Palladium-Catalyzed α-Arylation of Oxindoles

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Supporting Information

General Information: All reactions were performed under an inert atmosphere of argon, in oven or flame dried glassware unless otherwise stated. Argon was passed through a Drierite® filled drying tube before use.

Analytical thin layer chromatography was carried out using pre-coated aluminium-backed silica plates (Merck Kieselgel $60F_{254}$) and pre-coated plastic backed silica plates (Polygram® Sil G/UV_{254}). Plates were visualised under ultraviolet light (254 nm) or by staining with $KMnO_4$, vanillin or ceric ammonium molybdate (CAM). Flash column chromatography was carried out using Zeochem ZEOprep hyd. 40-63 micron silica with pre-absorption of the crude product onto silica. Pressure was applied at the column head *via* hand bellows.

Tetrahydrofuran, purchased from Rathburn (HPLC grade), was distilled from Na/benzophenone and stored over 4Å molecular sieves prior to use. Where required, solvents were degassed with argon. All chemicals were purchased from Acros, Aldrich, Alfa Aesar or Strem chemical companies and without further purification.

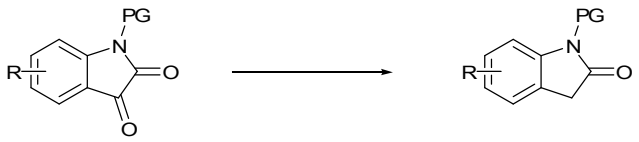
Melting points were determined using a Leica Galen III hot-stage microscope and are reported uncorrected. Infrared measurements were carried out as liquid films on NaCl discs using a Bruker Tensor 27 FT-IR with internal calibration in the range 4000-500 cm^{-1}. Mass spectrometry was carried out on a Bruker MicroTOF mass spectrometer by the internal service at the Department of Organic Chemistry, University of Oxford.

^{1}H, ^{13}C and ^{19}F nuclear magnetic resonance experiments were carried out using a Bruker AC-200 MHz, AC-250Mz, AC-300 MHz, AC-400 MHz or AC-500 MHz NMR spectrometers. Chemical shifts were reported from the residual solvent peak which was used as an internal standard. The multiplicities of the spectra are reported as follows: singlet (s), doublet (d), triplet (t), quartet (q) and multiplet (m). Sometimes apparent multiplicities (app.) were observed. Coupling constants (*J*) are given in Hz.

Preparation of Oxindoles

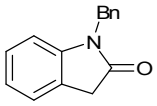
The *N*-protected oxindoles were prepared by one of two methods, either by reaction of the free oxindole with the appropriate anhydride and sodium carbonate or by reduction of the parent *N*-protected isatin with hydrazine monohydrate.

General procedure A: The reduction of *N*-protected isatins to oxindoles



Based on a procedure by Carreira and Marti;[1] A suspension of the protected isatin (1.88 mmol) in hydrazine hydrate (2 mL) was heated to reflux for 1.5 h. After cooling to room temperature, the reaction was diluted with water (20 mL) and ethyl acetate (20 mL), the phases separated and the aqueous phase extracted with ethyl acetate (3 × 10 mL). The combined organics were dried ($MgSO_4$) and reduced *in vacuo*. Purification by flash column chromatography (SiO_2, petrol/diethyl ether 2 : 1) and subsequent recrystallisation from diethyl ether gave the desired *N*-benzyl oxindole (appearance as described).

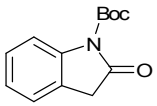
1-Benzylindolin-2-one (Table 2, entries 1-17, starting material)[1]



Prepared according to the general procedure **A**; Isolated as white needles (88%); ν_{max} (film)/cm^{-1} 1710 (C=O); ^{1}H NMR (400 MHz, $CDCl_3$) 7.35-7.24 (6H, m, H-4 and 5 × Ar-H (benzyl)), 7.18 (1H, dd, *J* 7.8 and 7.7, H-6), 7.02 (1H, dd, *J* 7.7 and 7.4, H-5), 6.74 (1H, d, *J* 7.8, H-7), 4.94 (2H, s, C*H*$_2$ (benzyl)), 3.64 (2H, s, 2 × H-3); ^{13}C NMR (100

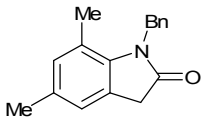
MHz, $CDCl_3$) 175.1, 144.2, 135.8, 128.7, 127.8, 127.6, 127.3, 124.4, 124.3, 122.3, 109.0, 43.7, 35.7. Data consistent with the literature.[1]

tert-Butyl 2-oxoindoline-1-carboxylate (Table 2, entry 18, starting material)[2]



Di-*tert*-butyldicarbonate (0.76 mL, 3.75 mmol) was added in one portion to a solution of oxindole (200 mg, 1.5 mmol), DMAP (approx. 5 mg) and anhydrous sodium carbonate (900 mg) in tetrahydrofuran (8 mL). After 20 h at 70 °C the reaction was diluted with dichloromethane (20 mL) and water (10 mL), the phases separated and the aqueous phase extracted with dichloromethane (3 × 10 mL). The combined organic phases were dried ($MgSO_4$) and reduced *in vacuo*. Purification by column chromatography (SiO_2, petrol/diethyl ether 4 : 1) gave the desired protected oxindole as a white powder (73%); m.p. 65-67 °C (lit. 66-67 °C);[2] ^{1}H NMR (300 MHz, $CDCl_3$) 7.79 (1H, d, *J* 8.1, H-7), 7.30 (1H, dd, *J* 8.1 and 7.7, H-6), 7.24 (1H, d, *J* 7.6, H-4), 7.13 (1H, dd, *J* 7.7 and 7.4, H-5), 3.65 (2H, s, 2 × H-3), 1.65 (9H, s, $C(CH_3)_3$); Data consistent with the literature.[2]

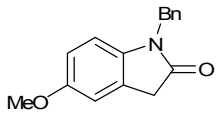
1-Benzyl-5,7-dimethylindolin-2-one (Table 2, entry 19, starting material)



Prepared according to the general procedure **A**; Isolated as white needles (66%); m.p. 138-139 °C (Et_2O); ν_{max} (film)/cm^{-1} 3030, 2923, 1693 (C=O), 1483, 1358, 1212, 1017, 899, 712; ^{1}H NMR (400 MHz, $CDCl_3$) 7.28 (2H, dd (app. t), *J* 7.3, 2 × Ar-H (benzyl)), 7.21 (1H, t, *J* 7.3, Ar-H (benzyl)), 7.13 (2H, d, *J* 7.3, 2 × Ar-H (benzyl)), 6.94 (1H, s, H-

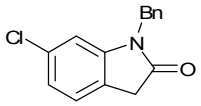
6), 6.73 (1H, s, H-4), 5.15 (2H, s, CH_2 (benzyl)), 3.60 (2H, s, 2 × H-3), 2.25 (3H, s, CH_3), 2.20 (3H, s, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) 176.0, 139.8, 137.6, 132.0, 131.8, 128.7, 127.0, 125.5, 125.1, 123.0, 119.4, 44.8, 35.5, 20.6, 18.4; *m/z* (ESI$^+$, [*M* + Na]$^+$) $C_{17}H_{17}NNaO$ requires 274.1202, found 274.1206.

1-Benzyl-5-methoxyindolin-2-one (Table 2, entry 20, starting material)



Prepared according to the general procedure **A**; Isolated as white needles (62%); m.p. 50-52 °C (Et_2O); ν_{max} (film)/cm^{-1} 3062, 3031, 2938, 1706 (C=O), 1602, 1494, 1344, 1219, 1037, 804, 706; ^{1}H NMR (400 MHz, $CDCl_3$) 7.30-7.19, (5H, m, 5 × Ar-H (benzyl), 6.84 (1H, d, *J* 2.5, H-4), 6.65 (1H, dd, *J* 8.5 and 2.5, H-6), 6.56 (1H, d, *J* 8.5, H-7) 4.85 (2H, s, CH_2 (benzyl)), 3.71 (3H, s, OCH_3), 3.57 (2H, s, 2 × H-3); ^{13}C NMR (100 MHz, $CDCl_3$) 174.7, 155.8, 137.8, 135.9, 128.7, 127.5, 127.3, 125.8, 112.1, 111.9, 109.3, 55.7, 43.8, 36.1; *m/z* (ESI$^+$, [*M* + Na]$^+$) $C_{16}H_{15}NNaO_2$ requires 276.0995, found 276.0992.

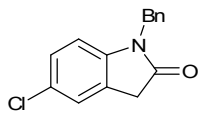
1-Benzyl-6-chloroindolin-2-one (Table 2, entry 21, starting material)



Prepared according to the general procedure **A**; Isolated as white needles (46%); m.p. 115 °C (Et_2O); ν_{max} (film)/cm^{-1} 3062, 3029, 2973, 1707 (C=O), 1614, 1489, 1367, 1221, 950, 917, 893; ^{1}H NMR (400 MHz, $CDCl_3$) 7.36-7.28 (5H, m, 5 × Ar-H (benzyl)), 7.15 (1H, d, *J* 7.9, H-4), 6.98 (1H, dd, *J* 7.9 and 1.8, H-5), 6.71 (1H, d, *J* 1.8, H-7), 4.88 (2H, s, CH_2 (benzyl)), 3.59 (2H, s, 2 × H-3); ^{13}C NMR (100 MHz, $CDCl_3$) 175.0, 145.5, 135.3, 133.6,

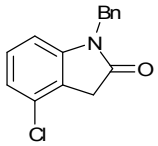
128.9, 127.8, 127.3, 125.3, 122.7, 122.3, 109.6, 43.9, 35.3; *m/z* (ESI$^+$, [*M* + Na]$^+$) $C_{15}H_{12}ClNNaO$ requires 280.0500, found 280.0499.

1-Benzyl-5-chloroindolin-2-one (Table 2, entry 22, starting material)



Prepared according to the general procedure **A**; Isolated as white needles (70%); m.p. 103 °C (Et_2O; lit: 103-104 °C); ν_{max} (film)/cm^{-1} 3064, 3031, 2923, 1711 (C=O), 1484, 1338, 1196, 1074, 808, 732, 699; ^{1}H NMR (400 MHz, $CDCl_3$) 7.30-7.21 (5H, m, 5 × Ar-H (benzyl)), 7.18 (1H, d, *J* 2.4, H-4), 7.08 (1H, dd, *J* 8.3 and 2.4, H-6), 6.57 (1H, d, *J* 8.3, H-7), 4.85 (2H, s, C*H*$_2$ (benzyl)), 3.57 (2H, s, 2 × H-3); ^{13}C NMR (100 MHz, $CDCl_3$) 174.4, 142.8, 135.4, 128.8, 127.73, 127.71, 127.2, 126.0, 124.8, 109.9, 43.8, 35.6, (one carbon signal not observed); *m/z* (ESI$^+$, [*M* + Na]$^+$) $C_{15}H_{12}ClNNaO$ requires 280.0500, found 280.0497.

1-Benzyl-4-chloroindolin-2-one (Table 2, entry 23, starting material)

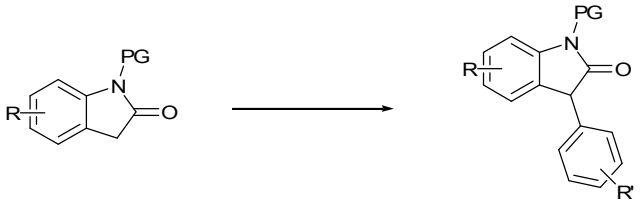


Prepared according to the general procedure **A**; Isolated as white needles (69%); m.p. 121 °C (Et_2O); ν_{max} (film)/cm^{-1} 3033, 3008, 2929, 1703 (C=O), 1608, 1480, 1358, 1159, 771, 706; ^{1}H NMR (400 MHz, $CDCl_3$) 7.35-7.24 (5H, m, 5 × Ar-H (benzyl)), 7.11 (1H, dd (app. t), *J* 8.0, H-6), 6.98 (1H, d, *J* 8.0, H-5), 6.61 (1H, d, *J* 7.0, H-7), 4.90 (2H, s, C*H*$_2$ (benzyl)), 3.62 (2H, s, 2 × H-3); ^{13}C NMR (100 MHz, $CDCl_3$) 174.1, 145.3, 135.4, 130.4,

129.2, 128.8, 127.7, 127.3, 123.0, 122.5, 107.3, 44.0, 35.3; *m/z* (ESI$^+$, [*M* + Na]$^+$) $C_{15}H_{12}ClNNaO$ requires 280.0500, found 280.0497.

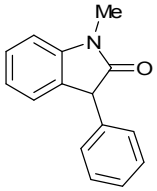
Oxindole Arylation

General procedure B: C-3 arylation of oxindoles



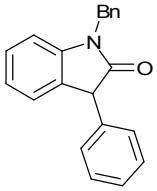
A small reaction tube (diameter 12 mm, depth 84 mm) was charged with the oxindole (0.25 mmol), $Pd(dba)_2$ (0.005 mmol, 2.9 mg) and 2-dicyclohexylphosphino-2′,4′,6′-tri*iso*propylbiphenyl **4** (0.07 mmol, 3.3 mg), sealed with a rubber septum, then vacuum purged three times with argon. Anhydrous, degassed tetrahydrofuran (0.4 mL) and the aryl bromide/triflate/chloride (0.275 mmol) were added sequentially and the mixture heated to 70 °C. Potassium bis(trimethylsilyl)amide (0.5 M solution in toluene, 0.55 mL, 0.275 mmol) was added in one portion and the reaction stirred for 30 minutes. After quenching with saturated ammonium chloride (1 mL), the mixture was diluted with dichloromethane (10 mL) and water (10 mL), the phases separated and the aqueous phase extracted with further dichloromethane (2 × 10 mL). The combined organic phases were dried ($MgSO_4$) and the solvents reduced *in vacuo*. Purification by flash column chromatography (as described) gave the desired C-3 aryl oxindole.

1-Methyl-3-phenylindolin-2-one (Table 1)[3]



Prepared according to the general procedure **B**; Flash column chromatography (petrol/diethyl ether 5 : 1) and subsequent recrystallisation from hexane gave the oxindole as white crystalline needles (95%); ^{1}H NMR (400 MHz, $CDCl_3$) 7.36-7.28 (4H, m, H-6 and 3 × Ar-H), 7.22-7.16 (3H, m, H-5 and 2 × Ar-H), 7.07 (1H, ddd, *J* 7.5, 7.5 and 0.8, H-4), 6.91 (1H, d, *J* 7.8, H-7), 4.62 (1H, s, H-3), 3.26 (3H, s, NCH_3); ^{13}C NMR (100 MHz, $CDCl_3$) 175.9, 144.4, 136.5, 128.8, 128.7, 128.3, 127.5, 125.0, 122.6, 108.1, 51.9, 26.4, (one carbon signal not observed). Data consistent with the literature.[3]

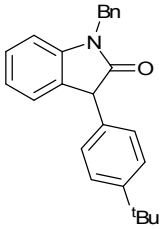
1-Benzyl-3-phenylindolin-2-one (Table 2, entries 1-3)[3]



Prepared according to the general procedure **B**; Flash column chromatography (petrol/diethyl ether 5 : 1) and subsequent recrystallisation from hexane gave the oxindole as white needles (89%); ν_{max} (film)/cm^{-1} 3060, 3030, 2923, 1713 (C=O), 1612, 1488, 1349, 1183, 1080, 892, 696; ^{1}H NMR (400 MHz, $CDCl_3$) 7.39-7.19 (11H, m, H-6, 5 × Ar-H (benzyl) and 5 × Ar-H), 7.17 (1H, d, *J* 7.4, H-4), 7.03 (1H, dd, *J* 7.5 and 7.4, H-5), 6.80 (1H, d, *J* 7.8, H-7), 5.01 (1H, d, *J* 15.6, C*H* (benzyl), 4.91 (1H, d, *J* 15.6, C*H* (benzyl)), 4.72 (1H, s, H-3); ^{13}C NMR (100 MHz, $CDCl_3$) 176.1, 143.6, 136.7, 135.9,

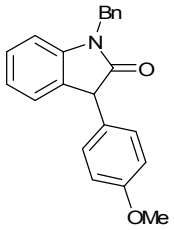
129.0, 128.9, 128.8, 128.5, 128.3, 127.7, 127.6, 127.4, 125.1, 122.8, 109.2, 58.1, 44.0. Data consistent with the literature.[3]

1-Benzyl-3-(4-*tert*-butylphenyl)indolin-2-one (Table 2, entry 4)



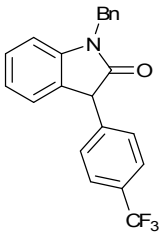
Prepared according to the general procedure **B**; Flash column chromatography (petrol/diethyl ether 5 : 1) and subsequent recrystallisation from hexane gave the oxindole as white needles (79%); m.p. 116-117 °C (hexane); ν_{max} (film)/cm^{-1} 3031, 2962, 2903, 2868, 1714 (C=O), 1611, 1516, 1488, 1347, 1203, 1182, 750, 697; ^{1}H NMR (400 MHz, $CDCl_3$) 7.38 (2H, d, *J* 8.3, 2 × Ar-H), 7.36-7.26 (5H, m, 5 × Ar-H (benzyl)), 7.23-7.16 (4H, m, H-6, H-4 and 2 × Ar-H), 7.03 (1H, dd (app. t), *J* 7.5, H-5), 6.79 (1H, d, *J* 7.7, H-7), 5.01 (1H , d, *J* 15.6, C*H* (benzyl)), 4.92 (1H, d, *J* 15,6, C*H* (benzyl)), 4.71 (1H, s, H-3), 1.32 (9H, s, $(CH_3)_3$); ^{13}C NMR (100 MHz, $CDCl_3$) 176.3, 150.3, 143.5, 135.9, 133.5, 129.0, 128.7, 128.2, 128.0, 127.6, 127.3, 125.9, 125.1, 122.6, 109.1, 51.6, 43.9, 34.5, 31.3; *m/z* (ESI$^+$, $[M + H]^+$) $C_{25}H_{26}NO$ requires 356.2009, found 356.2003.

1-Benzyl-3-(4-methoxyphenyl)indolin-2-one (Table 2, entries 5 and 6)



Prepared according to the general procedure **B**; Flash column chromatography (petrol/diethyl ether 5 : 1) and subsequent recrystallisation from hexane gave the oxindole as white needles (85%); m.p. 109-110 °C (hexane); ν_{max} (film)/cm^{-1} 3032, 2928, 1712 (C=O), 1611, 1512, 1488, 1466, 1347, 1249, 1179, 1031, 751, 698; ^{1}H NMR (400 MHz, $CDCl_3$) 7.35-7.26 (5H, m, 5 × Ar-H (benzyl)), 7.21 (1H, dd, *J* 7.8 and 7.5, H-6), 7.18-7.13 (3H, m, 2 × Ar-H and H-4), 7.03 (1H, dd (app. t), *J* 7.5, H-5), 6.89 (2H, d, *J* 8.6, 2 × Ar-H), 6.79 (1H, d, *J* 7.8, H-7), 5.00 (1H, d, *J* 15.6, C*H* (benzyl)), 4.90 (1H, d, *J* 15.6, C*H* (benzyl)), 4.66 (1H, s, H-3), 3.80 (3H, s, OCH_3); ^{13}C NMR (100 MHz, $CDCl_3$) 176.4, 159.0, 143.5, 135.9, 129.4, 129.1, 128.7, 128.7, 128.2, 127.6, 127.3, 125.0, 122.7, 114.4, 109.1, 55.3, 51.2, 43.9; *m/z* (ESI$^+$, [*M* + Na]$^+$) $C_{22}H_{19}NNaO_2$ requires 352.1308, found 352.1301.

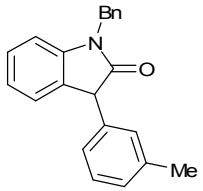
1-Benzyl-3-(4-(trifluoromethyl)phenyl)indolin-2-one (Table 2, entries 7 and 8)



Prepared according to the general procedure **B**; Flash column chromatography (petrol/diethyl ether 5 : 1) and subsequent recrystallisation from hexane gave the oxindole as white needles (80%); m.p. 120-121 °C (hexane); ν_{max} (film)/cm^{-1} 3061, 3034, 2925,

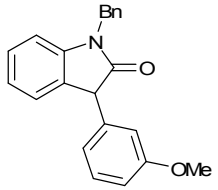
1714 (C=O), 1612, 1326, 1165, 1069, 752, 699; ^{1}H NMR (400 MHz, $CDCl_3$) 7.62 (2H, d, *J* 8.1, 2 × Ar-H), 7.37 (2H, d, *J* 8.1, 2 × Ar-H), 7.35-7.27 (5H, m, 5 × Ar-H (benzyl)), 7.25 (1H, dd, *J* 7.8 and 7.5, H-6), 7.16 (1H, d, *J* 7.5, H-4), 7.06 (1H, dd (app. t), *J* 7.5, H-5), 6.84 (1H, d, *J* 7.8, H-7), 5.00 (1H, d, *J* 15.6, C*H* (benzyl)), 4.91 (1H, d, *J* 15.6, C*H* (benzyl)), 4.78 (1H, s, H-3); ^{13}C NMR (100 MHz, $CDCl_3$) 175.2, 143.5, 140.7, 135.6, 129.9 (q, *J* 32.5), 128.8, 128.8, 128.7, 127.8, 127.7, 127.3, 125.8, 125.1, 124.0 (q, *J* 272.2), 122.9, 109.4, 51.7, 44.0; ^{19}F NMR (376.5 MHz, $CDCl_3$) -62.5; *m/z* (ESI$^+$, [*M* + H]$^+$) $C_{22}H_{17}F_3NO$ requires 368.1257, found 368.1260.

1-Benzyl-3-*m*-tolylindolin-2-one (Table 2, entry 9)



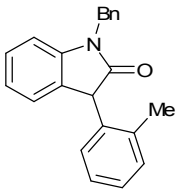
Prepared according to the general procedure **B**; Flash column chromatography (petrol/diethyl ether 5 : 1) gave the oxindole as a viscous pale yellow oil (77%); ν_{max} (film)/cm^{-1} 3032, 2921, 1715 (C=O), 1612, 1488, 1348, 1182, 1081, 752, 695; ^{1}H NMR (400 MHz, $CDCl_3$) 7.38-7.27 (5H, m, 5 × Ar-H (benzyl)), 7.25-7.21 (3H, m, H-6, H-5 and H-4), 7.14 (1H, d, *J* 7.6, Ar-H), 7.08-7.01 (3H, m, 3 × Ar-H), 6.82 (1H, d, *J* 7.8, H-7), 5.03 (1H, d, *J* 15.6, C*H* (benzyl)), 4.93 (1H, d, *J* 15.6, C*H* (benzyl)), 4.69 (1H, s, H-3), 2.36 (3H, s, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) 176.2, 143.4, 138.5, 136.6, 135.9, 129.1, 129.0, 128.7, 128.6, 128.4, 128.2, 127.6, 127.3, 125.4, 125.0, 122.7, 109.1, 52.0, 43.9, 21.4; *m/z* (ESI$^+$, [*M* + Na]$^+$) $C_{22}H_{19}NNaO$ requires 336.1359, found 336.1361.

1-Benzyl-3-(3-methoxyphenyl)indolin-2-one (Table 2, entry 10)



Prepared according to the general procedure **B**; Flash column chromatography (petrol/diethyl ether 5 : 1) and subsequent recrystallisation from hexane gave the oxindole as pale yellow needles (85%); m.p. 69-70 °C (hexane); ν_{max} (film)/cm^{-1} 3058, 3031, 2835, 1714 (C=O), 1612, 1489, 1244, 1047, 752, 693; ^{1}H NMR (400 MHz, $CDCl_3$) 7.35-7.25 (6H, m, 5 × Ar-H (benzyl) and Ar-H), 7.24-7.16 (2H, m, H-6 and H-4), 7.02 (1H, ddd (app. td), *J* 7.5 and 0.9, H-5), 6.87-6.77 (4H, m, H-7 and 3 × Ar-H), 5.01 (1H, d, *J* 15.6, C*H* (benzyl)), 4.90 (1H, d, *J* 15.6, C*H* (benzyl)), 4.68 (1H, s, H-3), 3.78 (3H, s, OCH_3); ^{13}C NMR (100 MHz, $CDCl_3$) 175.9, 159.9, 143.5, 138.1, 135.9, 129.9, 128.7, 128.7, 128.3, 127.6, 127.3, 125.1, 122.7, 120.7, 114.2, 113.0, 109.2, 55.2, 52.0, 43.9; *m/z* (ESI$^+$, $[M + Na]^+$) $C_{22}H_{19}NNaO_2$ requires 352.1308, found 352.1307.

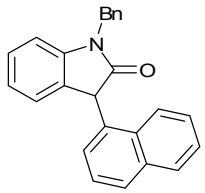
1-Benzyl-3-o-tolylindolin-2-one (Table 2, entries 11 and 12)



Prepared according to the general procedure **B**; Flash column chromatography (petrol/diethyl ether 5 : 1) and subsequent recrystallisation from hexane gave the oxindole as white crystalline needles (74%); m.p. 85-86 °C (hexane); ^{1}H NMR (250 MHz, d_6-DMSO, 90 °C) 7.42-7.02 (9H, m, 5 × Ar-H (benzyl) and 4 × Ar-H), 7.02-6.94 (3H, m, 3 × Ar-H), 6.91 (1H, d, *J* 7.2, H-7), 5.10 (1H, s, H-3), 4.96 (2H, s, CH_2 (benzyl)), 2.26 (3H, s, CH_3); ^{13}C NMR (62.5 MHz, d_6-DMSO, 90 °C) 176.4, 144.2, 137.8, 137.4, 136.9,

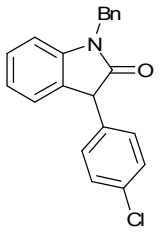
131.5, 130.3, 129.8, 129.4, 128.8, 128.3, 128.2, 128.1, 126.9, 125.0, 123.2, 109.9, 50.6, 44.1, 19.9; *m/z* (ESI$^+$, [*M* + H]$^+$) $C_{22}H_{20}NO$ requires 314.1539, found 314.1539.

1-Benzyl-3-(naphthalen-1-yl)indolin-2-one (Table 2, entry 13)



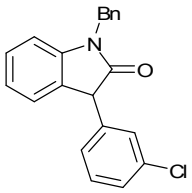
Prepared according to the general procedure **B**; Flash column chromatography (petrol/diethyl ether 3 : 1) and subsequent recrystallisation from hexane gave the oxindole as pale yellow plates (80%); m.p. 63-65 °C (hexane); ν_{max} (film)/cm^{-1} 3058, 2924, 1712 (C=O), 1611, 1487, 1346, 1170, 899, 751, 698; ^{1}H NMR (250 MHz, d_6-DMSO, 100 °C) 7.96-7.88 (3H, m, 3 × Ar-H (naphthyl)), 7.56-7.12 (10H, m, H-6, 5 × Ar-H (benzyl) and 4 × Ar-H (naphthyl), 7.06 (1H, d, *J* 7.8, H-5), 7.09-6.90 (2H, m, H-7 and H-4), 5.65 (1H, s, H-3), 5.07 (1H, d, *J* 15.6, C*H* (benzyl)), 4.99 (1H, d, *J* 15.6, C*H* (benzyl)); ^{13}C NMR (62.5 MHz, d_6-DMSO, 100 °C) 176.5, 143.9, 137.4, 137.3, 134.9, 134.7, 132.7, 130.7, 130.6, 129.5, 129.4, 129.4, 128.9, 128.3, 128.2, 127.0, 126.6, 126.3, 125.1, 125.0, 123.2, 110.1, 44.2; *m/z* (ESI$^+$, [*M* + Na]$^+$) $C_{25}H_{19}NNaO$ requires 372.1359, found 372.1357.

1-Benzyl-3-(4-chlorophenyl)indolin-2-one (Table 2, entries 14 and 17)



Prepared according to the general procedure **B**; Flash column chromatography (petrol/diethyl ether 5 : 1) and subsequent recrystallisation from hexane gave the oxindole as white needles (70%); m.p. 126-127 °C (hexane); ν_{max} (film)/cm^{-1} 3061, 1712 (C=O), 1612, 1488, 1408, 1201, 1015, 892, 751, 697; ^{1}H NMR (400 MHz, $CDCl_3$) 7.37-7.26 (7H, m, 5 × Ar-H (benzyl) and 2 × Ar-H), 7.24 (1H, dd (app. t), *J* 7.8, H-6), 7.20-7.15 (3H, m, H-4 and 2 × Ar-H), 7.05 (1H, dd (app. t), *J* 7.8, H-5), 6.82 (1H, d, *J* 7.8, H-7), 5.00 (1H, d, *J* 15.6, C*H* (benzyl)), 4.91 (1H, d, *J* 15.6, C*H* (benzyl)), 4.70 (1H, s, H-3); ^{13}C NMR (100 MHz, $CDCl_3$) 175.6, 143.6, 135.8, 135.2, 133.6, 129.8, 129.1, 128.8, 128.6, 128.3, 127.7, 127.4, 125.1, 122.9, 109.4, 51.4, 44.0; *m/z* (ESI$^+$, [*M* + H]$^+$) $C_{21}H_{17}ClNO$ requires 334.0993, found 334.0987.

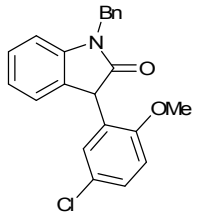
1-Benzyl-3-(3-chlorophenyl)indolin-2-one (Table 2, entry 15)



Prepared according to the general procedure **B**; Flash column chromatography (petrol/diethyl ether 5 : 1) and subsequent recrystallisation from hexane gave the oxindole as white needles (73%); m.p. 81-82 °C (hexane); ν_{max} (film)/cm^{-1} 3060, 2923, 1713 (C=O), 1612, 1488, 1347, 1201, 1080, 778, 721; ^{1}H NMR (400 MHz, $CDCl_3$) 7.35-7.27 (7H, m, 5 × Ar-H (benzyl) and Ar-H), 7.26-7.20 (2H, m, H-6 and Ar-H), 7.18-7.13 (2H,

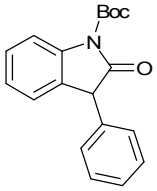
m, Ar-H and H-4), 7.05 (1H, dd (app. t), *J* 7.5, H-5), 6.82 (1H, d, *J* 7.8, H-7), 4.99 (1H, d, *J* 15.6, C*H* (benzyl)), 4.92 (1H, d, *J* 15.6, C*H* (benzyl)), 4.69 (1H, s, H-3); ^{13}C NMR (100 MHz, $CDCl_3$) 175.4, 143.5, 138.6, 135.7, 134.7, 130.1, 128.8, 128.6, 128.5, 128.0, 127.9, 127.7, 127.3, 126.8, 125.1, 122.9, 109.3, 51.5, 44.0; *m/z* (ESI$^+$, [*M* + Na]$^+$) $C_{21}H_{16}ClNNaO$ requires 356.0813, found 356.0813.

1-Benzyl-3-(5-chloro-2-methoxyphenyl)indolin-2-one (Table 2, entry 16)



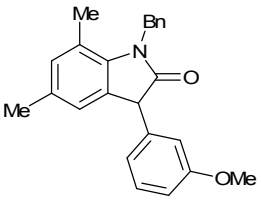
Prepared according to the general procedure **B**; Flash column chromatography (SiO_2, petrol/diethyl ether 4 : 1) and subsequent recrystallisation from hexane gave the oxindole as pale yellow needles (77%); m.p. 123-125 °C (hexane); ν_{max} (film)/cm^{-1} 3059, 2940, 2838, 1714 (C=O), 1612, 1489, 1358, 1153, 1027, 809, 650; ^{1}H NMR (400 MHz, $CDCl_3$) 7.41 (2H, d, *J* 7.6, 2 × Ar-H (benzyl)), 7.35 (2H, dd, *J* 7.6 and 7.1, 2 × Ar-H (benzyl)), 7.30 (1H, d, *J* 7.1, Ar-H (benzyl)), 7.25 (1H, dd, *J* 8.8 and 2.6, Ar-H), 7.17 (1H, dd, *J* 7.9 and 7.4, H-6), 7.12 (1H, br s, Ar-H), 7.05 (1H, d, *J* 7.4, H-4), 6.96 (1H, dd (app. t), *J* 7.4, H-5), 6.83 (1H, d, *J* 8.8, Ar-H), 6.80 (1H, d, *J* 7.9, H-7), 5.09 (1H, d, *J* 15.6, C*H* (benzyl)), 4.90 (1H, d, *J* 15.6, C*H* (benzyl)), 4.88 (1H, s, H-3), 3.62 (3H, s, OCH_3); ^{13}C NMR (125 MHz, $CDCl_3$) 175.9, 156.1, 143.3, 136.0, 130.2, 128.8, 128.6, 128.6, 127.9, 127.5, 127.5, 127.3, 125.5, 124.0, 122.5, 112.5, 108.9, 55.8, 48.0, 43.9; *m/z* (ESI$^+$, [*M* + Na]$^+$) $C_{22}H_{18}ClNNaO_2$ requires 386.0918, found 386.0911.

***tert*-Butyl 2-oxo-3-phenylindoline-1-carboxylate (Table 2, entry 18)**



Prepared according to the general procedure **B**; Flash column chromatography (petrol/diethyl ether 5 : 1) and subsequent recrystallisation from hexane gave the oxindole as white needles (60%); m.p. 108-109 °C (hexane); ν_{max} (film)/cm^{-1} 3060, 3030, 2981, 2933, 1769 (C=O), 1729 (C=O), 1495, 1370, 1291, 1148, 848, 722; ^{1}H NMR (500 MHz, $CDCl_3$) 7.94 (1H, d, *J* 8.2, H-7), 7.40-7.29 (4H, m, H-6 and 3 × Ar-H), 7.24-7.16 (4H, m, H-5, H-4 and 2 × Ar-H), 4.74 (1H, s, H-3), 1.64 (9H, s, C(C*H*$_3$)$_3$); ^{13}C NMR (125 MHz, $CDCl_3$) 173.9, 149.4, 140.5, 136.3, 128.9, 128.6, 127.9, 127.4, 125.1, 124.6, 115.1, 84.4, 52.6, 28.1; *m/z* (ESI$^+$, [*M* + Na]$^+$) $C_{19}H_{19}NNaO_3$ requires 332.1257, found 332.1260.

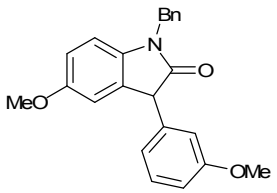
1-Benzyl-3-(3-methoxyphenyl)-5,7-dimethylindolin-2-one (Table 2, entry 19)



Prepared according to the general procedure **B**; Flash column chromatography (SiO_2, petrol/diethyl ether 2 : 1) gave the oxindole as a viscous pale yellow oil (67%); ν_{max} (film)/cm^{-1} 3060, 3030, 2935, 1710 (C=O), 1600, 1481, 1342, 1263, 1177, 1039, 728, 698; ^{1}H NMR (400 MHz, $CDCl_3$) 7.35-7.25 (4H, m, 3 × Ar-H (benzyl) and Ar-H), 7.21 (2H, d, *J* 7.1, 2 × Ar-H (benzyl)), 6.91-6.89 (2H, m, Ar-H), 6.88-6.86 (1H, m, H-4), 6.85-6.83 (1H, m, H-6), 6.82 (1H, s, Ar-H), 5.28 (1H, d, *J* 16.8, C*H* (benzyl)), 5.20 (1H, d, *J* 16.8, C*H* (benzyl)), 4.69 (1H, s, H-3), 3.81 (3H, s, OC*H*$_3$), 2.31 (3H, s, C*H*$_3$), 2.26 (3H, s,

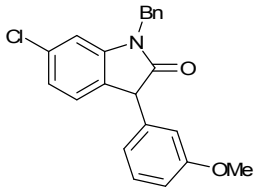
C*H*$_3$); ^{13}C NMR (100 MHz, $CDCl_3$) 177.0, 160.0, 139.2, 138.8, 137.9, 132.7, 132.4, 129.9, 129.7, 128.9, 127.2, 125.8, 123.9, 120.9, 119.6, 114.4, 113.0, 55.3, 51.9, 45.2, 20.8, 18.7; *m/z* (ESI$^+$, [*M* + MeCN + NH_4]$^+$) $C_{26}H_{30}N_3$ requires 416.2333, found 416.2330.

1-Benzyl-5-methoxy-3-(3-methoxyphenyl)indolin-2-one (Table 2, entry 20)



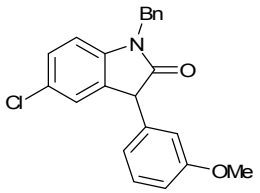
Prepared according to the general procedure **B**; Flash column chromatography (SiO_2, petrol/diethyl ether 1 : 1) gave the oxindole as a viscous pale yellow oil (76%); ν_{max} (film)/cm^{-1} 3030, 2938, 2835, 1708 (C=O), 1600, 1492, 1279, 1177, 777, 696; ^{1}H NMR (400 MHz, $CDCl_3$) 7.35-7.26 (6H, m, 5 × Ar-H (benzyl) and Ar-H), 6.89-6.83 (2H, m, 2 × Ar-H), 6.82-6.79 (2H, m, H-4 and Ar-H), 6.75 (1H, dd, *J* 8.5 and 2.4, H-6), 6.69 (1H, d, *J* 8.5, H-7), 5.00 (1H, d, *J* 15.6, C*H* (benzyl)), 4.89 (1H, d, *J* 15.6, C*H* (benzyl)), 4.68 (1H, s, H-3), 3.79 (3H, s, C(aryl)-OC*H*$_3$), 3.72 (3H, s, C(5)-OC*H*$_3$); ^{13}C NMR (100 MHz, $CDCl_3$) 175.6, 159.8, 156.0, 138.1, 136.6, 135.9, 130.0, 129.9, 128.7, 127.5, 127.2, 120.7, 114.1, 113.0, 112.8, 112.1, 109.5, 55.6, 55.1, 52.4, 43.9; *m/z* (ESI$^+$, [*M* + Na]$^+$) $C_{23}H_{21}NNaO_3$ requires 382.1414, found 382.1410.

1-Benzyl-6-chloro-3-(3-methoxyphenyl)indolin-2-one (Table 2, entry 21)



Prepared according to the general procedure **B**, reaction time: 1 h; Flash column chromatography (SiO_2, petrol/diethyl ether 4 : 1) and subsequent recrystallisation from hexane gave the oxindole as white needles (66%); m.p. 90-91 °C (hexane); ν_{max} (film)/cm^{-1} 3064, 3032, 2937, 1716 (C=O), 1609, 1489, 1369, 1184, 1080, 779, 700; ^{1}H NMR (400 MHz, $CDCl_3$) 7.38-7.28 (6H, m, 5 × Ar-H (benzyl) and Ar-H), 7.10 (1H, d, *J* 7.9, H-4), 7.01 (1H, dd, *J* 7.9 and 1.8, H-5), 6.87 (1H, dd, *J* 8.3 and 1.9, Ar-H), 6.82-6.79 (2H, m, H-7 and Ar-H), 6.76-6.73 (1H, m, Ar-H), 4.99 (1H, d, *J* 15.7, C*H* (benzyl)), 4.87 (1H, d, *J* 15.7, C*H* (benzyl)), 4.66 (1H, s, H-3), 3.79 (3H, s, OCH_3); ^{13}C NMR (100 MHz, $CDCl_3$) 175.8, 159.9, 144.6, 137.5, 135.3, 134.0, 130.0, 128.9, 127.8, 127.2, 127.1, 126.0, 122.7, 120.6, 114.1, 113.2, 109.7, 55.2, 51.5, 44.0; *m/z* (ESI$^+$, [*M* + Na]$^+$) $C_{22}H_{18}ClNNaO_2$ requires 386.0918, found 386.0917.

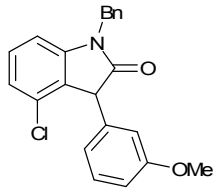
1-Benzyl-5-chloro-3-(3-methoxyphenyl)indolin-2-one (Table 2, entry 22)



Prepared according to the general procedure **B**, reaction time: 1 h; Flash column chromatography (SiO_2, petrol/diethyl ether 1 : 1) gave the oxindole as a viscous pale yellow oil (70%); ν_{max} (film)/cm^{-1} 3063, 3031, 2936, 1717 (C=O), 1608, 1485, 1339, 1183, 1081, 742, 695; ^{1}H NMR (400 MHz, $CDCl_3$) 7.37-7.28 (6H, m, 5 × Ar-H (benzyl)

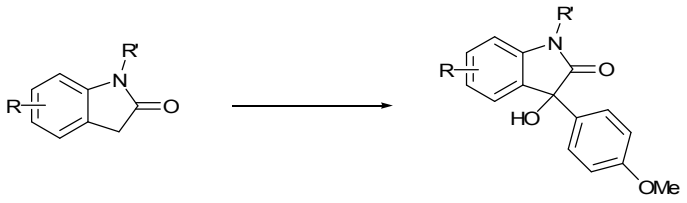
and Ar-H), 7.18 (1H, dd, *J* 8.3 and 2.4, H-6), 7.17-7.15 (1H, m, H-4), 6.88 (1H, dd, *J* 7.9 and 1.9, Ar-H), 6.80 (1H, d, *J* 7.6, Ar-H), 6.77-6.74 (1H, m, Ar-H), 6.71 (1H, d, *J* 8.3, H-7), 5.01 (1H, d, *J* 15.6, C*H* (benzyl)), 4.89 (1H, d, *J* 15.6, C*H* (benzyl)), 4.68 (1H, s, H-3), 3.80 (3H, s, OCH_3); ^{13}C NMR (100 MHz, $CDCl_3$) 175.4, 160.0, 141.9, 137.3, 135.4, 130.4, 130.0, 128.9, 128.3, 128.1, 127.8, 127.2, 125.4, 120.6, 114.2, 113.1, 110.1, 55.2, 52.0, 44.0; *m/z* (ESI$^+$, [*M* + Na]$^+$) $C_{22}H_{18}ClNNaO_2$ requires 386.0918, found 386.0921.

1-Benzyl-4-chloro-3-(3-methoxyphenyl)indolin-2-one (Table 2, entry 23)



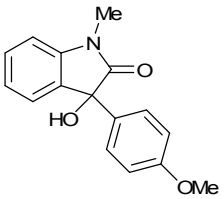
Prepared according to the general procedure **B**, reaction time: 2.5 h; Flash column chromatography (SiO_2, petrol/diethyl ether 3 : 1) and recrystallisation from hexane gave the oxindole as red plates (61%); m.p. 130-131 °C (hexane); ν_{max} (film)/cm^{-1} 3029, 2935, 1719 (C=O), 1606, 1459, 1332, 1138, 772, 695; ^{1}H NMR (400 MHz, $CDCl_3$) 7.37-7.27 (6H, m, 5 × Ar-H (benzyl) and Ar-H), 7.19 (1H, dd (app. t), *J* 8.1 and 7.9, H-6), 7.01 (1H, d, *J* 8.1, H-5), 6.87 (1H, dd, *J* 8.3 and 2.4, Ar-H), 6.79 (1H, d, *J* 7.7, Ar-H), 6.74-6.72 (1H, m, Ar-H), 6.71 (1H, d, *J* 7.9, H-7), 5.00 (1H, d, *J* 15.6, C*H* (benzyl)), 4.86 (1H, d, *J* 15.6, C*H* (benzyl)), 4.71 (1H, s, H-3), 3.80 (3H, s, OCH_3); ^{13}C NMR (100 MHz, $CDCl_3$) 175.1, 159.8, 145.1, 136.2, 135.4, 131.5, 129.8, 129.7, 128.8, 127.7, 127.3, 126.2, 123.3, 120.4, 114.0, 113.0, 107.5, 55.2, 51.9, 44.1; *m/z* (ESI$^+$, [*M* + Na]$^+$) $C_{22}H_{18}ClNNaO_2$ requires 386.0918, found 386.0920.

General Procedure C: One-Pot C3-Arylation/Hydroxylation of Oxindoles



A small reaction tube (diameter 12 mm, depth 84 mm) was charged with the oxindole (0.25 mmol), $Pd(dba)_2$ (0.005 mmol, 2.9 mg) and -dicyclohexylphosphino-2′,4′,6′-tri*iso*propylbiphenyl **4** (0.07 mmol, 3.3 mg), sealed with a rubber septum and vacuum purged three times with argon. Anhydrous, argon deoxygenated tetrahydrofuran (0.4 mL) and 4-bromoanisole (34 μL, 0.275 mmol) were added sequentially and the mixture heated to 70 °C. Potassium bis(trimethylsilyl)amide (0.5 M solution in toluene, 0.55 mL, 0.275 mmol) was added in one portion and the reaction stirred for 30 minutes. The reaction was then carefully purged with air and the rubber septum removed. After a further 5 minutes the reaction was cooled to room temperature, diluted with dichloromethane (10 mL) and filtered through a celite pad. Purification by flash column chromatography (SiO_2, petrol/diethyl ether 1 : 1) and subsequent recrystallisation from diethyl ether/hexane gave the desired product as described.

3-Hydroxy-3-(4-methoxyphenyl)-1-methylindolin-2-one, 7



Prepared according to the general procedure **C**; Isolated as white needles (97%); m.p. 147-148 °C (Et_2O/hexane); ν_{max} (film)/cm^{-1} 3385 (OH), 3058, 2936, 2837, 1707 (C=O), 1612, 1510, 1470, 1251, 1174, 1030, 826, 756; ^{1}H NMR (400 MHz, $CDCl_3$) 7.35 (1H, ddd (app t), *J* 7.7 and 1.2, H-6), 7.33-7.29 (3H, m, H-4 and 2 × Ar-H), 7.10 (1H, ddd

(app. t), *J* 7.7 and 0.7, H-5), 6.89 (1H, d, *J* 7.7, H-7), 6.84 (2H, d, *J* 8.9, 2 × Ar-H), 3.83 (1H, br s, O*H*), 3.77 (3H, s, OCH_3), 3.21 (3H, s, NCH_3); ^{13}C NMR (100 MHz, $CDCl_3$) 177.7, 159.5, 143.3, 132.1, 131.6, 129.7, 126.8, 124.8, 123.4, 113.9, 108.6, 77.5, 55.2, 26.4; *m/z* (ESI$^+$, [*M* + Na]$^+$) $C_{16}H_{15}NNaO_3$ requires 292.0944, found 292.0943.

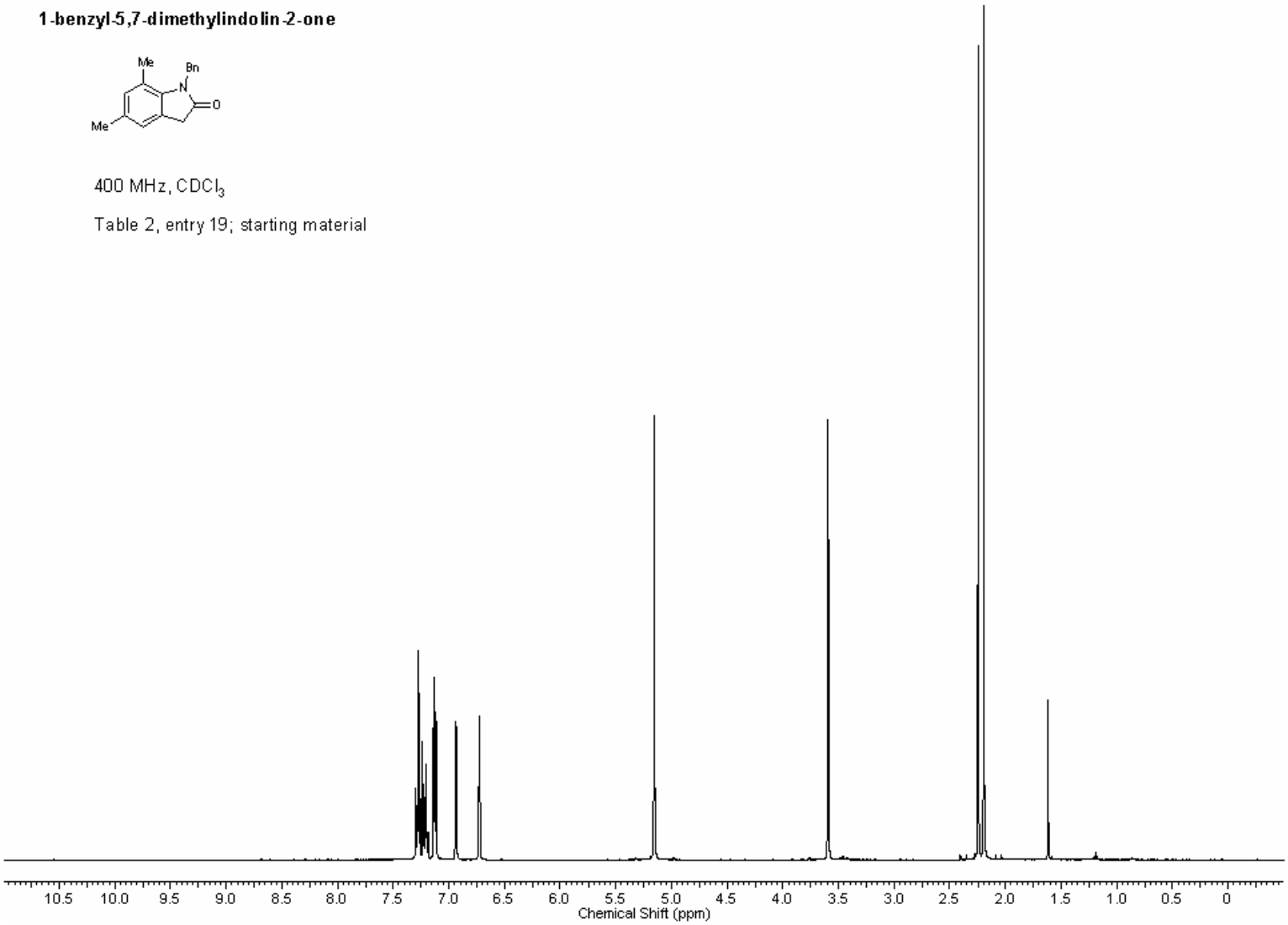
References

1. Carreira, E. M.; Marti, C., *J. Am. Chem. Soc.* **2005**, 127, 11505-11515.
2. Vazquez, E.; Payback, J. F., *Tetrahedron Lett.* **2004**, 45, 6549-6550.
3. Trost, B. M.; Frederiksen, M. U., *Angew. Chem. Int. Ed.* **2005**, 44, 308-310.

1-benzyl-5,7-dimethylindolin-2-one

400 MHz, $CDCl_3$

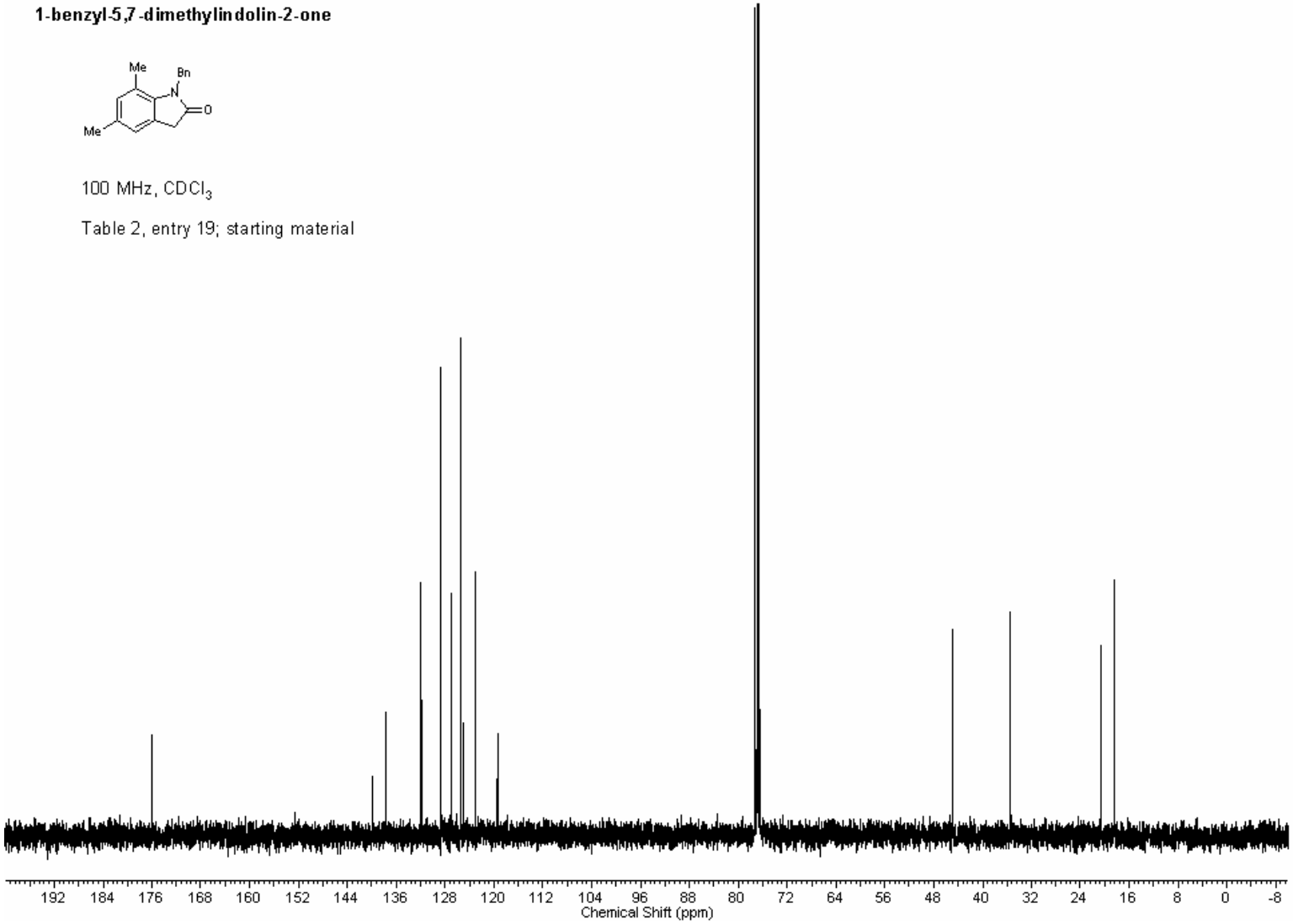
Table 2, entry 19; starting material



1-benzyl-5,7-dimethylindolin-2-one

100 MHz, $CDCl_3$

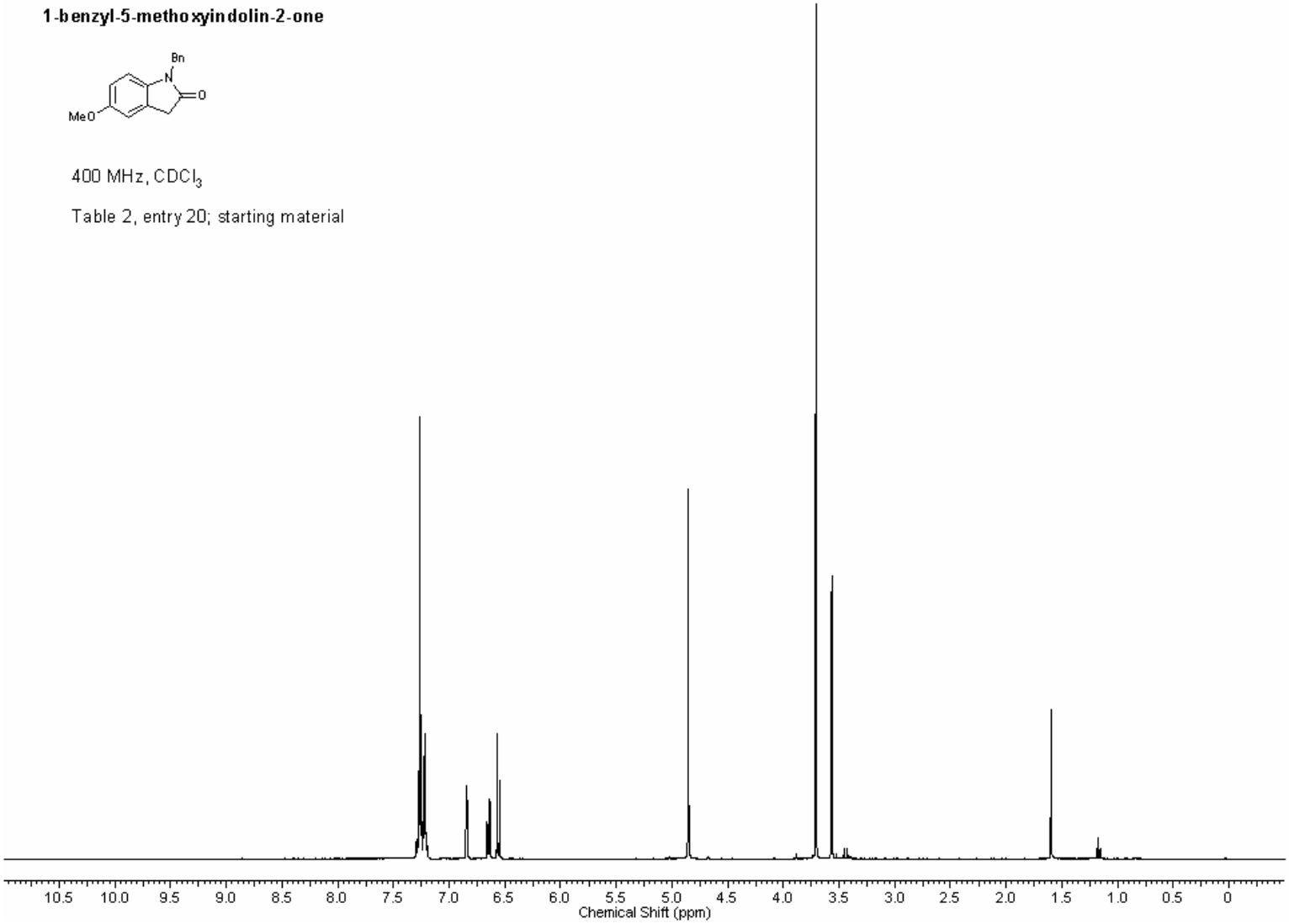
Table 2, entry 19; starting material



1-benzyl-5-methoxyindolin-2-one

400 MHz, $CDCl_3$

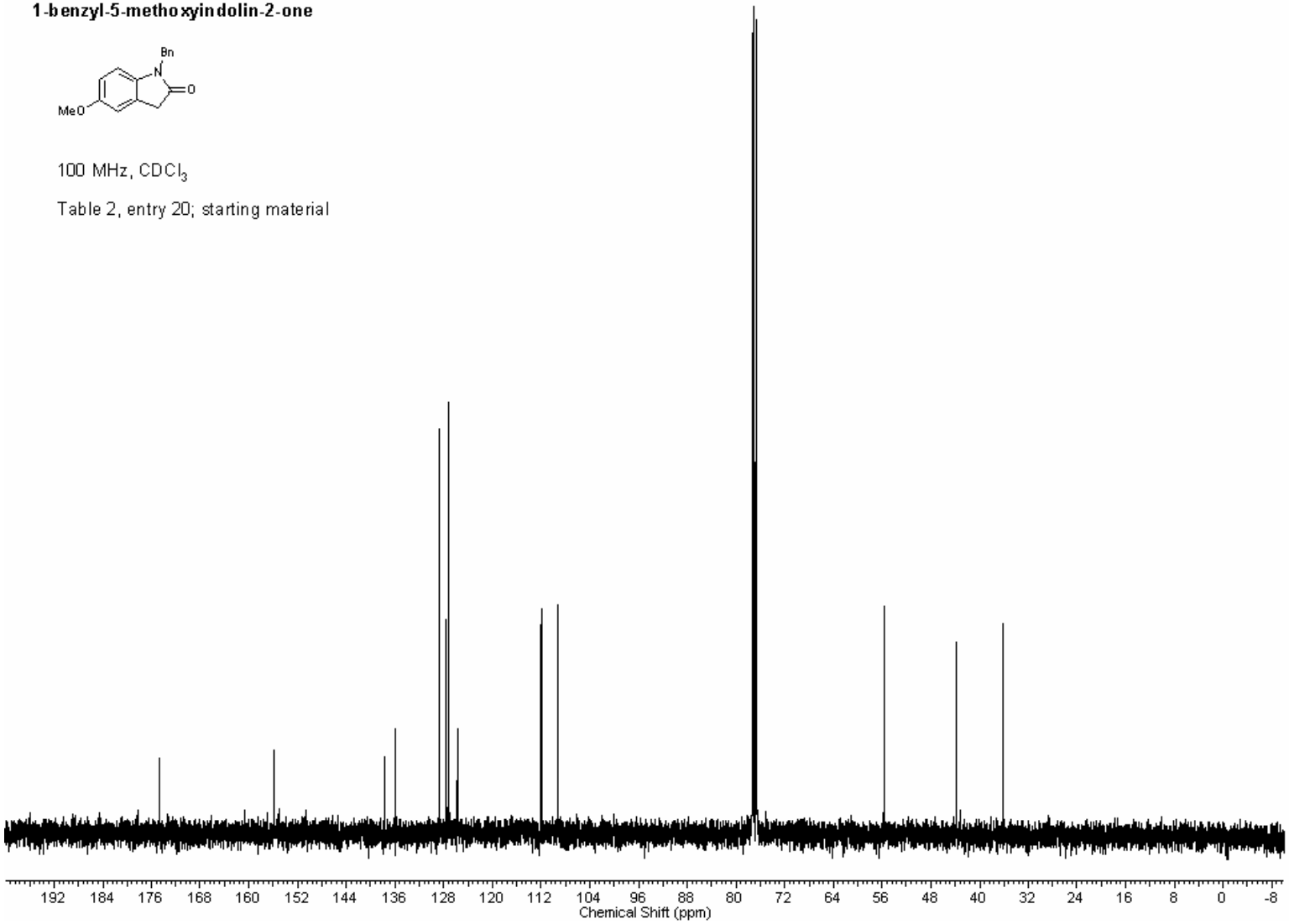
Table 2, entry 20; starting material



1-benzyl-5-methoxyindolin-2-one

100 MHz, $CDCl_3$

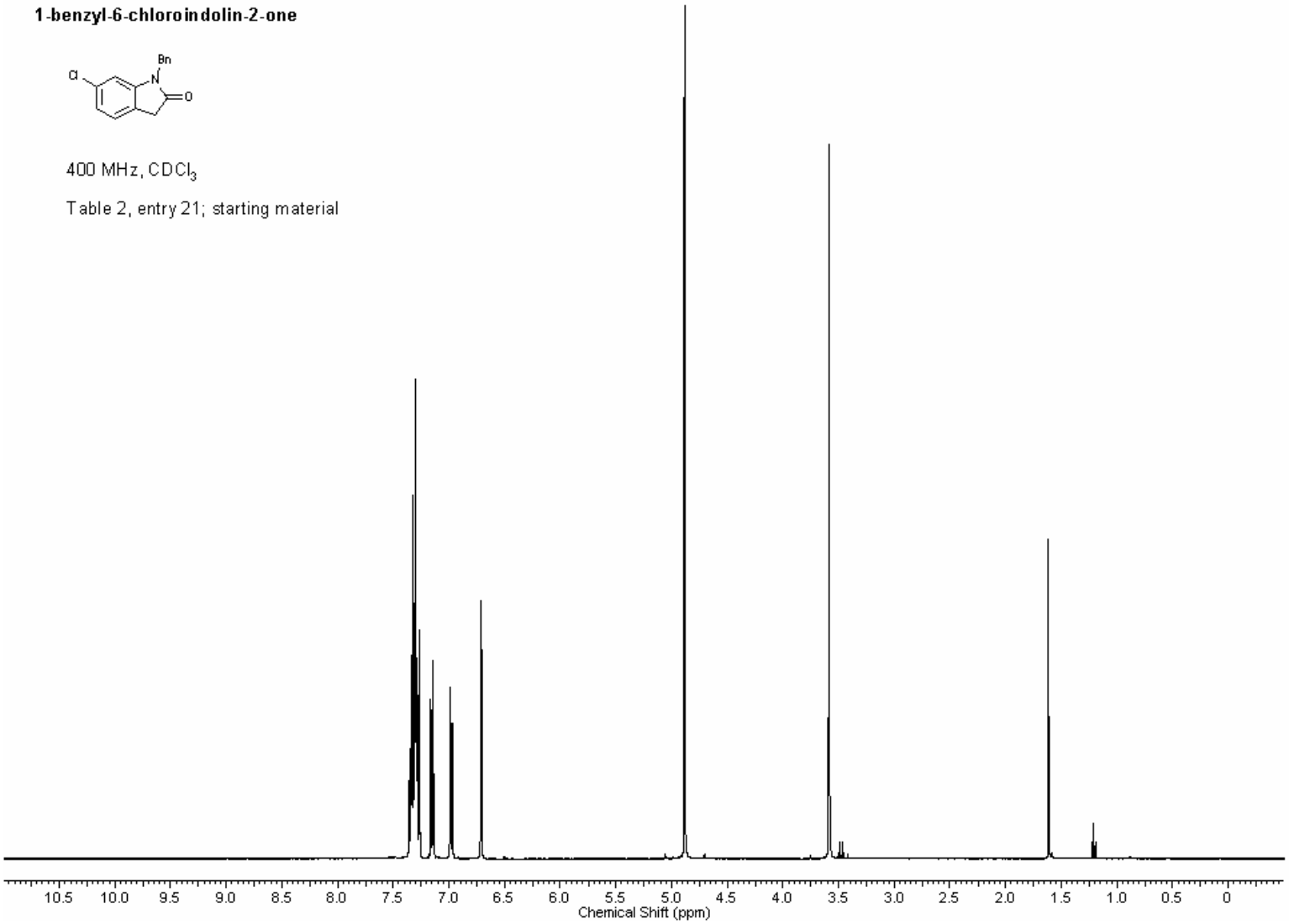
Table 2, entry 20; starting material



1-benzyl-6-chloroindolin-2-one

400 MHz, $CDCl_3$

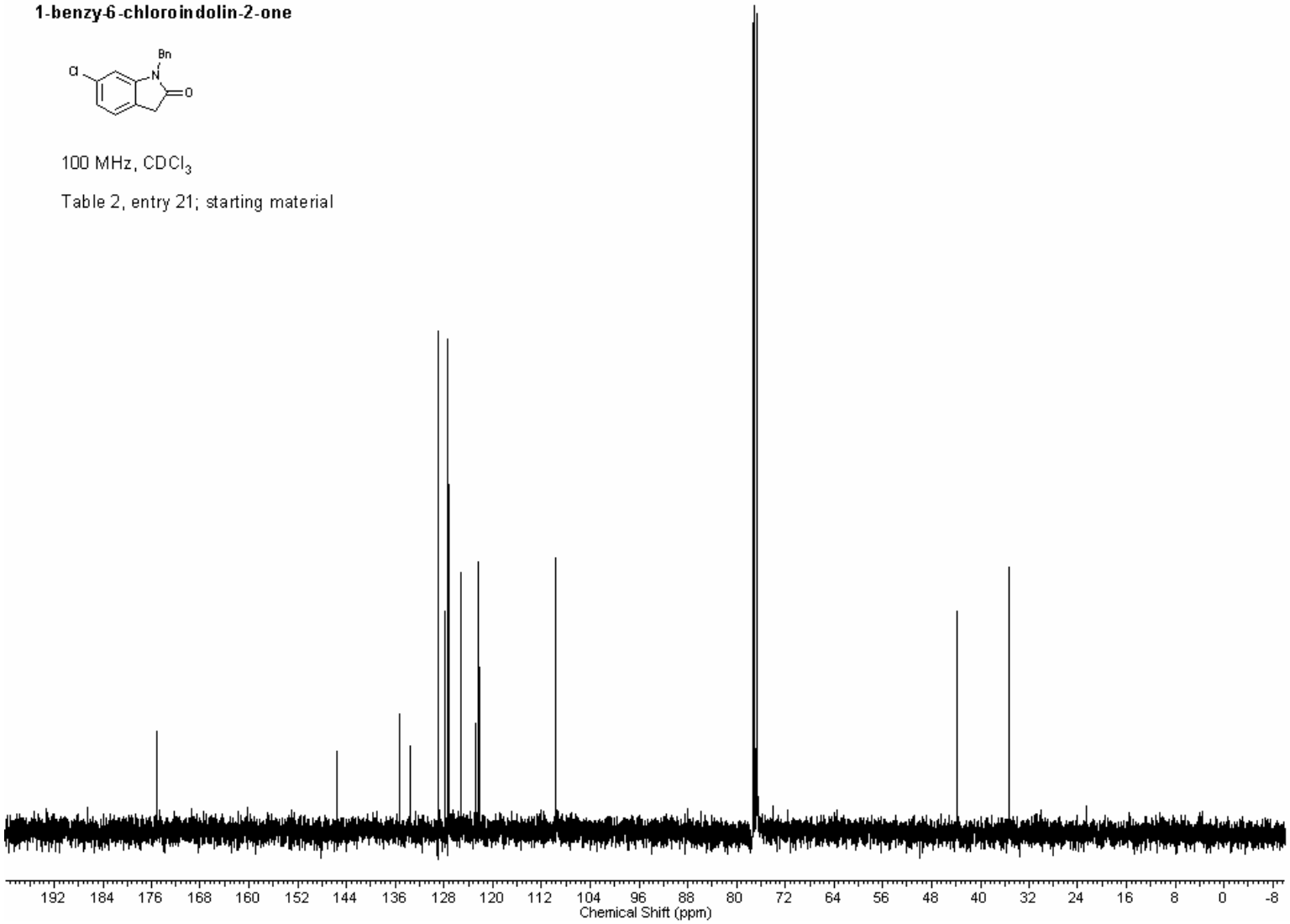
Table 2, entry 21; starting material



1-benzy-6-chloroindolin-2-one

100 MHz, $CDCl_3$

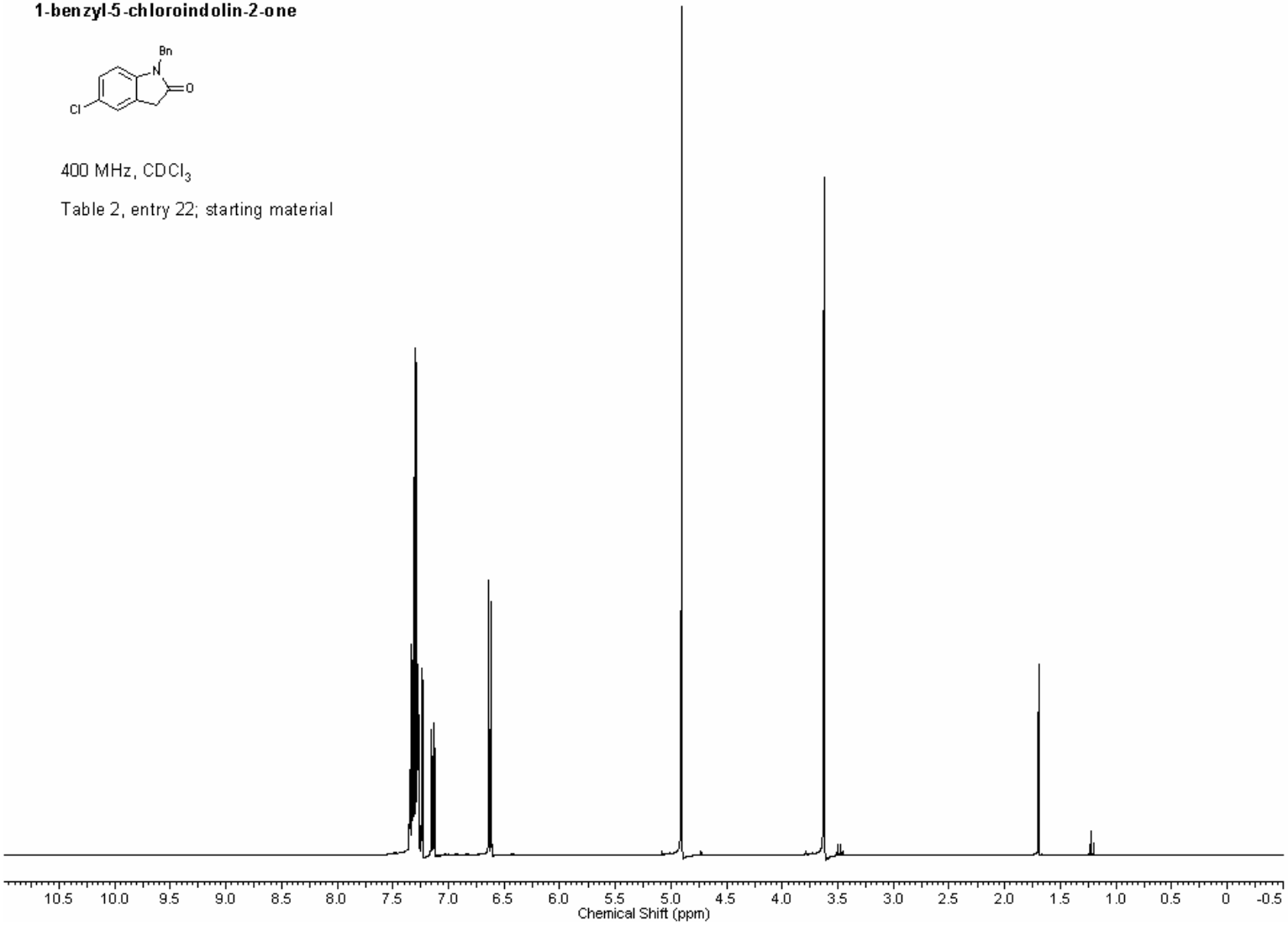
Table 2, entry 21; starting material



1-benzyl-5-chloroindolin-2-one

400 MHz, $CDCl_3$

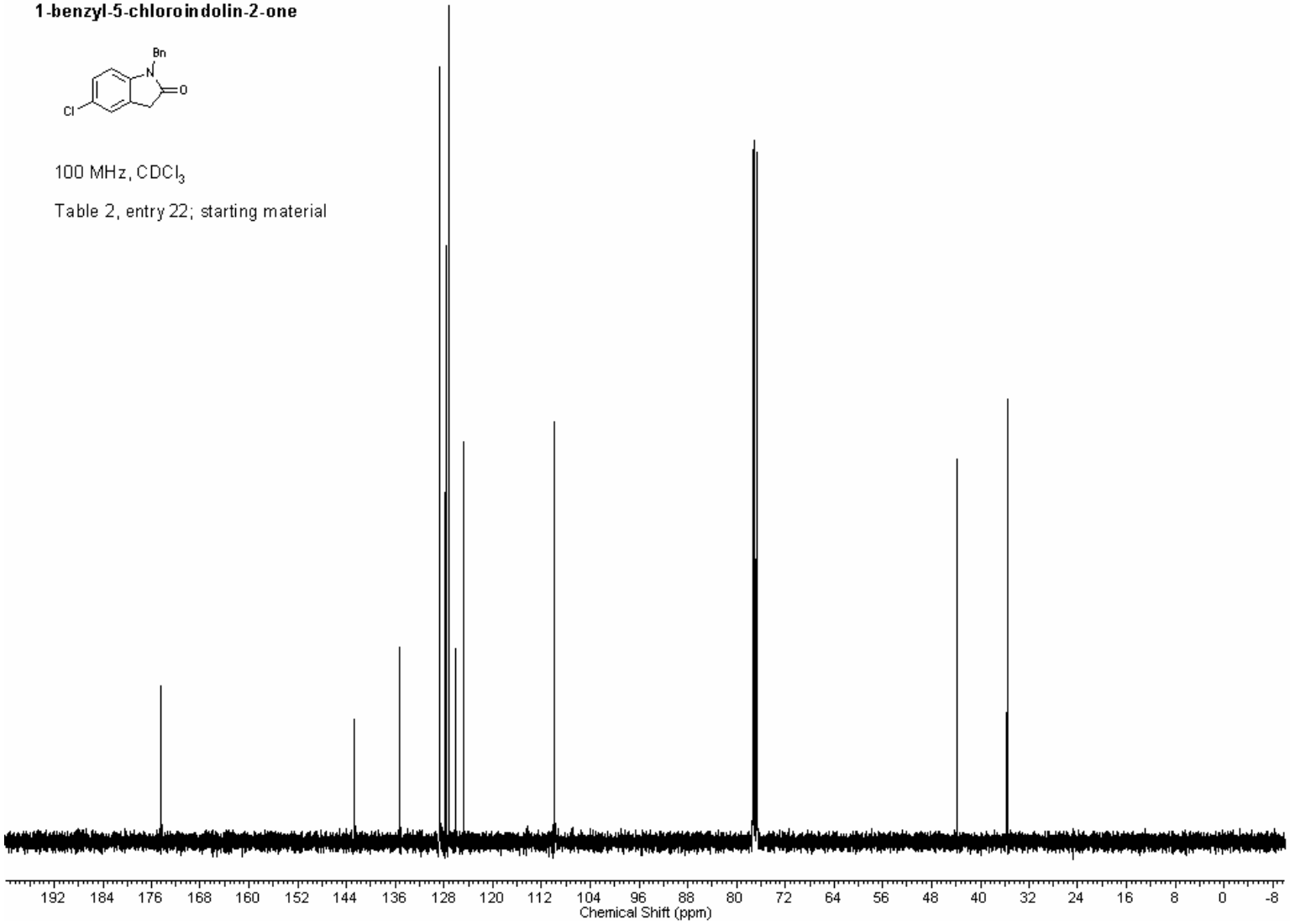
Table 2, entry 22; starting material



1-benzyl-5-chloroindolin-2-one

100 MHz, $CDCl_3$

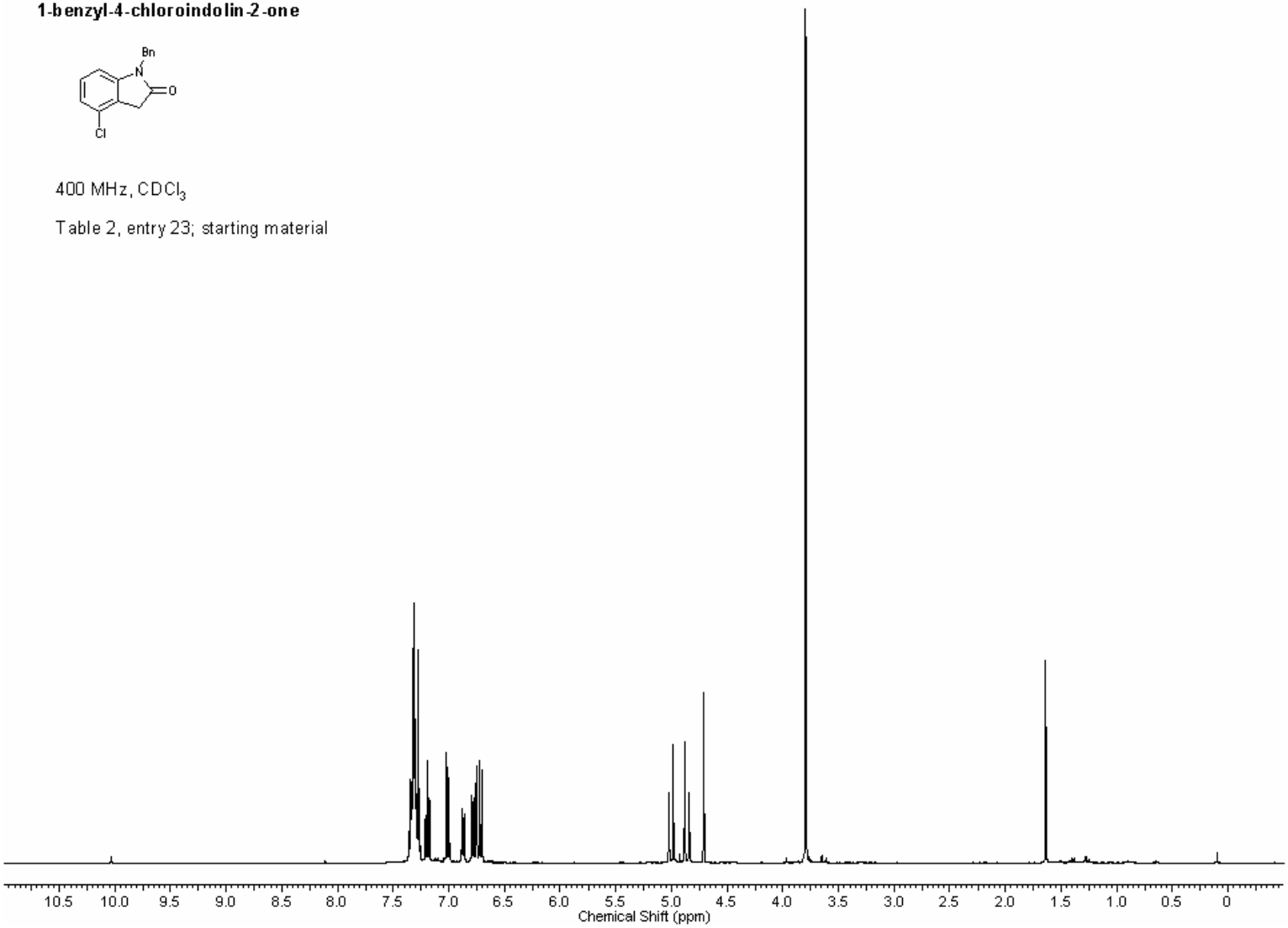
Table 2, entry 22; starting material



1-benzyl-4-chloroindolin-2-one

400 MHz, $CDCl_3$

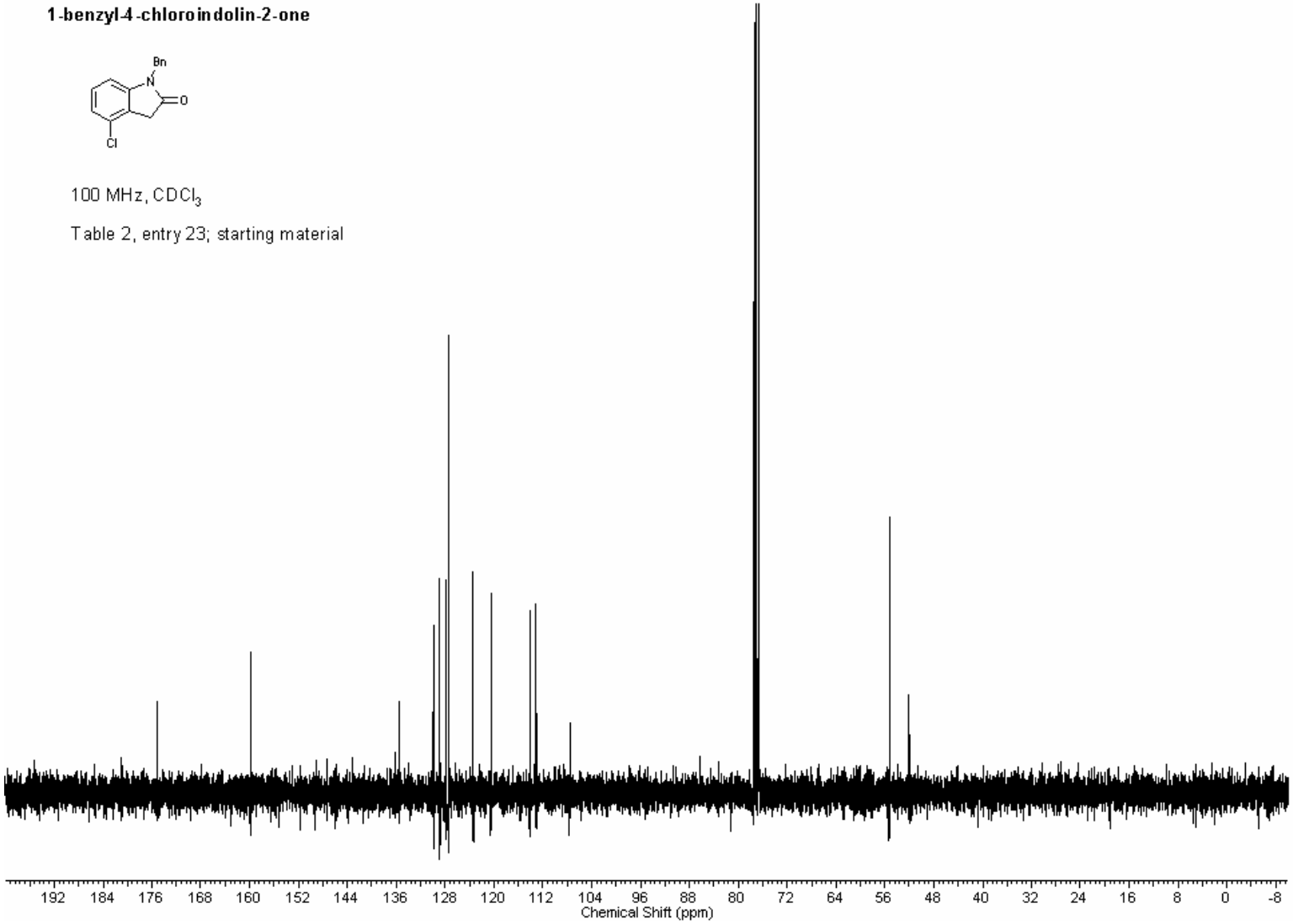
Table 2, entry 23; starting material



1-benzyl-4-chloroindolin-2-one

100 MHz, $CDCl_3$

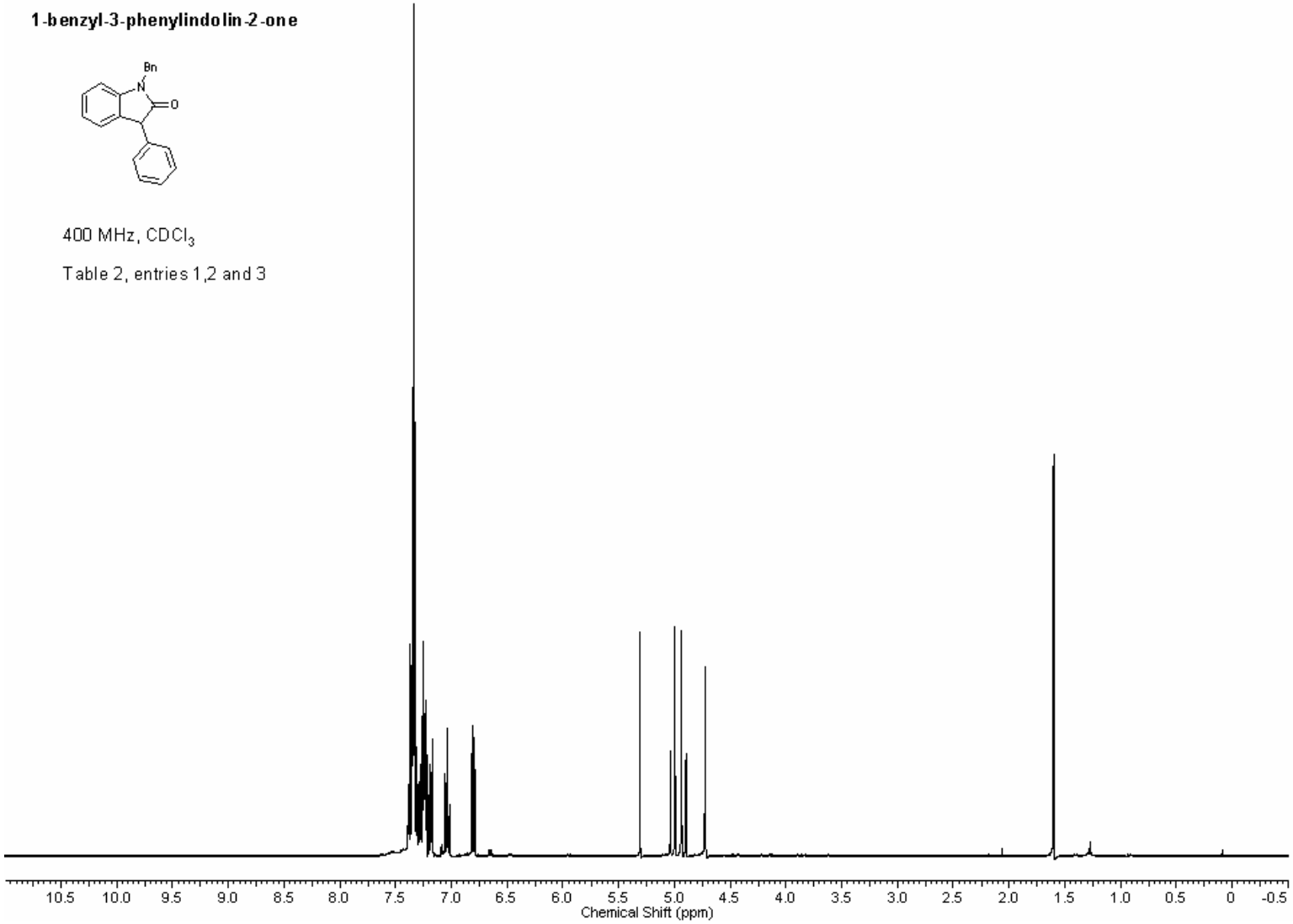
Table 2, entry 23; starting material



1-benzyl-3-phenylindolin-2-one

400 MHz, $CDCl_3$

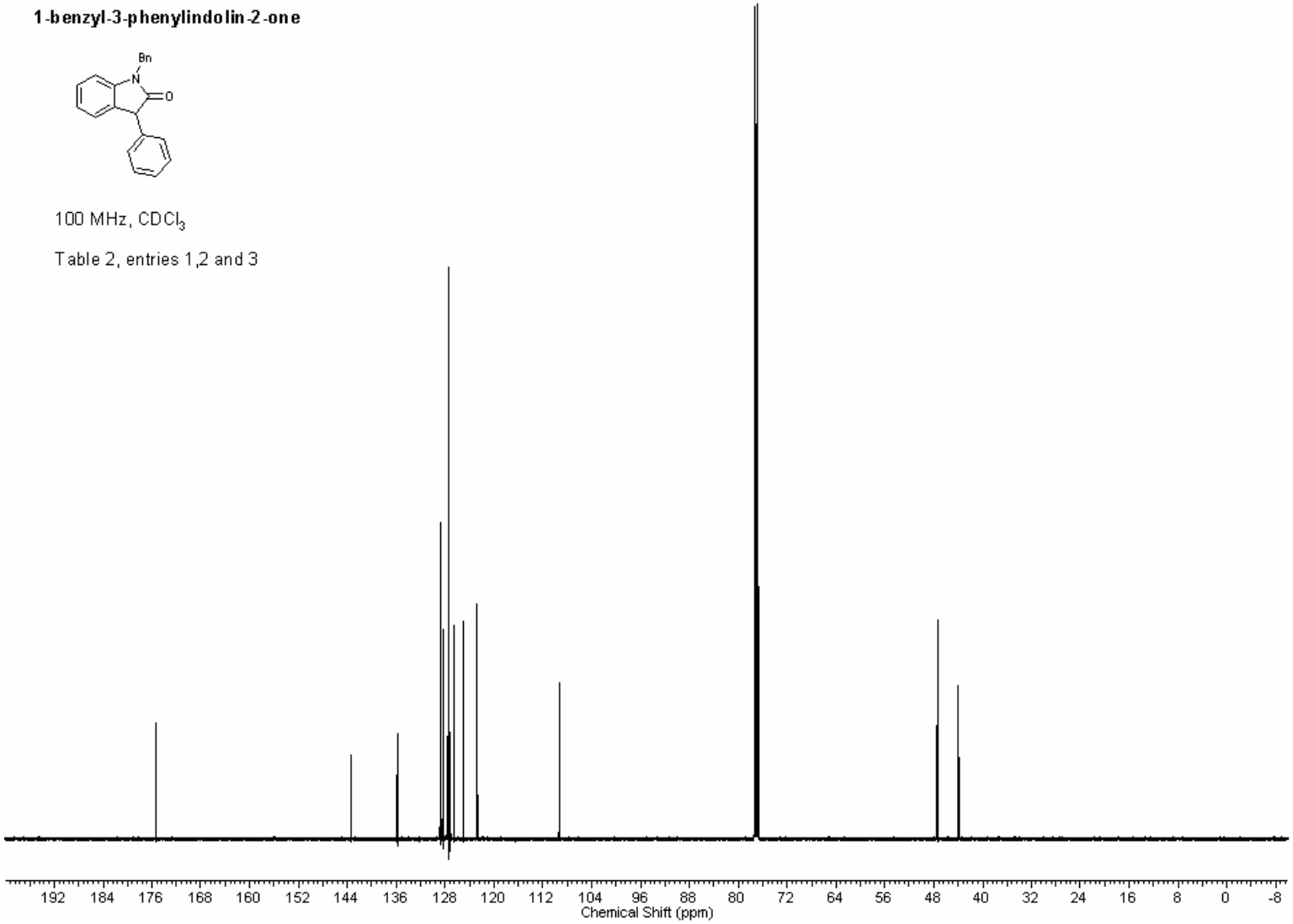
Table 2, entries 1,2 and 3



1-benzyl-3-phenylindolin-2-one

100 MHz, $CDCl_3$

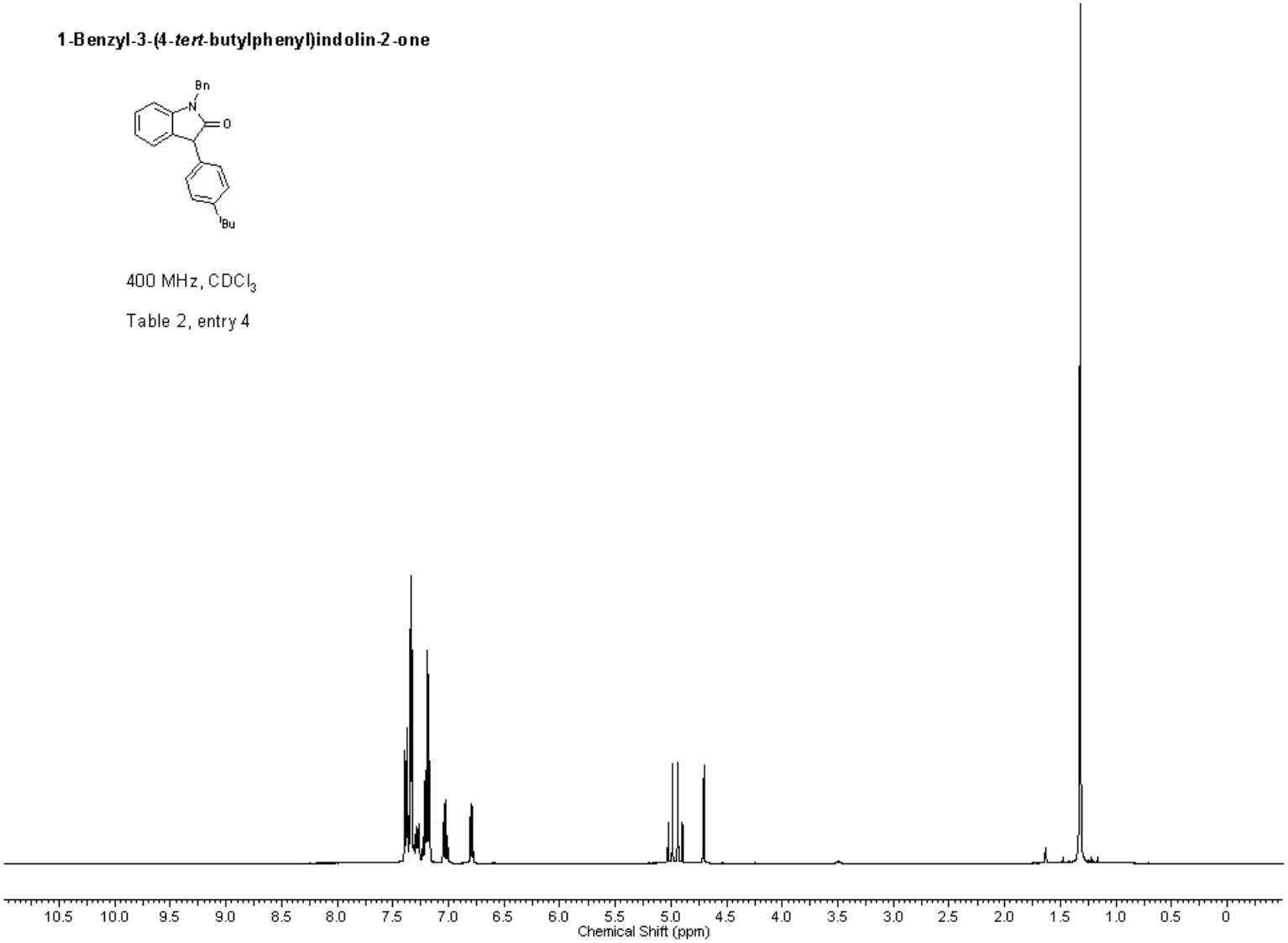
Table 2, entries 1,2 and 3



1-Benzyl-3-(4-*tert*-butylphenyl)indolin-2-one

400 MHz, $CDCl_3$

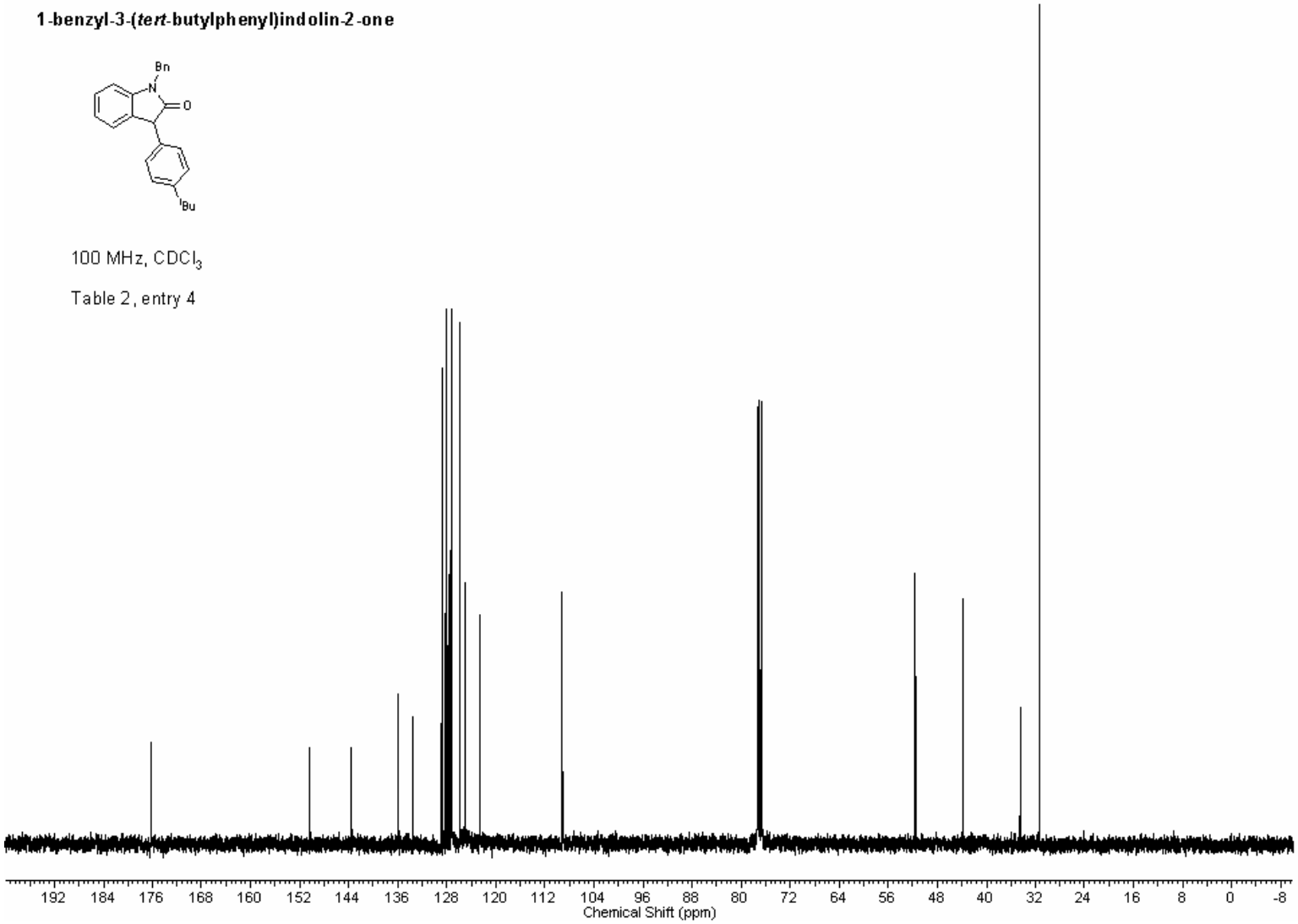
Table 2, entry 4



1-benzyl-3-(*tert*-butylphenyl)indolin-2-one

100 MHz, $CDCl_3$

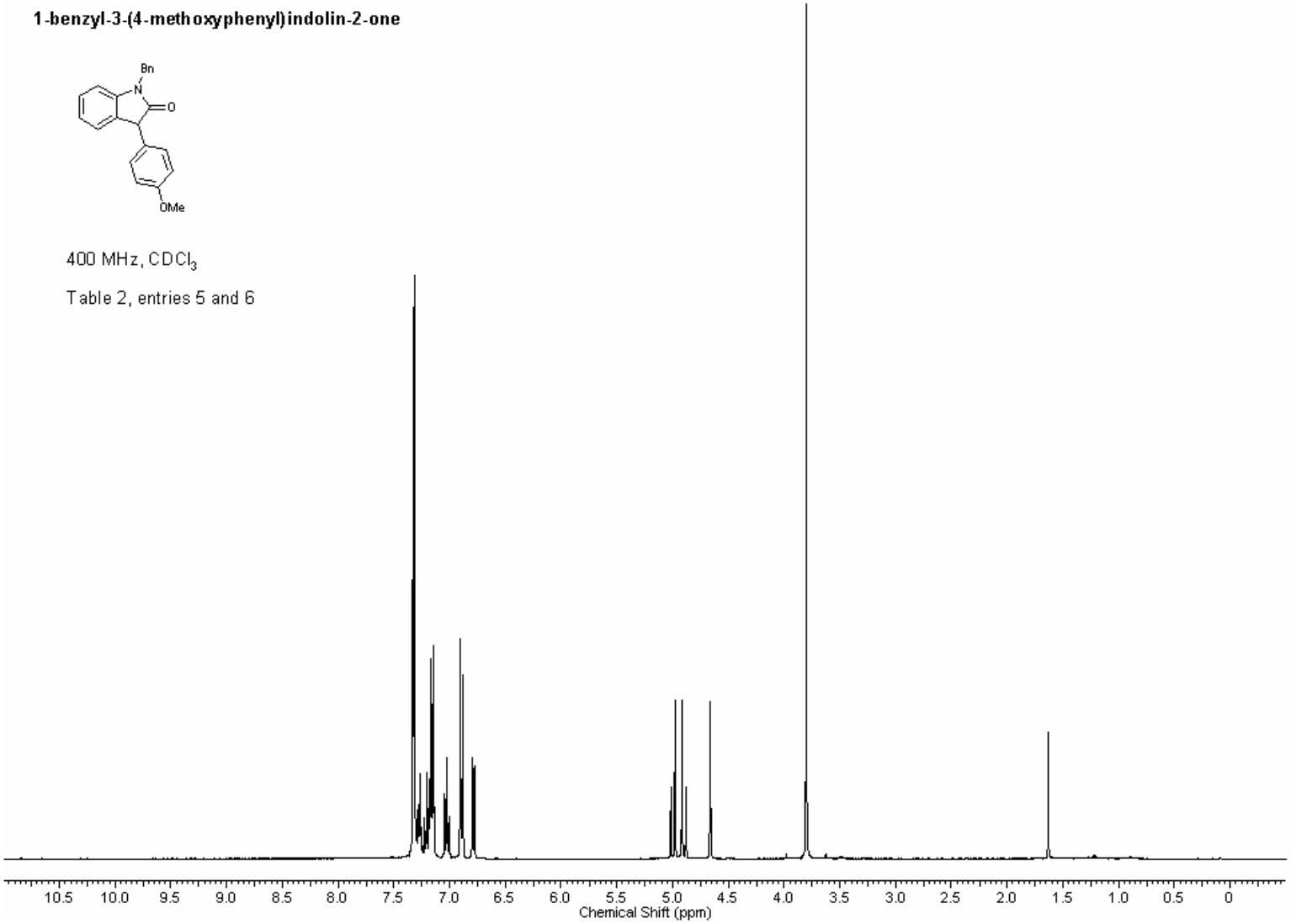
Table 2, entry 4



1-benzyl-3-(4-methoxyphenyl)indolin-2-one

400 MHz, $CDCl_3$

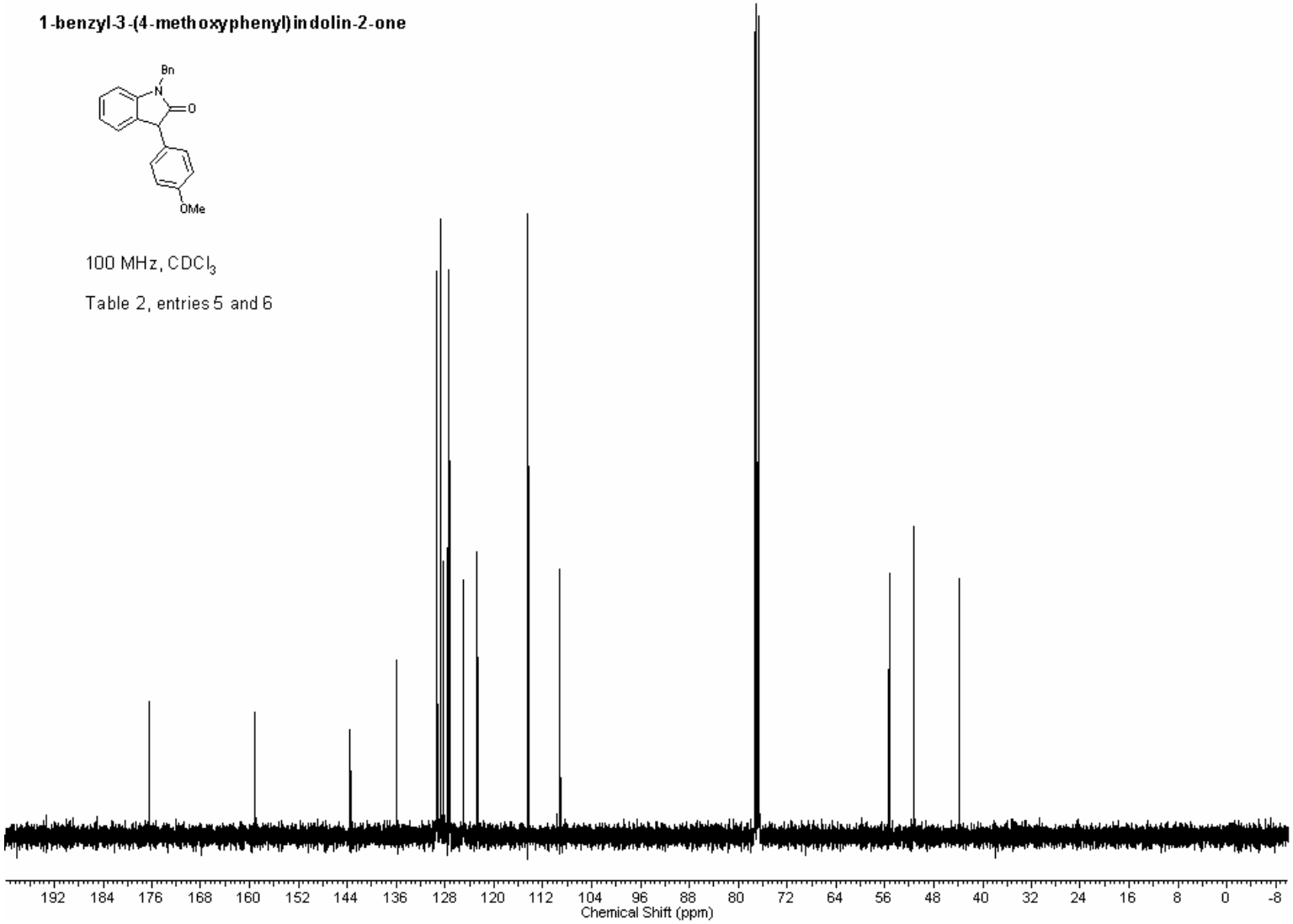
Table 2, entries 5 and 6



1-benzyl-3-(4-methoxyphenyl)indolin-2-one

100 MHz, $CDCl_3$

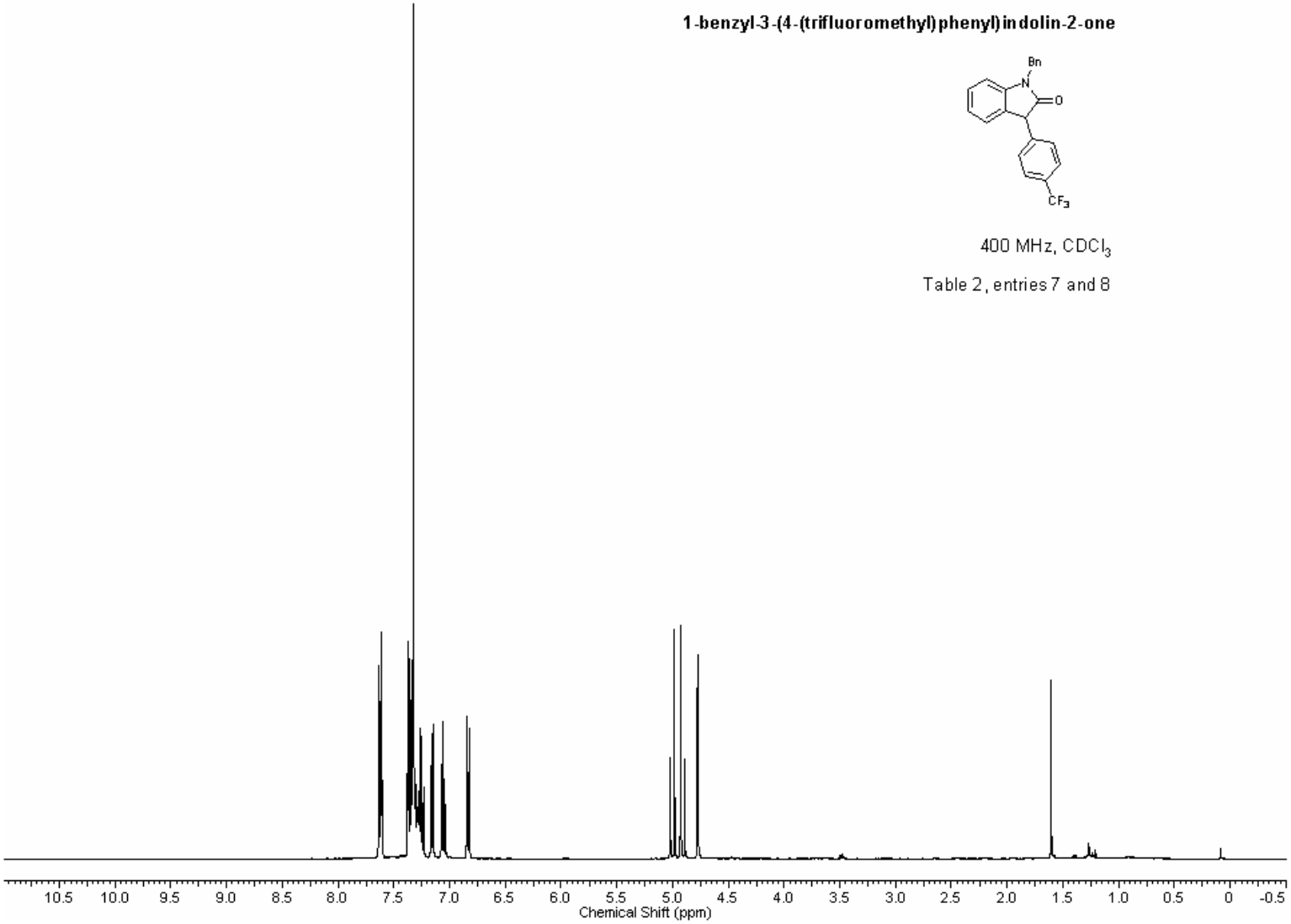
Table 2, entries 5 and 6



1-benzyl-3-(4-(trifluoromethyl)phenyl)indolin-2-one

400 MHz, $CDCl_3$

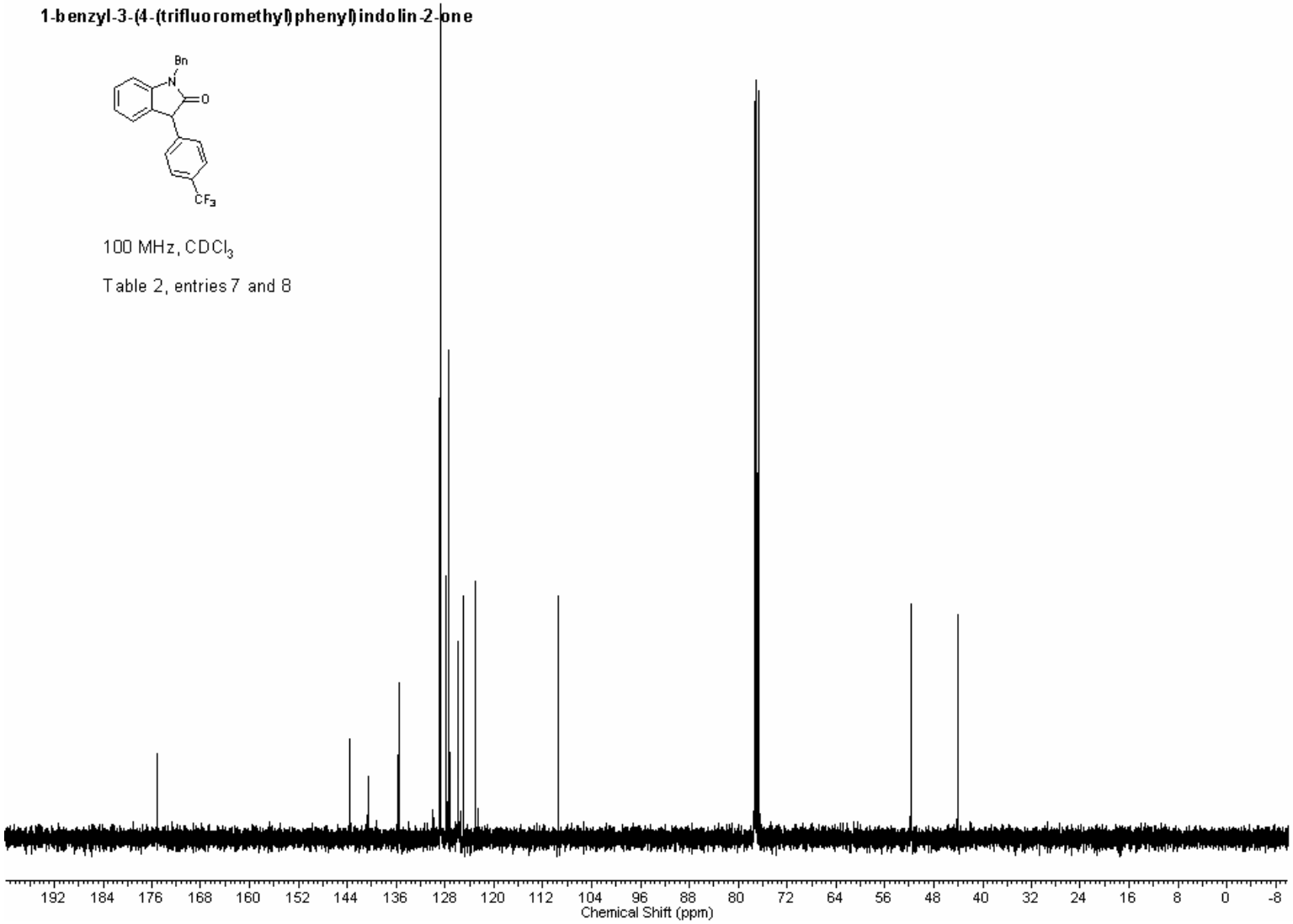
Table 2, entries 7 and 8



1-benzyl-3-(4-(trifluoromethyl)phenyl)indolin-2-one

100 MHz, $CDCl_3$

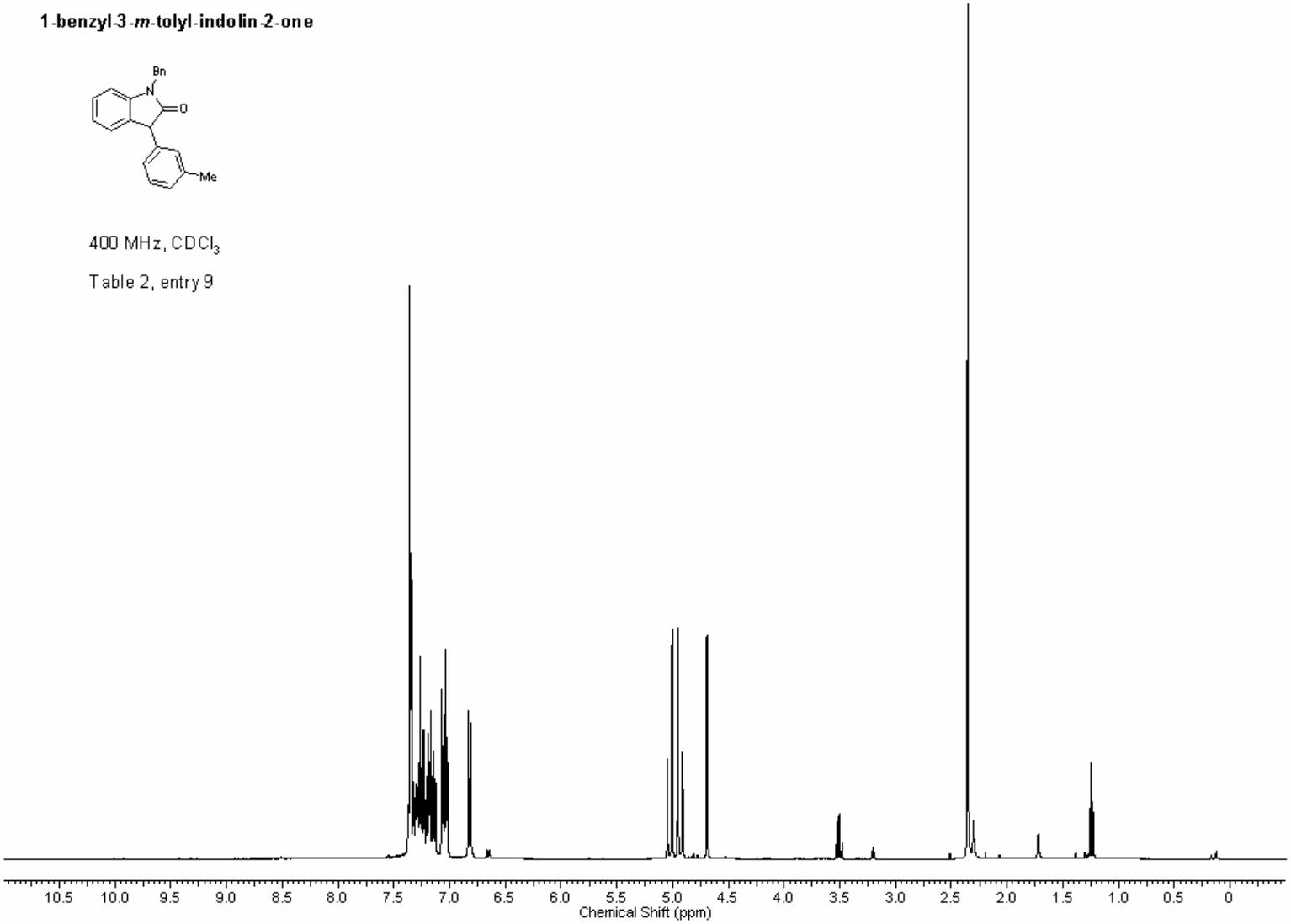
Table 2, entries 7 and 8



1-benzyl-3-*m*-tolyl-indolin-2-one

400 MHz, $CDCl_3$

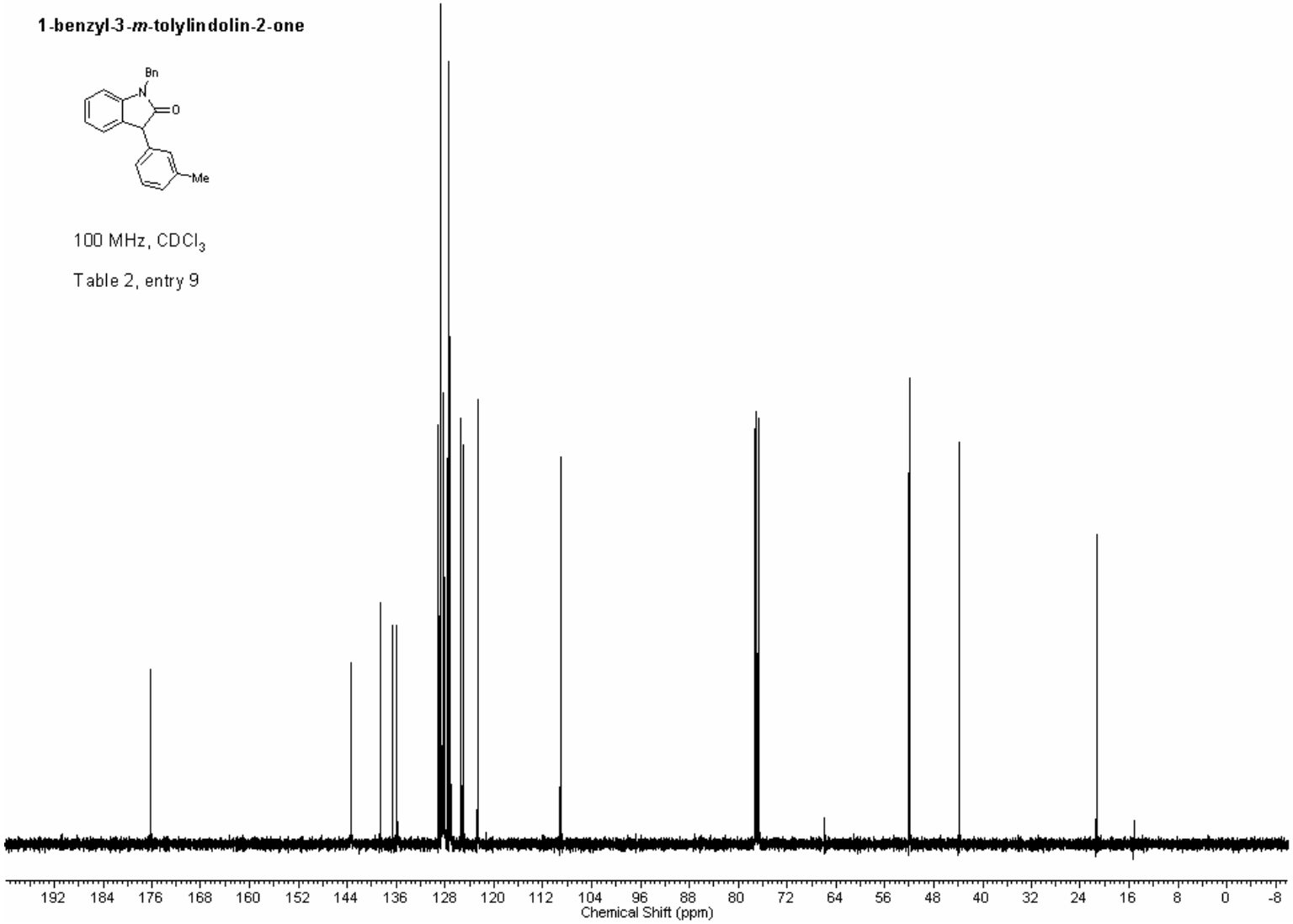
Table 2, entry 9



1-benzyl-3-*m*-tolylindolin-2-one

100 MHz, $CDCl_3$

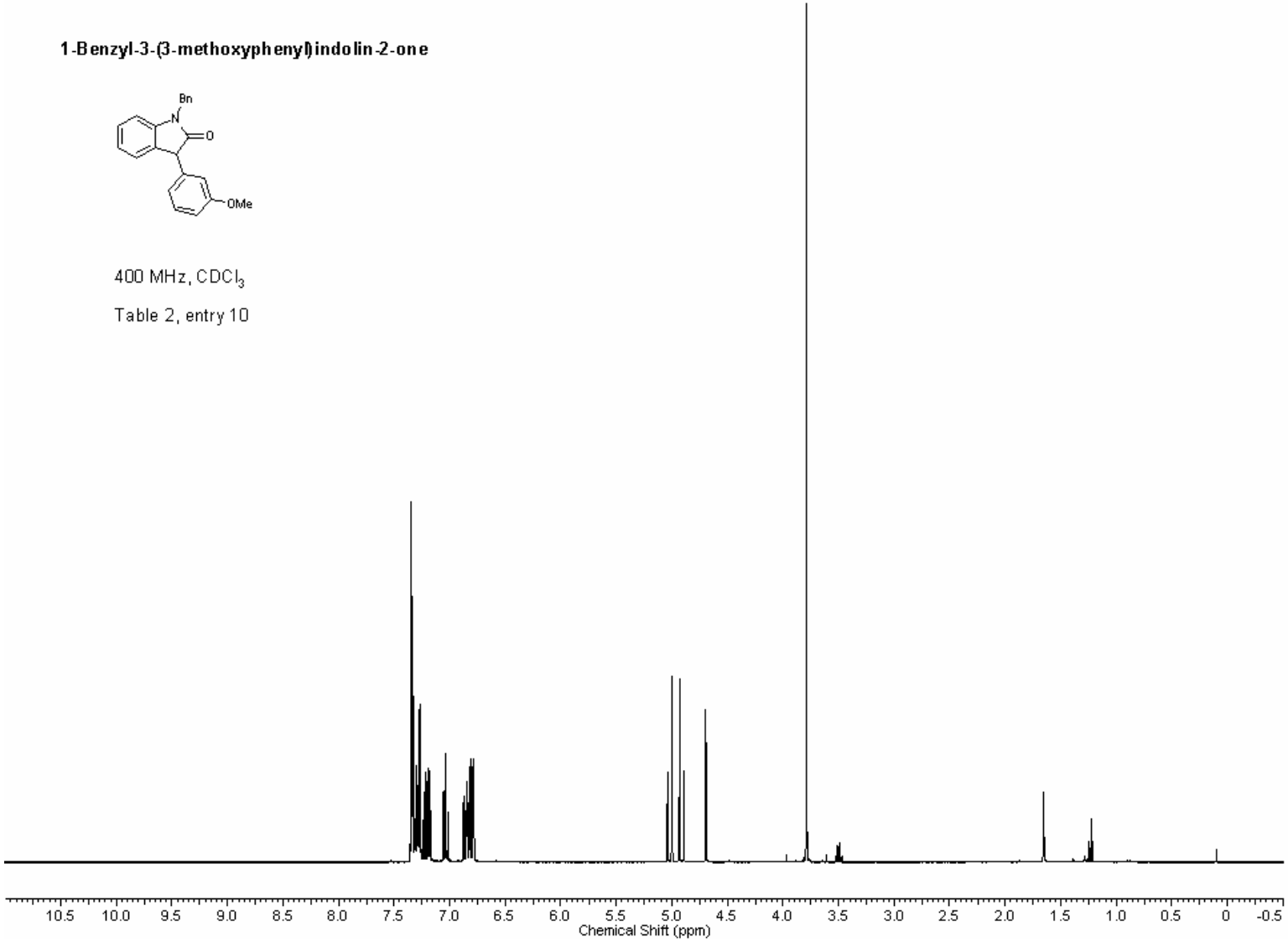
Table 2, entry 9

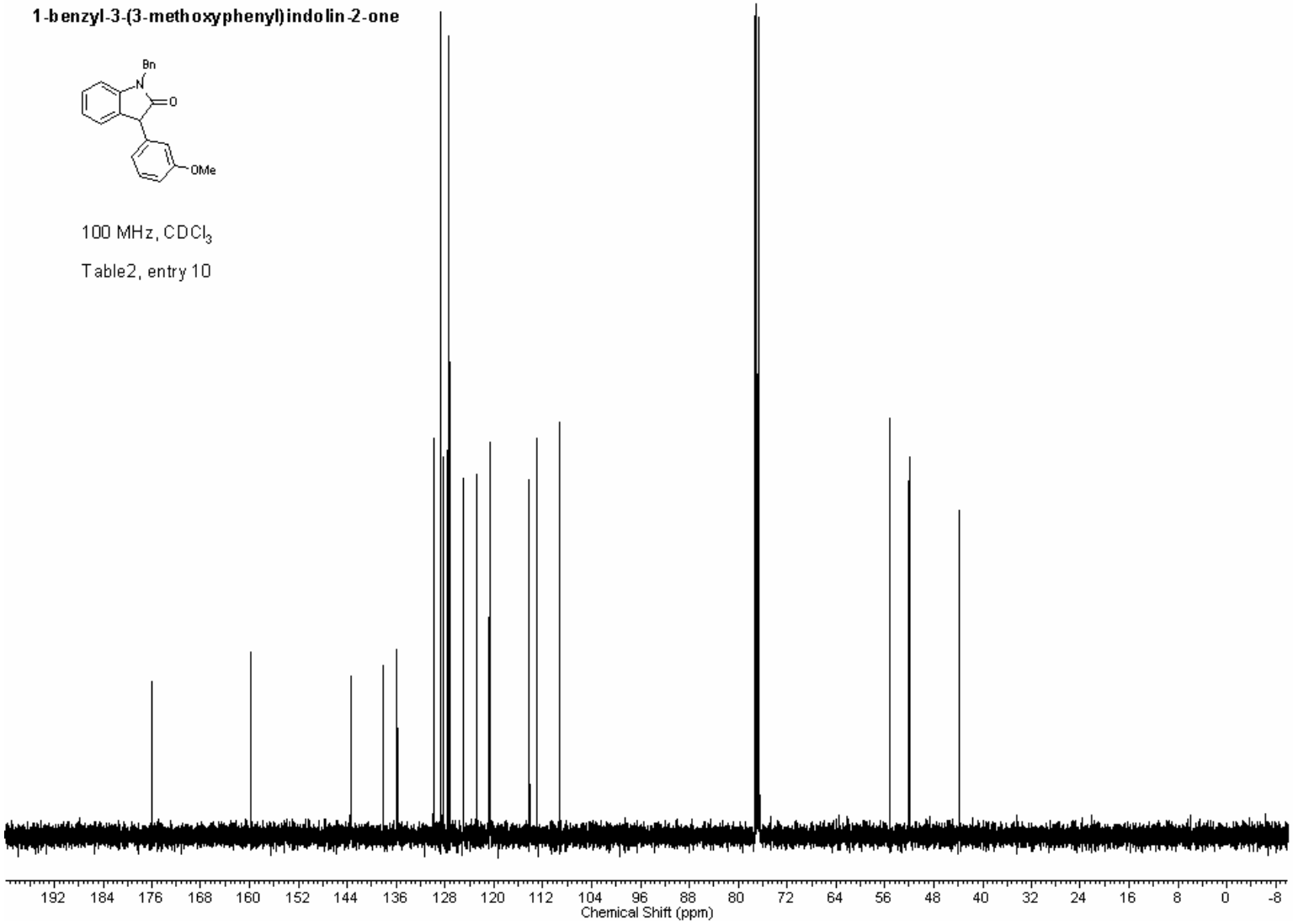


1-Benzyl-3-(3-methoxyphenyl)indolin-2-one

400 MHz, $CDCl_3$

Table 2, entry 10

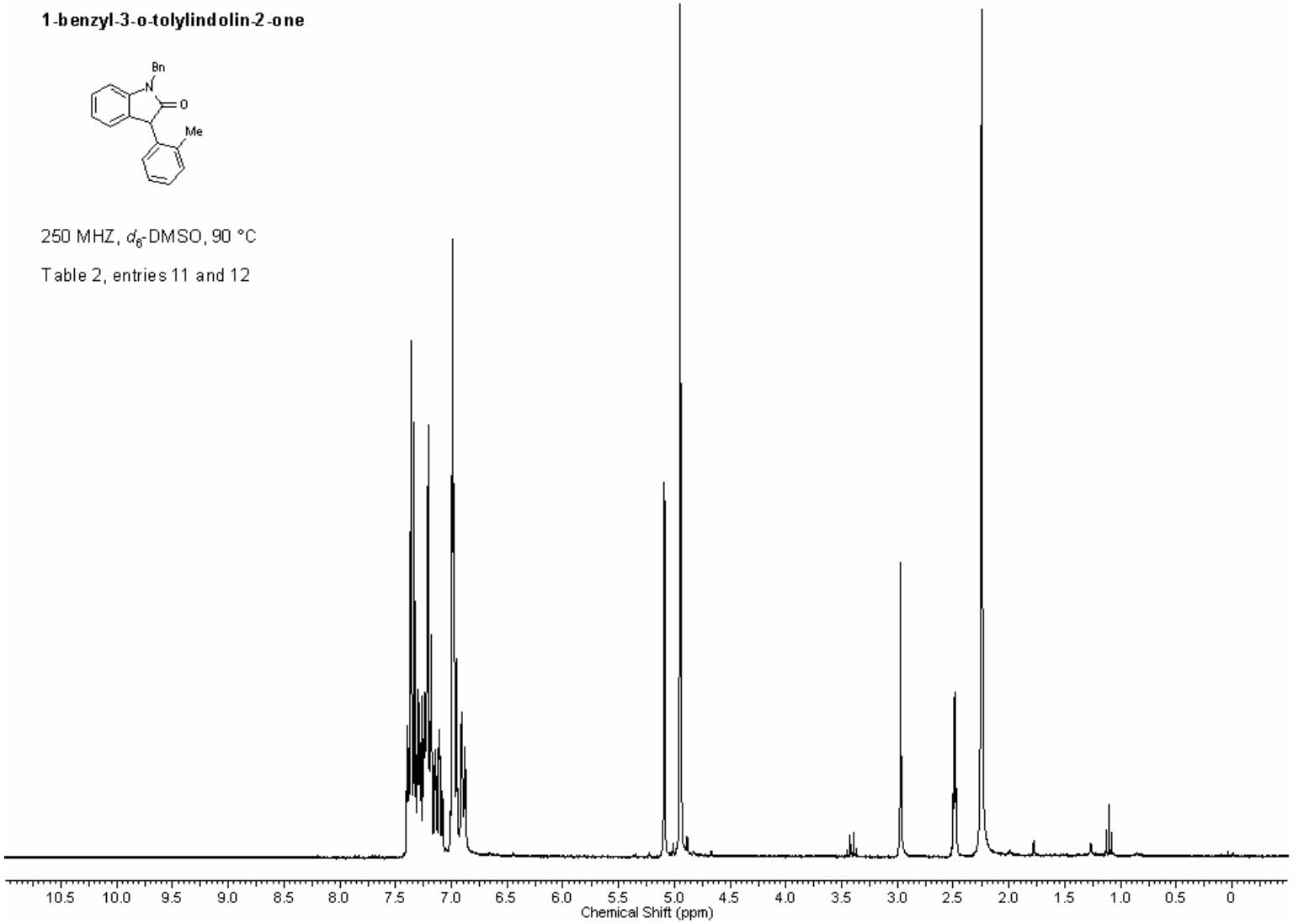



1-benzyl-3-(3-methoxyphenyl)indolin-2-one
Bn
N
O
OMe
100 MHz, CDCl3
Table2, entry 10
192 184 176 168 160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8 0 -8
Chemical Shift (ppm)

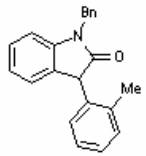
1-benzyl-3-o-tolylindolin-2-one

250 MHZ, d_6-DMSO, 90 °C

Table 2, entries 11 and 12

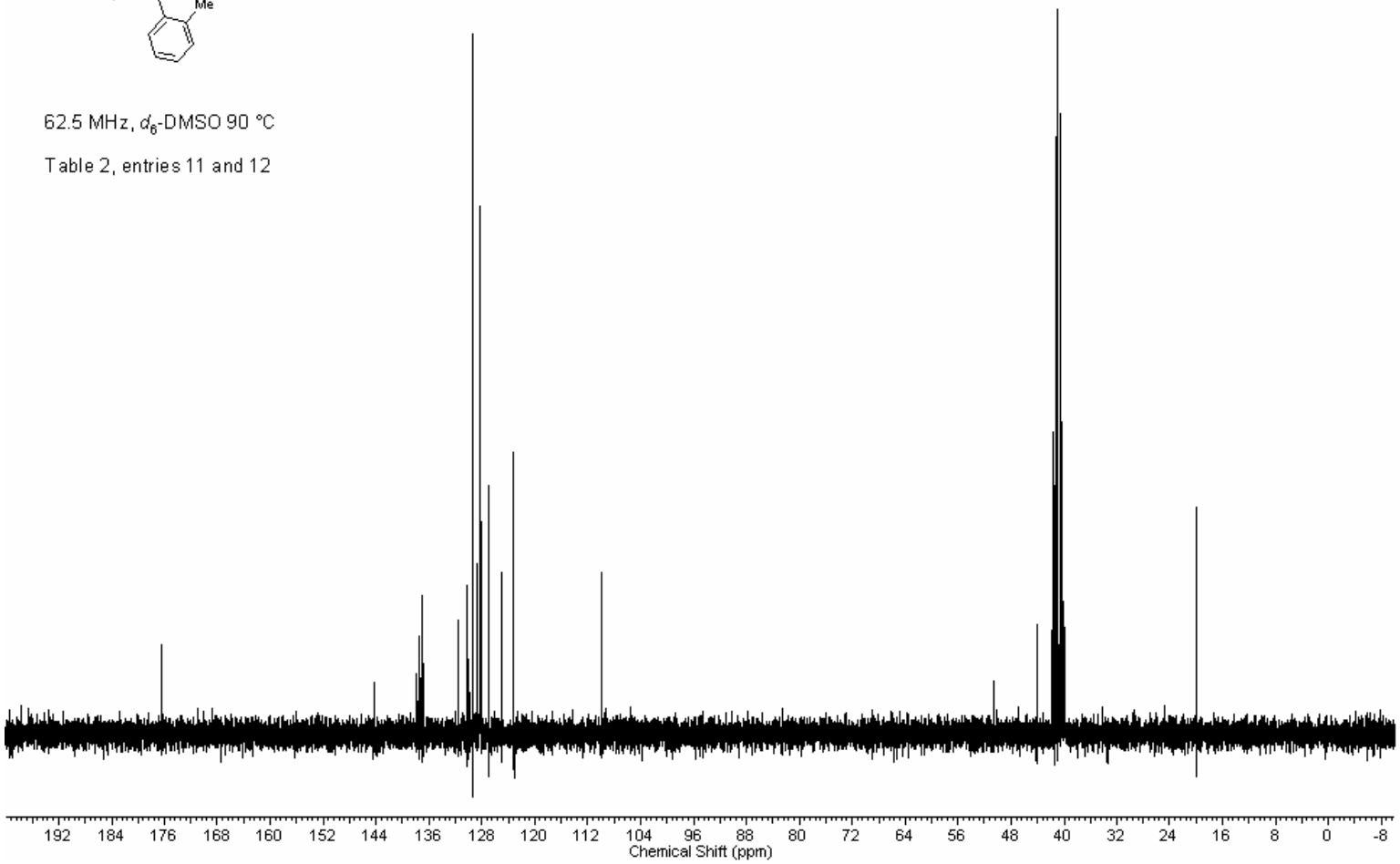


1-benzyl-3-*o*-tolylindolin-2-one

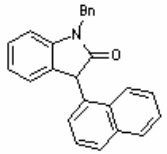


62.5 MHz, d_6-DMSO 90 °C

Table 2, entries 11 and 12

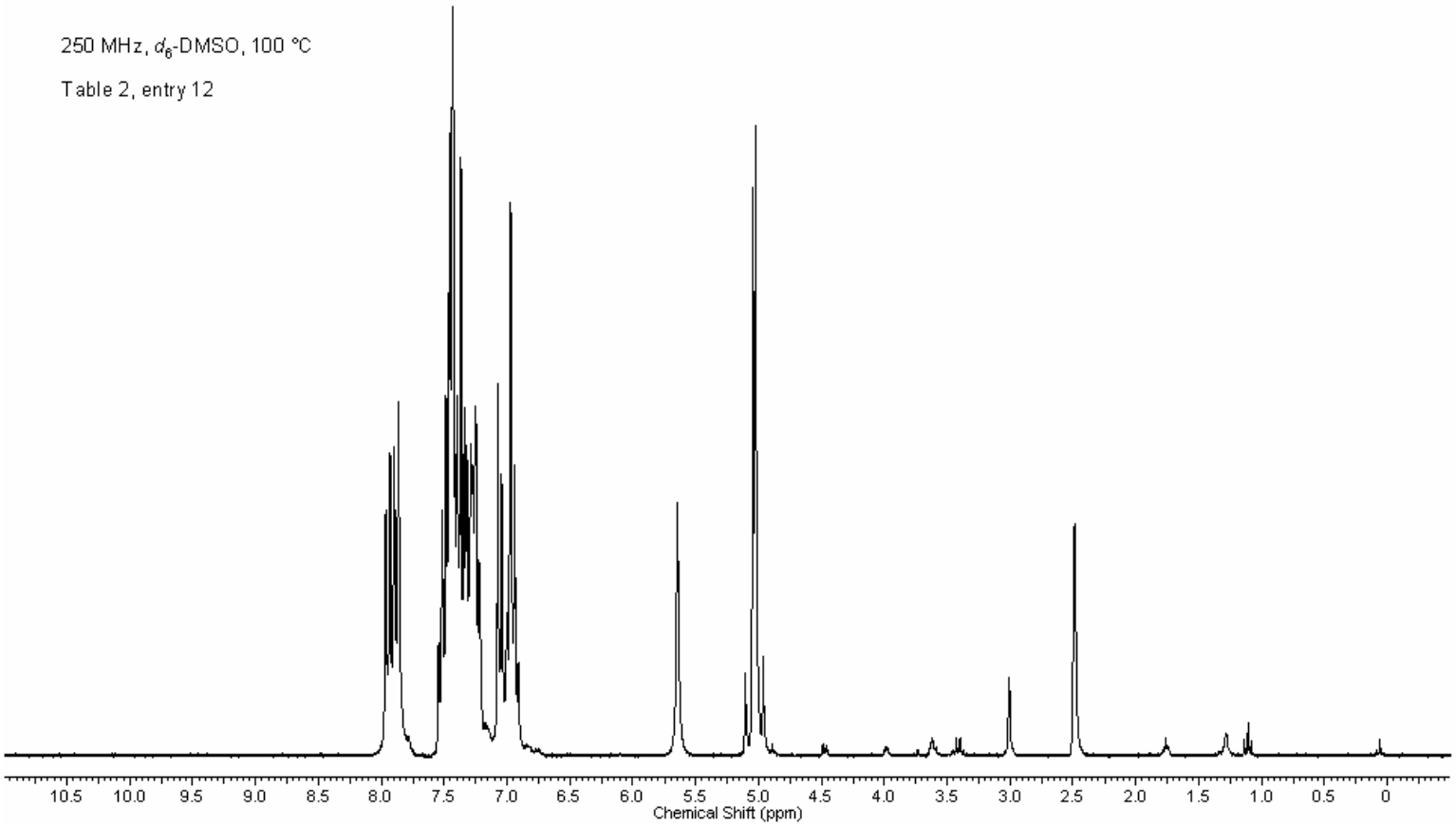


1-benzyl-3-(naphthalen-1-yl)indolin-2-one



250 MHz, d_6-DMSO, 100 °C

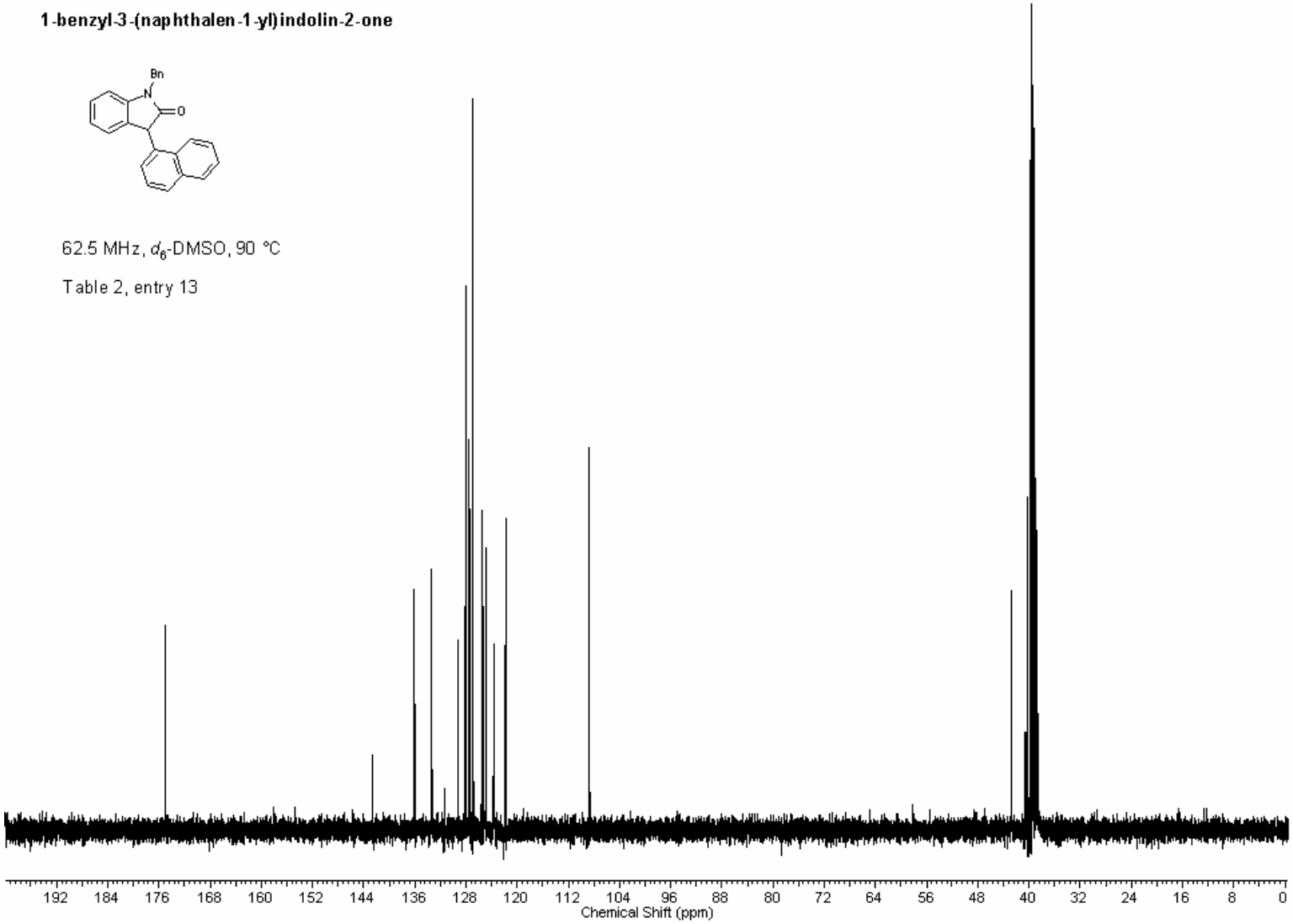
Table 2, entry 12



1-benzyl-3-(naphthalen-1-yl)indolin-2-one

62.5 MHz, d_6-DMSO, 90 °C

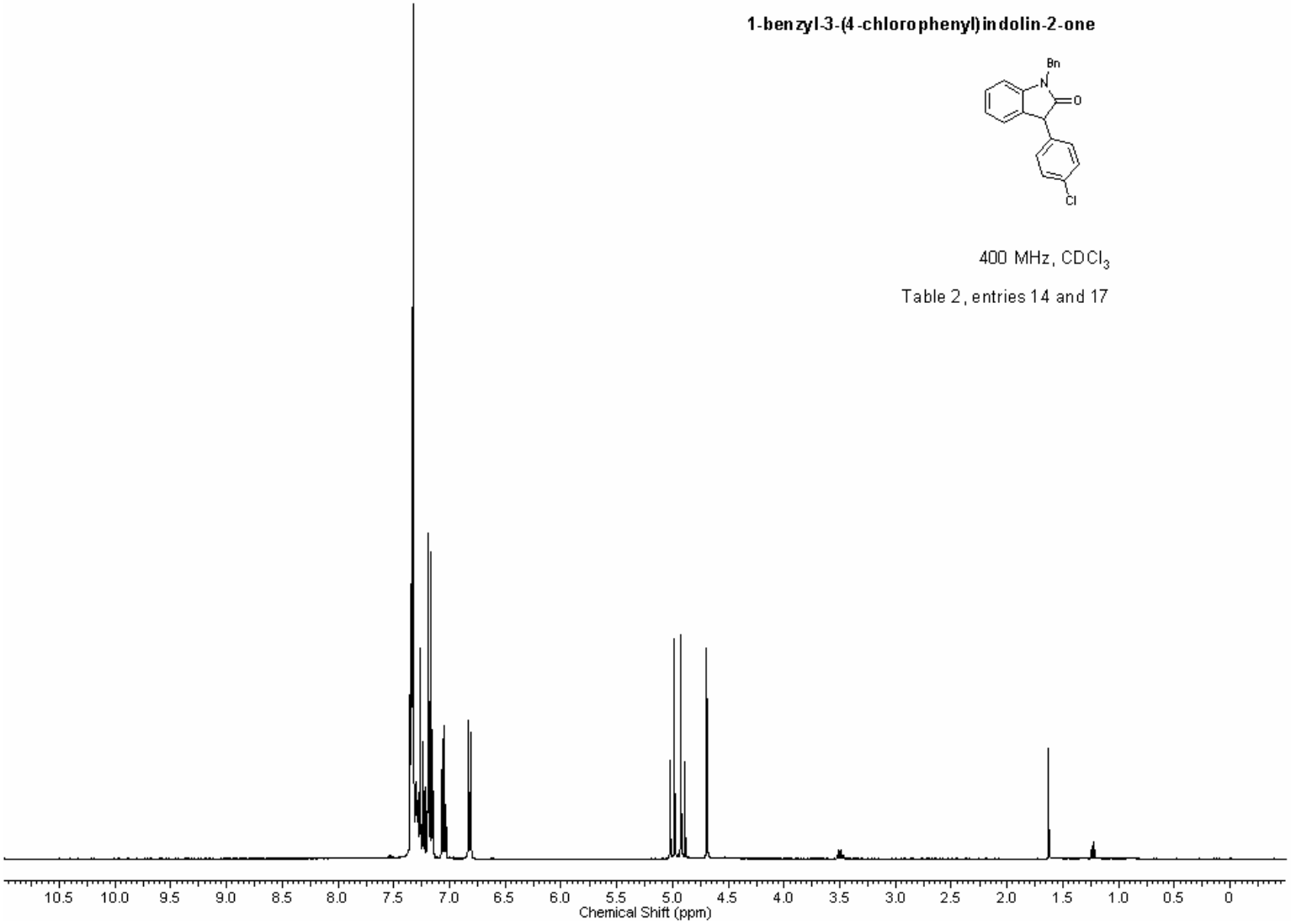
Table 2, entry 13



1-benzyl-3-(4-chlorophenyl)indolin-2-one

400 MHz, $CDCl_3$

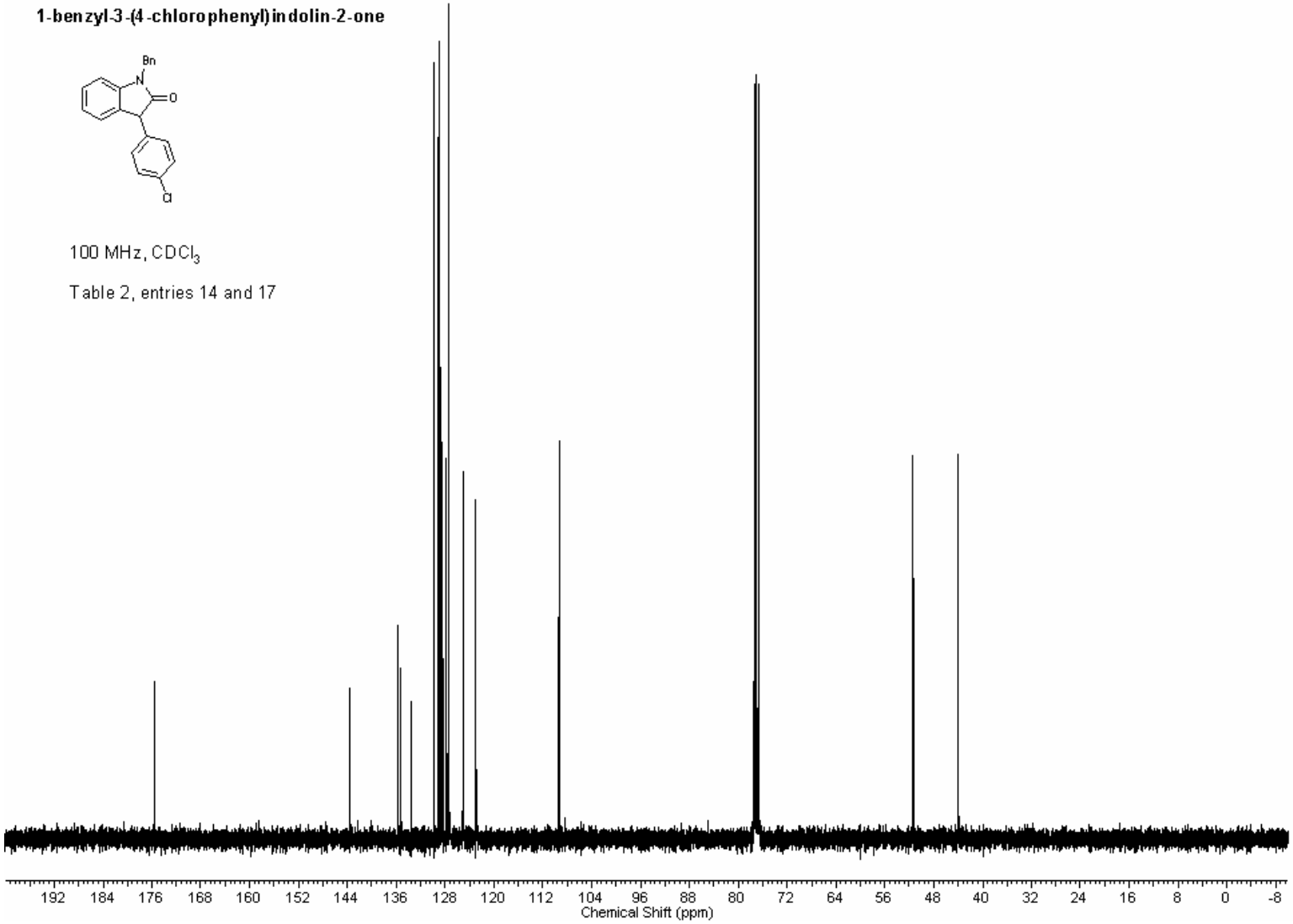
Table 2, entries 14 and 17



1-benzyl-3-(4-chlorophenyl)indolin-2-one

100 MHz, $CDCl_3$

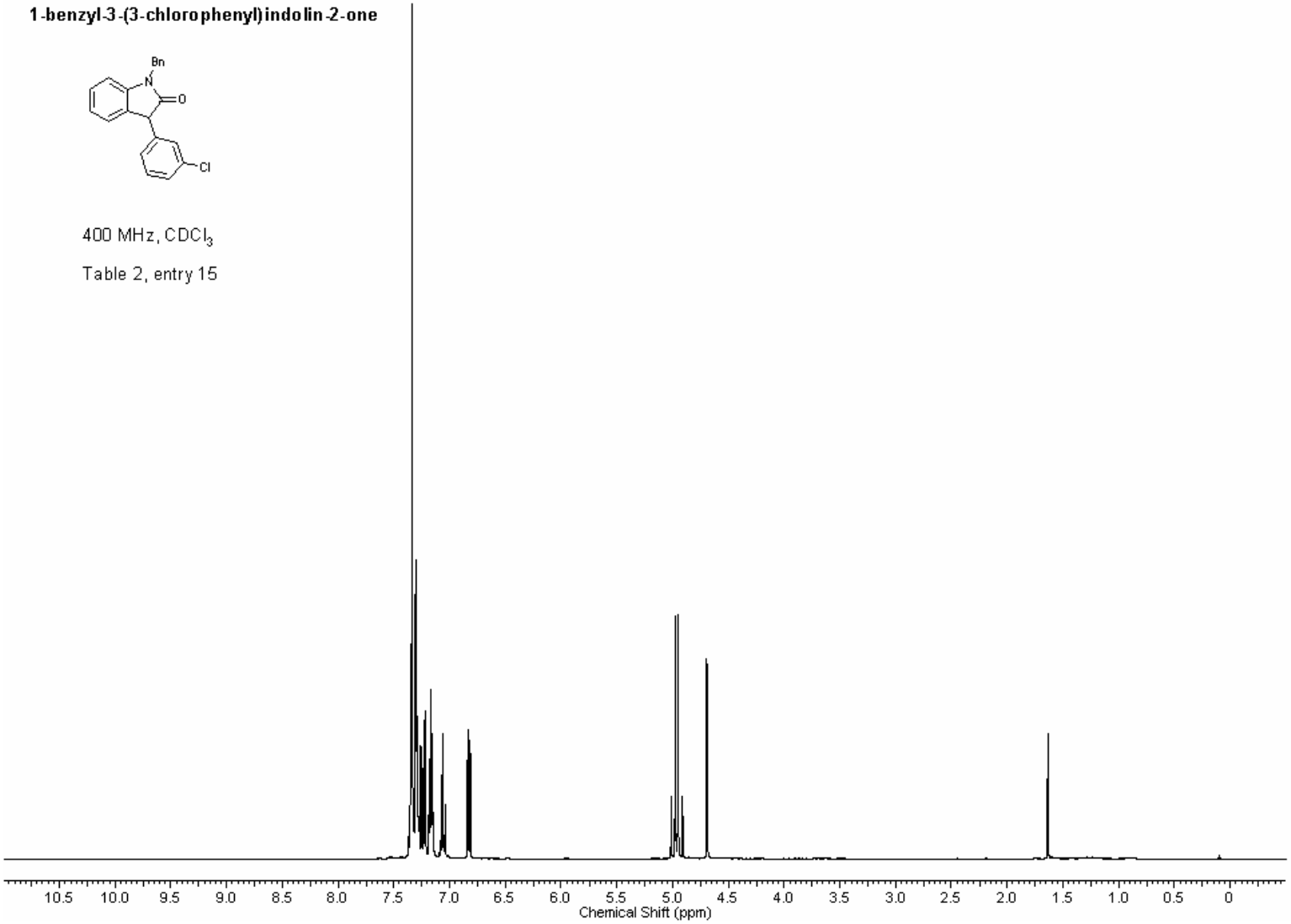
Table 2, entries 14 and 17

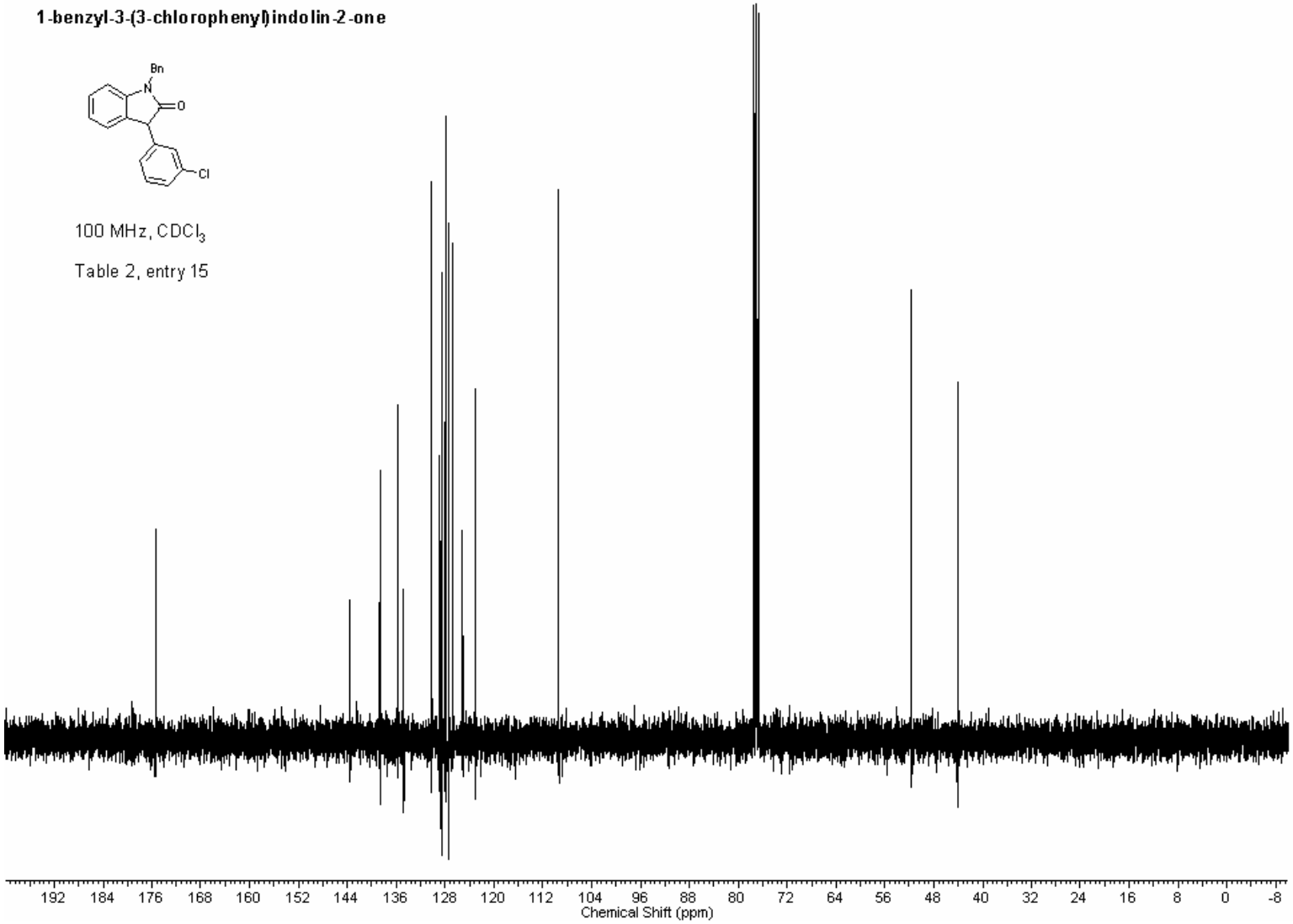


1-benzyl-3-(3-chlorophenyl)indolin-2-one

400 MHz, $CDCl_3$

Table 2, entry 15

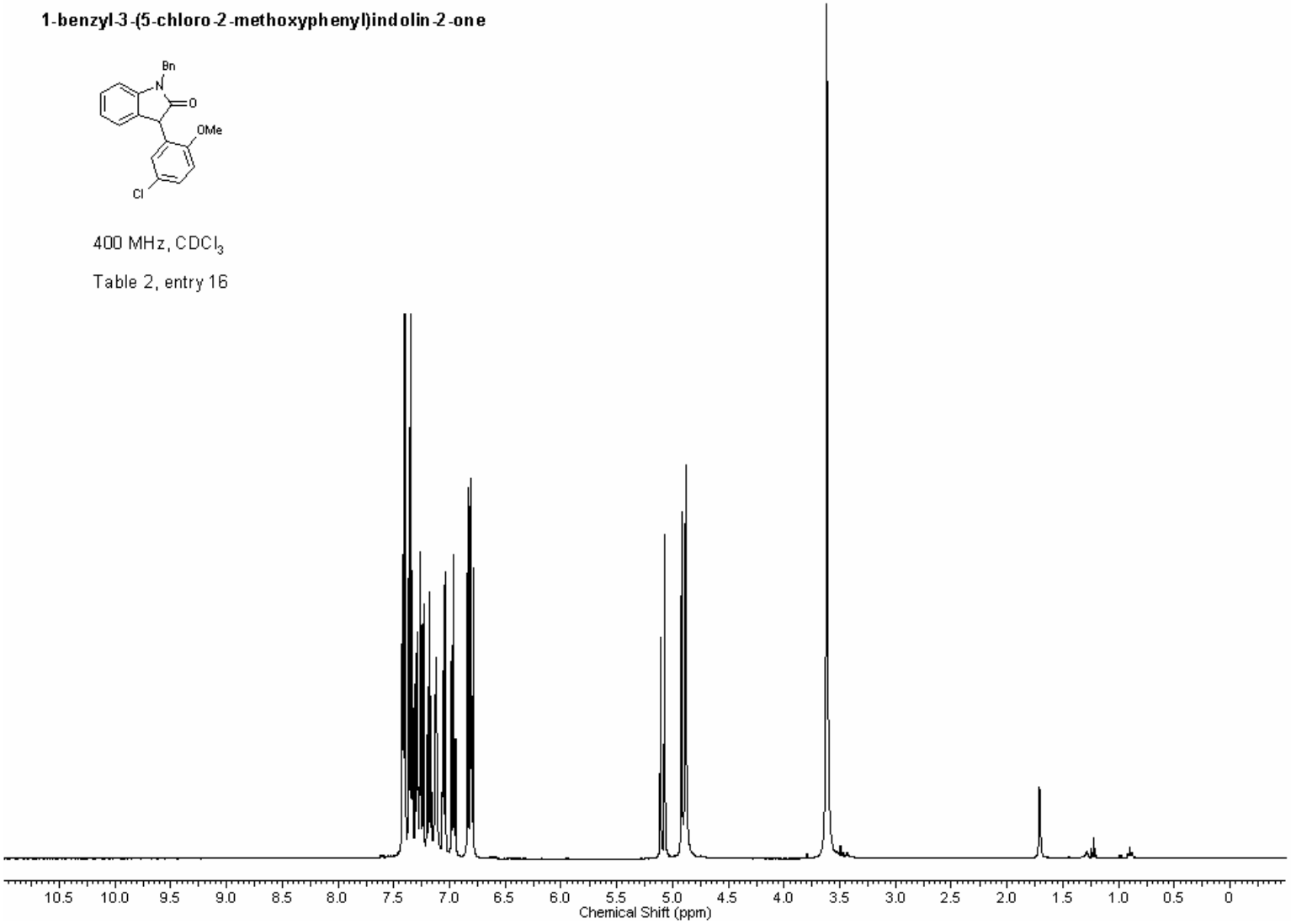



1-benzyl-3-(3-chlorophenyl)indolin-2-one
Bn
N
O
Cl
100 MHz, CDCl3
Table 2, entry 15
192 184 176 168 160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8 0 -8
Chemical Shift (ppm)

1-benzyl-3-(5-chloro-2-methoxyphenyl)indolin-2-one

400 MHz, $CDCl_3$

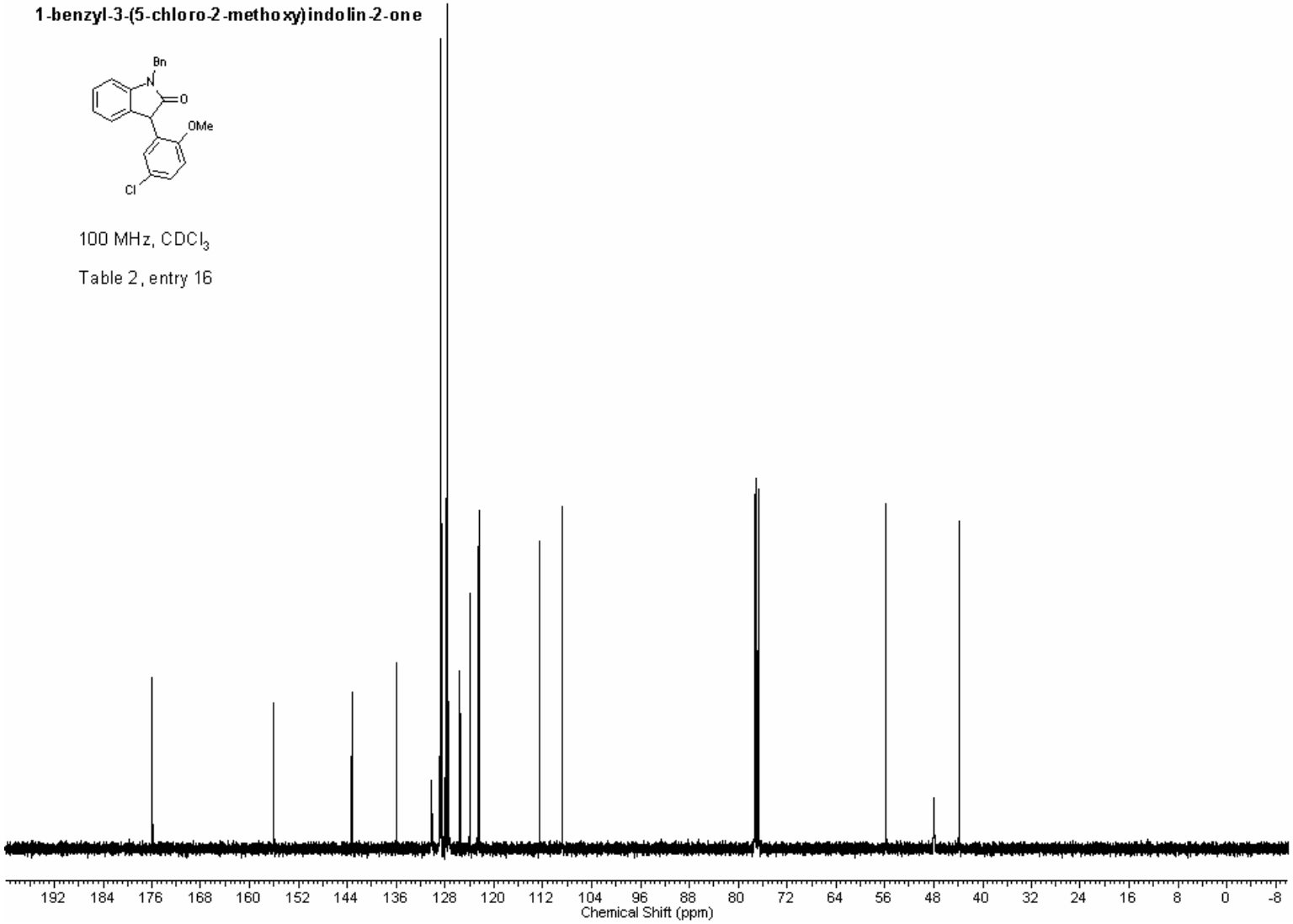
Table 2, entry 16



1-benzyl-3-(5-chloro-2-methoxy)indolin-2-one

100 MHz, $CDCl_3$

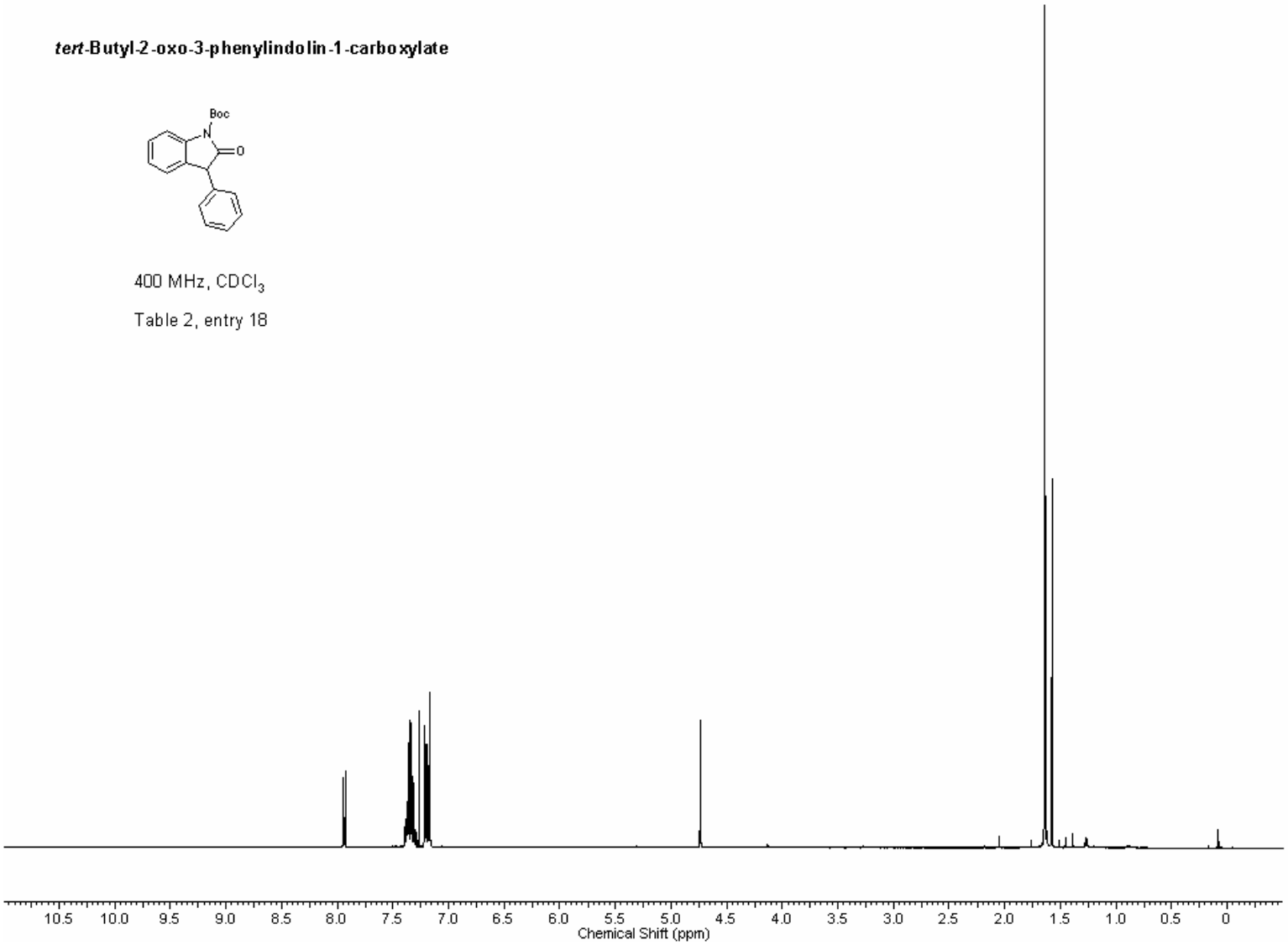
Table 2, entry 16



***tert*-Butyl-2-oxo-3-phenylindolin-1-carboxylate**

400 MHz, $CDCl_3$

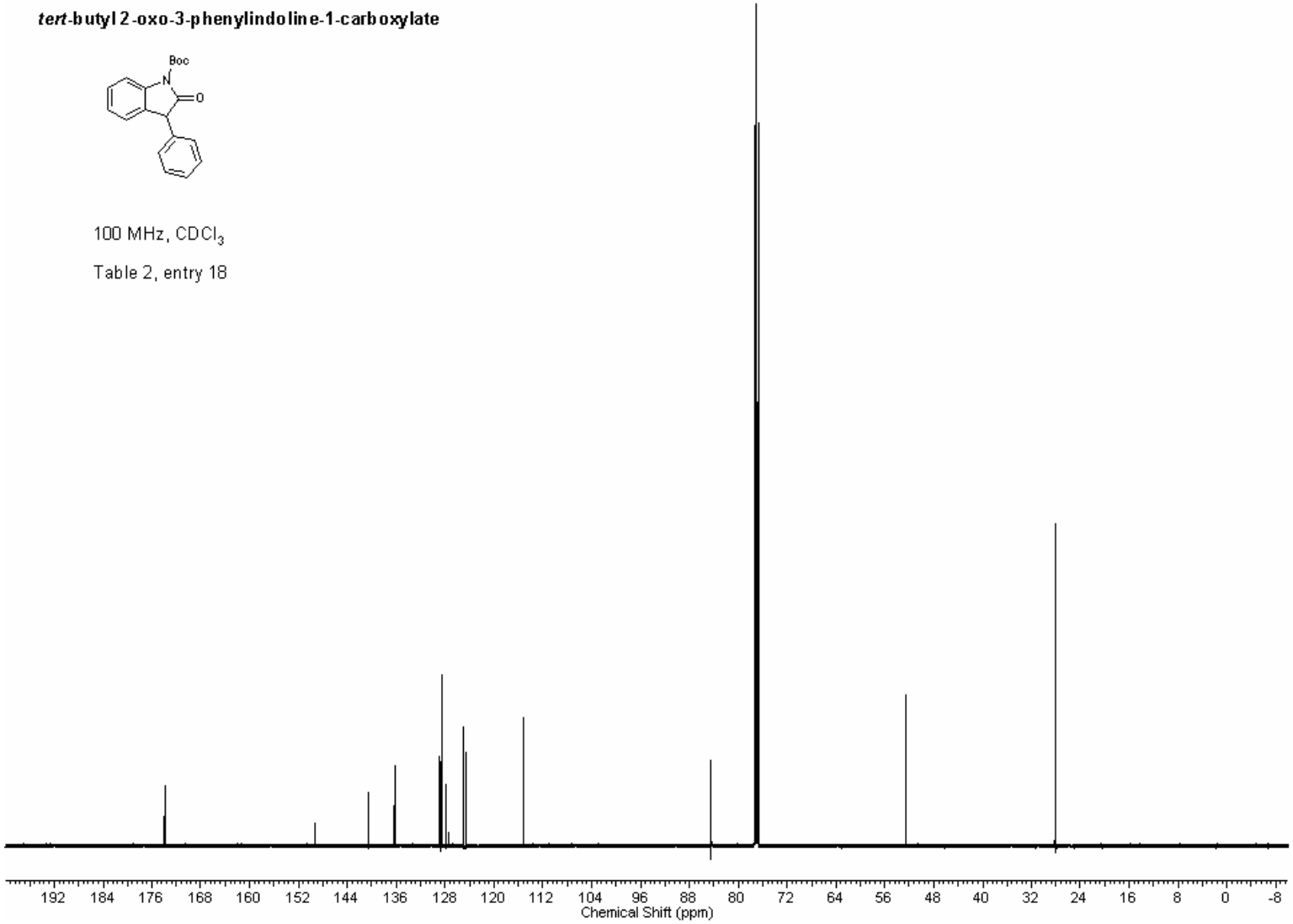
Table 2, entry 18



***tert*-butyl 2-oxo-3-phenylindoline-1-carboxylate**

100 MHz, $CDCl_3$

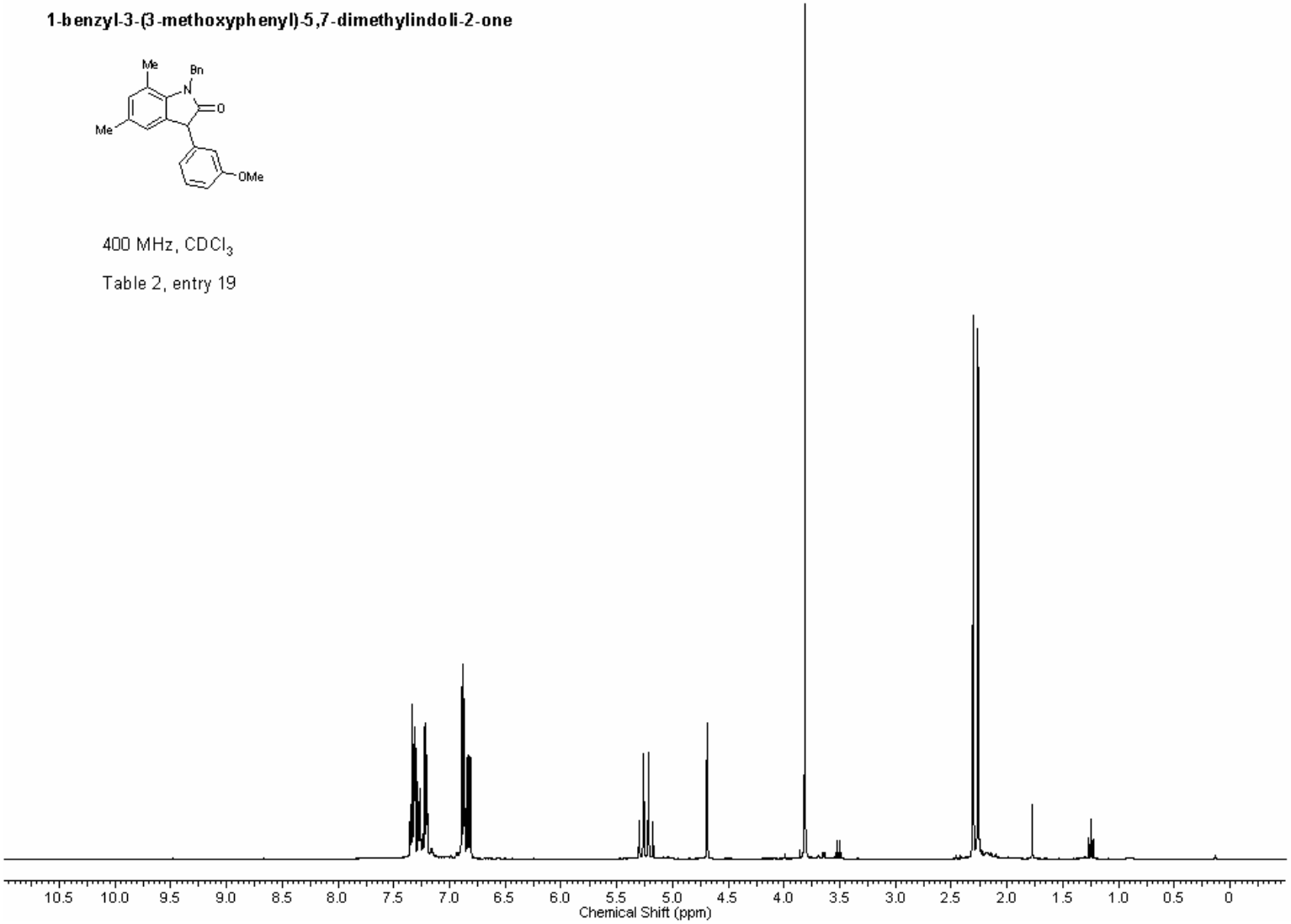
Table 2, entry 18



1-benzyl-3-(3-methoxyphenyl)-5,7-dimethylindoli-2-one

400 MHz, $CDCl_3$

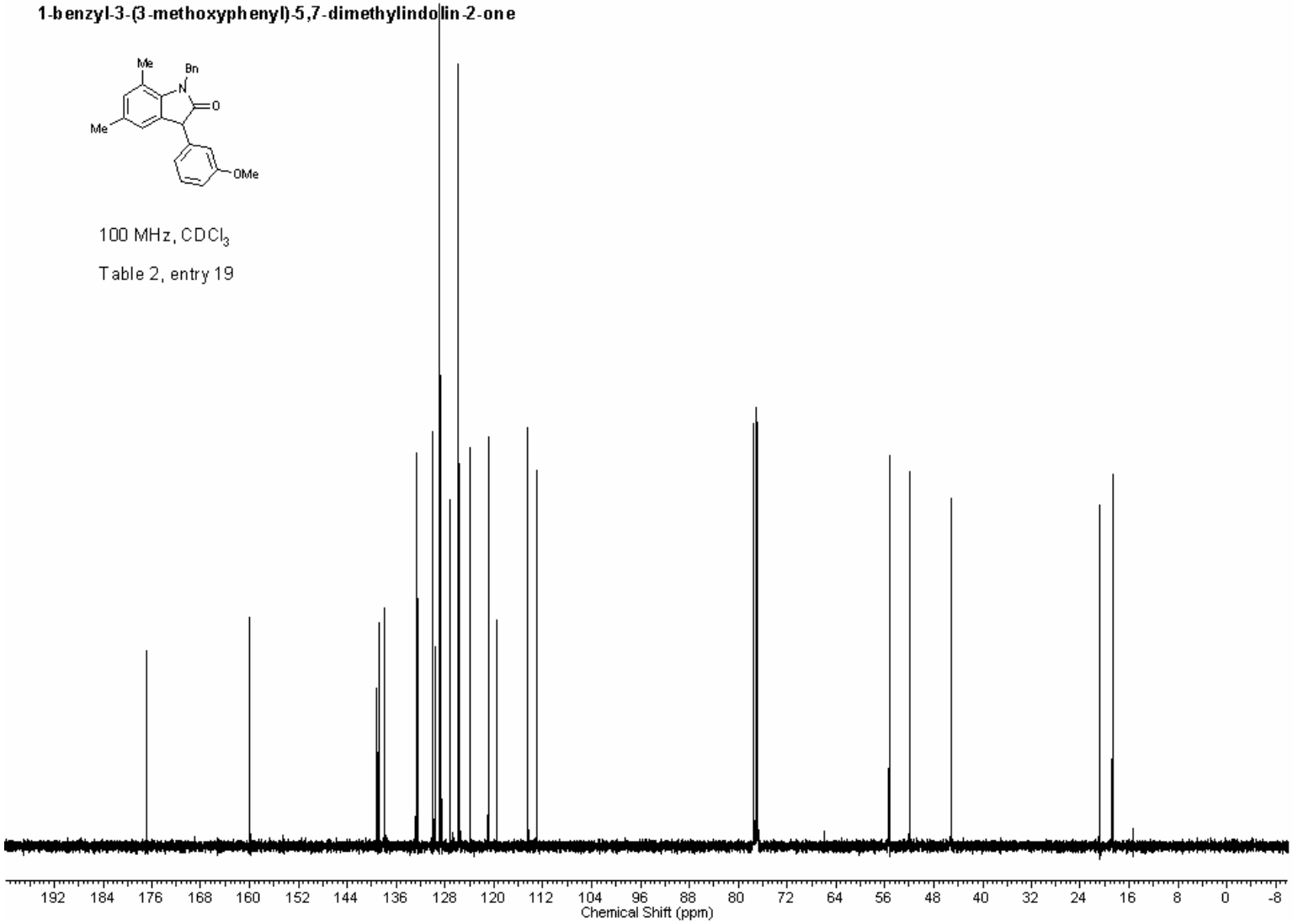
Table 2, entry 19



1-benzyl-3-(3-methoxyphenyl)-5,7-dimethylindolin-2-one

100 MHz, $CDCl_3$

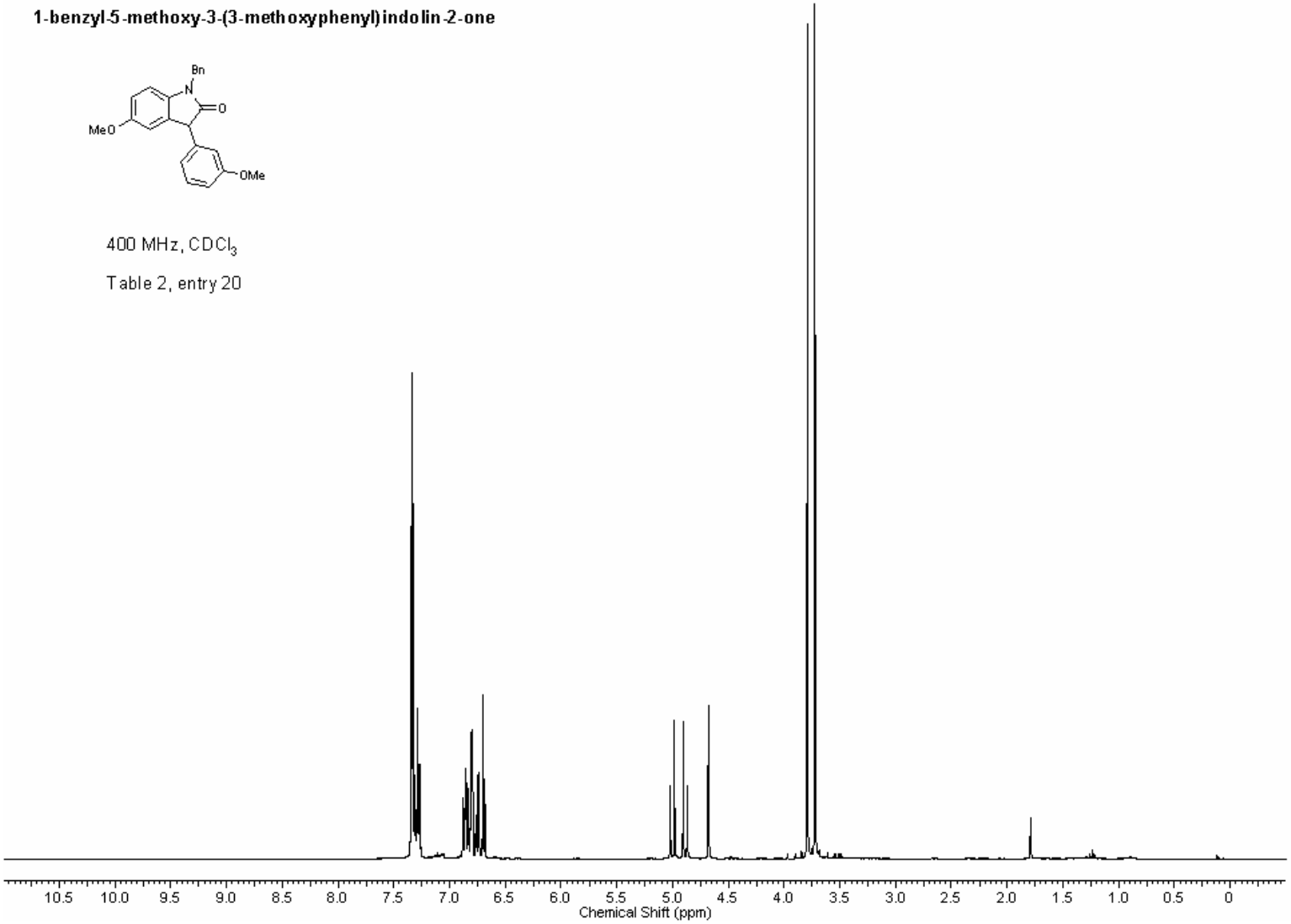
Table 2, entry 19

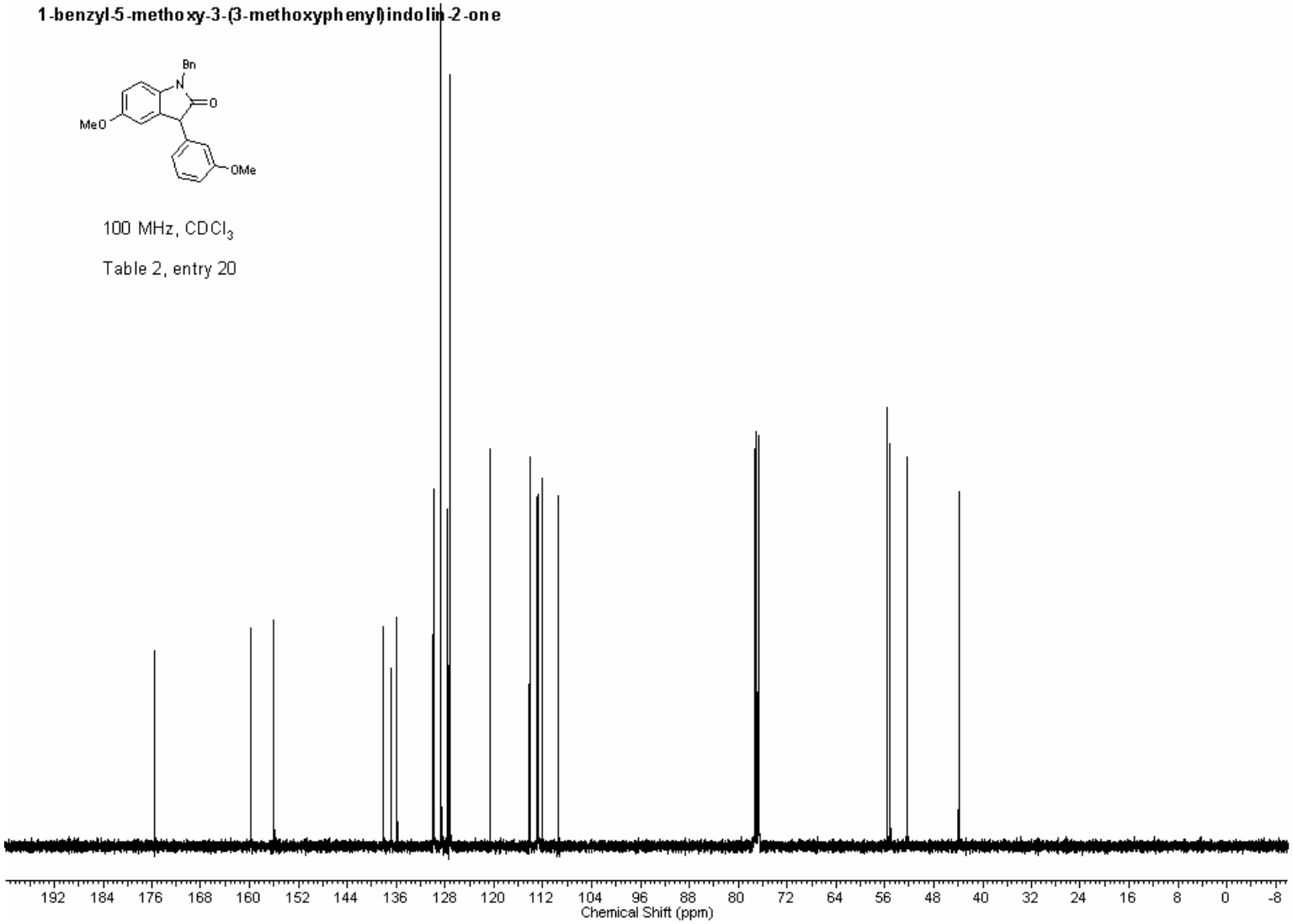


1-benzyl-5-methoxy-3-(3-methoxyphenyl)indolin-2-one

400 MHz, $CDCl_3$

Table 2, entry 20

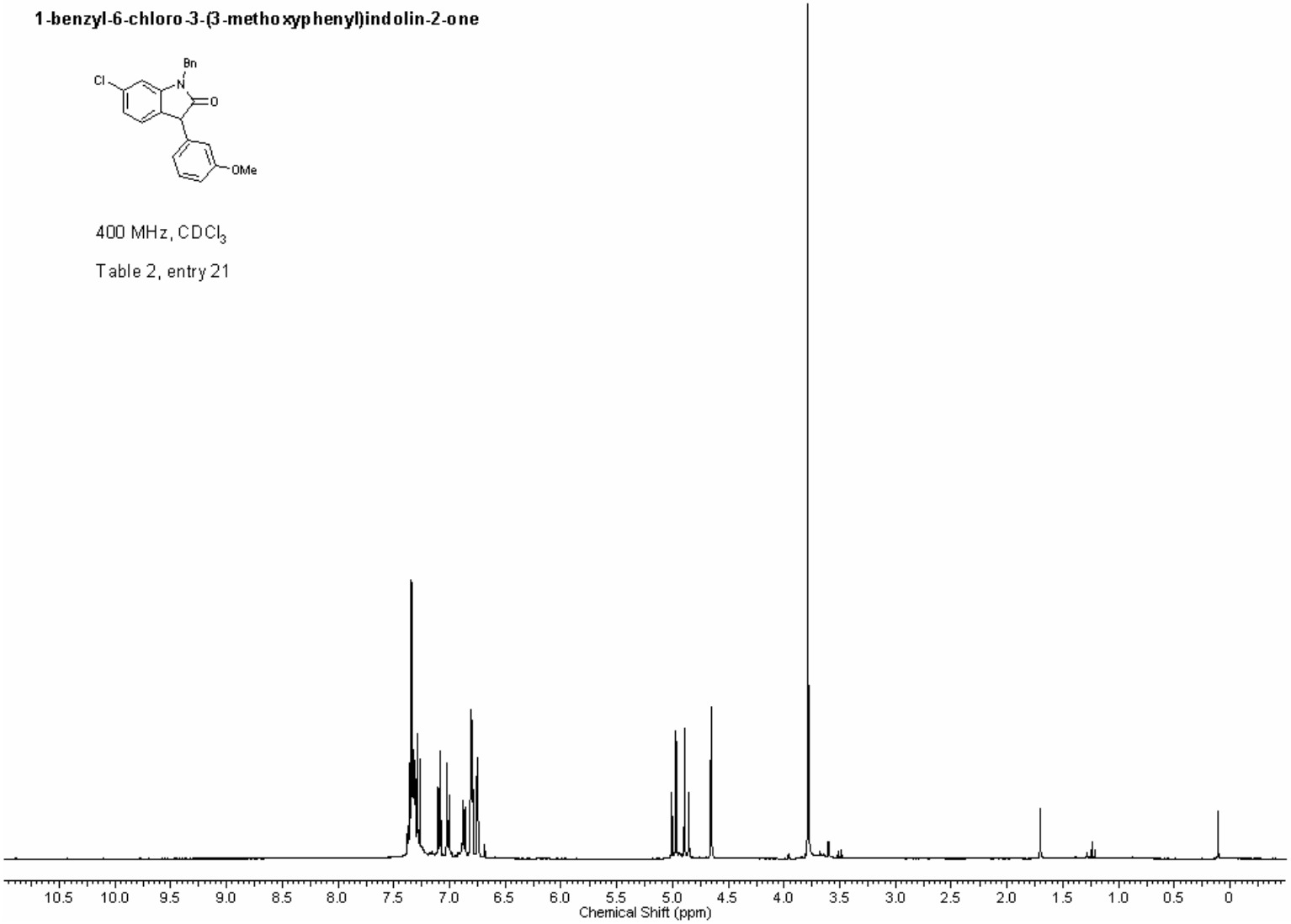


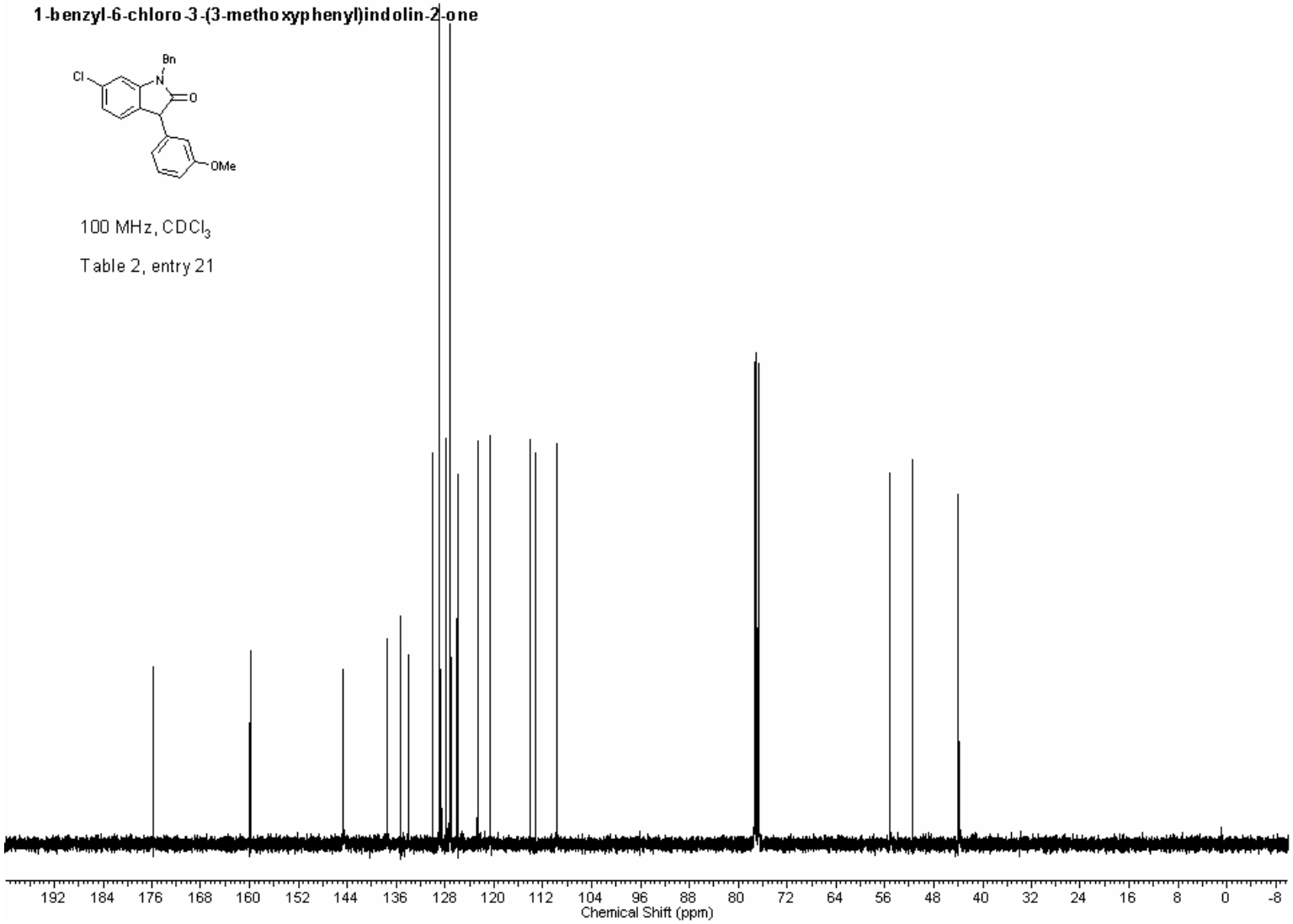

1-benzyl-5-methoxy-3-(3-methoxyphenyl)indolin-2-one
Bn
N
O
MeO
OMe
100 MHz, CDCl3
Table 2, entry 20
192 184 176 168 160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8 0 -8
Chemical Shift (ppm)

1-benzyl-6-chloro-3-(3-methoxyphenyl)indolin-2-one

400 MHz, $CDCl_3$

Table 2, entry 21

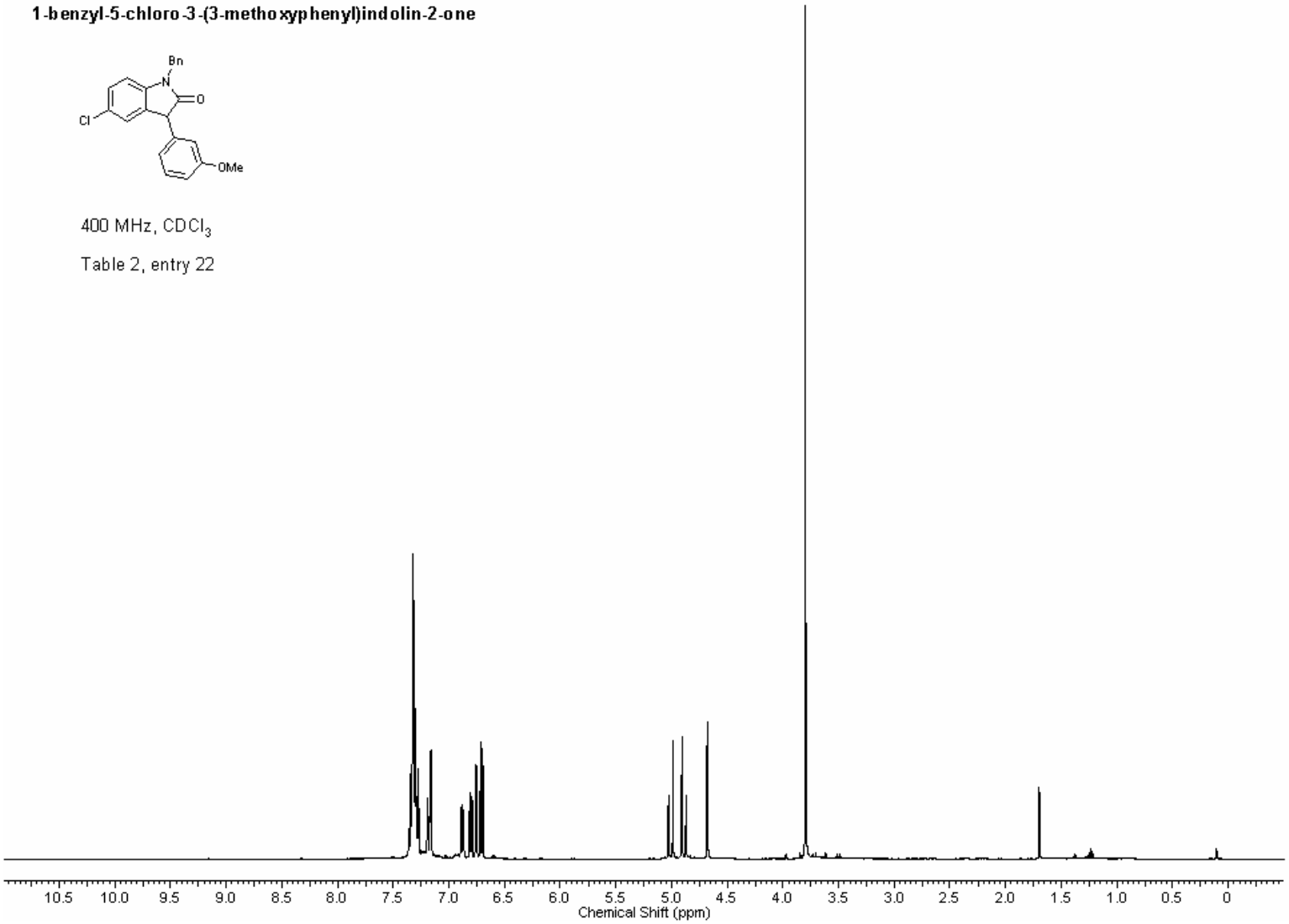



1-benzyl-6-chloro-3-(3-methoxyphenyl)indolin-2-one
Bn
N
Cl
O
OMe
100 MHz, CDCl3
Table 2, entry 21
192 184 176 168 160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8 0 -8
Chemical Shift (ppm)

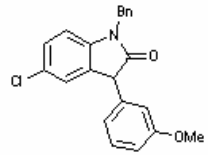
1-benzyl-5-chloro-3-(3-methoxyphenyl)indolin-2-one

400 MHz, $CDCl_3$

Table 2, entry 22

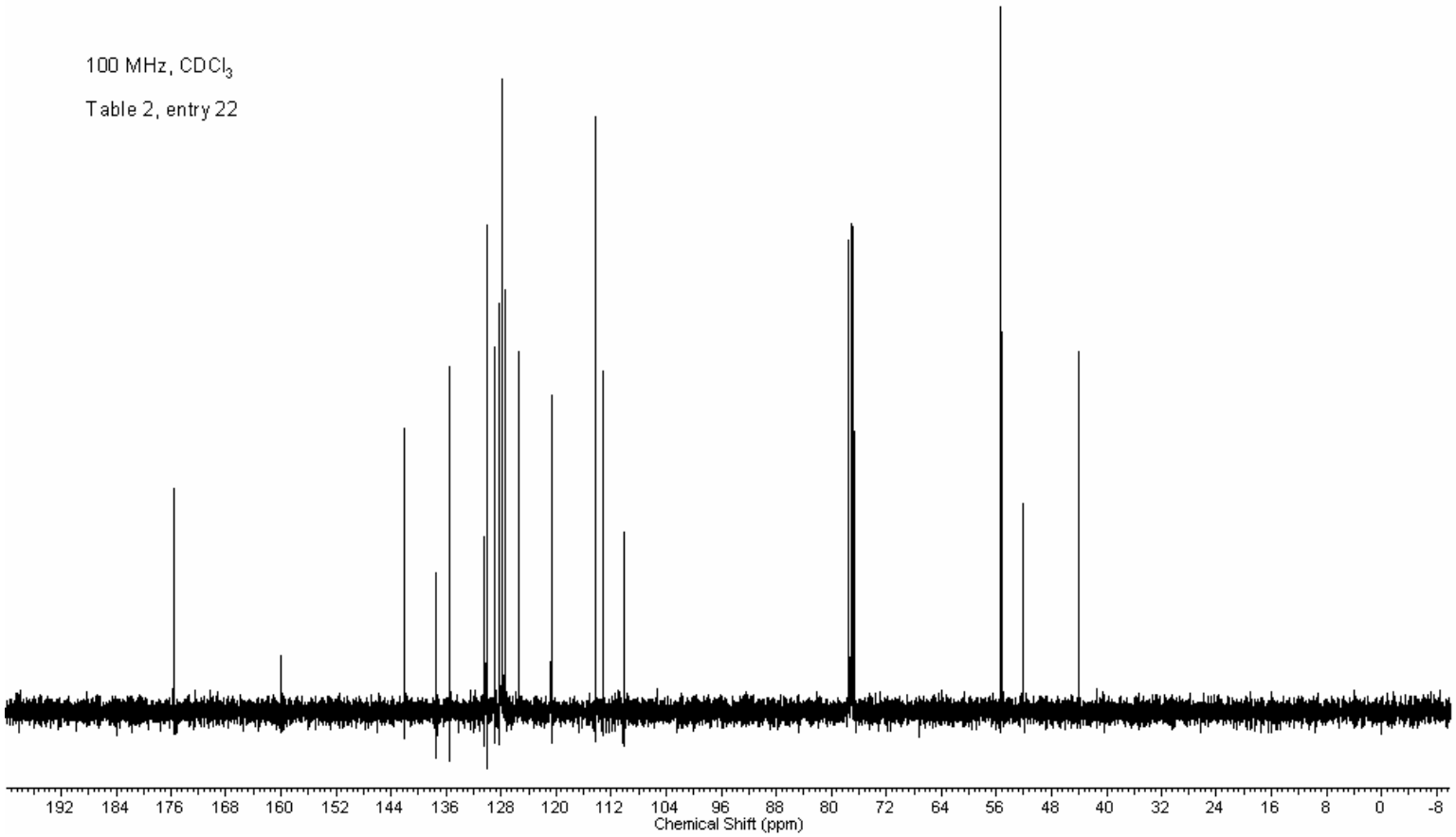


1-benzyl-5-chloro-3-(3-methoxyphenyl)indolin-2-one



100 MHz, $CDCl_3$

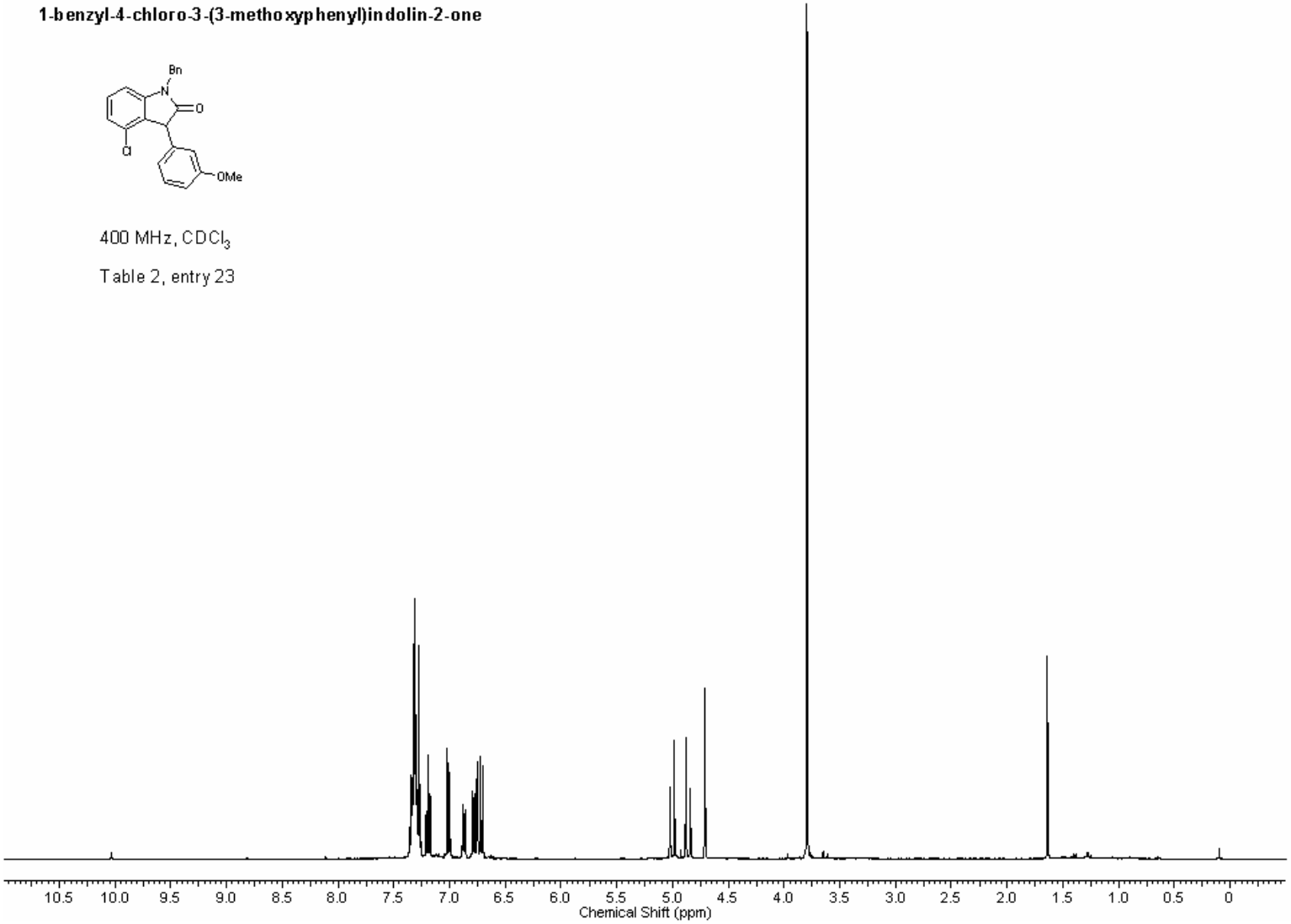
Table 2, entry 22



1-benzyl-4-chloro-3-(3-methoxyphenyl)indolin-2-one

400 MHz, $CDCl_3$

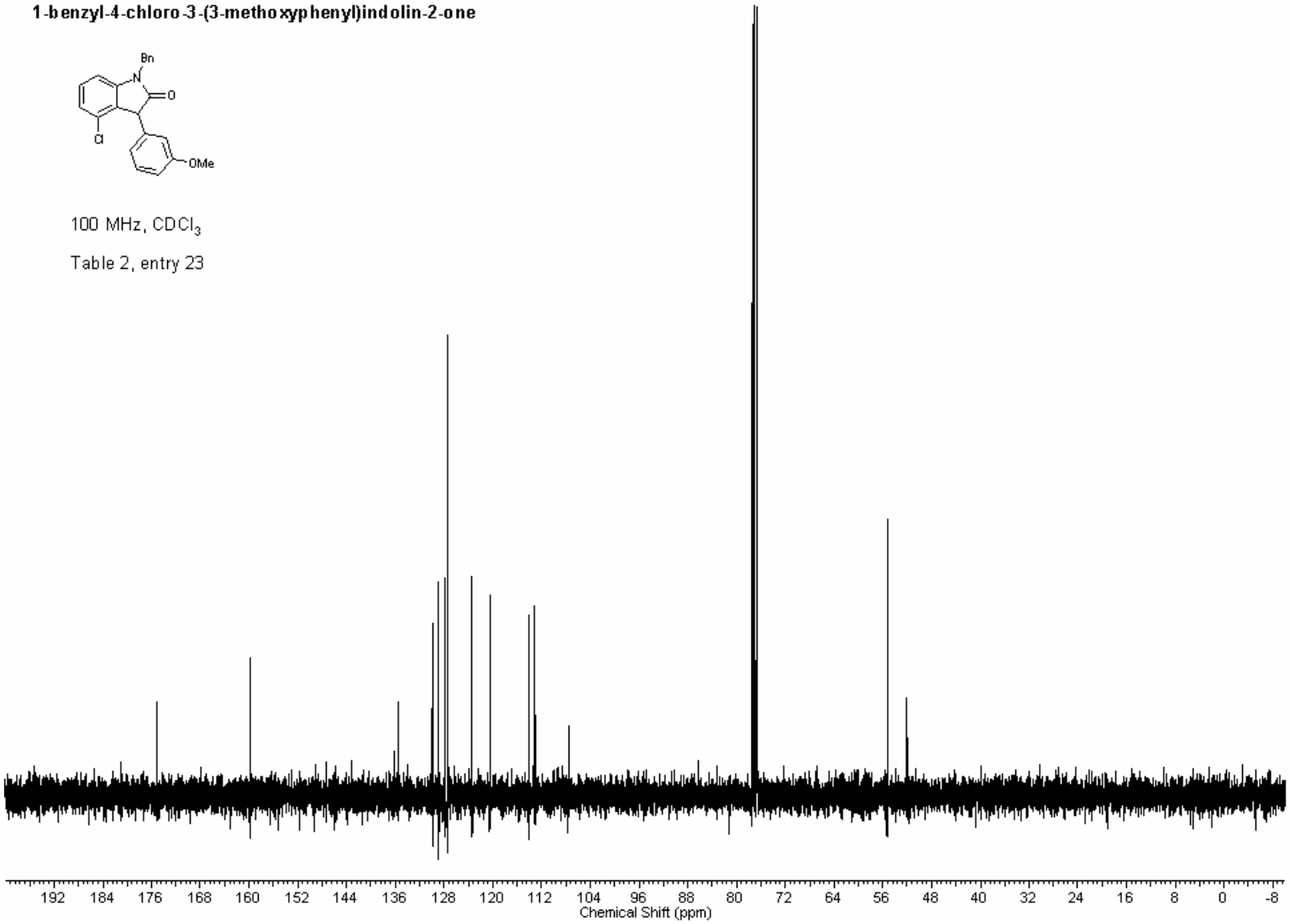
Table 2, entry 23



1-benzyl-4-chloro-3-(3-methoxyphenyl)indolin-2-one

100 MHz, $CDCl_3$

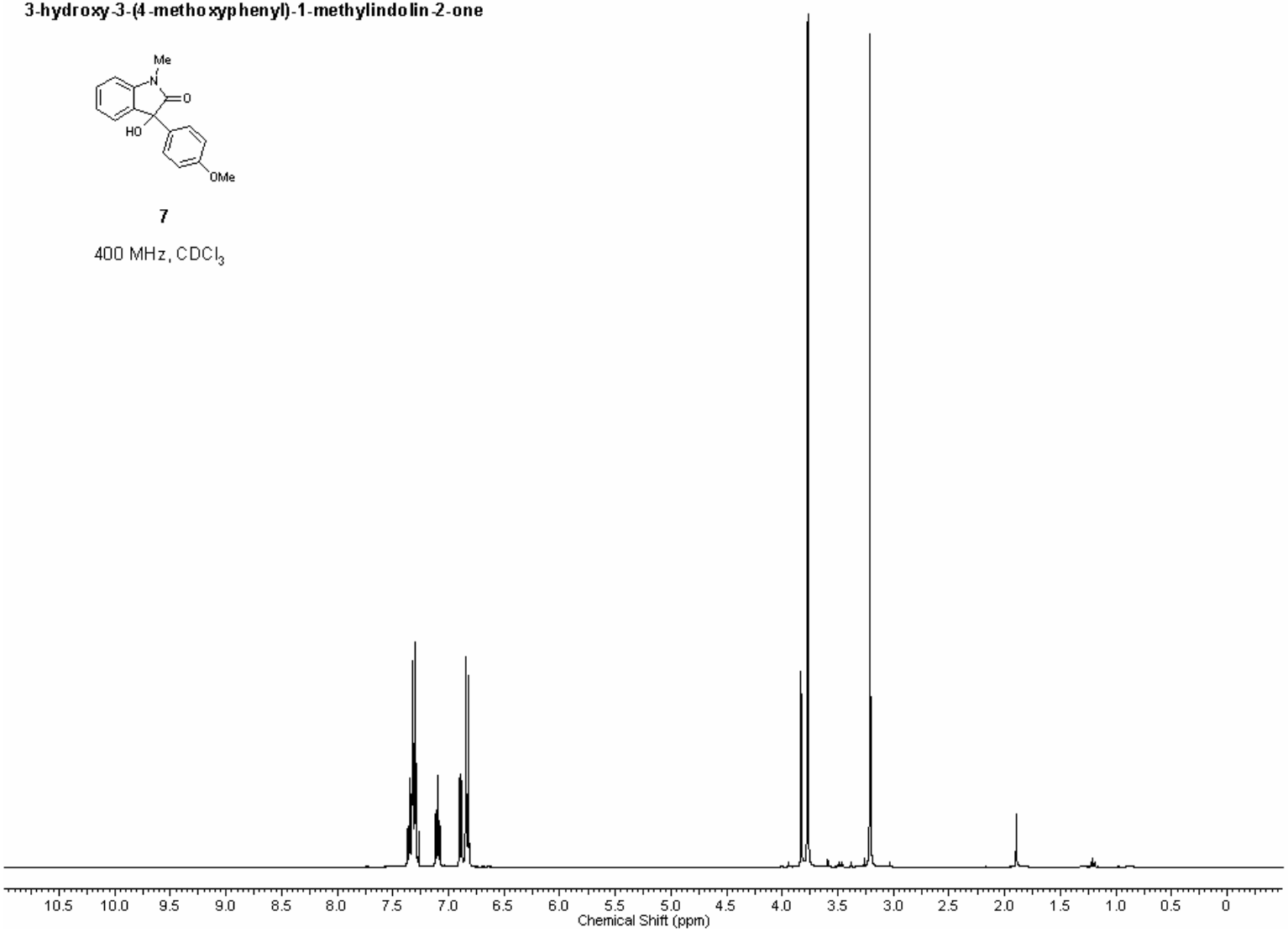
Table 2, entry 23

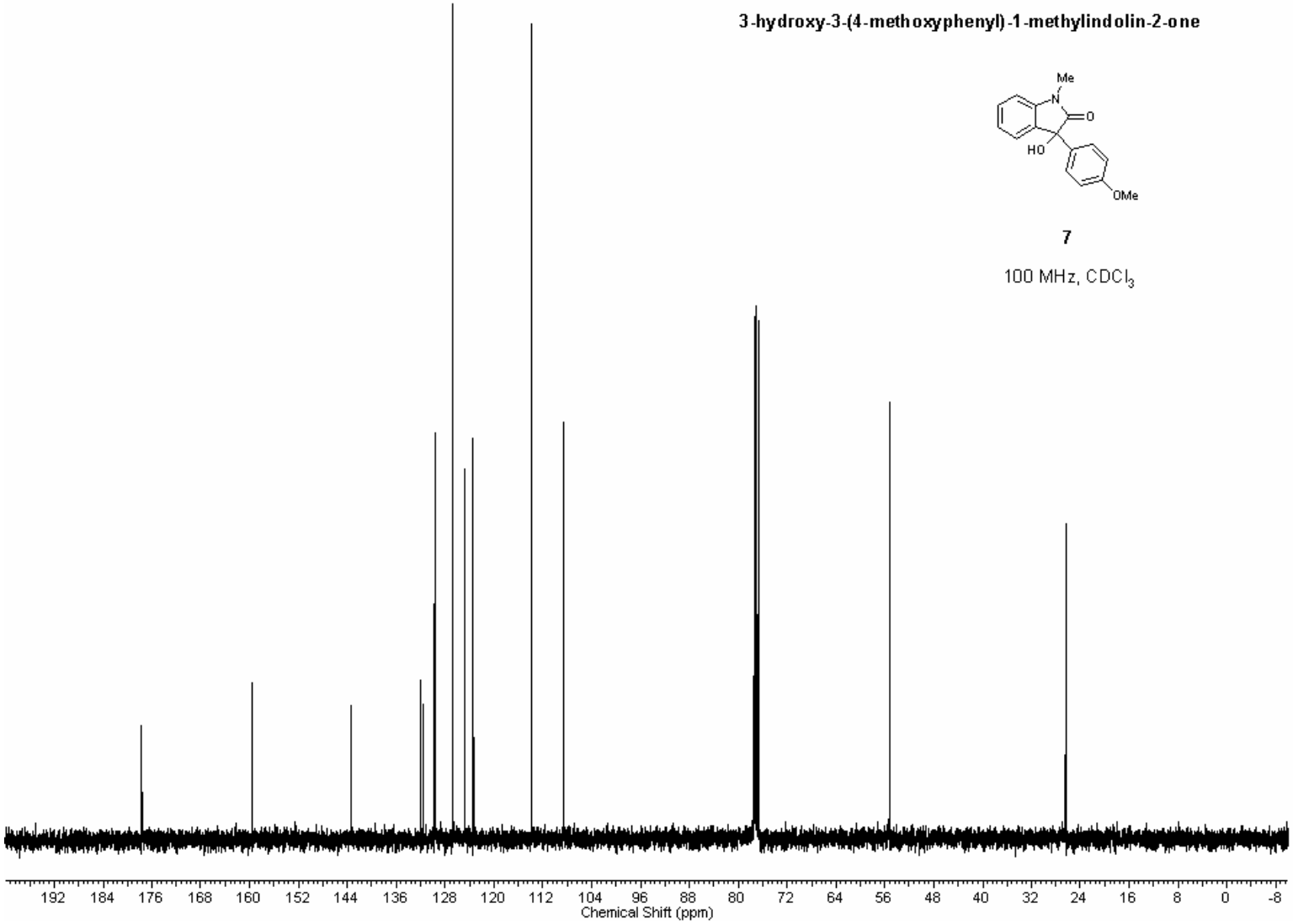


3-hydroxy-3-(4-methoxyphenyl)-1-methylindolin-2-one

7

400 MHz, $CDCl_3$




3-hydroxy-3-(4-methoxyphenyl)-1-methylindolin-2-one
Me
N
O
HO
OMe
7
100 MHz, CDCl3
192 184 176 168 160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8 0 -8
Chemical Shift (ppm)