.8, 55.5, 47.7. IR (film, cm^{-1}): 1028, 1053, 1170, 1247, 1311, 1336, 1367, 1446, 1485, 1529, 1697, 2233. Melting point: 195-201 °C. HRMS (ESI) m/z: $(M + H)^+$ calcd. for $C_{24}H_{20}N_3O_2$ 382.1550, found 382.1555.



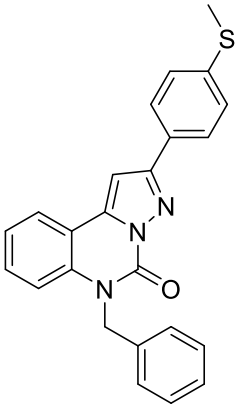
6-Benzyl-2-(3,4-dimethoxyphenyl)pyrazolo[1,5-*c*]quinazolin-5(6*H*)-one (2y)

53 mg of the desired compound were obtained with procedure G in 64% yield as a white solid. TLC: Rf = 0.5 (Cyclohexane/Ethyl acetate = 4/1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.91 (dd, *J* = 8.1, 1.4 Hz, 1H), 7.75 (d, *J* = 2.0 Hz, 1H), 7.55 (dd, *J* = 8.3, 2.0 Hz, 1H), 7.45 - 7.39 (m, 1H), 7.36 – 7.34 (m, 3H), 7.32 – 7.27 (m, 4H), 7.16 (s, 1H), 6.96 (d, *J* = 8.3 Hz, 1H), 5.60 (s, 2H), 4.03 (s, 3H), 3.95 (s, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) *δ* 156.4, 150.3, 149.4, 146.5, 141.0, 135.8, 135.3, 130.5, 129.0 (2 C), 127.8, 126.9 (2 C), 124.9, 124.6, 123.7, 119.9, 115.8, 113.7, 111.1, 109.8, 97.9, 56.3, 56.0, 47.7. IR (film, cm^{-1}): 1028, 1116, 1161, 1217, 1247,1313, 1365, 1435, 1473, 1485, 1529, 1570, 1620, 1708. Melting point: 217-222 °C. HRMS (ESI) m/z: $(M + H)^+$ calcd. for $C_{25}H_{22}N_3O_3$ 412.1656, found 412.1662.



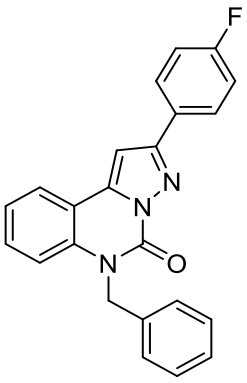
6-Benzyl-2-(3,4,5-trimethoxyphenyl)pyrazolo[1,5-*c*]quinazolin-5(6*H*)-one (2z)

50 mg of the desired compound were obtained with procedure G in 56% yield as a white solid. TLC: Rf = 0.5 (Cyclohexane/Ethyl acetate = 3/1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.91 (dd, *J* = 8.1, 1.6 Hz, 1H), 7.44 – 7.38 (m, 1H), 7.33 – 7.24(m, 9H), 7.16 (s, 1H), 5.58 (s, 2H), 3.97 (s, 6H), 3.91 (s, 3H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) *δ* 156.4, 153.6, 146.4, 141.1, 139.5, 135.7 (2 C), 135.3, 130.6, 129.0 (2 C), 127.8, 127.4, 126.9 (2 C), 124.6, 123.8, 115.8, 113.7, 104.3 (2 C), 98.2, 61.0, 56.5 (2 C), 47.8. IR (film, cm^{-1}): 1122, 1157, 1190, 1232, 1251, 1309, 1361, 1460, 1485, 1568, 1616, 1705. Melting point: 195-201 °C. HRMS (ESI) m/z: $(M + H)^+$ calcd. for $C_{26}H_{24}N_3O_4$ 442.1761, found 442.1768.



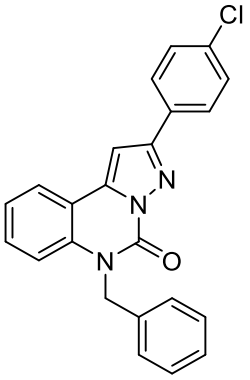
6-benzyl-2-(*p*-tolyl)pyrazolo[1,5-c]quinazolin-5(6H)-one (2aa)

59 mg of the desired compound were obtained with procedure G in 81% yield as a white solid. TLC: Rf = 0.4 (Cyclohexane/Ethyl acetate = 3/1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.00 (d, J = 8.5 Hz, 2H), 7.89 (d, J = 7.8 Hz, 1H), 7.43 – 7.26 (m, 10H), 7.15 (s, 1H), 5.59 (s, 2H), 2.53 (s, 3H). ^{13}C{1H} NMR (75 MHz, $CDCl_3$) δ 155.9, 146.3, 141.0, 140.2, 135.6, 135.2, 130.4, 128.9 (2 C), 128.4, 127.7, 127.2 (2 C), 126.8 (2 C), 126.3 (2 C), 124.5, 123.6, 115.7, 113.6, 97.8, 47.6, 15.5. IR (film, cm^{-1}): 1025, 1088, 1124, 1199, 1214, 1365, 1397, 1468, 1526, 1678, 1698, 1745. Melting point: 147-151 °C. HRMS (ESI) m/z: $(M + H)^+$ calcd. for $C_{24}H_{20}N_3OS$ 398.1322, found 398.1325.



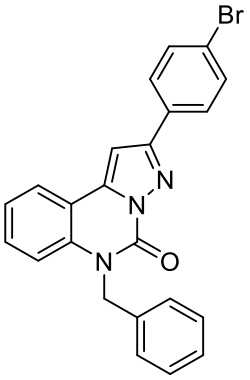
6-Benzyl-2-(4-fluorophenyl)pyrazolo[1,5-*c*]quinazolin-5(6*H*)-one (2ab)

45 mg of the desired compound were obtained with procedure G in 60% yield as a white solid. TLC: Rf = 0.4 (Cyclohexane/Ethyl acetate = 5/1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.10 – 8.03 (m, 2H), 7.91 (dd, J = 8.1, 1.5 Hz, 1H), 7.45 – 7.24 (m, 8H), 7.19 – 7.12 (m, 3H), 5.60 (s, 2H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 163.7 (d, J = 249.2 Hz), 155.6, 146.4, 141.3, 135.7, 135.4, 130.7, 129.1 (2 C), 128.9, 128.8, 128.2 (d, J = 3.8 Hz), 127.9, 126.9 (2 C), 124.6, 123.8, 115.9 (2 C), 115.8 (d, J = 21.0 Hz), 113.8, 98.0, 47.8. ^{19}F NMR (188 MHz, $CDCl_3$) δ -111.99. IR (film, cm^{-1}): 1014, 1155, 1174, 1220, 1255, 1313, 1332, 1438, 1483, 1527, 1570, 1670, 1602, 1618. Melting point: 205-210 °C. HRMS (ESI) m/z: $(M + H)^+$ calcd. for $C_{23}H_{17}FN_3O$ 370.1350, found 370.1356.



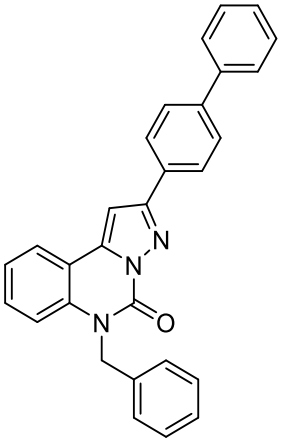
6-Benzyl-2-(4-chlorophenyl)pyrazolo[1,5-*c*]quinazolin-5(6*H*)-one (2ac)

52 mg of the desired compound were obtained with procedure G in 67% yield as a white solid. TLC: Rf = 0.4 (Cyclohexane/Ethyl acetate = 5/1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.90 – 7.85 (m, 2H), 7.75 (d, *J* = 7.8 Hz, 1H), 7.32 – 7.25 (m, 3H), 7.20 – 7.10 (m, 7H), 7.02 (s, 1H), 5.46 (s, 2H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 155.4, 146.4, 141.3, 135.7, 135.4, 135.3, 130.7, 130.4, 129.1 (3 C), 128.2 (3 C), 127.9, 126.9 (2 C), 124.6, 123.9, 115.9, 113.7, 98.1, 47.8. IR (film, cm^{-1}): 1012, 1022, 1053, 1109, 1249, 1309, 1328, 1369, 1433, 1485, 1560, 1591, 1614, 1712. Melting point: 242-247 °C. HRMS (ESI) m/z: $(M + H)^+$ calcd. for $C_{23}H_{17}ClN_3O$ 386.1055, found 386.1060.



6-Benzyl-2-(4-chlorophenyl)pyrazolo[1,5-*c*]quinazolin-5(6*H*)-one (2ad)

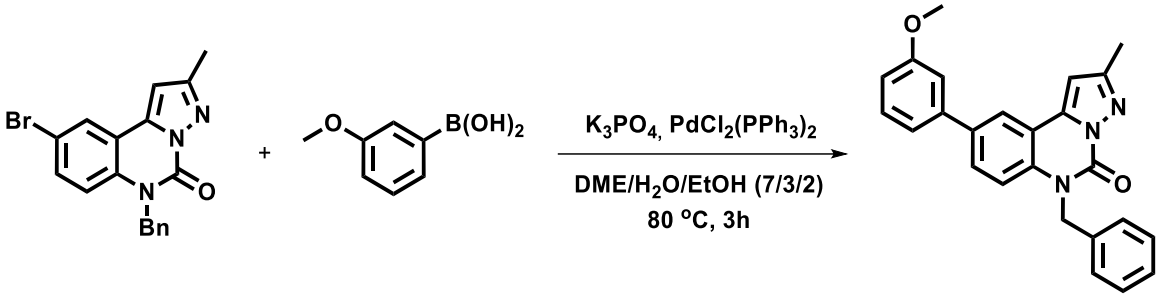
54 mg of the desired compound were obtained with procedure G in 62% yield as a white solid. TLC: Rf = 0.5 (Cyclohexane/Ethyl acetate = 3/1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.90 - 7.81 (m, 3H), 7.54 – 7.50 (m, 2H), 7.38 – 7.32 (m, 1H), 7.26 – 7.18 (m, 7H), 7.09 (s, 1H), 5.52 (s, 2H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 155.4, 146.4, 141.3, 135.7, 135.3, 132.1 (2 C), 130.9, 130.7, 129.1 (2 C), 128.5 (2 C), 127.9, 126.9 (2 C), 124.7, 123.9, 123.7, 115.9, 113.7, 98.1, 47.8. IR (film, cm^{-1}): 1005, 1056, 1079, 1115, 1199, 1268, 1358, 1402, 1468, 1496, 1555, 1569, 1659, 1701, 1712. Melting point: 250-255 °C. HRMS (ESI) m/z: $(M + H)^+$ calcd. for $C_{23}H_{17}BrN_3O$ 430.0550, found 430.0551.



2-([1,1'-Biphenyl]-4-yl)-6-benzylpyrazolo[1,5-*c*]quinazolin-5(6*H*)-one (2ae)

51 mg of the desired compound were obtained with procedure G in 60% yield as a white solid. TLC: Rf = 0.5 (Cyclohexane/Ethyl acetate = 5/1). ^{1}H NMR (300 MHz, $(CD_3)_2SO$) δ 8.15 (d, *J* = 8.0 Hz, 3H), 7.86 – 7.75 (m, 5H), 7.53 – 7.26 (m, 11H), 5.59 (s, 2H). $^{13}C\{^{1}H\}$ NMR (75 MHz, $(CD_3)_2SO$) *δ* 154.7, 145.5, 141.0, 140.8, 139.4, 136.1, 134.8, 130.8, 130.6, 129.0 (2 C), 128.7 (2 C), 127.7, 127.3, 127.2 (2 C), 126.8 (2 C), 126.6 (2 C), 126.5 (2 C), 124.6, 123.6, 115.9, 113.1, 98.8, 46.6. IR (film, cm^{-1}): 1056, 1118, 1174, 1224, 1257, 1303, 1315, 1336, 1440, 1485, 1570, 1598, 1618, 1707. Melting point: 218-224 °C. HRMS (ESI) m/z: $(M + H)^+$ calcd. for $C_{29}H_{22}N_3O$ 428.1757, found 428.1760.

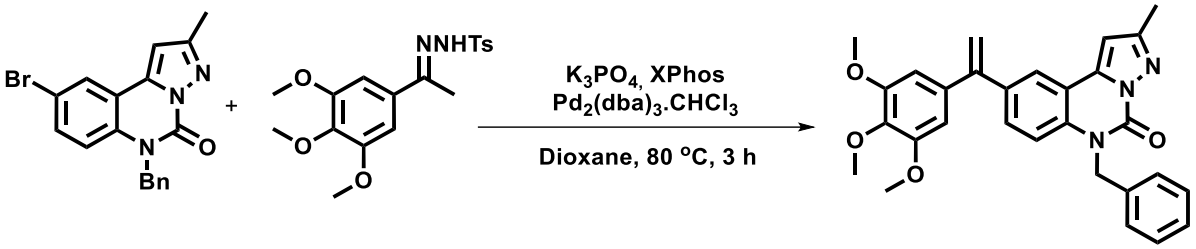
Post-functionalization reactions



6-Benzyl-9-(3-methoxyphenyl)-2-methylpyrazolo[1,5-*c*]quinazolin-5(6*H*)-one (3)

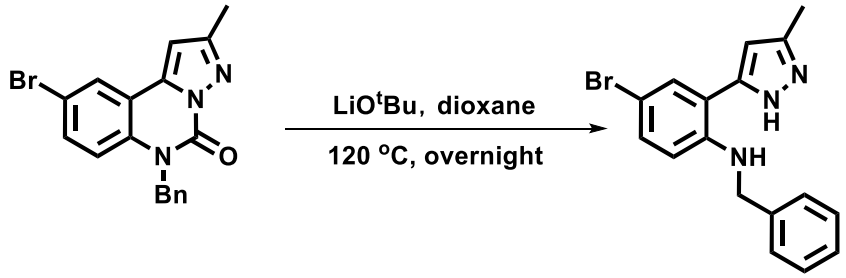
To an oven-dried sealed tube, under argon atmosphere, the bromo compound (73 mg, 0.2 mmol, 1.0 equiv.) and potassium phosphate (84 mg, 0.4 mmol, 2.0 equiv.), 3-methoxyphenylboronic acid (37 mg, 0.2 mmol, 1.2 equiv.), dichlorobis(triphenylphosphine)palladium(II) (7 mg, 0.01 mmol, 5 mol%) were dissolved into a solvent mixture of 1,2-dimethoxy ethane/water/ethanol (7/3/2, 2.4 mL). The reaction was stirred at 80 °C for 3 hours. The crude mixture was then extracted three times with ethyl acetate. The organic phase was washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (Cyclohexane/Ethyl acetate: 4/1) as eluent to obtain the corresponding product. 60 mg of the desired compound was obtained in 83% yield as a white solid. TLC: Rf = 0.5 (Cyclohexane/Ethyl acetate = 3/1). ^{1}H NMR (300 MHz, $CDCl_3$) *δ* 7.86 (d, *J* = 2.1 Hz, 1H), 7.47 (dd, *J* = 8.8, 2.1 Hz, 1H), 7.29 – 7.14 (m, 7H), 7.06 – 7.02 (m, 1H), 7.00

– 6.96 (m, 1H), 6.83 – 6.79 (m, 1H), 6.64 (s, 1H), 5.47 (s, 2H), 3.76 (s, 3H), 2.43 (s, 3H). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 160.2, 155.1, 146.2, 140.9, 140.4, 136.6, 135.8, 134.5, 130.1, 129.1, 129.0 (2 C), 127.7, 126.8 (2 C), 122.6, 119.4, 116.2, 114.0, 113.0 (2 C), 101.3, 55.4, 47.5, 14.3. IR (film, cm^{-1}): 1001, 1045, 1247, 1340, 1450, 1479, 1510, 1558, 1600, 1722. Melting point: 92-96 °C. HRMS (ESI) m/z: $(M + H)^+$ calcd. for $C_{25}H_{22}N_3O_2$ 396.1707, found 396.1710.



6-Benzyl-2-methyl-9-(1-(3,4,5-trimethoxyphenyl)vinyl)pyrazolo[1,5-*c*]quinazolin-5(6*H*)-one (4)

To an oven-dried sealed tube, under argon atmosphere, the bromo compound (73 mg, 0.2 mmol, 1.0 equiv.) and potassium phosphate (84 mg, 0.4 mmol, 2.0 equiv.), *N*-tosylhydrazone (90 mg, 0.24 mmol, 1.2 equiv.), XPhos (9.5 mg, 0.02 mmol, 10 mol%), $Pd_2(dba)_3.CHCl_3$ (10 mg, 0.01 mmol, 5 mol%) were dissolved in dioxane (1 mL). Then, the reaction was stirred at 80 °C for 3 hours. The crude mixture was extracted three times with ethyl acetate, and the organic phase was concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (Cyclohexane/Ethyl acetate: 6/1) as eluent to obtain the corresponding product. 58 mg of the desired compound was obtained in 60% yield as a white solid. TLC: Rf = 0.5 (Cyclohexane/Ethyl acetate = 2/1). ^1H NMR (300 MHz, $CDCl_3$) δ 7.74 (d, J = 2.0 Hz, 1H), 7.32 (dd, J = 8.8, 2.0 Hz, 1H), 7.26 - 7.24 (m, 3H), 7.21 – 7.14 (m, 3H), 6.62 (s, 1H), 6.46 (s, 2H), 5.51 (s, 2H), 5.40 (s, 2H), 3.83 (s, 3H), 3.73 (s, 6H), 2.45 (s, 3H). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 155.1, 153.2 (2 C), 148.6, 146.2, 140.3, 138.3, 136.8, 136.5, 135.8, 134.8, 130.3, 129.0 (2 C), 127.7, 126.9 (2 C), 123.8, 115.6, 114.6, 113.6, 105.8 (2 C), 101.3, 61.0, 56.3 (2 C), 47.6, 14.2. IR (film, cm^{-1}): 1025, 1037, 1124, 1232, 1338, 1340, 1409, 1500, 1577, 1598, 1712. Melting point: 110-114 °C. HRMS (ESI) m/z: $(M + H)^+$ calcd. for $C_{29}H_{28}N_3O_4$ 482.2074, found 482.2077.



***N*-Benzyl-4-bromo-2-(3-methyl-1*H*-pyrazol-5-yl)aniline (5)**

A mixture of bromo compound (73 mg, 0.2 mmol, 1.2 equiv.) and LiO^tBu (32 mg, 0.8 mmol, 2.0 equiv.) was added in dioxane (2 mL). The reaction mixture was stirred at 120 °C overnight. Then, the solvent was evaporated under vacuum, and the reaction crude was purified by column chromatography on silica gel (Petroleum ether/EtOAc = 12/1) to afford the corresponding product. 22 mg of the desired compound was obtained in 32% yield as a white solid. TLC: Rf = 0.5 (Cyclohexane/Ethyl acetate = 8/1). ^1H NMR (300 MHz, $CDCl_3$) δ 7.82 (d, J = 2.4 Hz, 1H), 7.55 (d, J = 2.4 Hz, 1H), 7.32 – 7.18 (m, 5H), 7.13 (dd, J = 8.8, 2.4 Hz, 1H), 6.47 (d, J = 8.8 Hz, 1H), 6.32 (s, 1H), 4.39 (s, 2H), 2.27 (s, 3H). $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 152.1,

145.1, 139.7, 139.5, 131.2, 130.7, 128.7 (2 C), 127.2 (2 C), 127.1, 118.2, 112.9, 107.4, 102.9, 47.7, 10.9. IR (film, cm^{-1}): 1026, 1145, 1240, 1292, 1319, 1354, 1450, 1508, 1570, 2850, 3112, 3423. Melting point: 83-88 °C. HRMS (ESI) m/z: $(M + H)^+$ calcd. for $C_{17}H_{17}BrN_3$ 342.0600, found 342.0605.

Crystallographic data collection, structure determination and refinement

Crystals suitable for Single crystal X-ray diffraction (SCXRD) were obtained by dissolving the compound **2a** in acetone, followed by slow solvent evaporation. X-ray diffraction experiment was performed at room temperature on a colorless massive crystal using a RIGAKU XtaLabPro diffractometer. Its microfocus sealed tube mm003 generator coupled to a double-bounce confocal Max-Flux® multilayer optics, emitted the diffracted radiation at the Mo Ka wavelength, which was captured by an HPAD PILATUS3R 200K detector. The data processing was performed using *CrysAlisPro*.[9] A combination of absorption correction methods was employed, including a numerical method based on Gaussian integration over a multifaceted crystal model and an empirical method using spherical harmonics, as implemented in the SCALE3 ABSPACK scaling algorithm. The structure was solved by Intrinsic Phasing methods (*SHELXT* program),[10] and refined with full-matrix least-squares methods on F^2 using *SHELX-L*.[11] Displacement parameters for all non-hydrogen atoms within the asymmetric unit (asu) of the centrosymmetric triclinic cell were refined anisotropically. Aromatic hydrogen atoms were positioned geometrically and refined with U_{iso} set to $1.2U_{eq}$(C) of the parent carbon atom. The methyl groups were refined as an idealized rigid group that could rotate but not tip (AFIX 137), and U(H) values were fixed at $1.5U_{eq}$ (C). The final structure was achieved through Hirshfeld atom refinement (HAR)[12] using aspherical scattering factors via *NoSpherA2* [13] partitioning in *Olex2*.[14] This was based on electron density obtained from iterative single-determinant SCF single-point DFT calculations using *ORCA* [15] with a PBE[16] functional using non-relativistic Hamiltonian and a cc-pVTZ basis set.[17] Any of these wavefunctions were read by the *NoSpherA2* software and the related electron-density was partitioned into Hirshfeld atoms. The Fourier transforms are these atoms are the non-spherical scattering factors, which were then tabulated in a .tsc file and provided to *olex2.refine* [18] for the L-M refinement. In this HAR approach, all hydrogen atoms were refined independently and anisotropically. There are currently nine structures of pyrazolo-[1,5-*c*]quinazolinone present in the Cambridge Structural Database (CSD; [19] Conquest 2023.3.0; CSD version 5.45, update of March 2024). Similarly to **2a,** all these structures show a quasi-planar hetero-membered tricyclic platform. One structure is monosubstituted in C10 (acetate group) (CCDC RefCode HUGHAV);[20] two structures are disubstituted like **2a** (in C9 (methyl group) and N1 (benzyl group)): CCDC RefCode VACJOB,[21] in C10 (methoxyphenyl group) and N1 (benzyl group) and CCDC RefCode ERAPOF,[22] in C9 (nitrophenyl group) and C10 (acetate group). Two structures have a phenyl group fused with the pyrazol moiety and a substitution in N1 (benzyl group, (respectively, phenyl group): CCDC RefCode TEGCAM [23] (resp., AYEXAG [24]). Four structures are three-times substituted: CCDC RefCode JUMNEM,[25] in C9 (dimethoxy phosphate group), in C10 (benzaldehyde group), and in C5 (F atom), CCDC RefCode HEZNAE, [26] in C9 (difluoroalkyl group), in C10 (acetate group), and in N1 (methyl group), and CCDC RefCode WIQPOF [27] and

XEXQOK,[28] in N1 (benzyl group) and alternately in 9 and C10 with a formate group and a CF3 group.

Crystal data, data collection and structure refinement details are summarized in Table S1. CCDC 2341570 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Figure S1

Ortep view of the structure of product **2a**. Displacement ellipsoids are shown at the 50% probability level. The hydrogen atoms are represented as ellipsoids as well.

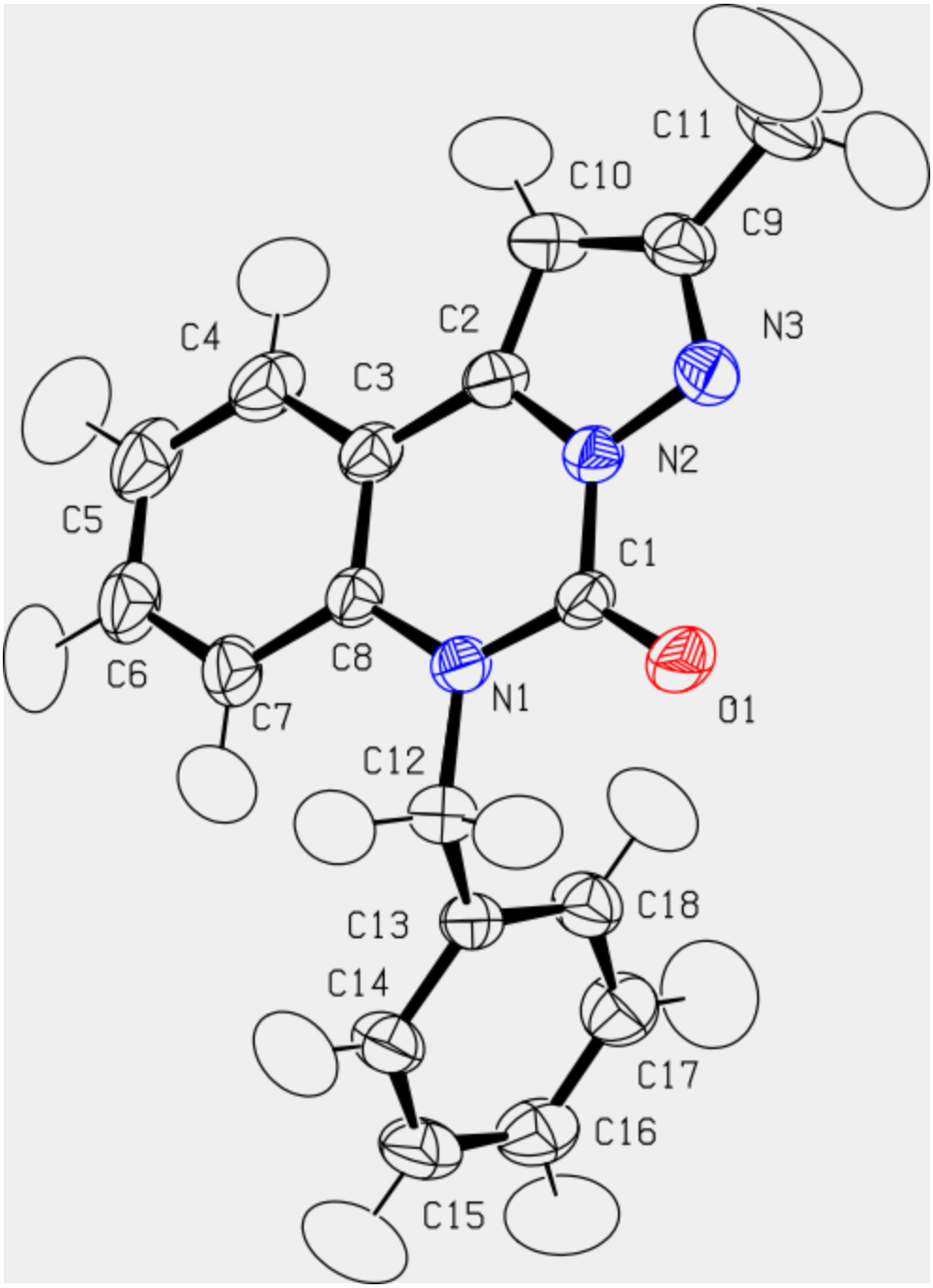
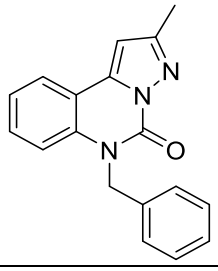


Table S1 Crystal data, data collection and structure refinement details for the product **2a.**

Compound		***Product 2a***
		
Chemical name		*6-benzyl-2-methylpyrazolo[1,5-c]quinazolin-5(6H)-one*
Empirical formula		$C_{18}\,H_{15}\,N_3\,O$
Formula weight		289.34
Temperature (K)		293(2)
Wavelength (Å)		0.71073
Crystal system, space group		Monoclinic, *P* 2_1/c
Unit cell dimensions	a | (Å) b c β | (°)	15.8567(6) 9.2722(4) 9.8086(4) 96.020(4)
Volume (Å^3)		1434.17(10)
Z, Calculated density (Mg/m^3)		4, 1.340
Absorption coefficient (mm^{-1})		0.086
F(000)		608
Crystal size (mm)		0.48 x 0.23 x 0.09
θ range for data collection (°)		3.03 to 30.50
Limiting indices		$-23 \le h \le 22$, $-13 \le k \le 14$, $-14 \le l \le 11$
Reflections collected / unique [R(int)		26314 / 4365 0.0307
Completeness to θ_{full} (%)		99.9
Absorption correction		Gaussian/Semi-empirical from equivalents
Max. and min. transmission		1.000 and 0.639
Refinement method		HAR, Full-matrix least-squares on F^2
Data / restraints / parameters		4365 / 0 / 335
Goodness-of-fit on F^2		1.0994
Final R indices [$I>2\sigma(I)$]	R1 wR2	0.0242 0.0441
R indices (all data)	R1 wR2	0.0377, 0.0474
Extinction coefficient		0.0187(13)
Largest Δ peak and hole (e.Å^{-3})		0.121 and -0.134
CCDC deposit number		2341570

References

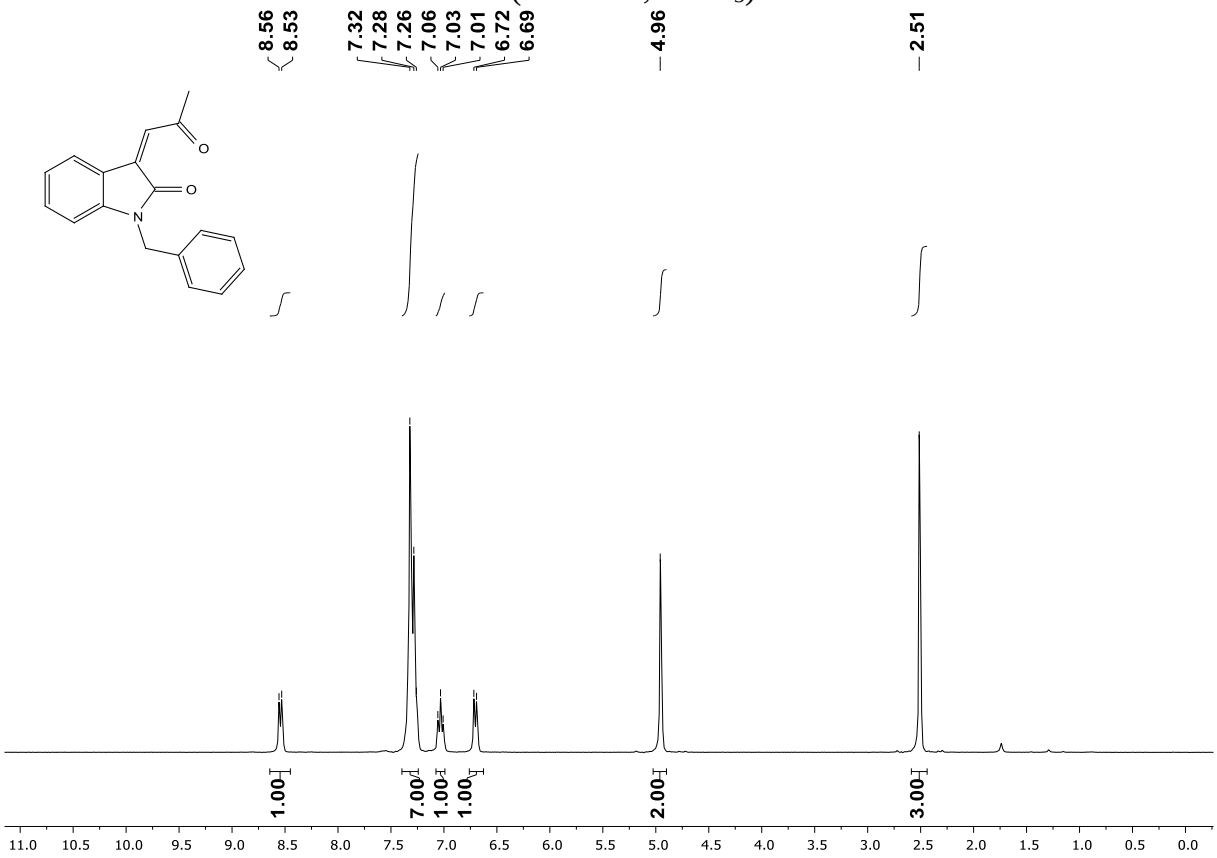
1. Zhang, X.-C.; Cao, S.-H.; Wei, Y.; Shi, M., Phosphine-catalyzed highly diastereoselective [3+2] cyclization of isatin derived electron-deficient alkenes with α-allenic esters. *Chem. Commun.* **2011,** *47* (5), 1548-1550.
2. Nagle, A. A.; Reddy, S. A.; Bertrand, H.; Tajima, H.; Dang, T.-M.; Wong, S.-C.; Hayes, J. D.; Wells, G.; Chew, E.-H., 3-(2-Oxoethylidene)indolin-2-one Derivatives Activate Nrf2 and Inhibit NF-κB: Potential Candidates for Chemoprevention. *ChemMedChem* **2014,** *9* (8), 1763-1774.
3. Majik, M. S.; Rodrigues, C.; Mascarenhas, S.; D'Souza, L., Design and synthesis of marine natural product-based 1H-indole-2,3-dione scaffold as a new antifouling/antibacterial agent against fouling bacteria. *Bioorg. Chem.* **2014,** *54*, 89-95.
4. Tang, Q.-G.; Cai, S.-L.; Wang, C.-C.; Lin, G.-Q.; Sun, X.-W., Organocatalytic Aza-Michael/Michael Cyclization Cascade Reaction: Enantioselective Synthesis of Spiro-oxindole Piperidin-2-one Derivatives. *Org. Lett.* **2020,** *22* (9), 3351-3355.
5. Sohail, M.; Tanaka, F., Dynamic Kinetic Asymmetric Transformation of Racemic Diastereomers: Diastereo- and Enantioconvergent Michael–Henry Reactions to Afford Spirooxindoles Bearing Furan-Fused Rings. *Angew. Chem. Int. Ed.* **2021,** *60* (39), 21256-21260.
6. Cao, S.-H.; Zhang, X.-C.; Wei, Y.; Shi, M., Chemoselective Reduction of Isatin-Derived Electron-Deficient Alkenes Using Alkylphosphanes as Reduction Reagents. *Eur. J. Org. Chem.* **2011,** *2011* (14), 2668-2672.
7. Pramanik, S.; Saha, P.; Ghosh, P.; Mukhopadhyay, C., Steric-Hindrance-Induced Diastereoselective Radical Nitration of 3-Alkylidene-2-oxindoles Followed by Tosylhydrazine-Mediated Sulfonation. *J. Org. Chem.* **2023,** *88* (6), 3386-3402.
8. Petrini, M.; Chiurchiù, E.; Rossi, F. V.; Palmieri, A., Oxidative Conversion of Sulfonyl Indoles into 3-Alkylidene-2-oxindoles under Flow Chemical Conditions. *Synthesis* **2018,** *50* (02), 371-376.

9 Rigaku OD (2015). *CrysAlis PRO*. Rigaku Oxford Diffraction, Yarnton, Oxfordshire, England.
10 Sheldrick, G. M. (2015). *Acta Crystallogr.*, **C**71, 3-8.
11 Sheldrick, G. M. (2015). *Acta Crystallogr.*, **A**71, 3-8.
12 Fugel, M., Jayatilaka, D., Hupf, E., Overgaard, J., Hathwar, V. R., Macchi, P., Turner, M. J., Howard, J. A. K., Dolomanov, O. V., Puschmann, H., Iversen, B. B., Bürgi, H.-B. & Grabowsky, S. (2018). *IUCrJ*, 5, 32–44.
13 Kleemiss, F., Dolomanov, O. V., Bodensteiner, M., Peyerimhoff, N., Midgley, L., Bourhis, L. J., Genoni, A., Malaspina, L. A., Jayatilaka, D., Spencer, J. L., White, F., Grundkötter-Stock, B., Steinhauer, S., Lentz, D., Puschmann, H. & Grabowsky, S. (2021). *Chem. Sci.* 12, 1675–1692; Midgley, L., Bourhis, L. J., Dolomanov, O. V., Grabowsky, S., Kleemiss, F., Puschmann, H. & Peyerimhoff, N. (2021). *Acta Cryst.* A77, 519–533.
14 Dolomanov, O. V., Bourhis, L. J., Gildea, R. J., Howard, J. A. K. & Puschmann, H. (2009). *J. Appl. Cryst.* 42, 339–341.
15 Neese, F. (2012). *WIREs Comput. Mol. Sci.* 2, 73–78; Neese, F., Wennmohs, F., Becker, U. & Riplinger, C. (2020). *J. Chem. Phys.* 152, 224108.
16 Adamo, C. & Barone, V. (1999). *J. Chem. Phys.* 110, 6158–6170.
17 Dunning, T. H. (1989). *J. Chem. Phys.* 90, 1007–1023.
18 Bourhis, L. J., Dolomanov, O. V., Gildea, R. J., Howard, J. A. K. & Puschmann, H. (2015). *Acta Cryst.* A71, 59–75.
19 Groom, C. R. & Allen, F. H. (2014). *Angew. Chem. Int. Ed.* **53**, 662-671.

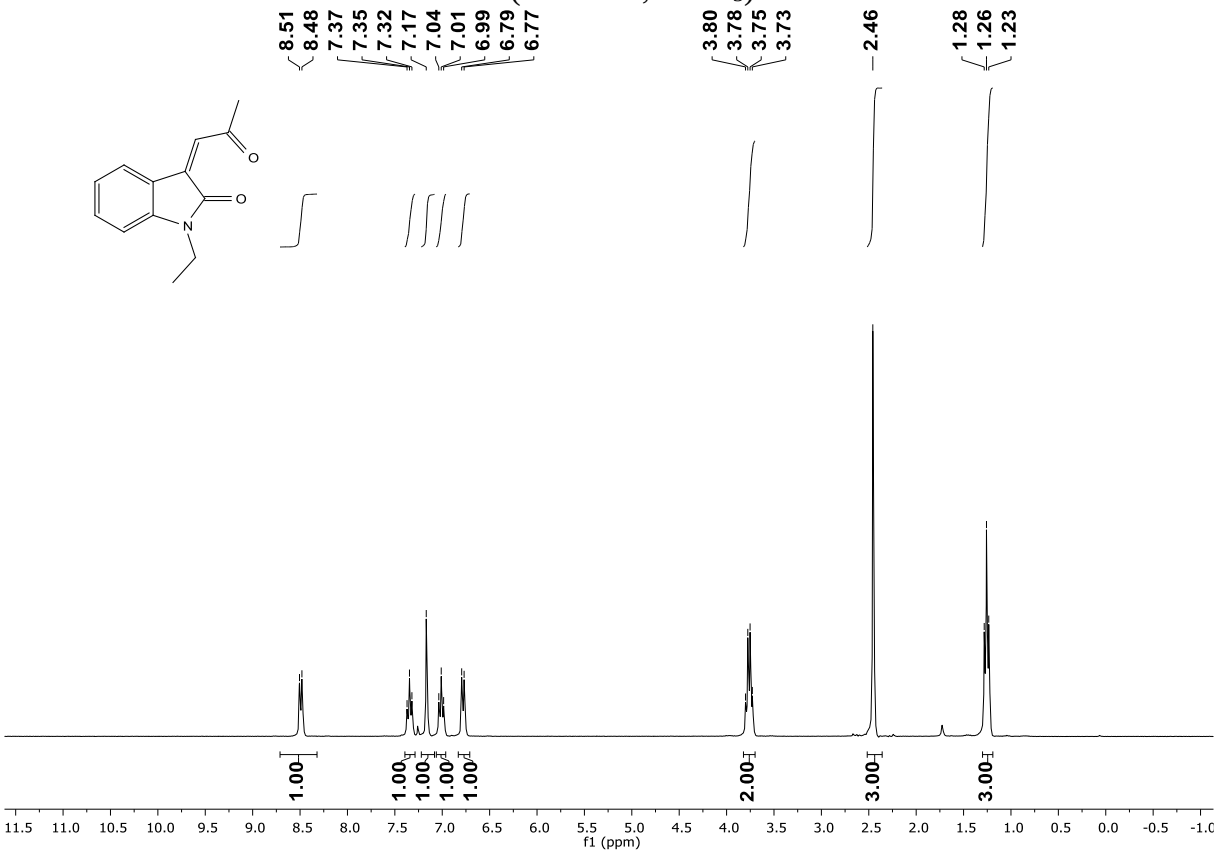
20 Ramu, G., Tangella, Y., Ambala, S., Babu, B.N. (2020) *J.Org.Chem.*, **85,** 5370-5378.
21 Chen, Q., Li, K., Lu, T., Zhou, Q. (2016) *RSC Advances*, **6,** 24792-24796.
22 Ramu, G., Krishna, N.H., Pawar, G., Visweswara Sastry, K.N., Nanubolu, J.B., Babu, B.N. (2018) *ACS Omega*, **3,** 12349-12360.
23 Cheng, B., Zu, B., Bao, B., Li, Y., Wang, R., Zhai, H. (2017) *J.Org.Chem.*, **82,** 8228-8233.
24 Cheng, B., Wang, T., Zhai, H., He, Y., Zhang, X., Li, H., Ding, Z., Feng, L., Sun, H. (2021) *Synthesis* ,**53,** 3578-3584.
25 Gupta, A.K., Ahamad, S., Gupta, E., Kant, R., Mohanan, K. (2015) *Org.Biomol.Chem.* ,**13,** 9783-9788.
26 Han, W-J., Wang, J-S., Zhao, J., Long, L., Cui, B-D., Wan, N-W., Chen, Y-Z (2018) *J.Org.Chem.* , **83,** 6556-6565.
27 Qiu, L-Y., Ren, N., Deng, Z., Chen, J., Deng, H., Zhang, H., Cao, W., Tang, X-J. (2023) *J.Org.Chem.*, **88**, 14, 10180–10189.
28 Tang, (2023) *CSD Communication (Private Communication).*

^{1}H, ^{13}C, and ^{19}F NMR Spectra

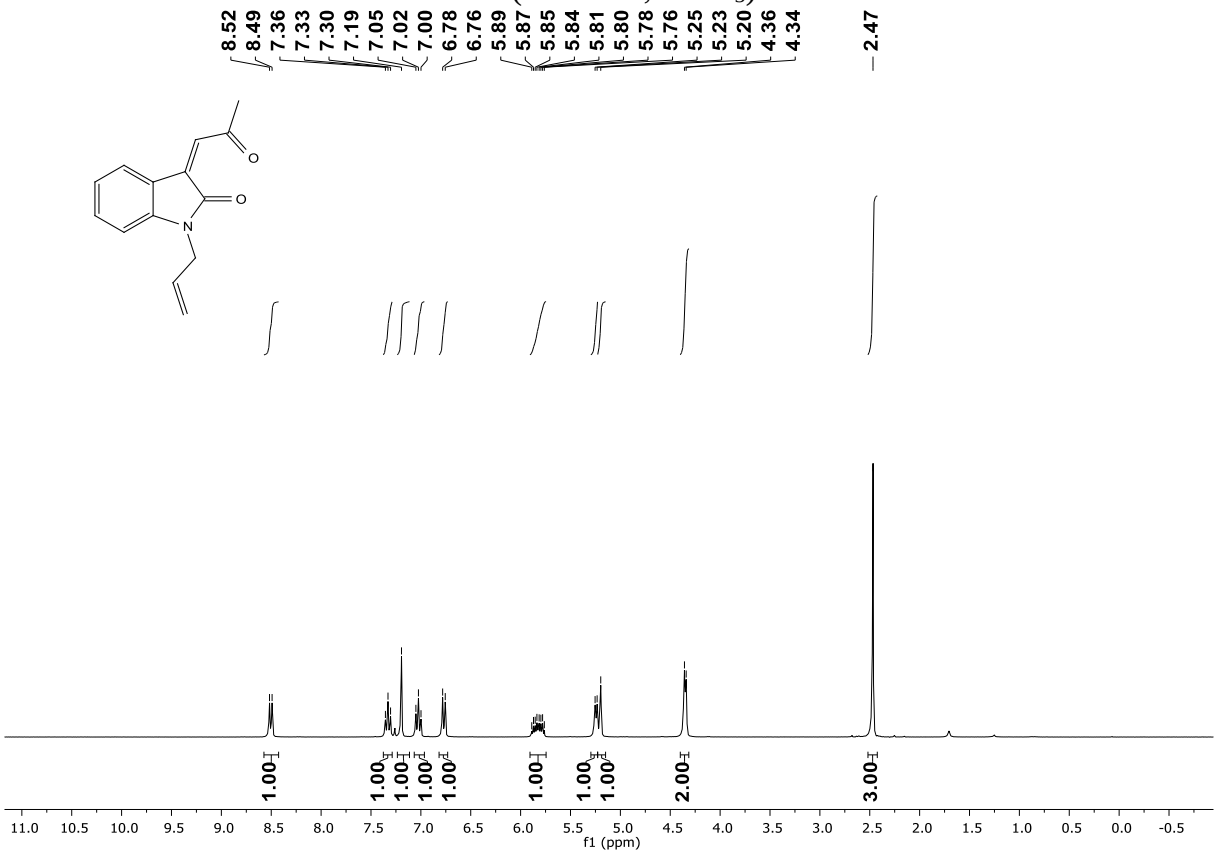
^{1}H NMR (300 MHz, $CDCl_3$) of **1a**



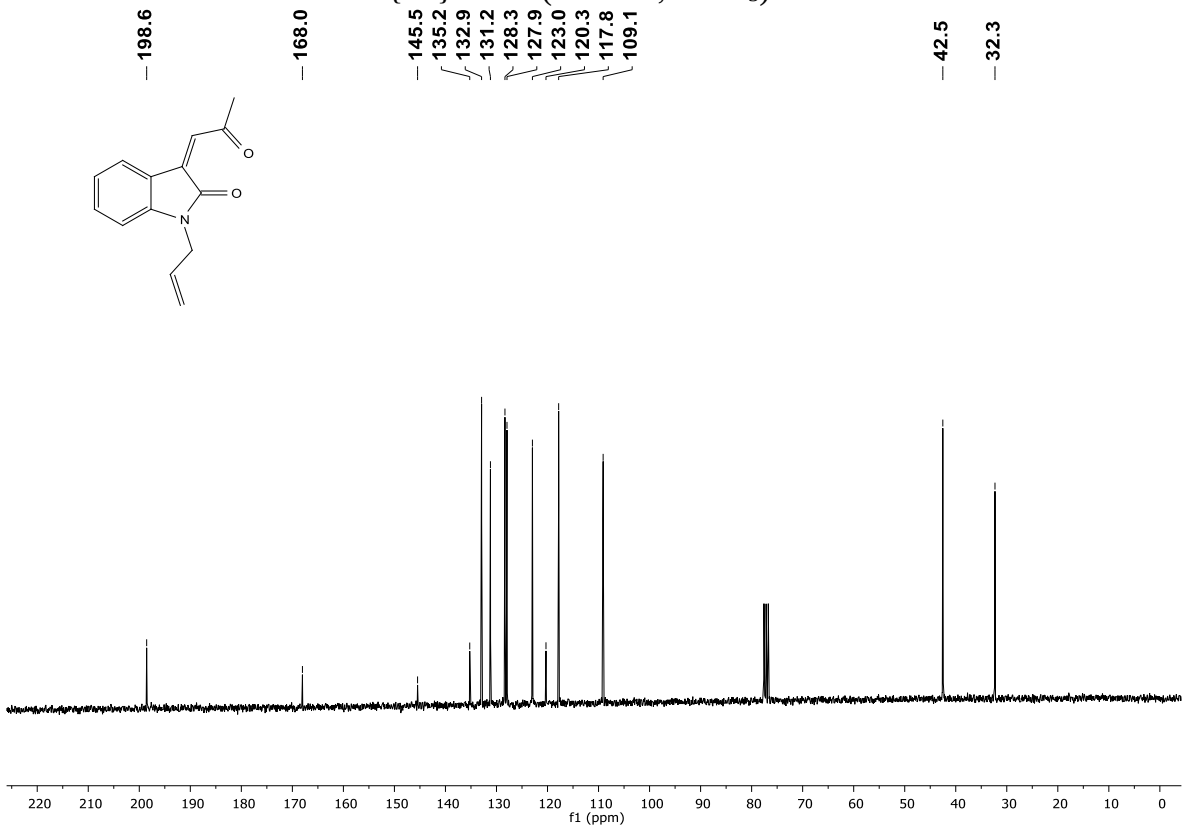
^{1}H NMR (300 MHz, $CDCl_3$) of **1b**



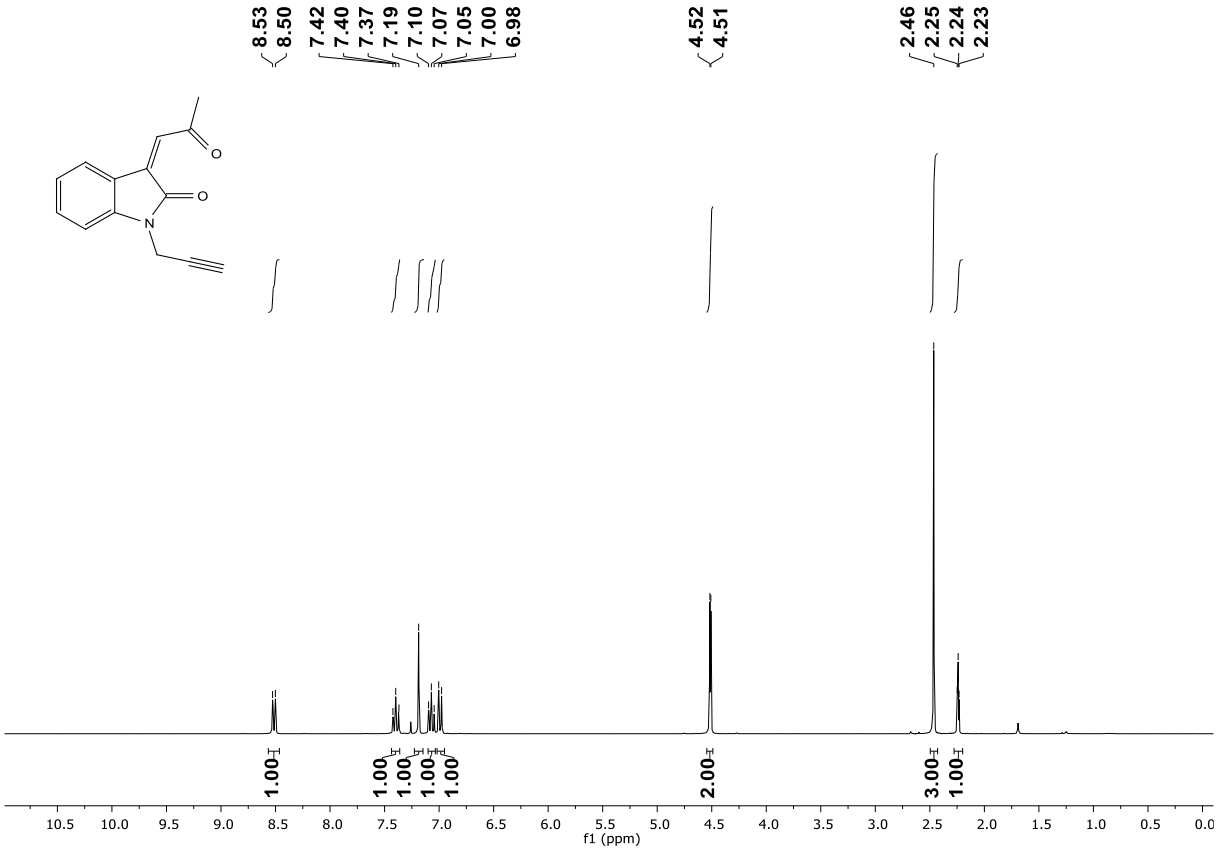
^{1}H NMR (300 MHz, $CDCl_3$) of **1c**



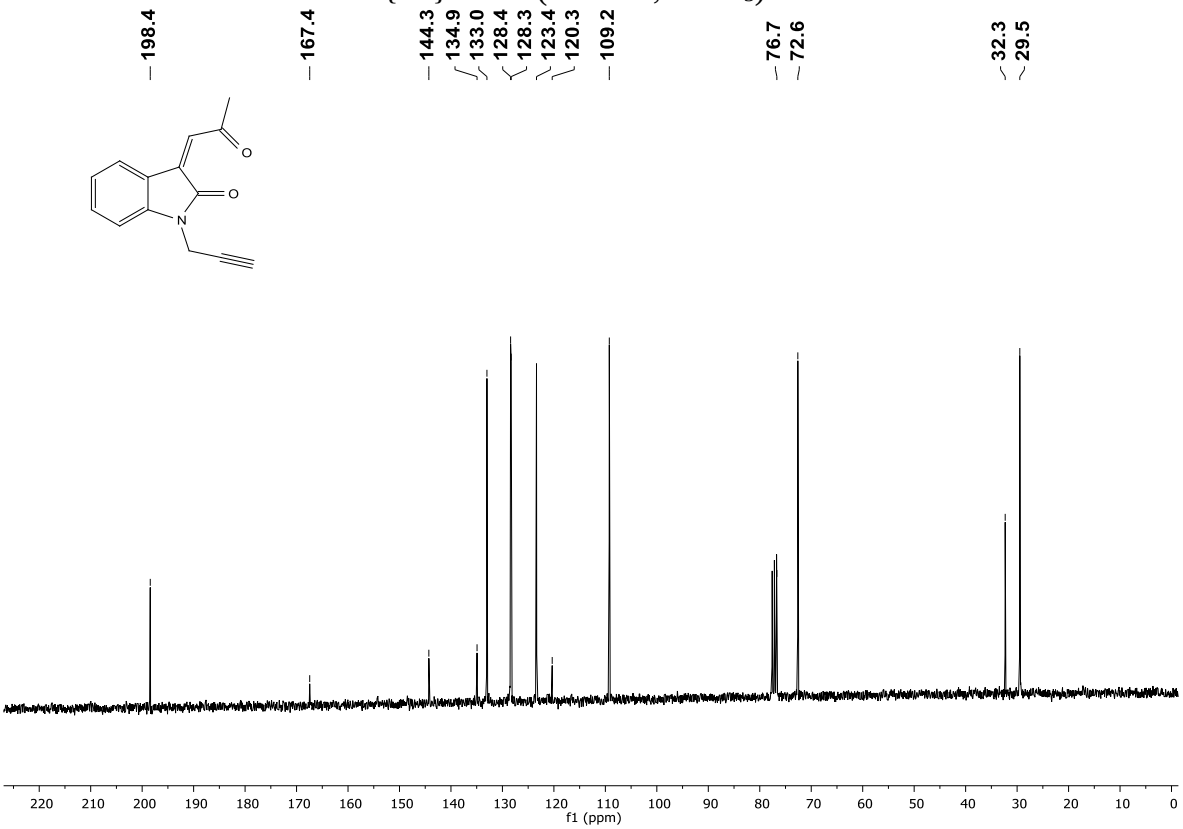
$^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) of **1c**



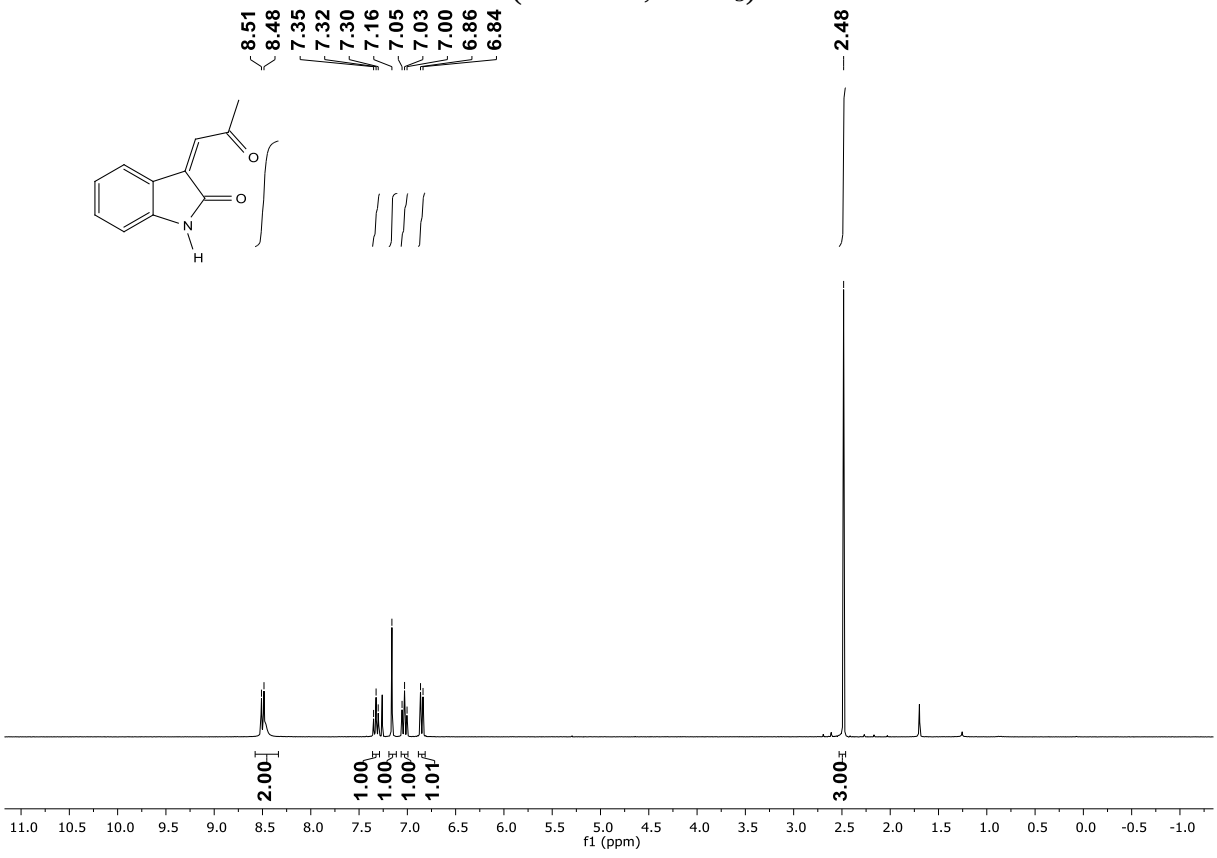
^{1}H NMR (300 MHz, $CDCl_3$) of **1d**



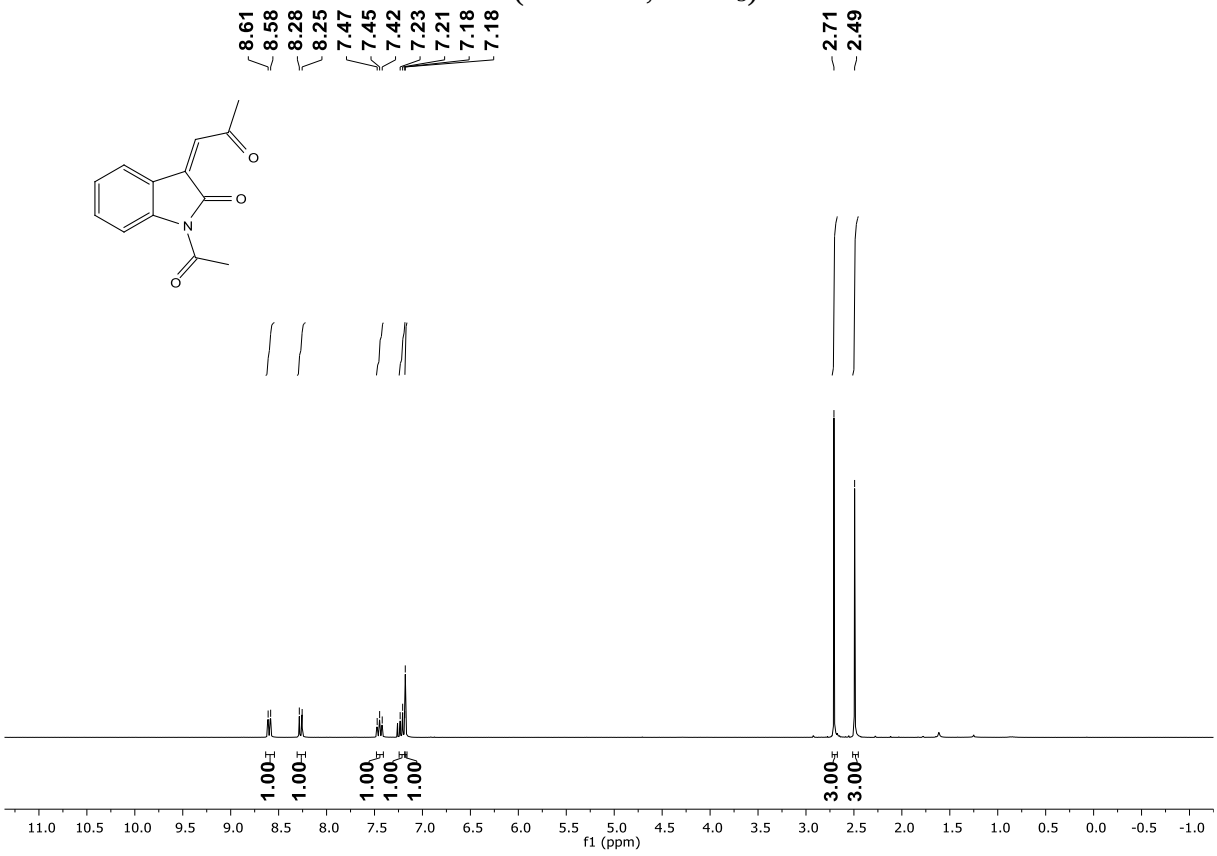
$^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) of **1d**



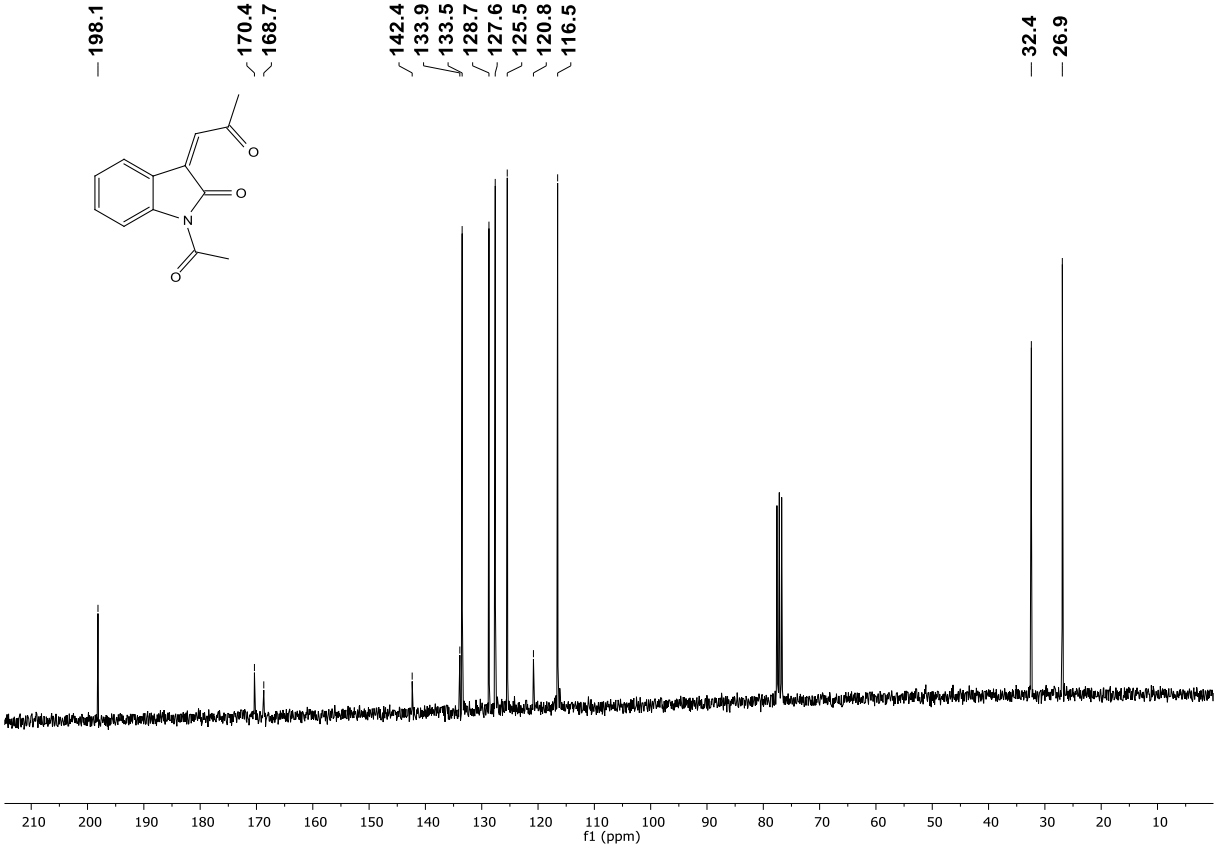
^{1}H NMR (300 MHz, $CDCl_3$) of **1e**



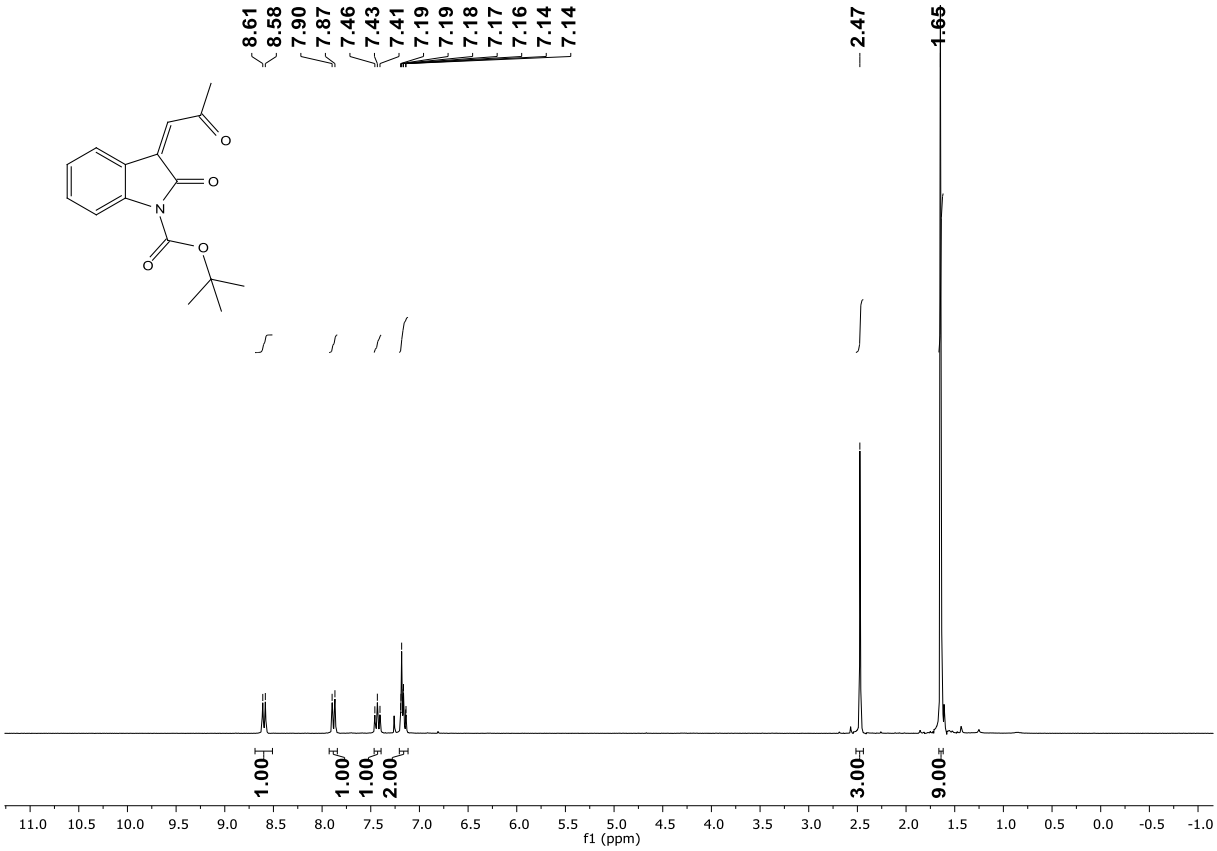
^{1}H NMR (300 MHz, $CDCl_3$) of **1f**



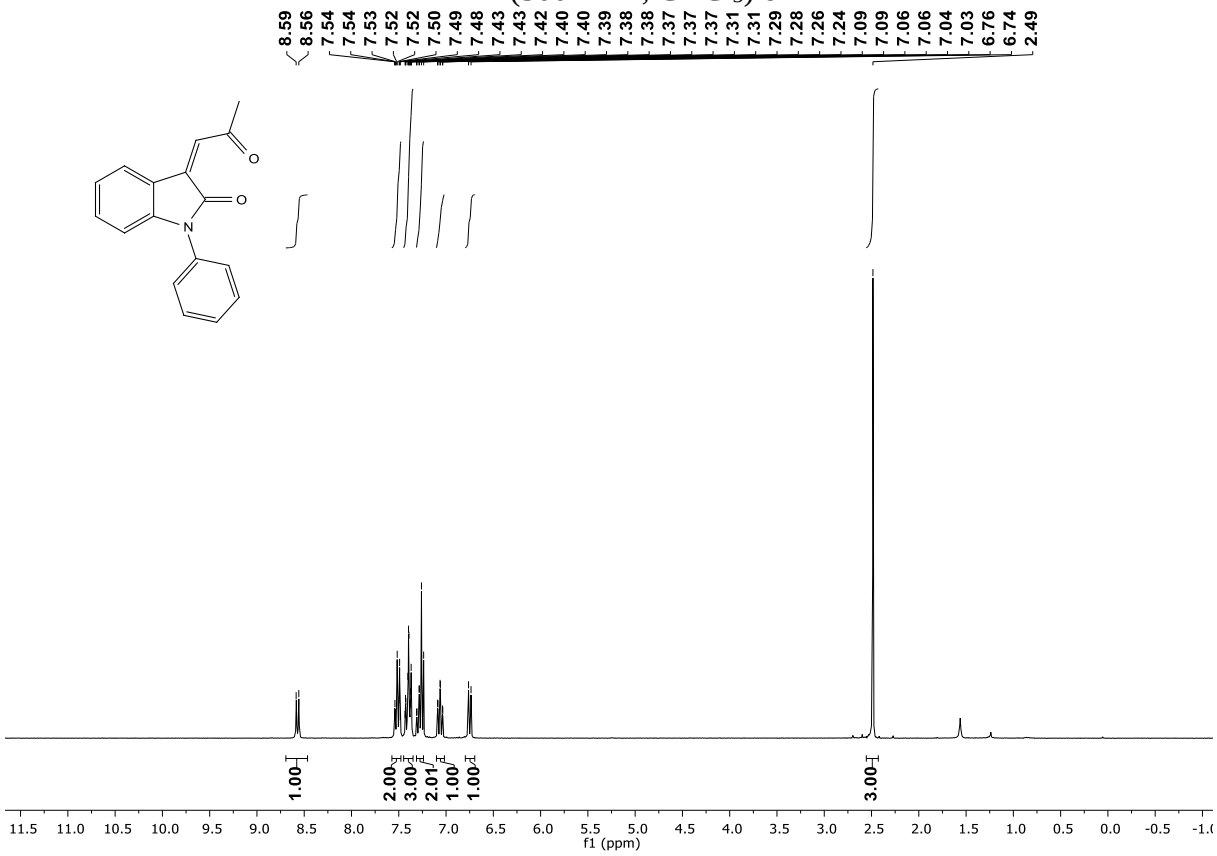
^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) of **1f**



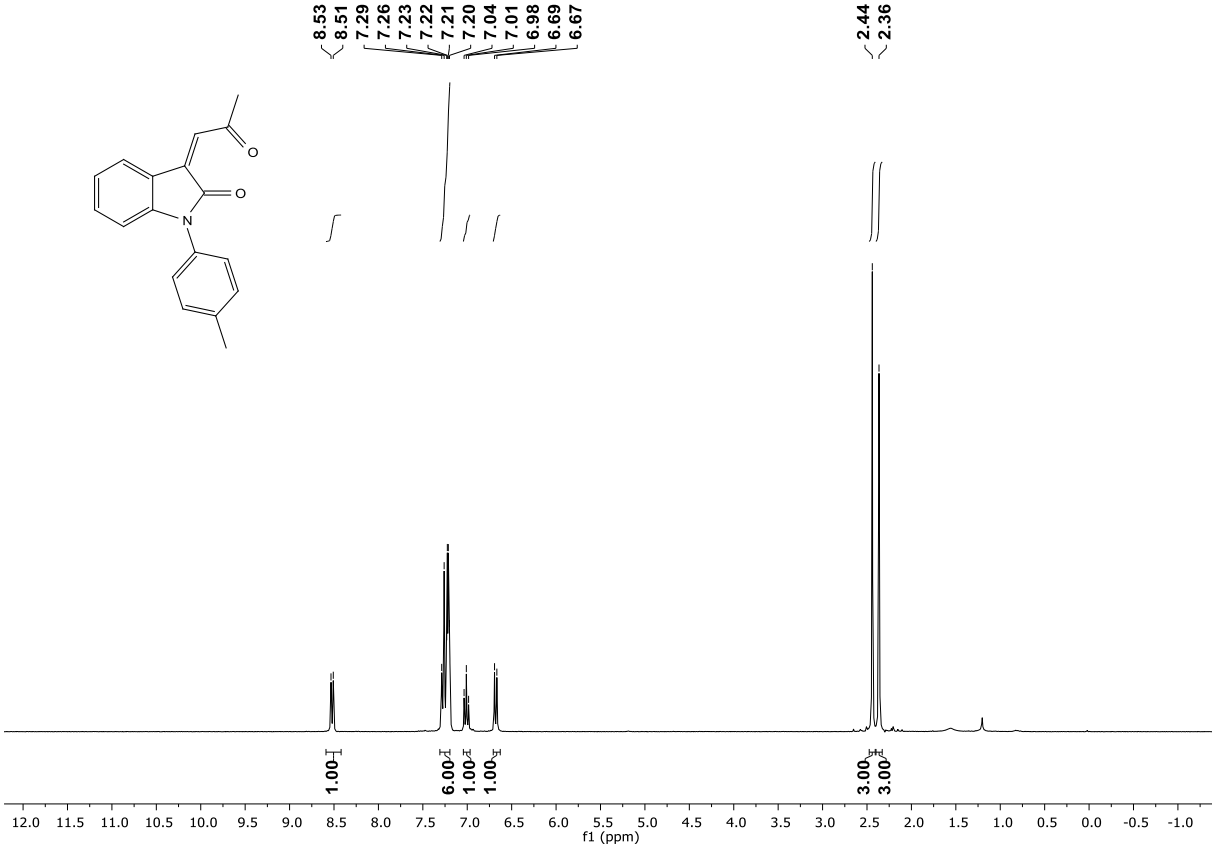
^{1}H NMR (300 MHz, $CDCl_3$) of **1g**



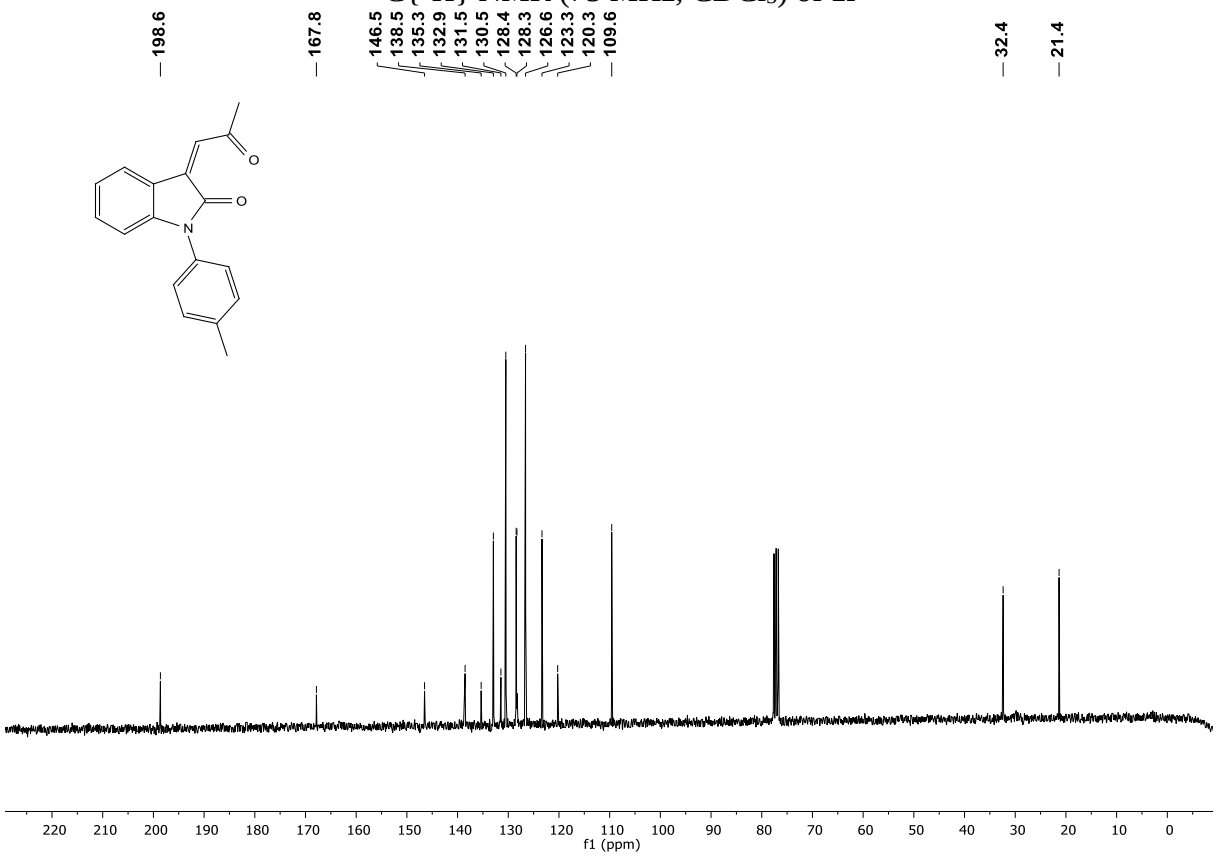
^{1}H NMR (300 MHz, $CDCl_3$) of **1h**



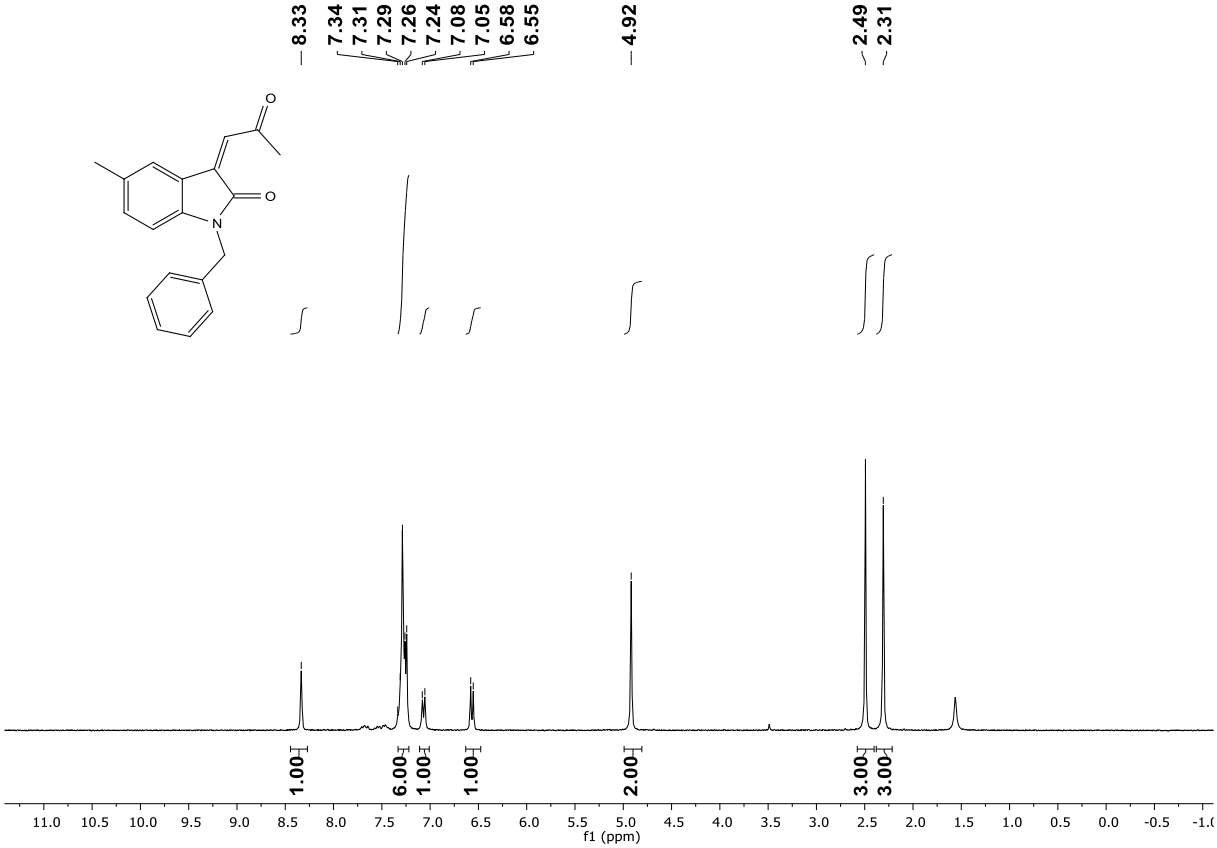
^{1}H NMR (300 MHz, $CDCl_3$) of **1i**



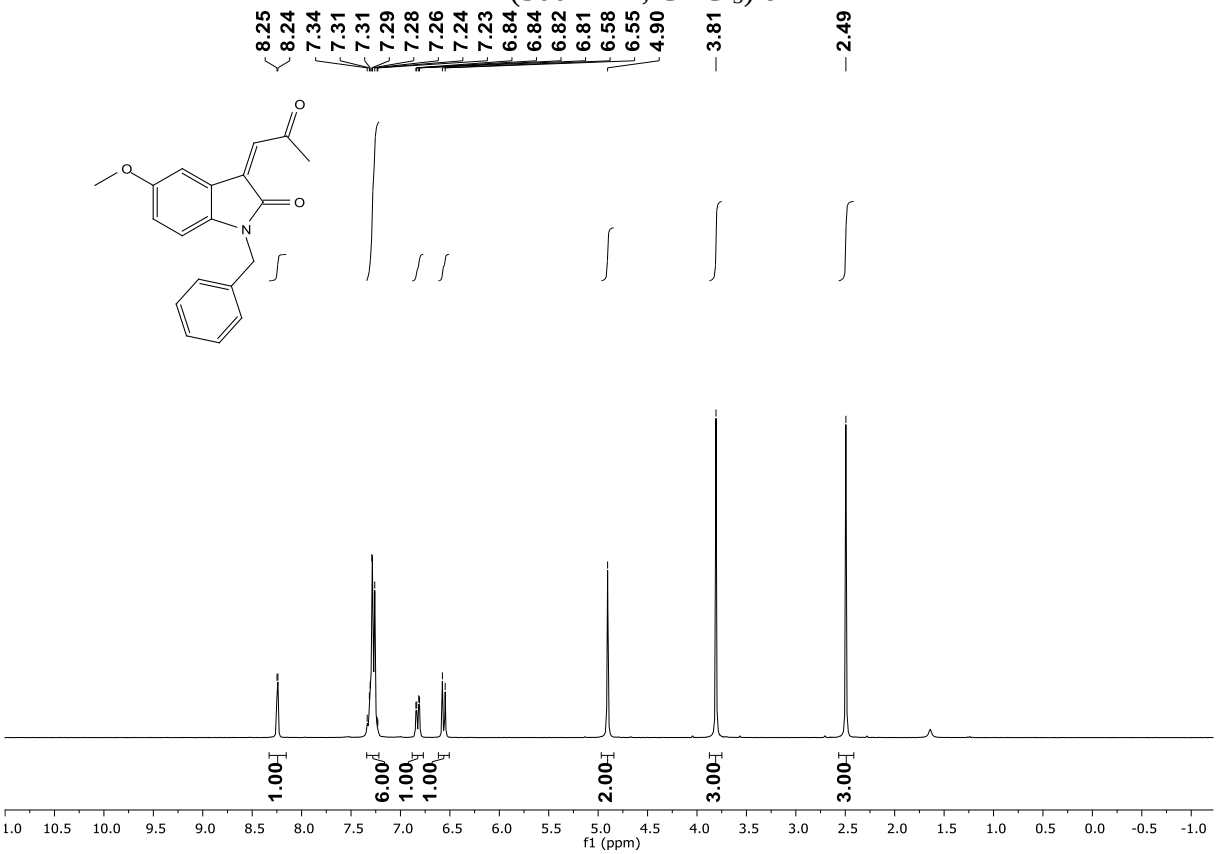
^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) of **1i**



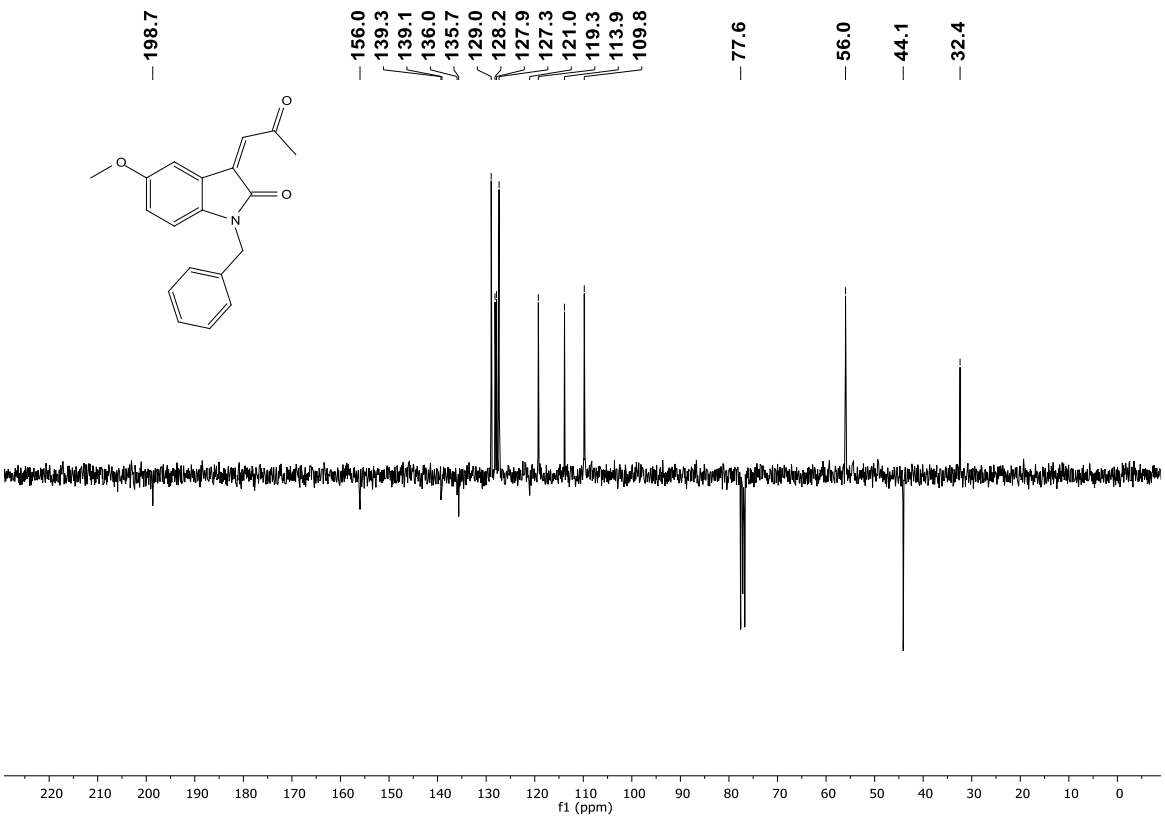
^{1}H NMR (300 MHz, $CDCl_3$) of **1j**



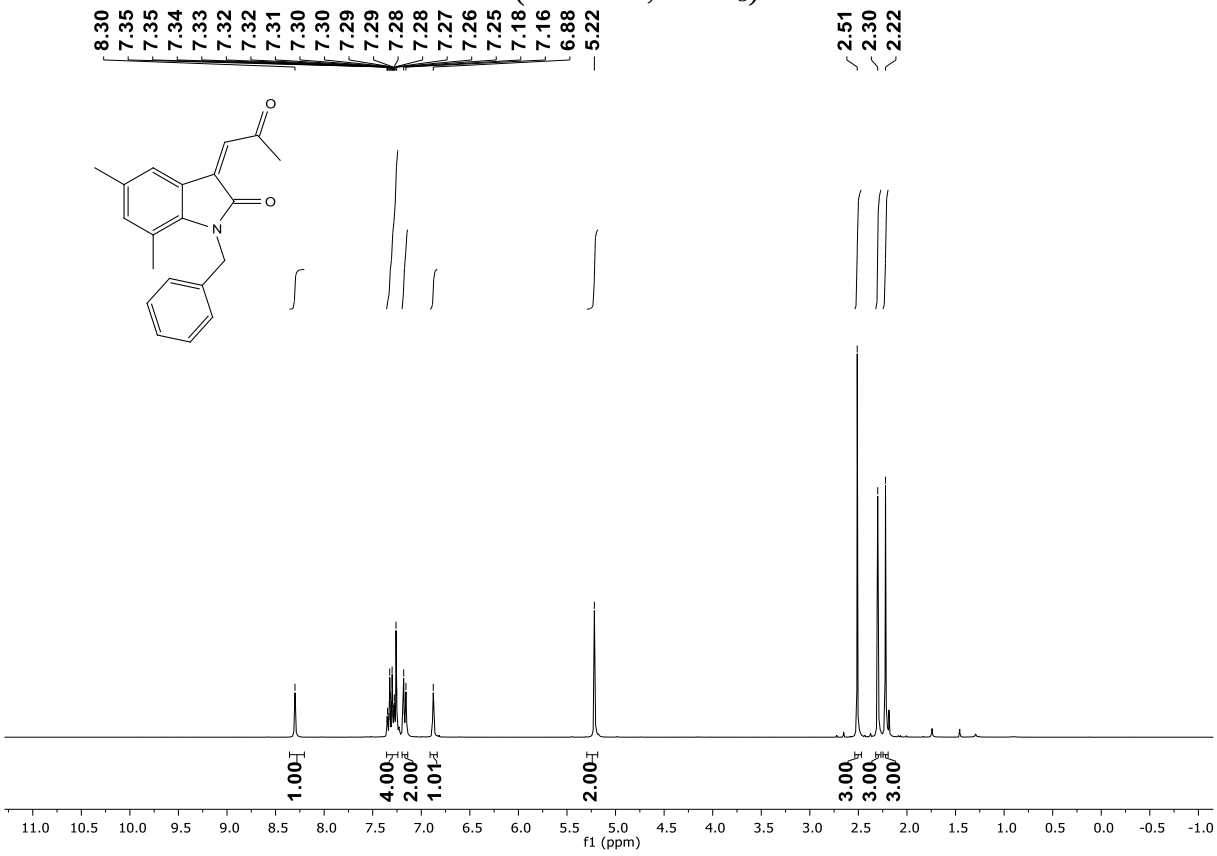
^{1}H NMR (300 MHz, $CDCl_3$) of **1k**



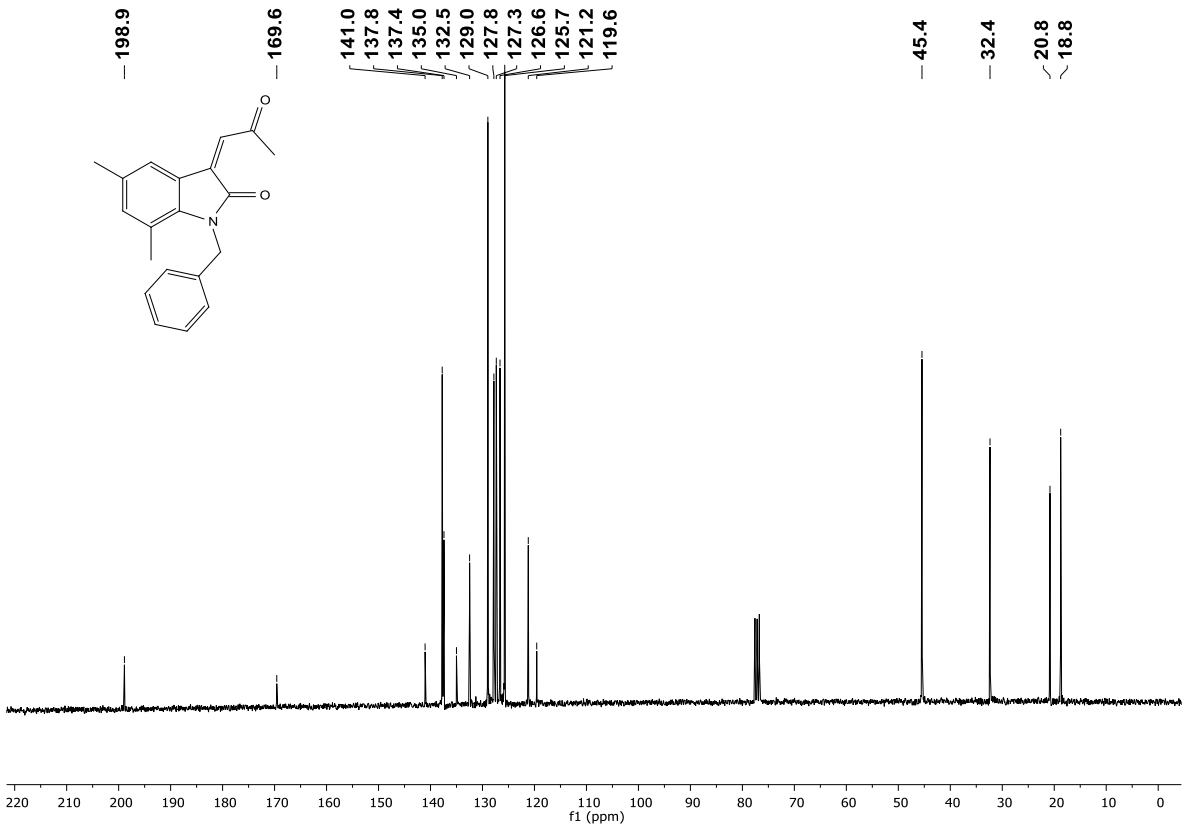
$^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) of **1k**



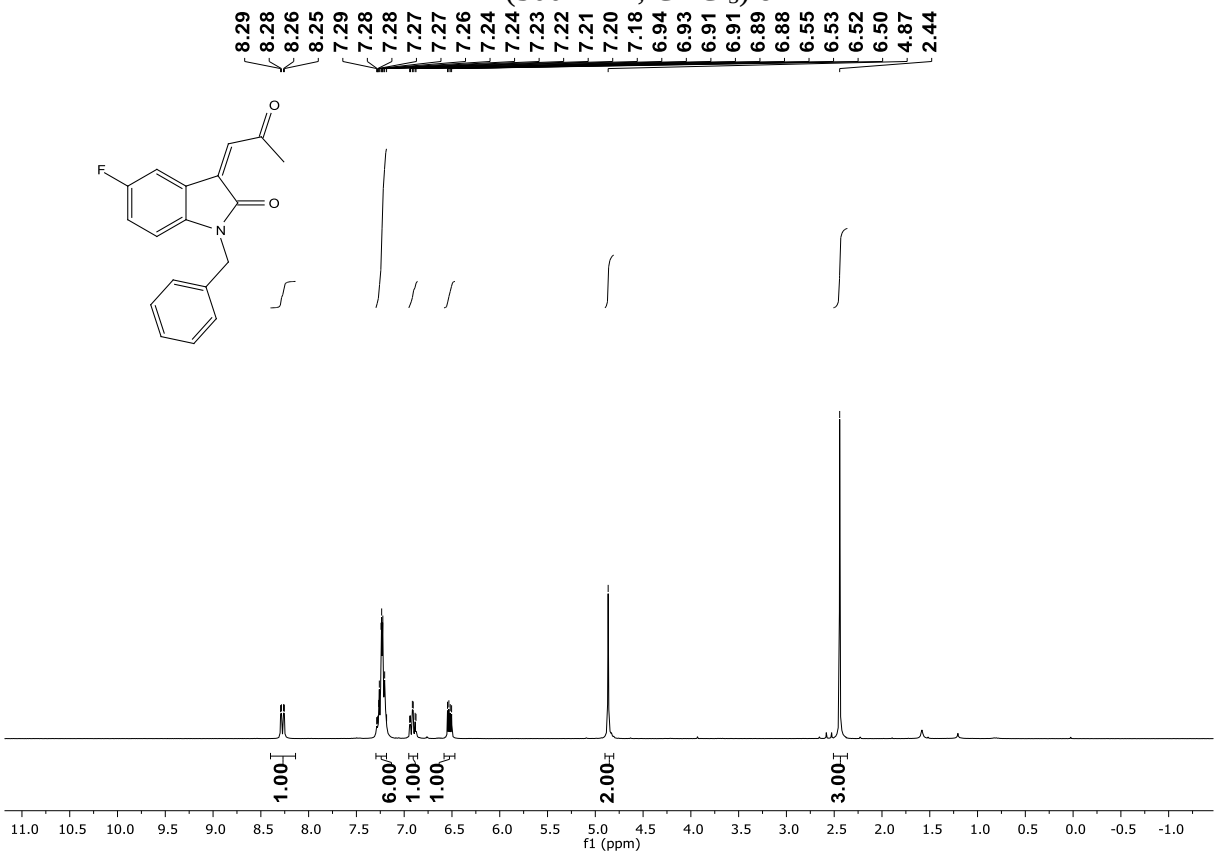
^{1}H NMR (300 MHz, $CDCl_3$) of **1l**



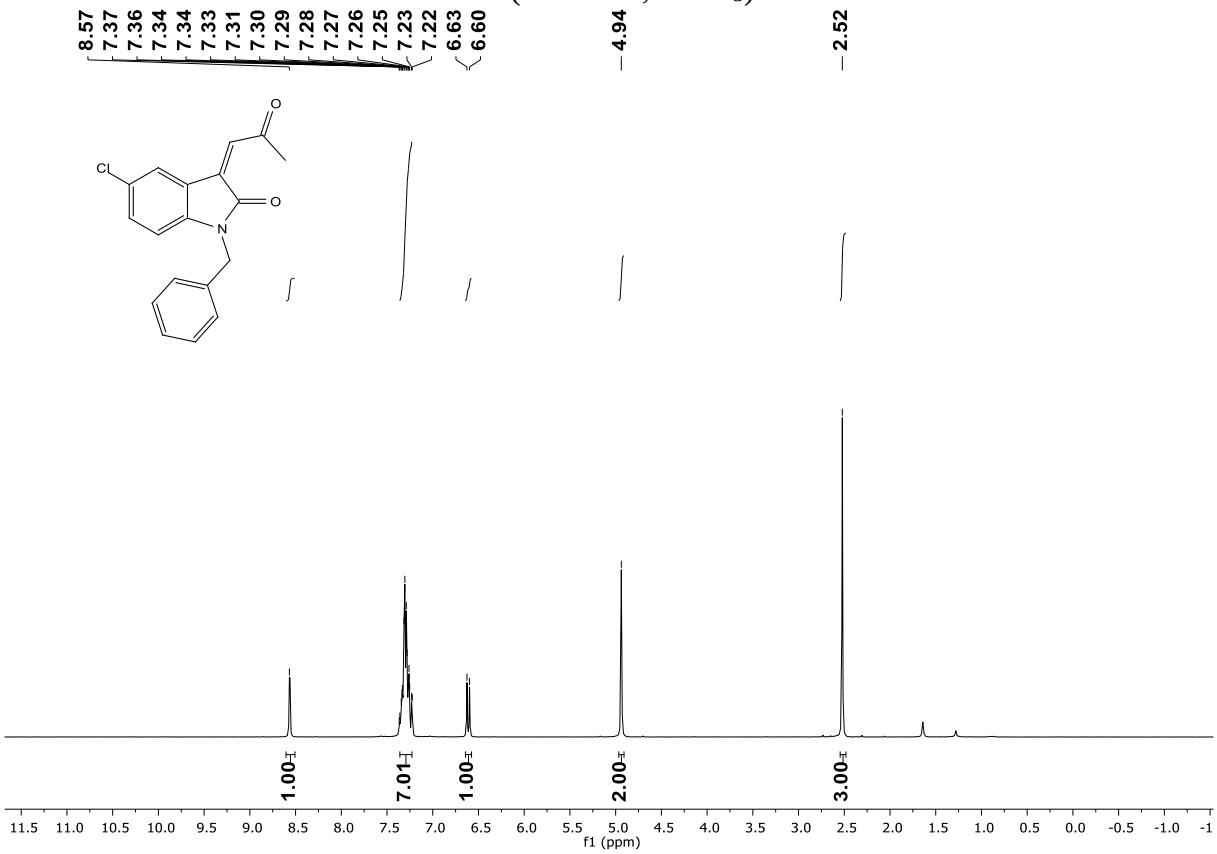
$^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) of **1l**



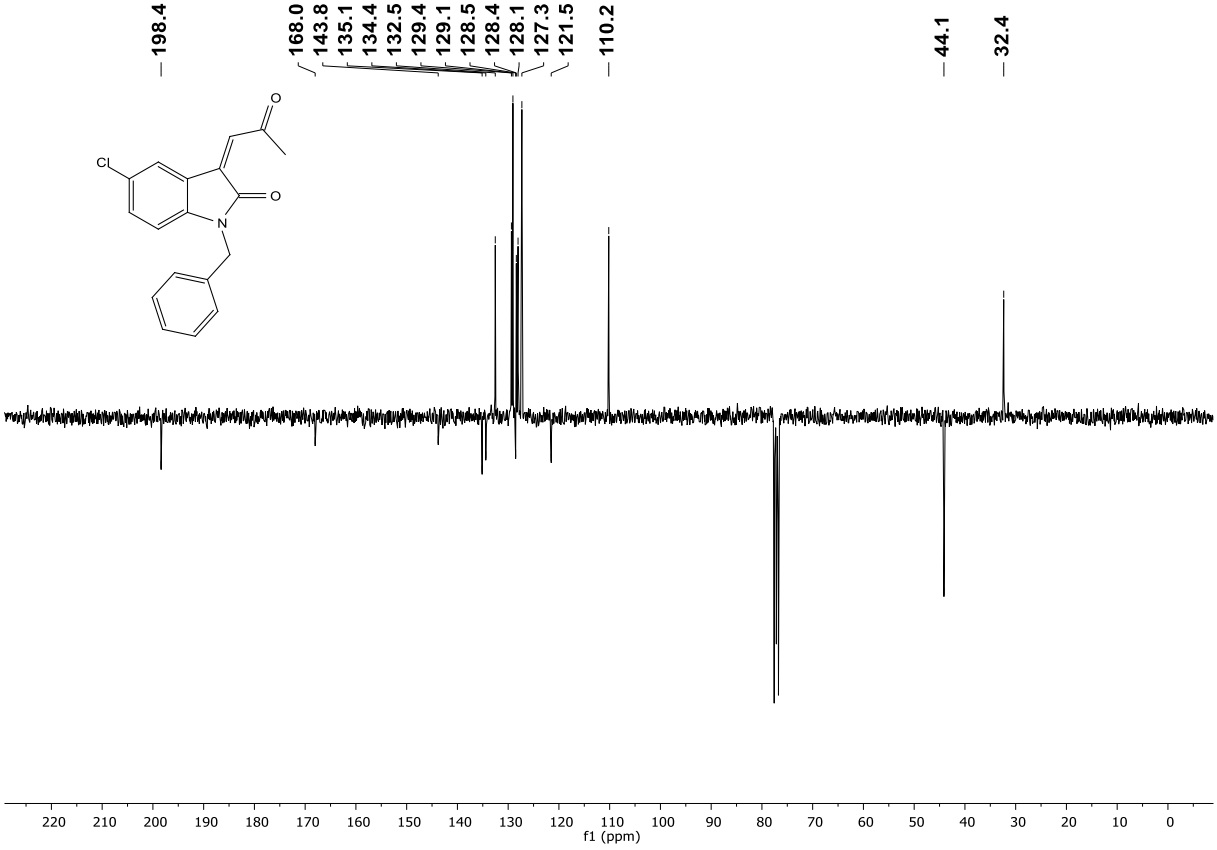
^{1}H NMR (300 MHz, $CDCl_3$) of **1m**



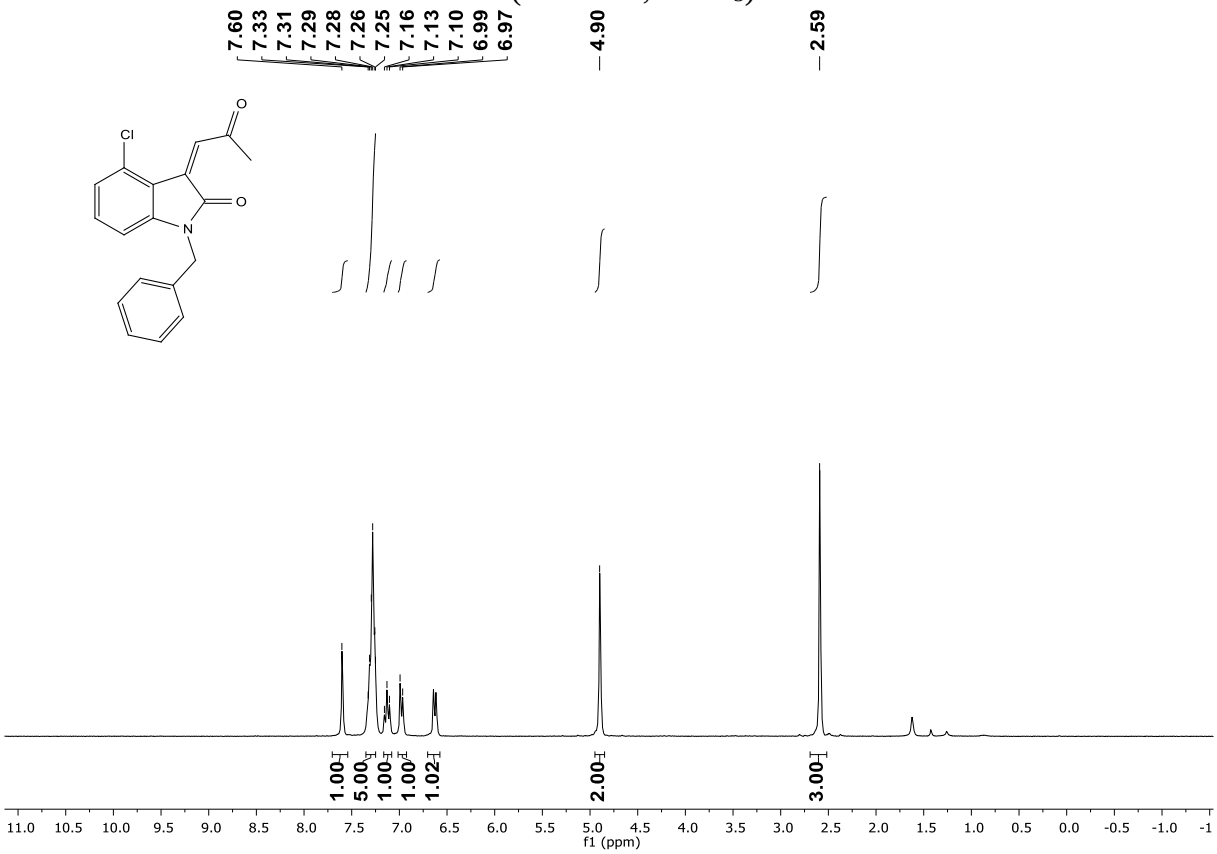
^{1}H NMR (300 MHz, $CDCl_3$) of **1n**



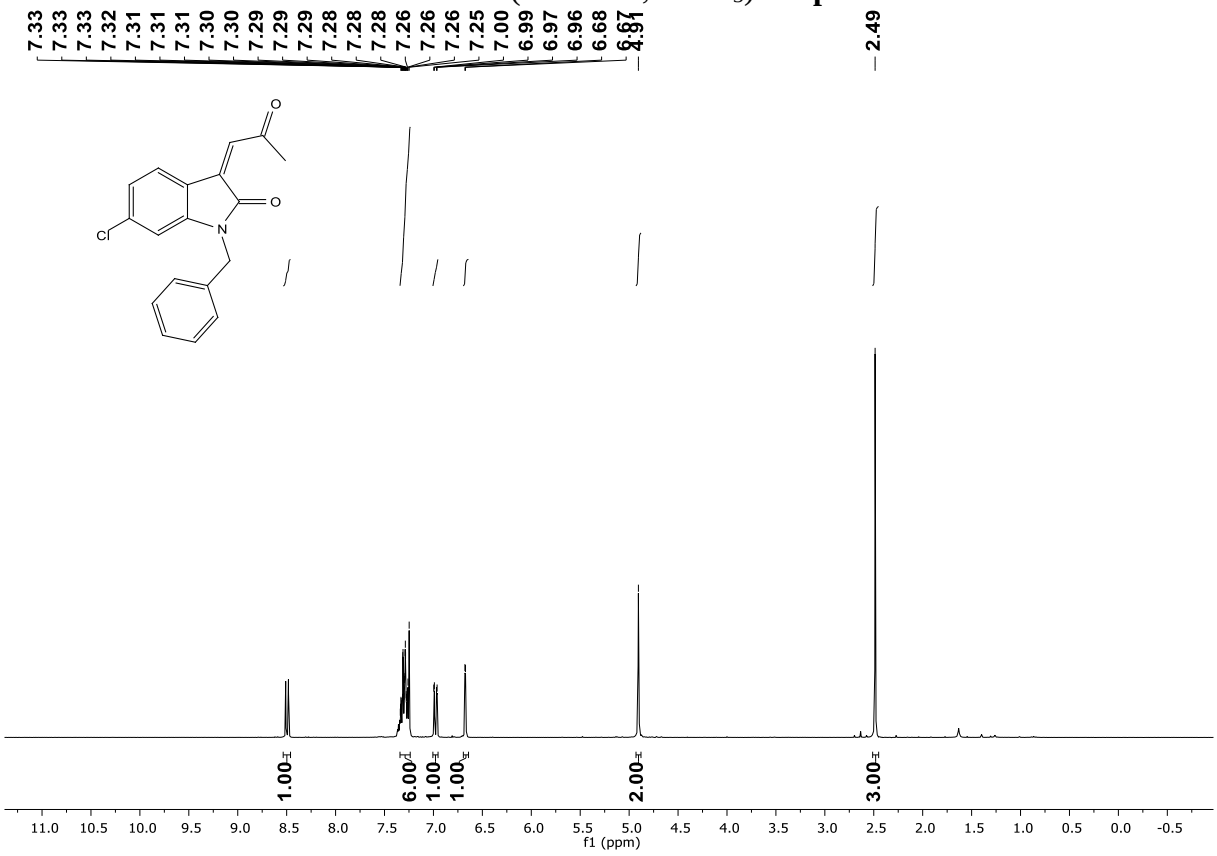
^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) of **1n**



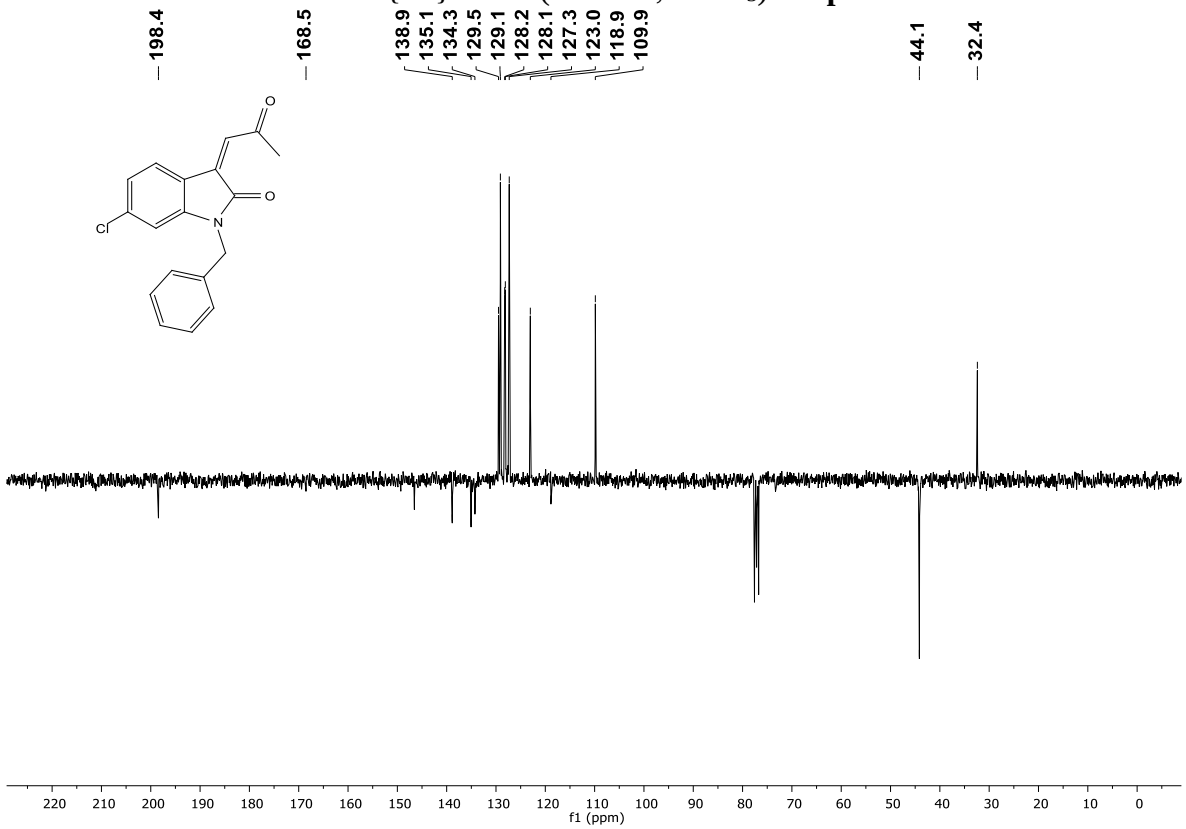
^{1}H NMR (300 MHz, $CDCl_3$) of **1o**



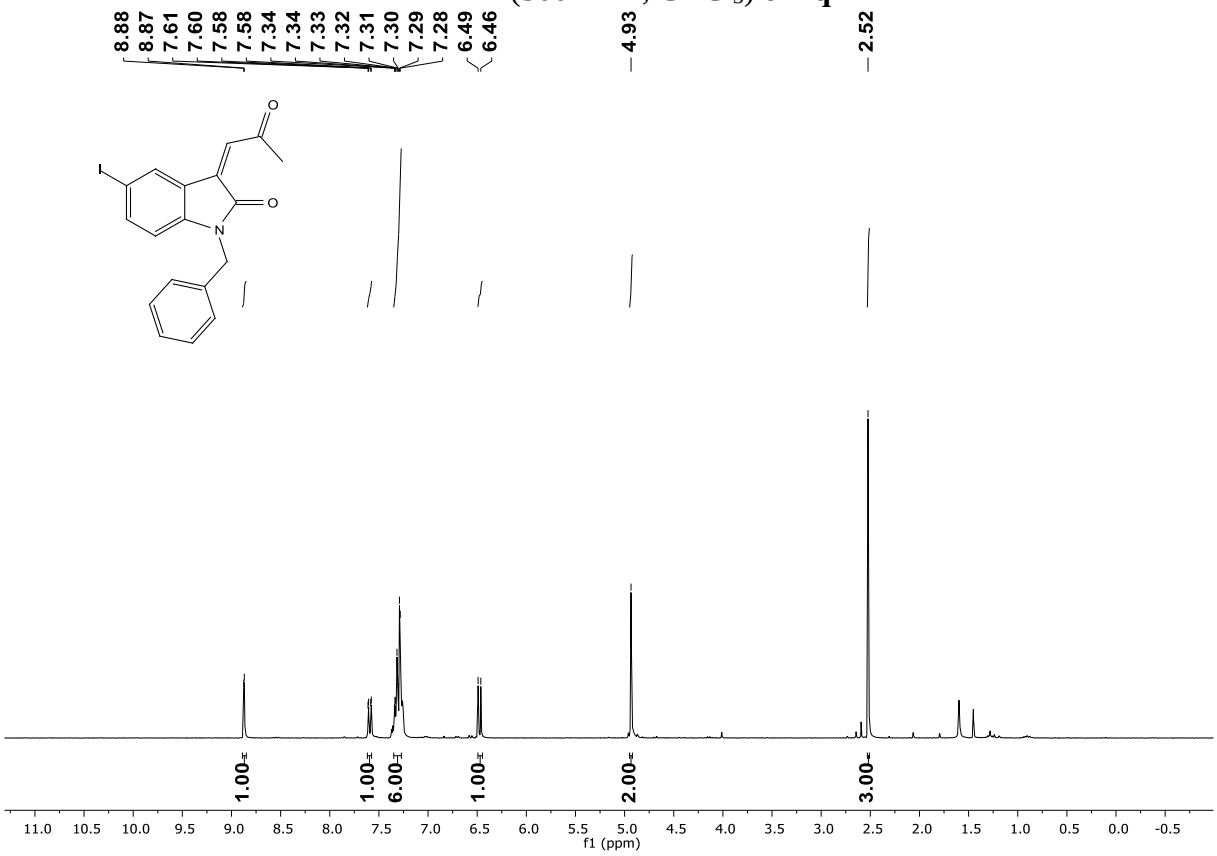
^{1}H NMR (300 MHz, $CDCl_3$) of **1p**



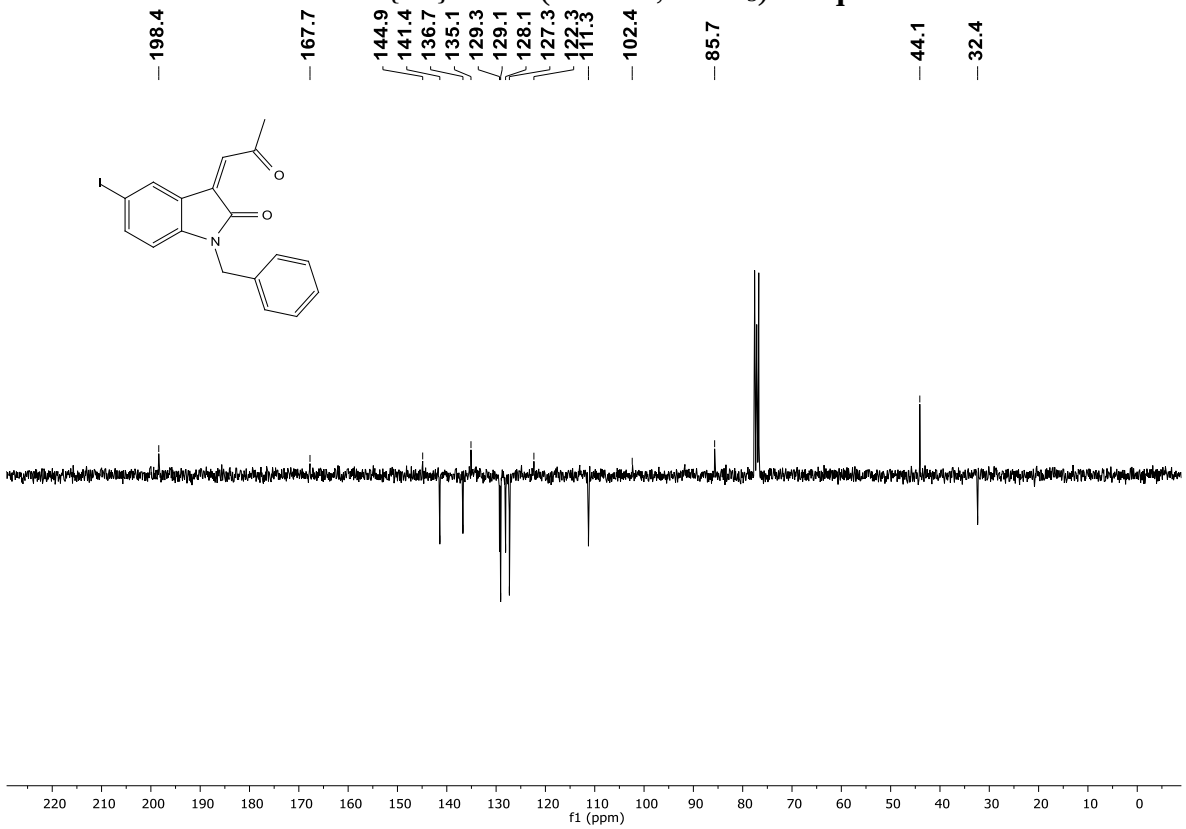
$^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) of **1p**



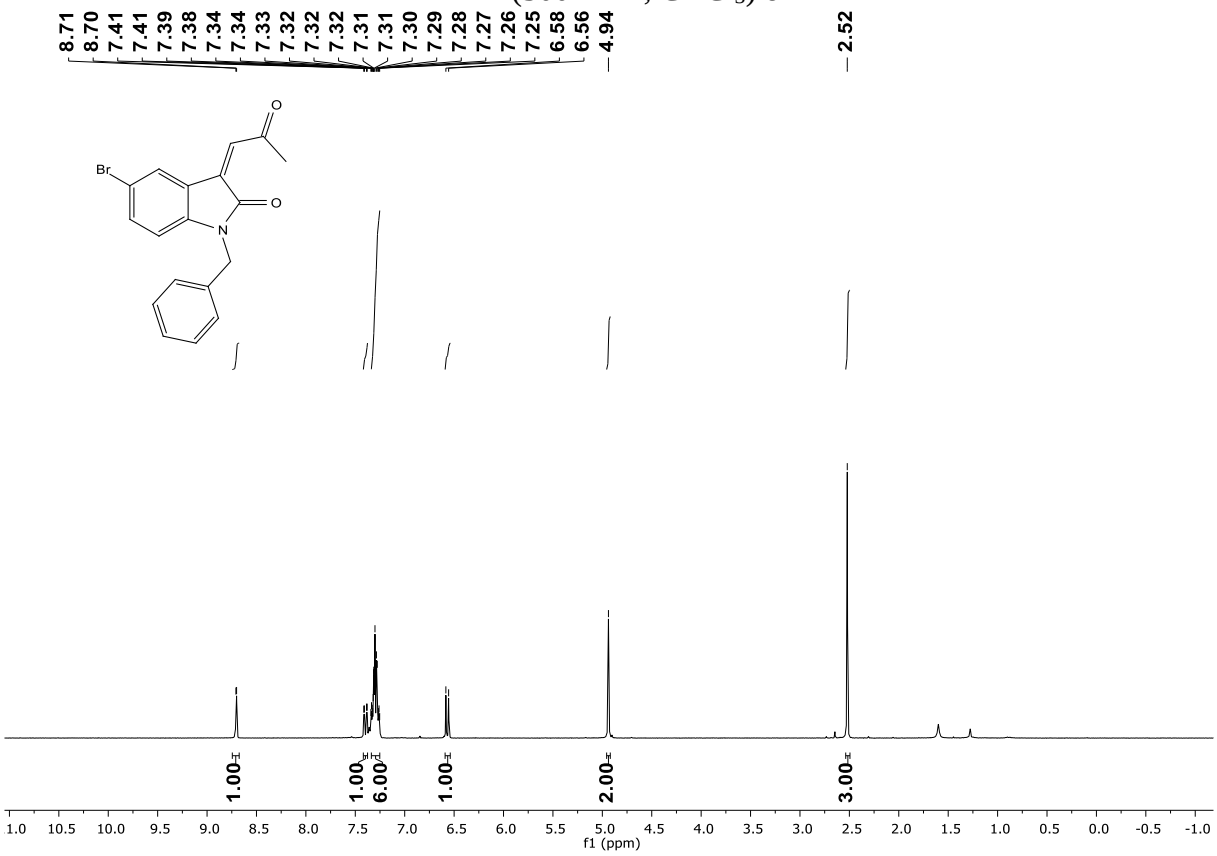
^{1}H NMR (300 MHz, $CDCl_3$) of **1q**



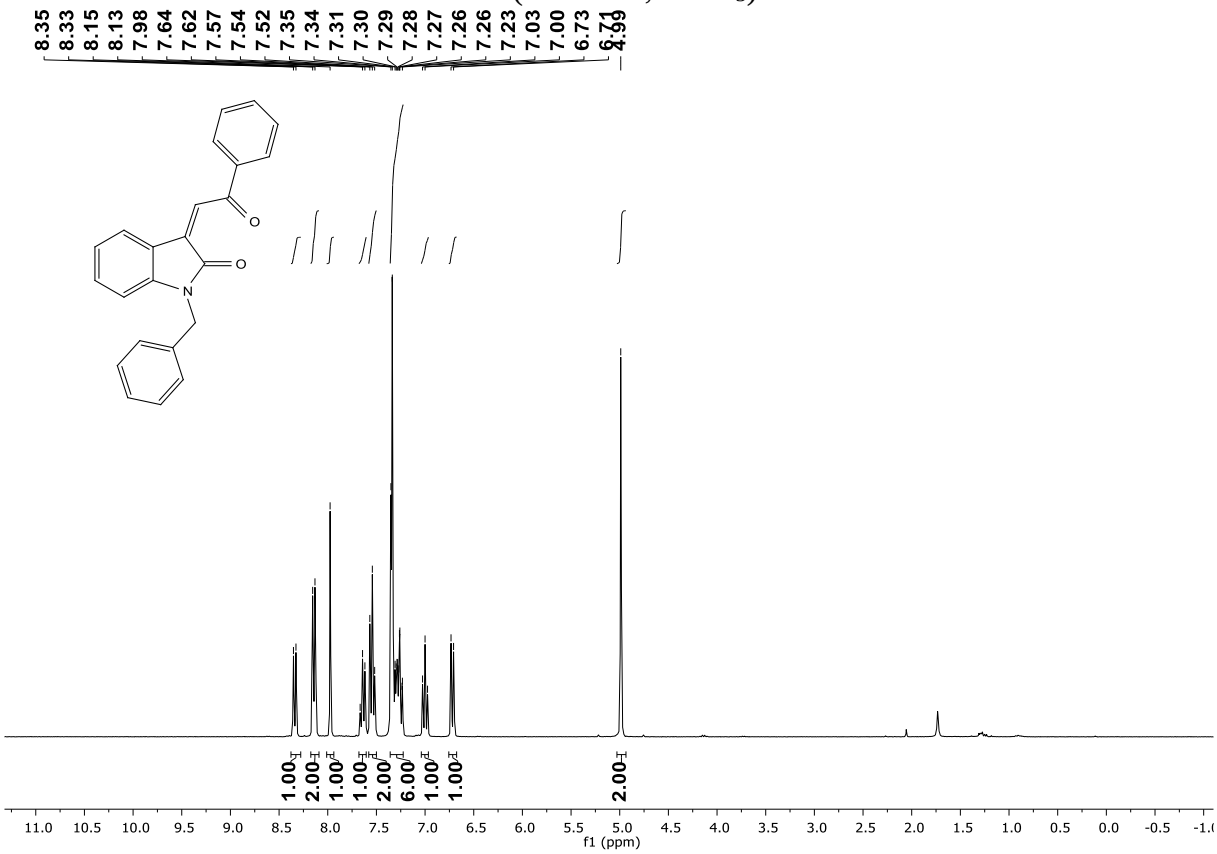
$^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) of **1q**



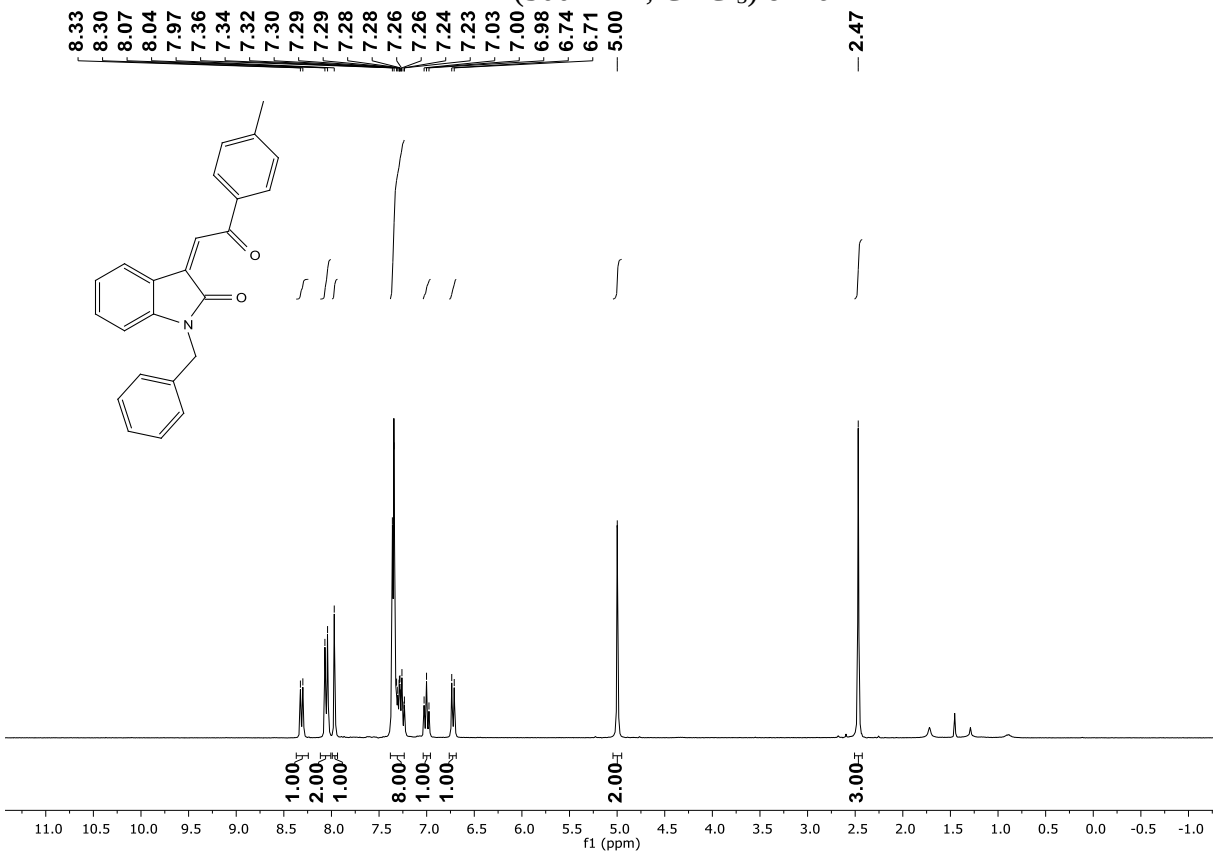
^{1}H NMR (300 MHz, $CDCl_3$) of **1r**



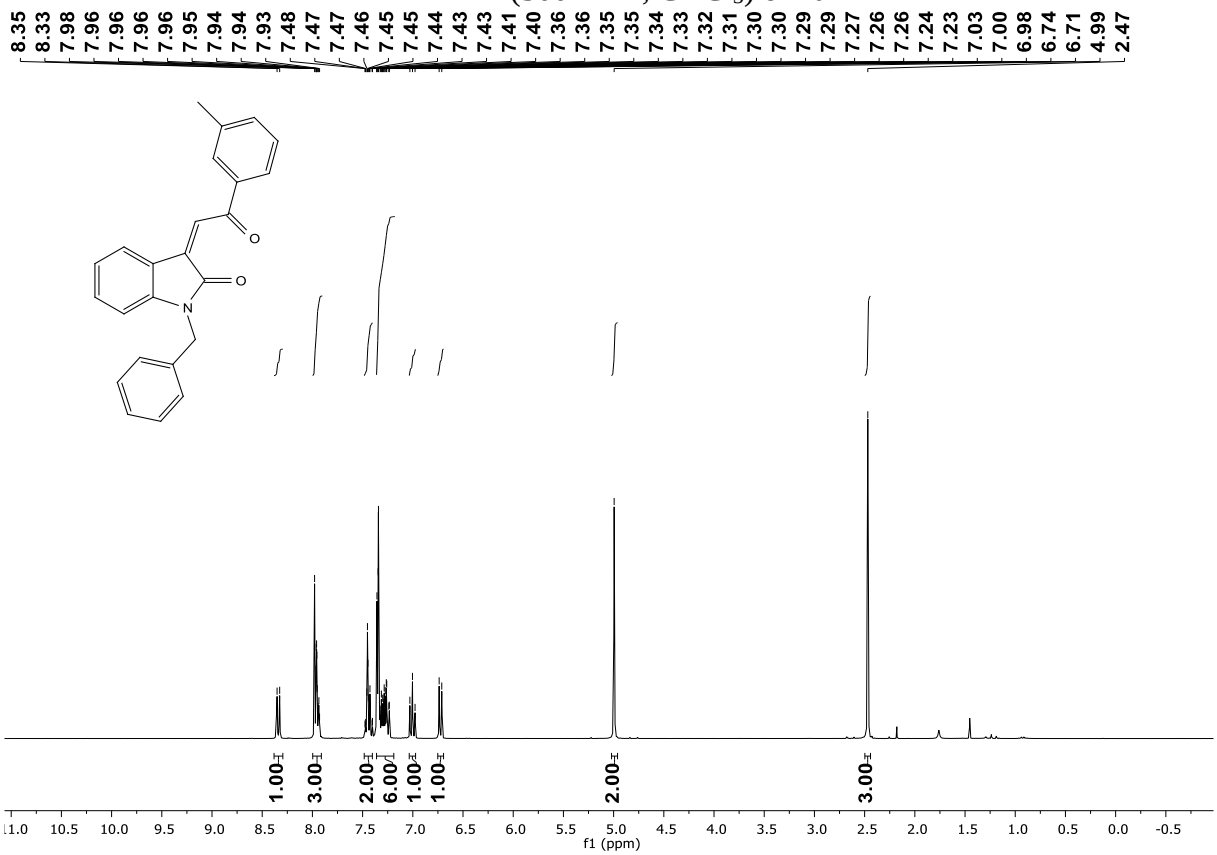
^{1}H NMR (300 MHz, $CDCl_3$) of **1s**



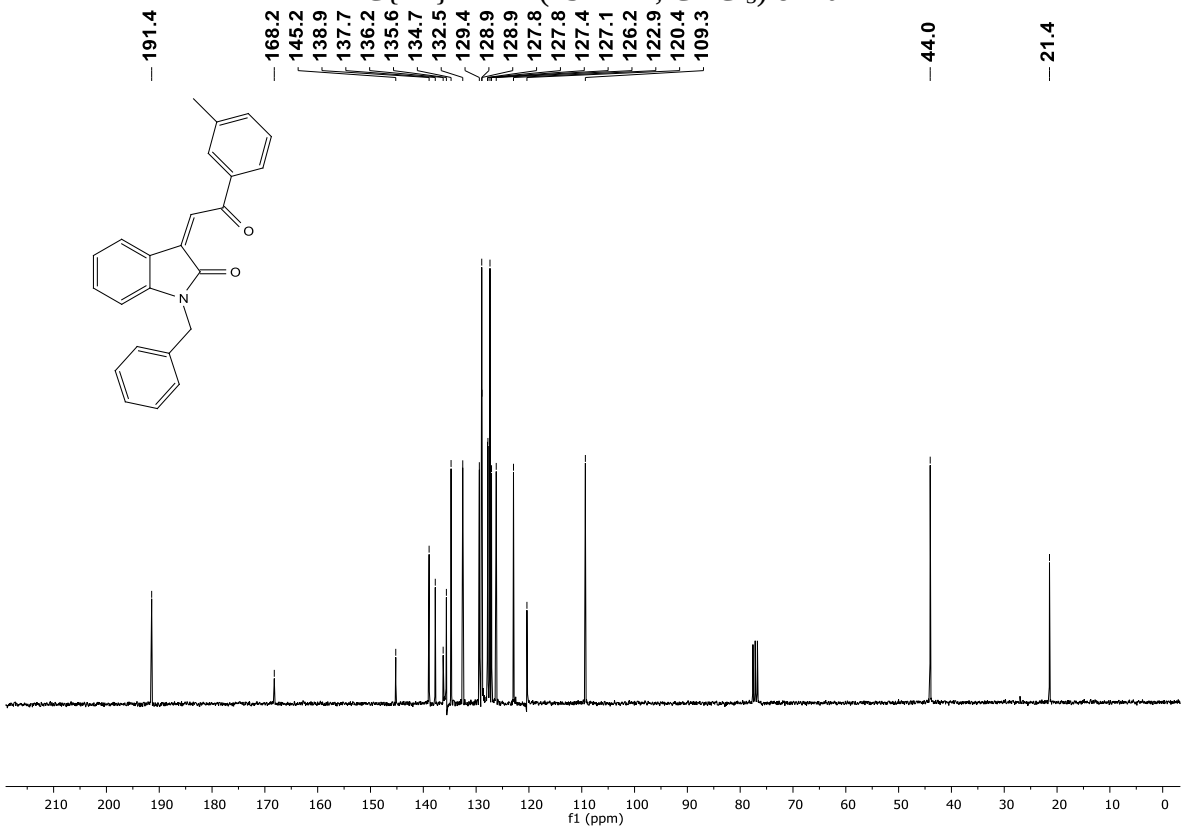
^{1}H NMR (300 MHz, $CDCl_3$) of **1t**



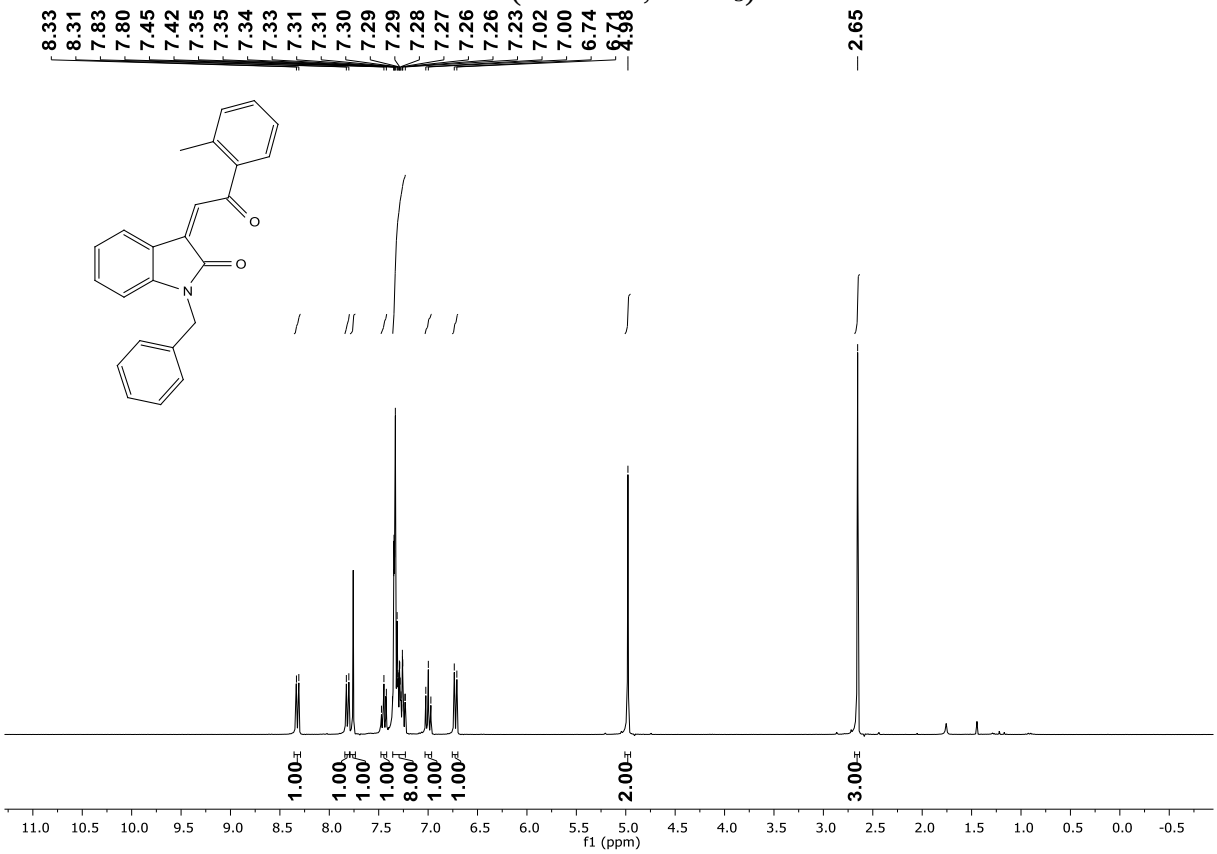
^{1}H NMR (300 MHz, $CDCl_3$) of **1u**



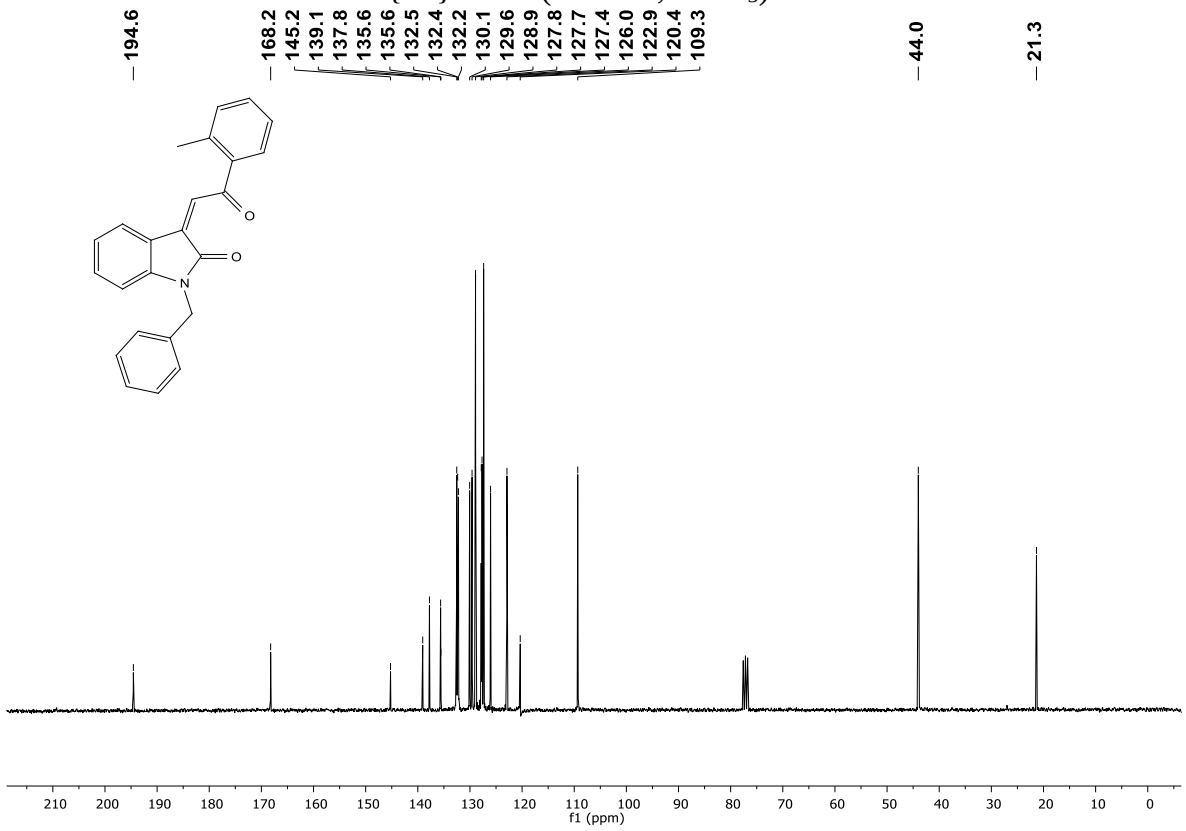
^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) of **1u**



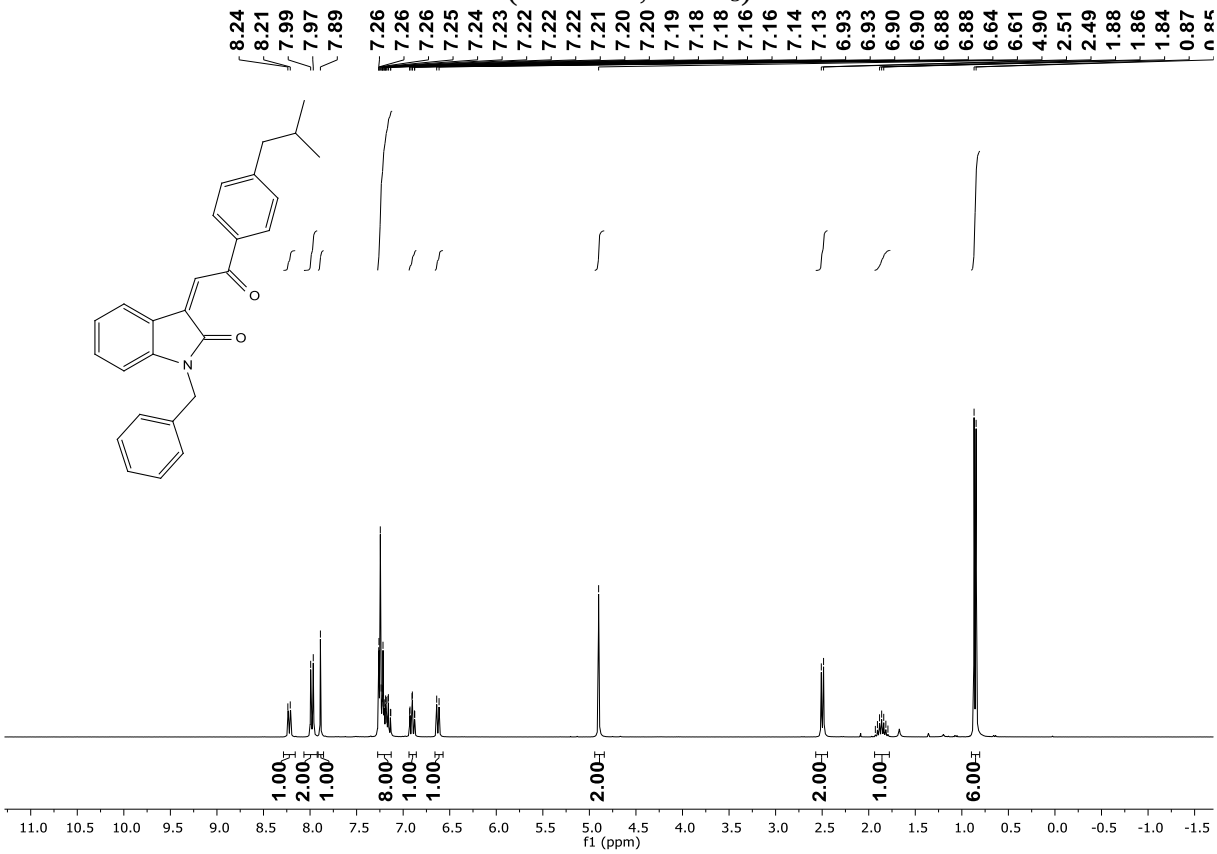
^{1}H NMR (300 MHz, $CDCl_3$) of **1v**



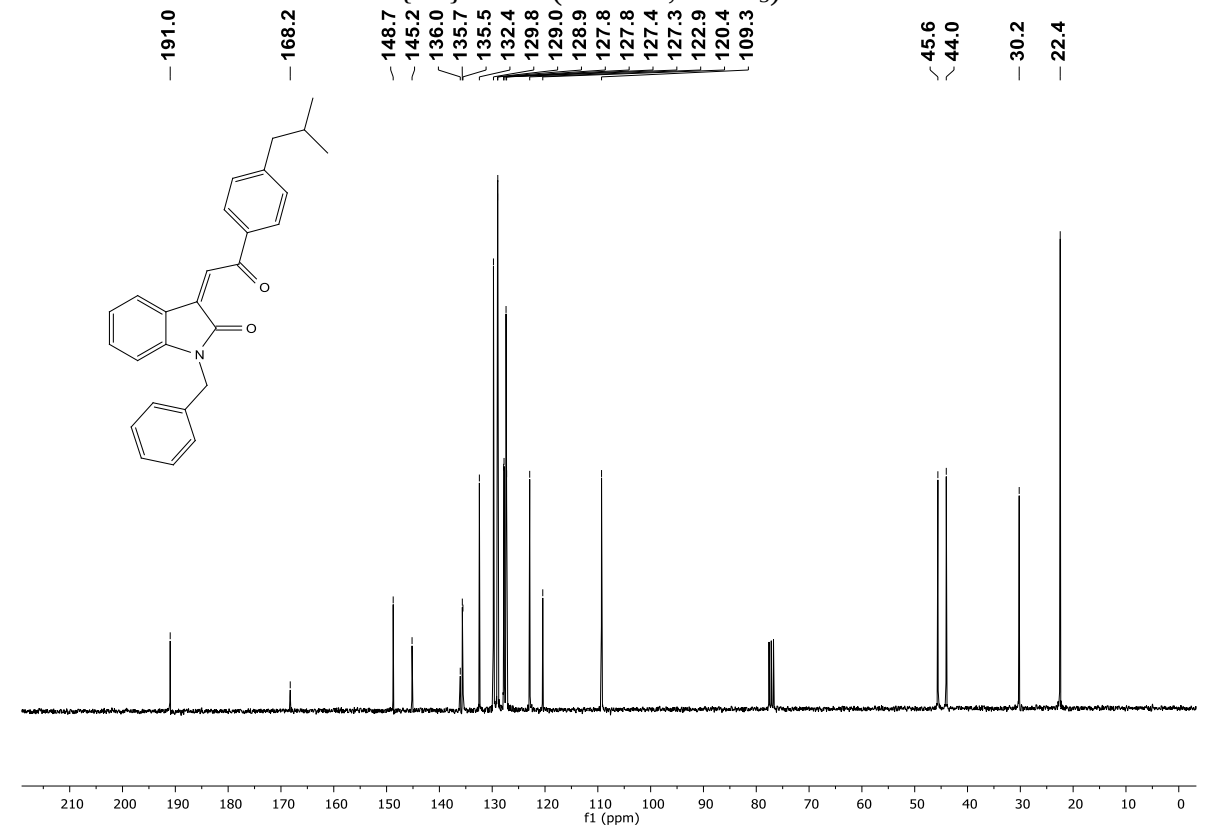
^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) of **1v**



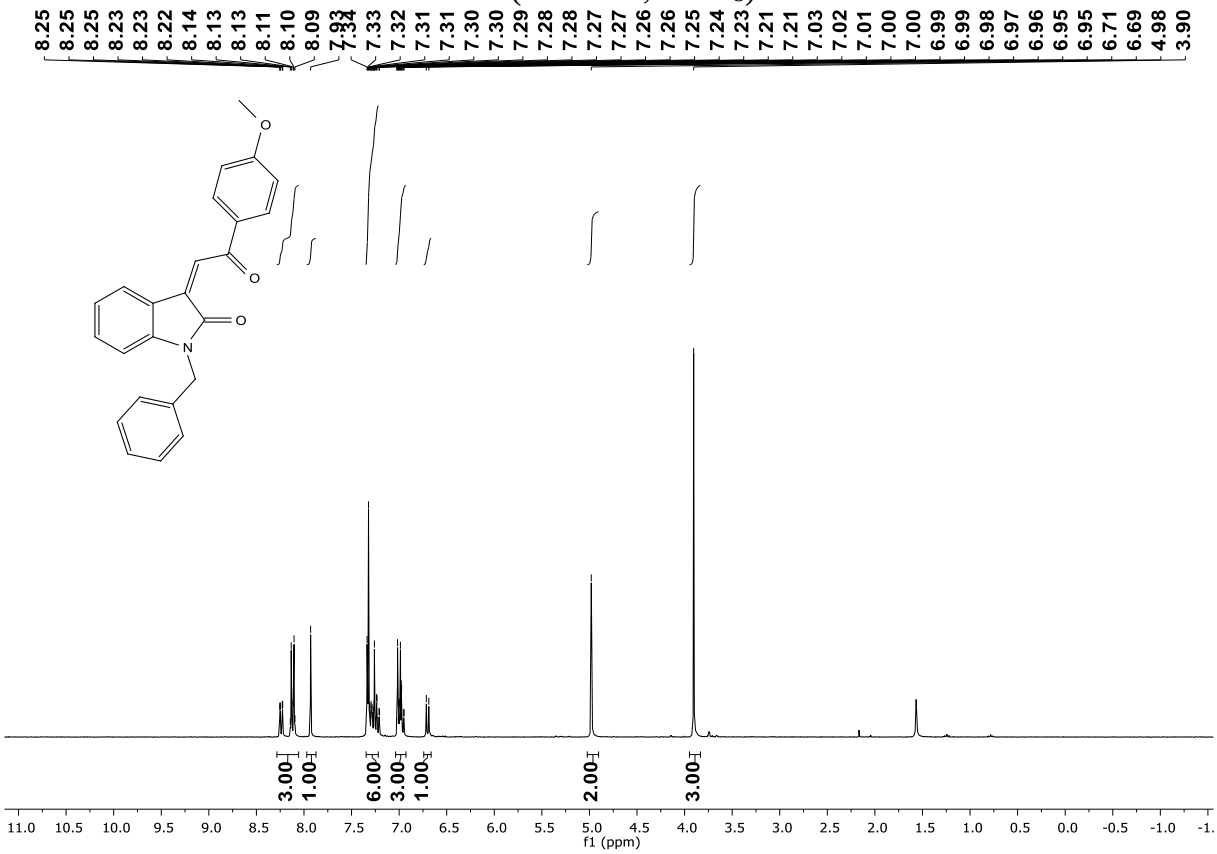
^{1}H NMR (300 MHz, $CDCl_3$) of **1w**



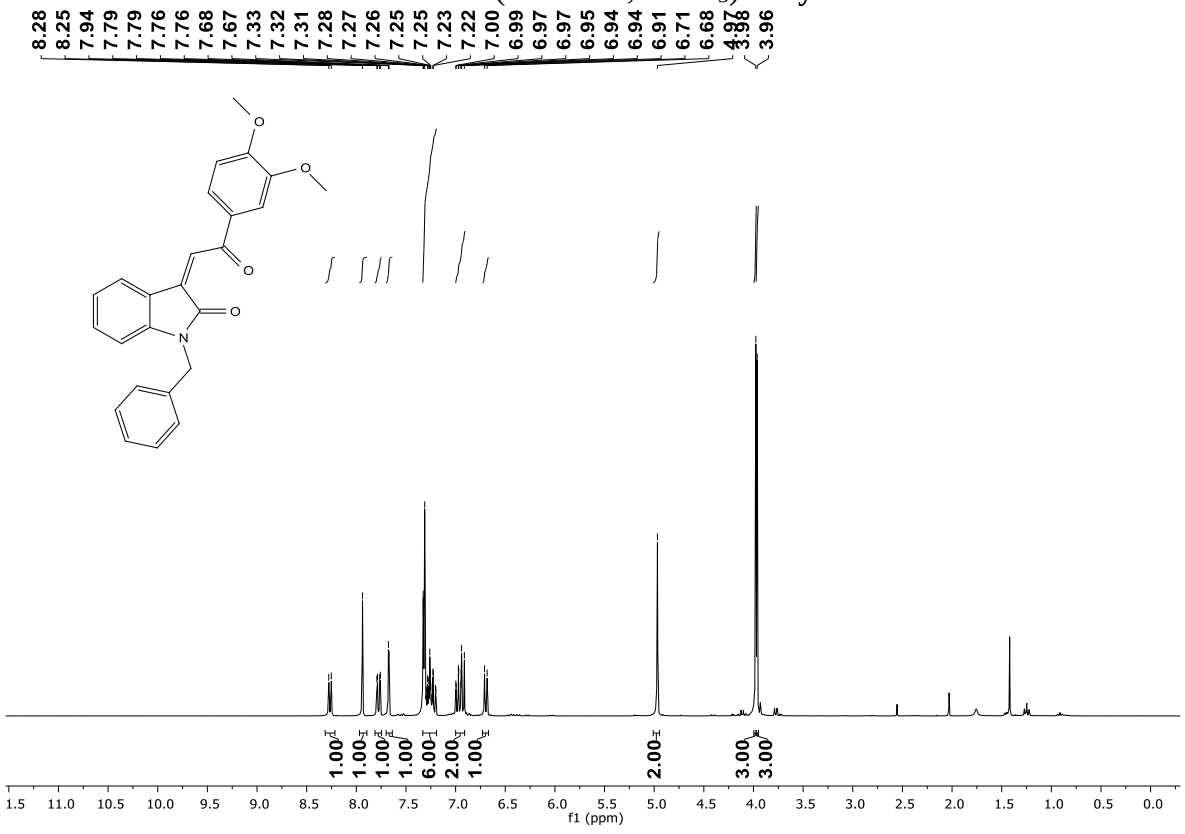
^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) of **1w**



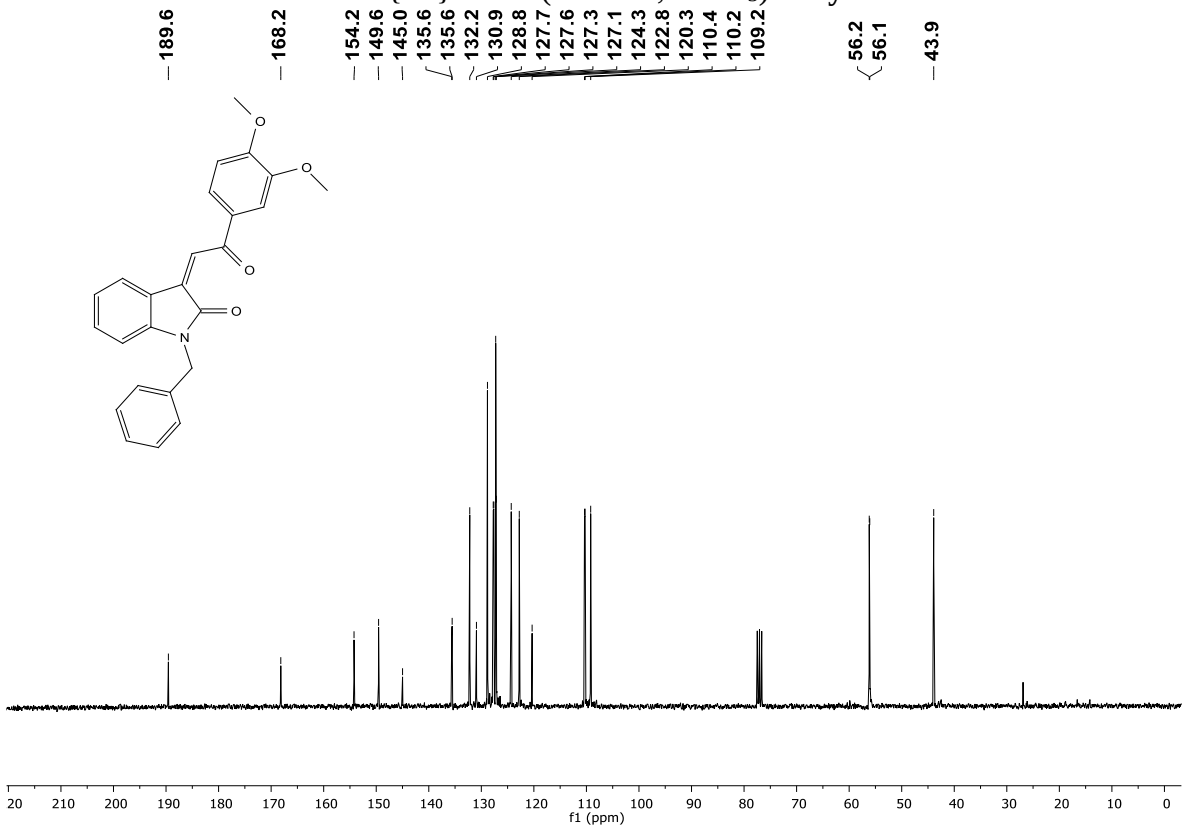
^{1}H NMR (300 MHz, $CDCl_3$) of **1x**



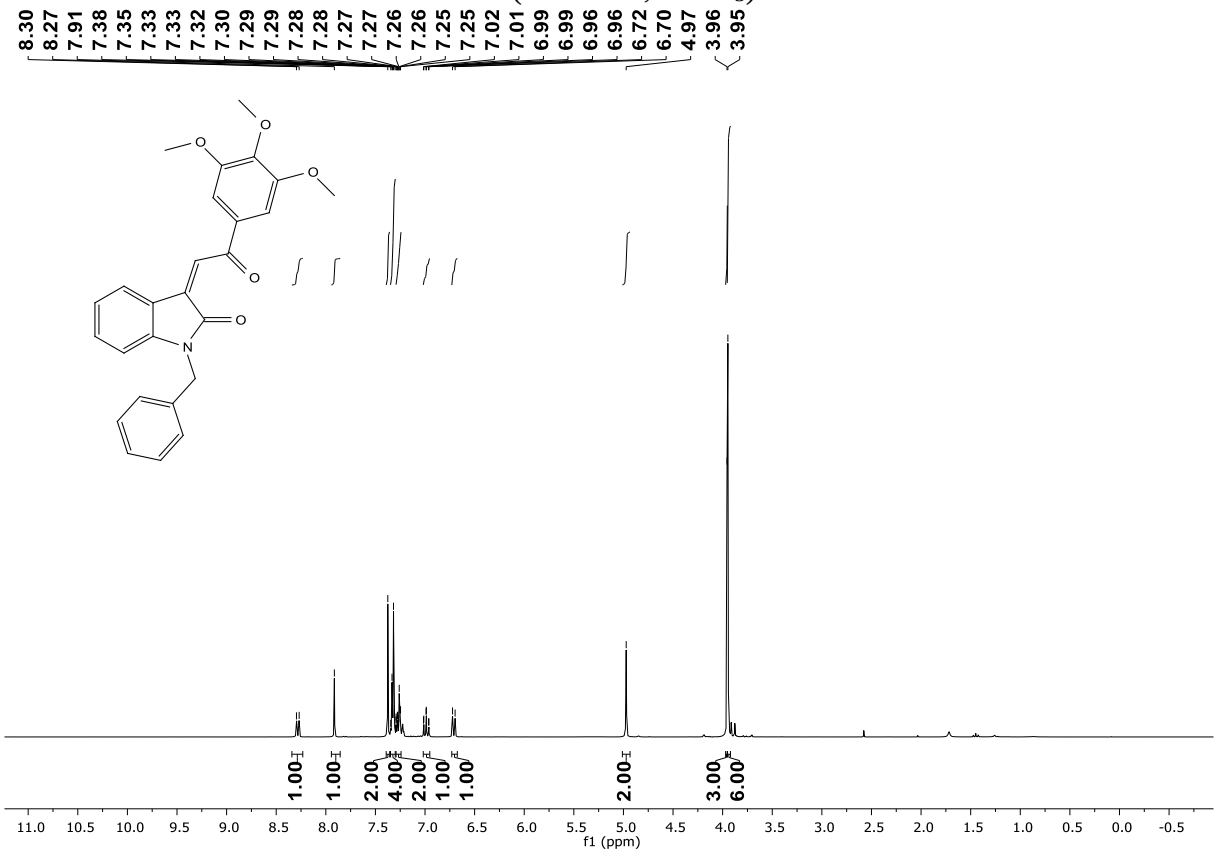
^{1}H NMR (300 MHz, $CDCl_3$) of **1y**



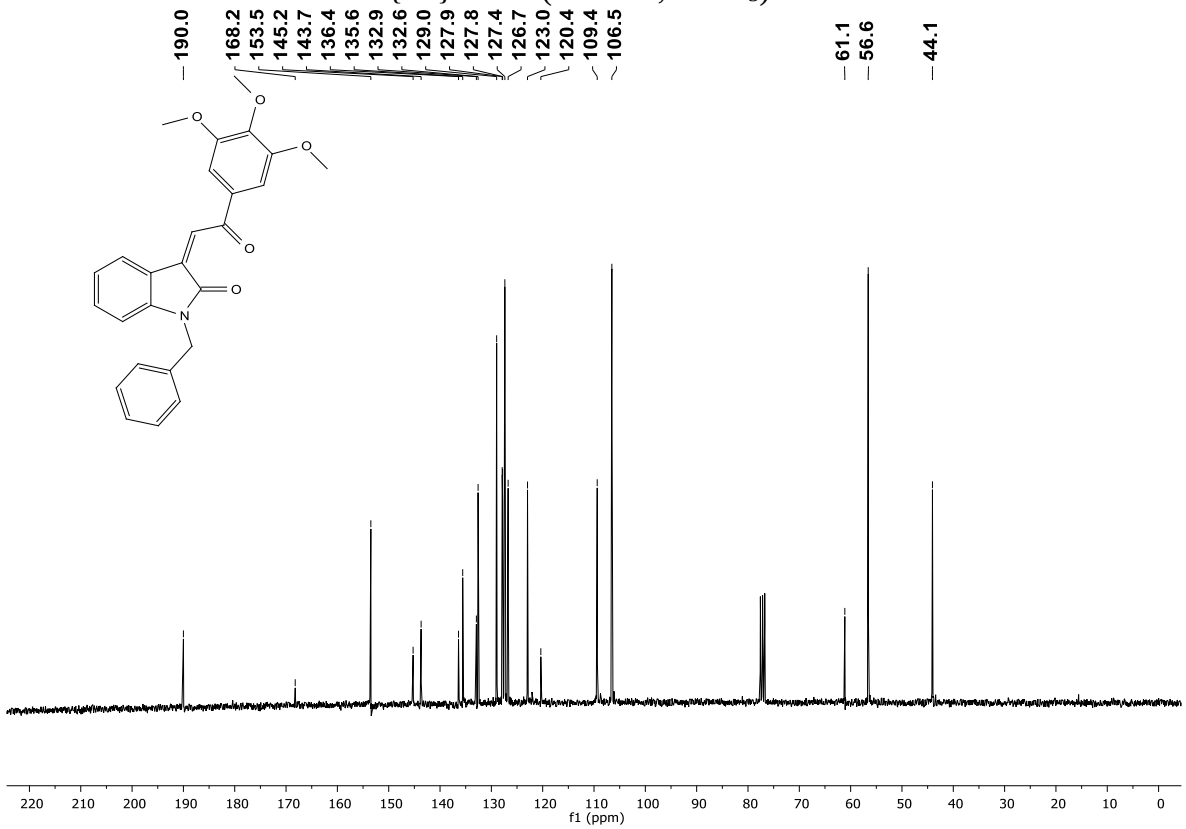
$^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) of **1y**



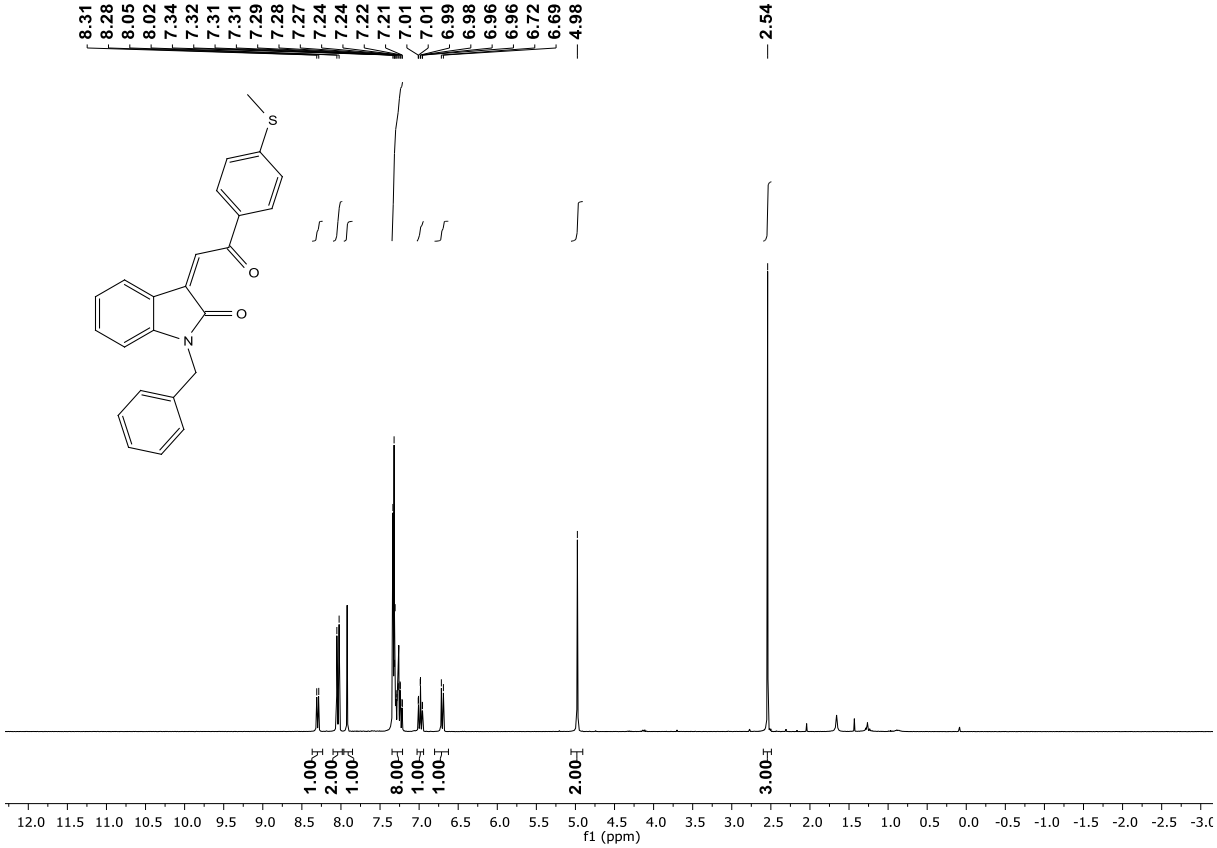
^{1}H NMR (300 MHz, $CDCl_3$) of **1z**



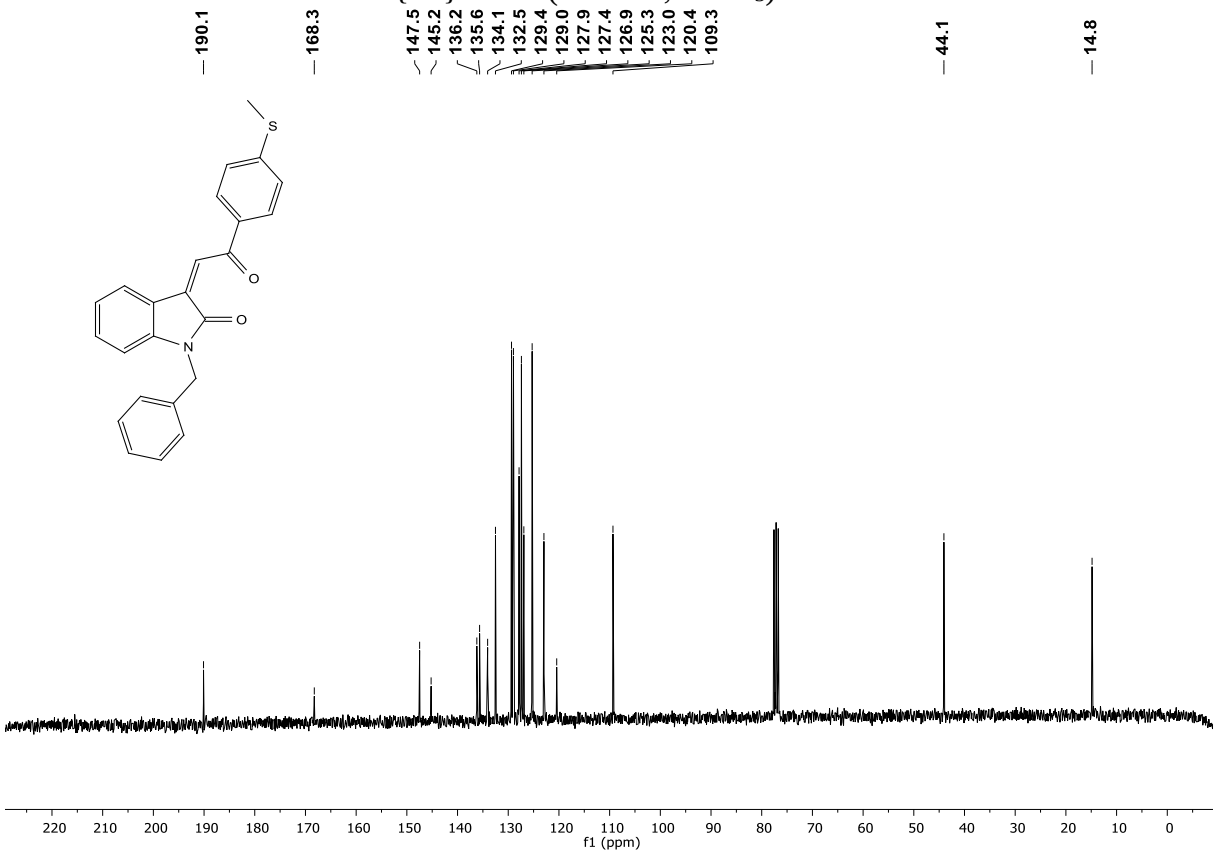
$^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) of **1z**



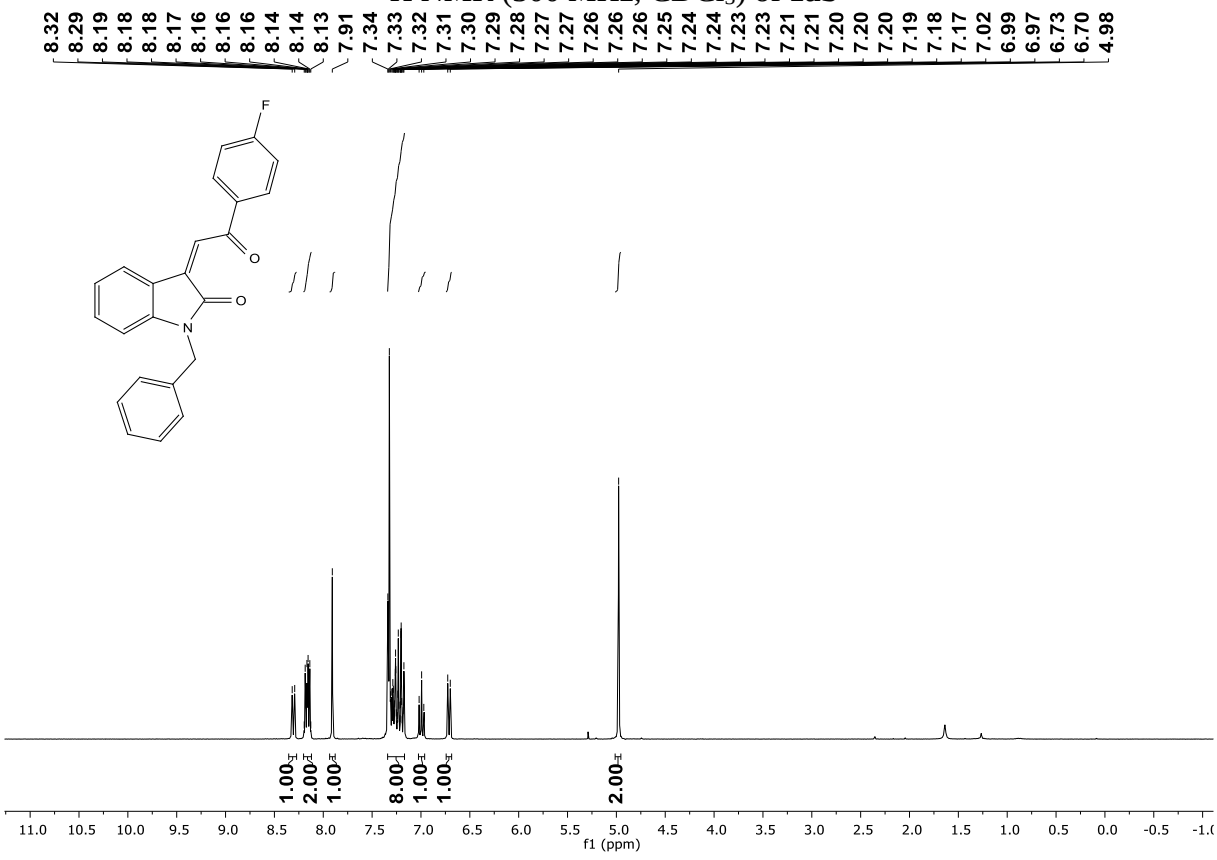
^{1}H NMR (300 MHz, $CDCl_3$) of **1aa**



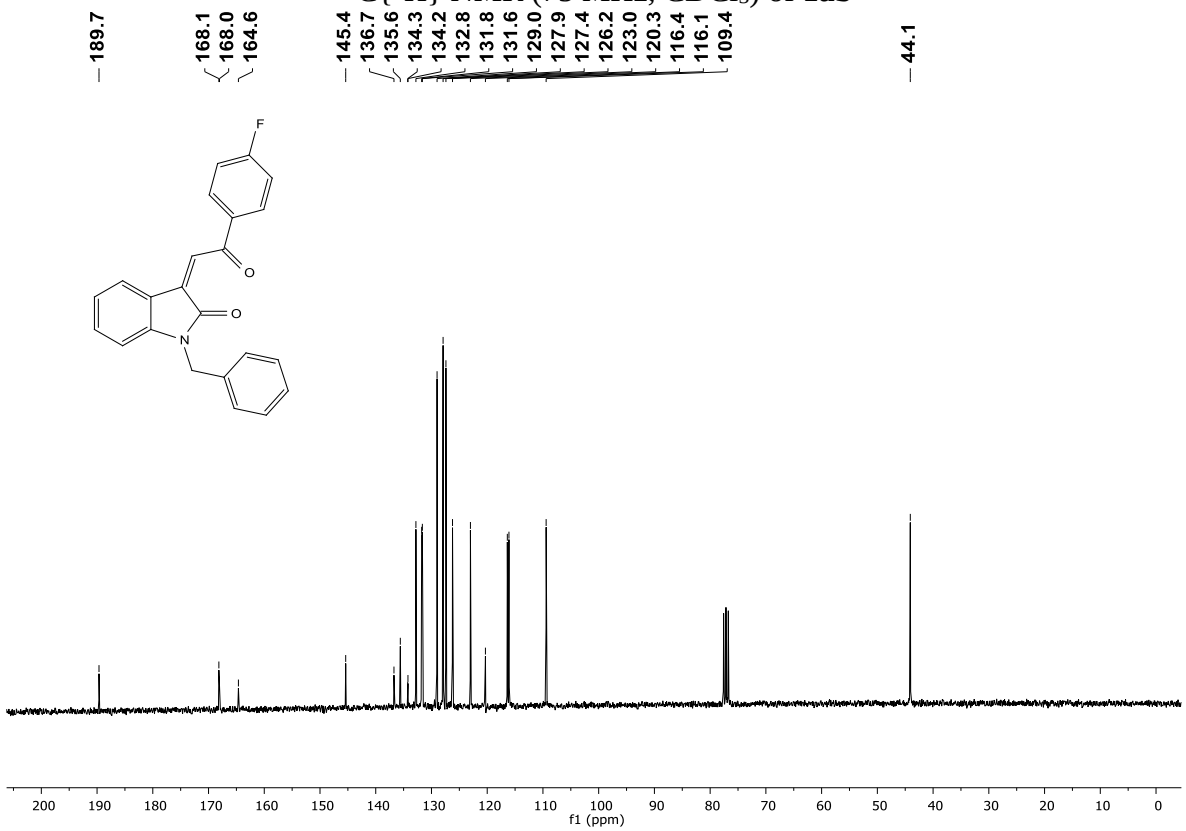
$^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) of **1aa**



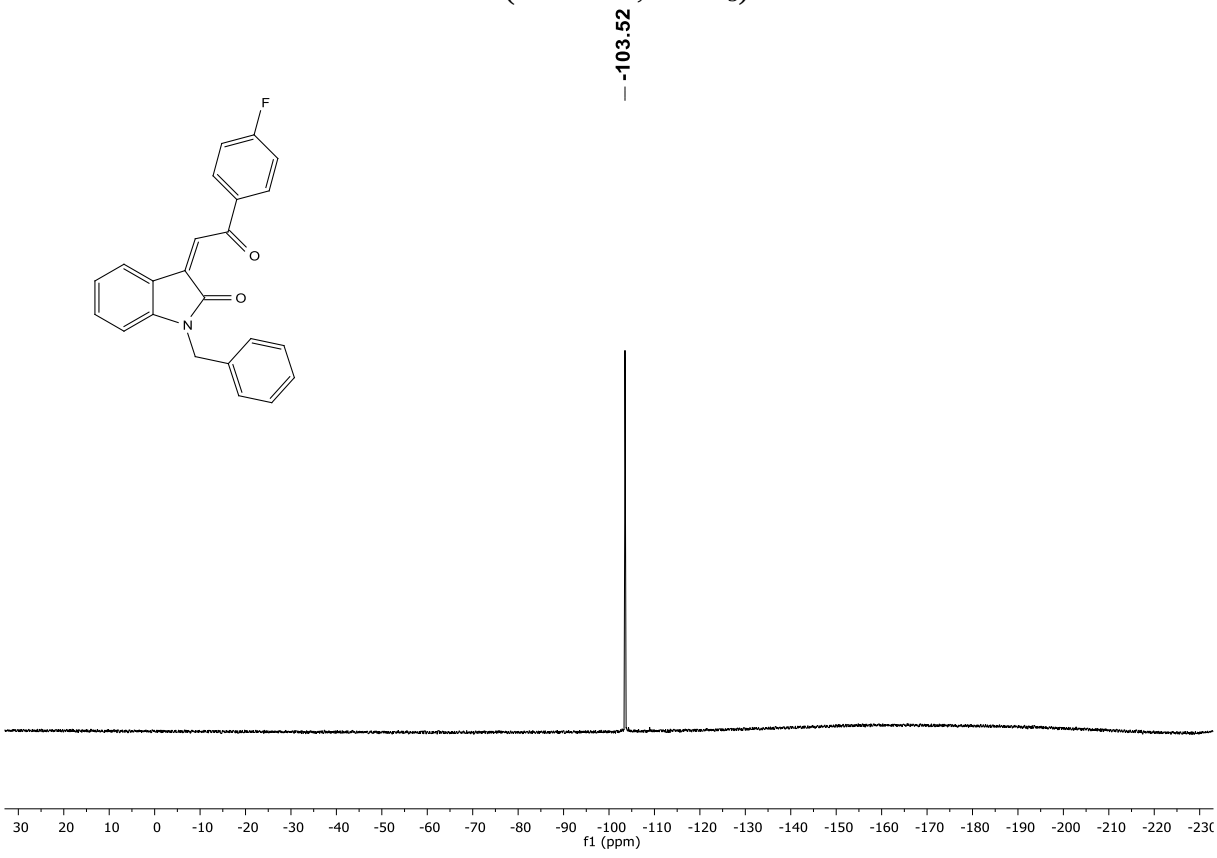
^{1}H NMR (300 MHz, $CDCl_3$) of **1ab**



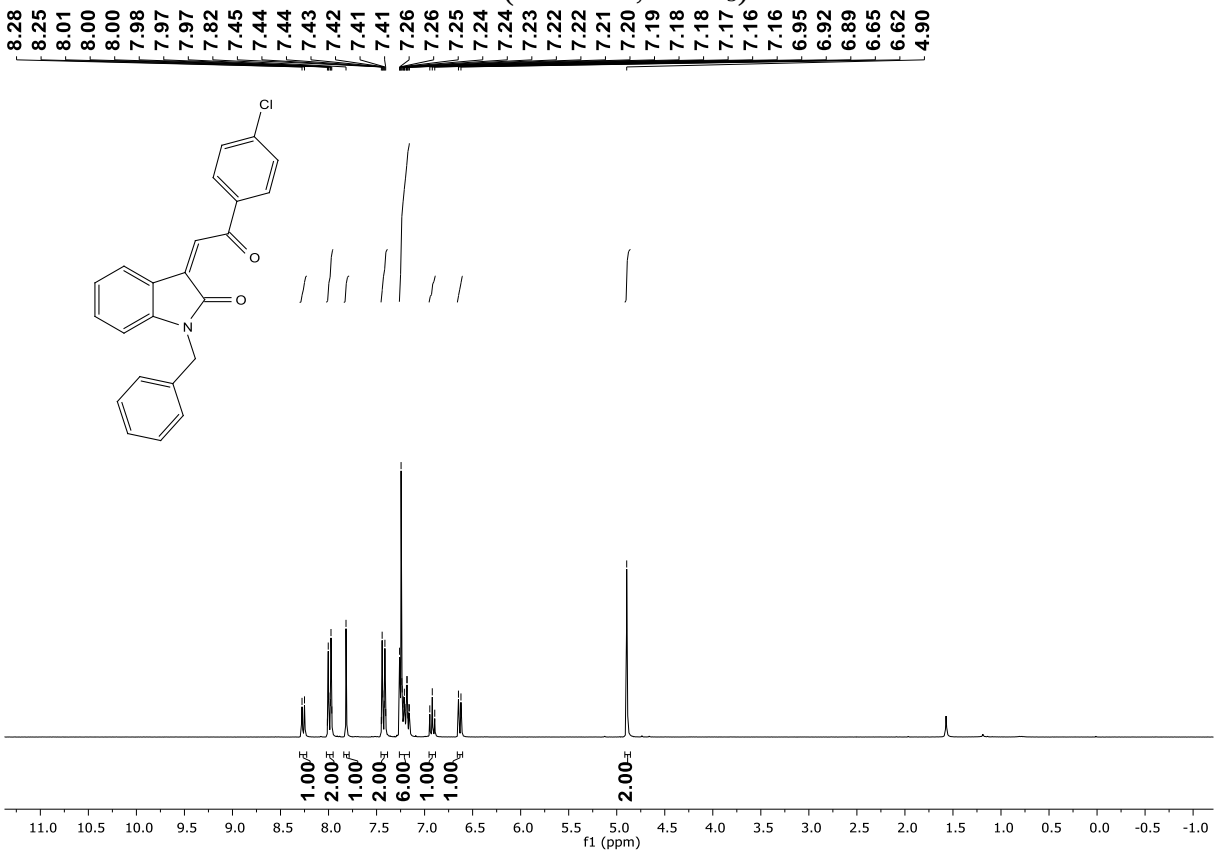
$^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) of **1ab**



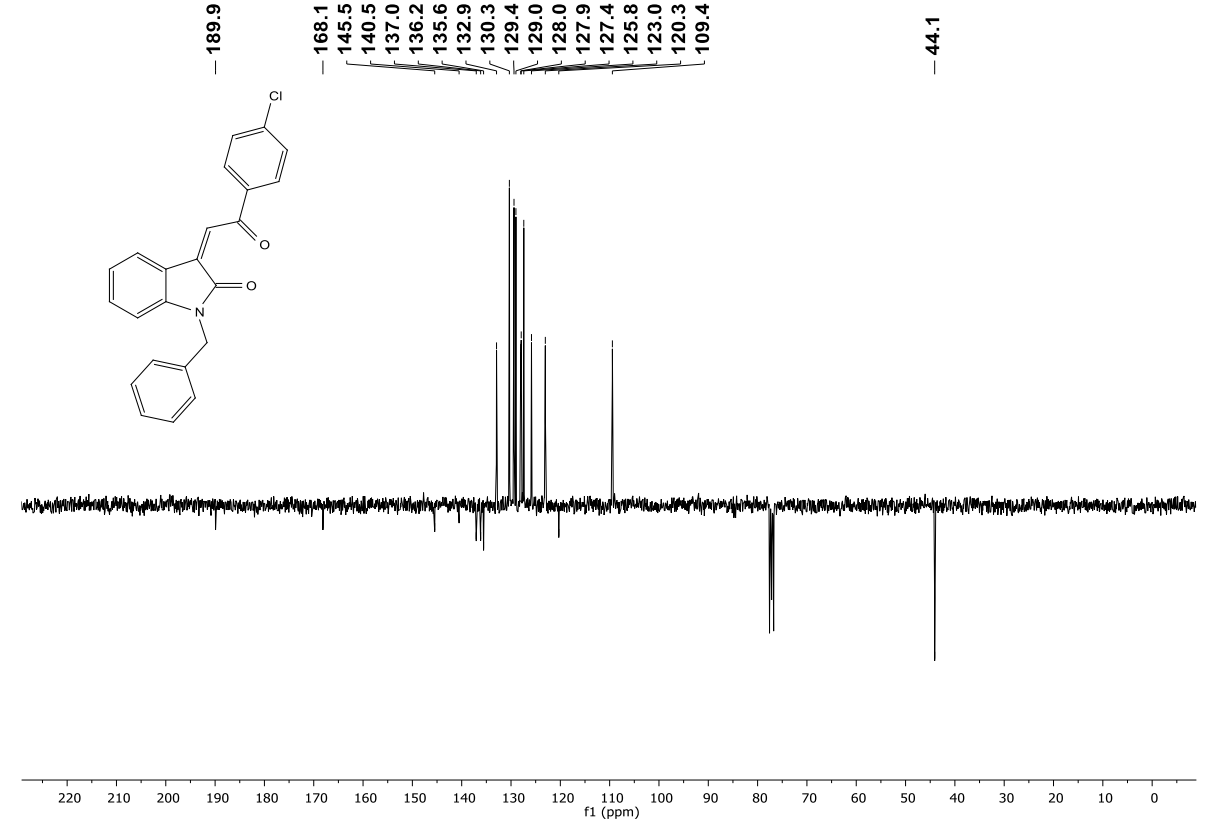
^{19}F NMR (188 MHz, $CDCl_3$) of **1ab**



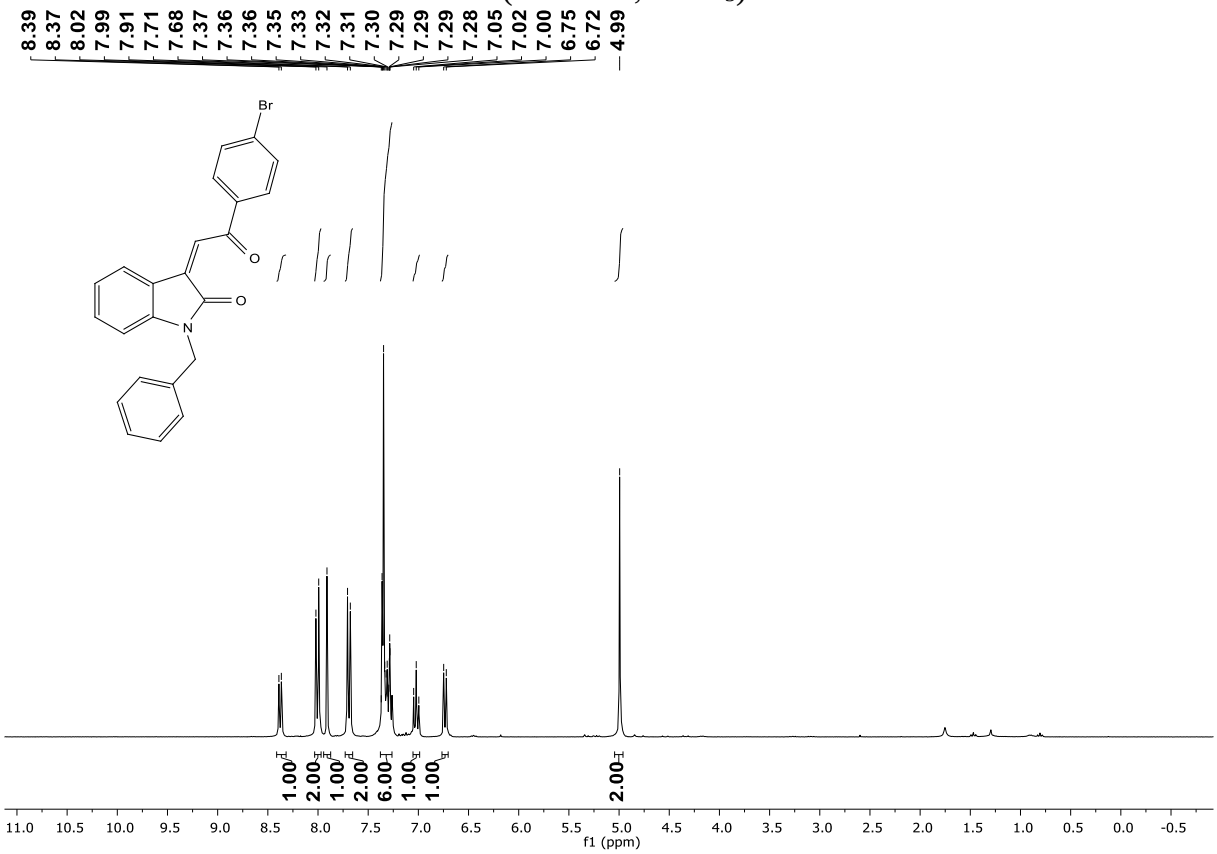
^{1}H NMR (300 MHz, $CDCl_3$) of **1ac**



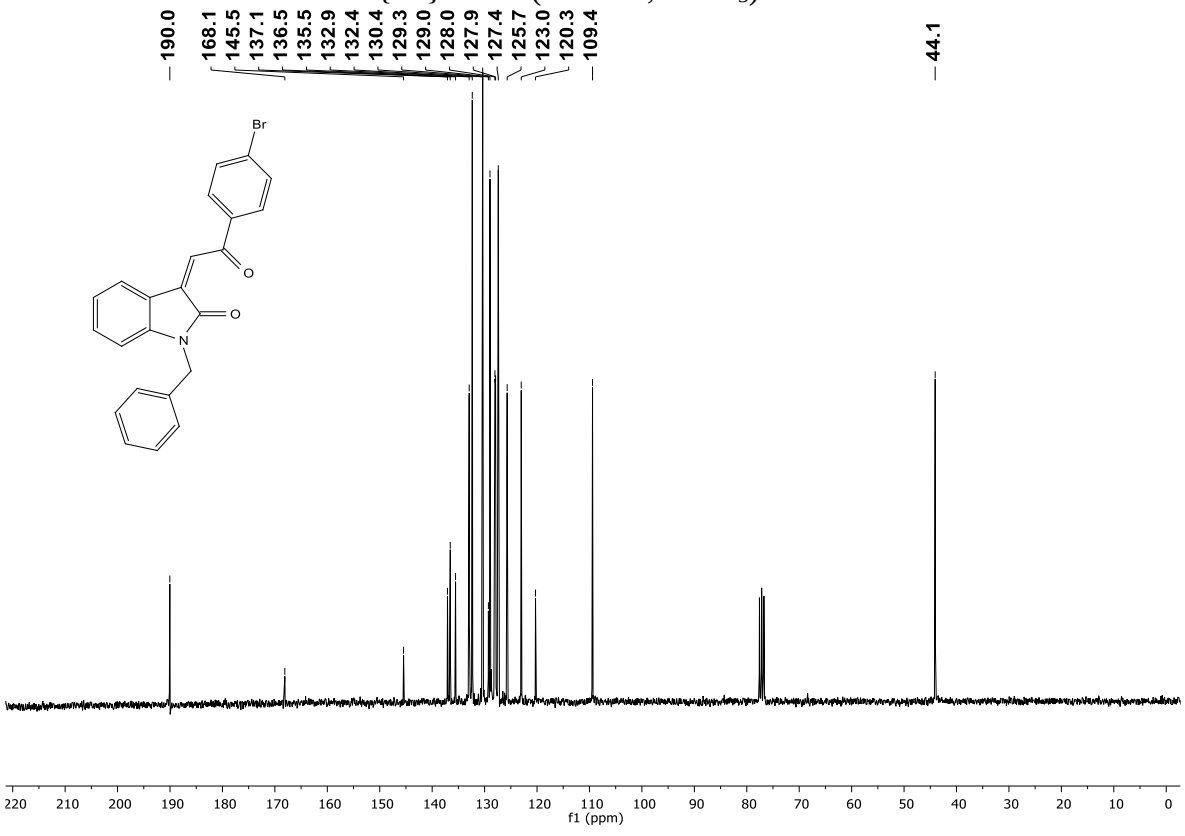
^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) of **1ac**



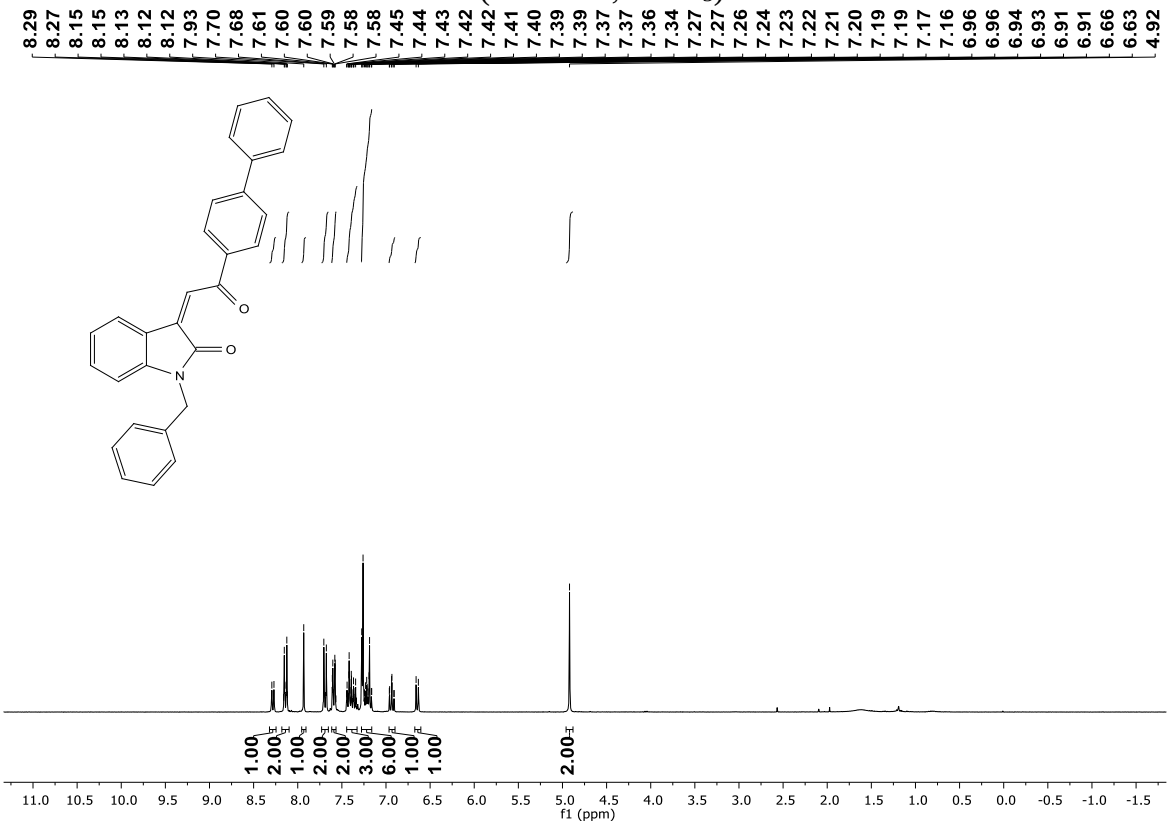
^{1}H NMR (300 MHz, $CDCl_3$) of **1ad**



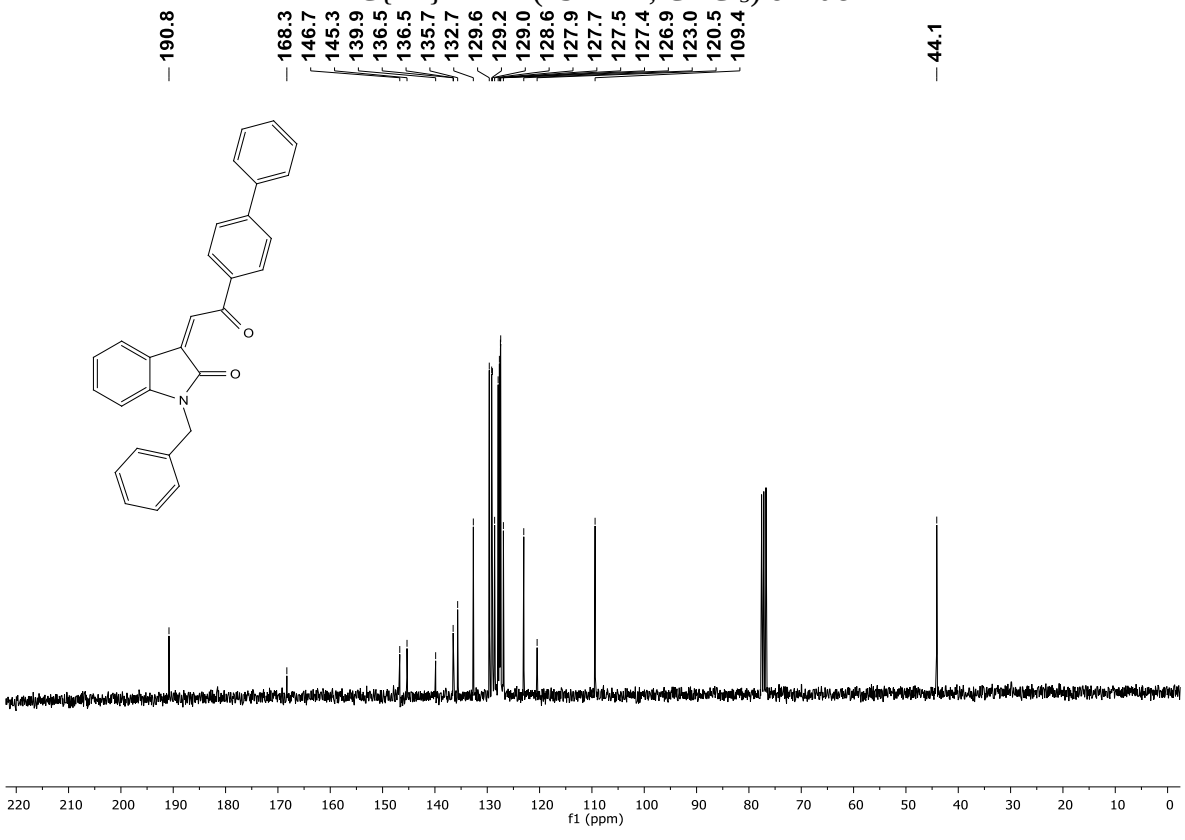
$^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) of **1ad**



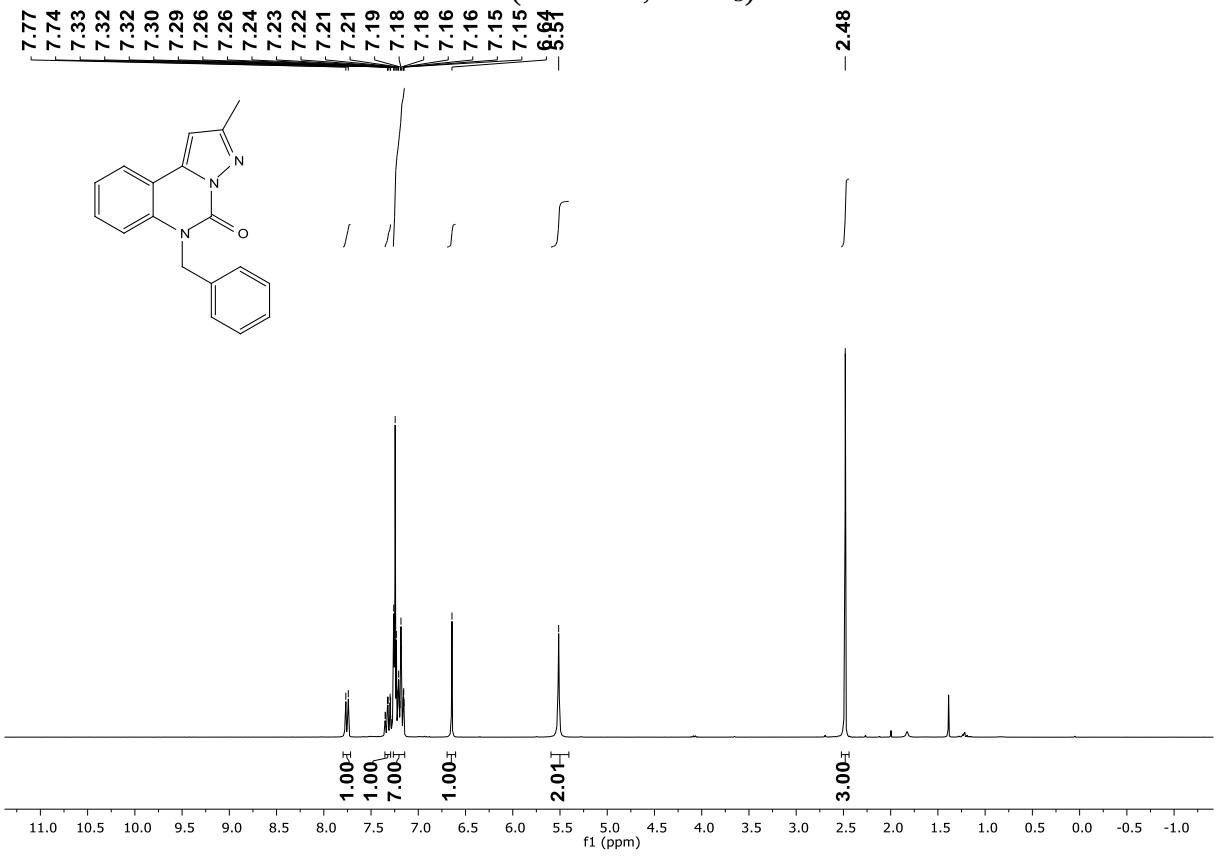
^{1}H NMR (300 MHz, $CDCl_3$) of **1ae**



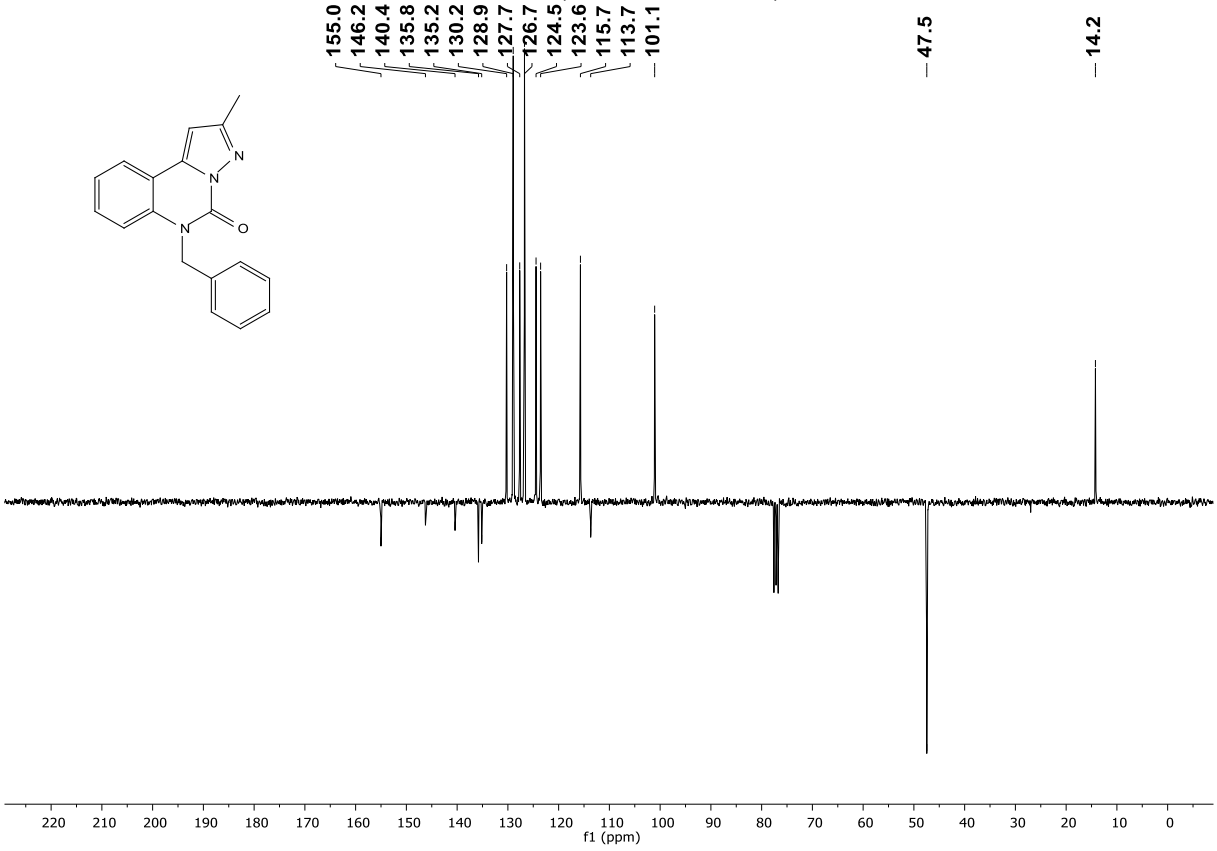
^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) of **1ae**



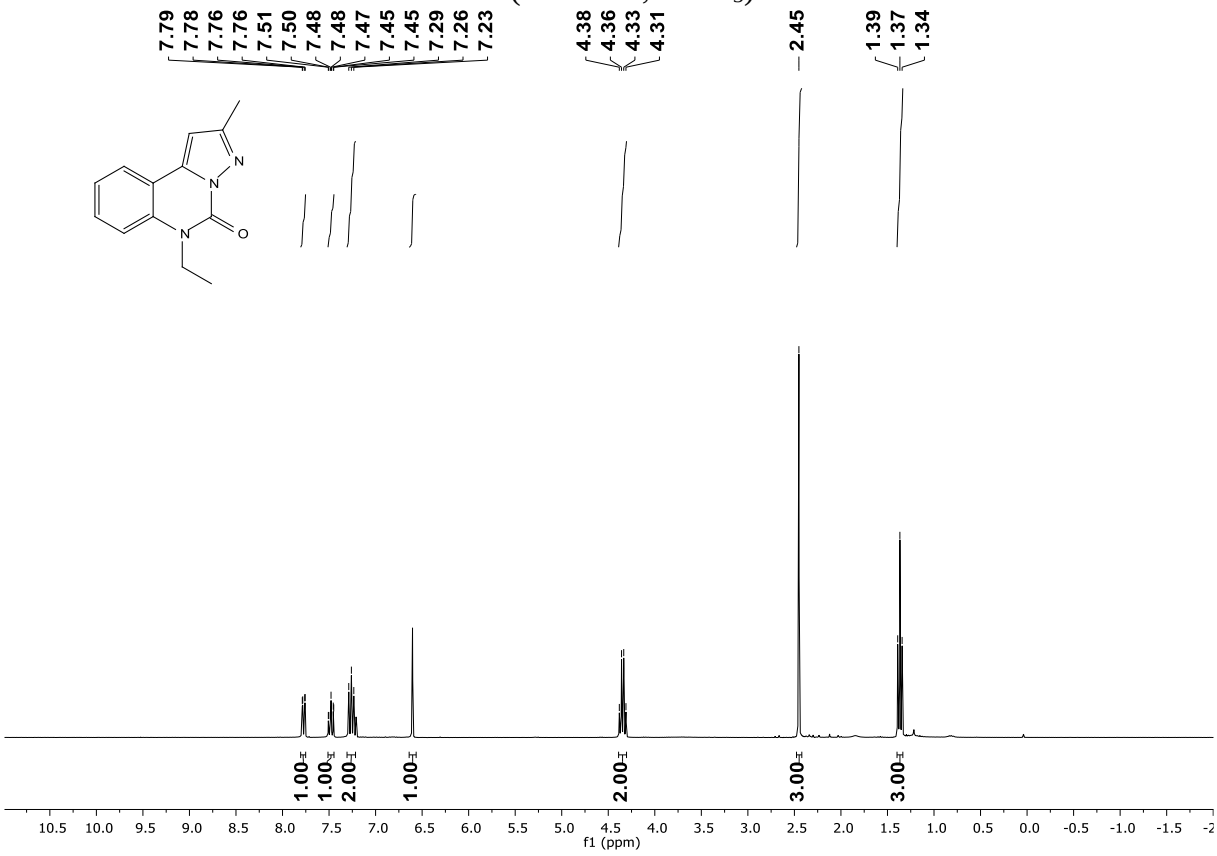
^{1}H NMR (300 MHz, $CDCl_3$) of **2a**



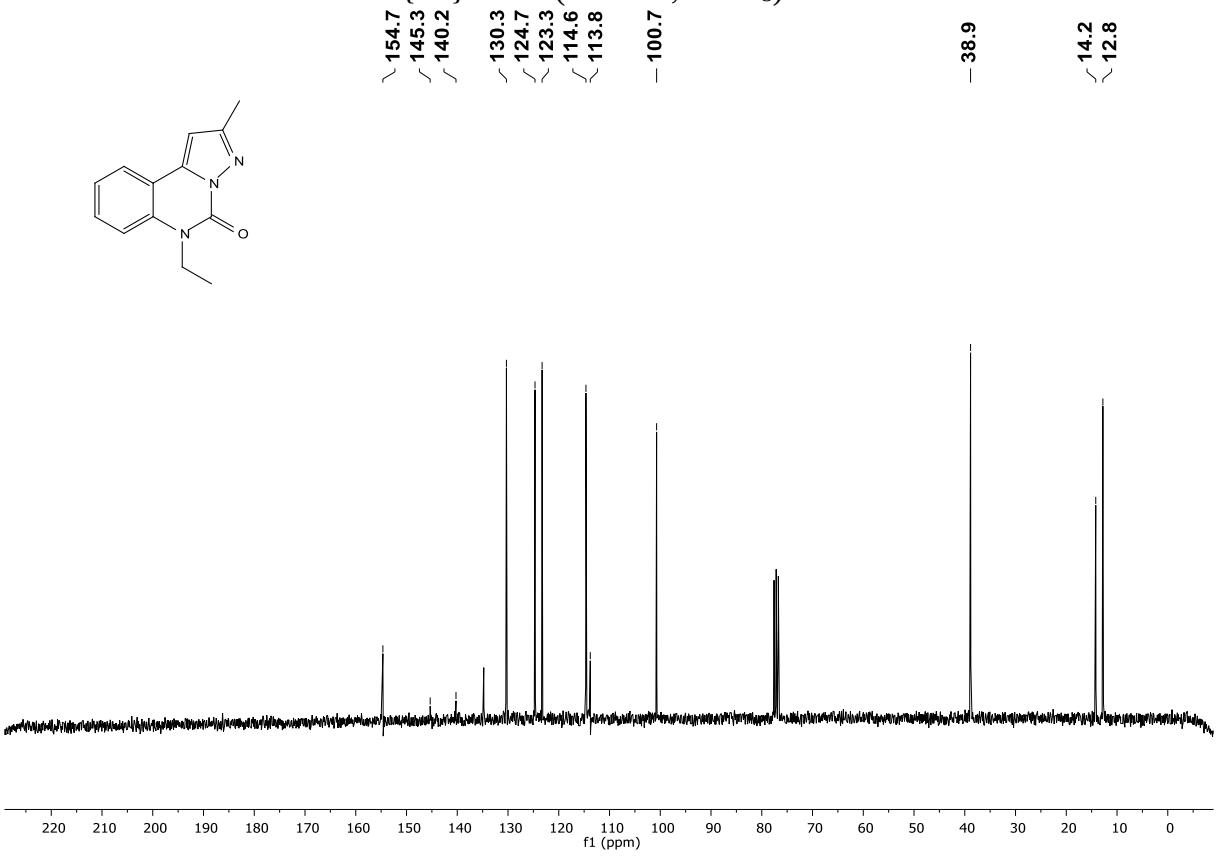
$^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) of **2a**



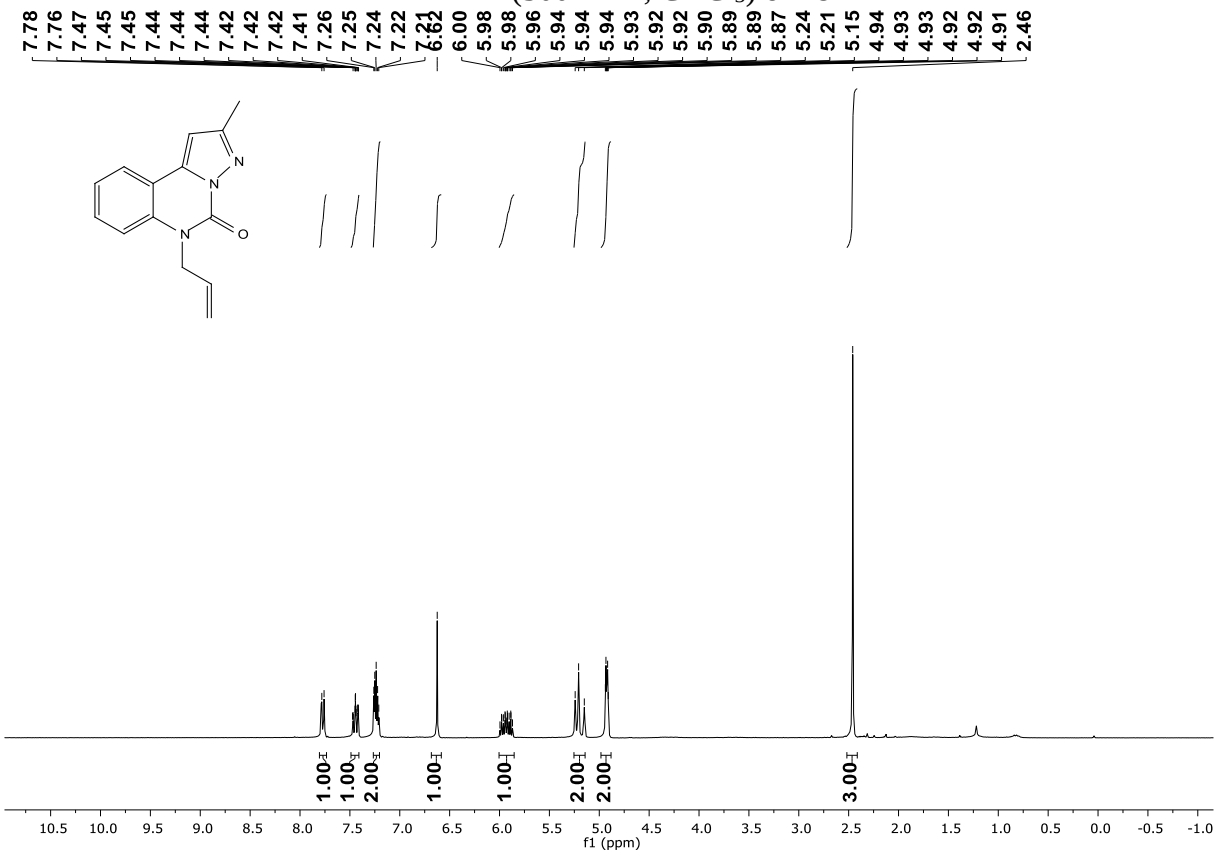
^{1}H NMR (300 MHz, $CDCl_3$) of **2b**



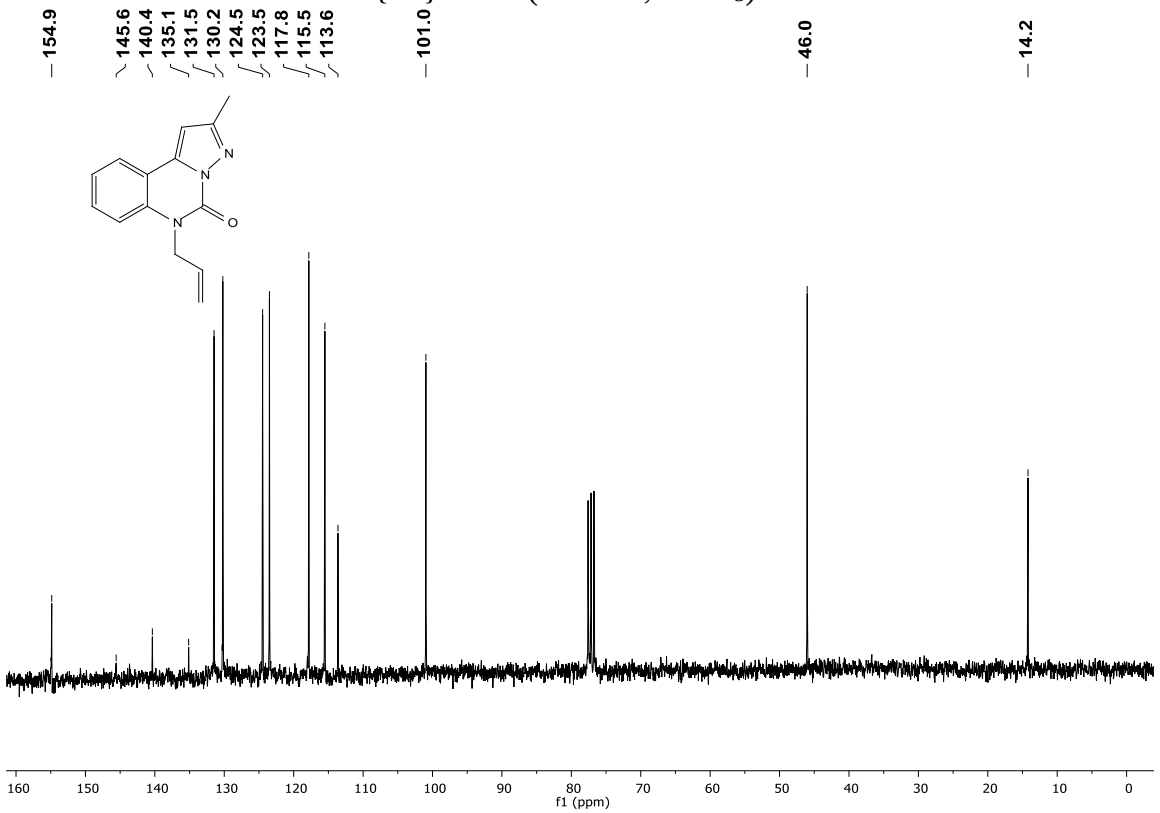
$^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) of **2b**



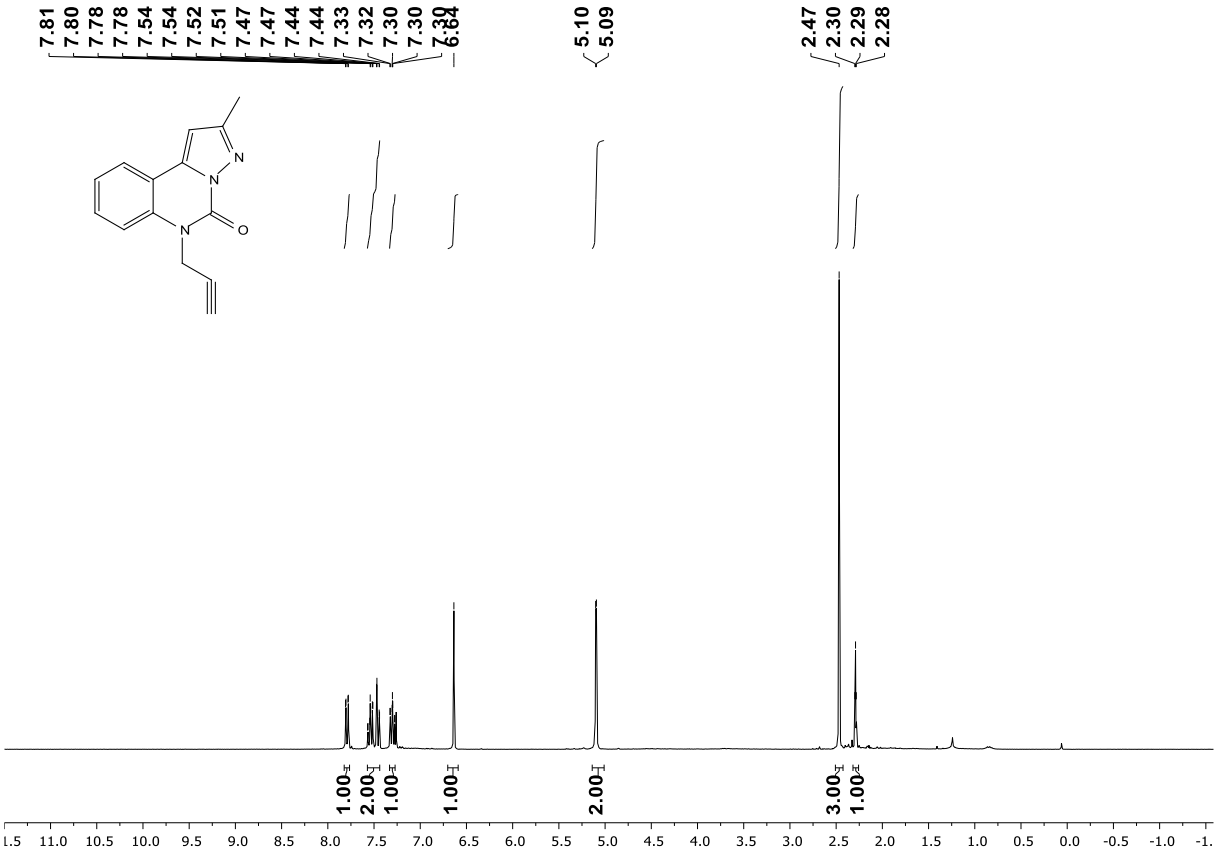
^{1}H NMR (300 MHz, $CDCl_3$) of **2c**



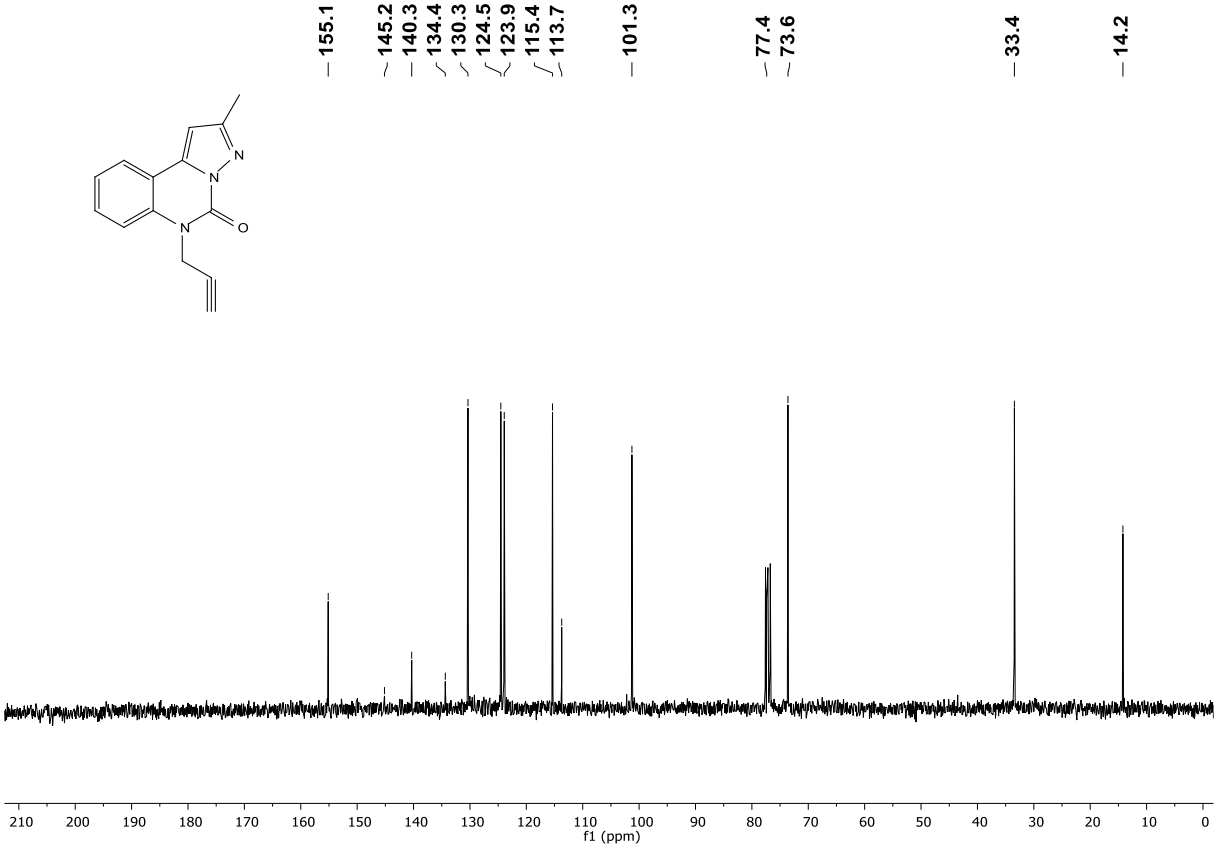
$^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) of **2c**



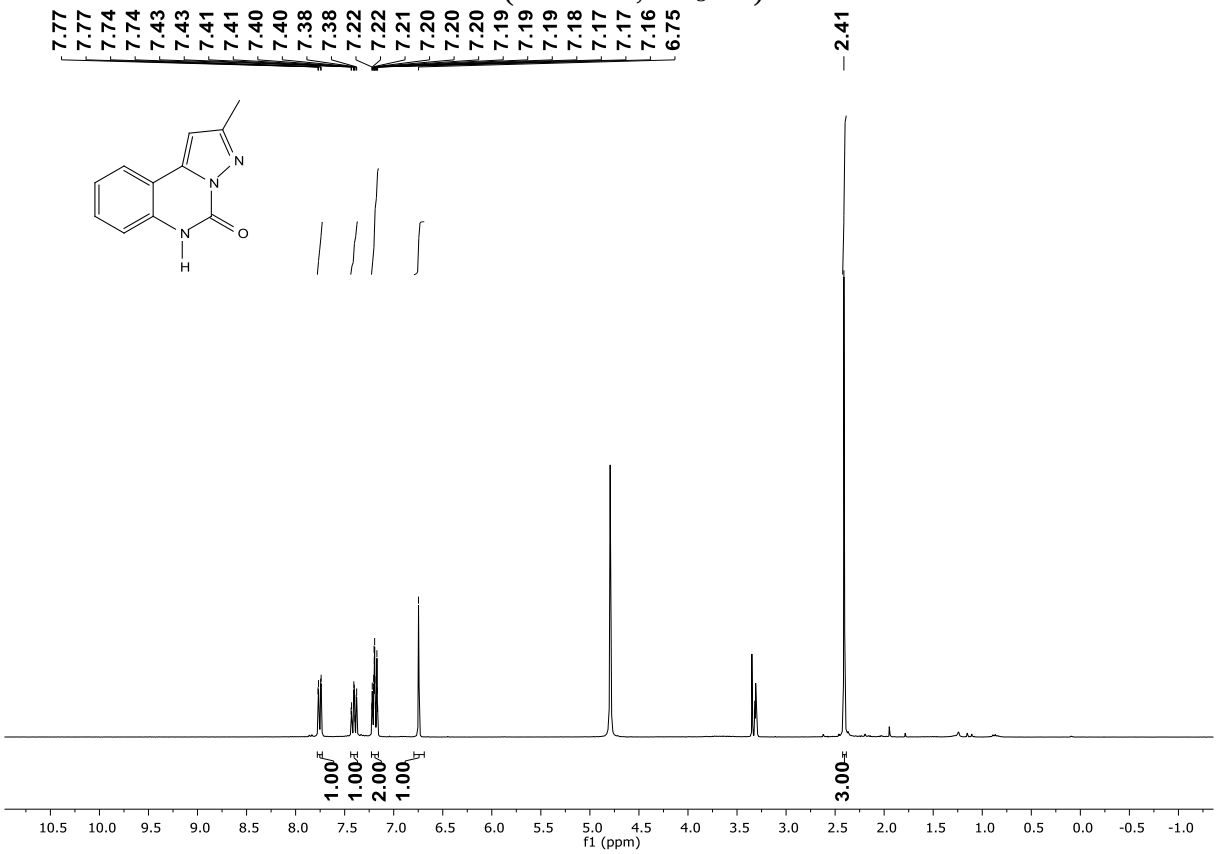
^{1}H NMR (300 MHz, $CDCl_3$) of **2d**



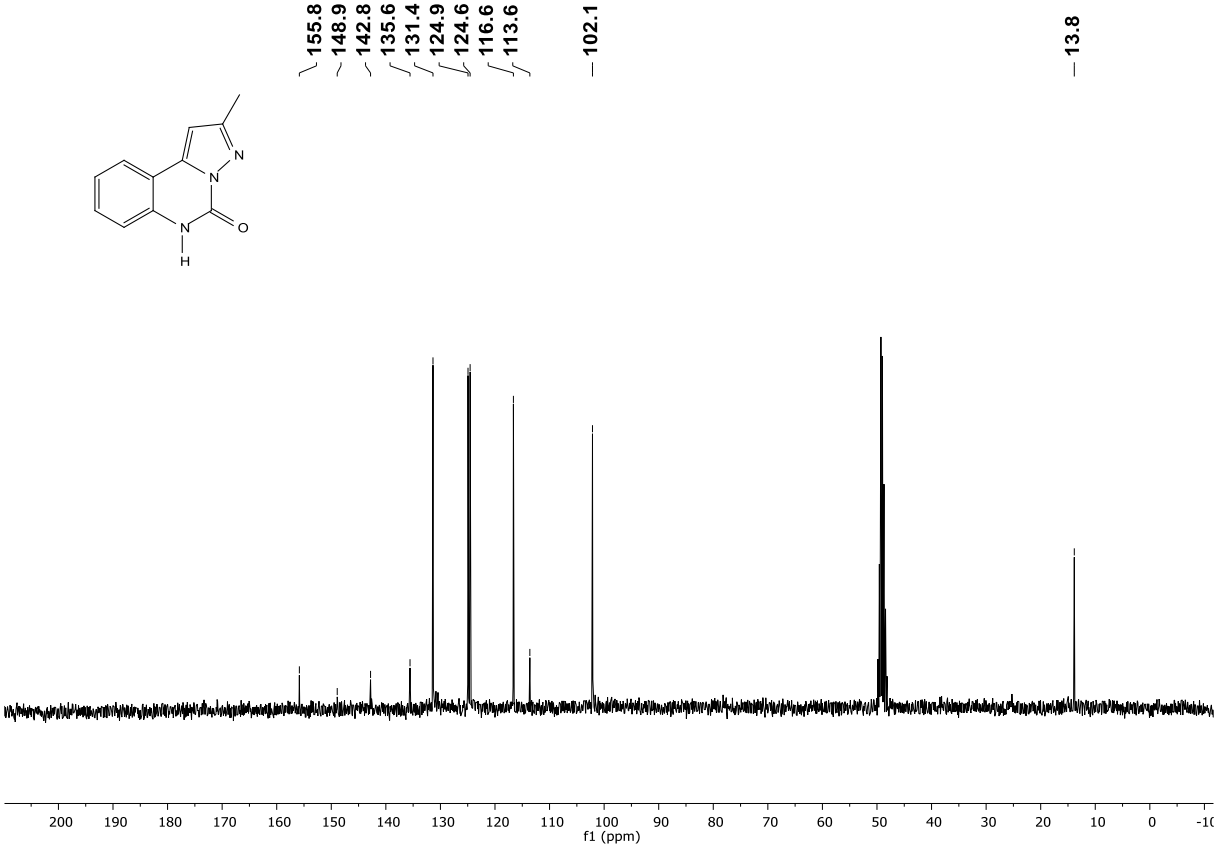
$^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) of **2d**



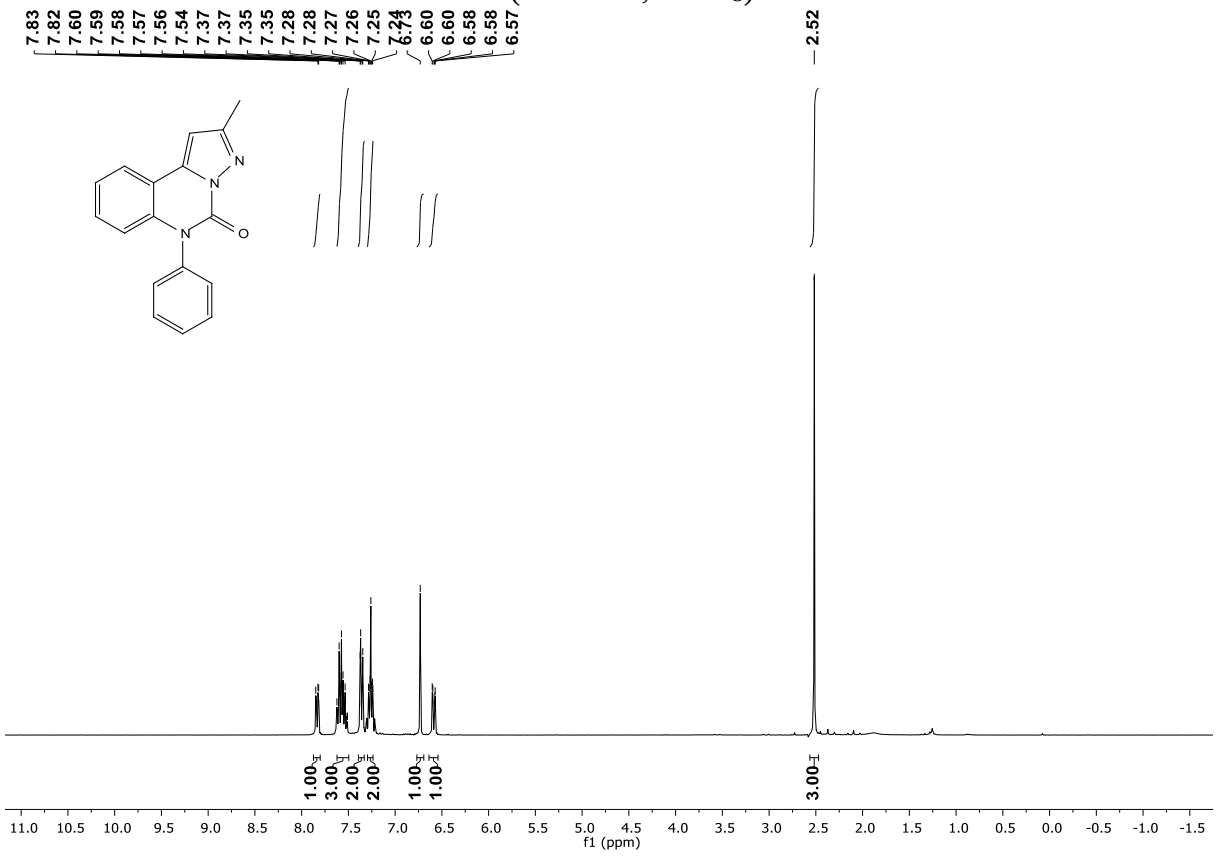
^{1}H NMR (300 MHz, CD_3OD) of **2e**



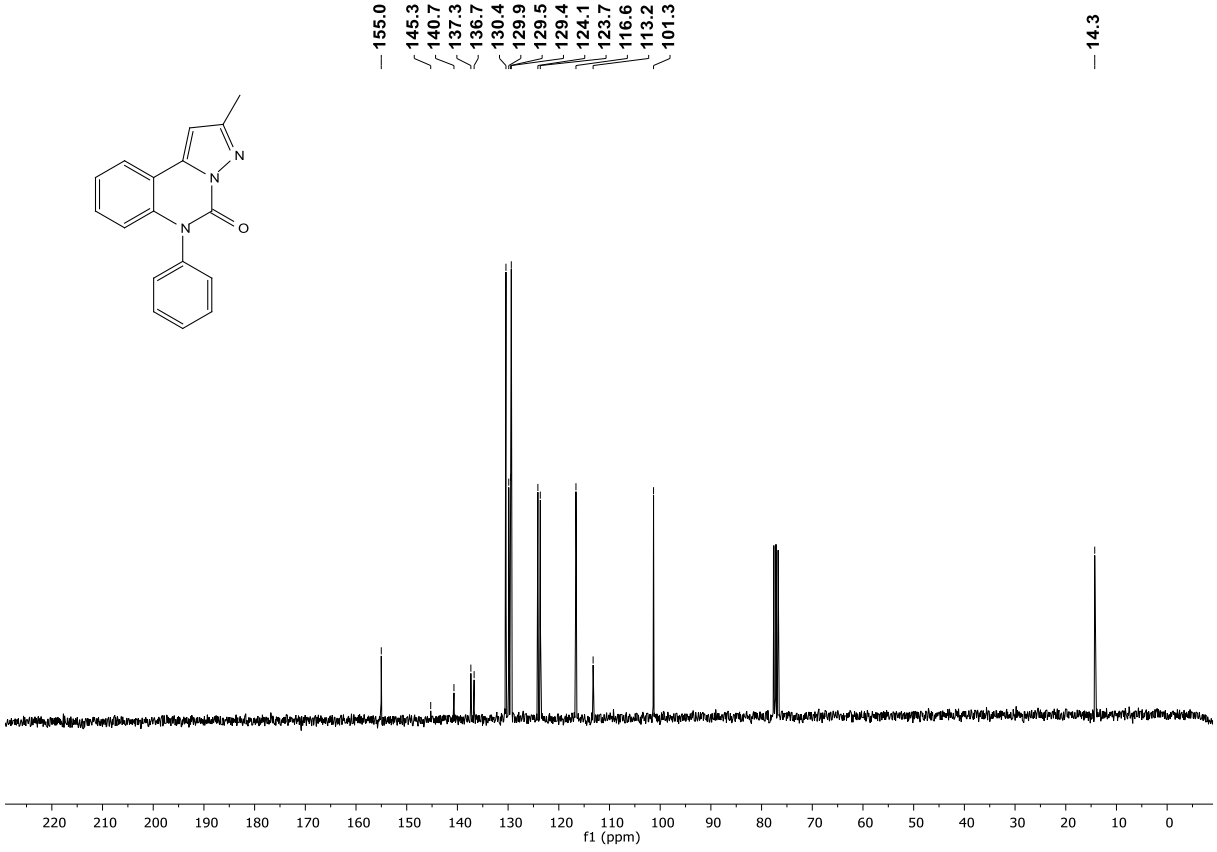
^{13}C{^{1}H} NMR (75 MHz, CD_3OD) of **2e**



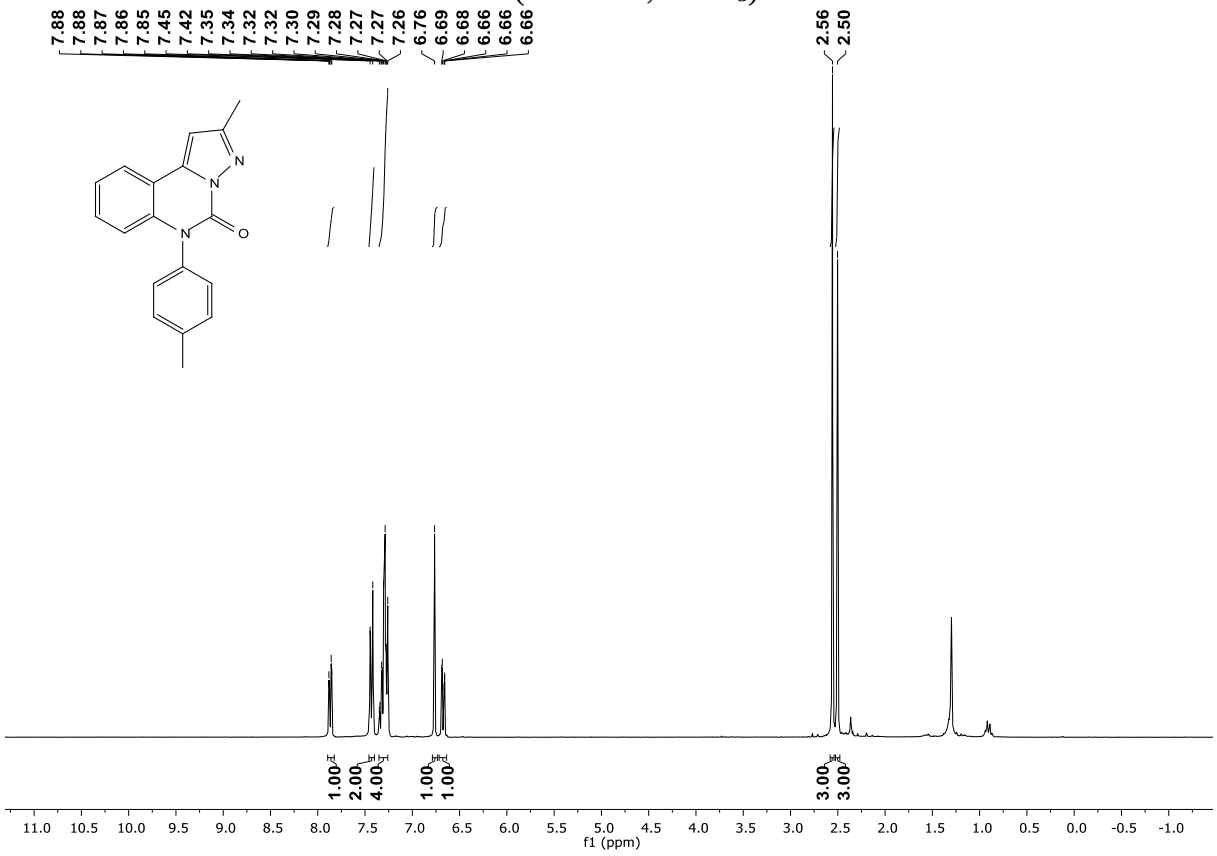
^{1}H NMR (300 MHz, $CDCl_3$) of **2h**



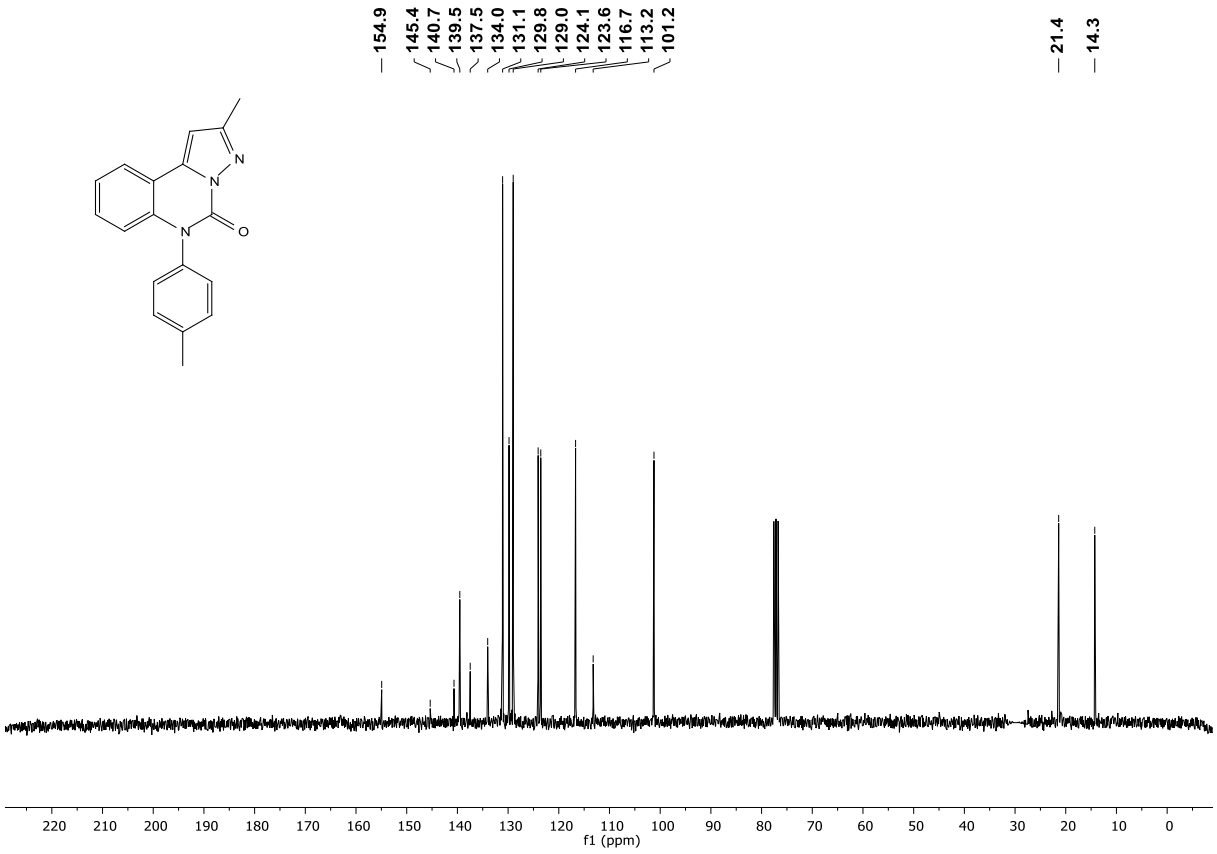
^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) of **2h**



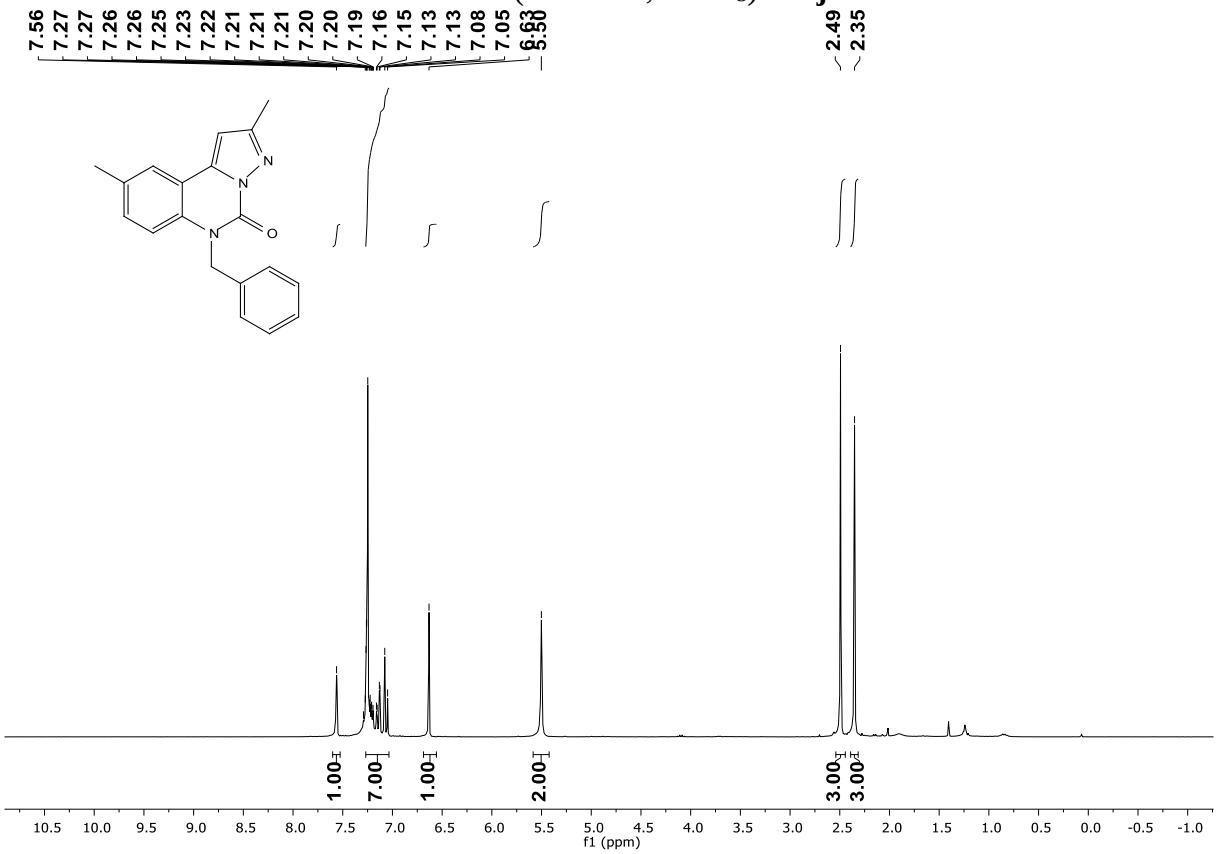
^{1}H NMR (300 MHz, $CDCl_3$) of **2i**



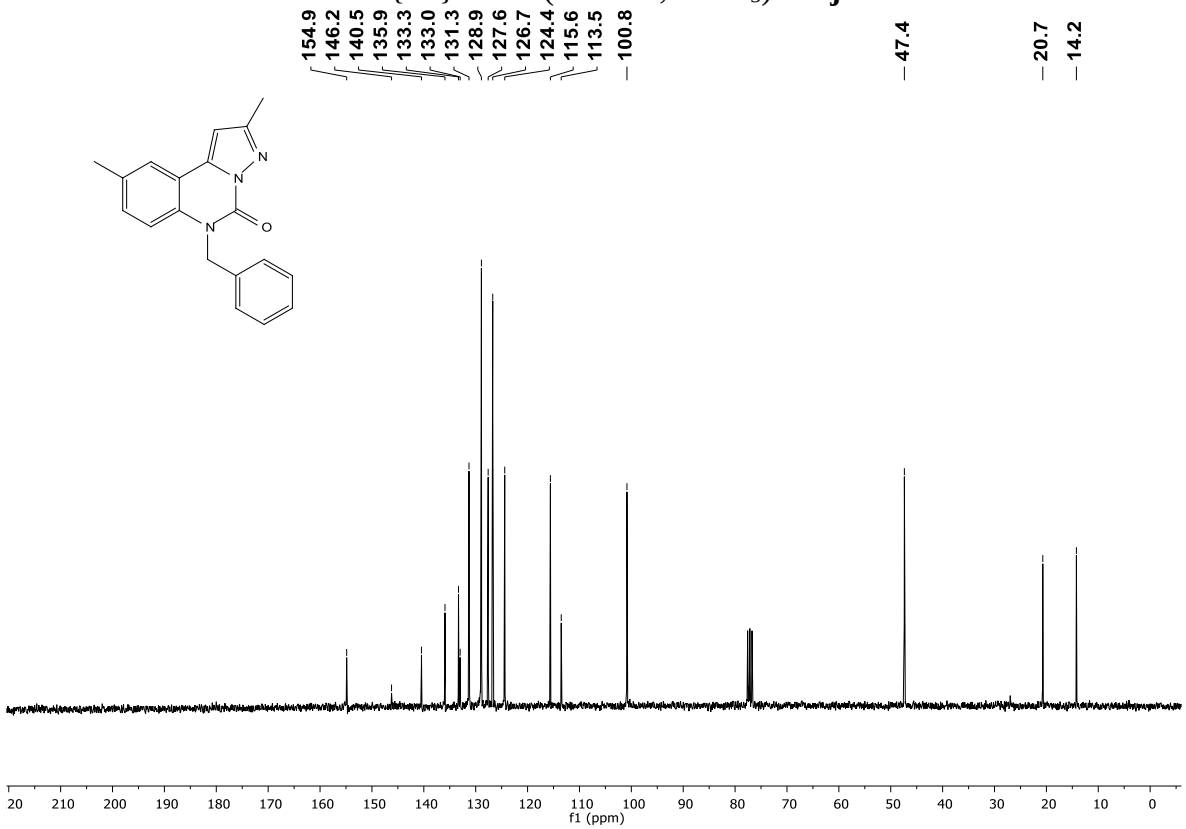
$^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) of **2i**



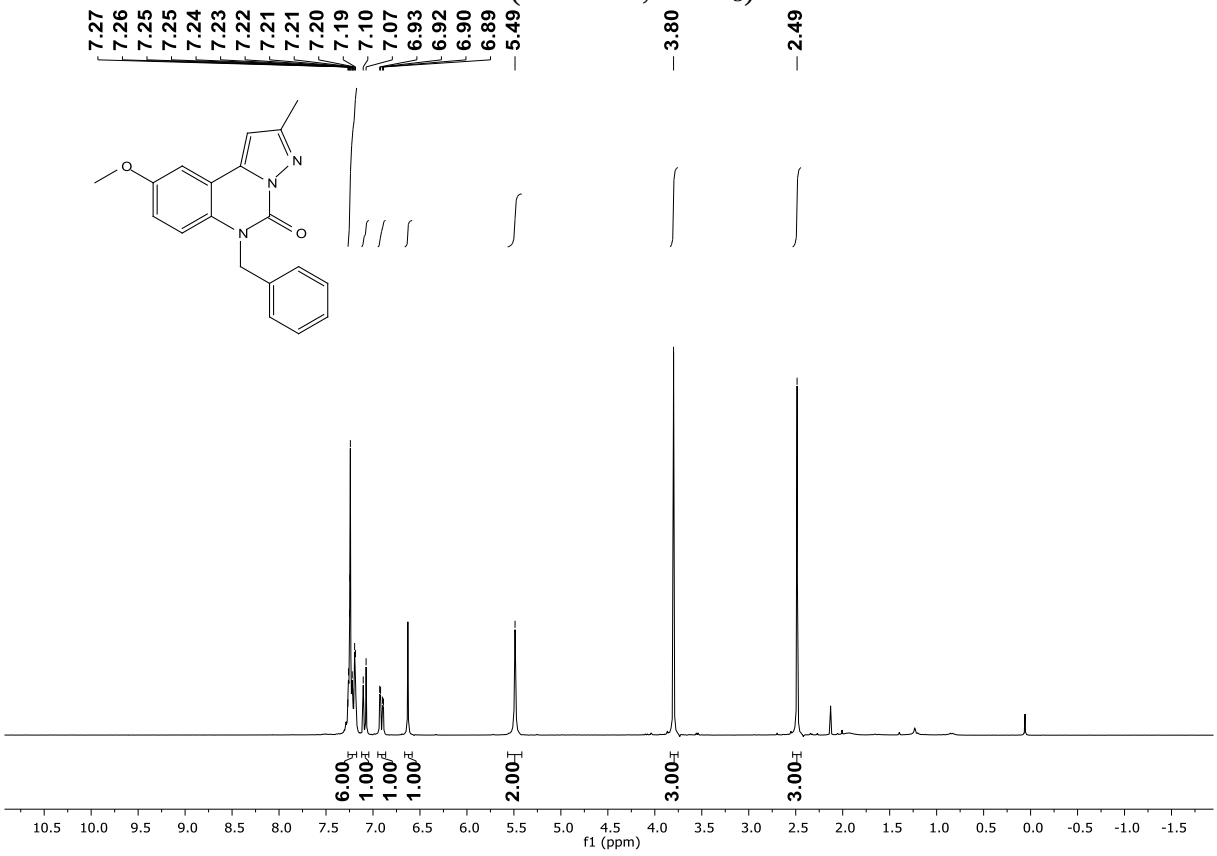
^{1}H NMR (300 MHz, $CDCl_3$) of **2j**



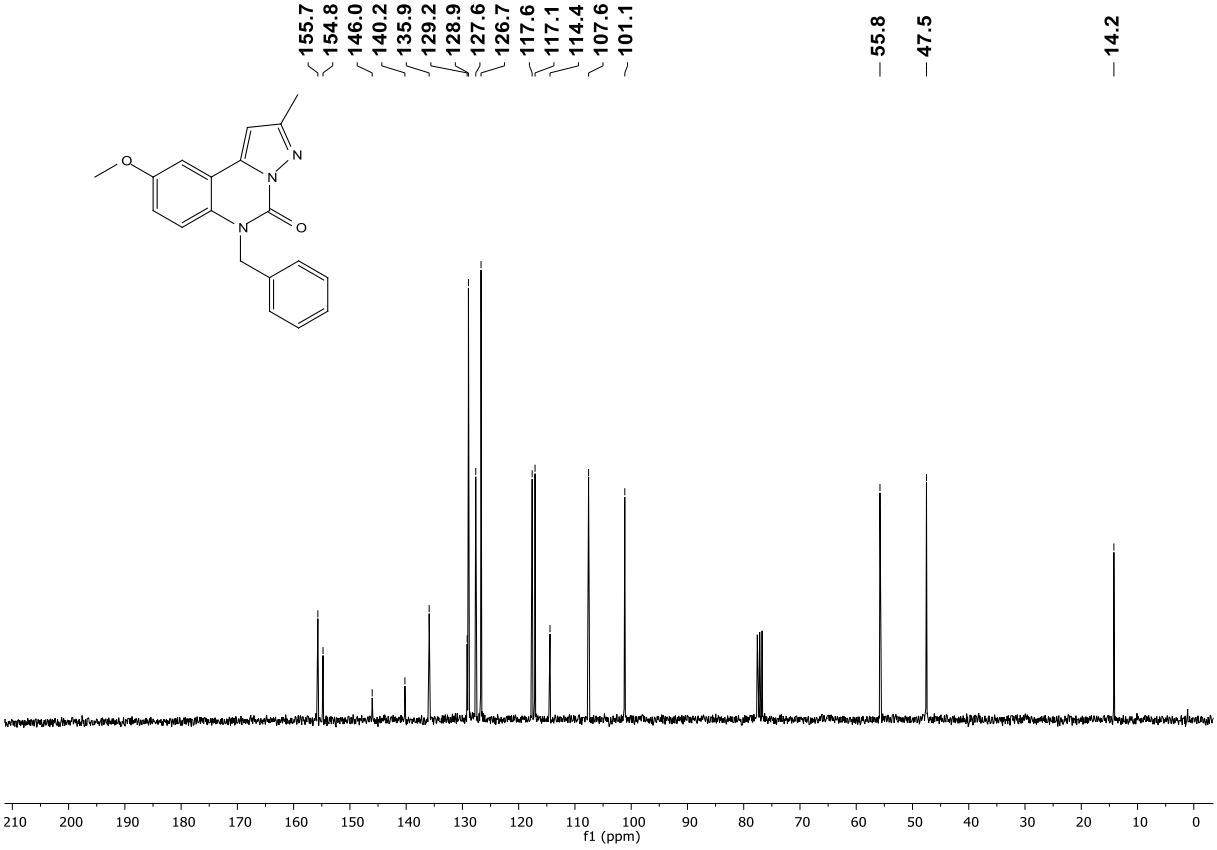
$^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) of **2j**



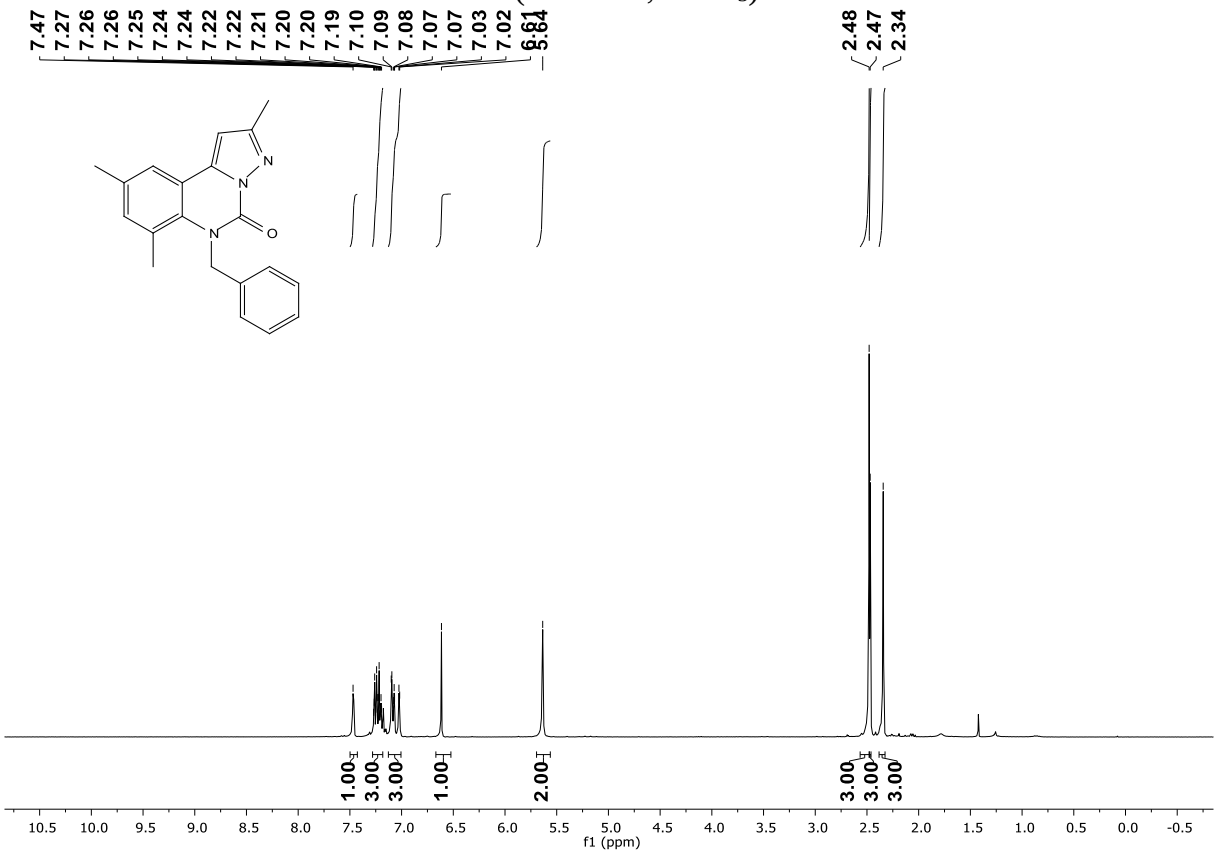
^{1}H NMR (300 MHz, $CDCl_3$) of **2k**



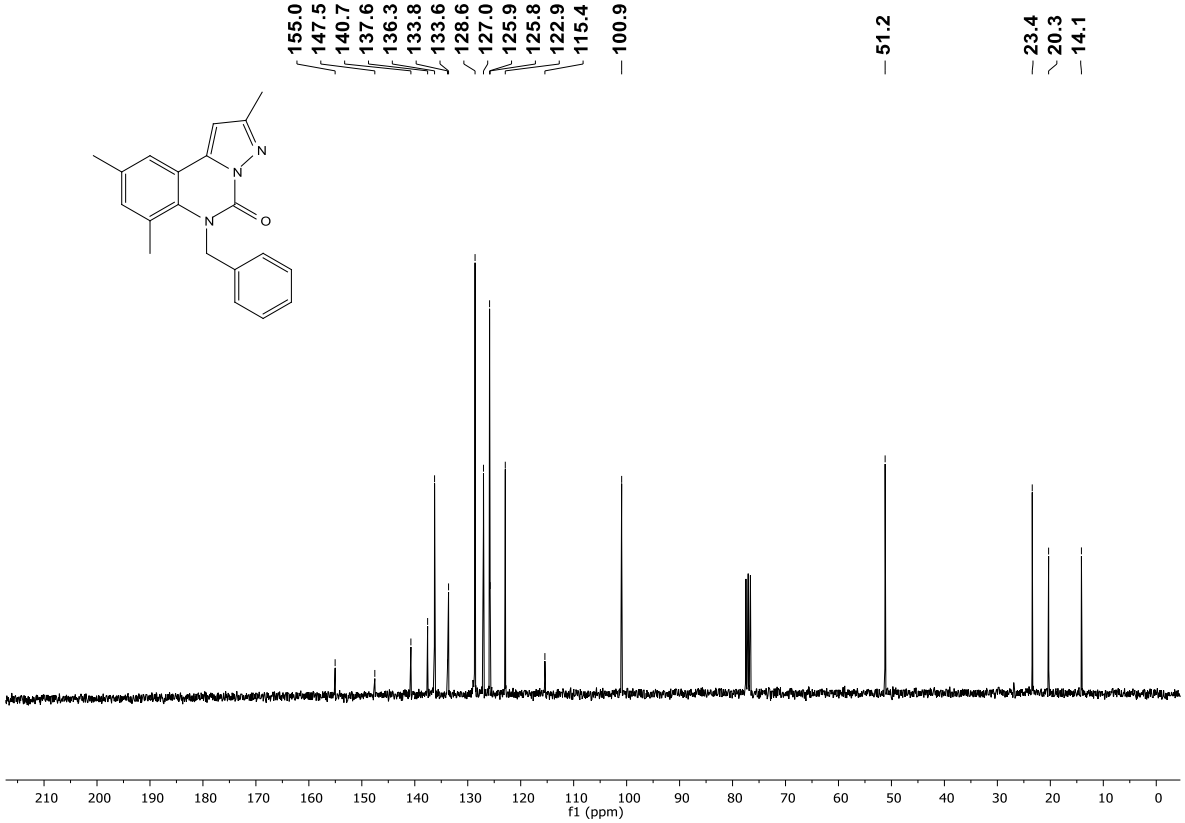
^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) of **2k**



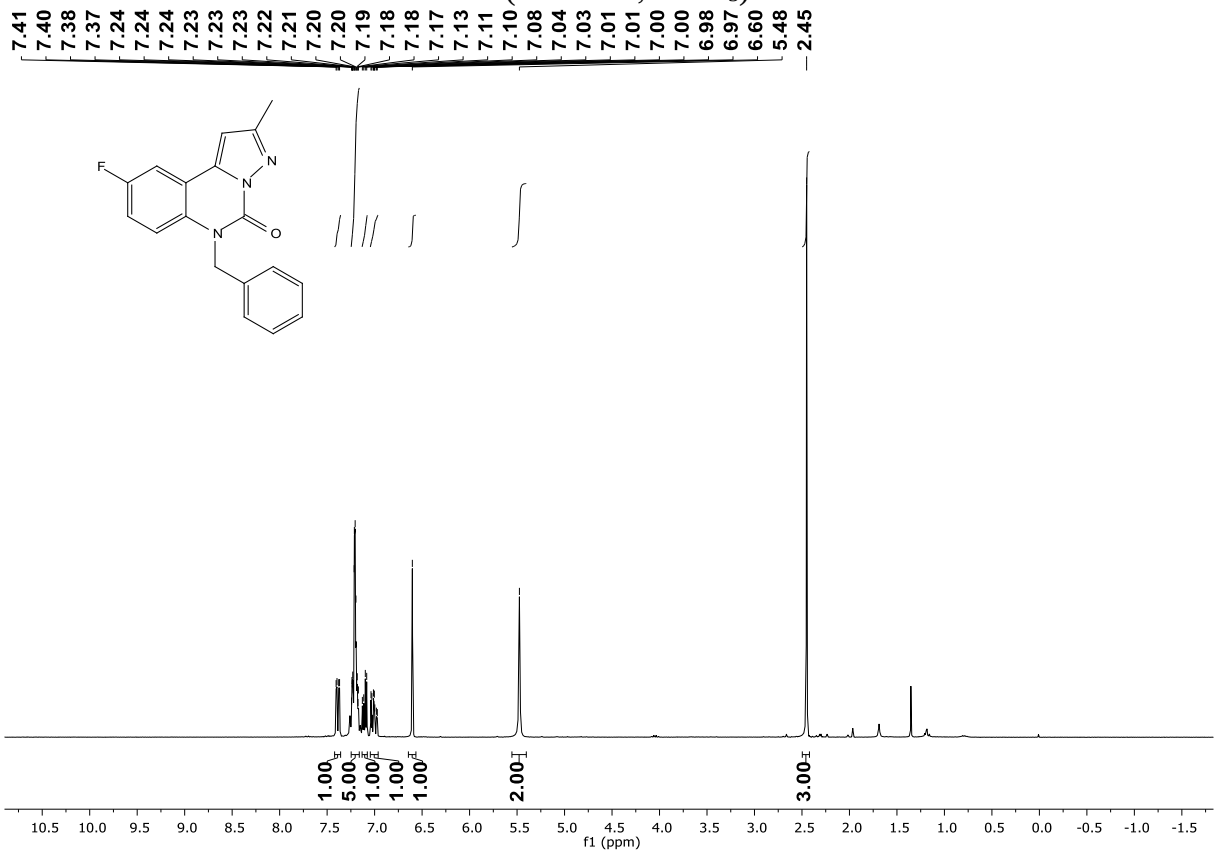
^{1}H NMR (300 MHz, $CDCl_3$) of **2l**



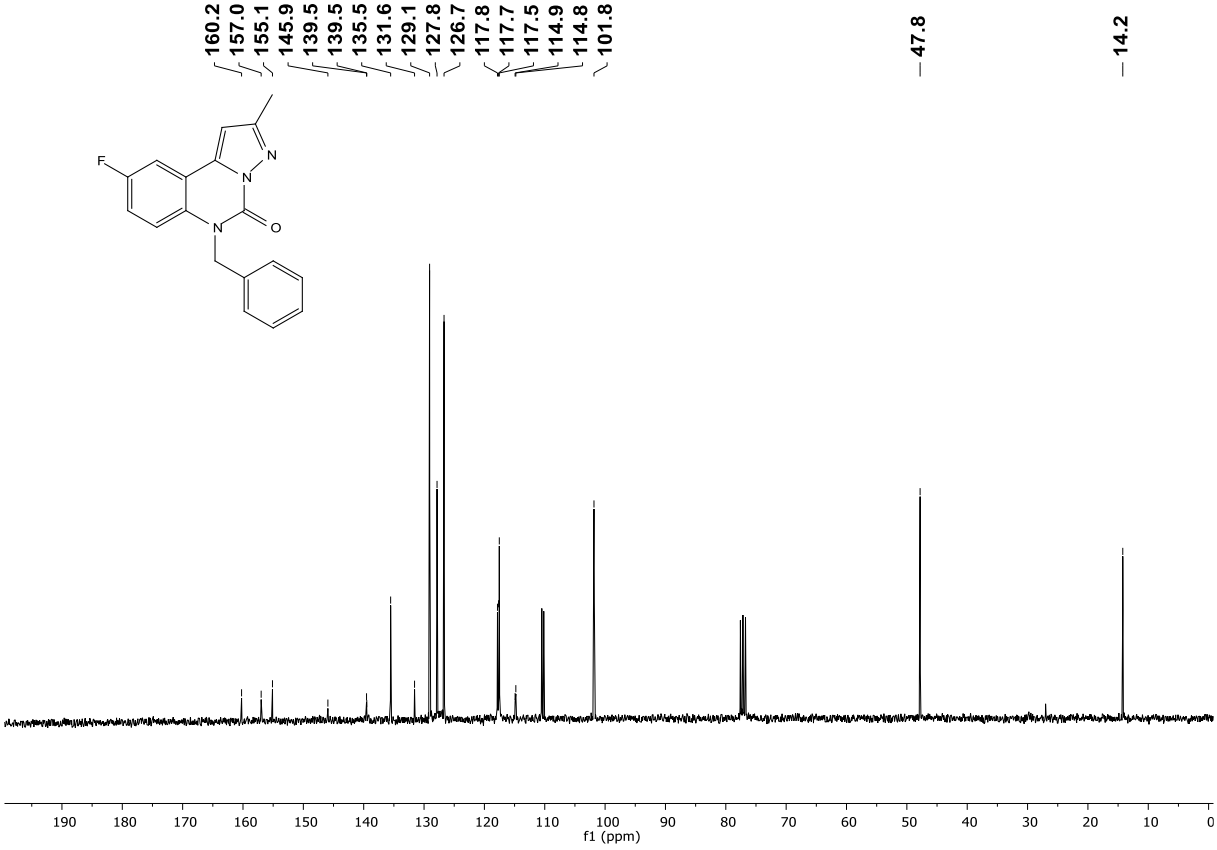
^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) of **2l**



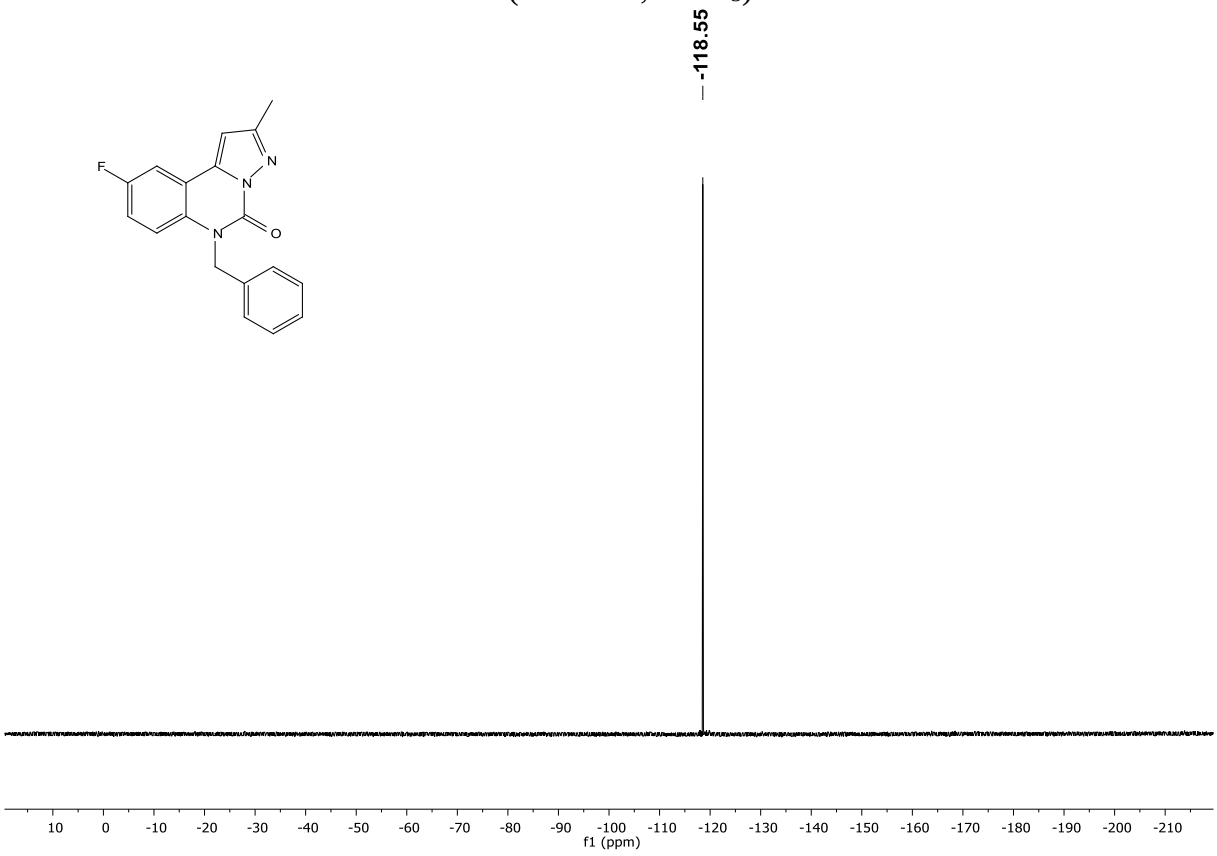
^{1}H NMR (300 MHz, $CDCl_3$) of **2m**



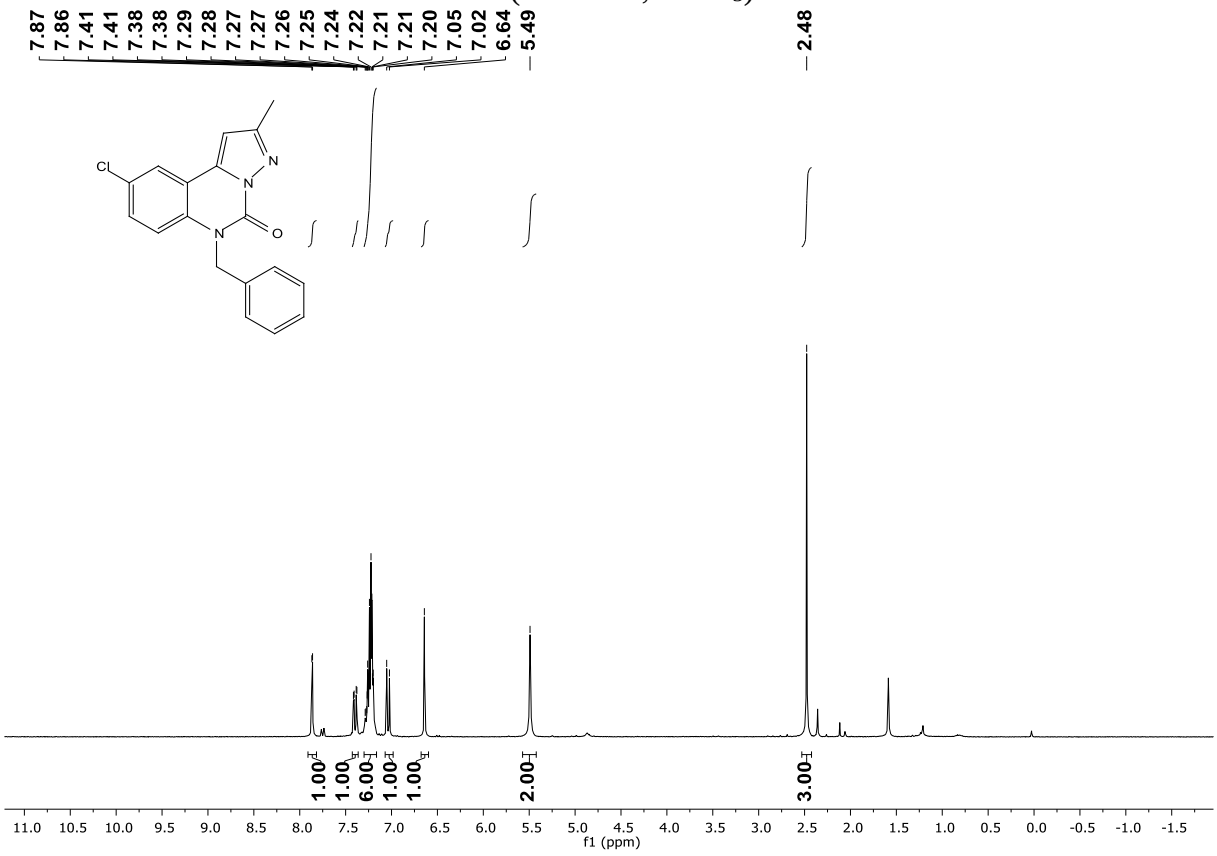
$^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) of **2m**



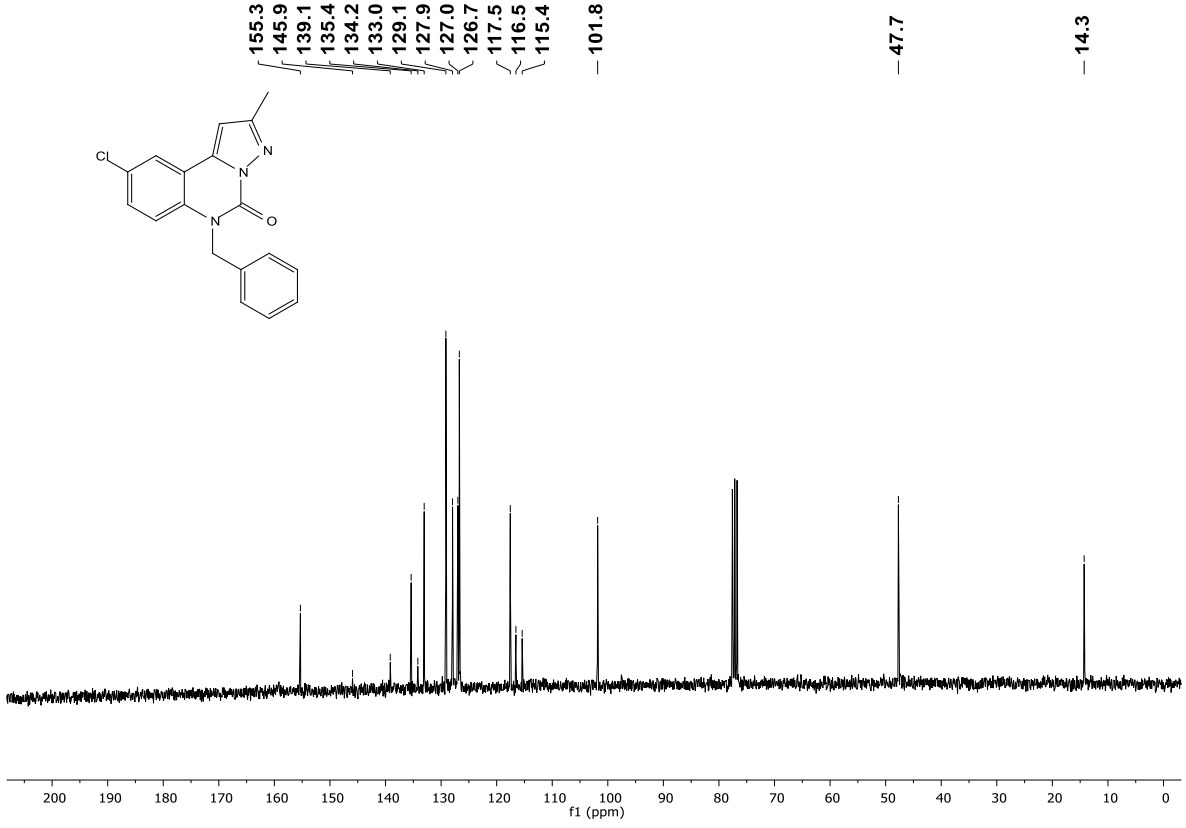
^{19}F NMR (188 MHz, $CDCl_3$) of **2m**



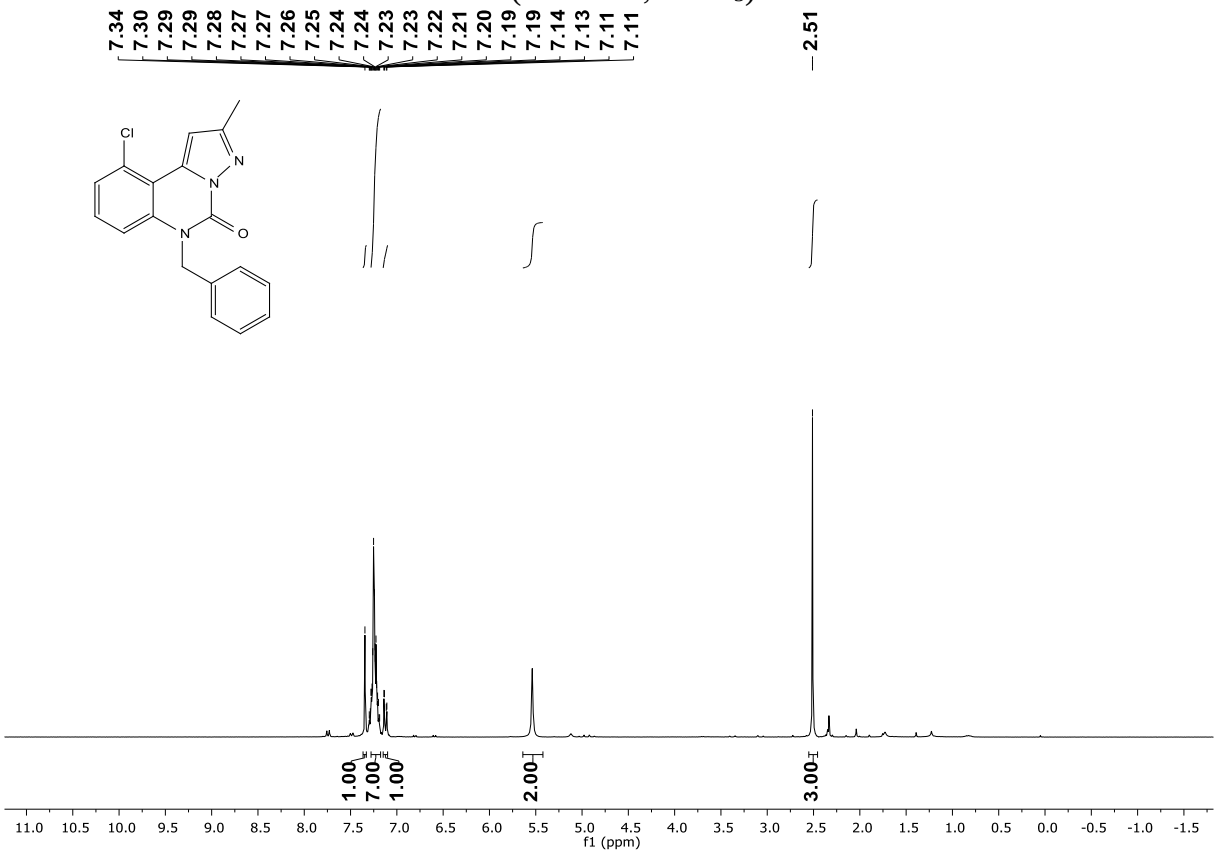
^{1}H NMR (300 MHz, $CDCl_3$) of **2n**



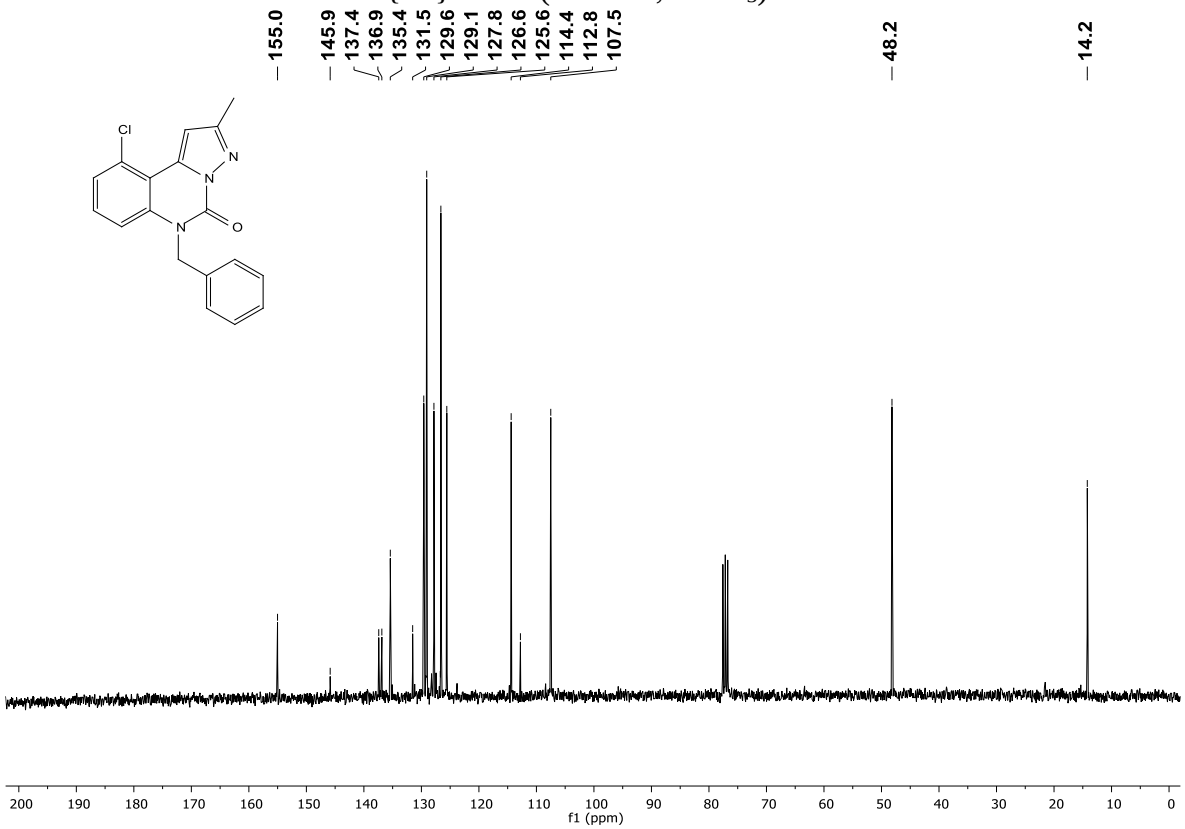
^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) of **2n**



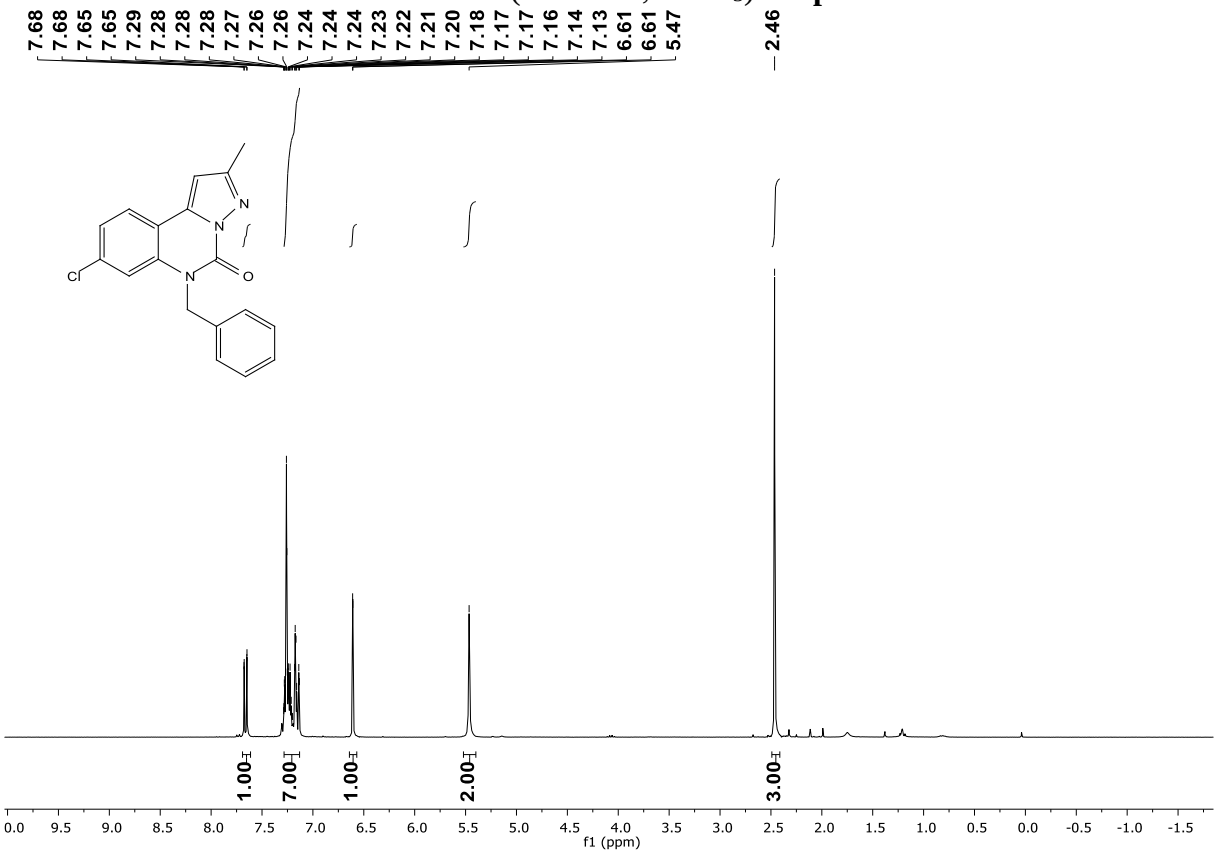
^{1}H NMR (300 MHz, $CDCl_3$) of **2o**



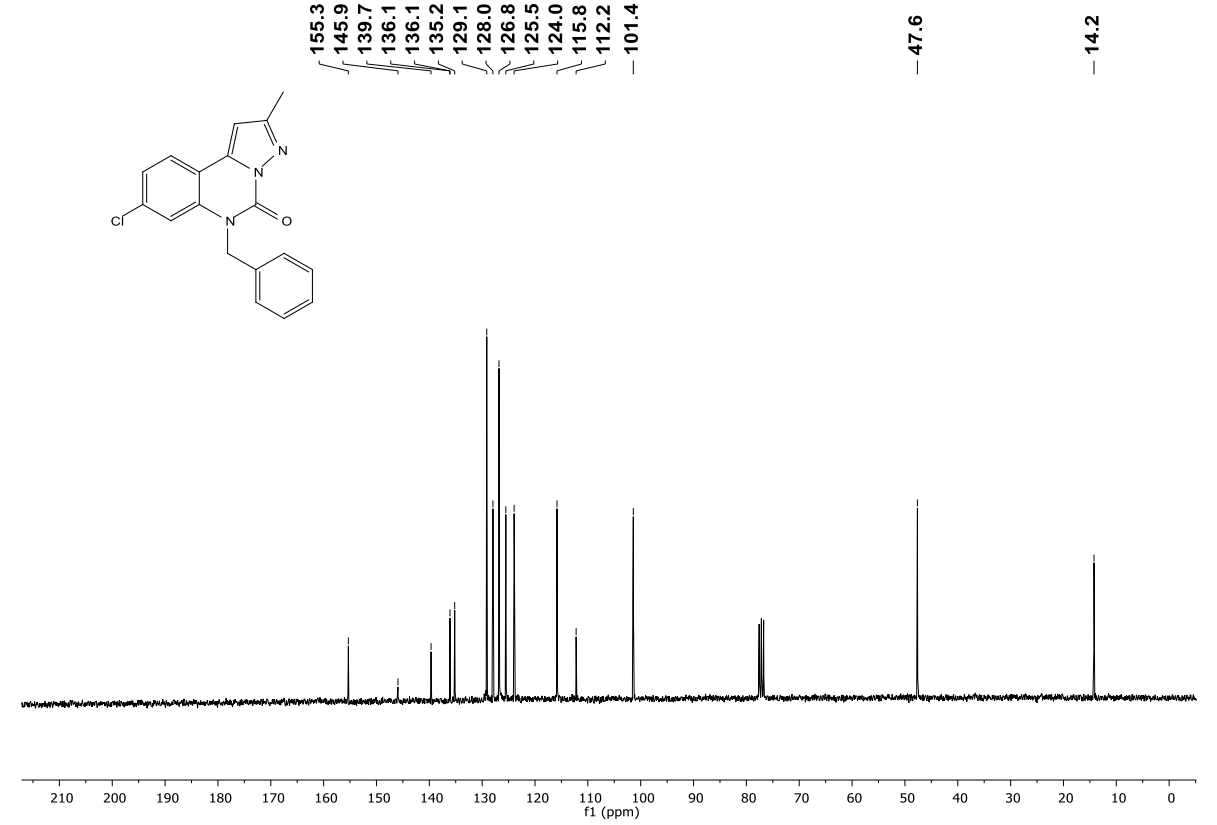
^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) of **2o**



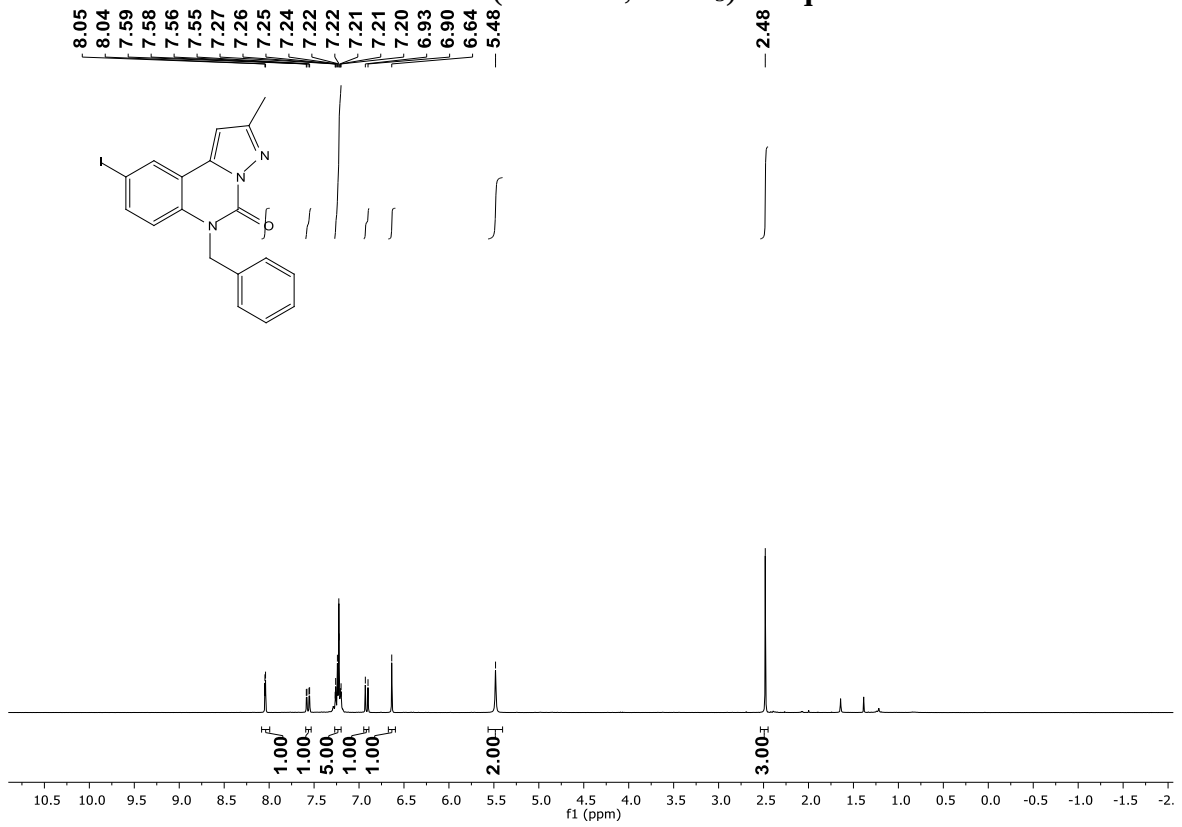
^{1}H NMR (300 MHz, $CDCl_3$) of **2p**



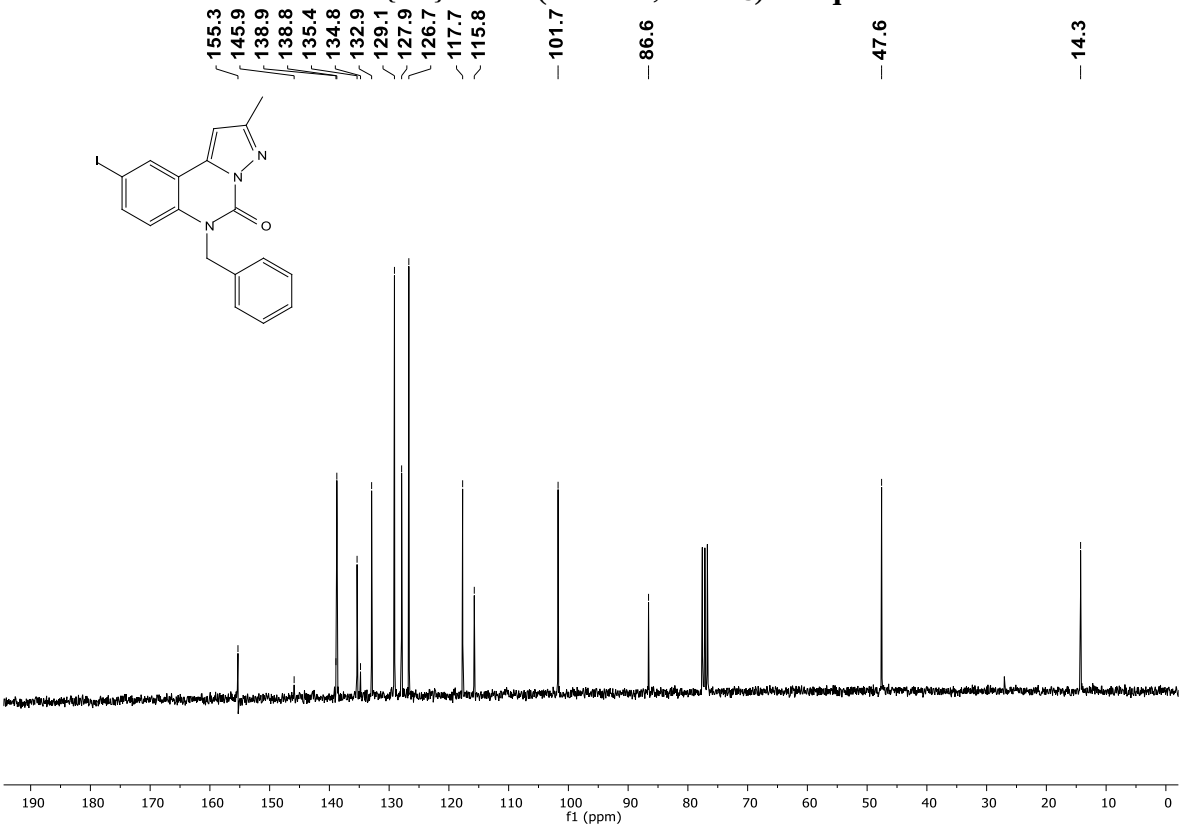
^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) of **2p**



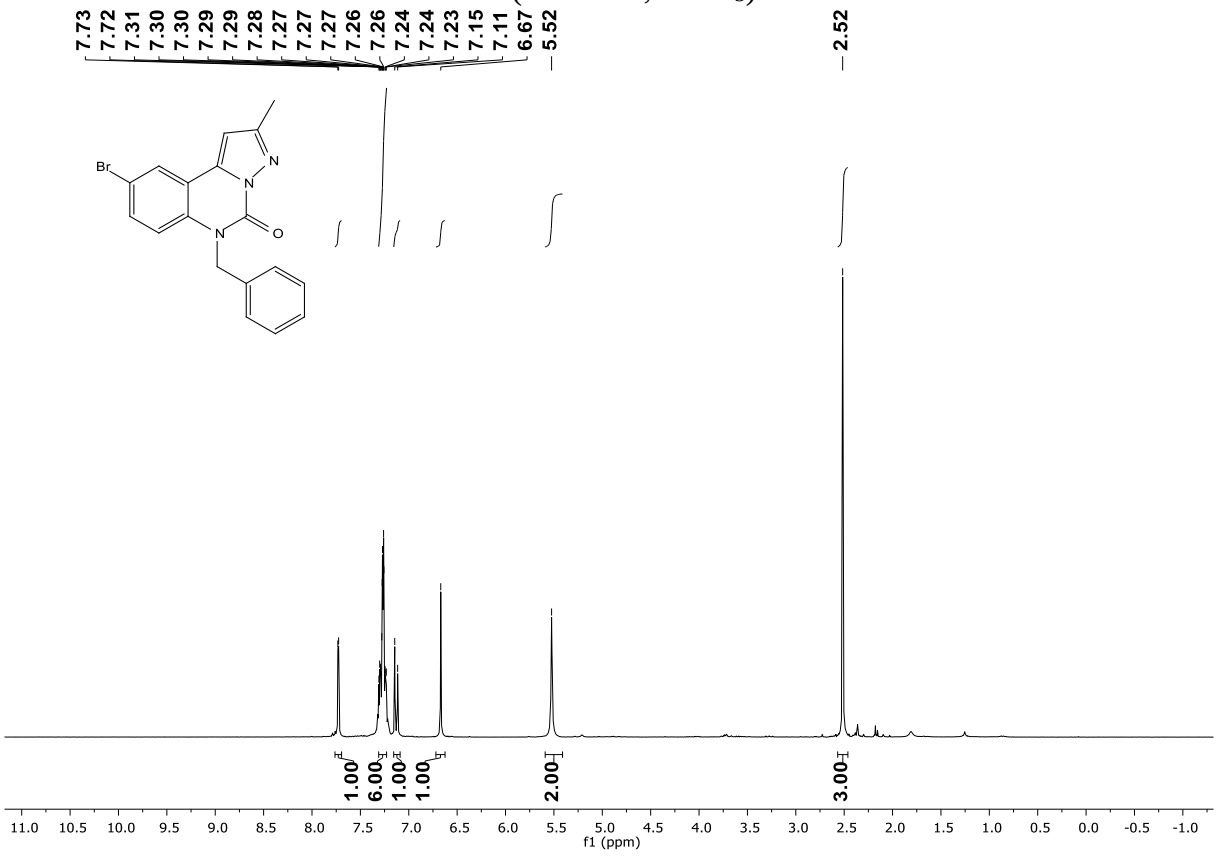
^{1}H NMR (300 MHz, $CDCl_3$) of **2q**



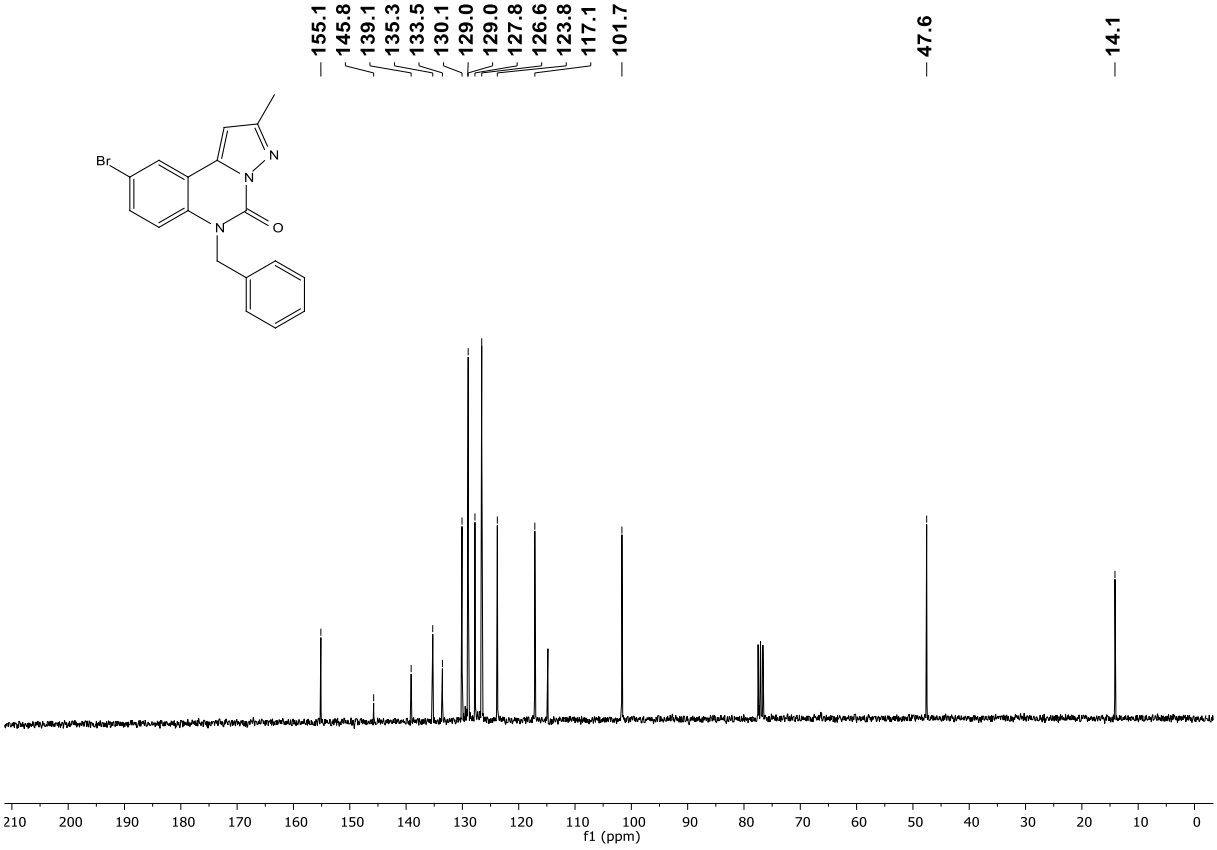
^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) of **2q**



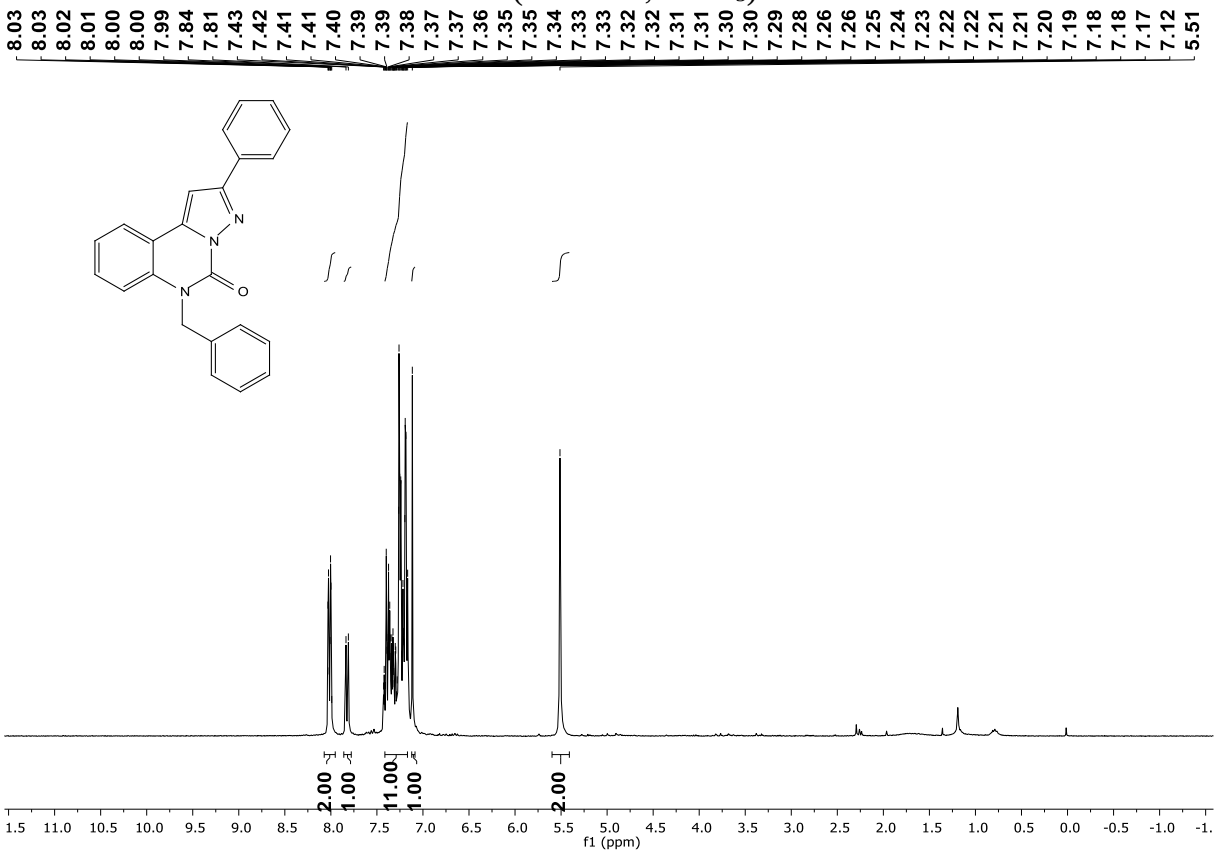
^{1}H NMR (300 MHz, $CDCl_3$) of **2r**



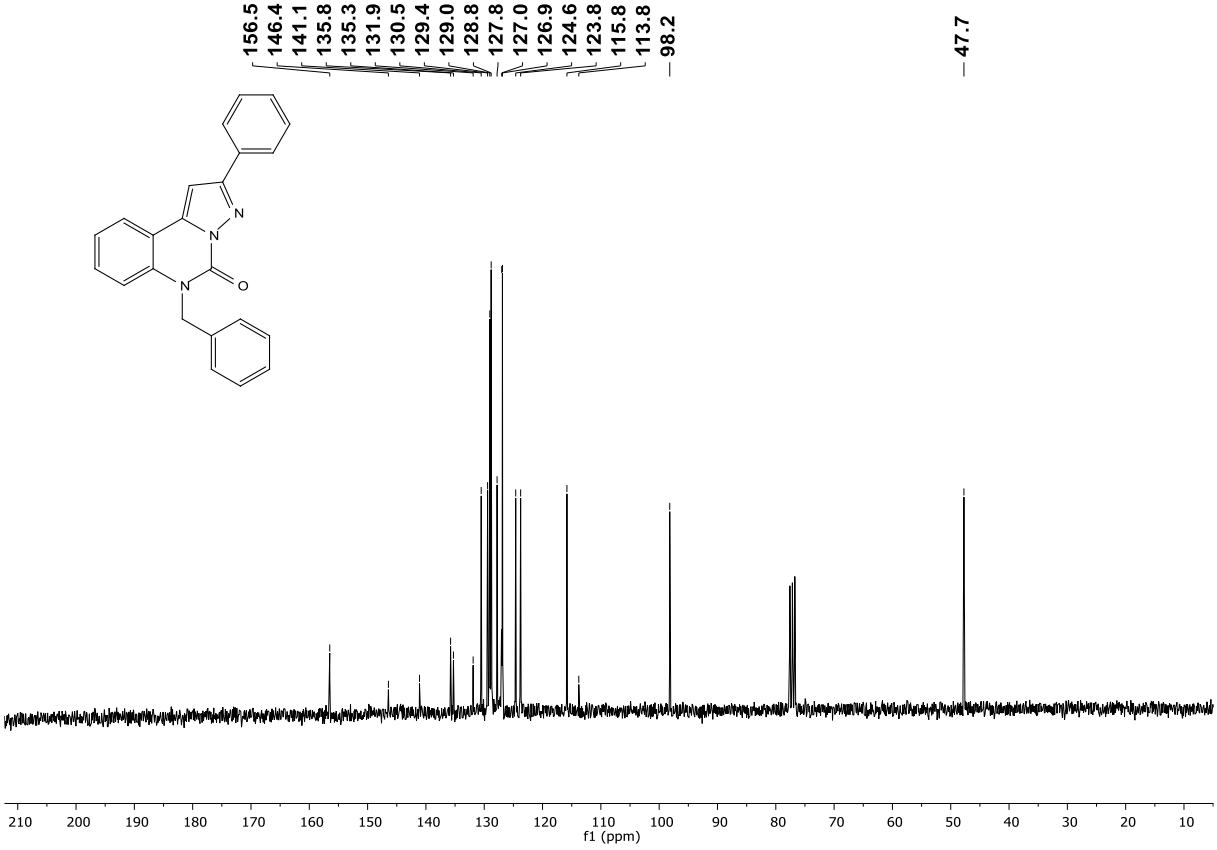
^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) of **2r**



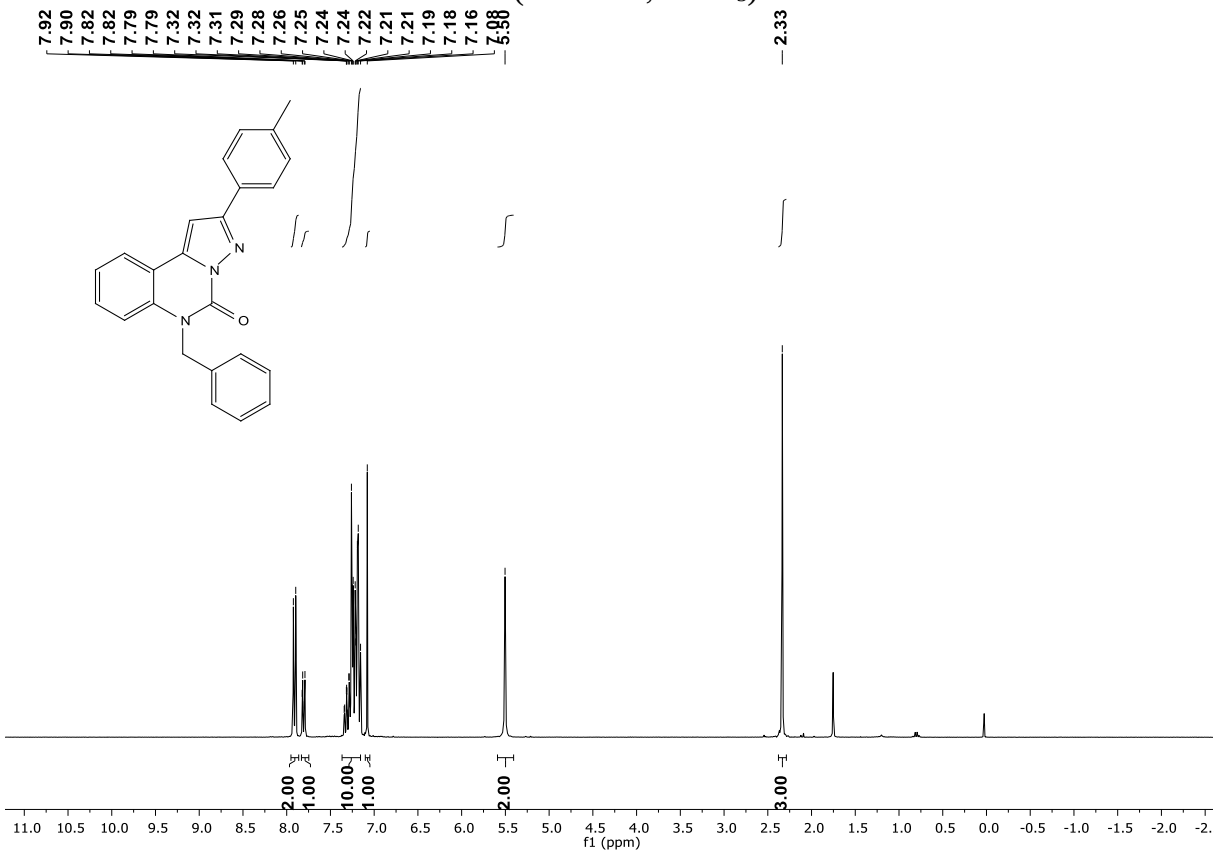
^{1}H NMR (300 MHz, $CDCl_3$) of **2s**



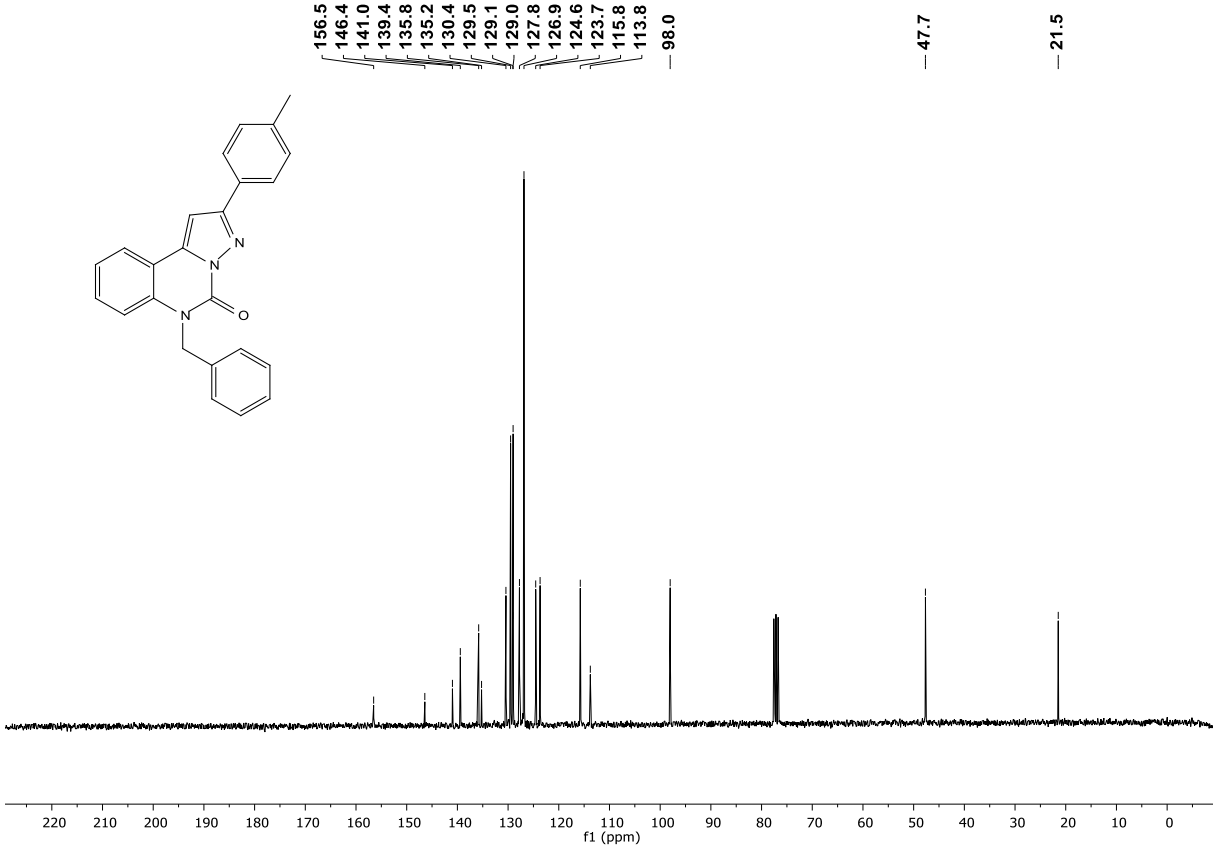
^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) of **2s**



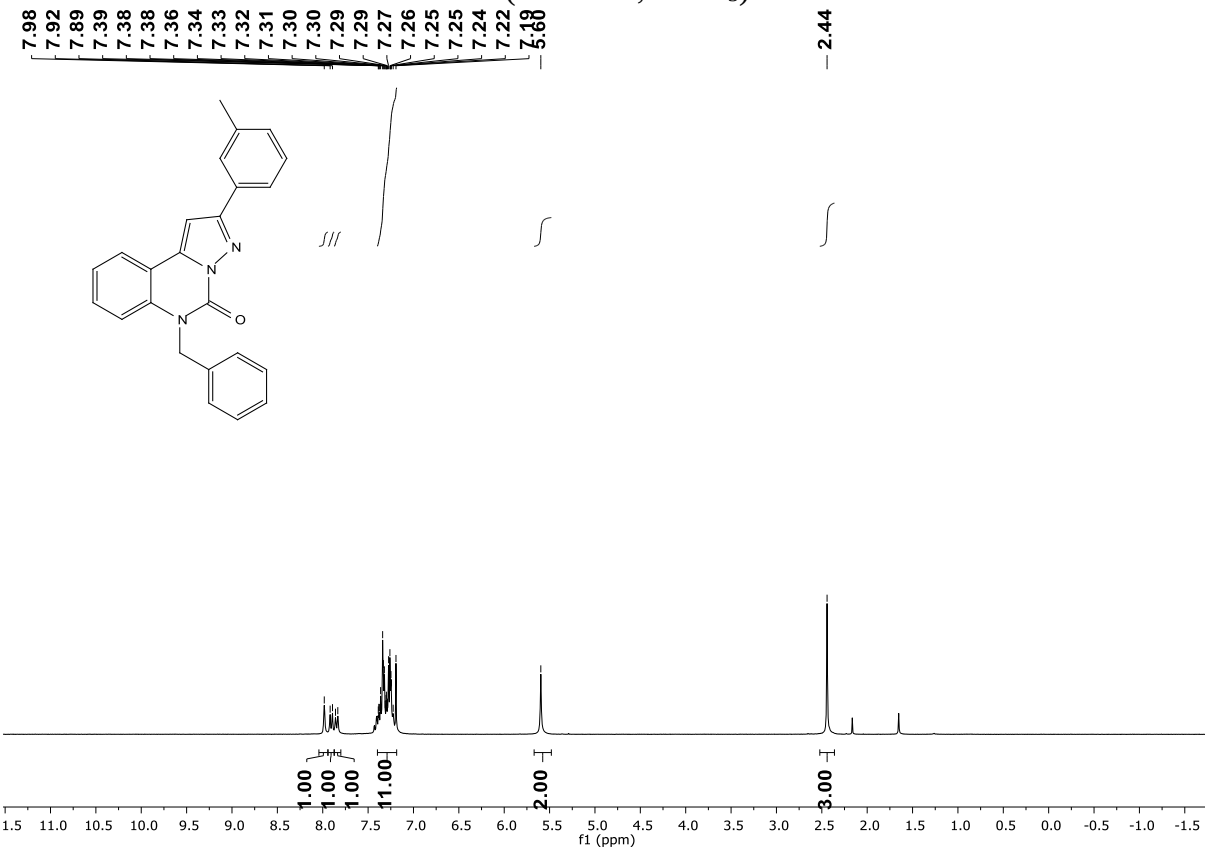
^{1}H NMR (300 MHz, $CDCl_3$) of **2t**



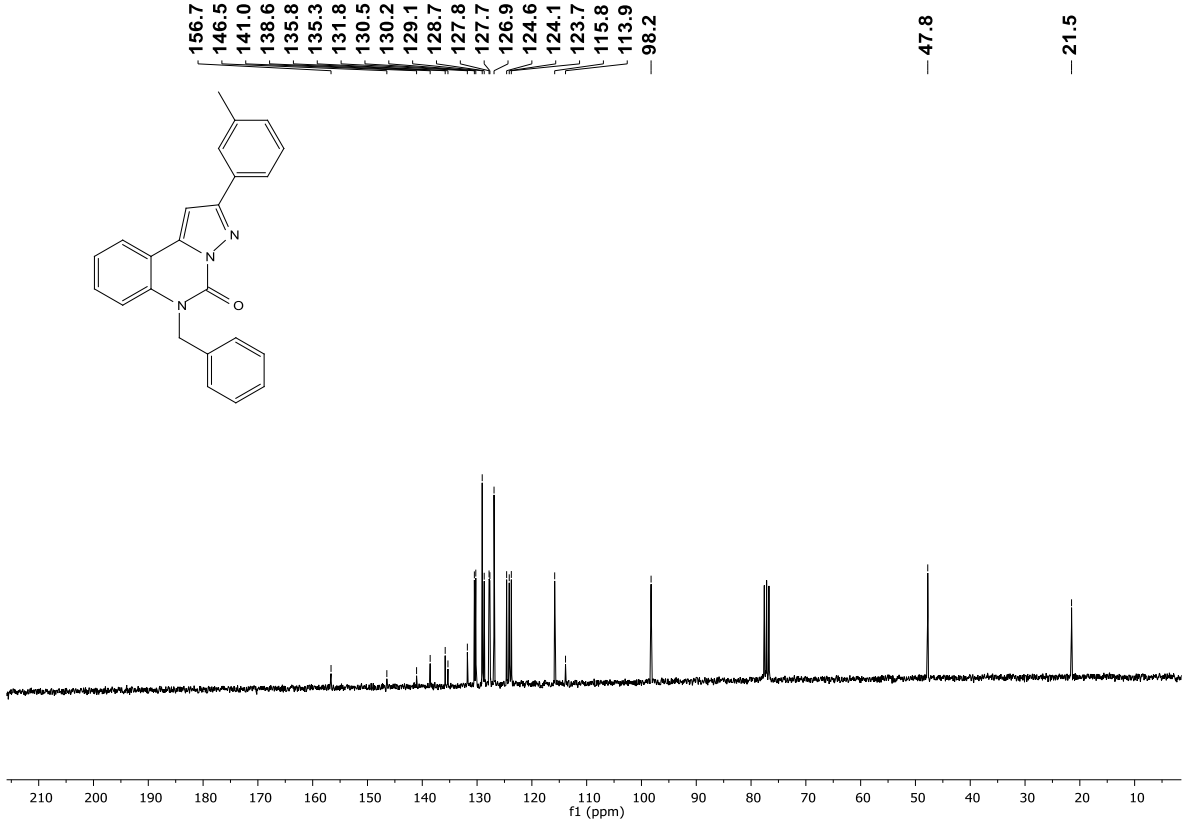
^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) of **2t**



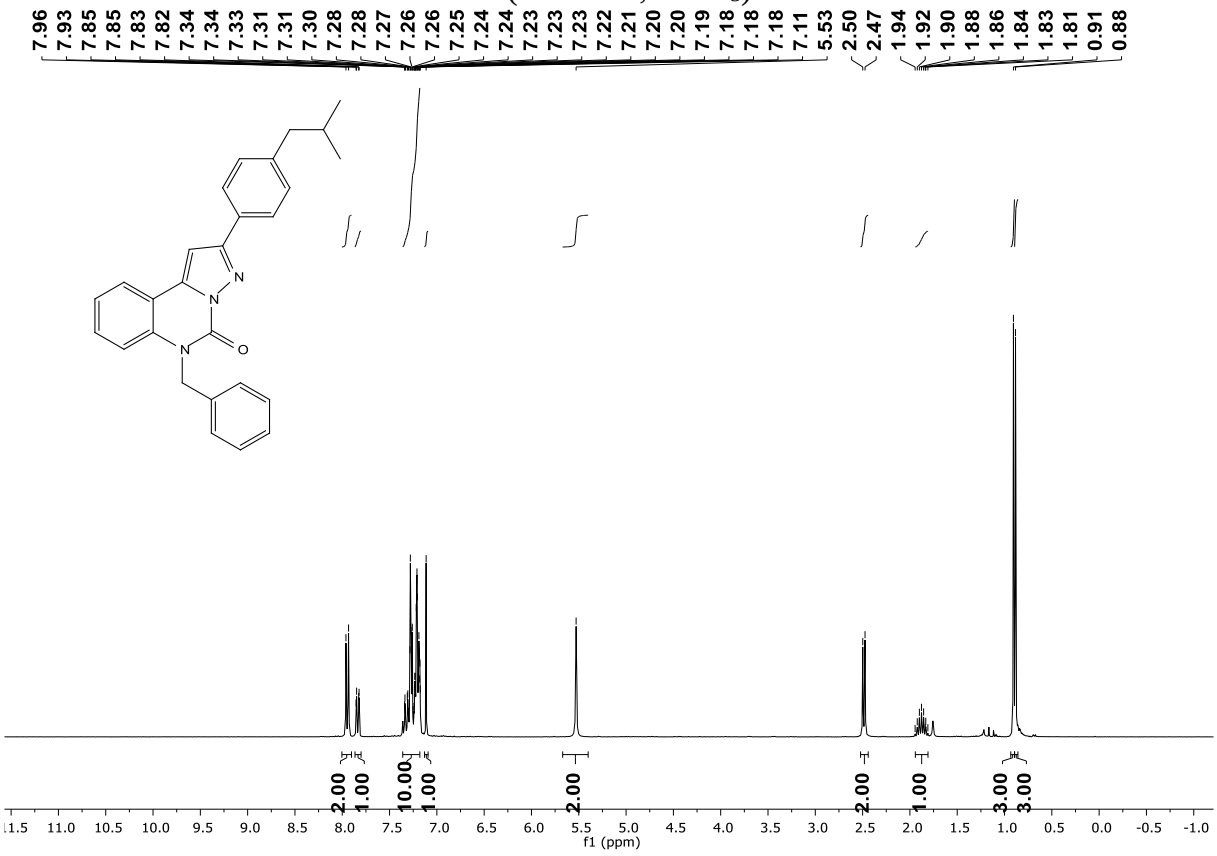
^{1}H NMR (300 MHz, $CDCl_3$) of **2u**



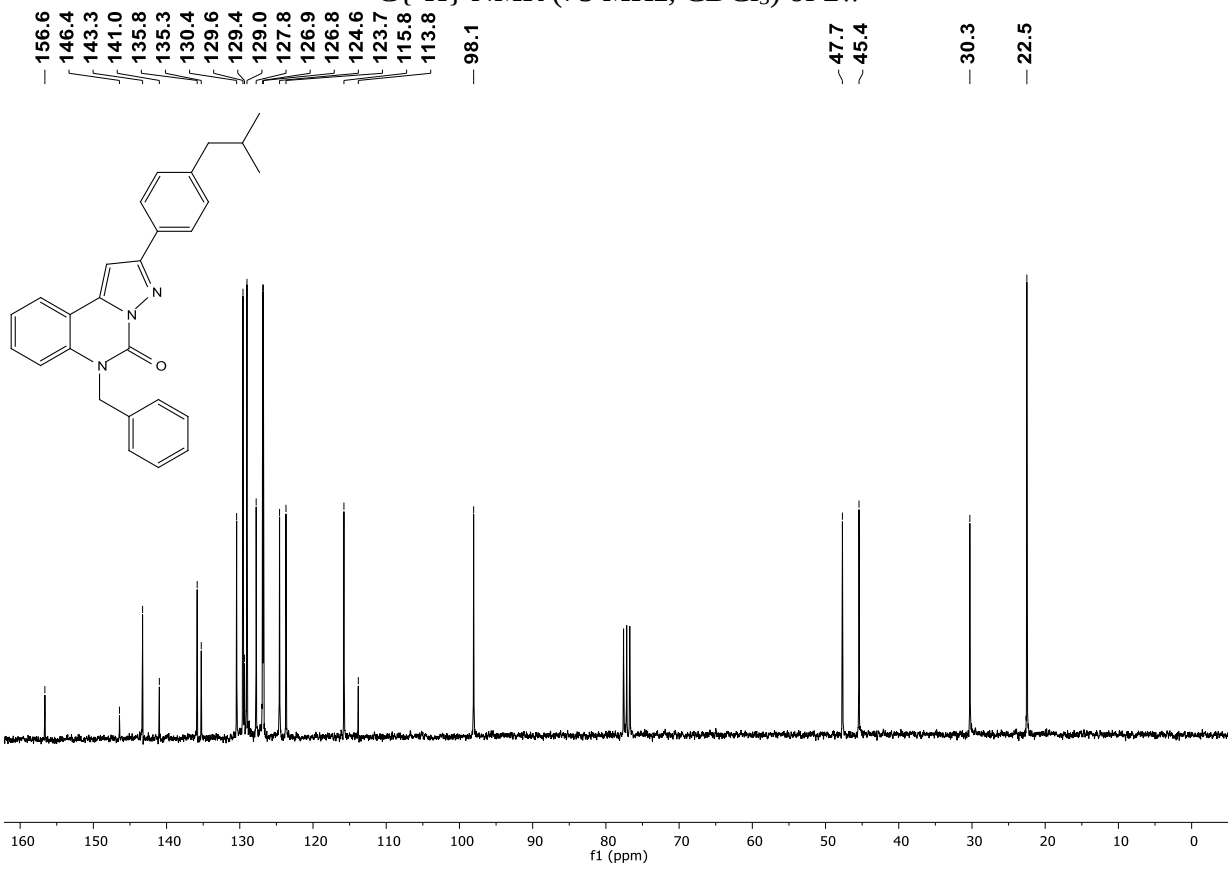
^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) of **2u**



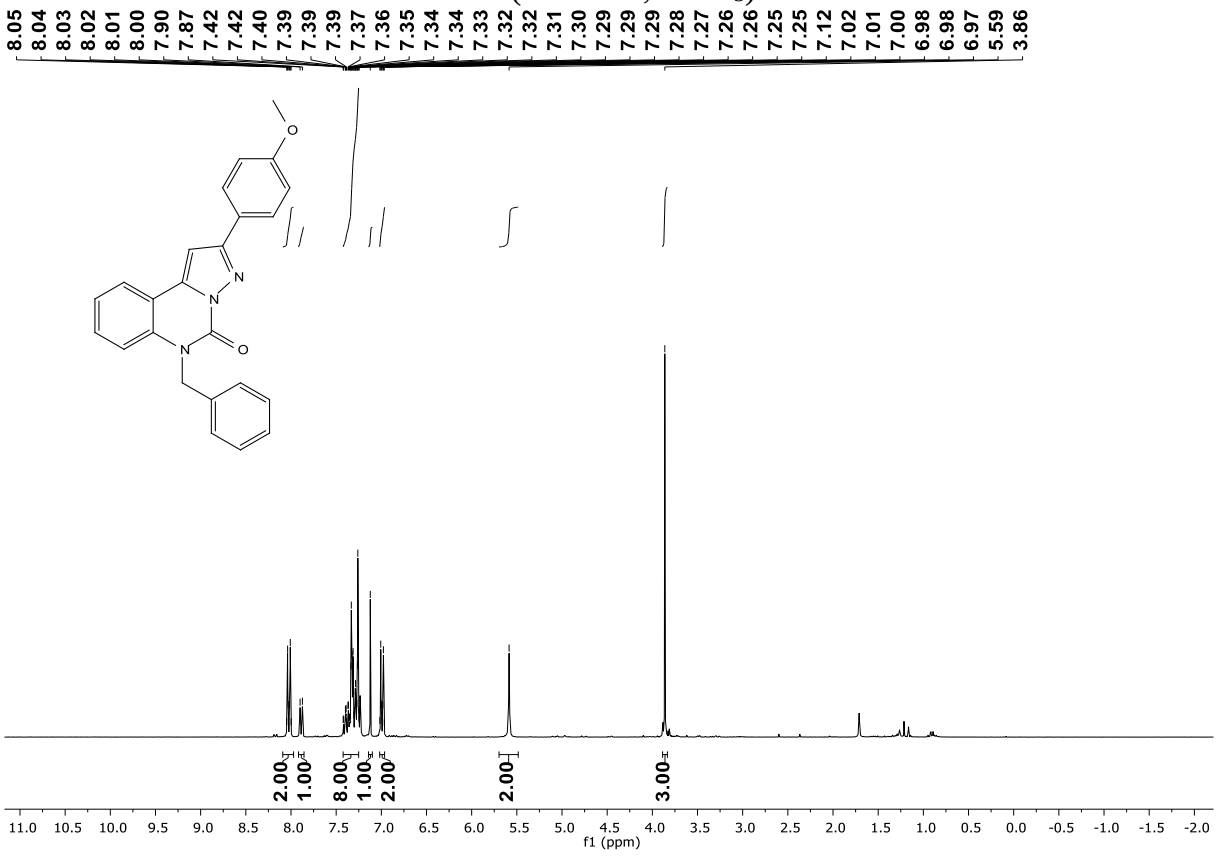
^{1}H NMR (300 MHz, $CDCl_3$) of **2w**



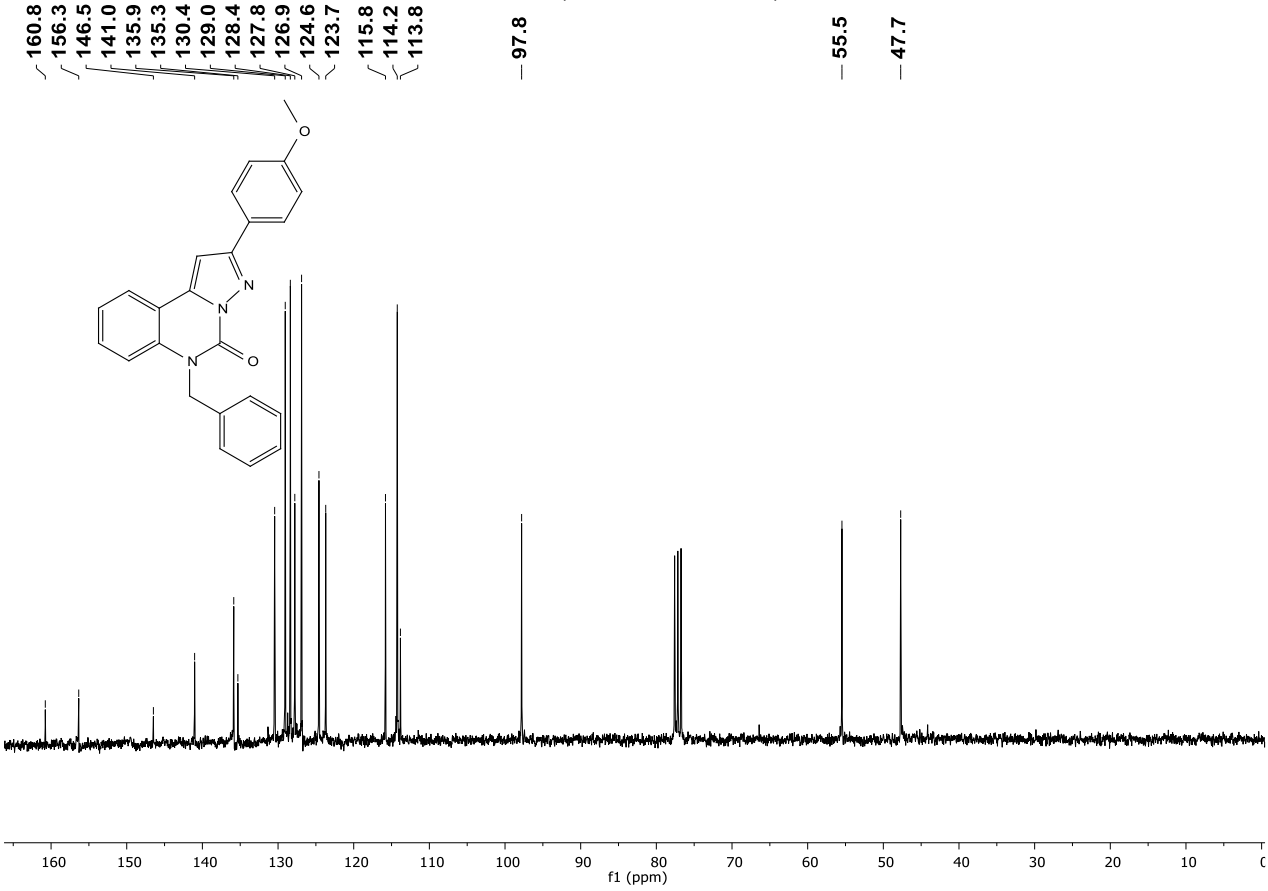
$^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) of **2w**



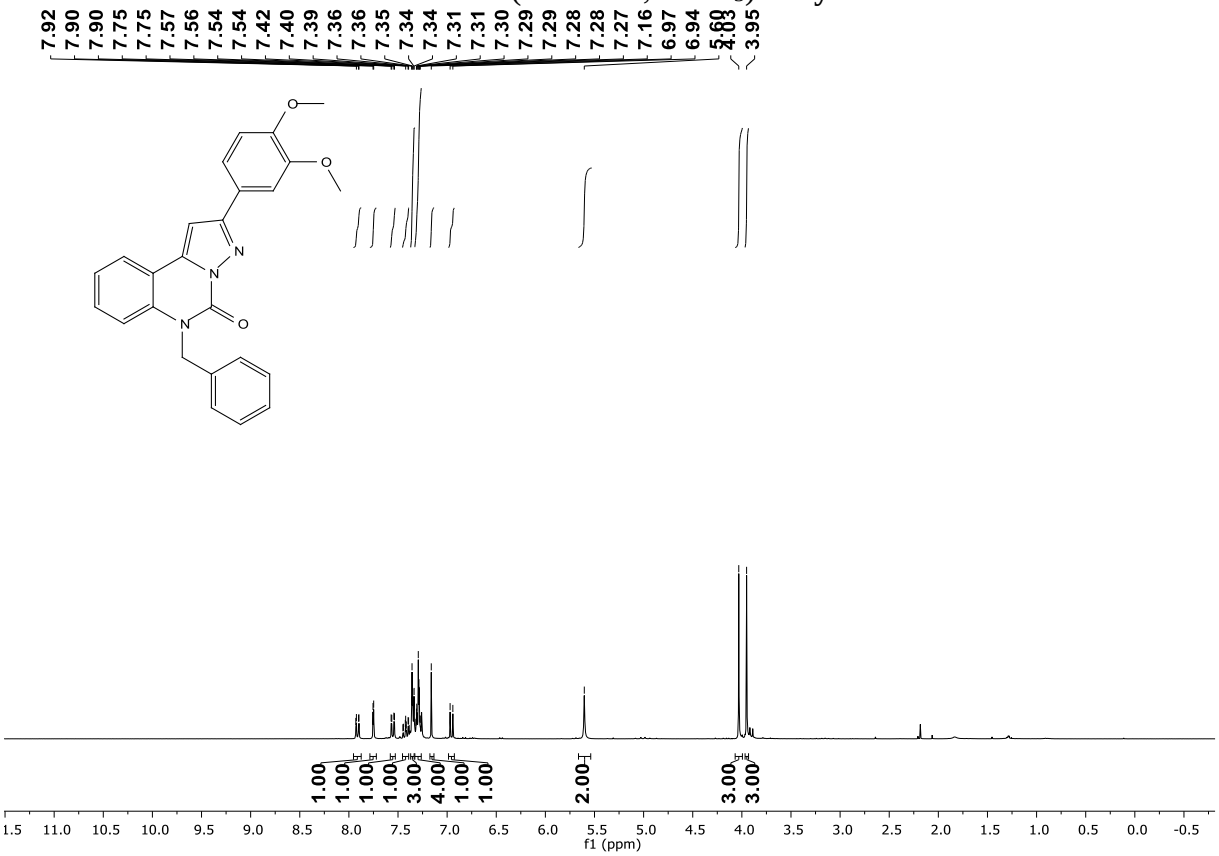
^{1}H NMR (300 MHz, $CDCl_3$) of **2x**



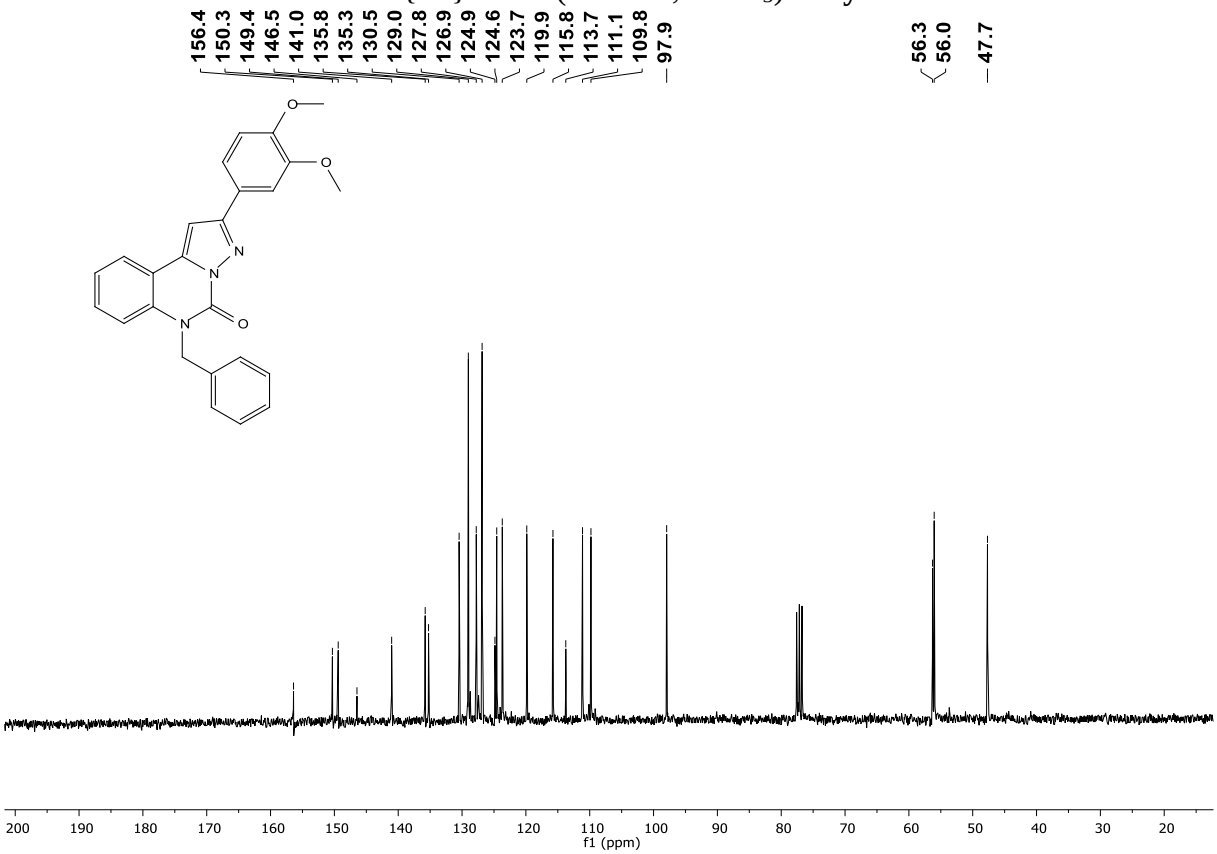
^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) of **2x**



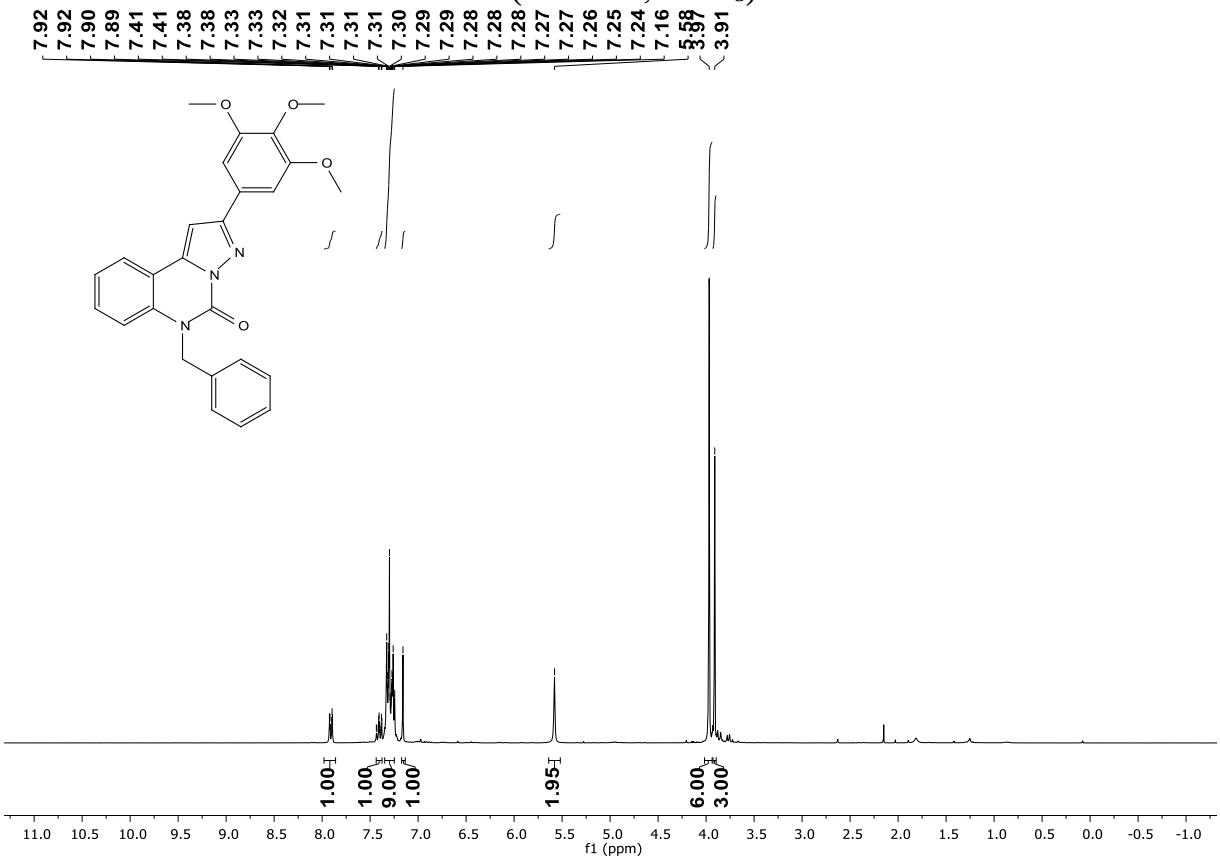
^{1}H NMR (300 MHz, $CDCl_3$) of **2y**



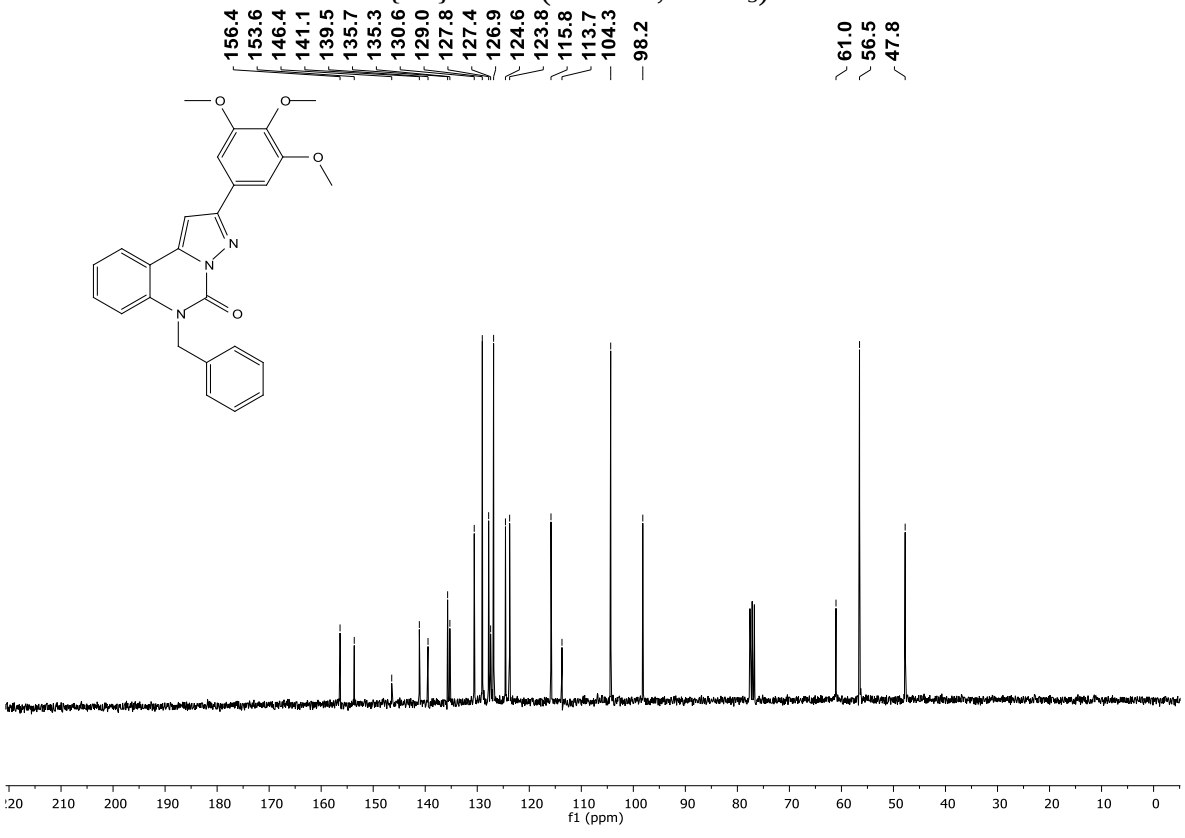
^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) of **2y**



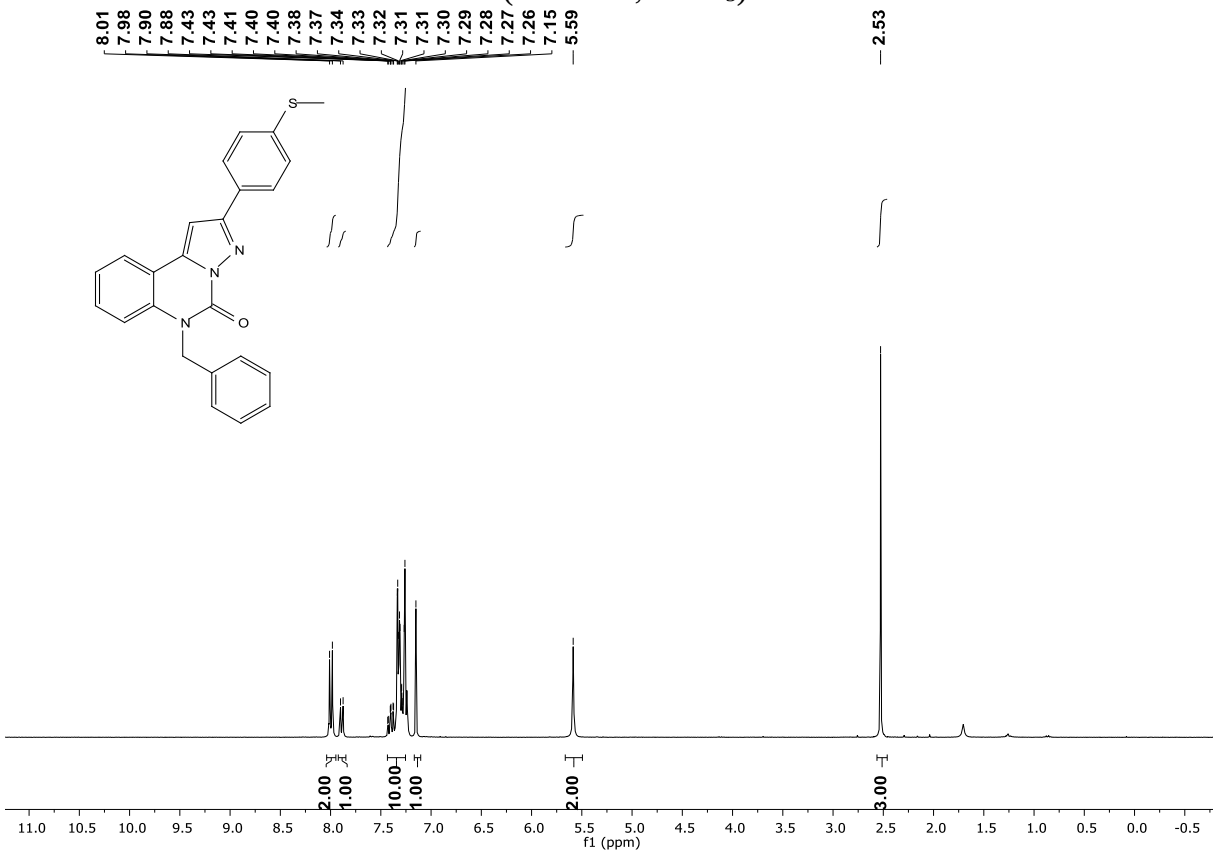
^{1}H NMR (300 MHz, $CDCl_3$) of **2z**



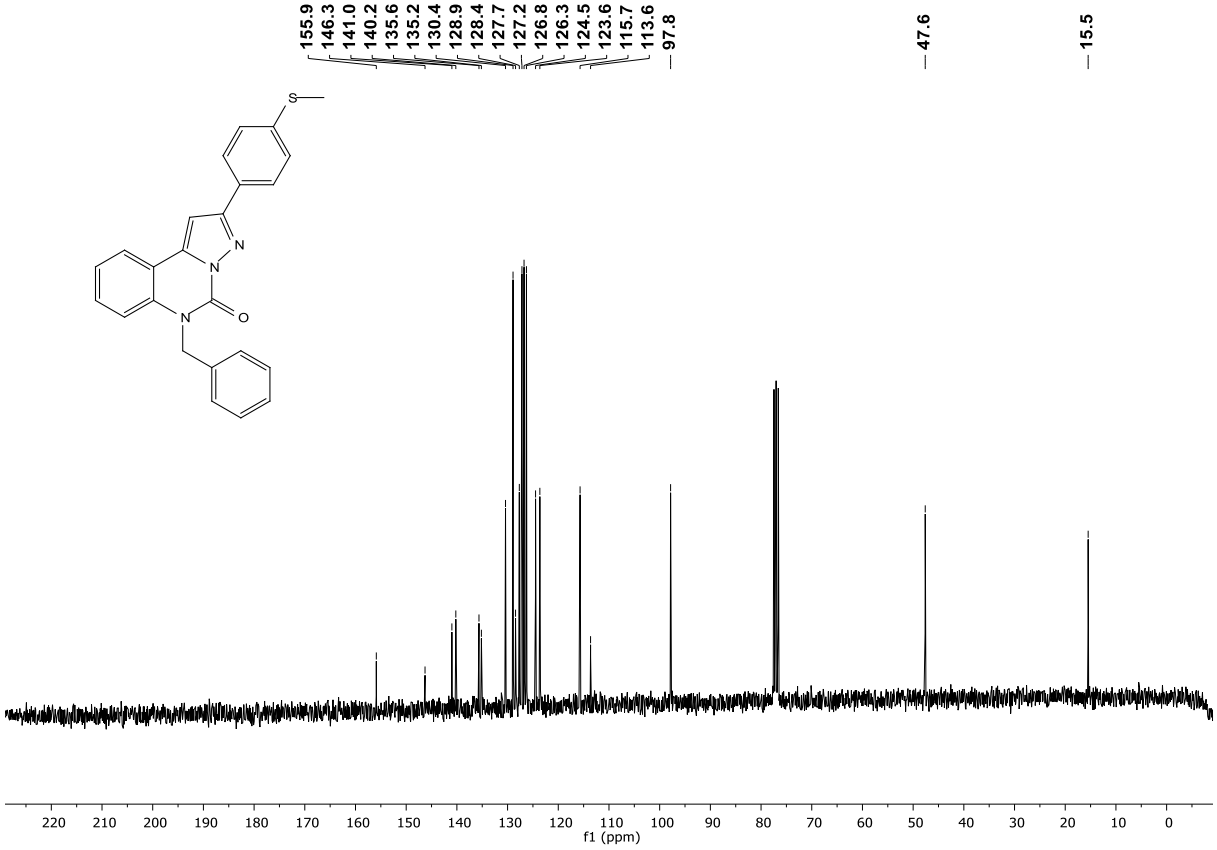
$^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) of **2z**



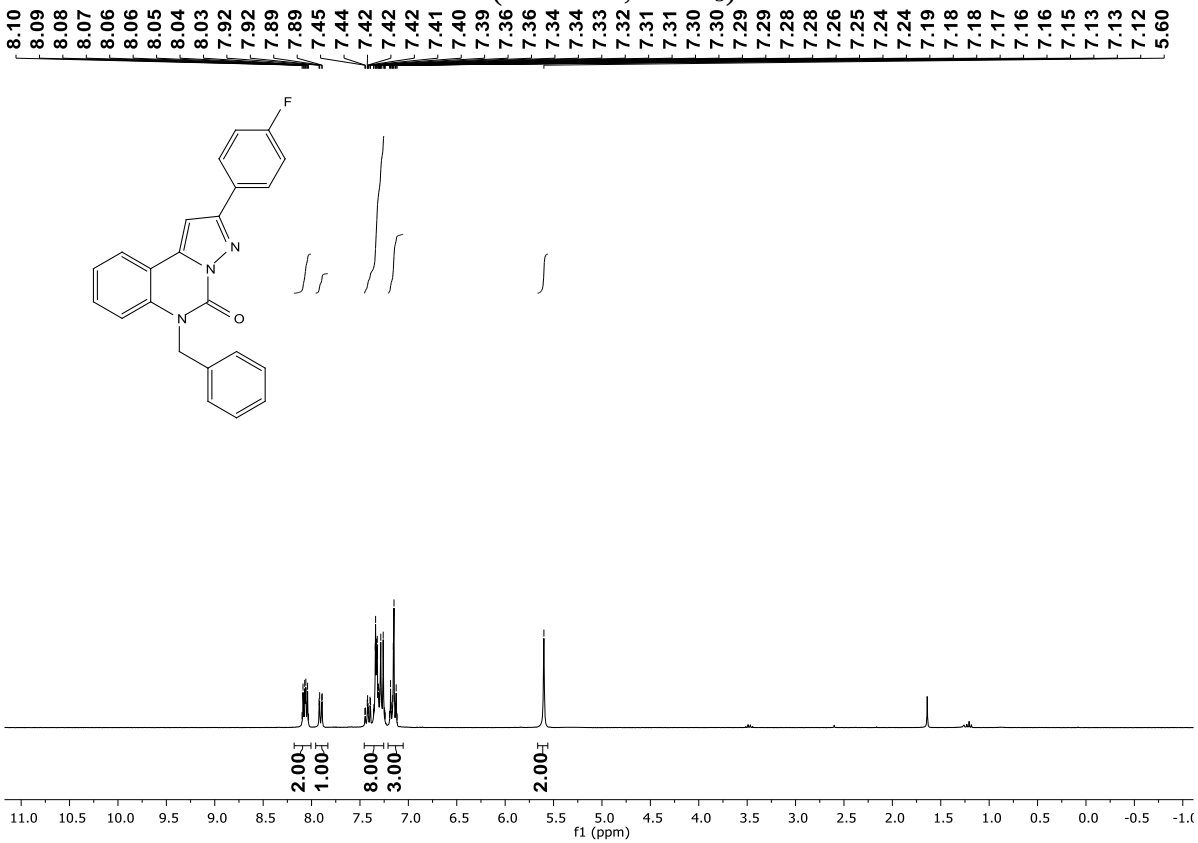
^{1}H NMR (300 MHz, $CDCl_3$) of **2aa**



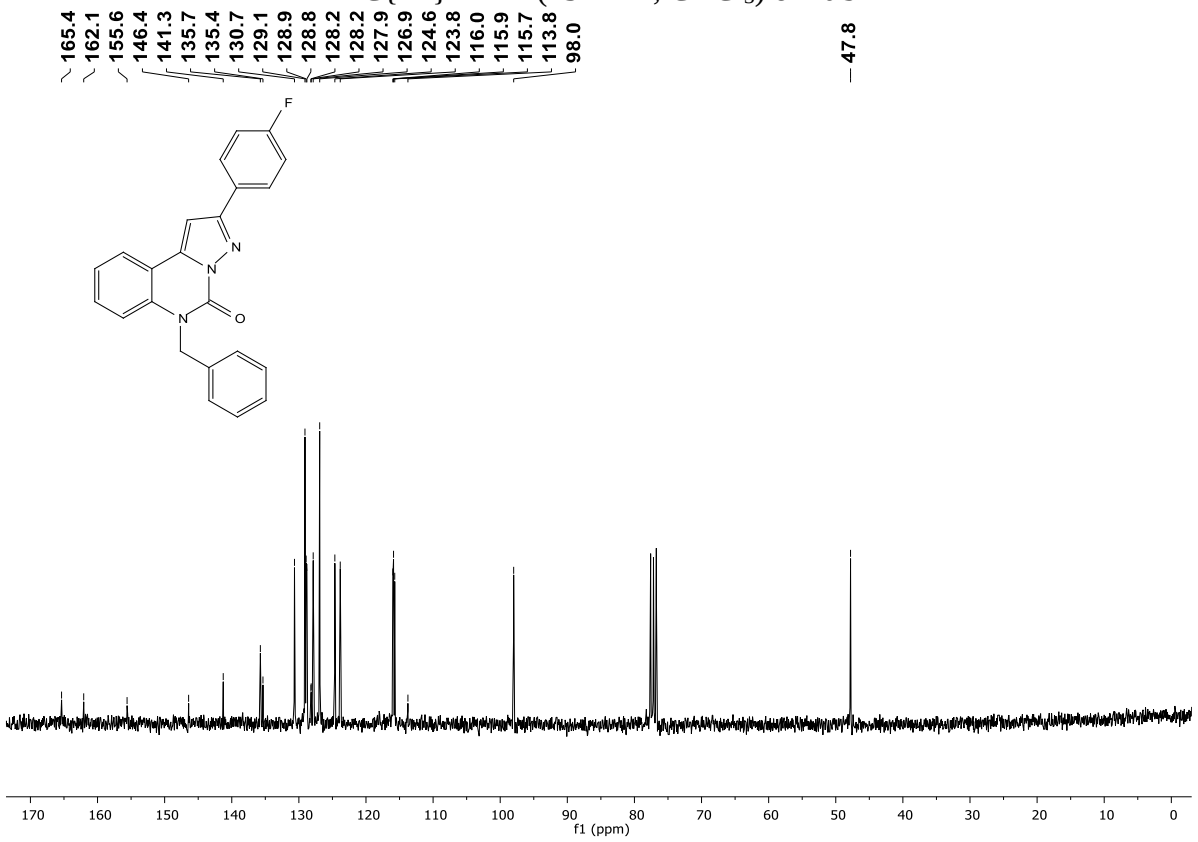
^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) of **2aa**



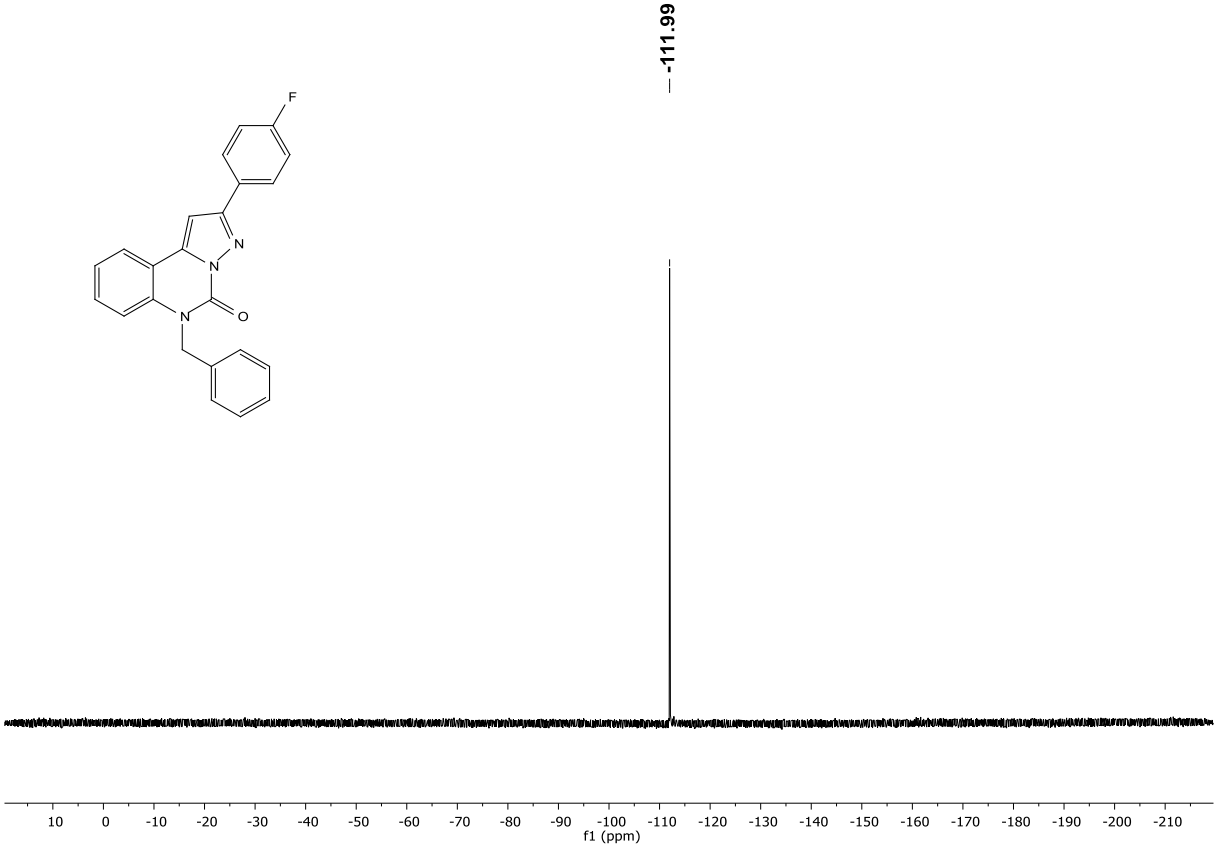
^{1}H NMR (300 MHz, $CDCl_3$) of **2ab**



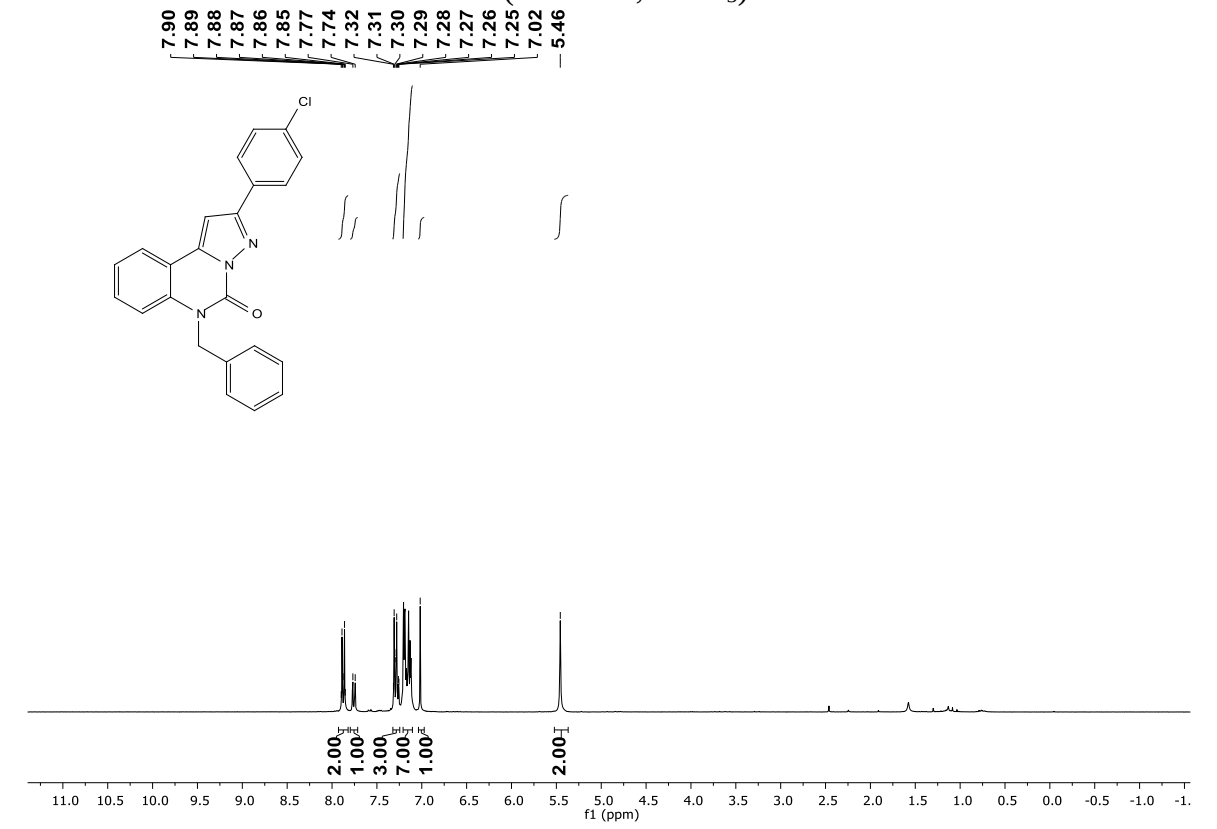
^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) of **2ab**



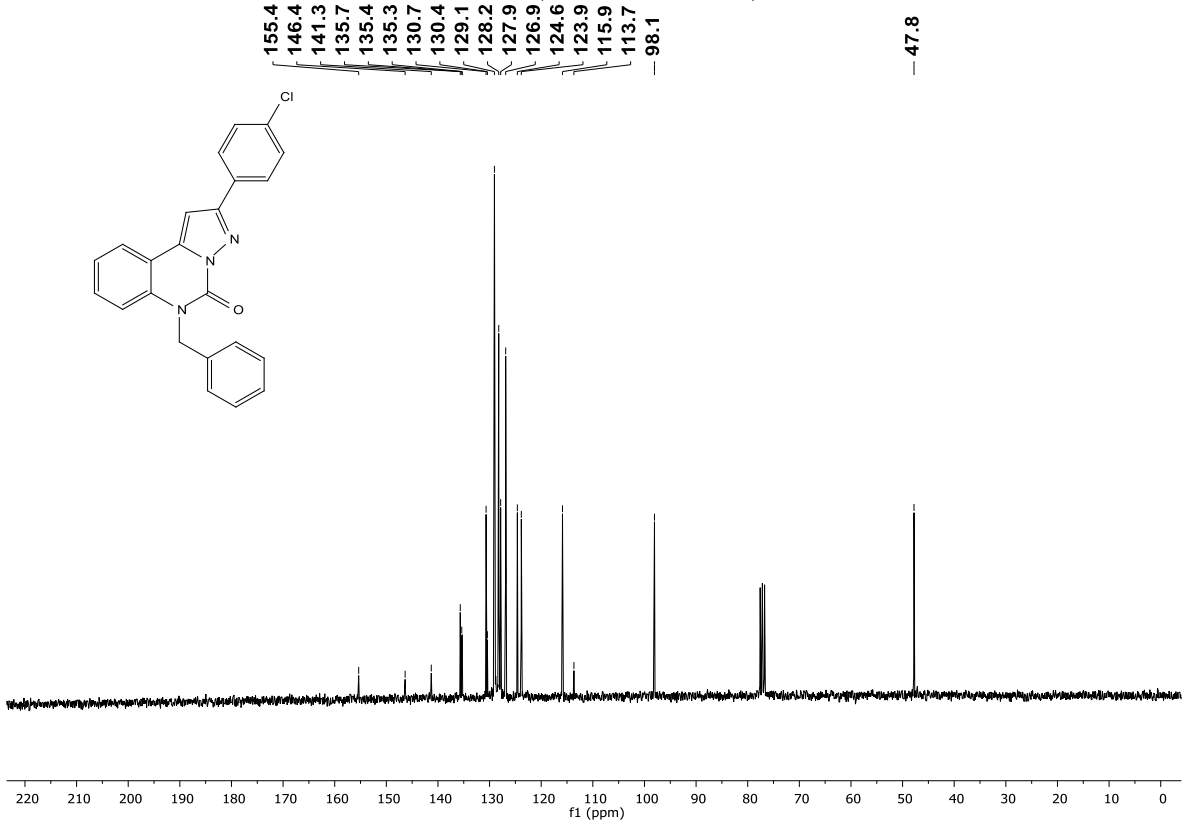
^{19}F NMR (188 MHz, $CDCl_3$) of **2ab**



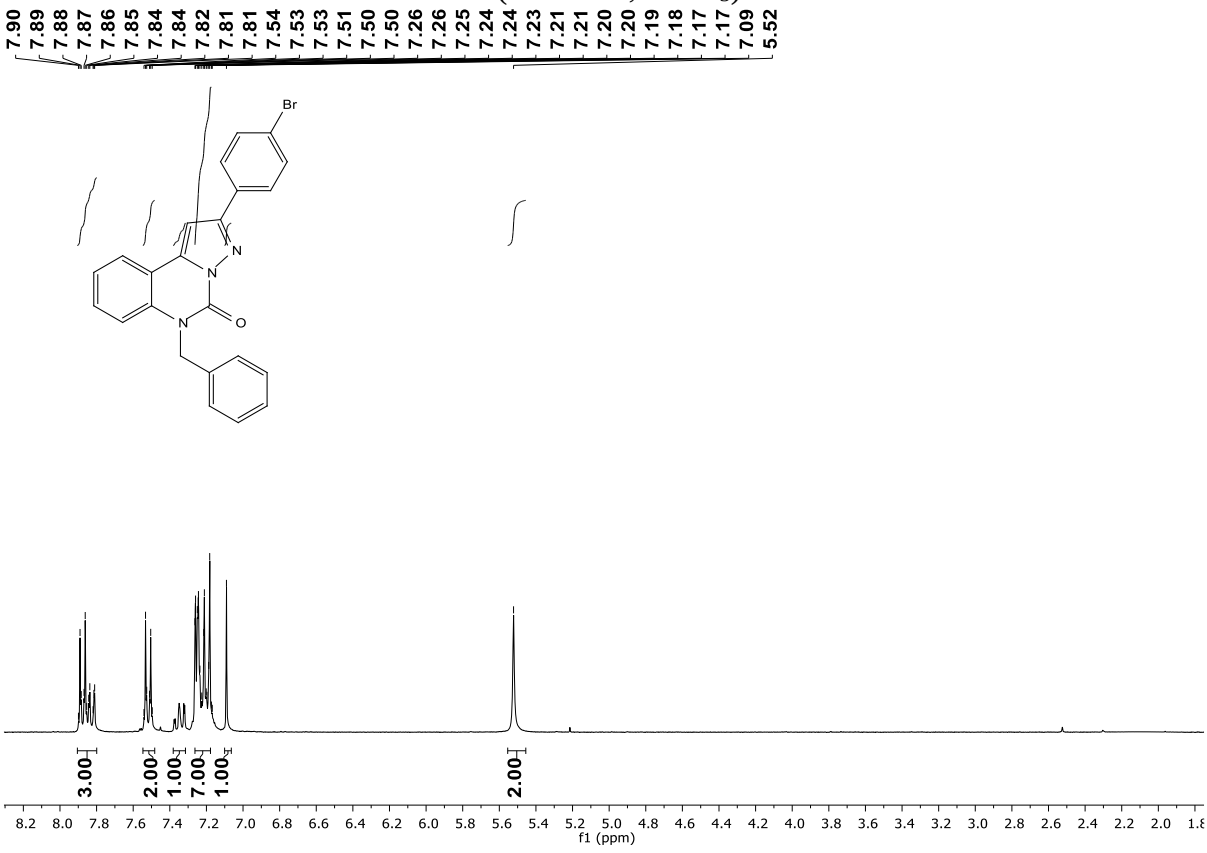
^{1}H NMR (300 MHz, $CDCl_3$) of **2ac**



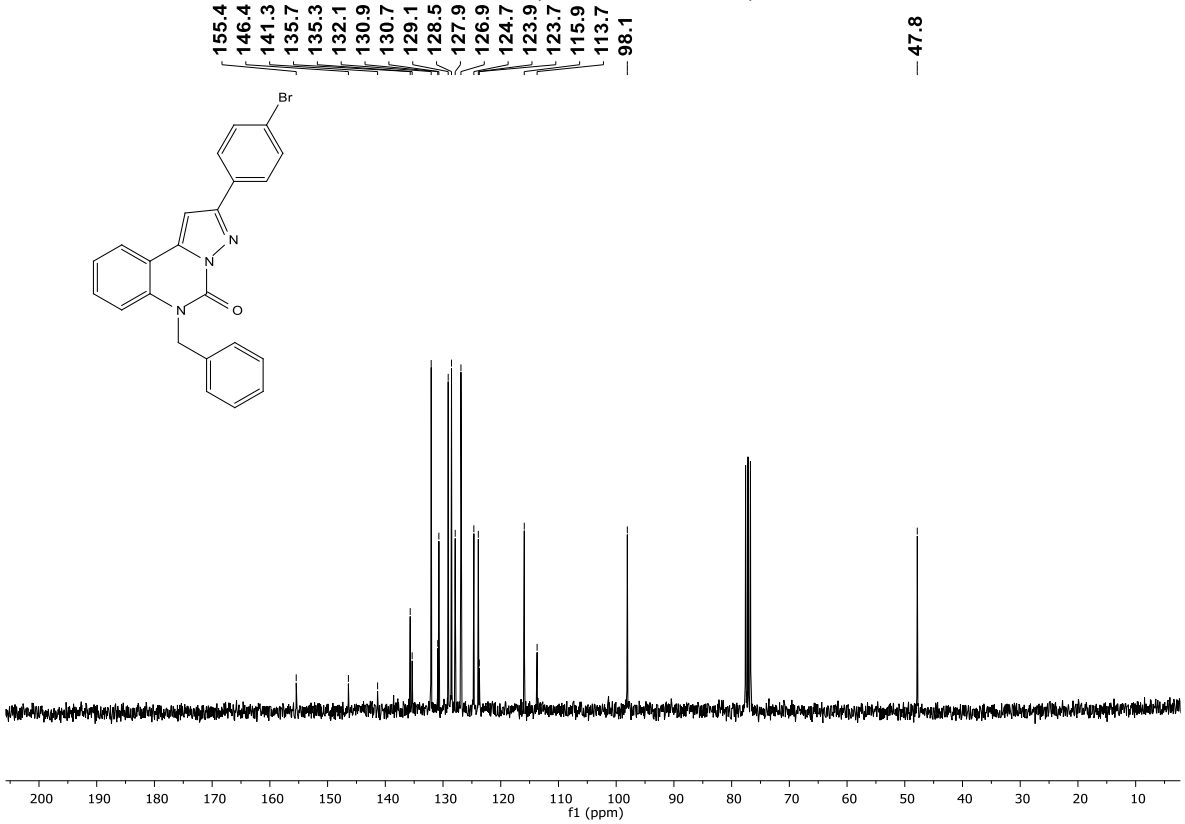
$^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) of **2ac**



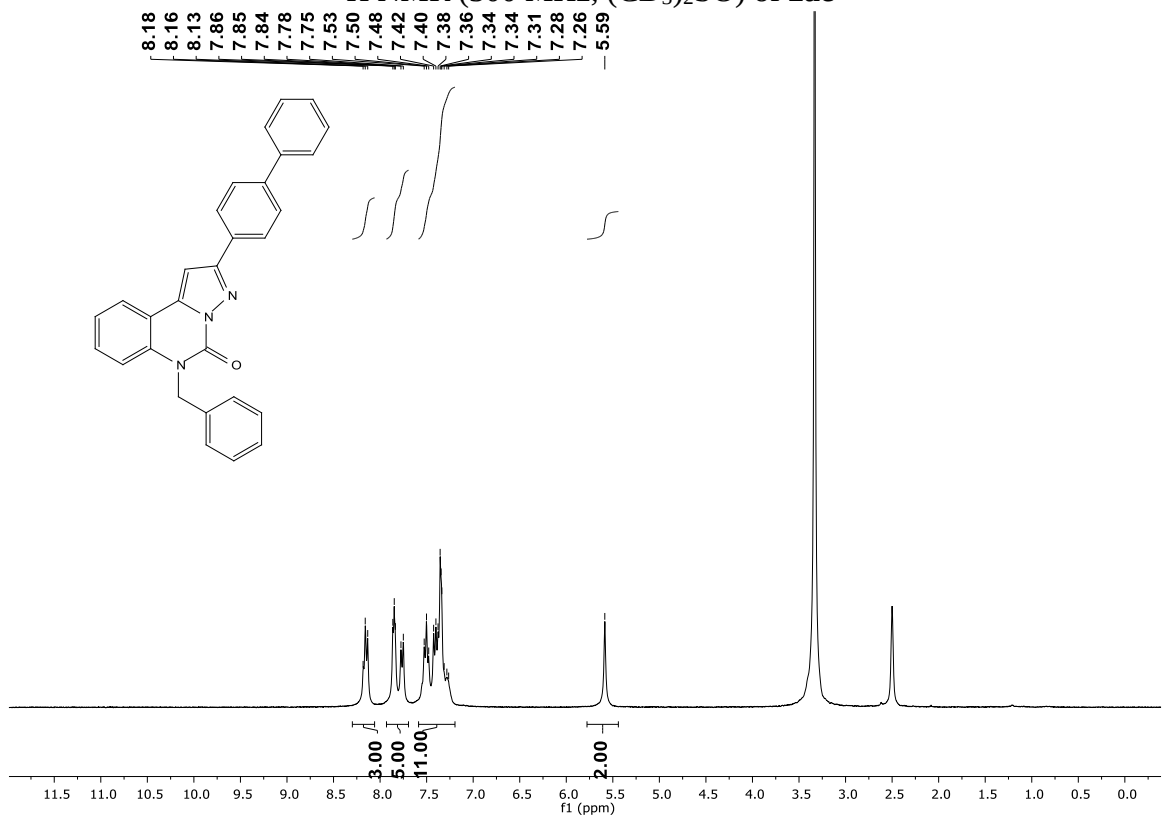
^{1}H NMR (300 MHz, $CDCl_3$) of **2ad**



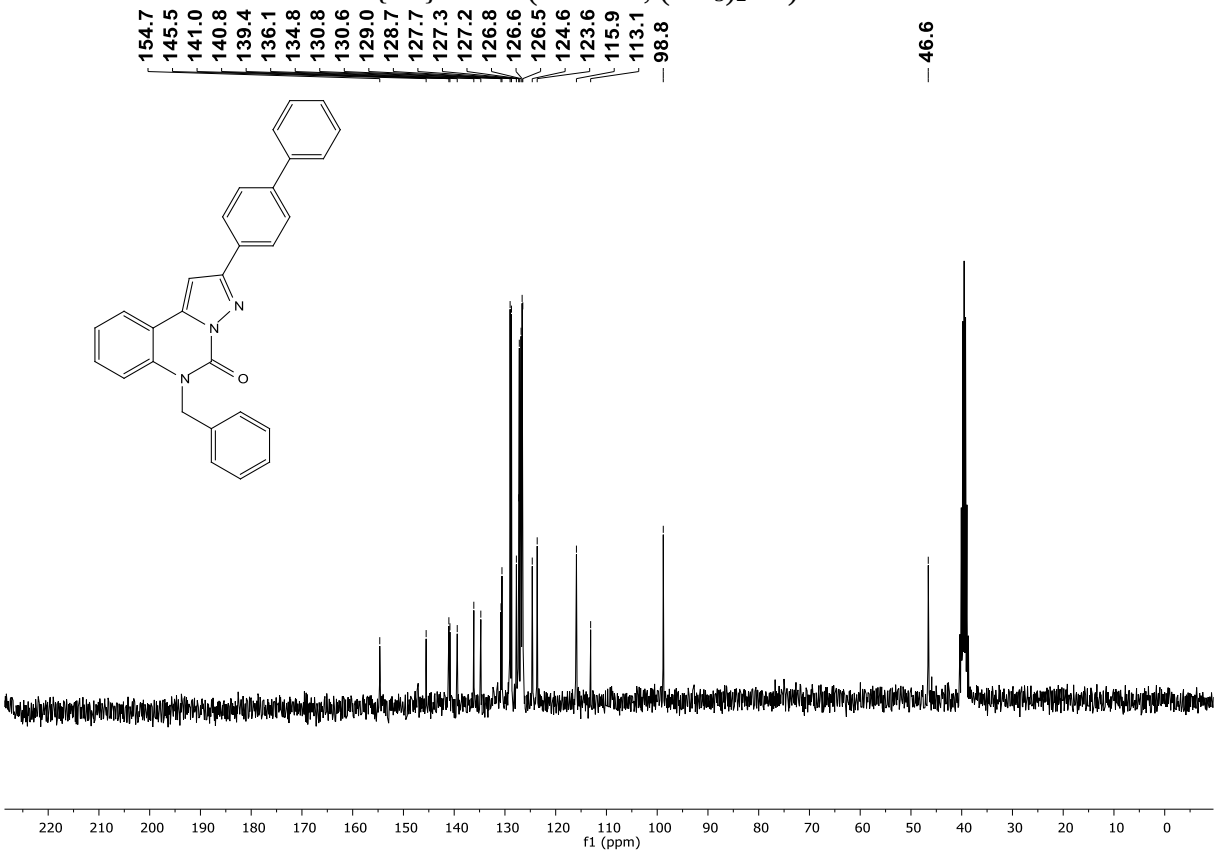
$^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) of **2ad**



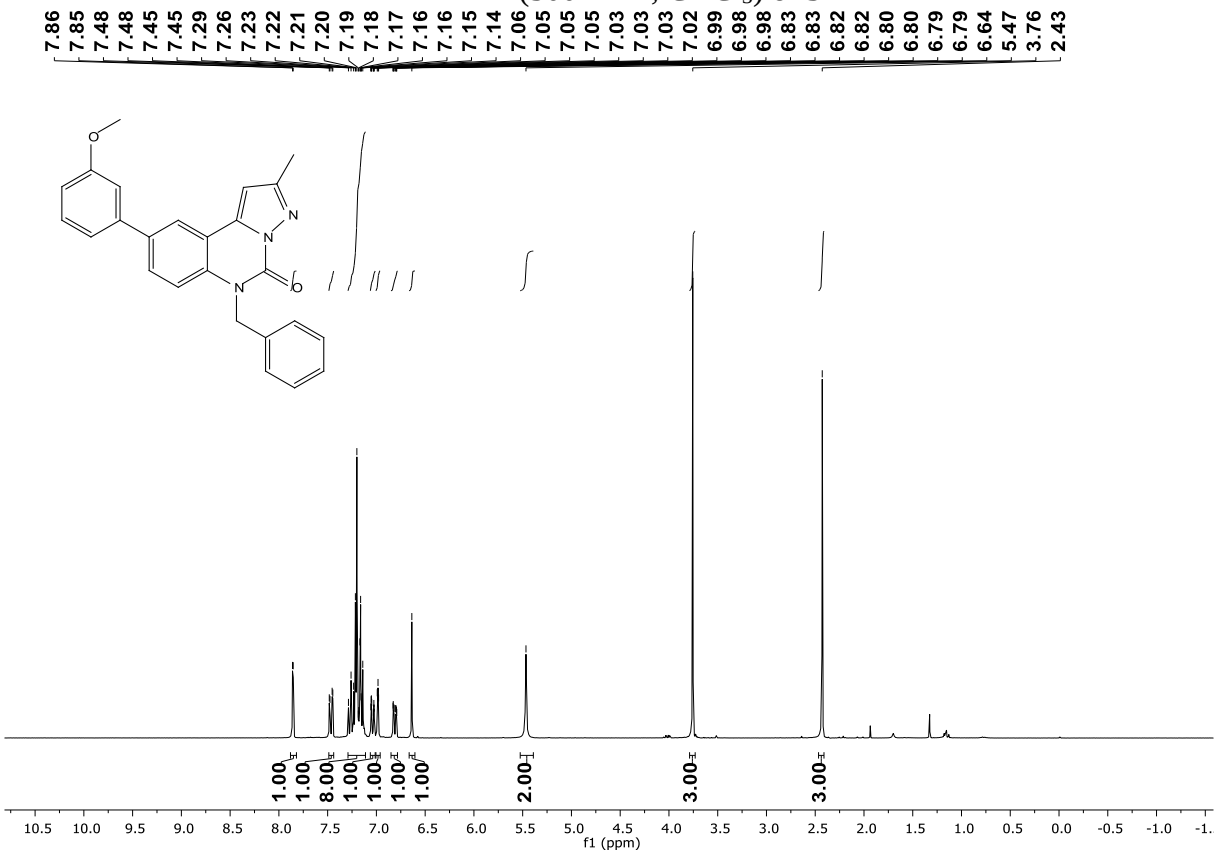
^{1}H NMR (300 MHz, $(CD_3)_2SO$) of **2ae**



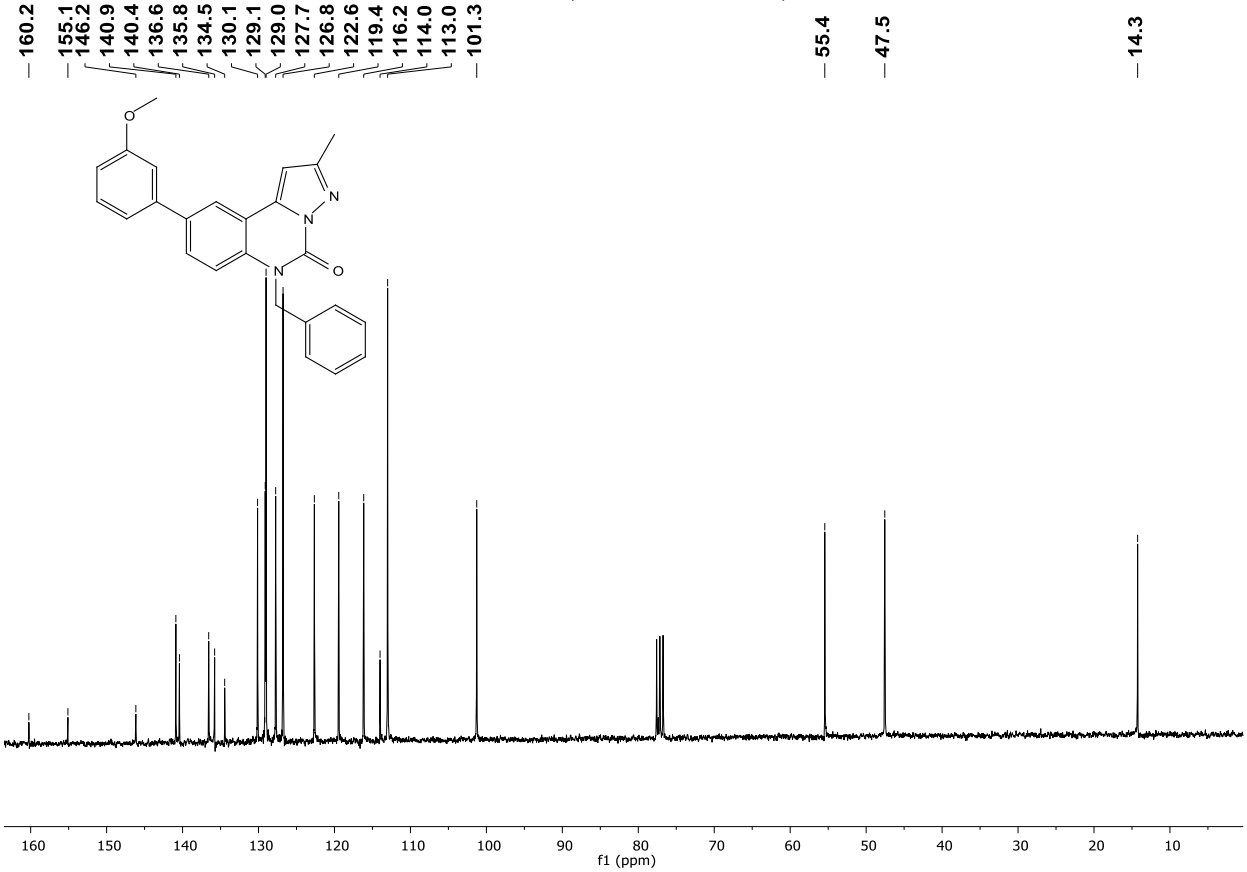
$^{13}C\{^{1}H\}$ NMR (75 MHz, $(CD_3)_2SO$) of **2ae**



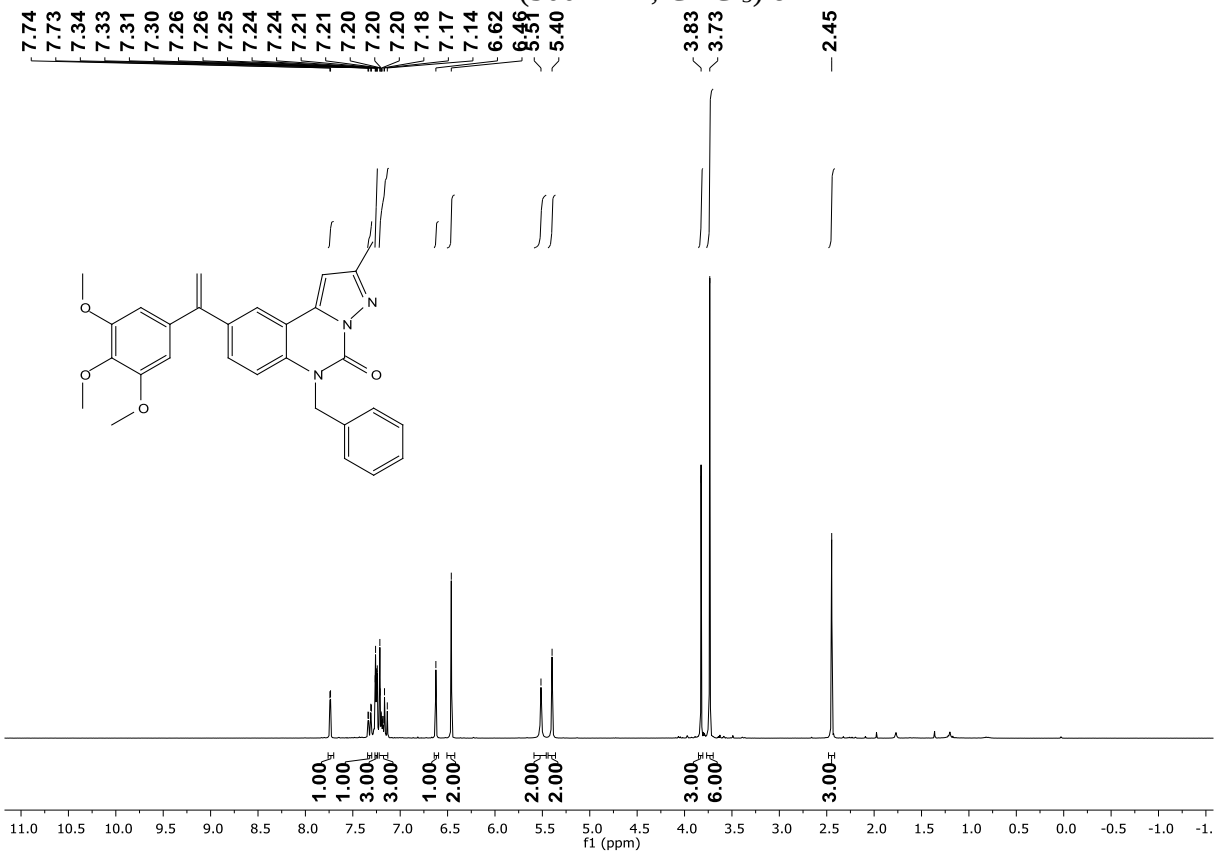
^{1}H NMR (300 MHz, $CDCl_3$) of **3**



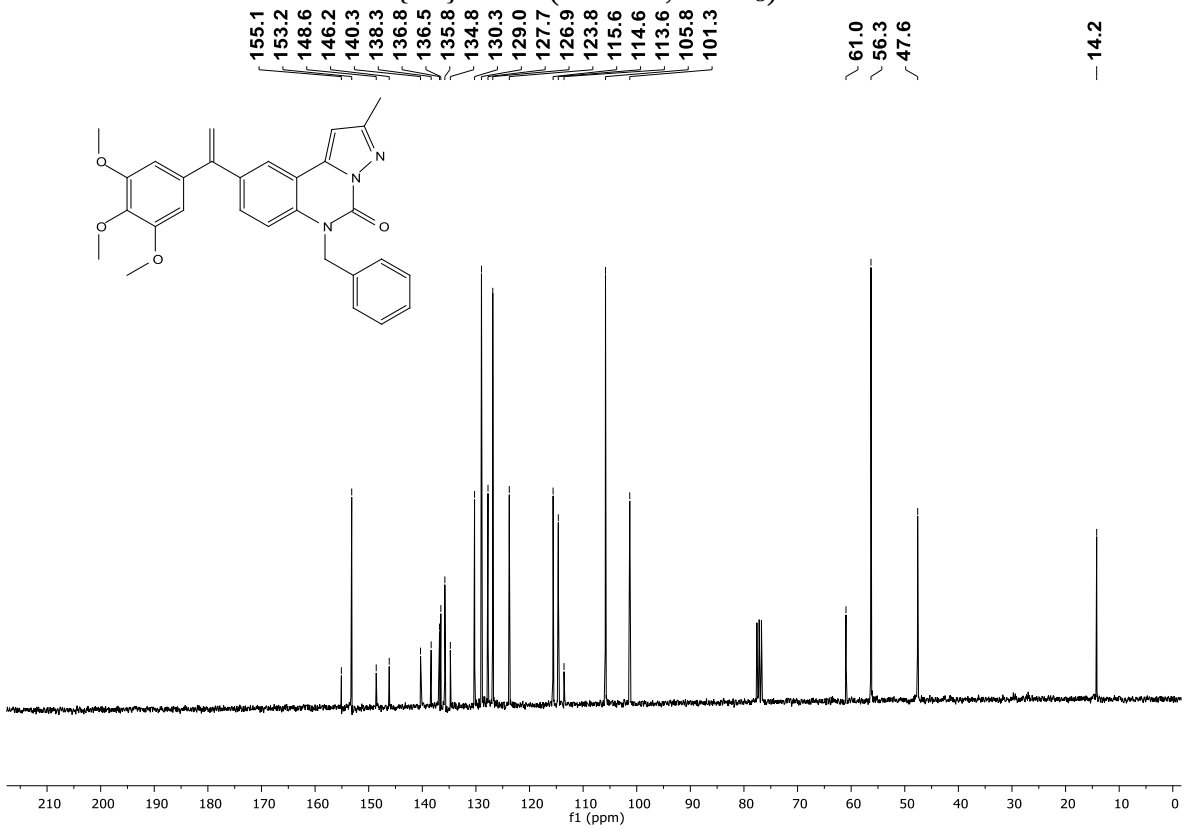
$^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) of **3**



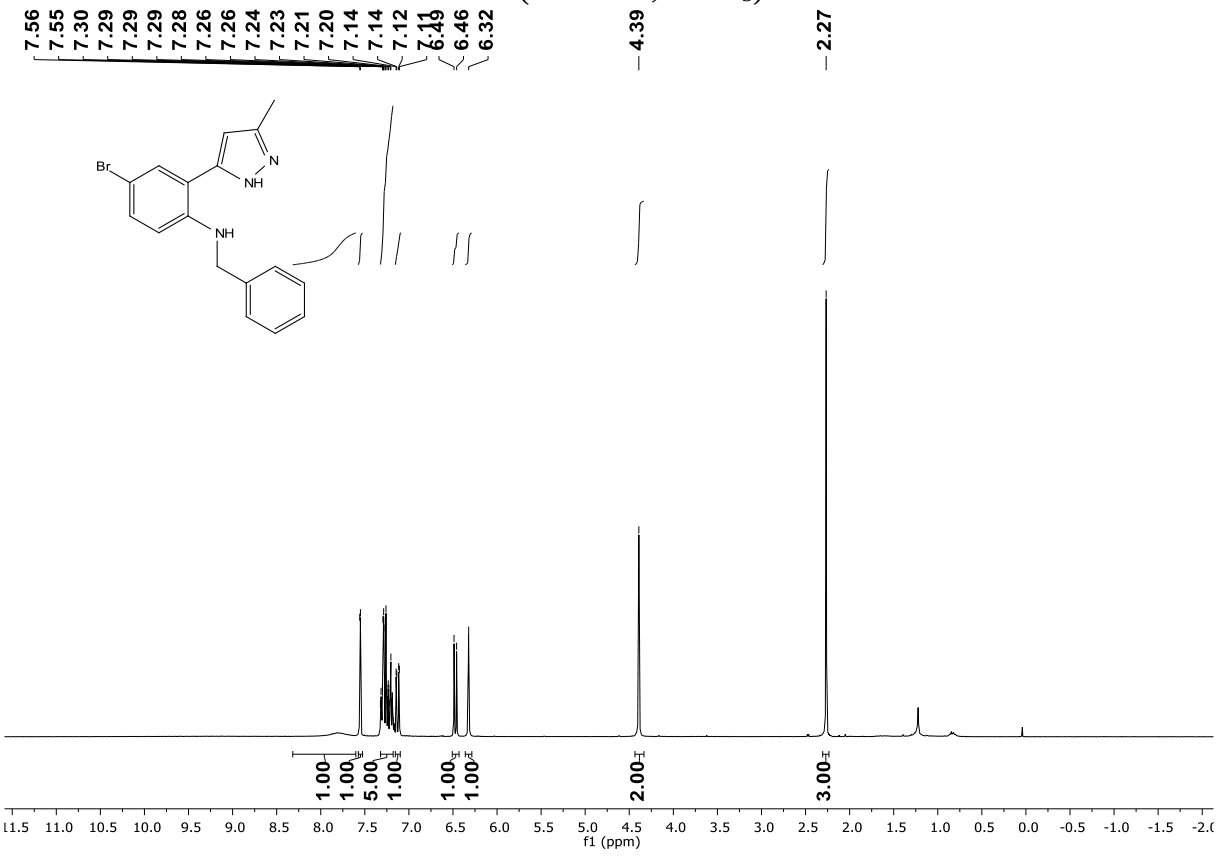
^{1}H NMR (300 MHz, $CDCl_3$) of **4**



$^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) of **4**



^{1}H NMR (300 MHz, $CDCl_3$) of **5**



$^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) of **5**