Cascade Reaction of Isatins with Nitro-substituted Enamines: Highly Selectively Synthesis of Functionalized (*Z*)-3-(1-(Arylamino)-2-oxoarylidene)indolin-2-ones

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Supporting Information

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General Information

All compounds were fully characterised by spectroscopic data. The NMR spectra were recorded on a Bruker DRX600. Chemical shifts (δ) are expressed in ppm, J values are given in Hz, and deuterated DMF-d_7 was used as solvent. IR spectra were recorded on a FT-IR Thermo Nicolet Avatar 360 using a KBr pellet. The reactions were monitored by thin layer chromatography (TLC) using silica gel GF_{254}. The melting points were determined on a XT-4A melting point apparatus and are uncorrected; HRMS were performed on an Agilent LC/Msd TOF instrument.

The materials were purchased from Adamas-beta Corporation Limited. All chemicals and solvents were used as received without further purification unless otherwise stated. Column chromatography was performed on silica gel (200–300 mesh). The *N*-(2-nitro-1-phenylvinyl)anilines **2** were prepared according to the literature.[1]

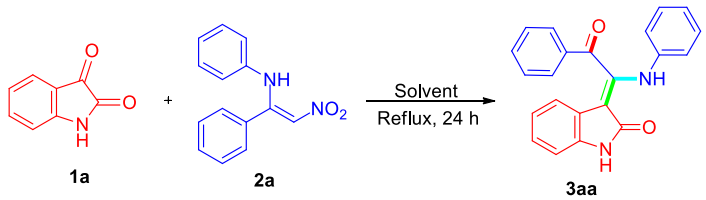
Screening the Optimal Conditions for Synthesis of 3-(1-(Arylamino)-2-oxoarylidene)indolin-2-ones 3

To determine the optimal conditions, different reaction parameters including solvents and catalysts were screened, and the results indicated that the reactions in different solvents including acetonitrile, ethanol, 1,4-dioxane and toluene did not occur in the absence of a catalyst at reflux conditions (Table S1, entries 1−4). Then, HOAc was used as the acid catalyst and was added in this reaction, and it was found that HOAc can catalyze this cascade reaction (Table S1, entries 5−8). Among the examined solvents, ethanol was found to be the best solvent, with its use leading to the target compound yield of 36%. Based on these results, other acids including *p*-TsOH, NH_2SO_3H and HCl were used in this reaction (Table S1, entries 9−11). It was found that NH_2SO_3H can catalyze this reaction remarkably well and gives compound **3aa** with a moderate yield (60%) (Table S1, entry 10). Next, basic catalysts such as NEt_3, Pyridine, Cs_2CO_3 and K_2CO_3 were screened in the ethanol optimal solvent, and it was found that basic catalysts could not promote this cascade reaction. While these results show that NH_2SO_3H is the optimal catalyst and ethanol is the best solvent, but ideal yields were not obtained for this reaction due to the poor solubility of the NH_2SO_3 catalyst in ethanol. To increase the solubility of the NH_2SO_3H, EtOH/H_2O mixed solvents with different volume ratios were used, and the desired

product **3aa** was obtained in higher yield compared to ethanol (Table S1, entry 10 vs.16−18). More importantly, the target compound **3aa** precipitated from the mixed solvent with no further purification. The presence of water not only facilitated the reaction proceeding smoothly, but also allowed the products to crystallize out of the system. Finally, the optimal catalyst amounts were also examined (Table S1, entries 19−20), and it was found that the optimal amount of catalyst is 0.1 equivalent (Table S1, entry 17 vs. 19−20).

Based on the above results, we find that the optimal conditions are EtOH/H_2O with volume ratio of 1:1 as the solvent, and 0.1 equivalent NH_2SO_3 as the catalyst at reflux for about 24 hours (Table S1, entry 17).

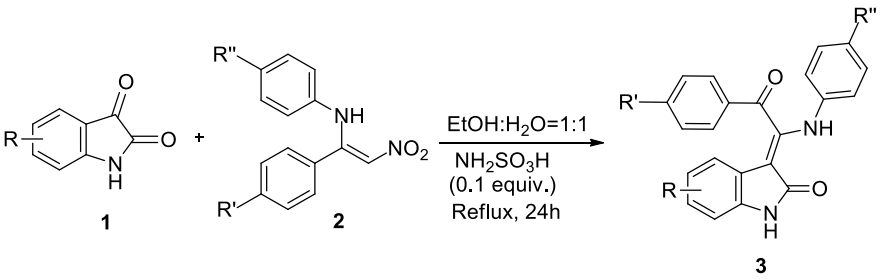
Table S1 Optimization of the reaction conditions for the model reaction[a]



Entry	Solvent	Catalyst	*t*/^{0}C	Yield/%
1	CH_3CN	–	reflux	n.r
2	EtOH	–	reflux	n.r
3	1,4-dioxane	–	reflux	n.r
4	Toluene	–	reflux	n.r
5	CH_3CN	HOAc	reflux	3
6	EtOH	HOAc	reflux	36
7	1,4-dioxane	HOAc	reflux	12
8	Toluene	HOAc	reflux	7
9	EtOH	*p*-TsOH	reflux	51
10	EtOH	NH_2SO_3H	reflux	60
11	EtOH	HCl	reflux	18
12	EtOH	NEt_3	reflux	12
13	EtOH	Pyridine	reflux	15
14	EtOH	Cs_2CO_3	reflux	n.r
15	EtOH	K_2CO_3	reflux	6
16	EtOH/H_2O (2:1)	NH_2SO_3H	reflux	72
17	EtOH/H_2O (1:1)	NH_2SO_3H	reflux	85
18	EtOH/H_2O (1:2)	NH_2SO_3H	reflux	61
19	EtOH/H_2O (1:1)	NH_2SO_3H[b]	reflux	83
20	EtOH/H_2O (1:1)	NH_2SO_3H[c]	reflux	80

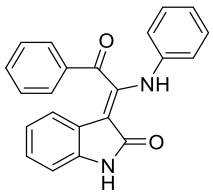
[a] Unless otherwise mentioned, the reaction conditions are **1a** (1.0 mmol), **2a** (1.0 mmol), catalyst (0.1 mmol), solvent (4 mL), mixed solvent volume ration = 1:1. [b] **1a**/**2a**/catalyst ration of 1:1:0.2. [c] **1a**/**2a**/catalyst ration of 1:1:0.05.

General Procedure for the Synthesis of 3-(1-(Arylamino)-2-oxoarylidene)indolin-2-ones 3



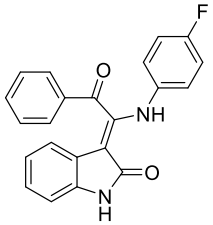
Isatins **1** (1.0 mmol) and *N*-(2-nitro-1-phenylvinyl)aniline **2** (1.0 mmol) were charged into a round bottom flask, then 4 mL mixture solvent ($V_{ethanol}$:V_{H2O}=1:1) was added. Finally, NH_2SO_3H (0.1 equivalent) was added to the mixture. The reaction mixture was stirred at reflux, and then precipitate was formed in the process of reaction. The mixture was stirred until completion of reaction (monitored by TLC), and cooled to room temperature. The formed precipitate was then filtered and washed with cool ethanol to produce the pure products **3**. The products were further identified by FTIR spectroscopy, NMR spectroscopy and HRMS.

(*Z*)-3-(2-oxo-2-phenyl-1-(phenylamino)ethylidene)indolin-2-one (3aa)



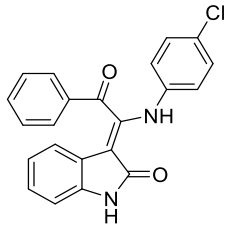
Yield: 290 mg (85 %), yellow solid. Mp: 287.2-287.6 °C; IR (KBr): 3469, 1606, 1359, 1192, 1108, 790, 748, 651, 619, 548 cm^{-1}; ^1H NMR (600 MHz, DMF-d_7): δ = 6.74-6.75 (m, 2H, ArH), 7.03-7.04 (m, 2H, ArH), 7.09-7.10 (m, 1H, ArH), 7.16-7.18 (m, 2H, ArH), 7.27-7.30 (m, 2H, ArH), 7.59-7.61 (m, 2H, ArH), 7.72-7.73 (m, 1H, ArH), 8.15-8.17 (m, 2H, ArH), 10.84 (s, 1H, ArNH), 11.99 (s, 1H, CONH); ^{13}C NMR (150 MHz, DMSO-d_7): δ = 97.6, 109.9, 118.5, 120.8, 122.0, 122.2, 124.9, 125.3, 129.6, 129.7, 134.4, 135.7, 137.9, 138.6, 150.9, 170.9, 192.0; HRMS (TOF ES^+): *m/z* calcd for $C_{22}H_{17}N_2O_2^+$ [$(M+H)^+$], 341.1285; found, 341.1282.

(*Z*)-3-(1-((4-fluorophenyl)amino)-2-oxo-2-phenylethylidene)indolin-2-one (3ab)



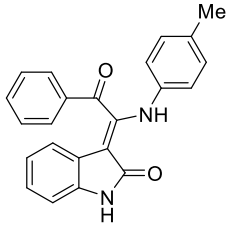
Yield: 316 mg (88 %), yellow solid. Mp: 282.1-282.5 °C; IR (KBr): 3461, 1605, 1390, 1351, 1107, 884, 780, 714, 690, 620, 565 cm^{-1}; ^1H NMR (600 MHz, DMF-d_7): δ = 6.73-6.76 (m, 2H, ArH), 7.02-7.04 (m, 2H, ArH), 7.09- 7.14 (m, 2H, ArH), 7.23-7.26 (m, 2H, ArH), 7.58-7.61 (m, 2H, ArH), 7.72-7.74 (m, 1H, ArH), 8.11-8.14 (m, 2H, ArH), 10.82 (s, 1H, ArNH), 11.84 (s, 1H, CONH); ^{13}C NMR (150 MHz, DMF-d_7): δ = 97.5, 109.9, 116.2 (d, J = 24.0 Hz), 118.43, 120.8, 122.2, 125.0 (d, J = 7.5 Hz), 129.6, 129.7, 134.4, 135.0, 135.7, 137.9, 151.3, 160.1 (d, J = 249.0 Hz), 170.9, 191.9; ^{19}F NMR (470 MHz, DMSO-d_7) δ = −118.0 (d, J = −4.7 Hz); HRMS (TOF ES^+): *m/z* calcd for $C_{22}H_{16}FN_2O_2^+$ [$(M+H)^+$], 359.1190; found, 359.1186.

(*Z*)-3-(1-((4-chlorophenyl)amino)-2-oxo-2-phenylethylidene)indolin-2-one (3ac)



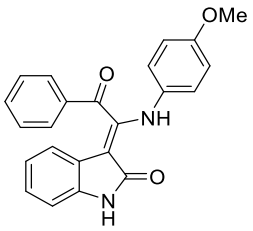
Yield: 326 mg (87 %), yellow solid. Mp: 274.1-274.6 °C; IR (KBr): 3435, 1651, 1597, 1385, 1104, 739, 690, 651, 606, 539 cm^{-1}; ^1H NMR (600 MHz, DMF-d_7): δ = 6.75-6.76 (m, 2H, ArH), 7.03-7.06 (m, 2H, ArH), 7.20-7.22 (m, 2H, ArH), 7.33-7.35 (m, 2H, ArH), 7.59-7.62 (m, 2H, ArH), 7.73-7.76 (m, 1H, ArH), 8.15-8.17 (m, 2H, ArH), 10.86 (s, 1H, ArNH), 11.94 (s, 1H, CONH); ^{13}C NMR (150 MHz, DMF-d_7): δ = 98.3, 110.0, 118.7, 120.9, 122.0, 123.7, 125.2, 129.6, 129.8, 134.3, 135.8, 137.7, 138.1, 150.3, 170.8, 191.9; HRMS (TOF ES^+): *m/z* calcd for $C_{22}H_{16}ClN_2O_2^+$ [$(M+H)^+$], 375.0895; found, 375.0888.

(*Z*)-3-(2-oxo-2-phenyl-1-(*p*-tolylamino)ethylidene)indolin-2-one (3ad)



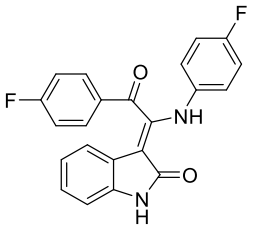
Yield: 294 mg (83 %), yellow solid. Mp: 261.0-261.5 °C; IR (KBr): 3476, 1661, 1601, 1396, 1357, 1229, 1108, 780, 749, 650, 598 cm^{-1}; ^1H NMR (600 MHz, DMF-d_7): δ = 2.36 (s, 3H, $ArCH_3$), 6.90-6.91 (m, 2H, ArH), 7.19-7.20 (m, 2H, ArH), 7.23-7.26 (m, 4H, ArH), 7.75-7.78 (m, 2H, ArH), 7.88-7.90 (m, 1H, ArH), 8.31-8.32 (m, 2H, ArH), 10.98 (s, 1H, ArNH), 12.11 (s, 1H, CONH); ^{13}C NMR (150 MHz, DMF-d_7): δ = 20.1, 97.2, 110.0, 118.5, 120.9, 122.4, 124.9, 129.8, 129.9, 130.3, 134.6, 135.3, 135.8, 136.2, 137.9, 151.5, 171.0, 192.2; HRMS (TOF ES^+): *m/z* calcd for $C_{23}H_{19}N_2O_2^+$ [$(M+H)^+$], 355.1441; found, 355.1437.

(*Z*)-3-(1-((4-methoxyphenyl)amino)-2-oxo-2-phenylethylidene)indolin-2-one (3ae)



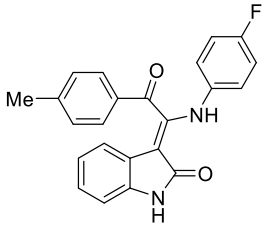
Yield: 308 mg (83 %), yellow solid. Mp: 257.8-258.3 °C; IR (KBr): 3505, 1650, 1604, 1518, 1394, 1351, 1220, 1112, 840, 733, 692, 598 cm^{-1}; ^1H NMR (600 MHz, DMF-d_7): δ = 3.74 (s, 3H, OCH_3), 6.71-6.74 (m, 2H, ArH), 6.85-6.87 (m, 2H, ArH), 7.01-7.02 (m, 2H, ArH), 7.14-7.16 (m, 2H, ArH), 7.58-7.61 (m, 2H, ArH), 7.72-7.73 (m, 1H, ArH), 8.12-8.14 (m, 2H, ArH), 10.77 (s, 1H, ArNH), 11.80 (s, 1H, CONH); ^{13}C NMR (150 MHz, DMF-d_7): δ = 55.2, 96.3, 109.8, 114.7, 118.1, 120.6, 122.4, 124.5, 124.8, 129.6, 129.7, 131.3, 134.5, 135.6, 137.6, 152.1, 157.7, 170.9, 192.0; HRMS (TOF ES^+): *m/z* calcd for $C_{23}H_{19}N_2O_3^+$ [$(M+H)^+$], 371.1390; found, 371.1385.

(Z)-3-(2-(4-fluorophenyl)-1-((4-fluorophenyl)amino)-2-oxoethylidene)indolin-2-one (3af)



Yield: 304 mg (81 %), yellow solid. Mp: 279.5-280.1 °C; IR (KBr): 3451, 1601, 1514, 1383, 1104, 884, 818, 719, 678, 645, 551 cm^{-1}; ^1H NMR (600 MHz, DMF-d_7): δ = 6.74-6.78 (m, 2H, ArH), 7.03-7.07 (m, 2H, ArH), 7.12-7.15 (m, 2H, ArH), 7.23-7.26 (m, 2H, ArH), 7.40-7.43 (m, 2H, ArH), 8.24-8.26 (m, 2H, ArH), 10.82 (s, 1H, ArNH), 11.79 (s, 1H, CONH); ^{13}C NMR (150 MHz, DMF-d_7): δ = 97.6, 110.0, 116.3 (d, J = 22.5 Hz), 116.9 (d, J = 22.5 Hz), 118.5, 120.8, 122.1, 125.1 (d, J = 12.0 Hz), 125.2, 131.2, 132.9 (d, J = 10.5 Hz), 134.9, 138.0, 150.8, 160.2 (d, J = 243.0 Hz), 166.7 (d, J = 240.0 Hz), 170.9, 190.3; ^{19}F NMR (470 MHz, DMF-d_7) δ = −117.9, −102.5; HRMS (TOF ES^+): *m/z* calcd for $C_{23}H_{18}FN_2O_2^+$ [$(M+H)^+$], 377.1096; found, 377.108.

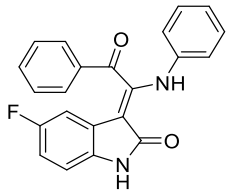
(*Z*)-3-(1-((4-fluorophenyl)amino)-2-oxo-2-(*p*-tolyl)ethylidene)indolin-2-one (3ag)



Yield: 316 mg (85 %), yellow solid. Mp: 283.2-283.5 °C; IR (KBr): 3464, 1657, 1607, 1387, 1214, 1107, 847, 747, 655, 608, 563 cm^{-1}; ^1H NMR (600 MHz, DMF-d_7): δ = 2.37 (s, 3H, $ArCH_3$), 6.74-6.75(m, 2H, ArH), 7.03 (d, J = 3.3 Hz, 2H, ArH), 7.11-7.14 (m, 2H, ArH), 7.24-7.26 (m, 2H, ArH), 7.40 (d, J = 8.1 Hz, 2H, ArH), 8.03 (d, J = 8.2

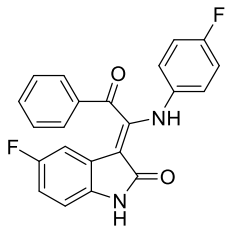
Hz, 2H, ArH), 10.81 (s, 1H, ArNH), 11.87 (s, 1H, CONH); ^{13}C NMR (150 MHz, DMF-d_7): δ = 21.1, 97.3, 109.9, 116.2 (d, J = 24.0 Hz), 118.5, 120.7, 122.2, 124.8 (d, J = 7.5 Hz), 129.7, 129.8, 130.4, 132.0, 135.1 (d, J = 3.0 Hz), 137.8, 147.1, 151.5, 160.1 (d, J = 243.0 Hz), 170.9, 191.3; ^{19}F NMR (470 MHz, DMF-d_7) δ = −118.1; HRMS (TOF ES$^+$): *m/z* calcd for $C_{22}H_{15}FN_2O_2^+$ [(M+H)$^+$], 373.1347; found, 373.1339.

(*Z*)-5-fluoro-3-(2-oxo-2-phenyl-1-(phenylamino)ethylidene)indolin-2-one (3ba)



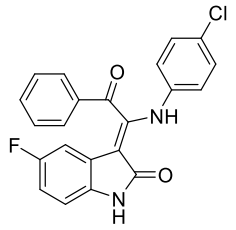
Yield: 326 mg (91 %), yellow solid. Mp: 266.4-266.7 °C; IR (KBr): 3468, 1657, 1605, 1469, 1386, 1310, 1130, 853, 790, 761, 690 cm^{-1}, 617, 527; ^{1}H NMR (600 MHz, DMF-d_7): δ = 6.60-6.62 (m, 1H, ArH), 7.02-7.03 (m, 1H, ArH), 7.18-7.21 (m, 1H, ArH), 7.28-7.29 (m, 1H, ArH), 7.35-7.37 (m, 2H, ArH), 7.45-7.48 (m, 2H, ArH), 7.76-7.79 (m, 2H, ArH), 7.90-7.91 (m, 1H, ArH), 8.32-8.34 (m, 2H, ArH), 11.05 (s, 1H, ArNH), 12.25 (s, 1H, CONH); ^{13}C NMR (150 MHz, DMF-d_7): δ = 97.4, 105.2 (d, J = 27.0 Hz), 110.7 (d, J = 9.0 Hz), 111.1 (d, J = 24.0 Hz), 122.5, 123.6 (d, J = 9.0 Hz), 125.9, 129.8, 130.0, 134.3 (d, J = 10.5 Hz), 136.1, 138.5, 152.2, 158.2 (d, J = 232.5 Hz), 171.2, 191.9; ^{19}F NMR (470 MHz, DMF-d_7) δ = −123.9; HRMS (TOF ES$^+$): *m/z* calcd for $C_{22}H_{16}FN_2O_2^+$ [(M+H)$^+$], 359.1190; found, 359.1188.

(*Z*)-5-fluoro-3-(1-((4-fluorophenyl)amino)-2-oxo-2-phenylethylidene)indolin-2-on e (3bb)



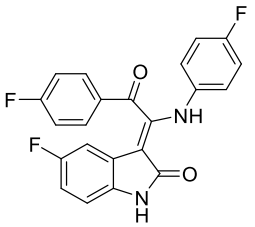
Yield: 350 mg (93 %), yellow solid. Mp: 271.0-271.4 °C; IR (KBr): 3438, 1649, 1590, 1517, 1304, 1163, 1106, 847, 808, 769, 708, 619, 557 cm^{-1}; ^{1}H NMR (600 MHz, DMF-d_7): δ = 6.42-6.44 (m, 1H, ArH), 6.84-6.88 (m, 1H, ArH), 7.02-7.04 (m, 1H, ArH), 7.12-7.15 (m, 2H, ArH), 7.26-7.29 (m, 2H, ArH), 7.60-7.62 (m, 2H, ArH), 7.74-7.77 (m, 1H, ArH), 8.14-8.16 (m, 2H, ArH), 10.86 (s, 1H, ArNH), 11.91 (s, 1H, CONH); ^{13}C NMR (150 MHz, DMF-d_7): δ = 97.1, 150.0 (d, J = 24.0 Hz), 110.5 (d, J = 7.5 Hz), 111.0 (d, J = 24.0 Hz), 116.3 (d, J = 24.0 Hz), 123.4 (d, J = 9.0 Hz), 125.3 (d, J = 7.5 Hz), 129.6, 129.8, 134.1, 134.7, 135.9, 152.4, 158.0 (d, J = 233.0 Hz), 160.4 (d, J = 243.0 Hz), 171.0, 191.6; ^{19}F NMR (470 MHz, DMF-d_7) δ = −124.1, −117.5; HRMS (TOF ES$^+$): *m/z* calcd for $C_{22}H_{15}F_2N_2O_2^+$ [(M+H)$^+$], 377.1096; found, 377.1092.

(*Z*)-3-(1-((4-chlorophenyl)amino)-2-oxo-2-phenylethylidene)-5-fluoroindolin-2-one (3bc)



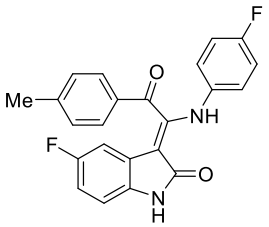
Yield: 352 mg (90 %), yellow solid. Mp: 305.4-305.8 °C; IR (KBr): 3400, 1601, 1518, 1359, 1117, 718, 658, 606, 584, 544 cm^{-1}; ^{1}H NMR (600 MHz, DMF-d_7): δ = 6.98-6.99 (m, 1H, ArH), 7.16-7.17 (m, 1H, ArH), 7.18-7.19 (m, 1H, ArH), 7.39-7.40 (m, 2H, ArH), 7.52-7.53 (m, 2H, ArH), 7.77-7.80 (m, 2H, ArH), 7.92-7.93 (m, 1H, ArH), 8.32-8.34 (m, 2H, ArH), 11.06 (s, 1H, ArNH), 12.18 (s, 1H, CONH); ^{13}C NMR (150 MHz, DMF-d_7): δ = 98.1, 105.4 (d, J = 27.0 Hz), 110.8 (d, J = 9.0 Hz), 111.4 (d, J = 24.0 Hz), 123.4, 124.2, 129.8, 130.0, 130.4, 134.2, 134.4, 136.2, 137.5, 151.6, 158.0 (d, J = 233.0 Hz), 171.1, 191.8; ^{19}F NMR (470 MHz, DMF-d_7) δ = −123.9; HRMS (TOF ES^+): *m/z* calcd for $C_{22}H_{15}ClFN_2O_2^+$ [$(M+H)^+$], 393.0801; found, 393.0796.

(*Z*)-5-fluoro-3-(2-(4-fluorophenyl)-1-((4-fluorophenyl)amino)-2-oxoethylidene) indolin-2-one (3bf)



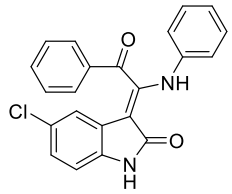
Yield: 346 mg (88 %), yellow solid. Mp: 271.1-271.5 °C; IR (KBr): 3449, 1651, 1595, 1510, 1360, 1196, 1155, 1104, 845, 716, 685, 599, 558 cm^{-1}; ^{1}H NMR (600 MHz, DMF-d_7): δ = 6.59-6.61 (m, 1H, ArH), 7.04-7.05 (m, 1H, ArH), 7.19-7.21 (m, 1H, ArH), 7.30-7.32 (m, 2H, ArH), 7.42-7.45 (m, 2H, ArH), 7.57-7.60 (m, 2H, ArH), 8.42-8.44 (m, 2H, ArH), 11.04 (s, 1H, ArNH), 12.05 (s, 1H, CONH); ^{13}C NMR (150 MHz, DMF-d_7): δ = 97.4, 105.2 (d, J = 25.5 Hz), 110.7 (d, J = 9.0 Hz), 111.2 (d, J = 24.0 Hz), 116.5 (d, J = 24.0 Hz), 117.2 (d, J = 22.5 Hz), 123.5 (d, J = 10.5 Hz), 125.6 (d, J = 7.5 Hz), 131.1, 133.2 (d, J = 9.0 Hz), 134.3, 134.8, 152.1, 155.5 (d, J = 232.5 Hz), 160.6 (d, J = 243.0 Hz), 167.1 (d, J = 256.5 Hz), 171.2, 190.2; ^{19}F NMR (470 MHz, DMF-d_7) δ = −124.1, −117.4, −102.0; HRMS (TOF ES^+): *m/z* calcd for $C_{22}H_{15}ClFN_2O_2^+$ [$(M+H)^+$], 395.1002; found, 395.0995.

(*Z*)-5-fluoro-3-(1-((4-fluorophenyl)amino)-2-oxo-2-(*p*-tolyl)ethylidene)indolin-2-one (3bg)



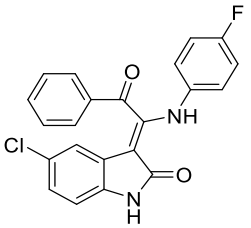
Yield: 352 mg (90 %), yellow solid. Mp: 289.6-290.0 °C; IR (KBr): 3440, 1647, 1606, 1516, 1358, 1119, 851, 804, 714, 684, 627, 560 cm^{-1}; ^1H NMR (600 MHz, DMF-d_7): δ = 2.38 (s, 3H, $ArCH_3$), 6.42-6.44 (m, 1H, ArH), 6.84-7.87 (m, 1H, ArH), 7.01-7.03 (m, 1H, ArH), 7.13-7.16 (m, 2H, ArH), 7.27-7.28 (m, 2H, ArH), 7.29-7.42 (m, 2H, ArH), 8.04-8.05 (m, 2H, ArH), 10.85 (s, 1H, ArNH), 11.94 (s, 1H, CONH); ^{13}C NMR (150 MHz, DMF-d_7): δ = 21.1, 96.9, 105.0 (d, J = 25.5 Hz), 110.5 (d, J = 9.0 Hz), 110.9 (d, J = 24.0 Hz), 116.3 (d, J = 24.0 Hz), 123.5 (d, J = 9.0 Hz), 125.2 (d, J = 9.0 Hz), 129.8, 130.5, 131.7, 134.1, 134.7 (d, J = 1.5 Hz), 147.2, 152.7, 158.0 (d, J = 232.5 Hz), 160.3 (d, J = 243.0 Hz), 171.0, 190.9; ^{19}F NMR (470 MHz, DMF-d_7) δ = −124.1, −117.6; HRMS (TOF ES^+): *m/z* calcd for $C_{23}H_{17}F_2N_2O_2^+$ [$(M+H)^+$], 391.1253; found, 391.1246.

(*Z*)-5-chloro-3-(2-oxo-2-phenyl-1-(phenylamino)ethylidene)indolin-2-one (3ca)



Yield: 326 mg (87 %), yellow solid. Mp: 243.8-244.1 °C; IR (KBr): 3448, 1651, 1602, 1360, 1308, 1224, 1192, 1111, 871, 814, 721, 671, 600, 566 cm^{-1}; ^1H NMR (600 MHz, DMF-d_7): δ = 6.70 (d, J = 1.50 Hz, 1H, ArH), 7.05-7.07 (m, 2H, ArH), 7.08-7.13 (m, 1H, ArH), 7.18-7.20 (m, 2H, ArH), 7.28-7.31 (m, 2H, ArH), 7.60-7.62 (m, 2H, ArH), 7.74-7.76 (m, 1H, ArH), 8.14-8.16 (m, 2H, ArH), 10.95 (s, 1H, ArNH), 12.04 (s, 1H, CONH); ^{13}C NMR (150 MHz, DMF-d_7): δ = 96.6, 111.2, 117.9, 122.4, 124.0, 124.4, 125.4, 125.8, 129.6, 129.7, 129.9, 134.2, 135.9, 136.5, 138.2, 152.2, 170.7, 191.7; HRMS (TOF ES^+): *m/z* calcd for $C_{22}H_{16}ClN_2O_2^+$ [$(M+H)^+$], 375.0895; found, 375.0888.

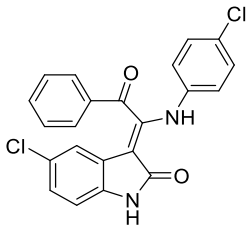
(*Z*)-5-chloro-3-(1-((4-fluorophenyl)amino)-2-oxo-2-phenylethylidene)indolin-2-one (3cb)



Yield: 348 mg (89 %), yellow solid. Mp: 236.4-236.8 °C; IR (KBr): 3442, 1604, 1384, 1358, 1102, 755, 712, 610, 569, 543 cm^{-1}; ^1H NMR (600 MHz, DMF-d_7): δ = 6.68 (d,

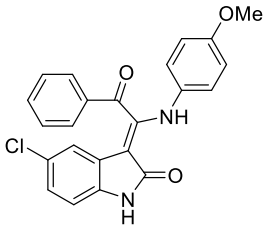
J = 1.60 Hz, 1H, ArH), 7.06-7.07 (m, 2H, ArH), 7.11-7.14 (m, 2H, ArH), 7.25-7.28 (m, 2H, ArH), 7.59-7.62 (m, 2H, ArH), 7.74-7.75 (m, 1H, ArH), 8.12-8.13 (m, 2H, ArH), 10.92 (s, 1H, ArNH), 11.88 (s, 1H, CONH); ^{13}C NMR (150 MHz, DMF-d_7): δ = 96.4, 111.2, 116.3 (d, *J* = 24.0 Hz), 117.8, 124.0, 124.4, 125.4 (d, *J* = 10.5 Hz), 125.5, 129.6, 129.8, 134.1, 134.6, 136.0, 136.5, 152.5, 160.2 (d, *J* = 241.0 Hz), 170.7, 191.6; HRMS (TOF ES$^+$): *m/z* calcd for $C_{22}H_{15}ClFN_2O_2^+$ [(M+H)$^+$], 393.0801; found, 393.0797.

(*Z*)-5-chloro-3-(1-((4-chlorophenyl)amino)-2-oxo-2-phenylethylidene)indolin-2-one (3cc)



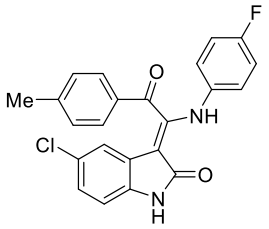
Yield: 350 mg (86 %), yellow solid. Mp: 307.3-307.8 °C; IR (KBr): 3458, 1599, 1599, 1386, 1357, 1111, 867, 773, 708, 682, 655, 545 cm^{-1}; ^{1}H NMR (600 MHz, DMF-d_7): δ = 6.86 (d, *J* = 1.9 Hz, 1H, ArH), 7.21-7.26 (m, 2H, ArH), 7.38-7.40 (m, 2H, ArH), 7.50-7.53 (m, 2H, ArH), 7.77-7.79 (m, 2H, ArH), 7.91-7.94 (m, 1H, ArH), 8.31-8.32 (m, 2H, ArH), 11.12 (s, 1H, ArNH), 12.14 (s, 1H, CONH); ^{13}C NMR (150 MHz, DMF-d_7): δ = 97.4, 111.4, 118.2, 124.0, 124.4, 124.8, 125.6, 129.8, 130.1, 130.5, 134.2, 136.2, 136.8, 137.5, 151.8, 170.8, 191.8; HRMS (TOF ES$^+$): *m/z* calcd for $C_{22}H_{15}Cl_2N_2O_2^+$ [(M+H)$^+$], 409.0505; found, 409.0496.

(*Z*)-5-chloro-3-(1-((4-methoxyphenyl)amino)-2-oxo-2-phenylethylidene)indolin-2-one (3ce)



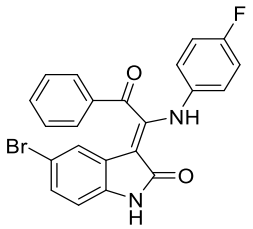
Yield: 354 mg (85 %), yellow solid. Mp: 262.7-263.1 °C; IR (KBr): 3483, 1639, 1600, 1114, 916, 782, 753, 702, 649, 607, 574 cm^{-1}; ^{1}H NMR (600 MHz, DMF-d_7): δ = 3.72 (s, 3H, OCH_3), 6.64- 6.65 (m, 1H, ArH), 6.85-6.87 (m, 2H, ArH), 7.04-7.05 (m, 2H, ArH), 7.16-7.18 (m, 2H, ArH), 7.60-7.62 (m, 2H, ArH), 7.74-7.76 (m, 1H, ArH), 8.12-8.14 (m, 2H, ArH), 10.96 (s, 1H, ArNH), 11.86 (s, 1H, CONH); ^{13}C NMR (150 MHz, DMF-d_7): δ = 55.2, 95.3, 111.1, 114.7, 117.5, 123.9, 124.2, 125.1, 125.2, 129.6, 129.8, 130.8, 134.1, 135.9, 136.2, 153.2, 158.0, 170.7, 191.7; HRMS (TOF ES$^+$): *m/z* calcd for $C_{23}H_{18}ClN_2O_3^+$ [(M+H)$^+$], 405.1000; found, 405.0992.

(*Z*)-5-chloro-3-(1-((4-fluorophenyl)amino)-2-oxo-2-(*p*-tolyl)ethylidene)indolin-2-one (3cg)



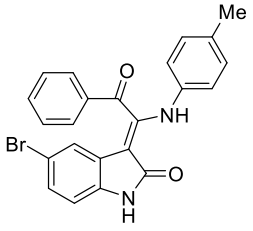
Yield: 354 mg (87 %), yellow solid. Mp: 292.5-292.8 °C; IR (KBr): 3462, 1651, 1607, 1358, 1220, 1121, 853, 730, 675, 638, 572 cm^{-1}; ^1H NMR (600 MHz, DMF-d_7): δ = 2.37 (s, 3H, $ArCH_3$), 6.68 (s, 1H, ArH), 7.06-7.07 (m, 2H, ArH), 7.14-7.16 (m, 2H, ArH), 7.27-7.29 (m, 2H, ArH), 7.41-7.42 (m, 2H, ArH), 8.03-8.04 (m, 2H, ArH), 10.99 (s, 1H, ArNH), 11.90 (s, 1H, CONH); ^{13}C NMR (150 MHz, DMF-d_7): δ = 21.1, 96.2, 111.1, 116.3 (d, J = 24.0 Hz), 117.8, 124.0, 124.3, 125.3 (d, J = 7.5 Hz), 129.6, 130.5, 131.7, 134.6, 136.4, 147.5, 152.8, 160.4 (d, J = 243.0 Hz), 170.7, 191.0; ^{19}F NMR (470 MHz, DMF-d_7) δ = −117.4; HRMS (TOF ES^+): *m/z* calcd for $C_{23}H_{17}ClFN_2O_2^+$ [$(M+H)^+$], 407.0957; found, 407.0949.

(*Z*)-5-bromo-3-(1-((4-fluorophenyl)amino)-2-oxo-2-phenylethylidene)indolin-2-one (3db)



Yield: 392 mg (90 %), yellow solid. Mp: 235.8-236.2 °C; IR (KBr): 3453, 1649, 1593, 1359, 1304, 1220, 1116, 716, 680, 621, 565 cm^{-1}; ^1H NMR (600 MHz, DMF-d_7): δ = 6.99-6.70 (m, 1H, ArH), 7.16-7.18 (m, 1H, ArH), 7.29-7.32 (m, 2H, ArH), 7.37-7.39 (m, 1H, ArH), 7.43-7.45 (m, 2H, ArH), 7.76-7.79 (m, 2H, ArH), 7.91-7.94 (m, 1H, ArH), 8.30-8.32 (m, 2H, ArH), 11.14 (s, 1H, ArNH), 12.11 (s, 1H, CONH); ^{13}C NMR (150 MHz, DMF-d_7): δ = 96.5, 111.8, 113.0, 116.5 (d, J = 24.0 Hz), 120.8, 124.7, 125.6 (d, J = 7.5 Hz), 127.4, 129.8, 130.0, 134.3, 134.8 (d, J = 3.0 Hz), 136.1, 137.1, 152.6, 160.6 (d, J = 241.5 Hz), 170.7, 191.8; ^{19}F NMR (470 MHz, DMF-d_7) δ = −117.2; HRMS (TOF ES^+): *m/z* calcd for $C_{22}H_{15}BrFN_2O_2^+$ [$(M+H)^+$], 437.0295; found, 437.0290.

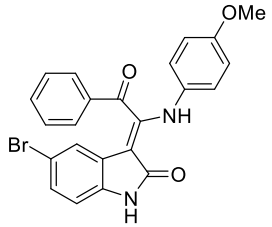
(*Z*)-5-bromo-3-(2-oxo-2-phenyl-1-(*p*-tolylamino)ethylidene)indolin-2-one (3dd)



Yield: 398 mg (92 %), yellow solid. Mp: 261.5-261.9 °C; IR (KBr): 3456, 1647, 1602, 1386, 1358, 1106, 765, 690, 617, 573 cm^{-1}; ^1H NMR (600 MHz, DMF-d_7): δ = 2.19 (s,

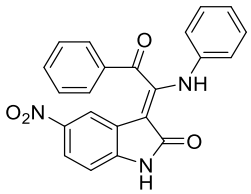
3H, $ArCH_3$), 6.81-6.82 (m, 1H, ArH), 7.01-7.03 (m, 1H, ArH), 7.10-7.11 (m, 4H, ArH), 7.19-7.21 (m, 1H, ArH), 7.60-7.63 (m, 2H, ArH), 7.74-7.77 (m, 1H, ArH), 8.15-8.16 (m, 2H, ArH), 11.05 (s, 1H, ArNH), 12.00 (s, 1H, CONH); ^{13}C NMR (150 MHz, DMF-d_7): δ = 20.0, 95.8, 111.7, 112.9, 120.5, 122.6, 124.6, 127.0, 129.6, 129.9, 130.2, 134.1, 135.6, 135.7, 136.0, 136.6, 152.5, 170.5, 191.7; HRMS (TOF ES^+): *m/z* calcd for $C_{23}H_{18}BrN_2O_2^+$ [$(M+H)^+$], 433.0546; found, 433.0546.

(*Z*)-5-bromo-3-(1-((4-methoxyphenyl)amino)-2-oxo-2-phenylethylidene)indolin -2-one (3de)



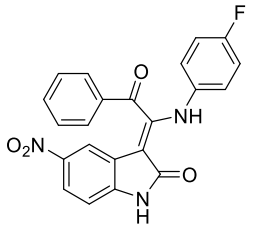
Yield: 416 mg (93 %), yellow solid. Mp: 256.2-256.8 °C; IR (KBr): 3451, 1647, 1600, 1382, 1352, 1166, 785, 656, 602, 567 cm^{-1}; ^1H NMR (600 MHz, DMF-d_7): δ = 3.88 (s, 3H, OCH_3), 6.95-6.97 (m, 1H, ArH), 7.01-7.03 (m, 2H, ArH), 7.17-7.18 (m, 1H, ArH), 7.32-7.35 (m, 3H, ArH), 7.76-7.78 (m, 2H, ArH), 7.90-7.93 (m, 1H, ArH), 8.28-8.30 (m, 2H, ArH), 11.13 (s, 1H, ArNH), 12.05 (s, 1H, CONH); ^{13}C NMR (150 MHz, DMF-d_7): δ = 55.2, 95.2, 111.6, 112.8, 114.7, 120.3, 124.7, 125.1, 126.8, 129.6, 129.8, 130.8, 134.1, 135.9, 136.5, 153.2, 158.0, 170.5, 191.7; HRMS (TOF ES^+): *m/z* calcd for $C_{23}H_{18}BrN_2O_3^+$ [$(M+H)^+$], 449.0495; found, 449.0489.

(*Z*)-5-nitro-3-(2-oxo-2-phenyl-1-(phenylamino)ethylidene)indolin-2-one (3ea)



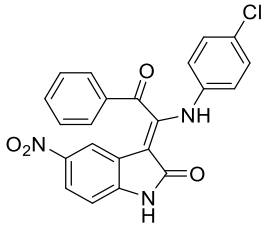
Yield: 358 mg (93 %), yellow solid. Mp: 273.8-274.3 °C; IR (KBr): 3444, 1659, 1604, 1514, 1384, 1200, 1107, 769, 712, 690, 616, 544 cm^{-1}; ^1H NMR (600 MHz, DMF-d_7): δ = 7.32-7.34 (m, 1H, ArH), 7.38-7.39 (m, 1H, ArH), 7.42-7.43 (m, 1H, ArH), 7.48-7.51 (m, 2H, ArH), 7.77-7.81 (m, 3H, ArH), 7.91-7.93 (m, 1H, ArH), 8.17-8.21 (m, 2H, ArH), 8.37-8.38 (m, 2H, ArH), 11.64 (s, 1H, ArNH), 12.22 (s, 1H, CONH); ^{13}C NMR (150 MHz, DMF-d_7): δ = 96.0, 109.8, 113.4, 121.2, 123.0, 126.4, 129.9, 130.0, 134.3, 136.2, 138.2, 142.2, 143.2, 153.5, 171.3, 191.6; HRMS (TOF ES^+): *m/z* calcd for $C_{22}H_{16}N_3O_4^+$ [$(M+H)^+$], 386.1135; found, 386.1126.

(*Z*)-3-(1-((4-fluorophenyl)amino)-2-oxo-2-phenylethylidene)-5-nitroindolin-2-one (3eb)



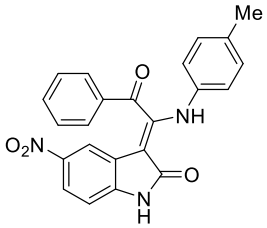
Yield: 382 mg (95 %), yellow solid. Mp: 297.4-297.9 °C; IR (KBr): 3463, 1665, 1604, 1388, 1361, 1101, 898, 841, 759, 696, 629, 572 cm^{-1}; ^1H NMR (600 MHz, DMF-d_7): δ = 7.13-7.18 (m, 2H, ArH), 7.20-7.22 (m, 1H, ArH), 7.32-7.34 (m, 2H, ArH), 7.60-7.63 (m, 2H, ArH), 7.75-7.77 (m, 1H, ArH), 8.01-8.04 (m, 2H, ArH), 8.18-8.19 (m, 2H, ArH), 11.41 (s, 1H, ArNH), 11.90 (s, 1H, CONH); ^{13}C NMR (150 MHz, DMF-d_7): δ = 95.9, 109.7, 113.3, 116.5 (d, J = 24.0 Hz), 121.2, 123.0, 126.0 (d, J = 9.0 Hz), 129.8, 130.0, 134.2, 134.5, 136.2, 142.1, 143.2, 153.9, 160.8 (d, J = 243.0 Hz), 171.2, 191.5; ^{19}F NMR (470 MHz, DMF-d_7) δ = −116.7; HRMS (TOF ES^+): *m/z* calcd for $C_{22}H_{15}FN_3O_4^+$ [$(M+H)^+$], 404.1041; found, 404.1035.

(*Z*)-3-(1-((4-chlorophenyl)amino)-2-oxo-2-phenylethylidene)-5-nitroindolin-2-one (3ec)



Yield: 382 mg (91 %), yellow solid. Mp: 298.6-299.1 °C; IR (KBr): 3458, 1600, 1384, 1354, 1196, 1109, 808, 710, 665, 601, 572 cm^{-1}; ^1H NMR (600 MHz, DMF-d_7): δ = 7.37-7.39 (m, 1H, ArH), 7.45-7.46 (m, 2H, ArH), 7.52-7.56 (m, 2H, ArH), 7.77-7.81 (m, 2H, ArH), 7.92-7.94 (m, 1H, ArH), 8.18-8.19 (m, 2H, ArH), 8.37-8.38 (m, 2H, ArH), 11.64 (s, 1H, ArNH), 12.15 (s, 1H, CONH); ^{13}C NMR (150 MHz, DMF-d_7): δ = 96.6, 109.8, 113.6, 121.5, 122.9, 124.8, 129.8, 129.9, 130.1, 131.0, 134.2. 136.3, 137.2, 142.2, 143.4, 153.0, 171.2, 191.5; HRMS (TOF ES^+): *m/z* calcd for $C_{22}H_{15}ClN_3O_4^+$ [$(M+H)^+$], 420.0746; found, 420.0734.

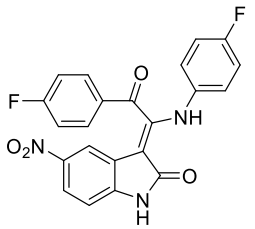
(*Z*)-5-nitro-3-(2-oxo-2-phenyl-1-(*p*-tolylamino)ethylidene)indolin-2-one (3ed)



Yield: 368 mg (92 %), yellow solid. Mp: 298.6-299.1 °C; IR (KBr): 3438, 1665, 1603, 1518, 1358, 1108, 876, 761, 697, 626, 600, 520 cm^{-1}; ^1H NMR (600 MHz, DMF-d_7): δ = 2.22 (s, 3H, $ArCH_3$), 7.13-7.17 (m, 4H, ArH), 7.21-7.22 (m, 1H, ArH), 7.61-7.63 (m, 3H, ArH), 7.75-7.76 (m, 1H, ArH), 8.00-8.02 (m, 1H, ArH), 8.21-8.22 (m, 2H,

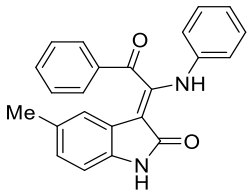
ArH), 11.45 (s, 1H, ArNH), 12.01 (s, 1H, CONH); ^{13}C NMR (150 MHz, DMF-d_7): δ = 20.0, 95.3, 109.5, 113.1, 120.9, 122.9, 129.7, 129.9, 130.2, 134.1, 135.4, 136.0, 136.1, 142.0, 142.9, 153.7, 171.1, 191.4; HRMS (TOF ES$^+$): *m/z* calcd for $C_{23}H_{18}N_3O_4^+$ [(M+H)$^+$], 400.1292; found, 400.1281.

(*Z*)-3-(2-(4-fluorophenyl)-1-((4-fluorophenyl)amino)-2-oxoethylidene)-5-nitroindolin-2-one (3ef)



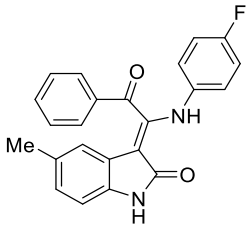
Yield: 378 mg (90 %), yellow solid. Mp: 325.0-325.5 °C; IR (KBr): 3451, 1663, 1600, 1504, 1333, 1208, 1100, 882, 837, 780, 715, 663, 619, 528 cm^{-1}; ^{1}H NMR (600 MHz, DMF-d_7): δ = 7.29-7.41 (m, 3H, ArH), 7.49-7.52 (m, 2H, ArH), 7.59-7.61 (m, 2H, ArH), 7.78-7.79 (m, 1H, ArH), 8.19-8.21 (m, 1H, ArH), 8.47-8.49 (m, 2H, ArH), 11.62 (s, 1H, ArNH), 12.05 (s, 1H, CONH); ^{13}C NMR (150 MHz, DMF-d_7): δ = 96.0, 109.8, 113.4, 116.5 (d, J = 22.5 Hz), 117.3 (d, J = 22.5 Hz), 121.3, 123.0, 126.1 (d, J = 7.5 Hz), 131.1, 133.2 (d, J = 10.5 Hz), 134.5, 142.2, 143.3, 153.4, 160.9 (d, J = 243.0 Hz), 167.2 (d, J = 255.5 Hz), 171.2, 190.0; ^{19}F NMR (470 MHz, DMF-d_7) δ = −116.5, −101.6; HRMS (TOF ES$^+$): *m/z* calcd for $C_{22}H_{14}F_2N_3O_4^+$ [(M+H)$^+$], 422.0947; found, 422.0953.

(*Z*)-5-methyl-3-(2-oxo-2-phenyl-1-(phenylamino)ethylidene)indolin-2-one (3fa)



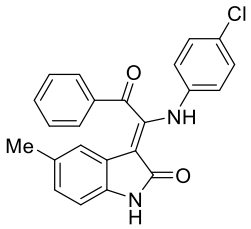
Yield: 266 mg (75 %), yellow solid. Mp: 260.4-260.9 °C; IR (KBr): 3406, 1603, 1361, 1194, 1115, 794, 751, 669, 605, 528 cm^{-1}; ^{1}H NMR (600 MHz, DMF-d_7): δ = 2.25 (s, 3H, ArCH$_3$), 6.76 (s, 1H, ArH), 7.02-7.03 (m, 1H, ArH), 7.06-7.08 (m, 1H, ArH), 7.23-7.25 (m, 1H, ArH), 7.32-7.33 (m, 2H, ArH), 7.43-7.46 (m, 2H, ArH), 7.75-7.77 (m, 2H, ArH), 7.88-7.91 (m, 1H, ArH), 8.32-8.34 (m, 2H, ArH), 10.81 (s, 1H, ArNH), 12.21 (s, 1H, CONH); ^{13}C NMR (150 MHz, DMF-d_7): δ = 20.8, 98.0, 109.7, 119.4, 122.0, 122.4, 125.2, 125.7, 129.7, 129.8, 134.8, 135.7, 136.0, 139.0, 150.7, 171.2, 192.2; HRMS (TOF ES$^+$): *m/z* calcd for $C_{23}H_{19}N_2O_2^+$ [(M+H)$^+$], 355.1441; found, 355.1439.

(*Z*)-3-(1-((4-fluorophenyl)amino)-2-oxo-2-phenylethylidene)-5-methylindolin-2-one (3fb)



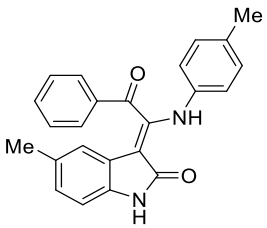
Yield: 294 mg (79 %), yellow solid. Mp: 234.6-235.0 °C; IR (KBr): 3441, 1601, 1392, 1359, 1206, 1109, 837, 802, 759, 660, 618, 550 cm^{-1}; ^1H NMR (600 MHz, DMF-d_7): δ = 2.08 (s, 3H, $ArCH_3$), 6.60 (s, 1H, ArH), 6.86-6.87 (m, 1H, ArH), 6.92-6.93 (m, 1H, ArH), 7.05-7.07 (m, 1H, ArH), 7.09-7.14 (s, 1H, ArH), 7.22-7.25 (m, 2H, ArH), 7.59-7.61 (m, 2H, ArH), 7.73-7.75 (m, 1H, ArH), 8.14-8.15 (m, 2H, ArH), 10.65 (s, 1H, ArNH), 11.90 (s, 1H, CONH); ^{13}C NMR (150 MHz, DMF-d_7): δ = 20.6, 97.8, 109.6, 116.2 (d, J = 22.5 Hz), 119.2, 122.3, 124.8 (d, J = 9.0 Hz), 125.6, 129.6, 129.7, 134.6, 135.2, 135.5, 135.9, 150.9, 160.8 (d, J = 241.5 Hz), 171.0, 191.9; ^{19}F NMR (470 MHz, DMF-d_7) δ = −118.3; HRMS (TOF ES^+): *m/z* calcd for $C_{23}H_{18}FN_2O_2^+$ [$(M+H)^+$], 373.1347; found, 373.1349.

(*Z*)-3-(1-((4-chlorophenyl)amino)-2-oxo-2-phenylethylidene)-5-methylindolin-2-one (3fc)



Yield: 302 mg (78 %), yellow solid. Mp: 288.2-288.7 °C; IR (KBr): 3453, 1649, 1593, 1359, 1304, 1220, 1116, 716, 680, 621, 565 cm^{-1}; ^1H NMR (600 MHz, DMF-d_7): δ =2.09 (s, 3H, $ArCH_3$), 6.59 (s, 1H, ArH), 6.87-6.91 (m, 2H, ArH), 7.19-2.20 (m, 2H, ArH), 7.34-7.36 (m, 2H, ArH), 7.60-7.62 (m, 2H, ArH), 7.74-7.75 (m, 1H, ArH), 8.16-8.18 (m, 2H, ArH), 10.73 (s, 1H, ArNH), 11.99 (s, 1H, CONH); ^{13}C NMR (150 MHz, DMF-d_7): δ = 20.6, 98.6, 109.6, 119.4, 123.5, 125.9, 129.6, 129.7, 134.5, 135.7, 136.0, 137.9, 149.9, 170.9, 191.9; HRMS (TOF ES^+): *m/z* calcd for $C_{23}H_{18}ClN_2O_2^+$ [$(M+H)^+$], 389.1051; found, 389.1044.

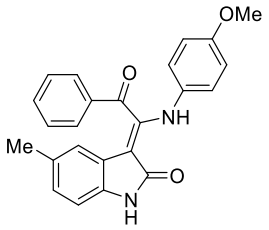
(*Z*)-5-methyl-3-(2-oxo-2-phenyl-1-(*p*-tolylamino)ethylidene)indolin-2-one (3fd)



Yield: 280 mg (76 %), yellow solid. Mp: 268.5-268.7 °C; IR (KBr): 3450, 1599, 1386, 1358, 1206, 1118, 886, 782, 661, 603, 565 cm^{-1}; ^1H NMR (600 MHz, DMF-d_7): δ = 2.25 (s, 3H, $ArCH_3$), 2.37 (s, 3H, $ArCH_3$), 6.73 (s, 1H, ArH), 7.01-7.02 (m, 1H, ArH),

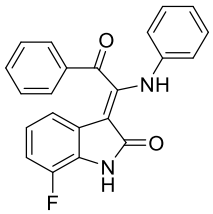
7.06-7.07 (m, 1H, ArH), 7.22-7.27 (m, 4H, ArH), 7.76-7.78 (m, 2H, ArH), 7.89-7.90 (m, 1H, ArH), 8.32-8.33 (m, 2H, ArH), 10.85 (s, 1H, ArNH), 12.16 (s, 1H, CONH); ^{13}C NMR (150 MHz, DMF-d_7): δ = 20.1, 20.8, 97.4, 109.7, 119.2, 122.2, 122.5, 125.5, 129.6, 129.8, 129.9, 130.2, 134.8, 135.1, 135.7, 135.8, 136.4, 151.1, 171.2, 192.2; HRMS (TOF ES$^+$): *m/z* calcd for $C_{24}H_{21}N_2O_2^+$ [(M+H)$^+$], 369.1598; found, 369.1593.

(*Z*)-3-(1-((4-methoxyphenyl)amino)-2-oxo-2-phenylethylidene)-5-methylindolin -2-one (3fe)



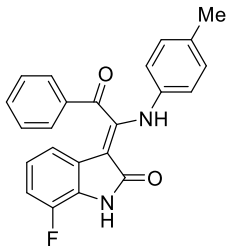
Yield: 288 mg (75 %), yellow solid. Mp: 264.5-264.9 °C; IR (KBr): 3429, 1601, 1358, 1117, 880, 837, 695, 616, 572, 544 cm^{-1}; ^{1}H NMR (600 MHz, DMF-d_7): δ = 2.08 (s, 3H, $ArCH_3$), 3.73 (s, 3H, OCH_3), 6.56 (s, 1H, ArH), 6.83-6.86 (m, 3H, ArH), 6.89-6.90 (m, 1H, ArH), 7.13-7.14 (m, 2H, ArH), 7.58-7.61 (m, 2H, ArH), 7.72-7.73 (m, 1H, ArH), 8.13-8.14 (m, 2H, ArH), 10.57 (s, 1H, ArNH), 11.86 (s, 1H, CONH); ^{13}C NMR (150 MHz, DMF-d_7): δ = 20.6, 55.2, 96.6, 109.4, 114.7, 118.9, 122.5, 124.6, 125.1, 129.4, 129.6, 131.5, 134.7, 135.4, 135.6, 151.7, 157.6, 171.0, 192.0; HRMS (TOF ES$^+$): *m/z* calcd for $C_{24}H_{21}N_2O_3^+$ [(M+H)$^+$], 385.1547; found, 385.1547.

(*Z*)-7-fluoro-3-(2-oxo-2-phenyl-1-(phenylamino)ethylidene)indolin-2-one (3ga)



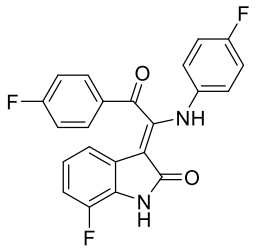
Yield: 316 mg (88 %), yellow solid. Mp: 245.5-245.8 °C; IR (KBr): 3411, 2024, 1605, 1360, 1124, 884, 715, 672, 599, 558 cm^{-1}; ^{1}H NMR (600 MHz, DMF-d_7): δ = 6.72-6.73 (m, 1H, ArH), 6.93-6.94 (m, 1H, ArH), 7.06-7.10(m, 1H, ArH), 7.28-7.30 (m, 1H, ArH), 7.36-7.38 (m, 2H, ArH), 7.46-7.48 (m, 2H, ArH), 7.75-7.78 (m, 2H, ArH), 7.89-7.91 (m, 1H, ArH), 8.32-8.33 (m, 2H, ArH), 11.55 (s, 1H, ArNH), 12.26 (s, 1H, CONH); ^{13}C NMR (150 MHz, DMF-d_7): δ = 97.1, 111.3 (d, J = 18.0 Hz), 114.6, 121.6 (d, J = 6.0 Hz), 122.6, 124.7 (d, J = 13.5 Hz), 125.6, 125.9, 129.8, 130.0, 134.4, 136.0, 138.4, 147.6 (d, J = 238.5 Hz), 152.5, 170.8, 191.8; ^{19}F NMR (470 MHz, DMF-d_7) δ = −135.1; HRMS (TOF ES$^+$): *m/z* calcd for $C_{22}H_{16}FN_2O_2^+$ [(M+H)$^+$], 359.1190; found, 359.1190.

(*Z*)-7-fluoro-3-(2-oxo-2-phenyl-1-(*p*-tolylamino)ethylidene)indolin-2-one (3gd)



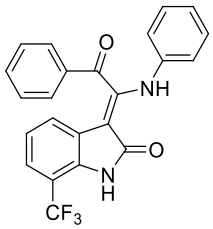
Yield: 324 mg (87 %), yellow solid. Mp: 283.7-284.1 °C; IR (KBr): 3421, 1655, 1606, 1516, 1401, 1357, 1208, 1124, 786, 631, 572 cm^{-1}; ^1H NMR (600 MHz, DMF-d_7): δ = 2.21 (s, 3H, $ArCH_3$), 6.54-6.56 (m, 1H, ArH), 6.74-6.77 (m, 1H, ArH), 6.89-6.92 (m, 1H, ArH), 7.09-7.13 (m, 4H, ArH), 7.59-7.62 (m, 2H, ArH), 7.73-7.76 (m, 1H, ArH), 8.15-8.17 (m, 2H, ArH), 11.32 (s, 1H, ArNH), 12.04 (s, 1H, CONH); ^{13}C NMR (150 MHz, DMF-d_7): δ = 96.4, 110.9 (d, J = 18.0 Hz), 114.3, 121.3 (d, J = 6.0 Hz), 122.6, 124.4 (d, J = 12.0 Hz), 125.6 (d, J = 4.5 Hz), 129.6, 129.8, 130.1, 134.3, 135.6, 135.7, 147.8 (d, J = 240.0 Hz), 152.6, 170.6, 191.6; ^{19}F NMR (470 MHz, DMF-d_7) δ = −135.3; HRMS (TOF ES^+): *m/z* calcd for $C_{23}H_{18}FN_2O_2^+$ [$(M+H)^+$], 373.1347; found, 373.1348.

(*Z*)-7-fluoro-3-(2-(4-fluorophenyl)-1-((4-fluorophenyl)amino)-2-oxoethylidene) indolin-2-one (3gf)



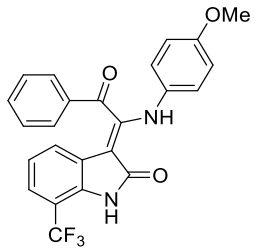
Yield: 354 mg (90 %), yellow solid. Mp: 252.5-252.8 °C; IR (KBr): 3436, 1659, 1606, 1511, 1211, 1155, 1106, 188, 700, 656, 598 cm^{-1}; ^1H NMR (600 MHz, DMF-d_7): δ = 6.54-6.56 (m, 1H, ArH), 6.77-6.80 (m, 1H, ArH), 6.91-6.94 (m, 1H, ArH), 7.14-7.17 (m, 1H, ArH), 7.22-7.29 (m, 1H, ArH), 7.37-7.43 (m, 2H, ArH), 7.91-7.93 (m, 1H, ArH), 8.14-8.17 (m, 1H, ArH), 8.24-8.26 (m, 1H, ArH), 11.36 (s, 1H, ArNH), 11.87 (s, 1H, CONH); ^{13}C NMR (150 MHz, DMF-d_7): δ = 96.9, 111.2 (d, J = 16.5 Hz), 114.4, 115.2 (d, J = 22.5 Hz), 115.4 (d, J = 22.5 Hz), 116.3 (d, J = 22.5 Hz), 117.0 (d, J = 21.0 Hz), 121.5 (d, J = 7.5 Hz), 122.4 (d, J = 7.5 Hz), 125.4, 125.6 (d, J = 9.0 Hz), 130.5 (d, J = 9.0 Hz), 131.0, 133.0 (d, J = 10.5 Hz), 134.6, 146.7, 152.3, 160.5 (d, J = 243.0 Hz), 164.0 (d, J = 242.0 Hz), 165.2 (d, J = 244.0 Hz), 170.6, 190.0; ^{19}F NMR (470 MHz, DMF-d_7) δ = −135.1, −117.3, −102.2; HRMS (TOF ES^+): *m/z* calcd for $C_{22}H_{14}F_3N_2O_2^+$ [$(M+H)^+$], 395.1002; found, 395.1165.

(*Z*)-3-(2-oxo-2-phenyl-1-(phenylamino)ethylidene)-7-(trifluoromethyl)indolin-2-o ne (3ia)



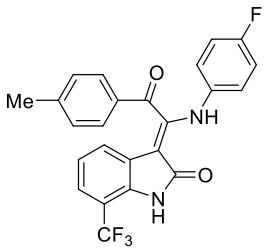
Yield: 350 mg (86 %), yellow solid. Mp: 243.7-244.1 °C; IR (KBr): 3418, 1606, 1360, 1116, 881, 667, 613, 573, 553 cm^{-1}; ^1H NMR (600 MHz, DMF-d_7): δ = 6.96-6.98 (m, 2H, ArH), 7.13-7.16 (m, 1H, ArH), 7.22-7.24 (m, 2H, ArH), 7.30-7.34 (m, 3H, ArH), 7.59-7.62 (m, 2H, ArH), 7.74-7.77 (m, 1H, ArH), 8.17-8.18 (m, 2H, ArH), 11.35 (s, 1H, ArNH), 12.10 (s, 1H, CONH); ^{13}C NMR (150 MHz, DMF-d_7): δ = 95.8, 120.7, 120.9, 121.6, 122.7, 124.2, 126.0, 129.7, 129.8, 134.0, 134.1, 136.0, 138.1, 152.9, 171.1, 191.6; ^{19}F NMR (470 MHz, DMF-d_7) δ = −61.4; HRMS (TOF ES$^+$): *m/z* calcd for $C_{23}H_{16}F_3N_2O_2^+$ [$(M+H)^+$], 409.1158; found, 409.1157.

(*Z*)-3-(1-((4-methoxyphenyl)amino)-2-oxo-2-phenylethylidene)-7-(trifluoromethyl) indolin-2-one (3ie)



Yield: 372 mg (85 %), yellow solid. Mp: 232.8-233.1 °C; IR (KBr): 3429, 1607, 1516, 1361, 1119, 892, 722, 689, 647, 613, 559 cm^{-1}; ^1H NMR (600 MHz, DMF-d_7): δ = 3.81 (s, 3H, OCH_3), 7.03-7.05 (m, 2H, ArH), 7.10-7.11 (m, 2H, ArH), 7.35-7.37 (m, 2H, ArH), 7.47-7.48 (m, 1H, ArH), 7.76-7.78 (m, 2H, ArH), 7.90-7.93 (m, 1H, ArH), 8.30-8.32 (m, 2H, ArH), 11.44 (s, 1H, ArNH), 12.09 (s, 1H, CONH); ^{13}C NMR (150 MHz, DMF-d_7): δ = 55.4, 94.4, 114.8, 120.6, 120.7, 121.4, 124.6, 125.5, 129.8, 130.0, 130.8, 133.9, 134.3, 136.0, 154.1, 158.3, 171.2, 191.8; ^{19}F NMR (470 MHz, DMF-d_7) δ = −61.3; HRMS (TOF ES$^+$): *m/z* calcd for $C_{24}H_{18}F_3N_2O_3^+$ [$(M+H)^+$], 439.1264; found, 439.1264.

(*Z*)-3-(1-((4-fluorophenyl)amino)-2-oxo-2-(*p*-tolyl)ethylidene)-7-(trifluoromethyl)i ndolin-2-one (3ig)

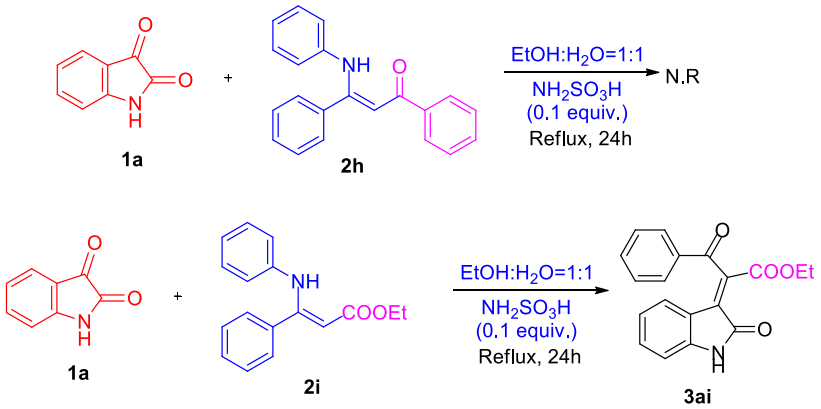


Yield: 382 mg (87%), yellow solid. Mp: 255.4-255.8 °C; IR (KBr): 3467, 1665, 1612,

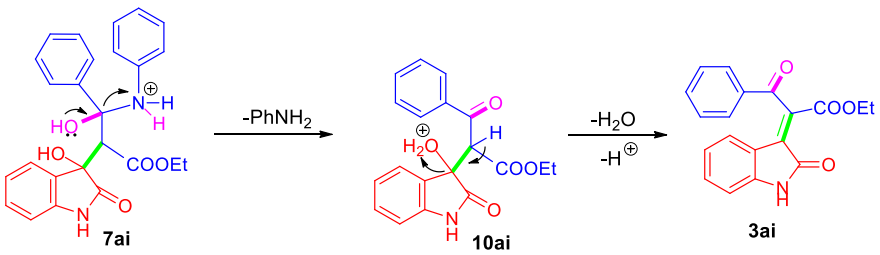
1518, 1324, 1223, 1182, 1118, 808, 709, 627, 601, 565 cm^{-1}; ^1H NMR (600 MHz, DMF-d_7): δ = 2.54 (s, 3H, $ArCH_3$), 7.12-7.13 (m, 2H, ArH), 7.31-7.34 (m, 2H, ArH), 7.46-7.50 (m, 3H, ArH), 7.57-7.58 (m, 2H, ArH), 8.20-8.22 (m, 2H, ArH), 11.46 (s, 1H, ArNH), 12.11 (s, 1H, CONH); ^{13}C NMR (150 MHz, DMF-d_7): δ = 21.3, 95.3, 116.5 (d, J = 22.5 Hz), 120.9 (d, J = 10.5 Hz), 121.7, 124.5, 125.5, 125.8, 130.0, 130.6, 131.8, 134.2, 134.6, 147.6, 153.7, 160.7 (d, J = 241.5 Hz), 171.2, 191.0; ^{19}F NMR (470 MHz, DMF-d_7) δ = −116.9, −61.2; HRMS (TOF ES^+): *m/z* calcd for $C_{24}H_{17}F_4N_2O_2^+$ [$(M+H)^+$], 441.1221; found, 441.1221.

Control experiments

Scheme S1. Different enamines used as substrate to detect the cascade reaction

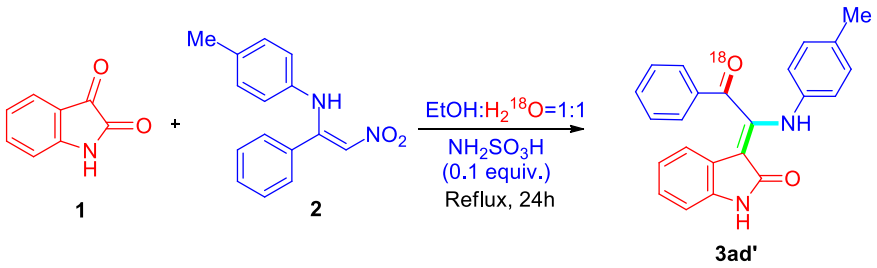


Other analogues of compound **2** in which NO_2 was replaced by ester/acyl were used as the substrates in this cascade reaction. It was found that isatins **1a** could not react with acyl substrate **2h**, so that we could not obtain any intermediate or final products. This may be because substrate **2h** was not sufficiently reactive, and the reactions of intermediates **4**-**7** were carried out through three reversible reactions, resulting in an unfavorable equilibrium for the forward reaction (Paper, Scheme 2). The ester substrate **2i** reacted with substrate **1a** to form (*Z*)-ethyl 3-oxo-2-(2-oxoindolin-3-ylidene)-3-phenylpropanoate **3ai** with very low yield (8%). This result showed that the ester group could not be removed from intermediate **7**, and therefore the arylamino group could not undergo the 1,2-migration rearrangement to form intermediate **8** (Paper, Scheme 2). The arylamino group was removed from the intermediate **7ai** to obtain intermediate **10ai**, and then intermediate **10ai** lost one water molecule and one proton to produce (*Z*)-ethyl 3-oxo-2-(2-oxoindolin-3-ylidene)-3-phenylpropanoate **3ai**.



Ethyl 3-oxo-2-(2-oxoindolin-3-ylidene)-3-phenylpropanoate (3ai): Yield: 26 mg (8 %), yellow semisolid; ^{1}H NMR (600 MHz, DMSO-d_6): δ = 1.13 (t, J = 7.1 Hz, 3H, CH_3), 4.29 (q, J = 7.0 Hz, 2H, CH_2), 6.91 (d, J = 7.8 Hz, 1H, ArH), 7.06-7.08 (m, 1H, ArH), 7.39-7.42 (m, 1H, ArH), 7.52-7.55 (m, 2H, ArH), 7.64-7.66 (m, 1H, ArH), 7.92-7.93 (m, 2H, ArH), 8.05-8.06 (m, 1H, ArH), 10.84 (s, 1H, CONH); ^{13}C NMR (150 MHz, DMSO-d_6): δ = 14.2, 62.7, 111.1, 119.5, 122.5, 127.5, 128.8, 129.3, 130.0, 133.5, 134.0, 134.7, 135.5, 136.3, 145.6, 163.9, 167.3, 192.7.

Scheme S2. H_2O^{18} instead of H_2O to verify the mechanism



Most importantly, a control experiment using H_2O^{18} instead of H_2O was carried out to verify that the oxygen atom in the carbonyl of compound **3** originated from water rather that from the substrate isatins **1** (SI, Figures S104−S106).

(*Z*)-3-(2-^{18}O-2-phenyl-1-(*p*-tolylamino)ethylidene)indolin-2-one (3ad'): Yield: 303 mg (85 %), yellow solid. Mp: 261-262 °C;^{1}H NMR (600 MHz, DMF-d_7): δ = 2.20 (s, 3H, CH_3), 6.74-6.75 (m, 2H, ArH), 7.02-7.03 (m, 2H, ArH), 7.07-7.11 (m, 4H, ArH), 7.59-7.62 (m, 2H, ArH), 7.73-7.74 (m, 1H, ArH), 8.17-8.18 (m, 2H, ArH), 10.81 (s, 1H, ArNH), 11.98 (s, 1H, CONH); ^{13}C NMR (150 MHz, DMF-d_7): δ = 20.0, 97.0, 109.8, 118.3, 120.7, 122.2, 122.3, 124.7, 129.6, 129.7, 130.1, 134.4, 135.0, 135.6, 136.1, 137.8, 151.2, 170.8, 191.9; HRMS (ES^{+}): *m/z* calcd for $C_{23}H_{19}N_2{}^{18}O^{16}O$ [(M+H)$^{+}$], 357.1490; found, 357.1496.

X-ray Structure and Data of 3aa[2]

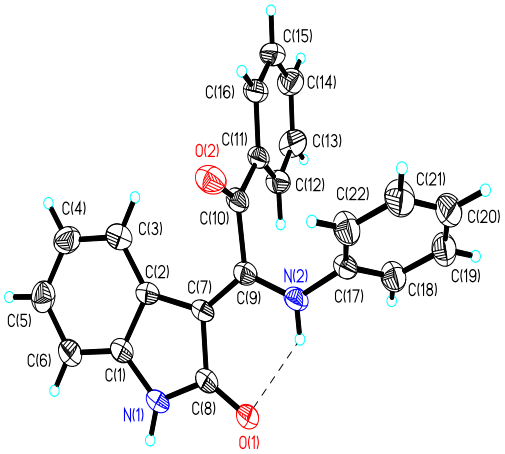


Figure S1.X-Ray crystal structure of **3aa**, ellipsoids are drawn at the 30% probability level.

Table S2. Crystal data and structure refinement for **3aa**

Empirical formula	$C_{22}H_{16}N_2O_2$
Formula weight	340.37
Temperature	293(2) K
Wavelength	0.71073 A
Crystal system, space group	Monoclinic, P2(1)/c
Unit cell dimensions	a = 9.3098(15) A alpha = 90 deg. b = 10.3197(17) A beta = 91.529(2) deg. c = 18.503(3) A gamma = 90 deg.
Volume	1777.0(5) A^3
Z, Calculated density	4, 1.272 Mg/m^3
Absorption coefficient	0.083 mm^-1
F(000)	712
Crystal size	0.20 x 0.18 x 0.15 mm
Theta range for data collection	2.188 to 25.993 deg.
Limiting indices	-11<=h<=8, -12<=k<=12, -20<=l<=22
Reflections collected / unique	10634 / 3482 [R(int) = 0.0791]
Completeness to theta = 25.242	99.7 %
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3482 / 0 / 235
Goodness-of-fit on F^2	0.864
Final R indices [I>2sigma(I)]	R1 = 0.0494, wR2 = 0.0940
R indices (all data)	R1 = 0.1567, wR2 = 0.1189
Extinction coefficient	n/a
Largest diff. peak and hole	0.159 and -0.200 e.A^-3

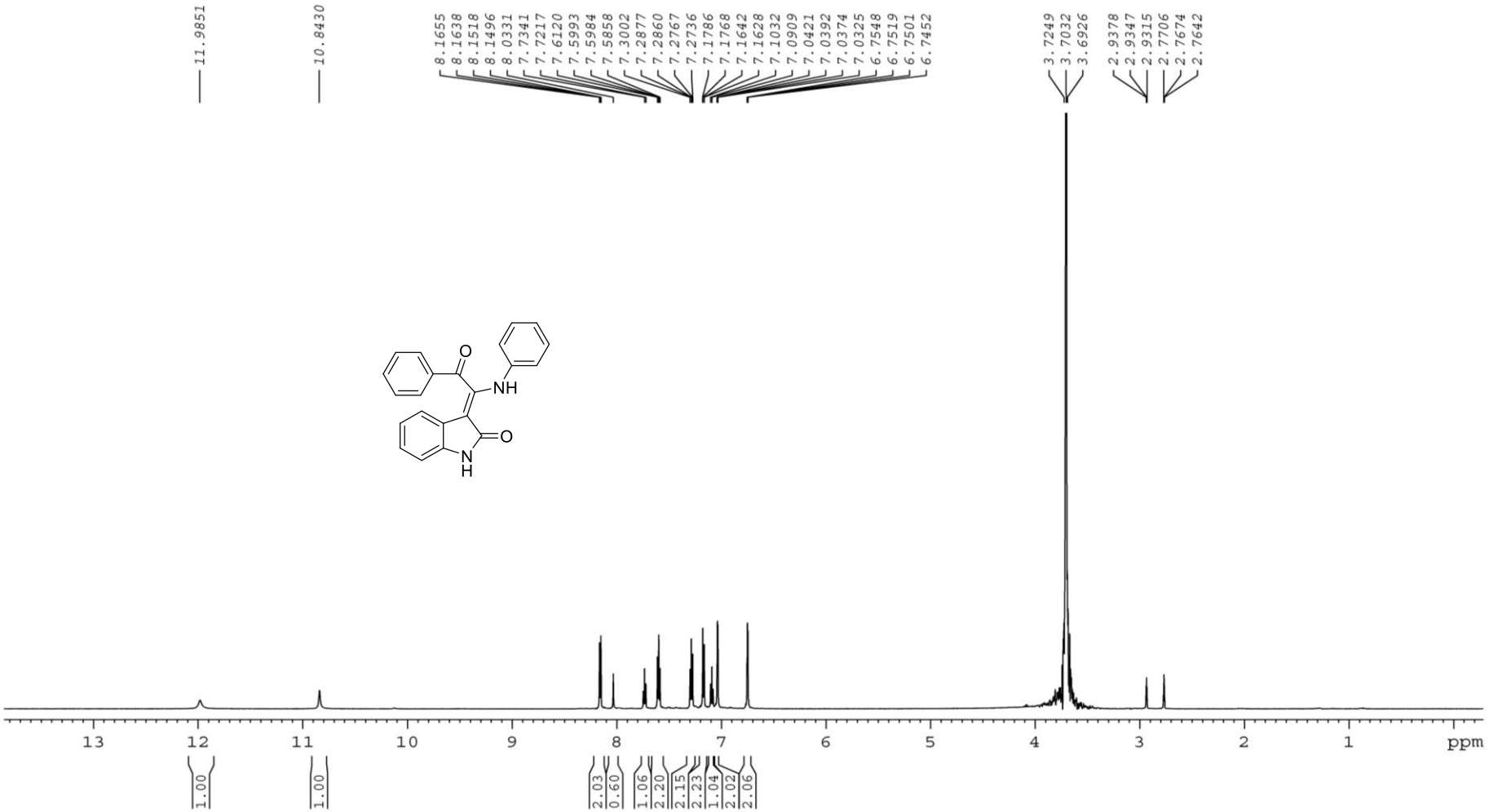


Figure S2. ^{1}H NMR (600 MHz, DMF-d_7) spectra of compound **3aa**

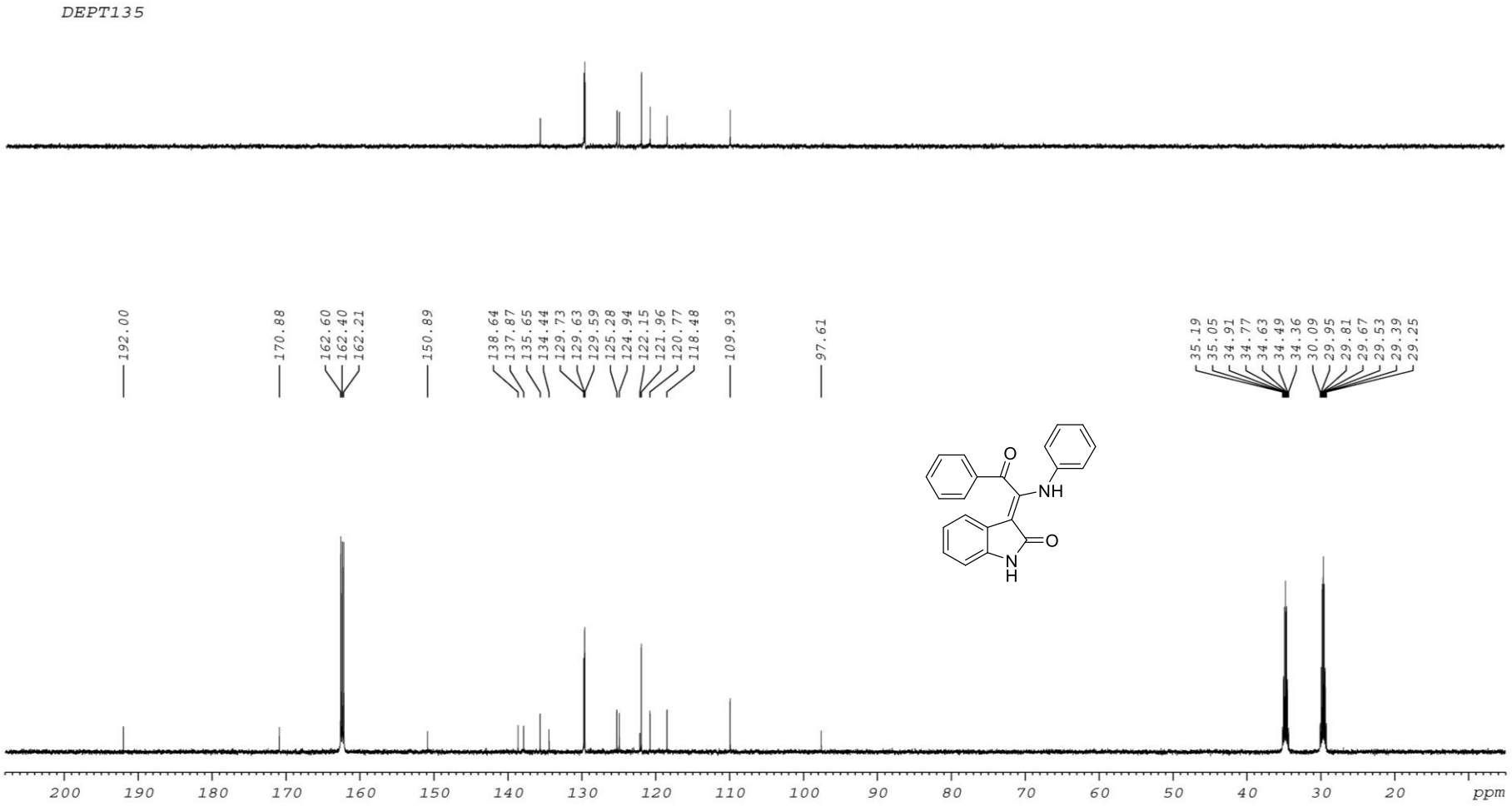


Figure S3. ^{13}C NMR (150 MHz, DMF-d_7) spectra of compound **3aa**

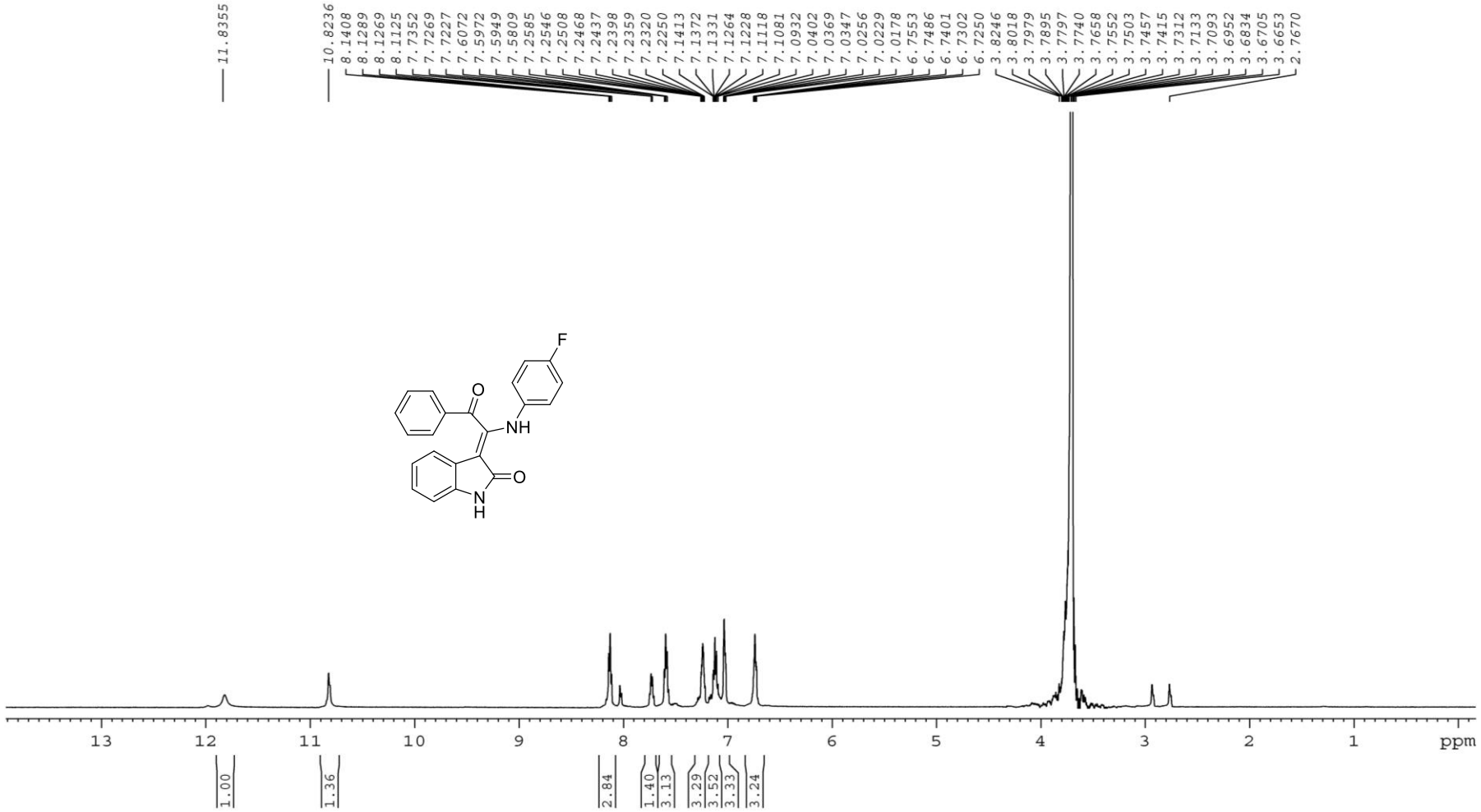


Figure S4. ^{1}H NMR (600 MHz, DMF-d_7) spectra of compound **3ab**

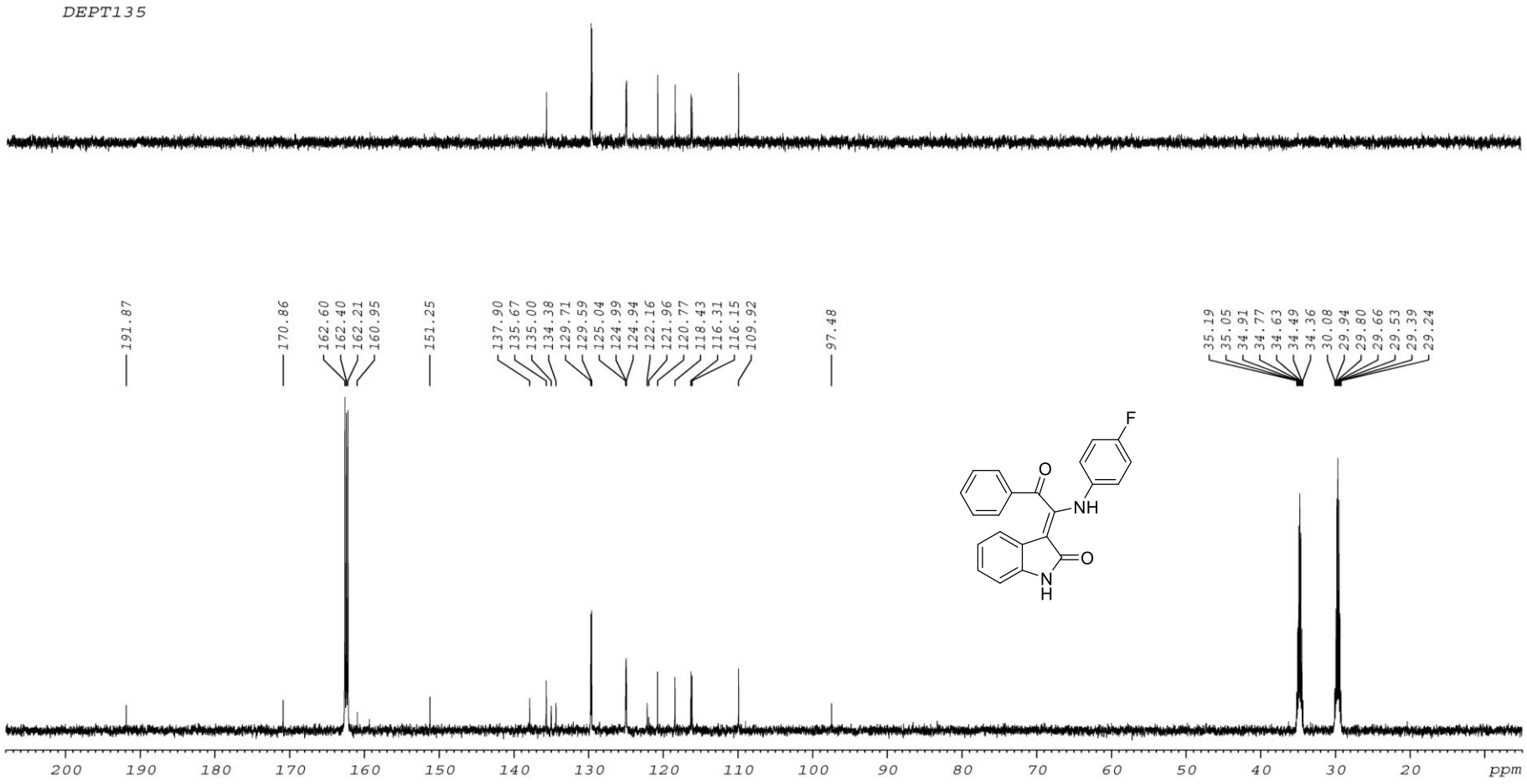


Figure S5. ^{13}C NMR (150 MHz, DMF-d_7) spectra of compound **3ab**

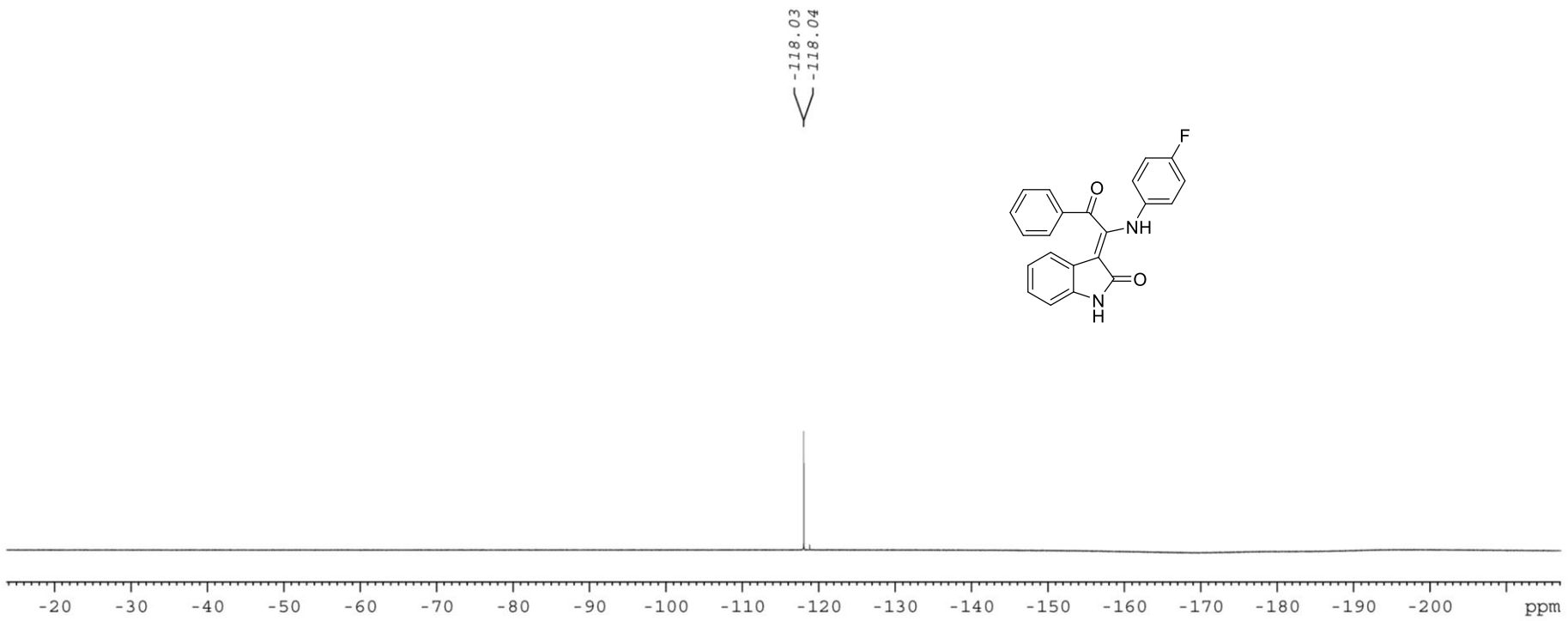


Figure S6. ^{19}F NMR (470 MHz, DMF-d_7) spectra of compound **3ab**

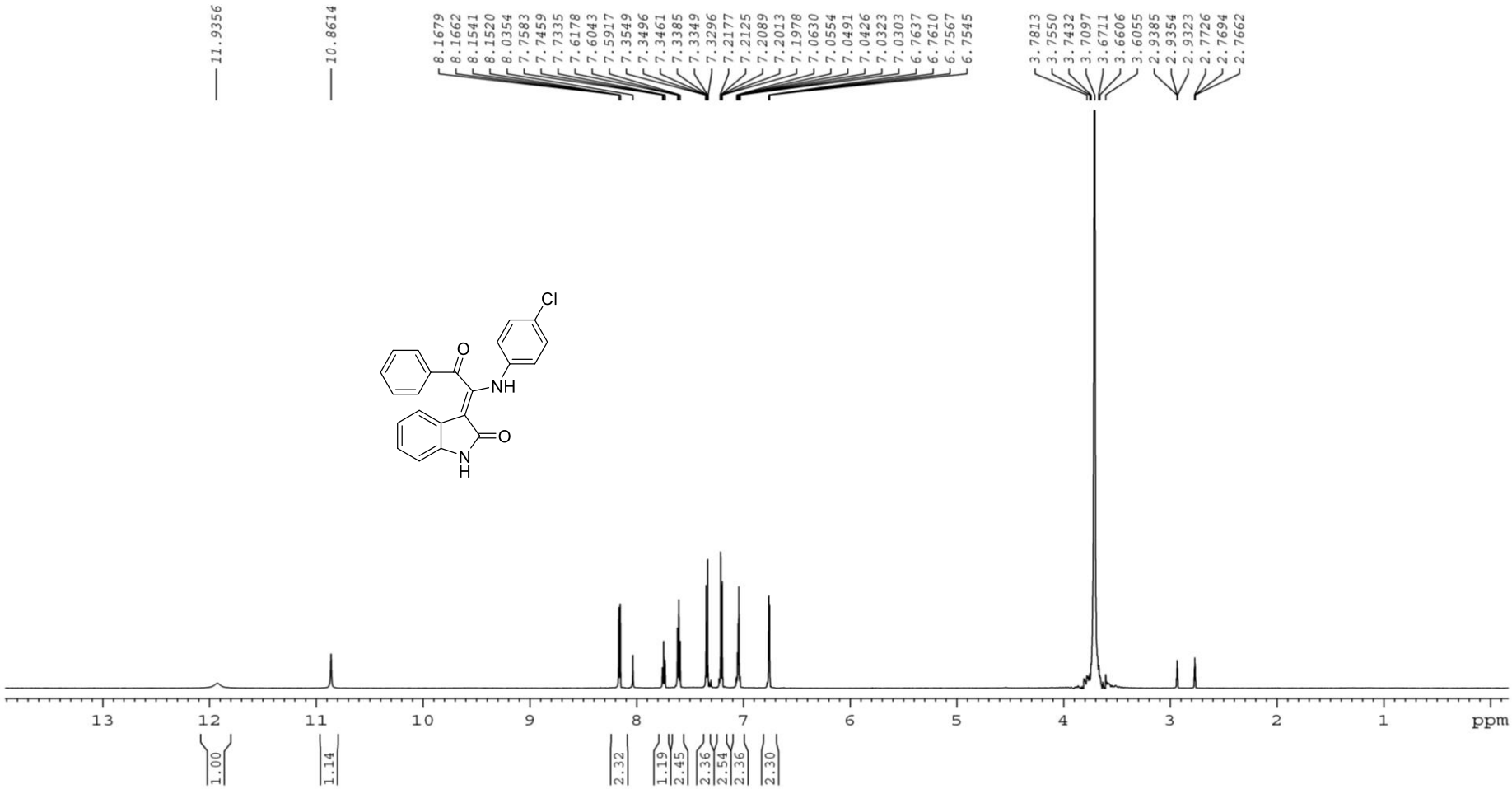


Figure S7. ^{1}H NMR (600 MHz, DMF-d_7) spectra of compound **3ac**

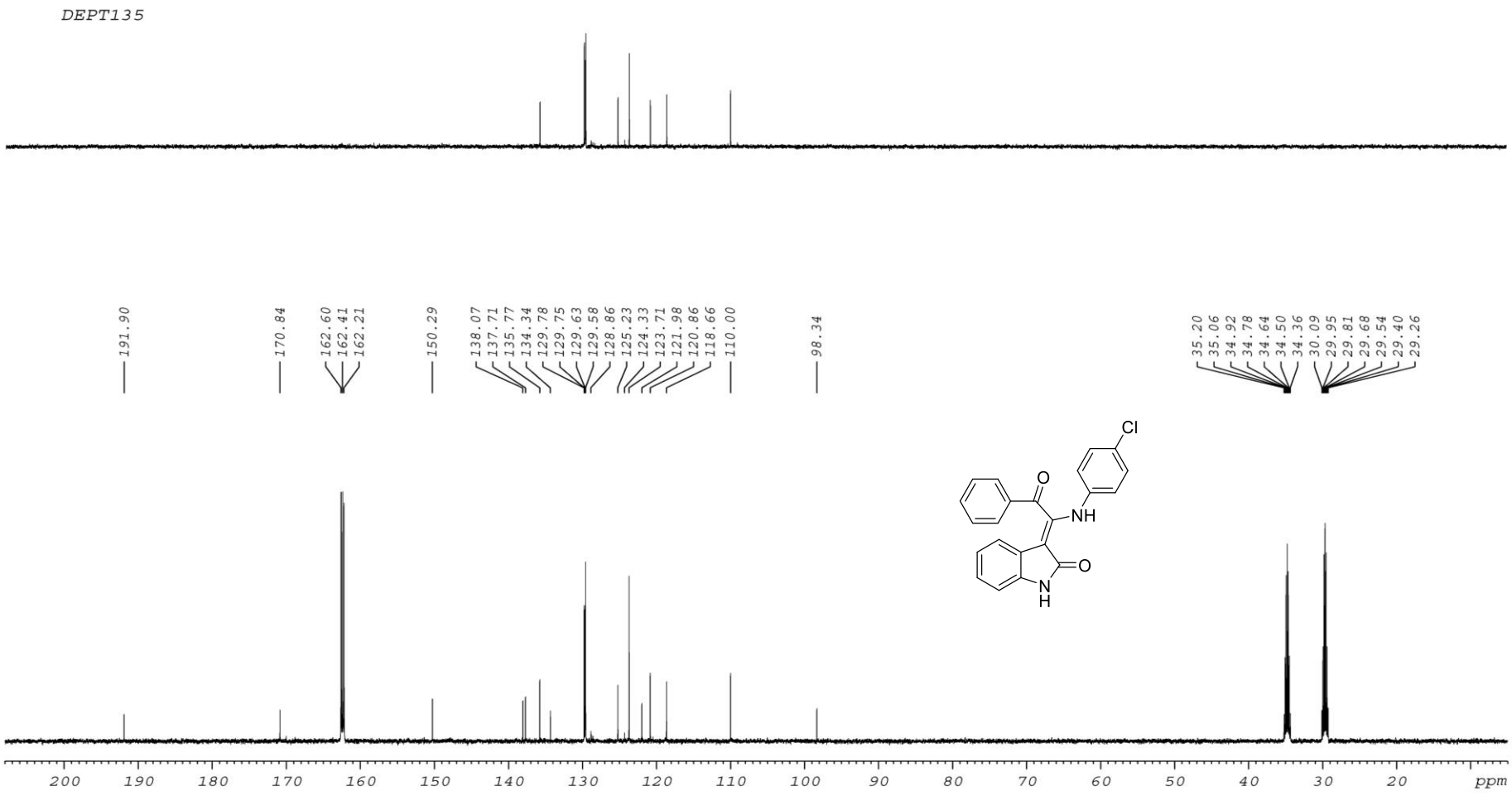


Figure S8. ^{13}C NMR (150 MHz, DMF-d_7) spectra of compound **3ac**

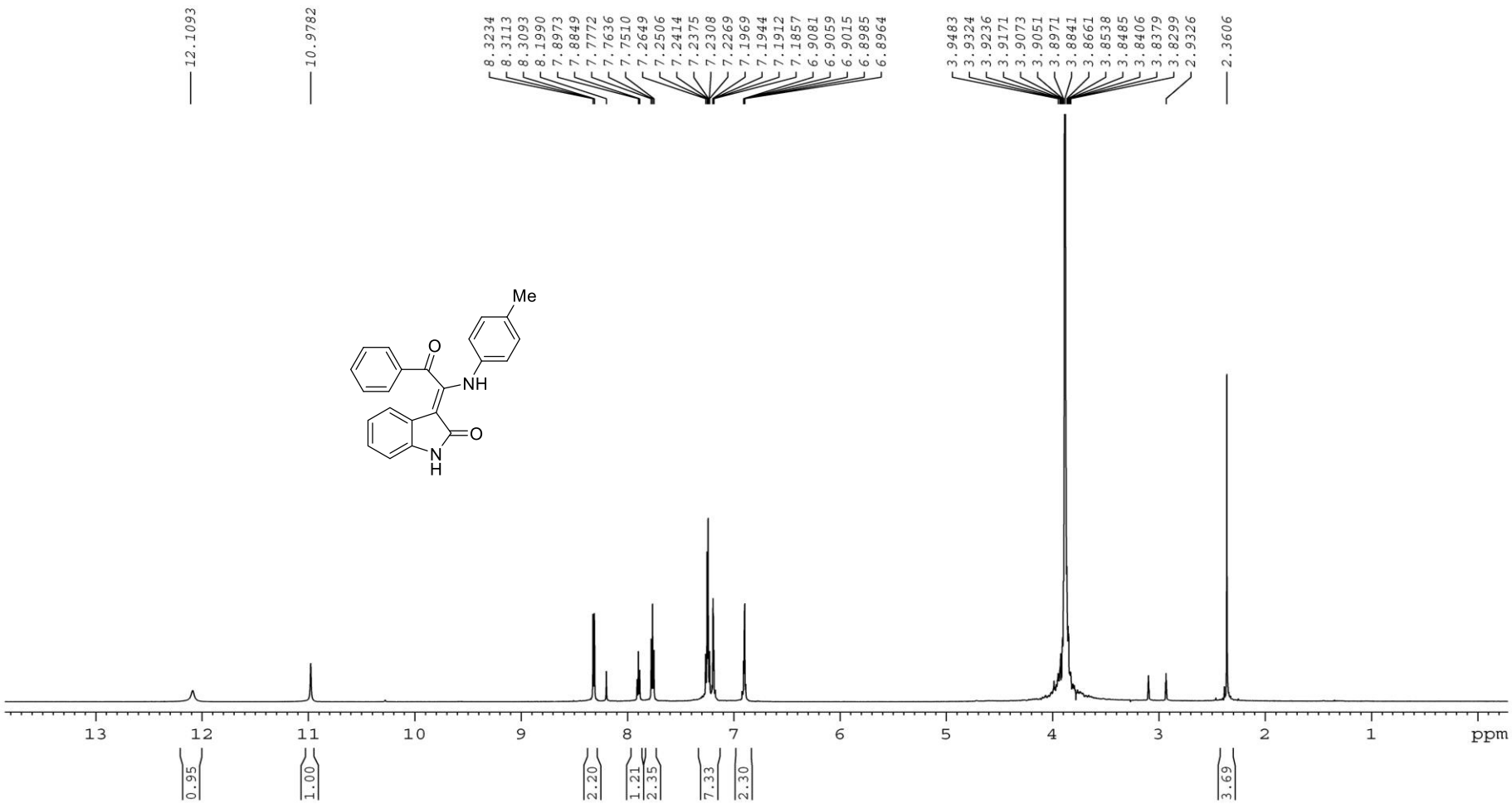


Figure S9. ^{1}H NMR (600 MHz, DMF-d_7) spectra of compound **3ad**

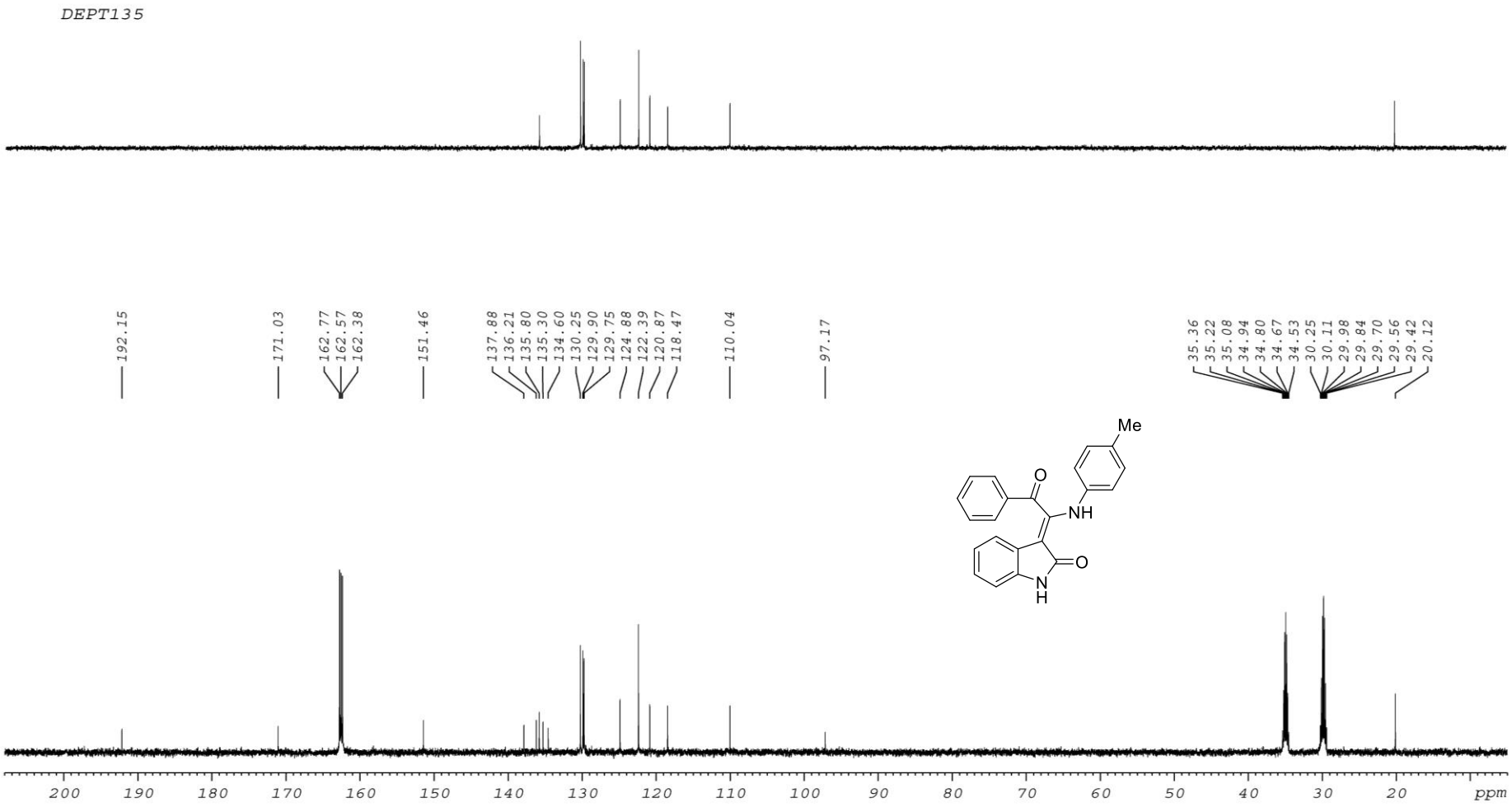


Figure S10. ^{13}C NMR (150 MHz, DMF-d_7) spectra of compound **3ad**

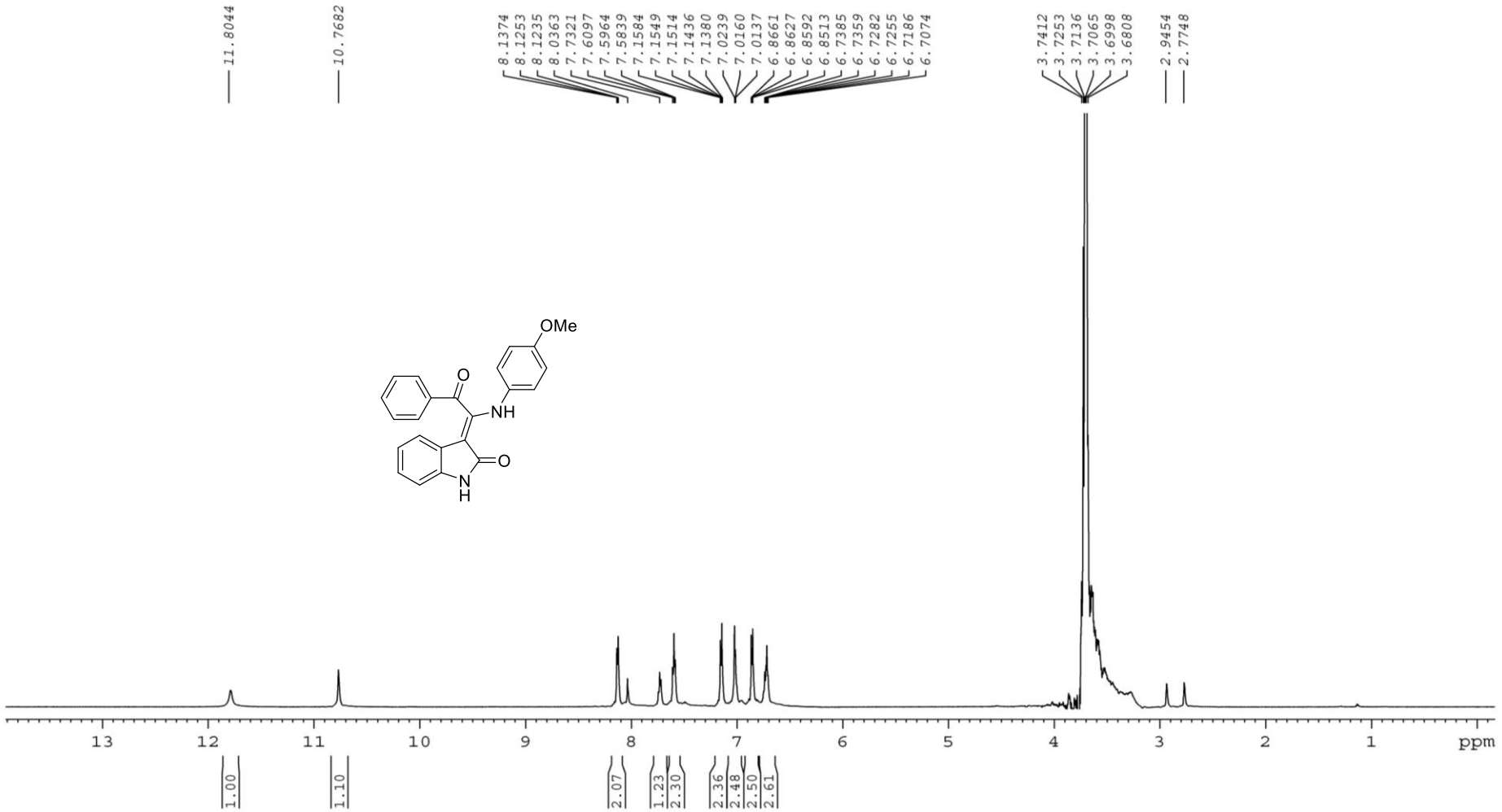


Figure S11. ^{1}H NMR (600 MHz, DMF-d_7) spectra of compound **3ae**

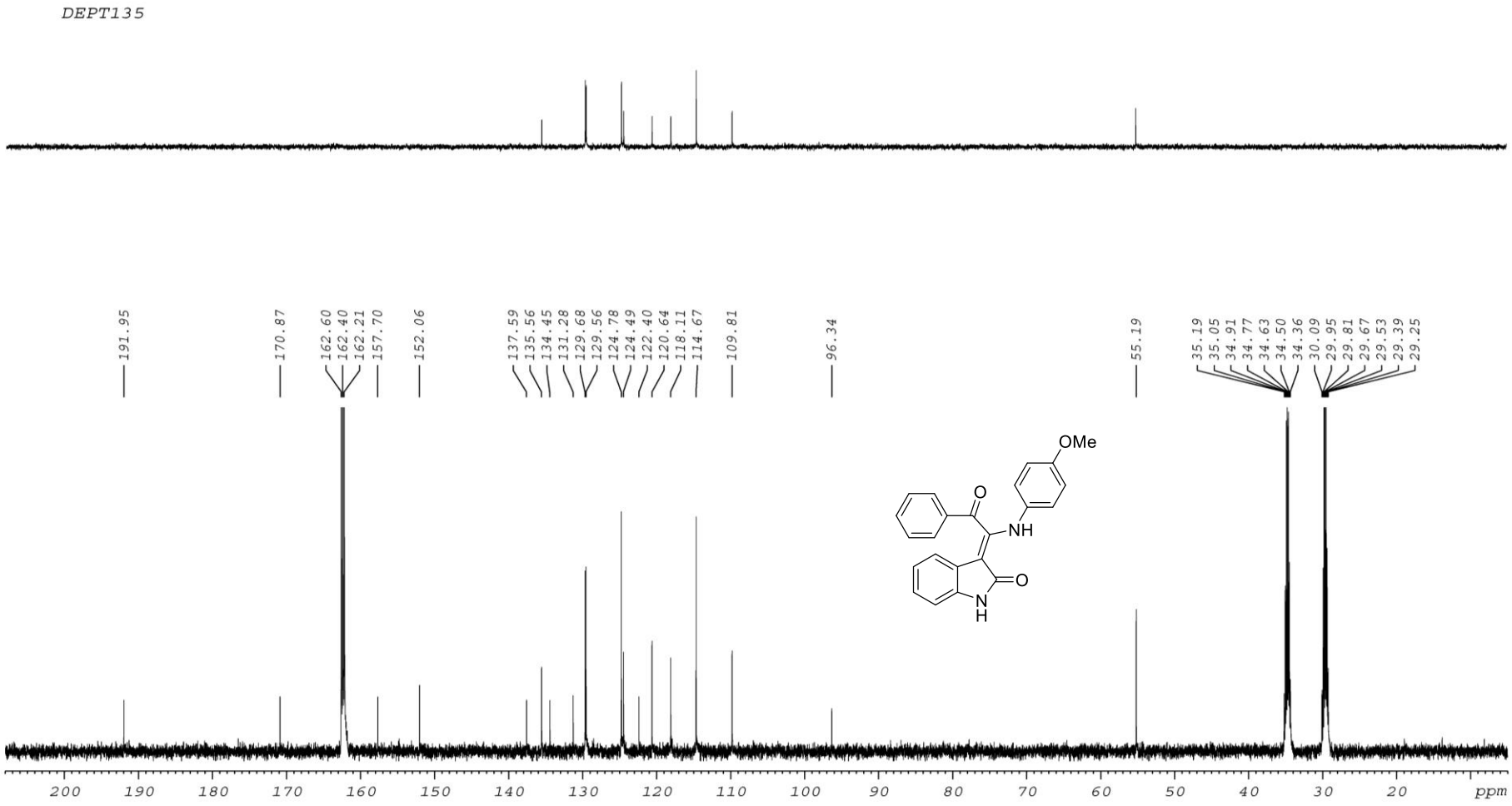


Figure S12. ^{13}C NMR (150 MHz, DMF-d_7) spectra of compound **3ae**

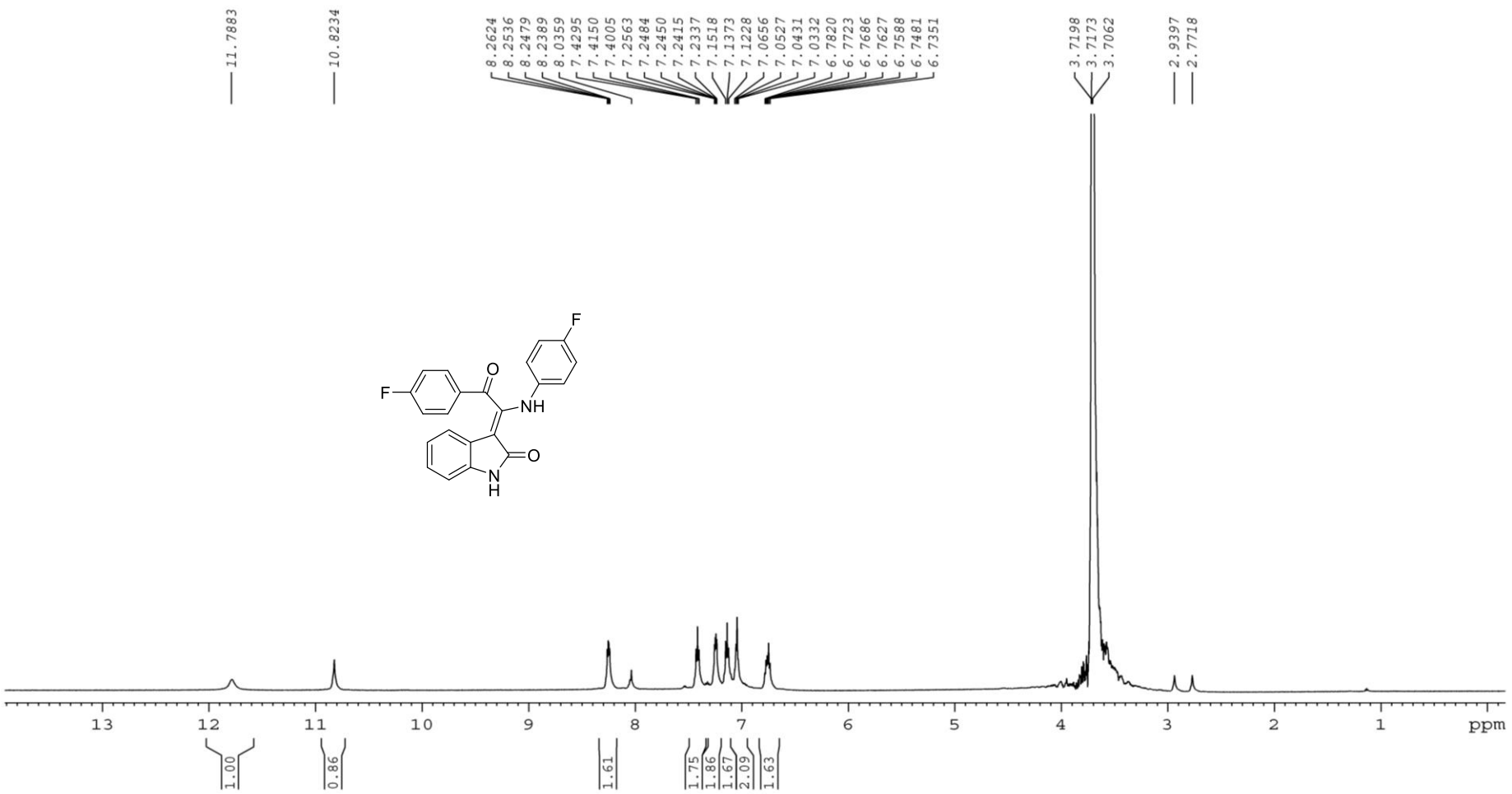


Figure S13. ^{1}H NMR (600 MHz, DMF-d_7) spectra of compound **3af**

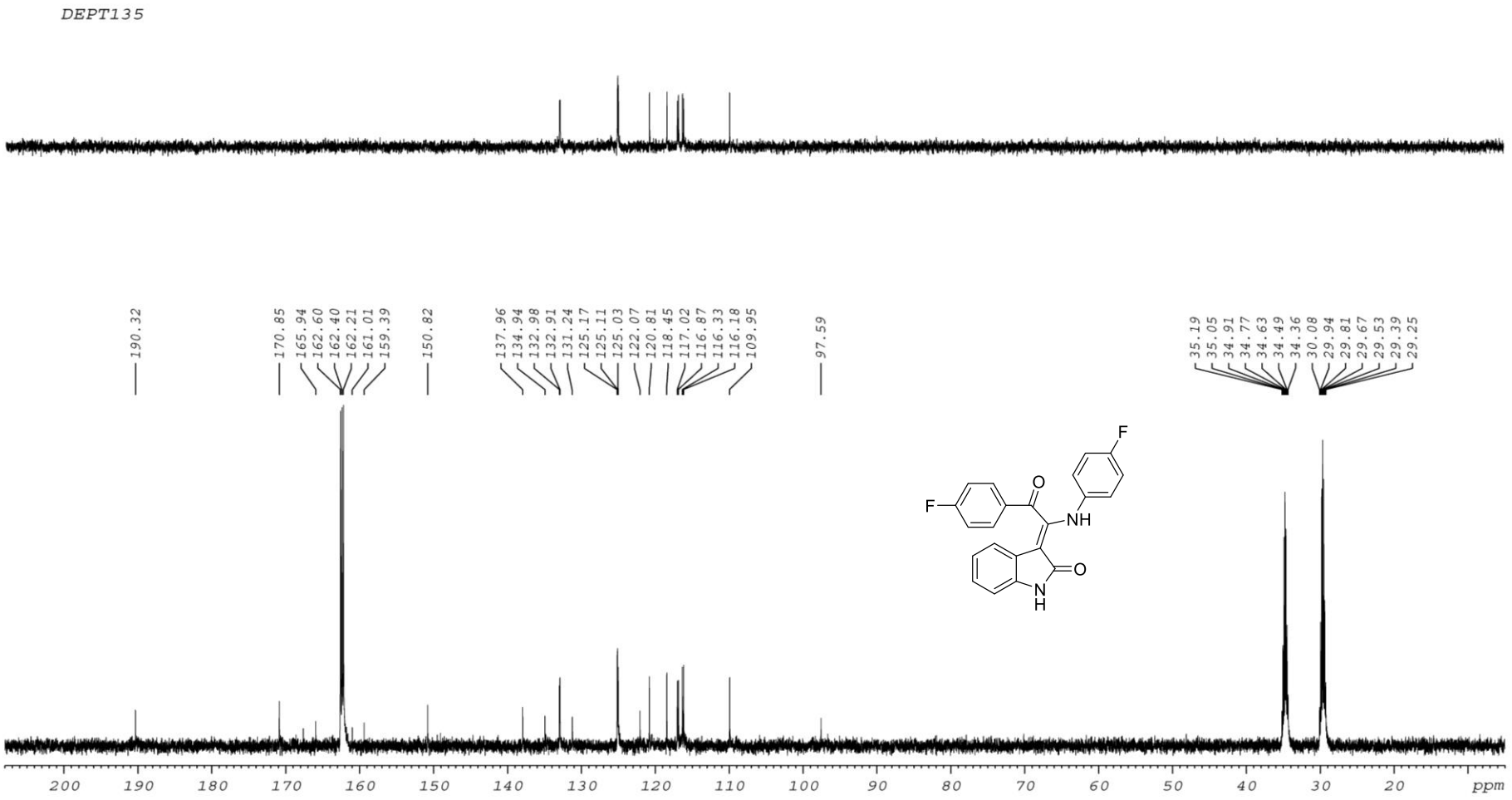


Figure S14. ^{13}C NMR (150 MHz, DMF-d_7) spectra of compound **3af**

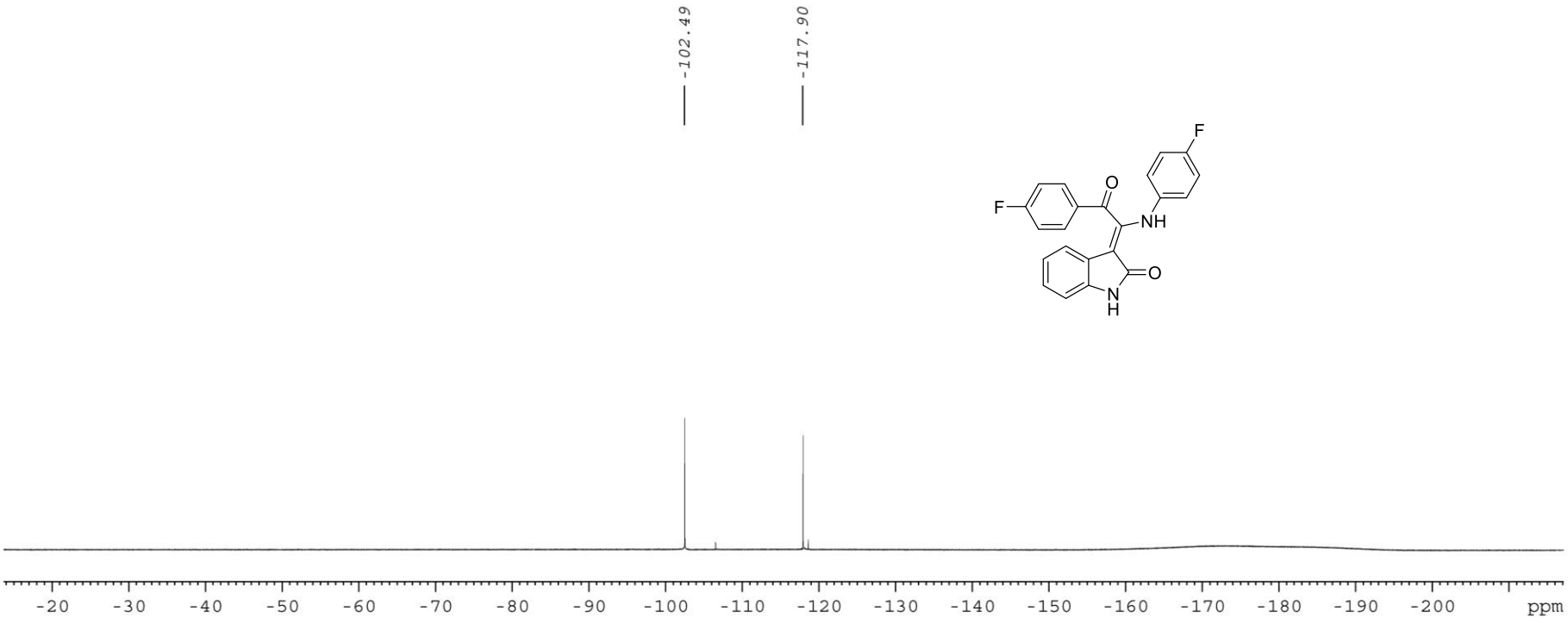


Figure S15. ^{19}F NMR (470 MHz, DMF-d_7) spectra of compound **3af**

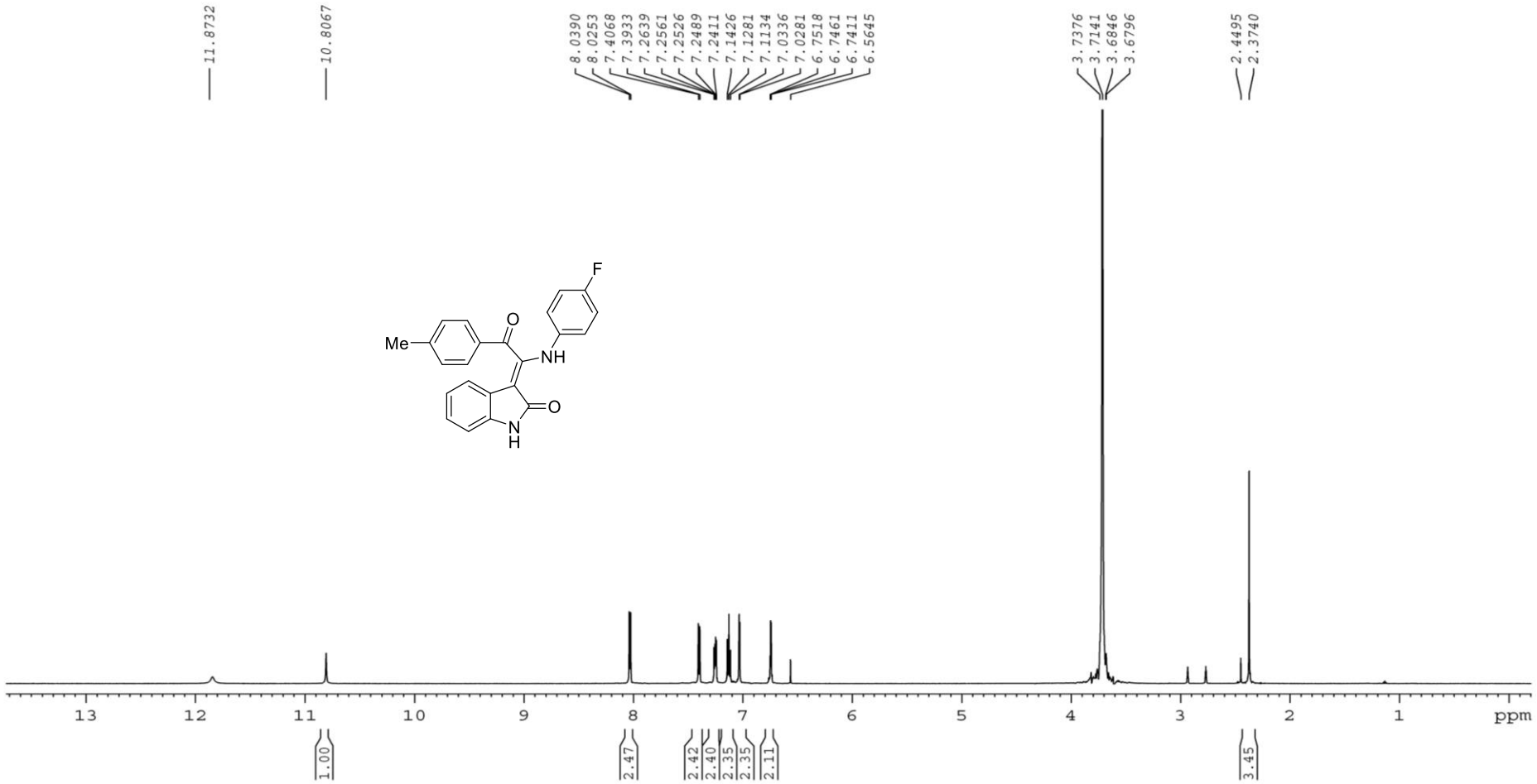


Figure S16. ^{1}H NMR (600 MHz, DMF-d_7) spectra of compound **3ag**

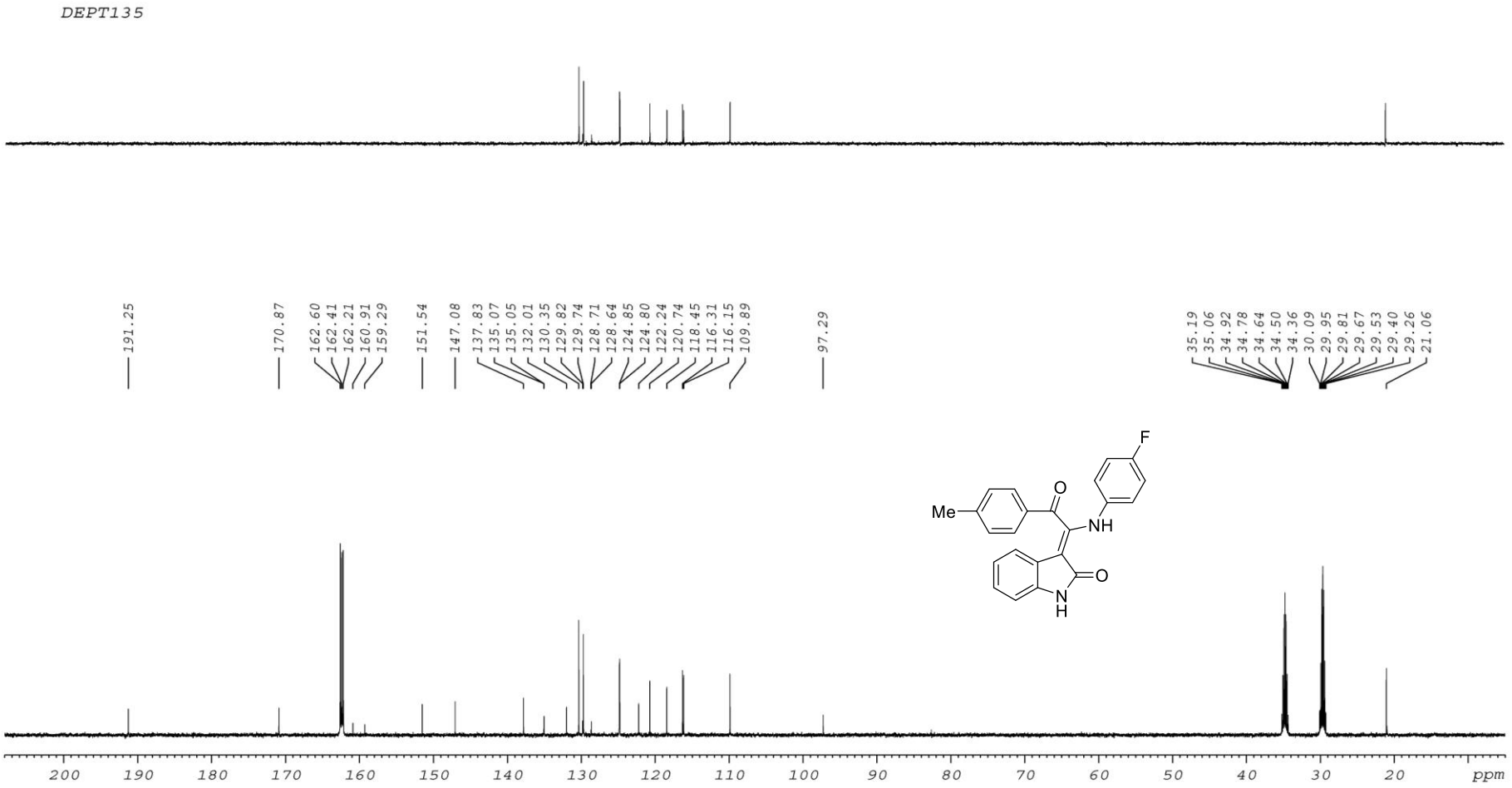


Figure S17. ^{13}C NMR (150 MHz, DMF-d_7) spectra of compound **3ag**

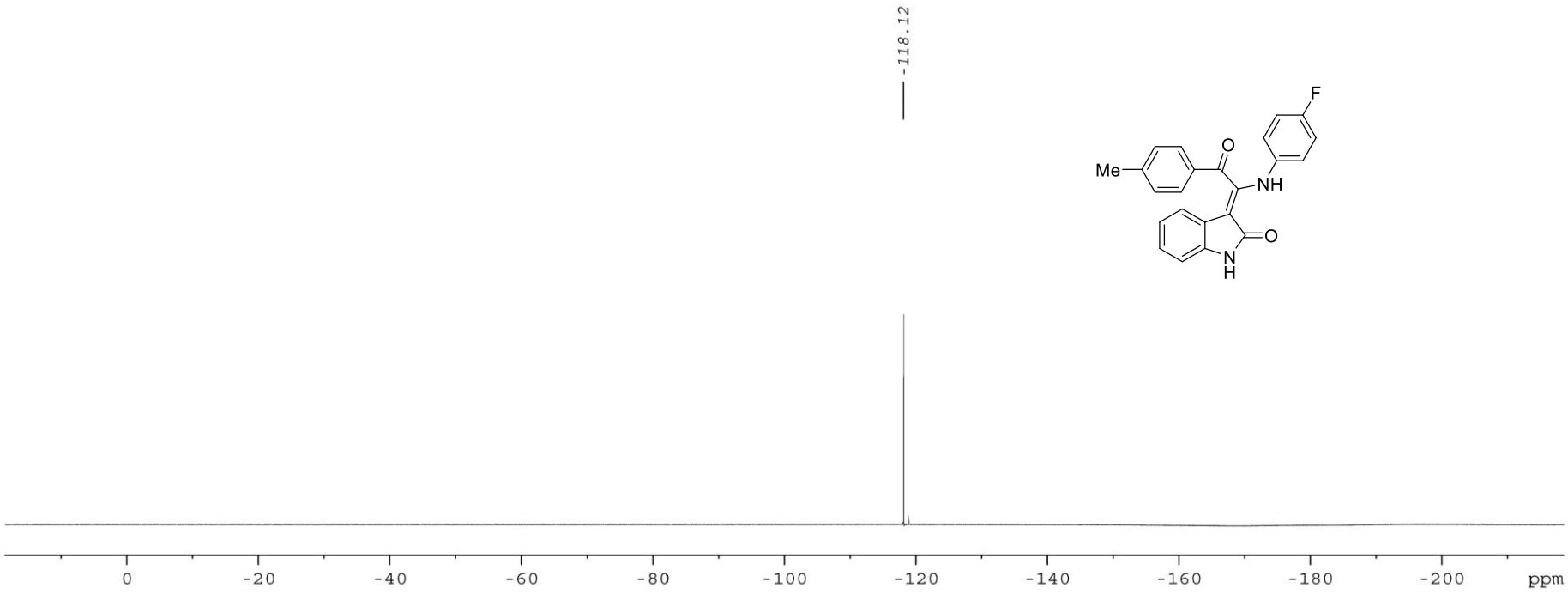


Figure S18. ^{19}F NMR (470 MHz, DMF-d_7) spectra of compound **3ag**

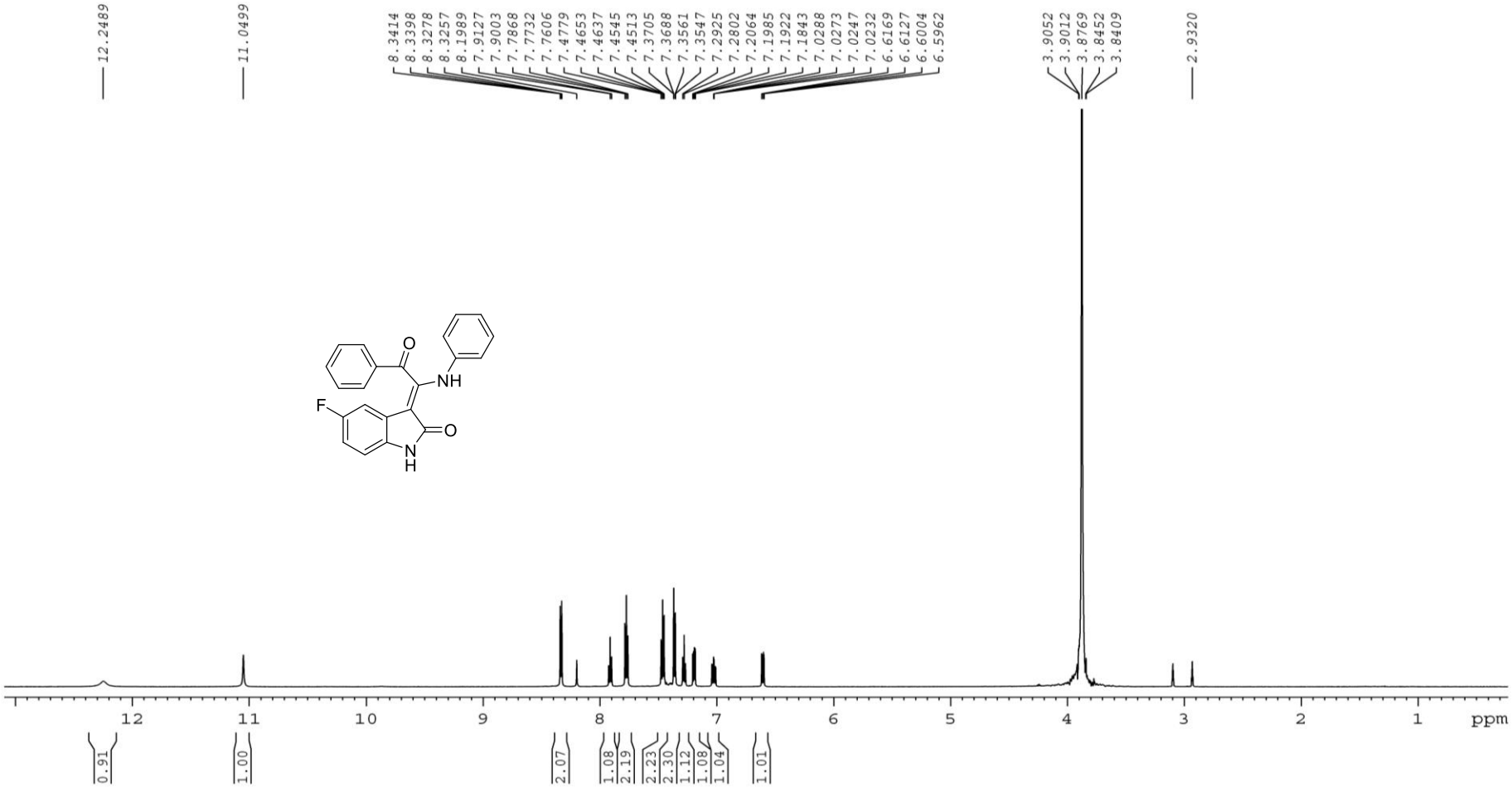


Figure S19. ^{1}H NMR (600 MHz, DMF-d_7) spectra of compound **3ba**

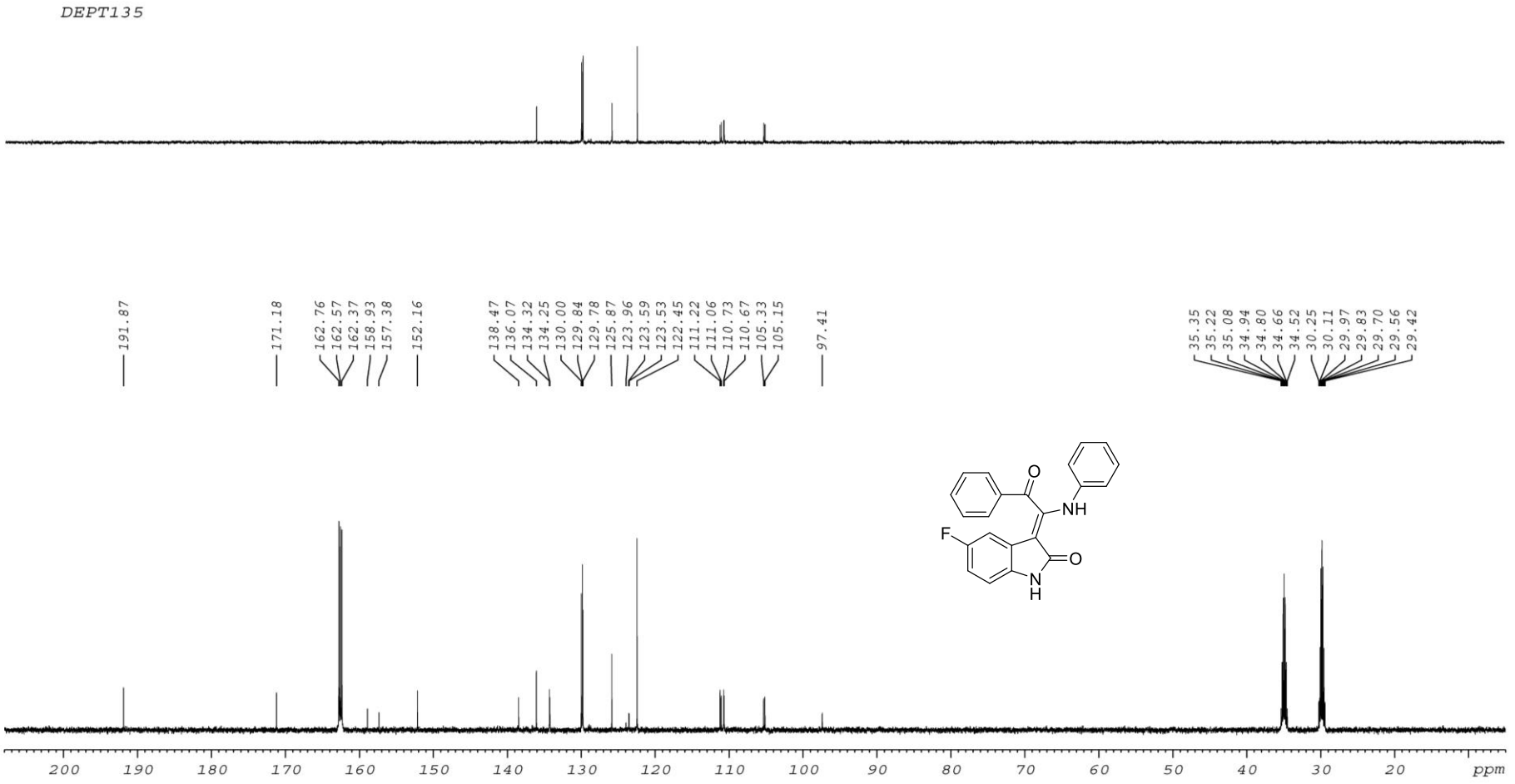


Figure S20. ^{13}C NMR (150 MHz, DMF-d_7) spectra of compound **3ba**

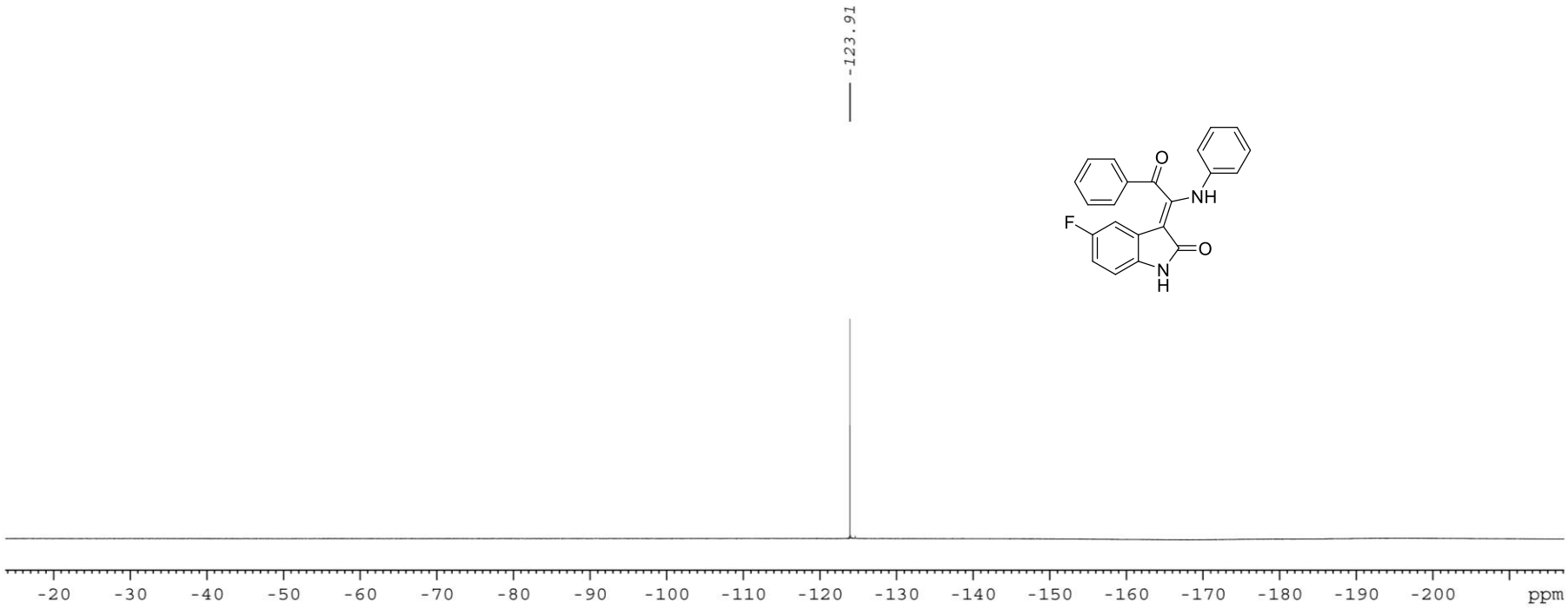


Figure S21. ^{19}F NMR (470 MHz, DMF-d_7) spectra of compound **3ba**

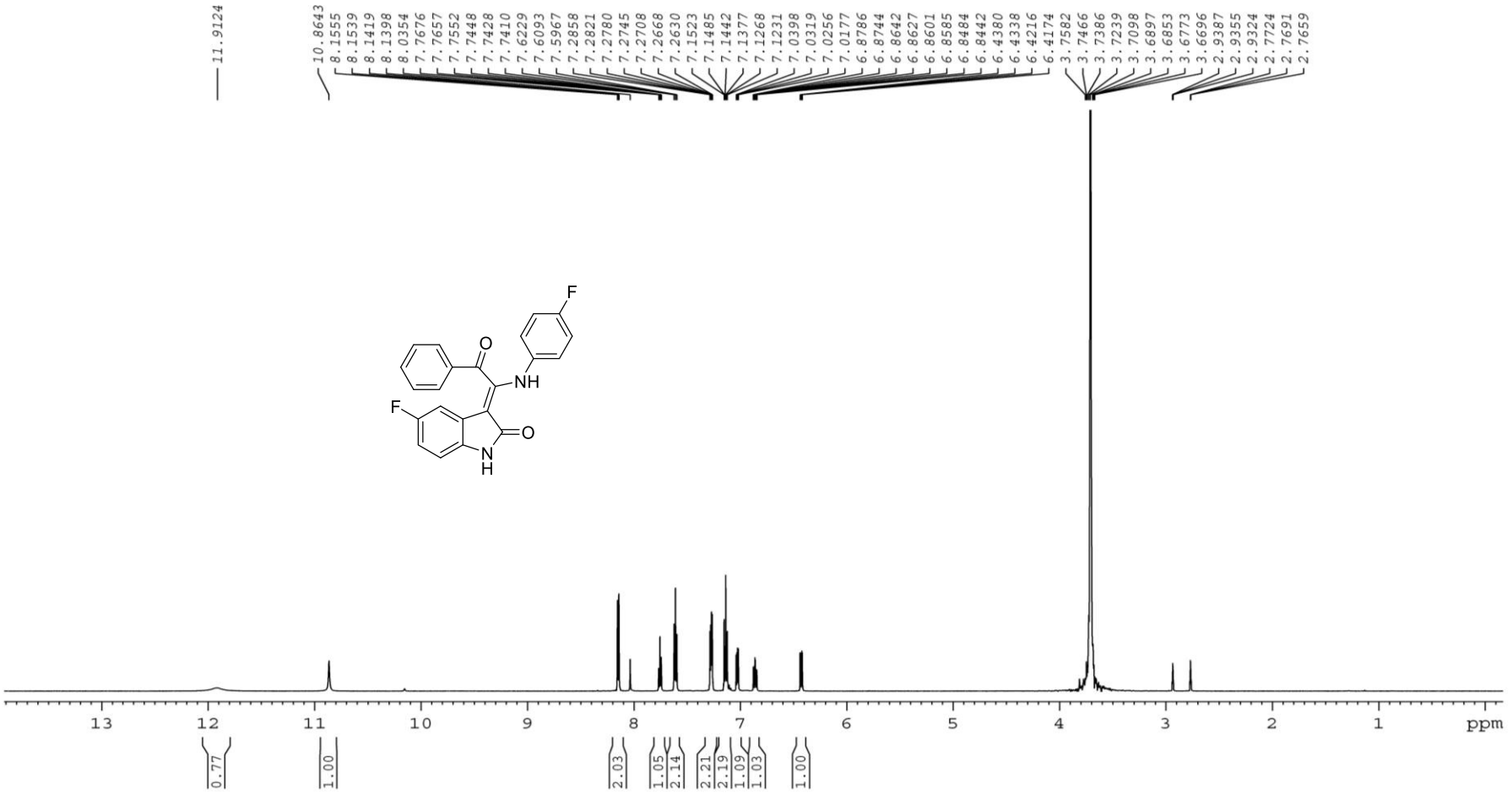


Figure S22. ^{1}H NMR (600 MHz, DMF-d_7) spectra of compound **3bb**

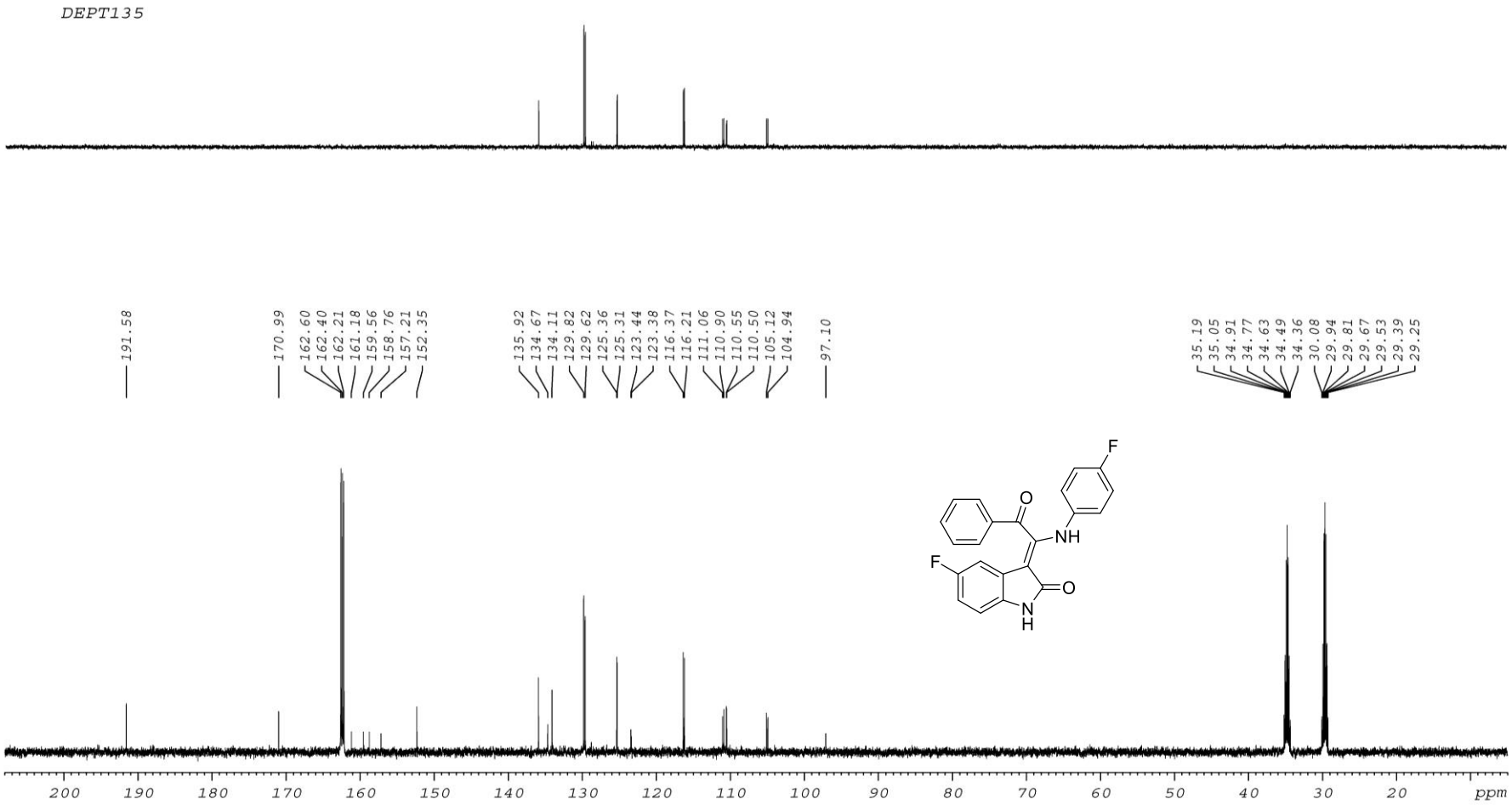


Figure S23. ^{13}C NMR (150 MHz, DMF-d_7) spectra of compound **3bb**

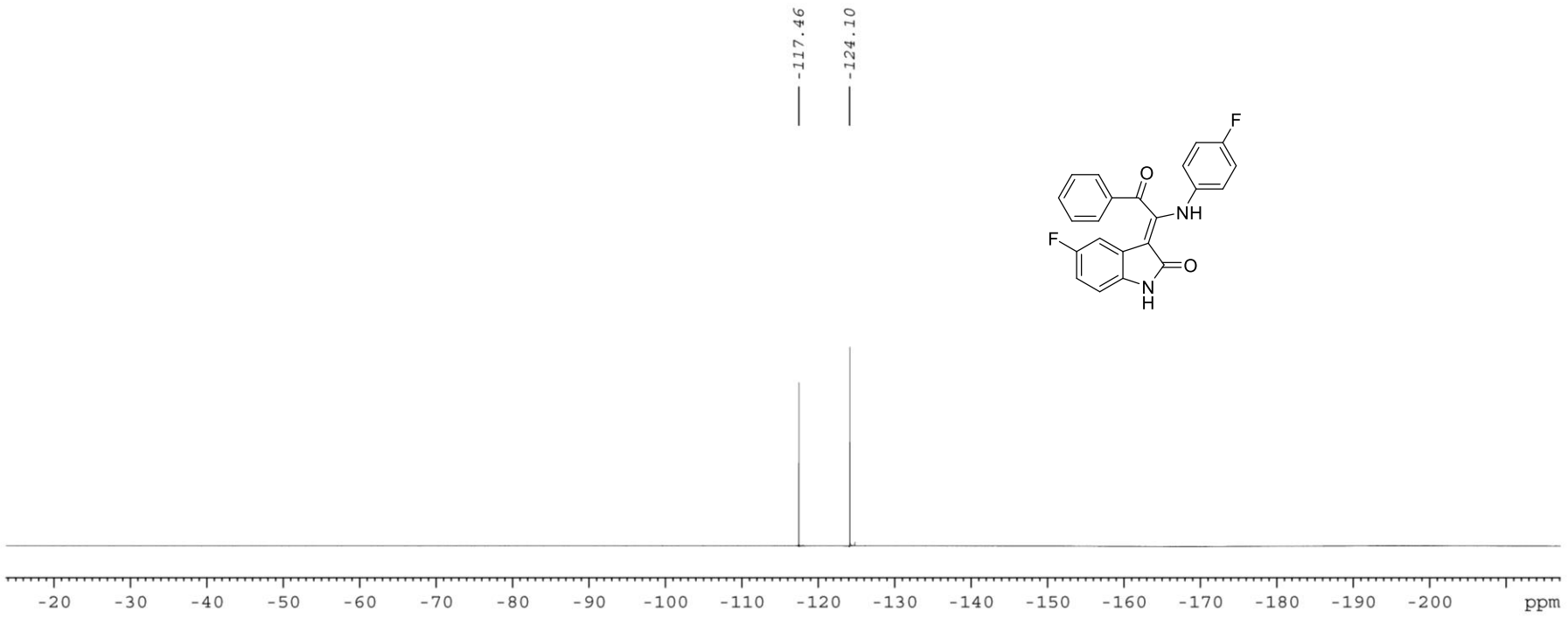


Figure S24. ^{19}F NMR (470 MHz, DMF-d_7) spectra of compound **3bb**

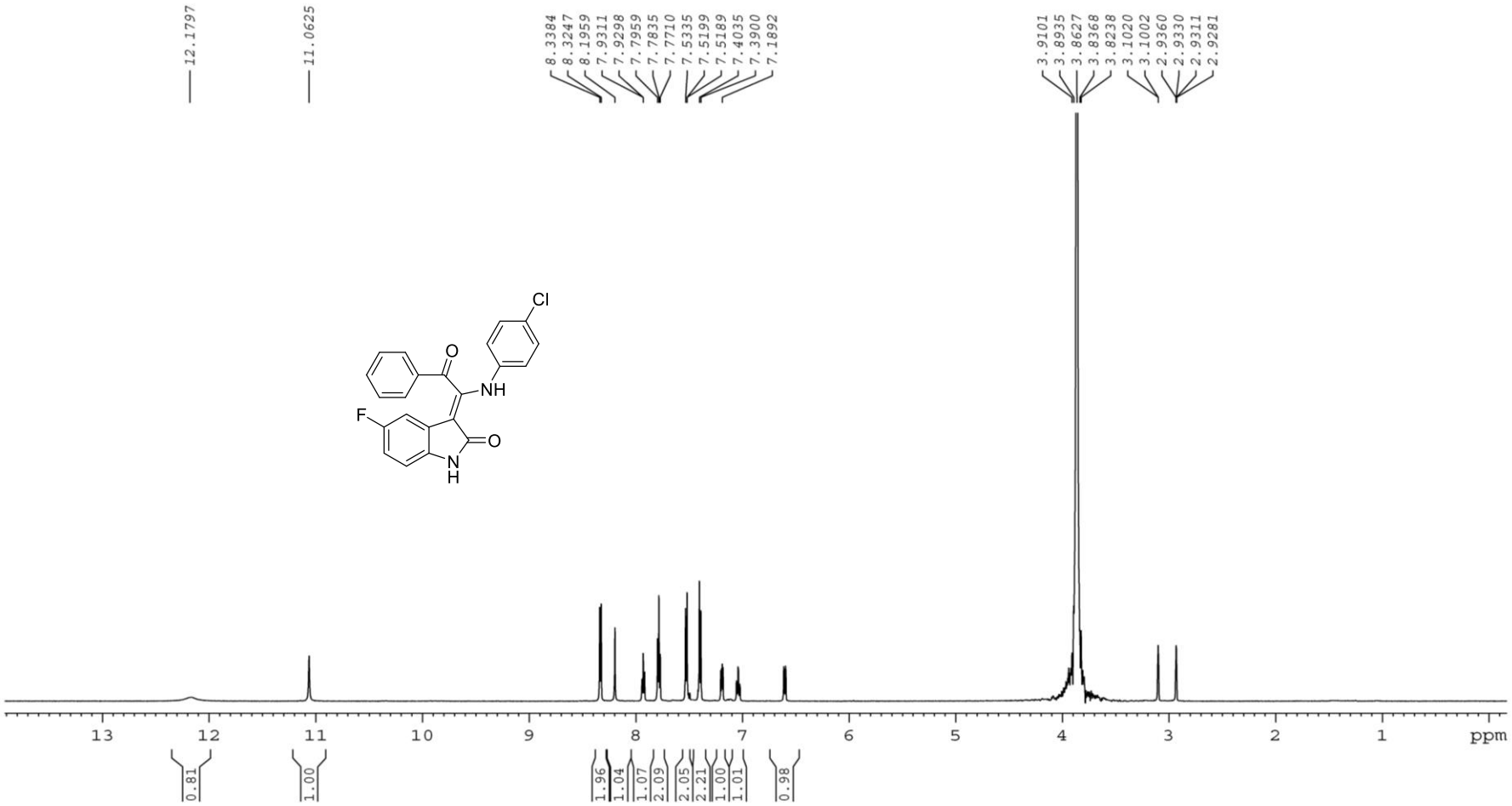


Figure S25. ^{1}H NMR (600 MHz, DMF-d_7) spectra of compound **3bc**

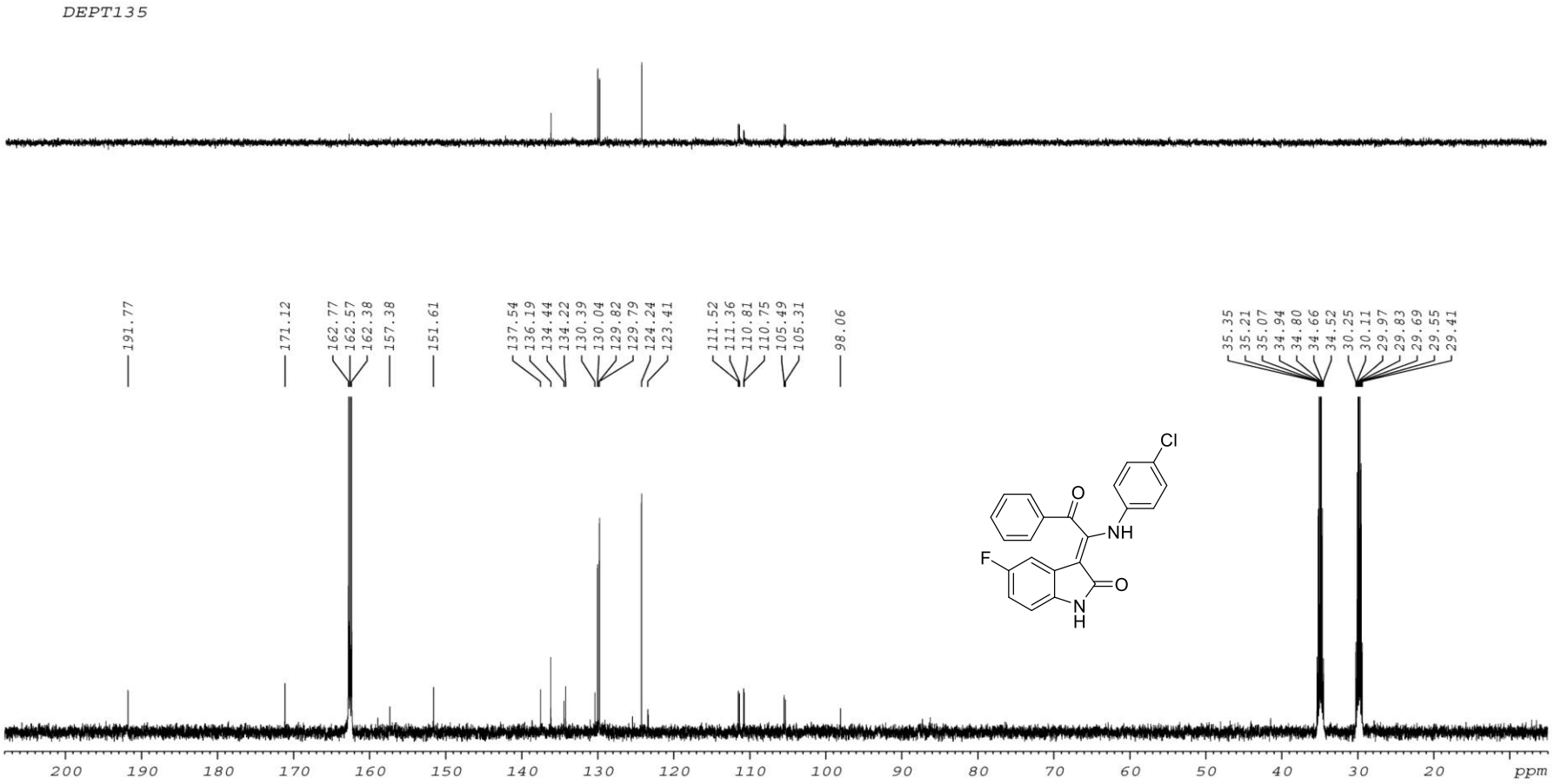


Figure S26. ^{13}C NMR (150 MHz, DMF-d_7) spectra of compound **3bc**

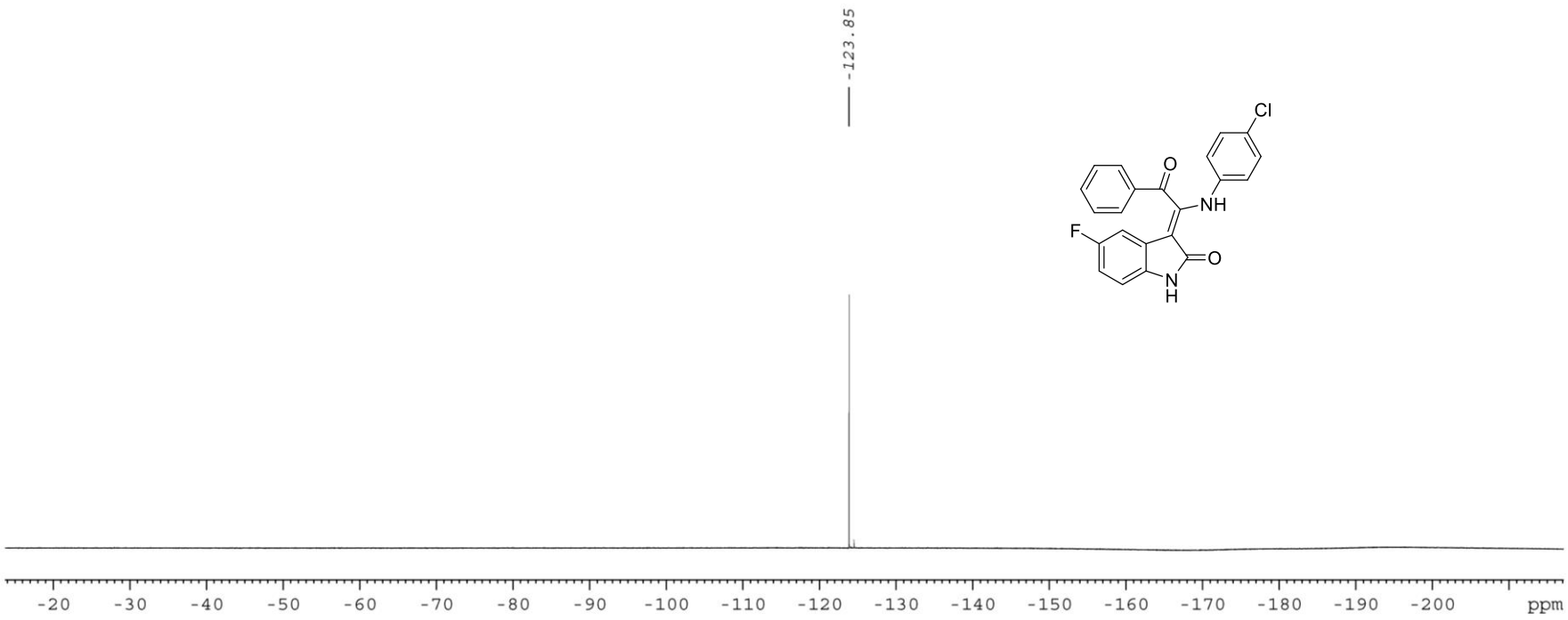


Figure S27. ^{19}F NMR (470 MHz, DMF-d_7) spectra of compound **3bc**

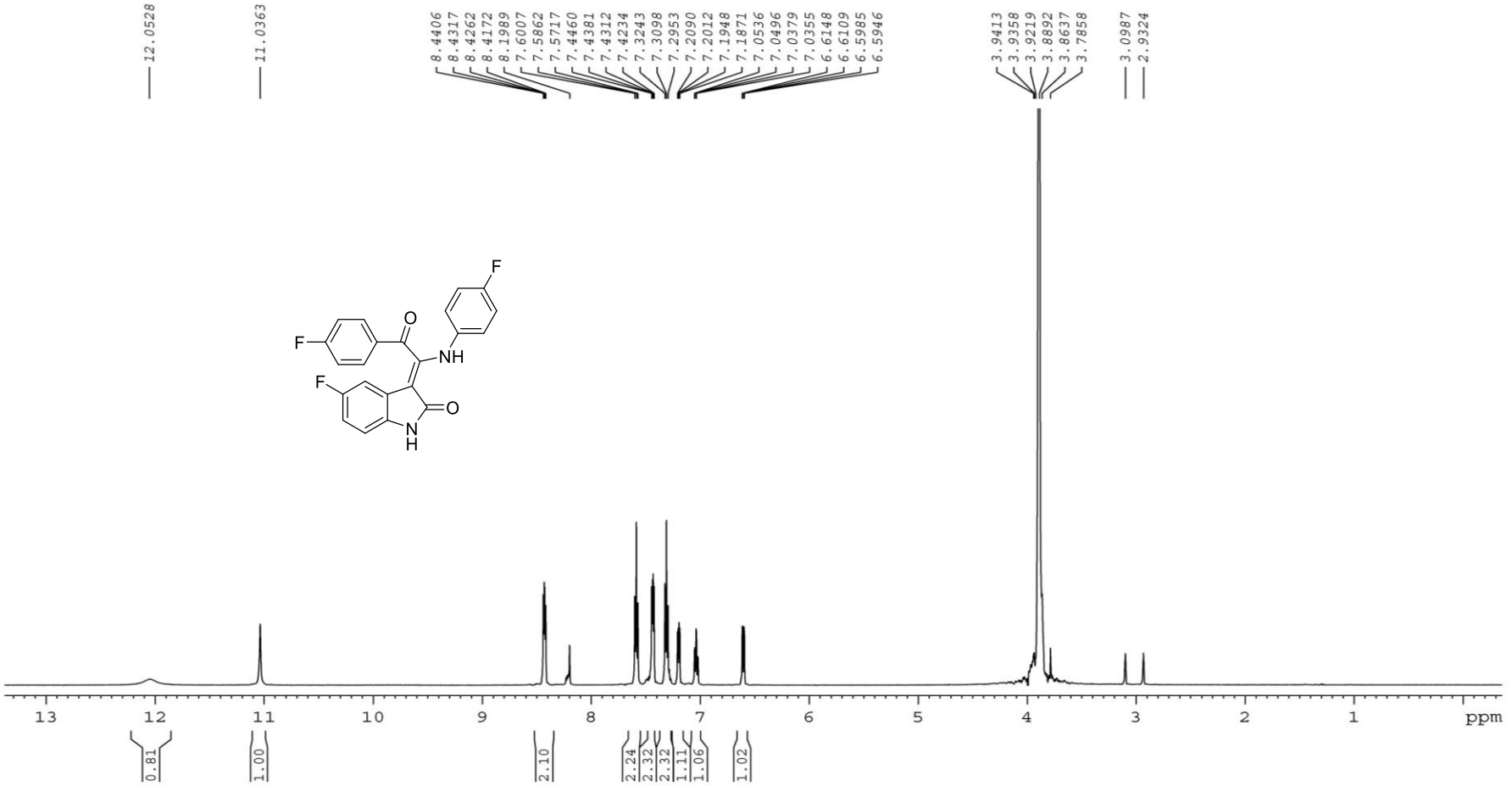


Figure S28. ^{1}H NMR (600 MHz, DMF-d_7) spectra of compound **3bf**

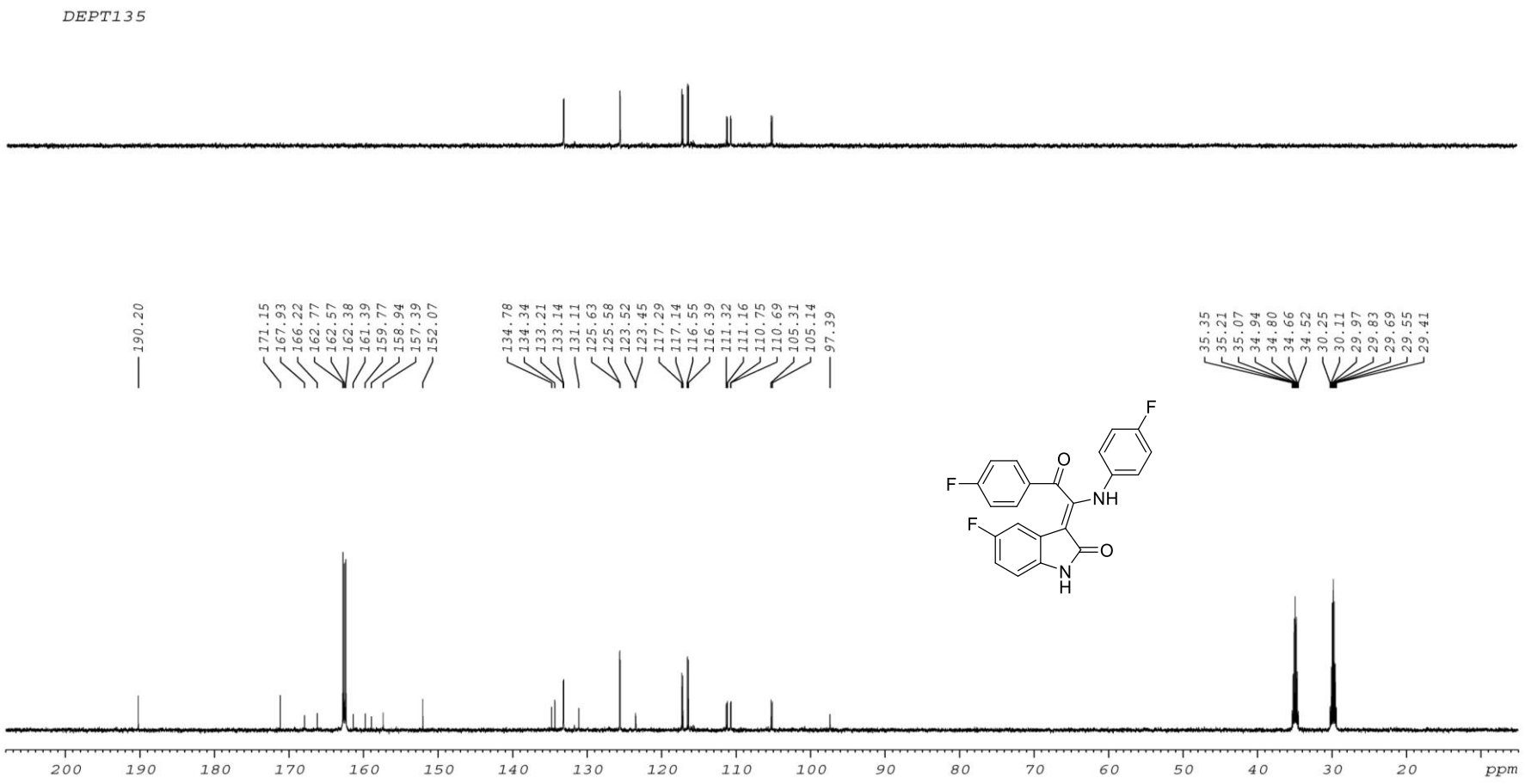


Figure S29. ^{13}C NMR (150 MHz, DMF-d_7) spectra of compound **3bf**

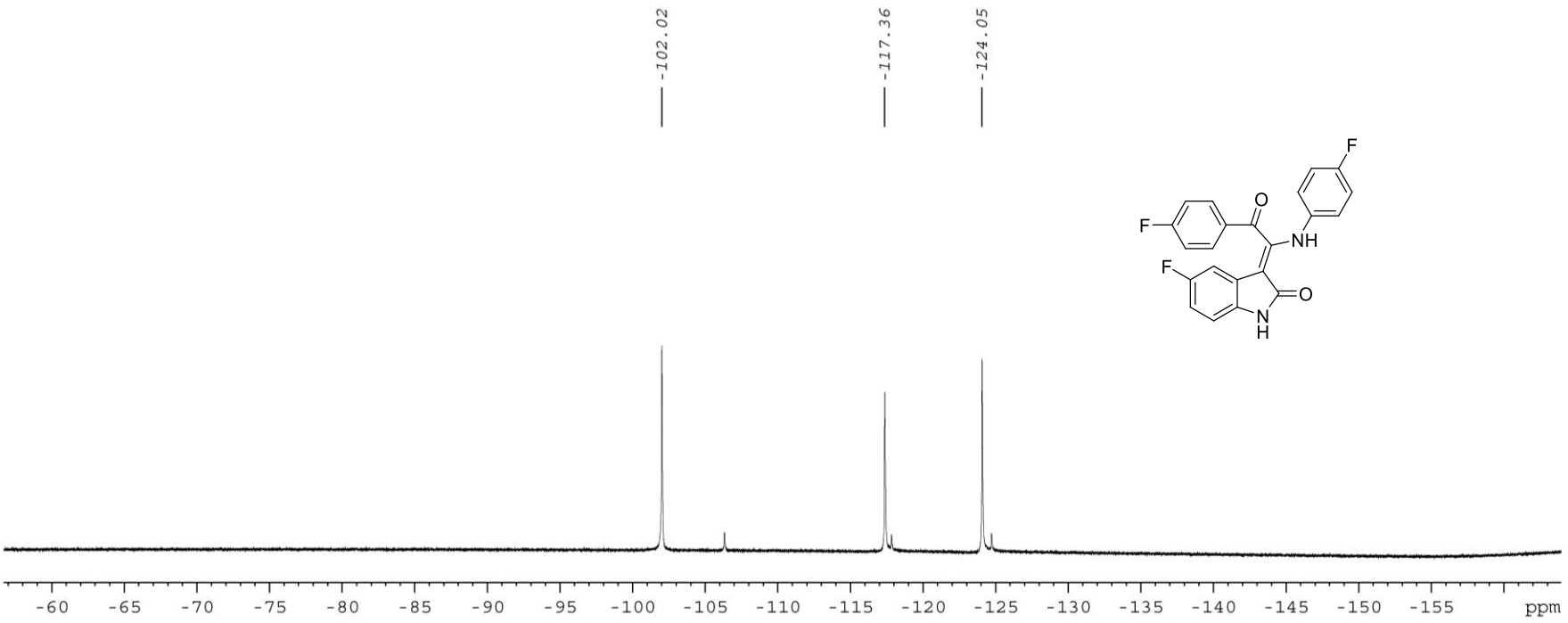


Figure S30. ^{19}F NMR (470 MHz, DMF-d_7) spectra of compound **3bf**

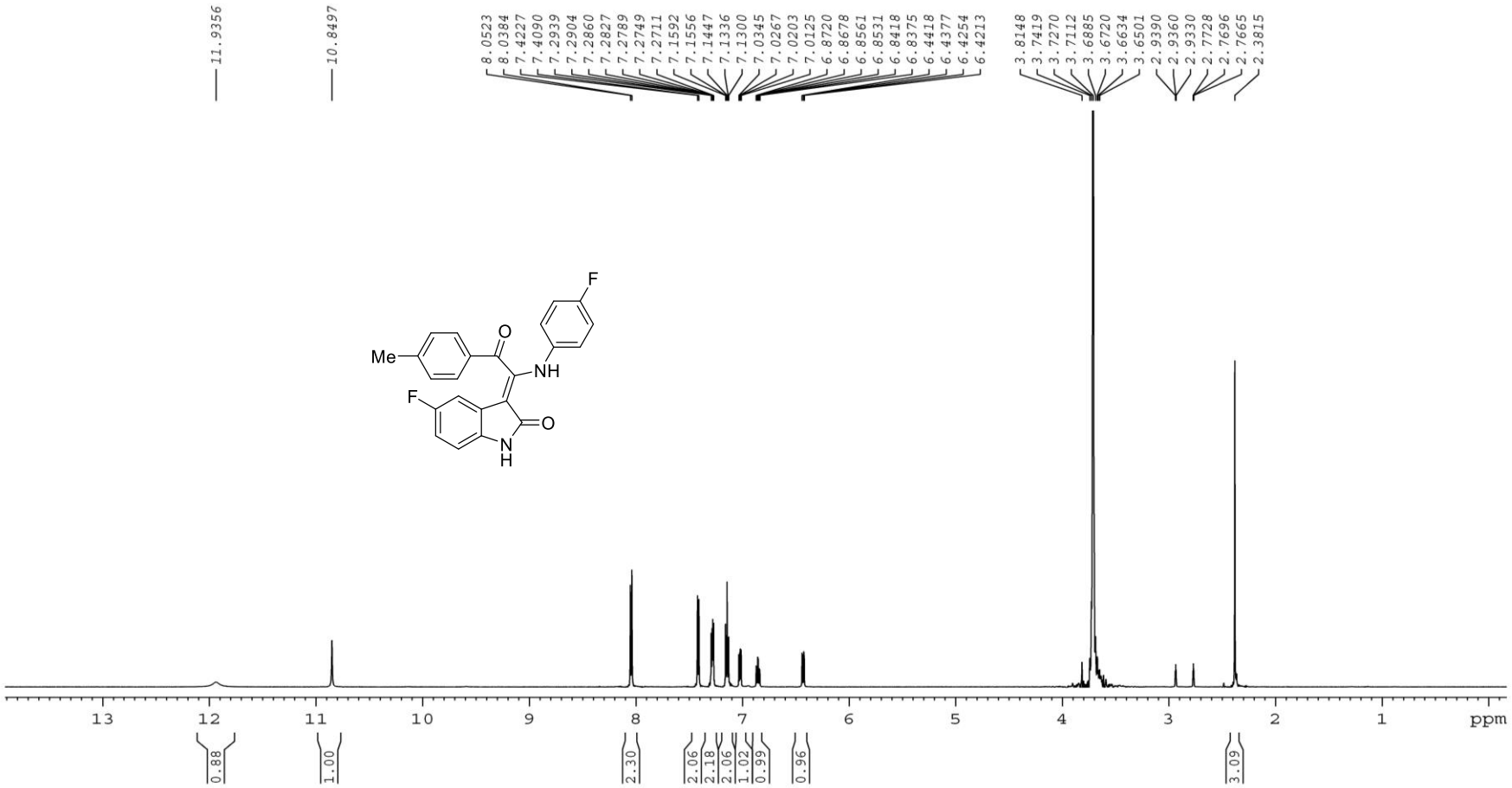


Figure S31. ^{1}H NMR (600 MHz, DMF-d_7) spectra of compound **3bg**

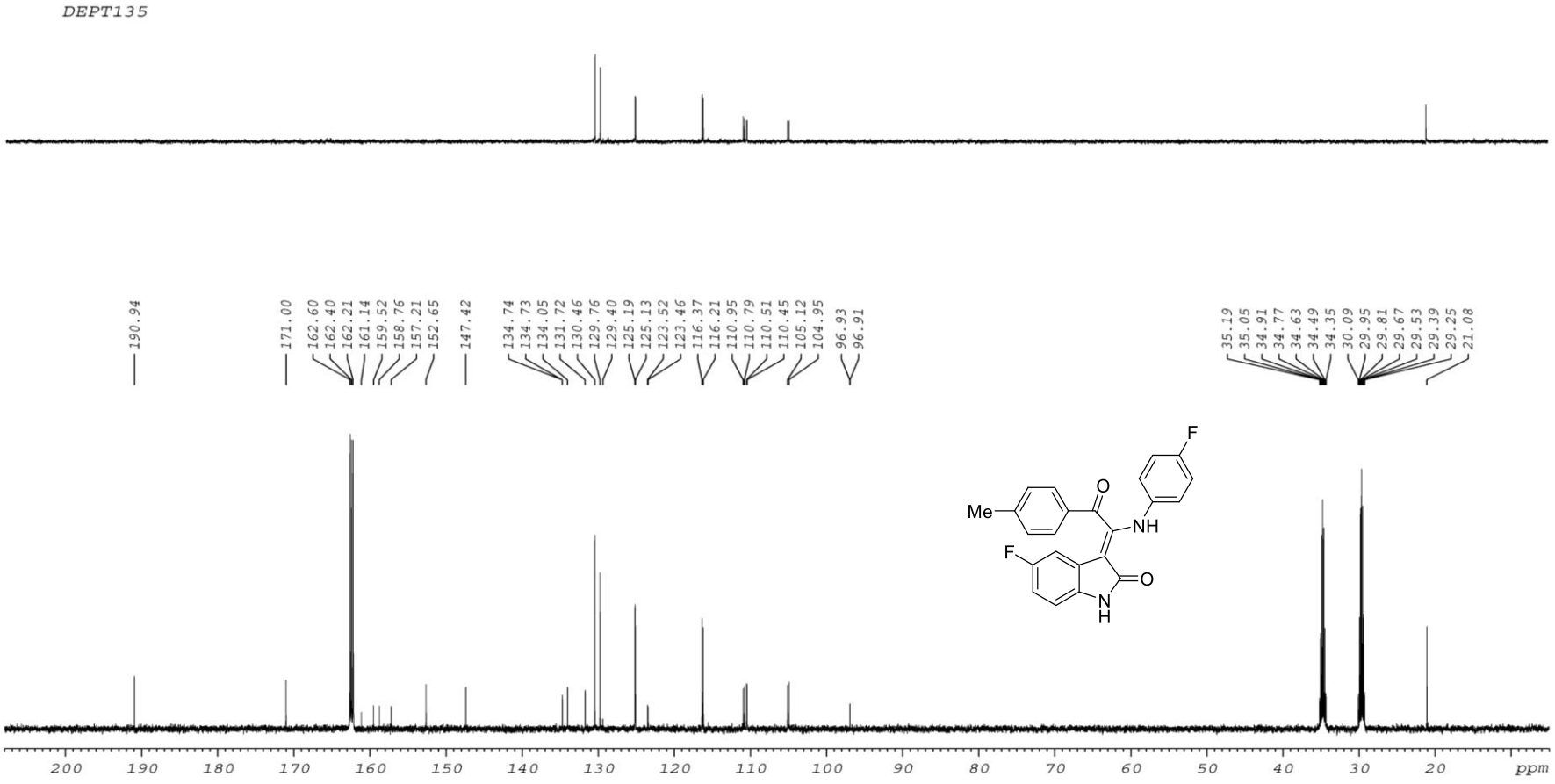


Figure S32. ^{13}C NMR (150 MHz, DMF-d_7) spectra of compound **3bg**

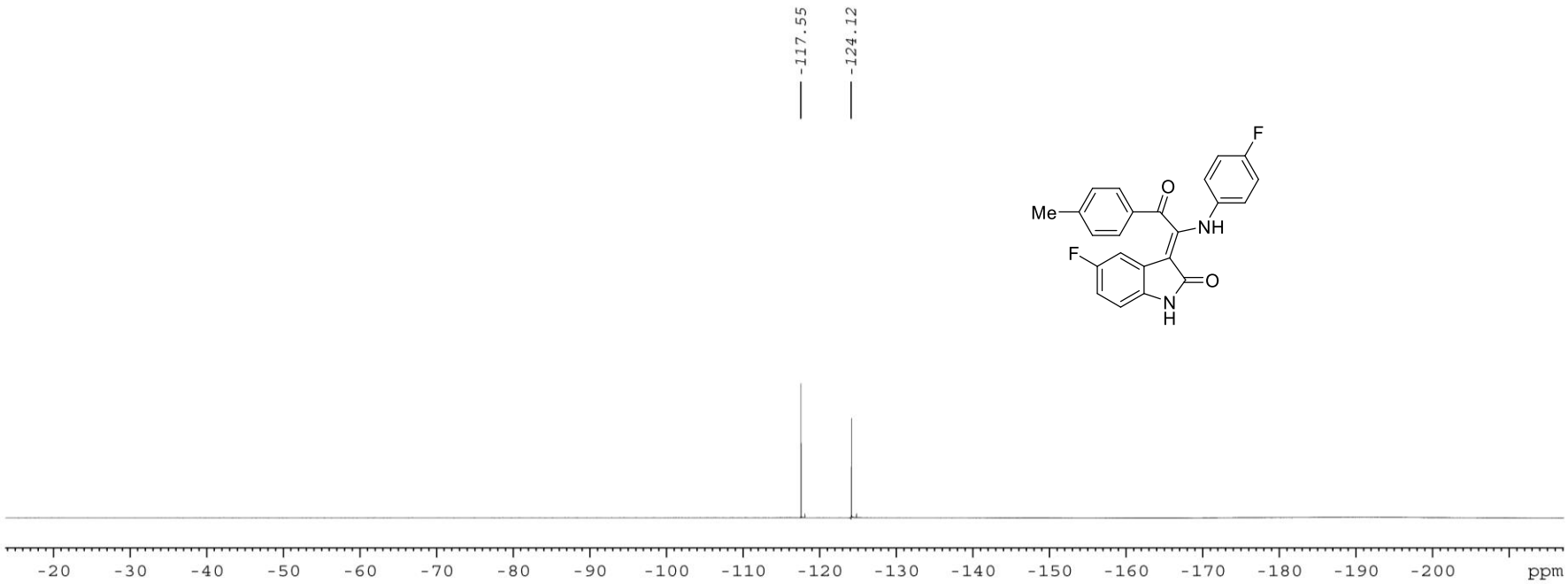


Figure S33. ^{19}F NMR (470 MHz, DMF-d_7) spectra of compound **3bg**

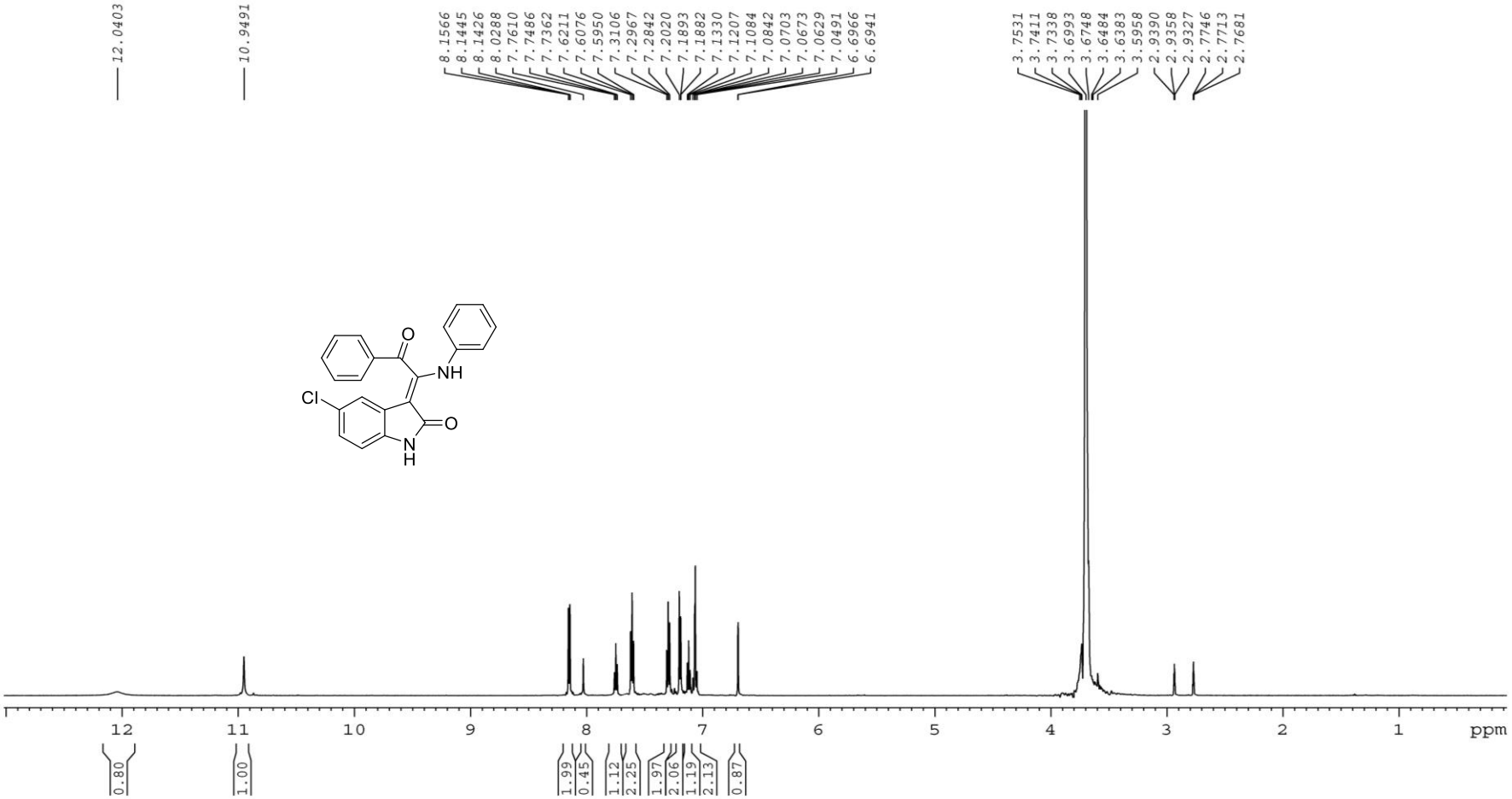


Figure S34. ^{1}H NMR (600 MHz, DMF-d_7) spectra of compound **3ca**

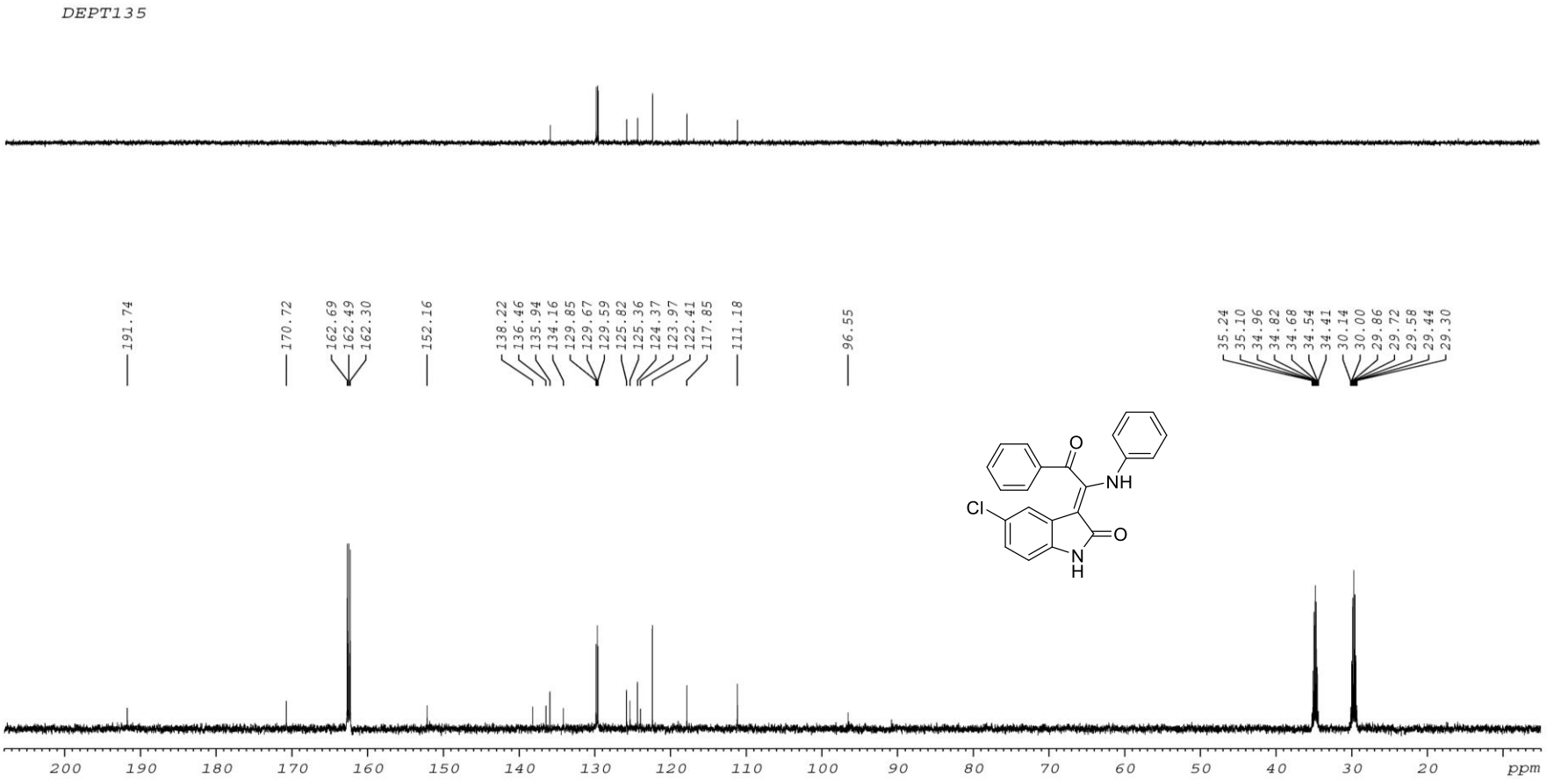


Figure S35. ^{13}C NMR (150 MHz, DMF-d_7) spectra of compound **3ca**

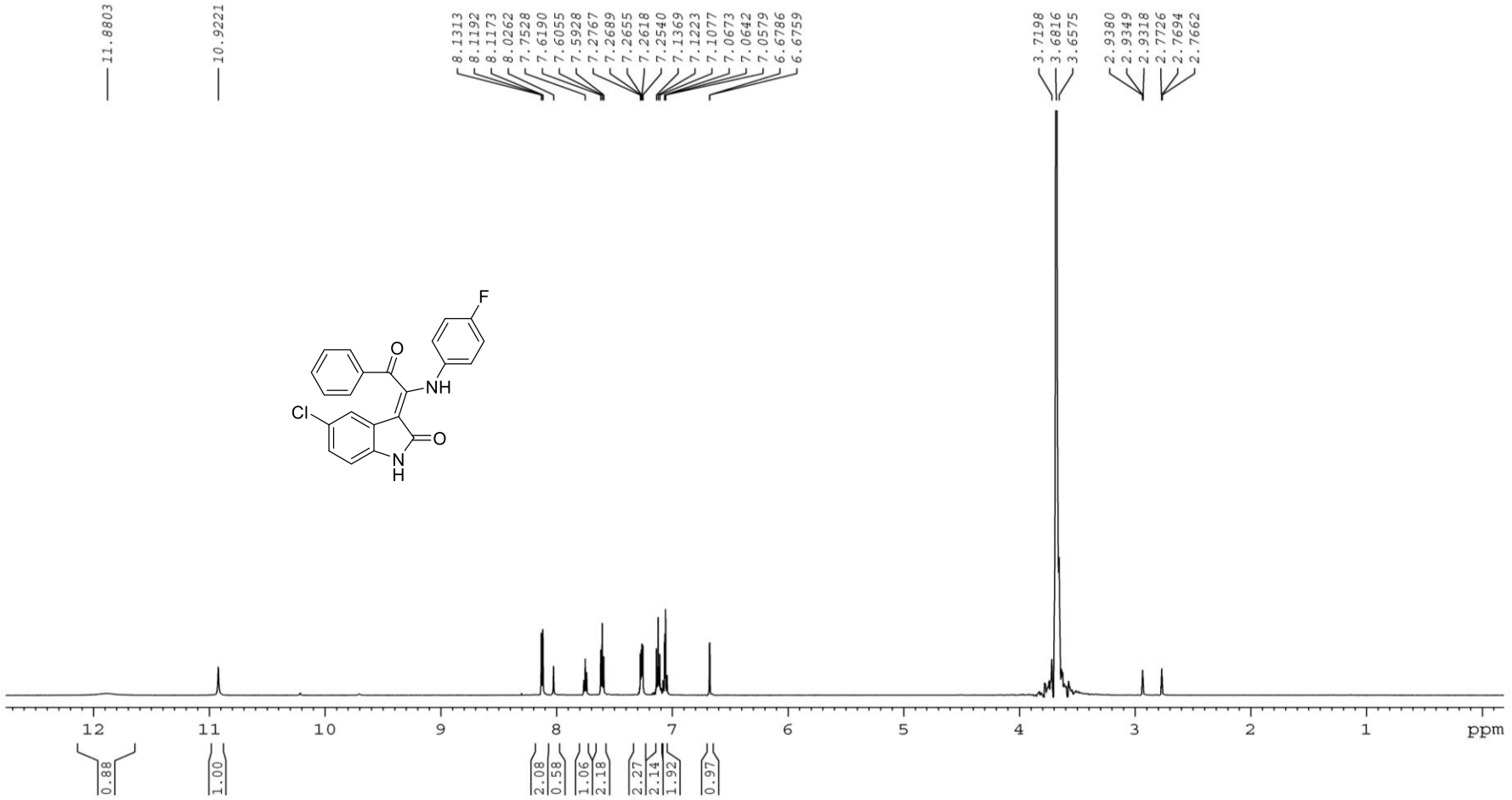


Figure S36. ^{1}H NMR (600 MHz, DMF-d_7) spectra of compound **3cb**

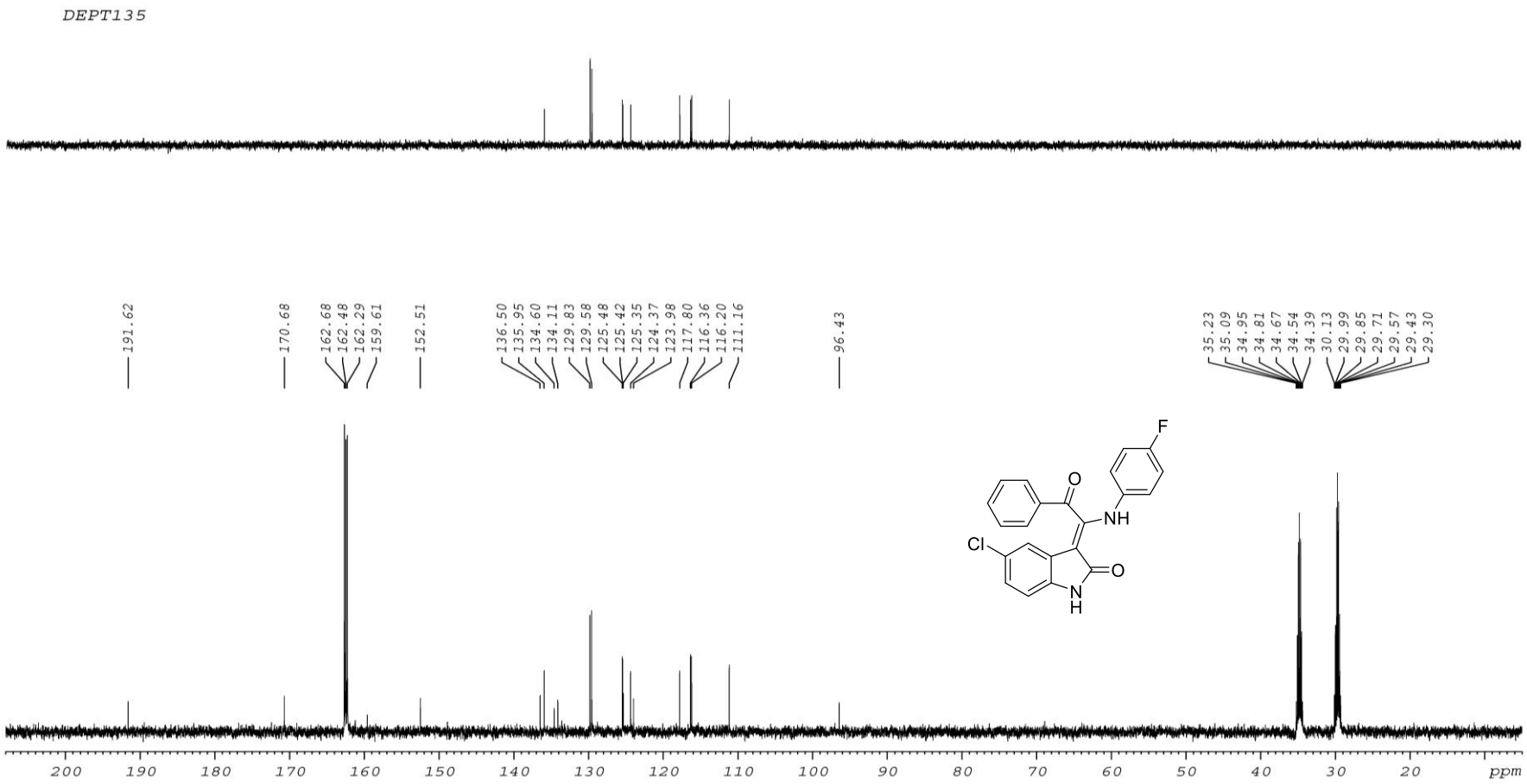


Figure S37. ^{13}C NMR (150 MHz, DMF-d_7) spectra of compound **3cb**

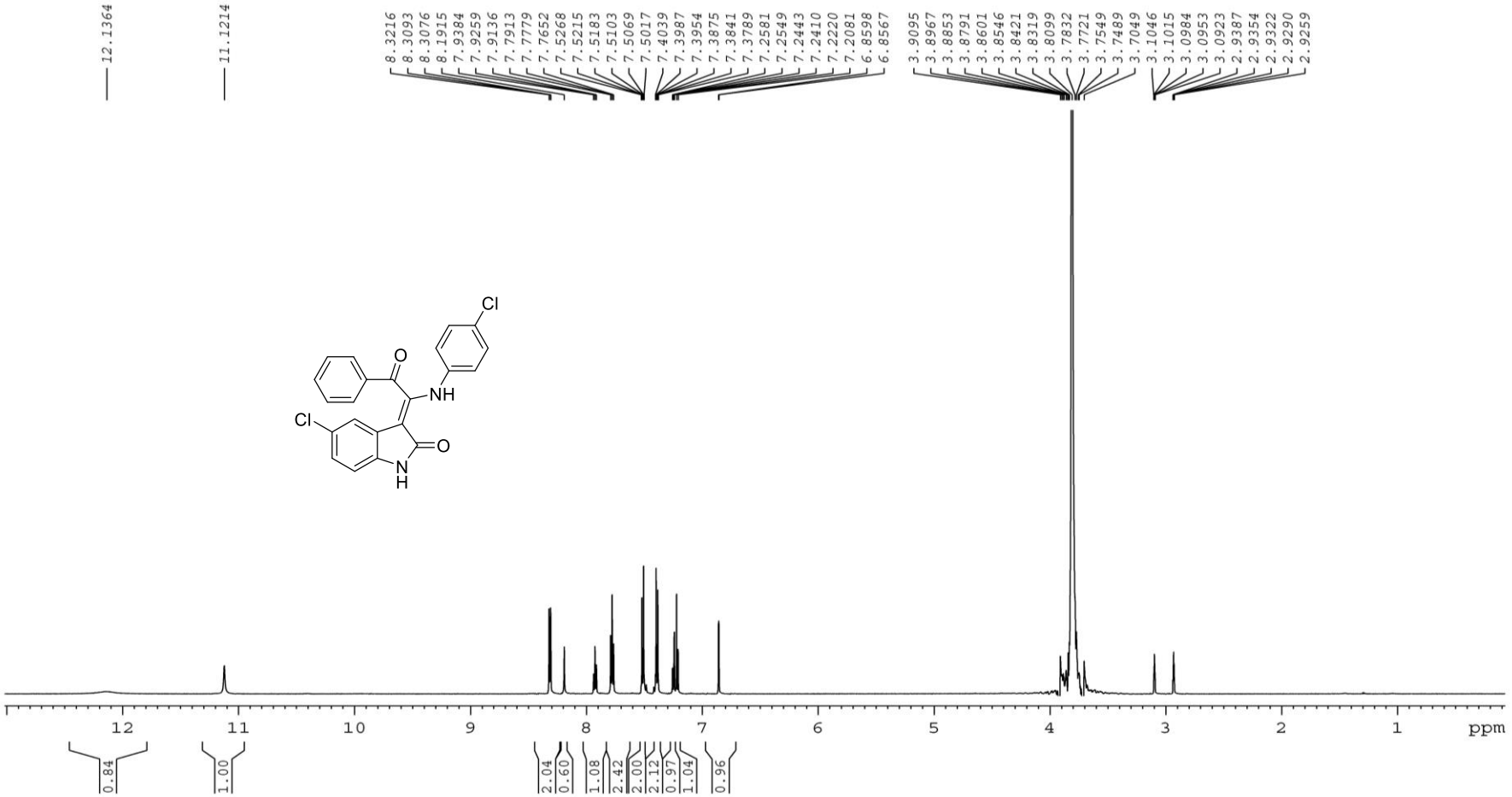


Figure S38. ^{1}H NMR (600 MHz, DMF-d_7) spectra of compound **3cc**

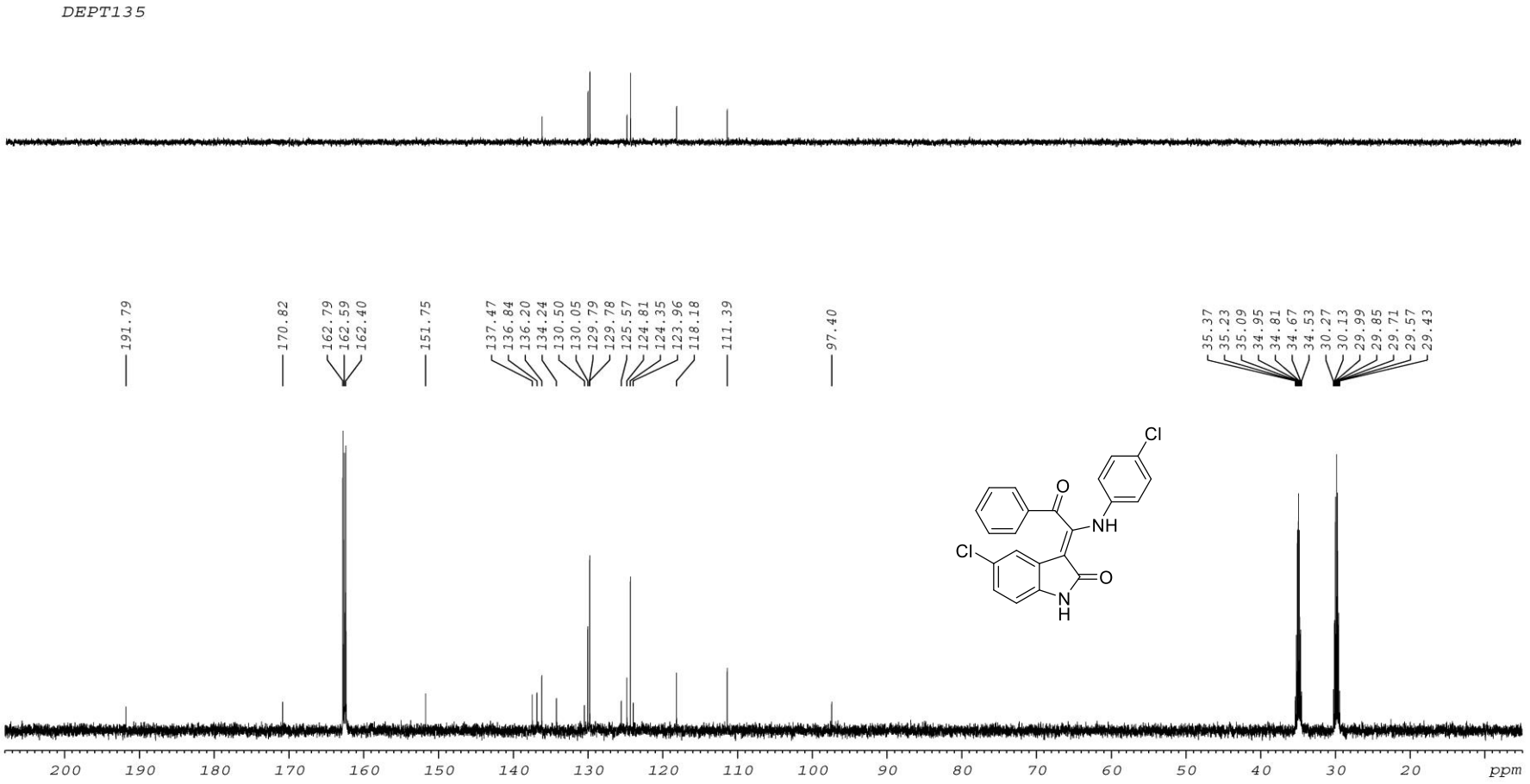


Figure S39. ^{13}C NMR (150 MHz, DMF-d_7) spectra of compound **3cc**

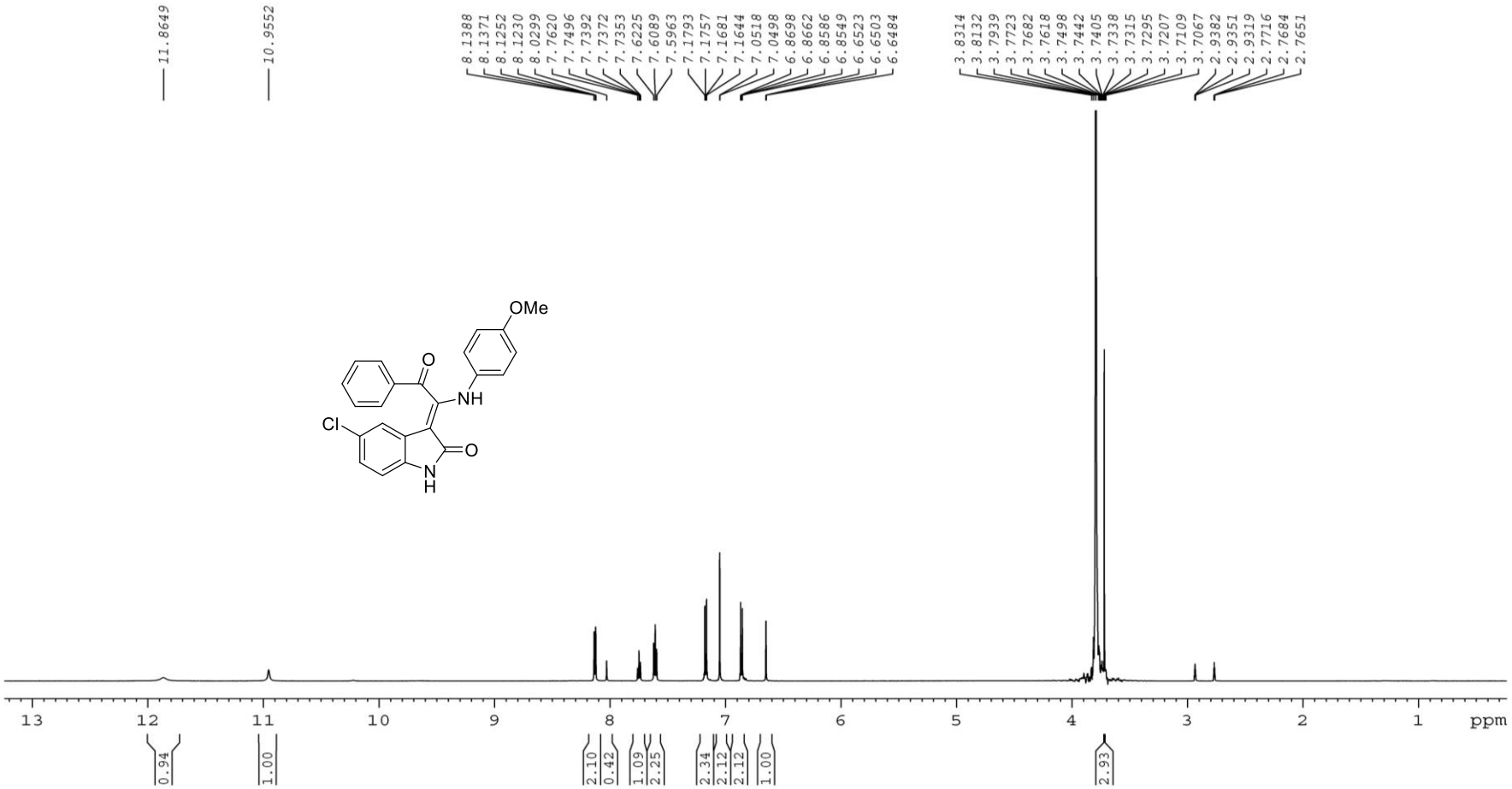


Figure S40. ^{1}H NMR (600 MHz, DMF-d_7) spectra of compound **3ce**

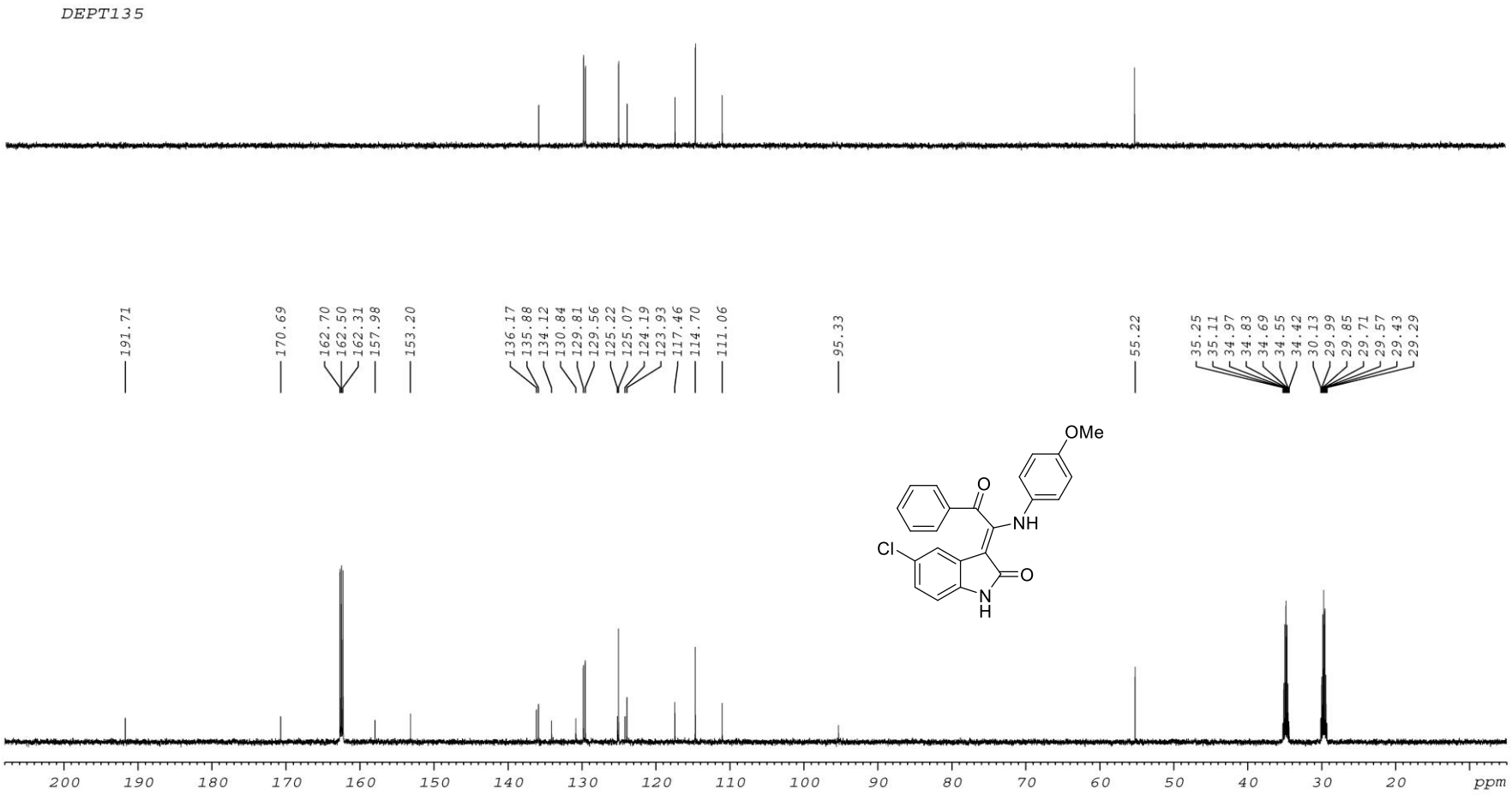


Figure S41. ^{13}C NMR (150 MHz, DMF-d_7) spectra of compound **3ce**

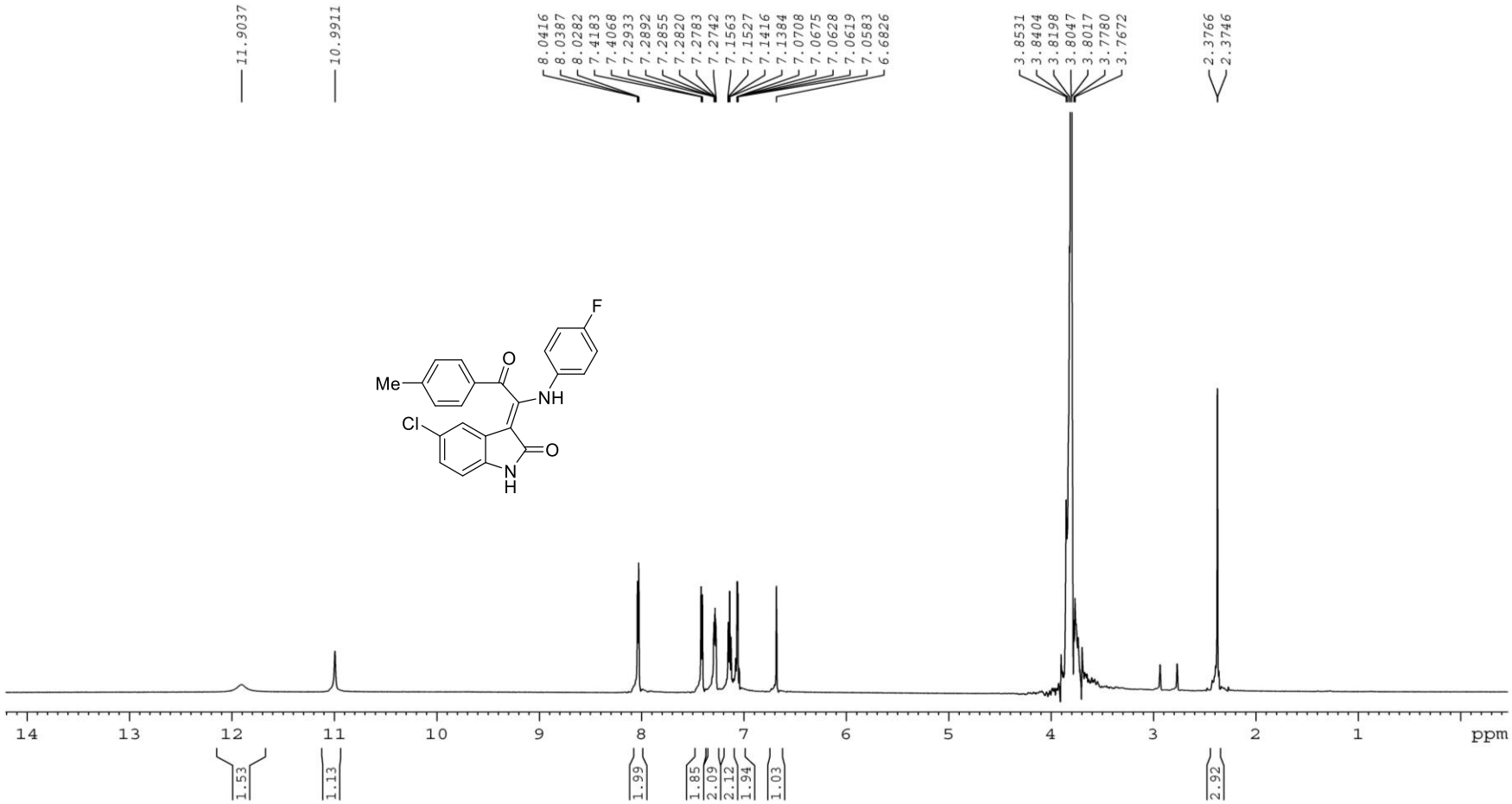


Figure S42. ^{1}H NMR (600 MHz, DMF-d_7) spectra of compound **3cg**

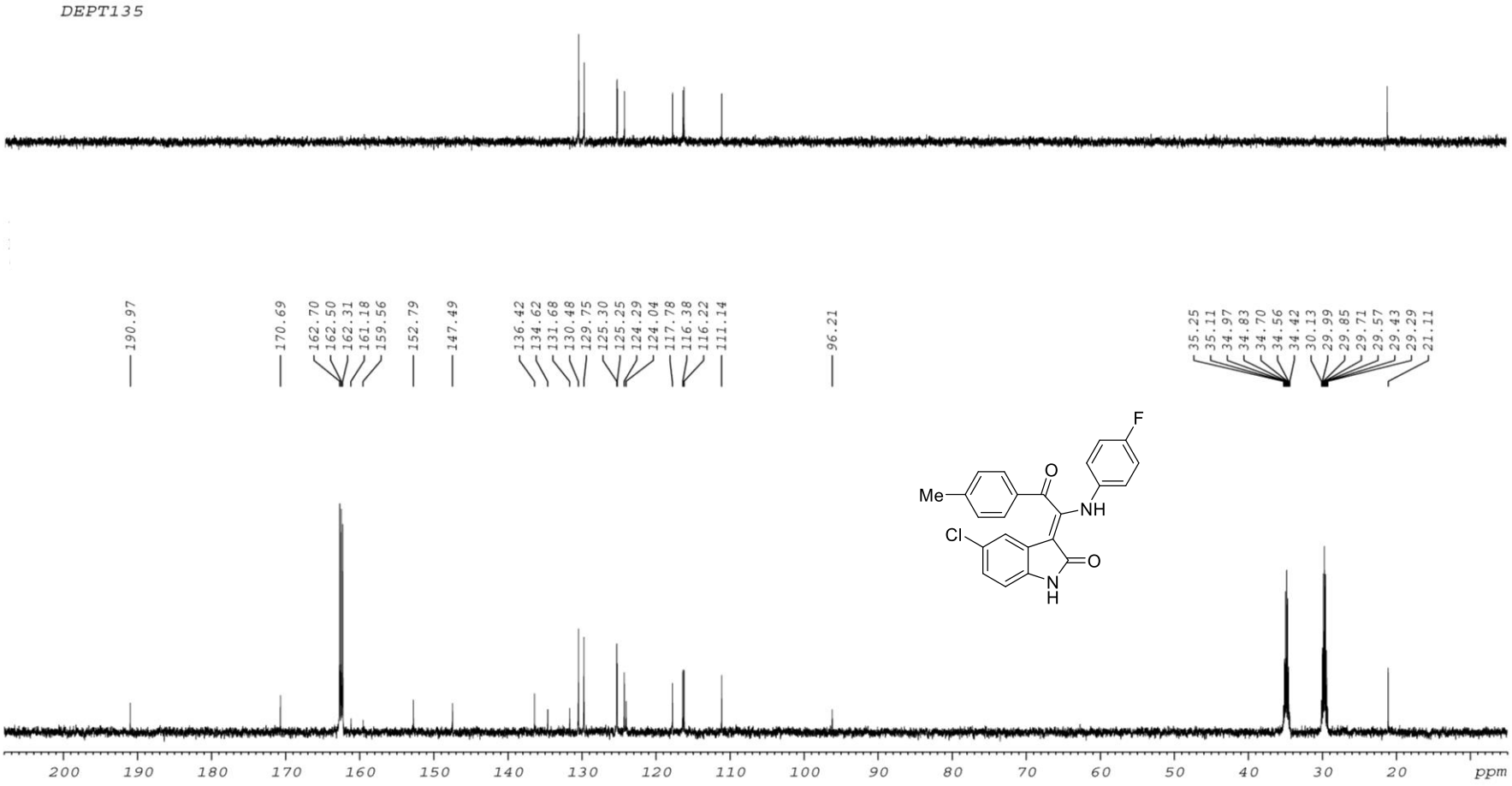


Figure S43. ^{13}C NMR (150 MHz, DMF-d_7) spectra of compound **3cg**

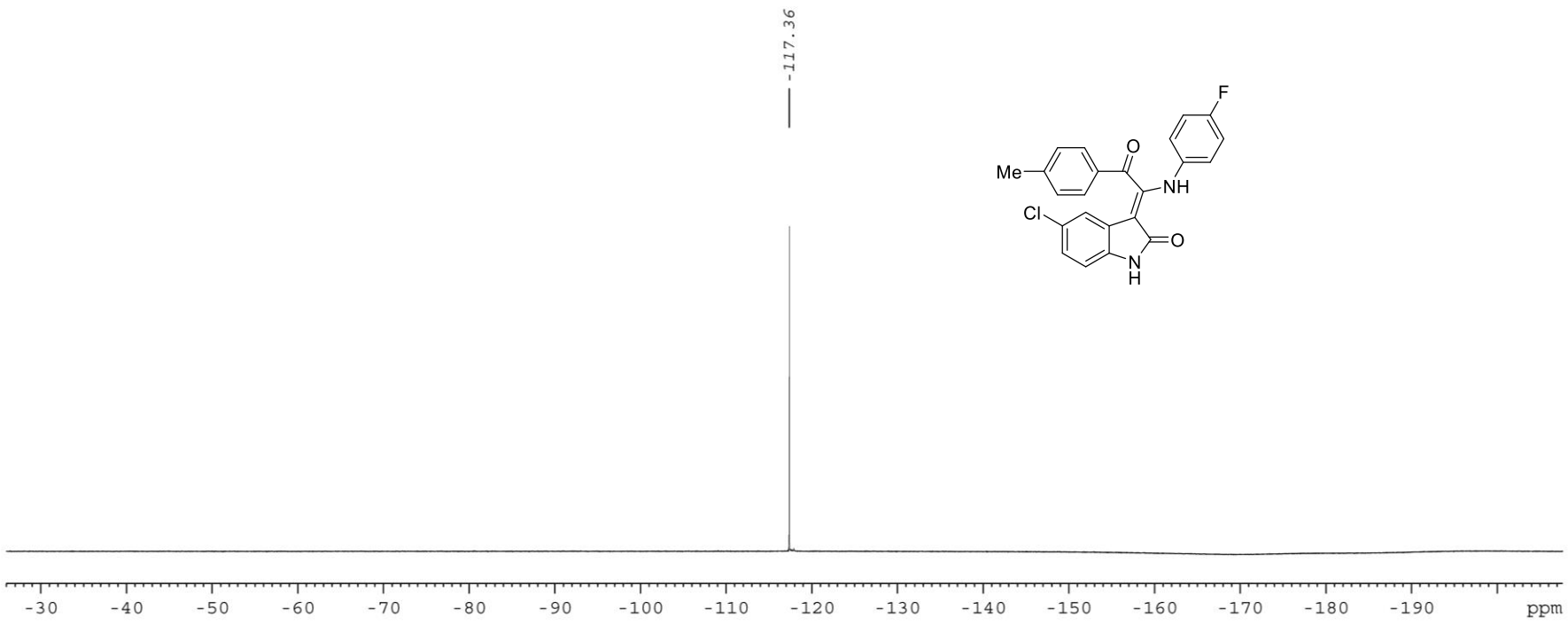


Figure S44. ^{19}F NMR (470 MHz, DMF-d_7) spectra of compound **3cg**

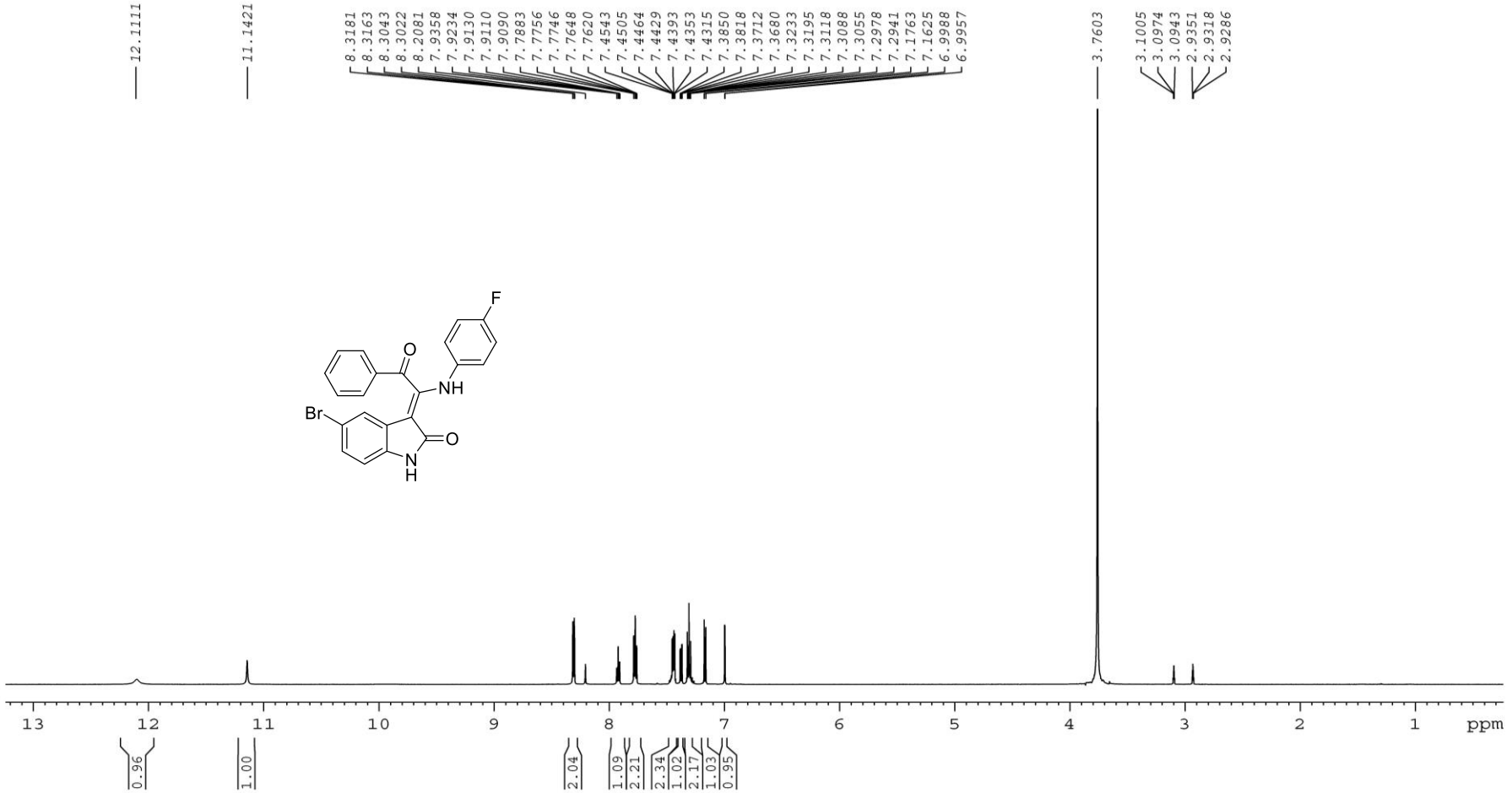


Figure S45. ^{1}H NMR (600 MHz, DMF-d_7) spectra of compound **3db**

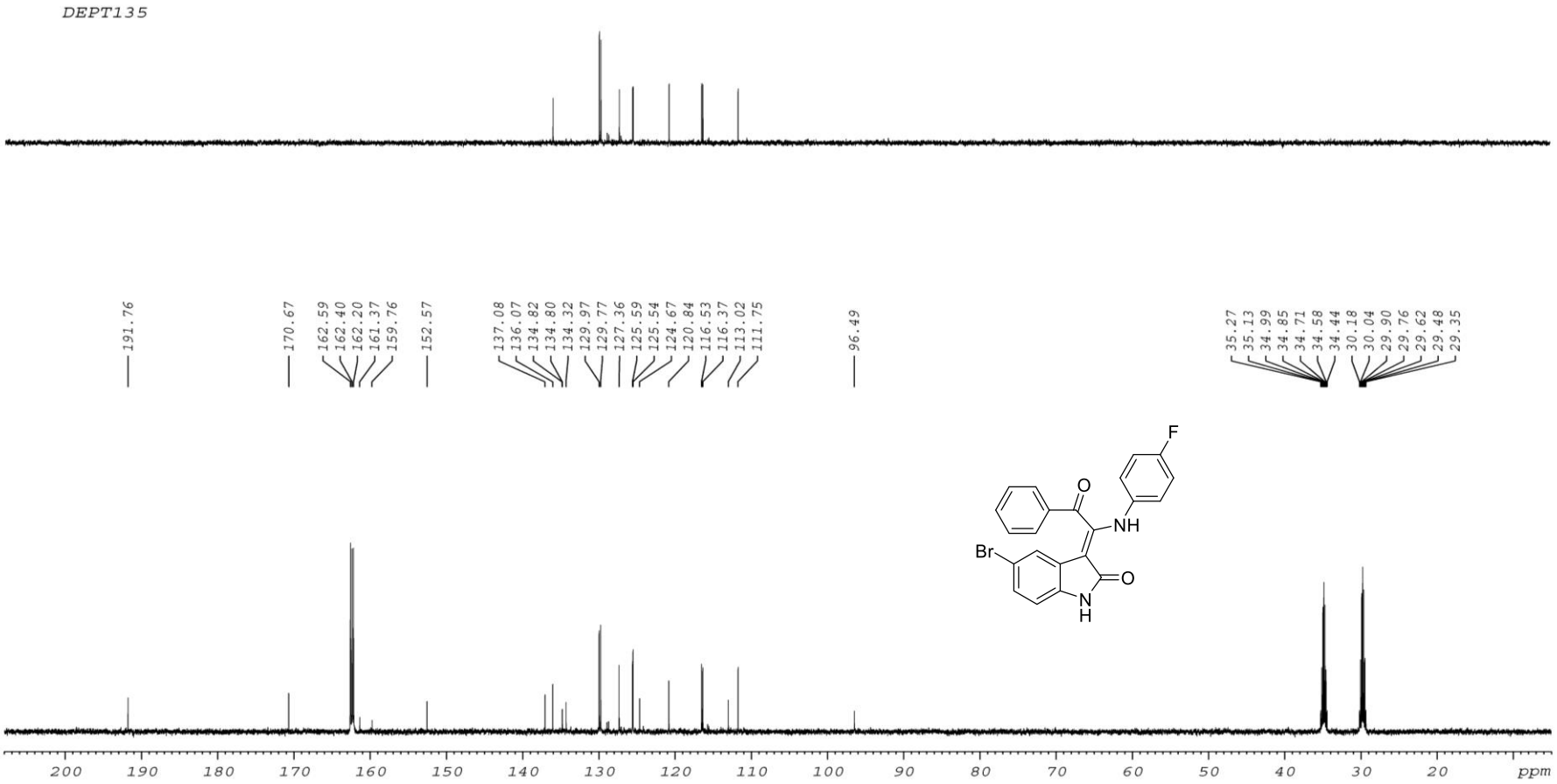


Figure S46. ^{13}C NMR (150 MHz, DMF-d_7) spectra of compound **3db**

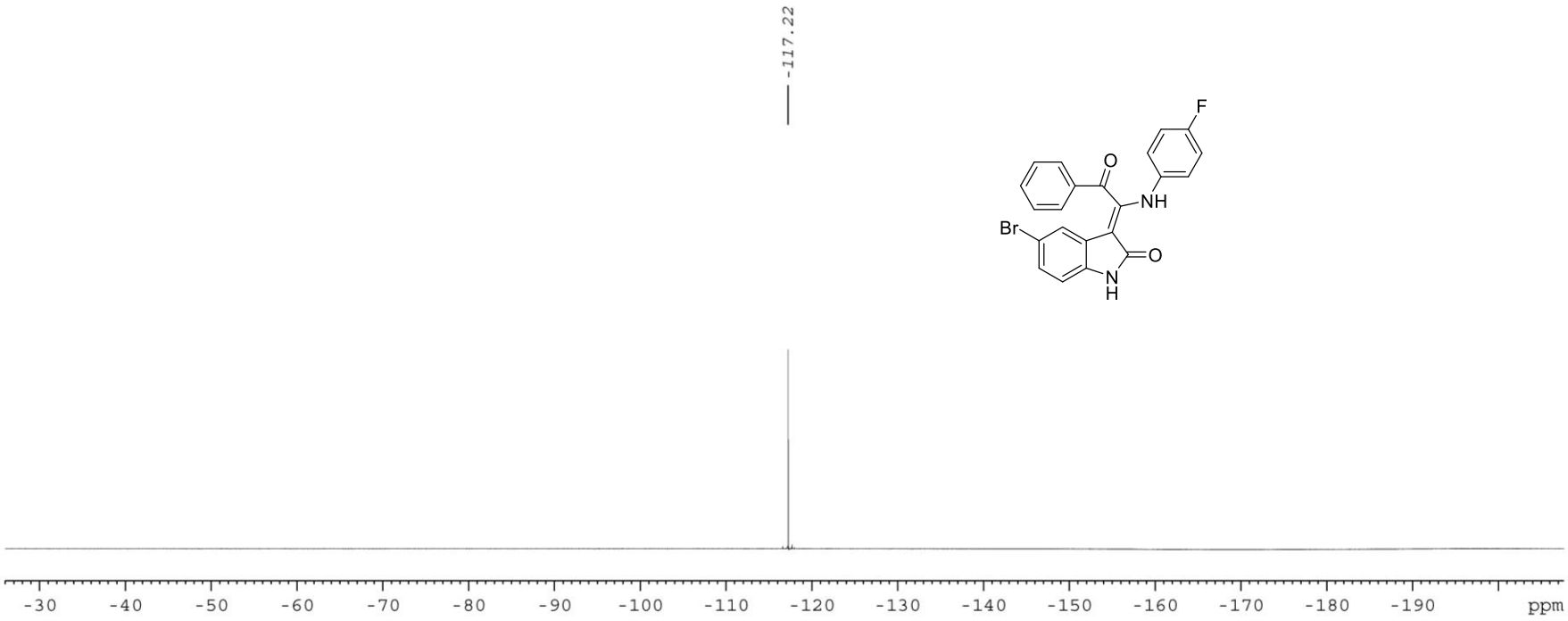


Figure S47. ^{19}F NMR (470 MHz, DMF-d_7) spectra of compound **3db**

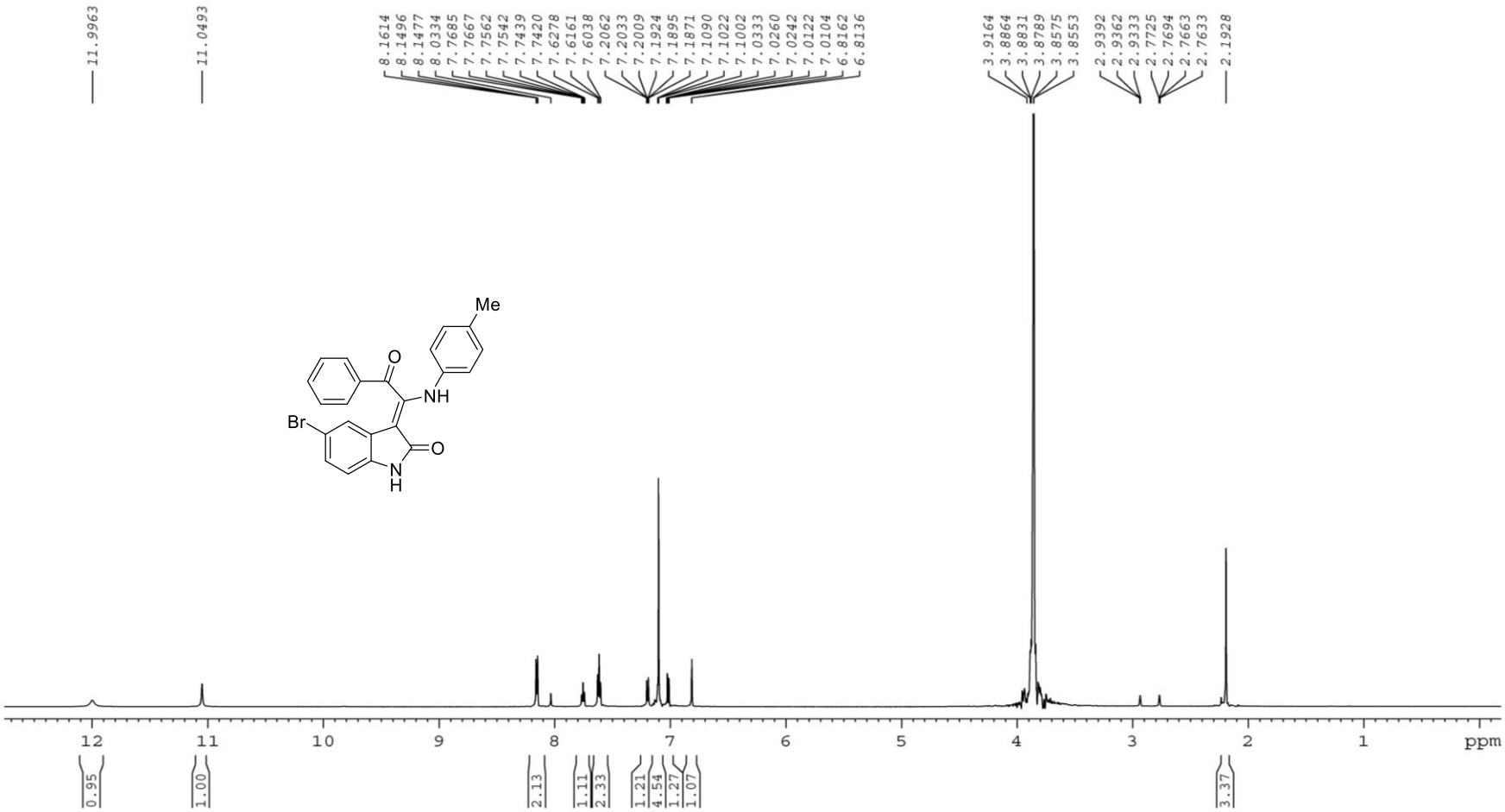


Figure S48. ^{1}H NMR (600 MHz, DMF-d_7) spectra of compound **3dd**

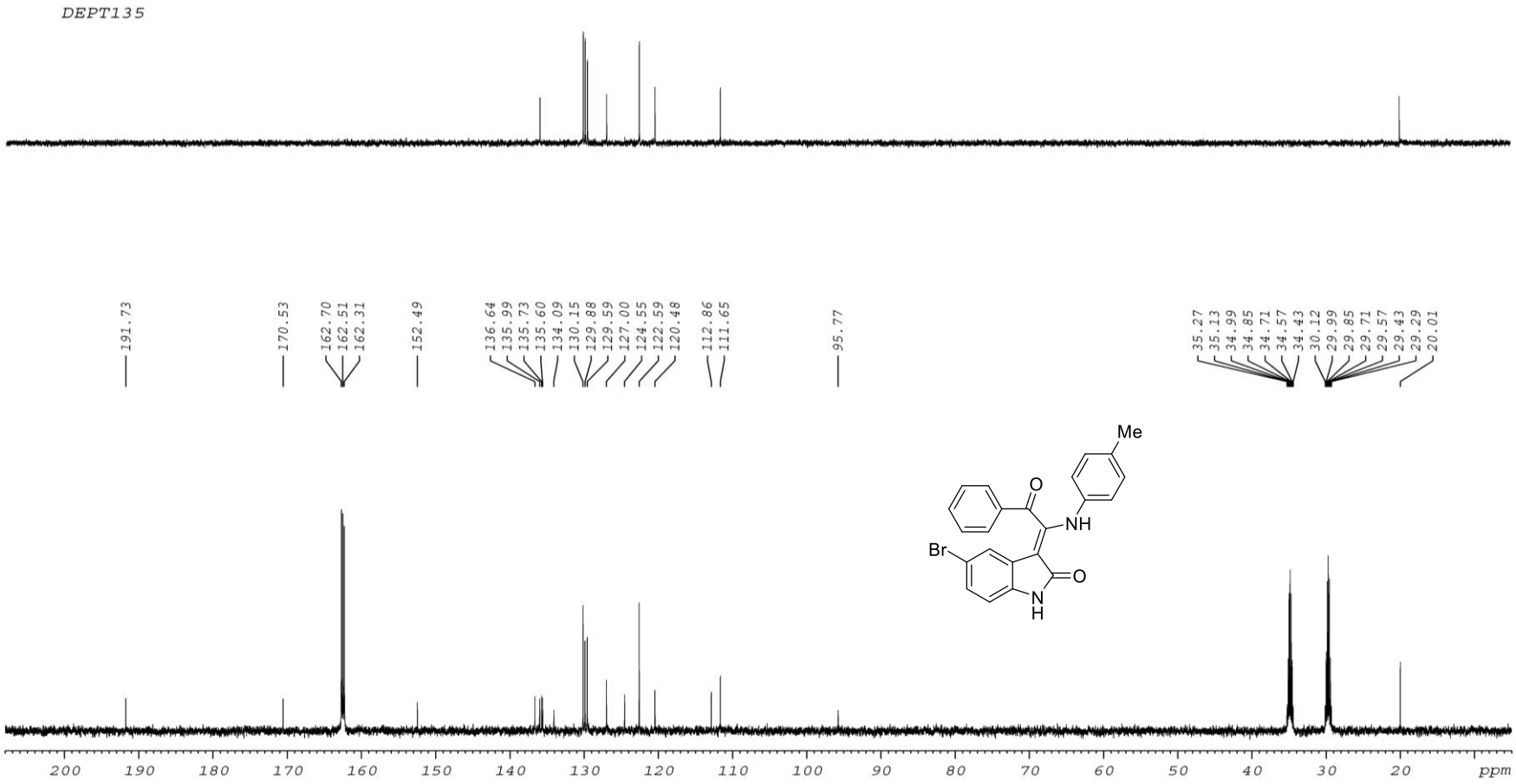


Figure S49. ^{13}C NMR (150 MHz, DMF-d_7) spectra of compound **3dd**

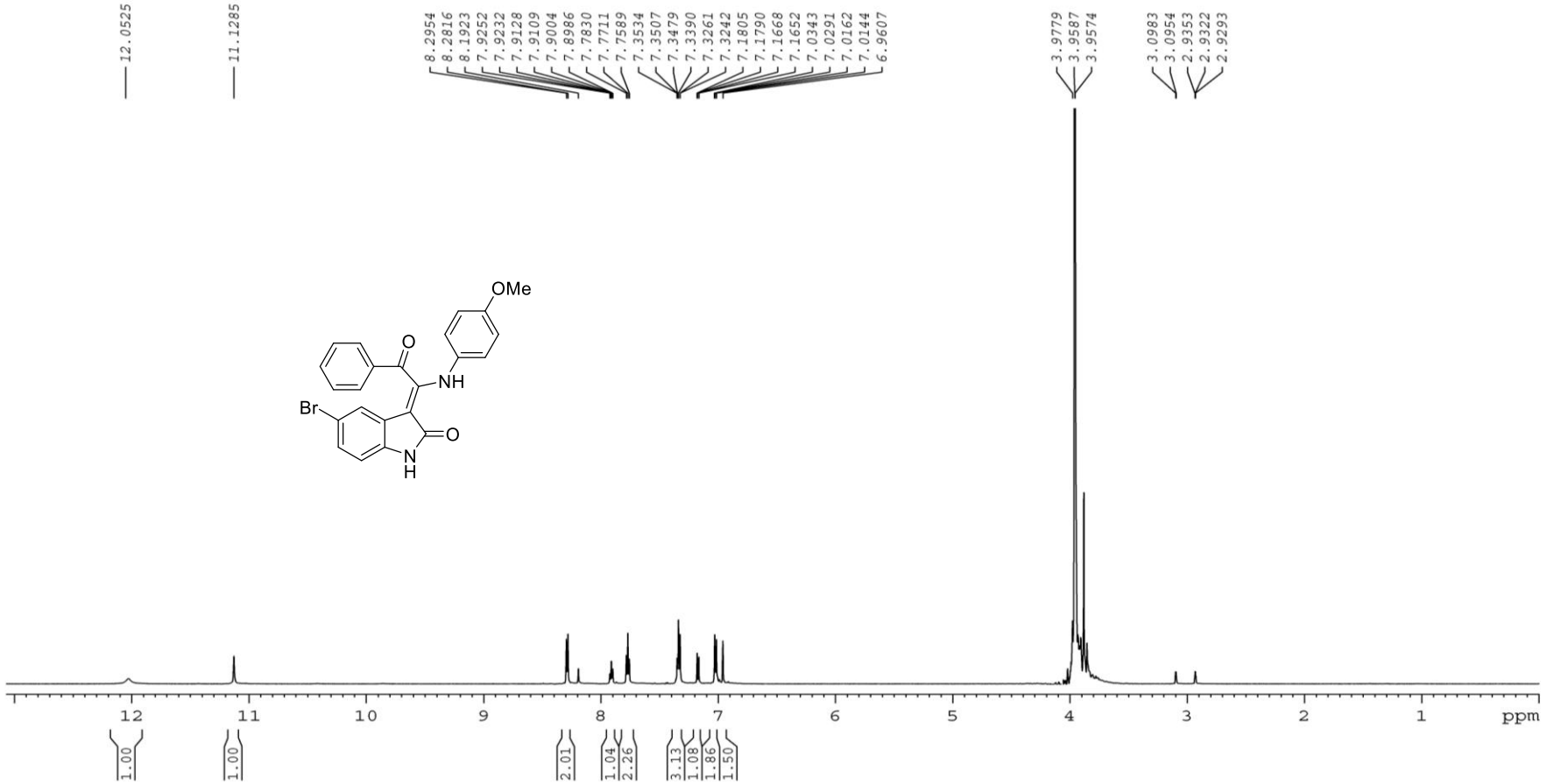


Figure S50. ^{1}H NMR (600 MHz, DMF-d_7) spectra of compound **3de**

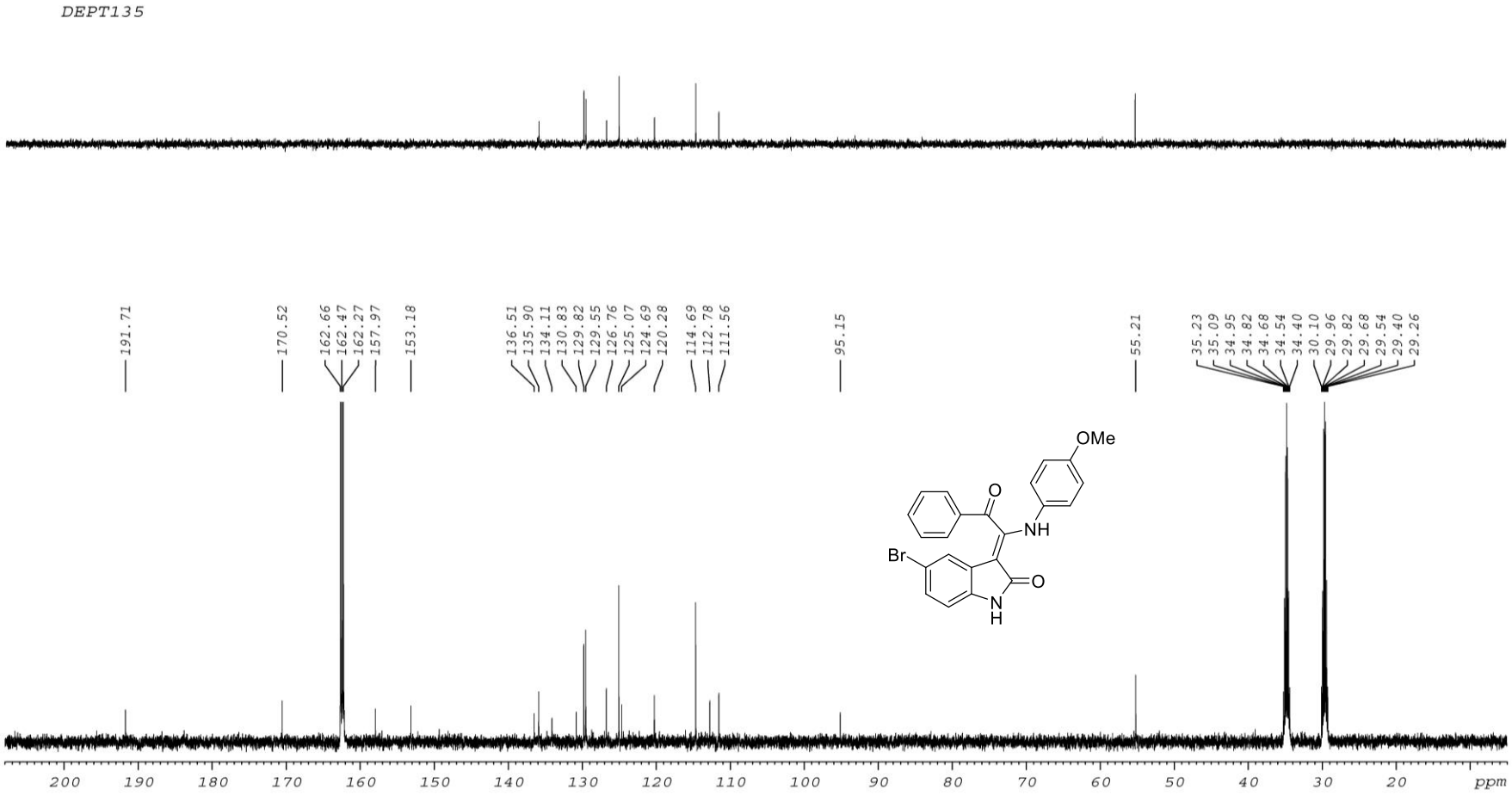


Figure S51. ^{13}C NMR (150 MHz, DMF-d_7) spectra of compound **3de**

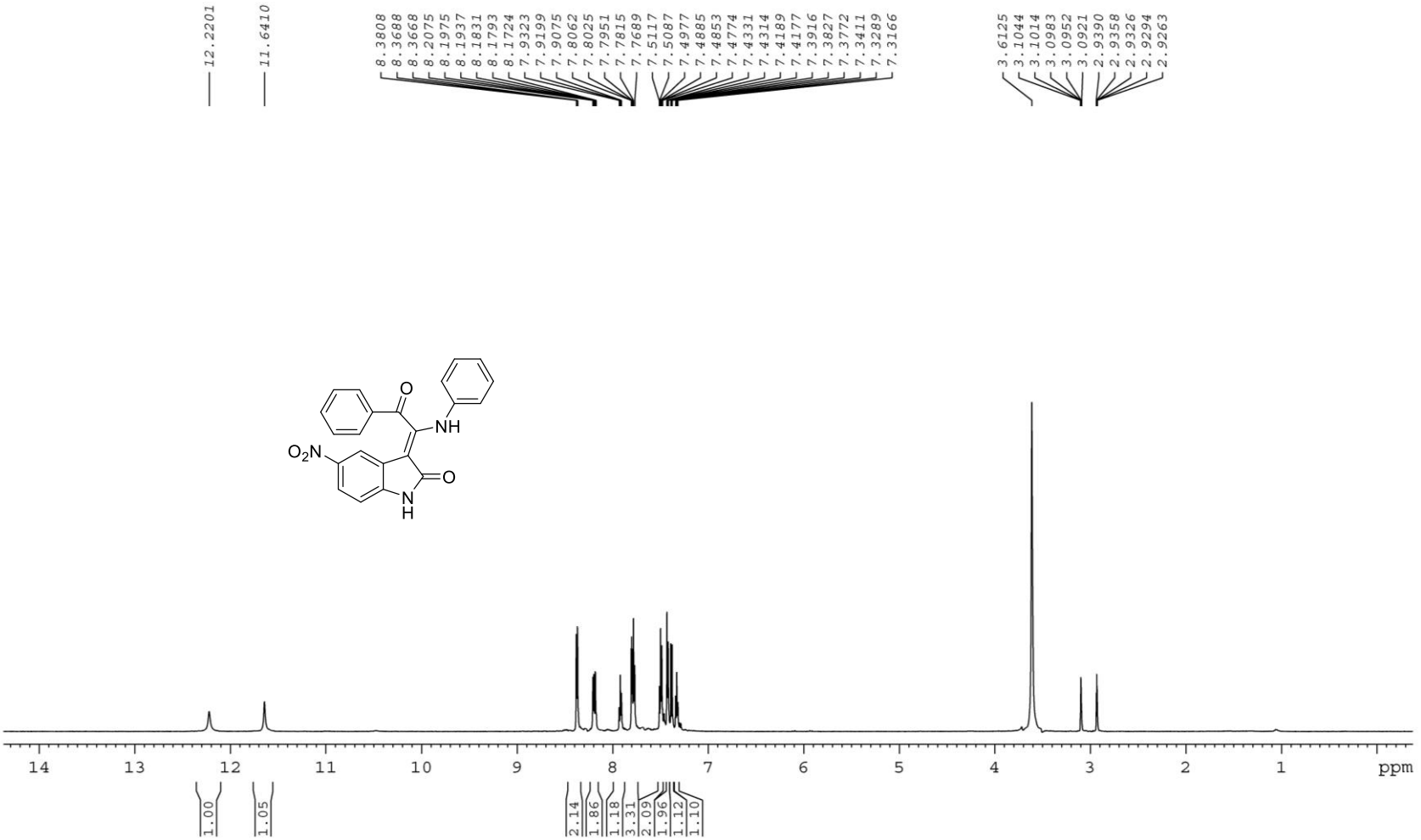


Figure S52. ^{1}H NMR (600 MHz, DMF-d_7) spectra of compound **3ea**

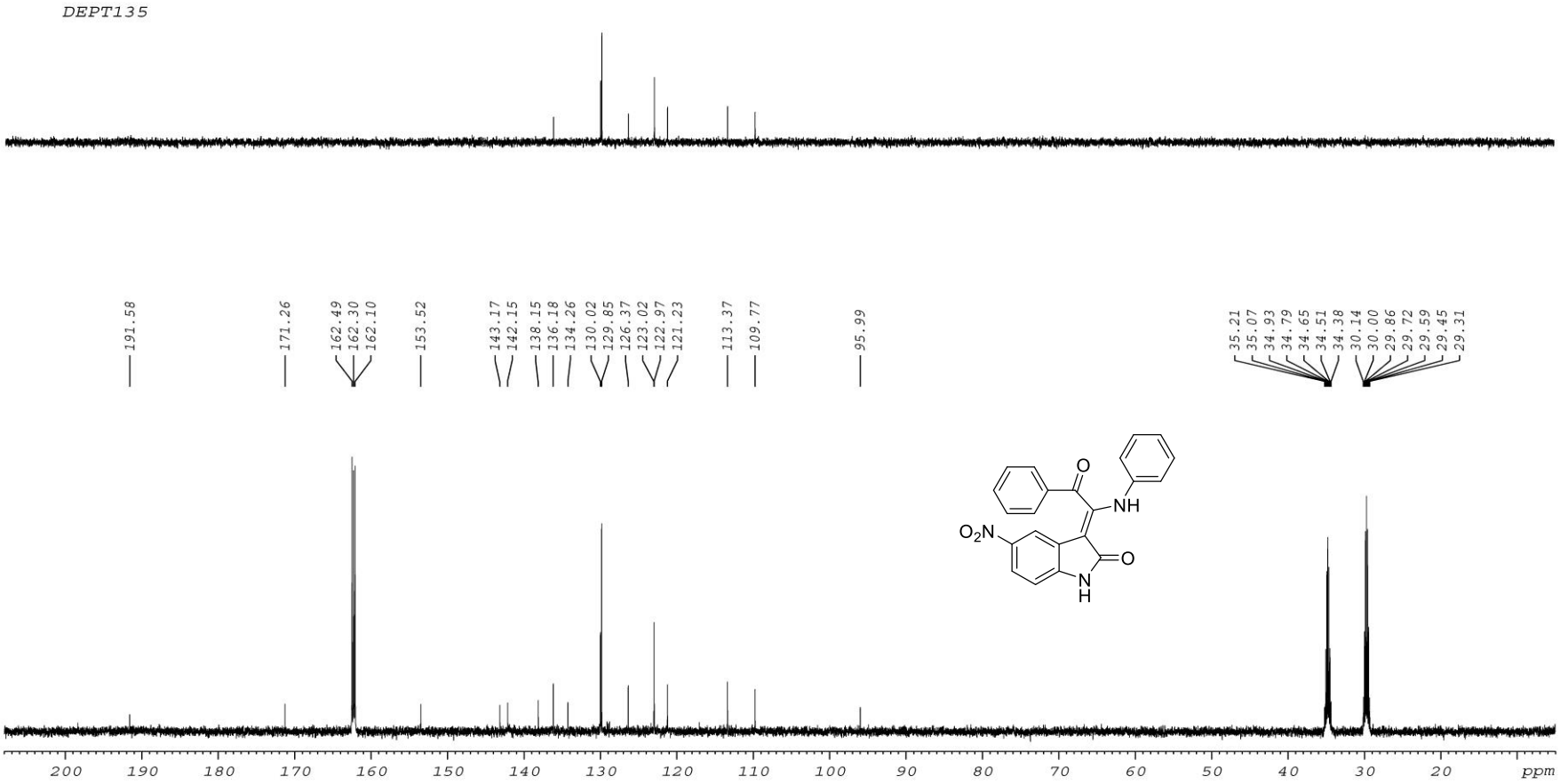


Figure S53. ^{13}C NMR (150 MHz, DMF-d_7) spectra of compound **3ea**

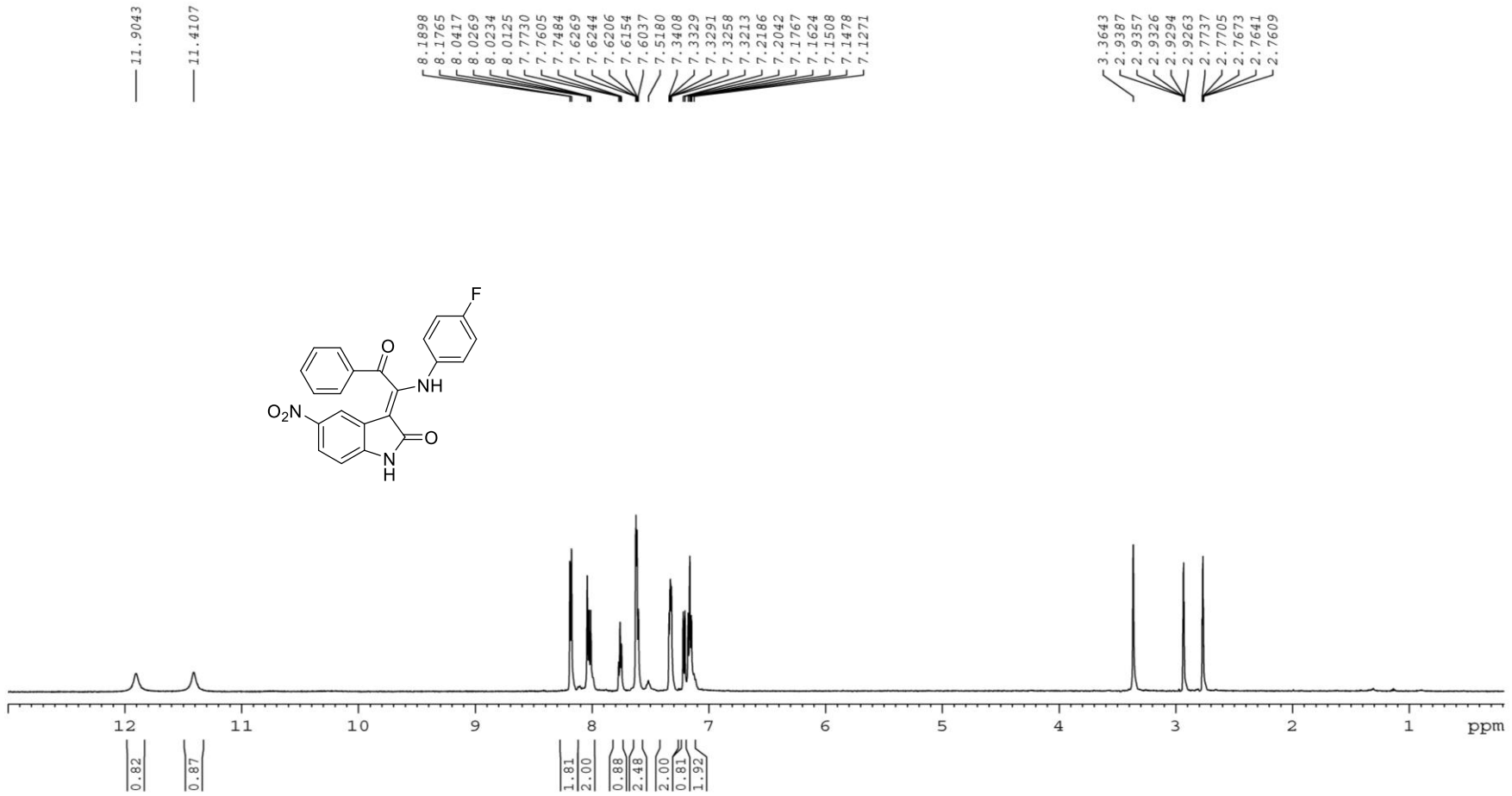


Figure S54. ^{1}H NMR (600 MHz, DMF-d_7) spectra of compound **3eb**

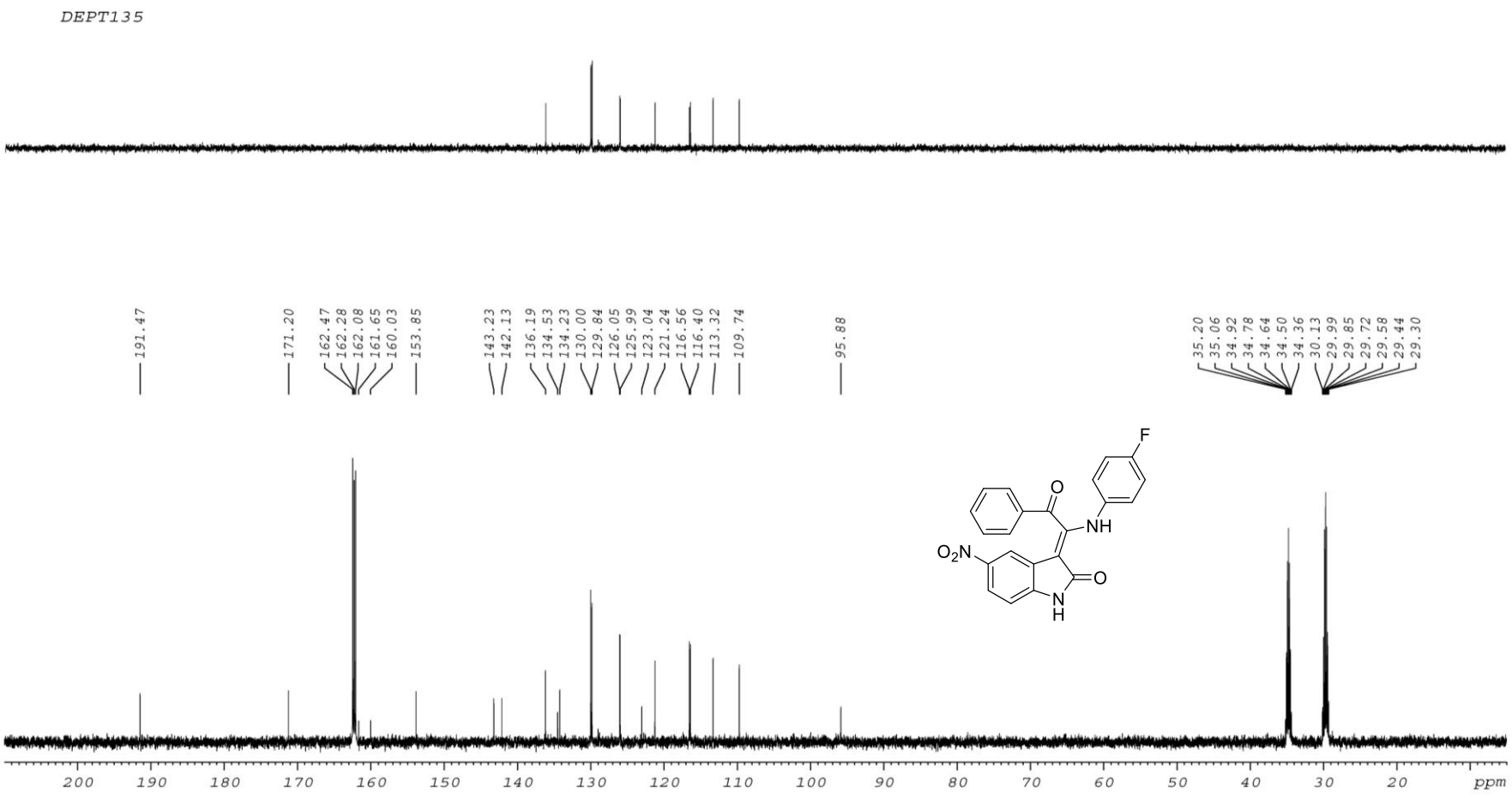


Figure S55. ^{13}C NMR (150 MHz, DMF-d_7) spectra of compound **3eb**

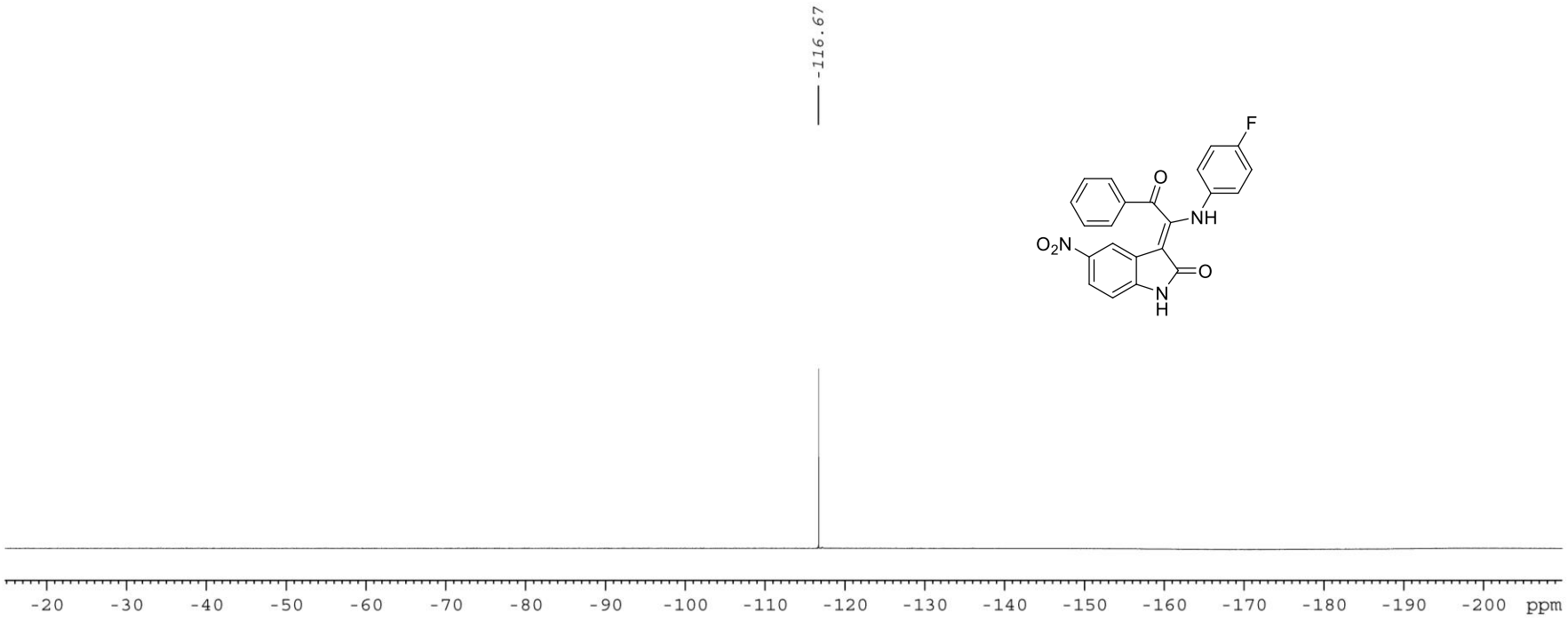


Figure S56. ^{19}F NMR (470 MHz, DMF-d_7) spectra of compound **3eb**

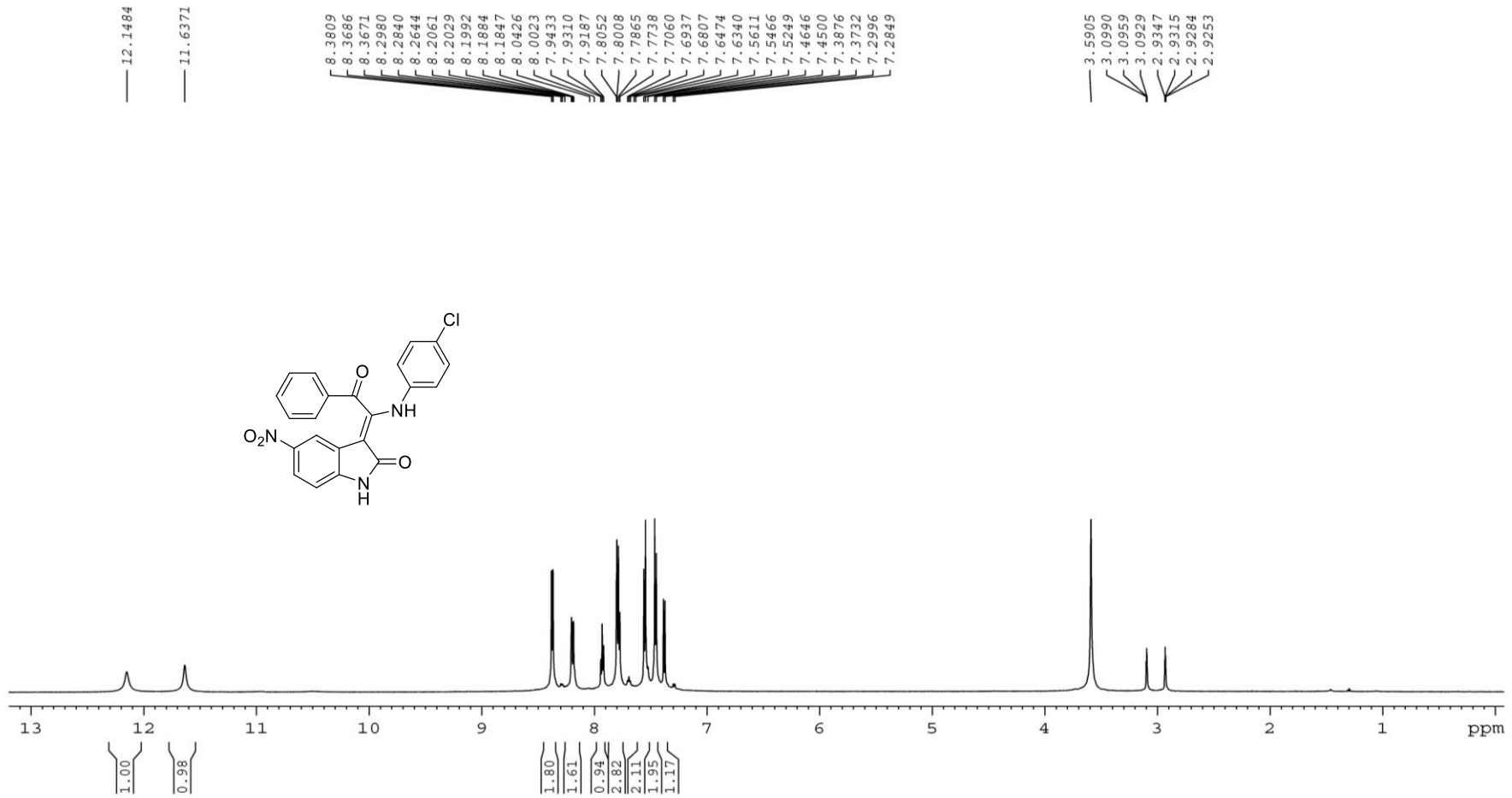


Figure S57. ^{1}H NMR (600 MHz, DMF-d_7) spectra of compound **3ec**

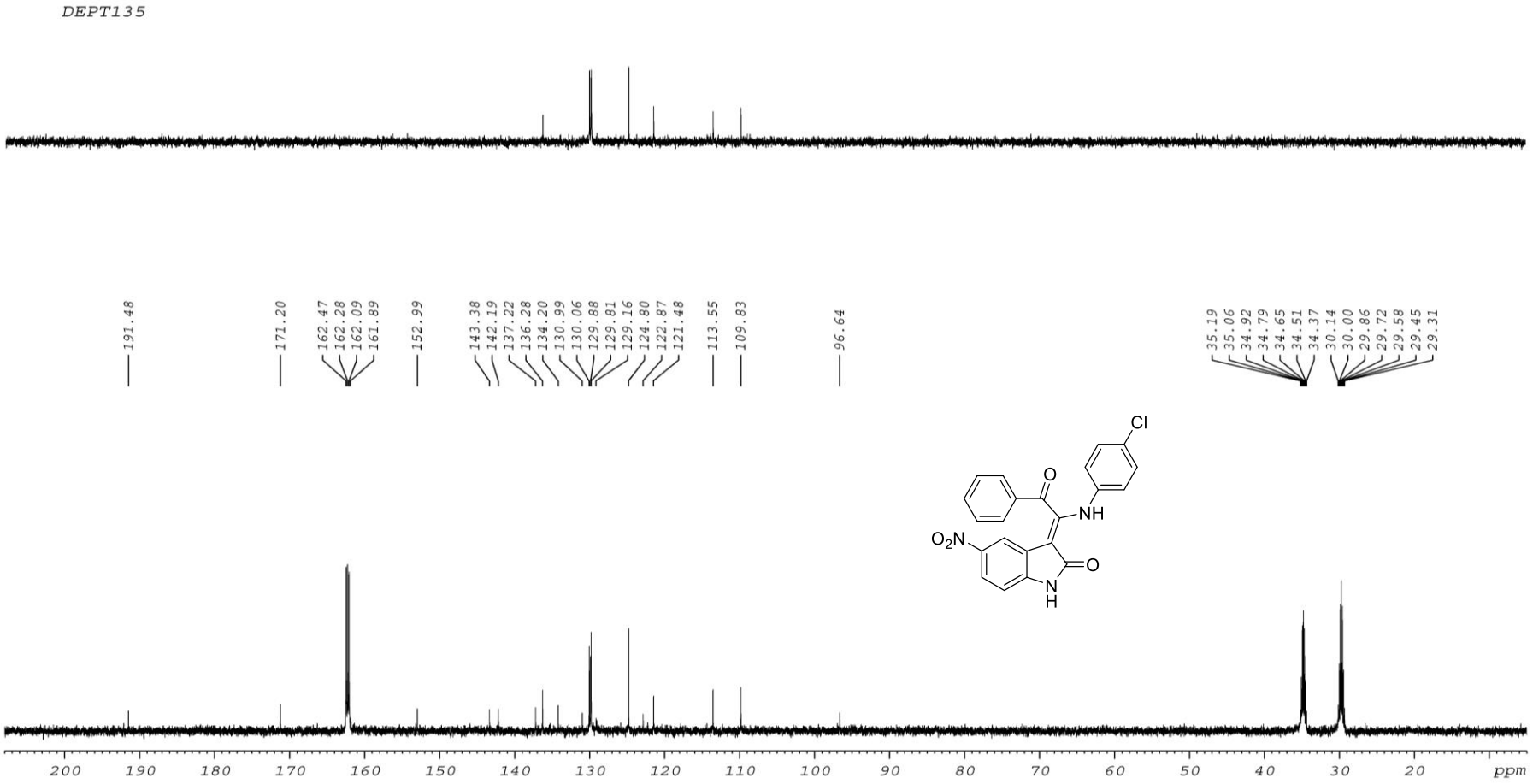


Figure S58. ^{13}C NMR (150 MHz, DMF-d_7) spectra of compound **3ec**

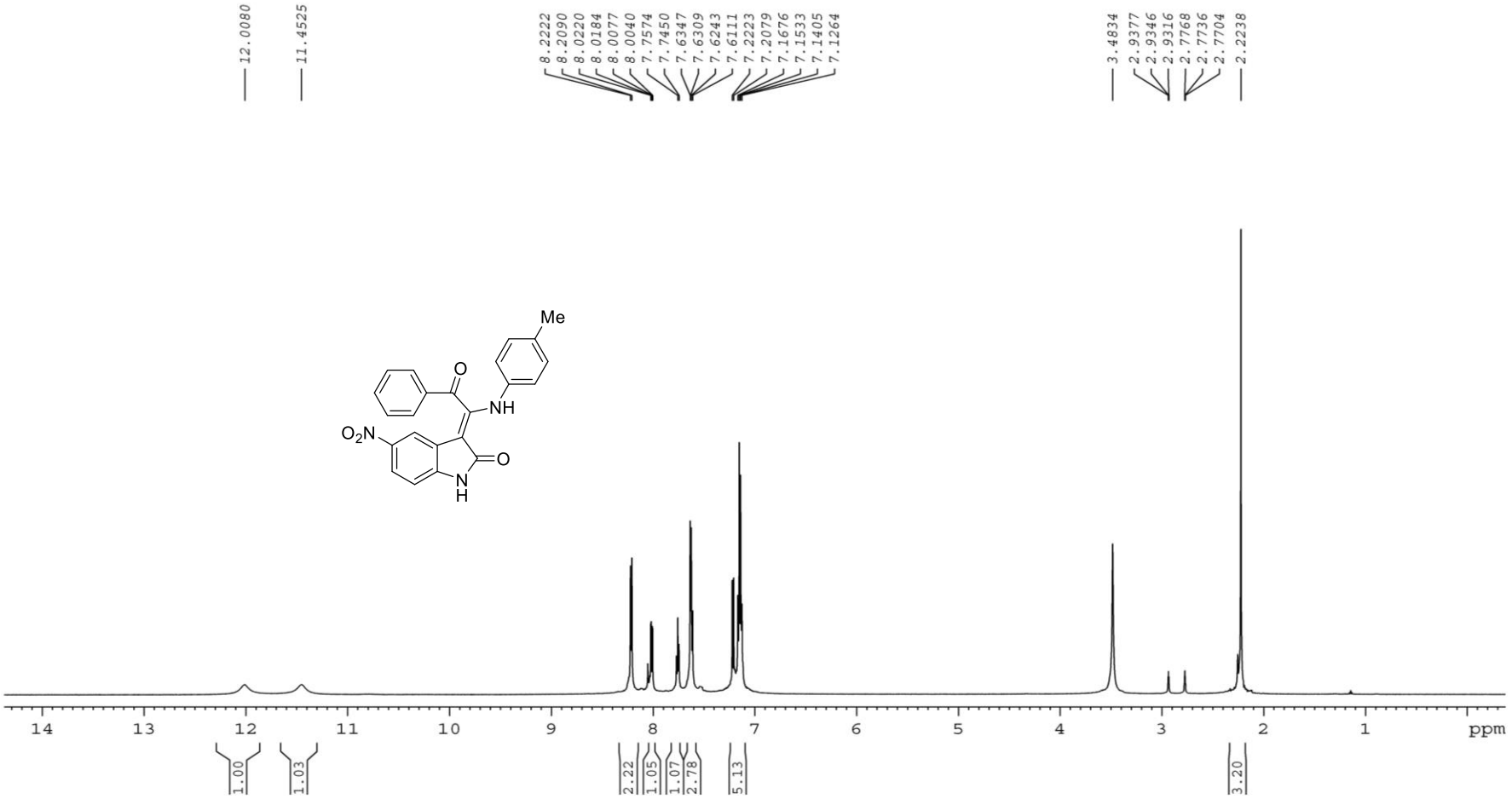


Figure S59. ^{1}H NMR (600 MHz, DMF-d_7) spectra of compound **3ed**

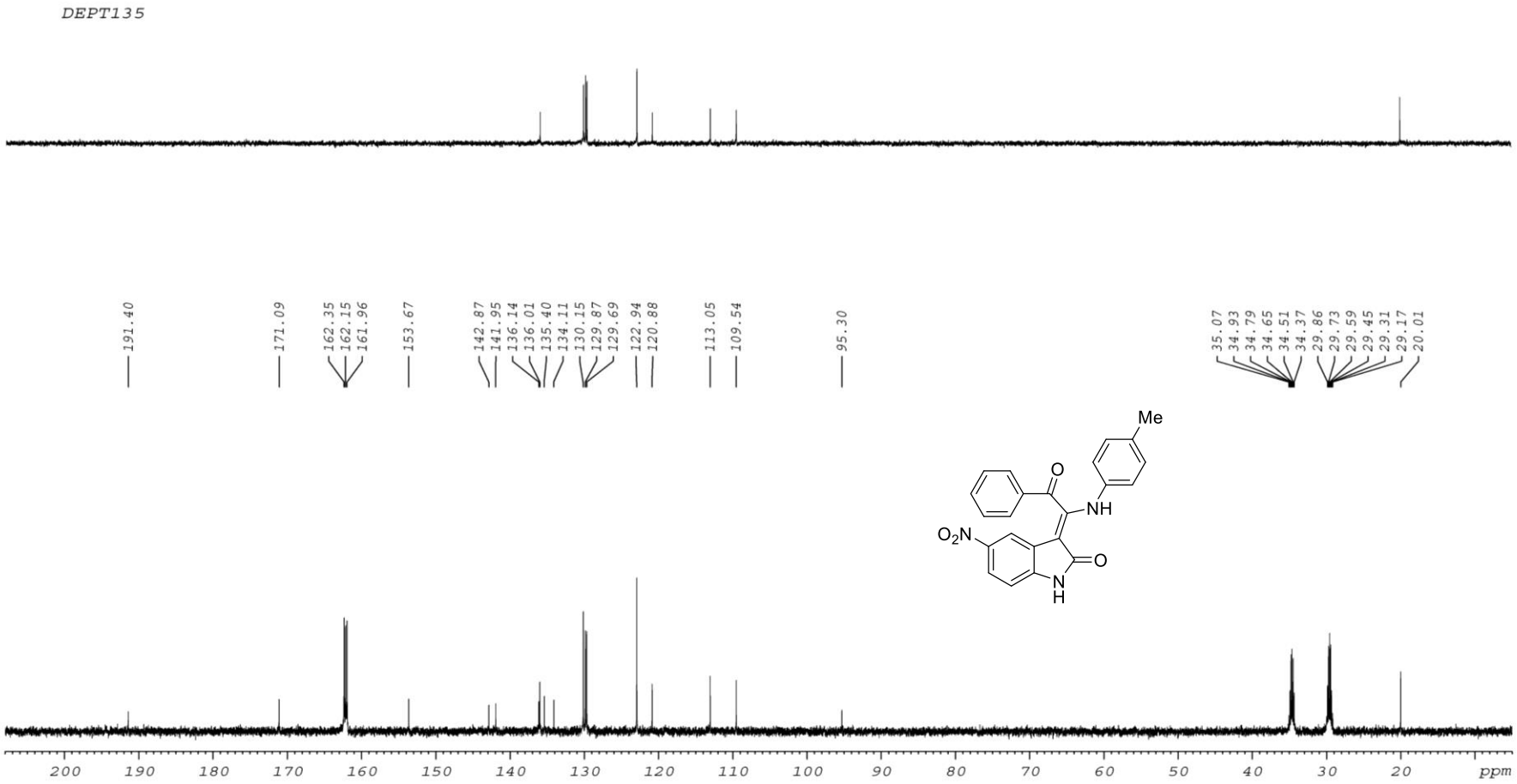


Figure S60. ^{13}C NMR (150 MHz, DMF-d_7) spectra of compound **3ed**

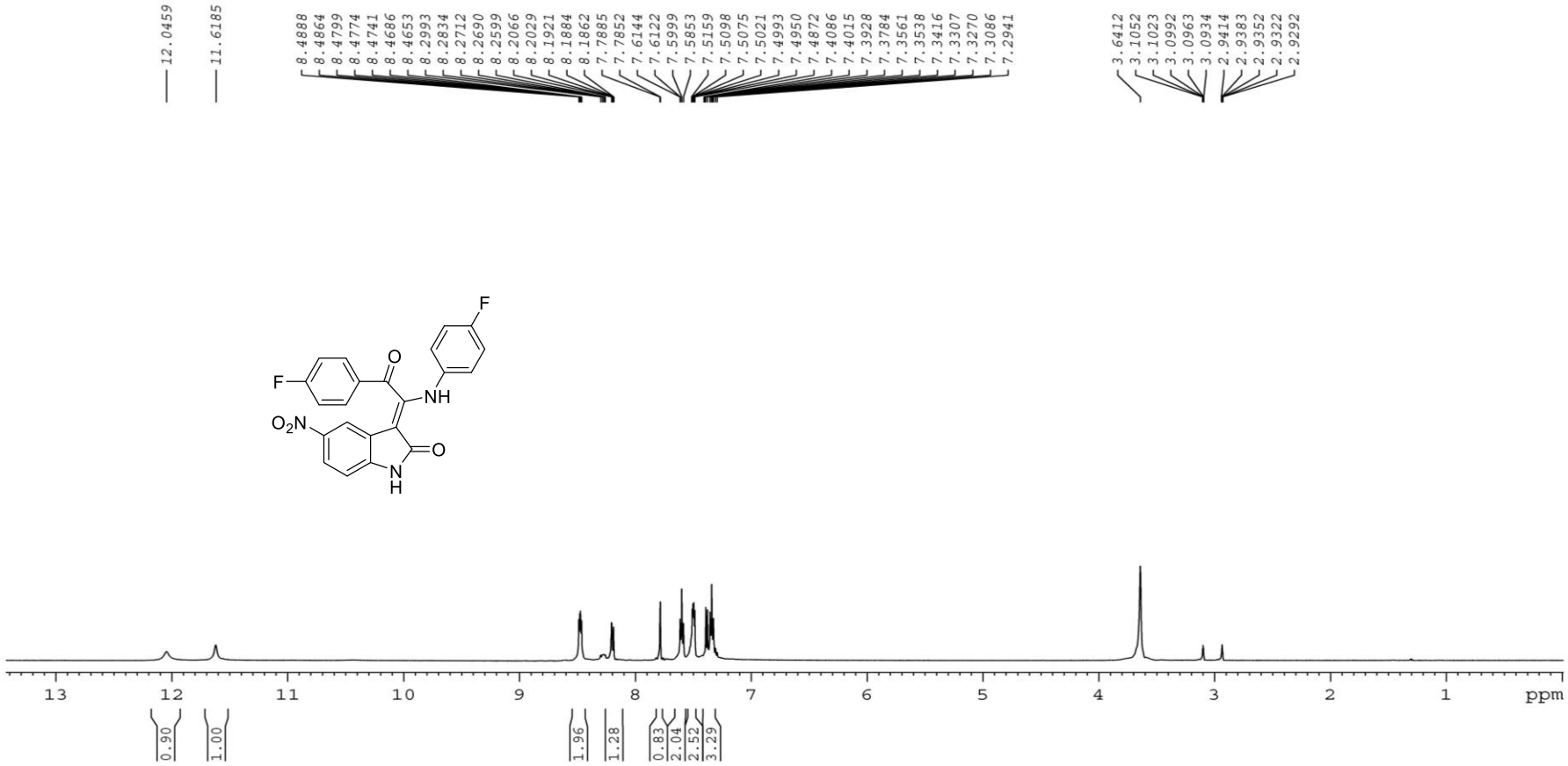


Figure S61. ^{1}H NMR (600 MHz, DMF-d_7) spectra of compound **3ef**

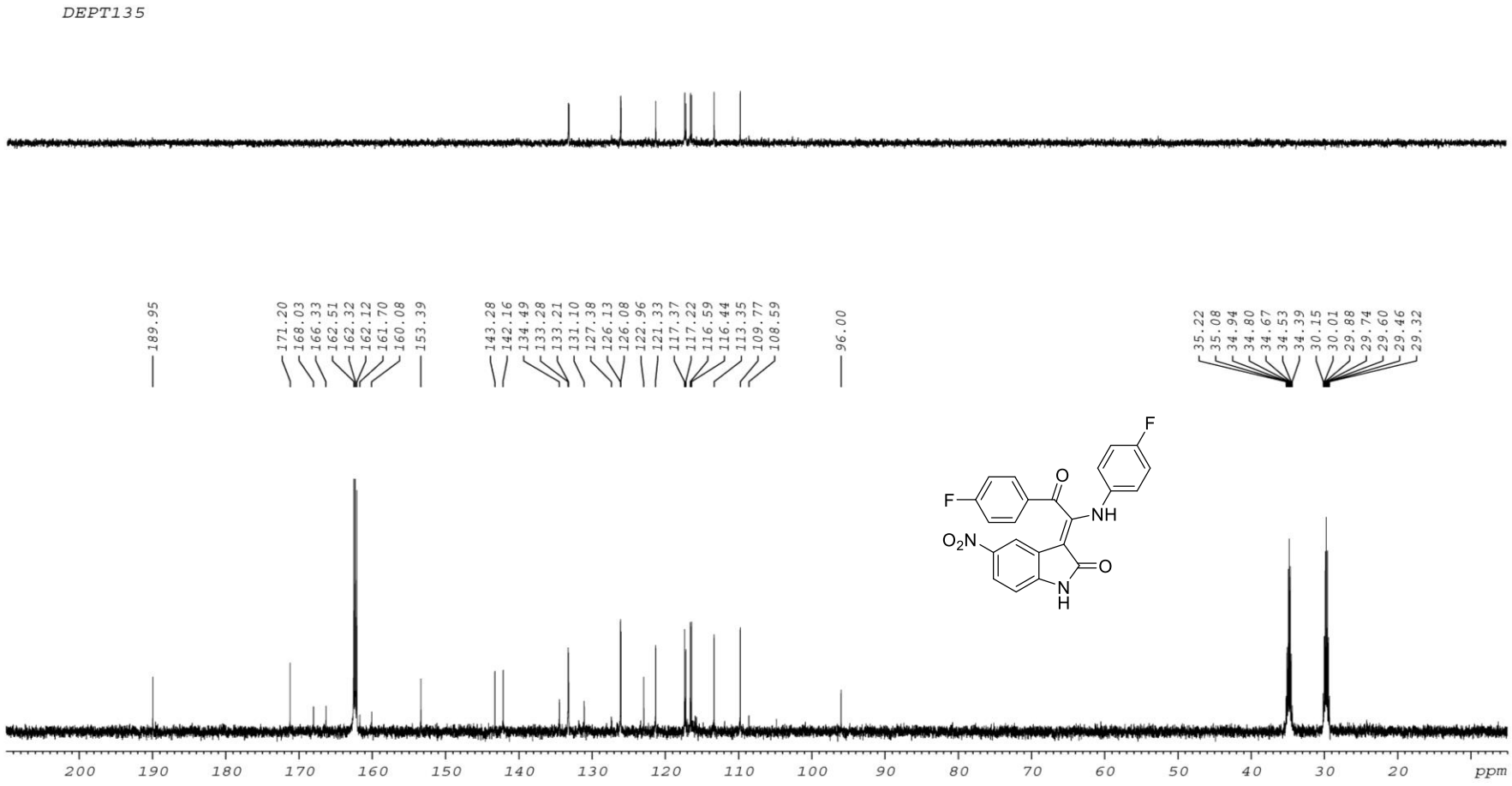


Figure S62. ^{13}C NMR (150 MHz, DMF-d_7) spectra of compound **3ef**

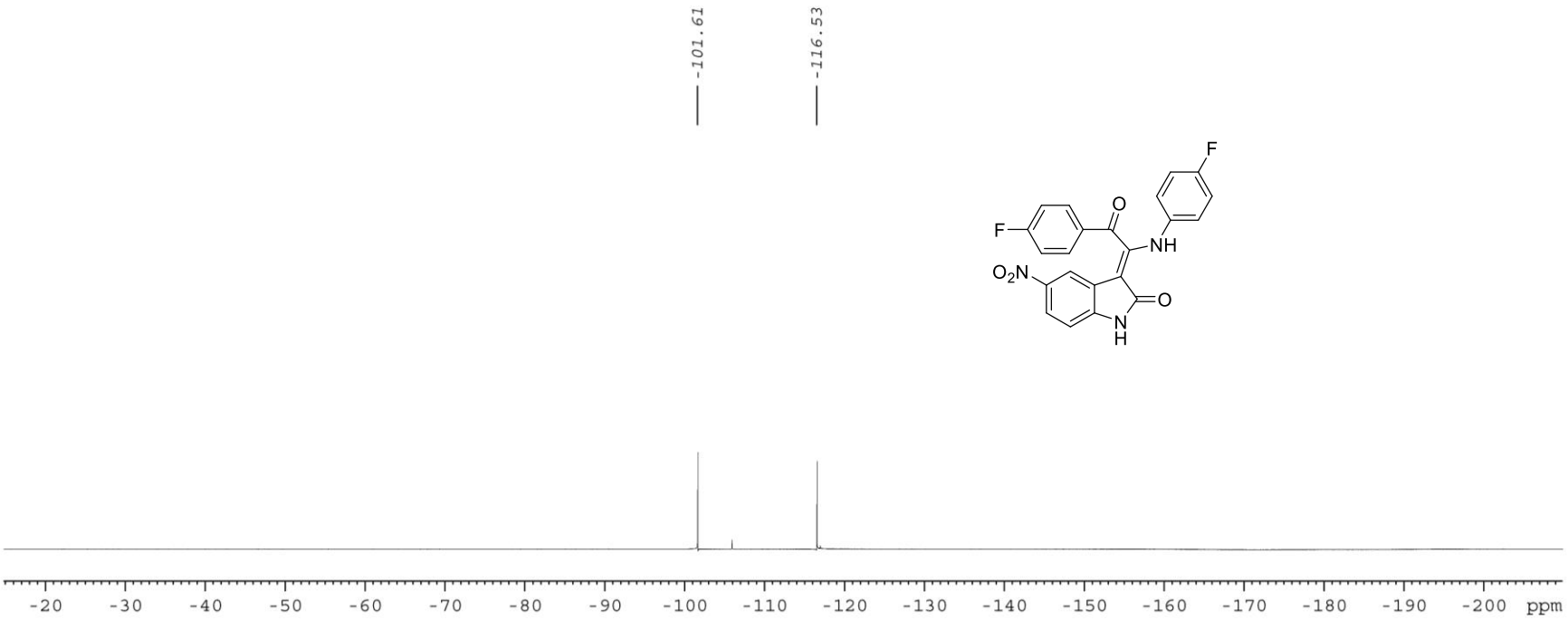


Figure S63. ^{19}F NMR (470 MHz, DMF-d_7) spectra of compound **3ef**

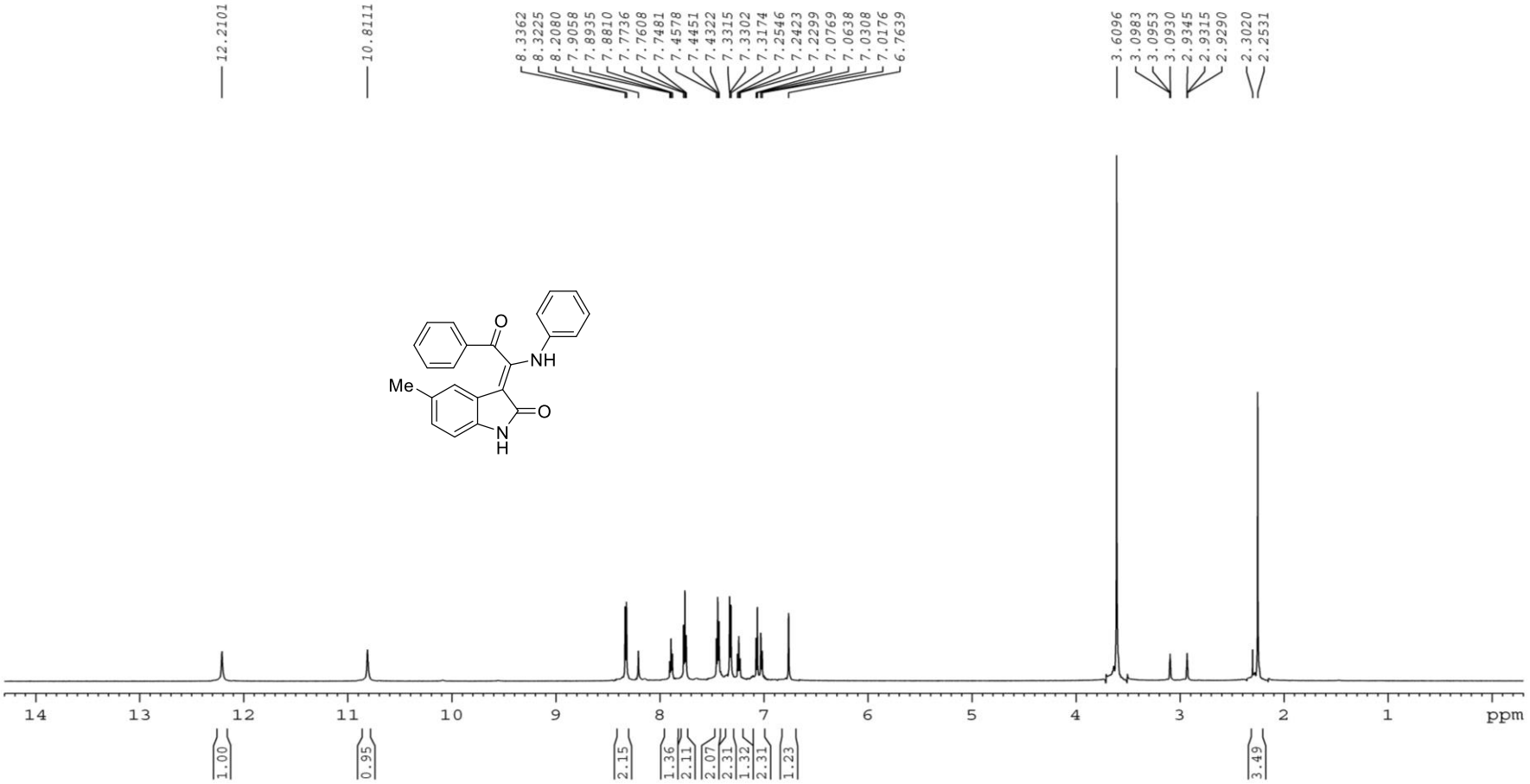


Figure S64. ^{1}H NMR (600 MHz, DMF-d_7) spectra of compound **3fa**

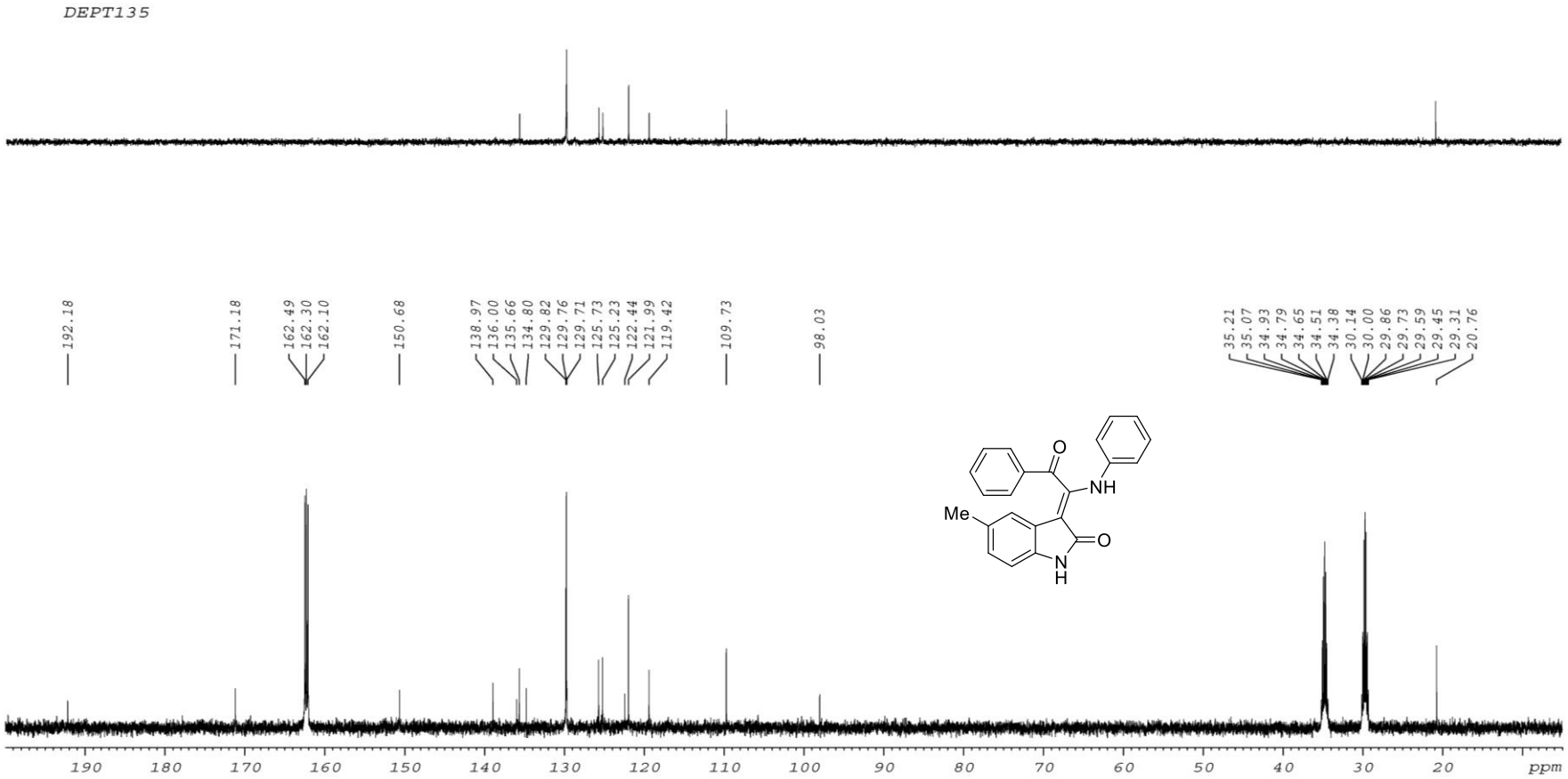


Figure S65. ^{13}C NMR (150 MHz, DMF-d_7) spectra of compound **3fa**

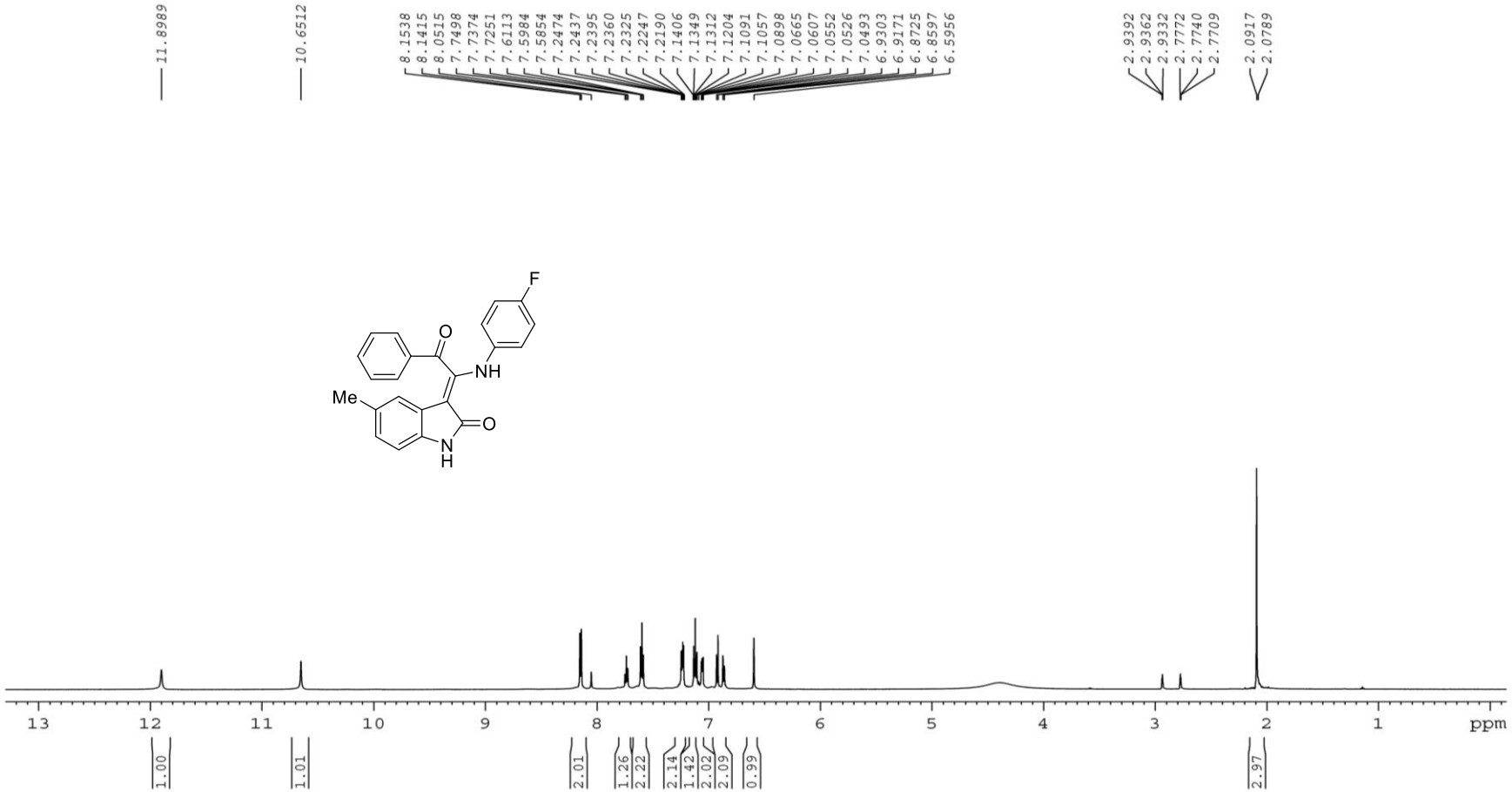


Figure S66. ^{1}H NMR (600 MHz, DMF-d_7) spectra of compound **3fb**

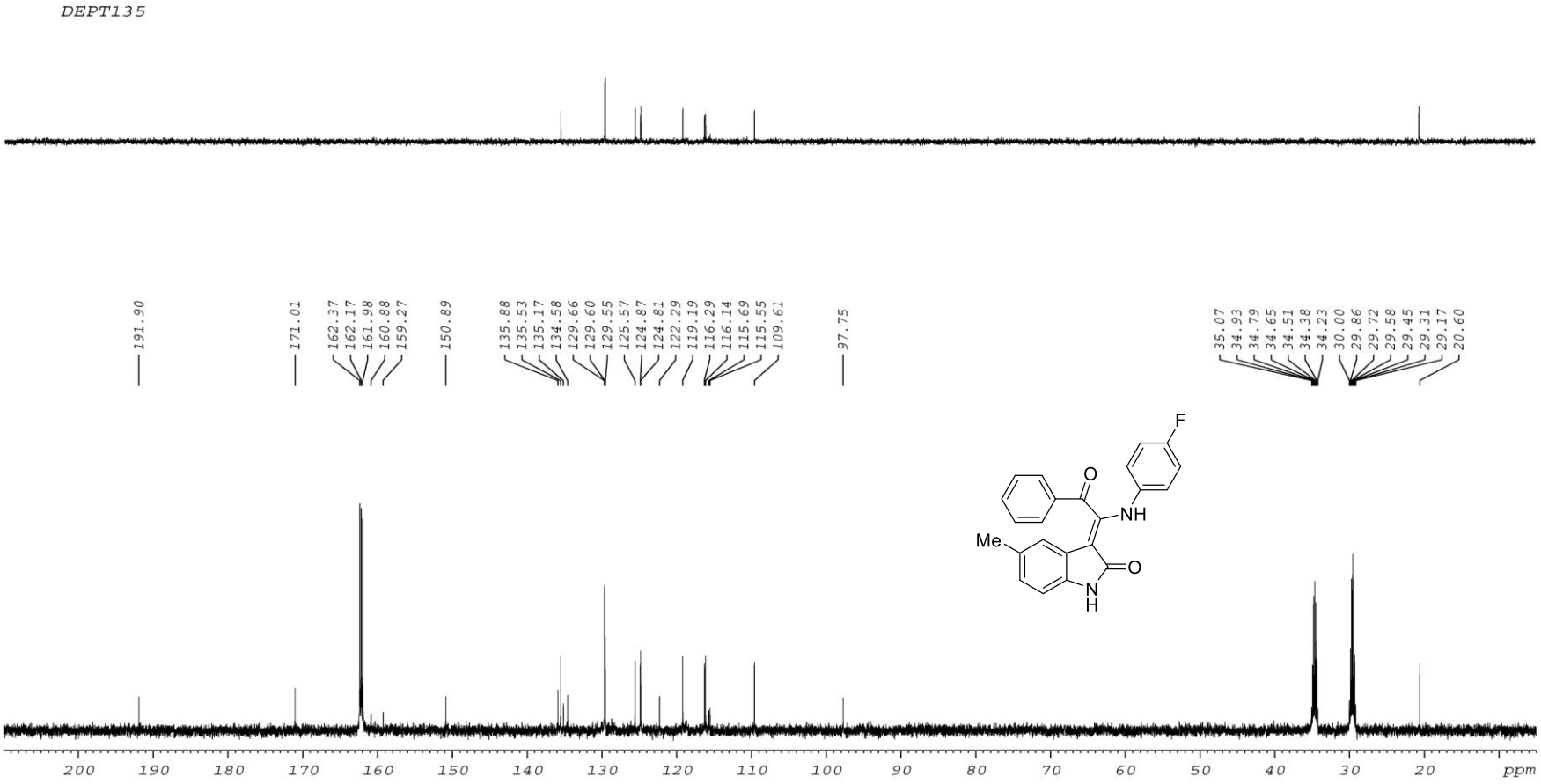


Figure S67. ^{13}C NMR (150 MHz, DMF-d_7) spectra of compound **3fb**

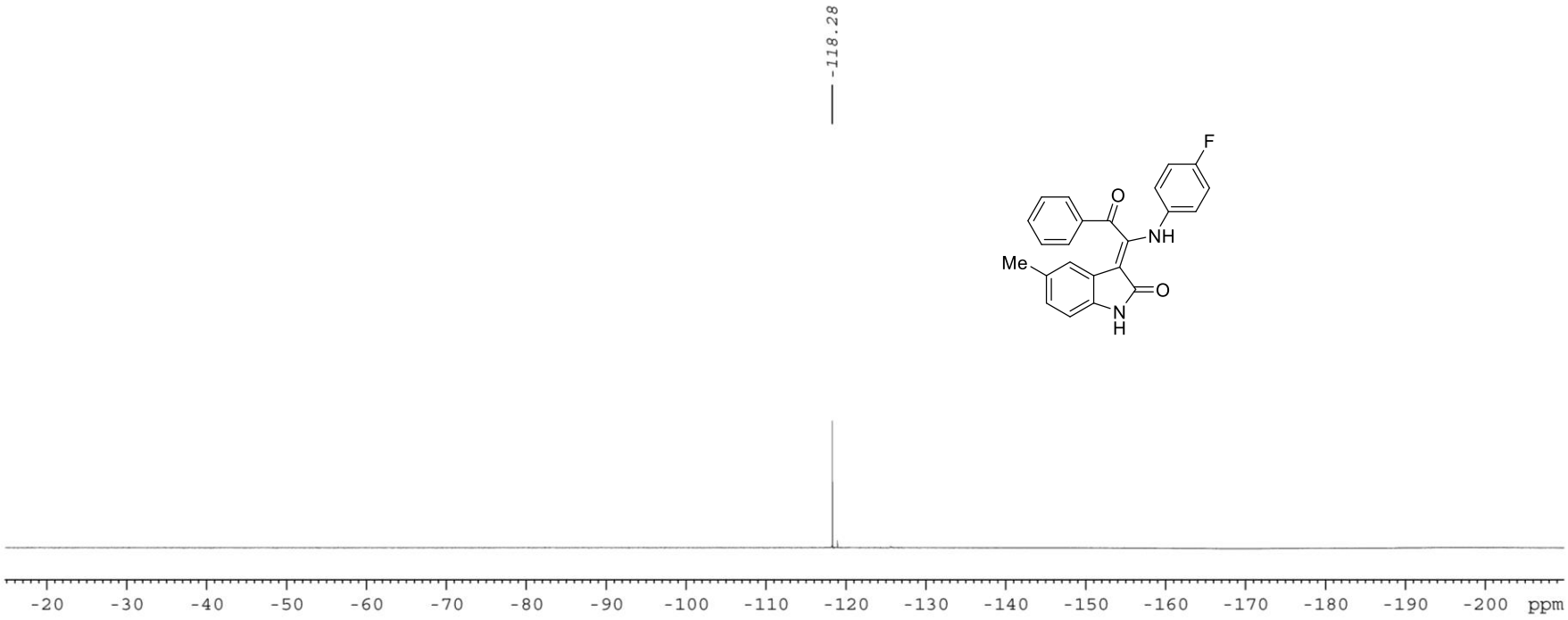


Figure S68. ^{19}F NMR (470 MHz, DMF-d_7) spectra of compound **3fb**

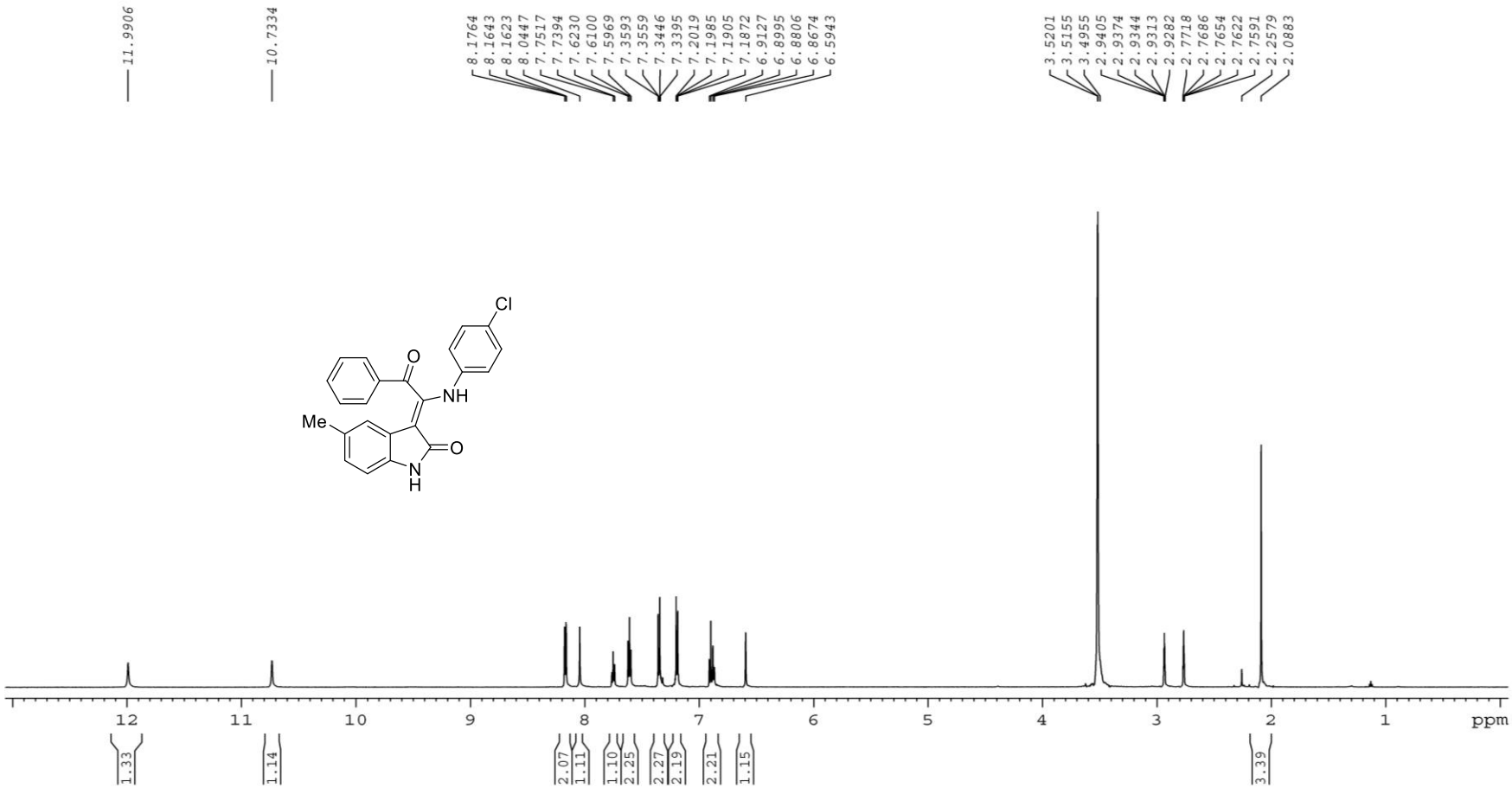


Figure S69. ^{1}H NMR (600 MHz, DMF-d_7) spectra of compound **3fc**

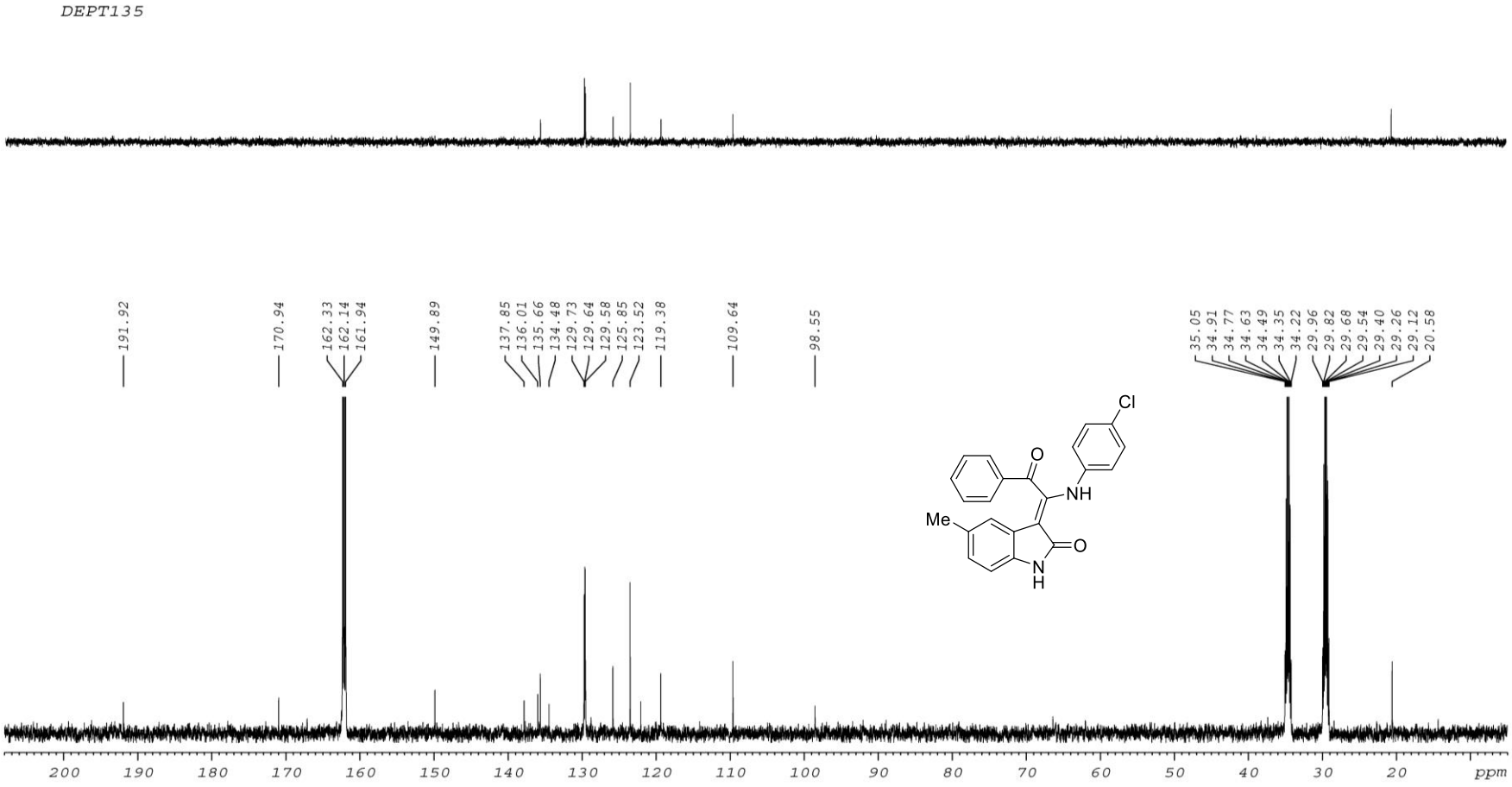


Figure S70. ^{13}C NMR (150 MHz, DMF-d_7) spectra of compound **3fc**

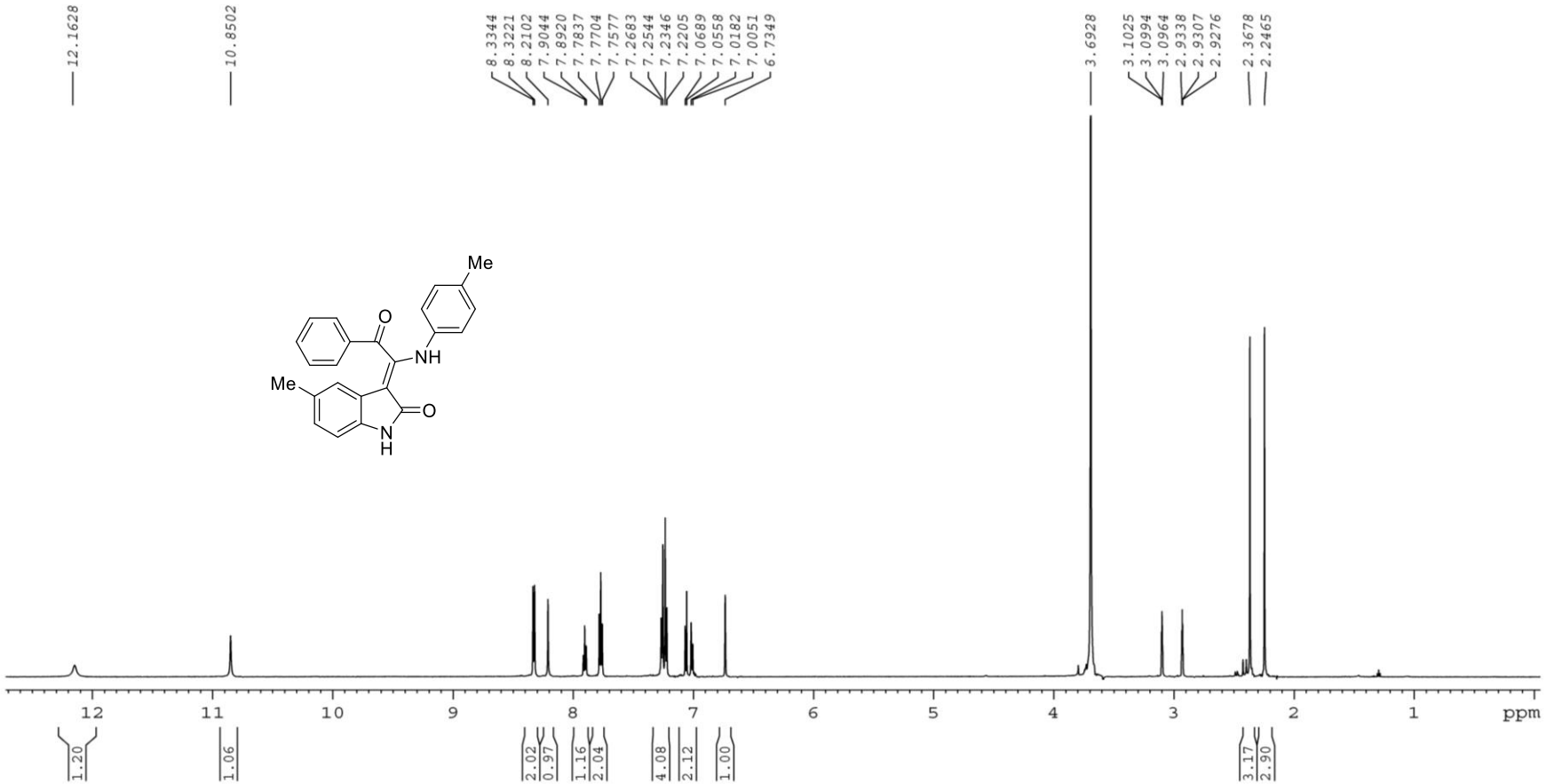


Figure S71. ^{1}H NMR (600 MHz, DMF-d_7) spectra of compound **3fd**

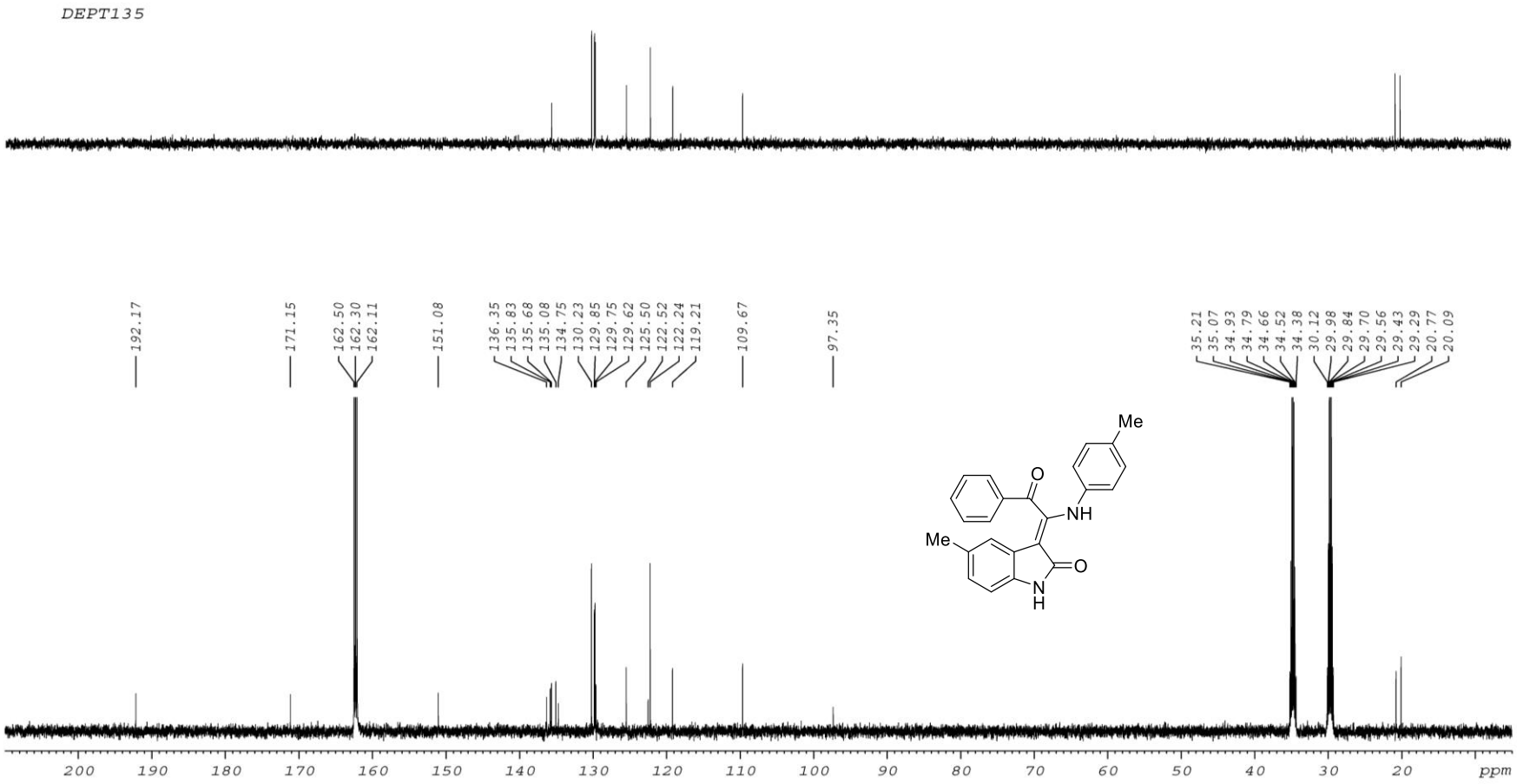


Figure S72. ^{13}C NMR (150 MHz, DMF-d_7) spectra of compound **3fd**

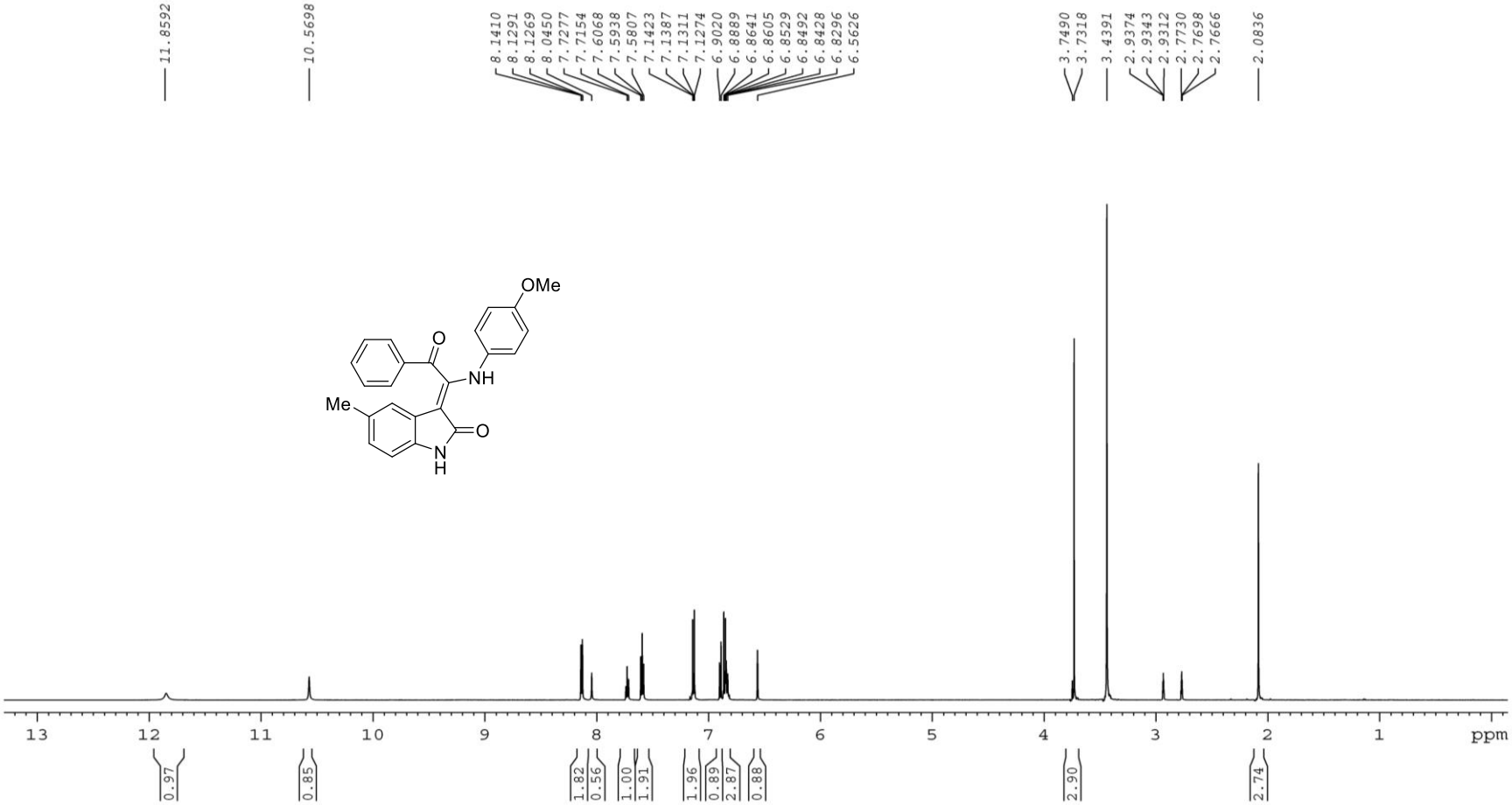


Figure S73. ^{1}H NMR (600 MHz, DMF-d_7) spectra of compound **3fe**

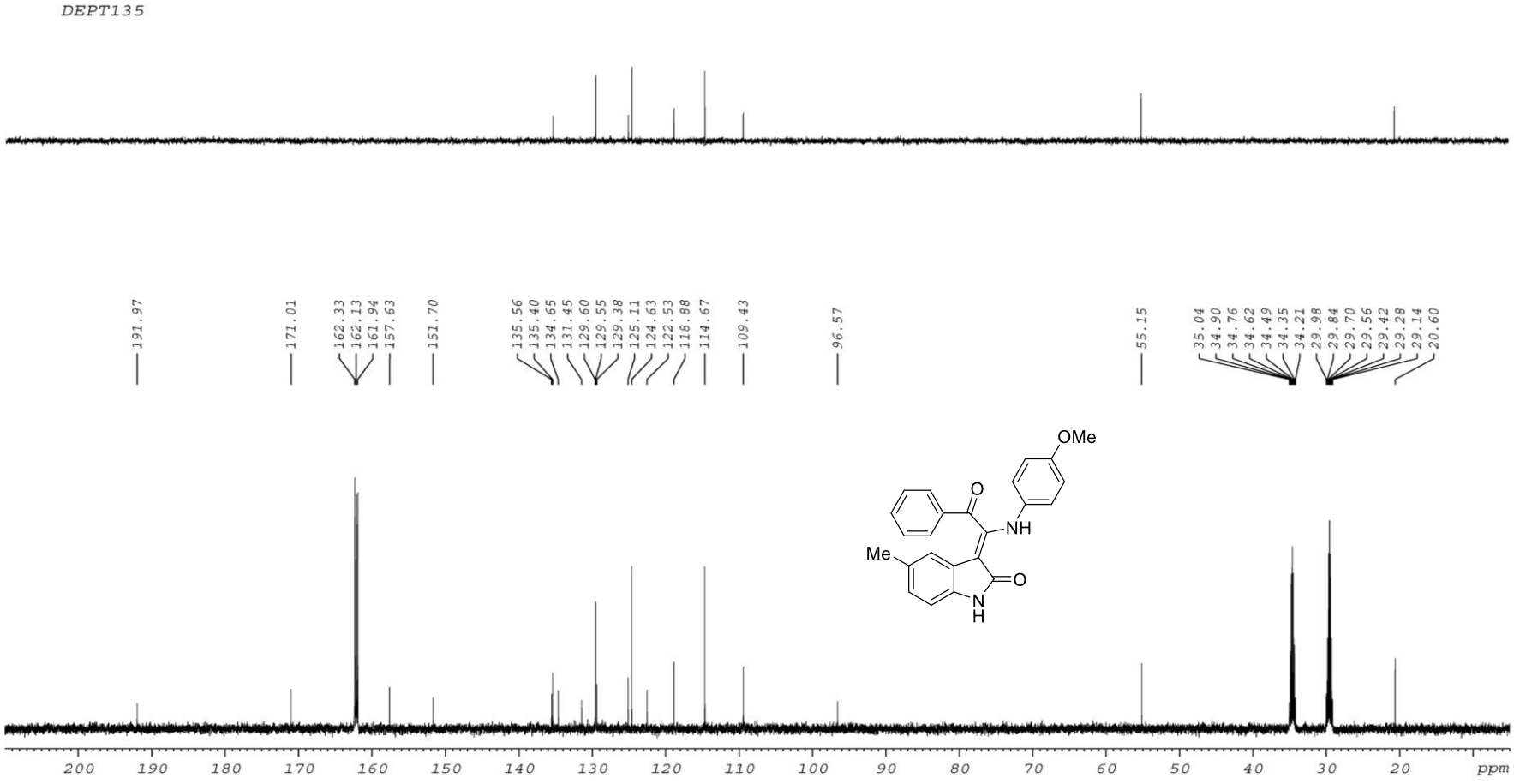


Figure S74. ^{13}C NMR (150 MHz, DMF-d_7) spectra of compound **3fe**

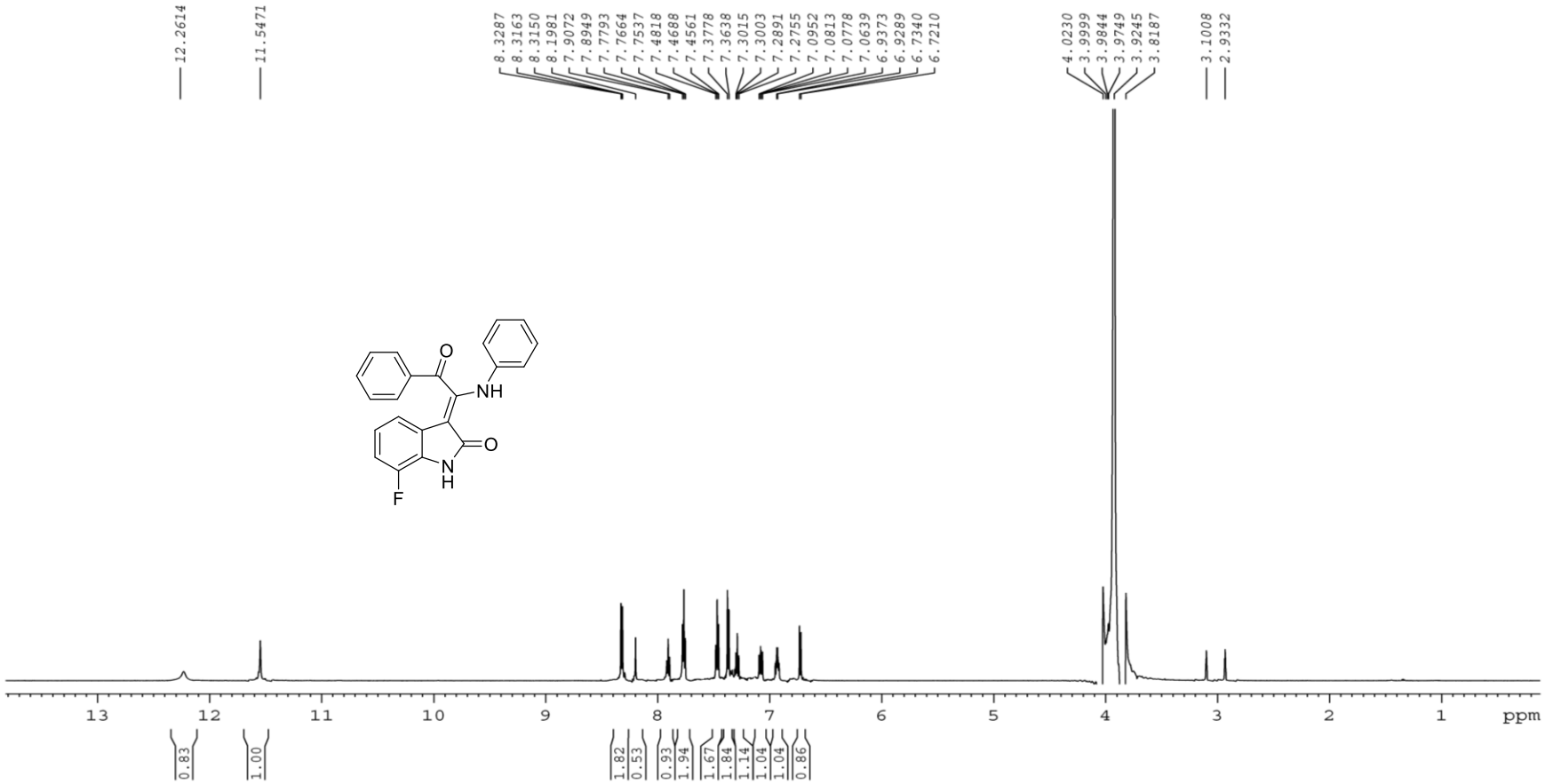


Figure S75. ^{1}H NMR (600 MHz, DMF-d_7) spectra of compound **3ga**

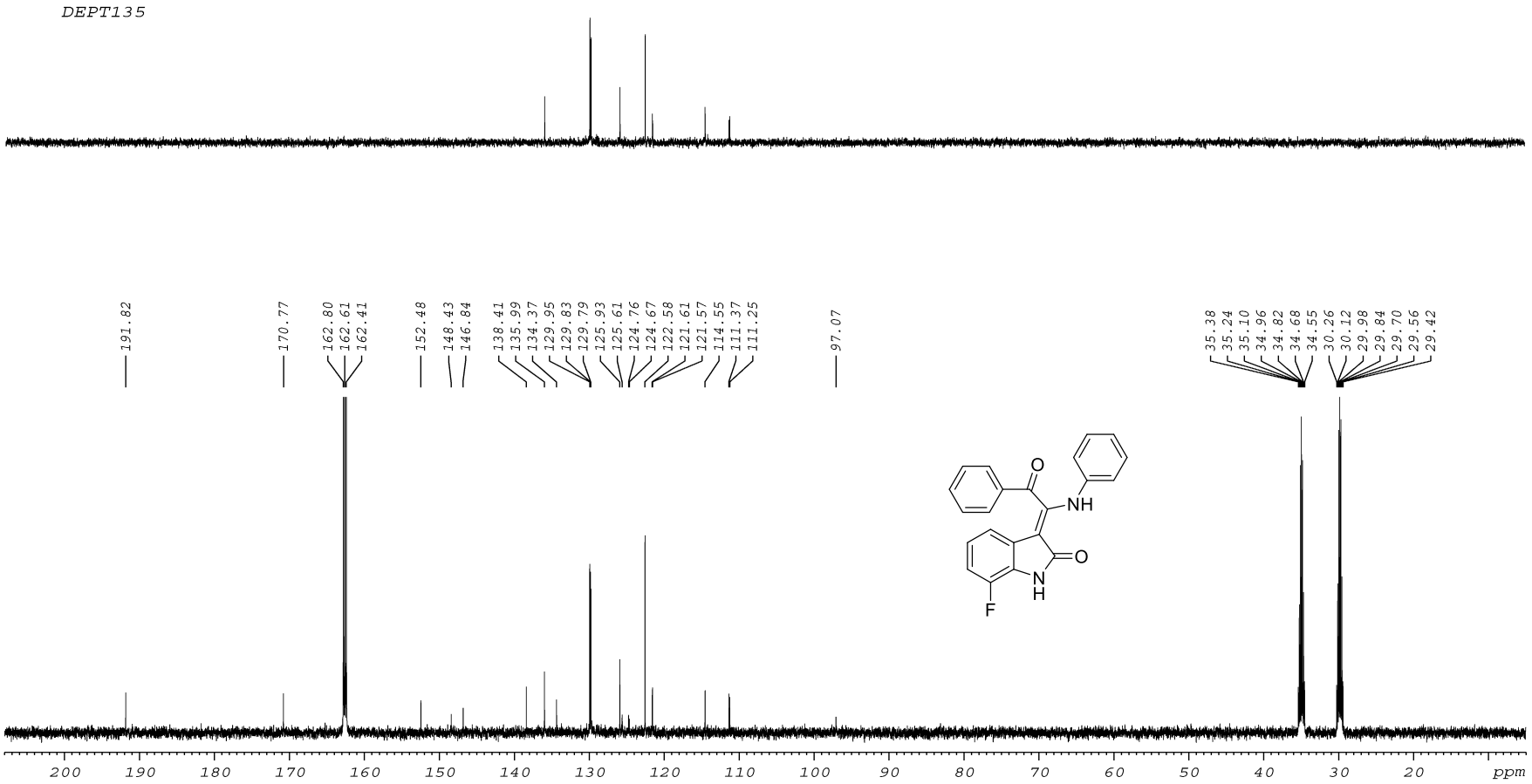


Figure S76. ^{13}C NMR (150 MHz, DMF-d_7) spectra of compound **3ga**

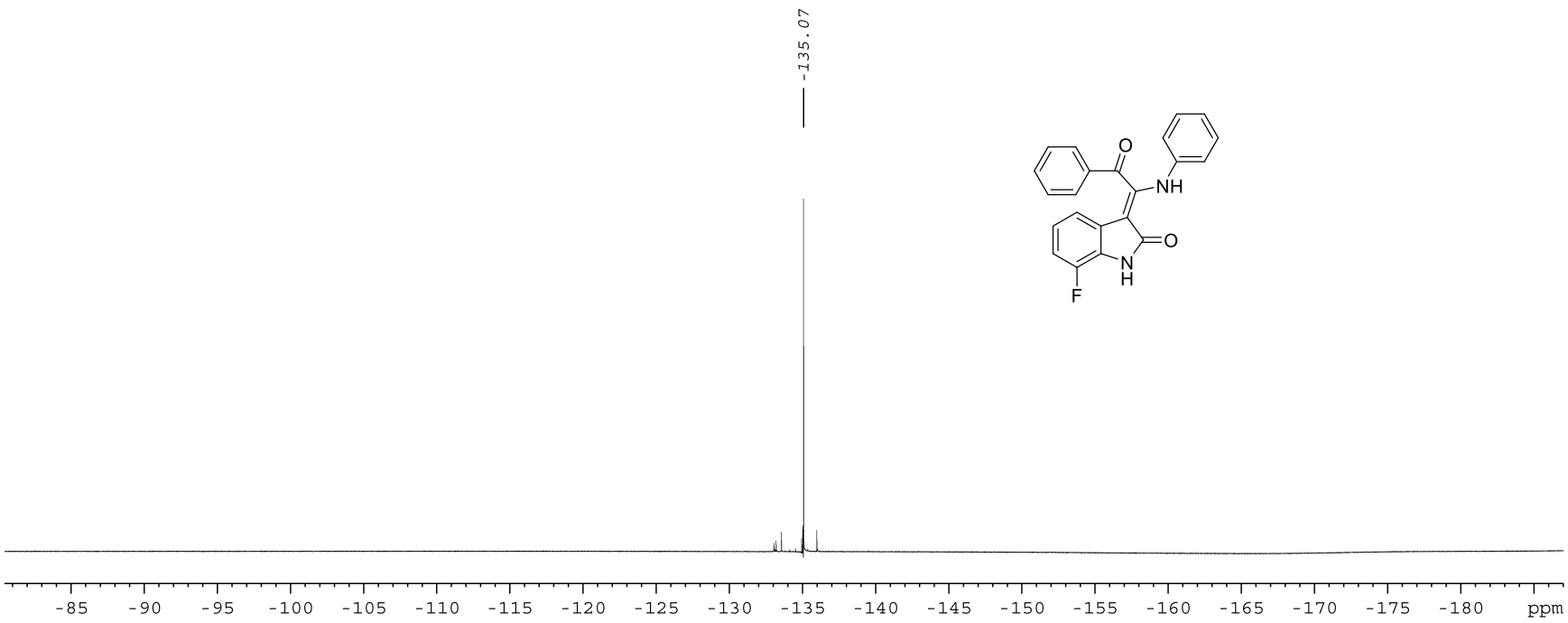


Figure S77. ^{19}F NMR (470 MHz, DMF-d_7) spectra of compound **3ga**

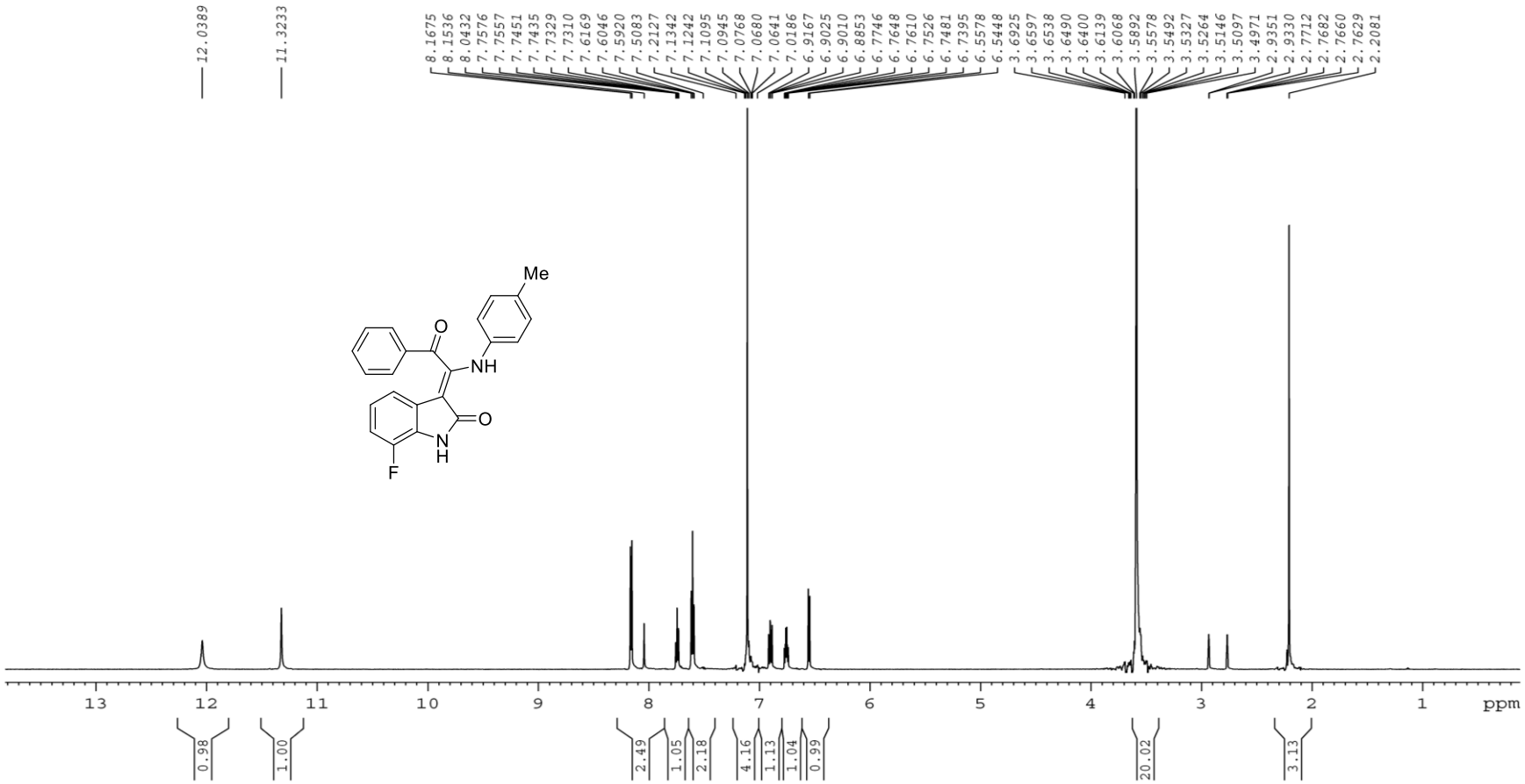


Figure S78. ^{1}H NMR (600 MHz, DMF-d_7) spectra of compound **3gd**

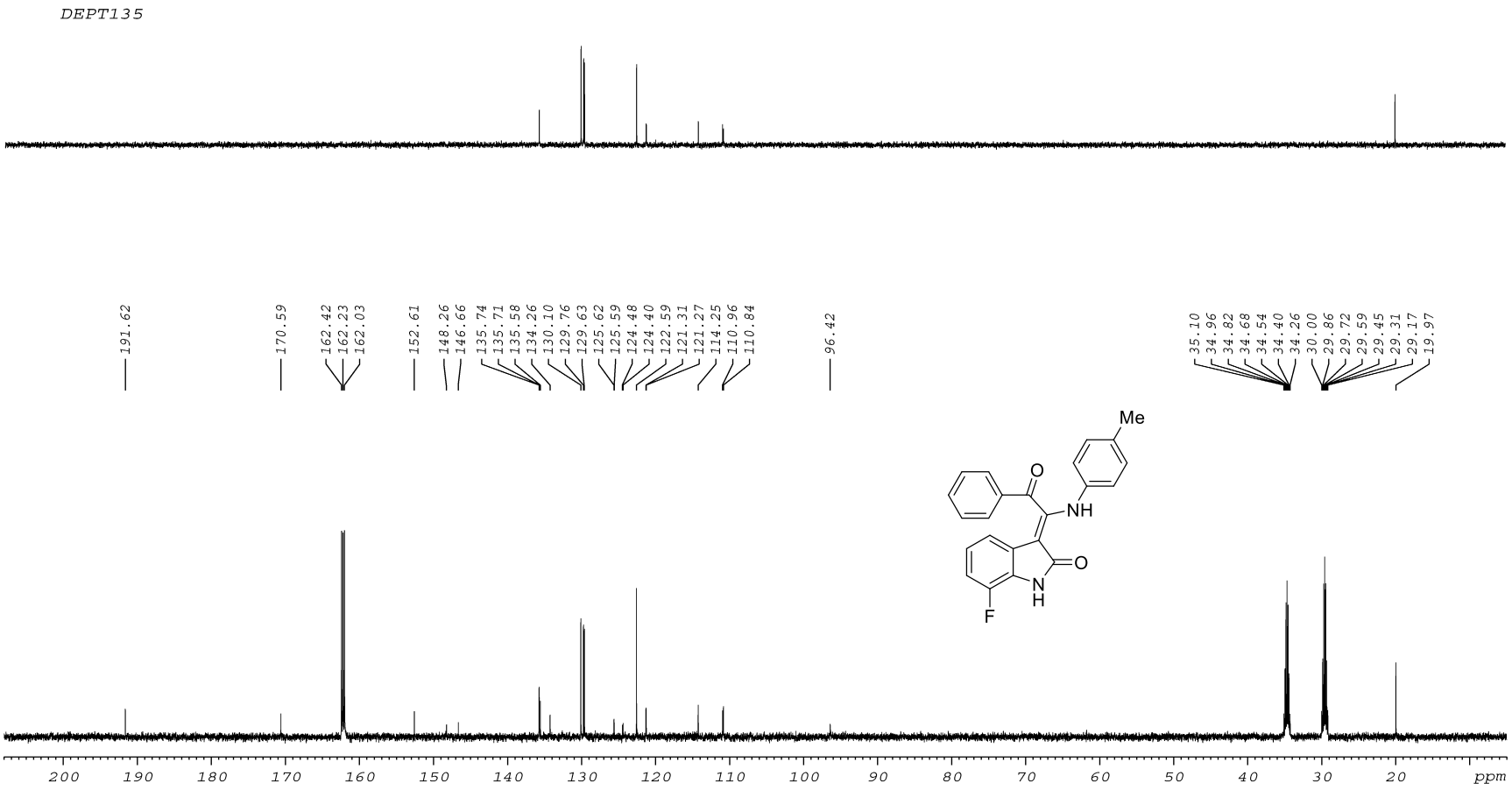


Figure S79. ^{13}C NMR (150 MHz, DMF-d_7) spectra of compound **3gd**

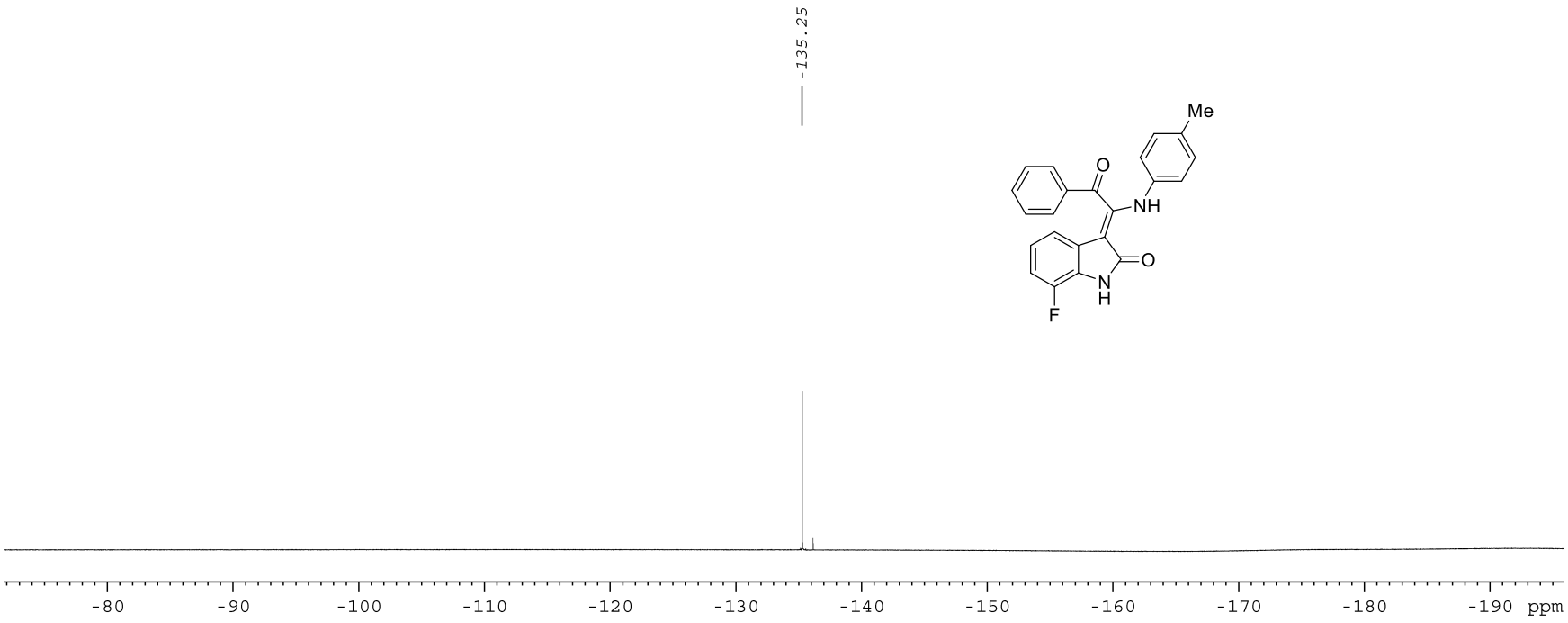


Figure S80. ^{19}F NMR (470 MHz, DMF-d_7) spectra of compound **3gd**

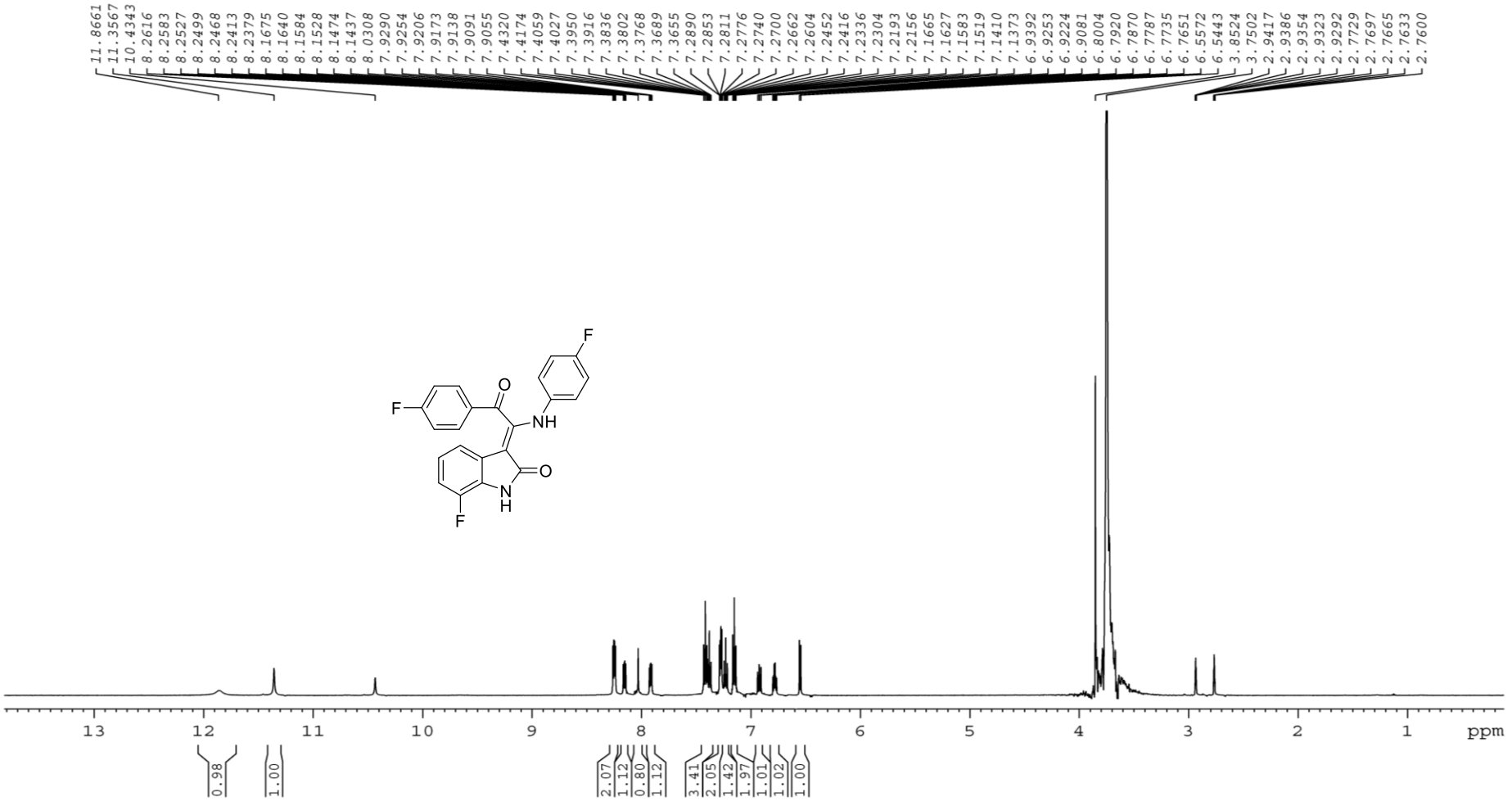


Figure S81. ^{1}H NMR (600 MHz, DMF-d_7) spectra of compound **3gf**

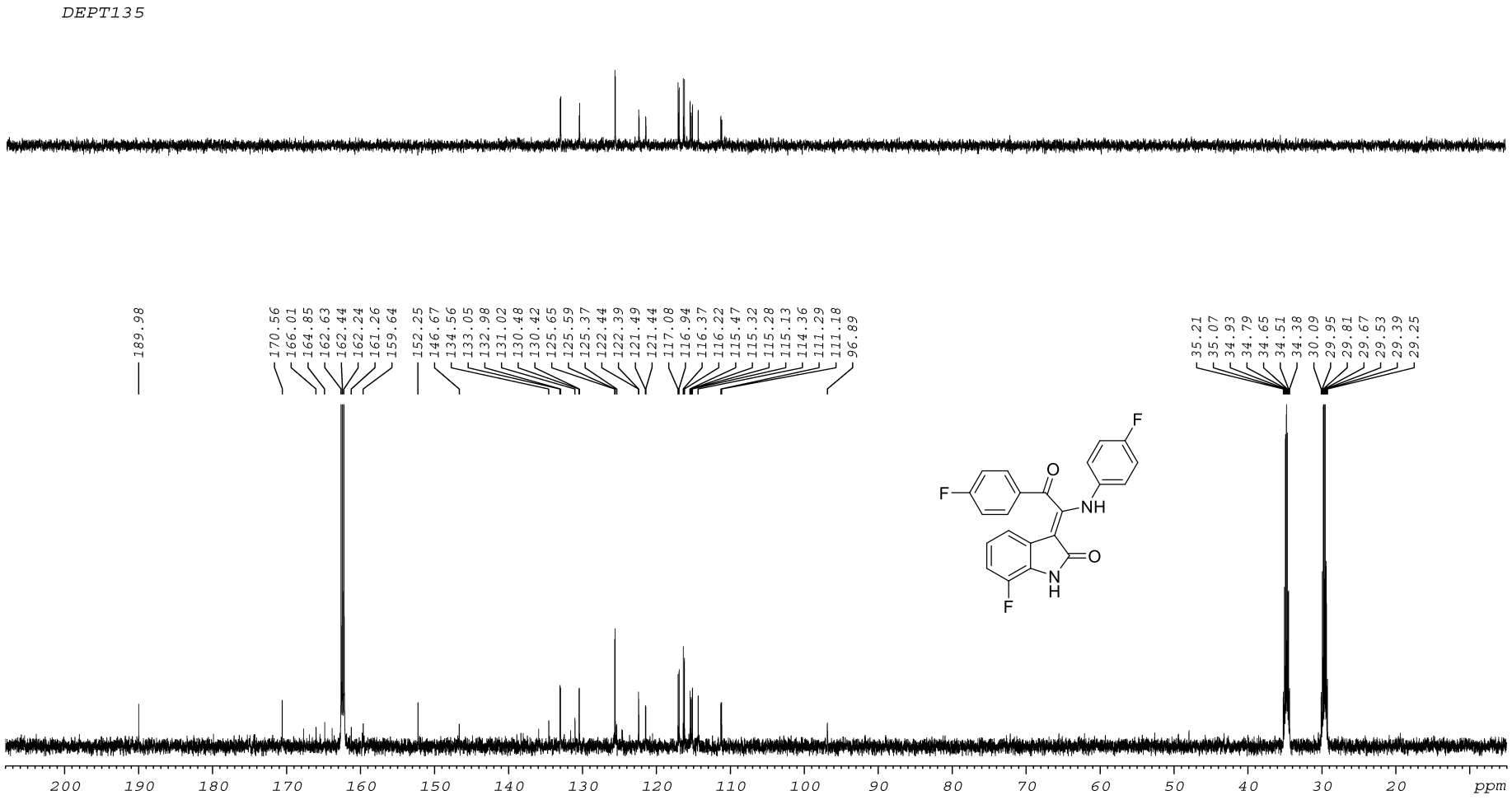


Figure S82. ^{13}C NMR (150 MHz, DMF-d_7) spectra of compound **3gf**

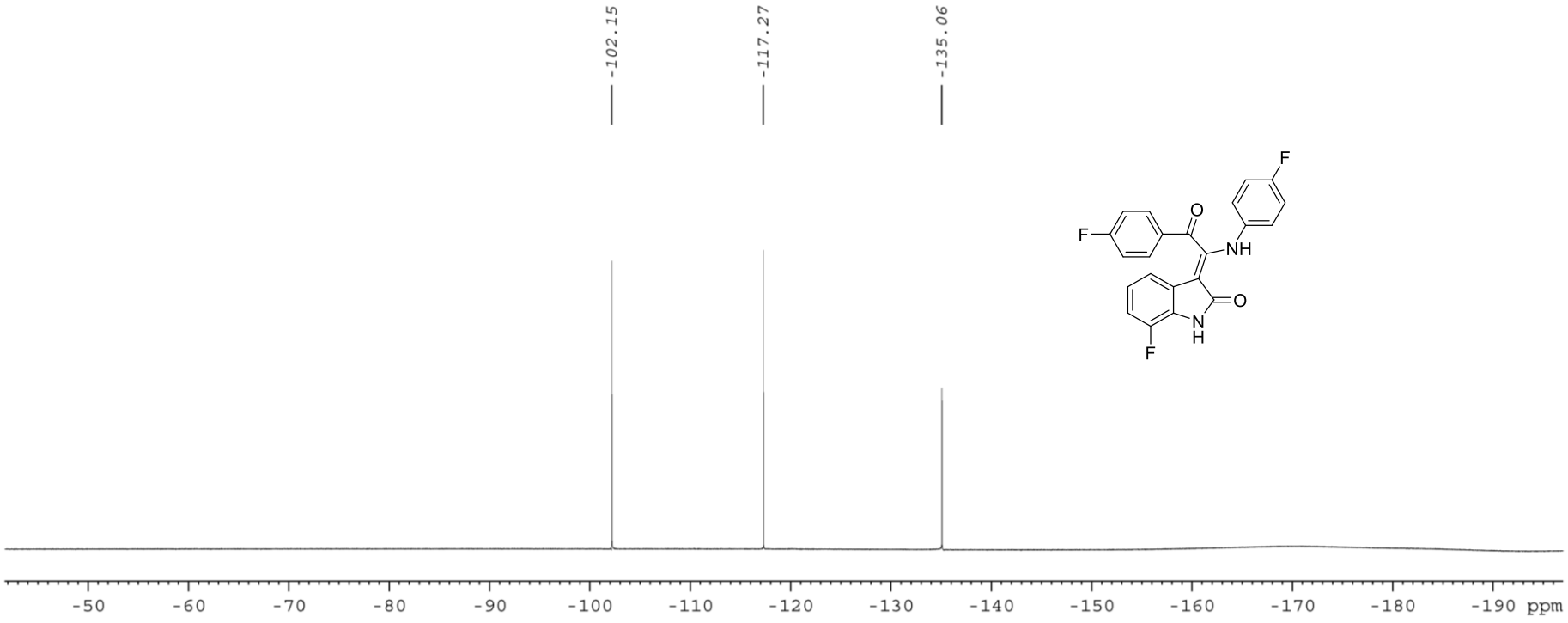


Figure S83. ^{19}F NMR (470 MHz, DMF-d_7) spectra of compound **3gf**

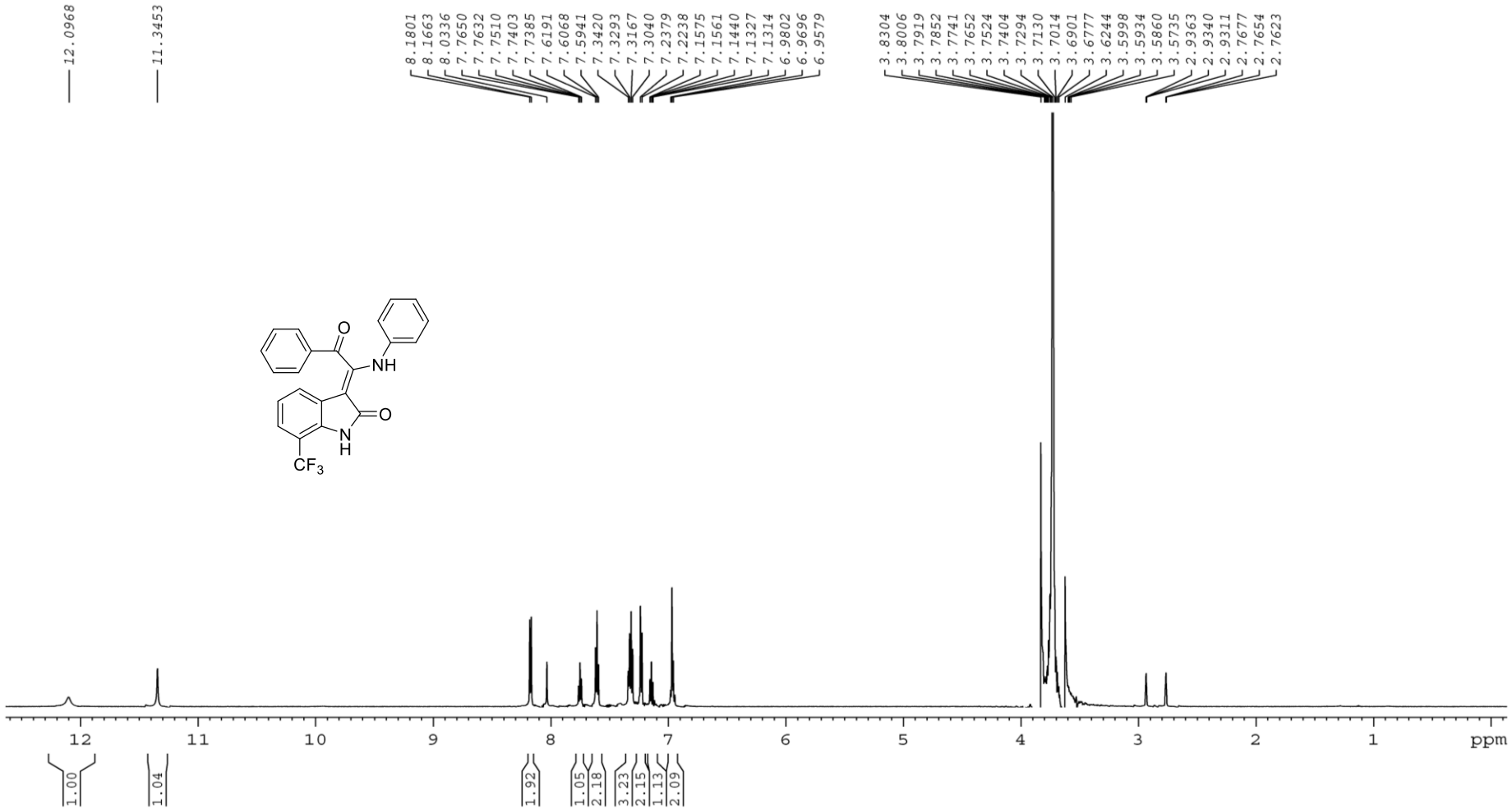


Figure S84. ^{1}H NMR (600 MHz, DMF-d_7) spectra of compound **3ha**

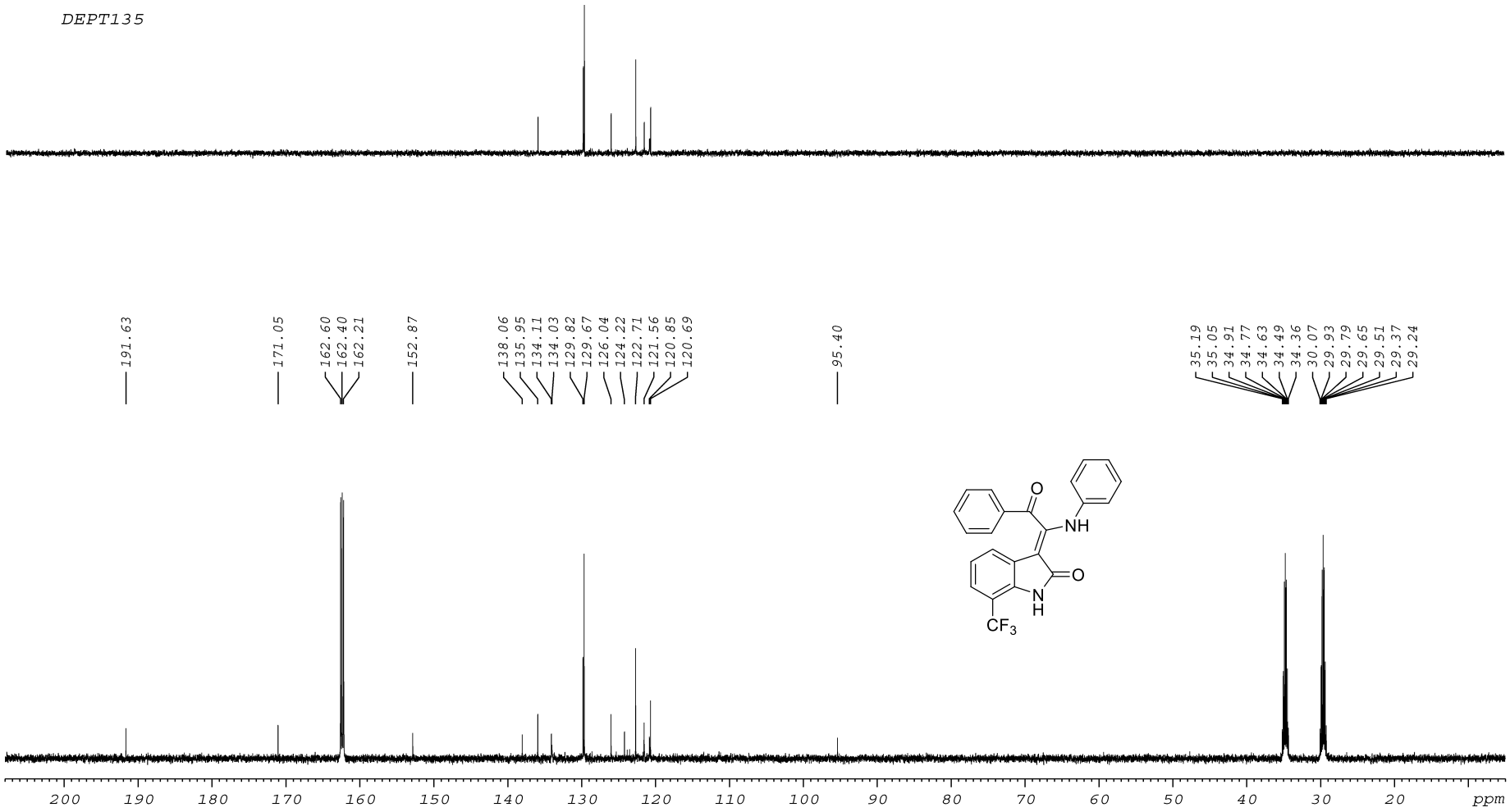


Figure S85. ^{13}C NMR (150 MHz, DMF-d_7) spectra of compound **3ha**

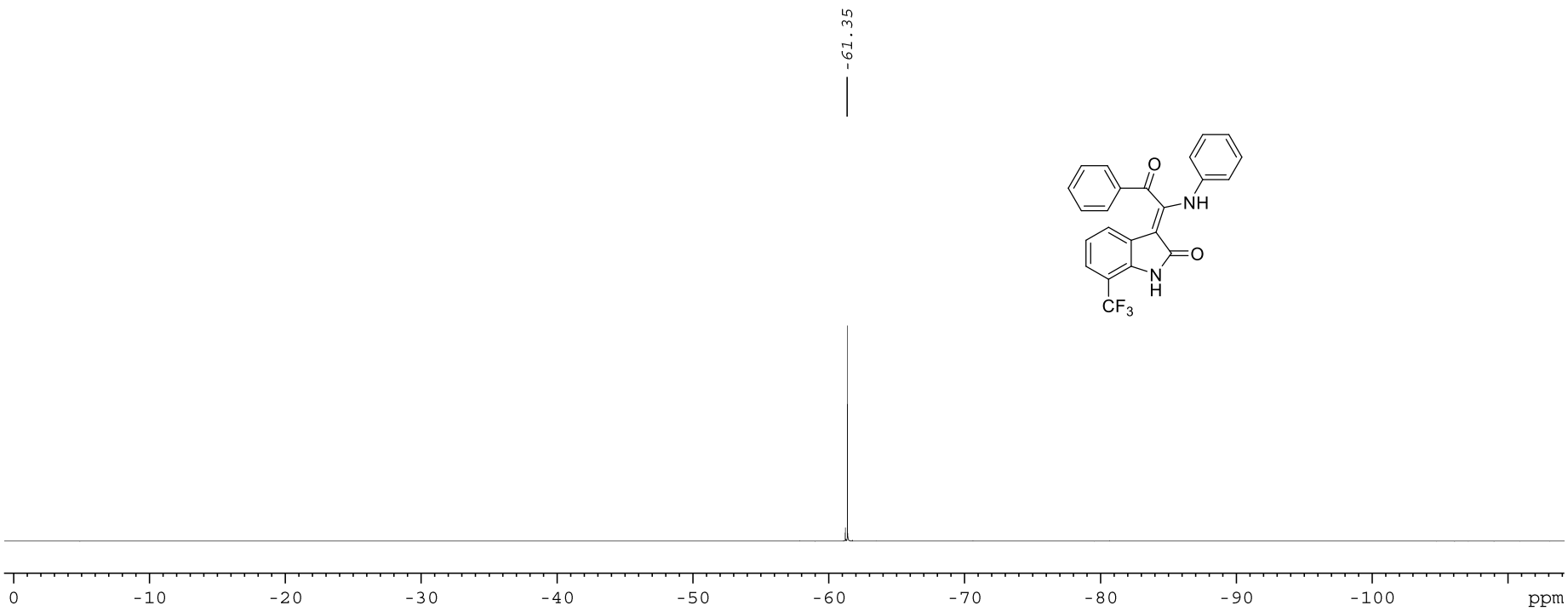


Figure S86. ^{19}F NMR (470 MHz, DMF-d_7) spectra of compound **3ha**

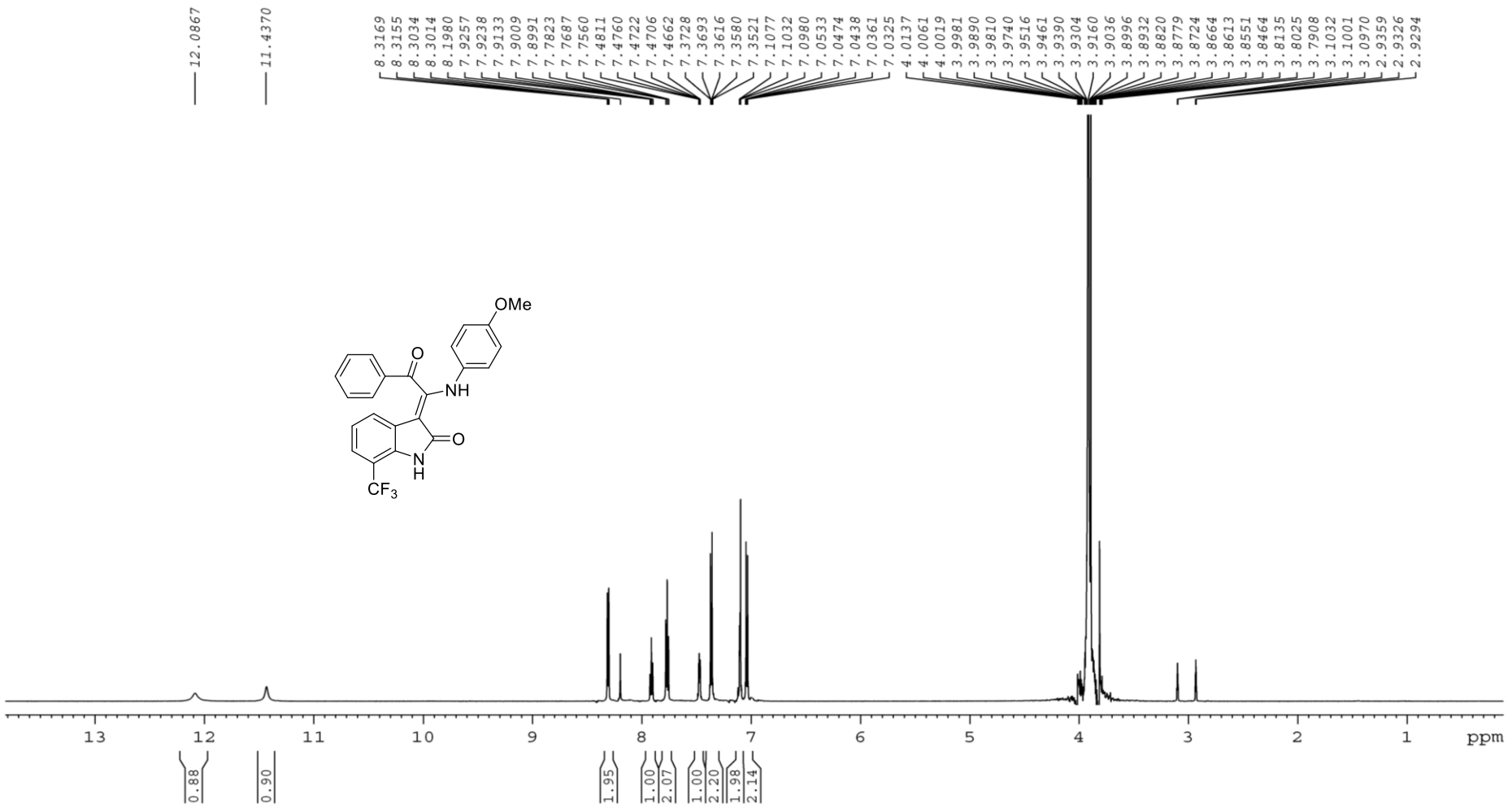


Figure S87. ^{1}H NMR (600 MHz, DMF-d_7) spectra of compound **3he**

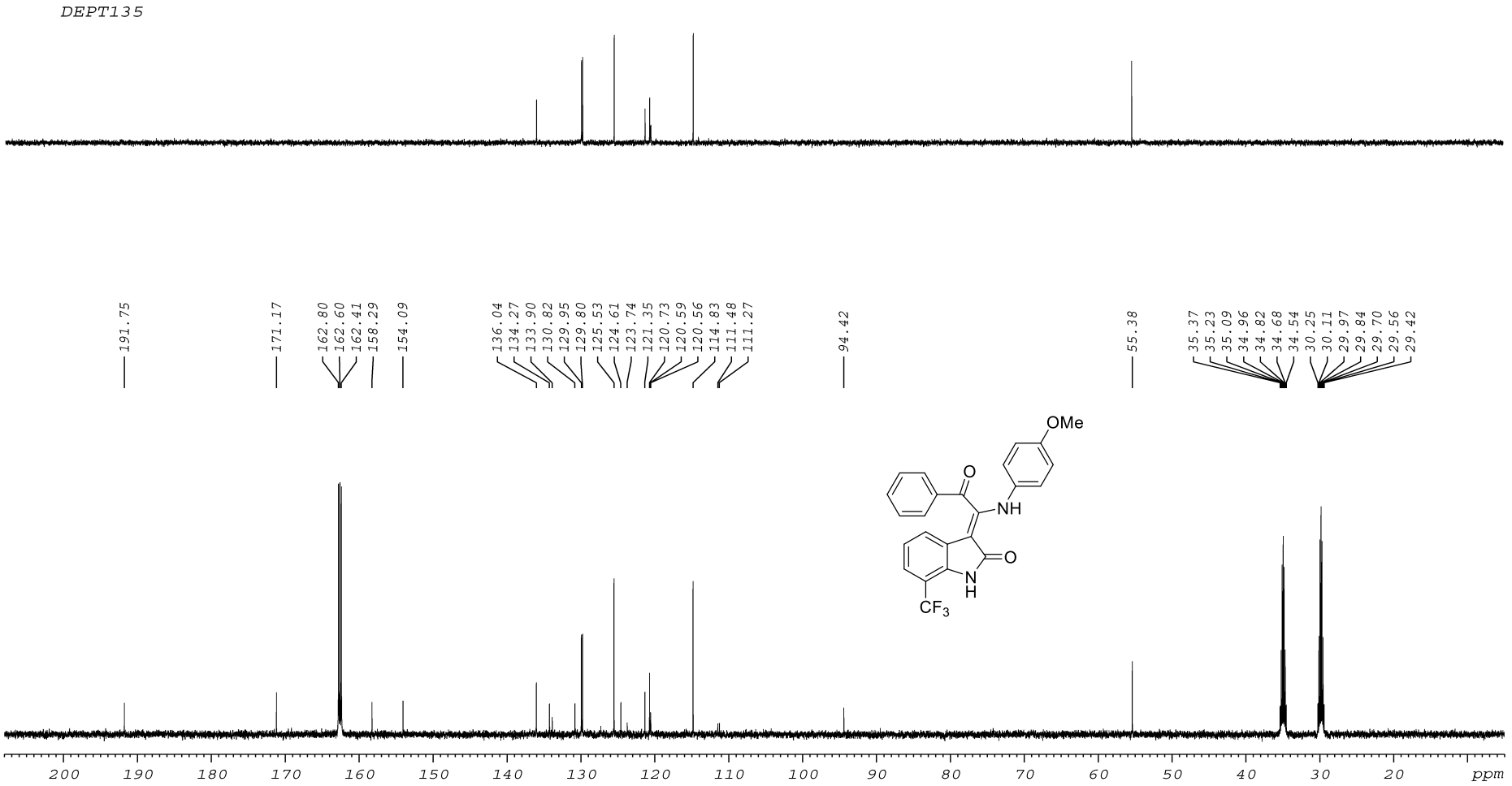


Figure S88. ^{13}C NMR (150 MHz, DMF-d_7) spectra of compound **3he**

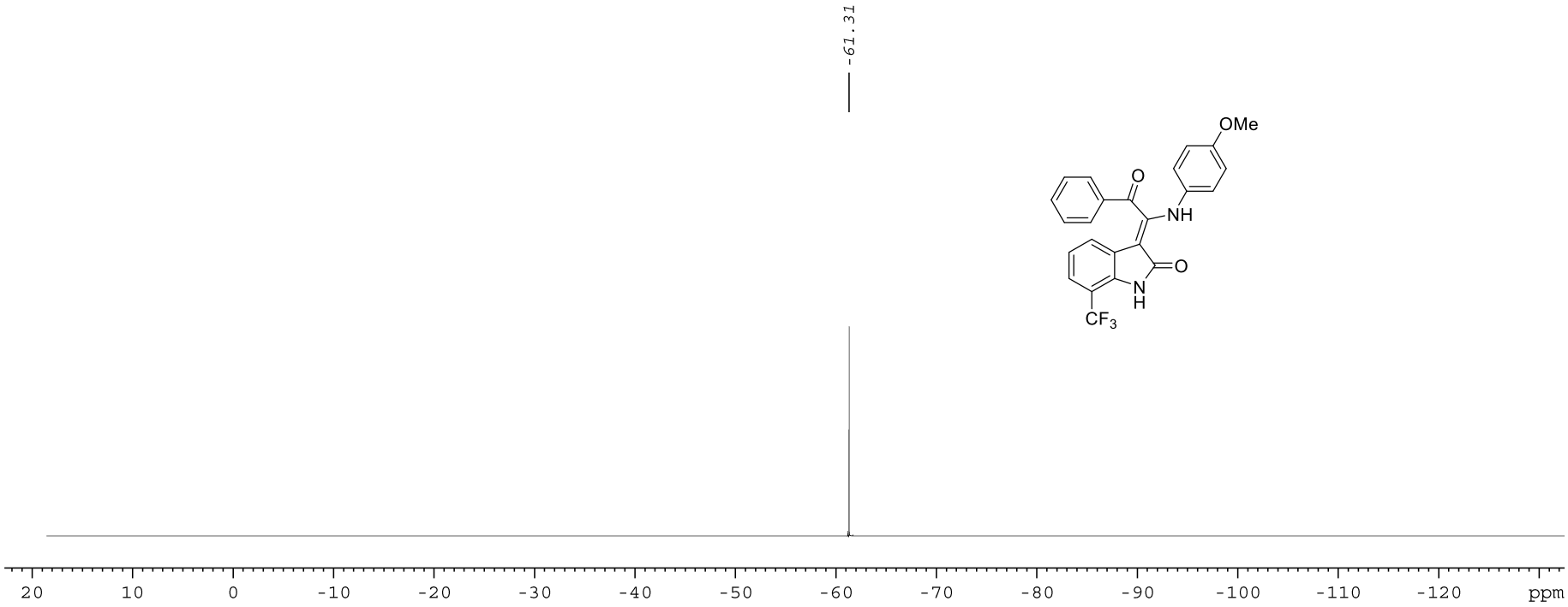


Figure S89. ^{19}F NMR (470 MHz, DMF-d_7) spectra of compound **3he**

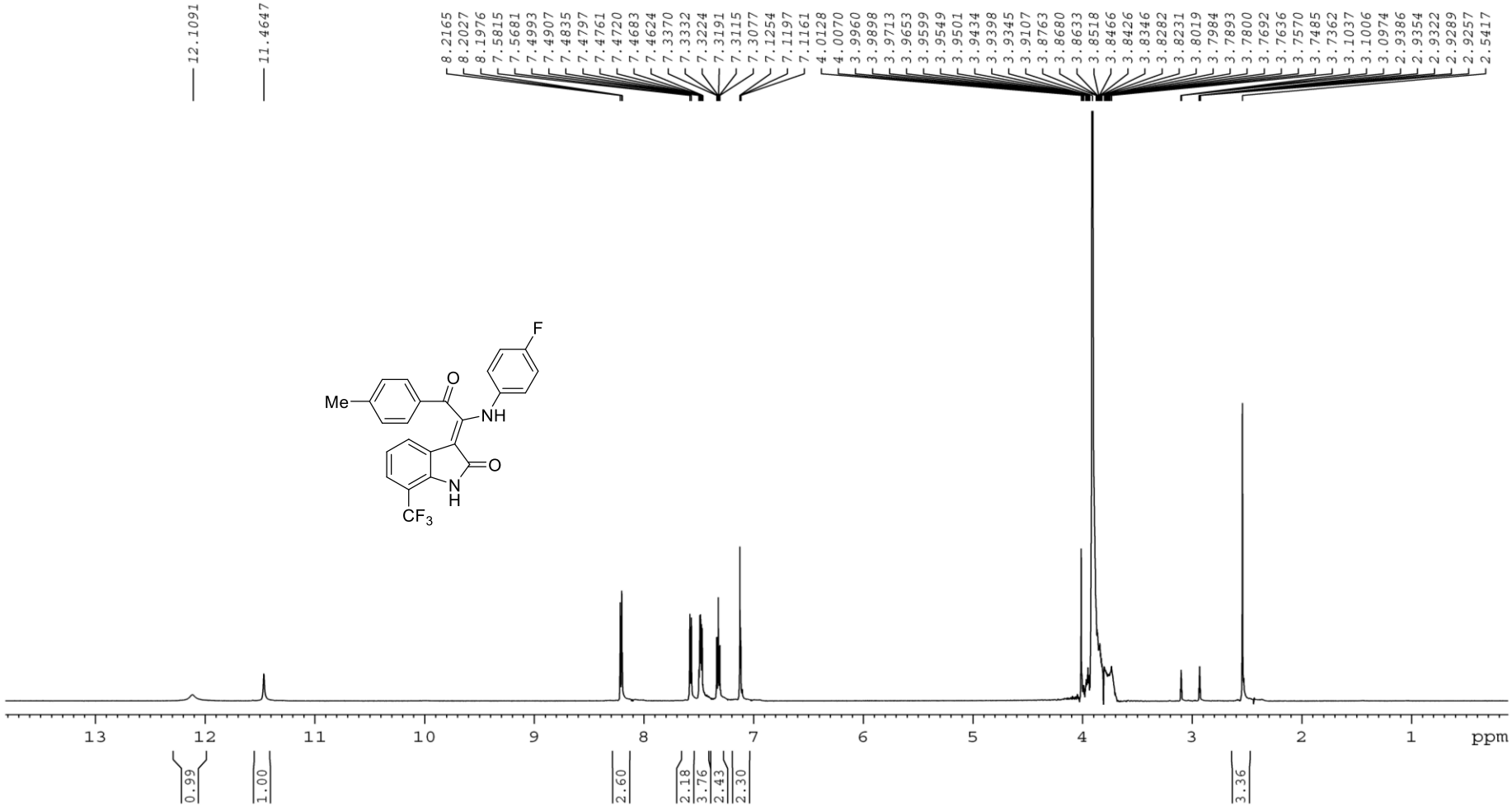


Figure S90. ^{1}H NMR (600 MHz, DMF-d_7) spectra of compound **3hg**

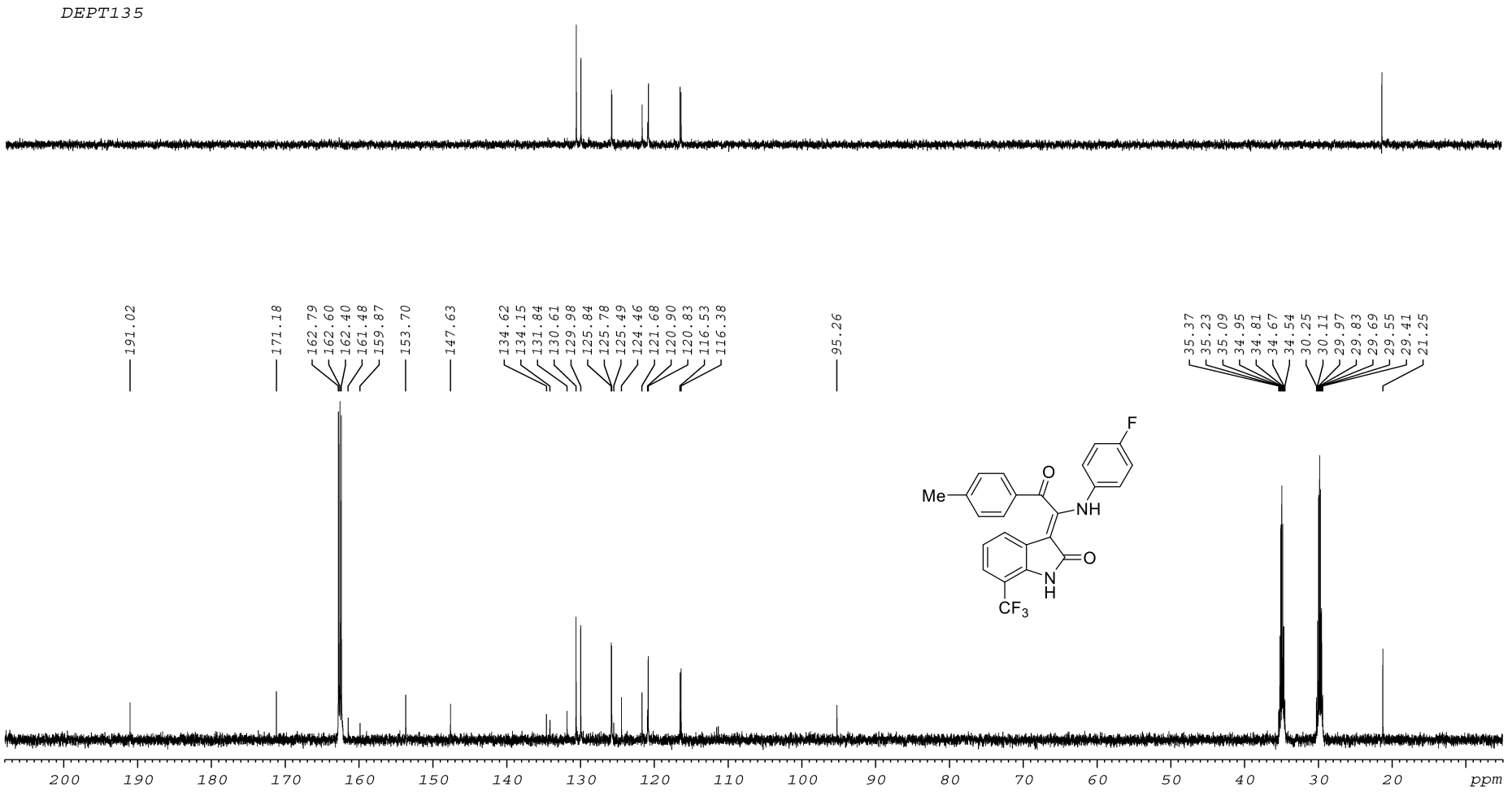


Figure S91. ^{13}C NMR (150 MHz, DMF-d_7) spectra of compound **3hg**

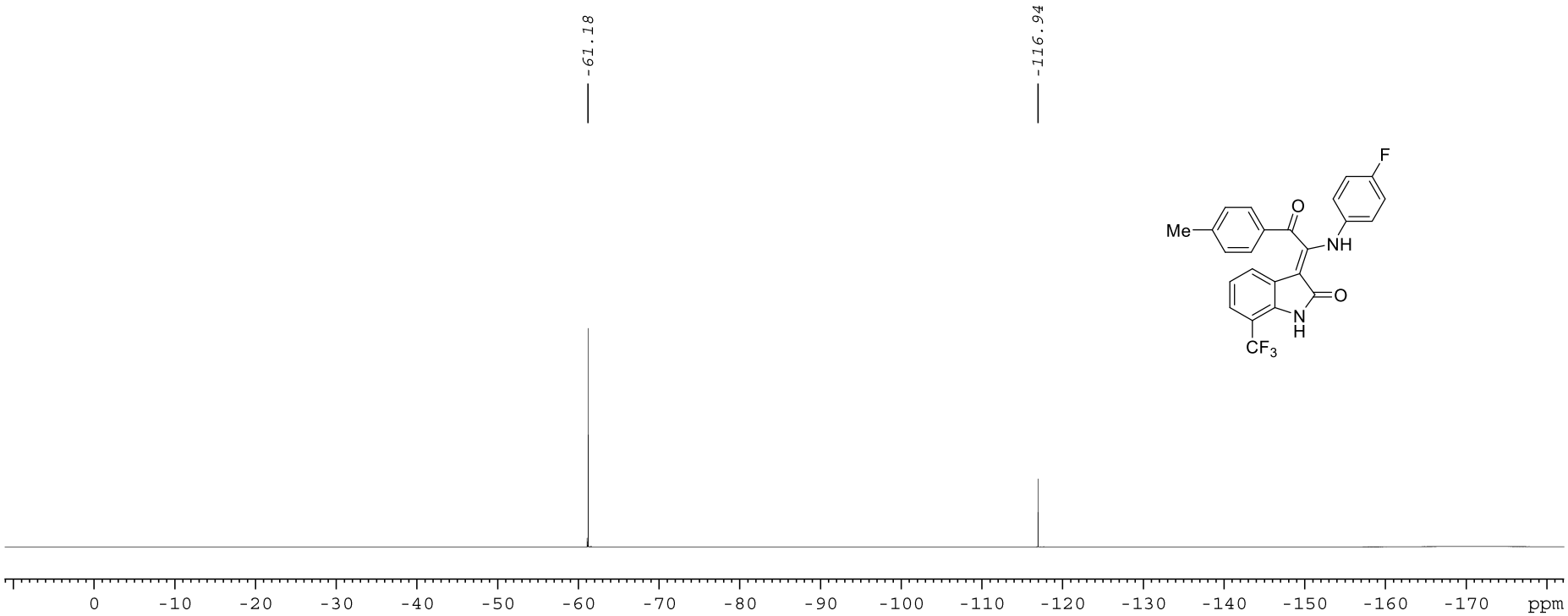


Figure S92. ^{19}F NMR (470 MHz, DMF-d_7) spectra of compound **3hg**

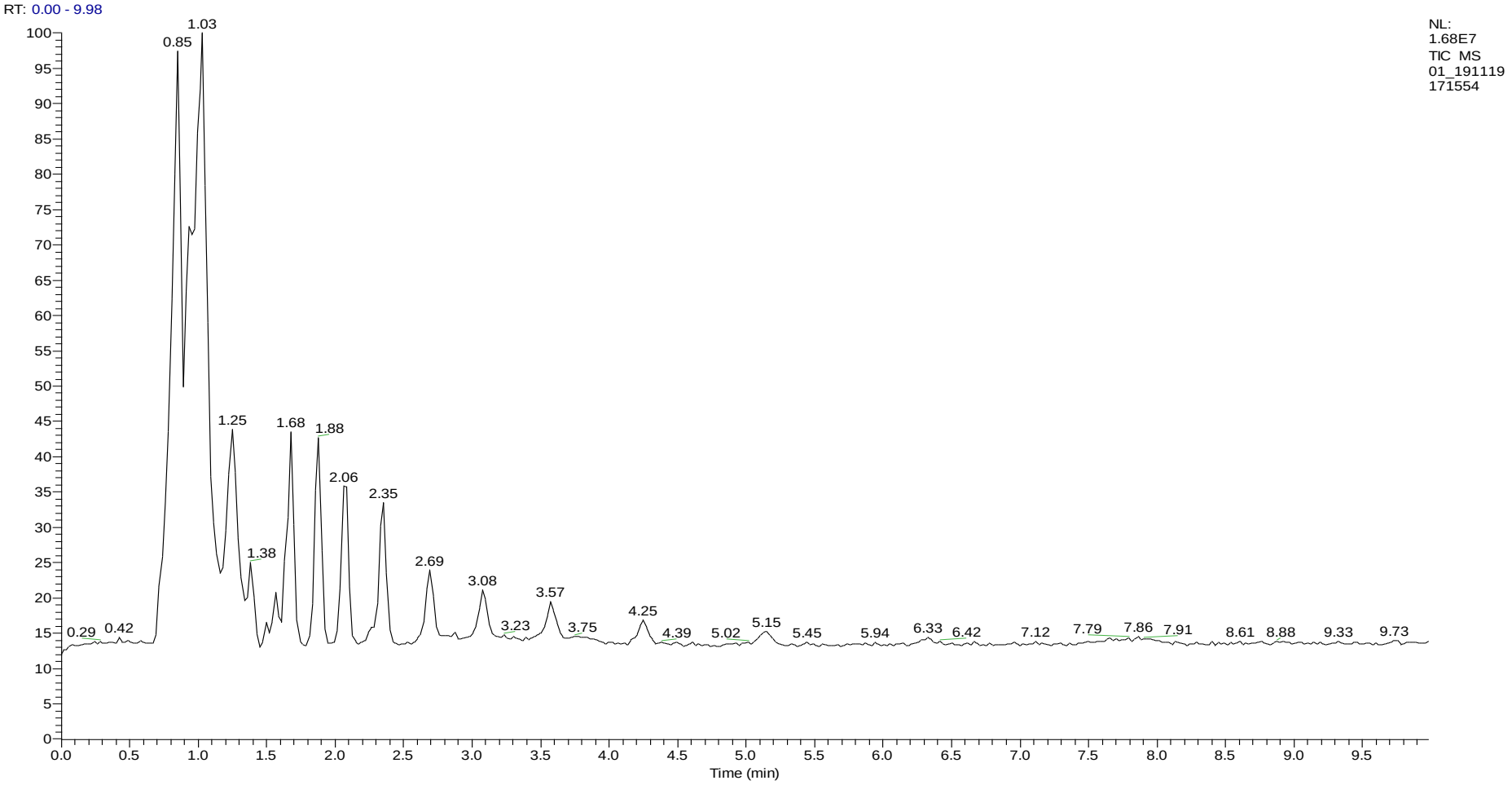


Figure S93. HPLC total ion flow diagram of the reaction mixture

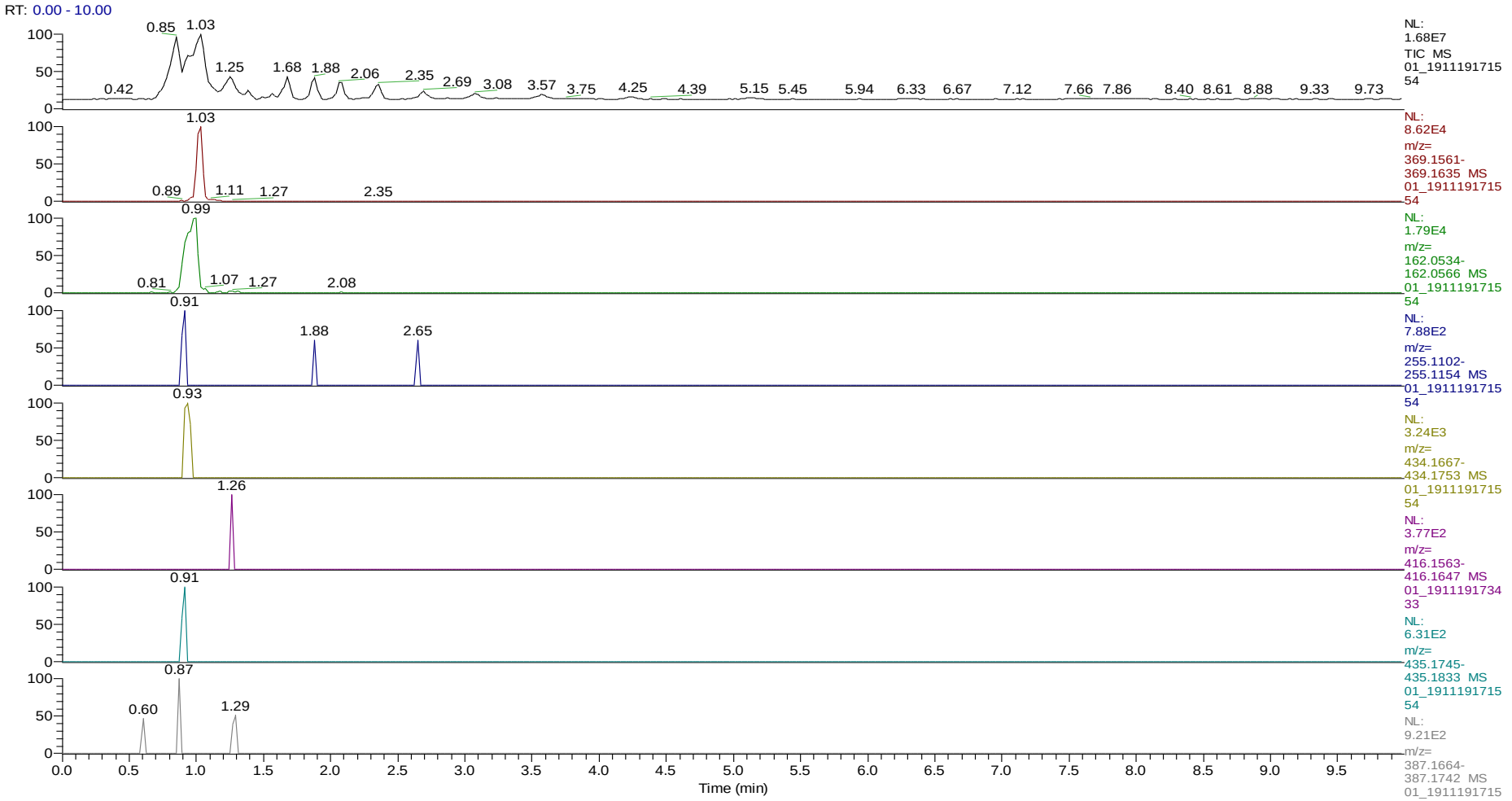


Figure S94. HPLC extracted ion flow diagrams of the reaction mixture

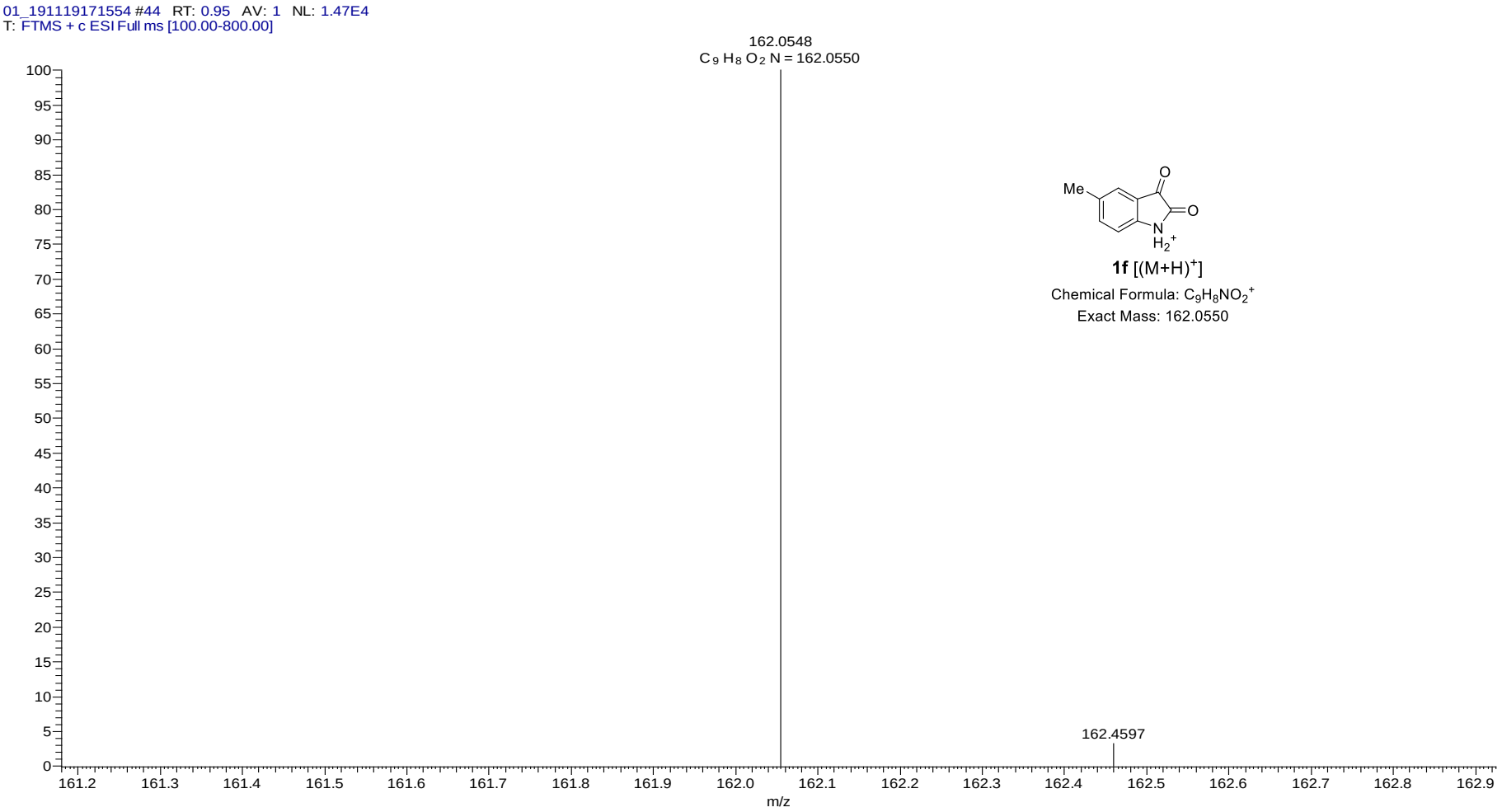


Figure S95. HPLC of the substrate **1f**

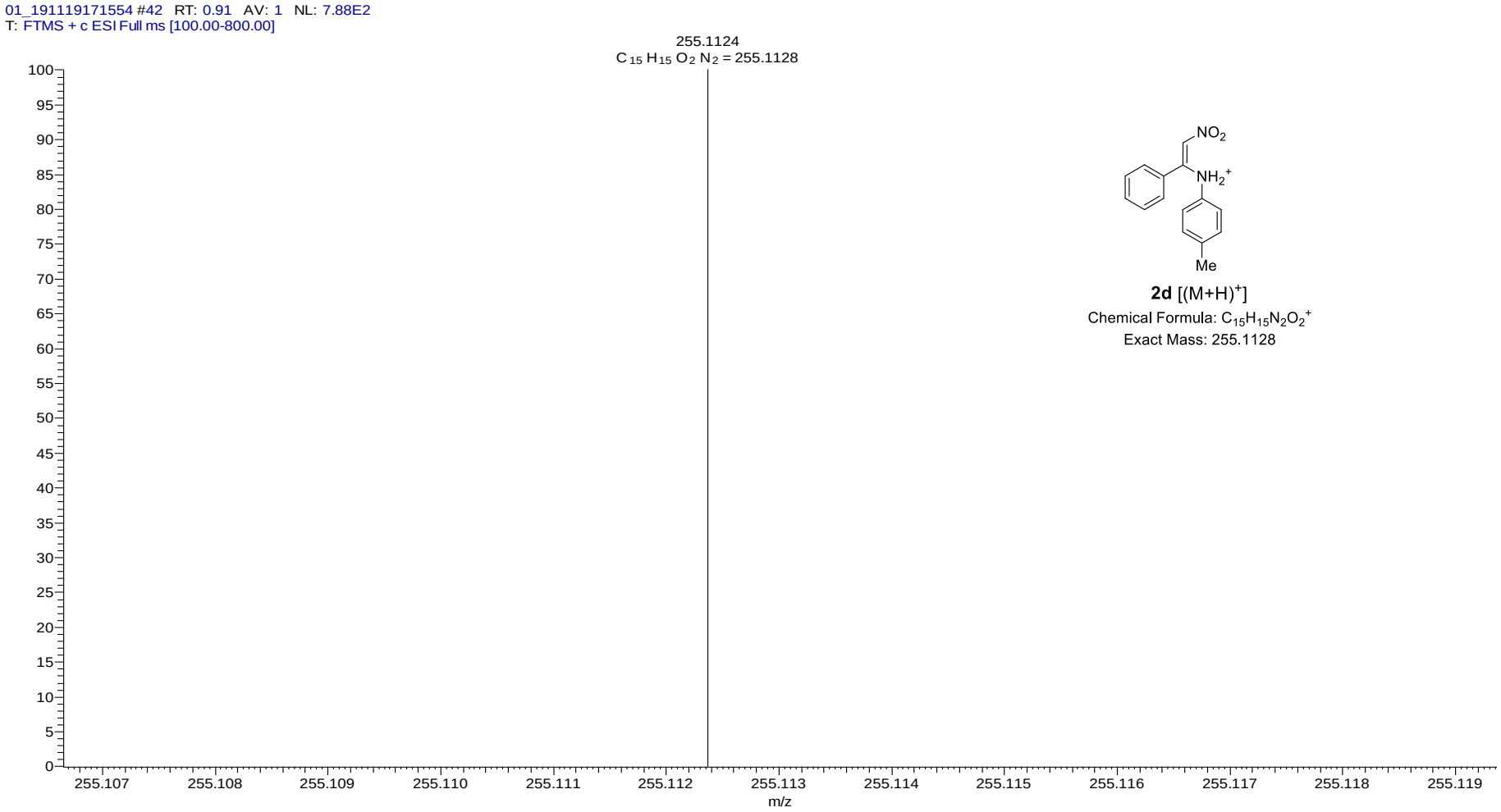


Figure S96. HPLC of the substrate **2d**

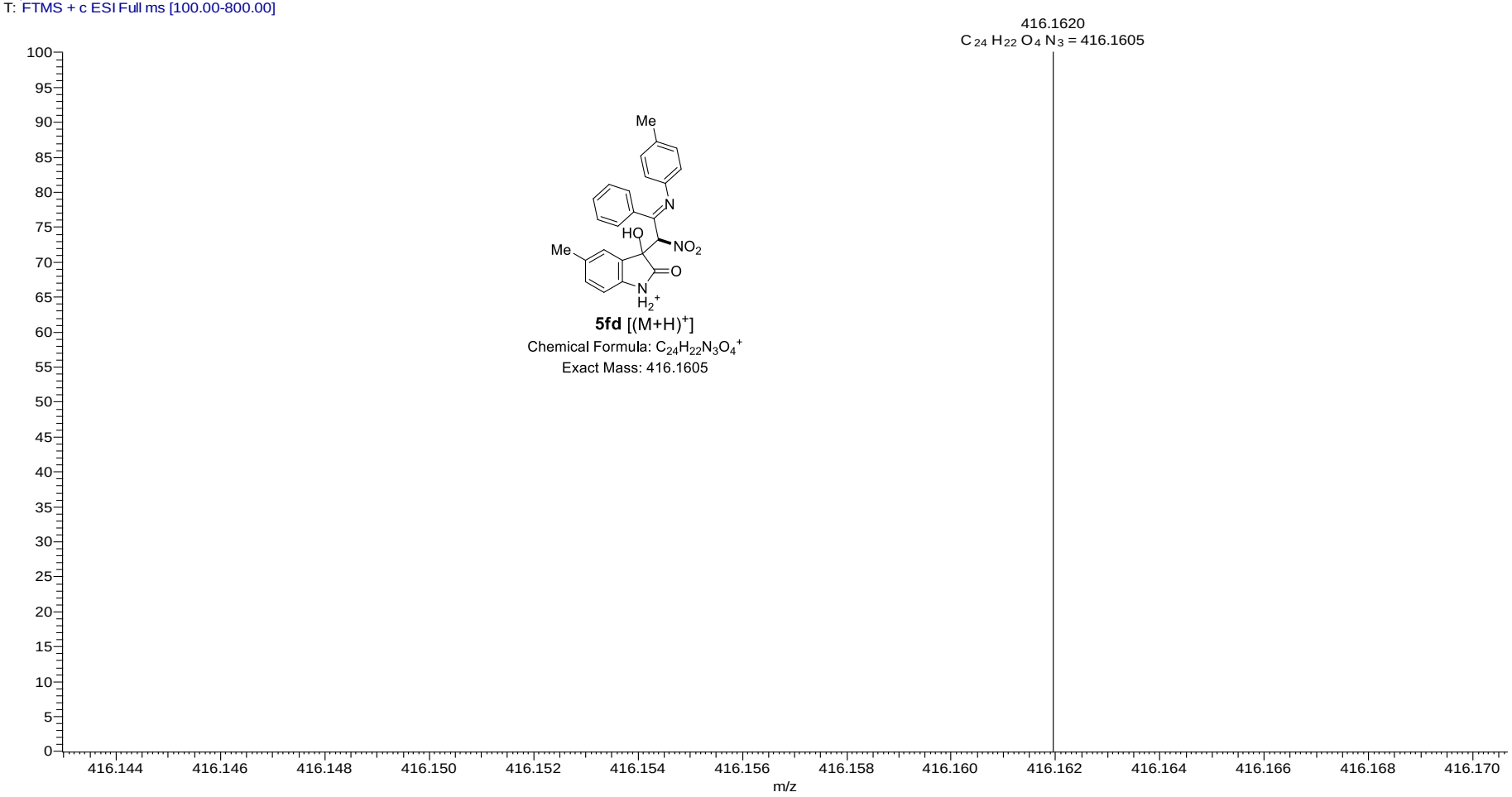


Figure S97. HPLC of the intermediate **5fd**

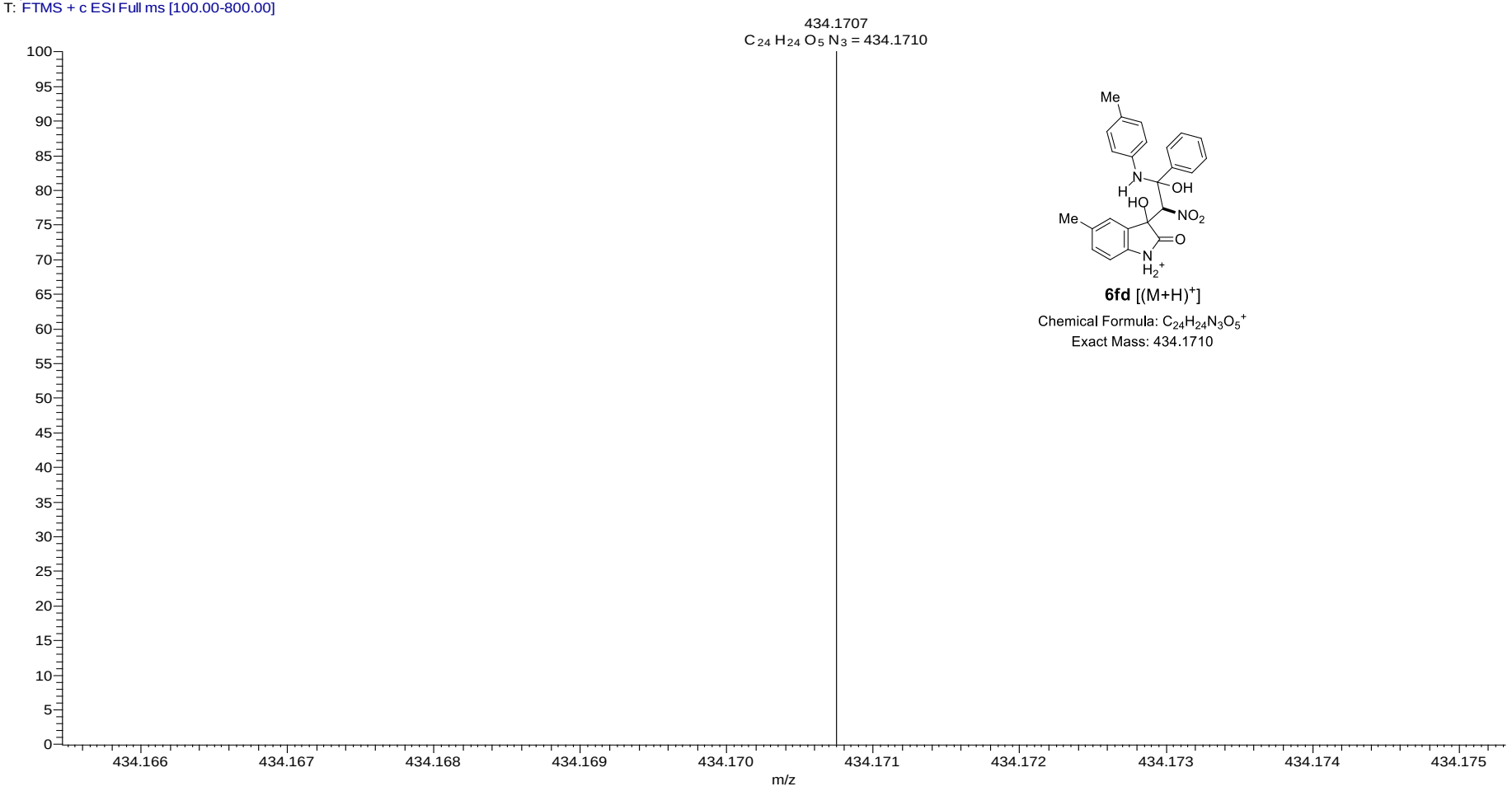


Figure S98. HPLC of the intermediate **6fd**

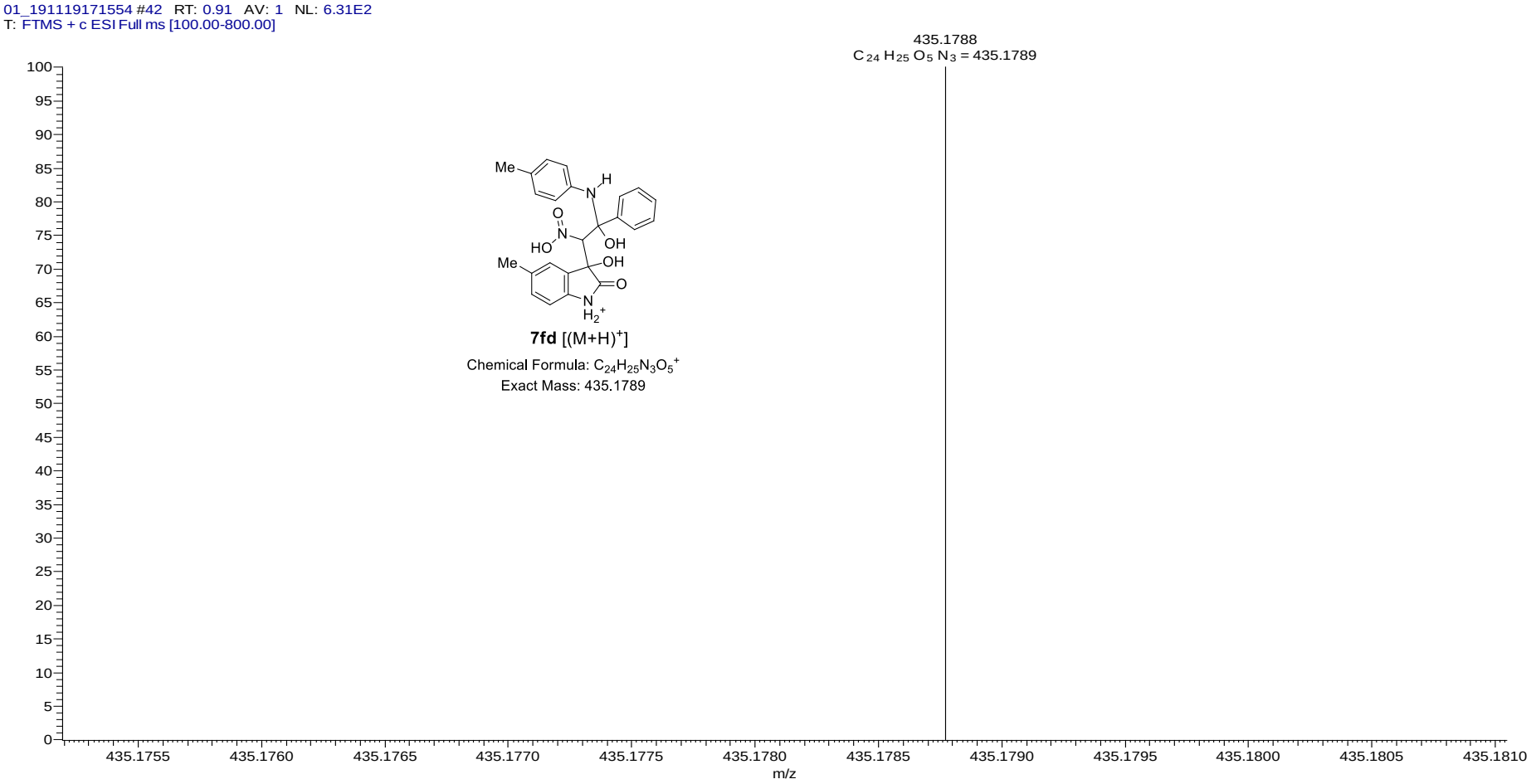


Figure S99. HPLC of the intermediate **7fd**

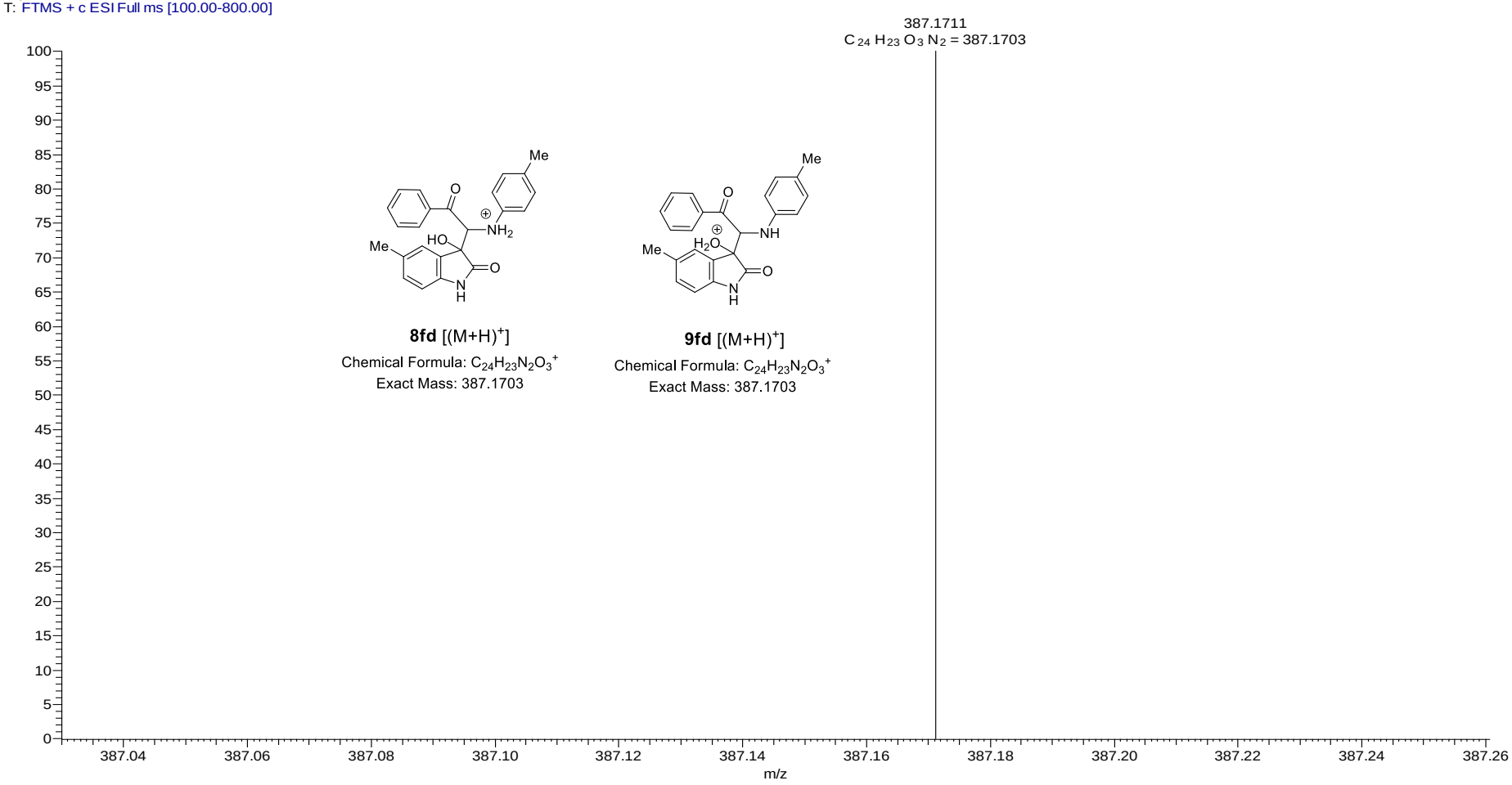


Figure S100. HPLC of the intermediate **8fd** or **9fd**

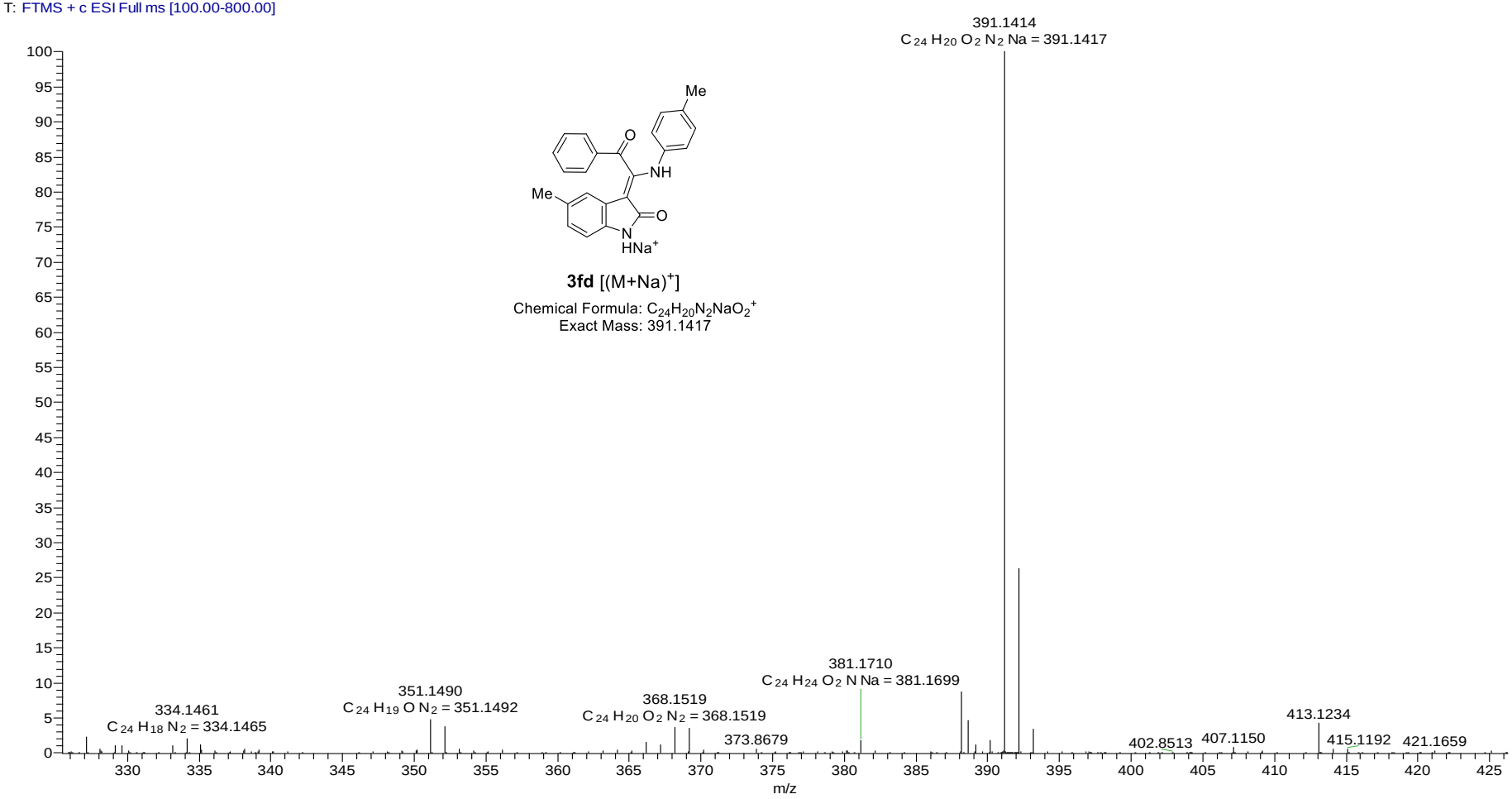


Figure S101. HPLC of the target compound **3fd**

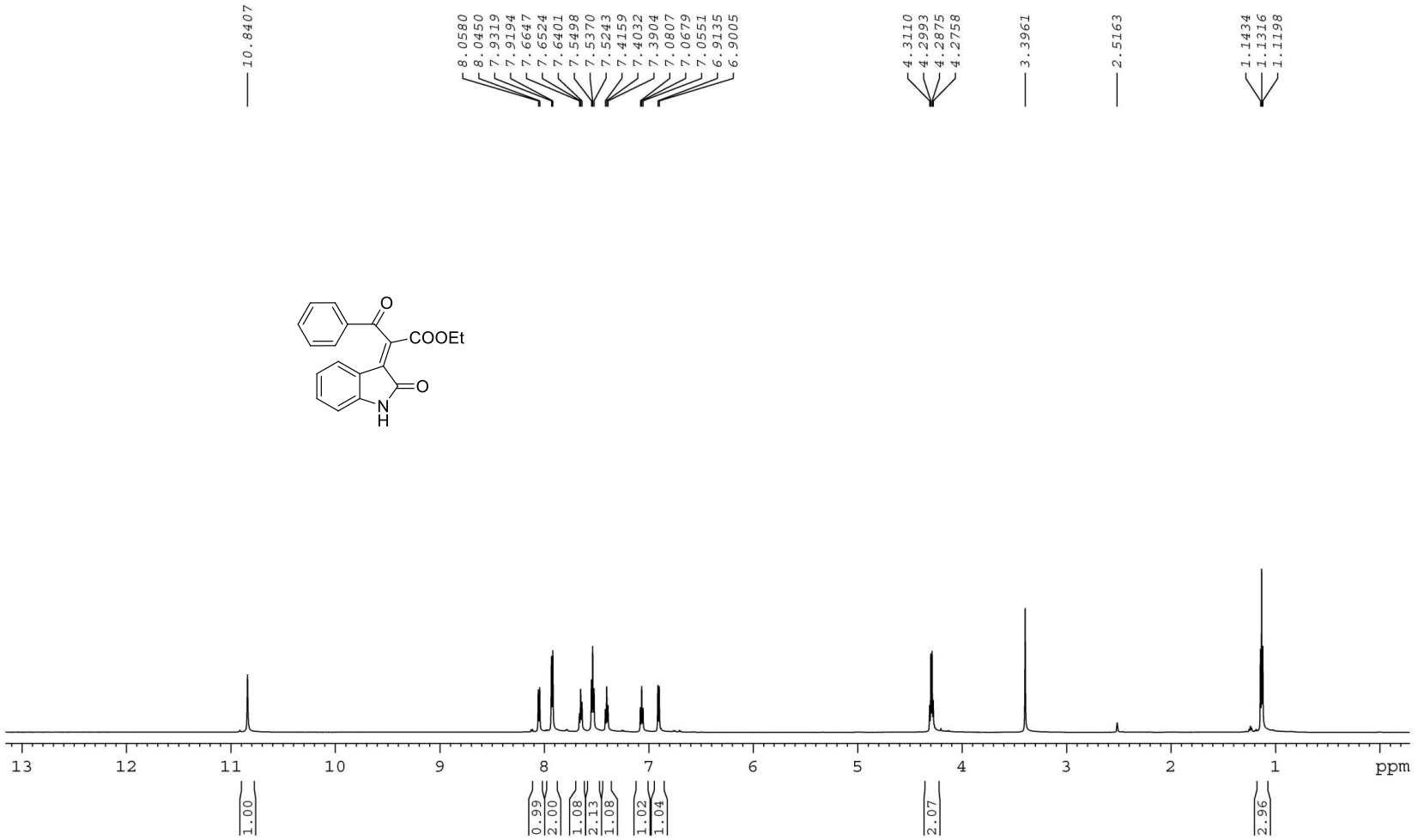


Figure S102. ^{1}H NMR (600 MHz, DMF-d_7) spectra of compound **3ai**

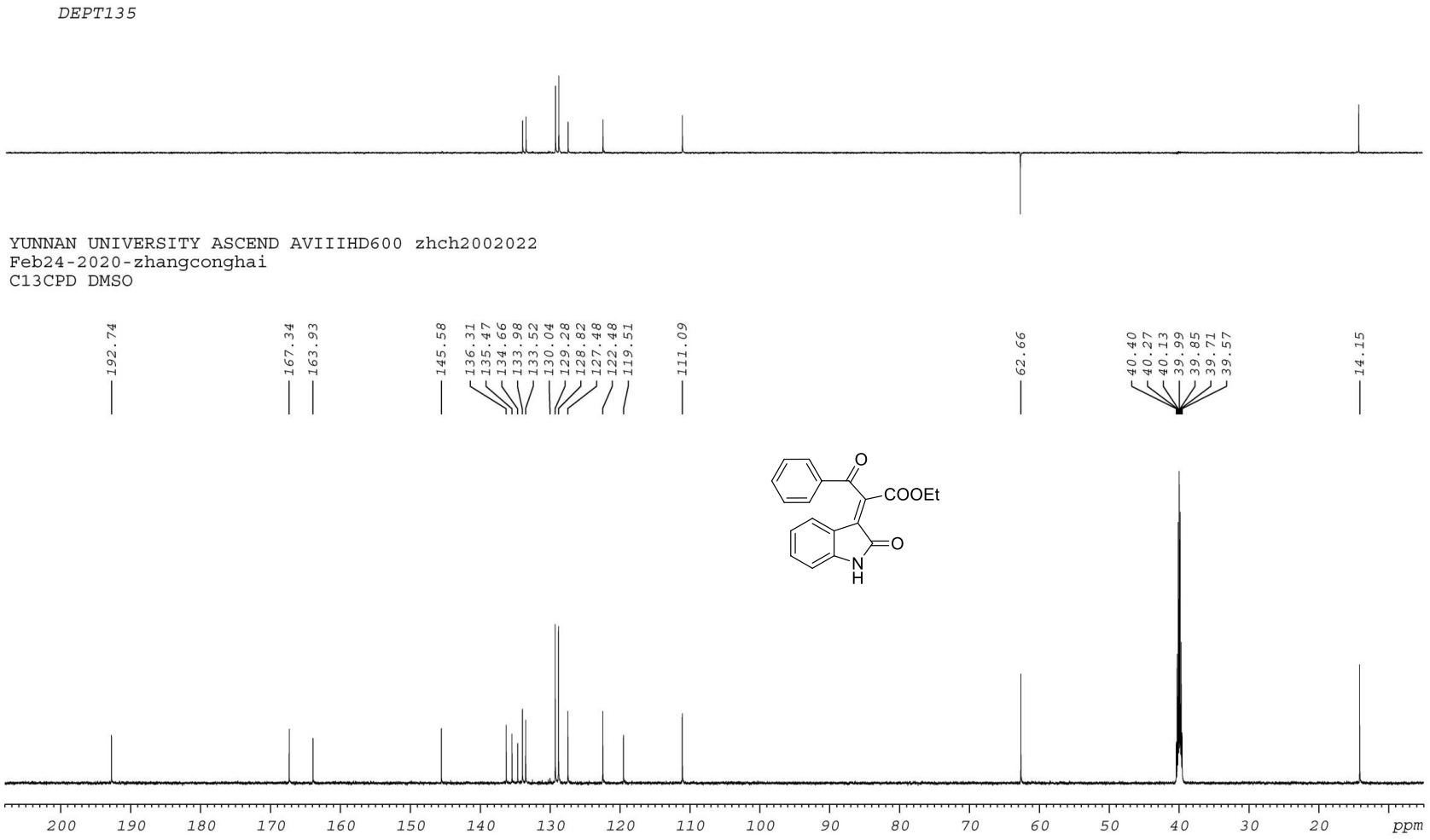


Figure S103. ^{13}C NMR (150 MHz, DMF-d_7) spectra of compound **3ai**

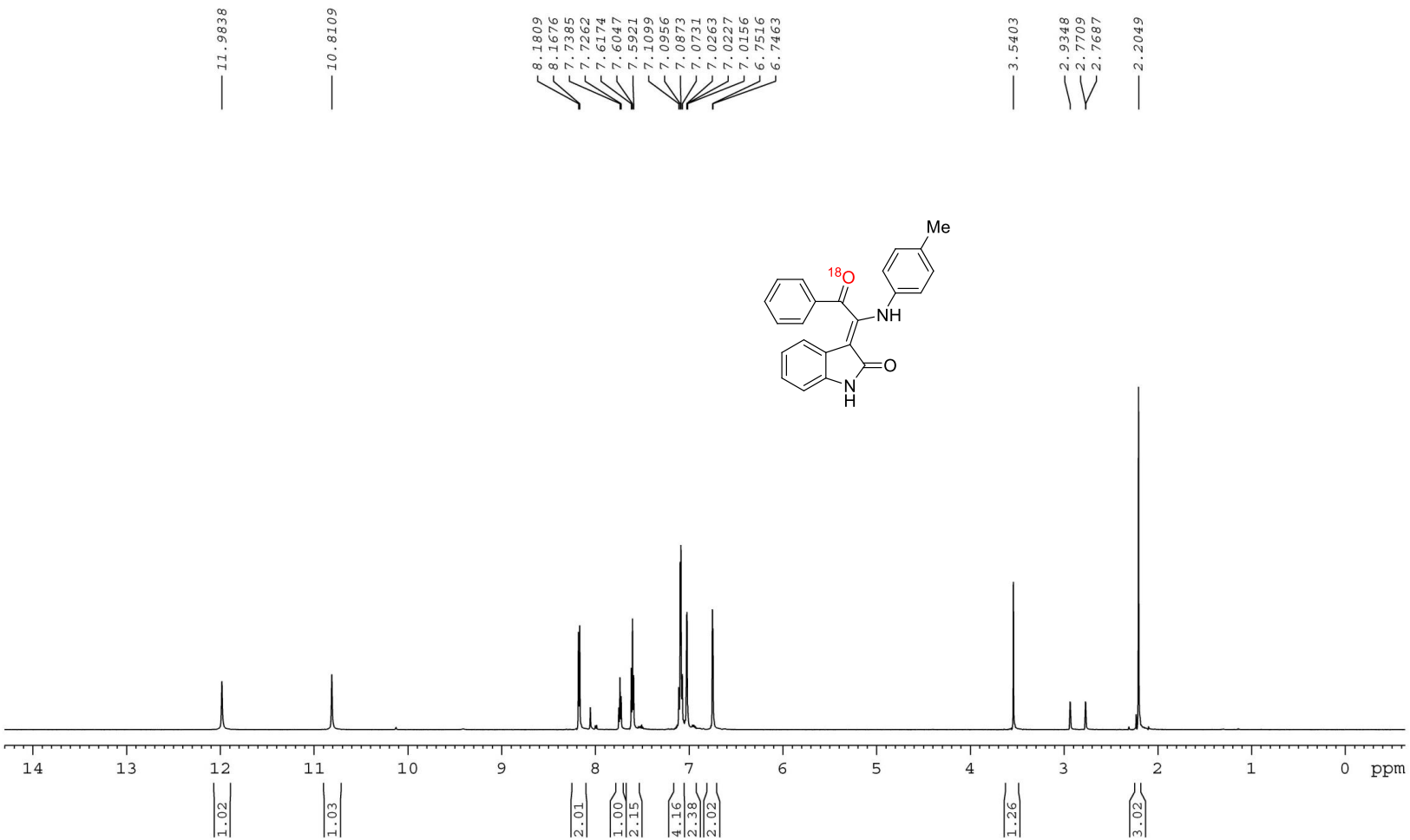


Figure S104. ^{1}H NMR (600 MHz, DMF-d_7) spectra of compound **3ad'**

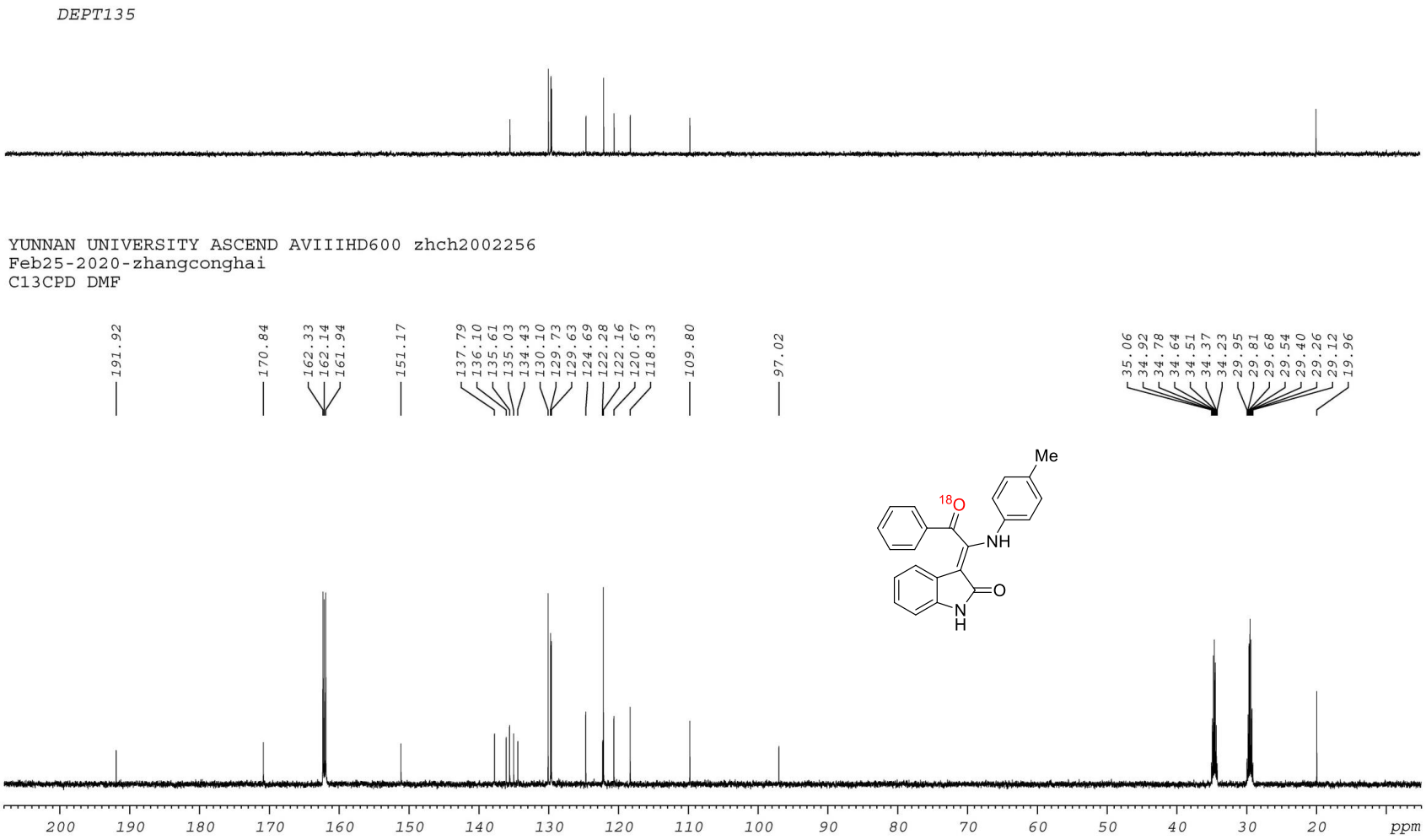


Figure S105. ^{13}C NMR (150 MHz, DMF-d_7) spectra of compound **3ad'**

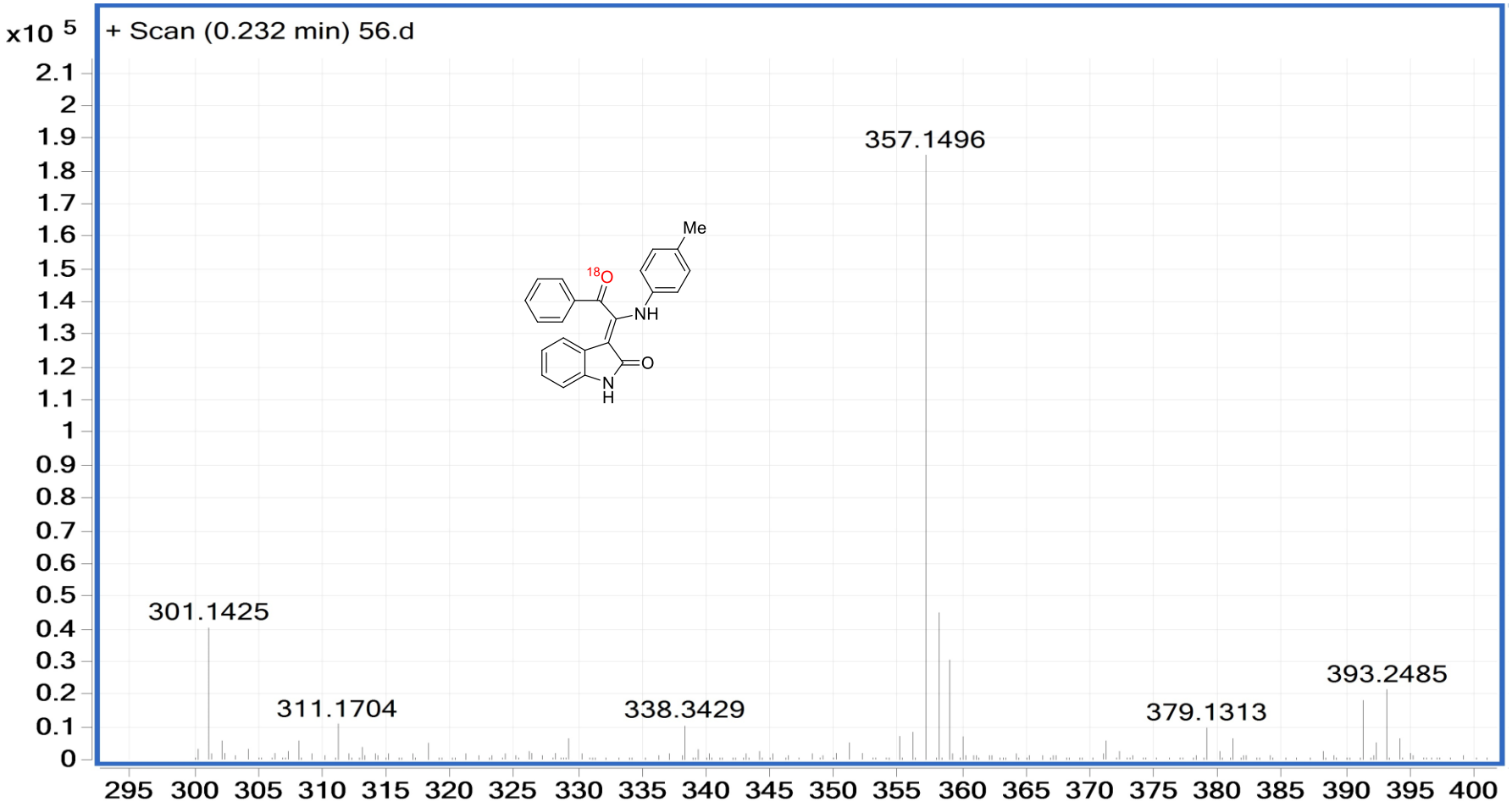


Figure S106. HRMs of compound **3ad'**

References and Notes

1. Klára Aradi, Ádám Mészáros, Balázs L. Tóth, Zoltán Vincze, and Zoltán Novák, *J. Org. Chem.* **2017**, 82, 11752-11764

2. CCDC 1970776 contain the supplementary crystallographic data for compound **3aa**. These data can be obtained free of charge from The Cambridge Crystallographic Data Center *via* www.ccdc.cam.ac.uk/data_request/cif