Unusual C-2 selectivity of Grignard additions to *N*-Boc-protected isatin 3-imines

Alexandra Mary Plakas,[a,b] Kamogelo Rosinah Butsi,[a,b] Sahil Lala,[b,c] Robyn Lynne van Zyl,[b,c] Manuel Antonio Fernandes,[a] Songeziwe Ntsimango,[a] Moira Leanne Bode[a] and Amanda Louise Rousseau*[a,b]

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1. Experimental

1.1 Chemistry

All reagents were purchased from Sigma-Aldrich (South Africa) and used as received. Solvents used for reactions were distilled over the appropriate drying agents under inert environments. THF was dried over sodium wire in the presence of an indicator, benzophenone. DCM and DMF were distilled from calcium hydride. DMF was later stored over activated molecular sieves (4Å) under N_2 atmosphere. Absolute ethanol was obtained from commercial sources without any further purification. Solvents for column chromatography (ethyl acetate and hexane) were purified by distillation. Thin Layer Chromatography (TLC) was carried out using Merck aluminium foil F_{254} backed plates coated with silica gel 60. Normal column chromatography was performed on Macherey-Nagel silica gel 60 particle size 0.063 – 0.200 mm and Merck silica gel of particle size 0.035 – 0.070 mm was employed for flash columns. All melting points were determined using a Stuart SMP10 melting point apparatus and are uncorrected. ^{1}H and ^{13}C Nuclear Magnetic Resonance data were recorded on a Bruker 300 or 500 MHz spectrometer using specified deuterated solvents. For those compounds soluble in deuterated chloroform ($CDCl_3$), chemical shifts were referenced against the internal standard tetramethyl silane (TMS) which occurs at zero parts per million. Chemical shifts are recorded in ppm, while coupling constants are recorded in Hertz. Infrared spectra were acquired from a Bruker Tensor-27 Fourier Transform spectrometer. Measurements are made by directly loading samples to the diamond cell. Signals are reported on the wavenumber scale (ν, cm^{-1}). High Resolution Mass Spectra (HRMS) were obtained on a SYNAPT G2 HDMS mass spectrometer (ESI) at Stellenbosch University.

1.1.1 General procedure for benzyl protection of isatins.

To a solution of isatin **5** (20.4 mmol) in dry DMF (90 mL) under argon was added K_2CO_3 (24.5 mmol). After stirring the resulting solution for 1 h, KI (4.08 mmol) and the appropriate benzyl bromide (25 mmol) were added. The reaction was stirred at 80ºC for 5 h. The reaction mixture was cooled to room temperature and neutralised with aqueous HCl (32%), extracted with ethyl acetate (3 x 40 mL), and washed with brine (3 x 50 mL). The combined organic layers were dried over $MgSO_4$ and filtered over a celite pad. The filtrate was concentrated under reduced pressure and the solid obtained was purified by recrystallization from EtOAc/hexane. Bn-protected isatins **7a-b** were prepared using this procedure.

1-Benzylindoline-2,3-dione 7a[16] was isolated as bright orange crystals (3.6 g, 75%). R_f 0.24 (3:7 EtOAc/Hex); mp 134-135 °C (lit. mp 136 °C)[22]; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.61 (1H, ddd, J = 7.5, 1.4, 0.6 Hz), 7.48 (1H, td, J = 7.8, 1.4 Hz), 7.40 – 7.29 (5H, m), 7.09 (1H, td, J = 7.5,

0.8 Hz), 6.78 (1H, d, *J* = 8.0 Hz), 4.93 (2H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 183.2, 158.3, 150.7, 138.3, 134.5, 129.1, 128.2, 127.4, 125.4, 123.8, 117.7, 111.0, 44.1.

1-(4-Methoxybenzyl)indoline-2,3-dione 7b was isolated as an orange crystalline solid (3.9 g, 72%). R_f 0.36 (3:7 EtOAc/Hex); mp 169-170 °C (lit. mp 170-171 °C)[23]; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.59 (1H, dd, *J* = 7.4, 1.3 Hz), 7.48 (1H, td, *J* = 7.8, 1.4 Hz), 7.32 – 7.24 (2H, m), 7.08 (1H, td, *J* = 7.5, 0.9 Hz), 6.91 – 6.84 (2H, m), 6.81 (1H, d, *J* = 7.9 Hz), 4.86 (2H, s), 3.78 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 183.4, 159.5, 158.2, 150.8, 138.2, 128.9, 126.5, 125.4, 123.8, 117.7, 114.4, 111.0, 55.3, 43.5.[24]

1.1.2 General procedure for the synthesis of ketimines.

Isatin (3.00 g, 20.4 mmol) and a substituted aniline (1.0 eq., 20.4 mmol) were dissolved in absolute ethanol (120 mL) and treated with a catalytic amount of glacial acetic acid (0.8 mL). The resulting mixture was stirred at reflux (100 °C) under a nitrogen atmosphere for 5-15 h. The reaction was then cooled and concentrated by removal of the solvent under reduced pressure to allow the product to precipitate out of solution. The mixture was filtered, and the filter cake was further purified by recrystallization from ethanol to afford the desired imine. Imines **6a**-**f** were prepared using this procedure.

3-(*p*-Tolylimino)indolin-2-one 6a[25] was isolated as a yellow solid (2.94 g, 61%) in an isomeric ratio of *E:Z* = 3:1. R_f 0.47 (3:7 EtOAc/Hex); mp 232-233 °C (lit. mp 222 °C); ^{1}H NMR (300 MHz, DMSO-d_6) *E* Isomer δ 10.97 (1H, s), 7.32 (1H, td, *J* = 7.7, 1.3 Hz), 7.26 (2H, d, *J* = 8.0 Hz), 6.93 – 6.85 (3H, m), 6.72 (1H, td, *J* = 7.7, 1.0 Hz), 6.49 (1H, dd, *J* = 7.8, 1.2 Hz), 2.35 (3H, s); *Z* isomer δ 10.85 (1H, s), 7.57 (1H, dd, *J* = 7.5, 1.2 Hz), 7.43 (1H, td, *J* = 7.7, 1.3 Hz), 7.11 (2H, d, *J* = 8.0 Hz), 7.05 (1H, td, *J* = 7.6, 0.9 Hz), 6.94 (2H, d, *J* = 8.2 Hz), 6.91 – 6.81 (1H, m), 2.30 (3H, s); ^{13}C NMR (75 MHz, DMSO-d_6) *E* Isomer δ 163.5, 154.7, 147.8, 146.9, 134.2, 134.1, 130.0, 125.2, 121.6, 117.4, 115.7, 111.4, 20.5; *Z* Isomer δ 158.4, 152.5, 146.1, 145.4, 134.0, 133.9, 128.7, 122.5, 122.2, 119.6, 115.7, 110.6, 20.5; HRMS (*m/z*), calculated for $C_{15}H_{13}N_2O^+$: 237.1022, found $(M + H)^+$: 237.1022.

3-((4-Bromophenyl)imino)indolin-2-one 6b[25] was isolated as an orange solid (4.05 g, 66%) in an isomeric ratio of *E:Z* = 4:1. R_f 0.12 (3:7 EtOAc/Hex); mp 278-279 °C (lit. mp 270 °C); ^{1}H NMR (300 MHz, DMSO-d_6) *E* Isomer δ 10.97 (1H, s), 7.65 (2H, d, *J* = 8.6 Hz), 7.35 (1H, td, *J* = 7.7, 1.3 Hz), 6.97 (2H, d, *J* = 8.6 Hz), 6.89 (1H, d, *J* = 7.9 Hz), 6.77 (1H, td, *J* = 7.7, 1.1 Hz), 6.43 (1H, dd, *J* = 7.8, 1.2 Hz); *Z* Isomer δ 10.97 (1H, s), 7.59 (1H, d, *J* = 7.5 Hz), 7.51 – 7.41 (3H, m), 7.06 (1H, td, *J* = 7.6, 1.0 Hz), 6.97 (2H, d, *J* = 8.4 Hz), 6.95 – 6.82 (1H, m); ^{13}C NMR (75 MHz, DMSO-d_6) *E* Isomer δ 163.3, 155.3, 149.6, 147.1, 134.7, 132.4, 125.4, 121.8, 119.7, 117.1, 115.6, 111.6; *Z* Isomer δ 158.5, 153.5, 148.4, 145.8, 134.4, 131.1, 122.9, 122.3, 121.2,

116.6, 115.6, 110.8; HRMS (*m/z*), calculated for $C_{14}H_{10}{}^{79}BrN_2O^+$: 300.9971, found (*M* + H)$^+$: 300.9969.

3-((4-Chlorophenyl)imino)indolin-2-one 6c[26] was isolated as an orange solid (2.54 g, 72%), in an isomeric ratio of *E:Z* = 2.3:1. R_f 0.22 (3:7 EtOAc/Hex); mp 268-279 °C (lit. mp 240 °C); ^{1}H NMR (300 MHz, DMSO-d_6) *E* Isomer δ 10.98 (1H, s), 7.52 (2H, d, *J* = 8.6 Hz), 7.36 (1H, td, *J* = 7.6, 1.2 Hz), 7.04 (2H, d, *J* = 8.6 Hz), 6.90 (1H, d, *J* = 7.9 Hz), 6.77 (1H, td, *J* = 7.7, 1.0 Hz), 6.44 (1H, dd, *J* = 7.8, 1.2 Hz); *Z* Isomer δ 10.98 (1H, s), 7.58 (1H, dd, *J* = 7.6, 1.2 Hz), 7.45 (1H, td, *J* = 7.7, 1.3 Hz), 7.37 (2H,d, *J* = 7.8 Hz), 7.11 – 7.00 (3H, m), 6.88 (1H, d, *J* = 7.3 Hz); ^{13}C NMR (75 MHz, DMSO-d_6) *E* Isomer δ 163.3, 155.4, 149.2, 147.1, 134.7, 129.6, 129.0, 125.4, 121.8, 119.4, 115.6, 111.6; *Z* Isomer δ 158.5, 153.6, 148.0, 145.8, 134.4, 128.5, 128.2, 122.9, 122.3, 121.2, 120.9, 110.8; HRMS (*m/z*), calculated for $C_{14}H_{10}{}^{35}ClN_2O^+$: 257.0476, found (*M* + H)$^+$: 257.0472.

3-((4-Methoxyphenyl)imino)indolin-2-one 6d[25] was isolated as an orange solid (8.06 g, 94%) in an isomeric ratio of *E:Z* = 4:1. R_f 0.16 (3:7 EtOAc/Hex); mp 241-242 °C (lit. mp 230 °C); ^{1}H NMR (300 MHz, DMSO-d_6) *E* Isomer δ 10.95 (1H, s), 7.33 (1H, td, *J* = 7.7, 1.4 Hz), 7.03 (2H, d, *J* = 8.9 Hz), 6.98 (2H, d, *J* = 8.9 Hz), 6.94 – 6.86 (1H, m), 6.75 (1H, td, *J* = 7.6, 1.0 Hz), 6.66 (1H, dd, *J* = 7.8, 1.3 Hz), 3.80 (3H, s); *Z* Isomer δ 10.84 (1H, s), 7.55 (1H, dd, *J* = 7.6, 1.2 Hz), 7.41 (1H, td, *J* = 7.7, 1.3 Hz), 7.18 (2H, d, *J* = 8.8 Hz), 7.11 – 6.94 (3H, m), 6.85 (1H, d, *J* = 7.8 Hz), 3.77 (3H, s); ^{13}C NMR (75 MHz, DMSO-d_6) *E* Isomer δ 163.6, 157.1, 154.5, 146.8, 143.0, 134.1, 124.9, 121.6, 119.4, 115.8, 114.7, 111.4, 55.3; *Z* Isomer δ 158.6, 157.5, 151.6, 145.0, 141.0, 133.5, 122.7, 122.3, 122.2, 122.1, 113.4, 110.5, 55.2; HRMS (*m/z*), calculated for $C_{15}H_{13}N_2O_2^+$: 253.0972, found (*M* + H)$^+$: 253.0968.

3-((3,4-Dimethylphenyl)imino)indolin-2-one 6e was isolated as an olive green solid (4.65 g, 91%) as a mixture of isomers in a *E:Z* ratio of 5.7:1. R_f 0.26 (3:7 EtOAc/Hex); mp 202-203 °C; IR ν_{max} (cm^{-1}) 3192, 2919, 1743, 1650; ^{1}H NMR (300 MHz, DMSO-d_6) *E* Isomer δ 10.96 (1H, s), 7.32 (1H, td, *J* = 7.7, 1.3 Hz), 7.21 (1H, d, *J* = 7.9 Hz), 6.89 (1H, d, *J* = 7.8 Hz), 6.82 – 6.65 (3H, m), 6.52 (1H, dd, *J* = 7.8, 1.1 Hz), 2.26 (3H, s), 2.24 (3H, s); *Z* Isomer δ 10.84 (1H, s), 7.56 (1H, dd, *J* = 7.6, 1.2 Hz), 7.43 (1H, td, *J* = 7.7, 1.3 Hz), 7.05 (2H, d, *J* = 7.7 Hz), 6.86 – 6.81 (1H, m), 6.82 – 6.65 (2H, m), 2.20 (3H, s), 2.19 (3H, s); ^{13}C NMR (75 MHz, DMSO-d_6) *E* Isomer δ 163.5, 154.5, 148.1, 146.8, 137.5, 134.2, 132.8, 130.3, 125.2, 121.6, 118.5, 115.7, 114.6, 111.4, 19.4, 18.9; *Z* Isomer δ 158.4, 152.2, 146.5, 145.3, 135.9, 133.8, 132.7, 129.2, 122.5, 122.2, 120.7, 116.9, 111.5, 110.6, 19.4, 18.9; HRMS (*m/z*), calculated for $C_{16}H_{15}N_2O^+$: 251.1179, found (*M* + H)$^+$: 251.1178.

5-Chloro-3-(*p*-tolylimino)indolin-2-one 6f was isolated as orange needles (3.06 g, 74 %) in an isomeric ratio of *E:Z*= 5:1. R_f 0.15 (3:7 EtOAc/Hex); mp 197-200 °C (lit. mp 202 °C)[27]; IR ν_{max} (cm^{-1}) 3250, 3089, 3030, 2978, 2925, 1786, 1733, 1648; 1593, 1155; ^{1}H NMR (300 MHz, DMSO-

d_6) *E* Isomer δ 11.12 (1H, s), 7.40 (1H, dd, *J* = 8.4, 2.2 Hz), 7.30 (2H, d, *J* = 8.2 Hz), 6.90 (3H, app. d, *J* = 8.2 Hz, H-7), 6.40 (1H, d, *J* = 2.2 Hz), 2.37 (3H, s); *Z* isomer δ 10.99 (1H, s), 7.56 (1H, d, *J* = 2.2 Hz, H-4), 7.47 (1H, dd, *J* = 8.3, 2.2 Hz), 7.13 (2H, d, *J* = 8.2 Hz), 6.99 (2H, d, *J* = 8.2 Hz), 6.87 (1H, d, *J* = 8.3 Hz), 2.30 (3H, s); ^{13}C NMR (101 MHz, DMSO-d_6) *E* Isomer δ 163.2, 153.8, 147.4, 145.7, 134.7, 133.6, 130.0, 125.2, 124.6, 117.5, 116.9, 113.1, 20.6 *Z* Isomer δ 158.2, 151.6, 148.0, 144.1, 134.6, 133.2, 128.8, 126.4, 123.3, 122.1, 120.0, 112.3, 20.6; HRMS (*m/z*), calculated for $C_{15}H_{12}ClN_2O^+$: 271.0633, found $(M + H)^+$: 271.0633.

1-Benzyl-3-(*p*-tolylimino)indoline-2-one 4g was isolated as an orange solid (3.2 g, 78%) in an isomeric ratio of *E:Z* = 9:1. R_f 0.60 (3:7 EtOAc/Hex); mp 164-166 °C; IR ν_{max} (cm^{-1}) 3029, 2936, 2863, 1717, 1597; ^{1}H NMR (400 MHz, $CDCl_3$) *E* isomer δ 7.40 – 7.28 (5H, m), 7.25 – 7.20 (3H, m), 6.95 (2H, d, *J* = 8.2 Hz), 6.81 – 6.67 (3H, m), 5.02 (2H, s), 2.41 (3H, s); ^{13}C NMR (101 MHz, $CDCl_3$) *E* isomer δ 163.6, 154.1, 147.8, 147.2, 135.3, 135.3, 134.0, 130.1, 129.0, 128.0, 127.6, 126.2, 122.8 , 118.2, 116.1, 110.4, 44.1, 21.2; HRMS (*m/z*), calculated for $C_{22}H_{19}N_2O^+$: 326.1419, found $(M + H)^+$: 327.1497.

1-Benzyl-3-((4-bromophenyl)imino)indolin-2-one 4h was isolated as a yellow solid (4.5 g, 90%). R_f 0.52 (3:7 EtOAc/Hex); mp 151 °C; IR ν_{max} (cm^{-1}) 2981, 2919, 1732, 1650; ^{1}H NMR (300 MHz, $CDCl_3$) *E* isomer δ 7.60 – 7.52 (2H, m), 7.42 – 7.28 (6H, m), 6.99 – 6.89 (2H, m), 6.81 – 6.68 (3H, m), 5.01 (2H, s); ^{13}C NMR (75 MHz, $CDCl_3$) *E* isomer δ 163.1, 149.2, 147.4, 135.0, 134.4, 132.6, 131.7, 129.0, 128.0, 127.5, 126.2, 122.8, 119.8, 118.5, 115.7, 110.5, 44.1; HRMS (*m/z*), calculated for $C_{21}H_{16}{}^{79}BrN_2O^+$: 391.0446, found $(M + H)^+$: 391.0439.

1-Benzyl-3-((4-chlorophenyl)imino)indolin-2-one 4i was isolated as a yellow solid (3.0 g, 67%). R_f 0.54 (3:7 EtOAc/Hex); mp 199-200 °C; IR ν_{max} (cm^{-1}) 2930, 1732, 1655; ^{1}H NMR (300 MHz, $CDCl_3$) *E* isomer δ 7.47 – 7.28 (8H, m), 7.04 – 6.95 (2H, m), 6.82 – 6.69 (3H, m), 5.01 (2H, s); ^{13}C NMR (75 MHz, $CDCl_3$) *E* isomer δ 163.2 , 154.6, 148.7, 147.4, 135.0, 134.4, 130.8, 129.6, 129.0, 128.0, 127.5, 126.2, 122.8, 119.4, 115.7, 110.5, 44.1; HRMS (*m/z*), calculated for $C_{21}H_{16}{}^{35}ClN_2O^+$: 347.0951, found $(M + H)^+$: 347.0943.

1-(4-Methoxybenzyl)-3-(*p*-tolylimino)indolin-2-one 4j was isolated as an orange solid (1.89 g, 65%, in an isomeric ratio of *E:Z* = 8:1. R_f 0.56 (3:7 EtOAc/Hex); mp 180-182 °C; IR ν_{max} (cm^{-1}) 3062, 2993, 2853, 1727, 1660, 1604; ^{1}H NMR (400 MHz, $CDCl_3$) *E* isomer δ 7.34 – 7.29 (2H, m), 7.25 – 7.21 (3H, m), 6.97 – 6.92 (2H, m), 6.89 – 6.85 (2H, m), 6.78 – 6.70 (3H, m), 4.95 (2H, s), 3.78 (3H, s), 2.40 (3H, s); ^{13}C NMR (101 MHz, $CDCl_3$) *E* isomer δ 163.5, 159.4, 154.2, 147.8, 147.2, 135.3, 133.9, 130.1, 129.1, 127.3, 126.2, 122.7, 118.1, 116.1, 114.4, 110.4, 55.4, 43.6, 21.2; HRMS (*m/z*), calculated for $C_{23}H_{21}N_2O_2^+$: 357.1598, found $(M + H)^+$: 357.1594.

1.1.3 General procedure for *tert*-butoxycarbonyl protection of ketimines.

To a solution of one of the imines **6a**-**e** (4.98 mmol) in dry THF (10 mL) was added DMAP (0.270 mmol), followed by slow addition of di-*tert*-butyl dicarbonate (1.1 eq., 5.48 mmol). The reaction was stirred under an atmosphere of N_2 at room temperature for 3 h. After complete consumption of the starting material, water was added to the solution and a yellow solid precipitated. The filtered paste-like precipitate was dissolved in EtOAc, dried over $MgSO_4$ and filtered through a pad of Celite. In instances where a paste-like precipitate did not form, the aqueous reaction mixture was extracted with ethyl acetate. The filtrate was concentrated under reduced pressure and the solid obtained was purified by recrystallization from EtOAc/hexane. Boc-protected imines **4a**-**f** and benzylidene **11** were prepared using this procedure.

***tert*-Butyl 2-oxo-3-(*p*-tolylimino)indoline-1-carboxylate 4a** was isolated as a yellow solid (2.77 g, 97%) in an *E*:*Z* isomeric ratio of 9:1. R_f 0.66 (3:7 EtOAc/Hex); mp 132 °C; IR ν_{max} (cm^{-1}) 3031, 1785, 1733,1653; ^{1}H NMR (300 MHz, $CDCl_3$) *E* Isomer δ 8.00 (1H, d, *J* = 8.3 Hz), 7.46 – 7.37 (1H, m), 7.23 (2H, d, *J* = 8.3 Hz), 6.92 – 6.84 (4H, m), 2.41 (3H, s), 1.67 (9H, s); *Z* Isomer δ 7.92 (1H, d, *J* = 8.1 Hz), 7.80 (1H, d, *J* = 7.5 Hz), 7.56 – 7.47 (1H, m), 7.29 – 7.20 (2H, m), 7.17 (1H, d, *J* = 8.3 Hz), 6.97 (2H, d, *J* = 8.3 Hz), 2.37 (3H, s), 1.60 (9H, s); ^{13}C NMR (75 MHz, $CDCl_3$) *E* Isomer δ 160.9, 152.2, 148.9, 147.6, 144.4, 135.4, 134.2, 130.2 (2C), 125.7, 124.3, 117.8, 116.1, 85.1, 28.2, 21.2; *Z* Isomer δ 157.0, 151.2, 147.6, 146.5, 144.3, 135.7, 133.8, 130.2, 129.4 (2C), 119.7, 116.8, 115.6, 85.0, 28.2, 21.3; HRMS (*m/z*), calculated for $C_{20}H_{21}N_2O_3$: 337.1547^+, found $(M + H)^+$: 337.1554.

***tert*-Butyl 3-((4-bromophenyl)imino)-2-oxoindoline-1-carboxylate 4b** was isolated as a yellow solid (1.96 g, 98%) in an isomeric ratio of *E*:*Z* = 3:1. R_f 0.74 (3:7 EtOAc/Hex); mp 277-278 °C; IR ν_{max} (cm^{-1}) 2981, 1783, 1731, 1654; ^{1}H NMR (300 MHz, $CDCl_3$) *E* Isomer δ 8.02 (1H, d, *J* = 8.3 Hz), 7.63 – 7.52 (2H, m), 7.50 – 7.41 (1H, m), 6.99 – 6.78 (4H, m), 1.67 (9H, s); *Z* isomer δ 7.94 (1H, d, *J* = 8.2 Hz), 7.79 (1H, dd, *J* = 7.5, 1.4 Hz), 7.62 – 7.50 (2H, m), 7.49 – 7.40 (1H, m), 7.00 – 6.76 (3H, m), 1.60 (9H, s); ^{13}C NMR (75 MHz, $CDCl_3$) *E* Isomer δ 160.6, 152.7, 149.0, 148.7, 147.8, 144.6, 134.7, 132.7, 125.7, 124.4, 119.4, 118.5, 116.3, 85.3, 28.1; *Z* Isomer δ 160.6, 158.5, 151.8, 148.8, 147.4, 143.3, 134.4, 131.8, 125.0, 123.0, 120.7, 118.6, 115.7, 85.2, 28.1; HRMS (*m/z*), calculated for $C_{19}H_{18}{}^{79}BrN_2O_3^+$: 401.0495, found $(M + H)^+$: 401.0492.

***tert*-Butyl 3-((4-chlorophenyl)imino)-2-oxoindoline-1-carboxylate 4c** was isolated as a yellow solid (1.03 g, 74%) in an isomeric ratio of *E*:*Z* = 3:1. R_f 0.90 (3:7 EtOAc/Hex); mp 267 °C; IR ν_{max} (cm^{-1}) 2983, 1718, 1731, 1656; ^{1}H NMR (300 MHz, $CDCl_3$) *E* Isomer δ 8.01 (1H, d, *J* = 8.3 Hz), 7.45 (1H, t, *J* = 8.0 Hz), 7.42 – 7.39 (2H, m), 6.98 – 6.89 (3H, m), 6.82 (1H, d, *J* = 7.7 Hz), 1.67 (9H, s); *Z* Isomer δ 7.93 (1H, d, *J* = 8.3 Hz), 7.79 (1H, d, *J* = 7.5 Hz), 7.54 (1H, t, *J* = 8.0 Hz), 7.35 – 7.29 (2H, m), 6.98 – 6.89 (3H, m), 1.60 (9H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ

160.6, 152.9, 148.6, 144.7, 134.8, 131.0, 129.9, 128.9, 125.8, 124.5, 120.6, 119.2, 116.4, 85.4, 28.2; HRMS (*m/z*), calculated for $C_{19}H_{18}{}^{35}ClN_2O_3^+$: 357.1000, found $(M + H)^+$: 357.1012.

***tert*-Butyl 3-((4-methoxyphenyl)imino)-2-oxoindoline-1-carboxylate 4d** was isolated as a yellow solid (2.49 g, 89%) as an isomeric mixture in an *E:Z* ratio of 4:1. R_f 0.57 (3:7 EtOAc/Hex); mp 110-111 °C; IR ν_{max} (cm^{-1}) 2987.58, 1733.19, 1655.55, 1602.15; ^{1}H NMR (500 MHz, $CDCl_3$) *E* Isomer δ 8.00 (1H, d, *J* = 8.3 Hz), 7.42 (1H, ddd, *J* = 8.3, 7.6, 1.4 Hz), 7.06 (1H, dd, *J* = 7.8, 1.5 Hz), 7.03 – 6.95 (4H, m), 6.94 – 6.88 (1H, m), 3.86 (3H, s), 1.67 (9H, s); *Z* Isomer δ 7.89 (1H, d, *J* = 8.2 Hz), 7.78 (1H, d, *J* = 7.6 Hz), 7.63 – 7.56 (1H, m), 7.49 (1H, ddd, *J* = 8.3, 7.5, 1.4 Hz), 7.25 – 7.20 (4H, m), 6.91 – 6.88 (1H, m), 3.83 (3H, s), 1.61 (9H, s); ^{13}C NMR (126 MHz, $CDCl_3$) *E* Isomer δ 161.0, 158.0, 151.9, 148.9, 144.3, 142.9, 134.2, 125.2, 124.3, 120.0, 116.1, 114.7, 113.9, 85.1, 55.6, 28.2; *Z* Isomer δ 158.8, 155.0, 149.2, 148.0, 142.5, 141.1, 133.4, 124.9, 123.2, 122.6, 116.8, 115.5, 114.5, 84.9, 55.6, 28.4; HRMS (*m/z*), calculated for $C_{20}H_{21}N_2O_4^+$: 353.1496, found $(M + H)^+$: 353.1502.

***tert*-Butyl 3-((3,4-dimethylphenyl)imino)-2-oxoindoline-1-carboxylate 4e** was isolated as an orange solid (2.39 g, 82%). R_f 0.87 (3:7 EtOAc/Hex); mp 149-150 °C; IR ν_{max} (cm^{-1}) 2982, 1730, 1655, 1602; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.99 (1H, dd, *J* = 8.3, 0.9 Hz), 7.41 (1H, m), 7.17 (1H, d, *J* = 7.9 Hz), 6.94 – 6.85 (2H, m), 6.78 (1H, d, *J* = 2.2 Hz), 6.72 (1H, dd, *J* = 7.9, 2.2 Hz), 2.31 (3H, s), 2.28 (3H, s), 1.67 (9H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.0, 152.0, 149.0 148.0, 144.3, 138.0, 134.1, 134.0, 130.6, 125.7, 124.3, 119.1, 116.9, 116.1, 115.0, 85.1, 28.2, 20.0, 19.5; HRMS (*m/z*), calculated for $C_{21}H_{23}N_2O_3^+$: 351.1703, found $(M + H)^+$ 351.1710.

***tert*-Butyl-5-chloro-2-oxo-3-(*p*-tolylimino)indoline-1-carboxylate 4f** was isolated as dark orange crystals (1.49, 81%) in an isomeric ration of *E:Z* = 6:1. R_f 0.76 (3:7 EtOAc/Hex); mp 178-180 °C; IR ν_{max} (cm^{-1}) 2977, 1789, 1733, 1648, 1458; ^{1}H NMR (400 MHz, CD_3OD) *E* isomer δ 8.13 (1H, d, *J* = 8.9 Hz), 7.90 (1H, d, *J* = 2.5 Hz), 7.63 – 7.56 (3H, m), 7.20 (2H, d, *J* = 8.1 Hz), 2.34 (3H, s), 1.49 (9H, s); *Z* isomer δ 7.85 (1H, d, *J* = 8.8 Hz), 7.79 (1H, d, *J* = 2.7 Hz), 7.46 (2H, d, *J* = 8.4 Hz), 7.31 (1H, dd, *J* = 8.9, 2.7 Hz), 7.12 (2H, d, *J* = 8.4 Hz), 2.29 (3H, s), 1.43 (9H, s); ^{13}C NMR (101 MHz, CD_3OD) *E* Isomer δ 191.9, 163.3, 154.5, 141.5, 136.1, 136.0, 133.2, 130.5, 130.2, 128.1, 122.9, 122.7, 121.6, 82.4, 28.5, 21.0; HRMS (*m/z*), calculated for $C_{20}H_{19}N_2O_3{}^{35}Cl$: 370.1084, found $(M + CH_3OH + H)^+$: 403.1397.

1.1.4 General procedure for Grignard addition reaction to *N*-protected ketimines.

The Grignard reagent was prepared prior to use from a suitably substituted phenethyl bromide[27] (2.0 eq., 4.98 mmol) treated with magnesium turnings (2.10 eq., 5.48 mmol) in THF (5 mL). Heat was applied to initiate the reaction. The mixture was then stirred at room temperature under a N_2 atmosphere for 1 h until all the magnesium had been consumed. *N*-Boc-protected ketimines **4a-f** (1.0 eq., 2.49 mmol) were dissolved in THF (30 mL), while *N*-Bn and *N*-PMB-protected

ketimines **4g-i** (1.0 eq., 2.49 mmol) were dissolved in DCM (30 mL). The solution was treated with $MgBr_2$ (2.0 eq., 4.98 mmol) and the heterogeneous mixture was cooled to -40 °C for 20 min. The previously prepared Grignard reagent was then added slowly to the cooled solution. The reaction mixture was stirred at -40 °C for 1 h and then allowed to warm to room temperature overnight under an atmosphere of N_2. The reaction mixture was quenched with a saturated aqueous NH_4Cl solution (30 mL) and extracted into EtOAc (3 × 40 mL). The organic layer was dried ($MgSO_4$), filtered through a pad of Celite and concentrated under reduced pressure. The resulting residue was purified by flash silica gel column chromatography (5% EtOAc/Hex) to afford the desired product. Oxindoles **2a-d** and **3a-3aa** were prepared using this procedure.

1-Benzyl-3-(2-chlorophenethyl)-3-(*p*-tolylamino)indolin-2-one 2a was isolated as a yellow powder (0.055 g, 4.7%). R_f 0.71 (3:7 EtOAc/Hex); mp 133-134 °C; IR ν_{max} (cm^{-1}) 3331, 3062, 2961, 2857, 1707, 1610, 1515; ^1H NMR (400 MHz, CD_3OD) *E* isomer δ 7.45 (1H, dd, *J* = 7.4, 0.8 Hz), 7.35 – 7.28 (1H, m), 7.26 – 7.22 (4H, m), 7.19 – 7.12 (6H, m), 6.80 – 6.70 (3H, m), 6.22 (2H, d, *J* = 8.4 Hz), 5.08 (1H, d, *J* = 15.5 Hz), 4.75 (1H, d, *J* = 15.5 Hz), 3.22 (1H, s), 2.69 – 2.53 (2H, m), 2.40 – 2.29 (1H, m), 2.28 – 2.19 (1H, m), 2.17 (3H, s); ^{13}C NMR (101 MHz, $CDCl_3$) δ 177.8, 142.7, 142.4, 138.4, 135.6, 133.8, 130.4, 129.6, 129.5, 129.5, 129.4, 129.1, 128.7, 127.7, 127.6, 127.6, 126.9, 124.2, 123.1, 117.2, 109.6, 65.5, 44.0, 40.0, 27.5, 20.5; HRMS (*m/z*), calculated for $C_{30}H_{28}{}^{35}ClN_2O^+$: 467.1885, found $(M + H)^+$: 467.1870.

1-Benzyl-3-((4-bromophenyl)amino)-3-(4-methoxyphenethyl)indolin-2-one 2b was isolated as a yellow solid (80 mg, 6%). The reaction was repeated using DCM as a solvent, to afford the product in a slightly improved yield of 11%. R_f 0.68 (3:7 EtOAc/Hex); mp 192-193 °C; IR ν_{max} (cm^{-1}) 3307, 2956, 1703; ^1H NMR (300 MHz, $CDCl_3$) δ 7.39 – 7.32 (1H, m), 7.32 – 7.17 (6H, m), 7.13 – 7.05 (1H, m), 7.03 – 6.95 (4H, m), 6.87 – 6.75 (3H, m), 6.16 – 6.00 (2H, m), 5.09 (1H, d, *J* = 15.4 Hz), 4.70 (1H, d, *J* = 15.4 Hz), 4.34 (1H, s), 3.77 (3H, s), 2.58 – 2.18 (4H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 177.4, 158.1, 144.3,142.3, 135.5, 132.4, 131.8, 129.3, 129.3, 129.3, 128.8, 127.9, 127.8, 123.9, 123.3, 117.9, 113.9, 111.9, 109.8, 65.2, 55.3, 44.2, 42.2, 28.4; HRMS (*m/z*), calculated for $C_{30}H_{28}{}^{79}BrN_2O_2^+$: 527.1334, found $(M + H)^+$: 527.1328.

1-Benzyl-3-((4-chlorophenyl)amino)-3-(4-methoxyphenethyl)indolin-2-one 2c was isolated as an off-white solid (74 mg, 12%). R_f 0.68 (3:7 EtOAc/Hex); mp 187 °C; IR ν_{max} (cm^{-1}) 3308, 2931, 2838, 1703; ^1H NMR (300 MHz, $CDCl_3$) δ 7.37 (1H, dd, J = 7.3, 1.3 Hz), 7.33 – 7.15 (6H, m), 7.14 – 7.05 (1H, m), 7.03 – 6.95 (2H, m), 6.91 – 6.73 (5H, m), 6.18 – 6.11 (2H, m), 5.09 (1H, d, *J* = 15.4 Hz), 4.69 (1H, d, *J* = 15.4 Hz) 3.77 (3H, s, OCH3), 2.58 – 2.21 (3H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 177.4, 158.1, 143.8, 142.3, 135.5, 132.4, 130.7, 129.3, 129.3, 128.9, 128.7, 127.8, 127.7, 124.7, 123.9, 123.3, 117.7, 113.9, 109.8, 65.3, 55.3, 44.1, 42.2, 28.4; HRMS (*m/z*), calculated for $C_{30}H_{28}{}^{35}ClN_2O_2^+$: 483.1839, found $(M + H)^+$: 483.1840.

1-3-(2-Methoxyphenethyl)-1-(4-methoxybenzyl)-3-(*p*-tolylamino)indolin-2-one 2d was isolated as a yellow powder (10 mg, 2%). R_f 0.49 (3:7 EtOAc/Hex); mp 88 – 89 °C; IR ν_{max} (cm^{-1}) 3328, 2996, 2953, 1698, 1587; ^1H NMR (400 MHz, DMSO-d_6) δ 7.32 (2H, d, *J* = 8.6 Hz), 7.31 – 7.22 (2H, m), 7.15 (1H, t, *J* = 7.6 Hz), 7.10 – 7.02 (2H, m), 6.98 (1H, d, *J* = 7.3 Hz), 6.92 – 6.82 (3H, m, H-7), 6.82 (1H, t, *J* = 7.6 Hz), 6.62 (2H, d, *J* = 8.3 Hz), 6.11 (1H, s), 6.04 (2H, d, *J* = 8.3 Hz), 4.98 – 4.78 (2H, m), 3.72 (3H, s), 3.68 (3H, s), 2.39 – 2.26 (1H, m), 2.24 – 2.08 (3H, m), 2.04 (3H, s); ^{13}C NMR (101 MHz, DMSO-d_6) δ 177.4, 158.6, 156.9, 143.9, 142.0, 130.1, 129.3, 129.2, 128.9, 128.7, 128.6, 128.3, 127.4, 125.5, 123.2, 122.6, 120.3, 113.9, 113.9, 110.6, 109.4, 64.0, 55.2, 55.4, 42.5, 39.7, 23.2, 19.9; HRMS (*m/z*), calculated for $C_{32}H_{33}N_2O_3^+$: 493.6265, found $(M + H)^+$: 493.2475.

***tert*-Butyl 2-hydroxy-2-(4-methoxyphenethyl)-3-(*p*-tolylimino)indoline-1-carboxylate 3a** was isolated as a yellow powder (0.25 g, 35 %). R_f 0.77 (3:7 EtOAc/Hex); mp 109-110 °C; IR ν_{max} (cm^{-1}) 3179, 2966, 2923, 1699; ^1H NMR (300 MHz, $CDCl_3$) δ 7.88 (1H, br s), 7.36 (1H, ddd, *J* = 8.6, 7.2, 1.5 Hz), 7.19 (2H, d, *J* = 7.9 Hz), 6.99 (2H, d, *J* = 8.5 Hz), 6.84 – 6.68 (5H, m), 6.67 – 6.60 (1H, m), 4.49 (1H, s), 3.77 (3H, s), 2.99 – 2.77 (1H, m), 2.76 – 2.60 (1H, m), 2.59 – 2.41 (2H, m), 2.40 (3H, s), 1.64 (9H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.6, 157.9, 151.4, 148.3, 148.1, 133.8, 133.4, 132.9, 130.1, 129.2, 126.4, 122.3, 119.7, 117.9, 116.0, 113.8, 91.8, 83.3, 55.2, 41.2, 29.6, 28.5, 21.0; HRMS (*m/z*), calculated for $C_{29}H_{33}N_2O_4^+$: 473.2435, found $(M + H)^+$: 473.2432.

^{13}C NMR (101 MHz, $CDCl_3$) δ 165.52, 157.89, 151.45, 148.30, 133.87, 133.43, 132.86, 130.12, 129.19, 129.15, 126.41, 122.36, 119.75, 117.93, 116.04, 113.83, 91.83, 83.35, 55.27, 41.26, 29.56, 28.48, 20.99.

***tert*-Butyl 2-hydroxy-2-(4-chlorophenethyl)-3-(*p*-tolylimino)indoline-1-carboxylate 3b** was isolated as a yellow oil (0.28 g, 38%). R_f 0.58 (3:7 EtOAc/Hex); ^1H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, *J* = 15.0 Hz, 1H), 7.36 (t, *J* = 7.6 Hz, 1H), 7.21 – 7.12 (m, 4H), 6.96 (d, *J* = 7.9 Hz, 2H), 6.81 – 6.69 (m, 3H), 6.64 (d, *J* = 7.8 Hz, 1H), 4.50 (s, 1H), 2.98 – 2.77 (m, 1H), 2.76 – 2.62 (m, 1H), 2.59 – 2.43 (m, 2H), 2.39 (s, 3H), 1.62 (s, 9H); ^{13}C NMR (101 MHz, CDCl3) δ 165.5, 152.8, 151.5, 148.3, 143.0, 139.4, 134.1, 133.6, 131.8, 130.3, 129.8, 128.6, 126.6, 122.6, 118.0, 116.2, 91.8, 83.6, 40.7, 30.0, 28.6, 21.1; HRMS (*m/z*), calculated for $C_{28}H_{30}{}^{35}ClN_2O_3^+$: 477.1939, found $(M + H)^+$: 477.1957.

***tert*-Butyl 2-hydroxy-2-(3-chlorophenethyl)-3-(*p*-tolylimino)indoline-1-carboxylate 3c** was isolated as a yellow solid (0.14 g, 19%). R_f 0.87 (3:7 EtOAc/Hex); mp 98 °C; IR ν_{max} (cm^{-1}) 3293, 2972, 2918, 1703; ^1H NMR (300 MHz, $CDCl_3$) δ 7.82 (1H, br s), 7.36 (1H, ddd, *J* = 8.6, 7.2, 1.5 Hz), 7.24 – 7.14 (2H, m), 7.15 – 7.08 (2H, m), 6.98 (1H, br s), 6.96 – 6.90 (1H, m), 6.84 – 6.76 (2H, m), 6.73 (1H, dd, *J* = 7.2, 1.0 Hz), 6.65 (1H, ddd, 7.9, 1.5, 0.6 Hz), 4.54 (1H, s), 2.97 – 2.77 (1H, m), 2.75 – 2.63 (1H, m), 2.62 – 2.46 (2H, m), 2.40 (3H, s), 1.63 (9H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.5, 151.6, 148.3, 148.1, 142.9, 134.2, 134.1, 133.6, 130.3, 129.7, 128.6, 126.6,

126.5, 126.3, 122.6, 119.7, 118.0, 116.2, 91.8, 83.6, 40.5, 30.3, 28.6, 21.1; HRMS (*m/z*), calculated for $C_{28}H_{30}{}^{35}ClN_2O_3^+$: 477.1939, found $(M + H)^+$: 477.1929.

***tert*-Butyl 2-hydroxy-2-(2,4-dichlorophenethyl)-3-(*p*-tolylamino)indoline-1-carboxylate 3d** as a brown oil (0.082 g, 10%). R_f 0.90 (3:7 EtOAc/Hex); IR ν_{max} (cm^{-1}) 3429, 2976, 2927, 1709; ^1H NMR (500 MHz, $CDCl_3$) δ 7.87 (1H, br s), 7.36 (1H, ddd, *J* = 8.5, 7.2, 1.4 Hz), 7.32 (1H, d, *J* = 2.1 Hz), 7.23 – 7.17 (2H, m), 7.09 (1H, dd, *J* = 8.2, 2.2 Hz), 6.99 (1H, d, *J* = 8.2 Hz), 6.85 – 6.79 (2H, m), 6.75 (1H, ddd, *J* = 8.2, 7.2, 1.0 Hz), 6.67 (1H, ddd, *J* = 7.8, 1.4, 0.7 Hz), 4.53 (1H, s), 2.90 – 2.73 (1H, m), 2.70 – 2.57 (3H, m), 2.40 (3H, s), 1.64 (9H, s); ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.3, 151.5, 148.4, 144.0, 137.2, 134.6, 134.1, 133.7, 132.7, 131.4, 130.3, 129.4, 127.3, 126.6, 122.7, 119.8, 118.0, 116.2, 91.8, 83.7, 39.0, 28.6, 28.2, 21.1; HRMS (*m/z*), calculated for $C_{28}H_{29}{}^{35}Cl_2N_2O_3^+$: 511.1550, found $(M + H)^+$: 511.1558.

***tert*-Butyl 3-((4-bromophenyl)imino)-2-hydroxy-2-(4-methoxyphenethyl)indoline-1-carboxylate 3e** was isolated as a lime green solid (0.60 g, 45%). R_f 0.87 (3:7 EtOAc/Hex); mp 143-144 °C; IR ν_{max} (cm^{-1}) 3302, 2980, 2836, 1710; ^1H NMR (300 MHz, $CDCl_3$) δ 8.02 – 7.75 (1H, m), 7.50 (2H, d, *J* = 8.6 Hz), 7.39 (1H, ddd, *J* = 8.6, 7.3, 1.4 Hz), 6.95 (2H, d, *J* = 8.6 Hz), 6.80 – 6.73 (5H, m), 6.63 (1H, d, *J* = 7.3 Hz), 4.15 (1H, br s), 3.76 (3H, s), 2.98 – 2.73 (1H, m), 2.65 (1H, dt, *J* = 13.2, 7.8 Hz), 2.46 (2H, t, *J* = 8.0 Hz), 1.64 (9H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.3, 158.1, 151.5, 150.0, 148.4, 134.5, 132.8, 132.7, 129.3, 126.5, 122.7, 120.1, 119.5, 117.0, 116.3, 114.0, 92.1, 83.7, 55.4, 41.2, 29.7, 28.6; HRMS (*m/z*), calculated for $C_{28}H_{30}{}^{79}BrN_2O_4^+$: 537.1383, found $(M + H)^+$: 537.1379.

***tert*-Butyl 3-((4-bromophenyl)imino)-2-hydroxy-2-(4-chlorophenethyl)indoline-1-carboxylate 3f** was isolated as a yellow solid (0.23 g, 34%). R_f 0.90 (3:7 EtOAc/Hex); mp 129-130 °C; IR ν_{max} (cm^{-1}) 3177, 2976, 2930, 1720; ^1H NMR (300 MHz, $CDCl_3$) δ 7.89 – 7.78 (1H, m), 7.49 (2H, d, *J* = 8.6 Hz), 7.39 (1H, ddd, *J* = 8.6, 7.3, 1.4 Hz), 7.15 (2H, d, *J* = 8.4 Hz), 6.92 (2H, d, *J* = 8.4 Hz), 6.82 – 6.68 (3H, m), 6.62 (1H, dd, 7.9, 1.3 Hz), 4.61 (1H, s), 3.00 – 2.75 (1H, m), 2.72 – 2.58 (1H, m), 2.53 – 2.44 (2H, m), 1.62 (9H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.2, 151.4, 149.8, 148.3, 139.1, 134.5, 132.7 (2C), 131.8, 129.7, 128.5, 126.4, 122.7, 120.0, 119.3, 117.0, 116.4, 91.9, 83.7, 77.2, 40.5, 29.9, 28.5; HRMS (*m/z*), calculated for $C_{27}H_{27}{}^{79}Br{}^{35}ClN_2O_3^+$: 541.0888, found $(M + H)^+$: 541.0901.

***tert*-Butyl 3-((4-bromophenyl)imino)-2-hydroxy-2-(3-chlorophenethyl)indoline-1-carboxylate 3g** was isolated as a yellow solid (0.26 g, 39%). R_f 0.90 (3:7 EtOAc/Hex); mp 108 °C; IR ν_{max} (cm^{-1}) 3191, 2979,1702; ^1H NMR (300 MHz, $CDCl_3$) δ 7.83 (1H, br s), 7.53 – 7.47 (2H, m), 7.39 (1H, ddd, *J* = 8.6, 7.3, 1.4 Hz), 7.15 – 7.10 (2H, m), 6.96 (1H, d, *J* = 1.5 Hz), 6.93 – 6.86 (1H, m), 6.82 – 6.71 (3H, m), 6.62 (1H, dd, *J* = 8.0, 1.2 Hz), 4.61 (1H, s, NH), 2.87 (1H, dt, *J* = 13.3, 7.8 Hz), 2.76 – 2.59 (1H, m), 2.55 – 2.45 (2H, m), 1.62 (9H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.0, 151.3, 149.7, 148.1, 142.6, 134.5, 134.1, 132.6, 129.6, 128.5, 126.5, 126.3,

126.2, 122.7, 120.0, 119.2, 116.9, 116.3, 91.8, 83.7, 40.3, 30.2, 28.4; HRMS (*m/z*), calculated for $C_{27}H_{27}{}^{79}Br^{35}ClN_2O_3^+$: 541.0888, found $(M + H)^+$: 541.0897.

***tert*-Butyl 3-((4-bromophenyl)imino)-2-hydroxy-2-(2,4-dichlorophenethyl)indoline-1-carboxylate 3h** was isolated as a brown oil (0.19 g, 27%). R_f 0.90 (3:7 EtOAc/Hex); IR ν_{max} (cm^{-1}): 3304, 2976, 2931, 1702; ^1H NMR (300 MHz, $CDCl_3$) δ 7.88 (1H, br s), 7.50 (2H, d, *J* = 8.6 Hz), 7.40 (1H, ddd, *J* = 8.6, 7.2, 1.4 Hz), 7.30 (1H, d, *J* = 2.1 Hz), 7.07 (1H, dd, *J* = 8.2, 2.1 Hz), 6.95 (1H, d, *J* = 8.3 Hz), 6.87 – 6.72 (3H, m), 6.66 (1H, dd, *J* = 7.9, 1.4 Hz), 4.73 (1H, s), 2.93 – 2.53 (4H, m), 1.64 (9H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.9, 151.3, 149.8, 148.3, 136.9, 134.5, 134.4, 132.7, 132.6, 131.2, 129.3, 127.1, 126.4, 122.6, 120.0, 119.1, 116.9, 116.3, 91.7, 83.7, 38.8, 28.4, 28.0; HRMS (*m/z*), calculated for $C_{27}H_{26}{}^{79}Br^{35}Cl_2N_2O_3^+$: 575.0498, found $(M + H)^+$: 575.0504.

***tert*-Butyl 3-((4-chlorophenyl)imino)-2-hydroxy-2-(4-methoxyphenethyl)indoline-1-carboxylate 3i** was isolated as an off-white solid (0.32 g, 50%). R_f 0.81 (3:7 EtOAc/Hex); mp 125 °C; IR ν_{max} (cm^{-1}) 3118, 2980, 2837, 1708; ^1H NMR (300 MHz, $CDCl_3$) δ 7.83 (1H, d, *J* = 10.0 Hz), 7.45 – 7.30 (3H, m), 6.99 – 6.89 (2H, m), 6.86 – 6.70 (5H, m), 6.62 (1H, dd, *J* = 8.0, 1.4 Hz), 4.49 (1H, s), 3.76 (3H, s), 3.07 – 2.26 (4H, m), 1.63 (9H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.3, 158.0, 151.4, 149.5, 148.4, 134.5, 132.8, 129.8, 129.4, 129.3, 126.4, 122.6, 119.7, 119.5, 116.3, 114.0, 92.0, 83.7, 55.4, 41.3, 29.7, 28.6; HRMS (*m/z*), calculated for $C_{28}H_{40}{}^{35}ClN_2O_4^+$: 493.1889, found $(M + H)^+$: 493.1882.

***tert*-Butyl 3-((4-chlorophenyl)imino)-2-hydroxy-2-(4-chlorophenethyl)indoline-1-carboxylate 3j** was isolated as a brown solid (0.74 g, 53%). R_f 0.87 (3:7 EtOAc/Hex); mp 122 - 123 °C; IR ν_{max} (cm^{-1}) 3196, 2981, 2931, 1714; ^1H NMR (300 MHz, $CDCl_3$) δ 7.86 (1H, br s), 7.44 – 7.36 (1H, m), 7.33 (2H, d, *J* = 8.7 Hz), 7.14 (2H, d, *J* = 8.3 Hz), 6.91 (2H, d, *J* = 8.3 Hz), 6.82 – 6.69 (3H, m), 6.61 (1H, dd, *J* = 8.0, 1.3 Hz), 4.68 (1H, s), 2.87 (1H, dt, *J* = 13.2, 7.9 Hz), 2.74 – 2.57 (1H, m), 2.48 (2H, t, *J* = 7.8 Hz), 1.61 (9H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.3, 151.3, 149.2, 148.3, 139.1, 134.4, 131.7, 129.7, 129.6, 129.3, 128.4, 126.3, 122.5, 119.6, 119.2, 116.3, 91.8, 83.5, 40.4, 29.8, 28.4; HRMS (*m/z*), calculated for $C_{27}H_{27}{}^{35}Cl_2N_2O_3^+$: 497.1393, found $(M + H)^+$: 497.1400.

***tert*-Butyl 3-((4-chlorophenyl)imino)-2-hydroxy-2-(3-chlorophenethyl)indoline-1-carboxylate 3k** was isolated as a yellow solid (0.66 g, 48 %). R_f 0.87 (3:7 EtOAc/Hex); mp 119 °C; IR ν_{max} (cm^{-1}) 3177, 2980, 2930, 1702; ^1H NMR (300 MHz, $CDCl_3$) δ 7.83 (1H, d, *J* = 9.2 Hz), 7.45 – 7.30 (3H, m), 7.16 – 7.08 (2H, m), 6.95 (1H, d, *J* = 1.6 Hz), 6.94 – 6.86 (1H, m), 6.85 – 6.72 (3H, m), 6.62 (1H, dd, *J*=8.0, 1.3 Hz), 4.63 (1H, s), 2.98 – 2.41 (4H, m), 1.62 (9H, s); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.3, 151.4, 149.3, 148.2, 142.6, 134.6, 134.2, 129.8, 129.7, 129.4, 128.6, 126.6, 126.4, 126.3, 122.8, 119.7, 119.3, 116.4, 91.9, 83.8, 40.4, 30.3, 28.5; HRMS (*m/z*), calculated for $C_{27}H_{27}{}^{35}Cl_2N_2O_3^+$: 497.1393, found $(M + H)^+$: 497.1398.

***tert*-Butyl 3-((4-chlorophenyl)imino)-2-hydroxy-2-(2,4-dichlorophenethyl)indoline-1-carboxylate 3l** was isolated as a brown oil (0.22 g, 15%). R_f 0.90 (3:7 EtOAc/Hex); IR ν_{max} (cm^{-1}) 3413, 2976, 2928, 1710; ^1H NMR (500 MHz, $CDCl_3$) δ 7.88 (1H, br s), 7.42 – 7.33 (3H, m), 7.30 (1H, d, *J* = 2.1 Hz), 7.07 (1H, dd, *J* = 8.2, 2.1 Hz), 6.96 (1H, d, *J* = 8.3 Hz), 6.86 (2H, d, *J* = 8.6 Hz), 6.77 (1H, td, *J* = 7.6, 1.0 Hz), 6.66 (1H, dd, *J* = 8.1, 1.4 Hz), 4.79 (1H, s), 2.82 – 2.75 (1H, m), 2.70 – 2.52 (3H, m), 1.64 (9H, s); ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.1, 152.9, 151.4, 149.3, 148.3, 136.9, 134.6, 134.5, 132.6, 131.3, 129.8, 129.4, 129.3, 127.2, 126.4, 122.7, 119.6, 116.3, 91.8, 83.8, 38.8, 28.5, 28.1; HRMS (*m/z*), calculated for $C_{27}H_{26}{}^{35}Cl_3N_2O_3^+$: 531.1004, found $(M + H)^+$: 531.0986.

***tert*-Butyl 2-hydroxy-2-(4-methoxyphenethyl)-3-((4-methoxyphenyl)imino)indoline-1-carboxylate 3m** was isolated as a yellow solid (0.22 g, 32%). R_f 0.52 (3:7 EtOAc/Hex); mp 145-146 °C; IR ν_{max} (cm^{-1}) 3127, 2983, 1703; ^1H NMR (500 MHz, $CDCl_3$) δ 7.85 (1H, br s), 7.36 (1H, ddd, *J* = 8.5, 7.2, 1.5 Hz), 7.00 – 6.90 (4H, m), 6.86 – 6.80 (2H, m), 6.78 – 6.71 (3H, m), 6.69 (1H, ddd, *J* = 8.0, 1.5, 0.6 Hz), 4.52 (1H, br s), 3.85 (3H, s), 3.76 (3H, s), 2.91 – 2.75 (1H, m), 2.73 – 2.60 (1H, m), 2.543 – 2.38 (2H, m), 1.64 (9H, s); ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.0, 158.0, 156.6 (2C), 144.2, 134.0, 133.0, 129.3, 129.1, 126.4, 122.5, 119.9, 119.4, 116.2, 114.9, 113.9, 92.0, 83.5, 55.4, 41.4, 29.7, 28.6; HRMS (*m/z*), calculated for $C_{29}H_{33}N_2O_5^+$: 489.2384, found $(M + H)^+$: 489.2394.

***tert*-Butyl 2-hydroxy-2-(4-chlorophenethyl)-3-((4-methoxyphenyl)imino)indoline-1-carboxylate 3n** was isolated as a yellow powder (0.27 g, 39%). R_f 0.48 (3:7 EtOAc/Hex); mp 138-139 °C; IR ν_{max} (cm^{-1}) 3172, 2965, 1702; ^1H NMR (500 MHz, $CDCl_3$) δ 7.36 (1H, ddd, *J* = 8.6, 7.2, 1.5 Hz), 7.26 – 7.21 (1H, m), 7.18 – 7.13 (2H, m), 7.13 – 7.08 (1H, m), 6.98 – 6.88 (3H, m), 6.82 – 6.78 (2H, m), 6.74 (1H, td, *J* = 7.6, 1.0 Hz), 6.68 (1H, dd, *J* = 7.9, 1.4 Hz), 3.84 (3H, s), 2.94 – 2.81 (1H, m), 2.72 – 2.61 (1H, m), 2.57 – 2.41 (2H, m), 1.62 (9H, s); ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.0, 156.6, 143.9, 133.2, 137.2, 134.0, 132.2, 131.7, 130.4, 129.7, 128.5, 126.3, 122.5, 119.3, 116.2, 114.9, 91.8, 83.5, 55.5, 38.5, 29.9, 28.5; HRMS (*m/z*), calculated for $C_{28}H_{30}{}^{35}ClN_2O_4^+$: 493.1889, found $(M + H)^+$: 493.1895.

***tert*-Butyl 2-hydroxy-2-(3-chlorophenethyl)-3-((4-methoxyphenyl)imino)indoline-1-carboxylate 3o** was isolated as a yellow solid (0.28 g, 40%). R_f 0.61 (3:7 EtOAc/Hex); mp 132-133 °C; IR ν_{max} (cm^{-1}) 3140, 2969, 2931, 1702; ^1H NMR (500 MHz, $CDCl_3$) δ 7.82 (1H, br s), 7.37 (1H, ddd, *J* = 8.6, 7.2, 1.5 Hz), 7.19 (1H, br s),7.15 – 7.09 (2H, m), 7.00 – 6.89 (3H, m), 6.85 – 6.79 (2H, m), 6.74 (1H, ddd, *J* = 8.2, 7.2, 1.0 Hz), 6.69 (1H, dd, *J* = 7.9, 1.4 Hz), 4.65 (1H, s), 3.84 (3H, s), 2.94 – 2.82 (1H, m), 2.69 (1H, ddd, *J* = 13.4, 9.5, 6.1 Hz), 2.60 – 2.43 (4H, m), 1.62 (9H, s); ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.0, 156.6, 143.9, 142.8, 134.1, 134.0, 129.8, 129.6, 129.1, 128.6, 126.6, 126.3, 126.2, 122.5, 119.3, 116.2, 114.9, 91.8, 83.5, 55.5, 38.9, 30.2, 28.5; HRMS (*m/z*), calculated for $C_{28}H_{30}{}^{35}ClN_2O_4^+$: 493.1889, found $(M + H)^+$: 493.1896.

***tert*-Butyl 2-hydroxy-2-(2,4-dichlorophenethyl)-3-((4-methoxyphenyl)imino)indoline-1-carboxylate 3p** was isolated as a brown oil (0.23 g, 33%). R_f 0.65 (3:7 EtOAc/Hex); IR ν_{max} (cm^{-1}) 3330, 2966, 2936, 1706; ^1H NMR (500 MHz, $CDCl_3$) δ 7.88 (1H, br s), 7.36 (1H, ddd, *J* = 8.6, 6.7, 2.0 Hz), 7.31 (1H, d, *J* = 2.1 Hz), 7.08 (1H, dd, *J* = 8.2, 2.1 Hz), 7.00 – 6.91 (3H, m), 6.89 – 6.82 (2H, m), 6.77 – 6.67 (2H, m), 4.55 (1H, br s), 3.84 (3H, s), 2.91 – 2.72 (1H, m), 2.68 – 2.51 (3H, m), 1.64 (9H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.8, 156.7, 151.5, 148.1, 140.0, 137.1, 134.6, 134.1, 132.6, 131.4, 129.3, 127.2, 126.4, 122.6, 119.6, 119.3, 116.2, 115.0, 91.8, 83.6, 55.6, 39.0, 28.5, 28.0; HRMS (*m/z*), calculated for $C_{28}H_{29}{}^{35}Cl_2N_2O_4^+$: 527.1499, found $(M + H)^+$: 527.1502.

***tert*-Butyl 3-((3,4-dimethylphenyl)imino)-2-hydroxy-2-(4-chlorophenethyl)indoline-1-carboxylate 3q** was isolated as a yellow solid (0.11 g, 15%). R_f 0.90 (3:7 EtOAc/Hex); mp 138 °C; IR ν_{max} (cm^{-1}) 3171, 2972, 2920, 1703; ^1H NMR (500 MHz, $CDCl_3$) δ 7.83 (1H, br s), 7.36 (1H, ddd, *J* = 8.5, 7.2, 1.5 Hz), 7.19 – 7.14 (2H, m), 7.13 (1H, d, *J* = 7.9 Hz), 6.97 (2H, d, *J* = 8.4 Hz), 6.76 – 6.70 (1H, m), 6.69 – 6.62 (2H, m), 6.61 (1H, dd, *J* = 7.9, 2.2 Hz), 4.53 (1H, s), 2.94 – 2.79 (1H, m), 2.69 (1H, ddd, *J* = 13.4, 9.7, 5.9 Hz), 2.60 – 2.42 (2H, m), 2.30 (3H, s), 2.27 (3H, s), 1.63 (9H, s); ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.3, 151.5, 148.6, 148.0, 139.4, 137.9, 133.9, 132.2, 131.8, 130.7, 129.8, 128.5, 126.6, 122.5, 119.8, 119.2, 116.1, 115.2, 91.8, 83.5, 40.7, 30.0, 28.5, 20.0, 19.4; HRMS (*m/z*), calculated for $C_{29}H_{32}{}^{35}ClN_2O_3^+$: 491.2096, found $(M + H)^+$: 491.2108.

***tert*-Butyl 3-((3,4-dimethylphenyl)imino)-2-hydroxy-2-(3-chlorophenethyl)indoline-1-carboxylate 3r** was isolated as a yellow solid (0.12 g, 18%). R_f 0.97 (3:7 EtOAc/Hex); mp 129 °C; IR ν_{max} (cm^{-1}) 3166, 2972, 2928, 1702; ^1H NMR (500 MHz, $CDCl_3$) δ 7.84 (1H, br s), 7.36 (1H, ddd, *J* = 8.6, 7.2, 1.5 Hz), 7.17 – 7.10 (3H, m), 6.99 (1H, br s), 6.96 – 6.92 (1H, m), 6.74 (1H, ddd, *J* = 8.2, 7.3, 1.0 Hz), 6.67 (2H, dd, *J* = 7.9, 1.6 Hz), 6.63 (1H, dd, *J* = 7.8, 2.3 Hz), 4.57 (1H, s), 2.94 – 2.79 (1H, m), 2.70 (1H, ddd, *J* = 13.4, 9.6, 6.0 Hz), 2.61 – 2.44 (2H, m), 2.30 (3H, s), 2.27 (3H, s), 1.63 (9H, s); ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.3, 151.5, 148.6, 148.0, 143.0, 137.9, 134.1, 134.0, 132.2, 130.7, 129.7, 128.6, 126.6, 126.6, 126.3, 122.6, 119.8, 119.2, 116.2, 115.2, 91.8, 83.5, 40.5, 30.3, 28.6, 20.0, 19.4; HRMS (*m/z*), calculated for $C_{29}H_{32}{}^{35}ClN_2O_3^+$: 491.2096, found $(M + H)^+$: 491.2113.

***tert*-Butyl-5-chloro-2-(4-methoxyphenethyl)-2-hydroxy-3-(*p*-tolylimino)indoline-1-carboxylate 3s** was isolated as a yellow powder (0.086 g, 13%) from the starting isatin ketimine **4f** (0.500 g, 1.35 mmol). R_f 0.54 (3:7 EtOAc/Hex); mp 121-122 °C; IR ν_{max} (cm^{-1}) 3167, 2971, 1707, 1652, 1508; ^1H NMR (400 MHz, CD_3OD) δ 8.03 (1H, d, *J* = 8.8 Hz), 7.39 (1H, dd, *J* = 8.8, 2.3 Hz), 7.27 (2H, d, *J* = 7.8 Hz), 6.92 (2H, d, *J* = 8.6 Hz), 6.77 – 6.70 (4H, m), 6.39 (1H, d, *J* = 2.3 Hz), 3.73 (3H, s), 3.04 – 2.93 (1H, m), 2.60 – 2.42 (1H, m), 2.47 – 2.33 (5H, m), 1.63 (9H, s); ^{13}C NMR (101 MHz, CD_3OD) δ 168.6, 159.5, 152.5, 149.3, 148.9, 135.5, 134.8, 133.9, 131.4,

130.3, 127.8, 126.7, 121.6, 118.9, 118.7, 114.8, 93.8, 83.9, 55.7, 41.3, 30.6, 28.6, 21.0; HRMS (*m/z*), calculated for $C_{29}H_{32}{}^{35}ClN_2O_4^+$: 507.2045, found $(M + H)^+$: 507.2068.

***tert*-Butyl-5-chloro-2-(3-methoxyphenethyl)-2-hydroxy-3-(*p*-tolylimino)indoline-1-carboxylate 3t** was isolated as a yellow powder (0.084 g, 12%) from the starting isatin ketimine **4f** (0.500 g, 1.35 mmol). R_f 0.53 (3:7 EtOAc:Hex); mp 126 – 127 °C; IR ν_{max} (cm^{-1}) 3175, 3085, 2853, 1703, 1654; ^1H NMR (400 MHz, CD_3OD) δ 8.03 (1H, d, *J* = 8.9 Hz), 7.40 (1H, dd, *J* = 8.9, 2.2 Hz), 7.27 (2H, d, *J* = 8.0 Hz), 7.09 (1H, t, *J* = 7.8 Hz), 6.75 – 6.68 (3H, m), 6.61 (1H, d, *J* = 7.8 Hz), 6.56 – 6.52 (1H, m), 6.39 (1H, d, *J* = 2.2 Hz), 3.70 (3H, s), 3.08 – 2.98 (1H, m), 2.63 – 2.53 (1H, m), 2.52 – 2.42 (2H, m), 2.41 (3H, s), 1.63 (9H, s); ^{13}C NMR (101 MHz, CD_3OD) δ 168.6 (C-3), 161.1, 152.5, 149.3, 148.9, 143.6, 135.5, 134.8, 131.4, 130.4, 127.9, 126.7, 121.8, 121.6, 118.9, 118.7, 115.3, 112.4, 93.8, 83.9, 55.5, 40.9, 31.6, 28.6 (C-10, C-10' and C-10''), 20.97 (C-12); HRMS (*m/z*), calculated for $C_{29}H_{32}{}^{35}ClN_2O_4^+$: 507.2045, found $(M + H)^+$: 507.2072.

***tert*-Butyl-5-chloro-2-(2-methoxyphenethyl)-2-hydroxy-3-(*p*-tolylimino)indoline-1-carboxylate 3u** was isolated as a yellow powder (0.10 g, 19%) from the starting isatin ketimine **4f** (0.500 g, 1.35 mmol). R_f 0.55 (3:7 EtOAc:Hex); mp 118 – 119 °C; IR ν_{max} (cm^{-1}) 3211, 2976, 2853, 1700, 1654, 1594, 1498; ^1H NMR (400 MHz, CD_3OD) δ 8.06 (1H, d, *J* = 8.8 Hz), 7.39 (1H, dd, *J* = 8.8, 2.4 Hz), 7.28 (2H, d, *J* = 8.1 Hz), 7.12 (1H, td, *J* = 8.0, 1.6 Hz), 6.91 (1H, dd, *J* = 7.4, 1.6 Hz), 6.84 (1H, d, *J* = 8.0 Hz), 6.78 – 6.73 (3H, m), 6.40 (1H, d, *J* = 2.4 Hz), 3.73 (3H, s), 3.01 – 2.91 (1H, m), 2.58 – 2.48 (1H, m), 2.48 – 2.42 (2H, m), 2.41 (3H, s), 1.63 (9H, s); ^{13}C NMR (101 MHz, CD_3OD) δ 168.6, 158.7, 152.6, 149.4, 149.0, 135.5, 134.7, 131.4, 130.9, 130.1, 128.5, 127.8, 126.6, 121.6, 121.4, 118.9, 118.6, 111.4, 93.9, 83.8, 55.7, 39.8, 28.6, 25.7, 21.0; HRMS (*m/z*), calculated for $C_{29}H_{32}{}^{35}ClN_2O_4^+$: 507.2045, found $(M + H)^+$: 507.2069.

***tert*-Butyl-5-chloro-2-(4-chlorophenethyl)-2-hydroxy-3-(*p*-tolylimino)indoline-1-carboxylate 3v** was isolated as a yellow powder (0.18 g, 37%) from the starting isatin ketimine **4f** (0.349 g, 0.94 mmol). R_f 0.58 (3:7 EtOAc:Hex); mp 125 – 126 °C; IR ν_{max} (cm^{-1}) 3149, 2982, 2857, 1707, 1658, 1506; ^1H NMR (400 MHz, CD_3OD) δ 8.02 (1H, d, *J* = 9.0 Hz), 7.41 (1H, dd, *J* = 9.0, 2.3 Hz), 7.29 (2H, d, *J* = 8.1 Hz), 7.08 – 7.01 (2H, m), 6.95 – 6.89 (2H, m), 6.77 (2H, d, *J* = 8.1 Hz), 6.43 (1H, d, *J* = 2.2 Hz), 3.07 – 2.94 (1H, m), 2.61 – 2.51 (1H, m), 2.48 – 2.42 (1H, m), 2.41 (3H, s), 1.62 (9H, s); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.5, 152.5, 149.3, 148.9, 138.0, 135.6, 134.9, 131.4, 131.0, 128.0, 126.7, 121.5, 119.3, 118.9, 118.7, 116.0, 93.7, 84.0, 41.0, 30.6, 28.6, 21.0; HRMS (*m/z*), calculated for $C_{28}H_{29}{}^{35}Cl_2N_2O_3^+$: 511.1550, found $(M + H)^+$: 511.15124.

***tert*-Butyl-5-chloro-2-(3-chlorophenethyl)-2-hydroxy-3-(*p*-tolylimino)indoline-1-carboxylate 3w** was isolated as a yellow powder (0.24 g, 49%) from the starting isatin ketimine **4f** (0.349 g, 0.941 mmol). R_f 0.60 (3:7 EtOAc:Hex); mp 122 – 124 °C; IR ν_{max} (cm^{-1}) 3135, 2979, 2927, 2863, 1709, 1656, 1507, 1252; ^1H NMR (400 MHz, CD_3OD) δ 7.98 (1H, d, *J* = 8.7 Hz),

7.39 (1H, dd, *J* = 8.7, 2.3 Hz), 7.26 (2H, d, *J* = 8.1 Hz), 7.18 – 7.12 (2H, m), 6.97 – 6.93 (2H, m), 6.73 (2H, d, *J* = 8.1 Hz), 6.39 (1H, d, *J* = 2.3 Hz), 3.07 – 2.97 (1H, m), 2.62 – 2.51 (1H, m), 2.51 – 2.42 (1H, m), 2.40 (3H, s), 1.61 (9H, s); ^{13}C NMR (101 MHz, CD_3OD) δ 168.4, 152.4, 149.2, 148.8, 144.4, 135.6, 135.1, 134.9, 131.4, 130.9, 129.6, 128.0, 128.0, 127.2, 126.7, 121.5, 118.9, 118.7, 93.7, 84.0, 40.6, 31.3, 28.6, 21.0; HRMS (*m/z*), calculated for $C_{28}H_{29}{}^{35}Cl_2N_2O_3^+$: 511.1550, found $(M + H)^+$: 511.1577.

***tert*-Butyl-5-chloro-2-(2-chlorophenethyl)-2-hydroxy-3-(*p*-tolylimino)indoline-1-carboxylate 3x** was isolated as a yellow powder (0.52 g, 42%) from the starting isatin ketimine **4f** (0.891 g, 2.40 mmol). R_f 0.62 (3:7 EtOAc:Hex); mp 129 – 131 °C; IR ν_{max} (cm^{-1}) 3175, 3125, 2930, 1710, 1657, 1508, 1465, 1253; ^{1}H NMR (400 MHz, CD_3OD) δ 7.35 – 7.28 (2H, m), 7.23 (2H, d, *J* = 8.1 Hz), 7.15 – 7.04 (4H, m), 6.82 (2H, d, *J* = 8.1 Hz), 6.60 (1H, d, *J* = 2.2 Hz), 2.92 – 2.75 (1H, m), 2.70 – 2.58 (3H, m), 2.41 (3H, s), 1.64 (9H, s); ^{13}C NMR (101 MHz, CD_3OD) δ 164.2, 147.8, 138.3, 134.2, 133.9, 133.7, 133.8, 130.6, 131.4, 129.7, 128.8, 127.8, 127.6, 127.1, 126.1, 117.8, 117.3, 92.2, 84.0, 39.4, 28.6, 28.6, 21.2; HRMS (*m/z*), calculated for $C_{28}H_{29}{}^{35}Cl_2N_2O_3^+$: 511.1550, found $(M + H)^+$: 511.1550.

***tert*-Butyl-5-chloro-2-(2,4-dichlorophenethyl)-2-hydroxy-3-(*p*-tolylimino)indoline-1-carboxylate 3y** was isolated as a yellow powder (0.099 g, 22%) from the starting isatin ketimine **4f** (0.300 g, 0.808 mmol). R_f 0.64 (3:7 EtOAc:Hex); mp 132 – 133 °C; IR ν_{max} (cm^{-1}) 3166, 2971, 2854, 1710, 1650, 1506, 1276; ^{1}H NMR (400 MHz, CD_3OD) δ 8.05 (1H, d, *J* = 8.8 Hz), 7.41 (1H, dd, *J* = 8.8, 2.3 Hz), 7.37 (1H, d, *J* = 2.1 Hz), 7.29 (2H, d, *J* = 8.1 Hz), 7.18 – 7.13 (1H, m), 7.05 (1H, d, *J* = 8.3 Hz), 6.80 (2H, d, *J* = 8.1 Hz), 6.45 (1H, d, *J* = 2.3 Hz), 3.07 – 2.91 (1H, m), 2.66 – 2.50 (3H, m), 2.42 (3H, s), 1.62 (9H, s); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.2, 152.4, 149.3, 148.9, 142.2, 138.6, 135.6, 134.9, 133.8, 132.9, 131.5, 130.1, 128.4, 128.0, 126.7, 121.4, 118.9, 118.8, 95.6, 84.0, 38.9, 28.8, 28.6, 21.0; HRMS (*m/z*), calculated for $C_{28}H_{28}{}^{35}Cl_3N_2O_3^+$: 545.1160, found $(M + H)^+$: 545.1150.

***tert*-Butyl-5-chloro-2-(4-fluorophenethyl)-2-hydroxy-3-(*p*-tolylimino)indoline-1-carboxylate 3z** as a yellow powder (0.194 g, 48%). R_f 0.63 (3:7 EtOAc:Hex); mp 139 – 141 °C; IR ν_{max} (cm^{-1}) 3338, 2964, 2854, 1717, 1683, 1505, 1455, 1253; ^{1}H NMR (400 MHz, CD_3OD) δ 8.02 (1H, d, *J* = 8.8 Hz), 7.41 (1H, dd, *J* = 8.8, 2.3 Hz), 7.29 (2H, d, *J* = 8.1 Hz), 7.08 – 7.01 (2H, m), 6.96 – 6.88 (2H, m), 6.77 (2H, d, *J* = 8.1 Hz), 6.43 (1H, d, 2.3 Hz), 3.06 – 2.96 (1H, m), 2.60 – 2.51 (1H, m), 2.48 – 2.42 (2H, m), 2.41 (3H, s), 1.62 (9H, s); ^{13}C NMR (101 MHz, CD_3OD) δ 168.5, 162.8 (d, J_{C-F} = 243 Hz), 152.5, 149.3, 148.9, 138.0, 135.6, 134.9, 131.4, 131.0 (d, J_{C-F} = 7.9 Hz), 128.0, 126.7, 121.5, 118.9, 118.7, 116.0 (d, J_{C-F} = 21.4 Hz), 93.7, 84.0, 41.0, 30.6, 28.6, 21.0; HRMS (*m/z*), calculated for $C_{28}H_{29}{}^{35}ClFN_2O_3^+$: 495.1845, found $(M + H)^+$: 495.1849.

***tert*-Butyl-5-chloro-2-(2-fluorophenethyl)-2-hydroxy-3-(*p*-tolylimino)indoline-1-carboxylate 3aa** was isolated as a yellow powder (0.083 g, 23%). R_f 0.64 (3:7 EtOAc:Hex); mp

148 – 149 °C; IR ν_{max} (cm^{-1}) 3344, 2975, 2927, 2857, 1710, 1667, 1596, 1495, 1364, 1246; ^{1}H NMR (400 MHz, CD_3OD) δ 8.06 (1H, d, *J* = 9.0 Hz), 7.40 (1H, dd, *J* = 9.0, 2.3 Hz), 7.29 (2H, d, *J* = 8.1 Hz), 7.22 – 7.09 (1H, m), 7.08 – 6.94 (3H, m), 6.78 (2H, d, *J* = 8.1 Hz), 6.42 (1H, d, *J* = 2.3 Hz), 3.09 – 2.94 (1H, m), 2.62 – 2.43 (3H, m), 2.41 (3H, s), 1.63 (9H, s); ^{13}C NMR (101 MHz, CD_3OD) δ 168.4, 162.4 (d, J_{C-F} = 244 Hz), 152.5, 149.3, 149.0, 135.5, 134.9, 131.9 (d, J_{C-F} = 4.8 Hz), 131.4, 129.2 (d, J_{C-F} = 8.1 Hz), 128.8 (d, J_{C-F} = 15.8 Hz), 127.9, 126.6, 125.3, 121.5, 118.9, 118.7, 116.2 (d, J_{C-F} = 22 Hz), 93.6, 84.0, 39.8, 28.6, 24.8, 21.0; HRMS (*m/z*), calculated for $C_{28}H_{29}{}^{35}ClFN_2O_3^+$: 495.1845, found $(M + H)^+$: 495.1818.

1.1.5 General procedure for the addition reaction of ethynyl benzenes to ketimines.

A stirred solution of an appropriately substituted phenylacetylene (2.0 eq., 4.23 mmol) in THF (20 mL) under argon was treated with freshly sublimed potassium *tert*-butoxide (3.0 eq., 6.35 mmol). The resulting solution was left to stir for 30 min at room temperature. After this time, 3-(*p*-tolylimino)indolin-2-one **4a** (1.0 eq., 2.12 mmol) and CuI (0.10 eq., 0.42 mmol) were added, and the resulting solution was left to stir overnight. The reaction mixture was quenched with saturated NH_4Cl (40 mL), and the product was extracted with EtOAc (3 x 30 mL). The combined organic layers were stirred with activated charcoal and Na_2SO_4 at 74 °C before filtration over a bed of celite. The filtrate was reduced *in vacuo,* and the resulting crude was purified by recrystallisation in DCM to afford the desired product. Oxindoles **11a-e** were prepared using this procedure.

3-(Phenylethynyl)-3-(*p*-tolylamino)indolin-2-one 11a[21] was isolated as a yellow powder (0.454 g, 63%). R_f 0.18 (4:6 EtOAc:Hex); mp 184-185 °C; IR ν_{max} (cm^{-1}) 3308, 3080, 3025, 2623, 2195, 1719, 1675, 1618; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.88 (1H, s), 7.45 – 7.34 (6H, m), 7.30 (1H, td, *J* = 7.7, 1.3 Hz), 7.04 (1H, td, *J* = 7.7, 1.1 Hz), 6.95 (1H, d, *J* = 7.7 Hz), 6.79 (2H, d, *J* = 8.4 Hz), 6.64 (1H, s), 6.44 (2H, d, *J* = 8.4 Hz), 2.09 (3H, s); ^{13}C NMR (101 MHz, DMSO-d_6) δ 174.3, 143.0, 140.9, 131.5, 129.7, 129.6, 129.1, 129.0, 128.7, 126.4, 124.1, 122.7, 121.3, 114.8, 110.5, 87.2, 83.3, 59.0, 20.0; HRMS (*m/z*), calculated for $C_{23}H_{19}N_2O^+$: 339.1492, found $(M + H)^+$: 339.1489.

3-((4-Methoxyphenyl)ethynyl)-3-(*p*-tolylamino)indolin-2-one 11b was isolated as a white powder (0.339 g, 43%). R_f 0.22 (4:6 EtOAc:Hex); mp 193-194 °C; IR ν_{max} (cm^{-1}) 3305, 3150, 3028, 2220, 1720, 1618, 1293; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.84 (1H, s), 7.39 – 7.32 (3H, m), 7.29 (1H, td, *J* = 7.7, 1.2 Hz), 7.03 (1H, td, *J* = 7.7, 0.7 Hz), 6.96 – 6.89 (3H, m), 6.78 (2H, d, *J* = 8.4 Hz), 6.59 (1H, s), 6.41 (2H, d, *J* = 8.4 Hz), 3.76 (3H, s), 2.08 (3H, s); ^{13}C NMR (101 MHz, DMSO-d_6) δ 174.5, 159.7, 143.1, 140.9, 133.1, 129.8, 129.6, 129.0, 126.3, 124.0, 122.6, 114.7, 114.3, 113.2, 110.5, 85.7, 83.3, 59.0, 55.2, 20.0; HRMS (*m/z*), calculated for $C_{24}H_{21}N_2O_2^+$: 369.1598, found $(M + H)^+$: 369.1592.

3-((3-Methoxyphenyl)ethynyl)-3-(*p*-tolylamino)indolin-2-one 11c as a white powder (0.311 g, 40%). R_f 0.43 (4:6 EtOAc:Hex); mp 179-180 °C; IR ν_{max} (cm^{-1}) 3312, 3146, 3087, 2227, 1718, 1617, 1517, 1291; ^1H NMR (400 MHz, DMSO-d_6) δ 10.87 (1H, s), 7.37 (1H, d, *J* = 7.33 Hz), 7.34 – 7.24 (2H, m), 7.03 (1H, td, *J* = 7.55, 0.70 Hz), 7.00 – 6.90 (4H, m), 6.79 (2H, d, *J* = 8.30 Hz), 6.62 (1H, s), 6.43 (2H, d, *J* = 8.45 Hz), 3.74 (3H, s), 2.09 (3H, s); ^{13}C NMR (101 MHz, DMSO-d_6) δ 174.3, 159.1, 143.0, 140.9, 129.9, 129.7, 129.5, 129.0, 126.5, 124.1, 124.0, 122.7, 122.4, 116.0, 115.8, 114.8, 110.5, 87.0, 83.3, 59.0, 55.2, 20.0; HRMS (*m/z*), calculated for $C_{24}H_{21}N_2O_2^+$: 369.1598, found $(M + H)^+$: 369.1593.

3-((2-Methoxyphenyl)ethynyl)-3-(*p*-tolylamino)indolin-2-one 11d was isolated as a white powder (0.350 g, 45%). R_f 0.35 (4:6 EtOAc:Hex); mp 160-161 °C; IR ν_{max} (cm^{-1}) 3297, 3132, 3083, 2202, 1716, 1617, 1518, 1269; ^1H NMR (400 MHz, DMSO-d_6) δ 10.80 (1H, s), 7.40 – 7.25 (4H, m), 7.08 – 6.98 (2H, m), 6.96 – 6.89 (2H, m), 6.79 (2H, d, *J* = 8.11 Hz), 6.51 (2H, d, *J* = 8.19 Hz), 6.46 (1H, s), 3.75 (3H, s), 2.09 (3H, s); ^{13}C NMR (101 MHz, DMSO-d_6) δ 174.3, 159.9, 143.1, 140.9, 133.5, 130.7, 129.9, 129.6, 128.9, 126.4, 124.1, 122.6, 120.4, 115.1, 111.5, 110.4, 110.4, 90.6, 80.3, 59.1, 55.7, 20.0; HRMS (*m/z*), calculated for $C_{24}H_{21}N_2O_2^+$: 369.1598, found $(M + H)^+$: 369.1592.

3-((2-Fluorophenyl)ethynyl)-3-(*p*-tolylamino)indolin-2-one 11e was isolated as a white powder (0.356 g, 47 %). R_f 0.30 (4:6 EtOAc:Hex); mp 178-179 °C; IR ν_{max} (cm^{-1}) 3296, 3121, 3082, 3029, 1721, 1618, 1518, 1299; ^1H NMR (400 MHz, DMSO-d_6) δ 10.89 (1H, s), 7.53 – 7.42 (2H, m), 7.38 (1H, d, *J* = 7.00 Hz), 7.33 – 7.25 (2H, m), 7.22 (1H, td, *J* = 7.62, 0.99 Hz), 7.04 (1H, td, *J* = 7.68, 0.61 Hz), 6.94 (1H, d, *J* = 7.72 Hz), 6.79 (2H, d, *J* = 8.30 Hz), 6.63 (1H, s), 6.47 (2H, d, *J* = 8.44 Hz), 2.09 (3H, s); ^{13}C NMR (101 MHz, DMSO-d_6) δ 174.0, 160.8 (J_{C-F} = 238 Hz), 142.9, 140.9, 133.7, 131.5 (J_{C-F} = 5.00 Hz), 129.8, 129.4, 129.0, 126.6, 124.8 (J_{C-F} = 3.03 Hz), 124.2, 124.4, 122.7, 115.8 (J_{C-F} = 20.2 Hz), 115.0, 110.5, 85.6, 76.9, 59.1, 20.0; HRMS (*m/z*), calculated for $C_{23}H_{18}FN_2O^+$: 357.1398 found $(M + H)^+$: 357.1394.

1.1.6 General procedure for the hydrogenation of phenethynyl indoline-2-ones.

In a high-pressure reactor vessel, the appropriately substituted 3-ethynyl-3-(*p*-tolylamino)indolin-2-one **8a-e** (0.200 g, 0.59 mmol) was dissolved in EtOH (10 mL). To the stirred solution, 10% Pd/C (0.020 g, 0.019 mmol) and Na_2CO_3 (0.625 g, 5.9 mmol) were added, and the mixture was stirred overnight under a hydrogen atmosphere (200 mbar). After this time, the reaction mixture was filtered through a pad of celite, and the solvent removed under rotary evaporation. A 1:1 DCM/Hexane solution (5 mL) was added to the flask, and the resulting precipitate was collected by filtration and washed with cold DCM. The final product was obtained after drying. Oxindoles **2e-i** were obtained using this procedure.

3-Phenethyl-3-(*p*-tolylamino)indolin-2-one 2e was isolated as a white solid (0.166 g, 82%). R_f 0.35 (4:6 EtOAc:Hex); mp 202-204 °C; IR ν_{max} (cm^{-1}) 3320, 3140, 2950, 2933, 1703, 1660, 1334; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.67 (1H, s), 7.28 – 7.20 (4H, m), 7.16 (1H, t, *J* = 7.33), 7.10 (2H, d, *J* = 7.03 Hz), 6.99 (1H, t, *J* = 7.48 Hz), 6.93 (1H, d, *J* = 7.66 Hz), 6.70 (2H, d, *J* = 8.28 Hz), 6.17 (1H, s), 6.12 (2H, d, *J* = 8.44 Hz), 2.47 – 2.27 (2H, m), 2.18 – 1.97 (5H, m); ^{13}C NMR (101 MHz, DMSO-d_6) δ 179.2, 144.3, 141.3, 141.0, 130.7, 129.0, 128.7, 128.4, 128.1, 125.9, 125.2, 123.5, 122.0, 113.5, 110.0, 64.1, 41.4, 28.5, 19.9; HRMS (*m/z*), calculated for $C_{23}H_{23}N_2O^+$: 343.1805, found $(M + H)^+$: 343.1802.

3-(4-Methoxyphenethyl)-3-(*p*-tolylamino)indolin-2-one 2f was isolated as white crystals (0.158 g, 78%). R_f 0.53 (4:6 EtOAc:Hex); mp 163-164 °C; IR ν_{max} (cm^{-1}) 3328, 3136, 2936, 2915, 1711, 1616, 1333; ^{1}H NMR (400 MHz, DMSO-d_6): δ 10.66 (1H, s), 7.28 – 7.20 (2H, m), 7.04 – 6.96 (3H, m), 6.93 (1H, d, *J* = 7.73 Hz), 6.83 – 6.78 (2H, m), 6.70 (2H, d, *J* = 8.30 Hz), 6.18 – 6.08 (3H, m), 3.70 (3H, s), 2.44 – 2.26 (2H, m), 2.14 – 1.94 (5H, m); ^{13}C NMR (101 MHz, DMSO-d_6) δ 179.2, 157.5, 144.3, 141.3, 132.8, 130.7, 129.1, 129.0, 128.7, 125.1, 123.5, 121.9, 113.8, 113.5, 110.0, 64.1, 55.0, 41.7, 27.6, 19.9; HRMS (*m/z*), calculated for $C_{24}H_{25}N_2O_2$: 373.1911, found $(M + H)^+$: 373.1907.

3-(3-Methoxyphenethyl)-3-(*p*-tolylamino)indolin-2-one 2g was isolated as white crystals (0.142 g, 70%). R_f 0.33 (4:6 EtOAc:Hex); mp 160-162 °C; IR ν_{max} (cm^{-1}) 3321, 3141, 2918, 1704, 1618, 1302; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.67 (1H, s), 7.29 – 7.20 (2H, m), 7.15 (1H, t, *J* = 7.33), 7.00 (1H, t, *J* = 7.44 Hz), 6.94 (1H, d, *J* = 7.67 Hz), 6.75 – 6.66 (5H, m), 6.17 (1H, s), 6.13 (2H, d, *J* = 8.43 Hz), 3.71 (3H, s), 2.48 – 2.33 (2H, m), 2.18 – 1.99 (5H, m); ^{13}C NMR (101 MHz, DMSO-d_6) δ 179.2, 159.3, 144.2, 142.6, 141.3, 130.7, 129.4, 129.0, 128.7, 125.2, 123.5, 121.9, 120.3, 113.6, 113.5, 111.6, 110.0, 64.1, 54.9, 41.2, 28.6, 19.9; HRMS (*m/z*), calculated for $C_{24}H_{25}N_2O_2^+$: 373.1911, found $(M + H)^+$: 373.1906.

3-(2-Methoxyphenethyl)-3-(*p*-tolylamino)indolin-2-one 2h was isolated as white crystals (0.154 g, 76%). R_f 0.32 (4:6 EtOAc:Hex); mp 176-178 °C; IR ν_{max} (cm^{-1}) 3316, 3250, 2981, 1705, 1618, 1313 1225; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.65 (1H, s), 7.26 (1H, t, *J* = 7.48 Hz), 7.19 (1H, d, *J* = 7.46), 7.19 (1H, d, *J* = 7.46 Hz), 7.15 (1H, t, *J* = 7.75 Hz), 7.04 – 6.98 (2H, m), 6.94 – 6.87 (2H, m), 6.83 (1H, t, *J* = 7.37 Hz), 6.70 (2H, d, *J* = 8.31 Hz), 6.12 (2H, d, *J* = 8.44 Hz), 6.07 (1H, s), 3.68 (3H, s), 2.46 – 2.35 (2H, m), 2.09 – 2.02 (5H, m); ^{13}C NMR (101 MHz, DMSO-d_6) δ 179.1, 156.9, 144.2, 141.4, 130.7, 129.1, 129.0, 128.9, 128.6, 127.3, 125.1, 123.4, 121.9, 120.3, 113.5, 110.6, 109.8, 64.2, 55.2, 39.5 (overlapped with DMSO-d_6), 23.0, 19.9; HRMS (*m/z*), calculated for $C_{24}H_{25}N_2O_2^+$: 373.1911, found $(M + H)^+$: 373.1907.

3-(2-Fluorophenethyl)-3-(*p*-tolylamino)indolin-2-one 2i was isolated as white crystals (0.146 g, 72%). R_f 0.26 (4:6 EtOAc:Hex); mp 228-229 °C; IR ν_{max} (cm^{-1}) 3323, 3135, 1703, 1618, 1523, 1336; **¹**H NMR (400 MHz, DMSO-d_6) δ 10.70 (1H, s), 7.29 – 7.16 (4H, m), 7.12 – 7.05 (2H, m),

6.99 (1H, t, *J* = 7.53 Hz), 6.94 (1H, d, *J* = 7.69 Hz), 6.70 (2H, d, *J* = 8.33 Hz), 6.17 (1H, s), 6.13 (2H, d, *J* = 8.56 Hz), 2.59 – 2.51 (1H, m), 2.40 – 2.29 (1H, m), 2.17 – 1.96 (5H, m); ^{13}C NMR (101 MHz, DMSO-d_6) δ 179.0, 160.3 (J_{C-F} = 244 Hz), 144.2, 141.4, 130.5 (J_{C-F} = 5.05 Hz), 129.0, 128.8, 128.1 (J_{C-F} = 8.08 Hz), 127.6, 127.5, 125.3, 124.5 (J_{C-F} = 3.03 Hz), 123.4, 122.0, 115.1 (J_{C-F} = 22.2 Hz), 113.6, 110.0, 64.0, 39.8 (overlapped with DMSO-d_6), 21.8, 19.9; HRMS (*m/z*), calculated for $C_{23}H_{22}FN_2O^+$: 361.1711, found $(M + H)^+$: 361.1705.

1.1.7 Preparation of (*E*)-3-(4-Methylbenzylidene)indolin-2-one 9.

To a stirred solution of oxindole (1.00 g, 7.51 mmol) in ethanol (30 mL) was added piperidine (74.2 µL, 0.751 mmol). After 5 minutes, *p*-tolualdehyde (1.34 g, 9.01 mmol) was added and the mixture was refluxed under argon for 4 h. After this time, the reaction mixture was cooled, and the resulting precipitate was isolated by filtration. The crude solid was recrystallised from methanol and isolated as bright yellow crystals (1.42 g, 6.03 mmol, 80%, *E:Z* = 8:1). R_f 0.45 (3:7 EtOAc:Hex); mp 194 – 196 °C (lit. mp 197 – 198 °C)[28]; IR ν_{max} (cm^{-1}) 3131, 3075, 2886, 1691, 1599; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24 (1H, s), 7.82 (1H, s), 7.71 (1H, d, *J* = 7.60 Hz), 7.59 (2H, d, *J* = 7.60), 7.28 (2H, d, *J* = 7.78 Hz), 7.21 (1H, td, *J* = 7.67 Hz, 0.91 Hz), 6.92 – 6.86 (2H, m), 2.43 (3H,); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.2, 141.4, 140.3, 138.1, 132.0, 129.8, 129.7, 129.5, 126.8, 123.2, 122.1, 122.0, 110.2, 21.7; HRMS (*m/z*), calculated for $C_{16}H_{13}NO^+$: 236.1070, found $(M + H)^+$: 236.1060.

1.1.8 Preparation of (*E*)-*tert*-butyl 3-(4-methylbenzylidene)-2-oxoindoline-1-carboxylate 10.

(*E*)-3-(4-methylbenzylidene) indolin-2-one **9** (0.500 g, 2.13 mmol), DMAP (0.039 g, 0.32 mmol) and di-*tert*-butyl dicarbonate (0.557 g, 2.55 mmol) were reacted in 30 mL THF for 24 hr. The resulting crude was purified by column chromatography (30 % EtOAc/Hex) to afford (*E*)-*tert*-butyl 3-(4-methylbenzylidene)-2-oxoindoline-1-carboxylate **10** (0.521 g, 1.55 mmol, 73%) as yellow crystals. R_f 0.89 (3:7 EtOAc:Hex); mp 86 – 88 °C (lit. mp 97 – 98 °C)[29]; IR ν_{max} (cm^{-1}) 3056, 3004, 2925, 1746, 1717, 1626, 1599; ^{1}H NMR ((400 MHz, $CDCl_3$) δ 7.91 (1H, d, *J* = 8.19 Hz), 7.85 (1H, s), 7.75 (1H, d, *J* = 7.67 Hz), 7.54 (2H, d, *J* = 7.93), 7.33 – 7.25 (3H, m), 7.00 (1H, t, *J* = 8.05 Hz), 2.43 (3H, s), 1.67 (9H, s); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.0, 149.5, 140.5, 140.0, 138.8, 131.8, 129.9, 129.6, 129.5, 125.5, 123.8, 122.4, 121.9, 115.3, 84.3, 28.3, 21.7; HRMS (*m/z*), calculated for $C_{21}H_{21}NO_3Na^+$: 358.1414, found $(M + Na)^+$: 358.1410.

1.19 Synthesis of 3-allyl-1-benzyl-3-((4-chlorophenyl)amino)indolin-2-one

1-Benzyl-3-((4-chlorophenyl)imino)indolin-2-one **4i** (0.500 g, 1.44 mmol) and $MgBr_2$ (0.130 g, 2.88 mmol) were dissolved in DCM (20 ml) and the temperature of the reaction mixture was reduced to -40 ˚C for 20 min. AllylMgBr (1.59 ml, 1.59 mmol, 1M in diethyl ether) was then added and the temperature was kept at -40 ˚C for an hour. The temperature was raised to room temperature, and the reaction mixture was left stirring overnight under a N_2 atmosphere. The

reaction mixture was quenched with saturated aqueous NH_4Cl. The organic layer was extracted into DCM, dried over $MgSO_4$, and filtered through a pad of celite. After removal of solvent under reduced pressure the resulting residue was purified by silica gel column chromatography (5% EtOAc/Hex) to yield 3-allyl-1-benzyl-3-((4-chlorophenyl)amino)indolin-2-one as yellow solid (0.29 g, 52%). R_f = 0.52 (3:7 EtOAc/Hex); mp 140 ˚C; IR ν_{max} (cm^{-1}) 3317, 3025, 2927, 1705, 1613; ^1H NMR (400 MHz, $CDCl_3$) δ 7.33 – 7.19 (7H, m), 7.04 (1H, td, *J* = 7.5, 1.0 Hz), 6.89 – 6.83 (2H, m), 6.81 (1H, d, *J* = 7.9 Hz), 6.19 – 6.08 (2H, m), 5.81 – 5.66 (1H,m), 5.29 – 5.16 (2H, m), 5.10 – 4.99 (1H, m), 4.77 (1H, d, *J* = 15.4 Hz, 1H), 4.37 (s, 1H), 2.80 – 2.70 (1H, m), 2.61 (dd, *J* = 13.3, 7.9 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 177.3, 143.7, 141.9, 135.5, 130.2, 129.3, 129.1, 128.8, 128.7, 127.8, 127.7, 124.2, 123.9, 123.0, 121.1, 117.0, 109.7, 64.1, 44.5, 44.1; HRMS (*m*/z), calculated for $C_{24}H_{22}{}^{35}ClN_2O^+$: 389.1415, found $(M + H)^+$: 389.1414.

1.2 Biology

1.2.1 Antiplasmodial activity

The chloroquine-resistant (FCR3) and chloroquine-sensitive (NF54) strains of *P. falciparum* were separately maintained in continuous culture *in vitro* in supplemented RPMI-1640 culture media at 37 °C and gassed with a mixture of 5% CO_2, 3% O_2 and 92% N_2.[30] D-sorbitol (5% w/v) was used to synchronise the culture in the ring stage.[31] To determine the antimalarial activity of the compounds, the synchronised ring-stage parasites were adjusted to a final parasitaemia of 2% and 2% haematocrit, to which serial dilutions of the compounds and positive controls, chloroquine and quinine were added to a sterile 96 well plate. Negative controls included uninfected erythrocytes and drug-free parasitised erythrocytes. Following a 48h or a 72h incubation period, the plates were frozen at -70°C for 1 h and thawed for 1 h. Lysate (25 µl) was transferred to a second plate, to which 100 µL Malstat™ and 20 µl nitroblue tetrazolium-phenazine ethosulfate (1:1) mixture was added to each well and incubated for 40 min at 37°C to quantify the parasite lactate dehydrogenase (pLDH) activity.[32] Thereafter, 5% acetic acid (50 µl) was added to each well, and the absorbance of the products read at 620 nm, as an indicator of parasite viability. The percentage parasite growth, taking the appropriate controls into account, were calculated and used to determine the concentration required to inhibit parasite growth by 50% (IC_{50} value) from log sigmoid dose-response curves using the GraphPad Prism® 9.0.0 software. Each experiment was repeated at least in triplicate.[33]

1.2.2 Cytotoxicity assay

2. To determine if the test compounds caused general cell death to mammalian cells, the tetrazolium cytotoxicity assay was undertaken. The 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay is a quantitative colourimetric assay that involves

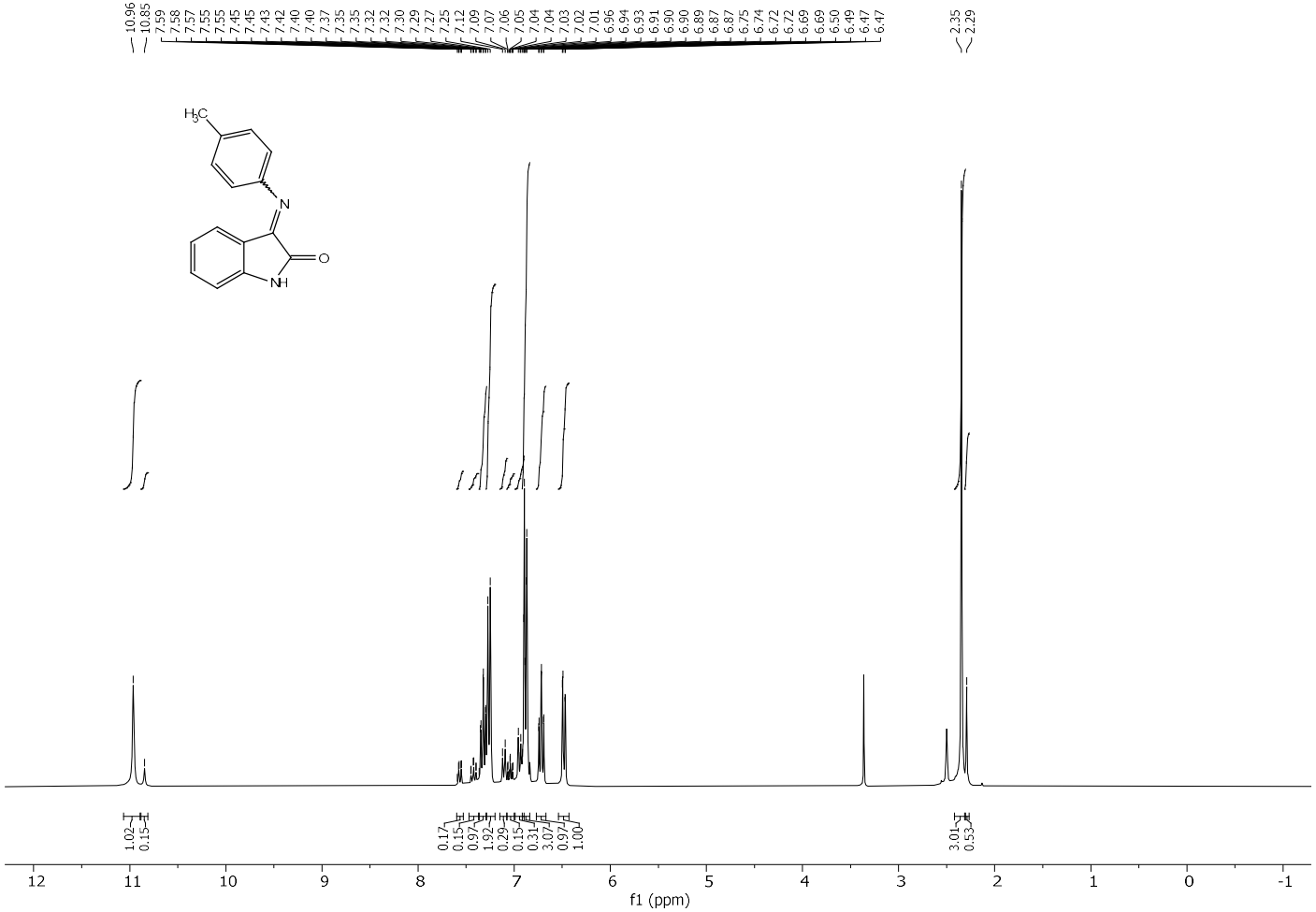
the cleavage of the yellow MTT by succinate dehydrogenase found in the mitochondria of living cells. After the tetrazolium ring is cleaved, this produced water-insoluble purple formazan crystals.[34] The MTT method as described by Mosmann[34] and Van Zyl *et al.*[35] was performed on the human embryonic kidney epithelial cell (HEK293; Graham) over 48h for those compounds with >50% antimalarial effects, with cisplatin and chloroquine as the positive control and untreated cells as the negative control.

Table 1: **Summary of biological evaluation of compounds**

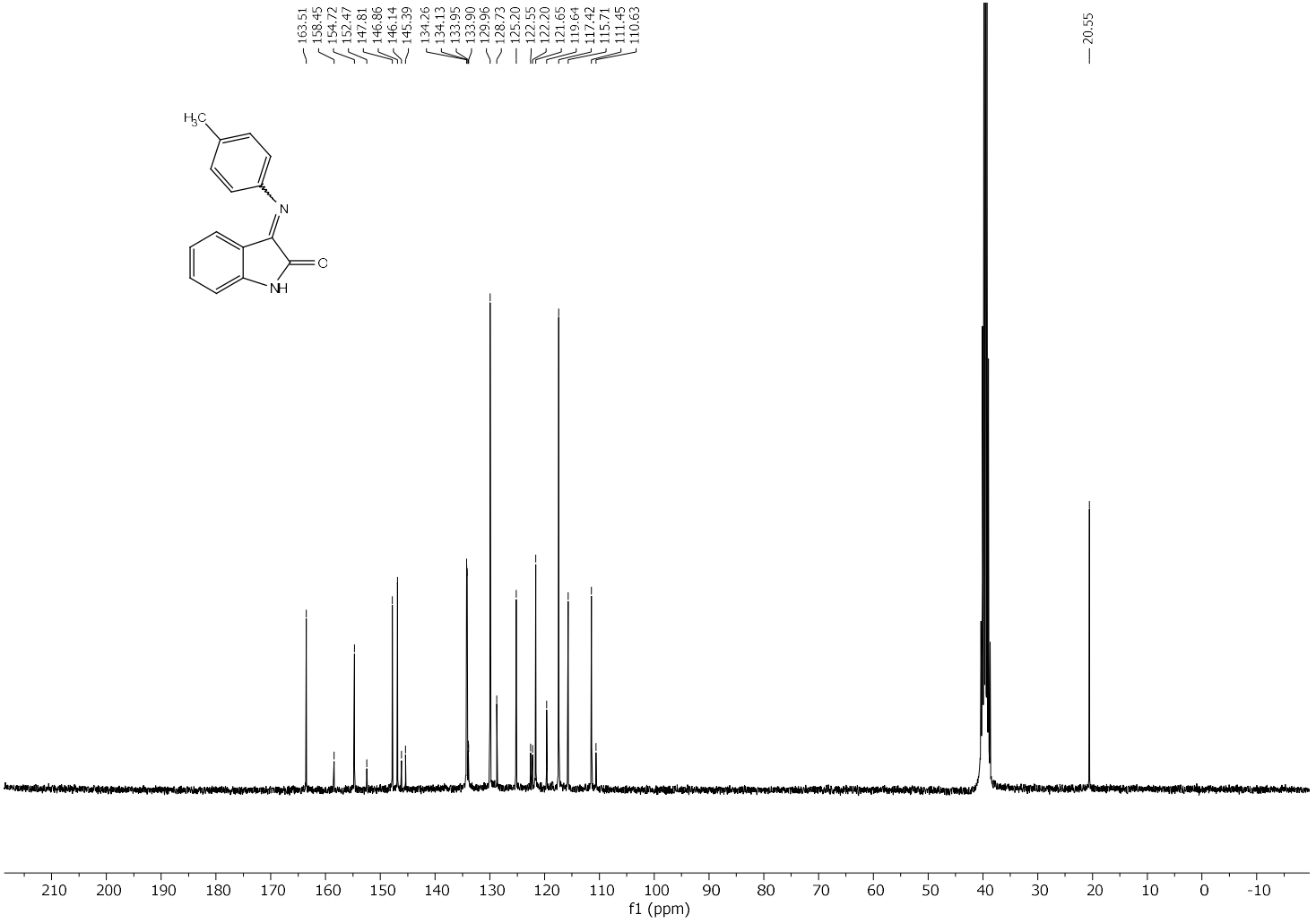
Compound	R^1	R^2	R^3	R^4	*P. falciparum* NF54		*Pf* FCR3	Cytotoxicity (HEK293)	
					% Parasitaemia at 10 µM	Average IC_{50} (µM)	Average IC_{50} (µM)	% Cell Growth (10 µM)	% Cell Growth (0.1 µM)
2a	H	Bn	4-Me	2-Cl	26.68 ± 22.64 [a]	2.84 ± 0.21	0.50 ± 0.06	84.26 ± 6.48	94.66 ± 5.46
2e	H	H	4-Me	H	59.28 ± 7.19 [b]				
2f	H	H	4-Me	4-OMe	94.08 ± 6.35 [b]				
2g	H	H	4-Me	3-OMe	76.49 ± 1.43 [b]				
2h	H	H	4-Me	2-OMe	81.72 ± 5.39 [b]				
2i	H	H	4-Me	2-F	63.78 ± 2.64 [b]				
3a	H	Boc	4-Me	4-OMe	20.54 ± 3.65 [a]	1.08 ± 0.59	0.37 ± 0.09	57.15 ± 6.24	99.74 ± 7.25
3b	H	Boc	4-Me	4-Cl	10.49 ± 16.71 [a]	1.03 ± 0.04	5.36 ± 0.41	49.31 ± 8.06	97.96 ± 8.79
3c	H	Boc	4-Me	3-Cl	5.59 ± 18.92 [a]	0.11 ± 0.01	0.41 ± 0.01	55.09 ± 7.46	92.13 ± 5.75
3d	H	Boc	4-Me	2,4-diCl	20.94 ± 12.84 [a]	0.71 ± 0.34	0.63 ± 0.11	79.40 ± 4.49	93.86 ± 4.42
3f	H	Boc	4-Br	4-Cl	24.36 ± 18.64 [a]	0.99 ± 0.20	3.57 ± 0.51	58.22 ± 4.75	99.21 ± 4.11
3r	H	Boc	3,4-diMe	3-Cl	3.83 ± 16.62 [a]	0.76 ± 0.40	1.64 ± 0.02	72.86 ± 2.26	95.29 ± 4.70
3s	Cl	Boc	4-Me	4-OMe	12.13 ± 22.84 [a]	1.44 ± 0.30	4.32 ± 0.22	80.92 ± 7.61	89.47 ± 2.68
3t	Cl	Boc	4-Me	3-OMe	11.62 ± 15.03 [a]	4.01 ± 1.48	3.44 ± 0.92	76.14 ± 0.04	97.18 ± 9.14
3u	Cl	Boc	4-Me	2-OMe	13.49 ± 19.44 [a]	7.83 ± 0.60	5.67 ± 1.09	77.70 ± 2.13	95.42 ± 6.61
3v	Cl	Boc	4-Me	4-Cl	37.10 ± 8.64 [a]	5.01 ± 2.62	7.37 ± 0.12	73.72 ± 4.56	89.82 ± 1.92
3w	Cl	Boc	4-Me	3-Cl	34.77 ± 7.15 [a]	3.30 ± 0.85	1.63 ± 0.05	67.30 ± 2.17	88.85 ± 8.76
3x	Cl	Boc	4-Me	2-Cl	56.25 ± 0.04 [a]	1.14 ± 0.24	4.20 ± 0.26	95.84 ± 1.19	89.43 ± 9.74
3z	Cl	Boc	4-Me	4-F	35.26 ± 1.08 [a]	0.85 ± 0.05	0.35 ± 0.01	62.54 ± 2.42	81.38 ± 9.77
3aa	Cl	Boc	4-Me	2-F	26.26 ± 7.46 [a]	1.40 ± 0.46	0.99 ± 0.07	65.46 ± 1.58	92.63 ± 5.70
Controls	Chloroquine				0.06 ± 0.21	0.04 ± 0.01	0.14 ± 0.03	-	-
	Quinine				0.01 ± 13.49	0.08 ± 0.02	0.03 ± 0.01		-
	Cisplatin				-	-	-	42.53 ± 7.70	75.56 ± 8.35

[a]run for 72 h; [b]run for 48 h

3. NMR spectra 6a ^{1}H NMR spectrum



6a ^{13}C NMR spectrum



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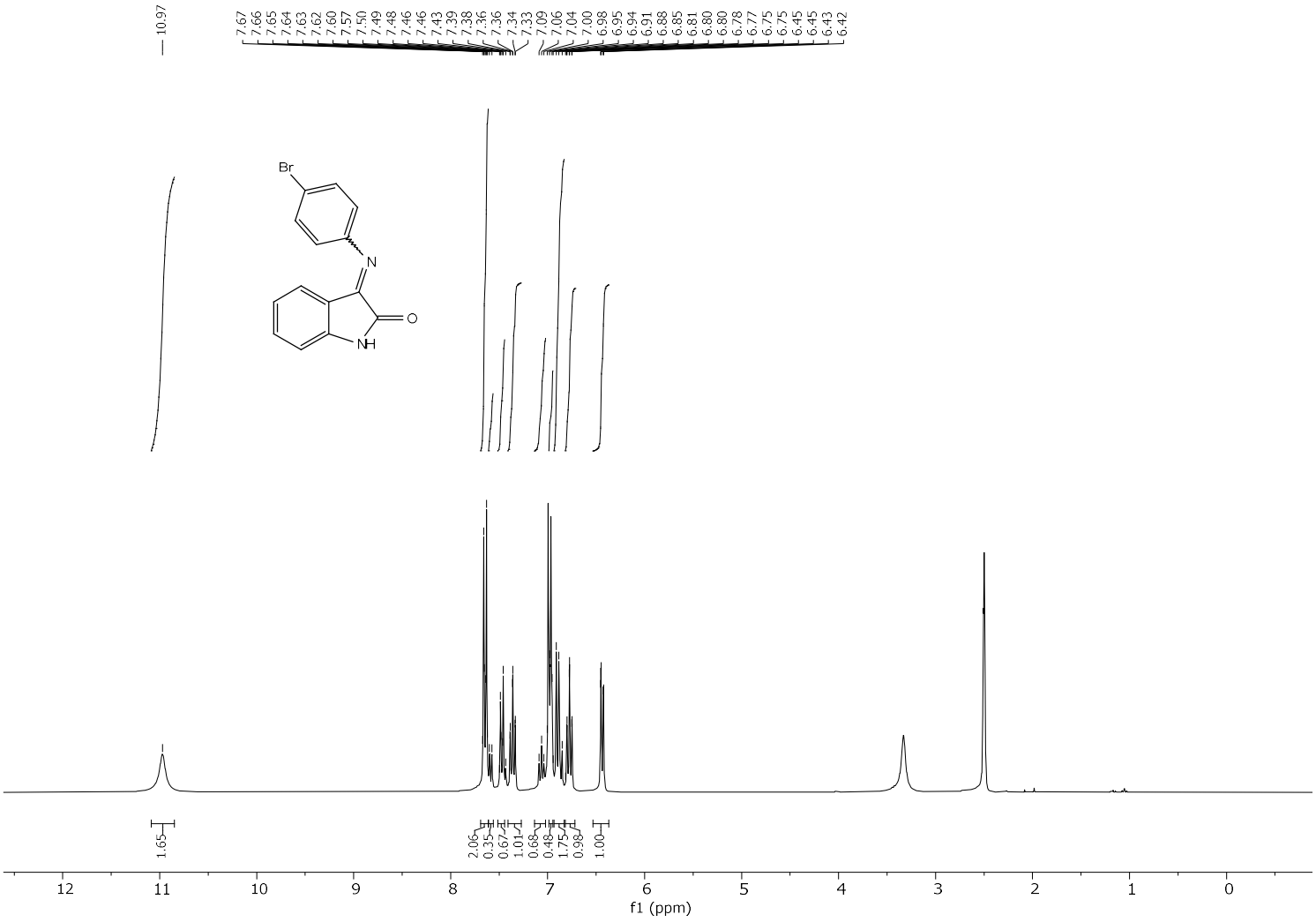

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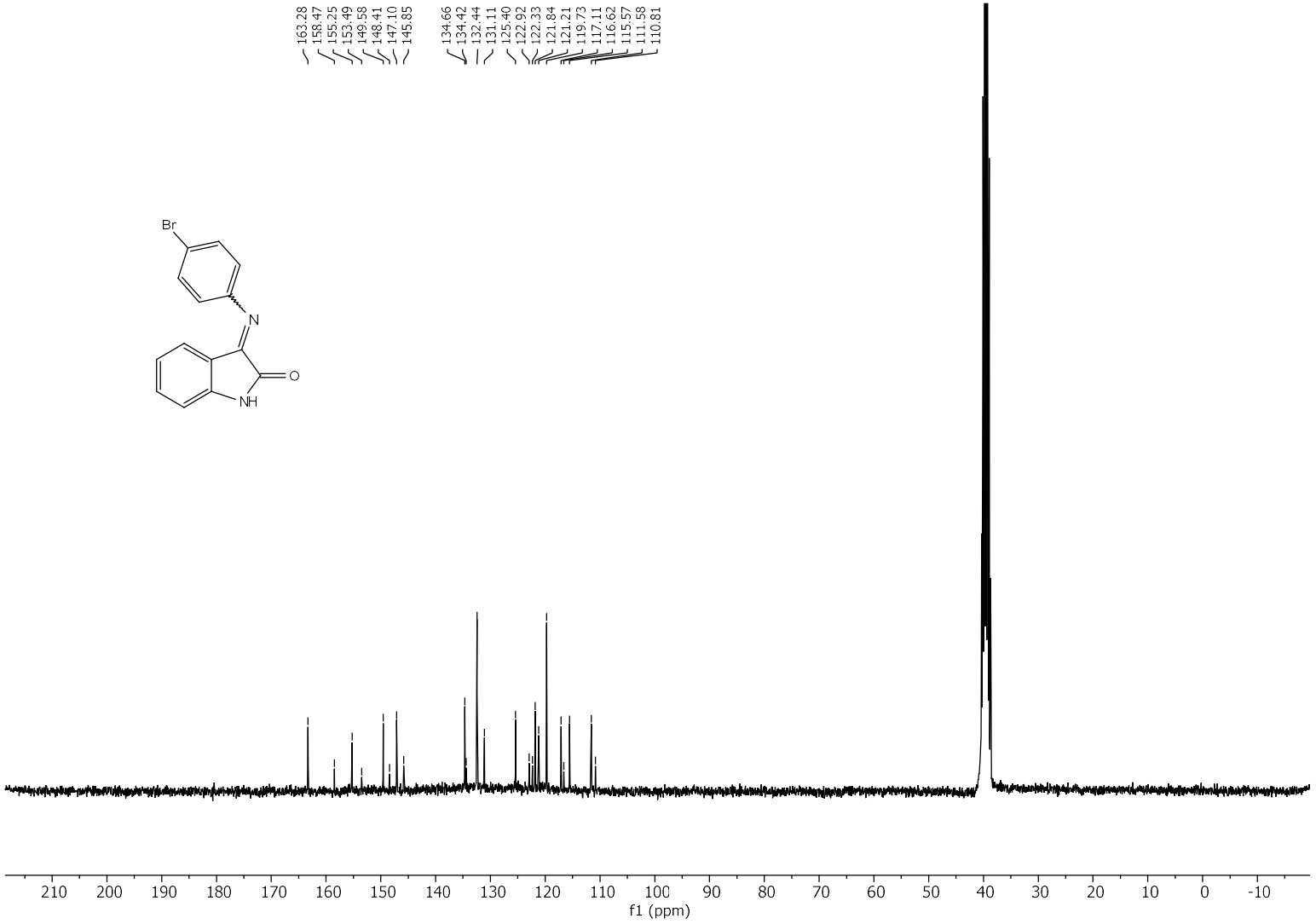

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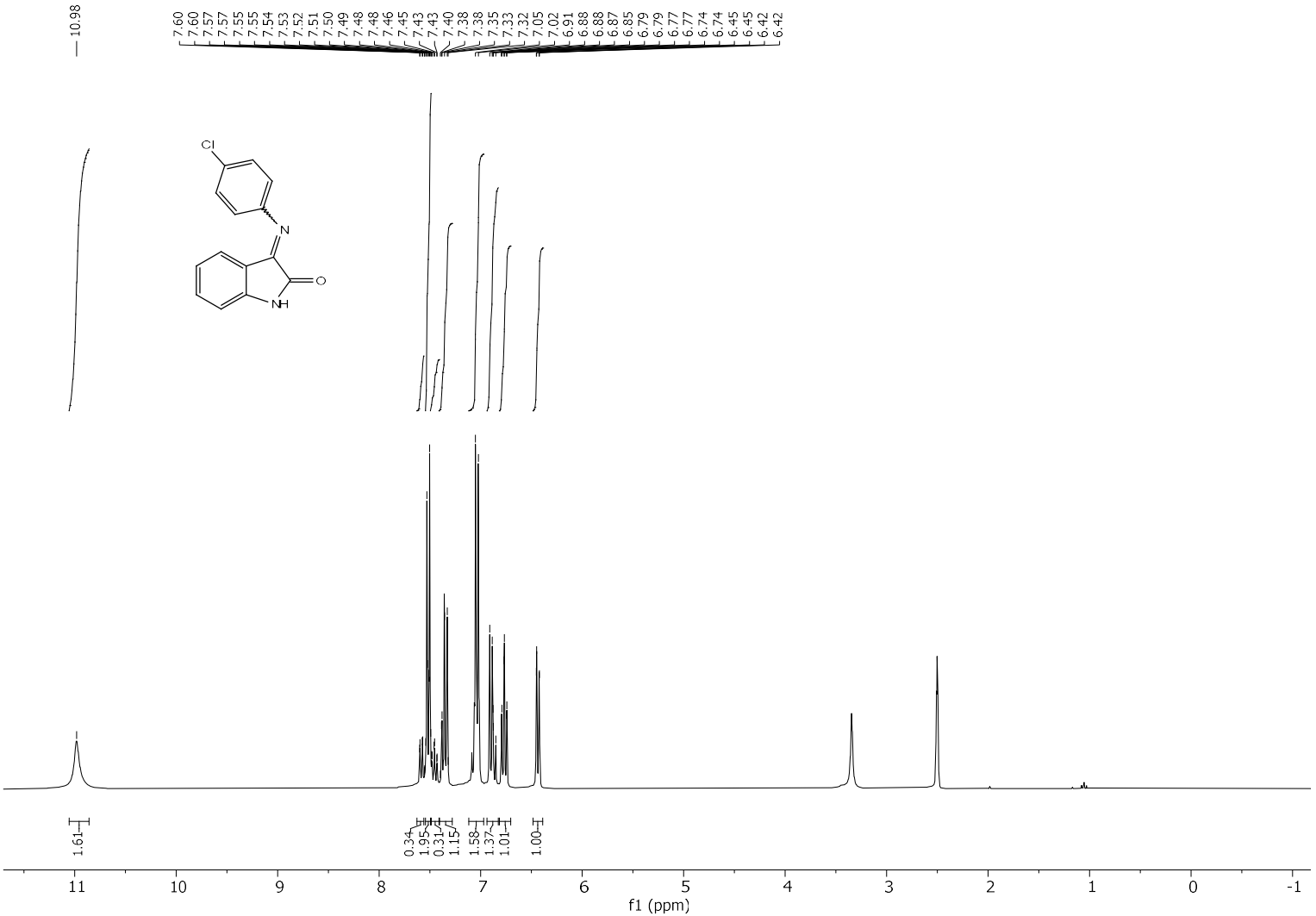

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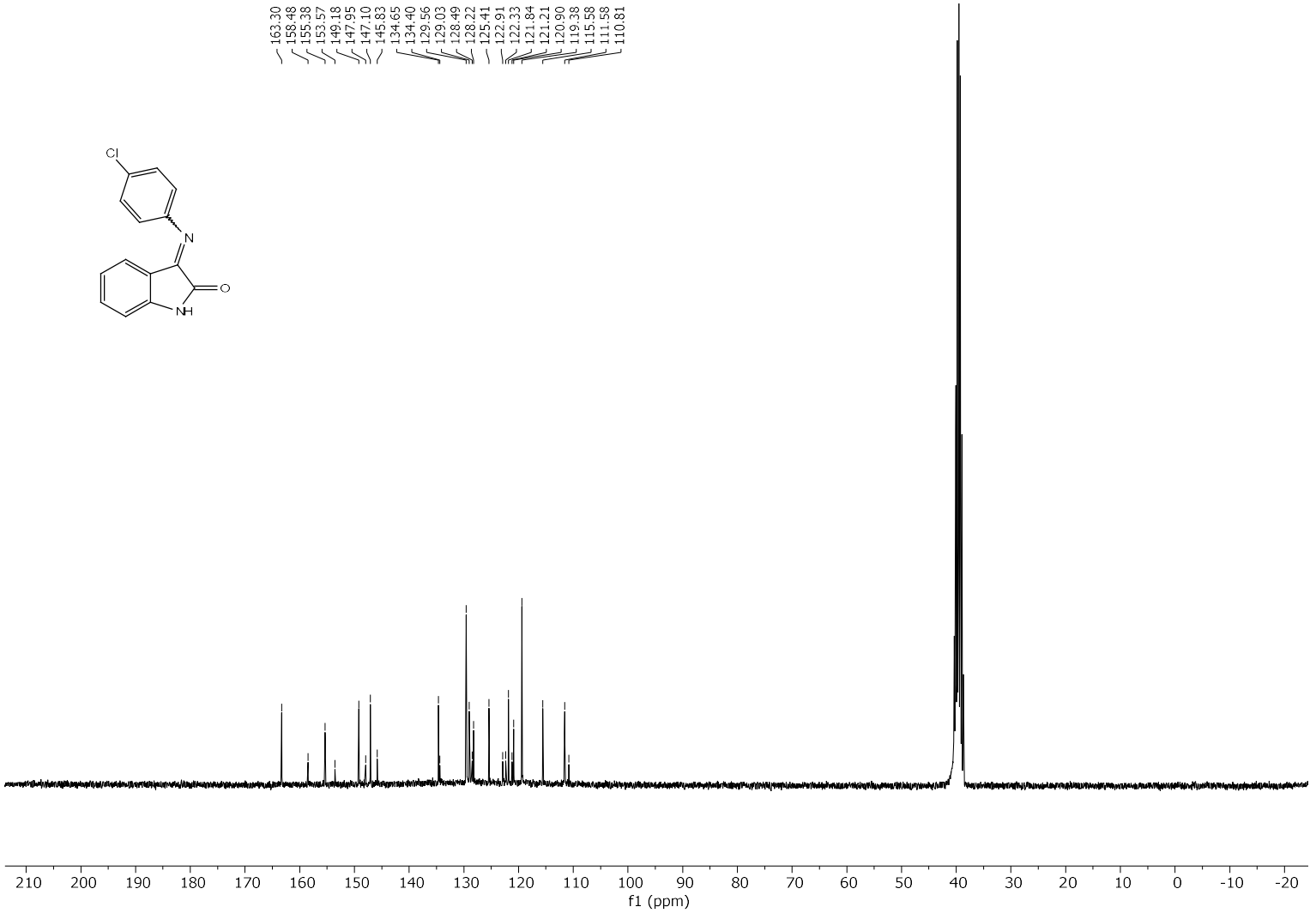

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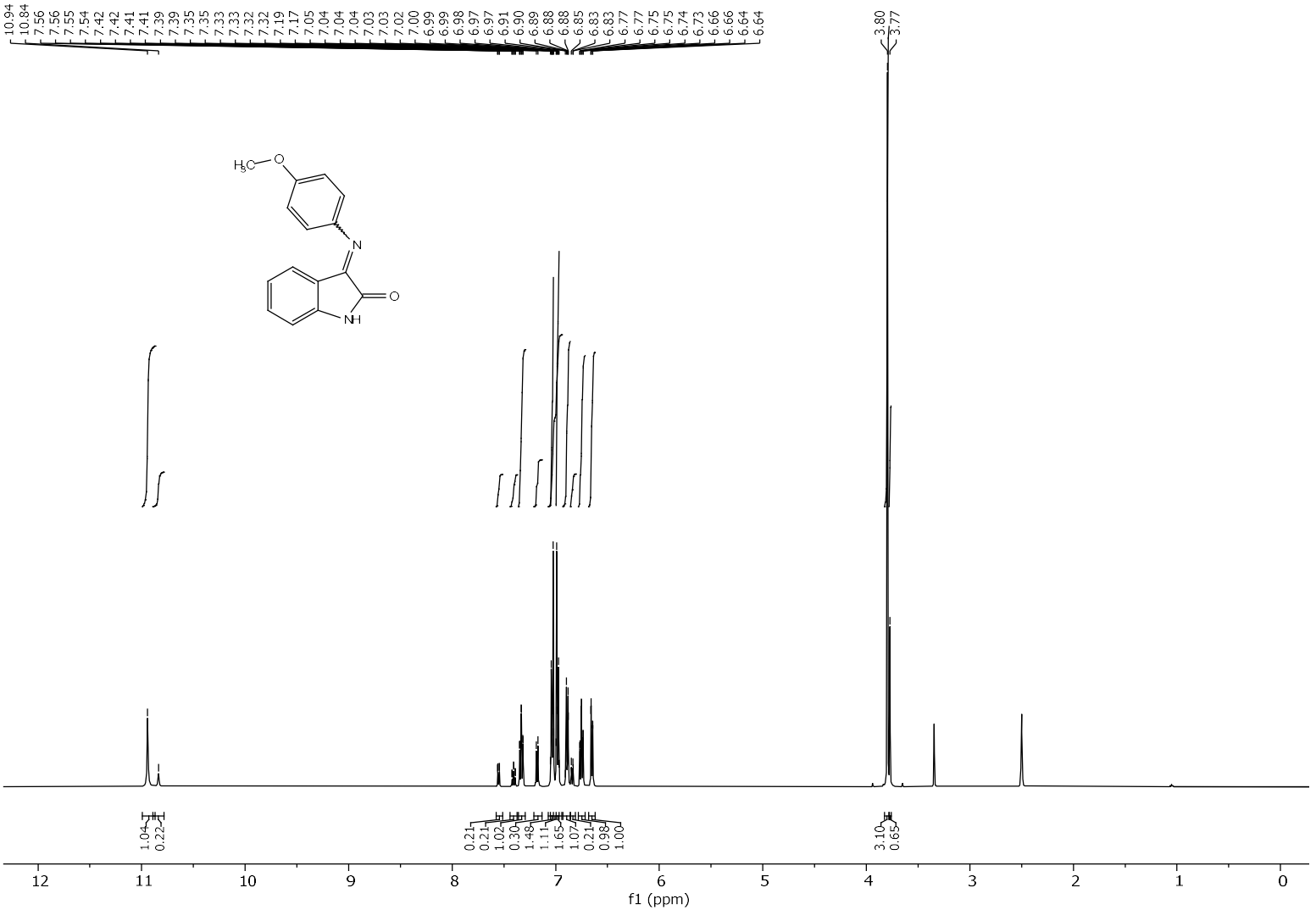

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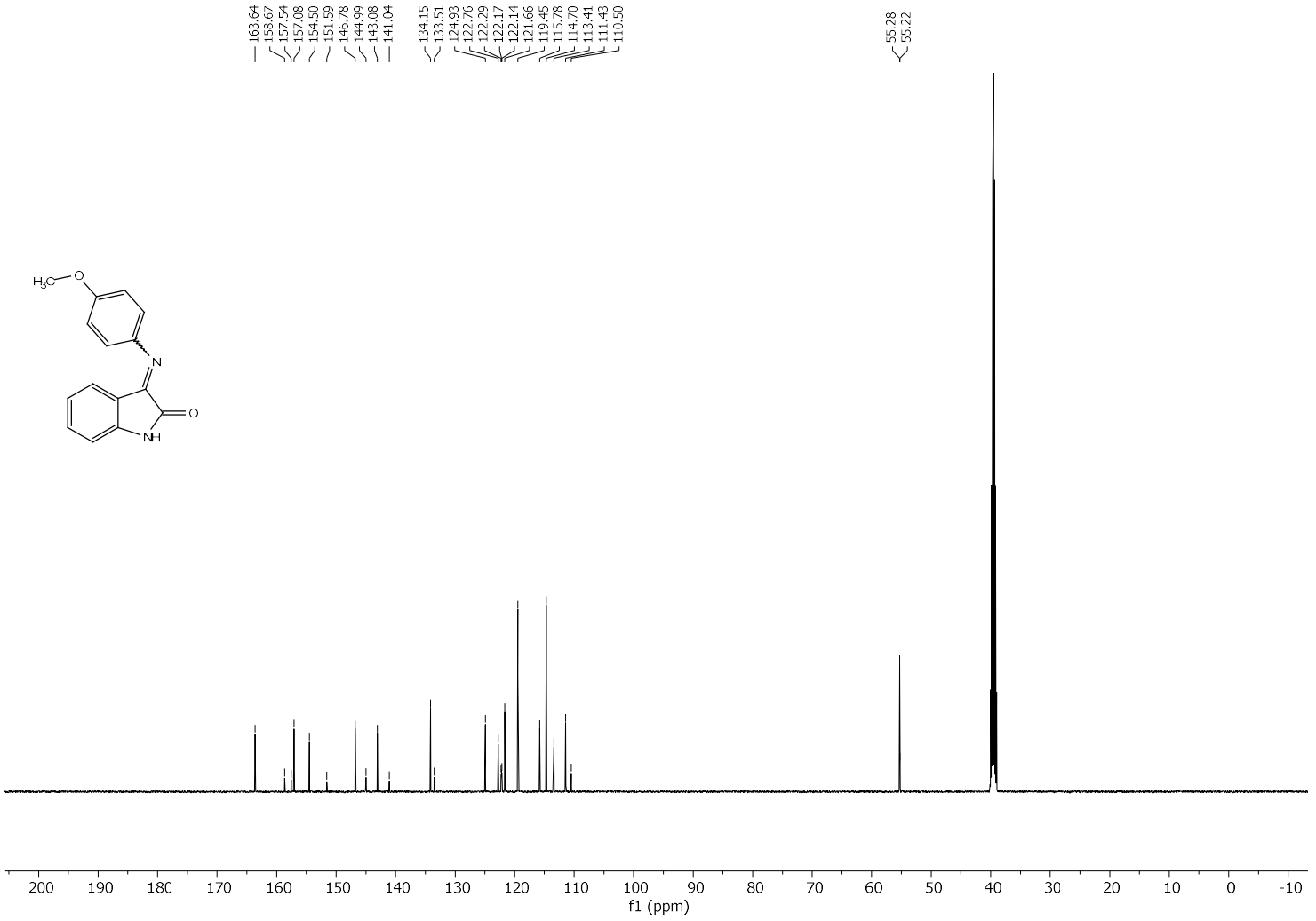

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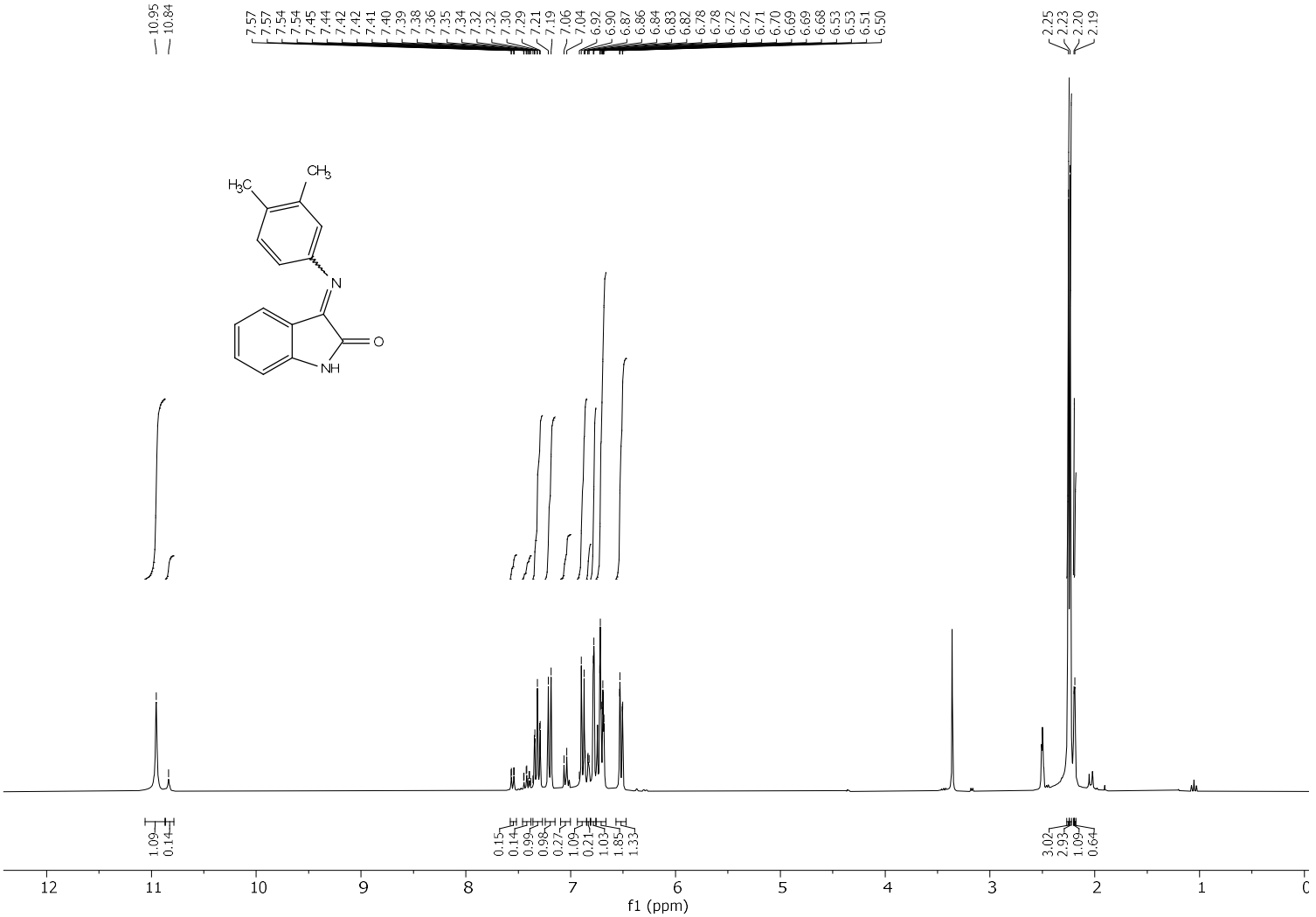

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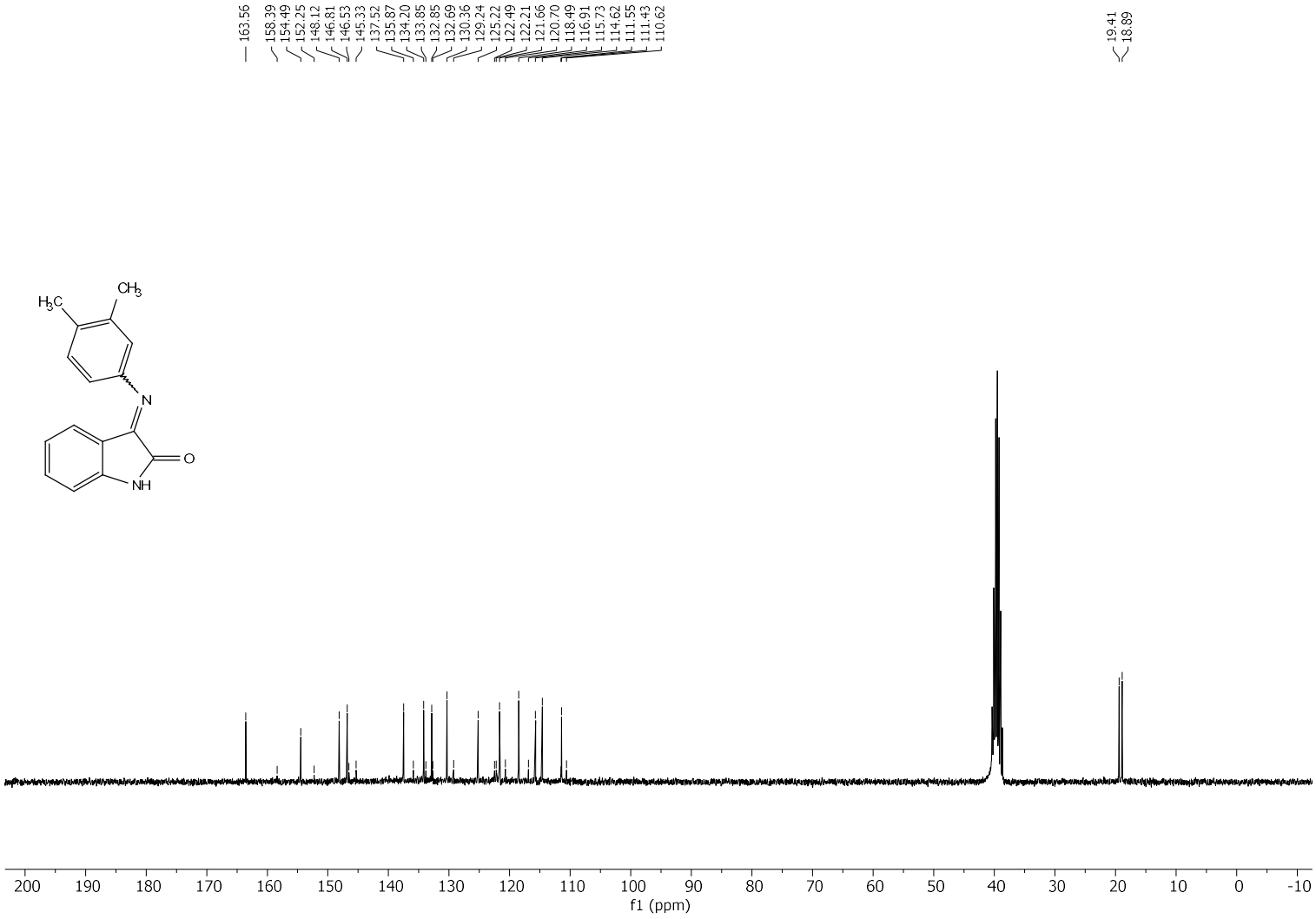
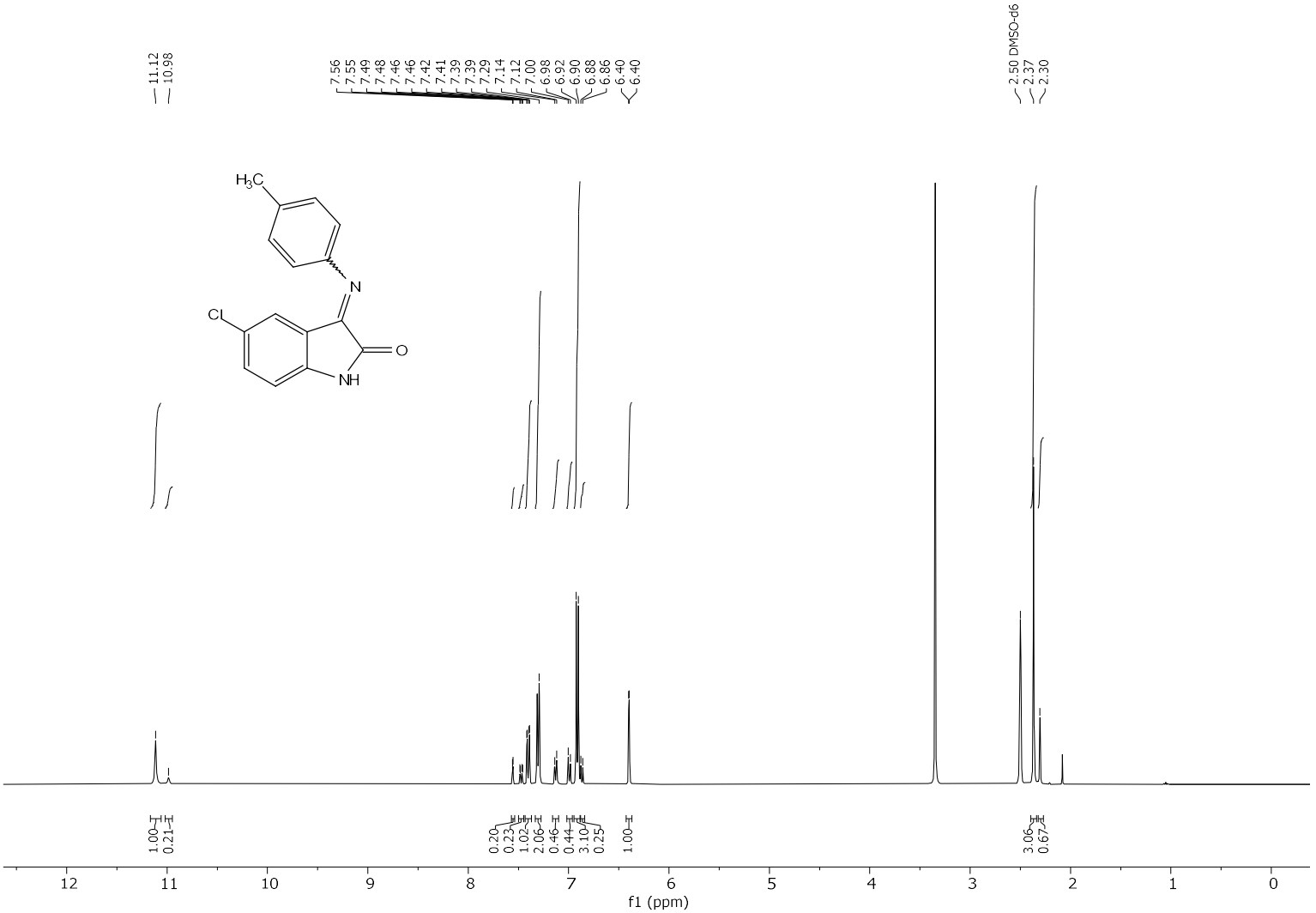


6f ^{1}H NMR spectrum



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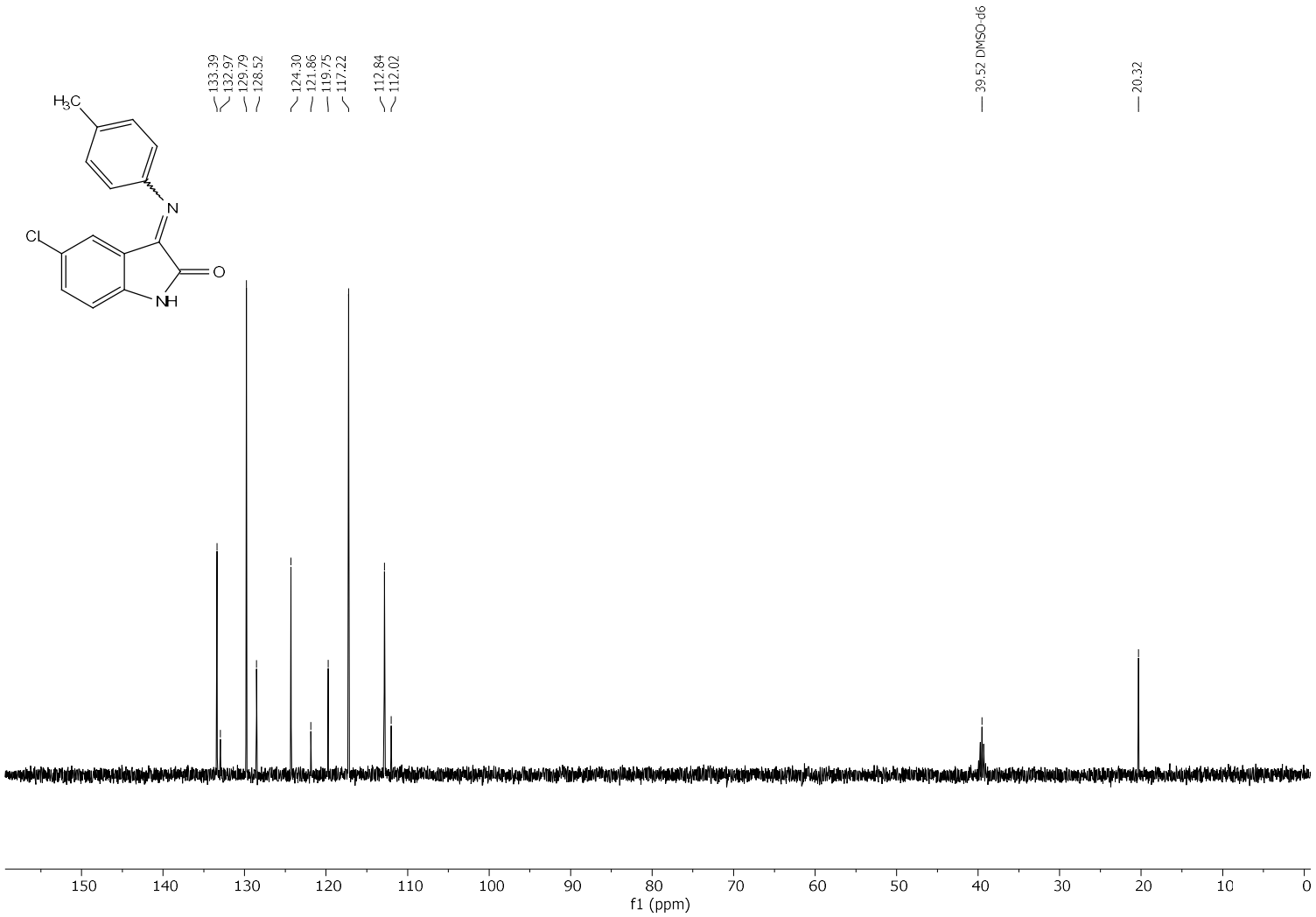
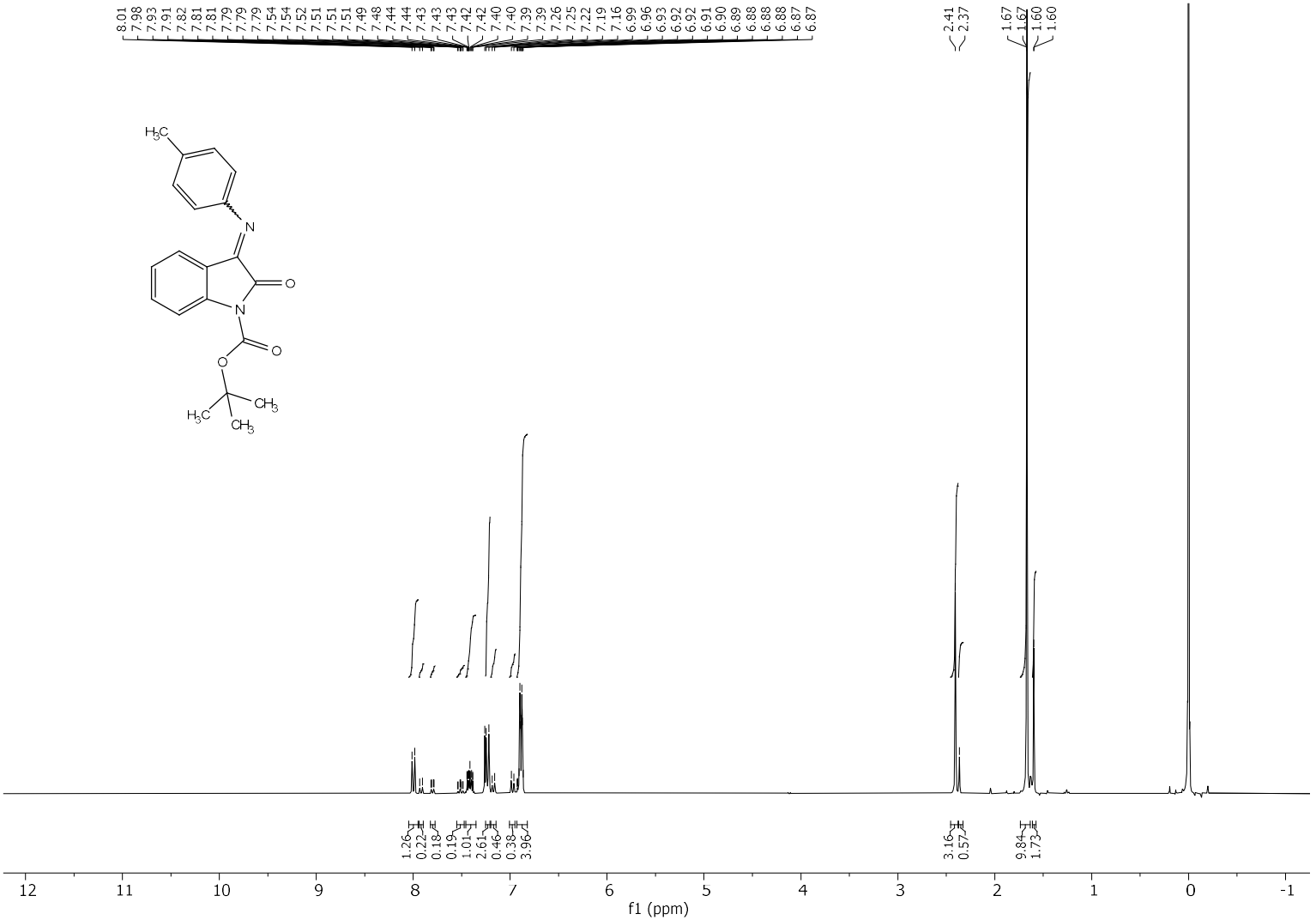


4a ^{1}H NMR spectrum



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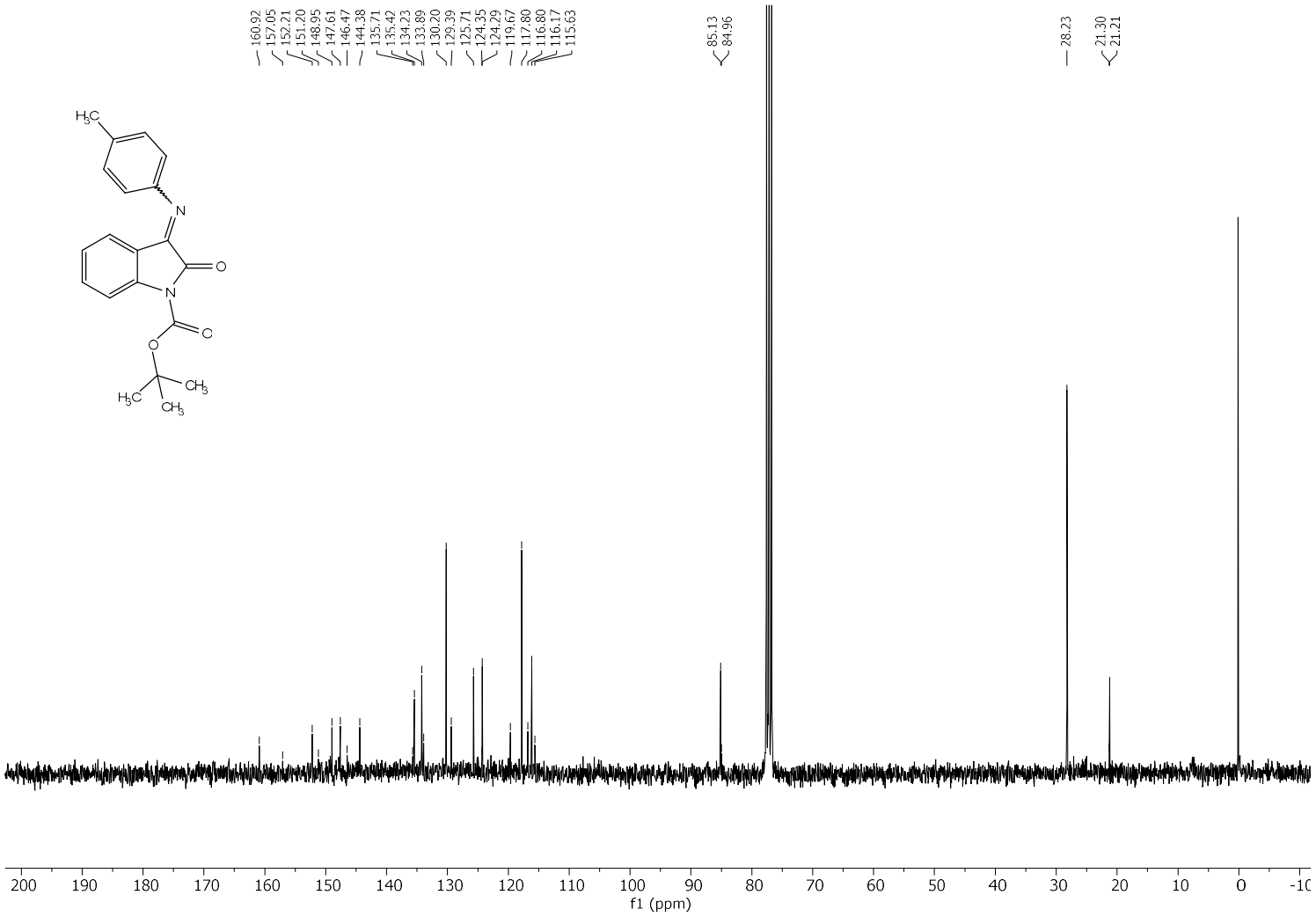

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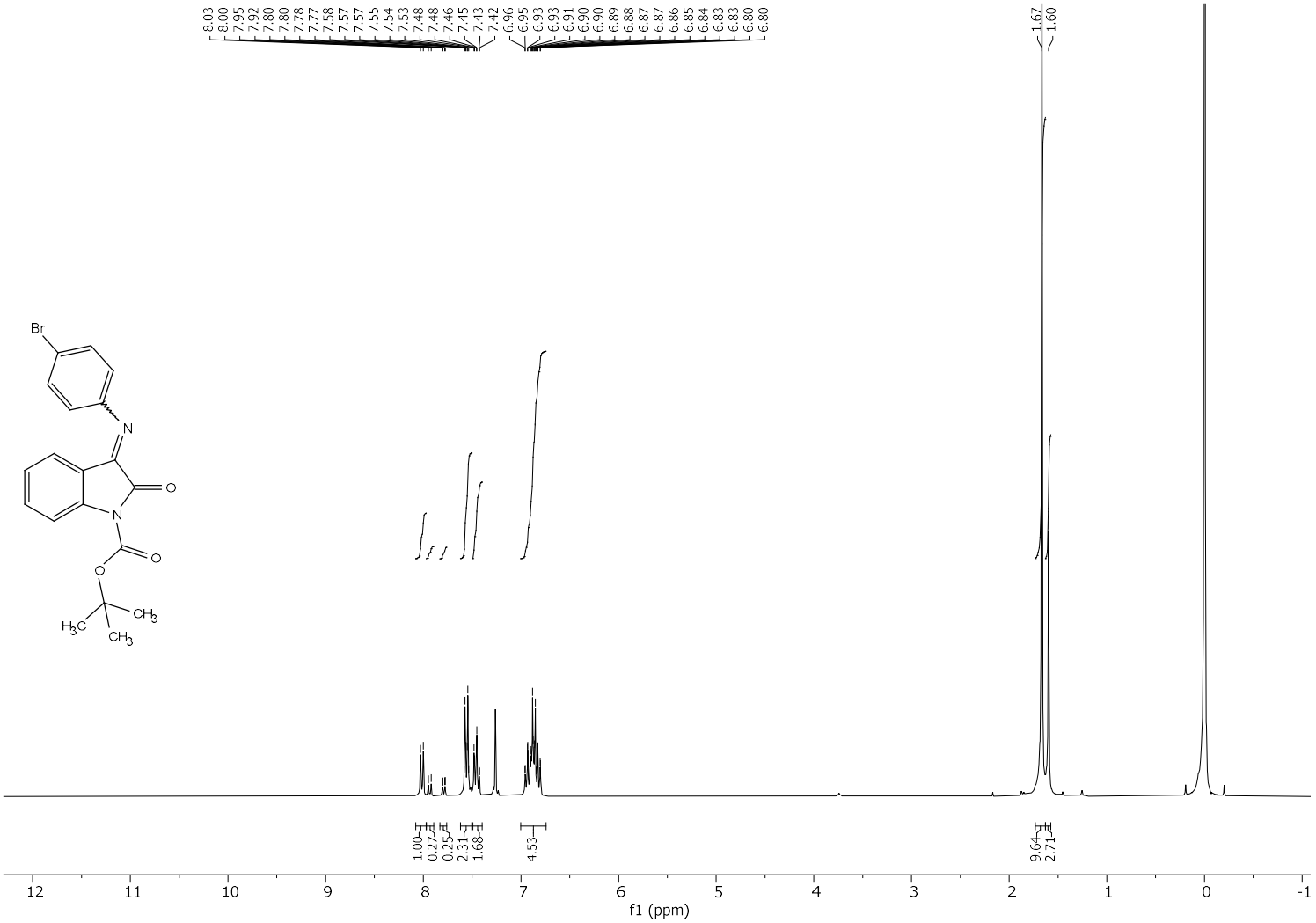

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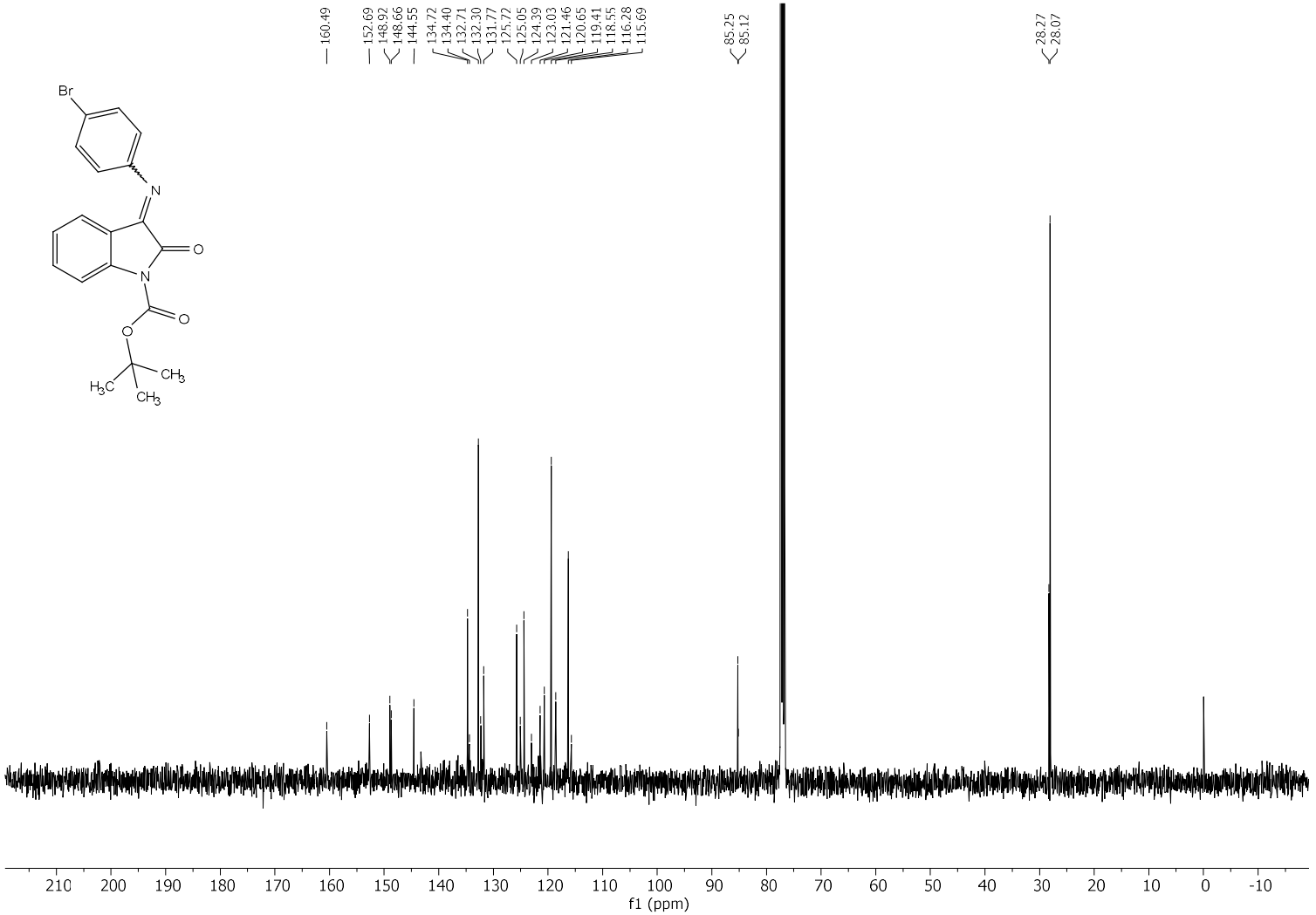

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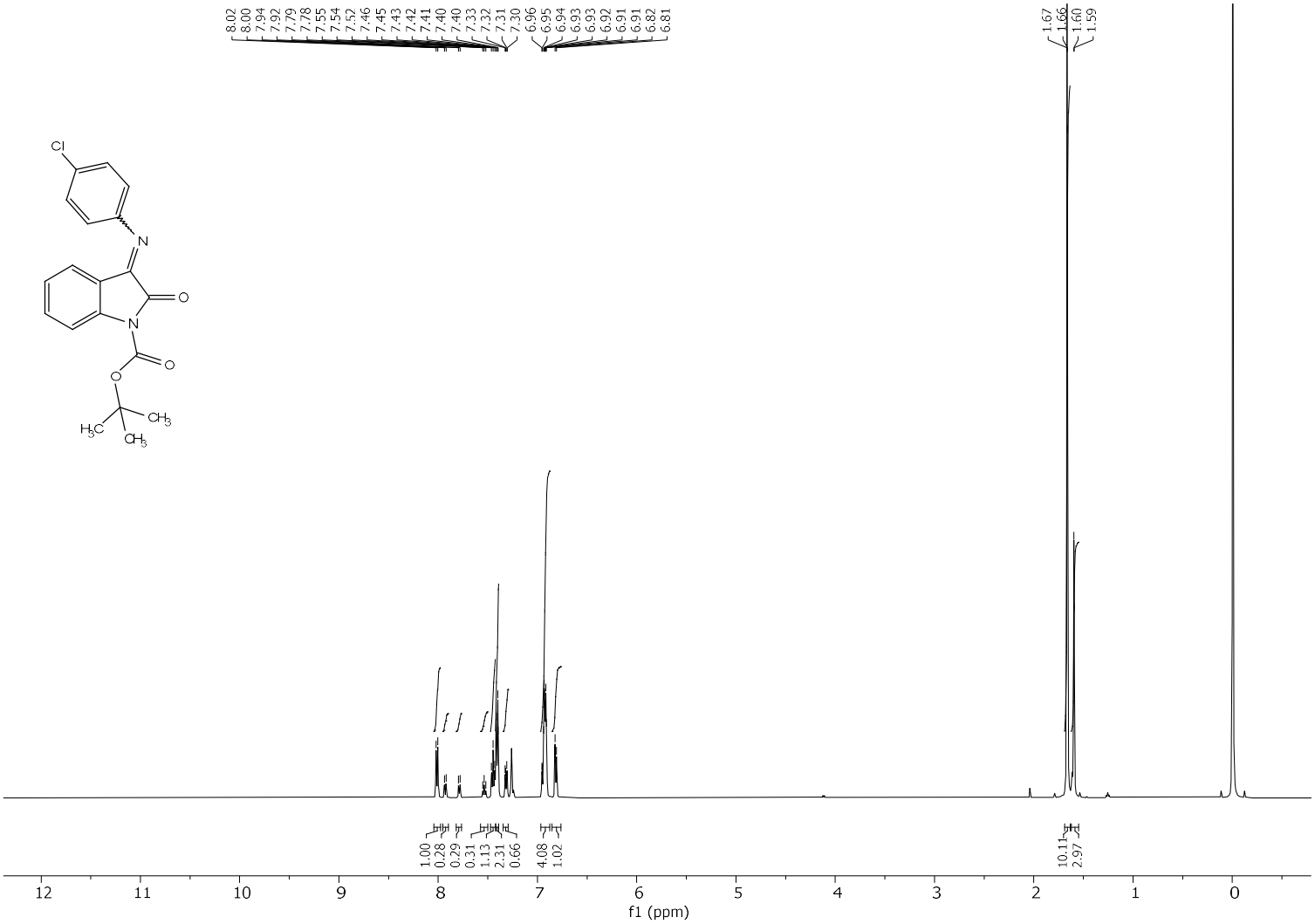

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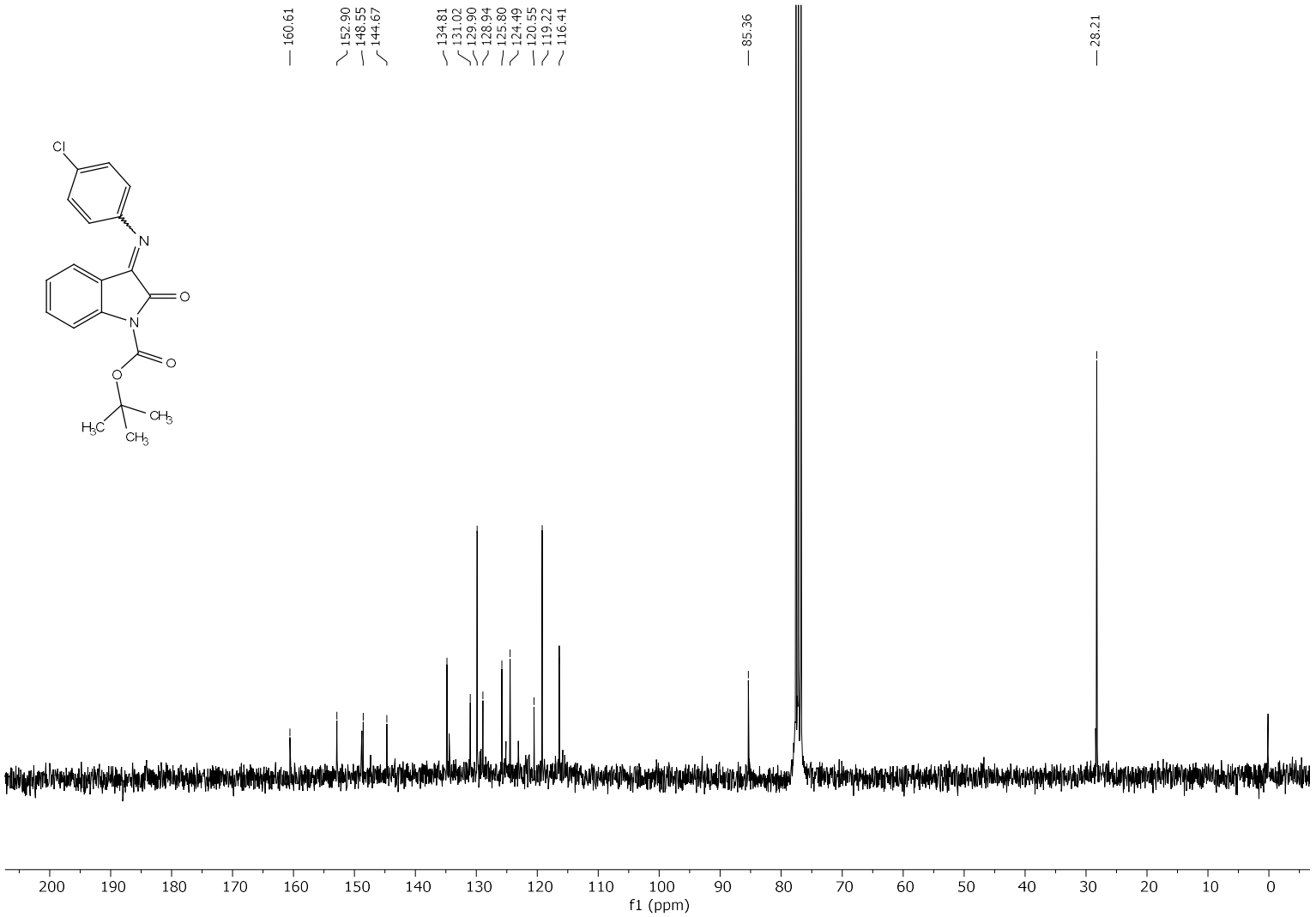

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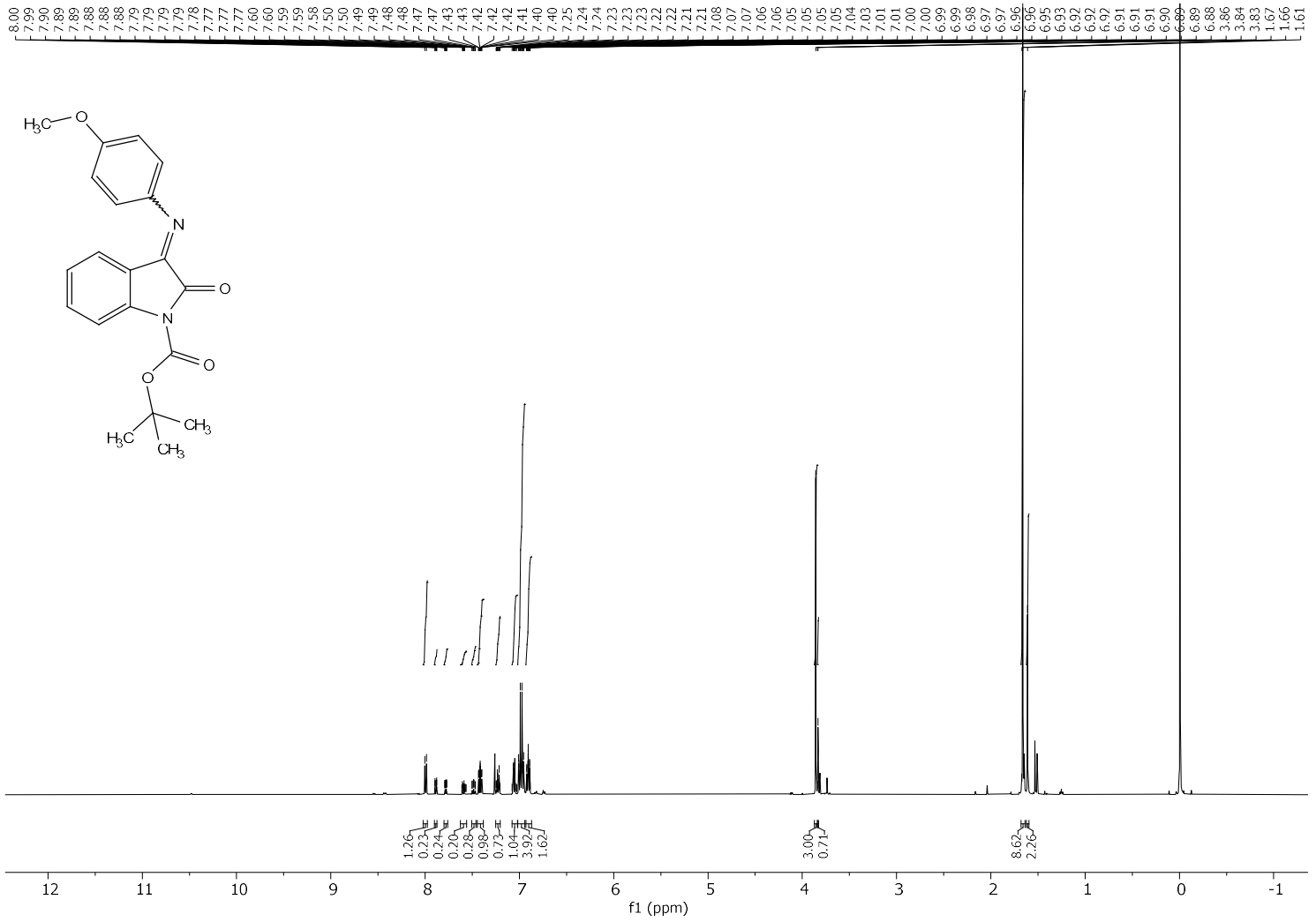

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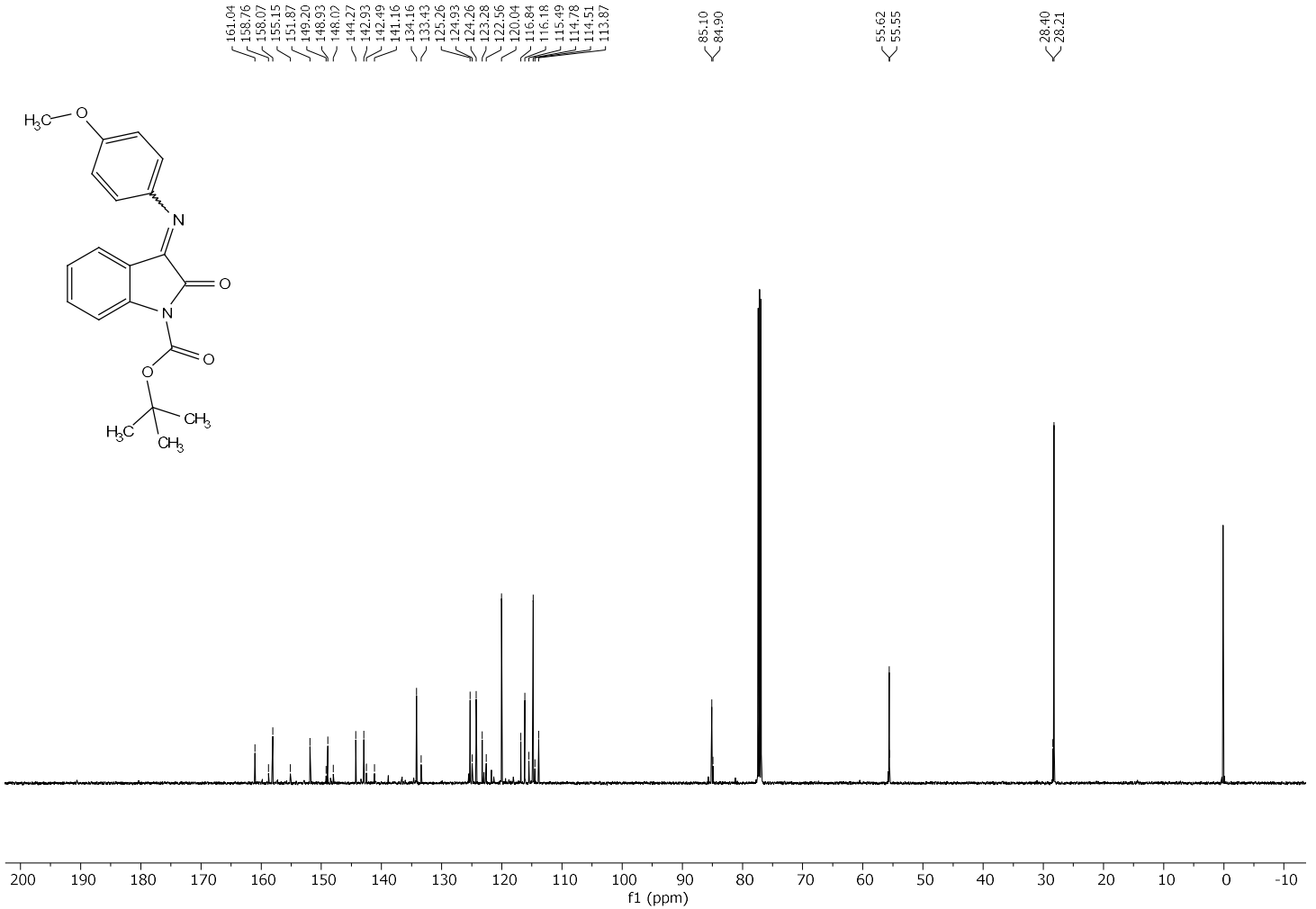

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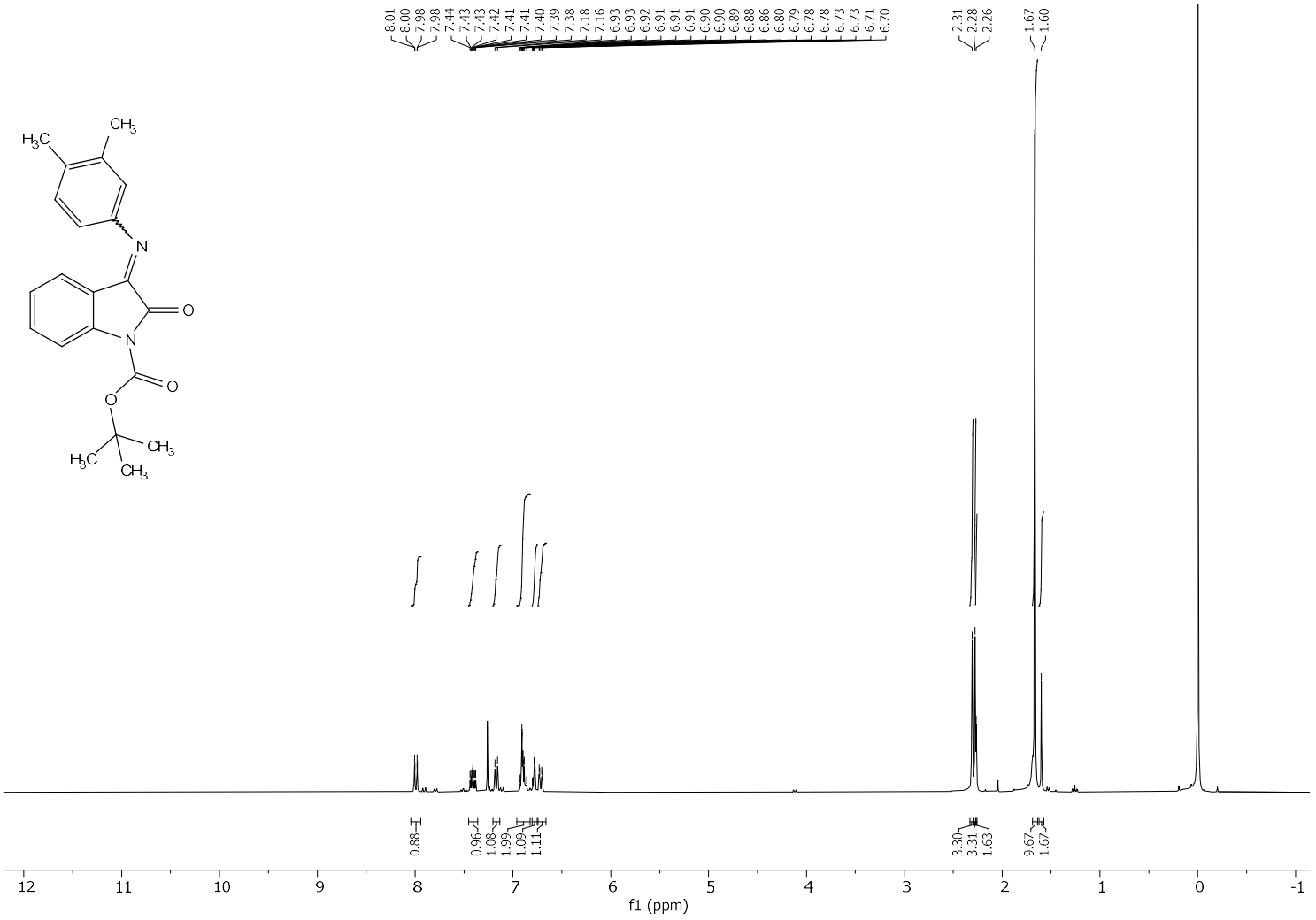

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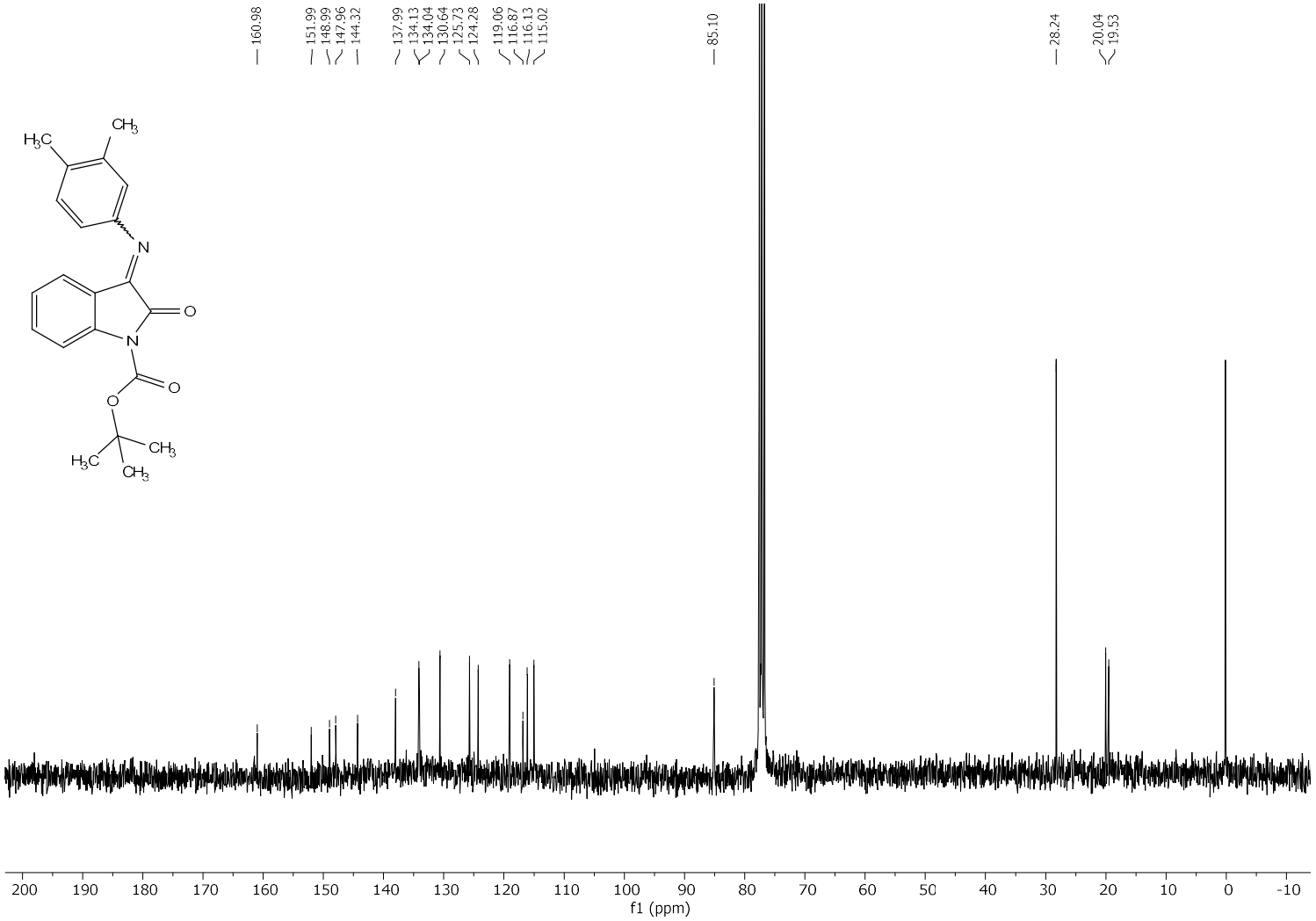

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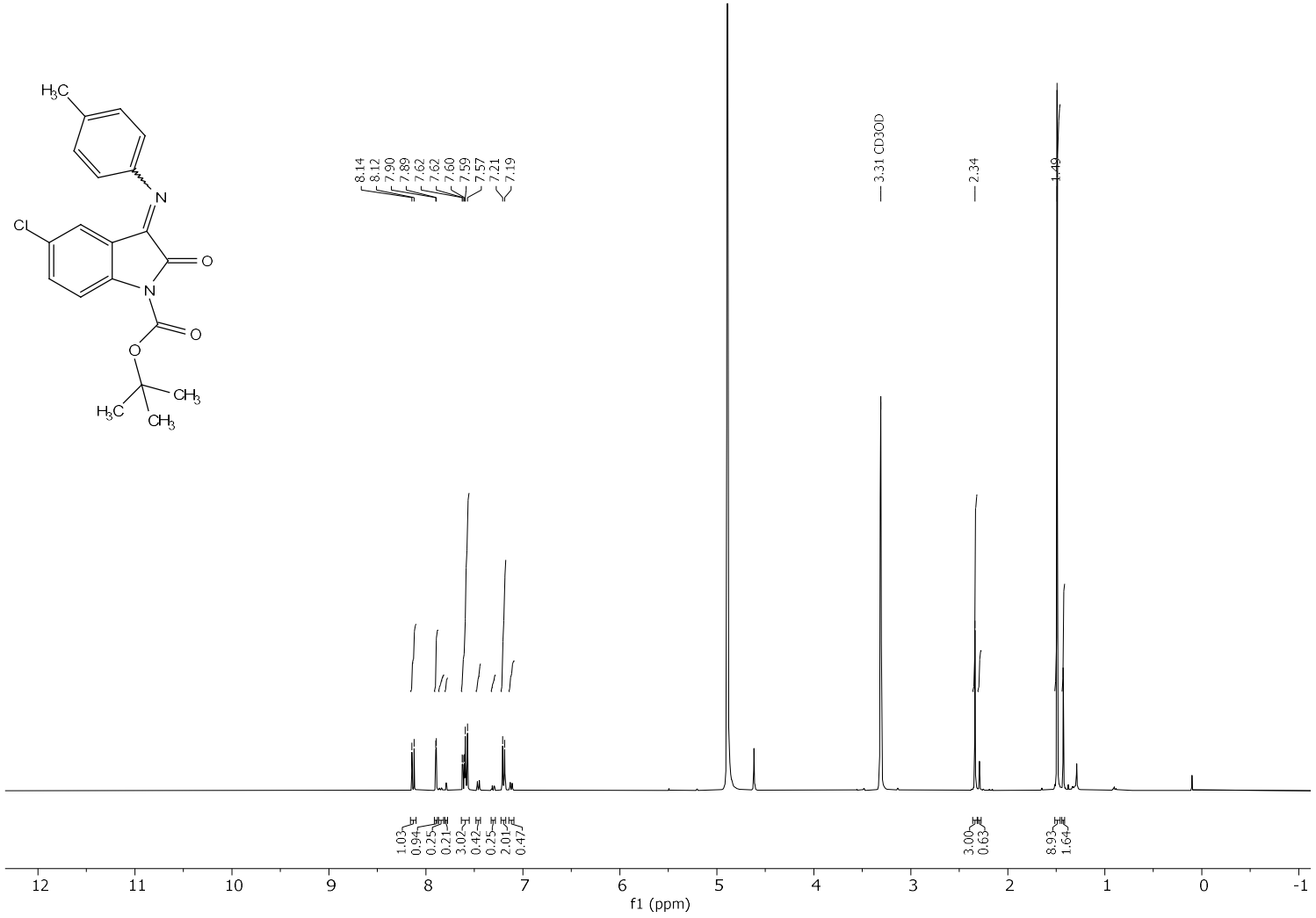

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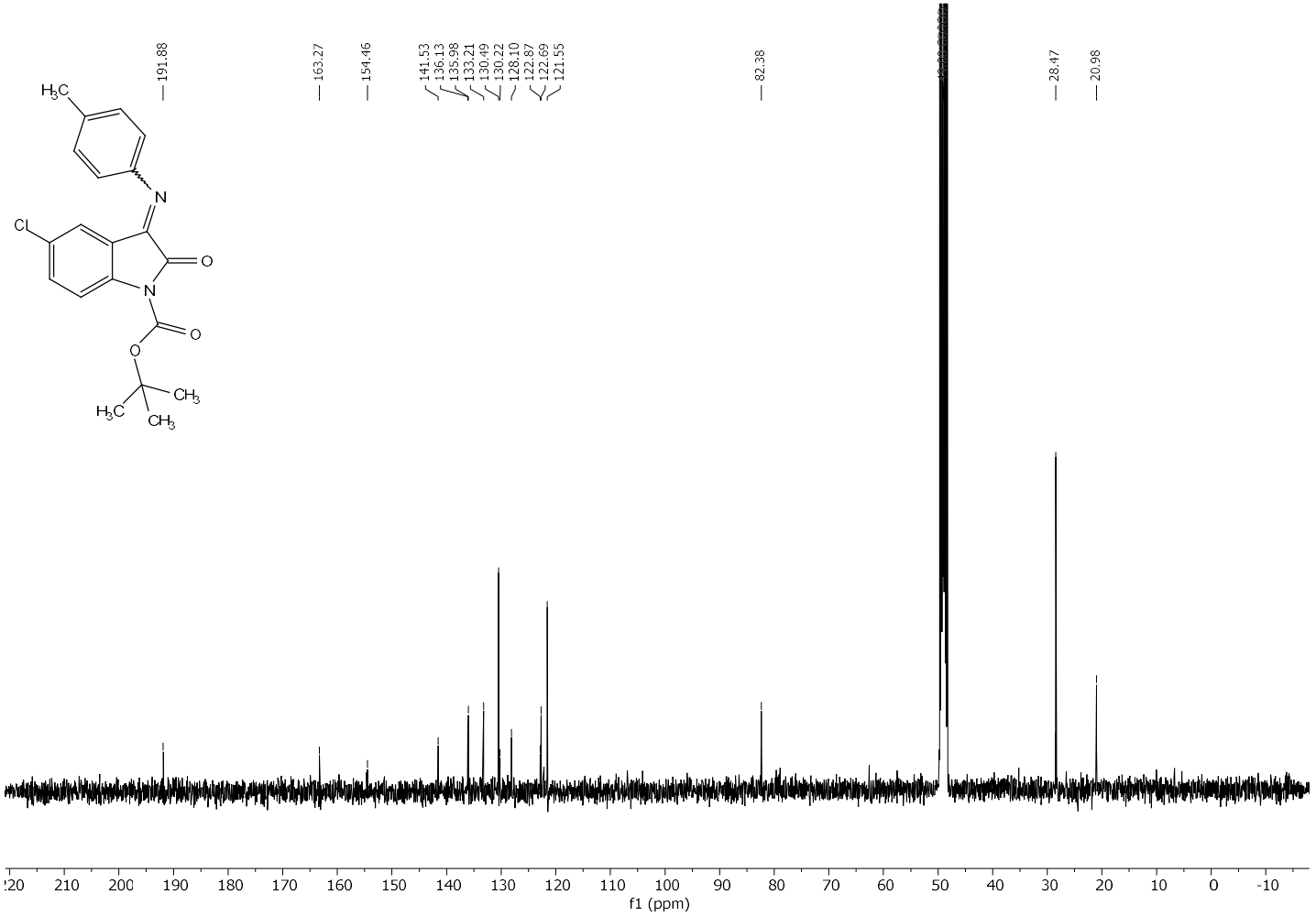

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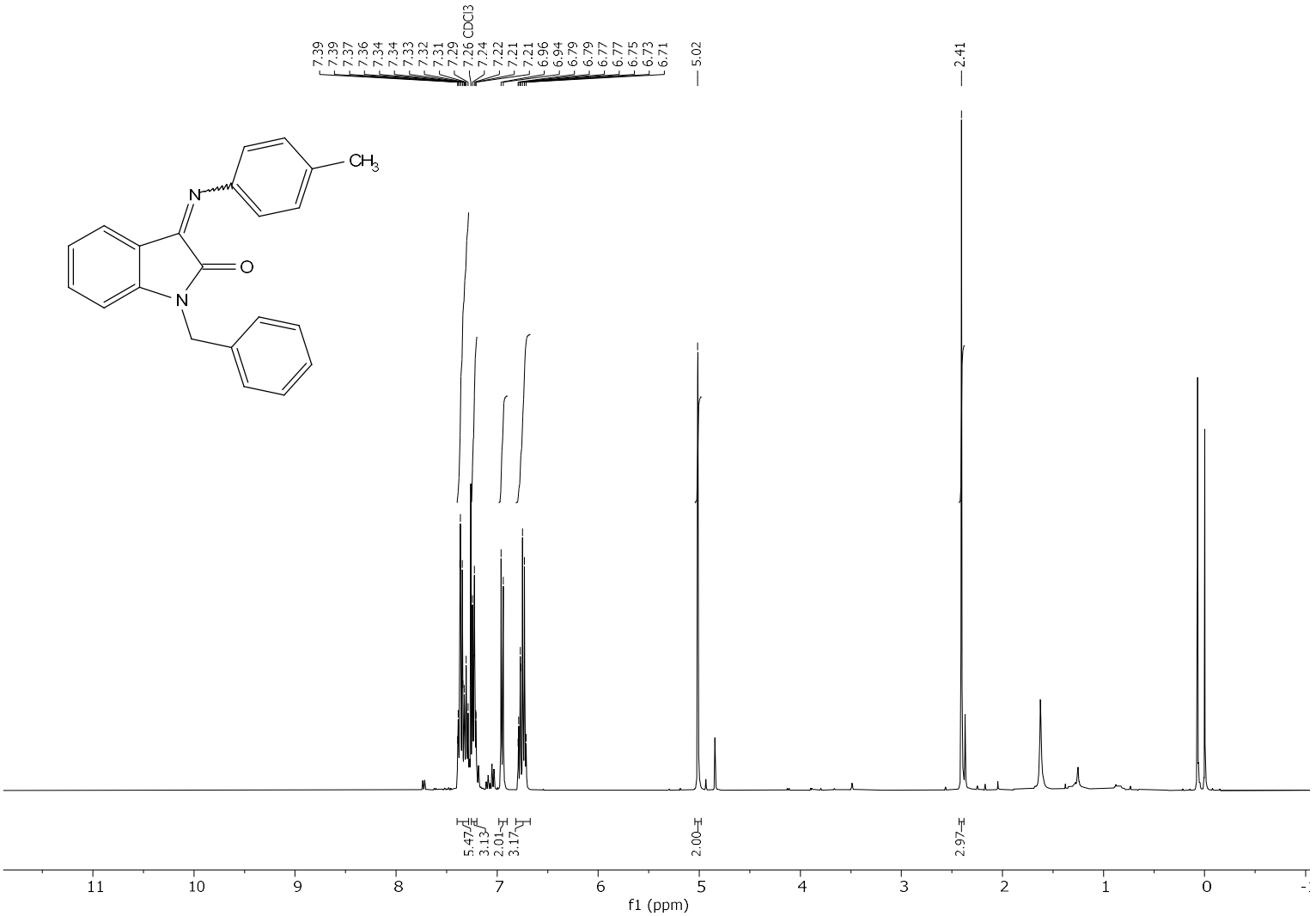

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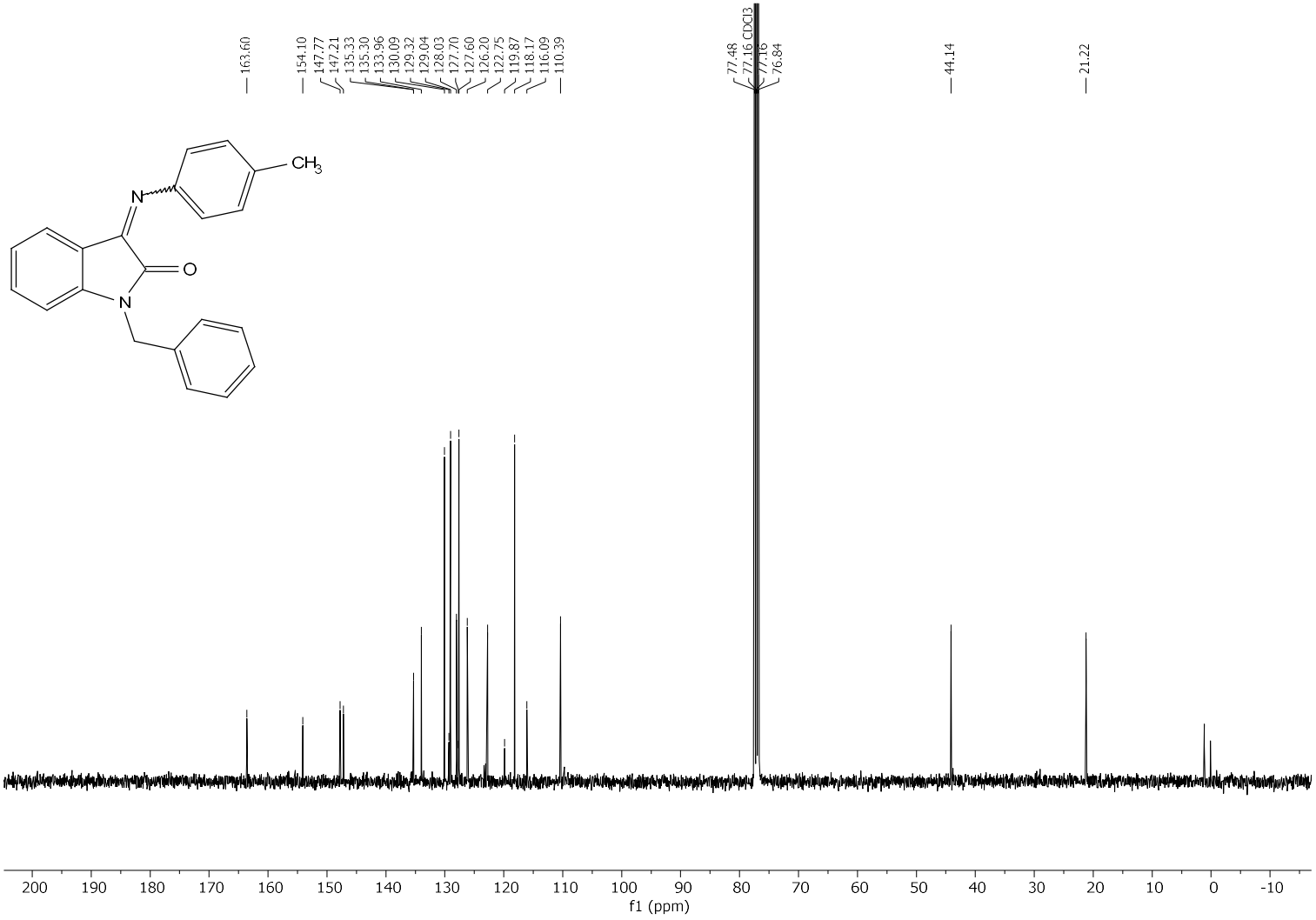

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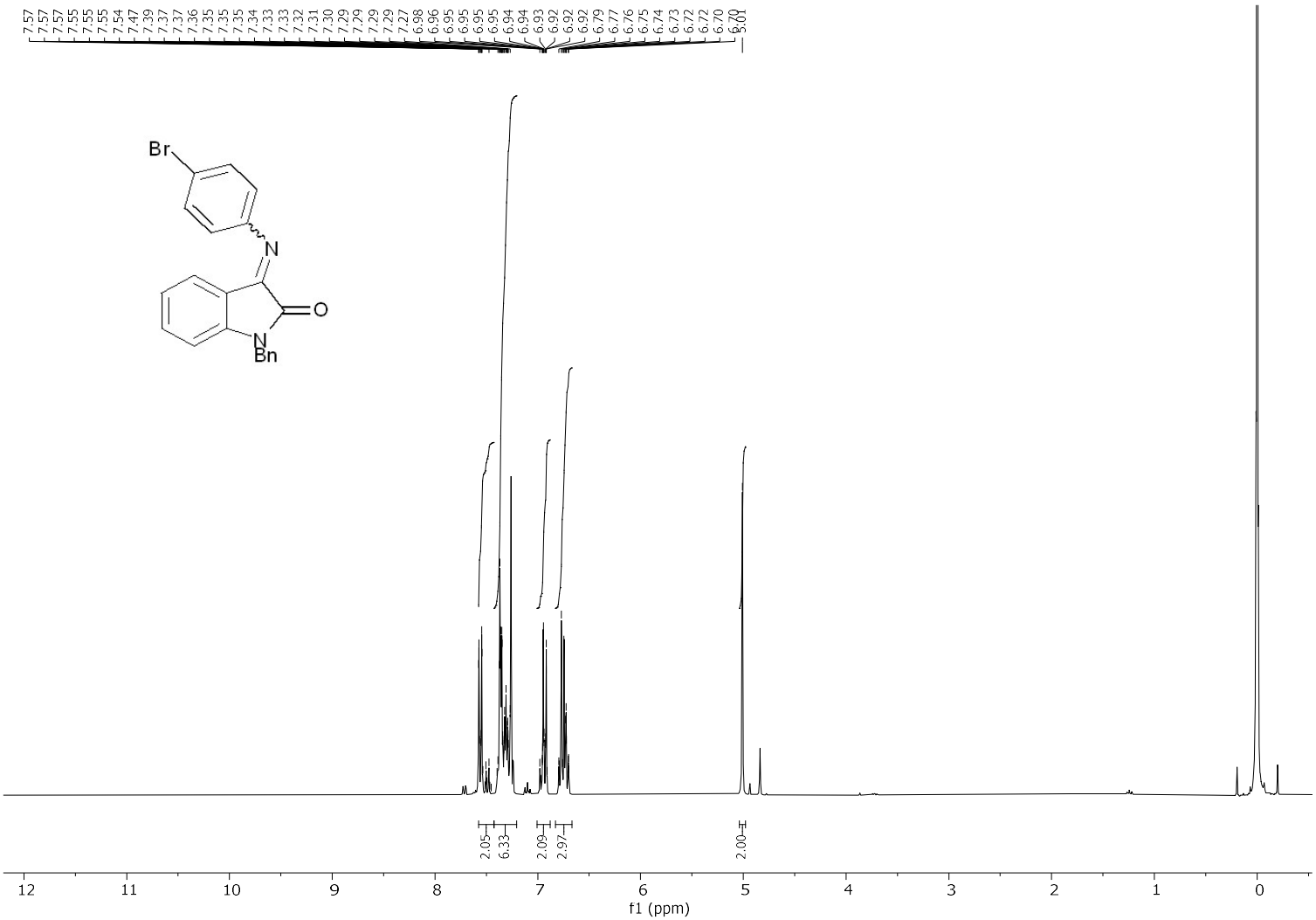

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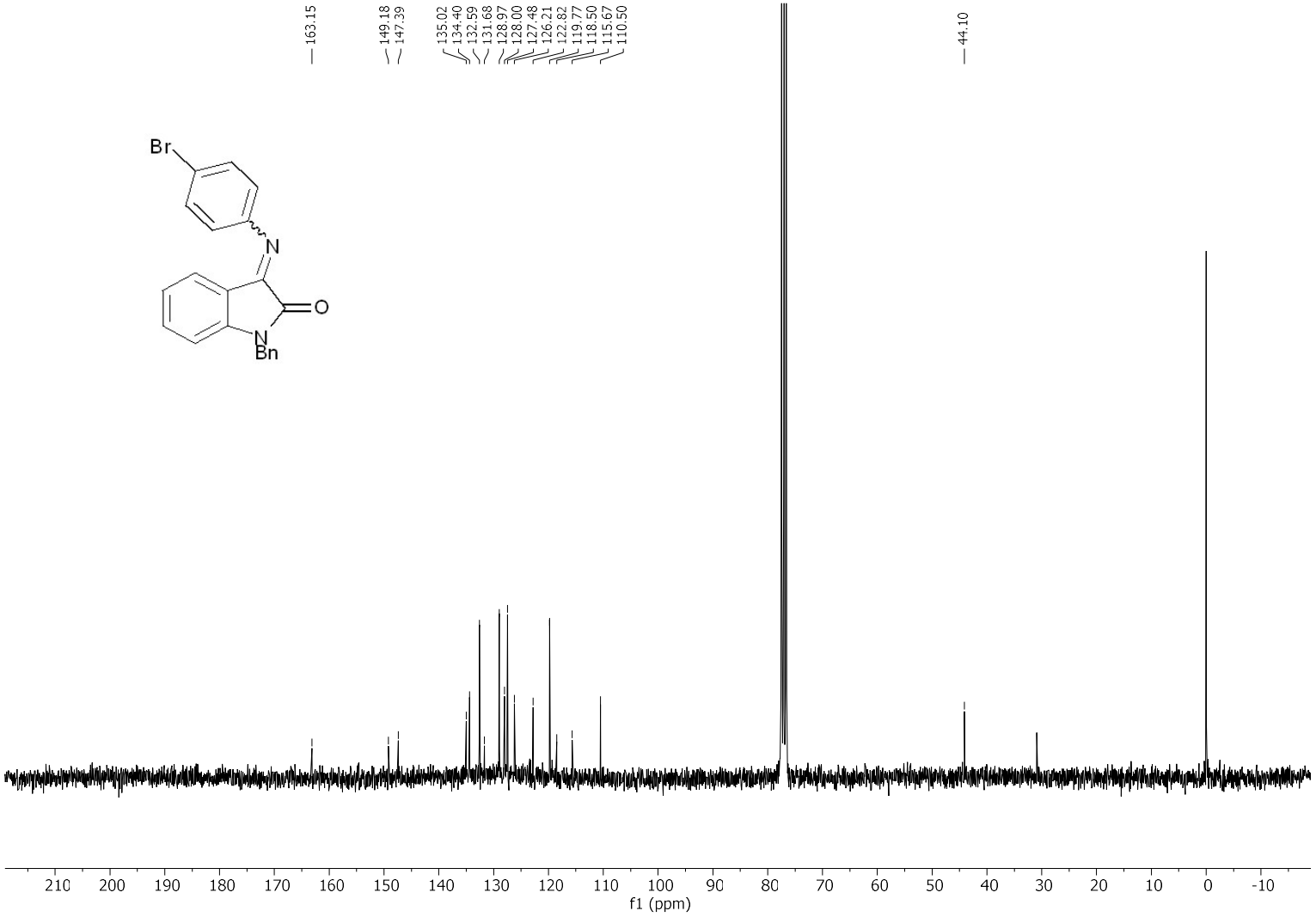

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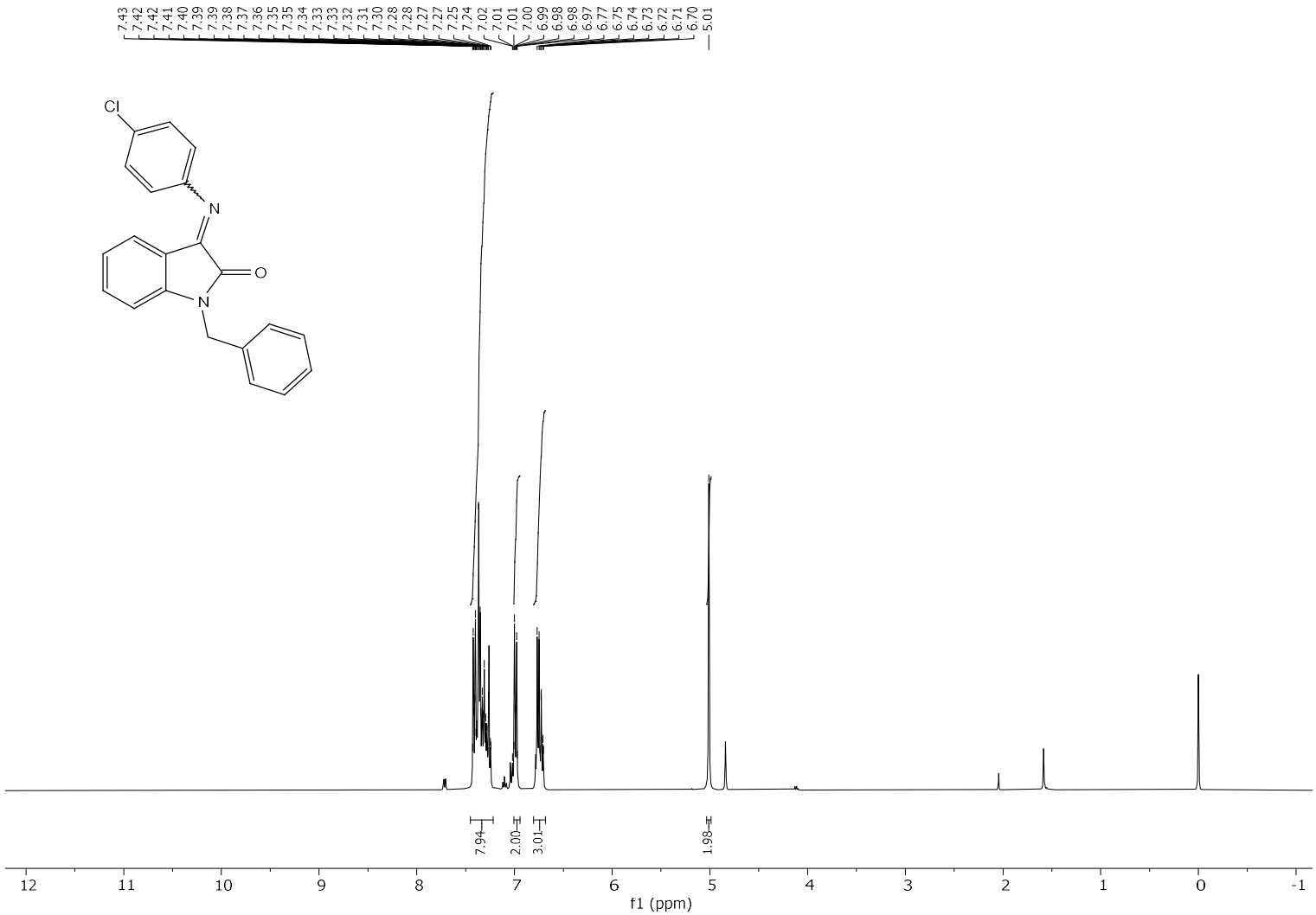

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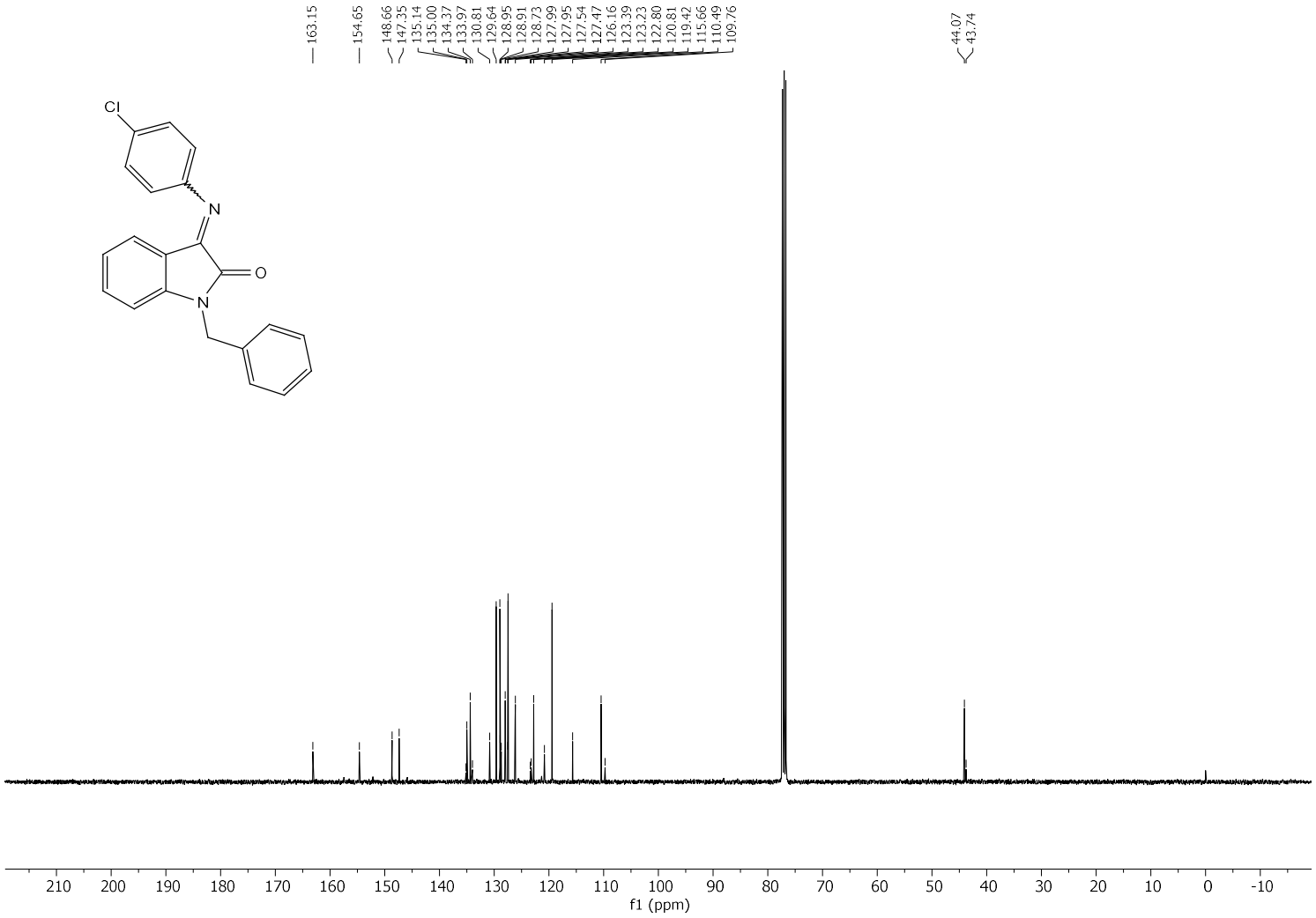

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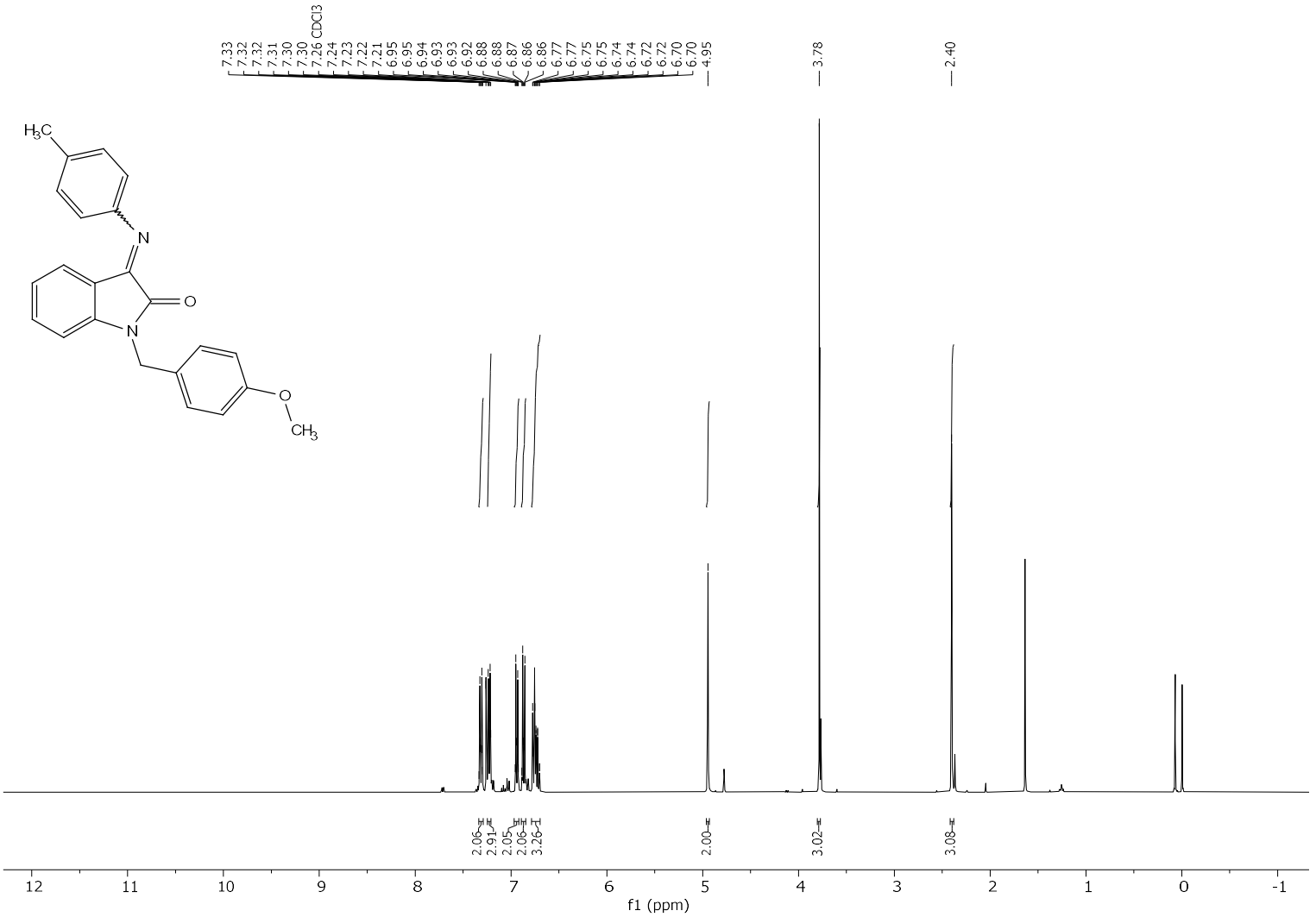

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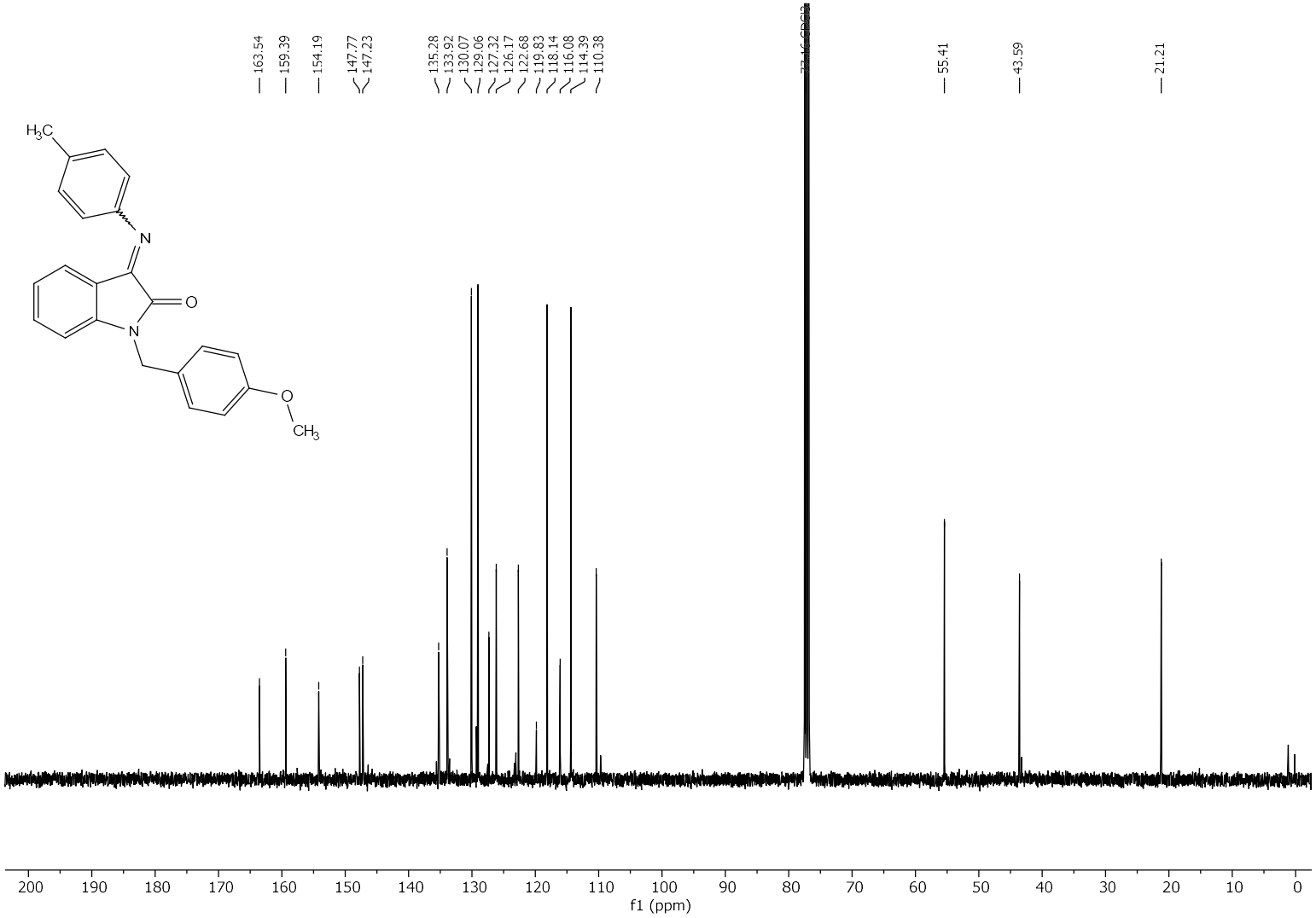
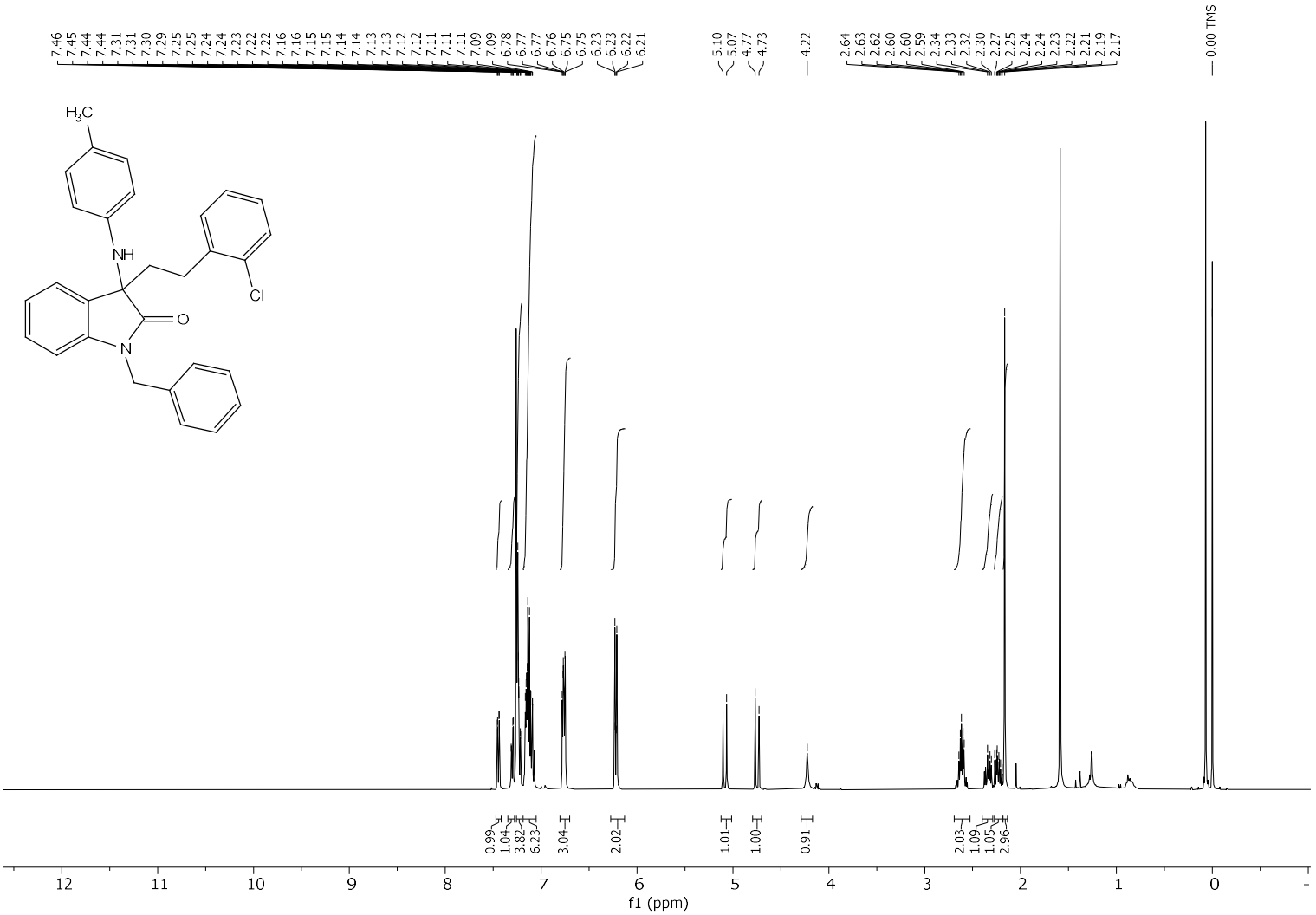


2a ^{1}H NMR spectrum



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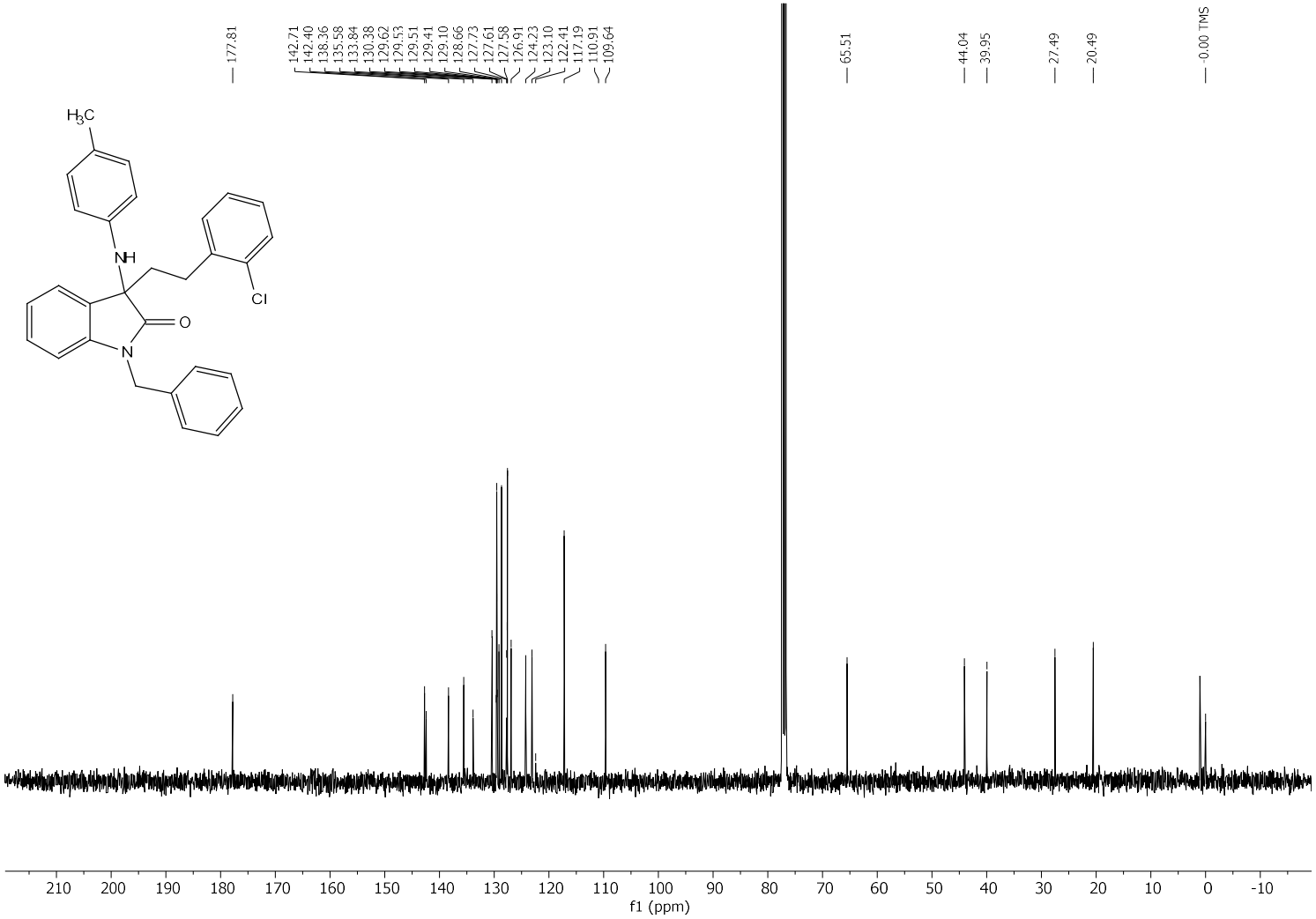

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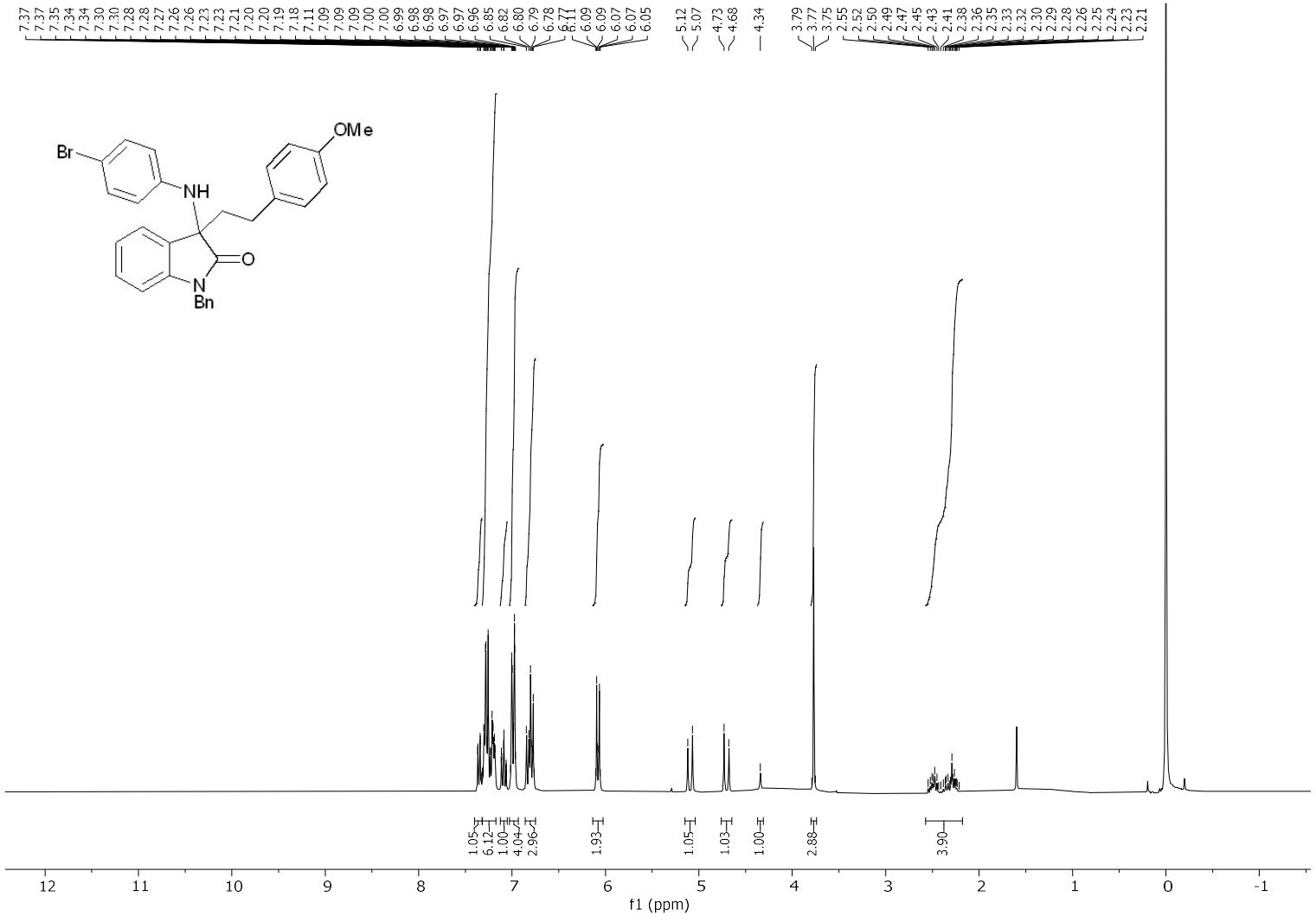

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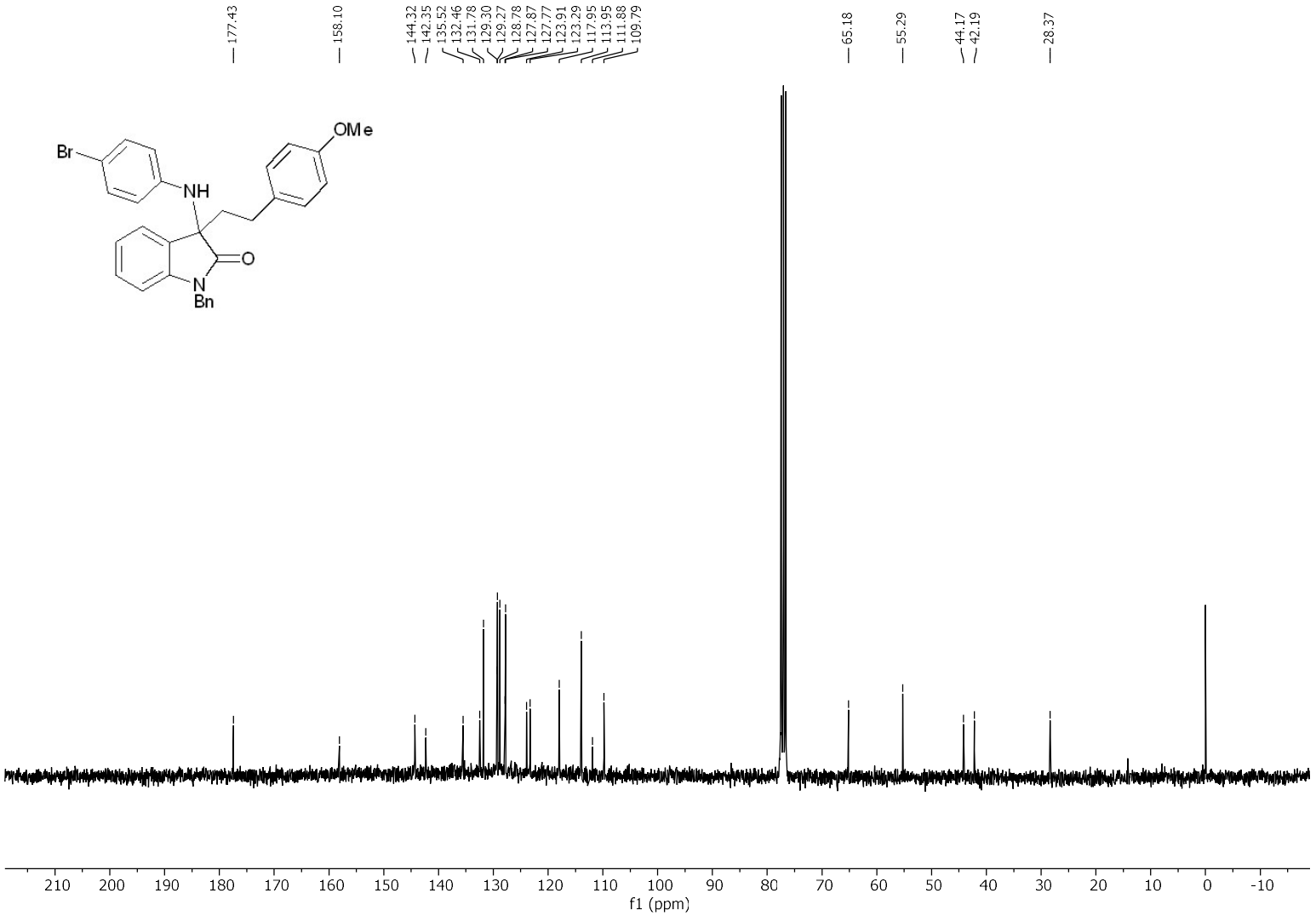

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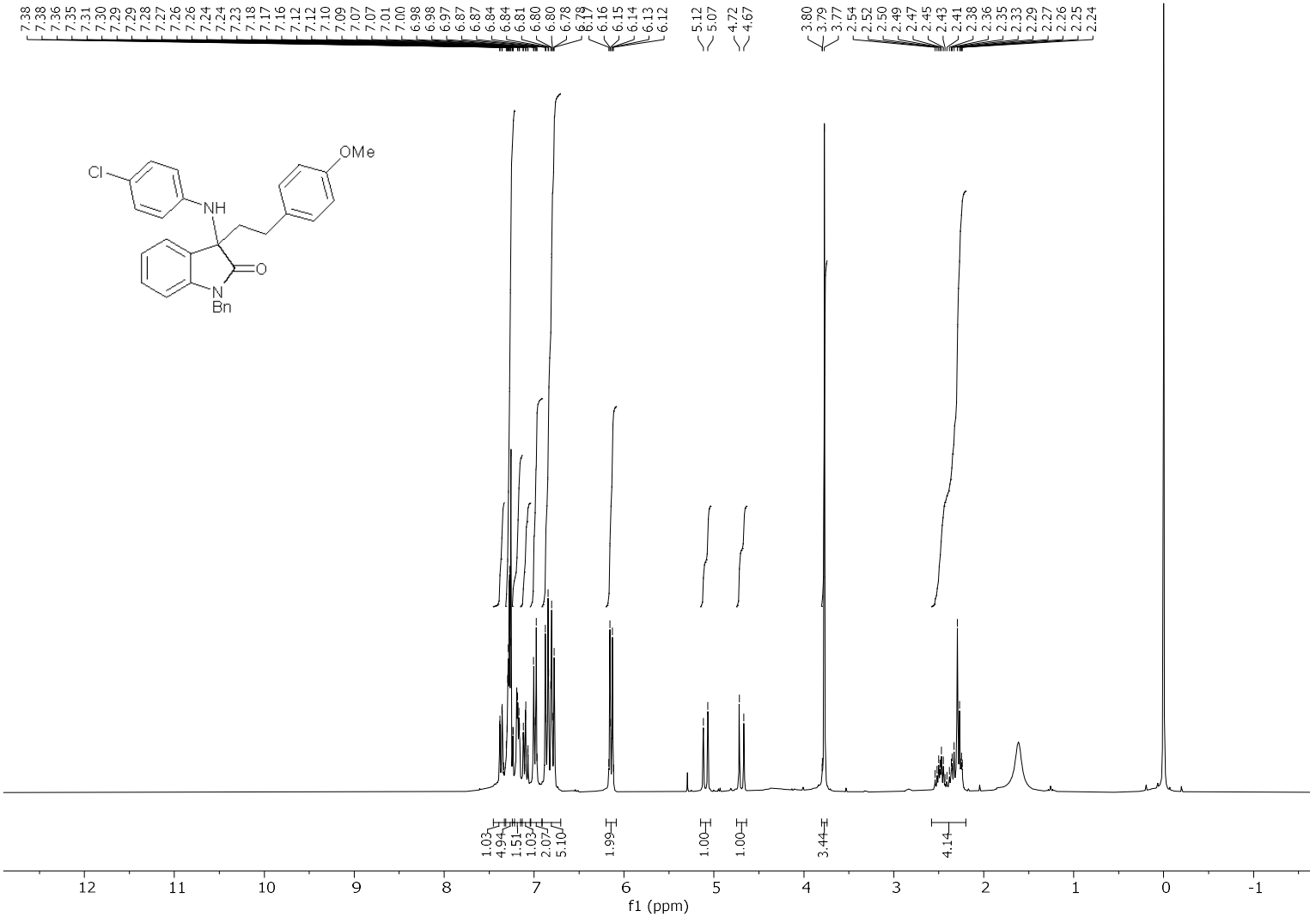

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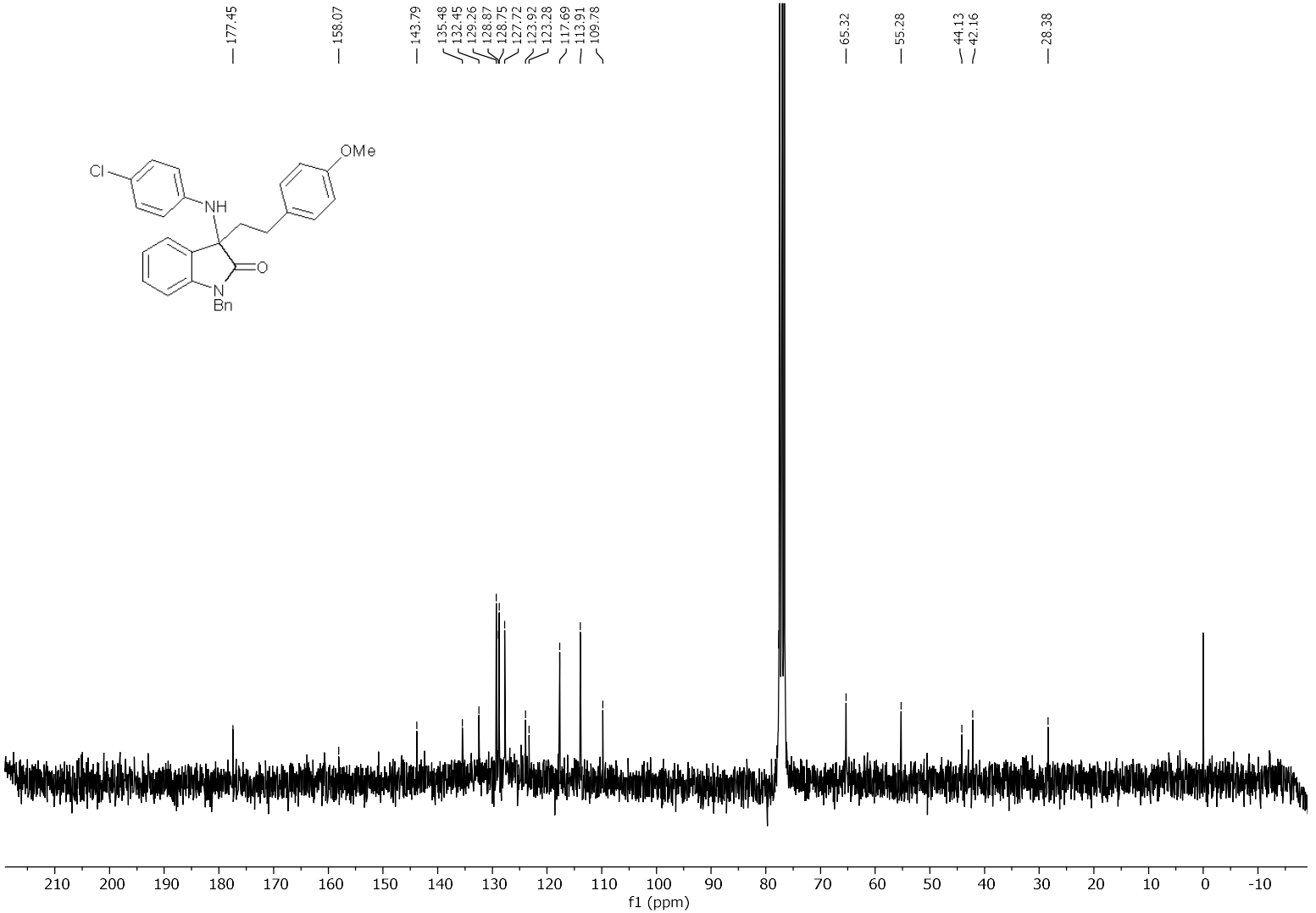

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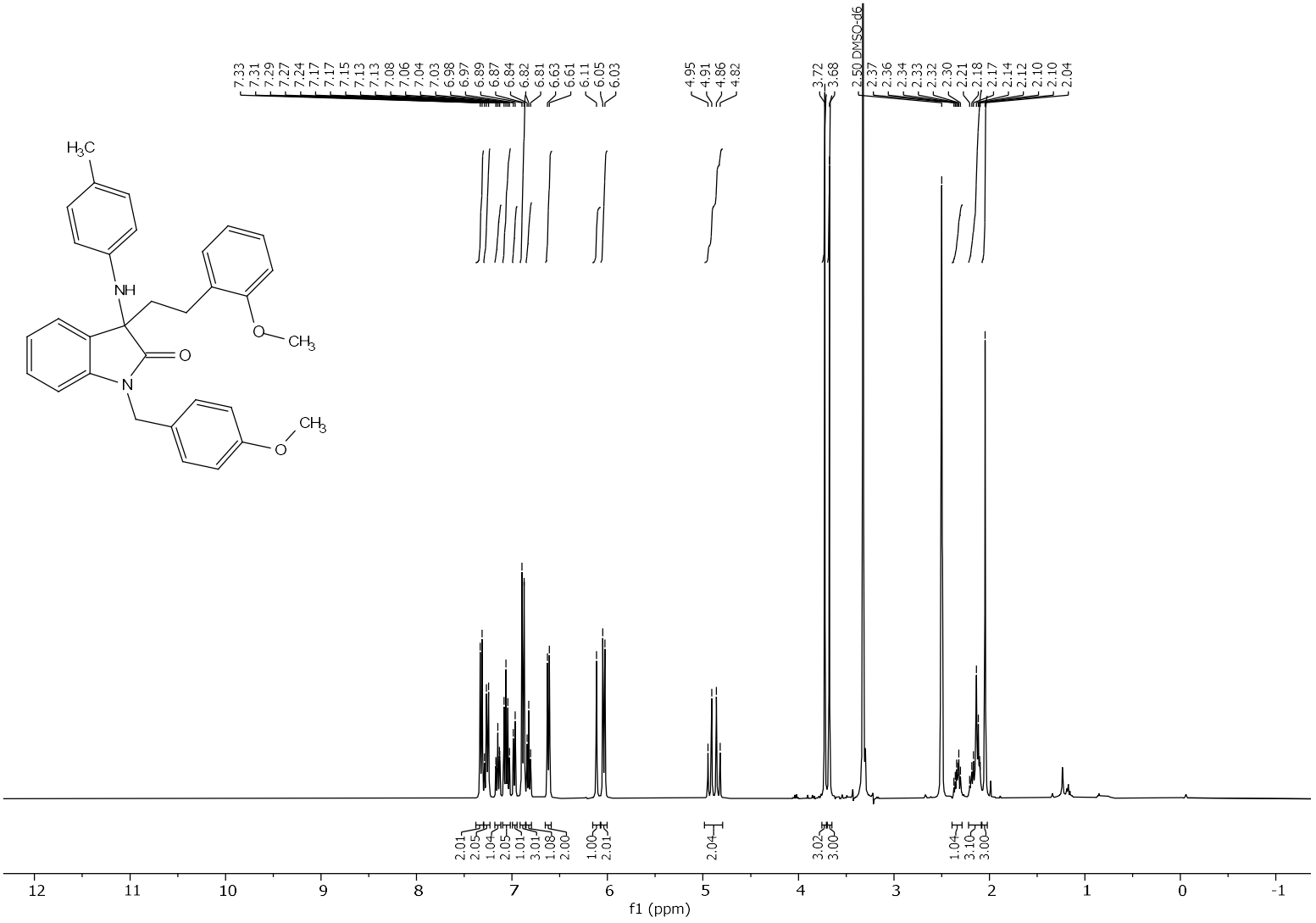
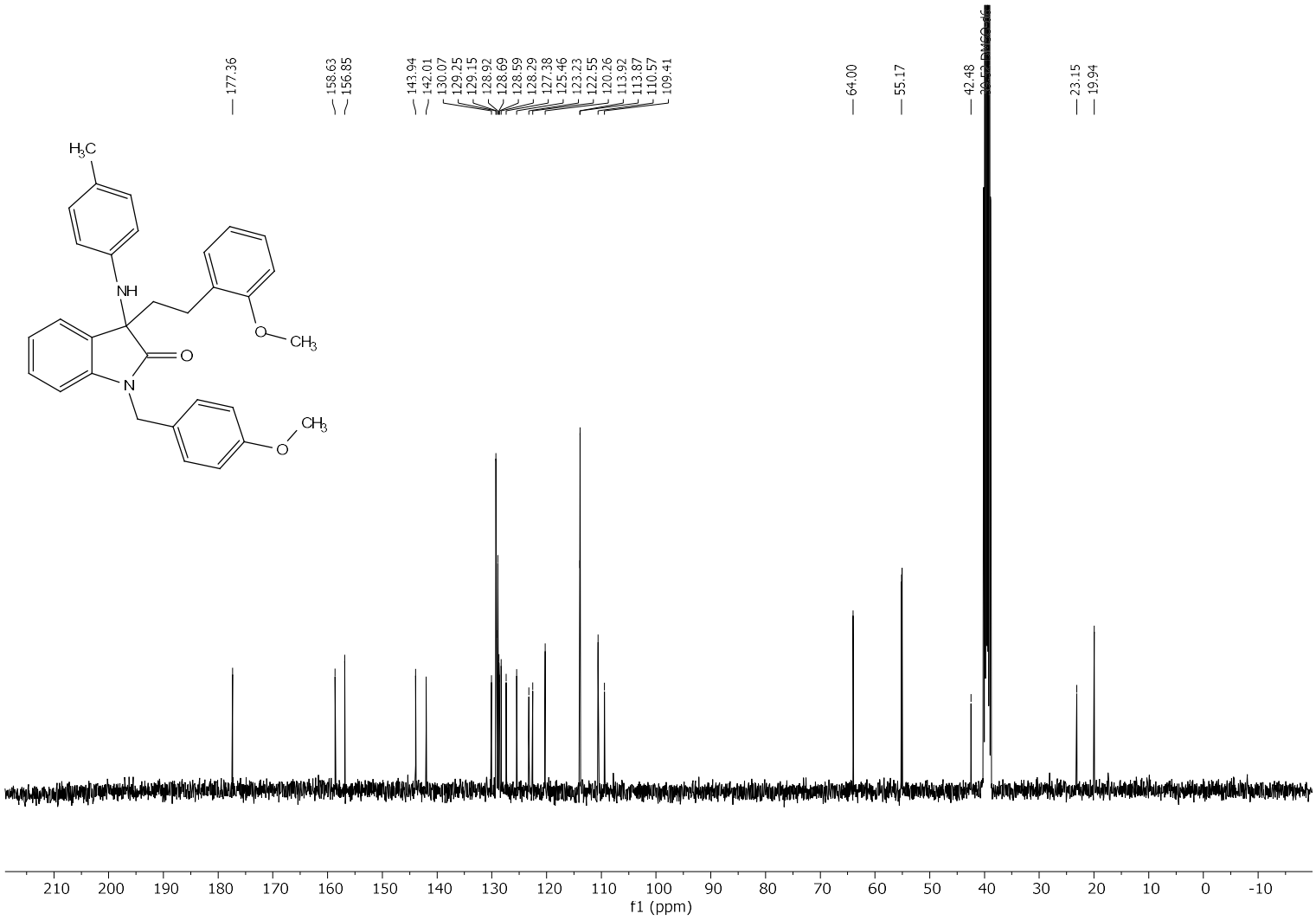
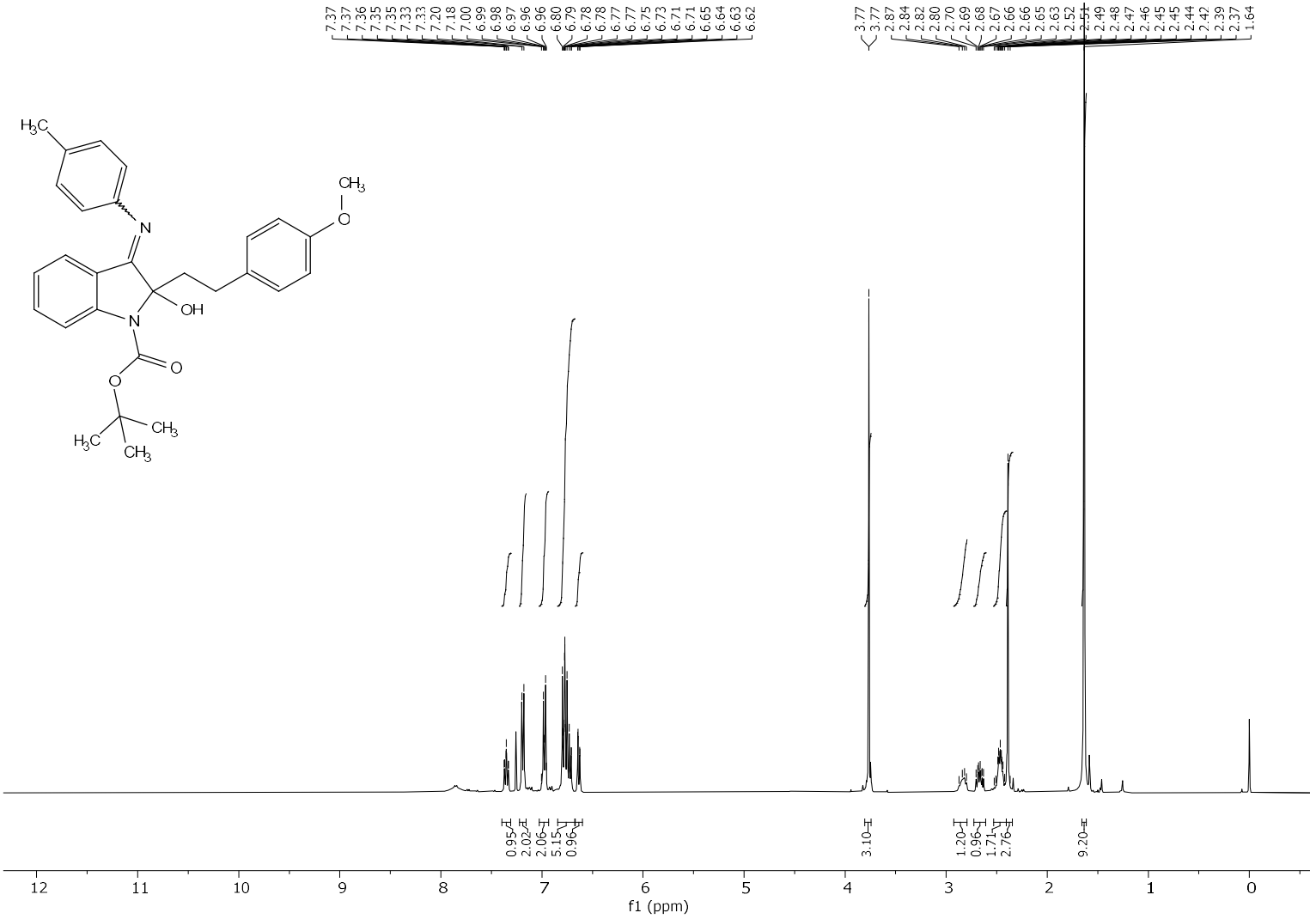


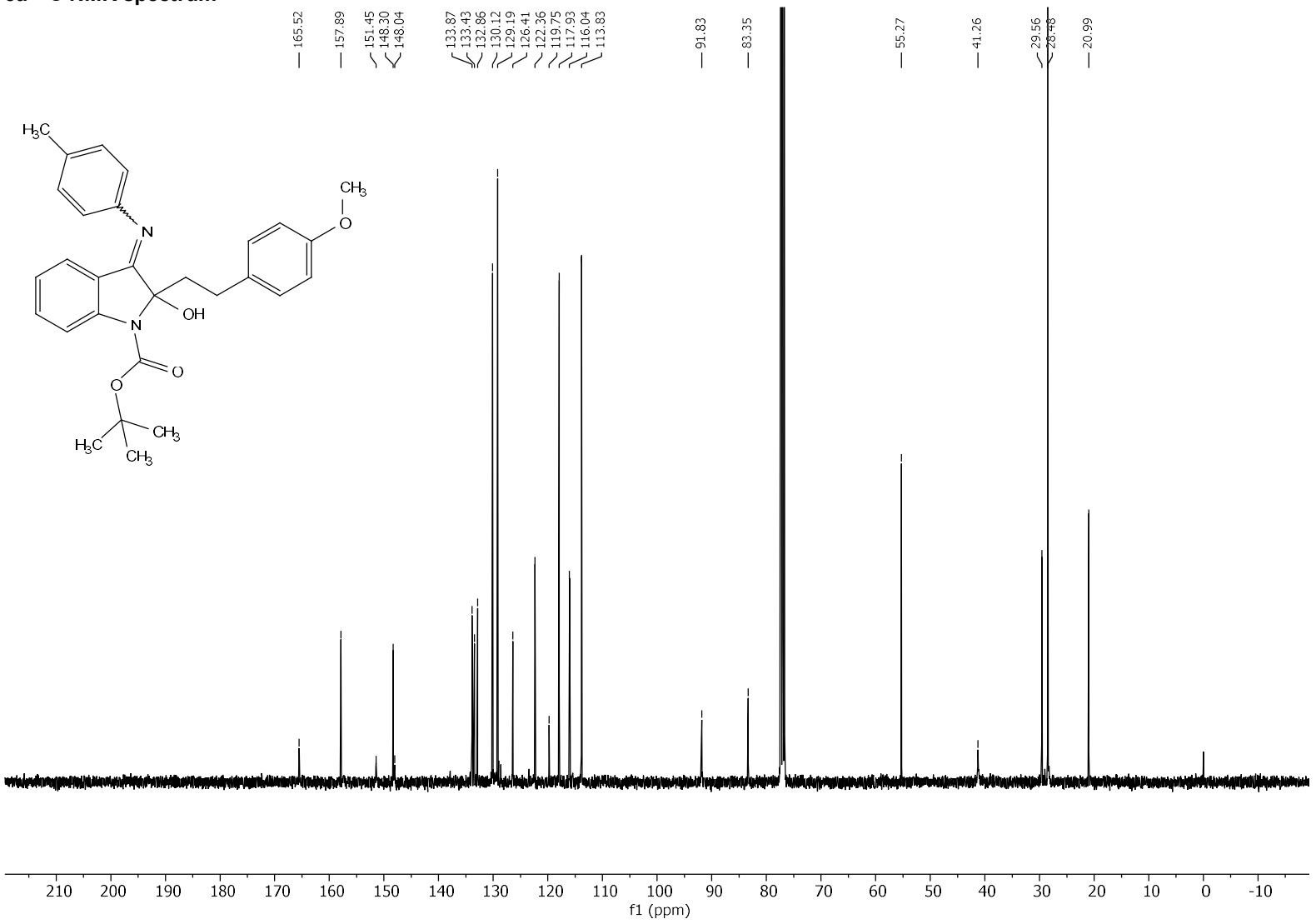
2d ^{13}C NMR spectrum



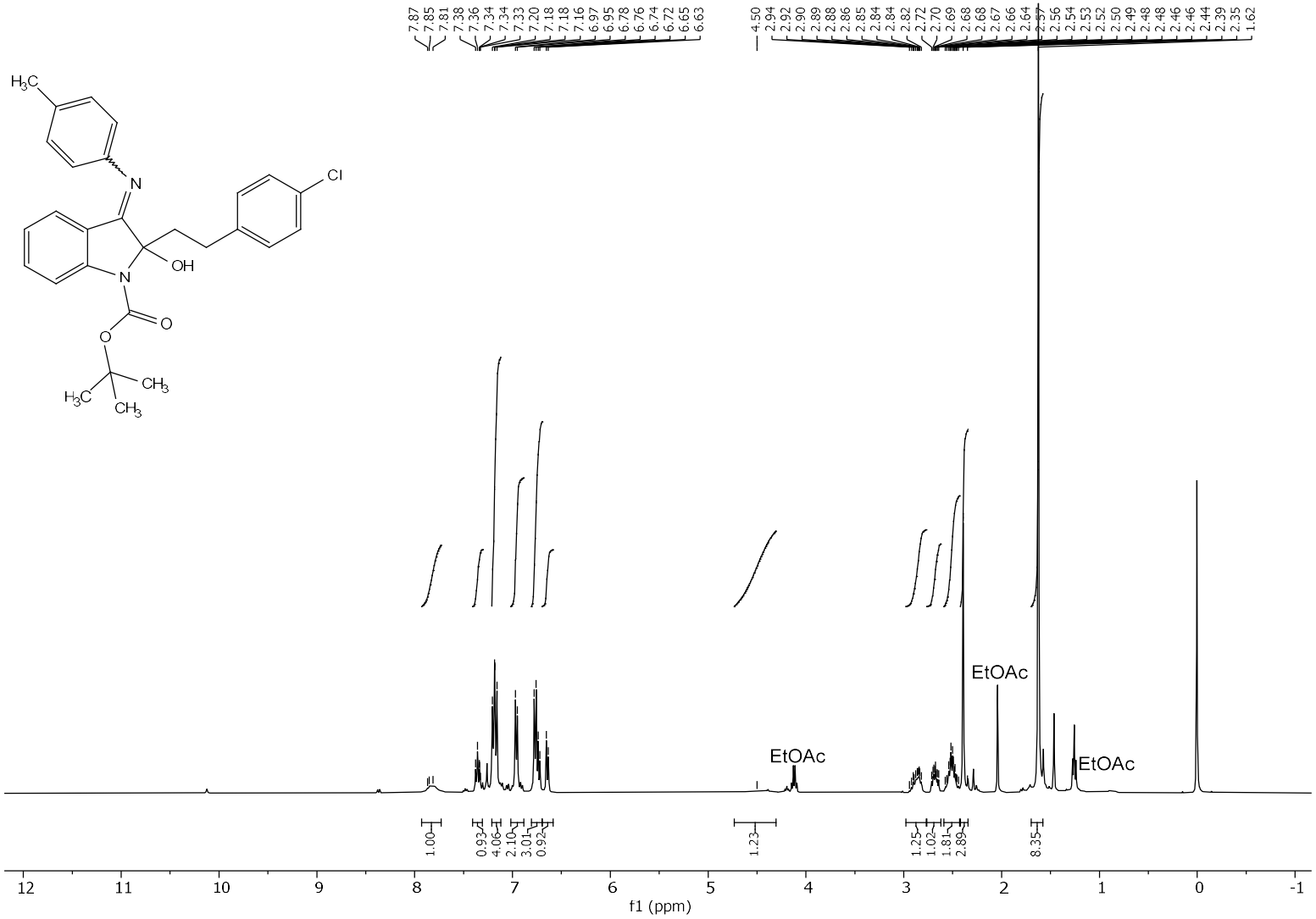
3a ^{1}H NMR spectrum



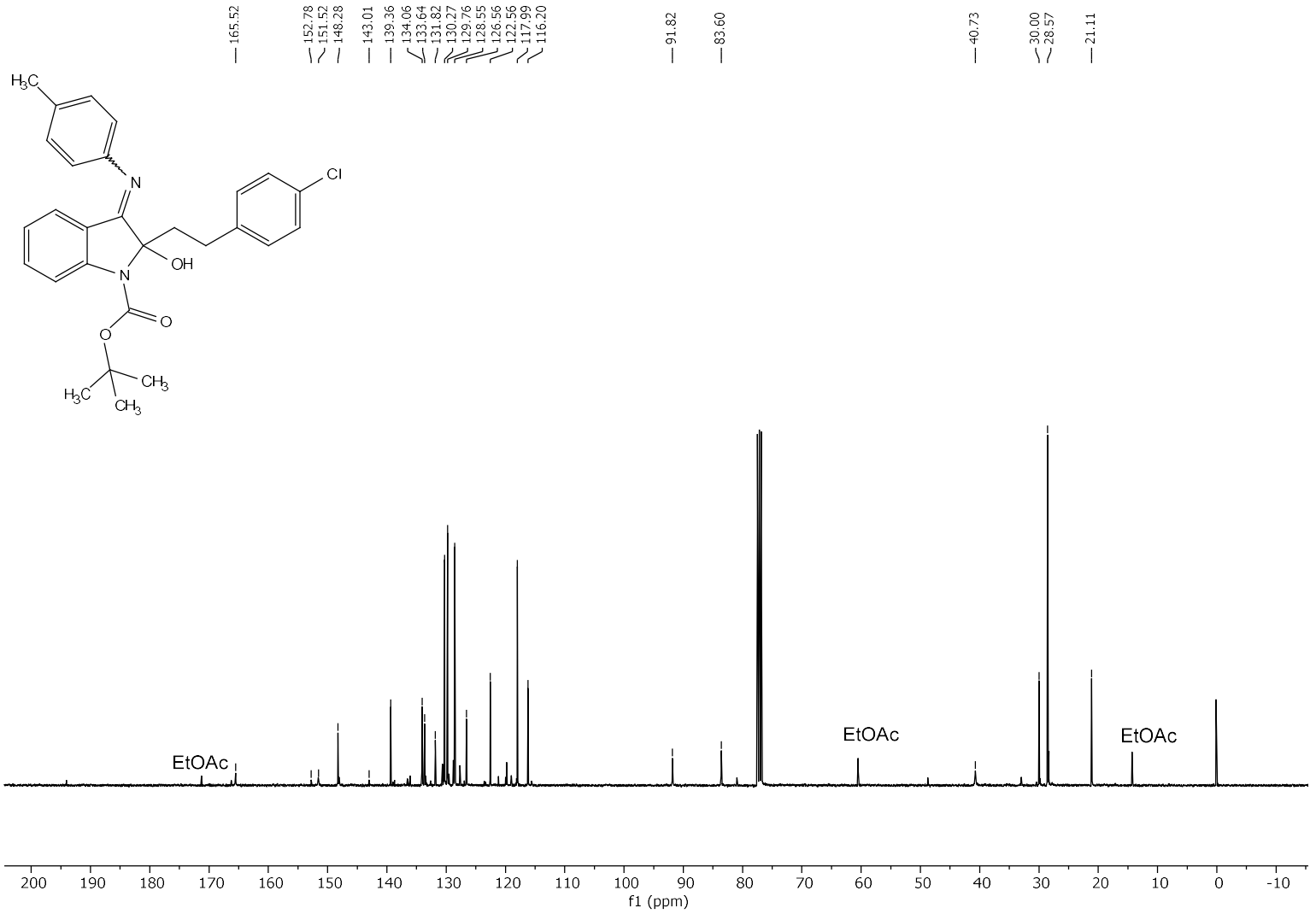
3a ^{13}C NMR spectrum



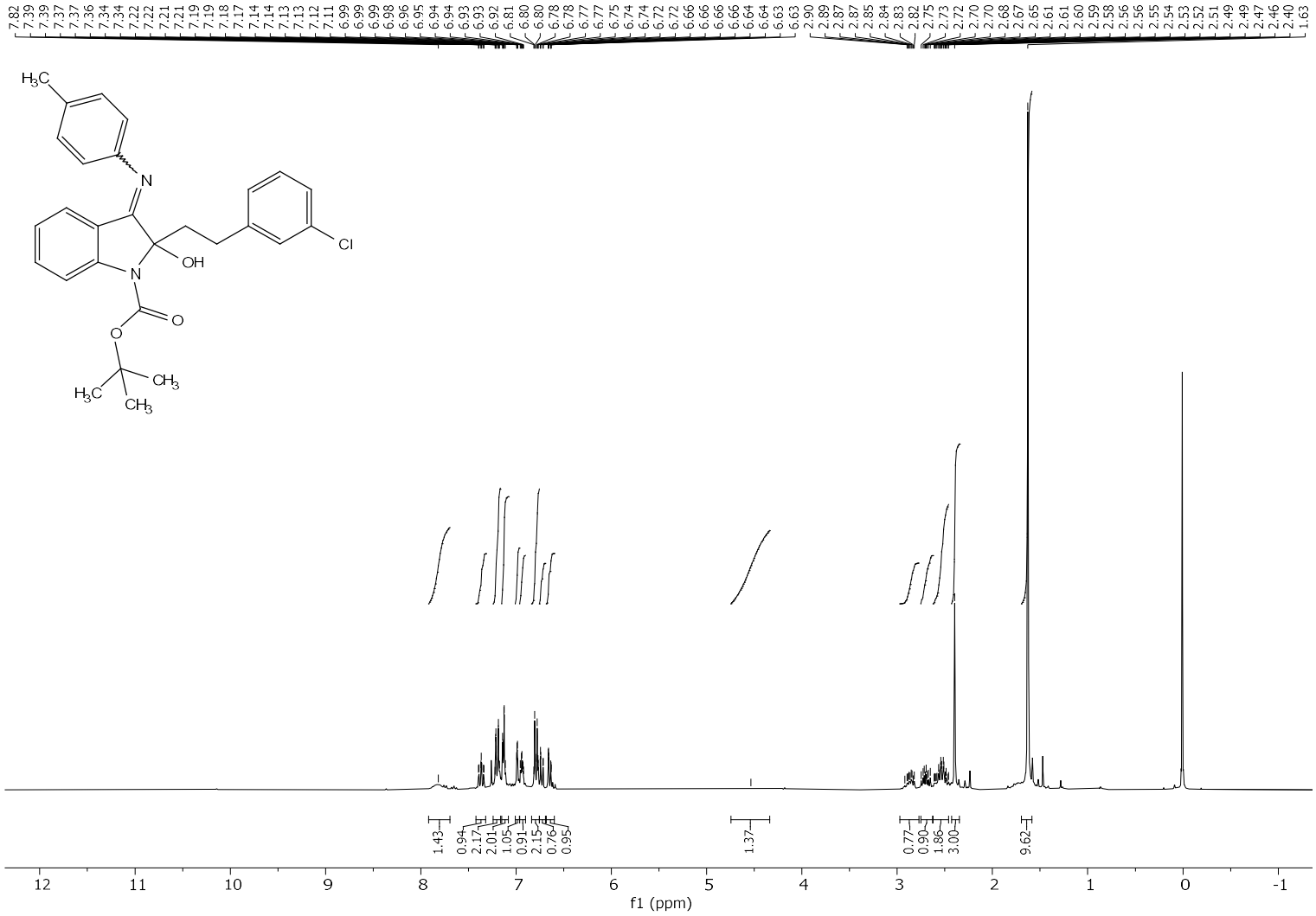
3b ^{1}H NMR spectrum



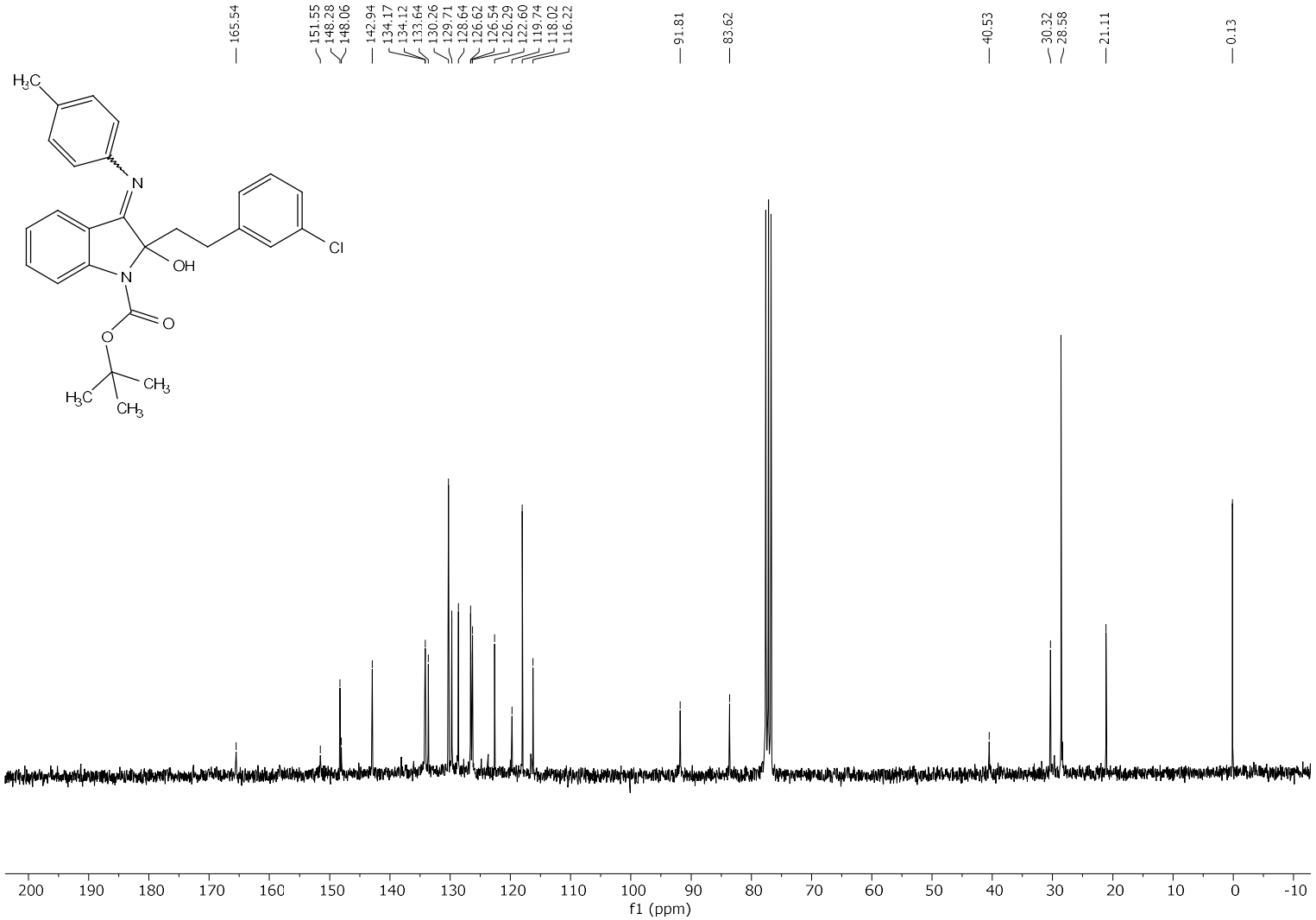
3b ^{13}C NMR spectrum



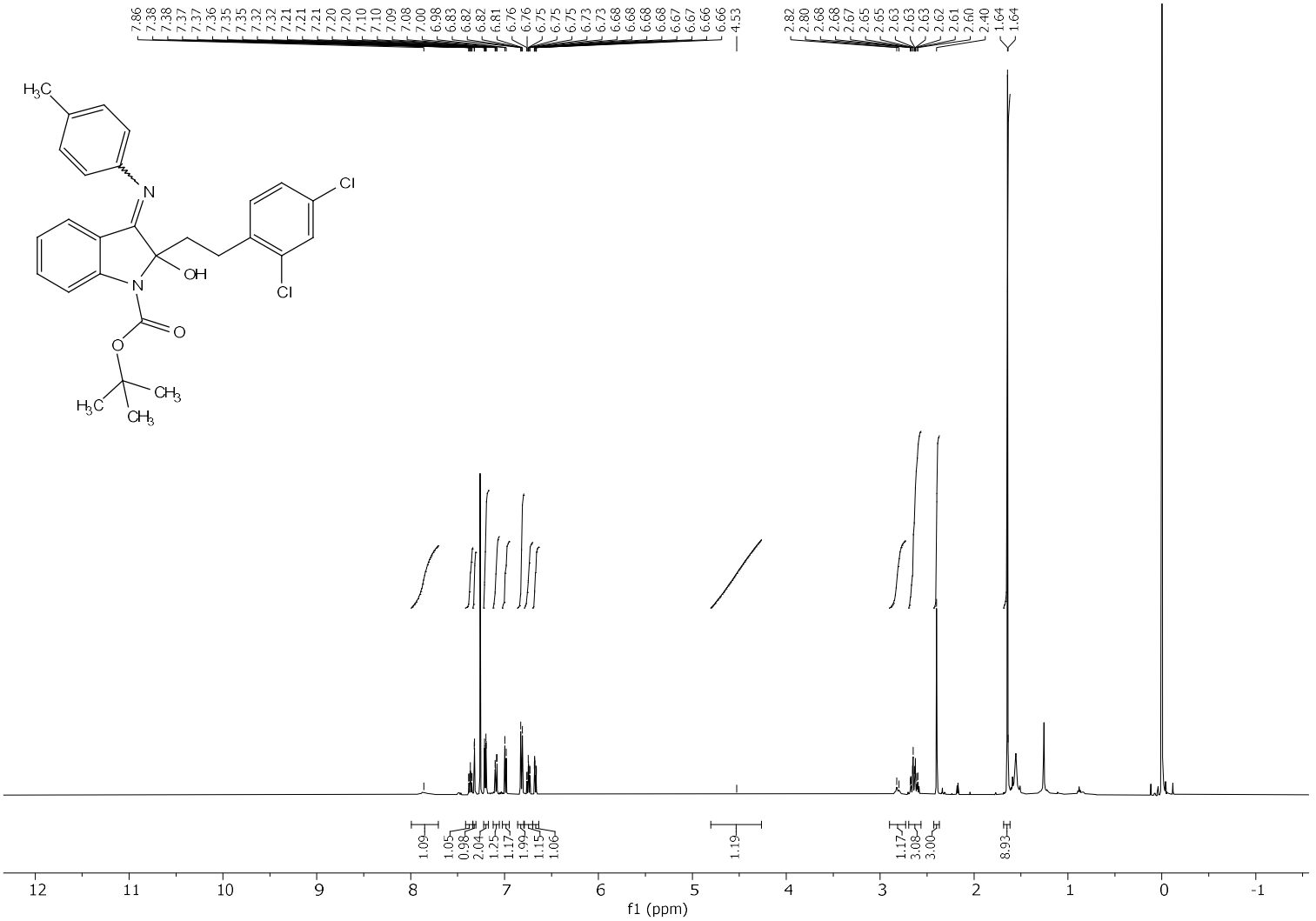
3c ^{1}H NMR spectrum



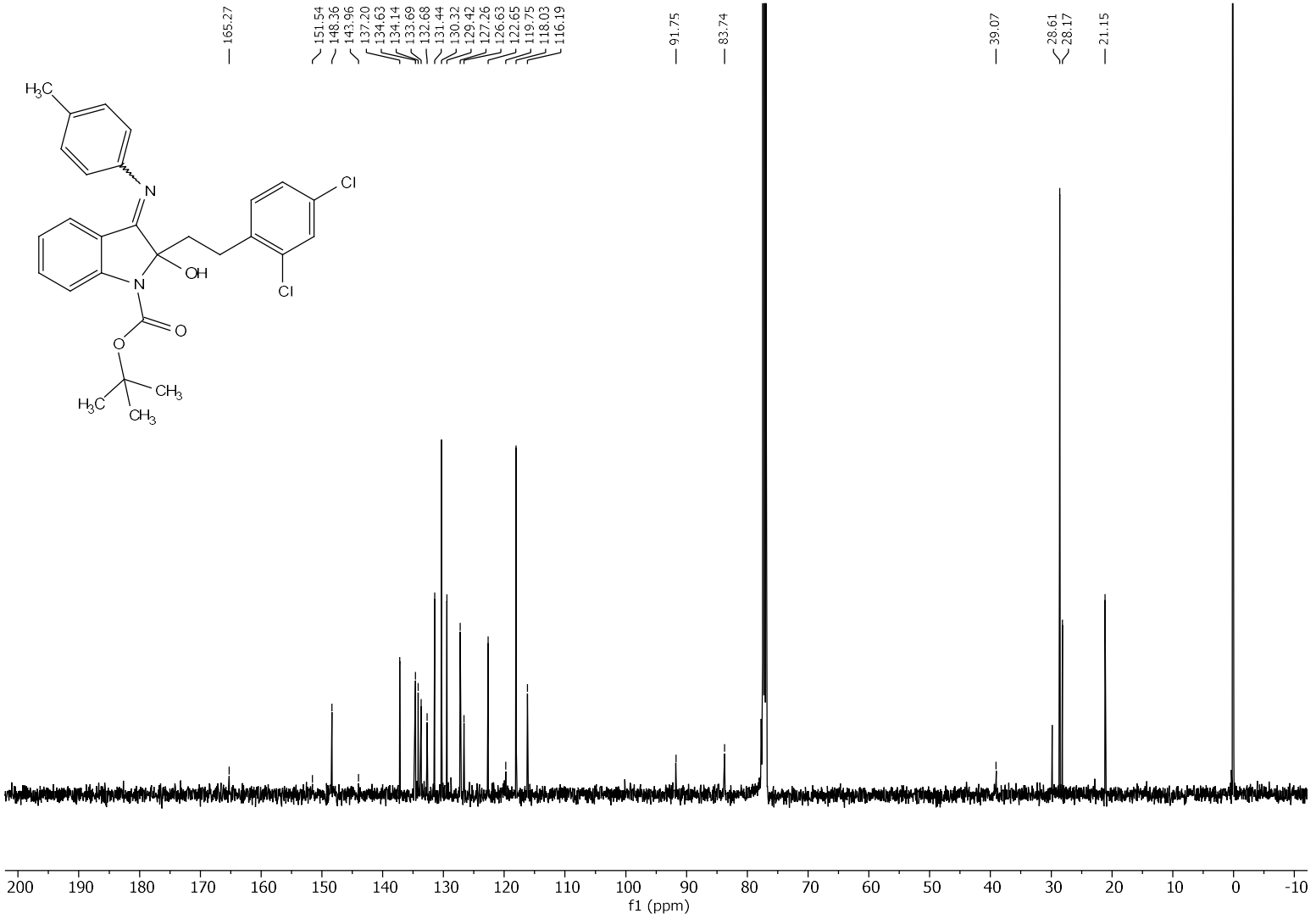
3c ^{13}C NMR spectrum



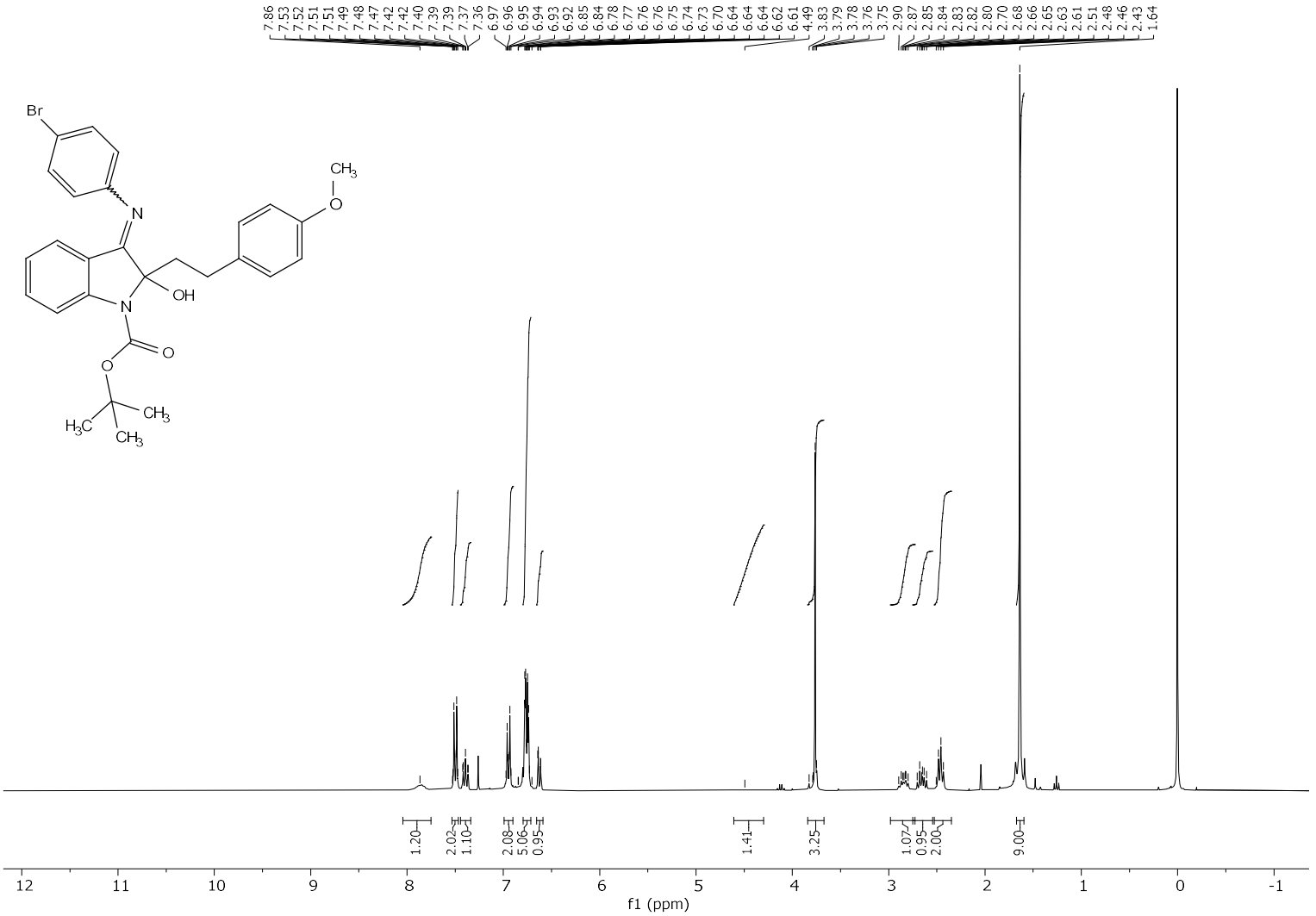
3d ^{1}H NMR spectrum



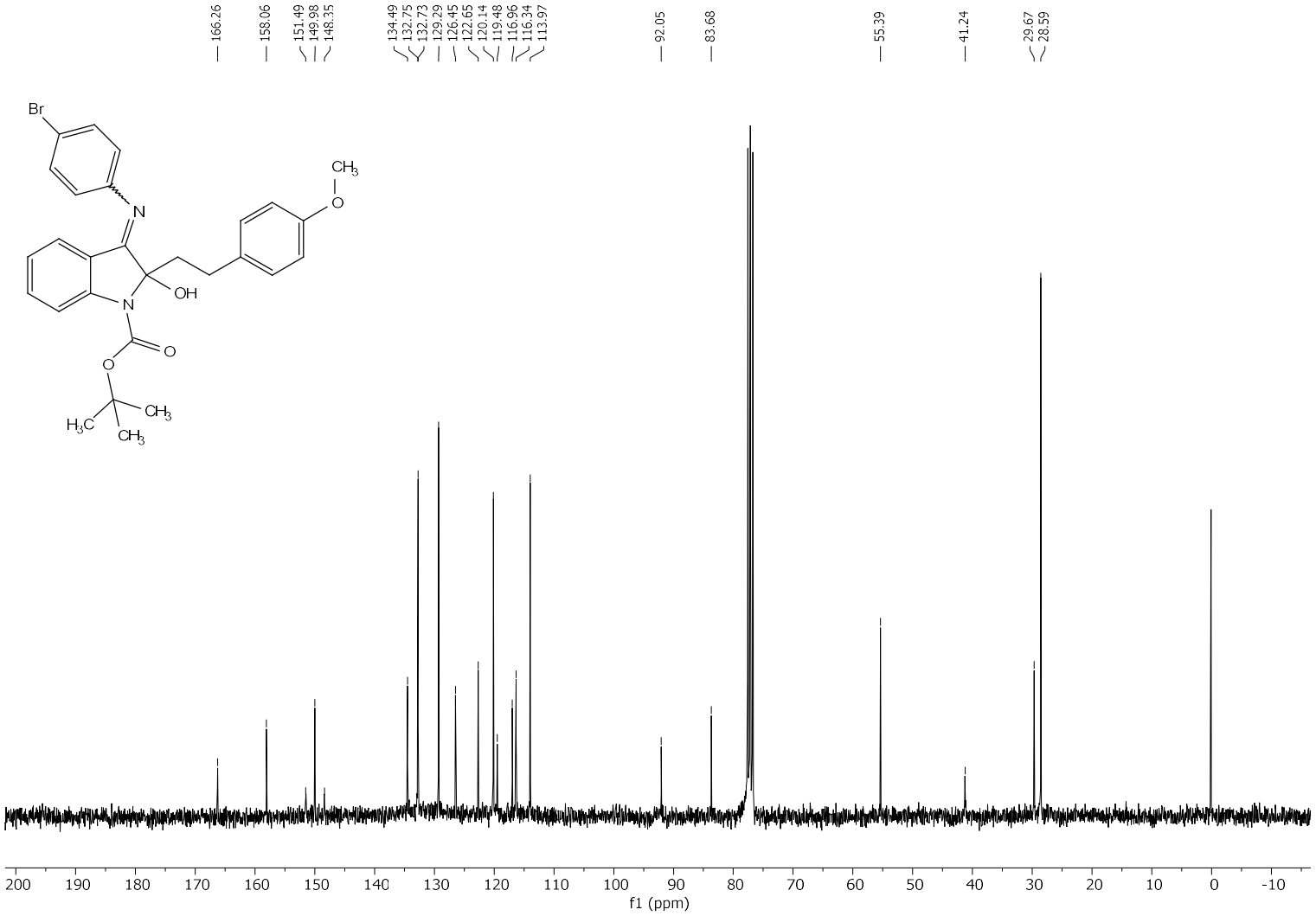
3d ^{13}C NMR spectrum



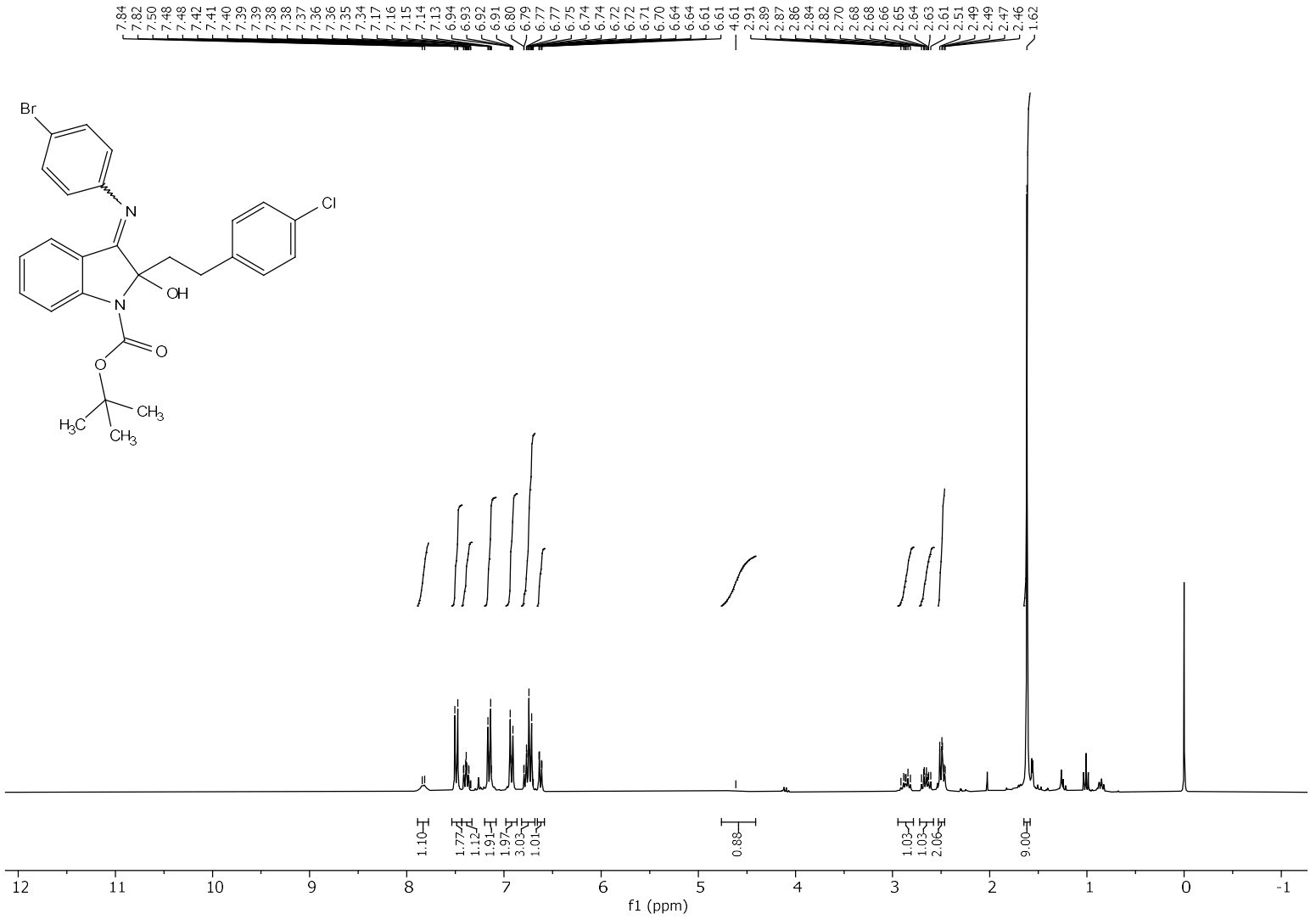
3e ^{1}H NMR spectrum



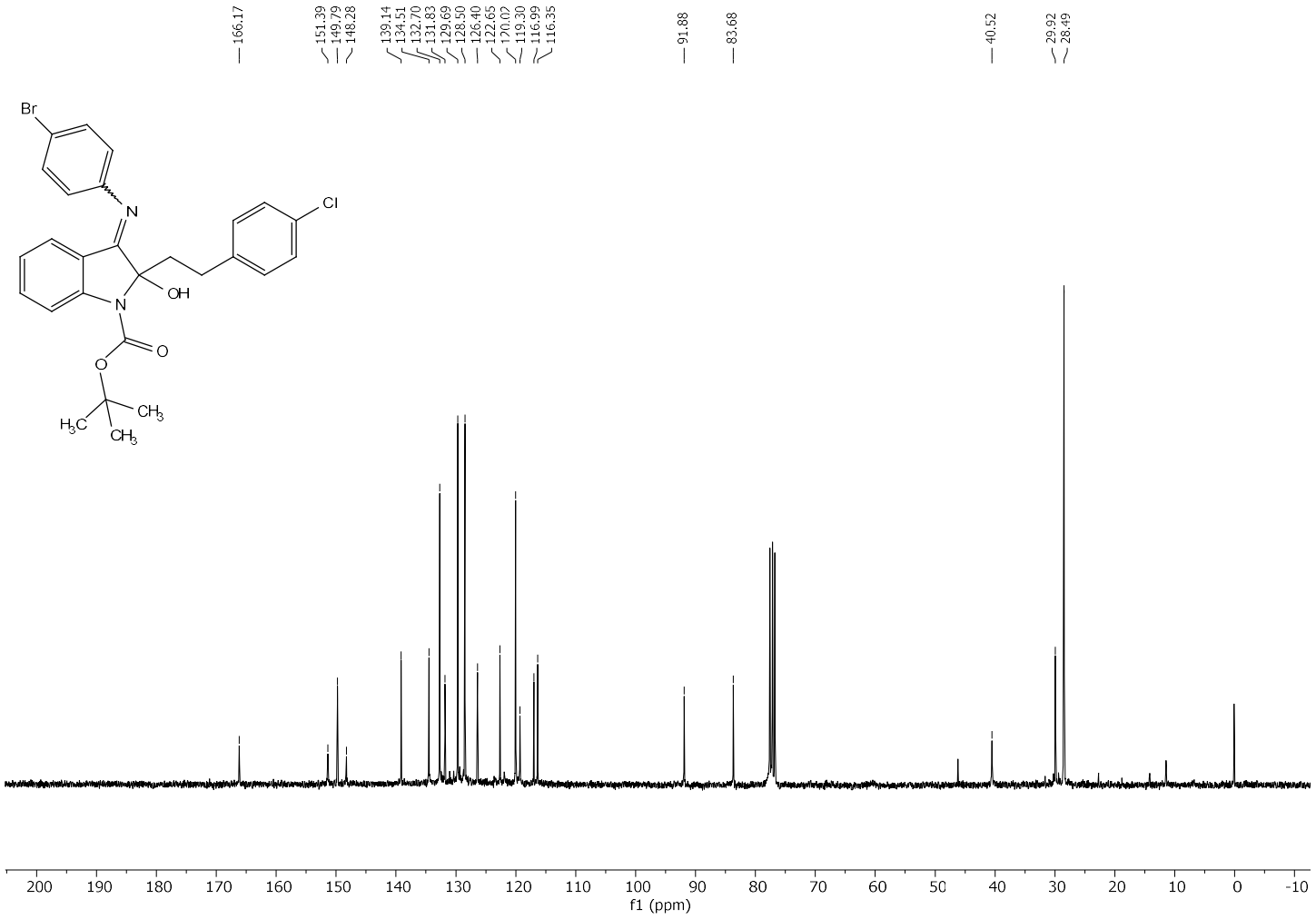
3e ^{13}C NMR spectrum



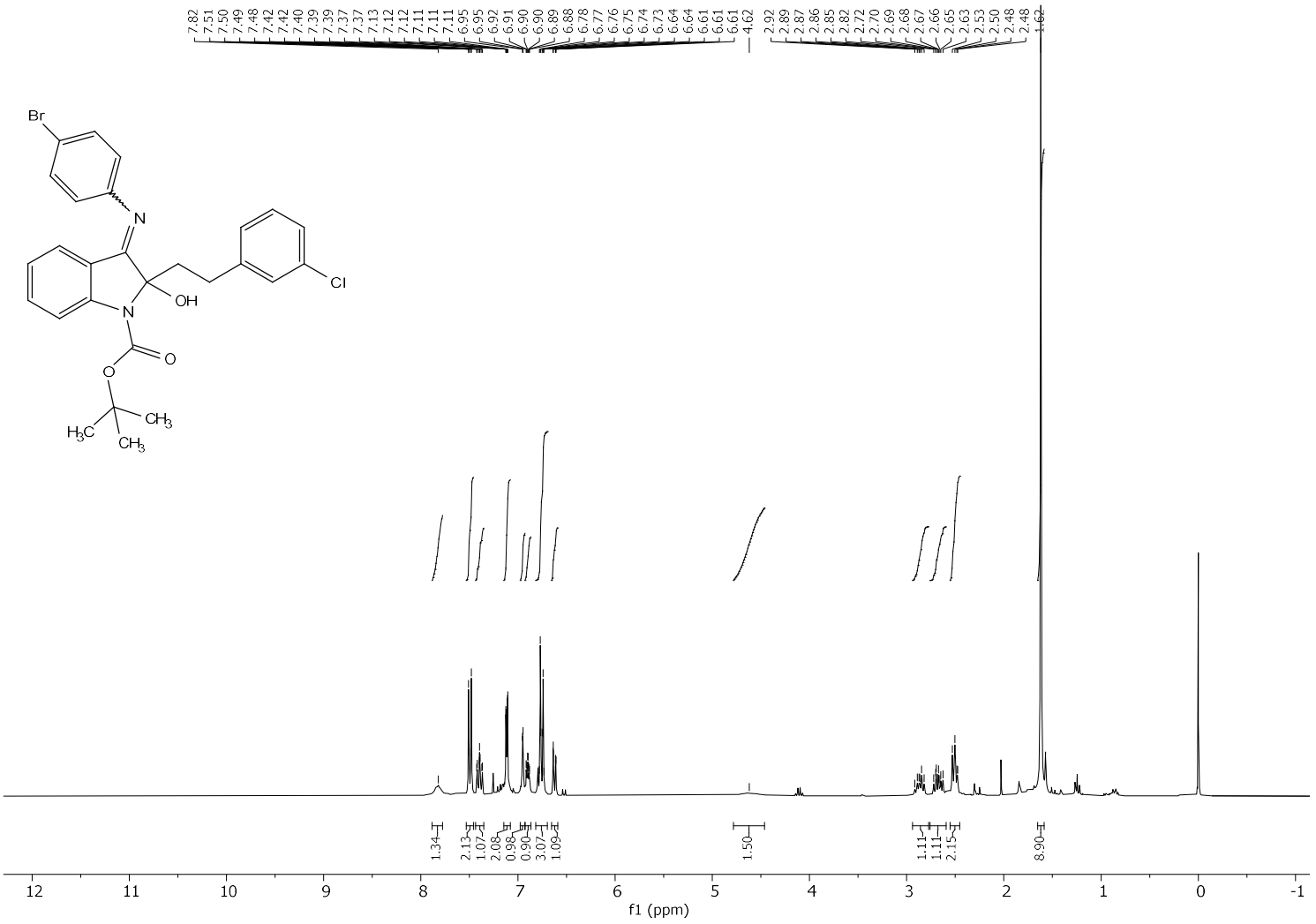
3f ^{1}H NMR spectrum



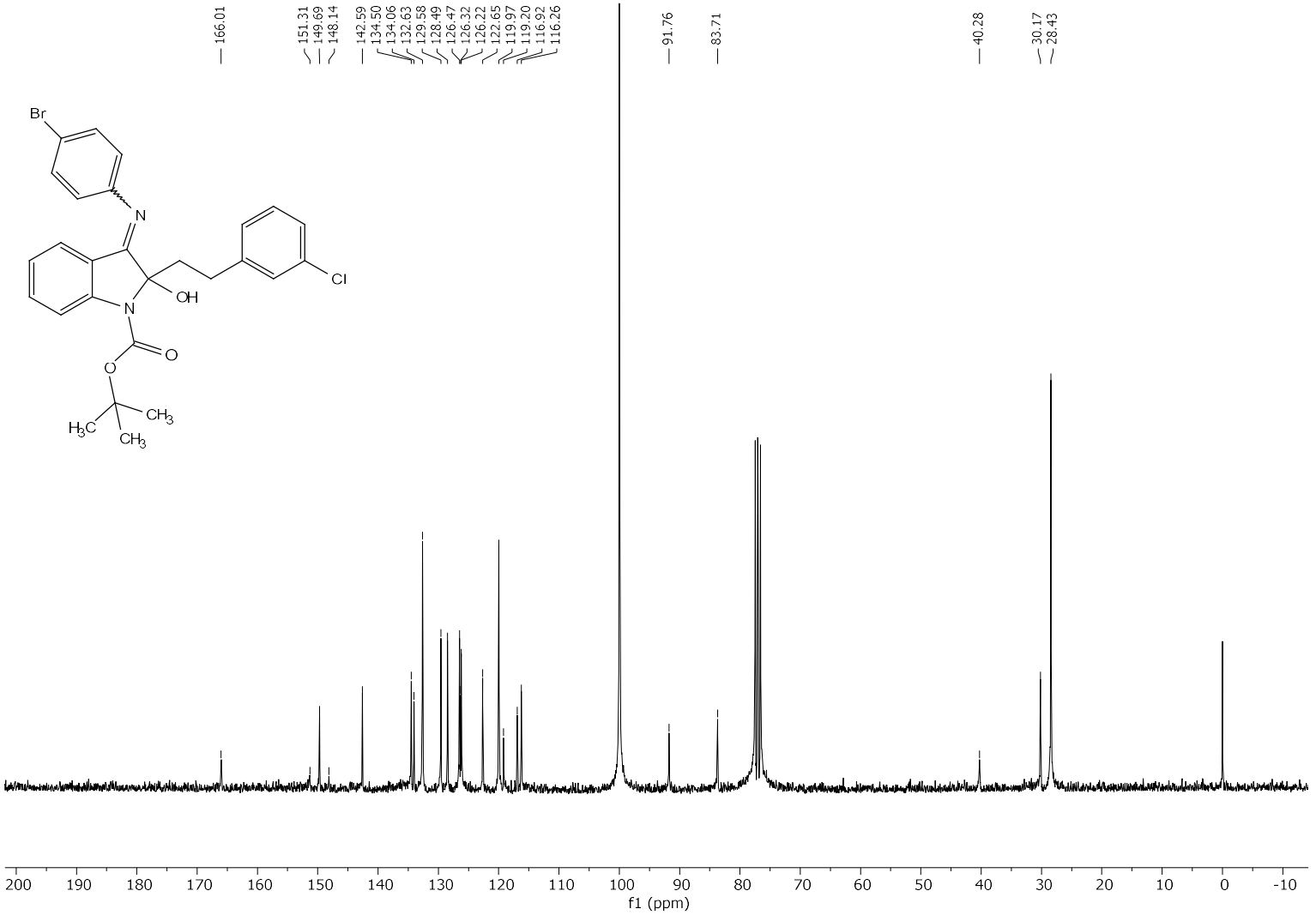
3f ^{13}C NMR spectrum



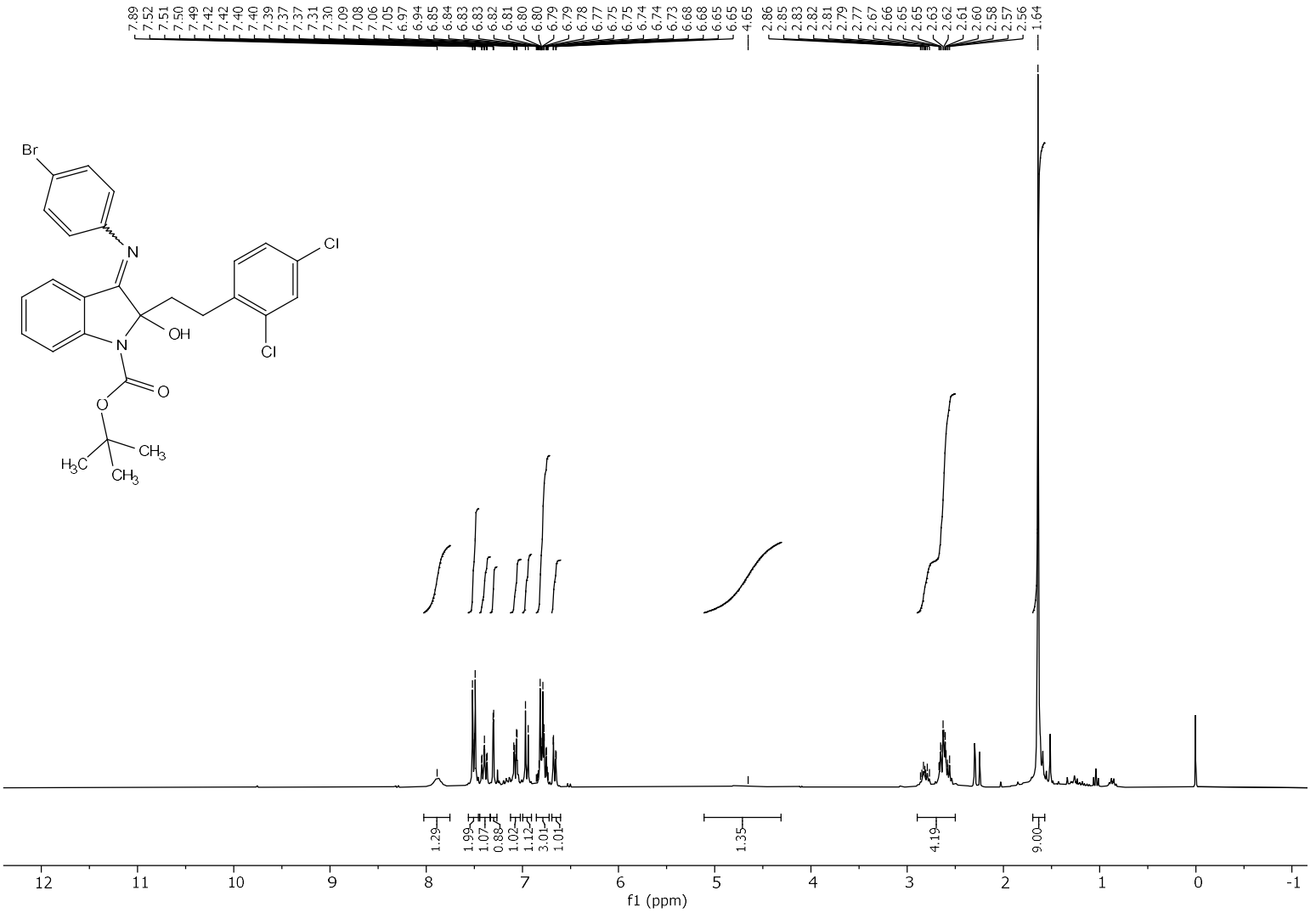
3g ^{1}H NMR spectrum



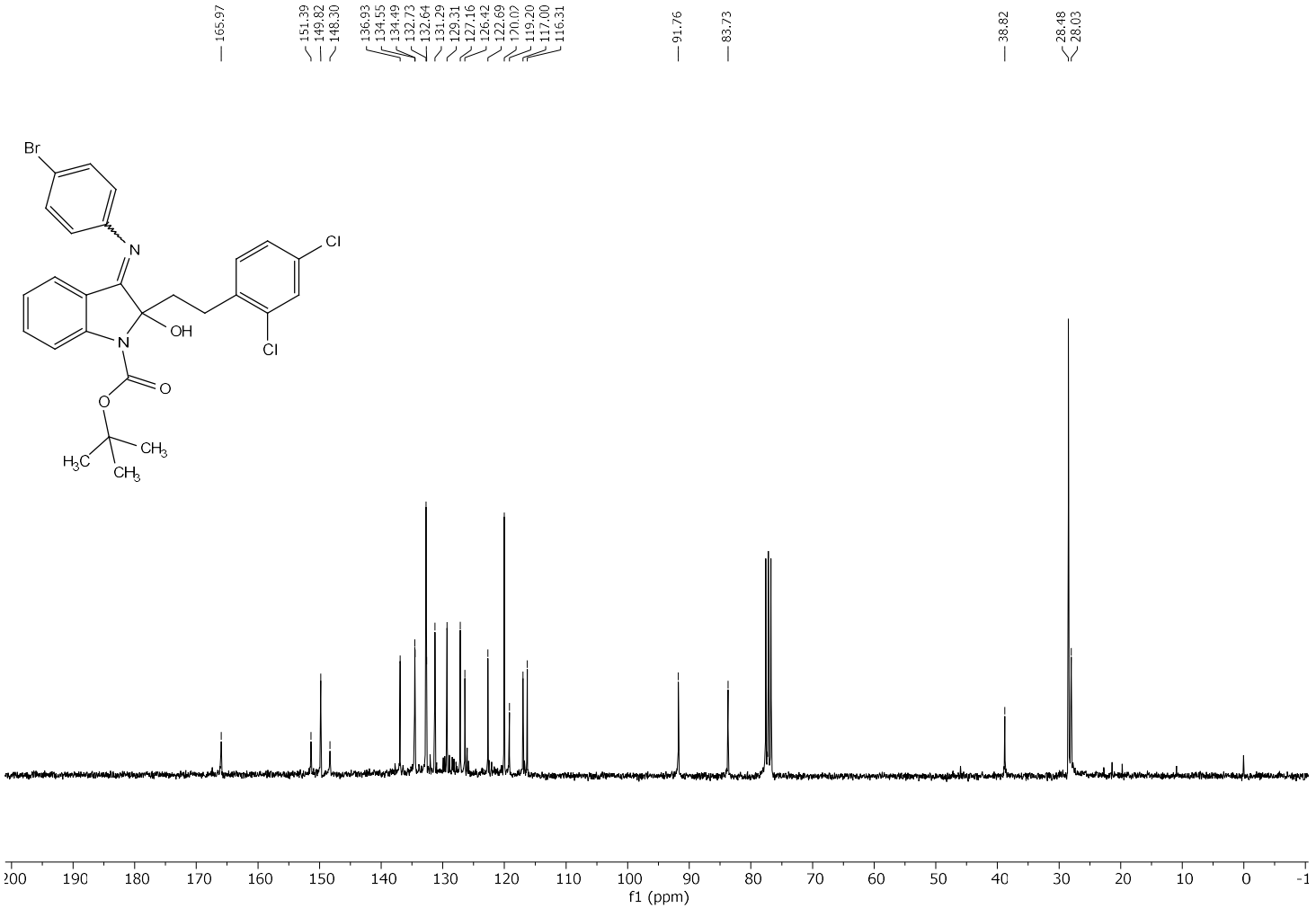
3g ^{13}C NMR spectrum



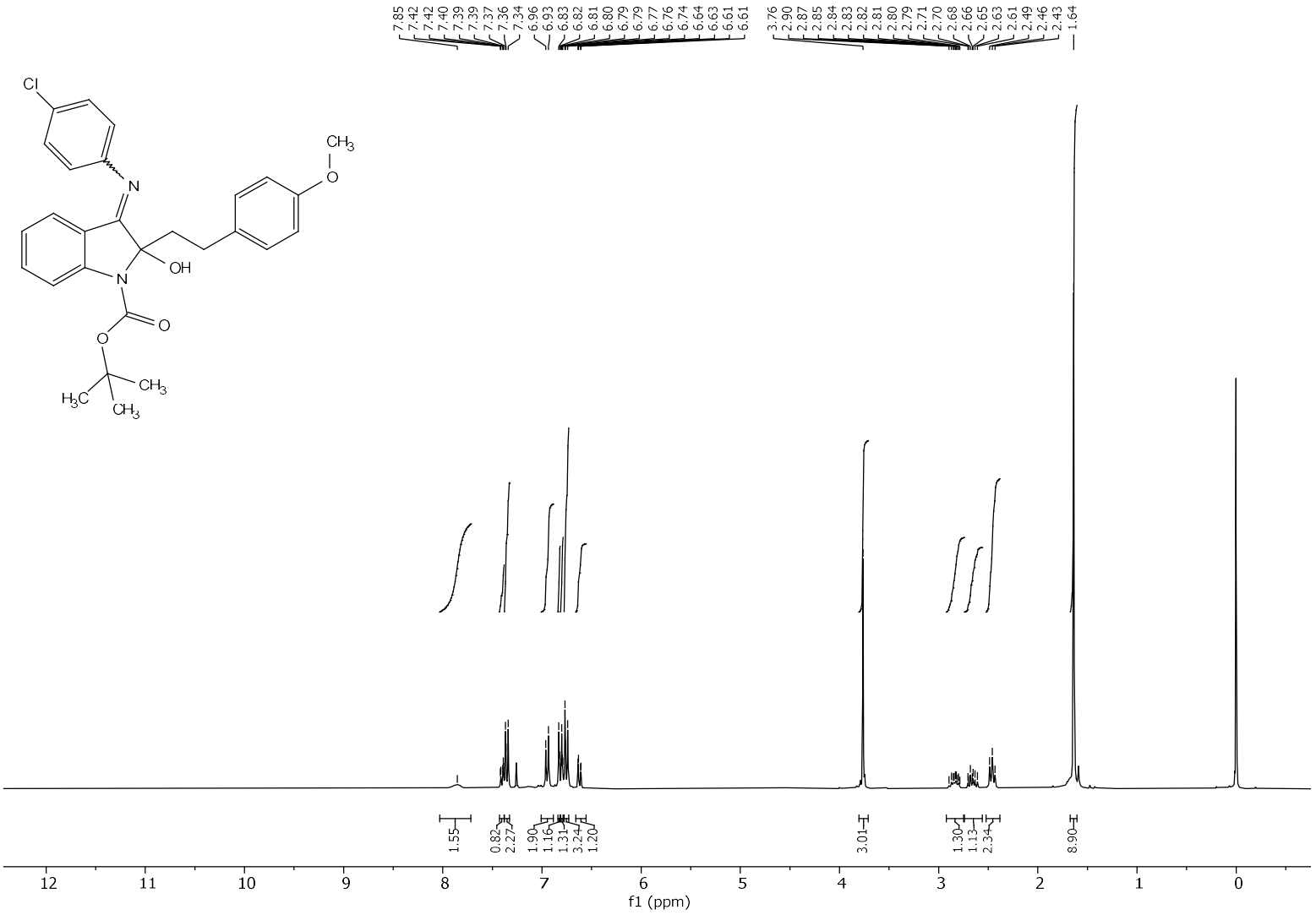
3h ^{1}H NMR spectrum



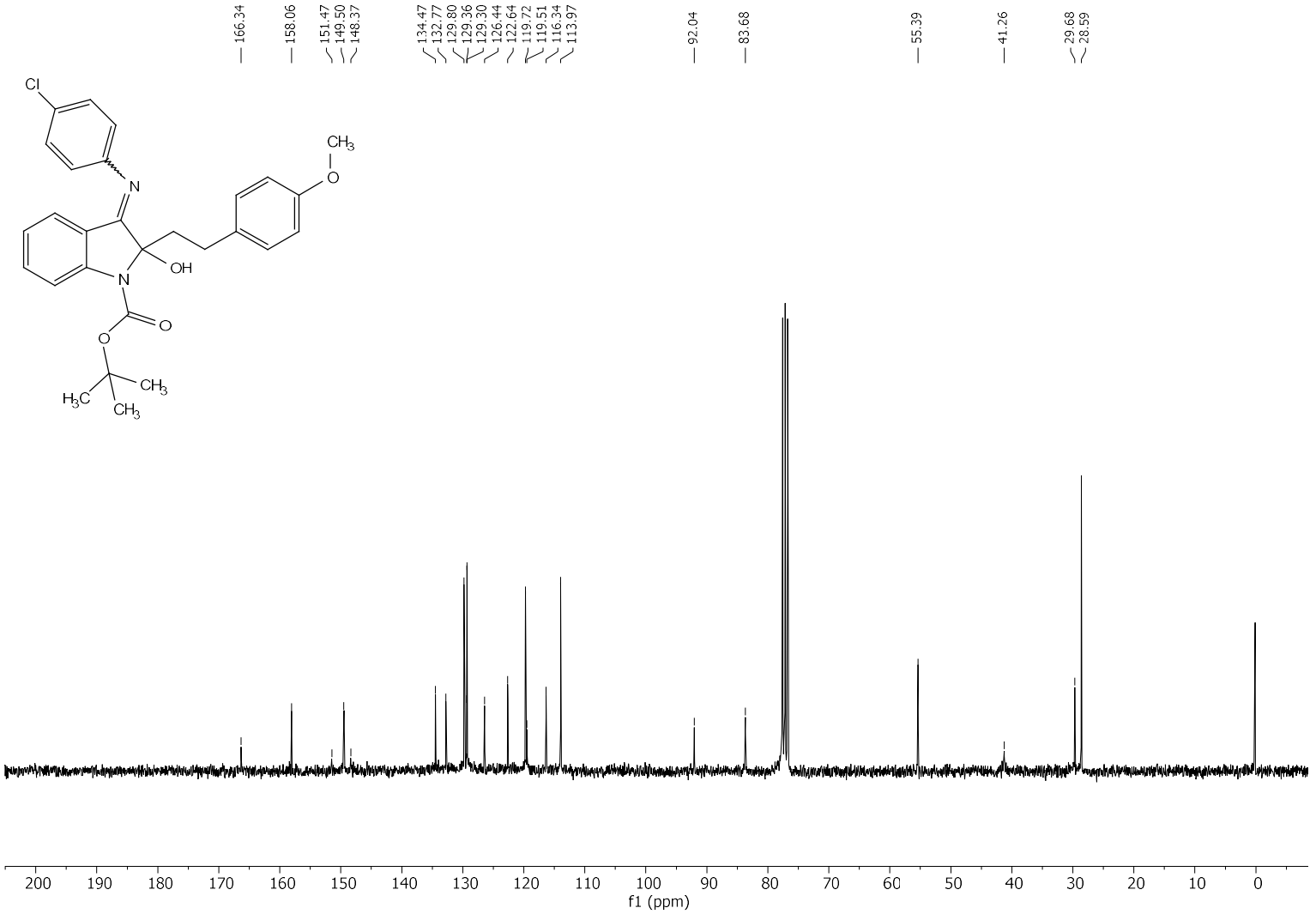
3h ^{13}C NMR spectrum



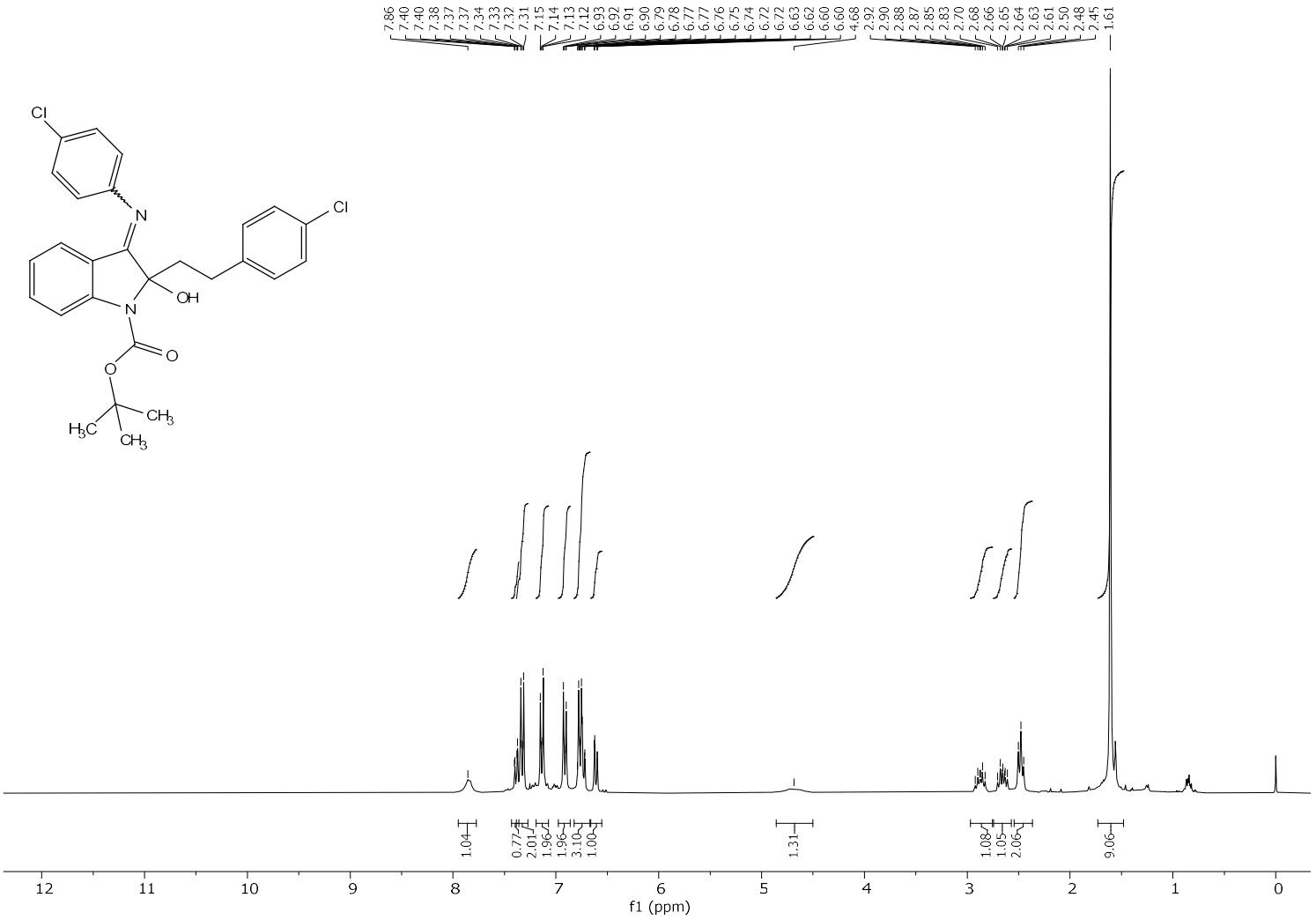
3i ^{1}H NMR spectrum



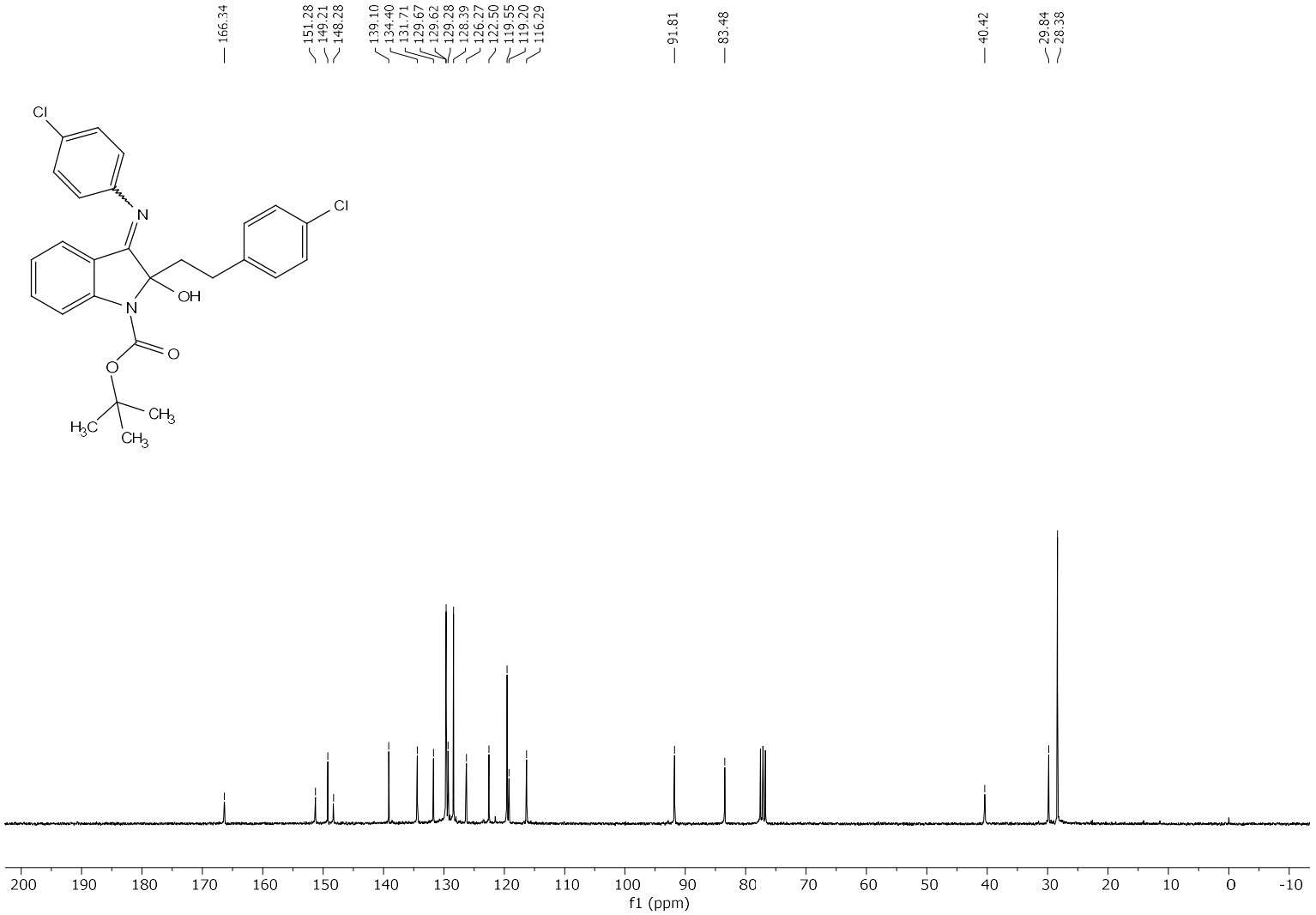
3i ^{13}C NMR spectrum



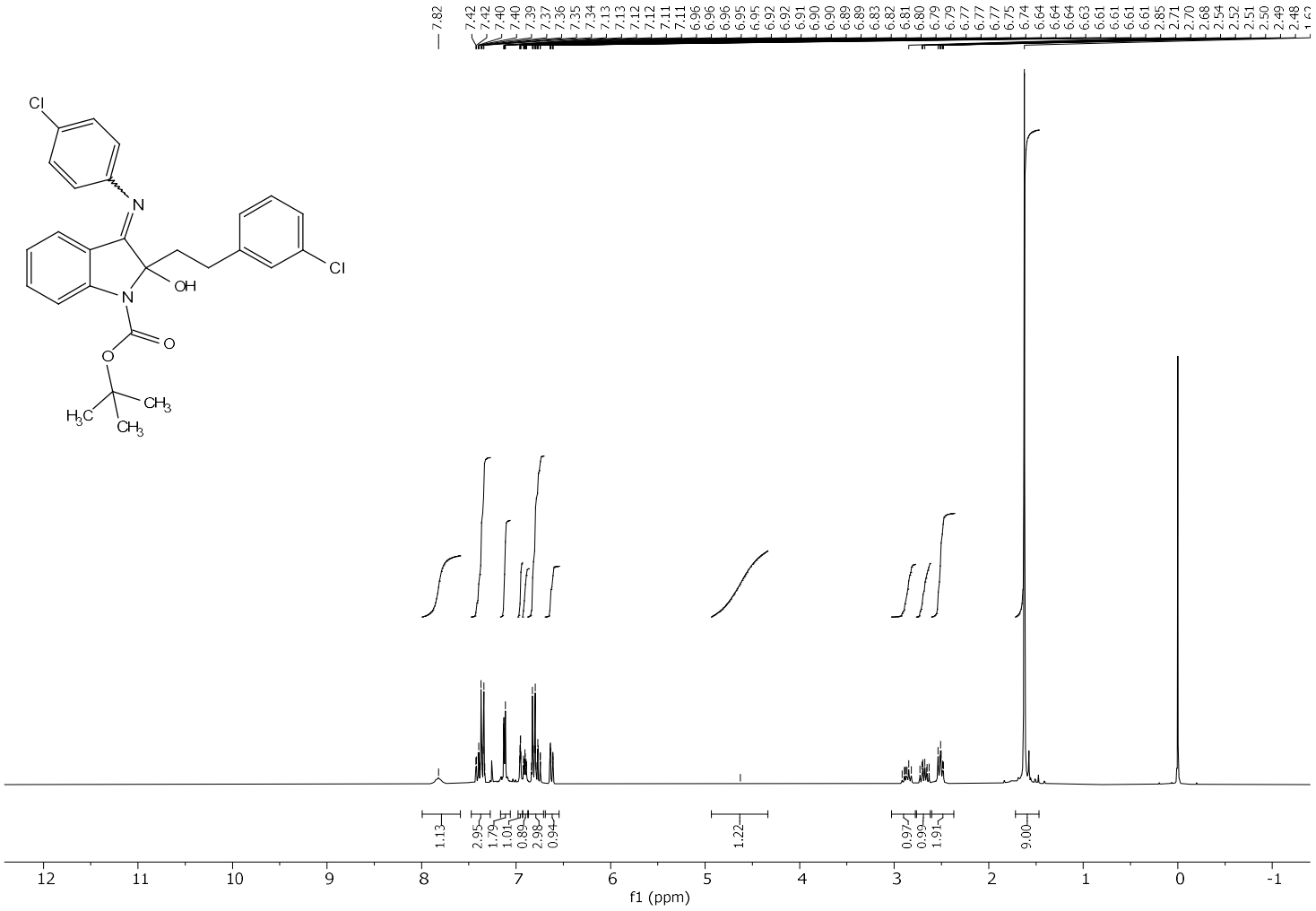
3j ^{1}H NMR spectrum



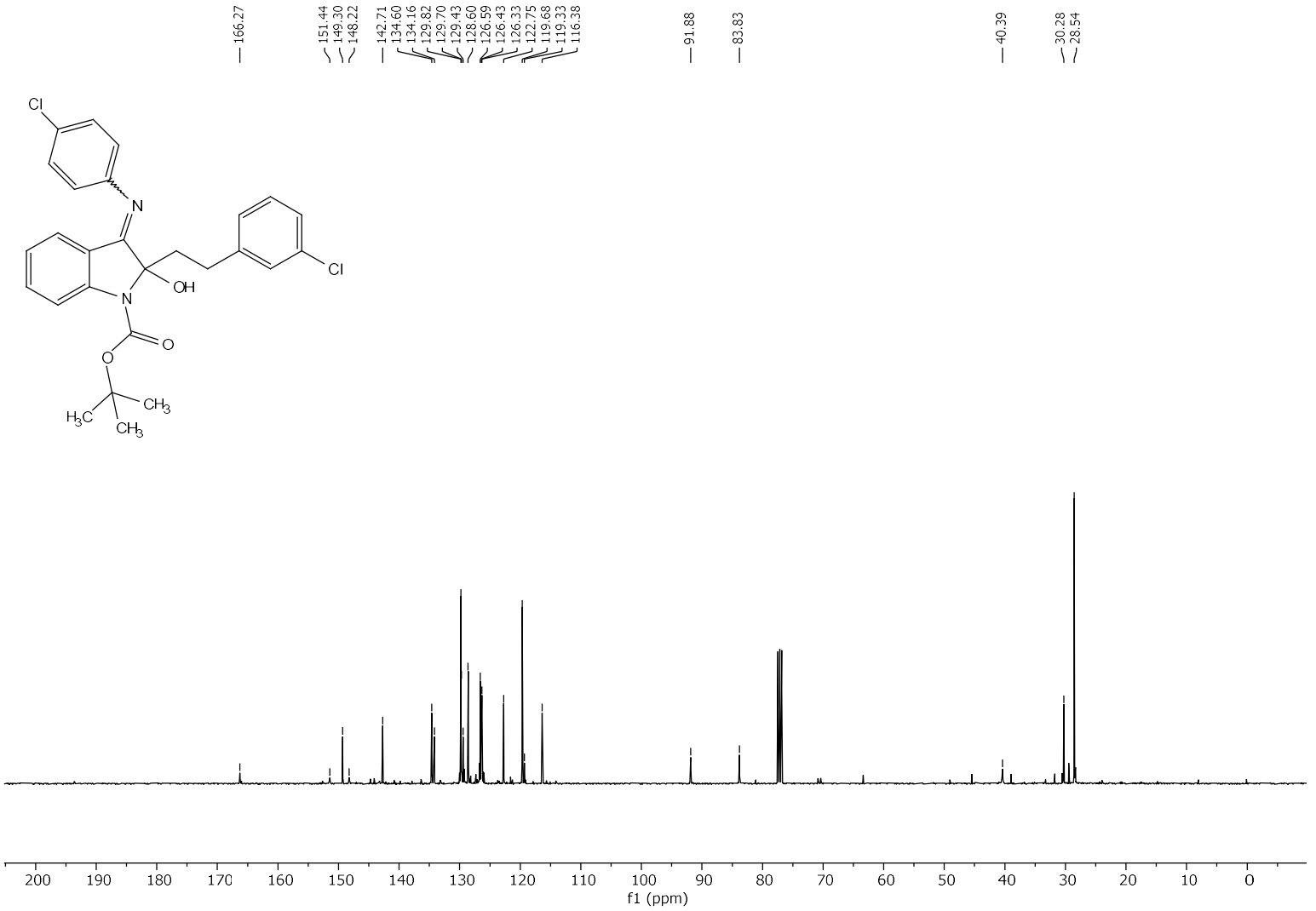
3j ^{13}C NMR spectrum



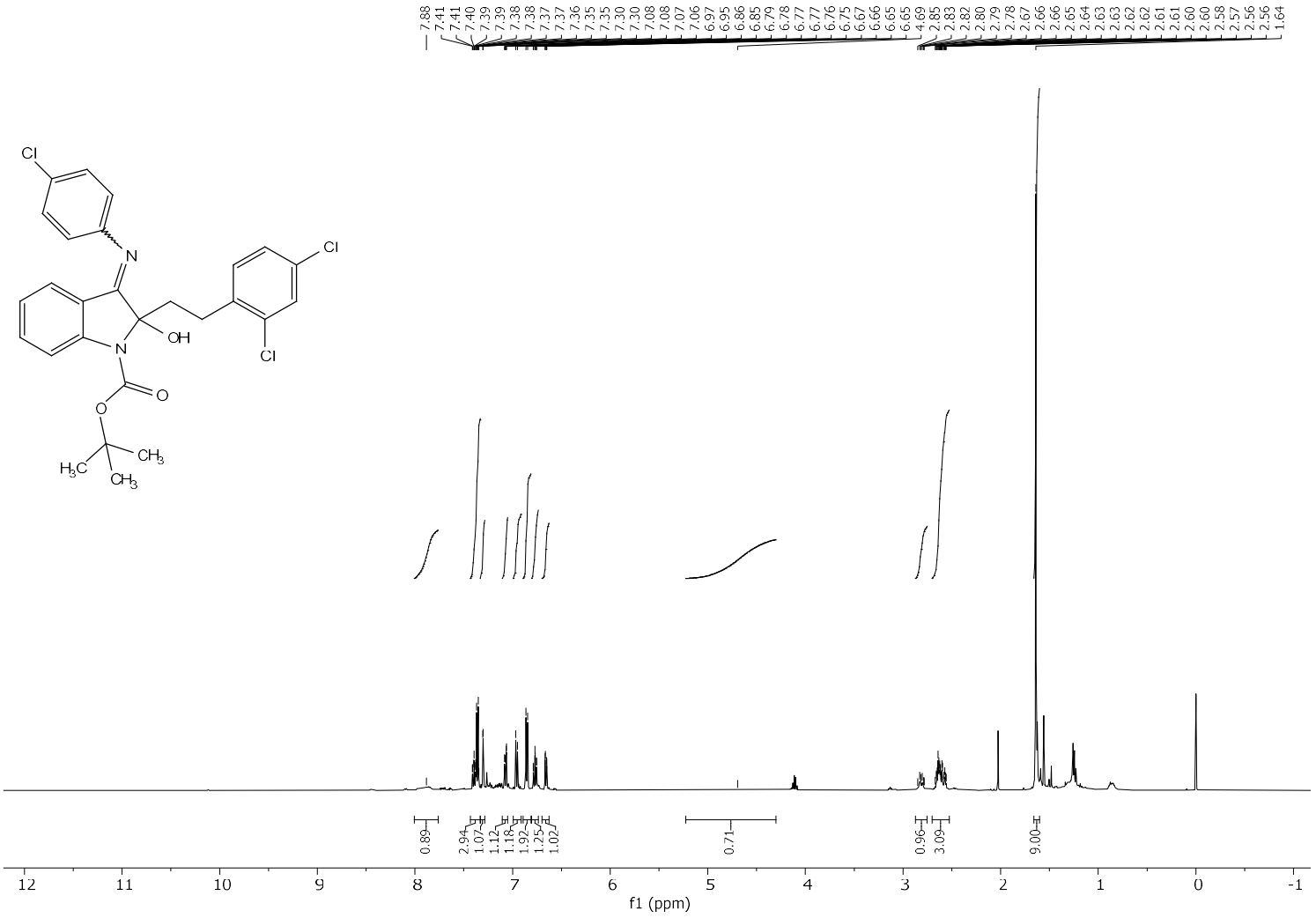
3k ^{1}H NMR spectrum



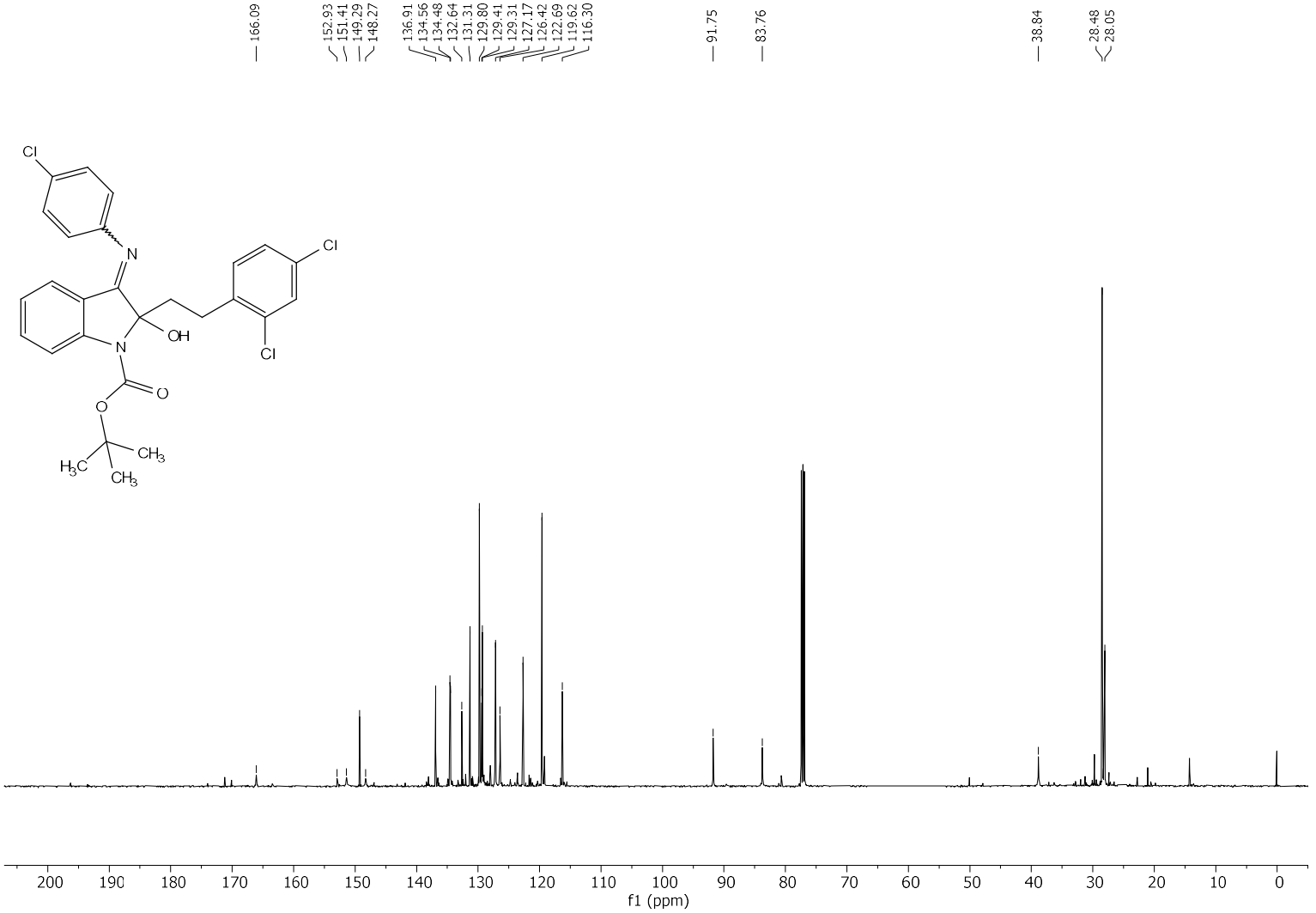
3k ^{13}C NMR spectrum



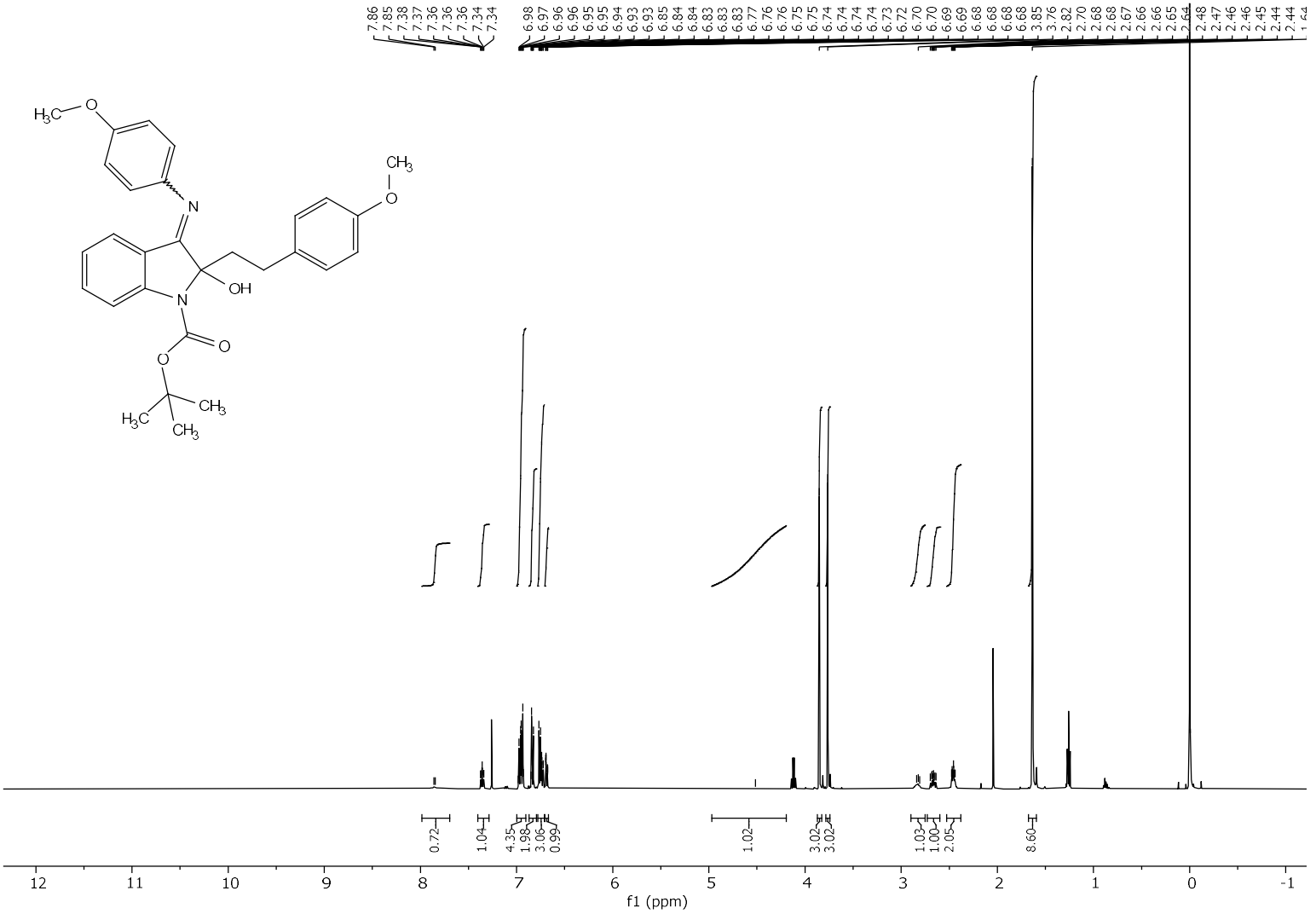
3l ^{1}H NMR spectrum



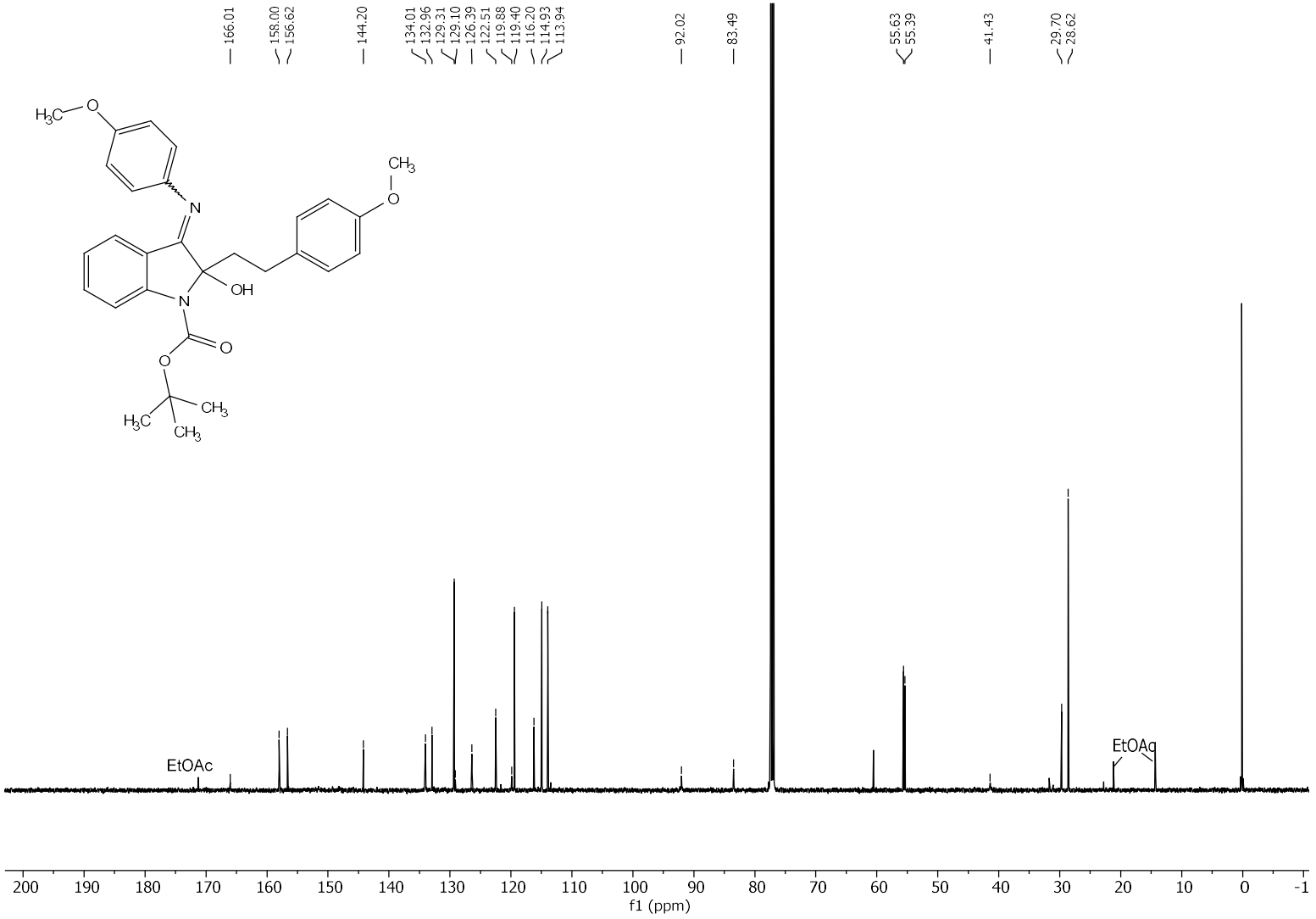
3l ^{13}C NMR spectrum



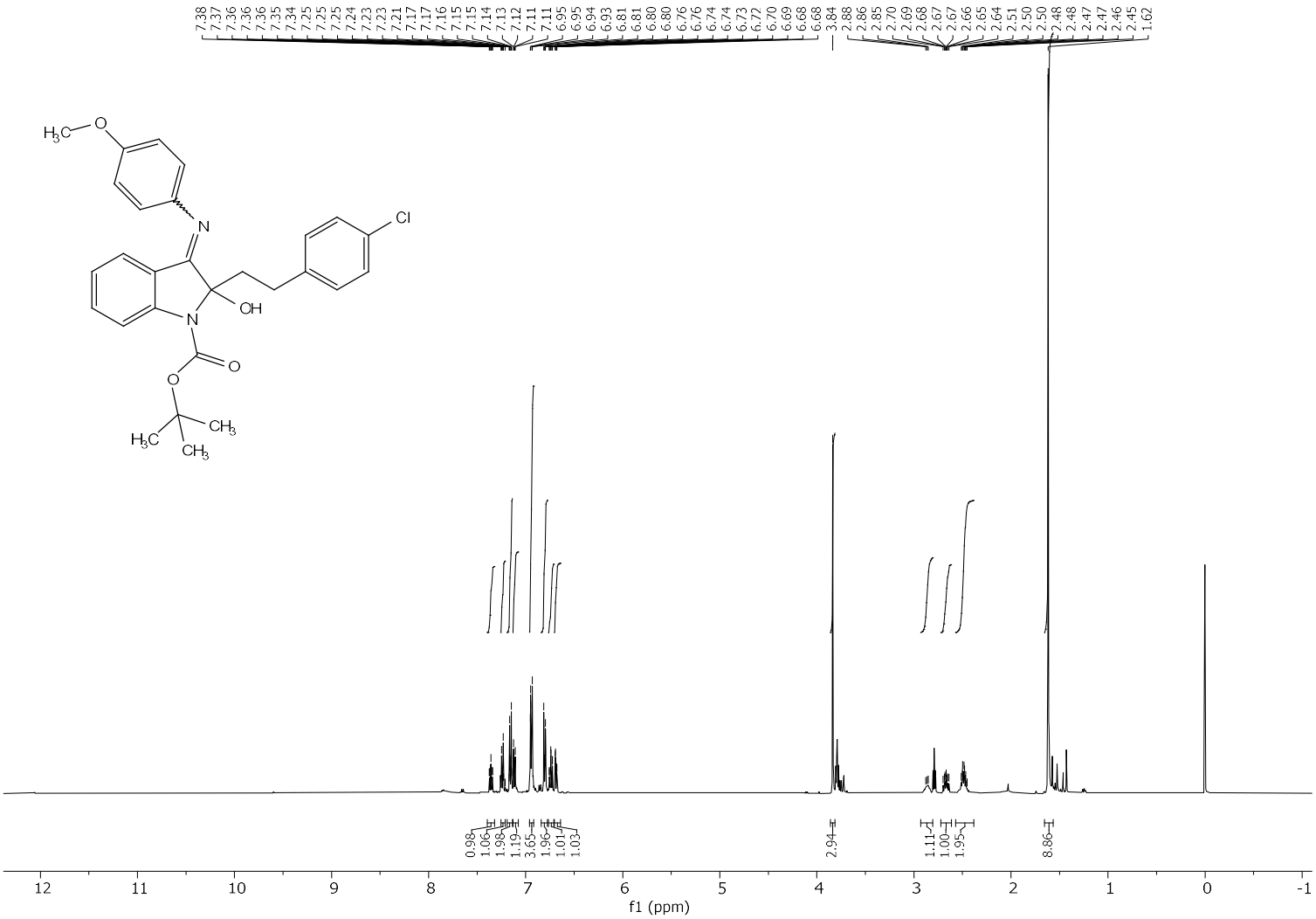
3m ^{1}H NMR spectrum



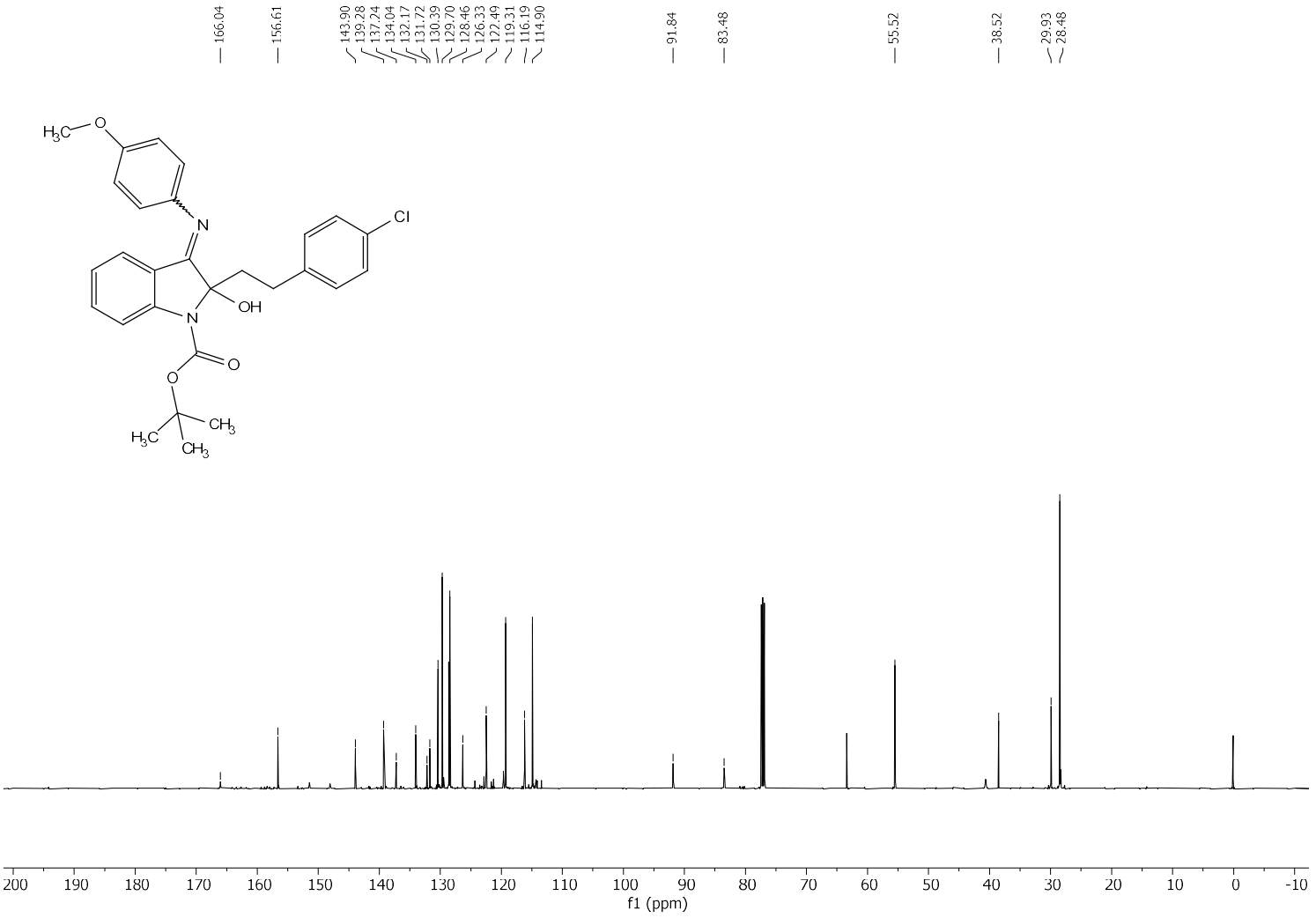
3m ^{13}C NMR spectrum



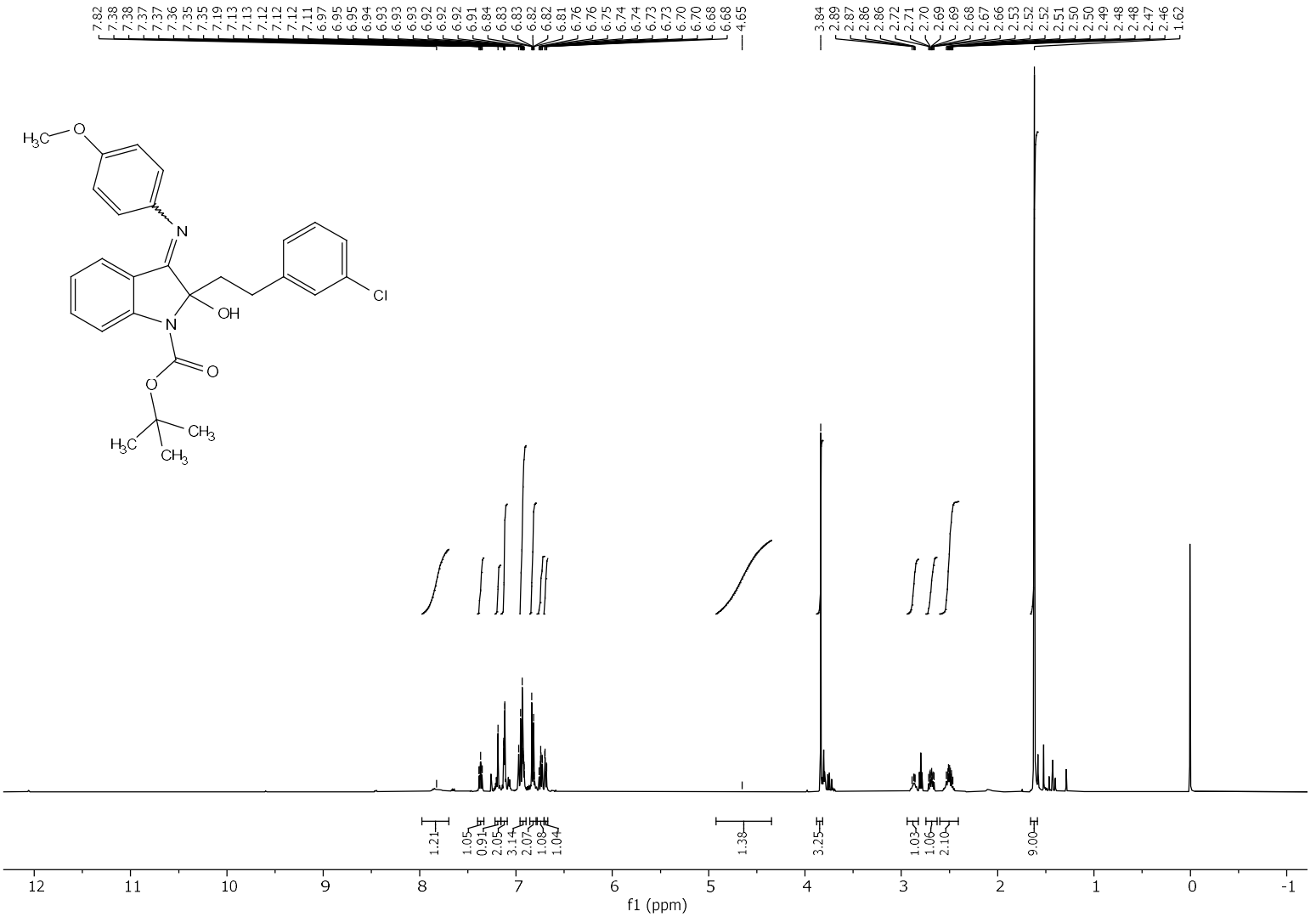
3n ^{1}H NMR spectrum



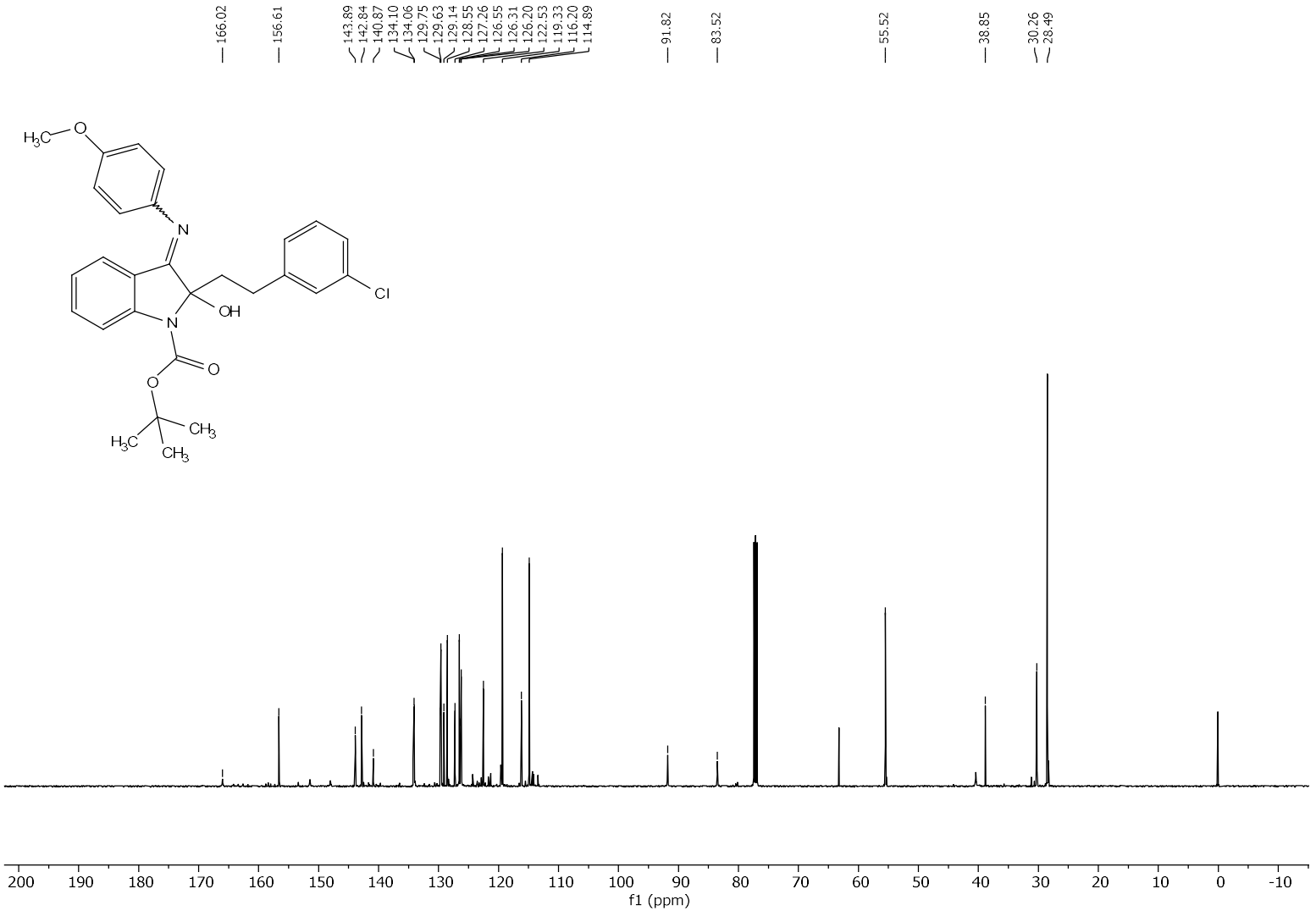
3n ^{13}C NMR spectrum



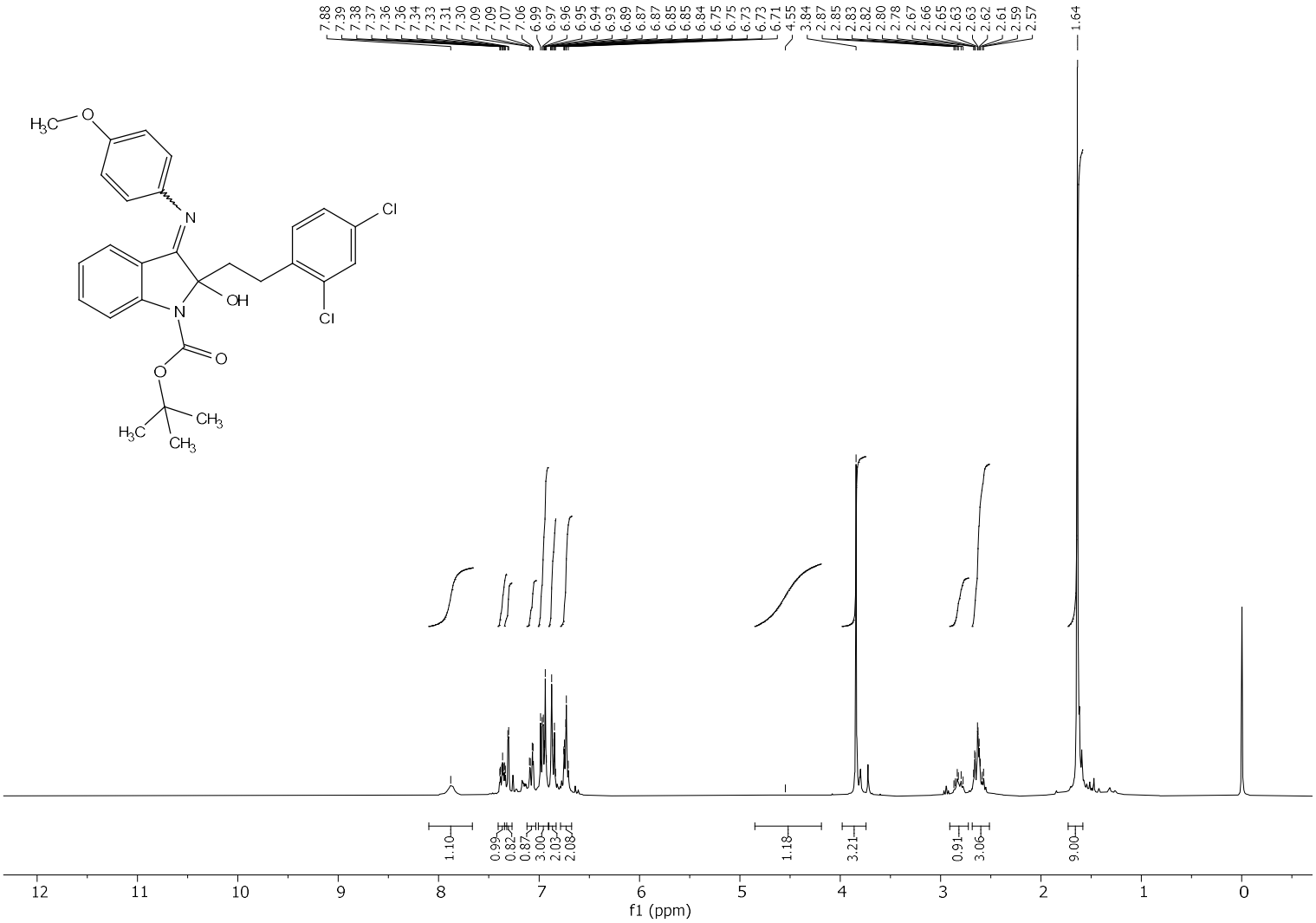
3o ^{1}H NMR spectrum



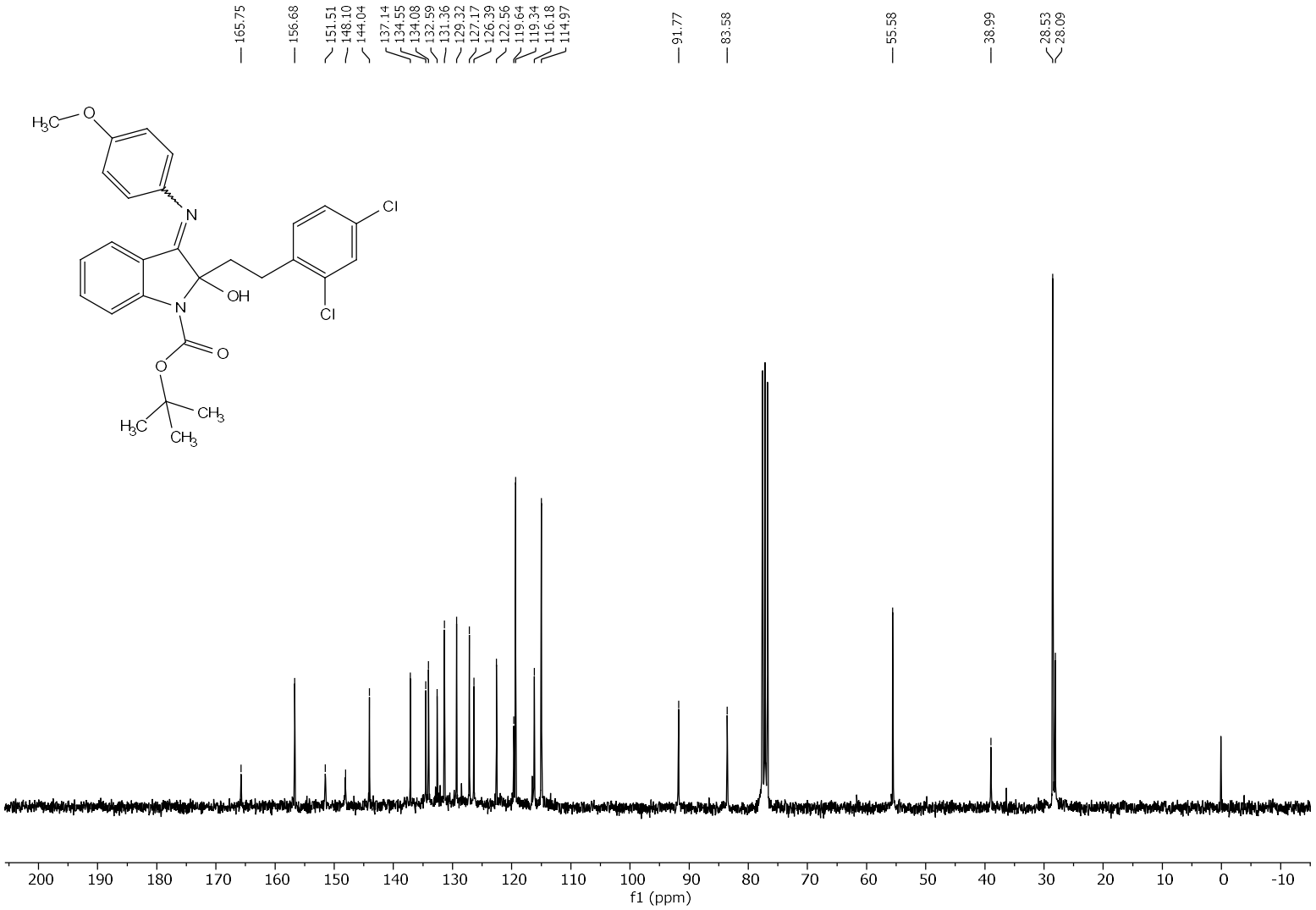
3o ^{13}C NMR spectrum



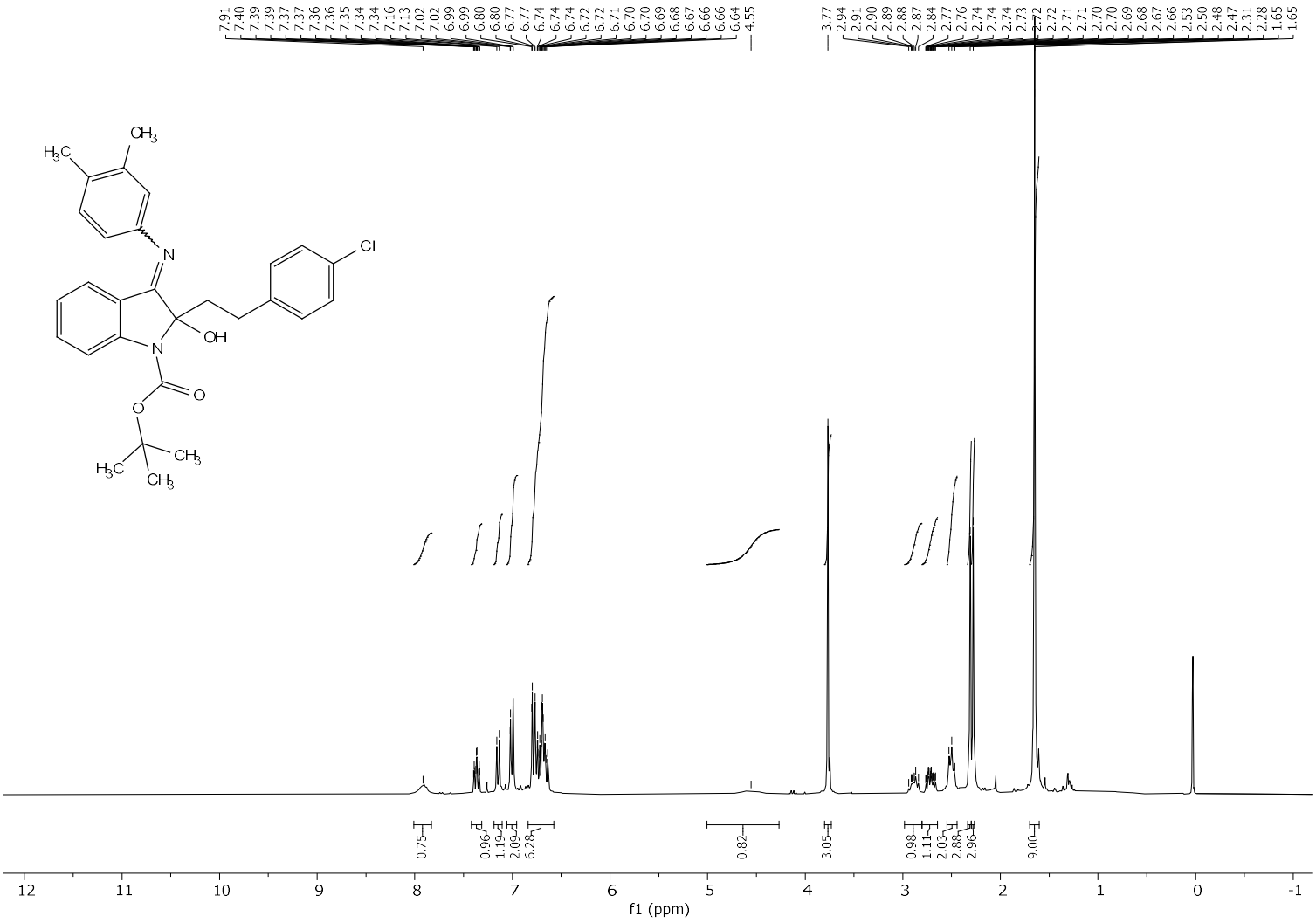
3p ^{1}H NMR spectrum



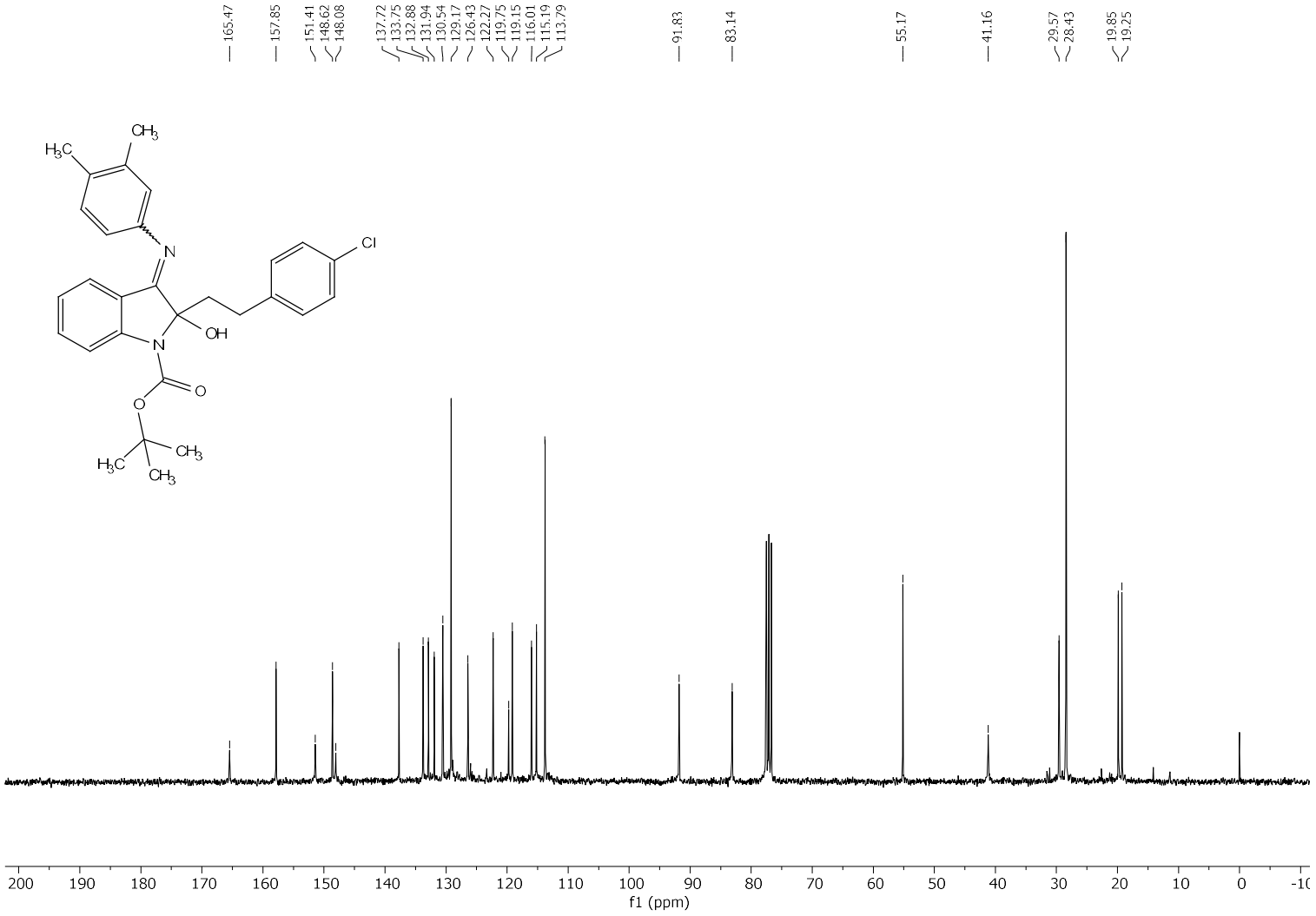
3p ^{13}C NMR spectrum



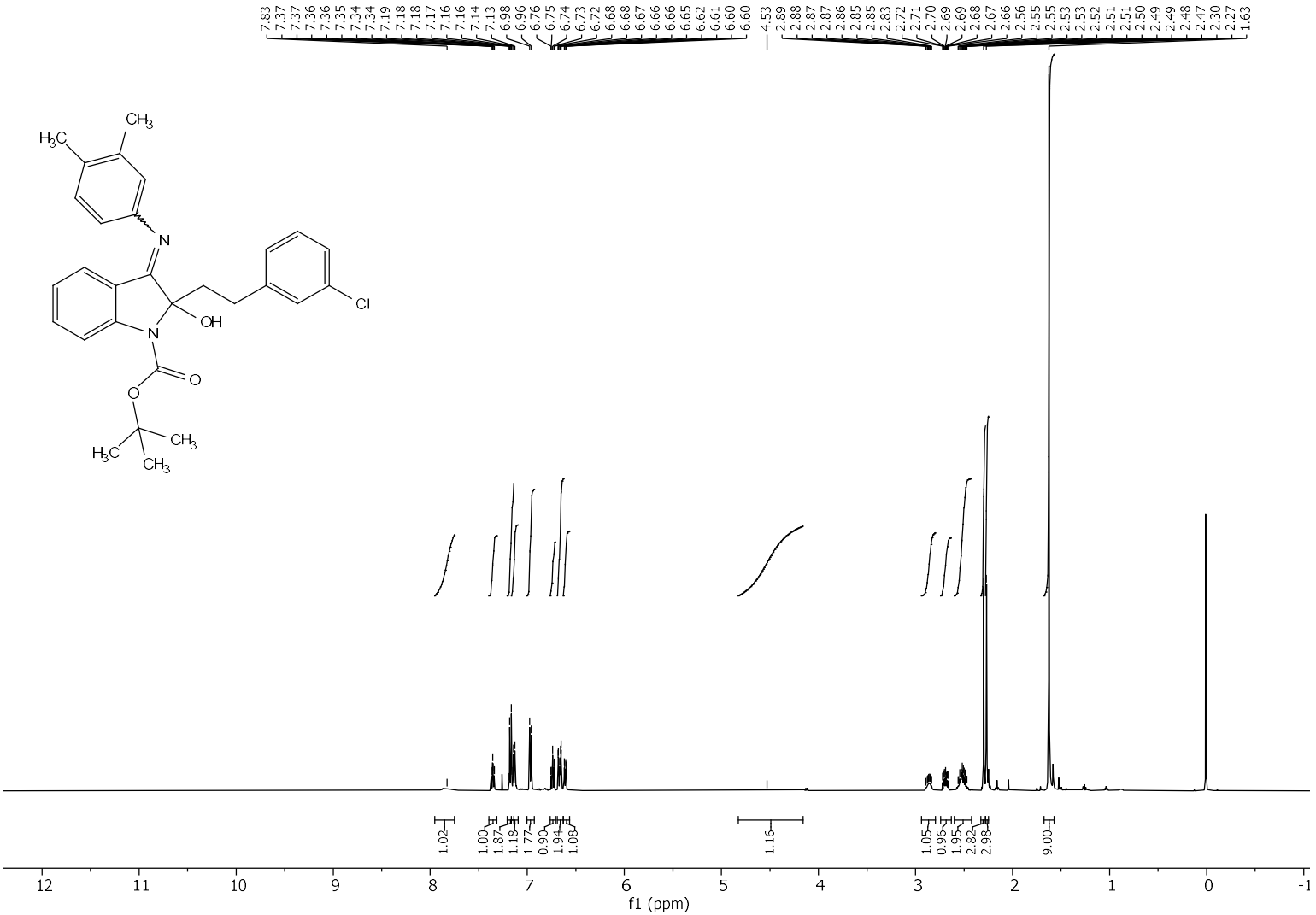
3q ^{1}H NMR spectrum



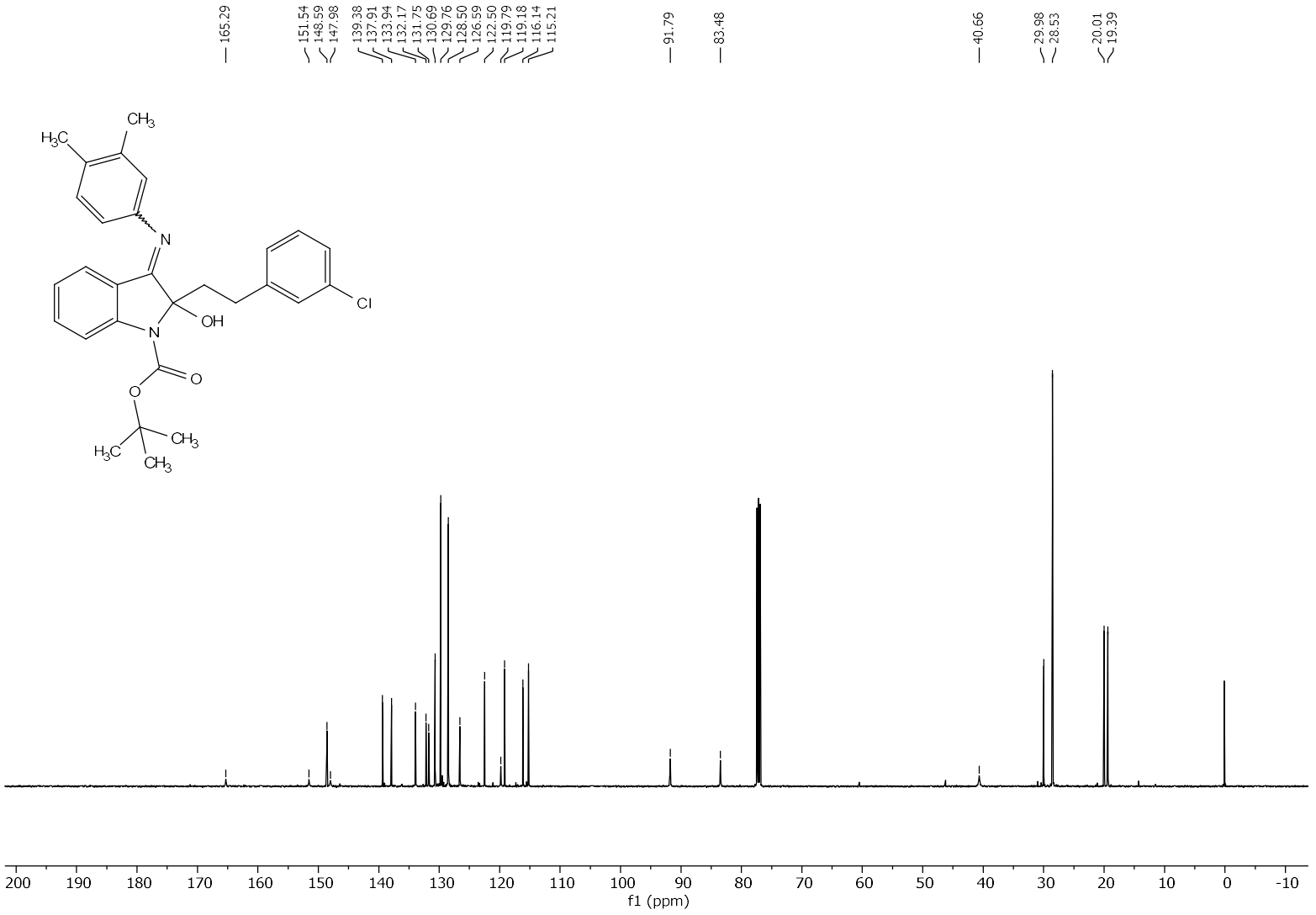
3q ^{13}C NMR spectrum



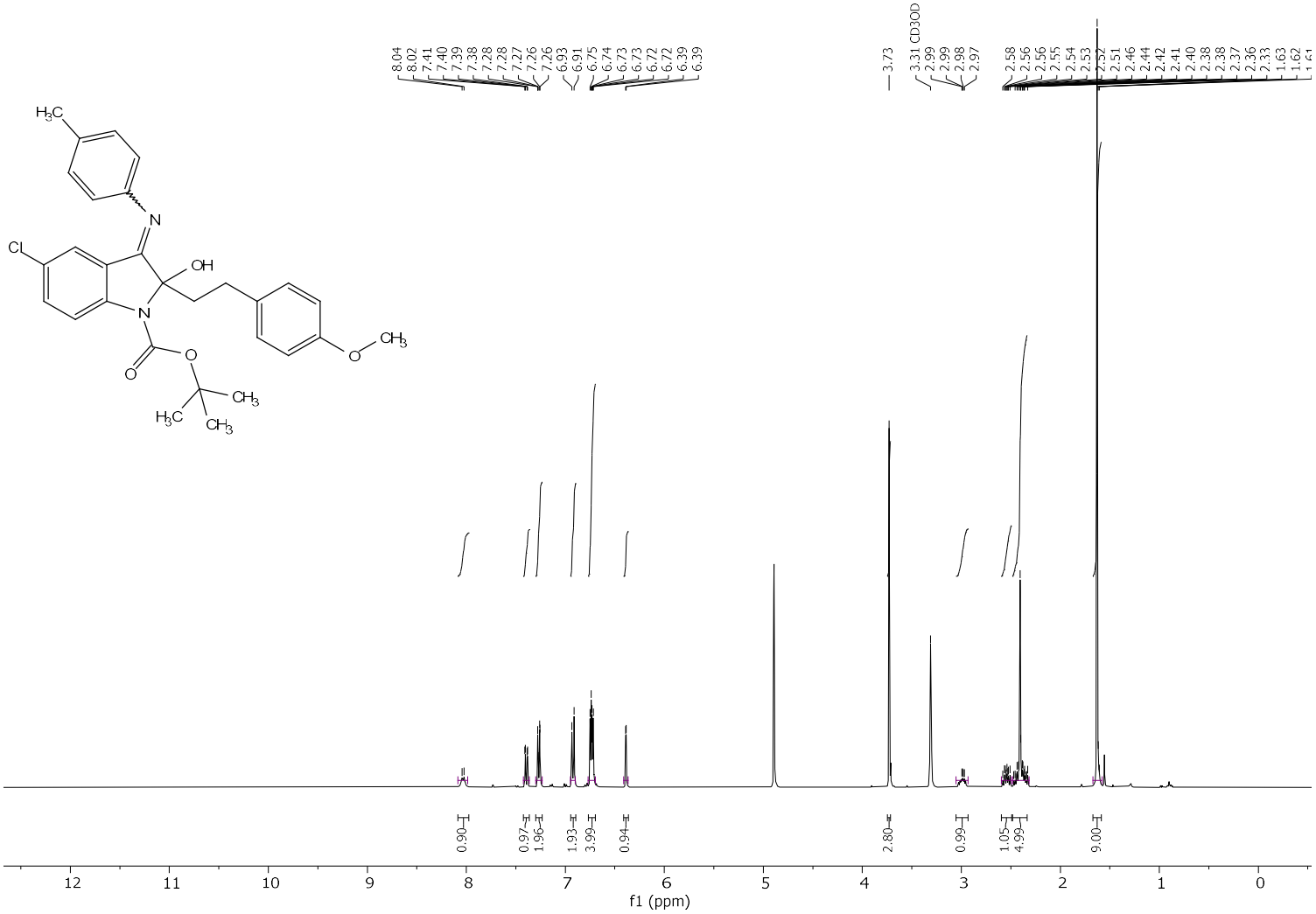
3r ^{1}H NMR spectrum



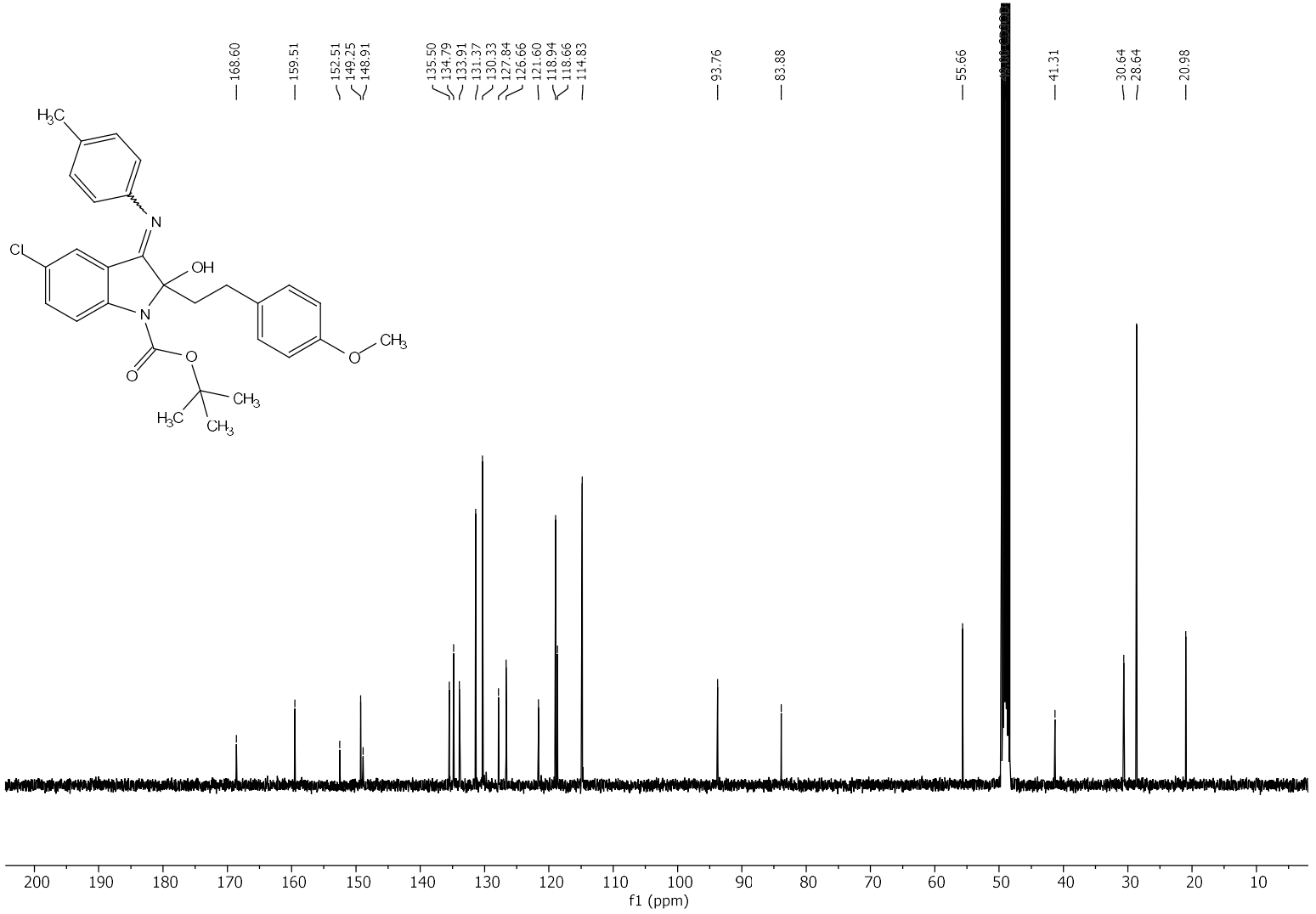
3r ^{13}C NMR spectrum



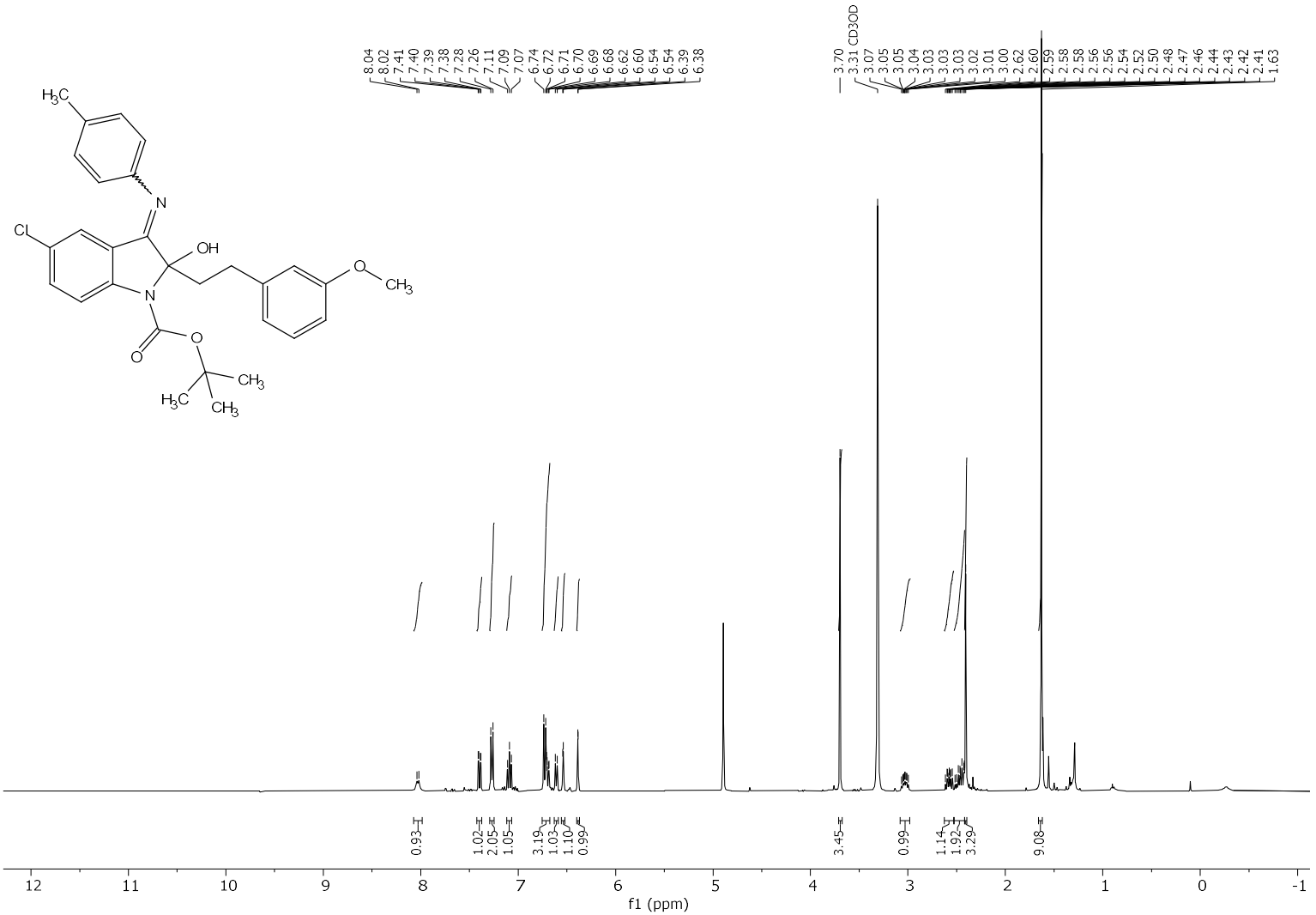
3s ^{1}H NMR spectrum



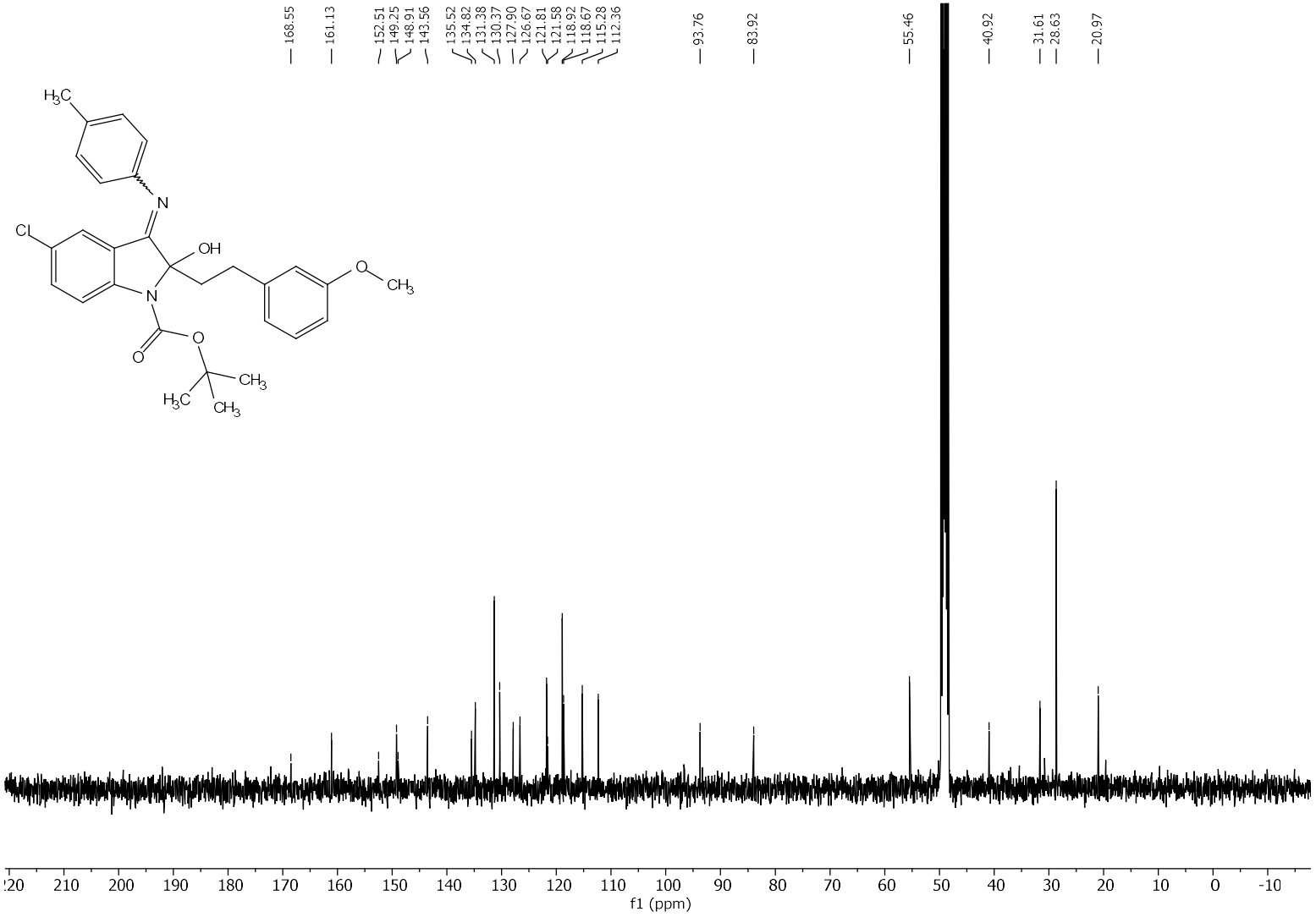
3s ^{13}C NMR spectrum



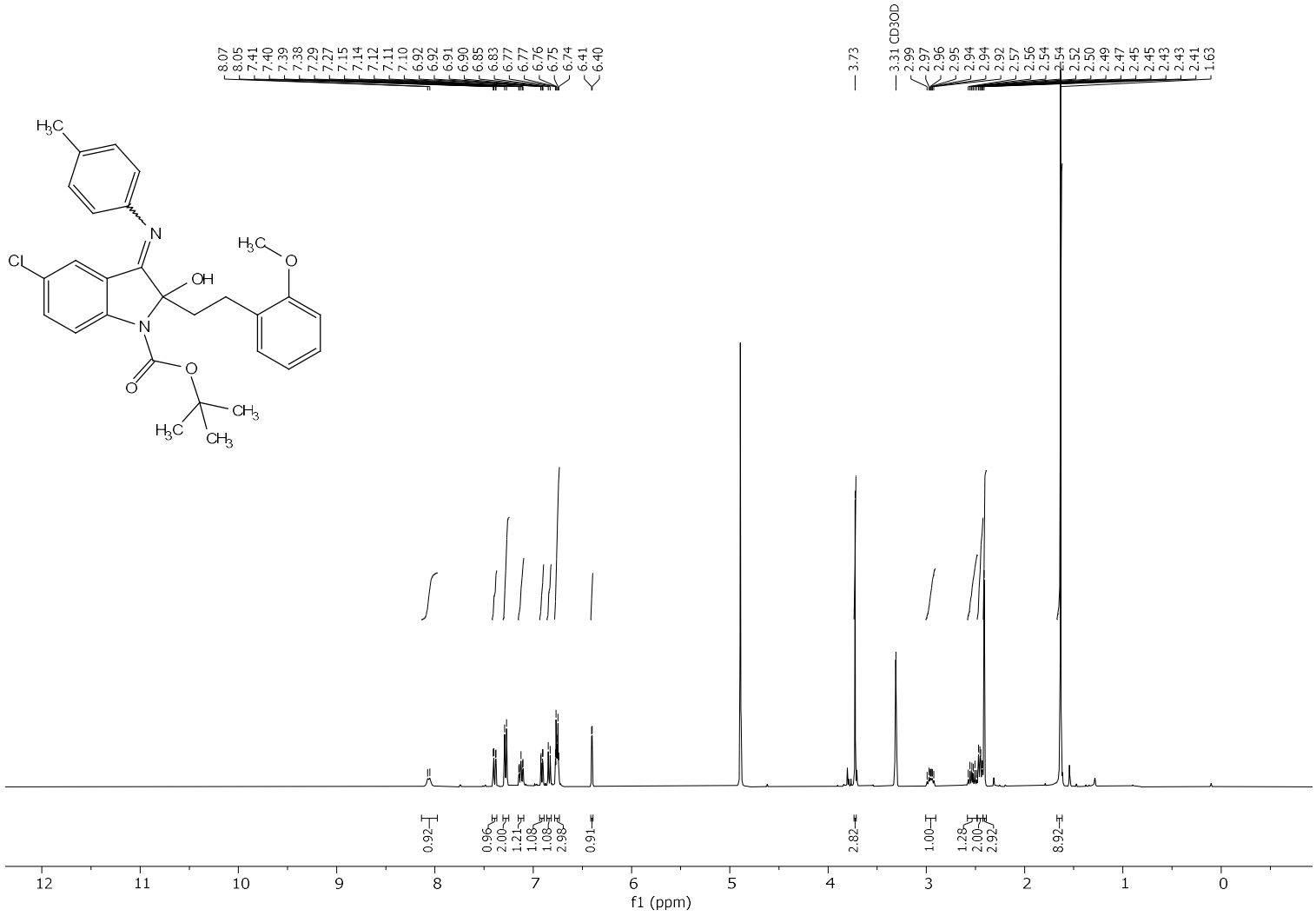
3t ^{1}H NMR spectrum



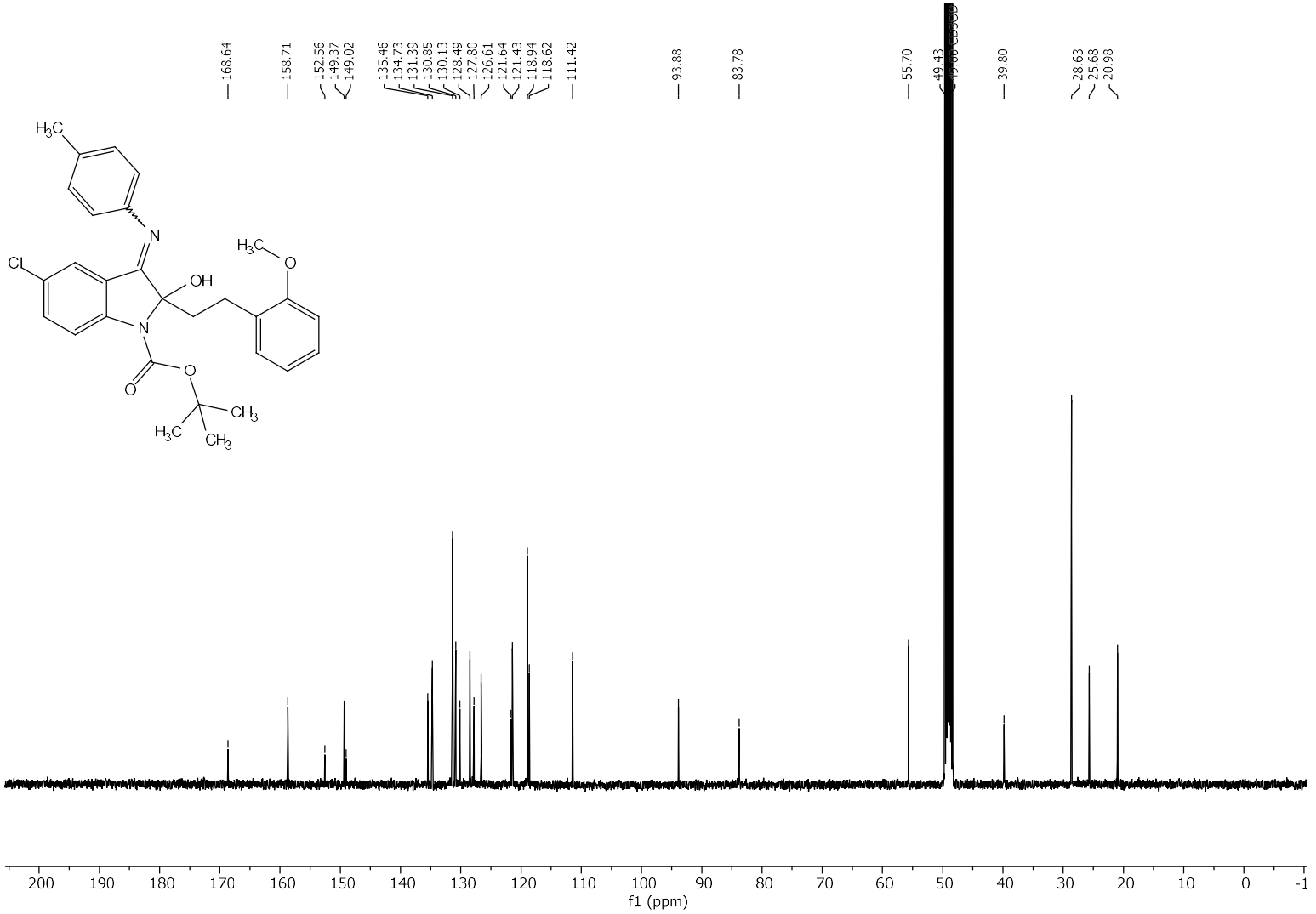
3t ^{13}C NMR spectrum



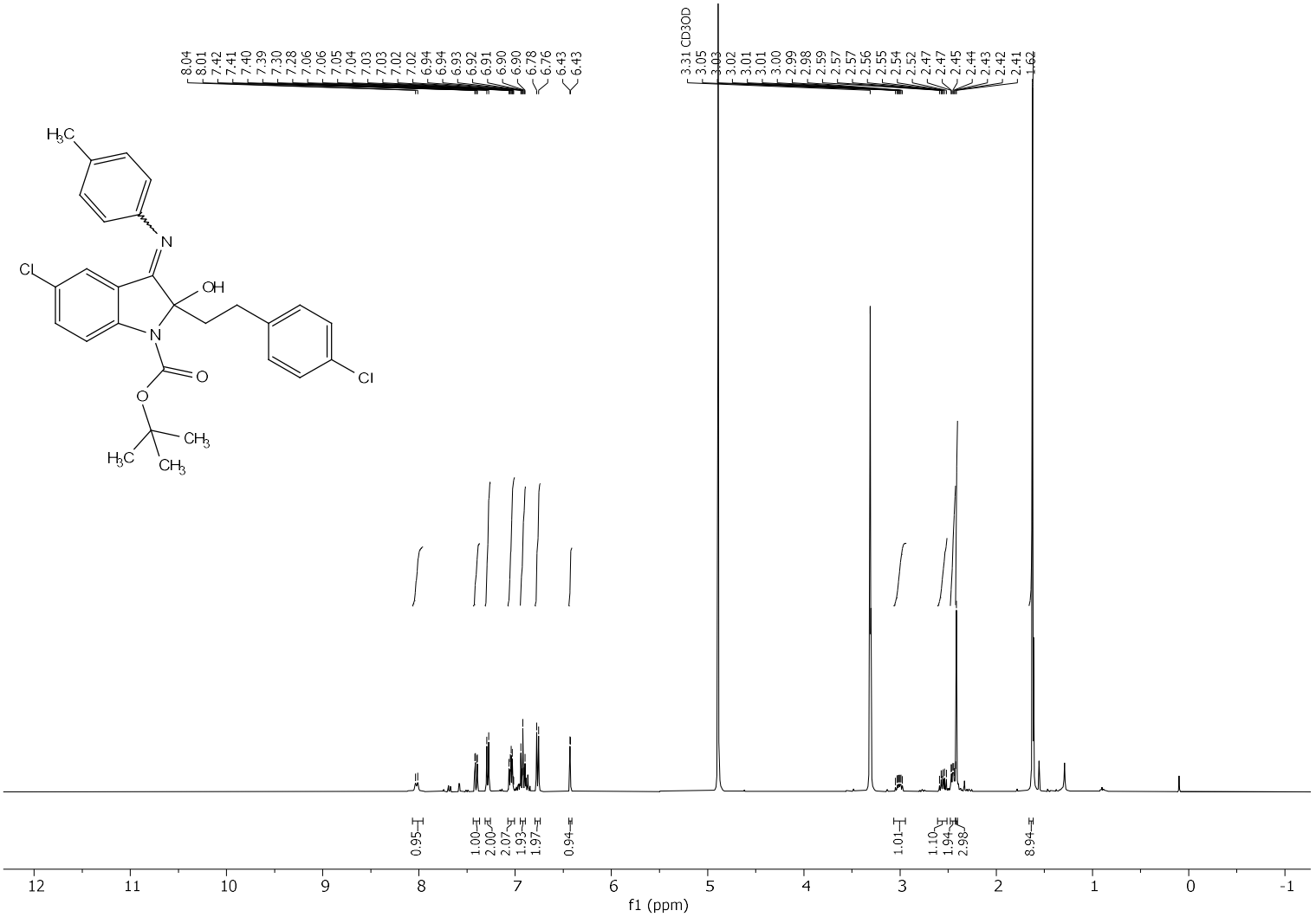
3u ^{1}H NMR spectrum



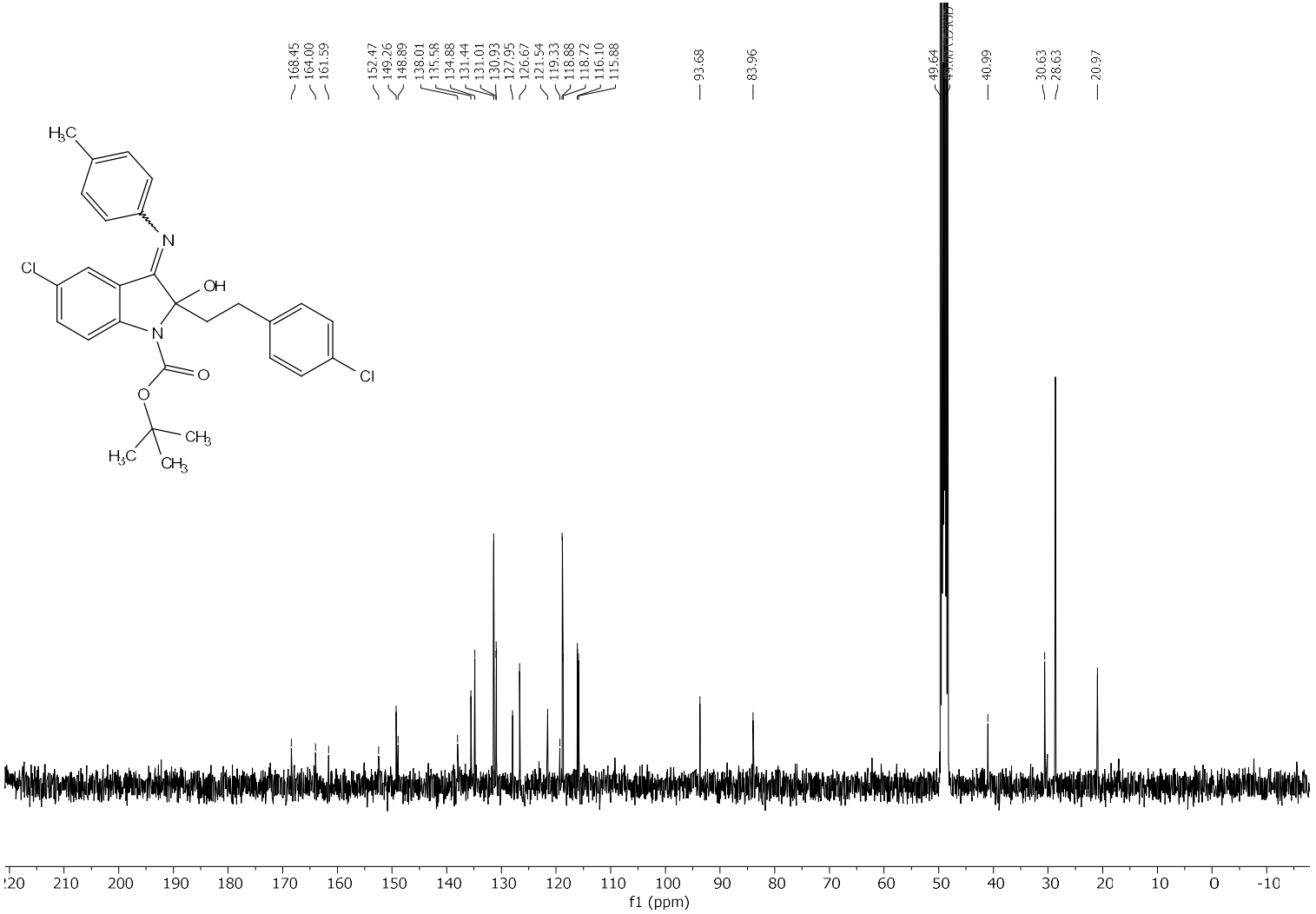
3u ^{13}C NMR spectrum



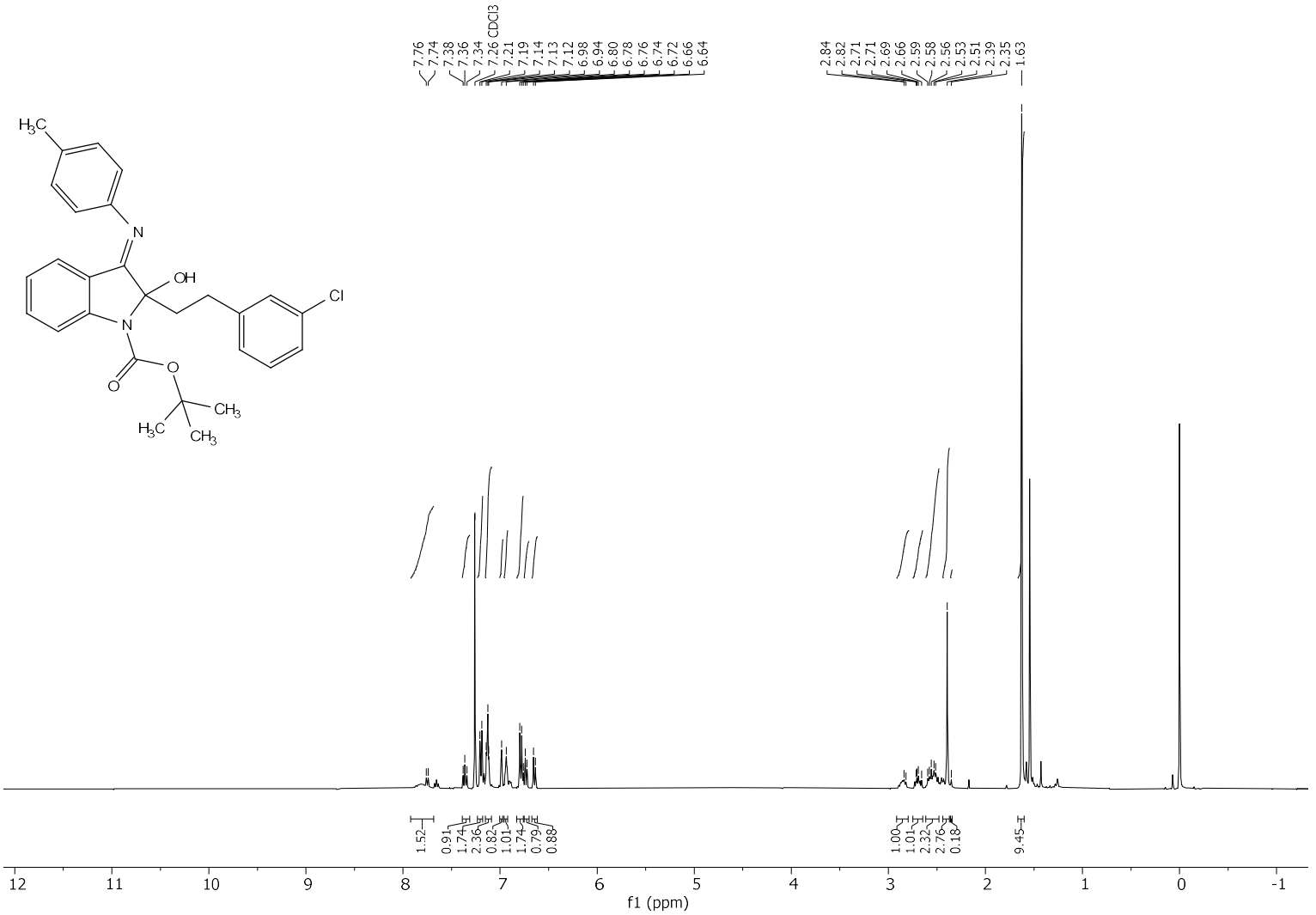
3v ^{1}H NMR spectrum



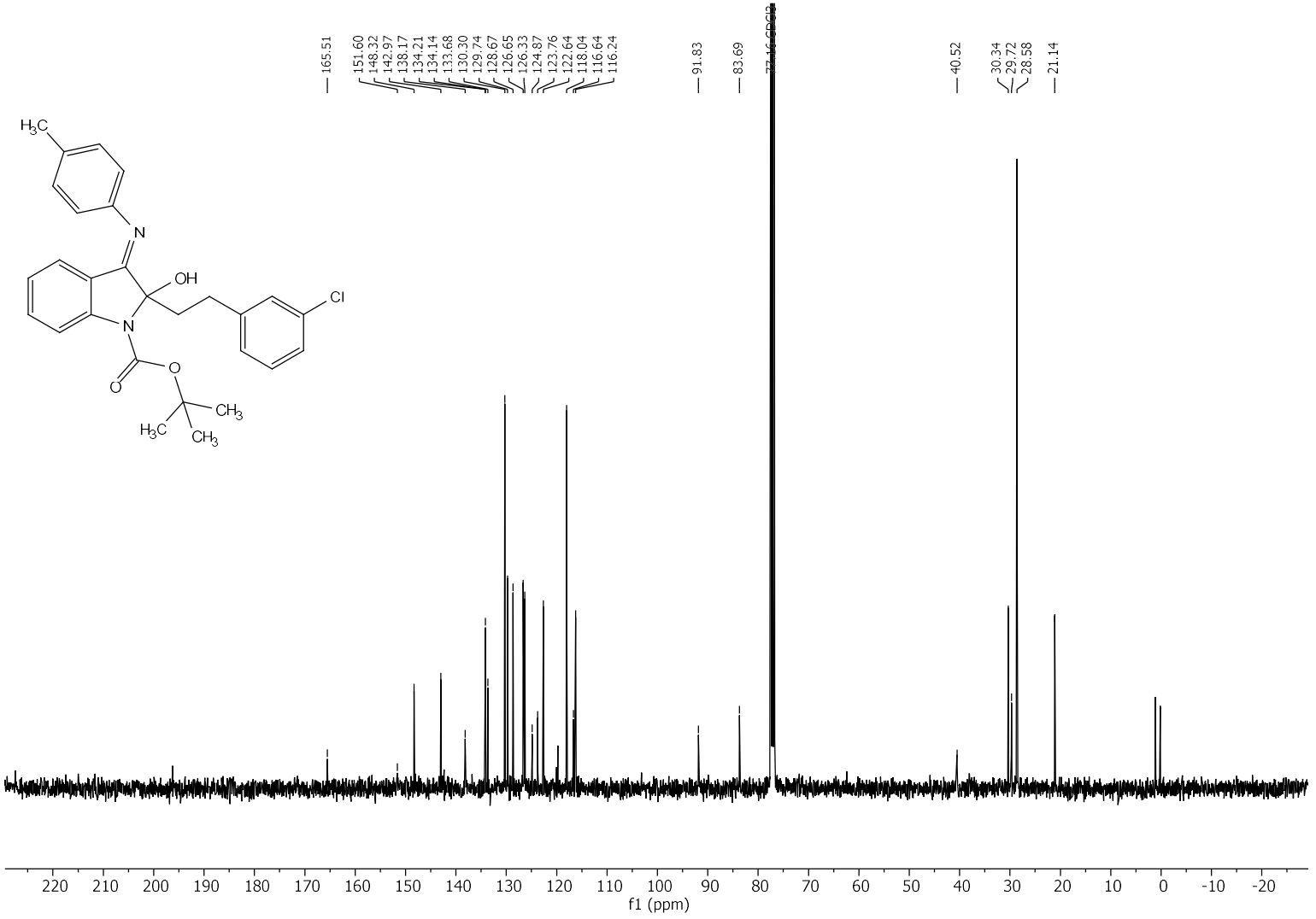
3v ^{13}C NMR spectrum



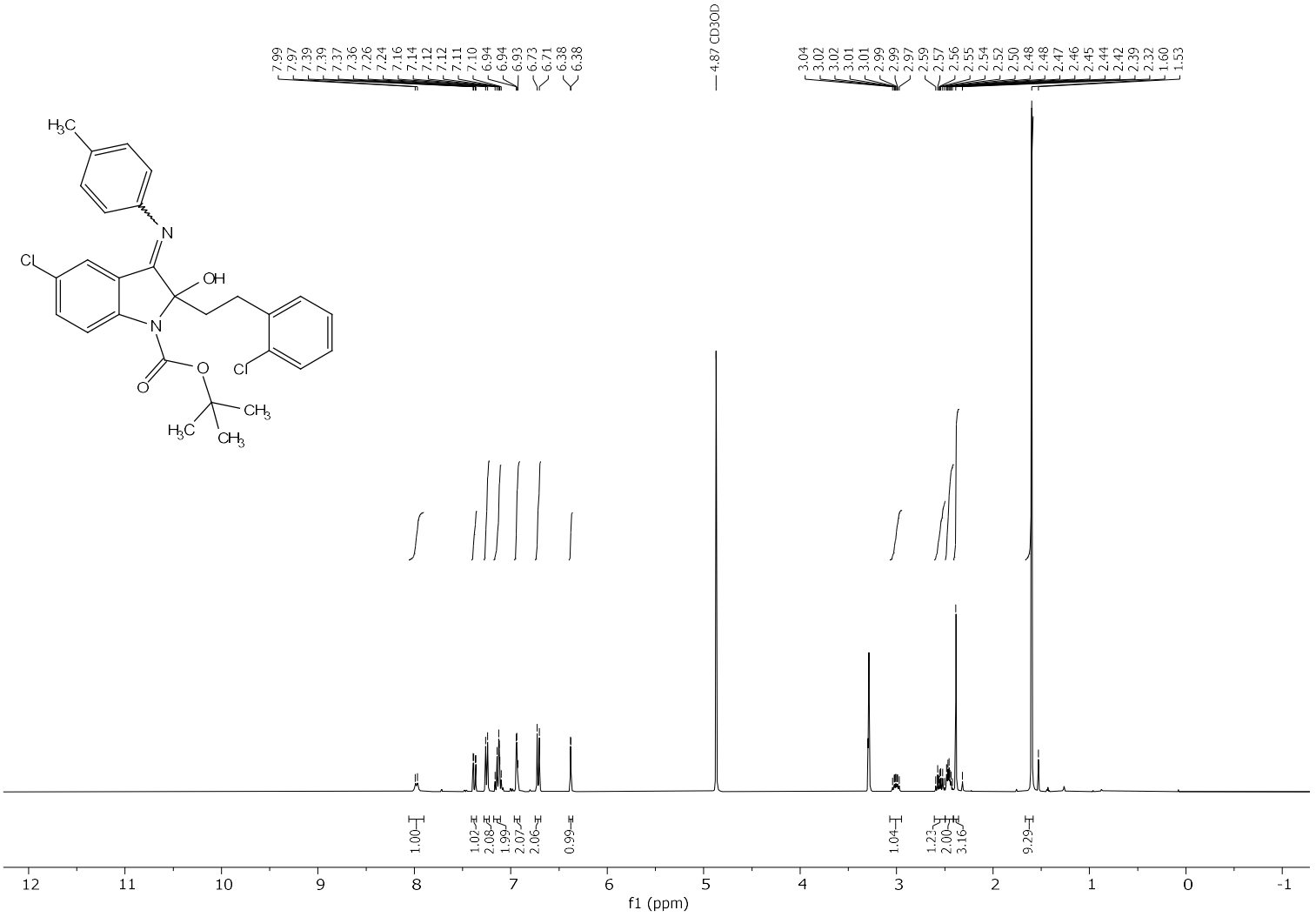
3w ^{1}H NMR spectrum



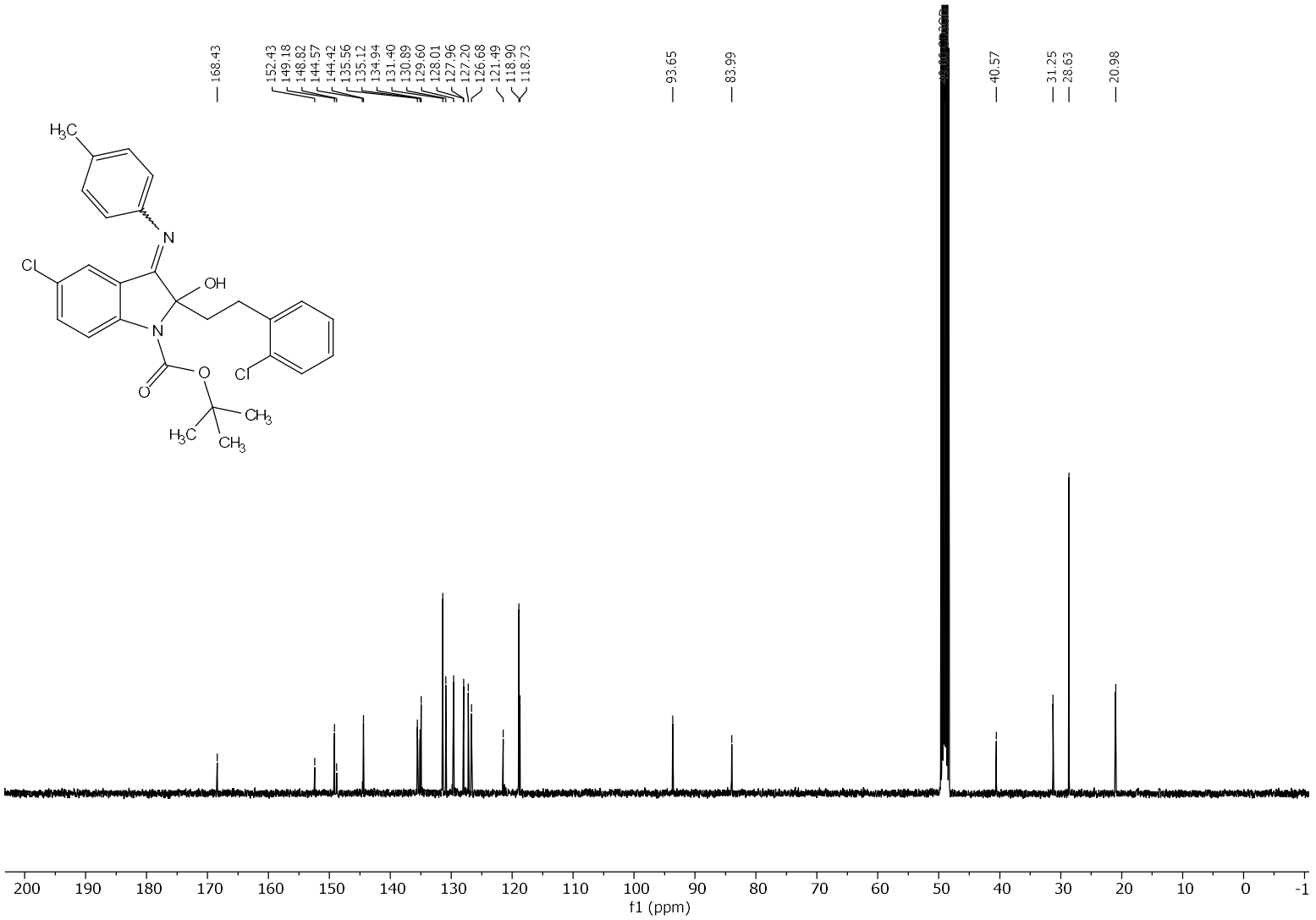
3w ^{13}C NMR spectrum



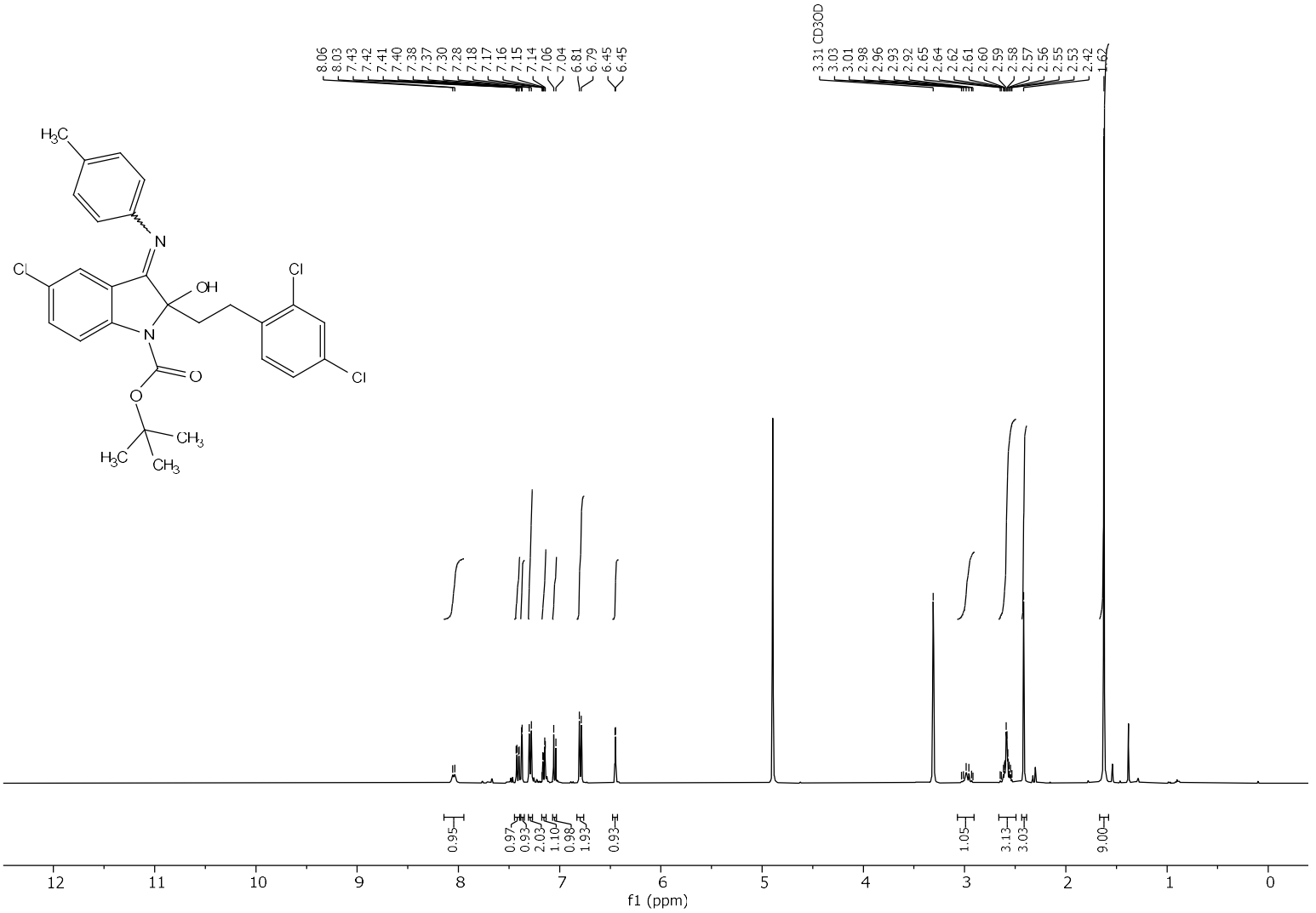
3x ^{1}H NMR spectrum



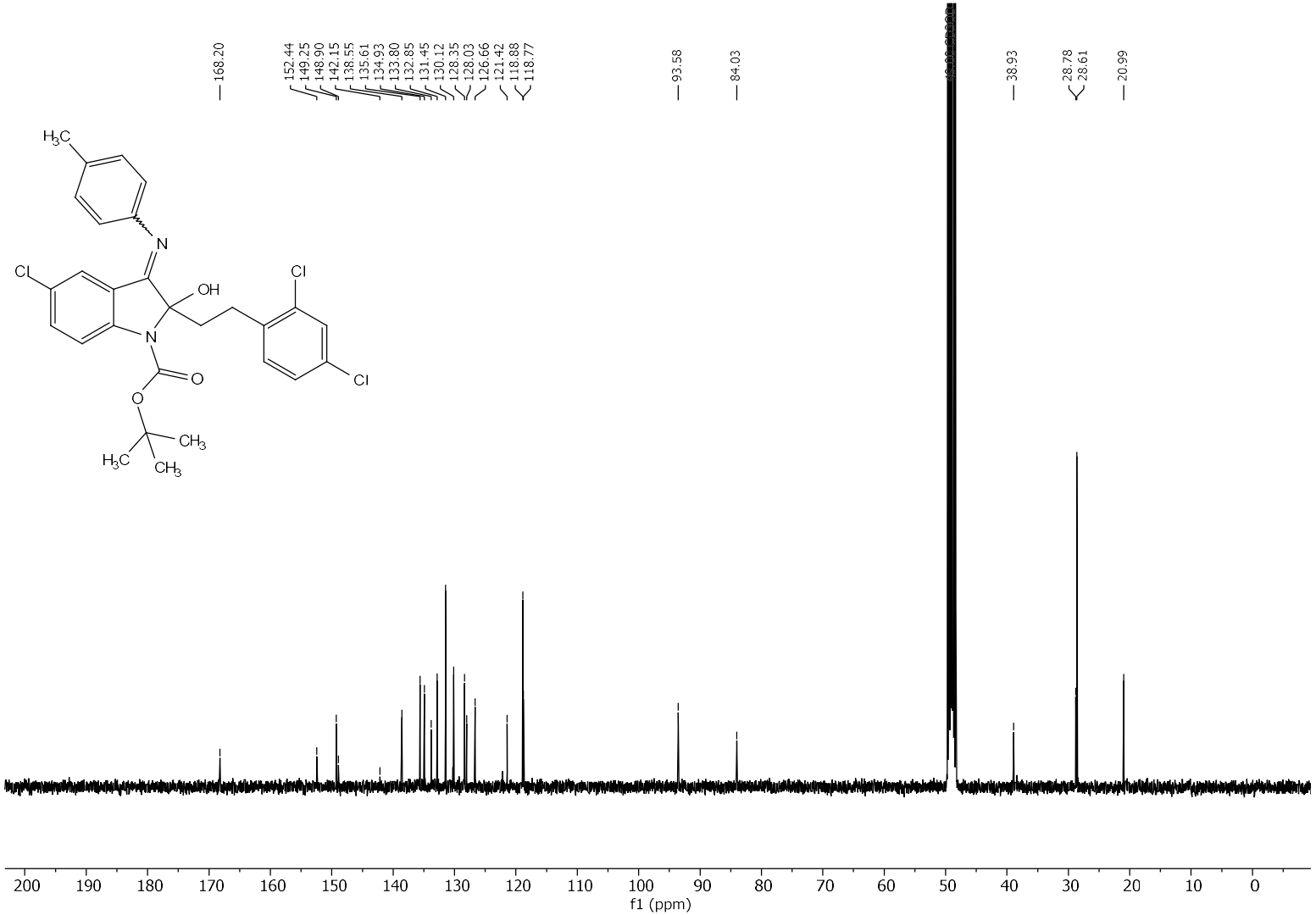
3x ^{13}C NMR spectrum



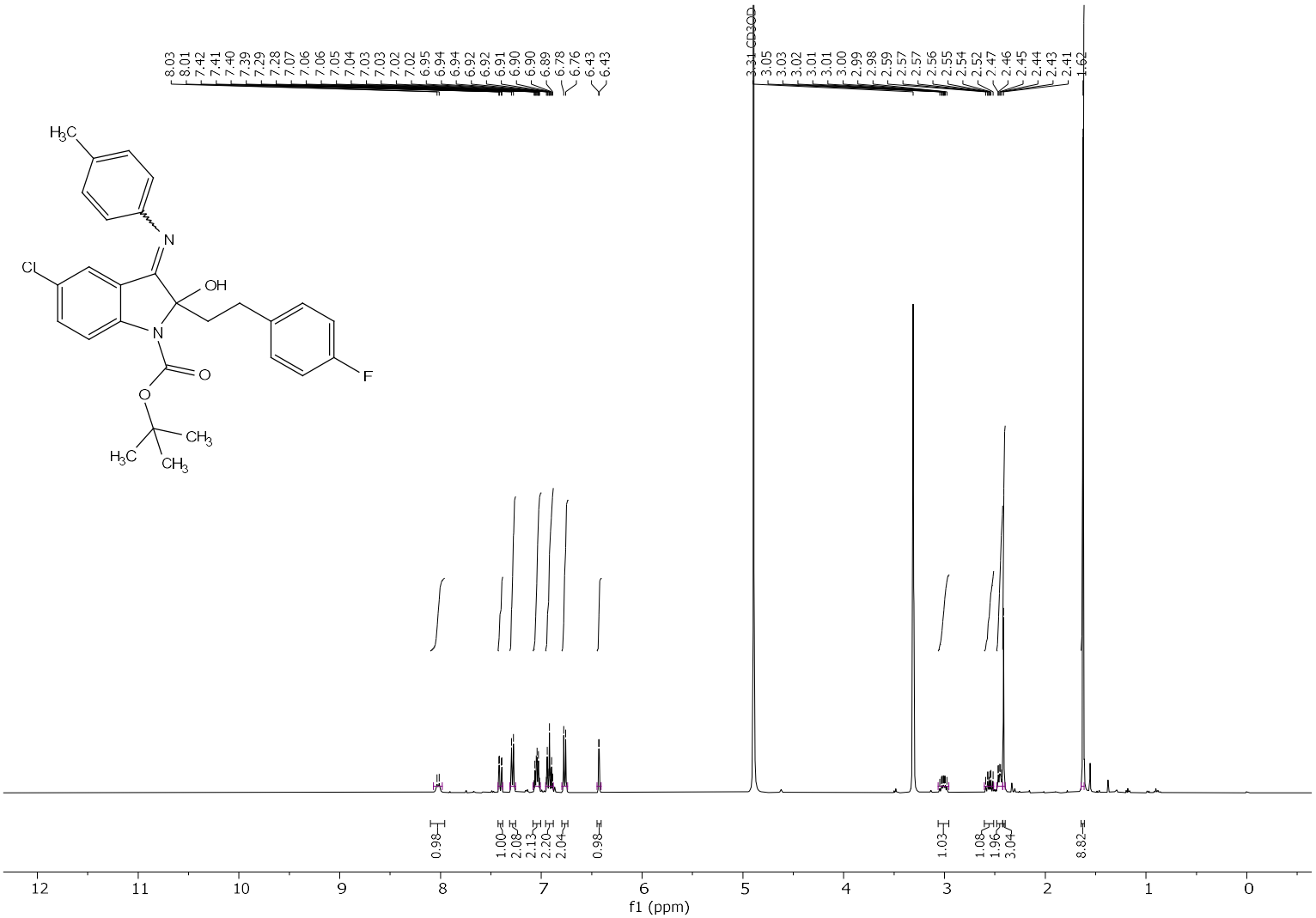
3y ^{1}H NMR spectrum



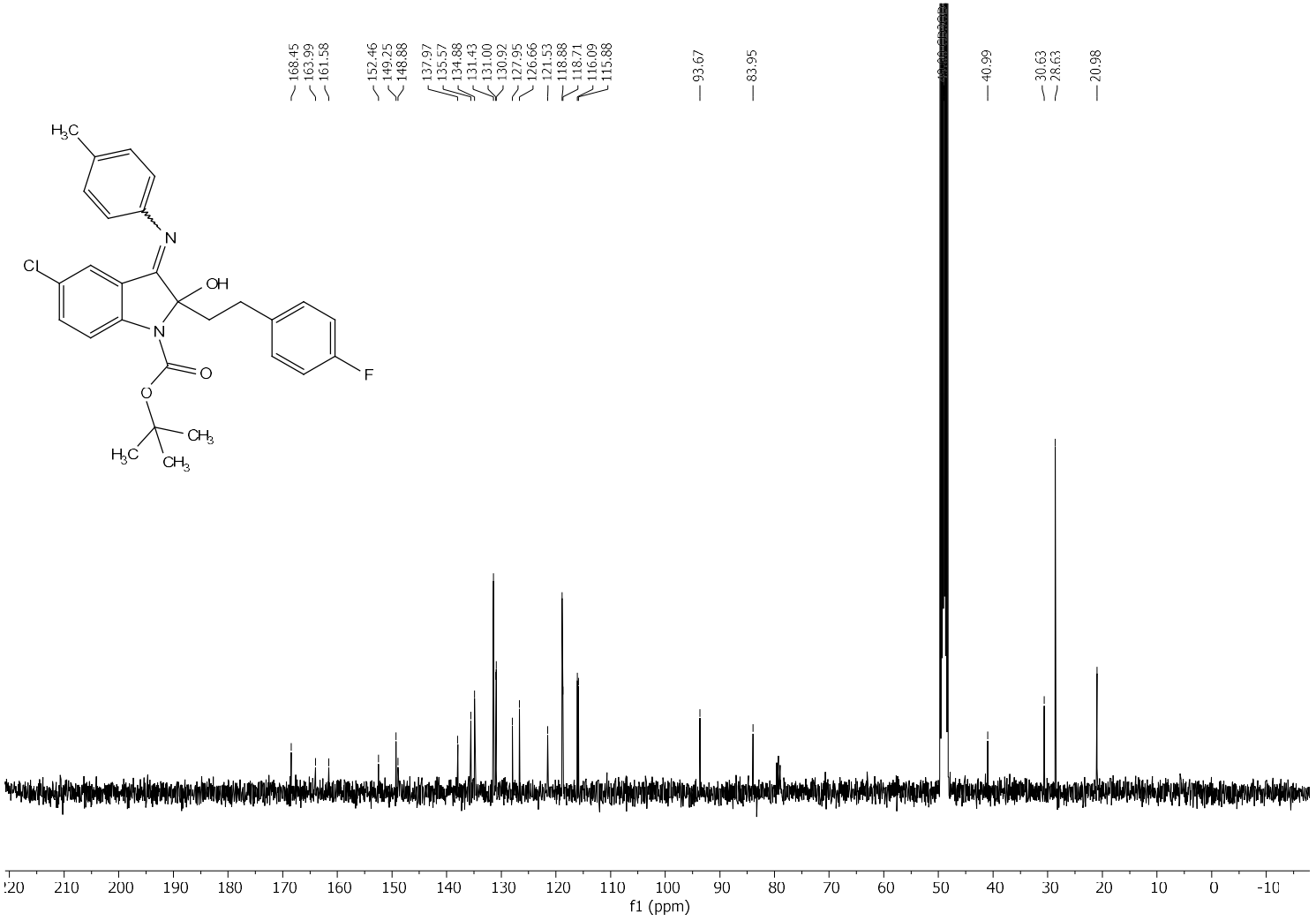
3y ^{13}C NMR spectrum



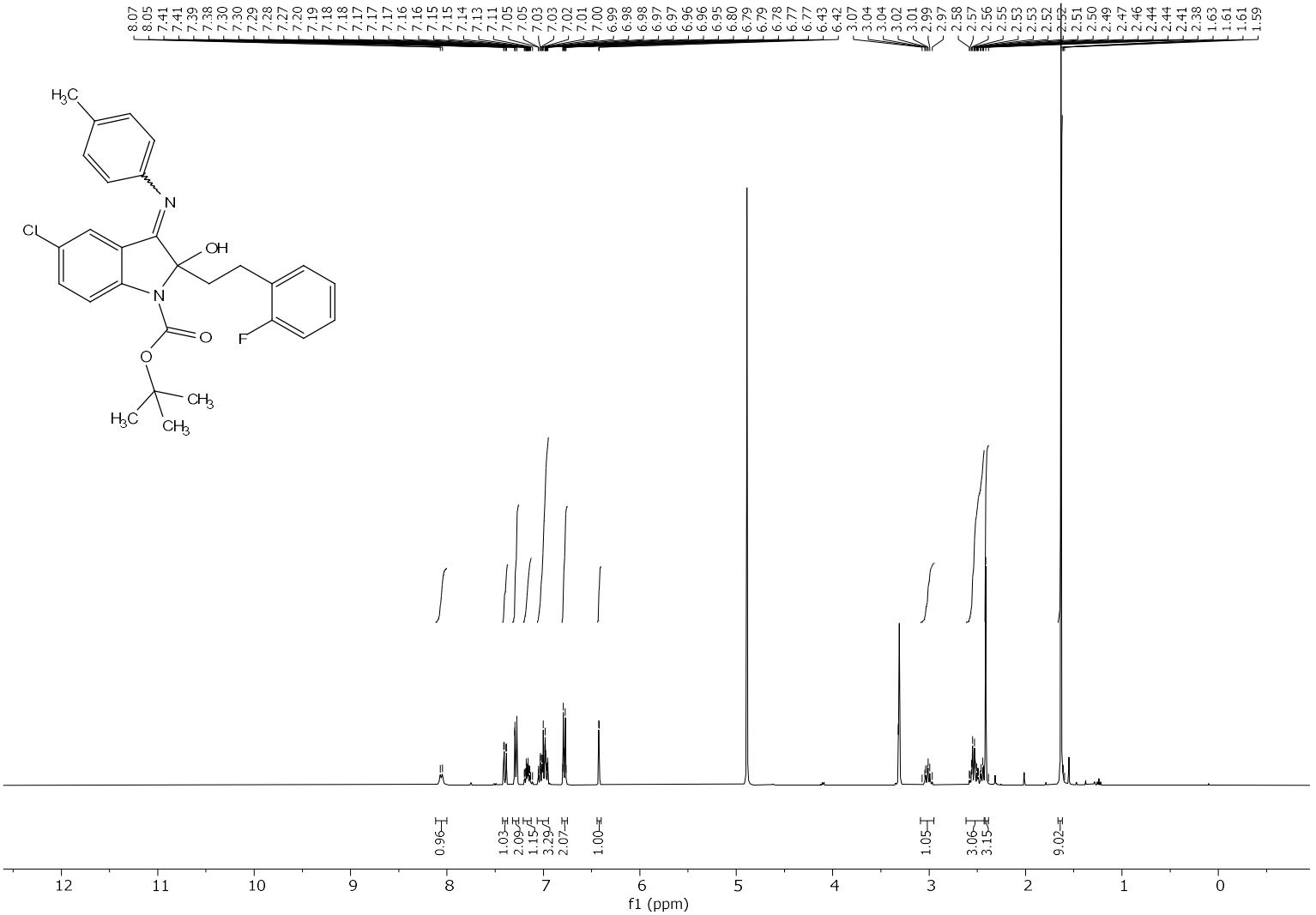
3z ^{1}H NMR spectrum



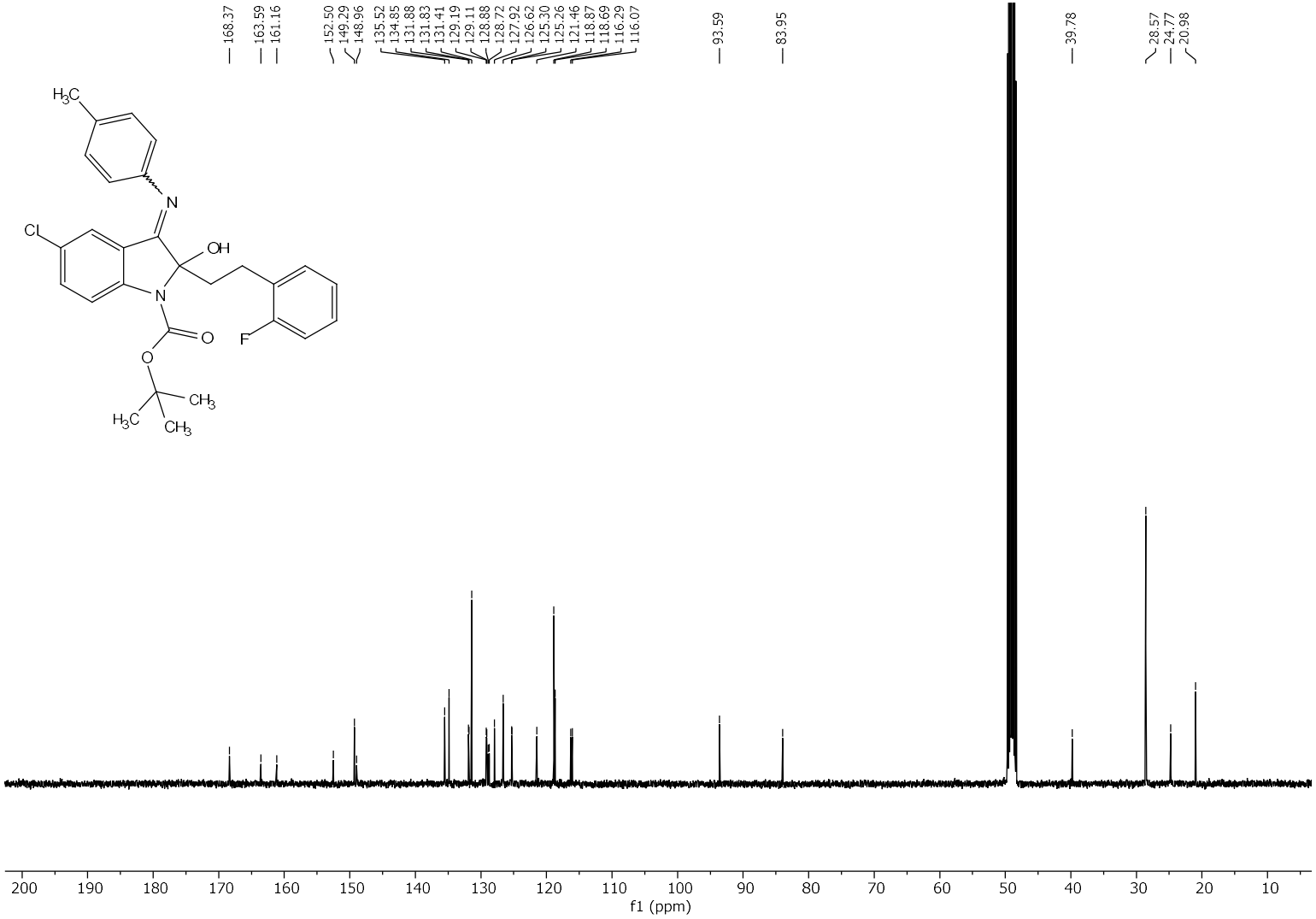
3z ^{13}C NMR spectrum



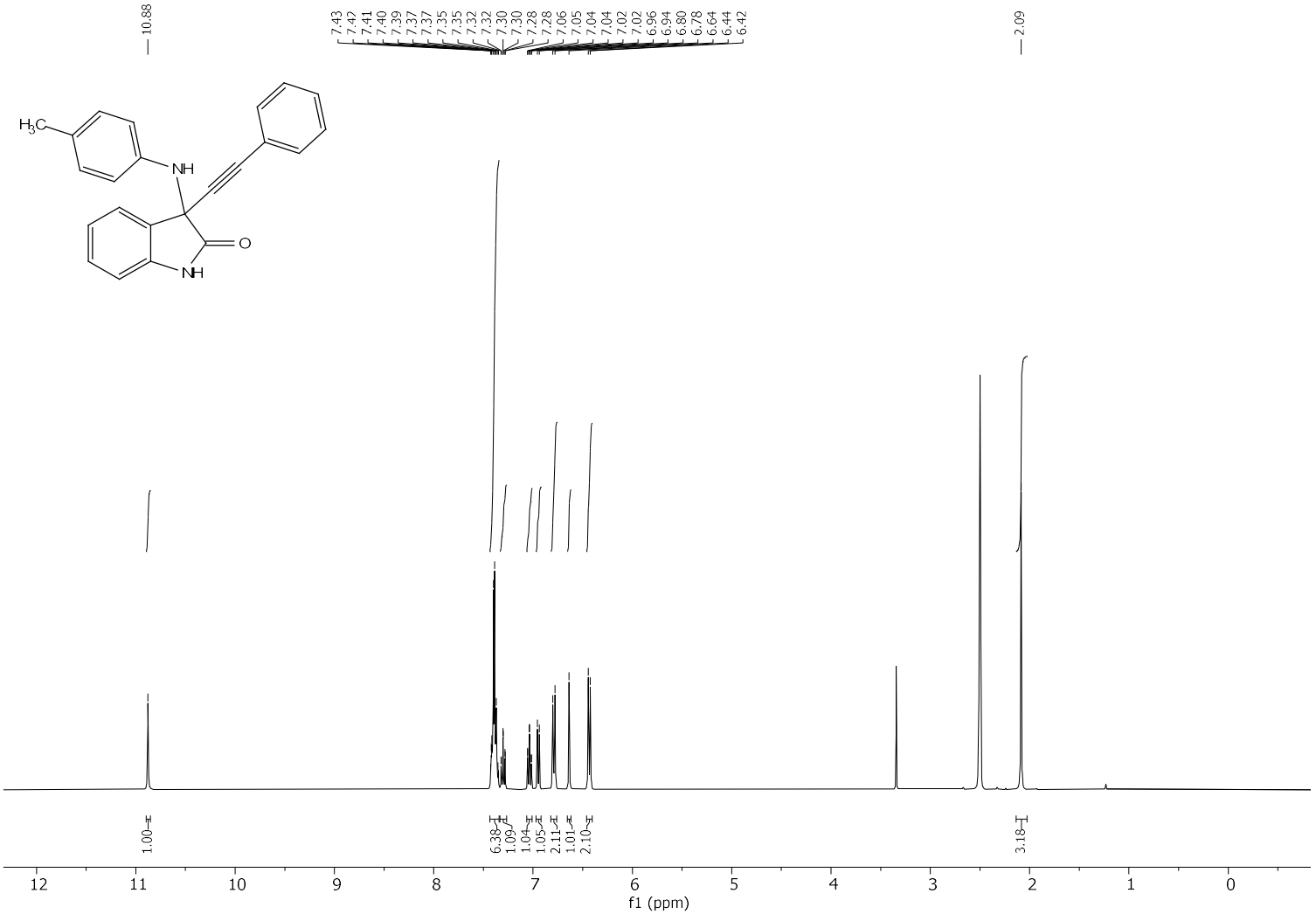
3aa ^{1}H NMR spectrum



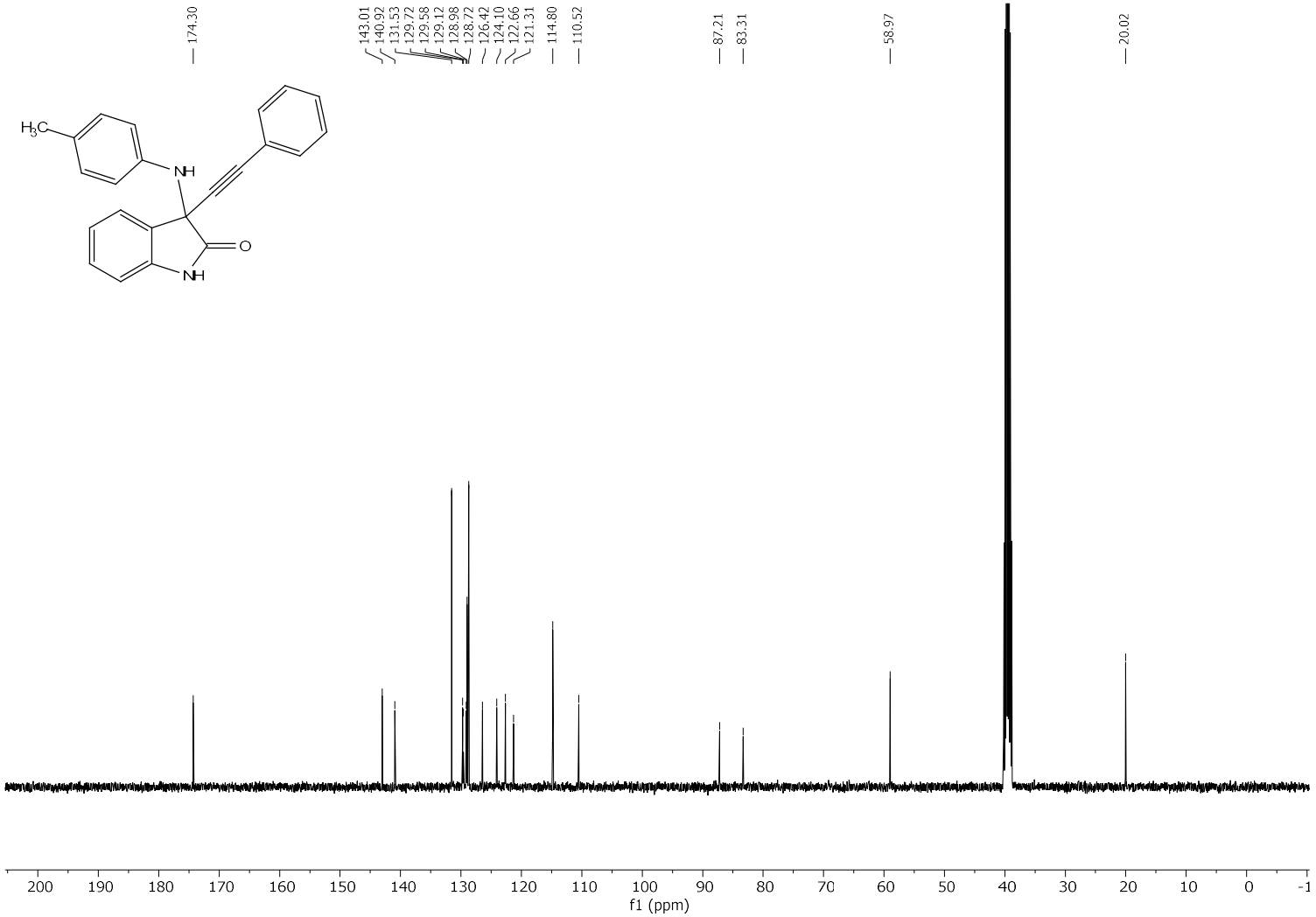
3aa ^{13}C NMR spectrum



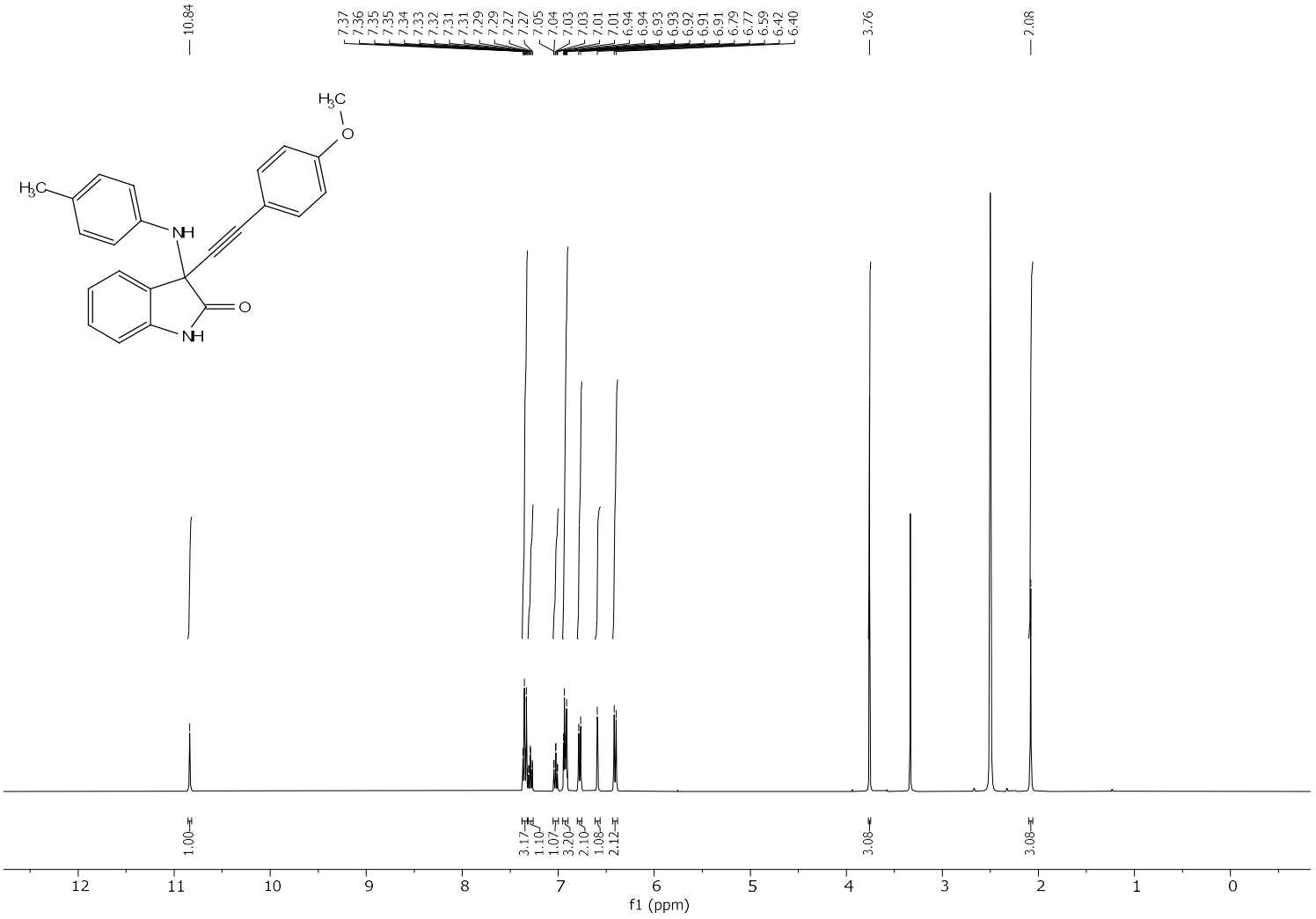
8a ^{1}H NMR spectrum



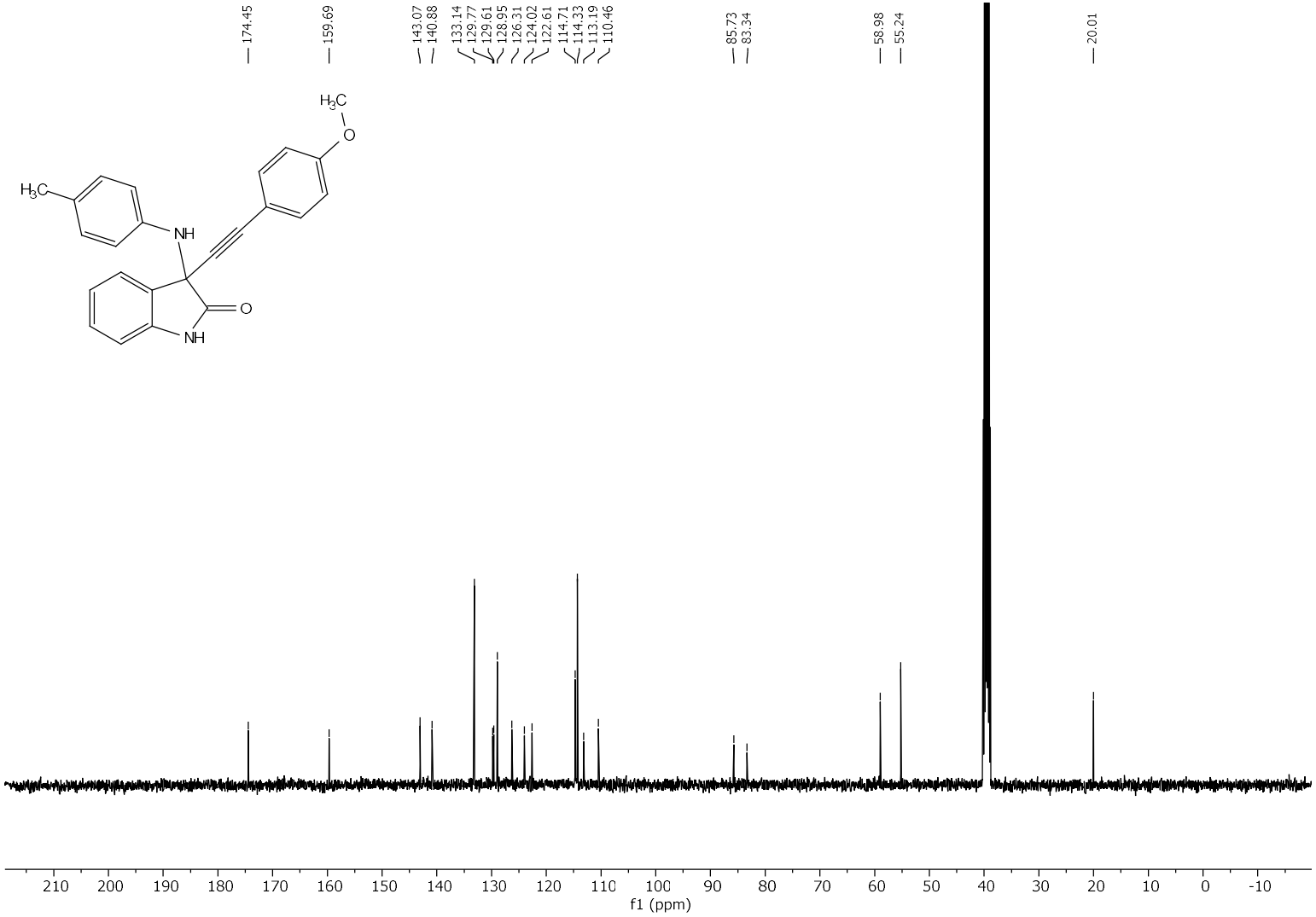
8a ^{13}C NMR spectrum



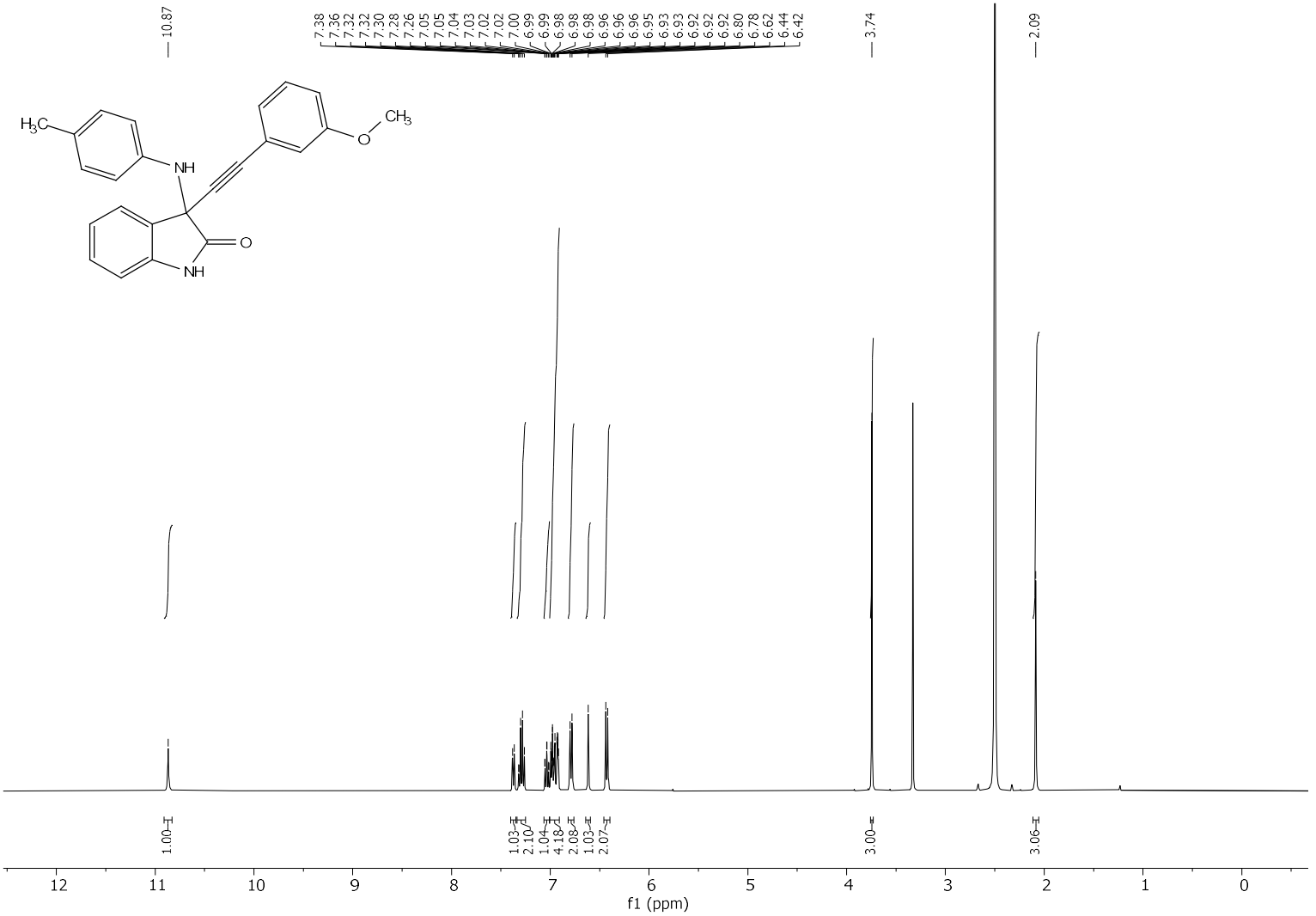
8b ^{1}H NMR spectrum



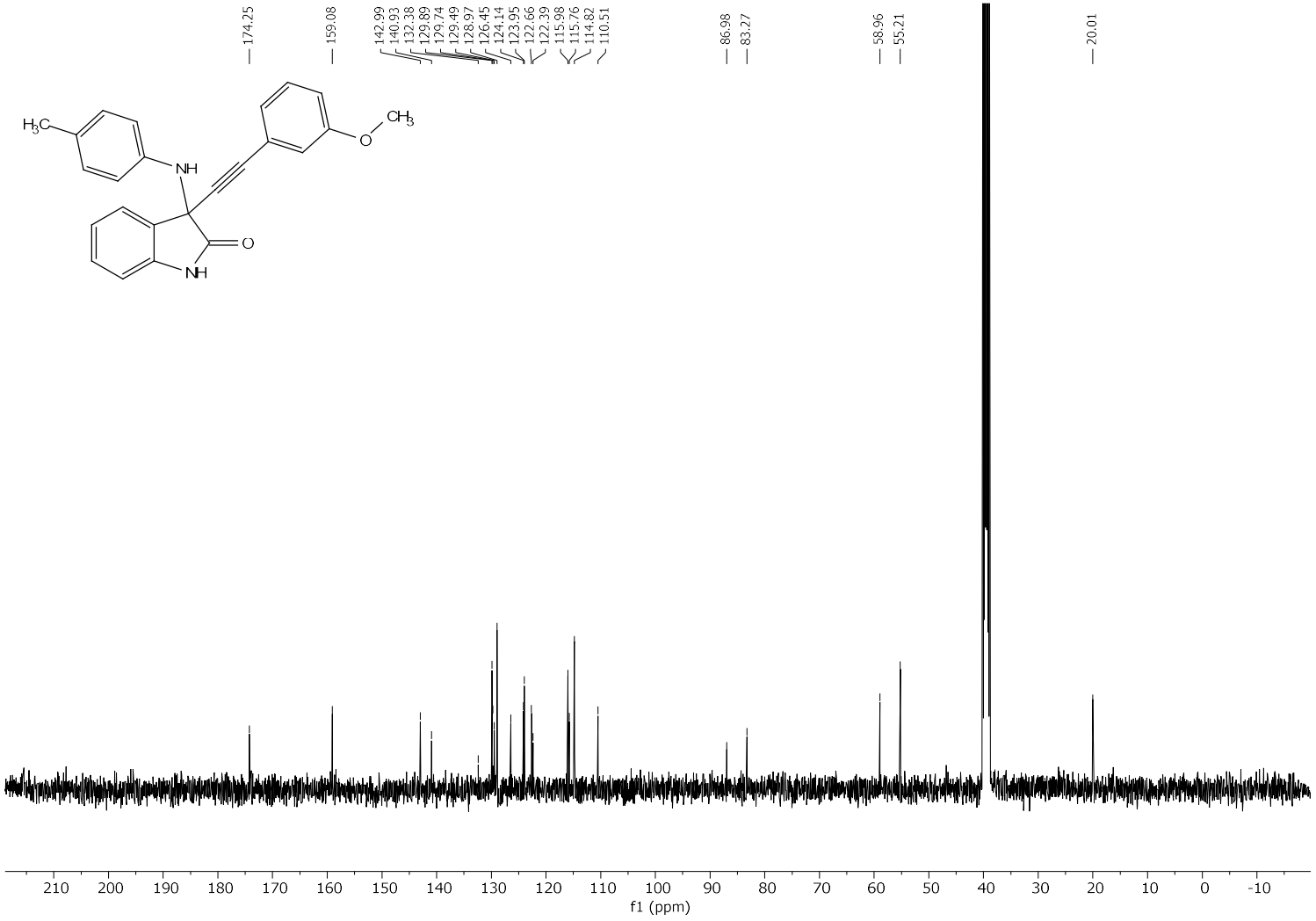
8b ^{13}C NMR spectrum



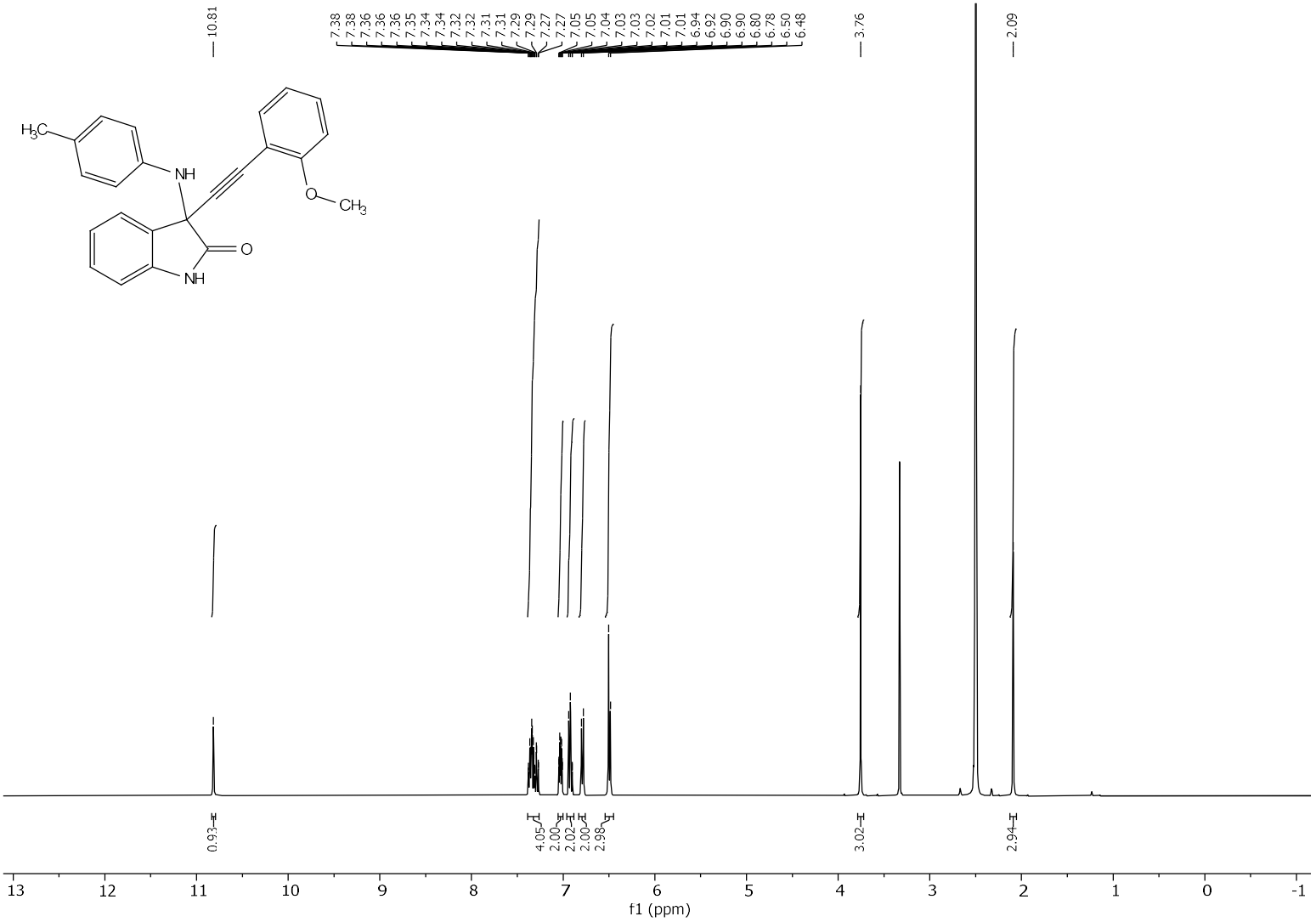
8c ^{1}H NMR spectrum



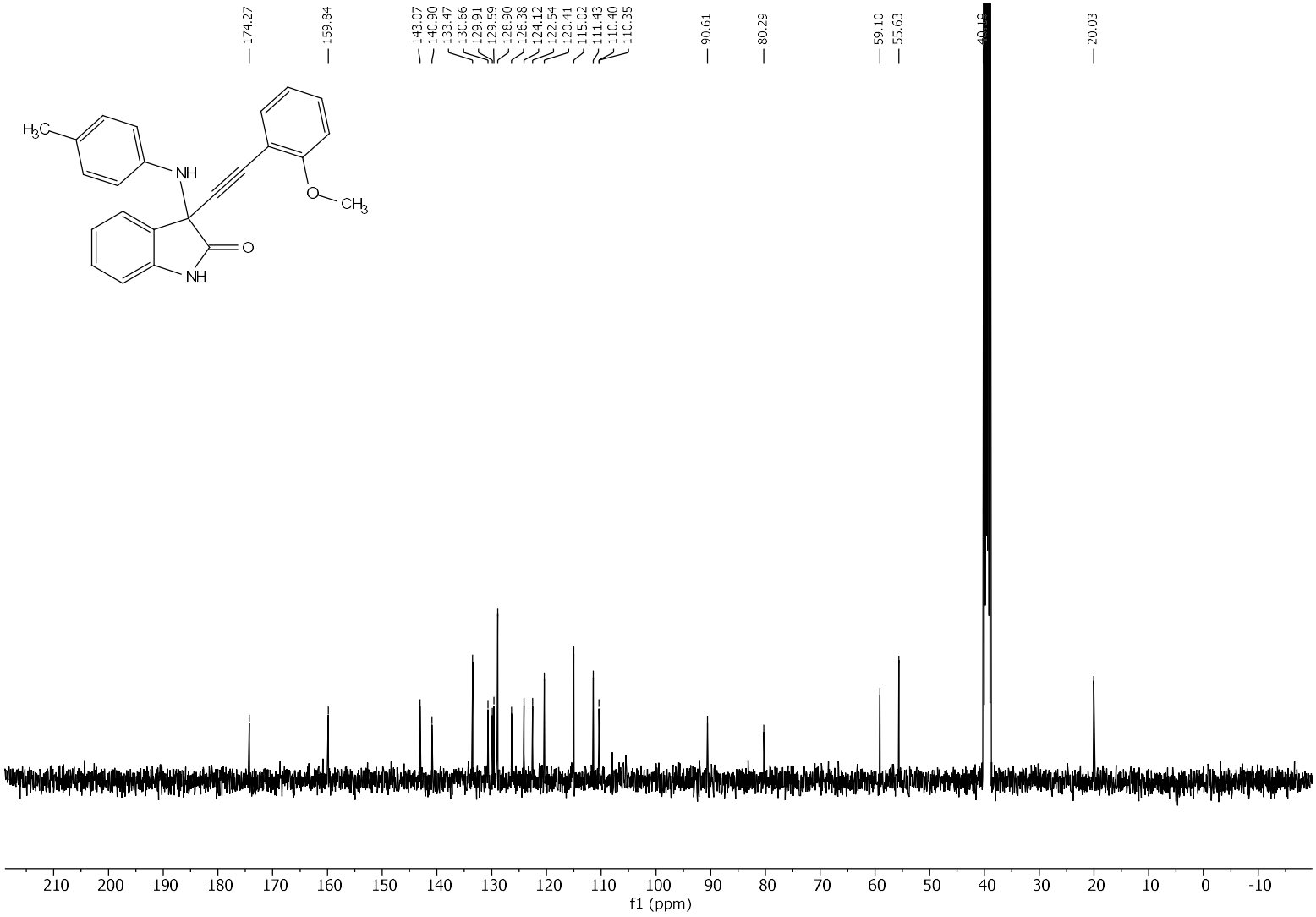
8c ^{13}C NMR spectrum



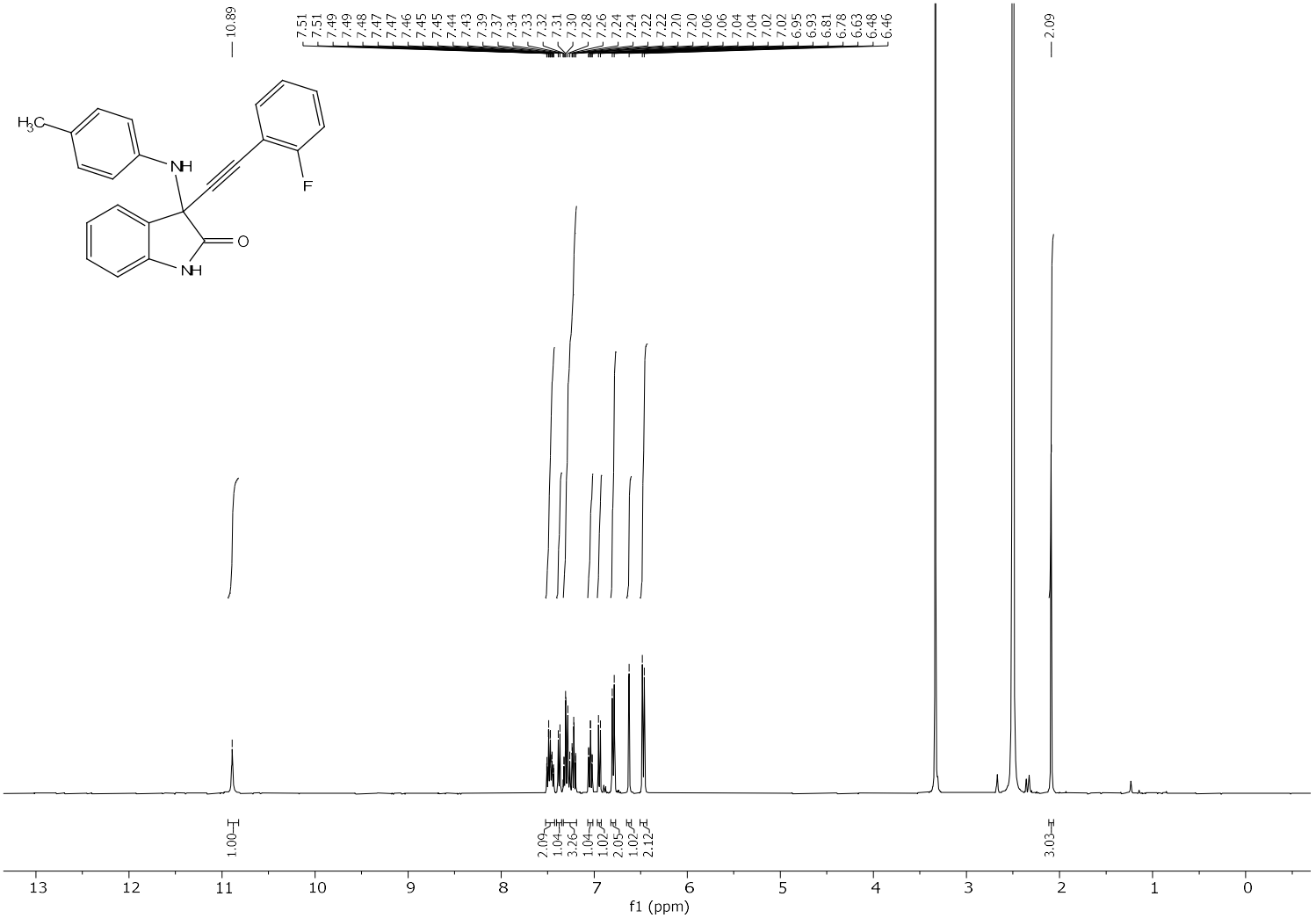
8d ^{1}H NMR spectrum



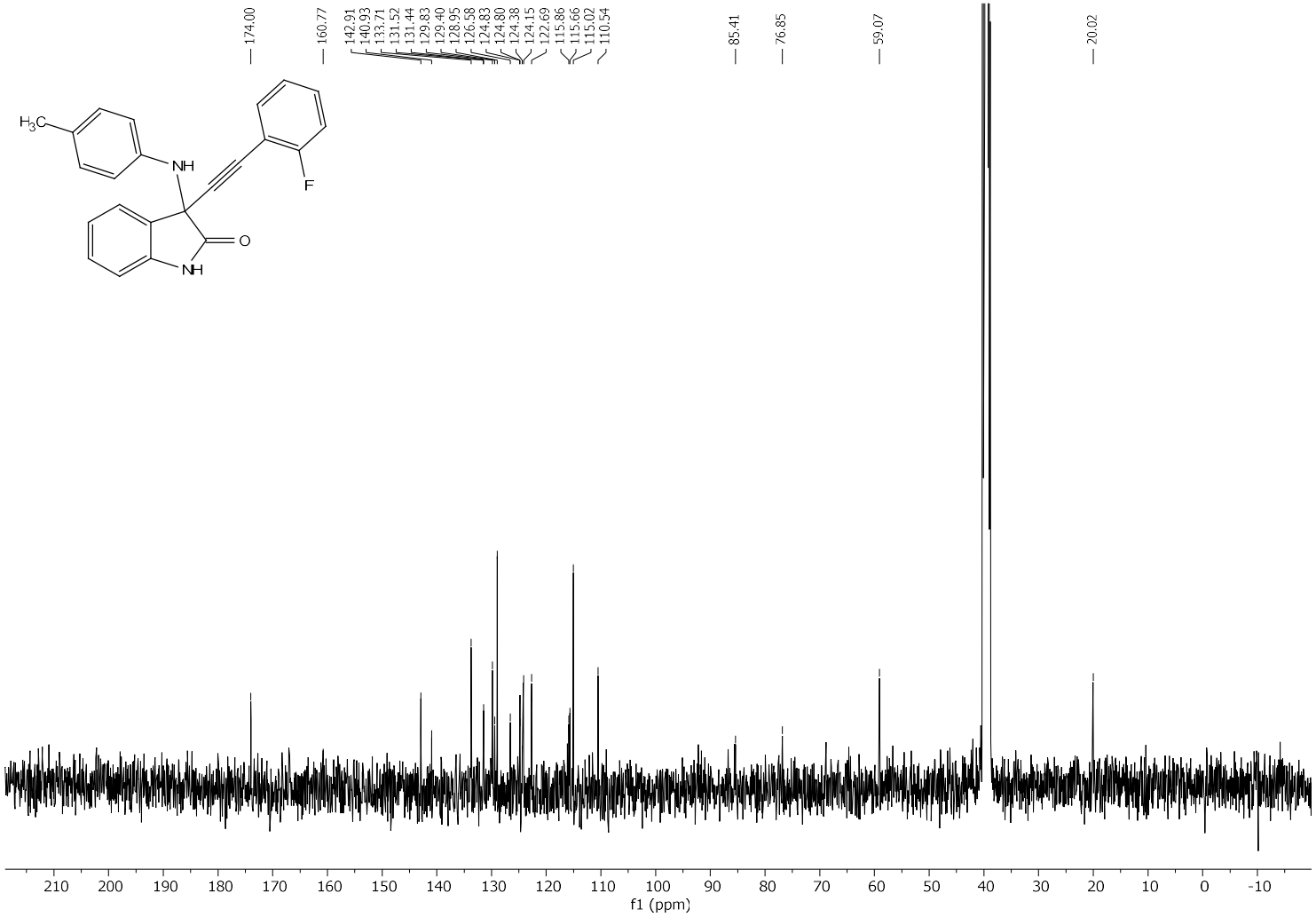
8d ^{13}C NMR spectrum



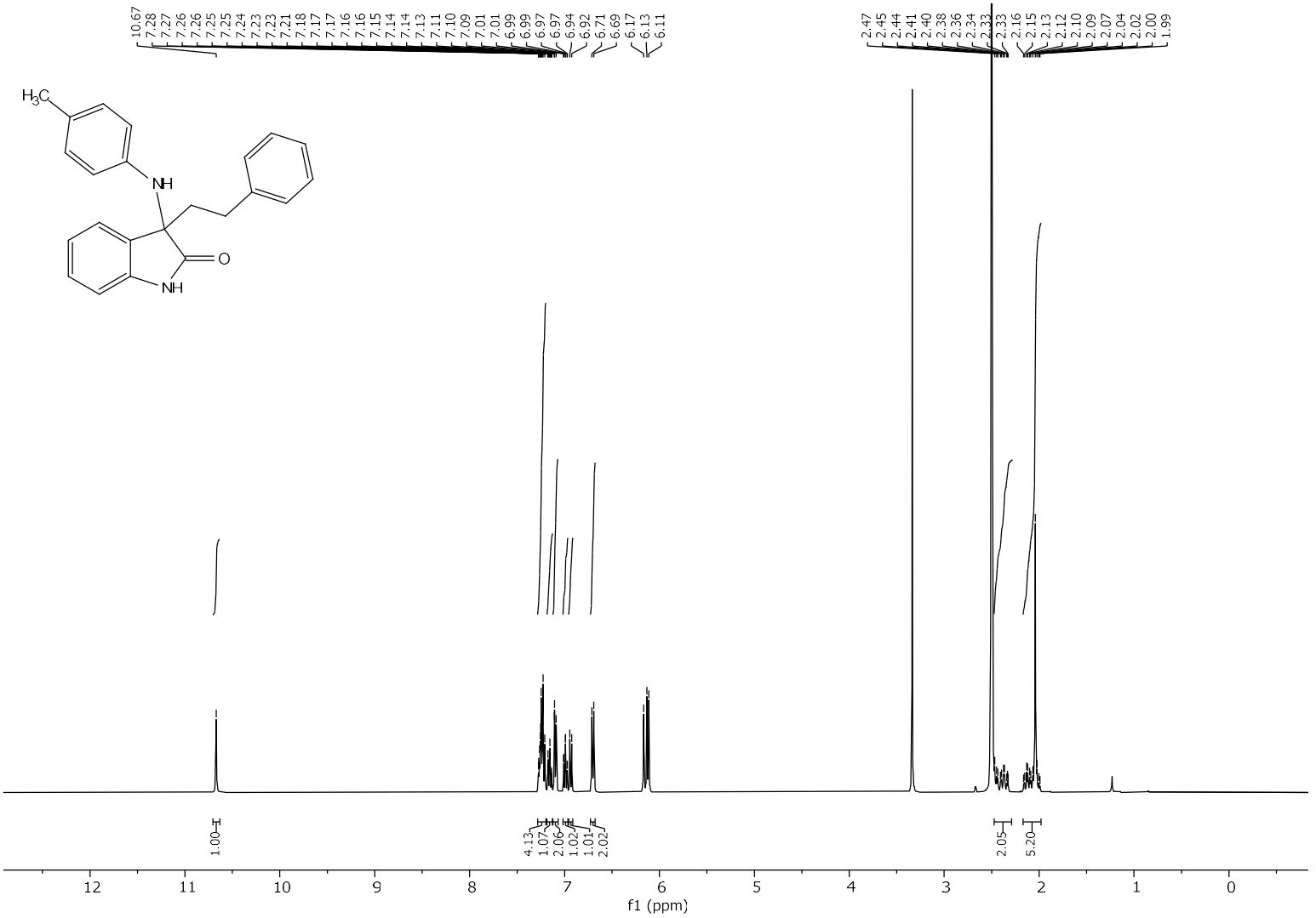
8e ^{1}H NMR spectrum



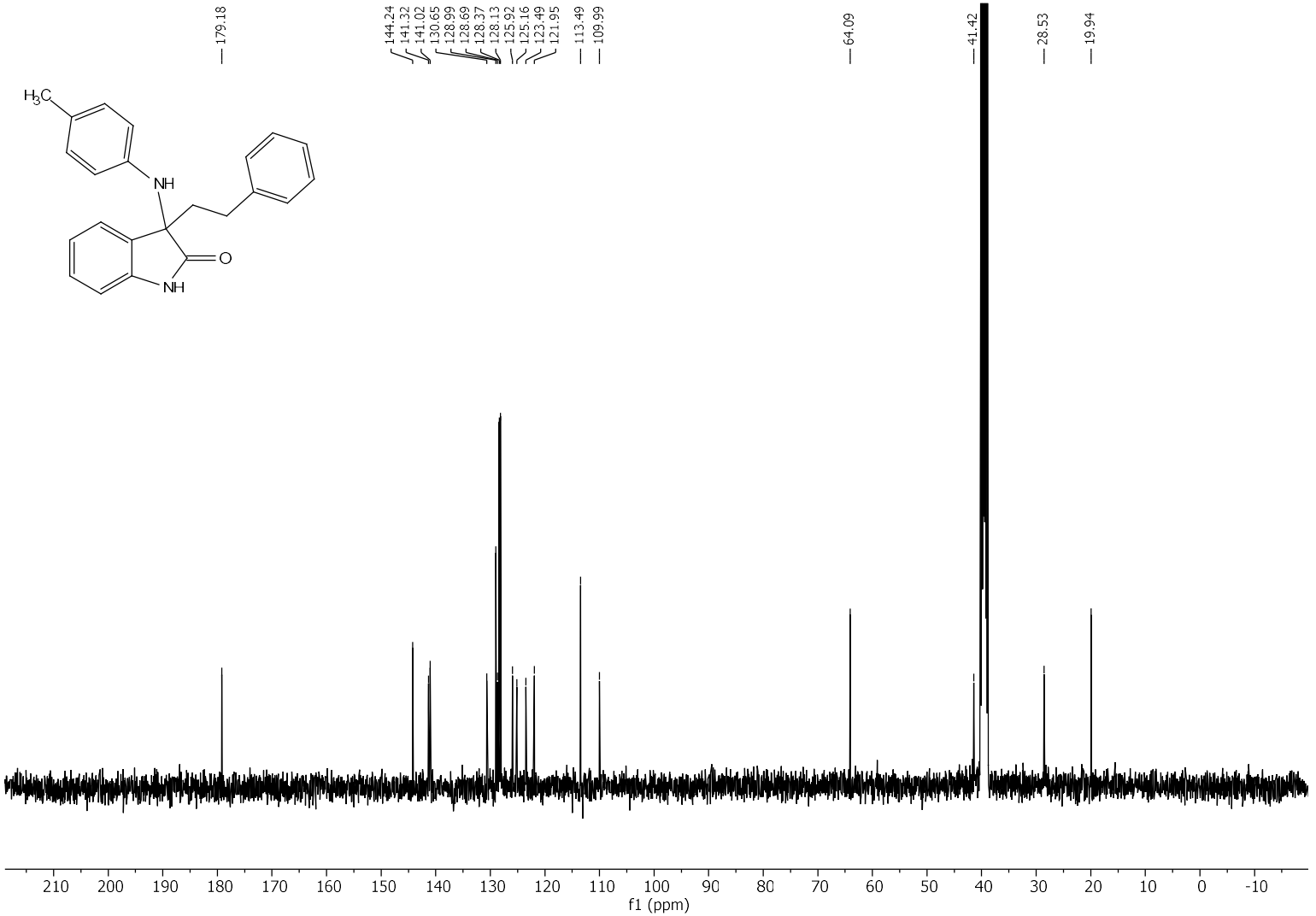
8e ^{13}C NMR spectrum



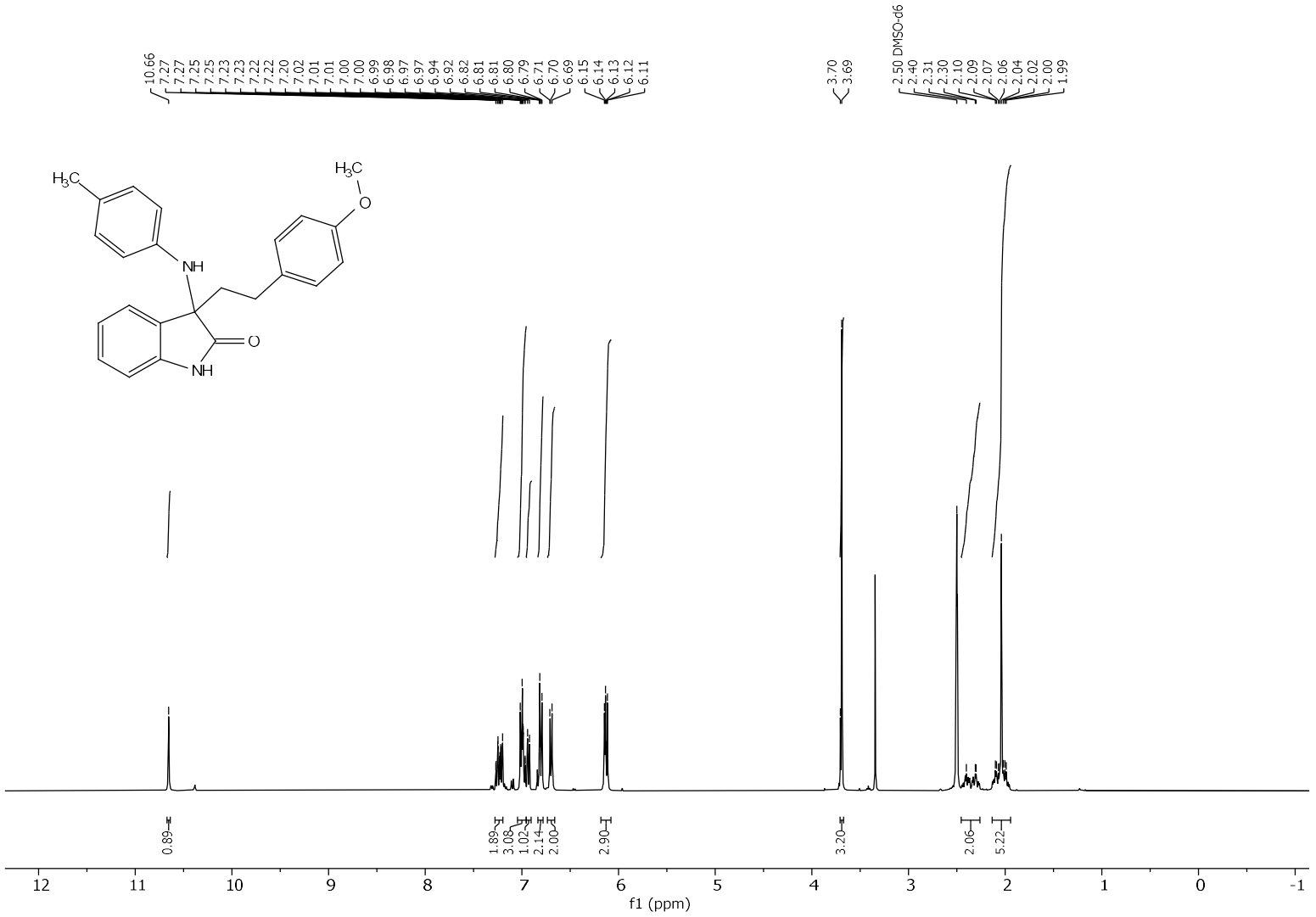
2e ^{1}H NMR spectrum



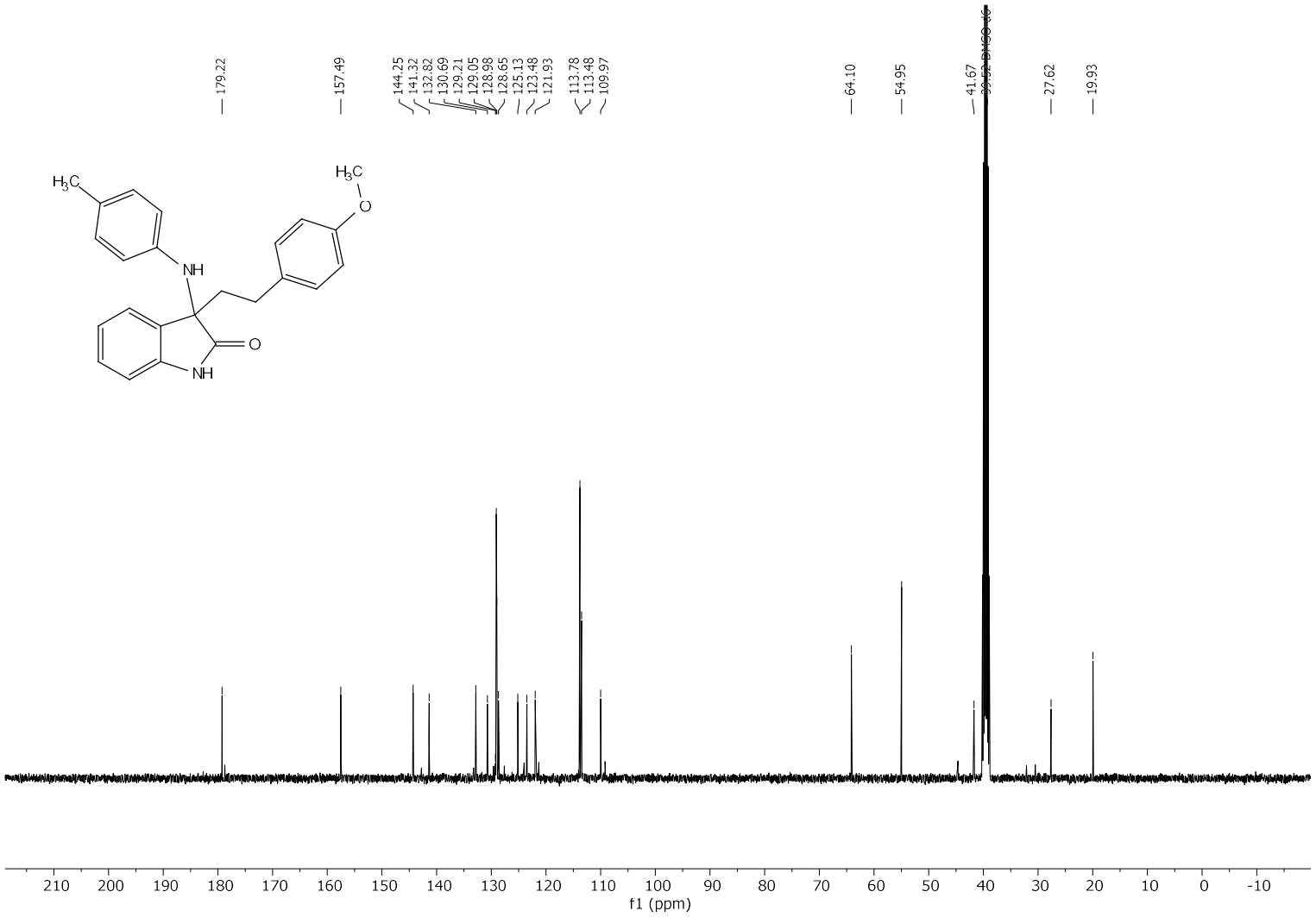
2e ^{13}C NMR spectrum



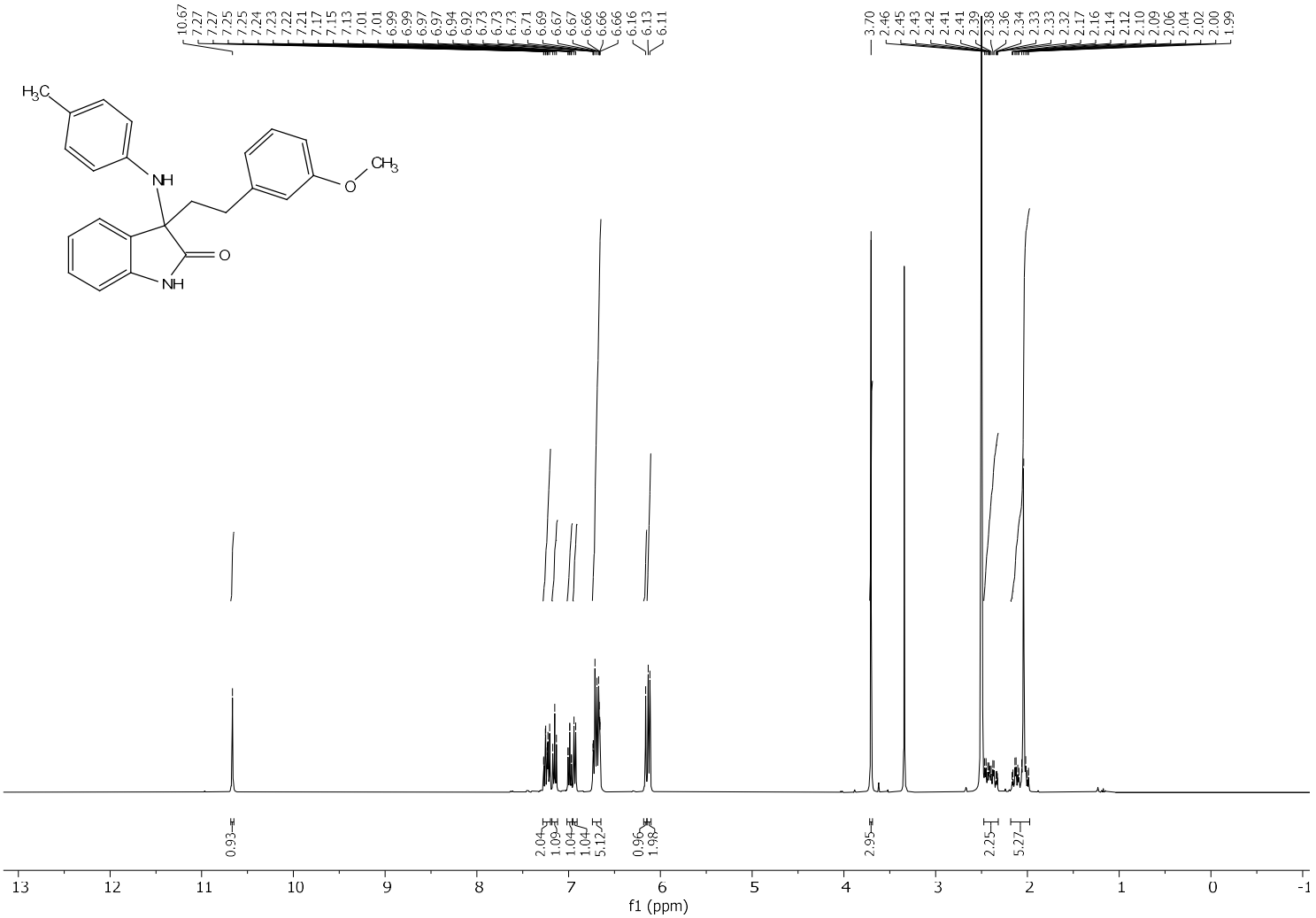
2f ^{1}H NMR spectrum



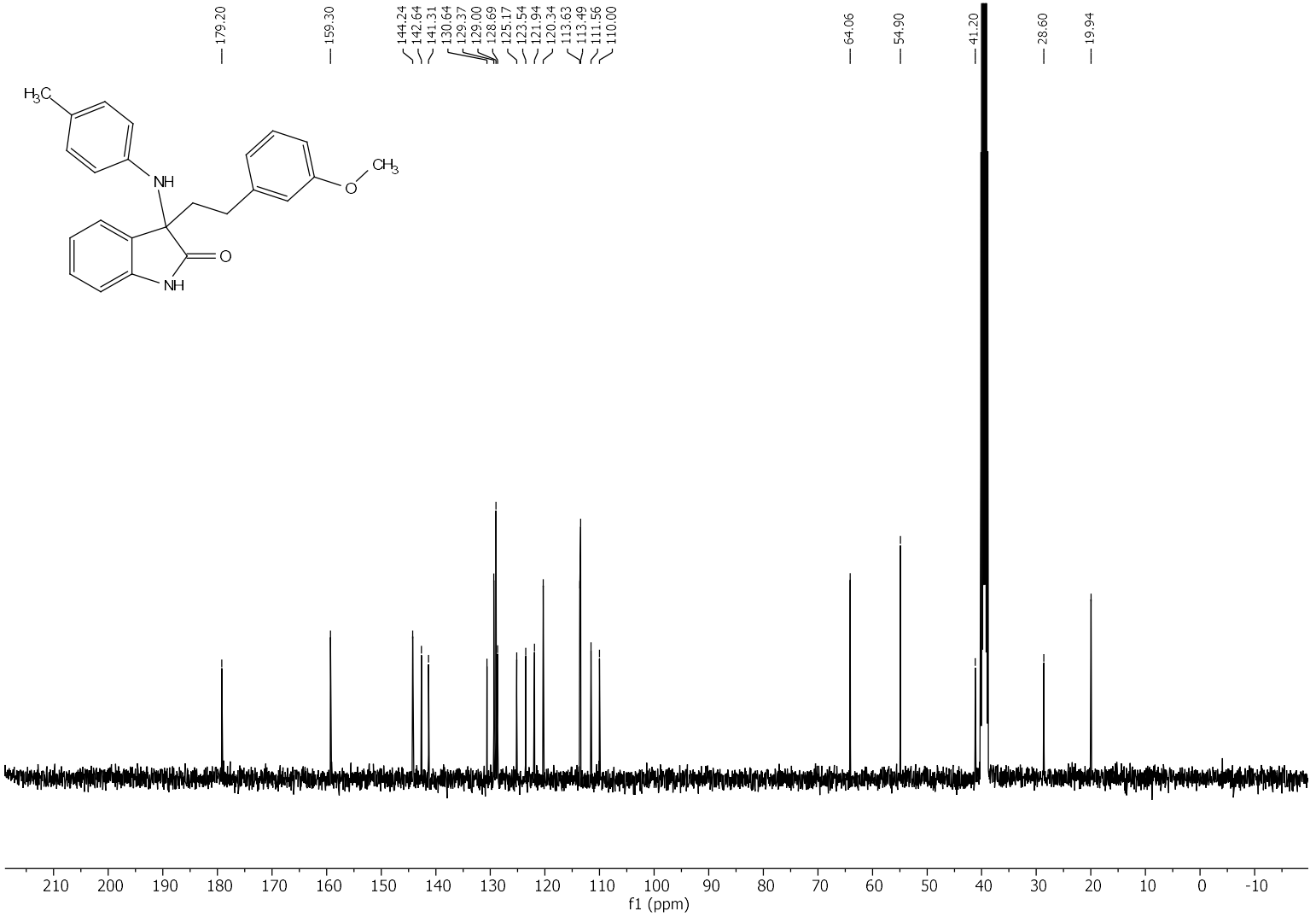
2f ^{13}C NMR spectrum



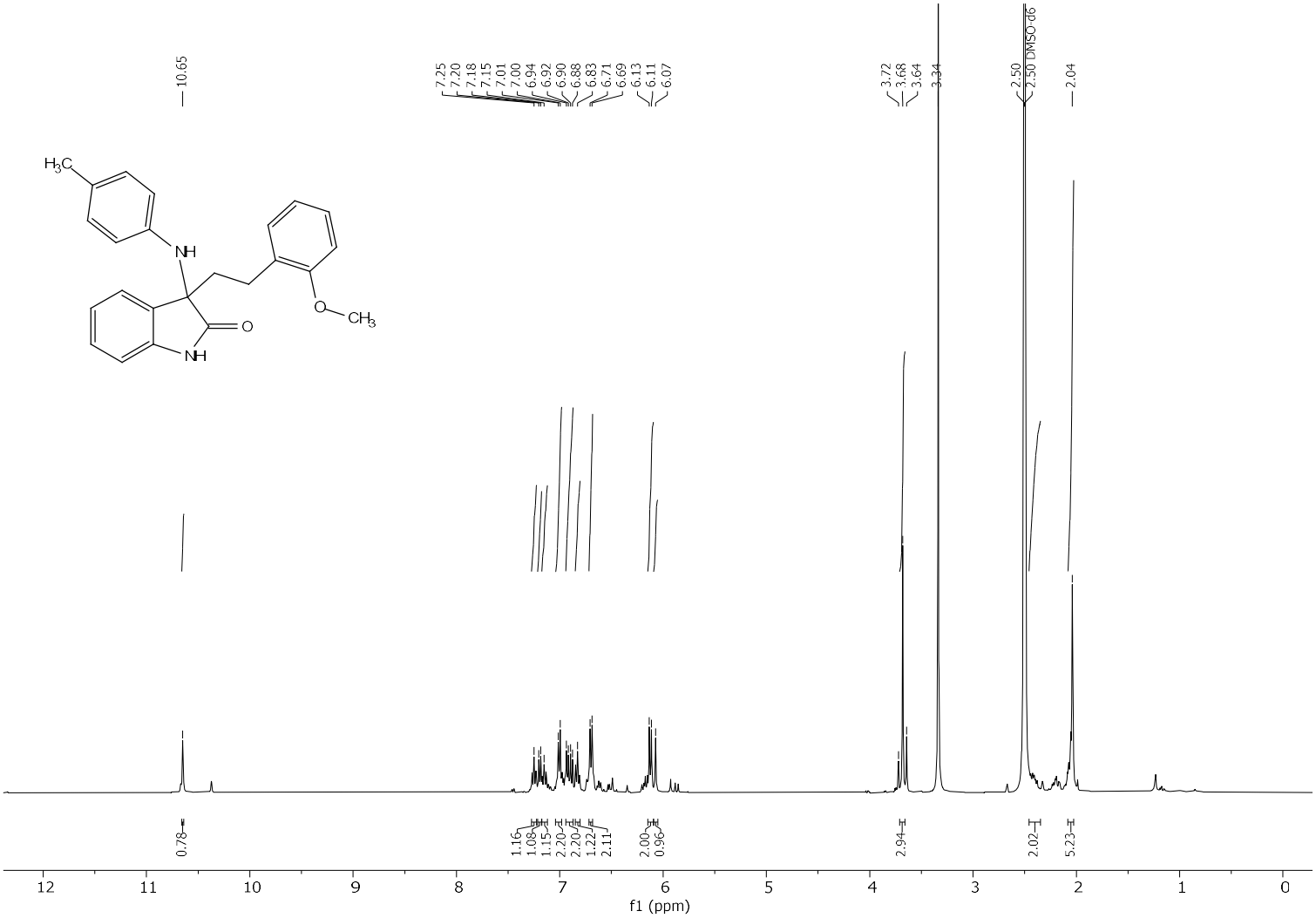
2g ^{1}H NMR spectrum



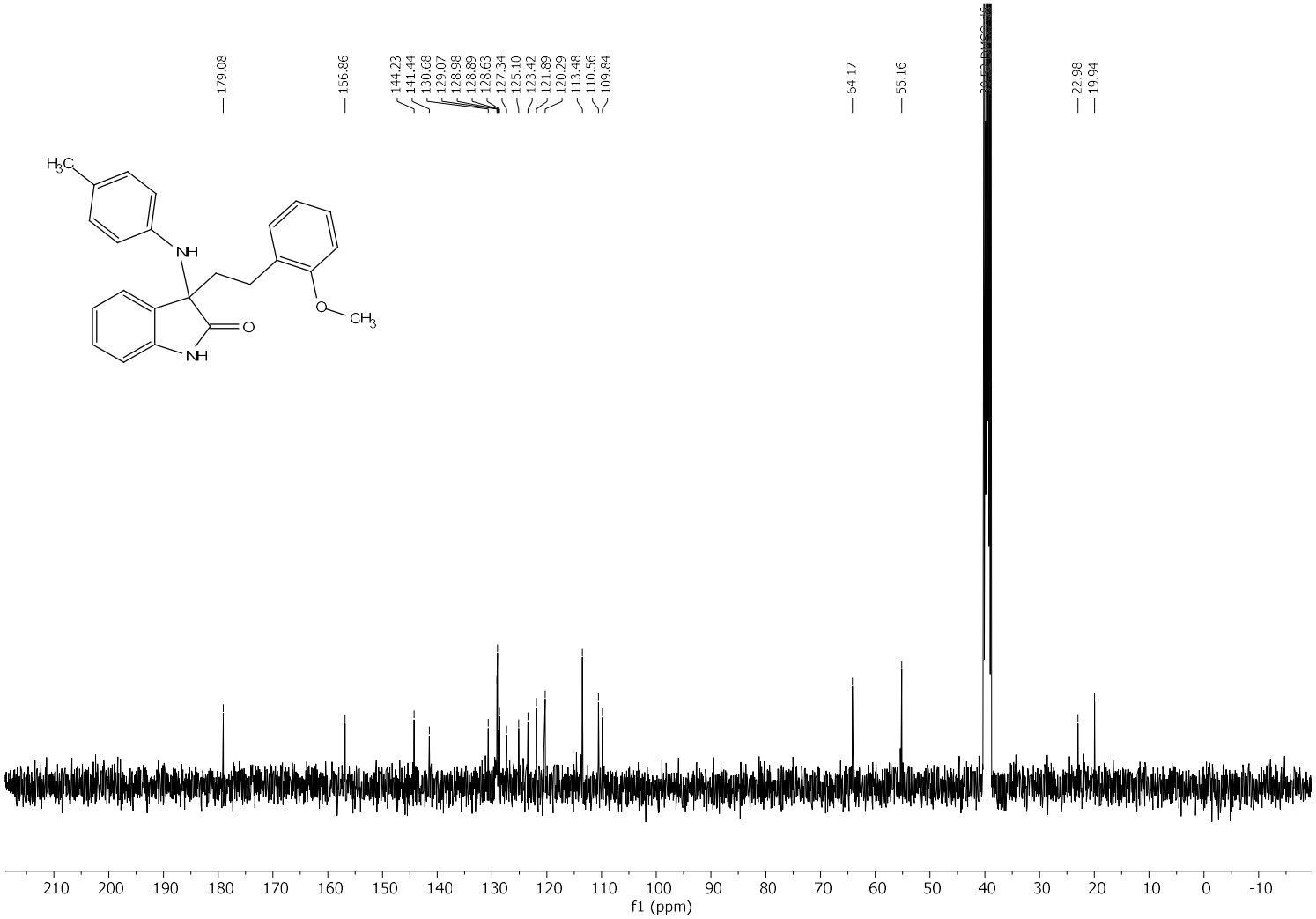
2g ^{13}C NMR spectrum



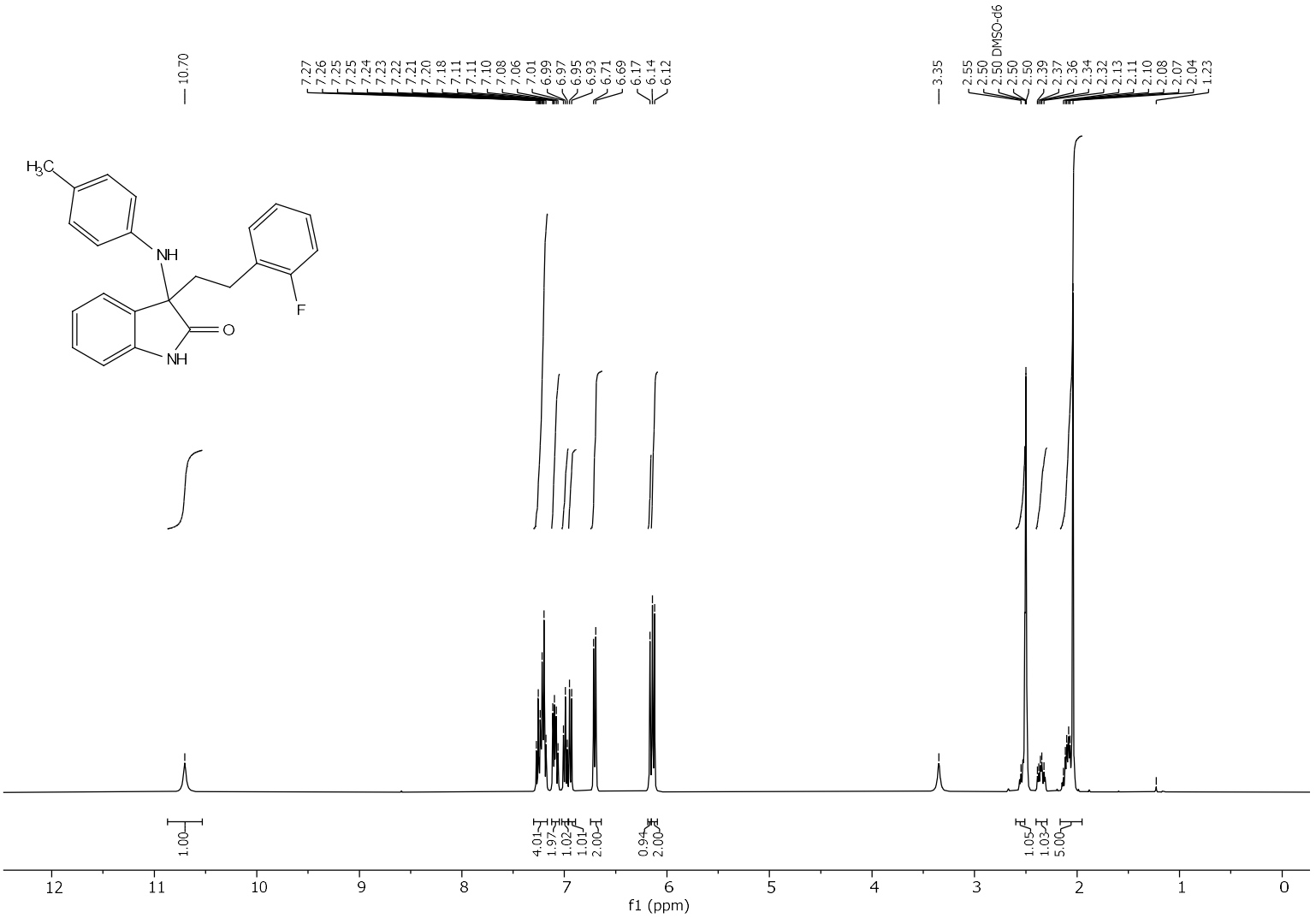
2h ^{1}H NMR spectrum



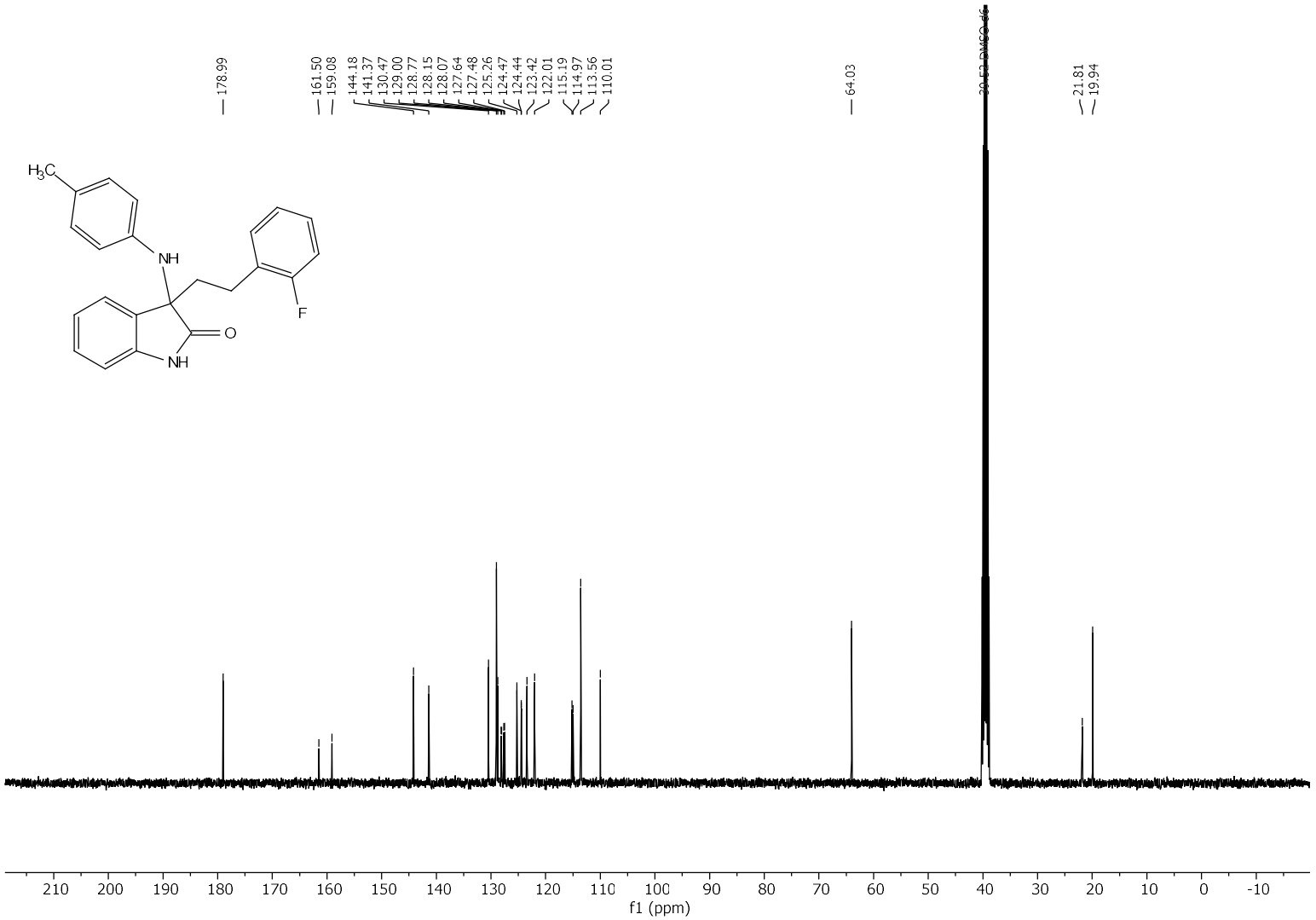
2h ^{13}C NMR spectrum



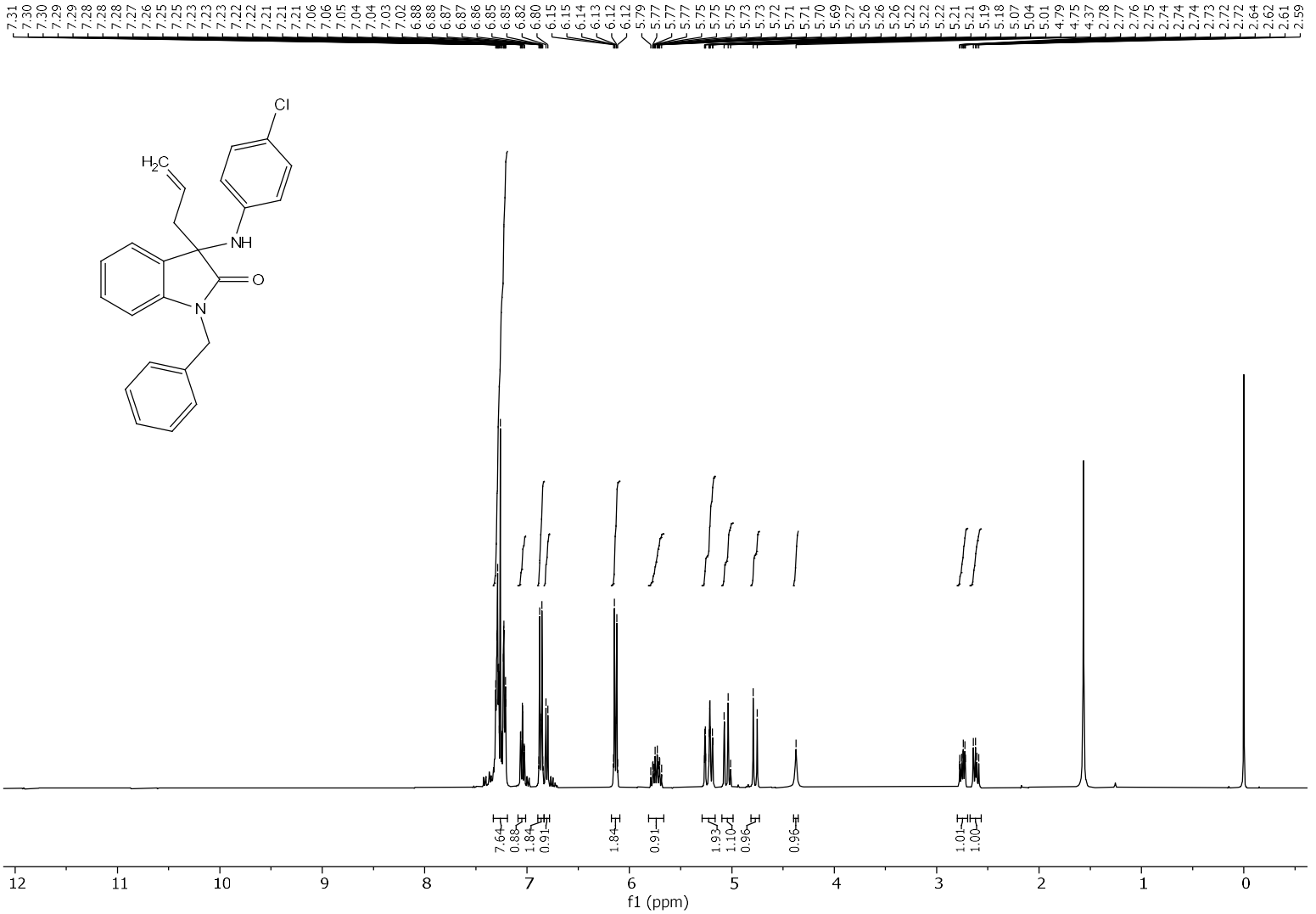
2i ^{1}H NMR spectrum



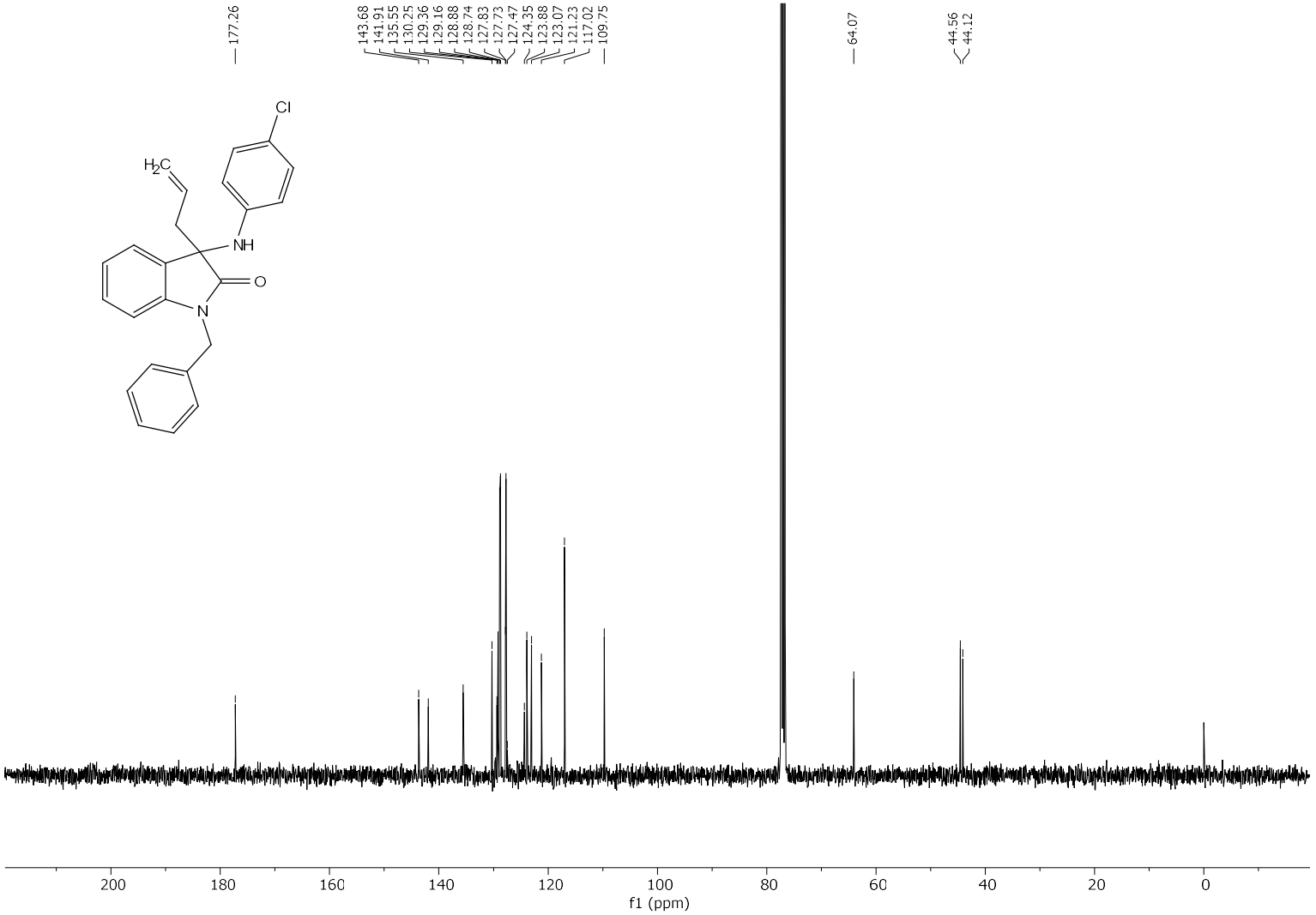
2i ^{13}C NMR spectrum



3-Allyl-1-benzyl-3-((4-chlorophenyl)amino)indolin-2-one ^{1}H NMR spectrum



3-Allyl-1-benzyl-3-((4-chlorophenyl)amino)indolin-2-one ^{13}C NMR spectrum



3. X-Ray Crystallography

3.1 Crystal data collection and refinement

Intensity data for compounds **2c** and **3e** were collected on a Bruker D8 Venture Bio PHOTON III 28 pixel array area detector (208 ×128 mm 2) diffractometer with a Mo Kα IμS DIAMOND source (50kV, 1.4 mA) at -100 °C. The collection method involved ω- and φ-scans, and 1536 × 1024 bit data frames. The unit cell and full data set were collected using APEX4[36], SAINT was used to integrate the data, and SADABS was used to make empirical absorption corrections and scale the data. Space group assignments were made using XPREP on all compounds. Using OLEX2[37], the crystal structures were solved with the ShelXT[38] structure solution program using Intrinsic Phasing and refined with the ShelXL[39] refinement package using Least Squares minimization. Non-hydrogen atoms were first refined isotropically followed by anisotropic refinement by full matrix least-squares calculations based on F^2.

3.2 Crystallographic data and structure refinement details

Crystal structure determination for 1-benzyl-3-((4-chlorophenyl)amino)-3-(4-methoxyphenethyl)indolin-2-one 2c A purified sample of 1-benzyl-3-((4-chlorophenyl)amino)-3-(4-methoxyphenethyl)indolin-2-one **2c** was recrystallised by slow evaporation in DCM at ambient temperature. Crystal Data for $C_{30}H_{27}N_2O_2Cl$ (M = 482.98 g/mol): triclinic, space group P-1 (no. 2), a = 9.8224(3) Å, b = 10.4896(3) Å, c = 12.9397(4) Å, α = 107.5160(10)°, β = 95.1060(10)°, γ = 103.4500(10)°, V = 1218.22(6) Å^3, Z = 2, T = 173(1) K, μ(MoKα) = 0.188 mm^{-1}, $Dcalc$ = 1.317 g/cm^3, 45607 reflections measured (4.232° ≤ 2Θ ≤ 57.156°), 6119 unique (R_{int} = 0.0535, R_{sigma} = 0.0341) which were used in all calculations. The final R_1 was 0.0386 (I > 2σ(I)) and wR_2 was 0.1015 (all data). CCDC deposition number: 2513396.

Crystal structure determination for *tert*-butyl 3-((4-bromophenyl)imino)-2-hydroxy-2-(4-methoxyphenethyl)indoline-1-carboxyla 3e A purified sample of *tert*-butyl 3-((4-bromophenyl)imino)-2-hydroxy-2-(4-methoxyphenethyl)indoline-1-carboxylate **3e** was recrystallised by slow evaporation in DCM at ambient temperature. Crystal Data for $C_{28}H_{29}BrN_2O_4$ (M = 537.44 g/mol): colourless needle, monoclinic, space group $P2_1/c$ (no. 14), a = 14.1456(18) Å, b = 17.8889(19) Å, c = 10.4103(13) Å, β = 103.055(4)°, V = 2566.2(5) Å^3, Z = 4, T = 173(1) K, μ(MoKα) = 1.638 mm^{-1}, $Dcalc$ = 1.391 g/cm^3, 44998 reflections measured (4.554° ≤ 2Θ ≤ 54°), 5591 unique (R_{int} = 0.1113, R_{sigma} = 0.0554) which were used in all calculations. The final R_1 was 0.0410 (I > 2σ(I)) and wR_2 was 0.0900 (all data). CCDC deposition number: 2513397.

3.3 Crystallographic information

3.3.1 1-Benzyl-3-((4-chlorophenyl)amino)-3-(4-methoxyphenethyl)indolin-2-one 2c

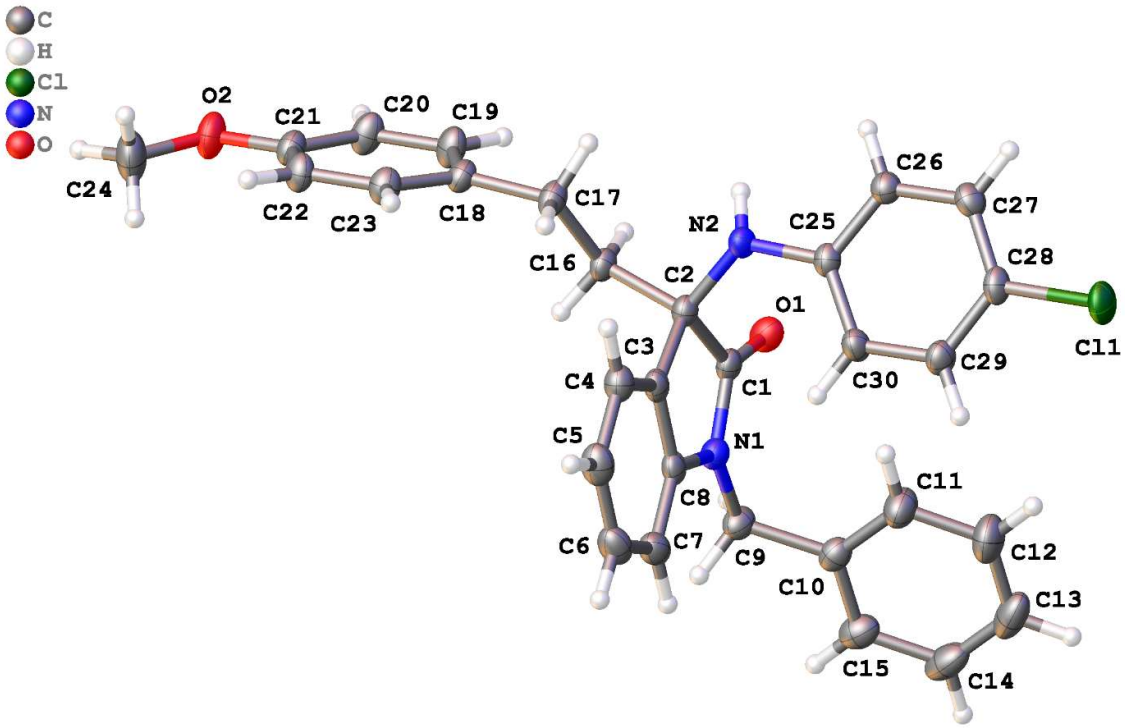


Figure 1. Single crystal X-ray structure of compound 2c. ORTEP diagram drawn at 50% probability level.

Table 2 Crystal data and structure refinement for 1-benzyl-3-((4-chlorophenyl)amino)-3-(4-methoxyphenethyl)indolin-2-one 2c

Empirical formula	**$C_{30}H_{27}N_2O_2Cl$**
Formula weight	482.98
Temperature/K	173(1)
Crystal system	triclinic
Space group	*P*-1
a/Å	9.8224(3)
b/Å	10.4896(3)
c/Å	12.9397(4)
α/°	107.5160(10)

β/°	95.1060(10)
γ/°	103.4500(10)
Volume/Å^3	1218.22(6)
Z	2
ρ_{calc}g/cm^3	1.317
μ/mm^{-1}	0.188
F(000)	508.0
Crystal size/mm^3	0.243 × 0.151 × 0.1
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	4.232 to 57.156
Index ranges	-13 ≤ h ≤ 13, -14 ≤ k ≤ 14, -17 ≤ l ≤ 17
Reflections collected	45607
Independent reflections	6119 [R_{int} = 0.0535, R_{sigma} = 0.0341]
Data/restraints/parameters	6119/0/321
Goodness-of-fit on F^2	1.040
Final R indexes [I>=2σ (I)]	R_1 = 0.0386, wR_2 = 0.0961
Final R indexes [all data]	R_1 = 0.0463, wR_2 = 0.1015
Largest diff. peak/hole / e Å^{-3}	0.32/-0.26

Table 3 Fractional Atomic Coordinates ($\times 10^4$) and Equivalent Isotropic Displacement Parameters ($Å^2 \times 10^3$) for 1-benzyl-3-((4-chlorophenyl)amino)-3-(4-methoxyphenethyl)indolin-2-one 2e. U_{eq} is defined as 1/3 of the trace of the orthogonalised U_{IJ}.

Atom	*x*	*y*	*z*	U(eq)
Cl1	6260.1(4)	9917.6(3)	2234.1(3)	35.06(10)
O1	3808.0(10)	3738.4(10)	3530.9(7)	29.1(2)
O2	8520.9(11)	-166.6(11)	7221.9(9)	36.4(2)
N1	4749.5(11)	2706.3(11)	2048.7(8)	23.7(2)
N2	6844.3(11)	5622.1(11)	4219.0(9)	23.3(2)
C1	4831.7(13)	3546.8(13)	3098.5(10)	22.9(2)
C2	6419.8(13)	4137.0(12)	3649.0(10)	21.9(2)
C3	7147.4(13)	3620.2(12)	2681.0(10)	23.1(2)
C4	8566.5(14)	3860.9(14)	2583.4(11)	28.1(3)
C5	8930.5(15)	3204.0(15)	1576.0(12)	33.6(3)
C6	7886.0(16)	2348.3(15)	689.2(12)	34.4(3)
C7	6450.4(15)	2119.6(14)	767.3(11)	29.6(3)
C8	6113.8(13)	2759.4(12)	1775.3(10)	23.1(2)
C9	3411.3(14)	1866.6(13)	1338.5(11)	28.2(3)
C10	2692.7(14)	2615.2(14)	718.3(10)	27.4(3)
C11	3072.7(17)	4041.3(16)	990.9(13)	38.3(3)
C12	2357.3(19)	4680.0(19)	409.7(15)	47.2(4)
C13	1257.3(18)	3902(2)	-438.0(14)	46.8(4)
C14	855.9(17)	2478(2)	-703.7(12)	44.2(4)
C15	1568.1(15)	1832.7(17)	-134.1(11)	35.3(3)
C16	6576.5(13)	3395.1(13)	4503.2(10)	23.4(2)
C17	8027.7(14)	3902.6(14)	5250.7(11)	28.0(3)

Atom	*x*	*y*	*z*	U(eq)
C18	8224.0(13)	2893.7(13)	5837.6(10)	24.9(2)
C19	7211.1(14)	2409.6(15)	6423.7(11)	31.0(3)
C20	7349.8(14)	1403.0(16)	6881.4(12)	32.0(3)
C21	8507.7(14)	859.4(14)	6768.2(11)	27.2(3)
C22	9557.1(14)	1363.9(14)	6238.5(11)	29.6(3)
C23	9399.3(14)	2376.2(14)	5779.1(11)	28.0(3)
C24	9631(2)	-834.3(19)	7047.7(16)	48.4(4)
C25	6657.5(12)	6590.1(12)	3717.8(10)	21.9(2)
C26	6737.8(13)	7939.3(13)	4392.6(10)	25.1(2)
C27	6615.6(14)	8964.3(13)	3948.4(11)	27.5(3)
C28	6399.8(13)	8640.8(13)	2815.1(11)	25.7(3)
C29	6312.1(14)	7324.1(13)	2132.2(11)	27.1(3)
C30	6447.3(14)	6303.1(13)	2580.0(10)	25.7(3)

Table 4 Anisotropic Displacement Parameters ($Å^2×10^3$) for 1-benzyl-3-((4-chlorophenyl)amino)-3-(4-methoxyphenethyl)indolin-2-one 2c. The Anisotropic displacement factor exponent takes the form: $-2π^2[h^2a^{*2}U_{11}+2hka^*b^*U_{12}+…]$.

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
Cl1	44.8(2)	27.07(17)	43.35(19)	21.52(14)	9.59(15)	15.05(14)
O1	26.5(4)	37.1(5)	27.8(4)	13.1(4)	6.9(4)	12.4(4)
O2	35.5(5)	38.8(6)	48.5(6)	29.6(5)	9.2(4)	15.4(4)
N1	25.1(5)	23.9(5)	24.0(5)	10.0(4)	2.8(4)	7.9(4)
N2	29.9(5)	20.9(5)	22.3(5)	10.1(4)	5.2(4)	9.2(4)
C1	26.0(6)	23.3(6)	24.2(5)	13.0(5)	3.9(4)	9.3(5)
C2	23.2(6)	22.2(6)	23.6(5)	10.8(5)	4.0(4)	8.3(4)
C3	28.1(6)	20.8(5)	26.3(6)	12.5(5)	6.9(5)	10.9(5)
C4	28.1(6)	28.0(6)	33.1(7)	14.6(5)	6.8(5)	10.5(5)
C5	33.2(7)	37.0(7)	41.1(8)	19.9(6)	16.3(6)	16.5(6)
C6	44.9(8)	33.4(7)	33.5(7)	14.1(6)	17.5(6)	19.0(6)
C7	40.2(7)	25.5(6)	25.9(6)	9.8(5)	7.2(5)	12.2(6)
C8	28.2(6)	19.6(5)	27.3(6)	12.4(5)	6.7(5)	10.7(5)
C9	29.6(6)	24.9(6)	28.7(6)	10.9(5)	0.3(5)	4.1(5)
C10	26.1(6)	34.5(7)	25.4(6)	13.1(5)	5.7(5)	10.4(5)
C11	39.8(8)	34.9(8)	41.2(8)	16.9(6)	-2.9(6)	10.0(6)
C12	53.5(10)	46.7(9)	54.8(10)	29.7(8)	7.1(8)	23.1(8)
C13	46.5(9)	72.8(12)	40.9(8)	32.3(8)	11.8(7)	34.7(9)
C14	35.5(8)	70.6(12)	28.7(7)	15.4(7)	2.0(6)	21.8(8)
C15	30.8(7)	44.7(8)	29.0(7)	10.4(6)	3.7(5)	10.4(6)
C16	25.4(6)	22.9(6)	25.6(6)	13.1(5)	3.2(5)	7.4(5)
C17	26.9(6)	28.3(6)	32.3(6)	17.1(5)	0.7(5)	6.6(5)

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
C18	24.4(6)	26.8(6)	25.5(6)	12.4(5)	1.0(5)	7.2(5)
C19	26.3(6)	39.9(7)	37.4(7)	21.6(6)	9.1(5)	16.1(6)
C20	26.8(6)	43.0(8)	37.4(7)	25.2(6)	10.7(5)	12.9(6)
C21	27.5(6)	28.0(6)	29.2(6)	15.0(5)	1.2(5)	7.8(5)
C22	25.7(6)	33.8(7)	36.4(7)	17.1(6)	6.6(5)	13.9(5)
C23	24.5(6)	31.7(7)	32.6(6)	16.3(5)	7.0(5)	8.3(5)
C24	57.3(10)	46.8(9)	61.5(11)	32.2(8)	17.5(8)	31.2(8)
C25	20.0(5)	21.8(6)	27.3(6)	11.9(5)	5.2(4)	6.6(4)
C26	26.7(6)	23.5(6)	25.9(6)	9.3(5)	3.7(5)	7.1(5)
C27	29.1(6)	20.6(6)	32.4(6)	8.2(5)	5.2(5)	7.0(5)
C28	25.6(6)	22.5(6)	35.0(7)	16.5(5)	6.7(5)	8.0(5)
C29	32.1(7)	27.1(6)	27.6(6)	14.4(5)	7.4(5)	10.5(5)
C30	32.5(6)	21.3(6)	26.5(6)	9.8(5)	6.7(5)	10.4(5)

Table 5 Bond Lengths for 1-benzyl-3-((4-chlorophenyl)amino)-3-(4-methoxyphenethyl)indolin-2-one 2c.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
Cl1	C28	1.7468(12)	C10	C15	1.3881(19)
O1	C1	1.2210(15)	C11	C12	1.392(2)
O2	C21	1.3743(15)	C12	C13	1.370(3)
O2	C24	1.4262(19)	C13	C14	1.377(3)
N1	C1	1.3622(16)	C14	C15	1.386(2)
N1	C8	1.4091(16)	C16	C17	1.5306(17)
N1	C9	1.4516(16)	C17	C18	1.5121(16)
N2	C2	1.4478(15)	C18	C19	1.3978(18)
N2	C25	1.3953(15)	C18	C23	1.3840(18)
C1	C2	1.5529(17)	C19	C20	1.3832(18)
C2	C3	1.5181(16)	C20	C21	1.3862(18)
C2	C16	1.5473(16)	C21	C22	1.3793(18)
C3	C4	1.3818(18)	C22	C23	1.3947(18)
C3	C8	1.3943(17)	C25	C26	1.4013(17)
C4	C5	1.3996(19)	C25	C30	1.3968(17)
C5	C6	1.385(2)	C26	C27	1.3858(17)
C6	C7	1.392(2)	C27	C28	1.3864(18)
C7	C8	1.3835(17)	C28	C29	1.3756(18)
C9	C10	1.5150(17)	C29	C30	1.3880(17)
C10	C11	1.379(2)			

Table 6 Bond Angles for 1-benzyl-3-((4-chlorophenyl)amino)-3-(4-methoxyphenethyl)indolin-2-one 2c.

Atom	Atom	Atom	Angle/˚	Atom	Atom	Atom	Angle/˚
C21	O2	C24	117.48(11)	C10	C11	C12	120.56(15)
C1	N1	C8	110.99(10)	C13	C12	C11	120.51(16)
C1	N1	C9	122.95(11)	C12	C13	C14	119.29(14)
C8	N1	C9	126.06(10)	C13	C14	C15	120.60(15)
C25	N2	C2	123.32(10)	C14	C15	C10	120.34(15)
O1	C1	N1	124.64(12)	C17	C16	C2	115.22(10)
O1	C1	C2	126.76(11)	C18	C17	C16	111.45(10)
N1	C1	C2	108.52(10)	C19	C18	C17	121.72(11)
N2	C2	C1	114.01(10)	C23	C18	C17	120.79(11)
N2	C2	C3	116.18(10)	C23	C18	C19	117.45(11)
N2	C2	C16	108.48(10)	C20	C19	C18	121.02(12)
C3	C2	C1	101.23(10)	C19	C20	C21	120.21(12)
C3	C2	C16	111.74(10)	O2	C21	C20	115.59(11)
C16	C2	C1	104.55(9)	O2	C21	C22	124.40(12)
C4	C3	C2	131.47(12)	C22	C21	C20	120.01(12)
C4	C3	C8	119.68(11)	C21	C22	C23	119.01(12)
C8	C3	C2	108.84(10)	C18	C23	C22	122.18(12)
C3	C4	C5	118.74(13)	N2	C25	C26	118.28(11)
C6	C5	C4	120.56(13)	N2	C25	C30	123.58(11)
C5	C6	C7	121.38(12)	C30	C25	C26	118.10(11)
C8	C7	C6	117.15(13)	C27	C26	C25	121.19(11)
C3	C8	N1	109.95(10)	C26	C27	C28	119.17(12)
C7	C8	N1	127.56(12)	C27	C28	Cl1	120.10(10)

Atom	Atom	Atom	Angle/˚	Atom	Atom	Atom	Angle/˚
C7	C8	C3	122.46(12)	C29	C28	Cl1	118.97(10)
N1	C9	C10	114.79(10)	C29	C28	C27	120.93(11)
C11	C10	C9	122.82(12)	C28	C29	C30	119.76(12)
C11	C10	C15	118.69(13)	C29	C30	C25	120.85(11)
C15	C10	C9	118.44(12)				

Table 7 Torsion Angles for 1-benzyl-3-((4-chlorophenyl)amino)-3-(4-methoxyphenethyl)indolin-2-one 2c.

A	B	C	D	Angle/°	A	B	C	D	Angle/°
Cl1	C28	C29	C30	178.80(10)	C8	C3	C4	C5	-1.37(18)
O1	C1	C2	N2	-50.66(16)	C9	N1	C1	O1	-3.88(18)
O1	C1	C2	C3	-176.16(12)	C9	N1	C1	C2	173.18(10)
O1	C1	C2	C16	67.63(15)	C9	N1	C8	C3	-176.77(11)
O2	C21	C22	C23	177.87(13)	C9	N1	C8	C7	5.36(19)
N1	C1	C2	N2	132.36(10)	C9	C10	C11	C12	-178.56(14)
N1	C1	C2	C3	6.86(12)	C9	C10	C15	C14	178.25(13)
N1	C1	C2	C16	-109.34(10)	C10	C11	C12	C13	0.4(3)
N1	C9	C10	C11	-15.07(19)	C11	C10	C15	C14	0.7(2)
N1	C9	C10	C15	167.45(12)	C11	C12	C13	C14	0.6(3)
N2	C2	C3	C4	50.66(17)	C12	C13	C14	C15	-1.0(2)
N2	C2	C3	C8	-129.52(11)	C13	C14	C15	C10	0.4(2)
N2	C2	C16	C17	-52.14(14)	C15	C10	C11	C12	-1.1(2)
N2	C25	C26	C27	177.53(11)	C16	C2	C3	C4	-74.52(16)
N2	C25	C30	C29	-177.97(11)	C16	C2	C3	C8	105.30(11)
C1	N1	C8	C3	2.31(13)	C16	C17	C18	C19	-51.30(17)
C1	N1	C8	C7	-175.57(12)	C16	C17	C18	C23	126.37(13)
C1	N1	C9	C10	85.30(14)	C17	C18	C19	C20	174.74(13)
C1	C2	C3	C4	174.70(12)	C17	C18	C23	C22	-174.91(12)
C1	C2	C3	C8	-5.48(12)	C18	C19	C20	C21	0.3(2)
C1	C2	C16	C17	-174.13(10)	C19	C18	C23	C22	2.9(2)
C2	N2	C25	C26	162.86(11)	C19	C20	C21	O2	-177.94(13)
C2	N2	C25	C30	-19.62(18)	C19	C20	C21	C22	2.8(2)

A	B	C	D	Angle/°	A	B	C	D	Angle/°
C2	C3	C4	C5	178.43(12)	C20	C21	C22	C23	-2.9(2)
C2	C3	C8	N1	2.44(13)	C21	C22	C23	C18	0.1(2)
C2	C3	C8	C7	-179.56(11)	C23	C18	C19	C20	-3.0(2)
C2	C16	C17	C18	-164.83(10)	C24	O2	C21	C20	175.03(14)
C3	C2	C16	C17	77.20(13)	C24	O2	C21	C22	-5.7(2)
C3	C4	C5	C6	1.09(19)	C25	N2	C2	C1	-55.32(15)
C4	C3	C8	N1	-177.72(11)	C25	N2	C2	C3	61.84(15)
C4	C3	C8	C7	0.28(18)	C25	N2	C2	C16	-171.34(10)
C4	C5	C6	C7	0.3(2)	C25	C26	C27	C28	0.47(19)
C5	C6	C7	C8	-1.4(2)	C26	C25	C30	C29	-0.45(18)
C6	C7	C8	N1	178.72(12)	C26	C27	C28	Cl1	-179.35(10)
C6	C7	C8	C3	1.09(18)	C26	C27	C28	C29	-0.3(2)
C8	N1	C1	O1	177.01(11)	C27	C28	C29	C30	-0.3(2)
C8	N1	C1	C2	-5.93(13)	C28	C29	C30	C25	0.7(2)
C8	N1	C9	C10	-95.72(14)	C30	C25	C26	C27	-0.12(18)

Table 8 Hydrogen Atom Coordinates (Å×10^4) and Isotropic Displacement Parameters (Å^2×10^3) for 1-benzyl-3-((4-chlorophenyl)amino)-3-(4-methoxyphenethyl)indolin-2-one 2c.

Atom	*x*	*y*	*z*	U(eq)
H2	6661(17)	5844(17)	4896(14)	34(4)
H4	9281.47	4460.88	3188.71	34
H5	9902.36	3346.56	1499.98	40
H6	8154.53	1907.92	13.21	41
H7	5732.65	1548.62	154.64	36
H9A	2753.51	1520.05	1791.8	34
H9B	3583.07	1048.79	798.64	34
H11	3829.45	4592.59	1580.48	46
H12	2633.79	5663.26	602.36	57
H13	776.68	4339.7	-838.27	56
H14	83.68	1934.11	-1282.74	53
H15	1285.24	849.38	-328.07	42
H16A	5839.57	3515.89	4970.5	28
H16B	6387.75	2387.91	4105.38	28
H17A	8786.21	4016.61	4804.07	34
H17B	8115.2	4820.96	5800.97	34
H19	6415.22	2777.64	6508.97	37
H20	6649.28	1083.31	7274.63	38
H22	10375.04	1026.78	6187.32	36
H23	10122.58	2722.06	5413.97	34
H24A	9635.47	-1206.53	6257	73
H24B	9473.33	-1595.15	7353.06	73
H24C	10546.94	-159.84	7413.29	73

Atom	*x*	*y*	*z*	U(eq)
H26	6878.5	8155.29	5168.61	30
H27	6678.82	9877.07	4414.54	33
H29	6159.57	7114.38	1356.82	33
H30	6396.29	5397.32	2106.59	31

3.3.2 *tert*-Butyl 3-((4-bromophenyl)imino)-2-hydroxy-2-(4-methoxyphenethyl)indoline-1-carboxylate 3e

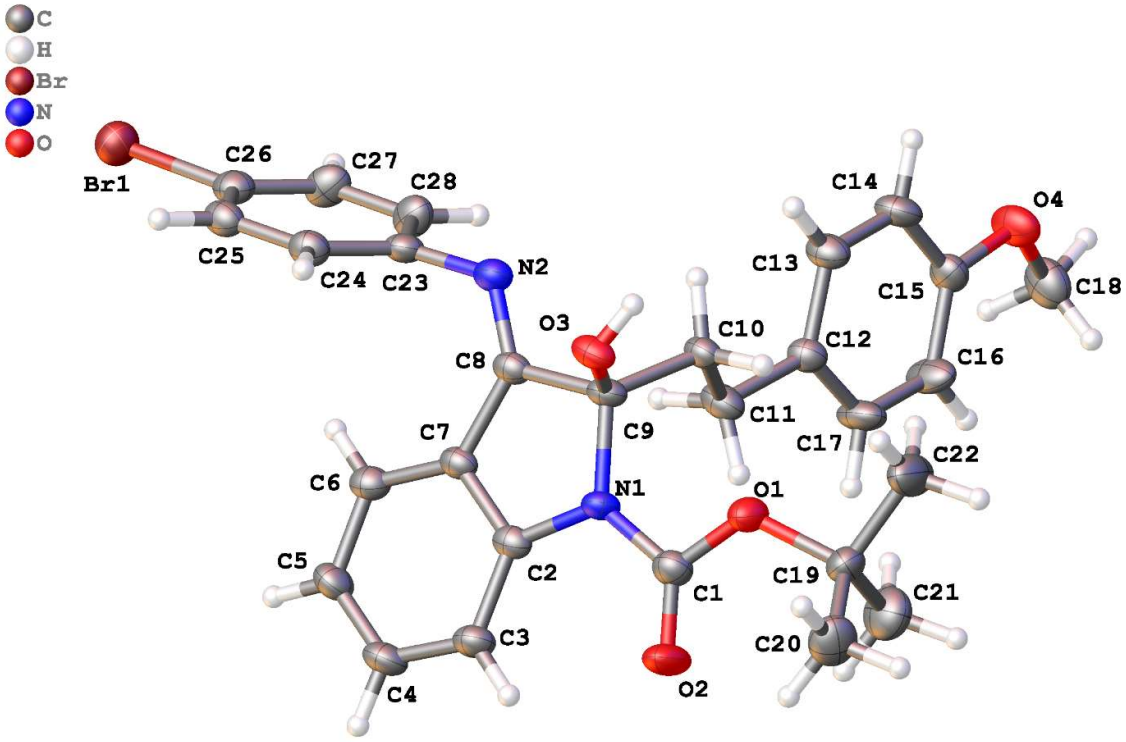


Figure 2. Single crystal X-ray structure of compound 3e. ORTEP diagram drawn at 50% probability level.

Table 9 Crystal data and structure refinement for 3-((4-bromophenyl)imino)-2-hydroxy-2-(4-methoxyphenethyl)indoline-1-carboxylate 3e.

Empirical formula	**$C_{28}H_{29}BrN_2O_4$**
Formula weight	537.44
Temperature/K	173(1)
Crystal system	monoclinic
Space group	$P2_1/c$
a/Å	14.1456(18)
b/Å	17.8889(19)
c/Å	10.4103(13)
α/°	90
β/°	103.055(4)
γ/°	90
Volume/Å^3	2566.2(5)
Z	4
ρ_{calc}g/cm^3	1.391
μ/mm^{-1}	1.638
F(000)	1112.0
Crystal size/mm^3	0.478 × 0.167 × 0.052
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	4.554 to 54
Index ranges	-18 ≤ h ≤ 18, -22 ≤ k ≤ 22, -13 ≤ l ≤ 13
Reflections collected	44998
Independent reflections	5591 [R_{int} = 0.1113, R_{sigma} = 0.0554]
Data/restraints/parameters	5591/0/324
Goodness-of-fit on F^2	1.034
Final R indexes [I>=2σ (I)]	R_1 = 0.0410, wR_2 = 0.0783
Final R indexes [all data]	R_1 = 0.0702, wR_2 = 0.0900
Largest diff. peak/hole / e Å^{-3}	0.33/-0.56

Table 10 Fractional Atomic Coordinates ($\times 10^4$) and Equivalent Isotropic Displacement Parameters ($Å^2 \times 10^3$) for 3-((4-bromophenyl)imino)-2-hydroxy-2-(4-methoxyphenethyl)indoline-1-carboxylate 3e. U_{eq} is defined as 1/3 of the trace of the orthogonalised U_{IJ}.

Atom	*x*	*y*	*z*	U(eq)
Br1	591.9(2)	4321.6(2)	3455.4(3)	38.91(10)
O1	7534.0(13)	6342.3(10)	1573.6(17)	32.6(4)
O2	7500.0(15)	7145.0(11)	3234(2)	48.4(6)
O3	5504.6(13)	5940.8(9)	375.7(17)	28.2(4)
O4	8547.4(15)	1864.9(9)	4223.8(19)	40.1(5)
N1	6259.1(15)	6331.5(10)	2504.0(19)	23.8(4)
N2	4330.7(15)	5011.5(11)	1727(2)	26.3(5)
C1	7141.9(19)	6651.6(13)	2495(3)	29.1(6)
C2	5679.8(18)	6559.0(12)	3370(2)	24.4(5)
C3	5803.2(19)	7174.2(13)	4220(3)	29.5(6)
C4	5135(2)	7279.6(14)	4979(3)	31.9(6)
C5	4360(2)	6793.2(14)	4940(3)	31.1(6)
C6	4228.8(19)	6194.0(13)	4079(2)	27.7(6)
C7	4879.6(18)	6084.4(12)	3272(2)	23.7(5)
C8	4903.1(18)	5538.9(12)	2233(2)	23.7(5)
C9	5807.0(18)	5688.4(13)	1678(2)	24.1(5)
C10	6444.2(18)	4989.6(13)	1793(2)	25.4(5)
C11	6837(2)	4745.6(14)	3210(3)	31.9(6)
C12	7348.8(19)	3996.0(13)	3397(2)	26.3(5)
C13	7060(2)	3386.8(14)	2566(3)	31.3(6)
C14	7478(2)	2689.1(14)	2858(3)	33.3(6)
C15	8189.9(19)	2580.9(13)	3992(3)	30.7(6)

Atom	*x*	*y*	*z*	U(eq)
C16	8497(2)	3177.2(15)	4812(3)	41.5(7)
C17	8083(2)	3874.6(14)	4500(3)	38.9(7)
C18	9079(2)	1699.8(16)	5528(3)	43.2(7)
C19	8577.6(19)	6446.2(15)	1619(3)	32.5(6)
C20	8801(2)	7255.3(16)	1363(3)	46.1(8)
C21	9158(2)	6175.9(18)	2932(3)	51.7(8)
C22	8721(2)	5938.1(19)	520(4)	55.2(9)
C23	3464.0(18)	4872.4(13)	2163(2)	26.0(5)
C24	2661.2(19)	5334.4(13)	1790(2)	27.6(6)
C25	1814.7(19)	5176.2(13)	2183(2)	29.4(6)
C26	1767.6(19)	4550.2(14)	2945(2)	29.7(6)
C27	2556(2)	4081.9(14)	3318(3)	34.7(6)
C28	3406.2(19)	4243.9(14)	2923(3)	33.8(6)

Table 11 Anisotropic Displacement Parameters ($Å^2×10^3$) for 3-((4-bromophenyl)imino)-2-hydroxy-2-(4-methoxyphenethyl)indoline-1-carboxylate 3e. The Anisotropic displacement factor exponent takes the form: $-2π^2[h^2a^{*2}U_{11}+2hka^*b^*U_{12}+…]$.

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
Br1	35.15(16)	37.29(15)	45.04(17)	-1.65(14)	10.64(12)	-2.57(13)
O1	29.0(10)	37.6(10)	32.3(10)	-11.1(8)	8.9(8)	-7.3(8)
O2	41.8(12)	45.5(12)	60.3(14)	-31.6(11)	16.6(11)	-17.1(10)
O3	39.2(11)	22.0(8)	21.3(9)	-2.8(8)	2.0(8)	4.2(8)
O4	48.1(13)	23.2(9)	43.5(12)	-1.1(8)	-1.5(10)	8.1(8)
N1	27.6(11)	18.8(10)	24.3(10)	-4.7(8)	4.5(9)	-4.0(8)
N2	28.3(12)	21.6(10)	27.2(11)	-3.0(9)	2.5(9)	-0.4(9)

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
C1	32.0(15)	22.5(12)	31.9(14)	-2.3(11)	5.3(12)	-0.2(11)
C2	29.8(14)	19.4(11)	21.4(12)	0.2(10)	0.4(10)	3.0(10)
C3	33.7(15)	21.8(12)	30.9(14)	-5.1(11)	3.2(12)	-2.2(11)
C4	41.7(17)	23.9(13)	28.9(14)	-8.0(11)	5.4(12)	0.3(11)
C5	36.6(16)	29.4(13)	28.4(14)	-7.2(11)	9.6(12)	2.6(11)
C6	30.9(14)	25.0(12)	24.8(13)	-1.9(10)	1.1(11)	-0.3(10)
C7	28.2(14)	18.6(11)	22.2(12)	-1.2(10)	1.5(10)	2.5(10)
C8	29.0(13)	17.9(11)	22.2(12)	-0.7(9)	1.5(10)	2.5(9)
C9	30.3(13)	18.7(11)	21.3(12)	-3.8(10)	1.4(10)	-1.3(10)
C10	29.6(14)	19.9(11)	24.7(13)	-4.0(10)	2.3(11)	3.1(10)
C11	41.5(17)	25.5(13)	26.2(13)	-3.6(11)	2.7(12)	5.8(11)
C12	30.9(14)	21.9(12)	25.0(13)	-0.9(10)	4.0(11)	-0.2(10)
C13	37.7(16)	27.1(13)	25.2(13)	-3.4(11)	-0.9(12)	2.8(11)
C14	43.8(17)	23.9(13)	30.2(14)	-8.7(11)	4.2(12)	-2.9(11)
C15	31.2(15)	21.2(12)	38.5(15)	-1.3(11)	5.4(12)	2.7(10)
C16	38.6(17)	31.5(14)	42.1(17)	-6.1(13)	-16.7(14)	5.2(12)
C17	42.8(17)	24.3(13)	41.3(16)	-11.3(12)	-7.7(14)	-0.2(12)
C18	49.8(19)	36.1(15)	42.4(17)	4.8(14)	7.7(15)	13.8(13)
C19	24.5(14)	33.5(14)	38.3(15)	-7.4(12)	4.7(12)	-4.0(11)
C20	43.2(19)	38.6(16)	59(2)	4.6(15)	17.6(16)	-6.5(13)
C21	42.4(19)	52.3(19)	54(2)	3.1(16)	-1.7(16)	10.8(15)
C22	40.2(19)	67(2)	64(2)	-32.0(18)	25.1(17)	-15.4(16)
C23	29.4(14)	20.9(12)	25.9(13)	-6.3(10)	2.4(11)	-2.6(10)
C24	32.6(15)	21.1(12)	27.5(13)	1.1(10)	3.6(11)	0.8(10)
C25	32.7(15)	24.1(12)	28.6(14)	-1.9(11)	1.0(11)	4.5(10)

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
C26	31.1(15)	27.9(13)	27.4(13)	-4.6(11)	1.1(11)	-1.6(11)
C27	34.6(16)	25.6(13)	40.8(16)	7.8(12)	1.9(13)	-2.2(11)
C28	28.6(14)	24.6(13)	44.9(16)	4.0(12)	1.5(12)	3.0(11)

Table 12 Bond Lengths for 3-((4-bromophenyl)imino)-2-hydroxy-2-(4-methoxyphenethyl)indoline-1-carboxylate 3e.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
Br1	C26	1.901(3)	C8	C9	1.541(3)
O1	C1	1.332(3)	C9	C10	1.530(3)
O1	C19	1.478(3)	C10	C11	1.518(3)
O2	C1	1.205(3)	C11	C12	1.515(3)
O3	C9	1.401(3)	C12	C13	1.394(3)
O4	C15	1.378(3)	C12	C17	1.381(4)
O4	C18	1.427(3)	C13	C14	1.385(4)
N1	C1	1.376(3)	C14	C15	1.381(4)
N1	C2	1.408(3)	C15	C16	1.374(4)
N1	C9	1.491(3)	C16	C17	1.385(4)
N2	C8	1.277(3)	C19	C20	1.518(4)
N2	C23	1.423(3)	C19	C21	1.506(4)
C2	C3	1.399(3)	C19	C22	1.510(4)
C2	C7	1.400(3)	C23	C24	1.387(3)
C3	C4	1.375(4)	C23	C28	1.387(3)
C4	C5	1.393(4)	C24	C25	1.380(4)
C5	C6	1.383(3)	C25	C26	1.383(4)
C6	C7	1.393(3)	C26	C27	1.379(4)

Atom	Atom	Length/Å	Atom	Atom	Length/Å
C7	C8	1.463(3)	C27	C28	1.387(4)

Table 13 Bond Angles for 3-((4-bromophenyl)imino)-2-hydroxy-2-(4-methoxyphenethyl)indoline-1-carboxylate 3e.

Atom	Atom	Atom	Angle/˚	Atom	Atom	Atom	Angle/˚
C1	O1	C19	120.00(19)	C11	C10	C9	113.0(2)
C15	O4	C18	116.9(2)	C12	C11	C10	116.0(2)
C1	N1	C2	123.0(2)	C13	C12	C11	123.2(2)
C1	N1	C9	126.1(2)	C17	C12	C11	119.6(2)
C2	N1	C9	110.88(19)	C17	C12	C13	117.0(2)
C8	N2	C23	120.6(2)	C14	C13	C12	121.1(2)
O1	C1	N1	111.0(2)	C15	C14	C13	120.5(2)
O2	C1	O1	125.5(3)	O4	C15	C14	116.6(2)
O2	C1	N1	123.5(2)	C16	C15	O4	124.1(2)
C3	C2	N1	128.7(2)	C16	C15	C14	119.3(2)
C3	C2	C7	120.4(2)	C15	C16	C17	119.7(2)
C7	C2	N1	110.9(2)	C12	C17	C16	122.4(2)
C4	C3	C2	117.9(2)	O1	C19	C20	111.1(2)
C3	C4	C5	122.4(2)	O1	C19	C21	108.9(2)
C6	C5	C4	119.5(2)	O1	C19	C22	101.8(2)
C5	C6	C7	119.3(2)	C21	C19	C20	111.9(2)
C2	C7	C8	107.8(2)	C21	C19	C22	110.8(3)
C6	C7	C2	120.3(2)	C22	C19	C20	111.8(3)
C6	C7	C8	131.9(2)	C24	C23	N2	121.1(2)
N2	C8	C7	132.8(2)	C24	C23	C28	119.5(2)

Atom	Atom	Atom	Angle/˚	Atom	Atom	Atom	Angle/˚
N2	C8	C9	118.4(2)	C28	C23	N2	119.3(2)
C7	C8	C9	108.7(2)	C25	C24	C23	120.3(2)
O3	C9	N1	107.88(18)	C24	C25	C26	119.6(2)
O3	C9	C8	108.73(19)	C25	C26	Br1	119.5(2)
O3	C9	C10	112.63(19)	C27	C26	Br1	119.6(2)
N1	C9	C8	101.62(18)	C27	C26	C25	120.8(3)
N1	C9	C10	114.64(19)	C26	C27	C28	119.3(2)
C10	C9	C8	110.67(19)	C27	C28	C23	120.3(2)

Table 14 Torsion Angles for 3-((4-bromophenyl)imino)-2-hydroxy-2-(4-methoxyphenethyl)indoline-1-carboxylate 3e.

A	B	C	D	Angle/˚	A	B	C	D	Angle/˚
Br1	C26	C27	C28	178.8(2)	C7	C2	C3	C4	2.1(4)
O3	C9	C10	C11	175.7(2)	C7	C8	C9	O3	-112.6(2)
O4	C15	C16	C17	-179.2(3)	C7	C8	C9	N1	1.0(2)
N1	C2	C3	C4	-179.9(2)	C7	C8	C9	C10	123.2(2)
N1	C2	C7	C6	177.7(2)	C8	N2	C23	C24	75.5(3)
N1	C2	C7	C8	-3.3(3)	C8	N2	C23	C28	-107.7(3)
N1	C9	C10	C11	51.8(3)	C8	C9	C10	C11	-62.4(3)
N2	C8	C9	O3	65.9(3)	C9	N1	C1	O1	4.1(3)
N2	C8	C9	N1	179.5(2)	C9	N1	C1	O2	-175.8(2)
N2	C8	C9	C10	-58.4(3)	C9	N1	C2	C3	-174.1(2)
N2	C23	C24	C25	177.6(2)	C9	N1	C2	C7	4.1(3)
N2	C23	C28	C27	-177.6(2)	C9	C10	C11	C12	171.2(2)
C1	O1	C19	C20	-67.2(3)	C10	C11	C12	C13	-35.8(4)

A	B	C	D	Angle/˚	A	B	C	D	Angle/˚
C1	O1	C19	C21	56.5(3)	C10	C11	C12	C17	150.3(3)
C1	O1	C19	C22	173.6(2)	C11	C12	C13	C14	-172.6(3)
C1	N1	C2	C3	8.6(4)	C11	C12	C17	C16	171.9(3)
C1	N1	C2	C7	-173.1(2)	C12	C13	C14	C15	0.5(4)
C1	N1	C9	O3	-71.6(3)	C13	C12	C17	C16	-2.4(5)
C1	N1	C9	C8	174.1(2)	C13	C14	C15	O4	178.3(3)
C1	N1	C9	C10	54.7(3)	C13	C14	C15	C16	-1.7(4)
C2	N1	C1	O1	-179.1(2)	C14	C15	C16	C17	0.8(5)
C2	N1	C1	O2	1.0(4)	C15	C16	C17	C12	1.3(5)
C2	N1	C9	O3	111.2(2)	C17	C12	C13	C14	1.5(4)
C2	N1	C9	C8	-3.0(2)	C18	O4	C15	C14	-163.8(3)
C2	N1	C9	C10	-122.4(2)	C18	O4	C15	C16	16.2(4)
C2	C3	C4	C5	1.0(4)	C19	O1	C1	O2	16.5(4)
C2	C7	C8	N2	-176.9(3)	C19	O1	C1	N1	-163.3(2)
C2	C7	C8	C9	1.3(3)	C23	N2	C8	C7	0.8(4)
C3	C2	C7	C6	-3.9(4)	C23	N2	C8	C9	-177.2(2)
C3	C2	C7	C8	175.1(2)	C23	C24	C25	C26	-0.5(4)
C3	C4	C5	C6	-2.3(4)	C24	C23	C28	C27	-0.7(4)
C4	C5	C6	C7	0.5(4)	C24	C25	C26	Br1	-178.69(19)
C5	C6	C7	C2	2.5(4)	C24	C25	C26	C27	0.0(4)
C5	C6	C7	C8	-176.2(2)	C25	C26	C27	C28	0.1(4)
C6	C7	C8	N2	2.0(5)	C26	C27	C28	C23	0.2(4)
C6	C7	C8	C9	-179.9(2)	C28	C23	C24	C25	0.8(4)

Table 15 Hydrogen Atom Coordinates (Å×10^4) and Isotropic Displacement Parameters (Å^2×10^3) for 3-((4-bromophenyl)imino)-2-hydroxy-2-(4-methoxyphenethyl)indoline-1-carboxylate 3e.

Atom	*x*	*y*	*z*	U(eq)
H3A	6332.18	7508.67	4272.38	35
H4	5203.58	7699.83	5550.7	38
H5	3924.84	6872.62	5501.13	37
H6	3700.34	5860.3	4038.84	33
H10A	6059.61	4575.84	1300.96	30
H10B	6995.4	5090.42	1376.96	30
H11A	7296.88	5131.9	3656.75	38
H11B	6290.88	4728.84	3658.52	38
H13	6567.12	3451.1	1785.78	38
H14	7273.91	2282.25	2275.19	40
H16	8992.18	3111.52	5589.08	50
H17	8312.7	4284.07	5066.05	47
H18A	9207.95	1161.58	5609.82	65
H18B	8699.53	1851.67	6163.73	65
H18C	9695.88	1972.83	5707.68	65
H20A	8384.48	7418.44	525.08	69
H20B	9483.07	7300.49	1317.7	69
H20C	8679.21	7569.35	2079.69	69
H21A	9044.92	6507.68	3631.97	78
H21B	9849.34	6177.26	2926.51	78
H21C	8955.68	5666.83	3093.26	78
H22A	8548.69	5424.85	705.13	83
H22B	9401.49	5955.04	458.1	83

Atom	*x*	*y*	*z*	U(eq)
H22C	8305.15	6104.63	-315.53	83
H24	2694.6	5761.91	1260.16	33
H25	1267.39	5495.36	1931.52	35
H27	2517.14	3652.41	3840.33	42
H28	3951.83	3922.9	3172.93	41
H3	5620(20)	5633(16)	-160(30)	41(9)