The Simple Route to 2,3-Benzodiazepines from Substituted Indenes

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General information

Solvents were purchased from commercial sources and were absolutized before use if it's necessary. Thin layer chromatography was performed using pre-coated plates obtained from E. Merck (TLC silica gel 60 F254). TLC plates were visualized by exposure to ultraviolet light (UV). Silica gel chromatography purifications were performed by flash chromatography using EM Science silica gel 60 (230-400 mesh). All other reagents were commercially available and were used without further purification.

All new compounds were characterized by ^{1}H NMR, ^{13}C NMR, ^{19}F NMR, ^{1}H-^{13}C HSQC, ^{1}H-^{13}C HMBC, ^{1}H-^{15}N HMBC NMR, FTIR and High Resolution Mass Spectrometry (HRMS). NMR spectra were obtained on a Bruker "Ascend™ 400" (400 MHz ^{1}H, 101 MHz ^{13}C, 376 MHz ^{19}F, 40.55 ^{15}N). Coupling constants *J* are given in Hertz as positive values regardless of their real individual signs. The multiplicity of the signals is indicated as ''s", ''d", "t" or ''m" for singlet, doublet, triplet or multiplet, respectively. Mass analysis was performed on an "Agilent 1260" Infinity liquid chromatograph combined with a Bruker MaXis Impact mass spectrometer with electrospray ionization method (ESI) or AB Sciex TripleTOF 6500+ equipped with different ionization sources. Eluents used: 80% MeCN, 20% H_2O and direct injection of the sample (no chromatography column) were performed.

Crystallographic data: Crystals of *N*-aminoquinoline **3c-3 (**$C_{21}H_{24}N_2O_5$, M=384.42 g/mol) are triclinic, space group P-1 (no. 2), a = 7.6144(9) Å, b = 9.7829(11) Å, c = 14.1330(15) Å, α = 78.875(5)°, β = 83.922(4)°, γ = 70.003(4)°, V = 969.81(19) Å^3, Z = 2, μ(MoKα) = 0.094 mm^{-1}, F(000) = 408.0, *Dcalc* = 1.316 g/cm^3. Intensities of 14038 reflections were measured at 296.15 K with a Bruker APEX-II CCD diffractometer (2.94° ≤ 2Θ ≤ 51.994°), 3794 unique (R_{int} = 0.0244, R_{sigma} = 0.0287) which were used in all calculations. The final R_1 was 0.0442 (I > 2σ(I)) and wR_2 was 0.1458 (all data). Using Olex2[1], the structure was solved with the SHELXT[2] structure solution program using Intrinsic Phasing and refined with the XL[3] refinement package using Least Squares minimization. CCDC 2426778 contains the supplementary crystallographic information for *N*-aminoquinoline **3c-3**.

Kinetic experiments

*Kinetic experiment 1. Cyclization of 1'-(2'-benzoyl-5'-methoxyphenyl)propan-2-one (***2c***) with hydrazine hydrate with the AcOH addition.*

Kinetic experiments were carried out *in situ* directly in the NMR tube. 50 mg (0.19 mmol) of 1'-(2'-benzoyl-5'-methoxyphenyl)propan-2-one (**2c**) and 5.9 mg (0.1 mmol, 0.53 eq) glacial acetic acid were dissolved in CD_3OD (0.7 ml). After the spectrum was registered 46.6 mg

(0.933 mmol) hydrazine hydrate was added to the tube and the NMR data were collected in 2, 5, 15, 30, 45, 60, 90, 120, 180, 240, 480, 720 and 1080 min. The ratios of each component were determined by measuring the peaks areas in relation to the methyl group of acetic acid signal (1.98 ppm), which is constant during the experiment.

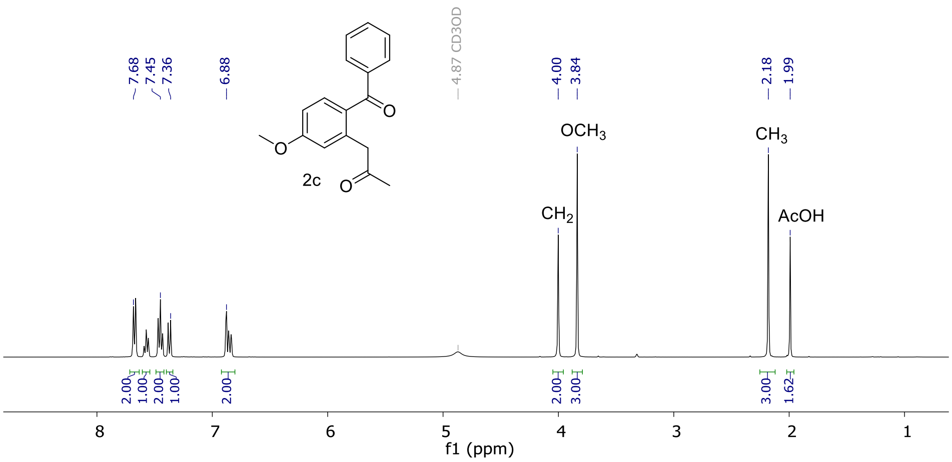


Figure S1.1 ^{1}H NMR (600 MHz, CD_3OD) of mixture 1'-(2'-benzoyl-5'-methoxyphenyl)propan-2-one (**2c**) and acetic acid.

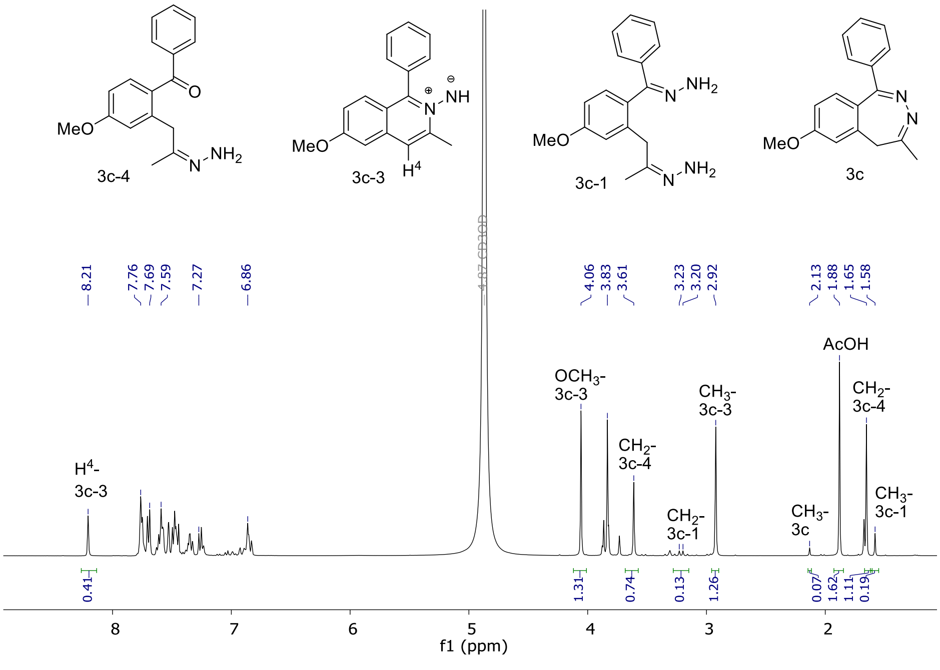


Figure S1.2 ^{1}H NMR (600 MHz, CD_3OD) of reaction of 1'-(2'-benzoyl-5'-methoxyphenyl)propan-2-one (**2c**), acetic acid and $N_2H_4 \cdot H_2O$ in 2 min.

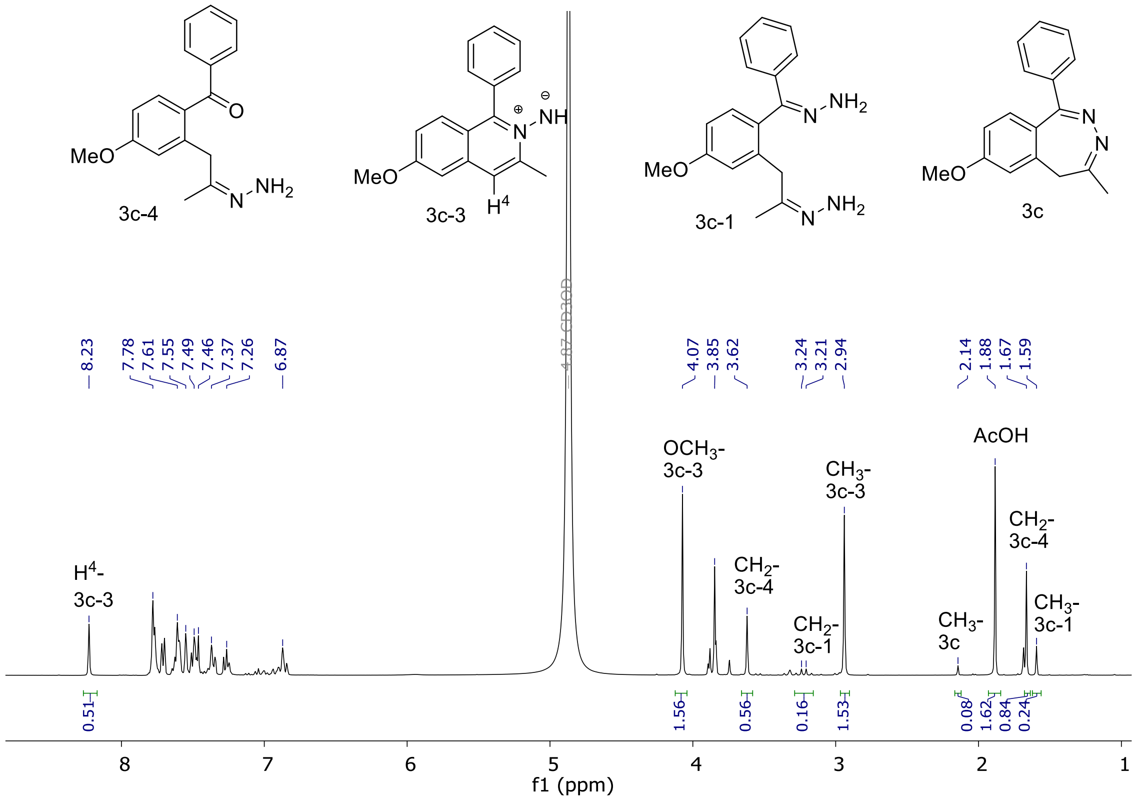


Figure S1.3. [1]H NMR (600 MHz, CD_3OD) spectrum of reaction of 1'-(2'-benzoyl-5'-methoxyphenyl)propan-2-one (**2c**), acetic acid and $N_2H_4{\cdot}H_2O$ in 5 min

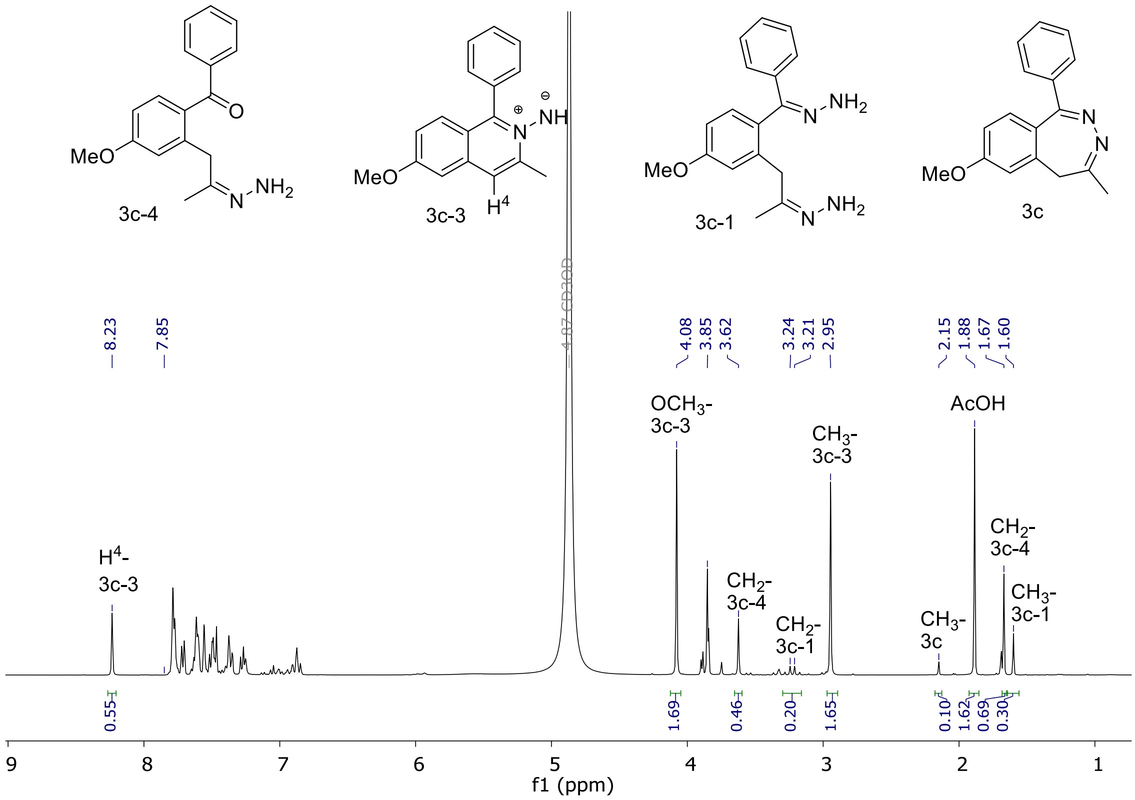


Figure S1.4. [1]H NMR (600 MHz, CD_3OD) spectrum of reaction of 1'-(2'-benzoyl-5'-methoxyphenyl)propan-2-one (**2c**), acetic acid and $N_2H_4{\cdot}H_2O$ in 15 min

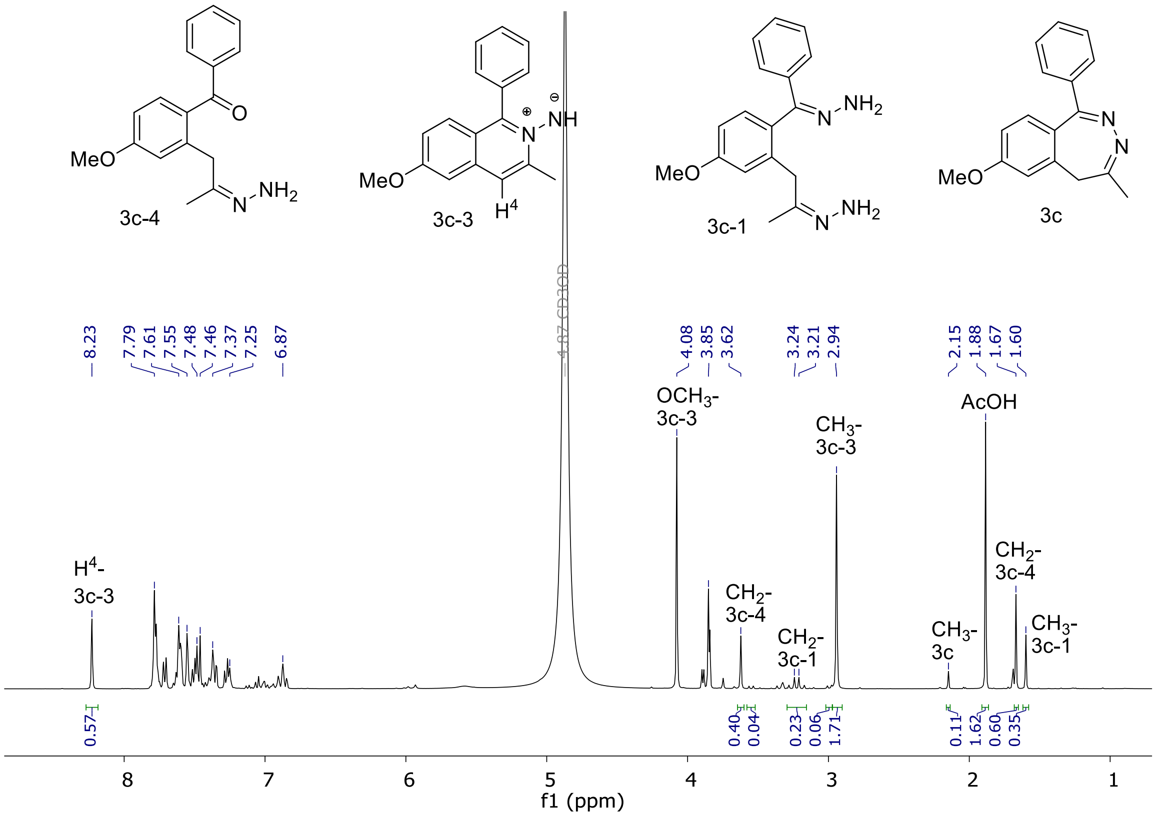


Figure S1.5. ^{1}H NMR (600 MHz, CD_3OD) spectrum of reaction of 1'-(2'-benzoyl-5'-methoxyphenyl)propan-2-one (**2c**), acetic acid and $N_2H_4{\cdot}H_2O$ in 30 min

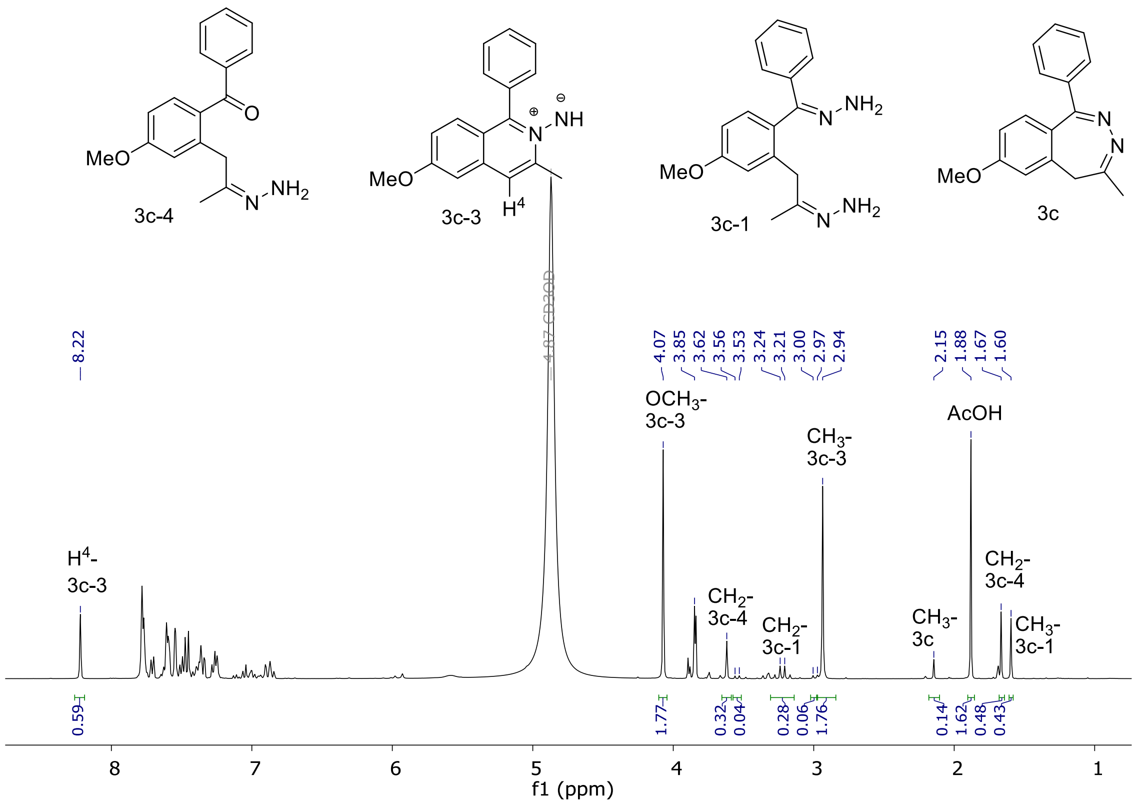


Figure S1.6. ^{1}H NMR (600 MHz, CD_3OD) spectrum of reaction of 1'-(2'-benzoyl-5'-methoxyphenyl)propan-2-one (**2c**), acetic acid and $N_2H_4{\cdot}H_2O$ in 60 min

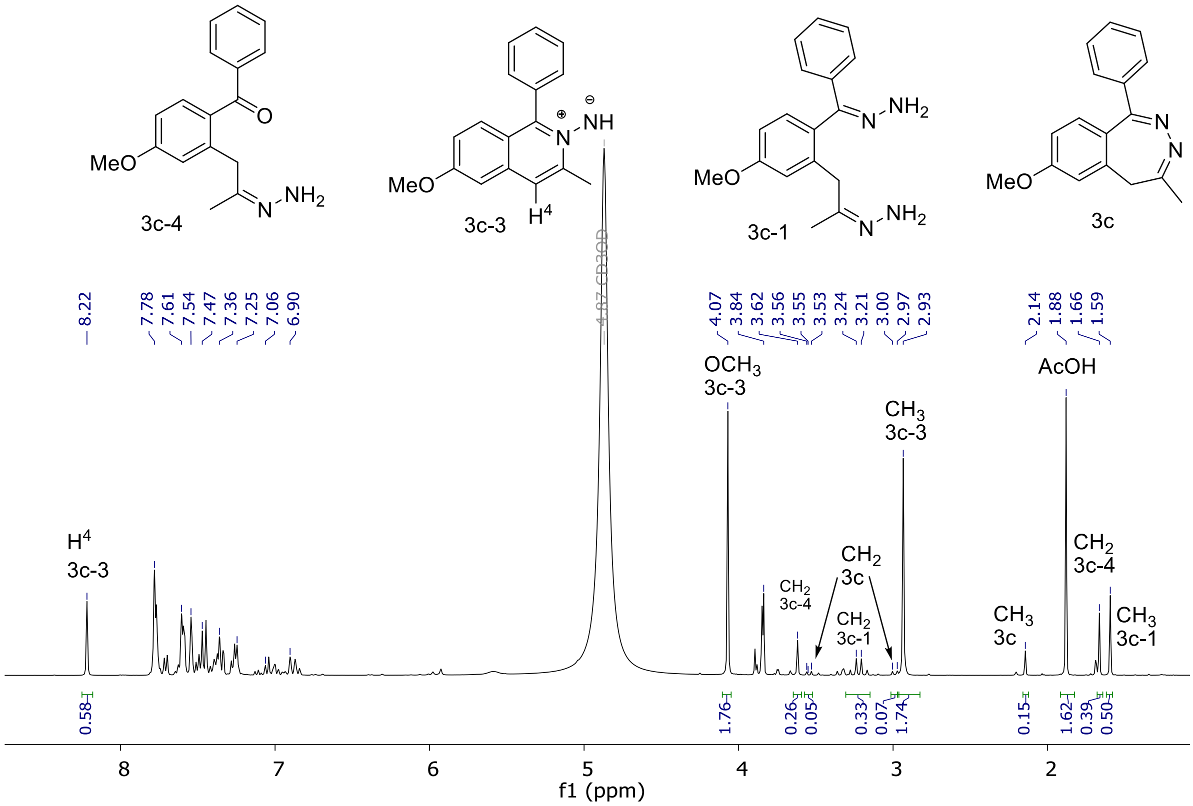


Figure S1.7. ^{1}H NMR (600 MHz, CD_3OD) spectrum of reaction of 1'-(2'-benzoyl-5'-methoxyphenyl)propan-2-one (**2c**), acetic acid and $N_2H_4{\cdot}H_2O$ in 90 min

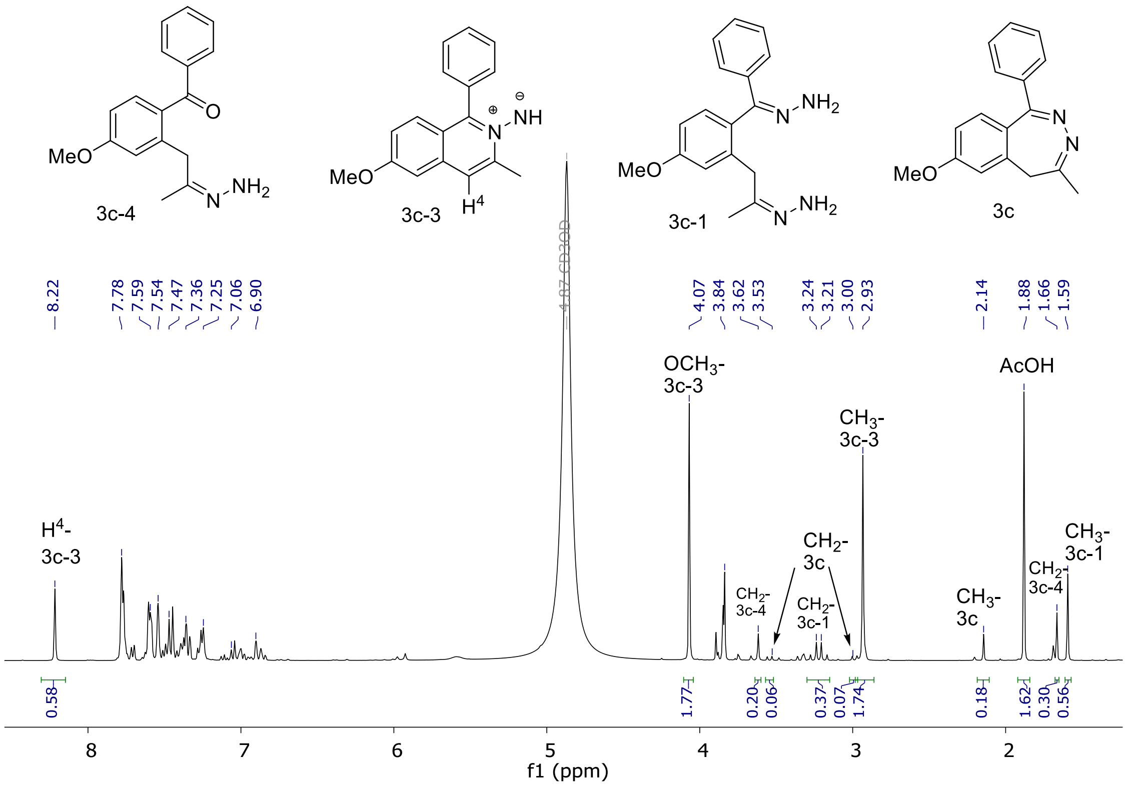


Figure S1.8. ^{1}H NMR (600 MHz, CD_3OD) spectrum of reaction of 1'-(2'-benzoyl-5'-methoxyphenyl)propan-2-one (**2c**), acetic acid and $N_2H_4{\cdot}H_2O$ in 2 h

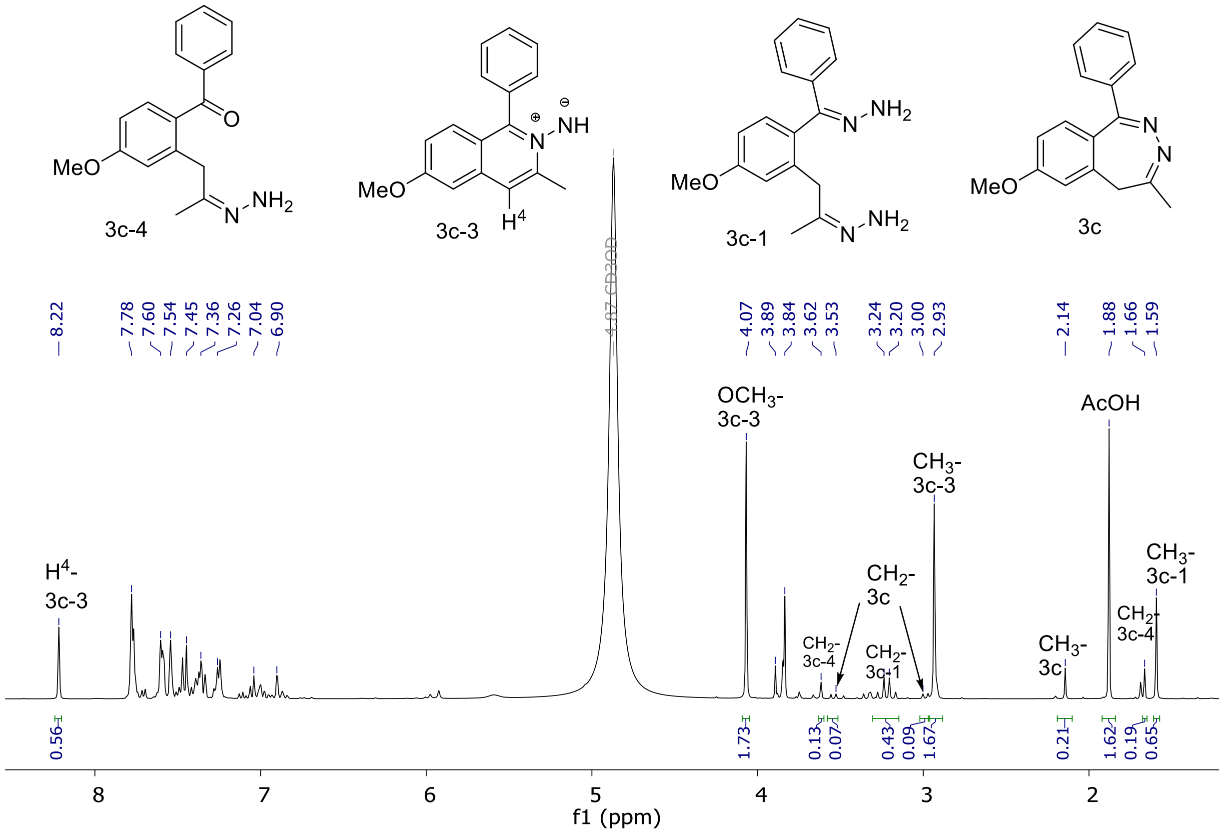


Figure S1.9. ^{1}H NMR (600 MHz, CD_3OD) spectrum of reaction of 1'-(2'-benzoyl-5'-methoxyphenyl)propan-2-one (**2c**), acetic acid and $N_2H_4 \cdot H_2O$ in 3 h

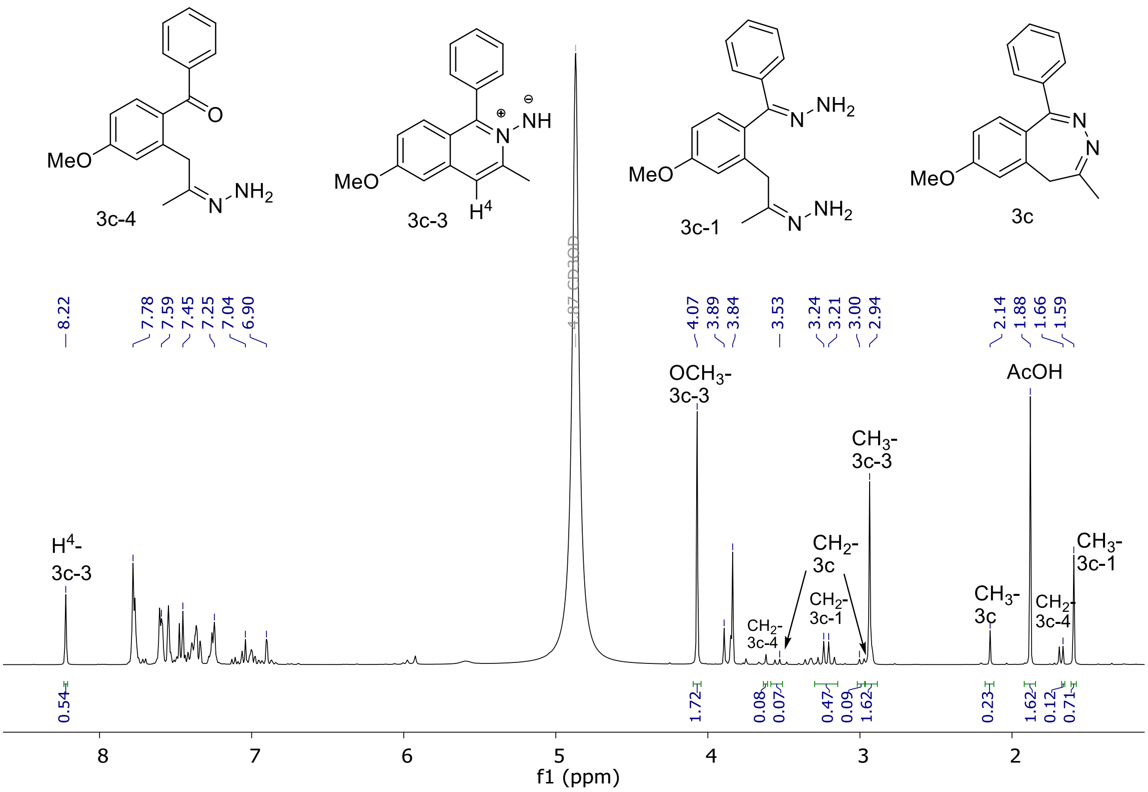


Figure S1.10. ^{1}H NMR (600 MHz, CD_3OD) spectrum of reaction of 1'-(2'-benzoyl-5'-methoxyphenyl)propan-2-one (**2c**), acetic acid and $N_2H_4xH_2O$ in 4 h

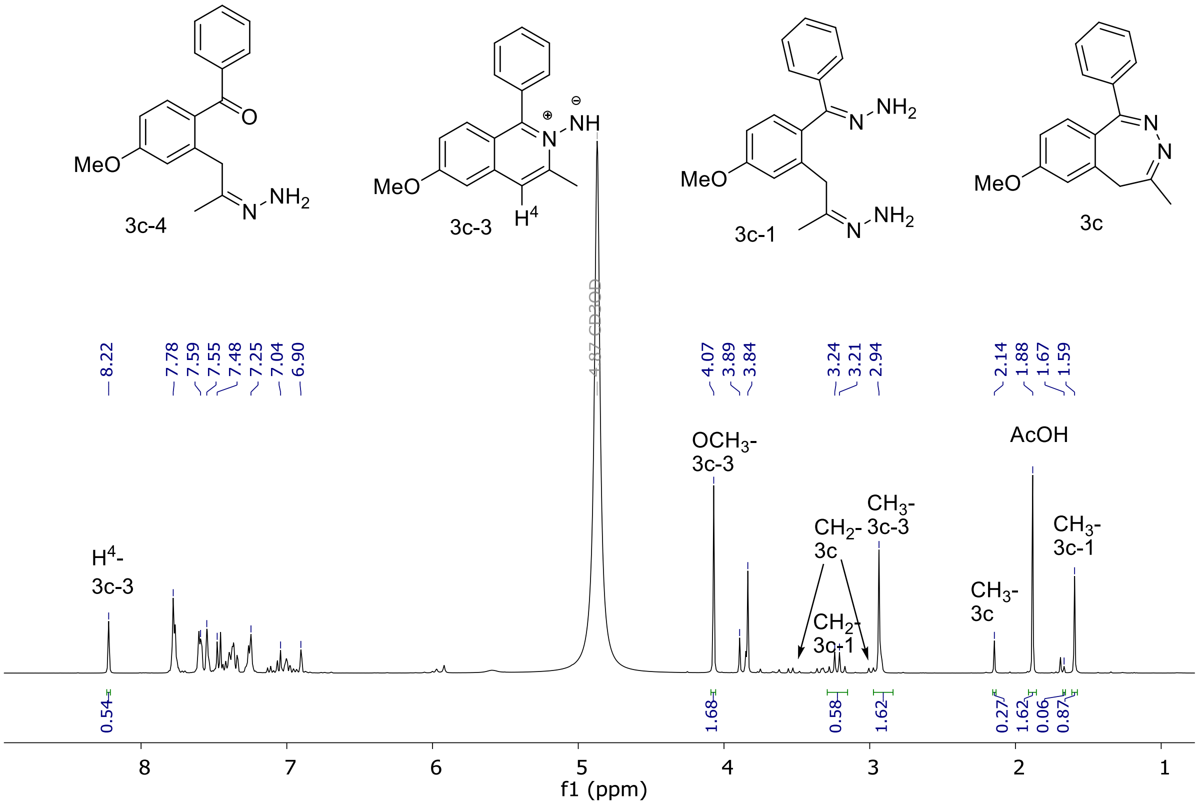


Figure S1.11. ^{1}H NMR (600 MHz, CD_3OD) spectrum of reaction of 1'-(2'-benzoyl-5'-methoxyphenyl)propan-2-one (**2c**), acetic acid and $N_2H_4 \cdot H_2O$ in 6 h.

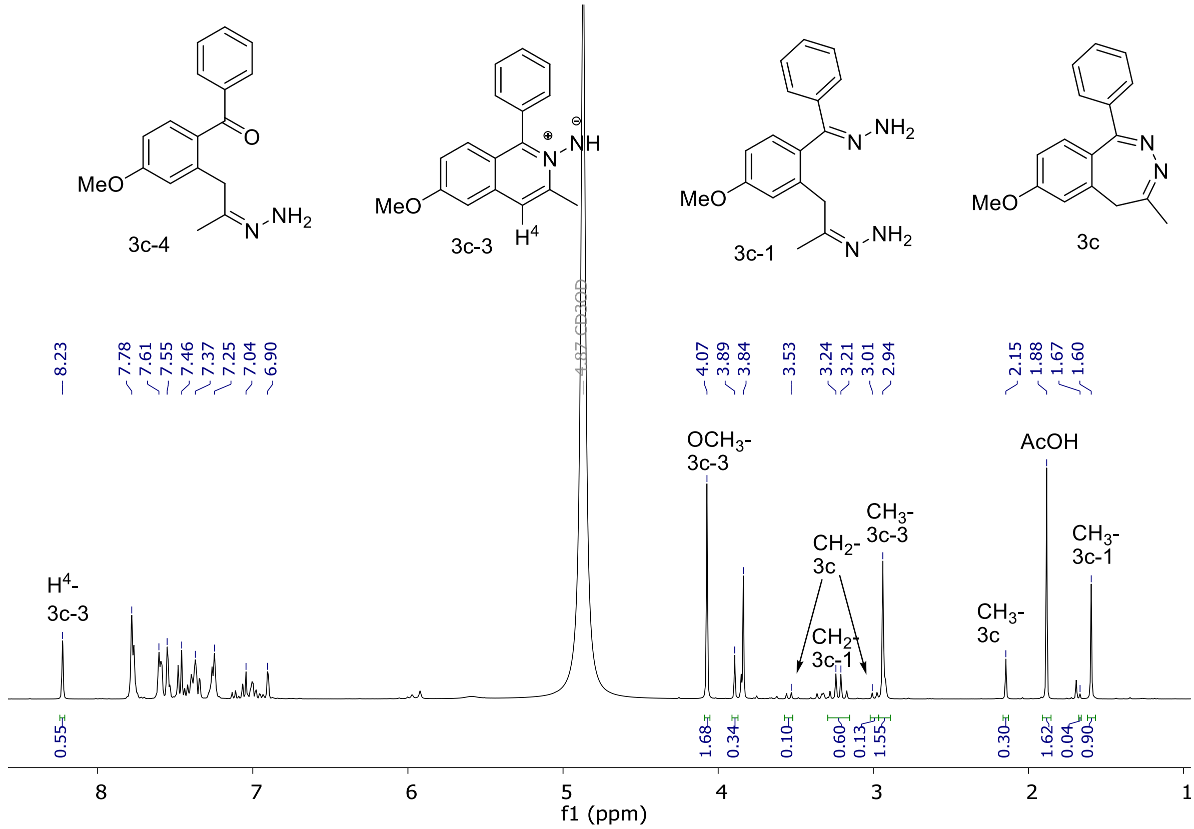


Figure S1.12. ^{1}H NMR (600 MHz, CD_3OD) spectrum of reaction of 1'-(2'-benzoyl-5'-methoxyphenyl)propan-2-one (**2c**), acetic acid and $N_2H_4 \cdot H_2O$ in 8 h

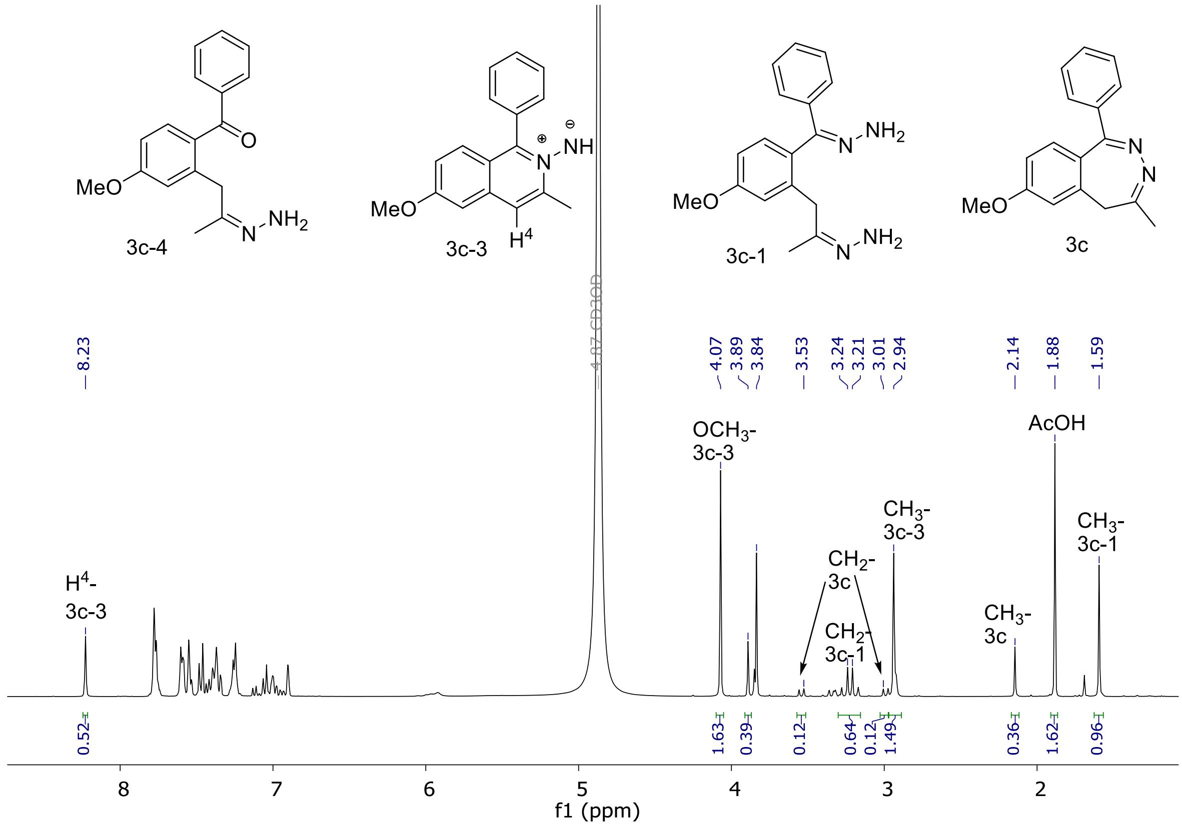


Figure S1.13. ^{1}H NMR (600 MHz, CD_3OD) spectrum of reaction of 1'-(2'-benzoyl-5'-methoxyphenyl)propan-2-one (**2c**), acetic acid and $N_2H_4 \cdot H_2O$ in 12 h

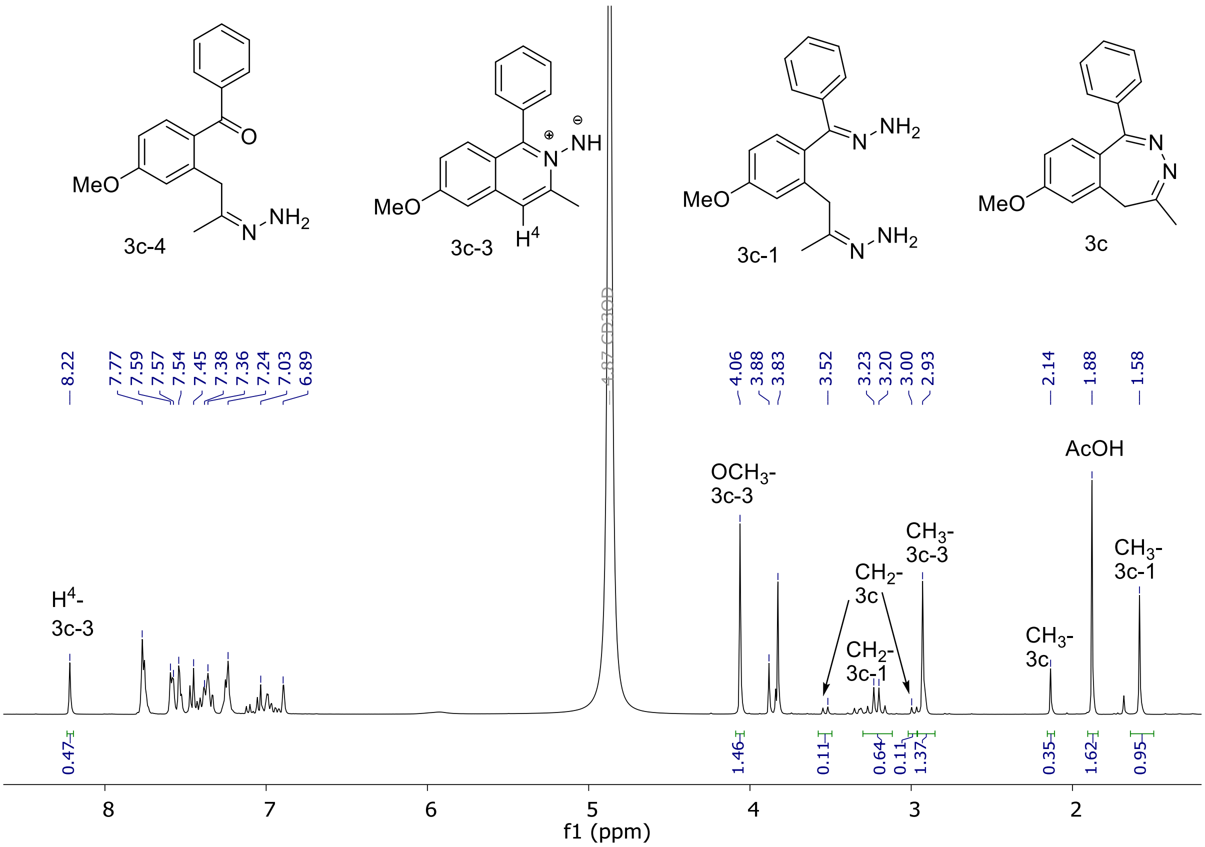


Figure S1.14. ^{1}H NMR (600 MHz, CD_3OD) spectrum of reaction of 1'-(2'-benzoyl-5'-methoxyphenyl)propan-2-one (**2c**), acetic acid and $N_2H_4 \cdot H_2O$ in 18 h

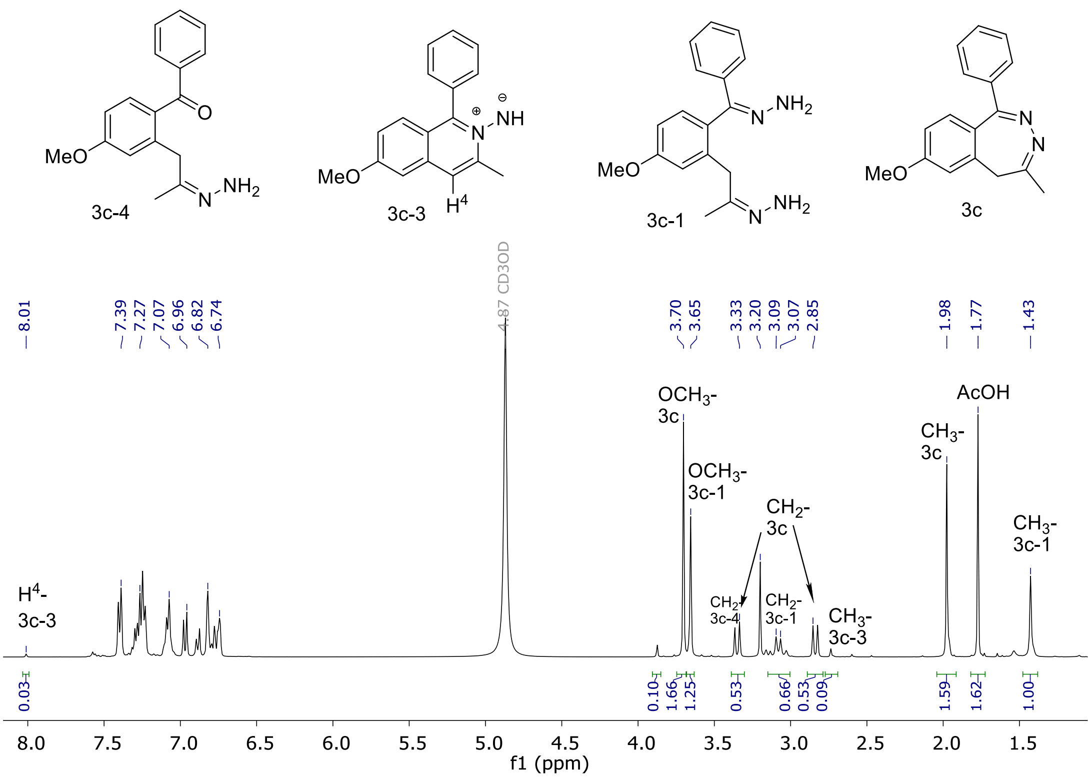


Figure S1.15. ^{1}H NMR (600 MHz CD_3OD) spectrum of reaction of 1'-(2'-benzoyl-5'-methoxyphenyl)propan-2-one (**2c**), acetic acid and $N_2H_4{\cdot}H_2O$ after evaporation of the solvent

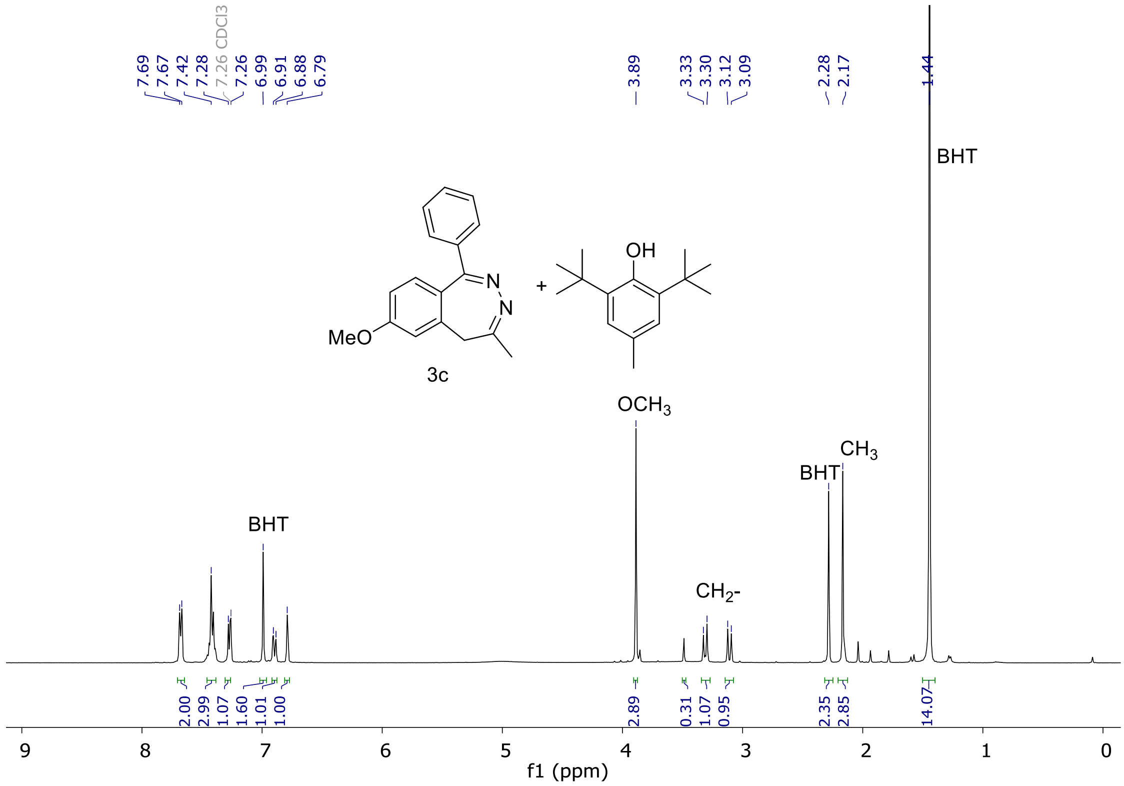


Figure S1.16. ^{1}H NMR (600 MHz, $CDCl_3$) spectrum of reaction residue (1'-(2'-benzoyl-5'-methoxyphenyl)propan-2-one (**2c**), acetic acid and $N_2H_4{\cdot}H_2O$) after the treatment of reaction mixture (solvent evaporation followed by flash chromatography on a silica column, eluent CH_2Cl_2/EtOAc 9:1). BHT was added as internal standard.

Figure	Time, min	Mono-hydrazone **3c-4**, %	*N*-Aminoquinoline **3c-3**, %	Bis-hydrazone **3c-1**, %	2,3-Benzodi-azepine **3c**, %
Figure S1.2	2	37	42	6	2
Figure S1.3	5	28	51	8	2
Figure S1.4	15	23	55	10	3
Figure S1.5	30	20	57	11	3
Figure S1.6	60	16	59	14	4
Figure S1.7	90	13	58	16	5
Figure S1.8	120	10	58	18	6
Figure S1.9	180	6	56	21	7
Figure S1.10	240	4	54	23	7
Figure S1.11	360	2	54	29	9
Figure S1.12	480	1	51	30	10
Figure S1.13	720	0	50	32	12
Figure S1.14	1080	0	46	32	11
Figure S1.15	After evaporation	0	3	33	53
Figure S1.16	After SiO_2 column	0	0	0	75

Table S1. Change in ratio of main products in the reaction of (1'-(2'-benzoyl-5'-methoxyphenyl)propan-2-one (**2c**), acetic acid and $N_2H_4 \cdot H_2O$ over time

*Kinetic experiment 2. Cyclization of 1'-(2'-benzoyl-5'-methoxyphenyl)propan-2-one (**2c**) with hydrazine hydrate*

Kinetic experiments were carried out *in situ* directly in the NMR tube. 1'-(2'-Benzoyl-5'-methoxyphenyl)propan-2-one (**2c**) (50 mg, 0.19 mmol) and 4.35 mg (5 mkl, 0.036 mmol, 0.19 eq) of 1,3,5-trimethylbenzene (TMB) were dissolved in CD_3OD (0.7 ml). After the spectrum was registered hydrazine hydrate (46.6 mg, 0.933 mmol) was added to the tube and the ^1H NMR data was collected in 2, 60, 120, 240, 600 min. The ratios of each component were determined by measuring the peaks areas in relation to the 1,3,5-trimethylbenzene signal (2.25 ppm – CH_3-group), which is constant during the experiment.

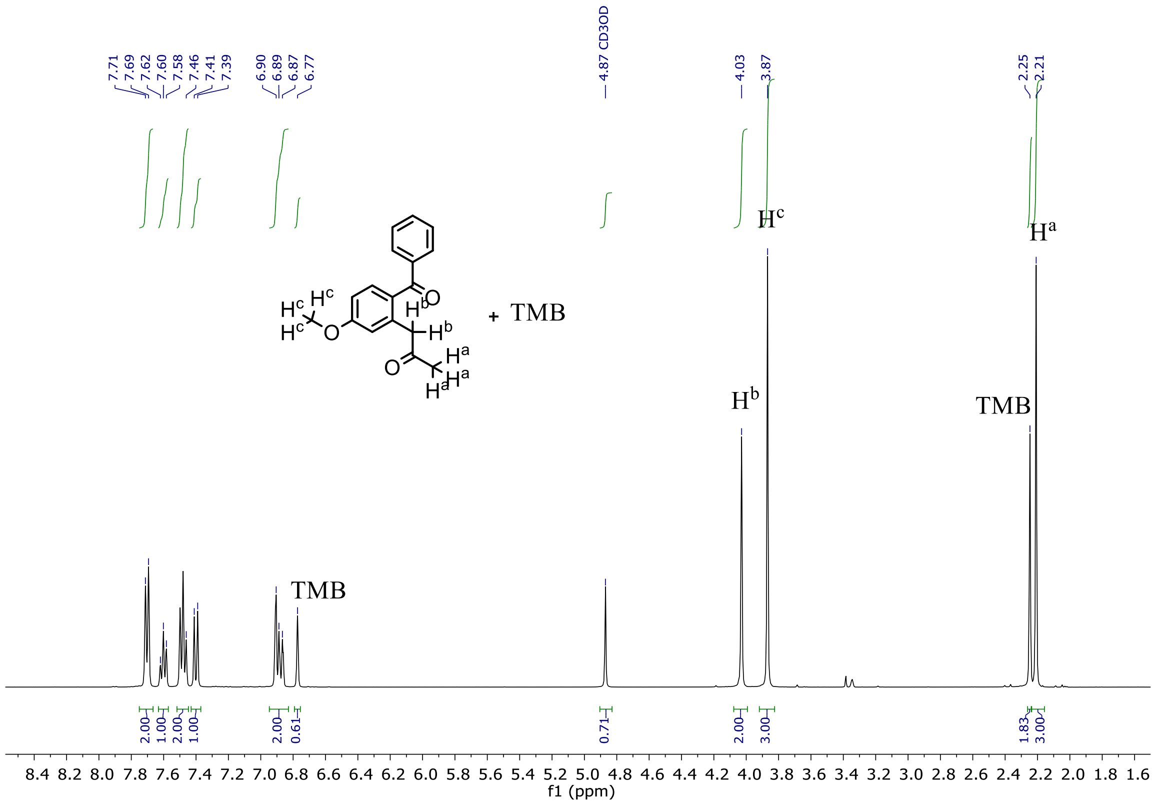


Figure S2.1. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of mixture 1'-(2'-benzoyl-5'-methoxyphenyl)propan-2-one (2c) with TMB.

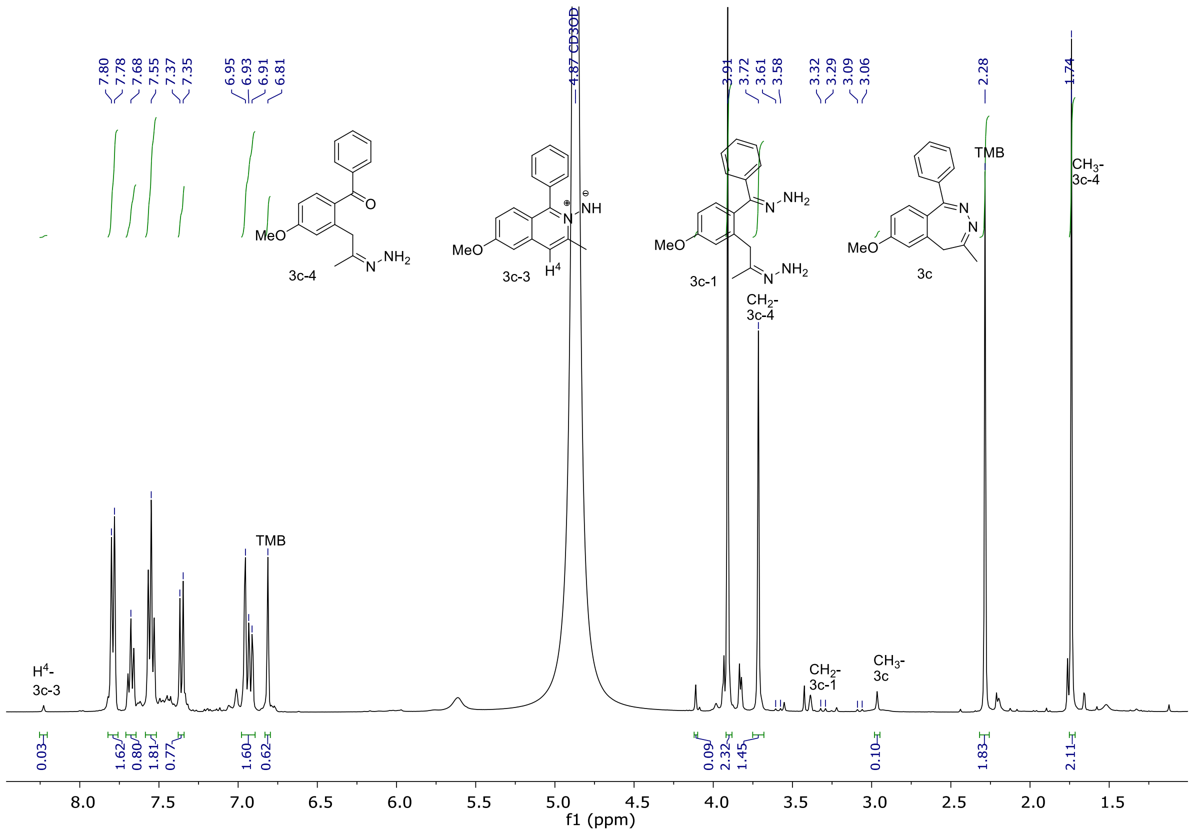


Figure S2.2. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of reaction of 1'-(2'-benzoyl-5'-methoxyphenyl)propan-2-one (**2c**), and $N_2H_4 \cdot H_2O$ in 2 min

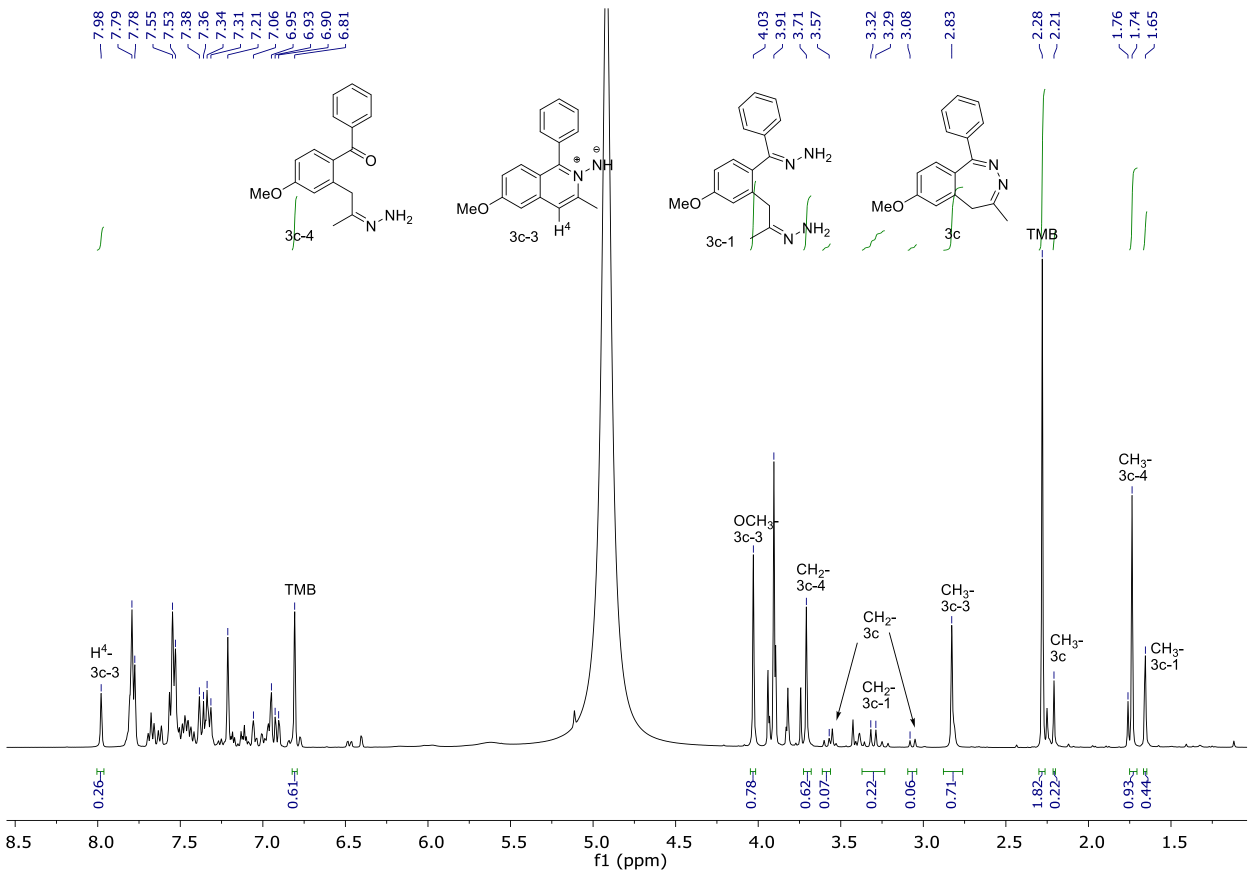


Figure S2.3. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of reaction of 1'-(2'-benzoyl-5'-methoxyphenyl)propan-2-one (**2c**), and $N_2H_4{\cdot}H_2O$ in 60 min

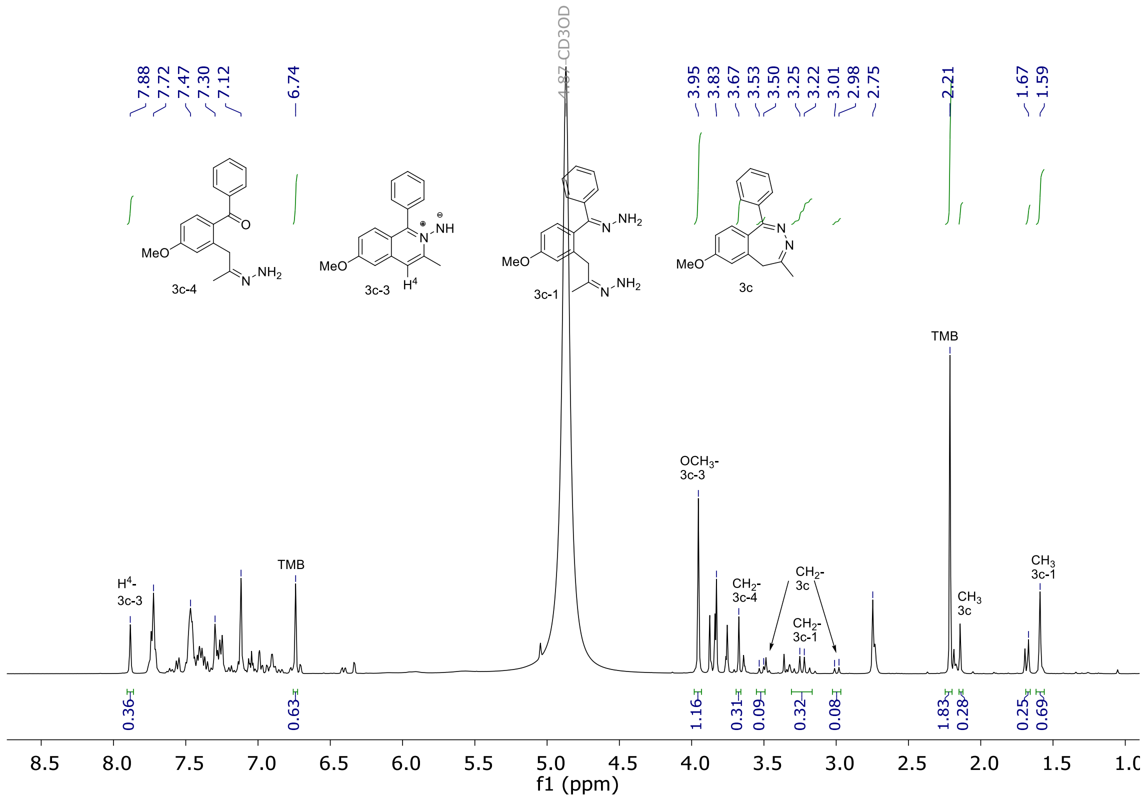


Figure S2.4. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of reaction of 1'-(2'-benzoyl-5'-methoxyphenyl)propan-2-one (**2c**), and $N_2H_4{\cdot}H_2O$ in 120 min

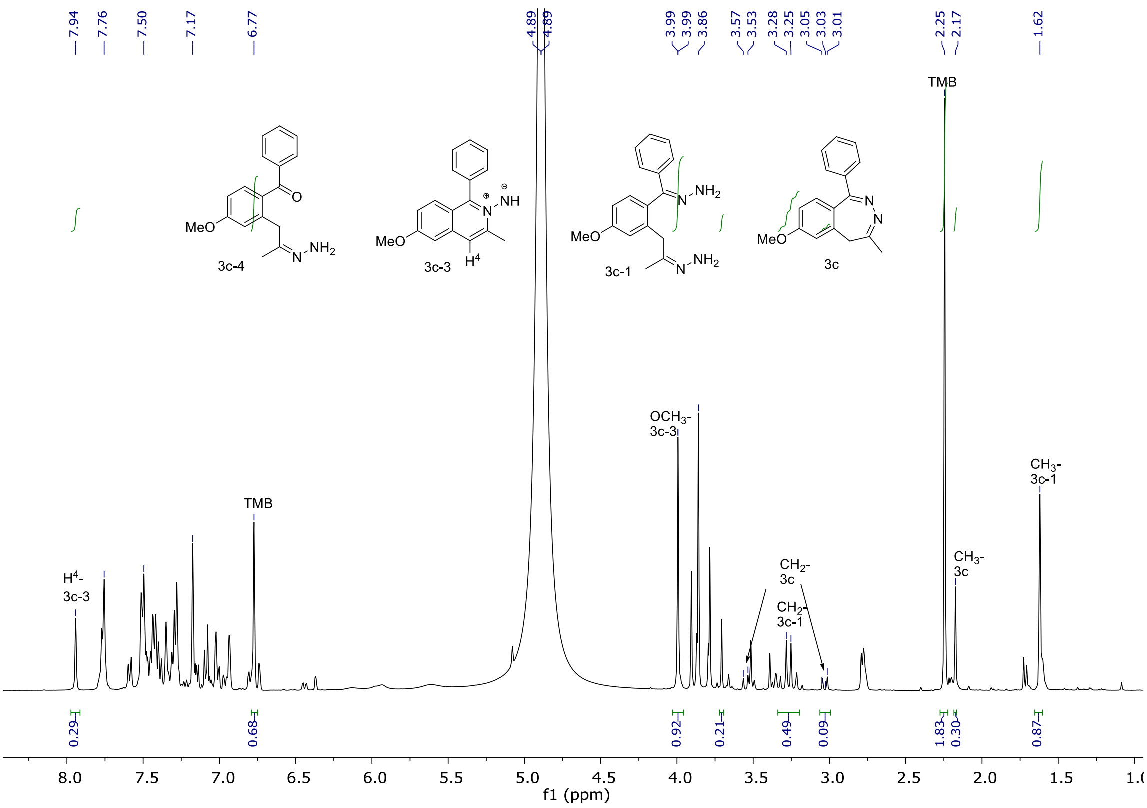


Figure S2.5. [1]H NMR (400 MHz, $CDCl_3$) spectrum of reaction of 1'-(2'-benzoyl-5'-methoxyphenyl)propan-2-one (**2c**), and $N_2H_4 \cdot H_2O$ in 240 min

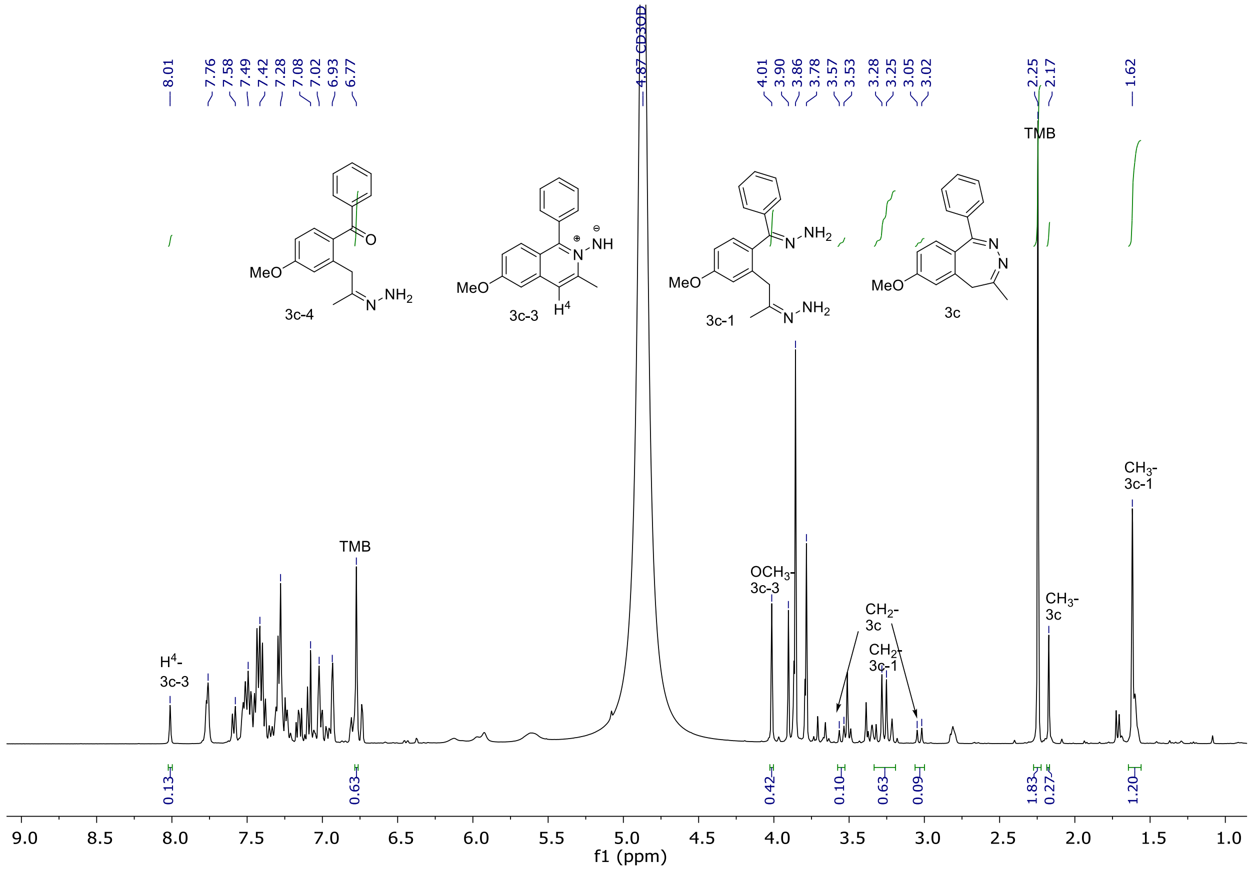


Figure S2.6. [1]H NMR (400 MHz, $CDCl_3$) spectrum of reaction of 1'-(2'-benzoyl-5'-methoxyphenyl)propan-2-one (**2c**), and $N_2H_4 \cdot H_2O$ in 600 min

Figure	Time, min	Mono-hydrazone **3c-4**, %	*N*-Aminoquinoline **3c-3**, %	Bis-hydrazone **3c-1**, %	2,3-Benzodiazepine **3c**, %
Figure S2.2	2	72	3	2	-
Figure S2.3	60	31	26	11	7
Figure S2.4	120	15	36	16	8
Figure S2.5	240	-	29	25	9
Figure S2.6	600	-	13	32	9

Table S2. Change in ratio of main products in the reaction of (1'-(2'-benzoyl-5'-methoxyphenyl)propan-2-one (**2c**), and $N_2H_4{\cdot}H_2O$ over time

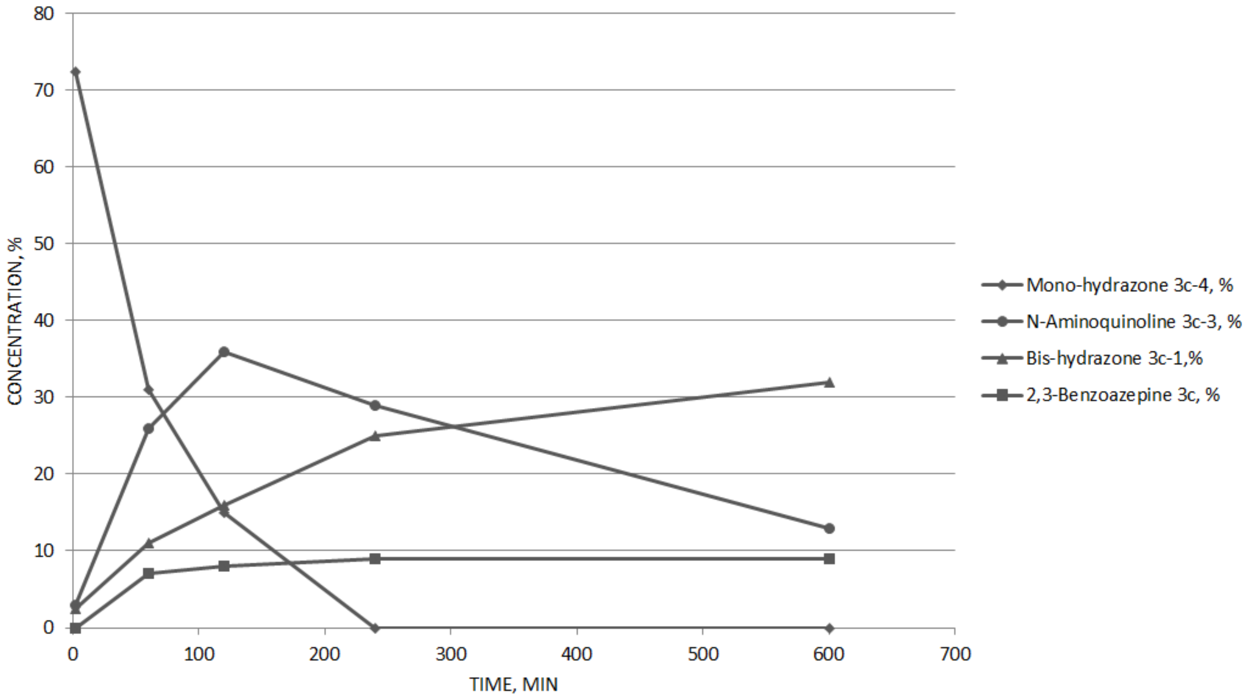


Figure S2.7. Change in ratio of main products in the reaction of (1'-(2'-benzoyl-5'-methoxyphenyl)propan-2-one (**2c**), and $N_2H_4{\cdot}H_2O$ over time

Kinetic experiment 3. Reaction of 7-methoxy-4-methyl-1-phenyl-5H-benzo[d][1,2]diazepine (3c) and hydrazine hydrate

Kinetic experiments were carried out *in situ* directly in the NMR tube. 14.2 mg (0.06 mmol) of 7-methoxy-4-methyl-1-phenyl-5*H*-benzo[*d*][1,2]diazepine (**3c**) and 5.3 mg (0.044 mmol) 1,3,5-trimethylbenzene were dissolved in CD_3OD (0.7 ml). After the spectra was registered 17 mkl of the solution containing of 15 mg (0.3 mmol, 5 eq) hydrazine hydrate and 1.82 mg (0.5 eq) acetic acid was added to the tube and the NMR data were collected in 2 min, 4 h and 8 h.

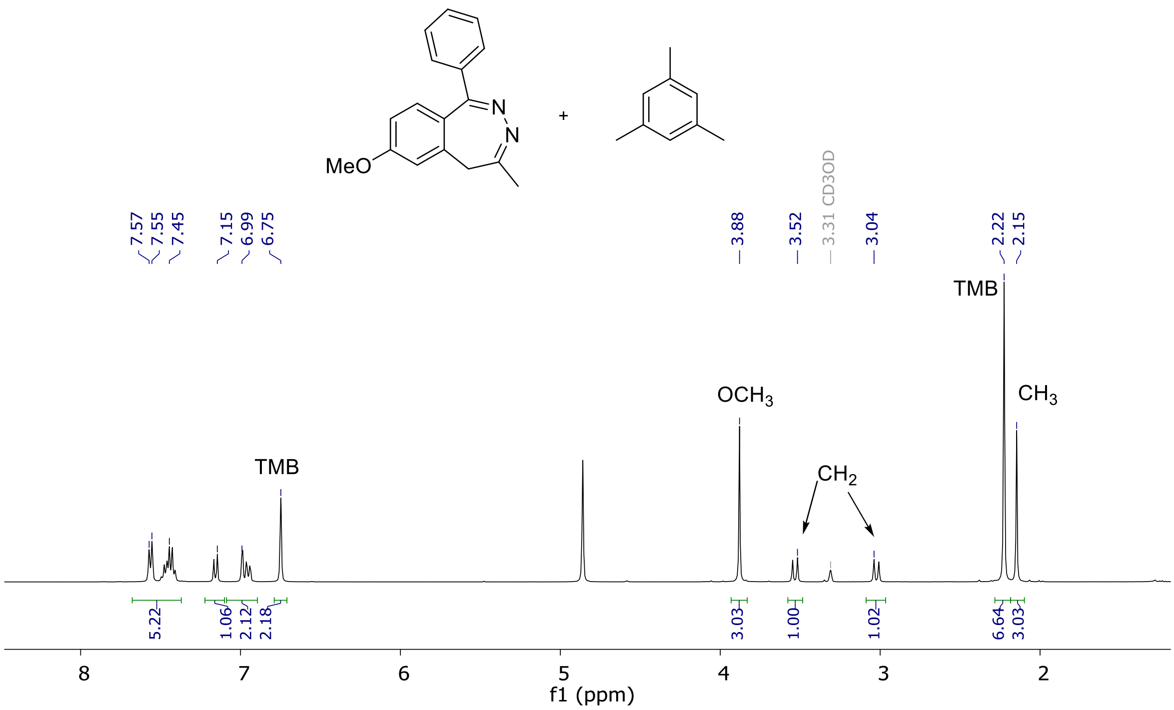


Figure S3.1. ^{1}H NMR (600 MHz, CD_3OD) of 7-methoxy-4-methyl-1-phenyl-5*H*-benzo[*d*][1,2]diazepine (**3c)** and TMB

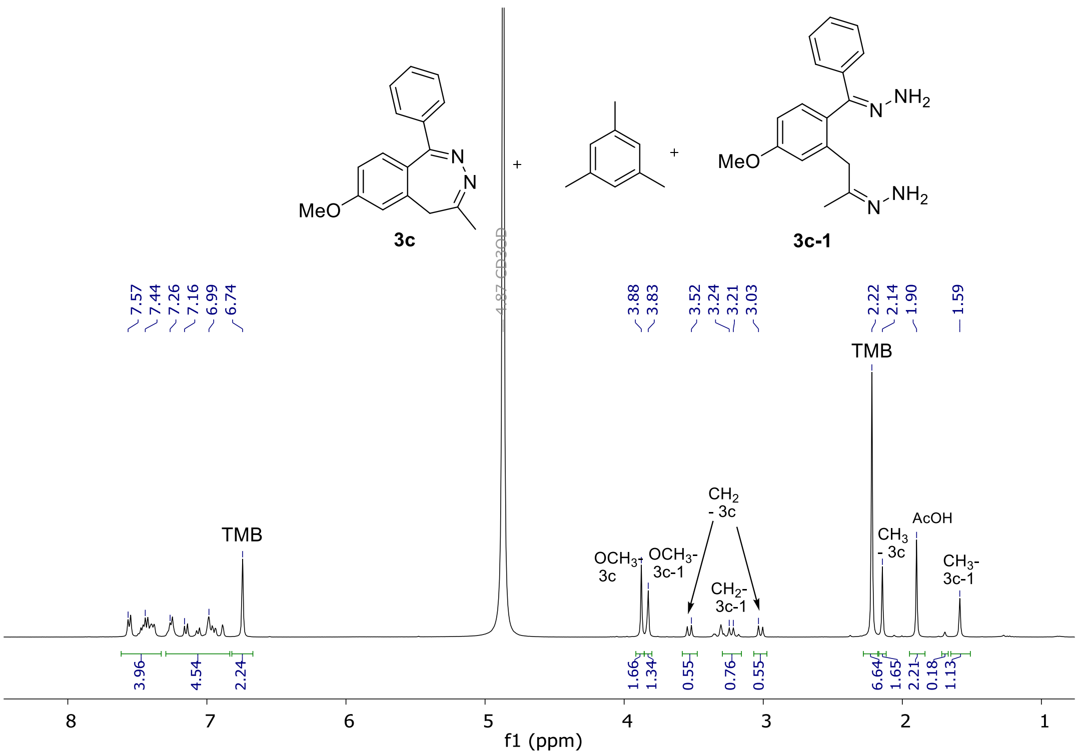


Figure S3.2. ^{1}H NMR (600 MHz, CD_3OD) spectrum of reaction mixture of 7-methoxy-4-methyl-1-phenyl-5*H*-benzo[*d*][1,2]diazepine (**3c),** acetic acid and $N_2H_4{\cdot}H_2O$ in presence of TMB in 2 min

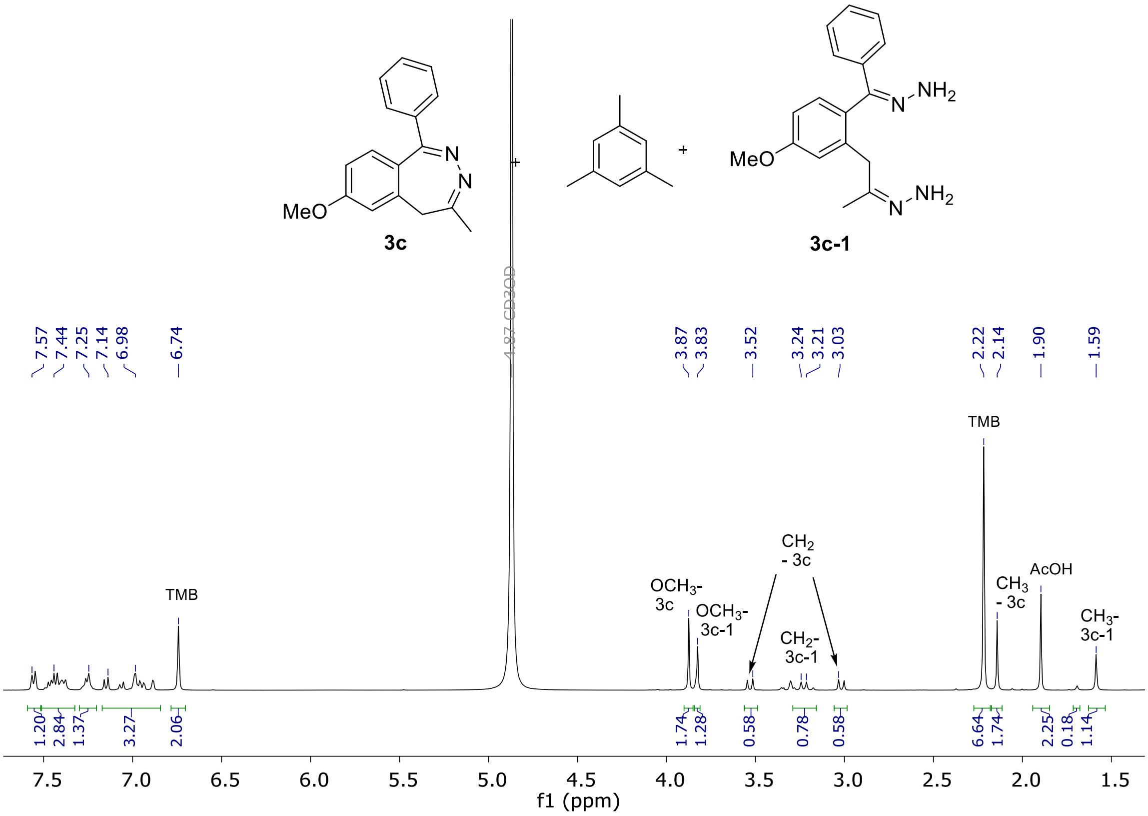


Figure S3.3. ^{1}H NMR (600 MHz, CD_3OD) spectrum of reaction mixture of 7-methoxy-4-methyl-1-phenyl-5*H*-benzo[*d*][1,2]diazepine (**3c**), acetic acid and $N_2H_4 \cdot H_2O$ in presence of TMB in 4 h

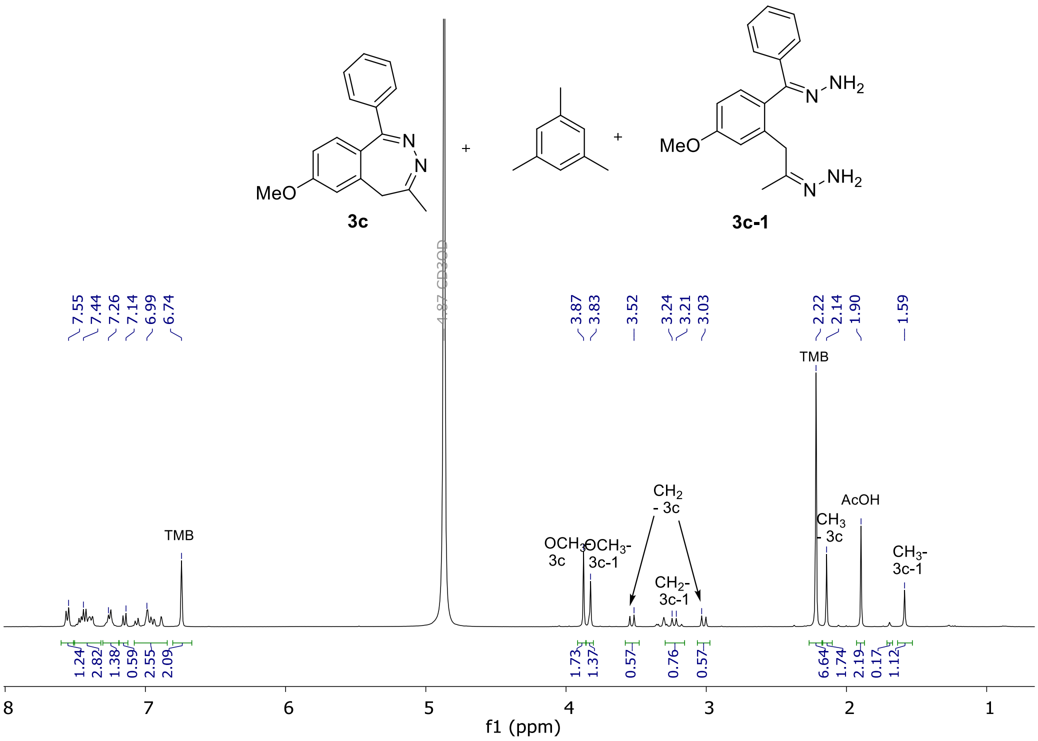


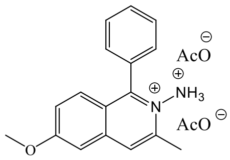
Figure S3.4. ^{1}H NMR (600 MHz, CD_3OD) spectrum of reaction mixture of 7-methoxy-4-methyl-1-phenyl-5*H*-benzo[*d*][1,2]diazepine (**3c**), acetic acid and $N_2H_4 \cdot H_2O$ in presence of TMB in 8 h

Preparation of *N*-aminoquinoline 3c-3

2-ammonio-6-methoxy-3-methyl-1-phenylisoquinolinium acetate.

Diketone **2c** (1.5 g, 5.6 mmol) and hydrazine monohydrate (1.4 g, 28 mmol, 5 eq) were stirred in acetic acid (5 ml) under argon atmosphere at room temperature for 16 hours. Then the solvent was removed under reduced pressure, reaction mixture was diluted with DCM and solid hydrazine acetate was filtered off. The mixture was evaporated; the residue was crystallized with acetonitrile, filtered and recrystallized from acetonitrile.

Yield 1 g (67%); white crystals, m.p. 105.5-106.8°C.



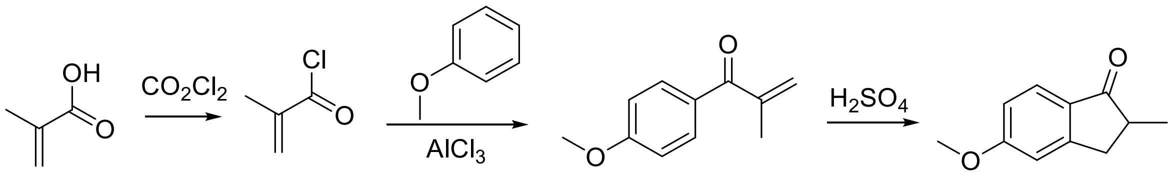
^{1}H NMR (400 MHz, $CDCl_3$) δ = 10.08 (s, 3H), 7.82 (s, 1H), 7.71 – 7.67 (m, 3H), 7.64 – 7.59 (m, 2H), 7.35 (d, *J*=9.3, 1H), 7.21 – 7.12 (m, 2H), 3.98 (s, 3H), 2.96 (s, 3H), 1.84 (s, 6H).

^{13}C {^{1}H} ^{13}C NMR (101 MHz, $CDCl_3$) δ = 176.3, 164.0, 151.3, 144.4, 138.4, 131.8, 130.8, 130.2, 129.9, 128.1, 123.5, 123.3, 122.6, 104.1, 56.2, 23.1, 20.1.

^{15}N NMR (41 MHz, $CDCl_3$) δ = 211.2, 106.7.

Preparation of indanones

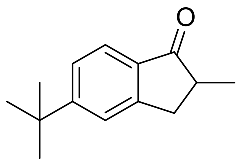
5-methoxy-2,3-dihydro-1H-inden-1-one.



To freshly distilled 2-methylprop-2-enoic acid (20 g, 0.232 mol) in dry dichloromethane (200 ml) while cooling with ice water bath oxalyl chloride (31 g, 0.244 mol, 1.05 eq) was added dropwise. DMF (0.1 ml) was added and the reaction mixture was stirred 3 h. at room temperature until a gas evolution was ended. The reaction mixture was cooled with an ice water bath, then $AlCl_3$ (31 g, 0.232 mol) was added in portion, after that anisole (22.8 g, 0,232 mol) was added dropwise and the reaction mixture was stirred 12 hours at room temperature. The reaction was quenched with cold 1N HCl (100 ml). Organic layer was separated and water phase was extracted with DCM (2x50 ml). Combined organic phase was dried over Na_2SO_4, filtered and evaporated. The residue was mixed with 120 ml concentrated H_2SO_4. The mixture was stirred at 65°C 1h, than diluted with ice water, extracted with DCM (3x50 ml). Combined organic phase was washed with aq. $NaHCO_3$, dried over Na_2SO_4, filtered and evaporated. The residue was purified on silica gel (eluent – DCM). Yield 30 g (74%). NMR data are in agreement with previously published[4, 5].

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, *J* = 8.4 Hz, 1H), 6.93 – 6.83 (m, 2H), 3.87 (s, 3H), 3.37 – 3.29 (m, 1H), 2.75 – 2.61 (m, 2H), 1.29 (d, *J* = 7.3 Hz, 3H).

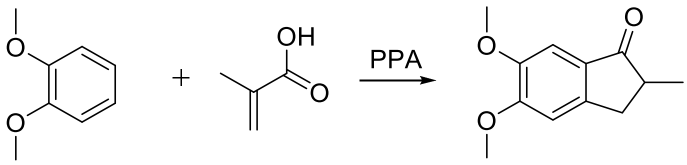
5-t-Butyl-2,3-dihydro-1H-inden-1-one



Compound was synthesized in the same way. Yield 20 g (50%). NMR data are in agreement with previously published[6].

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, *J* = 8.1 Hz, 1H), 7.44 (s, 1H), 7.42 (d, *J* = 8.2 Hz, 1H), 3.37 (dd, *J* = 17.8, 8.6 Hz, 1H), 2.70 (dt, *J* = 12.1, 3.0 Hz, 2H), 1.35 (s, 9H), 1.30 (d, *J* = 7.2 Hz, 3H).

5,6-dimethoxy-2,3-dihydro-1H-inden-1-one



Concentrated H_3PO_4 (20 ml) was put in a round-bottom flask which was then placed in an ice bath. After that, 30 g of P_2O_5 was slowly added to the mixture with stirring so that a homogeneous mixture is formed. Then the flask was placed on an oil bath, the reaction mass was warmed to 80 °C and then stirred for 30 min. Obtained polyphosphoric acid (15 ml) was put in a round-bottom flask, 1,2-dimethoxybenzene (1 g, 7.25 mmol) and methacrylic acid (1.24 g , 14.5 mmol) were added. The reaction mass was placed on an oil bath and stirred at 50 °C overnight. The progress of the reaction was monitored by TLC (eluent: CH_2Cl_2) after pretreatment of the sample with Na_2CO_3. Then the reaction mixture was dissolved in distill water and treated with Na_2CO_3 until the acid was neutralized. After that, the reaction products were extracted with CH_2Cl_2. After drying over anhydrous Na_2SO_4, the combined organic extract was concentrated by rotary evaporation. The crude product was purified by flash chromatography on silica gel (eluent: CH_2Cl_2). Yield 1.45 g (97%).NMR data are in agreement with previously published[7].

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.18 (s, 1H), 6.86 (s, 1H), 3.96 (s, 3H), 3.90 (s, 3H), 3.30 (dd, *J* = 16.7, 7.3 Hz, 1H), 2.70 (td, *J* = 7.4, 3.5 Hz, 1H), 2.63 (dd, *J* = 16.7, 3.4 Hz, 1H), 1.29 (d, *J* = 7.4 Hz, 3H).

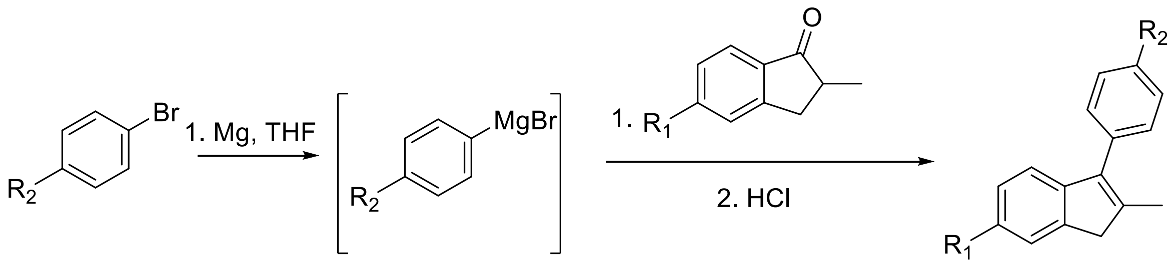
Preparation of indenes

*General Procedure 1 (**GP-1**)*[8]

3,4-Diaryl butadiene sulfone (10 mmol) was heated in *o*-dichlorobenzene (5 ml/mmol; 10 ml/mmol for methoxy-substituted indenes) in a round-bottom flask under inert atmosphere for 5 hours. After that the reaction mixture was cooled to 65 °C and $BF_3{\cdot}Et_2O$ (2 mmol) was added. The reaction mixture was stirred for 2 hours at 65 °C, allowed to cool to RT, quenched with 2 mL of methanol and the solvent was removed under reduced pressure. The crude product was purified by flash chromatography on silica gel (eluent: CH_2Cl_2/hexane = from 3:1 to 1:1 by volume).

Indenes **1i-1p** were synthesized according the literature procedure ***GP-1.*** NMR data for **1i**, **1m**, **1n** and **1p** are in agreement with previously published[8].

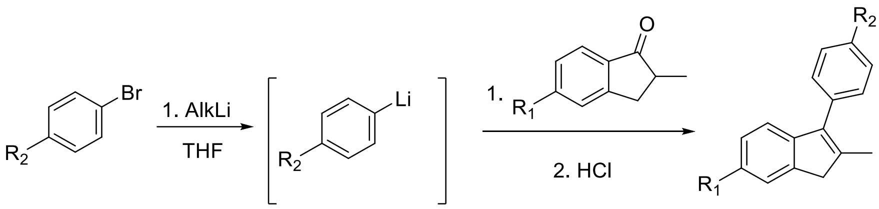
*General Procedure 2 (**GP-2**)*



Under argon atmosphere to Mg powder (1.36 g, 0.057 mol, 2 eq) in 50 ml THF_{abs}, a crop of iodine and one drop of 1,2-dibromoethane were added. The mixture was heated on an oil bath and stirred under reflux until Mg was activated. After that, the mixture was cooled to 40-45 °C, and Aryl bromide (0.042 mol, 1.5 eq) was added dropwise to keep the reaction mixture at gentle reflux. After that the reaction mixture was refluxed with stirring for approximately 1 h before was cooled to RT and the solution of conforming 5-methoxy-2-methyl-2,3-dihydro-1*H*-inden-1-one or 5-tert-butyl-2-methyl-2,3-dihydro-1*H*-inden-1-one (0.028 mol) in 30 ml THF_{abs} was added dropwise . Then the reaction mixture was stirred for 2 h at 40 °C, then cooled to RT and stirred overnight. The reaction mixture was decanted from unreacted Mg to saturated NH_4Cl solution (20 ml), concentrated HCl (3 ml) was added to the mixture and stirred for 30 min. After that the product was extracted with ethyl acetate (2x50 ml). The combined organic layer was dried over Na_2SO_4, filtered and concentrated by rotary evaporation. The crude product was purified by column chromatography on silica gel (eluent: CH_2Cl_2/petroleum ether = 1:1).

Indenes **1a-1g** were obtained using procedure ***GP-2***.

*General Procedure 3 (**GP-3**)*

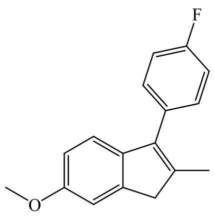


To the solution of 4-bromo-1.2-dimethoxybenzene (1.1 g, 5.1 mmol) in THF_{abs} (20 ml) in inert atmosphere was added a solution of *t*-BuLi (6.0 ml, 10.2 mmol, 2 eq, 1.7M in pentane) at -78°C. The reaction was stirred at this temperature for an hour. Then the solution of corresponding indanon (4.1 mmol, 0.8 eq) in THF_{abs} (10 ml) was added, and after that the stirring continued for 7h at RT. After the reaction was complete, water (10 ml) and conc. hydrochloric acid (2 ml) were added to obtain pH = 1, and the reaction mixture was stirred 30 min. The RM was diluted with water, extracted with ethyl acetate and purified by column chromatography on silica gel (eluent: petroleum ether/CH_2Cl_2 = 2:1).

Indenes **1h, 1q, 1r** and **1s** were obtained using procedure ***GP-3***.

Analytical data of indens:

*3-(4-fluorophenyl)-6-methoxy-2-methyl-1H-indene **(1a)***



Yield 3.41 g (48%); red-orange solid, m.p. 67.2-69.2°C

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.33 (m, 2H), 7.18 – 7.12 (m, 2H), 7.10 – 7.04 (m, 2H), 6.80 (dd, *J* = 8.3, 2.4 Hz, 1H), 3.84 (s, 3H), 3.42 (s, 2H), 2.10 (s, 3H).

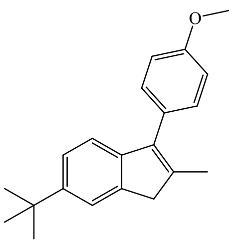
^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ 157.6, 144.2, 138.5, 130.8, 130.7, 119.4, 115.6, 115.4, 111.6, 110.5, 55.8, 43.1, 14.9.

^{19}F NMR (376 MHz, $CDCl_3$) δ -115.3.

IR (KBr, cm^{-1}) ν_{max} = 1602, 1580, 1508, 1475, 1463, 1432, 1389, 1351, 1328, 1286, 1244, 1219, 1170, 1153, 1108, 1092, 1031, 1013, 1007.

HRMS calc. for $C_{17}H_{16}FO$ $[M+H]^+$ = 255.1180; found 255.1184.

*6-tert-butyl-3-(4-methoxyphenyl)-2-methyl-1H-indene **(1b)***



Yield 5,97 g (73%); orange liquid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 – 7.52 (m, 1H), 7.40 – 7.35 (m, 2H), 7.31 (dd, *J* = 8.0, 1.8 Hz, 1H), 7.20 (d, *J* = 8.0 Hz, 1H), 7.06 – 7.01 (m, 2H), 3.89 (s, 3H), 3.46 (s, 2H), 2.16 (s, 3H), 1.40 (s, 9H).

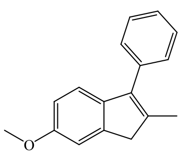
^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ 158.6, 147.2, 144.2, 142.5, 139.5, 137.9, 130.3, 128.2, 123.2, 120.8, 118.8, 113.9, 55.4, 43.2, 34.7, 31.8, 15.0.

IR (KBr, cm^{-1}) ν_{max} = 2959, 2904, 2869, 1601, 1510, 1462, 1441, 1362, 1286, 1245, 1173, 1160, 1093, 1034.

HRMS calc. for $C_{21}H_{25}O$ $[M+H]^+$ = 293.1900; found 293.1897.

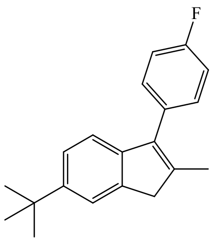
*6-methoxy-2-methyl-3-phenyl-1H-indene **(1c)***

Yield 6.47 g (98%); white solid, m.p. 89.4-90.2°C



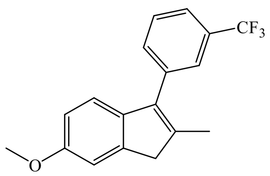
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 (t, *J* = 7.5 Hz, 2H), 7.42 (d, *J* = 7.5 Hz, 2H), 7.36 (t, *J* = 7.2 Hz, 1H), 7.14 (d, *J* = 8.3 Hz, 1H), 7.07 (s, 1H), 6.81 (dd, *J* = 8.3, 1.7 Hz, 1H), 3.84 (s, 3H), 3.44 (s, 2H), 2.13 (s, 3H).
^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ 157.5, 144.3, 139.7, 138.3, 138.1, 135.8, 129.2, 128.5, 127.0, 119.6, 111.5, 110.4, 55.7, 43.2, 14.9.
IR (KBr, cm^{-1}) ν_{max} = 1579, 1492, 1473, 1439, 1389, 1352, 1328, 1282, 1243, 1218, 1173, 1132, 1107, 1076, 1031, 1009.
HRMS calc. for $C_{17}H_{17}O$ $[M+H]^+$ = 237.1274; found 237.1276.

*6-tert-butyl-3-(4-fluorophenyl)-2-methyl-1H-indene **(1d)***



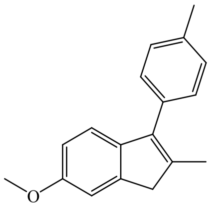
Yield 5.7 g (73%); yellow solid, m.p. 55.7-57.1°C
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 – 7.51 (m, 1H), 7.40 – 7.34 (m, 2H), 7.30 (dd, *J* = 8.0, 1.8 Hz, 1H), 7.19 – 7.11 (m, 3H), 3.46 (s, 2H), 2.13 (s, 3H), 1.38 (s, 9H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 162.0 (d, *J* = 245.6 Hz), 147.5, 143.8, 142.4, 140.3, 137.5, 131.7 (d, *J* = 3.3 Hz), 130.8 (d, *J* = 7.9 Hz), 123.3, 120.8, 118.6, 115.5 (d, *J* = 21.2 Hz), 43.3, 34.8, 31.8, 14.9.
^{19}F NMR (376 MHz, $CDCl_3$) δ -115.4.
IR (KBr, cm^{-1}) ν_{max} = 2960, 2905, 2872, 1721, 1658, 1598, 1506, 1479, 1424, 1387, 1364, 1294, 1261, 1222, 1202, 1155, 1094, 1014.
HRMS calc. for $C_{20}H_{22}F$ $[M+H]^+$ = 281.1700; found 281.1704.

*6-methoxy-2-methyl-3-(3-(trifluoromethyl)phenyl)-1H-indene **(1e)***



Yield 6,2 g (73%); bright orange solid, m.p. 50.5-52.5°C
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (s, 1H), 7.63 – 7.56 (m, 3H), 7.11 – 7.05 (m, 2H), 6.81 (dd, *J* = 8.3, 2.4 Hz, 1H), 3.84 (s, 3H), 3.45 (s, 2H), 2.12 (s, 3H).
^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ 157.8, 144.2, 139.6, 139.0, 137.0, 136.7, 132.5, 131.0 (q, *J* = 31.7 Hz), 129.0, 125.9 (q, *J* = 3.7 Hz), 124.4 (q, *J* = 272.0 Hz), 123.8 (q, *J* = 3.8 Hz), 119.3, 111.7, 110.6, 55.8, 43.3, 14.9.
^{19}F NMR (376 MHz, $CDCl_3$) δ -62.5.
IR (KBr, cm^{-1}) ν_{max} = 1605, 1479, 1468, 1442, 1354, 1321, 1309, 1265, 1166, 1110, 1091, 1072, 1030.
HRMS calc. for $C_{18}H_{16}F_3O$ $[M+H]^+$ = 305.1148; found 305.1151.

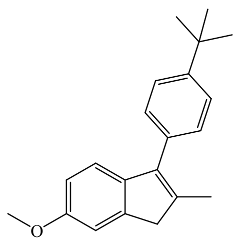
*6-methoxy-2-methyl-3-p-tolyl-1H-indene **(1f)***



Yield 6.09 g (87%); white solid, m.p. 98.9-99.3°C
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 – 7.27 (m, 4H), 7.15 (d, *J* = 8.3 Hz, 1H), 7.07 (s, 1H), 6.81 (d, *J* = 8.3 Hz, 1H), 3.85 (s, 3H), 3.43 (s, 2H), 2.44 (s, 3H), 2.13 (s, 3H).
^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ 157.5, 144.3, 139.8, 138.0, 138.0, 136.6, 132.8, 129.2, 129.1, 119.6, 111.5, 110.4, 55.7, 43.1, 21.4, 14.9.

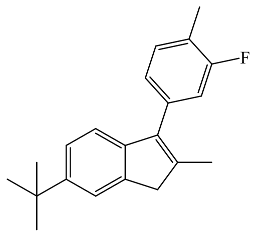
IR (KBr, cm^{-1}) ν_{max} = 1617, 1602, 1576, 1507, 1473, 1460, 1431, 1350, 1326, 1287, 1245, 1216, 1197, 1169, 1135, 1107, 1037, 1005.
HRMS calc. for $C_{18}H_{19}O$ $[M+H]^+$ = 251.1430; found 251.1434.

3-(4-tert-butylphenyl)-6-methoxy-2-methyl-1H-indene ***(1g)***



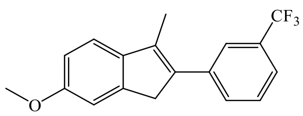
Yield 6,1 g (75%); pale orange solid, m.p. 112.6-113.3°C
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.51 – 7.47 (m, 2H), 7.39 – 7.34 (m, 2H), 7.19 (d, *J* = 8.3 Hz, 1H), 7.06 (d, *J* = 2.4 Hz, 1H), 6.80 (dd, *J* = 8.3, 2.4 Hz, 1H), 3.84 (s, 3H), 3.42 (s, 2H), 2.14 (d, *J* = 1.0 Hz, 3H), 1.40 (s, 9H).
^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ 157.5, 149.8, 144.3, 139.8, 138.0, 137.9, 132.8, 128.8, 125.4, 119.8, 111.5, 110.4, 55.7, 43.2, 34.7, 31.6, 15.0.
IR (KBr, cm^{-1}) ν_{max} = 2952, 2933, 2901, 1617, 1582, 1510, 1476, 1460, 1431, 1396, 1350, 1328, 1288, 1268, 1247, 1222, 1202, 1174, 1137, 1111, 1037, 1005.
HRMS calc. for $C_{21}H_{25}O$ $[M+H]^+$ = 293.1900; found 293.1901.

6-tert-butyl-3-(3-fluoro-4-methylphenyl)-2-methyl-1H-indene ***(1h)***



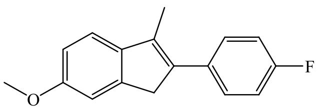
Yield 0.96 g (82%); yellow caramel.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (d, *J* = 1.1 Hz, 1H), 7.29 (dd, *J* = 8.1, 1.8 Hz, 1H), 7.25 (d, *J* = 7.1 Hz, 1H), 7.17 (d, *J* = 8.0 Hz, 1H), 7.11 – 7.04 (m, 2H), 3.45 (s, 2H), 2.35 (d, *J* = 1.6 Hz, 3H), 2.14 (s, 3H), 1.37 (s, 9H).
^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ 161.5 (d, *J* = 244.4 Hz), 147.4, 143.6, 142.4, 140.5, 137.4 (d, *J* = 1.9 Hz), 135.3 (d, *J* = 8.0 Hz), 131.5 (d, *J* = 5.6 Hz), 124.7 (d, *J* = 3.3 Hz), 123.4 (d, *J* = 17.1 Hz), 123.3, 120.8, 118.7, 115.6 (d, *J* = 22.1 Hz), 43.3, 34.8, 31.8, 15.0, 14.6 (d, *J* = 3.5 Hz).
^{19}F NMR (376 MHz, $CDCl_3$) δ -117.8.
IR (KBr, cm^{-1}) ν_{max} = 2964, 2952, 2929, 2905, 2867, 1571, 1505, 1479, 1462, 1441, 1414, 1389, 1364, 1292, 1267, 1245, 1221, 1199, 1162, 1154, 1126, 1115, 1022.
HRMS calc. for $C_{21}H_{24}F$ $[M+H]^+$ = 295.1856; found 295.1822

6-methoxy-3-methyl-2-(3-(trifluoromethyl)phenyl)-1H-indene ***(1j)***



Yield 2.04 g (67%); orange solid, m.p. 50.0-50.6°C
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30 (s, 1H), 8.25 (d, *J* = 7.8 Hz, 1H), 7.93 (d, *J* = 8.7 Hz, 1H), 7.83 (d, *J* = 7.8 Hz, 1H), 7.64 (t, *J* = 7.8 Hz, 1H), 6.90 (dd, *J* = 8.7, 2.6 Hz, 1H), 6.78 (d, *J* = 2.6 Hz, 1H), 4.62 (s, 2H), 3.88 (s, 3H), 2.52 (s, 3H).
^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ 158.6, 144.3, 140.4, 138.6, 136.6, 136.2, 131.3, 130.9 (q, *J* = 31.9 Hz), 128.9, 124.7 (q, *J* = 3.8 Hz), 124.4 (q, *J* = 272.6 Hz), 123.0 (q, *J* = 3.8 Hz), 120.0, 112.3, 110.1, 55.7, 40.8, 12.2.
^{19}F NMR (376 MHz, $CDCl_3$) δ -62.6.
IR (KBr, cm^{-1}) ν_{max} = 1607, 1595, 1583, 1481, 1441, 1381, 1345, 1309, 1288, 1247, 1227, 1157, 1142, 1123, 1066, 1030, 1004,.
HRMS calc. for $C_{18}H_{16}F_3O$ $[M+H]^+$ = 305.1148 ; found 305.1152

2-(4-fluorophenyl)-6-methoxy-3-methyl-1H-indene ***(1l)****)*



Yield 1.21 g (48%); ivory solid, m.p. 109.0-109.5°C

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 (dd, *J* = 8.1, 5.8 Hz, 2H), 7.27 (d, *J* = 8.3 Hz, 1H), 7.15 – 7.06 (m, 3H), 6.91 (dd, *J* = 8.4, 2.4 Hz, 1H), 3.87 (s, 3H), 3.68 (s, 2H), 2.27 (s, 3H).

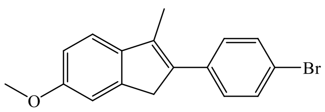
^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ 161.6 (d, *J* = 245.9 Hz), 158.2, 144.1, 140.7, 137.1, 134.4, 133.9 (d, *J* = 3.3 Hz), 129.6 (d, *J* = 7.8 Hz), 119.6, 115.4 (d, *J* = 21.2 Hz), 112.1, 110.1, 55.7, 41.1, 12.1.

^{19}F NMR (376 MHz, $CDCl_3$) δ -115.9.

IR (KBr, cm^{-1}) ν_{max} = 1607, 1584, 1504, 1482, 1469, 1453, 1429, 1399, 1381, 1328, 1286, 1278, 1269, 1246, 1223, 1158, 1142, 1115, 1073, 1023.

HRMS calc. for $C_{17}H_{16}FO$ $[M+H]^+$ 255.1180; found 255.1184.

2-(4-bromophenyl)-6-methoxy-3-methyl-1H-indene ***(1o)***



Yield 2.01 g (64%); ivory solid, m.p. 106.0-106.5°C

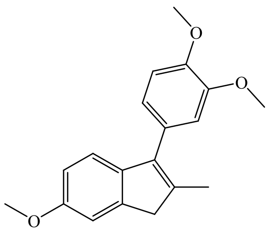
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 – 7.49 (m, 2H), 7.34 – 7.30 (m, 2H), 7.27 (d, *J* = 8.3 Hz, 1H), 7.07 (d, *J* = 2.1 Hz, 1H), 6.90 (dd, *J* = 8.3, 2.4 Hz, 1H), 3.86 (s, 3H), 3.69 – 3.65 (m, 2H), 2.27 (t, *J* = 2.1 Hz, 3H).

^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ 158.4, 144.2, 140.6, 136.9, 136.7, 135.3, 131.6, 129.7, 120.3, 119.8, 112.2, 110.1, 55.7, 40.8, 12.3.

IR (KBr, cm^{-1}) ν_{max} = 1608, 1574, 1482, 1454, 1426, 1397, 1379, 1340, 1288, 1276, 1264, 1226, 1209, 1185, 1146, 1135, 1109, 1073, 1065, 1025, 1006.

HRMS calc. for $C_{17}H_{16}BrO$ $[M+H]^+$ = 315.0379; found 315.0379.

3-(3,4-dimethoxyphenyl)-6-methoxy-2-methyl-1H-indene ***(1q)***



Yield 0.78 g (64%); grey solid, m.p. 103.1-104.9°C

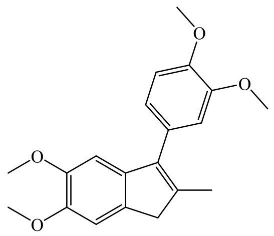
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.14 (d, *J* = 8.3 Hz, 1H), 7.05 (s, 1H), 7.00 – 6.93 (m, 3H), 6.80 (dd, *J* = 8.3, 3.2 Hz, 1H), 3.94 (s, 3H), 3.90 (s, 3H), 3.83 (s, 3H), 3.41 (s, 2H), 2.12 (s, 3H).

^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ 157.5, 148.9, 148.1, 144.2, 139.8, 137.8, 128.5, 121.6, 119.5, 112.3, 111.5, 111.3, 110.5, 56.0, 55.7, 43.1, 15.0.

IR (KBr, cm^{-1}) ν_{max} = 2998, 2961, 2931, 2834, 1608, 1579, 1516, 1474, 1460, 1452, 1430, 1405, 1360, 1328, 1291, 1258, 1234, 1201, 1157, 1140, 1111, 1045, 1038, 1026, 1020.

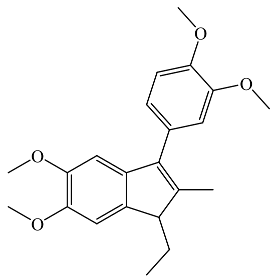
HRMS calc. for $C_{19}H_{21}O_3$ $[M+H]^+$ = 297.1485; found 297.1487.

3-(3,4-dimethoxyphenyl)-5,6-dimethoxy-2-methyl-1H-indene ***(1r)***



Yield 1,25 g (94%); beige solid, m.p. 131.5-132.6°C
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.05 (s, 1H), 6.99 (d, *J* = 8.0 Hz, 1H), 6.97 – 6.93 (m, 2H), 6.81 (s, 1H), 3.94 (s, 3H), 3.90 (d, *J* = 2.9 Hz, 6H), 3.83 (s, 3H), 3.38 (s, 2H), 2.12 (s, 3H).
^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ 148.9, 148.3, 148.1, 146.7, 139.4, 138.8, 138.0, 134.6, 128.4, 121.5, 112.3, 111.4, 108.2, 103.4, 56.5, 56.3, 56.1, 56.0, 42.9, 15.0.
IR (KBr, cm^{-1}) ν_{max} = 1600, 1578, 1512, 1492, 1466, 1456 1438, 1410, 1345, 1293, 1251, 1212, 1174, 1139, 1102, 1045, 1026, 1010.
HRMS calc. for $C_{20}H_{23}O_4$ $[M+H]^+$ = 327.1591; found 327.1595.

3-(3,4-dimethoxyphenyl)-1-ethyl-5,6-dimethoxy-2-methyl-1H-indene ***(1s)***



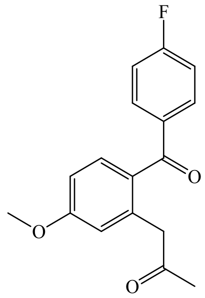
Yield 0.72 g (90%); white solid, m.p. 95.7-97.0°C
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.03 – 6.91 (m, 4H), 6.78 (s, 1H), 3.96 – 3.88 (m, 6H), 3.82 (s, 3H), 3.35 (t, *J* = 4.8 Hz, 1H), 2.11 – 2.04 (m, 1H), 2.01 (s, 3H), 1.96 – 1.86 (m, 1H), 0.64 (t, *J* = 7.3 Hz, 3H).
^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ 148.9, 148.3, 148.1, 146.8, 141.9, 139.0, 138.5, 137.9, 128.6, 121.6, 112.4, 111.4, 107.6, 103.3, 56.6, 56.2, 56.0, 56.0, 52.9, 23.0, 13.3, 8.6.
IR (KBr, cm^{-1}) ν_{max} = 2995, 2950, 2921, 2909, 2857, 2831, 1599, 1578, 1511, 1492, 1465, 1444, 1439, 1417, 1409, 1346, 1335, 1322, 1292, 1272, 1253, 1229, 1205, 1186, 1171, 1158, 1139, 1115, 1084, 1026, 1015, 1007.
HRMS calc. for $C_{22}H_{27}O_4$ $[M+H]^+$ = 355.1904; found 355.1910.

Preparation of 1,5-diketones from indenes

Corresponding indene (0.013 mol) and $NaIO_4$ (11.1 g, 0.052 mol, 4.0 eq) were placed in a round-bottom flask, and then a mixture of CH_2Cl_2, CH_3CN and H_2O 1:2:1 (50 ml) was added. The flask was cold in an ice bath, and $RuCl_3$ (0.134 g, 0.65 mmol, 5 mol%) was added to the reaction mixture. After that, the reaction was stirred at RT 2-16 hour. The progress of the reaction was monitored by TLC (eluent: CH_2Cl_2/petroleum ether = 1:1). The reaction mixture was treated with 50 ml of saturated $Na_2S_2O_3$ and then extracted by CH_2Cl_2. The combined organic extract was dried over anhydrous Na_2SO_4, filtered and concentrated by rotary evaporation. The crude product was purified by column chromatography on silica gel (eluent: CH_2Cl_2).

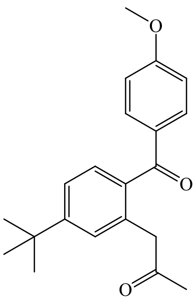
Analytical data of 1,5-diketones:

1-(2-(4-fluorobenzoyl)-5-methoxyphenyl)propan-2-one ***(2a)***



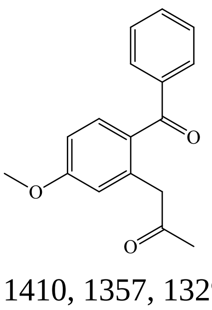
Yield 2.68 g (72%); yellow crystals, m.p. 69.8-70.3°C
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 – 7.74 (m, 2H), 7.39 (d, *J* = 8.6 Hz, 1H), 7.15 – 7.08 (m, 2H), 6.84 – 6.77 (m, 2H), 4.00 (s, 2H), 3.86 (s, 3H), 2.23 (s, 3H).
^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ 205.6, 196.0, 165.4 (d, *J* = 253.8 Hz), 162.0, 138.0, 135.1 (d, *J* = 3.0 Hz), 133.5, 132.8 (d, *J* = 9.2 Hz), 129.9, 118.4, 115.5 (d, *J* = 21.8 Hz), 111.2, 55.6, 48.7, 30.0.
^{19}F NMR (376 MHz, $CDCl_3$) δ -106.3.
IR (KBr, cm^{-1}) ν_{max} = 3064, 3056, 3020, 3001, 2979, 2953, 2919, 2847, 1928, 1709, 1648, 1609, 1598, 1567, 1502, 1463, 1457, 1430, 1421, 1407, 1354, 1329, 1304, 1296, 1293, 1281, 1254, 1226, 1200, 1183, 1168, 1157, 1152, 1110, 1100, 1042, 1011.
HRMS calc. for $C_{17}H_{16}FO_3$ $[M+H]^+$ = 287.1078; found 287.1084.

1-(5-tert-butyl-2-(4-methoxybenzoyl)phenyl)propan-2-one ***(2b)***



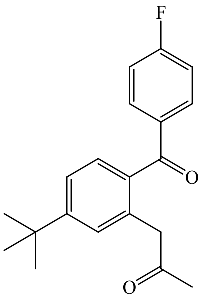
Yield 3.36 g (80%); pale yellow crystals, m.p. 76.3-77.0°C
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 – 7.79 (m, 2H), 7.35 (d, *J* = 8.0 Hz, 1H), 7.32 (dd, *J* = 8.1, 1.8 Hz, 1H), 7.25 (d, *J* = 1.5 Hz, 1H), 6.96 – 6.90 (m, 2H), 3.96 (s, 2H), 3.87 (s, 3H), 2.16 (s, 3H), 1.35 (s, 9H).
^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ 206.0, 197.0, 163.5, 154.2, 135.7, 134.2, 132.8, 130.9, 130.2, 129.2, 123.3, 113.6, 55.6, 48.6, 35.0, 31.3, 30.0.
IR (KBr, cm^{-1}) ν_{max} = 1717, 1653, 1601, 1576, 1507, 1498, 1483, 1465, 1455, 1436, 1419, 1397, 1365, 1362, 1354, 1324, 1305, 1276, 1251, 1202, 1191, 1181, 1158, 1130, 1115, 1097, 1024.
HRMS calc. for $C_{21}H_{25}O_3$ $[M+H]^+$ = 325.1798; found 325.1804.

1-(2-benzoyl-5-methoxyphenyl)propan-2-one ***(2c)***



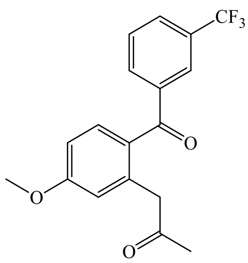
Yield 3.41 g (98%); 83%; white crystals, m.p. 74.4-75.0°C
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 – 7.71 (m, 2H), 7.57 – 7.52 (m, 1H), 7.47 – 7.40 (m, 3H), 6.80 (dq, *J* = 4.7, 2.6 Hz, 2H), 4.00 (s, 2H), 3.86 (s, 3H), 2.24 (s, 3H).
^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ 205.6, 197.4, 161.9, 138.9, 138.1, 133.9, 132.4, 130.1, 129.9, 128.3, 118.3, 111.1, 55.5, 48.8, 30.0.
IR (KBr, cm^{-1}) ν_{max} = 1719, 1654, 1603, 1595, 1577, 1503, 1468, 1453, 1447, 1410, 1357, 1329, 1319, 1308, 1279, 1246, 1187, 1175, 1160, 1097, 1076, 1031, 1016.
HRMS calc. for $C_{17}H_{17}O_3$ $[M+H]^+$ = 269.1172; found 269.1176.

*1-(5-tert-butyl-2-(4-fluorobenzoyl)phenyl)propan-2-one **(2d)***



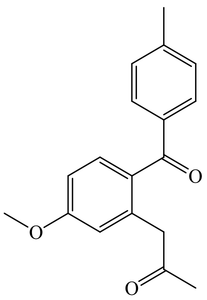
Yield 2,75 g (68%); yellow liquid.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 – 7.81 (m, 2H), 7.33 (d, *J* = 1.2 Hz, 2H), 7.25 (s, 1H), 7.16 – 7.09 (m, 2H), 4.02 (s, 2H), 2.19 (s, 3H), 1.35 (s, 9H).
^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ 205.9, 196.8, 165.6 (d, *J* = 254.2 Hz), 154.8, 135.0, 134.6, 134.6 (d, *J* = 2.8 Hz), 133.0 (d, *J* = 9.2 Hz), 130.5, 129.4, 123.4, 115.5 (d, *J* = 21.8 Hz), 48.7, 35.0, 31.3, 30.0.
^{19}F NMR (376 MHz, $CDCl_3$) δ -105.9.
IR (KBr, cm^{-1}) ν_{max} = 1717, 1659, 1596, 1570, 1505, 1478, 1463, 1410, 1357, 1299, 1275, 1231, 1154, 1132, 1095, 1062, 1014.
HRMS calc. for $C_{20}H_{22}FO_2$ $[M+H]^+$ = 313.1599; found 313.1603.

*1-(5-methoxy-2-(3-(trifluoromethyl)benzoyl)phenyl)propan-2-one **(2e)***



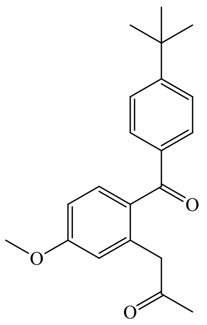
Yield 3.18 g (73%); yellow liquid.
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (s, 1H), 7.91 (d, *J* = 7.7 Hz, 1H), 7.81 (d, *J* = 7.8 Hz, 1H), 7.58 (t, *J* = 7.8 Hz, 1H), 7.42 – 7.35 (m, 1H), 6.85 – 6.77 (m, 2H), 4.05 (s, 2H), 3.87 (s, 3H), 2.26 (s, 3H).
^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ 205.4, 195.9, 162.4, 139.7, 138.5, 133.9, 133.4, 131.0 (q, *J* = 32.9 Hz), 129.1, 128.9, 128.7 (q, *J* = 3.6 Hz), 126.8 (q, *J* = 3.9 Hz), 123.9 (q, *J* = 272.5 Hz), 118.8, 111.2, 55.6, 48.9, 30.1.
^{19}F NMR (376 MHz, $CDCl_3$) δ -62.7.
IR (KBr, cm^{-1}) ν_{max} = 1722, 1717, 1661, 1651, 1601, 1572, 1568, 1501, 1464, 1429, 1357, 1338, 1316, 1254, 1158, 1113, 1094, 1072, 1045.
HRMS calc. for $C_{18}H_{16}F_3O_3$ $[M+H]^+$ = 337.1046; found 337.1052.

*1-(5-methoxy-2-(4-methylbenzoyl)phenyl)propan-2-one **(2f)***



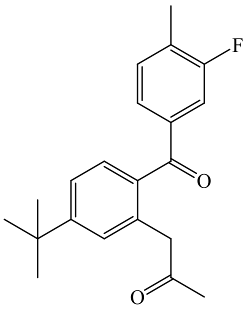
Yield 2.45 g (77%); pale orange solid, m.p. 86.0-86.8°C
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, *J* = 8.0 Hz, 2H), 7.42 (d, *J* = 9.3 Hz, 1H), 7.25 (d, *J* = 8.0 Hz, 2H), 6.80 (d, *J* = 6.8 Hz, 2H), 3.97 (s, 2H), 3.86 (s, 3H), 2.42 (s, 3H), 2.22 (s, 3H).
^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ 205.6, 197.2, 161.7, 143.2, 137.8, 136.2, 133.5, 130.4, 130.3, 129.0, 118.2, 111.1, 55.5, 48.7, 30.0, 21.7.
IR (KBr, cm^{-1}) ν_{max} = 1717, 1646, 1604, 1568, 1496, 1467, 1455, 1446, 1423, 1406, 1355, 1328, 1311, 1296, 1275, 1256, 1213, 1184, 1166, 1148, 1115, 1046, 1015.
HRMS calc. for $C_{18}H_{19}O_3$ $[M+H]^+$ = 283.1329; found 283.1334.

*1-(2-(4-tert-butylbenzoyl)-5-methoxyphenyl)propan-2-one **(2g)***



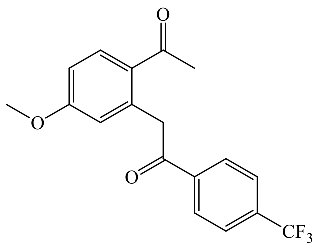
Yield 3.45 g (82%); yellow liquid.
[1]H NMR (400 MHz, Chloroform-*d*) δ 7.72 – 7.67 (m, 2H), 7.48 – 7.43 (m, 3H), 6.82 – 6.77 (m, 2H), 3.98 (s, 2H), 3.86 (s, 3H), 2.23 (s, 3H), 1.35 (s, 9H).
[13]C {[1]H} NMR (101 MHz, $CDCl_3$) δ 205.7, 197.1, 161.7, 156.1, 137.9, 136.1, 133.6, 130.3, 130.2, 125.3, 118.2, 111.1, 55.5, 48.7, 35.2, 31.2, 30.0.
IR (KBr, cm^{-1}) ν_{max} = 1724, 1719, 1648, 1643, 1597, 1571, 1561, 1499, 1473, 1465, 1458, 1430, 1420, 1396, 1355, 1314, 1294, 1249, 1195, 1179, 1161, 1110, 1045.
HRMS calc. for $C_{21}H_{25}O_3$ $[M+H]^+$ = 325.1798; found 325.1801.

*1-(5-tert-butyl-2-(3-fluoro-4-methylbenzoyl)phenyl)propan-2-one **(2h)***



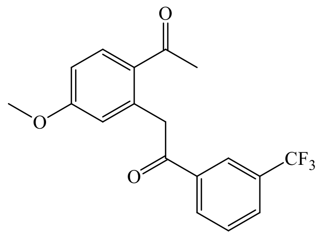
Yield 2.97 g (70%); yellow liquid.
[1]H NMR (400 MHz, $CDCl_3$) δ 7.47 – 7.40 (m, 2H), 7.30 (d, *J* = 8.1 Hz, 1H), 7.27 (dd, *J* = 8.1, 1.8 Hz, 1H), 7.23 – 7.17 (m, 2H), 3.96 (s, 2H), 2.29 (d, *J* = 2.1 Hz, 3H), 2.14 (s, 3H), 1.30 (s, 9H).
[13]C {[1]H} NMR (101 MHz, $CDCl_3$) δ 205.8, 196.7 (d, *J* = 2.1 Hz), 161.0 (d, *J* = 246.4 Hz), 154.8, 137.9 (d, *J* = 6.4 Hz), 134.8, 134.6, 131.3 (d, *J* = 4.9 Hz), 130.6, 130.4 (d, *J* = 17.6 Hz), 129.4, 126.2 (d, *J* = 3.3 Hz), 123.4, 116.6 (d, *J* = 23.5 Hz), 48.7, 35.0, 31.2, 30.0, 14.9 (d, *J* = 3.5 Hz).
[19]F NMR (376 MHz, $CDCl_3$) δ -116.5.
IR (KBr, cm^{-1}) ν_{max} = 1722, 1656, 1618, 1606, 1574, 1498, 1414, 1355, 1304, 1267, 1220, 1190, 1160, 1114, 1085.
HRMS calc. for $C_{21}H_{24}FO_2$ $[M+H]^+$ = 327.1755; found 327.1759.

*2-(2-acetyl-5-methoxyphenyl)-1-(4-(trifluoromethyl)phenyl)ethanone **(2i)***



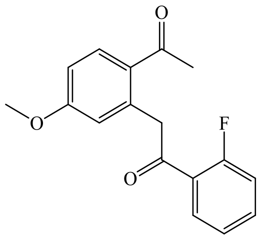
Yield 2.62 g (60%); beige solid, m.p. 114.0-115.0°C
[1]H NMR (400 MHz, $CDCl_3$) δ 8.16 (d, *J* = 8.2 Hz, 2H), 7.93 (d, *J* = 8.7 Hz, 1H), 7.76 (d, *J* = 8.2 Hz, 2H), 6.90 (dd, *J* = 8.7, 2.6 Hz, 1H), 6.78 (d, *J* = 2.6 Hz, 1H), 4.60 (s, 2H), 3.87 (s, 3H), 2.51 (s, 3H).
[13]C {[1]H} NMR (101 MHz, $CDCl_3$) δ 198.9, 196.4, 162.7, 140.4, 138.3, 134.2 (q, *J* = 32.6 Hz), 133.7, 128.6, 125.8 (q, *J* = 3.7 Hz), 123.8 (q, *J* = 272.6 Hz), 119.5, 112.0, 55.6, 45.9, 28.3.
[19]F NMR (376 MHz, $CDCl_3$) δ -63.0.
IR (KBr, cm^{-1}) ν_{max} = 1690, 1663, 1608, 1567, 1508, 1427, 1406, 1359, 1315, 1296, 1251, 1213, 1160, 1138, 1107, 1071, 1064, 1035, 1014, 1002.
HRMS calc. for $C_{18}H_{16}F_3O_3$ $[M+H]^+$ = 337.1046; found 337.1050.

2-(2-acetyl-5-methoxyphenyl)-1-(3-(trifluoromethyl)phenyl)ethanone ***(2j)***



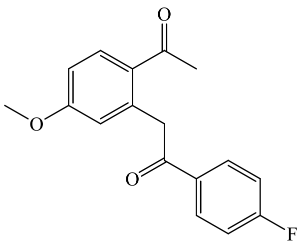
Yield 2.92 g (67%); beige solid, m.p. 93.2-93.9°C
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30 (s, 1H), 8.25 (d, *J* = 7.9 Hz, 1H), 7.93 (d, *J* = 8.7 Hz, 1H), 7.83 (d, *J* = 7.8 Hz, 1H), 7.64 (t, *J* = 7.8 Hz, 1H), 6.90 (dd, *J* = 8.7, 2.6 Hz, 1H), 6.78 (d, *J* = 2.6 Hz, 1H), 4.62 (s, 2H), 3.88 (s, 3H), 2.52 (s, 3H).
^{13}C {^{1}H} NMR δ (101 MHz, $CDCl_3$) δ 198.9, 195.9, 162.7, 138.3, 138.1, 133.7, 131.5, 131.27 (q, *J* = 32.8 Hz), 129.4, 128.8, 125.1 (q, *J* = 3.9 Hz), 123.9 (q, *J* = 272.5 Hz) 119.4, 112.0, 55.6, 45.8, 28.4.
^{19}F NMR (376 MHz, $CDCl_3$) δ -62.66.
IR (KBr, cm^{-1}) ν_{max} = 1767, 1684, 1671, 1605, 1570, 1505, 1466, 1458, 1440, 1409, 1358, 1350, 1331, 1319, 1284, 1244, 1212, 1187, 1171, 1117, 1100, 1071, 1061, 1026, 1012.
HRMS calc. for $C_{18}H_{16}F_3O_3$ $[M+H]^+$ = 337.1046; found 337.1052.

2-(2-acetyl-5-methoxyphenyl)-1-(2-fluorophenyl)ethanone ***(2k)***



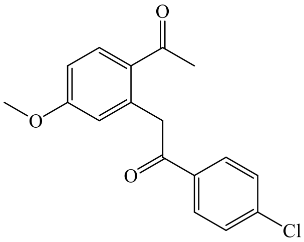
Yield 2.60 g (70%); pink-brown solid, m.p. 99.1-100.4°C
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 – 7.88 (m, 2H), 7.55 – 7.48 (m, 1H), 7.28 – 7.22 (m, 1H), 7.19 – 7.13 (m, 1H), 6.88 (dd, *J* = 8.7, 2.6 Hz, 1H), 6.79 (d, *J* = 2.6 Hz, 1H), 4.57 (d, *J* = 2.7 Hz, 2H), 3.87 (s, 3H), 2.52 (s, 3H).
^{13}C {^{1}H} NMR (101 MHz, Chloroform-*d*) δ 198.7, 195.5 (d, *J* = 4.5 Hz), 162.54, 161.9 (d, *J* = 253.6 Hz), 138.6 (d, *J* = 2.3 Hz), 134.3 (d, *J* = 8.9 Hz), 133.4, 131.0 (d, *J* = 2.9 Hz), 129.0, 126.4 (d, *J* = 13.3 Hz), 124.6 (d, *J* = 3.3 Hz), 119.2, 116.7 (d, *J* = 23.8 Hz), 112.0, 55.5, 50.3 (d, *J* = 8.4 Hz), 28.4.
^{19}F NMR (376 MHz, $CDCl_3$) δ -109.5.
IR (KBr, cm^{-1}) ν_{max} 1692, 1677, 1669, 1662, 1627, 1601, 1574, 1480, 1465, 1453, 1417, 1401, 1357, 1339, 1318, 1307, 1277, 1266, 1241, 1212, 1205, 1197, 1190, 1178, 1162 , 1154, 1122, 1102, 1063, 1029, 1004.
HRMS calc. for $C_{17}H_{16}FO_3$ $[M+H]^+$ = 287.1078; found 287.1082.

2-(2-acetyl-5-methoxyphenyl)-1-(4-fluorophenyl)ethanone ***(2l)***



Yield 2.53 g (68%); white solid, m.p. 137.9-138.4°C
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 – 8.05 (m, 2H), 7.91 (d, *J* = 8.7 Hz, 1H), 7.19 – 7.11 (m, 2H), 6.89 (dd, *J* = 8.7, 2.6 Hz, 1H), 6.76 (d, *J* = 2.6 Hz, 1H), 4.59 (s, 2H), 3.87 (s, 3H), 2.52 (s, 3H).
^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ 199.0, 195.8, 165.8 (d, *J* = 253.9 Hz), 162.5, 138.7, 133.9 (d, *J* = 3.2 Hz), 133.5, 130.9 (d, *J* = 9.5 Hz), 129.0, 119.3, 115.8 (d, *J* = 21.9 Hz), 111.9, 55.6, 45.5, 28.4.
^{19}F NMR (376 MHz, $CDCl_3$) δ -105.97.
IR (KBr, cm^{-1}) ν_{max} = 1685, 1672, 1603, 1569, 1507, 1466, 1421, 1409, 1360, 1337, 1318, 1243, 1225, 1215, 1186, 1180, 1161, 1123, 1065, 1028, 1007.
HRMS calc. for $C_{17}H_{16}FO_3$ $[M+H]^+$ = 287.1078; found 287.1082.

2-(2-acetyl-5-methoxyphenyl)-1-(4-chlorophenyl)ethanone ***(2m)***



Yield 3.1 g (79%); white solid, m.p. 134.5-134.9°C

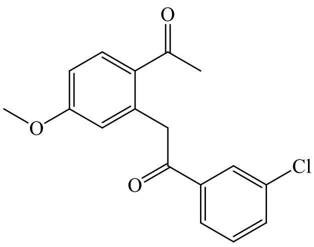
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 – 7.97 (m, 2H), 7.91 (d, *J* = 8.7 Hz, 1H), 7.48 – 7.44 (m, 2H), 6.89 (dd, *J* = 8.7, 2.6 Hz, 1H), 6.76 (d, *J* = 2.6 Hz, 1H), 4.58 (s, 2H), 3.87 (s, 3H), 2.52 (s, 3H).

^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ 198.98, 196.23, 162.59, 139.35, 138.59, 135.91, 133.57, 129.76, 129.03, 128.92, 119.34, 112.00, 55.59, 45.54, 28.44.

IR (KBr, cm^{-1}) ν_{max} = 1685, 1668, 1602, 1587, 1570, 1487, 1465, 1421, 1400, 1359, 1334, 1319, 1306, 1297, 1281, 1244, 1215, 1191, 1182, 1173, 1122, 1090, 1064, 1028, 1015, 1004.

HRMS calc. for $C_{17}H_{16}ClO_3$ $[M+H]^+$ = 303.0783; found 303.0787.

2-(2-acetyl-5-methoxyphenyl)-1-(3-chlorophenyl)ethanone ***(2n)***



Yield 3.53 g (90%); beige crystalls, m.p. 122.5-124.0°C

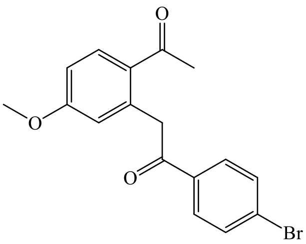
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (t, *J* = 1.8 Hz, 1H), 7.96 – 7.90 (m, 2H), 7.56 – 7.53 (m, 1H), 7.44 (t, *J* = 7.9 Hz, 1H), 6.90 (dd, *J* = 8.7, 2.6 Hz, 1H), 6.76 (d, *J* = 2.6 Hz, 1H), 4.58 (s, 2H), 3.88 (s, 3H), 2.52 (s, 3H).

^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ 198.9, 196.0, 162.6, 139.1, 138.4, 135.0, 133.6, 132.9, 130.1, 128.9, 128.4, 126.4, 119.4, 112.0, 55.6, 45.7, 28.4.

IR (KBr, cm^{-1}) ν_{max} 1686, 1666, 1661, 1624, 1601, 1571, 1478, 1467, 1422, 1413, 1407, 1357, 1336, 1320, 1306, 1297, 1242, 1211, 1187, 1179, 1124, 1063, 1029, 1007, 1001.

HRMS calc. for $C_{17}H_{16}ClO_3$ $[M+H]^+$ = 303.0783; found 303.0789.

2-(2-acetyl-5-methoxyphenyl)-1-(4-bromophenyl)ethanone ***(2o)***



Yield 3.14 g (70%); white crystals, m.p. 121.6-122.1°C

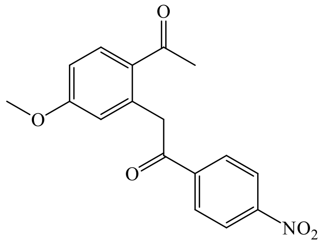
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 – 7.87 (m, 3H), 7.65 – 7.60 (m, 2H), 6.89 (dd, *J* = 8.7, 2.6 Hz, 1H), 6.76 (d, *J* = 2.6 Hz, 1H), 4.57 (s, 2H), 3.87 (s, 3H), 2.51 (s, 3H).

^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ 198.9, 196.4, 162.6, 138.5, 136.3, 133.6, 132.0, 129.9, 128.9, 128.0, 119.3, 112.0, 55.6, 45.5, 28.4.

IR (KBr, cm^{-1}) ν_{max} = 1694, 1658, 1607, 1585, 1571, 1567, 1488, 1470, 1441, 1430, 1410, 1398, 1357, 1332, 1321, 1293, 1272, 1255, 1249, 1214, 1177, 1163, 1138, 1115, 1104, 1065, 1028, 1012.

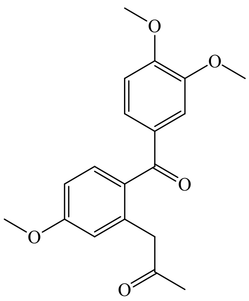
HRMS calc. for $C_{17}H_{16}BrO_3$ $[M+H]^+$ = 347.0277; found 347.0279.

*2-(2-acetyl-5-methoxyphenyl)-1-(4-nitrophenyl)ethanone **(2p)***



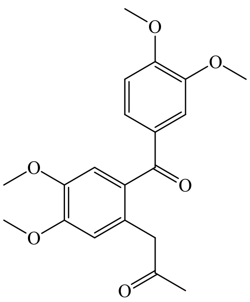
Yield 3.2 g (79%); bright yellow crystals, m.p. 157.0-157.5°C
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36 – 8.31 (m, 2H), 8.23 – 8.17 (m, 2H), 7.94 (d, *J* = 8.7 Hz, 1H), 6.91 (dd, *J* = 8.7, 2.6 Hz, 1H), 6.79 (d, *J* = 2.6 Hz, 1H), 4.58 (s, 2H), 3.88 (s, 3H), 2.51 (s, 3H).
^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ 198.8, 195.9, 162.8, 150.3, 142.4, 138.0, 133.9, 129.3, 128.3, 124.0, 119.6, 112.1, 55.6, 46.1, 28.3.
IR (KBr, cm^{-1}) ν_{max} = 1695, 1664, 1609, 1571, 1524, 1519, 1458, 1427, 1412, 1402, 1355, 1346, 1334, 1320, 1298, 1274, 1257, 1213, 1166, 1138, 1109, 1073, 1032, 1021, 1005.
HRMS calc. for $C_{17}H_{16}NO_5$ $[M+H]^+$ = 314.1023; found 314.1027.

*1-(2-(3,4-dimethoxybenzoyl)-5-methoxyphenyl)propan-2-one **(2q)***



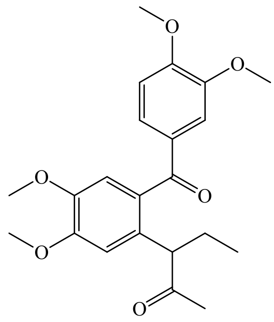
Yield 2.98 g (70%); orange crystals, m.p. 91.6-93.5°C
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 – 7.40 (m, 2H), 7.29 (dd, *J* = 8.3, 2.0 Hz, 1H), 6.86 (d, *J* = 8.4 Hz, 1H), 6.82 – 6.78 (m, 2H), 3.94 (s, 5H), 3.91 (s, 3H), 3.86 (s, 3H), 2.20 (s, 3H).
^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ 205.7, 196.2, 161.5, 153.0, 149.0, 137.5, 133.0, 131.5, 130.6, 125.6, 118.0, 112.1, 111.2, 109.9, 56.2, 56.1, 55.5, 48.6, 29.9.
IR (KBr, cm^{-1}) ν_{max} = 1716, 1636, 1608, 1596, 1583, 1570, 1514, 1463, 1455, 1441, 1417, 1395, 1358, 1347, 1329, 1292, 1274, 1253, 1234, 1185, 1160, 1153, 1135, 1110, 1046, 1042, 1024.
HRMS calc. for $C_{19}H_{21}O_5$ $[M+H]^+$ = 329.1384; found 329.1388.

*1-(2-(3,4-dimethoxybenzoyl)-4,5-dimethoxyphenyl)propan-2-one **(2r)***



Yield 4.14 g (89%); beige solid, m.p. 89.9-90.6°C
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (d, *J* = 2.0 Hz, 1H), 7.32 (dd, *J* = 8.4, 2.0 Hz, 1H), 6.96 (s, 1H), 6.87 (d, *J* = 8.4 Hz, 1H), 6.75 (s, 1H), 3.95 (d, *J* = 3.0 Hz, 6H), 3.93 (s, 3H), 3.85 (s, 2H), 3.81 (s, 3H), 2.18 (s, 3H).
^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ 206.2, 196.1, 153.3, 151.0, 149.1, 146.9, 131.2, 130.5, 128.5, 125.7, 114.6, 113.8, 112.0, 110.0, 56.3 (d, *J* = 3.7 Hz), 56.2 – 56.1 (m), 48.0, 29.8.
IR (KBr, cm^{-1}) ν_{max} = 1641, 1593, 1581, 1510, 1467, 1461, 1445, 1415, 1388, 1343, 1291, 1260, 1230, 1210, 1183, 1158, 1142, 1097, 1040, 1034, 1021, 1009.
HRMS calc. for $C_{20}H_{23}O_6$ $[M+H]^+$ = 359.1489; found 359.1495.

*3-(2-(3,4-dimethoxybenzoyl)-4,5-dimethoxyphenyl)pentan-2-one **(2s)***



Yield 4.2 g (84%); ivory solid, m.p. 155.8-157.0°C
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.5 (s, 1H), 7.3 – 7.3 (m, 1H), 6.9 – 6.8 (m, 2H), 6.8 (s, 1H), 4.0 – 3.9 (m, 7H), 3.9 (s, 3H), 3.8 (s, 3H), 2.1 (s, 3H), 2.0 – 1.9 (m, 1H), 1.7 – 1.6 (m, 1H), 0.7 (t, *J* = 7.4 Hz, 3H).
^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ 209.3, 196.3, 153.7, 150.9, 149.3, 146.8, 131.9, 131.7, 131.2, 126.1, 112.2, 111.7, 110.4, 109.9, 56.3, 56.2, 56.2, 55.6, 29.9, 25.7, 12.2.
IR (KBr, cm^{-1}) ν_{max} = 1707, 1655, 1594, 1583, 1507, 1449, 1439, 1418, 1347, 1321, 1294, 1263, 1235, 1222, 1205, 1186, 1166, 1156, 1140, 1113, 1097, 1078, 1035, 1018, 1001.
HRMS calc. for $C_{23}H_{27}O_6$ $[M+H]^+$ = 387.1802; found 387.1806.

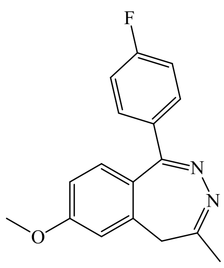
Preparation of 2,3-benzodiazepines 3a-3s from 1,5-diketones 2a-2s

General procedure

Corresponding 1,5-diketone (1 mmol) and hydrazine monohydrate (5 mmol, 5 eq) were stirred in methanol (5 ml) under argon atmosphere at room temperature for 16 hours. Then the solvent was removed under reduced pressure, and the crude product was purified by flash chromatography on silica gel (eluent: 5% EtOAc in CH_2Cl_2).

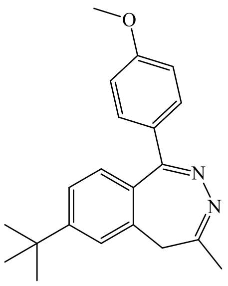
Analytical data for 2,3-benzodiazepines:

*1-(4-fluorophenyl)-7-methoxy-4-methyl-5H-benzo[d][1,2]diazepine **(3a)***



Yield 248 mg (88%); pale yellow solid, m.p. 147.5-149.1°C
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 – 7.61 (m, 2H), 7.23 (d, *J* = 8.6 Hz, 1H), 7.12 – 7.03 (m, 2H), 6.88 (dd, *J* = 8.6, 2.5 Hz, 1H), 6.77 (d, *J* = 2.5 Hz, 1H), 3.87 (s, 3H), 3.30 (d, *J* = 12.0 Hz, 1H), 3.07 (d, *J* = 12.0 Hz, 1H), 2.14 (s, 3H).
^{13}C {^{1}H } NMR (101 MHz, $CDCl_3$) δ 164.0 (d, *J* = 249.8 Hz), 162.4, 157.5, 155.0, 141.2, 135.4 (d, *J* = 3.1 Hz), 132.1, 131.6 (d, *J* = 8.4 Hz), 123.1, 115.3 (d, *J* = 21.6 Hz), 113.0, 111.2, 55.6, 39.1, 23.2.
^{19}F NMR (376 MHz, $CDCl_3$) δ -111.6.
IR (KBr, cm^{-1}) ν_{max} = 1603, 1599, 1574, 1505, 1498, 1469, 1450, 1445, 1402, 1372, 1334, 1309, 1295, 1278, 1250, 1237, 1228, 1196, 1187, 1161, 1152, 1136, 1096, 1048, 1029, 1014.
HRMS calc. for $C_{18}H_{16}FN_2O$ $[M+H]^+$= 283.1241; found 283.1246.

7-tert-butyl-1-(4-methoxyphenyl)-4-methyl-5H-benzo[d][1,2]diazepine ***(3b)***



Yield 301 mg (94%); beige crystals, m.p. 177.6-178.3°C

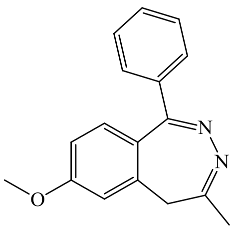
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (d, *J* = 8.7 Hz, 2H), 7.35 (dd, *J* = 8.2, 1.7 Hz, 1H), 7.25 – 7.20 (m, 2H), 6.90 (d, *J* = 8.7 Hz, 2H), 3.82 (s, 3H), 3.29 (d, *J* = 12.0 Hz, 1H), 3.07 (d, *J* = 12.0 Hz, 1H), 2.11 (s, 3H), 1.34 (s, 9H).

^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ 161.1, 158.3, 155.3, 139.3, 131.7, 131.1, 130.4, 127.5, 124.2, 122.9, 113.7, 55.5, 39.2, 35.1, 31.4, 23.3.

IR (KBr, cm^{-1}) ν_{max} = 1734, 1605, 1580, 1563, 1510, 1475, 1469, 1455, 1443, 1437, 1429, 1415, 1367, 1326, 1305, 1286, 1251, 1204, 1183, 1173, 1150, 1114, 1093, 1044, 1031.

HRMS calc. for $C_{21}H_{25}N_2O$ $[M+H]^+$ = 321.1962; found 321.1966.

7-methoxy-4-methyl-1-phenyl-5H-benzo[d][1,2]diazepine ***(3c)***



Yield 219 mg (98%); ocher crystals, m.p. 160-162°C

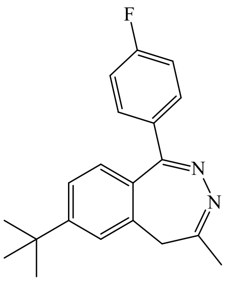
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 – 7.63 (m, 2H), 7.43 – 7.36 (m, 3H), 7.25 (d, *J* = 8.6 Hz, 1H), 6.88 (dd, *J* = 8.6, 2.4 Hz, 1H), 6.77 (d, *J* = 2.3 Hz, 1H), 3.87 (s, 3H), 3.30 (d, *J* = 12.1 Hz, 1H), 3.09 (d, *J* = 12.0 Hz, 1H), 2.15 (s, 3H).

^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ 162.3, 158.6, 154.9, 141.3, 139.3, 132.2, 129.8, 128.3, 123.3, 112.9, 111.1, 55.6, 39.1, 23.3.

IR (KBr, cm^{-1}) ν_{max} = 1613, 1601, 1568, 1510, 1497, 1489, 1462, 1451, 1442, 1432, 1422, 1369, 1323, 1309, 1284, 1277, 1246, 1236, 1181, 1134, 1110, 1049, 1035, 1023.

HRMS calc. for $C_{17}H_{17}N_2O$ $[M+H]^+$ = 265.1336; found 265.1339.

7-tert-butyl-1-(4-fluorophenyl)-4-methyl-5H-benzo[d][1,2]diazepine ***(3d)***



Yield 246 mg (80%); beige crystals, m.p. 169.9-171.4°C

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 – 7.65 (m, 2H), 7.39 (dd, *J* = 8.2, 1.9 Hz, 1H), 7.28 – 7.22 (m, 2H), 7.11 – 7.05 (m, 2H), 3.35 (d, *J* = 12.1 Hz, 1H), 3.08 (d, *J* = 12.1 Hz, 1H), 2.15 (s, 3H), 1.37 (s, 9H).

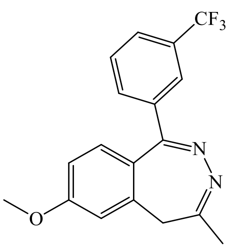
^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ 164.0 (d, *J* = 249.7 Hz), 157.9, 155.4, 155.3, 139.3, 135.2 (d, *J* = 3.2 Hz), 131.6 (d, *J* = 8.4 Hz), 130.1, 127.2, 124.4, 123.0, 115.3 (d, *J* = 21.6 Hz), 39.2, 35.1, 31.4, 23.3.

^{19}F NMR (376 MHz, $CDCl_3$) δ -111.6.

IR (KBr, cm^{-1}) ν_{max} = 1603, 1563, 1506, 1477, 1460, 1433, 1403, 1396, 1371, 1365, 1329, 1301, 1284, 1262, 1232, 1219, 1200, 1161, 1148, 1103, 1092, 1050, 1011.

HRMS calc. for $C_{20}H_{22}FN_2$ $[M+H]^+$ = 309.1762; found 309.1766.

7-methoxy-4-methyl-1-(3-(trifluoromethyl)phenyl)-5H-benzo[d][1,2]diazepine ***(3e)***



Yield 269 mg (81%); beige crystals, m.p. 131.8-132.4°C

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (s, 1H), 7.87 (d, *J* = 7.8 Hz, 1H), 7.68 (d, *J* = 7.8 Hz, 1H), 7.52 (t, *J* = 7.8 Hz, 1H), 7.22 (d, *J* = 8.6 Hz, 1H), 6.91 (dd, *J* = 8.6, 2.5 Hz, 1H), 6.80 (d, *J* = 2.4 Hz, 1H), 3.88 (s, 3H), 3.33 (d, *J* = 12.1 Hz, 1H), 3.06 (d, *J* = 12.1 Hz, 1H), 2.16 (s, 3H).

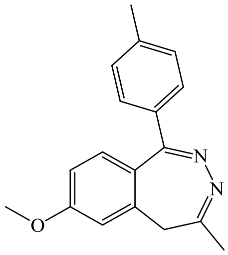
^{13}C {^{1}H} ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.6, 157.4, 155.0, 141.4, 140.0, 132.9, 131.8, 130.8 (q, *J* = 32.4 Hz), 128.8, 126.5 (q, *J* = 3.9 Hz), 126.4 (q, *J* = 3.7 Hz), 124.1 (q, *J* = 272.5 Hz), 122.7, 113.3, 111.4, 55.6, 39.2, 23.3.

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.6.

IR (KBr, cm^{-1}) ν_{max} = 1599, 1574, 1502, 1485, 1472, 1465, 1448, 1437, 1417, 1374, 1342, 1332, 1322, 1309, 1276, 1252, 1236, 1197, 1188, 1169, 1158, 1140, 1118, 1101, 1094, 1074, 1052, 1032.

HRMS calc. for $C_{18}H_{16}F_3N_2O$ $[M+H]^+$ = 333.1209; found 333.1215.

7-methoxy-4-methyl-1-p-tolyl-5H-benzo[d][1,2]diazepine ***(3f)***



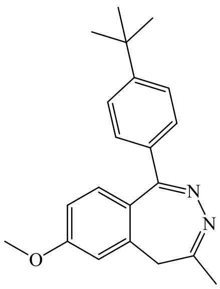
Yield 227 mg (82%); beige crystals, m.p. 121.3-122.0°C

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (d, *J* = 8.1 Hz, 2H), 7.26 (d, *J* = 8.6 Hz, 1H), 7.20 (d, *J* = 8.0 Hz, 2H), 6.87 (dd, *J* = 8.6, 2.4 Hz, 1H), 6.77 (d, *J* = 2.4 Hz, 1H), 3.87 (s, 3H), 3.28 (d, *J* = 12.0 Hz, 1H), 3.09 (d, *J* = 12.0 Hz, 1H), 2.39 (s, 3H), 2.14 (s, 3H).

^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ 162.2, 158.4, 154.9, 141.2, 140.0, 136.5, 132.3, 129.7, 129.0, 123.4, 112.9, 111.0, 55.6, 39.1, 23.3, 21.4.

IR (KBr, cm^{-1}) ν_{max} = 3054 (W), 3027 (M), 3003 (M), 2969 (M), 2921 (M), 2840 (M), 2047 (VW), 1919 (W), 1668 (W), 1598 (VS), 1580 (S), 1508 (S), 1496 (VS), 1470 (M), 1450 (S), 1415 (M), 1372 (S), 1334 (VS), 1311 (S), 1304 (S), 1276 (VS), 1248 (VS), 1236 (VS), 1216 (M), 1176 (S), 1158 (S), 1136 (M), 1111 (M), 1095 (VS), 1048 (S), 1028 calc. for $C_{18}H_{19}N_2O$ $[M+H]^+$ = 279.1492; found 279.1494.

1-(4-tert-butylphenyl)-7-methoxy-4-methyl-5H-benzo[d][1,2]diazepine ***(3g)***



Yield 304 mg (95%); yellow crystals, m.p. 184.0-185.8°C

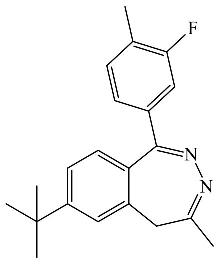
^{1}H NMR 1H NMR (400 MHz, $CDCl_3$) δ 7.64 – 7.57 (m, 2H), 7.44 – 7.39 (m, 2H), 7.30 (d, *J* = 8.6 Hz, 1H), 6.88 (dd, *J* = 8.6, 2.5 Hz, 1H), 6.77 (d, *J* = 2.5 Hz, 1H), 3.87 (s, 3H), 3.28 (d, *J* = 12.0 Hz, 1H), 3.08 (d, *J* = 12.0 Hz, 1H), 2.14 (s, 3H), 1.34 (s, 9H).

^{13}C {^{1}H} (101 MHz, $CDCl_3$) δ 162.2, 158.4, 154.8, 153.1, 141.2, 136.4, 132.4, 129.5, 125.3, 123.4, 112.9, 111.0, 55.6, 39.1, 34.9, 31.4, 23.3.

IR (KBr, cm^{-1}) ν_{max} = 3068 (W), 3036 (W), 3002 (M), 2963 (VS), 2938 (S), 2867 (M), 2833 (M), 2066 (VW), 1723 (VW), 1601 (VS), 1573 (S), 1558 (S), 1518 (S), 1495 (VS), 1475 (M), 1460 (S), 1435 (S), 1422 (S), 1400 (M), 1369 (S), 1321 (S), 1309 (M), 1293 (VS), 1276 (VS), 1255 (S), 1243 (VS), 1203 (M), 1177 (M), 1156 (M), 1142 (VS), 1114 (VS), 1102 (S), 1053 (M), 1037 (S), 1015 (M), 974 (S), 942 (M), 930 (S), 912 (M), 879 (S), 850 (S), 840 (S), 832 (S), 807 (S), 763 (M), 750 (M), 701 (M), 677 (S), 650 (W), 626 (M), 583 (M), 561 (M), 535 (S), 500 (W), 480 (M), 471 (M), 427 (VW).

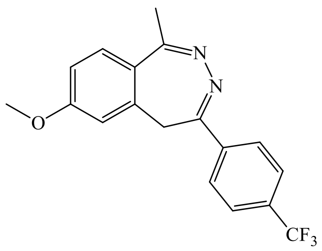
HRMS calc. for $C_{21}H_{25}N_2O$ $[M+H]^+$ = 321.1961; found 321.1966.

*7-tert-butyl-1-(3-fluoro-4-methylphenyl)-4-methyl-5H-benzo[d][1,2]diazepine **(3h)***



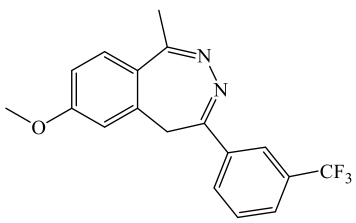
Yield 264 mg (82%); pale yellow crystals, m.p. 157.2-158.1°C
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 – 7.34 (m, 3H), 7.29 – 7.24 (m, 2H), 7.20 (t, *J* = 8.0 Hz, 1H), 3.33 (d, *J* = 12.1 Hz, 1H), 3.07 (d, *J* = 12.1 Hz, 1H), 2.32 (d, *J* = 1.6 Hz, 3H), 2.15 (s, 3H), 1.37 (s, 9H).
^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ 161.2 (d, *J* = 244.3 Hz), 157.8, 155.4, 155.3, 139.4, 138.7 (d, *J* = 7.4 Hz), 131.2 (d, *J* = 5.3 Hz), 130.2, 127.1, 126.7 (d, *J* = 17.3 Hz), 125.1 (d, *J* = 3.3 Hz), 124.4, 123.0, 116.1 (d, *J* = 23.8 Hz), 39.2, 35.1, 31.4, 23.3, 14.7 (d, *J* = 3.4 Hz).
^{19}F NMR (376 MHz, $CDCl_3$) δ -117.6.
IR (KBr, cm^{-1}) ν_{max} = 1601, 1576, 1561, 1508, 1498, 1475, 1457, 1449, 1429, 1412, 1403, 1378, 1370, 1326, 1304, 1294, 1267, 1250, 1241, 1223, 1201, 1188, 1160, 1147, 1128, 1115, 1087, 1049, 1004.
HRMS calc. for $C_{21}H_{24}FN_2$ $[M+H]^+$ = 323.1918; found 323.1922

*7-methoxy-1-methyl-4-(4-(trifluoromethyl)phenyl)-5H-benzo[d][1,2]diazepine **(3i)***



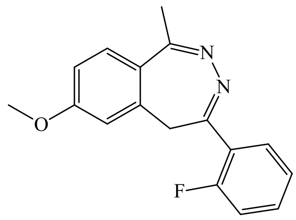
Yield 259 mg (78%); beige solid, m.p. 153.9-154.4°C
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (d, *J* = 8.2 Hz, 2H), 7.65 (d, *J* = 8.3 Hz, 2H), 7.49 (d, *J* = 8.7 Hz, 1H), 6.92 (dd, *J* = 8.7, 2.5 Hz, 1H), 6.81 (d, *J* = 2.4 Hz, 1H), 3.97 (d, *J* = 13.0 Hz, 1H), 3.84 (s, 3H), 3.19 (d, *J* = 13.0 Hz, 1H), 2.57 (s, 3H).
^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ 162.3, 156.8, 152.7, 140.3, 139.4, 131.5 (d, *J* = 32.7 Hz), 129.7, 127.6, 125.7 (q, *J* = 3.8 Hz), 125.5, 124.1 (d, *J* = 272.2 Hz), 113.3, 111.6, 55.6, 34.8, 25.4.
^{19}F NMR (376 MHz, $CDCl_3$) δ -62.78.
IR (KBr, cm^{-1}) ν_{max} = 1609, 1576, 1536, 1496, 1460, 1441, 1427, 1406, 1373, 1364, 1324, 1286, 1266, 1253, 1194, 1159, 1143, 1112, 1072, 1038, 1012.
HRMS calc. for $C_{18}H_{16}F_3N_2O$ $[M+H]^+$ = 333.1209; found 333.1215.

*7-methoxy-1-methyl-4-(3-(trifluoromethyl)phenyl)-5H-benzo[d][1,2]diazepine **(3j)***



Yield 315 mg (95%); green-brown solid , m.p. 106.7-108.0°C
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.2 (s, 1H), 8.1 (d, *J* = 7.9 Hz, 1H), 7.6 (d, *J* = 7.8 Hz, 1H), 7.5 (dd, *J* = 13.3, 8.2 Hz, 2H), 7.5 (s, 0H), 6.9 (dd, *J* = 8.6, 2.6 Hz, 1H), 6.8 (d, *J* = 2.5 Hz, 1H), 4.0 (d, *J* = 13.0 Hz, 1H), 3.8 (s, 3H), 3.2 (d, *J* = 13.0 Hz, 1H), 2.6 (s, 3H).
^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ 162.3, 156.8, 152.5, 140.2, 136.8, 131.2 (q, *J* = 32.5 Hz), 130.4, 129.6, 129.2, 126.4 (q, *J* = 3.7 Hz), 125.5, 124.1 (q, *J* = 3.9 Hz), 124.0 (d, *J* = 272.4 Hz), 113.5, 111.4, 55.6, 34.7, 25.4.
^{19}F NMR (376 MHz, $CDCl_3$) δ -62.8.
IR (KBr, cm^{-1}) ν_{max} = 1603, 1581, 1560, 1538, 1502, 1488, 1443, 1429, 1375, 1329, 1307, 1293, 1276, 1254, 1242, 1162, 1153, 1134, 1115, 1094, 1073, 1035, 1026.
HRMS calc. for $C_{18}H_{16}F_3N_2O$ $[M+H]^+$ = 333.1209; found 333.1212.

4-(2-fluorophenyl)-7-methoxy-1-methyl-5H-benzo[d][1,2]diazepine ***(3k)***



Yield 206 mg (73%); green-brown solid, m.p. 83.5-84.5°C

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (td, *J* = 7.8, 1.8 Hz, 1H), 7.47 (d, *J* = 8.6 Hz, 1H), 7.38 – 7.31 (m, 1H), 7.15 – 7.05 (m, 2H), 6.93 (dd, *J* = 8.6, 2.6 Hz, 1H), 6.82 (t, *J* = 2.8 Hz, 1H), 3.90 (dd, *J* = 12.8, 2.1 Hz, 1H), 3.84 (s, 3H), 3.24 (d, *J* = 12.8 Hz, 1H), 2.55 (s, 3H).

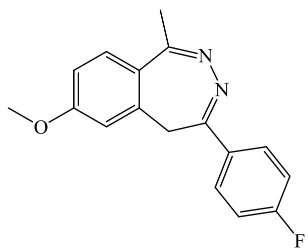
^{13}C {^{1}H} NMR ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.9, 161.2 (d, *J* = 250.3 Hz), 157.0, 152.7 (d, *J* = 2.9 Hz), 140.9, 131.4 (d, *J* = 11.4 Hz), 131.4, 129.1, 125.7, 125.0 (d, *J* = 11.8 Hz), 124.5 (d, *J* = 3.3 Hz), 116.2 (d, *J* = 22.5 Hz), 113.7, 112.3 (d, *J* = 3.7 Hz), 55.5, 37.4 (d, *J* = 5.6 Hz), 25.5.

^{19}F NMR (376 MHz, $CDCl_3$) δ -112.0.

IR (KBr, cm^{-1}) ν_{max} = 1608, 1578, 1541, 1495, 1484, 1457, 1445, 1430, 1423, 1371, 1329, 1289, 1263, 1246, 1208, 1151, 1141, 1100, 1074, 1038, 1032, 1010.

HRMS calc. for $C_{17}H_{16}FN_2O$ $[M+H]^+$ = 283.1241; found 283.1245.

4-(4-fluorophenyl)-7-methoxy-1-methyl-5H-benzo[d][1,2]diazepine ***(3l)***



Yield 240 mg (85%); beige crystals, m.p. 118.8-120.9°C

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 – 7.86 (m, 2H), 7.48 (d, *J* = 8.6 Hz, 1H), 7.10 – 7.03 (m, 2H), 6.90 (dd, *J* = 8.6, 2.5 Hz, 1H), 6.79 (d, *J* = 2.5 Hz, 1H), 3.94 (d, *J* = 12.9 Hz, 1H), 3.83 (s, 3H), 3.15 (d, *J* = 12.9 Hz, 1H), 2.55 (s, 3H).

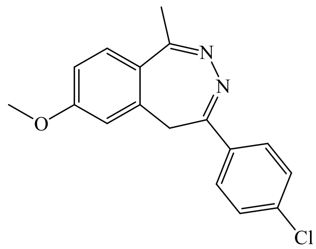
^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ 163.9 (d, *J* = 250.3 Hz), 162.1, 156.7, 152.8, 140.5, 132.2 (d, *J* = 3.3 Hz), 129.5, 129.3 (d, *J* = 8.5 Hz), 125.6, 115.7 (d, *J* = 21.7 Hz), 113.1, 111.6, 55.6, 34.9, 25.4.

^{19}F NMR (376 MHz, $CDCl_3$) δ -111.0.

IR (KBr, cm^{-1}) ν_{max} = 1605, 1597, 1558, 1533, 1508, 1503, 1464, 1449, 1413, 1407, 1369, 1326, 1292, 1266, 1245, 1233, 1188, 1165, 1128, 1105, 1068, 1027, 1022.

HRMS calc. for $C_{17}H_{16}FN_2O$ $[M+H]^+$ = 283.1241; found 283.1246.

4-(4-chlorophenyl)-7-methoxy-1-methyl-5H-benzo[d][1,2diazepine ***(3m)***



Yield 195 mg (99%); white solid, m.p. 150.0-151.0°C

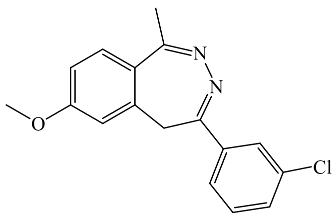
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 – 7.80 (m, 2H), 7.47 (d, *J* = 8.6 Hz, 1H), 7.38 – 7.33 (m, 2H), 6.90 (dd, *J* = 8.6, 2.5 Hz, 1H), 6.78 (d, *J* = 2.5 Hz, 1H), 3.93 (d, *J* = 12.9 Hz, 1H), 3.83 (s, 3H), 3.14 (d, *J* = 12.9 Hz, 1H), 2.55 (s, 3H).

^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ 162.1, 156.7, 152.8, 140.4, 136.0, 134.5, 129.5, 128.9, 128.6, 125.6, 113.2, 111.5, 55.6, 34.7, 25.4.

IR (KBr, cm^{-1}) ν_{max} = 1602, 1583, 1554, 1538, 1492, 1465, 1453, 1436, 1397, 1368, 1325, 1292, 1263, 1243, 1169, 1153, 1131, 1093, 1069, 1029, 1017, 1011.

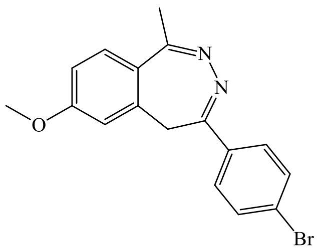
HRMS calc. for $C_{17}H_{16}ClN_2O$ $[M+H]^+$ = 299.0946; found 299.0951.

4-(3-chlorophenyl)-7-methoxy-1-methyl-5H-benzo[d][1,2]diazepine ***(3n)***



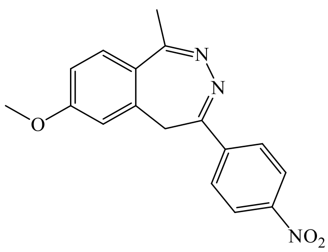
Yield 283 mg (95%); ocher solid, m.p. 102.0-103.1°C
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 – 7.86 (m, 1H), 7.79 – 7.74 (m, 1H), 7.48 (d, *J* = 8.6 Hz, 1H), 7.36 – 7.29 (m, 2H), 6.91 (dd, *J* = 8.6, 2.5 Hz, 1H), 6.80 (d, *J* = 2.4 Hz, 1H), 3.92 (d, *J* = 13.0 Hz, 1H), 3.84 (s, 3H), 3.15 (d, *J* = 12.9 Hz, 1H), 2.56 (s, 3H).
^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ 162.2, 156.7, 152.6, 140.4, 137.8, 134.8, 129.9, 129.9, 129.6, 127.4, 125.5, 125.4, 113.3, 111.6, 55.6, 34.8, 25.4.
IR (KBr, cm^{-1}) ν_{max} = 1608, 1576, 1553, 1534, 1498, 1475, 1461, 1453, 1440, 1423, 1407, 1368, 1325, 1304, 1290, 1272, 1260, 1250, 1190, 1164, 1149, 1144, 1074, 1042, 1025.
HRMS calc. for $C_{17}H_{16}ClN_2O$ [M+H]$^+$ = 299.0946; found 299.0949.

4-(4-bromophenyl)-7-methoxy-1-methyl-5H-benzo[d][1,2]diazepine ***(3o)***



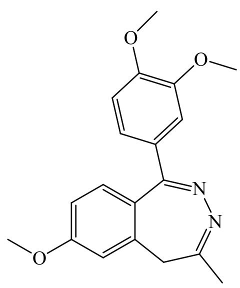
Yield 307 mg (90%); brown crystals, m.p. 171.0-171.8°C
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 – 7.73 (m, 2H), 7.53 – 7.49 (m, 2H), 7.47 (d, *J* = 8.6 Hz, 1H), 6.90 (dd, *J* = 8.6, 2.5 Hz, 1H), 6.78 (d, *J* = 2.5 Hz, 1H), 3.92 (d, *J* = 12.9 Hz, 1H), 3.83 (s, 3H), 3.14 (d, *J* = 12.9 Hz, 1H), 2.55 (s, 3H).
^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ 162.1, 156.6, 152.8, 140.4, 134.9, 131.9, 129.5, 128.8, 125.6, 124.4, 113.2, 111.5, 55.6, 34.6, 25.4.
IR (KBr, cm^{-1}) ν_{max} = 1602, 1587, 1553, 1537, 1502, 1494, 1488, 1471, 1465, 1453, 1435, 1392, 1368, 1324, 1294, 1284, 1263, 1243, 1192, 1170, 1153, 1132, 1075, 1068, 1028, 1017, 1009.
HRMS calc. for $C_{17}H_{16}BrN_2O$ [M+H]$^+$ = 343.0441; found 343.0442.

7-methoxy-1-methyl-4-(4-nitrophenyl)-5H-benzo[d][1,2]diazepine ***(3p)***



Yield 296 mg (96%); light yellow crystals, m.p. 197.5-198.5°C
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 – 8.21 (m, 2H), 8.07 – 8.02 (m, 2H), 7.50 (d, *J* = 8.6 Hz, 1H), 6.94 (dd, *J* = 8.7, 2.5 Hz, 1H), 6.82 (d, *J* = 2.5 Hz, 1H), 3.97 (d, *J* = 13.1 Hz, 1H), 3.85 (s, 3H), 3.21 (d, *J* = 13.1 Hz, 1H), 2.57 (s, 3H).
^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ 162.4, 156.8, 152.1, 148.5, 142.0, 140.1, 129.8, 128.1, 125.4, 123.9, 113.5, 111.6, 55.6, 34.7, 25.5.
IR (KBr, cm^{-1}) ν_{max} = 1609, 1581, 1552, 1535, 1514, 1438, 1375, 1348, 1324, 1294, 1247, 1170, 1134, 1069, 1027, 1011.
HRMS calc. for $C_{17}H_{16}N_3O_3$ [M+H]$^+$ = 310.1186; found 310.1192.

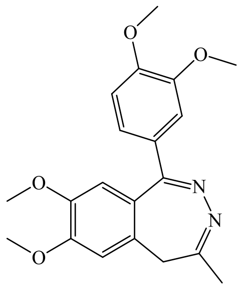
1-(3,4-dimethoxyphenyl)-7-methoxy-4-methyl-5H-benzo[d][1,2]diazepine ***(3q)***



Yield 243 mg (75%); pale yellow crystals, m.p. 176.3-177.1°C
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (d, *J* = 2.0 Hz, 1H), 7.31 (d, *J* = 8.6 Hz, 1H), 6.99 (dd, *J* = 8.4, 2.0 Hz, 1H), 6.89 (dd, *J* = 8.6, 2.5 Hz, 1H), 6.84 (d, *J* = 8.4 Hz, 1H), 6.77 (d, *J* = 2.5 Hz, 1H), 3.93 (s, 3H), 3.91 (s, 3H), 3.88 (s, 3H), 3.28 (d, *J* = 12.0 Hz, 1H), 3.10 (d, *J* = 12.0 Hz, 1H), 2.14 (s, 3H).

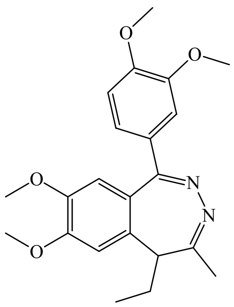
^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ 162.3, 158.0, 155.0, 150.7, 149.0, 141.2, 132.4, 132.0, 123.7, 123.1, 112.8, 111.7, 111.0, 110.3, 56.1, 55.6, 39.1, 23.3.
IR (KBr, cm^{-1}) ν_{max} = 1599, 1568, 1511, 1498, 1476, 1459, 1445, 1431, 1424, 1412, 1379, 1371, 1339, 1315, 1306, 1288, 1274, 1248, 1231, 1195, 1185, 1166, 1159, 1143, 1136, 1107, 1044, 1030.
HRMS calc. for $C_{19}H_{21}N_2O_3$ $[M+H]^+$ = 325.1547; found 325.1553.

1-(3,4-dimethoxyphenyl)-7,8-dimethoxy-4-methyl-5H-benzo[d][1,2]diazepine ***(3r)***



Yield 230 mg (65%); orange crystals, m.p. 151.7-153.4°C
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (d, *J* = 2.0 Hz, 1H), 7.04 (dd, *J* = 8.4, 2.0 Hz, 1H), 6.84 (t, *J* = 4.2 Hz, 2H), 6.72 (s, 1H), 3.96 (s, 3H), 3.91 (d, *J* = 2.5 Hz, 6H), 3.75 (s, 3H), 3.24 (d, *J* = 12.2 Hz, 1H), 3.02 (d, *J* = 12.2 Hz, 1H), 2.13 (s, 3H).
^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$) δ 157.9, 155.0, 152.1, 150.7, 149.0, 147.9, 133.1, 131.8, 123.5, 122.4, 112.8, 111.7, 110.4, 108.6, 56.3, 56.2, 56.1, 56.1, 38.5, 23.2.
IR (KBr, cm^{-1}) ν_{max} = 1600, 1514, 1467, 1461, 1442, 1429, 1412, 1356, 1310, 1276, 1263, 1251, 1231, 1213, 1165, 1145, 1101, 1037, 1024, 1008.
HRMS calc. for $C_{20}H_{23}N_2O_4$ $[M+H]^+$ = 355.1653; found 355.1655.

1-(3,4-dimethoxyphenyl)-5-ethyl-7,8-dimethoxy-4-methyl-5H-benzo[d][1,2]diazepine ***(3s)***



Diketone **2s** (150 mg, 0.39 mmol) was placed in a vial and dissolved in CH_2Cl_2 (5 ml). Tetrafluoroboric acid 50% in water (0.16 g, 1.17 mmol, 3 eq) was added to the solution. The reaction then was stirred at 40°C for 4 hours. The reaction mixture was cooled to the RT, and then diethyl ether was added until no more precipitate formed. The resulting precipitate was filtrated and dried in vacuo. The yield of the resulting pyrylium tetrafluoroborate was 172 mg (94%). After that pyrylium tetrafluoroborate (172 mg, 0.37 mmol) was placed in a vial, dissolved in 5 ml of methanol. Then hydrazine monohydrate (185 mg, 3,7 mmol, 10 eq) was added to the mixture. The reaction was stirred at RT for 30 minutes. The crude product was purified by column chromatography on silica gel (eluent: ethyl acetate/CH_2Cl_2 = 2:1). The yield of 3s is 134 mg (95%).
Instead of tetrafluoroboric acid 20% solution of HCl in dioxane (1.17 mmol, 3 eq) could be used. Then the yield of the pyrylium chloride is 0.137g (87%).
Yield 134 mg (90% from diketone); white crystals, m.p. 155.0-156.5°C
Major isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (d, *J* = 1.7 Hz, 1H), 7.06 (dd, *J* = 8.4, 1.8 Hz, 1H), 6.90 – 6.83 (m, 2H), 6.73 (s, 1H), 3.97 (s, 3H), 3.93 (s, 3H), 3.91 (s, 3H), 3.75 (s, 3H), 2.76 (t, *J* = 7.5 Hz, 1H), 2.21 – 2.04 (m, 2H), 1.97 (s, 3H), 1.09 (t, *J* = 7.3 Hz, 3H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 157.1, 156.8, 152.3, 150.6, 149.0, 147.7, 135.6, 131.7, 123.6, 122.3, 112.7, 111.5, 110.4, 104.5, 56.2, 56.1, 56.1, 56.1, 46.0, 20.0, 18.0, 12.7.
Minor isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, *J* = 1.7 Hz, 1H), 6.96 (dd, *J* = 8.3, 1.8 Hz, 1H), 6.84 (d, *J* = 3.0 Hz, 1H), 6.79 (s, 1H), 6.64 (s, 1H), 3.96 (s, 3H), 3.92 (s, 3H), 3.91 (s, 3H), 3.73 (s, 3H), 3.40 (t, *J* = 8.2 Hz, 1H), 2.15 (s, 3H), 1.67 (dq, *J* = 15.0, 7.4 Hz, 1H), 1.50 (dq, *J* = 14.2, 7.6 Hz, 1H), 0.85 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 157.3, 156.9, 152.0, 150.5, 149.0, 147.9, 137.1, 132.5, 123.6, 123.1, 121.2, 113.9, 111.8, 110.5, 56.2, 56.1, 56.1, 56.1, 54.2, 26.0, 18.7, 13.1.

IR (KBr, cm^{-1}) ν_{max} = 1508, 1460, 1445, 1412, 1369, 1358, 1345, 1279, 1266, 1253, 1246, 1231, 1220, 1206, 1185, 1164, 1145, 1128, 1095, 1077, 1040, 1031, 1017, 1006.

HRMS calc. for $C_{22}H_{27}N_2O_4$ $[M+H]^+$ = 383.1965; found 383.1969.

Tofisopam (BIOCOM)

Major isomer: ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.59 (d, *J* = 2.0 Hz, 1H), 7.26 (s, 1H), 7.06 (dd, *J* = 8.4, 2.0 Hz, 1H), 6.88 (s, 1H), 6.85 (d, *J* = 8.4 Hz, 1H), 6.74 (s, 1H), 3.97 (s, 3H), 3.94 (s, 3H), 3.92 (s, 3H), 3.76 (s, 3H), 2.16 – 2.07 (m, 2H), 1.98 (s, 3H), 1.09 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 157.2, 156.9, 152.3, 150.6, 149.1, 147.7, 135.6, 131.7, 123.7, 122.3, 112.7, 111.5, 110.4, 104.5, 56.3, 56.2, 56.1, 56.1, 46.0, 20.0, 18.0, 12.7.

Minor isomer: ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.47 (d, *J* = 2.0 Hz, 1H), 6.96 (dd, *J* = 8.3, 2.0 Hz, 1H), 6.84 (d, *J* = 8.3 Hz, 2H), 6.80 (s, 1H), 6.64 (s, 1H), 3.96 (s, 3H), 3.92 (s, 3H), 3.91 (s, 3H), 3.73 (s, 3H), 3.41 (t, *J* = 8.2 Hz, 1H), 2.16 (s, 3H), 1.73 – 1.60 (m, 1H), 1.56 – 1.45 (m, 1H), 0.85 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 157.4, 157.0, 152.0, 150.5, 149.0, 147.9, 137.1, 132.5, 123.7, 123.2, 121.2, 113.9, 111.8, 110.5, 56.3, 56.2, 56.1, 56.1, 54.3, 26.0, 18.7, 13.2.

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^{1}H, ^{13}C NMR, ^{19}F and 2D NMR spectra

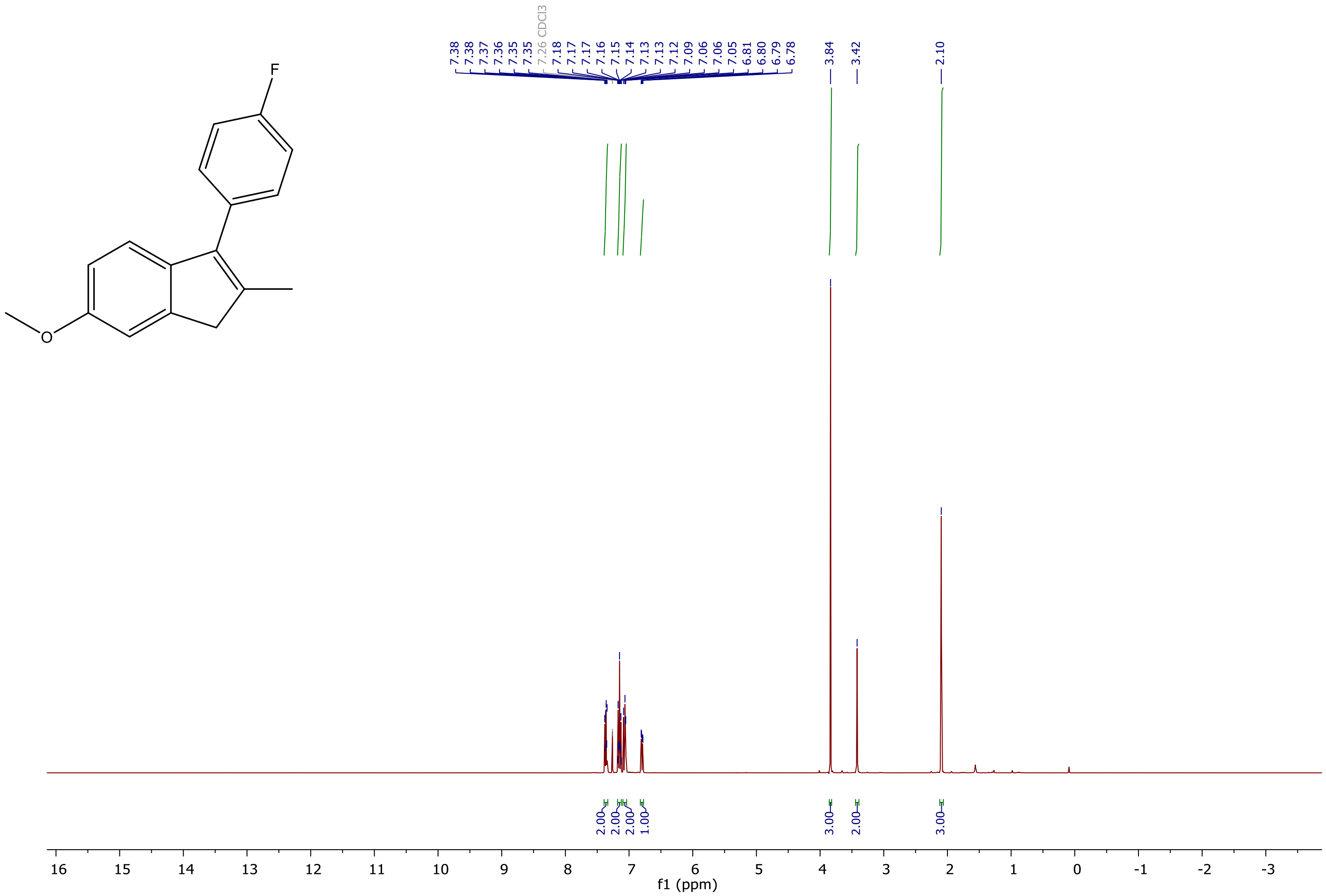


Figure S4.1. ^{1}H NMR (400MHz, $CDCl_3$) of 3-(4-fluorophenyl)-6-methoxy-2-methyl-1H-indene (1a)

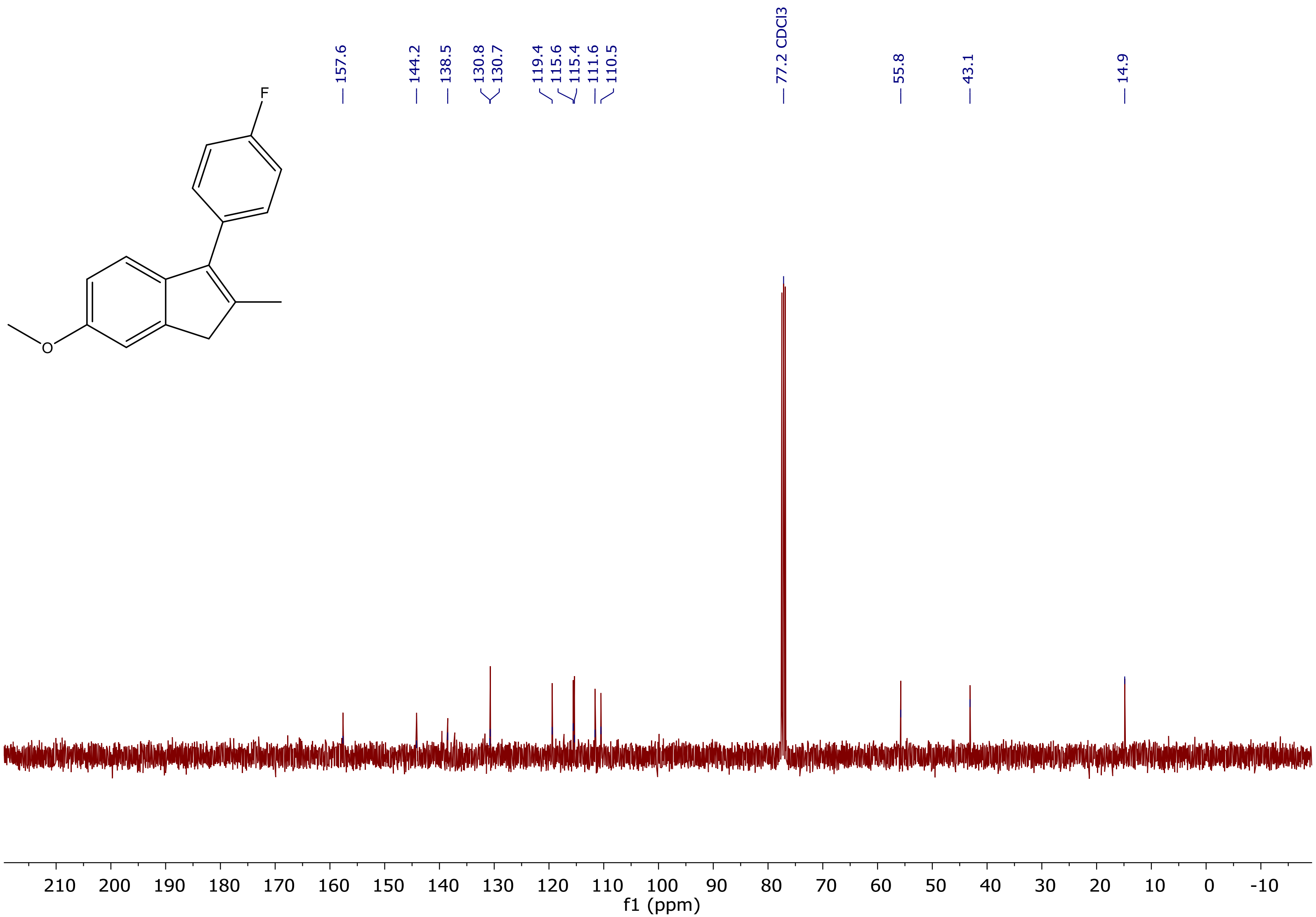


Figure S4.2. ^{13}C {^{1}H} NMR (101MHz, $CDCl_3$) of 3-(4-fluorophenyl)-6-methoxy-2-methyl-1H-indene (1a)

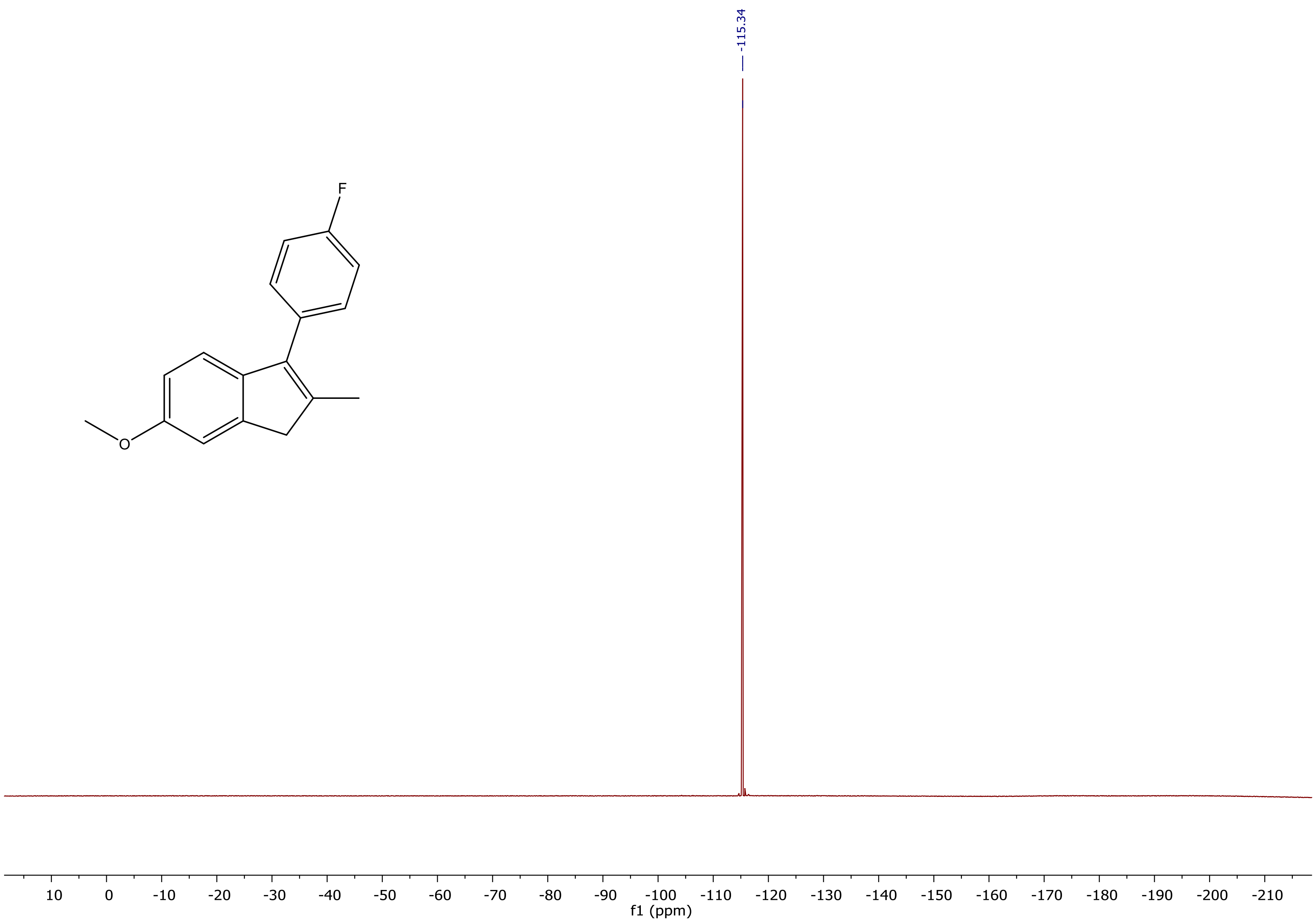


Figure S4.3. ^{19}F NMR (376 MHz, $CDCl_3$) of 3-(4-fluorophenyl)-6-methoxy-2-methyl-1H-indene (1a)

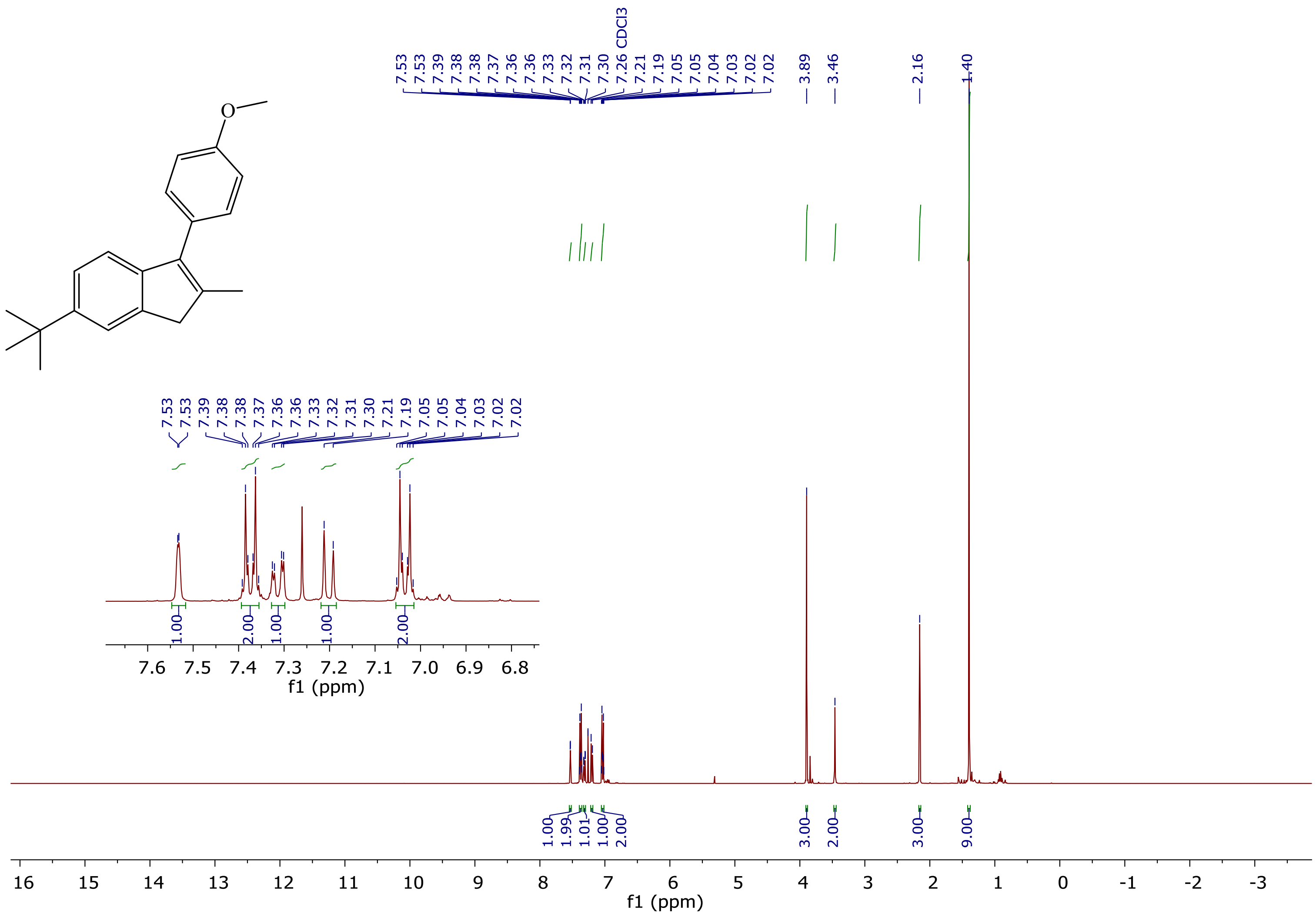


Figure S4.4. ^{1}H NMR (400MHz, $CDCl_3$) of 6-tert-butyl-3-(4-methoxyphenyl)-2-methyl-1H-indene (1b)

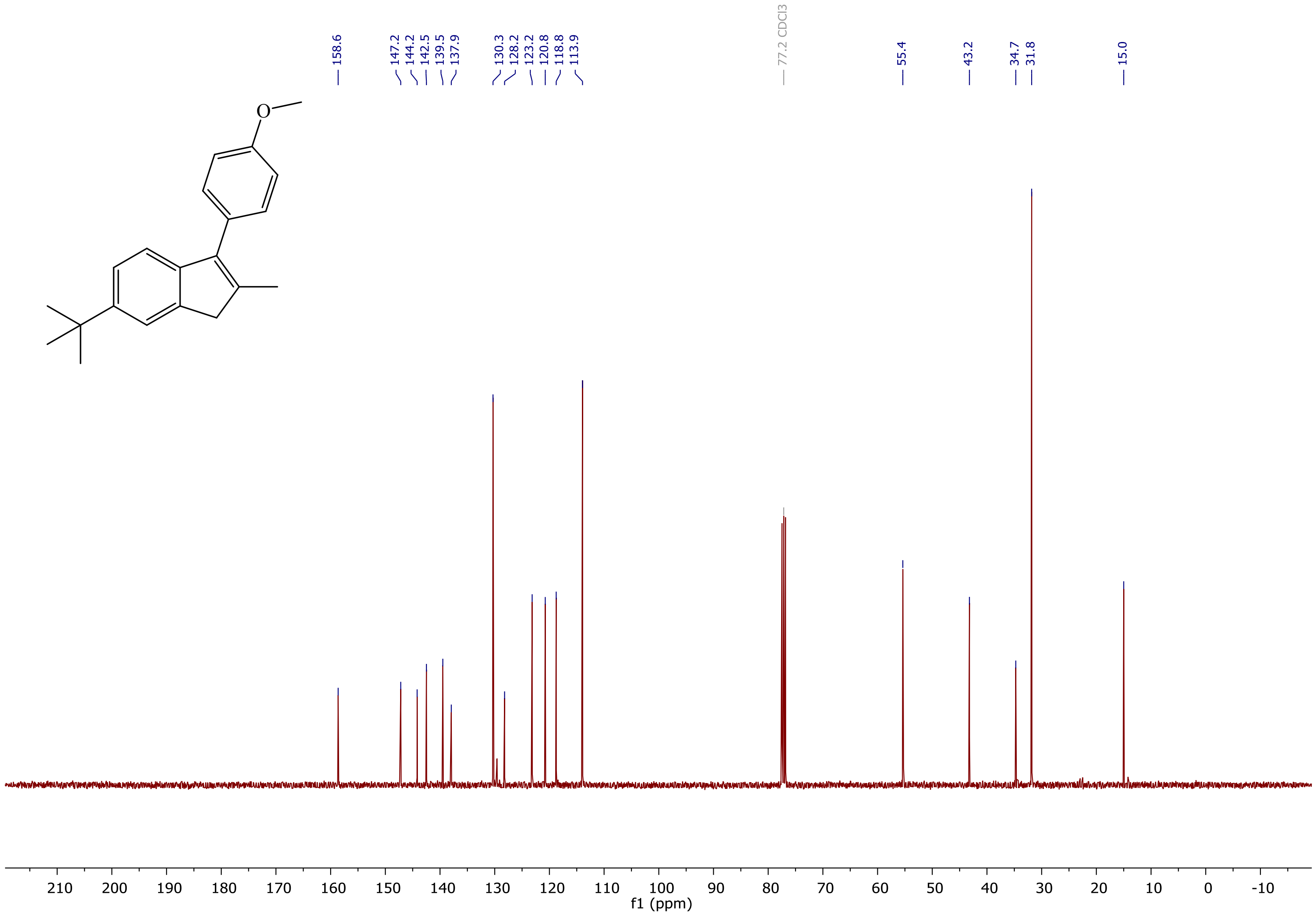


Figure S4.5. $^{13}C\ \{^{1}H\}$ **NMR (101MHz,** $CDCl_3$**) of 6-tert-butyl-3-(4-methoxyphenyl)-2-methyl-1H-indene (1b)**

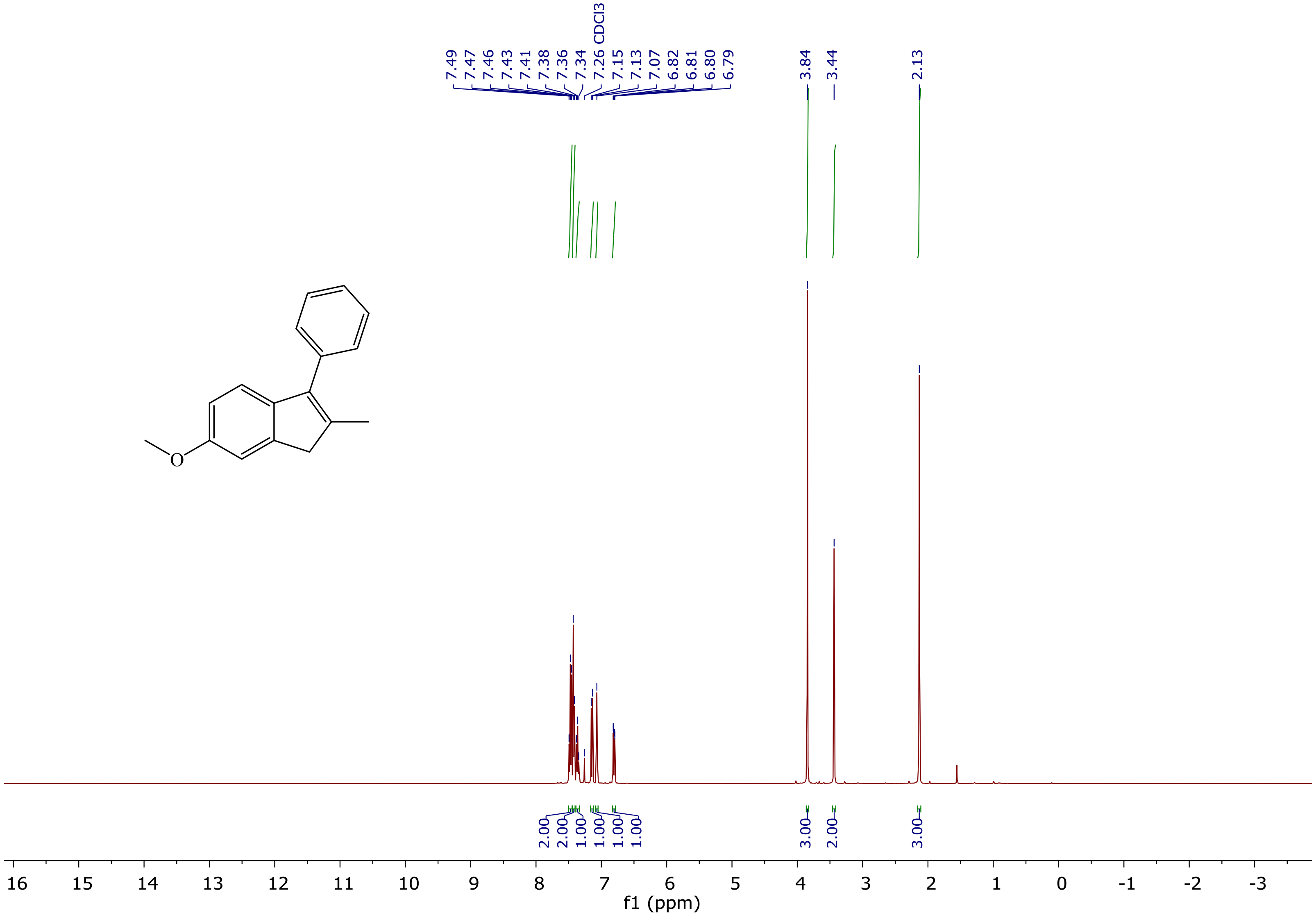


Figure S4.6. [1]H NMR (400MHz, $CDCl_3$) of 6-methoxy-2-methyl-3-phenyl-1H-indene (1c)

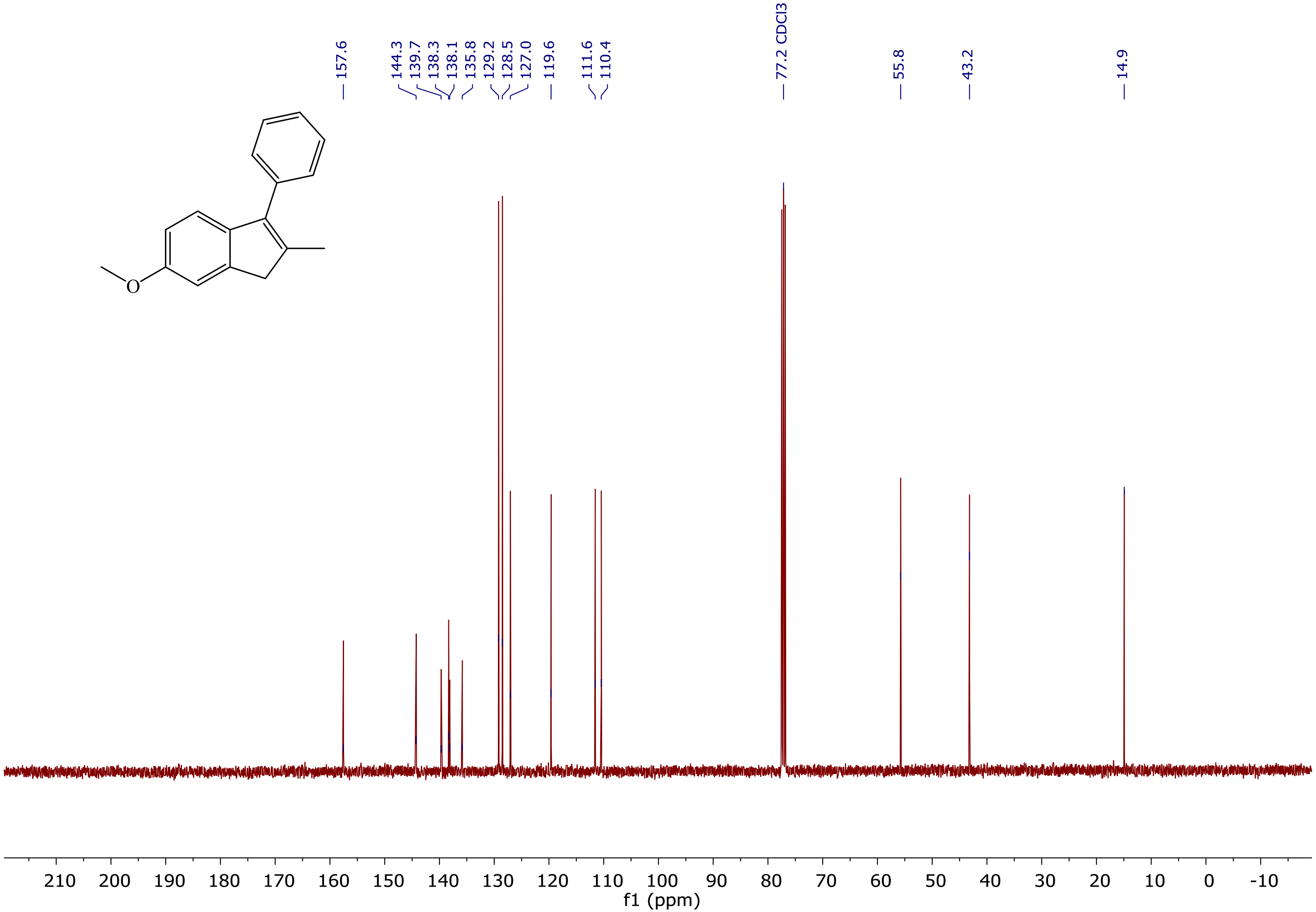


Figure S4.7. $^{13}C\{^{1}H\}$ **NMR (101MHz,** $CDCl_3$**) of 6-methoxy-2-methyl-3-phenyl-1H-indene (1c)**

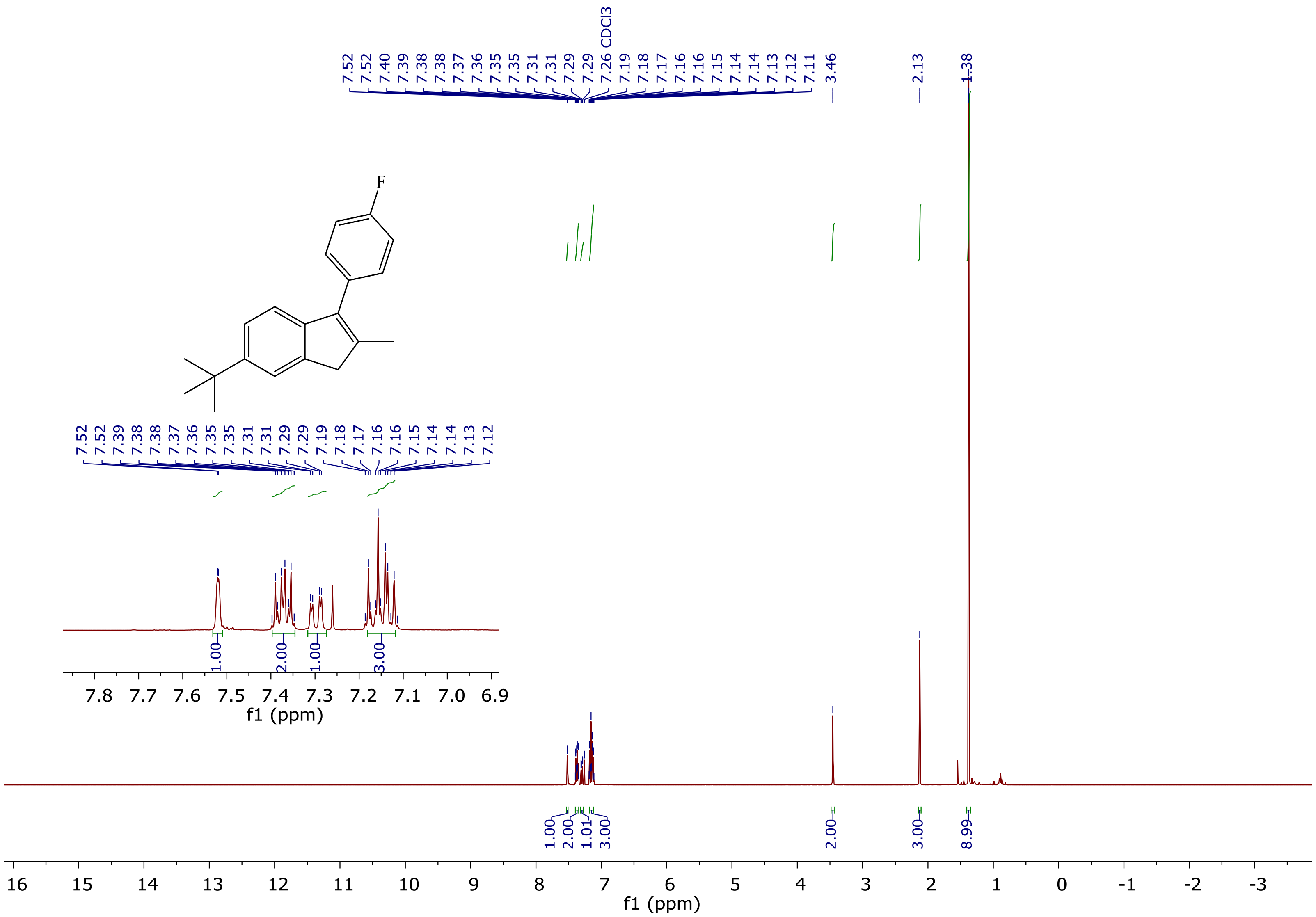


Figure S4.8. ^{1}H NMR (400MHz, $CDCl_3$) of 6-tert-butyl-3-(4-fluorophenyl)-2-methyl-1H-indene (1d)

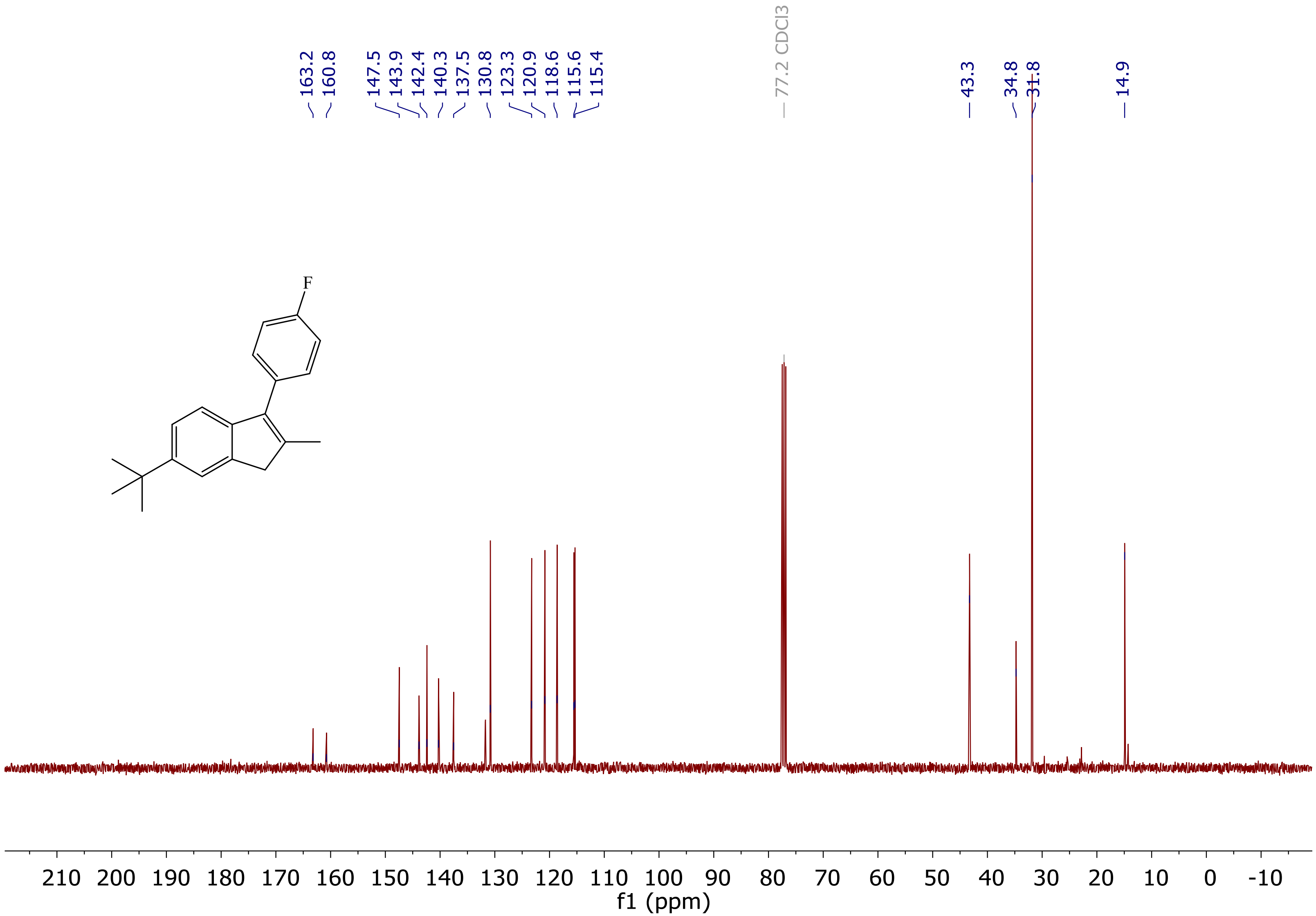


Figure S4.9. $^{13}C\{^1H\}$ **NMR (101MHz,** $CDCl_3$**) of 6-tert-butyl-3-(4-fluorophenyl)-2-methyl-1H-indene (1d)**

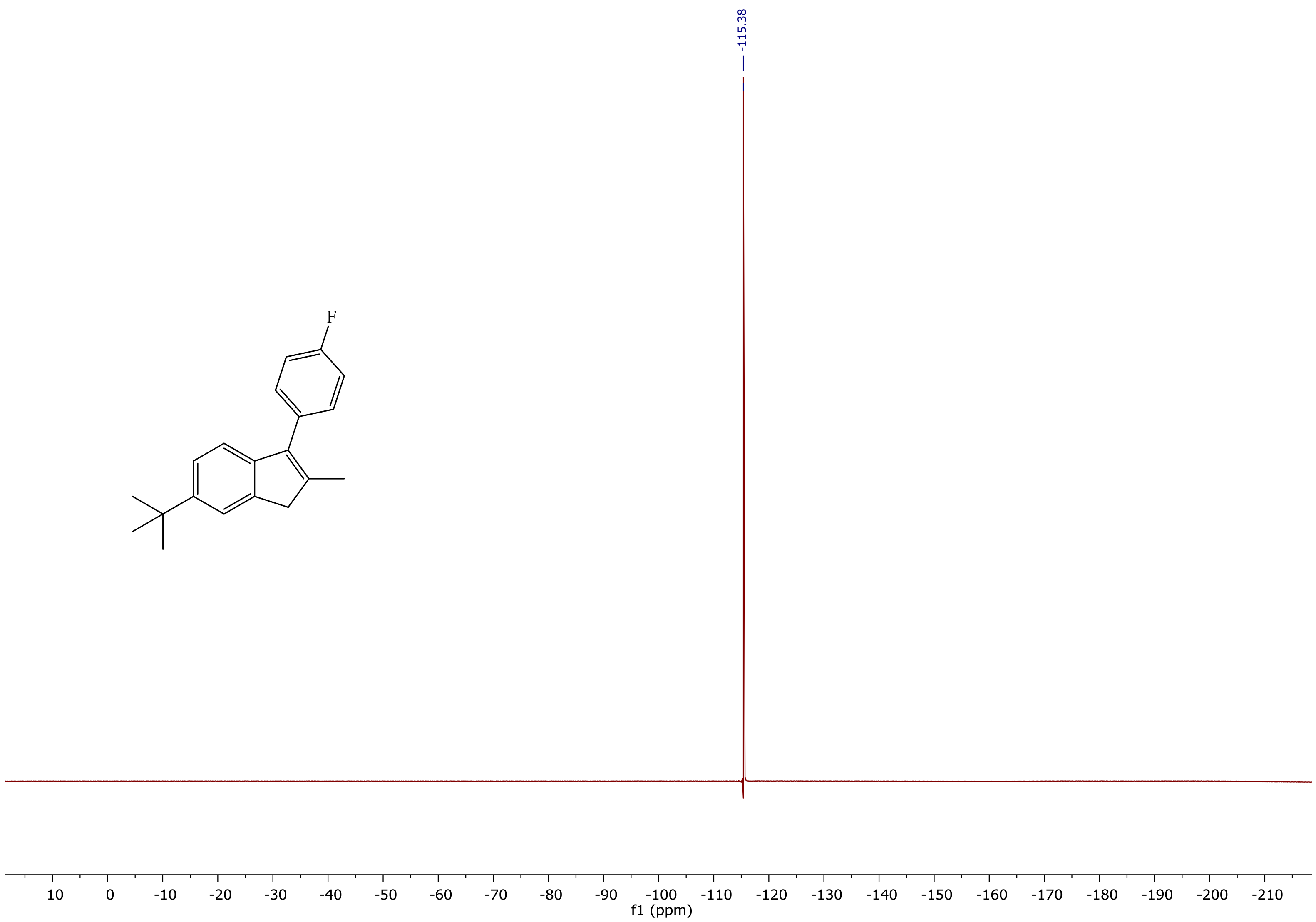


Figure S4.10. [19]F NMR (376 MHz, $CDCl_3$) of 6-tert-butyl-3-(4-fluorophenyl)-2-methyl-1H-indene (1d)

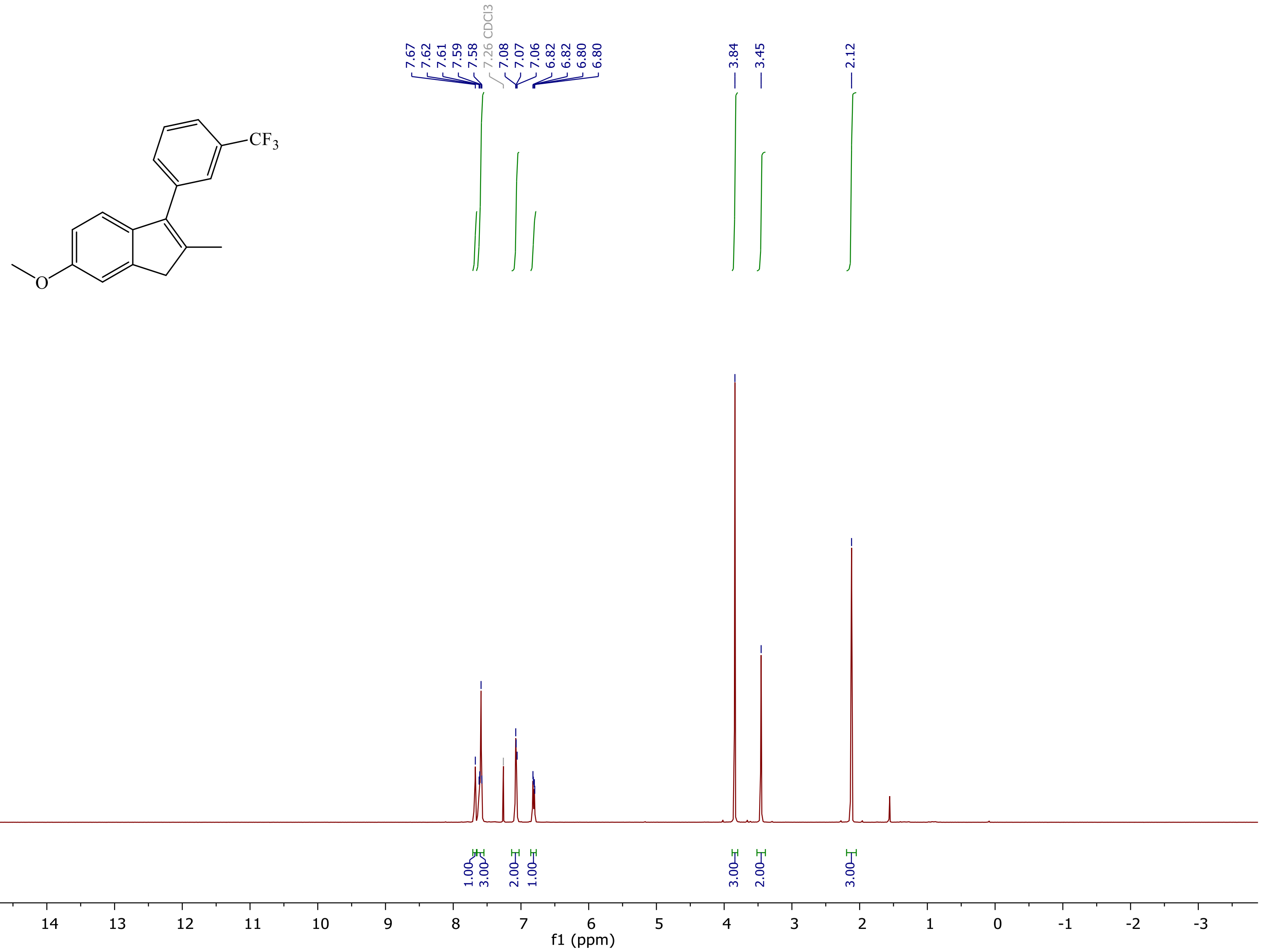


Figure S4.11. ^{1}H NMR (400MHz, $CDCl_3$) of 6-methoxy-2-methyl-3-(3-(trifluoromethyl)phenyl)-1H-indene (1e)

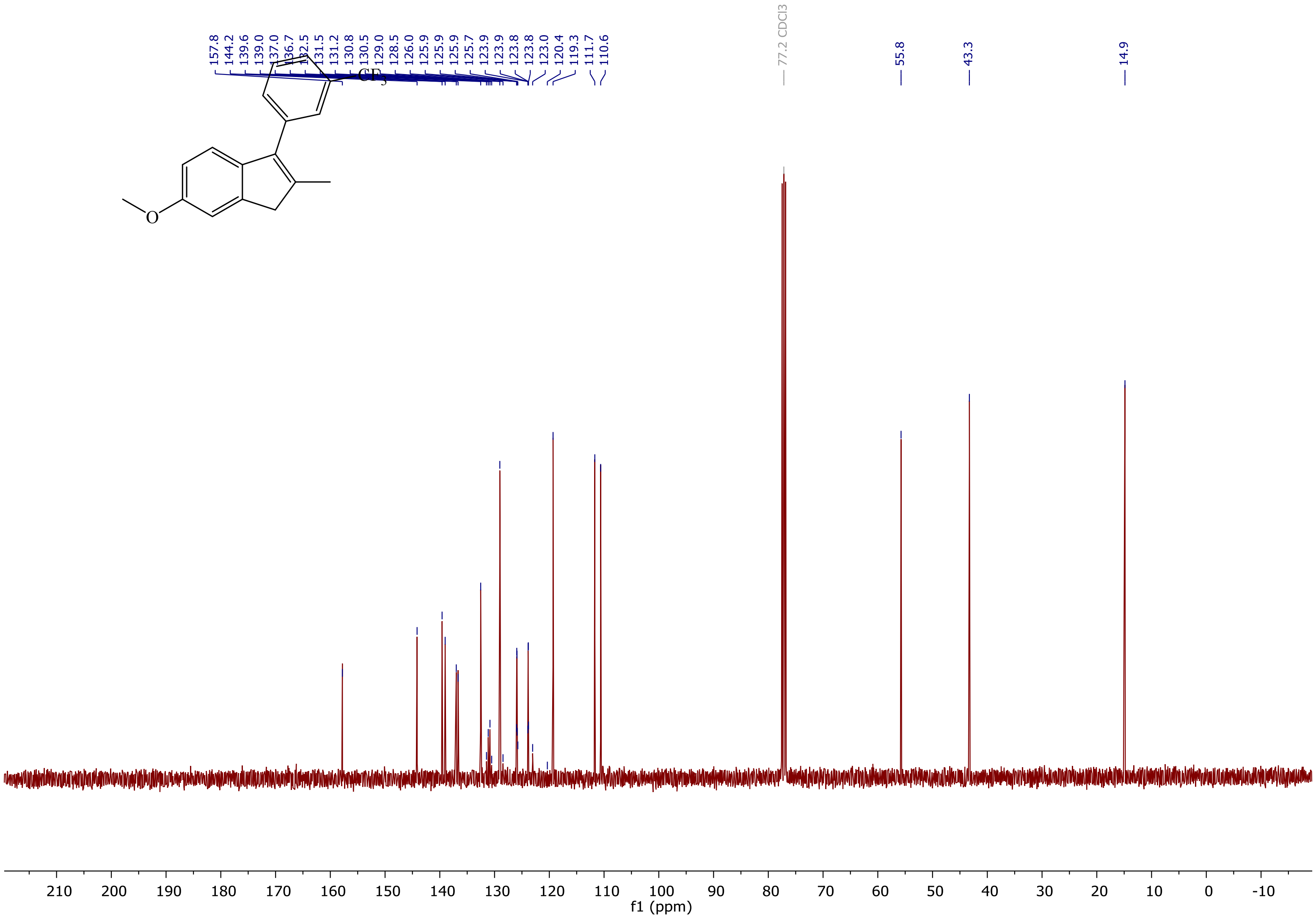


Figure S4.12. $^{13}C\ \{^{1}H\}$ NMR (101MHz, $CDCl_3$) of 6-methoxy-2-methyl-3-(3-(trifluoromethyl)phenyl)-1H-indene (1e)

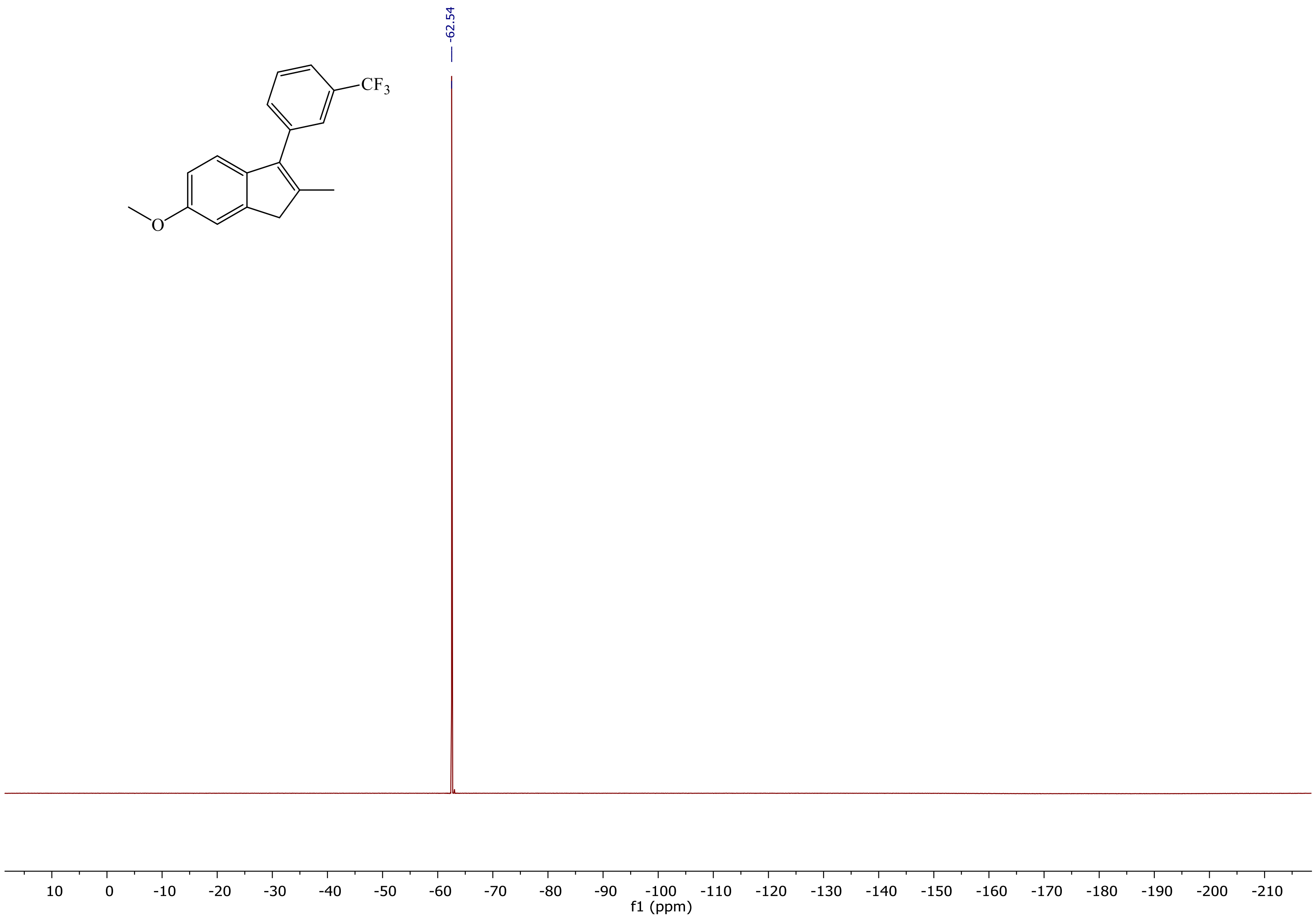


Figure S4.13. ^{19}F NMR (376MHz, $CDCl_3$) of 6-methoxy-2-methyl-3-(3-(trifluoromethyl)phenyl)-1H-indene (1e)

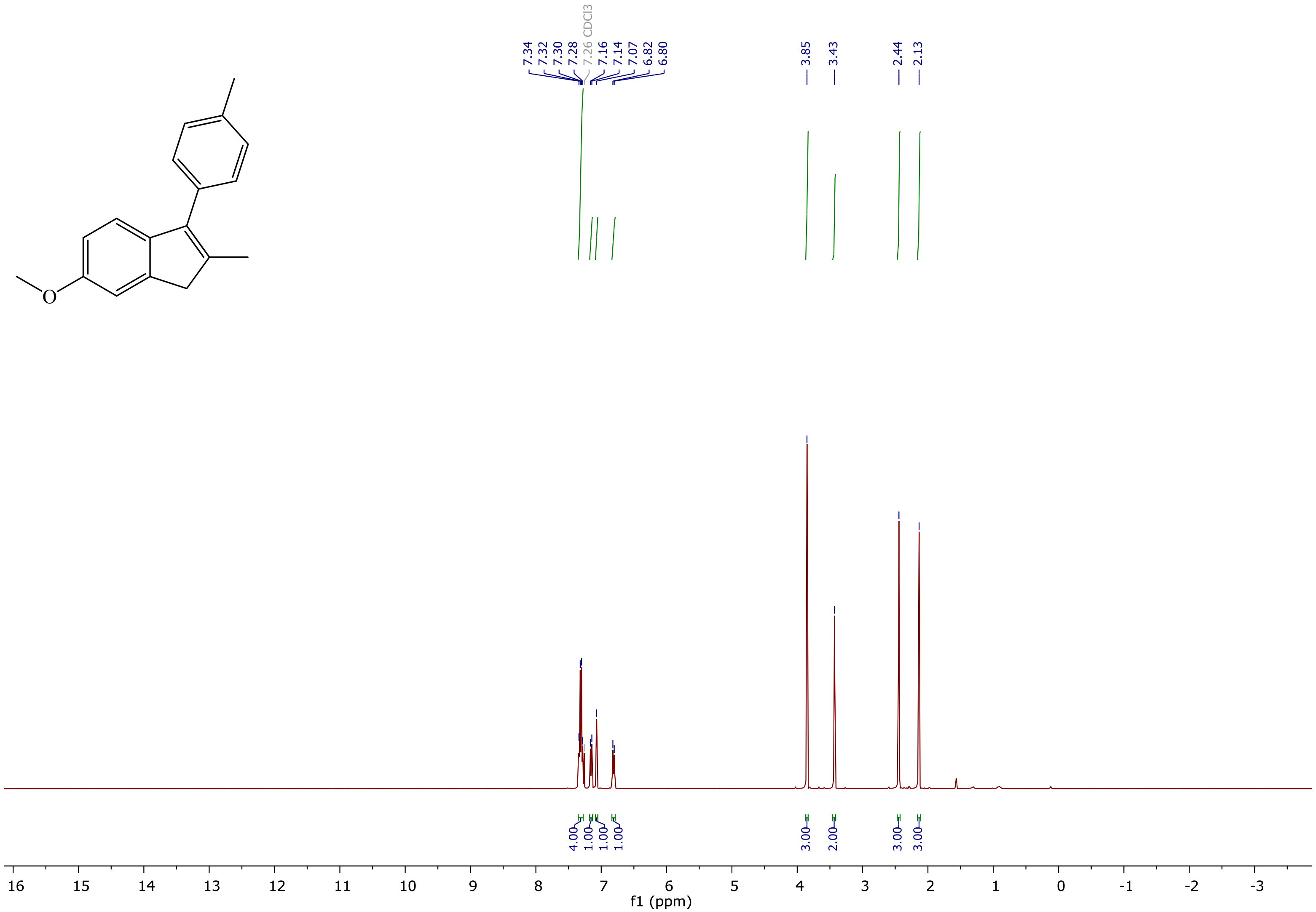


Figure S4.14. ^{1}H NMR (400MHz, $CDCl_3$) of 6-methoxy-2-methyl-3-p-tolyl-1H-indene (1f)

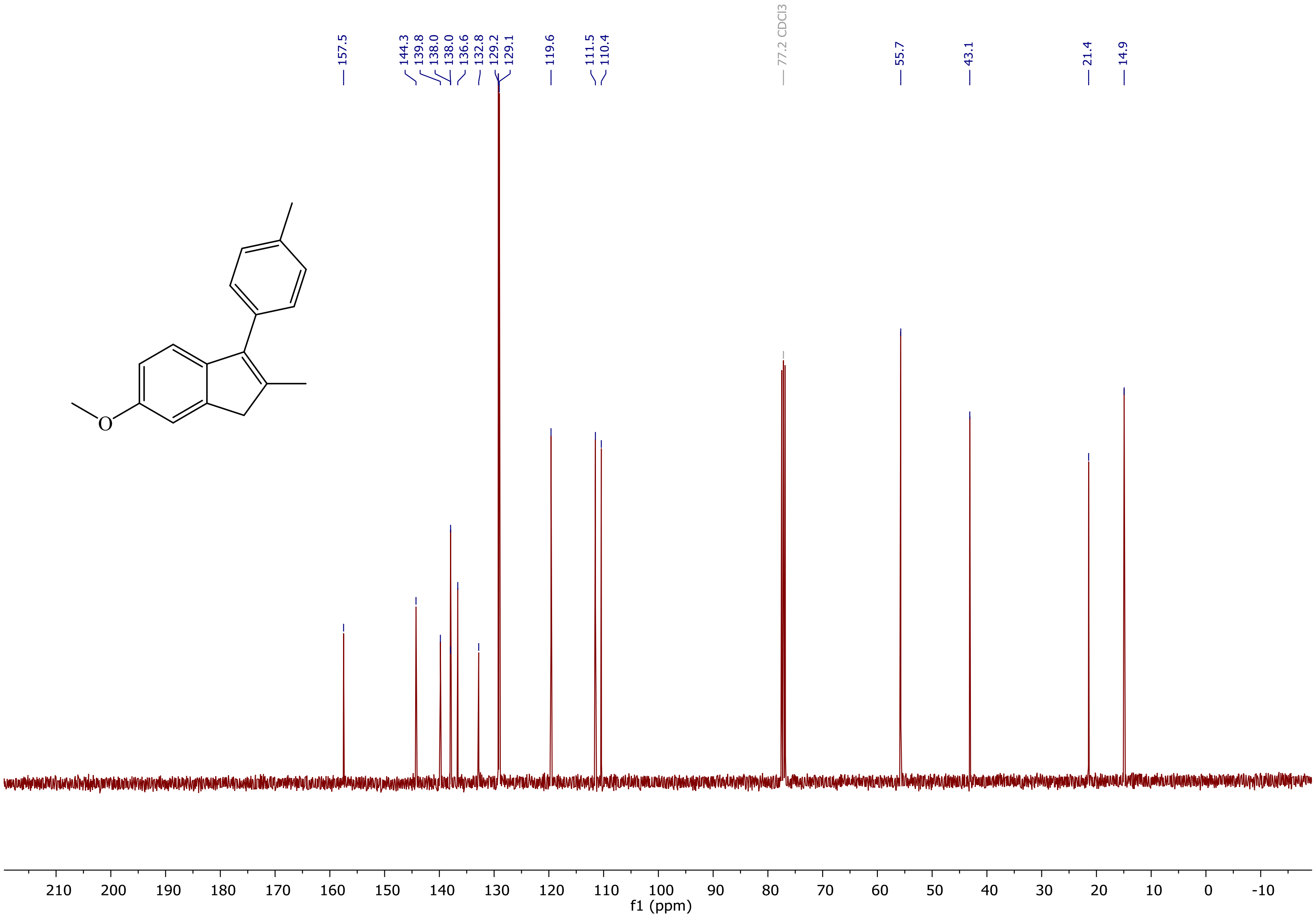


Figure S4.15. ^{13}C {^{1}H} NMR (101MHz, $CDCl_3$) of 6-methoxy-2-methyl-3-p-tolyl-1H-indene (1f)

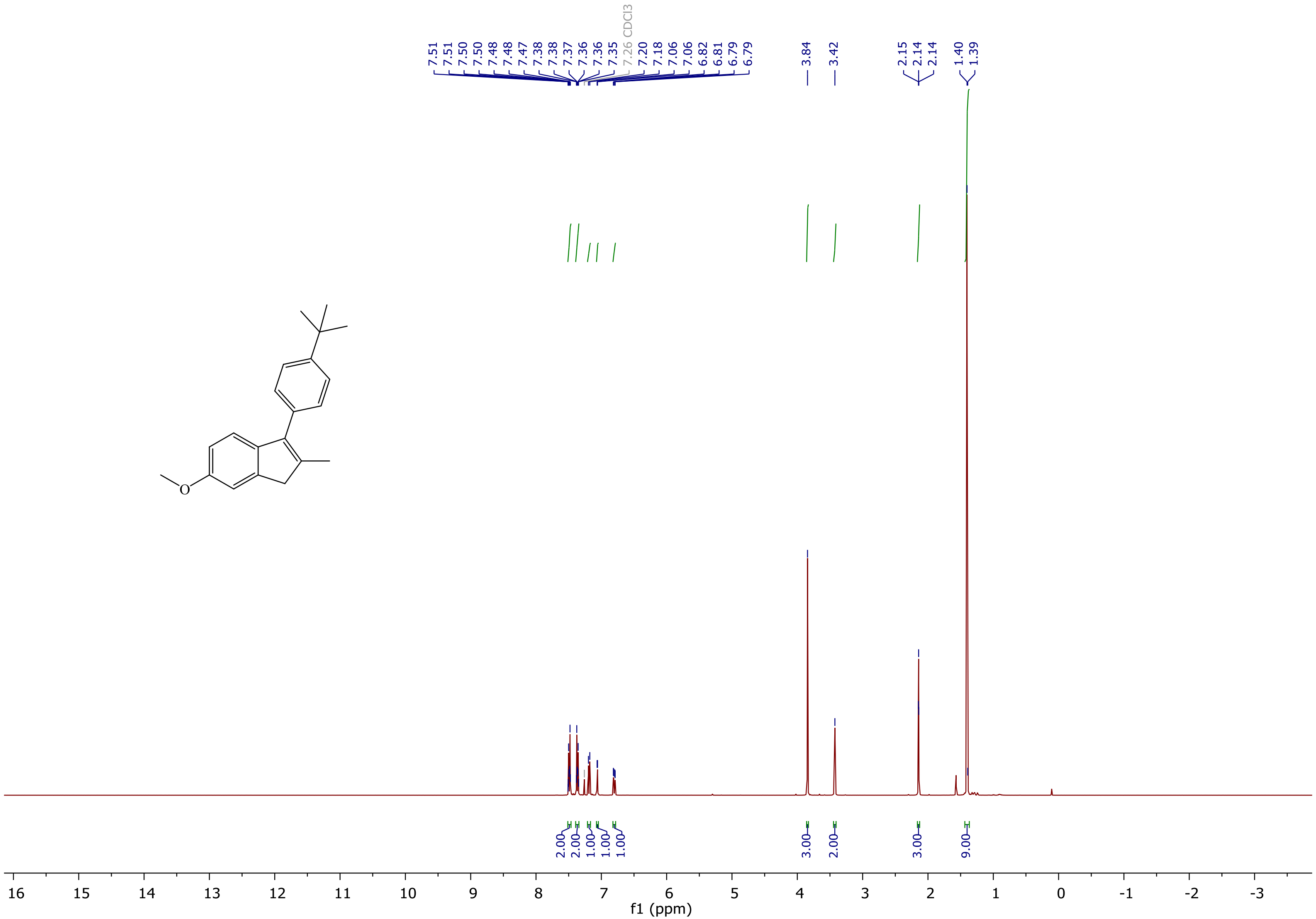


Figure S4.16. ^{1}H NMR (400MHz, $CDCl_3$) of 3-(4-tert-butylphenyl)-6-methoxy-2-methyl-1H-indene (1g)

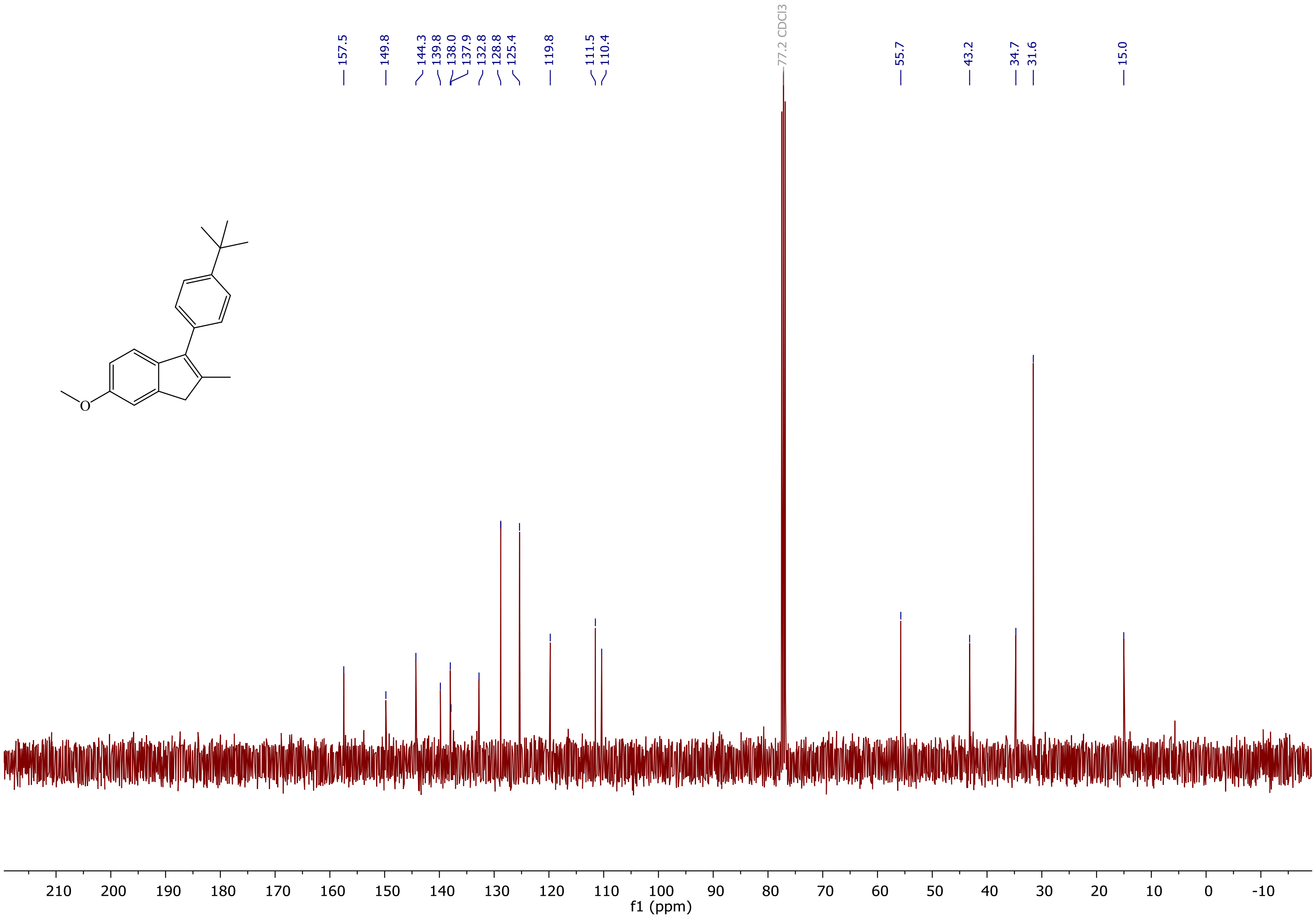


Figure S4.17. $^{13}C\{^{1}H\}$ **NMR (101MHz,** $CDCl_3$**) of 3-(4-tert-butylphenyl)-6-methoxy-2-methyl-1H-indene (1g)**

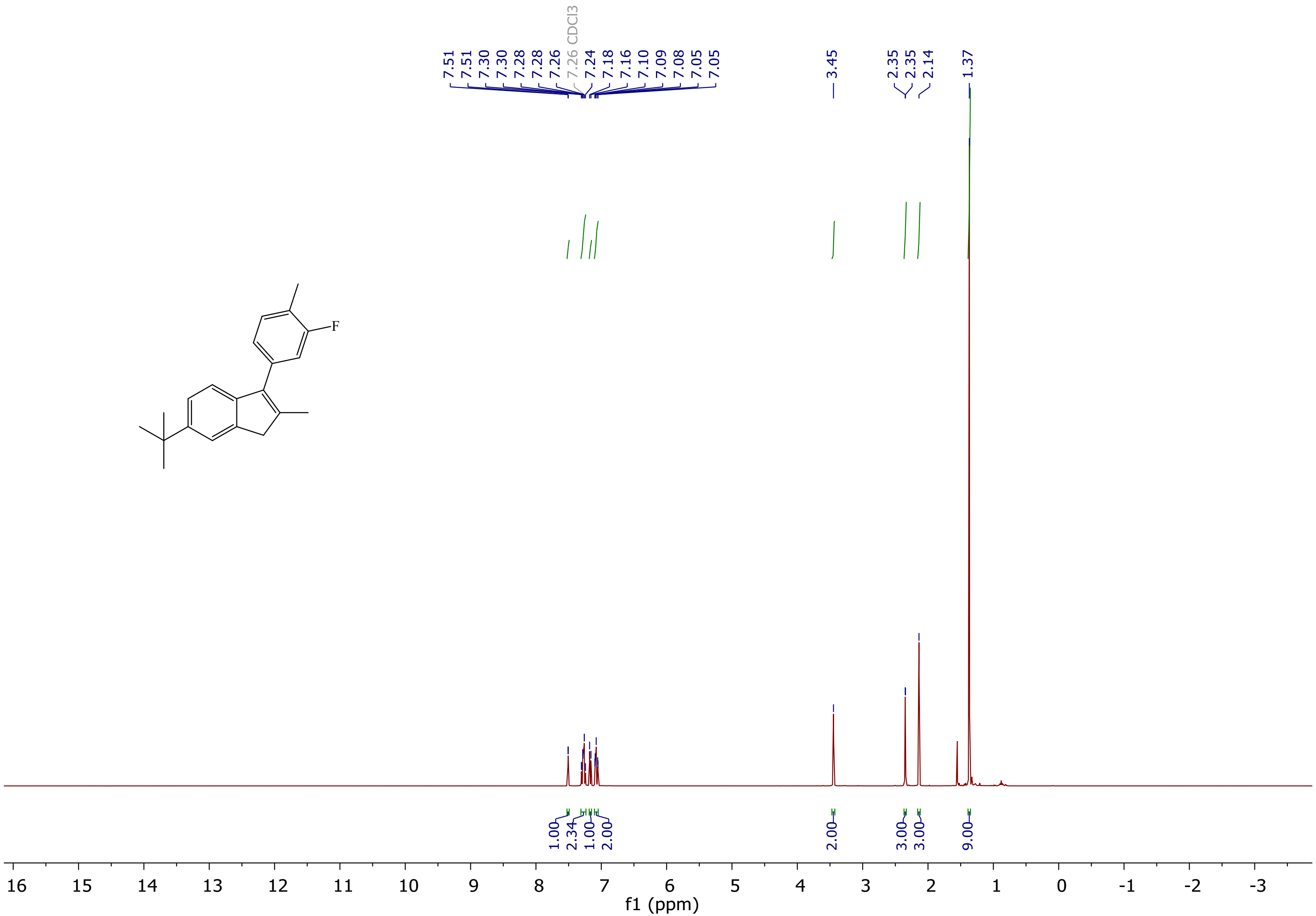


Figure S4.18. ^{1}H NMR (400MHz, $CDCl_3$) of 6-tert-butyl-3-(3-fluoro-4-methylphenyl)-2-methyl-1H-indene (1h)

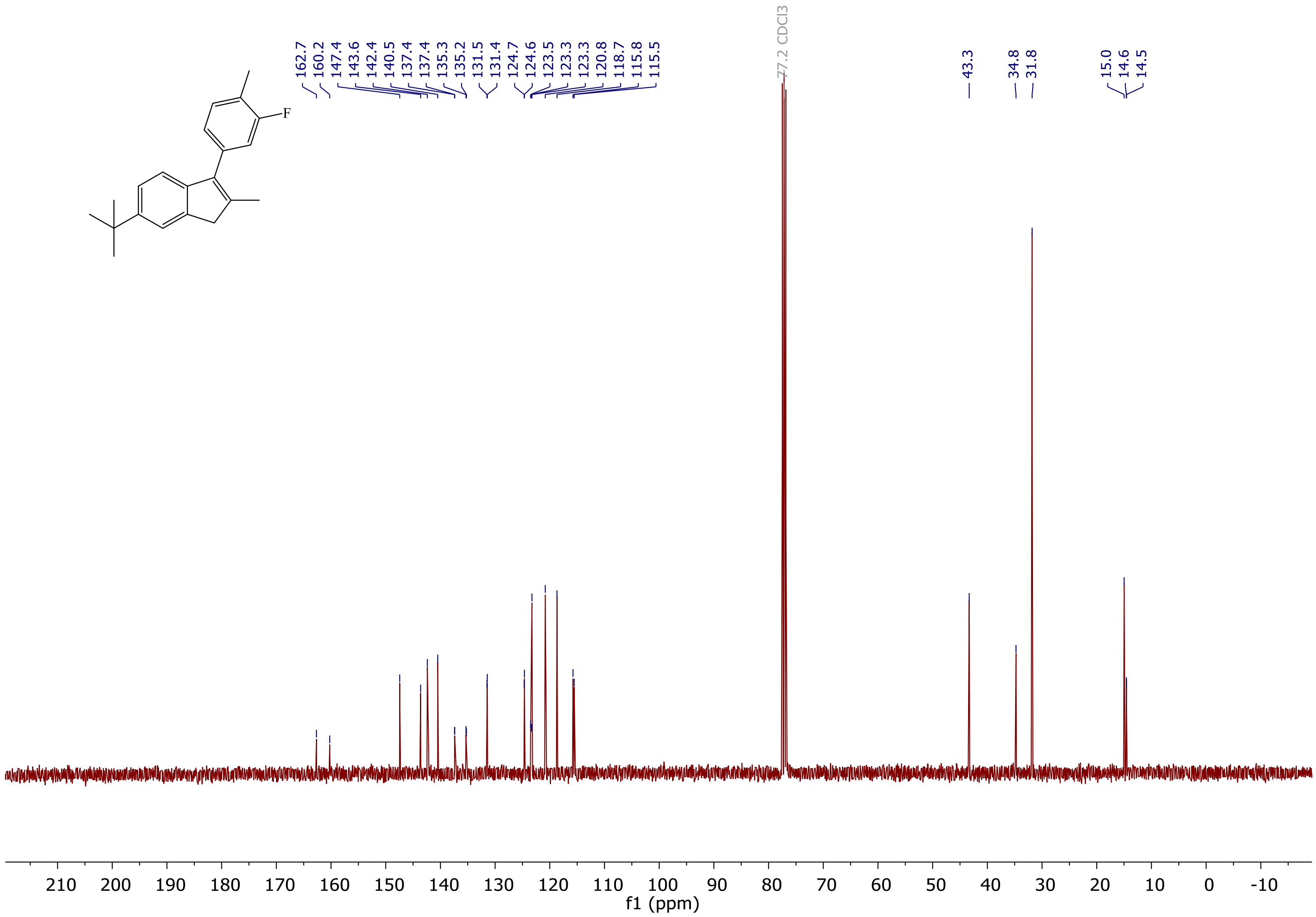


Figure S4.19. $^{13}C\{^1H\}$ **NMR (101MHz,** $CDCl_3$**) of 6-tert-butyl-3-(3-fluoro-4-methylphenyl)-2-methyl-1H-indene (1h)**

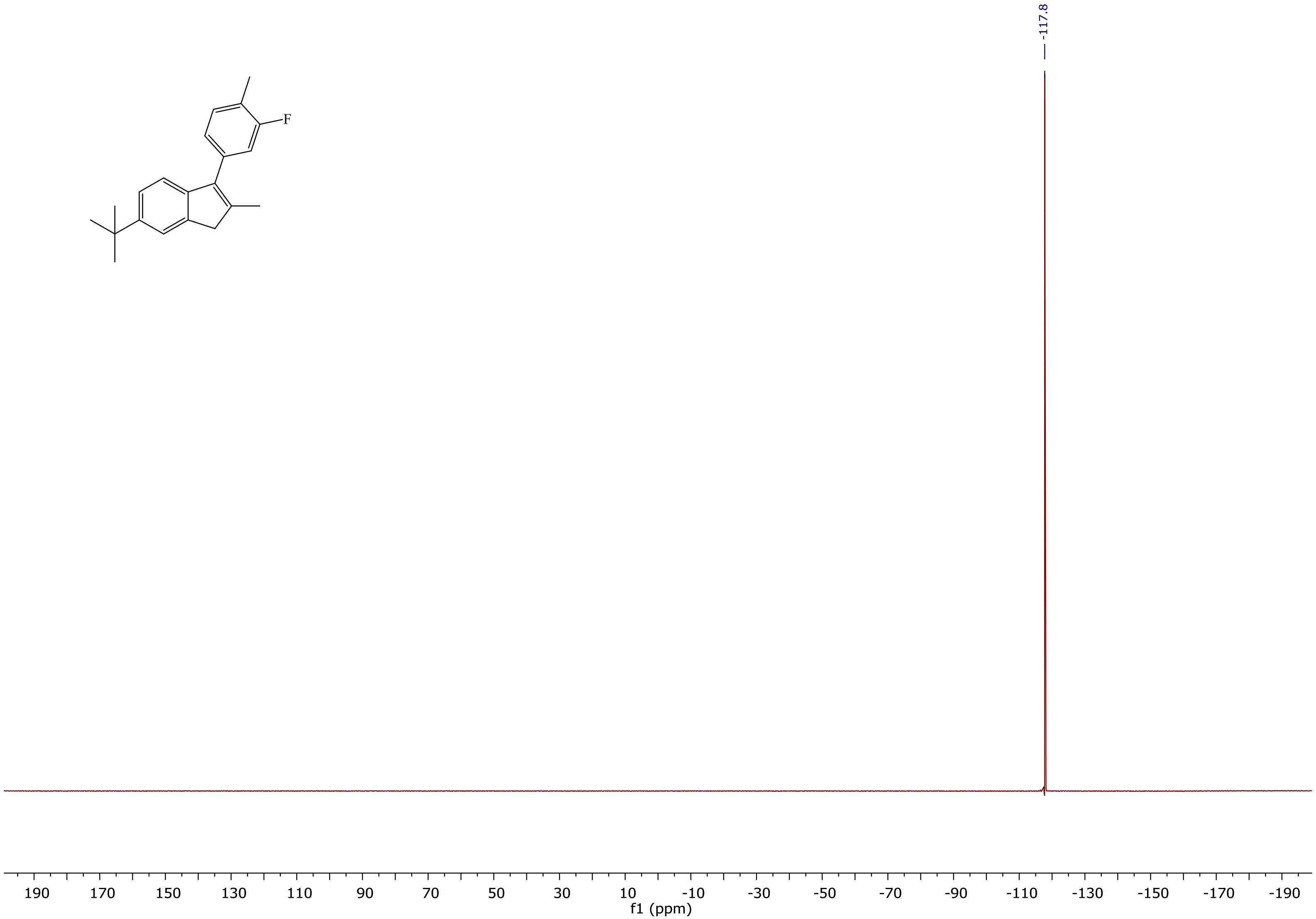


Figure S4.20. ^{19}F NMR (376 MHz, $CDCl_3$) of 6-tert-butyl-3-(3-fluoro-4-methylphenyl)-2-methyl-1H-indene (1h)

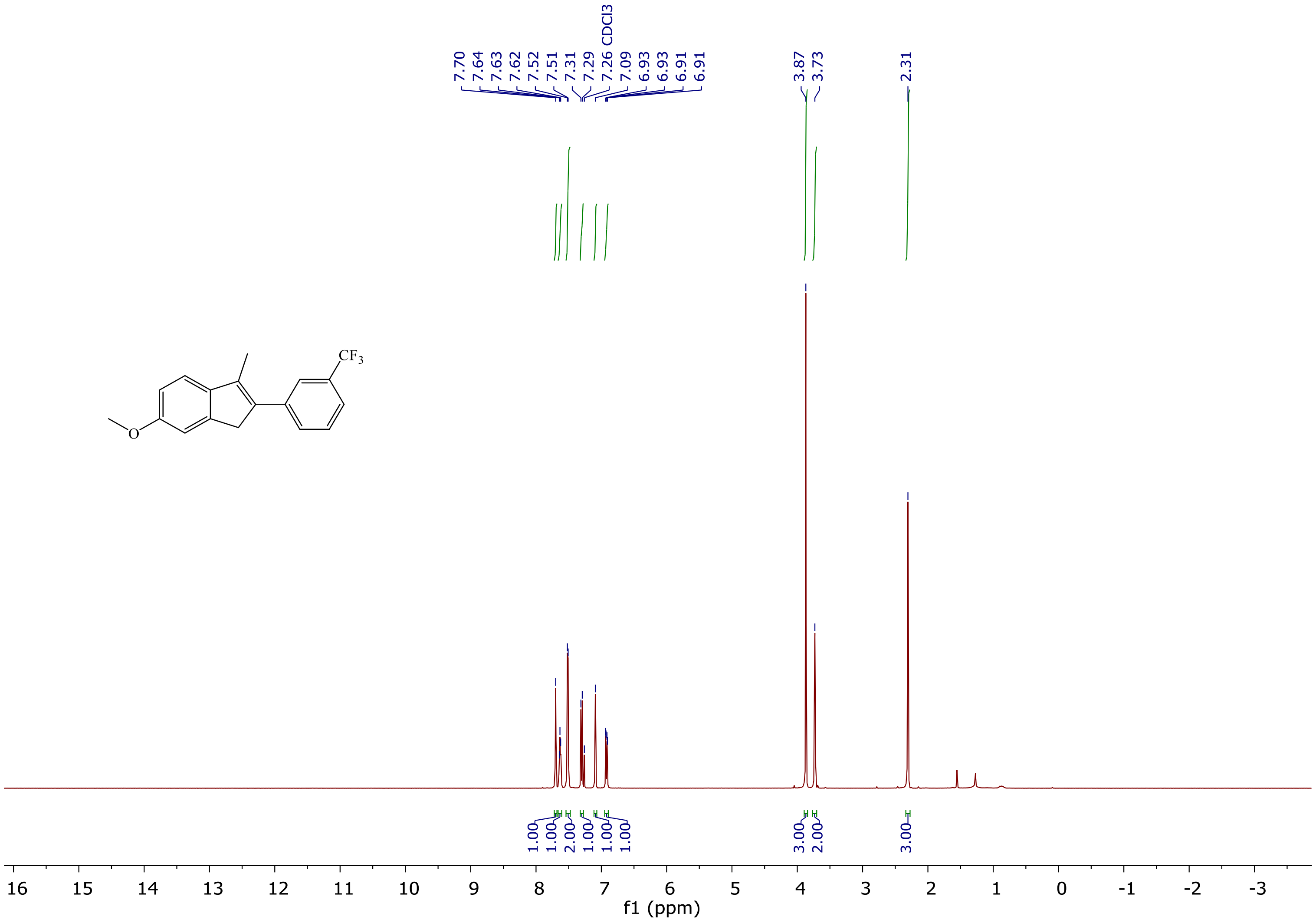


Figure S4.21. ^{1}H NMR (400MHz, $CDCl_3$) of 6-methoxy-3-methyl-2-(3-(trifluoromethyl)phenyl)-1H-indene (1j)

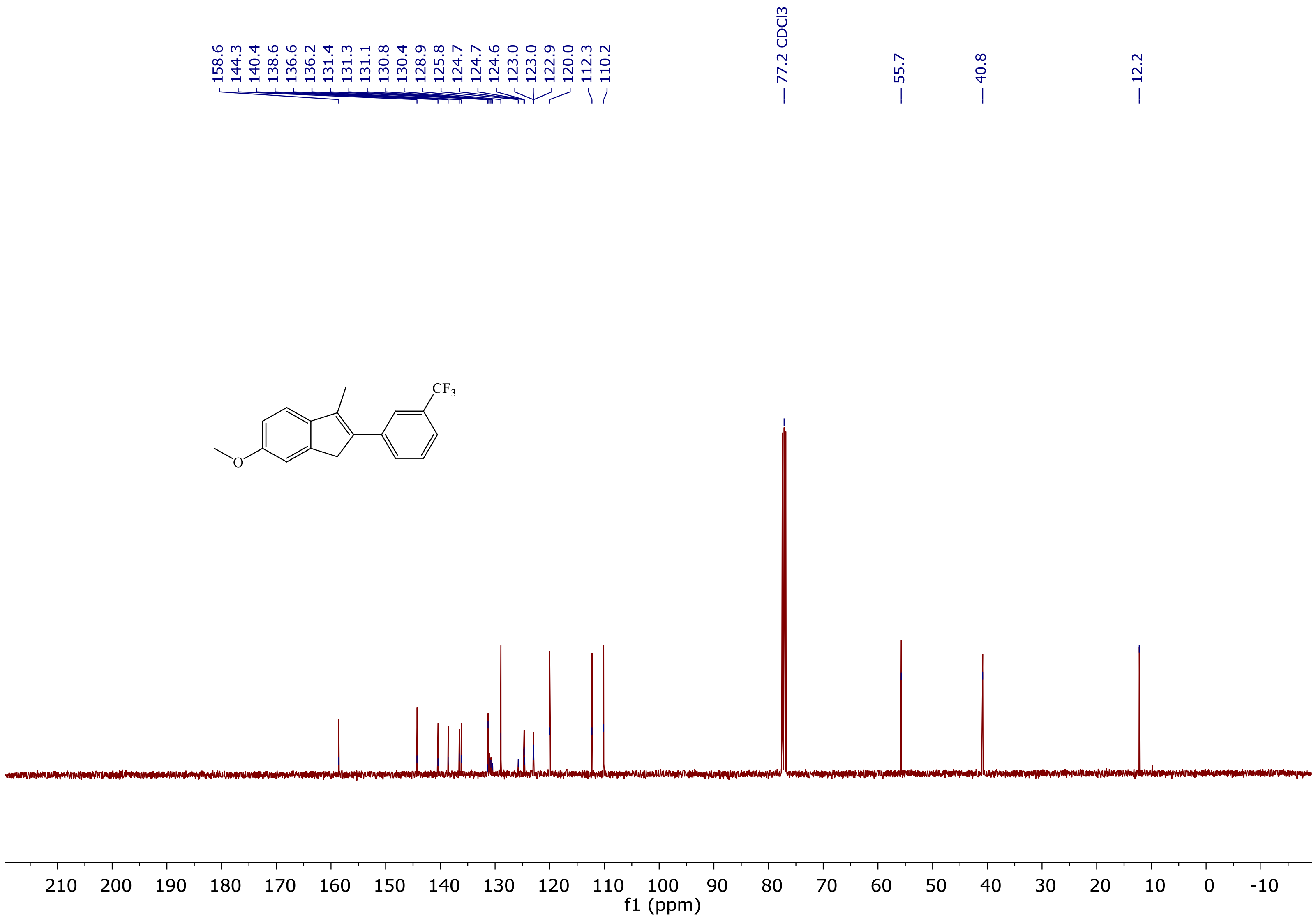


Figure S4.22. $^{13}C\{^1H\}$ **NMR (101MHz,** $CDCl_3$**) of 6-methoxy-3-methyl-2-(3-(trifluoromethyl)phenyl)-1H-indene (1j)**

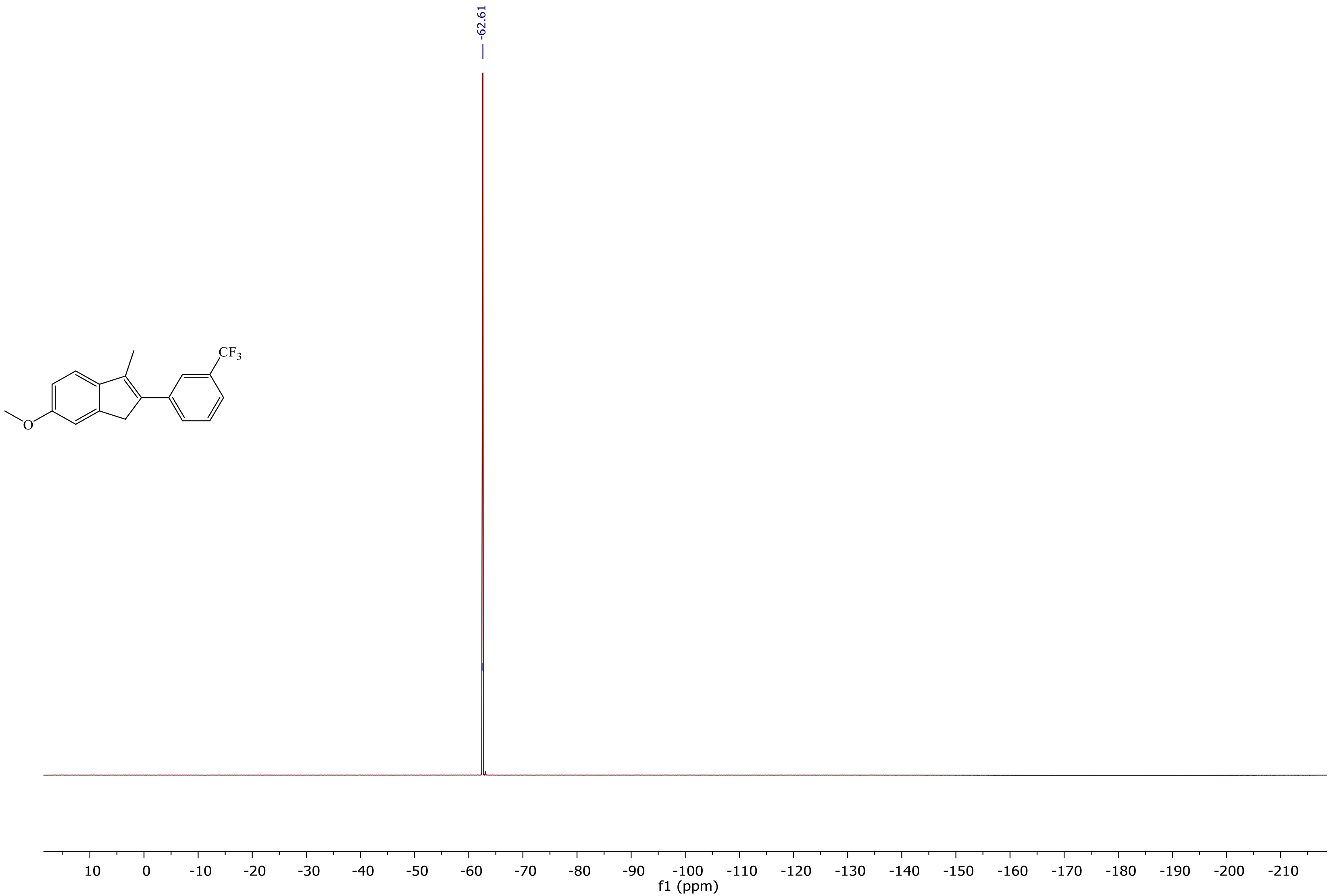


Figure S4.23. [19]F NMR (101MHz, $CDCl_3$) of 6-methoxy-3-methyl-2-(3-(trifluoromethyl)phenyl)-1H-indene (1j)

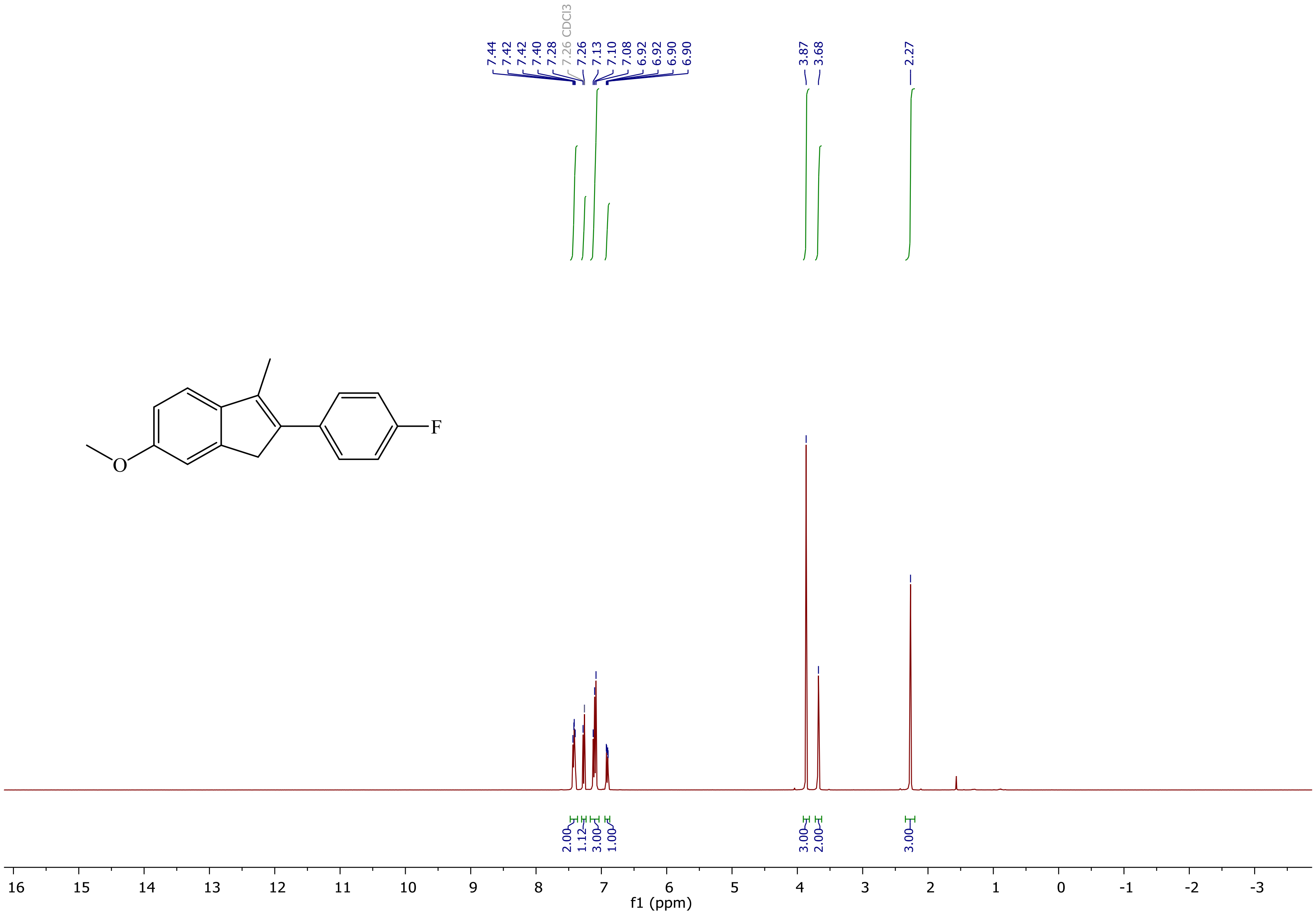


Figure S4.24. [1]H NMR (400MHz, $CDCl_3$) of 2-(4-fluorophenyl)-6-methoxy-3-methyl-1H-indene (1l)

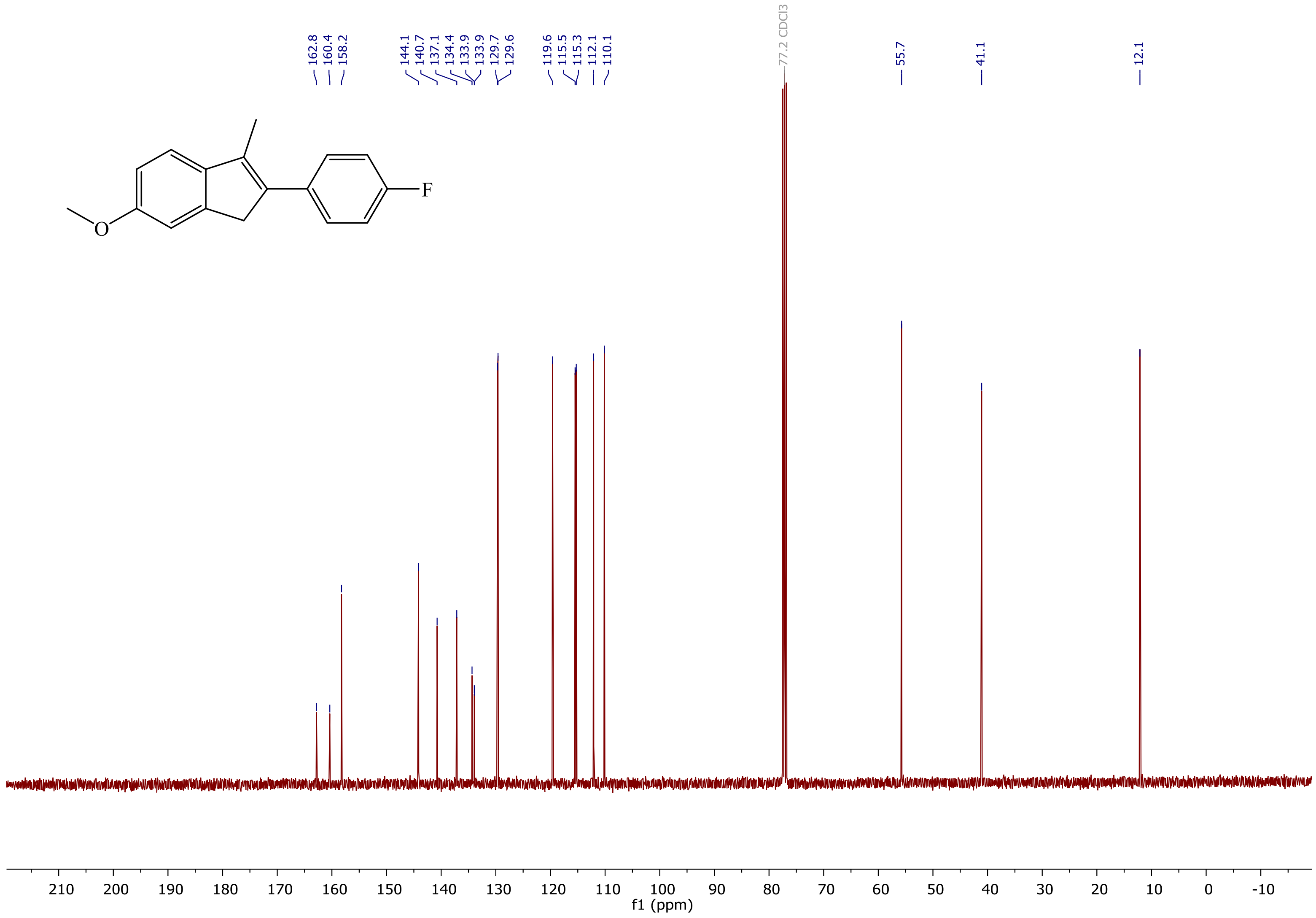


Figure S4.25. $^{13}C\{^1H\}$ **NMR (101MHz, $CDCl_3$) of 2-(4-fluorophenyl)-6-methoxy-3-methyl-1H-indene (1l)**

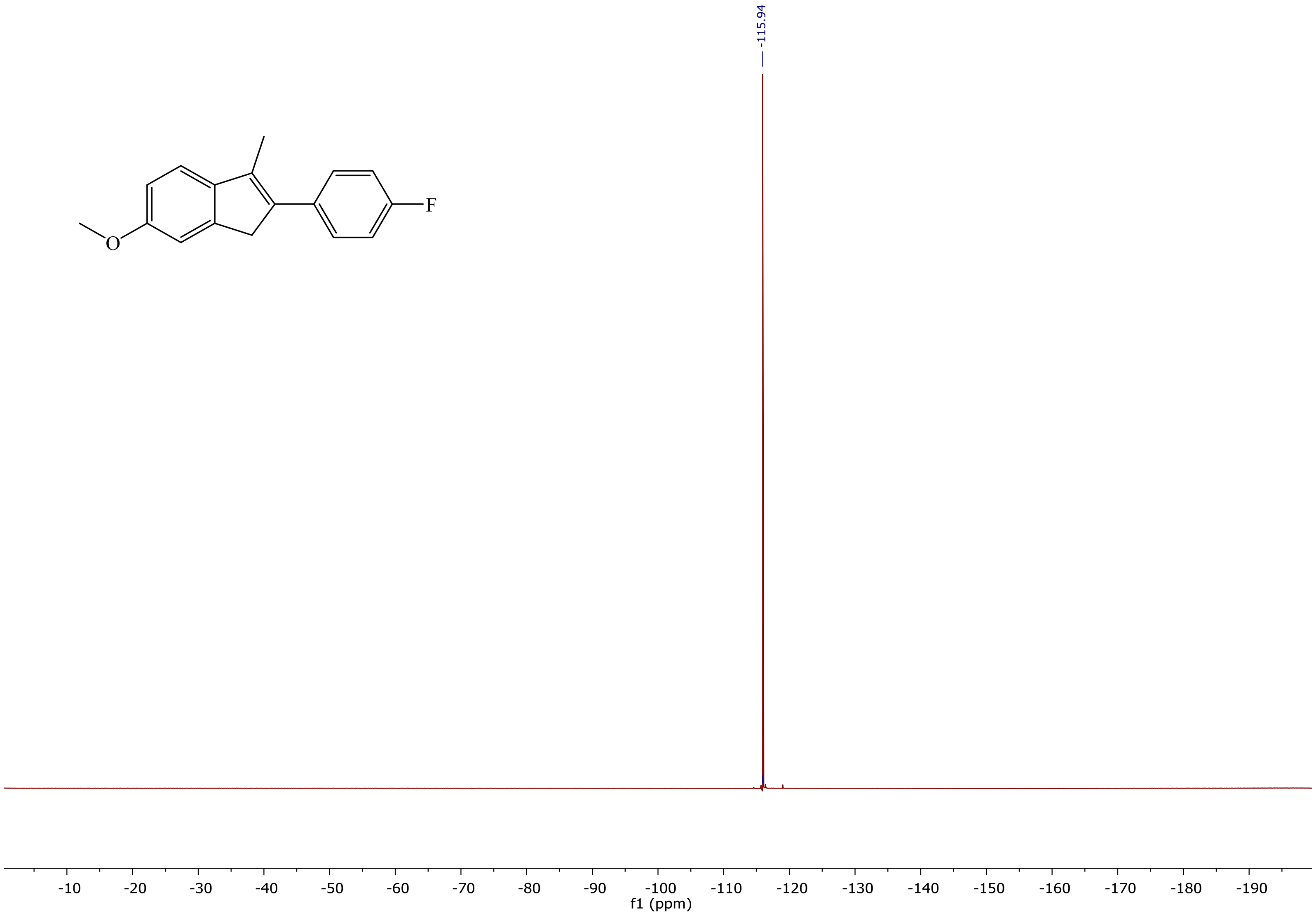


Figure S4.26. ^{19}F NMR (101MHz, $CDCl_3$) of 2-(4-fluorophenyl)-6-methoxy-3-methyl-1H-indene (1l)

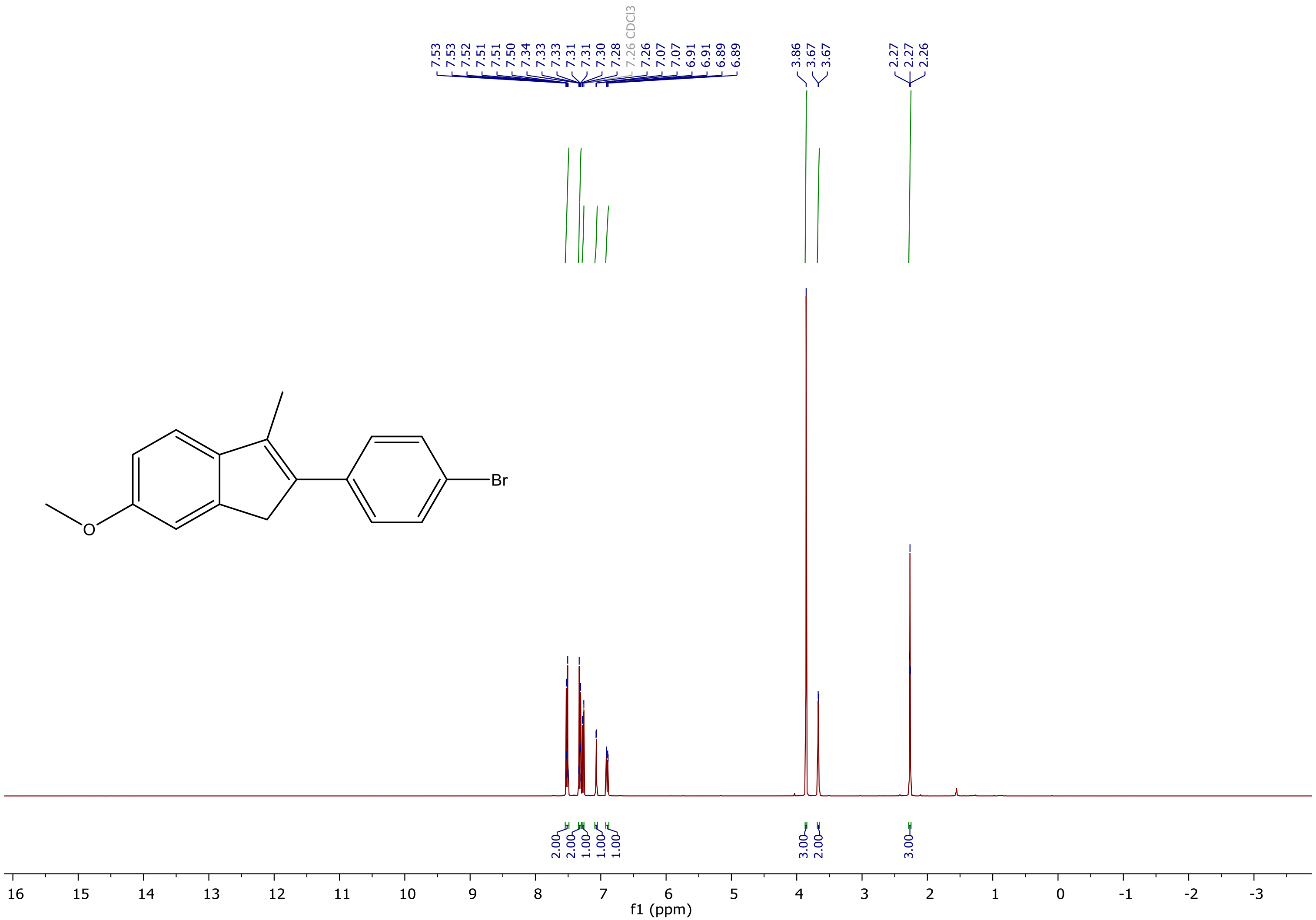


Figure S4.27. [1]H NMR (400MHz, $CDCl_3$) of 2-(4-bromophenyl)-6-methoxy-3-methyl-1H-indene (1o)

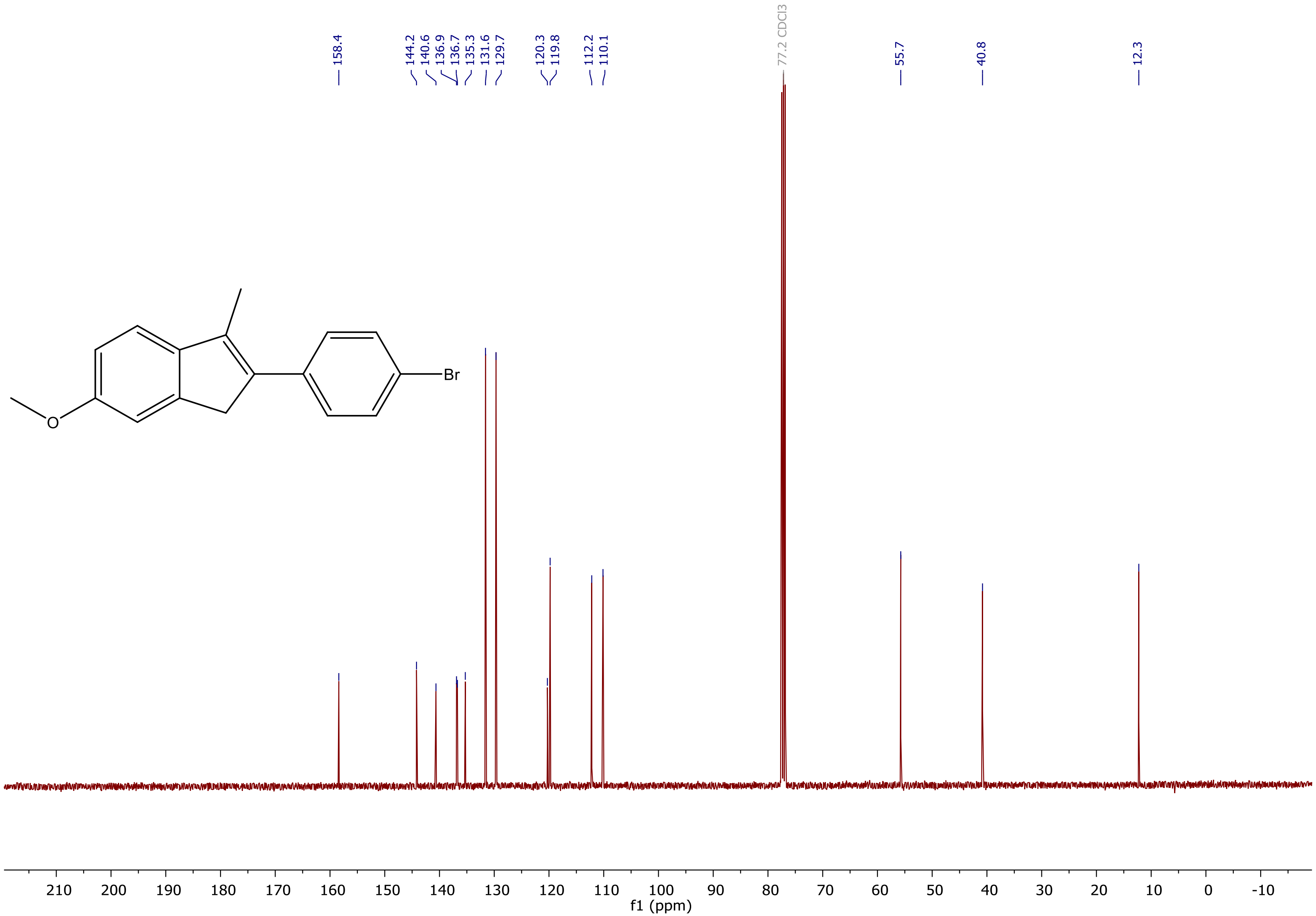


Figure S4.28. $^{13}C\{^{1}H\}$ NMR (101MHz, $CDCl_3$) of 2-(4-bromophenyl)-6-methoxy-3-methyl-1H-indene (1o)

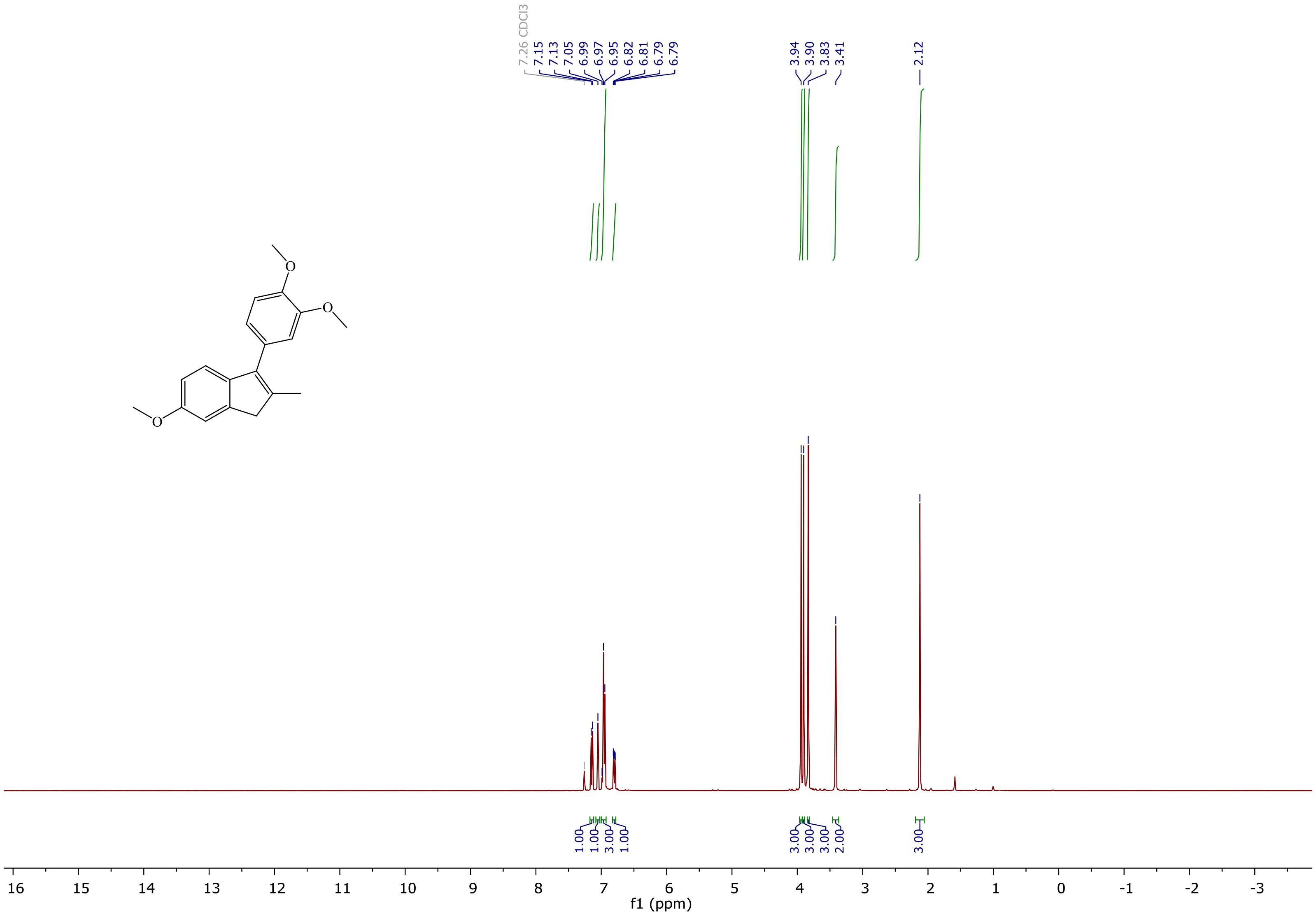


Figure S4.29. ¹H NMR (400MHz, CDCl$_3$) of 3-(3,4-dimethoxyphenyl)-6-methoxy-2-methyl-1H-indene (1q)

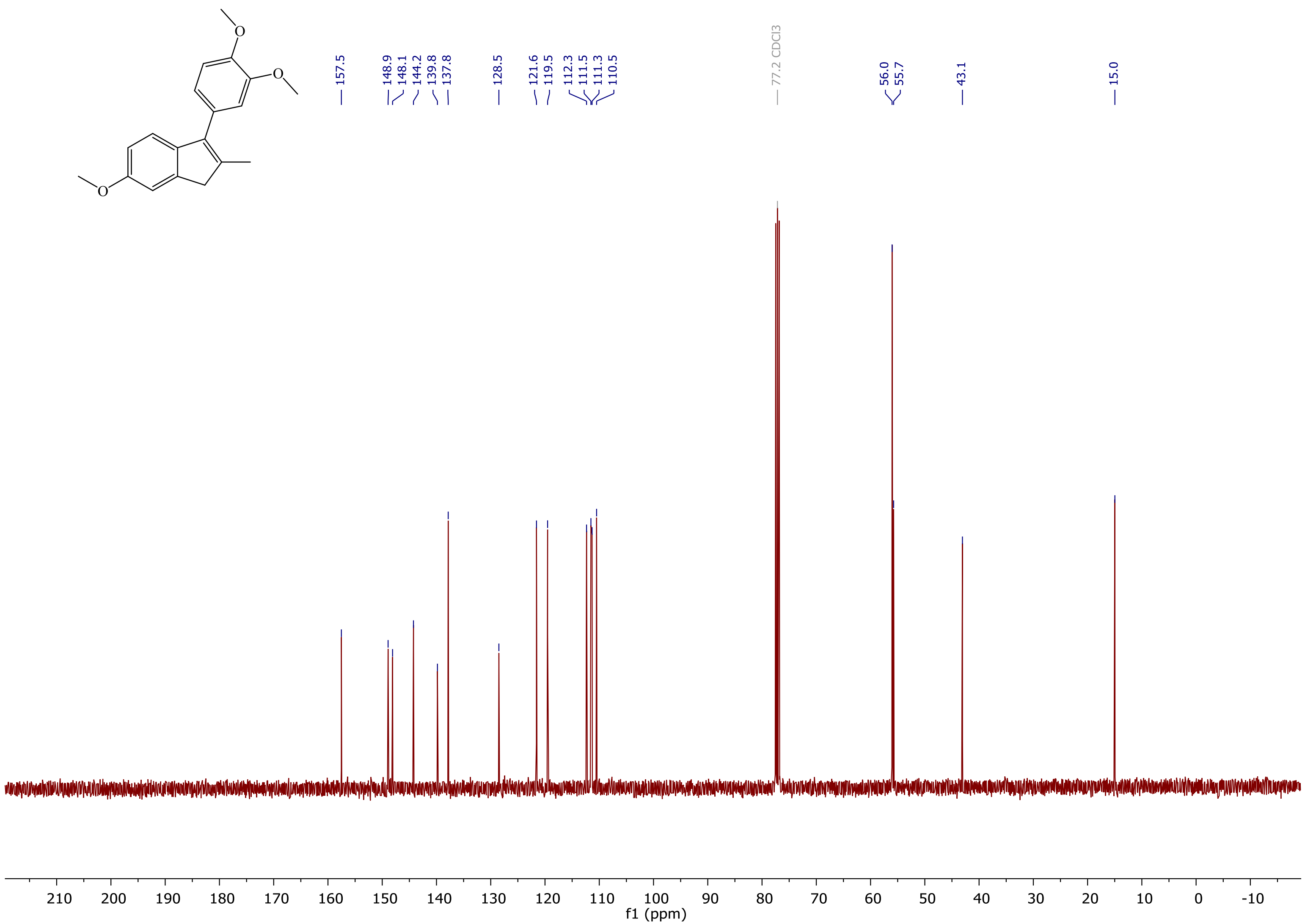


Figure S4.30. ^{13}**C {**^{1}**H} NMR (101MHz, CDCl**$_3$**) of 3-(3,4-dimethoxyphenyl)-6-methoxy-2-methyl-1H-indene (1q)**

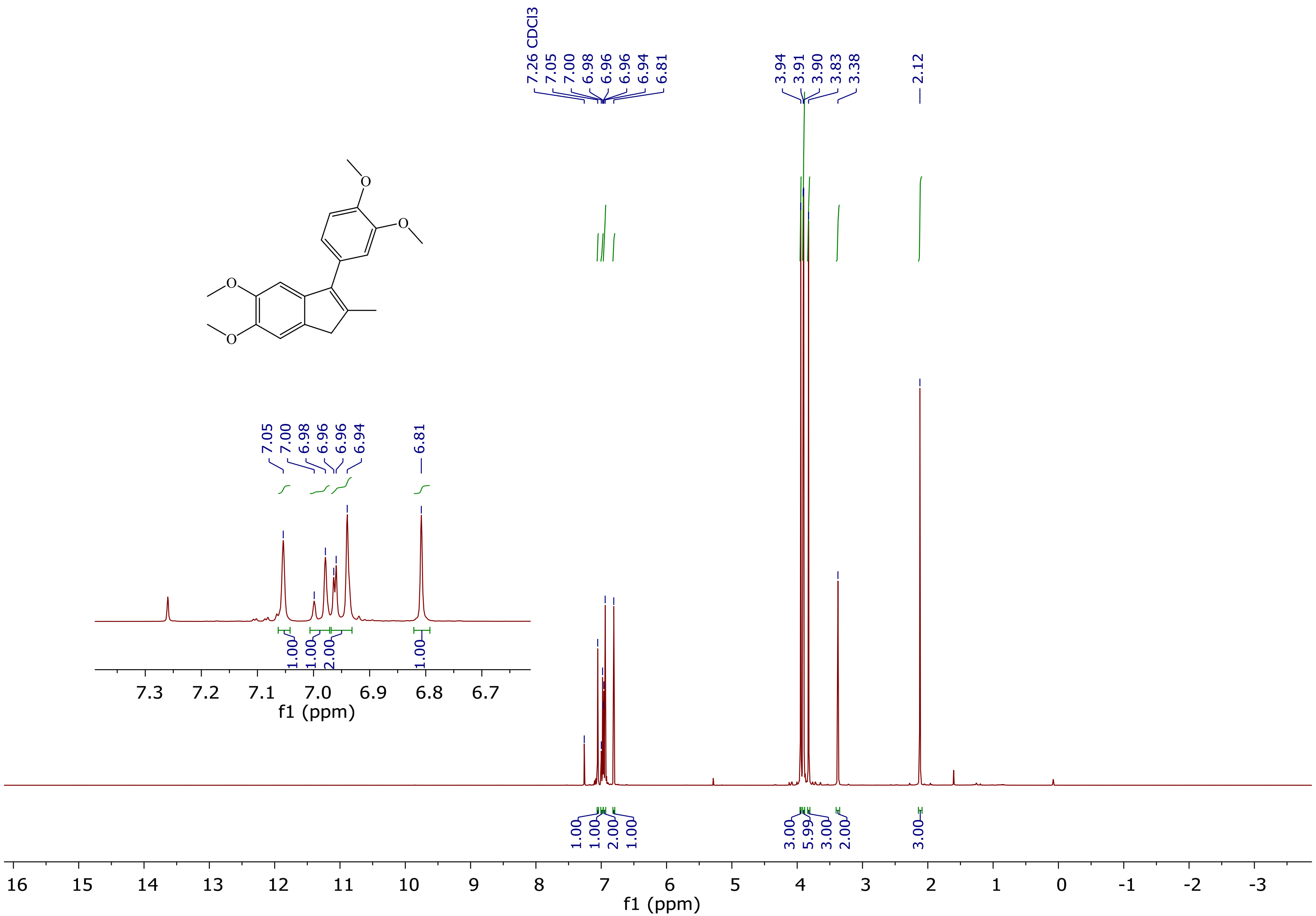


Figure S4.31. [1]H NMR (400MHz, $CDCl_3$) of 3-(3,4-dimethoxyphenyl)-5,6-dimethoxy-2-methyl-1H-indene (1r)

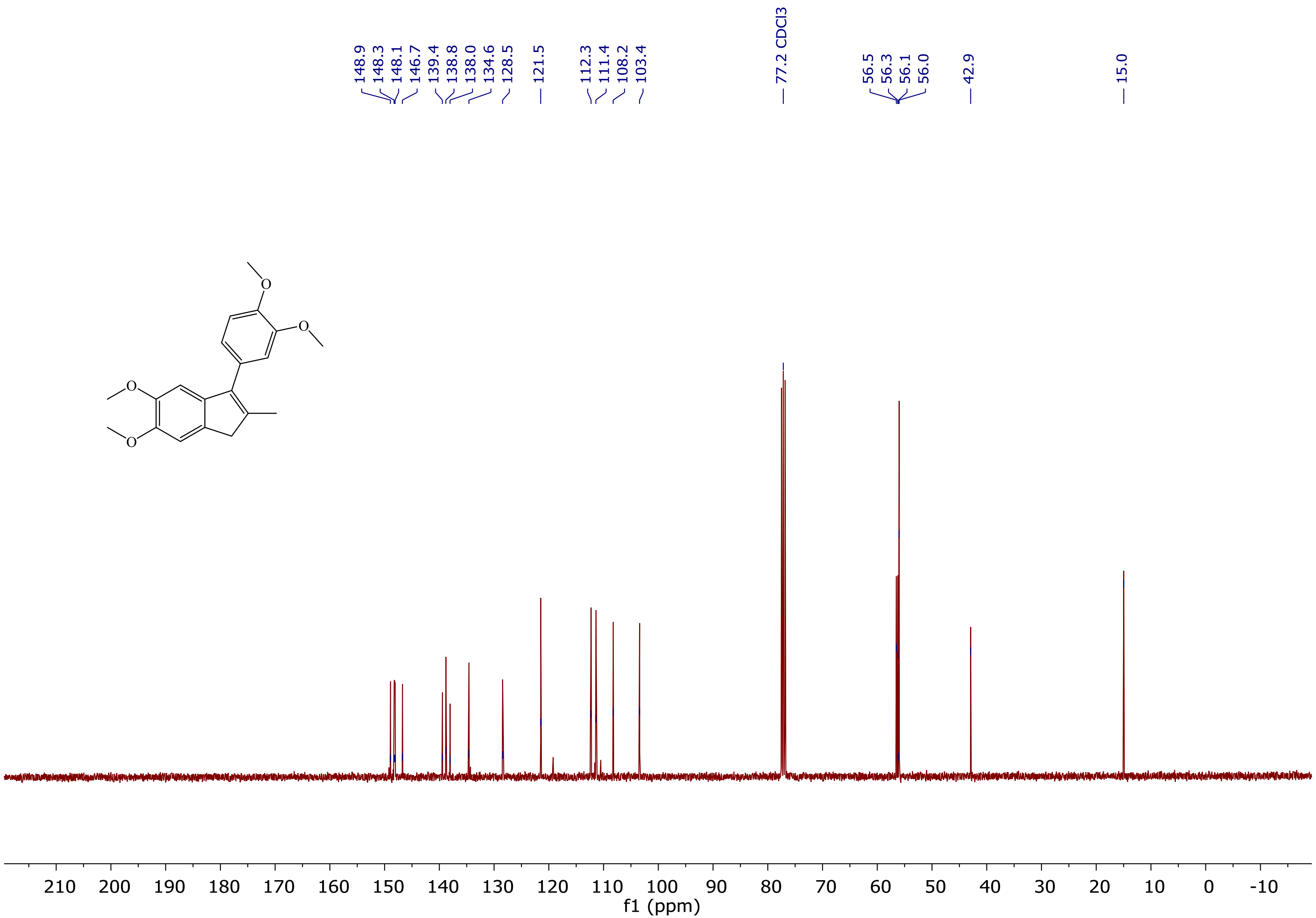


Figure S4.32. $^{13}C\ \{^{1}H\}$ **NMR (101MHz,** $CDCl_3$**) of 3-(3,4-dimethoxyphenyl)-5,6-dimethoxy-2-methyl-1H-indene (1r)**

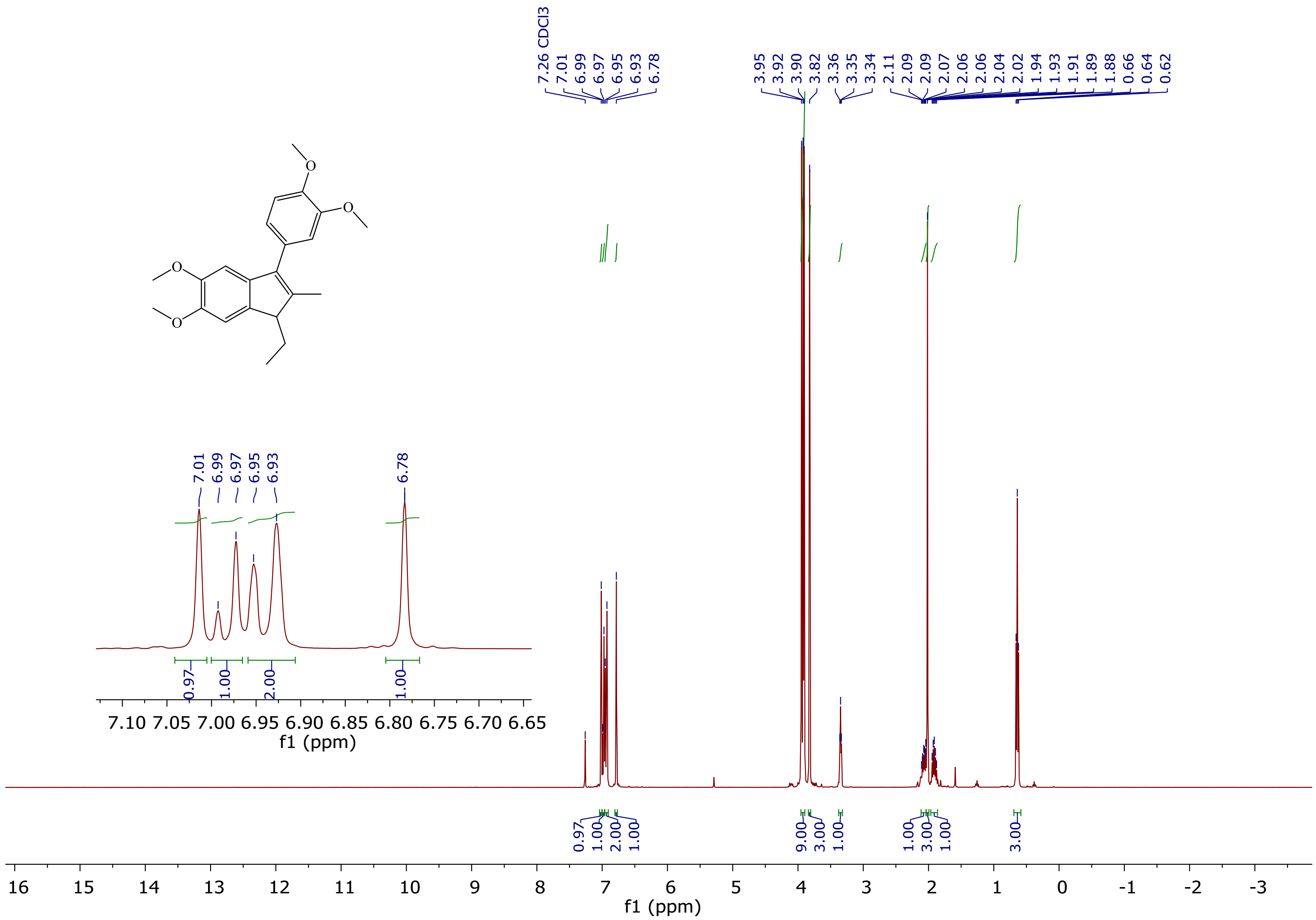


Figure S4.33. ^{1}H NMR (400MHz, $CDCl_3$) of 3-(3,4-dimethoxyphenyl)-1-ethyl-5,6-dimethoxy-2-methyl-1H-indene (1s)

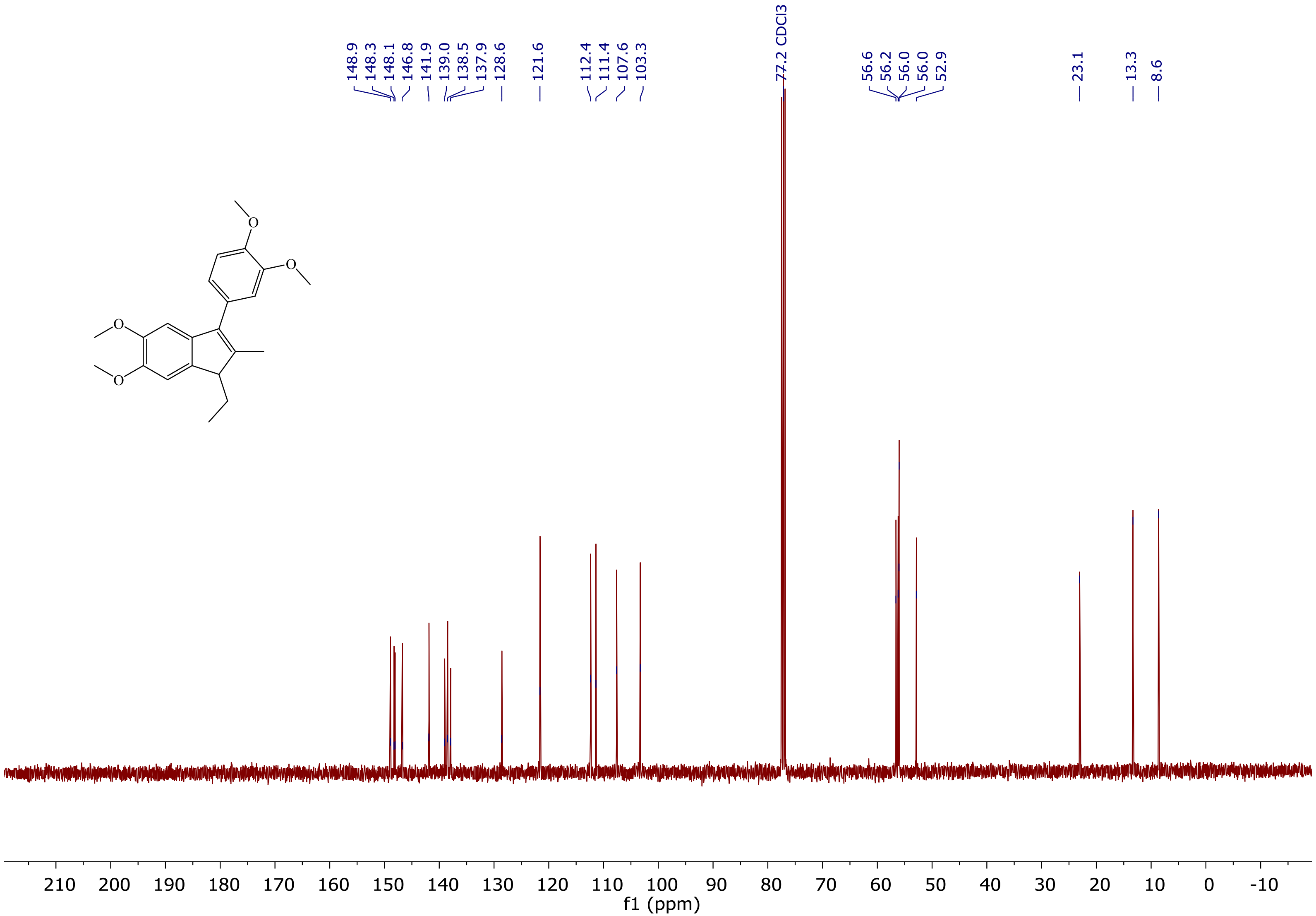


Figure S4.34. $^{13}C\{^1H\}$ **NMR (101MHz,** $CDCl_3$**) of 3-(3,4-dimethoxyphenyl)-1-ethyl-5,6-dimethoxy-2-methyl-1H-indene (1s)**

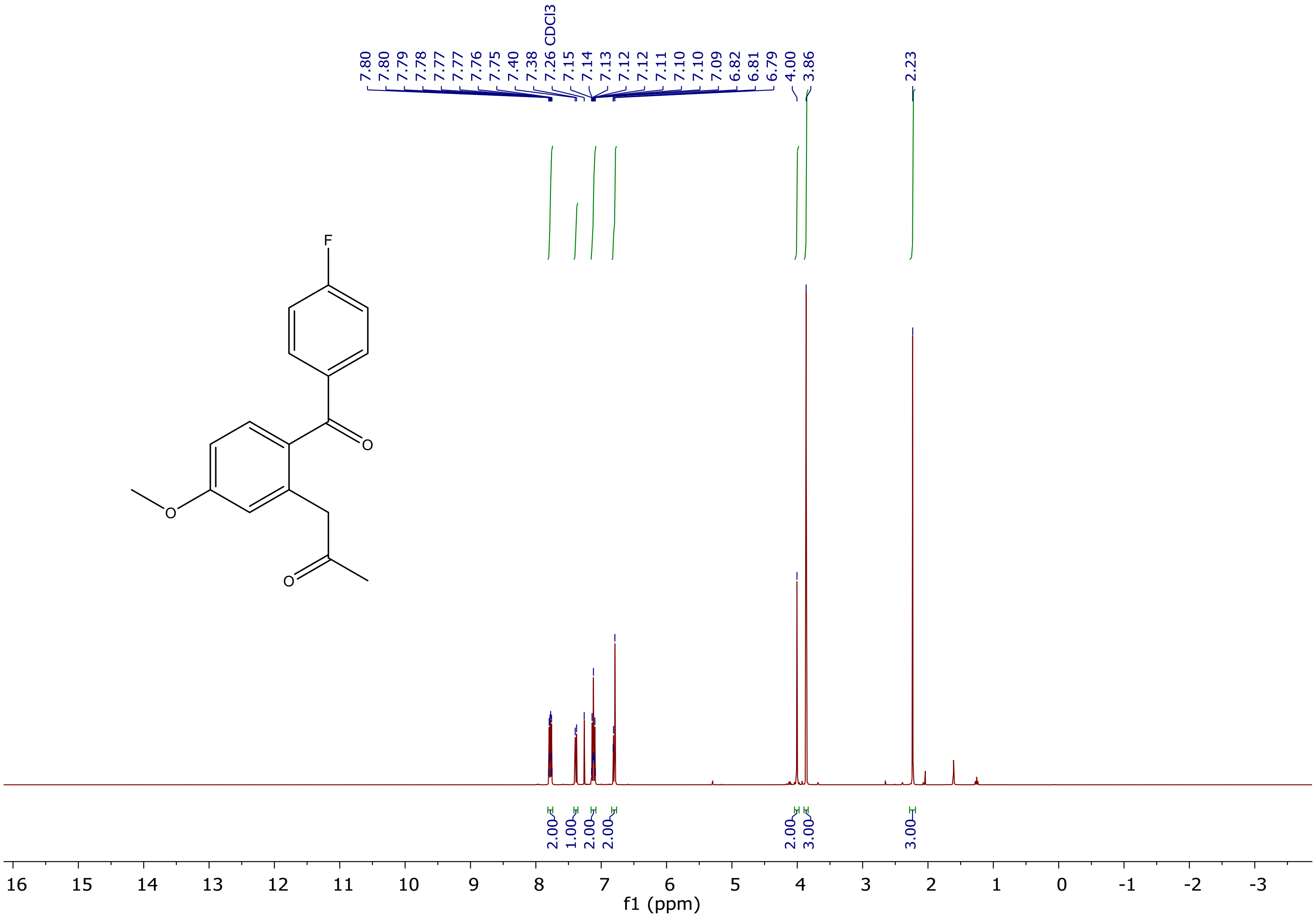


Figure S4.35. ^{1}H NMR (400MHz, $CDCl_3$) of 1-(2-(4-fluorobenzoyl)-5-methoxyphenyl)propan-2-one (2a)

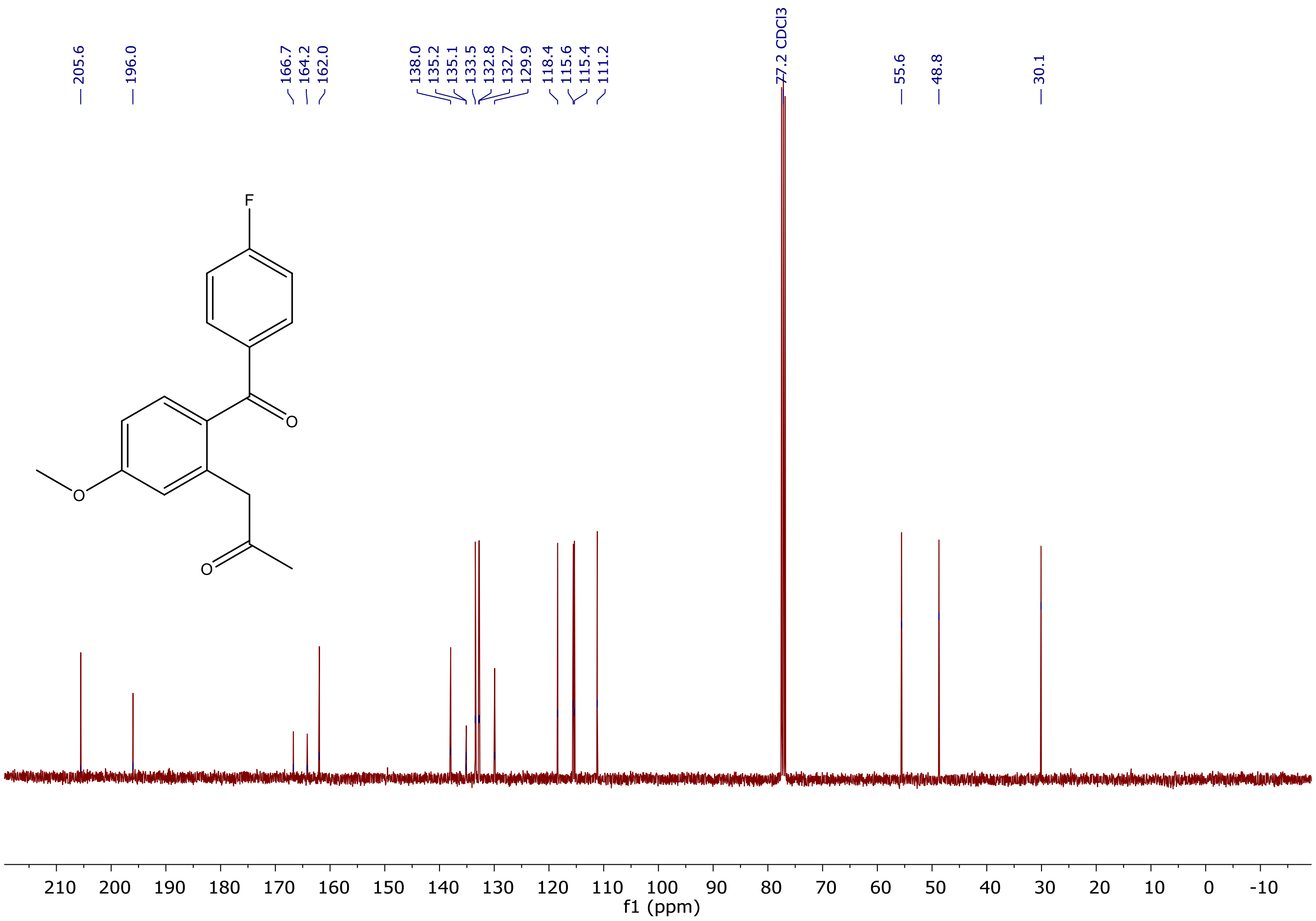


Figure S4.37. ^{13}C {^{1}H} NMR (101MHz, $CDCl_3$) of 1-(2-(4-fluorobenzoyl)-5-methoxyphenyl)propan-2-one (2a)

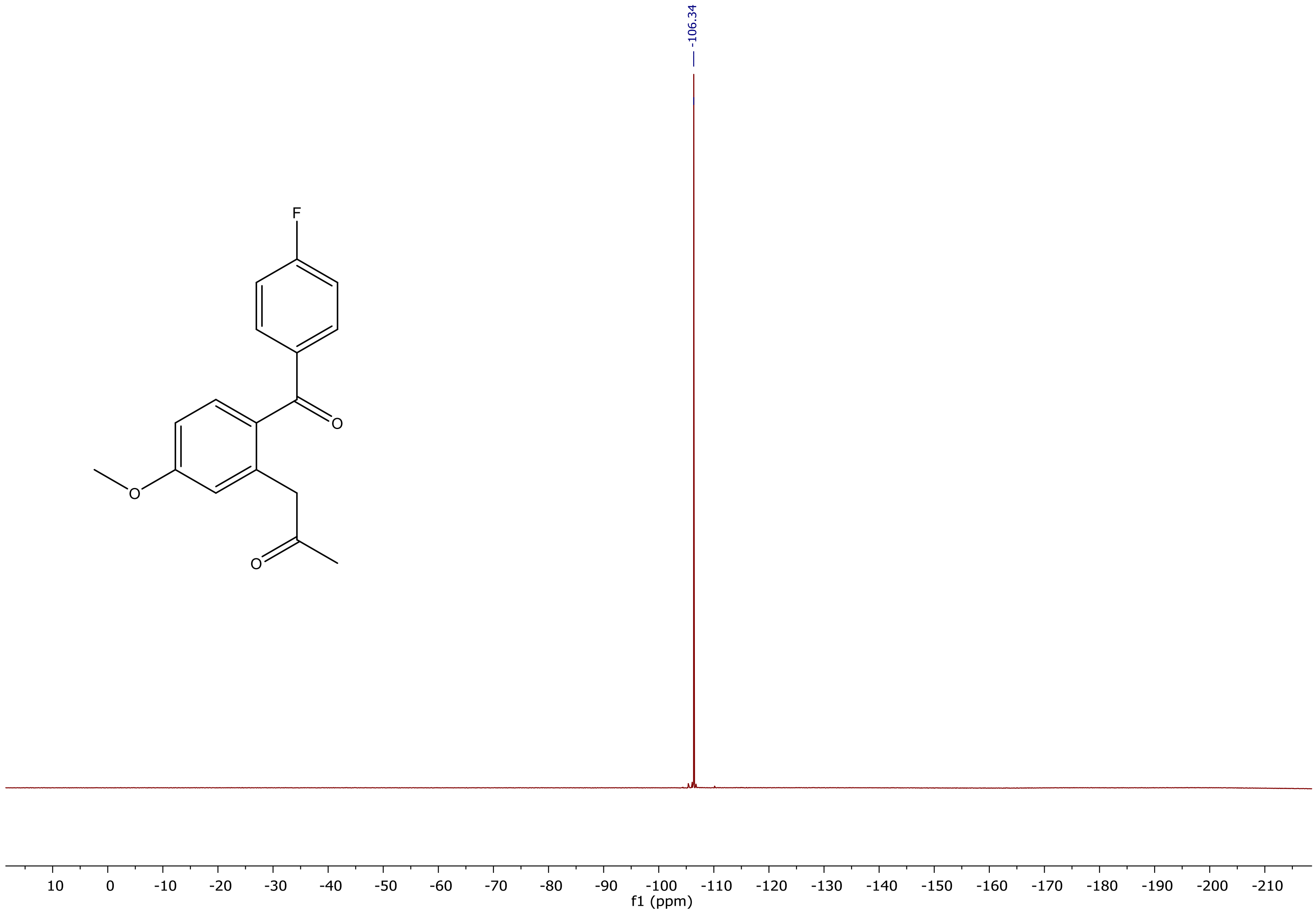


Figure S4.38. ^{19}**F NMR (376 MHz, CDCl**$_3$**) of 1-(2-(4-fluorobenzoyl)-5-methoxyphenyl)propan-2-one (2a)**

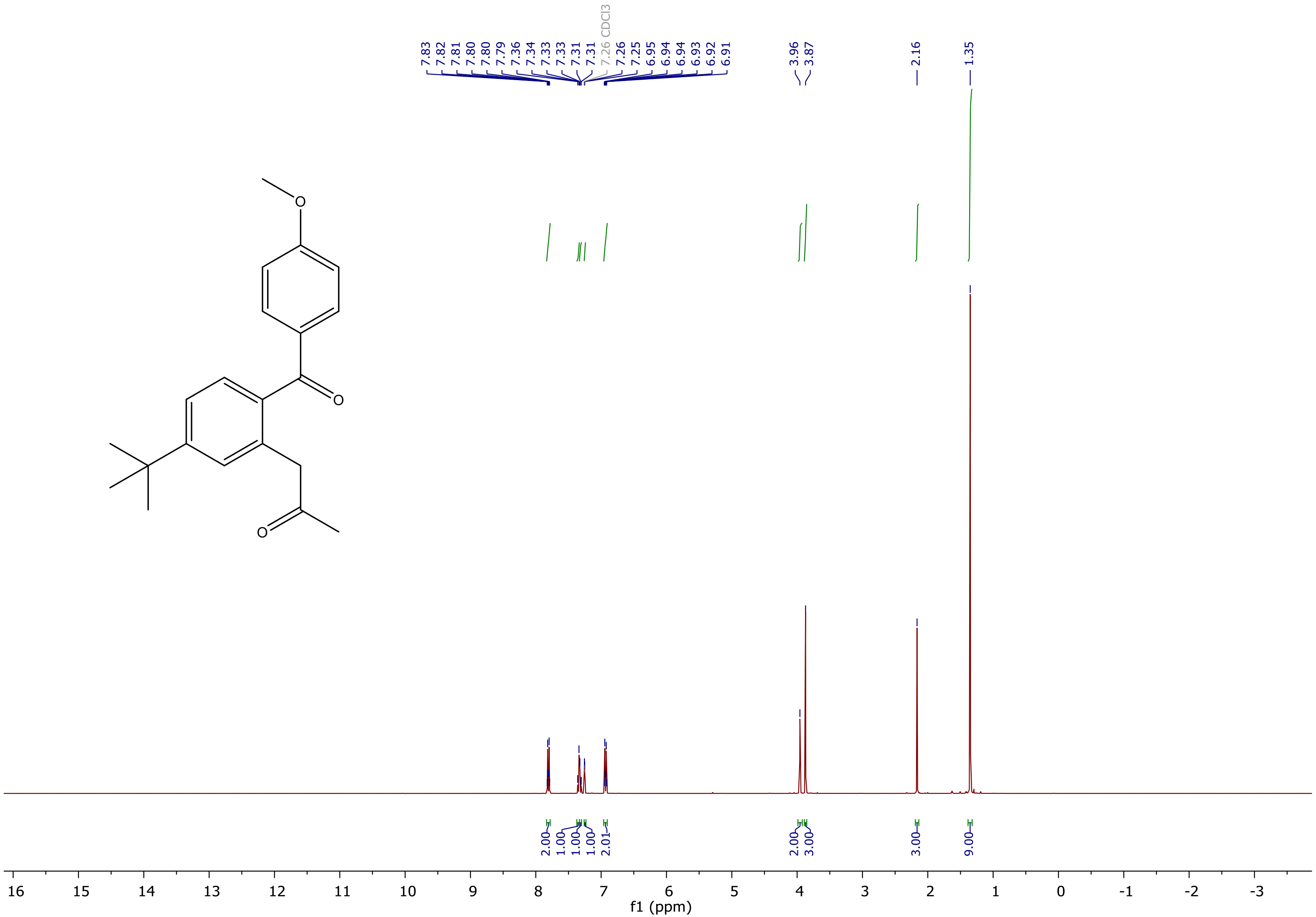


Figure S4.39. ^{1}H NMR (400MHz, $CDCl_3$) of 1-(5-tert-butyl-2-(4-methoxybenzoyl)phenyl)propan-2-one (2b)

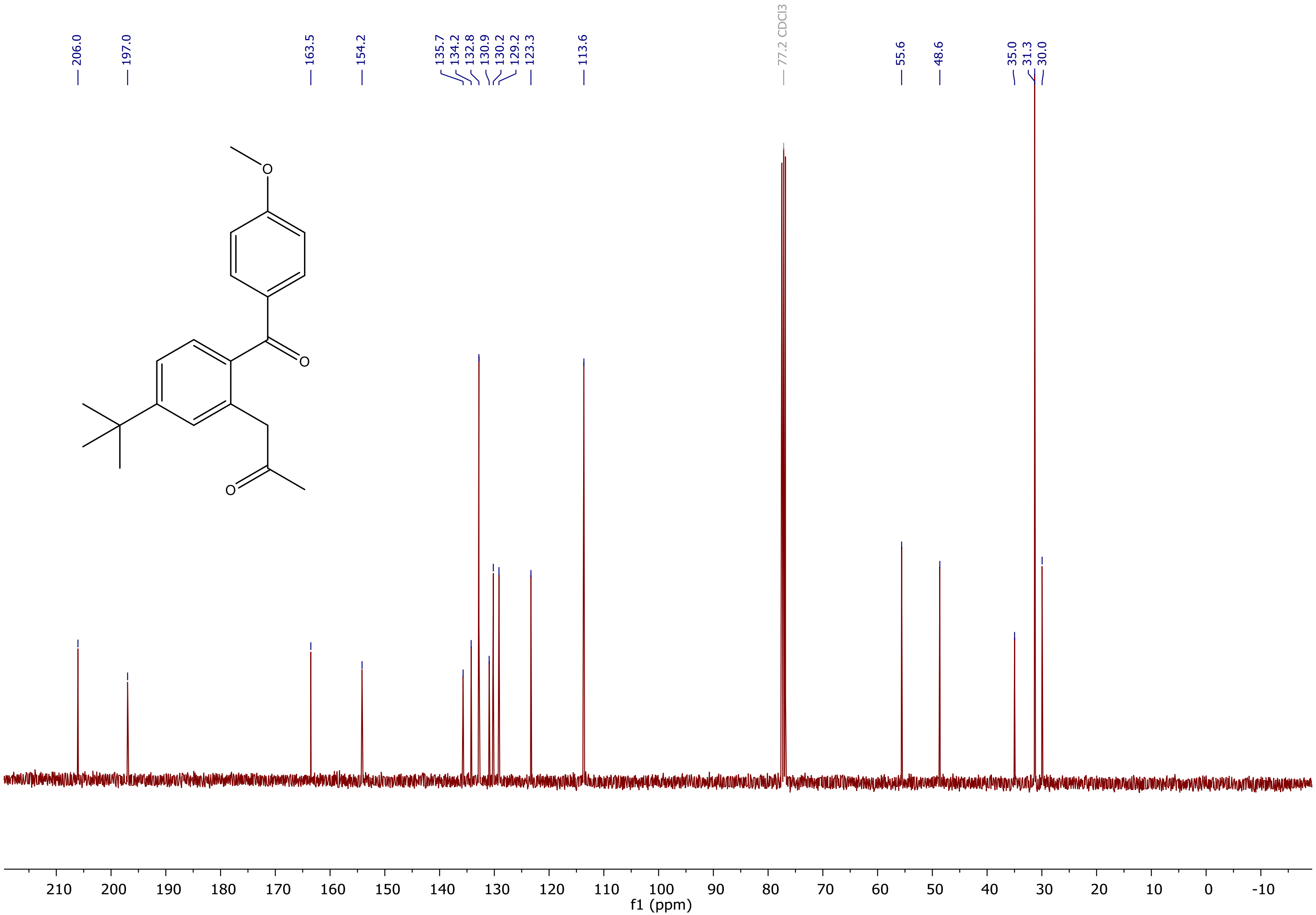


Figure S4.40. $^{13}C\ \{^1H\}$ **NMR (101MHz, $CDCl_3$) of 1-(5-tert-butyl-2-(4-methoxybenzoyl)phenyl)propan-2-one (2b)**

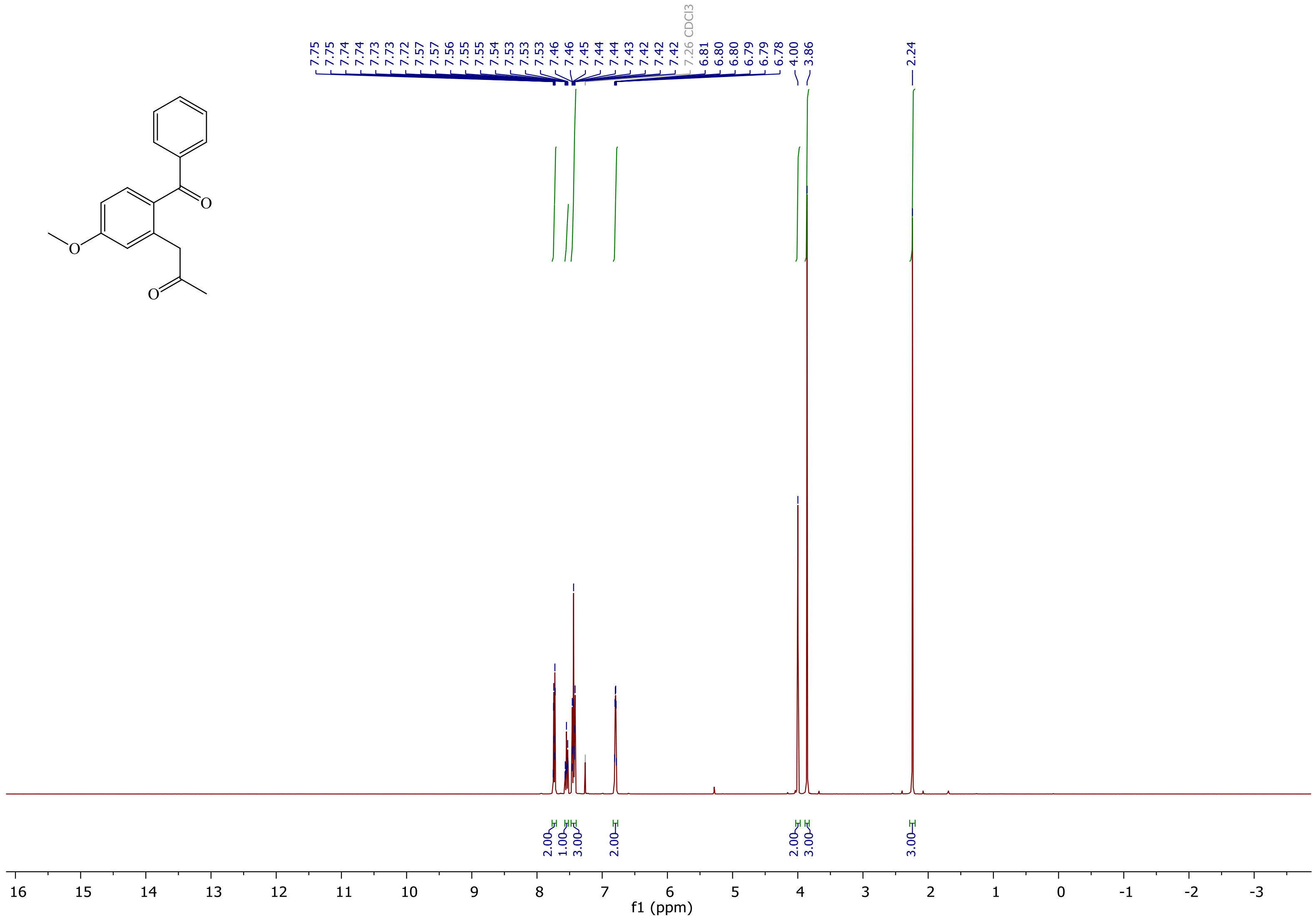


Figure S4.41. ^{1}H NMR (400MHz, $CDCl_3$) of 1-(2-benzoyl-5-methoxyphenyl)propan-2-one (2c)

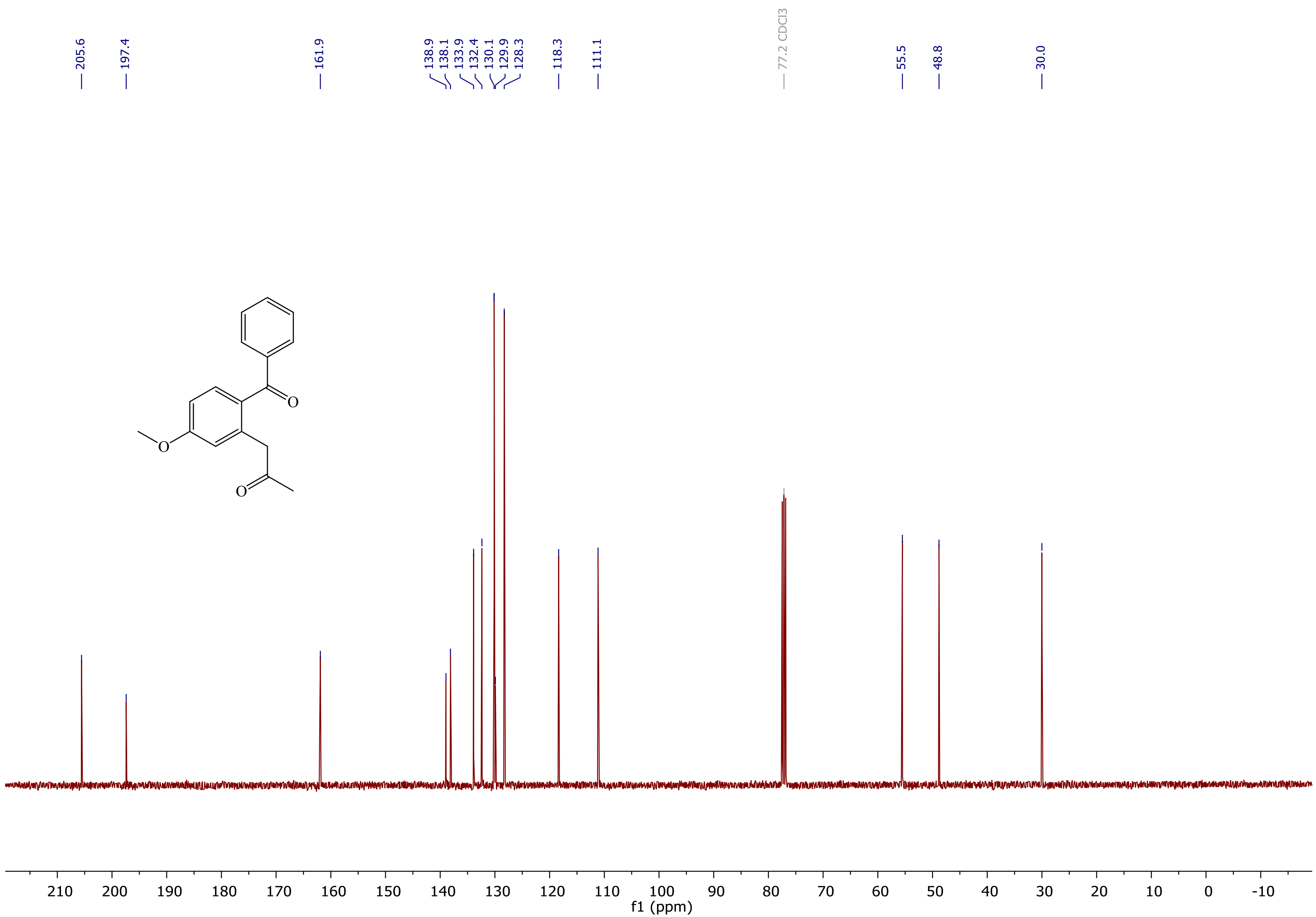


Figure S4.42. ^{13}**C {**^{1}**H} NMR (101MHz,** $CDCl_3$**) of 1-(2-benzoyl-5-methoxyphenyl)propan-2-one (2c)**

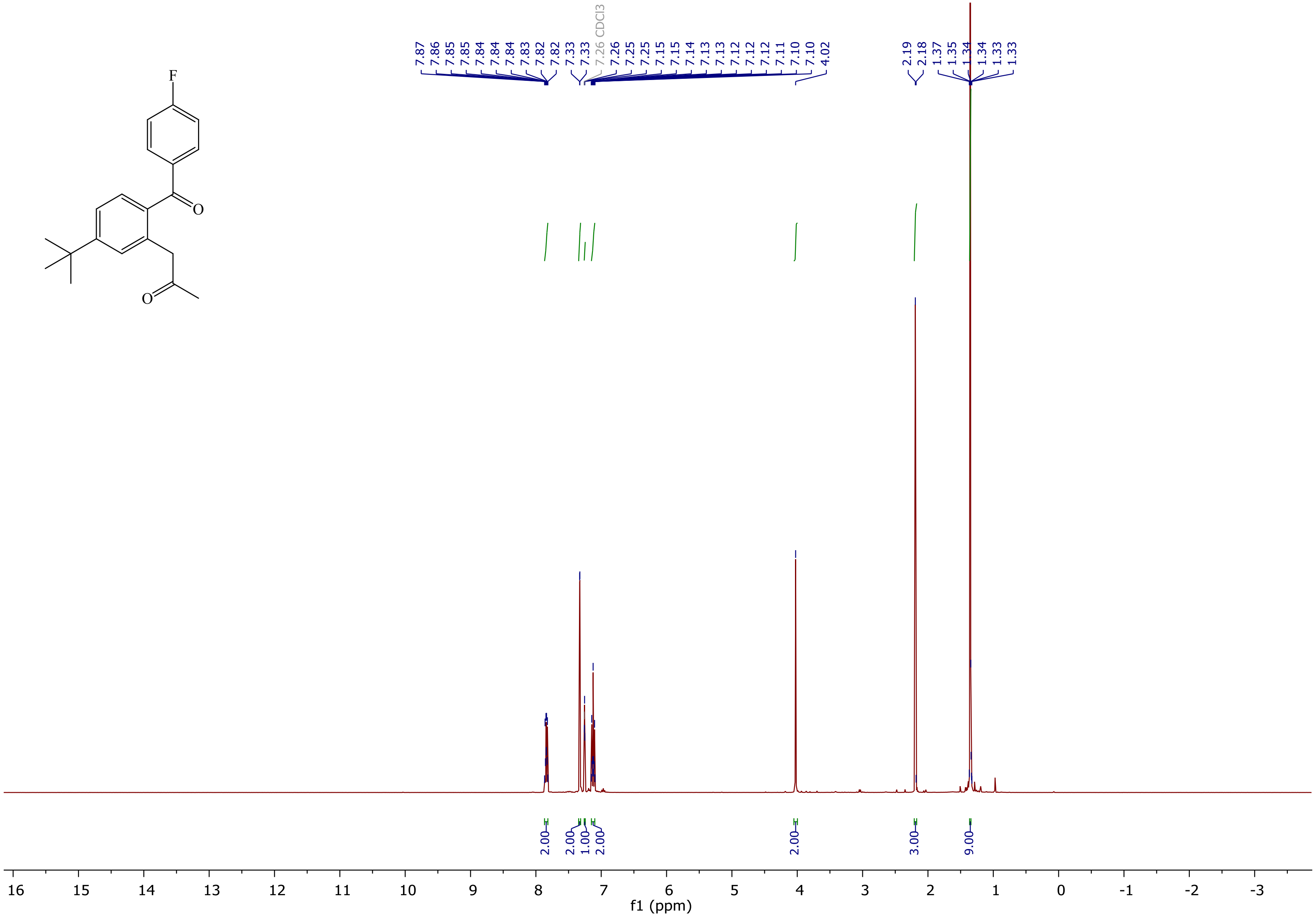


Figure S4.43. ^{1}H NMR (400MHz, $CDCl_3$) of 1-(5-tert-butyl-2-(4-fluorobenzoyl)phenyl)propan-2-one (2d)

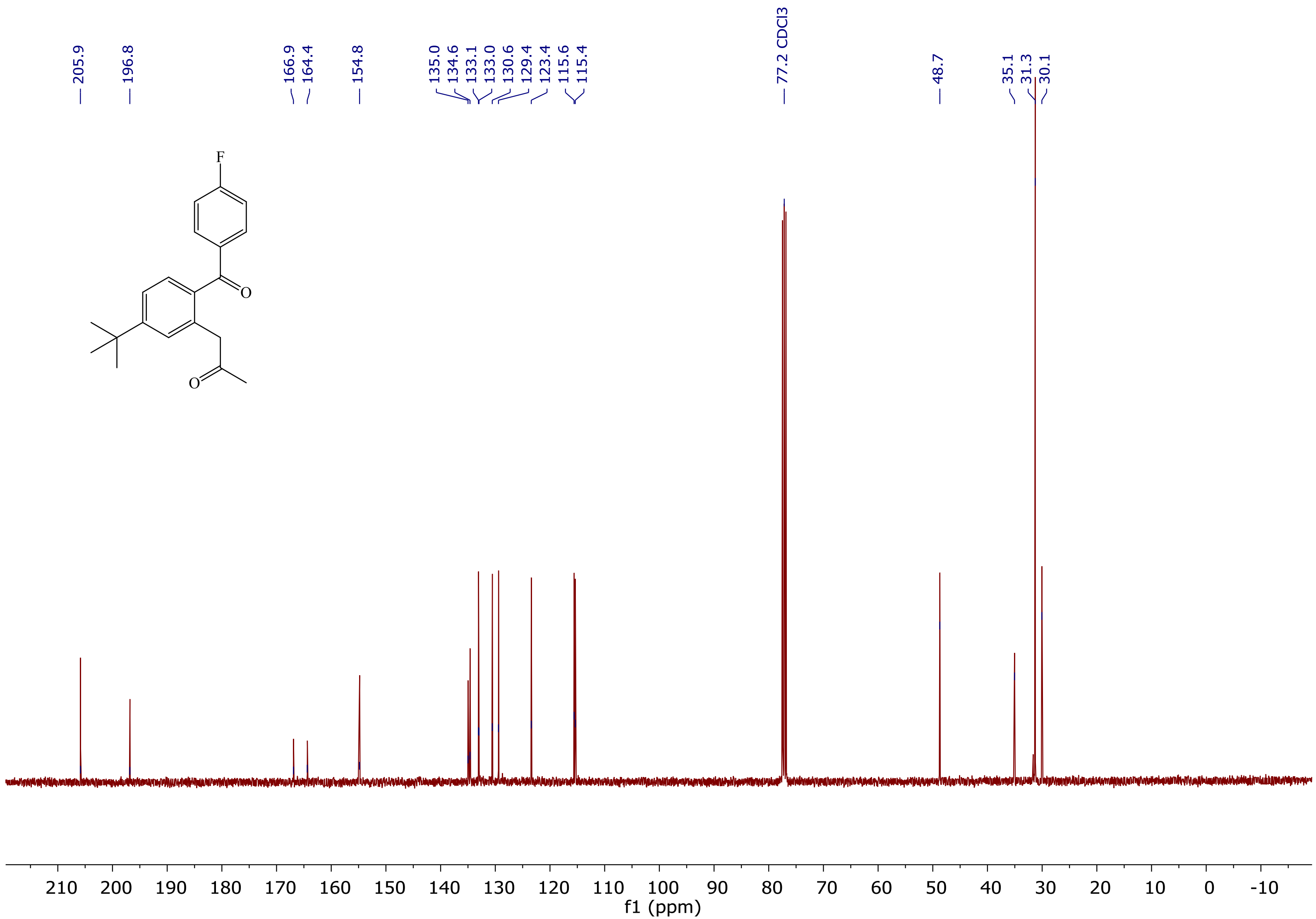


Figure S4.44. ^{13}C {^{1}H} NMR (101MHz, $CDCl_3$) of 1-(5-tert-butyl-2-(4-fluorobenzoyl)phenyl)propan-2-one (2d)

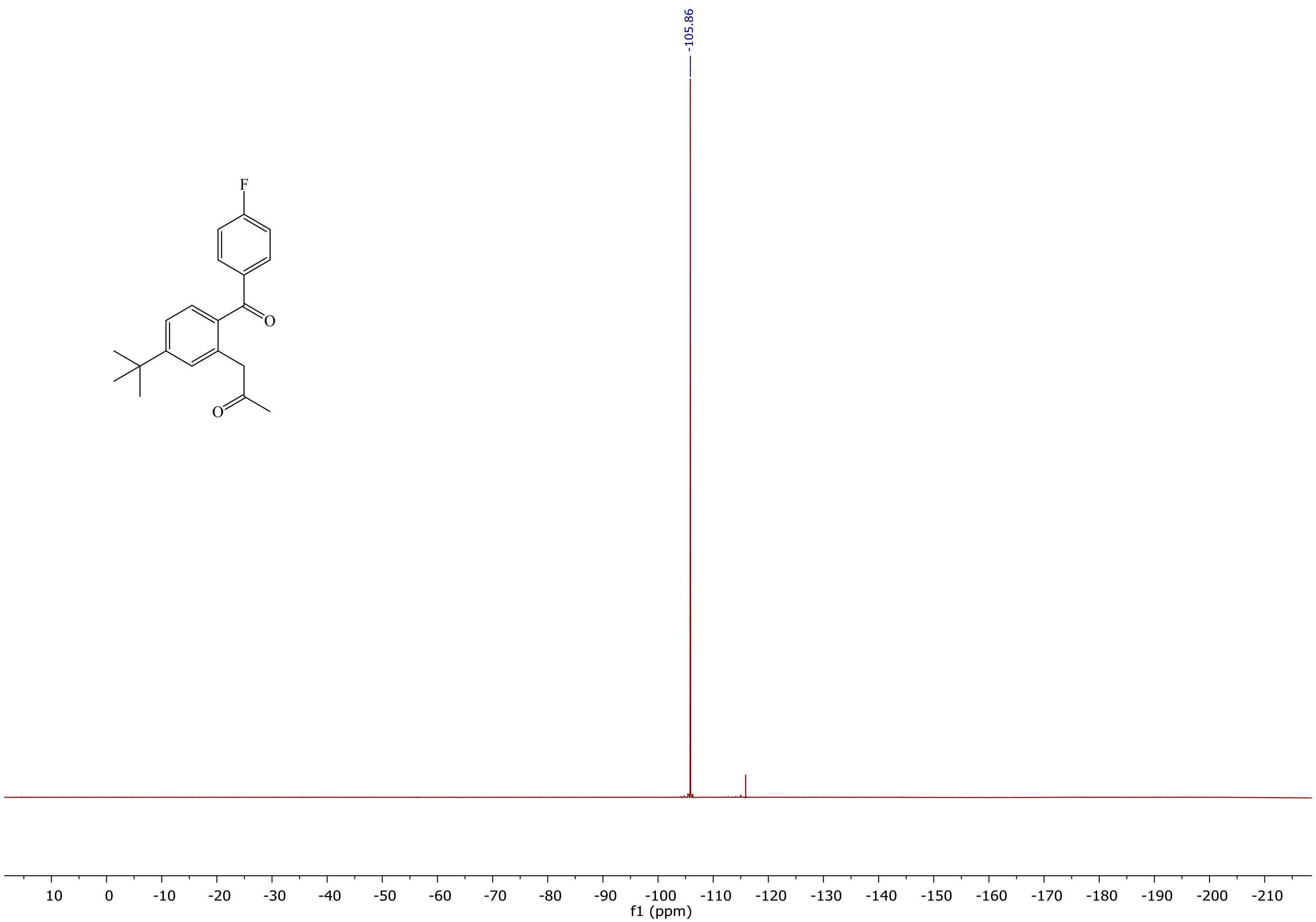


Figure S4.45. ^{19}F NMR (376 MHz, $CDCl_3$) of 1-(5-tert-butyl-2-(4-fluorobenzoyl)phenyl)propan-2-one (2d)

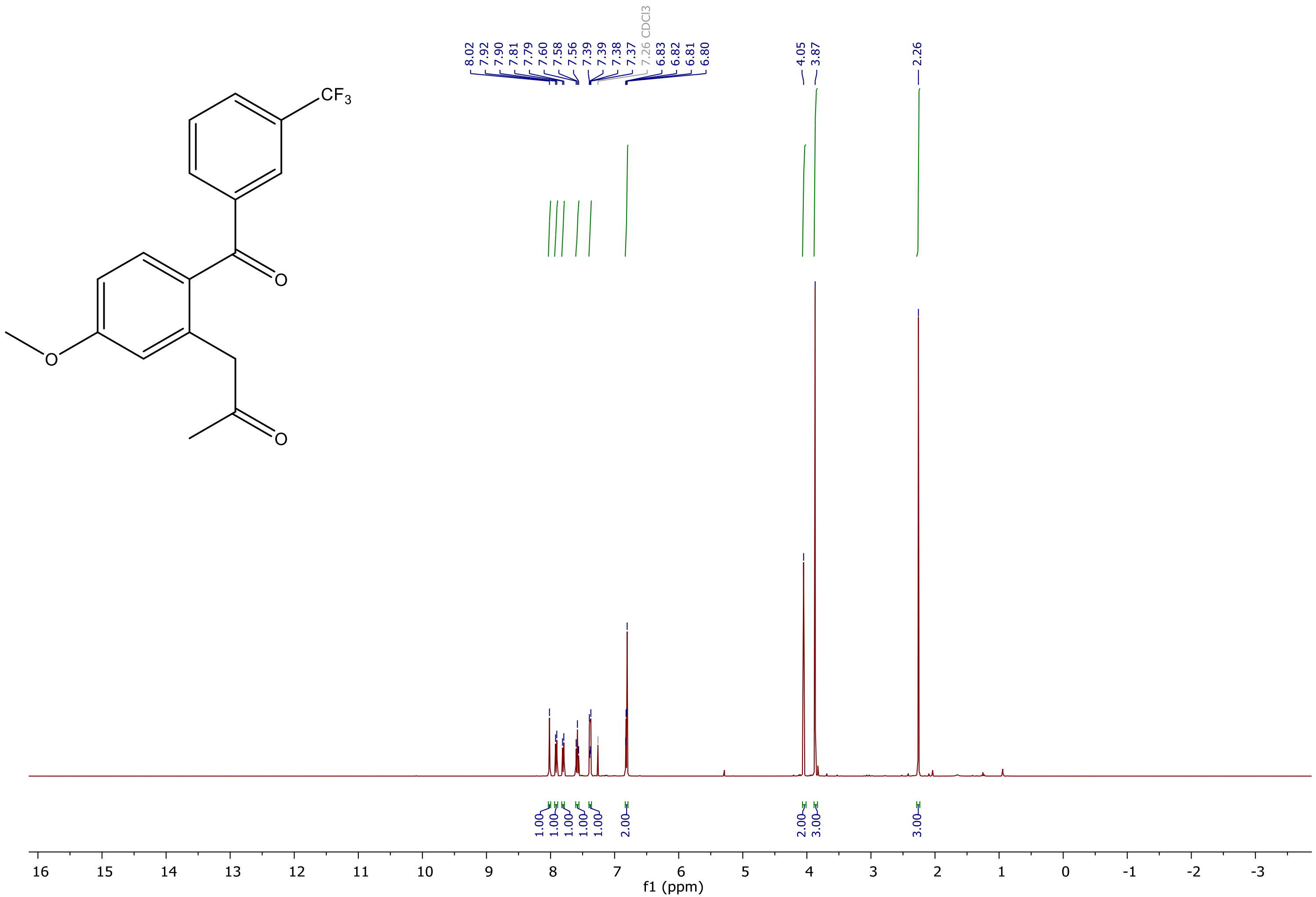


Figure S4.46. ^{1}H NMR (400MHz, $CDCl_3$) of 1-(5-methoxy-2-(3-(trifluoromethyl)benzoyl)phenyl)propan-2-one (2e)

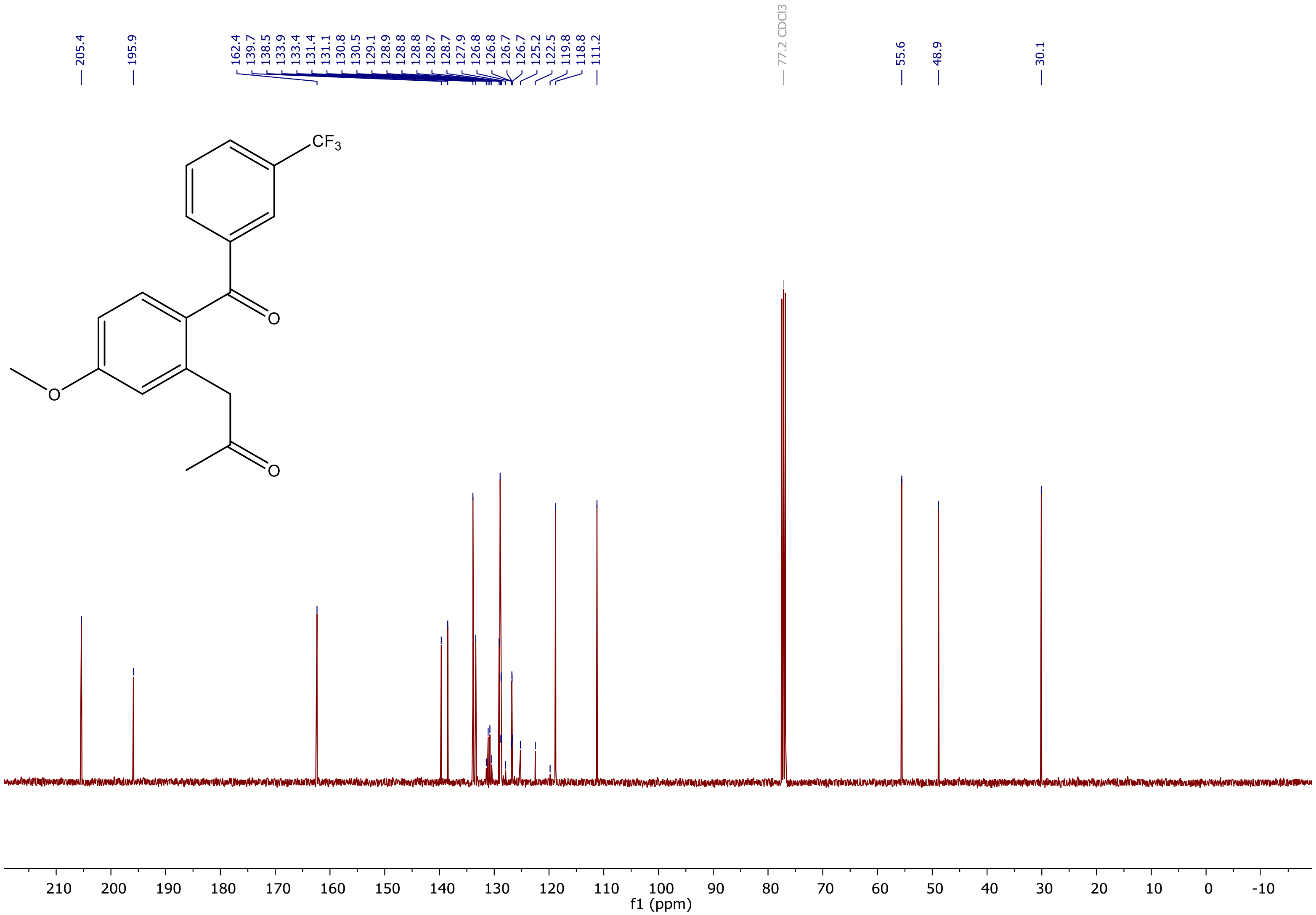


Figure S4.47. ^{13}C {^{1}H} **NMR (101MHz, $CDCl_3$) of 1-(5-methoxy-2-(3-(trifluoromethyl)benzoyl)phenyl)propan-2-one (2e)**

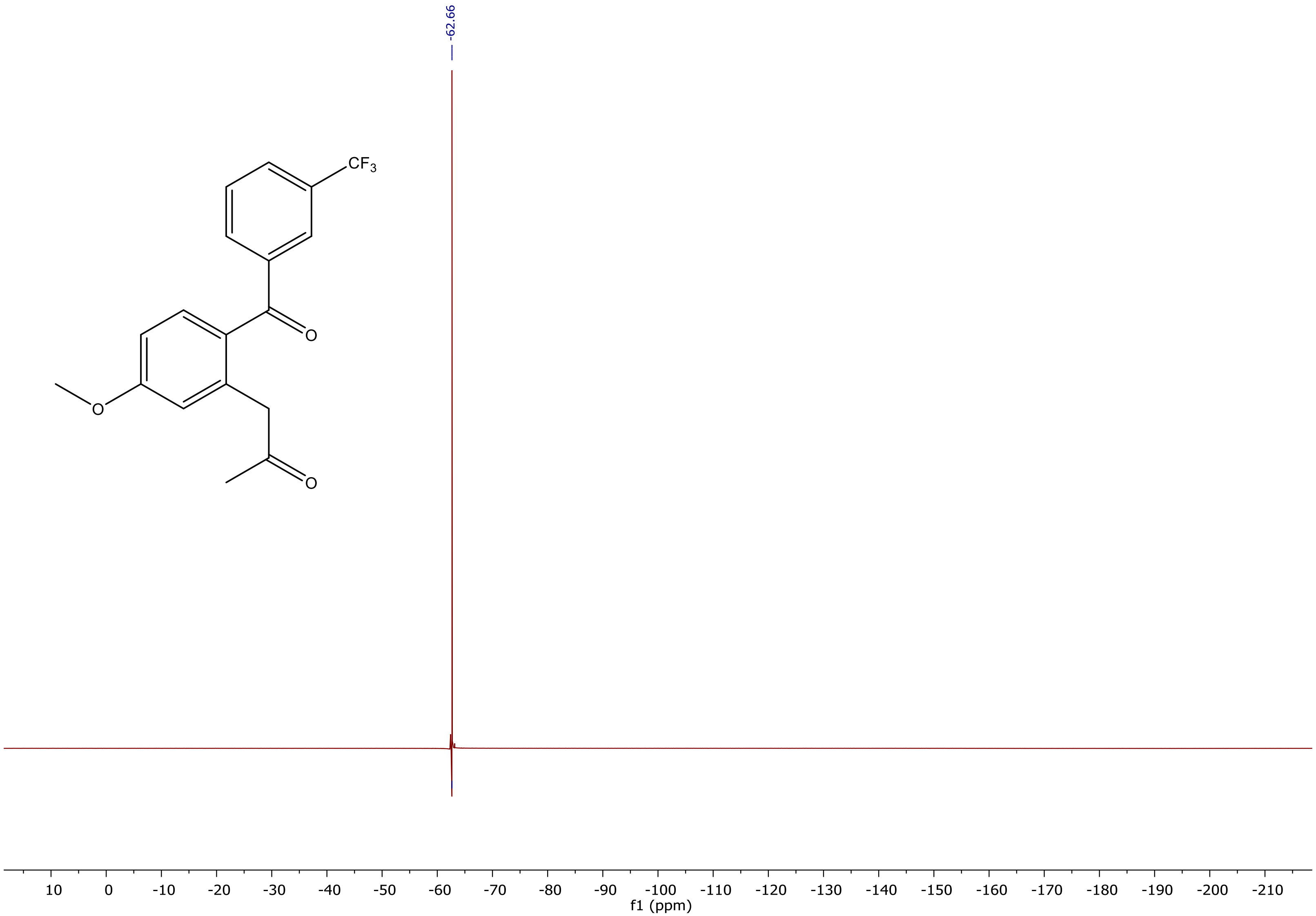


Figure S4.48. [19]F NMR (376 MHz, $CDCl_3$) of 1-(5-methoxy-2-(3-(trifluoromethyl)benzoyl)phenyl)propan-2-one (2e)

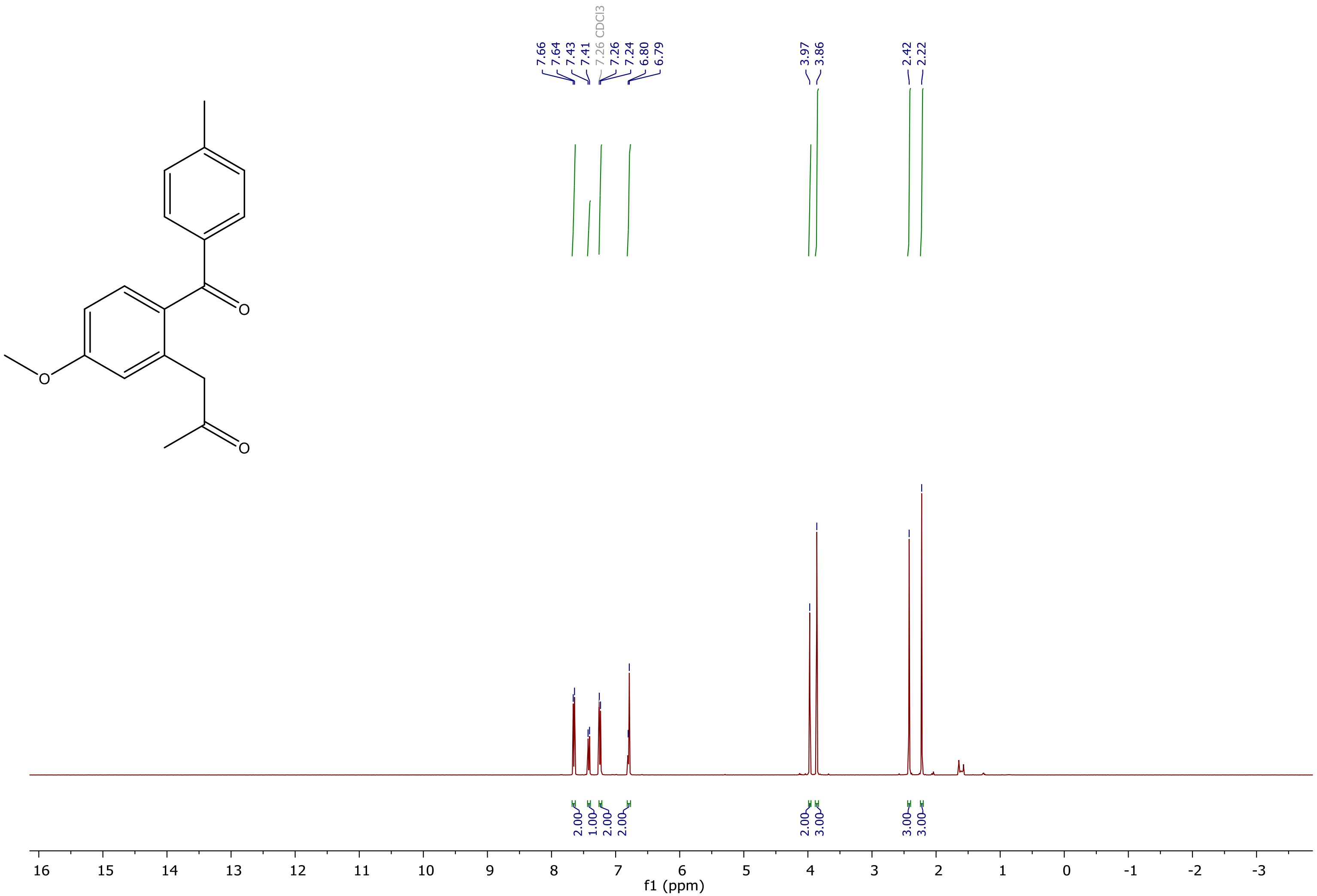


Figure S4.49. **[1]H NMR (400MHz, $CDCl_3$) of 1-(5-methoxy-2-(4-methylbenzoyl)phenyl)propan-2-one (2f)**

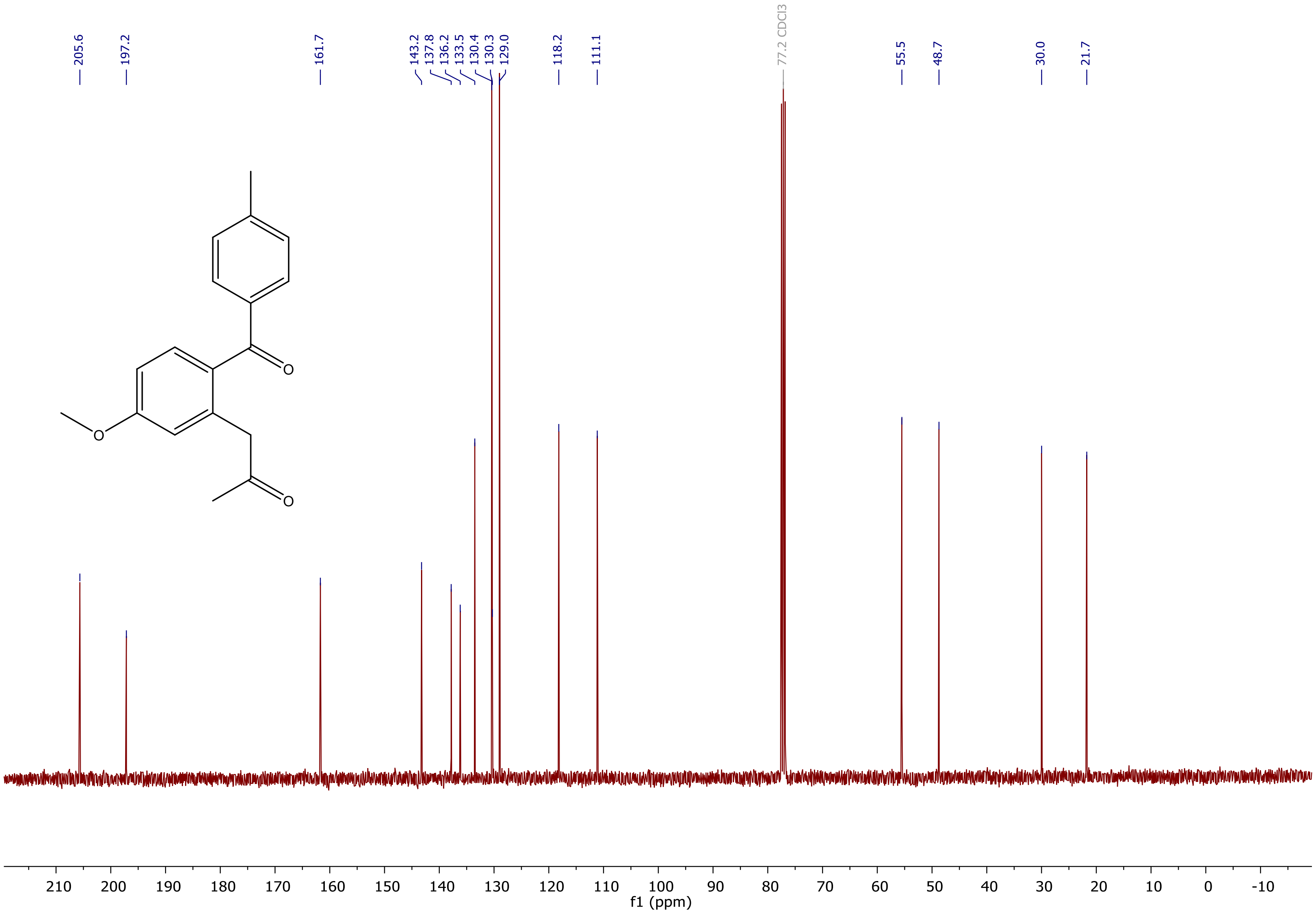


Figure S4.50. $^{13}C\{^1H\}$ **NMR (101MHz,** $CDCl_3$**) of 1-(5-methoxy-2-(4-methylbenzoyl)phenyl)propan-2-one (2f)**

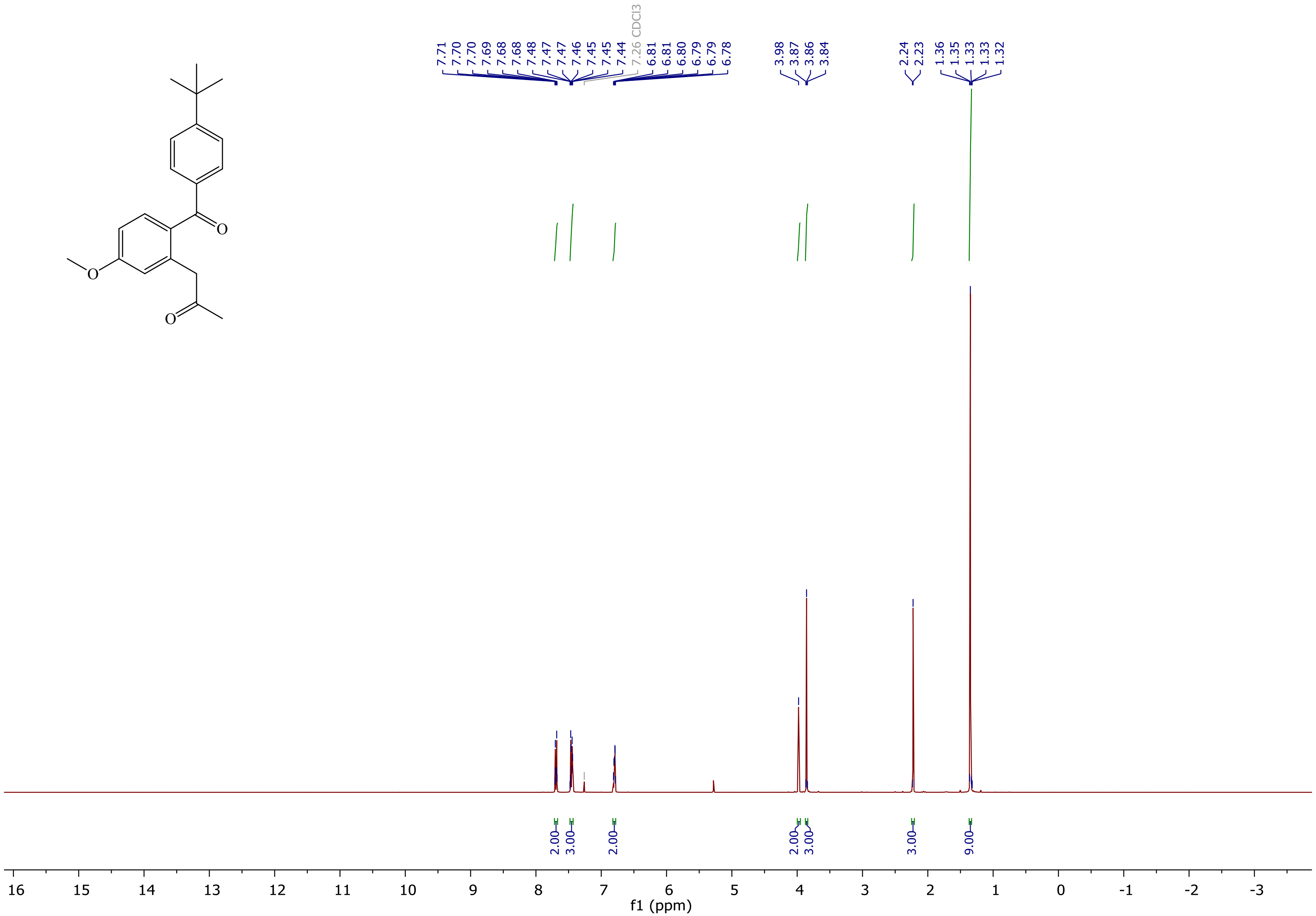


Figure S4.51. ^{1}**H NMR (400MHz, CDCl$_3$) of 1-(2-(4-tert-butylbenzoyl)-5-methoxyphenyl)propan-2-one (2g)**

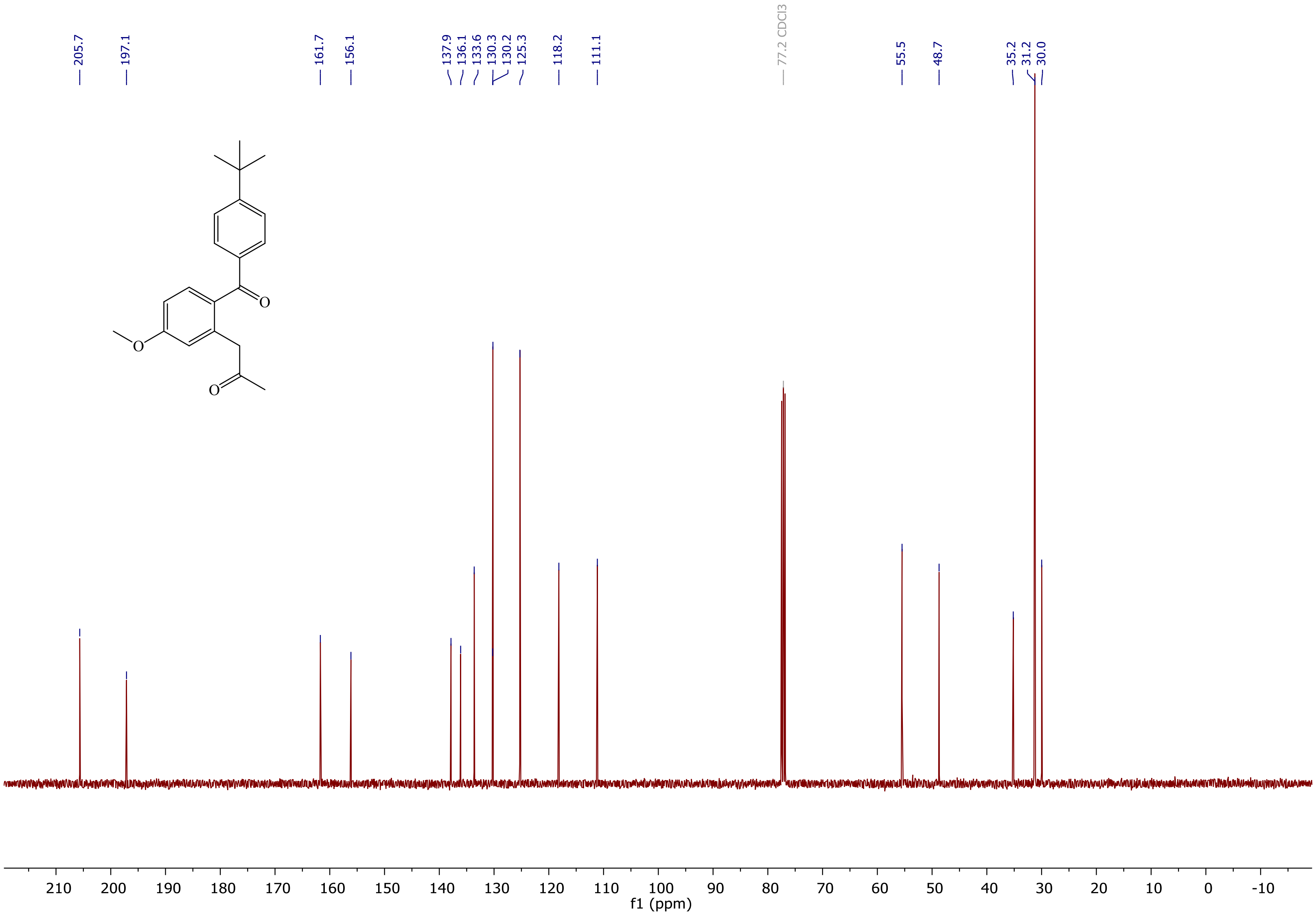


Figure S4.52. $^{13}C\{^1H\}$ **NMR (101MHz, $CDCl_3$) of 1-(2-(4-tert-butylbenzoyl)-5-methoxyphenyl)propan-2-one (2g)**

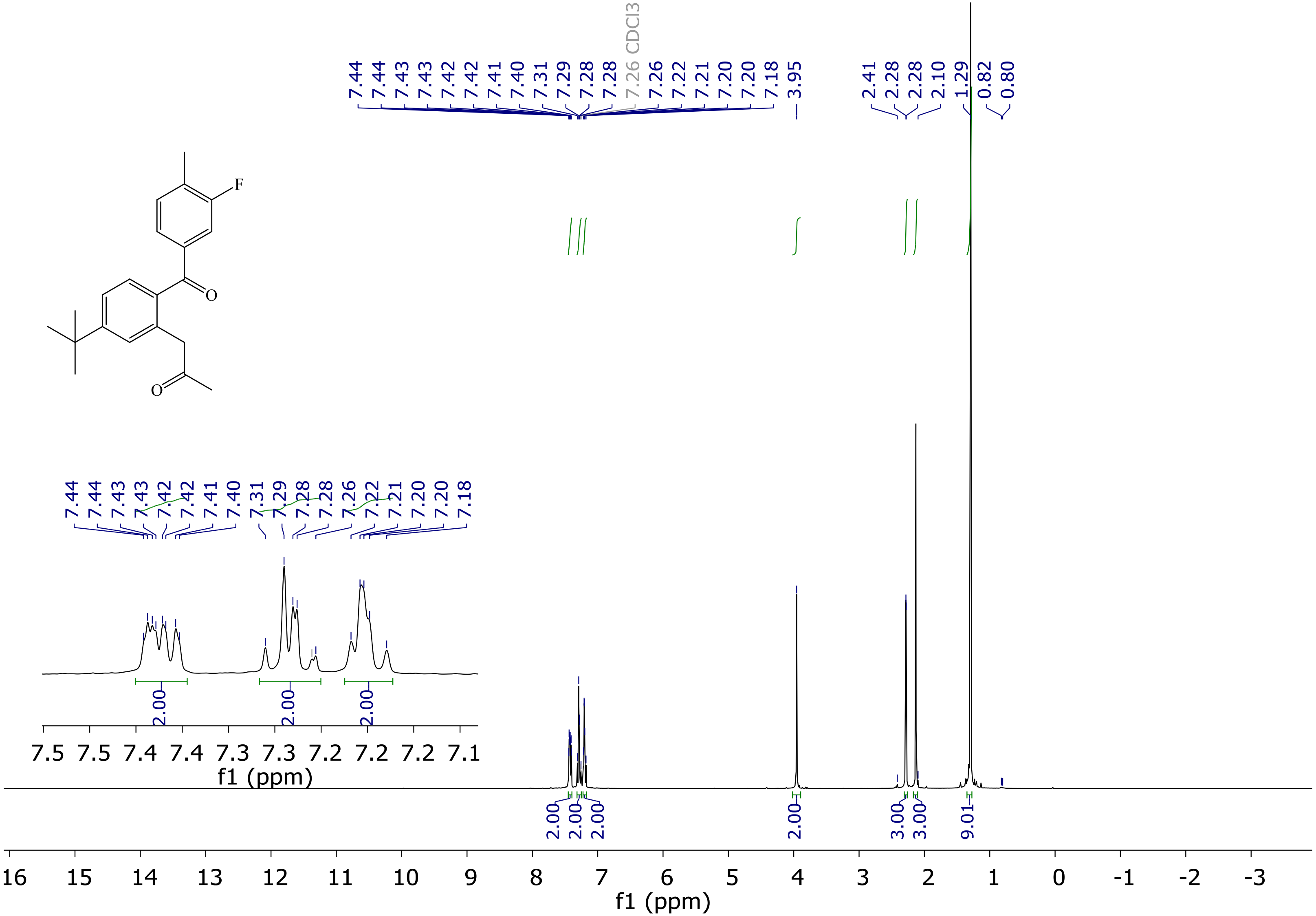


Figure S4.53. ^{1}H NMR (400MHz, $CDCl_3$) of 1-(5-tert-butyl-2-(3-fluoro-4-methylbenzoyl)phenyl)propan-2-one (2h)

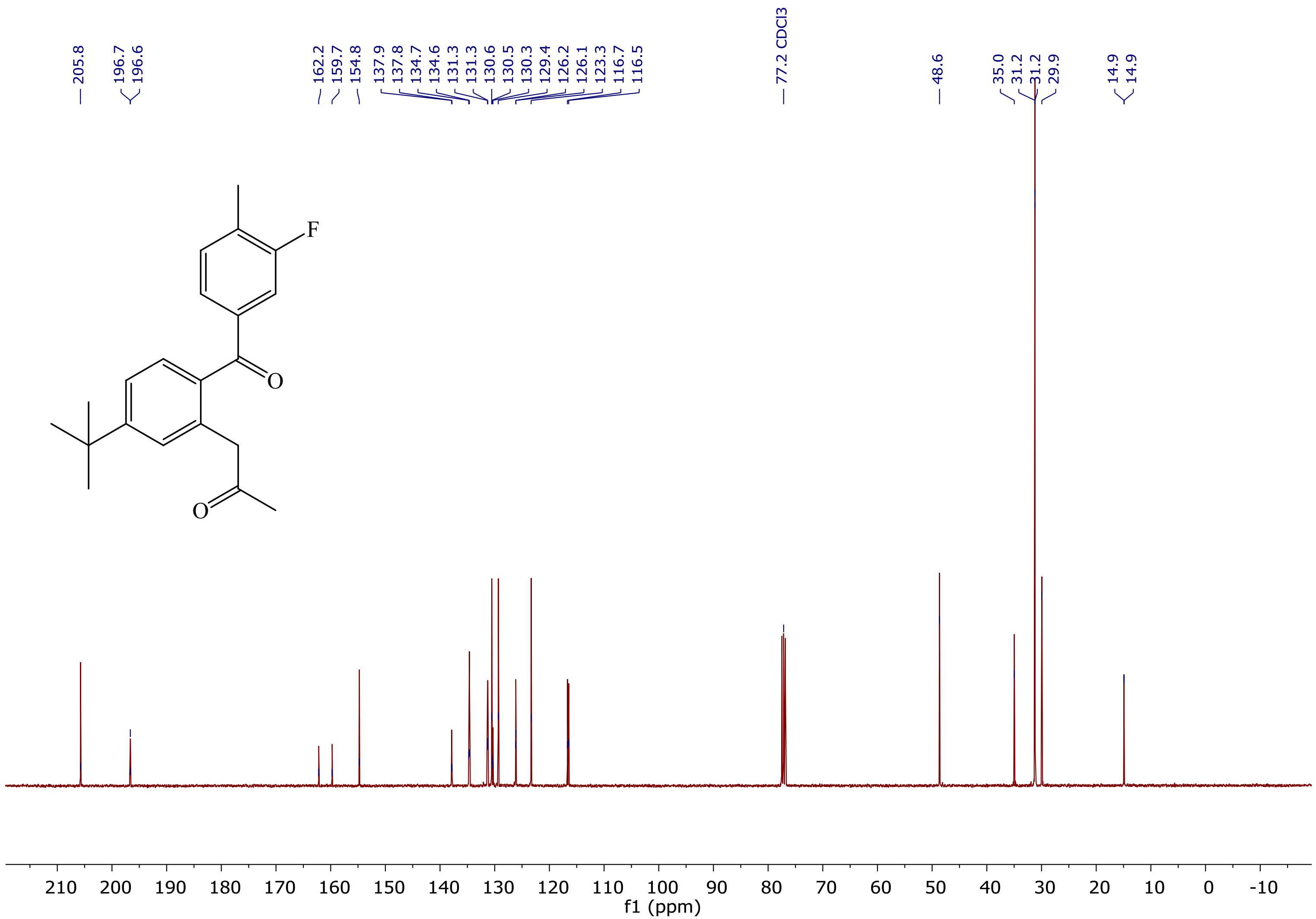


Figure S4.54. $^{13}C\{^1H\}$ **NMR (101MHz,** $CDCl_3$**) of 1-(5-tert-butyl-2-(3-fluoro-4-methylbenzoyl)phenyl)propan-2-one (2h)**

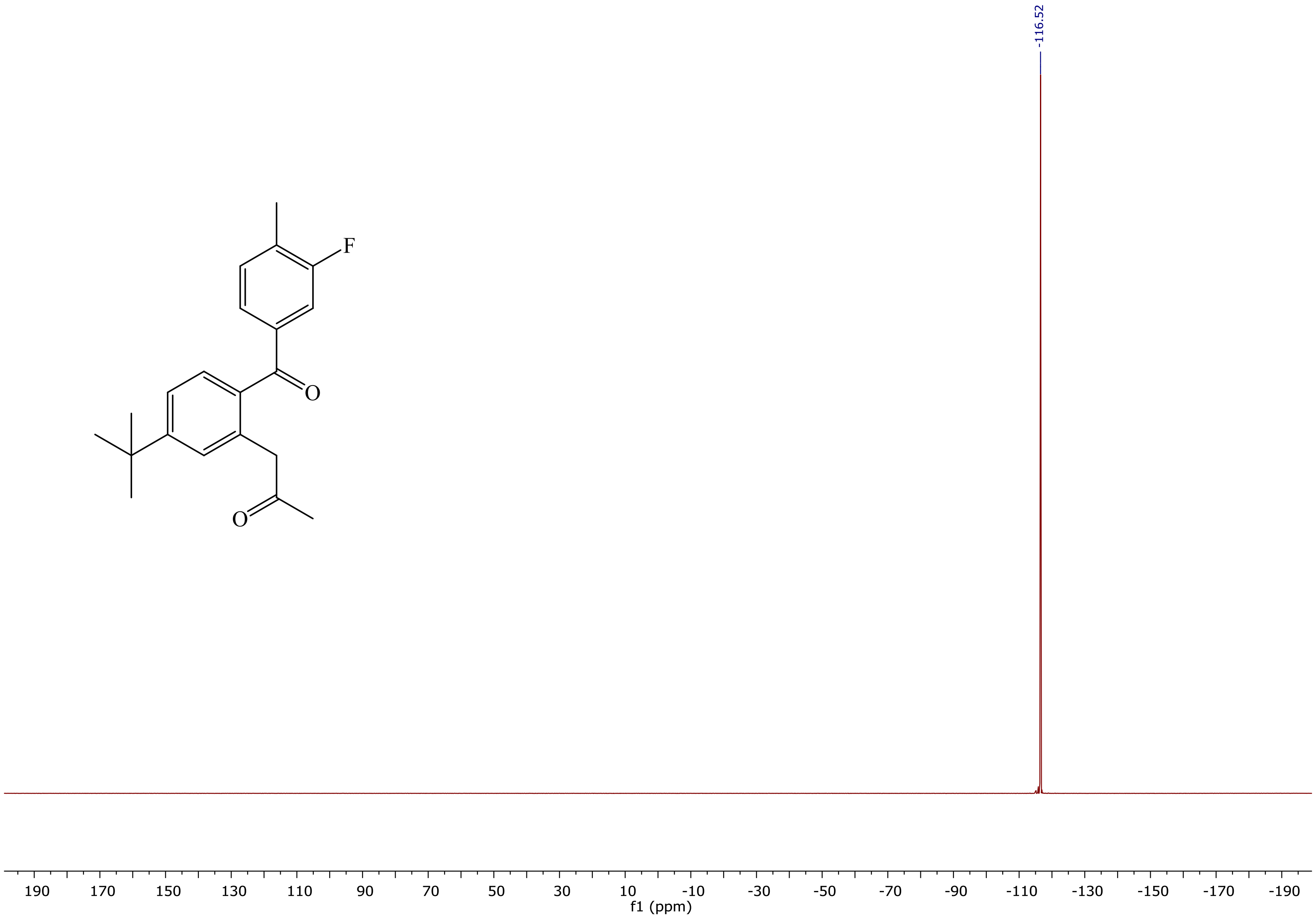


Figure S4.55. ^{19}F NMR (376 MHz, CDCl$_3$) of 1-(5-tert-butyl-2-(3-fluoro-4-methylbenzoyl)phenyl)propan-2-one (2h)

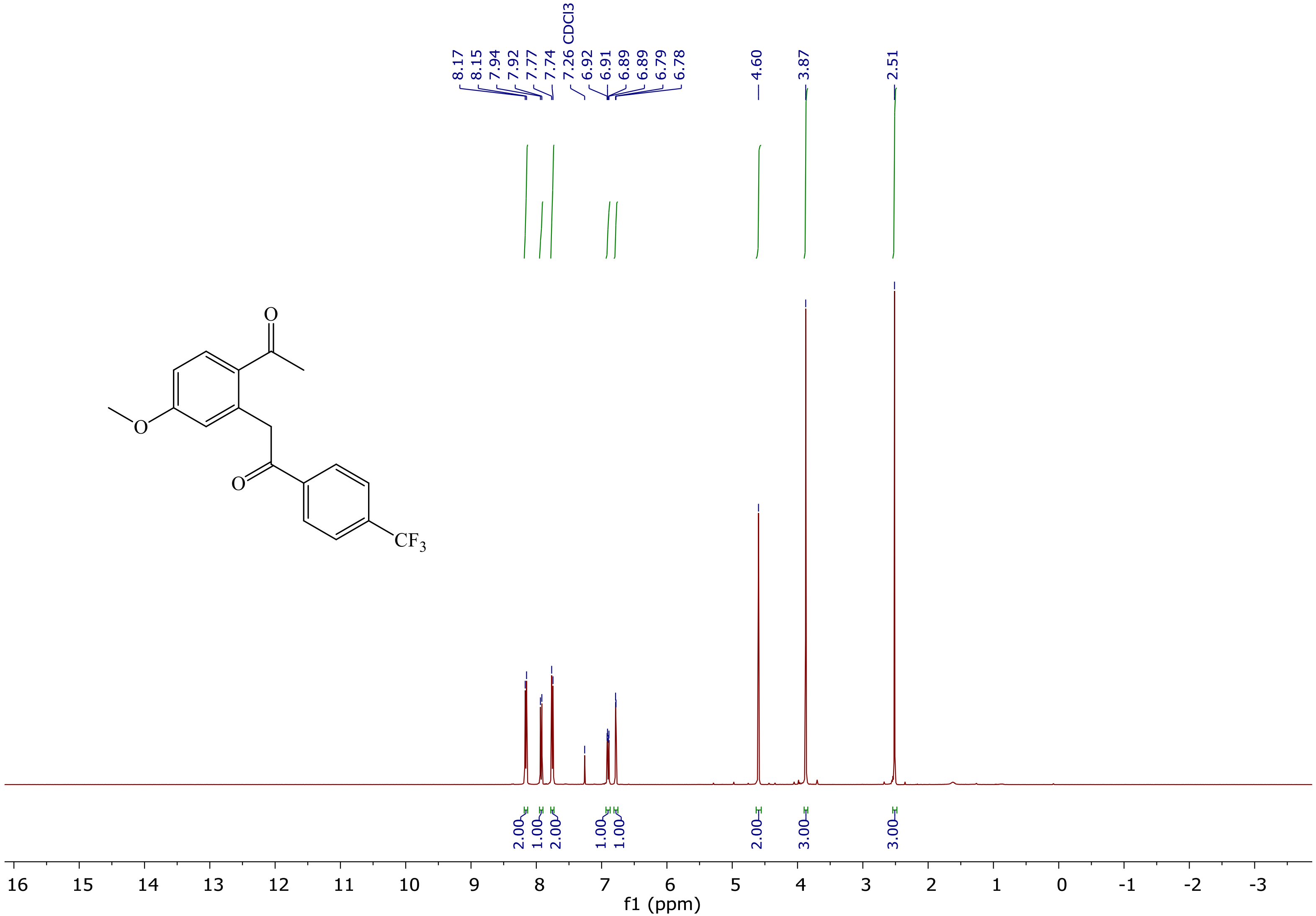


Figure S4.56. [1]H NMR (400MHz, $CDCl_3$) of 2-(2-acetyl-5-methoxyphenyl)-1-(4-(trifluoromethyl)phenyl)ethanone (2i)

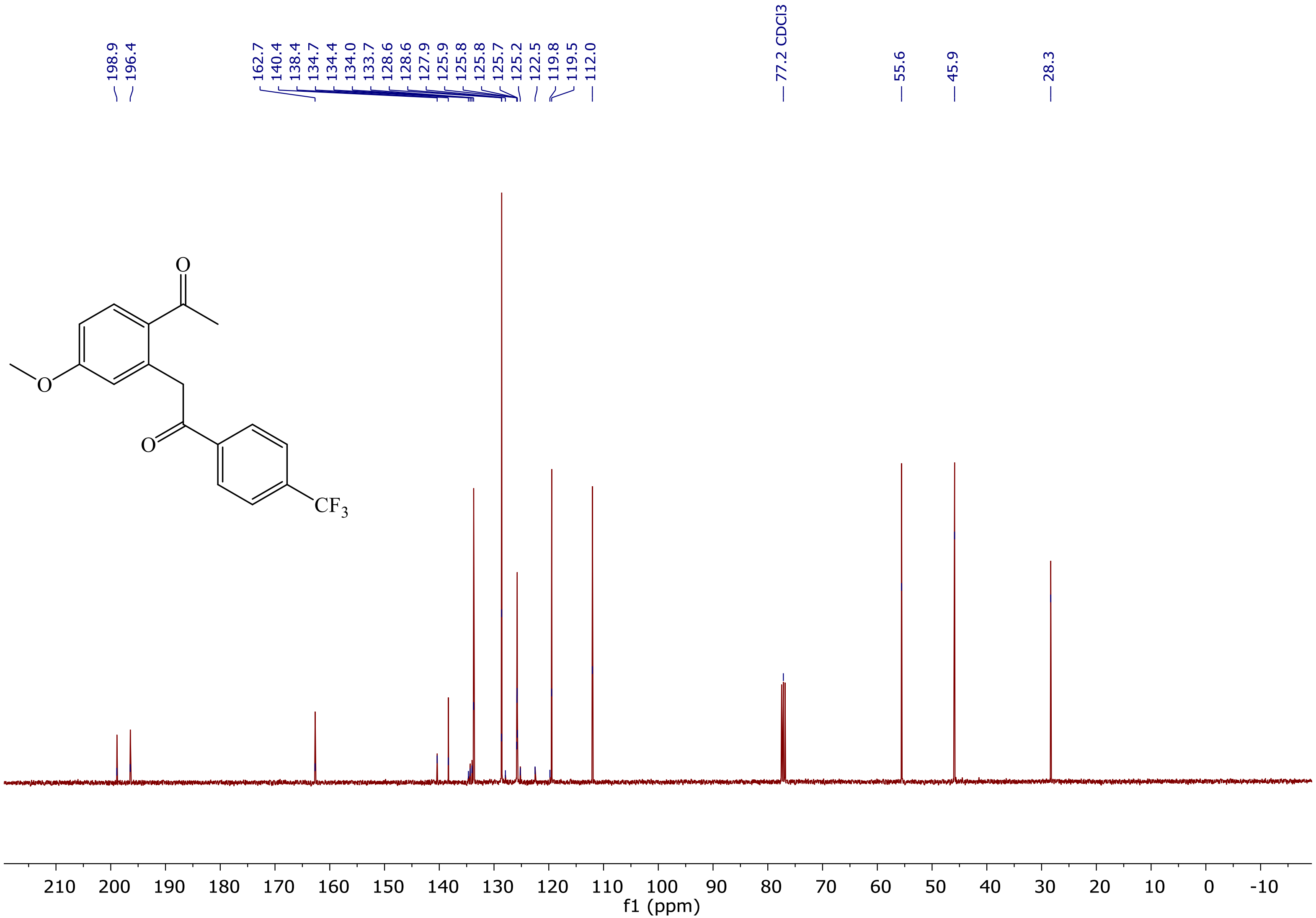


Figure S4.57. ^{13}C {^{1}H} **NMR (101MHz, $CDCl_3$) of 2-(2-acetyl-5-methoxyphenyl)-1-(4-(trifluoromethyl)phenyl)ethanone (2i)**

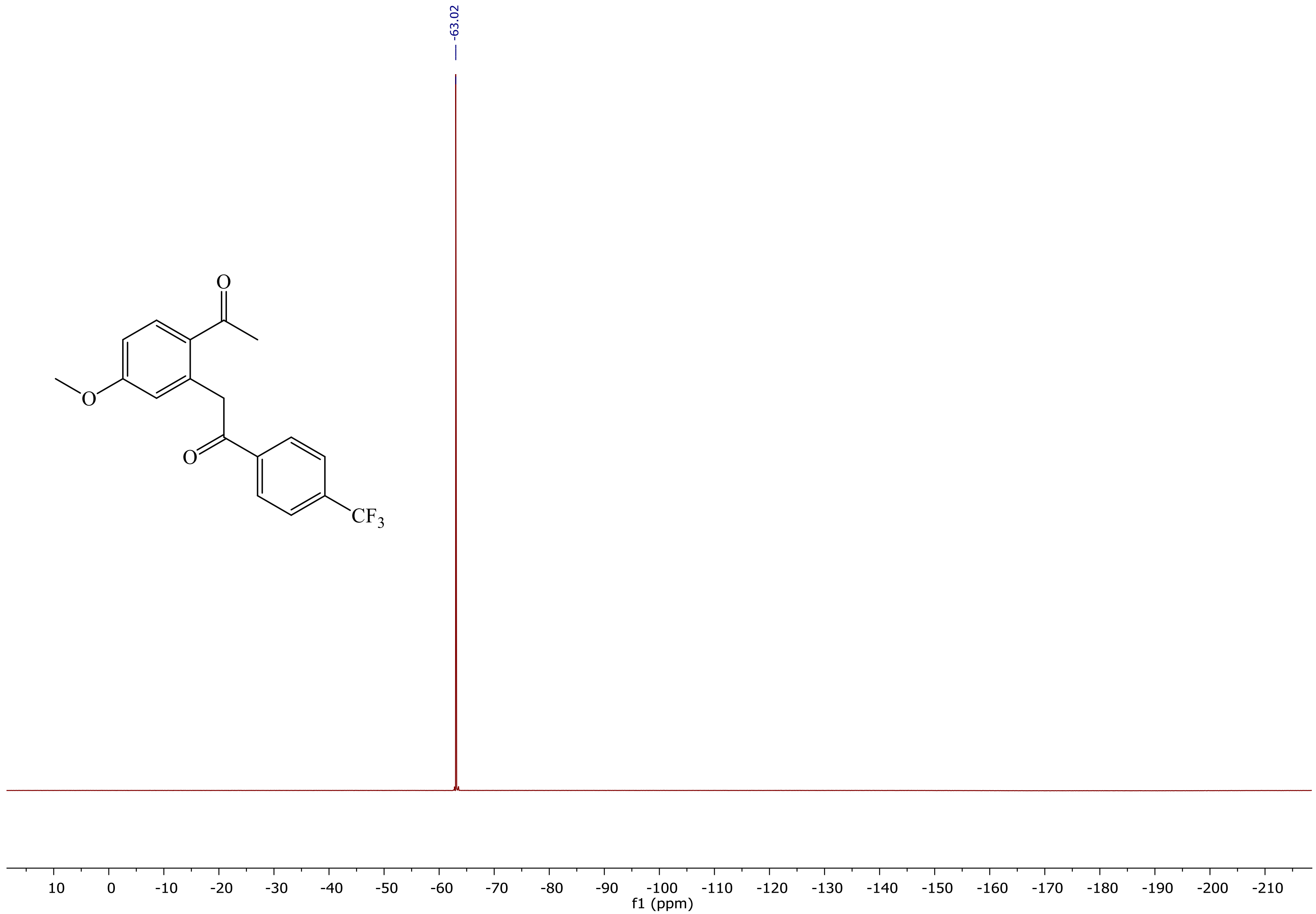


Figure S4.58. ^{19}F NMR (376 MHz, $CDCl_3$) of 2-(2-acetyl-5-methoxyphenyl)-1-(4-(trifluoromethyl)phenyl)ethanone (2i)

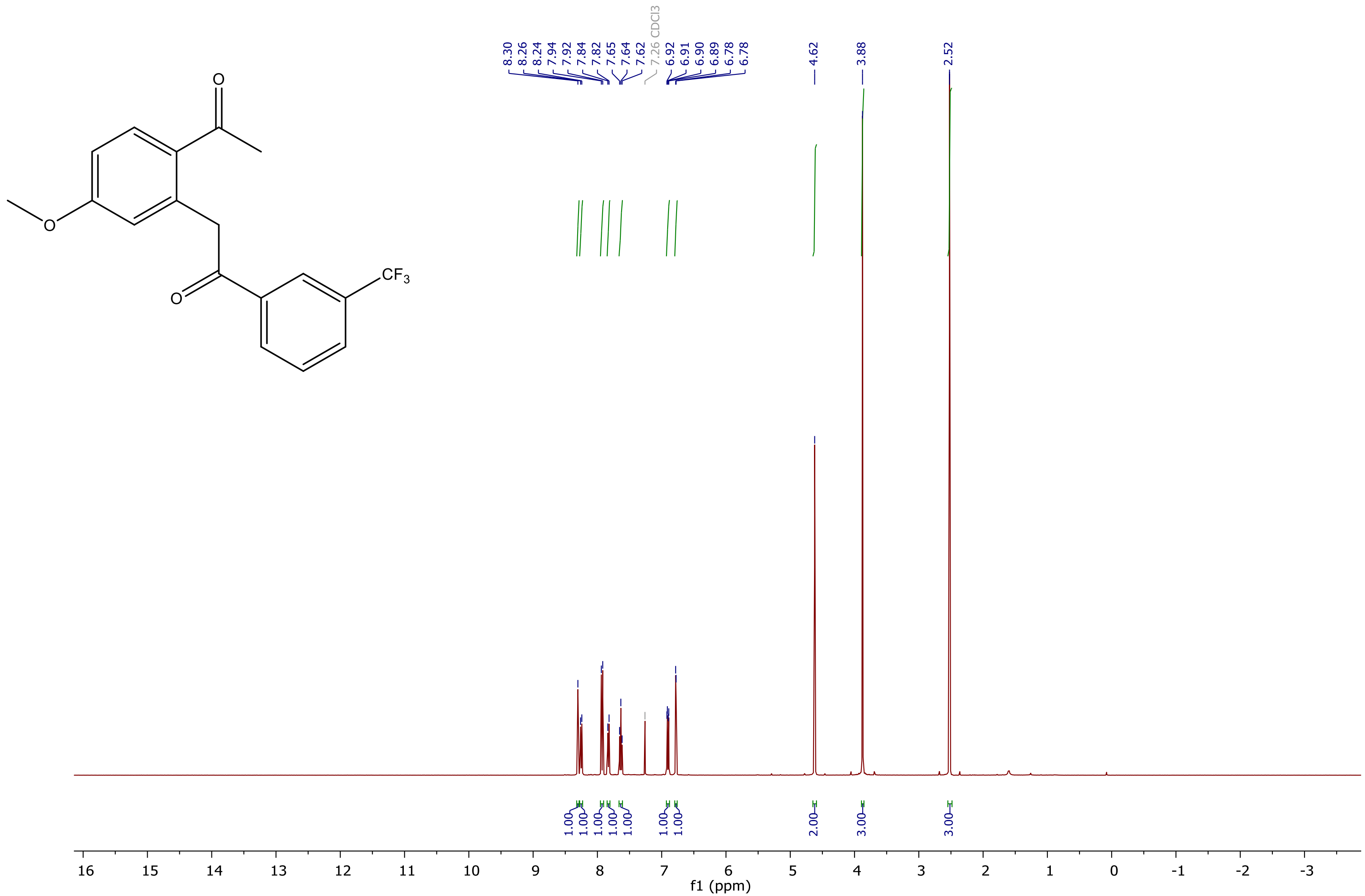


Figure S4.59. [1]H NMR (400MHz, $CDCl_3$) of 2-(2-acetyl-5-methoxyphenyl)-1-(3-(trifluoromethyl)phenyl)ethanone (2j)

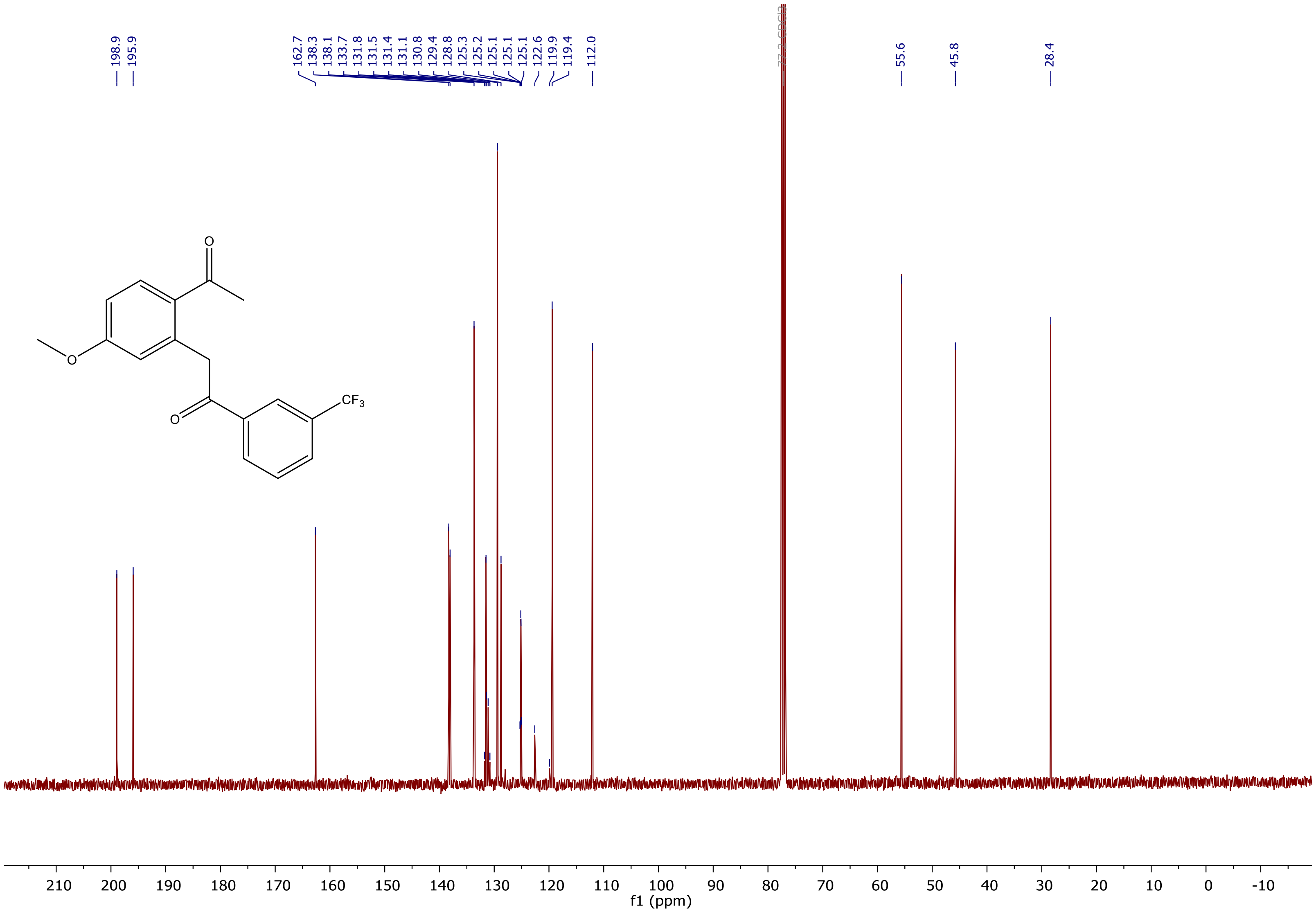


Figure S4.60. ^{13}C {^{1}H} **NMR (101MHz, $CDCl_3$) of 2-(2-acetyl-5-methoxyphenyl)-1-(3-(trifluoromethyl)phenyl)ethanone (2j)**

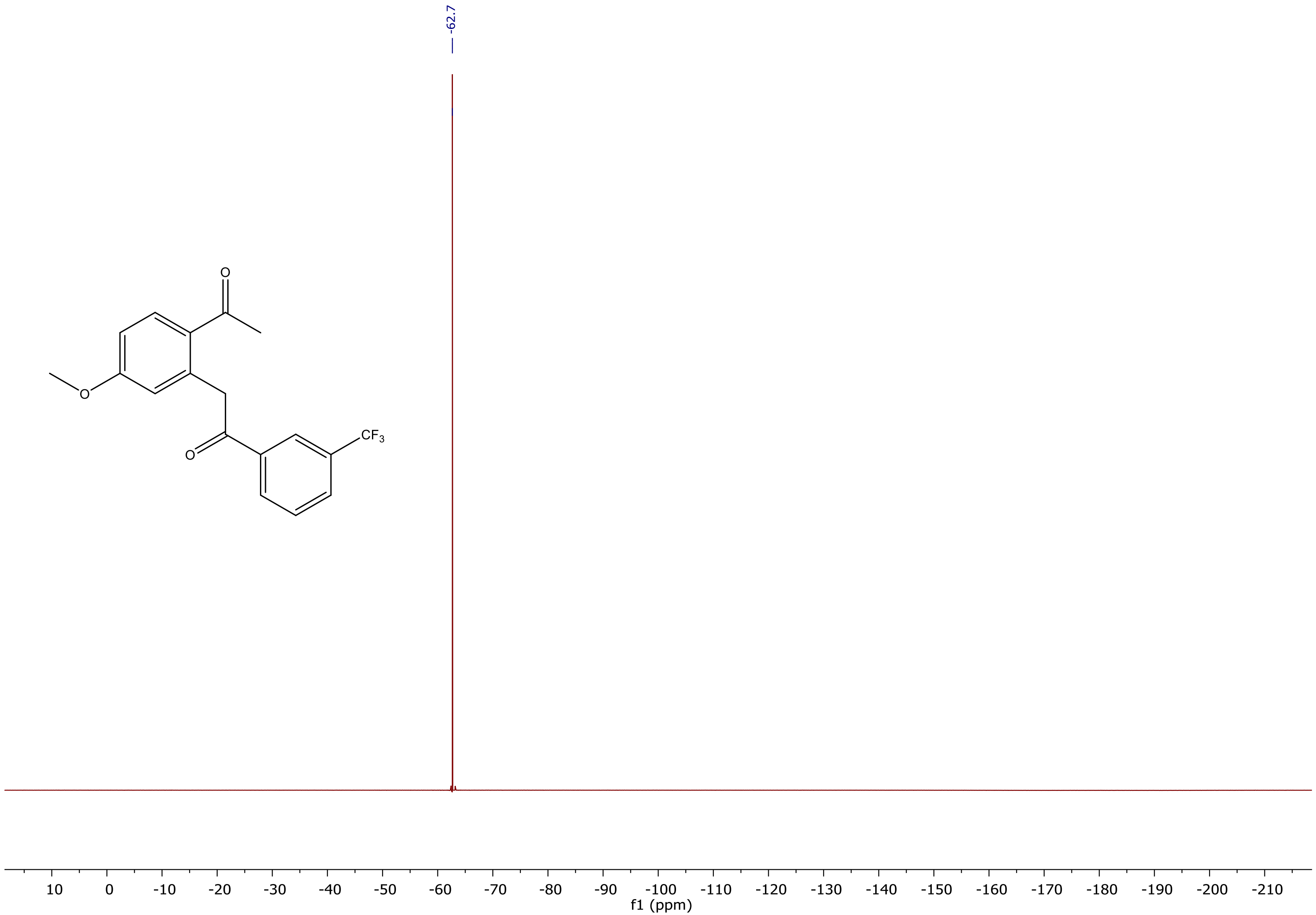


Figure S4.61. ^{19}**F NMR (376 MHz,** $CDCl_3$**) of 2-(2-acetyl-5-methoxyphenyl)-1-(3-(trifluoromethyl)phenyl)ethanone (2j)**

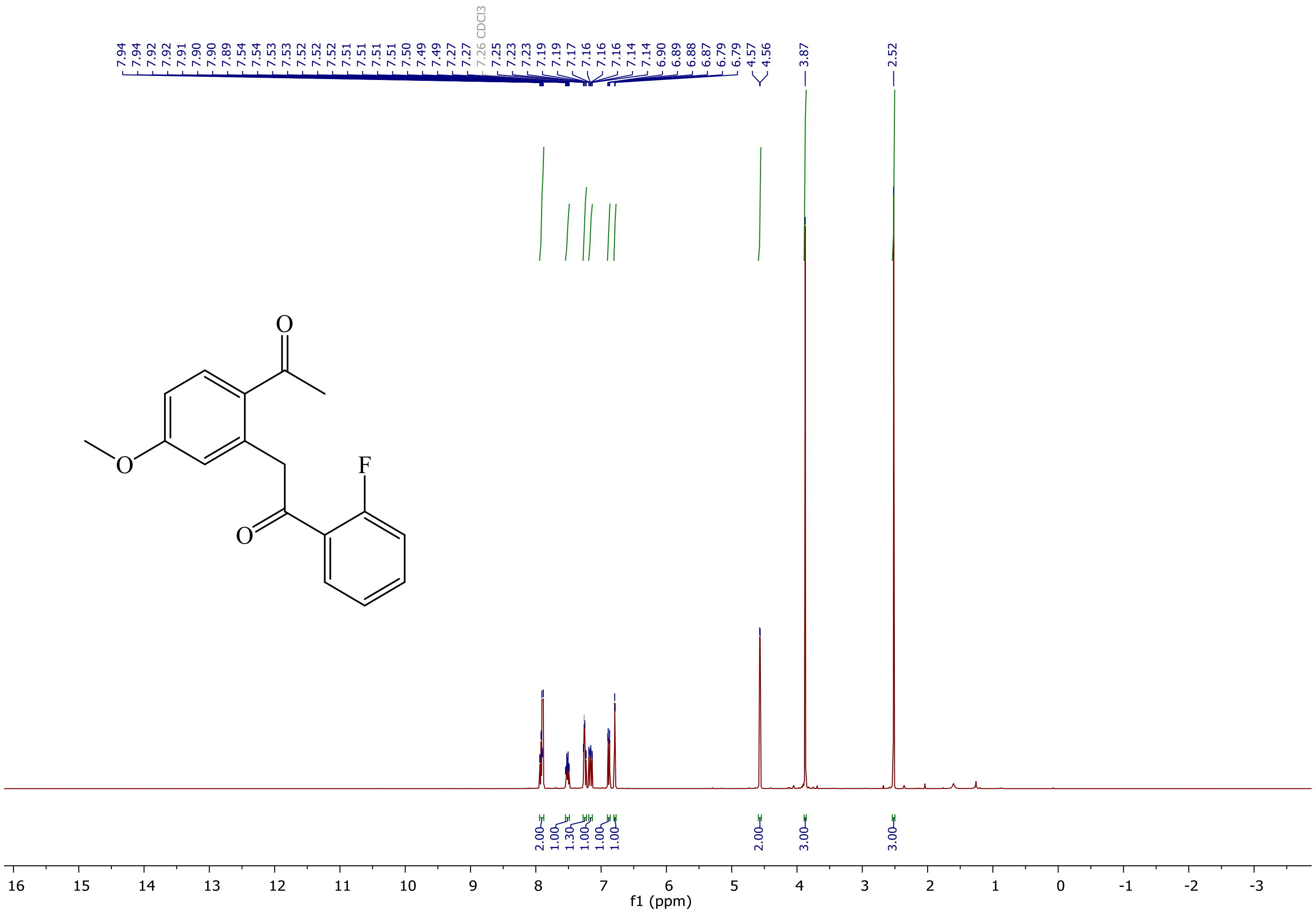


Figure S4.62. ^{1}H NMR (400MHz, $CDCl_3$) of 2-(2-acetyl-5-methoxyphenyl)-1-(2-fluorophenyl)ethanone (2k)

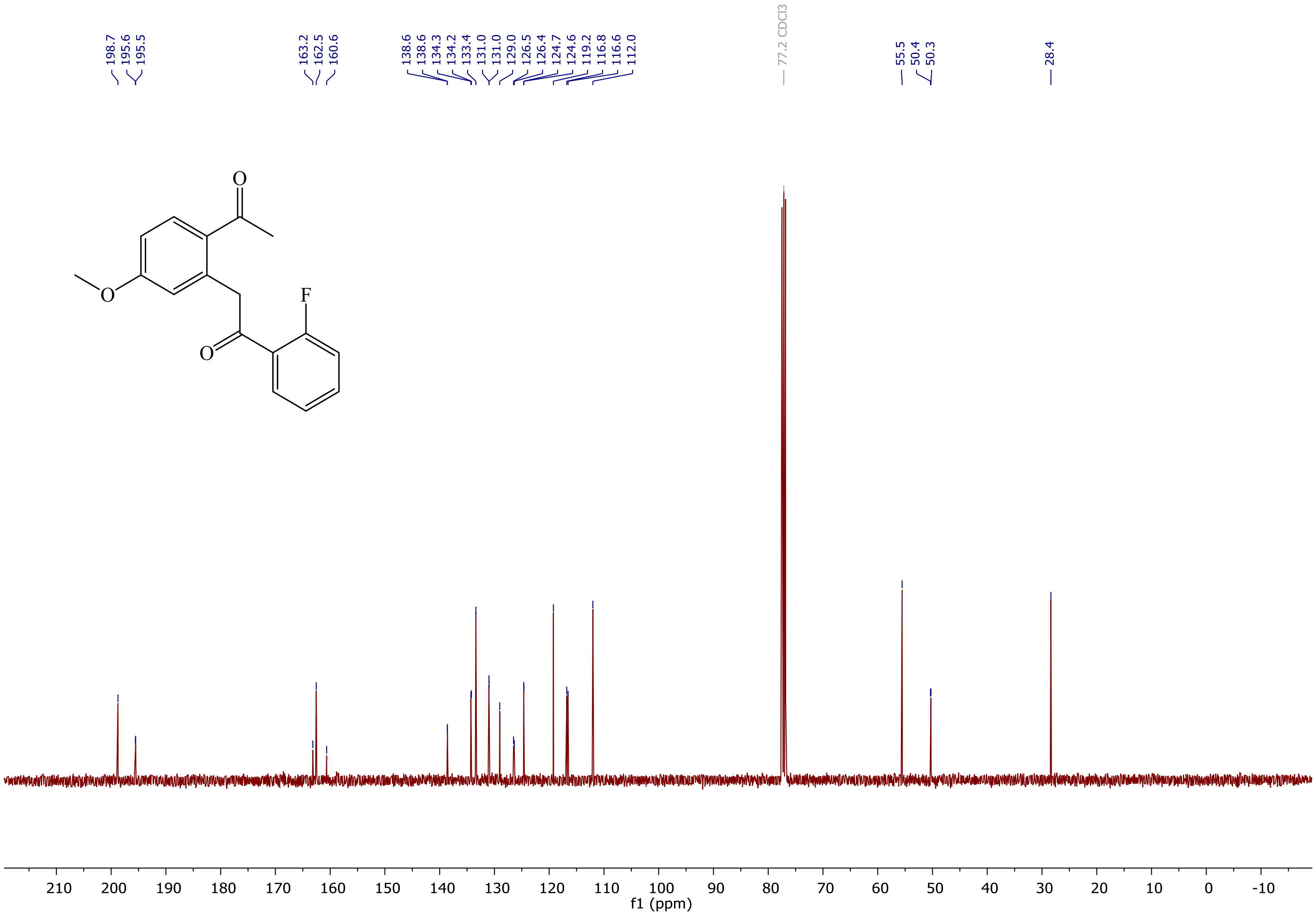


Figure S4.63. $^{13}C\{^{1}H\}$ **NMR (101MHz,** $CDCl_3$**) of 2-(2-acetyl-5-methoxyphenyl)-1-(2-fluorophenyl)ethanone (2k)**

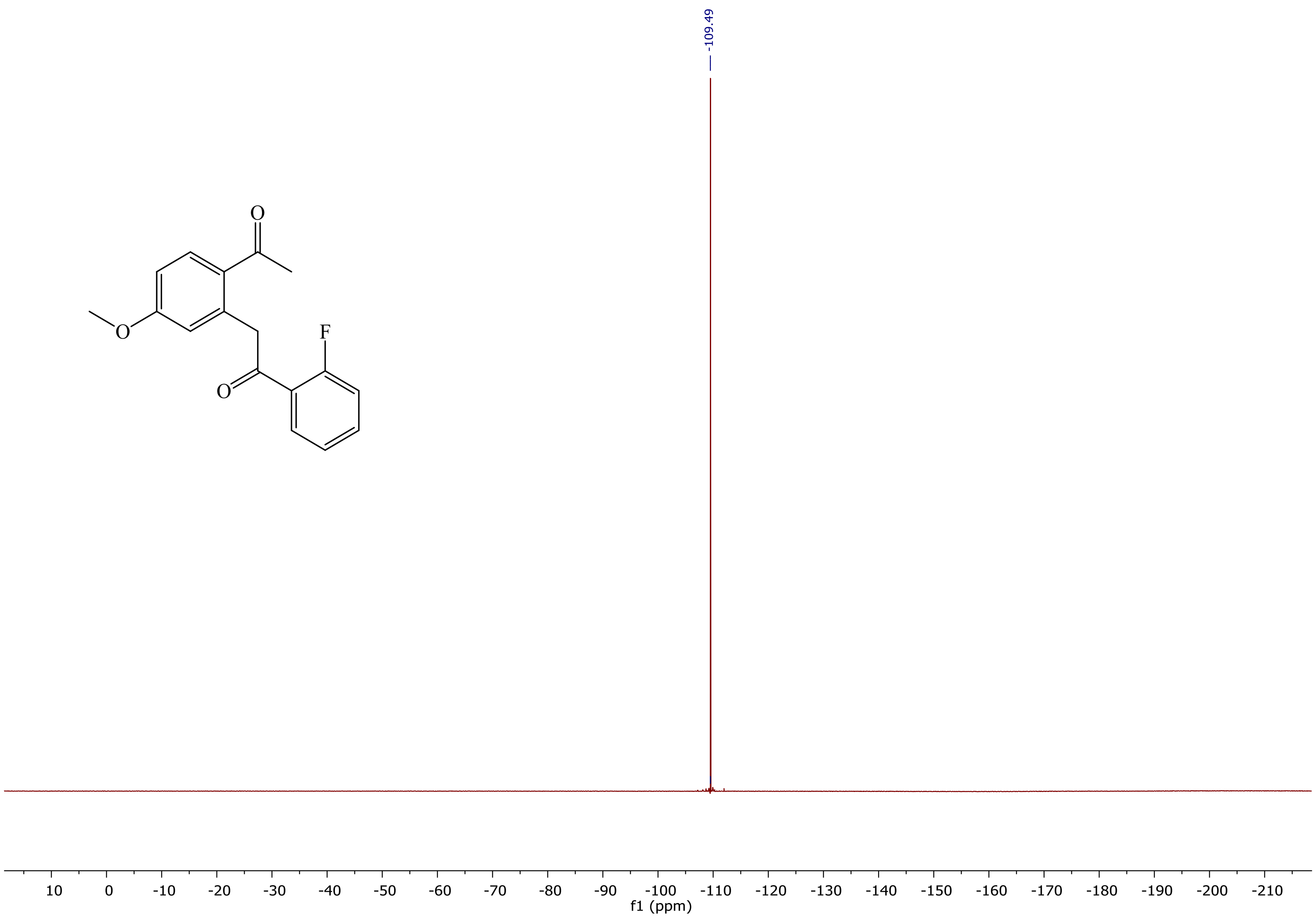


Figure S4.64. ^{19}F NMR (376 MHz, $CDCl_3$) of 2-(2-acetyl-5-methoxyphenyl)-1-(2-fluorophenyl)ethanone (2k)

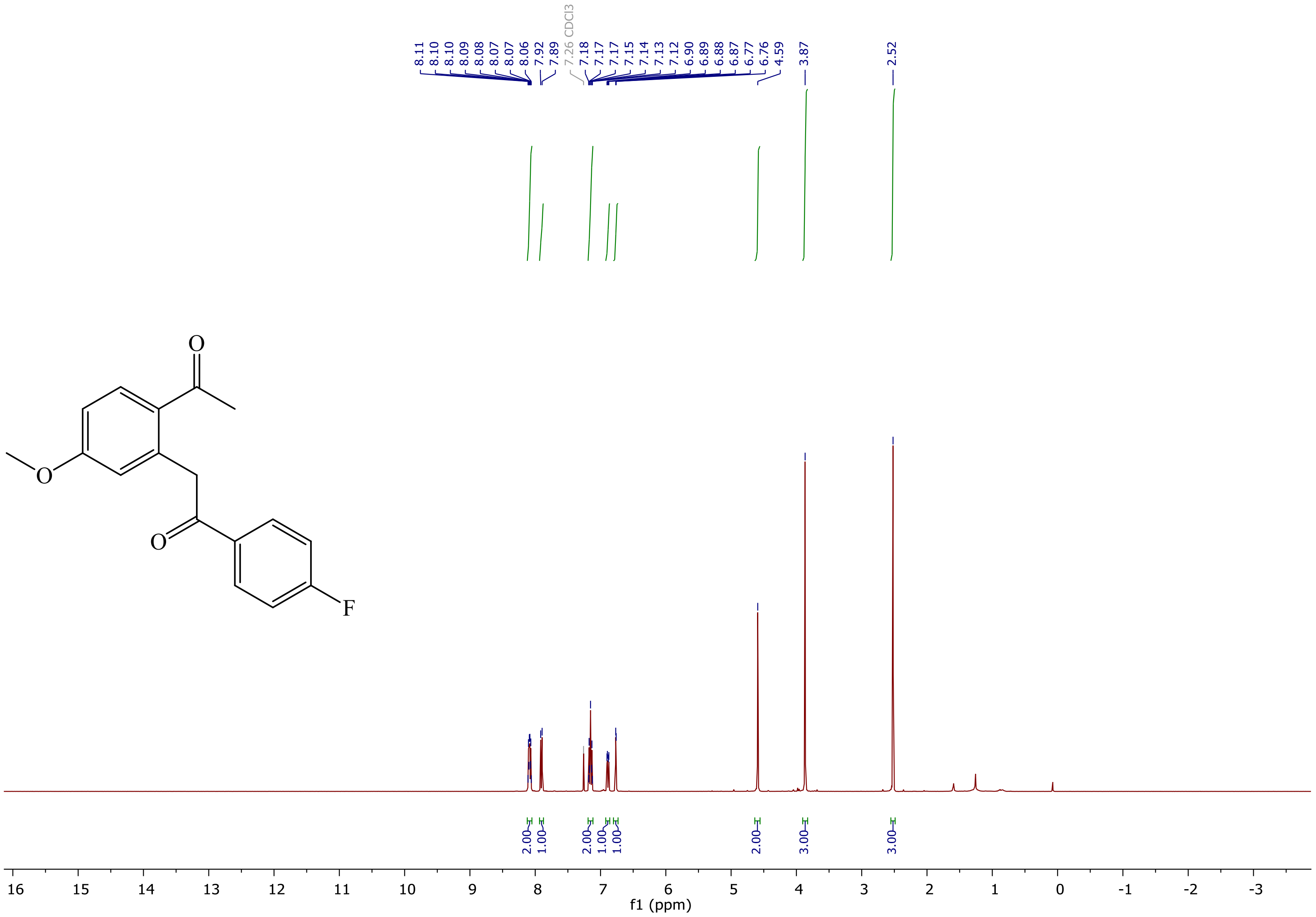


Figure S4.65. ^{1}H NMR (400MHz, $CDCl_3$) of 2-(2-acetyl-5-methoxyphenyl)-1-(4-fluorophenyl)ethanone (2l)

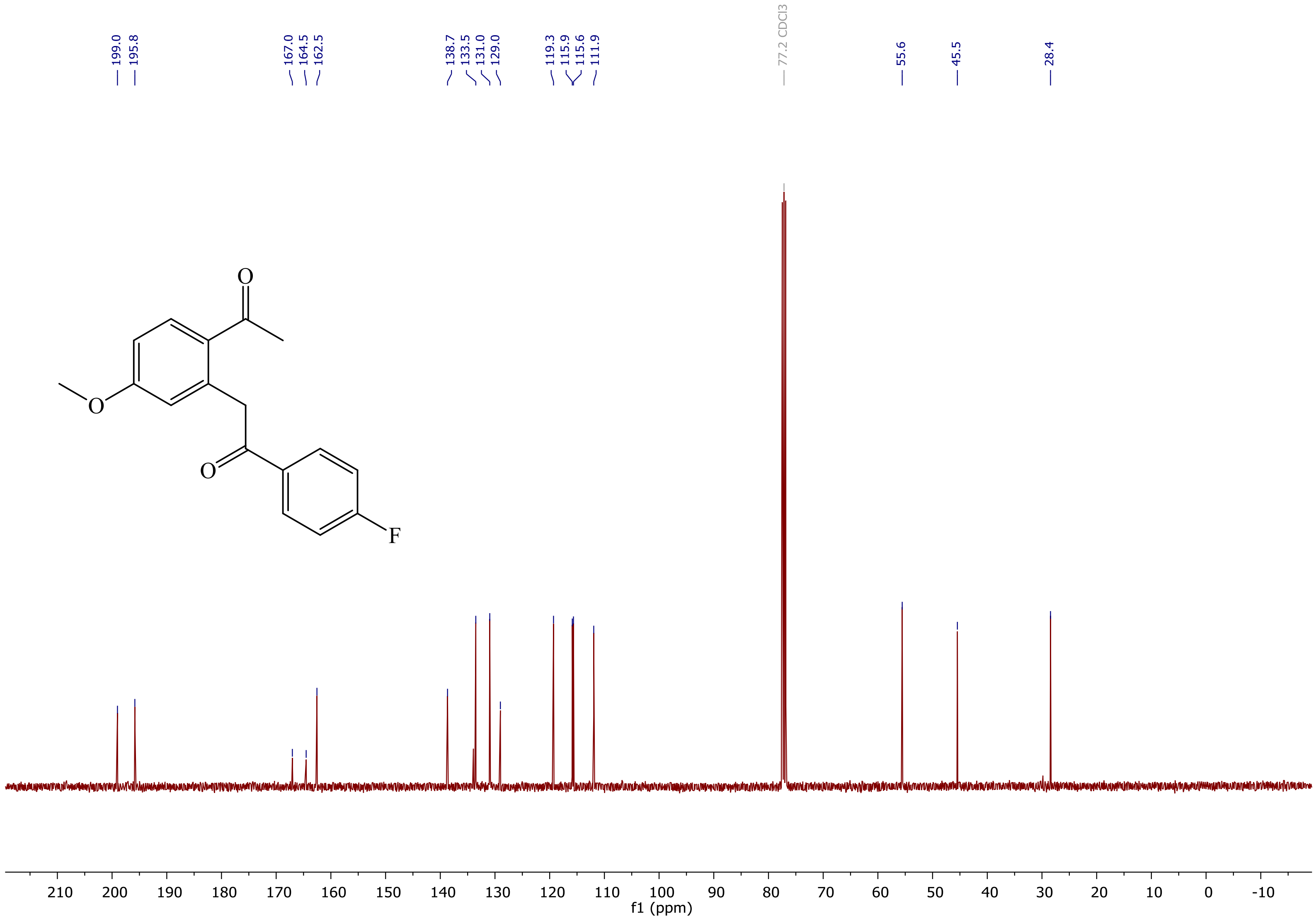


Figure S4.66. ^{13}C {^{1}H} NMR (101MHz, $CDCl_3$) of 2-(2-acetyl-5-methoxyphenyl)-1-(4-fluorophenyl)ethanone (2l)

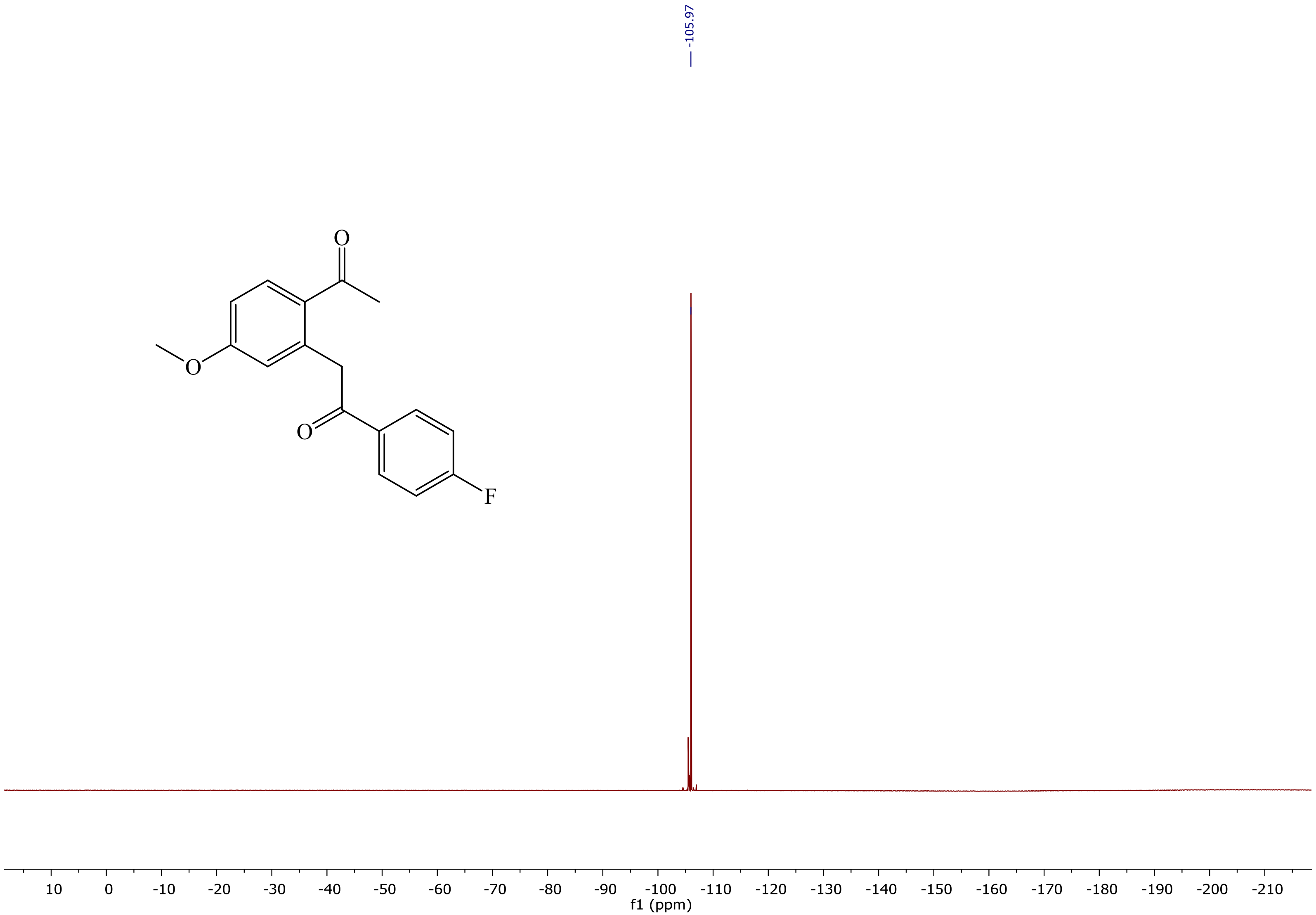


Figure S4.67. [19]F NMR (376 MHz, $CDCl_3$) of 2-(2-acetyl-5-methoxyphenyl)-1-(4-fluorophenyl)ethanone (2l)

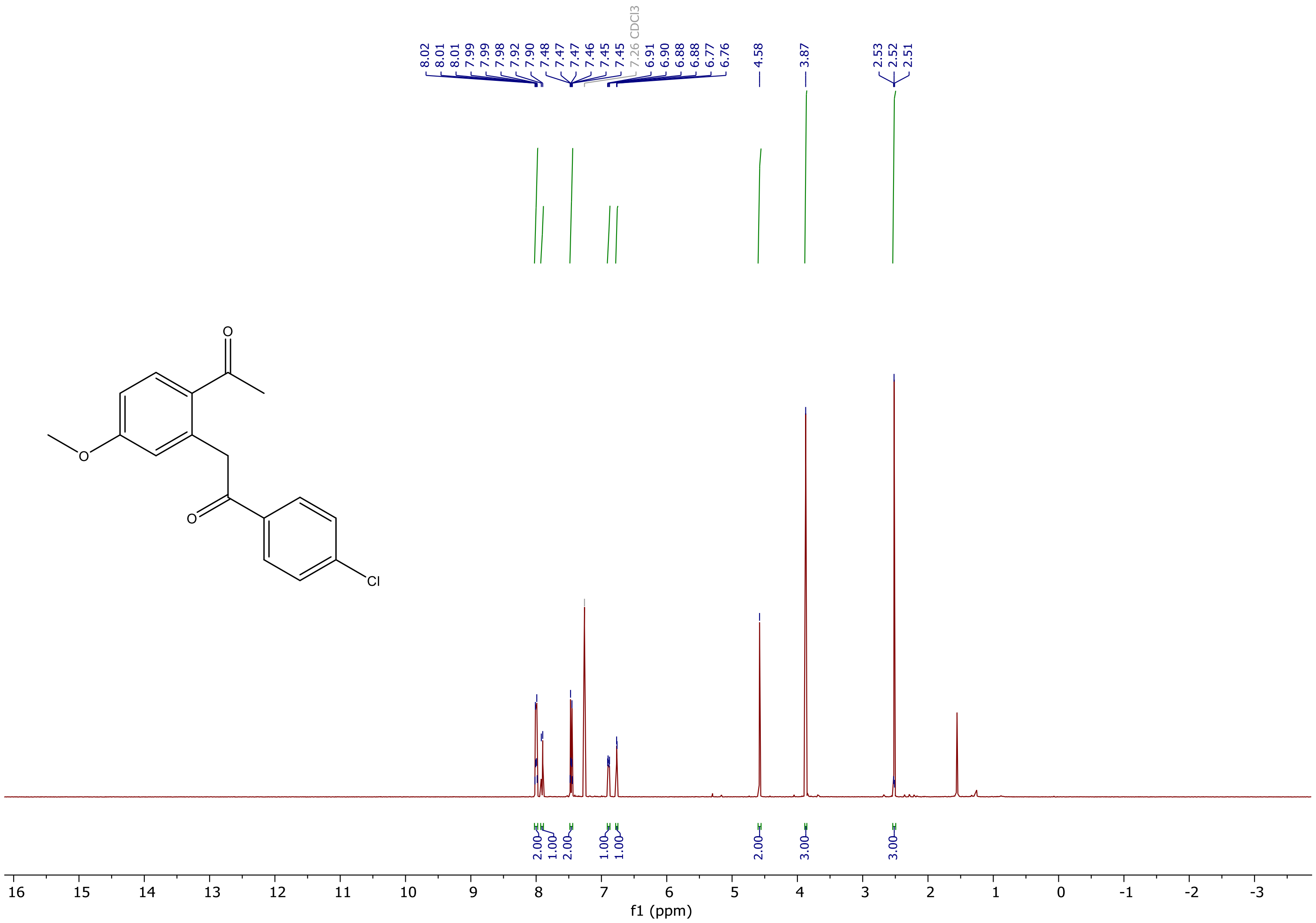


Figure S4.68. ^{1}H NMR (400MHz, $CDCl_3$) of 2-(2-acetyl-5-methoxyphenyl)-1-(4-chlorophenyl)ethanone (2m)

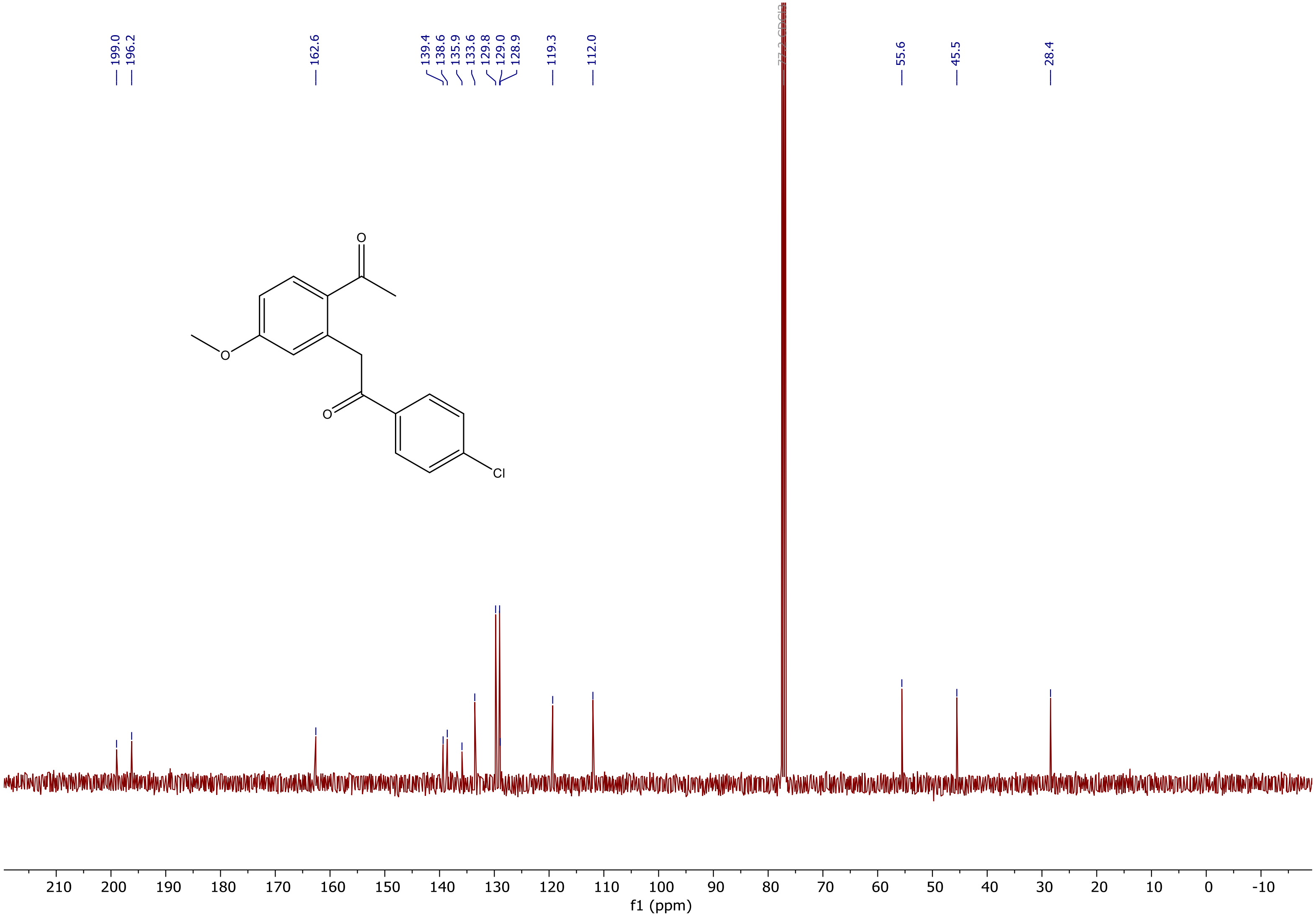


Figure S4.69. $^{13}C\{^1H\}$ NMR (101MHz, $CDCl_3$) of 2-(2-acetyl-5-methoxyphenyl)-1-(4-chlorophenyl)ethanone (2m)

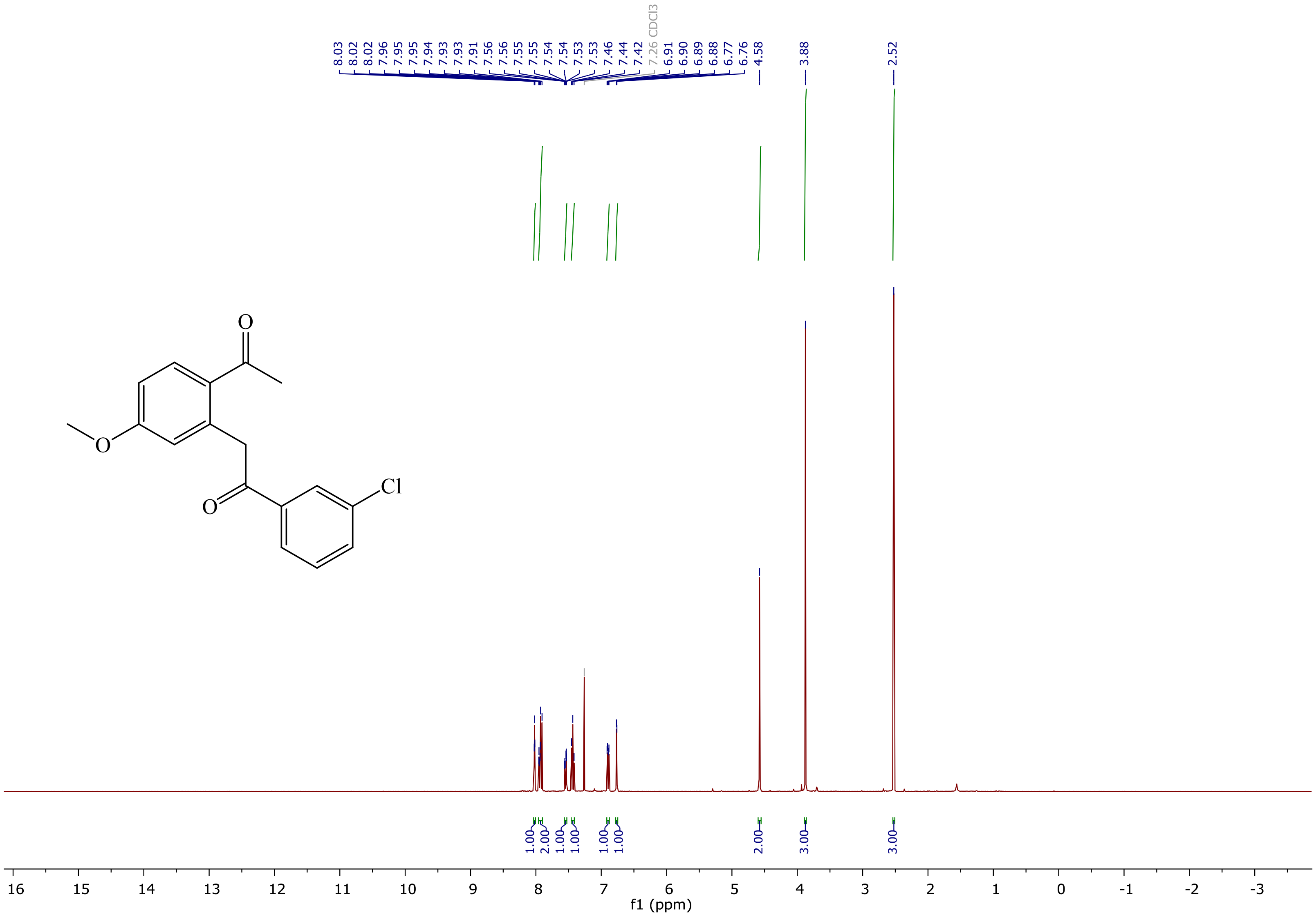


Figure S4.70. ^{1}H NMR (400MHz, $CDCl_3$) of 2-(2-acetyl-5-methoxyphenyl)-1-(3-chlorophenyl)ethanone (2n)

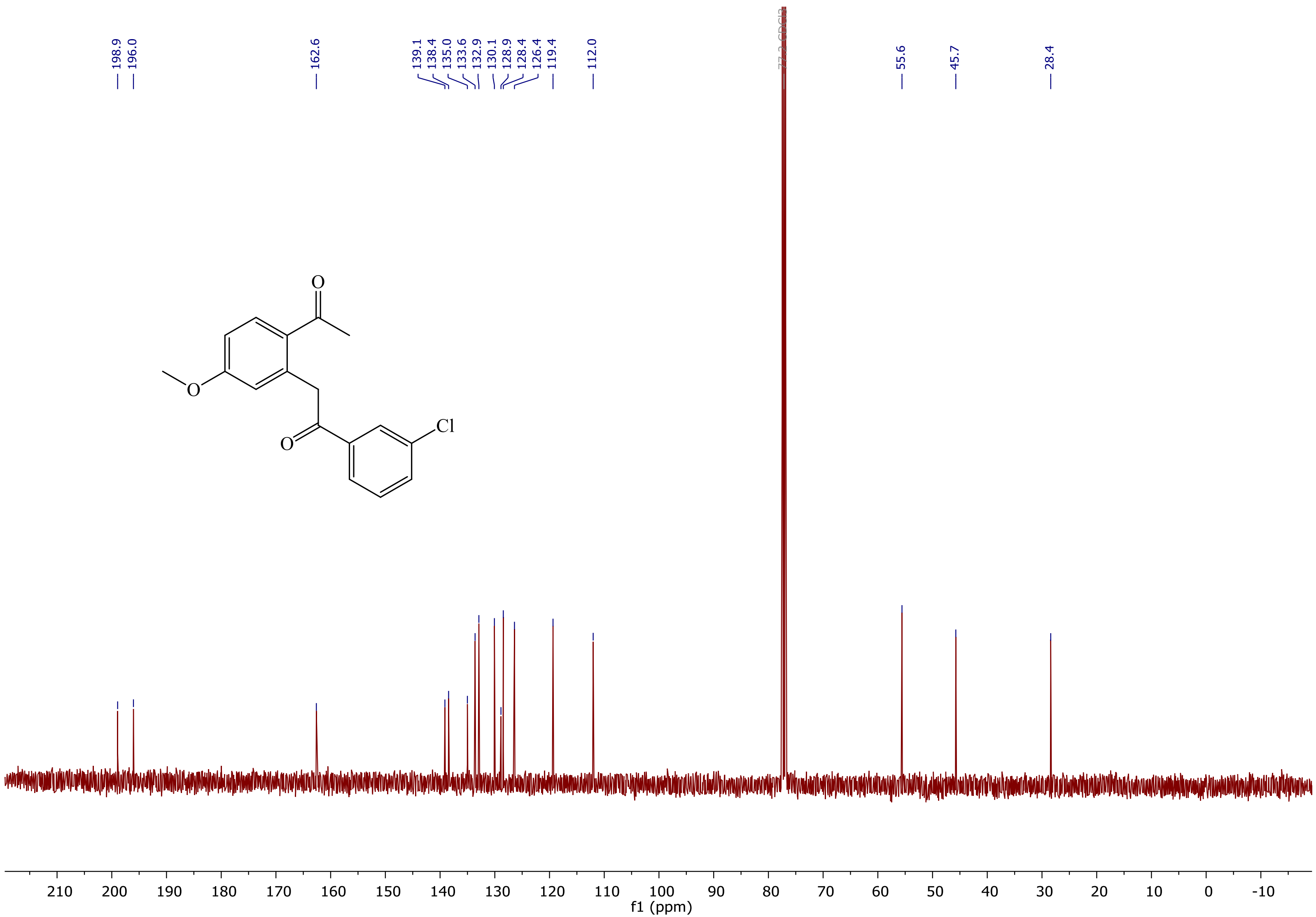


Figure S4.71. $^{13}C\ \{^{1}H\}$ **NMR (101MHz,** $CDCl_3$**) of 2-(2-acetyl-5-methoxyphenyl)-1-(3-chlorophenyl)ethanone (2n)**

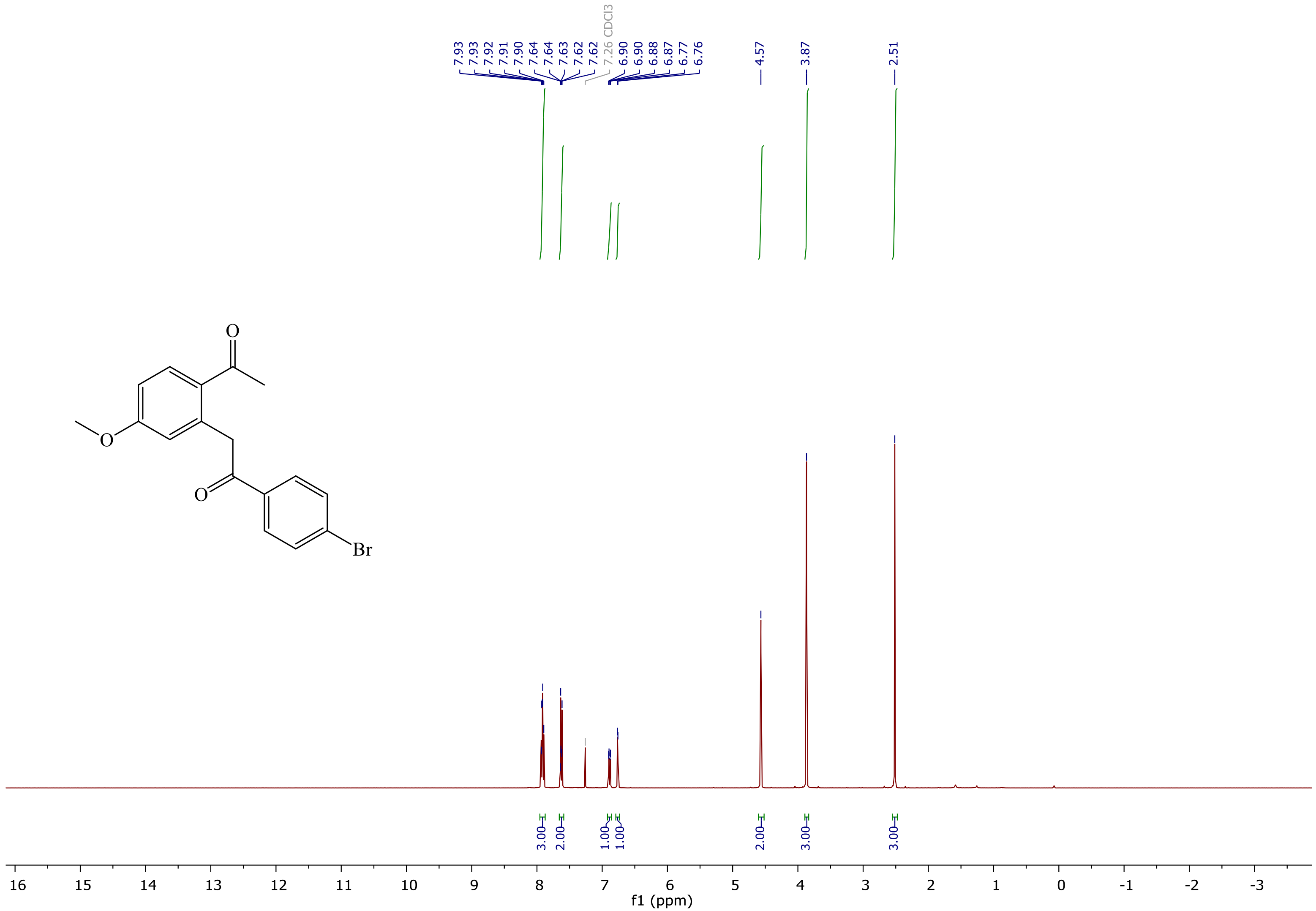


Figure S4.72. [1]H NMR (400MHz, $CDCl_3$) of 2-(2-acetyl-5-methoxyphenyl)-1-(4-bromophenyl)ethanone (2o)

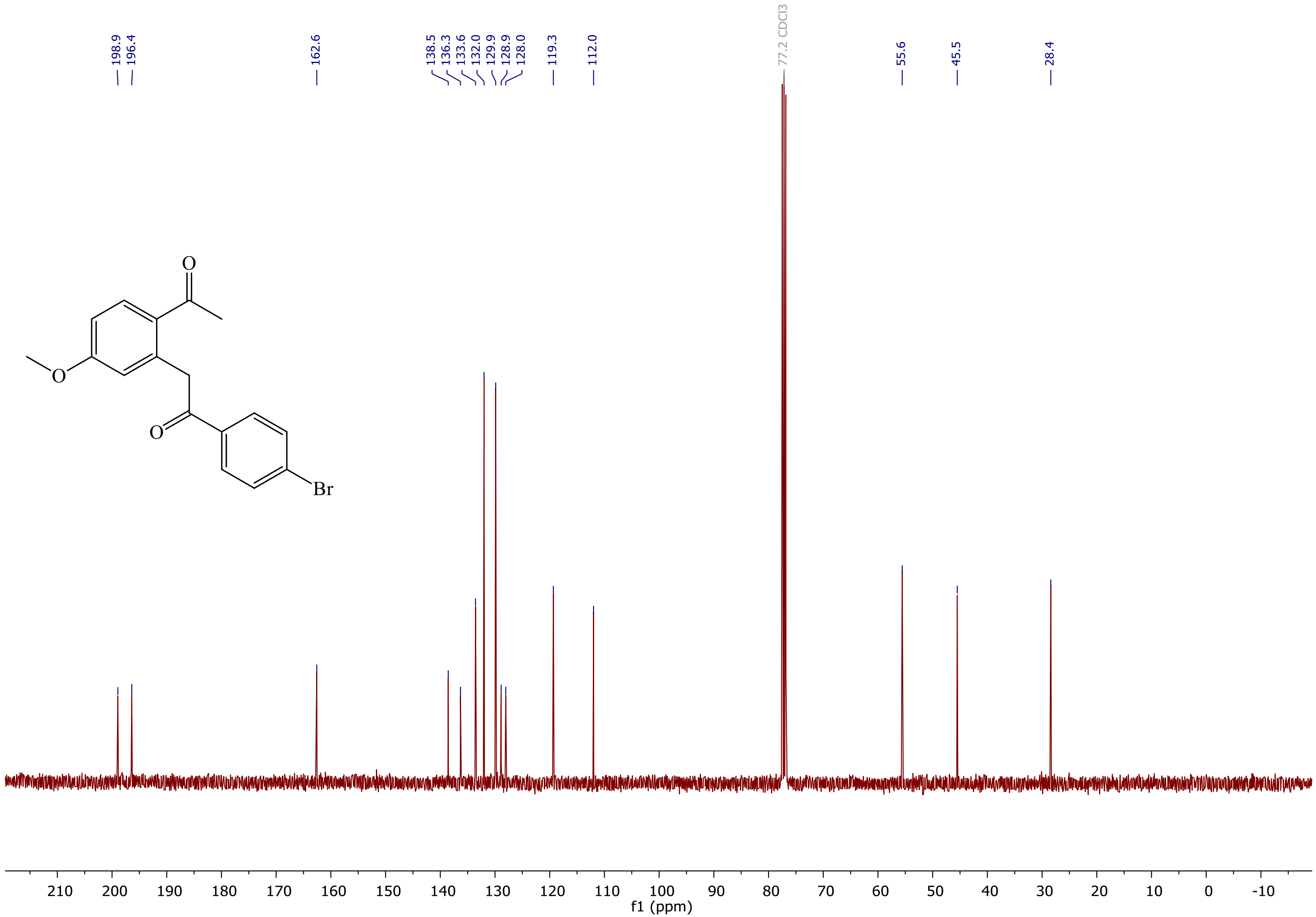


Figure S4.7. $^{13}C\{^1H\}$ **NMR (101MHz, CDCl$_3$) of 2-(2-acetyl-5-methoxyphenyl)-1-(4-bromophenyl)ethanone (2o)**

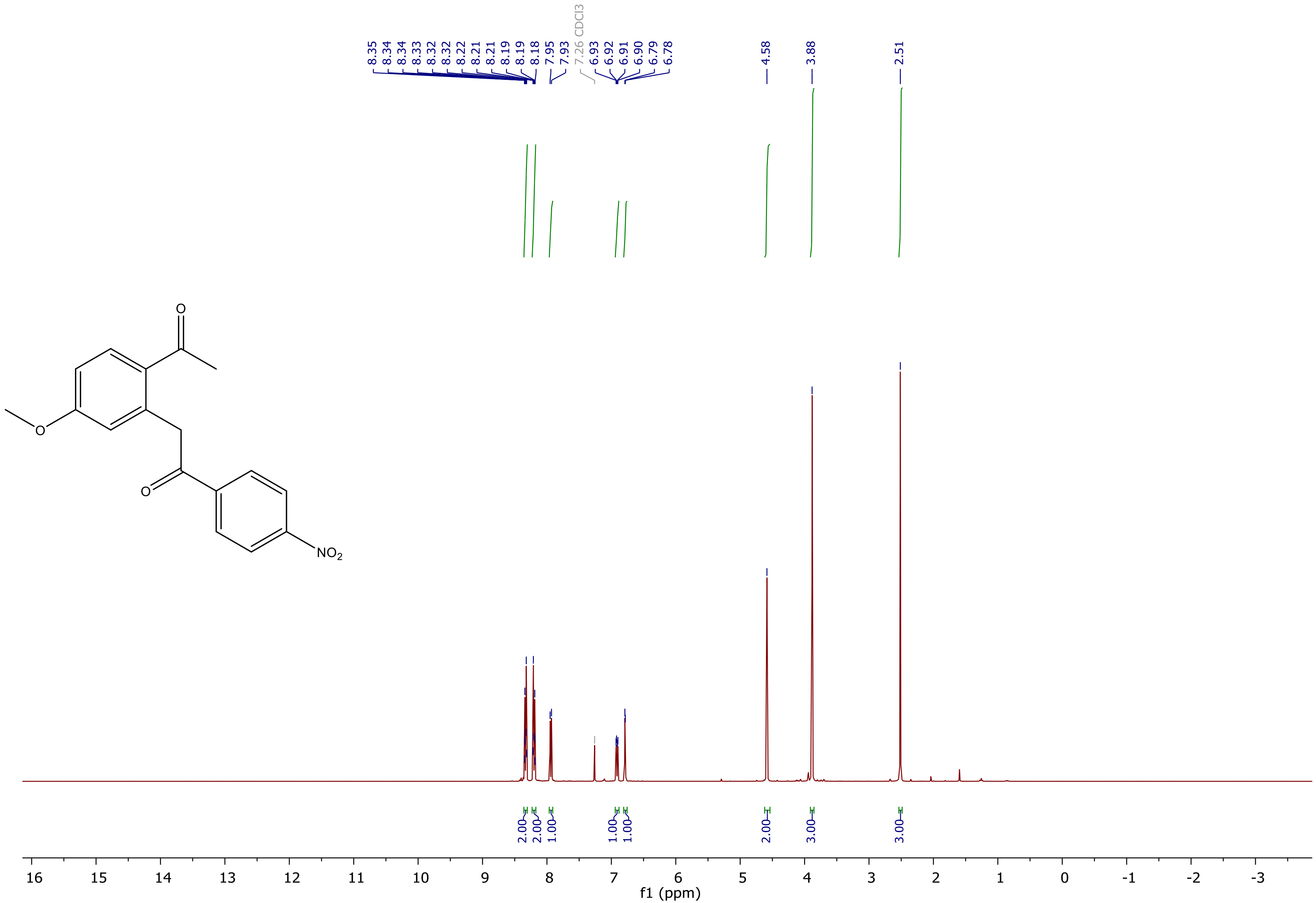


Figure S4.74. ^{1}H NMR (400MHz, $CDCl_3$) of 2-(2-acetyl-5-methoxyphenyl)-1-(4-nitrophenyl)ethanone (2p)

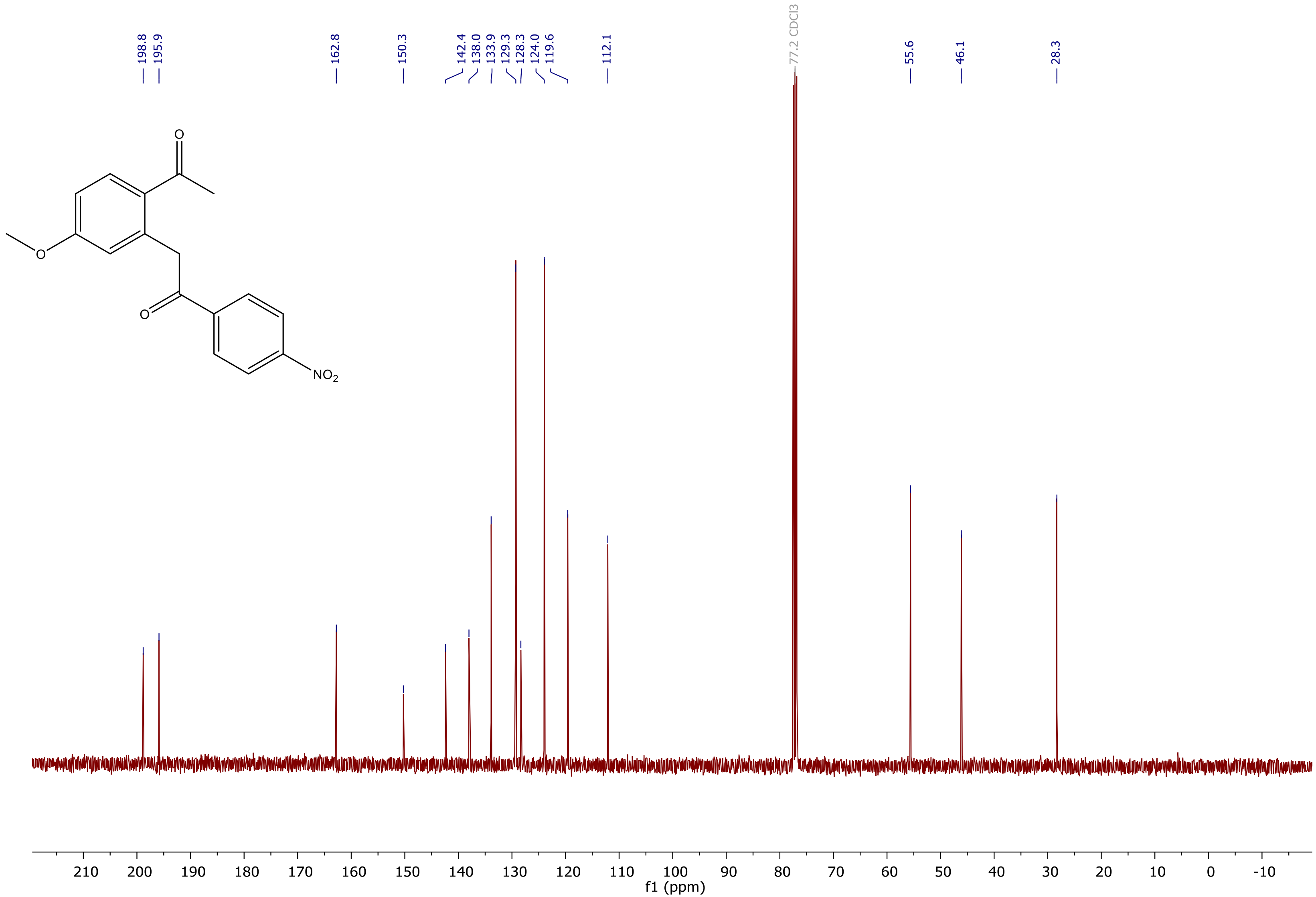


Figure S4.75. ^{13}C {^{1}H} NMR (101MHz, $CDCl_3$) of 2-(2-acetyl-5-methoxyphenyl)-1-(4-nitrophenyl)ethanone (2p)

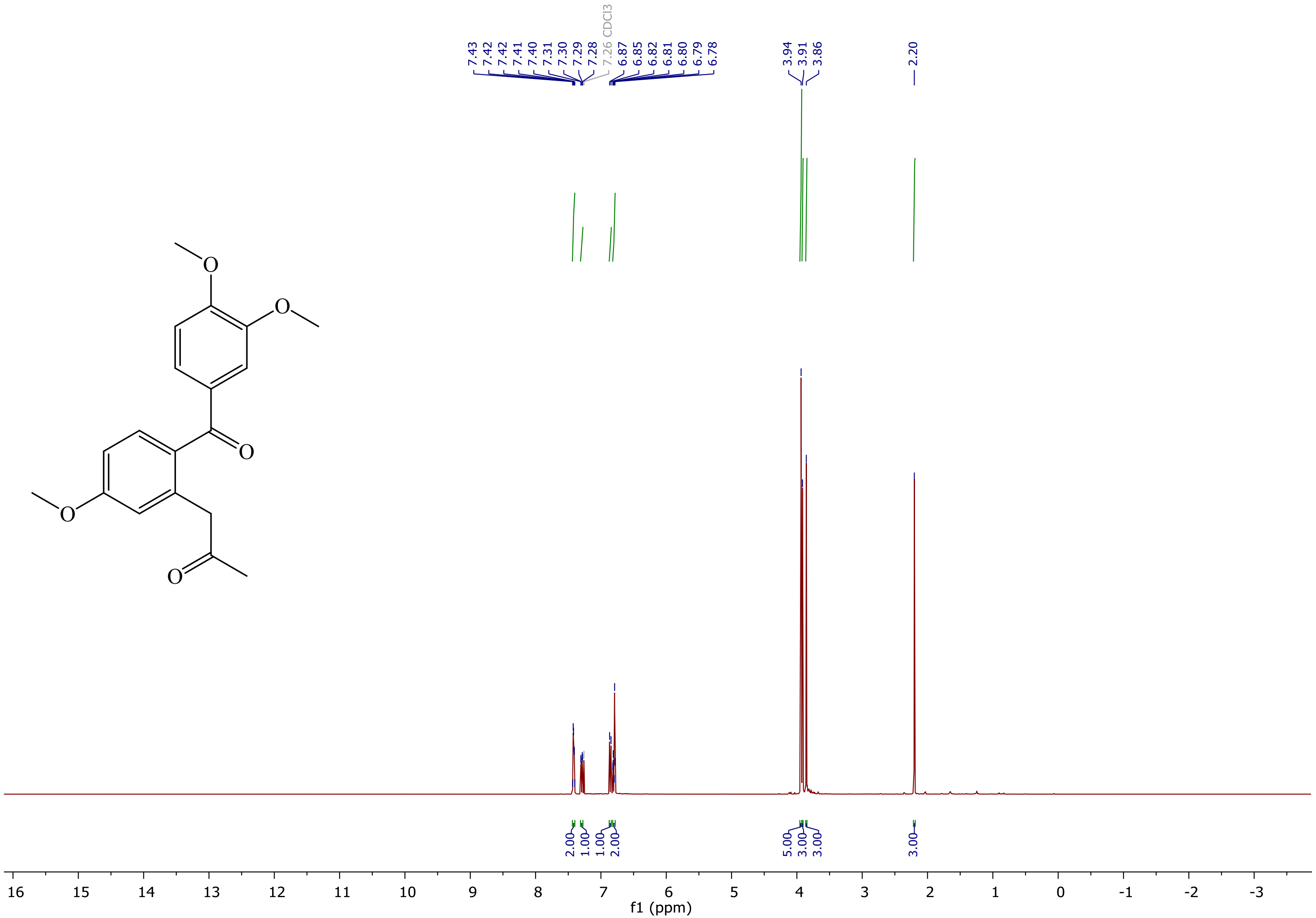


Figure S4.76. ^{1}H NMR (400MHz, $CDCl_3$) of 1-(2-(3,4-dimethoxybenzoyl)-5-methoxyphenyl)propan-2-one (2q)

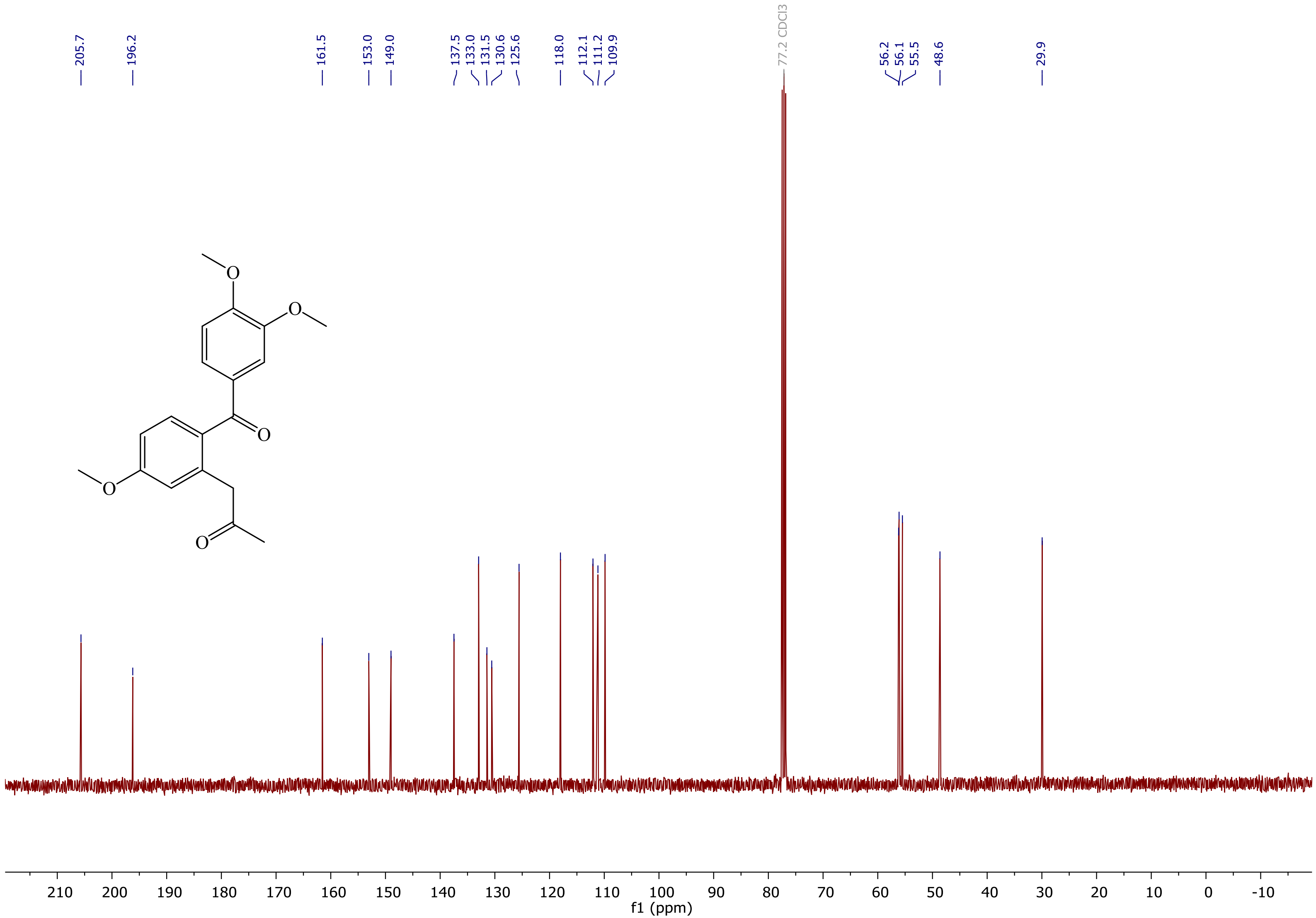


Figure S4.77. ^{13}C {^{1}H} NMR (101MHz, $CDCl_3$) of 1-(2-(3,4-dimethoxybenzoyl)-5-methoxyphenyl)propan-2-one (2q)

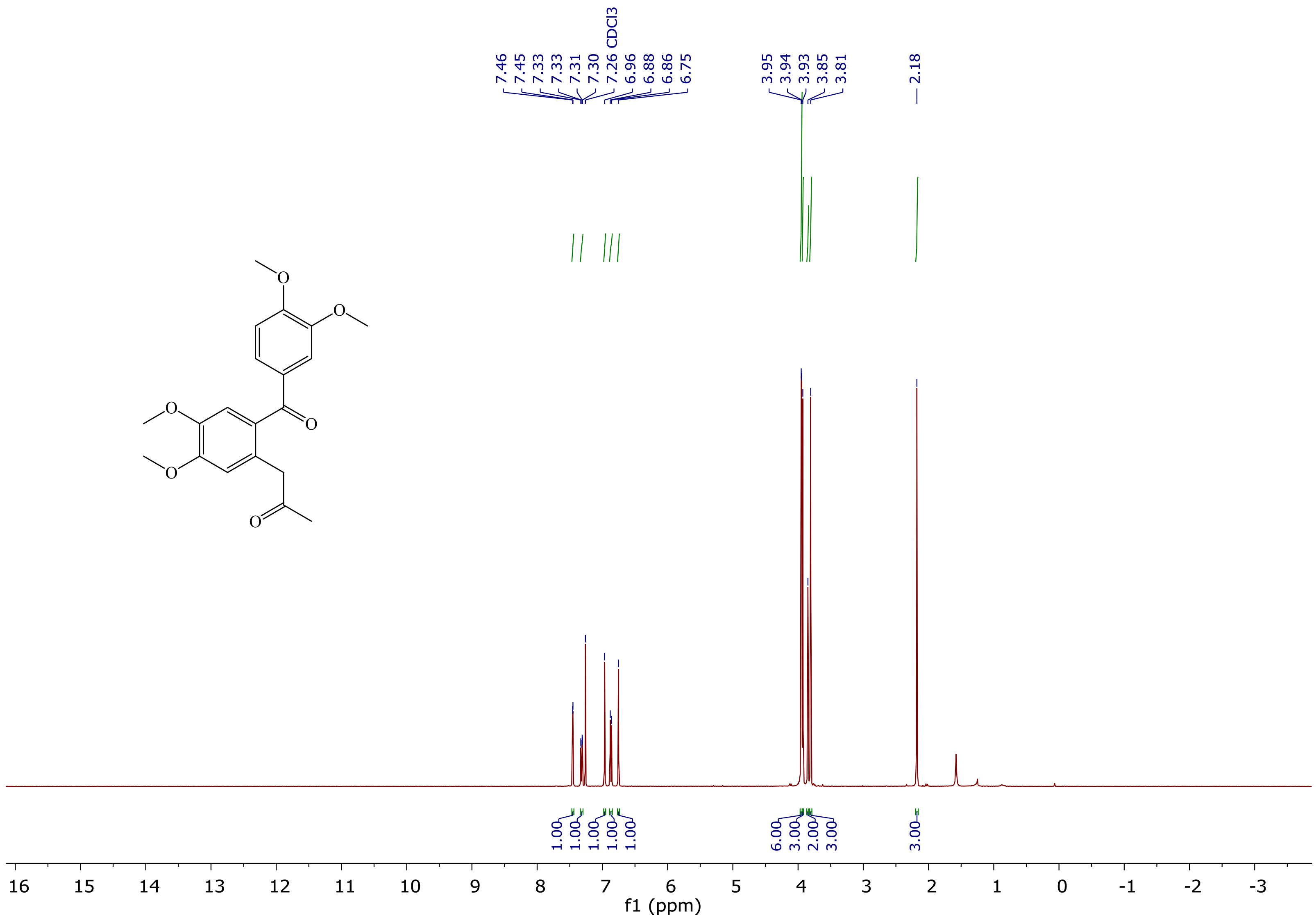


Figure S4.78. ^{1}H NMR (400MHz, $CDCl_3$) of 1-(2-(3,4-dimethoxybenzoyl)-4,5-dimethoxyphenyl)propan-2-one (2r)

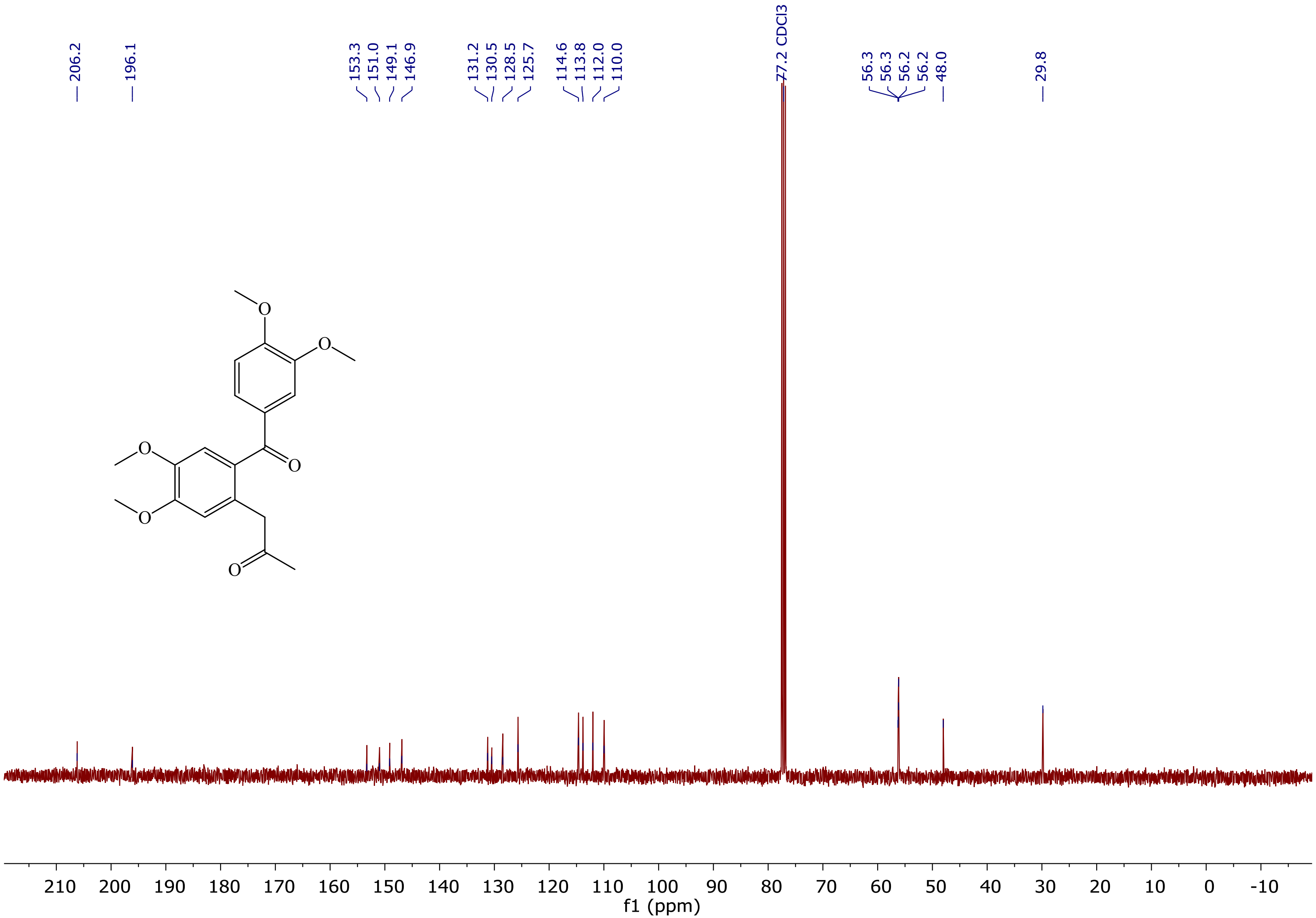


Figure S4.79. $^{13}C\ \{^1H\}$ **NMR (101MHz, $CDCl_3$) of 1-(2-(3,4-dimethoxybenzoyl)-4,5-dimethoxyphenyl)propan-2-one (2r)**

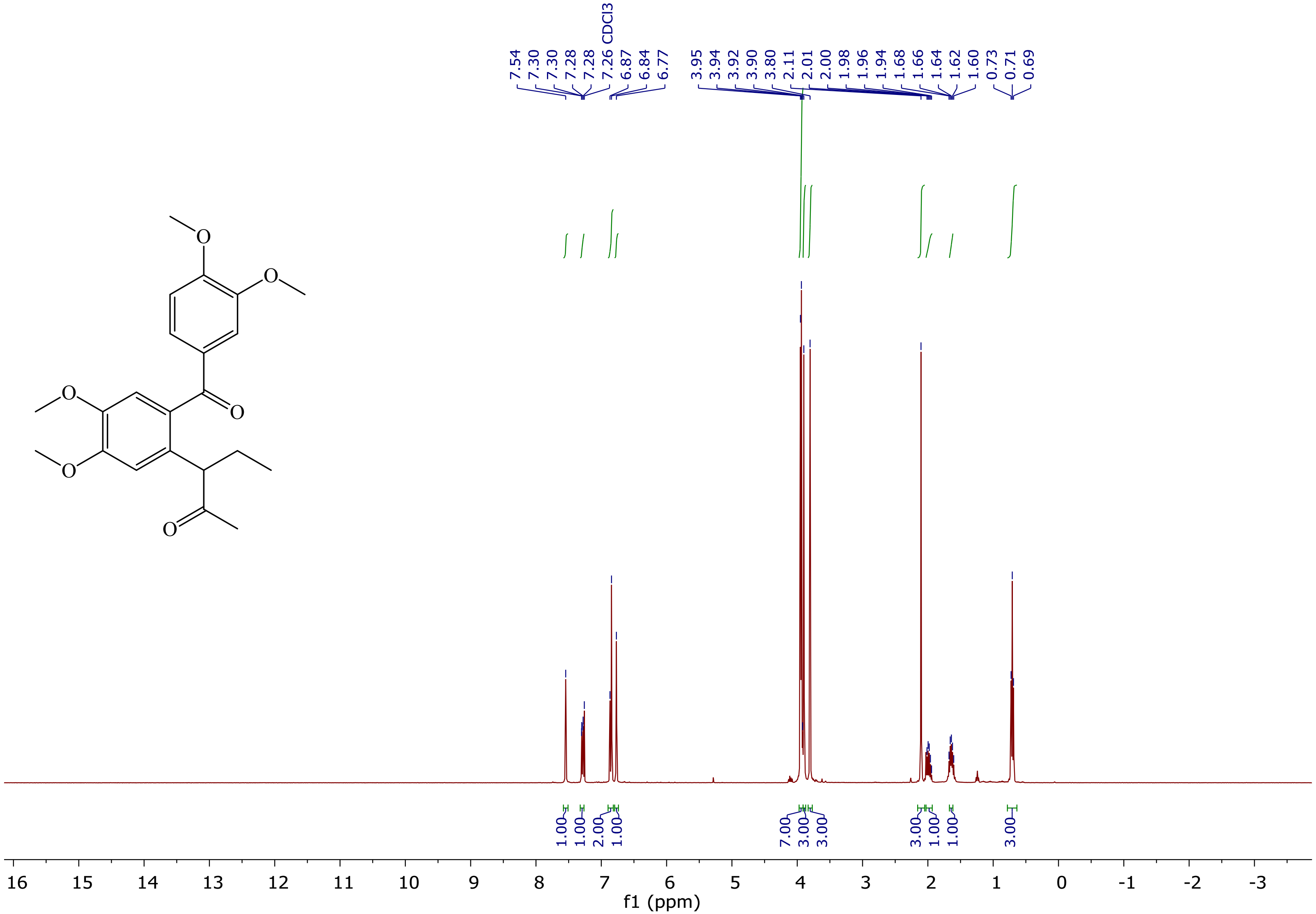


Figure S4.80. ^{1}H NMR (400MHz, $CDCl_3$) of 3-(2-(3,4-dimethoxybenzoyl)-4,5-dimethoxyphenyl)pentan-2-one (2s)

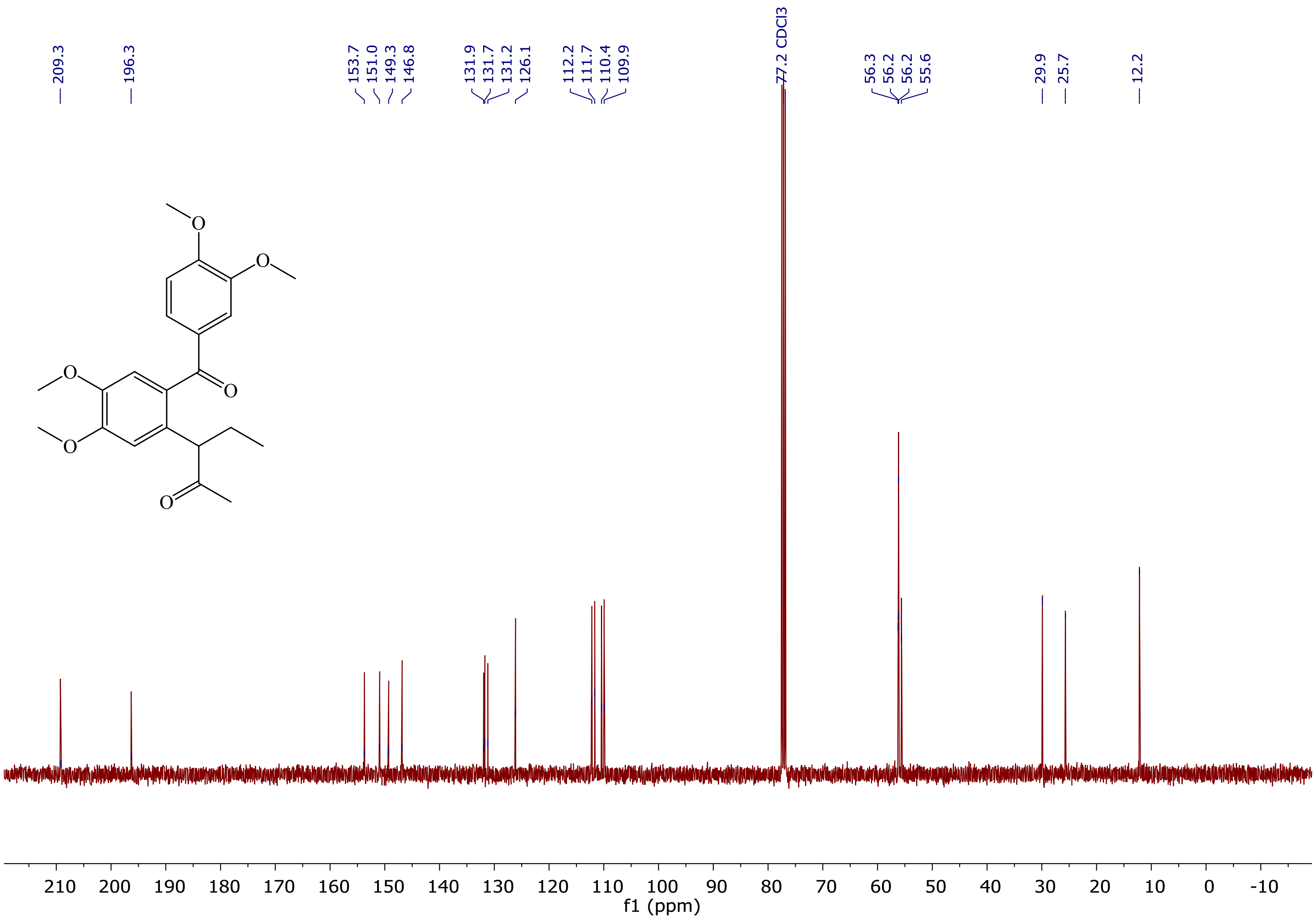


Figure S4.81. $^{13}C\{^1H\}$ **NMR (101MHz,** $CDCl_3$**) of 3-(2-(3,4-dimethoxybenzoyl)-4,5-dimethoxyphenyl)pentan-2-one (2s)**

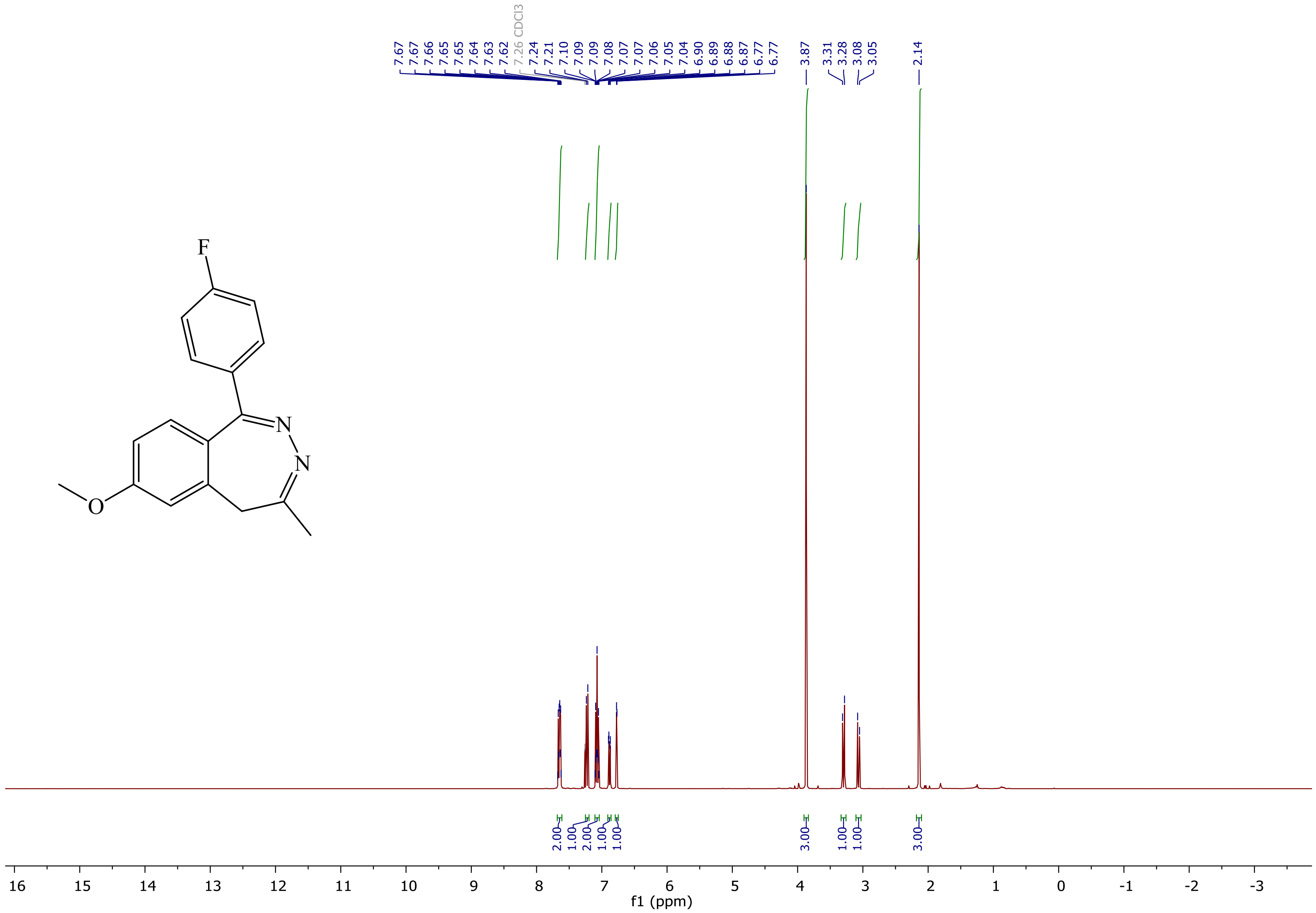


Figure S4.82. ^{1}H NMR (400MHz, $CDCl_3$) of 1-(4-fluorophenyl)-7-methoxy-4-methyl-5H-benzo[d][1,2]diazepine (3a)

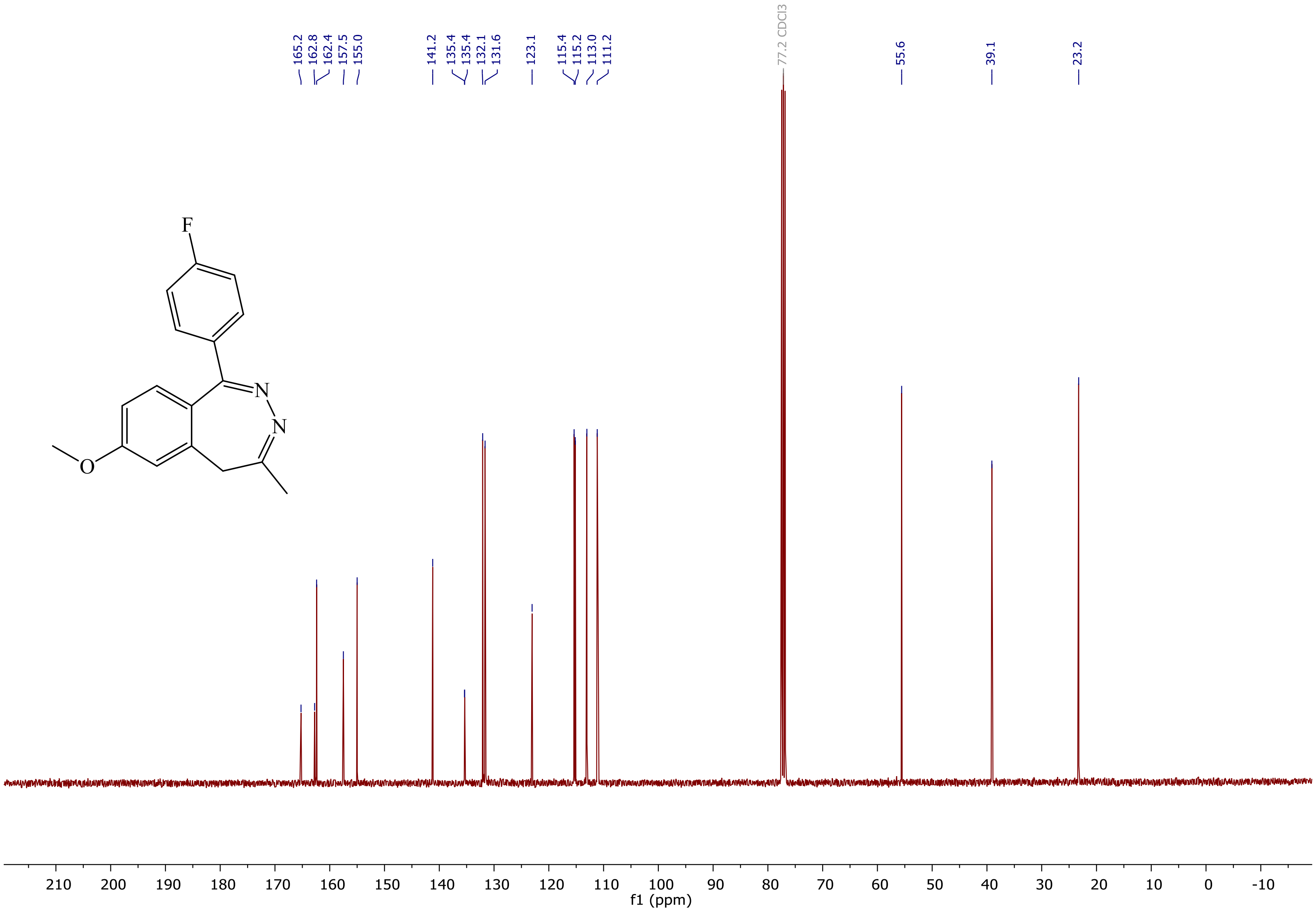


Figure S4.83. $^{13}C\ \{^{1}H\}$ **NMR (101MHz, CDCl₃) of 1-(4-fluorophenyl)-7-methoxy-4-methyl-5H-benzo[d][1,2]diazepine (3a)**

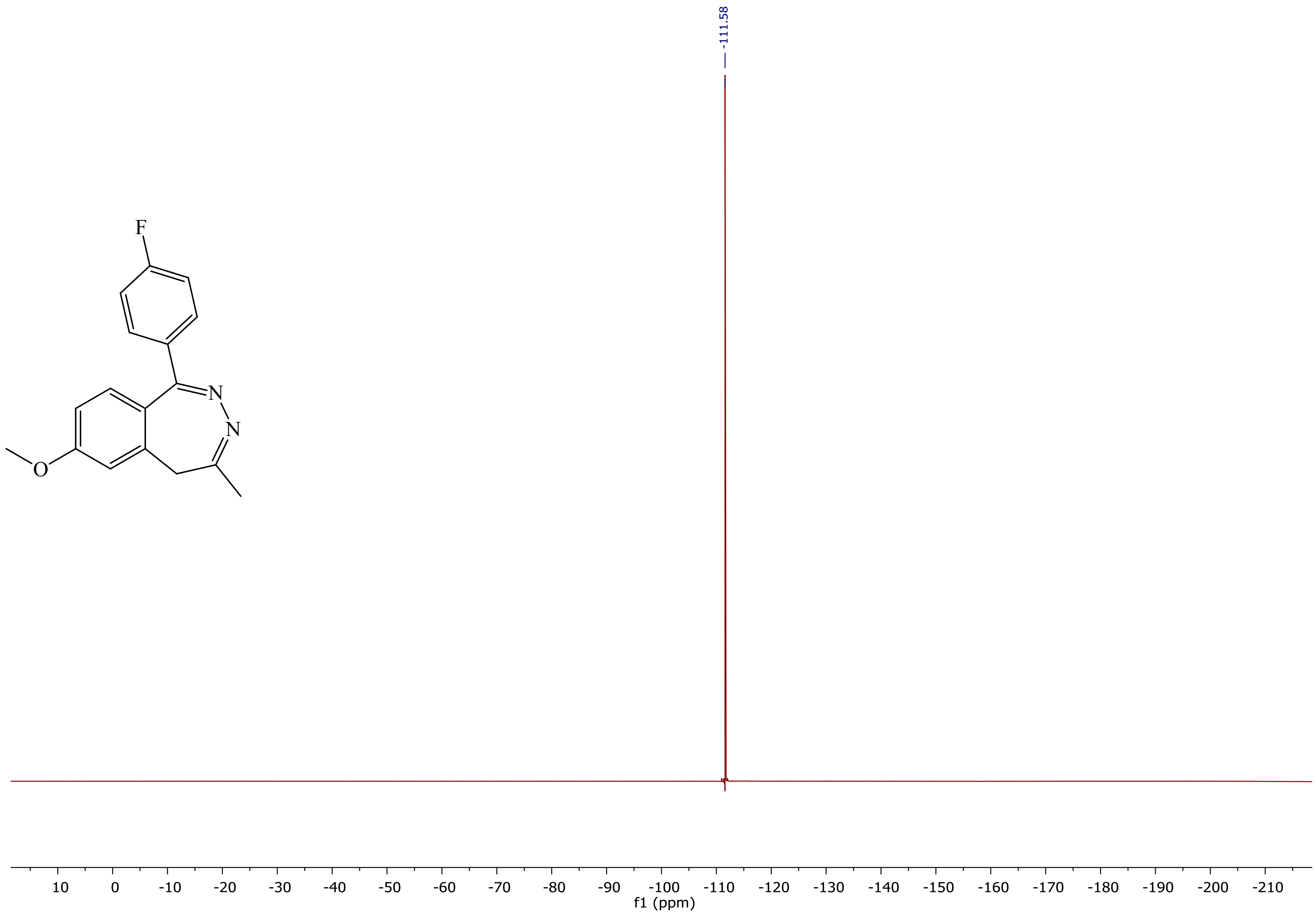


Figure S4.84. ^{19}F NMR (376 MHz, $CDCl_3$) of 1-(4-fluorophenyl)-7-methoxy-4-methyl-5H-benzo[d][1,2]diazepine (3a)

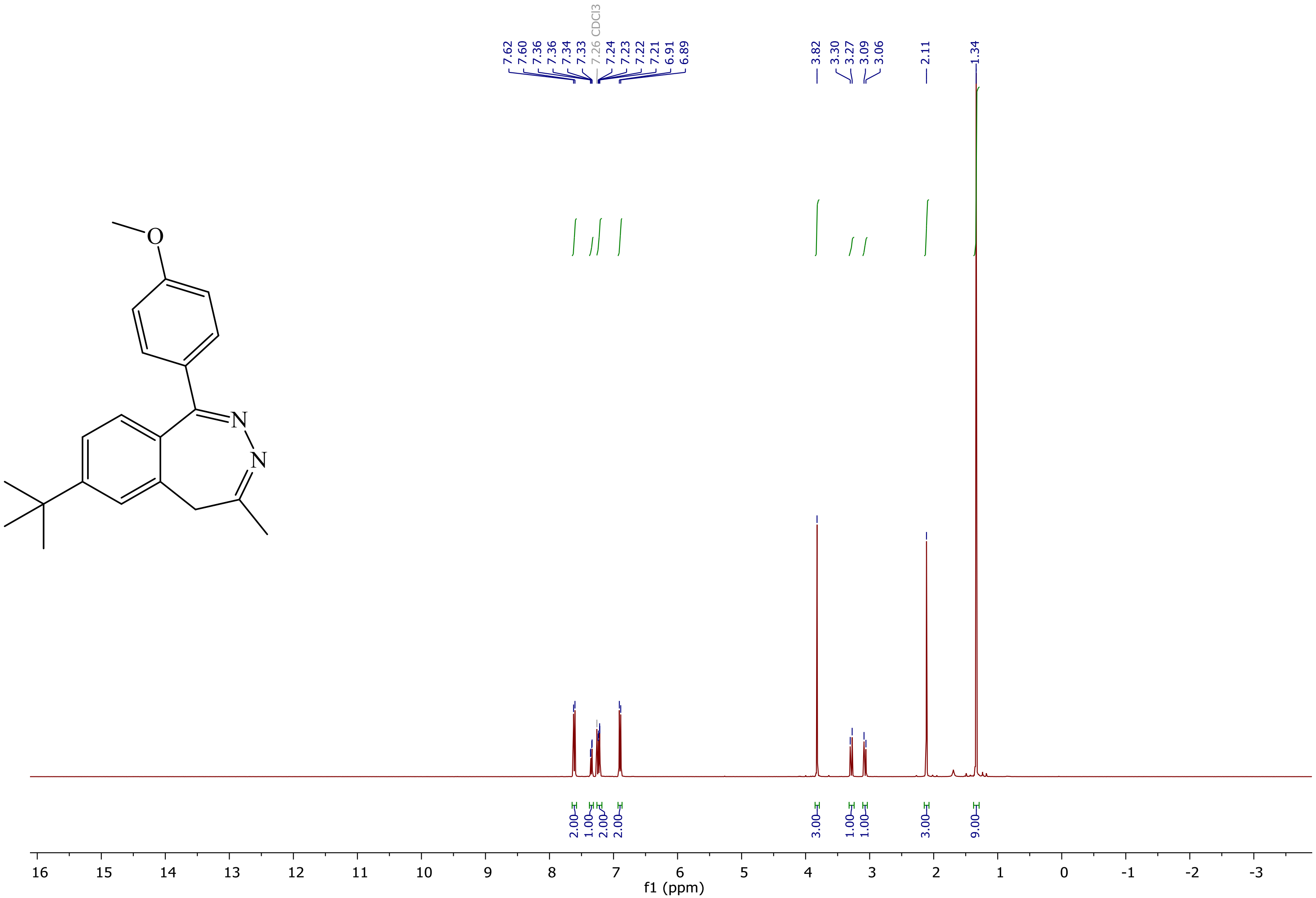


Figure S4.85. [1]H NMR (400MHz, $CDCl_3$) of 7-tert-butyl-1-(4-methoxyphenyl)-4-methyl-5H-benzo[d][1,2]diazepine (3b)

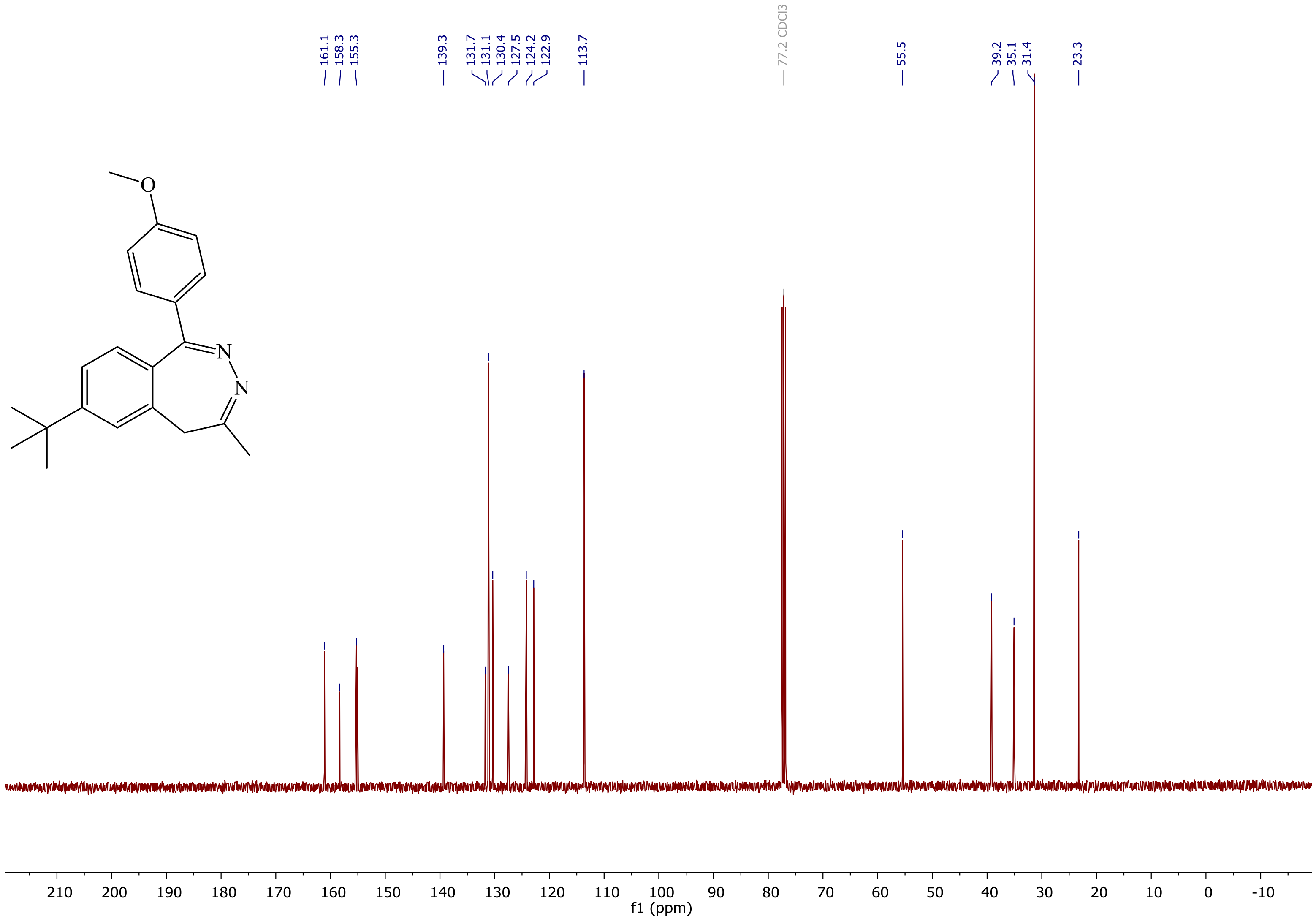


Figure S4.86. ^{13}C {^{1}H} NMR (101MHz, $CDCl_3$) of 7-tert-butyl-1-(4-methoxyphenyl)-4-methyl-5H-benzo[d][1,2]diazepine (3b)

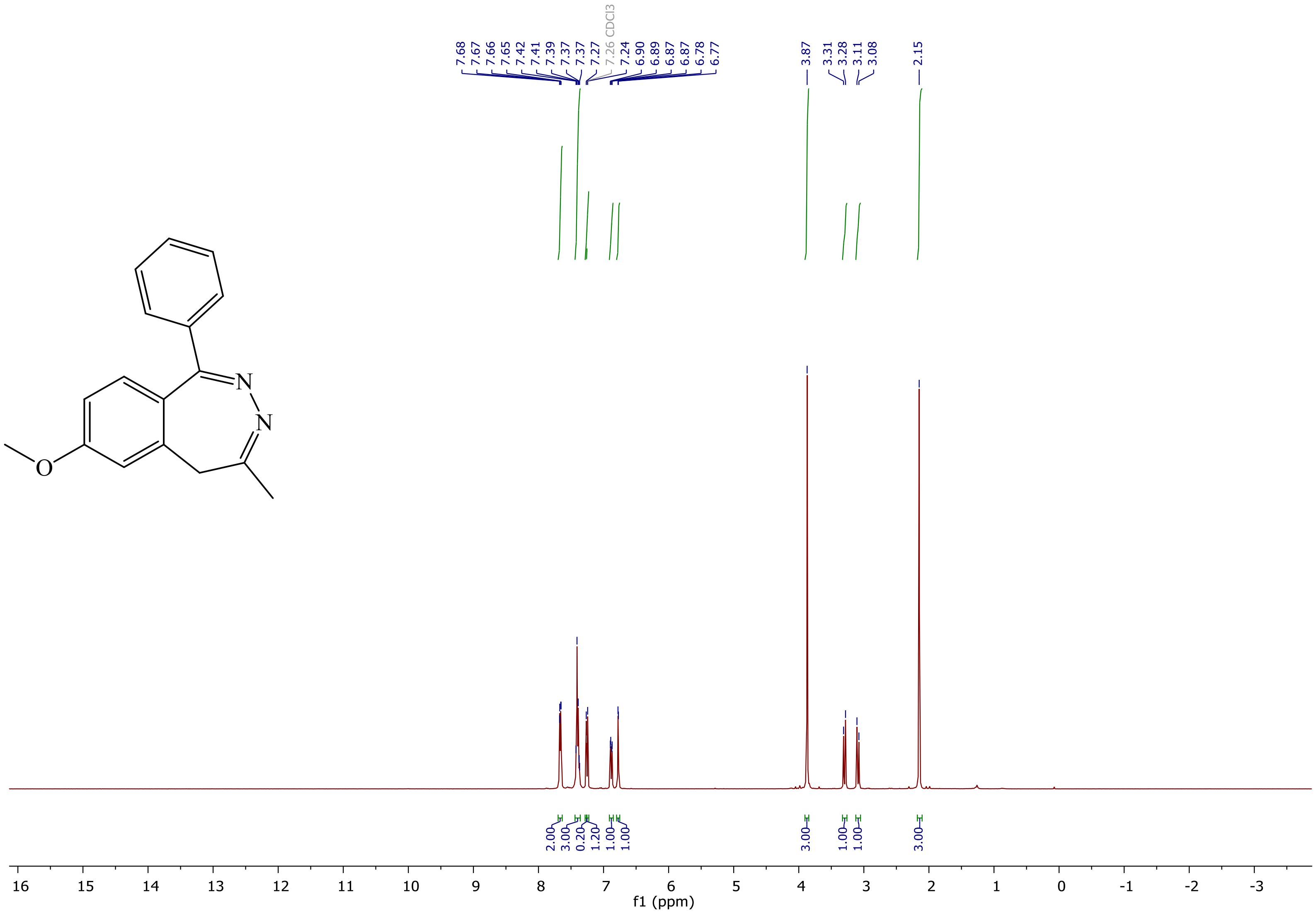


Figure S4.87. ^{1}H NMR (400MHz, $CDCl_3$) of 7-methoxy-4-methyl-1-phenyl-5H-benzo[d][1,2]diazepine (3c)

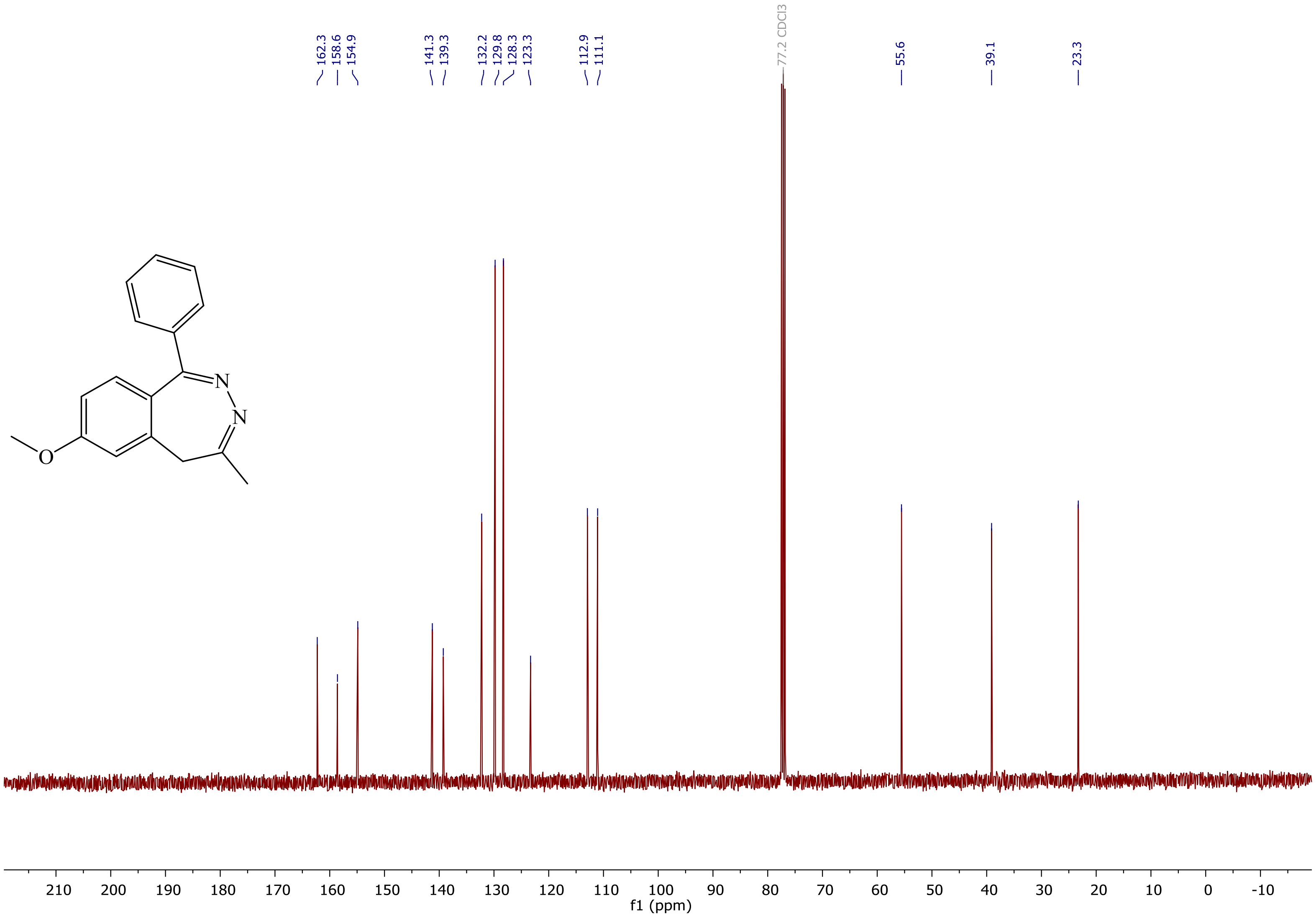


Figure S4.88. $^{13}C\ \{^{1}H\}$ NMR (101MHz, $CDCl_3$) of 7-methoxy-4-methyl-1-phenyl-5H-benzo[d][1,2]diazepine (3c)

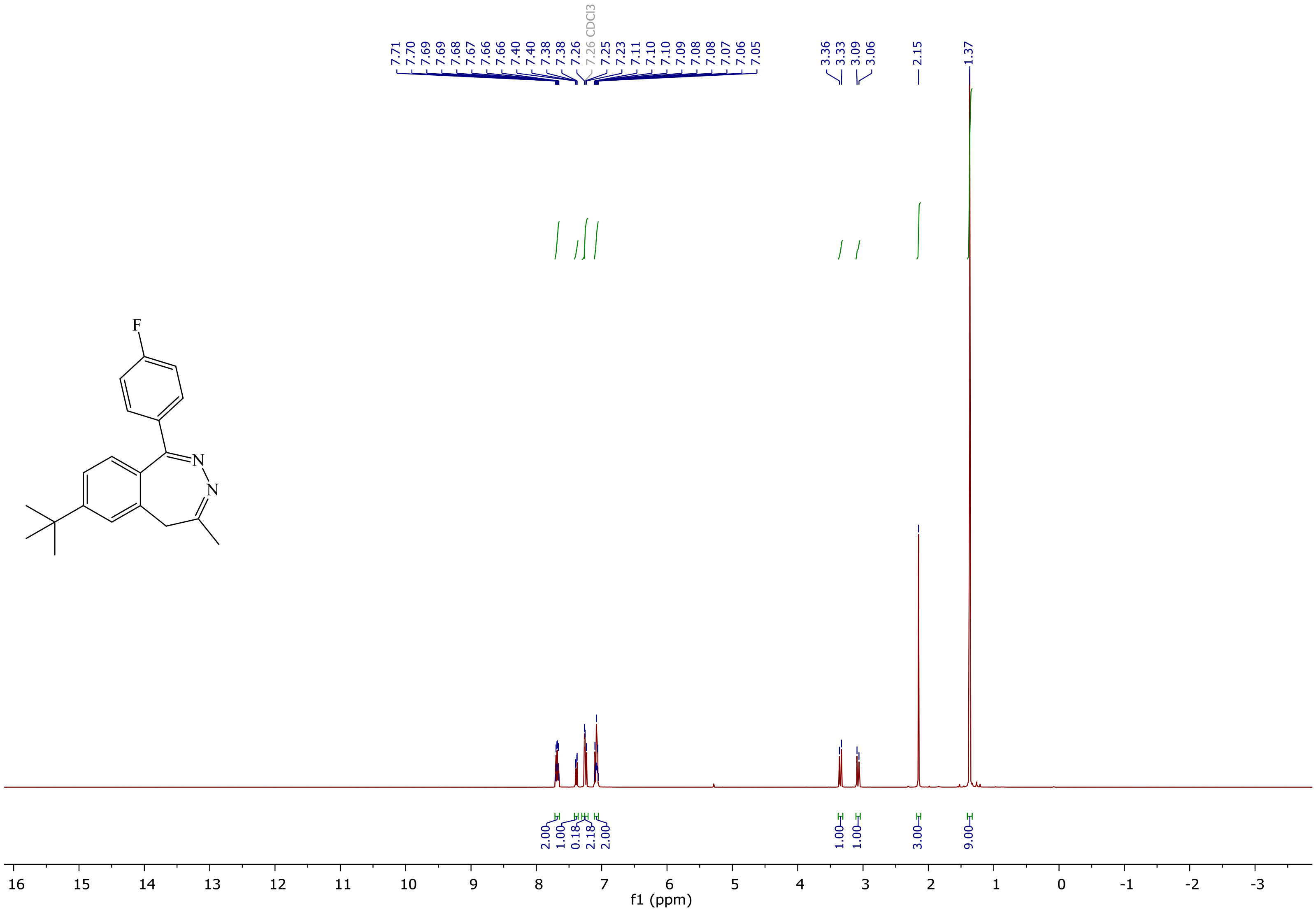


Figure S4.89. **[1]H NMR (400MHz, $CDCl_3$) of 7-tert-butyl-1-(4-fluorophenyl)-4-methyl-5H-benzo[d][1,2]diazepine (3d)**

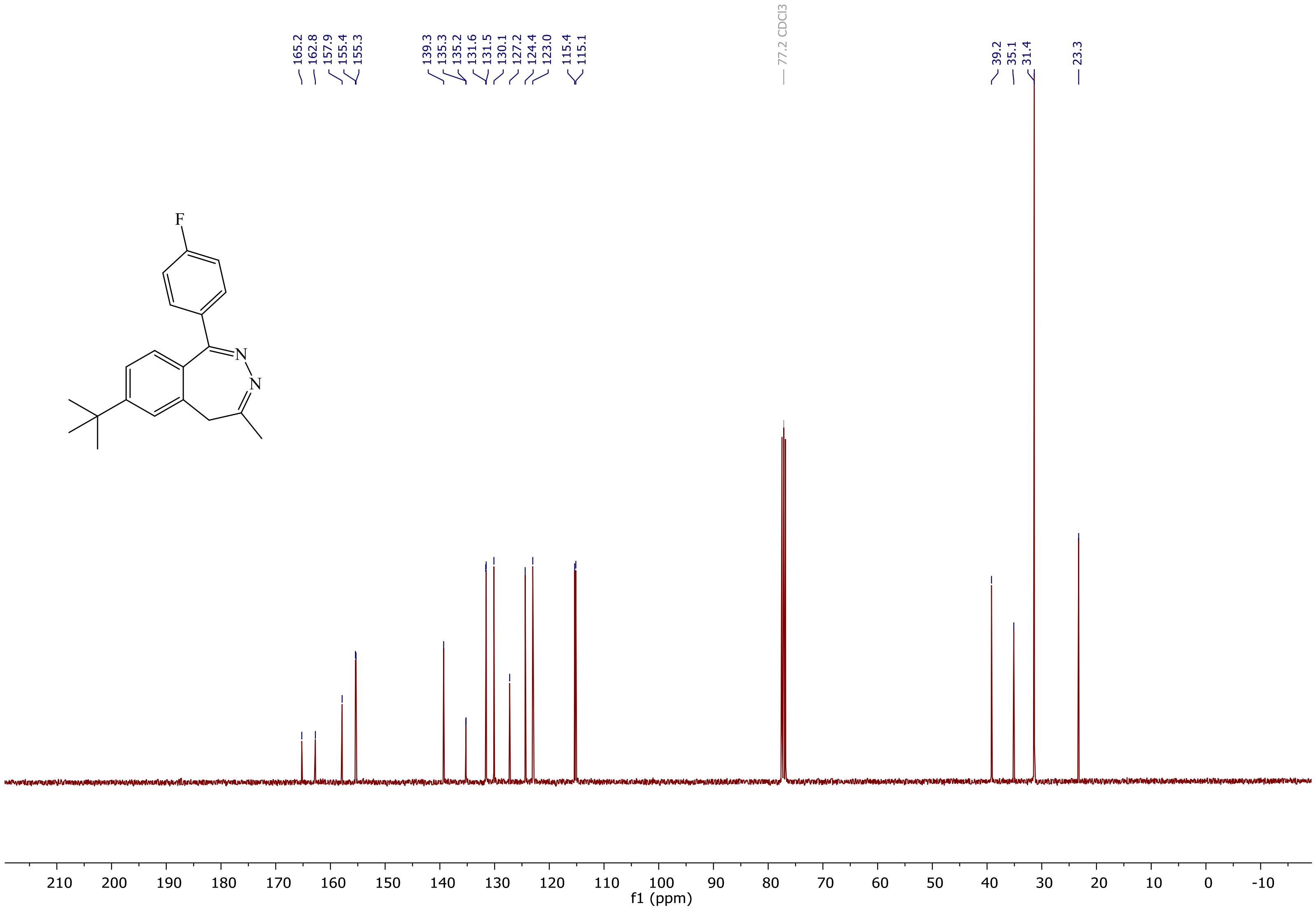


Figure S4.90. $^{13}C\{^1H\}$ **NMR (101MHz, $CDCl_3$) of 7-tert-butyl-1-(4-fluorophenyl)-4-methyl-5H-benzo[d][1,2]diazepine (3d)**

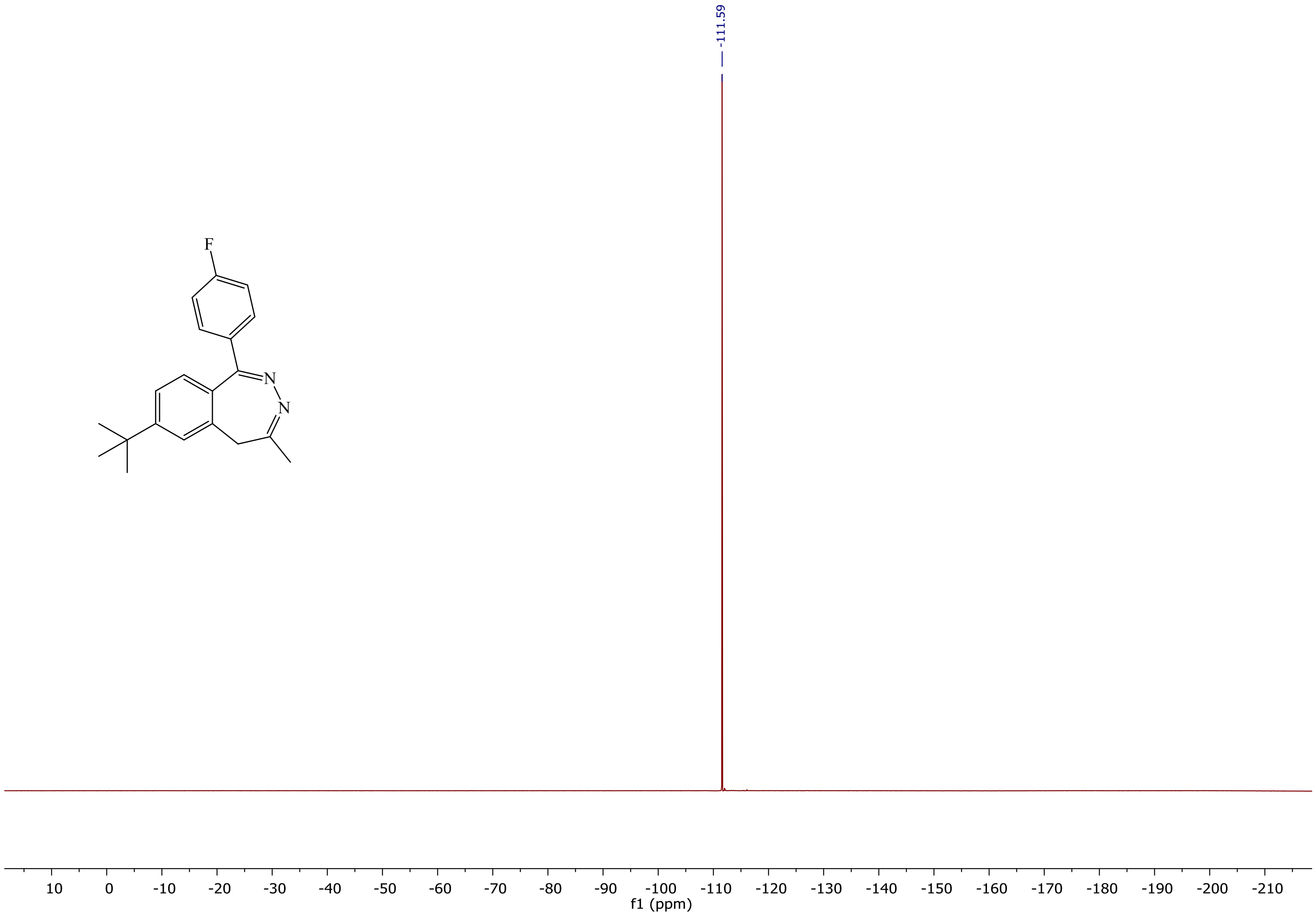


Figure S4.91. [19]F NMR (376 MHz, $CDCl_3$) of 7-tert-butyl-1-(4-fluorophenyl)-4-methyl-5H-benzo[d][1,2]diazepine (3d)

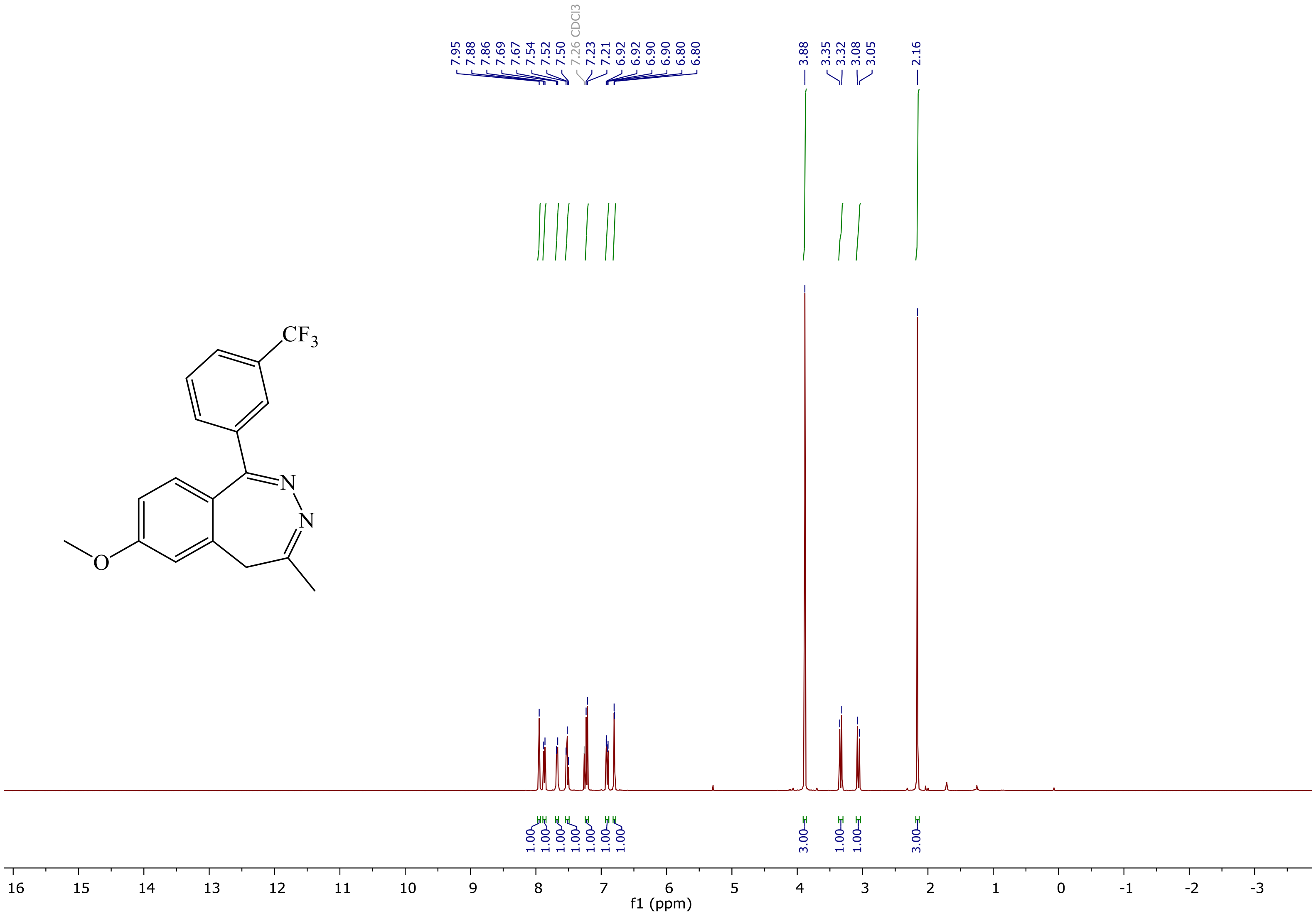


Figure S4.92. ^{1}H NMR (400MHz, $CDCl_3$) of 7-methoxy-4-methyl-1-(3-(trifluoromethyl)phenyl)-5H-benzo[d][1,2]diazepine (3e)

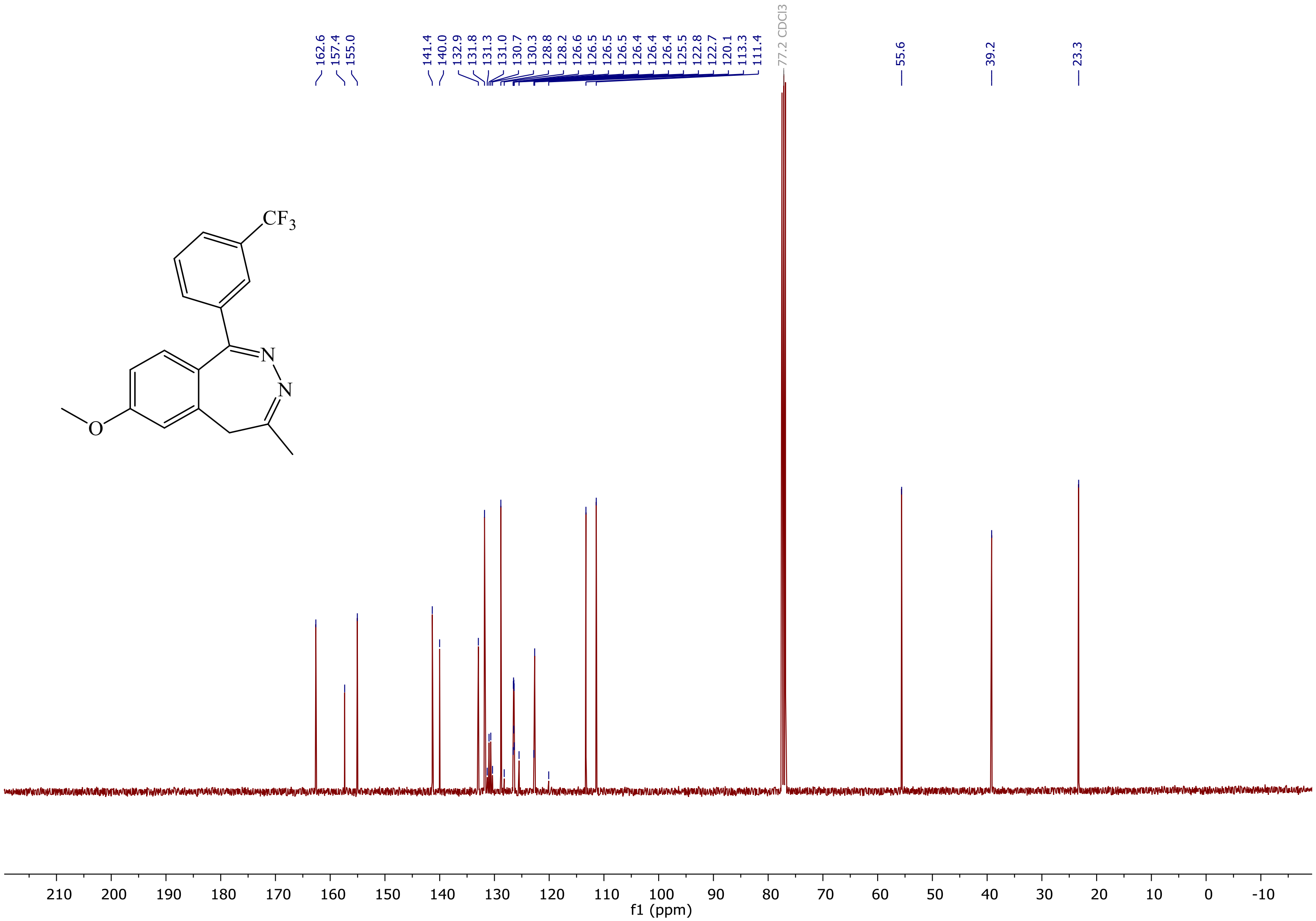


Figure S4.93. $^{13}C\ \{^1H\}$ **NMR (101MHz,** $CDCl_3$**) of 7-methoxy-4-methyl-1-(3-(trifluoromethyl)phenyl)-5H-benzo[d][1,2]diazepine (3e)**

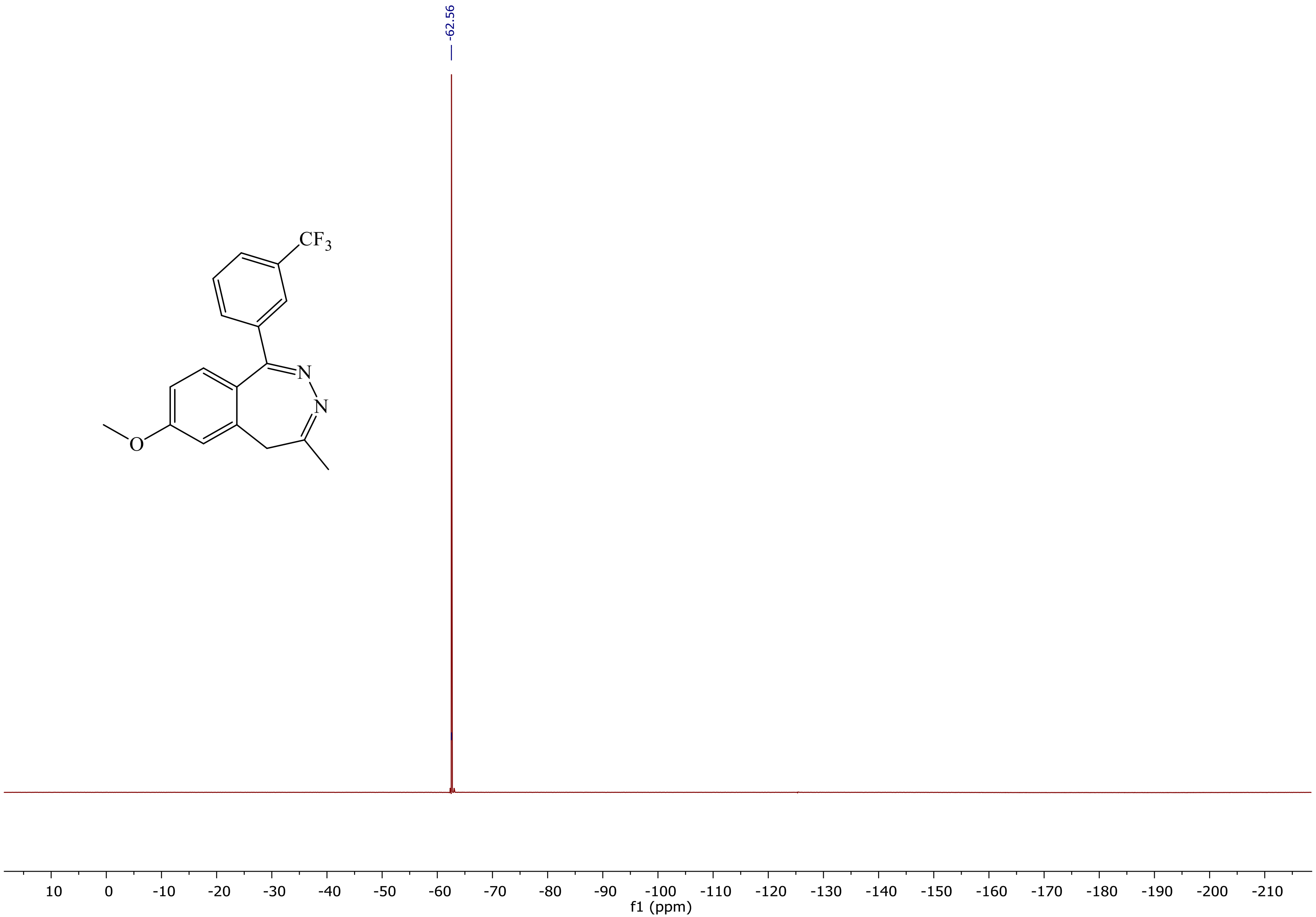
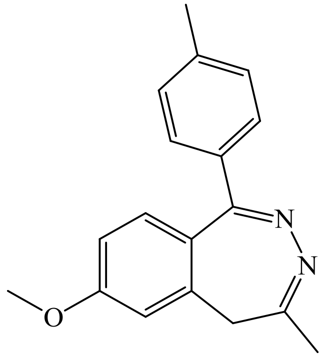


Figure S4.94. ^{19}F NMR (376 MHz, $CDCl_3$) of 7-methoxy-4-methyl-1-(3-(trifluoromethyl)phenyl)-5H-benzo[d][1,2]diazepine (3e)



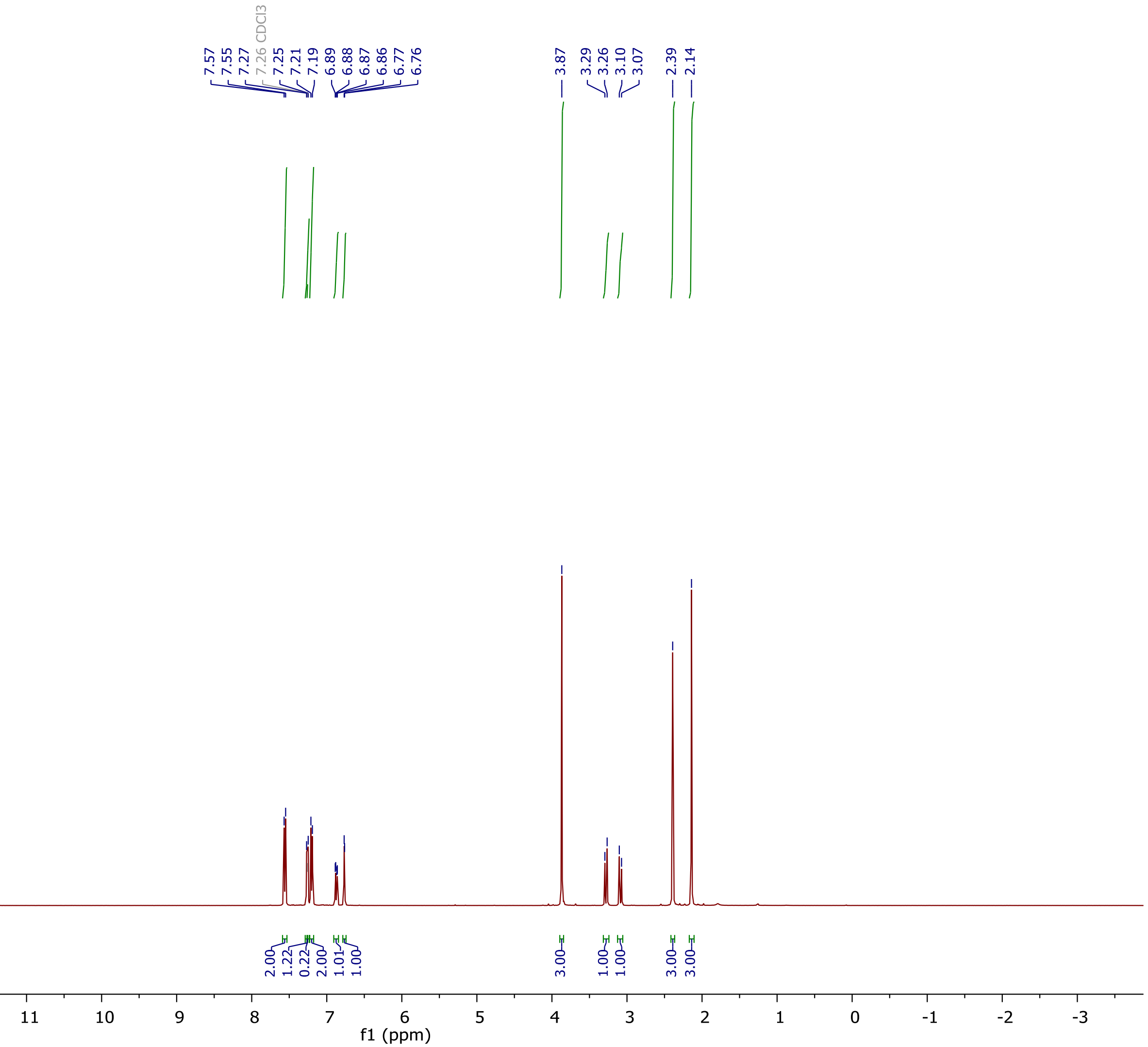


Figure S4.95. ^{1}H NMR (400MHz, $CDCl_3$) of 7-methoxy-4-methyl-1-p-tolyl-5H-benzo[d][1,2]diazepine (3f)

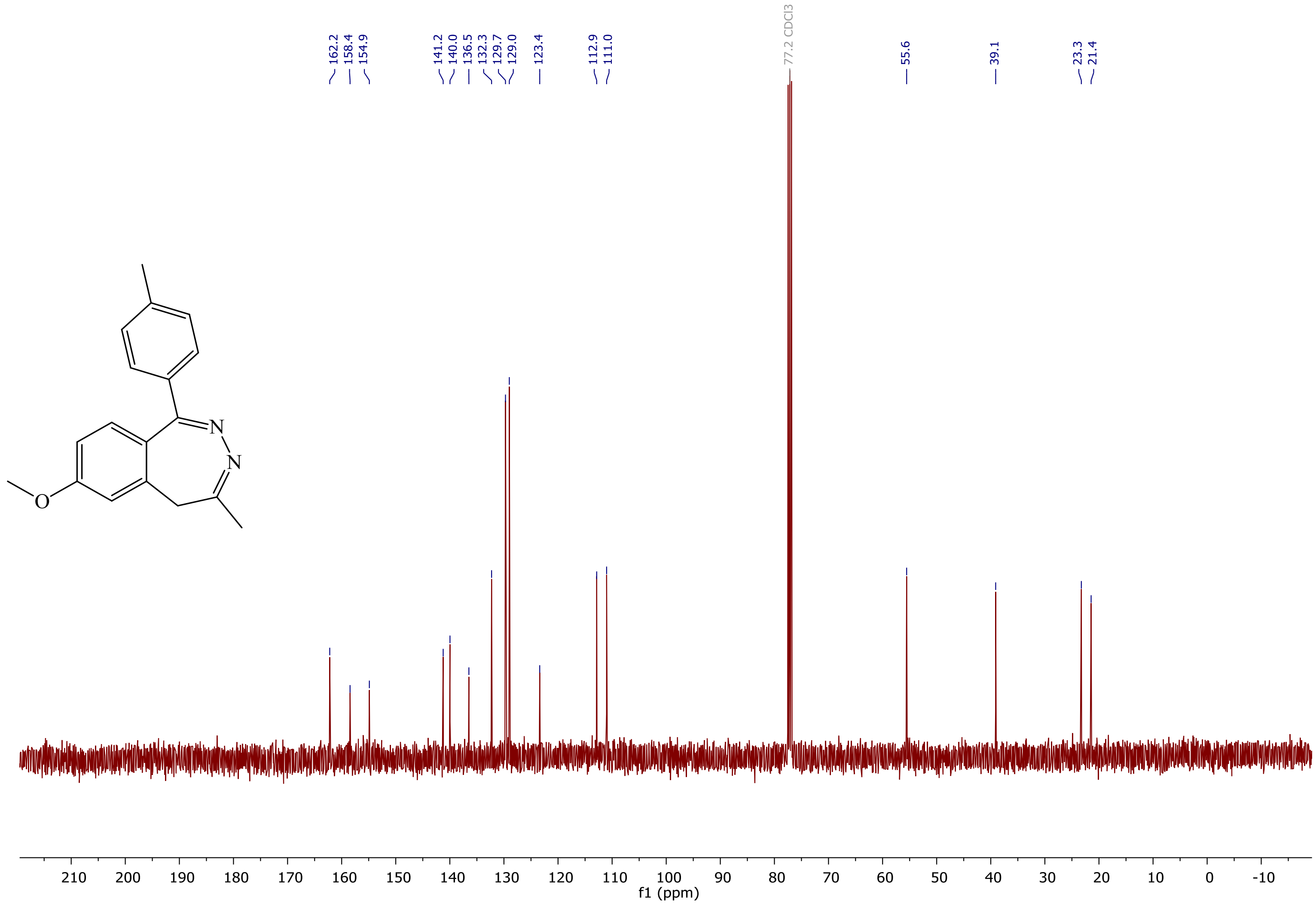


Figure S4.96. $^{13}C\{^{1}H\}$ NMR (101MHz, $CDCl_3$) of 7-methoxy-4-methyl-1-p-tolyl-5H-benzo[d][1,2]diazepine (3f)

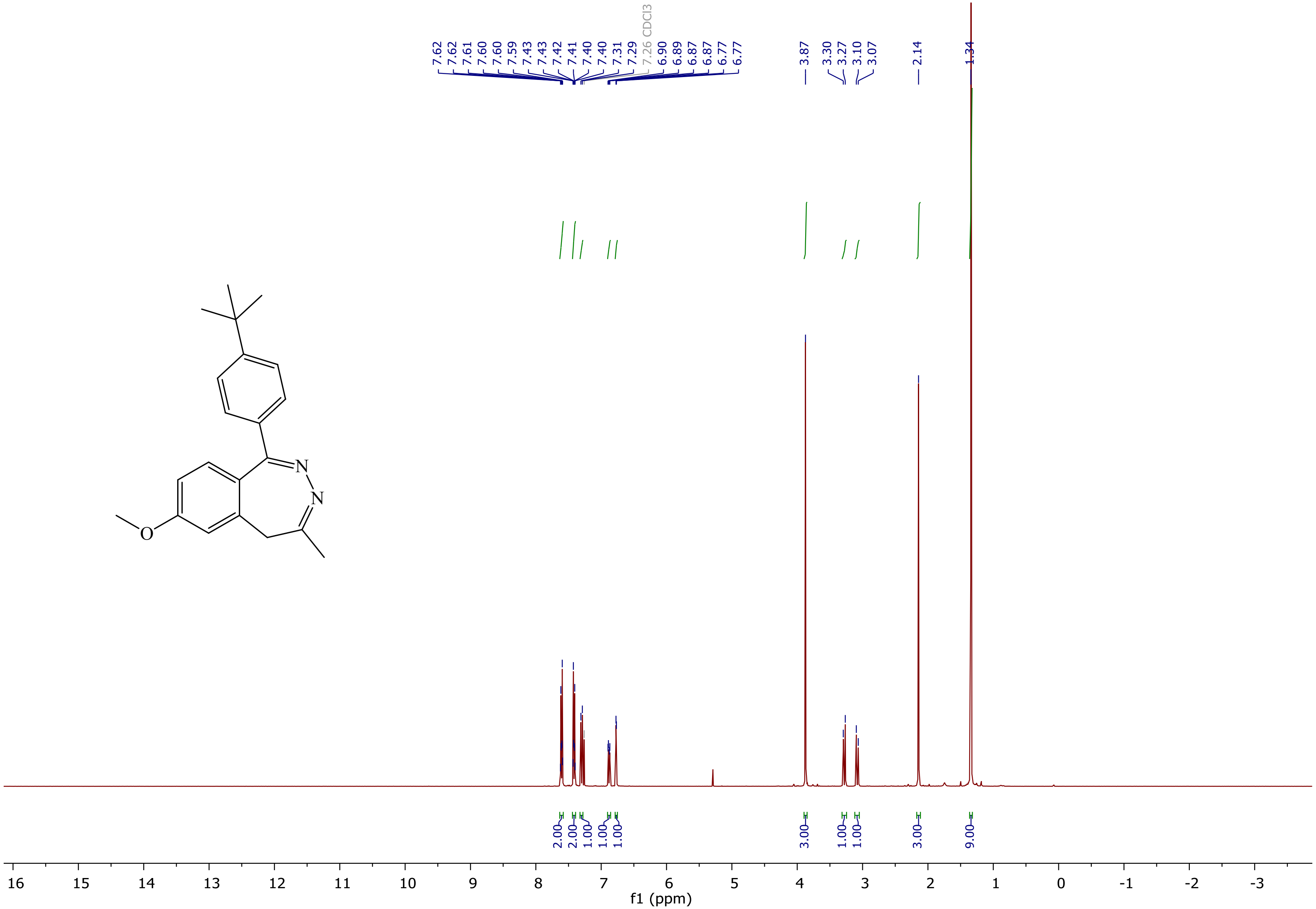


Figure S4.97. ^{1}H NMR (400MHz, $CDCl_3$) of 1-(4-tert-butylphenyl)-7-methoxy-4-methyl-5H-benzo[d][1,2]diazepine (3g)

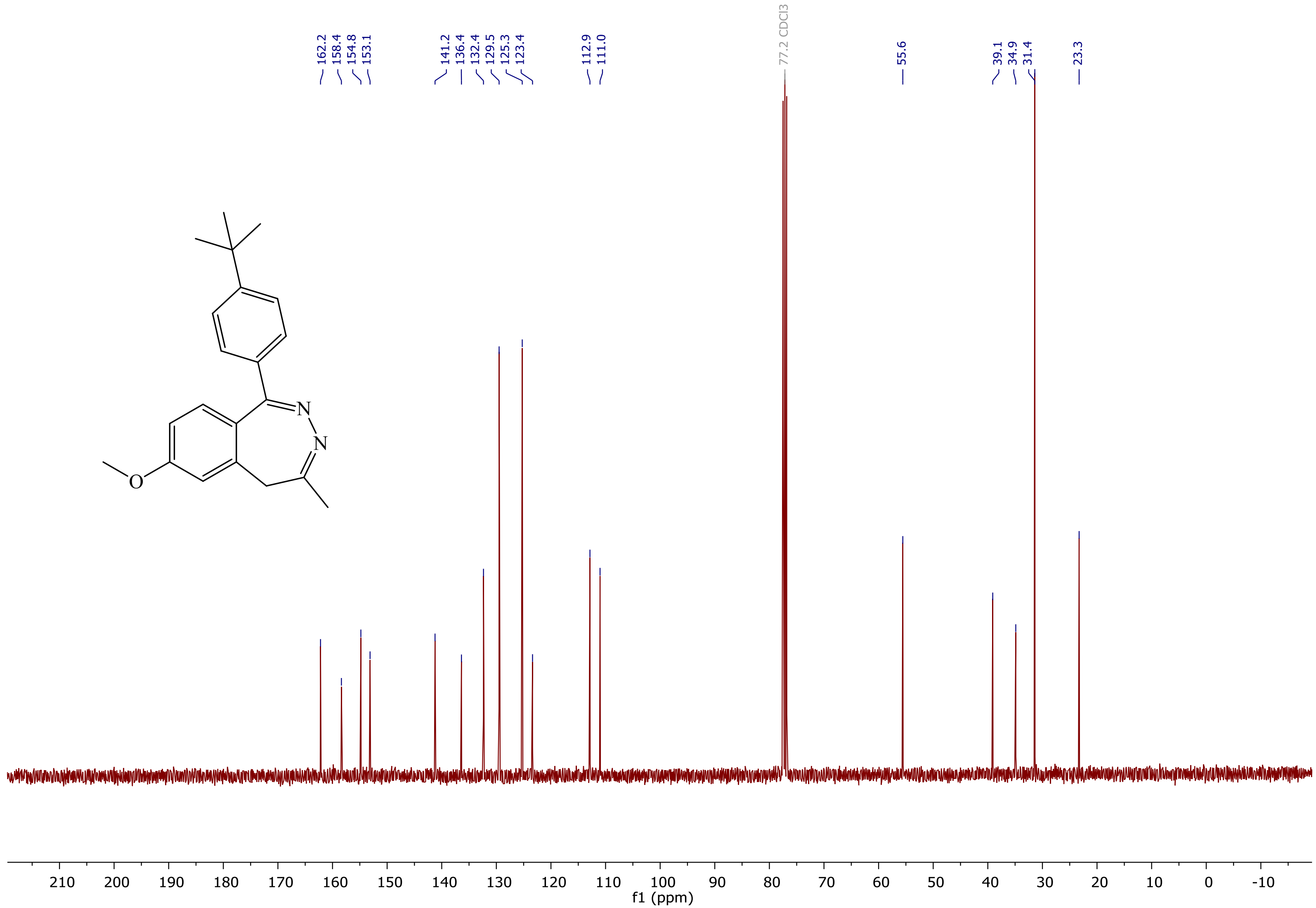


Figure S4.98. $^{13}C\ \{^1H\}$ **NMR (101MHz,** $CDCl_3$**) of 1-(4-tert-butylphenyl)-7-methoxy-4-methyl-5H-benzo[d][1,2]diazepine (3g)**

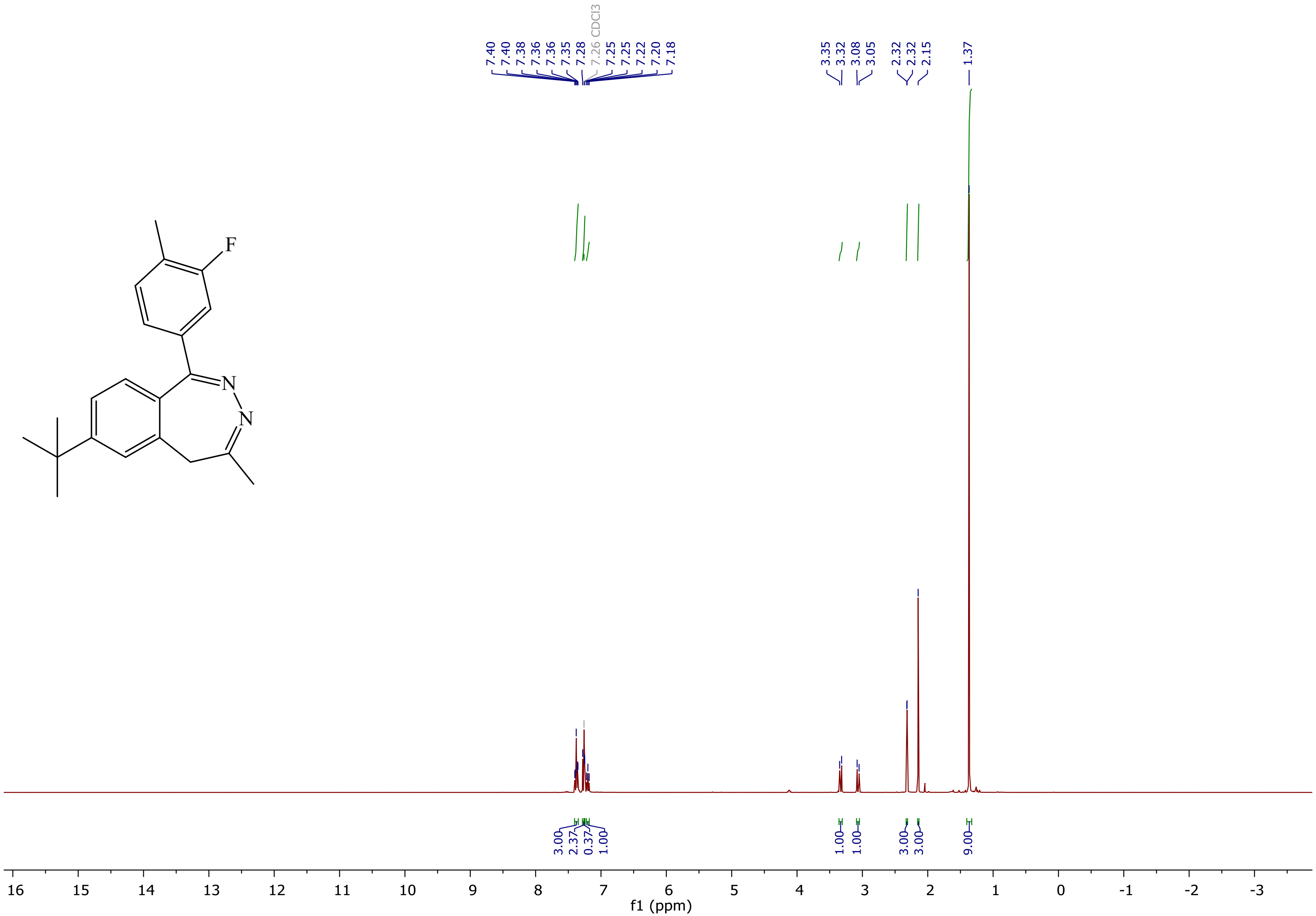


Figure S4.99. ^{1}**H NMR (400MHz,** $CDCl_3$**) of 7-tert-butyl-1-(3-fluoro-4-methylphenyl)-4-methyl-5H-benzo[d][1,2]diazepine (3h)**

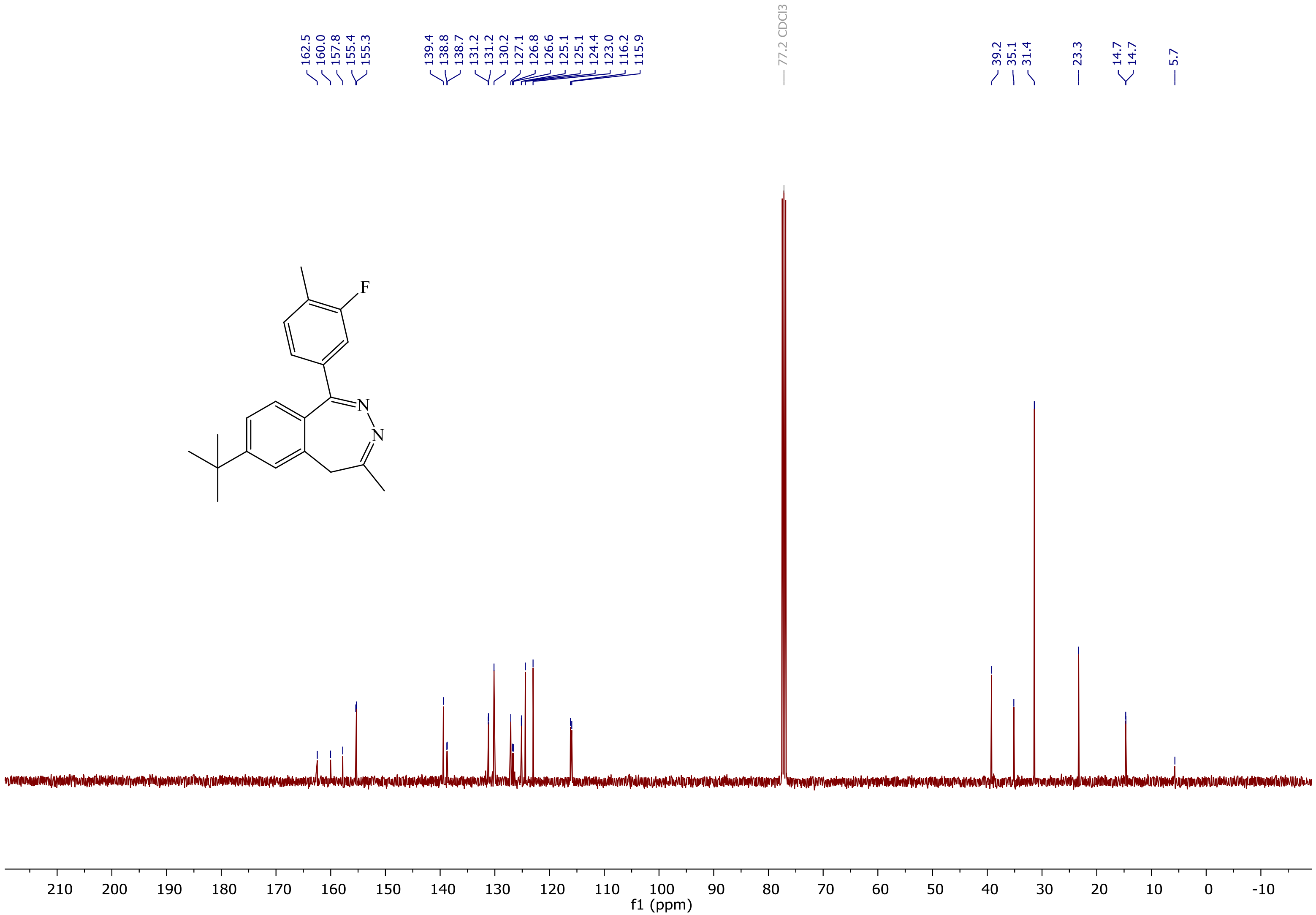


Figure S4.100. $^{13}C\ \{^1H\}$ **NMR (101MHz, CDCl$_3$) of 7-tert-butyl-1-(3-fluoro-4-methylphenyl)-4-methyl-5H-benzo[d][1,2]diazepine (3h)**

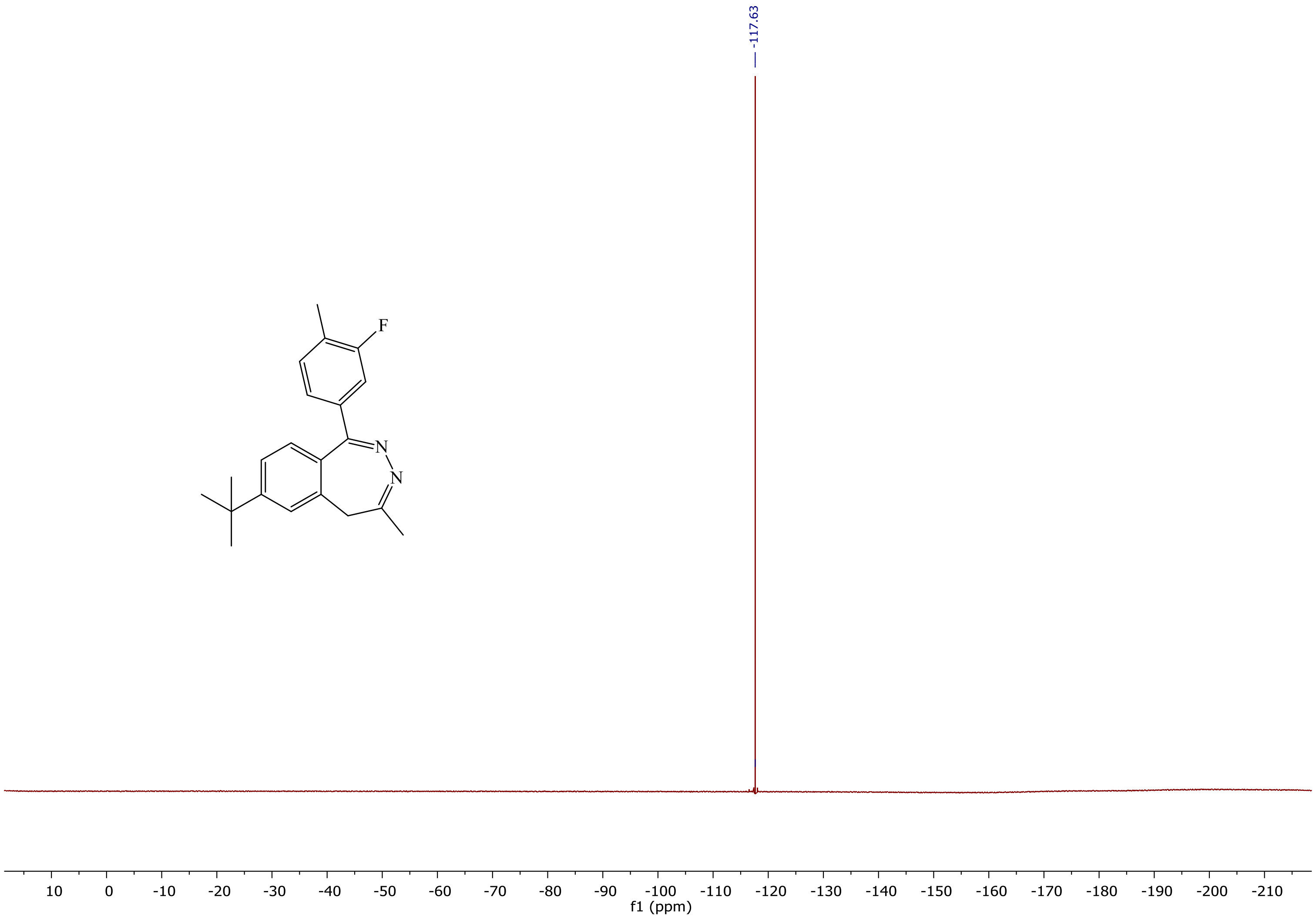


Figure S4.101. [19]F NMR (376 MHz, $CDCl_3$) of 7-tert-butyl-1-(3-fluoro-4-methylphenyl)-4-methyl-5H-benzo[d][1,2]diazepine (3h)

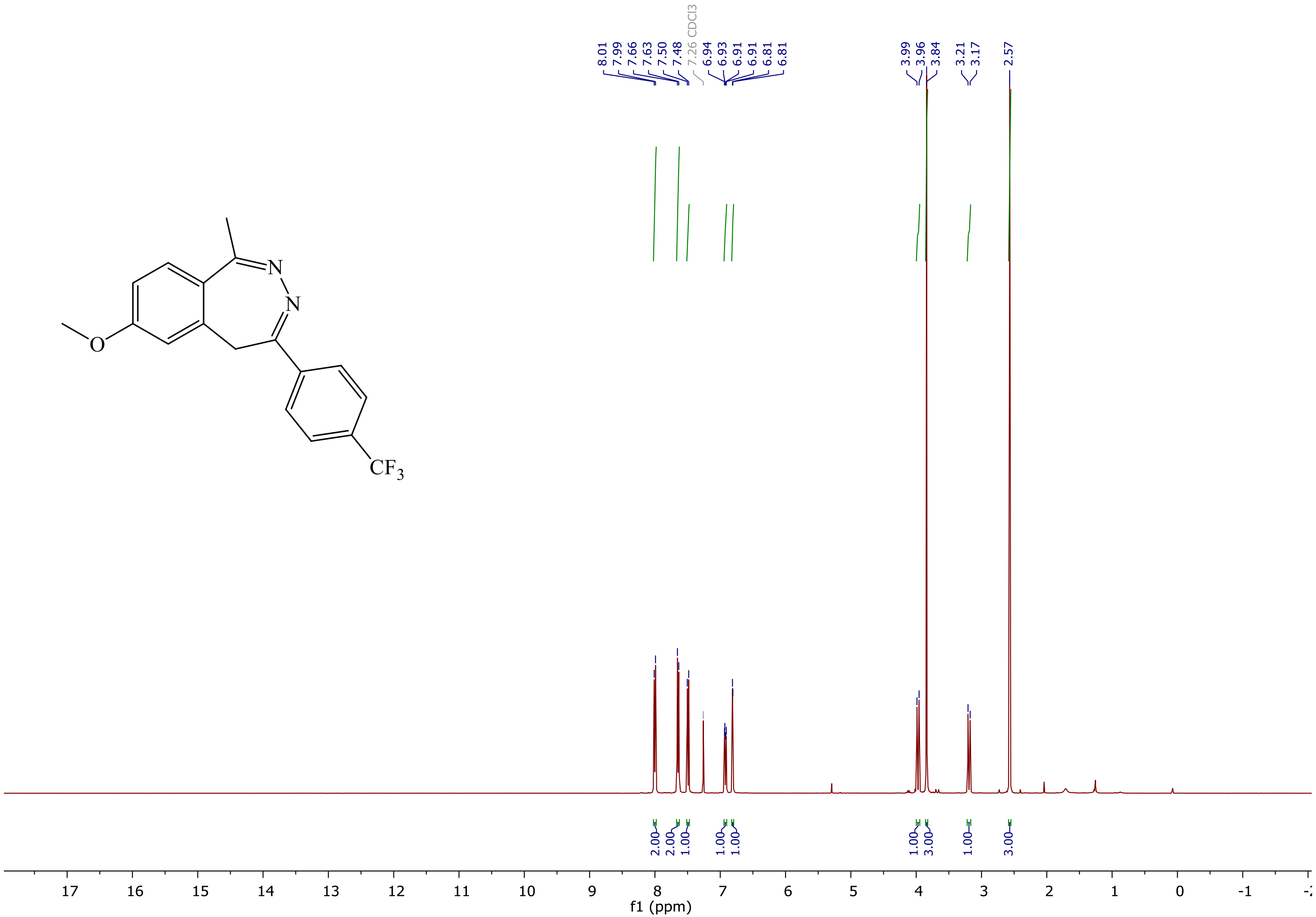


Figure S4.102. ¹H NMR (400MHz, $CDCl_3$) of 7-methoxy-1-methyl-4-(4-(trifluoromethyl)phenyl)-5H-benzo[d][1,2]diazepine (3i)

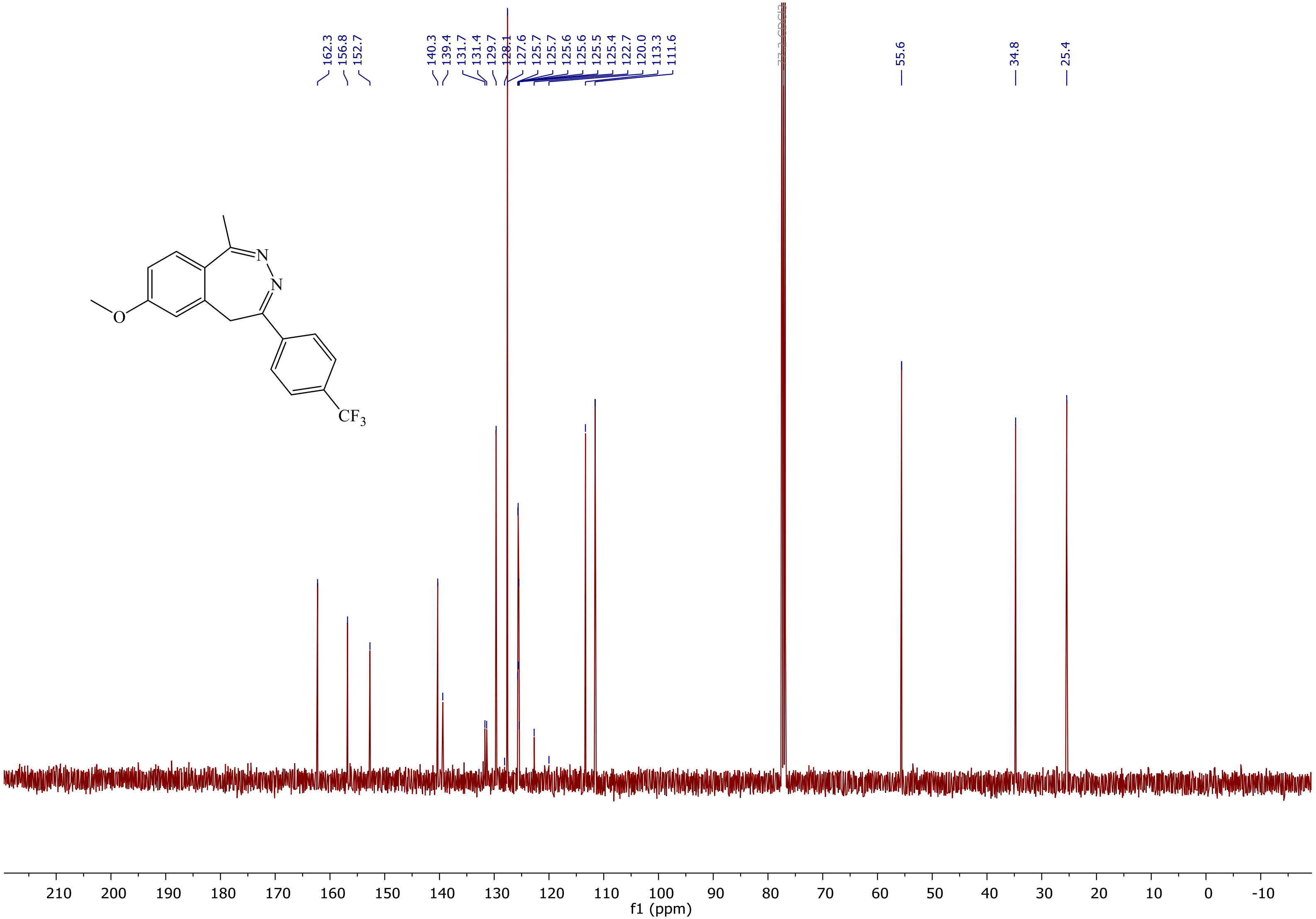


Figure S4.103. $^{13}C\{^{1}H\}$ **NMR (101MHz, $CDCl_3$) of 7-methoxy-1-methyl-4-(4-(trifluoromethyl)phenyl)-5H-benzo[d][1,2]diazepine (3i)**

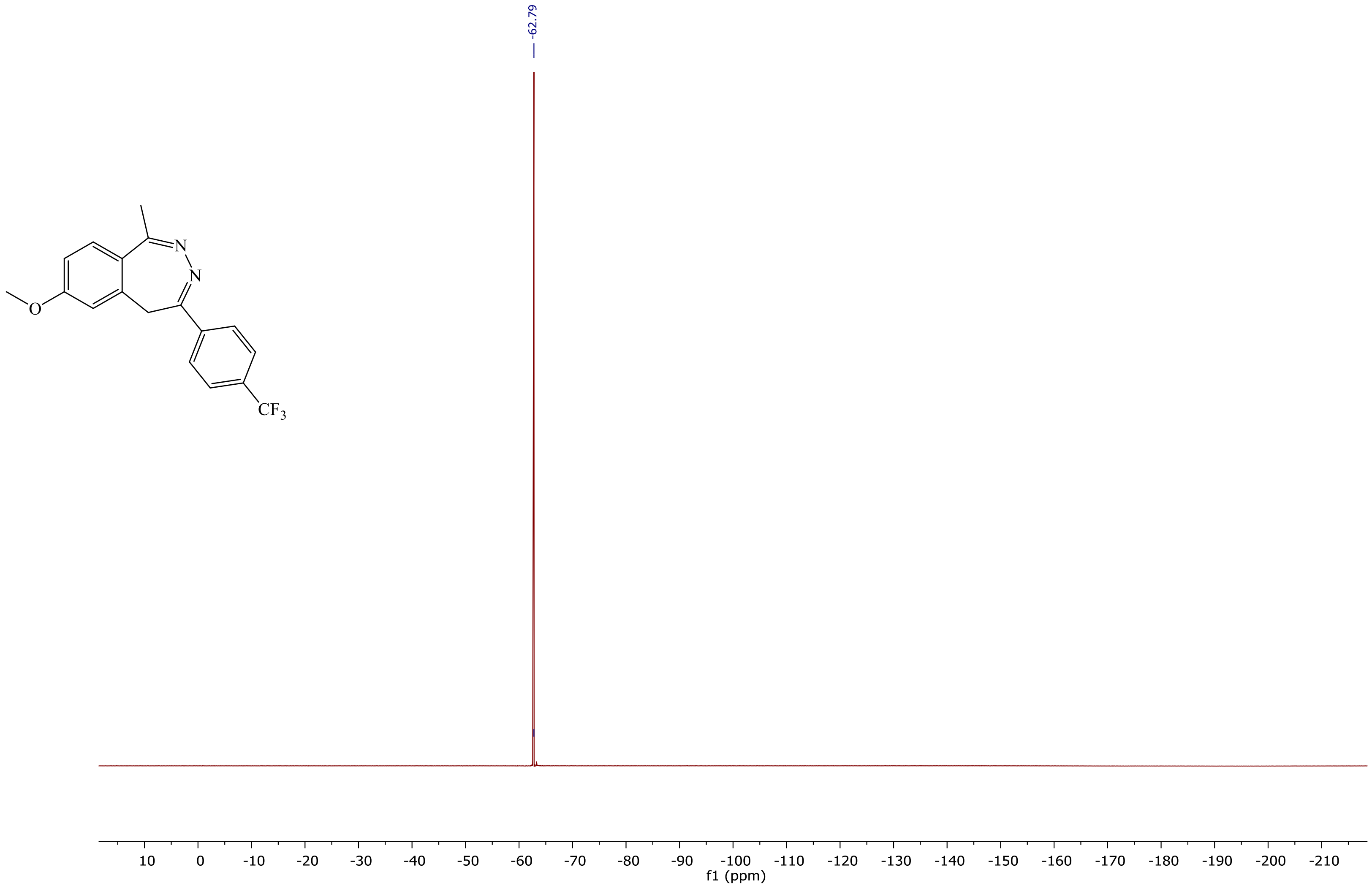


Figure S4.104. ^{19}F NMR (376 MHz, $CDCl_3$) of 7-methoxy-1-methyl-4-(4-(trifluoromethyl)phenyl)-5H-benzo[d][1,2]diazepine (3i)

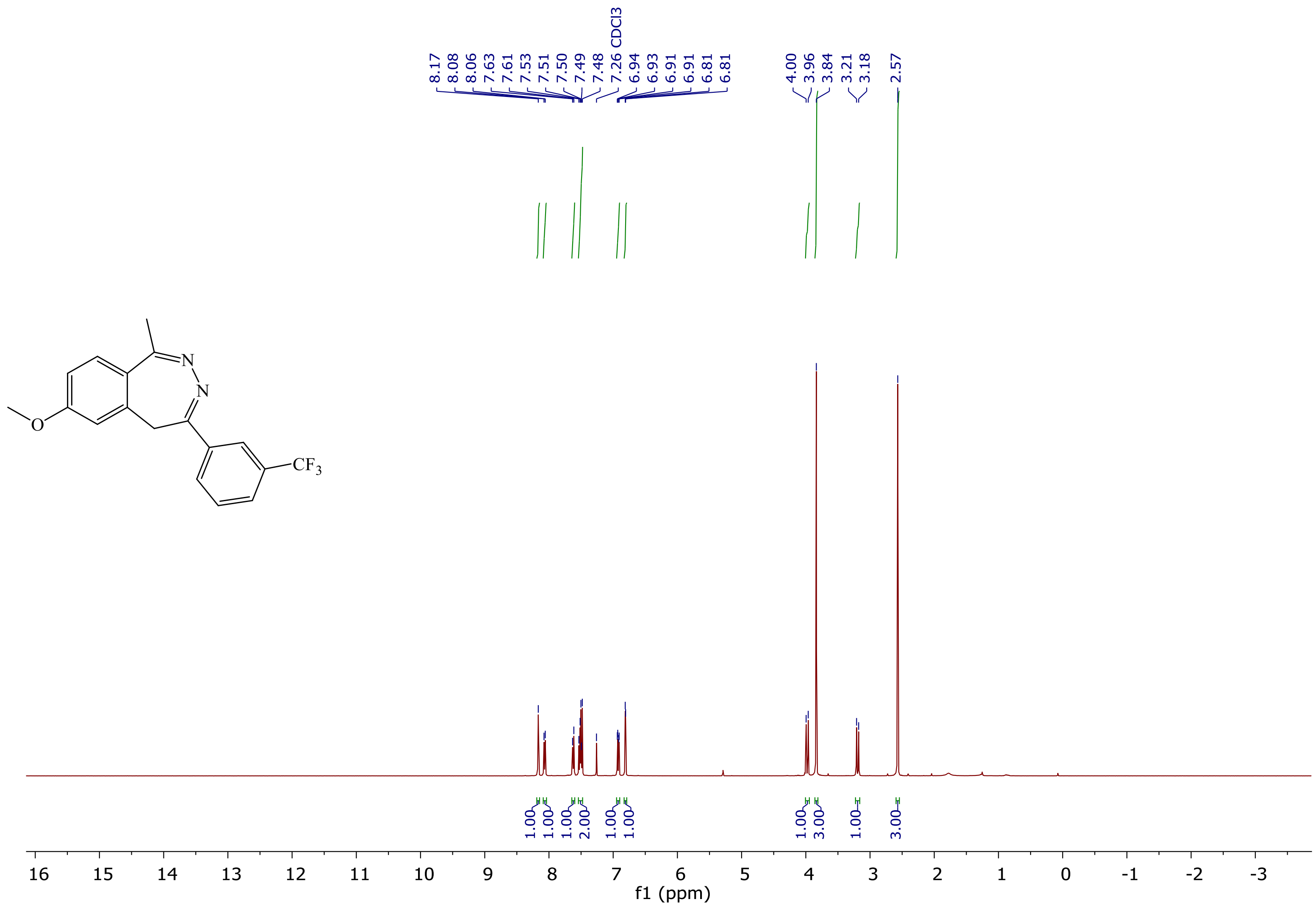


Figure S4.105. ^{1}H NMR (400MHz, $CDCl_3$) of 7-methoxy-1-methyl-4-(3-(trifluoromethyl)phenyl)-5H-benzo[d][1,2]diazepine (3j)

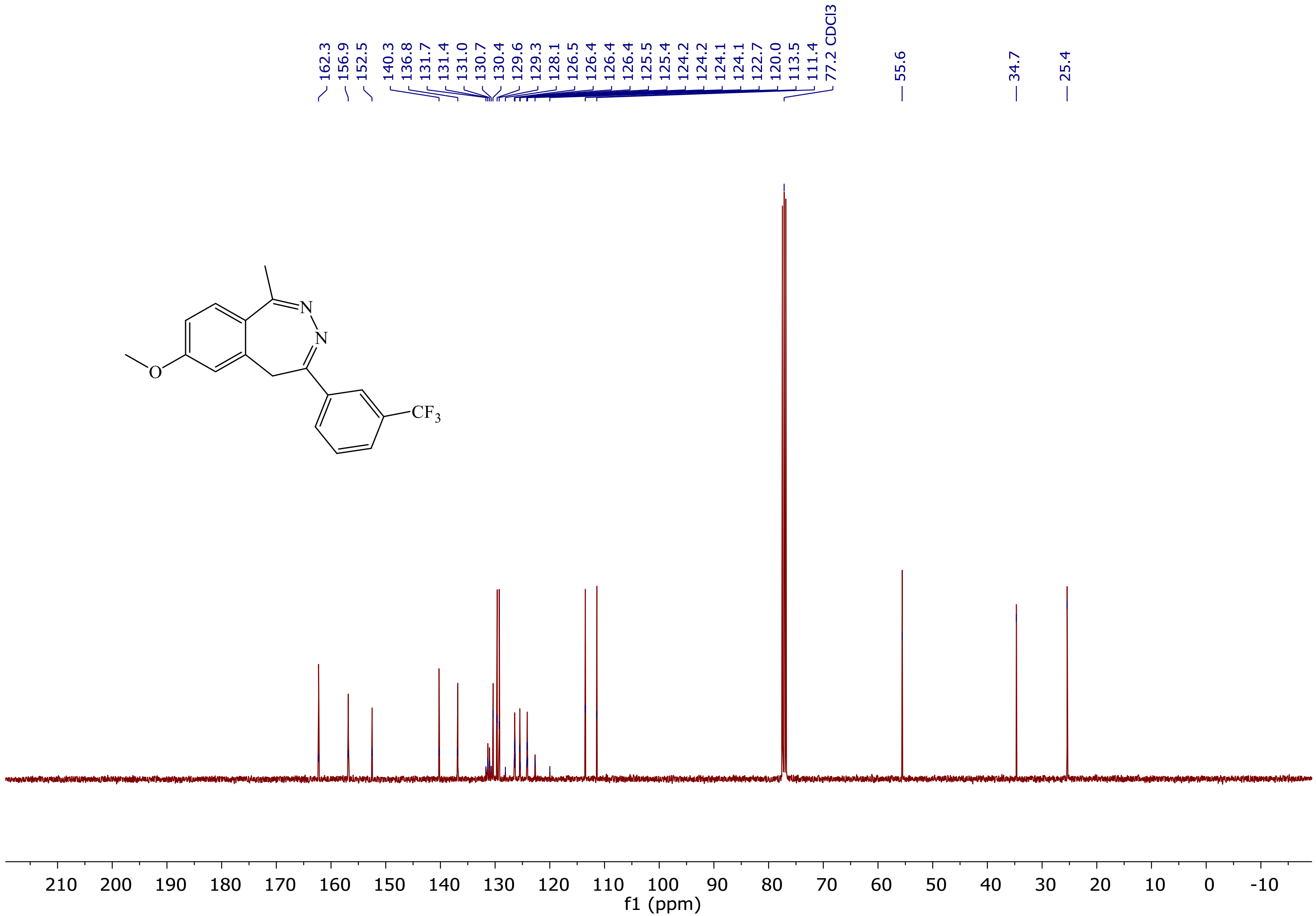


Figure S4.106. $^{13}C\ \{^{1}H\}$ **NMR (101MHz,** $CDCl_3$**) of 7-methoxy-1-methyl-4-(3-(trifluoromethyl)phenyl)-5H-benzo[d][1,2]diazepine (3j)**

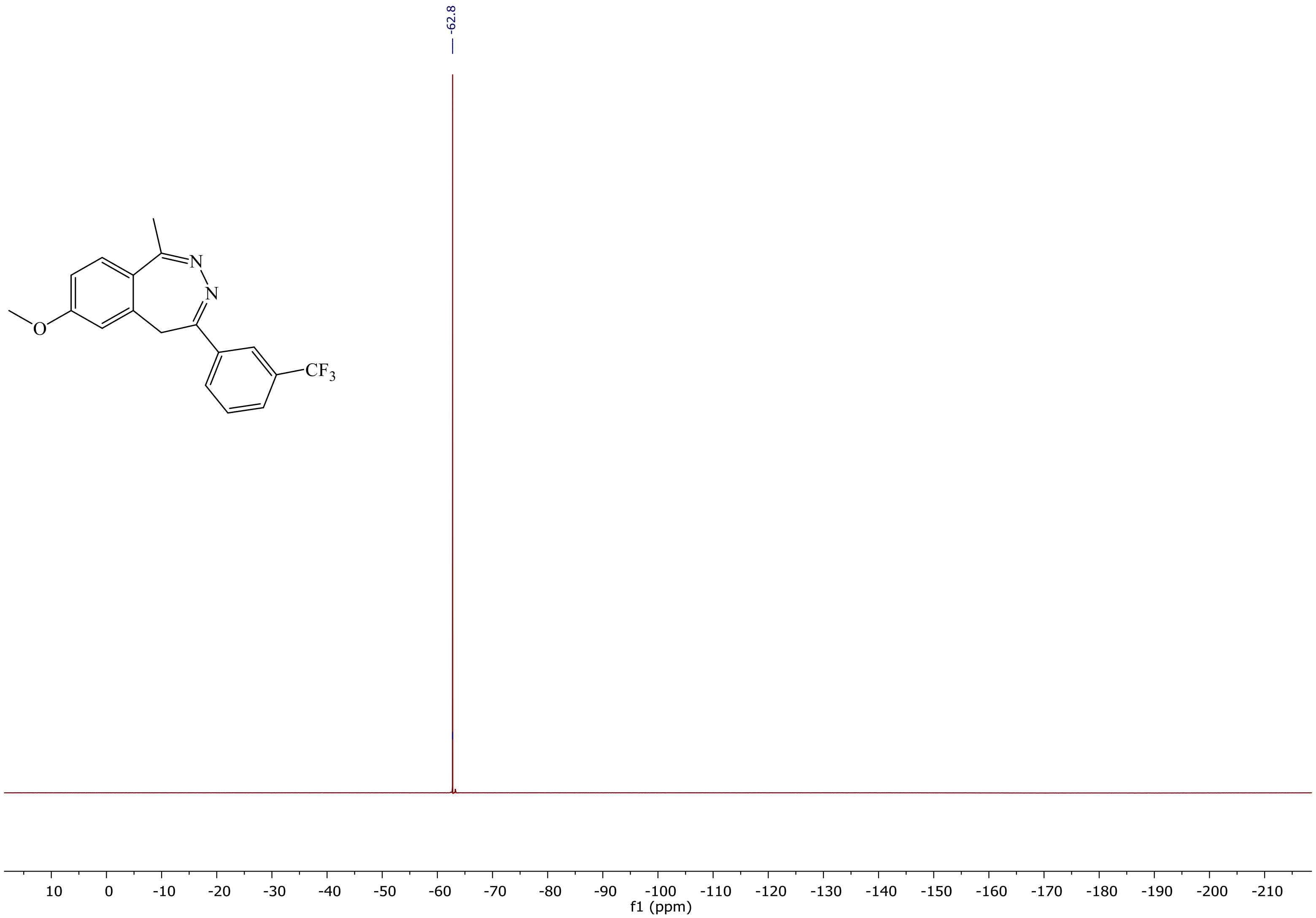


Figure S4.107. ^{19}**F NMR (376 MHz,** $CDCl_3$**) of 7-methoxy-1-methyl-4-(3-(trifluoromethyl)phenyl)-5H-benzo[d][1,2]diazepine (3j)**

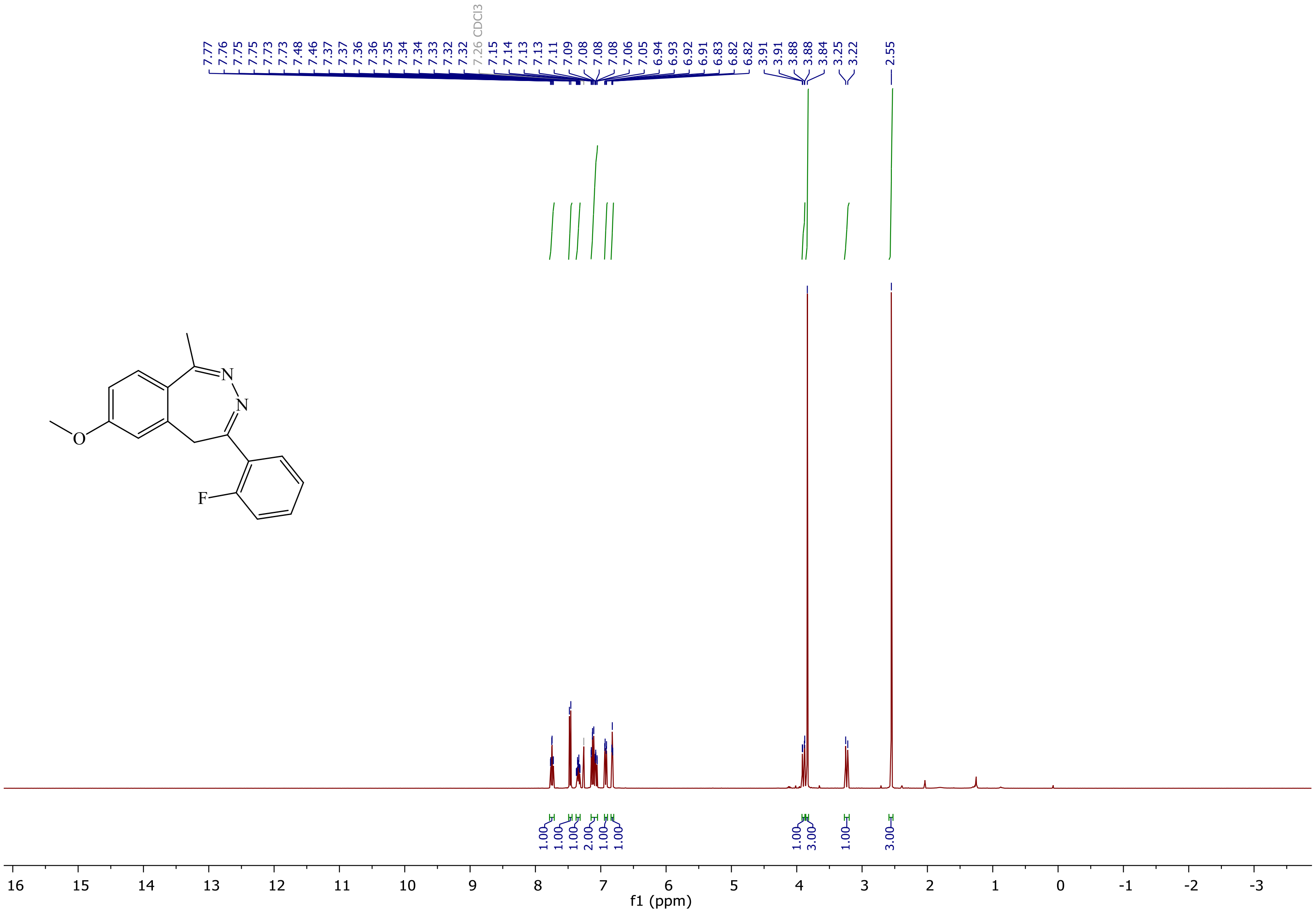


Figure S4.108. ^{1}H NMR (400MHz, $CDCl_3$) of 4-(2-fluorophenyl)-7-methoxy-1-methyl-5H-benzo[d][1,2]diazepine (3k)

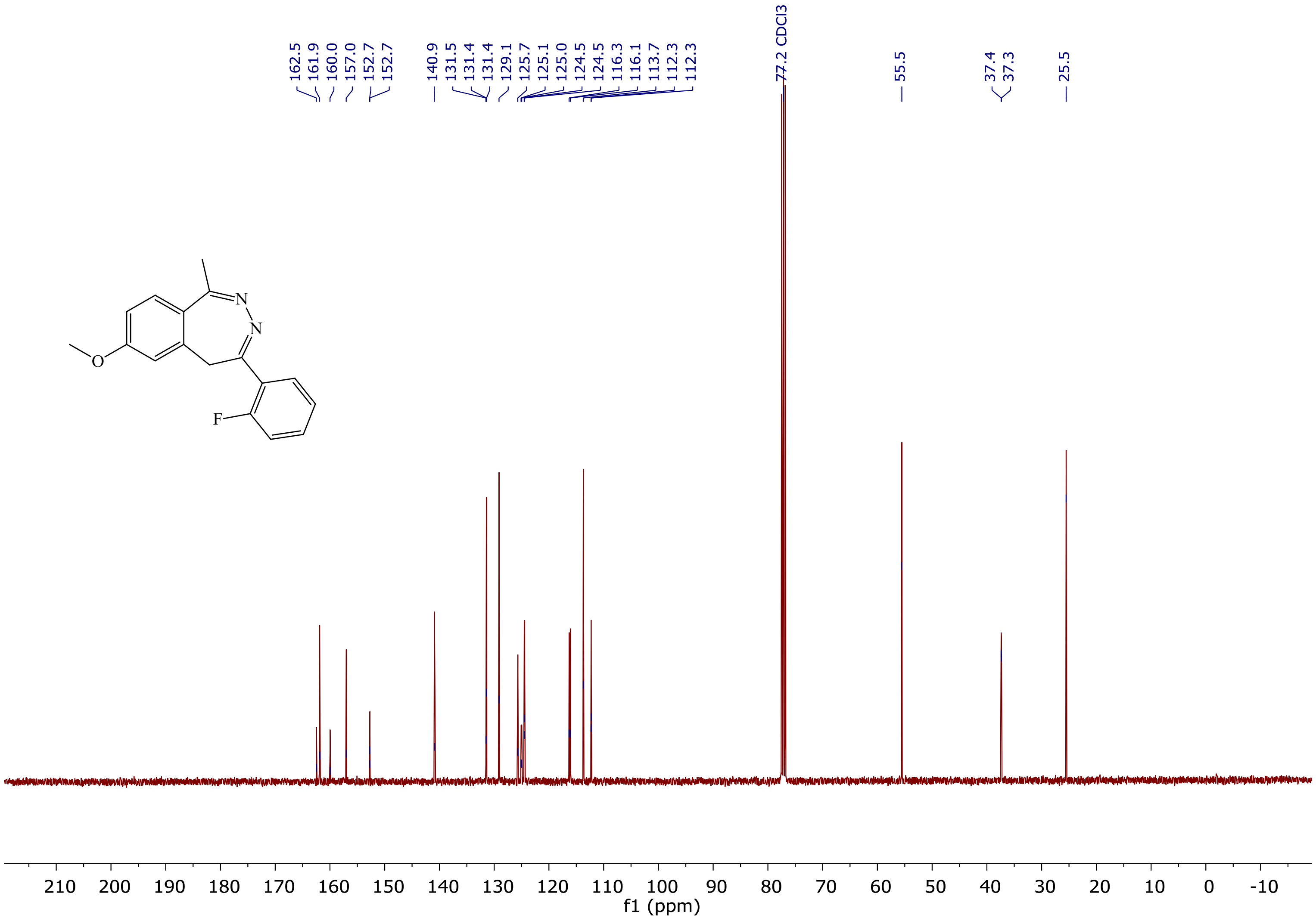


Figure S4.109. ^{13}C {^1H} **NMR (101MHz, $CDCl_3$) of 4-(2-fluorophenyl)-7-methoxy-1-methyl-5H-benzo[d][1,2]diazepine (3k)**

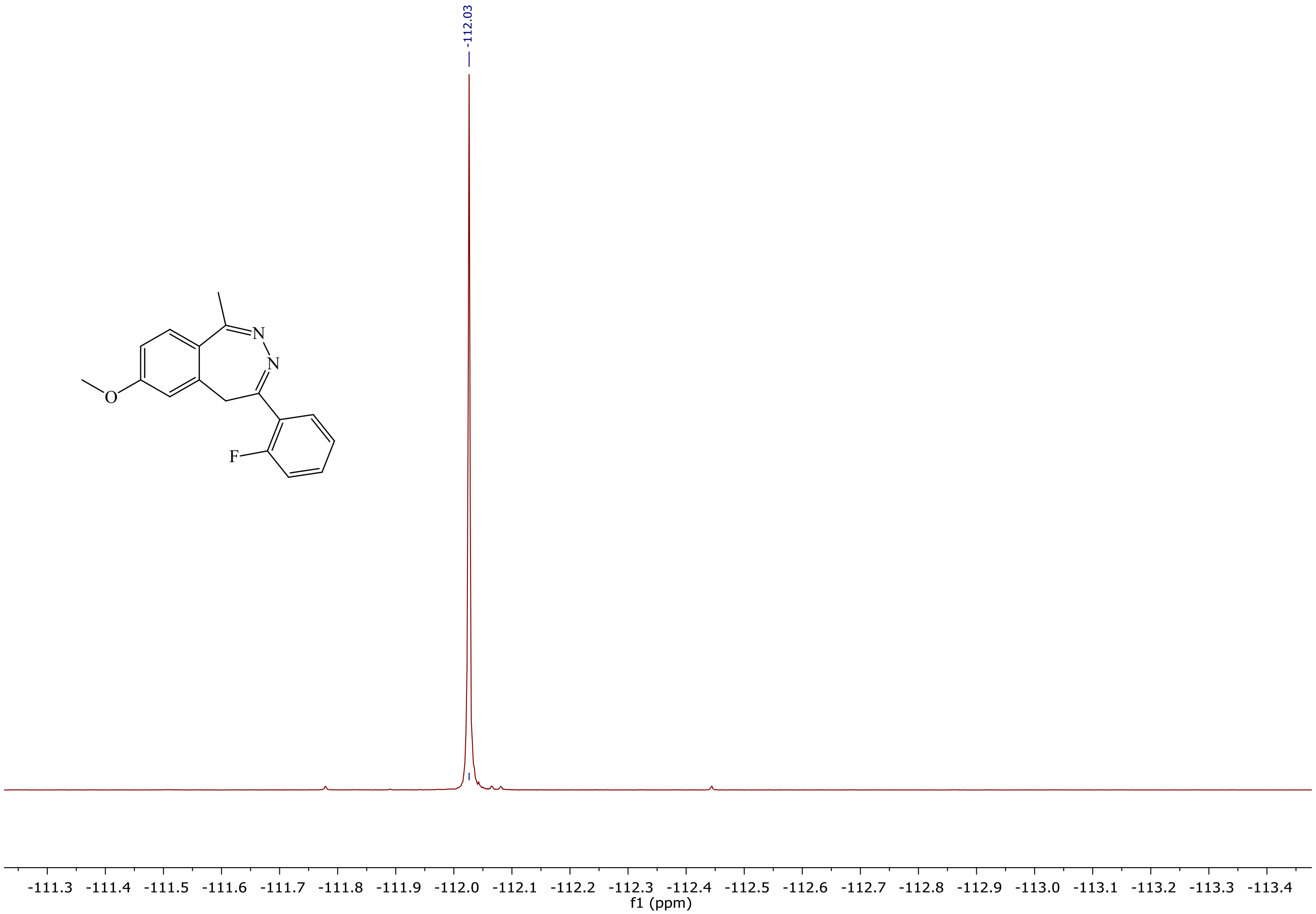


Figure S4.110. ^{19}F NMR (376 MHz, $CDCl_3$) of 4-(2-fluorophenyl)-7-methoxy-1-methyl-5H-benzo[d][1,2]diazepine (3k)

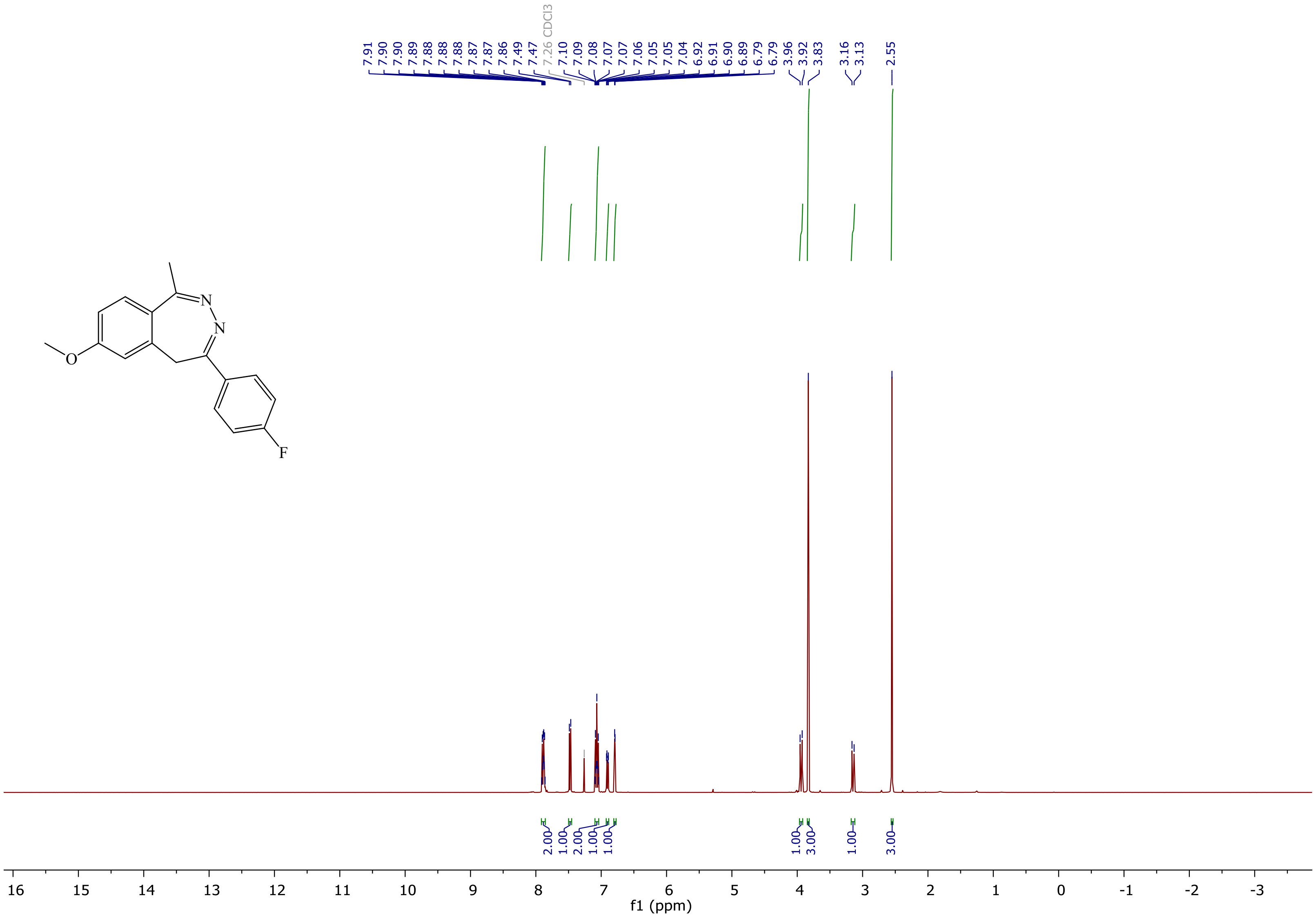


Figure S4.111. ^{1}H NMR (400MHz, $CDCl_3$) of 4-(4-fluorophenyl)-7-methoxy-1-methyl-5H-benzo[d][1,2]diazepine (3l)

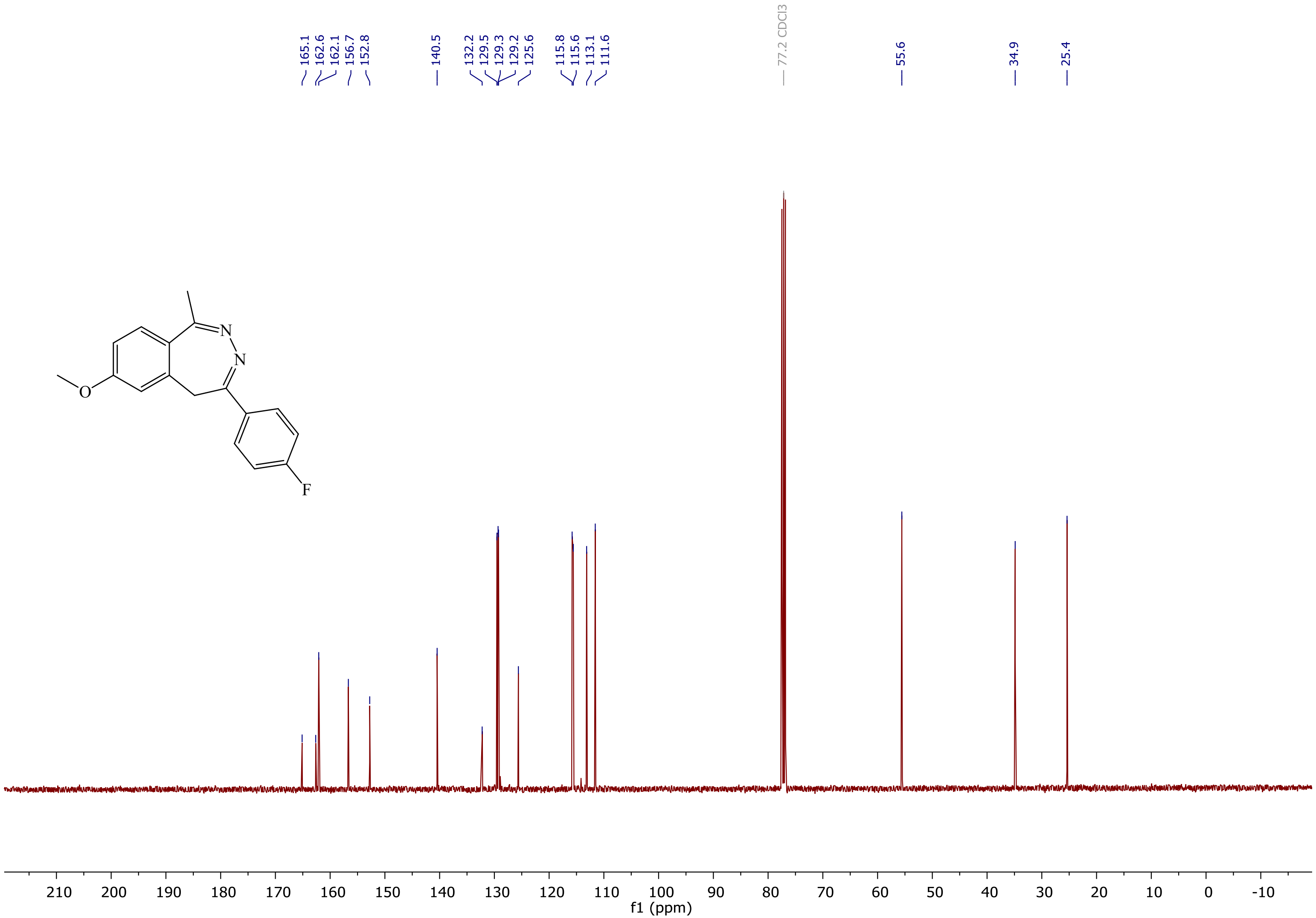


Figure S4.112. ^{13}C {^{1}H} NMR (101MHz, $CDCl_3$) of 4-(4-fluorophenyl)-7-methoxy-1-methyl-5H-benzo[d][1,2]diazepine (3l)

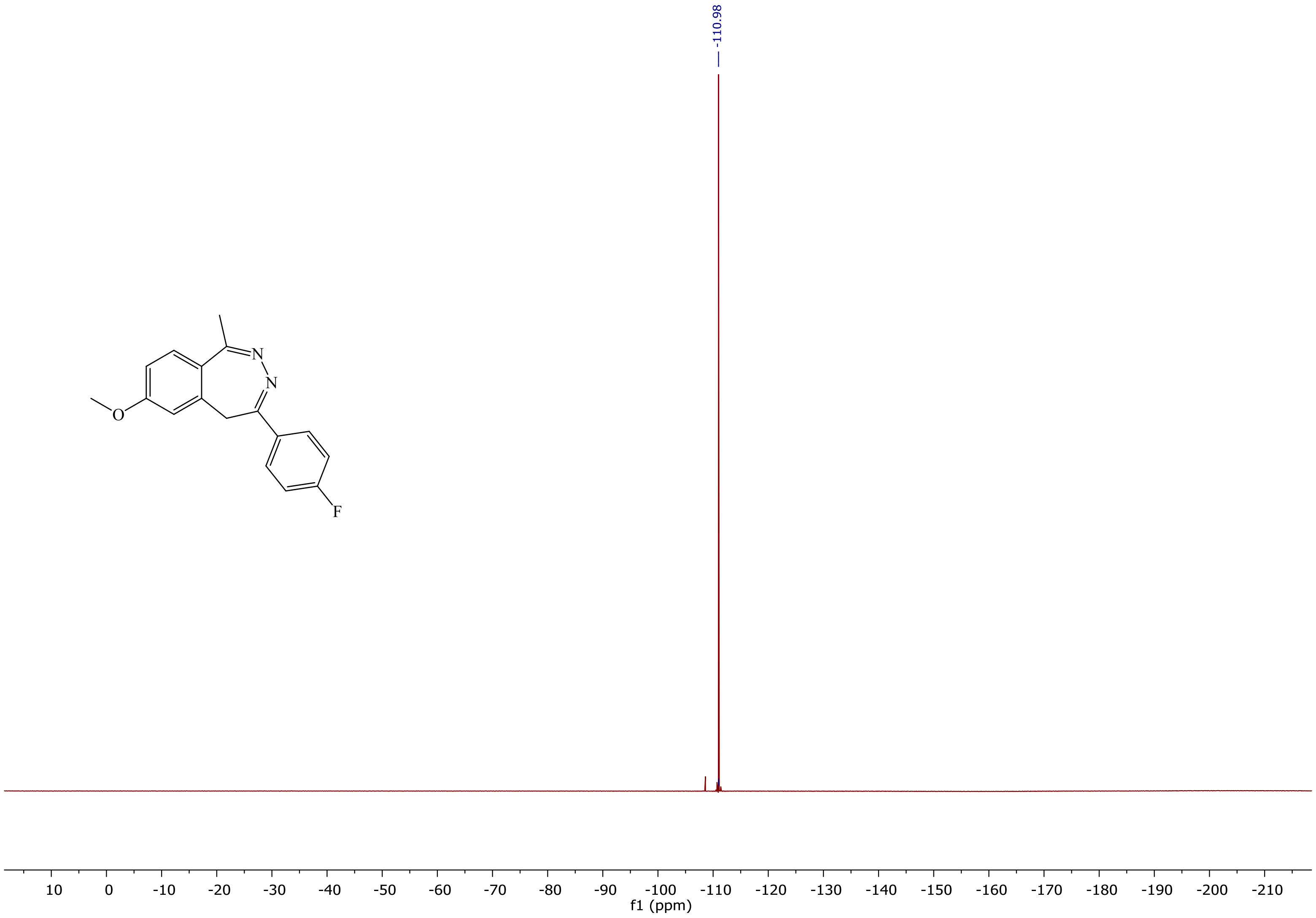


Figure S4.113. ^{19}F NMR (376 MHz, $CDCl_3$) of 4-(4-fluorophenyl)-7-methoxy-1-methyl-5H-benzo[d][1,2]diazepine (3l)

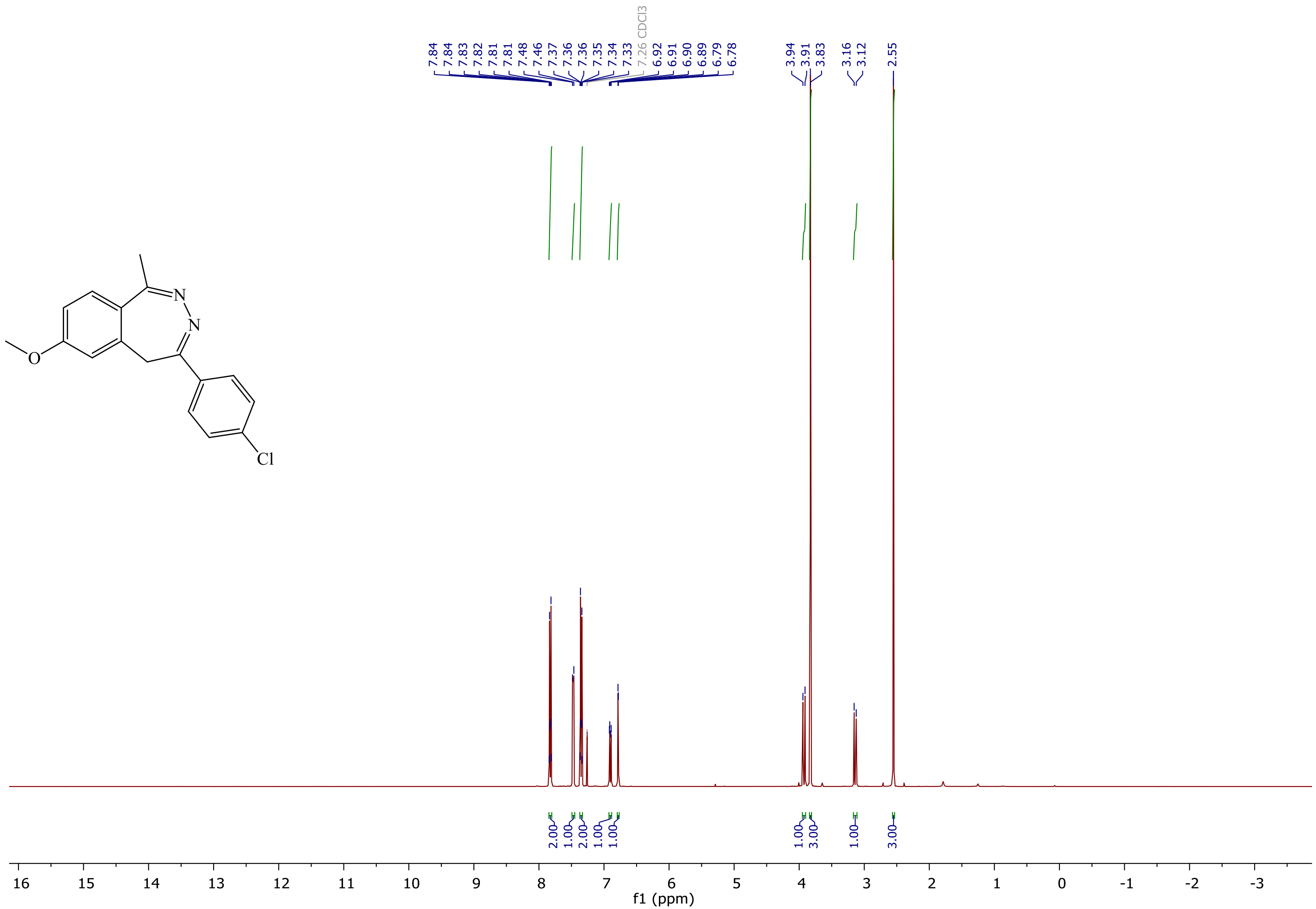


Figure S4.114. ^{1}H NMR (400MHz, $CDCl_3$) of 4-(4-chlorophenyl)-7-methoxy-1-methyl-5H-benzo[d][1,2]-diazepine (3m)

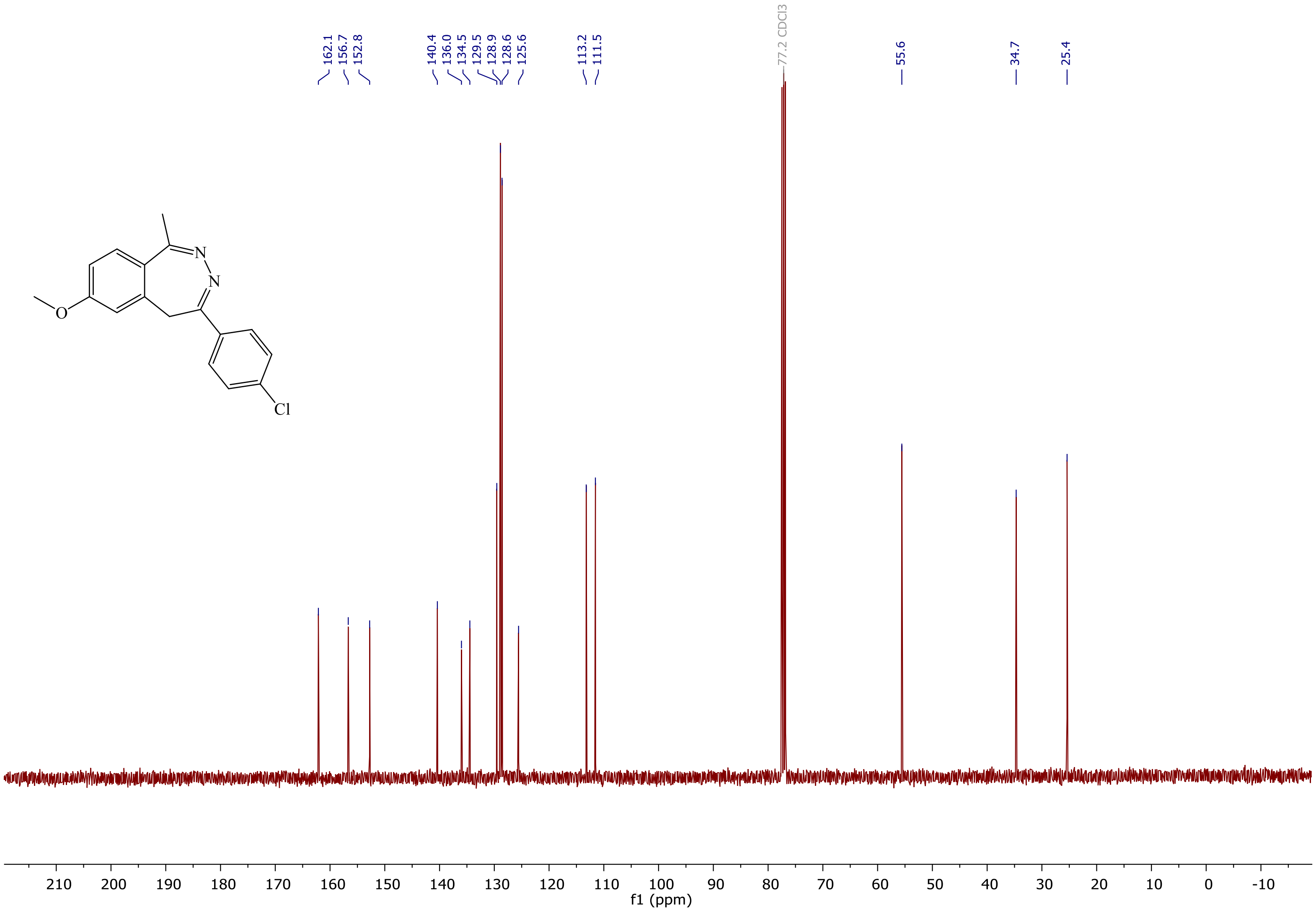


Figure S4.115. ^{13}C {^{1}H} NMR (101MHz, $CDCl_3$) of 4-(4-chlorophenyl)-7-methoxy-1-methyl-5H-benzo[d][1,2]-diazepine (3m)

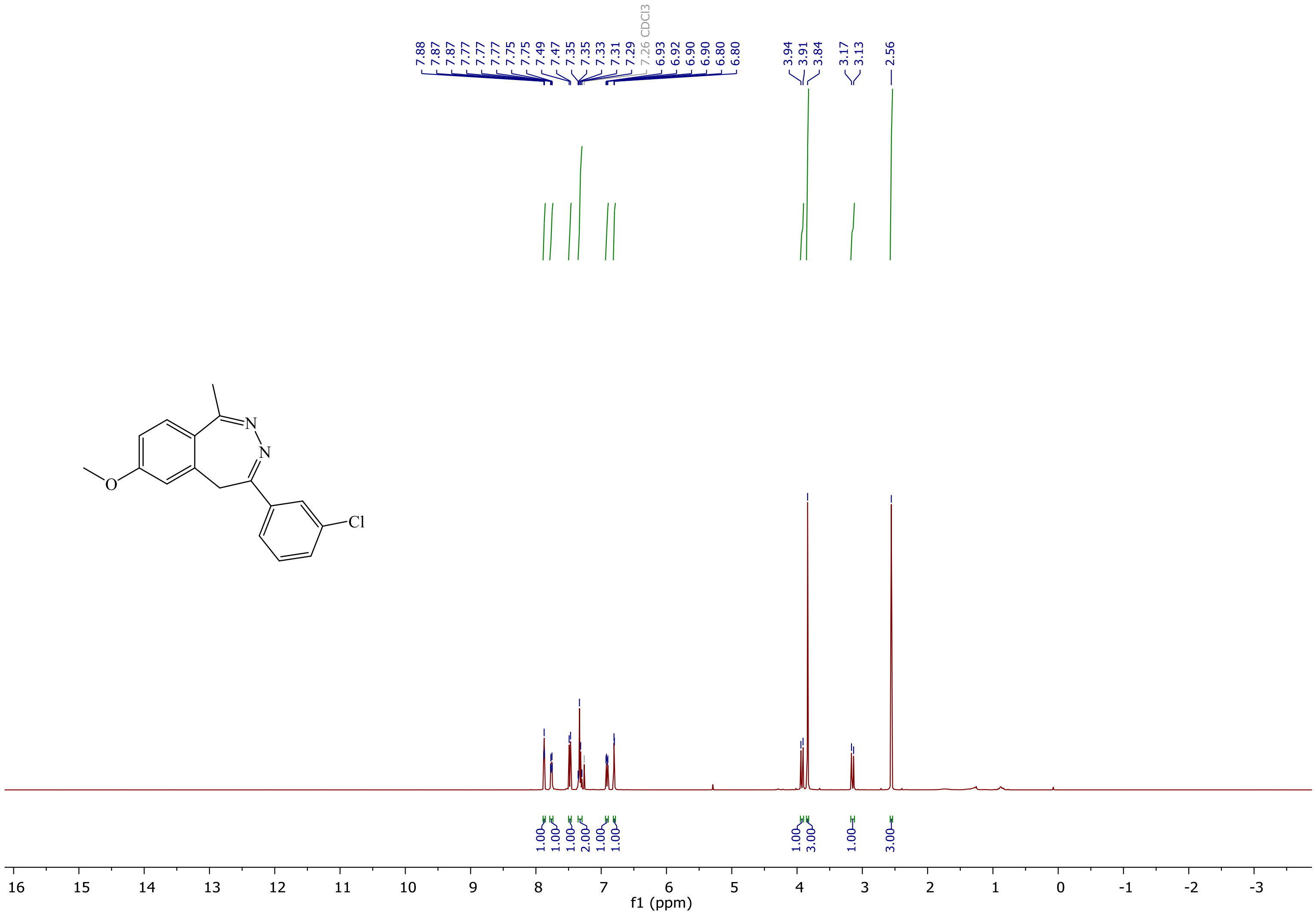


Figure S4.116. ^{1}H NMR (400MHz, $CDCl_3$) of 4-(3-chlorophenyl)-7-methoxy-1-methyl-5H-benzo[d][1,2]diazepine (3n)

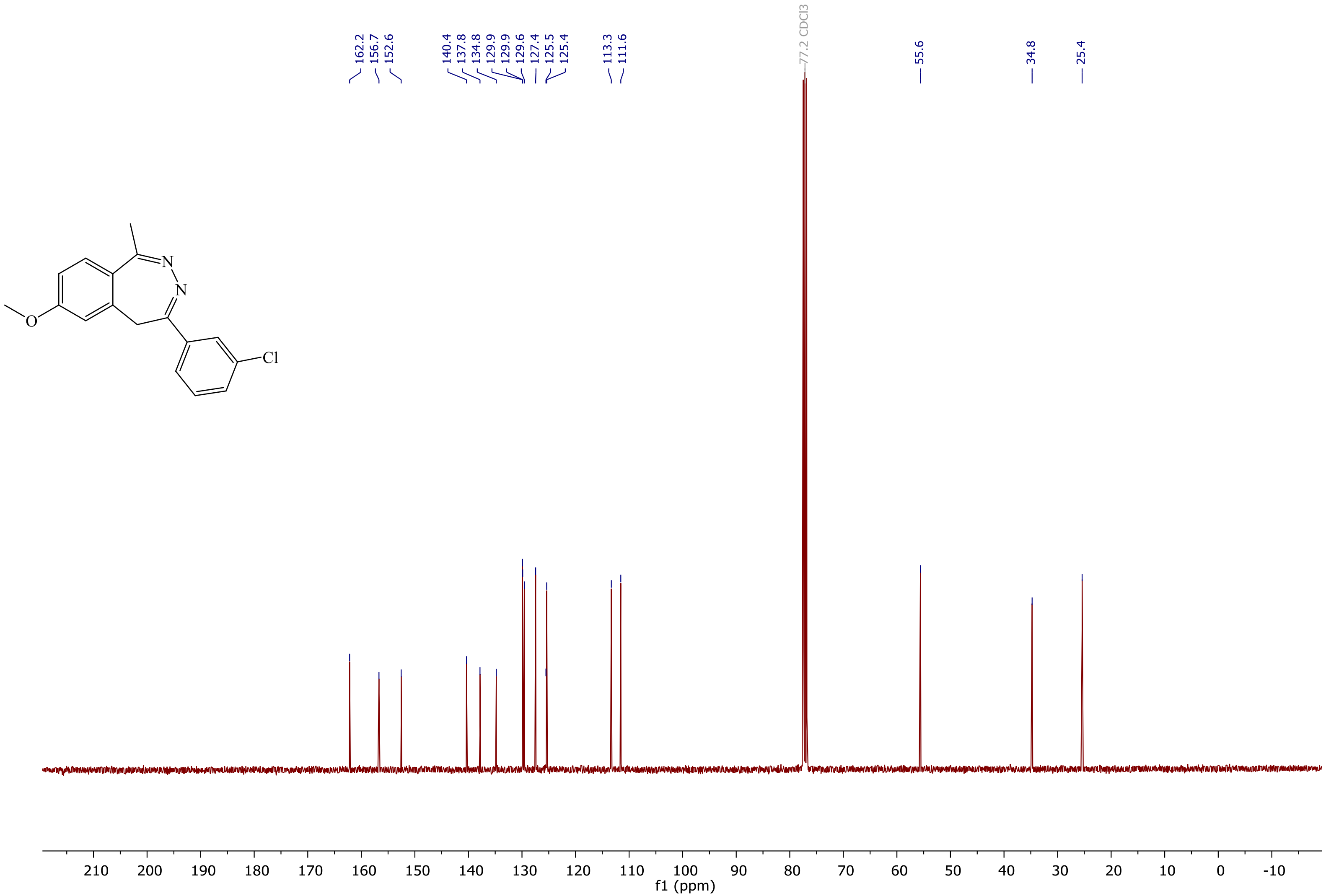


Figure S4.117. $^{13}C\ \{^1H\}$ NMR (101MHz, $CDCl_3$) of 4-(3-chlorophenyl)-7-methoxy-1-methyl-5H-benzo[d][1,2]diazepine (3n)

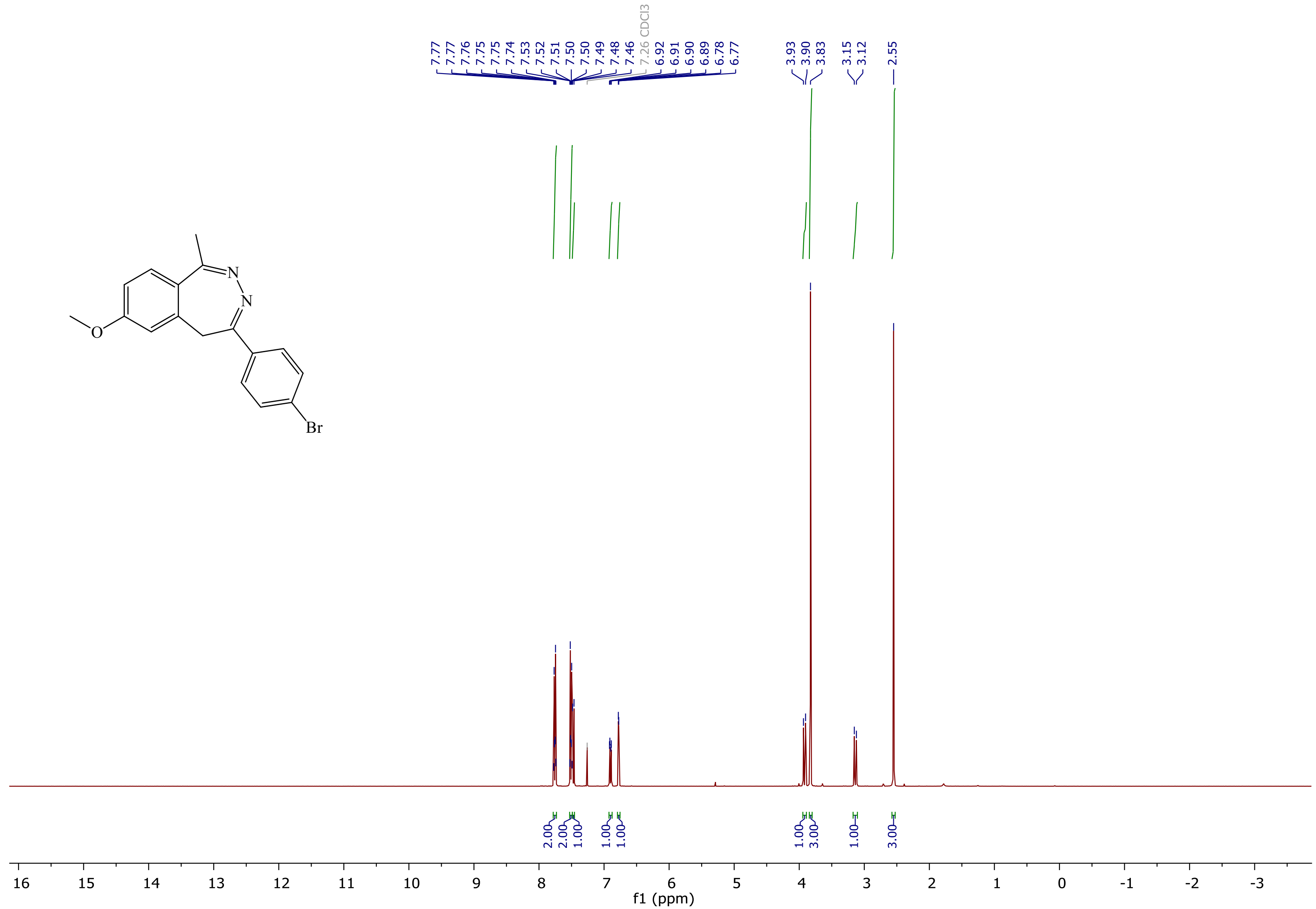


Figure S4.118. ^{1}H NMR (400MHz, $CDCl_3$) of 4-(4-bromophenyl)-7-methoxy-1-methyl-5H-benzo[d][1,2]diazepine (3o)

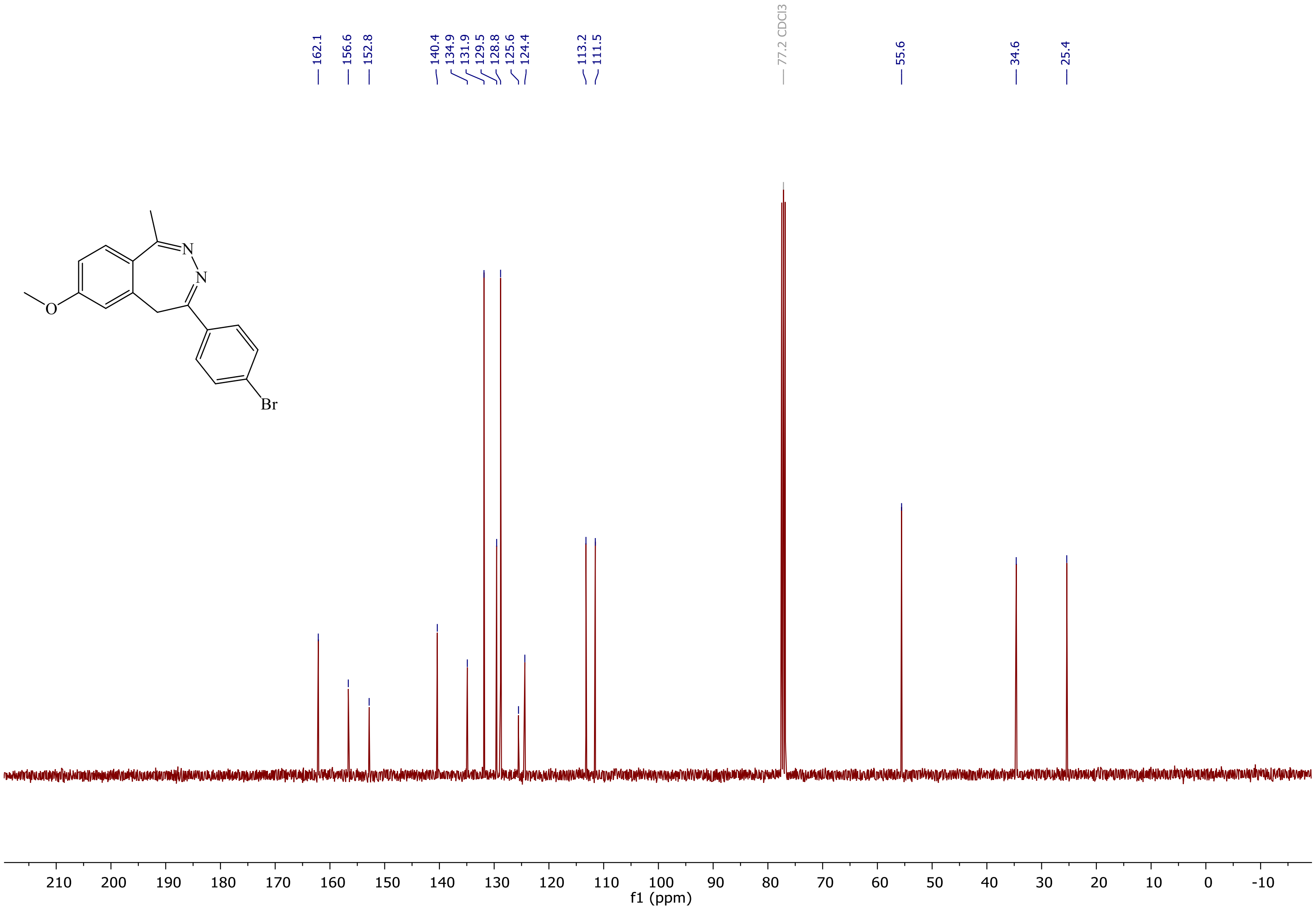


Figure S4.119 $^{13}C\ \{^{1}H\}$ NMR (101MHz, $CDCl_3$) of 4-(4-bromophenyl)-7-methoxy-1-methyl-5H-benzo[d][1,2]diazepine (3o)

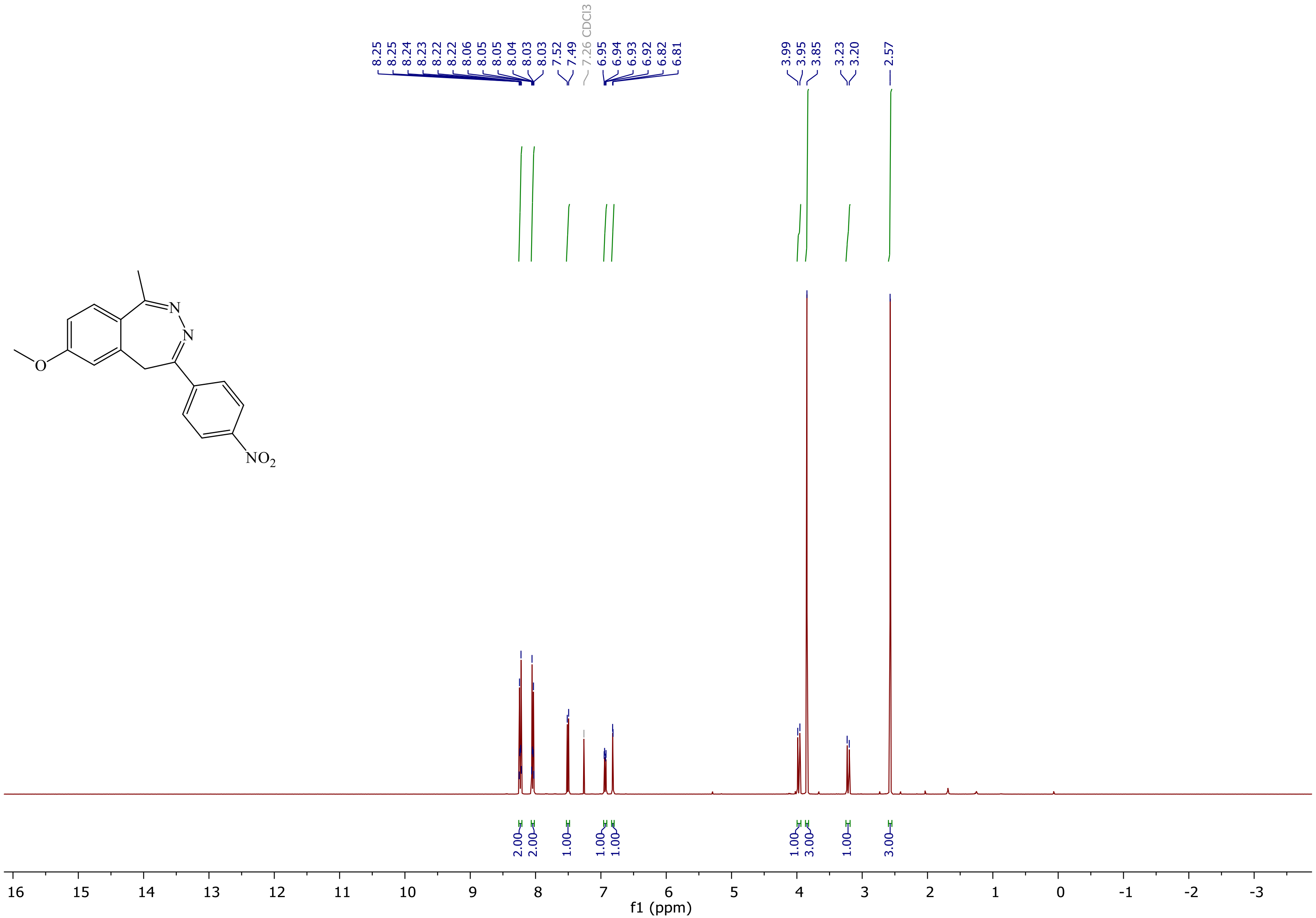


Figure S4.120. [1]H NMR (400MHz, $CDCl_3$) of 7-methoxy-1-methyl-4-(4-nitrophenyl)-5H-benzo[d][1,2]diazepine (3p)

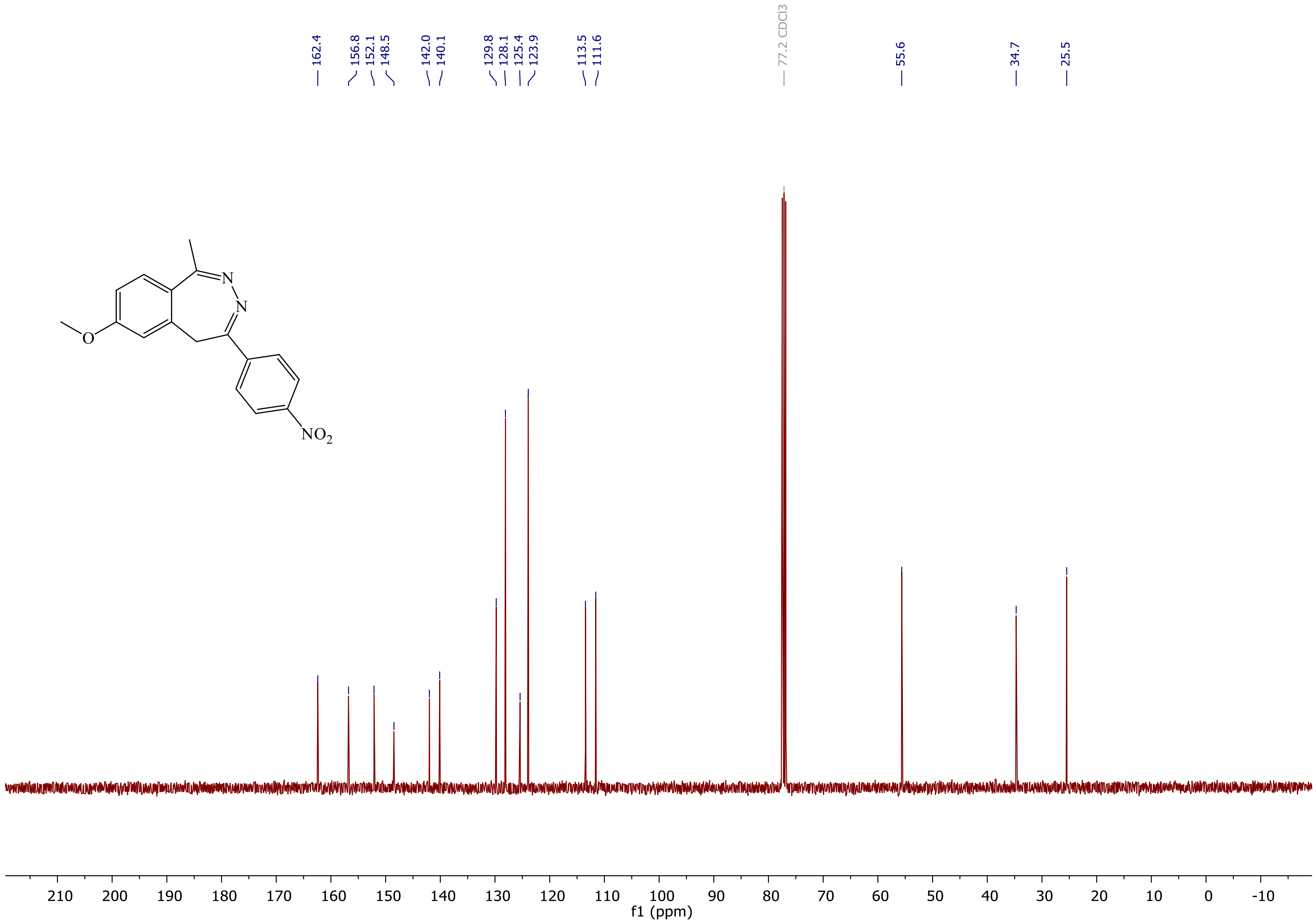


Figure S4.121 ^{13}C {^{1}H} NMR (101MHz, $CDCl_3$) of 7-methoxy-1-methyl-4-(4-nitrophenyl)-5H-benzo[d][1,2]diazepine (3p)

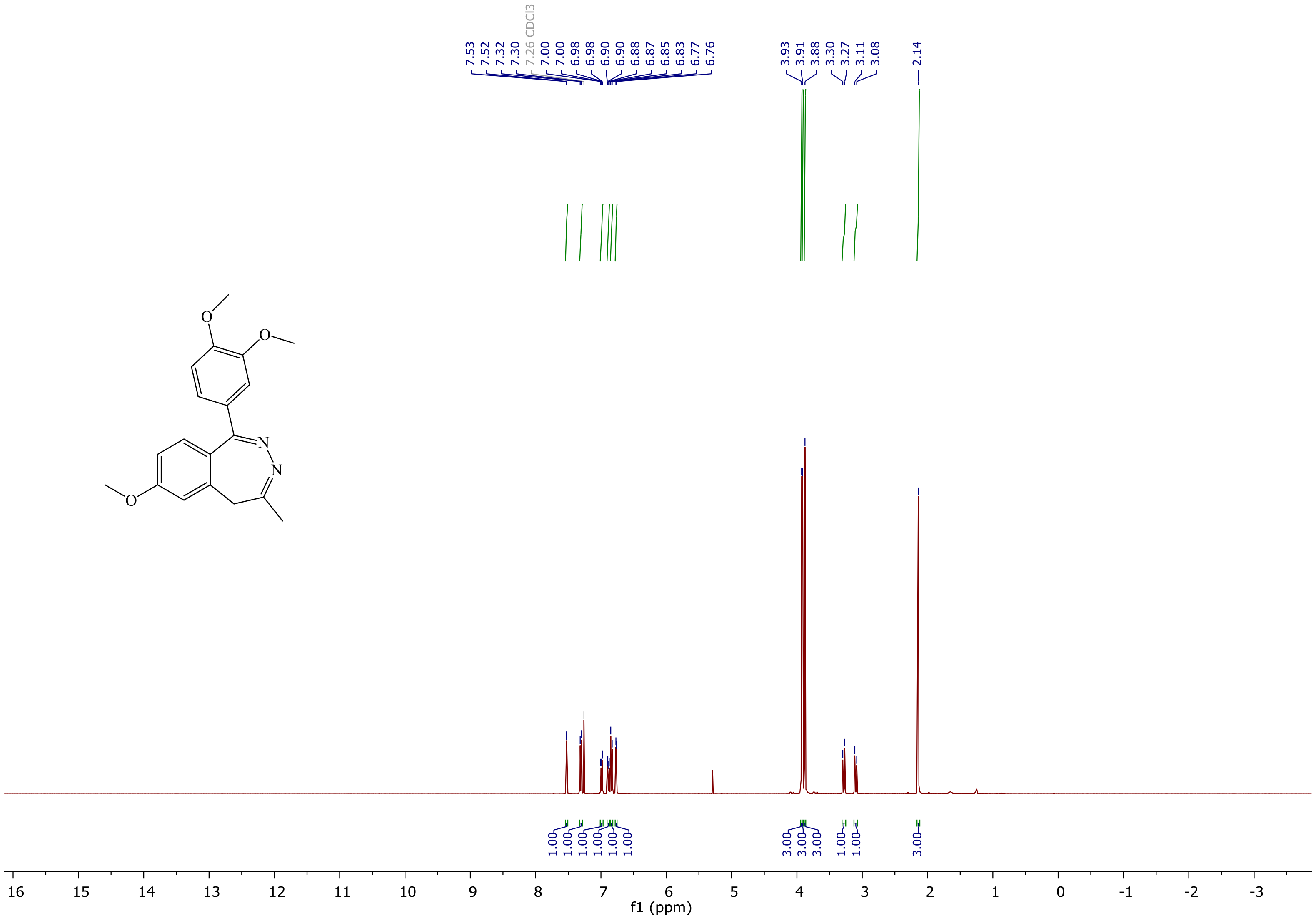


Figure S4.122. ¹H NMR (400MHz, $CDCl_3$) of 1-(3,4-dimethoxyphenyl)-7-methoxy-4-methyl-5H-benzo[d][1,2]diazepine (3q)

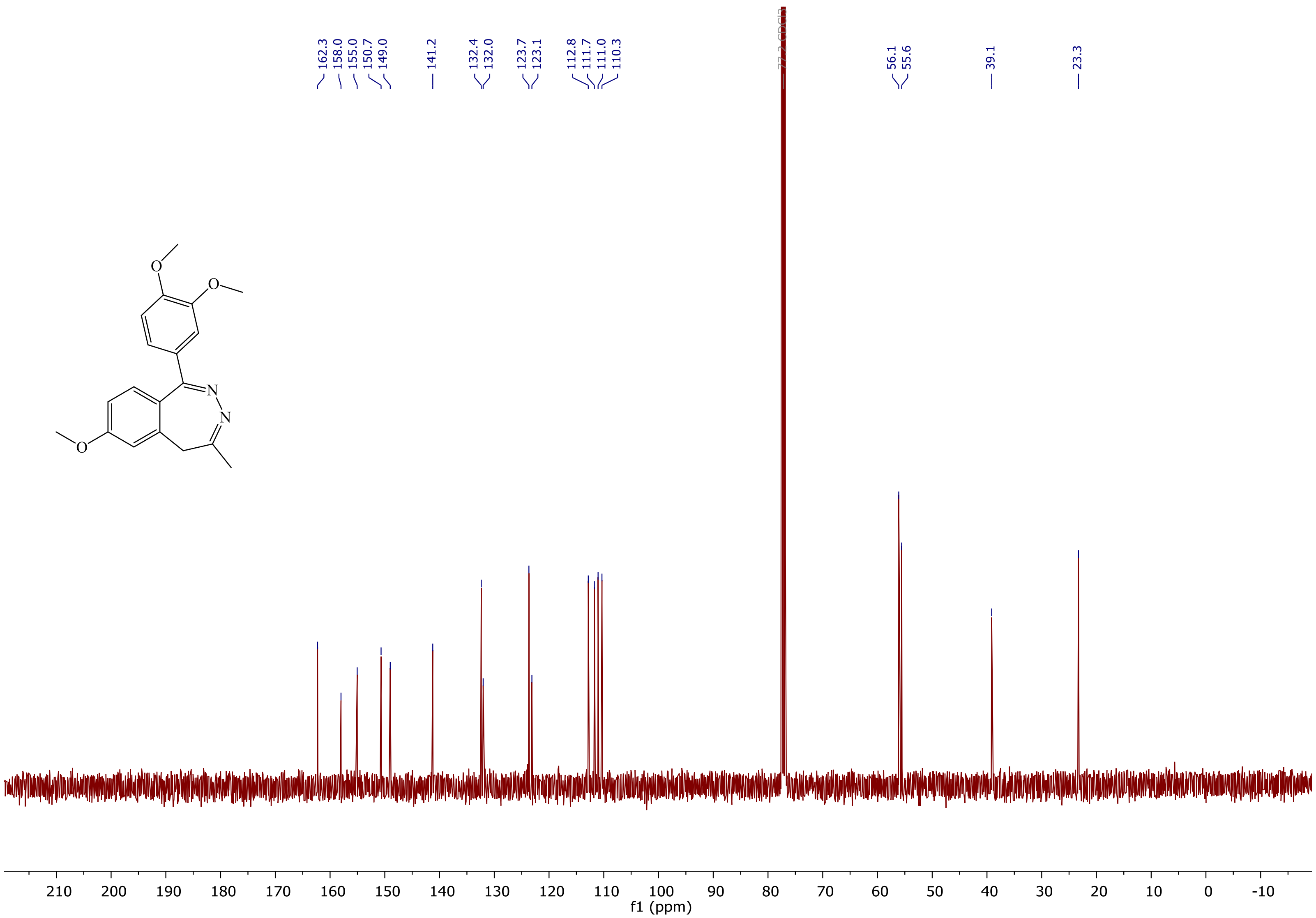
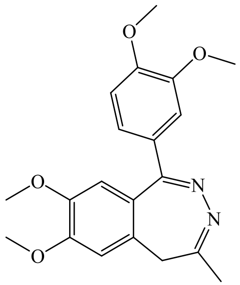


Figure S4.123. $^{13}C\ \{^{1}H\}$ NMR (101MHz, $CDCl_3$) of 1-(3,4-dimethoxyphenyl)-7-methoxy-4-methyl-5H-benzo[d][1,2]diazepine (3q)



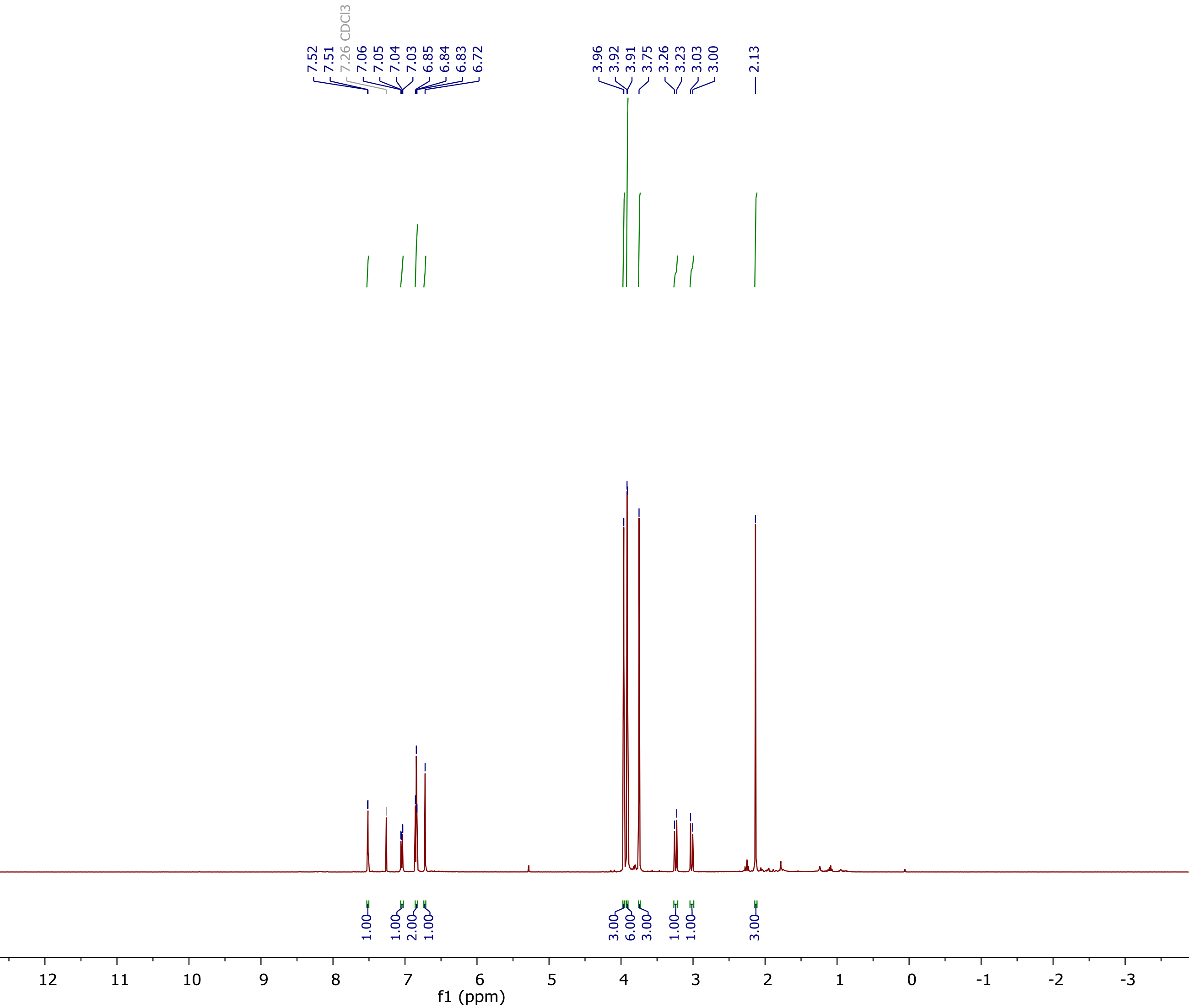


Figure S4.124. ^{1}**H NMR (400MHz,** $CDCl_3$**) of 1-(3,4-dimethoxyphenyl)-7,8-dimethoxy-4-methyl-5H-benzo[d][1,2]diazepine (3r)**

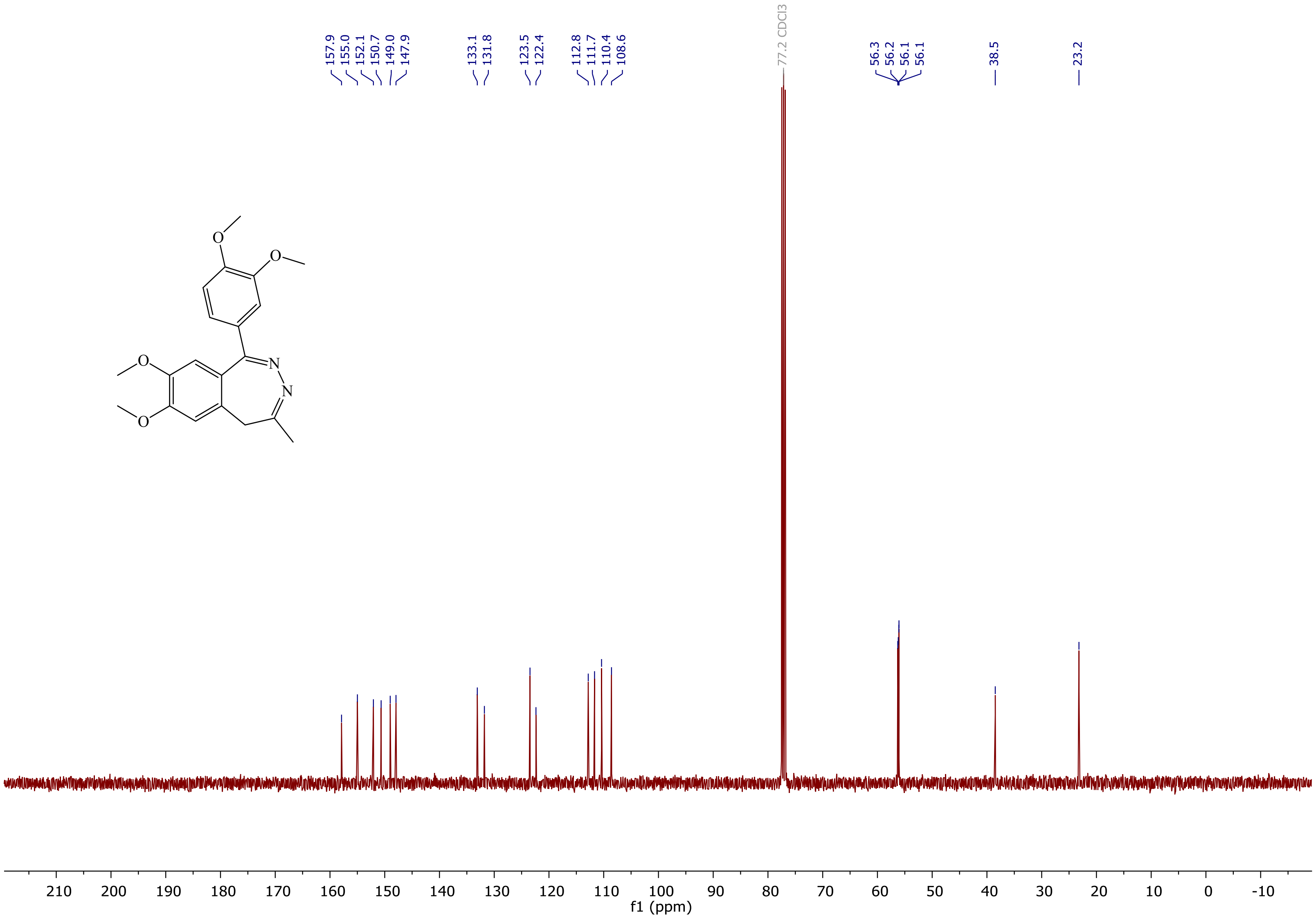


Figure S4.125. **^{13}C {^{1}H} NMR (101MHz, $CDCl_3$) of 1-(3,4-dimethoxyphenyl)-7,8-dimethoxy-4-methyl-5H-benzo[d][1,2]diazepine (3r)**

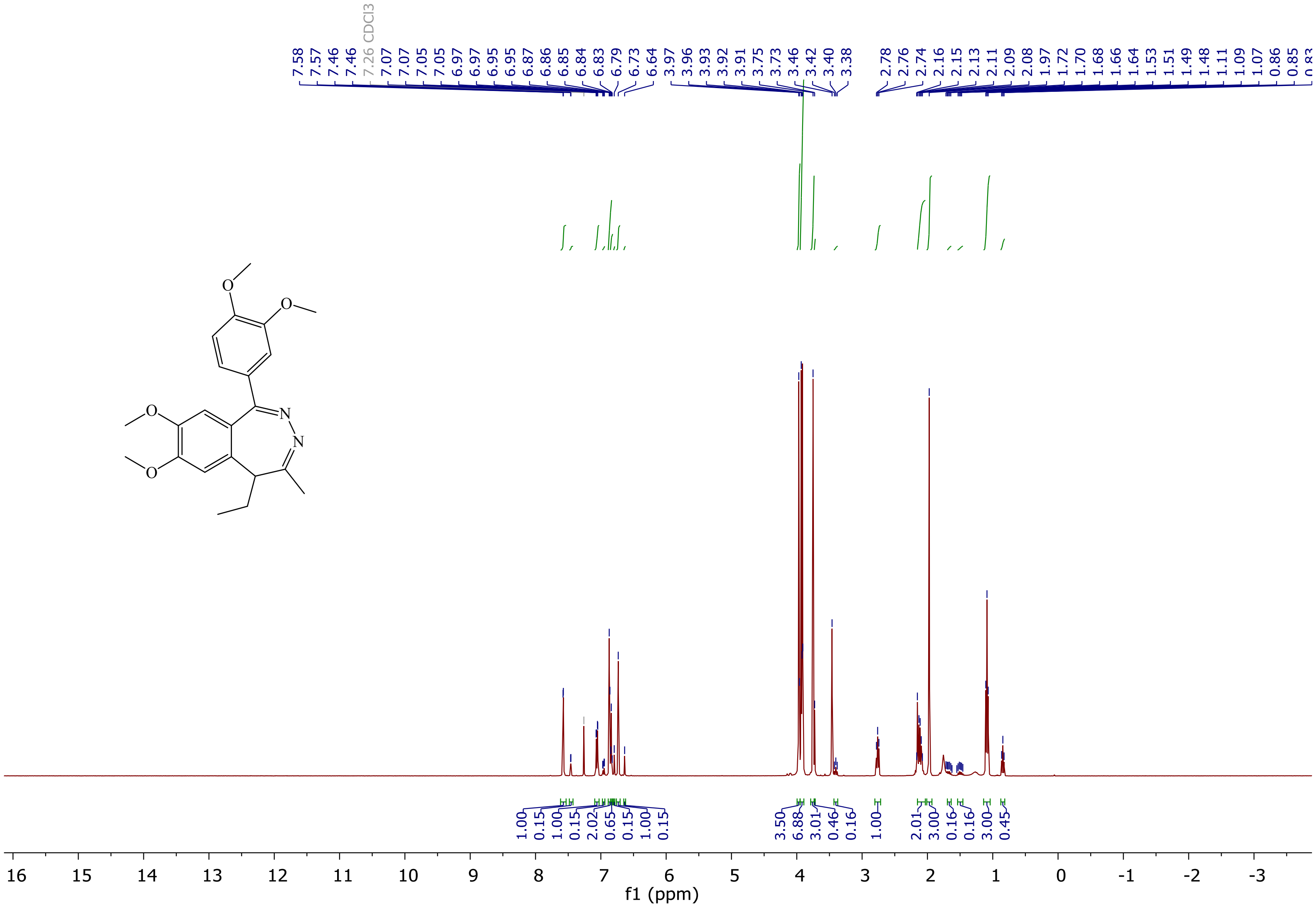


Figure S4.126. [1]H NMR (400MHz, $CDCl_3$) of 1-(3,4-dimethoxyphenyl)-5-ethyl-7,8-dimethoxy-4-methyl-5H-benzo[d][1,2]diazepine (3s)

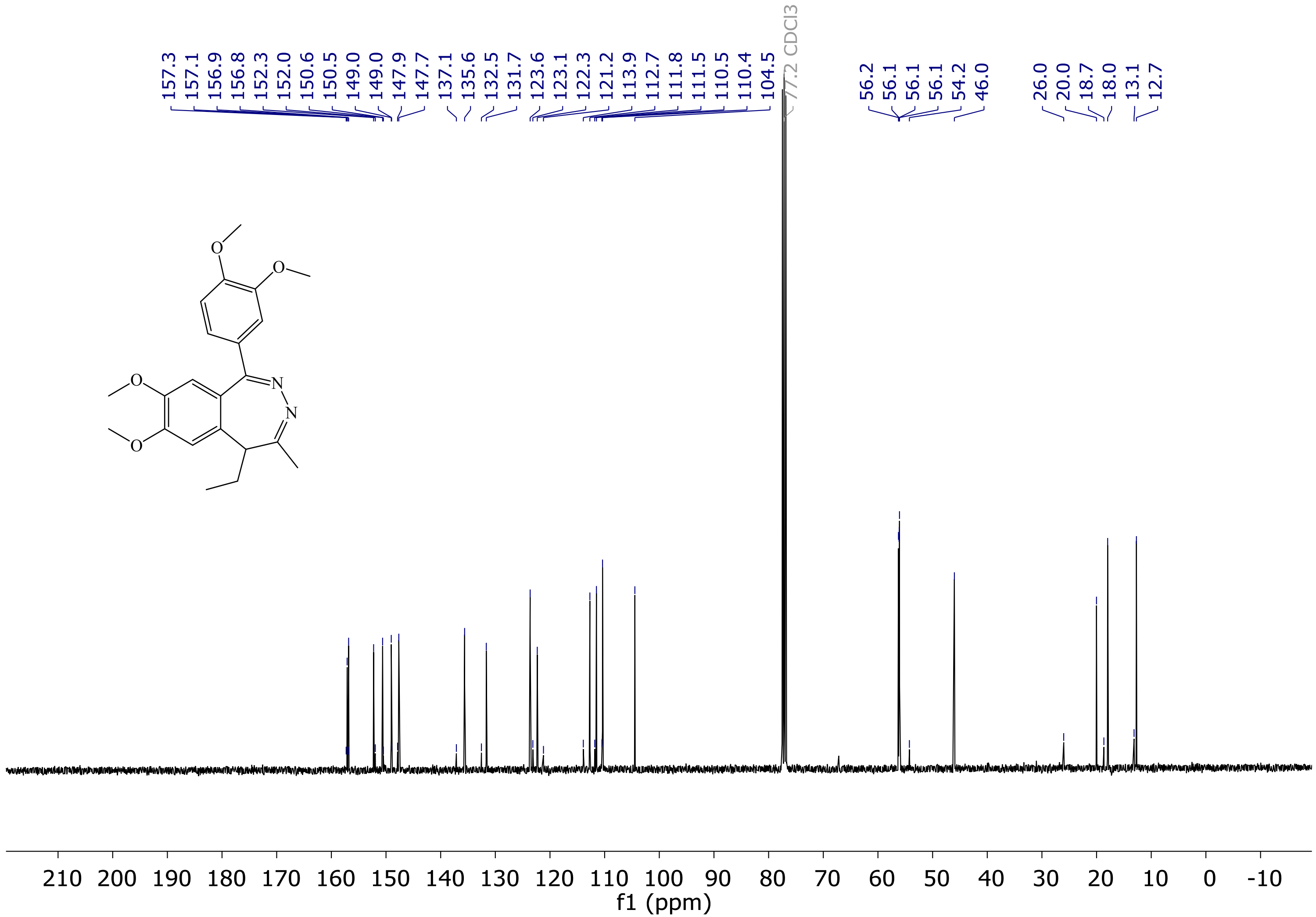


Figure S4.127. $^{13}C\ \{^{1}H\}$ NMR (101MHz, $CDCl_3$) of 1-(3,4-dimethoxyphenyl)-5-ethyl-7,8-dimethoxy-4-methyl-5H-benzo[d][1,2]diazepine (3s)

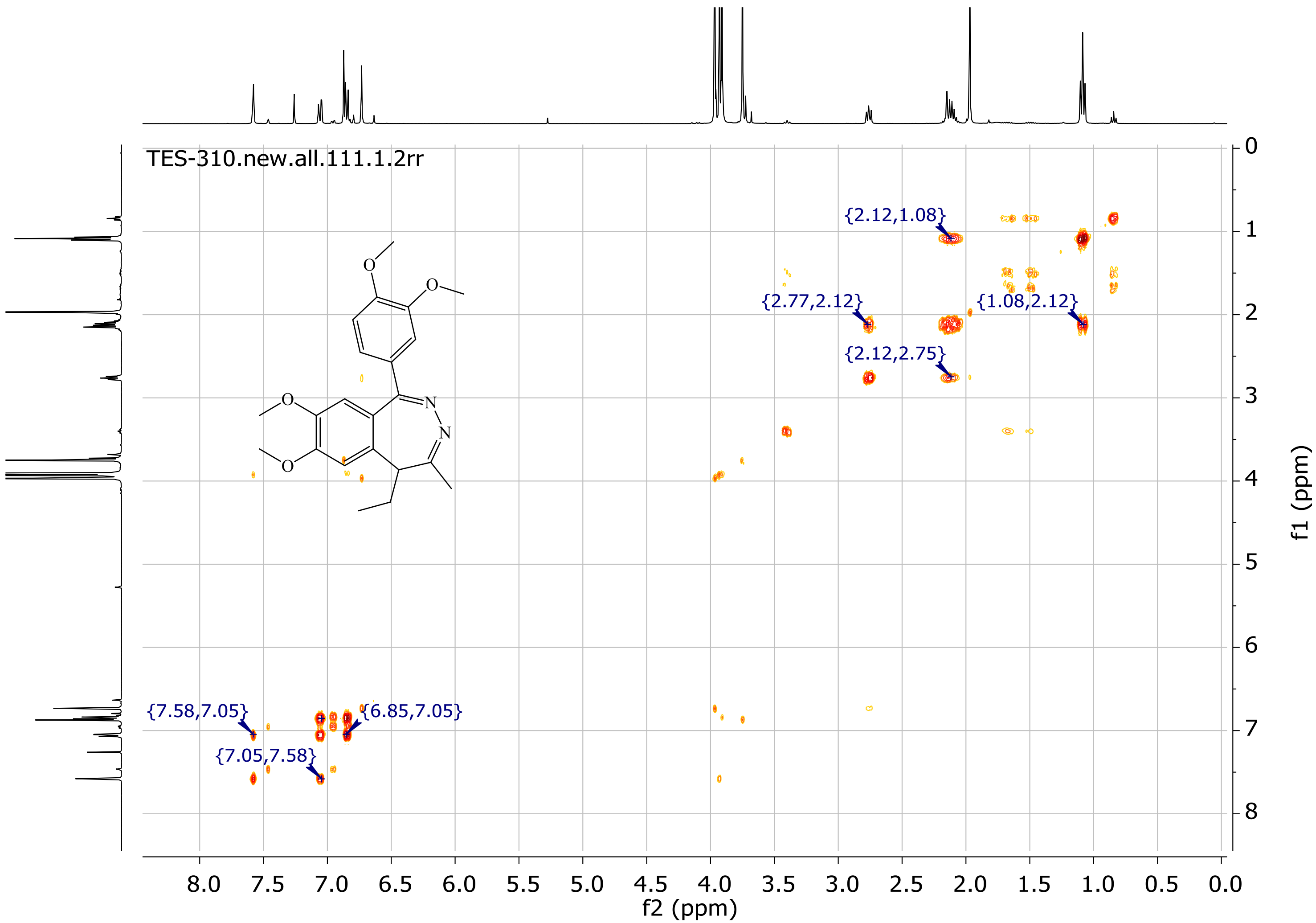


Figure S4.128. COSY NMR spectrum (400MHz, $CDCl_3$) of 1-(3,4-dimethoxyphenyl)-5-ethyl-7,8-dimethoxy-4-methyl-5H-benzo[d][1,2]diazepine, major isomer (3s)

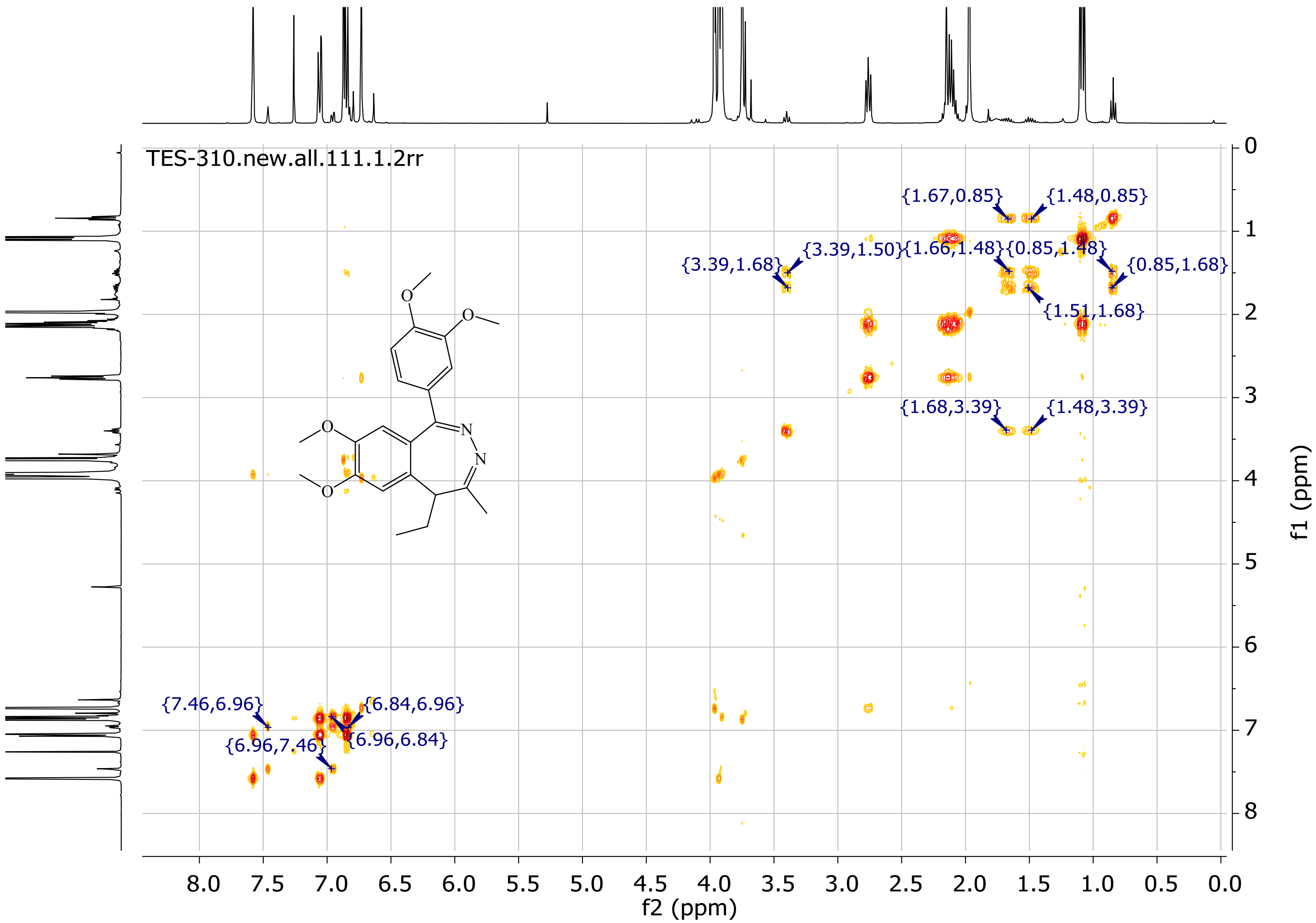


Figure S4.129. COSY NMR spectrum (400MHz, $CDCl_3$) of 1-(3,4-dimethoxyphenyl)-5-ethyl-7,8-dimethoxy-4-methyl-5H-benzo[d][1,2]diazepine, minor isomer (3s)

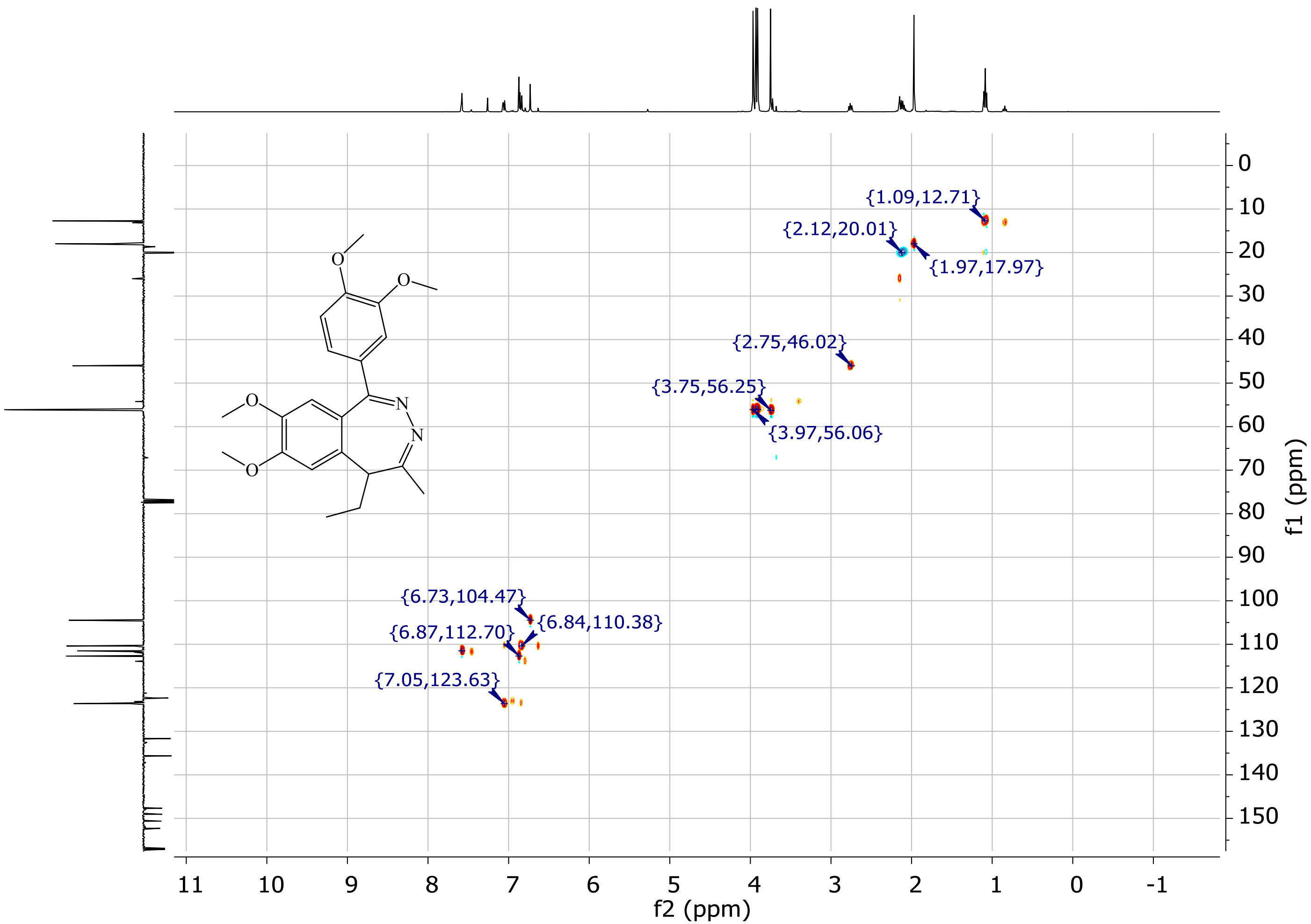


Figure S4.130. HSQC NMR spectrum (101, 400MHz, $CDCl_3$) 3r ^{1}H-^{13}C-HSQC 1-(3,4-dimethoxyphenyl)-5-ethyl-7,8-dimethoxy-4-methyl-5H-benzo[d][1,2]diazepine, major isomer (3s)

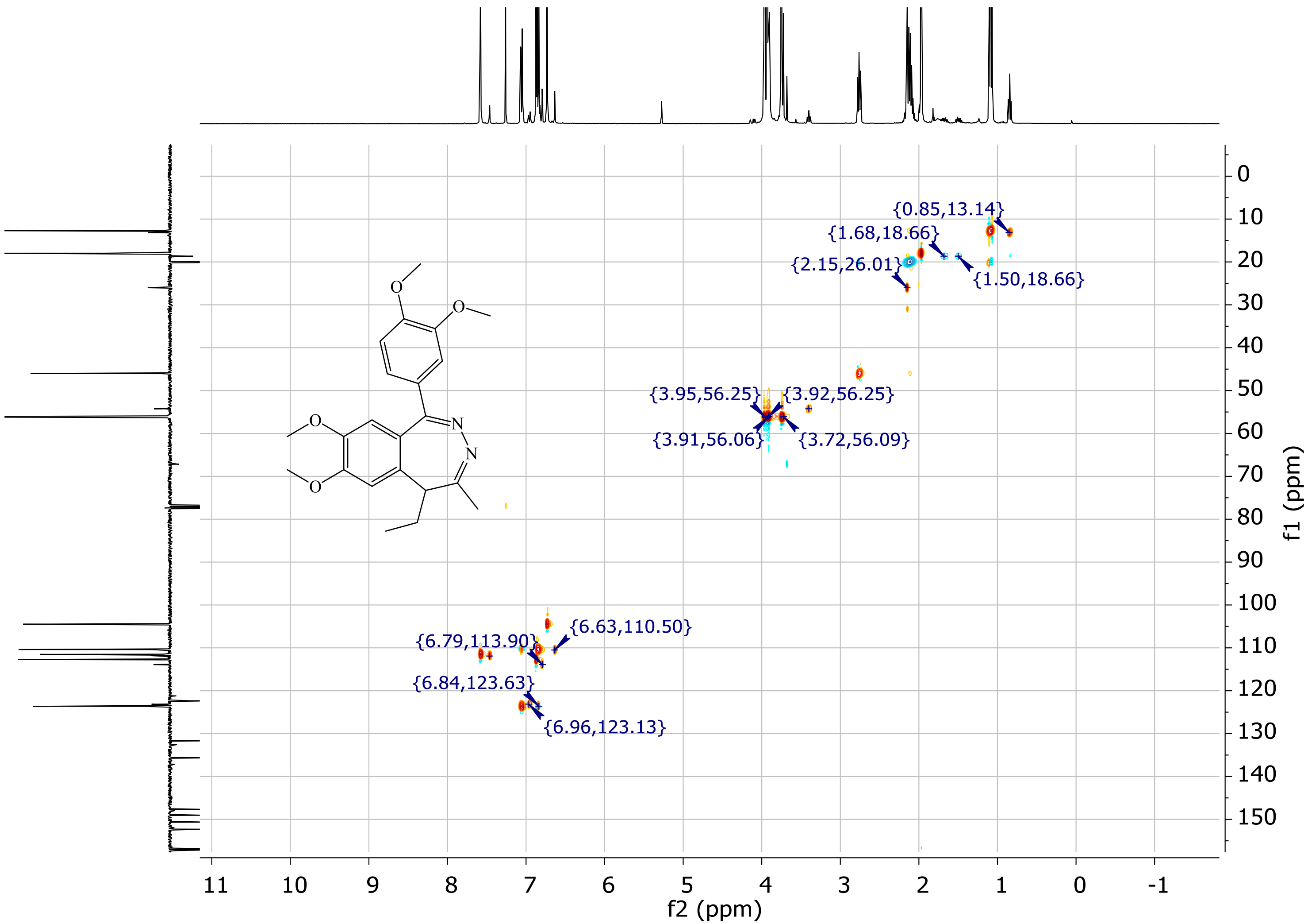


Figure S4.131. HSQC NMR spectrum (101, 400MHz, $CDCl_3$) of ^{1}H-^{13}C-HSQC of 1-(3,4-dimethoxyphenyl)-5-ethyl-7,8-dimethoxy-4-methyl-5H-benzo[d][1,2]diazepine, minor isomer (3s)

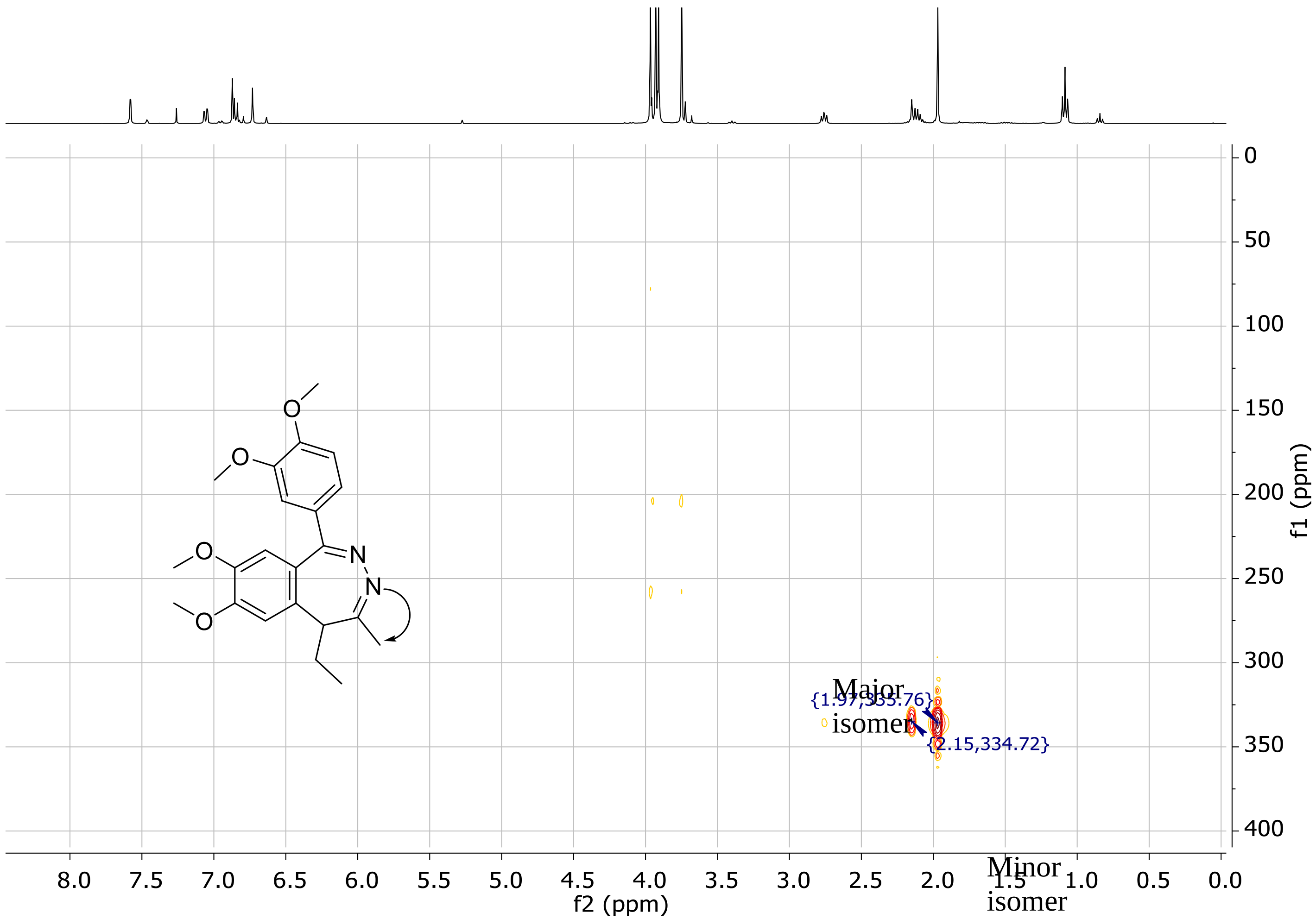


Figure S4.132. $^{1}H^{15}N$-HMBC spectra of 1-(3,4-dimethoxyphenyl)-5-ethyl-7,8-dimethoxy-4-methyl-5H-benzo[d][1,2]diazepine, two isomers (3s)

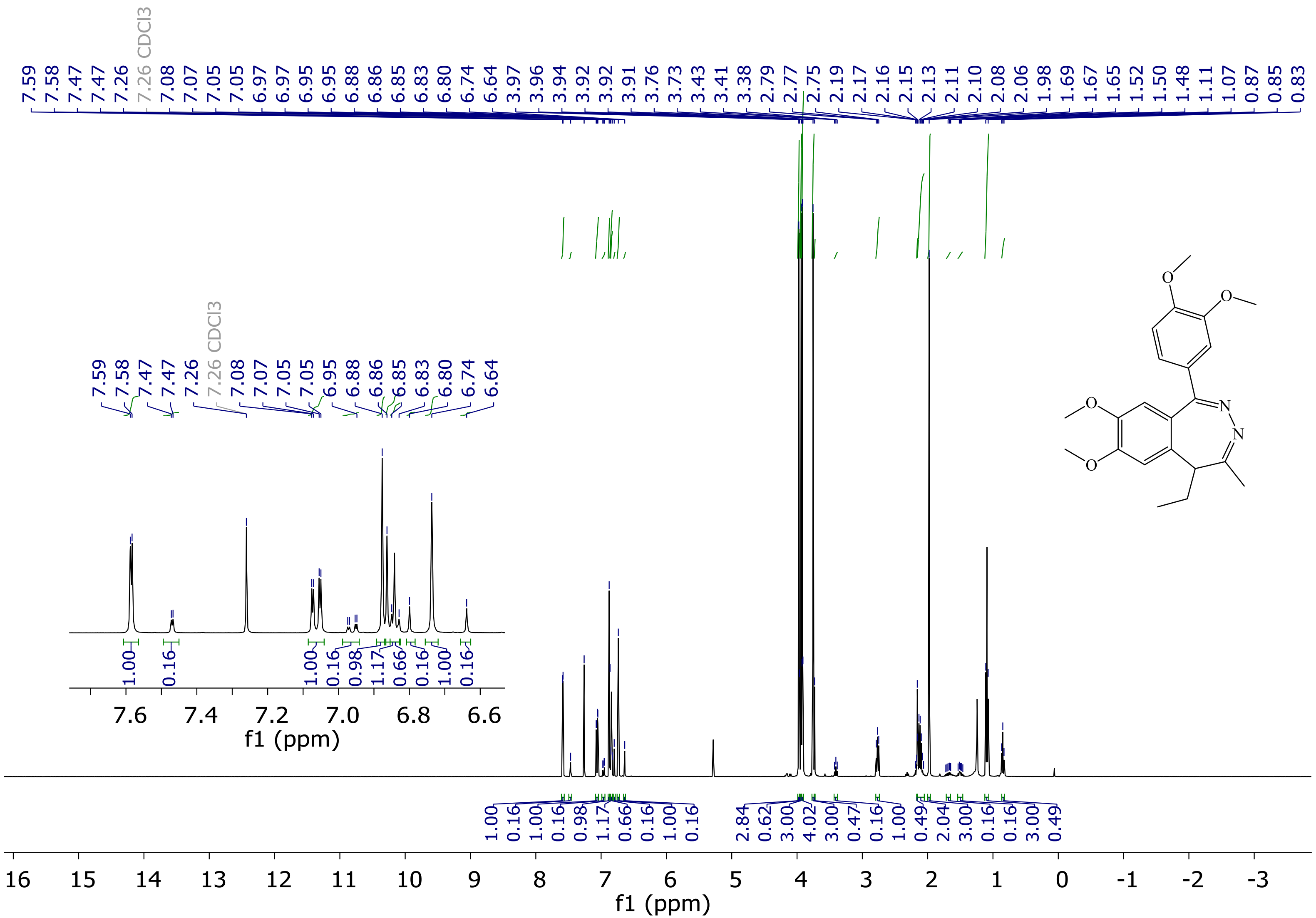


Figure S4.133. ^{1}H NMR (400MHz, $CDCl_3$) of Tofisopam (BIOCOM)

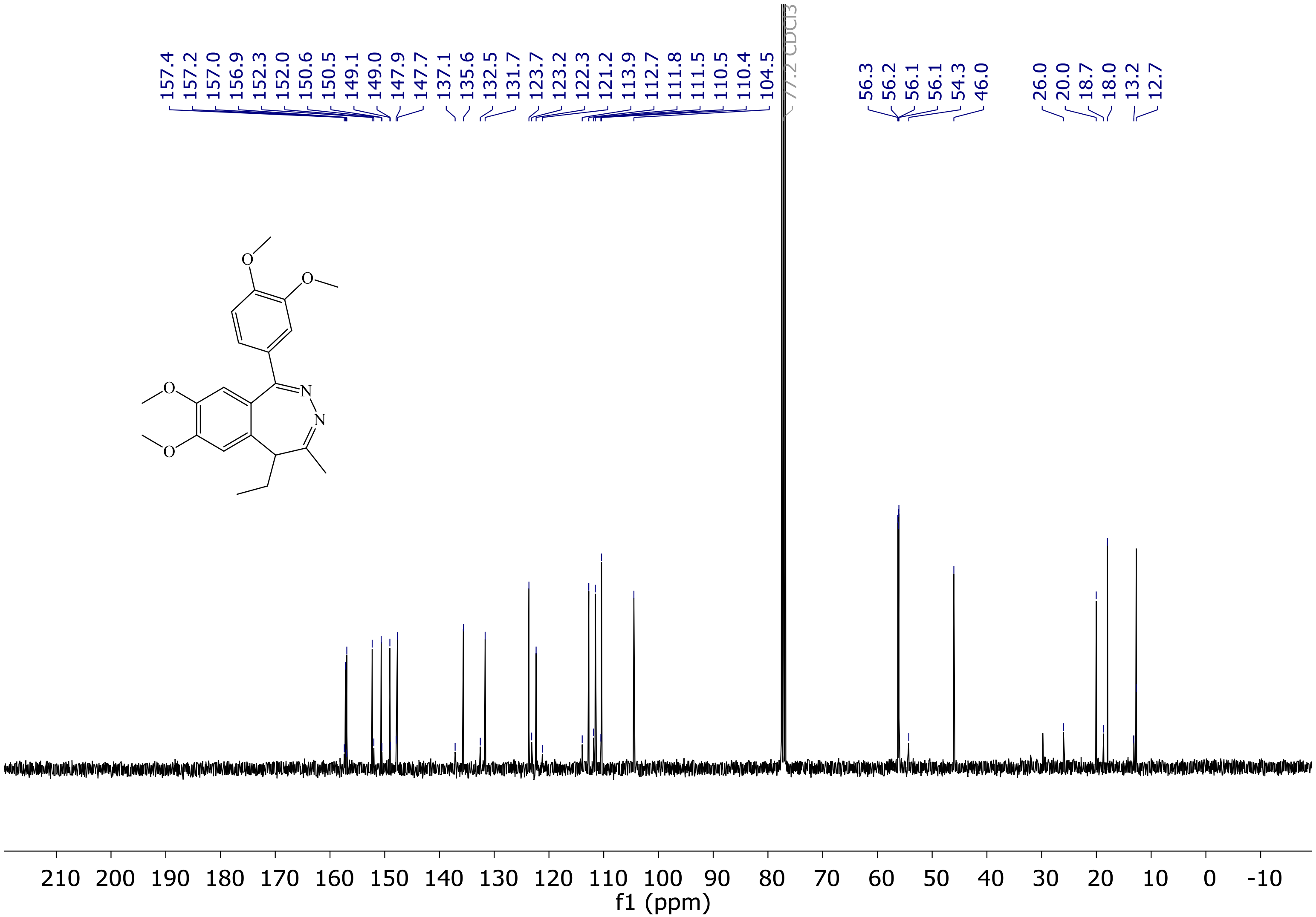


Figure S4.134. $^{13}C\{^{1}H\}$ **NMR (101MHz,** $CDCl_3$**) of Tofisopam (BIOCOM)**

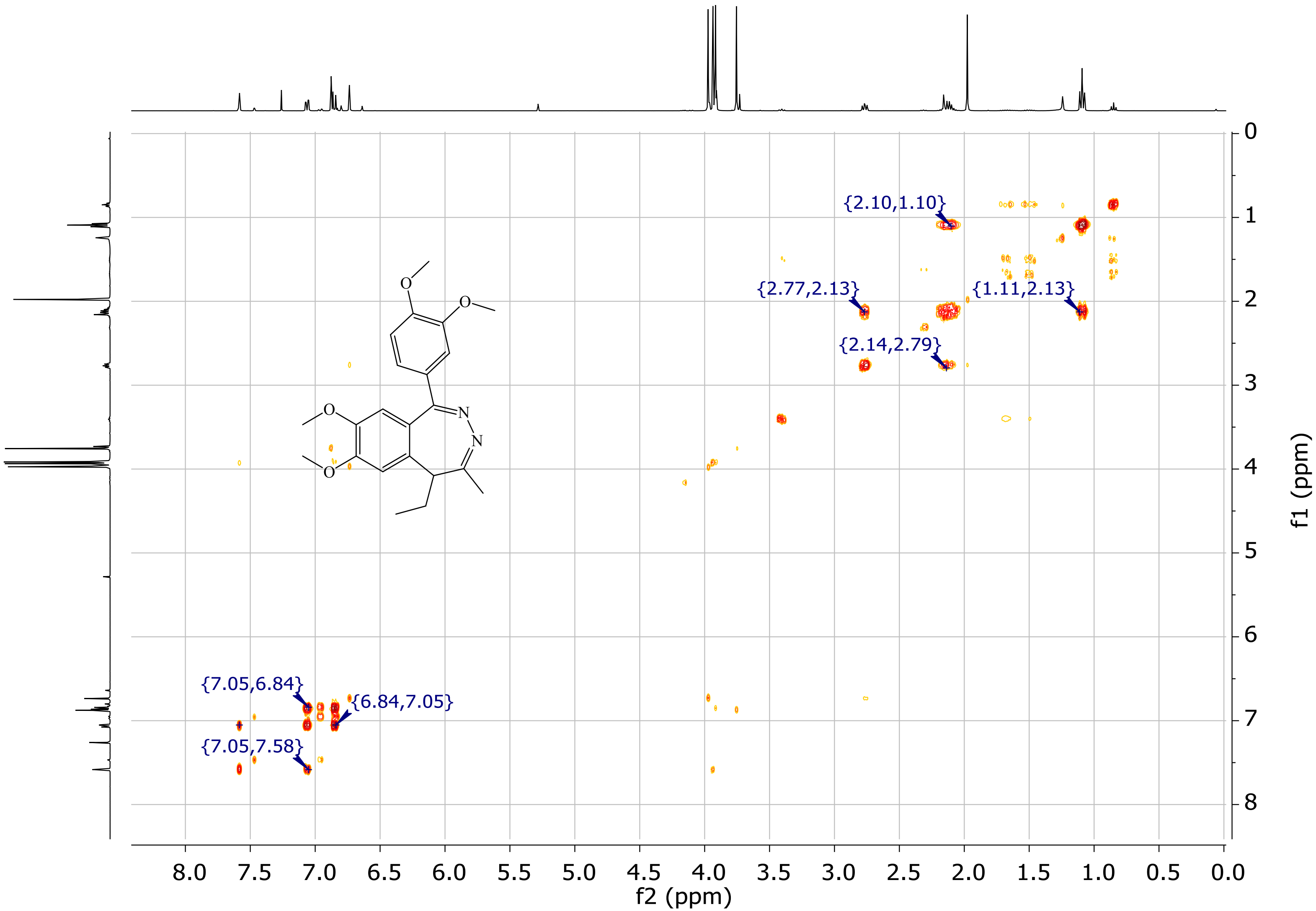


Figure S4.135. COSY NMR spectrum (400MHz, $CDCl_3$) of Tofisopam (BIOCOM) major isomer

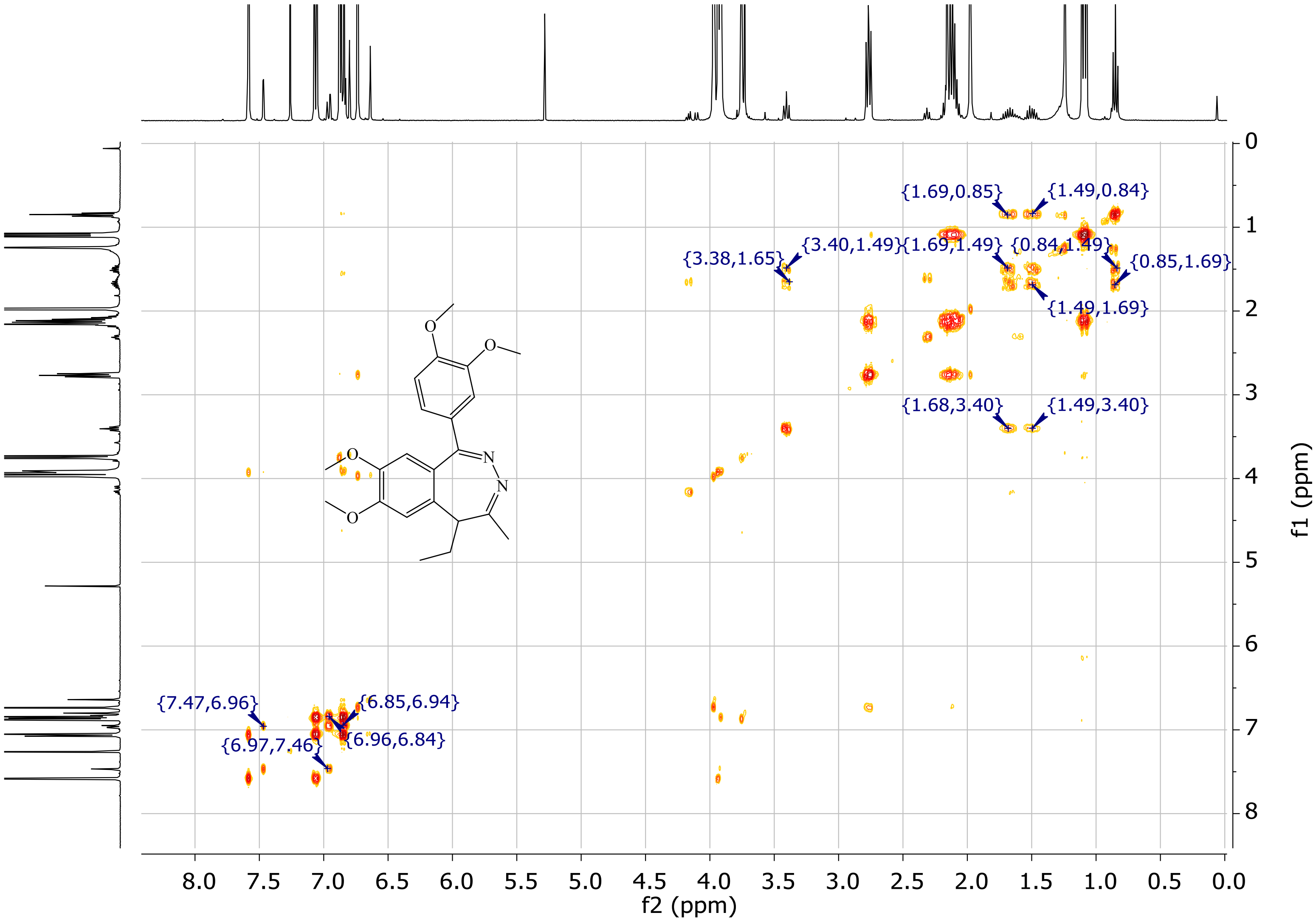


Figure S4.136. COSY NMR spectrum (400MHz, $CDCl_3$) of Tofisopam (BIOCOM) minor isomer

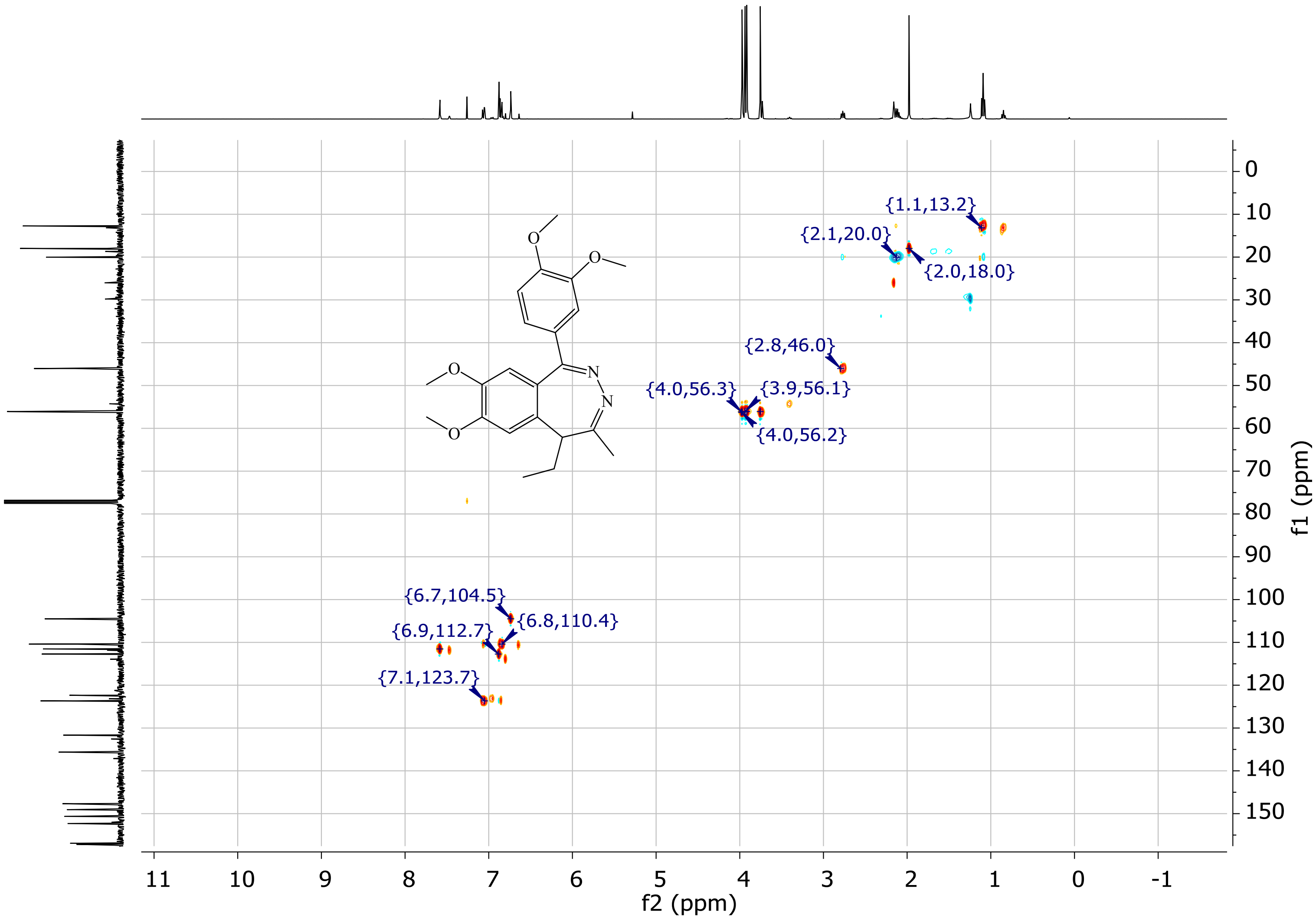


Figure S4.137. [1]H-[13]C-HSQC NMR spectrum (101, 400MHz, $CDCl_3$) of Tofisopam (BIOCOM) major isomer

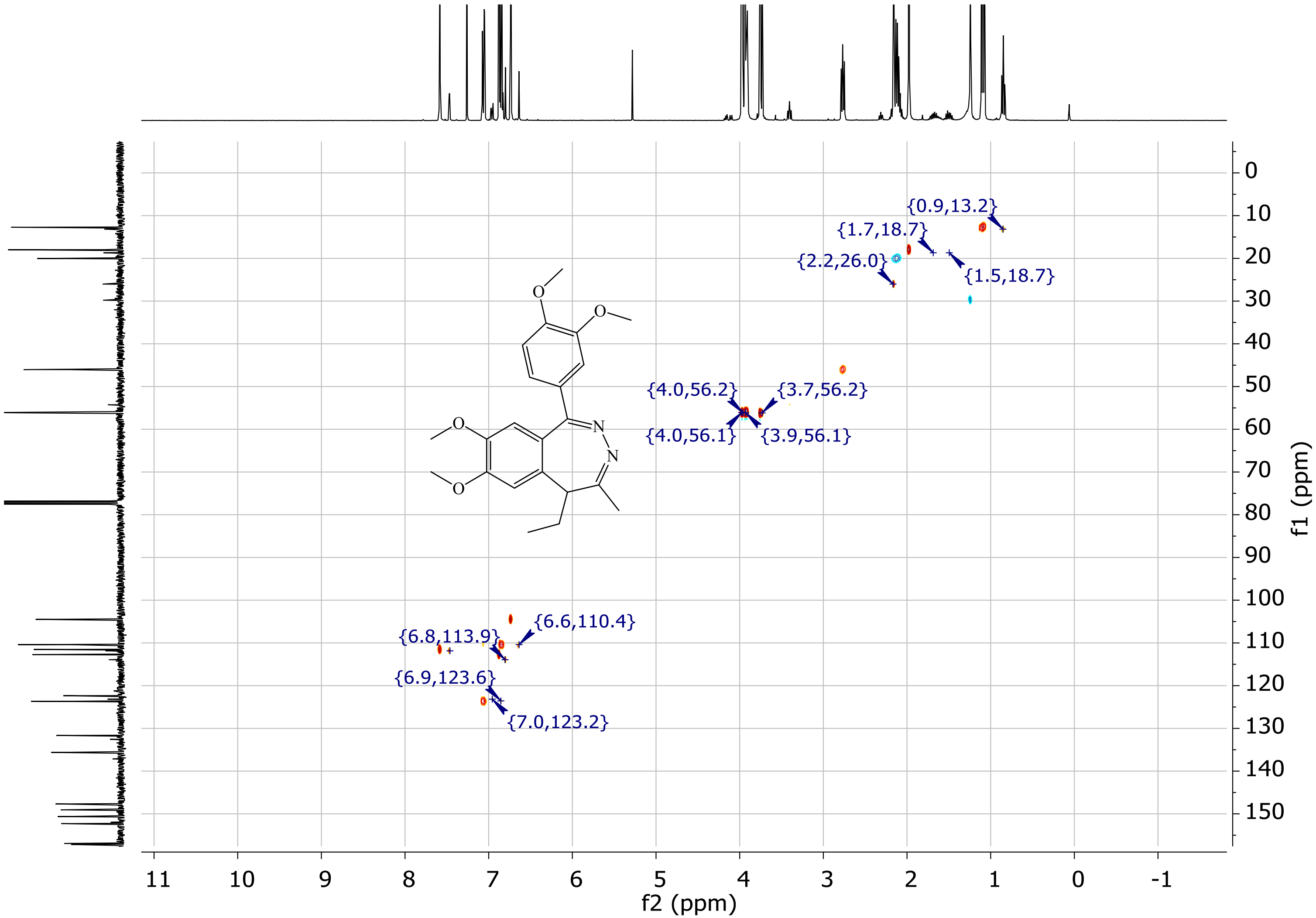


Figure S4.138. **^{1}H-^{13}C-HSQC NMR spectrum (101, 400MHz, $CDCl_3$) of Tofisopam (BIOCOM) minor isomer**

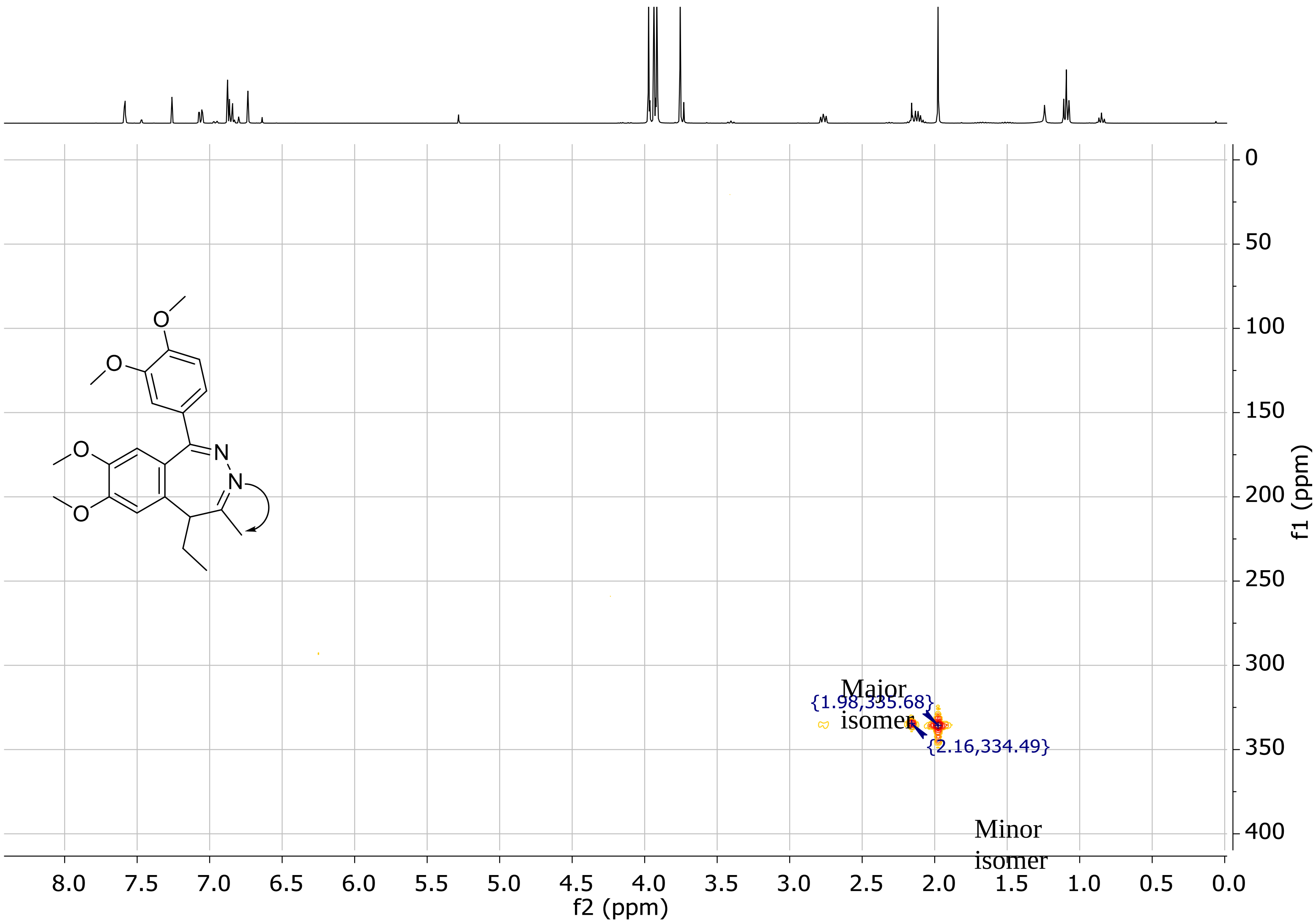


Figure S4.139. ^{1}H-^{15}N-HMBC spectra of Tofisopam (BIOCOM), two isomers

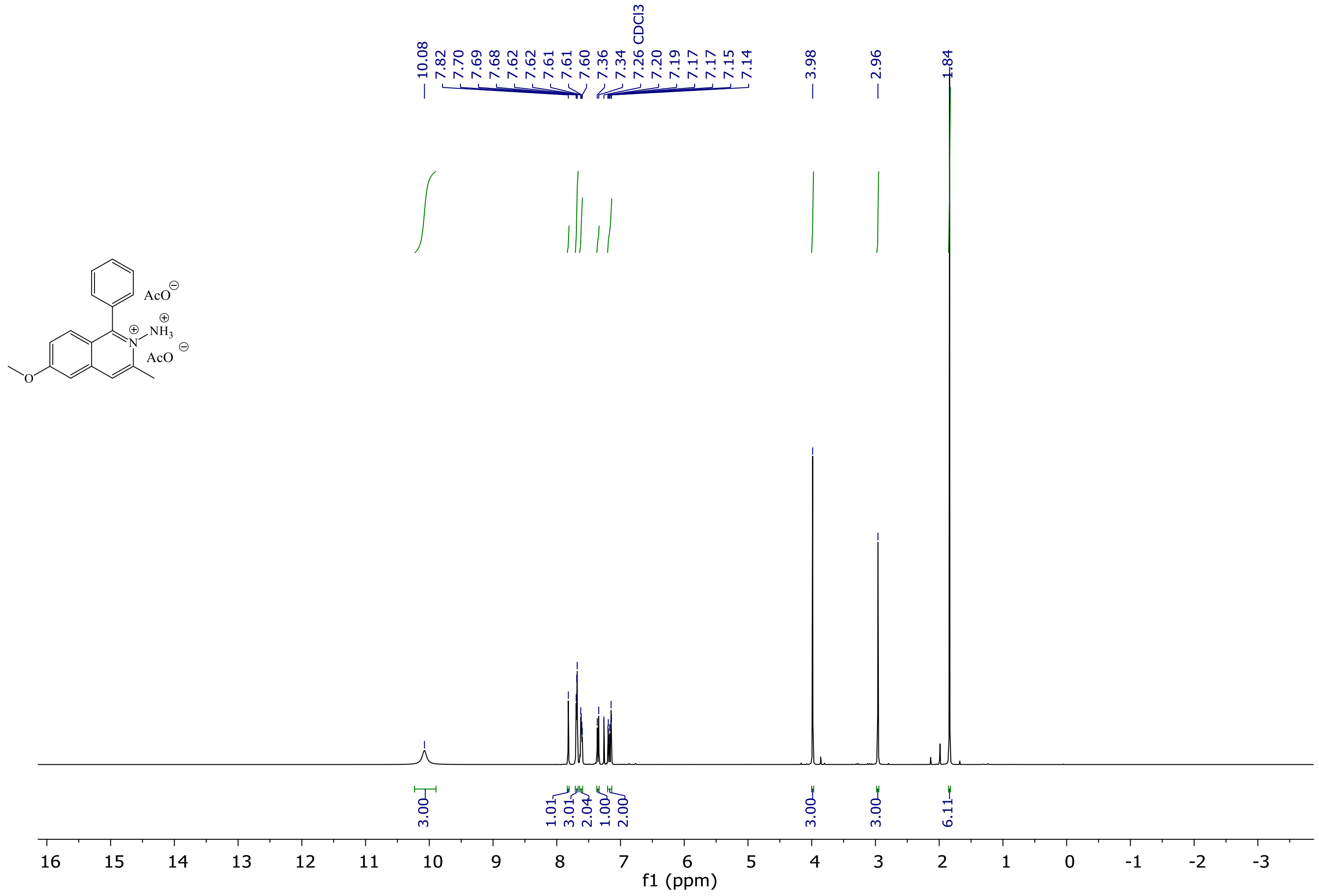


Figure S4.140. [1]H NMR (400MHz, $CDCl_3$) of 2-ammonio-6-methoxy-3-methyl-1-phenylisoquinolinium acetate (3c-3)

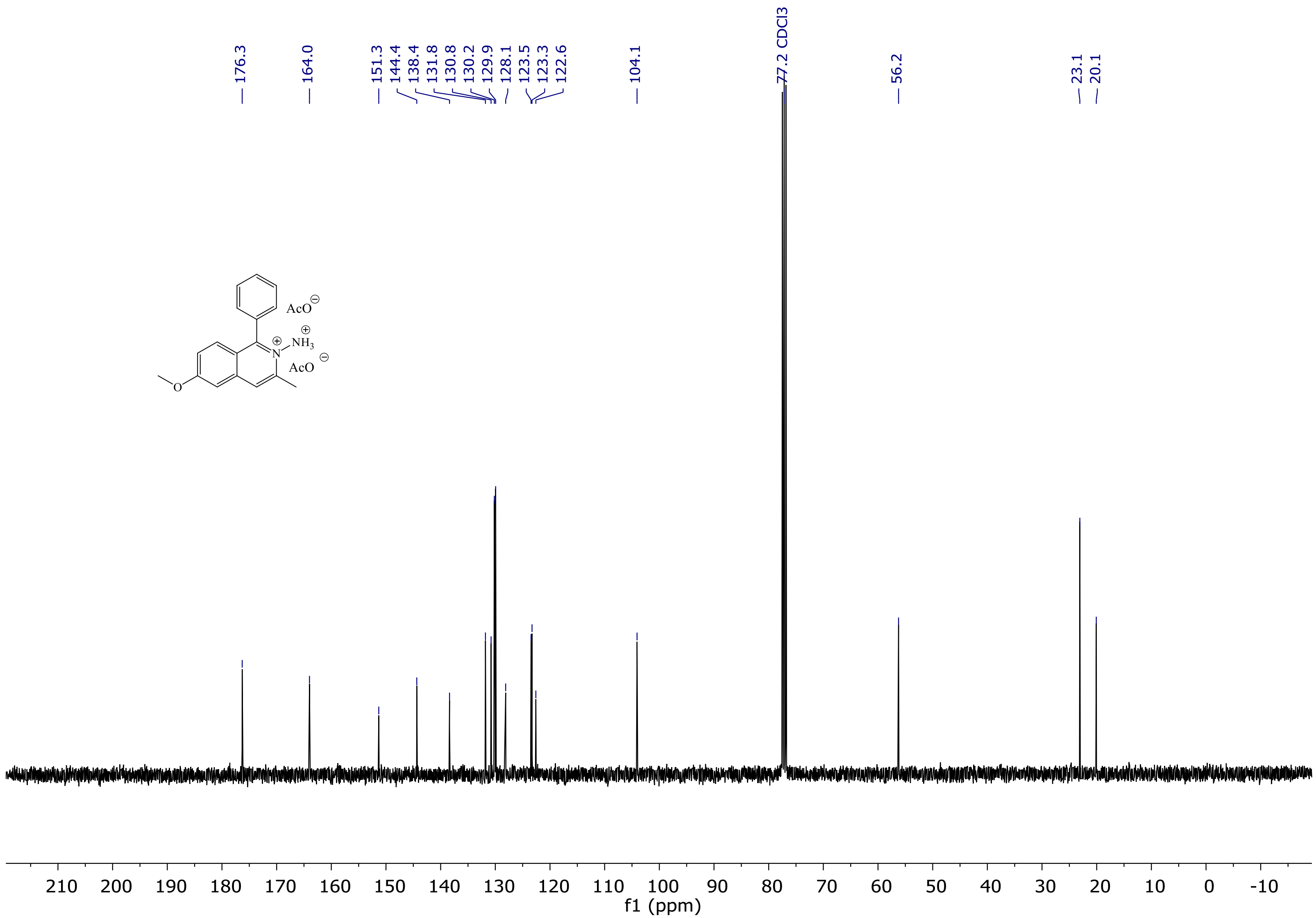


Figure S4.141. $^{13}C\{^1H\}$ **NMR (101MHz,** $CDCl_3$**) of 2-ammonio-6-methoxy-3-methyl-1-phenylisoquinolinium acetate (3c-3)**

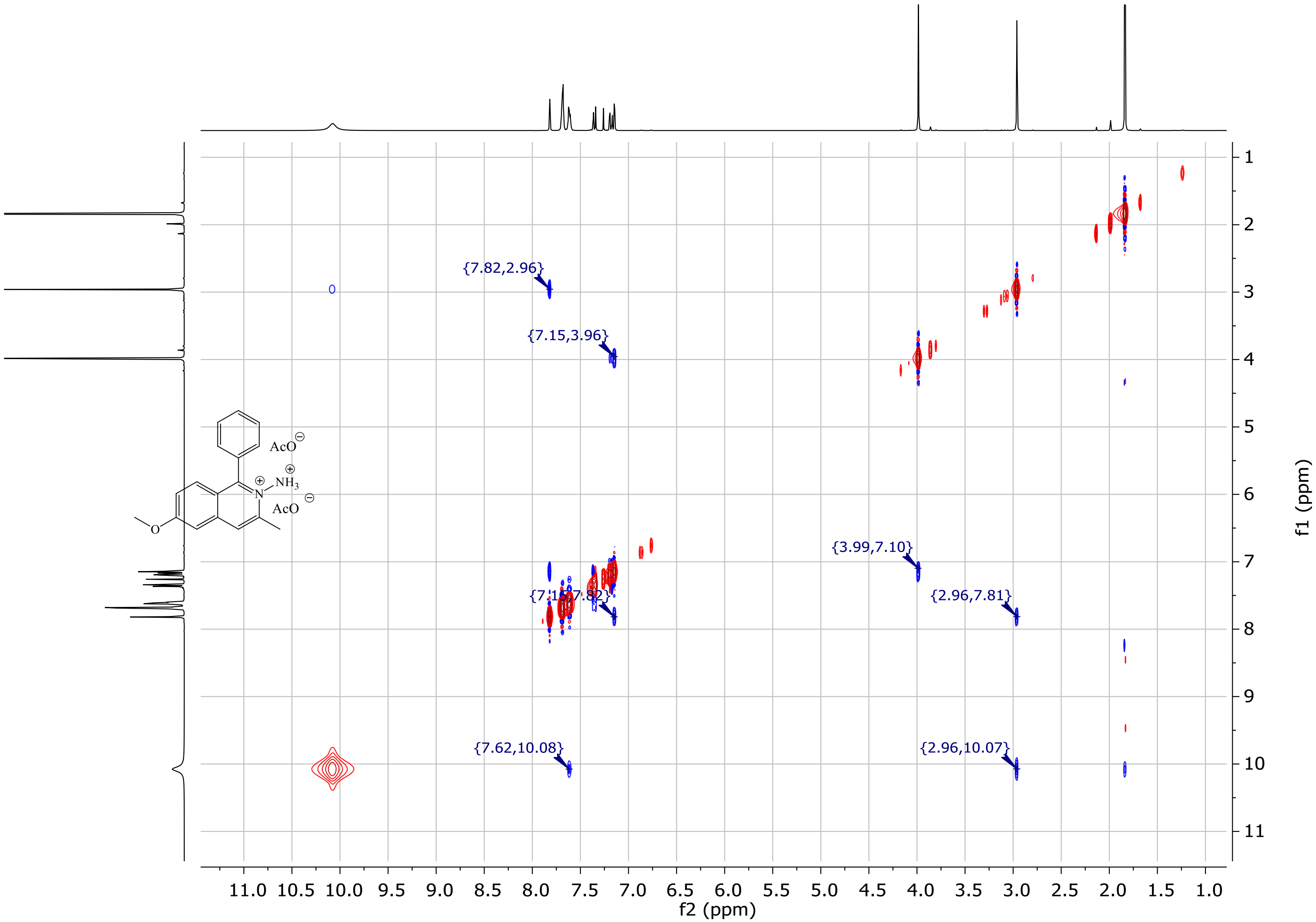


Figure S4.142. NOESY NMR spectrum (400MHz, $CDCl_3$) of 2-ammonio-6-methoxy-3-methyl-1-phenylisoquinolinium acetate (3c-3)

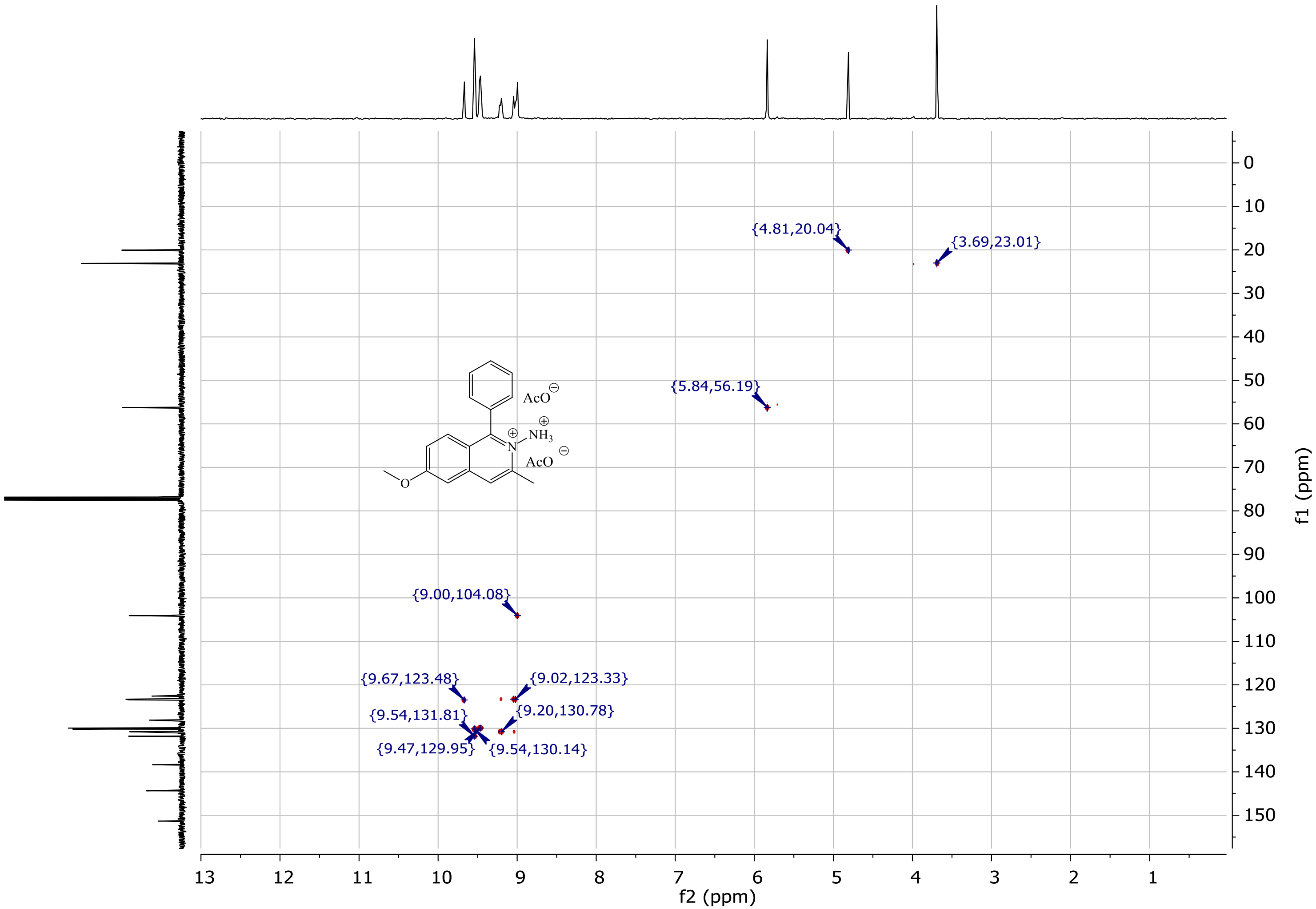


Figure S4.143. [1]H-[13]C-HSQC NMR spectrum (101, 400MHz, $CDCl_3$) of 2-ammonio-6-methoxy-3-methyl-1-phenylisoquinolinium acetate (3c-3)

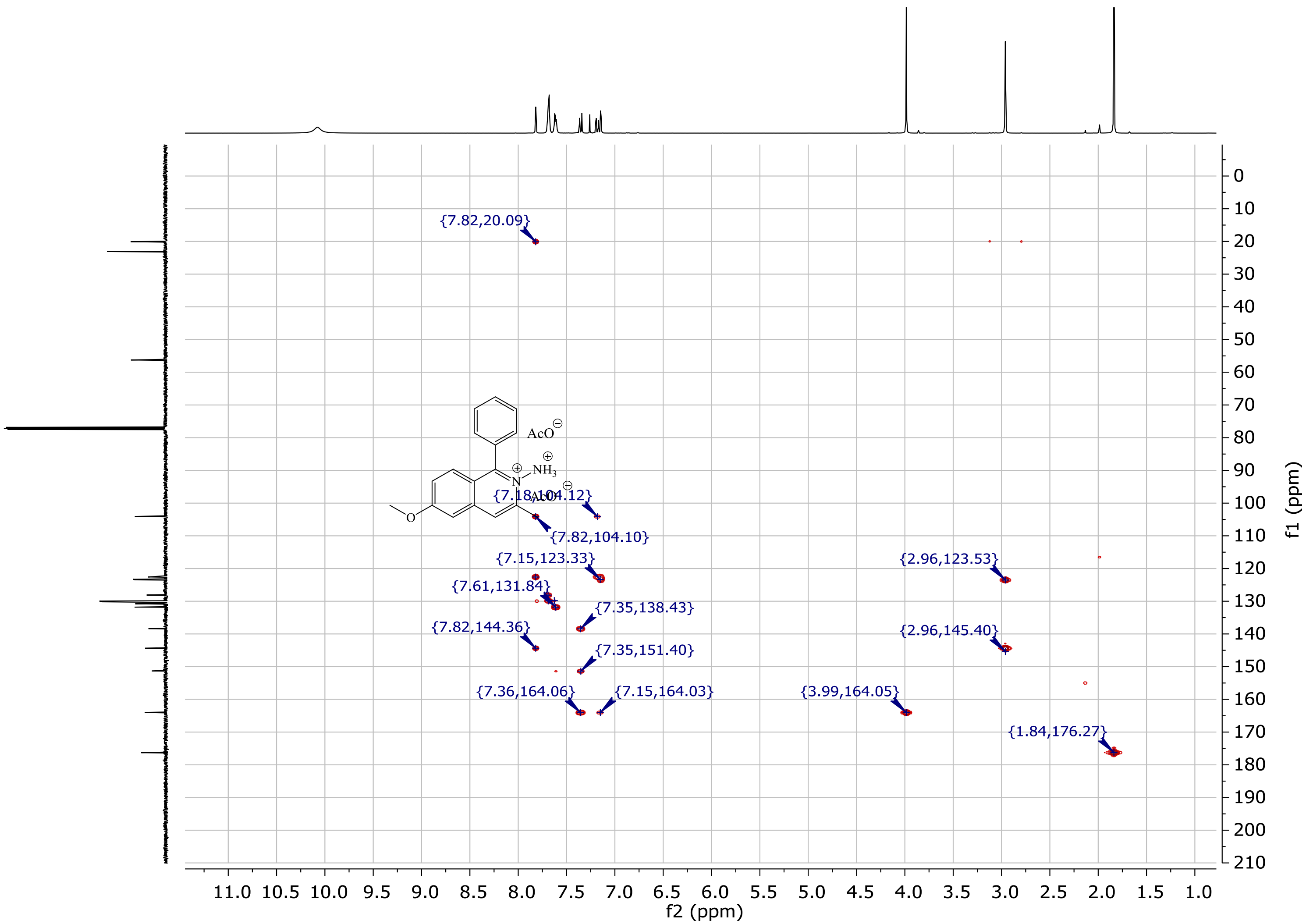


Figure S4.144. ^{1}H-^{13}C HMBC NMR spectrum (101, 400MHz, $CDCl_3$) of 2-ammonio-6-methoxy-3-methyl-1-phenylisoquinolinium acetate (3c-3)

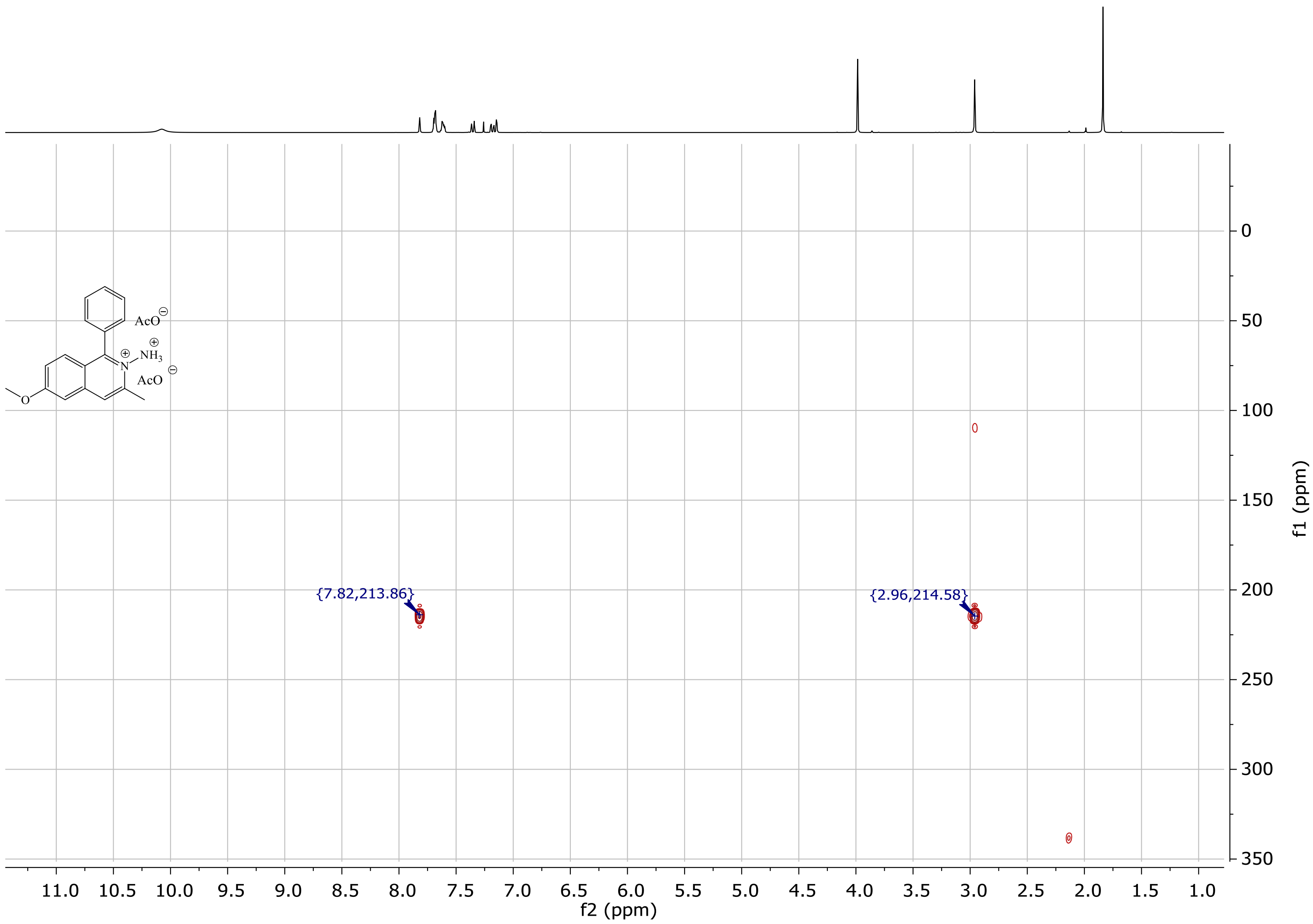


Figure S4.144. $^{1}H^{15}N$-HMBC spectra of 2-ammonio-6-methoxy-3-methyl-1-phenylisoquinolinium acetate (3c-3)

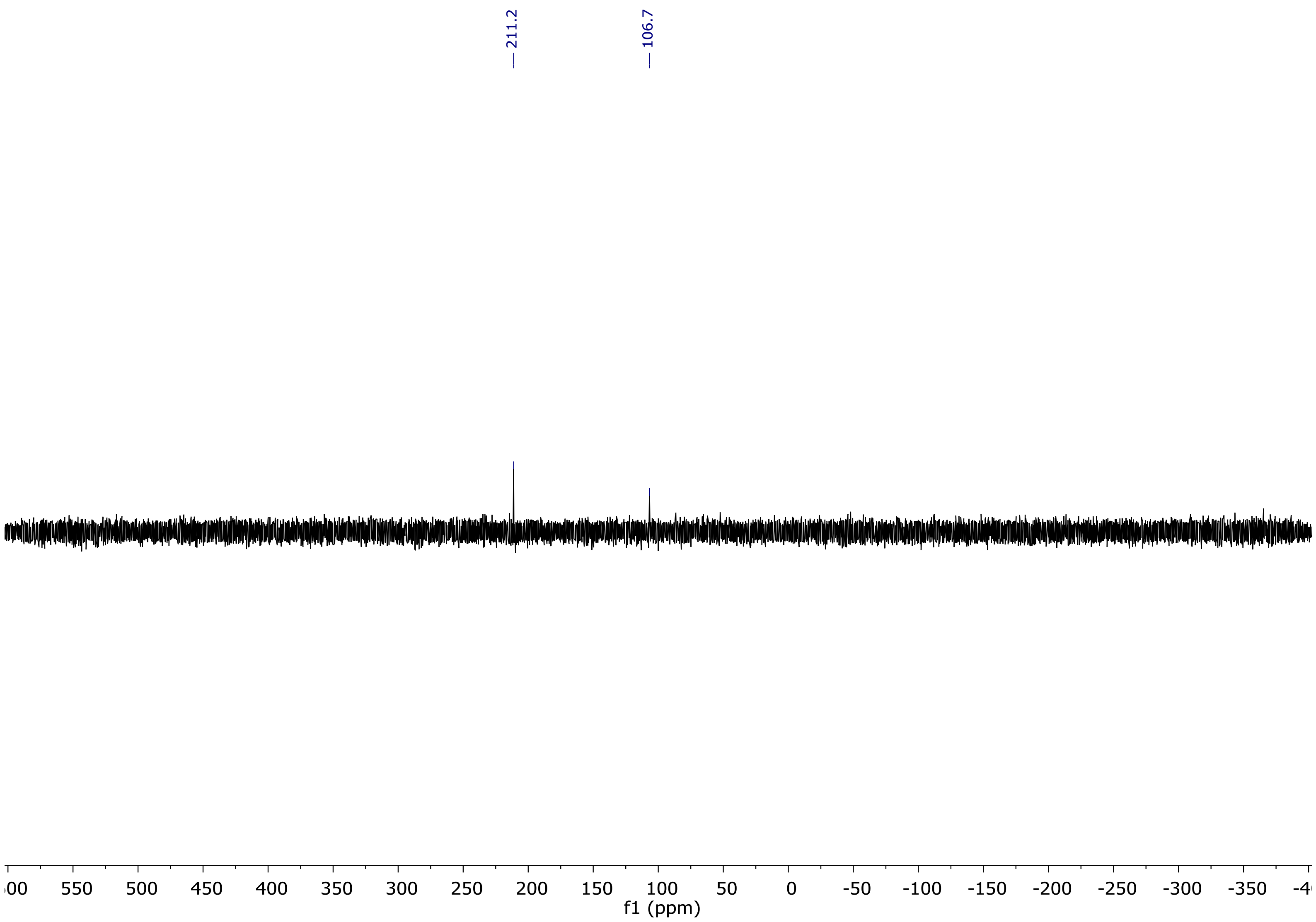


Figure S4.145. ^{15}**N NMR (41 MHz,** $CDCl_3$**) of 2-ammonio-6-methoxy-3-methyl-1-phenylisoquinolinium acetate (3c-3)**