

Direct Conversion of Indoles to 3,3-Difluoro-2-oxindoles *via* Electrophilic Fluorination

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SUPPORTING INFORMATION

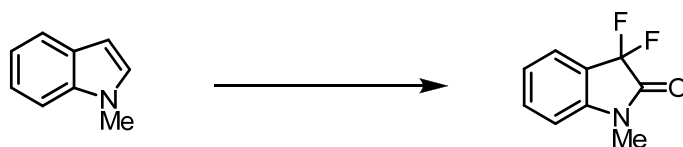
1. **Experimental procedures and spectroscopic data for compounds**
2. **References**
3. **Abbreviations**
4. **^1H , ^{13}C and ^{19}F NMR spectra of compounds**

Experimental Procedures and Spectroscopic Data for Compounds

General procedures. All reactions were carried out under an argon atmosphere with dry solvents under anhydrous conditions, unless otherwise noted. Dry tetrahydrofuran (THF), *N,N'*-dimethylformamide (DMF), and methylene chloride (CH₂Cl₂) were obtained by passing commercially available pre-dried, oxygen-free formulations through activated alumina columns. Yields refer to chromatographically and spectroscopically (¹H NMR) homogeneous materials, unless otherwise stated. Reagents were purchased at the highest commercial quality and used without further purification, unless otherwise stated. Reactions were monitored by thin-layer chromatography (TLC) carried out on 0.25 mm E. Merck silica gel plates (60F-254) using UV light as visualizing agent. E. Merck silica gel (60, particle size 0.040–0.063 mm) was used for flash column chromatography. Preparative thin-layer chromatography (PTLC) separations were carried out on 0.25 or 0.50 mm E. Merck silica gel plates (60F-254).

NMR spectra were recorded on Bruker DRX-400 or DRX-600 instruments and calibrated using residual undeuterated solvent (CDCl₃: δ_H = 7.26 ppm, δ_C = 77.16 ppm) as an internal reference. The following abbreviations were used to designate the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, quin = quintet, m = multiplet, br = broad. Infrared (IR) spectra were recorded on a Perkin–Elmer Spectrum One FT-IR spectrometer. High resolution mass spectra (HRMS) were recorded on an Agilent 6210 Series 1969A ESI-TOF (time of flight) mass spectrometer using EI (electron ionization) or ESI (electrospray ionization).

Detailed Screening & Optimization results



Entry ^a	F+	Oxidant	Additive	Solvent	T (°C)	Time (min)	Yield (%) ^b
1	3 eq Selectfluor	None	None	MeCN	70	60	0
2	3 eq Selectfluor	None	None	MeCN/H ₂ O (1:1)	70	60	trace
3	3 eq Selectfluor	None	None	MeCN/H ₂ O (1:1)	25	overnight	trace
4	3 eq F-py-BF ₄	None	None	MeCN	70	60	0
5	3 eq NFSI	None	None	CH ₂ Cl ₂	70	60	10
6	3 eq NFSI	None	None	THF	70	60	10
7	3 eq NFSI	None	None	CHCl ₃	70	60	17
8	3 eq NFSI	None	None	Acetone	70	60	17
9	3 eq NFSI	None	None	MeCN	70	60	3
10	3 eq NFSI	None	None	PhH	70	60	8

Entry ^a	F+	Oxidant	Additive	Solvent	T (°C)	Time (min)	Yield (%) ^b
11	3 eq NFSI	None	None	MeOH	70	60	3
12	3 eq NFSI	None	None	DMSO	70	60	4
13	3 eq NFSI	None	None	<i>t</i> BuOH	70	60	14
14	3 eq NFSI	None	None	PhH/MeCN (4:1)	70	60	16
15	3 eq NFSI	None	None	PhH/MeCN (1:1)	70	60	12
16	3 eq NFSI	None	None	PhH/MeCN (9:1)	70	60	11
17	3 eq NFSI	None	None	PhMe/MeCN (4:1)	70	60	18
18	3 eq NFSI	None	3 eq. Na ₂ CO ₃ + 3 eq. H ₂ O	PhMe/MeCN (4:1)	70	60	22
19	3 eq NFSI	None	3 eq. pyridine	PhMe/MeCN (4:1)	70	60	18
20	3 eq NFSI	None	3 eq. Na ₂ CO ₃	PhMe/MeCN (4:1)	70	60	21
21	3 eq NFSI	None	3 eq. <i>t</i> BuOH	PhMe/MeCN (4:1)	70	60	17
22	3 eq NFSI	3 eq. <i>t</i>-BuOOH	None	PhMe/MeCN (4:1)	70	60	32
23	3 eq NFSI	3 eq. <i>m</i> CPBA	None	PhMe/MeCN (4:1)	70	60	4
24	3 eq NFSI	3 eq PhI(OAc) ₂	None	PhMe/MeCN (4:1)	70	60	11
25	3 eq NFSI	3 eq. TEMPO	None	PhMe/MeCN (4:1)	70	60	2
26	3 eq NFSI	3 eq. oxone	None	PhMe/MeCN (4:1)	70	60	19
27	3 eq NFSI	5 eq. H ₂ O ₂	None	PhMe/MeCN (4:1)	70	60	33
28	3 eq NFSI	3 eq. <i>t</i>-BuOOH	None	PhMe/MeCN (4:1)	100	60	21
29	3 eq NFSI	3 eq. <i>t</i>-BuOOH	None	PhMe/MeCN (4:1)	70	120	36
30^c	3 eq NFSI	3 eq. <i>t</i>-BuOOH	None	PhMe/MeCN (4:1)	70	60	46
31 ^d	3 eq NFSI	3 eq. <i>t</i> -BuOOH	None	PhMe/MeCN (4:1)	70	60	29
32 ^e	3 eq NFSI	3 eq. <i>t</i> -BuOOH	None	PhMe/MeCN (4:1)	70	60	40
33 ^e	3 eq NFSI	3 eq. <i>t</i> -BuOOH	5 eq. NaHCO ₃	PhMe/MeCN (4:1)	70	60	47
34 ^e	3 eq NFSI	3 eq. <i>t</i> -BuOOH	5 eq. Na ₂ CO ₃	PhMe/MeCN (4:1)	70	60	40
35 ^e	3 eq NFSI	3 eq. <i>t</i> -BuOOH	5 eq. LiOH	PhMe/MeCN (4:1)	70	60	0
36 ^e	3 eq NFSI	3 eq. <i>t</i> -BuOOH	5 eq. NaOAc	PhMe/MeCN (4:1)	70	60	47
37 ^e	3 eq NFSI	3 eq. <i>t</i> -BuOOH	5 eq. K ₃ PO ₄	PhMe/MeCN (4:1)	70	60	41
38^e	3 eq NFSI	3 eq. <i>t</i>-BuOOH	5 eq. K₂HPO₄	PhMe/MeCN (4:1)	70	60	55
39 ^e	3 eq NFSI	3 eq. <i>t</i> -BuOOH	5 eq. KH ₂ PO ₄	PhMe/MeCN (4:1)	70	60	42
40 ^e	3 eq NFSI	3 eq. <i>t</i> -BuOOH	1 eq. K ₂ HPO ₄	PhMe/MeCN (4:1)	70	60	48
41^e	3 eq NFSI	3 eq. <i>t</i>-BuOOH	5 eq. K₂HPO₄	PhMe/MeCN (4:1)	25	960	13
42^e	3 eq NFSI	3 eq. <i>t</i>-BuOOH	5 eq. K₂HPO₄	PhMe/MeCN (4:1)	90	20	62
43 ^e	3 eq NFSI	3 eq. <i>t</i> -BuOOH	5 eq. K ₂ HPO ₄	CH ₂ Cl ₂	90	20	49

Entry ^a	F+	Oxidant	Additive	Solvent	T (°C)	Time (min)	Yield (%) ^b
44 ^c	3 eq NFSI	3 eq. <i>t</i> -BuOOH	5 eq. K ₂ HPO ₄	Acetone	90	20	30
45^f	3 eq NFSI	None	5 eq. K₂HPO₄	PhMe/MeCN (4:1)	90	20	23
46 ^c	3 eq NFSI	3 eq. <i>t</i> -BuOOH	5 eq. K ₂ HPO ₄	PhMe/CH ₂ Cl ₂ (1:1)	90	20	45
47 ^c	3 eq NFSI	3 eq. <i>t</i> -BuOOH	5 eq. K ₂ HPO ₄	CHCl ₃	90	20	55
48 ^c	3 eq NFSI	3 eq. <i>t</i> -BuOOH	5 eq. K ₂ HPO ₄	PhMe/MeCN (4:1)	120	20	57
49^c	3 eq NFSI	1.5 eq. <i>t</i>-BuOOH	5 eq. K₂HPO₄	PhMe/MeCN (4:1)	90	20	63
50 ^{c,g}	3 eq NFSI	3 eq. <i>t</i> -BuOOH	5 eq. K ₂ HPO ₄	PhMe/MeCN (4:1)	90	20	38
51 ^{c,h}	3 eq NFSI	3 eq. <i>t</i> -BuOOH	5 eq. K ₂ HPO ₄	PhMe/MeCN (4:1)	90	20	38
52 ^c	4 eq NFSI	3 eq. <i>t</i> -BuOOH	5 eq. K ₂ HPO ₄	PhMe/MeCN (4:1)	90	20	55
53 ^c	2 eq NFSI	3 eq. <i>t</i> -BuOOH	5 eq. K ₂ HPO ₄	PhMe/MeCN (4:1)	90	20	55
54 ^c	3 eq NFSI	1 eq. <i>t</i> -BuOOH	5 eq. K ₂ HPO ₄	PhMe/MeCN (4:1)	90	20	59
55 ^c	3 eq NFSI	5 eq. <i>t</i> -BuOOH	5 eq. K ₂ HPO ₄	PhMe/MeCN (4:1)	90	20	53
56 ⁱ	3 eq NFSI	1.5 eq. <i>t</i> -BuOOH	5 eq. K ₂ HPO ₄	PhMe/MeCN (4:1)	90	20	24
57 ^j	3 eq NFSI	1.5 eq. <i>t</i> -BuOOH	5 eq. K ₂ HPO ₄	PhMe/MeCN (4:1)	90	20	50
58^c	3 eq NFSI	3 eq. <i>t</i>-BuOOH	3 eq. K₂HPO₄	PhMe/MeCN (4:1)	90	20	51
59^c	3 eq Selectfluor	1.5 eq. <i>t</i>-BuOOH	5 eq. K₂HPO₄	PhMe/MeCN (4:1)	90	20	0

^a All reactions were carried at 0.05 M concentration (based on indole), monitored by TLC and proceeded with full conversion unless otherwise stated.

^b Yield determined by ¹⁹F NMR using 2-fluoro-1-nitrobenzene as an internal standard.

^c After the reaction, Et₃N (18 equiv) was added and the reaction mixture was further heated at 100 °C for 1 h before analysis.

^d After the reaction, Et₃N (18 equiv) was added and the reaction mixture was immediately analyzed.

^e After the reaction, Et₃N (18 equiv) was added and the reaction mixture was stirred at 25 °C for 16 h before analysis.

^f After the reaction, Et₃N (18 equiv) and 1.5eq TBHP was added, and the reaction mixture was stirred at 100 °C for 1 h before analysis.

^g Reaction was carried out at 0.1 M concentration (based on indole).

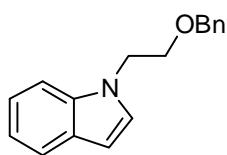
^h Reaction was carried out at 0.025 M concentration (based on indole).

ⁱ After the reaction, Et₃N (1 equiv) was added and the reaction mixture was further heated at 100 °C for 1 h before analysis.

^j After the reaction, Et₃N (5 equiv) was added and the reaction mixture was further heated at 100 °C for 1 h before analysis.

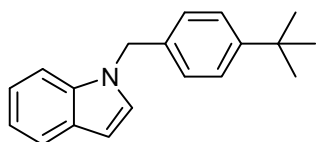
Indole **1a** was purchased from commercial sources and used as it is. For known indoles **1c-f**, **1j-k**, **3a-c**, **3f-g**, **3i-k**, they were synthesized according to reported literature procedures.^[1]

Preparation of 1-(2-(benzyloxy)ethyl)-1*H*-indole (1b). To a solution of 2-(1*H*-indol-1-yl)ethanol^[2] (487.7 mg, 3.03 mmol) in DMF (10 mL) was added portionwise NaH at 0 °C under argon flow. The reaction mixture was stirred at ambient temperature for 3 h then quenched with iced water. The crude was extracted with Et₂O (3 times). The combined organic layers were washed with H₂O



and then dried over MgSO_4 . After evaporation to dryness, purification by silica gel chromatography column (petroleum ether/EtOAc 95:5 to 90:10, v/v) gave the desired product (608 mg, 80%) as a white amorphous solid. **1b**: FT-IR (neat) ν_{max} 3028, 2969, 2933, 1463, 1366, 1229, 1111, 737, 698 cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ = 7.64 (dd, J = 7.9, 0.7 Hz, 1 H), 7.35 (d, J = 8.2 Hz, 1 H), 7.33–7.25 (m, 4H), 7.25–7.16 (m, 4 H), 7.15–7.06 (m, 1 H), 6.51 (d, J = 3.0 Hz, 1 H), 4.45 (s, 2 H), 4.33 (t, J = 5.7 Hz, 2 H), 3.80 (t, J = 5.7 Hz, 2 H) ppm; ^{13}C NMR (CDCl_3 , 100 MHz) δ = 138.0, 136.3, 128.8, 128.6 (2C), 128.5, 127.8, 127.7 (2C), 121.6, 121.1, 119.5, 109.4, 101.4, 73.5, 69.2, 46.5 ppm. HRMS (ESI-TOF) calcd for $\text{C}_{17}\text{H}_{17}\text{NONa}$ [$\text{M} + \text{Na}$] $^+$ 274.1202, found 274.1212.

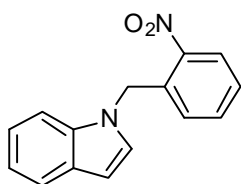
Preparation of 1-(4-(*tert*-butyl)benzyl)indole (1g). To indole (200 mg, 1.71 mmol, 1 equiv) was added NaH (82 mg, 2.05 mmol, 1.2 equiv) portionwise in DMF (30 mL) at 0 °C and slowly



warmed to room temperature and stirred for 30 minutes. 4-(*tert*-butyl)benzyl bromide (465 mg, 2.05 mmol, 1.2 equiv) in DMF (20 mL) was then added dropwise to the reaction mixture at 0 °C and slowly warmed to room temperature and stirred overnight. Water was then added and the reaction mixture was extracted with EtOAc. The

combined organic layers were then dried with Na_2SO_4 and concentrated in *vacuo* to give the crude product. Purification by silica gel column chromatography using 5-10% EtOAc:hexanes gave 1-(4-(*tert*-butyl)benzyl)indole (**1g**) as an amorphous solid (350 mg, 78%). **1g**: FT-IR (neat) ν_{max} 2961, 2865, 1509, 1484, 1461, 1443, 1395, 1361, 1336, 1308, 1269, 1253, 1177, 1109, 1009, 836, 756, 714, 675, 612, 556 cm^{-1} ; ^1H NMR (CDCl_3 , 600 MHz) δ = 7.65 (d, J = 7.8 Hz, 1 H), 7.30–7.33 (m, 3 H), 7.18 (td, J = 6.6, 1.2 Hz, 1 H), 7.13 (d, J = 3.0 Hz, 1 H), 7.11 (td, J = 7.8, 1.2 Hz, 1 H), 7.06 (d, J = 8.4 Hz, 1 H), 6.55 (dd, J = 3.6, 1.2 Hz, 1 H), 5.30 (s, 2 H), 1.29 (s, 9 H) ppm; ^{13}C NMR (CDCl_3 , 150 MHz) δ = 150.71, 136.46, 134.67, 128.82, 128.37, 126.69, 125.79, 125.76, 121.73, 121.08, 119.58, 109.84, 101.69, 49.87, 34.64, 31.45 ppm; HRMS (ESI-TOF) calcd for $\text{C}_{19}\text{H}_{21}\text{NH}^+$ [$\text{M} + \text{H}$] $^+$, 264.1752 found 264.1758.

Preparation of 1-(2-nitrobenzyl)indole (1h). To indole (300 mg, 2.56 mmol, 1 equiv) was added NaH (113 mg, 2.82 mmol, 1.1 equiv) portionwise in DMF (15 mL) at 0 °C and slowly

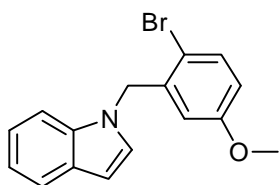


warmed to room temperature and stirred for 30 minutes. 2-nitrobenzyl bromide (553 mg, 2.56 mmol, 1 equiv) in DMF (10 mL) was then added dropwise to the reaction mixture at 0 °C and slowly warmed to room temperature and stirred overnight. Water was then added and the reaction mixture was extracted with EtOAc. The combined organic layers were

then dried with Na_2SO_4 and concentrated in *vacuo* to give the crude product. Purification by silica gel column chromatography using 10-15% EtOAc:hexanes gave **1h** as an amorphous solid (228 mg, 35%). **1h**: FT-IR (neat) ν_{max} 3057, 2924, 2853, 1609, 1578, 1523, 1482, 1461, 1446, 1421, 1398, 1335, 1317, 1305, 1261, 1195, 1163, 1048, 1012, 858, 788, 763, 741, 724, 677 cm^{-1} ; ^1H NMR (CDCl_3 , 600 MHz) δ = 8.18 (dd, J = 7.2, 1.8 Hz, 1 H), 7.72 (dd, J = 8.4, 1.2 Hz, 1 H),

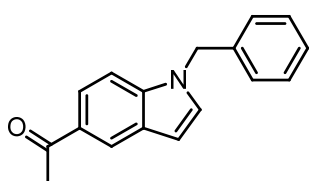
7.40-7.42 (m, 2 H), 7.15-7.20 (m, 4 H), 6.66 (d, $J = 3.3$ Hz, 1 H), 6.50 (dd, $J = 7.2, 1.2$ Hz, 1 H), 5.78 (s, 2 H) ppm; ^{13}C NMR (CDCl_3 , 150 MHz) $\delta = 147.20, 136.37, 134.35, 134.32, 128.86, 128.60, 128.45, 128.26, 125.32, 122.32, 121.32, 120.13, 109.57, 102.80, 47.69$ ppm; HRMS (ESI-TOF) calcd for $\text{C}_{15}\text{H}_{12}\text{N}_2\text{O}_2\text{Na}^+$ $[\text{M} + \text{Na}]^+$ 275.0791 found 275.0804.

Preparation of 1-(2-bromo-5-methoxybenzyl)indole (1i). To indole (200mg, 1.71 mmol, 1 equiv) was added NaH (82mg, 2.05 mmol, 1.2 equiv) portionwise in DMF (30 mL) at 0 °C and



slowly warmed to room temperature and stirred for 30 minutes. 2-bromo-5-methoxybenzyl bromide (574mg, 2.05 mmol, 1.2 equiv) in DMF (20 mL) was then added dropwise to the reaction mixture at 0 °C and slowly warmed to room temperature and stirred overnight. Water was then added and the reaction mixture was extracted with EtOAc. The combined organic layers were then dried with Na_2SO_4 and concentrated in *vacuo* to give the crude product. Purification by silica gel column chromatography using 5-10% EtOAc:hexanes gave **1i** as a solid/oil (490mg, 91%). **1i**: FT-IR (neat) ν_{max} 2961, 2834, 1595, 1571, 1511, 1461, 1429, 1416, 1397, 1349, 1318, 1291, 1271, 1259, 1227, 1194, 1154, 1135, 1120, 1090, 1055, 1016, 863, 801, 736, 719, 633, 600, 502 cm^{-1} ; ^1H NMR (CDCl_3 , 600 MHz) $\delta = 7.44$ (s, 1 H), 7.34 (t, $J = 7.2$ Hz, 1 H), 7.30 (t, $J = 7.2$ Hz, 1 H), 7.28 (s, 1 H), 7.11 (d, $J = 3.6$ Hz, 1 H), 7.06 (d, $J = 7.2$ Hz, 1 H), 6.55 (d, $J = 3.6$ Hz, 1 H), 5.83 (s, 2 H), 2.47 (s, 3 H) ppm; ^{13}C NMR (CDCl_3 , 150 MHz) $\delta = 159.41, 137.86, 136.36, 133.39, 128.74, 128.33, 121.99, 121.13, 119.80, 114.38, 114.23, 112.49, 109.69, 102.23, 55.26, 50.20$ ppm; HRMS (ESI-TOF) calcd for $\text{C}_{16}\text{H}_{14}\text{BrNOH}^+$ $[\text{M} + \text{H}]^+$, 316.0332 found 316.0325.

Preparation of 1-(1-benzyl-1H-indol-5-yl)ethanone (3d). To a solution of 1-(1H-indol-5-yl)ethanone (170 mg, 1.07 mmol) that was easily prepared from indole-5-carboxylic acid according to a reported procedure,^[3] in DMF (2 mL) were added

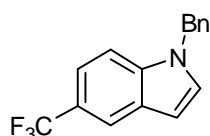


tetrabutylammonium iodide (20 mg, 0.05 mmol) and KOH (240 mg, 4.28 mmol). The mixture was stirred at room temperature, followed by addition of benzylbromide (0.19 mL, 1.60 mmol). The reaction mixture was stirred for another 3 h at room temperature and monitored by TLC. H_2O was then added and the resulted mixture was extracted with Et_2O (3×10 mL). The combined organic layers were washed with H_2O then dried over MgSO_4 and concentrated in *vacuo* to give the crude product. Purification by silica gel column chromatography using 10% EtOAc:petroleum ether gave the titled product as a white amorphous solid (207 mg, 78%). **3d**: FT-IR (neat) ν_{max} 3100, 3030, 2961, 2918, 1670, 1607, 1453, 1356, 1259, 1180, 810 cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) $\delta = 8.33$ (d, $J = 1.6$ Hz, 1 H), 7.85 (dd, $J = 8.7, 1.6$ Hz, 1 H), 7.35–7.23 (m, 4 H), 7.19 (d, $J = 3.1$ Hz, 1 H), 7.11 (m, 2 H), 6.67 (d, $J = 3.1$ Hz, 1 H), 5.35 (s, 2 H), 2.65 (s, 3 H) ppm; ^{13}C NMR (CDCl_3 , 100 MHz) $\delta = 198.3, 139.0, 137.0, 130.0$ (2C), 129.1 (2C), 128.4, 128.0, 126.9 (2C), 123.4, 122.3, 109.7, 103.8, 50.5, 26.8 ppm;

HRMS (ESI-TOF) calcd for $[M + H]^+$ 250.1226, found 250.1219; calcd for $[M + Na]^+$ 272.1046, found 272.1039.

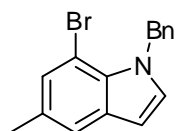
General procedure A for the preparation of *N*-benzylindoles (3e and 3l). To indole (1 equiv) was added NaH (1.2 equiv) portionwise in DMF at 0 °C and slowly warmed to room temperature and stirred for 30 minutes. Benzyl bromide (1.2 equiv) was then added dropwise to the reaction mixture at 0 °C and slowly warmed to room temperature and stirred overnight. Water was then added and the reaction mixture was extracted with EtOAc. The combined organic layers were then dried with Na₂SO₄ and concentrated in *vacuo* to give the crude product. Purification by silica gel column chromatography using 5-10% EtOAc:hexanes gave *N*-benzylindole as a solid/oil.

1-benzyl-5-(trifluoromethyl)-1*H*-indole (3e). Following general procedure A, 5-(trifluoromethyl)-1*H*-indole (200 mg, 1.09 mmol, 1 equiv) gave indole **3e** as an amorphous solid



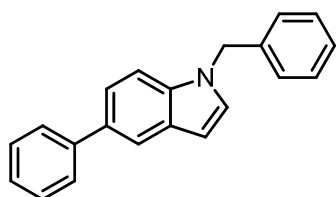
(212 mg, 71%). **3e**: FT-IR (neat) ν_{\max} 2923, 1619, 1510, 1496, 1450, 1399, 1365, 1347, 1327, 1286, 1276, 1260, 1202, 1184, 1164, 1141, 1094, 1076, 1052, 1029, 916, 891, 805, 733, 719, 696, 586, 505 cm^{-1} ; ¹H NMR (CDCl₃, 600 MHz) δ = 7.95 (s, 1 H), 7.40 (d, J = 9.0 Hz, 1 H), 7.28–7.35 (m, 4 H), 7.24 (d, J = 3.0 Hz, 1 H), 7.10 (d, J = 7.2 Hz, 2 H), 6.65 (d, J = 3.0 Hz, 1 H), 5.36 (s, 2 H) ppm; ¹³C NMR (CDCl₃, 150 MHz) δ = 137.66, 136.96, 130.17, 129.01, 128.31, 128.17, 126.84, 125.61 (q, J = 270 Hz), 122.06 (q, J = 31.5 Hz), 118.86 (q, J = 4.0 Hz), 118.57 (q, J = 4.0 Hz), 110.09, 102.87, 50.37 ppm; ¹⁹F NMR (CDCl₃, 376 MHz) δ = -60.00 ppm; HRMS (ESI-TOF) calcd for C₁₆H₁₂F₃NH⁺ $[M + H]^+$, 276.0995 found 276.1005.

1-benzyl-7-bromo-5-methyl-1*H*-indole (3l). Following general procedure A, 5-methyl-7-bromoindole (200 mg, 0.95 mmol, 1 equiv) gave indole **3l** as an amorphous solid (155 mg, 54%).



3l: FT-IR (neat) ν_{\max} 3027, 2917, 2849, 1604, 1551, 1495, 1486, 1450, 1409, 1389, 1357, 1319, 1301, 1192, 1173, 1040, 1030, 849, 805, 760, 731, 719, 692, 600, 503 cm^{-1} ; ¹H NMR (CDCl₃, 600 MHz) δ = 7.44 (s, 1 H), 7.34 (t, J = 7.2 Hz, 1 H), 7.30 (t, J = 7.2 Hz, 1H), 7.28 (s, 1 H), 7.11 (d, J = 3.6 Hz, 1 H), 7.06 (d, J = 7.2 Hz, 1 H), 6.55 (d, J = 3.6 Hz, 1 H), 5.83 (s, 2 H), 2.47 (s, 3 H) ppm; ¹³C NMR (CDCl₃, 150 MHz) δ = 139.32, 132.16, 131.45, 130.48, 128.71, 128.59, 127.33, 126.21, 120.33, 103.47, 101.91, 51.36, 20.85 ppm; HRMS (ESI-TOF) calcd for C₁₆H₁₄BrNH⁺ $[M + H]^+$, 300.0382 found 300.0385.

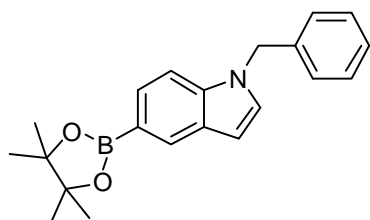
Preparation of 1-benzyl-5-phenyl-1*H*-indole (3h). To a solution of 1-benzyl-5-bromo-1*H*-indole **3a** (429.3 mg, 1.5 mmol) in THF (4 mL) were added phenylboronic acid (274.3 mg, 2.25



mmol) and Buchwald 2nd generation XPhos precatalyst (23.6 mg, 0.03 mmol). The solution was degassed with an argon flow for several minutes, following by addition of oxygen-free 0.5 M aqueous solution of K₃PO₄ (8 mL). The resulted biphasic mixture

was stirred at 60 °C overnight, followed by addition of H₂O and CH₂Cl₂. Two layers were separated and the aqueous layer was extracted with CH₂Cl₂. The organic layers were combined, dried over MgSO₄ and concentrated in *vacuo* to give the crude product. Purification by silica gel column chromatography using 10% EtOAc:petroleum ether gave the titled product as a white amorphous solid (320 mg, 75%). **3h**: FT-IR (neat) ν_{\max} 2928, 2850, 1476, 1454, 1184, 898, 807, 757, 737, 697 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz) δ = 7.86 (dd, *J* = 1.7, 0.8 Hz, 1 H), 7.71–7.61 (m, 2 H), 7.43 (m, 3 H), 7.38–7.23 (m, 5 H), 7.15 (m, 3 H), 6.61 (dd, *J* = 3.1, 0.8 Hz, 1 H), 5.35 (s, 2 H) ppm; ¹³C NMR (CDCl₃, 100 MHz) δ = 142.7, 137.6), 136.0, 133.3, 129.4, 129.1, 129.0 (2C), 128.8 (2C), 127.8, 127.5 (2C), 127.0 (2C), 121.8, 119.7, 110.1, 102.3, 50.4 ppm; HRMS (ESI-TOF) calcd for [M + H]⁺ 284.1434, found 284.1420; calcd for [M + Na]⁺ 306.1253, found 306.1244.

Preparation of 1-benzyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1*H*-indole (3m). A two-necked 250-mL round bottom flask containing 1-benzyl-5-bromo-1*H*-indole (**3a**) (630 mg,



2.2 mmol, 1 equiv), Pd₂(dba)₃ (20.15 mg, 0.02 mmol, 0.01 equiv) and XPhos (41.95 mg, 0.088 mmol, 0.04 equiv) was degassed with 3 vacuum/argon backfill cycles, then 1,4-dioxane (25 mL) and Et₃N (0.92 mL, 6.6 mmol, 3 equiv) were added under argon. Next, BHpin (0.96 mL, 6.6 mmol, 3 equiv) was added dropwise under argon, then the reaction mixture was stirred at 100 °C for 4 h. After TLC monitoring showed the reaction was complete, a

solution of sat. NaHCO₃ (50 mL) was added to the reaction mixture at 0 °C to quench the remaining BHpin, followed by extraction with CH₂Cl₂ (3 × 50 mL). The organic layers were combined, dried over MgSO₄ then concentrated in *vacuo* to give the crude product. Purification by silica gel column chromatography using 5-10% EtOAc:petroleum ether gave the titled product as a white amorphous solid (600 mg, 82%). **3m**: FT-IR (neat) ν_{\max} 3025, 2937, 1738, 1476, 1365, 1228, 1217, 898, 757, 737 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz) δ = 8.19 (s, 1 H), 7.63 (d, *J* = 8.0 Hz, 1 H), 7.37–7.17 (m, 5 H), 7.17–7.01 (m, 3 H), 6.57 (s, 1 H), 5.33 (s, 2 H), 1.36 (s, 12 H) ppm; ¹³C NMR (CDCl₃, 100 MHz) δ = 138.5, 137.6, 129.0, 128.9 (2 C), 128.6, 128.5, 128.0, 127.7, 126.9 (2 C), 109.2, 102.6, 83.6, 50.2, 25.1 (C adjacent to B atom does not show up) ppm; HRMS (ESI-TOF) calcd for [M + H]⁺ 334.1977, found 334.1973; calcd for [M + Na]⁺ 356.1798, found 356.1776.

General procedure B for the synthesis of difluorooxyindoles (4g and 4h). To the respective indole (1 equiv) was added *N*-fluorobenzenesulfonimide (3 equiv), *tert*-butyl hydroperoxide (1.5 equiv) and potassium phosphate dibasic (5 equiv) in a mixture of HPLC grade toluene:MeCN (4:1). The reaction mixture was heated from 70 °C for 1 h. Et₃N (excess) was added to quench the reaction followed by heating at 100 °C for 1 h. Water was then added and reaction mixture was extracted with EtOAc. The combined organic layers were dried with Na₂SO₄ and

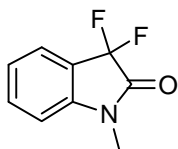
concentrated in *vacuo* to give a brown-black residue. Purification by column chromatography using 10–50% EtOAc:hexanes gave corresponding difluorooxyindole as an amorphous solid.

General procedure C for the synthesis of difluorooxyindoles (2a-2i, 4f and 4k). To the respective indole (1 equiv) was added *N*-fluorobenzenesulfonimide (3 equiv), *tert*-butyl hydroperoxide (1.5 equiv) and potassium phosphate dibasic (5 equiv) in a mixture of HPLC grade toluene:MeCN (4:1). The reaction mixture was heated from 90 °C for 20–70 min, depending on substrate. Et₃N (excess) was added to quench the reaction followed by heating at 100 °C for 1 h. Water was then added and reaction mixture was extracted with EtOAc. The combined organic layers were dried with Na₂SO₄ and concentrated in *vacuo* to give a brown-black residue. Purification by column chromatography using 10–50% EtOAc:hexanes gave corresponding difluorooxyindole as an amorphous solid.

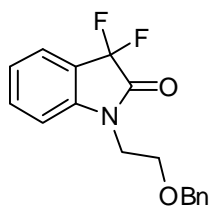
General procedure D for the synthesis of difluorooxyindoles (4b, 4d, 4e, 4i and 4l). To the respective indole (1 equiv) was added *N*-fluorobenzenesulfonimide (3 equiv), *tert*-butyl hydroperoxide (1.5 equiv) and potassium phosphate dibasic (5 equiv) in a mixture of HPLC grade toluene:MeCN (4:1). The reaction mixture was heated from 120 °C for 30–180 min depending on substrate. Et₃N (excess) was added to quench the reaction followed by heating at 100 °C for 1 h. Water was then added and reaction mixture was extracted with EtOAc. The combined organic layers were dried with Na₂SO₄ and concentrated in *vacuo* to give a brown-black residue. Purification by column chromatography using 10–50% EtOAc:hexanes gave corresponding difluorooxyindole as an amorphous solid.

General procedure E for the synthesis of difluorooxyindoles (2j, 2k and 4c). To the respective indole (1 equiv) was added *N*-fluorobenzenesulfonimide (3 equiv) and *tert*-butyl hydroperoxide (1.5 equiv) in a mixture of HPLC grade toluene:MeCN (4:1). The reaction mixture was heated from 120 °C for 2–5h, depending on substrate. Et₃N (excess) was added to quench the reaction followed by heating at 100 °C for 1 h. Water was then added and reaction mixture was extracted with EtOAc. The combined organic layers were dried with Na₂SO₄ and concentrated in *vacuo* to give a brown-black residue. Purification by column chromatography using 10–50% EtOAc:hexanes gave corresponding difluorooxyindole as an amorphous solid.

3,3-difluoro-1-methylindolin-2-one (2a). Following general procedure C for 20 min, indole **1a** (50 mg) gave the title compound **2a** (35 mg, 50%). **2a**: FT-IR (neat) ν_{\max} 2941, 1750, 1620, 1496, 1473, 1428, 1381, 1351, 1304, 1290, 1251, 1157, 1114, 1097, 1023, 856, 763, 752, 618 cm⁻¹; ¹H NMR (CDCl₃, 600 MHz) δ = 7.55 (d, *J* = 7.2 Hz, 1 H), 7.50 (t, *J* = 7.2 Hz, 1 H), 7.18 (t, *J* = 7.2 Hz, 1 H), 6.90 (d, *J* = 7.2 Hz, 1 H), 3.21 (s, 3 H) ppm; ¹³C NMR (CDCl₃, 150 MHz) δ = 165.45 (t, *J* = 30.0 Hz), 144.11 (t, *J* = 7.1 Hz), 133.71, 124.80, 124.07, 120.30 (t, *J* = 22.9 Hz), 110.99 (t, *J* = 248 Hz), 109.57, 26.45 ppm; ¹⁹F NMR (CDCl₃, 376 MHz) δ = -112.37 ppm; HRMS (ESI-TOF) calcd for C₉H₇F₂NONa⁺ [M + Na]⁺ 206.0388, found 206.0384.

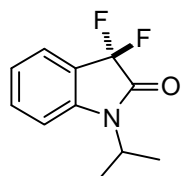


1-(2-(benzyloxy)ethyl)-3,3-difluoroindolin-2-one (2b). Following general procedure C for 20 min, indole **1b** (96.6 mg) gave the title compound **2b** (54 mg, 46%). **2b**: FT-IR (neat) ν_{\max} 2928,



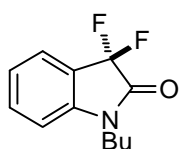
2807, 1753, 1622, 1490, 1472, 1375, 1313, 1286, 1197, 1158, 1086, 1032, 768, 701 cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ = 7.54 (dd, J = 7.4, 1.5 Hz, 1 H), 7.44 (td, J = 7.9, 1.2 Hz, 1 H), 7.33–7.24 (m, 2 H), 7.23–7.18 (m, 1 H), 7.15 (t, J = 7.6 Hz, 1 H), 7.05 (d, J = 8.0 Hz, 1 H), 4.50 (s, 1 H), 3.91 (t, J = 5.4 Hz, 1 H), 3.72 (t, J = 5.4 Hz, 1 H) ppm; ^{13}C NMR (CDCl_3 , 100 MHz) δ = 165.6 (t, J = 30.3 Hz), 143.9, 137.6, 133.3, 128.4 (2C), 127.8, 127.5 (2C), 124.5, 123.7 (t, J = 1.8 Hz), 120.1 (t, J = 23.0 Hz), 110.8 (t, J = 149 Hz), 73.2, 67.2, 40.6 ppm; ^{19}F NMR (CDCl_3 , 376 MHz) δ = -112.15 ppm; HRMS (ESI-TOF) calcd for $\text{C}_{17}\text{H}_{15}\text{F}_2\text{NO}_2\text{Na}^+$ $[\text{M} + \text{Na}]^+$ 326.0963, found 325.0973.

3,3-difluoro-1-isopropylindolin-2-one (2c). Following general procedure C for 20 min, indole **1c** (70 mg) gave the title compound **2c** (30 mg, 32%). **2c**: FT-IR (neat) ν_{\max} 2981, 2938, 2380,



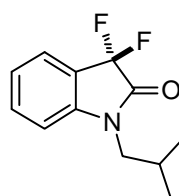
1749, 1623, 1483 cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ = 7.54 (dd, J = 7.4, 1.7 Hz, 1 H), 7.46 (td, J = 7.9, 1.3 Hz, 1 H), 7.14 (t, J = 7.4 Hz, 1 H), 7.02 (d, J = 7.9 Hz, 1 H), 4.50 (hept, J = 7.0 Hz, 1 H), 1.50 (d, J = 7.0 Hz, 6 H) ppm; ^{13}C NMR (CDCl_3 , 100 MHz) δ = 162.80 (t, J = 29.9 Hz), 140.72 (t, J = 7.1 Hz), 131.13 (t, J = 1.7 Hz), 122.7, 121.17 (t, J = 1.8 Hz), 118.42 (t, J = 23.0 Hz), 108.7, 108.3 (t, J = 248.6 Hz), 42.6, 17.0 ppm; ^{19}F NMR (CDCl_3 , 376 MHz) δ = -111.40 ppm; HRMS (ESI-TOF) calcd for $\text{C}_{21}\text{H}_{15}\text{F}_2\text{NNaO}^+$ $[\text{M} + \text{Na}]^+$ 234.0701, found 234.0704.

1-butyl-3,3-difluoroindolin-2-one (2d).^[4] Following general procedure C for 20 min, indole **1d** (50 mg) gave the title compound **2d** (31 mg, 47%). **2d**: ^1H NMR (CDCl_3 , 400 MHz) δ = 7.54 (dd,



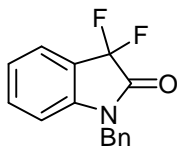
J = 7.4, 1.6 Hz, 1 H), 7.48 (td, J = 7.9, 1.2 Hz, 1 H), 7.16 (t, J = 7.6 Hz, 1 H), 6.90 (d, J = 7.9 Hz, 1 H), 3.69 (t, J = 7.4 Hz, 2 H), 1.88–1.59 (m, 2 H), 1.40 (dq, J = 14.7, 7.4 Hz, 2 H), 0.96 (t, J = 7.4 Hz, 3 H) ppm; ^{13}C NMR (CDCl_3 , 150 MHz) δ = 165.41 (t, J = 31.0 Hz), 143.6, 133.6, 124.9, 123.8, 120.45 (t, J = 24.4 Hz), 110.0 (t, J = 249.5 Hz), 109.9, 40.2, 29.3, 20.2, 13.8 ppm; ^{19}F NMR (CDCl_3 , 376 MHz) δ = -111.43 ppm. Data as reported in literature.^[4]

3,3-difluoro-1-isobutylindolin-2-one (2e). Following general procedure C for 20 min, indole **1e** (87 mg) gave the title compound **2e** (49 mg, 43%). **2e**: FT-IR (neat) ν_{\max} 2965, 2934, 2875,

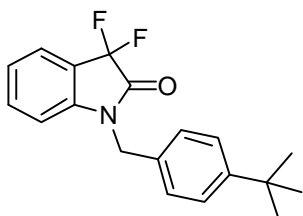


2256, 1750, 1621, 1473 cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ = 7.53 (dd, J = 7.4, 1.3 Hz, 1 H), 7.47 (td, J = 7.9, 1.2 Hz, 1 H), 7.15 (t, J = 7.4 Hz, 1 H), 6.90 (d, J = 7.9 Hz, 1 H), 3.49 (d, J = 7.5 Hz, 2 H), 2.31–2.04 (m, 1 H), 0.97 (d, J = 6.7 Hz, 6 H) ppm; ^{13}C NMR (CDCl_3 , 100 MHz) δ = 165.72 (t, J = 30.1 Hz), 143.97 (t, J = 7.1 Hz), 133.59 (t, J = 1.6 Hz), 124.8, 123.78 (t, J = 1.8 Hz), 120.31 (t, J = 23.1 Hz), 111.0 (t, J = 249.2), 110.1, 47.4, 27.0, 20.2 ppm; ^{19}F NMR (CDCl_3 , 376 MHz) δ = -111.40 ppm; HRMS (ESI-TOF) calcd for $\text{C}_{21}\text{H}_{15}\text{F}_2\text{NNaO}^+$ $[\text{M} + \text{Na}]^+$ 234.0701, found 234.0704.

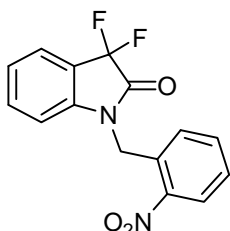
1-benzyl-3,3-difluoroindolin-2-one (2f). Following general procedure C for 20 min, indole **1f** (100 mg) gave the title compound **2f** (74.5 mg, 60%). **2f:** FT-IR (neat) ν_{\max} 2920, 1752, 1621, 1489, 1473, 1456, 1285, 1188, 1147, 1082, 631 cm^{-1} ; ^1H NMR (CDCl_3 , 600 MHz) δ = 7.56 (d, J = 7.8 Hz, 1 H), 7.40–7.32 (m, 3 H), 7.30–7.28 (m, 3 H), 7.14 (t, J = 7.8 Hz, 1 H), 6.77 (d, J = 7.8 Hz, 1 H), 4.90 (s, 2 H) ppm; ^{13}C NMR (CDCl_3 , 150 MHz) δ = 165.64 (t, J = 30.3 Hz), 143.26 (t, J = 6.9 Hz), 134.40, 133.61, 129.19, 128.29, 127.42, 124.87, 124.08, 120.32 (t, J = 22.8 Hz), 111.06 (t, J = 248 Hz), 110.66, 44.12 ppm; ^{19}F NMR (CDCl_3 , 376 MHz) δ = -111.75 ppm; HRMS (ESI-TOF) calcd for $\text{C}_{15}\text{H}_{11}\text{F}_2\text{ONa}^+ [\text{M} + \text{Na}]^+$ 282.0701, found 282.0697.



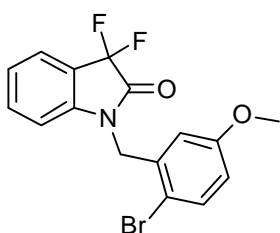
1-(4-tert-butylbenzyl)-3,3-difluoroindolin-2-one (2g). Following general procedure C for 45 min, indole **1g** (40.0 mg) gave the title compound **2g** (26.6 mg, 56%). **1g:** FT-IR (neat) ν_{\max} 2964, 1753, 1621, 1515, 1589, 1473, 1370, 1307, 1285, 1268, 1187, 1148, 1088, 1008, 768, 752, 504 cm^{-1} ; ^1H NMR (CDCl_3 , 600 MHz) δ = 7.55 (dd, J = 7.2, 1.2 Hz, 1 H), 7.39 (td, J = 7.8, 1.2 Hz, 1 H), 7.36 (d, J = 8.4 Hz, 2 H), 7.24 (d, J = 8.4 Hz, 2 H), 7.13 (t, J = 7.5 Hz, 1 H), 6.82 (d, J = 8.4 Hz, 1 H), 4.86 (s, 2 H), 1.29 (s, 9 H) ppm; ^{13}C NMR (CDCl_3 , 150 MHz) δ = 165.59 (t, J = 29.9 Hz), 151.33, 143.42 (t, J = 7.2 Hz), 133.60, 131.38, 127.25, 126.09, 124.83, 123.99, 120.35 (t, J = 23.0 Hz), 111.07 (t, J = 248 Hz), 110.70, 43.80, 34.70, 31.40 ppm; ^{19}F NMR (CDCl_3 , 376 MHz) δ = -111.86 ppm; HRMS (ESI-TOF) calcd for $\text{C}_{19}\text{H}_{19}\text{F}_2\text{NONa}^+ [\text{M} + \text{Na}]^+$ 338.1327, found 338.1332.



3,3-difluoro-1-(2-nitrobenzyl)indolin-2-one (2h). Following general procedure C for 70 min, indole **1h** (38.6 mg) gave the title compound **2h** (26.6 mg, 57%). **2h:** FT-IR (neat) ν_{\max} 2989, 2869, 1753, 1620, 1526, 1490, 1473, 1339, 1311, 1282, 1192, 1153, 1084, 1025, 1010, 859, 844, 788, 768, 753, 729 cm^{-1} ; ^1H NMR (CDCl_3 , 600 MHz) δ = 8.19 (d, J = 7.8 Hz, 1 H), 7.63 (d, J = 7.8 Hz, 1 H), 7.58 (t, J = 7.8 Hz, 1 H), 7.50 (t, J = 7.8 Hz, 1 H), 7.42 (t, J = 7.8 Hz, 1 H), 7.26–7.20 (m, 2 H), 6.69 (d, J = 7.8 Hz, 1 H), 5.34 (s, 2 H) ppm; ^{13}C NMR (CDCl_3 , 150 MHz) δ = 165.89 (t, J = 30.5 Hz), 148.00, 142.85 (t, J = 6.6 Hz), 134.49, 133.97, 130.19, 129.09, 127.48, 125.96, 125.23, 124.64, 120.20 (t, J = 23.0 Hz), 110.89 (t, J = 249 Hz), 110.27, 41.52 ppm; ^{19}F NMR (CDCl_3 , 376 MHz) δ = -111.19 ppm; HRMS (ESI-TOF) calcd for $\text{C}_{15}\text{H}_{10}\text{F}_2\text{N}_2\text{O}_3\text{Na}^+ [\text{M} + \text{Na}]^+$ 327.0552, found 327.0554.

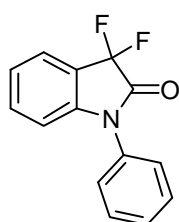


1-(2-bromo-5-methoxybenzyl)-3,3-difluoroindolin-2-one (2i). Following general procedure C for 30 min, indole **1i** (48.2 mg) gave the title compound **2i** (36.1 mg, 64%). **2i:** FT-IR (neat) ν_{\max} 2937, 1755, 1622, 1574, 1489, 1472, 1431, 1368, 1349, 1312, 1288, 1239, 1188, 1150, 1086, 1054, 1021, 1010, 769, 751 cm^{-1} ; ^1H NMR (CDCl_3 , 600 MHz) δ = 7.58 (d, J = 7.8 Hz, 1 H), 7.49 (d, J = 8.4 Hz, 1 H), 7.40 (t, J = 7.8 Hz, 1 H), 7.17 (t, J = 7.8 Hz, 1 H), 6.76 (d, J = 7.8 Hz, 1 H), 6.72 (dd, J = 8.4, 3.0 Hz, 1 H), 6.64 (d, J = 3.0 Hz, 1 H), 4.96



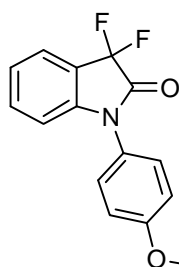
(s, 2 H), 3.68 (s, 3 H) ppm; ^{13}C NMR (CDCl_3 , 150 MHz) δ = 165.79 (t, J = 30.3 Hz), 159.58, 142.95 (t, J = 7.1 Hz), 134.24, 133.96, 133.85, 124.94, 124.35, 120.19 (t, J = 23.0 Hz), 115.14, 113.87, 113.09, 110.06 (t, J = 248 Hz), 110.79, 55.55, 44.08 ppm; ^{19}F NMR (CDCl_3 , 376 MHz) δ = -111.41 ppm; HRMS (ESI-TOF) calcd for $\text{C}_{16}\text{H}_{12}\text{BrF}_2\text{NO}_2\text{Na}^+$ [$\text{M} + \text{Na}$] $^+$ 389.9912 and 391.9893, found 389.9923 and 391.9905.

3,3-difluoro-1-phenylindolin-2-one (2j). Following general procedure E for 3 h, indole **1j** (29.6 mg) gave the title compound **2j** (15.0 mg, 40%). **2j**: FT-IR (neat) ν_{max} 2989, 2870, 1753, 1618,



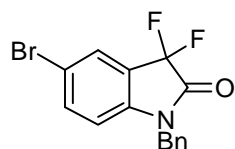
1596, 1499, 1471, 1375, 1301, 1289, 1202, 1126, 1084, 1003, 945, 843, 767, 750, 700 cm^{-1} ; ^1H NMR (CDCl_3 , 600 MHz) δ = 7.64 (d, J = 7.2 Hz, 1 H), 7.56 (t, J = 7.2 Hz, 2 H), 7.48–7.41 (m, 4 H), 7.22 (t, J = 8.4 Hz, 1 H), 6.87 (d, J = 8.4 Hz, 1 H) ppm; ^{13}C NMR (CDCl_3 , 150 MHz) δ = 164.70 (t, J = 30.5 Hz), 144.35 (t, J = 7.1 Hz), 133.64, 132.79, 130.08, 129.09, 126.36, 125.14, 124.52, 120.08 (t, J = 22.8 Hz), 110.91 (t, J = 246 Hz), 110.91 ppm; ^{19}F NMR (CDCl_3 , 376 MHz) δ = -110.65 ppm; HRMS (ESI-TOF) calcd for $\text{C}_{14}\text{H}_9\text{F}_2\text{NONa}^+$ [$\text{M} + \text{Na}$] $^+$ 268.0544, found 268.0547.

3,3-difluoro-1-(4-methoxyphenyl)indolin-2-one (2k). Following general procedure E for 2 h, indole **1k** (34.0 mg) gave the title compound **2k** (20.1 mg, 48%). **2k**: FT-IR (neat) ν_{max} 2966,



1756, 1622, 1515, 1470, 1379, 1299, 1251, 1203, 1127, 1085, 1033, 826, 767, 751, 631 cm^{-1} ; ^1H NMR (CDCl_3 , 600 MHz) δ = 7.61 (d, J = 7.2 Hz, 1 H), 7.56 (t, J = 7.8 Hz, 1 H), 7.32 (d, J = 9.0 Hz, 2 H), 7.20 (t, J = 7.2 Hz, 1 H), 7.05 (d, J = 9.0 Hz, 2 H), 6.81 (d, J = 8.4 Hz, 1 H), 3.87 (s, 3 H) ppm; ^{13}C NMR (CDCl_3 , 150 MHz) δ = 164.96 (t, J = 29.7 Hz), 159.93, 144.80 (t, J = 6.5 Hz), 133.63, 127.82, 125.24, 125.03, 124.36, 120.04 (t, J = 22.8 Hz), 115.33, 110.94 (t, J = 248 Hz), 110.81, 55.74 ppm; ^{19}F NMR (CDCl_3 , 376 MHz) δ = -110.91 ppm; HRMS (ESI-TOF) calcd for $\text{C}_{15}\text{H}_{11}\text{F}_2\text{NO}_2\text{Na}^+$ [$\text{M} + \text{Na}$] $^+$ 298.0650, found 298.0648.

1-benzyl-5-bromo-3,3-difluoroindolin-2-one (4a). To indole **3a** (110 mg, 0.381 mmol, 1 equiv) was added *N*-fluorobenzenesulfonimide (3 equiv), *tert*-butyl hydroperoxide (1.5 equiv) and

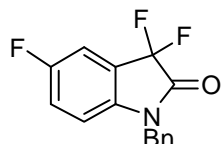


potassium phosphate dibasic (5 equiv) in a mixture of toluene:MeCN (4:1, 7.5 mL, 0.05 M). The reaction mixture was heated from 120 °C for 60 min. Et_3N (excess) was added to quench the reaction followed by heating at 100 °C for 1.5 h. Water was then added and reaction mixture was extracted

with EtOAc. The combined organic layers were dried with Na_2SO_4 and concentrated in *vacuo* to give a brown-black residue. Purification by column chromatography using 10–50% EtOAc:hexanes gave difluoroxyindole **4a** as an amorphous solid (78.2 mg, 60%). **4a**: FT-IR (neat) ν_{max} 3066, 2935, 1751, 1615, 1482, 1455, 1437, 1366, 1348, 1282, 1263, 1183, 1148, 1123, 1089, 816, 736, 698, 633, 529 cm^{-1} ; ^1H NMR (CDCl_3 , 600 MHz) δ = 7.67 (s, 1 H), 7.49 (d, J = 8.4 Hz, 1 H), 7.36–7.26 (m, 5 H), 6.64 (d, J = 8.4 Hz, 1 H), 4.88 (s, 2 H); ^{13}C NMR (CDCl_3 , 150

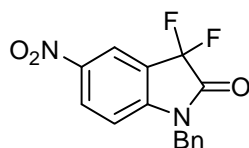
MHz) δ = 164.99 (t, J = 29.7 Hz), 142.20 (t, J = 6.3 Hz), 136.42, 133.90, 129.30, 128.49, 128.15, 127.37, 121.99 (t, J = 23.0 Hz), 116.75, 112.28, 110.37 (t, J = 250.1 Hz), 44.24 ppm; ^{19}F NMR (CDCl_3 , 376 MHz) δ = -111.70 ppm; HRMS (ESI-TOF) calcd for $\text{C}_{15}\text{H}_{10}\text{BrF}_2\text{NONa}^+$ [$\text{M} + \text{Na}$] $^+$ 359.9806, found 359.9818.

1-benzyl-3,3,5-trifluoroindolin-2-one (4b). Following general procedure D for 25 min, indole **3b** (85.9 mg) gave the title compound **4b** (59.9 mg, 57%). **4b**: FT-IR (neat) ν_{max} 3068, 1751,



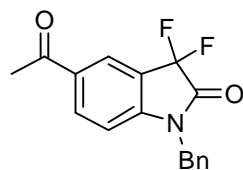
1628, 1491, 1469, 1456, 1372, 1350, 1294, 1263, 1201, 1179, 1138, 1090, 1018, 968, 883, 820, 792, 698, 638 cm^{-1} ; ^1H NMR (CDCl_3 , 600 MHz) δ = 7.37–7.27 (m, 6 H), 7.08 (t, J = 7.8 Hz, 1 H), 6.70 (d, J = 9.0 Hz, 1 H), 4.89 (s, 2 H) ppm; ^{13}C NMR (CDCl_3 , 150 MHz) δ = 165.37 (t, J = 30.0 Hz), 159.55 (d, J = 245 Hz), 139.14 (td, J = 6, 3 Hz), 134.05, 129.29, 128.45, 127.39, 121.50 (td, J = 22.5, 7.5 Hz), 120.12 (d, J = 24.0 Hz), 113.06 (d, J = 25.5 Hz) 111.81 (d, J = 7.5 Hz), 110.58 (t, J = 249 Hz), 44.29 ppm; ^{19}F NMR (CDCl_3 , 376 MHz) δ = -111.88 (s, 2 F), -117.437 (s, 1 F) ppm; HRMS (ESI-TOF) calcd for $\text{C}_{15}\text{H}_{10}\text{F}_3\text{NONa}^+$ [$\text{M} + \text{Na}$] $^+$ 300.0607, found 300.0609.

1-benzyl-3,3-difluoro-5-nitroindolin-2-one (4c). Following general procedure E for 5 h, indole **3c** (38.4 mg) gave the title compound **4c** (23.4 mg, 50%). **4c**: FT-IR (neat) ν_{max} 2988, 2869, 1765,



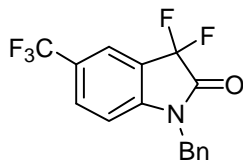
1622, 1529, 1486, 1455, 1380, 1341, 1279, 1184, 1145, 1085, 750, 698 cm^{-1} ; ^1H NMR (CDCl_3 , 600 MHz) δ = 8.45 (s, 1 H), 8.33 (d, J = 7.8 Hz, 1 H), 7.38 (t, J = 7.2 Hz, 2 H), 7.35 (t, J = 7.2 Hz, 1 H), 7.28 (d, J = 7.2 Hz, 2 H), 6.89 (d, J = 7.8 Hz, 1 H), 4.96 (s, 2 H) ppm; ^{13}C NMR (CDCl_3 , 150 MHz) δ = 165.34 (t, J = 30.0 Hz), 148.47 (t, J = 6.3 Hz), 144.34, 133.25, 130.63, 129.53, 128.87, 127.41, 121.08, 110.82, 109.57 (t, J = 251.0 Hz), 44.66 ppm; ^{19}F NMR (CDCl_3 , 376 MHz) δ = -112.11 ppm; HRMS (ESI-TOF) calcd for $\text{C}_{15}\text{H}_{10}\text{F}_2\text{N}_2\text{O}_3\text{Na}^+$ [$\text{M} + \text{Na}$] $^+$ 327.0552, found 327.0548.

5-acetyl-1-benzyl-3,3-difluoroindolin-2-one (4d). Following general procedure D for 3 h, indole **3d** (33.5 mg) gave the title compound **4d** (16.8 mg, 45%). **4d**: FT-IR (neat) ν_{max} 2989,

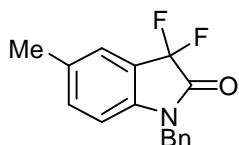


2871, 1760, 1682, 1622, 1493, 1456, 1362, 1299, 1236, 1188, 1145, 1091, 829, 698 cm^{-1} ; ^1H NMR (CDCl_3 , 600 MHz) δ = 8.16 (s, 1 H), 8.03 (d, J = 8.4 Hz, 1 H), 7.37–7.28 (m, 5 H), 6.85 (d, J = 7.2 Hz, 1 H), 4.93 (s, 2 H), 2.57 (s, 3 H) ppm; ^{13}C NMR (CDCl_3 , 150 MHz) δ = 195.64, 165.71 (t, J = 30.5 Hz), 147.09 (t, J = 6.6 Hz), 134.59, 133.84, 133.41, 129.35, 128.57, 127.41, 125.12, 120.54 (t, J = 23.6 Hz), 110.53, 110.31 (t, J = 249 Hz), 44.39, 26.51 ppm; ^{19}F NMR (CDCl_3 , 376 MHz) δ = -111.93 ppm; HRMS (ESI-TOF) calcd for $\text{C}_{17}\text{H}_{13}\text{F}_2\text{NO}_2\text{Na}^+$ [$\text{M} + \text{Na}$] $^+$ 324.0807, found 324.0814.

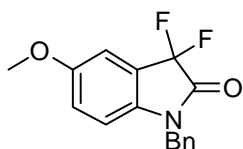
1-benzyl-3,3-difluoro-5-(trifluoromethyl)indolin-2-one (4e). Following general procedure D for 2 h, indole **3e** (41.6 mg) gave the title compound **4e** (22.8 mg, 46%). **4e**: FT-IR (neat) ν_{\max} 2867, 1761, 1634, 1608, 1502, 1456, 1377, 1334, 1265, 1192, 1170, 1124, 1096, 1065, 829, 774, 747, 699, 631, 553, 544, 534, 503 cm^{-1} ; ^1H NMR (CDCl_3 , 600 MHz) δ = 7.81 (s, 1 H), 7.66 (d, J = 8.4 Hz, 1 H), 7.38–7.28 (m, 5 H), 6.87 (d, J = 8.4 Hz, 1 H), 4.93 (s, 2 H) ppm; ^{13}C NMR (CDCl_3 , 150 MHz) δ = 165.32 (t, J = 29.9 Hz), 146.19 (t, J = 7.1 Hz), 133.68, 131.22, 129.40, 128.64, 127.40, 126.69 (q, J = 33.6 Hz), 123.60 (q, J = 270.3 Hz) 122.30, 120.86 (t, J = 23.3 Hz), 110.81, 110.10 (t, J = 249.5 Hz), 44.40 ppm; ^{19}F NMR (CDCl_3 , 376 MHz) δ = -62.240 (s, 3 F), -112.099 (s, 2 F) ppm; HRMS (ESI-TOF) calcd for $\text{C}_{16}\text{H}_{10}\text{F}_5\text{NONa}^+$ [$\text{M} + \text{Na}$] $^+$ 350.0575, found 350.0581.



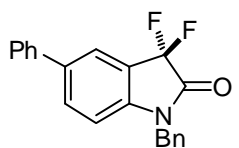
1-benzyl-3,3-difluoro-5-methylindolin-2-one (4f). Following general procedure C for 20 min, indole **3f** (21.4 mg) gave the title compound **4f** (14.3 mg, 54%). **4e**: FT-IR (neat) ν_{\max} 2988, 2926, 1746, 1628, 1606, 1496, 1455, 1370, 1350, 1300, 1278, 1179, 1141, 1125, 1081, 816, 698 cm^{-1} ; ^1H NMR (CDCl_3 , 600 MHz) δ = 7.37 (s, 1 H), 7.35–7.28 (m, 5 H), 7.16 (d, J = 7.8 Hz, 1 H), 6.65 (d, J = 7.8 Hz, 1 H), 4.87 (s, 2 H), 2.32 (s, 3 H) ppm; ^{13}C NMR (CDCl_3 , 150 MHz) δ = 165.67 (t, J = 30.8 Hz), 140.79 (t, J = 7.5 Hz), 134.54, 134.01, 133.82, 129.15, 128.23, 127.40, 125.47, 120.30 (t, J = 23.3 Hz), 111.30 (t, J = 248 Hz), 110.47, 44.11, 21.02 ppm; ^{19}F NMR (CDCl_3 , 376 MHz) δ = -111.62 ppm; HRMS (ESI-TOF) calcd for $\text{C}_{16}\text{H}_{13}\text{F}_2\text{NONa}^+$ [$\text{M} + \text{Na}$] $^+$ 296.0857, found 296.0843.



1-benzyl-3,3-difluoro-5-methoxyindolin-2-one (3g). Following general procedure B for 60 min, indole **3g** (49.8 mg) gave the title compound **4g** (25.5 mg, 42%). **4g**: FT-IR (neat) ν_{\max} 2940, 1744, 1606, 1489, 1437, 1350, 1342, 1293, 1266, 1231, 1178, 1143, 1080, 1025, 818, 782, 698, 635 cm^{-1} ; ^1H NMR (CDCl_3 , 600 MHz) δ = 7.36–7.28 (m, 5 H), 7.14 (s, 1 H), 6.88 (d, J = 8.4 Hz, 1 H), 6.66 (d, J = 8.4 Hz, 1 H), 4.87 (s, 2 H), 3.78 (s, 3 H) ppm; ^{13}C NMR (CDCl_3 , 150 MHz) δ = 165.52 (t, J = 30.0 Hz), 156.84, 136.26 (t, J = 7.5 Hz), 134.50, 129.18, 128.45, 127.41, 121.21 (t, J = 22.5 Hz), 118.56, 111.54, 111.22 (t, J = 248 Hz), 56.05, 44.19 ppm; ^{19}F NMR (CDCl_3 , 376 MHz) δ = -111.60 ppm; HRMS (ESI-TOF) calcd for $\text{C}_{16}\text{H}_{13}\text{F}_2\text{NO}_2\text{Na}^+$ [$\text{M} + \text{Na}$] $^+$ 312.0807, found 312.0813.

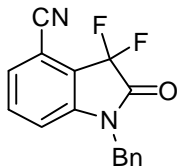


1-benzyl-3,3-difluoro-5-phenylindolin-2-one (4h). Following general procedure B for 60 min, indole **3h** (85 mg) gave the title compound **4h** (42 mg, 42%). **4h**: FT-IR (neat) ν_{\max} 3491, 3004, 1752, 1628, 1483 cm^{-1} ; ^1H NMR (CDCl_3 , 600 MHz) δ = 7.78 (s, 1 H), 7.59 (d, J = 8.2 Hz, 1 H), 7.51 (d, J = 7.5 Hz, 2 H), 7.44 (t, J = 7.7 Hz, 2 H), 7.38–7.31 (m, 6 H), 6.85 (d, J = 8.2 Hz, 1 H) ppm; ^{13}C NMR (CDCl_3 , 150 MHz) δ = 165.64 (t, J = 30.4 Hz), 142.32 (t, J = 6.9 Hz), 139.6, 137.8, 134.4, 132.2, 129.2, 129.1, 128.3, 127.9, 127.5, 126.9, 123.7, 120.87 (t, J =



23.0 Hz), 111.1 (t, $J = 250.2$ Hz), 111.0, 44.2 ppm; ^{19}F NMR (CDCl_3 , 376 MHz) $\delta = -111.52$ ppm; HRMS (ESI-TOF) calcd for $\text{C}_{21}\text{H}_{15}\text{F}_2\text{NNaO}^+ [\text{M} + \text{Na}]^+$ 358.1014, found 358.1025.

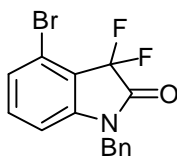
1-benzyl-3,3-difluoro-2-oxindoline-4-carbonitrile (4i). Following general procedure D for 2 h, indole **3i** (22.4 mg) gave the title compound **4i** (15.1 mg, 55%). **4i**: FT-IR (neat) ν_{max} 2926, 2236, 1758, 1603, 1462, 1363, 1285, 1218, 1145, 1092, 1010, 798, 763, 702 cm^{-1} ; ^1H



NMR (CDCl_3 , 600 MHz) $\delta = 7.48$ (t, $J = 8.1$ Hz, 1 H), 7.37–7.33 (m, 4 H), 7.25 (t, $J = 6.6$ Hz, 2 H), 6.98 (d, $J = 8.4$ Hz, 1 H), 4.90 (s, 2 H); ^{13}C NMR (CDCl_3 , 150 MHz) $\delta = 164.355$ (t, $J = 29.6$ Hz), 144.39 (t, $J = 6.3$ Hz), 134.41, 133.40, 129.43, 128.70, 127.37, 122.29 (t, $J = 22.0$ Hz), 114.79, 114.20, 109.52, 109.45 (t, $J = 251$ Hz), 44.42 ppm; ^{19}F NMR (CDCl_3 , 376 MHz) $\delta = -113.73$ ppm;

HRMS (ESI-TOF) calcd for $\text{C}_{16}\text{H}_{10}\text{F}_2\text{N}_2\text{ONa}^+ [\text{M} + \text{Na}]^+$ 307.0653, found 307.0654.

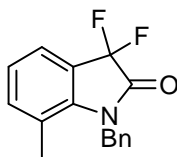
1-benzyl-4-bromo-3,3-difluoroindolin-2-one (4j). To indole **3j** (22.7 mg, 0.0793 mmol, 1 equiv) was added *N*-Fluorobenzenesulfonimide (3 equiv), *tert*-butyl hydroperoxide (1.5 equiv) and potassium phosphate dibasic (1 equiv) in a mixture of toluene:MeCN (4:1). The reaction mixture was heated at 120 °C for 40 min. Et_3N (excess) was added to



quench the reaction followed by heating at 100 °C for 1 h. Water was then added and reaction mixture was extracted with EtOAc. The combined organic layers were dried with Na_2SO_4 and concentrated in *vacuo* to give a brown-black residue. Purification by column chromatography using 10–50% EtOAc:hexanes gave difluoroxyindole **4j** as an amorphous solid (17.0 mg, 50%). **4j**: FT-IR (neat) ν_{max} 2989, 2870, 1757, 1611, 1591, 1454, 1364, 1280, 1235, 1171, 1154, 1135, 1093, 1008, 779, 761, 699 cm^{-1} ;

^1H NMR (CDCl_3 , 600 MHz) $\delta = 7.36$ –7.34 (m, 2 H), 7.32–7.30 (m, 1 H), 7.28–7.27 (m, 2 H), 7.23 (t, $J = 7.2$ Hz, 1 H), 7.21 (t, $J = 7.9$ Hz, 1 H), 6.70 (dd, $J = 7.6, 1.0$ Hz, 1 H), 4.88 (s, 2 H) ppm; ^{13}C NMR (CDCl_3 , 150 MHz) $\delta = 164.91$ (t, $J = 29.6$ Hz), 145.13 (t, $J = 5.6$ Hz), 134.60, 133.97, 129.29, 128.47, 128.06, 127.37, 120.05, 119.85, 110.83 (t, $J = 251$ Hz), 109.49, 44.24 ppm; ^{19}F NMR (CDCl_3 , 376 MHz) $\delta = -115.88$ ppm; HRMS (ESI-TOF) calcd for $\text{C}_{15}\text{H}_{10}\text{BrF}_2\text{NONa}^+ [\text{M} + \text{Na}]^+$ 359.9806, found 359.9806.

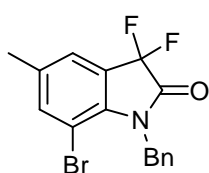
1-benzyl-3,3-difluoro-7-methylindolin-2-one (4k). Following general procedure C for 20 min, indole **3k** (21.4 mg) gave the title compound **4k** (15.4 mg, 58%). **4k**: FT-IR (neat) ν_{max} 3033, 1744, 1610, 1496, 1488, 1471, 1446, 1377, 1351, 1312, 1283, 1255, 1212, 1167, 1153, 1078, 1063, 1030, 996, 973, 872, 841, 786, 742, 732, 697 cm^{-1} ; ^1H



NMR (CDCl_3 , 600 MHz) $\delta = 7.45$ (d, $J = 7.2$ Hz, 1 H), 7.34 (t, $J = 7.2$ Hz, 2 H), 7.28 (t, $J = 7.2$ Hz, 1 H), 7.15 (t, $J = 7.2$ Hz, 3 H), 7.07 (t, $J = 7.2$ Hz, 1 H), 5.16 (s, 2 H), 2.25 (s, 3 H) ppm; ^{13}C NMR (CDCl_3 , 150 MHz) $\delta = 166.85$ (t, $J = 29.9$

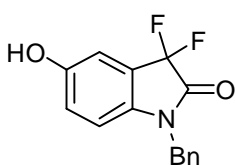
Hz), 141.16 (t, $J = 6.6$ Hz), 137.58, 136.11, 129.25, 127.83, 125.68, 124.30, 122.83, 121.68, 121.16 (t, $J = 22.7$ Hz), 110.66 (t, $J = 247$ Hz) 45.34, 18.80 ppm; ^{19}F NMR (CDCl_3 , 376 MHz) $\delta = -111.13$ ppm; HRMS (ESI-TOF) calcd for $\text{C}_{16}\text{H}_{13}\text{F}_2\text{NONa}^+ [\text{M} + \text{Na}]^+$ 296.0857, found 296.0852.

1-benzyl-7-bromo-3,3-difluoro-5-methylindolin-2-one (4l). Following general procedure D for 1 h, indole **3l** (45.2 mg) gave the title compound **4l** (24.4 mg, 46%). **4l**: FT-IR (neat) ν_{\max} 3033,



2926, 1753, 1626, 1578, 1497, 1477, 1454, 1422, 1362, 1345, 1299, 1230, 1156, 1087, 979, 865, 782, 732, 696, 632 cm^{-1} ; ^1H NMR (CDCl_3 , 600 MHz) δ = 7.36 (s, 2 H), 7.32 (t, J = 7.2 Hz, 2 H), 7.27 (t, J = 7.2 Hz, 1 H), 7.20 (d, J = 7.2 Hz, 2 H), 5.36 (s, 2 H), 2.33 (s, 3 H) ppm; ^{13}C NMR (CDCl_3 , 150 MHz) δ = 166.40 (t, J = 29.6 Hz), 139.42, 138.37 (t, J = 6.6 Hz), 136.00, 135.89, 128.90, 127.68, 126.40, 124.94, 123.30 (t, J = 23.0 Hz), 110.01 (t, J = 247 Hz), 103.55, 44.72, 20.48 ppm; ^{19}F NMR (CDCl_3 , 376 MHz) δ = -111.28 ppm; HRMS (ESI-TOF) calcd for $\text{C}_{16}\text{H}_{12}\text{BrF}_2\text{NONa}^+$ [$\text{M} + \text{Na}$] $^+$ 373.9963 and 375.9943, found 373.9962 and 375.9940.

1-benzyl-3,3-difluoro-5-hydroxyindolin-2-one (4m). To 1-benzyl-5-(4,5-dimethyl-1,3,2-dioxaborolan-2-yl)-1*H*-indole (**3m**) (46.0mg, 0.151mmol, 1 equiv) was added *N*-



Fluorobenzenesulfonimide (3 equiv), *tert*-butyl hydroperoxide (1.5 equiv) and potassium phosphate dibasic (1 equiv) in a mixture of toluene:MeCN (4:1). The reaction mixture was heated at 90 °C for 1 h. Et_3N (excess) was added to quench the reaction followed by heating at 100 °C for 1 h. Water was then added and reaction mixture was extracted with EtOAc. The combined organic layers were dried with Na_2SO_4 and concentrated in *vacuo* to give a brown-black residue. Purification by column chromatography using 10–50% EtOAc:hexanes gave difluorooxyindole **4m** as an amorphous solid (22.4mg, 54%). **4m**: FT-IR (neat) ν_{\max} 3309 (br), 2924, 1717, 1613, 1514, 1497, 1485, 1457, 1406, 1381, 1364, 1339, 1301, 1205, 1191, 1146, 1090, 1051, 1017, 971, 887, 824, 793, 693, 639, 504 cm^{-1} ; ^1H NMR (CDCl_3 , 600 MHz) δ = 7.35–7.27 (m, 5 H), 7.09 (d, J = 2.4 Hz, 1 H), 6.83 (dd, J = 8.4, 2.4 Hz, 1 H), 6.61 (d, J = 8.4 Hz, 1 H), 5.11 (br s, 1 H), 4.86 (s, 2 H) ppm; ^{13}C NMR (CDCl_3 , 150 MHz) δ = 165.56 (t, J = 30.1 Hz), 152.75, 136.31 (t, J = 7.2 Hz), 134.41, 129.20, 128.30, 127.40, 121.39 (t, J = 22.5 Hz), 119.79, 112.88, 111.68, 111.15 (t, J = 249 Hz), 44.22 ppm; ^{19}F NMR (CDCl_3 , 376 MHz) δ = -111.67 ppm; HRMS (ESI-TOF) calcd for $\text{C}_{15}\text{H}_{11}\text{O}_2\text{F}_2\text{NNa}^+$ [$\text{M} + \text{Na}$] $^+$ 298.0656, found 298.0631.

References

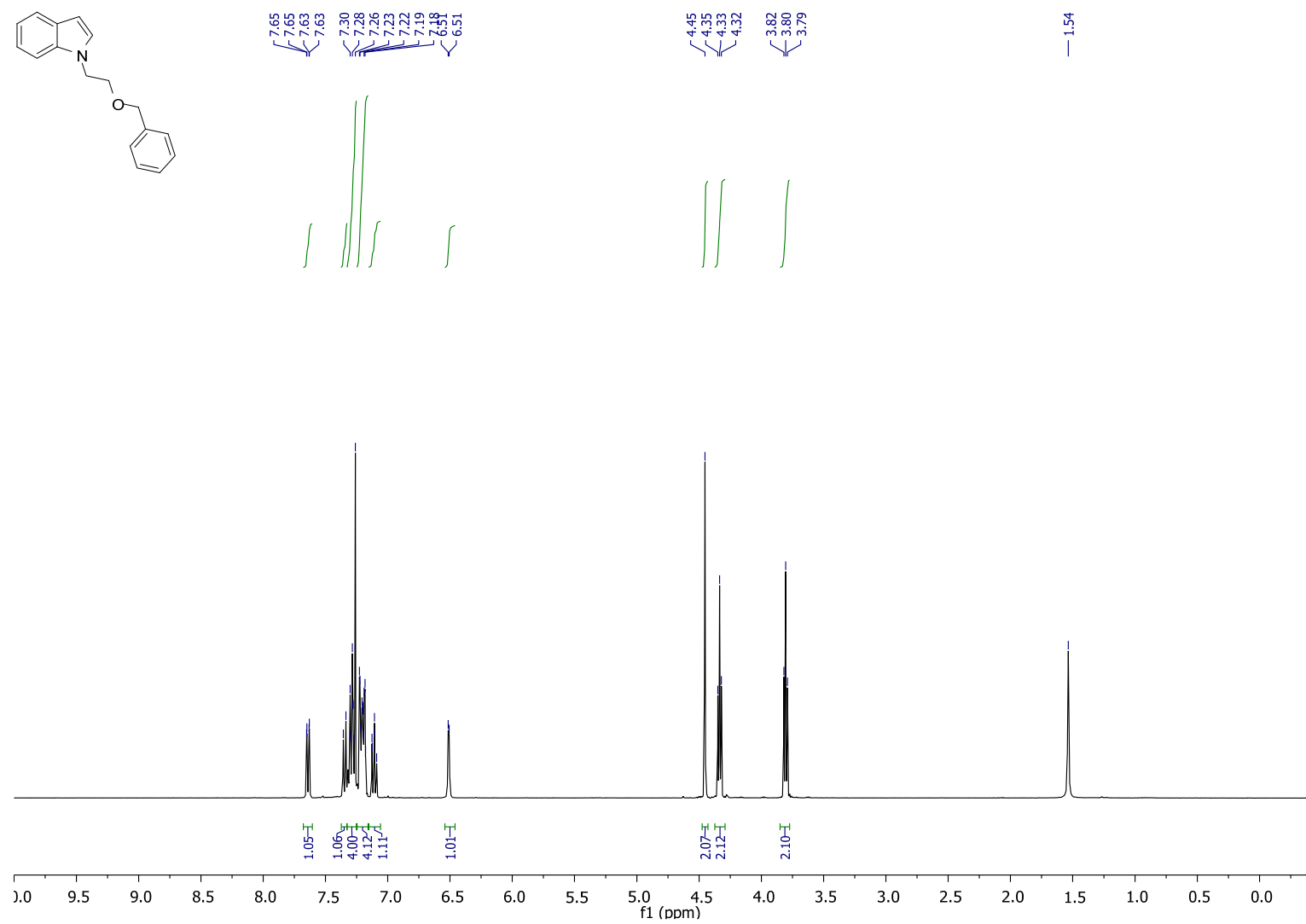
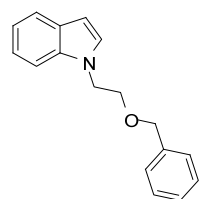
- [1] (a) Ghosh, S.; Golan, G.; Inbal, B.; Jacques, V.; Lobera, M. *Bicyclic compounds and methods of making and using same*. WO 2010/65743 A2. 2010-06-10. (b) Xu, X.-H.; Liu, G.-K.; Azuma, A.; Tokunaga, E.; Shibata, N. *Org. Lett.* **2011**, *13*, 4854. (c) Bremner, J. B.; Russell, H. F.; Skelton, B. W.; White, A. H. *Heterocycles* **2000**, *53*, 277. (d) Choy, P. Y.; Lau, C. P.; Kwong, F. Y. *J. Org. Chem.* **2011**, *76*, 80. (e) Hellal, M.; Singh, S.; Cuny, G. D. *J. Org. Chem.* **2012**, *77*, 4123. (f) Shuttleworth, S. J.; Silva, F. A. *Naphthridine derivatives as PI3K inhibitors for the treatment of cancer and immune-inflammatory diseases* WO2011/135351 A1. 2011-11-03.
- [2] Schiffner, J. A.; Wöste, T. H.; Oestreich, M. *Eur. J. Org. Chem.* **2010**, 174.
- [3] Bylund, J.; Ek, M.; Holenz, J.; Johansson, M. H.; Kers, A.; Närhi, K.; Nordvall, G.; Öhberg, L.; Sohn, D.; Viklund, J.; Von Berg, S. *Bis-(sulfonlamino) derivatives in therapy 066* WO 2009/064251 A1. 2009-05-22.
- [4] Zhu, J.; Zhang, W.; Zhang, L.; Liu, J.; Zheng, J.; Hu, J. *J. Org. Chem.* **2010**, *75*, 5505.

Abbreviations

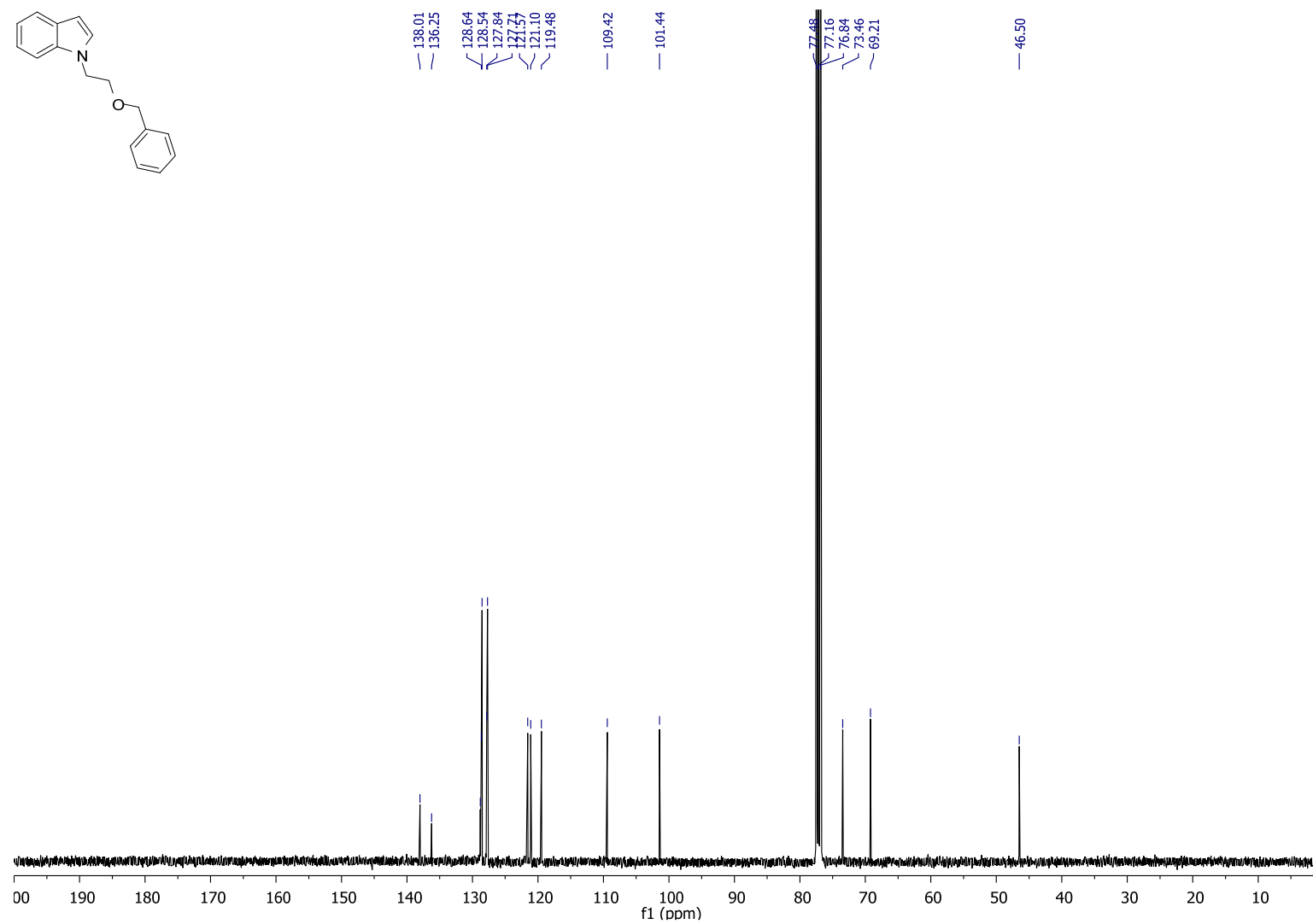
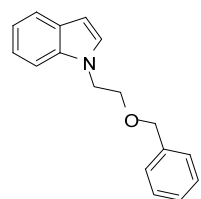
Bu	butyl
Bn	benzyl
DMF	<i>N,N'</i> -dimethylformamide
equiv	equivalents
EtOAc	ethyl acetate
h	hour
HPLC	high performance liquid chromatography
HRMS	high-resolution mass spectra
M	molar
min	minute
NMR	nuclear magnetic resonance
PTLC	preparative thin layer chromatography
R _f	retention factor
TLC	thin layer chromatography

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

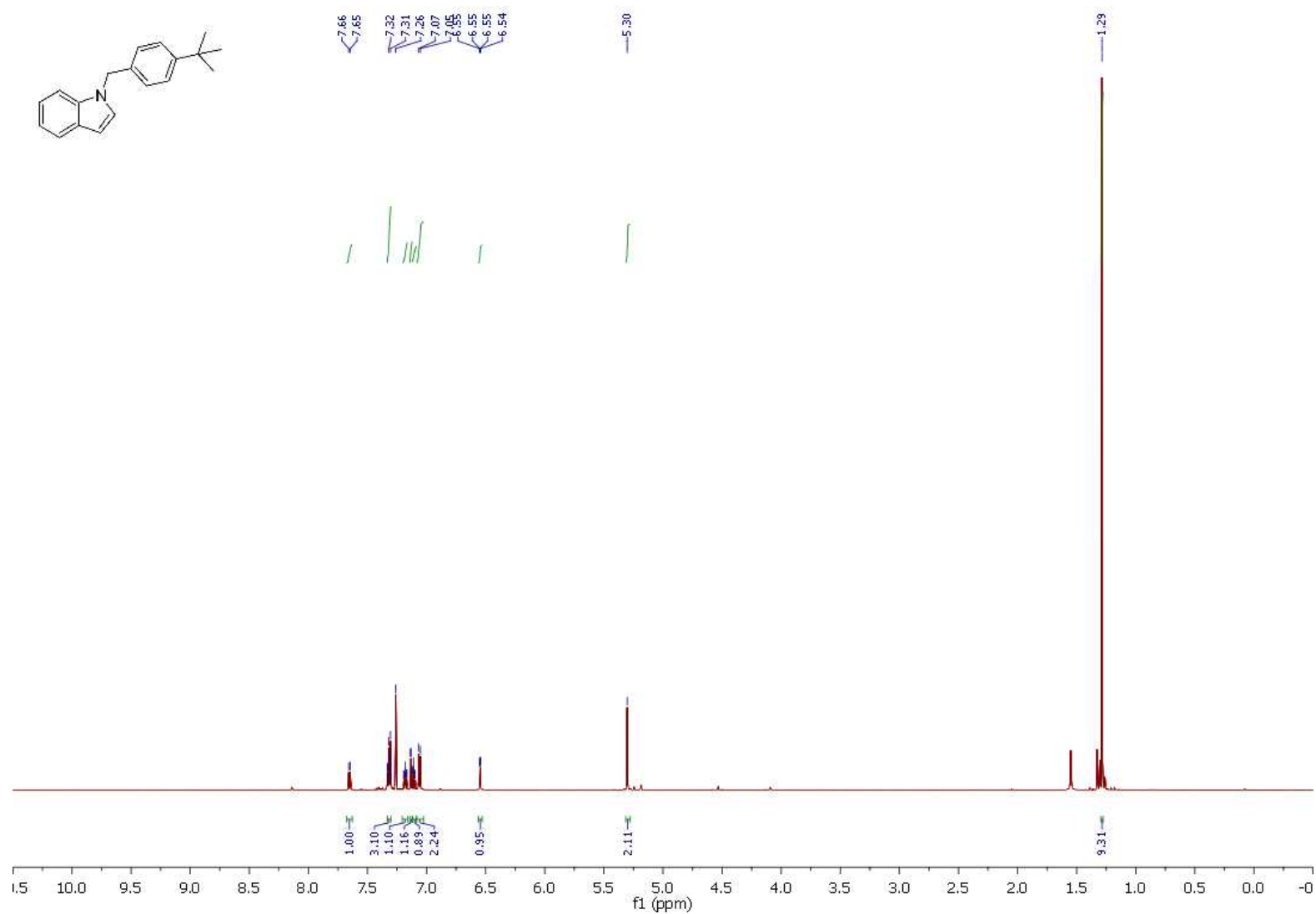
¹H NMR spectrum of compound **1b**



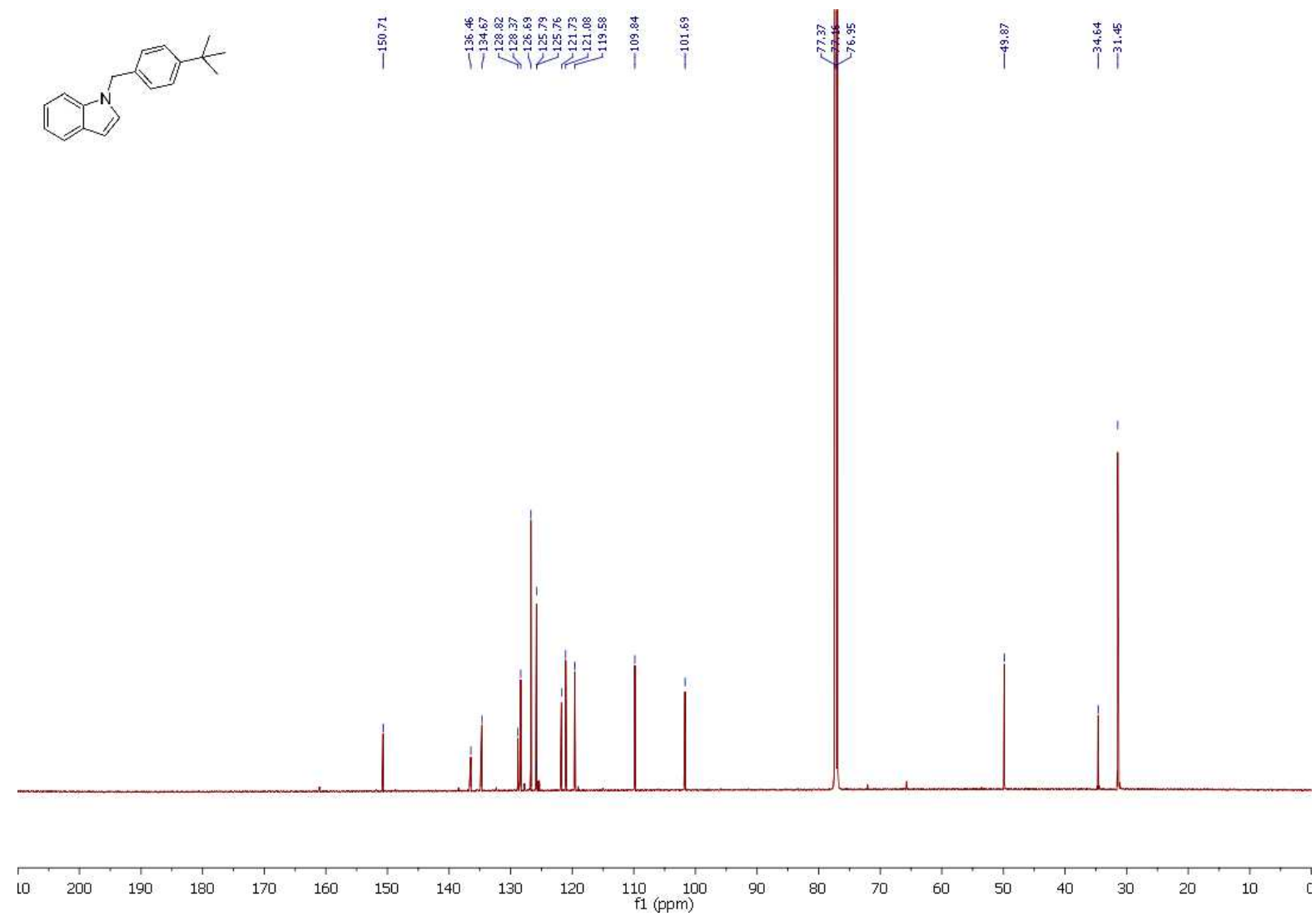
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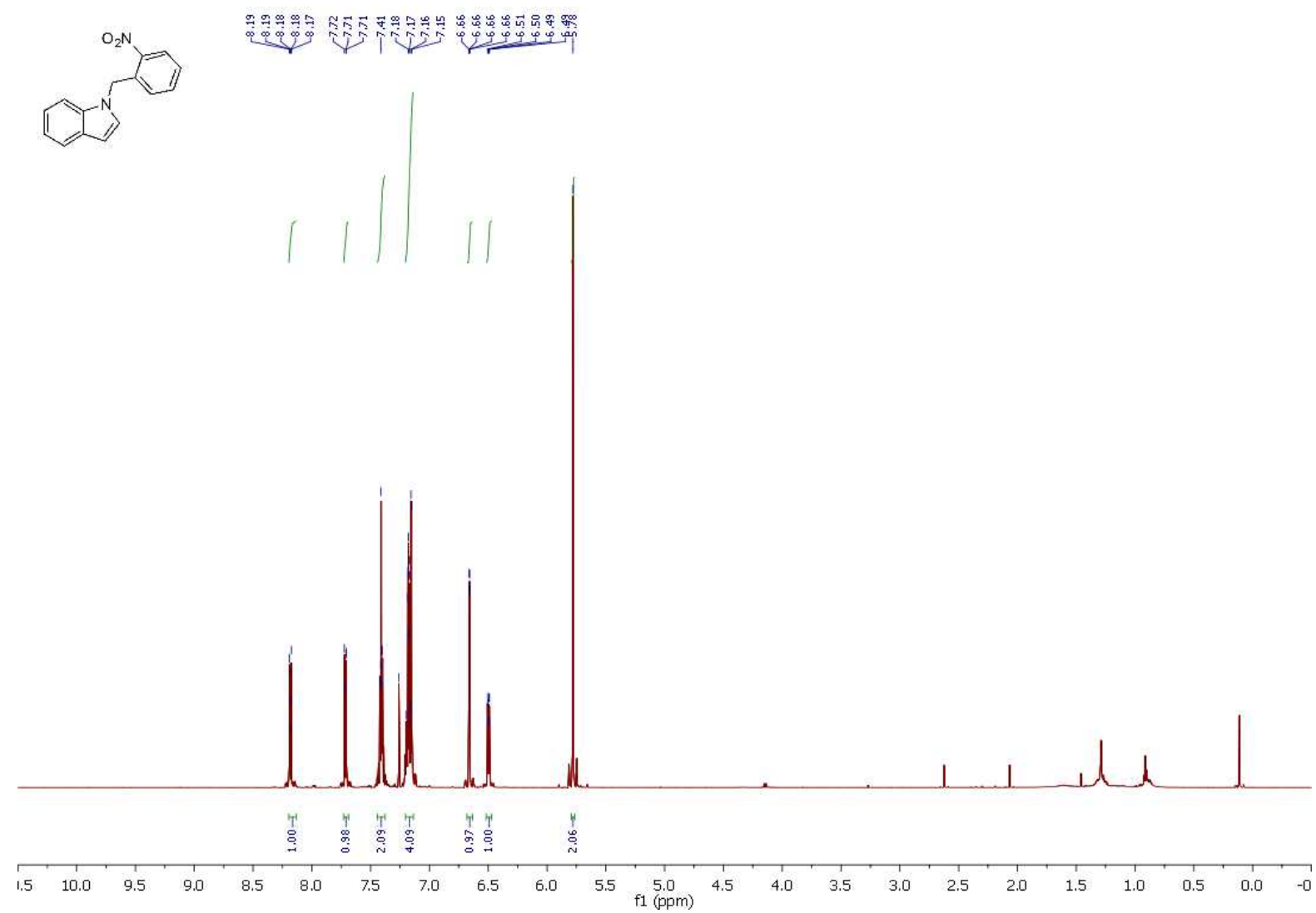
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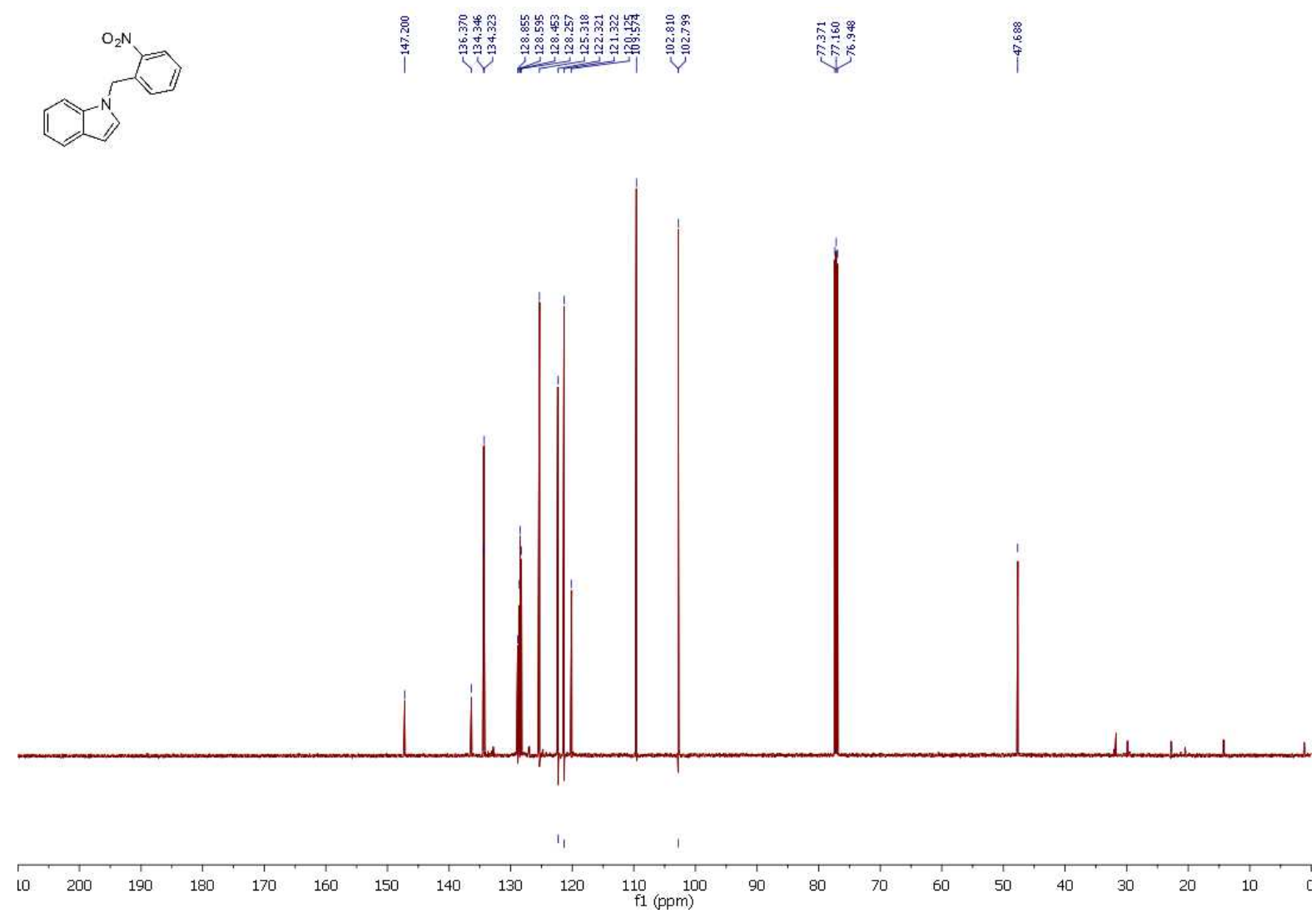
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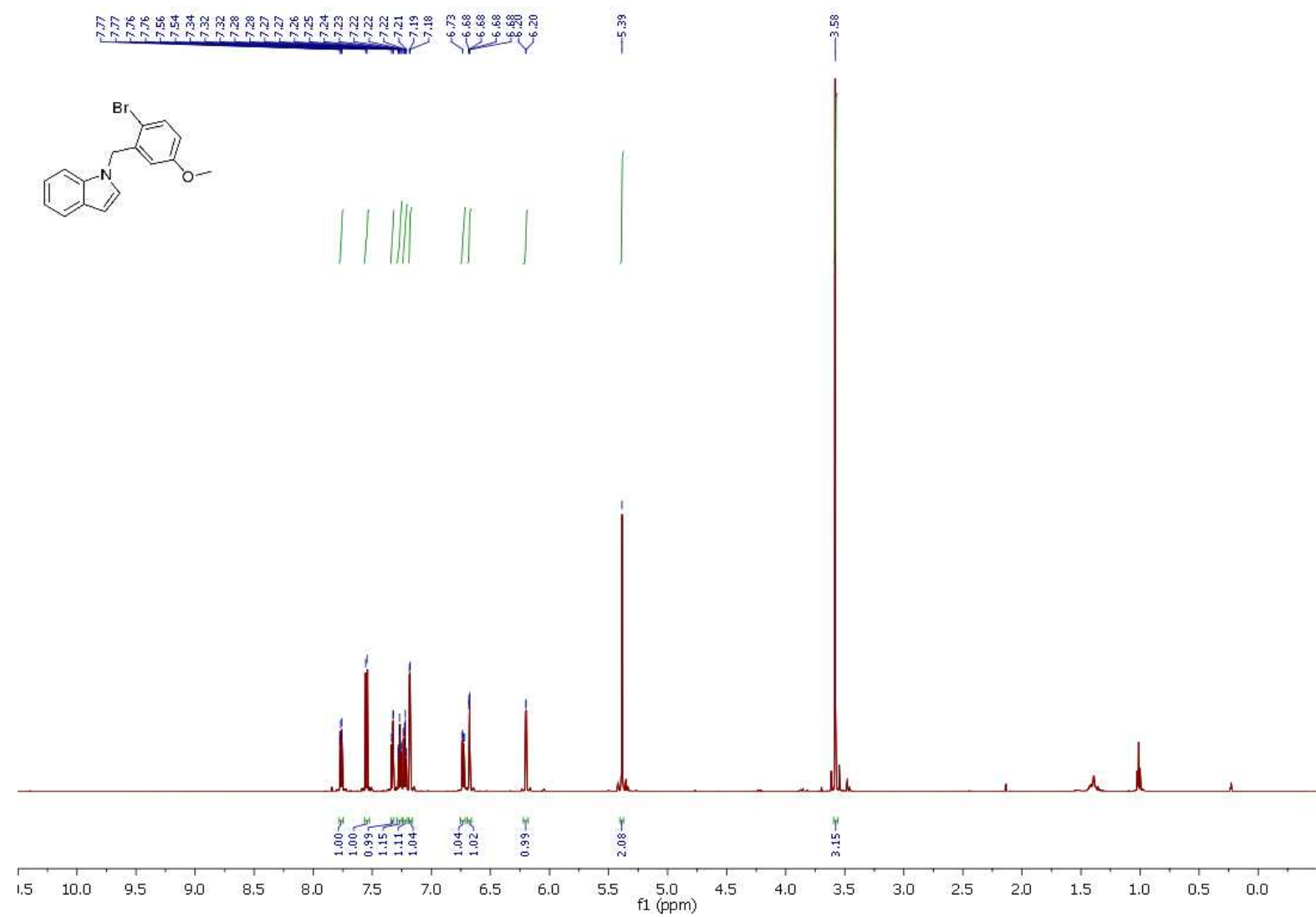
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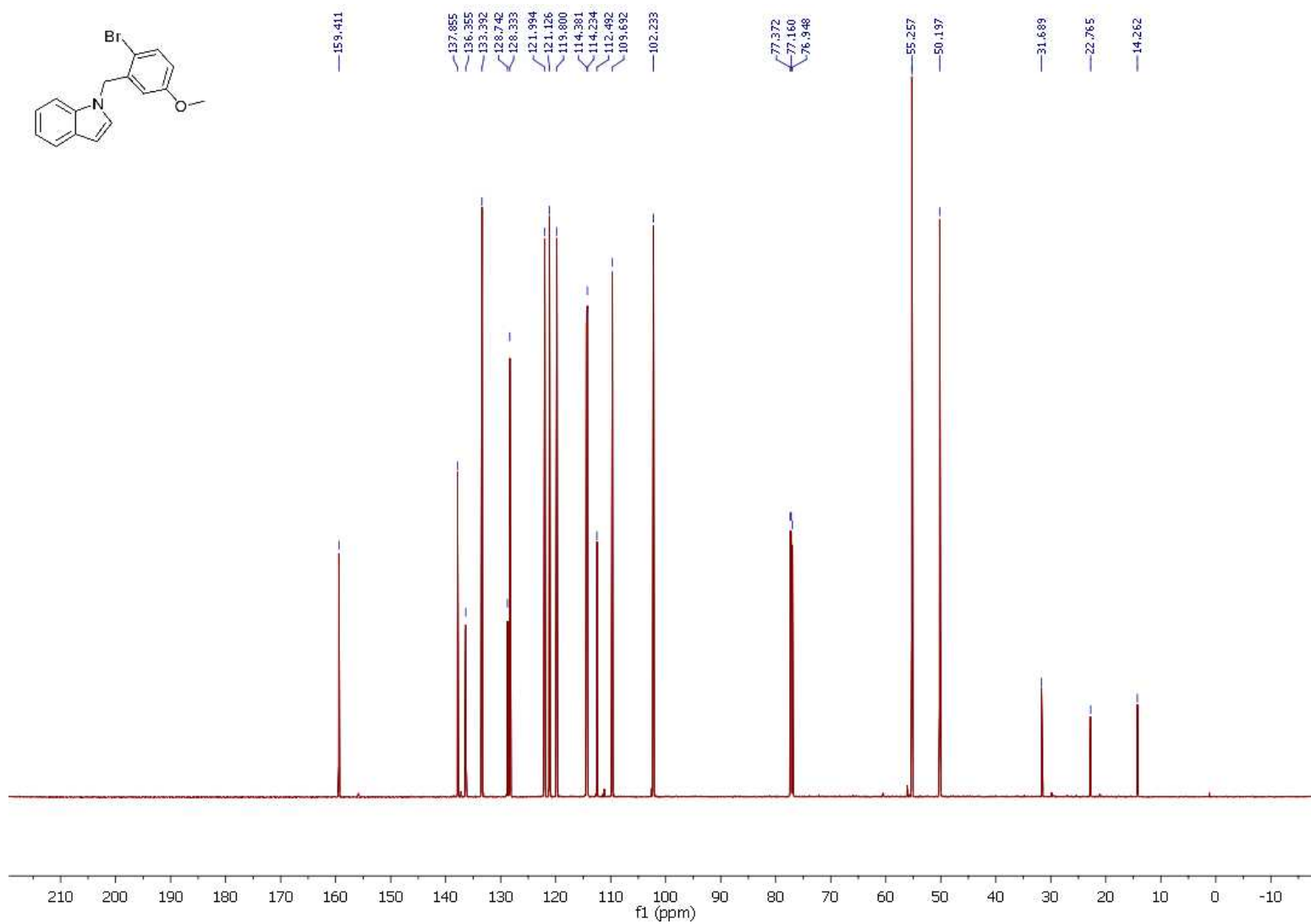
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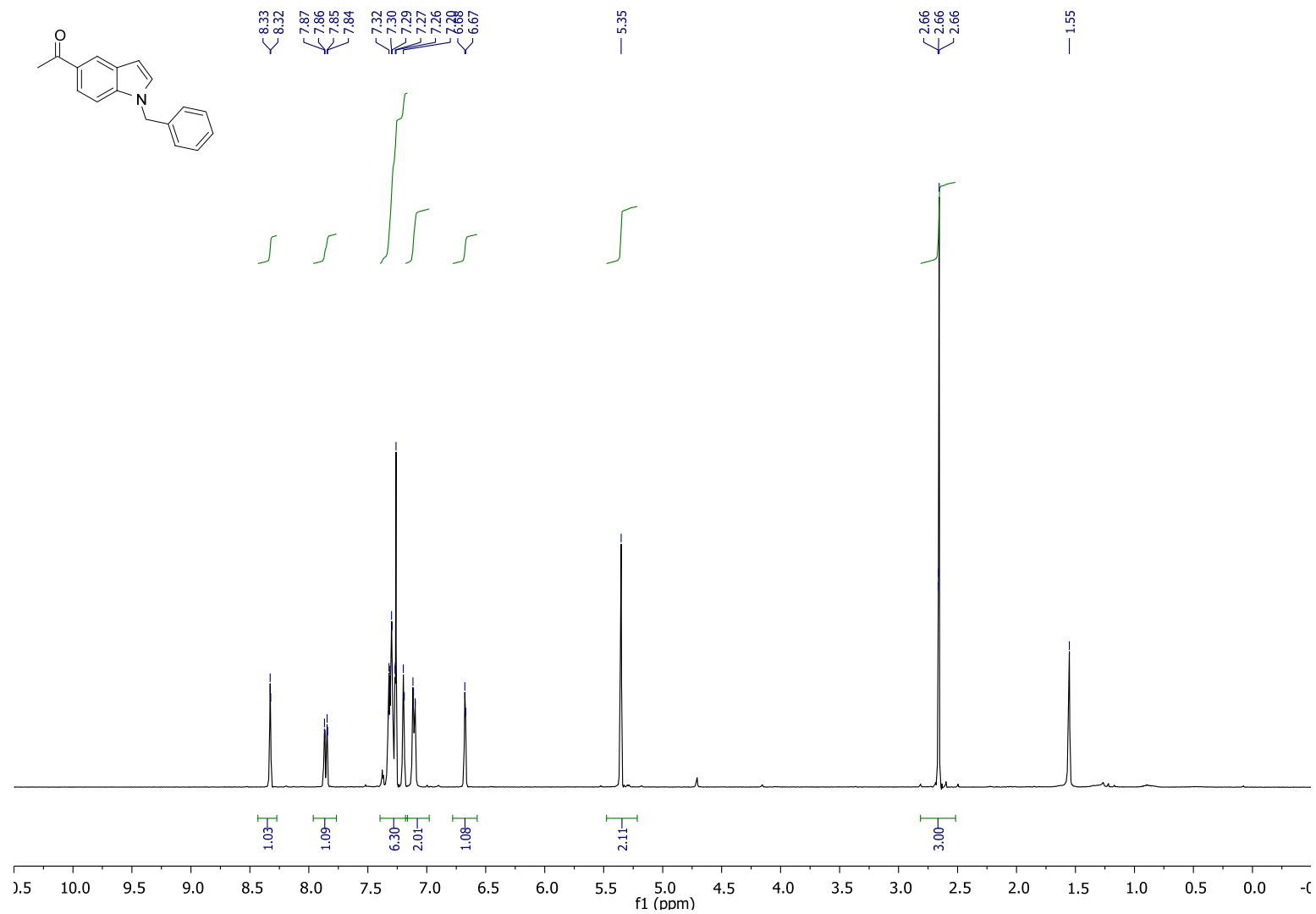
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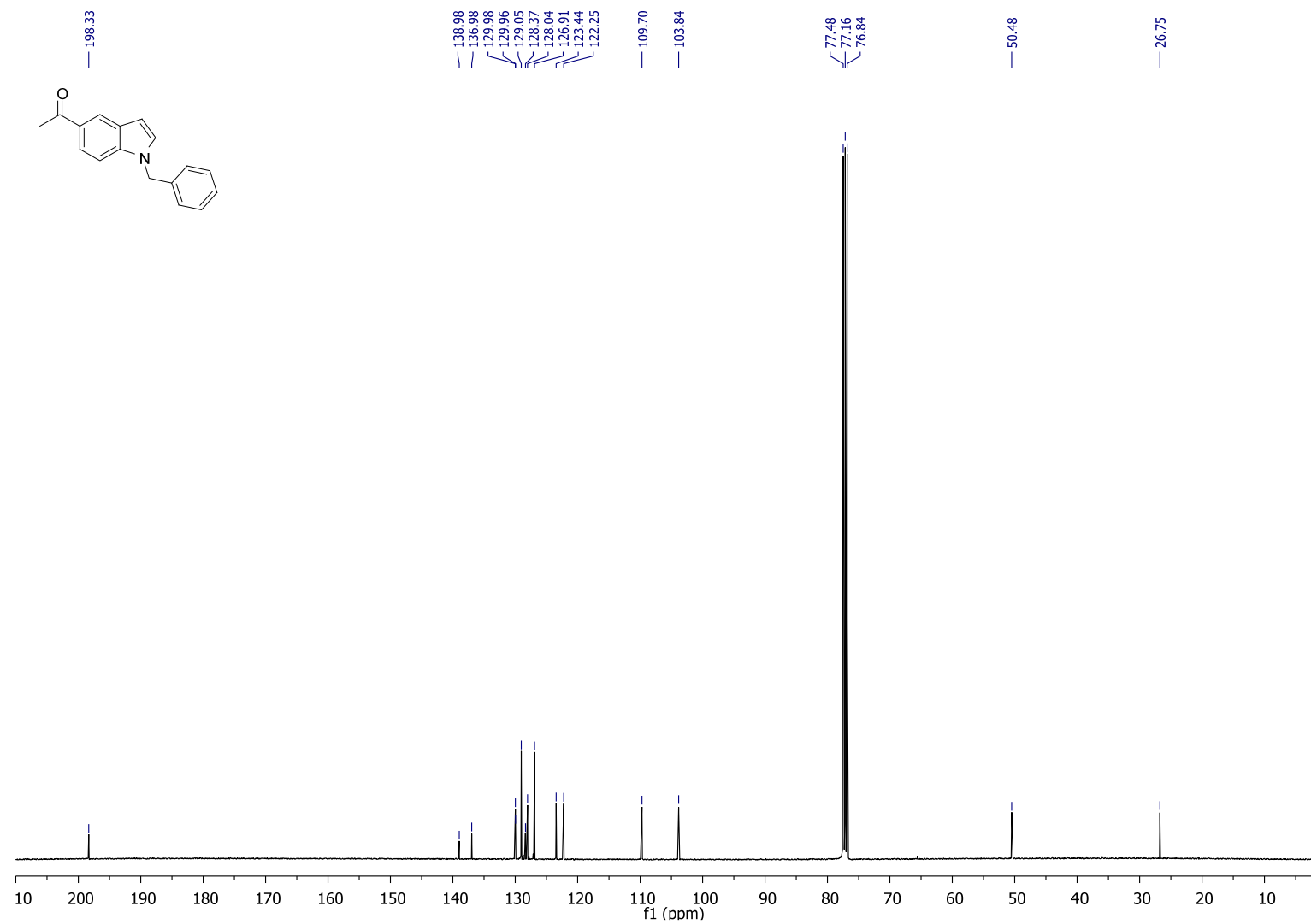
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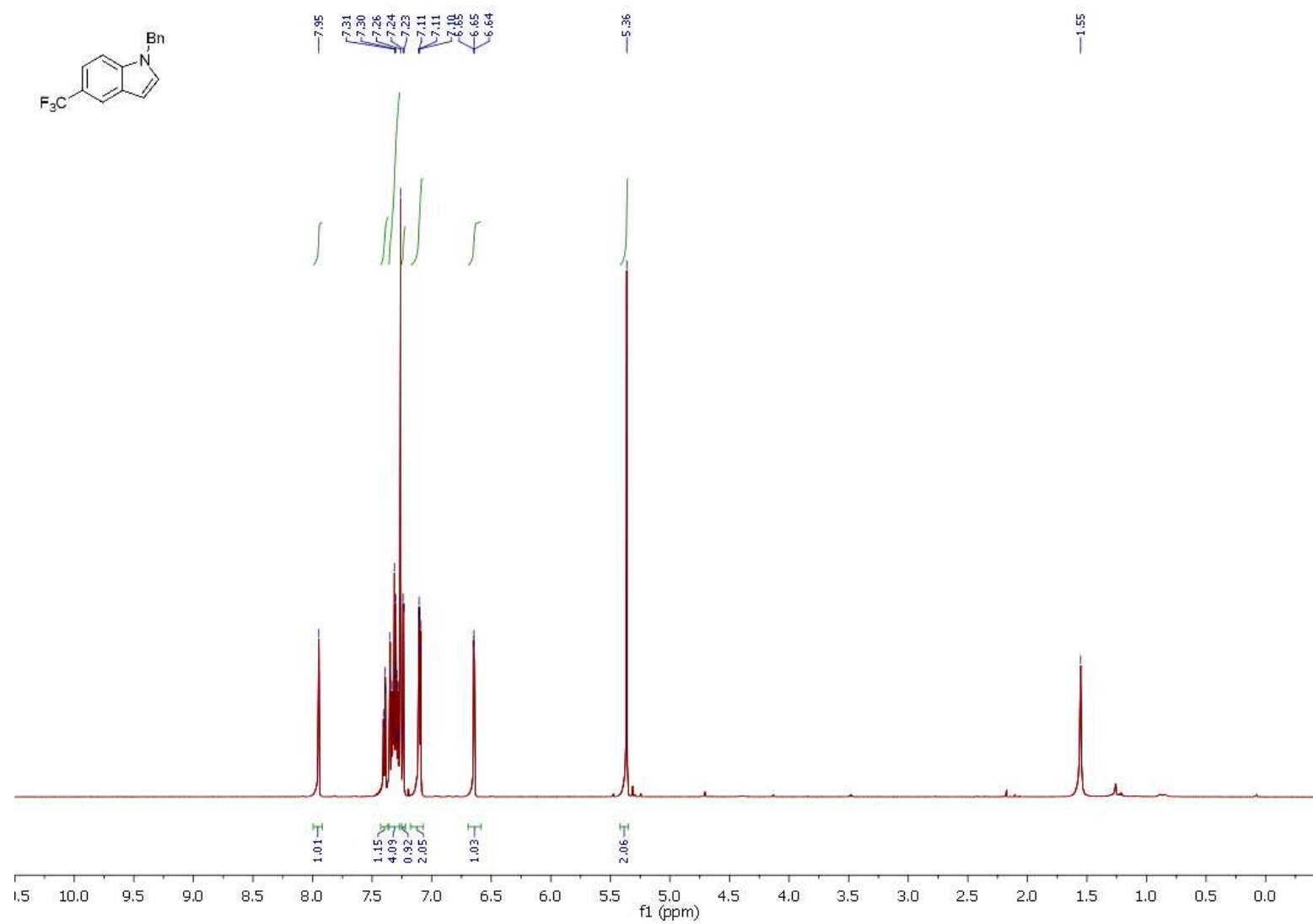
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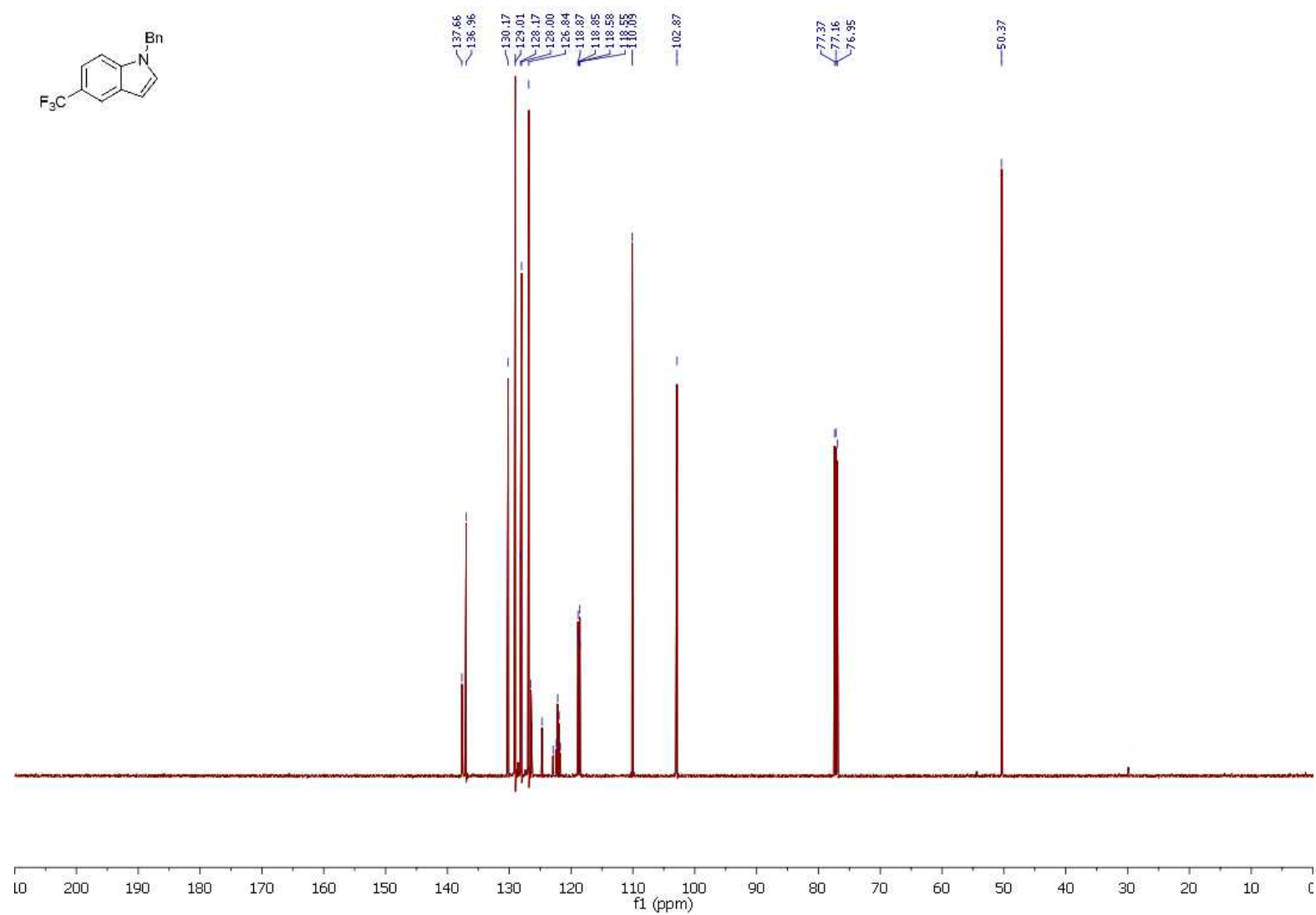
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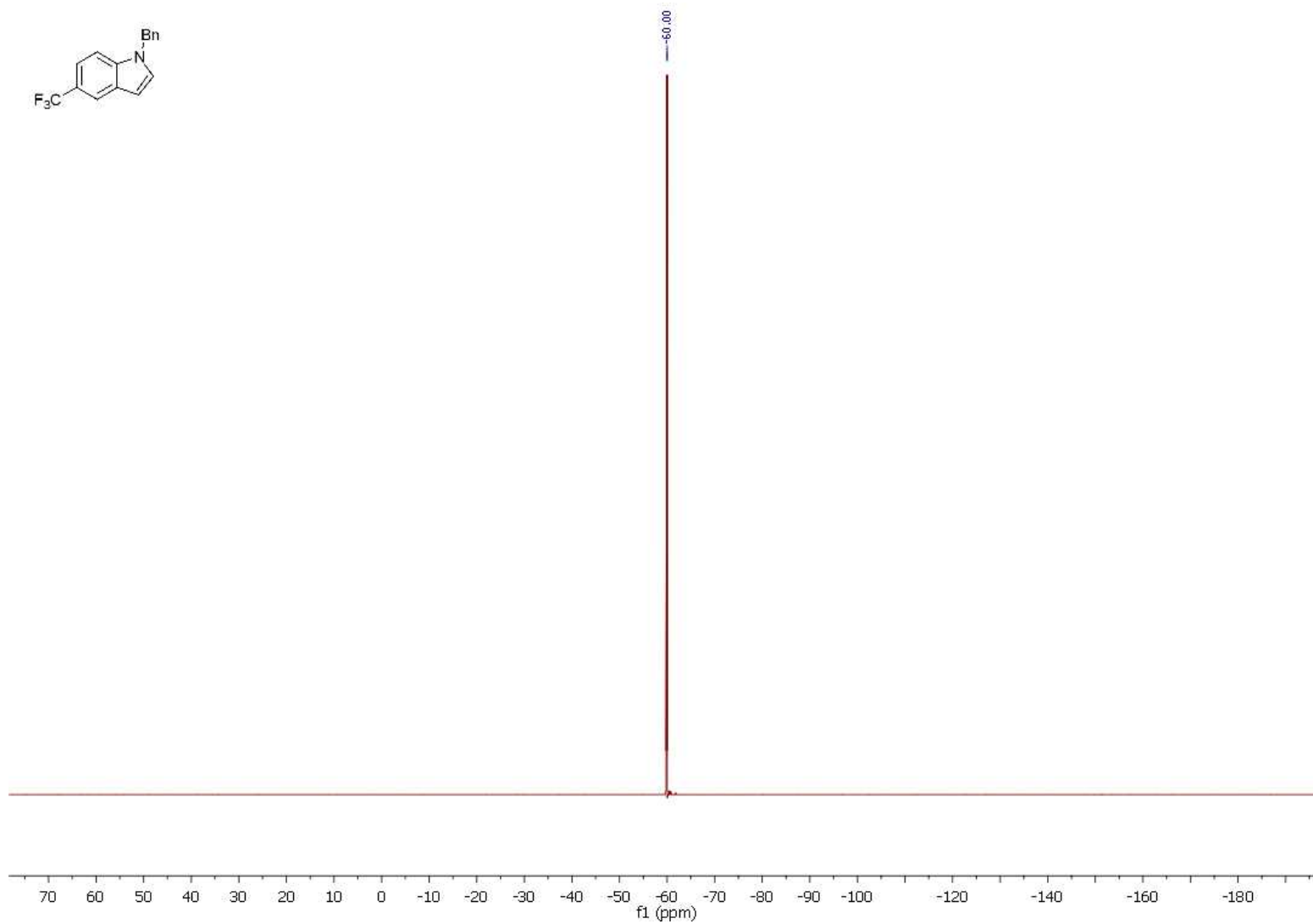
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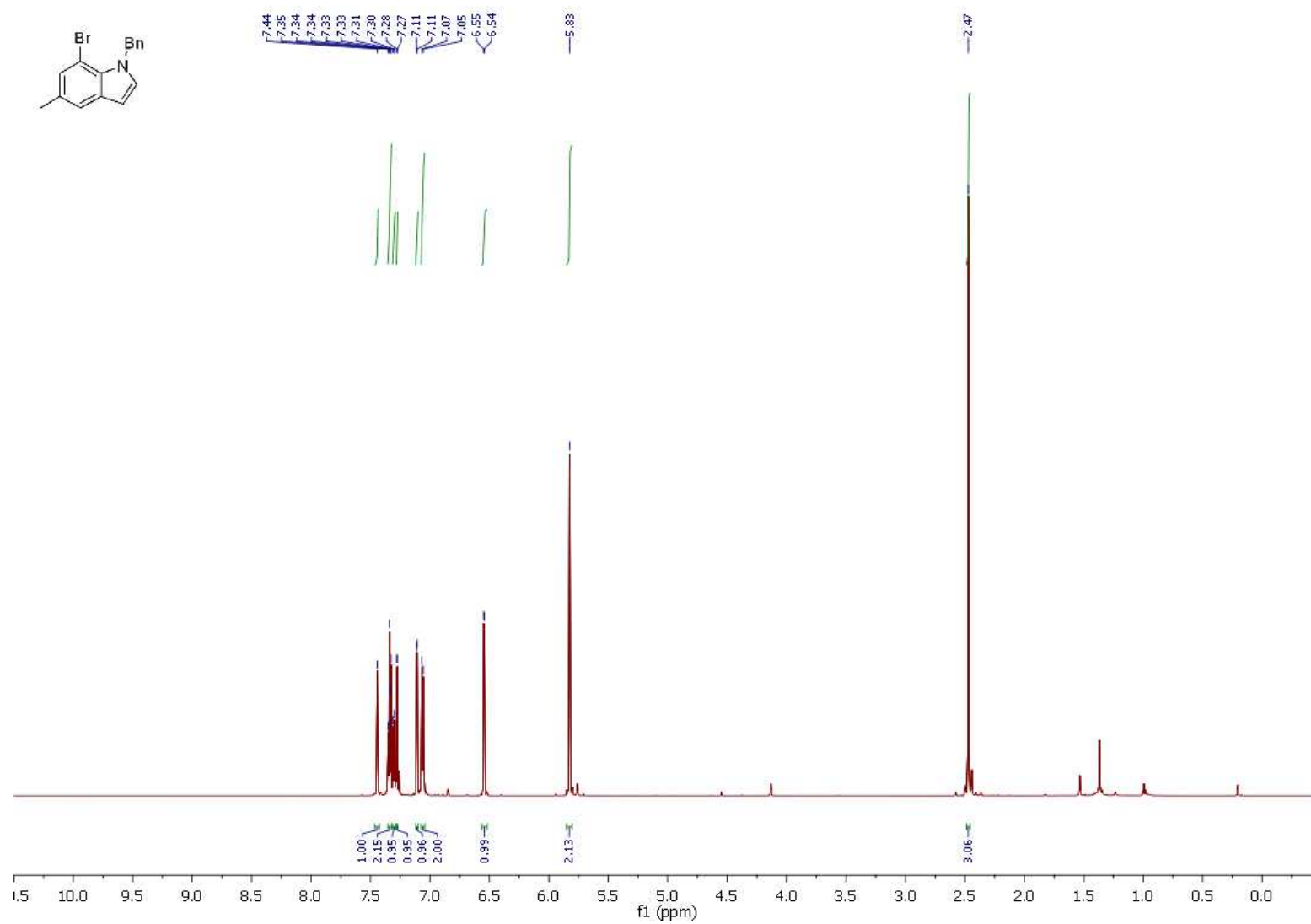
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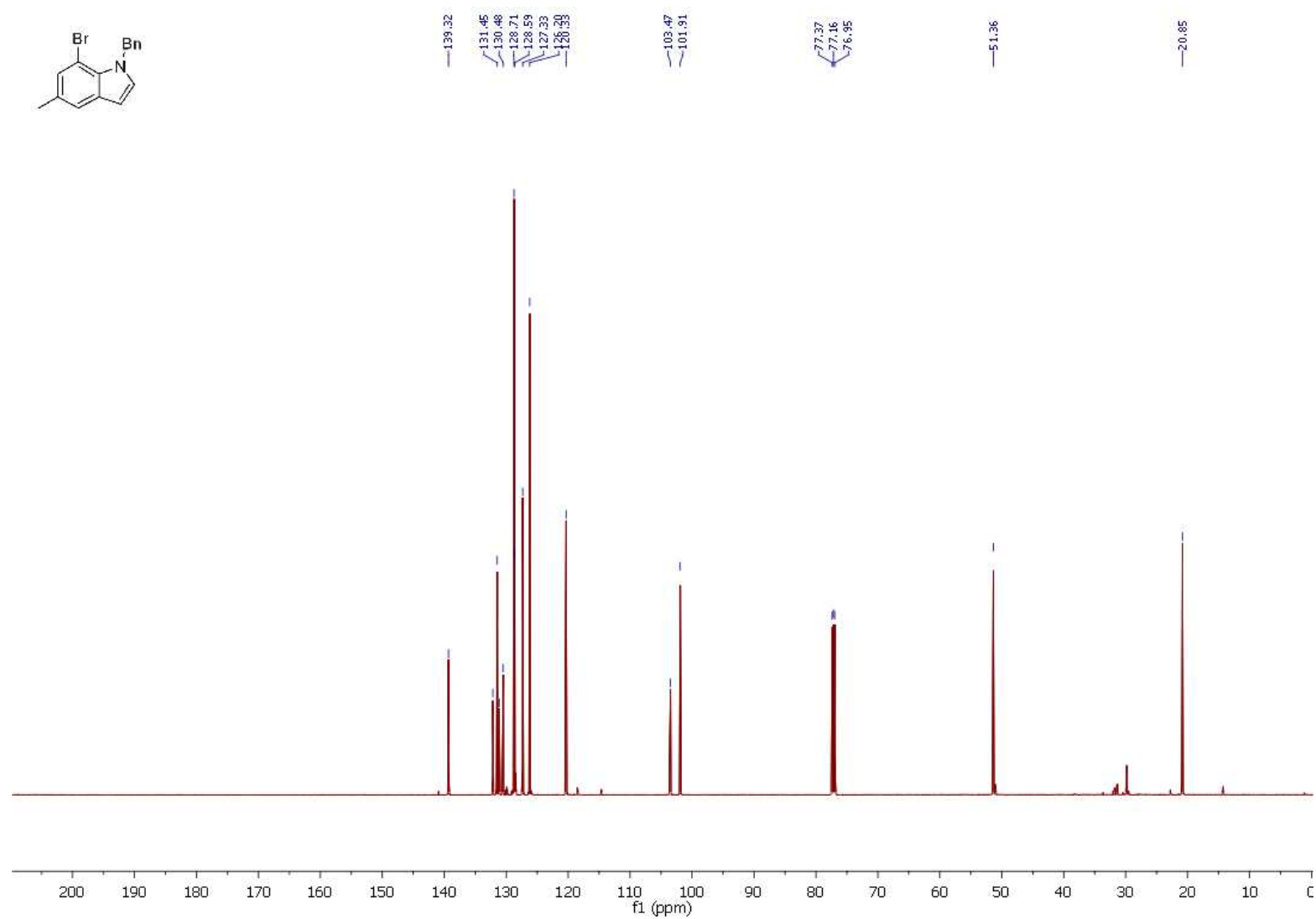
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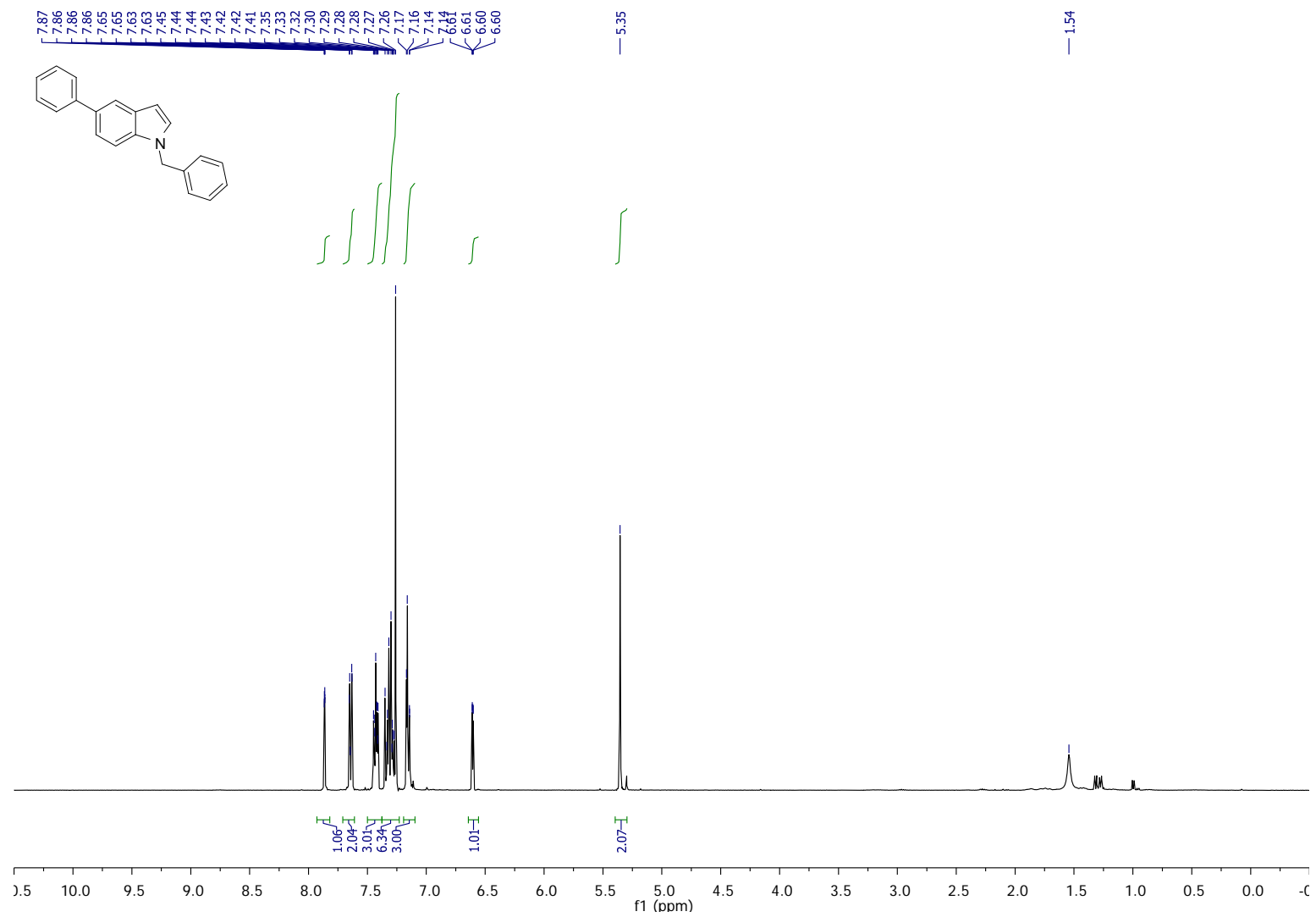
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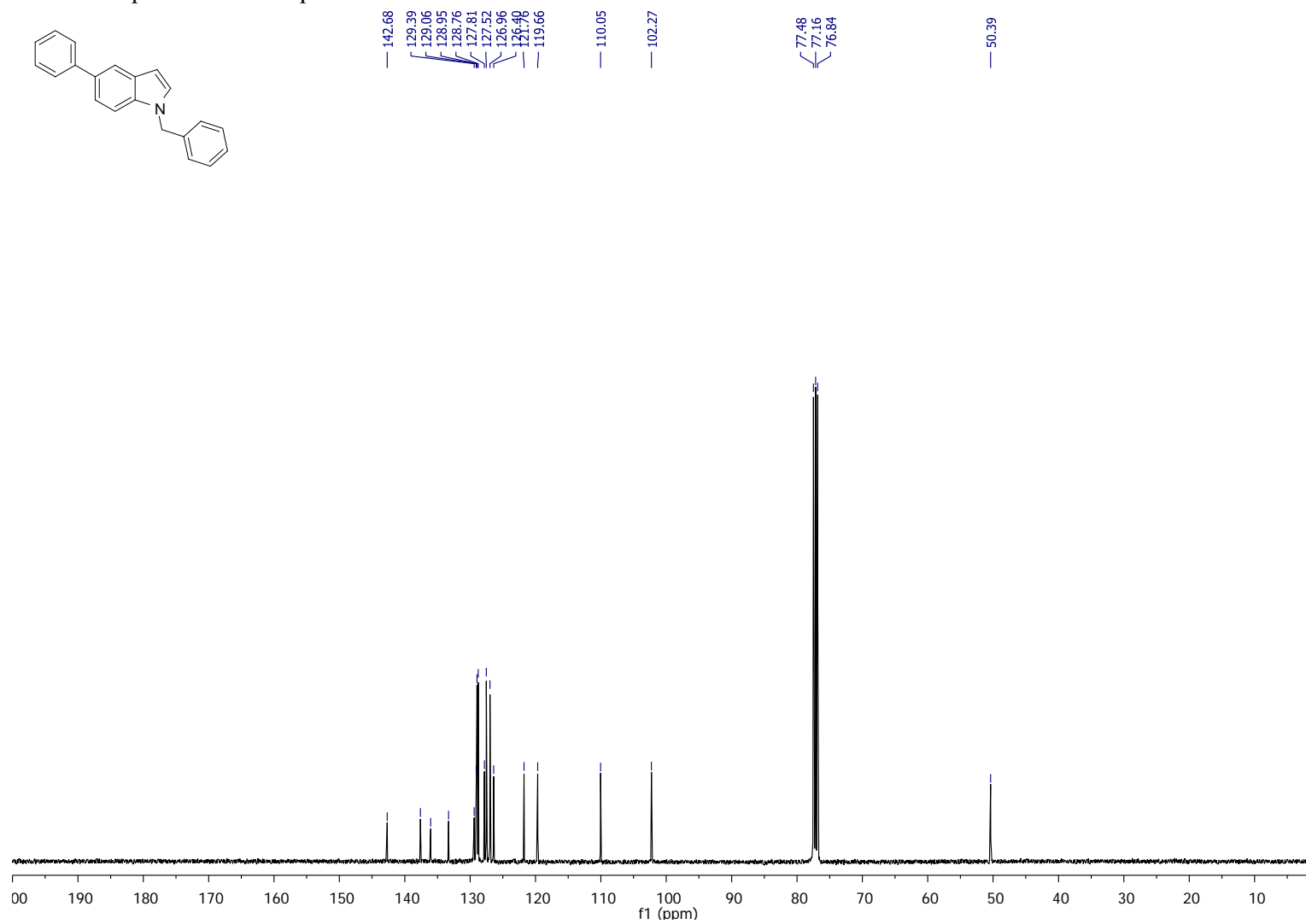
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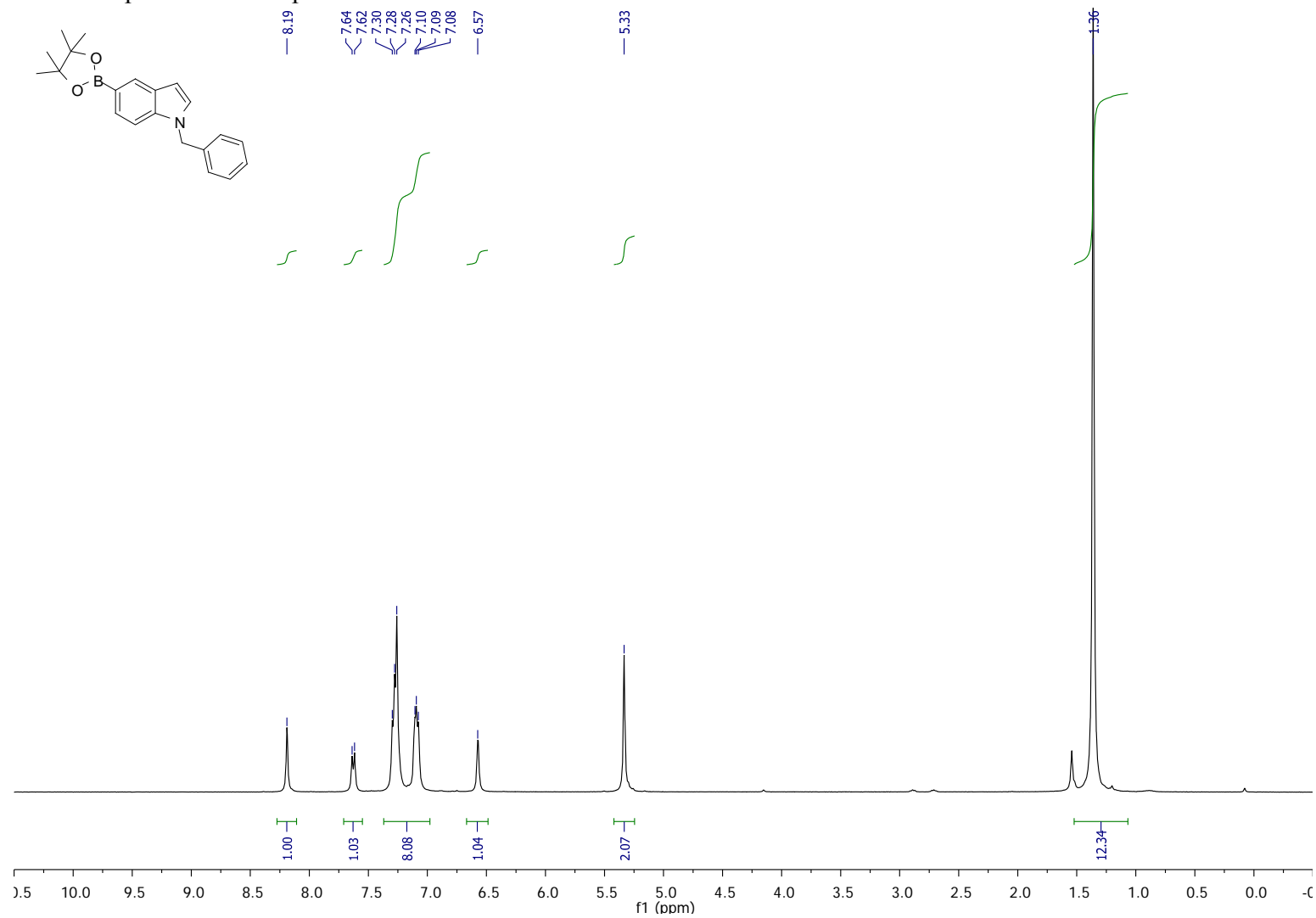
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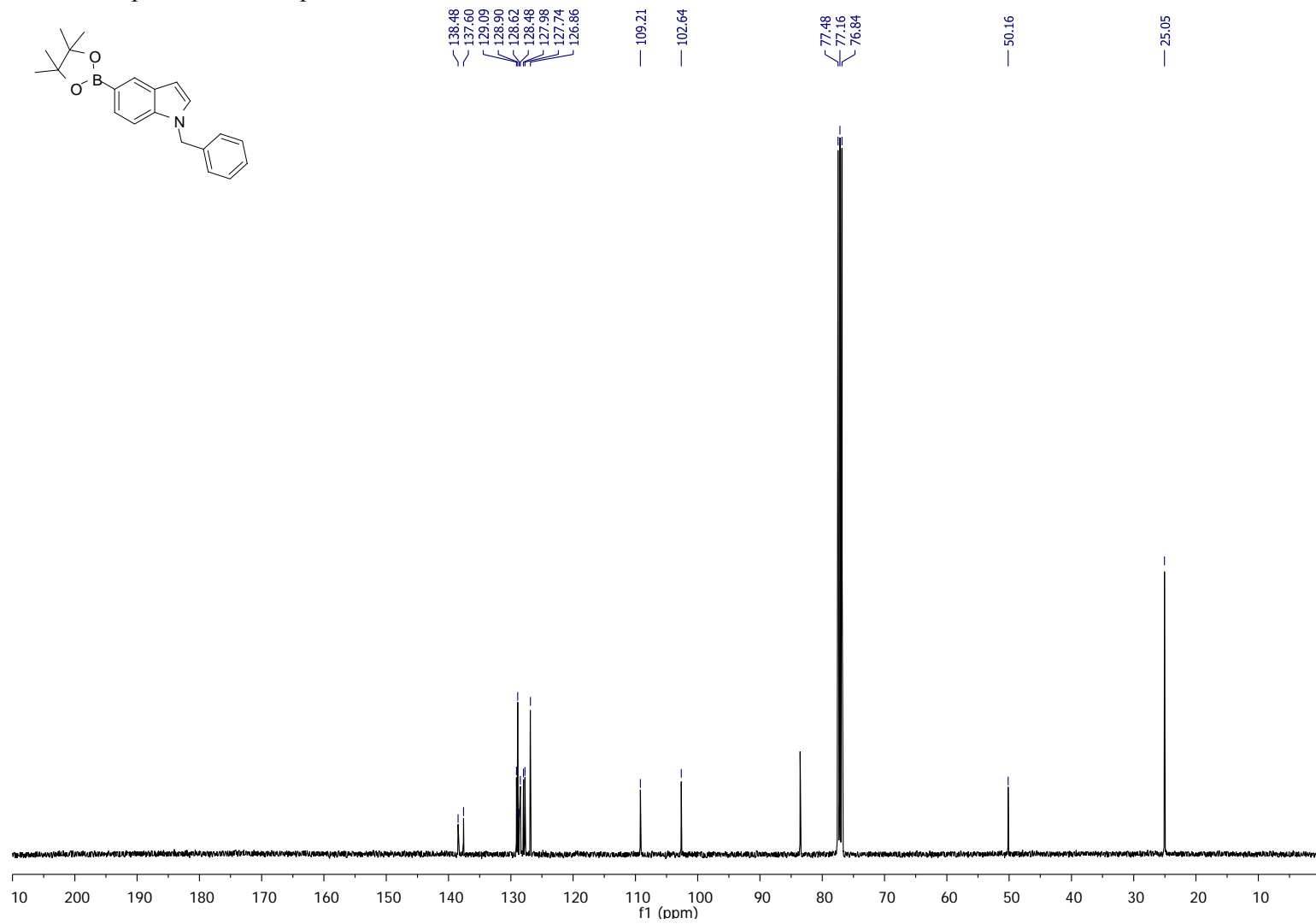
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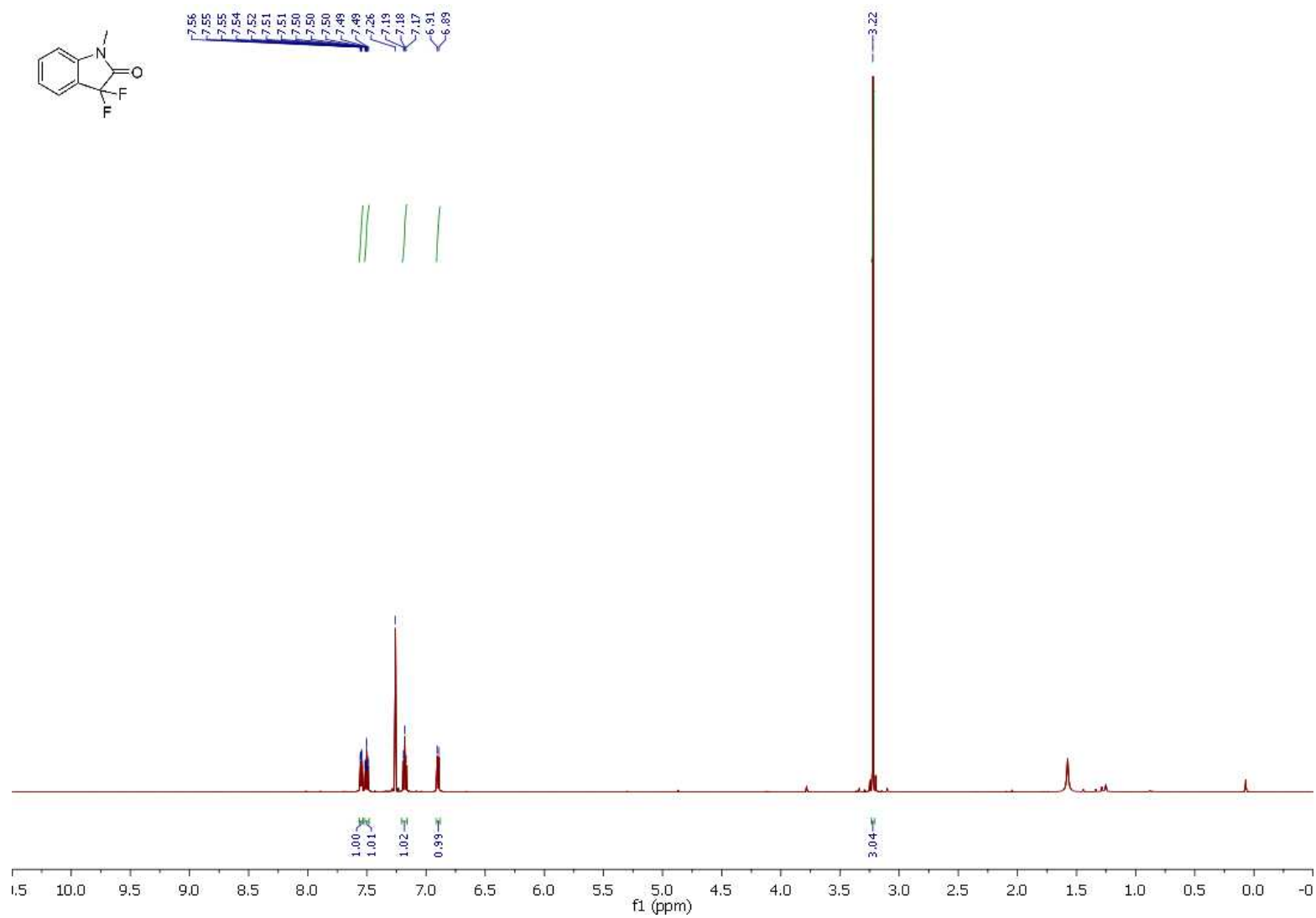
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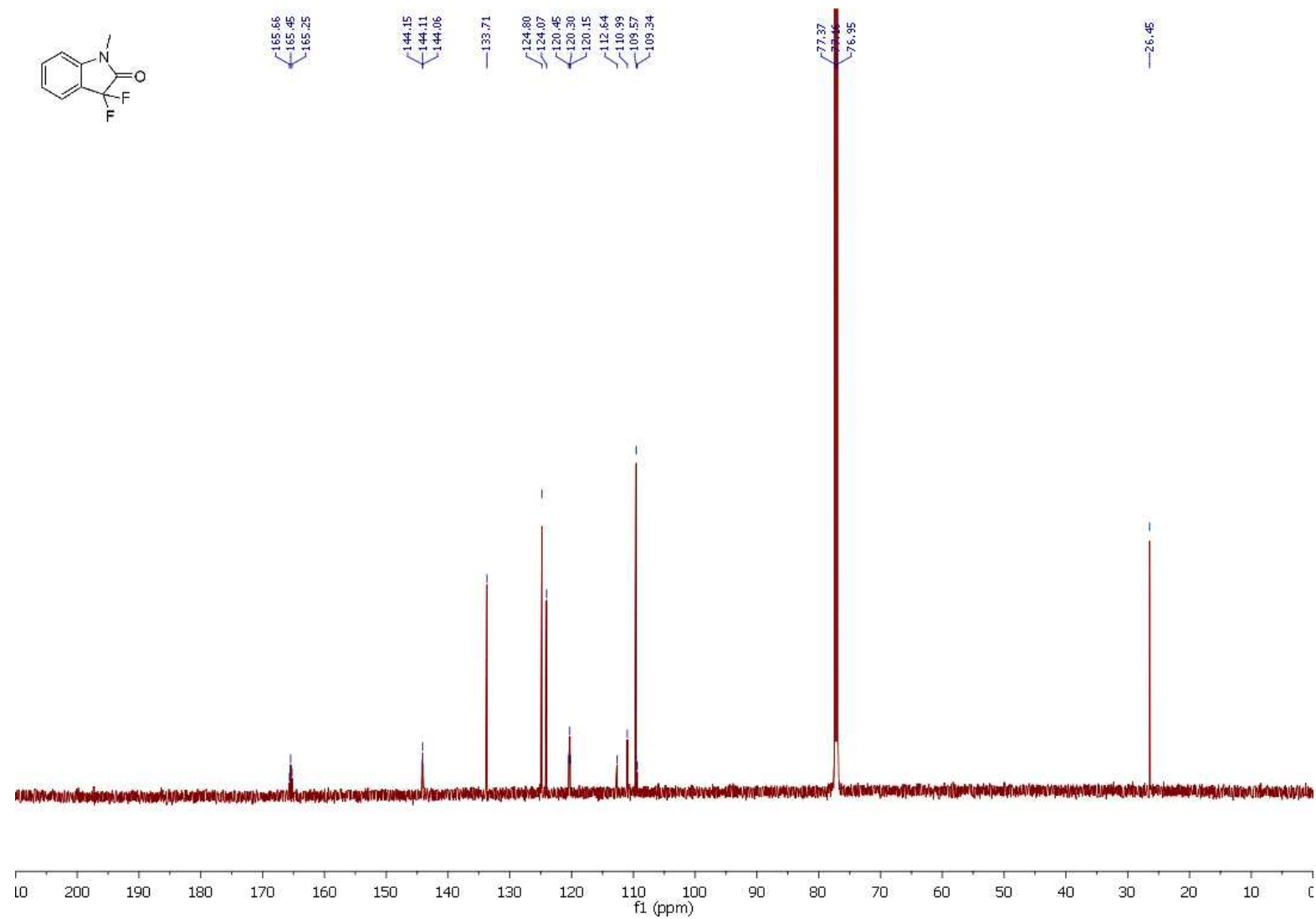
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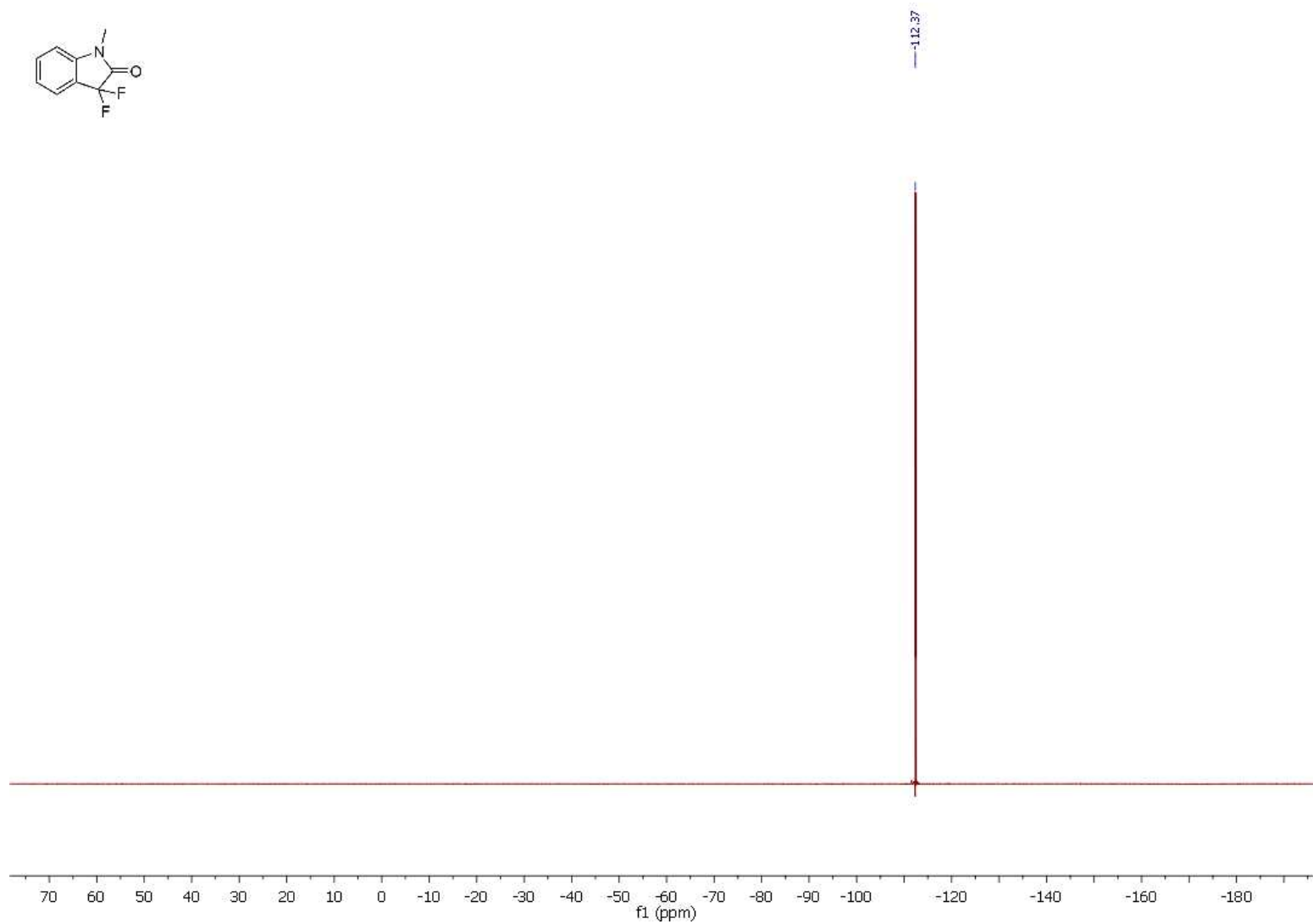
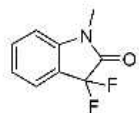
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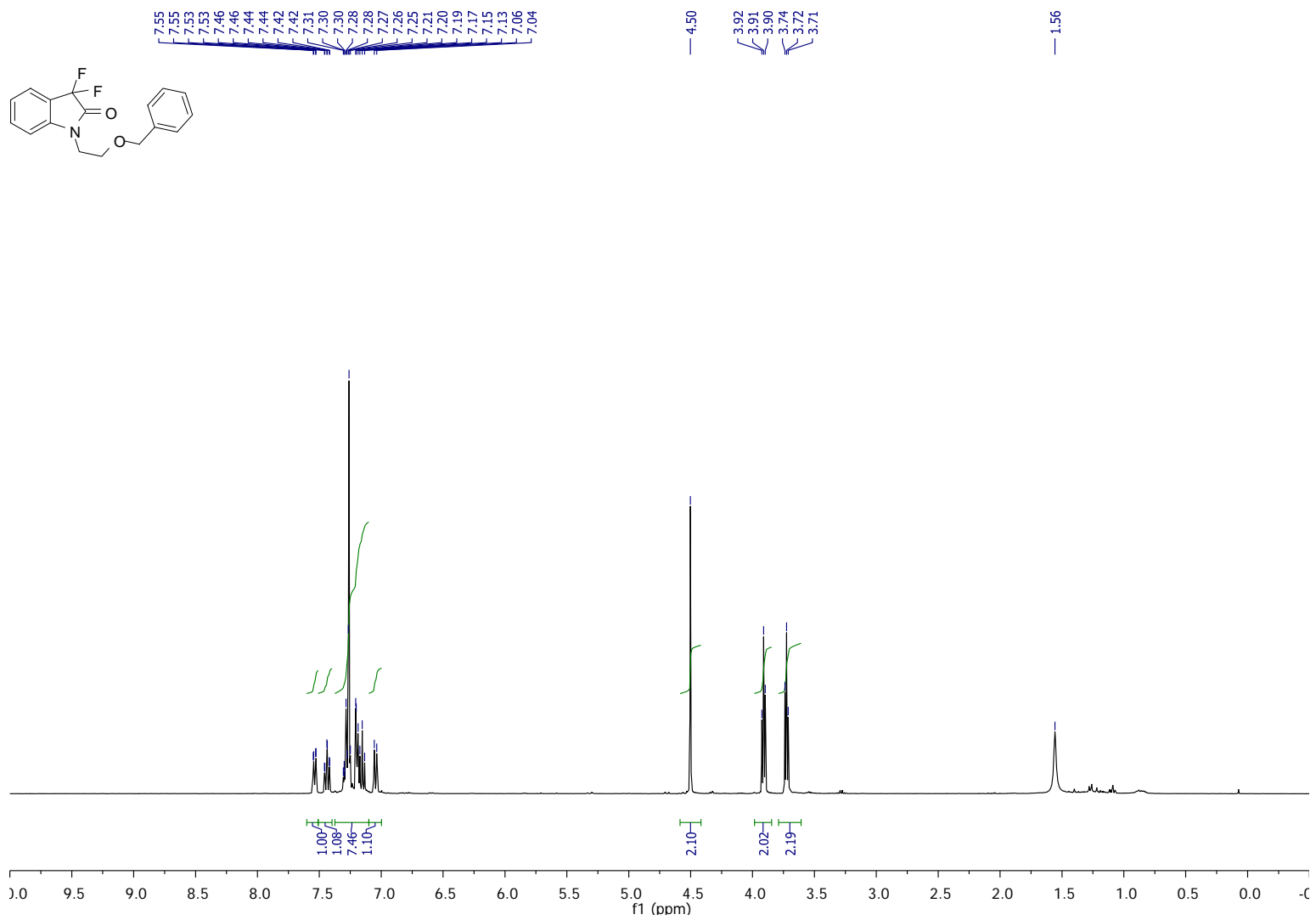
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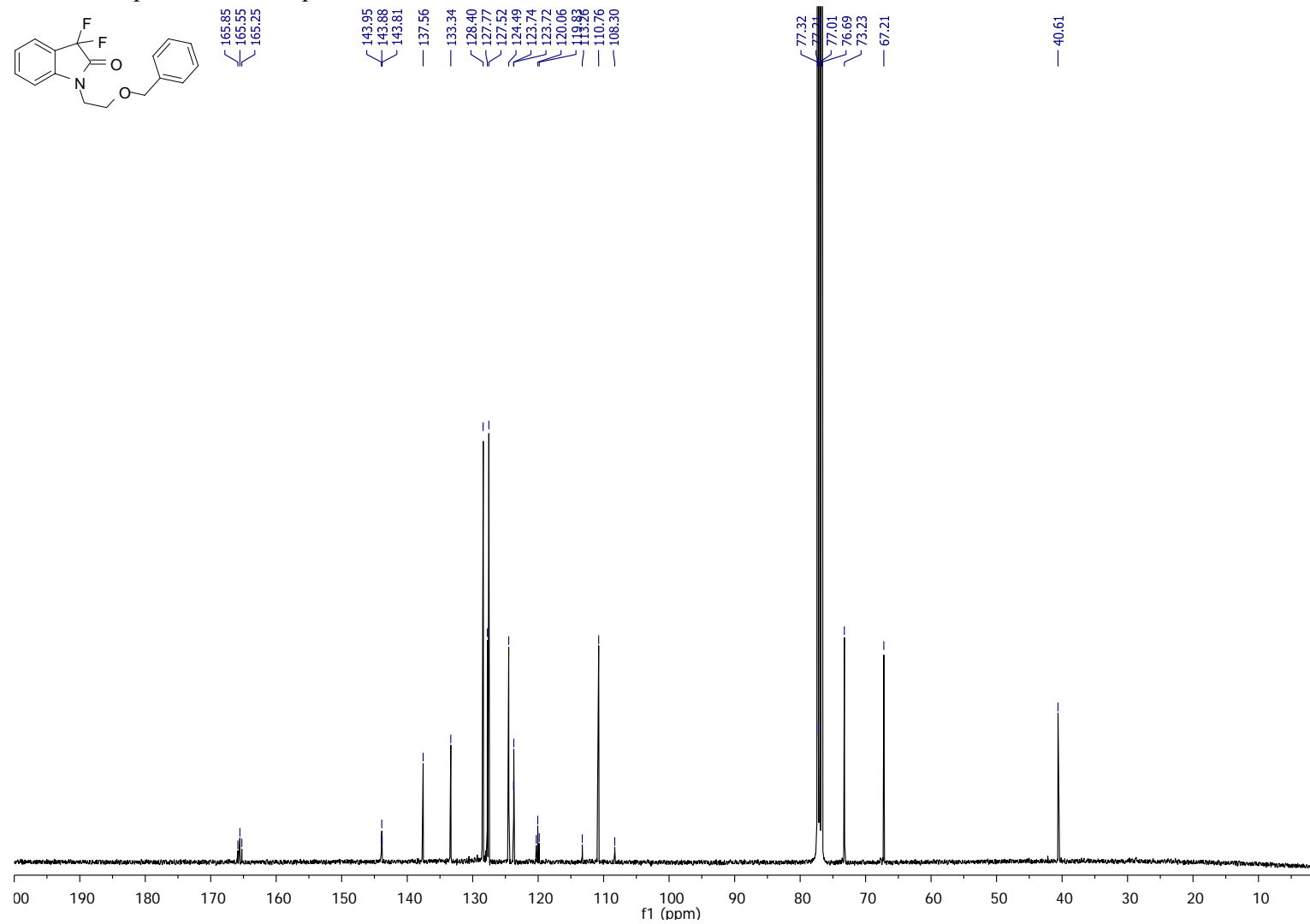
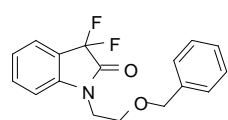
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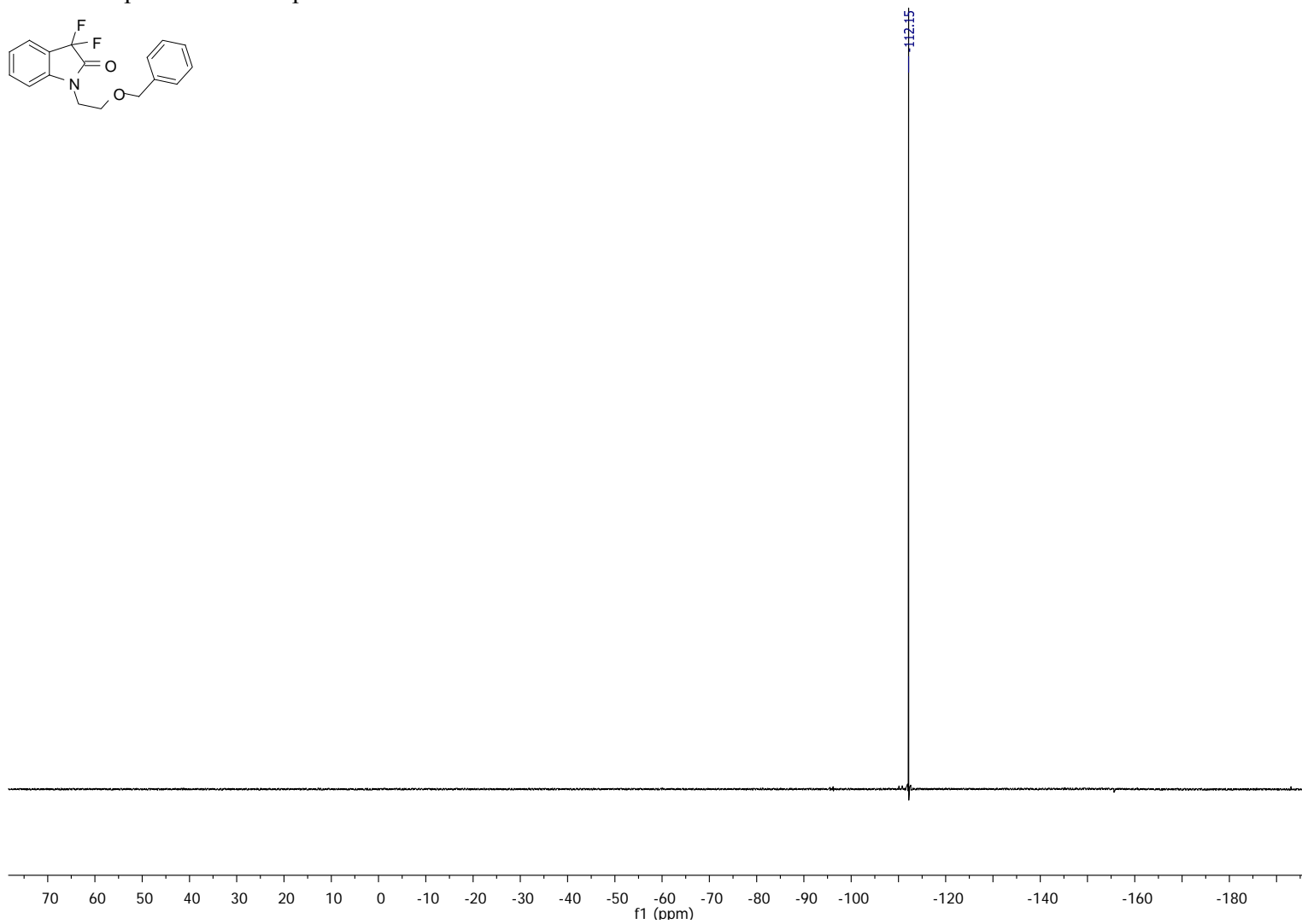
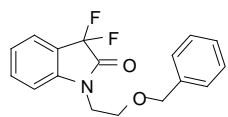
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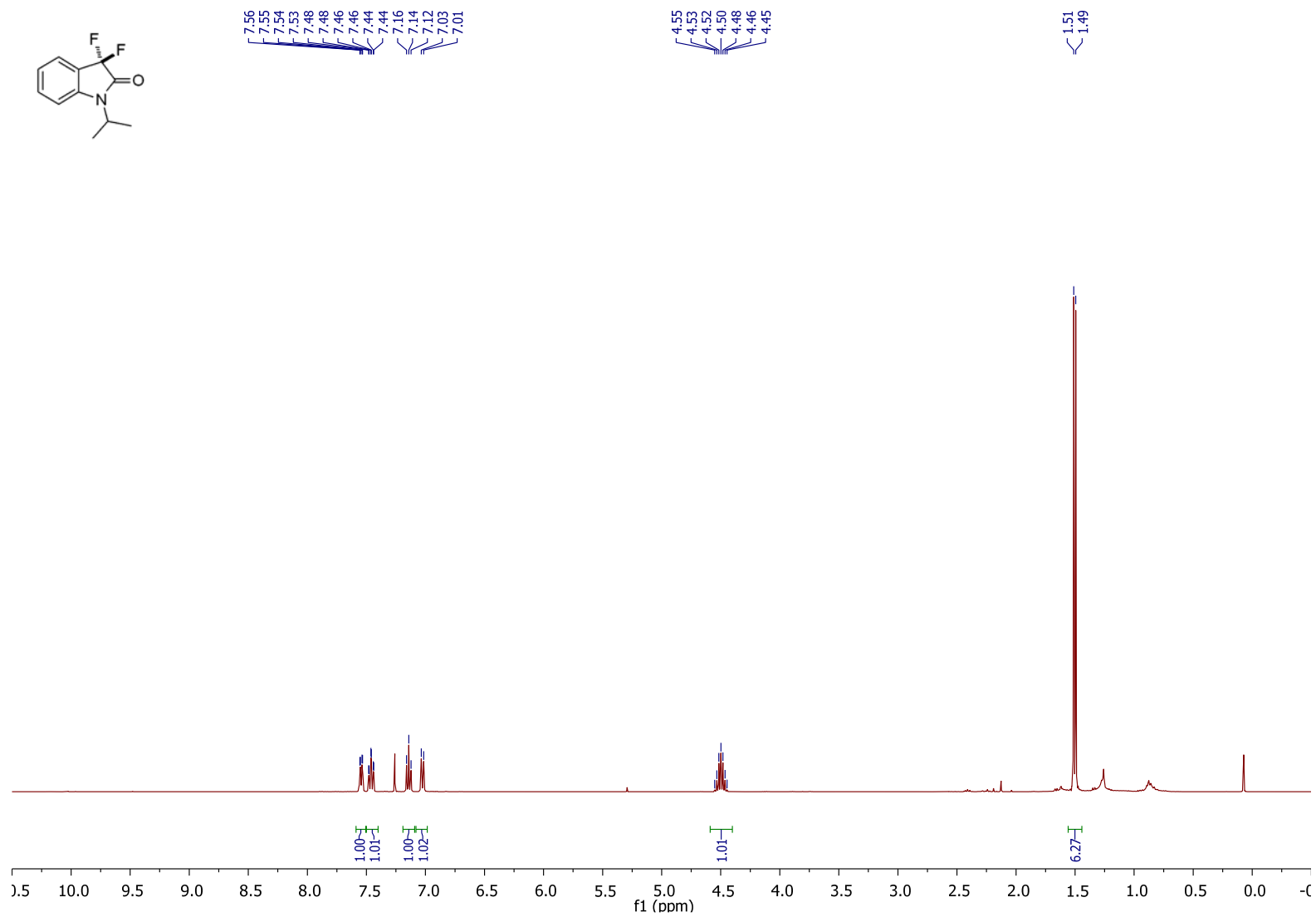
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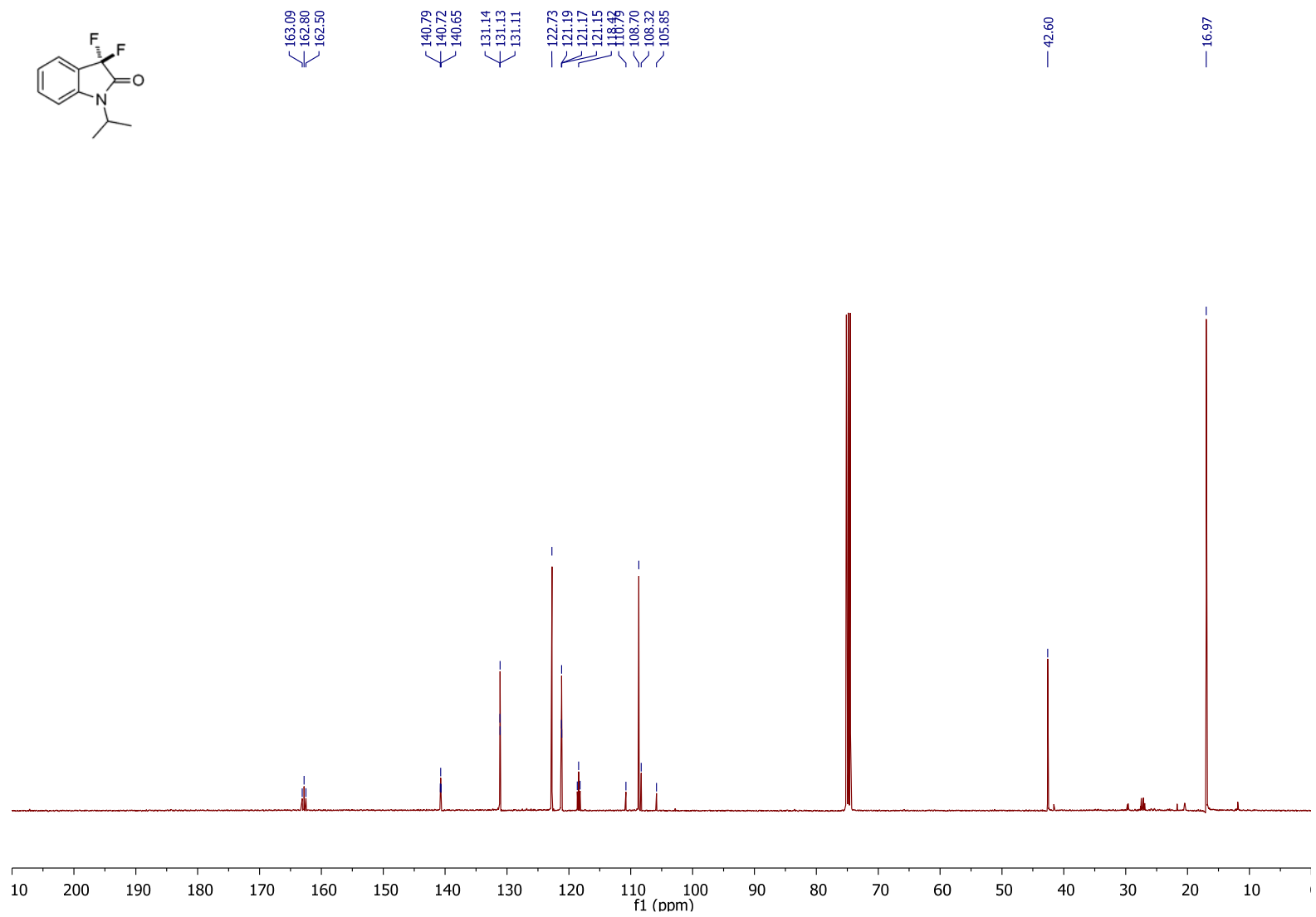
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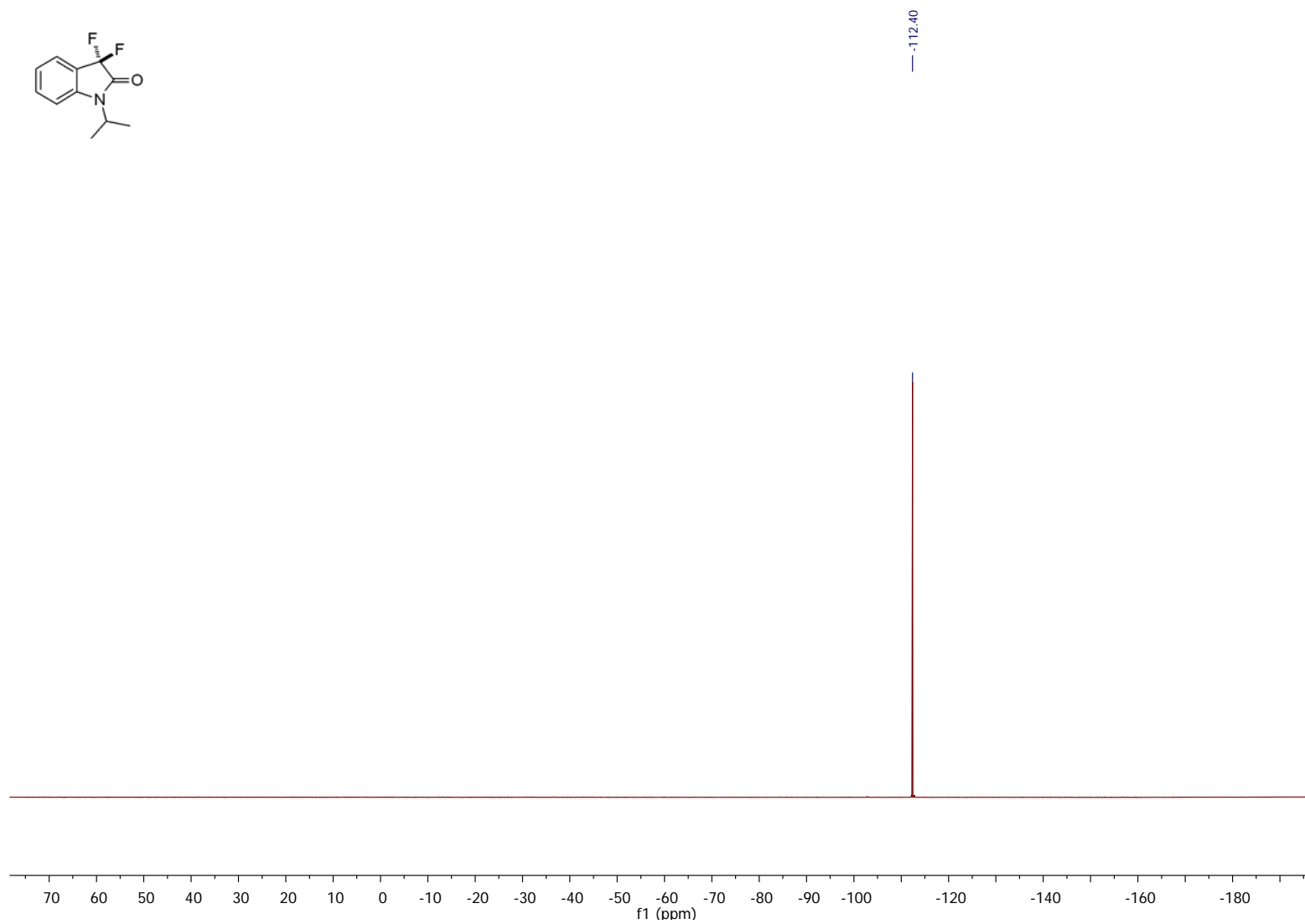
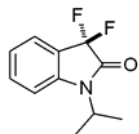
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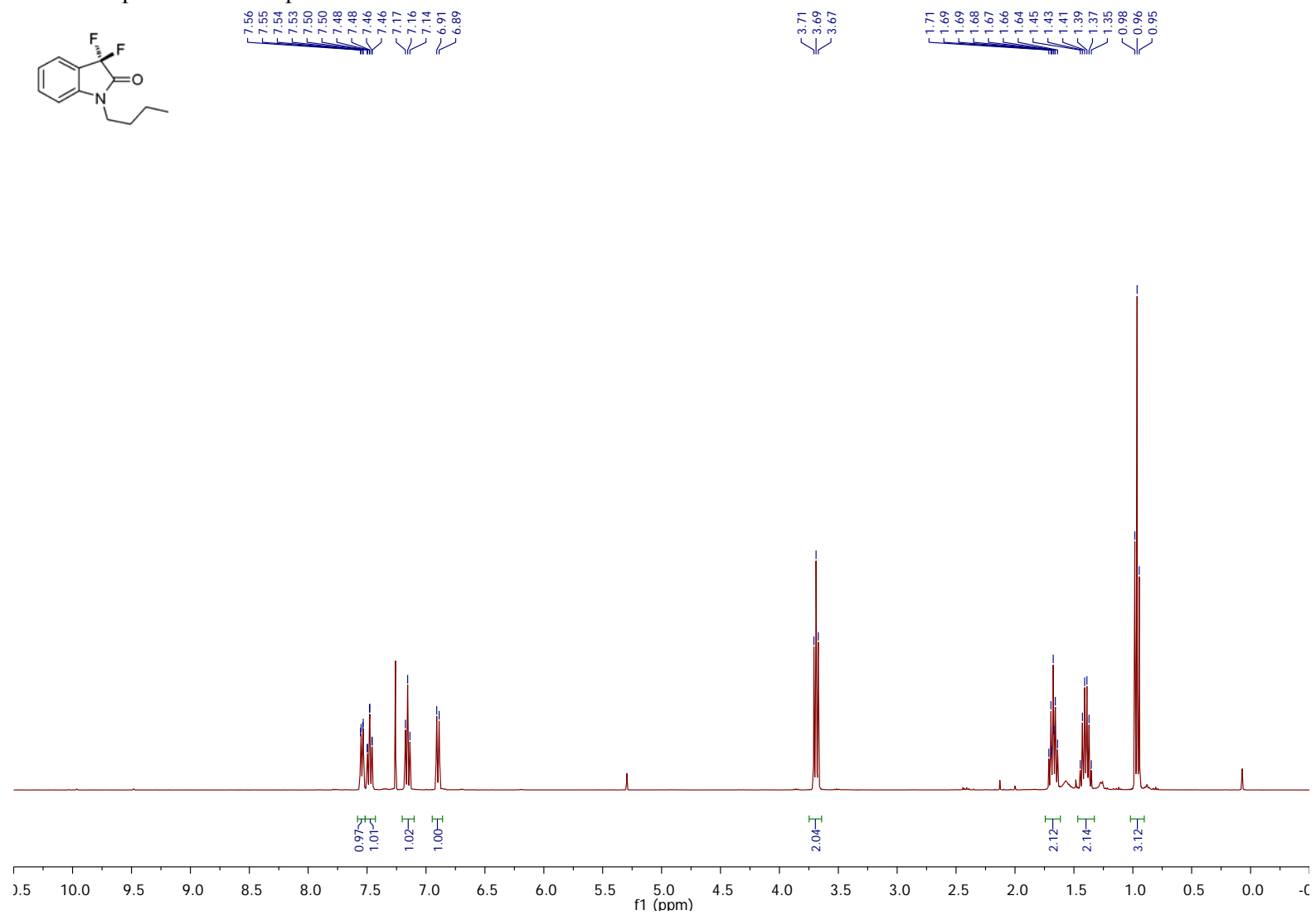
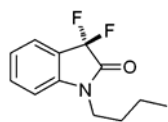
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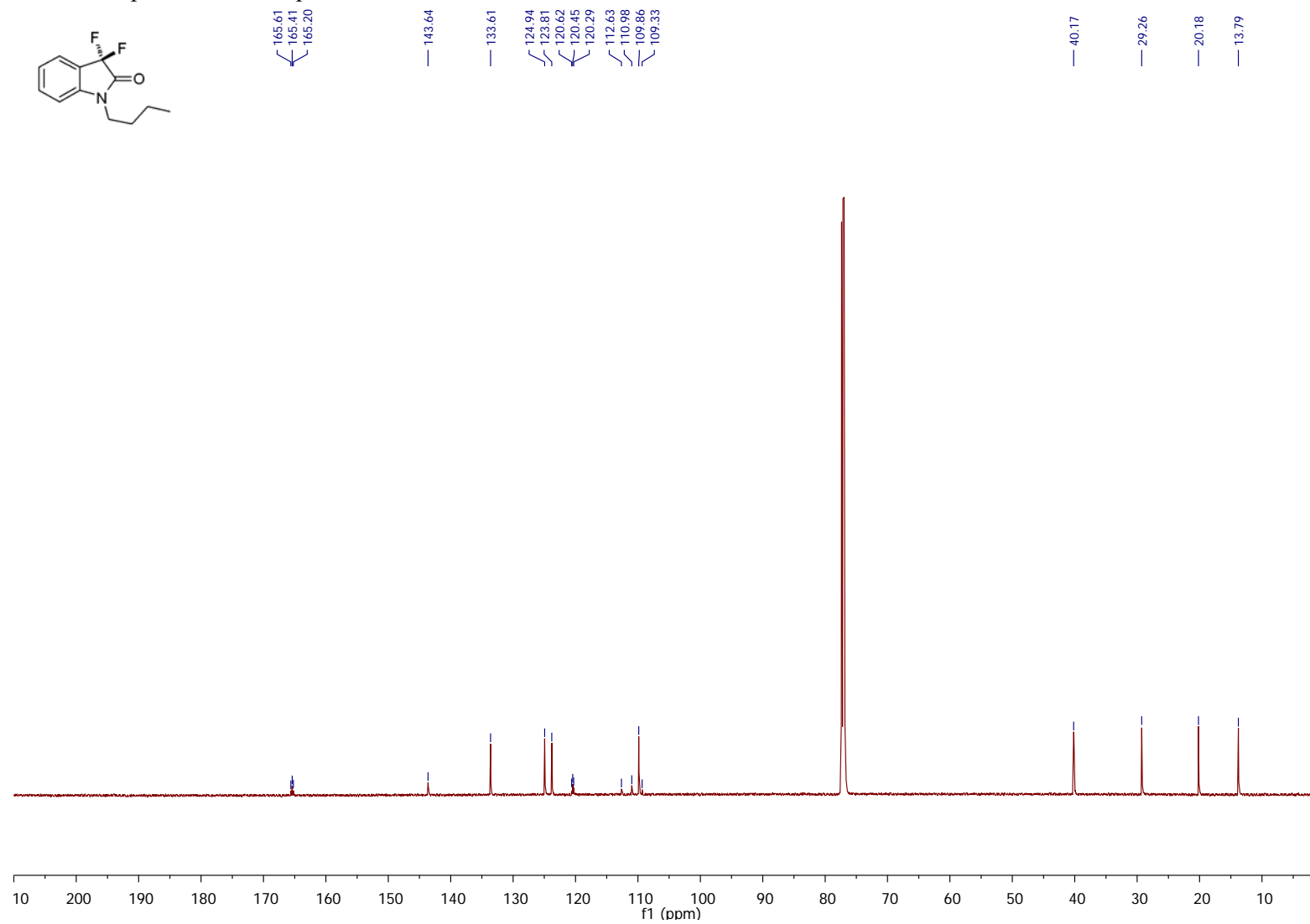
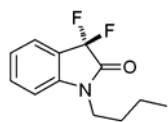
^{19}F NMR spectrum of compound **2c**



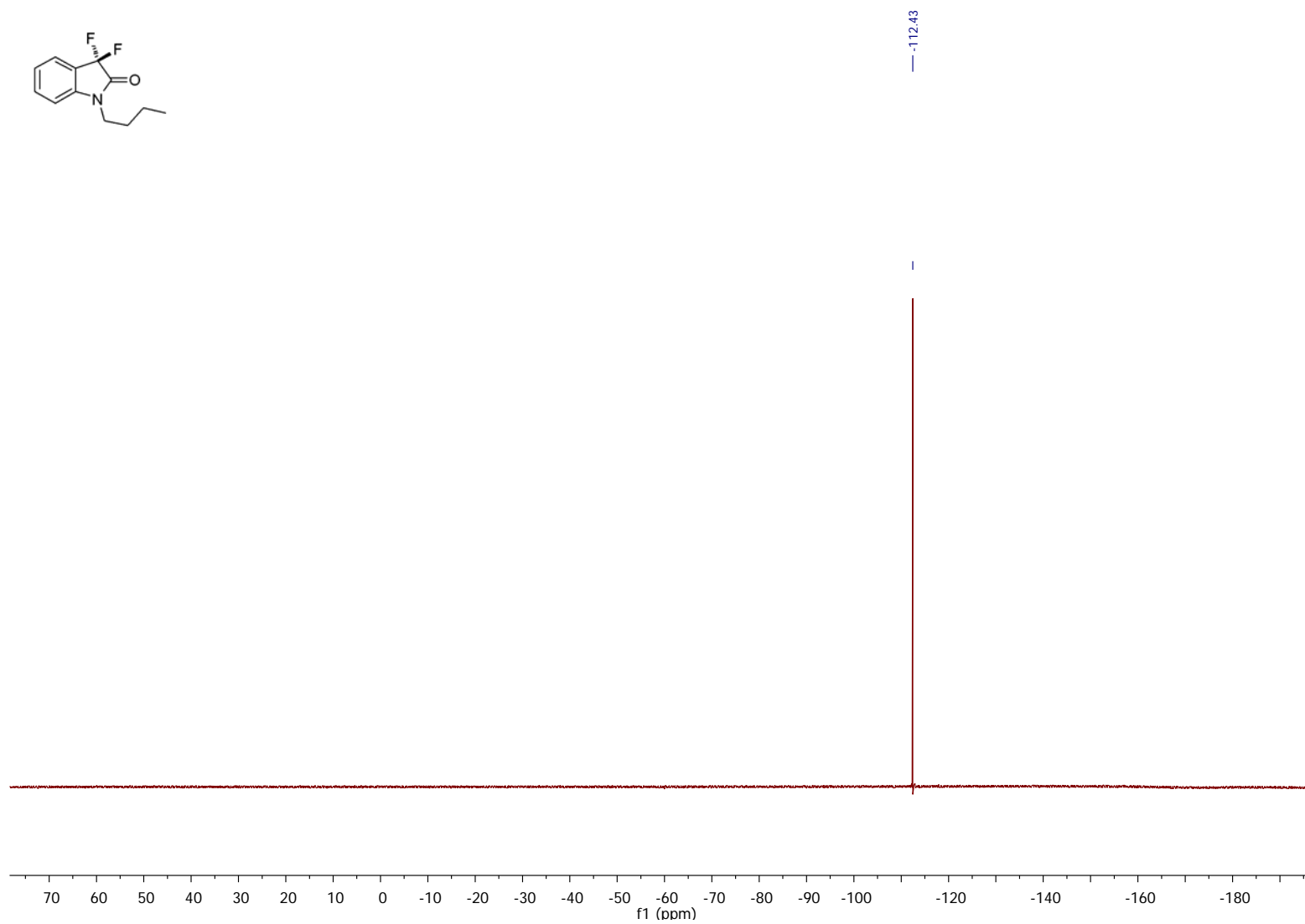
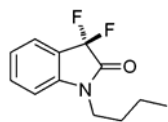
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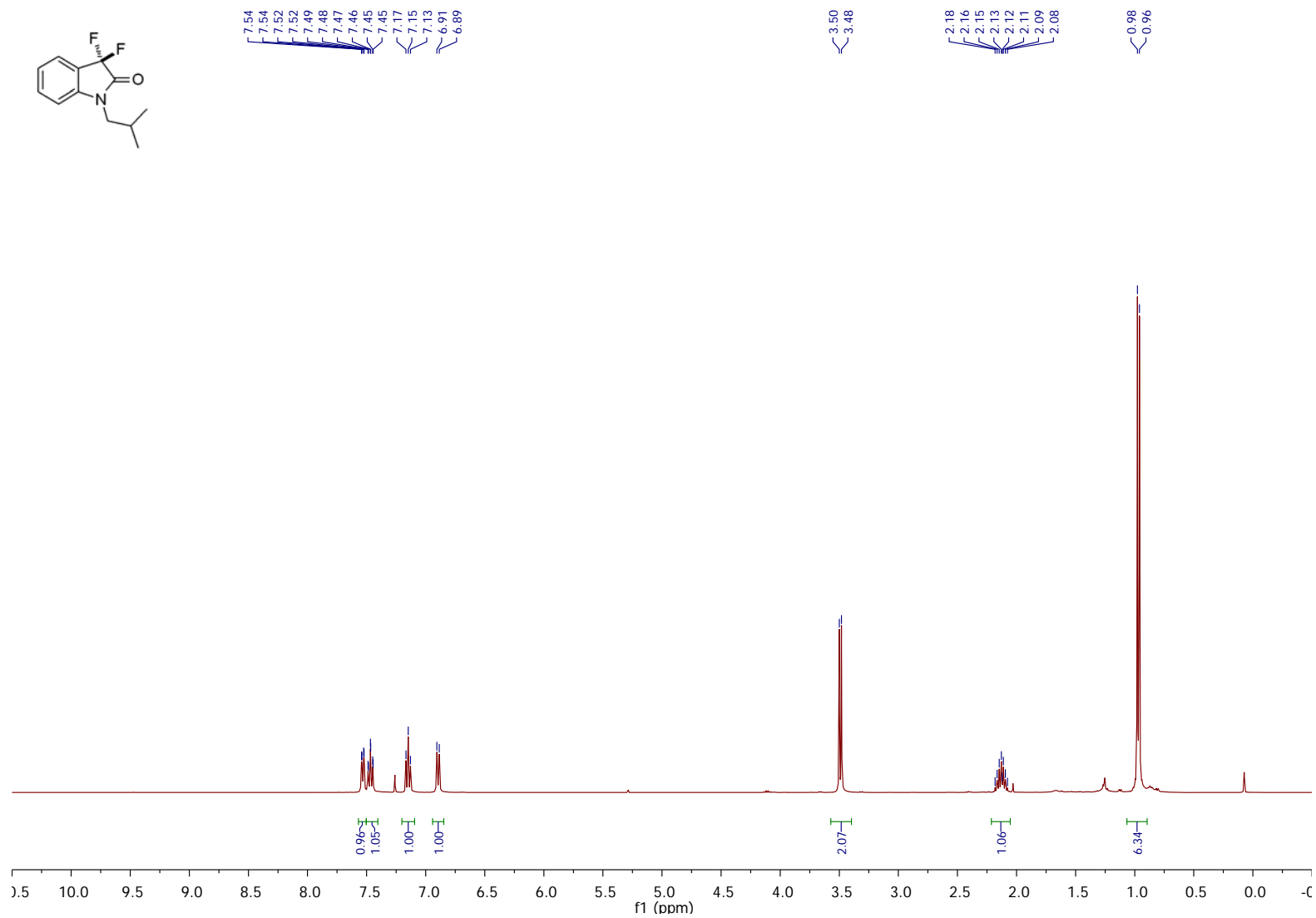
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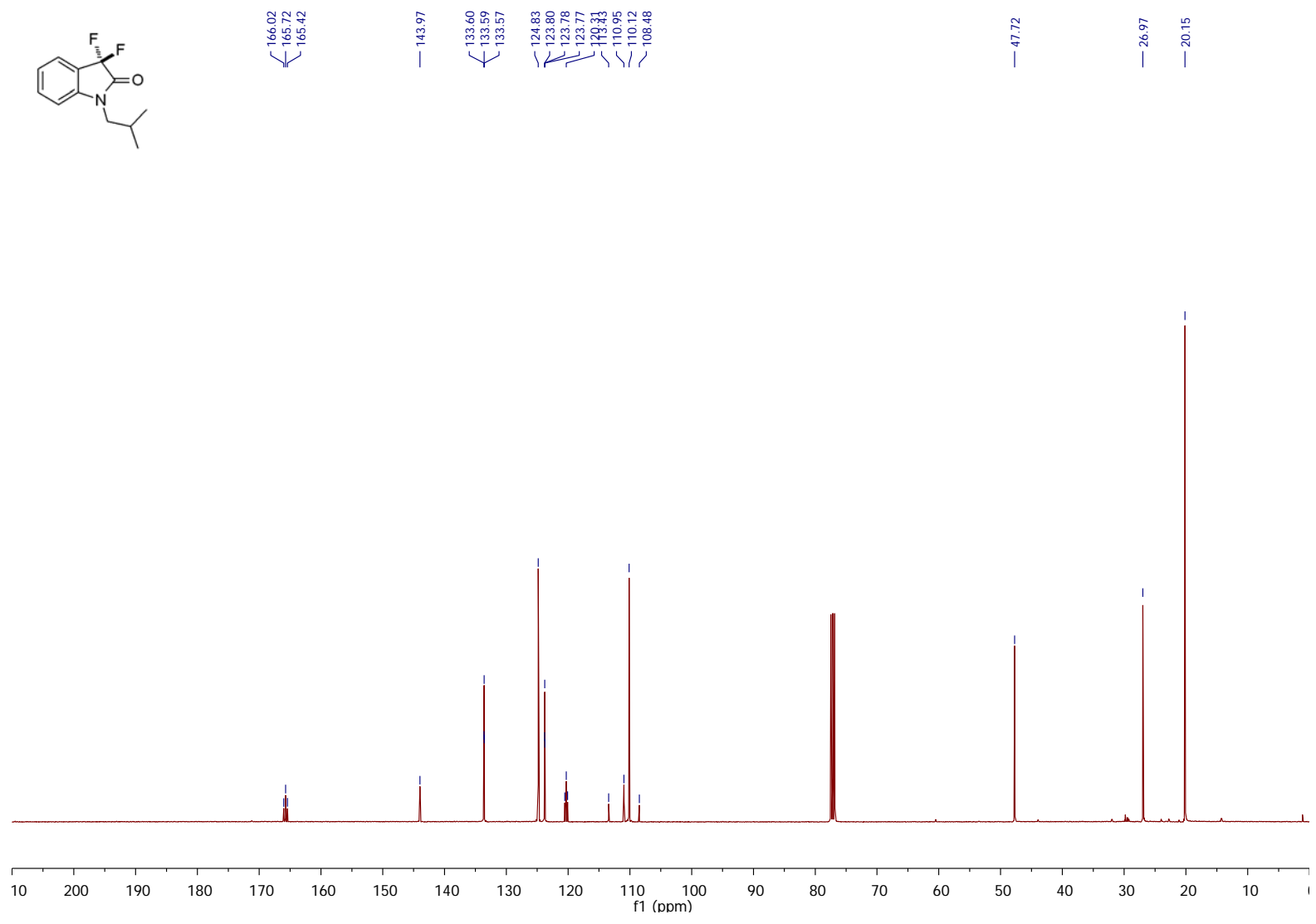
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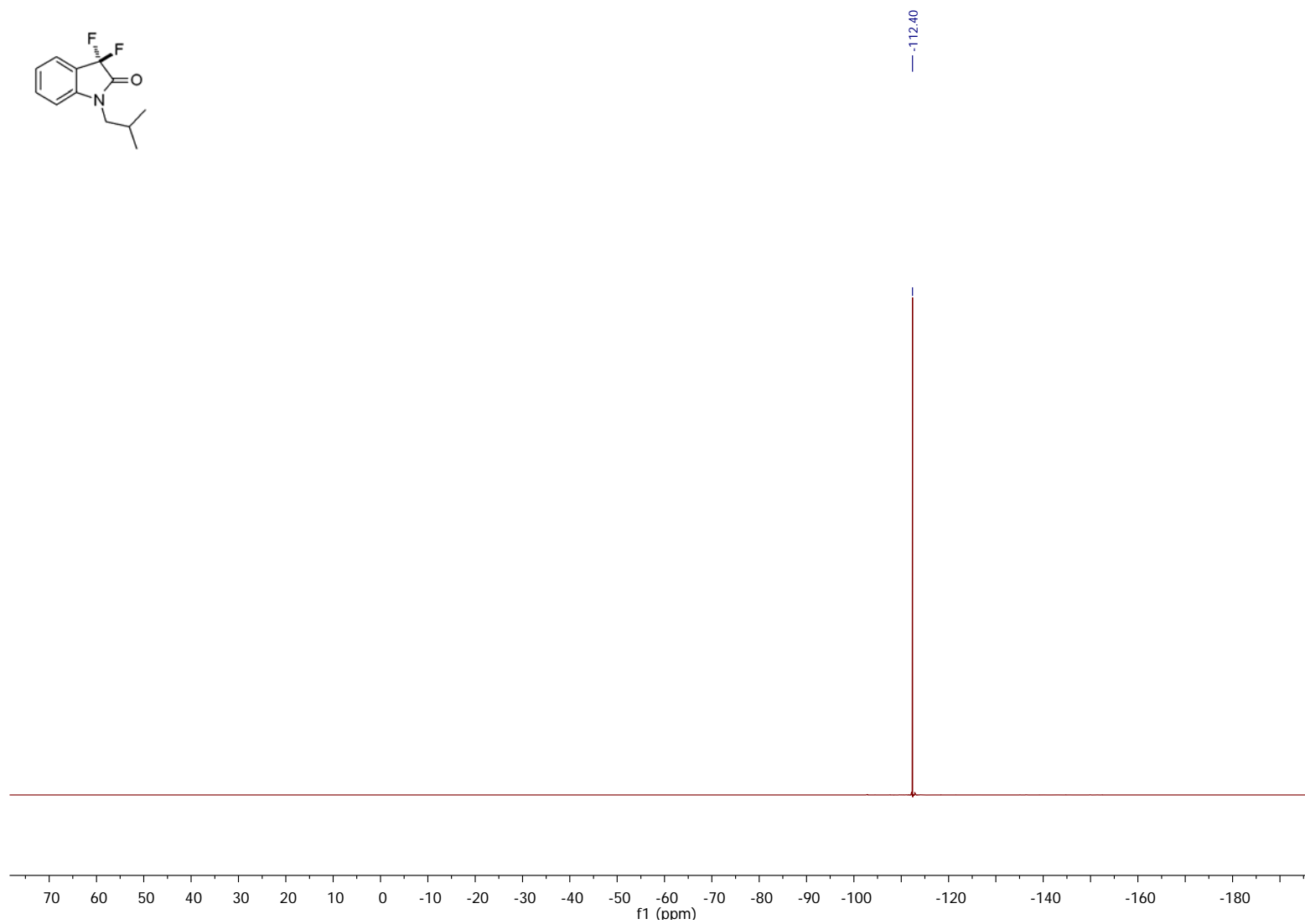
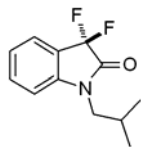
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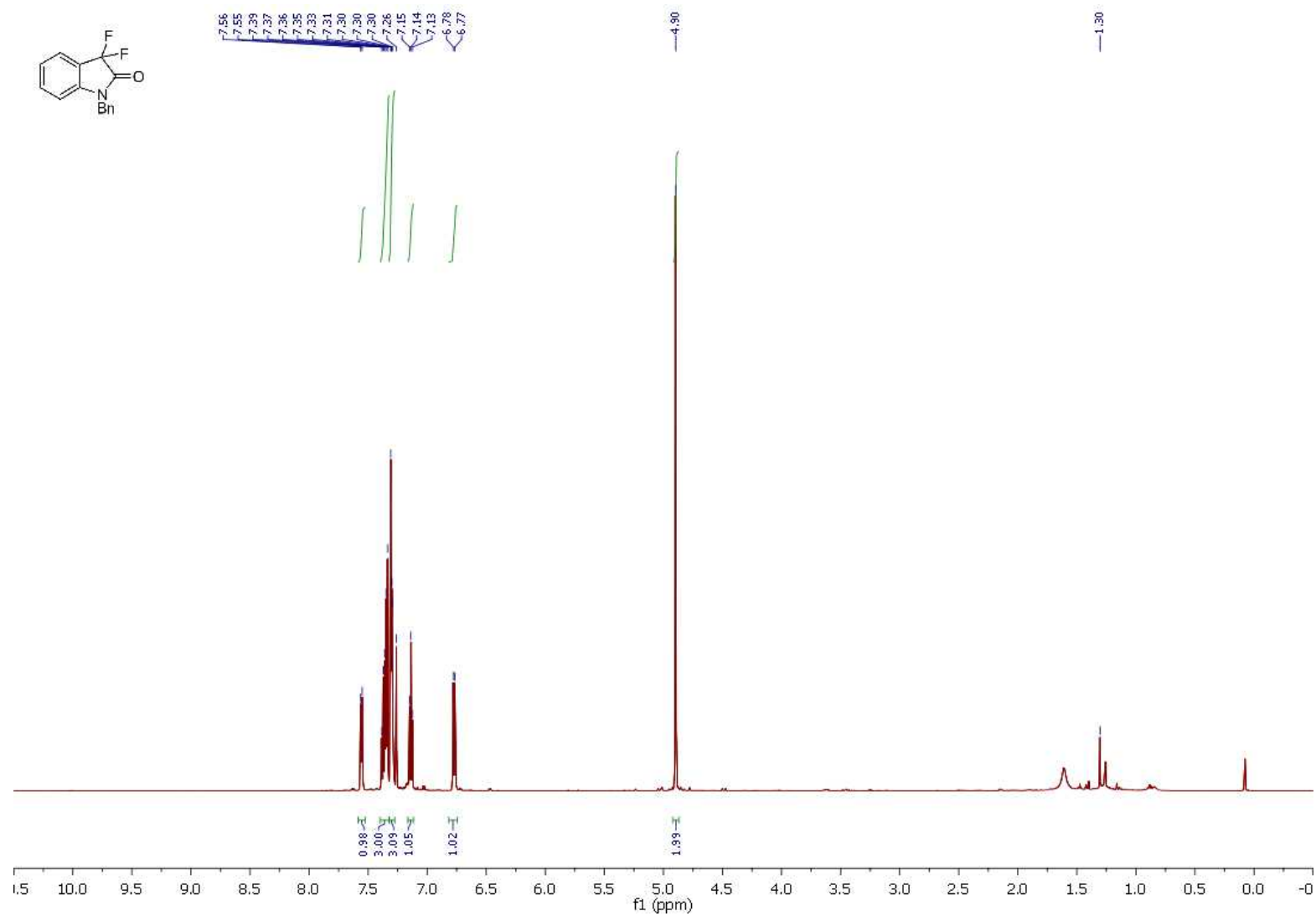
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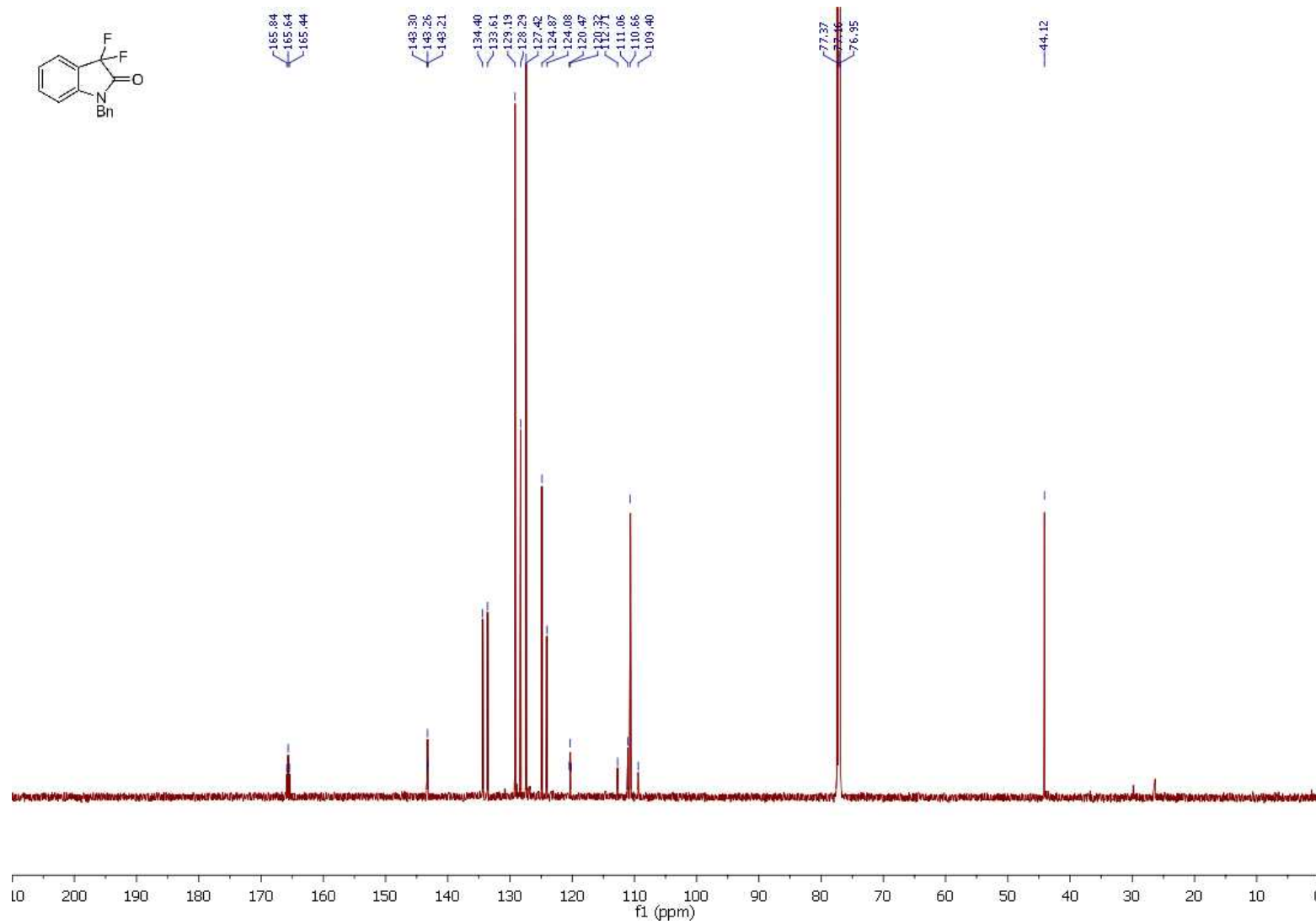
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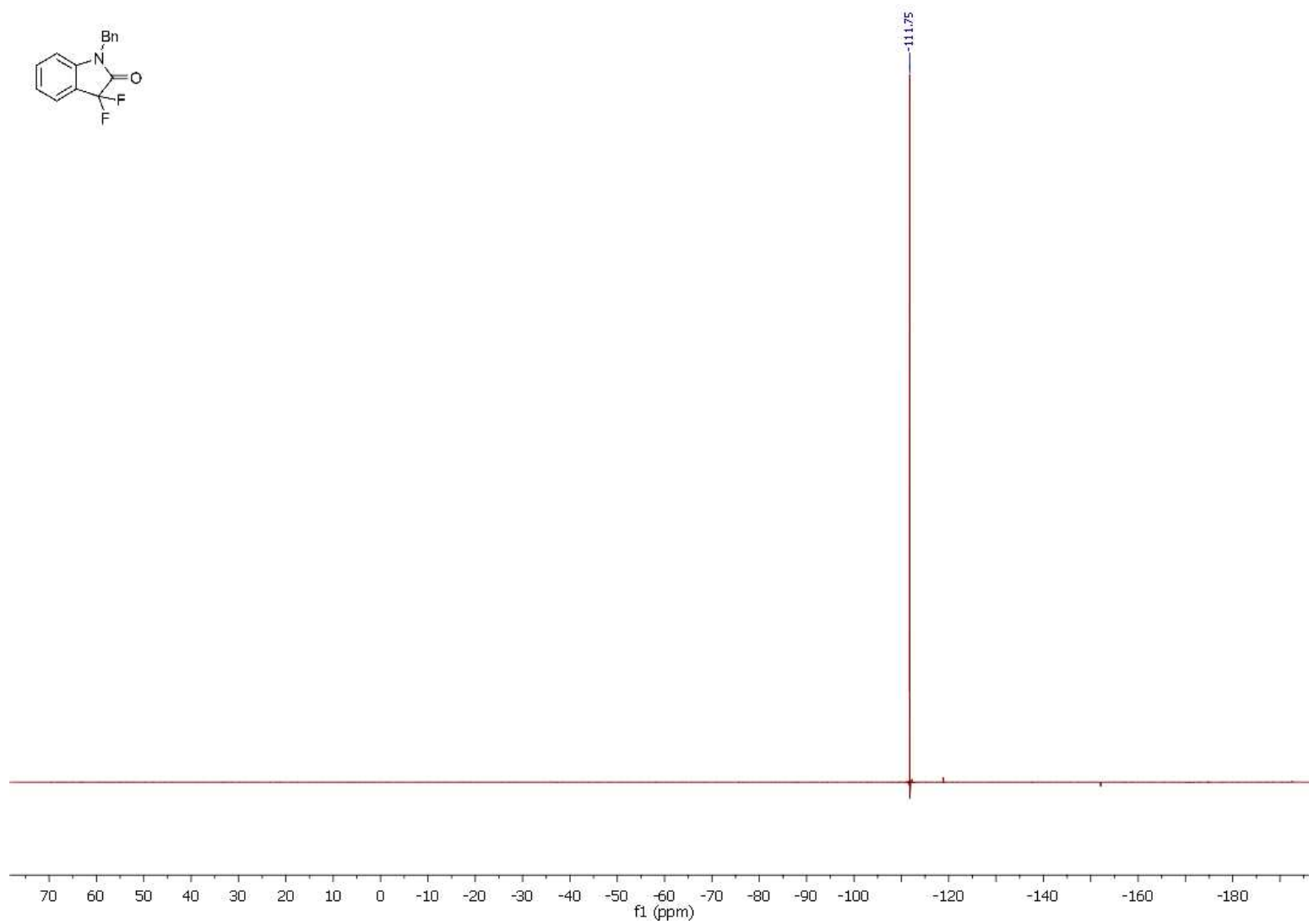
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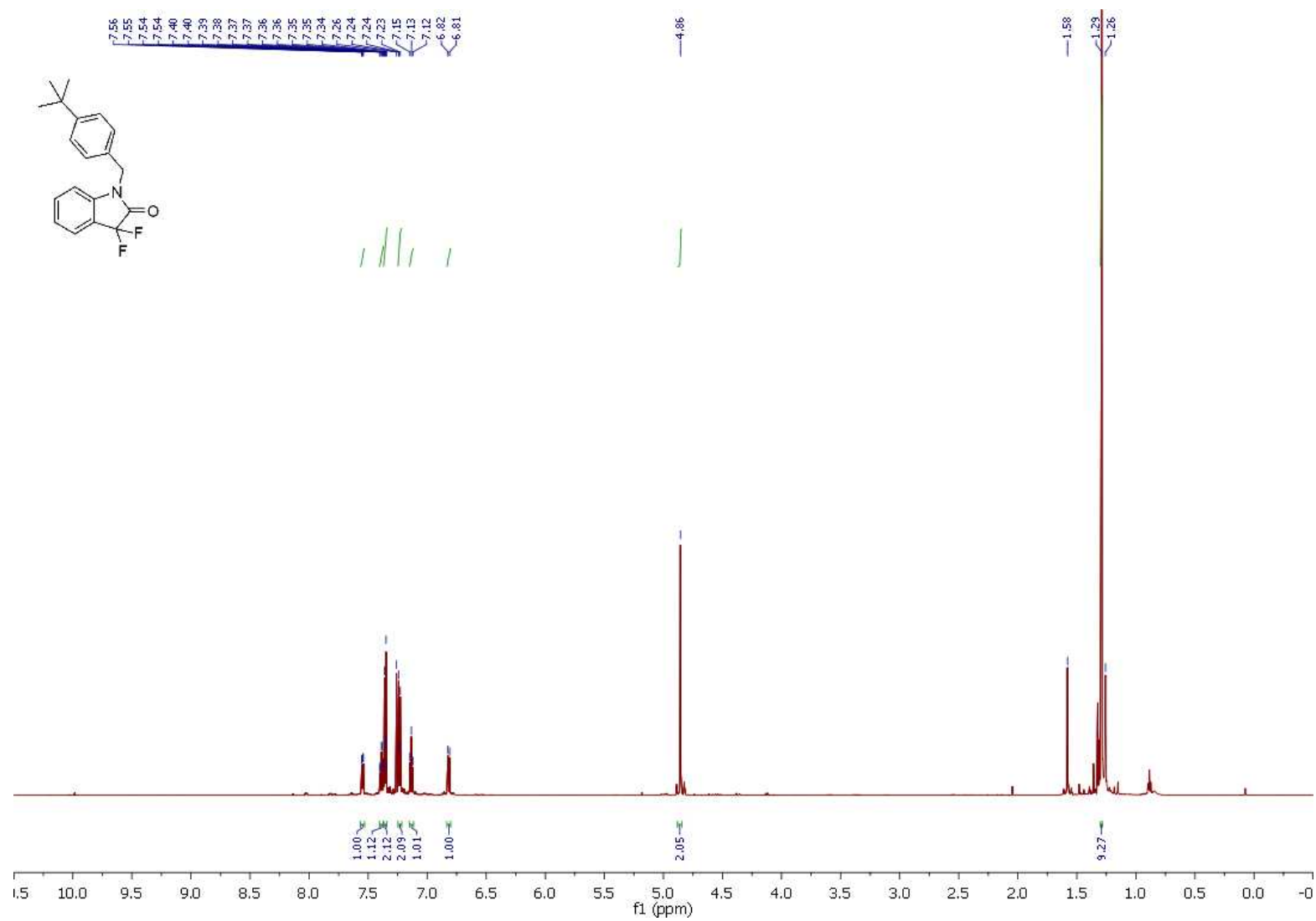
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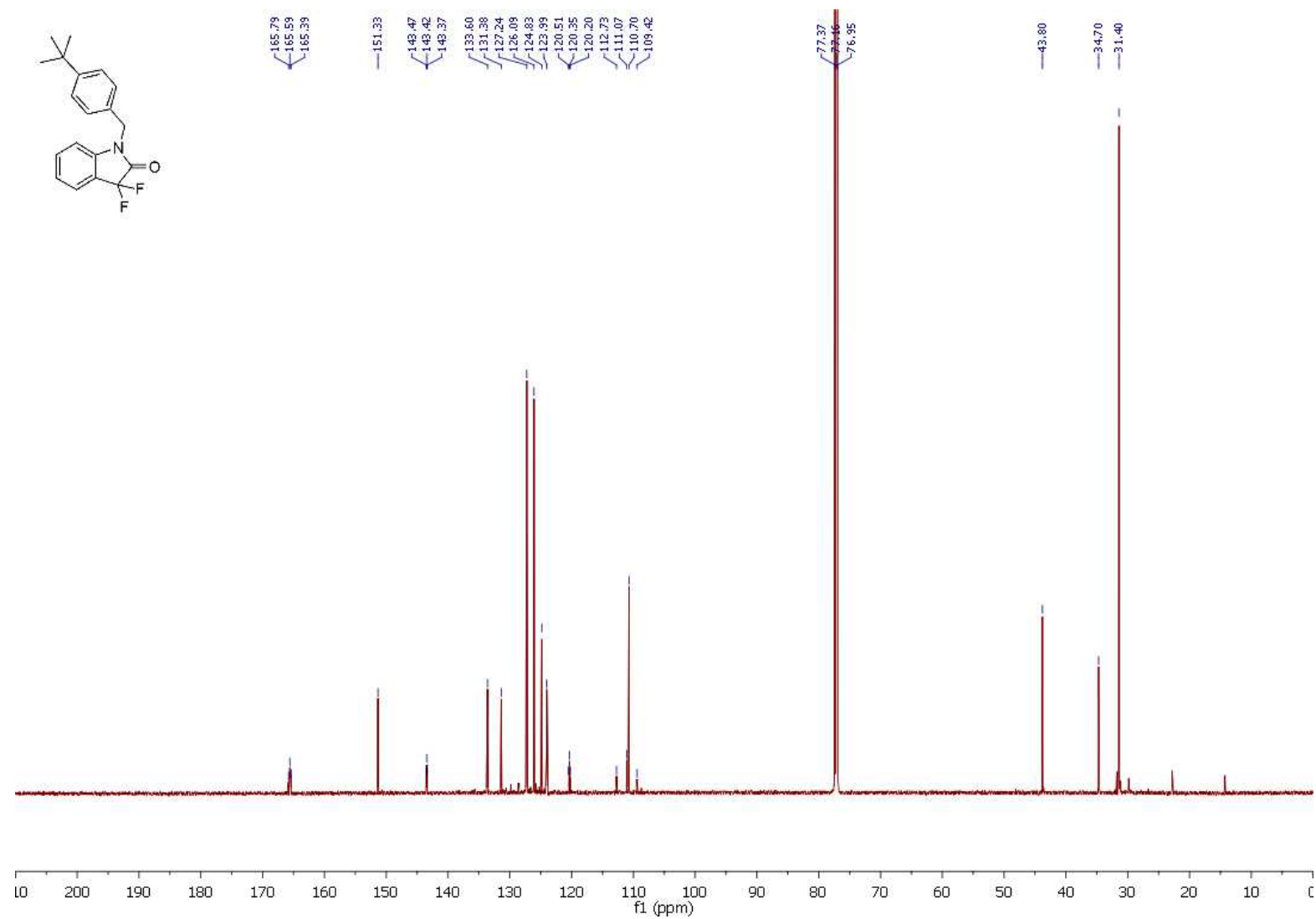
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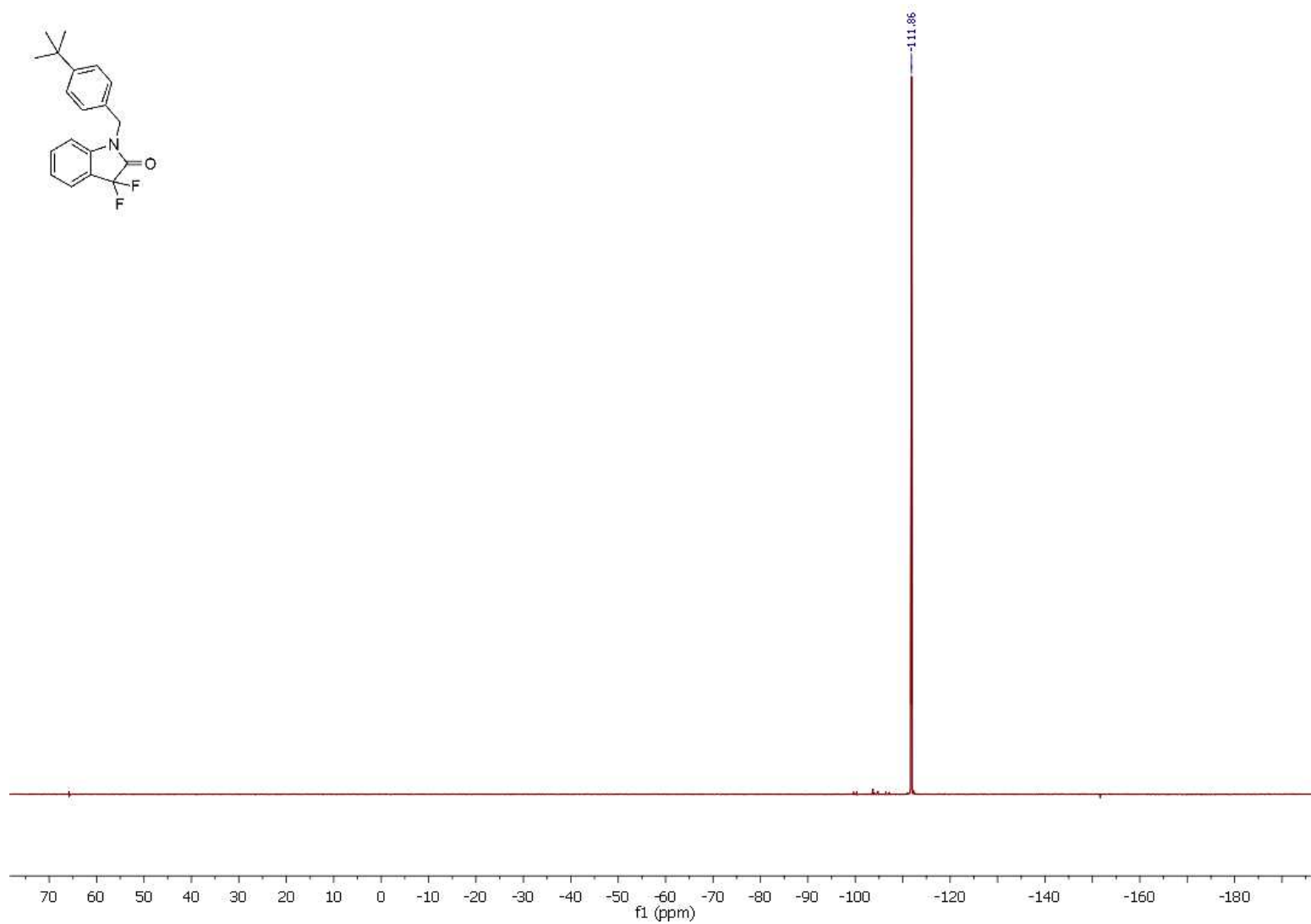
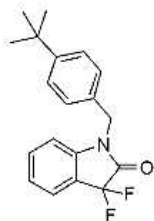
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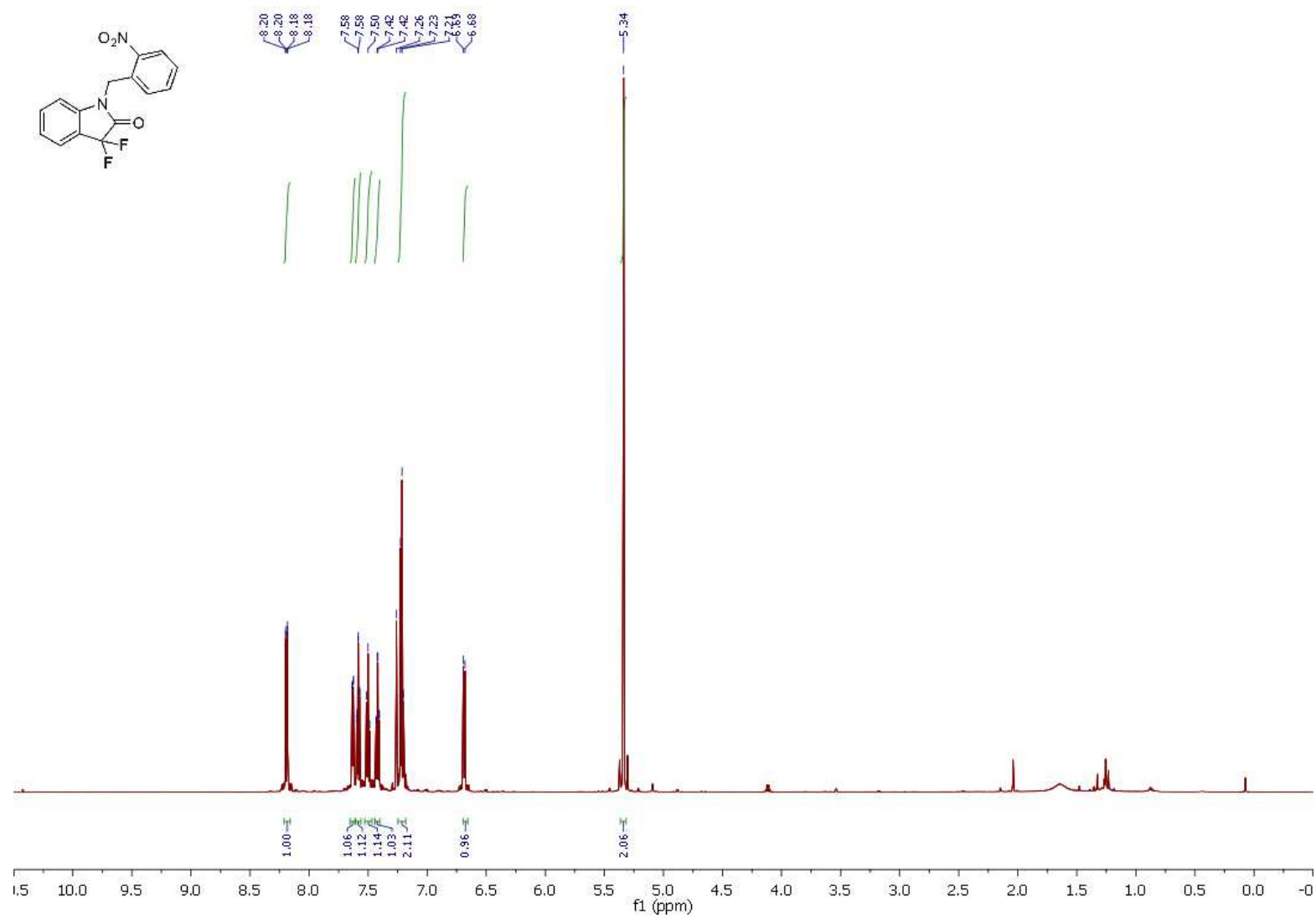
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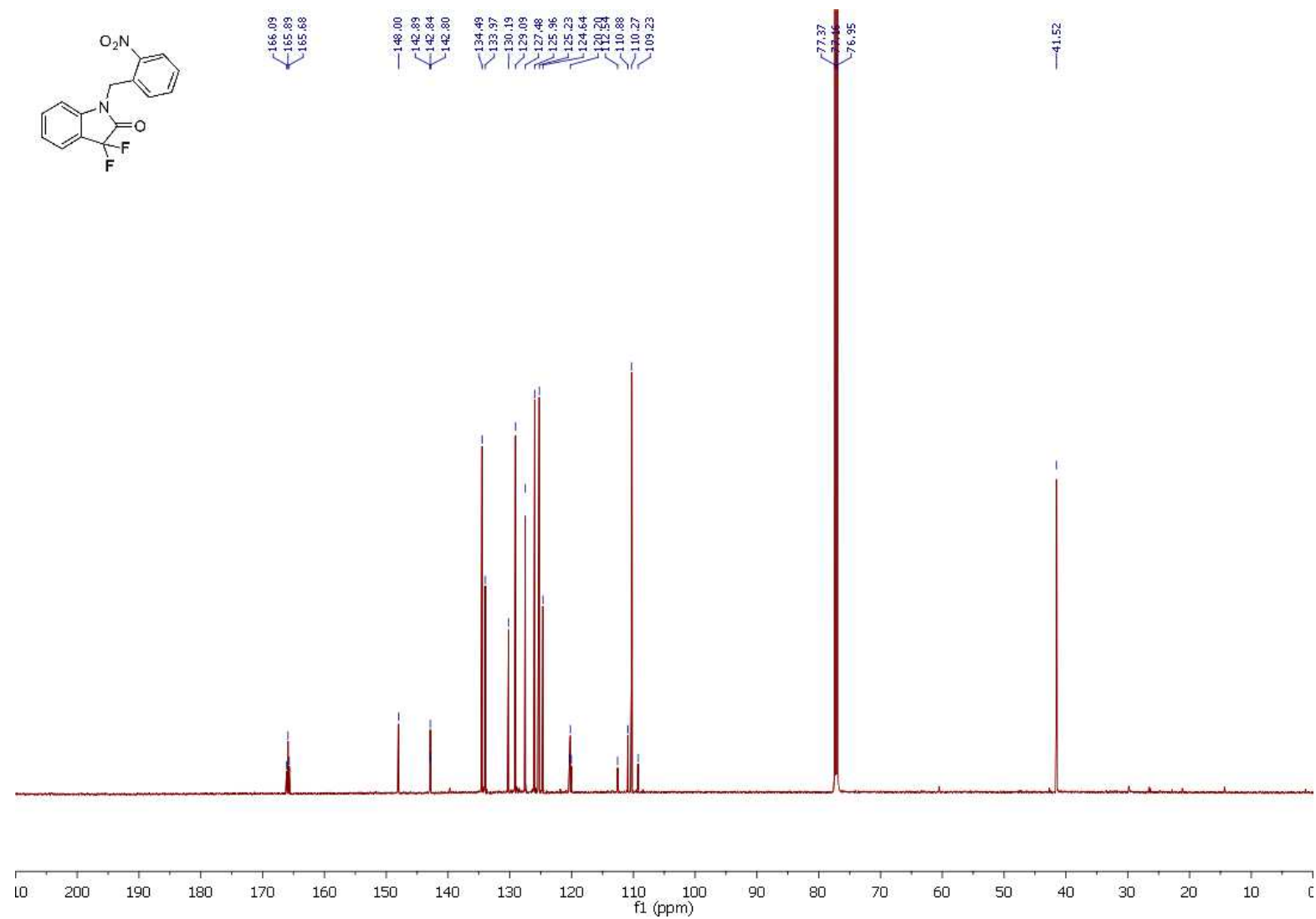
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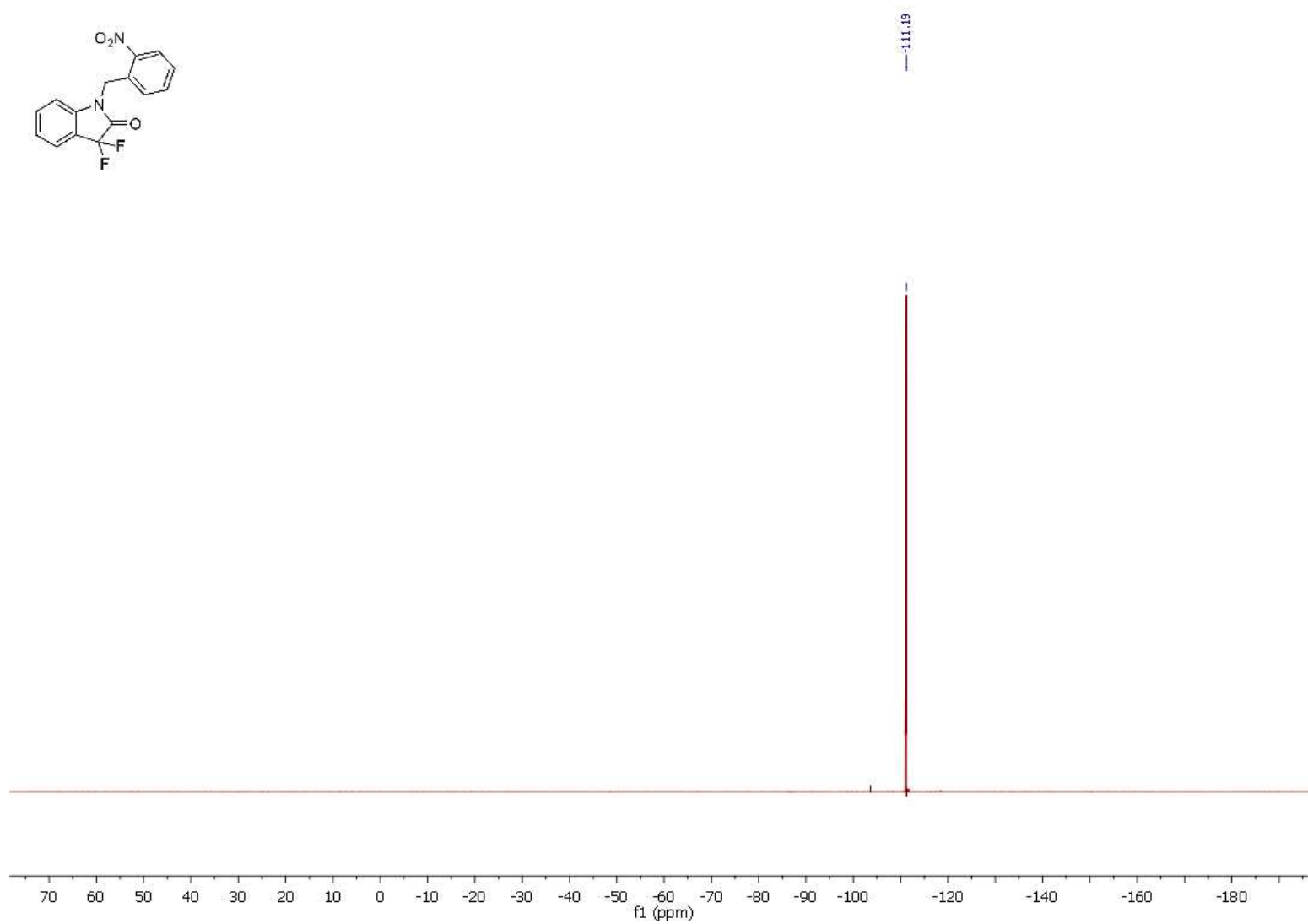
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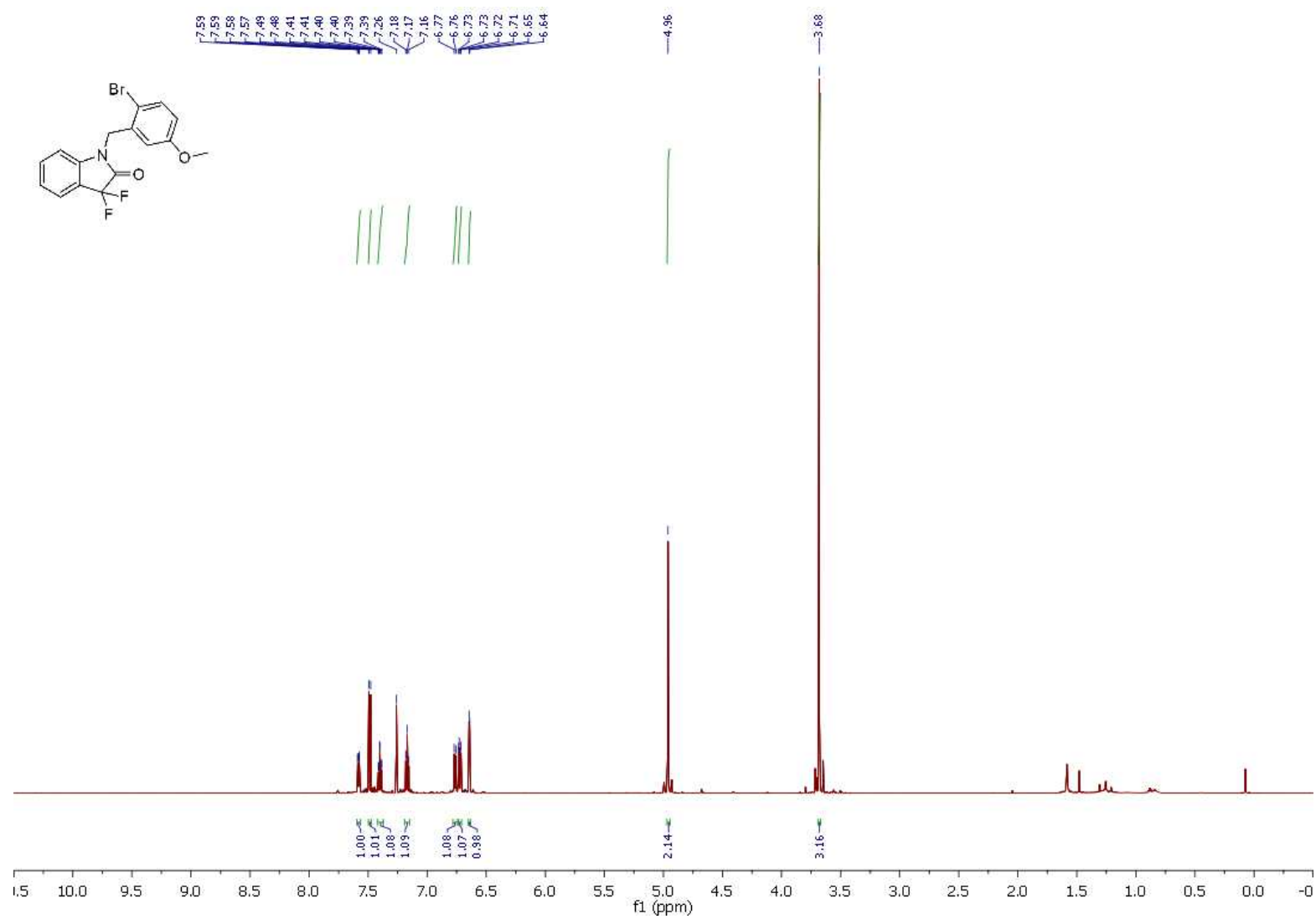
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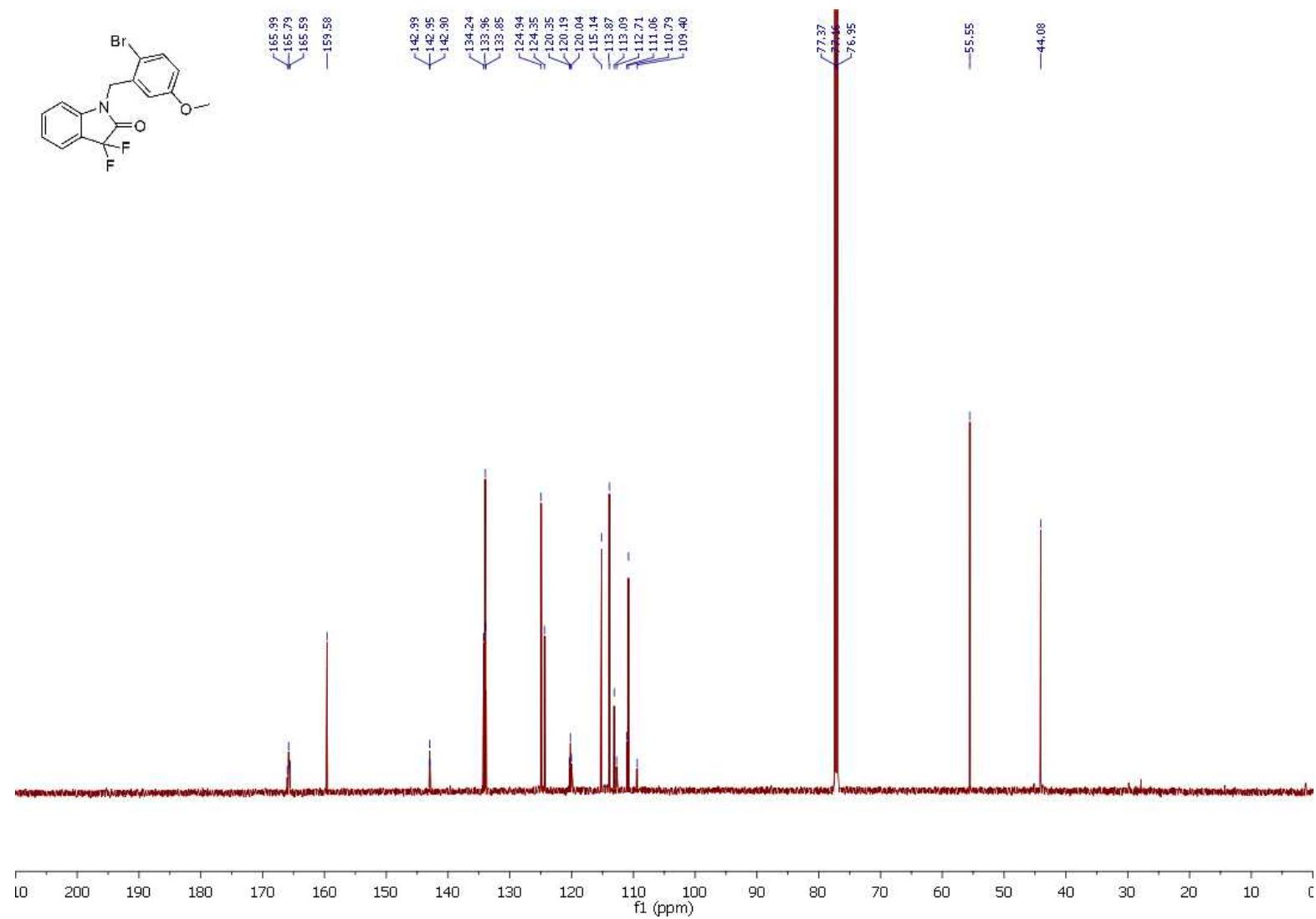
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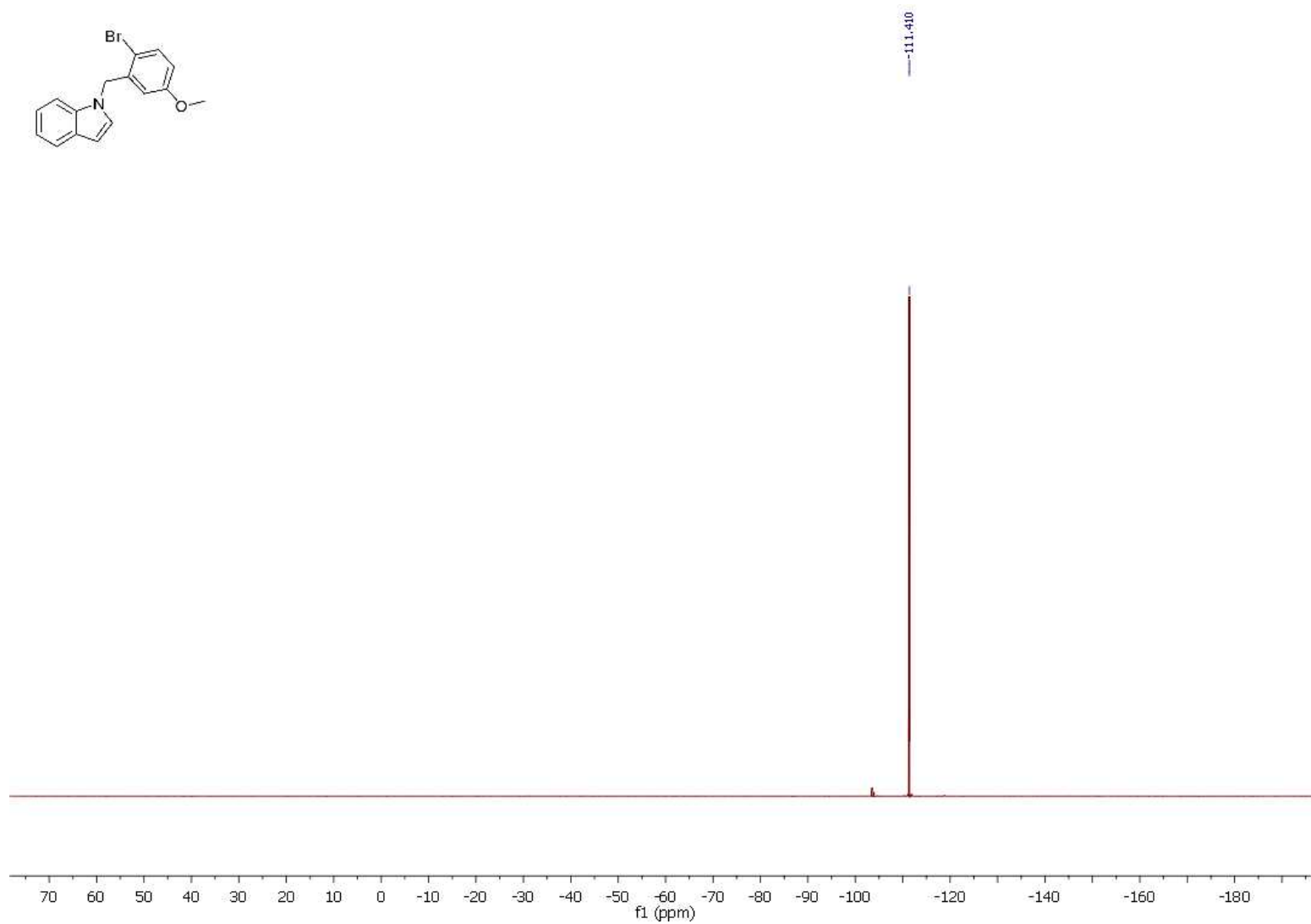
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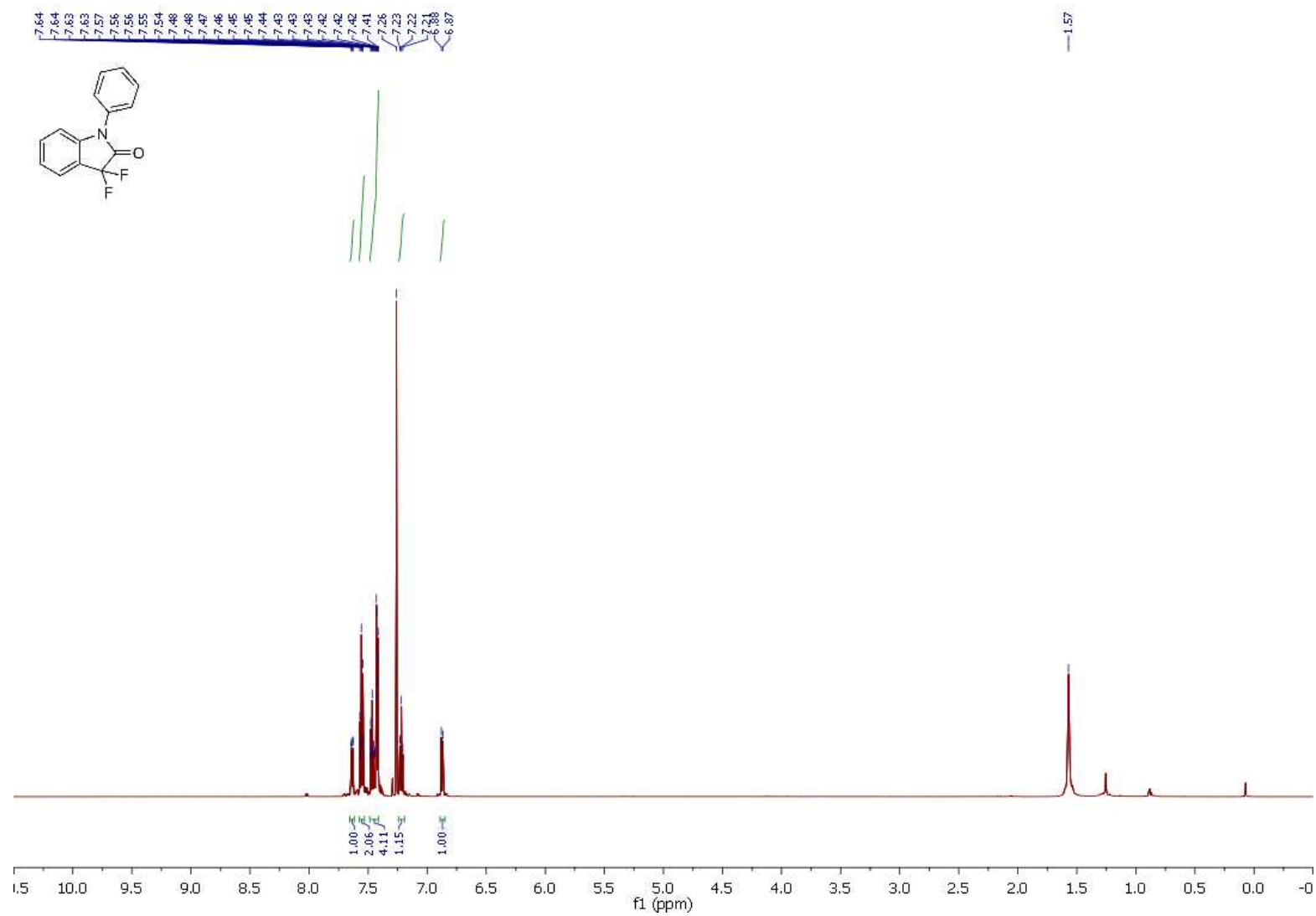
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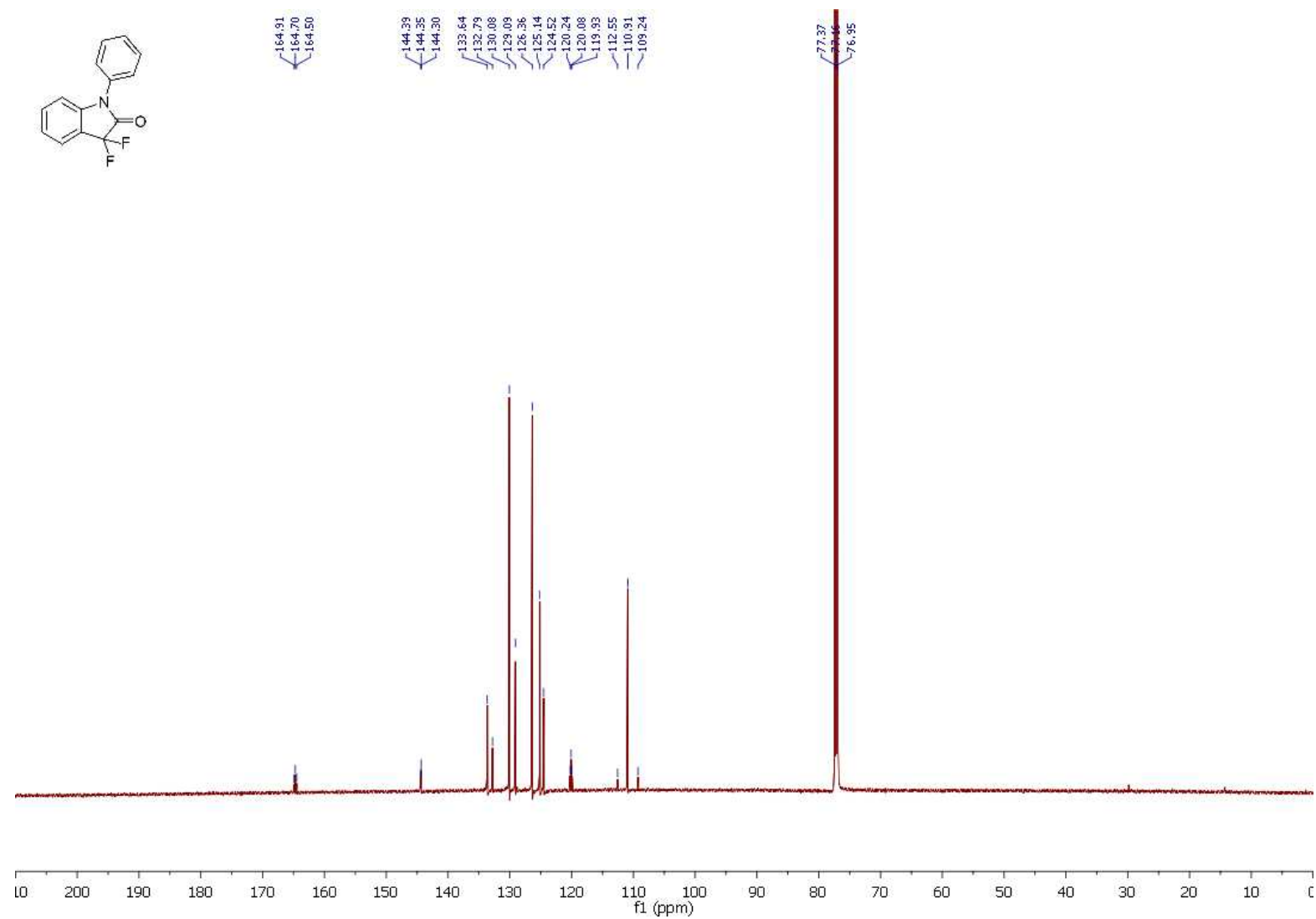
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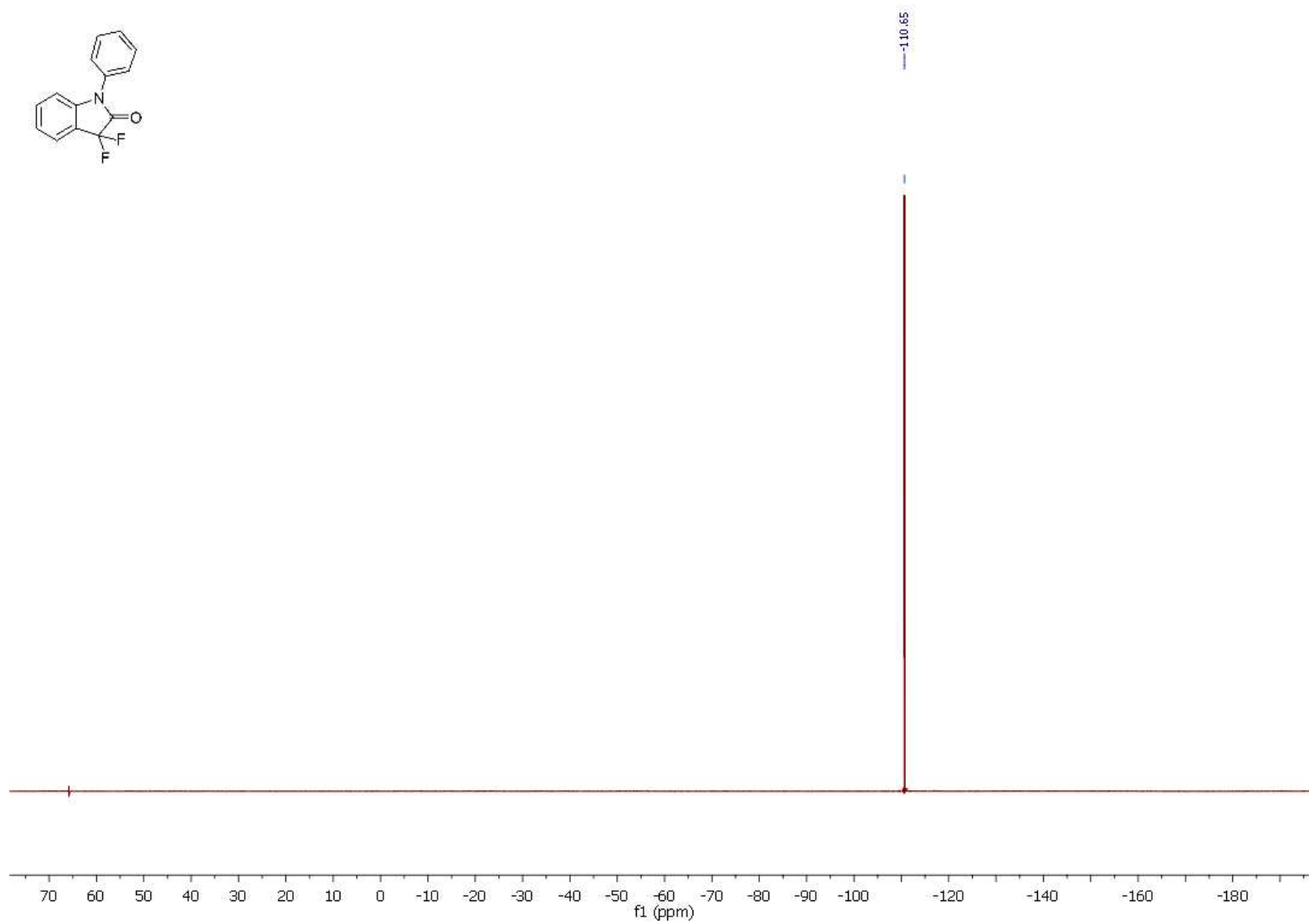
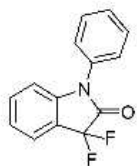
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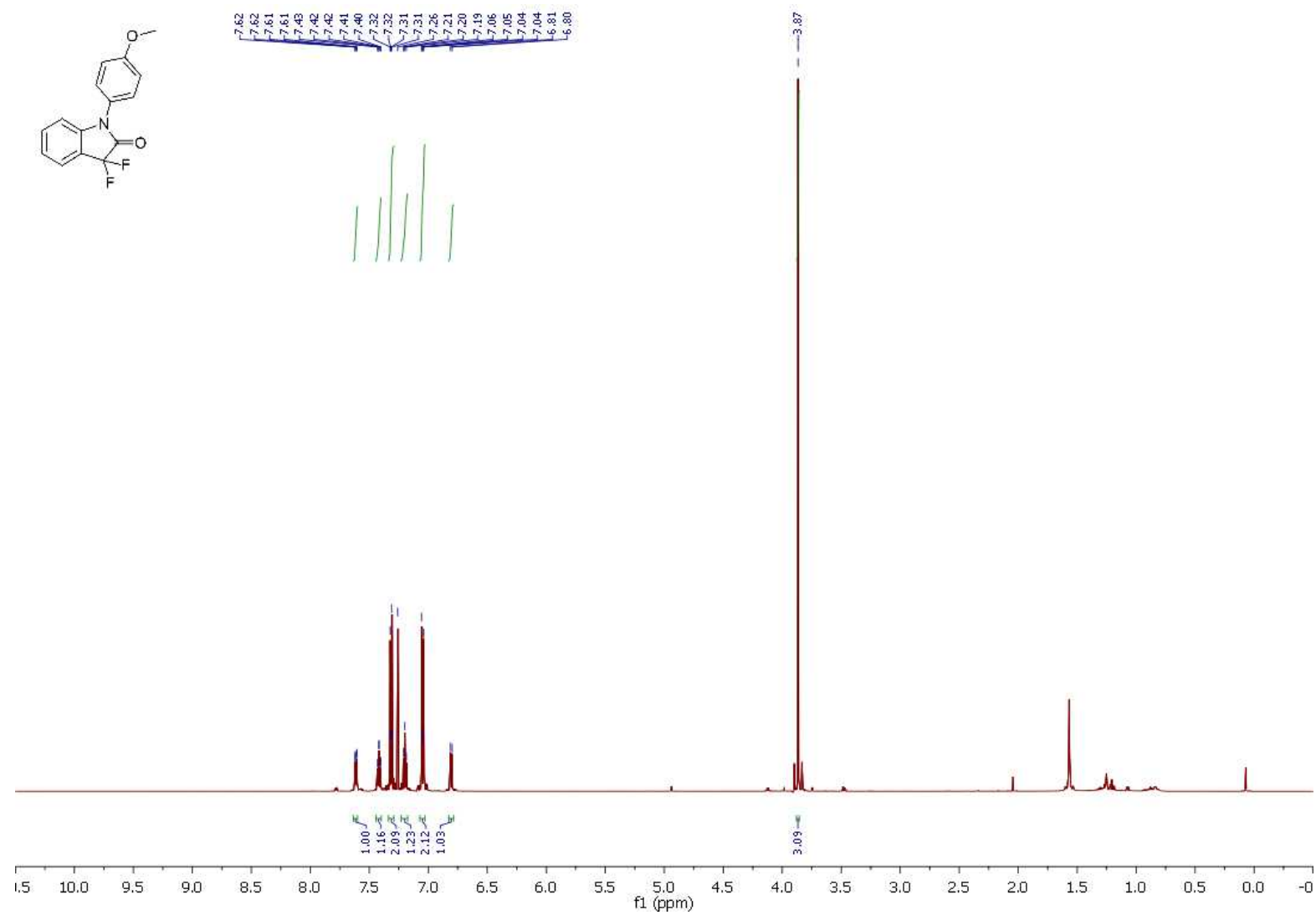
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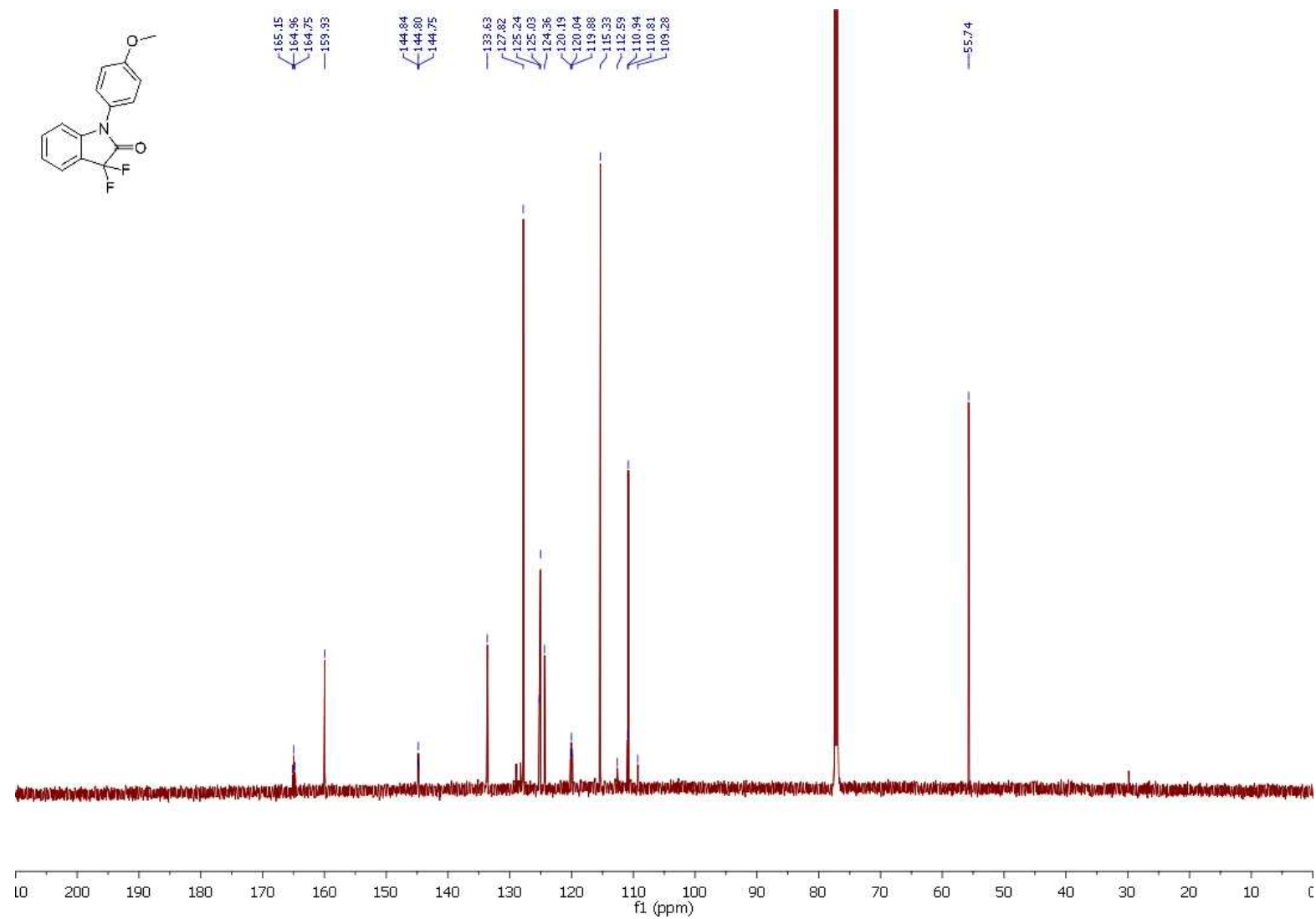
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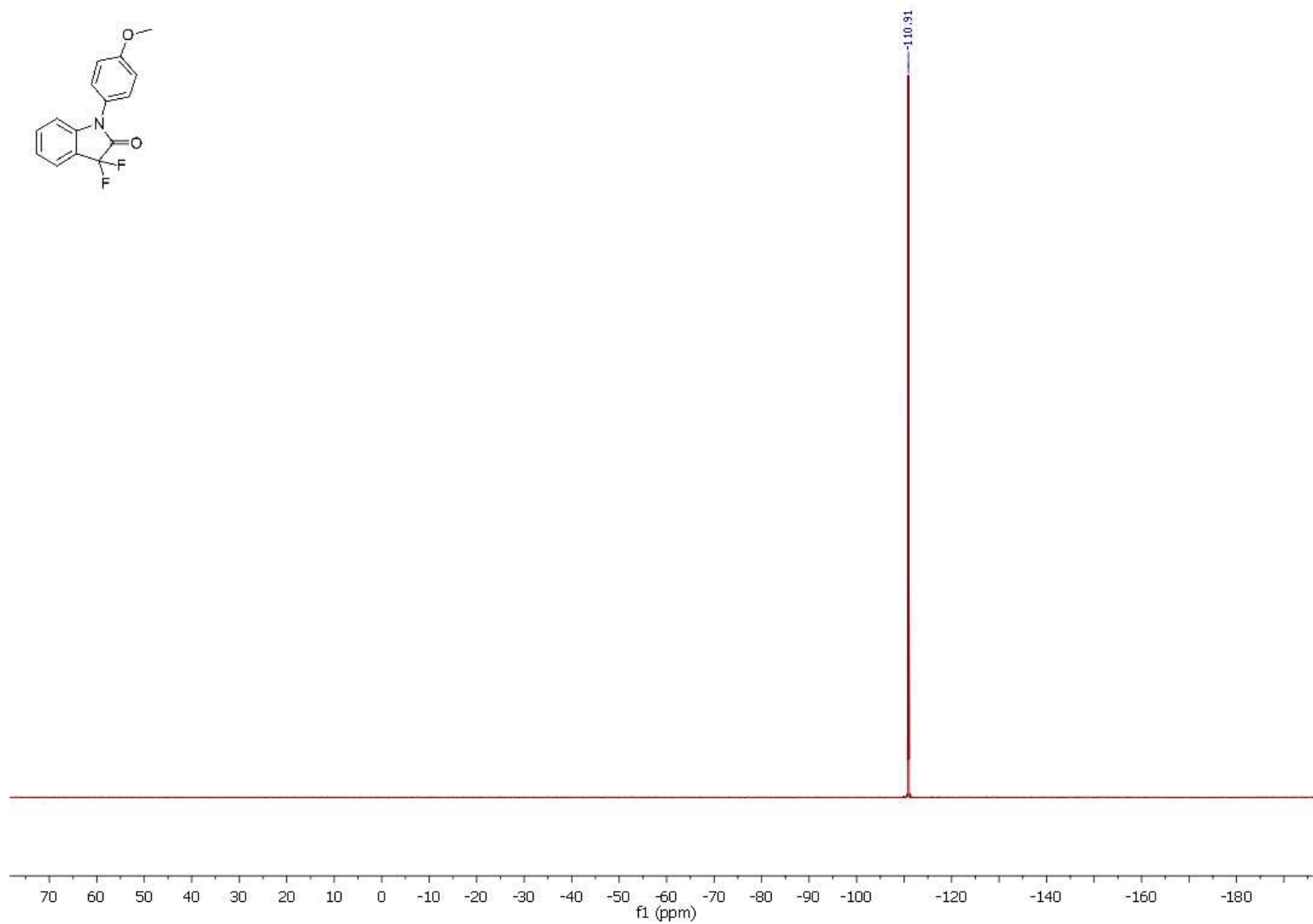
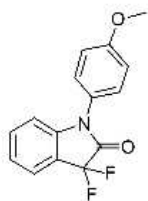
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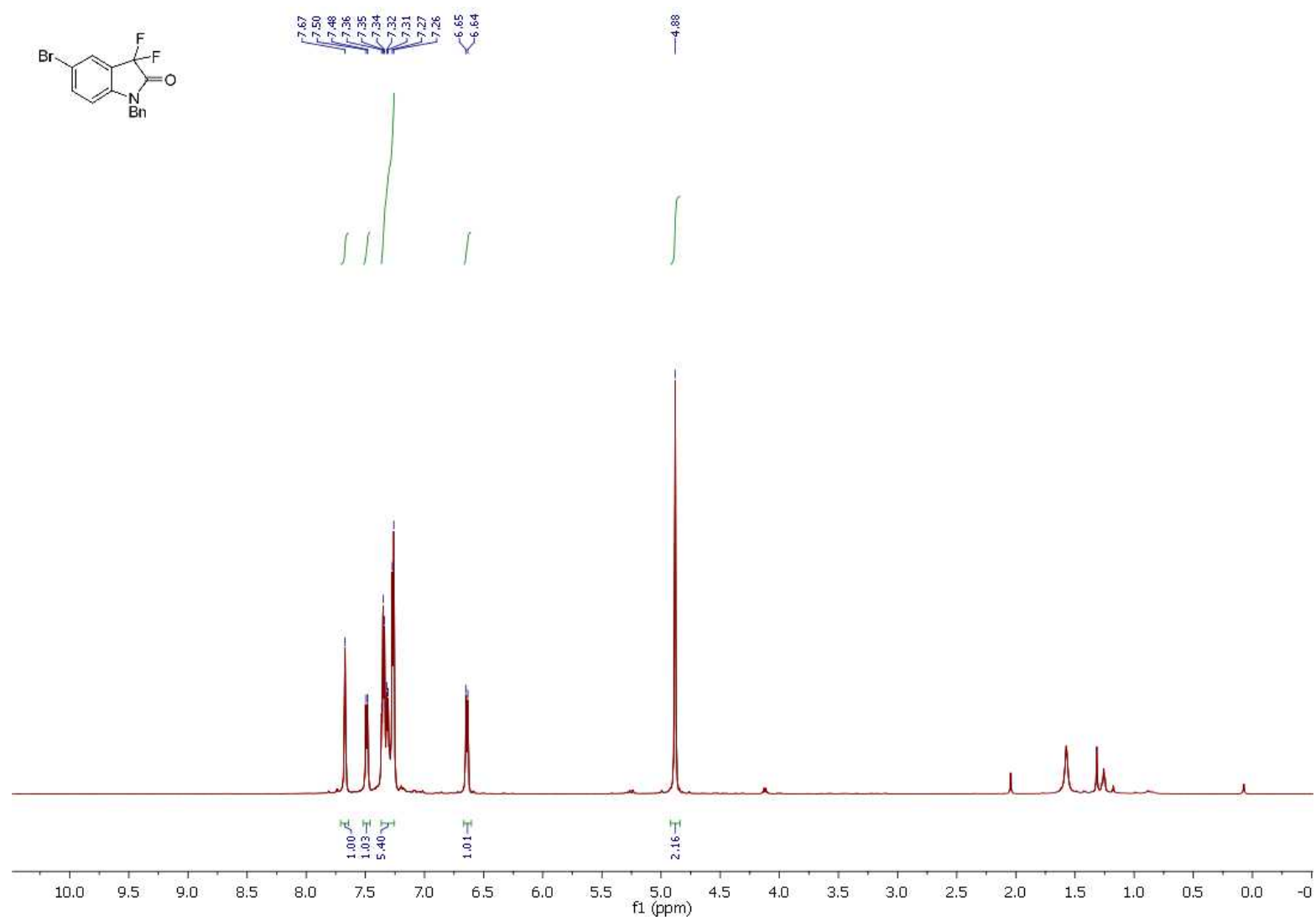
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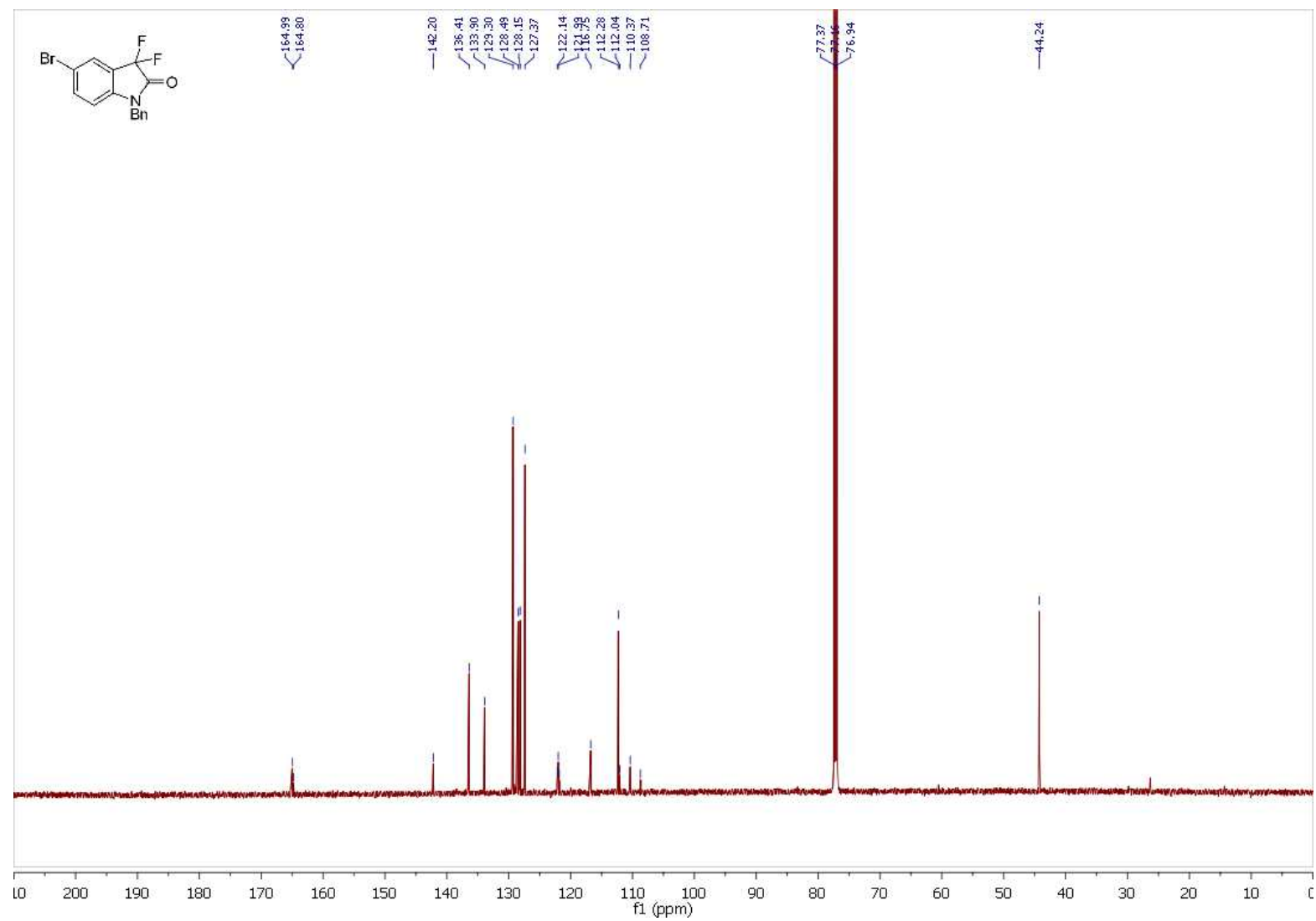
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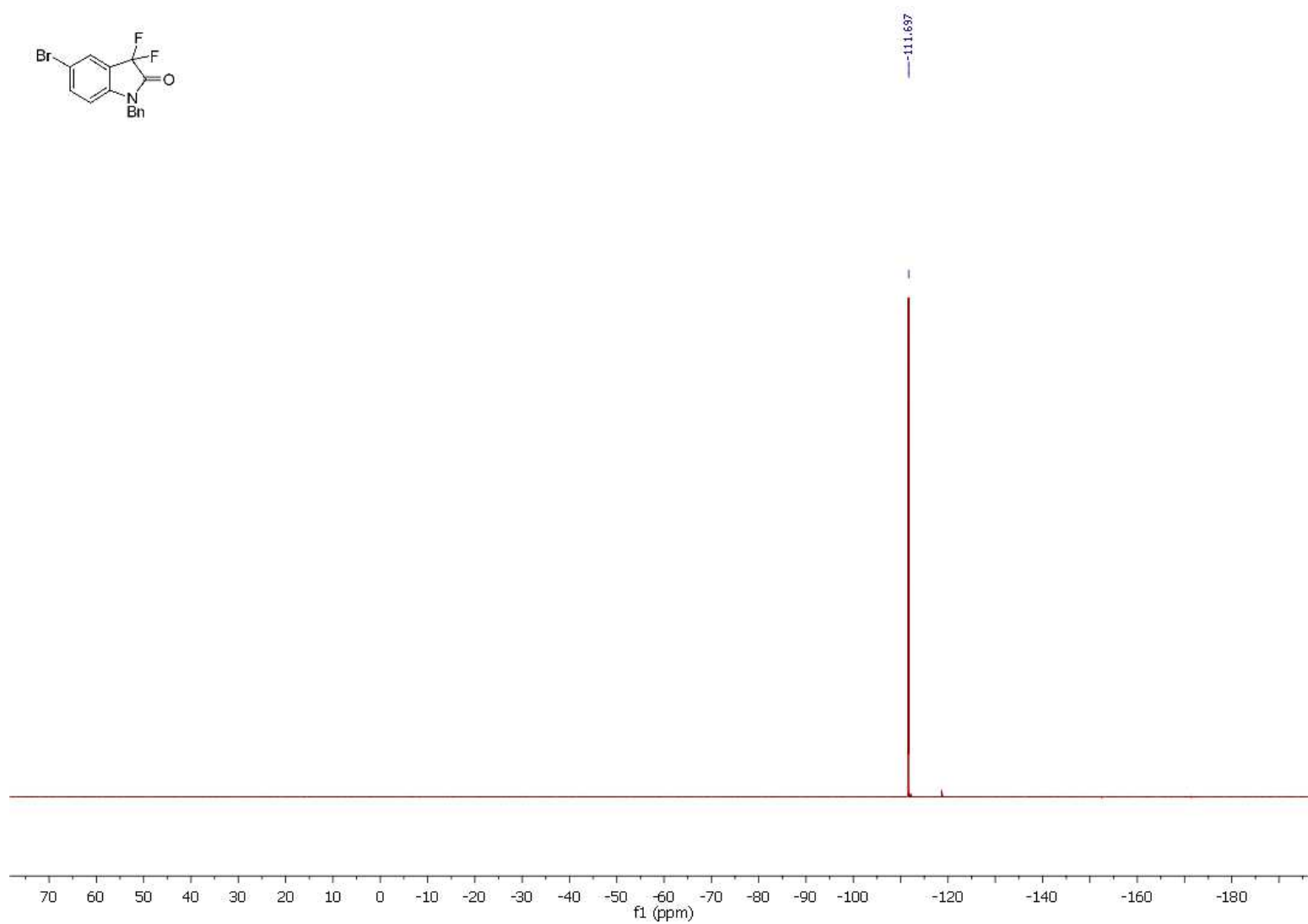
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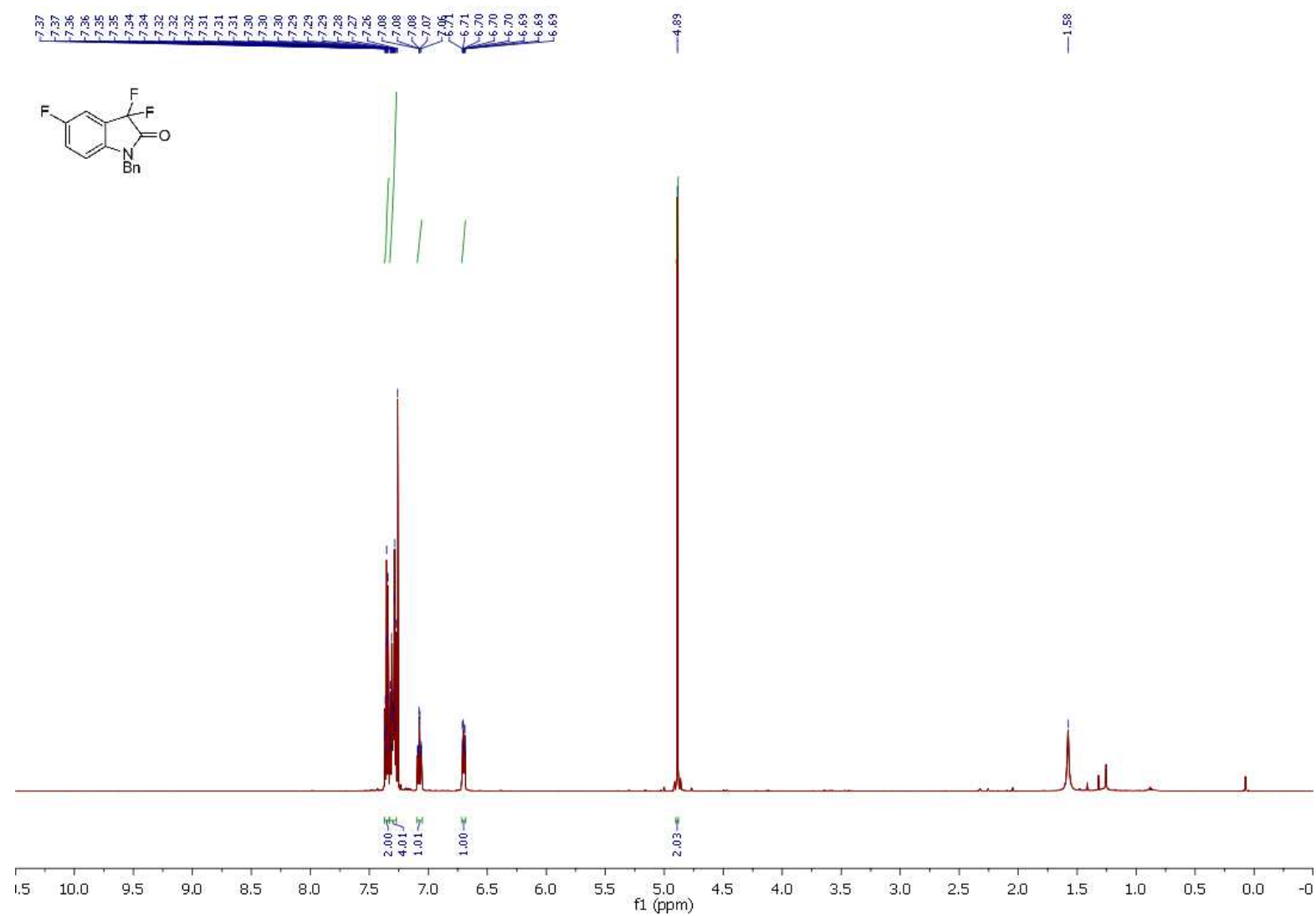
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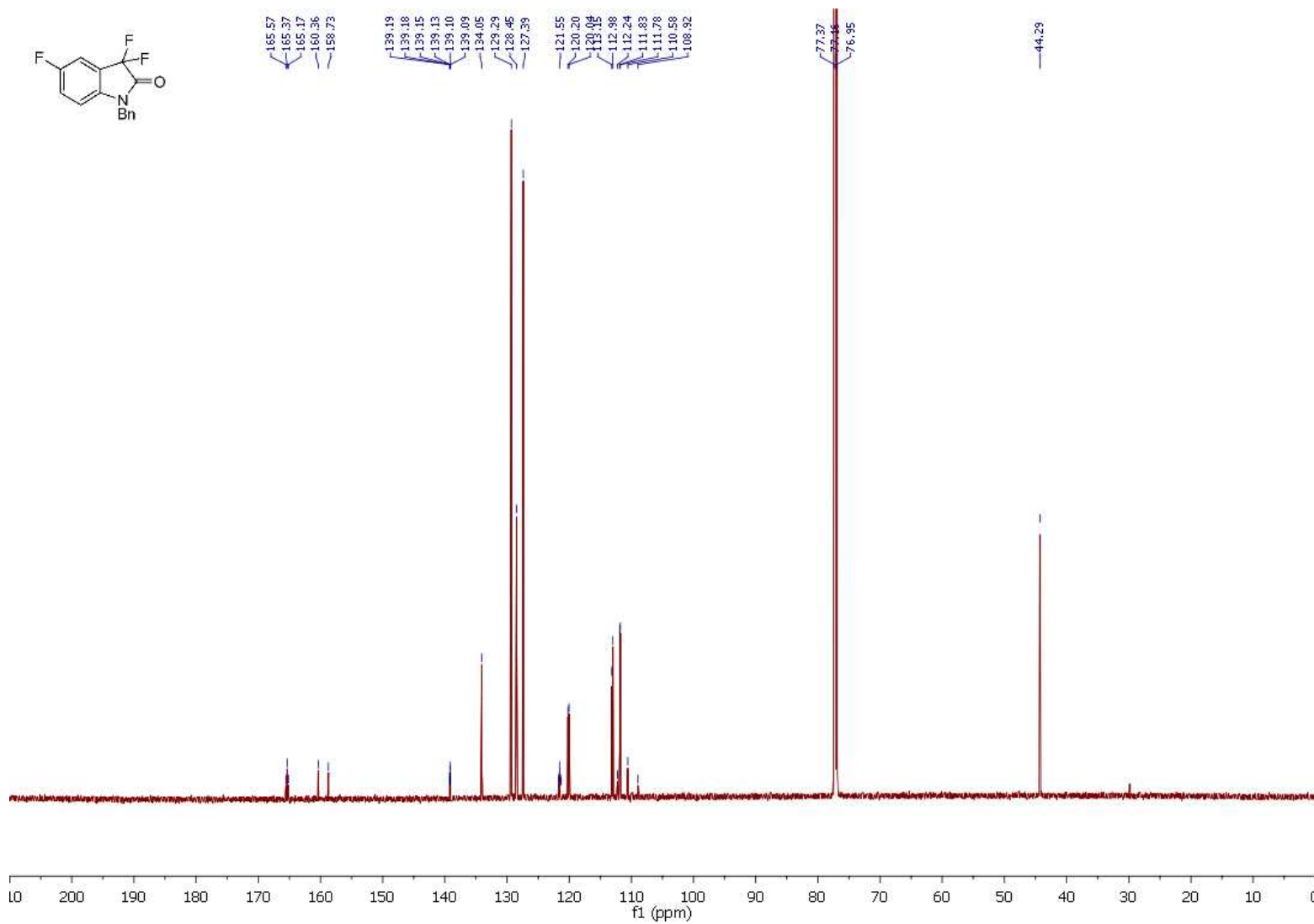
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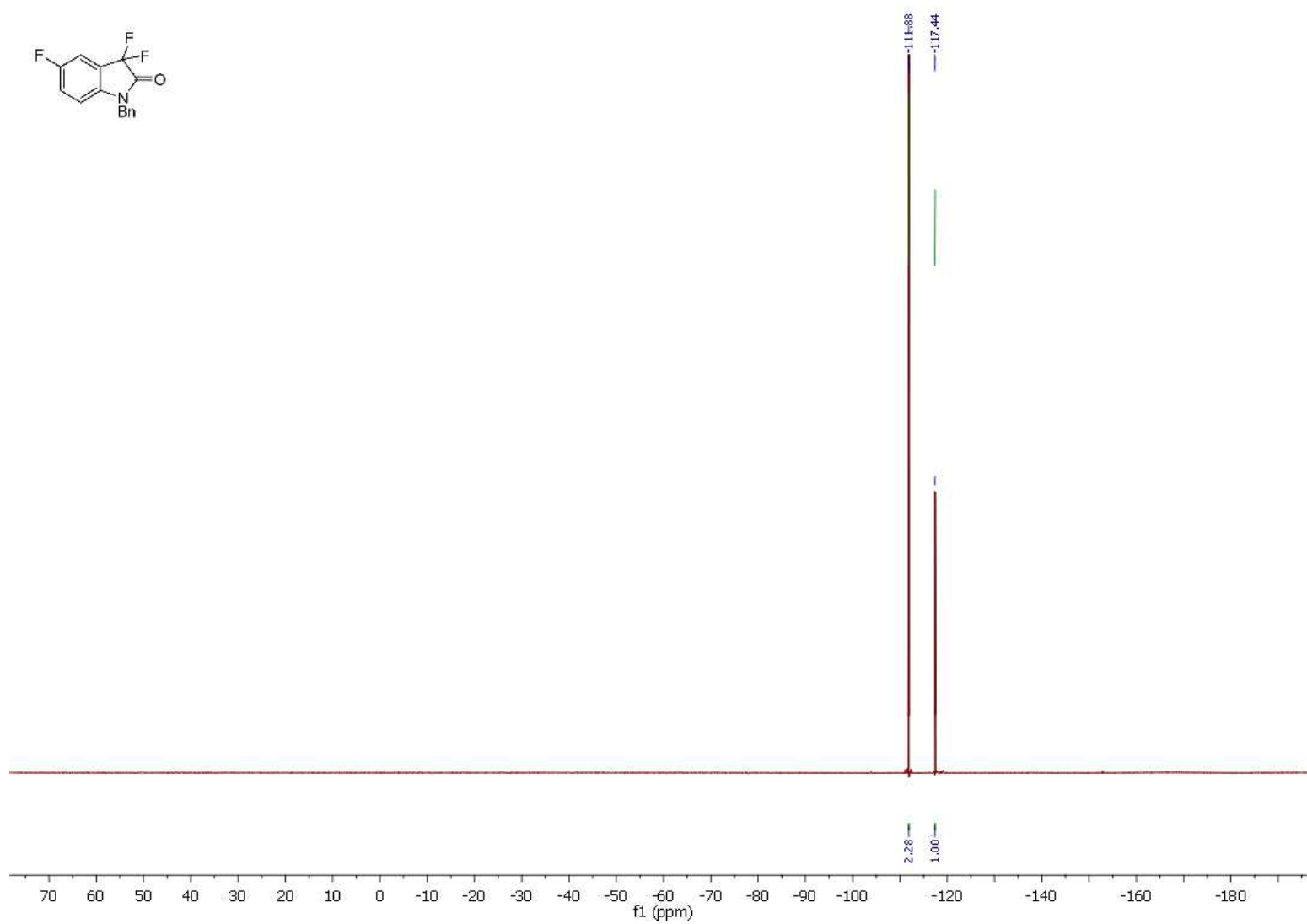
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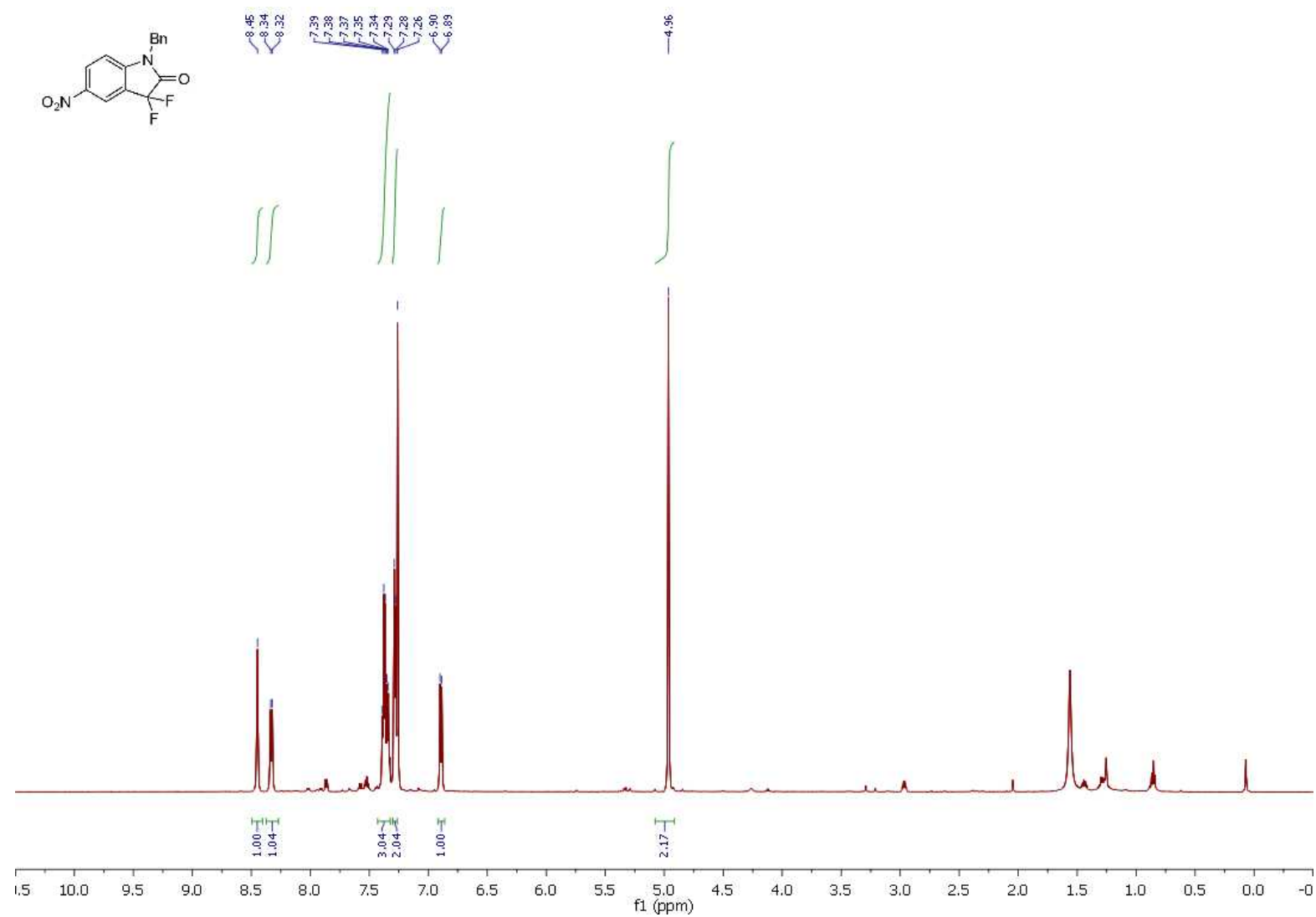
¹³C NMR spectrum of compound **4b**



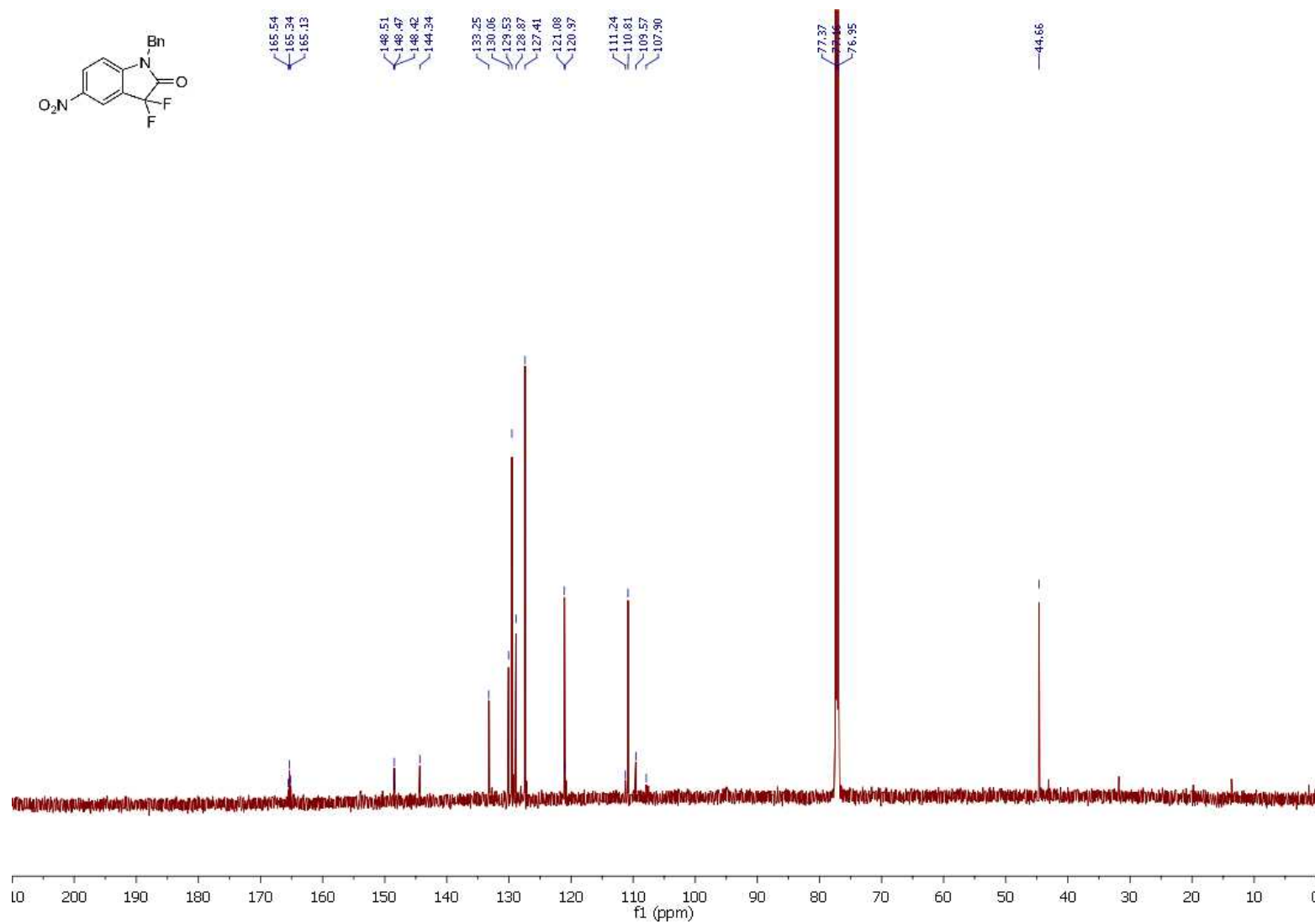
^{19}F NMR spectrum of compound **4b**



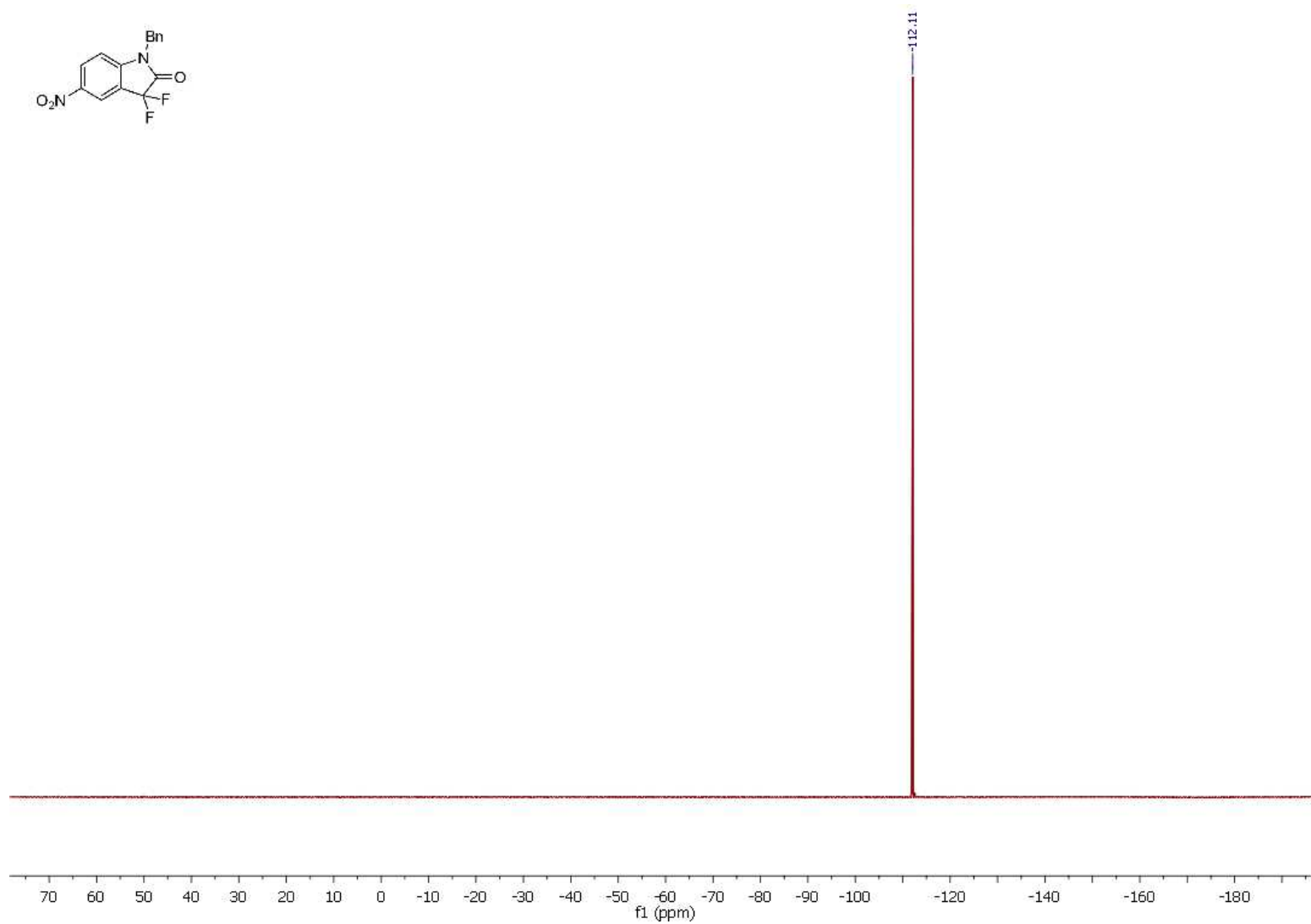
¹H NMR spectrum of compound **4c**



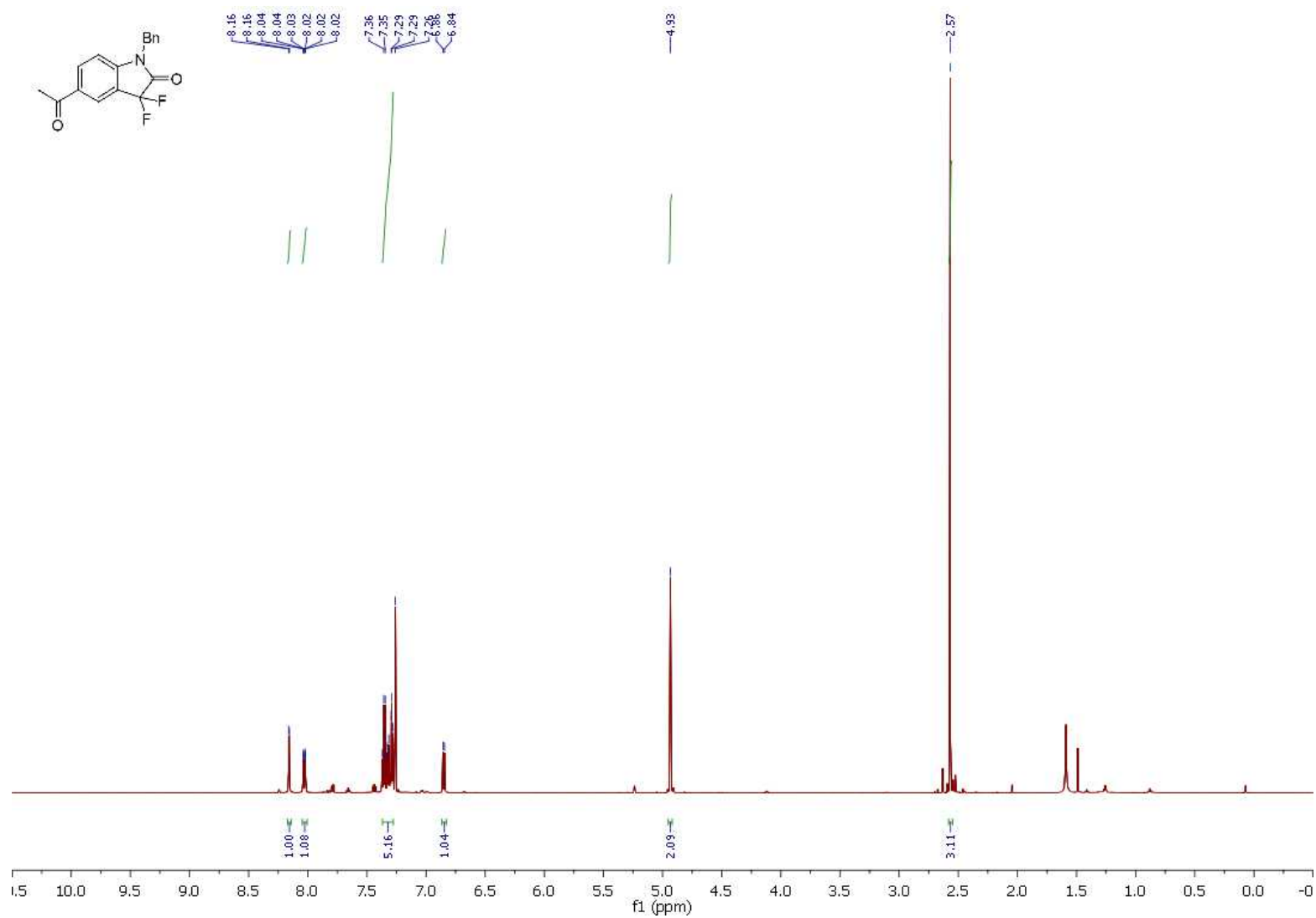
¹³C NMR spectrum of compound **4c**



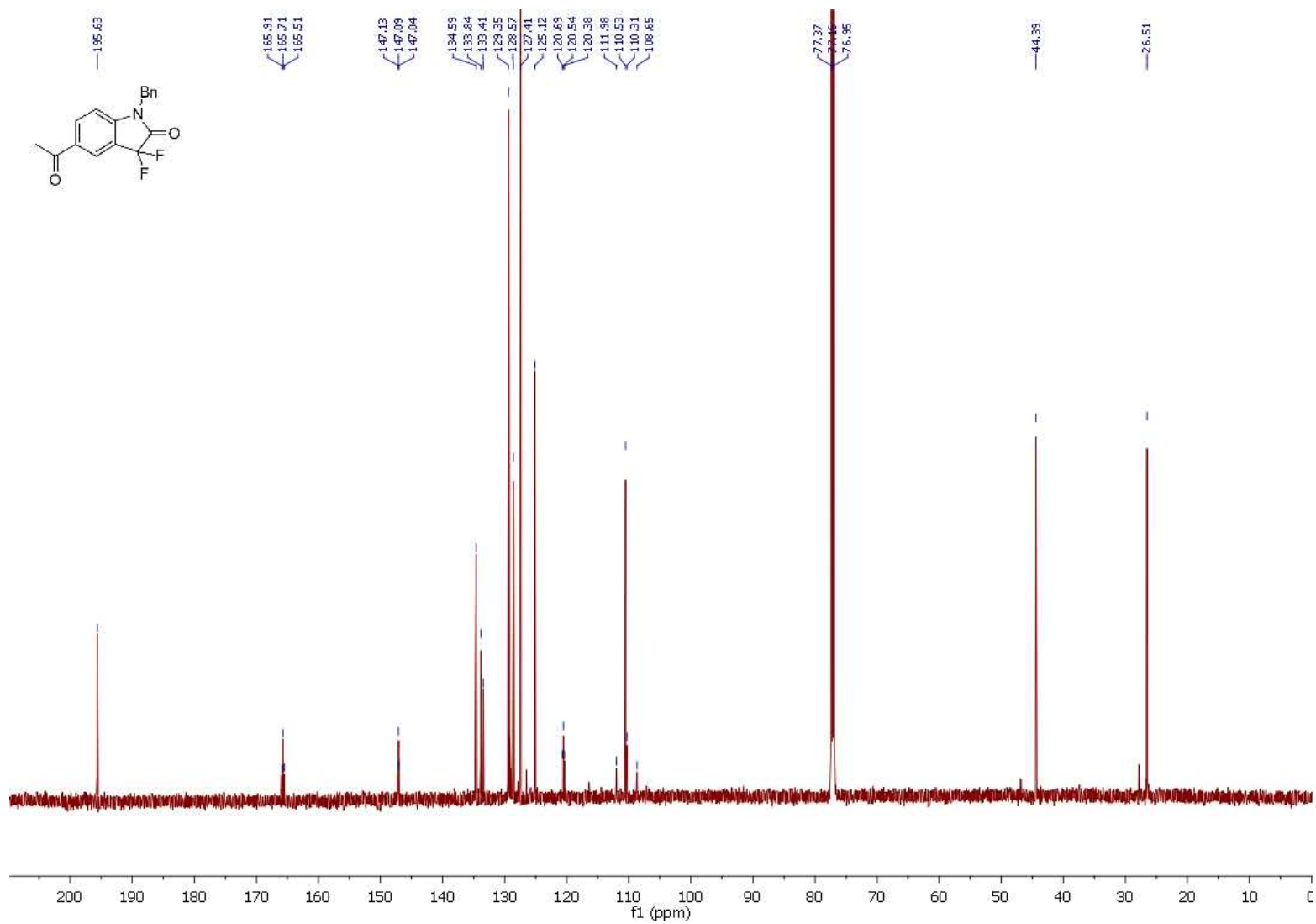
^{19}F NMR spectrum of compound **4c**



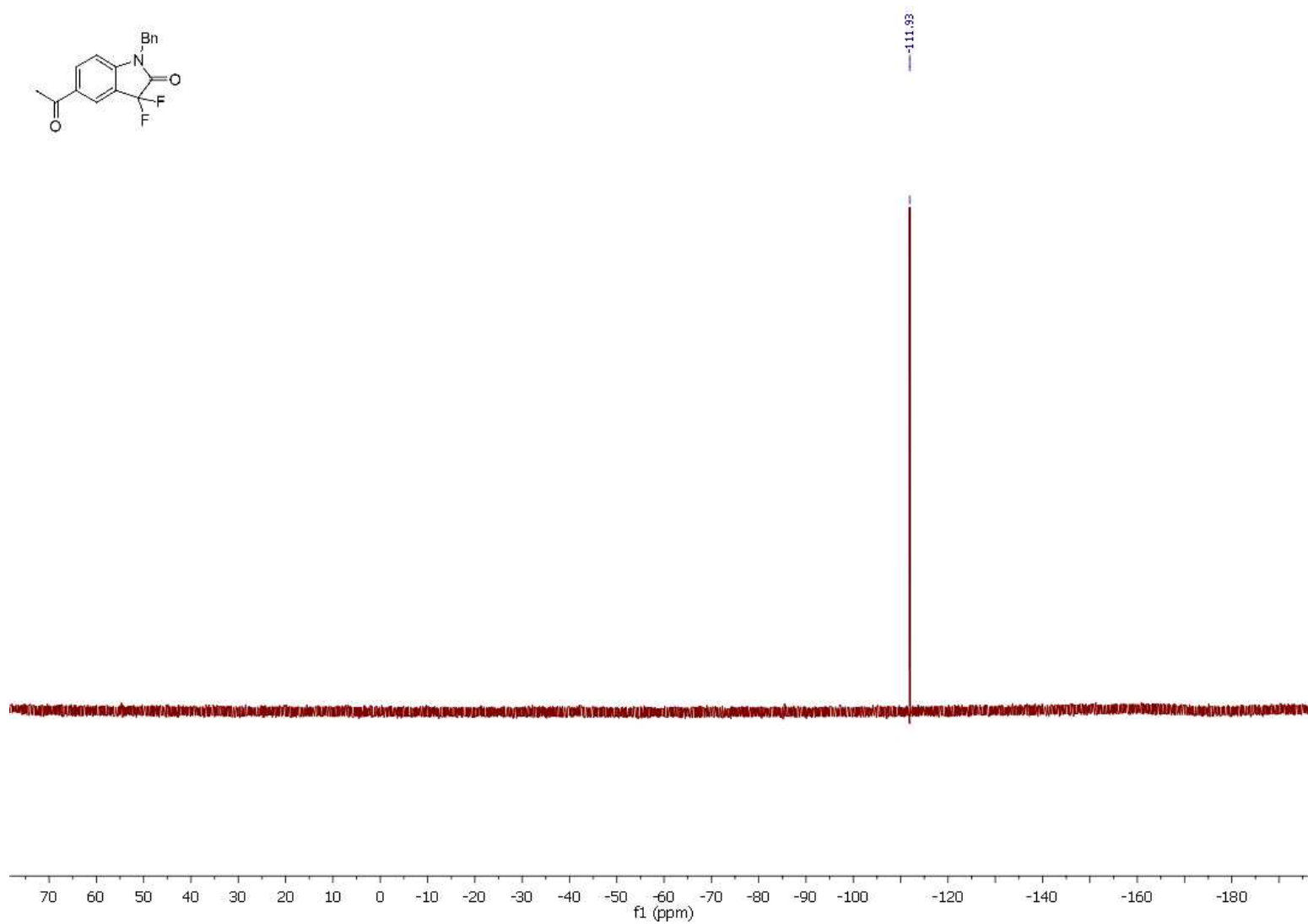
¹H NMR spectrum of compound **4d**



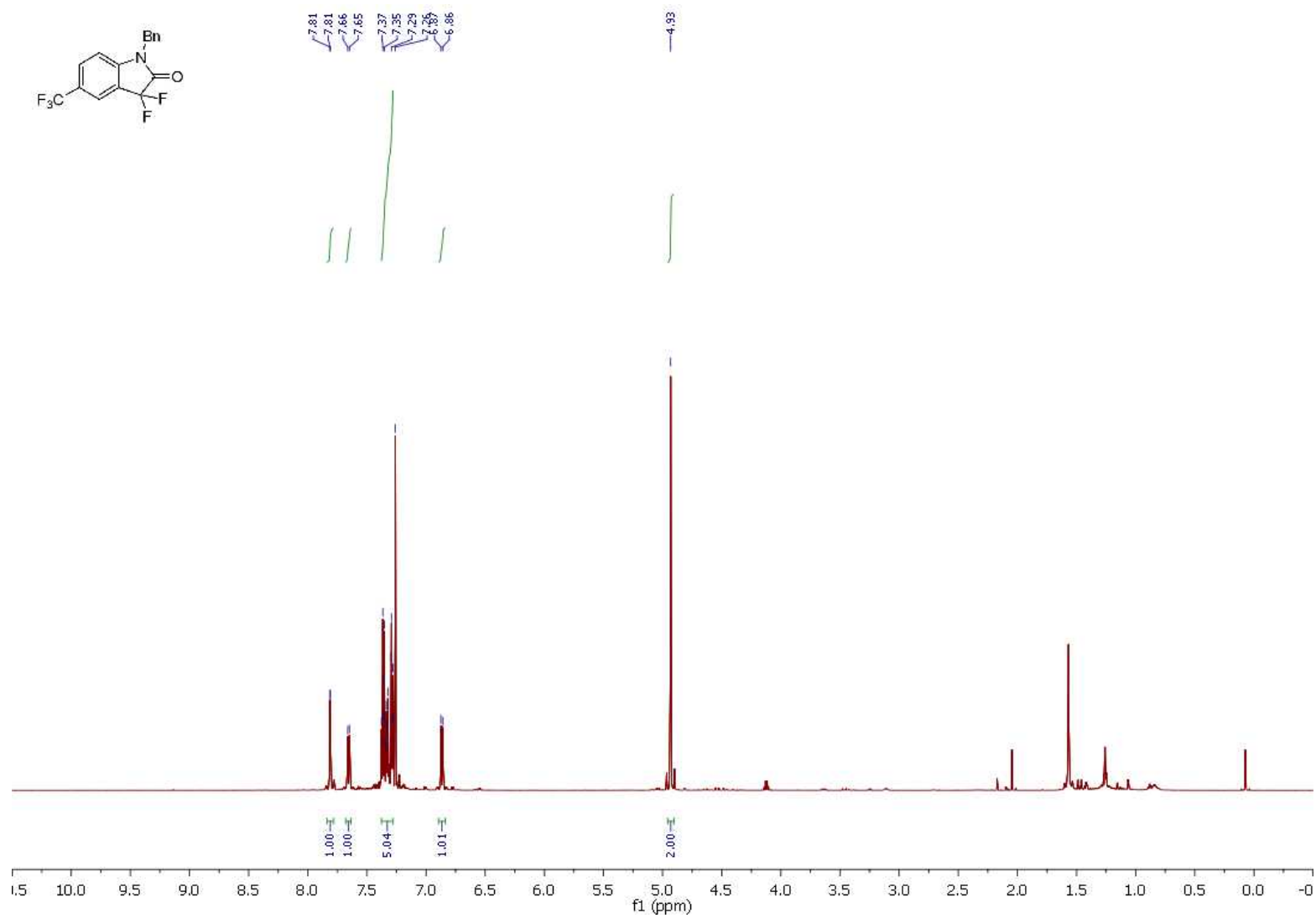
¹³C NMR spectrum of compound **4d**



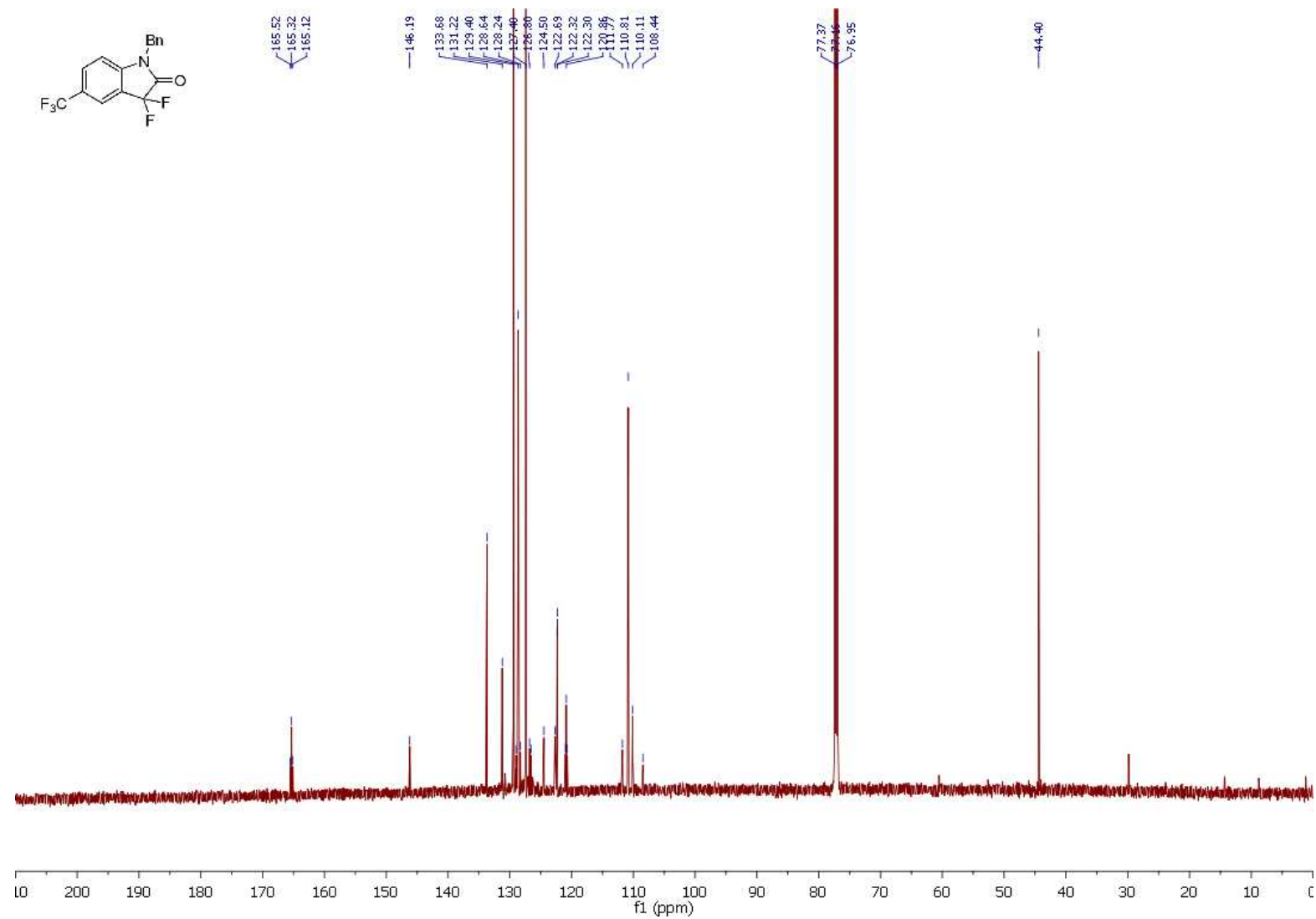
^{19}F NMR spectrum of compound **4d**



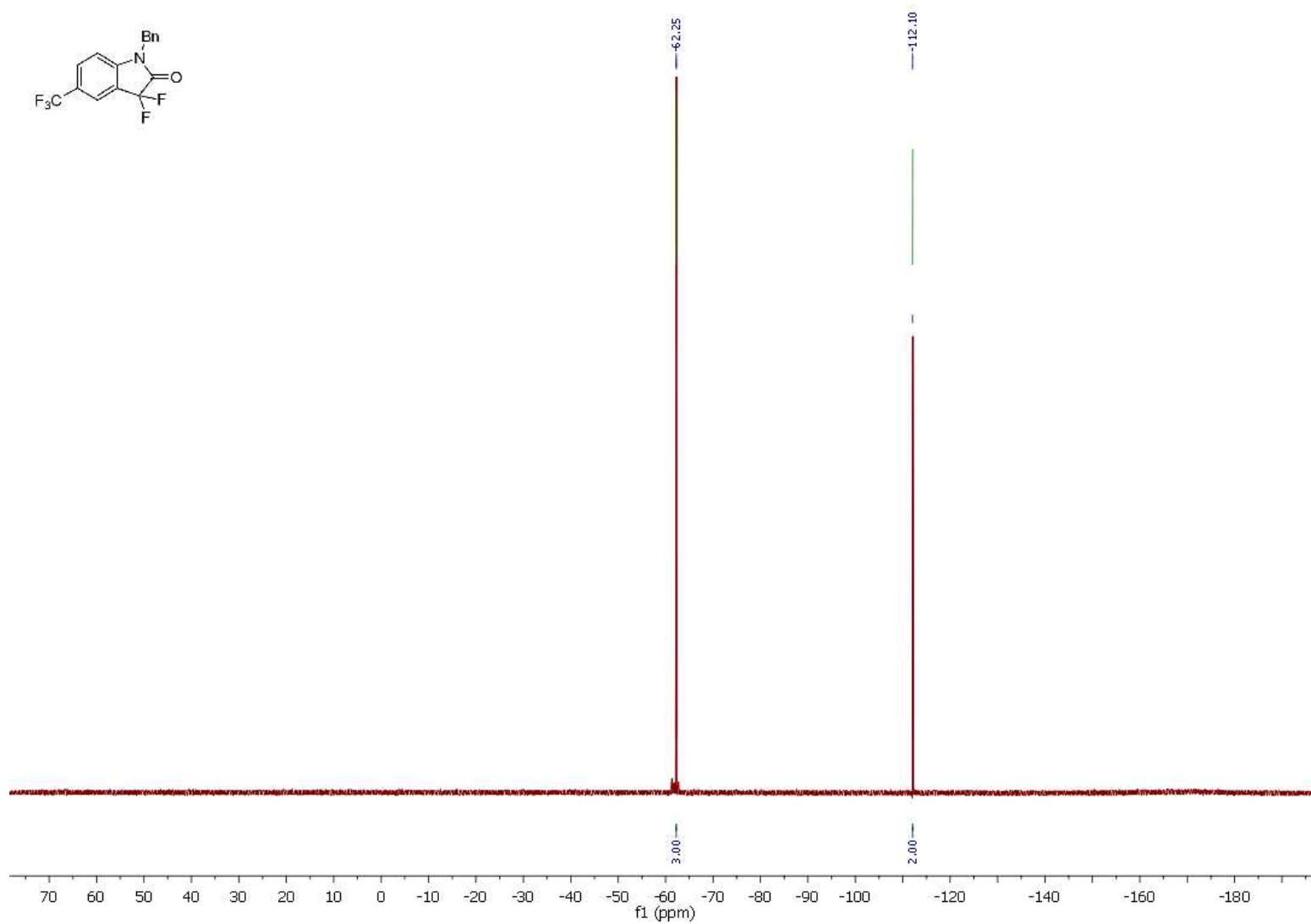
¹H NMR spectrum of compound **4e**



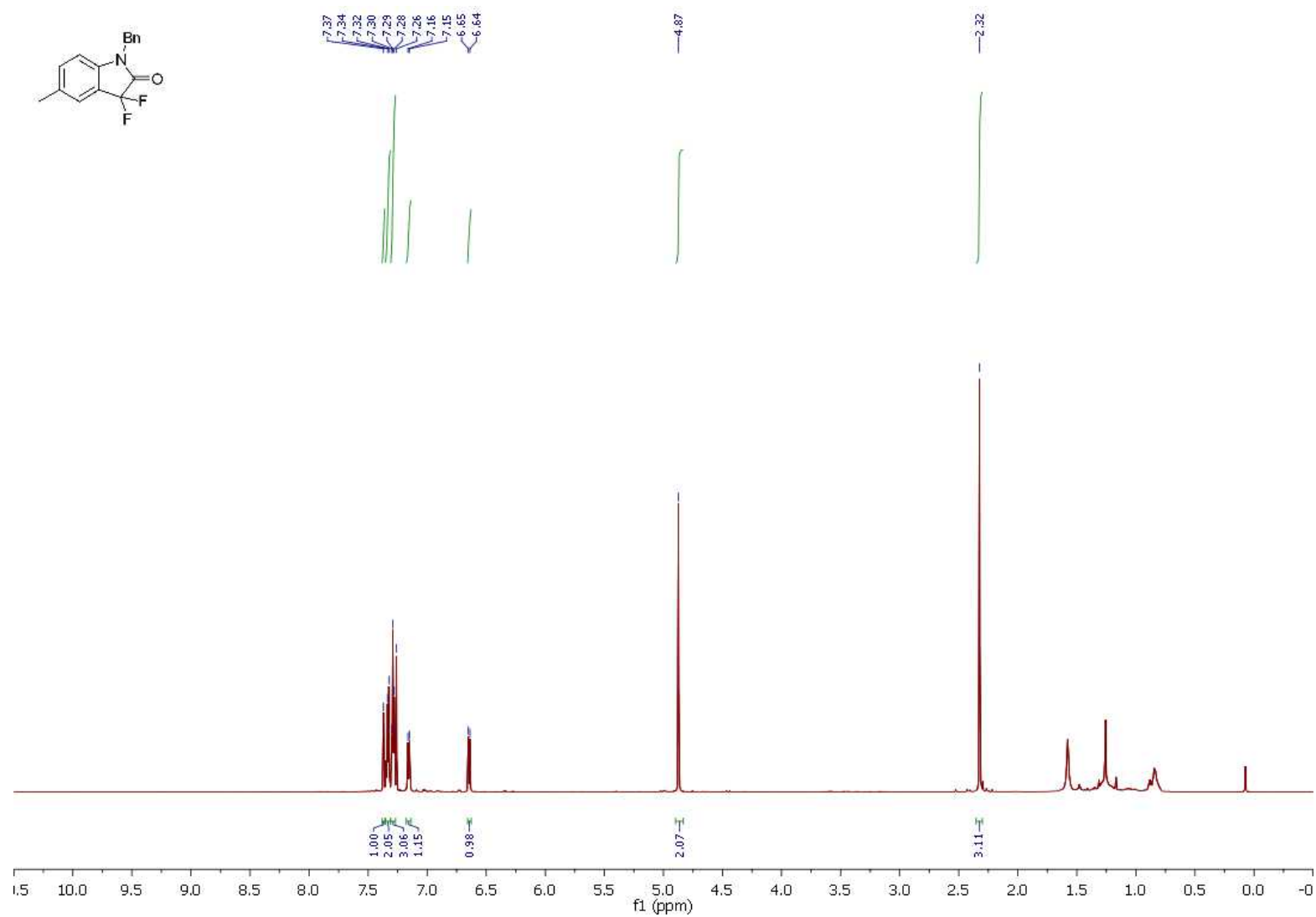
¹³C NMR spectrum of compound **4e**



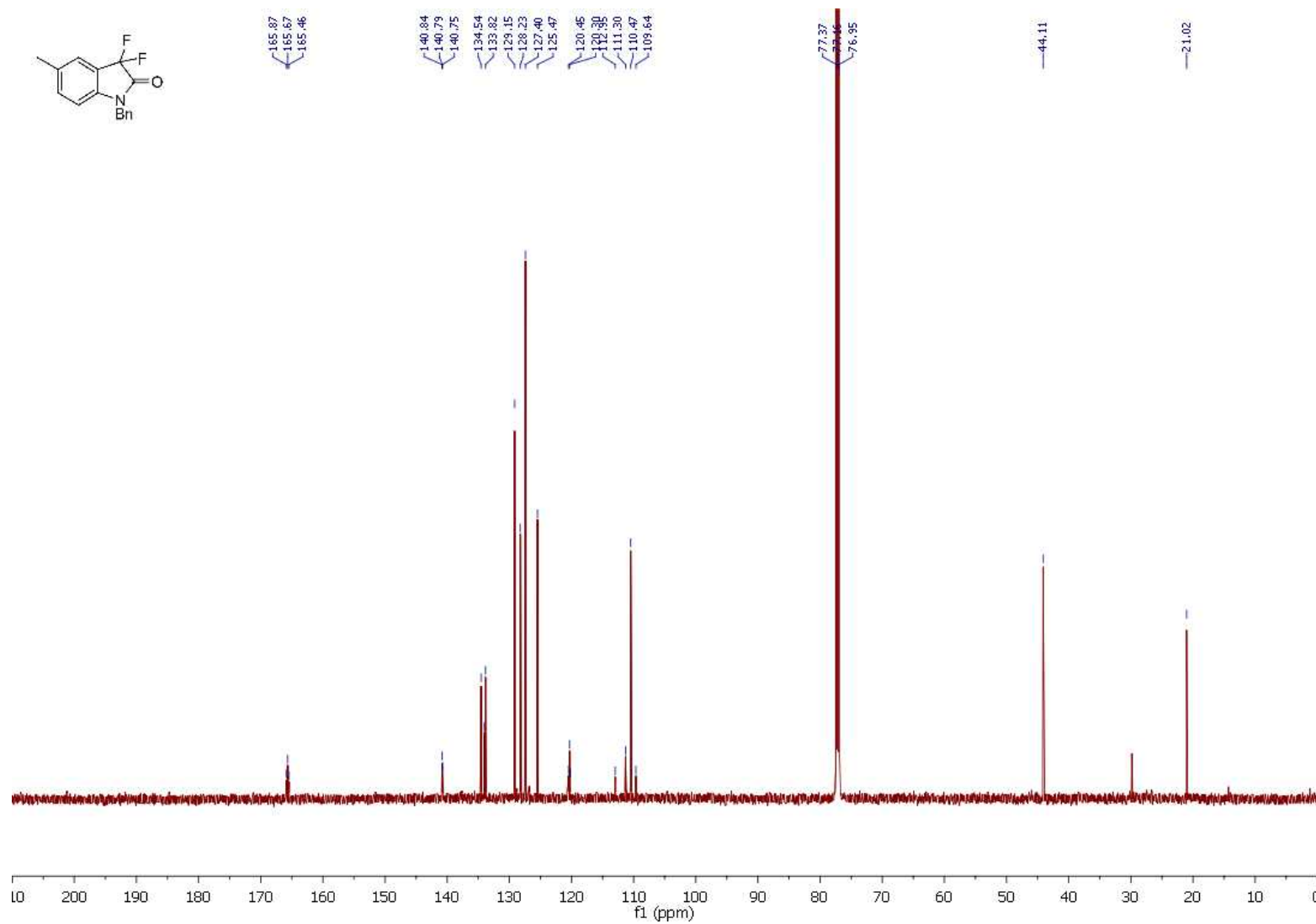
^{19}F NMR spectrum of compound **4e**



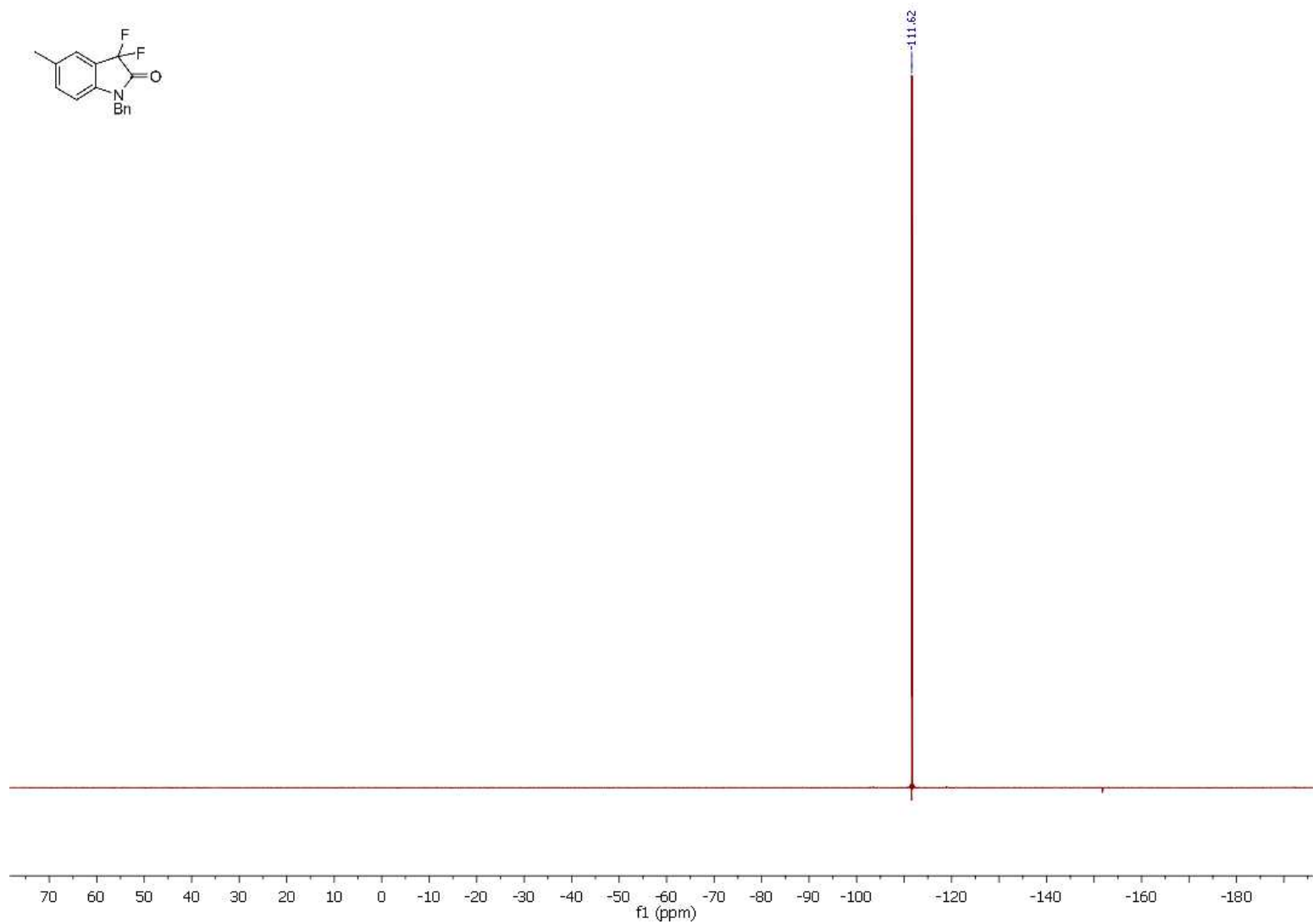
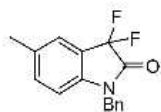
¹H NMR spectrum of compound **4f**



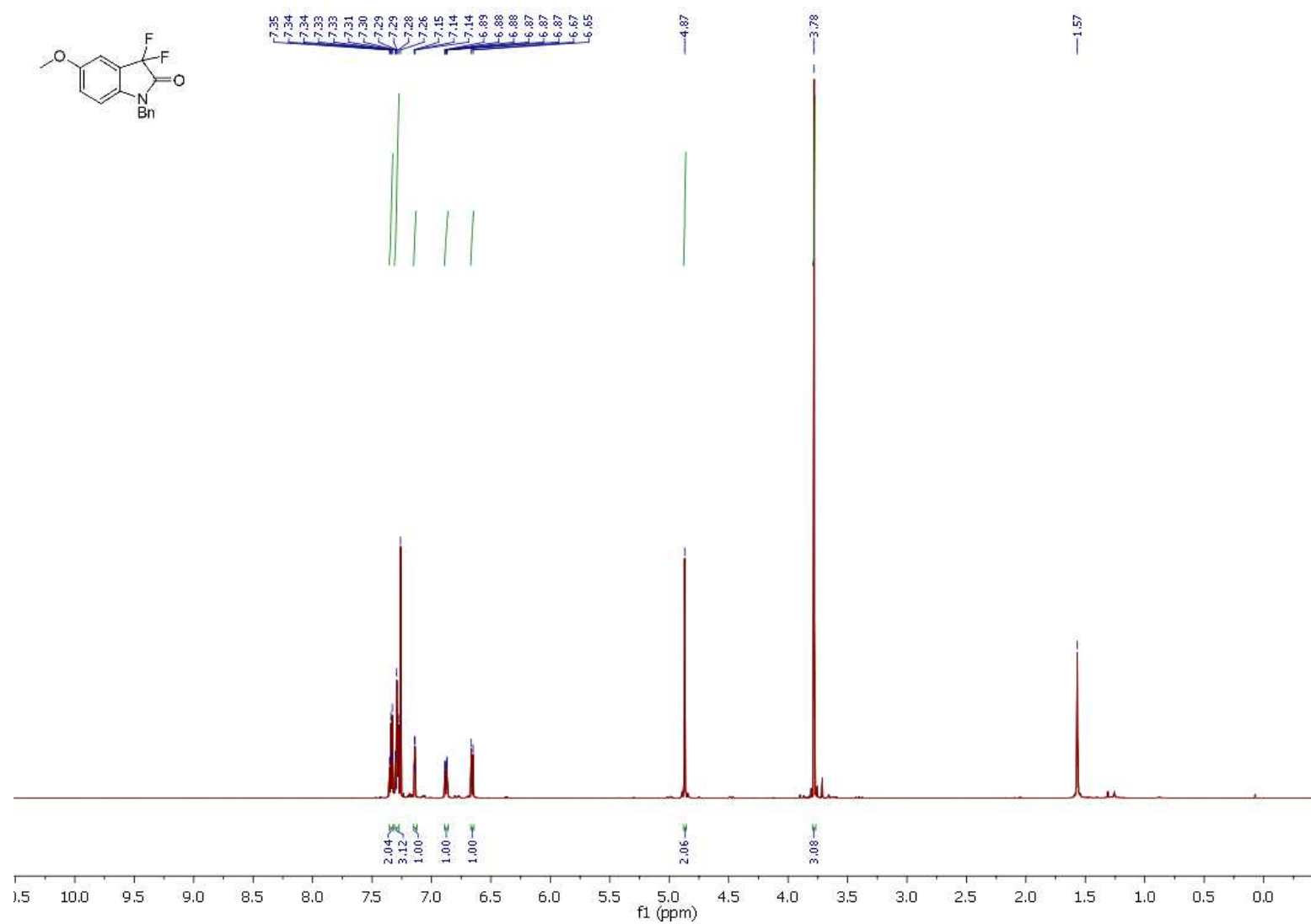
¹³C NMR spectrum of compound **4f**



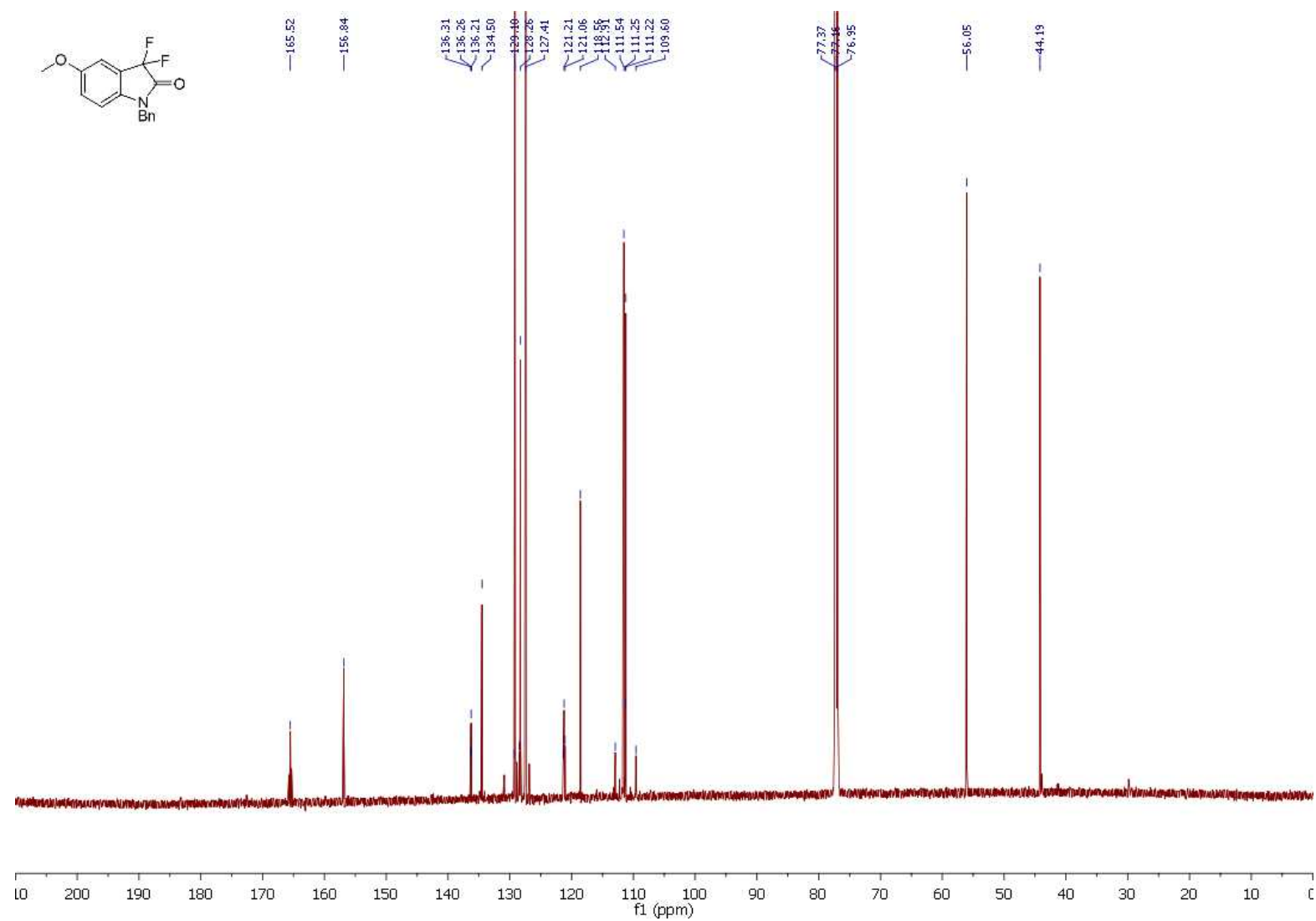
^{19}F NMR spectrum of compound **4f**



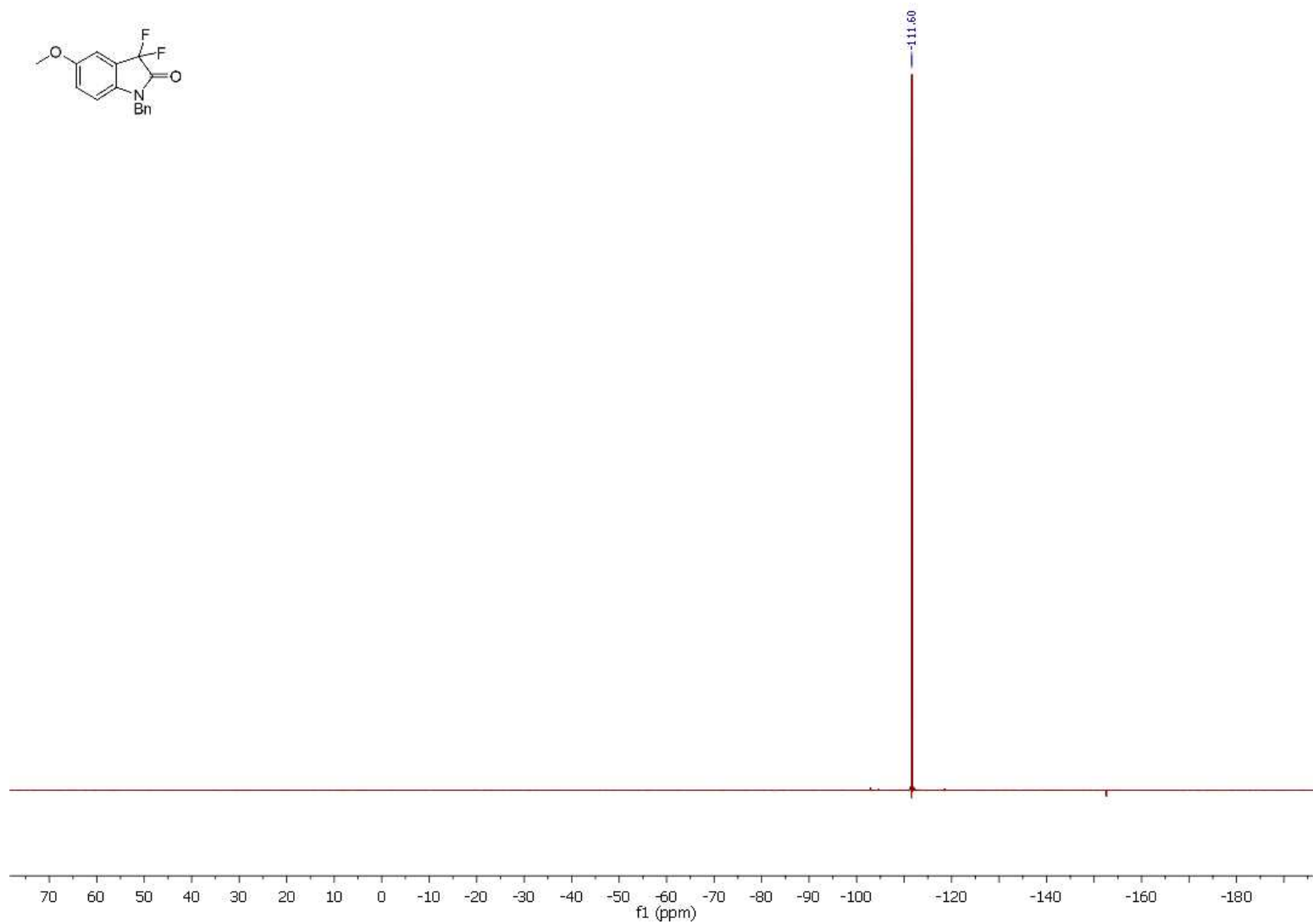
¹H NMR spectrum of compound **4g**



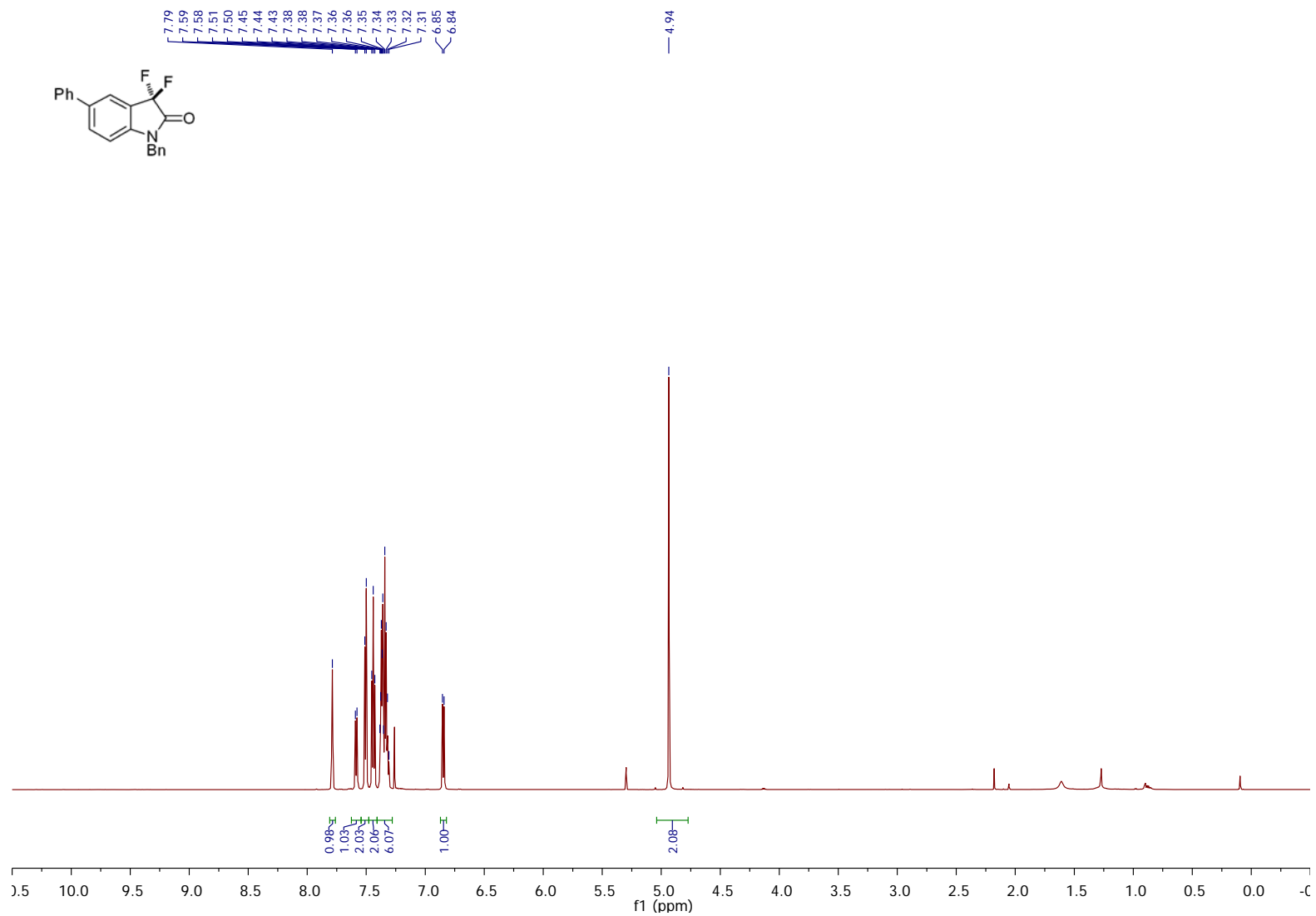
¹³C NMR spectrum of compound **4g**



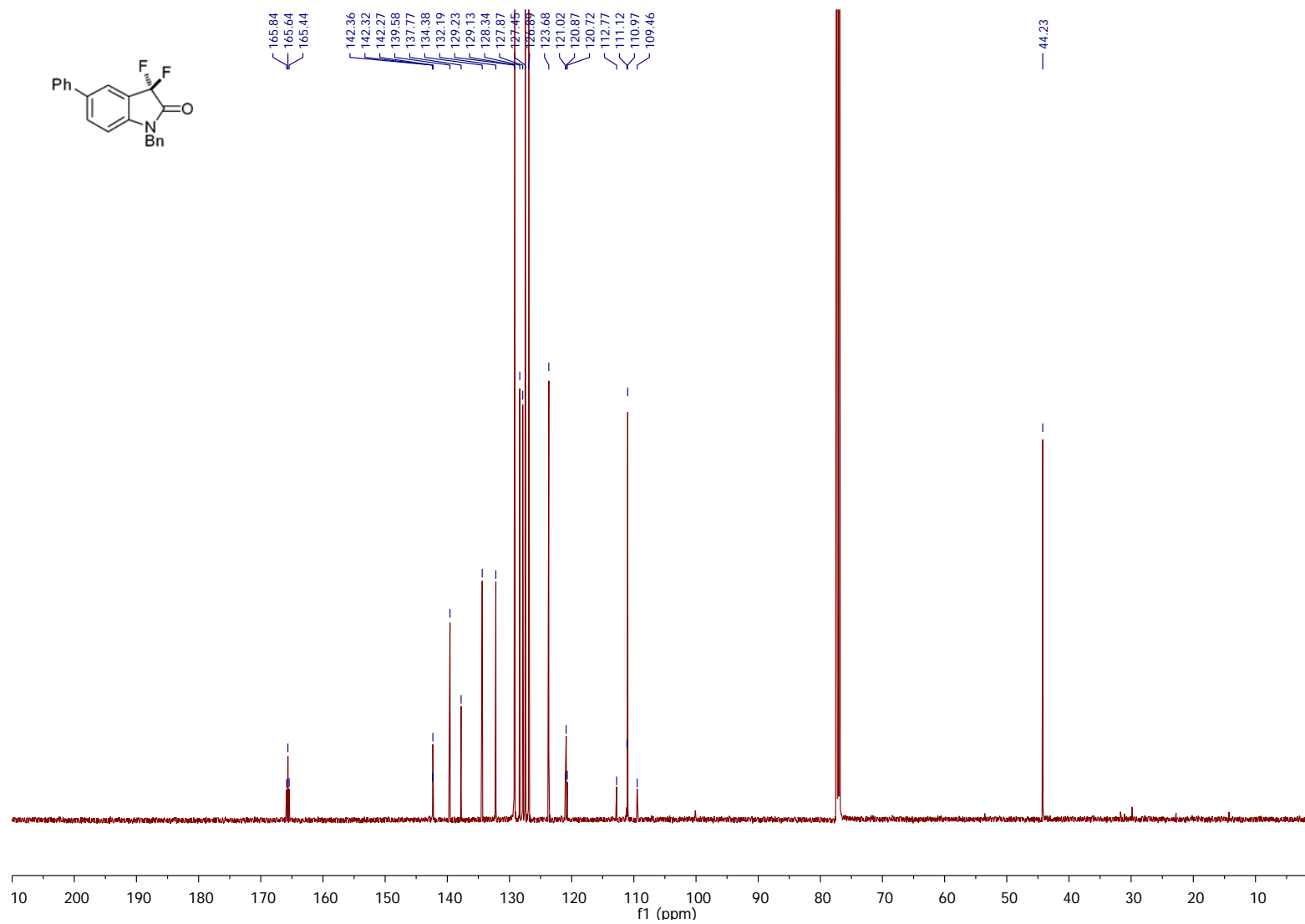
^{19}F NMR spectrum of compound **4g**



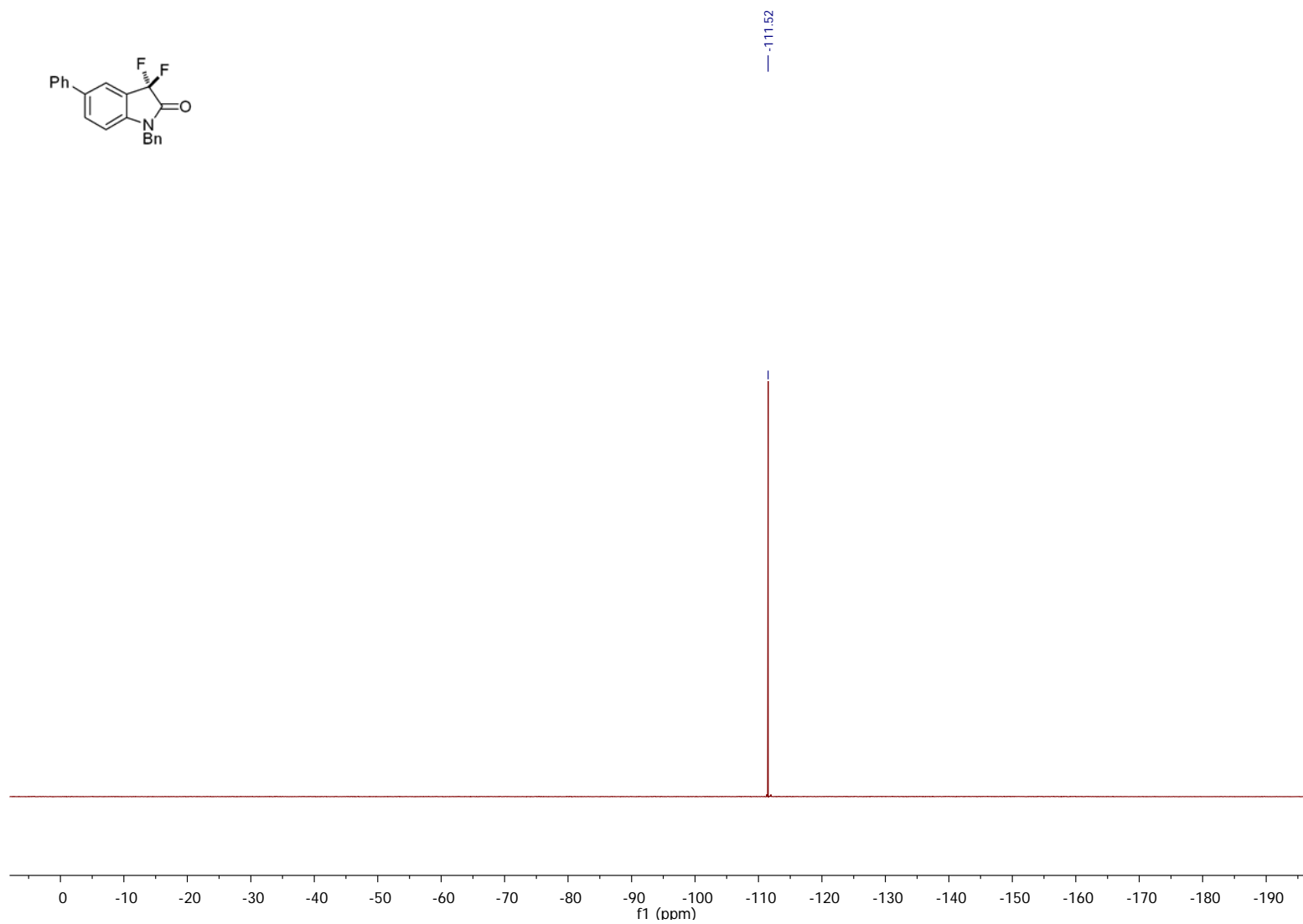
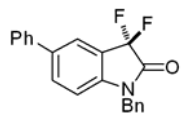
¹H NMR spectrum of compound **4h**



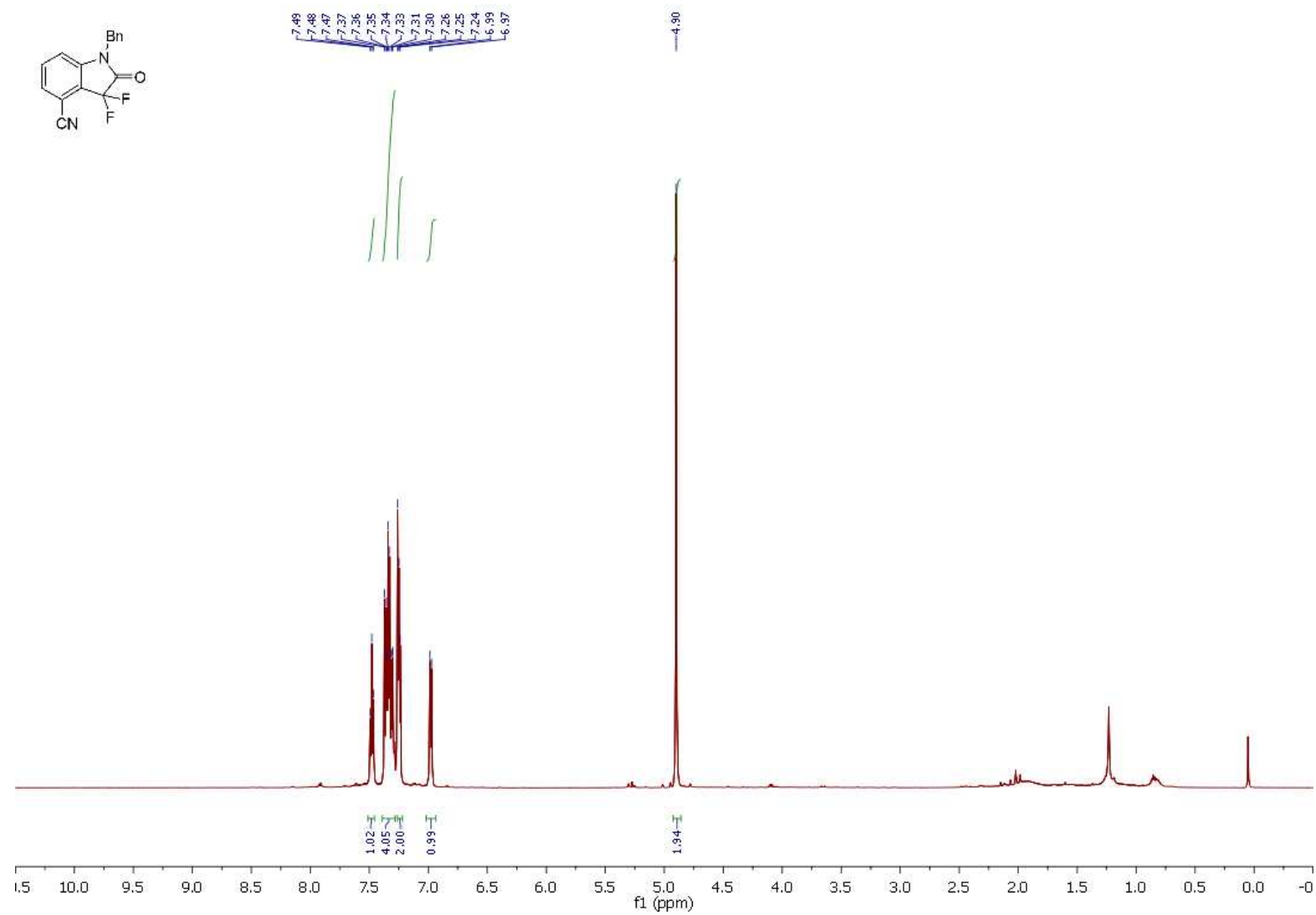
¹³C NMR spectrum of compound **4h**



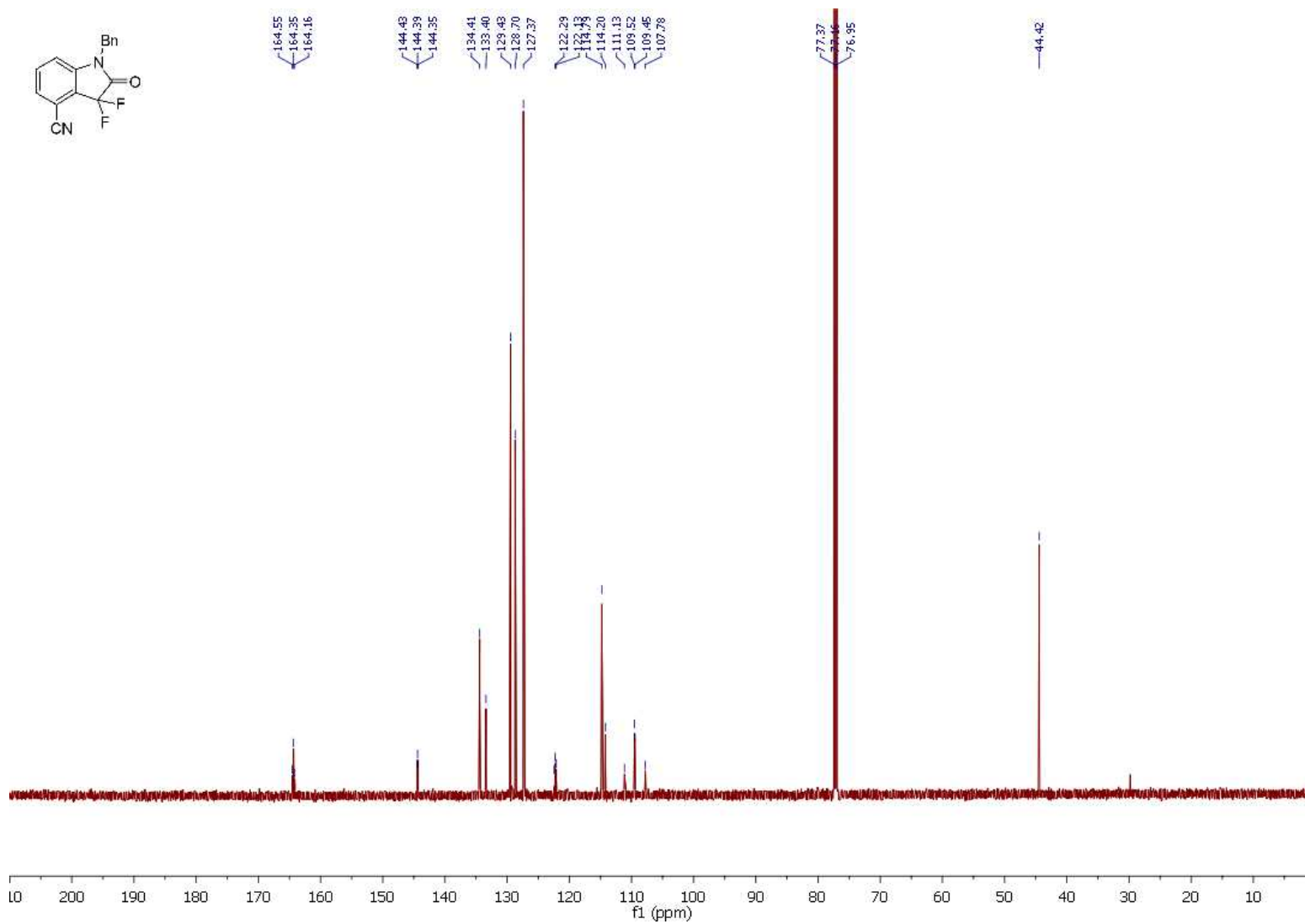
^{19}F NMR spectrum of compound **4h**



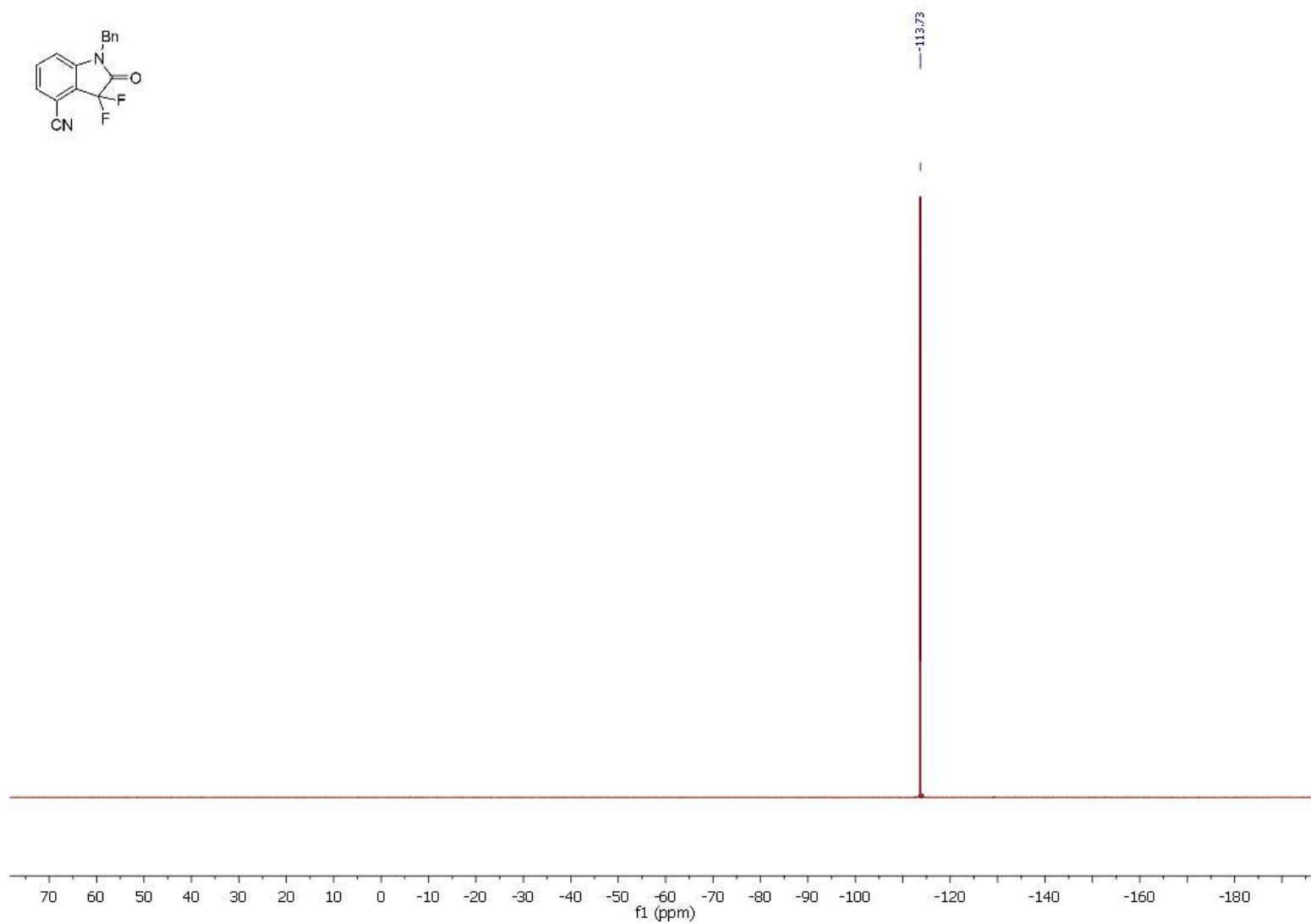
¹H NMR spectrum of compound **4i**



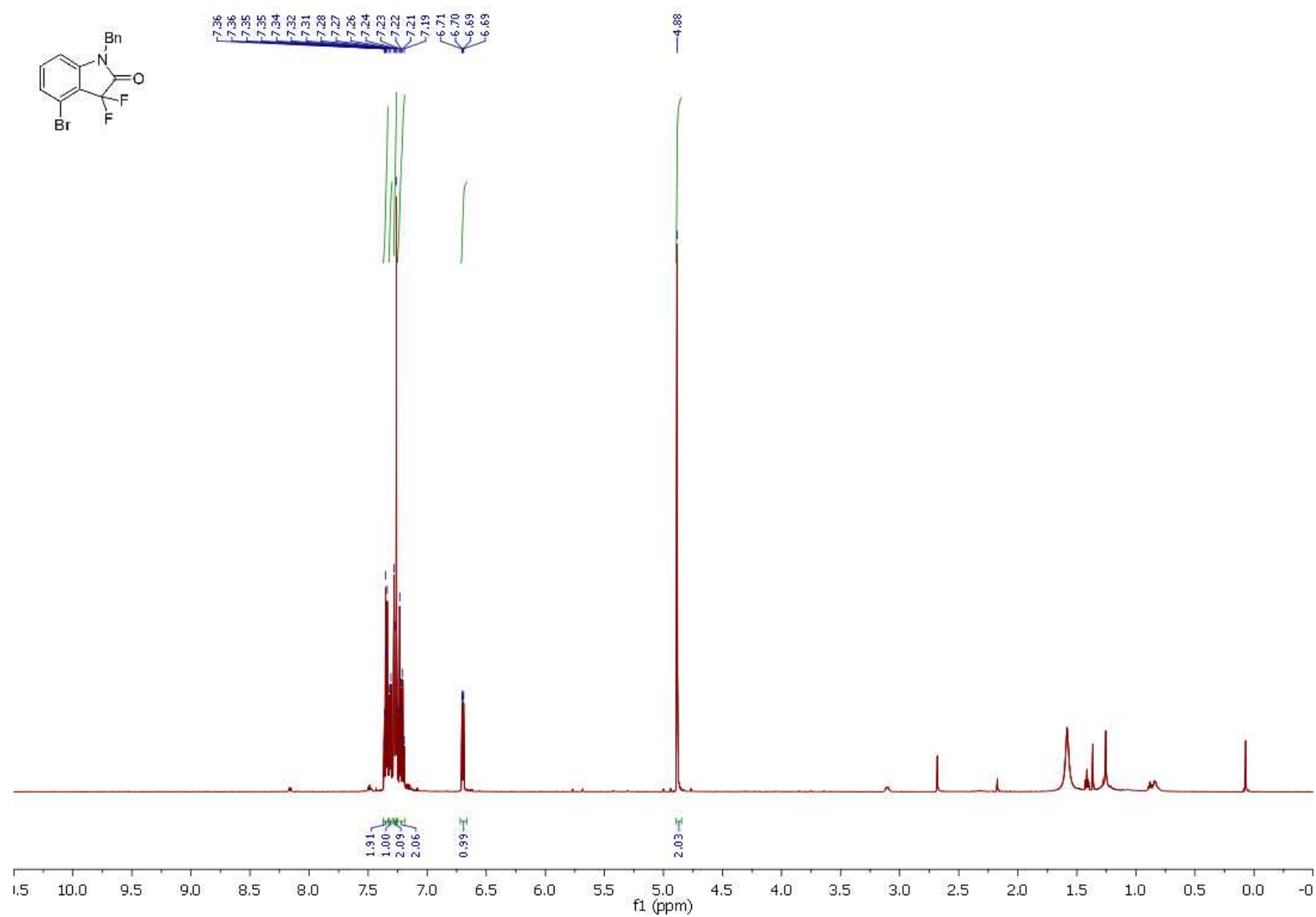
¹³C NMR spectrum of compound **4i**



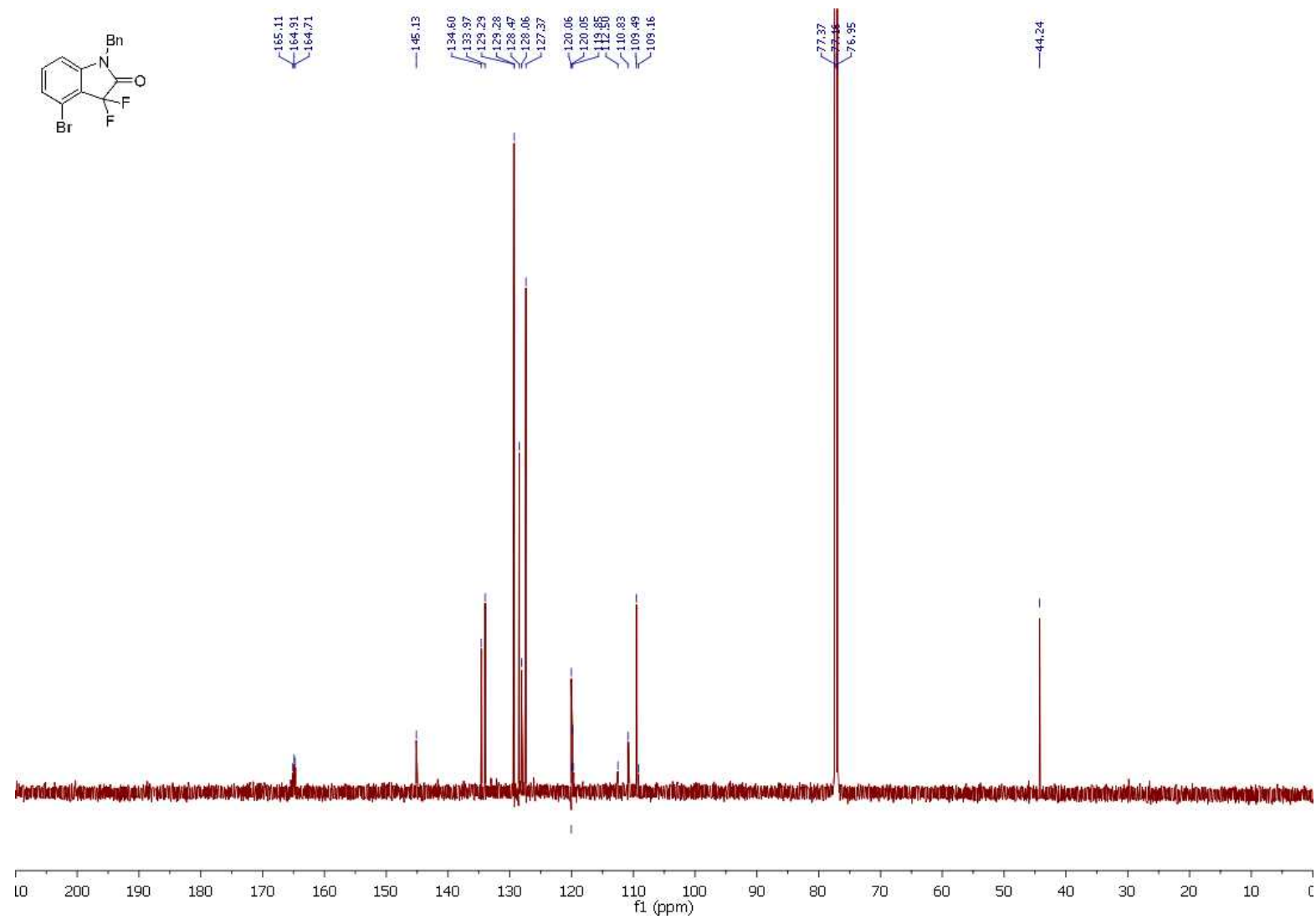
^{19}F NMR spectrum of compound **4i**



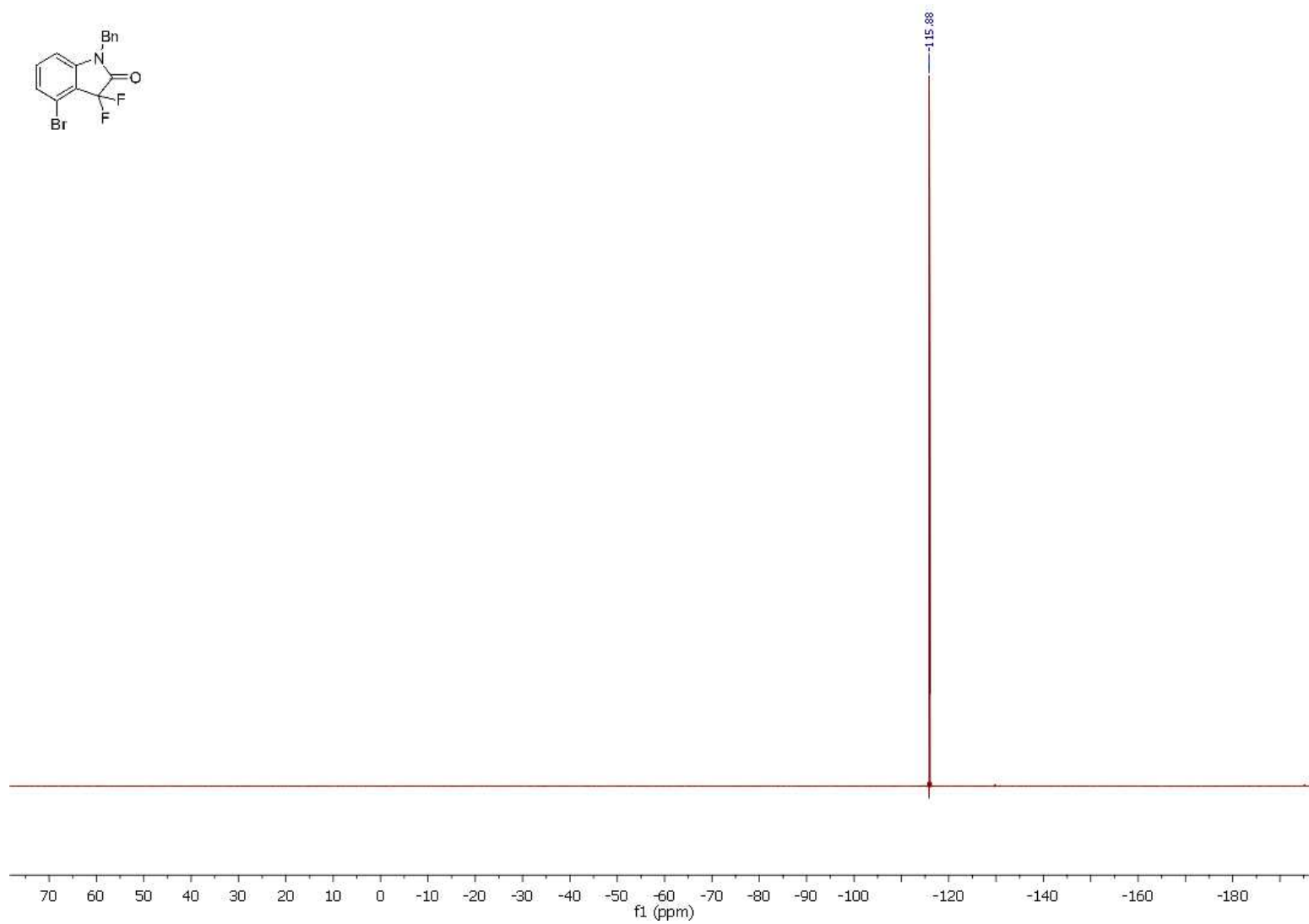
¹H NMR spectrum of compound **4j**



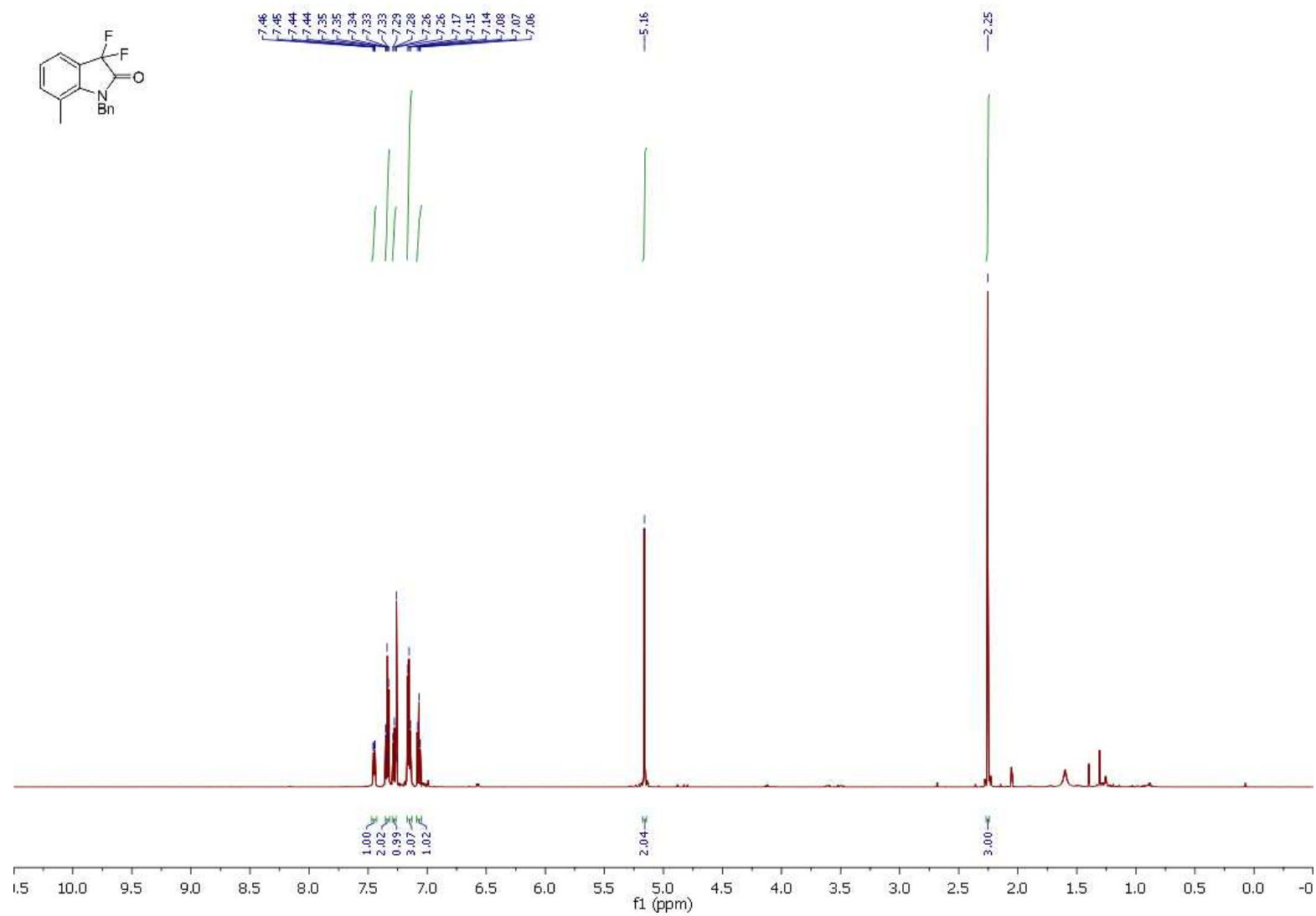
¹³C NMR spectrum of compound **4j**



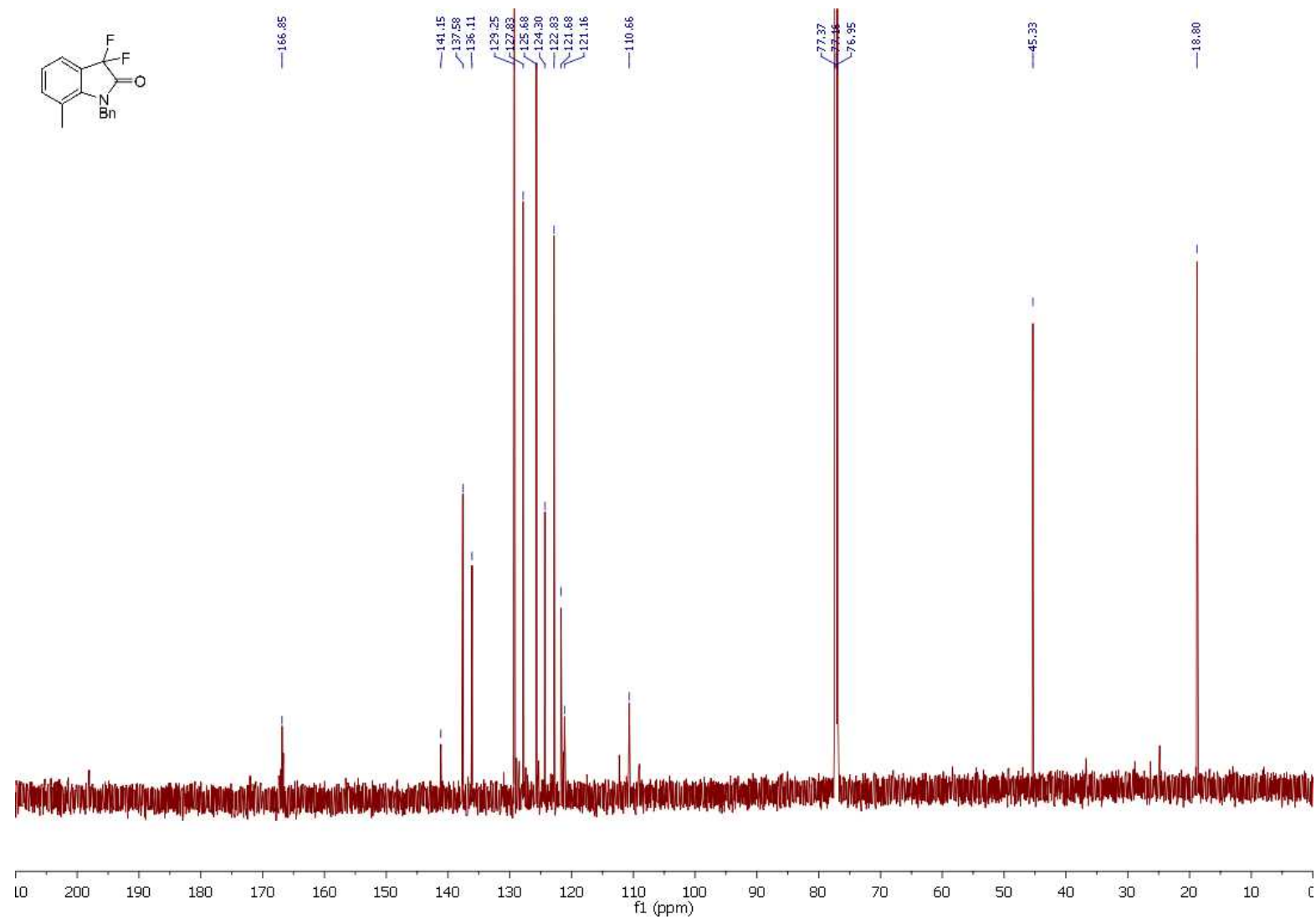
^{19}F NMR spectrum of compound **4j**



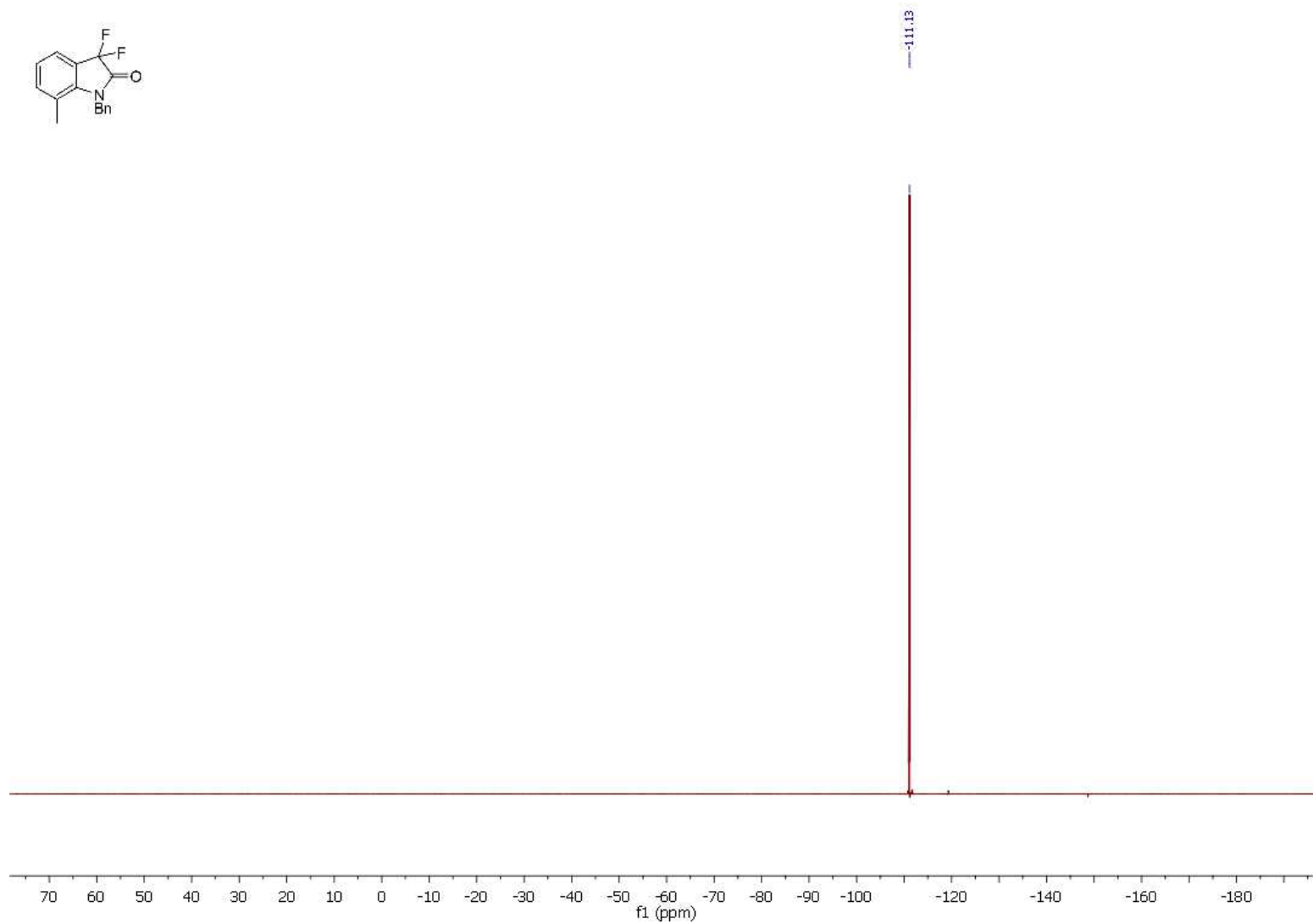
¹H NMR spectrum of compound **4k**



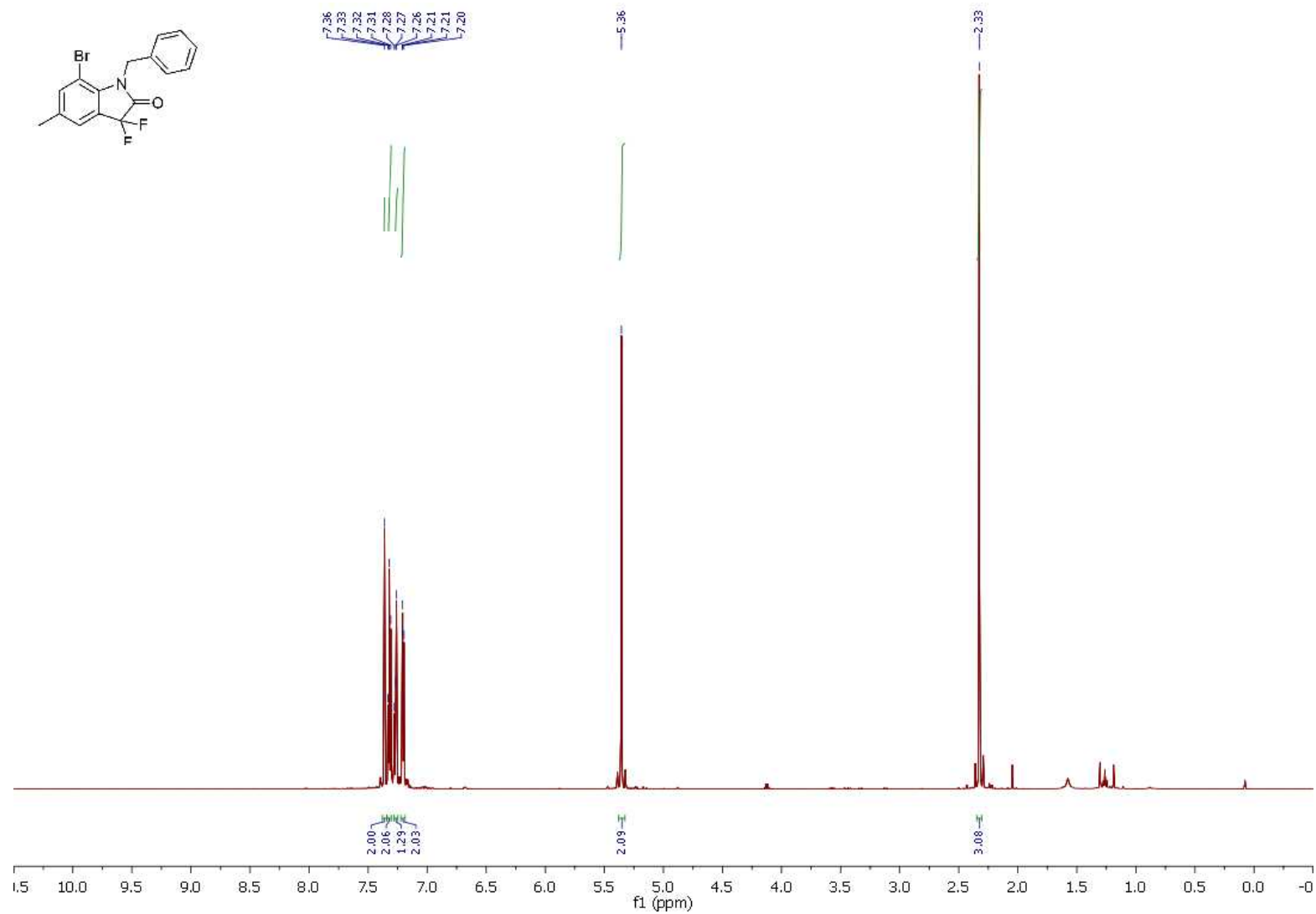
¹³C NMR spectrum of compound **4k**



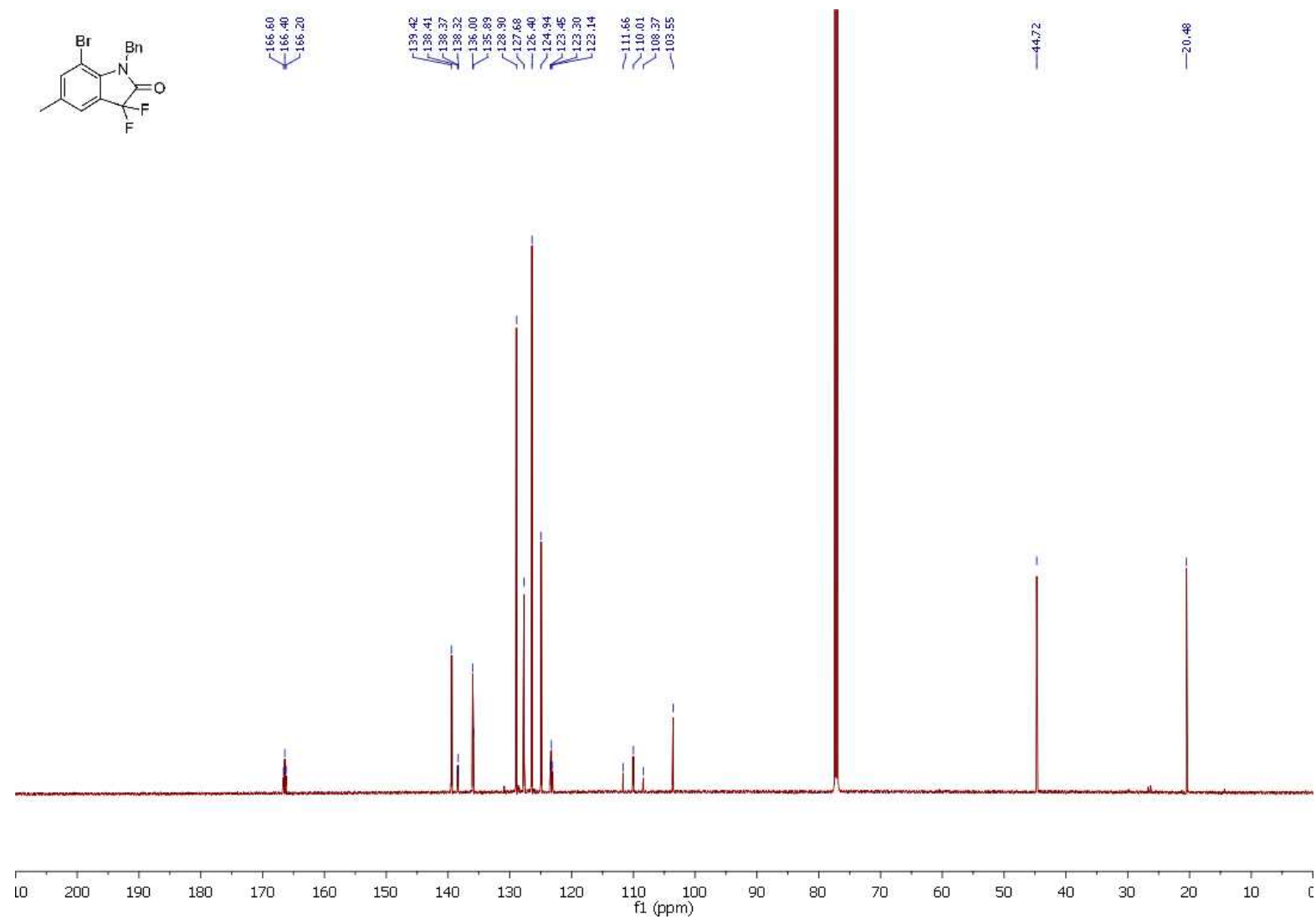
^{19}F NMR spectrum of compound **4k**



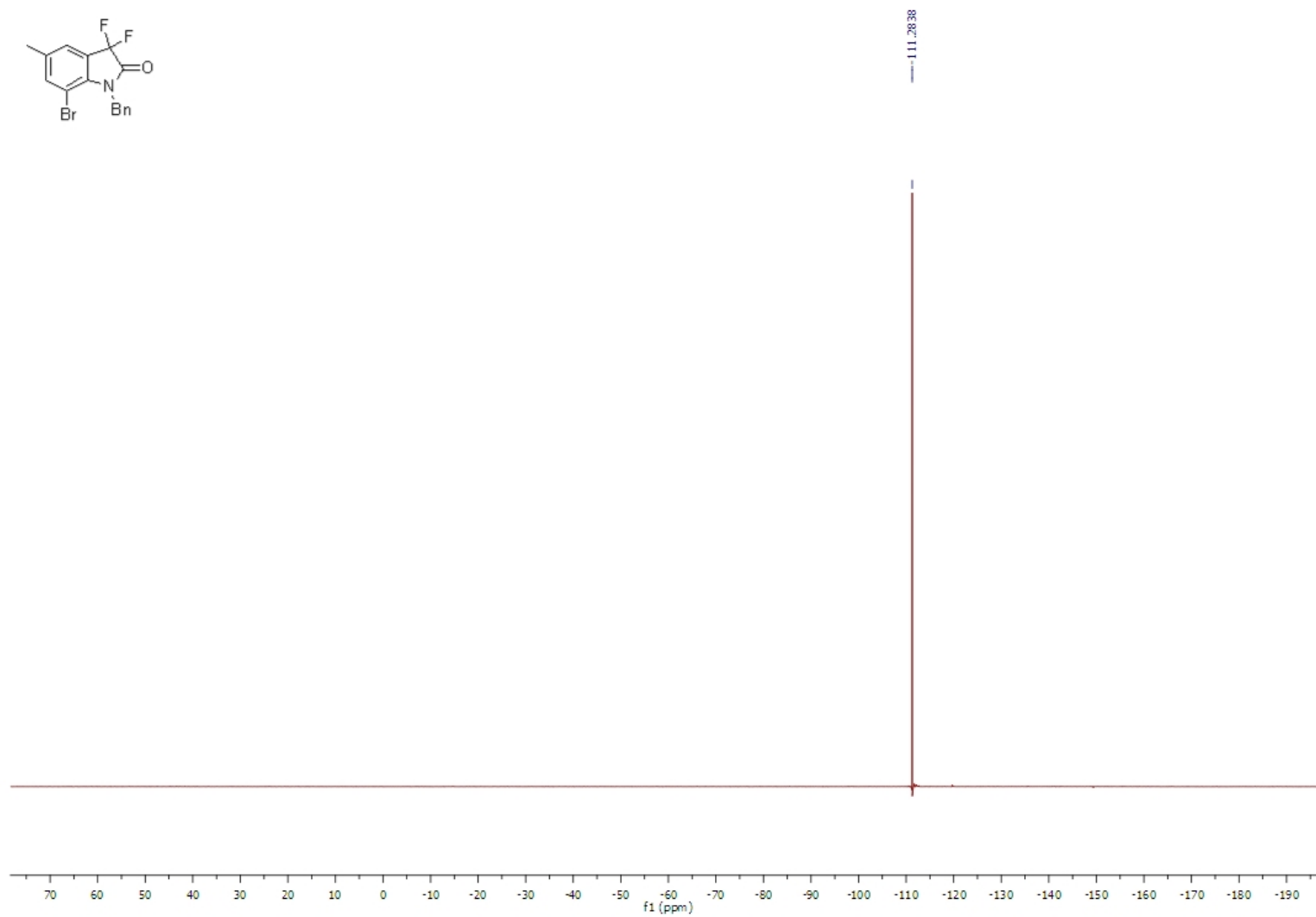
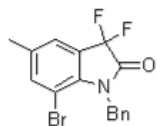
¹H NMR spectrum of compound **4l**



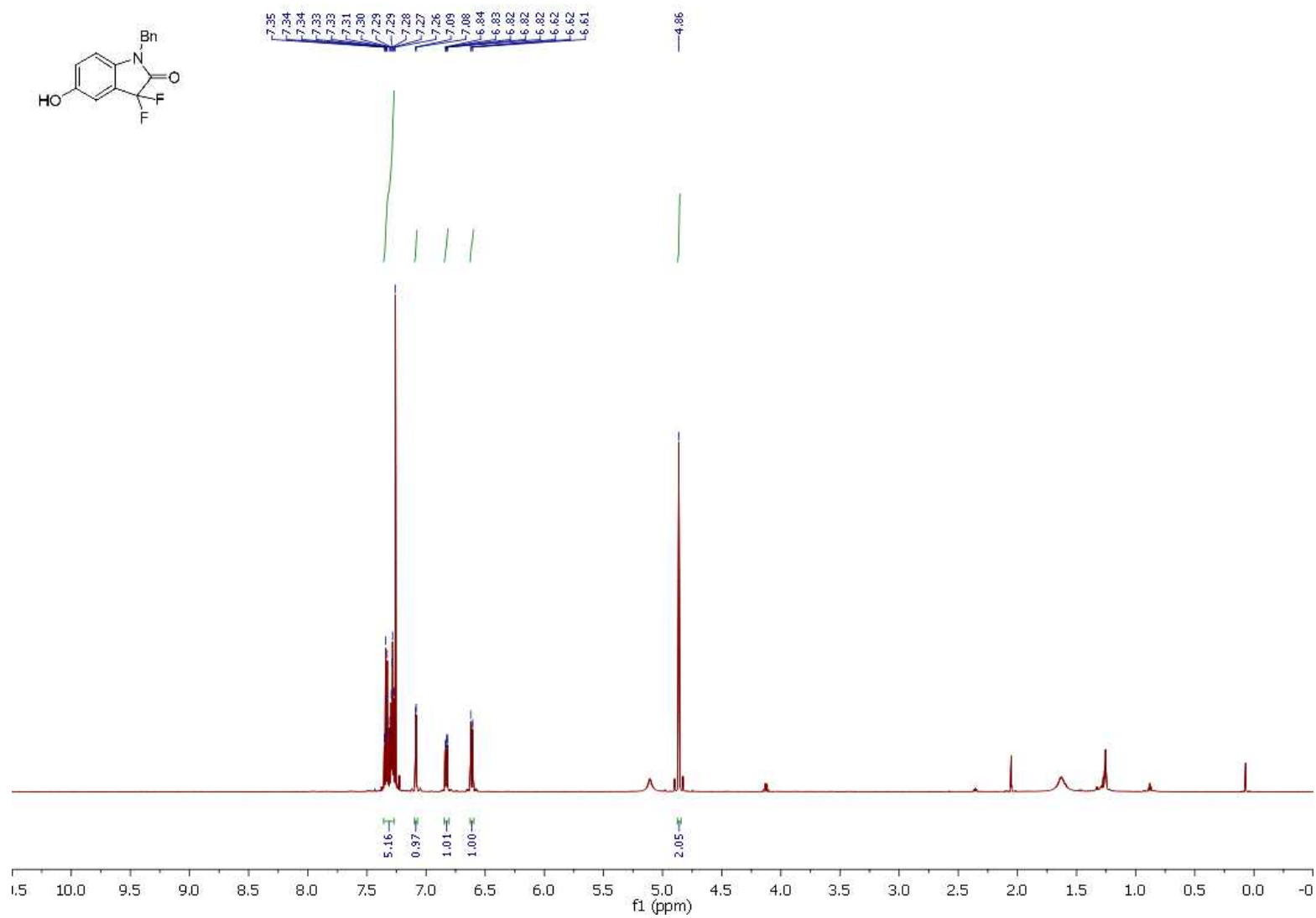
¹³C NMR spectrum of compound **41**



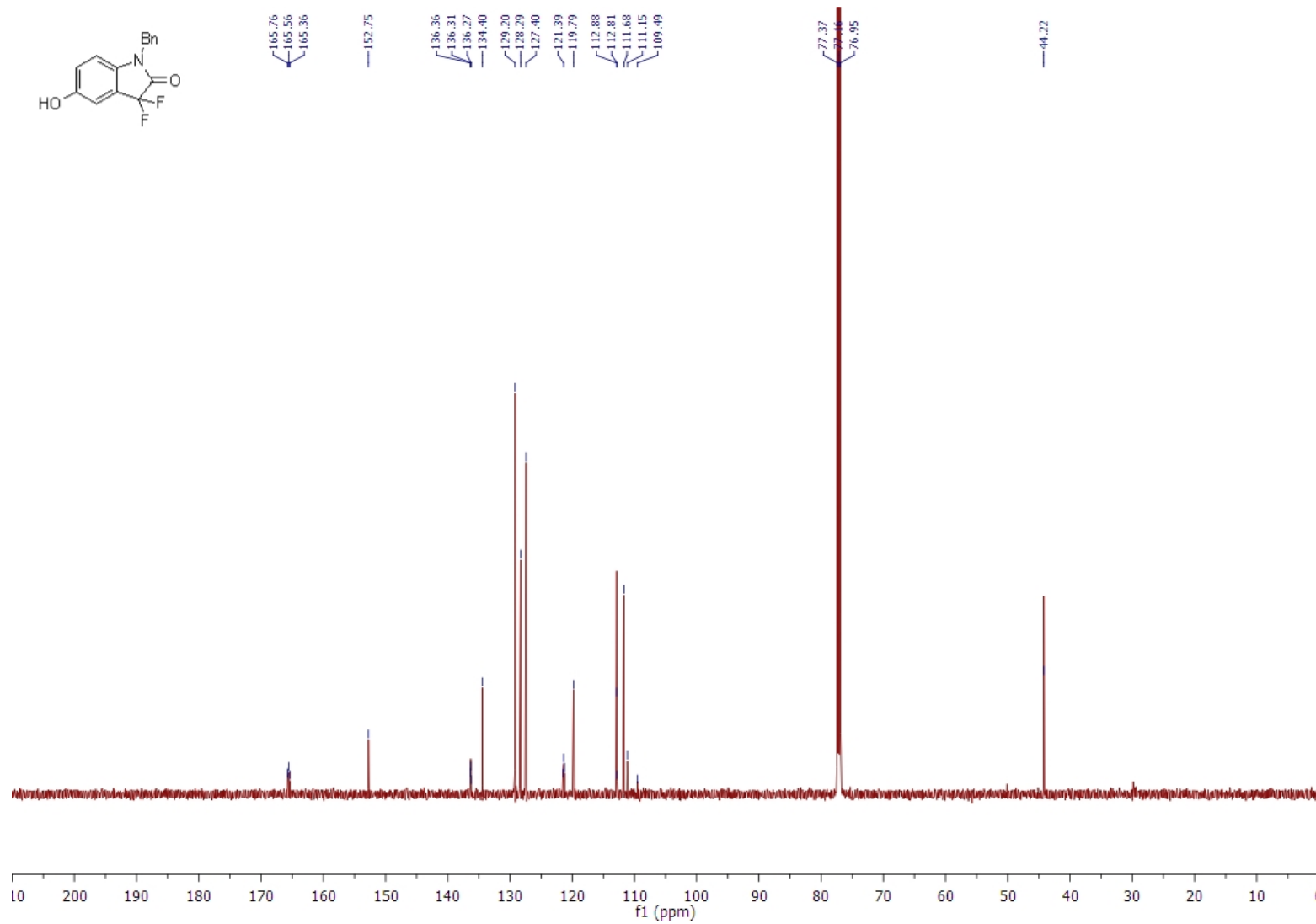
^{19}F NMR spectrum of compound **41**



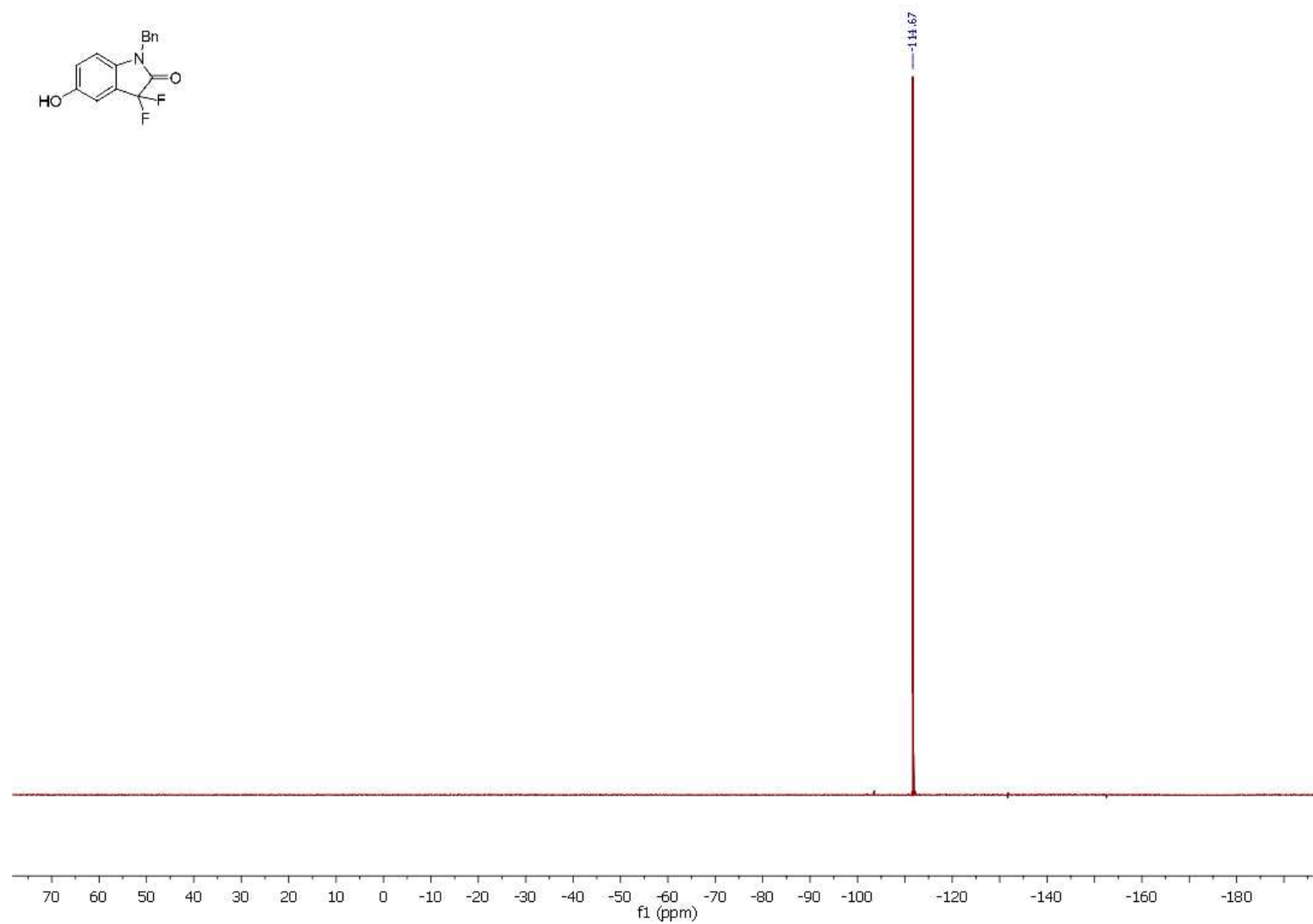
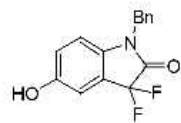
¹H NMR spectrum of compound **4m**



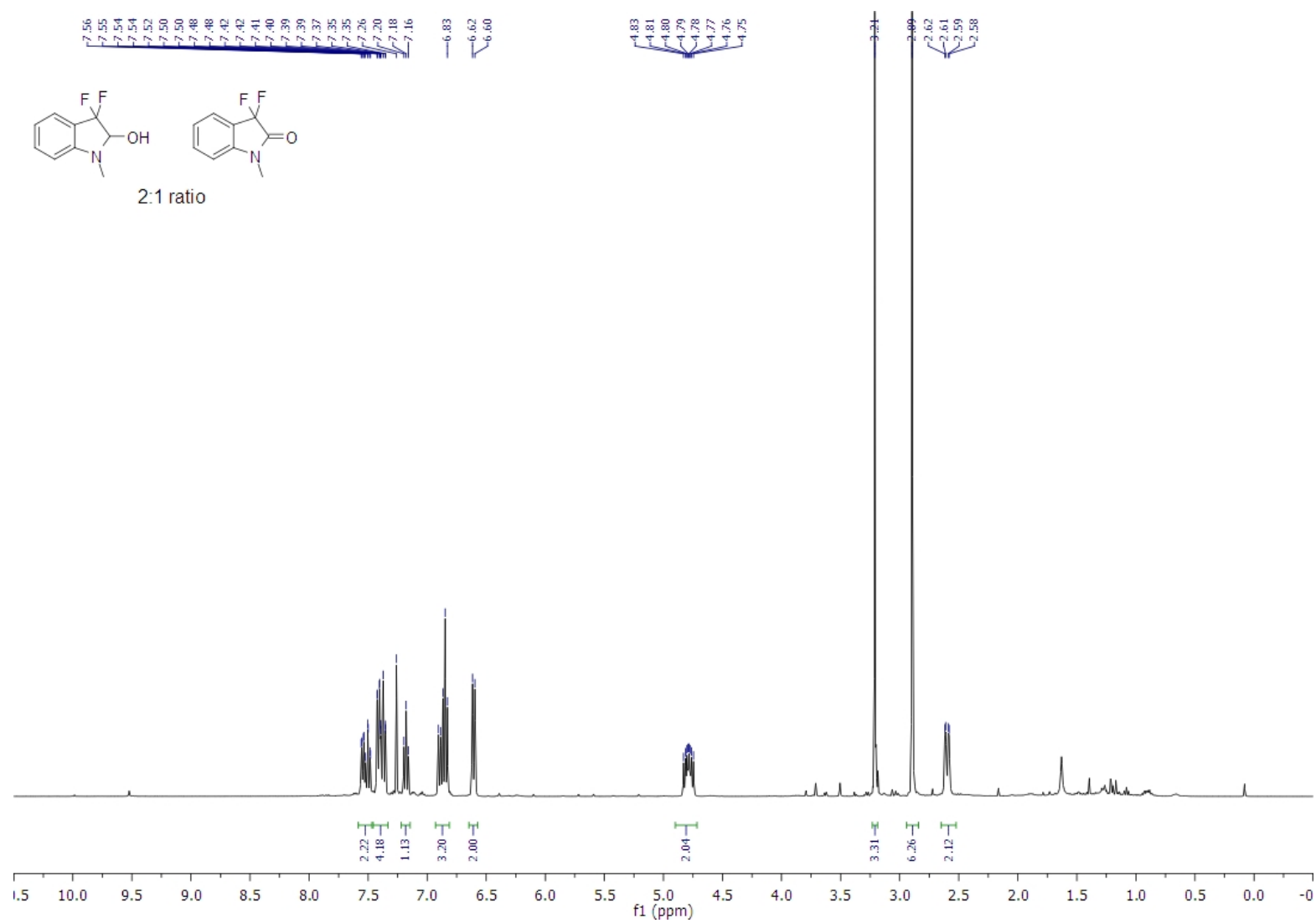
¹³C NMR spectrum of compound **4m**



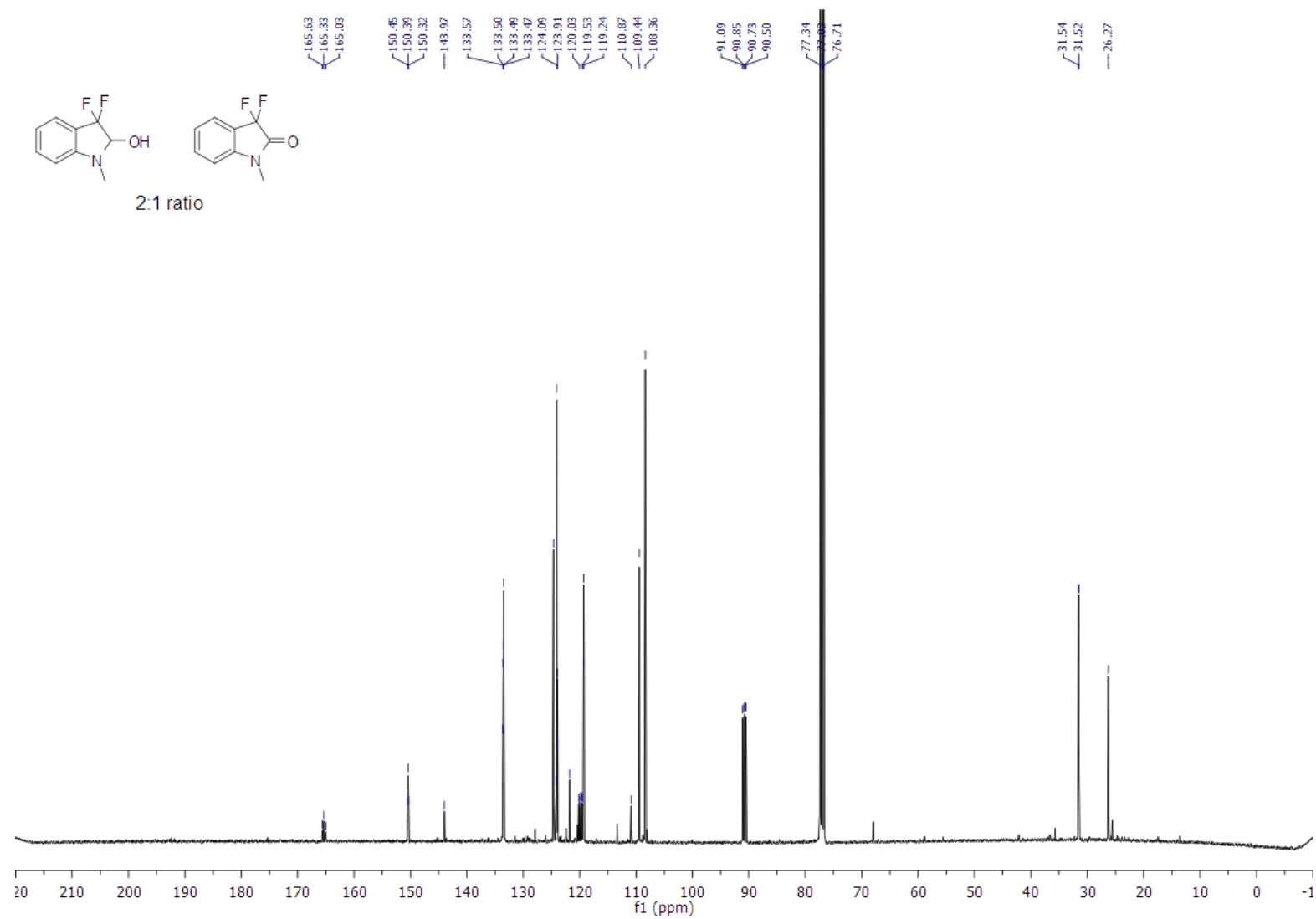
^{19}F NMR spectrum of compound **4m**



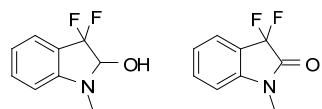
¹H NMR spectrum of the mixture of compound **V** and **IX** for the case of **1a**



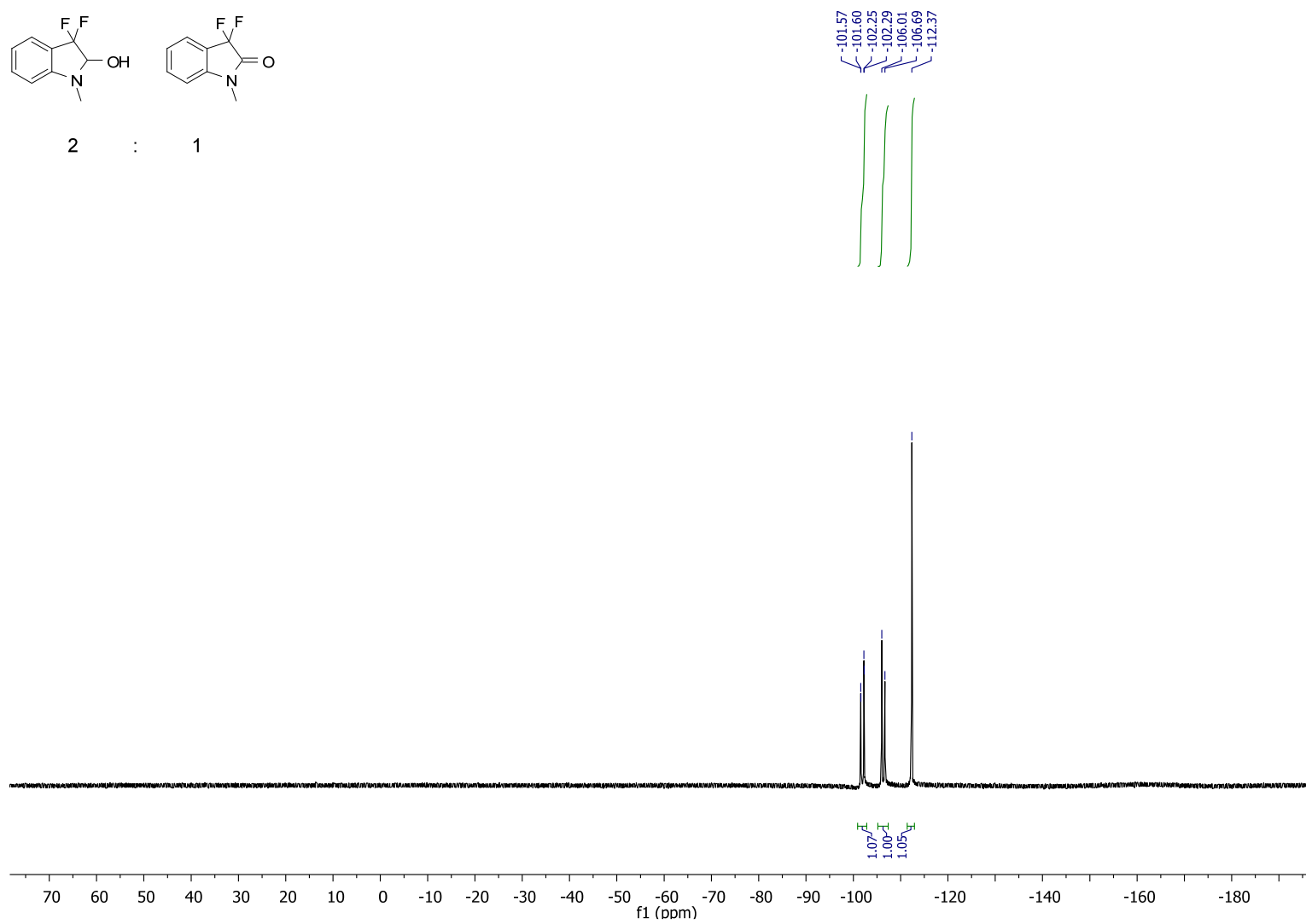
¹³C NMR spectrum of the mixture of compound **V** and **IX** for the case of **1a**



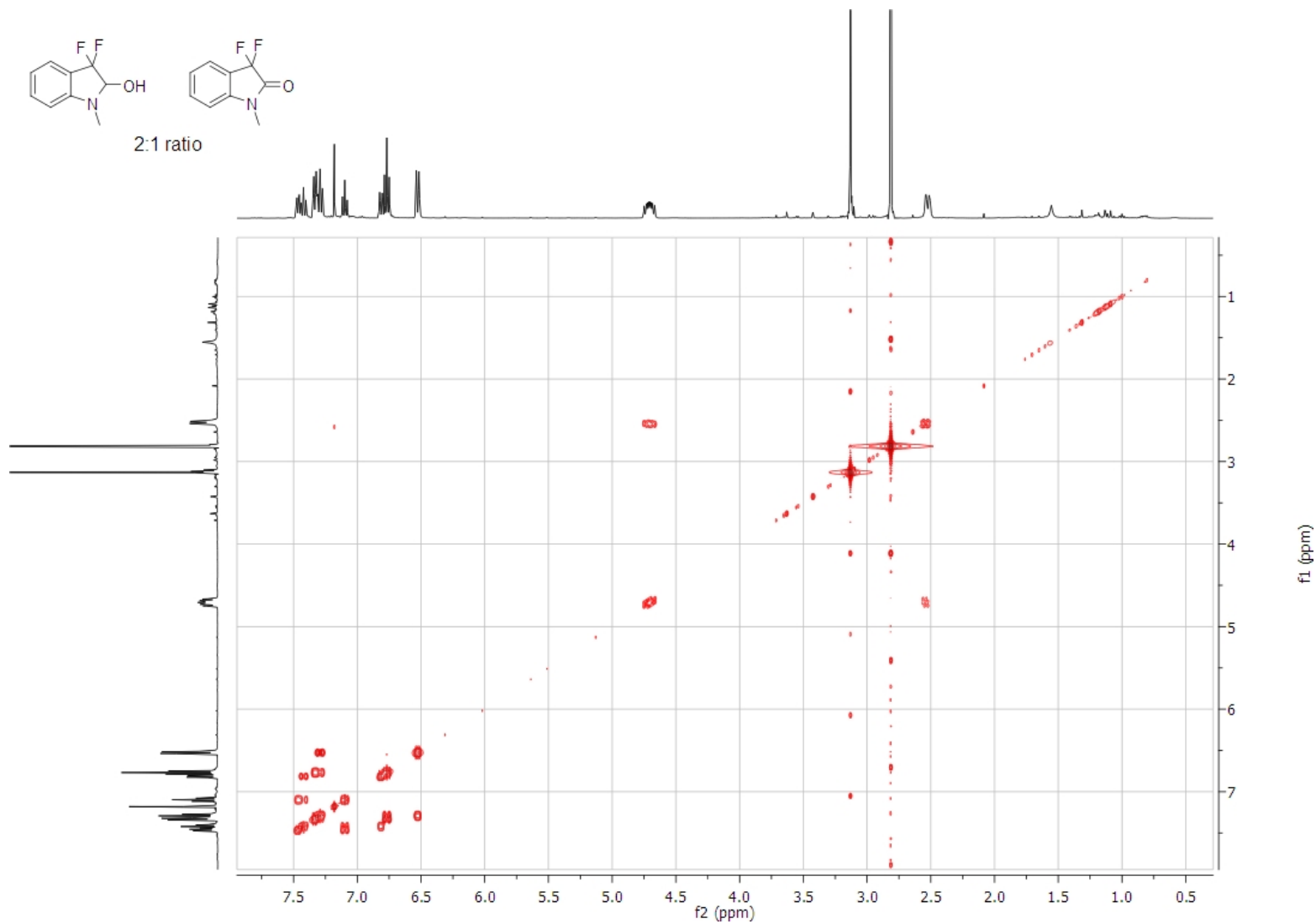
^{19}F NMR spectrum of the mixture of compound **V** and **IX** for the case of **1a**



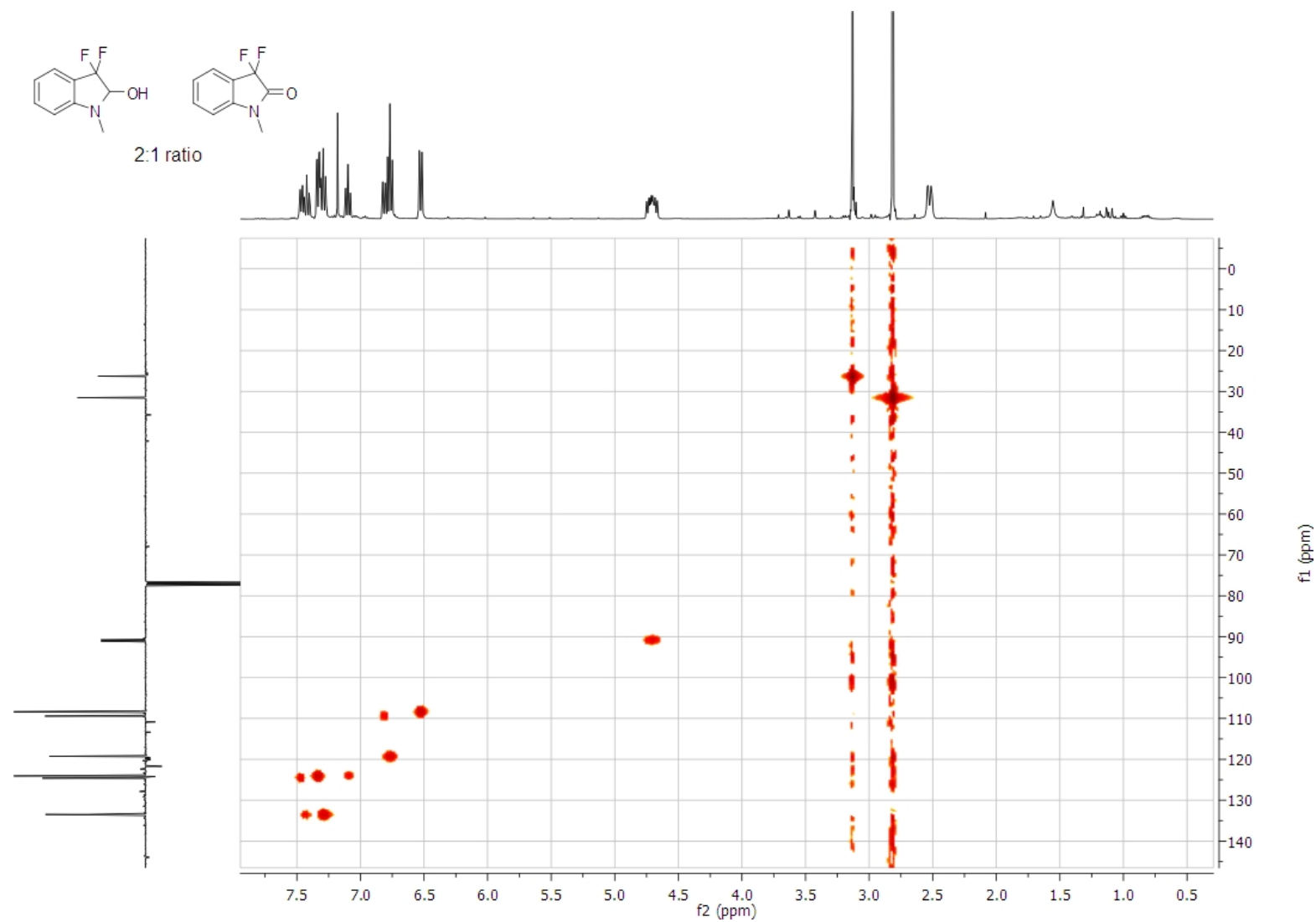
2 : 1



COSY spectrum of the mixture of compound **V** and **IX** for the case of **1a**



HMQC NMR spectrum of the mixture of compound **V** and **IX** for the case of **1a**



HMBC NMR spectrum of the mixture of compound **V** and **IX** for the case of **1a**

