Supporting Information

Diastereoselective Assembly of Complex Benzofuran-Annulated Spiro-Tetrahydroquinoline Frameworks via Povarov Cyclization

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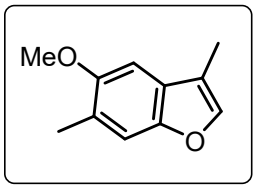
Section I. General information:

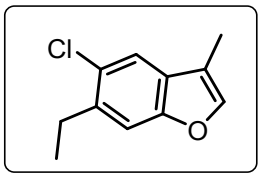
Unless otherwise stated, all reagents were purchased from commercial suppliers and used without purification. All reactions were monitored by thin-layer chromatography (TLC). Visualization of the spots on TLC plates was done by exposure to iodine vapor, under UV light or by spraying with Anisaldehyde-H_2SO_4-methanol solution and heating the plates at ~120°C. Commercial silica gel (100-200 mesh particle size) was used for column chromatography. ^{1}H and ^{13}C {^{1}H} NMR samples were recorded in $CDCl_3$, DMSO-d_6 and CD_3OD, chemical shifts are expressed in parts per million (δ) scale using tetramethylsilane as an internal standard. The standard abbreviations s, d, t, q, dd, dt and m refer to singlet, doublet, triplet, quartet, doublet of doublet, doublet of triplet and multiplet respectively. Coupling constants (J), whenever discernible, have been reported in Hz. Mass spectra were recorded using HRMS (ESI-TOF analyzer) equipment.

Section II. General procedure for the synthesis of substituted 3-Methylbenzofurans (6d-6m):

Reactant **6c** and **6d** were synthesized according to the procedure previously reported by our group.[1]

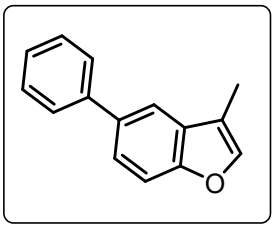


5-methoxy-3,6-dimethylbenzofuran 6d. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.23 (d, J = 1.2 Hz, 1H), 7.17-7.13 (m, 1H), 6.79 (s, 1H), 3.80 (s, 3H), 2.23 (s, 3H), 2.14 (s, 3H). **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 154.3, 149.9, 141.2, 127.0, 124.2, 115.7, 112.9, 99.6, 56.0, 17.1, 8.2. **ESI HRMS** m/z calc. for $C_{11}H_{13}O_2$ $[M+H]^+$: 177.0916, Found: 177.0915

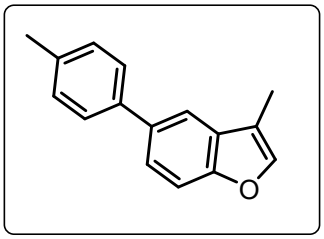


*5-chloro-6-ethyl-3-methylbenzofuran 6e.***^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.50 (s, 1H), 7.36 (d, J = 1.2 Hz, 1H), 7.32 (s, 1H), 2.85 (q, J = 7.5 Hz, 2H), 2.20 (s, 3H), 1.29 (t, J = 7.5 Hz, 3H). **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 154.3, 142.1, 137.7, 128.3, 128.1, 119.7, 115.3, 111.7, 27.3, 14.5, 8.0. **ESI HRMS** m/z calc. for $C_{11}H_{12}ClO[M+H]^+$: 195.0576, Found: 195.0575

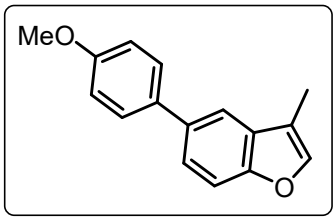
For reactants **6f-6m**, an oven dried round bottomed flask was charged with commercially available 5-bromo-3-methylbenzofuran (200 mg, 0.09 mmol, 1.0 equiv.), $Pd(PPh_3)_4$ (55 mg, 0.05 mmol, 0.05 equiv.), Na_2CO_3 (251 mg, 2.37 mmol, 2.5 equiv.) and Phenylboronic acid (139 mg, 1.14 mmol, 1.2 equiv.) in DME:H_2O (3:7,v/v, ~20 mL/mmol of phenylboronic acid) and the reaction mixture was refluxed at 90 °C for 8 h at constant stirring. The consumption of starting material was monitored by TLC analysis and upon complete consumption, the reaction mixture was cooled to room temperature, quenched with water (30 mL) and extracted with ethyl acetate (20 mL x 4). The combined organic layer was washed with brine, dried over anhydrous Na_2SO_4 and the solvent was removed under reduced pressure to obtain the crude product which was further purified by column chromatography using ethyl acetate: hexane (1:99, v/v) to afford pure **6f** as colorless liquid (118 mg, 0.57 mmol, 60% yield). Similar procedure was followed for the synthesis of **6g-6m**.



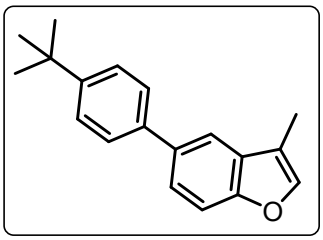
3-methyl-5-phenylbenzofuran (6f). This compound **6f** was prepared by using 5-bromo-3-methylbenzofuran (200 mg, 0.09 mmol, 1.0 equiv.), Phenylboronic acid (139 mg, 1.14 mmol, 1.2 equiv.), $Pd(PPh_3)_4$ (55 mg, 0.05 mmol, 0.05 equiv.), and Na_2CO_3 (251 mg, 2.37 mmol, 2.5 equiv.). The product **6f** was obtained by column chromatography (ethyl acetate: hexane, 1:99 v/v) as colorless liquid (118 mg, 0.57 mmol, 60% yield); m.p.: 48-50 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) *δ* 7.67 (d, *J* = 1.0 Hz, 1H), 7.61-7.55 (m, 2H), 7.46 (s, 2H), 7.42-7.33 (m, 3H), 7.33-7.26 (m, 1H), 2.20 (s, 3H). **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) *δ* 155.0, 142.1, 141.9, 136.1, 129.6, 128.8, 127.6, 126.9, 123.9, 118.0, 115.9, 111.5, 8.0. **ESI HRMS** *m/z* calc. for $C_{15}H_{13}O[M+H]^+$: 209.0966, Found: 209.0956.



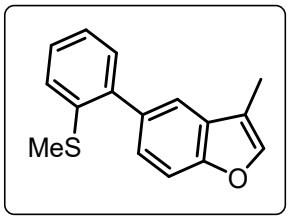
3-methyl-5-(p-tolyl)benzofuran (6g). This compound **6g** was prepared by using 5-bromo-3-methylbenzofuran (200 mg, 0.09 mmol, 1.0 equiv.), 3-methyl-5-(p-tolyl)benzofuran (155 mg, 1.12 mmol, 1.2 equiv.), $Pd(PPh_3)_4$ (55 mg, 0.05 mmol, 0.05 equiv.), and Na_2CO_3 (251 mg, 2.37 mmol, 2.5 equiv.). The product **6g** was obtained by column chromatography (ethyl acetate: hexane, 1:99 v/v) as white solid (116 mg, 0.52 mmol, 55% yield); m.p.: 60-62 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) *δ* 7.62 - 7.57 (m, 1H), 7.45 (d, *J* = 8.1 Hz, 2H), 7.41 (d, *J* = 1.4 Hz, 2H), 7.34 (d, *J* = 1.3 Hz, 1H), 7.21-7.11 (m, 2H), 2.32 (s, 3H), 2.19 (s, 3H). **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) *δ* 154.9, 142.1, 139.1, 136.7, 136.1, 129.6, 127.4, 123.8, 117.9, 116.0, 111.5, 21.2, 8.0. **ESI HRMS** *m/z* calc. for $C_{16}H_{15}O[M+H]^+$: 223.1123, Found: 223.1113.



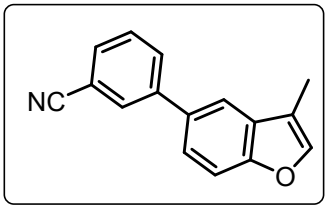
5-(4-methoxyphenyl)-3-methylbenzofuran (6h). This compound **6h** was prepared by using 5-bromo-3-methylbenzofuran (500 mg, 2.4 mmol, 1.0 equiv.), 4-methoxyphenylboronic acid (431 mg, 2.84 mmol, 1.2 equiv.), $Pd(PPh_3)_4$ (137 mg, 0.01 mmol, 0.05 equiv.), and Na_2CO_3 (628 mg, 6.0 mmol, 2.5 equiv.). The product **6h** was obtained by column chromatography (ethyl acetate: hexane, 3:47 v/v) as white solid (282 mg, 1.18 mmol, 50% yield); m.p.: 102-104 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) *δ* 7.70-7.67 (m, 1H), 7.61-7.56 (m, 2H), 7.50 (t, *J* = 1.2 Hz, 2H), 7.44 (d, *J* = 1.3 Hz, 1H), 7.06 -6.92 (m, 2H), 3.88 (s, 3H), 2.30 (s, 3H). **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) *δ* 159.0, 154.7, 142.1, 135.8, 134.5, 129.6, 128.6, 123.6, 117.6, 115.9, 114.3, 111.5, 55.5, 8.0. **ESI HRMS** *m/z* calc. for $C_{16}H_{15}O_2$ $[M+H]^+$: 239.1072, Found: 239.1060.



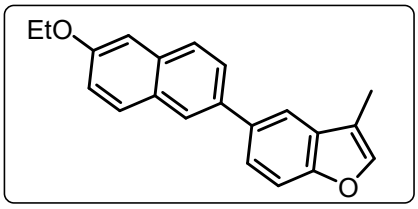
5-(4-(tert-butyl)phenyl)-3-methylbenzofuran (6i). This compound **6i** was prepared by using 5-bromo-3-methylbenzofuran (300 mg, 1.42 mmol, 1.0 equiv.), (4-(tert-butyl)phenyl)boronic acid (304 mg, 1.71 mmol, 1.2 equiv.), $Pd(PPh_3)_4$ (82 mg, 0.07 mmol, 0.05 equiv.), and Na_2CO_3 (377 mg, 3.5 mmol, 2.5 equiv.). The product **6i** was obtained by column chromatography (ethyl acetate: hexane, 1:99 v/v) as white solid (116 mg, 0.52 mmol, 55% yield); m.p.: 122-124 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) *δ* 7.73 (d, *J* = 0.8 Hz, 1H), 7.61 (d, *J* = 8.4 Hz, 2H), 7.536-7.49 (m, 4H), 7.45 (d, *J* = 1.0 Hz, 1H), 2.30 (s, 3H), 1.41 (s, 9H). **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) *δ* 154.9, 149.9, 142.1, 139.1, 136.0, 129.6, 127.2, 125.8, 123.8, 117.9, 116.0, 111.5, 34.6, 31.5, 8.1. **ESI HRMS** *m/z* calc. for $C_{19}H_{21}O$ $[M+H]^+$: 265.1592, Found: 265.1590.



3-methyl-5-(4-(methylthio)phenyl)benzofuran (6j). This compound **6j** was prepared by using 5-bromo-3-methylbenzofuran (500 mg, 2.4 mmol, 1.0 equiv.), 4-methylthiophenylboronic acid (47 mg, 2.84 mmol, 1.2 equiv.), $Pd(PPh_3)_4$ (137 mg, 0.01 mmol, 0.05 equiv.), and Na_2CO_3 (628 mg, 6.0 mmol, 2.5 equiv.). The product **6j** was obtained by column chromatography (ethyl acetate: hexane, 1:99 v/v) as white solid (362 mg, 1.42 mmol, 60% yield); m.p.: 60-62 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) *δ* 7.45-7.42 (m, 1H), 7.40-7.32 (m, 1H), 7.31 (s, 1H), 7.26-7.20 (m, 2H), 7.19.7.13 (m, 2H), 7.12-7.00 (m, 1H), 2.25 (s, 3H), 2.13 (s, 3H). **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) *δ* 154.8, 142.0, 141.2, 137.5, 134.9, 130.4, 129.1, 127.9, 125.7, 124.9, 124.6, 120.3, 115.9, 15.9, 8.0. **ESI HRMS** *m/z* calc. for $C_{16}H_{15}OS$ $[M+H]^+$: 255.0843, Found: 255.0842.

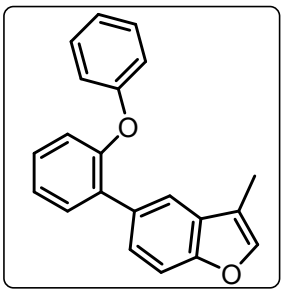


3-(3-methylbenzofuran-5-yl)benzonitrile (6k). This compound **6k** was prepared by using 5-bromo-3-methylbenzofuran (300 mg, 1.42 mmol, 1.0 equiv.), 3-cyanophenylboronic acid (251 mg, 1.71 mmol, 1.2 equiv.), $Pd(PPh_3)_4$ (82 mg, 0.07 mmol, 0.05 equiv.), and Na_2CO_3 (377 mg, 3.5 mmol, 2.5 equiv.). The product **6k** was obtained by column chromatography (ethyl acetate: hexane, 1:49 v/v) as white solid (166 mg, 0.71 mmol, 50% yield); m.p.: 179-181 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) *δ* 7.90 (t, *J* = 1.4 Hz, 1H), 7.88-7.81 (m, 1H), 7.68 (d, *J* = 1.4 Hz, 1H), 7.62 (dt, *J* = 7.7, 1.3 Hz, 1H), 7.54 (t, *J* = 8.3 Hz, 2H), 7.448-7.45 (m, 2H), 2.30 (s, 3H). **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) *δ* 155.4, 143.1, 142.6, 133.7, 131.9, 131.0, 130.3, 129.9, 129.6, 123.6, 119.1, 118.2, 116.0, 113.0, 112.0, 8.0. **ESI HRMS** *m/z* calc. for $C_{16}H_{12}NO$ $[M+H]^+$: 234,0919, Found: 234.0901.



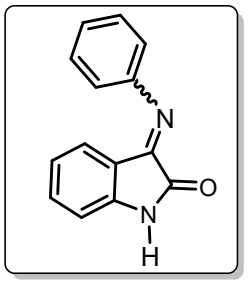
5-(6-ethoxynaphthalen-2-yl)-3-methylbenzofuran (6l). This compound **6l** was prepared by using 5-bromo-3-methylbenzofuran (500 mg, 2.4 mmol, 1.0 equiv.), 6-ethoxynaphthalen-2-ylboronic acid (512 mg, 2.84 mmol, 1.2 equiv.), $Pd(PPh_3)_4$ (137 mg, 0.01 mmol, 0.05 equiv.), and Na_2CO_3 (628 mg, 6.0 mmol, 2.5 equiv.). The product **6l** was obtained by column chromatography (ethyl acetate: hexane, 1:99 v/v) as white solid (358 mg, 1.18 mmol, 50% yield); m.p.: 136-138 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) *δ* 8.01 (s, 1H), 7.85-7.74 (m, 4H), 7.63 (dd, *J* = 8.5, 1.7 Hz, 1H), 7.55 (d, *J* = 8.5 Hz, 1H), 7.46 (s, 1H), 7.19 (dd, *J* = 11.3, 2.4 Hz, 2H), 4.18 (q, *J* = 7.0 Hz, 2H), 2.32 (s, 3H), 1.51 (t, *J* = 7.0 Hz, 3H). **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) *δ* 157.1, 154.9, 142.2, 137.0, 136.2, 133.7, 129.7,

129.7, 129.3, 127.3, 126.6, 125.8, 124.0, 119.5, 118.1, 116.0, 111.6, 106.5, 63.6, 15.0, 8.1. **ESI HRMS** *m/z* calc. for $C_{21}H_{19}O_2$ $[M+H]^+$: 303.1385, Found: 303.1372.



3-methyl-5-phenoxybenzofuran (6m). This compound **6m** was prepared by using 5-bromo-3-methylbenzofuran (500 mg, 2.4 mmol, 1.0 equiv.), 2-phenoxyphenylboronic acid (608 mg, 2.84 mmol, 1.2 equiv.), $Pd(PPh_3)_4$ (137 mg, 0.01 mmol, 0.05 equiv.), and Na_2CO_3 (628 mg, 6.0 mmol, 2.5 equiv.). The product **6m** was obtained by column chromatography as diastereomeric mixture (*d.r = 87:13*) (ethyl acetate: hexane, 1:49 v/v) as white solid (391 mg, 1.30 mmol, 55% yield); m.p.: 194-196 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) *δ* 7.66 (d, *J* = 1.3 Hz, 1H), 7.53-7.47 (m, 2H), 7.43-7.37 (m, 2H), 7.34-7.26 (m, 1H), 7.24-7.16 (m, 2H), 7.07-6.97 (m, 2H), 6.95-6.90 (m, 2H), 6.89-6.82 (m, 1H), 2.21(s, 3H). **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) *δ* 158.1, 154.7, 153.7, 141.8, 132.2, 131.8, 129.7, 129.5, 128.6, 125.8, 124.2, 122.7, 120.5, 120.2, 119.0, 118.1, 115.9, 110.9, 8.0. **ESI HRMS** *m/z* calc. for $C_{21}H_{17}O_2$ $[M+H]^+$: 301.1229, Found: 301.1221.

Section III. Procedure for the synthesis of Intermediate 7a:

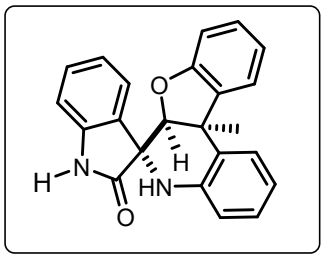


3-(phenylimino)indolin-2-one (7a). The compound **7a** was synthesized by using Isatin **4a** (100 mg, 0.67 mmol, 1.0 equiv.), Aniline **5a** (61 µL, 0.67 mmol, 1.0 equiv.), 3-Methylbenzofuran **6** (85 µL, 0.67 mmol, 1.0 equiv.) in presence of $Sc(OTf)_3$ (17 mg, 0.03 mmol, 0.05 equiv.) in 5 mL oven-dried reaction tube (reaction vial) with a magnetic stir bar. HFIP (2 mL) was employed as solvent. Then the tube was capped with PTFE made solid cap and the resulting mixture was stirred at 85 °C. The progress of the reaction was monitored by TLC. After 1 h, significant consumption of Isatin **4a** and Aniline **5a** was observed, accompanied by the formation of a major product **7a** along with the traces of **8a**. The reaction was quenched with water (10 mL), ethyl acetate (10 mL) and the layers were separated in a separating funnel. The aqueous layer was further extracted with ethyl acetate (10 mL x 2). The combined organic layers were washed with brine, dried over anhydrous sodium sulfate. Solvent was removed under reduced pressure to give the crude product, which was purified by column chromatography using ethyl acetate/hexane (3:7, v/v), resulted in compound **7a** (yellow solid) as EZ mixture (*E:Z = 97:3*) (66 mg, 0.29 mmol, 63% yield) with respect to recovered starting material (Isatin **4a,** 30 mg).**^{1}H NMR** (400 MHz, $CDCl_3$) *δ* 9.91 (s, 1H), 7.44 (t, *J* = 7.8 Hz, 2H), 7.34-7.22 (m, 2H), 7.04 (d, *J* = 7.5 Hz, 2H), 6.96 (d, *J* = 7.8 Hz, 1H), 6.74 (t, *J* = 7.6 Hz, 1H), 6.65 (d, *J* = 7.6 Hz, 1H). **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) *δ* 165.7, 160.2, 154.9, 150.2, 145.9, 138.8, 134.5, 134.1, 129.6, 129.4, 128.7, 126.5, 125.8, 125.6, 125.4, 124.0, 122.9, 119.2, 119.0, 118.1, 118.0, 116.3, 115.5, 112.9, 112.1. **ESI HRMS** *m/z* calc. for $C_{14}H_{11}N_2O[M+H]^+$: 223.0871, Found: 223.0868.

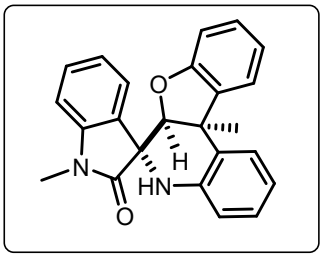
Section IV. General procedure for the synthesis of compounds 8a-8q:

A 5 mL oven-dried reaction tube (reaction vial) with a magnetic stir bar was charged with Isatin **4a** (100 mg, 0.67 mmol, 1.0 equiv.), Aniline **5a** (61 µL, 0.67 mmol, 1.0 equiv.), 3-Methylbenzofuran **6a** (85 µL, 0.67 mmol, 1.0 equiv.), $Sc(OTf)_3$ (17 mg, 0.03 mmol, 0.05 equiv.) and HFIP as solvent (2 mL). Then the tube was capped with PTFE made solid cap and the resulting mixture was stirred at

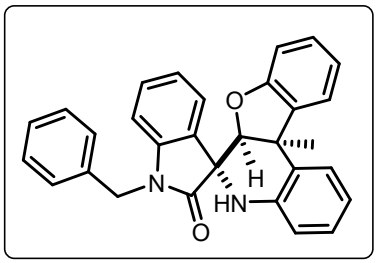
85 °C for 24 h. The reaction progress was monitored by TLC and upon the completion of the reaction, water (10 mL), ethyl acetate (10 mL) was added and the layers were separated in a separating funnel. The aqueous layer was further extracted with ethyl acetate (10 mL x 2). The combined organic layers were washed with brine, dried over anhydrous sodium sulfate. Solvent was removed under reduced pressure to give the crude product, which was purified by column chromatography using ethyl acetate/hexane (1:4, v/v) to result in compound **8a** as off-white solid (214 mg, 0.60 mmol, 89% yield). A similar procedure was followed for the synthesis of compounds **8b-q**.



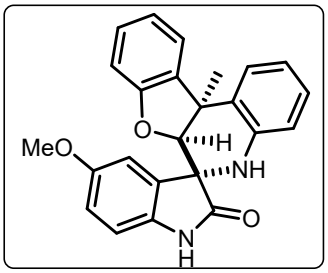
(6R,6aS,11bR)-11b-methyl-6a,11b-dihydro-5H-spiro[benzofuro[2,3-c]quinoline-6,3'-indolin]-2'-one (8a). The compound **8a** was prepared by using Isatin **4a** (100 mg, 0.67 mmol, 1.0 equiv.), Aniline 5**a** (61 µL, 0.67 mmol, 1.0 equiv.), 3-Methylbenzofuran **6a** (85 µL, 0.67 mmol, 1.0 equiv.) and $Sc(OTf)_3$ (17 mg, 0.03 mmol, 0.05 equiv.). The product **8a** was obtained by column chromatography (ethyl acetate: hexane, 1:4 v/v) as off-white solid (214 mg, 0.60 mmol, 89% yield); m.p.: 164-166 °C. **^{1}H NMR** (400 MHz, DMSO-d_6) δ 10.54 (s, 1H), 7.57 (dd, J = 13.2, 7.5 Hz, 2H), 7.16 (t, J = 7.5 Hz, 1H), 6.96 (dt, J = 13.6, 7.1 Hz, 3H), 6.87-6.78 (m, 2H), 6.74 -6.65 (m, 2H), 6.56 (dd, J = 18.3, 7.8 Hz, 2H), 6.40 (s, 1H), 4.74 (s, 1H), 1.76 (s, 3H). **^{13}C{^{1}H} NMR** (100 MHz, DMSO-d_6) δ 177.3, 156.9, 142.6, 142.0, 136.3, 129.2, 129.1, 128.0, 127.0, 126.8, 126.8, 126.5, 123.3, 120.9, 120.9, 118.3, 115.1, 109.4, 109.1, 89.2, 61.8, 45.3, 29.7. **ESI HRMS** *m/z* calc. for $C_{23}H_{19}N_2O_2[M+H]^+$: 355.1447, Found: 355.1437.



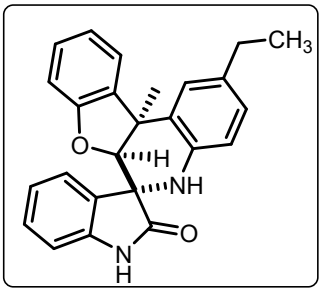
(6R,6aS,11bR)-1',11b-dimethyl-6a,11b-dihydro-5H-spiro[benzofuro[2,3-c]quinoline-6,3'-indolin]-2'-one (8b). The compound **8b** was prepared by using Isatin **4b** (50 mg, 0.33 mmol, 1.0 equiv.), Aniline **5a** (28 µL, 0.31 mmol, 1.0 equiv.), 3-Methylbenzofuran **6a** (39 µL, 0.31 mmol, 1.0 equiv.) and $Sc(OTf)_3$ (7 mg, 0.02 mmol, 0.05 equiv.). The product **8b** was obtained by column chromatography as diastereomeric mixture (*d.r = 96:4*) (ethyl acetate: hexane, 1:4 v/v) as white solid (97 mg, 0.26 mmol, 85% yield); m.p.: 128-130 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.64 (dd, J = 7.8, 1.2 Hz, 1H), 7.40 (dd, J = 7.5, 1.1 Hz, 1H), 7.21-7.16 (m, 1H), 7.09-7.03 (m, 1H), 6.98-6.91 (m, 2H), 6.87- 6.77 (m, 3H), 6.668-6.62 (m, 1H), 6.56 (dd, J = 7.9, 1.2 Hz, 1H), 6.45 (d, J = 8.0 Hz, 1H), 4.94 (s, 1H), 3.96 (s, 1H), 3.25 (s, 3H), 1.83 (s, 3H**)**. **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 175.9, 157.8, 143.6, 141.3, 135.5, 129.5, 128.3, 128.2, 127.9, 127.6, 127.2, 126.3, 122.9, 122.3, 121.2, 120.5, 116.2, 109.6, 108.0, 90.1, 63.0, 46.2, 31.2, 26.7. **ESI HRMS** *m/z* calc. for $C_{24}H_{21}N_2O_2[M+H]^+$: 369.1603, Found: 369.1600.



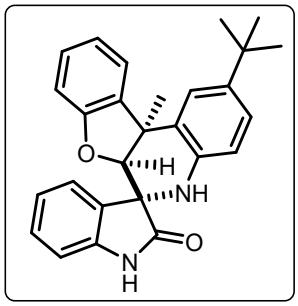
(6R,6aS,11bR)-1'-benzyl-11b-methyl-6a,11b-dihydro-5H-spiro[benzofuro[2,3-c]quinoline-6,3'-indolin]-2'-one (8c). The compound **8c** was prepared by using Isatin **4c** (50 mg, 0.21 mmol, 1.0 equiv.), Aniline **5a** (19 µL, 0.21 mmol, 1.0 equiv.), 3-Methylbenzofuran **6a** (26 µL, 0.21 mmol, 1.0 equiv.) and $Sc(OTf)_3$ (5 mg, 0.01 mmol, 0.05 equiv.). The product **8c** was obtained by column chromatography as diastereomeric mixture (*d.r = 94:6*) (ethyl acetate: hexane, 4:21 v/v) as off-white solid (82 mg, 0.18 mmol, 87% yield); m.p.: 162-164 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) *δ* 7.68 (dd, *J* = 7.7, 1.0 Hz, 1H), 7.43-7.28 (m, 6H), 7.12-7.06 (m, 1H), 7.02-6.97 (m, 2H), 6.92-6.87 (m, 1H), 6.83-6.87 (m, 1H), 6.67 (dd, *J* = 7.5, 0.8 Hz, 1H), 6.63-6.58 (m, 2H), 6.53-6.48 (m, 1H), 6.35 (d, *J* = 7.9 Hz, 1H), 5.25 (d, *J* = 15.8 Hz, 1H), 5.06 (s, 1H), 4.69 (d, *J* = 15.8 Hz, 1H), 4.05 (s, 1H), 1.84 (s, 3H). **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) *δ* 176.1, 157.8, 142.5, 141.4, 135.5, 135.4, 129.2, 128.9, 128.3, 128.2, 127.8, 127.7, 127.6, 127.5, 127.3, 126.1, 122.7, 122.1, 121.2, 120.5, 116.4, 109.6, 109.1, 90.3, 63.3, 46.2, 44.0, 31.5. **ESI HRMS** *m/z* calc. for $C_{30}H_{25}N_2O_2[M+H]^+$: 445.1916, Found: 445.1908.



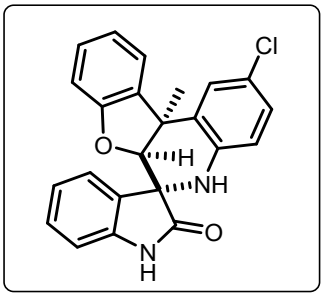
(6R,6aS,11bR)-5'-methoxy-11b-methyl-6a,11b-dihydro-5H-spiro[benzofuro[2,3-c]quinoline-6,3'-indolin]-2'-one (8d). The compound **8d** was prepared by using Isatin **4d** (100 mg, 0.56 mmol, 1.0 equiv.), Aniline **5a** (51 µL, 0.56 mmol, 1.0 equiv.), 3-Methylbenzofuran **6a** (70 µL, 0.56 mmol, 1.0 equiv.) and $Sc(OTf)_3$ (14 mg, 0.02 mmol, 0.05 equiv.). The product **8d** was obtained by column chromatography (ethyl acetate: hexane, 3:7 v/v) as white solid (167 mg, 0.43 mmol, 77% yield); m.p.: 287-289 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) *δ* 8.29 (s, 1H), 7.65 (dd, *J* = 7.8, 1.4 Hz, 1H), 7.44 (dd, *J* = 7.5, 1.1 Hz, 1H), 7.09-7.04 (m, 1H), 7.01-6.93 (m, 2H), 6.7-6.82 (m, 1H), 6.72 (d, *J* = 8.5 Hz, 1H), 6.67-6.63 (m, 1H), 6.58 (dd, *J* = 7.9, 1.1 Hz, 1H), 6.51-6.43 (m, 1H), 6.36 (d, *J* = 2.5 Hz, 1H), 4.98 (s, 1H), 3.38 (s, 3H), 3.07 (s, 1H), 1.83 (s, 3H). **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) *δ* 178.4, 157.6, 155.3, 140.9, 135.5, 133.6, 129.6, 128.3, 127.6, 127.5, 127.2, 122.6, 121.2, 120.6, 116.3, 115.4, 112.7, 110.3, 109.7, 89.8, 55.7, 46.0, 31.2. **ESI HRMS** *m/z* calc. for $C_{24}H_{21}N_2O_3[M+H]^+$: 385.1552, Found: 385.1538.



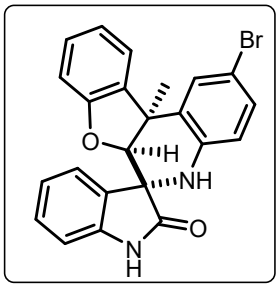
(6R,6aS,11bR)-2-ethyl-11b-methyl-6a,11b-dihydro-5H-spiro[benzofuro[2,3-c]quinoline-6,3'-indolin]-2'-one (8e). The compound **8e** was prepared by using Isatin **4a** (40 mg, 0.27 mmol, 1.0 equiv.), Aniline **5b** (34 µL, 0.27 mmol, 1.0 equiv.), 3-Methylbenzofuran **6a** (34 µL, 0.27 mmol, 1.0 equiv.) and $Sc(OTf)_3$ (7 mg, 0.01 mmol, 0.05 equiv.). The product **8e** was obtained by column chromatography (ethyl acetate: hexane, 3:17 v/v) as off-white solid (93 mg, 0.24 mmol, 89% yield); m.p.: 230-232 °C. **^{1}H NMR** (400 MHz, DMSO-*d*$_6$) *δ* 10.52 (s, 1H), 7.55 (d, *J* = 7.3 Hz, 1H), 7.42 (s, 1H), 7.13 (t, *J* = 7.4 Hz, 1H), 6.97 (t, *J* = 7.5 Hz, 1H), 6.88- 6.75 (m, 4H), 6.66 (t, *J* = 7.3 Hz, 1H), 6.51 (d, *J* = 7.6 Hz, 2H), 6.23 (s, 1H), 4.72 (s, 1H), 2.70-2.34 (m, 2H), 1.74 (s, 3H), 1.18 (t, *J* = 7.4 Hz, 3H). **^{13}C{^{1}H} NMR** (100 MHz, DMSO-*d*$_6$) δ 177.3, 157.0, 142.0, 140.4, 136.3, 133.4, 129.3, 129.0, 128.0, 126.5, 126.3, 126.2, 126.1, 123.3, 120.9, 120.8, 115.2, 109.3, 109.0, 89.37, 61.9, 45.3, 30.0, 27.6, 16.0. **ESI HRMS** *m/z* calc. for $C_{25}H_{23}N_2O_2[M+H]^+$: 383.1760, Found: 383.1748.



(6R,6aS,11bR)-2-(tert-butyl)-11b-methyl-6a,11b-dihydro-5H-spiro[benzofuro[2,3-c]quinoline-6,3'-indolin]-2'-one (8f). The compound **8f** was prepared by using Isatin **1a** (35 mg, 0.24 mmol, 1.0 equiv.), Aniline **2c** (38 µL, 0.24 mmol, 1.0 equiv.), 3-Methylbenzofuran **6a** (30 µL, 0.24 mmol, 1.0 equiv.) and $Sc(OTf)_3$ (6.0 mg, 0.01 mmol, 0.05 equiv.). The product **8f** was obtained by column chromatography (ethyl acetate: hexane, 4:21 v/v) as white solid (86 mg, 0.21 mmol, 88% yield); m.p.: 231-233 °C. **^{1}H NMR** (400 MHz, DMSO-d_6) δ 10.54 (s, 1H), 7.53 (s, 2H), 7.15 (s, 1H), 7.06 -6.78 (m, 5H), 6.70 (s, 1H), 6.53 (s, 2H), 6.27 (s, 1H), 4.73 (s, 1H), 1.78 (s, 3H), 1.29 (s, 9H). **^{13}C{^{1}H} NMR** (100 MHz, DMSO-d_6) δ 177.5, 156.9, 142.0, 140.3, 140.1, 136.5, 129.4, 129.0, 128.0, 126.5, 125.8, 123.6, 123.5, 123.2, 120.9, 114.7, 109.4, 109.2, 89.3, 61.9, 45.5, 33.9, 31.6, 29.7. **ESI HRMS** *m/z* calc. for $C_{27}H_{27}N_2O_2[M+H]^+$: 411.2061, Found: 411.2073.

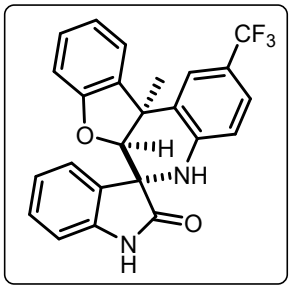


(6R,6aS,11bR)-2-chloro-11b-methyl-6a,11b-dihydro-5H-spiro[benzofuro[2,3-c]quinoline-6,3'-indolin]-2'-one (8g). The compound **8g** was prepared by using Isatin **4a** (100 mg, 0.67 mmol, 1.0 equiv.), Aniline **5f** (87 mg, 0.67 mmol, 1.0 equiv.), 3-Methylbenzofuran **6a** (85 µL, 0.67 mmol, 1.0 equiv.) and $Sc(OTf)_3$ (17 mg, 0.03 mmol, 0.05 equiv.). The product **8g** was obtained by column chromatography (ethyl acetate: hexane, 7:13 v/v) as white solid (233 mg, 0.60 mmol, 88% yield); m.p.: 297-299 °C. **^{1}H NMR** (400 MHz, DMSO-d_6) δ 10.59 (s, 1H), 7.59 (d, J = 7.1 Hz, 2H), 7.28 -7.12 (m, 2H), 7.05 (t, J = 7.5 Hz, 1H), 6.96 (d, J = 7.5 Hz, 1H), 6.87 (q, J = 6.0 Hz, 3H), 6.67- 6.59 (m, 3H), 4.74 (s, 1H), 1.82 (s, 3H). **^{13}C{^{1}H} NMR** (100 MHz, DMSO-d_6) δ 177.3, 156.7, 142.1, 141.8, 135.9, 129.4, 129.0, 128.9, 128.4, 127.1, 126.7, 126.4, 123.8, 121.5, 121.3, 121.2, 116.6, 109.6, 109.3, 88.9, 61.5, 45.5, 28.7. **ESI HRMS** m/z calcd. for $C_{23}H_{18}ClN_2O_2[M+H]^+$: 389.1057, Found: 389.1051.

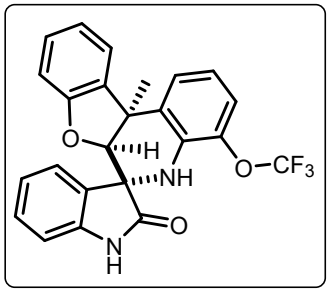


(6R,6aS,11bR)-2-bromo-11b-methyl-6a,11b-dihydro-5H-spiro[benzofuro[2,3-c]quinoline-6,3'-indolin]-2'-one (8h). The compound **8h** was prepared by using Isatin **4a** (100 mg, 0.67 mmol, 1.0 equiv.), Aniline **5g** (76 µL, 0.67 mmol, 1.0 equiv.), 3-Methylbenzofuran **6a** (85 µL, 0.67 mmol, 1.0 equiv.) and $Sc(OTf)_3$ (17 mg, 0.03 mmol, 0.05 equiv.). The product **8h** was obtained by column chromatography (ethyl acetate: hexane, 33:67 v/v) as off-white solid (247 mg, 0.57 mmol, 84% yield); m.p.: 284-286 °C. **^{1}H NMR** (400 MHz, DMSO-d_6) δ 10.57 (s, 1H), 7.66 (d, J = 1.7 Hz, 1H), 7.58 (d, J = 7.4 Hz, 1H), 7.27-7.16 (m, 2H), 7.05 (t, J = 7.5 Hz, 2H), 6.90-6.83 (m, 3H), 6.67-6.61 (m, 2H), 6.55 (d, J = 8.5 Hz, 1H), 4.72 (s, 1H), 1.80 (s, 3H). **^{13}C{^{1}H} NMR** (100 MHz, DMSO-d_6) δ 177.2, 156.6,

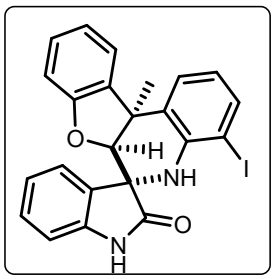
142.1, 142.1, 135.9, 129.4, 129.1, 128.8, 128.3, 127.1, 123.5, 121.3, 121.1, 117.0, 109.5, 109.2, 109.0, 88.79, 6.31, 5.43, 28.6. **ESI HRMS** *m/z* calc. for $C_{32}H_{18}BrN_2O_2[M+H]^+$: 433.0552, Found: 433.0538.



(6R,6aS,11bR)-11b-methyl-2-(trifluoromethyl)-6a,11b-dihydro-5H-spiro[benzofuro[2,3-c]quinoline-6,3'-indolin]-2'-one (8i). The compound **8i** was prepared by using Isatin **4a** (100 mg, 0.67 mmol, 1.0 equiv.), Aniline **5h** (86 µL, 0.67 mmol, 1.0 equiv.), 3-Methylbenzofuran **6a** (85 µL, 0.67 mmol, 1.0 equiv.) and $Sc(OTf)_3$ (17 mg, 0.03 mmol, 0.05 equiv.). The product **8i** was obtained by column chromatography (ethyl acetate: hexane, 21:29 v/v) as yellow solid (230 mg, 0.54 mmol, 80% yield); m.p.: 276-278 °C. **^{1}H NMR** (400 MHz, DMSO-d_6) δ 10.58 (s, 1H), 7.59 (d, J = 6.9 Hz, 1H), 7.53 (s, 1H), 7.28-7.16 (m, 2H), 7.05 (t, J = 7.0 Hz, 1H), 6.97-6.80 (m, 4H), 6.71 (s, 1H), 6.64 (d, J = 8.1 Hz, 2H), 4.75 (s, 1H), 1.82 (s, 3H). **^{13}C{^{1}H} NMR** (100 MHz, DMSO-d_6) δ 177.31, 156.63, 142.11, 142.01, 140.14, 135.96, 129.46, 128.86, 128.38, 128.11, 127.16, 123.50, 121.67, 121.33, 121.13, 120.04, 119.90, 119.15, 115.53, 109.57, 109.27, 88.67, 61.36, 45.53, 28.45. **^{19}F NMR** (377 MHz, DMSO-d_6) δ -57.23. **ESI HRMS** *m/z* calc. for $C_{24}H_{19}BrN_2O_2[M+H]^+$: 423.1325, Found: 423.1322.

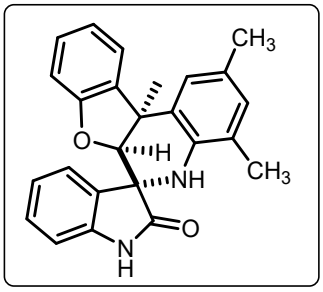


***(**6R,6aS,11bR)-11b-methyl-4-(trifluoromethoxy)-6a,11b-dihydro-5H-spiro[benzofuro[2,3-c]quinoline-6,3'-indolin]-2'-one (8j).* The compound **8j** was prepared by using Isatin **4a** (100 mg, 0.67 mmol, 1.0 equiv.), Aniline **5d** (93 µL, 0.67 mmol, 1.0 equiv.), 3-Methylbenzofuran **6a** (85 µL, 0.67 mmol, 1.0 equiv.) and $Sc(OTf)_3$ (17 mg, 0.03 mmol, 0.05 equiv.). The product **8j** was obtained by column chromatography (ethyl acetate: hexane, 2:3 v/v) as white solid (253 mg, 0.58 mmol, 85% yield); m.p.: 283-285 °C. **^{1}H NMR** (400 MHz, DMSO-d_6) δ 10.53 (s, 1H), 7.60 (dd, J = 21.8, 7.5 Hz, 2H), 7.16 (t, J = 7.6 Hz, 1H), 7.02 (dd, J = 17.7, 8.5 Hz, 2H), 6.92 (d, J = 7.3 Hz, 1H), 6.87-6.67 (m, 3H), 6.71 (t, J = 7.5 Hz, 1H), 6.62-6.51 (m, 2H), 4.73 (s, 1H), 1.78 (s, 3H). **^{13}C{^{1}H} NMR** (100 MHz, DMSO-d_6) δ 177.2, 156.7, 142.2, 136.0, 135.8, 135.3, 129.3, 129.2, 129.0, 128.4, 126.4, 126.2, 123.4, 121.7, 121.1, 120.9, 119.3, 119.2, 117.4, 109.4, 109.3, 88.7, 61.4, 45.3, 29.4. **ESI HRMS** *m/z* calc. for $C_{24}H_{18}F_3N_2O_3[M+H]^+$: 439.1270, Found: 439.1261. **^{19}F NMR** (377 MHz, DMSO-d_6) δ -56.40.

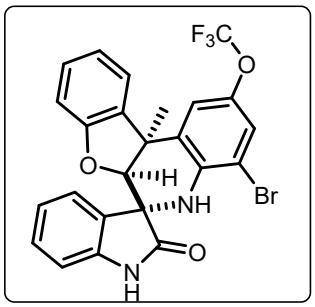


(6R,6aS,11bR)-4-iodo-11b-methyl-6a,11b-dihydro-5H-spiro[benzofuro[2,3-c]quinoline-6,3'-indolin]-2'-one 8k). The compound **8k** was prepared by using Isatin **4a** (50 mg, 0.33 mmol, 1.0 equiv.), Aniline **5e** (74 mg, 0.33 mmol, 1.0 equiv.), 3-Methylbenzofuran **6a** (42 µL, 0.33 mmol, 1.0 equiv.) and $Sc(OTf)_3$ (8.3 mg, 0.01 mmol, 0.05 equiv.). The product **8k** was obtained by column chromatography (ethyl acetate: hexane, 3:7 v/v) as off- white solid (142 mg, 0.30 mmol, 87% yield); m.p.: 256-258

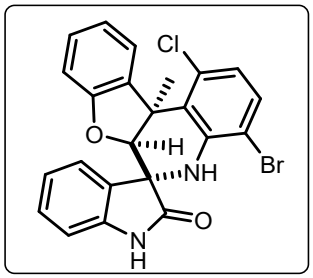
°C. **^{1}H NMR** (400 MHz, $CDCl_3$) *δ* 8.41 (s, 1H), 7.57 (t, *J* = 7.6 Hz, 2H), 7.36 (d, *J* = 7.2 Hz, 1H), 7.20 (t, *J* = 7.4 Hz, 1H), 7.08 (d, *J* = 7.4 Hz, 1H), 7.01 (t, *J* = 7.2 Hz, 1H), 6.88-6.78 (m, 3H), 6.67 (t, *J* = 7.8 Hz, 1H), 6.57 (d, *J* = 7.9 Hz, 1H), 4.88 (s, 1H), 4.61 (s, 1H), 1.88 (s, 3H). **^{13}C{^{1}H} NMR** (100 MHz, DMSO-d_6) *δ* 177.0, 156.5, 142.1, 141.7, 137.1, 136.1, 129.4, 128.8, 128.7, 128.3, 127.6, 126.6, 123.5, 121.2, 121.1, 120.7, 109.6, 109.3, 89.2, 85.4, 62.2, 46.0, 28.8. **ESI HRMS** *m/z* calc. for $C_{23}H_{18}IN_2O_2[M+H]^+$: 481.0413, Found: 481.0401.



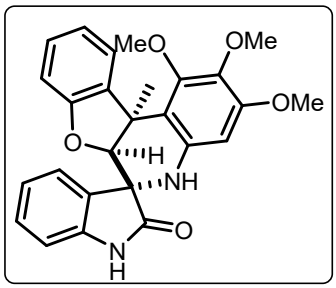
(6R,6aS,11bR)-2,4,11b-trimethyl-6a,11b-dihydro-5H-spiro[benzofuro[2,3-c]quinoline-6,3'-indolin]-2'-one (8l). The compound **8l** was prepared by using Isatin **4a** (100 mg, 0.67 mmol, 1.0 equiv.), Aniline **5i** (84 µL, 0.67 mmol, 1.0 equiv.), 3-Methylbenzofuran **6a** (85 µL, 0.67 mmol, 1.0 equiv.) and $Sc(OTf)_3$ (17 mg, 0.03 mmol, 0.05 equiv.). The product **8l** was obtained by column chromatography (ethyl acetate: hexane, 3:17 v/v) as off-white solid (231 mg, 0.60 mmol, 89% yield); m.p.: 180-182 °C. **^{1}H NMR** (400 MHz, DMSO-d_6) *δ* 10.50 (s, 1H), 7.54 (s, 1H), 7.29 (s, 1H), 7.01 (d, *J* = 55.8 Hz, 2H), 6.88-6.63 (m, 4H), 6.52 (d, *J* = 43.7 Hz, 2H), 5.43 (s, 1H), 4.69 (s, 1H), 2.22 (s, 3H), 1.97 (s, 3H), 1.70 (s, 3H). **^{13}C{^{1}H} NMR** (100 MHz, DMSO-d_6) δ 177.4, 156.9, 142.0, 138.1, 136.4, 129.8, 129.0, 128.6, 127.9, 126.2, 126.1, 125.9, 125.2, 123.2, 122.6, 120.8, 120.5, 109.1, 109.0, 89.4, 62.2, 45.1, 30.4, 20.4, 17.8. **ESI HRMS** *m/z* calc. for $C_{25}H_{23}N_2O_2[M+H]^+$: 383.1760, Found: 383.1749.



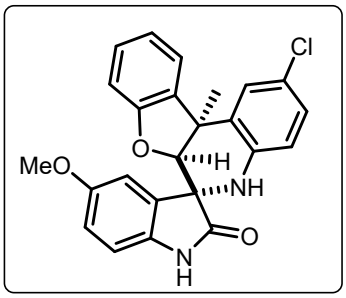
(6R,6aS,11bR)-4-bromo-11b-methyl-2-(trifluoromethoxy)-6a,11b-dihydro-5H-spiro[benzofuro[2,3-c]quinoline-6,3'-indolin]-2'-one (8m). The compound **8m** was prepared by using Isatin **4a** (40 mg, 0.27 mmol, 1.0 equiv.), Aniline **5k** (41 µL, 0.27 mmol, 1.0 equiv.), 3-Methylbenzofuran **6a** (34 µL, 0.27 mmol, 1.0 equiv.) and $Sc(OTf)_3$ (7 mg, 0.01 mmol, 0.05 equiv.). The product **8m** was obtained by column chromatography (ethyl acetate: hexane, 9:11 v/v) as white solid (118 mg, 0.23 mmol, 84% yield); m.p.: 310-312 °C. **^{1}H NMR** (400 MHz, DMSO-d_6) *δ* 10.57 (s, 1H), 7.65 (s, 2H), 7.31 (d, *J* = 47.3 Hz, 3H), 7.13-6.59 (m, 5H), 6.01 (s, 1H), 4.74 (s, 1H), 1.86 (s, 3H). **^{13}C{^{1}H} NMR** (100 MHz, DMSO-d_6) *δ* 177.1, 156.3, 142.2, 139.6, 135.7, 129.8, 129.4, 128.8, 128.6, 126.9, 123.6, 121.3, 120.2, 119.0, 109.6, 109.4, 107.9, 88.4, 61.6, 45.9, 27.8. **^{19}F NMR** (377 MHz, DMSO-d_6) *δ* -57.23. **ESI HRMS** m/z calcd. for $C_{24}H_{17}BrF_3N_2O_3[M+H]^+$: 517.0374, Found: 517.0367.



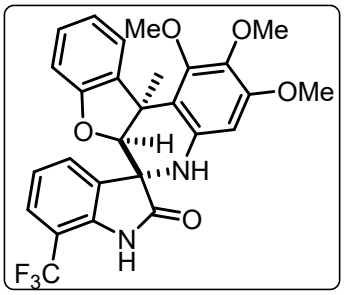
(6R,6aS,11bS)-4-bromo-1-chloro-11b-methyl-6a,11b-dihydro-5H-spiro[benzofuro[2,3-c]quinoline-6,3'-indolin]-2'-one (8n). The compound **8n** was prepared by using Isatin **4a** (35 mg, 0.24 mmol, 1.0 equiv.), Aniline **5j** (49 mg, 0.24 mmol, 1.0 equiv.), 3-Methylbenzofuran **6a** (30 µL, 0.24 mmol, 1.0 equiv.) and $Sc(OTf)_3$ (6.0 mg, 0.01 mmol, 0.05 equiv.). The product **8n** was obtained by column chromatography (ethyl acetate: hexane, 2:3 v/v) as white solid (93 mg, 0.20 mmol, 84% yield); m.p.: 300-302 °C. **^{1}H NMR** (400 MHz, DMSO-d_6) δ 10.57 (s, 1H), 7.90 (d, J = 7.7 Hz, 1H), 7.35 (d, J = 8.5 Hz, 1H), 7.20-2-15 (m, 1H), 7.10 (d, J = 7.4 Hz, 1H), 7.08-6.99 (m, 1H), 6.87- 6.75 (m, 3H), 6.72 (d, J = 8.5 Hz, 1H), 6.60 (d, J = 7.8 Hz, 1H), 6.17 (s, 1H), 4.66 (s, 1H), 2.03 (s, 3H). **^{13}C{^{1}H} NMR** (100 MHz, DMSO-d_6) δ 176.84, 157.39, 142.69, 142.10, 133.96, 132.66, 132.00, 129.22, 128.95, 128.83, 126.42, 126.12, 123.74, 121.53, 121.05, 120.53, 109.66, 109.55, 108.23, 90.94, 61.32, 47.04, 25.19. **ESI HRMS** *m/z* calc. for $C_{23}H_{17}BrClN_2O_2[M+H]^+$: 467.0162, Found: 467.0160.



(6R,6aS,11bS)-1,2,3-trimethoxy-11b-methyl-6a,11b-dihydro-5H-spiro[benzofuro[2,3-c]quinoline-6,3'-indolin]-2'-one (8o). The compound **8o** was prepared by using Isatin **4a** (50 mg, 0.33 mmol, 1.0 equiv.), Aniline **5l** (60 mg, 0.33 mmol, 1.0 equiv.), 3-Methylbenzofuran **6a** (42 µL, 0.67 mmol, 1.0 equiv.) and $Sc(OTf)_3$ (8.0 mg, 0.02 mmol, 0.05 equiv.). The product **8o** was obtained by column chromatography (ethyl acetate: hexane, 3:7 v/v) as off-white solid (136 mg, 0.31 mmol, 90% yield); m.p.: 280-282 °C. **^{1}H NMR** (400 MHz, DMSO-d_6) δ 10.54 (s, 1H), 7.67 (d, J = 7.4 Hz, 1H), 7.08 (t, J = 7.6 Hz, 1H), 6.91 (t, J = 7.5 Hz, 1H), 6.77 (d, J = 7.4 Hz, 3H), 6.58 (t, J = 7.5 Hz, 1H), 6.42 (d, J = 7.8 Hz, 1H), 6.28 (s, 1H), 6.06 (s, 1H), 4.62 (s, 1H), 3.95 (s, 3H), 3.66 (d, J = 12.4 Hz, 6H), 1.77 (s, 3H). **^{13}C{^{1}H} NMR** (100 MHz, DMSO-d_6) δ 177.1, 157.3, 152.5, 152.4, 141.9, 139.6, 136.1, 134.1, 129.2, 128.9, 127.9, 126.1, 125.3, 120.7, 120.7, 110.1, 109.3, 108.9, 94.7, 90.4, 61.8, 60.6, 60.4, 55.3, 45.6, 28.0. **ESI HRMS** *m/z* calc. for $C_{26}H_{25}N_2O_5[M+H]^+$: 445.1763, Found: 445.1753.



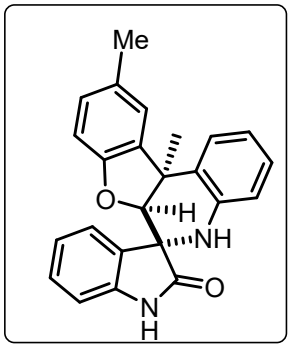
(6R,6aS,11bR)-2-chloro-5'-methoxy-11b-methyl-6a,11b-dihydro-5H-spiro[benzofuro[2,3-c]quinoline-6,3'-indolin]-2'-one (8p). The compound **8p** was prepared by using Isatin **4d** (100 mg, 0.56 mmol, 1.0 equiv.), Aniline **5f** (72 mg, 0.56 mmol, 1.0 equiv.), 3-Methylbenzofuran **6a** (70 µL, 0.56 mmol, 1.0 equiv.) and $Sc(OTf)_3$ (14 mg, 0.03 mmol, 0.05 equiv.). The product **8p** was obtained by column chromatography as diastereomeric mixture (*d.r = 93:7*) (ethyl acetate: hexane, 33:67 v/v) as white solid (180 mg, 0.46 mmol, 76% yield); m.p.: 227-229 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.72 (s, 1H), 7.54 (d, J = 1.7 Hz, 1H), 7.39 (d, J = 7.4 Hz, 1H), 7.26 (s, 1H), 7.07-6.96 (m, 2H), 6.89 (t, J = 7.4 Hz, 1H), 6.69 (dd, J = 8.5, 2.4 Hz, 1H), 6.64-6.52 (m, 3H), 6.47 (d, J = 8.5 Hz, 1H), 4.85 (s, 1H), 4.16 (s, 1H), 3.51 (s, 3H), 1.82 (s, 3H). **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 177.8, 157.5, 155.6, 139.8, 135.0, 133.9, 129.4, 129.3, 128.7, 127.6, 127.0, 124.9, 122.8, 121.5, 117.2, 115.4, 113.5, 110.5, 110.0, 89.5, 63.5, 55.9, 46.2, 30.5. **ESI HRMS** m/z calc. for $C_{24}H_{20}ClN_2O_3[M+H]^+$: 419.1162, Found: 419.1143.



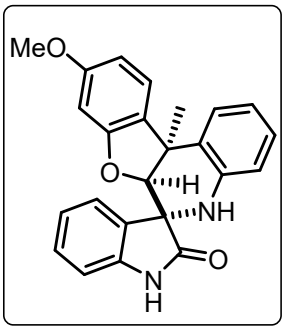
(6R,6aS,11bS)-1,2,3-trimethoxy-11b-methyl-7'-(trifluoromethyl)-6a,11b-dihydro-5H-spiro[benzofuro[2,3-c]quinoline-6,3'-indolin]-2'-one (8q).). The compound **8q** was prepared by using Isatin **4e** (100 mg, 0.46 mmol, 1.0 equiv.), Aniline **5l** (85 mg, 0.46 mmol, 1.0 equiv.), 3-Methylbenzofuran **6a** (57 µL, 0.46 mmol, 1.0 equiv.) and $Sc(OTf)_3$ (12 mg, 0.02 mmol, 0.05 equiv.). The product **8q** was obtained by column chromatography as diastereomeric mixture (*d.r = 82:18*) (ethyl acetate: hexane, 1:4 v/v) as white solid (185 mg, 0.15 mmol, 78% yield); m.p.: 274-276 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) 8.11 (s, 1H), 7.76 (d, *J* = 7.0 Hz, 1H), 7.62-7.43 (m, 1H), 7.34-7.15 (m, 1H), 7.00 -6.84 (m, 2H), 6.78 (t, *J* = 7.2 Hz, 1H), 6.72-6.59 (m, 1H), 6.36 (d, *J* = 7.4 Hz, 1H), 5.90 (s, 1H), 4.83 (s, 1H), 4.08 (s, 3H), 3.85 (s, 3H), 3.74 (s, 3H), 1.88 (s, 3H). **^{13}C{^{1}H} NMR** (100 MHz, CDCl3) *δ* 176.9, 157.8, 153.5, 153.2, 137.8, 137.8, 137.5, 136.4, 135.6, 130.3, 130.0, 128.3, 126.0, 125.9, 125.5, 121.9, 121.4, 111.5, 109.4, 95.4, 90.5, 62.3, 61.0, 60.9, 55.8, 46.7, 28.7. **^{19}F NMR** (377 MHz, CDCl3) *δ* -60.53. **ESI HRMS** *m/z* calc. for $C_{27}H_{24}F_3N_2O_5$ $[M+H]^+$: 513.1637, Found: 513.1628.

Section V. General procedure for the synthesis of compounds 9b-9m:

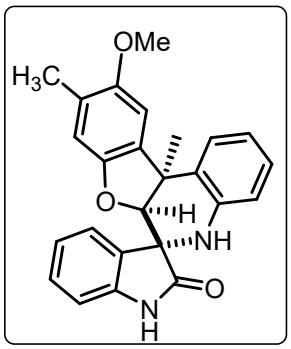
A similar procedure as described above for the synthesis of compounds **8a**-**8q**, was also followed for the synthesis of compounds **9b**-**9m**.



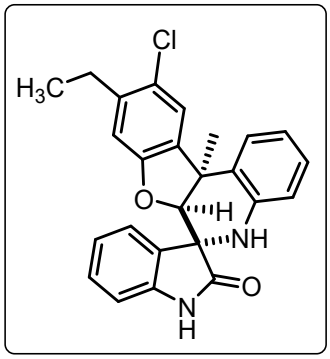
(6R,6aS,11bR)-10,11b-dimethyl-6a,11b-dihydro-5H-spiro[benzofuro[2,3-c]quinoline-6,3'-indolin]-2'-one (9b). The compound **9b** was prepared by using Isatin **4a** (100 mg, 0.67 mmol, 1.0 equiv.), Aniline **5a** (61 µL, 0.67 mmol, 1.0 equiv.), commercially available 3,5-dimethylbenzofuran **6b** (95.0 µL, 0.67 mmol, 1.0 equiv.) and $Sc(OTf)_3$ (17 mg, 0.03 mmol, 0.05 equiv.). The product **9b** was obtained by column chromatography (ethyl acetate: hexane, 1:5 v/v) as yellow solid (235 mg, 0.64 mmol, 94% yield); m.p.: 158-160 °C. **^{1}H NMR** (400 MHz, DMSO-d_6) *δ* 10.52 (s, 1H), 7.57 (d, *J* = 7.7 Hz, 1H), 7.35 (s, 1H), 7.16 (t, *J* = 7.7 Hz, 1H), 6.96-6.88 (m, 2H), 6.79 (t, *J* = 8.6 Hz, 2H), 6.71 (t, *J* = 7.5 Hz, 2H), 6.58 (d, *J* = 7.9 Hz, 1H), 6.47-6.31 (m, 2H), 4.69 (s, 1H), 2.22 (s, 3H), 1.74 (s, 3H). **^{13}C{^{1}H} NMR** (100 MHz, DMSO-d_6) *δ* 177.3, 154.8, 142.6, 142.0, 136.2, 129.5, 129.3, 129.0, 128.3, 126.9, 126.8, 126.7, 126.5, 123.7, 120.9, 118.2, 115.1, 109.3, 108.6, 89.3, 61.8, 45.3, 29.7, 20.6. **ESI HRMS** *m/z* calc. for $C_{24}H_{20}N_2O_2Na$ $[M+Na]^+$: 391.1422, Found: 391.1407



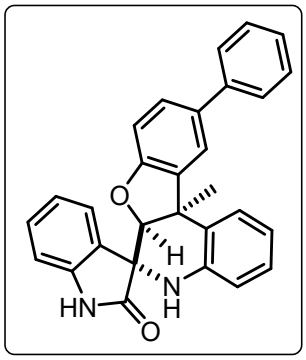
(6R,6aS,11bR)-9-methoxy-11b-methyl-6a,11b-dihydro-5H-spiro[benzofuro[2,3-c]quinoline-6,3'-indolin]-2'-one (9c). The compound **9c** was prepared by using Isatin **4a** (150 mg, 1.02 mmol, 1.0 equiv.), Aniline **5a** (93 µL, 1.02 mmol, 1.0 equiv.), commercially available 6-methoxy-3-methylbenzofuran **6c** (165 mg, 1.02 mmol, 1.0 equiv.) and $Sc(OTf)_3$ (25 mg, 0.05 mmol, 0.05 equiv.). The product **9c** was obtained by column chromatography (ethyl acetate: hexane, 1:5 v/v) as yellow solid (340 mg, 0.87 mmol, 87% yield); m.p.: 156-158 °C. **^{1}H NMR** (400 MHz, DMSO-d_6) δ 10.12 (s, 1H), 7.63 (d, J = 7.4 Hz, 1H), 7.41 (d, J = 7.3 Hz, 1H), 7.34 (d, J = 8.3 Hz, 1H), 7.31 -7.23 (m, 1H), 7.02 (t, J = 7.3 Hz, 1H), 6.96 (t, J = 7.1 Hz, 1H), 6.84 -6.73 (m, 2H), 6.66 (d, J = 7.9 Hz, 1H), 6.38 (dd, J = 8.3, 2.2 Hz, 1H), 6.33 (s, 1H), 6.28 (d, J = 2.2 Hz, 1H), 4.88 (s, 1H), 3.65 (s, 3H), 1.57 (s, 3H). **^{13}C{^{1}H} NMR** (100 MHz, DMSO-d_6) δ 176.3, 159.5, 158.3, 143.1, 142.5, 130.7, 129.34, 128.4, 128.0, 126.6, 126.5, 124.4, 122.9, 121.5, 118.2, 115.2, 109.3, 106.1, 95.8, 91.7, 62.0, 55.2, 44.9, 33.7. **ESI HRMS** *m/z* calc. for $C_{24}H_{20}N_2O_3Na$ $[M+Na]^+$: 407.1372, Found: 407.1349.



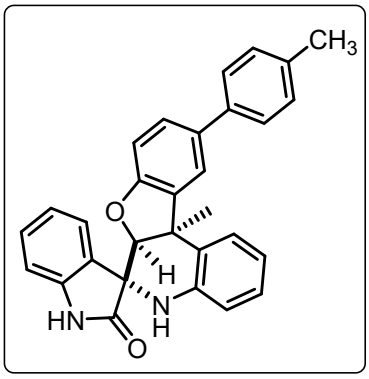
(6R,6aS,11bR)-10-methoxy-9,11b-dimethyl-6a,11b-dihydro-5H-spiro[benzofuro[2,3-c]quinoline-6,3'-indolin]-2'-one (9d). The compound **9d** was prepared by using Isatin **4a** (100 mg, 0.67 mmol, 1.0 equiv.), Aniline **5a** (61 µL, 0.67 mmol, 1.0 equiv.), 5-methoxy-3,6-dimethylbenzofuran **6d** (120 mg, 0.67 mmol, 1.0 equiv.) and $Sc(OTf)_3$ (17 mg, 0.03 mmol, 0.05 equiv.). The product **9d** was obtained by column chromatography as diastereomeric mixture (*d.r = 78:22*) (ethyl acetate: hexane, 3:7 v/v) as white solid (228 mg, 0.57 mmol, 84% yield); m.p.: 159-161 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.32 (s, 1H), 7.59 (d, J = 7.6 Hz, 1H), 7.13-7.02 (m, 2H), 6.88 (s, 1H), 6.70-6.62 (m, 3H), 6.58 (d, J = 7.7 Hz, 1H), 6.29 (s, 1H), 4.88 (s, 1H), 4.11 (s, 1H), 3.80 (s, 3H), 3.42 (s, 1H), 2.04 (s, 3H), 1.82 (s, 3H). **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 178.1, 152.8, 151.3, 141.3, 140.6, 132.9, 129.4, 128.8, 127.8, 127.5, 127.0, 127.0, 126.8, 122.2, 120.3, 116.3, 111.7, 110.1, 106.0, 90.2, 63.3, 56.7, 46.7, 30.8, 16.5. **ESI HRMS** *m/z* calc. for $C_{25}H_{23}N_2O_3[M+H]^+$: 399.1709, Found: 399.1707.



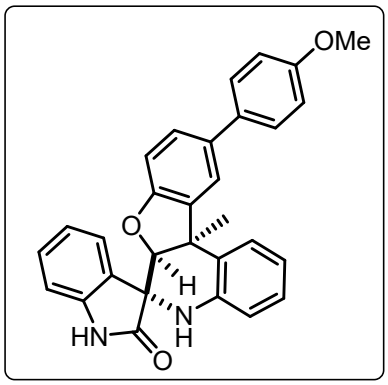
(6R,6aS,11bR)-10-chloro-9-ethyl-11b-methyl-6a,11b-dihydro-5H-spiro[benzofuro[2,3-c]quinoline-6,3'-indolin]-2'-one (9e). The compound **9e** was prepared by using Isatin **4a** (30 mg, 0.20 mmol, 1.0 equiv.), Aniline **5a** (18 µL, 0.20 mmol, 1.0 equiv.), 5-chloro-6-ethyl-3-methylbenzofuran **6e** (40 mg, 0.20 mmol, 1.0 equiv.) and $Sc(OTf)_3$ (5 mg, 0.01 mmol, 0.05 equiv.). The product **9e** was obtained by column chromatography as diastereomeric mixture (*d.r = 83:17*) (ethyl acetate: hexane, 1:3 v/v) as off-white solid (72 mg, 0.17 mmol, 85% yield); m.p.: 164-166 °C. **^{1}H NMR** (400 MHz, DMSO-d_6) δ 10.55 (s, 1H), 7.62-7.55 (m, 2H), 7.21-7.15(m, 1H), 7.01 (d, *J* = 7.3 Hz, 1H), 6.96-6.88 (m, 1H), 6.83 (d, *J* = 7.7 Hz, 1H), 6.78 (dd, *J* = 7.6, 0.8 Hz, 1H), 6.75-6.69 (m, 1H), 6.61-6.54 (m, 2H), 6.44 (s, 1H), 4.76 (s, 1H), 2.55-2.50 (m, 2H), 1.77 (s, 3H), 1.03 (t, *J* = 7.5 Hz, 3H). **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 178.3, 156.7, 141.8, 141.2, 140.6, 134.8, 129.5, 128.5, 127.8, 127.2, 127.1, 126.7, 125.3, 123.5, 122.3, 120.7, 116.3, 110.5, 110.1, 90.6, 63.5, 46.3, 30.9, 27.0, 14.2. **ESI HRMS** *m/z* calc. for $C_{25}H_{22}ClN_2O_2[M+H]^+$: 417.1370, Found: 417.1358.



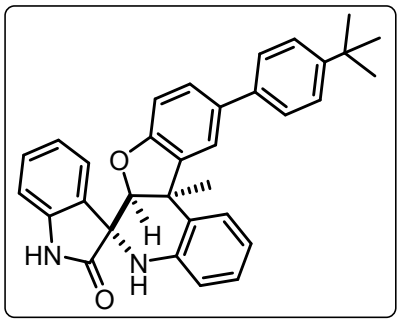
(6R,6aS,11bR)-11b-methyl-10-phenyl-6a,11b-dihydro-5H-spiro[benzofuro[2,3-c]quinoline-6,3'-indolin]-2'-one (9f). The compound **9f** was prepared by using Isatin **4a** (30 mg, 0.20 mmol, 1.0 equiv.), Aniline **5a** (18 µL, 0.20 mmol, 1.0 equiv.), 3-methyl-5-phenylbenzofuran **6f** (42 mg, 0.20 mmol, 1.0 equiv.) and $Sc(OTf)_3$ (5 mg, 0.01 mmol, 0.05 equiv.). The product **9f** was obtained by column chromatography as diastereomeric mixture (*d.r = 89:11*) (ethyl acetate: hexane, 1:4 v/v) as off-white solid (68 mg, 0.16 mmol, 78% yield); m.p.: 126-128 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.23 (s, 1H), 7.68 (d, *J* = 7.5 Hz, 1H), 7.60 (d, *J* = 1.6 Hz, 1H), 7.51 (d, *J* = 7.3 Hz, 2H), 7.41 (t, *J* = 7.6 Hz, 3H), 7.19 (dd, *J* = 8.2, 1.7 Hz, 1H), 7.15-7.02 (m, 2H), 6.98 (t, *J* = 7.5 Hz, 1H), 6.86 (d, *J* = 7.5 Hz, 1H), 6.79 (d, *J* = 7.7 Hz, 1H), 6.66- 6.57 (m, 2H), 6.54 (d, *J* = 8.2 Hz, 1H), 5.01 (s, 1H), 4.08 (s, 1H), 1.89 (s, 3H). **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 178.1, 157.4, 141.5, 141.2, 140.6, 136.2, 135.8, 135.0, 129.6, 128.8, 128.5, 127.7, 127.6, 127.5, 127.3, 127.0, 126.8, 122.3, 121.7, 120.6, 116.3, 110.0, 109.9, 90.5, 63.4, 46.2, 31.1. **ESI HRMS** *m/z* calc. for $C_{29}H_{23}N_2O_2$ $[M+H]^+$: 431.1755, Found: 431.1760.



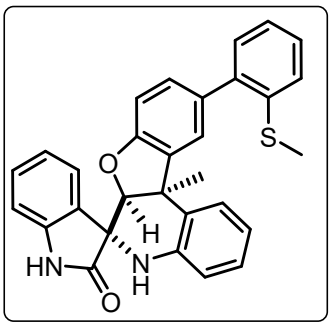
(*6R,6aS,11bR)-11b-methyl-10-(p-tolyl)-6a,11b-dihydro-5H-spiro[benzofuro[2,3-c]quinoline-6,3'-indolin]-2'-one (**9g**).* The compound **9g** was prepared by using Isatin **4a** (30 mg, 0.20 mmol, 1.0 equiv.), Aniline **5a** (18 µL, 0.20 mmol, 1.0 equiv.), 3-methyl-5-(p-tolyl)benzofuran **6g** (45 mg, 0.20 mmol, 1.0 equiv.) and $Sc(OTf)_3$ (5 mg, 0.01 mmol, 0.05 equiv.). The product **9g** was obtained by column chromatography as diastereomeric mixture (*d.r = 94:6*) (ethyl acetate: hexane, 3:7 v/v) as yellow solid (73 mg, 0.16 mmol, 81% yield); m.p.: 172-174 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) *δ* 8.46 (s, 1H), 7.68 (dd, *J* = 7.7, 1.1 Hz, 1H), 7.40 (d, *J* = 8.1 Hz, 2H), 7.22 (d, *J* = 7.9 Hz, 2H), 7.16 (dd, *J* = 8.3, 1.9 Hz, 1H), 7.12-7.05 (m, 2H), 6.99-6.94 (m, 1H), 6.83 (dd, *J* = 16.6, 7.5 Hz, 3H), 6.65-6.56 (m, 2H), 6.52 (d, *J* = 8.3 Hz, 1H), 5.00 (s, 1H), 4.09 (s, 1H), 2.39 (s, 3H), 1.88 (s, 3H). **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) *δ* 178.30, 157.2, 141.2, 140.5, 138.7, 136.5, 136.1, 134.9, 129.6, 129.5, 128.5, 127.7, 127.5, 127.3, 127.3, 126.9, 126.8, 122.3, 121.6, 120.6, 116.3, 110.0, 109.8, 90.4, 63.5, 46.2, 31.1, 21.2. **ESI HRMS** *m/z* calc. for $C_{30}H_{25}N_2O_2[M+H]^+$: 445.1916, Found: 445.1911.



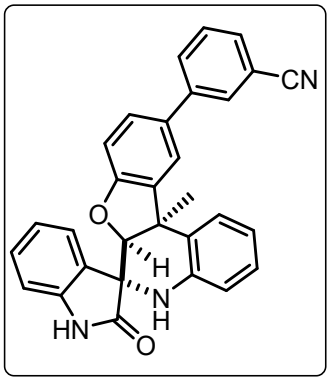
(6R,6aS,11bR)-10-(4-methoxyphenyl)-11b-methyl-6a,11b-dihydro-5H-spiro[benzofuro[2,3-c]quinoline-6,3'-indolin]-2'-one (9h). The compound **9h** was prepared by using Isatin **4a** (45 mg, 0.31 mmol, 1.0 equiv.), Aniline **5a** (28 µL, 0.31 mmol, 1.0 equiv.), 5-(4-methoxyphenyl)-3-methylbenzofuran **6h** (73 mg, 0.31 mmol, 1.0 equiv.) and $Sc(OTf)_3$ (10 mg, 0.02 mmol, 0.05 equiv.). The product **9h** was obtained by column chromatography as diastereomeric mixture (*d.r = 93:7*) (ethyl acetate: hexane, 1:5 v/v) as off-white solid (116 mg, 0.25 mmol, 82% yield); m.p.: 270-272 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) *δ* 8.44 (s, 1H), 7.68 (d, *J* = 7.6 Hz, 1H), 7.55 (s, 1H), 7.43 (d, *J* = 8.6 Hz, 2H), 7.12-7.04 (m, 3H), 6.97 (t, *J* = 8.4 Hz, 3H), 6.85 (d, *J* = 7.3 Hz, 1H), 6.75 (d, *J* = 7.7 Hz, 1H), 6.63 (t, *J* = 7.7 Hz, 1H), 6.57 (d, *J* = 7.8 Hz, 1H), 6.51 (d, *J* = 8.2 Hz, 1H), 4.98 (s, 1H), 4.06 (s, 1H), 3.85 (s, 3H), 1.88 (s, 3H**)**. **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) *δ* 207.6, 178.4, 159.2, 157.3, 141.6, 141.0, 136.5, 134.9, 134.6, 129.9, 128.9, 128.4, 128.0, 127.8, 127.6, 127.5, 127.1, 122.6, 121.7, 120.9, 116.6, 114.6, 110.3, 110.1, 90.7, 63.7, 55.9, 46.6, 31.4. **ESI HRMS** *m/z* calc. for $C_{30}H_{25}N_2O_3$ $[M+H]^+$: 461.1865, Found: 461.1855.



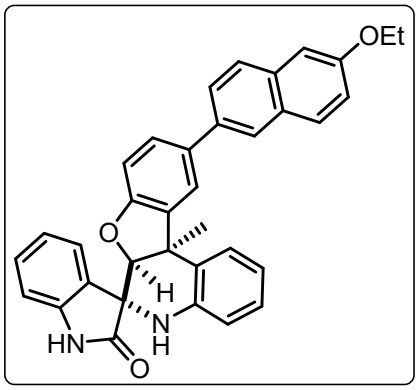
(6R,6aS,11bR)-10-(4-(tert-butyl)phenyl)-11b-methyl-6a,11b-dihydro-5H-spiro[benzofuro[2,3-c]quinoline-6,3'-indolin]-2'-one (9i). The compound **9i** was prepared by using Isatin **4a** (100 mg, 0.67 mmol, 1.0 equiv.), Aniline **5a** (61 µL, 0.67 mmol, 1.0 equiv.), 5-(4-(tert-butyl)phenyl)-3-methylbenzofuran **6i** (180 mg, 0.67 mmol, 1.0 equiv.) and $Sc(OTf)_3$ (17 mg, 0.03 mmol, 0.05 equiv.). The product **9i** was obtained by column chromatography (ethyl acetate: hexane, 3:17 v/v) as yellow solid (281 mg, 0.58 mmol, 85% yield); m.p.: 272-274 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) *δ* 7.95 (s, 1H), 7.67 (d, *J* = 7.4 Hz, 1H), 7.59 (s, 1H), 7.45 (s, 4H), 7.17 (d, *J* = 7.8 Hz, 1H), 7.15-7.04 (m, 2H), 6.96 (t, *J* = 7.4 Hz, 1H), 6.86 -6.78 (m, 2H), 6.61 (t, *J* = 7.9 Hz, 2H), 6.51 (d, *J* = 8.3 Hz, 1H), 5.01 (s, 1H), 4.07 (s, 1H), 1.88 (s, 3H), 1.36 (s, 9H). **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) *δ* 177.7, 157.3, 149.8, 141.2, 140.4, 138.7, 136.1, 134.8, 129.5, 128.6, 127.7, 127.5, 127.4, 127.6, 126.9, 126.7, 125.8, 122.3, 121.7, 120.7, 116.3, 109.8, 109.8, 90.4, 63.4, 46.3, 34.6, 31.5, 31.1. **ESI HRMS** *m/z* calc. for $C_{33}H_{31}N_2O_2$ M+H]$^+$: 487.2386, Found: 487.2377.



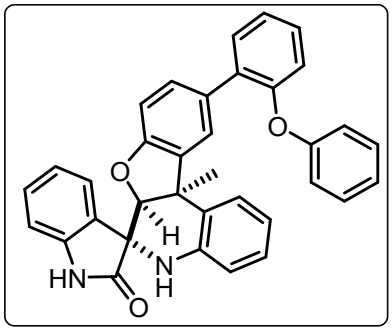
(6R,6aS,11bR)-11b-methyl-10-(2-(methylthio)phenyl)-6a,11b-dihydro-5H-spiro[benzofuro[2,3-c]quinoline-6,3'-indolin]-2'-one (9j). The compound **9j** was prepared by using Isatin **4a** (60 mg, 0.40 mmol, 1.0 equiv.), Aniline **5a** (37 µL, 0.40 mmol, 1.0 equiv.), 3-methyl-5-(2-(methylthio)phenyl)benzofuran **6j** (104 mg, 0.40 mmol, 1.0 equiv.) and $Sc(OTf)_3$ (10 mg, 0.02 mmol, 0.05 equiv.). The product **9j** was obtained by column chromatography as diastereomeric mixture (*d.r = 93:7*) (ethyl acetate: hexane, 1:4 v/v) as white solid (155 mg, 0.32 mmol, 80% yield); m.p.: 157-159 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) *δ* 8.28 (s, 1H), 7.67 (d, *J* = 7.4 Hz, 1H), 7.57 (d, *J* = 1.7 Hz, 1H), 7.43 (d, *J* = 8.4 Hz, 2H), 7.31 (d, *J* = 8.4 Hz, 2H), 7.16 (dd, *J* = 8.3, 1.9 Hz, 1H), 7.12-7.07 (m, 2H), 6.98 (t, *J* = 7.5 Hz, 1H), 6.86 (d, *J* = 7.5 Hz, 1H), 6.78 (d, *J* = 7.8 Hz, 1H), 6.63 (t, *J* = 7.6 Hz, 1H), 6.59 (d, *J* = 7.8 Hz, 1H), 6.53 (d, *J* = 8.3 Hz, 1H), 5.00 (s, 1H), 4.07 (s, 1H), 2.52 (s, 3H), 1.88 (s, 3H). **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) *δ* 178.1, 157.3, 141.2, 140.5, 137.5, 135.3, 133.7, 130.3, 129.4, 129.4, 128.6, 127.8, 127.7, 127.6, 127.4, 126.8, 125.1, 125.0, 124.7, 124.0, 122.5, 120.6, 116.3, 109.9, 109.3, 90.3, 63.6, 46.2, 31.4, 16.0. **ESI HRMS** *m/z* calc. for $C_{30}H_{25}N_2O_2S$ [M+H]$^+$: 477.1637, Found: 477.1626.



3-((6R,6aS,11bR)-11b-methyl-2'-oxo-6a,11b-dihydro-5H-spiro[benzofuro[2,3-c]quinoline-6,3'-indolin]-10-yl)benzonitrile (9k). The compound **9k** was prepared by using Isatin **4a** (50 mg, 0.33 mmol, 1.0 equiv.), Aniline **5a** (31 µL, 0.33 mmol, 1.0 equiv.), 3-(3-methylbenzofuran-5-yl)benzonitrile **6k** (79 mg, 0.33 mmol, 1.0 equiv.) and $Sc(OTf)_3$ (8 mg, 0.01 mmol, 0.05 equiv.). The product **9k** was obtained by column chromatography (ethyl acetate: hexane, 3:7 v/v) as yellow solid (118 mg, 0.26 mmol, 76% yield); m.p.: 273-275 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) *δ* 7.90 (s, 1H), 7.78 (d, *J* = 1.3 Hz, 1H), 7.75 -7.65 (m, 2H), 7.62-7.45 (m, 3H), 7.20-7.06 (m, 3H), 7.03-6.97(m, 1H), 6.91 (d, *J* = 7.1 Hz, 1H), 6.83 (d, *J* = 7.7 Hz, 1H), 6.70-6..64 (m, 1H), 6.63-6.57 (m, 2H), 5.02 (s, 1H), 4.09 (s, 1H), 1.90 (s, 3H). **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) *δ* 177.4, 158.3, 142.6, 141.2, 140.5, 136.9, 132.5, 131.3, 130.5, 130.2, 129.7, 129.7, 128.4, 127.8, 127.7, 127.2, 127.1, 126.9, 122.4, 121.7, 120.8, 119.2, 116.3, 113.0, 110.3, 109.9, 90.7, 63.2, 46.2, 31.0. **ESI HRMS** *m/z* calc. for $C_{30}H_{22}N_3O_2$ $[M+H]^+$: 456.1712, Found: 456.1704.



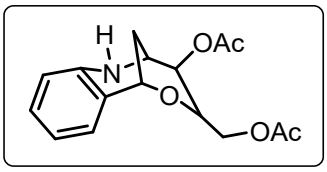
(6R,6aS,11bR)-10-(6-ethoxynaphthalen-2-yl)-11b-methyl-6a,11b-dihydro-5H-spiro[benzofuro[2,3-c]quinoline-6,3'-indolin]-2'-one (9l). The compound **9l** was prepared by using Isatin **4a** (50 mg, 0.33 mmol, 1.0 equiv.), Aniline **5a** (31 µL, 0.33 mmol, 1.0 equiv.), 5-(6-ethoxynaphthalen-2-yl)-3-methylbenzofuran **6l** (103 mg, 0.33 mmol, 1.0 equiv.) and $Sc(OTf)_3$ (8 mg, 0.02 mmol, 0.05 equiv.). The product **9l** was obtained by column chromatography (ethyl acetate: hexane, 3:7 v/v) as yellow solid (157 mg, 0.30 mmol, 88% yield); m.p.: 185-187 °C. **^{1}H NMR** (400 MHz, DMSO- d_6) *δ* 10.56 (s, 1H), 8.07 (s, 1H), 7.97 (s, 1H), 7.92-7.82 (m, 2H), 7.75 (d, *J* = 8.8 Hz, 2H), 7.43 (d, *J* = 8.3 Hz, 1H), 7.31 (s, 1H), 7.23-7.14 (m, 2H), 7.08 (d, *J* = 7.5 Hz, 1H), 6.93 (t, *J* = 7.2 Hz, 1H), 6.84 (d, *J* = 7.5 Hz, 1H), 6.80-6.66 (m, 3H), 6.60 (d, *J* = 7.8 Hz, 1H), 6.45 (s, 1H), 4.81 (s, 1H), 4.20-4.12 (m, 2H), 1.87 (s, 3H), 1.40 (t, *J* = 6.7 Hz, 3H). **^{13}C{^{1}H} NMR** (100 MHz, DMSO-d_6) *δ* 177.3, 156.5, 156.4, 142.6, 142.1`, 137.4, 135.3, 133.4, 133.2, 129.6, 129.6, 129.2, 128.8, 127.2, 127.1, 126.7, 126.7, 125.6, 124.3, 121.8, 121.0, 119.1, 118.3, 115.1, 109.5, 109.4, 106.3, 89.7, 74.9, 63.1, 61.7, 45.5, 29.4, 14.7. **ESI HRMS** *m/z* calc. for $C_{35}H_{29}N_2O_3$ $[M+H]^+$: 525.2178, Found: 525.2174.



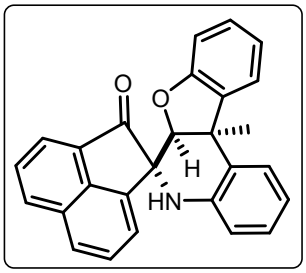
(6R,6aS,11bR)-11b-methyl-10-(2-phenoxyphenyl)-6a,11b-dihydro-5H-spiro[benzofuro[2,3-c]quinoline-6,3'-indolin]-2'-one (9m). The compound **9m** was prepared by using Isatin **4a** (40 mg, 0.27 mmol, 1.0 equiv.), Aniline **5a** (25 µL, 0.27 mmol, 1.0 equiv.), 3-methyl-5-(2-phenoxyphenyl)benzofuran **6m** (82 mg, 0.27 mmol, 1.0 equiv.) and $Sc(OTf)_3$ (7 mg, 0.01 mmol, 0.05 equiv.). The product **9m** was obtained by column chromatography (ethyl acetate: hexane, 7:13 v/v) as white solid (112 mg, 0.21 mmol, 79% yield); m.p.: 139-141 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) *δ* 8.54 (s, 1H), 7.64 (s, 1H), 7.41 (d, *J* = 6.3 Hz, 2H), 7.26 (s, 4H), 7.16-6.95 (m, 5H), 6.95. 6.69 (m, 4H), 6.53 (dd, *J* = 20.0, 6.4 Hz, 2H), 6.42-6.20 (m, 2H), 4.99 (s, 1H), 4.03 (s, 1H), 1.75 (s, 3H). **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) *δ* 178.0, 158.5, 157.3, 152.5, 141.1, 140.4, 135.2, 134.4, 131.2, 130.7, 129.7, 129.3, 129.2, 128.5, 128.4, 127.5, 127.5, 127.3, 126.5, 124.8, 123.9, 122.2, 122.1, 121.7, 120.6, 117.0, 116.3, 109.8, 109.4, 90.3, 63.6, 46.0, 31.3. **ESI HRMS** *m/z* calc. for $C_{35}H_{27}N_2O_3$ $[M+H]^+$: 523.2022, Found: 523.2021.

Section VI. Procedure for the synthesis of compounds 11 and 13:

A similar procedure as described above for the synthesis of compounds **8a**-**8q**, was also followed for the synthesis of compounds **11 and 13**. In case of **11**, triacetylglucal was used instead of 3-methylbenzofuran **6a** and incase of **13**, Acenaphthoquinone (**12**) was used instead of Isatin **4a.**



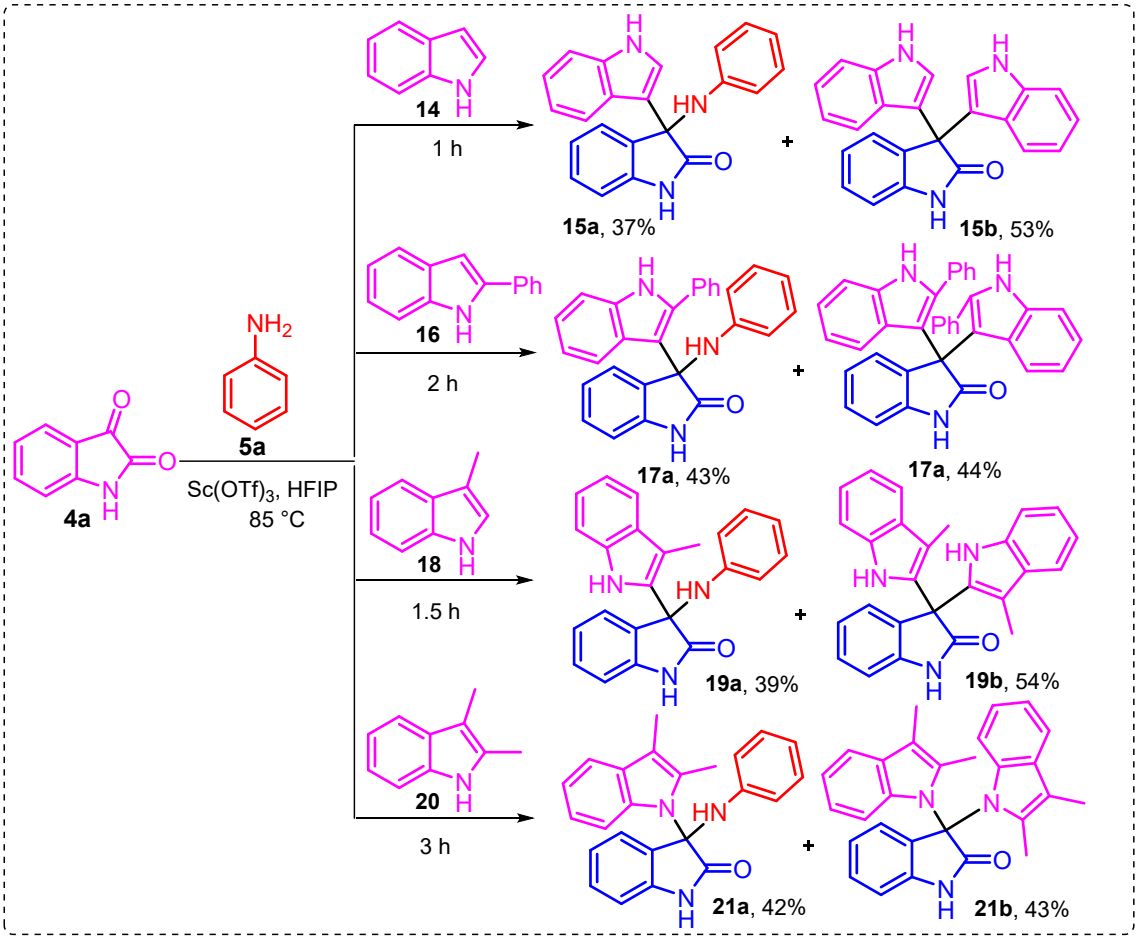
((2S,3R,6S)-3-acetoxy-1,3,4,6-tetrahydro-2H-2,6-methanobenzo[c][1,5]oxazocin-4-yl)methyl acetate (12). The compound **11** was prepared by using Isatin **4a** (100 mg, 0.67 mmol, 1.0 equiv.), Aniline **5a** (61 µL, 0.67 mmol, 1.0 equiv.), Triacetylglucal (104 mg, 0.34 mmol, 1.0 equiv.) and $Sc(OTf)_3$ (17 mg, 0.03 mmol, 0.05 equiv.). The product **11** was obtained by column chromatography (ethyl acetate: hexane, 1:9 v/v) as colourless liquid (86 mg, 0.22 mmol, 40% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.19-7.12 (m, 2H), 6.72-6.67 (m, 1H), 6.61 (d, *J* = 8.0 Hz, 1H), 4.87-4.80 (m, 2H), 4.44 (s, 1H), 4.19 (dd, *J* = 12.2, 4.4 Hz, 1H), 3.98 (dd, *J* = 12.2, 2.2 Hz, 1H), 3.85 (s, 1H), 3.61-3.56 (m, 1H), 2.31-2.26 (m, 1H), 2.11 (s, 3H), 2.06 (s, 3H), 1.99-1.94 (m, 1H). **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 171.1, 170.1, 145.2, 130.7, 130.1, 119.1, 117.4, 113.2, 72.0, 68.8, 67.6, 63.2, 46.8, 28.1, 21.2, 21.0. **ESI HRMS** *m/z* calc. for $C_{16}H_{19}NO_5Na$ $[M+Na]^+$: 328.1161, Found: 328.1161.



(1S,6a'S,11b'R)-11b'-methyl-6a',11b'-dihydro-2H,5'H-spiro[acenaphthylene-1,6'-benzofuro[2,3-c]quinolin]-2-one (13). The compound **13** was prepared by using Acenaphthoquinone **12** (100 mg, 0.55 mmol, 1.0 equiv.), Aniline **5a** (50 µL, 0.55 mmol, 1.0 equiv.), 3-Methylbenzofuran **6a** (68 µL,

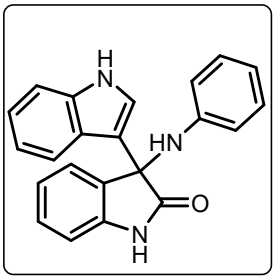
0.55 mmol, 1.0 equiv.) and $Sc(OTf)_3$ (14 mg, 0.03 mmol, 0.05 equiv.). The product **13** was obtained by column chromatography (ethyl acetate: hexane, 1:9 v/v) as yellow solid (92 mg, 0.24 mmol, 43% yield); m.p.: 250-252-50 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.12 (d, J = 8.1 Hz, 1H), 8.02 (d, J = 7.0 Hz, 1H), 7.83-7.64 (m, 3H), 7.46 (dd, J = 7.4, 1.2 Hz, 1H), 7.24 (s, 1H), 7.10-7.04 (m, 2H), 7.01-6.95 (m, 1H), 6.94 -6.82 (m, 2H), 6.55 (dd, J = 7.8, 1.0 Hz, 1H), 6.28 (dd, J = 7.8, 0.5 Hz, 1H), 5.08 (s, 1H), 4.13 (s, 1H), 1.86 (s, 3H). **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 203.3, 157.9, 142.2, 142.0, 137.7, 135.7, 132.3, 131.5, 130.5, 128.3, 128.1, 127.9, 127.6, 127.3, 125.2, 123.4, 123.0, 122.4, 121.2, 120.4, 116.1, 109.7, 90.3, 67.2, 46.4, 31.1. **ESI HRMS** *m/z* calc. for $C_{27}H_{20}NO_2[M+H]^+$: 390.1494, Found: 390.1485.

Section VII. General procedure for the synthesis of alkylated compounds 15a, 15b, 17a, 17b, 19a, 19b, 21a and 21b: The synthesis of these compounds was carried out using a similar procedure as described for the synthesis of **8a-8q** in Section **III**. Indole was used here instead of 3-methylbenzofuran **6** and the reaction follows alkylation pathway rather than cyclization.

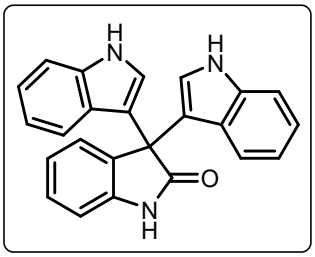


A 5 mL oven-dried reaction tube (reaction vial) with a magnetic stir bar was charged with Isatin **4a** (100 mg, 0.67 mmol, 1.0 equiv.), Aniline **5a** (61 µL, 0.67 mmol, 1.0 equiv.), Indole **14** (80 mg, 0.67 mmol, 1.0 equiv.), $Sc(OTf)_3$ (17 mg, 0.03 mmol, 0.05 equiv.) and HFIP as solvent (2 mL). Then the tube was capped with PTFE made solid cap and the resulting mixture was stirred at 85 °C for 1 h. The reaction progress was monitored by TLC and upon the completion of the reaction, water (10 mL), ethyl acetate (10 mL) was added and the layers were separated in a separating funnel. The aqueous layer was further extracted with ethyl acetate (10 mL x 2). The combined organic layers were washed with brine, dried over anhydrous sodium sulfate. Solvent was removed under reduced pressure to give the crude product, which was purified by column chromatography using ethyl acetate/hexane (1:4, v/v) to result in compounds **15a** (86 mg, 0.25 mmol, 37% yield) and **15b** (129 mg, 0.35 mmol, 53% yield) both appear as off-white solid. A

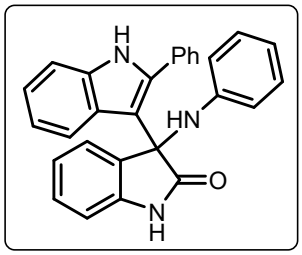
similar procedure was followed for the synthesis of the remaining compounds **17a, 17b, 19a, 19b, 21a and 21b**. These reactions even happened without $Sc(OTf)_3$ and heating as well.



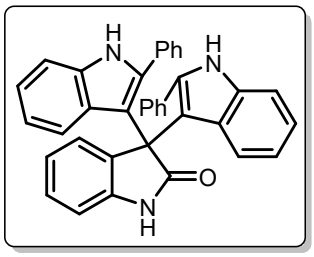
3-(1H-indol-3-yl)-3-(phenylamino)indolin-2-one (15a). The compound **15a** was prepared by using Isatin **4a** (100 mg, 0.67 mmol, 1.0 equiv.), Aniline **5a** (62 µL, 0.67 mmol, 1.0 equiv.), Indole **14** (80 mg, 0.67 mmol, 1.0 equiv.) and $Sc(OTf)_3$ (17 mg, 0.067 mmol, 0.05 equiv.). The product **15a** was obtained by column chromatography (ethyl acetate: hexane, 1:4 v/v) as off-white solid (86 mg, 0.25 mmol, 37% yield); m.p.: 186-188 °C. **^{1}H NMR** (400 MHz, DMSO-d_6) δ 10.94 (s, 1H), 10.52 (s, 1H), 7.33 (d, J = 7.6 Hz, 1H), 7.18 (d, J = 7.0 Hz, 2H), 7.09-6.87 (m, 6H), 6.78 (s, 2H), 6.47 (d, J = 7.4 Hz, 2H), 5.01 (s, 2H). **^{13}C{^{1}H} NMR** (100 MHz, DMSO-d_6) δ 179.2, 147.5, 141.2, 137.0, 134.9, 128.1, 127.7, 127.6, 125.7, 125.2, 124.3, 121.5, 121.0, 120.9, 118.3, 116.0, 113.6, 111.6, 109.6, 59.8, 56.5. **ESI HRMS** *m/z* calc. for $C_{22}H_{18}N_3O$ $[M+H]^+$: 340.1450, Found: 340.1449.



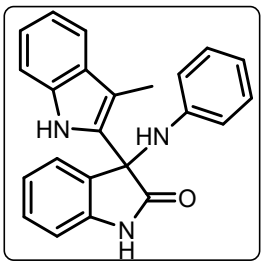
[3,3':3',3''-terindolin]-2'-one (15b). The compound **15b** was prepared by using Isatin **4a** (100 mg, 0.67 mmol, 1.0 equiv.), Aniline **5a** (62 µL, 0.67 mmol, 1.0 equiv.), Indole **14** (80 mg, 0.67 mmol, 1.0 equiv.) and $Sc(OTf)_3$ (17 mg, 0.067 mmol, 0.05 equiv.). The product **15b** was obtained by column chromatography (ethyl acetate: hexane, 1:5 v/v) as off-white solid (129 mg, 0.35 mmol, 53% yield); m.p.: 304-306 °C. **^{1}H NMR** (400 MHz, DMSO-d_6) δ 10.97 (s, 2H), 10.61 (s, 1H), 7.38-7.18 (m, 6H), 7.11-6.71 (m, 8H**)**. **^{13}C{^{1}H} NMR** (100 MHz, DMSO-d_6) δ 178.8, 141.4, 137.0, 134.6, 127.9, 125.7, 124.9, 124.3, 121.5, 121.0, 120.8, 118.3, 114.3, 111.6, 109.6, 52.6. **ESI HRMS** *m/z* calc. for $C_{24}H_{17}N_3NaO$ $[M+Na]^+$: 386.1269, Found: 386.1258.



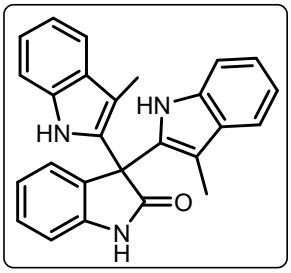
3-(2-phenyl-1H-indol-3-yl)-3-(phenylamino)indolin-2-one (17a). The compound **17a** was prepared by using Isatin **4a** (100 mg, 0.67 mmol, 1.0 equiv.), Aniline **5a** (62 µL, 0.67 mmol, 1.0 equiv.), Indole **16** (131 mg, 0.67 mmol, 1.0 equiv.) and $Sc(OTf)_3$ (17 mg, 0.067 mmol, 0.05 equiv.). The product **17a** was obtained by column chromatography (ethyl acetate: hexane, 1:5 v/v) as yellow solid (124 mg, 0.29 mmol, 43% yield); m.p.: 192-194 °C. **^{1}H NMR** (400 MHz, DMSO-d_6) δ 11.21 (s, 1H), 10.31 (s, 1H), 7.31 (d, J = 8.0 Hz, 1H), 7.27 – 7.12 (m, 4H), 7.10-6.96 (m, 4H), 6.89 (d, J = 7.6 Hz, 1H), 6.82 (t, J = 7.1 Hz, 3H), 6.74 (t, J =7.5 Hz, 1H), 6.61 (d, J = 8.0 Hz, 1H), 6.33 (d, J = 8.5 Hz, 2H), 4.94 (s, 2H). **^{13}C{^{1}H} NMR** (100 MHz, DMSO-d_6) δ 178.9, 147.3, 141.1, 136.7, 135.9, 135.1, 133.8, 129.18, 128.5, 127.9, 127.6, 127.3, 127.3, 125.3, 121.4, 121.0, 120.8, 118.4, 113.3, 111.7, 111.0, 109.4, 56.6. **ESI HRMS** *m/z* calc. for $C_{28}H_{22}N_3O$ $[M+H]^+$: 416.1763, Found: 416.1762.



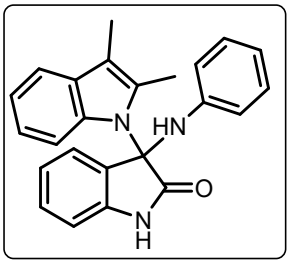
2,2''-diphenyl-[3,3':3',3''-terindolin]-2'-one (17b). The compound **17b** was prepared by using Isatin **4a** (100 mg, 0.67 mmol, 1.0 equiv.), Aniline **5a** (62 µL, 0.67 mmol, 1.0 equiv.), Indole **16** (131 mg, 0.67 mmol, 1.0 equiv.) and $Sc(OTf)_3$ (17 mg, 0.067 mmol, 0.05 equiv.). The product **17b** was obtained by column chromatography (ethyl acetate: hexane, 1:5 v/v) as yellow solid (154 mg, 0.29 mmol, 44% yield); m.p.: 313-315 °C. **^{1}H NMR** (400 MHz, DMSO-d_6) δ 11.04 (s, 1H), 10.73 (s, 1H), 10.45 (s, 1H), 7.29 (s, 7H), 7.19-6.80 (m, 11H), 6.64 (d, J = 14.9 Hz, 3H), 6.31 (s, 1H). **^{13}C{^{1}H} NMR** (100 MHz, DMSO-d_6) δ 177.8, 140.9, 135.5, 135.5, 135.3, 134.8, 134.1, 133.4, 128.9, 128.6, 127.8, 127.5, 127.3, 127.3, 127.2, 127.0, 126.6, 126.6, 126.6, 126.5, 125.9, 125.8, 125.8, 125.8, 125.8, 125.4, 121.5, 121.2, 120.5, 120.2, 118.3, 118.0, 111.6, 110.9, 110.4, 109.1, 52.9. **ESI HRMS** *m/z* calc. for $C_{36}H_{24}N_3O$ $[M-H]^+$: 514.1919, Found: 515.1909.



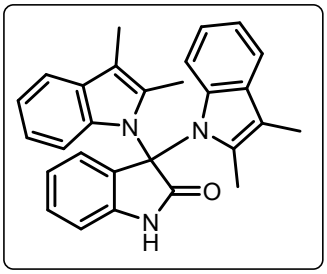
3-(3-methyl-1H-indol-2-yl)-3-(phenylamino)indolin-2-one (19a). The compound **19a** was prepared by using Isatin **4a** (100 mg, 0.67 mmol, 1.0 equiv.), Aniline **5a** (62 µL, 0.67 mmol, 1.0 equiv.), Indole **18** (89 mg, 0.67 mmol, 1.0 equiv.) and $Sc(OTf)_3$ (17 mg, 0.067 mmol, 0.05 equiv.). The product **19a** was obtained by column chromatography (ethyl acetate: hexane, 1:9 v/v) as yellow solid (93 mg, 0.26 mmol, 39% yield); m.p.: 184-186 °C. **^{1}H NMR** (400 MHz, DMSO- d_6) δ 11.94 (s, 1H), 11.43 (s, 1H), 10.56 (s, 1H), 7.56-7.33 (m, 2H), 7.20 (t, J = 7.6 Hz, 2H), 7.07 (d, J = 7.3 Hz, 2H), 6.95-6.87 (m, 2H), 6.84-6.70 (m, 2H), 6.40 (s, 2H), 2.09 (s, 3H). **^{13}C{^{1}H} NMR** (100 MHz, DMSO-d_6) δ 170.2, 164.1, 141.5, 137.0, 135.0, 131.4, 129.1, 128.1, 123.3, 122.6, 122.3, 121.0, 120.0, 119.5, 118.6, 117.8, 111.3, 111.2, 108.8, 106.4, 95.4, 21.8. **ESI HRMS** *m/z* calc. for $C_{25}H_{20}N_3O$ $[M+H]^+$: 354.1606, Found: 354.1604.



3,3''-dimethyl-[2,3':3',2''-terindolin]-2'-one (19b). The compound **19b** was prepared by using Isatin **4a** (100 mg, 0.67 mmol, 1.0 equiv.), Aniline **5a** (62 µL, 0.67 mmol, 1.0 equiv.), Indole **18** (89 mg, 0.67 mmol, 1.0 equiv.) and $Sc(OTf)_3$ (17 mg, 0.067 mmol, 0.05 equiv.). The product **19b** was obtained by column chromatography (ethyl acetate: hexane, 1:4 v/v) as yellow solid (143 mg, 0.36 mmol, 54% yield); m.p.: 296-298 °C. **^{1}H NMR** (400 MHz, DMSO-d_6) δ 10.82 (s, 1H), 10.46 (s, 2H), 7.50-7.20 (m, 6H), 7.01 (s, 6H), 1.91 (s, 6H). **^{13}C{^{1}H} NMR (**100 MHz, DMSO-d_6) δ 175.9, 141.5, 135.3, 131.6, 131.1, 129.0, 128.7, 125.6, 122.2, 120.9, 118.2, 117.8, 111.4, 109.9, 107.2, 54.6, 8.8. **ESI HRMS** *m/z* calc. for $C_{26}H_{22}N_3O$ $[M+H]^+$: 392.1763, Found: 392.1750.

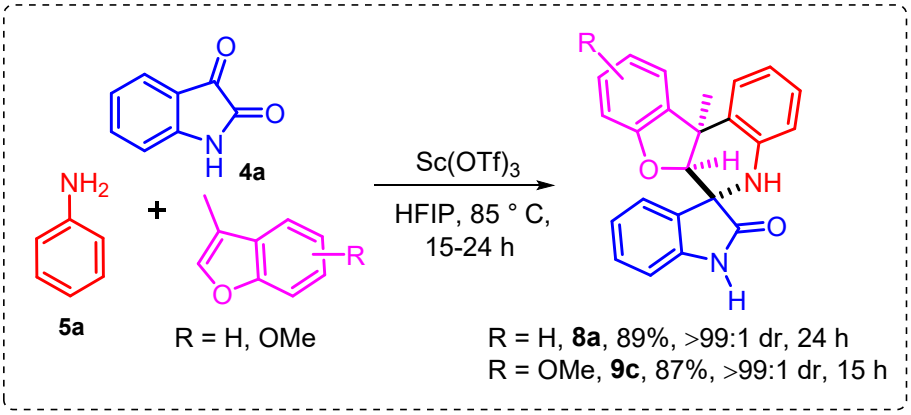


3-(2,3-dimethyl-1H-indol-1-yl)-3-(phenylamino)indolin-2-one (21a). The compound **21a** was prepared by using Isatin **4a** (100 mg, 0.67 mmol, 1.0 equiv.), Aniline **5a** (62 µL, 0.67 mmol, 1.0 equiv.), Indole **20** (99 mg, 0.67 mmol, 1.0 equiv.) and $Sc(OTf)_3$ (17 mg, 0.067 mmol, 0.05 equiv.). The product **21a** was obtained by column chromatography (ethyl acetate: hexane, 3:7 v/v) as yellow solid (107 mg, 0.29 mmol, 42% yield); m.p.: 188-190 °C. **^{1}H NMR** (400 MHz, DMSO-d_6) δ 10.52 (s, 2H), 7.28-7.12 (m, 4H), 7.03-6.82 (m, 6H), 6.73 (d, J = 8.2 Hz, 1H), 6.47 (d, J = 8.4 Hz, 2H), 5.03 (s, 2H), 2.26 (s, 3H), 2.10 (s, 3H). **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 181.1, 145.6, 140.2, 135.2, 135.1, 134.9, 132.2, 131.4, 129.7, 128.5, 127.8, 126.4, 122.6, 119.7, 117.8, 115.1, 110.4, 110.2, 106.9, 62.7, 11.6, 8.6. **ESI HRMS** *m/z* calc. for $C_{24}H_{22}N_3O$ $[M+H]^+$: 368.1763, Found: 368.1750.



2,2'',3,3''-tetramethyl-[1,3':3',1''-terindolin]-2'-one (21b). The compound **21b** was prepared by using Isatin **4a** (100 mg, 0.67 mmol, 1.0 equiv.), Aniline **5a** (62 µL, 0.67 mmol, 1.0 equiv.), Indole **20** (99 mg, 0.67 mmol, 1.0 equiv.) and $Sc(OTf)_3$ (17 mg, 0.067 mmol, 0.05 equiv.). The product **21b** was obtained by column chromatography (ethyl acetate: hexane, 1:9 v/v) as yellow solid (122 mg, 0.29 mmol, 43% yield); m.p.: 314-316 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.53 (s, 1H), 7.34 (d, J = 8.1 Hz, 2H), 7.12 (d, J =7.6 Hz, 2H), 7.06-6.92 (m, 5H), 6.85 (s, 3H), 2.20 (d, J = 36.5 Hz, 12H). **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 181.1, 140.3, 135.5, 135.3, 131.9, 128.5, 127.8, 126.4, 122.6, 119.5, 117.1, 111.6, 110.1, 106.7, 63.5, 11.6, 8.6. **ESI HRMS** *m/z* calc. for $C_{28}H_{26}N_3O$ $[M+H]^+$: 420.2076, Found: 420.2056.

***Section VIII. Gram scale synthesis of 8a and 9c*:**



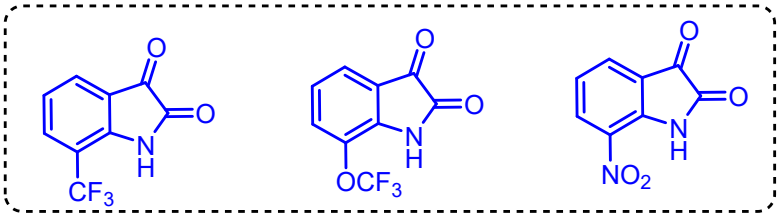
A 15 mL oven-dried reaction tube (seal tube) with a magnetic stir bar was charged with Isatin **4a** (700 mg, 4.76 mmol, 1.0 equiv.), Aniline **5a** (434 µL, 4.76 mmol, 1.0 equiv.), 3-Methylbenzofuran **6a** (593 µL, 4.76 mmol, 1.0 equiv.), $Sc(OTf)_3$ (117 mg, 0.24 mmol, 0.05 equiv.) and HFIP as solvent (17mL). Then the tube was capped with PTFE made solid cap and the resulting mixture was stirred

at 85 °C for 24 h. The reaction progress was monitored by TLC and upon the completion of the reaction, water (10 mL), ethyl acetate (10 mL) was added and the layers were separated in a separating funnel. The aqueous layer was further extracted with ethyl acetate (10 mL x 2). The combined organic layers were washed with brine, dried over anhydrous sodium sulfate. Solvent was removed under reduced pressure to give the crude product, which was purified by column chromatography using ethyl acetate/hexane (1:4, v/v) to result in compound **8a** as off-white solid (1500 mg, 4.23 mmol, 89% yield). A similar procedure was followed for the synthesis of compound **9c** using Isatin **4a** (500 mg, 3.40 mmol, 1.0 equiv.), Aniline **5a** (310 µL, 3.40 mmol, 1.0 equiv.), commercially available 6-methoxy-3-methylbenzofuran **6c** (551 mg, 3.40 mmol, 1.0 equiv.) and $Sc(OTf)_3$ (84 mg, 0.170 mmol, 0.05 equiv.). The product **9c** was obtained by column chromatography (ethyl acetate: hexane, 1:5 v/v) as yellow solid (1137 mg, 2.95 mmol, 87% yield).

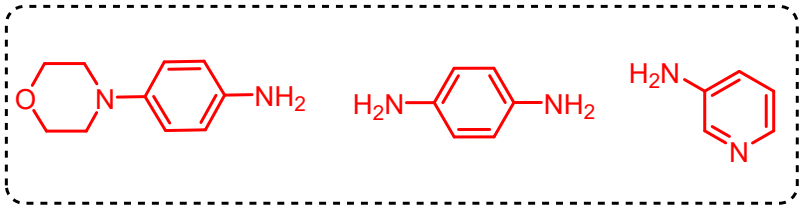
Section IX. Failed substrates:

Electron withdrawing groups (like CF_3, NO_2 and OCF_3) on the C-7 position of Isatin **4a** under optimized reaction conditions with aniline **5a** and 3-methylbenzofuran **6a** failed to give desired product. Although the reaction proceeds via an inverse electron-demand Diels-Alder pathway where the iminium ion acts as the electron poor diene, excessive electron withdrawal renders the iminium overly electron-deficient, diminishing effective orbital overlap with the dienophile and suppressing cycloaddition. In contrast, electron-rich anilines trimethoxy-substituted aniline **5l** donate electron density into the iminium system, tuning its frontier orbital energies and enabling the required povarov cyclization. In addition to isatins we have also faced failures in some aniline and benzofuran substrates possibly due to steric hindrance, deactivation effect or may be due to some related reasons.

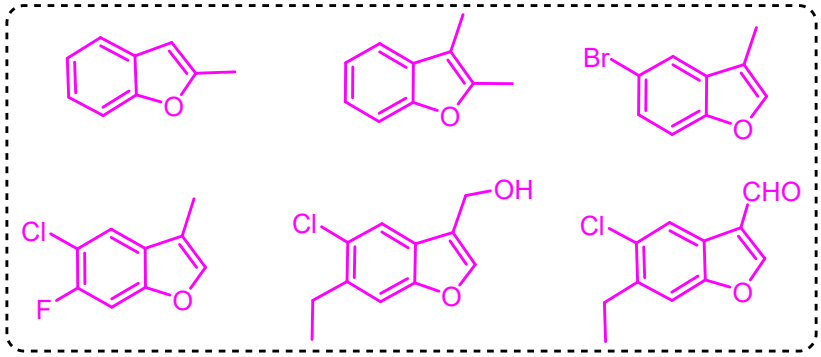
a). Isatin substrates:



b). Aniline substrates:

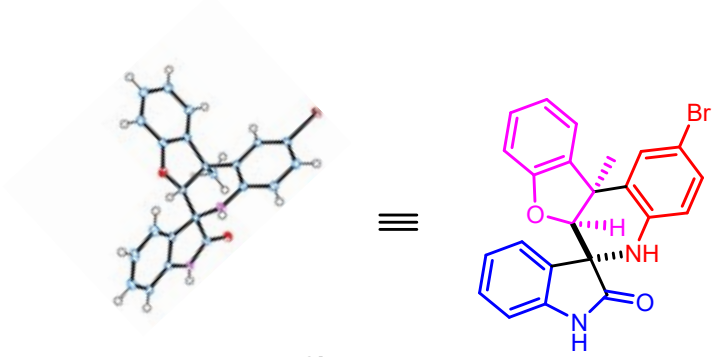


c). Benzofuran substrates:



Section X. Single Crystal XRD Studies:

***Sample preparation for crystallization of 8h*:** 15 mg of **8h** was dissolved in 2 mL of ethyl acetate, then 3 mL of hexane was added dropwise, and the resulting solution was left for slow evaporation for about 72 h which led to the formation of block shaped transparent crystals which were used for data collection. The crystals were mounted on a glass for diffraction experiments. Intensity data were collected on a Bruker Apex II CCD diffractometer with Mo Kα radiation (0.71073 Å) below room temperature.



ORTEP diagram of **8h**

Figure S1: ORTEP diagram of **8h**

CCDC number	2423086
Empirical formula	$C_{23}H_{17}BrN_2O_2$
Formula weight	433.29
Temperature [K]	296.15
Crystal system	Monoclinic
Space group (number)	$P2_1/c$ (14)
a [Å]	8.6102(2)
b [Å]	13.8584(4)
c [Å]	15.3809(5)
α [°]	90
β [°]	95.6250(10)
γ [°]	90
Volume [Å^3]	1826.47(9)
Z	4
ρ_{calc} [gcm^{-3}]	1.576
μ [mm^{-1}]	2.273
F(000)	880
Crystal size [mm^3]	0.18×0.18×0.21
Crystal colour	transparent
Crystal shape	block
Radiation	MoK_α (λ=0.71073 Å)
2θ range [°]	3.96 to 56.65 (0.75 Å)
Index ranges	−11 ≤ h ≤ 10 −15 ≤ k ≤ 18 −20 ≤ l ≤ 20
Reflections collected	41008
Independent reflections	4566 R_{int} = 0.0579

	R_{sigma} = 0.0301
Completeness to θ = 25.242°	100.0 %
Data / Restraints / Parameters	4566 / 0 / 254
Absorption correction T_{min}/T_{max} (method)	0.6302 / 0.7457 (multi-scan)
Goodness-of-fit on F^2	1.035
Final *R* indexes [$I \geq 2\sigma(I)$]	R_1 = 0.0284 wR_2 = 0.0683
Final *R* indexes [all data]	R_1 = 0.0350 wR_2 = 0.0706
Largest peak/hole [eÅ^{-3}]	0.58/−0.67

Check CIF file data of **8h** (CCDC 2423086) (**Figure S2**): Thermal ellipsoids are drawn at 50% probability in this ORTEP representation

.

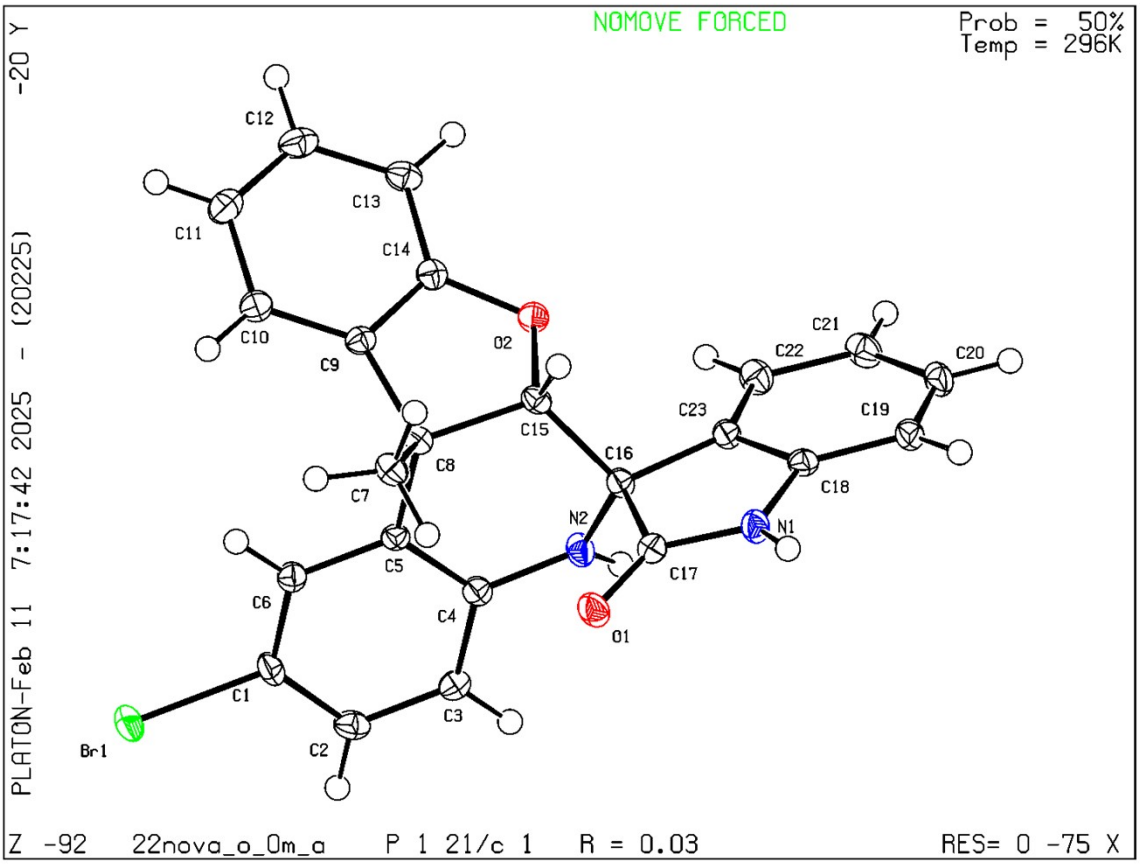


Figure S2: Check CIF file data of **8h**

Section XI. Computational studies:

All geometry optimizations were performed with the Gaussion 09 suite program.[2] The geometries were optimized at B3LYP functional[3] in a combination with the 6-31G(d) basis set.[4-6]Harmonic vibration frequency calculations were performed for all geometries to confirm the minima on their potential energy surface. Further, Grimme's dispersion correction (D3) was included by single-point calculation using the optimized geometries with the B3LYP-D3/6-311+G(d,p) (SMD,HFIP) level of theory.[7-11] Solvent effects were incorporated via single-point calculations using hexafluoro isopropanol (HFIP) in a combination with the SMD solvation model[12], consistent with the experimental conditions. The energies were calculated using the following equation,

$$\Delta E = E_{TS} - E_{Reactants} \ldots\ldots\ldots (1)$$

The frontier molecular orbitals (FMOs) were examined for the optimized geometries for the [4+2] cycloaddition at the B3LYP/6-31G(d) level of theory. The HOMO-LUMO band gaps were calculated using the following equation,

$$\Delta E = E_{LUMO} - E_{HOMO} \ldots\ldots\ldots (2)$$

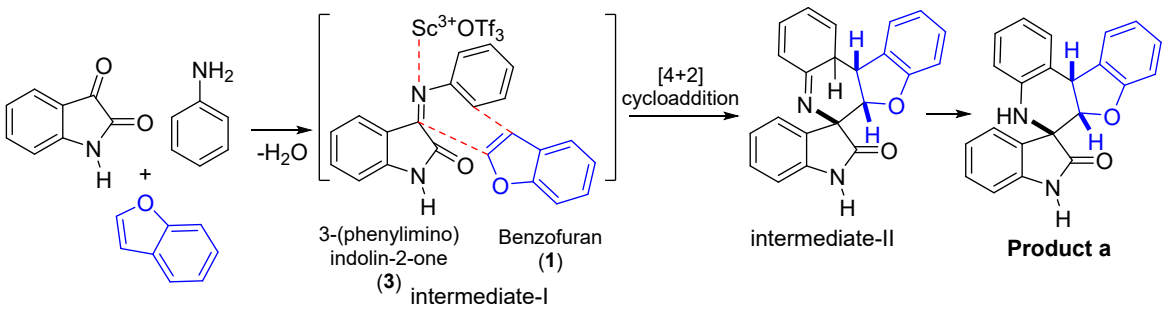
The calculations have been performed without the acid co-ordinated with the nitrogen center of intermediate-I (Scheme 1) for computational simplicity. Nervertheless, such coordination can influence the activation barrier of the reactions, however, it is presumed that such effects would be similar in both cases.

Results and Discussion:

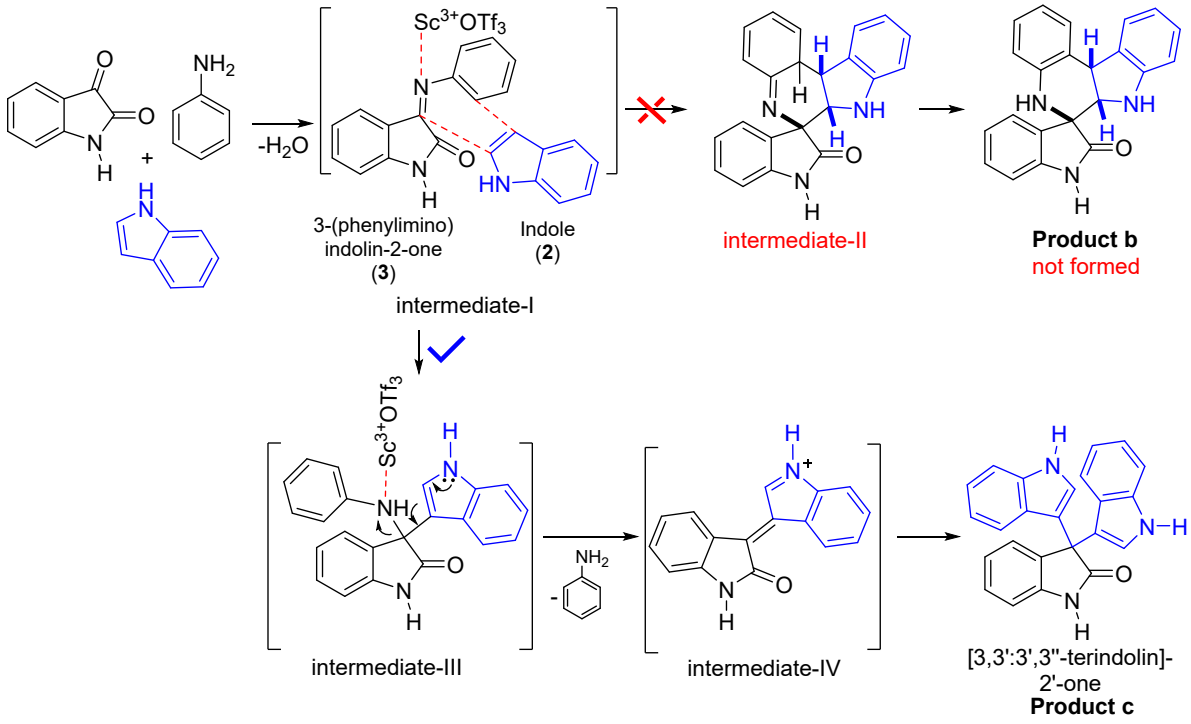
The experimental results indicate that benzofuran (**1**) undergoes a [4+2] cycloaddition reaction with 3-(phenylimino)indolin-2-one (**3**) to afford product **a**. In contrast, under similar reaction conditions, indole (**2**) reacts with the same partner via dialkylation rather than cycloaddition, leading to product **c**. The plausible mechanisms for these transformations are illustrated in **Scheme 1(a)** for benzofuran and **Scheme 1(b)** for indole.

To gain mechanistic insight, the [4+2] cycloaddition reactions of benzofuran (**1**) and indole (**2**) with 3-(phenylimino)indolin-2-one (**3**) were investigated using density functional theory (DFT) calculations, where benzofuran (**1**) and indole (**2**) act as dienophiles and compound (**3**) serves as the diene (**Scheme 2**).

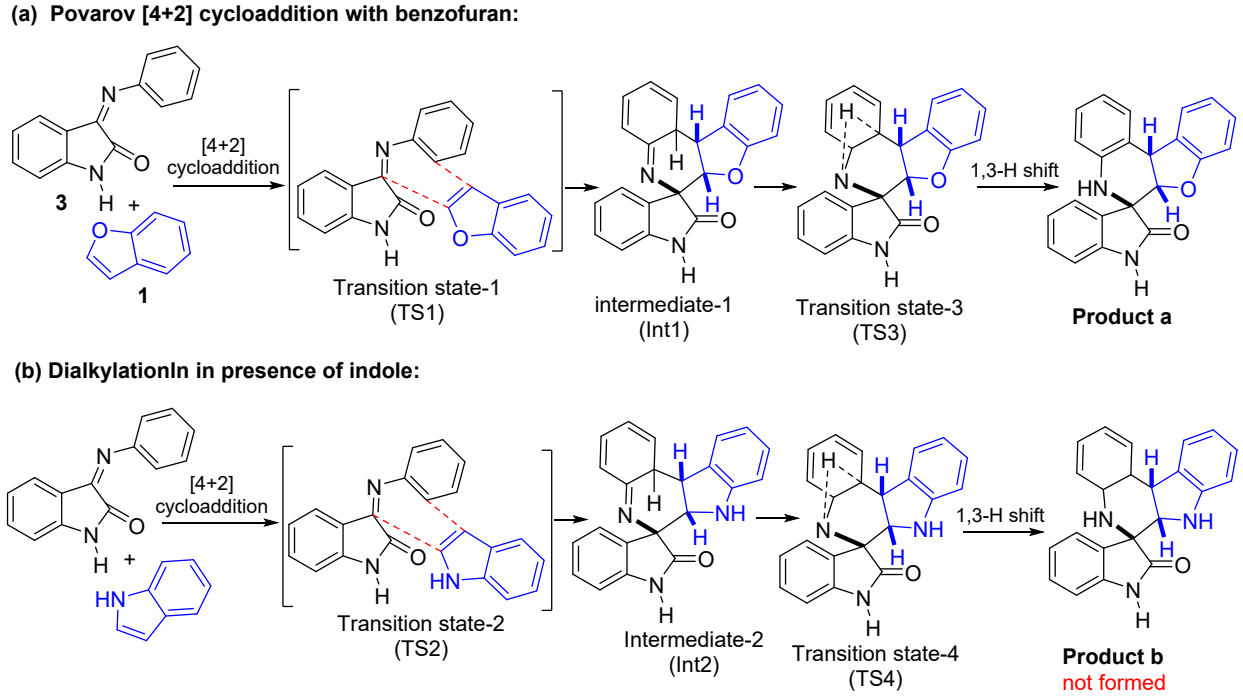
(a) [4+2] Povarov cyclization in presence of benzofuran:



(b) In presence of indole, it follows dialkylation



Scheme 1. Experimentally observed products formation for the reactions of benzofuran and indole with 3-(phenylimino)indolin-2-one.



Scheme 2. Computationally studied reaction mechanism for the [4+2] cycloaddition of benzofuran (**1**) and indole **2**) with 3-(phenylimino)indolin-2-one (**3**).

The potential energy surfaces were computed at the B3LYP/6-31G(d)//B3LYP-D3/6-311+G(d,p) (SMD, HFIP) level of theory (**Figure 1**).

The calculated activation energy (ΔE) for the cycloaddition step shows a clear preference for benzofuran (**1**), with transition state TS1 being lower in energy by ~4.0 kcal/mol compared to TS2 for indole (**2**). The corresponding cycloadduct intermediates are formed at −7.0 kcal/mol (Int1) for benzofuran and +2.2 kcal/mol (Int2) for indole. Subsequent 1,3-hydrogen shifts from these intermediates proceed via TS3 and TS4 and the former transition state is stable by ~7.0 kcal/mol compared to the later transition state relative to reactants.[13] These 1,3-H shift steps are the rate-determining step in both pathways.

The final products formed after the hydrogen shift are significantly stabilized, with energies of approximately −33.0 kcal/mol for benzofuran and −24.0 kcal/mol for indole. Overall, these results indicate that the [4+2] cycloaddition pathway is both kinetically and thermodynamically more favorable for benzofuran than for indole, in agreement with the experimental observations.

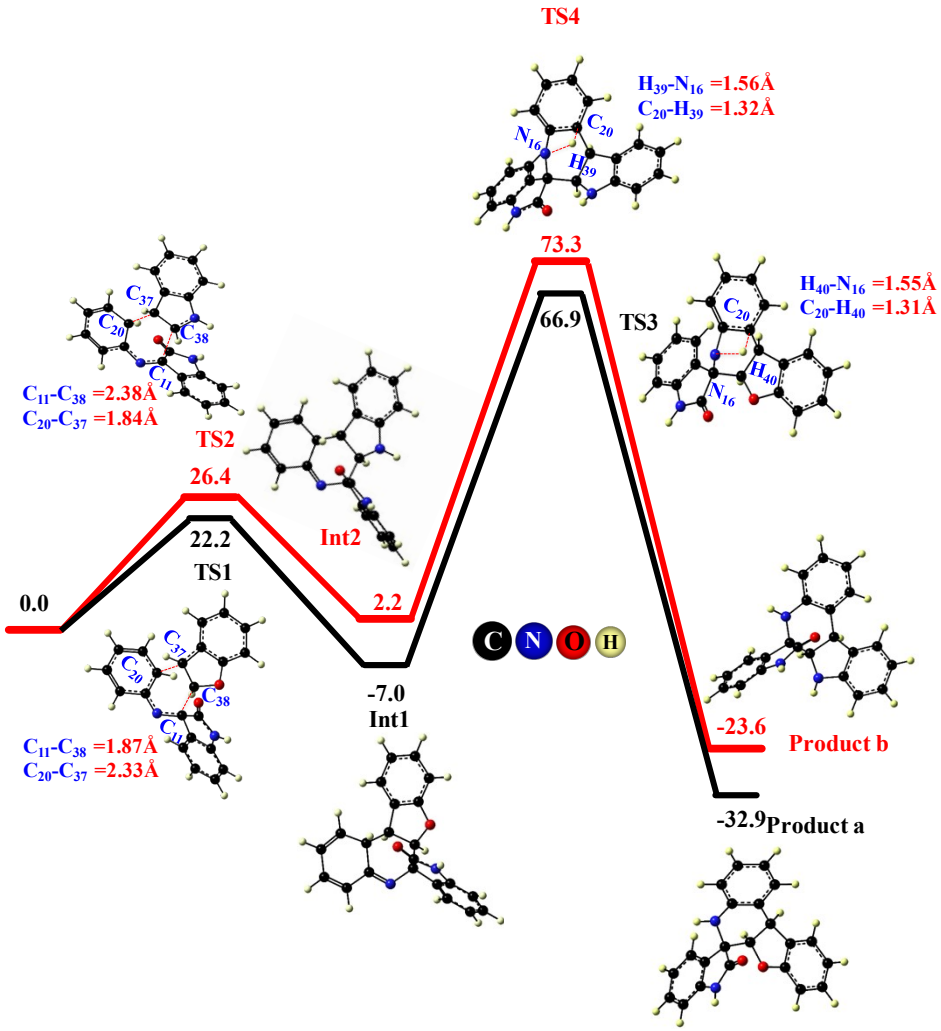


Figure 1. The calculated potential energy surface along with the optimized geometries at the B3LYP/6-31G(d)//B3LYP-D3/6-311+G(d,p)(SMD,HFIP) level of theory for the [4+2] cycloaddition of dienophiles, benzofuran (black graph) and indole (red graph) with the diene 3-(phenylimino)indolin-2-one. Electronic energies (ΔE in kcal/mol) are considered for the study.

Frontier molecular orbital (FMO) analysis further supports this preference. The interaction between the HOMO of the diene and the LUMO of the dienophile governs the feasibility of the cycloaddition.[14] In this case, the HOMO−1 of diene (**3**) was considered due to its appropriate orbital coefficients. The energy gaps were calculated as 5.80 eV for HOMO−1(**3**)–LUMO(**1**) (ΔE_1) and 6.20 eV for HOMO−1(**3**)–LUMO(**2**) (ΔE_2), indicating that benzofuran provides a more favorable orbital interaction by 8.8 kcal/mol compared to indole (**Figure 2**).

Additionally, Mulliken charge analysis of the dienophiles reveals that the alkene carbon (C37) in benzofuran (**1**) bears a less negative charge (−0.18537 a.u.) than the corresponding carbon in indole, **2** (−0.24073 a.u.). The more negatively charged alkene in indole leads to greater electronic repulsion with the electron-rich diene (**3**), disfavoring cycloaddition. In contrast, the relatively less negative character of benzofuran facilitates more favorable interactions with the diene, thereby promoting the [4+2] cycloaddition pathway.

Overall, the DFT results, FMO analysis, and charge distribution studies qualitatively explain that the benzofuran (**1**) preferentially undergoes [4+2] cycloaddition, whereas indole (**2**) would favor dialkylation under the same reaction conditions.

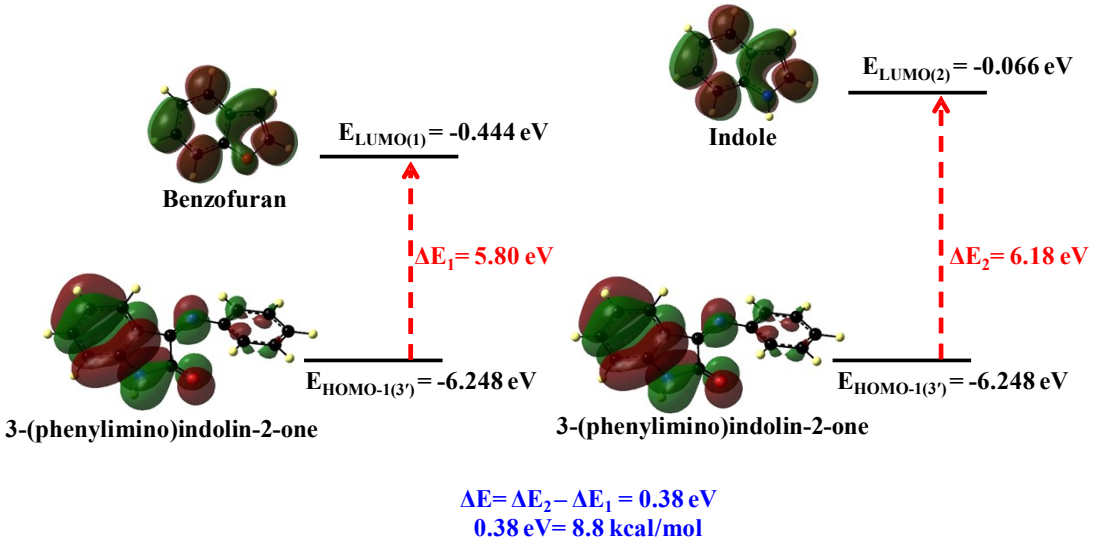


Figure 2. The (HOMO-1)-LUMO energy gaps for the [4+2] cycloaddition reaction of dienophiles, benzofuran and indole with the diene 3-(phenylimino)indolin-2-one, respectively, at the B3LYP/631G(d)level of theory.

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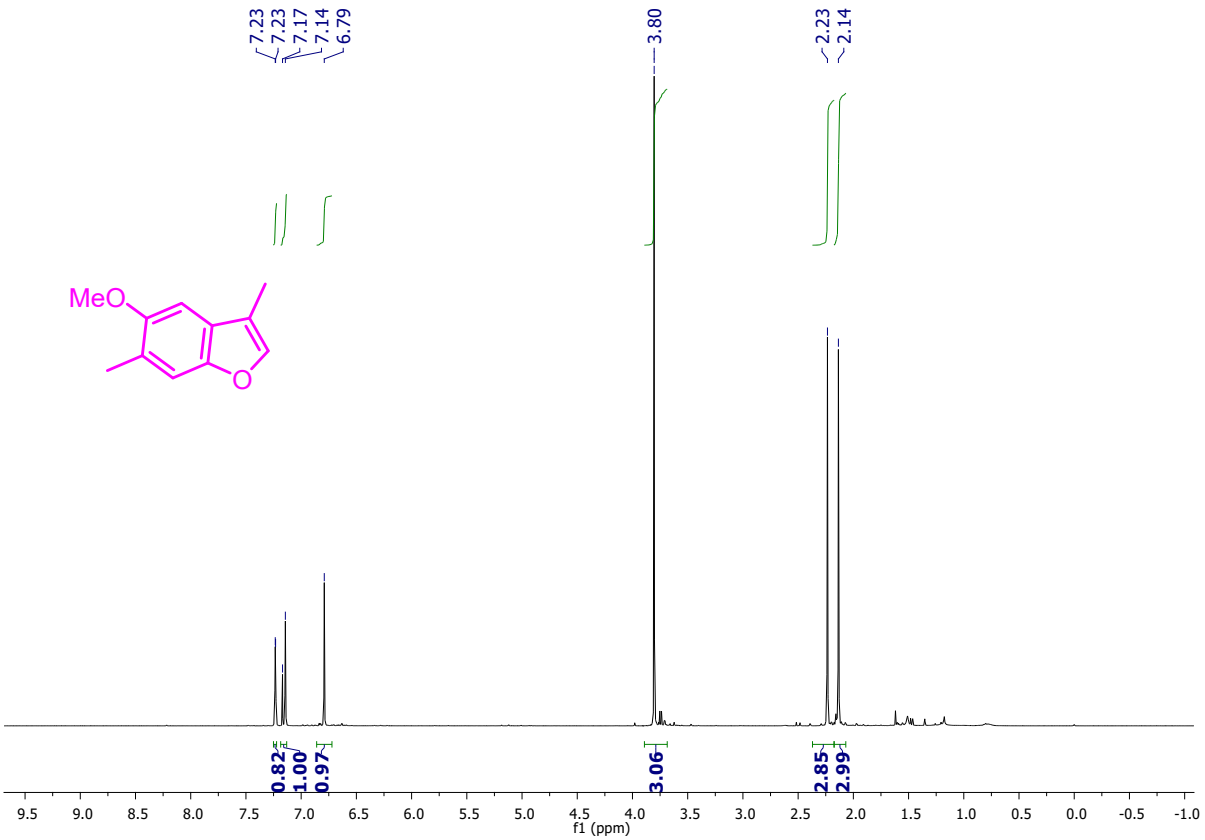
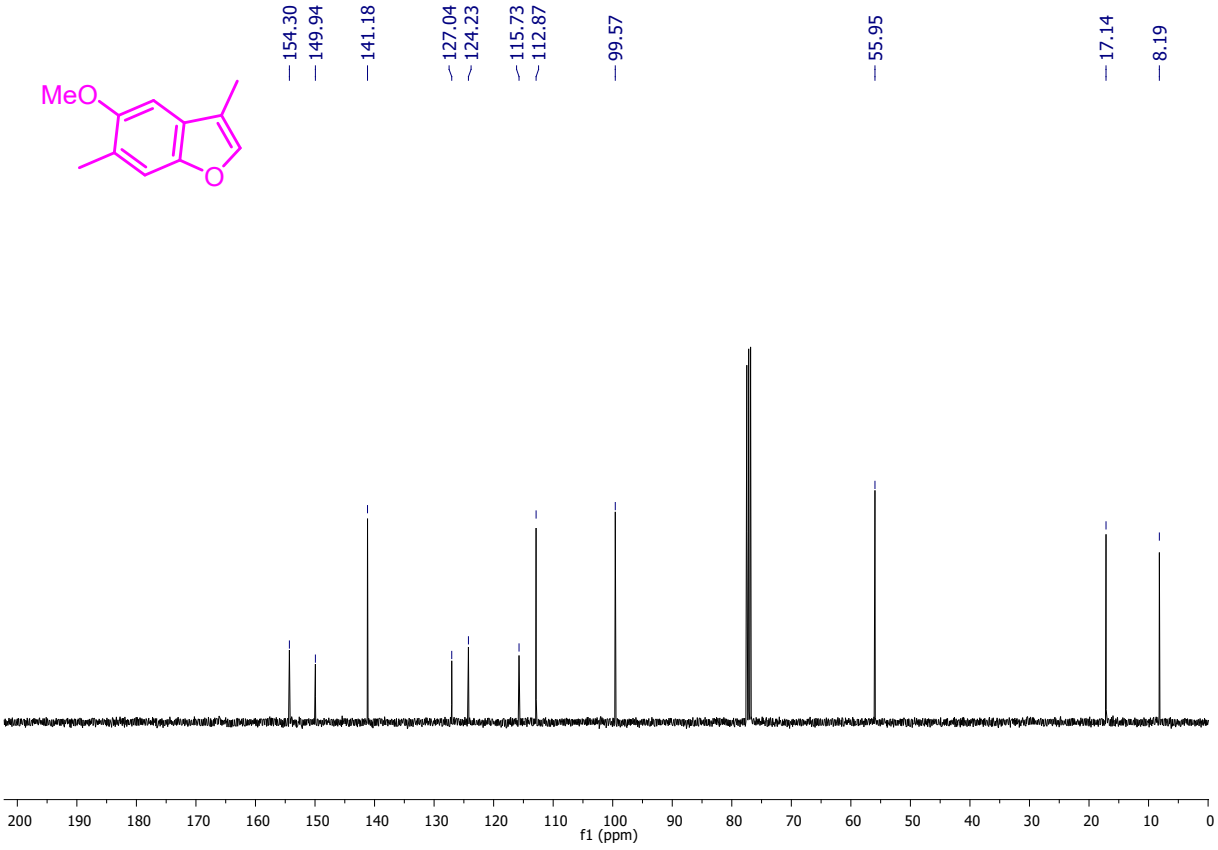
Section XIII. NMR Spectra:

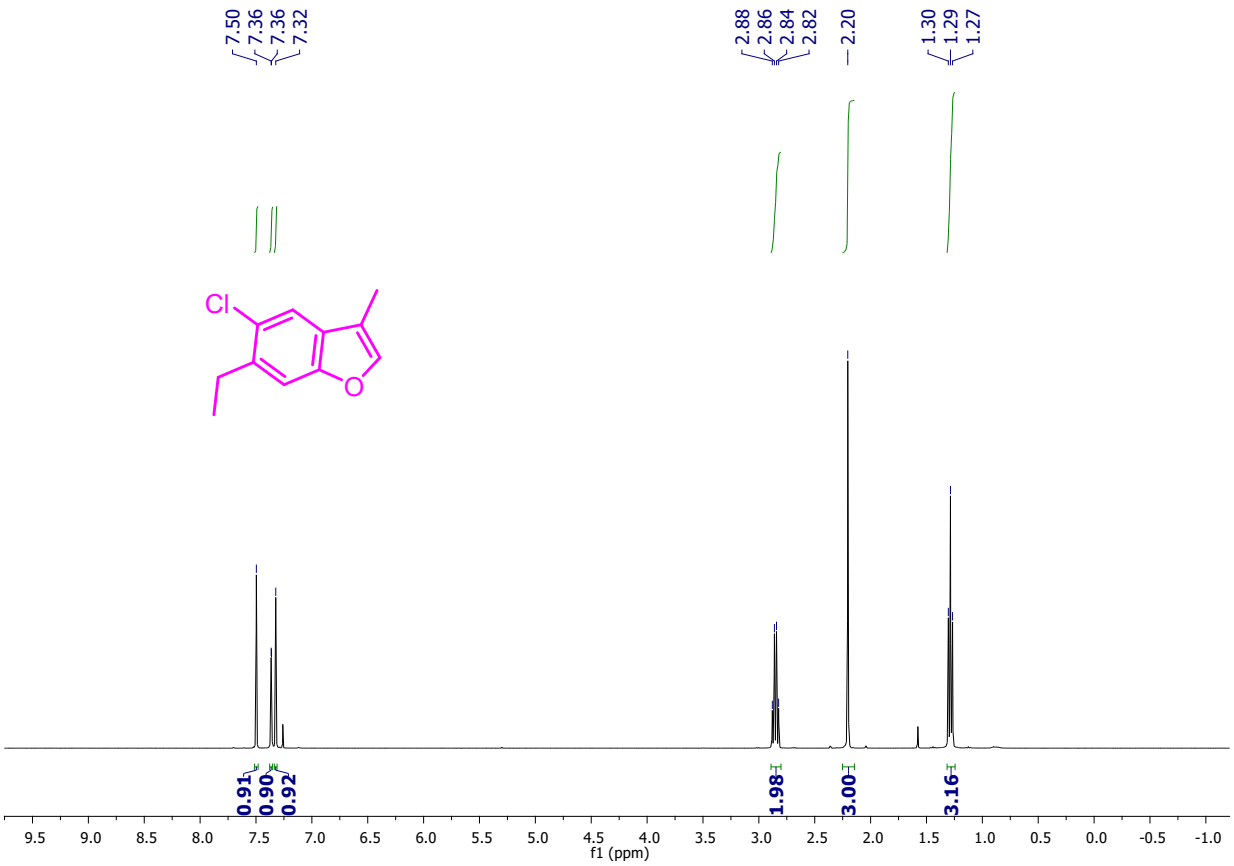
^{1}H NMR Spectrum of **6d** (400 MHz, $CDCl_3$)



^{13}C {^{1}H} NMR Spectrum of **6d** (100 MHz, $CDCl_3$)



^{1}H NMR Spectrum of **6e** (400 MHz, $CDCl_3$)



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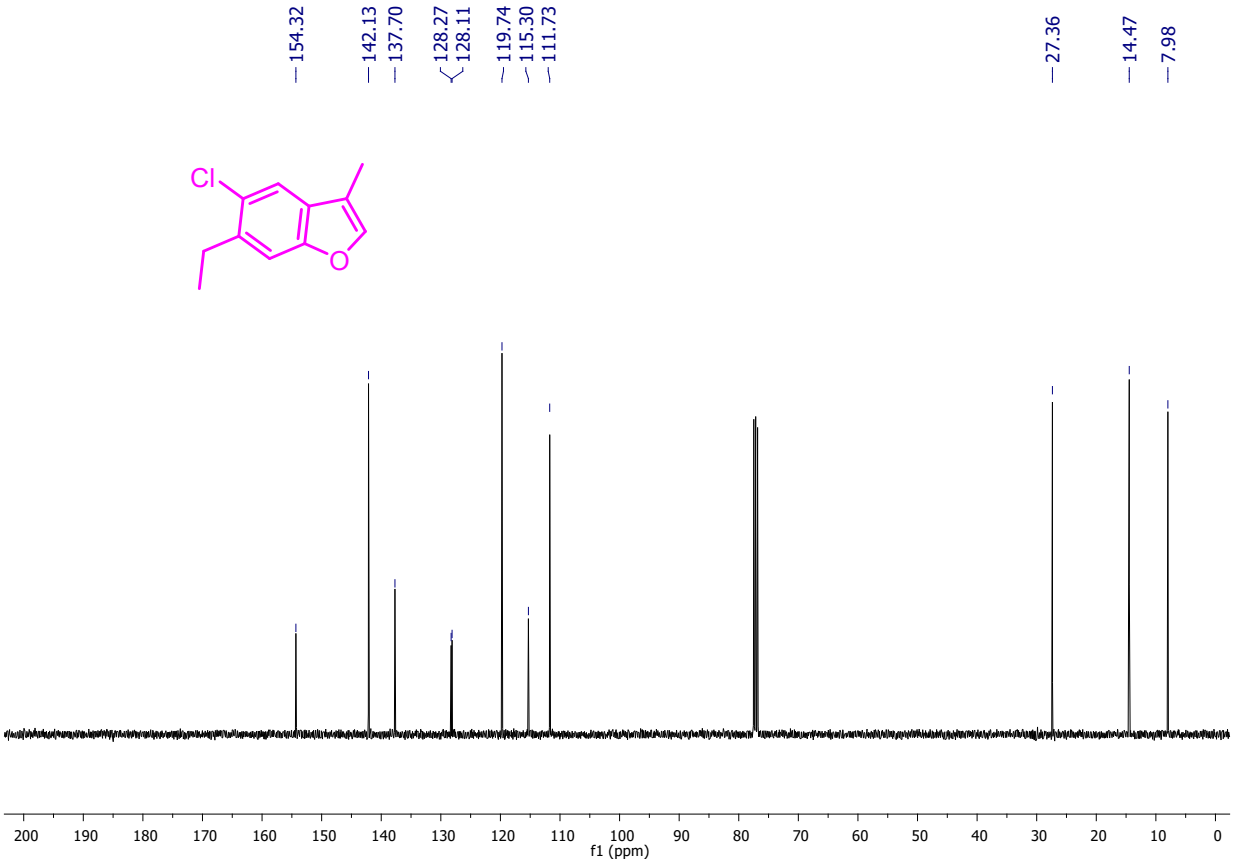
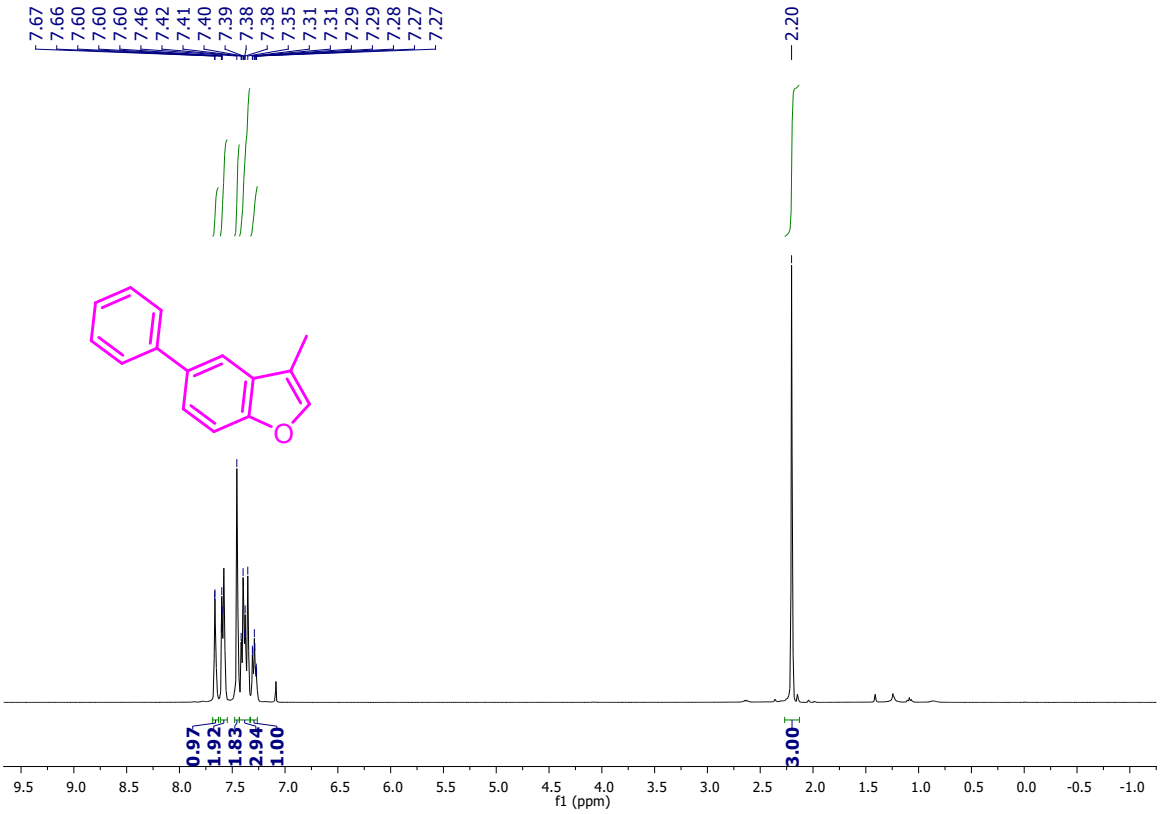


^{1}H NMR Spectrum of **6f** (400 MHz, $CDCl_3$)



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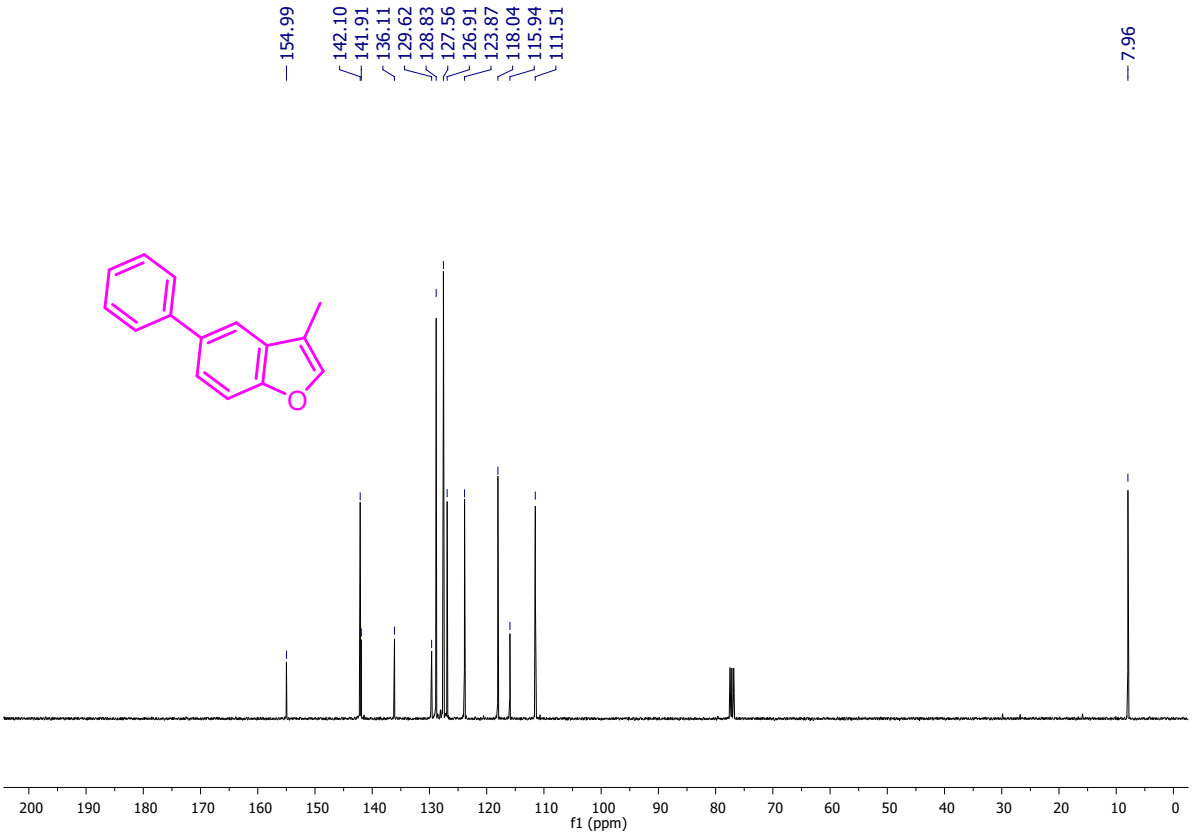
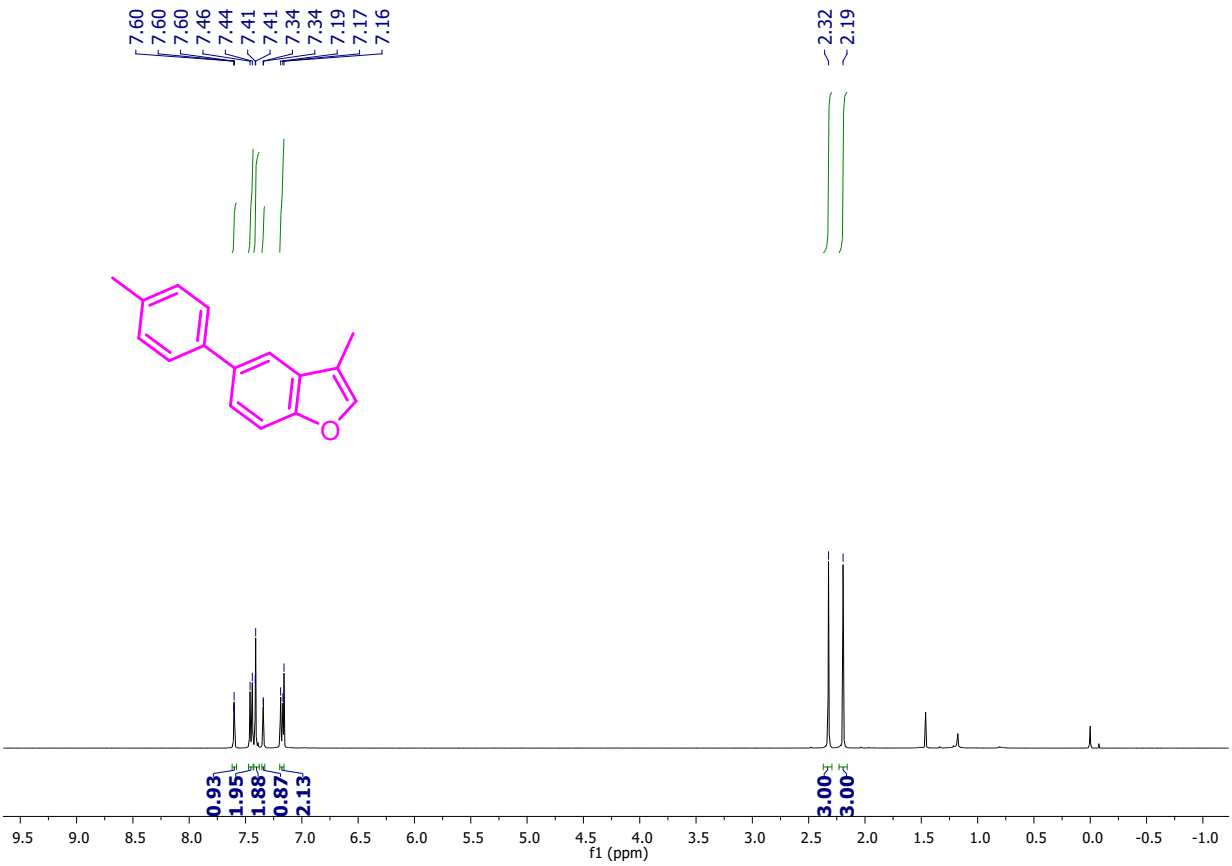
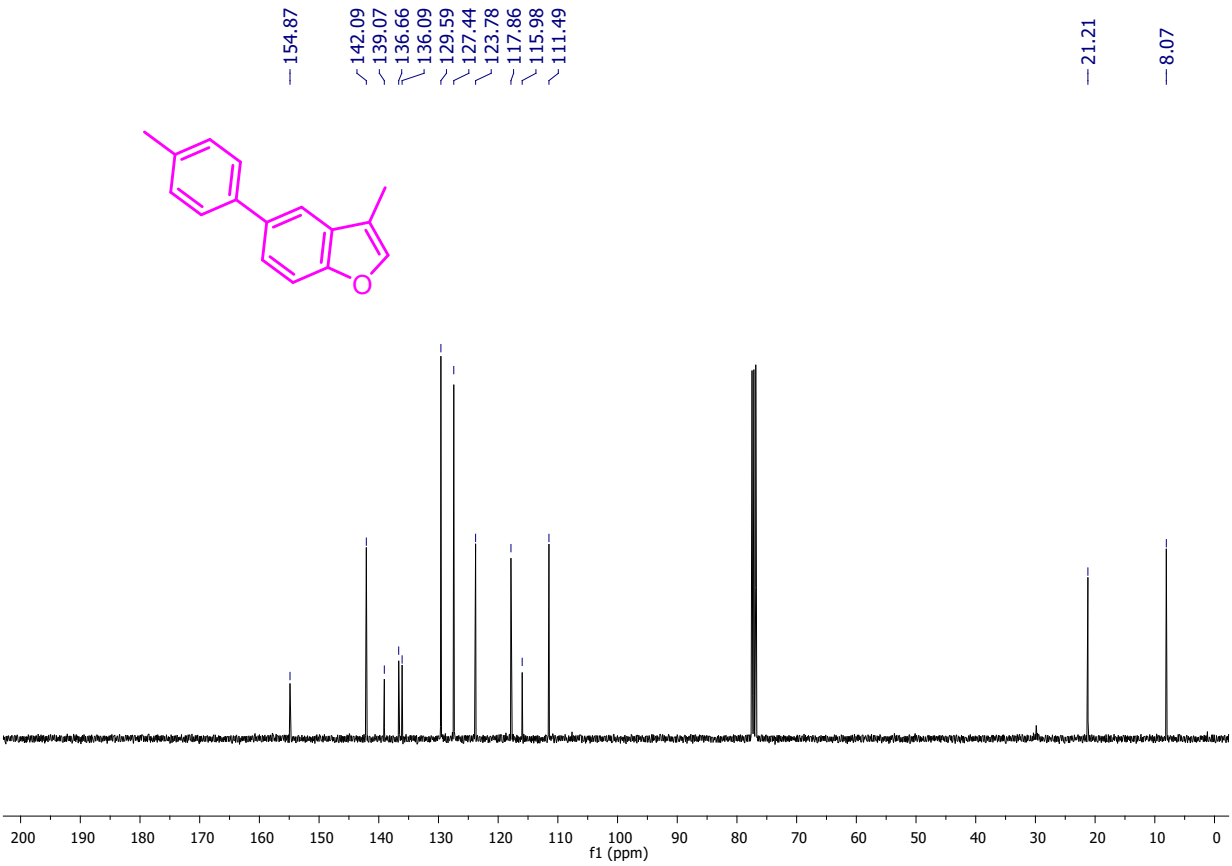


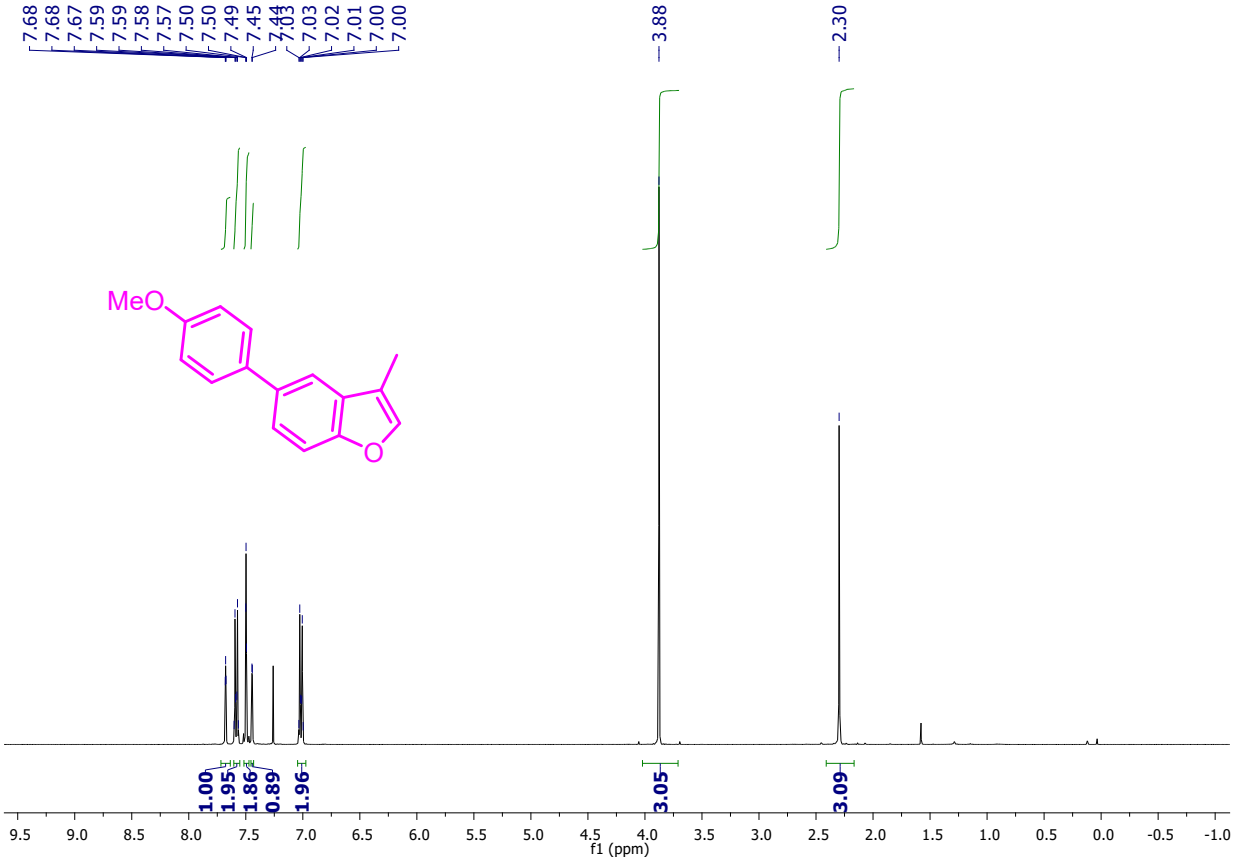
^{1}H NMR Spectrum of **6g** (400 MHz, $CDCl_3$)



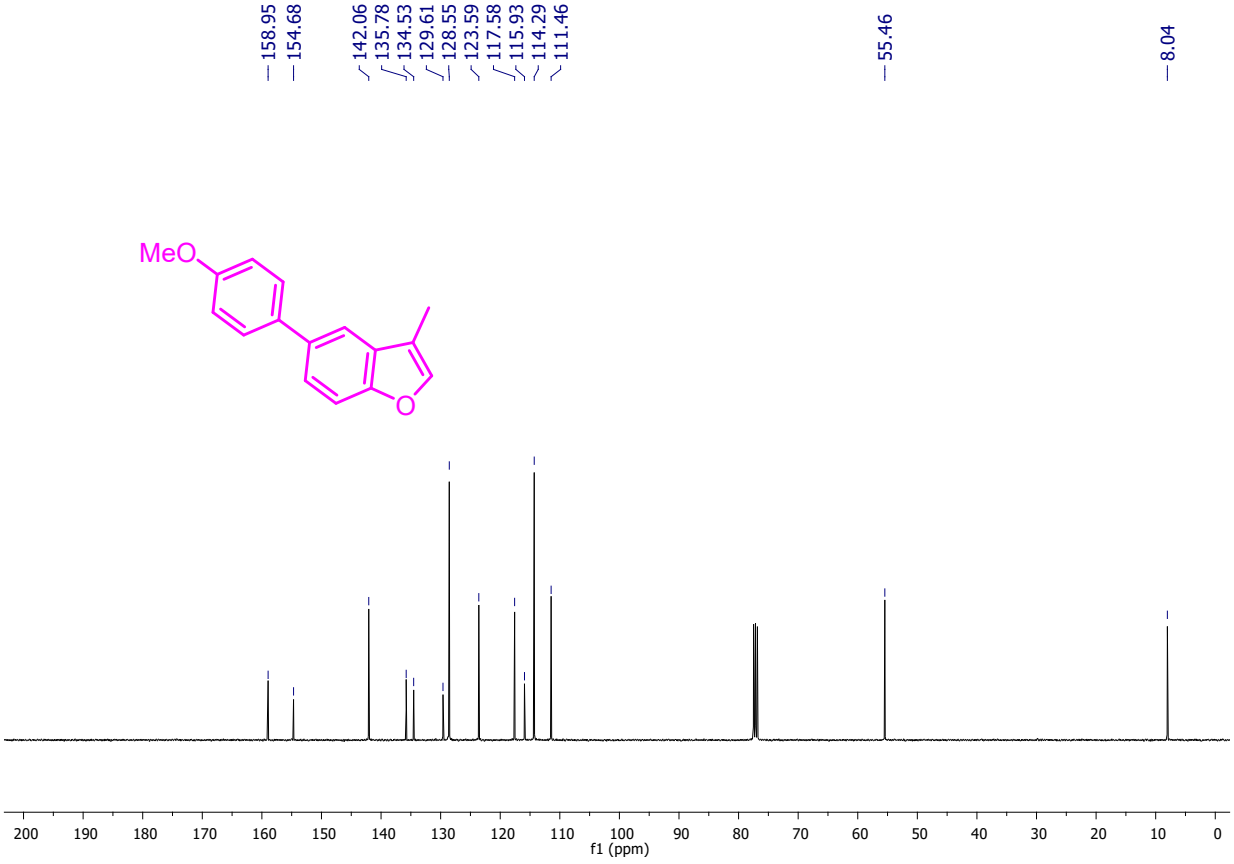
^{13}C {^{1}H} NMR Spectrum of **6g** (100 MHz, $CDCl_3$)



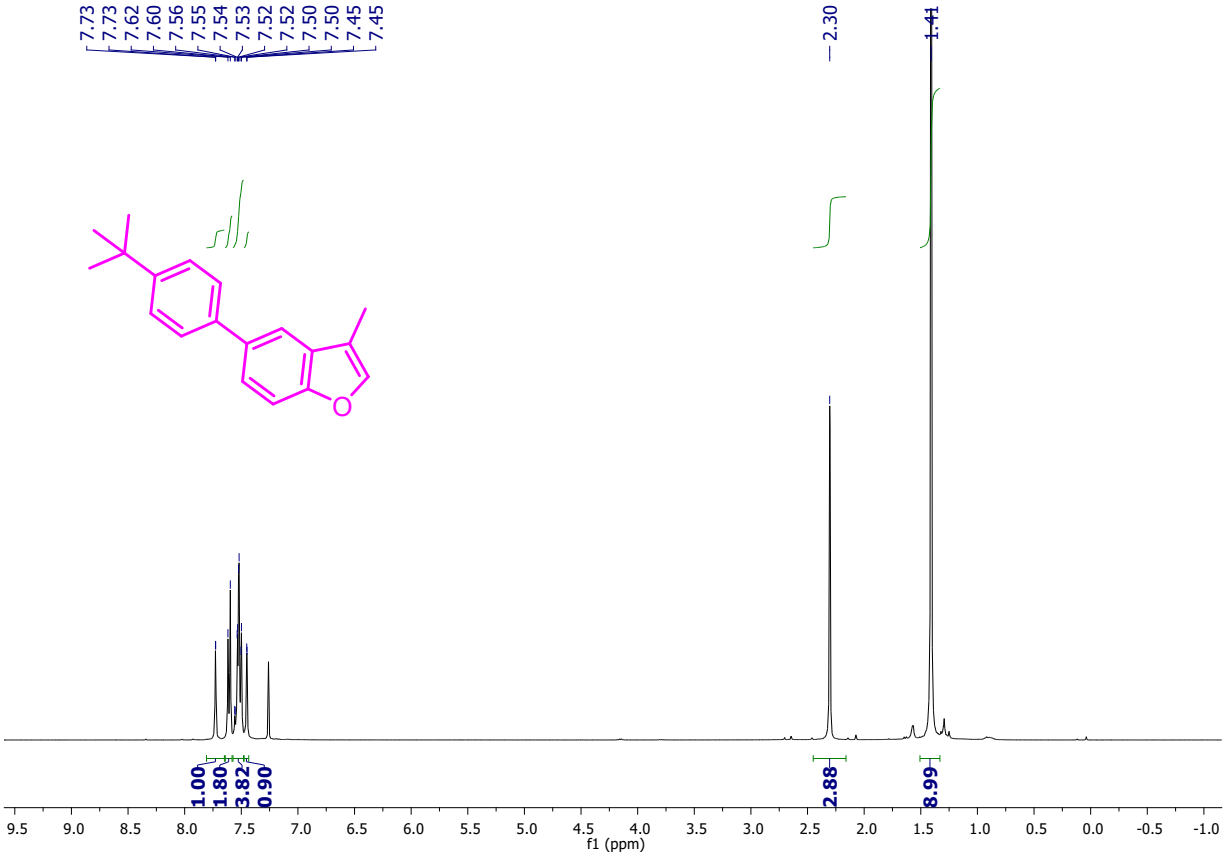
^{1}H NMR Spectrum of **6h** (400 MHz, $CDCl_3$)



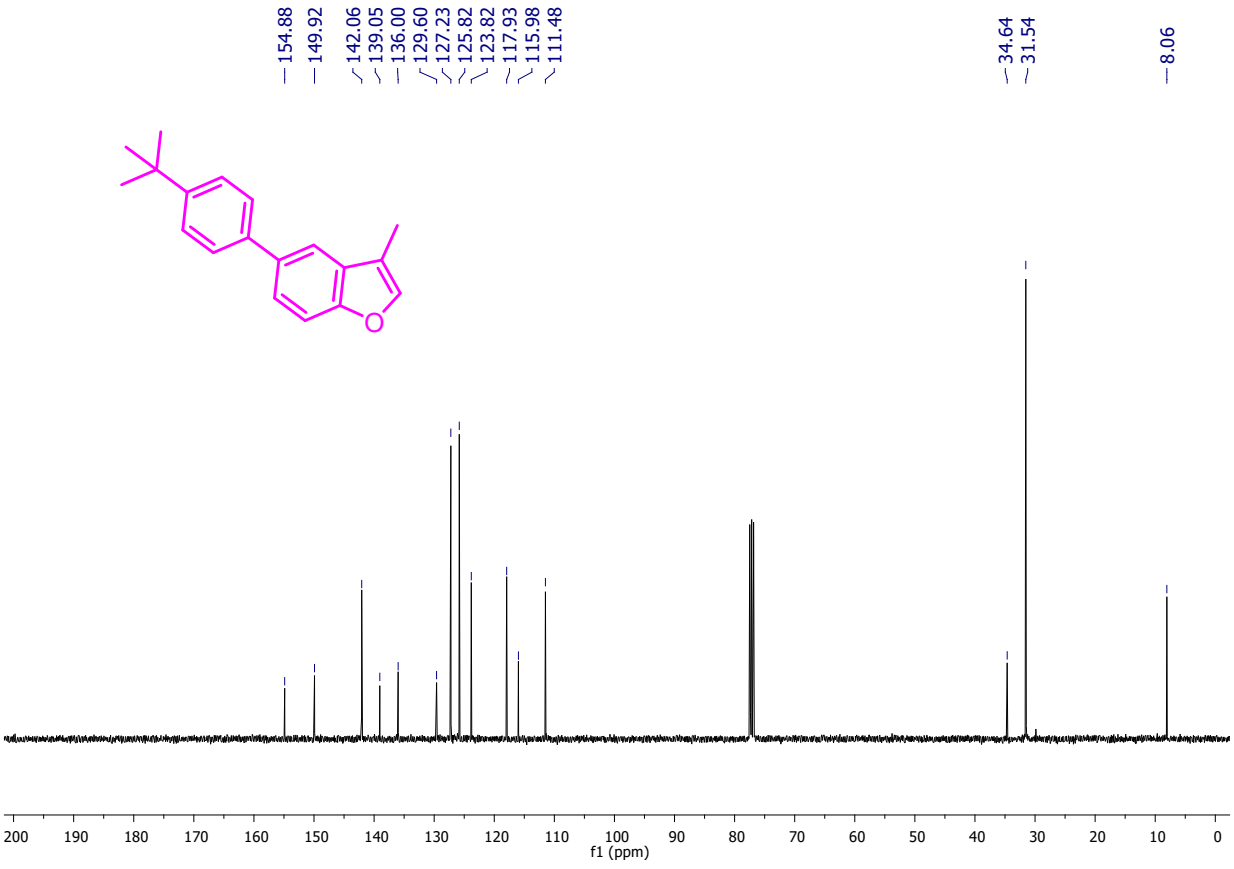
^{13}C {^{1}H} NMR Spectrum of **6h** (100 MHz, $CDCl_3$)



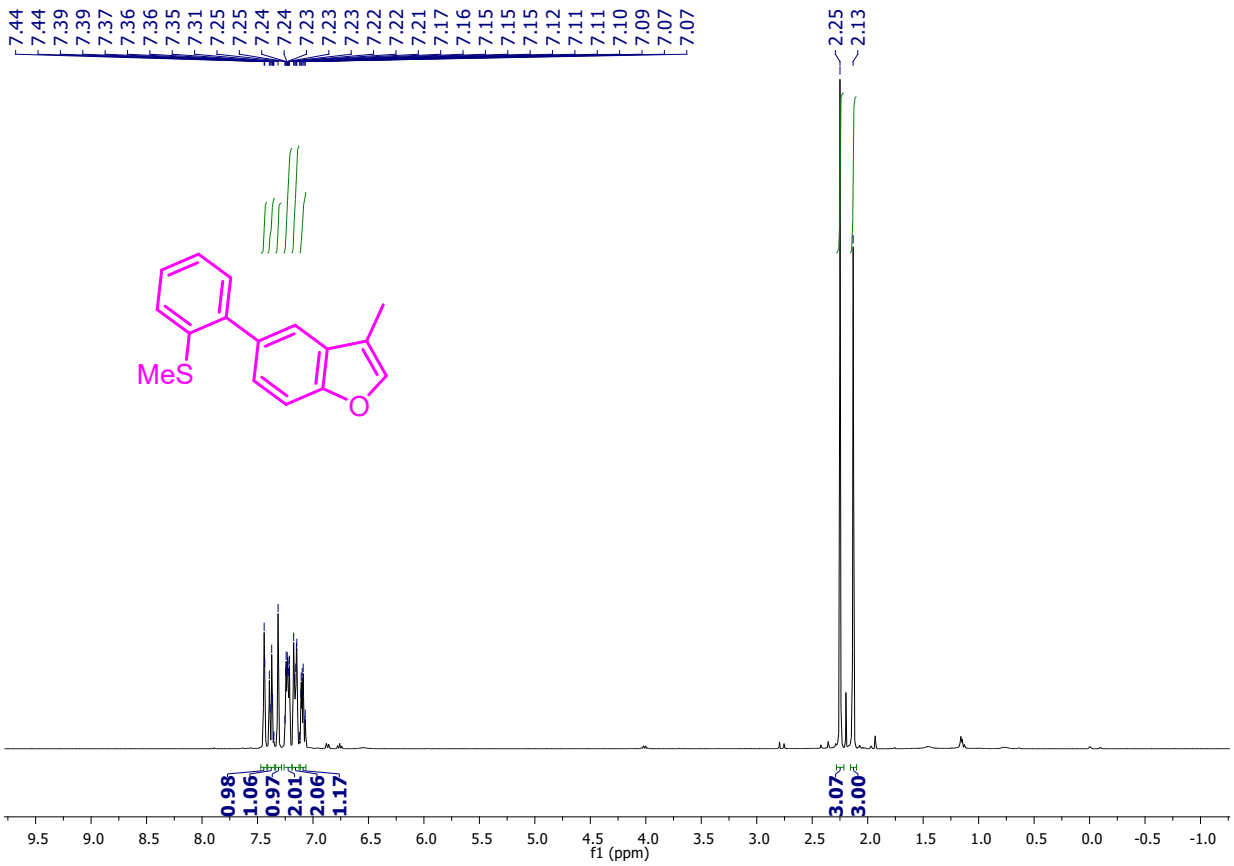
^{1}H NMR Spectrum of **6i** (400 MHz, $CDCl_3$)



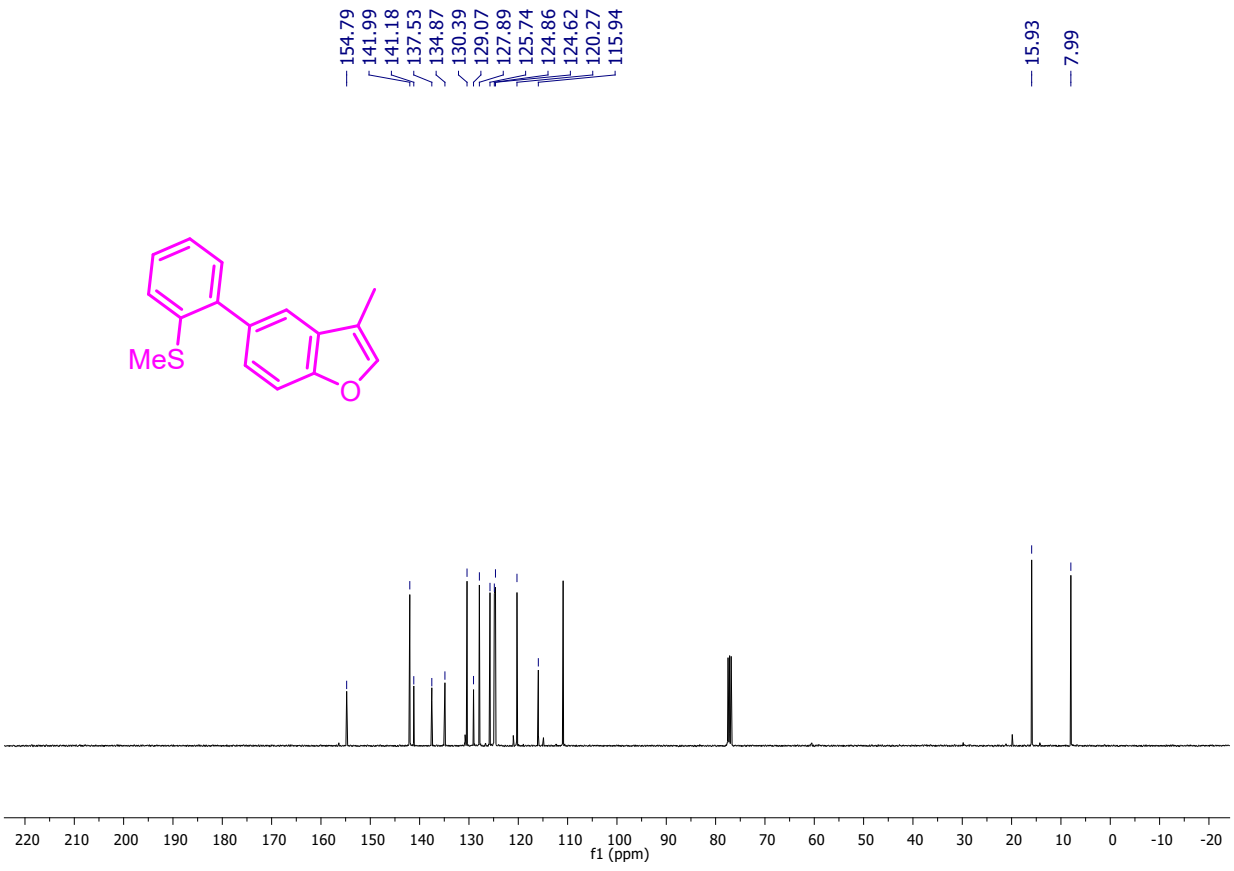
^{13}C {^{1}H} NMR Spectrum of **6i** (100 MHz, $CDCl_3$)



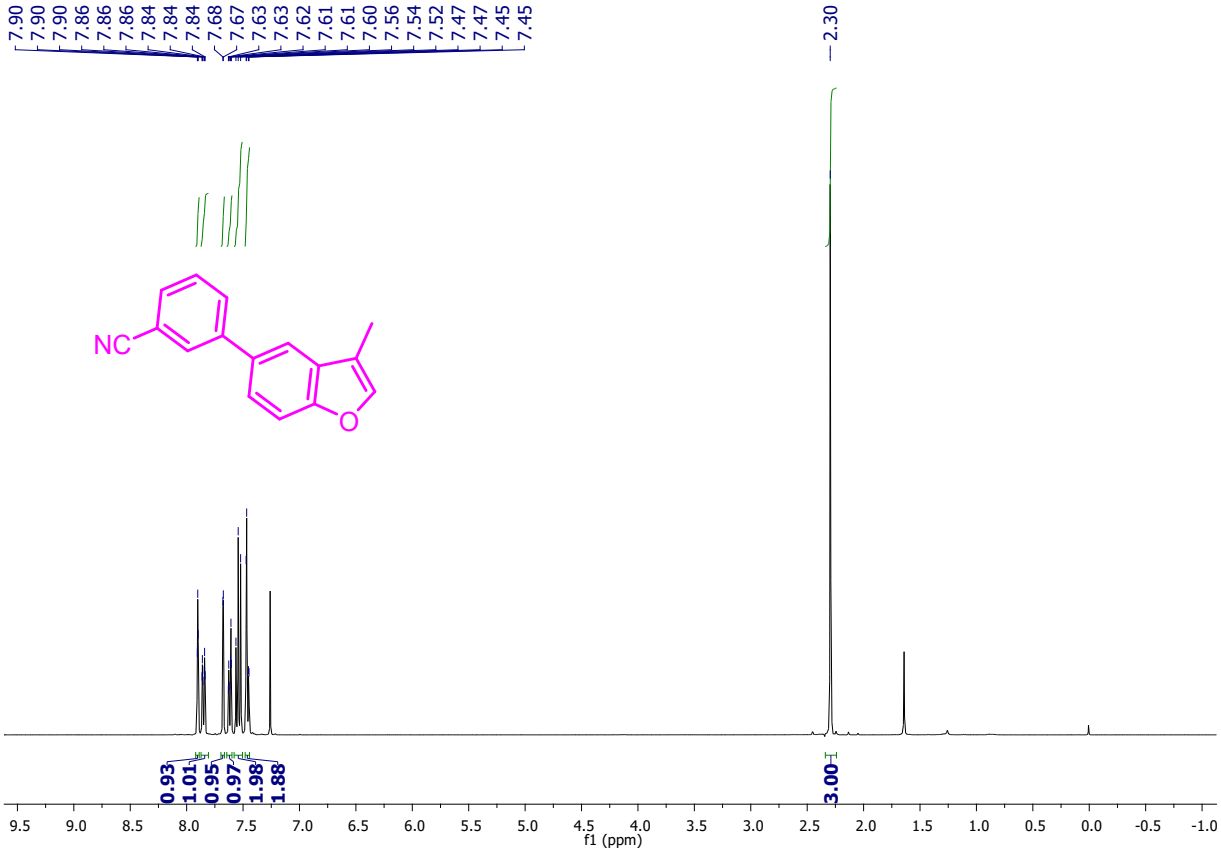
^{1}H NMR Spectrum of **6j** (400 MHz, $CDCl_3$)



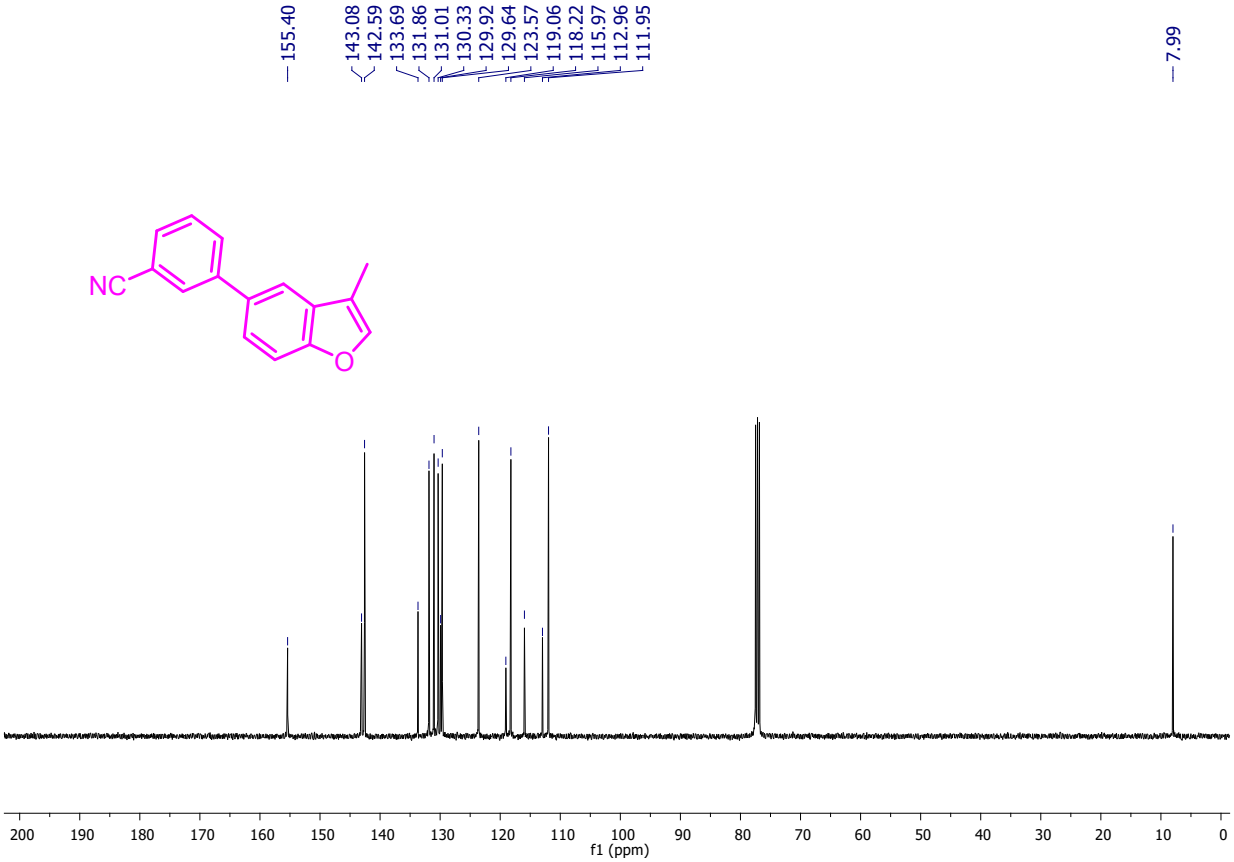
^{13}C {^{1}H} NMR Spectrum of **6j** (100 MHz, $CDCl_3$)



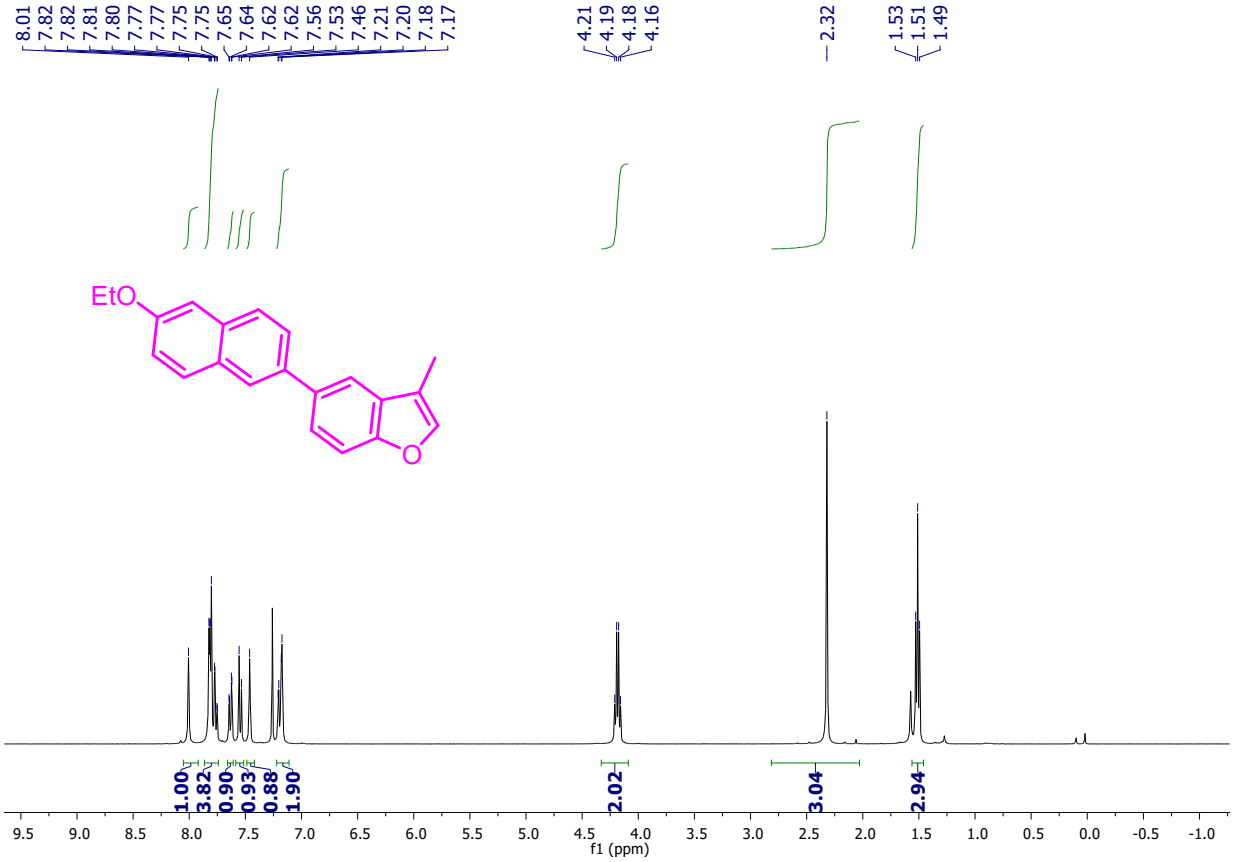
^{1}H NMR Spectrum of **6k** (400 MHz, $CDCl_3$)



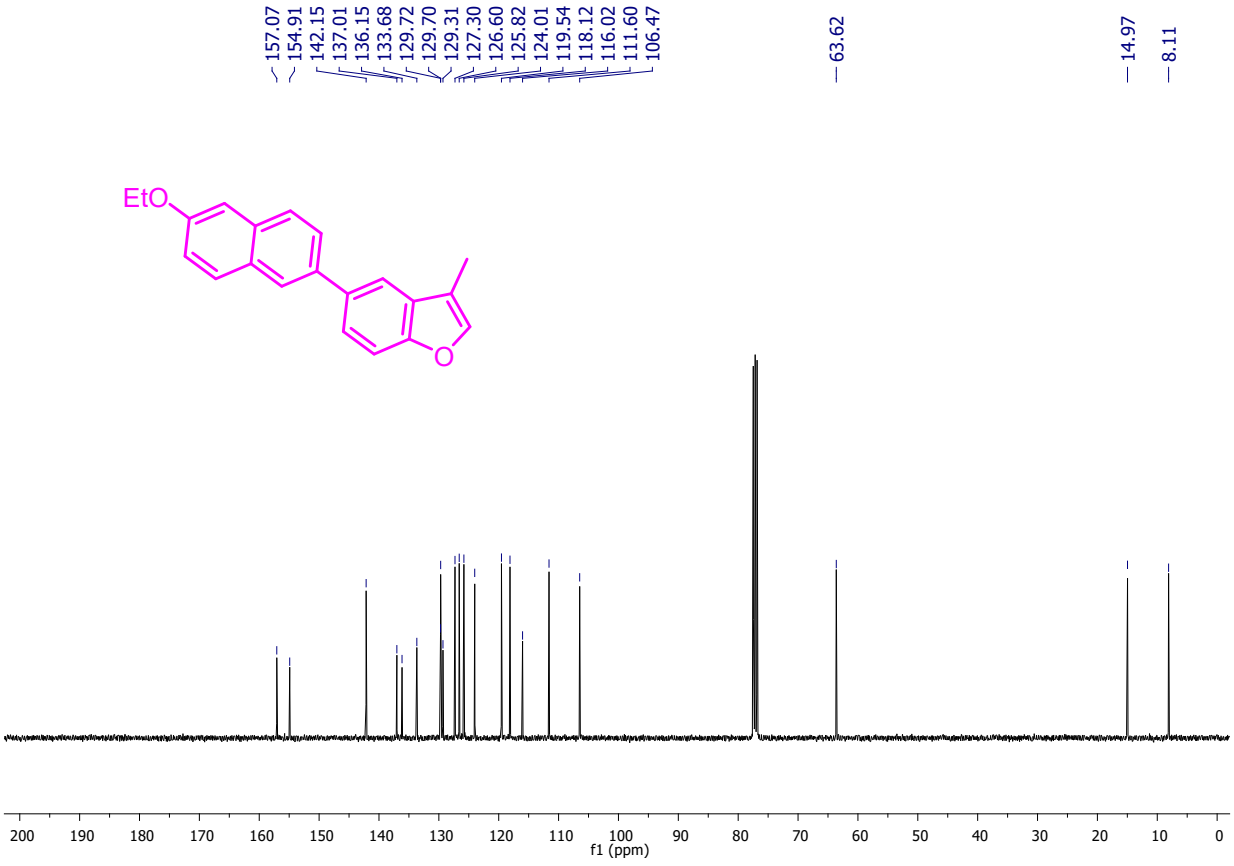
^{13}C {^{1}H} NMR Spectrum of **6k** (100 MHz, $CDCl_3$)



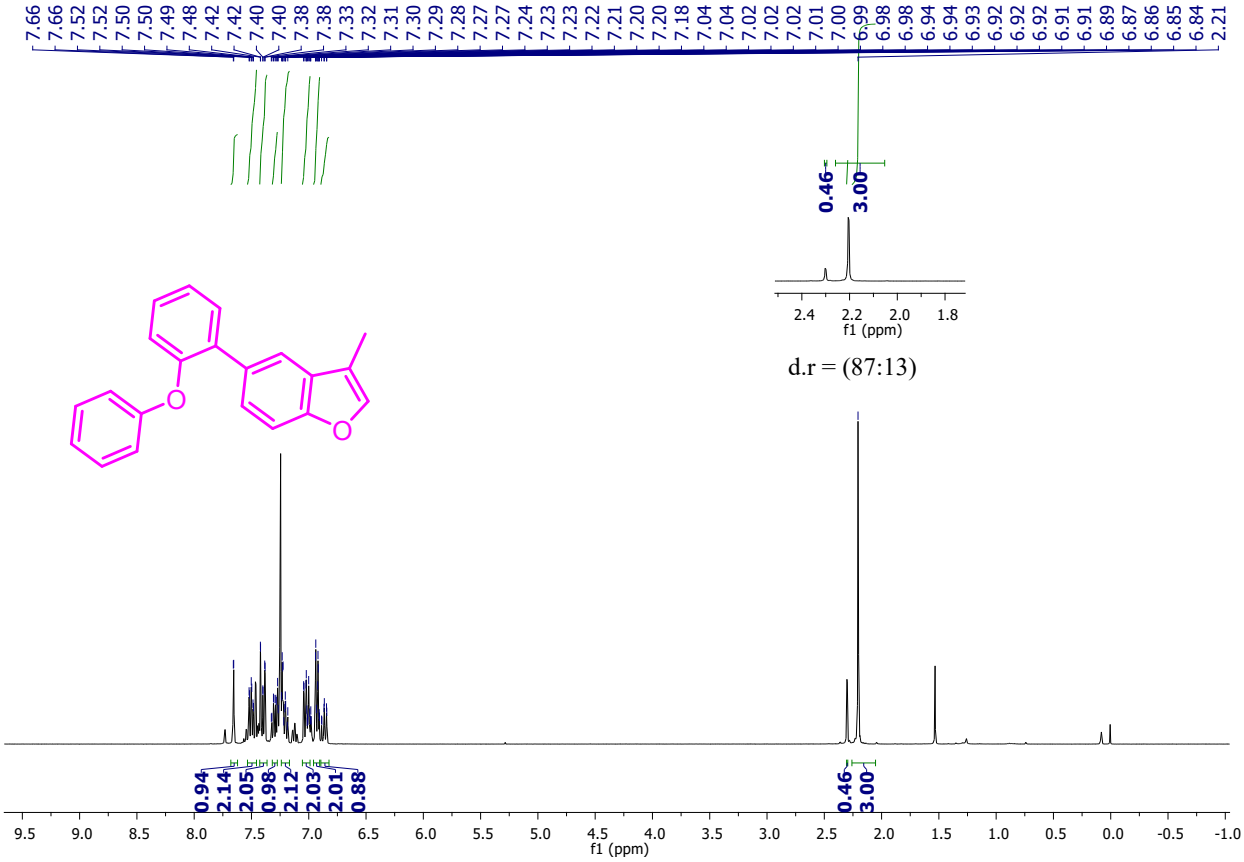
^{1}H NMR Spectrum of **6l** (400 MHz, $CDCl_3$)



^{13}C {^{1}H} NMR Spectrum of **6l** (100 MHz, $CDCl_3$)



^{1}H NMR Spectrum of **6m** (400 MHz, $CDCl_3$)



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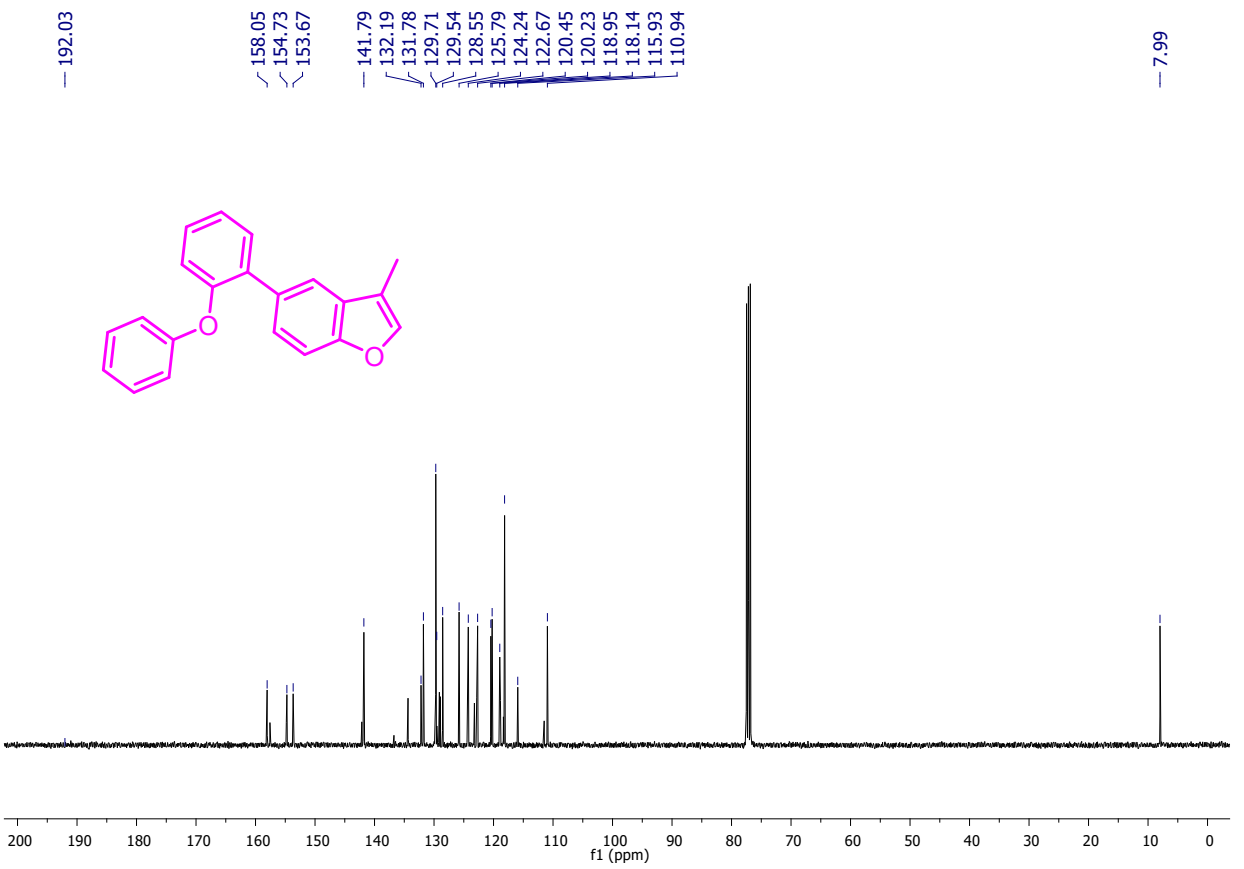
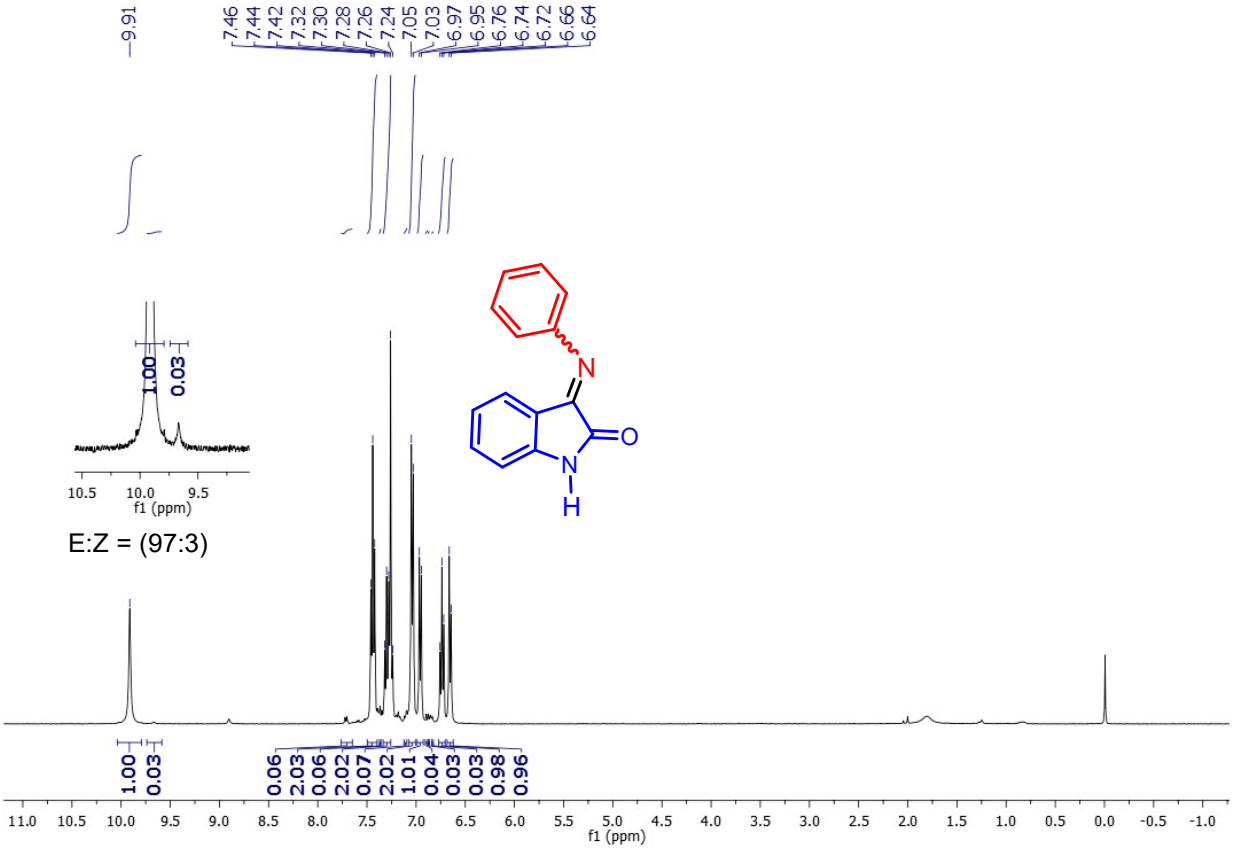
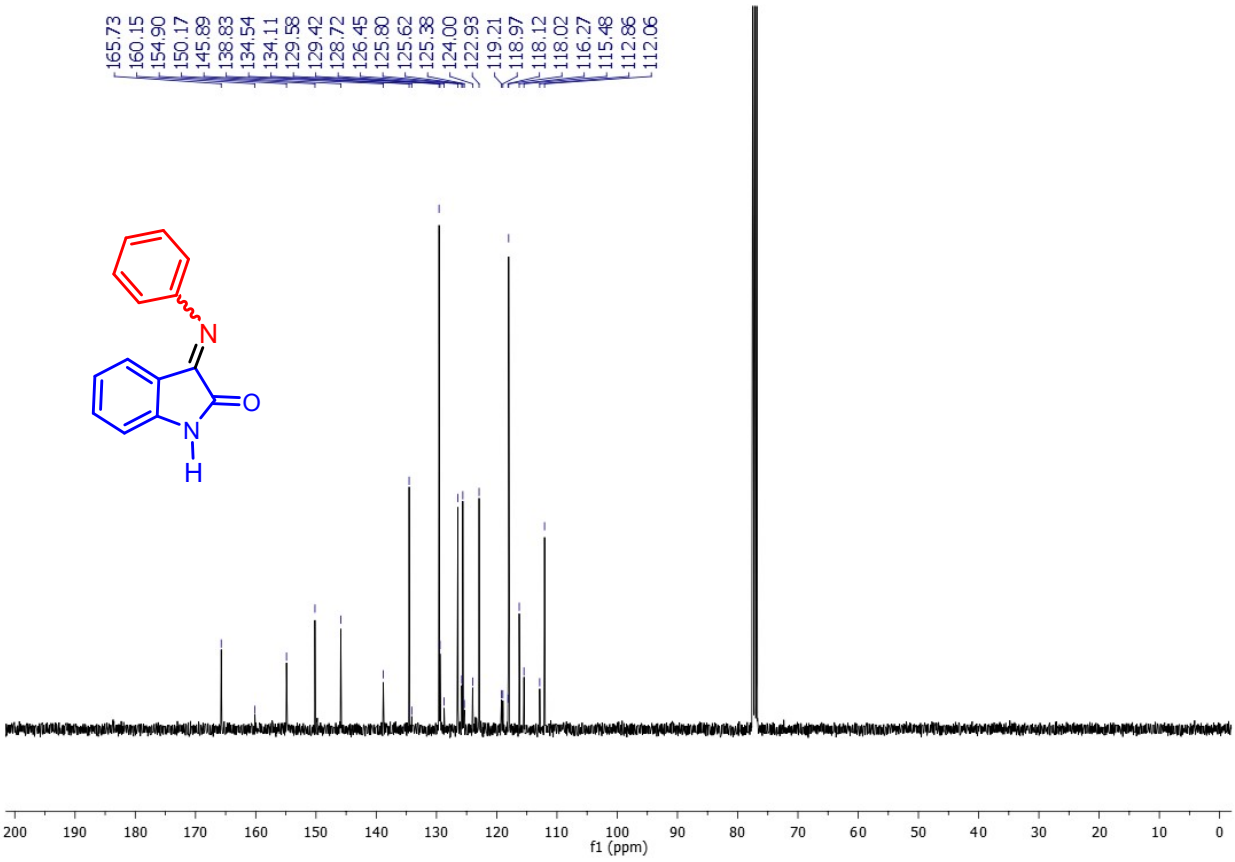


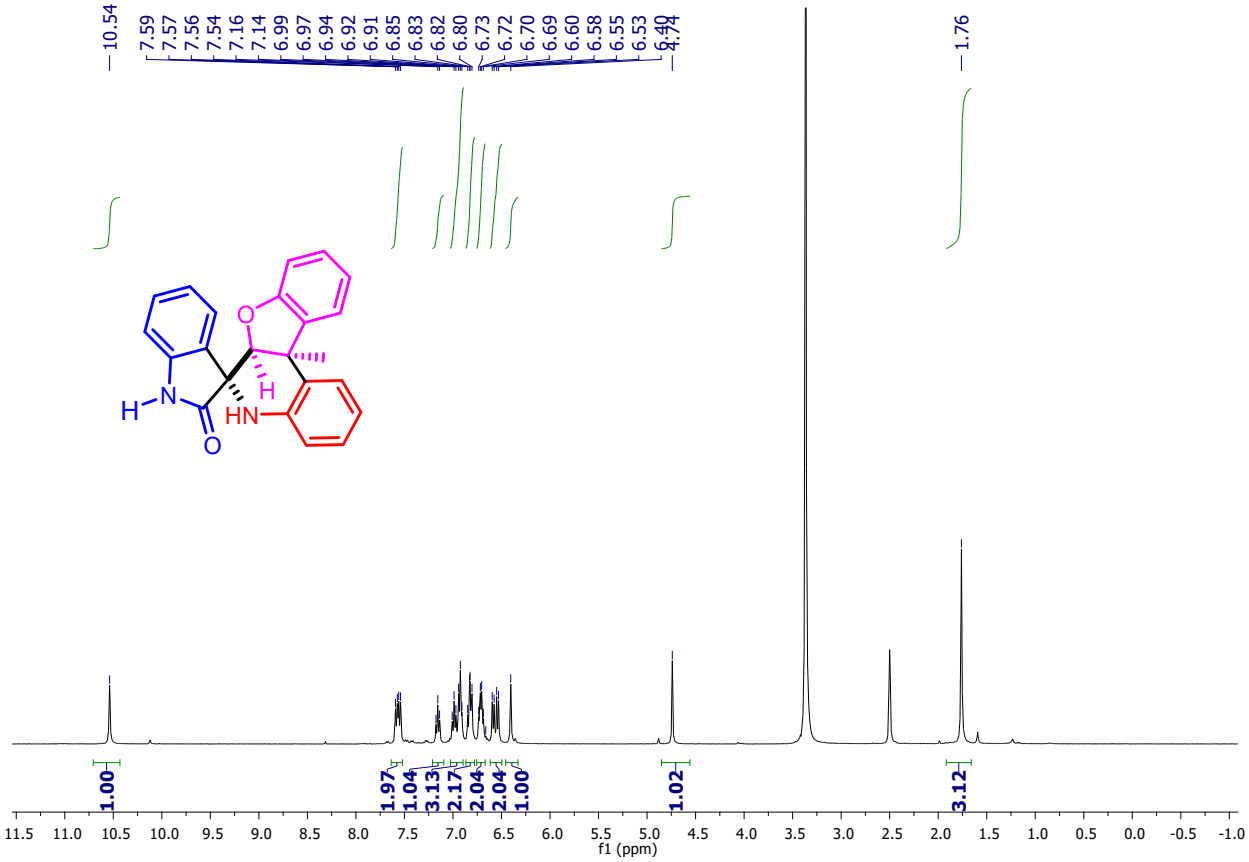
^{1}H NMR Spectrum of **7a** (400 MHz, $CDCl_3$)



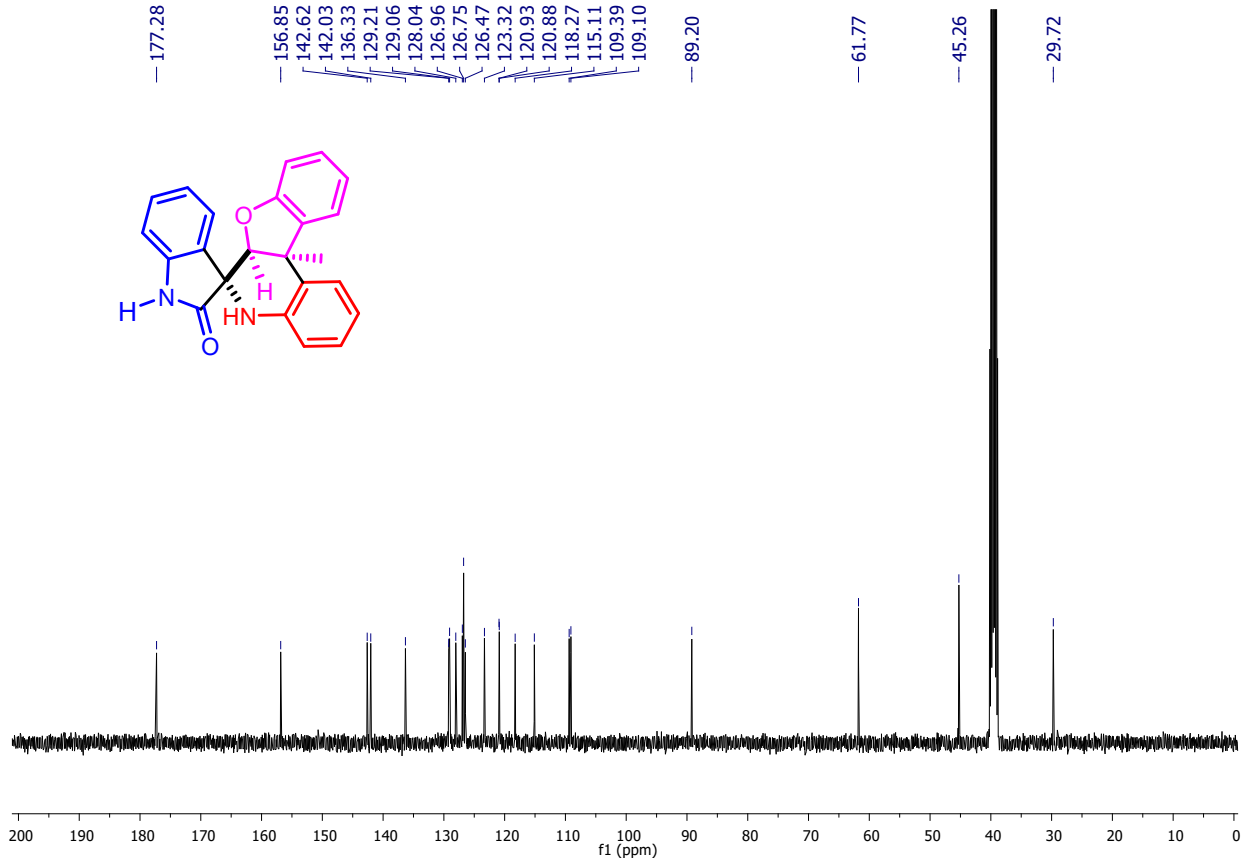
^{13}C NMR Spectrum of **7a** (400 MHz, $CDCl_3$)



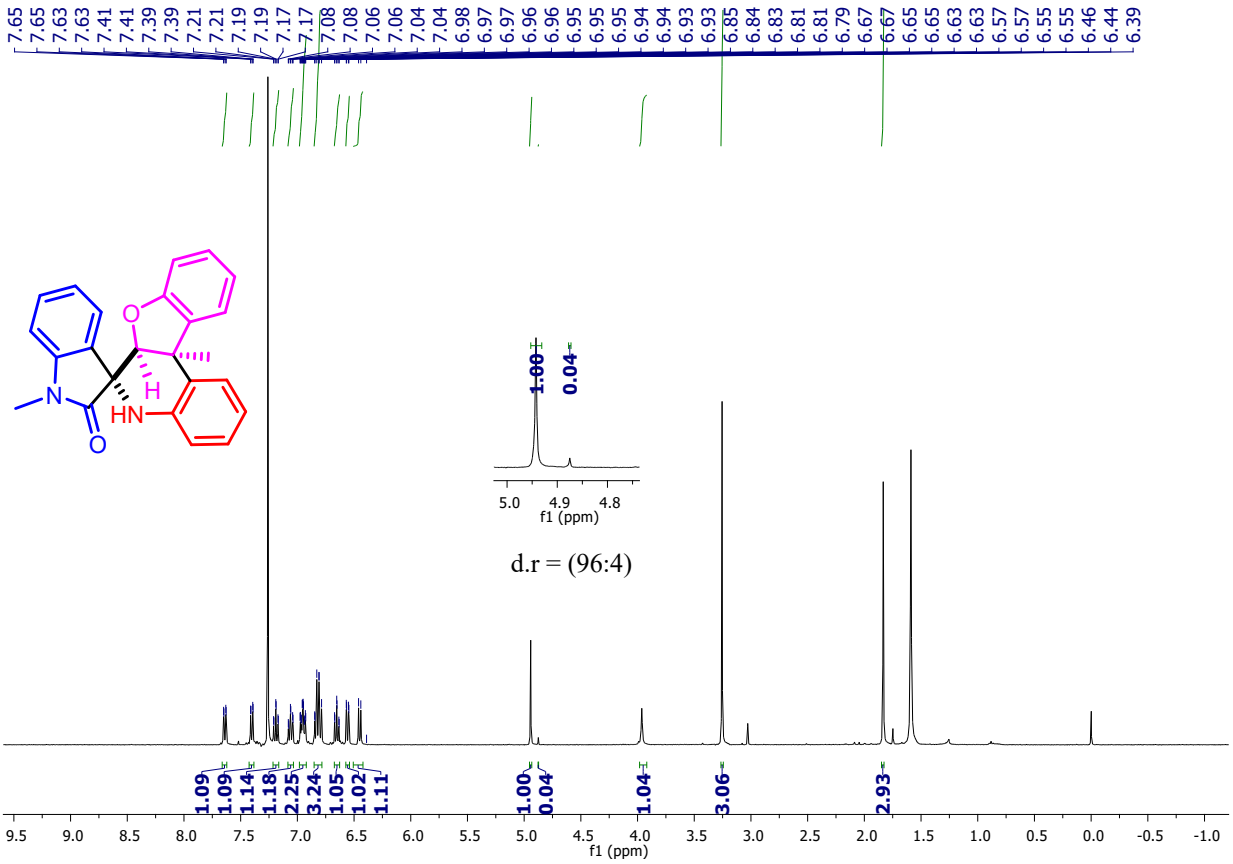
^{1}H NMR Spectrum of **8a** (400 MHz, DMSO-d_6)



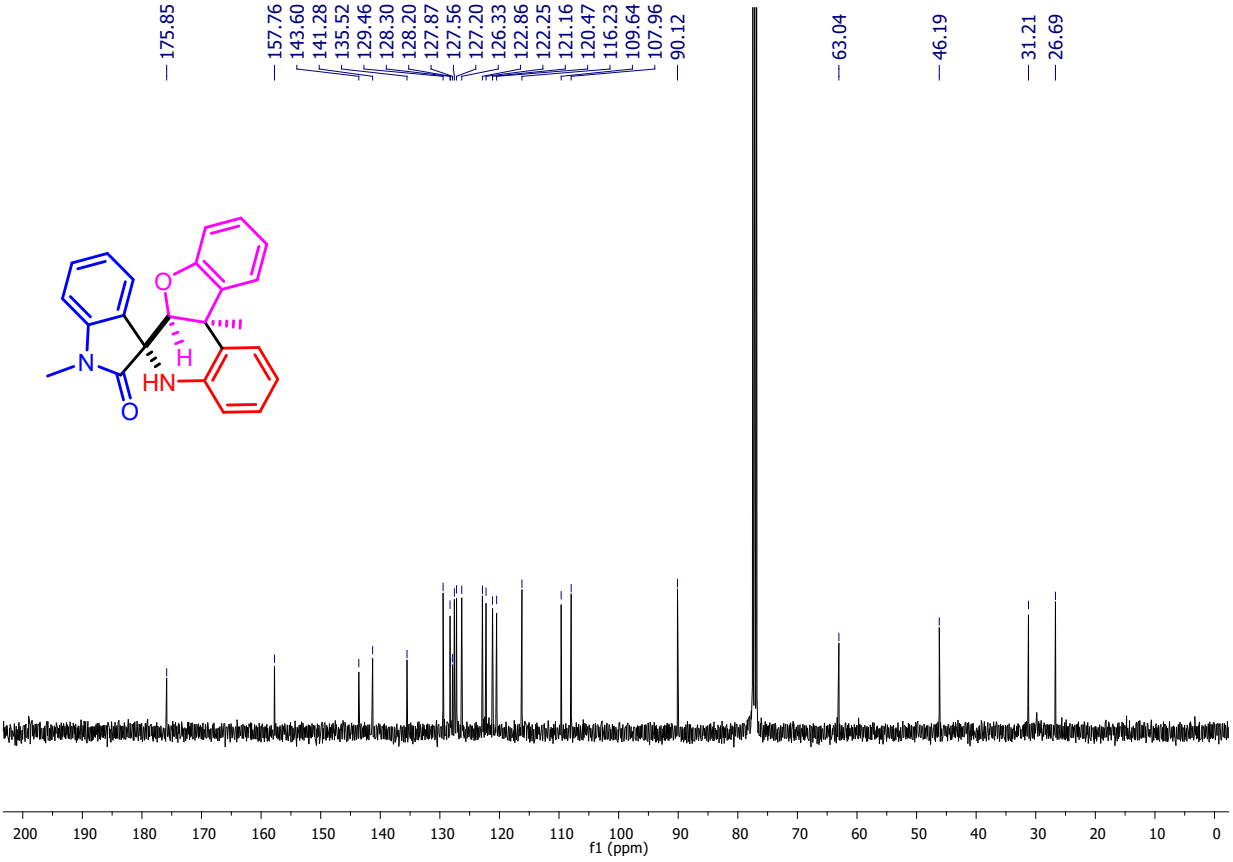
^{13}C {^{1}H} NMR Spectrum of **8a** (100 MHz, DMSO-d_6)



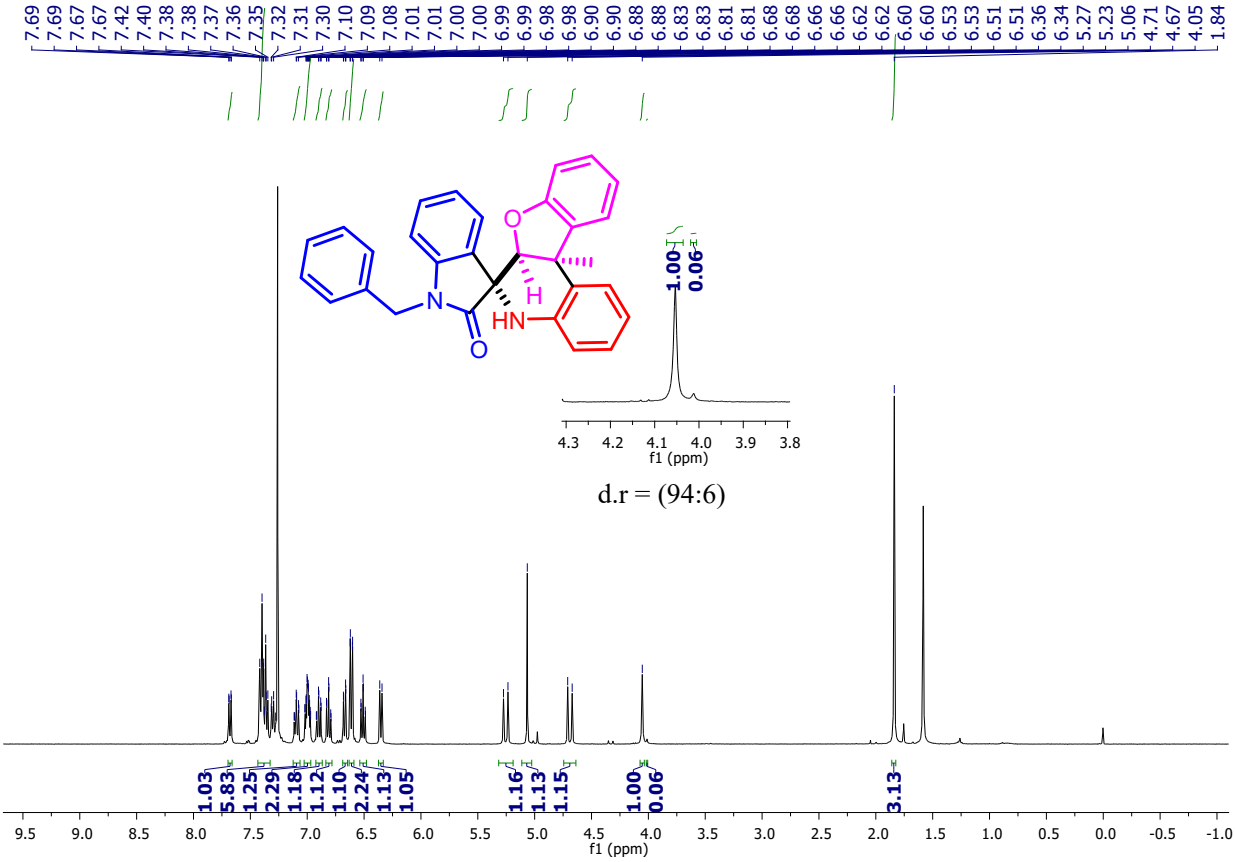
^{1}H NMR Spectrum of **8b** (400 MHz, $CDCl_3$)



^{13}C {^{1}H} NMR Spectrum of **8b** (100 MHz, $CDCl_3$)



^{1}H NMR Spectrum of **8c** (400 MHz, $CDCl_3$)



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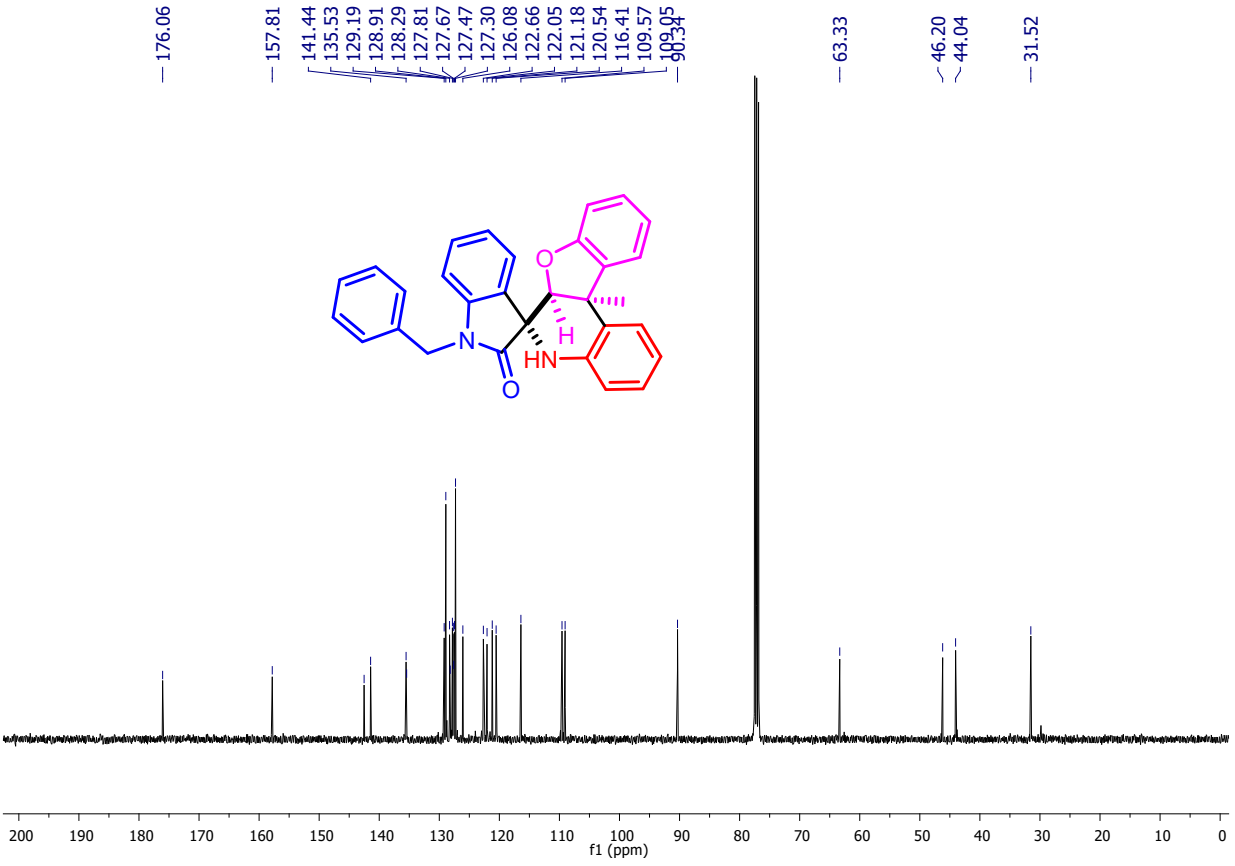
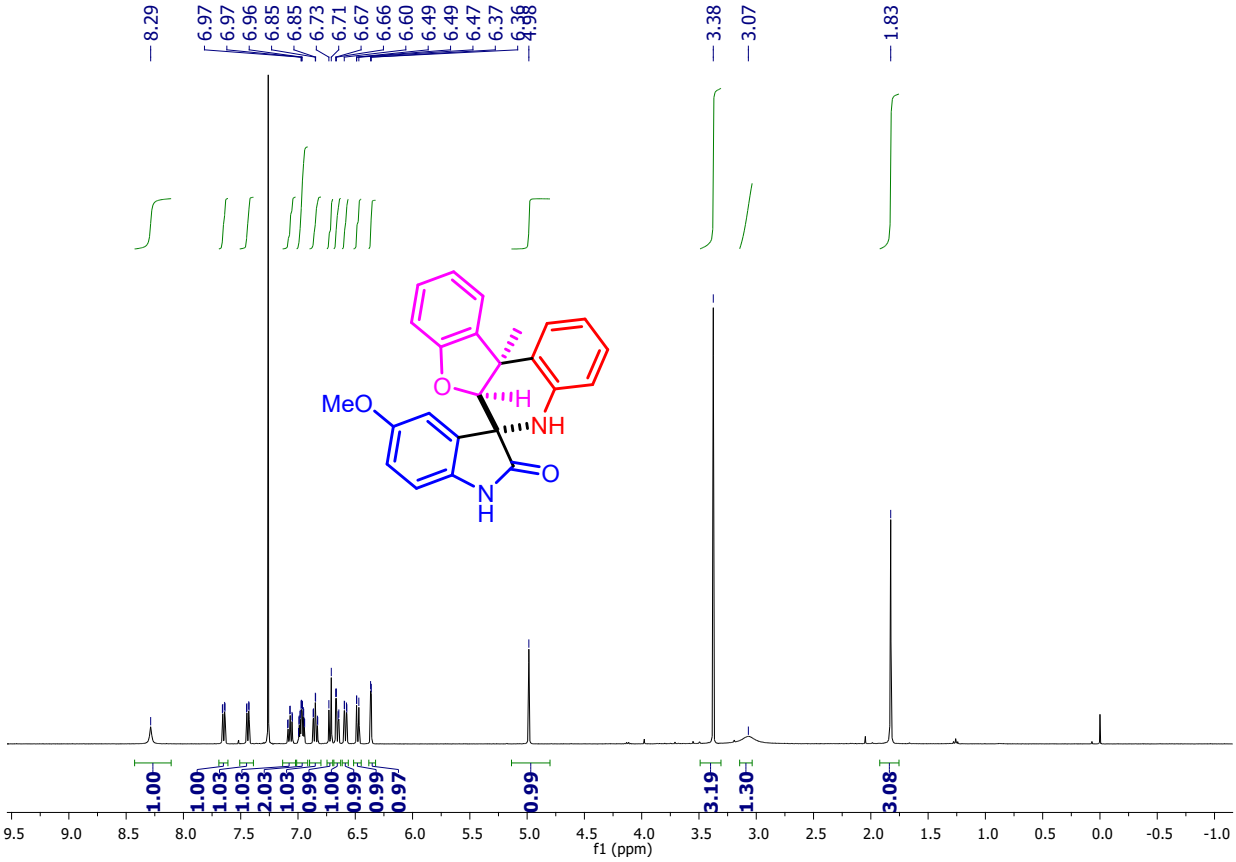
^{13}C {^{1}H} NMR Spectrum of **8c** (100 MHz, $CDCl_3$)



^{1}H NMR Spectrum of **8d** (400 MHz, $CDCl_3$)



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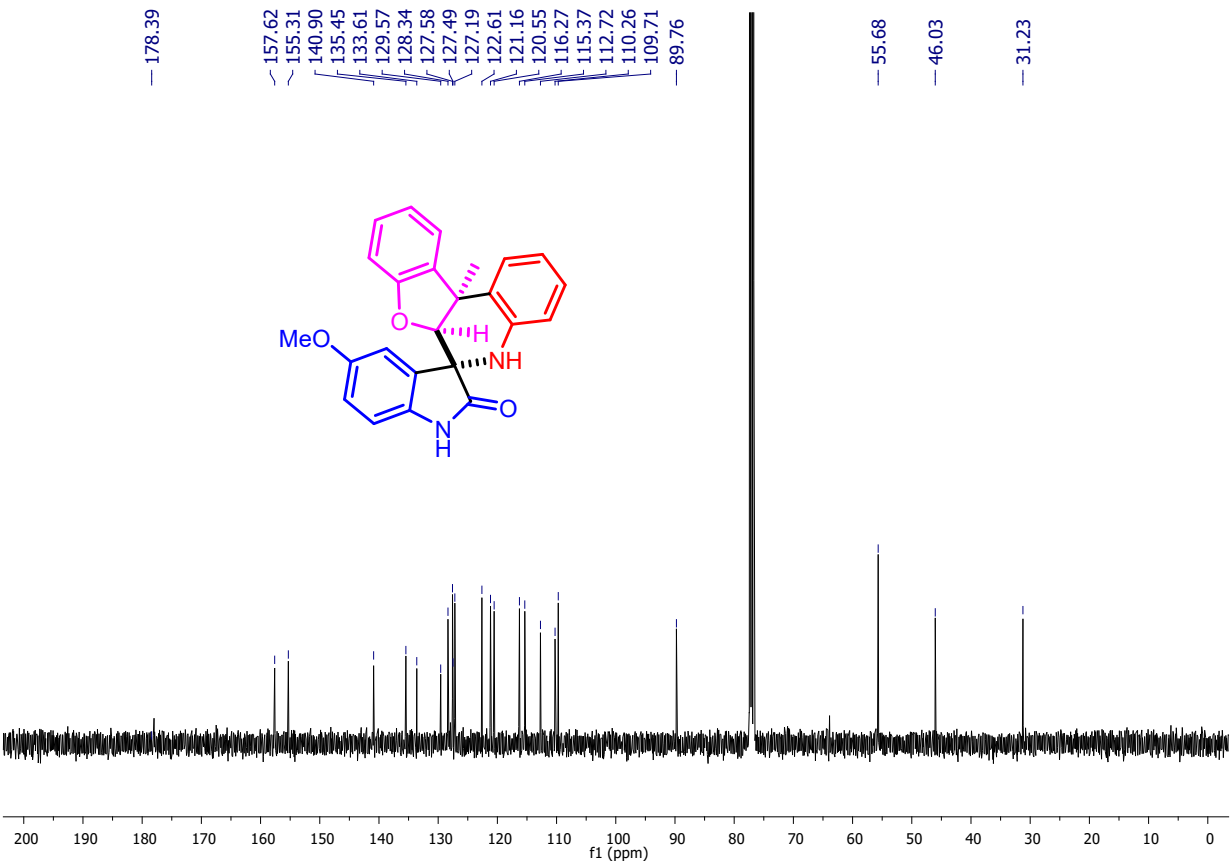
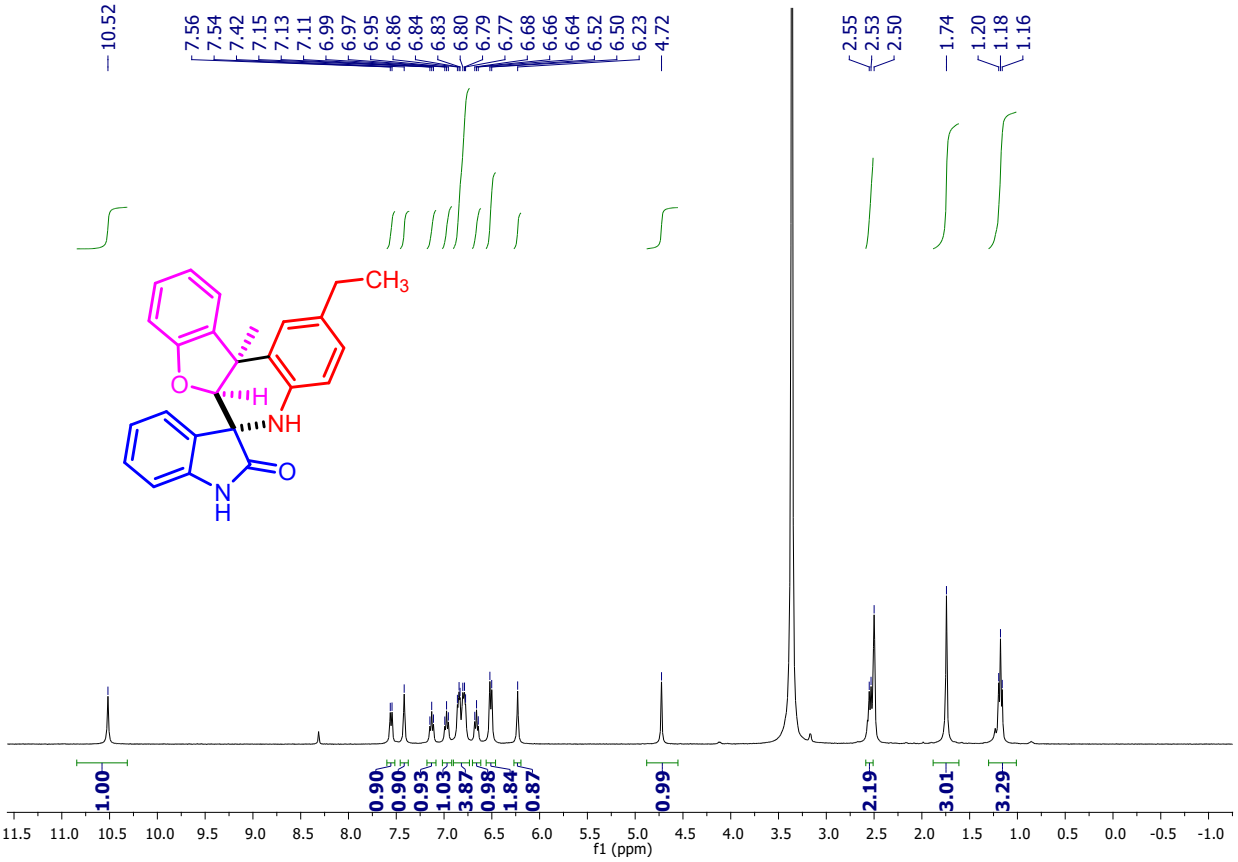
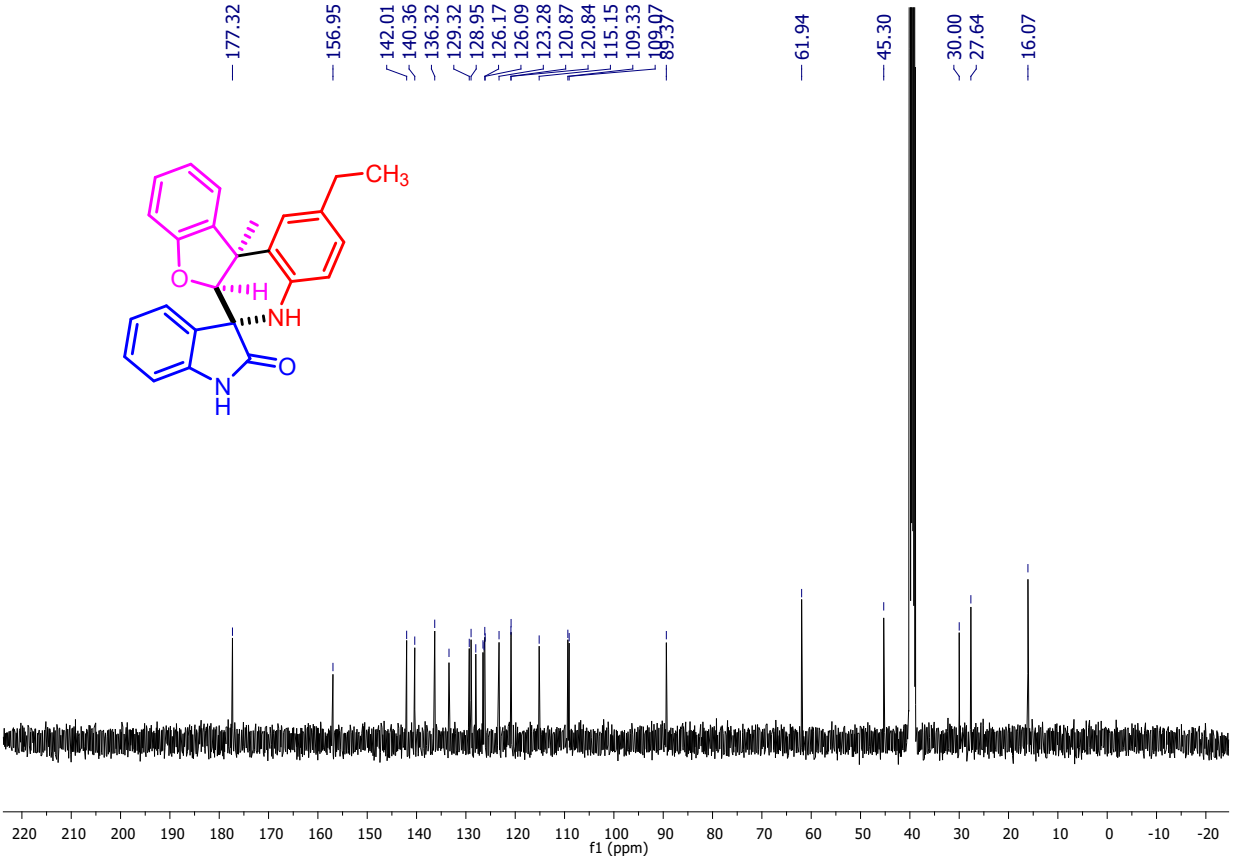


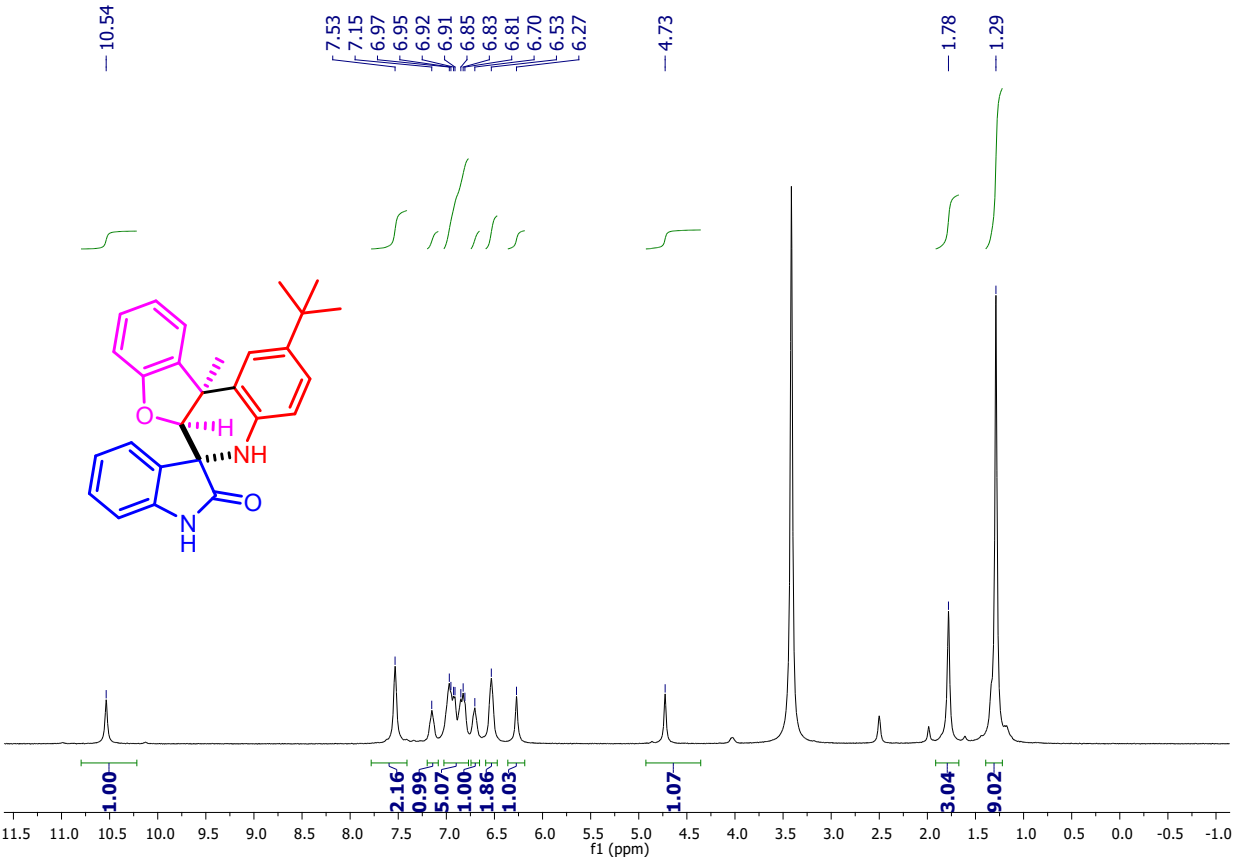
^{1}H NMR Spectrum of **8e** (400 MHz, DMSO-d_6)



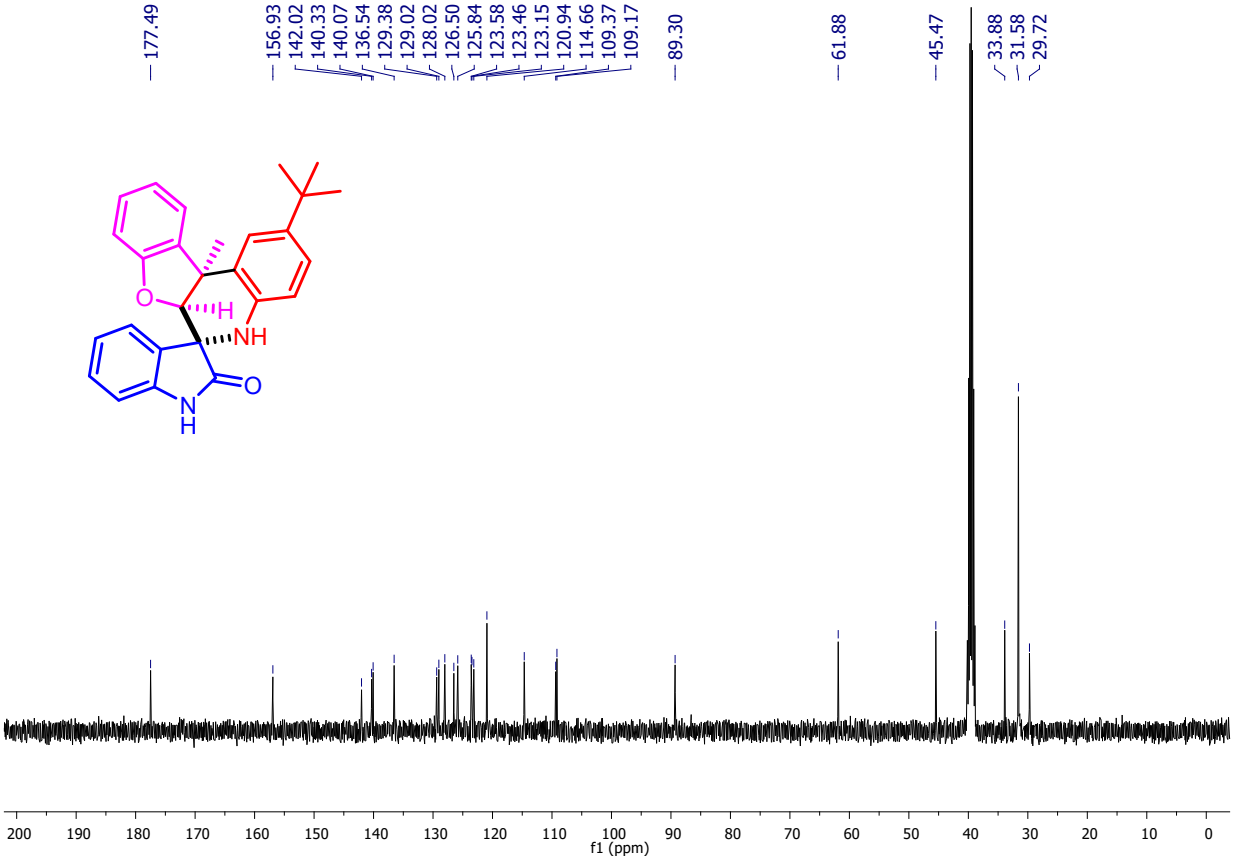
^{13}C {^{1}H} NMR Spectrum of **8e** (100 MHz, DMSO-d_6)



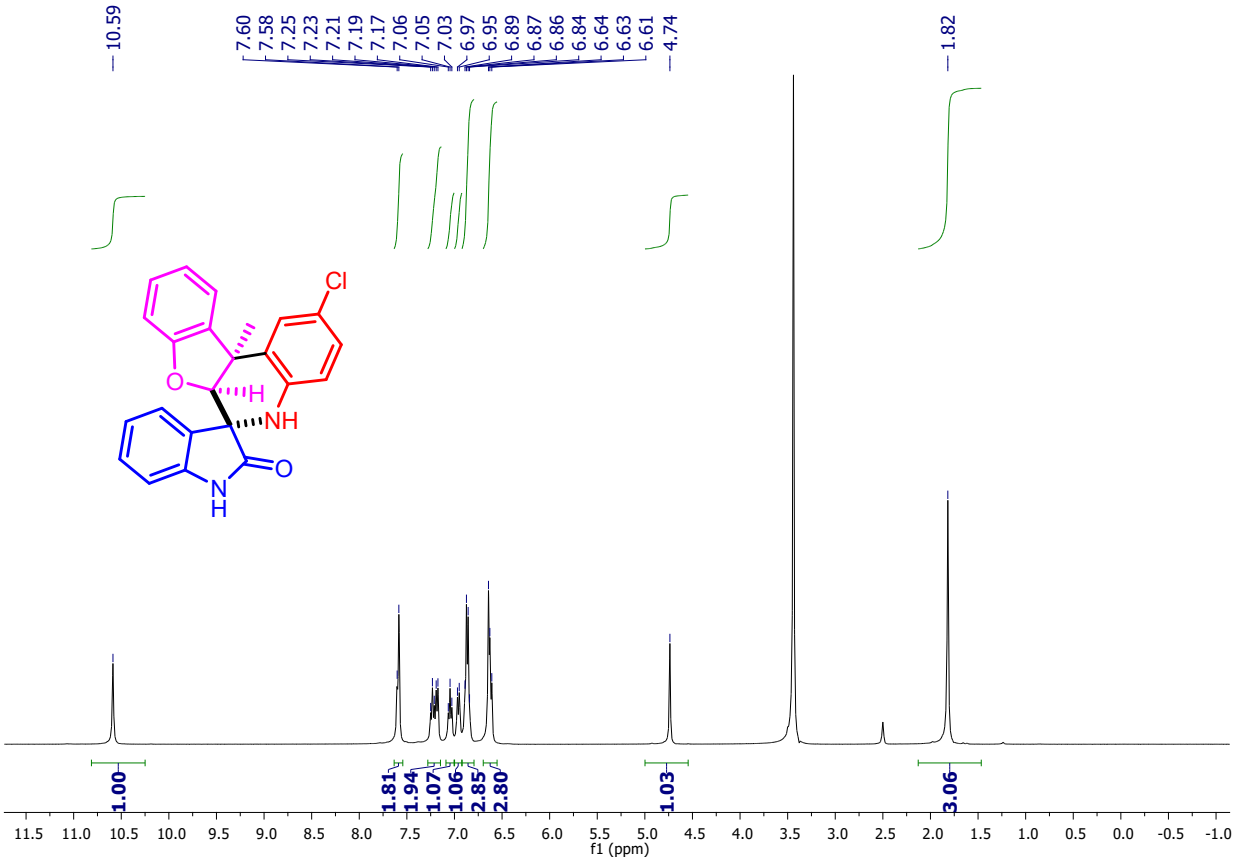
^{1}H NMR Spectrum of **8f** (400 MHz, DMSO-d_6)



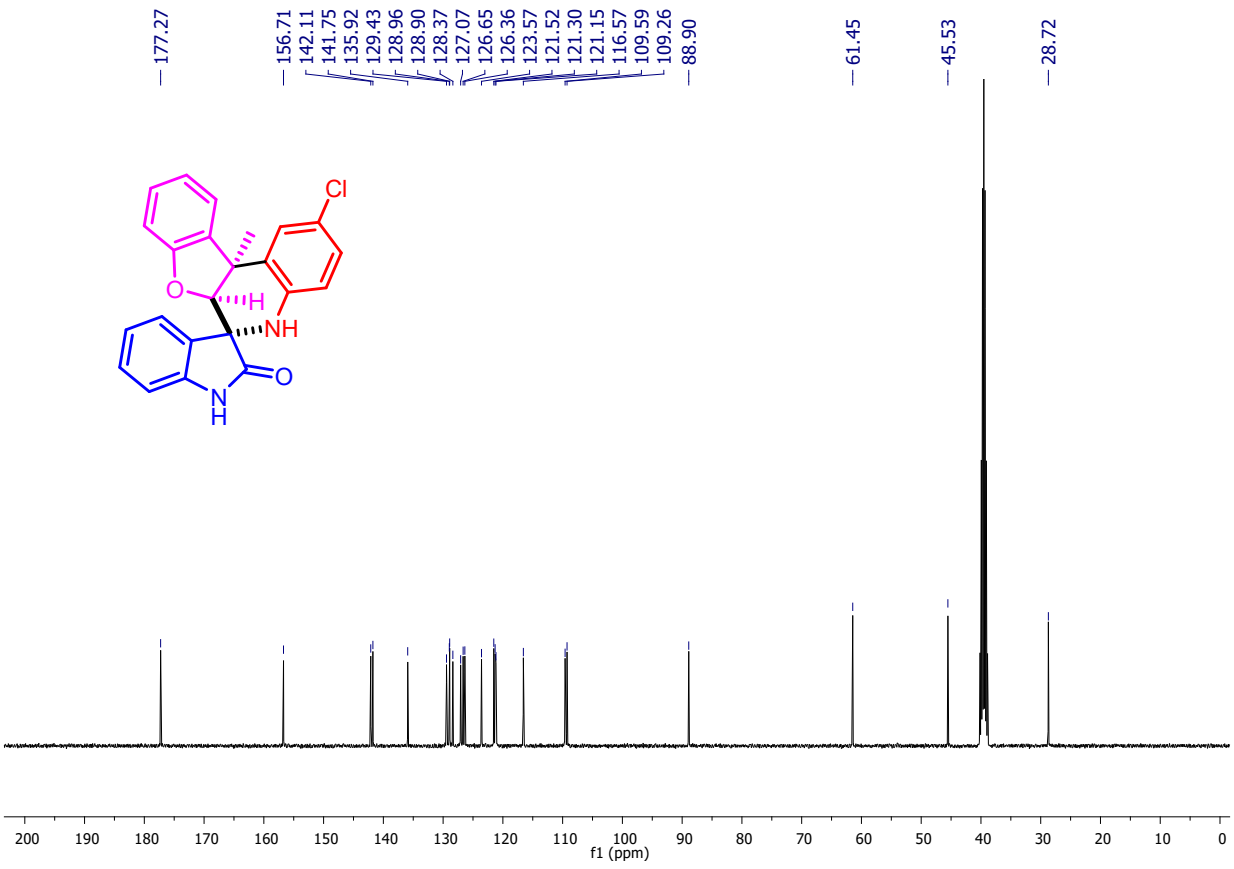
^{13}C {^{1}H} NMR Spectrum of **8f** (100 MHz, DMSO-d_6)



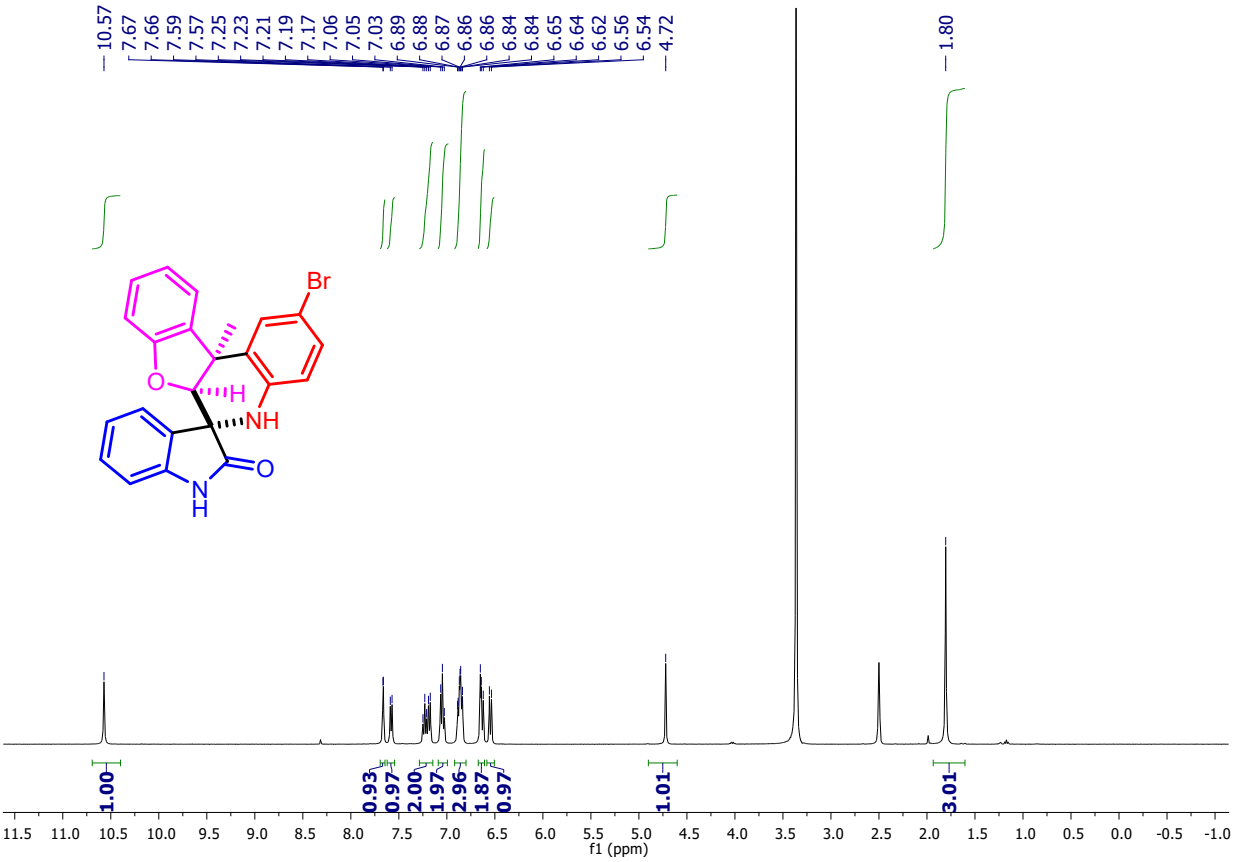
^{1}H NMR Spectrum of **8g** (400 MHz, DMSO-d_6)



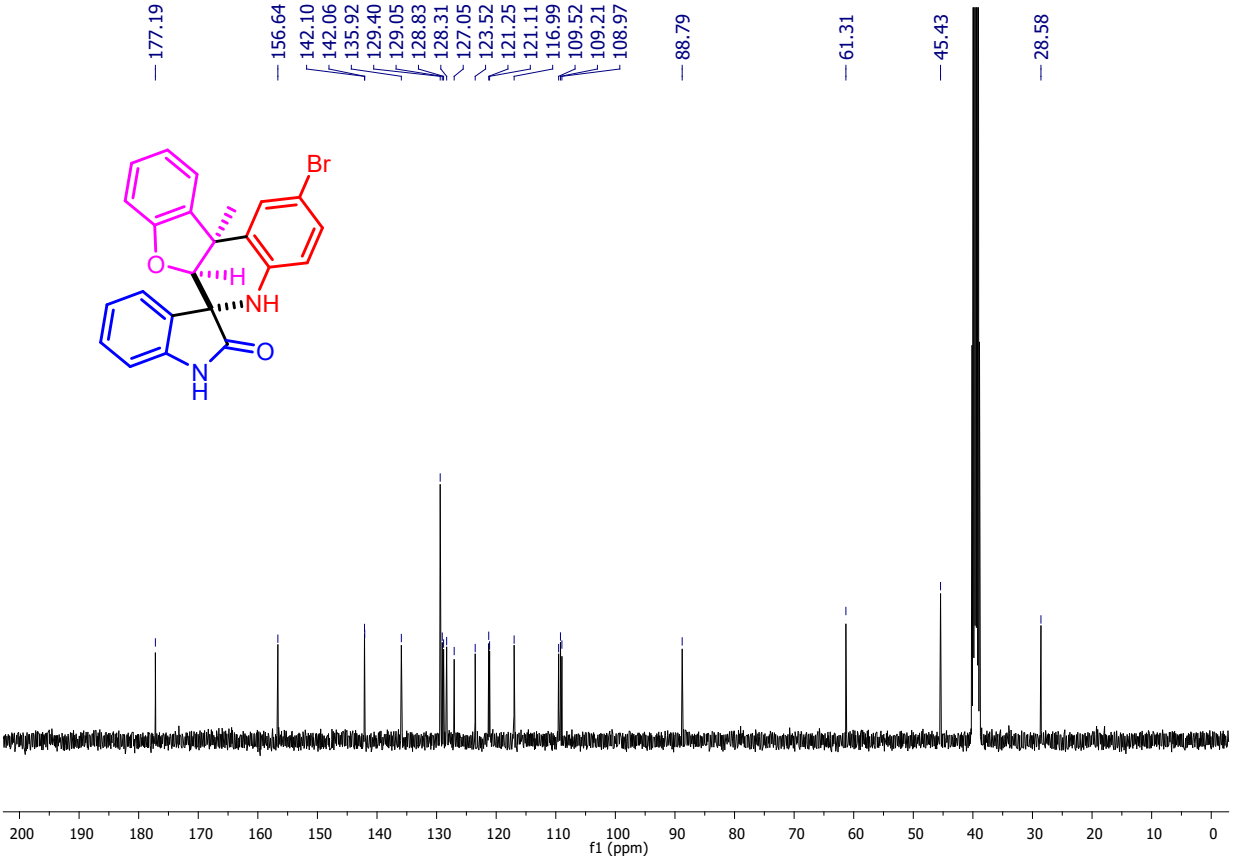
^{13}C {^{1}H} NMR Spectrum of **8g** (100 MHz, DMSO-d_6)



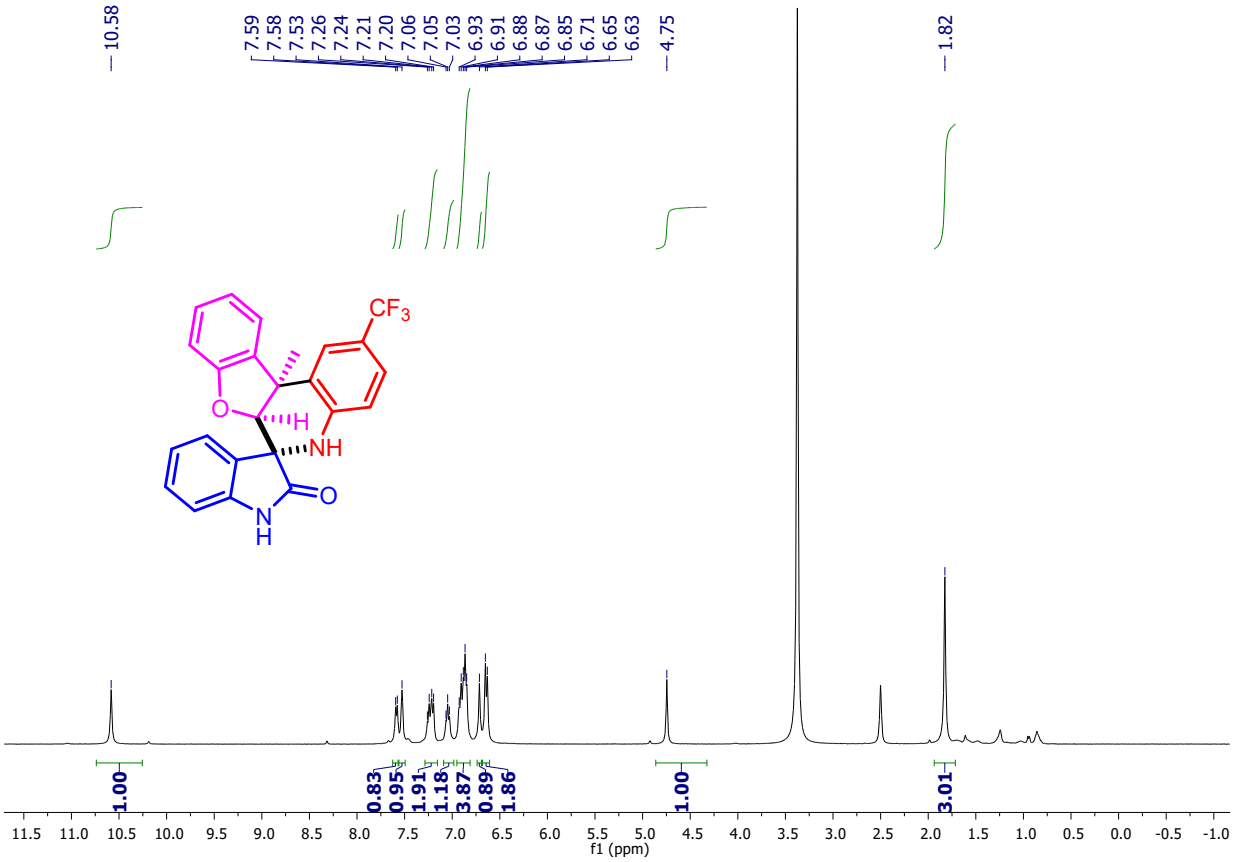
^{1}H NMR Spectrum of **8h** (400 MHz, DMSO-d_6)



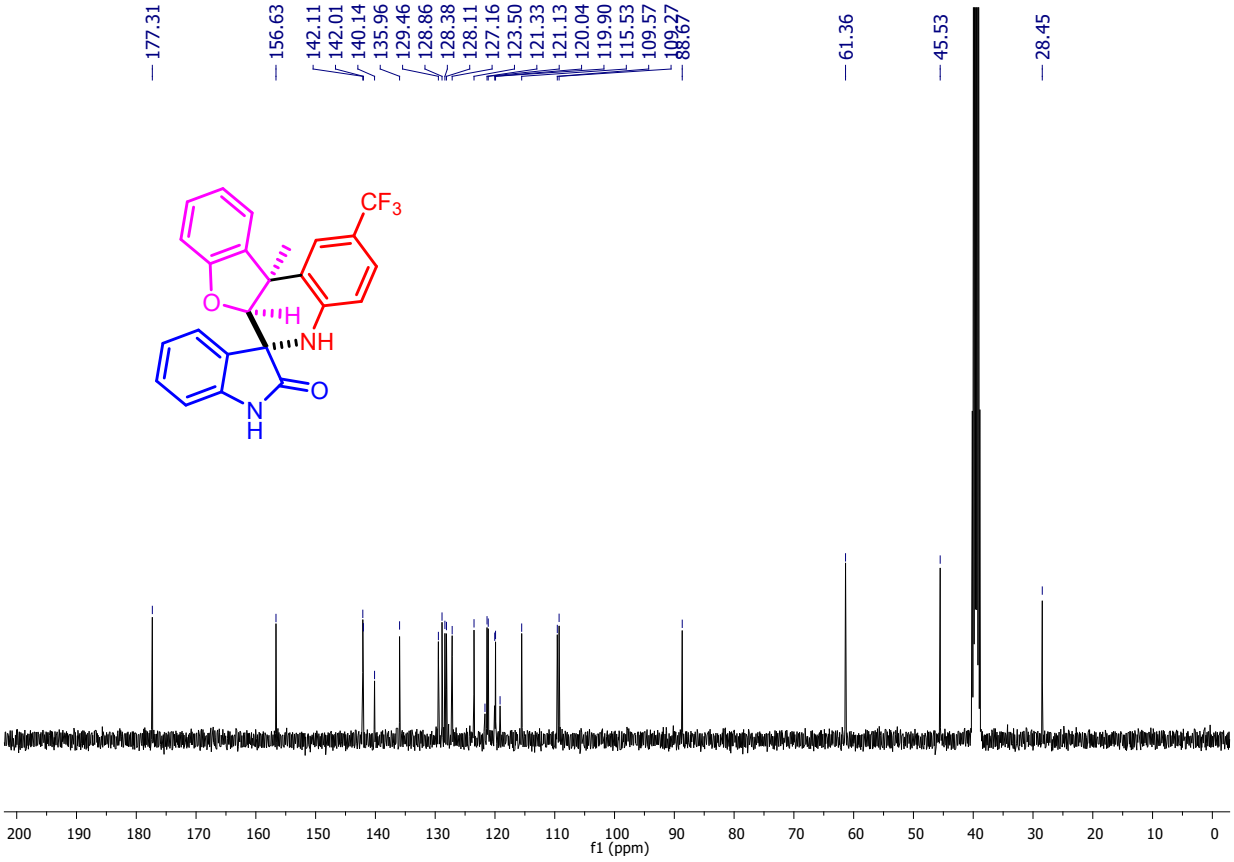
^{13}C {^{1}H} NMR Spectrum of **8h** (100 MHz, DMSO-d_6)



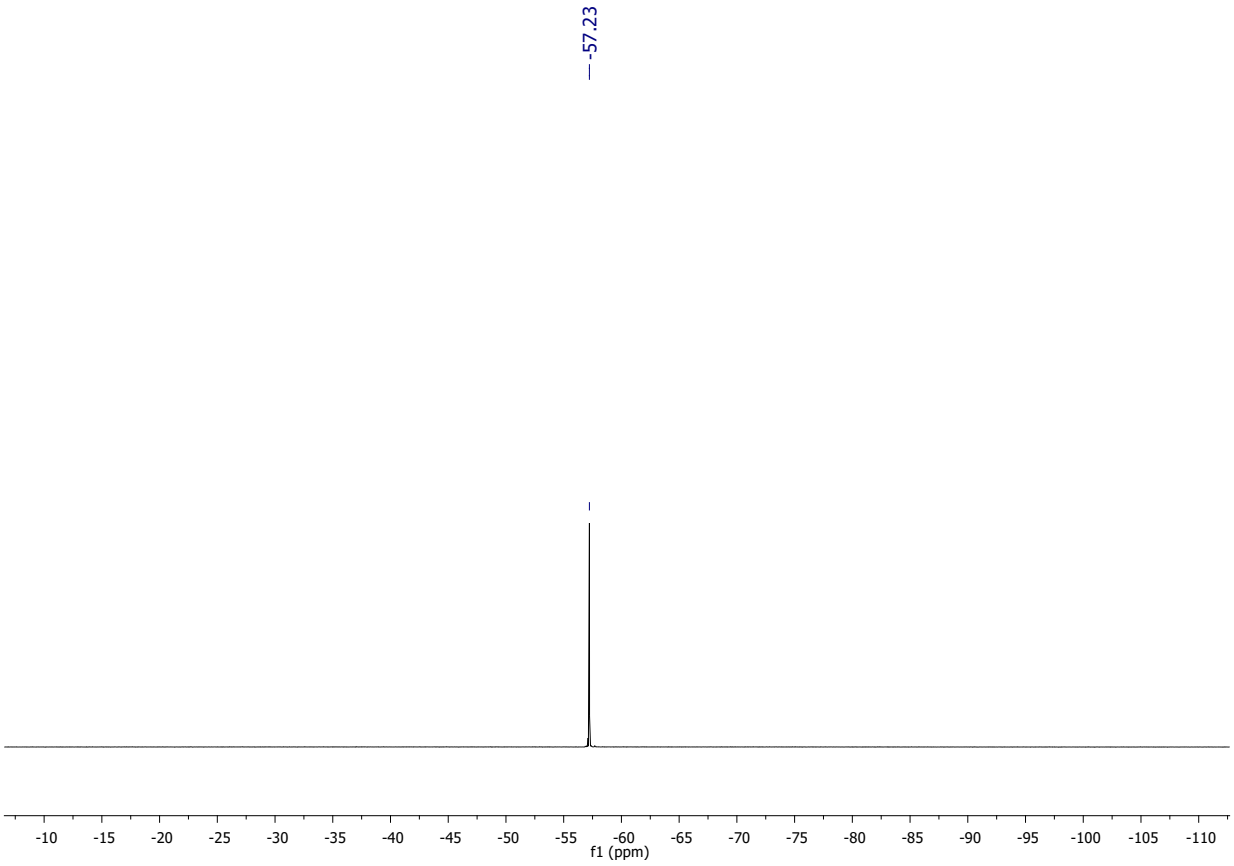
^{1}H NMR Spectrum of **8i** (400 MHz, DMSO-d_6)



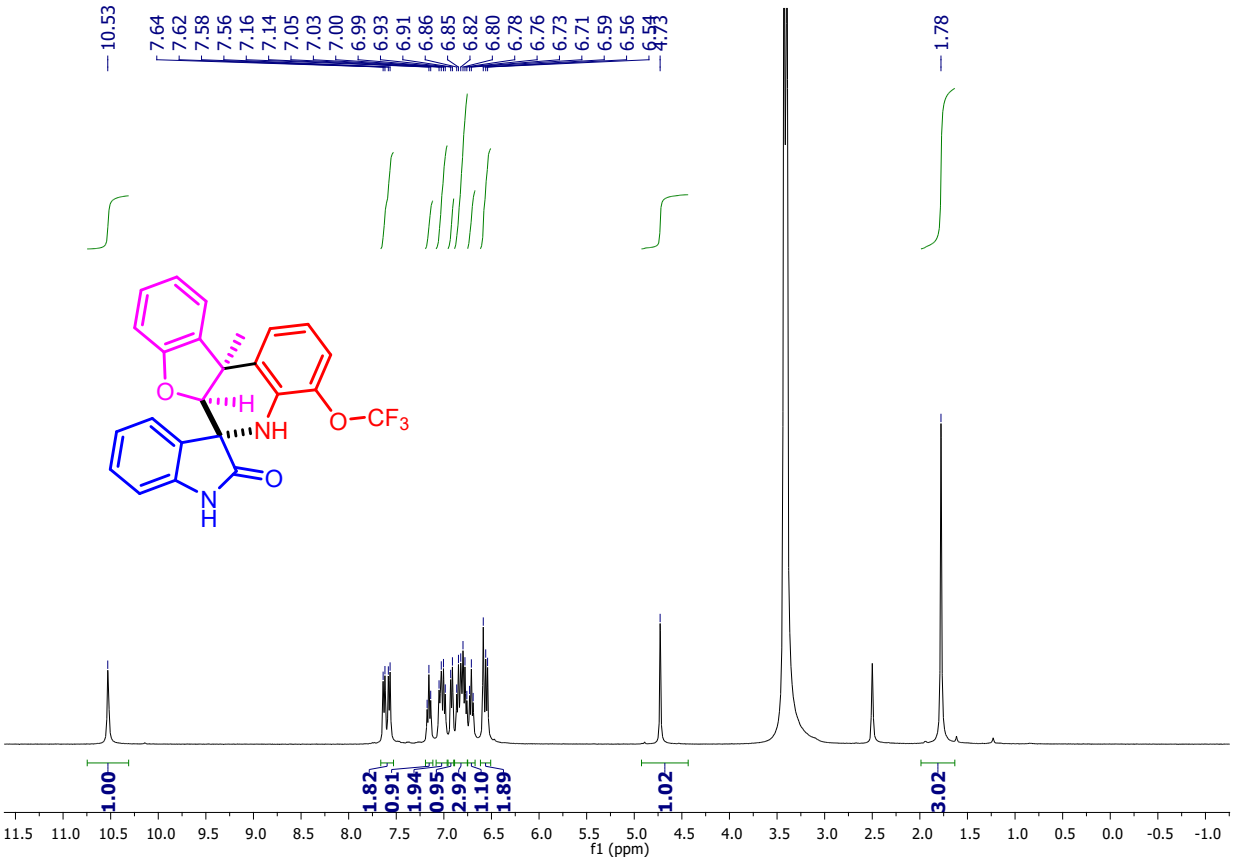
^{13}C {^{1}H} NMR Spectrum of **8i** (100 MHz, DMSO-d_6)



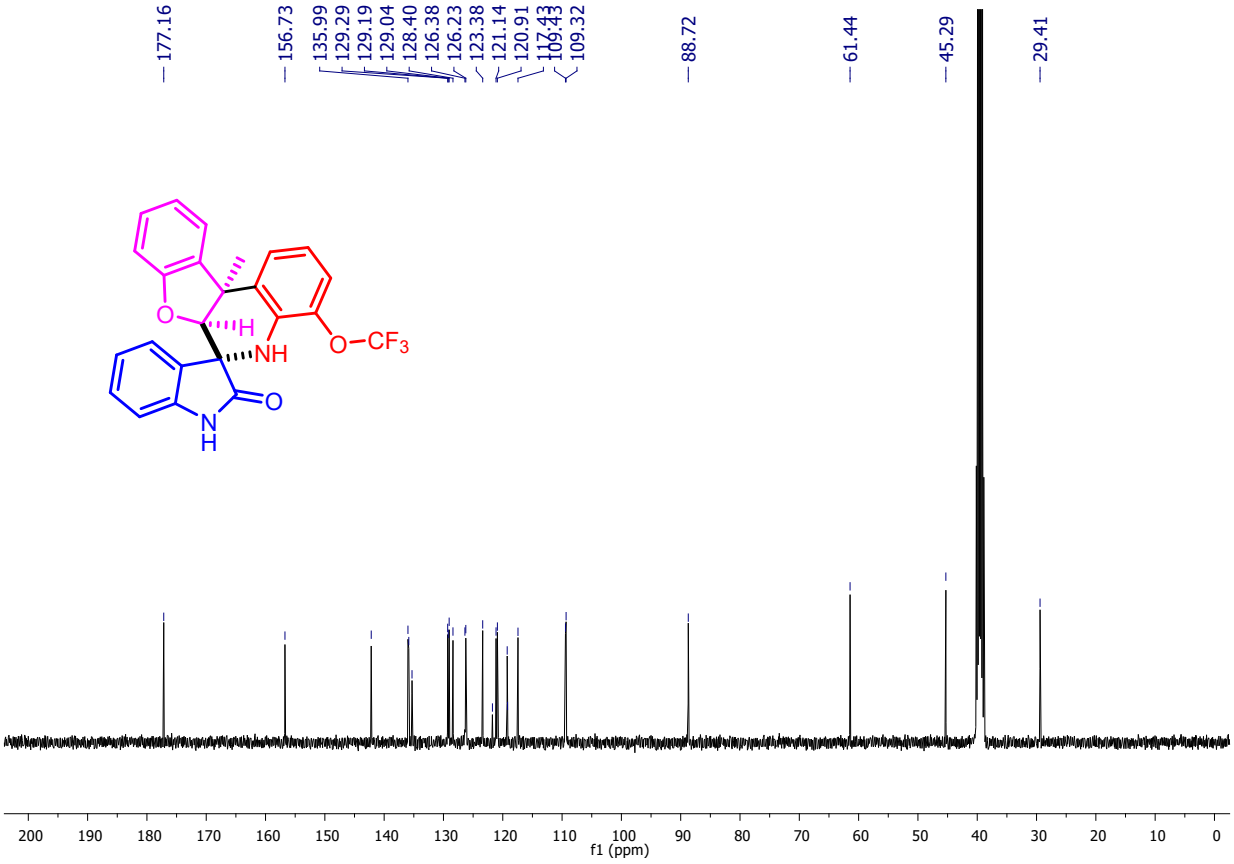
^{19}F NMR Spectrum of **8i** (377 MHz, DMSO-d_6)



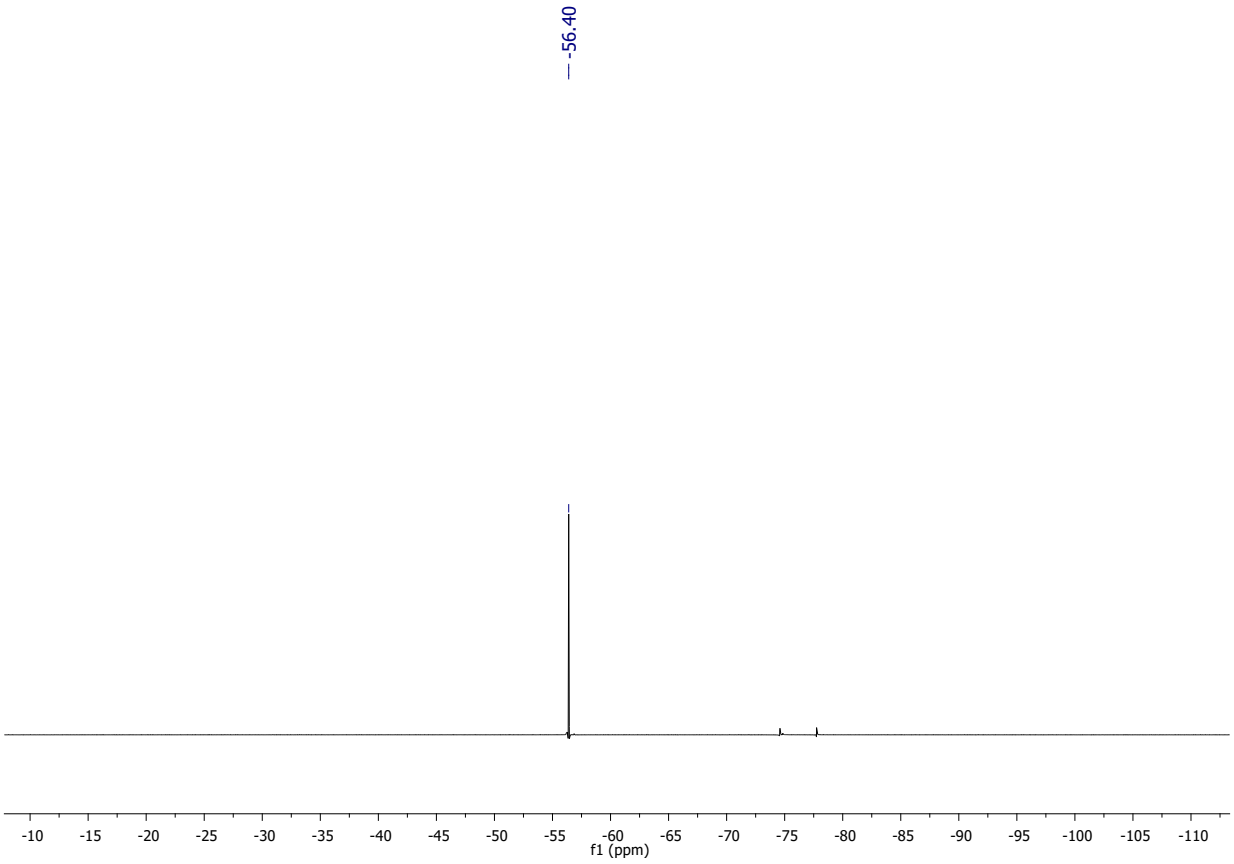
^{1}H NMR Spectrum of **8j** (400 MHz, DMSO-d_6)



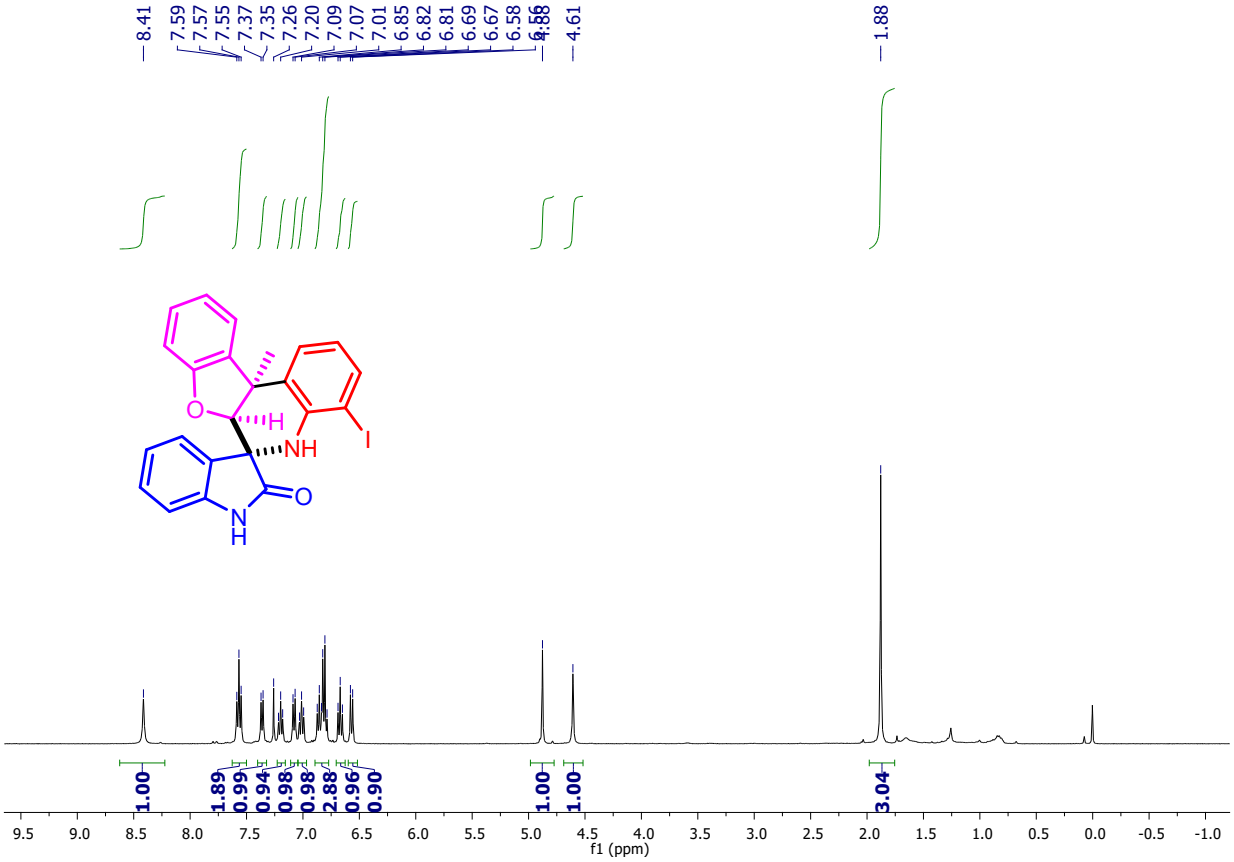
^{13}C {^{1}H} NMR Spectrum of **8j** (100 MHz, DMSO-d_6)



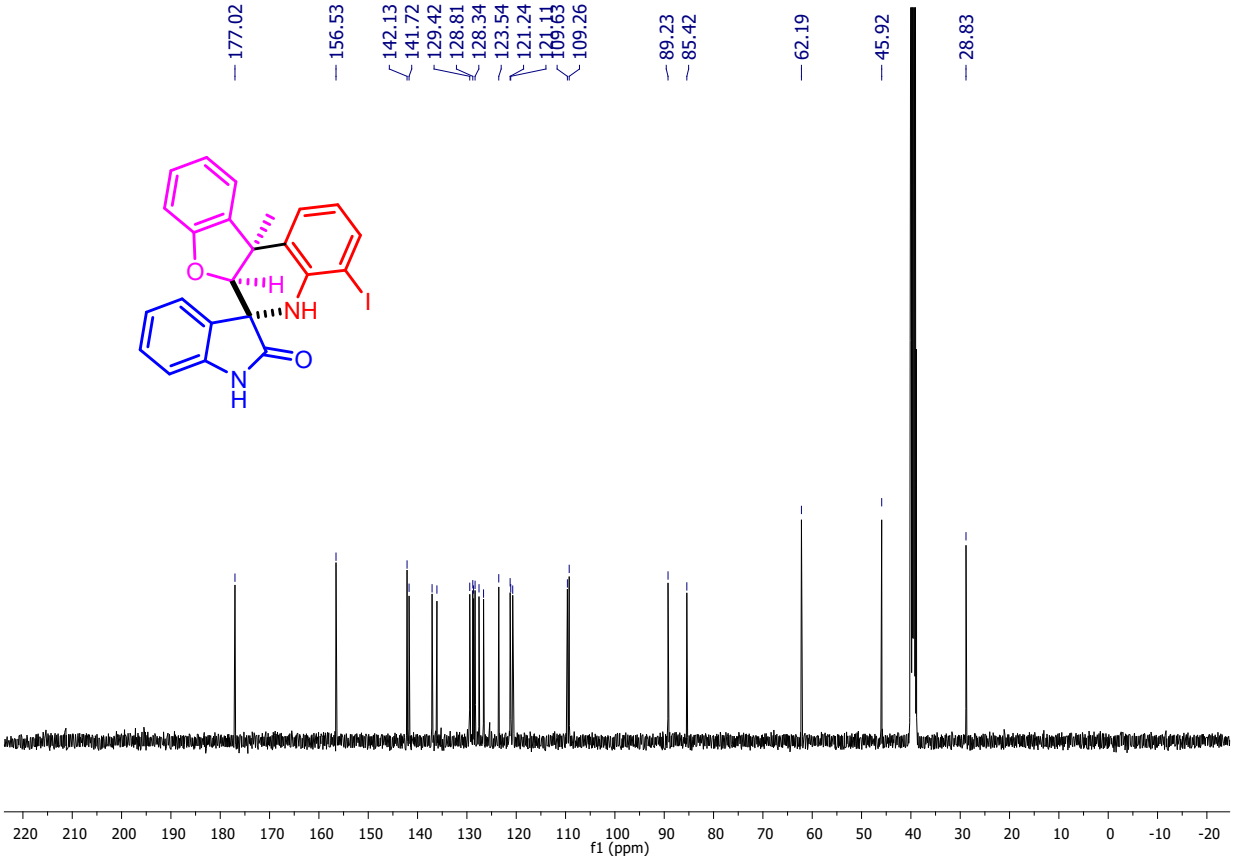
^{19}F NMR Spectrum of **8j** (377 MHz, DMSO-d_6)



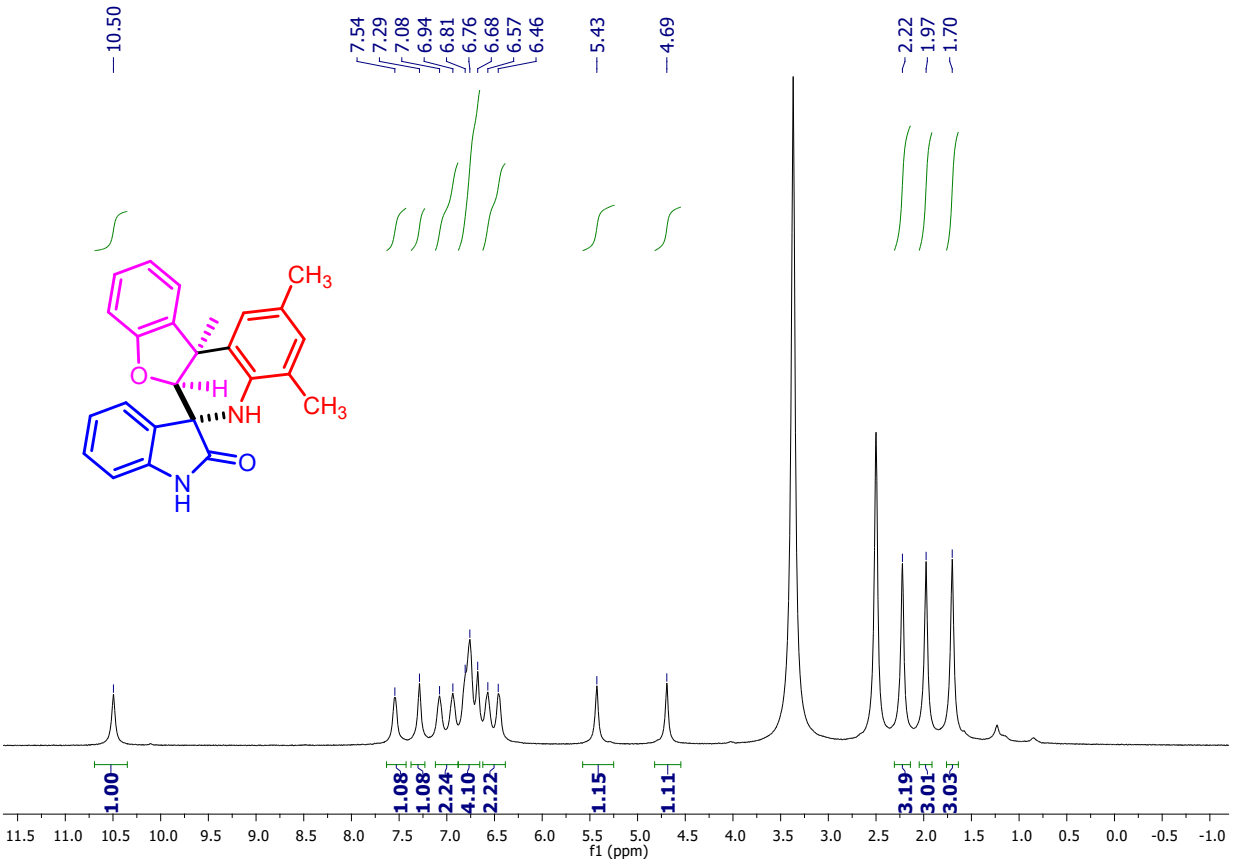
^{1}H NMR Spectrum of **8k** (400 MHz, $CDCl_3$)



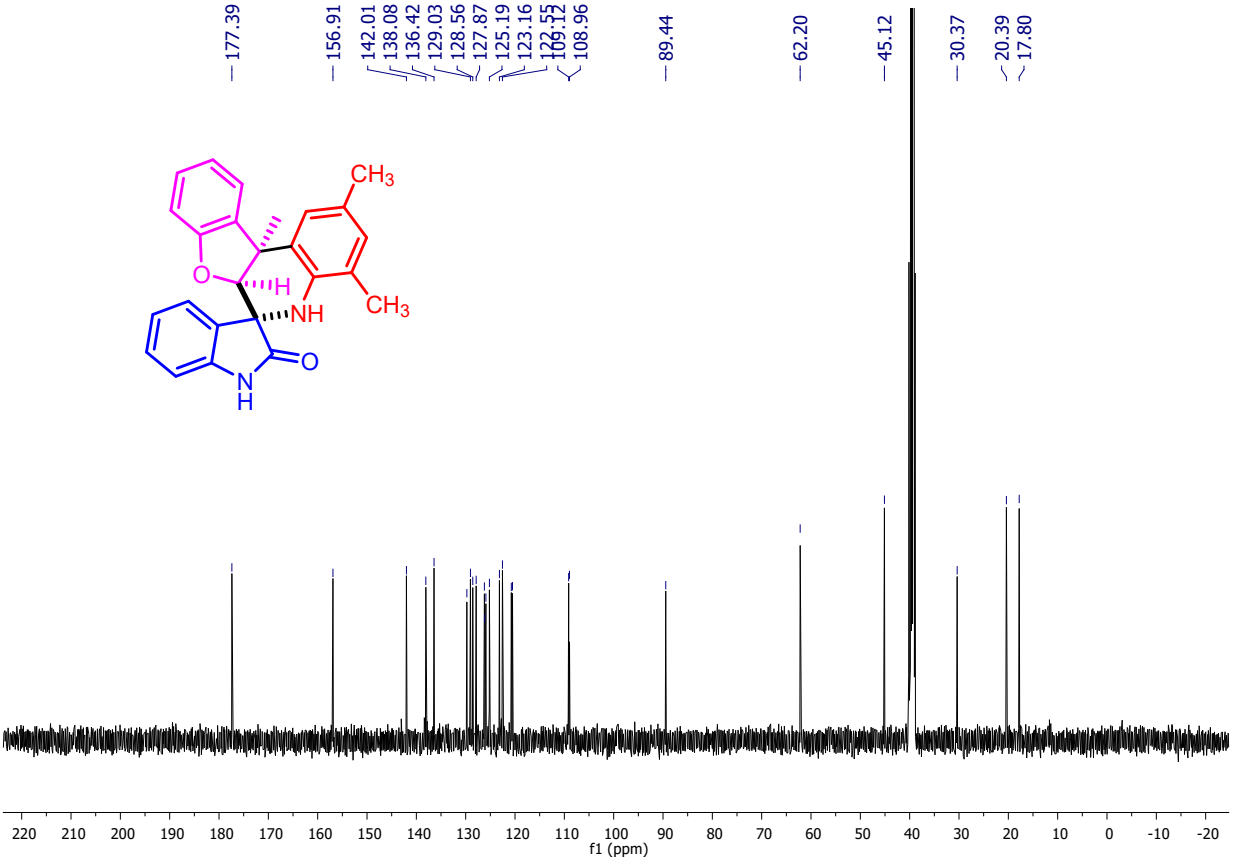
^{13}C {^{1}H} NMR Spectrum of **8k** (100 MHz, DMSO-d_6)



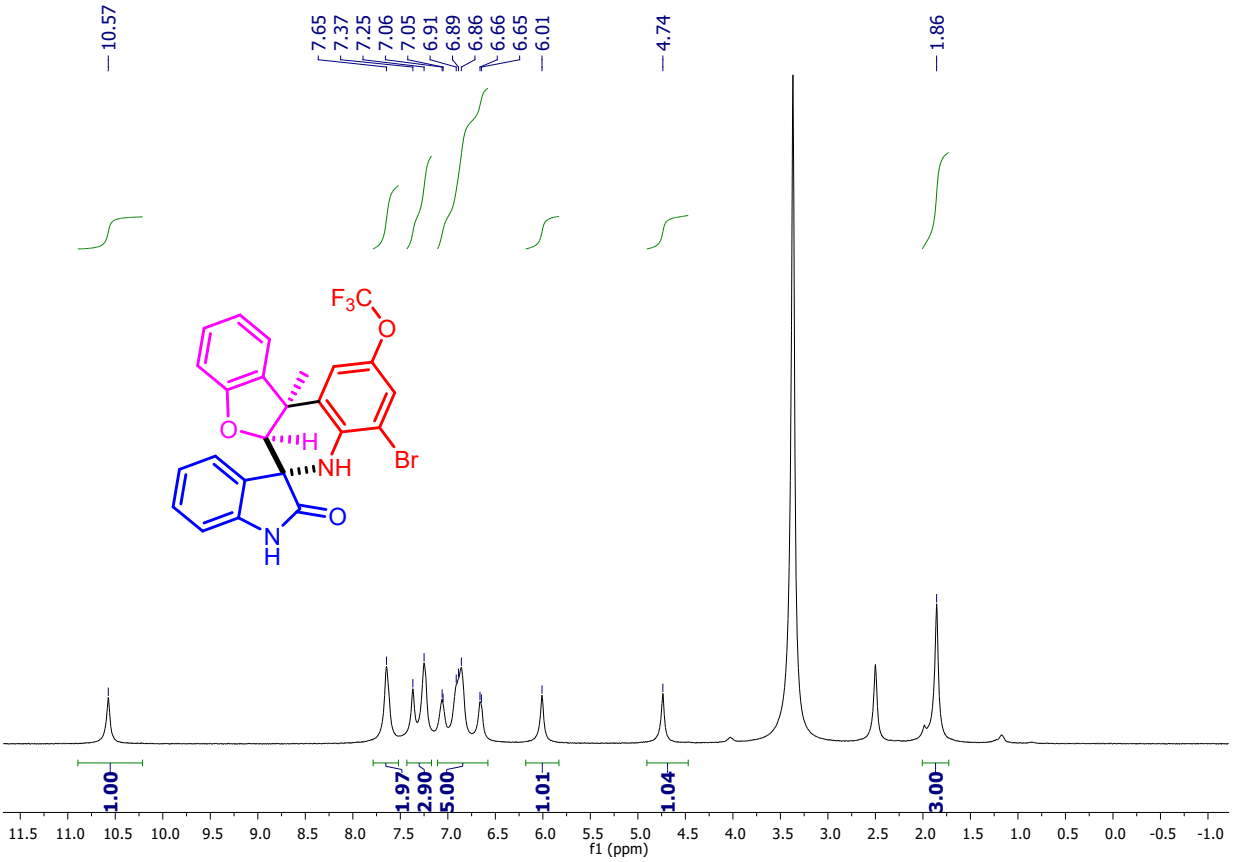
^{1}H NMR Spectrum of **8l** (400 MHz, DMSO-d_6)



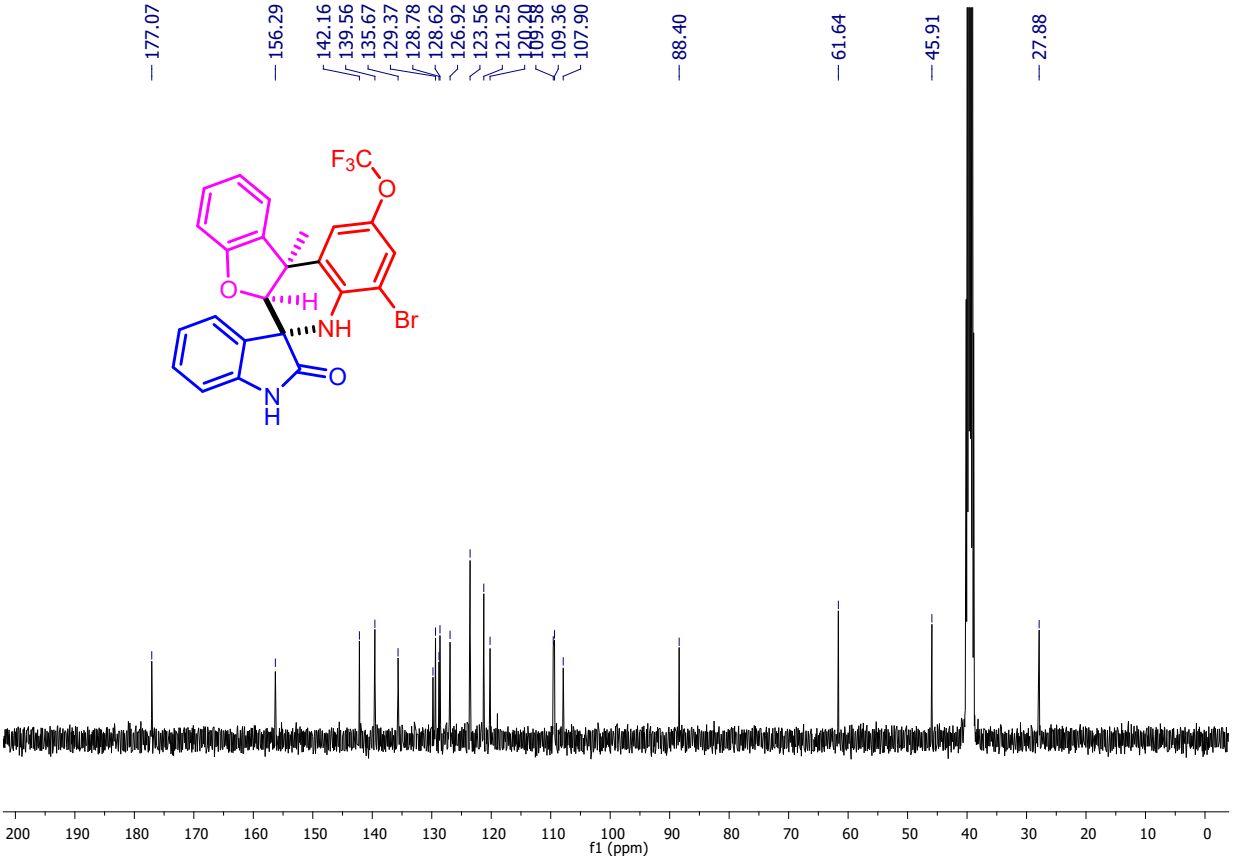
^{13}C {^{1}H} NMR Spectrum of **8l** (100 MHz, DMSO-d_6)



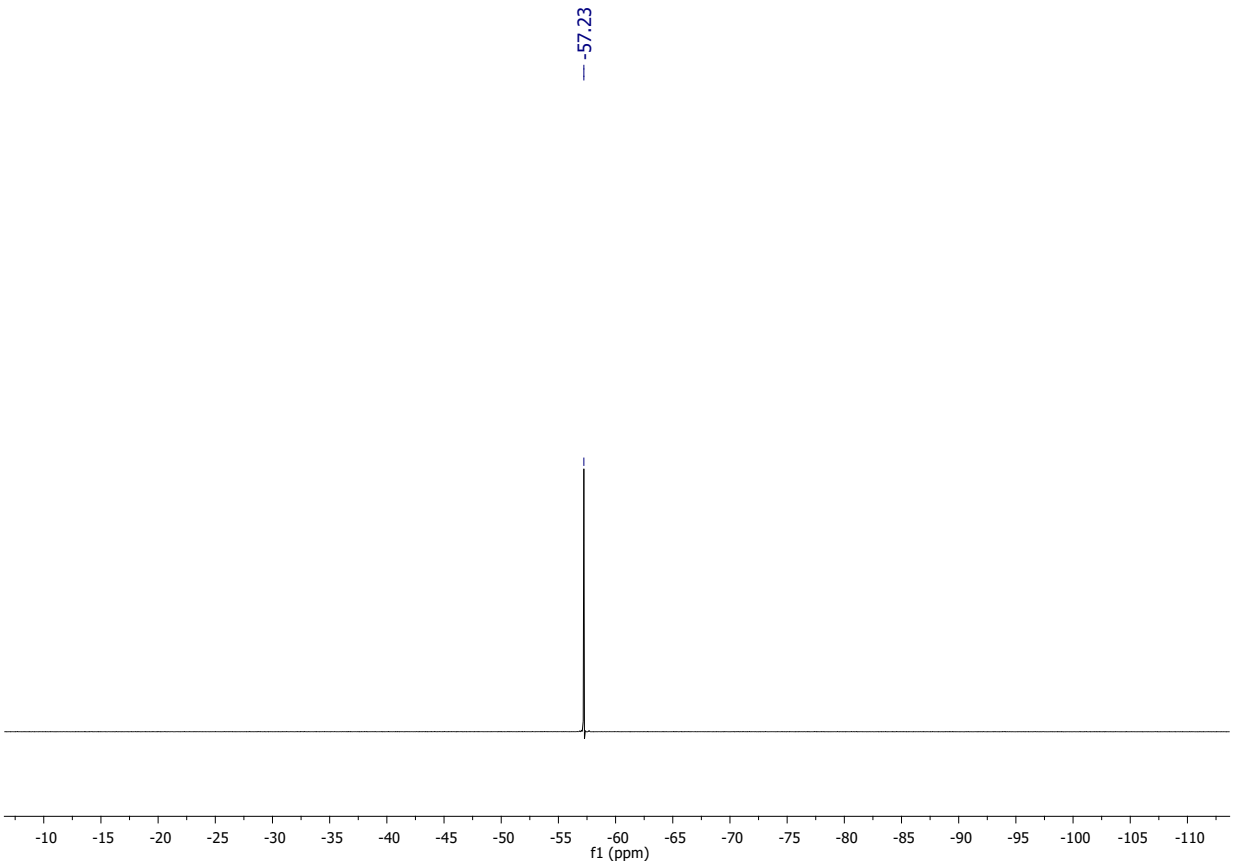
^{1}H NMR Spectrum of **8m** (400 MHz, DMSO-d_6)



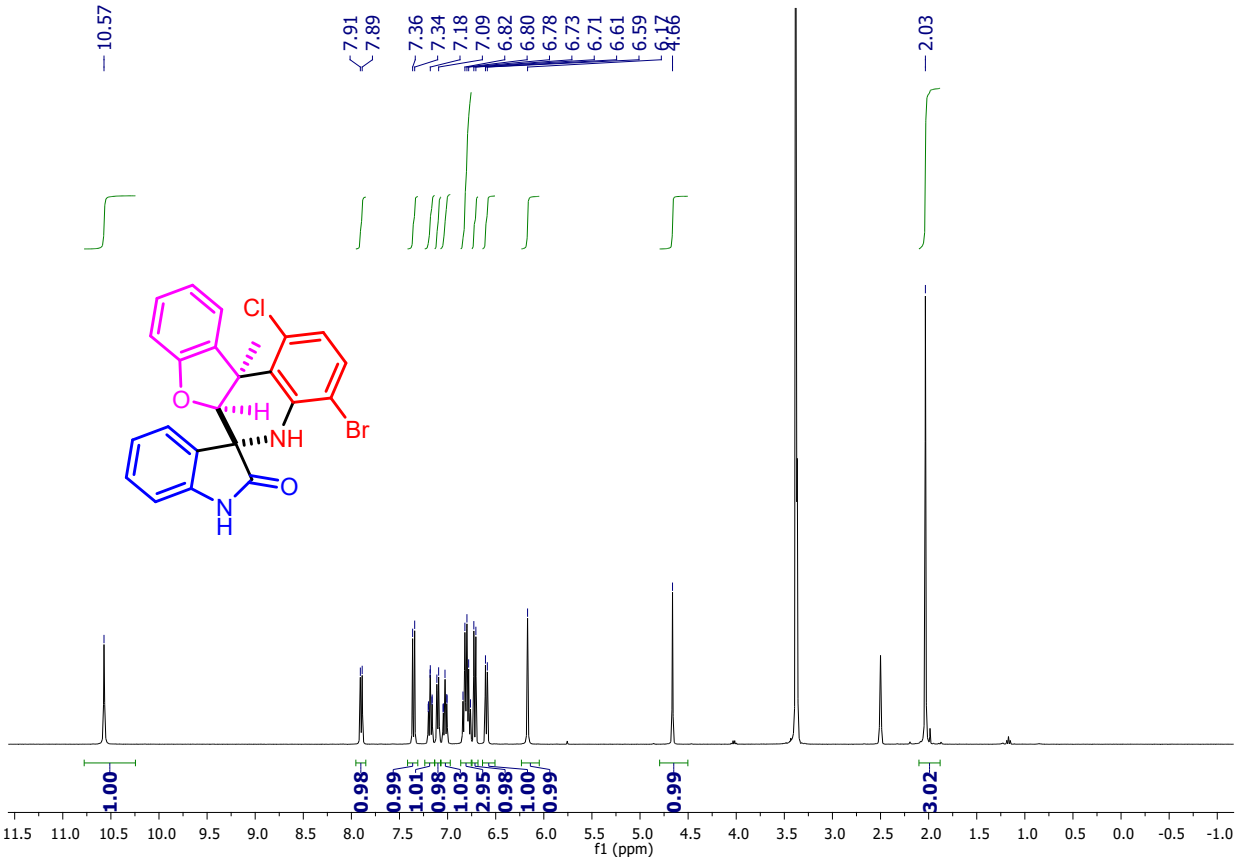
^{13}C {^{1}H} NMR Spectrum of **8m** (100 MHz, DMSO-d_6)



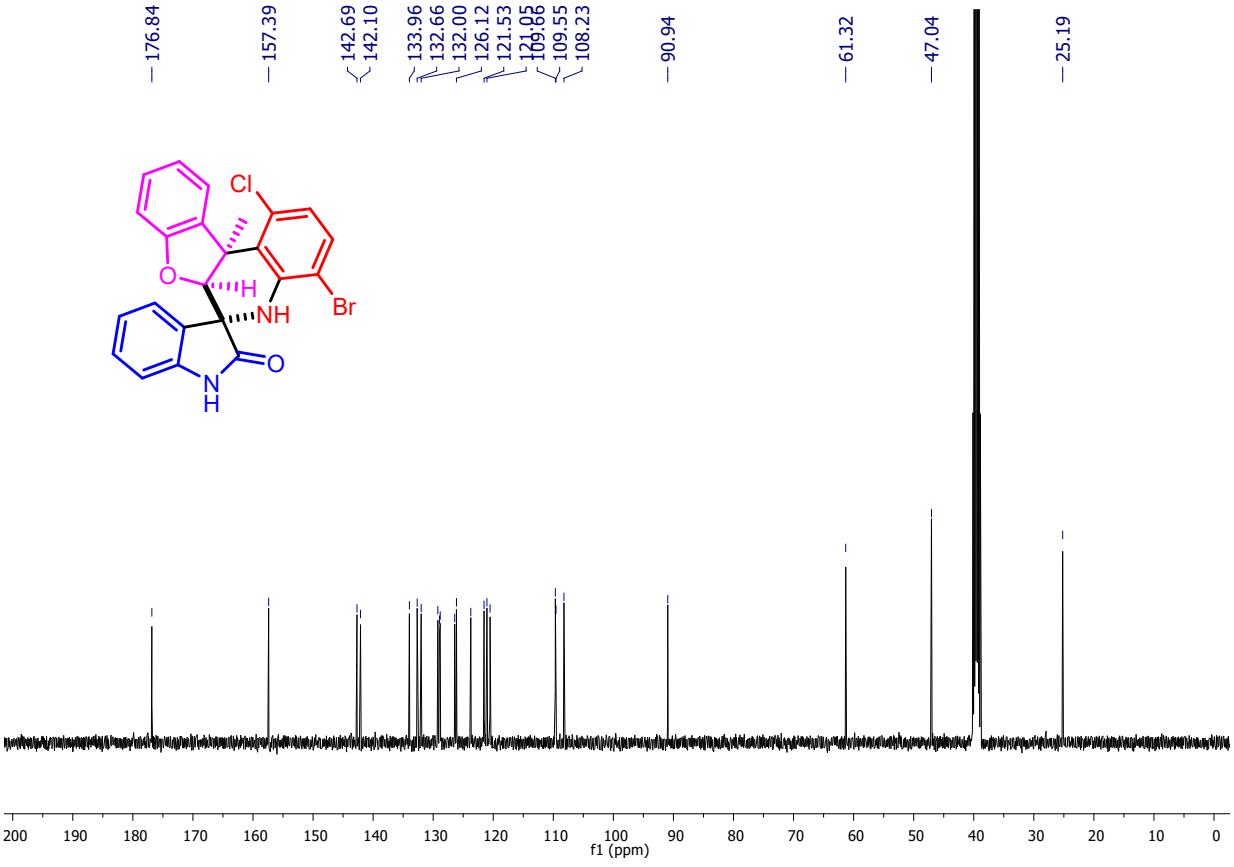
^{19}F NMR Spectrum of **8m** (377 MHz, DMSO-d_6)



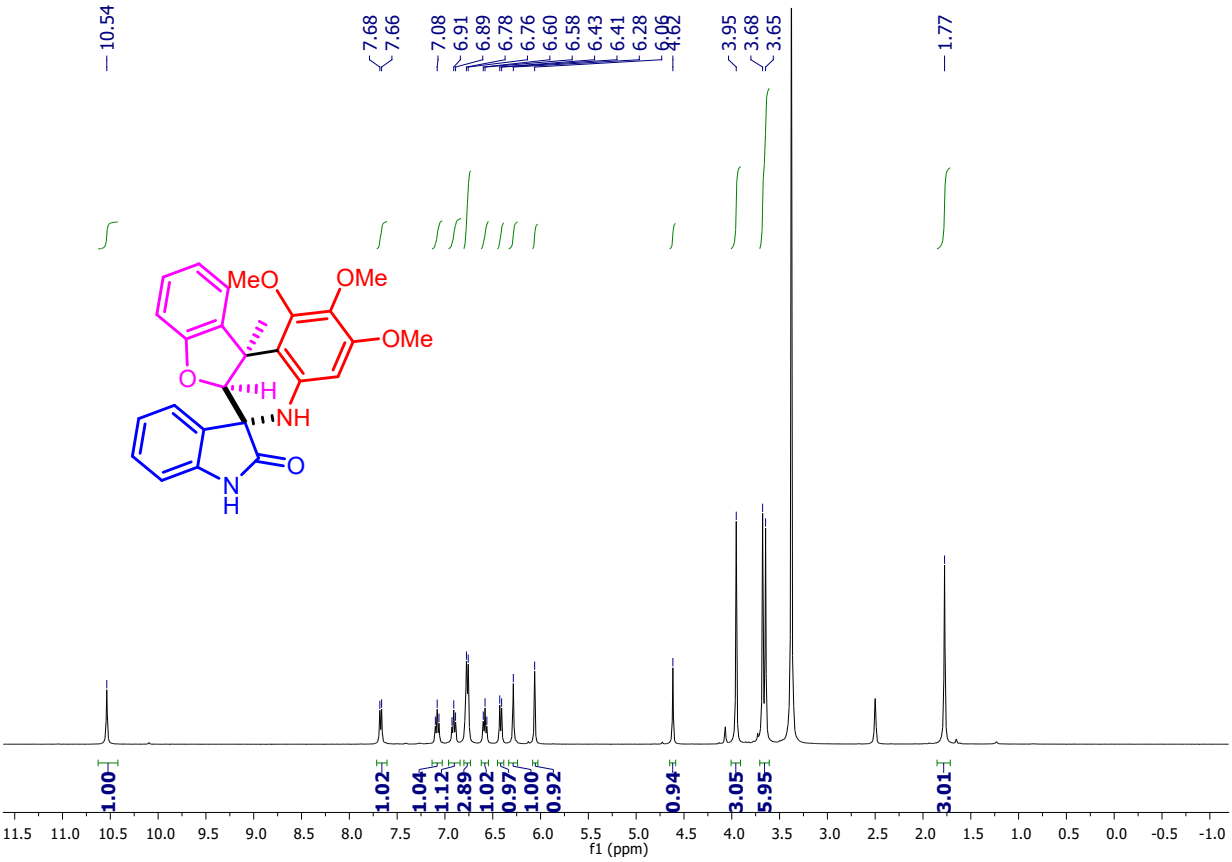
^{1}H NMR Spectrum of **8n** (400 MHz, DMSO-d_6)



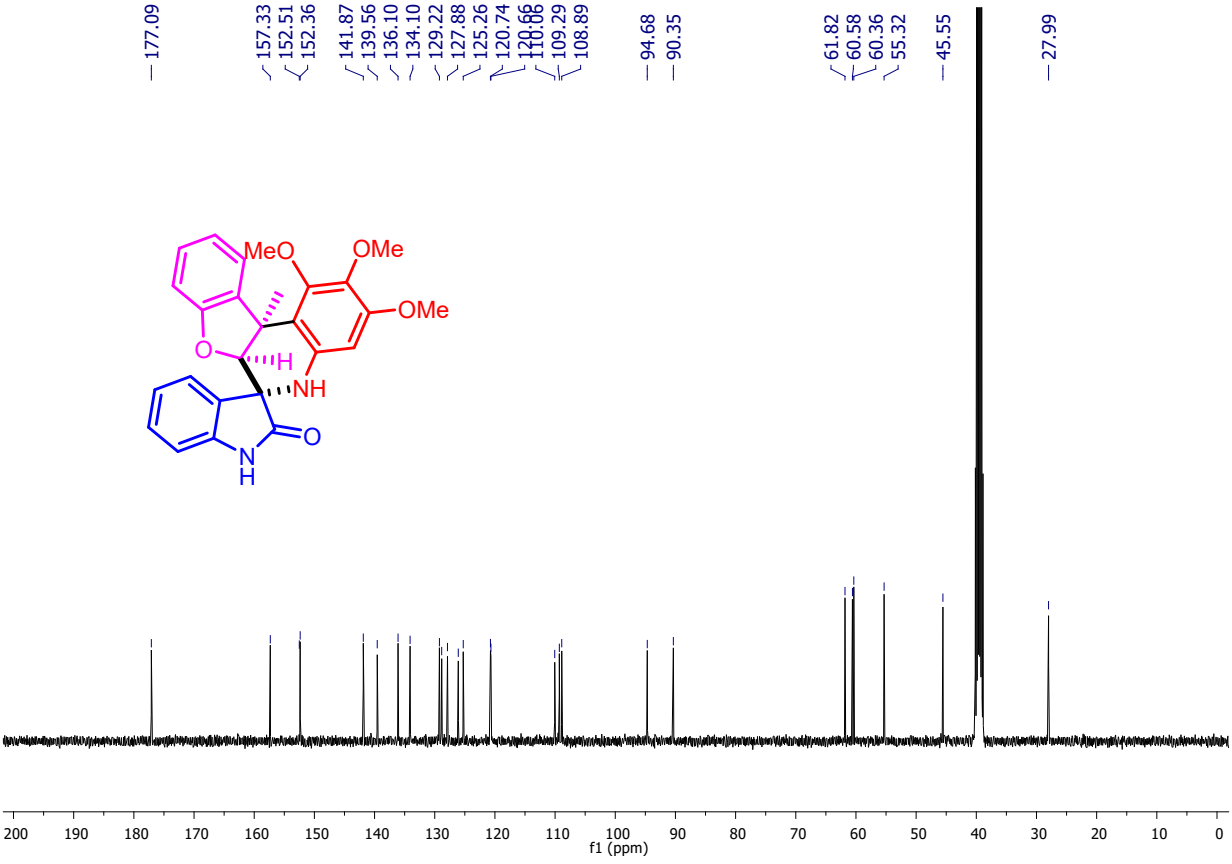
^{13}C {^{1}H} NMR Spectrum of **8n** (100 MHz, DMSO-d_6)



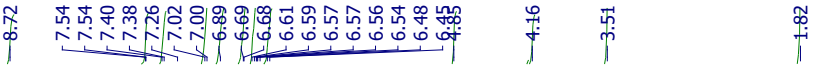
^{1}H NMR Spectrum of **8o** (400 MHz, DMSO-d_6)

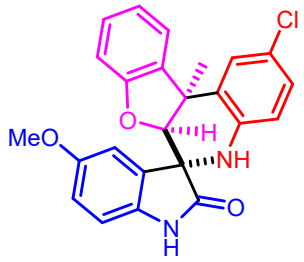


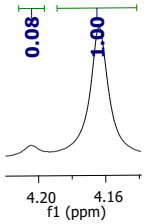
^{13}C {^{1}H} NMR Spectrum of **8o** (100 MHz, DMSO-d_6)



^{1}H NMR Spectrum of **8p** (400 MHz, $CDCl_3$)







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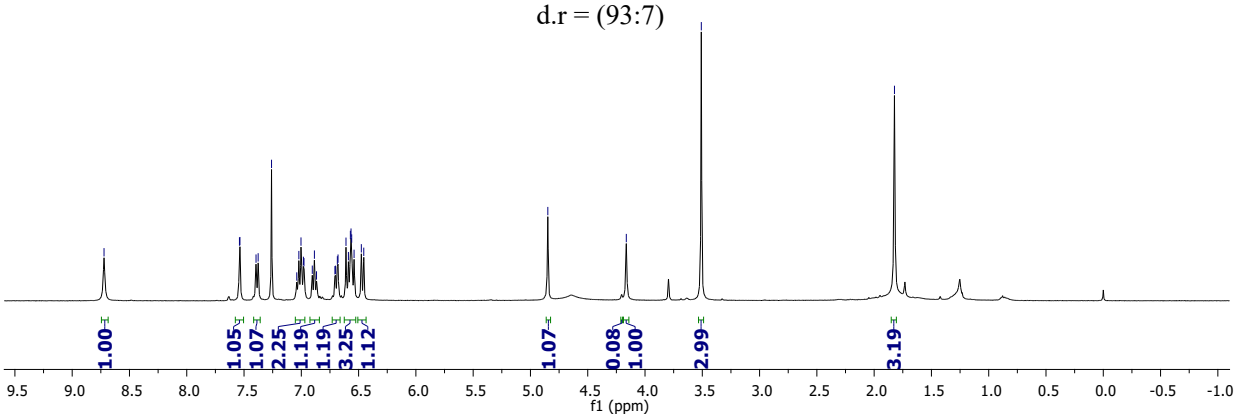
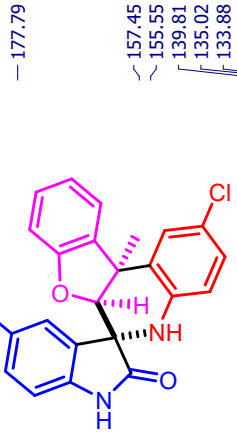
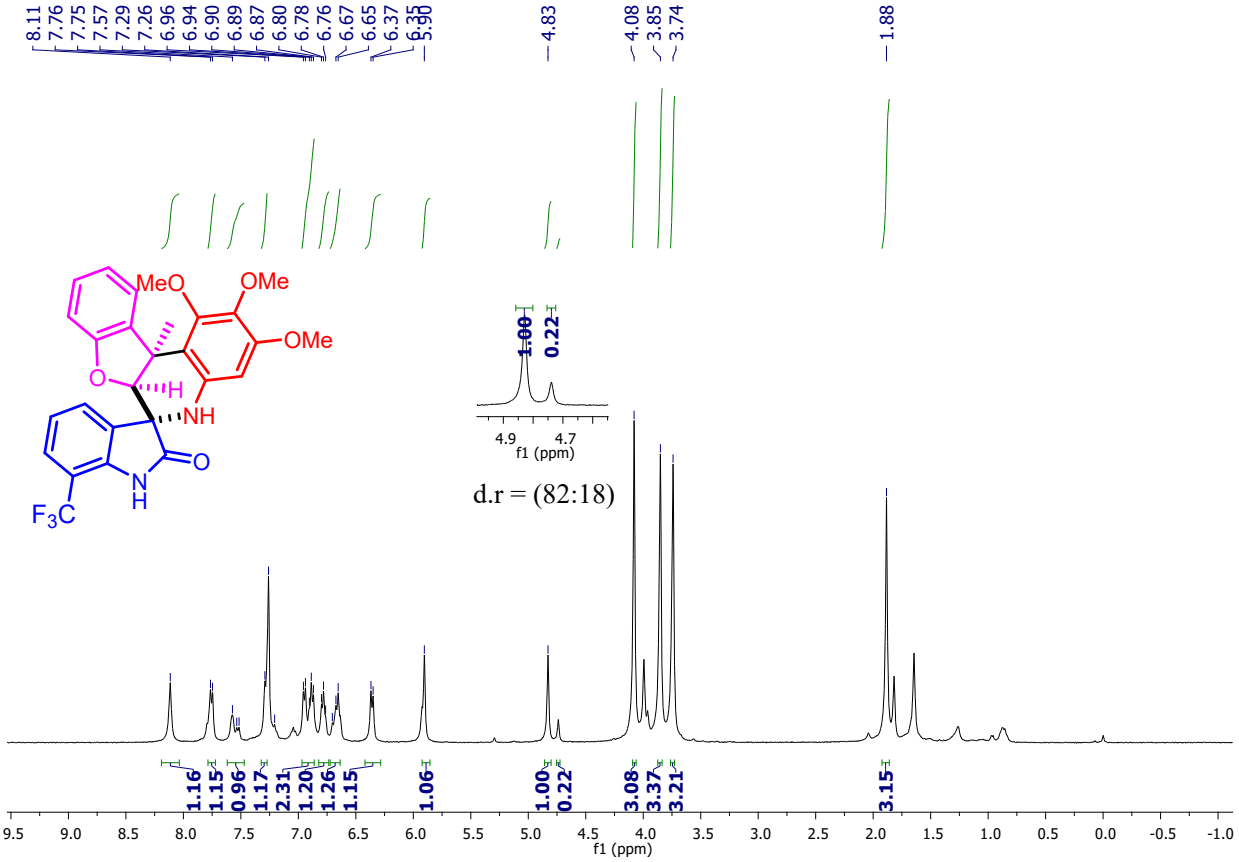


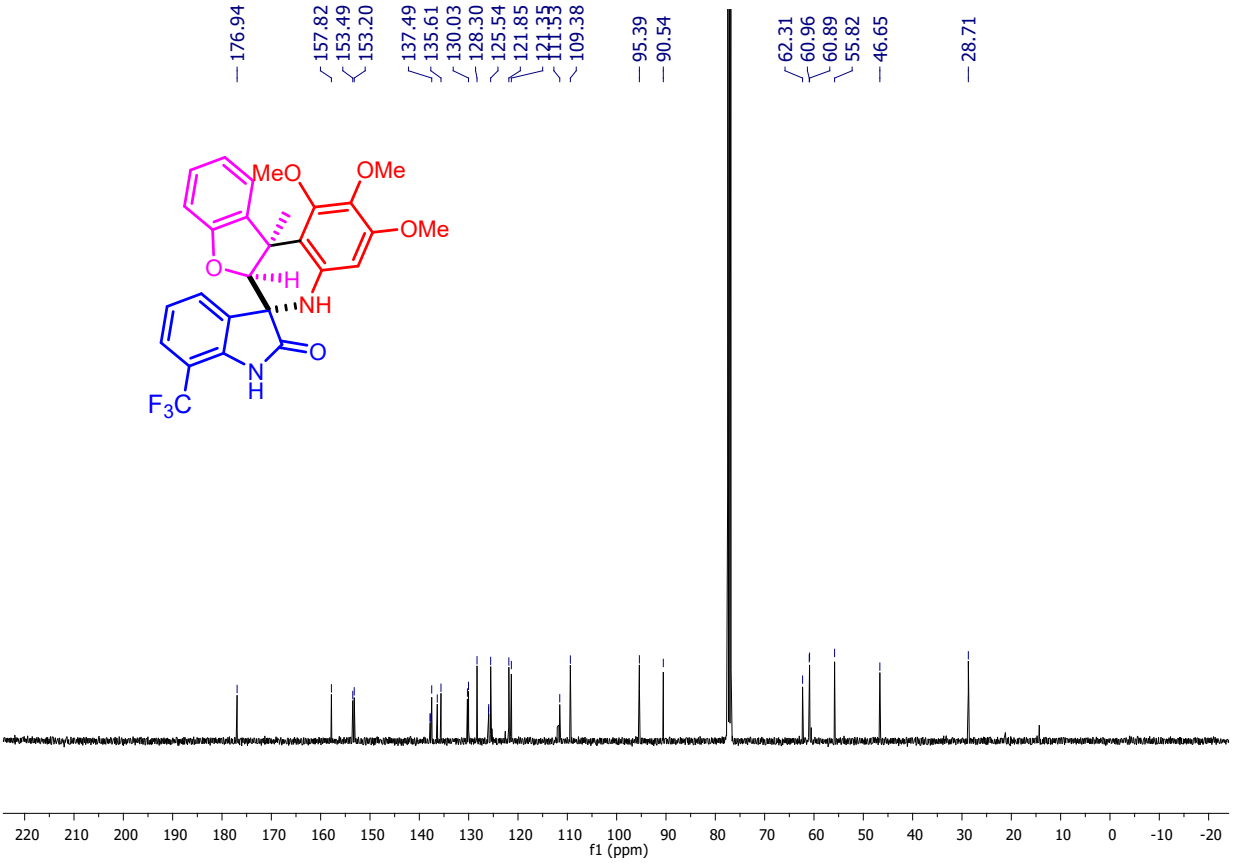
^{13}C {^{1}H} NMR Spectrum of **8p** (100 MHz, $CDCl_3$)



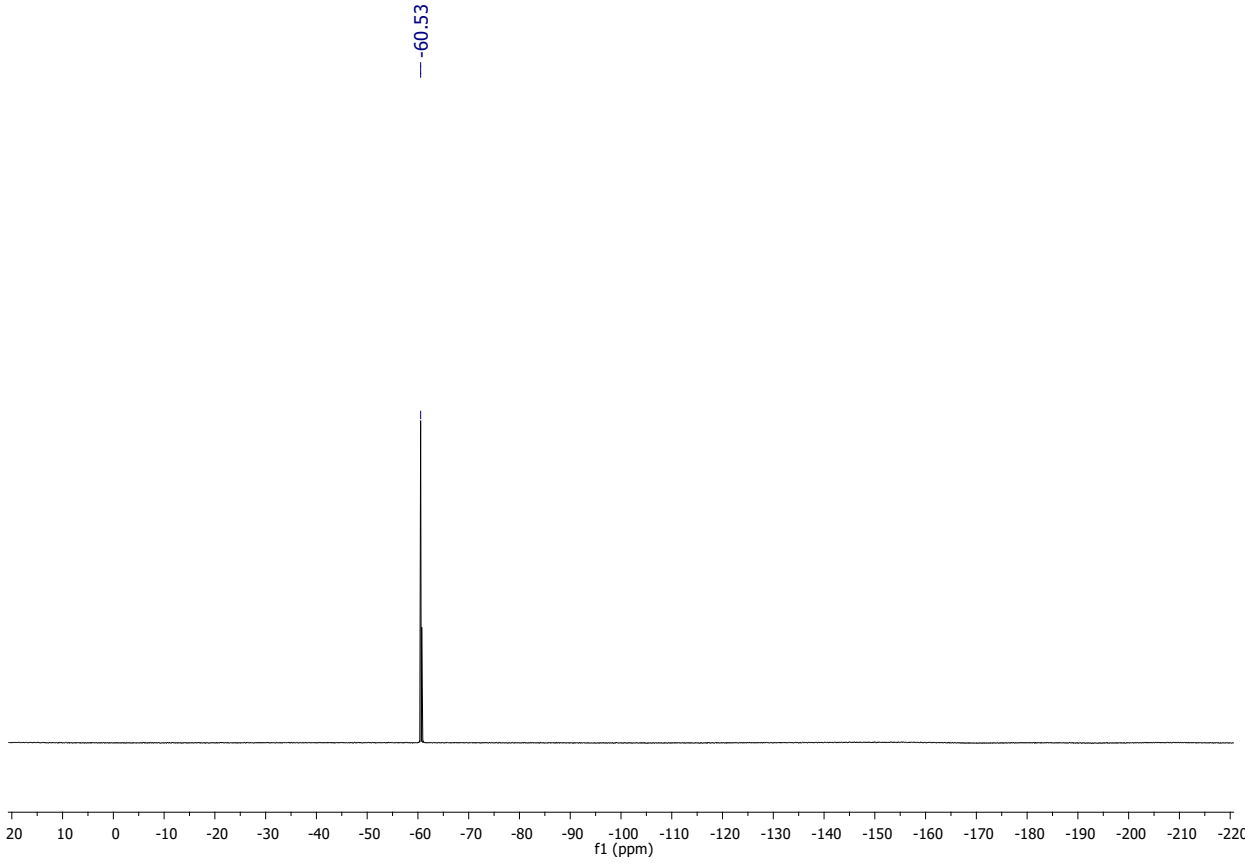
^{1}H NMR Spectrum of **8q** (400 MHz, $CDCl_3$)



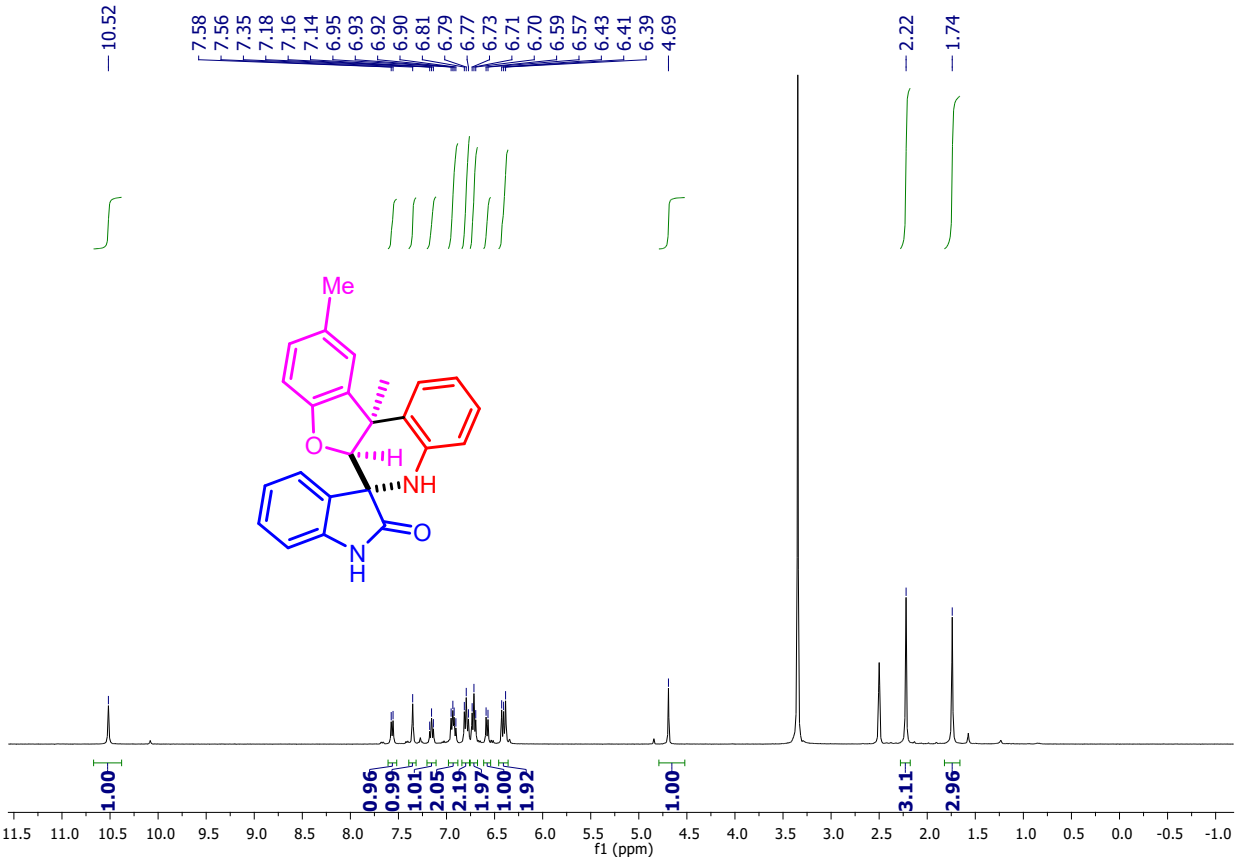
^{13}C {^{1}H} NMR Spectrum of **8q** (100 MHz, $CDCl_3$)



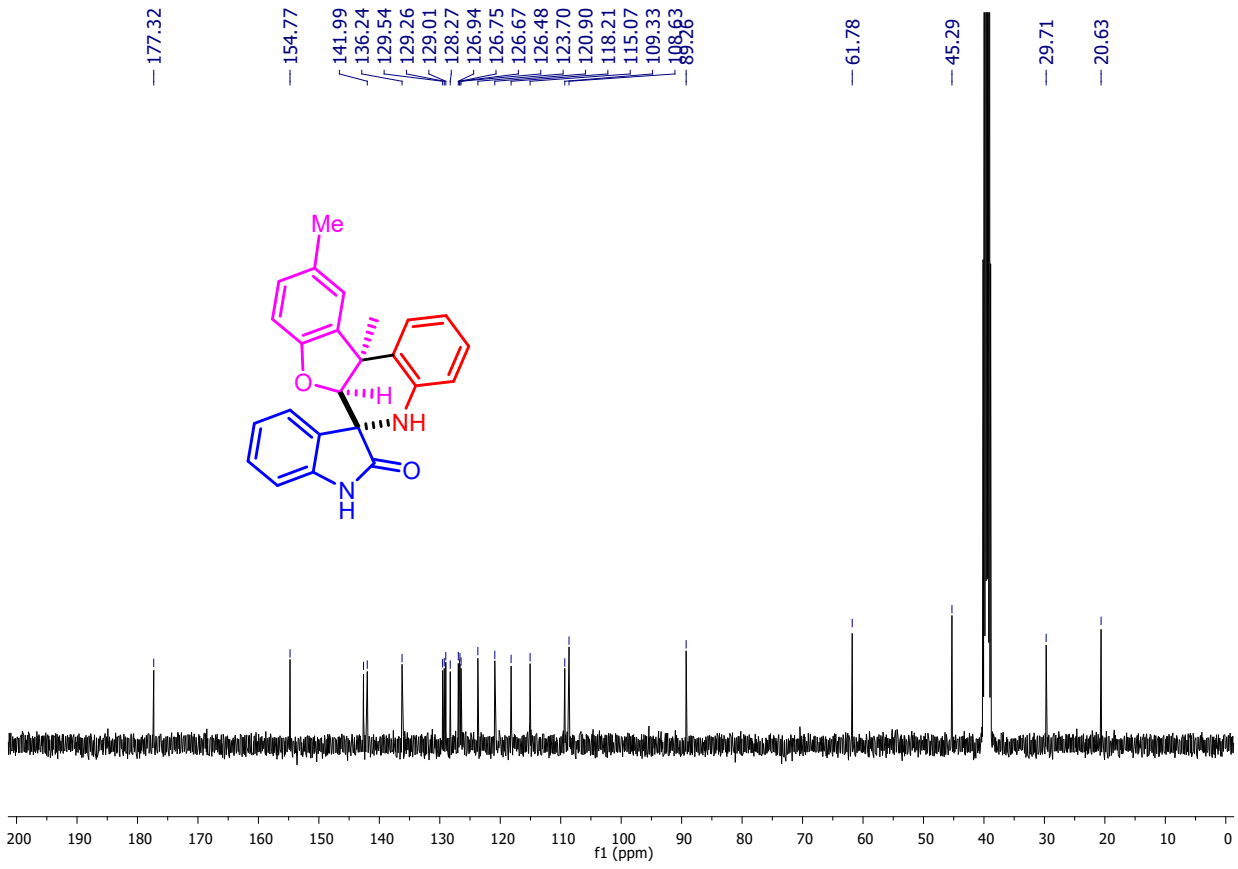
^{19}F NMR Spectrum of **8q** (377 MHz, $CDCl_3$)



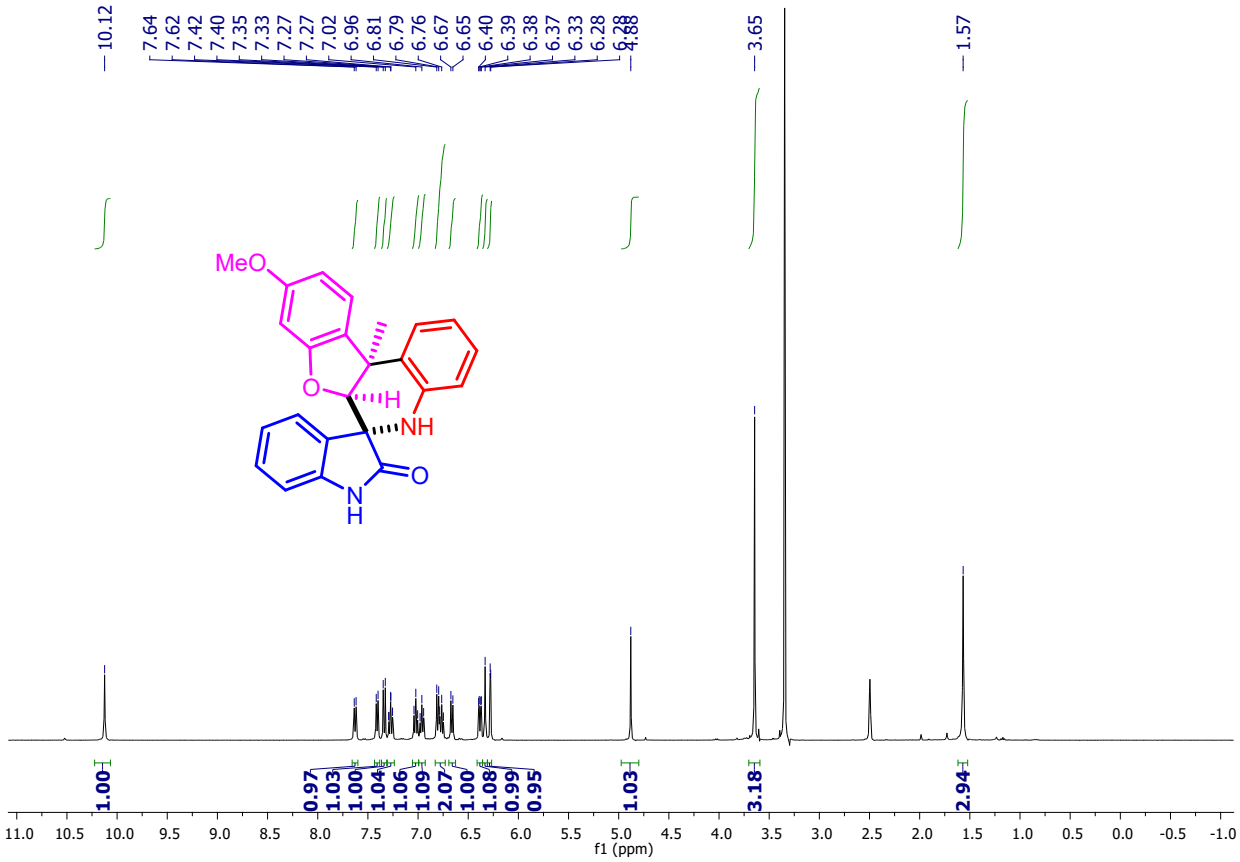
^{1}H NMR Spectrum of **9b** (400 MHz, DMSO-d_6)



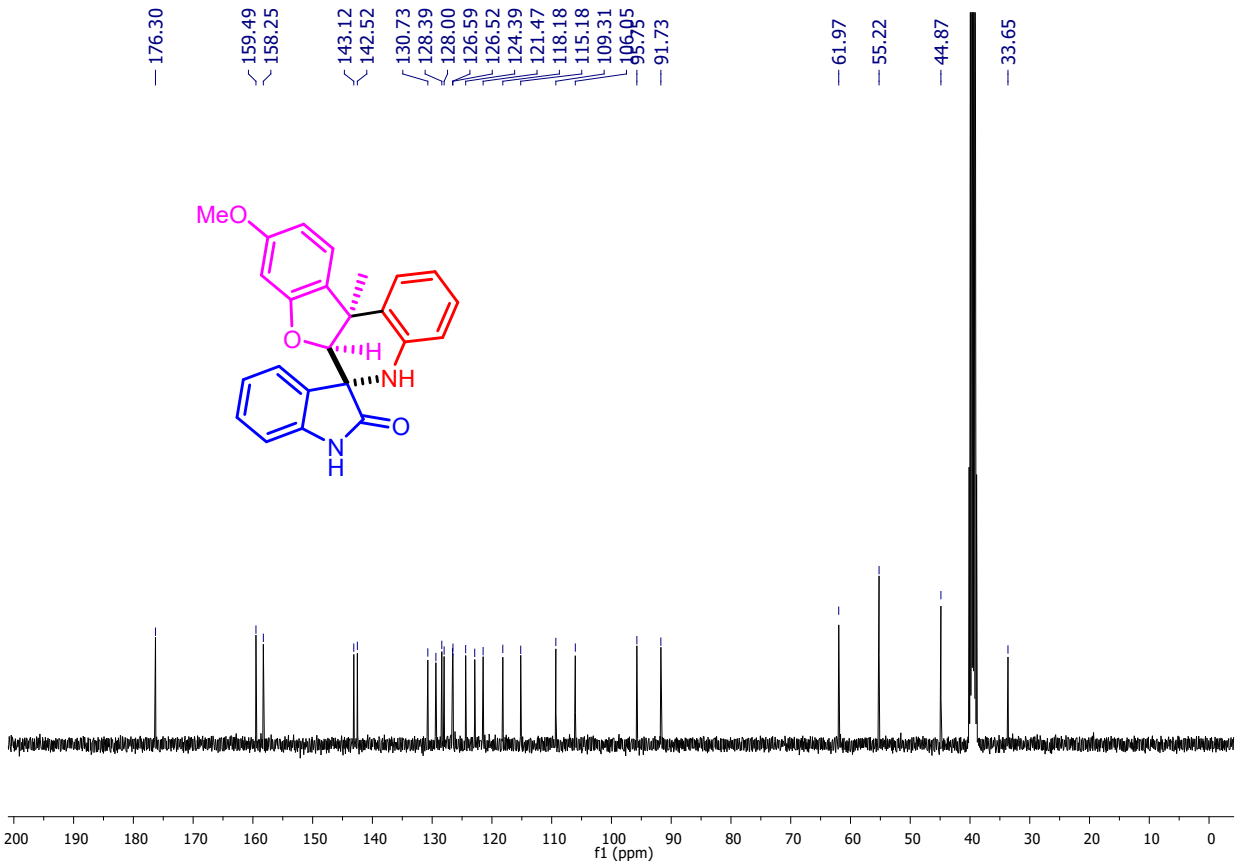
^{13}C {^{1}H} NMR Spectrum of **9b** (100 MHz, DMSO-d_6)



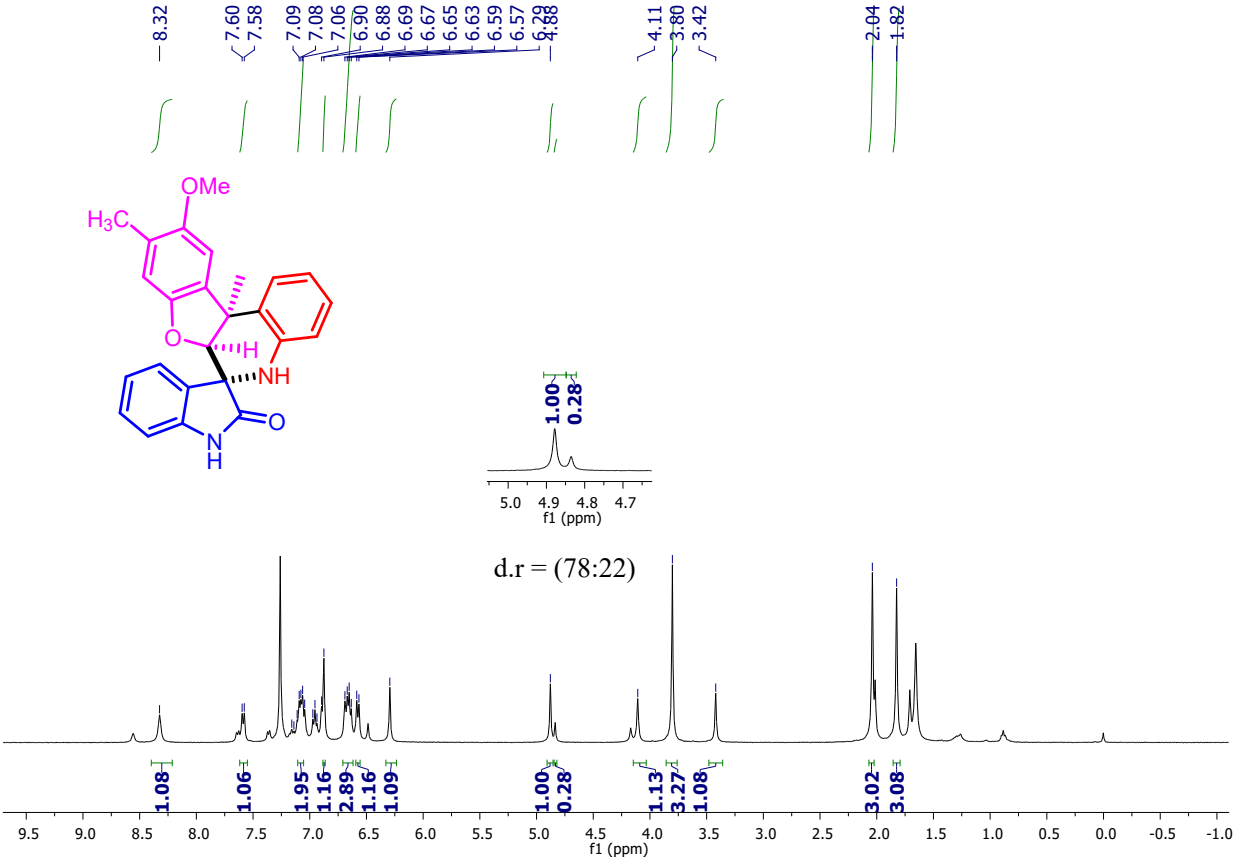
^{1}H NMR Spectrum of **9c** (400 MHz, DMSO-d_6)



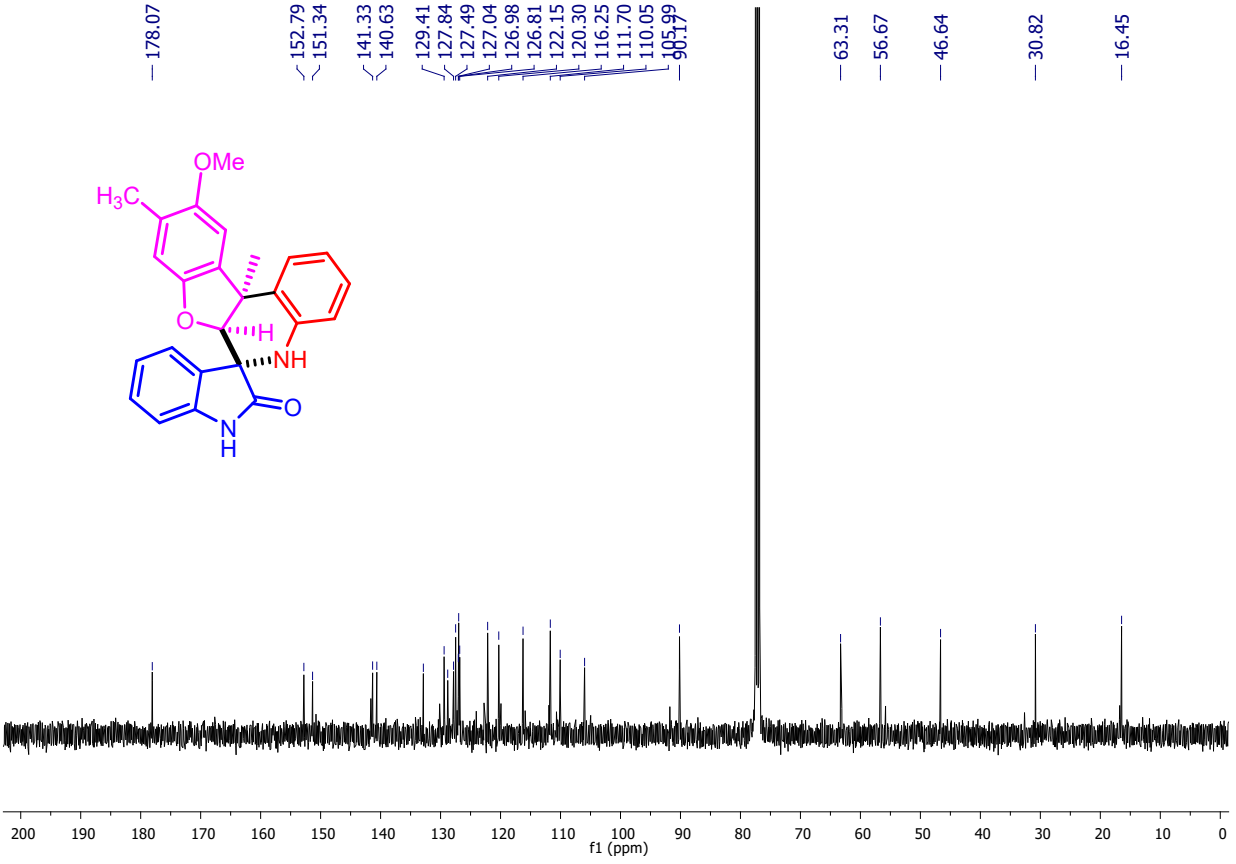
^{13}C {^{1}H} NMR Spectrum of **9c** (100 MHz, DMSO-d_6)



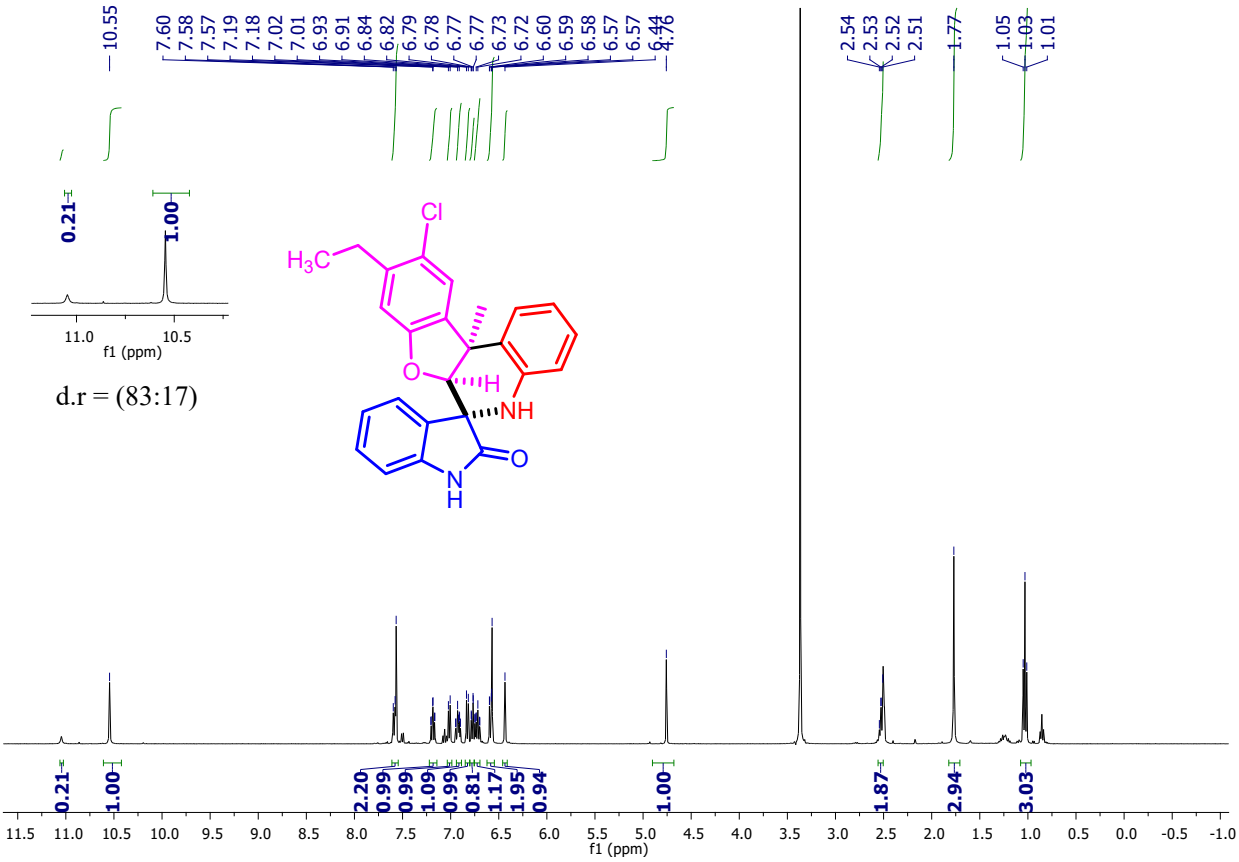
^{1}H NMR Spectrum of **9d** (400 MHz, $CDCl_3$)



^{13}C {^{1}H} NMR Spectrum of **9d** (100 MHz, $CDCl_3$)



^{1}H NMR Spectrum of **9e** (400 MHz, DMSO-d_6)



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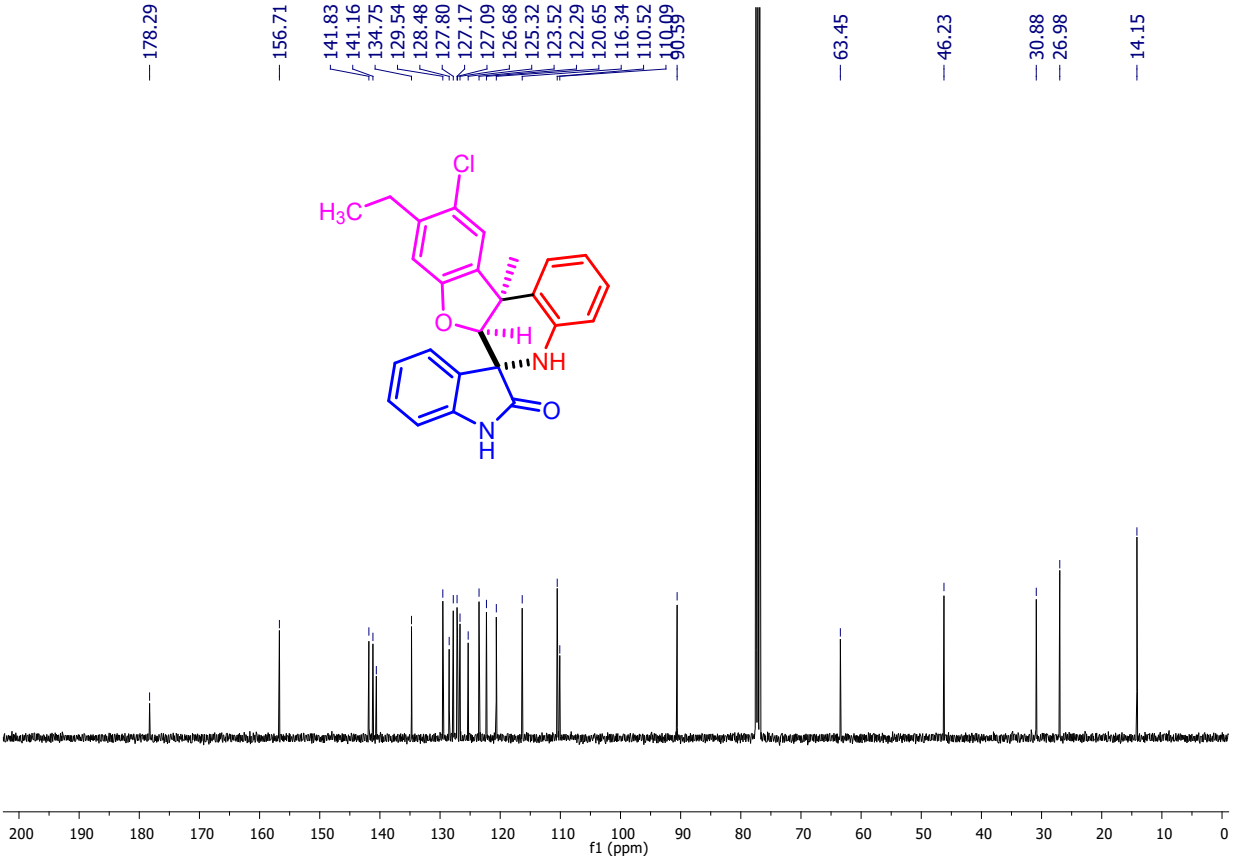
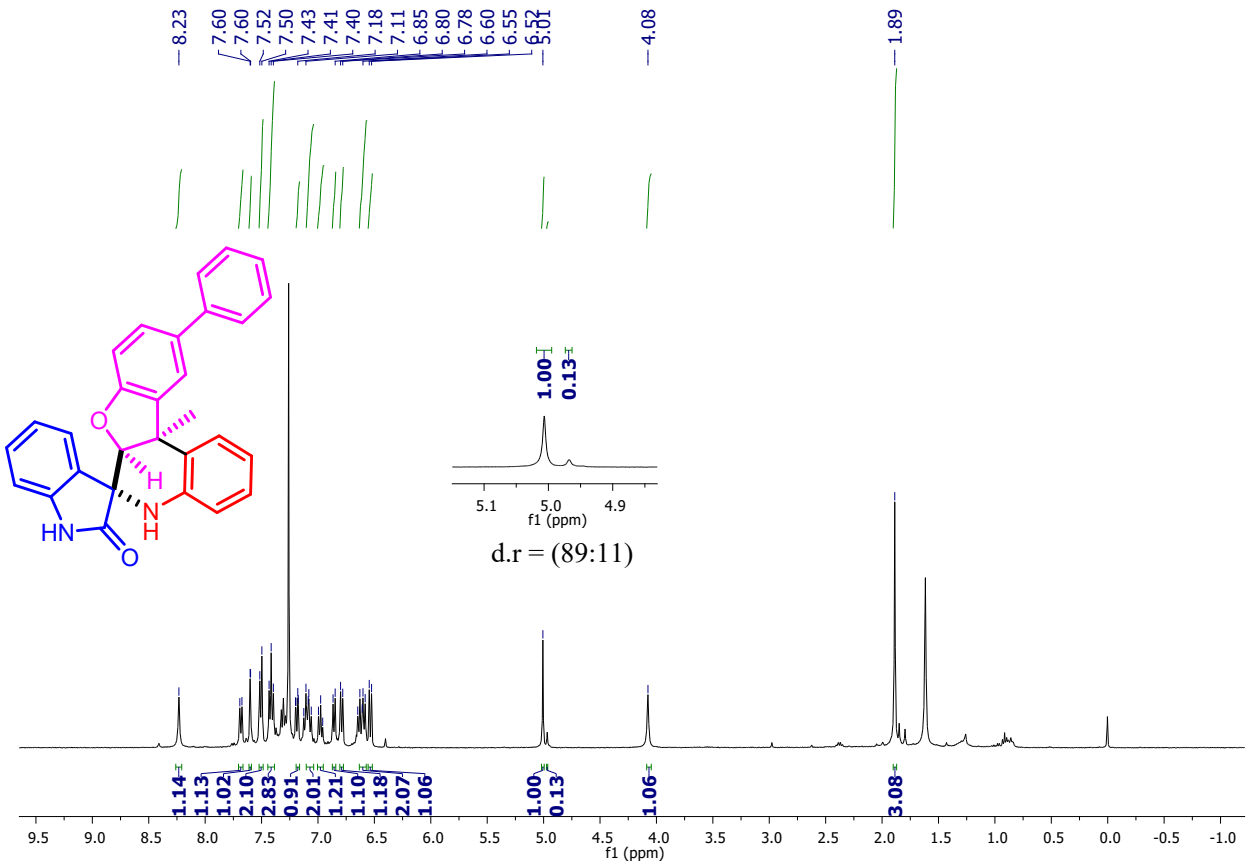
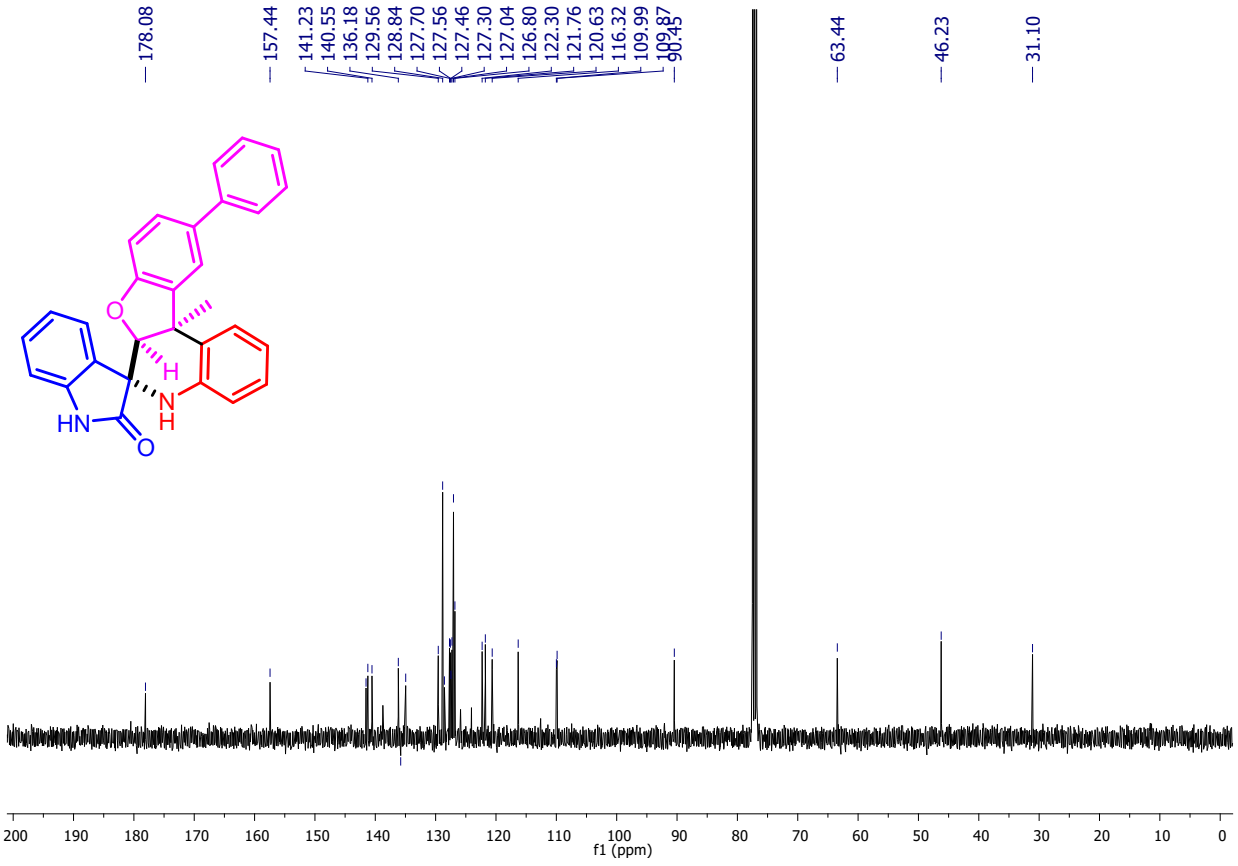
^{13}C {^{1}H} NMR Spectrum of **9e** (100 MHz, $CDCl_3$)



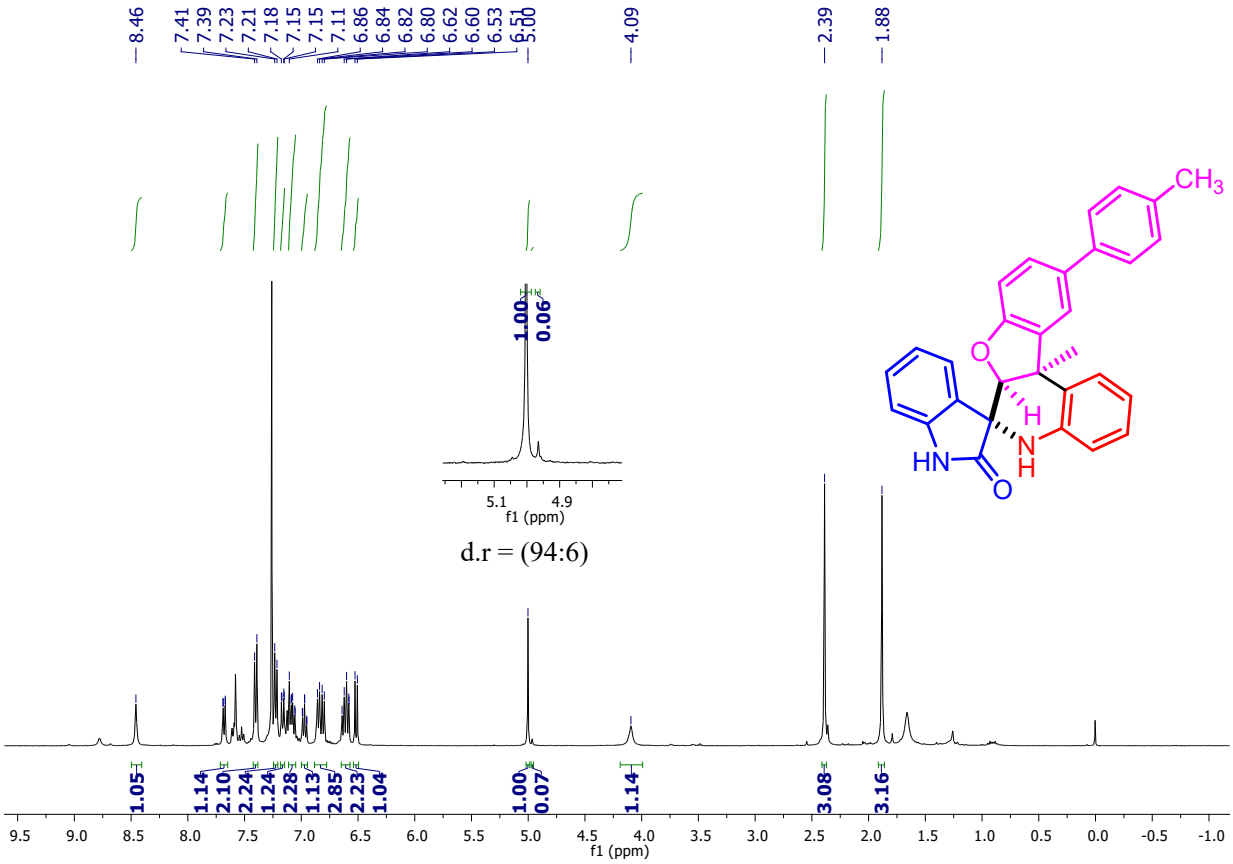
^{1}H NMR Spectrum of **9f** (400 MHz, $CDCl_3$)



^{13}C {^{1}H} NMR Spectrum of **9f** (100 MHz, $CDCl_3$)

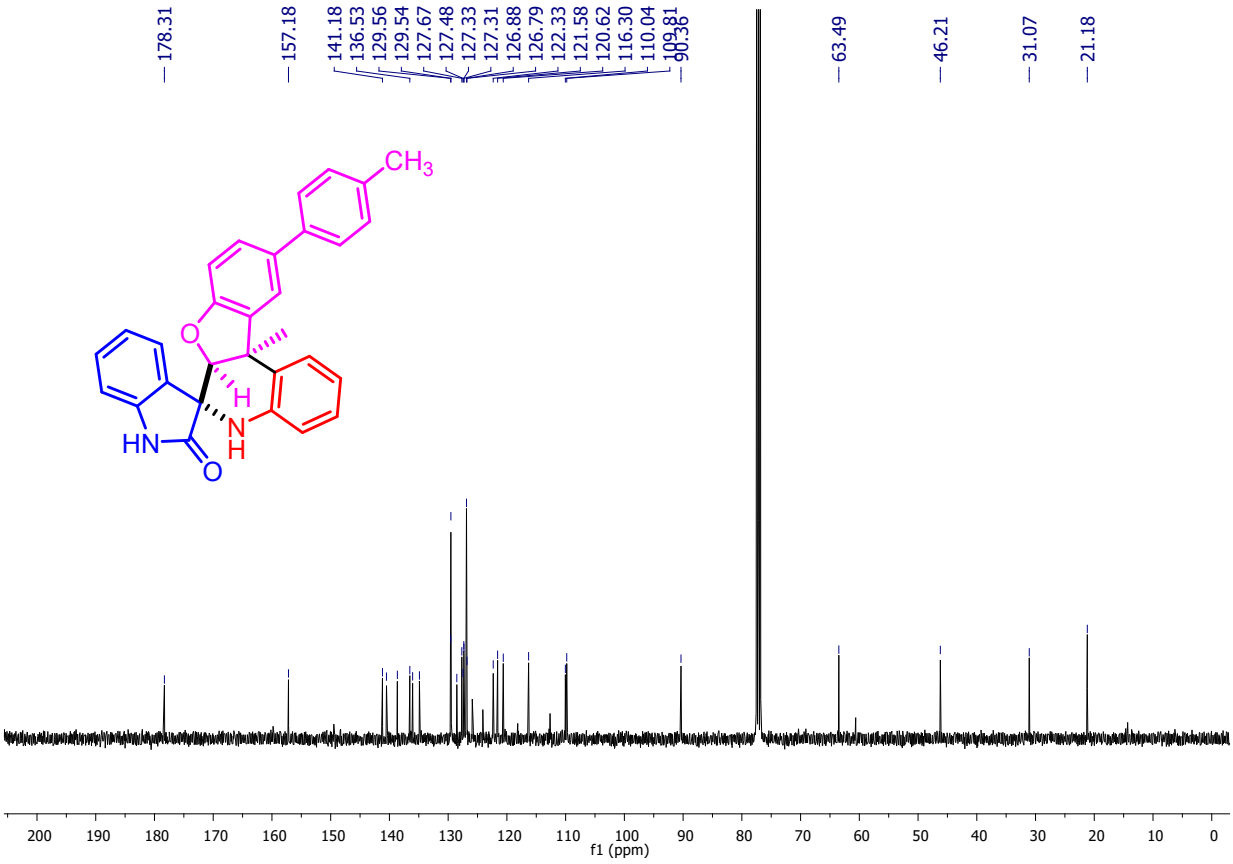


^{1}H NMR Spectrum of **9g** (400 MHz, $CDCl_3$)

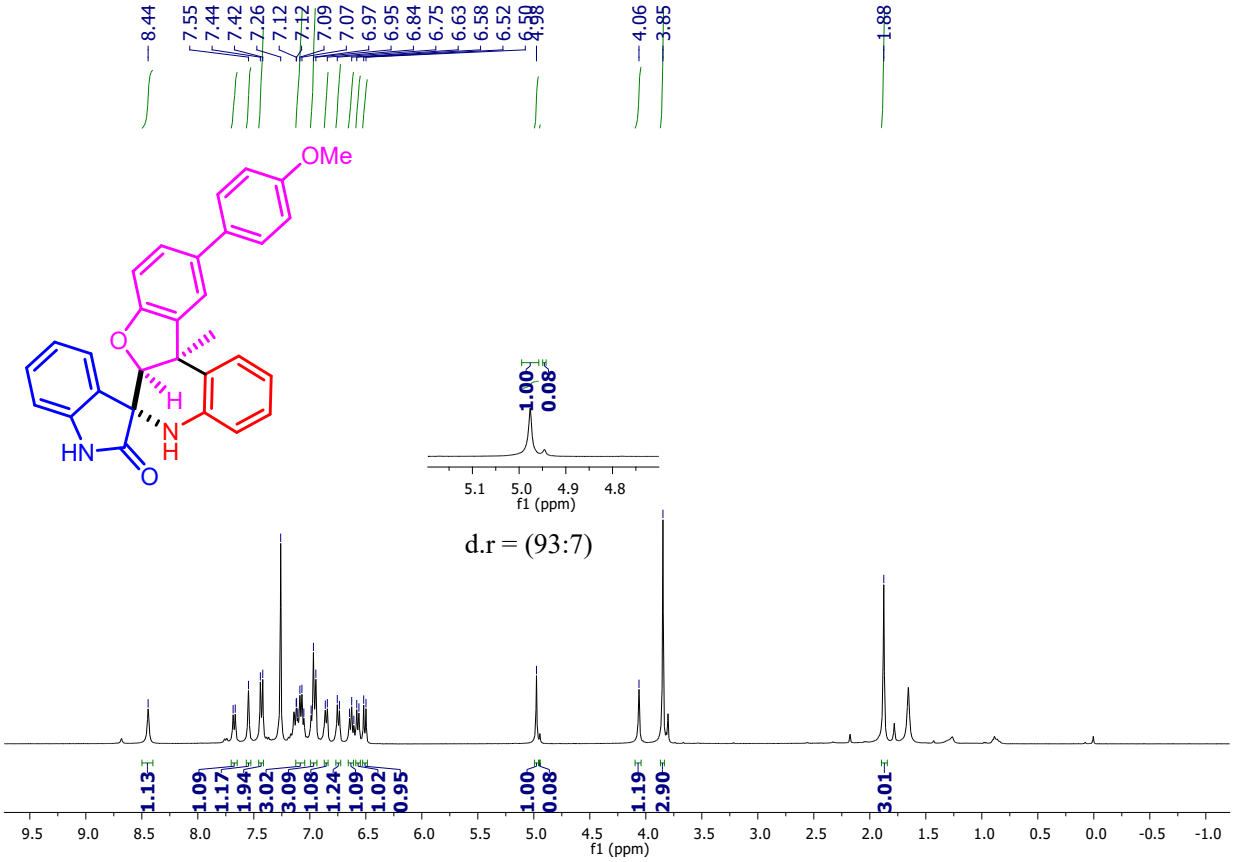


d.r = (94:6)

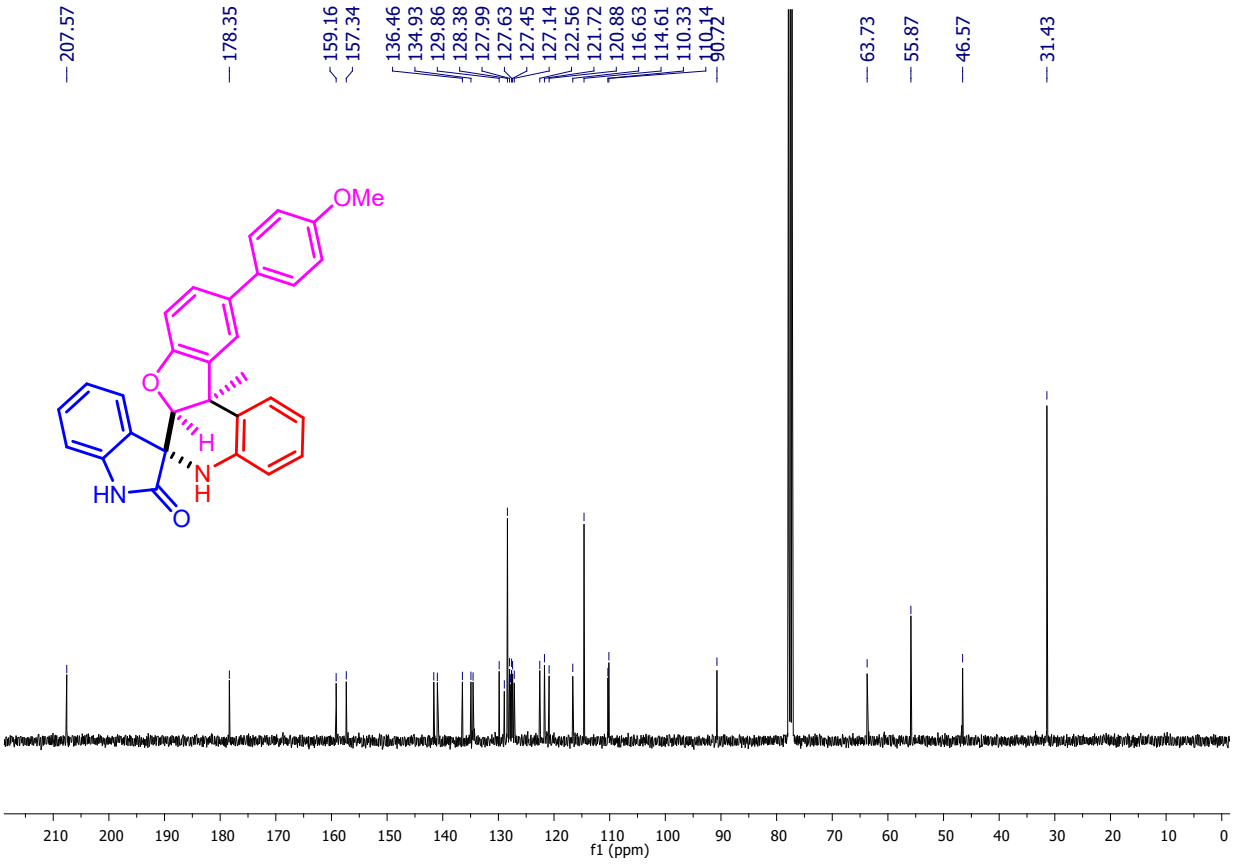
^{13}C {^{1}H} NMR Spectrum of **9g** (100 MHz, $CDCl_3$)



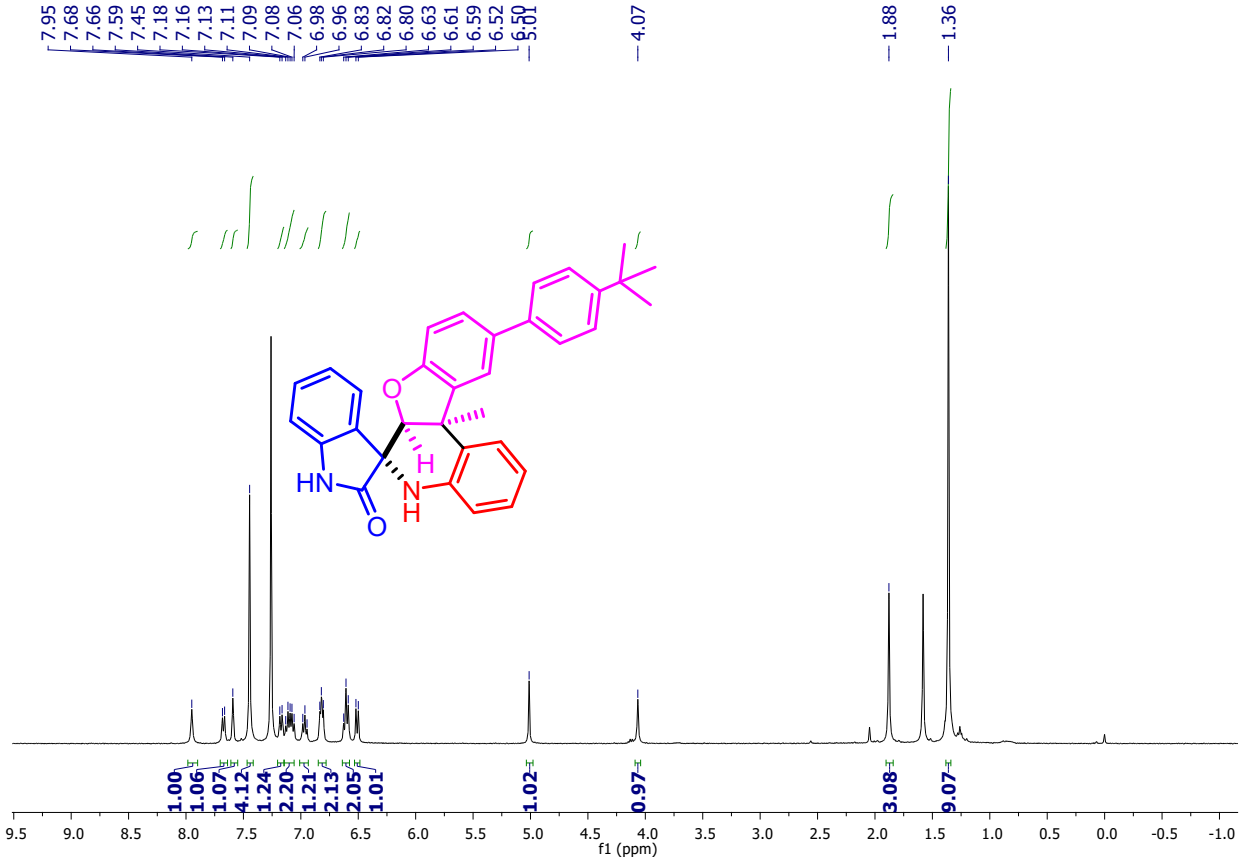
^{1}H NMR Spectrum of **9h** (400 MHz, $CDCl_3$)



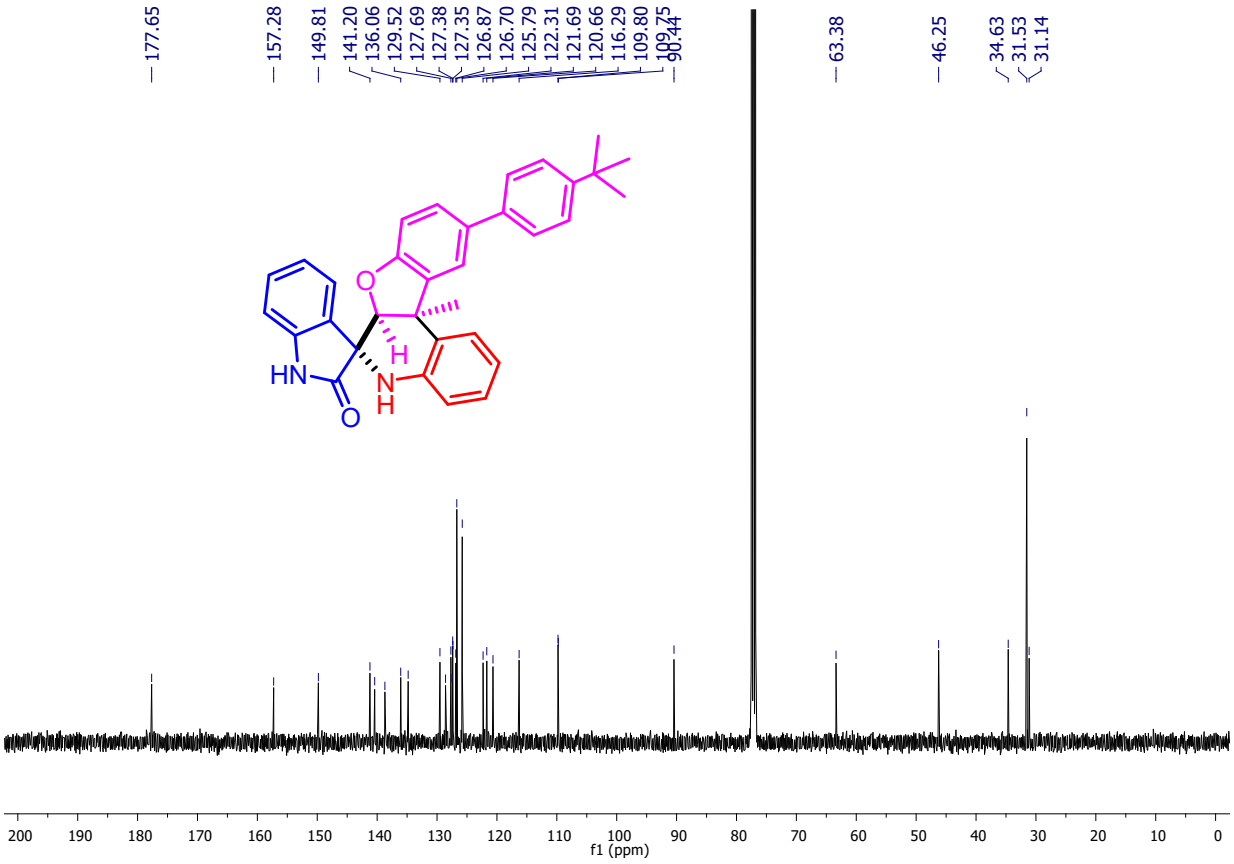
^{13}C {^{1}H} NMR Spectrum of **9h** (100 MHz, $CDCl_3$)



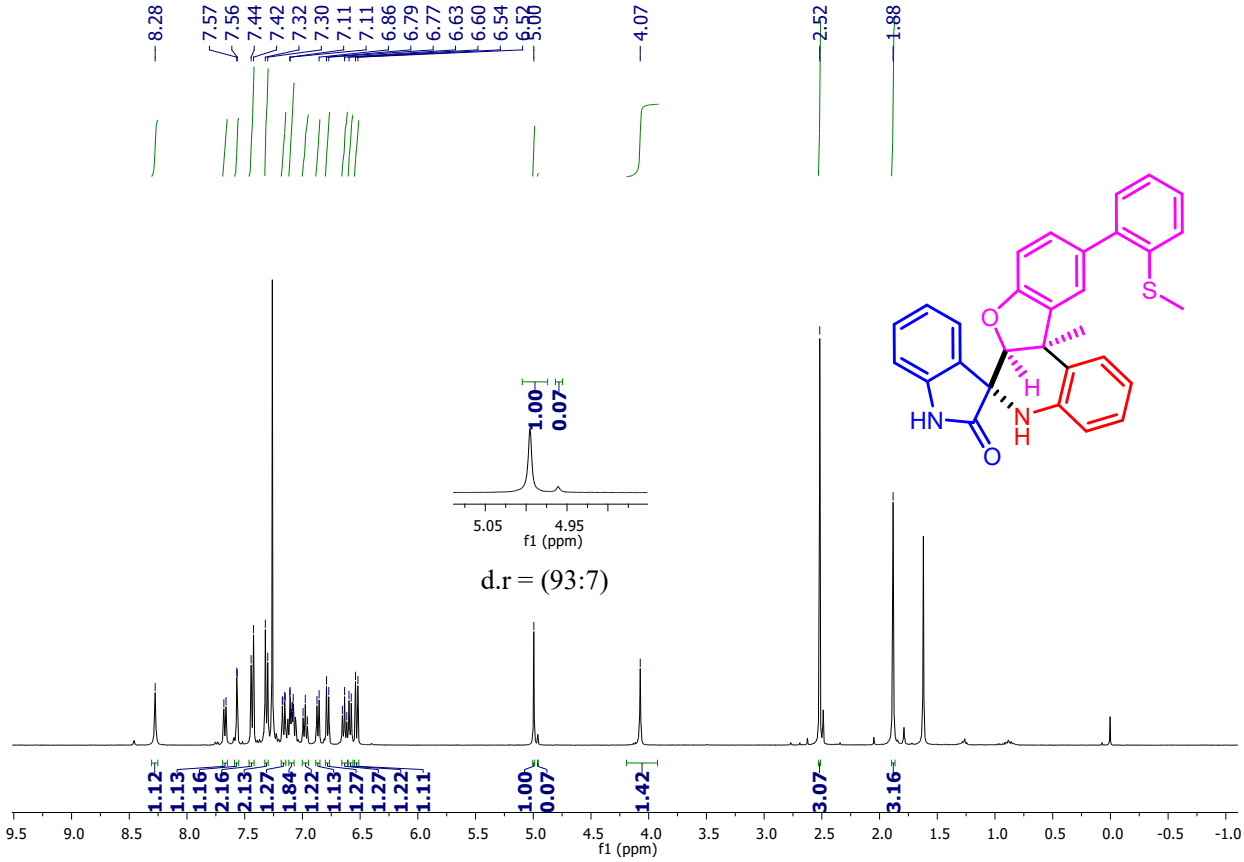
^{1}H NMR Spectrum of **9i** (400 MHz, $CDCl_3$)



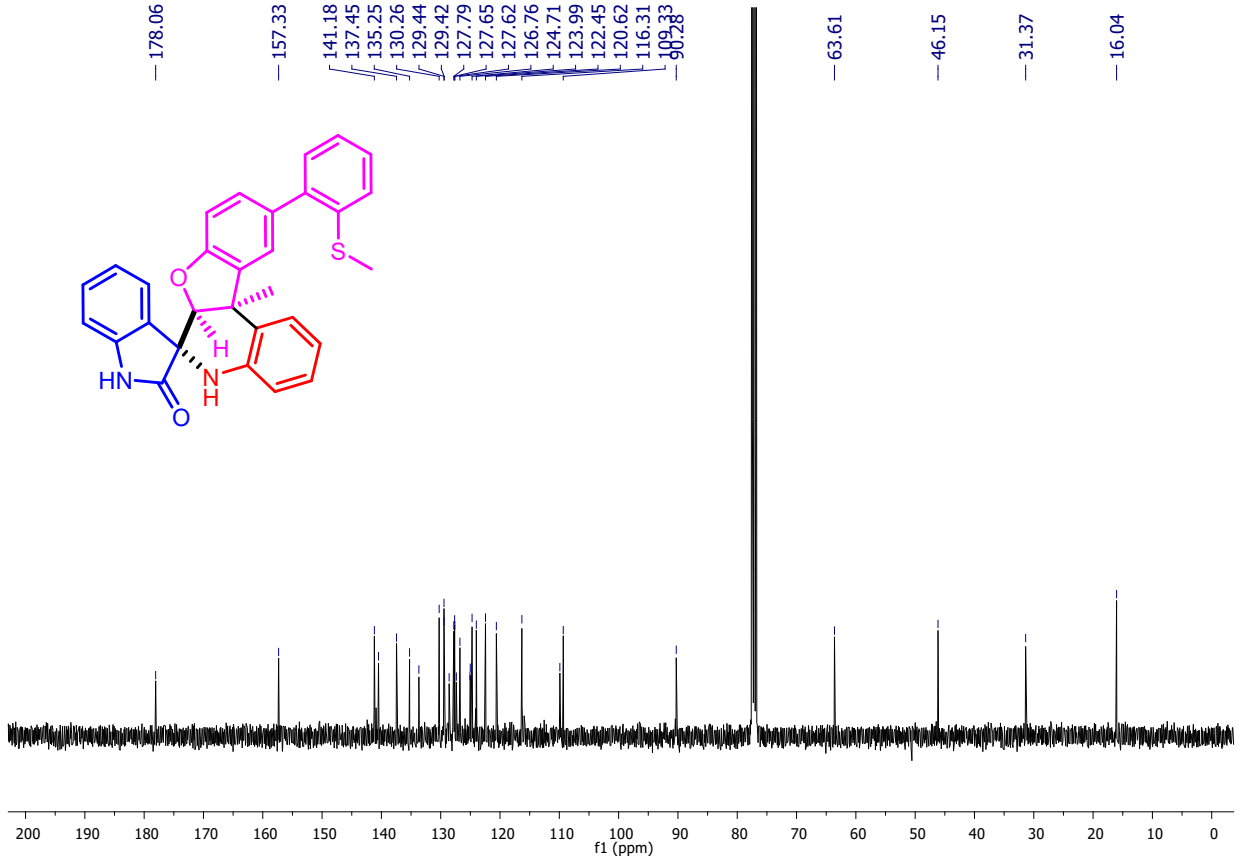
^{13}C {^{1}H} NMR Spectrum of **9i** (100 MHz, $CDCl_3$)



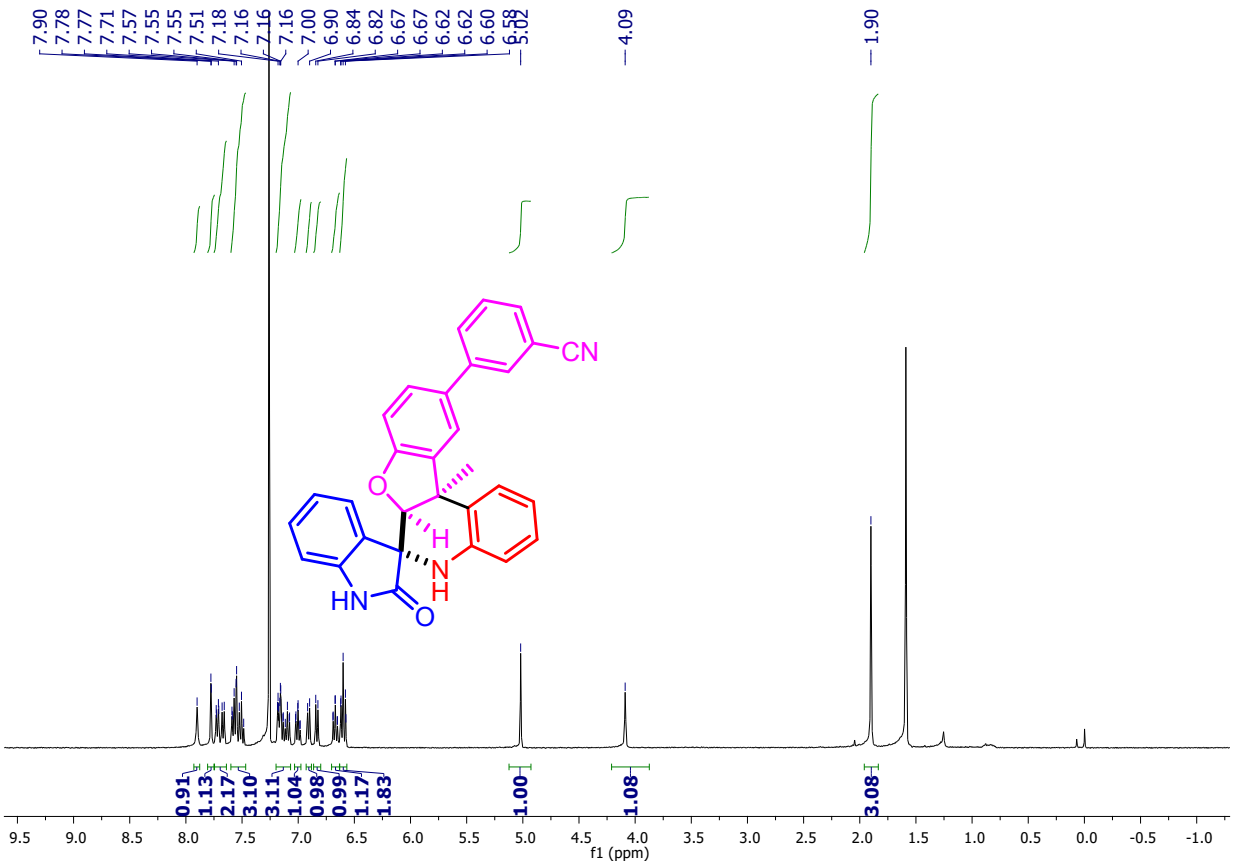
^{1}H NMR Spectrum of **9j** (400 MHz, $CDCl_3$)



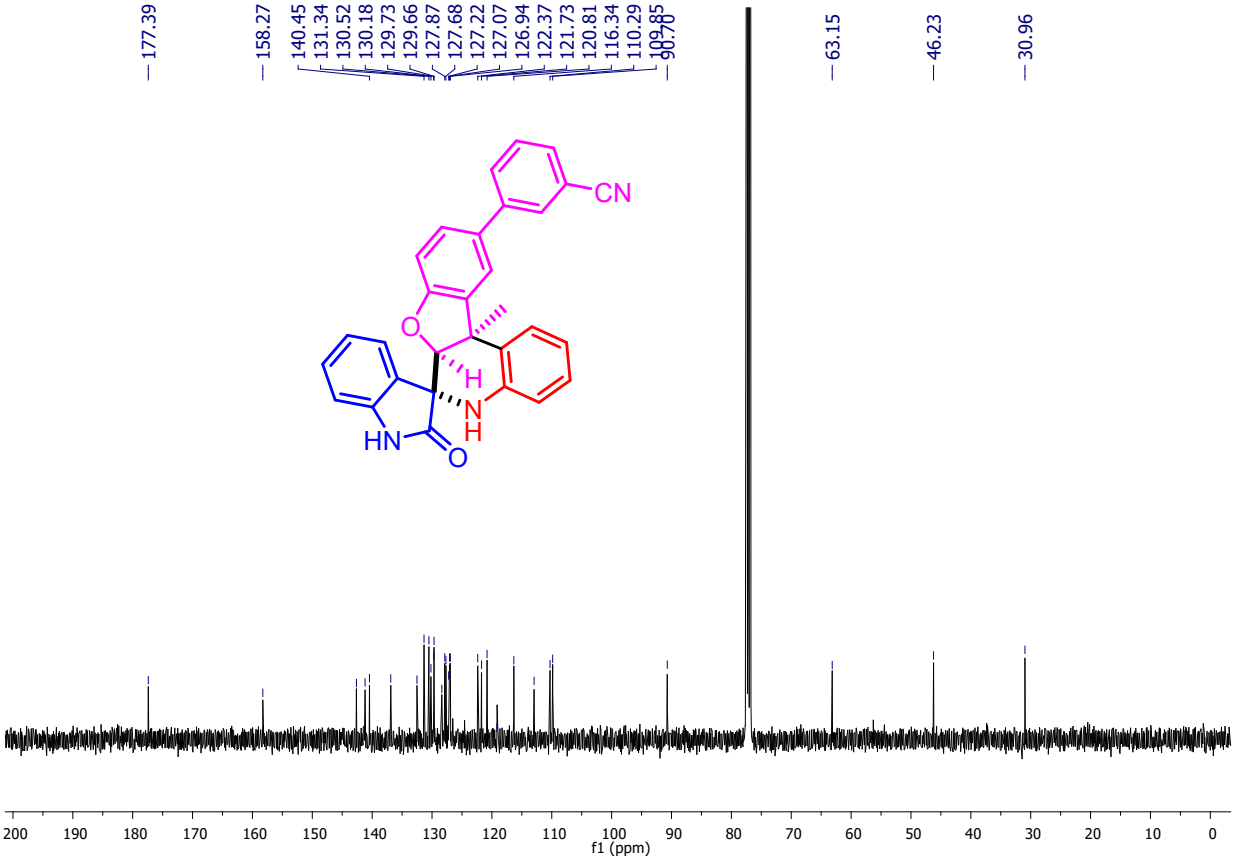
^{13}C {^{1}H} NMR Spectrum of **9j** (100 MHz, $CDCl_3$)



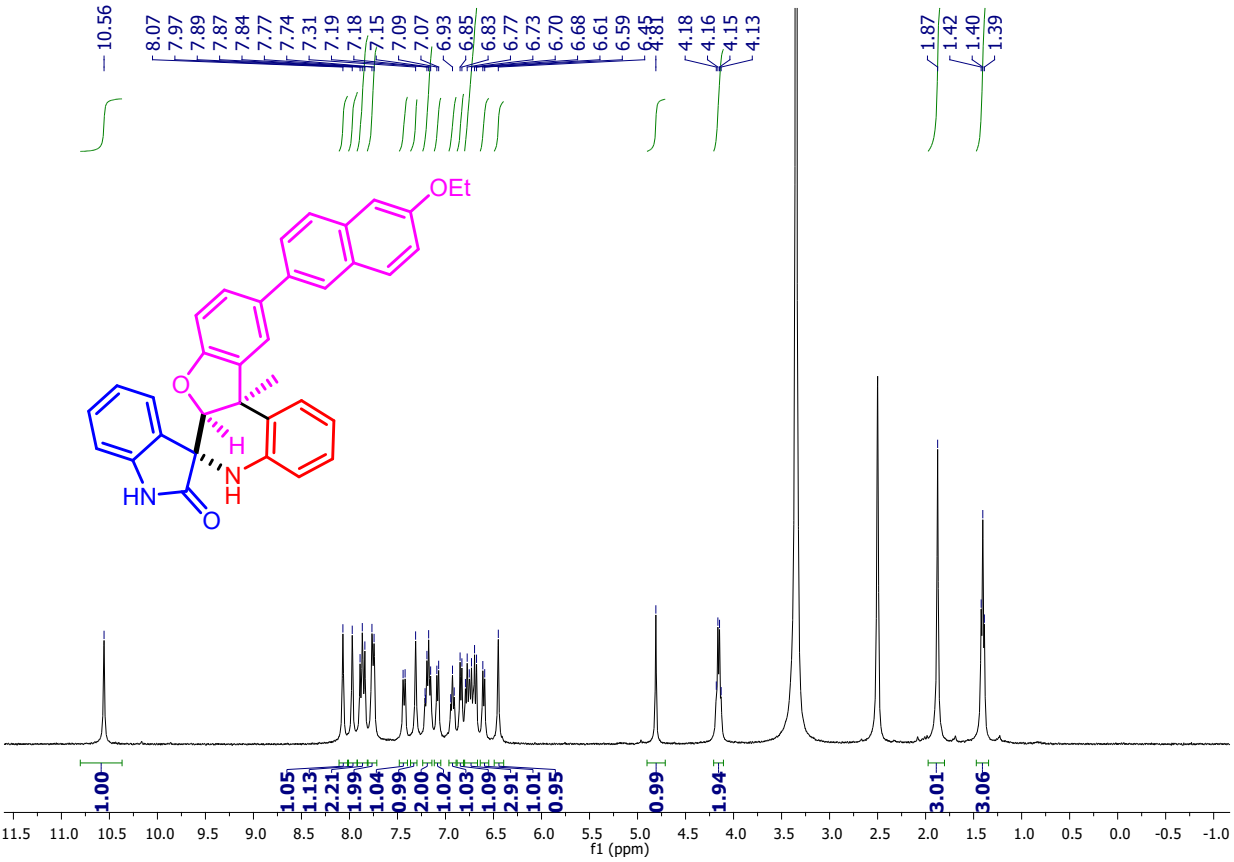
^{1}H NMR Spectrum of **9k** (400 MHz, $CDCl_3$)



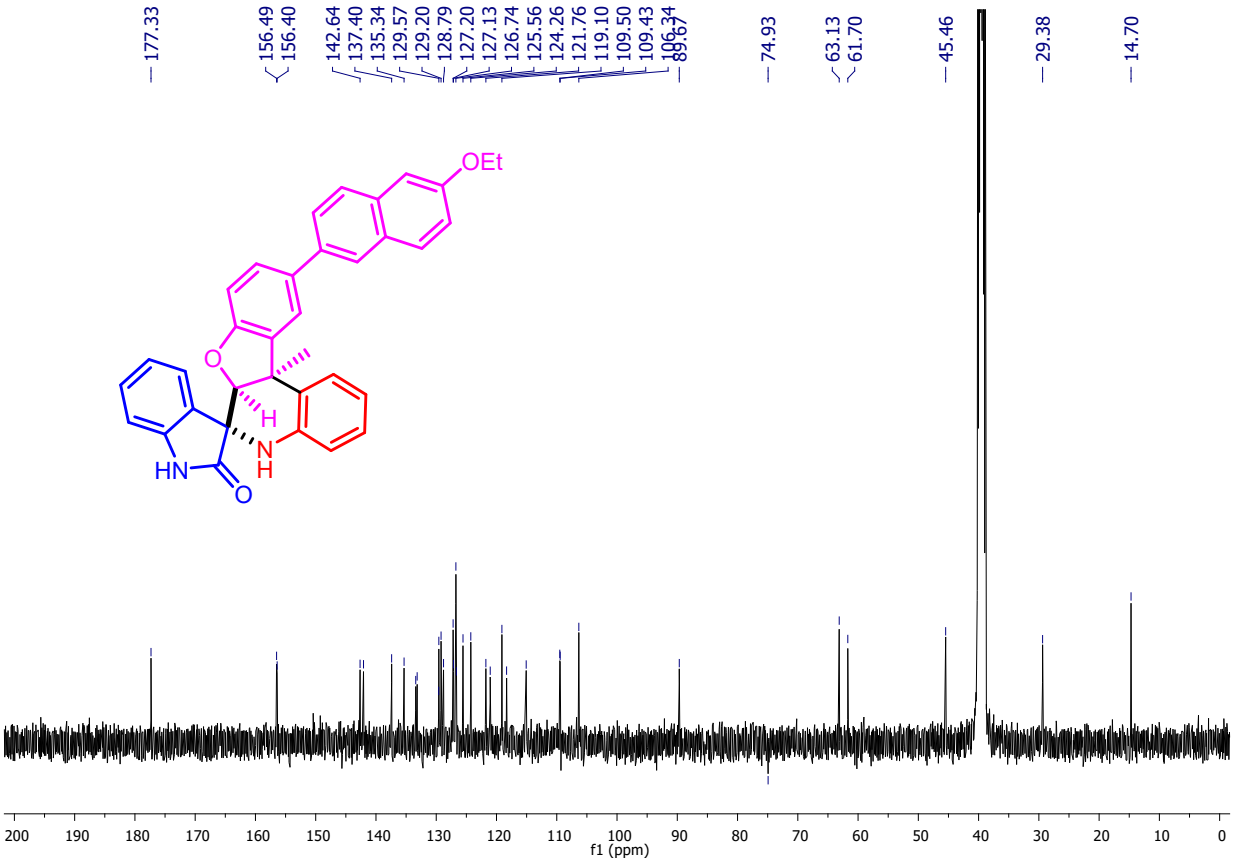
^{13}C {^{1}H} NMR Spectrum of **9k** (100 MHz, $CDCl_3$)



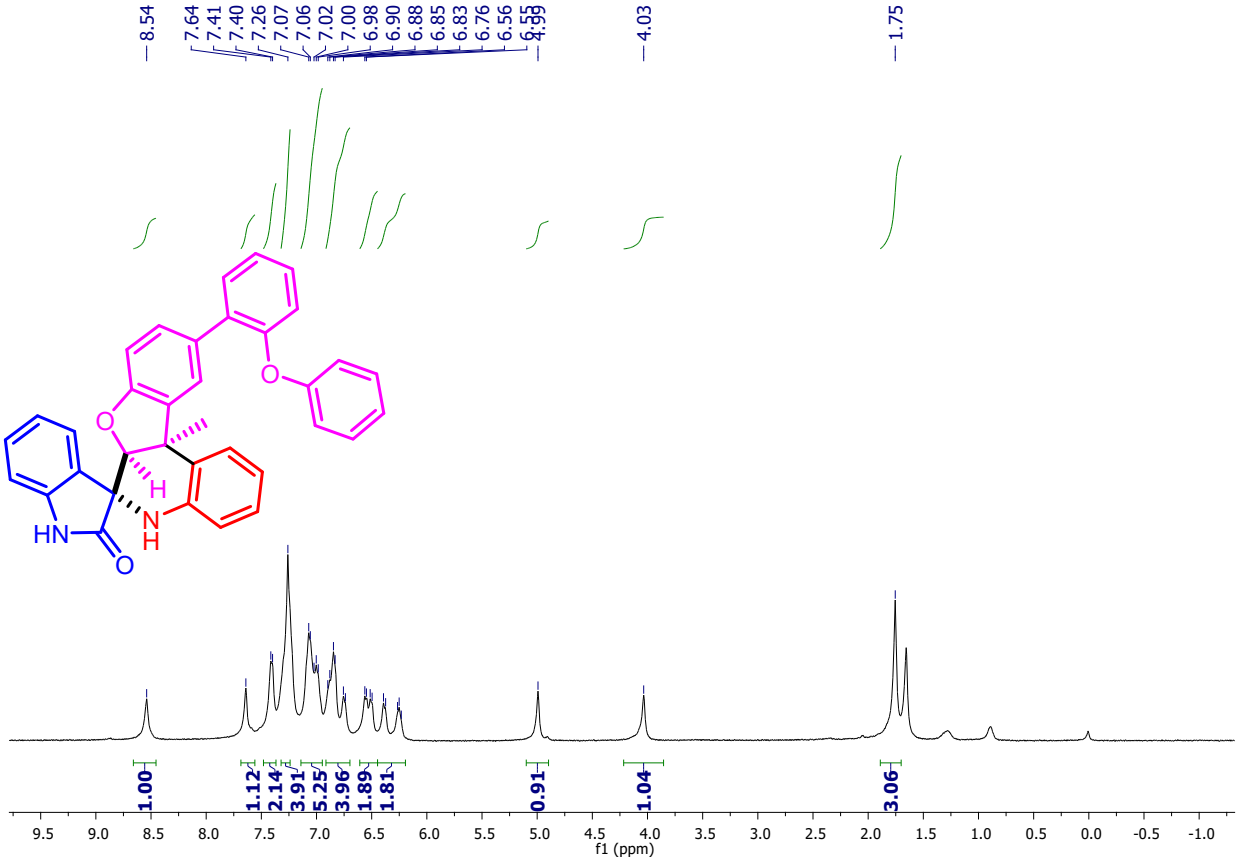
^{1}H NMR Spectrum of **9l** (400 MHz, $CDCl_3$)



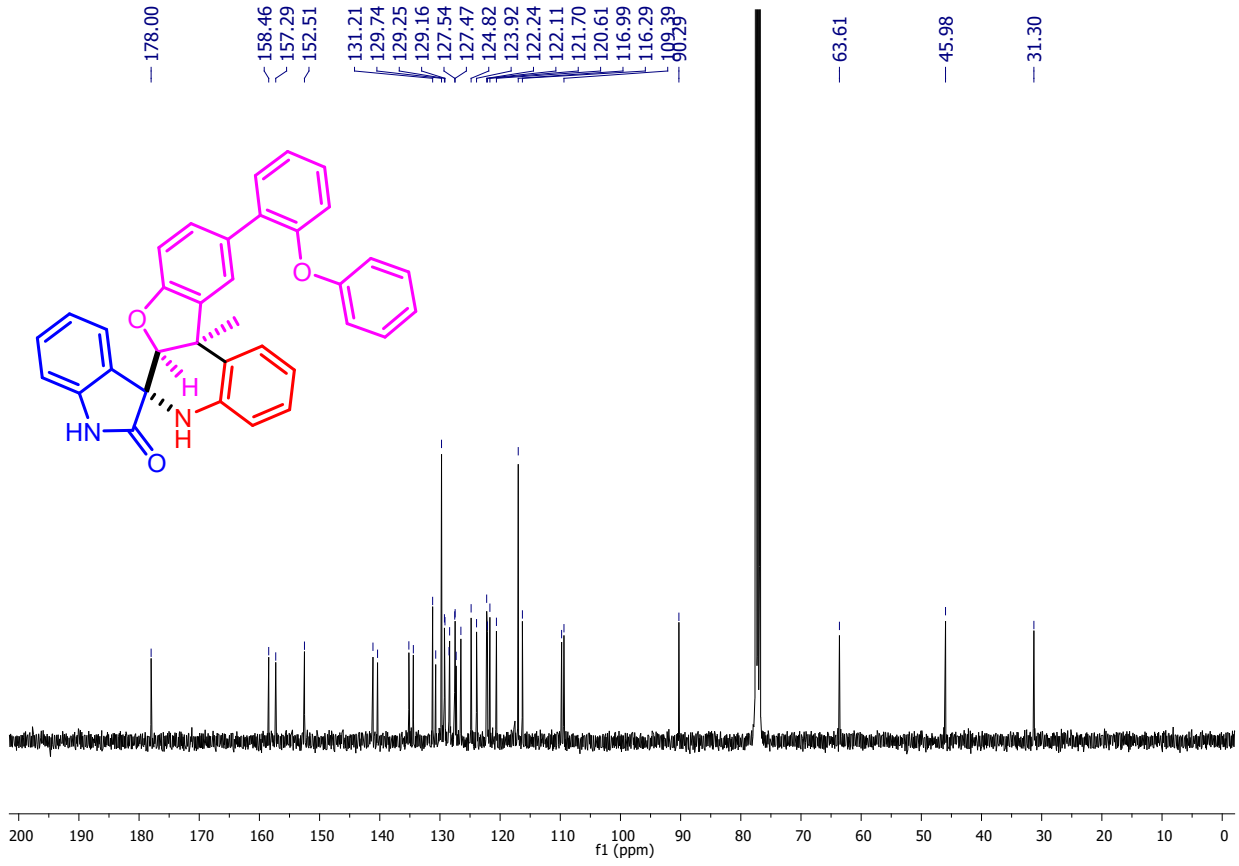
^{13}C {^{1}H} NMR Spectrum of **9l** (100 MHz, DMSO-d_6)



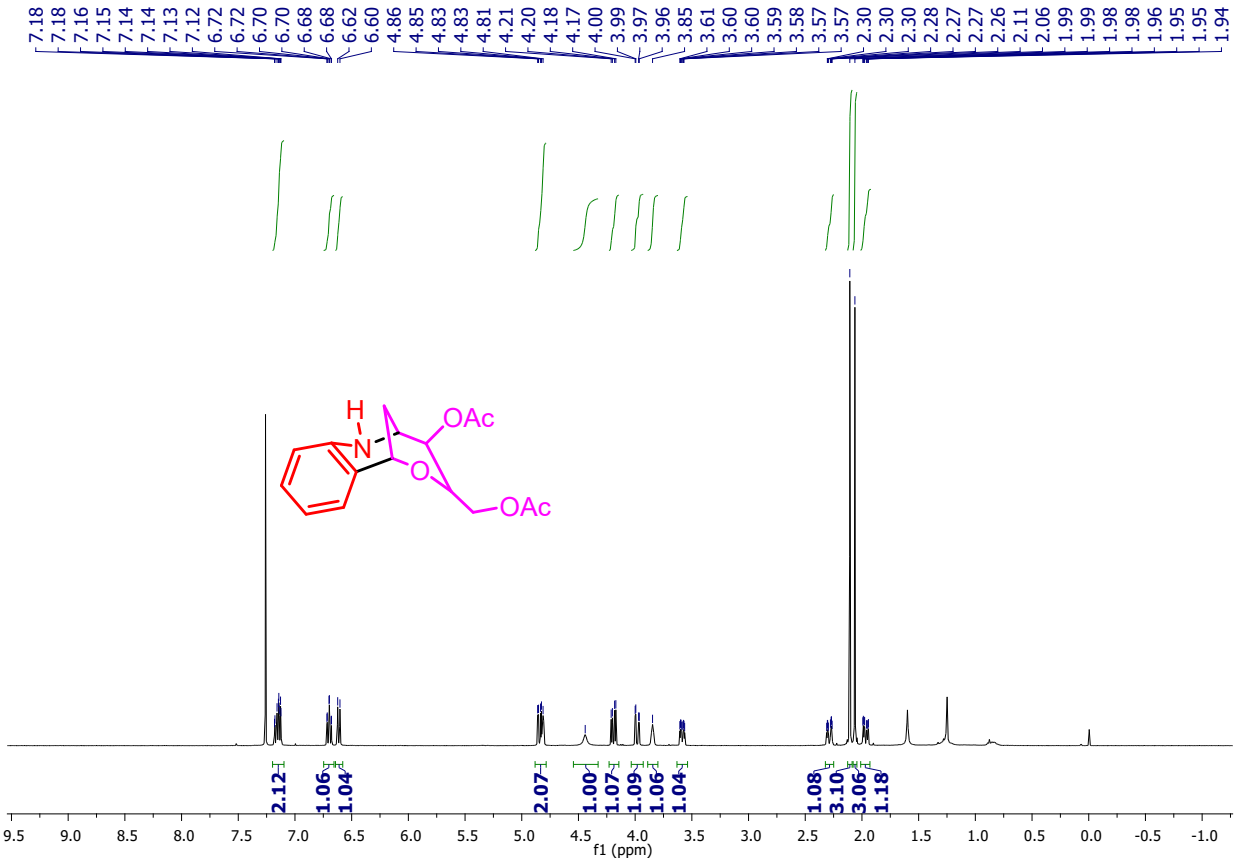
^{1}H NMR Spectrum of **9m** (400 MHz, $CDCl_3$)



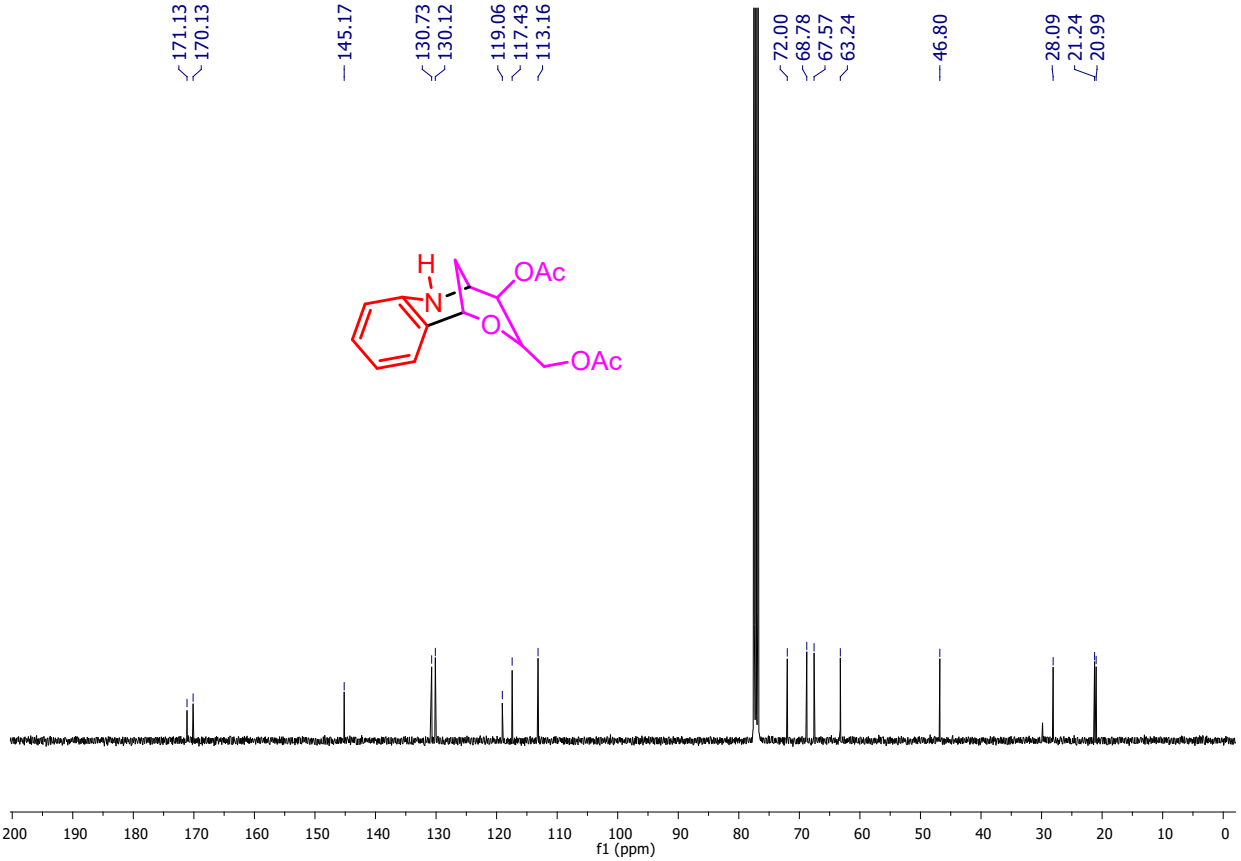
^{13}C {H} NMR Spectrum of **9m** (100 MHz, $CDCl_3$)



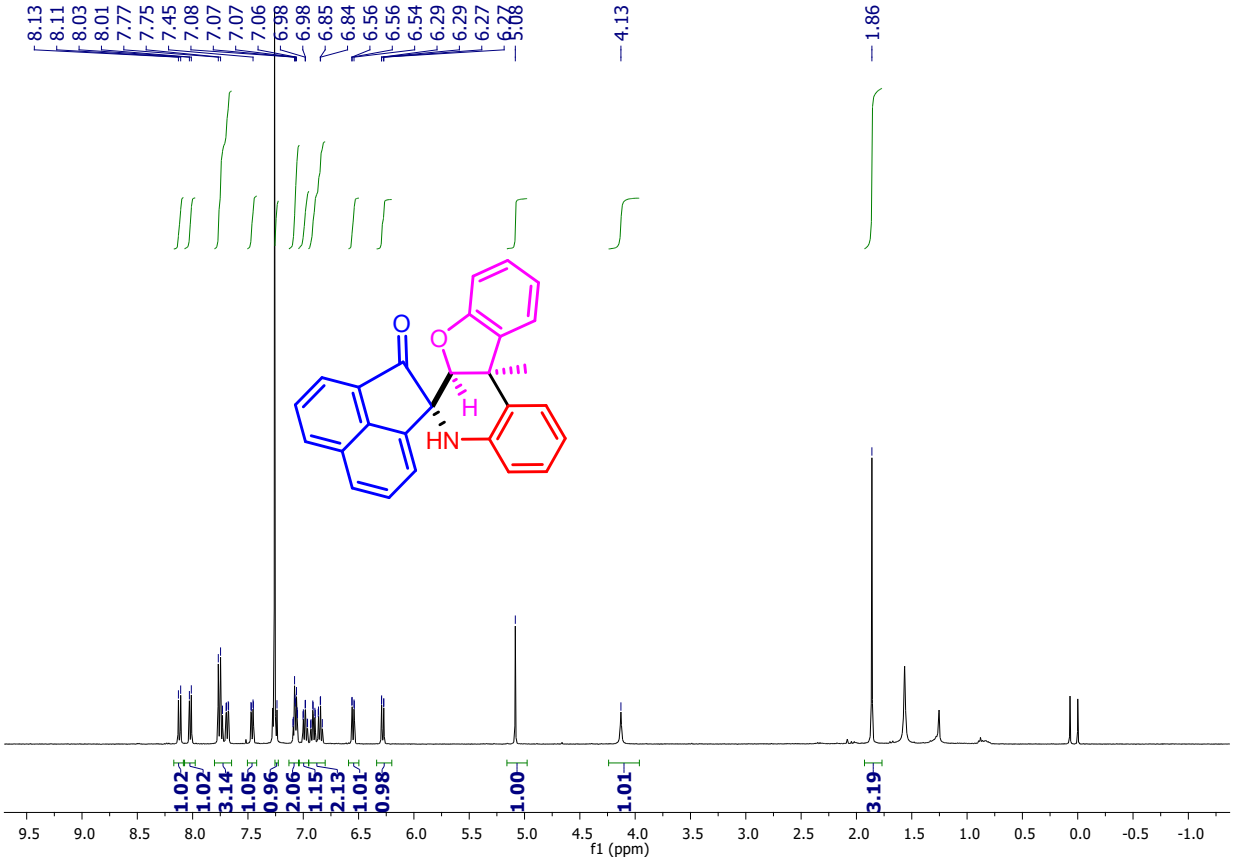
^{1}H NMR Spectrum of **11** (400 MHz, $CDCl_3$)



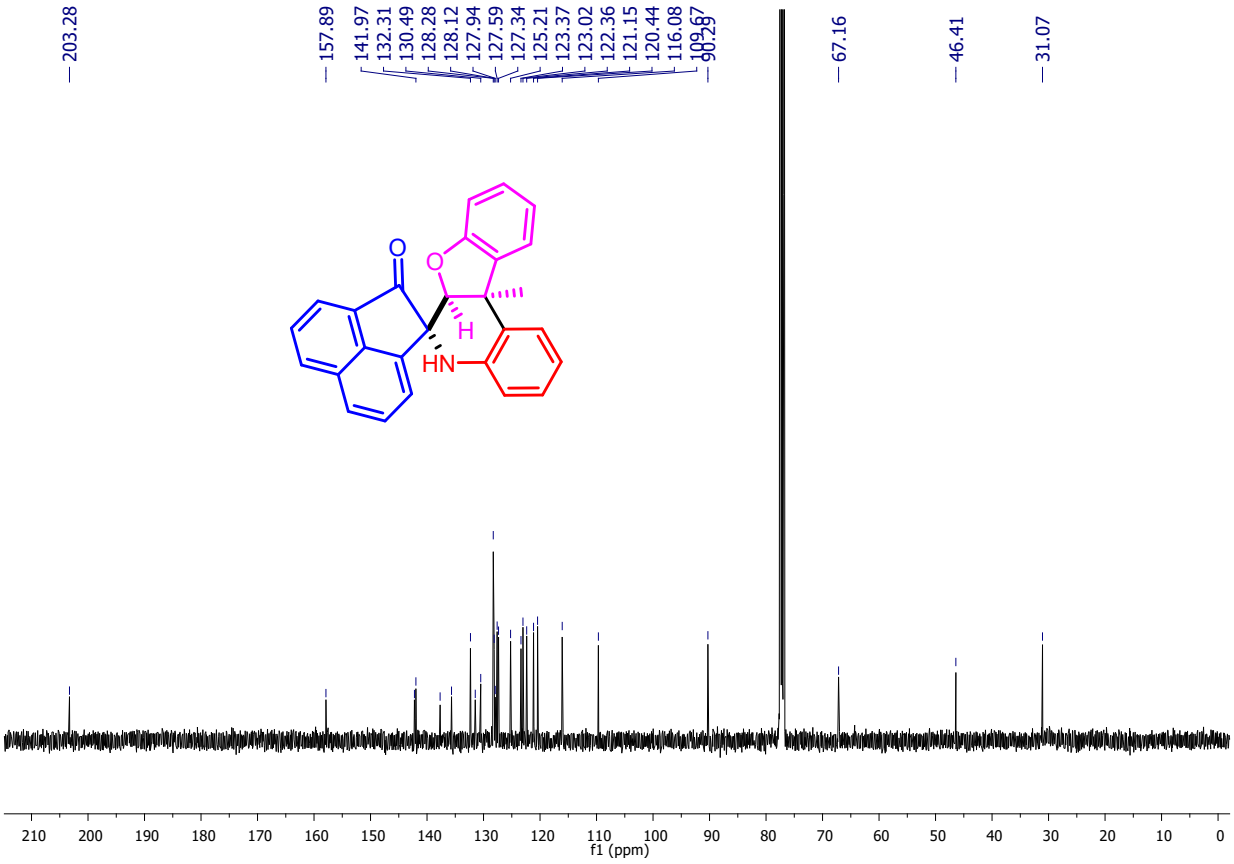
^{13}C {^{1}H} NMR Spectrum of **11** (100 MHz, $CDCl_3$)



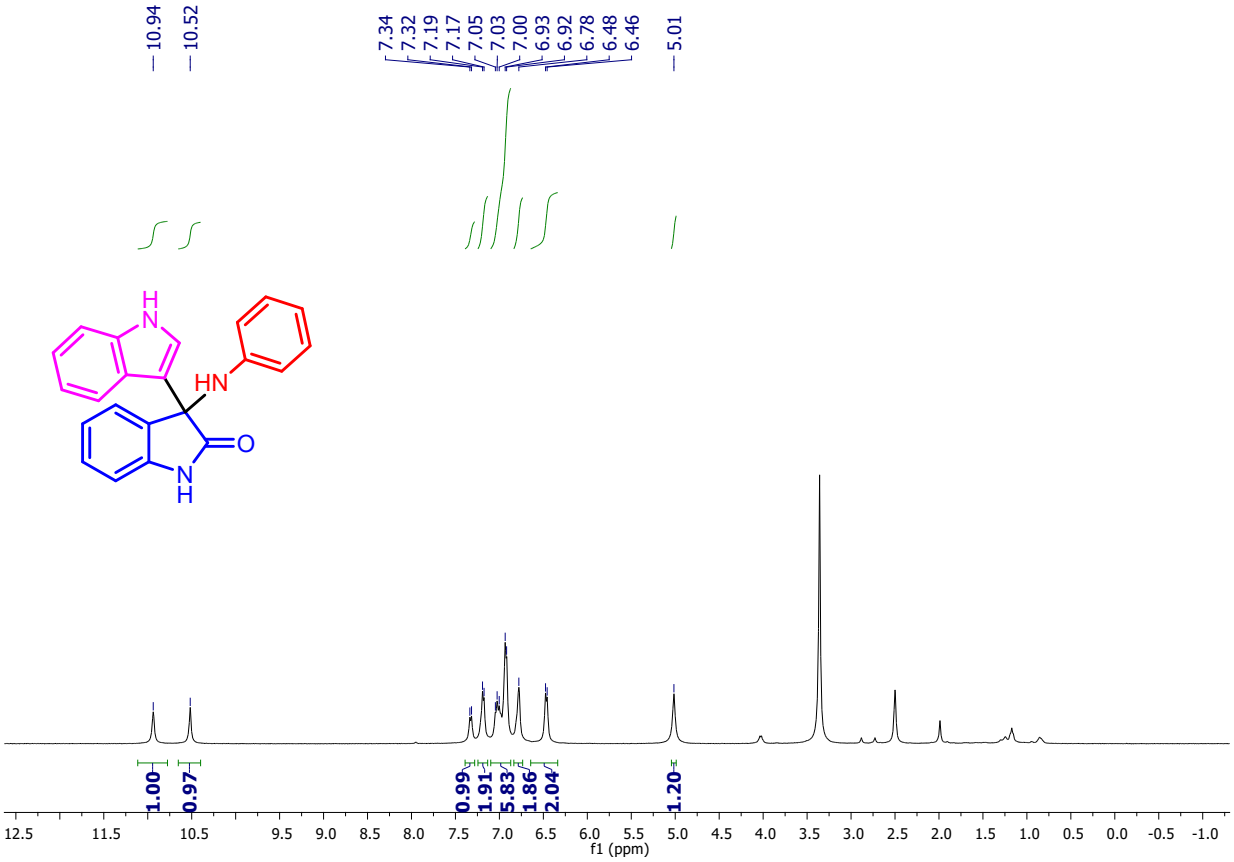
^{1}H NMR Spectrum of **13** (400 MHz, $CDCl_3$)



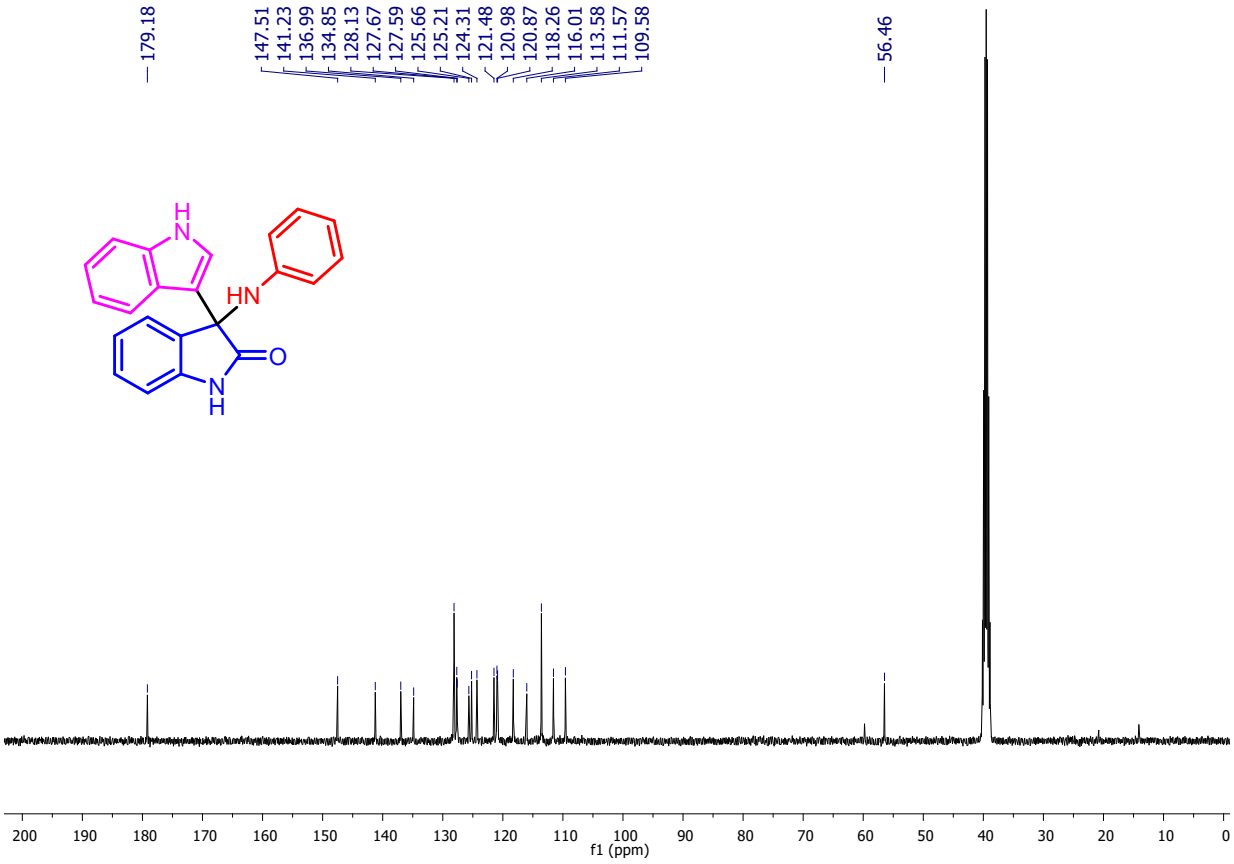
^{13}C {^{1}H} NMR Spectrum of **13** (100 MHz, $CDCl_3$)



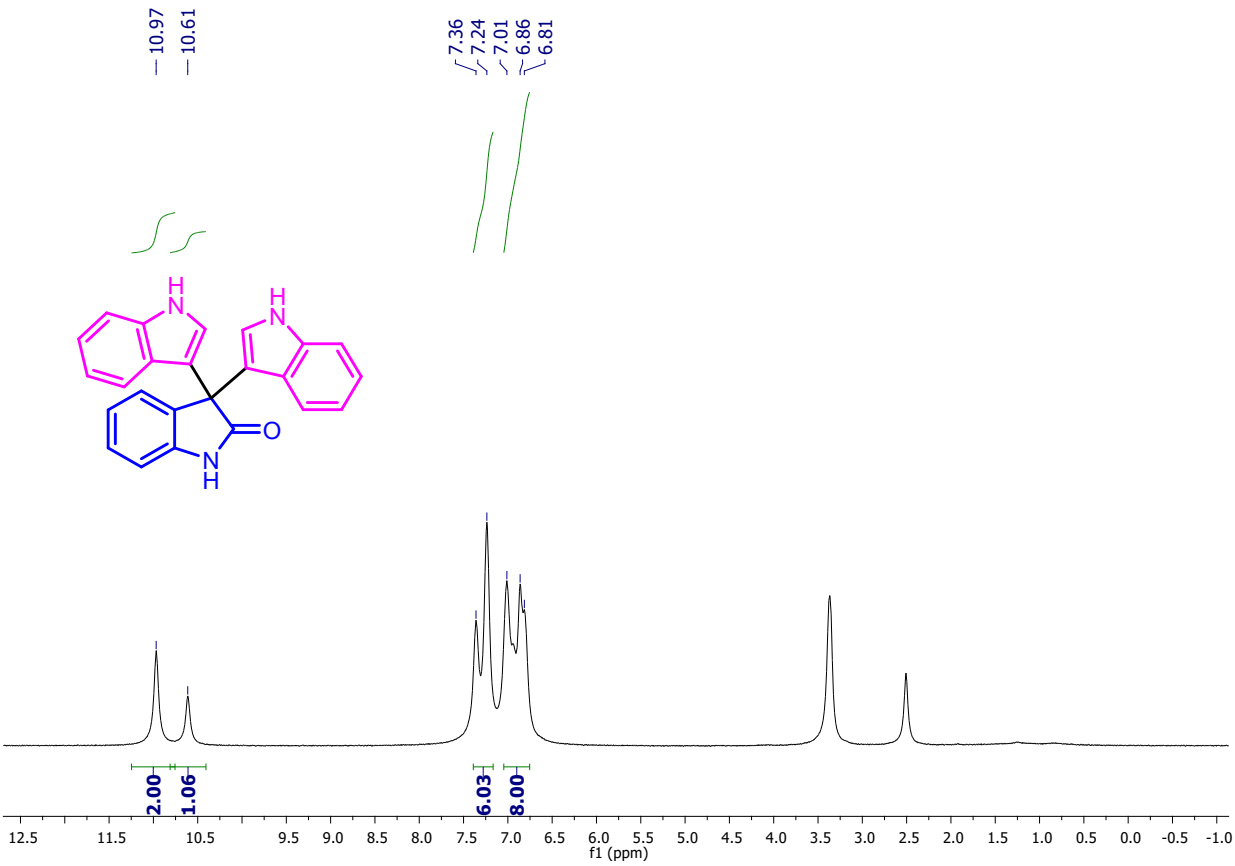
^{1}H NMR Spectrum of **15a** (400 MHz, DMSO-d_6)



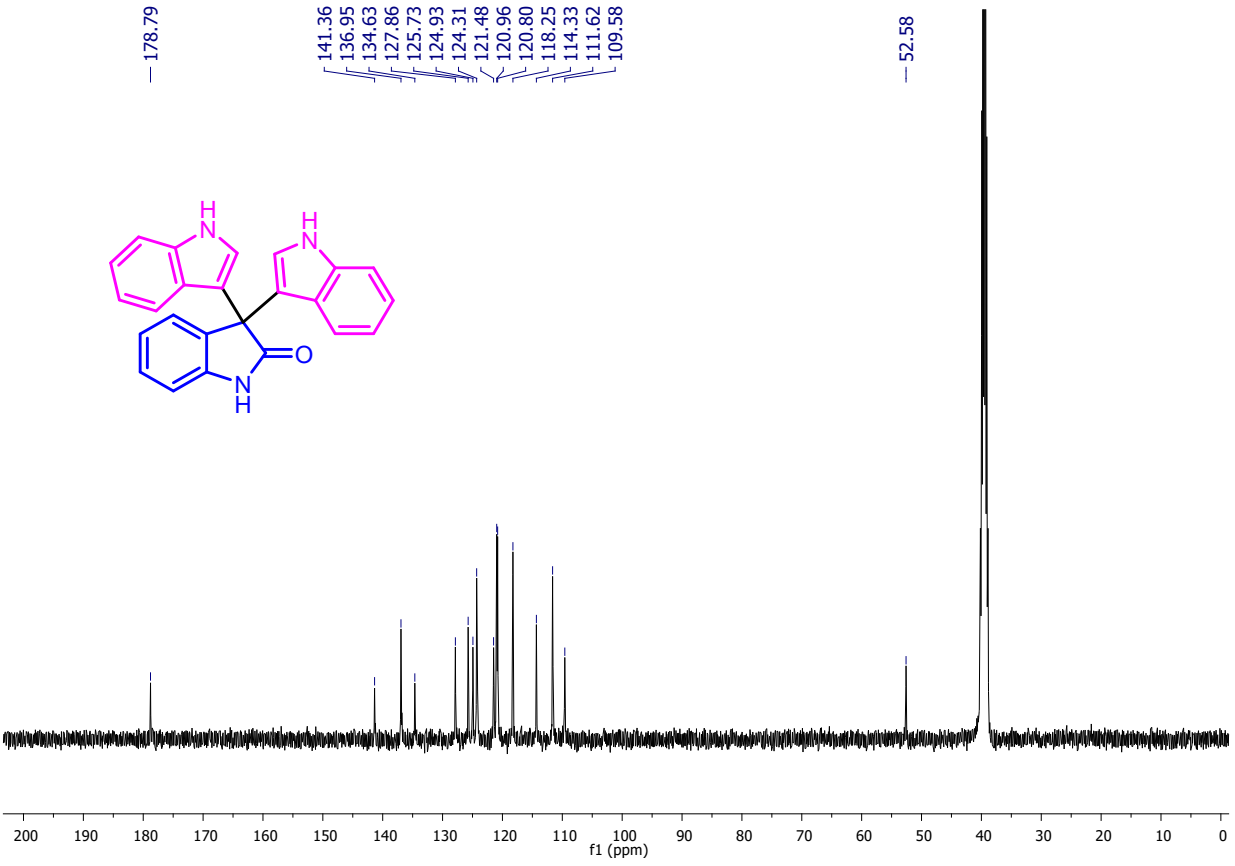
^{13}C {^{1}H} NMR Spectrum of **15a** (100 MHz, DMSO-d_6)



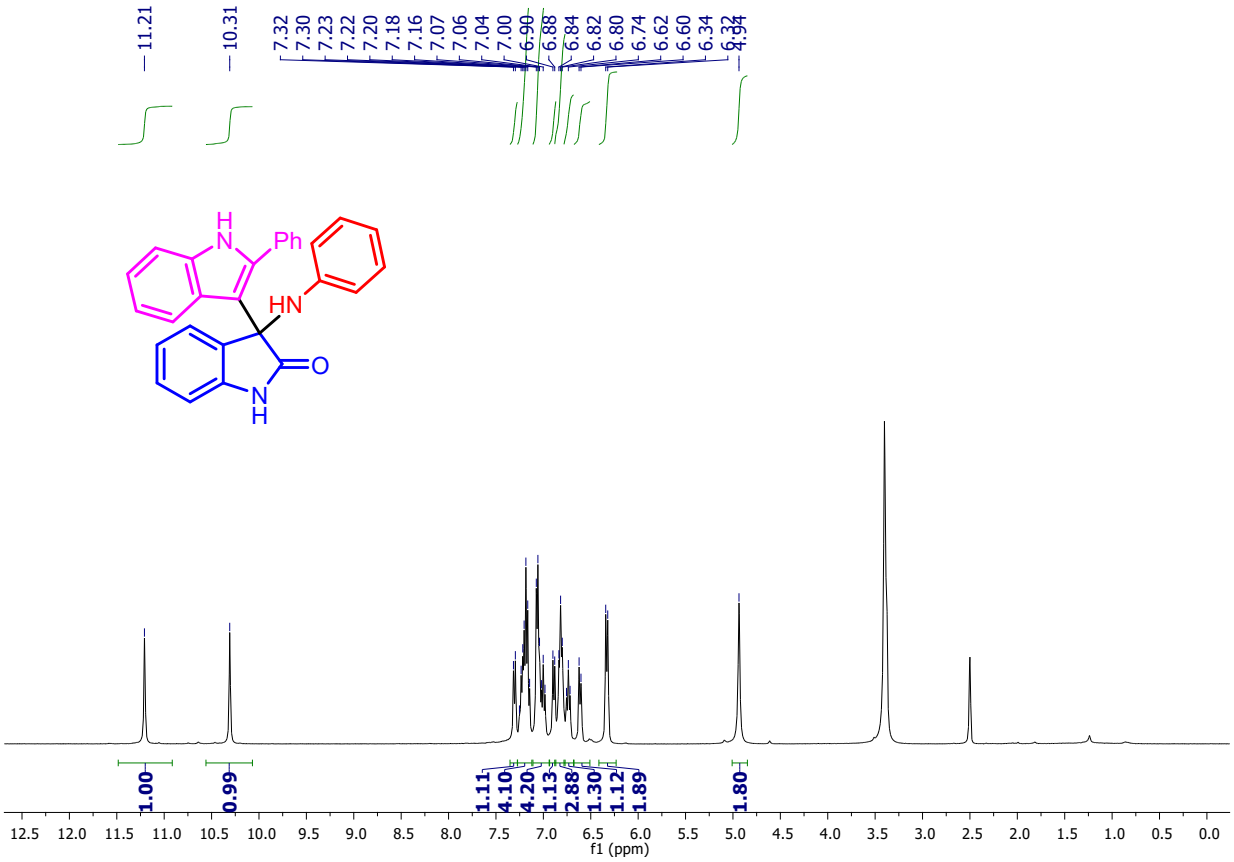
^{1}H NMR Spectrum of **15b** (400 MHz, DMSO-d_6)



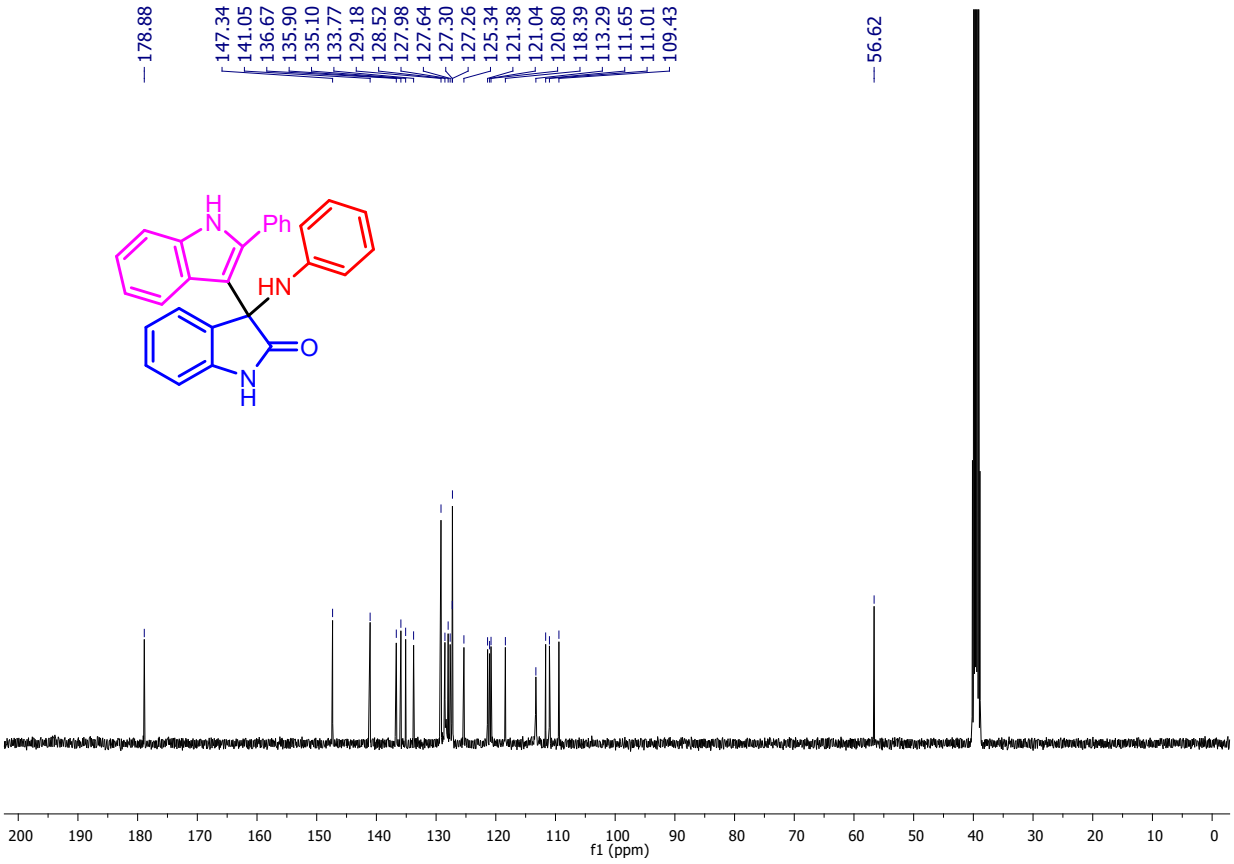
^{13}C {^{1}H} NMR Spectrum of **15b** (100 MHz, DMSO-d_6)



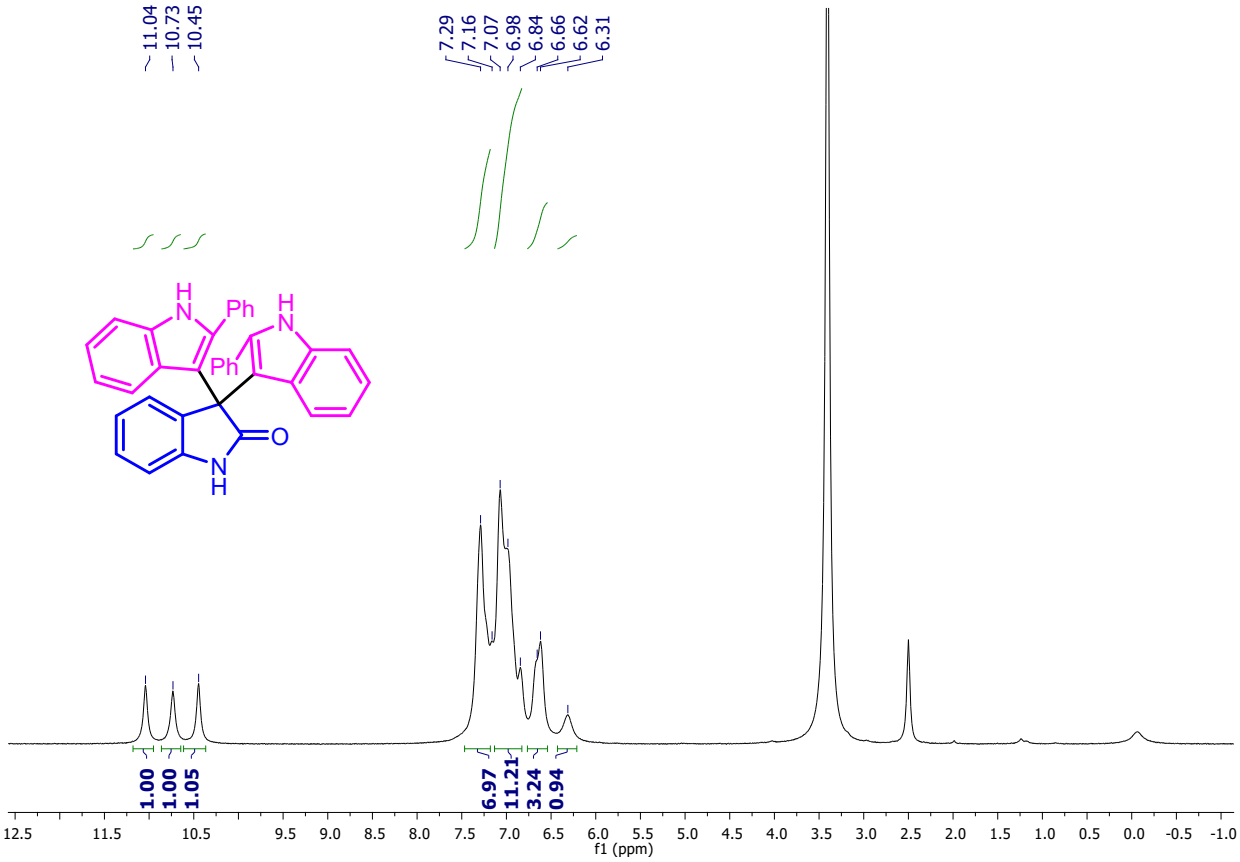
^{1}H NMR Spectrum of **17a** (400 MHz, DMSO-d_6)



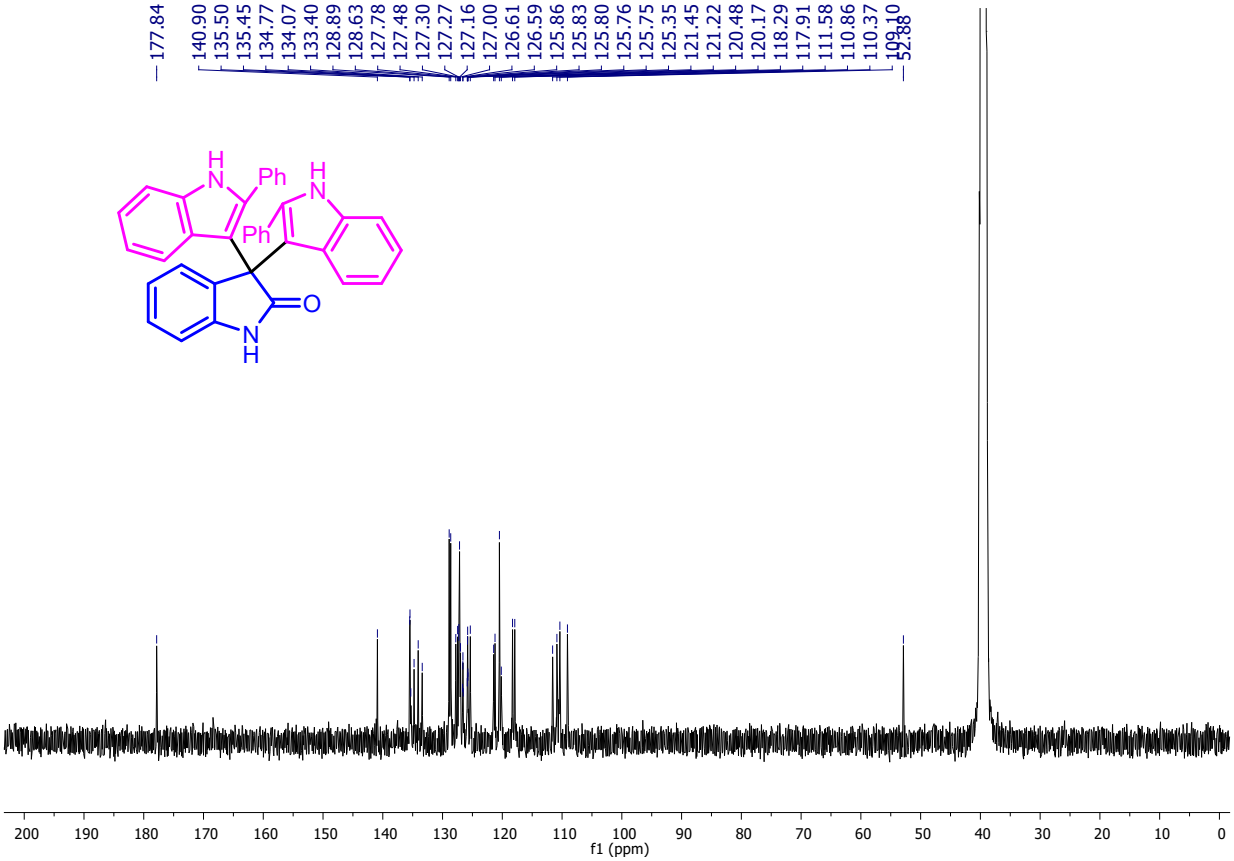
^{13}C {^{1}H} NMR Spectrum of **17a** (100 MHz, DMSO-d_6)



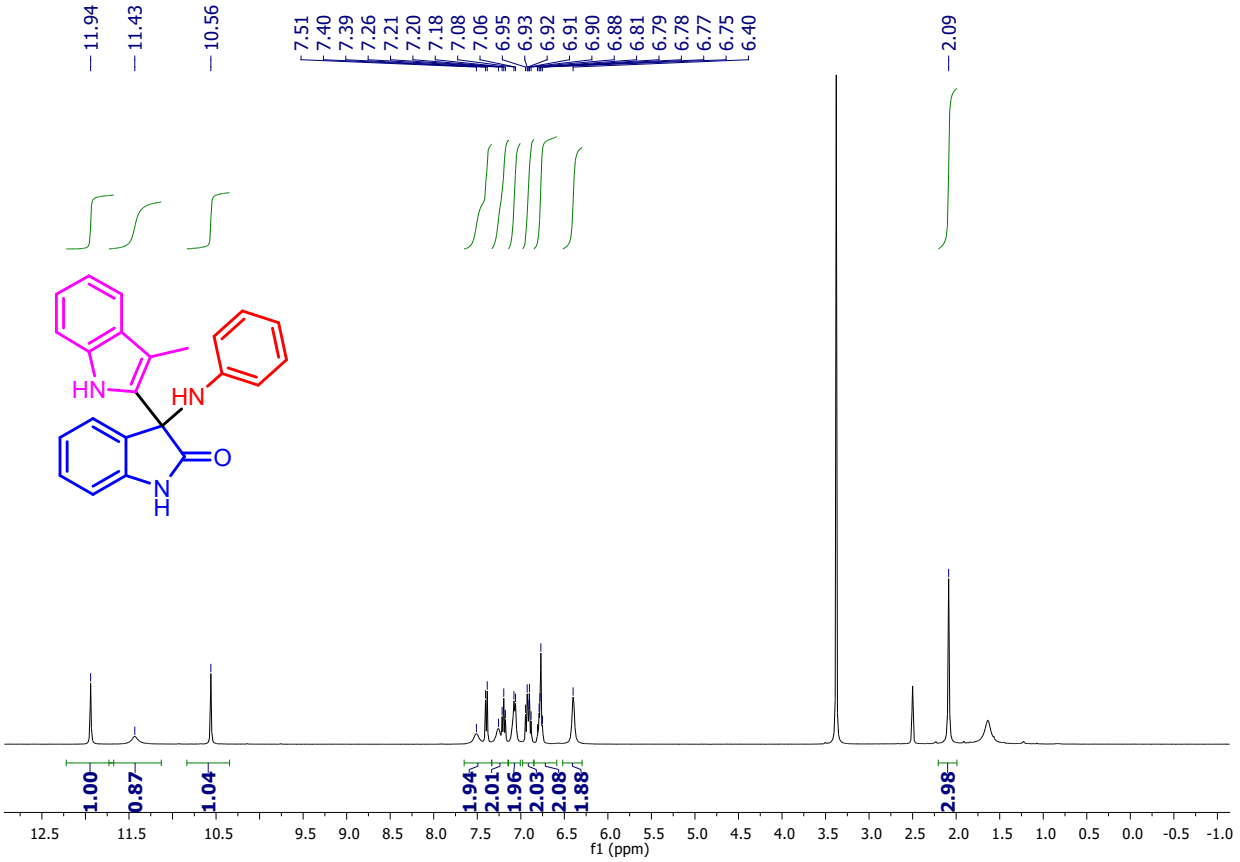
^{1}H NMR Spectrum of **17b** (400 MHz, DMSO-d_6)



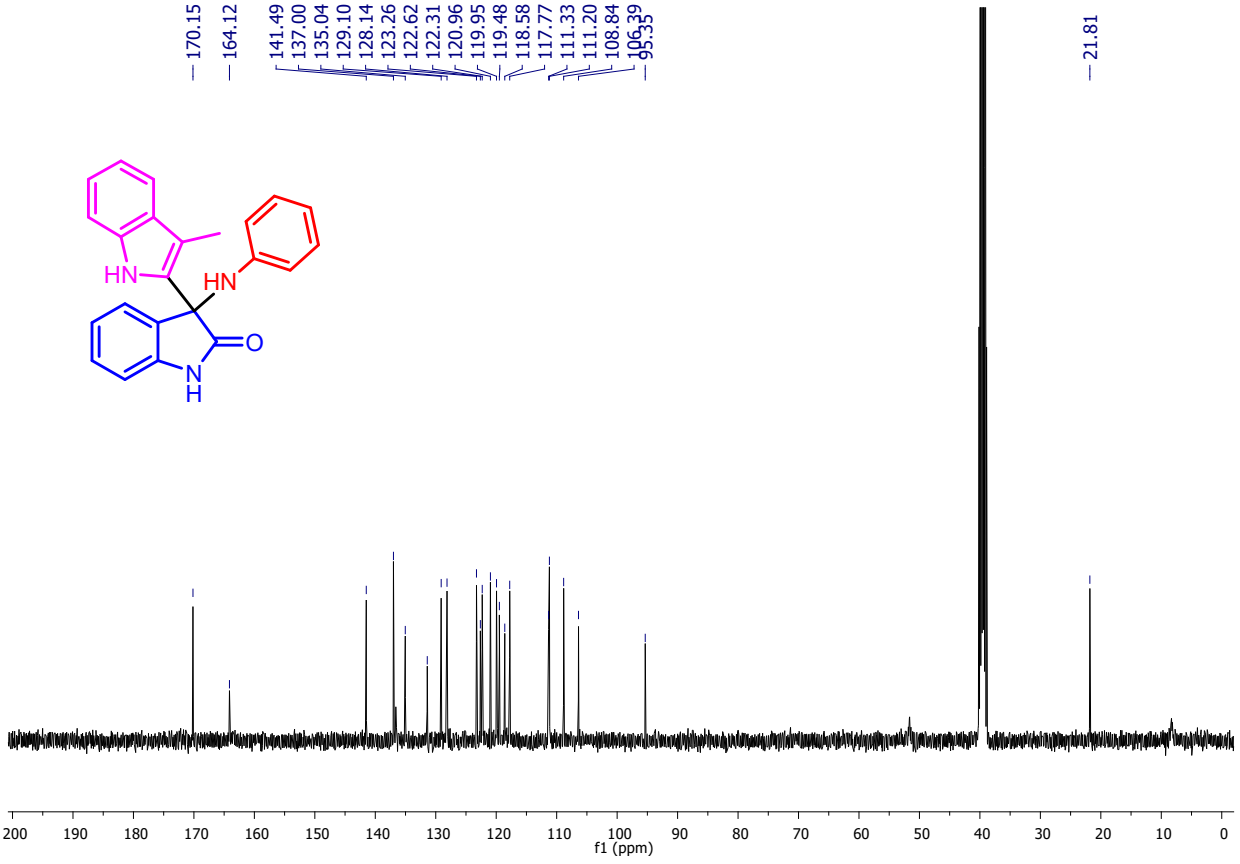
^{13}C {^{1}H} NMR Spectrum of **17b** (100 MHz, DMSO-d_6)



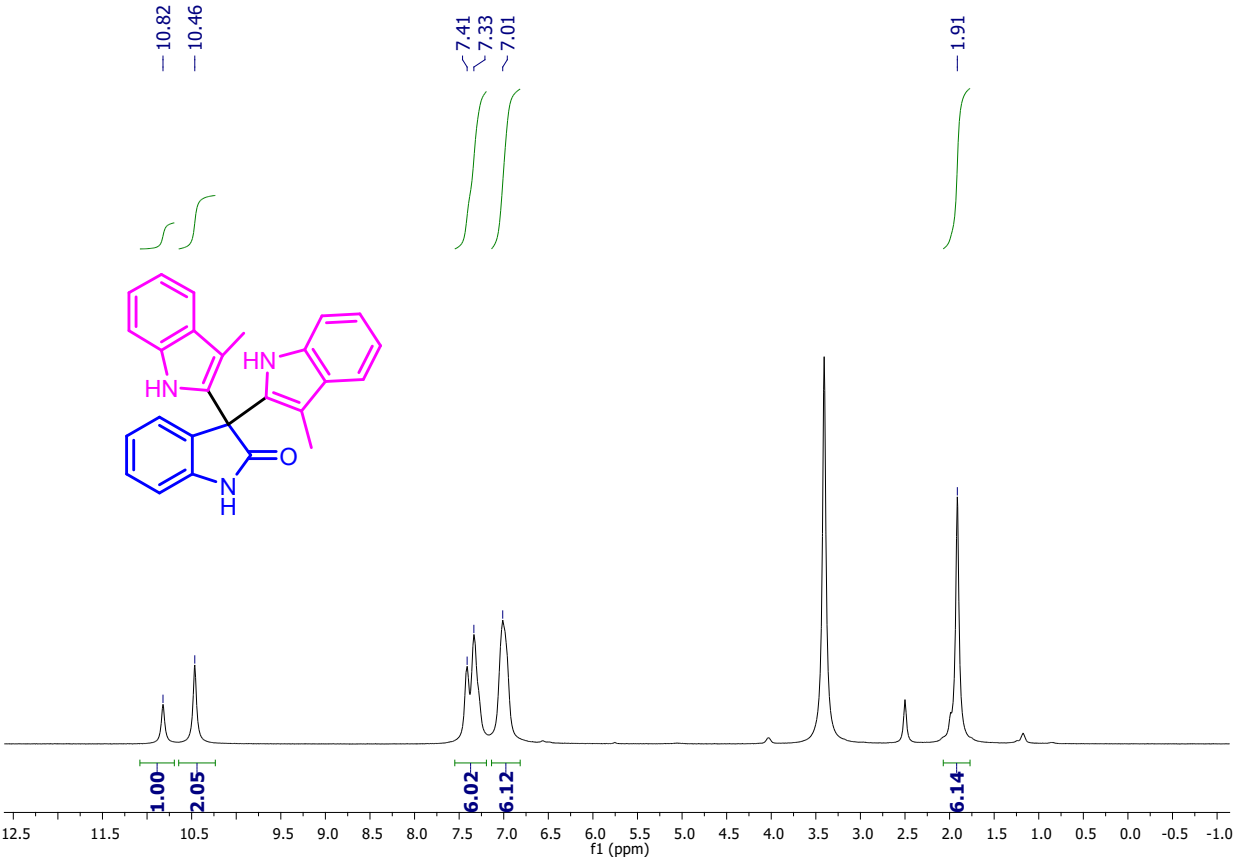
^{1}H NMR Spectrum of **19a** (400 MHz, DMSO-d_6)



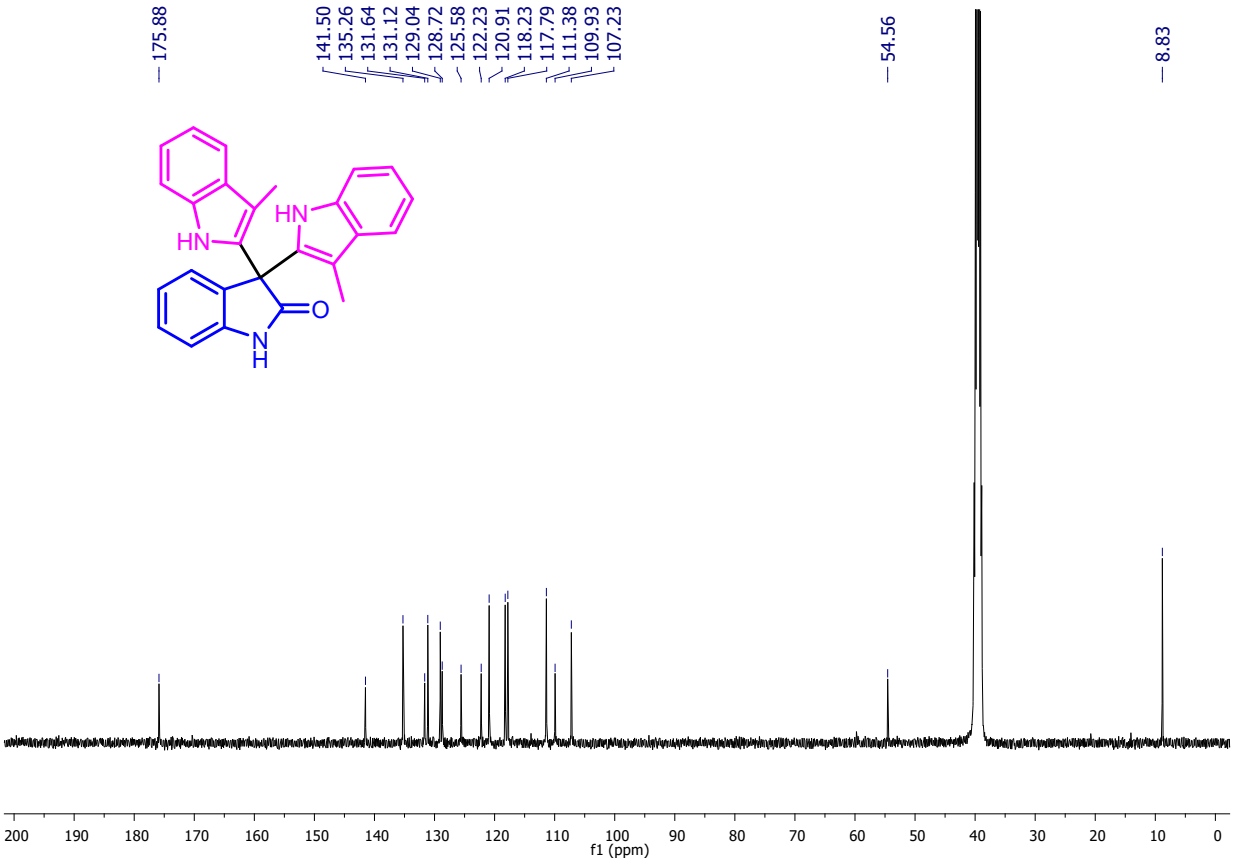
^{13}C {^{1}H} NMR Spectrum of **19a** (100 MHz, DMSO-d_6)



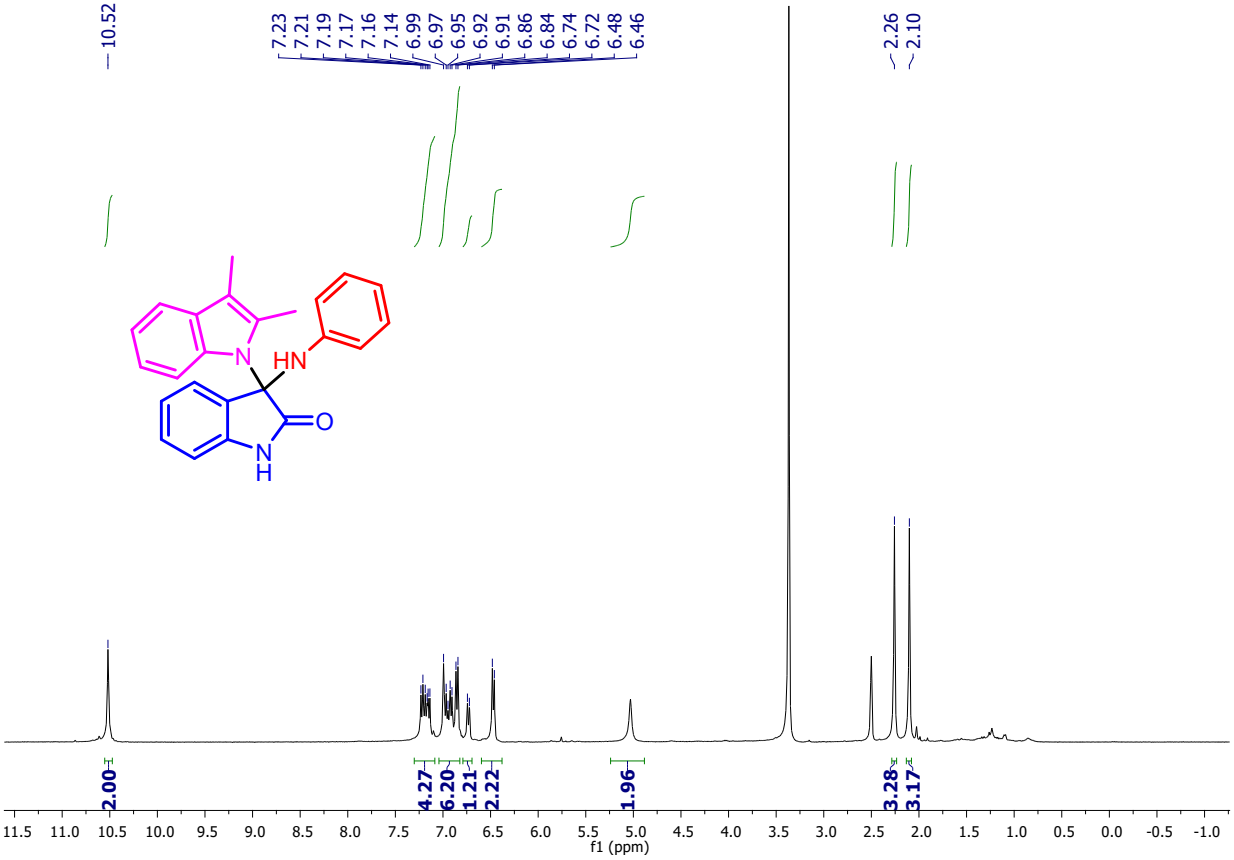
^{1}H NMR Spectrum of **19b** (400 MHz, DMSO-d_6)



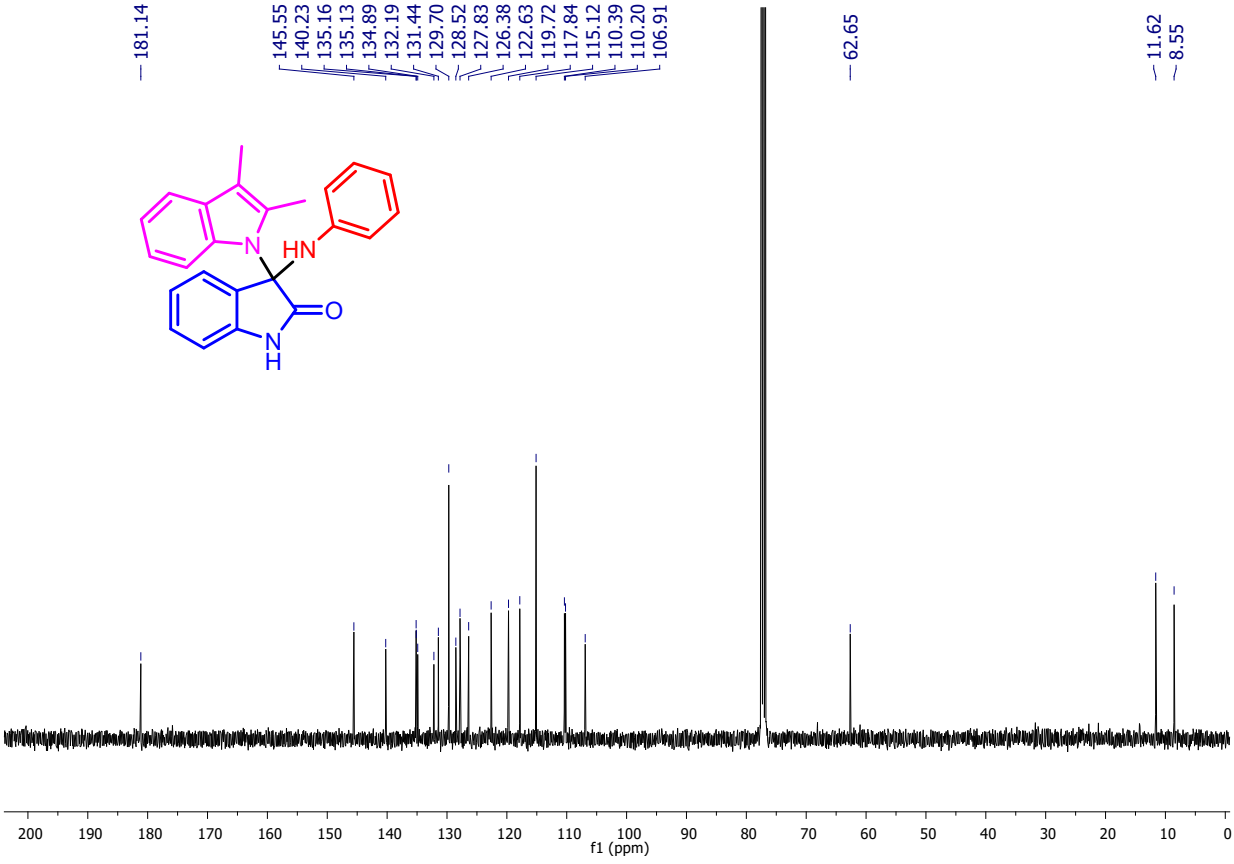
^{13}C {^{1}H} NMR Spectrum of **19b** (100 MHz, DMSO-d_6)



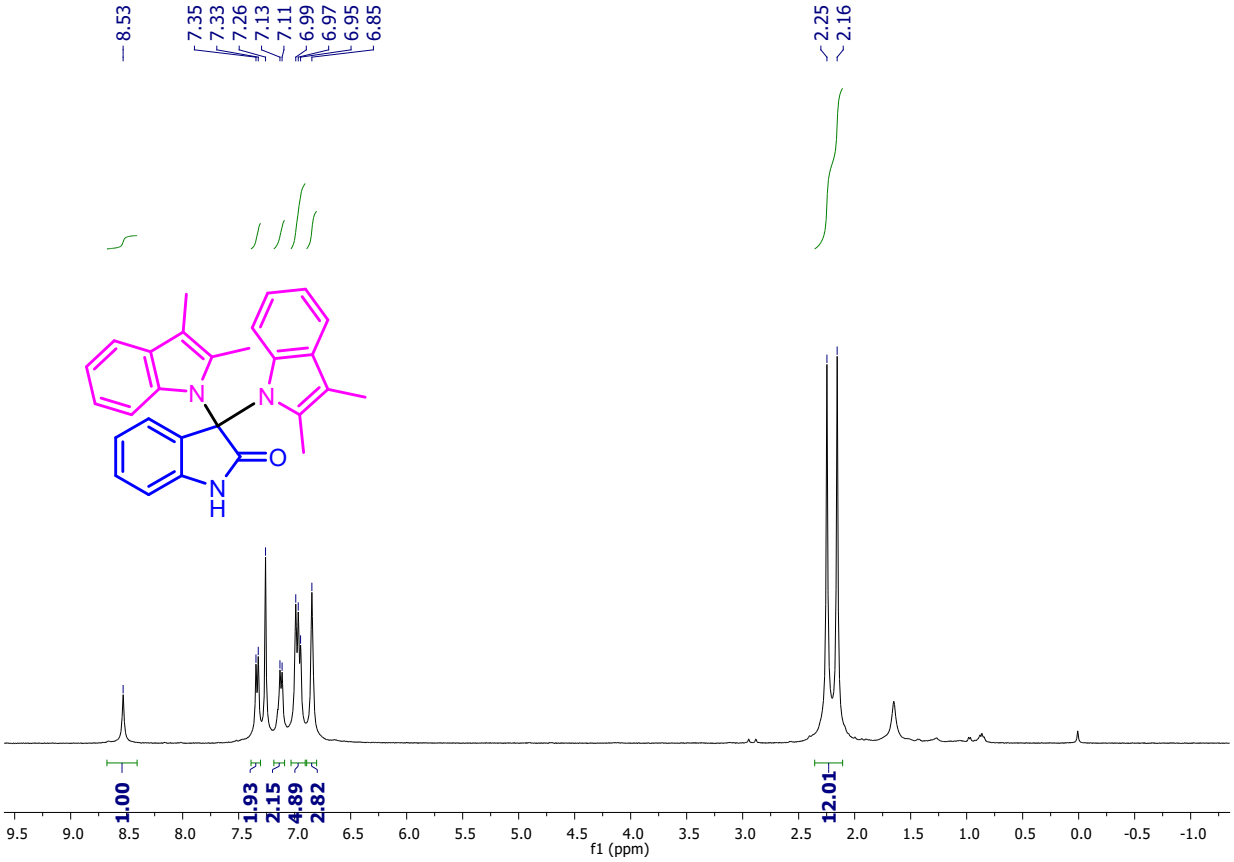
^{1}H NMR Spectrum of **21a** (400 MHz, DMSO-d_6)



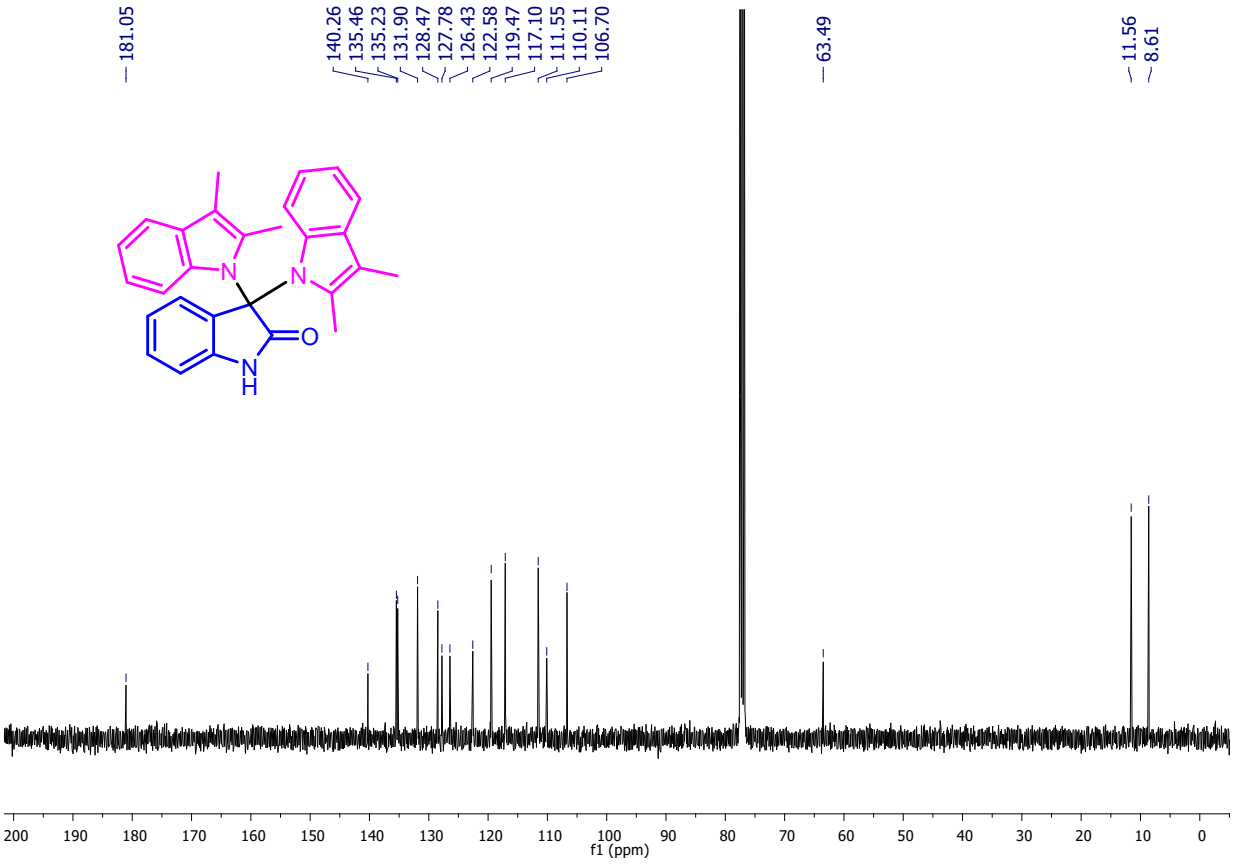
^{13}C {^{1}H} NMR Spectrum of **21a** (100 MHz, $CDCl_3$)



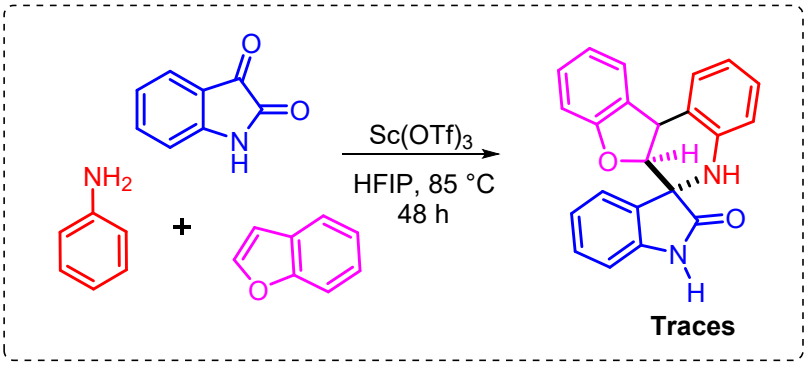
^{1}H NMR Spectrum of **21b** (400 MHz, $CDCl_3$)



^{13}C {^{1}H} NMR Spectrum of **21b** (100 MHz, $CDCl_3$)



Section XIV. Reaction with parent 1-Benzofuran:



Under the optimized reaction conditions, the reaction of simple benzofuran afforded only trace amounts of the desired product. The HRMS analysis indicated the presence of the expected molecular ion corresponding to the target product, confirming its formation in trace quantities. These results suggest that the C3-methyl group plays a crucial role in facilitating efficient cyclization, whereas unsubstituted benzofuran exhibits significantly lower reactivity under the same conditions.

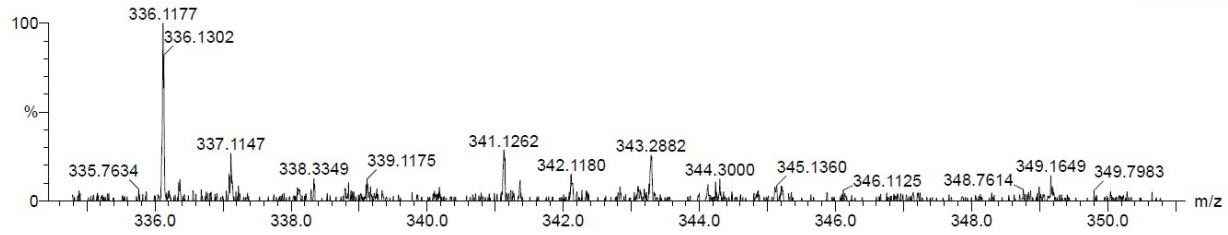
HRMS Report:

Elemental Composition Report **Page 1**

Single Mass Analysis
Tolerance = 50.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off

Monoisotopic Mass, Even Electron Ions
13 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)
Elements Used:
C: 0-22 H: 0-100 N: 0-2 O: 0-2

ART-02-SBFR QMI DIVISION, CSIR-IIIM JAMMU 23-Apr-2026
Xevo G2-XS QTOF YFC2015 15:51:14
23042026_19 19 (0.219) 1: TOF MS ES+
5.59e+002



Minimum:				-1.5	
Maximum:		2.0	50.0	50.0	
Mass	Calc. Mass	mDa	PPM	DBE	Formula
341.1262	341.1290	-2.8	-8.2	15.5	C22 H17 N2 O2