

Sulfonate Versus Sulfonate: Nickel and Palladium Multimetallic Cross-Electrophile Coupling of Aryl Triflates with Aryl Tosylates

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1. General Information

Reagents

Catalysts and Reductants: All metal catalysts and metal reductants, unless otherwise noted, were stored and handled in a N₂ filled glovebox. Palladium(II) dichloride (PdCl₂) was purchased from Alfa Aesar. Nickel(II) dichloride ethylene glycol dimethyl ether complex (NiCl₂(dme)) was purchased from Sigma-Aldrich. The reductant zinc powder (-325 mesh, 97%), zinc flake (-325 mesh, 99.9% metal basis), and manganese powder (-325 mesh) were purchased from Alfa Aesar. Zinc powder was used as the reductant for all the reactions unless otherwise noted.

Ligands: The optimal ligand for the nickel catalyst, 4,4'-diphenyl-2,2'-bipyridine, was purchased from Santa Cruz Biotechnology, Inc. Other amine ligands used for reaction optimization, 2,2':6',2''-terpyridine, 1,10-phenanthroline (phen), 2,2'-bipyridine (bpy), 4,4'-di-*tert*-butyl-2,2'-bipyridine, dimethyl 2,2'-bipyridine-4,4'-dicarboxylate, 6,6'-dimethyl-2,2'-bipyridine and 4,4'-dimethoxy-2,2'-bipyridine were purchased from Sigma-Aldrich or Alfa Aesar. The optimal ligand for the palladium catalyst, 1,4-bis(diphenylphosphino)butane (dppb), was purchased from Alfa Aesar. Other phosphine ligands used for reaction optimization, 1,3-bis(diphenylphosphino)propane (dppp), 1,2-bis(diphenylphosphino)ethane (dppe), triphenylphosphine (PPh₃), tricyclohexylphosphine (PCy₃), 4,5-bis(diphenylphosphino)-9,9-dimethylxanthene (Xantphos), 1,1'-bis(diphenylphosphino)ferrocene (dppf), 2-dicyclohexylphosphino-2',4',6'-triisopropylbiphenyl (XPhos) were purchased from Sigma-Aldrich or Alfa Aesar.

Salt Additives: Lithium bromide (LiBr), sodium bromide (NaBr), potassium bromide (KBr), tetra-*n*-butylammonium bromide (TBAB), lithium chloride (LiCl), and zinc bromide (ZnBr₂) were purchased from Alfa Aesar. All additives were used as received without further purification.

Solvents for Reactions: Anhydrous *N,N*-dimethylformamide (DMF, 99.9%) was purchased from Sigma-Aldrich. It was opened and stored in a N₂ filled glovebox. Dry dichloromethane (DCM) used for synthesis of starting materials was purchased from Fisher Chemical and purified by inert solvent purification system (PureSol MD 5) before use.

Starting Materials: Most aryl electrophiles used are known compounds and were synthesized according to reported procedures. Preparations and characterizations of unreported starting materials **1i**, **2o**, **7c**, **7f** and **7g** are described below in the synthesis of starting materials.

Methods

NMR Spectroscopy: ¹H nuclear magnetic resonance (NMR) spectroscopy chemical shifts are reported in ppm and referenced to tetramethylsilane (TMS) in solvent (for CDCl₃ δ = 0 ppm) or the residual solvent peaks (δ = 7.26 ppm for CDCl₃, δ = 7.15 ppm for C₆D₆, and δ = 2.50 ppm for DMSO-d₆). For ¹³C NMR chemical shifts, the residual solvent peak (δ = 77.20 ppm for CDCl₃, δ = 128.06 ppm for C₆D₆, and δ =

39.52 ppm for DMSO-d₆) were used as references. For ¹⁹F NMR chemical shifts, the external standard, α,α,α -trifluorotoluene ($\delta = 0$ ppm), was used as the reference. NMR spectra were recorded on Avance Bruker NMR spectrometers operating at either 400 MHz or 500 MHz and data analysis was performed with MestreNova. Chemical shifts are reported in parts per million (ppm), multiplicities are indicated by singlet (s), doublet (d), triplet (t), quartet (q), multiplet (m) and broad (br). Coupling constants (J) are reported in Hertz (Hz).

Gas Chromatography: GC analyses were performed on an Agilent 7890A GC equipped with dual DB-5 columns (20 m \times 180 μ m \times 0.18 μ m), dual FID detectors, and hydrogen as the carrier gas. A sample volume of 1 μ L was injected at a temperature of 300 °C and a 100:1 split ratio. The initial inlet pressure was 20.3 psi but varied as the column flow was held constant at 1.8 mL/min for the duration of the run. The initial oven temperature of 50 °C was held for 0.46 min followed by a temperature ramp of 65 °C/min up to 300 °C. The temperature was held at 300 °C for 3 min. The total run time was \sim 7.3 min and the FID temperature was 325 °C.

Mass Spectrometry: Mass spectrometry data was collected on a Thermo Q Exactive Plus (thermofisher.com) via flow injection with electrospray ionization or via ASAP-MS (asap-ms.com) by the chemistry mass spectrometry facility at the University of Wisconsin-Madison. The purchase of the Thermo Q Exactive Plus in 2015 was funded by NIH Award 1S10 OD020022 to the Department of Chemistry.

Supercritical Fluid Chromatography Mass Spectrometry: SFC/MS analyses were performed on a Waters ACQUITY UPC2 equipped with ACQUITY UPC2 PDA and ACQUITY QDa Detector. A Daicel Dcpack SFC-A column (3mm ID \times 150 mm L, 3 μ m PS) was used for separations. The eluent was a mixture (97:3 CO₂/ MeOH) with a flow rate of 2 mL/min at 40 °C with an ABPR at 1500 psi.

Infrared Spectroscopy: Solid state FT-IR spectroscopic data were collected in ATR mode using a Bruker TENSOR 27 spectrometer located in the Chemical Instrumentation Instructional Laboratory at the University of Wisconsin-Madison Department of Chemistry and are reported in wavenumbers (cm⁻¹).

Flash Chromatography for Isolations: Chromatography was performed on silica gel (EMD, silica gel 60, particle size 0.040-0.063 mm) using standard flash techniques or on 40-100 g HP Silica column using a Teledyne Isco Rf-200 (detection at 210 and 254 nm). Products were visualized by UV.

Melting Point: Melting points were measured using a DigiMelt M160 Melting Point Apparatus.

2. Reaction Optimization

2.1 General Procedure for Optimization Studies (Table S1, entries 1-20, 22-35 and 37)

The following procedures were conducted in a N₂ filled glovebox for convenience.

Preparation of nickel and palladium catalyst stock solutions (0.025 M with respect to Ni and Pd)

An oven-dried 1-dram vial equipped with a PTFE-coated stir-bar was charged with NiCl₂(dme) (11.0 mg, 0.050 mmol) and the listed amine ligand (**L1-L7**, 0.060 mmol). DMF (2.0 mL) was then added before the dram vial was capped with a screw cap fitted with a PTFE-faced silicone septum. The mixture was stirred (1000 rpm) at rt for 12 h before being used (vide infra). A second oven-dried 1-dram vial equipped with a PTFE-coated stir-bar was charged with PdCl₂ (8.9 mg, 0.050 mmol) and the listed phosphine ligand (0.060 mmol for dppb or **L8-L11** and 0.120 mmol for **L12-L14**). DMF (2.0 mL) was then added before the dram vial was capped with a screw cap fitted with a PTFE-faced silicone septum. The mixture was stirred (1000 rpm) at rt for 12 h before being used (vide infra).

Catalytic reaction setup

An oven-dried 1-dram vial equipped with a PTFE-coated stir-bar was charged sequentially with **1a** (64 mg, 0.25 mmol, 1.0 equiv), **1b** (62 mg, 0.25 mmol, 1.0 equiv), the listed salt additive (0 to 1.0 mmol, 0 to 4.0 equiv), and the listed reductant (Zn or Mn, 0.50 mmol, 2.0 equiv). Aliquots from both the 0.025 M nickel and palladium stock solutions (vide supra) were then added (30, 100 or 500 μ L for 0.3, 1.0 or 5.0 mol% catalyst loading, respectively), followed by dodecane as an internal standard (15-20 mg). Sufficient DMF was then added to bring the total volume of solvent to 1.0 mL. The vial was capped with a screw cap fitted with a PTFE-faced silicone septum, and the mixture was stirred (1000 rpm) for 5 min in the glovebox at rt. The reaction vial was then removed from the glovebox and heated in a reaction block set to the desired temperature (rt, 40, or 60 °C) with stirring (1250 rpm) for 14 h.

GC analysis

After 14 h, the reaction mixture (1 mL) was cooled to rt, diluted with ethyl acetate (5 mL), and filtered through a 2-cm silica gel plug in a Pasteur pipette. A 100 μ L aliquot of the resulting solution was added to a GC vial and further diluted with ethyl acetate (1 mL). The sample was analyzed by GC using our standard method and the yields were determined based on the peak area of the analyte compared to dodecane as an internal standard.



Figure S1. Screw cap fitted with a PTFE-faced silicone septum, 1-dram vial, and PTFE-coated stir-bar used in optimization studies and for isolated yields at up to 0.5 mmol scale.

2.2 Procedure for Benchtop Reaction Setup (Table S1, entry 21)

The following procedures were performed on the bench using standard Schlenk techniques and N₂ as the inert gas.

Preparation of nickel and palladium catalyst stock solutions (0.025 M with respect to Ni and Pd)

A 1-dram vial equipped with a PTFE-coated stir-bar was charged with NiCl₂(dme) (11.0 mg, 0.050 mmol) and **L1** (18.5 mg, 0.060 mmol) before it was capped with a screw cap fitted with a PTFE-faced silicone septum. The vial was connected to a Schlenk line via a needle through the septum. A second venting needle (open to air) was added, and the vial was purged with N₂ for 5 min. DMF (2.0 mL) was then added via syringe through the septum cap. The venting needle was removed, and the mixture was stirred (1000 rpm) under positive N₂ pressure at rt for 12 h before being used (vide infra). A second 1-dram vial with a PTFE-coated stir-bar was charged with PdCl₂ (8.9 mg, 0.050 mmol) and dppb (25.6 mg, 0.060 mmol) before it was capped with a screw cap fitted with a PTFE-faced silicone septum. The vial was connected to a Schlenk line via a needle through the septum. A second venting needle (open to air) was added, and the vial was purged with N₂ for 5 min. DMF (2.0 mL) was then added via syringe through the septum cap. The venting needle was removed, and the mixture was stirred (1000 rpm) under positive N₂ pressure at rt for 12 h before being used (vide infra).

Catalytic reaction setup

A 10 mL Schlenk tube (Figure S2, left) equipped with a PTFE-coated stir-bar was charged sequentially with **1a** (128 mg, 0.50 mmol, 1.0 equiv), **1b** (124 mg, 0.50 mmol, 1.0 equiv), LiBr (174 mg, 2.0 mmol, 4.0 equiv) and Zn (65 mg, 1.0 mmol, 2.0 equiv). The reaction tube was fitted with a rubber septum on the joint and the hose adapter was connected to a N₂ Schlenk line. The vessel was subjected to three evacuation/N₂ fill cycles. Under positive N₂ pressure, nickel catalyst stock solution (200 μ L for 1.0 mol% catalyst loading), palladium catalyst stock solution (200 μ L for 1.0 mol% catalyst loading), and DMF

(1.6 mL) were added by syringe through the septum cap. The vessel was sealed by closing the stopcock on the Schlenk flask, and the reaction mixture was stirred (1000 rpm) at rt for 10 min. The vessel was then placed into a 40 °C oil bath, and the mixture was stirred (1000 rpm) for 24 h (Figure S2, right).

Isolation and purification

When the reaction was judged complete (GC analysis), the reaction mixture was diluted with ethyl acetate (10 mL), filtered through a short plug of silica gel (1.5 cm × 3.0 cm), and the vessel and silica were washed with extra portions of ethyl acetate (15 mL × 5). Silica gel (2.5-3.0 g) was then added to the combined filtrate and the volatile solvents were removed by rotary evaporation. The resulting dry-loaded material was purified by flash chromatography on silica gel to provide the desired product.



Figure S2: (Left) the Schlenk tube and rubber septum used in the benchtop reaction (Table S1, entry 21); (Right) the reaction vessel in the oil bath (Table S1, entry 21).

2.3 Procedure for Lower Catalyst Loading Reactions (0.5 mol% Ni/Pd, 0.6 mol% ligands) (Table S1, entry 36)

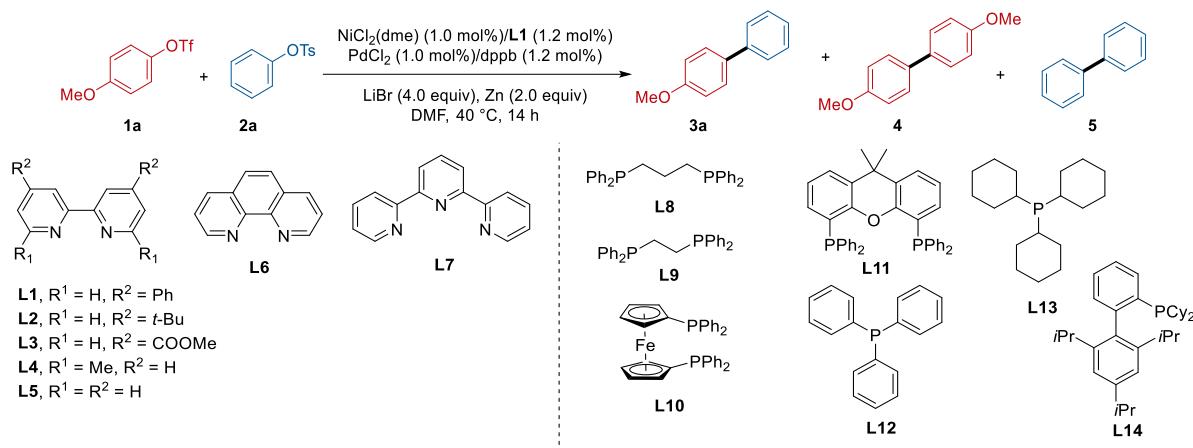
The following procedures were conducted in a N₂ filled glovebox for convenience. Nickel and palladium catalyst stock solutions were prepared following *general procedure for optimization studies* (page S4) using **L1** (18.5 mg, 0.060 mmol) as the amine ligand and dppb (25.6 mg, 0.060 mmol) as the phosphine ligand. GC analysis was performed following *general procedure for optimization studies* (page S4) after 24 h reaction time.

Catalytic Reaction Setup

An oven-dried 1-dram vial equipped with a PTFE-coated stir-bar was charged sequentially with **1a** (128 mg, 0.50 mmol, 1.0 equiv), **1b** (124 mg, 0.50 mmol, 1.0 equiv), LiBr (174 mg, 2.0 mmol, 4.0 equiv), and Zn (65 mg, 1.0 mmol, 2.0 equiv). Aliquots from both the 0.025 M nickel (100 μ L for 0.5 mol%) and

palladium (100 μ L for 0.5 mol%) stock solutions were added, followed by dodecane as an internal standard (15-20 mg). DMF (0.8 mL) was added before the vial was capped with a screw cap fitted with a PTFE-faced silicone septum. The reaction mixture was stirred (1000 rpm) for 10 min in the glovebox at rt. The vial was then removed from the glovebox and heated in a reaction block set to 40 °C with stirring (1250 rpm) for 24 h.

Table S1. Optimization of reaction parameters for cross-electrophile coupling of **1a** with **2a**^{a,b}



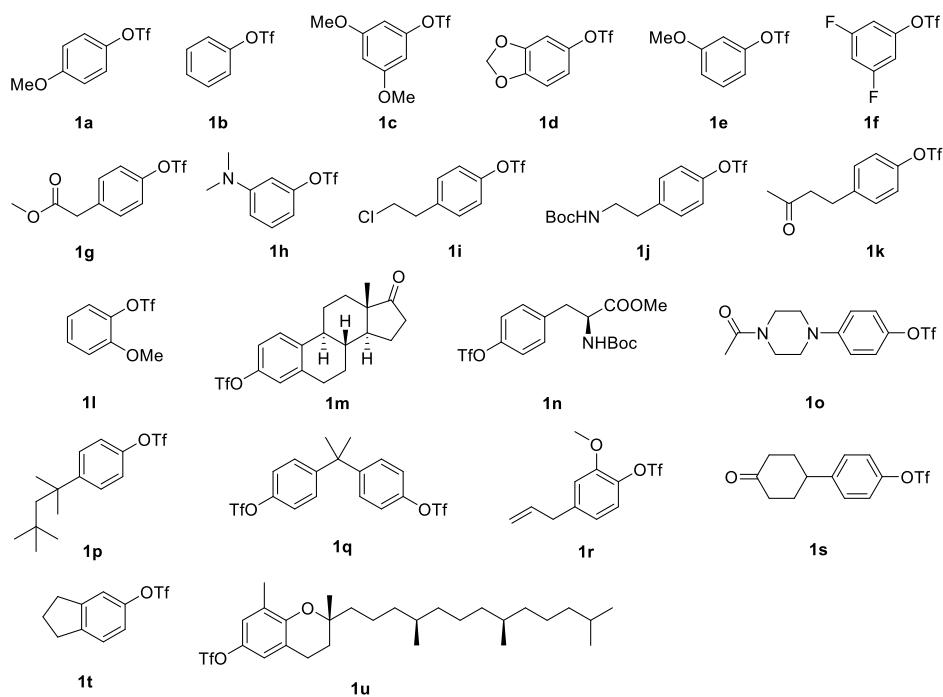
entry	variations from conditions above	3a (%)	4 (%)	5 (%)	1a (%)	2a (%)
1	none	76	12	13	0	0
2	without PdCl_2 and dppb	58	20	18	0	0
3	without $\text{NiCl}_2(\text{dme})$ and L1	<5	0	0	93	95
4	without PdCl_2	19	11	6	49	48
5	without $\text{NiCl}_2(\text{dme})$	0	0	0	98	96
6	without L1	0	0	0	98	98
7	without dppb	49	13	<5	13	30
8	without Zn	0	0	0	95	95
9	Mn instead of Zn	<5	0	0	91	95
10	without LiBr	8	3	1	82	91
11	2.0 equiv of LiBr	63	12	5	11	25
12	NaBr instead of LiBr	72	12	9	0	0
13	KBr instead of LiBr	73	12	5	0	9
14	$n\text{-Bu}_4\text{NBr}$ instead of LiBr	54	11	8	0	9
15	LiF instead of LiBr	5	<5	0	83	92
16	LiBF_4 instead of LiBr	9	<5	0	81	91
17	LiCl instead of LiBr	60	18	18	0	0
18	ZnBr_2 instead of LiBr	0	0	0	96	98
19	rt	64	10	6	9	6
20	60 °C	67	16	10	0	0
21	Reaction setup on benchtop	73 ^c	/	/	/	/
22	L2 instead of L1	32	6	8	43	48
23	L3 instead of L1	12	48	<5	0	58
24	L4 instead of L1	8	8	<5	79	83
25	L5 instead of L1	65	18	15	0	0
26	L6 instead of L1	62	19	14	0	5
27	L7 instead of L1	<5	8	<5	84	76
28	L8 instead of dppb	41	24	20	0	0
29	L9 instead of dppb	61	19	13	0	0
30	L10 instead of dppb	59	20	10	0	0
31	L11 instead of dppb	43	27	13	0	0
32	L12 instead of dppb	43	29	11	0	0
33	L13 instead of dppb	29	33	27	0	0
34	L14 instead of dppb	55	24	16	0	0
35	5.0 mol% $\text{NiCl}_2(\text{dme})$ /6.0 mol% L1 and 5.0 mol% PdCl_2 /6.0 mol% dppb	64	16	21	0	0
36	0.5 mol% $\text{NiCl}_2(\text{dme})$ /0.6 mol% L1 and 0.5 mol% PdCl_2 /0.6 mol% dppb	73 ^d	12	12	0	0
37	0.30 mol% $\text{NiCl}_2(\text{dme})$ /0.36 mol% L1 and 0.30 mol% PdCl_2 /0.36 mol% dppb	58	8	5	20	17

^aReactions were run on a 0.25 mmol scale in 1.0 mL DMF. DMF = *N,N*-dimethylformamide. ^bGC yields using dodecane as an internal standard. ^cIsolated yield from 0.50 mmol scale reaction. ^dReaction was run on 0.5 mmol scale in 1.0 mL DMF.

3. Synthesis of Starting Materials

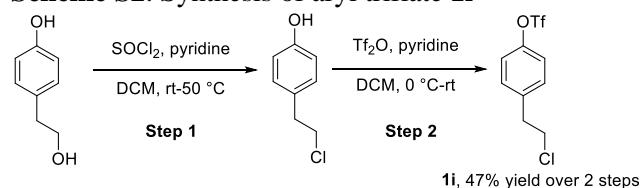
3.1 Synthesis of Aryl Triflates

Scheme S1. Aryl triflates used in this study



Known compounds **1a**¹, **1b**¹, **1c**², **1d**³, **1e**⁴, **1f**⁵, **1g**⁶, **1h**⁷, **1j**⁸, **1k**⁹, **1l**¹⁰, **1m**³, **1n**³, **1o**³, **1p**¹¹, **1q**¹², **1r**¹³, **1s**¹⁴, **1t**¹⁵ and **1u**¹ were prepared according to the reported procedures.

Scheme S2. Synthesis of aryl triflate **1i**



Procedure for the synthesis of **1i**

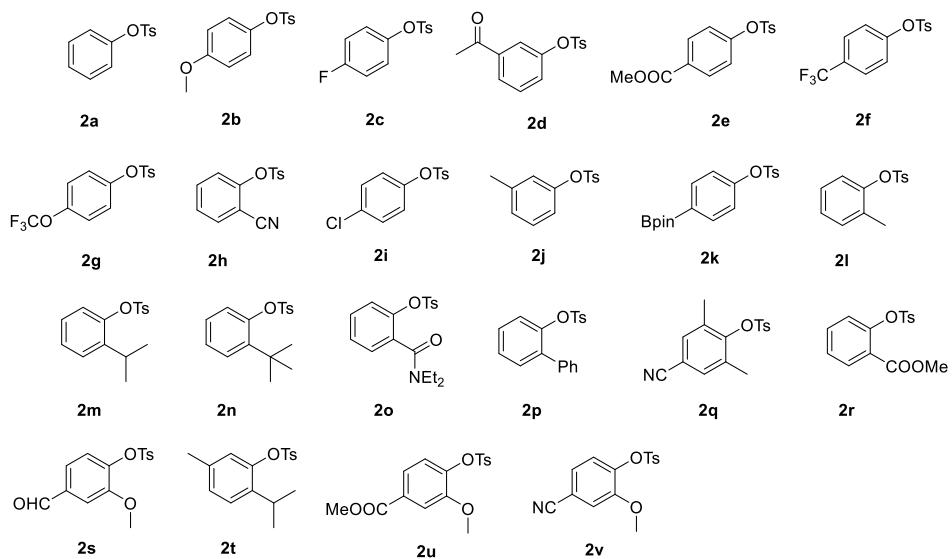
Step 1: A two-neck 100 mL round bottom flask equipped with a PTFE-coated stir-bar was fitted with a reflux condenser connected to a N_2 Schlenk line via a needle through a rubber septum (center neck). The flask was charged with 2-(4-hydroxyphenyl)ethanol (2000 mg, 14.5 mmol, 1.00 equiv) and pyridine (5728 mg, 72.5 mmol, 5.00 equiv) through the side-neck under positive N_2 flow. The reaction vessel was capped with a rubber septum and dry dichloromethane (40 mL) was added by syringe. The mixture was cooled in an ice-water bath for 10 min. A solution of thionyl chloride (8627 mg, 72.5 mmol, 5.00 equiv) in dry dichloromethane (10 mL) was added dropwise by syringe through the septum over 20 min with cooling.

The ice-water bath was then removed. The mixture was stirred at rt for 2 h, followed by heating the mixture to reflux in a 50 °C oil bath for 8 h. When the reaction was judged complete (TLC analysis, hexanes/ethyl acetate = 5/1, R_f = 0.3), the reaction mixture was cooled in an ice-water bath for 10 min before it was poured into 100 mL ice-cold water. The layers were separated in a 500 mL separatory funnel. The dichloromethane layer was set aside while the aqueous layer was washed further with dichloromethane (50 mL \times 3). The combined organic layers were dried over anhydrous MgSO₄, the resulting mixture was filtered to remove the MgSO₄, and the filtrate was concentrated by rotary evaporation. The residue was purified by flash chromatography on silica gel (hexanes/ethyl acetate = 5/1 to 3/1). The crude 2-(4-hydroxyphenyl)ethyl chloride product was directly used in the next step without further purification.

Step 2: A two-neck 100 mL round bottom flask equipped with a PTFE-coated stir-bar was connected to a N₂ Schlenk line via a needle through a rubber septum (center neck) and a second rubber septum was fitted to the side-neck. The flask was charged with 2-(4-hydroxyphenyl)ethyl chloride (1560 mg, 10.0 mmol, 1.00 equiv) obtained from Step 1 and pyridine (2291 mg, 29.0 mmol, 2.90 equiv) through the side-neck under positive N₂ flow. The side-neck was re-capped with a rubber septum after the addition, and dry dichloromethane (10 mL) was added by syringe. The reaction mixture was cooled in an ice-water bath for 10 min. A solution of trifluoromethanesulfonic anhydride (8178 mg, 29.0 mmol, 2.90 equiv) in dry dichloromethane (20 mL) was added dropwise by syringe through the side-neck septum over 20 min with cooling. After the addition was complete, the ice-water bath was removed, and the reaction mixture was allowed to recover to rt with stirring over 12 h. When the reaction was judged complete (TLC analysis, hexanes/ethyl acetate = 5/1, R_f = 0.8), the reaction mixture was poured into a 500 mL separatory funnel containing ice-cold water (50 mL) and dichloromethane (50 mL). The dichloromethane layer was set aside while the aqueous layer was washed further with dichloromethane (50 mL \times 3). The combined organic layers were dried over anhydrous MgSO₄, the resulting mixture was filtered to remove the MgSO₄, and the filtrate was concentrated by rotary evaporation. The crude material was purified by flash chromatography on silica gel (hexane/ethyl acetate = 50/1 to 10/1) to afford **4-(2-chloroethyl)phenyl trifluoromethanesulfonate (1i)** (1963 mg, 47% yield over 2 steps) as a colorless oil. ¹H NMR (400 MHz, CDCl₃) δ 7.31 (d, J = 8.7 Hz, 2 H), 7.23 (d, J = 8.7 Hz, 2 H), 3.72 (t, J = 7.1 Hz, 2 H), 3.10 (t, J = 7.1 Hz, 2 H); ¹³C{¹H} NMR (125 MHz, CDCl₃) δ 148.7, 138.8, 130.8, 121.6, 118.9 (q, J = 255.0 Hz), 44.6, 38.4; ¹⁹F{¹H} NMR (376 MHz, CDCl₃) δ -72.85 ppm. HRMS (ESI) m/z calcd for [M + H]⁺ 288.9908, found 288.9904. IR (cm⁻¹): 2957, 1416, 1205, 1135, 883, 608.

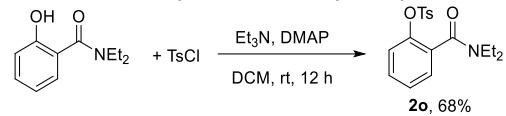
3.2 Synthesis of Aryl Tosylates

Scheme S3. Aryl tosylates used in this study



Known compounds **2a**¹⁶, **2b**¹⁷, **2c**¹⁷, **2d**¹⁸, **2e**¹⁷, **2f**¹⁹, **2g**¹⁸, **2h**²⁰, **2i**¹⁸, **2j**²¹, **2k**²², **2l**¹⁷, **2m**²³, **2n**²⁴, **2p**²⁵, **2q**²², **2r**¹⁶, **2s**²⁶, **2t**²⁷, **2u**²⁸ and **2v**²⁹ were prepared according to reported procedures.

Scheme S4. Synthesis of aryl tosylate **2o**



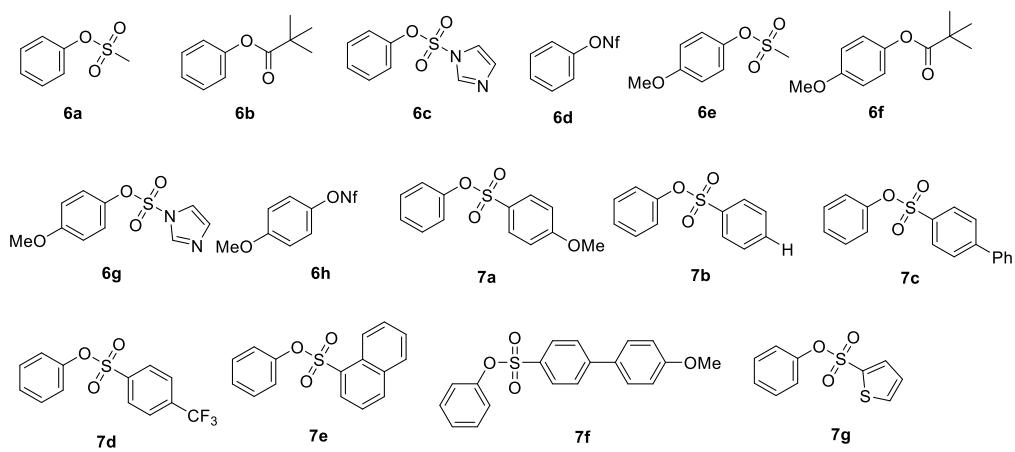
Procedure for the synthesis of aryl tosylate **2o**

A scintillation vial equipped with a PTFE-coated stir-bar was charged with *N,N*-diethylsalicylamide (965 mg, 5.00 mmol, 1.00 equiv), DMAP (61 mg, 0.50 mmol, 0.10 equiv), and triethylamine (1010 mg, 10.0 mmol, 2.00 equiv). Dry dichloromethane (10 mL) was added before the scintillation vial was capped with a rubber septum. The mixture was stirred at rt for 5 min. 4-toluenesulfonyl chloride (1143 mg, 6.00 mmol, 1.20 equiv) was then added in three portions over 2 min. The vial was recapped, and the mixture was stirred at rt for 12 h. When the reaction was judged complete (TLC analysis, hexanes/ethyl acetate = 5/1, R_f = 0.3), the reaction mixture was poured into a 250 mL separatory funnel containing water (30 mL) and dichloromethane (30 mL). The dichloromethane layer was set aside while the aqueous layer was washed further with dichloromethane (30 mL \times 3). The combined organic layers were dried over anhydrous MgSO_4 , the resulting mixture was filtered to remove the MgSO_4 , and the filtrate was concentrated by rotary evaporation. The crude material was purified by flash chromatography on silica gel (hexanes/ethyl acetate = 5/1 to 3/1) to afford **2-(diethylcarbamoyl)phenyl 4-methylbenzenesulfonate**

(2o) (1180 mg, 68% yield) as a colorless oil. ^1H NMR (500 MHz, CDCl_3) δ 7.75 (d, $J = 8.3$ Hz, 2 H), 7.29 (t, $J = 9.7$ Hz, 3 H), 7.26 – 7.21 (m, 3 H), 3.68 (s, 1 H), 3.11 (s, 3 H), 2.40 (s, 3 H), 1.13 (t, $J = 7.1$ Hz, 3 H), 1.02 (t, $J = 7.1$ Hz, 3 H); $^{13}\text{C}\{\text{H}\}$ NMR (125 MHz, CDCl_3) δ 166.4, 145.7, 145.5, 132.9, 131.4, 130.2, 130.0, 128.6, 128.4, 127.1, 122.2, 43.1, 39.1, 21.9, 14.0, 12.8 ppm. HRMS (ESI) m/z calcd for $[\text{M} + \text{H}]^+$ 348.1264, found 348.1258. IR: (cm^{-1}): 2972, 2934, 1623, 1518, 1289, 1244, 835, 763.

3.3 Synthesis of Other Phenol Derivatives

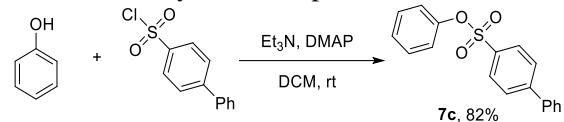
Scheme S5. Other phenol derivatives used in this study



Known compounds **6a**³⁰, **6b**³¹, **6c**³², **6d**³³, **6e**³⁰, **6f**³⁴, **6g**³², **6h**³⁵, **7a**³⁶, **7b**³⁷, **7d**³⁸ and **7e**³⁹ were prepared according to reported procedures.

Synthesis of phenol derivatives **7c**, **7f** and **7g**

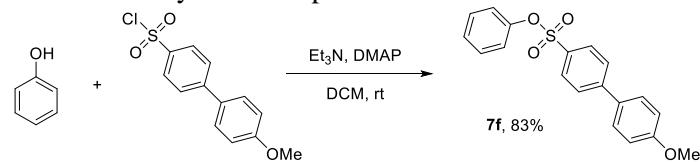
Scheme S6. Synthesis of phenol derivative **7c**



Phenyl [1,1'-biphenyl]-4-sulfonate (7c) [CAS: 20443-76-9] was synthesized following *procedure for the synthesis of aryl tosylate 2o* (page S11) using phenol (470 mg, 5.00 mmol, 1.00 equiv), DMAP (61 mg, 0.50 mmol, 0.10 equiv), triethylamine (1010 mg, 10.0 mmol, 2.00 equiv) and 4-phenylbenzenesulfonyl chloride (1512 mg, 6.00 mmol, 1.20 equiv) as starting materials and dry dichloromethane (10 mL) as solvent. After stirring at rt for 12 h, the reaction was quenched following the procedure and the crude material was purified by flash chromatography on silica gel (hexanes/ethyl acetate = 5/1 to 3/1) to afford the desired product (1271 mg, 82% yield) as a white solid. mp = 86 – 88 °C. ^1H NMR (500 MHz, CDCl_3 , TMS) δ 7.88 (d, $J = 8.5$ Hz, 2 H), 7.72 (d, $J = 8.5$ Hz, 2 H), 7.61 (d, $J = 7.1$ Hz, 2 H), 7.48 (t, $J = 7.4$ Hz, 2

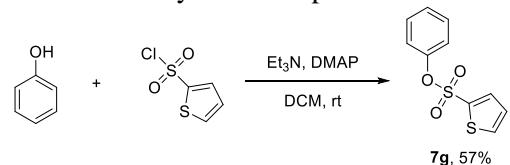
H), 7.43 (t, J = 7.3 Hz, 1 H), 7.30 (t, J = 7.5 Hz, 2 H), 7.25 (t, J = 7.3 Hz, 1 H), 7.03 (d, J = 7.7 Hz, 2 H); $^{13}\text{C}\{\text{H}\}$ NMR (100 MHz, CDCl_3) δ 149.8, 147.2, 138.9, 134.0, 129.8, 129.3, 129.2, 129.0, 127.8, 127.5, 127.3, 122.5 ppm. HRMS (ESI) m/z calcd for $[\text{M} + \text{Na}]^+$ 333.0556, found 333.0552. IR (cm^{-1}): 3062, 1593, 1483, 1349, 1182, 852, 762, 681.

Scheme S7. Synthesis of phenol derivative **7f**



Phenyl 4'-methoxy-[1,1'-biphenyl]-4-sulfonate (7f) was synthesized following *procedure for the synthesis of aryl tosylate 2o* (page S11) using phenol (282 mg, 3.00 mmol, 1.00 equiv), DMAP (37 mg, 0.30 mmol, 0.10 equiv), triethylamine (606 mg, 6.00 mmol, 2.00 equiv) and 4'-methoxybiphenyl-4-sulfonyl chloride (1015 mg, 3.60 mmol, 1.20 equiv) as starting materials and dry dichloromethane (6 mL) as solvent. After stirring at rt for 12 h, the reaction was quenched following the procedure and the crude material was purified by flash chromatography on silica gel (hexanes/ethyl acetate = 5/1 to 3/1) to afford the desired product (850 mg, 83% yield) as a white solid. mp = 100 – 102 °C. ^1H NMR (500 MHz, CDCl_3 , TMS) δ 7.85 (d, J = 8.6 Hz, 2 H), 7.68 (d, J = 8.5 Hz, 2 H), 7.57 (d, J = 8.7 Hz, 2 H), 7.30 (t, J = 7.5 Hz, 2 H), 7.28 – 7.24 (m, 1 H), 7.02 (m, 4 H), 3.87 (s, 3 H); $^{13}\text{C}\{\text{H}\}$ NMR (125 MHz, CDCl_3) δ 160.5, 149.8, 146.8, 133.1, 131.2, 129.8, 129.2, 128.7, 127.3, 127.1, 122.6, 114.7, 55.6 ppm. HRMS (ESI) m/z calcd for $[\text{M} + \text{H}]^+$ 341.0842, found 341.0841. IR (cm^{-1}): 3069, 2839, 1594, 1521, 1372, 1178, 860, 782, 634.

Scheme S8. Synthesis of phenol derivative **7g**



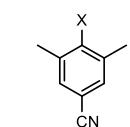
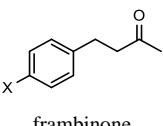
Phenyl thiophene-2-sulfonate (7g) was synthesized following *procedure for the synthesis of aryl tosylate 2o* (page S11) using phenol (282 mg, 3.00 mmol, 1.00 equiv), DMAP (37 mg, 0.30 mmol, 0.10 equiv), triethylamine (606 mg, 6.00 mmol, 2.00 equiv) and 2-thiophenesulfonyl chloride (655 mg, 3.60 mmol, 1.2 equiv) as starting materials and dry dichloromethane (6 mL) as solvent. After stirring at rt for 12 h, the reaction was quenched following the procedure and the crude material was purified by flash chromatography on silica gel (hexanes/ethyl acetate = 5/1) to afford the desired product (410 mg, 57% yield) as a colorless oil. ^1H NMR (500 MHz, CDCl_3 , TMS) δ 7.72 (dd, J = 5.0, 1.3 Hz, 1 H), 7.57 (dd, J = 3.8, 1.3 Hz, 1 H), 7.35 – 7.25 (m, 3 H), 7.10 (dd, J = 5.0, 3.8 Hz, 1 H), 7.04 (d, J = 8.1 Hz, 2 H); $^{13}\text{C}\{\text{H}\}$

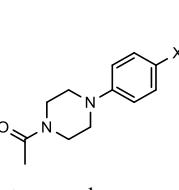
¹H NMR (125 MHz, CDCl₃) δ 149.7, 135.7, 134.8, 134.6, 129.9, 127.7, 127.6, 122.4 ppm. HRMS (ESI) m/z calcd for [M + Na]⁺ 262.9807, found 262.9806. IR (cm⁻¹): 3099, 1486, 1375, 1192, 1144, 861, 778, 728, 585.

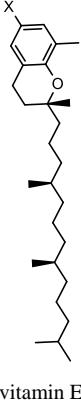
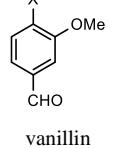
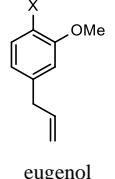
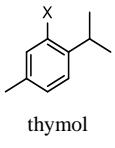
3.4 Availability Analysis of Selected Phenols and Their Aryl Halides (Halide = Cl, Br, I) Counterparts

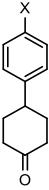
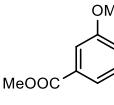
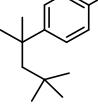
Phenols (Table S2, X = OH) can be a very convenient aryl source when their aryl halide counterparts (X = Cl, Br, I) are significantly more costly or not commercially available. Here we listed the detailed analysis of prices (US\$ per gram as well as US\$ per mol) for selected phenols (Scheme 2, *examples where Ar-OSO₂R is more convenient than Ar-X*) and their aryl halides counterparts (Table S2, entries 1-14). We also provided the availability analysis of other phenols we used as starting materials in Scheme 2 that are natural products, bioactive compounds, or precursors to important molecules (Table S2, entries 15-30). In many cases there is a wide variation in pricing or quantity available between different vendors. Therefore, for each compound we listed prices from at least 2 vendors (if there are 2 or more vendors). In each entry, compounds shaded in blue indicate the most commercially available variants of the molecules with the same substitution pattern. All the data provided here were from SciFinder search results for compounds' commercial sources on February 2nd, 2020.

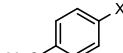
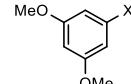
Table S2. Availability analysis of selected phenols and their aryl halides (X = Cl, Br, I) counterparts.

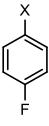
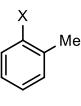
entry	compound structures and natural sources or applications when X= OH	X = OH	X = Cl	X = Br	X = I
1	 etravirine (Tibotec) precursor	CAS: 4198-90-7 Combi-Blocks (\$10/5g, \$290/mol) AA Blocks (\$6/5g, \$170/mol) Ambeed, Inc. (\$10/5g, \$290/mol)	CAS: 1097629-24-7 HE Chemical, China (\$7998/1g, \$1,320,000/mol) Aquila Pharmatech (Synthesis on demand)	CAS: 75344-77-3 Ambeed, Inc. (\$63/5g, \$2,600/mol) Combi-Blocks (\$80/5g, \$3,300/mol) Synthonix (\$80/5g, \$3,300/mol)	CAS: 127311-09-2 AA Blocks (\$32/100 mg, \$8,200/mol) Ambeed, Inc. (\$81/g, \$21,000/mol) Matrix Scientific (\$742/250 mg, \$762,000/mol)
2	 frambinone	CAS: 5471-51-2 Alfa Aeasr (\$41/25g, \$270/mol) Ambeed, Inc (\$6/25 g, \$40/mol) Santa Cruz Biotechnology (\$121/1kg, \$20/mol)	CAS: 3506-75-0 AA Blocks (\$200/250 mg, \$146,000/mol) Ambeed, Inc (\$250/g, \$46,000/mol) Matirx Scientific (\$90/5g, \$4,100/mol)	CAS: 89201-84-3 Ambeed, Inc (\$250/g, \$56,000/mol) Matirx Scientific (\$90/5g, \$4,100/mol) AURUM Pharmatech (\$284/250 mg, \$314,000/mol)	CAS: 918540-55-3 AA Blocks (\$1172/g, \$321,000/mol) Ambeed, Inc (\$300/g, \$82,000/mol) AURUM Pharmatech (\$806/g, \$221,000/mol)

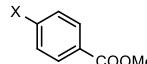
3	 estrone	CAS: 53-16-7 AA Blocks (\$10/g, \$2,700/mol) Combi-Blocks (\$10/g, \$2,700/mol) Santa Cruz Biotechnology (\$31/g, \$8,400/mol)	CAS: 5764-23-8 Only 1 vendor, no price provided	CAS: 1394922-25-8 Not commercially available	CAS: 1243197-32-1 Not commercially available
4	 L-tyrosine	CAS: 4326-36-7 AA Blocks (\$8/5g, \$470/mol) Ambeed, Inc (\$7/5g, \$410/mol) Combi-Blocks (\$11/5g, \$650/mol)	CAS: 172035-26-6 Only 3 vendors, no prices provided	CAS: 266306-18-7 AA Blocks (\$267/g, \$95,000/mol) Ambeed, Inc (\$222/g, \$79,000/mol)	CAS: 113850-76-3 AA Blocks (\$178/g, \$71,000/mol) Combi-Blocks (\$160/g, \$64,000/mol)
5	 ketoconazole precursor	CAS: 67914-60-7 AA Blocks (\$10/5g, \$440/mol) Alfa Aesar (\$29/25g, \$250/mol) Combi-Blocks (\$25/25g, \$220/mol)	CAS: 150557-99-6 AA Blocks (\$138/100 mg, \$328,000/mol) AURUM Pharmatech (\$869/5g, \$41,000/mol)	CAS: 678996-43-5 AA Blocks (\$223/g, \$63,000/mol) Combi-Blocks (\$200/g, \$56,000/mol)	CAS: 1197293-73-4 Only 1 vendor, no prices provided
6	 pleconaril (Picovir) precursor	CAS: 4421-08-3 AA Blocks (\$227/500g, \$68/mol) Alfa Aesar (\$159/100g, \$240/mol) Combi-Blocks (\$240/500g, \$72/mol)	CAS: 189620-40-8 AA Blocks (\$125/g, \$21,000/mol) Matrix Scientific (\$622/5g, \$21,000/mmol)	CAS: 120315-65-3 AA Blocks (\$220/25g, \$1,900/mol) Combi-Blocks (\$580/100g, \$1,200/mol)	CAS: 652997-56-3 Alicem product (\$677/g, 175,000/mol) FCH group reagents for synthesis (\$571/g, 148,000/mol)

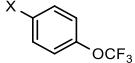
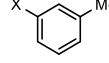
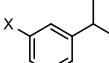
7	 vitamin E	CAS: 119-13-1 Santa Cruz Biotechnology (\$562/100 g, \$2,200/mol) Sigma-Aldrich (\$629/100 g, \$2,500/mol)	CAS: 1247868-59-2 Not commercially available	CAS: 1247868-54-7 Not commercially available	CAS: 2242797-94-8 Not commercially available
8	 vanillin	CAS: 121-33-5 AA Blocks (\$83/500g, \$25/mol) Alfa Aesar (\$63/500g, \$19/mol) Oakwood Chemical (\$55/500g, \$16/mol)	CAS: 13726-16-4 AA Blocks (\$13/g, \$2,200/mol) Combi-Blocks (\$12/g, \$2,100/mol) Oakwood Chemical (\$18/g, \$3,000/mmol)	CAS: 43192-34-3 AA Blocks (\$31/g, \$6,600/mol) Combi-Blocks (\$35/g, \$7,500/mol) Matrix Scientific (\$306/g, \$66,000/mol)	CAS: 121404-83-9 AA Blocks (\$217/250 mg, \$227,000/mol) Combi-Blocks (\$230/250mg, \$240,000/mol)
9	 eugenol	CAS: 97-53-0 AA Blocks (\$27/5g, \$880/mol) Alfa Aesar (\$33/100g, \$54/mol) Oakwood Chemical (\$55/500g, \$18/mol)	CAS: 1256467-57-8 Rieke Metals (\$566/g, \$103,000/mmol)	No CAS number Not commercially available	No CAS number Not commercially available
10	 thymol	CAS: 89-83-8 AA Blocks (\$96/100g, \$140/mol) Alfa Aesar (\$75/500g, \$22/mol) Oakwood Chemical (\$48/500g, \$14/mol)	CAS: 4395-80-6 Only 6 vendors, no prices provided.	CAS: 4478-10-8 Sigma-Aldrich (\$139/g, \$29,000/mmol)	CAS: 4395-81-7 Only 6 vendors, no prices provided.

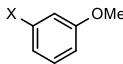
11	 precursor to liquid crystals after olefination and reduction	CAS: 105640-07-1 AA Blocks (\$177/100g, \$340/mol) Ambeed, Inc (\$142/100g, \$270/mol) TCI America (\$91/25g, \$690/mol)	CAS: 14472-80-1 AA Blocks (\$280/5g, \$11,600/mol) Ambeed, Inc (\$990/25g, \$8,230/mol) Combi-Blocks (\$165/g, \$34,000/mol)	CAS: 84892-43-3 Matrix Scientific (\$2400/10g, \$60,000/mol) AA Blocks (\$51/250mg, \$51,000/mol)	CAS: 1449768-19-7 Not commercially available
12	 precursor to carindacillin and candoxatril	CAS: 1470-94-6 AA Blocks (\$185/100g, \$250/mol) Oakwood Chemical (\$15/5g, \$400/mol) TCI America (\$114/100g, \$150/mol)	CAS: 60669-08-1 Matrix Scientific (\$1165/g, \$177,000/mol) Sigma-Aldrich (\$404/g, \$61,000/mol)	CAS: 6134-54-9 AA Blocks (\$106/100mg, \$208,000/mol) Sigma-Aldrich (\$39.9/100mg, \$78,000/mol)	CAS: 132464-83-6 AA Blocks (\$256/g, \$62,000/mol) Matrix Scientific (\$249/g, \$60,000/mol)
13	 from vanillic acid	CAS: 3943-74-6 AA Blocks (\$68/100g, \$120/mol) Ambeed, Inc (\$216/500g, \$76/mol) Combi-Blocks (\$225/500g, \$82/mol)	CAS: 116022-18-5 AA Blocks (\$682/100g, \$1,360/mol) Combi-Blocks (\$600/100g, \$1,200/mmol)	CAS: 17100-63-9 AA Blocks (\$589/100g, \$1,430/mol) Combi-Blocks (\$530/100g, \$1,290/mol)	CAS: 35387-92-9 AA Blocks (\$2000/100g, \$5,840/mol) Combi-Blocks (\$720/25g, \$8,400/mol)
14	 from 4- <i>tert</i> -octylphenol, a component of resins and paints	CAS: 140-66-9 Ambeed, Inc (\$17/25g, \$140/mol) Oakwood Chemical (\$20/100g, \$41/mol) TCI America (\$32/500g, \$13/mol)	No CAS number Not commercially available	CAS: 34549-13-8 Not commercially available	No CAS number Not commercially available

					CAS: 4387-36-4
15	 salicylonitrile, precursor to azoxystrobin	CAS: 611-20-1 Ambeed, Inc. (\$211/1 kg, \$25/mol)	CAS: 873-32-5 Combi-blocks (\$334/1 kg, \$46/mol)	CAS: 2042-37-7 AA Blocks (\$195/500 g, \$71/mol)	AA Blocks (\$118/100 g, \$270/mol)
		ChemScene (\$221/ 1 kg, \$26/mol)	Angene Chemical (\$106/500 g, \$29/mol)	Combi-Blocks (\$360/1 kg, \$66/mol)	Combi-Blocks (\$560/500 g, \$260/mol)
		Synthonix (\$311/1 kg, \$39/mol)	Oakwood Chemicals (\$39/100 g, \$53/mol)	Oakwood Chemicals (\$199/500 g, \$71/mol)	Oakwood Chemicals (\$118/100 g, \$270/mol)
16	 mequinol, a common active ingredient in topical drugs used for skin depigmentation	CAS: 150-76-5 AA Blocks (\$91/500 g, \$22/mol)	CAS: 623-12-1 AA Blocks (\$239/500 g, \$68/mol)	CAS: 104-92-7 AA Blocks (\$137/500 g, \$51/mol)	CAS: 696-62-8 AA Blocks (\$60/100 g, \$140/mol)
		Ambeed, Inc. (\$48/500 g, \$12/mol)	Ambeed, Inc. (\$112/500 g, \$32/mol)	Combi-Blocks (\$150/500 g, \$56/mol)	Ambeed, Inc. (\$205/500 g, \$96/mol)
		Combi-Blocks (\$250/1 kg, \$31/mol)	Combi-Blocks (\$150/500 g, \$43/mol)		Combi-Blocks (\$220/500 g, \$100/mol)
17	 phloroglucinol dimethyl ether (phloroglucinol is a chemical used for the treatment for gallstones, spasmodic pain and other related gastrointestinal problems)	CAS: 500-99-2 AA Blocks (\$60/25 g, \$370/mol)	CAS: 7051-16-3 AA Blocks (\$760/250 g, \$530/mol)	CAS: 20469-65-2 AA Blocks (\$400/500 g, \$170/mol)	CAS: 25245-27-6 AA Blocks (\$1167/100 g, \$3,100/mol)
		Ambeed, Inc. (\$113/25 g, \$700/mol)	Ambeed, Inc. (\$134/25 g, \$930/mol)	Ambeed, Inc. (\$287/500 g, \$120/mol)	Ambeed, Inc. (\$470/25 g, \$5,000/mol)
		Combi-Blocks (\$320/100 g, \$490/mol)	Combi-Blocks (\$160/25 g, \$1,100/mol)	Combi-Blocks (\$360/500 g, \$150/mol)	Combi-Blocks (\$1050/100 g, \$2,800/mol)

			CAS: 352-33-0		CAS: 352-34-1
18	 <p>precursor to cisapride, a drug that increases motility in the upper gastrointestinal tract</p>	<p>CAS: 371-41-5</p> <p>AA Blocks (\$110/500 g, \$25/mol)</p> <p>Ambeed, Inc. (\$199/1 kg, \$22/mol)</p> <p>Oakwood Chemicals (\$85/500 g, \$19/mol)</p>	<p>AA Blocks (\$15/25 g, \$78/mol)</p> <p>Oakwood Chemicals (\$145/500 g, \$38/mol)</p> <p>Matrix Scientific (\$125/500 g, \$33/mol)</p>	<p>CAS: 460-00-4</p> <p>AA Blocks (\$88/500 g, \$31/mol)</p> <p>Ambeed, Inc. (\$13/25 g, \$91/mol)</p> <p>Combi-Blocks (\$40/100 g, \$70/mol)</p>	<p>AA Blocks (\$283/500 g, \$120/mol)</p> <p>Ambeed, Inc. (\$142/500 g, \$63/mol)</p> <p>Combi-Blocks (\$320/1 kg, \$71/mol)</p>
19	 <p><i>o</i>-Cresol, one of the chemical compounds found in castoreum, widely used in the production of other chemicals</p>	<p>CAS: 95-48-7</p> <p>AA Blocks (\$61/500 g, \$13/mol)</p> <p>Oakwood Chemicals (\$60/500 g, \$13/mol)</p>	<p>CAS: 95-49-8</p> <p>AA Blocks (\$75/100 g, \$94/mol)</p> <p>Oakwood Chemicals (\$19/100 g, \$24/mol)</p> <p>Matrix Scientific (\$84/100 g, \$110/mol)</p>	<p>CAS: 95-46-5</p> <p>AA Blocks (\$283/500 g, \$97/mol)</p> <p>Combi-Blocks (\$320/1 kg, \$56/mol)</p> <p>Oakwood Chemicals (\$178/500 g, \$61/mol)</p>	<p>CAS: 615-37-2</p> <p>AA Blocks (\$50/100 g, \$110/mol)</p> <p>Ambeed, Inc. (\$172/500 g, \$75/mol)</p> <p>Combi-Blocks (\$400/1 kg, \$87/mol)</p>
20	 <p>phenol, a very important industrial commodity as a precursor to many materials and useful compounds</p>	<p>CAS: 108-95-2</p> <p>AA Blocks (\$98/500 g, \$18/mol)</p> <p>Oakwood Chemicals (\$40/500 g, \$7.3/mmol)</p>	<p>CAS: 108-90-7</p> <p>Combi-Blocks (\$40/100 g, \$45/mmol)</p> <p>Oakwood Chemicals (\$20/500 g, \$4.5/mol)</p> <p>TCI America (\$21/500 g, \$4.5/mol)</p>	<p>CAS: 108-86-1</p> <p>AA Blocks (\$40/100 g, \$63/mol)</p> <p>Combi-Blocks (\$250/1 kg, \$39/mol)</p> <p>Oakwood Chemicals (\$99/2.5 kg, \$6.2/mol)</p>	<p>CAS: 591-50-4</p> <p>AA Blocks (\$150/500 g, \$61/mol)</p> <p>Ambeed, Inc. (\$98/500 g, \$40/mol)</p> <p>Combi-Blocks (\$250/1 kg, \$51/mol)</p>
21	 <p>methyl salicylate, a drug used to temporarily relieve minor body aches and muscle and joint pain.</p>	<p>CAS: 119-36-8</p> <p>AA Blocks (\$57/500 g, \$17/mol)</p> <p>Ambeed, Inc. (\$30/500 g, \$8.9/mol)</p> <p>Combi-Blocks (\$250/1 kg, \$38/mol)</p>	<p>CAS: 610-96-8</p> <p>AA Blocks (\$238/500 g, \$81/mol)</p> <p>Combi-Blocks (\$360/1 kg, \$61/mol)</p> <p>Oakwood Chemicals (\$50/100 g, \$85/mol)</p>	<p>CAS: 610-94-6</p> <p>AA Blocks (\$187/500 g, \$80/mol)</p> <p>Ambeed, Inc. (\$197/1 kg, \$42/mol)</p> <p>Combi-Blocks (\$200/1 kg, \$43/mol)</p>	<p>CAS: 610-97-9</p> <p>AA Blocks (\$19/100 g, \$50/mol)</p> <p>Ambeed, Inc. (\$99/500 g, \$52/mol)</p> <p>Combi-Blocks (\$150/500 g, \$79/mol)</p>

22	 sesamol, a natural organic compound which is a component of sesame seeds and sesame oil.	CAS: 533-31-3 AA Blocks (\$15/25 g, \$83/mol) Ambeed, Inc. (\$267/500 g, \$74/mol) Oakwood Chemicals (\$90/100 g, \$124/mol)	CAS: 7228-38-8 AA Blocks (\$25/5 g, \$780/mol) Matrix Scientific (\$89/5 g, \$2,800/mol) Santa Cruz Biotechnology (\$40/10 g, \$620/mol)	CAS: 2635-13-4 AA Blocks (\$50/100 g, \$100/mol) Ambeed, Inc. (\$249/1000 g, \$50/mol) Combi-Blocks (\$220/500 g, \$88/mol)	CAS: 5876-51-7 AA Blocks (\$80/25 g, \$790/mol) Ambeed, Inc. (\$344/100 g, \$850/mol) Combi-Blocks (\$1,380/500 g, \$680/mol)
23	 3'-hydroxyacetophenone, a component of castoreum, the exudate from the castor sacs of the mature beaver.	CAS: 121-71-1 AA Blocks (\$34/100 g, \$46/mol) Ambeed, Inc. (\$98/500 g, \$27/mol) Combi-Blocks (\$250/1 kg, \$34/mol)	CAS: 99-02-5 AA Blocks (\$140/500 g, \$43/mol) Combi-Blocks (\$235/1 kg, \$36/mol) Oakwood Chemicals (\$270/1 kg, \$42/mol)	CAS: 2142-63-4 AA Blocks (\$181/500 g, \$72/mol) Ambeed, Inc. (\$256/1 kg, \$51/mol) Combi-Blocks (\$250/1 kg, \$50/mol)	CAS: 14452-30-3 AA Blocks (\$429/100 g, \$610/mol) Ambeed, Inc. (\$95/25 g, \$930/mol) Combi-Blocks (\$240/25 g, \$2400/mol)
24	 methylparaben, an anti-fungal agent often used in a variety of cosmetics and personal-care products.	CAS: 99-76-3 AA Blocks (\$14/100 g, \$21/mol) Ambeed, Inc. (\$87/1 kg, \$13/mol) Oakwood Chemicals (\$390/2.5 kg, \$24/mol)	CAS: 1126-46-1 AA Blocks (\$13/25 g, \$88/mol) Ambeed, Inc. (\$241/1 kg, \$41/mol) Combi-Blocks (\$250/1 kg, \$43/mol)	CAS: 619-42-1 AA Blocks (\$150/500 g, \$65/mol) Ambeed, Inc. (\$245/1 kg, \$53/mol) Combi-Blocks (\$250/1 kg, \$54/mol)	CAS: 619-44-3 AA Blocks (\$58/100 g, \$150/mol) Ambeed, Inc. (\$274/500 g, \$140/mol) Combi-Blocks (\$480/1 kg, \$130/mol)

25	 <p>precursor to delamanid, a medication used to treat tuberculosis</p>	<p>CAS: 828-27-3</p> <p>AA Blocks (\$193/500 g, \$69/mol)</p> <p>Ambeed, Inc. (\$247/1 kg, \$44/mol)</p> <p>Oakwood Chemicals (\$160/500 g, \$57/mol)</p>	<p>CAS: 461-81-4</p> <p>AA Blocks (\$50/100 g, \$98/mol)</p> <p>Ambeed, Inc. (\$248/1 kg, \$49/mol)</p> <p>Combi-Blocks (\$280/500 g, \$110/mol)</p>	<p>CAS: 407-14-7</p> <p>AA Blocks (\$12/25 g, \$120/mol)</p> <p>Ambeed, Inc. (\$248/1 kg, \$60/mol)</p> <p>Combi-Blocks (\$320/1 kg, \$77/mol)</p>	<p>CAS: 103962-05-6</p> <p>AA Blocks (\$145/100 g, \$420/mol)</p> <p>Ambeed, Inc. (\$346/1 kg, \$99/mol)</p> <p>Combi-Blocks (\$350/1 kg, \$100/mol)</p>
26	 <p>precursor to clofibrate, a drug for controlling the high cholesterol and triacylglyceride level in the blood</p>	<p>CAS: 106-48-9</p> <p>AA Blocks (\$181/500 g, \$46/mol)</p> <p>Oakwood Chemicals (\$14/25 g, \$72/mol)</p> <p>Santa Cruz Biotechnology (\$57/100 g, \$73/mol)</p>	<p>CAS: 106-46-7</p> <p>AA Blocks (\$60/100 g, \$88/mol)</p> <p>Combi-Blocks (\$250/1 kg, \$37/mol)</p>	<p>CAS: 106-39-8</p> <p>AA Blocks (\$5/25 g, \$38/mol)</p> <p>Ambeed, Inc. (\$60/1 kg, \$11/mol)</p> <p>Combi-Blocks (\$250/1 kg, \$48/mol)</p>	<p>CAS: 637-87-6</p> <p>AA Blocks (\$38/100 g, \$90/mol)</p> <p>Ambeed, Inc. (\$260/1 kg, \$62/mol)</p> <p>Combi-Blocks (\$250/1 kg, \$60/mol)</p>
27	 <p>precursor to numerous compounds (e.g., fenitrothion, synthetic vitamin E, and amylnmetacresol)</p>	<p>CAS: 108-39-4</p> <p>AA Blocks (\$40/100 g, \$43/mol)</p> <p>Combi-Blocks (\$250/1 kg, \$27/mol)</p> <p>Oakwood Chemicals (\$62/1 kg, \$6.7/mol)</p>	<p>CAS: 108-41-8</p> <p>AA Blocks (\$25/25 g, \$130/mol)</p> <p>Combi-Blocks (\$75/100 g, \$94/mol)</p> <p>Oakwood Chemicals (\$43/100 g, \$54/mol)</p>	<p>CAS: 591-17-3</p> <p>AA Blocks (\$182/500 g, \$62/mol)</p> <p>Combi-Blocks (\$400/1 kg, \$68/mol)</p> <p>Oakwood Chemicals (\$186/500 g, \$64/mol)</p>	<p>CAS: 625-95-6</p> <p>AA Blocks (\$200/500 g, \$87/mol)</p> <p>Ambeed, Inc. (\$372/1 kg, \$81/mol)</p> <p>Combi-Blocks (\$380/1 kg, \$83/mol)</p>
28	 <p>precursor to isoprocarb, an agricultural insecticide used on rice, cocoa, sugar cane, vegetables and other crops</p>	<p>CAS: 88-69-7</p> <p>AA Blocks (\$70/100 g, \$95/mol)</p> <p>Combi-Blocks (\$50/100 g, \$68/mol)</p> <p>Santa Cruz Biotechnology (\$185/500 g, \$50/mol)</p>	<p>CAS: 2077-13-6</p> <p>AA Blocks (\$198/250 mg, \$121,000/mol)</p> <p>Combi-Blocks (\$450/1 g, \$69,300/mol)</p>	<p>CAS: 7073-94-1</p> <p>AA Blocks (\$160/100 g, \$320/mol)</p> <p>Ambeed, Inc. (\$452/500 g, \$180/mol)</p> <p>Combi-Blocks (\$620/500 g, \$250/mol)</p>	<p>CAS: 19099-54-8</p> <p>AA Blocks (\$180/100 g, \$440/mol)</p> <p>Ambeed, Inc. (\$977/1000 g, \$240/mol)</p> <p>Combi-Blocks (\$180/100 g, \$440/mol)</p>

			CAS: 766-51-8		
29	 guaiacol, precursor to numerous compounds (e. g., eugenol and vanillin), and also used medicinally as an expectorant, antiseptic, and local anesthetic	CAS: 90-05-1 AA Blocks (\$6/25 g, \$30/mol) Ambeed, Inc. (\$21/500 g, \$5.2/mol) Combi-Blocks (\$250/1 kg, \$31/mol)	AA Blocks (\$50/100 g, \$71/mol) Combi-Blocks (\$360/1 kg, \$51/mol) Santa Cruz Biotechnology (\$51/50 g, \$140/mol)	CAS: 578-57-4 AA Blocks (\$82/250 g, \$61/mol) Ambeed, Inc. (\$114/500 g, \$43/mol) Combi-Blocks (\$250/1 kg, \$47/mol)	CAS: 529-28-2 AA Blocks (\$40/100 g, \$94/mol) Ambeed, Inc. (\$189/500 g, \$88/mol) Combi-Blocks (\$175/500 g, \$82/mol)
30	 2-phenylphenol, an agricultural fungicide	 CAS: 90-43-7 AA Blocks (\$40/100 g, \$68/mol) Combi-Blocks (\$40/100 g, \$68/mol) Oakwood Chemicals (\$16/100 g, \$27/mol)	 AA Blocks (\$534/100 g, \$1,000/mol) Combi-Blocks (\$480/100 g, \$900/mol) Santa Cruz Biotechnology (\$38/100 mg, \$71,440/mol)	 AA Blocks (\$178/100 g, \$410/mol) Combi-Blocks (\$470/1 kg, \$110/mol) Oakwood Chemicals (\$110/100 g, \$260/mol)	 CAS: 2051-60-7 AA Blocks (\$428/100 g, \$1,200/mol) Combi-Blocks (\$450/100 g, \$1,300/mol) Oakwood Chemicals (\$810/100 g, \$2,300/mol)
			CAS: 2052-07-5		CAS: 2113-51-1

4. Cross-Electrophile Couplings of Phenol Derivatives under Nickel and Palladium Multimetallic Conditions

4.1 Cross-Electrophile Couplings of Aryl Triflates with Aryl Tosylates

Procedure for cross-electrophile couplings of aryl triflates with aryl tosylates on 0.5 mmol scale

The following procedures were conducted in a N₂ filled glovebox for convenience. Nickel and palladium catalyst stock solutions were prepared following *general procedure for optimization studies* (page S4) using **L1** (18.5 mg, 0.060 mmol) as the amine ligand and dppb (25.6 mg, 0.060 mmol) as the phosphine ligand.

General procedure A: catalytic reactions at 1.0 mol% catalyst loading

An oven-dried 1-dram vial equipped with a PTFE-coated stir-bar was charged sequentially with aryl triflate (0.50 mmol, 1.0 equiv), aryl tosylate (0.50 mmol, 1.0 equiv or 0.75 mmol, 1.5 equiv), LiBr (174 mg, 2.0 mmol, 4.0 equiv), and Zn (65 mg, 1.0 mmol, 2.0 equiv). Aliquots from both the 0.025 M nickel (200 μ L for 1.0 mol%) and palladium (200 μ L for 1.0 mol%) catalyst stock solutions were added, followed by additional DMF (1.6 mL). The vial was capped with a screw cap fitted with a PTFE-faced silicone septum, and the reaction mixture was stirred (1000 rpm) for 10 min in the glovebox at rt. The vial was then removed from the glovebox and heated in a reaction block set to the desired temperature (40 or 60 °C) with stirring (1250 rpm) for 24 h.

General procedure B: catalytic reactions at 0.5 mol% catalyst loading

An oven-dried 1-dram vial equipped with a PTFE-coated stir-bar was charged sequentially with aryl triflate (0.50 mmol, 1.0 equiv), aryl tosylate (0.50 mmol, 1.0 equiv or 0.75 mmol, 1.5 equiv), LiBr (174 mg, 2.0 mmol, 4.0 equiv), and Zn (65 mg, 1.0 mmol, 2.0 equiv). Aliquots from both the 0.025 M nickel (100 μ L for 0.5 mol%) and palladium (100 μ L for 0.5 mol%) catalyst stock solutions were added, followed by additional DMF (0.8 mL). The vial was capped with a screw cap fitted with a PTFE-faced silicone septum, and the reaction mixture was stirred (1000 rpm) for 10 min in the glovebox at rt. The vial was then removed from the glovebox and heated in a reaction block set to the desired temperature (40 or 60 °C) with stirring (1250 rpm) for 24 h.

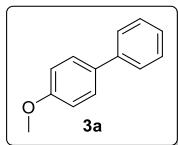
NOTE for Procedure B: we found that some aryl triflates slowly decomposed (a color change could be observed, usually from colorless to pale yellow) when they were stored in air at rt for several weeks. Reactions with these partially decomposed aryl triflates at 0.5 mol% catalyst loadings usually provided low yields due to low conversion of starting materials. Aryl triflates used in general procedure B were used within 3 days of preparation. However, these partially decomposed aryl triflates could be re-purified by flash chromatography on silica gel and used in reactions at 0.5 mol% catalyst loading.

GC and SFC-MS analysis

The reaction was monitored by GC analysis by cooling the reaction to rt and taking a 20 μ L aliquot of the crude reaction mixture with a gas-tight syringe. The aliquot was diluted with ethyl acetate (1 mL), filtered through a 2-cm silica gel plug in a Pasteur pipette, and collected in a GC vial. The sample was analyzed by GC to determine if the starting materials were consumed. SFC-MS analysis was used for reactions involving nonvolatile starting materials or products using the same workup as preparing GC samples.

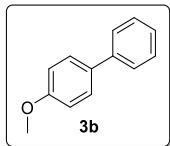
Isolation and purification

Reaction completion was judged by GC or SFC-MS analysis and was usually accompanied by a color change from grey to dark brown. The reaction mixture was diluted with ethyl acetate (10 mL), filtered through a short plug of silica gel (1.5 cm \times 3.0 cm), and extra portions of ethyl acetate (15 mL \times 5) were used to rinse the reaction vial and wash the silica gel pad. Silica gel (2.5-3.0 g) was then added to the combined filtrate and the volatile solvents were removed by rotary evaporation. The resulting dry-loaded material was purified by flash chromatography on silica gel to provide the desired product.

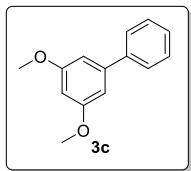


4-methoxy-1,1'-biphenyl (3a) [CAS: 613-37-6] was prepared following the general procedure A using **1a** (128 mg, 0.50 mmol) and **2a** (124 mg, 0.50 mmol) as starting materials. After stirring at 40 °C for 24 h, the reaction was quenched following general procedure and the crude material was purified by flash chromatography on silica gel (hexanes/ethyl acetate = 100/1 to 50/1) to afford the desired product (66.2 mg, 72%) as a white solid. ¹H NMR (400 MHz, CDCl₃): δ 7.56 (t, *J* = 8.4 Hz, 4 H), 7.43 (t, *J* = 7.7 Hz, 2 H), 7.31 (t, *J* = 6.9 Hz, 1 H), 6.99 (d, *J* = 8.7 Hz, 2 H), 3.86 (s, 3 H); ¹³C{¹H} NMR (100 MHz, CDCl₃): δ 159.3, 141.0, 134.0, 128.9, 128.3, 126.9, 126.8, 114.4, 55.5 ppm. Characterization data matched those reported in the literature.⁴⁰

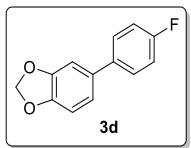
4-methoxy-1,1'-biphenyl (3a) [CAS: 613-37-6] was prepared following the general procedure B using **1a** (128 mg, 0.50 mmol) and **2a** (124 mg, 0.50 mmol) as starting materials. After stirring at 40 °C for 24 h, the reaction was quenched following general procedure and the crude material was purified by flash chromatography on silica gel (hexanes/ethyl acetate = 100/1 to 50/1) to afford the desired product (65.3 mg, 71%) as a white solid. ¹H NMR (400 MHz, CDCl₃) δ 7.57 (t, *J* = 8.5 Hz, 4 H), 7.44 (t, *J* = 7.7 Hz, 2 H), 7.33 (t, *J* = 7.3 Hz, 1 H), 7.01 (d, *J* = 8.8 Hz, 2 H), 3.87 (s, 3 H); ¹³C{¹H} NMR (100 MHz, CDCl₃) δ 159.3, 141.0, 133.9, 128.9, 128.3, 126.9, 126.8, 114.4, 55.5 ppm. Characterization data matched those reported in the literature.⁴⁰



4-methoxy-1,1'-biphenyl (3b) [CAS: 613-37-6] was prepared following the general procedure A using **1b** (113 mg, 0.50 mmol) and **2b** (139 mg, 0.50 mmol) as starting materials. After stirring at 40 °C for 24 h, the reaction was quenched following general procedure and the crude material was purified by flash chromatography on silica gel (hexanes/ethyl acetate = 100/1 to 50/1) to afford the desired product (57.0 mg, 62%) as a white solid. ¹H NMR (400 MHz, CDCl₃) δ 7.56 (t, *J* = 8.3 Hz, 4 H), 7.44 (t, *J* = 7.6 Hz, 2 H), 7.32 (t, *J* = 7.4 Hz, 1 H), 7.00 (d, *J* = 8.7 Hz, 2 H), 3.87 (s, 3 H); ¹³C{¹H} NMR (100 MHz, CDCl₃) δ 159.3, 141.0, 133.9, 128.9, 128.3, 126.9, 126.8, 114.4, 55.5 ppm. Characterization data matched those reported in the literature.⁴⁰



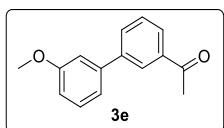
3,5-dimethoxy-1,1'-biphenyl (3c) [CAS: 64326-17-6] was prepared following the general procedure A using **1c** (143 mg, 0.50 mmol) and **2a** (124 mg, 0.50 mmol) as starting materials. After stirring at 40 °C for 24 h, the reaction was quenched following general procedure and the crude material was purified by flash chromatography on silica gel (hexanes/ethyl acetate = 50/1 to 30/1) to afford the desired product (75.5 mg, 70%) as a white solid. ^1H NMR (500 MHz, CDCl_3): δ 7.62 (dd, J = 8.2, 1.3 Hz, 2 H), 7.47 (t, J = 7.6 Hz, 2 H), 7.39 (t, J = 7.3 Hz, 1 H), 6.79 (d, J = 2.3 Hz, 2 H), 6.52 (t, J = 2.3 Hz, 1 H), 3.88 (s, 6 H); $^{13}\text{C}\{\text{H}\}$ NMR (125 MHz, CDCl_3): δ 161.2, 143.6, 141.4, 128.8, 127.7, 127.3, 105.6, 99.4, 55.5 ppm. Characterization data matched those reported in the literature.⁴¹



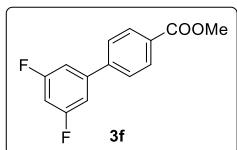
5-(4-fluorophenyl)benzo[d][1,3]dioxole (3d) [CAS: 157790-85-7] was prepared following the general procedure A using **1d** (135 mg, 0.50 mmol) and **2c** (133 mg, 0.50 mmol) as starting materials. After stirring at 40 °C for 24 h, the reaction was quenched following general procedure and the crude material was purified by flash chromatography on silica gel (hexanes/ethyl acetate = 100/1 to 50/1) to afford the desired product (79.2 mg, 73%) as a white solid. ^1H NMR (400 MHz, CDCl_3): δ 7.48 – 7.45 (m, 2 H), 7.10 (t, J = 8.7 Hz, 2 H), 7.03 – 6.99 (m, 2 H), 6.88 (d, J = 8.0 Hz, 1 H), 6.00 (s, 2 H); $^{13}\text{C}\{\text{H}\}$ NMR (100 MHz, CDCl_3): δ 162.5 (d, J = 247.5 Hz), 148.3, 147.2, 137.2 (d, J = 3.0 Hz), 134.8, 128.5 (d, J = 8.1 Hz), 120.6, 115.7 (d, J = 21.2 Hz), 108.8, 107.7, 101.4; $^{19}\text{F}\{\text{H}\}$ NMR (376 MHz, CDCl_3): δ –116. 20 ppm. Characterization data matched those reported in the literature.⁴²

5-(4-fluorophenyl)benzo[d][1,3]dioxole (3d) [CAS: 157790-85-7] was prepared following the general procedure B using **1d** (135 mg, 0.50 mmol) and **2c** (133 mg, 0.50 mmol) as starting materials. After stirring at 40 °C for 24 h, the reaction was quenched following general procedure and the crude material was purified by flash chromatography on silica gel (hexanes/ethyl acetate = 100/1 to 50/1) to afford the desired product (75.3 mg, 70%) as a white solid. ^1H NMR (400 MHz, CDCl_3) δ 7.48 – 7.45 (m, 2 H), 7.10 (t, J = 8.7 Hz, 2 H), 7.02 – 6.99 (m, 2 H), 6.88 (d, J = 7.9 Hz, 1 H), 6.00 (s, 2 H); $^{13}\text{C}\{\text{H}\}$ NMR (100 MHz, CDCl_3): δ 162.4 (d, J = 245.9 Hz), 148.3, 147.2, 137.2 (d, J = 3.2 Hz), 134.8, 128.6 (d, J = 7.9 Hz), 120.7,

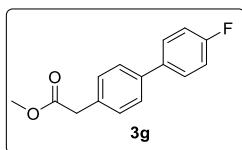
115.7 (d, $J = 21.4$ Hz), 108.8, 107.8, 101.4; $^{19}\text{F}\{\text{H}\}$ NMR (376 MHz, CDCl_3): δ -116.22 ppm. Characterization data matched those reported in the literature.⁴²



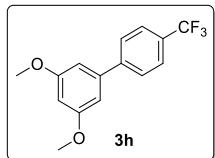
1-(3'-methoxy-[1,1'-biphenyl]-3-yl)ethan-1-one (3e) [CAS: 843734-63-9] was prepared following the general procedure A using **1e** (128 mg, 0.50 mmol) and **2d** (145 mg, 0.50 mmol) as starting materials. After stirring at 40 °C for 24 h, the reaction was quenched following general procedure and the crude material was purified by flash chromatography on silica gel (hexanes/ethyl acetate = 20/1 to 10/1) to afford the desired product (64.4 mg, 57%) as a white solid. ^1H NMR (400 MHz, CDCl_3): δ 8.18 (t, $J = 1.8$ Hz, 1 H), 7.94 (d, $J = 7.6$ Hz, 1 H), 7.78 (d, $J = 7.7$ Hz, 1 H), 7.53 (t, $J = 7.7$ Hz, 1 H), 7.39 (t, $J = 8.2$ Hz, 1 H), 7.20 (d, $J = 7.5$ Hz, 1 H), 7.14 (t, $J = 2.1$ Hz, 1 H), 6.94 (dd, $J = 7.8, 3.1$ Hz, 1 H), 3.88 (s, 3 H), 2.66 (s, 3 H); $^{13}\text{C}\{\text{H}\}$ NMR (125 MHz, CDCl_3): δ 198.2, 160.2, 141.9, 141.8, 137.8, 132.0, 130.1, 129.2, 127.5, 127.2, 119.8, 113.3, 113.2, 55.5, 27.0 ppm. Characterization data matched those reported in the literature.⁴³



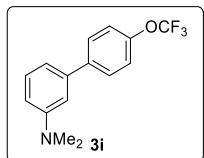
Methyl 3',5'-difluoro-[1,1'-biphenyl]-4-carboxylate (3f) [CAS: 1848978-85-7] was prepared following the general procedure A using **1f** (131 mg, 0.50 mmol) and **2e** (153 mg, 0.50 mmol) as starting materials. After stirring at 40 °C for 24 h, the reaction was quenched following general procedure and the crude material was purified by flash chromatography on silica gel (hexanes/ethyl acetate = 20/1 to 5/1) to afford the desired product (63.1 mg, 51%) as a white solid. ^1H NMR (500 MHz, CDCl_3): δ 8.11 (d, $J = 8.5$ Hz, 2 H), 7.60 (d, $J = 8.4$ Hz, 2 H), 7.12 (m, 2 H), 6.82 (tt, $J = 8.8, 2.3$ Hz, 1 H), 3.94 (s, 3 H); $^{13}\text{C}\{\text{H}\}$ NMR (125 MHz, CDCl_3): δ 166.8, 163.5 (dd, $J = 249.5, 13.9$ Hz), 143.4 (t, $J = 9.4$ Hz), 143.2 (t, $J = 2.5$ Hz), 130.4, 130.2, 127.1, 110.3 (m), 103.5 (t, $J = 25.2$ Hz), 52.4; $^{19}\text{F}\{\text{H}\}$ NMR (376 MHz, CDCl_3): δ -109.14 (s, 2 F) ppm. Characterization data matched those reported in the literature.⁴⁴



Methyl 2-(4'-fluoro-[1,1'-biphenyl]-4-yl)acetate (3g) [CAS: 1949812-56-9] was prepared following the general procedure A using **1g** (149 mg, 0.50 mmol) and **2c** (133 mg, 0.50 mmol) as starting materials. After stirring at 40 °C for 24 h, the reaction was quenched following general procedure and the crude material was purified by flash chromatography on silica gel (hexanes/ethyl acetate = 20/1 to 5/1) to afford the desired product (86.8 mg, 71%) as a colorless oil. ¹H NMR (400 MHz, CDCl₃): δ 7.55 – 7.50 (m, 4 H), 7.35 (d, *J* = 8.3 Hz, 2 H), 7.12 (t, *J* = 8.7 Hz, 2 H), 3.72 (s, 3 H), 3.68 (s, 2 H); ¹³C{¹H} NMR (125 MHz, CDCl₃): δ 172.2, 162.6 (d, *J* = 252.0 Hz), 139.3, 137.1 (d, *J* = 3.8 Hz), 133.2, 129.9, 128.8 (d, *J* = 7.6 Hz), 127.4, 115.8 (d, *J* = 21.4 Hz), 52.3, 40.9; ¹⁹F{¹H} NMR (376 MHz, CDCl₃): δ –115.74 ppm. HRMS (ESI) m/z calcd for [M + Na]⁺ 267.0792, found: 267.0787. IR (cm^{–1}): 3045, 2952, 1738, 1499, 1231, 1160, 807.

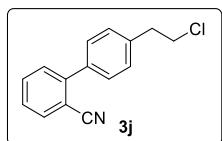


3,5-dimethoxy-4'-(trifluoromethyl)-1,1'-biphenyl (3h) [CAS: 216679-41-3] was prepared following the general procedure A using **1c** (143 mg, 0.50 mmol) and **2f** (158 mg, 0.50 mmol) as starting materials. After stirring at 40 °C for 24 h, the reaction was quenched following general procedure and the crude material was purified by flash chromatography on silica gel (hexanes/ethyl acetate = 50/1 to 10/1) to afford the desired product (85.3 mg, 60%) as a white solid. ¹H NMR (500 MHz, CDCl₃): δ 7.68 (s, 4 H), 6.72 (d, *J* = 5.0 Hz, 2 H), 6.52 (t, *J* = 5.0 Hz, 1 H), 3.86 (s, 6 H); ¹³C{¹H} NMR (125 MHz, CDCl₃): δ 161.4, 144.9, 142.1, 129.8 (q, *J* = 32.3 Hz), 127.7, 125.8 (q, *J* = 4.2 Hz), 124.4 (q, *J* = 273.4 Hz), 105.8, 100.1, 55.6; ¹⁹F{¹H} NMR (376 MHz, CDCl₃): δ –62.42 (s, 3 F) ppm. Characterization data matched those reported in the literature.⁴⁴

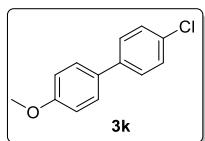


***N,N*-dimethyl-4'-(trifluoromethoxy)-[1,1'-biphenyl]-3-amine (3i) [CAS: 1261447-26-0]** was prepared following the general procedure A using **1h** (135 mg, 0.50 mmol) and **2g** (166 mg, 0.50 mmol) as starting materials. After stirring at 40 °C for 24 h, the reaction was quenched following general procedure and the crude material was purified by flash chromatography on silica gel (hexanes/ethyl acetate = 50/1 to 20/1) to afford the desired product (94.3 mg, 67%) as a colorless oil. *Compound 3i turned yellow immediately when it was dissolved in CDCl₃ and the NMR data were obtained in C₆D₆.* ¹H NMR (500 MHz, C₆D₆): δ 7.33 –

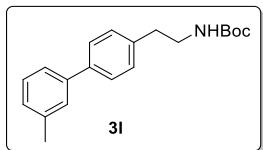
7.30 (m, 2 H), 7.24 (t, J = 8.0 Hz, 1 H), 7.00 (d, J = 7.3 Hz, 2 H), 6.86 (d, J = 7.7 Hz, 1 H), 6.76 (t, J = 2.1 Hz, 1 H), 6.59 (dd, J = 7.5, 2.7 Hz, 1 H), 2.54 (s, 6 H); $^{13}\text{C}\{\text{H}\}$ NMR (125 MHz, C_6D_6): δ 151.3, 148.8, 141.8, 141.2, 129.8, 129.0, 121.4, 121.3 (q, J = 257.0 Hz), 116.1, 112.4, 111.7, 40.2; $^{19}\text{F}\{\text{H}\}$ NMR (376 MHz, C_6D_6): δ -57.61 (s, 3 F) ppm. HRMS (ESI) m/z calcd for $[\text{M} + \text{H}]^+$ 282.1100, found 282.1099. IR (cm^{-1}): 3041, 2805, 1682, 1493, 1154, 837, 772.



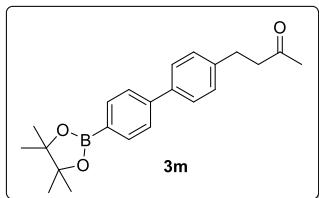
4'-(2-chloroethyl)-[1,1'-biphenyl]-2-carbonitrile (3j) was prepared following the general procedure A using **1i** (144 mg, 0.50 mmol) and **2h** (137 mg, 0.50 mmol) as starting materials. After stirring at 40 °C for 24 h, the reaction was quenched following general procedure and the crude material was purified by flash chromatography on silica gel (hexanes/ethyl acetate = 20/1 to 5/1) to afford the desired product (62.3 mg, 51%) as a colorless oil. ^1H NMR (500 MHz, CDCl_3): δ 7.76 (d, J = 7.2 Hz, 1 H), 7.63 (t, J = 7.7 Hz, 1 H), 7.52 (t, J = 8.0 Hz, 3 H), 7.44 (t, J = 7.6 Hz, 1 H), 7.35 (d, J = 8.0 Hz, 2 H), 3.77 (t, J = 7.4 Hz, 2 H), 3.14 (t, J = 7.4 Hz, 2 H); $^{13}\text{C}\{\text{H}\}$ NMR (125 MHz, CDCl_3): δ 145.3, 138.9, 136.9, 133.9, 133.0, 130.2, 129.4, 129.1, 127.7, 118.9, 111.3, 44.8, 39.0 ppm. HRMS (ESI) m/z calcd for $[\text{M} + \text{NH}_4]^+$ 259.0997, found 259.0993. IR (cm^{-1}): 3028, 2959, 2223, 1478, 1266, 762, 735.



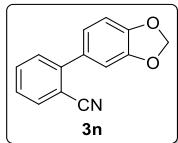
4-chloro-4'-methoxy-1,1'-biphenyl (3k) [CAS: 58970-19-7] was prepared following the general procedure A using **1a** (128 mg, 0.50 mmol) and **2i** (141 mg, 0.50 mmol) as starting materials. After stirring at 35 °C for 24 h, the reaction was quenched following general procedure and the crude material was purified by flash chromatography on silica gel (hexanes/ethyl acetate = 100/1 to 50/1) to afford the desired product (61.8 mg, 57%) as a white solid. ^1H NMR (500 MHz, CDCl_3): δ 7.49 (t, J = 8.3 Hz, 4 H), 7.38 (d, J = 8.5 Hz, 2 H), 6.98 (d, J = 8.7 Hz, 2 H), 3.86 (s, 3 H); $^{13}\text{C}\{\text{H}\}$ NMR (125 MHz, CDCl_3): δ 159.5, 139.4, 132.8, 132.6, 129.0, 128.2, 128.1, 114.5, 55.5 ppm. Characterization data matched those reported in the literature.⁴⁵



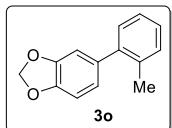
tert-butyl (2-(3'-methyl-[1,1'-biphenyl]-4-yl)ethyl)carbamate (3l) was prepared following the general procedure A using **1j** (135 mg, 0.50 mmol) and **2j** (131 mg, 0.50 mmol) as starting materials. After stirring at 40 °C for 24 h, the reaction was quenched following general procedure and the crude material was purified by flash chromatography on silica gel (hexanes/ethyl acetate = 50/1 to 20/1) to afford the desired product (116.3 mg, 75%) as a white solid. mp = 88 – 90 °C. ¹H NMR (500 MHz, CDCl₃): δ 7.55 (d, *J* = 8.2 Hz, 2 H), 7.38 (d, *J* = 11.8 Hz, 2 H), 7.34 (t, *J* = 7.5 Hz, 1 H), 7.28 (d, *J* = 7.8 Hz, 2 H), 7.18 (d, *J* = 7.4 Hz, 2 H), 4.64 (s, 1 H), 3.44 (q, *J* = 5.0 Hz, 2 H), 2.85 (t, *J* = 7.1 Hz, 2 H), 2.44 (s, 3 H), 1.47 (s, 9 H); ¹³C{¹H} NMR (125 MHz, CDCl₃): δ 156.0, 141.0, 139.6, 138.4, 138.1, 129.3, 128.8, 128.0, 127.9, 127.4, 124.2, 79.3, 41.9, 36.0, 28.6, 21.7 ppm. HRMS (ESI) m/z calcd for [M + Na]⁺ 334.1778, found 334.1773. IR (cm⁻¹): 3365, 2982, 1682, 1525, 1246, 1165, 777.



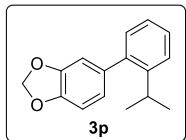
4-(4'-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-[1,1'-biphenyl]-4-yl)butan-2-one (3m) was prepared following the general procedure A using **1k** (148 mg, 0.50 mmol) and **2k** (280 mg, 0.75 mmol) as starting materials. After stirring at 40 °C for 24 h, the reaction was quenched following general procedure and the crude material was purified by flash chromatography on silica gel (hexanes/ethyl acetate = 10/1 to 5/1) to afford the desired product (118.5 mg, 68%) as a white solid. mp = 127 – 129 °C. ¹H NMR (500 MHz, CDCl₃): δ 7.88 (d, *J* = 8.1 Hz, 2 H), 7.69 (d, *J* = 8.1 Hz, 2 H), 7.55 (d, *J* = 8.1 Hz, 2 H), 7.26 (d, *J* = 8.0 Hz, 2 H), 2.95 (t, *J* = 7.6 Hz, 2 H), 2.80 (t, *J* = 7.7 Hz, 2 H), 2.16 (s, 3 H), 1.36 (s, 12 H); ¹³C{¹H} NMR (125 MHz, CDCl₃): δ 208.0, 143.7, 140.7, 139.0, 135.4, 128.9, 127.5, 126.4, 84.0, 45.3, 30.3, 29.5, 25.0 ppm. HRMS (ESI) m/z calcd for [M + NH₄]⁺ 368.2392, found 368.2393. IR (cm⁻¹): 2983, 2931, 1713, 1605, 1354, 1320, 1139, 853, 812, 656. The ¹³C NMR spectrum is missing one signal, which is the carbon directly bound to boron. Due to coupling with both quadrupolar boron isotopes, this carbon is challenging to resolve.⁴⁶



2-(benzo[d][1,3]dioxol-5-yl)benzonitrile (3n) [CAS: 475278-18-3] was prepared following the general procedure A using **1d** (135 mg, 0.50 mmol) and **2h** (137 mg, 0.50 mmol) as starting materials. After stirring at 40 °C for 24 h, the reaction was quenched following general procedure and the crude material was purified by flash chromatography on silica gel (hexanes/ethyl acetate = 20/1 to 5/1) to afford the desired product (80.2 mg, 72%) as a white solid. ¹H NMR (500 MHz, CDCl₃): 7.73 (dd, *J* = 7.7, 1.4 Hz, 1 H), 7.61 (td, *J* = 7.7, 1.4 Hz, 1 H), 7.46 (d, *J* = 7.9 Hz, 1 H), 7.40 (td, *J* = 7.6, 1.2 Hz, 1 H), 7.04 – 7.01 (m, 2 H), 6.92 (d, *J* = 7.8 Hz, 1 H), 6.03 (s, 2 H); ¹³C{¹H} NMR (125 MHz, CDCl₃): δ 148.3, 148.1, 145.3, 133.9, 132.9, 132.2, 130.1, 127.4, 122.9, 119.4, 111.3, 109.3, 108.7, 101.6 ppm. Characterization data matched those reported in the literature.⁴⁷



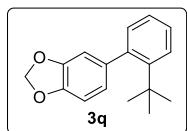
5-(o-tolyl)benzo[d][1,3]dioxole (3o) [CAS: 398470-00-3] was prepared following the general procedure A using **1d** (135 mg, 0.50 mmol) and **2l** (131 mg, 0.50 mmol) as starting materials. After stirring at 40 °C for 24 h, the reaction was quenched following general procedure and the crude material was purified by flash chromatography on silica gel (hexanes/ethyl acetate = 100/1 to 20/1) to afford the desired product (80.3 mg, 75%) as a white solid. ¹H NMR (400 MHz, CDCl₃, TMS): δ 7.25 – 7.18 (m, 4 H), 6.85 (d, *J* = 7.9 Hz, 1 H), 6.80 (d, *J* = 1.7 Hz, 1 H), 6.76 (dd, *J* = 7.9, 1.7 Hz, 1 H), 5.99 (s, 2 H), 2.27 (s, 3 H); ¹³C{¹H} NMR (125 MHz, CDCl₃): δ 147.4, 146.6, 141.7, 136.0, 135.6, 130.5, 130.0, 127.3, 125.9, 122.7, 110.0, 108.2, 101.2, 20.7 ppm. Characterization data matched those reported in the literature.⁴⁸



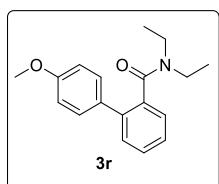
5-(2-isopropylphenyl)benzo[d][1,3]dioxole (3p) was prepared following the general procedure A using **1d** (135 mg, 0.50 mmol) and **2m** (218 mg, 0.75 mmol) as starting materials. After stirring at 60 °C for 24 h, the reaction was quenched following general procedure and the crude material was purified by flash chromatography on silica gel (hexanes/ethyl acetate = 100/1 to 20/1) to afford the desired product (83.0 mg, 69%) as a colorless oil. ¹H NMR (500 MHz, CDCl₃): δ 7.39 – 7.34 (m, 2 H), 7.22 – 7.16 (m, 2 H), 6.87

(d, $J = 7.9$ Hz, 1 H), 6.80 (d, $J = 1.6$ Hz, 1 H), 6.76 (dd, $J = 7.9, 1.6$ Hz, 1 H), 6.02 (s, 2 H), 3.11 (hept, $J = 6.9$ Hz, 1 H), 1.18 (d, $J = 6.9$ Hz, 6 H); $^{13}\text{C}\{\text{H}\}$ NMR (125 MHz, CDCl_3): δ 147.4, 146.7, 146.6, 140.8, 136.1, 130.2, 127.8, 125.7, 125.4, 122.7, 110.1, 108.1, 101.2, 29.5, 24.4 ppm. HRMS (ESI) m/z calcd for $[\text{M} + \text{H}]^+$ 241.1223, found 241.1220. IR (cm^{-1}): 3018, 1502, 1220, 1039, 907, 730.

5-(2-isopropylphenyl)benzo[d][1,3]dioxole (3p) was also prepared following the general procedure B using **1d** (135 mg, 0.50 mmol) and **2m** (218 mg, 0.75 mmol) as starting materials. After stirring at 60 °C for 24 h, the reaction was quenched following general procedure and the crude material was purified by flash chromatography on silica gel (hexanes/ethyl acetate = 100/1 to 20/1) to afford the desired product (96.2 mg, 80%) as a colorless oil. ^1H NMR (400 MHz, CDCl_3): δ 7.39 – 7.32 (m, 2 H), 7.22 – 7.15 (m, 2 H), 6.87 (d, $J = 7.9$ Hz, 1 H), 6.79 (d, $J = 1.6$ Hz, 1 H), 6.75 (dd, $J = 7.9, 1.7$ Hz, 1 H), 6.01 (s, 2 H), 3.10 (hept, $J = 6.9$ Hz, 1 H), 1.18 (d, $J = 6.9$ Hz, 6 H); $^{13}\text{C}\{\text{H}\}$ NMR (100 MHz, CDCl_3): 147.4, 146.7, 146.6, 140.8, 136.1, 130.2, 127.8, 125.7, 125.4, 122.7, 110.1, 108.1, 101.2, 29.5, 24.5 ppm.

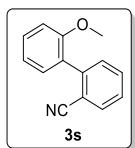


5-(2-(*tert*-butyl)phenyl)benzo[d][1,3]dioxole (3q) was prepared following the general procedure A using **1d** (135 mg, 0.50 mmol) and **2n** (228 mg, 0.75 mmol) as starting materials. After stirring at 60 °C for 24 h, the reaction was quenched following general procedure and the crude material was purified by flash chromatography on silica gel (hexanes/ethyl acetate = 100/1 to 20/1) to afford the desired product (69.2 mg, 54%) as a white solid. mp = 70 – 72 °C. ^1H NMR (500 MHz, CDCl_3): δ 7.53 (d, $J = 6.7$ Hz, 1 H), 7.30 (td, $J = 8.3, 7.8, 1.6$ Hz, 1 H), 7.17 (td, $J = 8.3, 7.8, 1.6$ Hz, 1 H), 7.02 (dd, $J = 7.3, 1.5$ Hz, 2 H), 6.81 – 6.76 (m, 2 H), 6.72 (dd, $J = 7.8, 1.6$ Hz, 1 H), 6.01 (s, 2 H), 1.23 (s, 9 H). $^{13}\text{C}\{\text{H}\}$ NMR (125 MHz, CDCl_3): δ 148.2, 146.7, 146.3, 141.7, 139.1, 133.0, 127.4, 126.9, 125.1, 123.4, 111.1, 107.3, 101.1, 36.8, 32.8 ppm. HRMS (ESI) m/z calcd for $[\text{M} + \text{H}]^+$ 255.1380, found 255.1377. IR (cm^{-1}): 2953, 2902, 1476, 1439, 1241, 1216, 1039, 757.

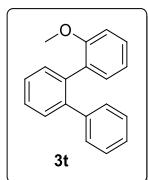


N,N-diethyl-4'-methoxy-[1,1'-biphenyl]-2-carboxamide (3r) [CAS: 1415045-57-6] was prepared following the general procedure A using **1a** (128 mg, 0.50 mmol) and **2o** (260 mg, 0.75 mmol) as starting

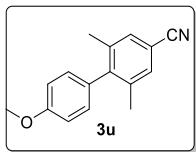
materials. After stirring at 60 °C for 24 h, the reaction was quenched following general procedure and the crude material was purified by flash chromatography on silica gel (hexanes/ethyl acetate = 5/1 to 3/1) to afford the desired product (116.3 mg, 82%) as a white solid. ^1H NMR (500 M, CDCl_3): δ 7.42 – 7.37 (m, 3 H), 7.36 (s, 1 H), 7.33 (m, 2 H), 6.90 (d, J = 8.7 Hz, 2 H), 3.81 (s, 3 H), 3.73 (m, 1 H), 3.03 (m, 1 H), 2.93 (m, 1 H), 2.66 (m, 1 H), 0.93 (t, J = 7.1 Hz, 3 H), 0.73 (t, J = 7.1 Hz, 3 H); $^{13}\text{C}\{^1\text{H}\}$ NMR (125 M, CDCl_3): δ 170.9, 159.4, 138.1, 136.4, 132.5, 130.1, 129.4, 129.0, 127.2, 127.1, 113.8, 55.4, 42.4, 38.5, 13.5, 12.3 ppm. Characterization data matched those reported in the literature.⁴⁹



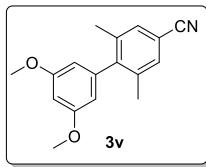
2'-methoxy-[1,1'-biphenyl]-2-carbonitrile (3s) [CAS: 150766-96-4] was prepared following the general procedure A using **1l** (128 mg, 0.50 mmol) and **2h** (205 mg, 0.75 mmol) as starting materials. After stirring at 60 °C for 24 h, the reaction was quenched following general procedure and the crude material was purified by flash chromatography on silica gel (hexanes/ethyl acetate = 10/1 to 5/1) to afford the desired product (63.7 mg, 61%) as a white solid. ^1H NMR (500 MHz, CDCl_3 , TMS) δ 7.71 (dd, J = 7.8, 1.4 Hz, 1 H), 7.61 (td, J = 7.7, 1.4 Hz, 1 H), 7.44 (d, J = 7.9 Hz, 1 H), 7.40 (td, J = 8.1, 1.9 Hz, 2 H), 7.25 (dd, J = 7.4, 1.7 Hz, 1 H), 7.05 (td, J = 7.5, 1.0 Hz, 1 H), 7.02 (d, J = 7.4 Hz, 1 H), 3.83 (s, 3 H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 M, CDCl_3): δ 156.6, 142.7, 132.9, 132.5, 131.0, 131.0, 130.5, 127.5, 127.4, 120.9, 118.8, 113.5, 111.4, 55.6 ppm. Characterization data matched those reported in the literature.⁵⁰



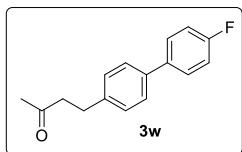
2-methoxy-1,1':2',1"-terphenyl (3t) [CAS: 54113-08-5] was prepared following the general procedure A using **1l** (128 mg, 0.50 mmol) and **2p** (243 mg, 0.75 mmol) as starting materials. After stirring at 60 °C for 24 h, the reaction was quenched following general procedure and the crude material was purified by flash chromatography on silica gel (hexanes/ethyl acetate = 50/1 to 10/1) to afford the desired product (74.0 mg, 57%) as a white solid. ^1H NMR (400 MHz, CDCl_3 , TMS): δ 7.41 (m, 2 H), 7.38 (m, 2 H), 7.23 – 7.11 (m, 7 H), 6.91 (td, J = 7.4, 1.1 Hz, 1 H), 6.68 (d, J = 9.2 Hz, 1 H), 3.33 (s, 3 H); $^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 156.4, 142.3, 141.8, 137.4, 131.8, 131.1, 130.8, 129.8, 129.1, 128.7, 127.7, 127.6, 127.3, 126.4, 120.5, 110.8, 55.1 ppm. Characterization data matched those reported in the literature.⁵¹



4'-methoxy-2,6-dimethyl-[1,1'-biphenyl]-4-carbonitrile (3u) was prepared following the general procedure A using **1a** (128 mg, 0.50 mmol) and **2q** (226 mg, 0.75 mmol) as starting materials. After stirring at 60 °C for 24 h, the reaction was quenched following general procedure and the crude material was purified by flash chromatography on silica gel (hexanes/ethyl acetate = 20/1 to 5/1) to afford the desired product (67.9 mg, 57%) as a white solid. mp = 118 – 120 °C. ¹H NMR (500 MHz, CDCl₃): 7.38 (s, 2 H), 7.02 – 6.97 (m, 4 H), 3.86 (s, 3 H), 2.05 (s, 6 H); ¹³C{¹H} NMR (125 MHz, CDCl₃): δ 159.0, 146.7, 138.2, 131.5, 130.8, 129.5, 129.4, 119.4, 114.3, 110.7, 55.4, 20.9 ppm. HRMS (ESI) m/z calcd for [M + H]⁺ 238.1226, found 238.1222. IR (cm⁻¹): 2965, 2837, 2221, 1610, 1516, 1288, 1242, 883.



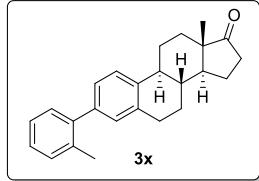
3',5'-dimethoxy-2,6-dimethyl-[1,1'-biphenyl]-4-carbonitrile (3v) was prepared following the general procedure A using **1c** (143 mg, 0.50 mmol) and **2q** (226 mg, 0.75 mmol) as starting materials. After stirring at 60 °C for 24 h, the reaction was quenched following general procedure and the crude material was purified by flash chromatography on silica gel (hexanes/ethyl acetate = 20/1 to 5/1) to afford the desired product (73.0 mg, 55%) as a white solid. mp = 164 – 166 °C. ¹H NMR (500 MHz, CDCl₃): 7.38 (s, 2 H), 6.47 (t, *J* = 2.3 Hz, 1 H), 6.23 (d, *J* = 2.3 Hz, 2 H), 3.80 (s, 6 H), 2.09 (s, 6 H); ¹³C{¹H} NMR (125 MHz, CDCl₃): δ 161.4, 146.8, 141.4, 137.7, 130.8, 119.4, 110.9, 106.4, 99.3, 55.6, 20.6 ppm. HRMS (ESI) m/z calcd for [M + NH₄]⁺ 285.1598, found 285.1594. IR (cm⁻¹): 2937, 2836, 2222, 1590, 1454, 1204, 1154, 1028, 836.



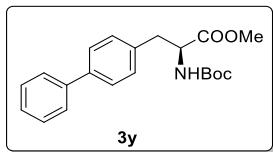
4-(4'-fluoro-[1,1'-biphenyl]-4-yl)butan-2-one (3w) [CAS: 1369389-99-0] was prepared following the general procedure A using **1k** (148 mg, 0.50 mmol) and **2c** (133 mg, 0.50 mmol) as starting materials. After stirring at 40 °C for 24 h, the reaction was quenched following general procedure and the crude material was purified by flash chromatography on silica gel (hexanes/ethyl acetate = 20/1 to 5/1) to afford the desired

product (88.0 mg, 73%) as a white solid. $\text{mp} = 64 - 66 \text{ }^\circ\text{C}$. ^1H NMR (400 MHz, CDCl_3 , TMS) δ 7.53 – 7.47 (m, 2 H), 7.44 (d, $J = 8.2 \text{ Hz}$, 2 H), 7.24 (d, $J = 8.0 \text{ Hz}$, 2 H), 7.09 (t, $J = 8.7 \text{ Hz}$, 2 H), 2.92 (t, $J = 7.5 \text{ Hz}$, 2 H), 2.78 (t, $J = 7.5 \text{ Hz}$, 2 H), 2.14 (s, 3 H); $^{13}\text{C}\{\text{H}\}$ NMR (100 MHz, CDCl_3) δ 207.9, 162.5 (d, $J = 246.1 \text{ Hz}$), 140.3, 138.2, 137.2 (d, $J = 3.2 \text{ Hz}$), 128.9, 128.6 (d, $J = 8.0 \text{ Hz}$), 127.2, 115.7 (d, $J = 21.4 \text{ Hz}$), 45.1, 30.2, 29.4; $^{19}\text{F}\{\text{H}\}$ -NMR (376 MHz, CDCl_3) δ –115.94 ppm. HRMS (ESI) m/z calcd for $[\text{M} + \text{NH}_4]^+$ 260.1445, found 260.1441. IR (cm^{-1}): 2955, 1715, 1497, 1373, 1227, 1159, 812.

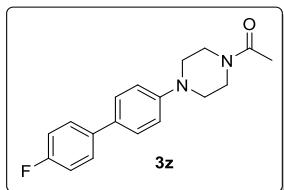
4-(4'-fluoro-[1,1'-biphenyl]-4-yl)butan-2-one (3w) [CAS: 1369389-99-0] was prepared following the general procedure B using **1k** (148 mg, 0.50 mmol) and **2c** (133 mg, 0.50 mmol) as starting materials. After stirring at 40 $^\circ\text{C}$ for 24 h, the reaction was quenched following general procedure and the crude material was purified by flash chromatography on silica gel (hexanes/ethyl acetate = 20/1 to 5/1) to afford the desired product (84.5 mg, 70%) as a white solid. ^1H NMR (400 MHz, CDCl_3 , TMS) δ 7.55 – 7.47 (m, 2 H), 7.44 (d, $J = 8.0 \text{ Hz}$, 2 H), 7.23 (d, $J = 7.8 \text{ Hz}$, 2 H), 7.09 (t, $J = 8.7 \text{ Hz}$, 2 H), 2.92 (t, $J = 7.5 \text{ Hz}$, 2 H), 2.78 (t, $J = 7.5 \text{ Hz}$, 2 H), 2.14 (s, 3 H); $^{13}\text{C}\{\text{H}\}$ NMR (100 MHz, CDCl_3) δ 207.9, 162.4 (d, $J = 246.0 \text{ Hz}$), 140.3, 138.2, 137.1 (d, $J = 3.2 \text{ Hz}$), 128.9, 128.6 (d, $J = 8.0 \text{ Hz}$), 127.2, 115.7 (d, $J = 21.3 \text{ Hz}$), 45.1, 30.12, 29.4; $^{19}\text{F}\{\text{H}\}$ -NMR (376 MHz, CDCl_3) δ –115.93 ppm.



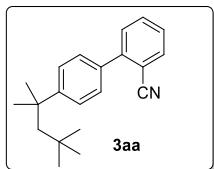
(8R,9S,13S,14S)-13-methyl-3-(o-tolyl)-6,7,8,9,11,12,13,14,15,16-decahydro-17H-cyclopenta[a]phenanthren-17-one (3x) was prepared following the general procedure A using **1m** (201 mg, 0.50 mmol) and **2l** (131 mg, 0.50 mmol) as starting materials. After stirring at 40 $^\circ\text{C}$ for 24 h, the reaction was quenched following general procedure and the crude material was purified by flash chromatography on silica gel (hexanes/ethyl acetate = 20/1 to 5/1) to afford the desired product (137.3 mg, 80%) as a white solid. $\text{mp} = 204 - 206 \text{ }^\circ\text{C}$. ^1H NMR (500 MHz, CDCl_3 , TMS) δ 7.32 (d, $J = 7.9 \text{ Hz}$, 1 H), 7.27 – 7.20 (m, 4 H), 7.12 (d, $J = 6.0 \text{ Hz}$, 1 H), 7.06 (s, 1 H), 2.95 (m, 2 H), 2.56 – 2.43 (m, 2 H), 2.36 (td, $J = 11.0, 4.0 \text{ Hz}$, 1 H), 2.29 (s, 3 H), 2.20 – 2.02 (m, 3 H), 1.99 (d, $J = 12.6 \text{ Hz}$, 1 H), 1.73 – 1.43 (m, 6 H), 0.93 (s, 3 H); $^{13}\text{C}\{\text{H}\}$ -NMR (125 MHz, CDCl_3): δ 221.0, 141.8, 139.6, 138.4, 136.3, 135.5, 130.4, 130.0, 129.9, 127.2, 126.8, 125.9, 125.2, 50.7, 48.2, 44.6, 38.3, 36.0, 31.8, 29.6, 26.7, 25.9, 21.8, 20.7, 14.0 ppm. HRMS (ESI) m/z calcd for $[\text{M} + \text{H}]^+$ 345.2213, found 345.2212. IR (cm^{-1}): 2927, 2858, 1736, 1480, 1453, 1155, 1006, 757, 732.



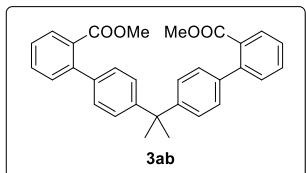
Methyl (S)-3-((1,1'-biphenyl)-4-yl)-2-((tert-butoxycarbonyl)amino)propanoate (3y) [CAS: 137255-96-8] was prepared following the general procedure A using **1n** (213 mg, 0.50 mmol) and **2a** (124 mg, 0.50 mmol) as starting materials. After stirring at 40 °C for 24 h, the reaction was quenched following general procedure and the crude material was purified by flash chromatography on silica gel (hexanes/ethyl acetate = 20/1 to 3/1) to afford the desired product (120.5 mg, 68%) as a white solid. ¹H NMR (400 MHz, CDCl₃): 7.56 (dd, *J* = 18.6, 7.8 Hz, 4 H), 7.44 (t, *J* = 7.6 Hz, 2 H), 7.34 (t, *J* = 7.5 Hz, 1 H), 7.21 (d, *J* = 7.8 Hz, 2 H), 5.05 (d, *J* = 8.4 Hz, 1 H), 4.64 (q, *J* = 6.7 Hz, 1 H), 3.74 (s, 3 H), 3.22 – 3.05 (m, 2 H), 1.43 (s, 9 H); ¹³C{¹H} NMR (100 MHz, CDCl₃): δ 172.5, 155.3, 140.9, 140.0, 135.2, 129.9, 128.9, 127.4, 127.2, 80.1, 54.5, 52.4, 38.1, 28.4 ppm. ¹H NMR data matched those reported in the literature,⁵² ¹³C{¹H} NMR data were not reported previously. The ¹³C NMR spectrum is missing one signal due to the overlap of two signals. Similar peak overlap was reported in the ¹³C NMR data of methyl 3-((1,1'-biphenyl)-4-yl)-2-((tert-butoxycarbonyl)amino)propanoate.⁵³



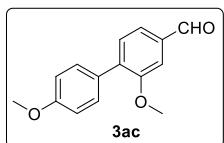
1-(4-(4'-fluoro-[1,1'-biphenyl]-4-yl)piperazin-1-yl)ethan-1-one (3z) was prepared following the general procedure A using **1o** (176 mg, 0.50 mmol) and **2c** (133 mg, 0.50 mmol) as starting materials. After stirring at 40 °C for 24 h, the reaction was quenched following general procedure and the crude material was purified by flash chromatography on silica gel (hexanes/ethyl acetate = 5/1 to 100% ethyl acetate) to afford the desired product (97.0 mg, 65%) as a white solid. mp = 188 – 190 °C. ¹H NMR (500 MHz, DMSO-d₆): δ 7.63 (dd, *J* = 8.7, 5.5 Hz, 2 H), 7.52 (d, *J* = 8.8 Hz, 2 H), 7.23 (t, *J* = 8.9 Hz, 2 H), 7.04 (d, *J* = 8.8 Hz, 2 H), 3.58 (q, *J* = 5.9 Hz, 4 H), 3.20 (t, *J* = 5.2 Hz, 2 H), 3.14 (t, *J* = 5.3 Hz, 2 H), 2.04 (s, 3 H); ¹³C{¹H} NMR (125 MHz, DMSO-d₆): δ 168.3, 161.3 (d, *J* = 243.2 Hz), 150.1, 136.5, 129.8, 127.7 (d, *J* = 8.0 Hz), 127.2, 116.0, 115.6 (d, *J* = 21.2 Hz), 48.4, 48.0, 45.4, 21.2; ¹⁹F{¹H} NMR (376 MHz, DMSO-d₆): δ –116.94 ppm. HRMS (ESI) m/z calcd for [M + H]⁺ 299.1554, found 299.1551. IR (cm^{–1}): 2828, 1618, 1501, 1231, 1001, 810, 558.



4'-(2,4,4-trimethylpentan-2-yl)-[1,1'-biphenyl]-2-carbonitrile (3aa) was prepared following the general procedure A using **1p** (169 mg, 0.50 mmol) and **2h** (137 mg, 0.50 mmol) as starting materials. After stirring at 40 °C for 24 h, the reaction was quenched following general procedure and the crude material was purified by flash chromatography on silica gel (hexanes/ethyl acetate = 10/1 to 5/1) to afford the desired product (122.4 mg, 83%) as a colorless oil. ¹H NMR (500 MHz, CDCl₃): δ 7.75 (d, *J* = 8.6 Hz, 1 H), 7.62 (t, *J* = 7.0 Hz, 1 H), 7.53 (d, *J* = 7.8 Hz, 1 H), 7.50 (s, 4 H), 7.41 (t, *J* = 7.6 Hz, 1 H), 1.79 (s, 2 H), 1.42 (s, 6 H), 0.76 (s, 9 H); ¹³C{¹H} NMR (125 MHz, CDCl₃): δ 151.2, 145.6, 135.2, 133.9, 132.9, 130.2, 128.3, 127.4, 126.7, 119.0, 111.4, 57.2, 38.8, 32.6, 32.0, 31.6 ppm. HRMS (ESI) m/z calcd for [M + H]⁺ 292.2060, found 292.2059. IR (cm⁻¹): 2952, 2901, 2223, 1732, 1477, 1365, 835, 754.

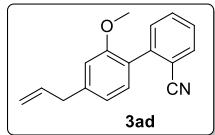


Dimethyl 4',4'''-(propane-2,2-diyl)bis([1,1'-biphenyl]-2-carboxylate) (3ab) was prepared following the general procedure A using **1q** (123 mg, 0.25 mmol) and **2r** (153 mg, 0.50 mmol) as starting materials. After stirring at 40 °C for 24 h, the reaction was quenched following general procedure and the crude material was purified by flash chromatography on silica gel (hexanes/ethyl acetate = 10/1 to 3/1) to afford the desired product (68.9 mg, 59%) as a colorless oil. ¹H NMR (500 MHz, CDCl₃): δ 7.80 (dd, *J* = 8.2, 1.4 Hz, 2 H), 7.52 (td, *J* = 7.8, 1.4 Hz, 2 H), 7.40 (d, *J* = 7.5 Hz, 4 H), 7.30 (d, *J* = 8.4 Hz, 4 H), 7.24 (d, *J* = 8.3 Hz, 4 H), 3.62 (s, 6 H), 1.77 (s, 6 H); ¹³C{¹H} NMR (125 MHz, CDCl₃): δ 169.5, 149.8, 142.3, 138.7, 131.4, 131.2, 130.8, 129.9, 128.2, 127.2, 126.7, 52.0, 42.9, 30.9 ppm. HRMS (ESI) m/z calcd for [M + NH₄]⁺ 482.2326, found 482.2324. IR (cm⁻¹): 2967, 1722, 1279, 1244, 1087, 839, 765, 745.

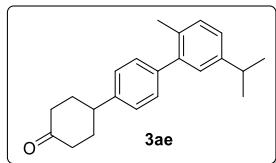


2,4-dimethoxy-[1,1'-biphenyl]-4-carbaldehyde (3ac) [CAS: 2039147-37-8] was prepared following the general procedure A using **1a** (128 mg, 0.50 mmol) and **2s** (153 mg, 0.50 mmol) as starting materials and 5.0 mol% NiCl₂(dme)/6.0 mol% 4,4'-dimethoxy-2,2'-bipyridine and 5.0 mol% PdCl₂/6.0 mol% dppb as

catalysts. After stirring at 40 °C for 24 h, the reaction was quenched following general procedure and the crude material was purified by flash chromatography on silica gel by flash chromatography on silica gel (hexanes/ethyl acetate = 10/1 to 3/1) afforded the desired product (76.0 mg, 64%) as a white solid. ¹H NMR (500 MHz, CDCl₃): δ 10.00 (s, 1 H), 7.53 – 7.46 (m, 5 H), 6.98 (d, *J* = 8.7 Hz, 2 H), 3.89 (s, 3 H), 3.86 (s, 3 H); ¹³C{¹H} NMR (125 MHz, CDCl₃): δ 192.0, 159.6, 157.2, 137.1, 136.5, 131.1, 130.8, 129.7, 124.7, 113.8, 109.7, 55.9, 55.5 ppm. Characterization data matched those reported in the literature.⁵⁴

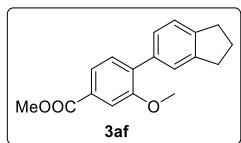


4'-allyl-2'-methoxy-[1,1'-biphenyl]-2-carbonitrile (3ad) was prepared following the general procedure A using **1r** (148 mg, 0.50 mmol) and **2h** (205 mg, 0.75 mmol) as starting materials. After stirring at 60 °C for 24 h, the reaction was quenched following general procedure and the crude material was purified by flash chromatography on silica gel (hexanes/ethyl acetate = 10/1 to 3/1) to afford the desired product (63.0 mg, 50%) as a white solid. mp = 59 – 61 °C. ¹H NMR (500 MHz, CDCl₃): δ 7.72 (d, *J* = 7.7 Hz, 1 H), 7.61 (t, *J* = 7.7 Hz, 1 H), 7.45 (d, *J* = 7.7 Hz, 1 H), 7.41 (t, *J* = 7.6 Hz, 1 H), 7.19 (d, *J* = 7.6 Hz, 1 H), 6.90 (d, *J* = 7.7 Hz, 1 H), 6.86 (s, 1 H), 6.02 (m, 1 H), 5.21 – 5.10 (m, 2 H), 3.84 (s, 3 H), 3.46 (d, *J* = 6.7 Hz, 2 H); ¹³C{¹H} NMR (125 MHz, CDCl₃): δ 156.6, 142.9, 142.7, 137.0, 133.0, 132.5, 131.1, 131.0, 127.4, 125.3, 121.1, 118.9, 116.5, 113.6, 111.8, 55.6, 40.6 ppm. HRMS (ESI) m/z calcd for [M + NH₄]⁺ 250.1226, found 250.1223. IR (cm⁻¹): 3003, 2910, 2224, 1610, 1411, 1162, 1036, 756, 548.



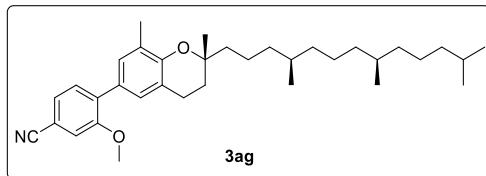
4-(2'-isopropyl-[1,1'-biphenyl]-4-yl)cyclohexan-1-one (3ae) was prepared following the general procedure A using **1s** (161 mg, 0.50 mmol) and **2t** (228 mg, 0.75 mmol) as starting materials. After stirring at 40 °C for 24 h, the reaction was quenched following general procedure and the crude material was purified by flash chromatography on silica gel (hexanes/ethyl acetate = 10/1 to 5/1) to afford the desired product (72.0 mg, 47%) as a white solid. mp = 82 – 84 °C. ¹H NMR (500 MHz, CDCl₃): δ 7.32 – 7.27 (m, 5 H), 7.19 (d, *J* = 8.0 Hz, 1 H), 7.03 (s, 1 H), 3.16 – 3.00 (m, 2 H), 2.60 – 2.50 (m, 4 H), 2.37 (s, 3 H), 2.37 – 2.29 (m, 2 H), 2.10 – 1.97 (m, 2 H), 1.18 (d, *J* = 6.9 Hz, 6 H); ¹³C{¹H} NMR (125 MHz, CDCl₃): δ 211.4, 143.6, 143.2, 140.8, 140.6, 134.9, 130.9, 129.6, 128.6, 126.4, 125.7, 42.6, 41.6, 34.2, 29.1, 24.6, 21.1 ppm.

HRMS (ESI) m/z calcd for $[M + H]^+$ 307.2056, found 307.2053. IR (cm^{-1}): 2958, 2865, 1715, 1493, 1161, 820.



Methyl 4-(2,3-dihydro-1*H*-inden-5-yl)-3-methoxybenzoate (3af) was prepared following the general procedure A using **1t** (133 mg, 0.50 mmol) and **2u** (168 mg, 0.50 mmol) as starting materials. After stirring at 40 °C for 24 h, the reaction was quenched following general procedure and the crude material was purified by flash chromatography on silica gel (hexanes/ethyl acetate = 10/1 to 3/1) to afford the desired product (117.0 mg, 83%) as a colorless oil. ^1H NMR (500 MHz, CDCl_3): δ 7.72 (dd, $J = 7.8, 1.5$ Hz, 1 H), 7.66 (d, $J = 1.4$ Hz, 1 H), 7.41 (s, 1 H), 7.38 (d, $J = 7.8$ Hz, 1 H), 7.31 (q, $J = 7.8$ Hz, 2 H), 3.96 (s, 3 H), 3.89 (s, 3 H), 2.97 (q, $J = 7.1$ Hz, 4 H), 2.13 (p, $J = 7.4$ Hz, 2 H); $^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 167.2, 156.6, 144.3, 144.0, 136.1, 135.6, 130.9, 130.1, 127.6, 125.6, 124.2, 122.3, 112.0, 55.9, 52.3, 33.0, 32.9, 25.6 ppm. HRMS (ESI) m/z calcd for $[M + H]^+$ 283.1329, found 283.1326. IR (cm^{-1}): 2949, 2842, 1718, 1397, 1286, 1227, 1109, 1035, 765.

Methyl 4-(2,3-dihydro-1*H*-inden-5-yl)-3-methoxybenzoate (3af) was prepared following the general procedure B using **1t** (133 mg, 0.50 mmol) and **2u** (168 mg, 0.50 mmol) as starting materials. After stirring at 40 °C for 24 h, the reaction was quenched following general procedure and the crude material was purified by flash chromatography on silica gel (hexanes/ethyl acetate = 10/1 to 3/1) to afford the desired product (111.5 mg, 79%) as a colorless oil. ^1H NMR (400 MHz, CDCl_3) δ 7.73 (dd, $J = 7.8, 1.6$ Hz, 1 H), 7.67 (d, $J = 1.6$ Hz, 1 H), 7.43 (s, 1 H), 7.40 (d, $J = 7.8$ Hz, 1 H), 7.33 (q, $J = 7.8$ Hz, 2 H), 3.97 (s, 3 H), 3.90 (s, 3 H), 2.99 (q, $J = 6.7$ Hz, 4 H), 2.14 (p, $J = 7.4$ Hz, 2 H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 167.1, 156.5, 144.3, 144.0, 136.0, 135.5, 130.9, 130.0, 127.6, 125.5, 124.2, 122.3, 112.0, 55.8, 52.3, 33.0, 32.8, 25.6 ppm.



4-((R)-2,8-dimethyl-2-((4*R*,8*R*)-4,8,12-trimethyltridecyl)chroman-6-yl)-3-methoxybenzonitrile (3ag) was prepared following the general procedure A using **1u** (267 mg, 0.50 mmol) and **2v** (152 mg, 0.50 mmol)

as starting materials. After stirring at 40 °C for 24 h, the reaction was quenched following general procedure and the crude material was purified by flash chromatography on silica gel (hexanes/ethyl acetate = 100/1 to 10/1) to afford the desired product (137.2 mg, 53%) as a colorless oil. ¹H NMR (500 MHz, CDCl₃): 7.37 (d, *J* = 7.8 Hz, 1 H), 7.30 (dd, *J* = 7.8, 1.5 Hz, 1 H), 7.16 (d, *J* = 1.5 Hz, 1 H), 7.14 (d, *J* = 2.7 Hz, 1 H), 7.08 (d, *J* = 2.2 Hz, 1 H), 3.85 (s, 3 H), 2.79 (m, 2 H), 2.21 (s, 3 H), 1.56 – 1.47 (m, 2 H), 1.44 – 1.32 (m, 5 H), 1.31 (s, 3 H), 1.29 – 1.18 (m, 6 H), 1.17 – 1.12 (m, 3 H), 1.10 – 1.03 (m, 3 H), 0.88 (d, *J* = 6.6 Hz, 9 H), 0.85 (d, *J* = 6.6 Hz, 3 H); ¹³C{¹H} NMR (125 MHz, CDCl₃): δ 156.7, 152.6, 136.2, 131.3, 129.5, 128.2, 127.0, 126.3, 125.0, 120.4, 119.4, 114.2, 110.9, 76.7, 56.0, 40.5, 39.5, 37.62, 37.60, 37.4, 33.0, 32.9, 31.2, 28.2, 25.0, 24.6, 24.6, 22.9, 22.8, 22.6, 21.2, 19.9, 19.8, 16.4 ppm. HRMS (ESI) m/z calcd for [M + NH₄]⁺ 535.4258, found 535.4259. IR (cm⁻¹): 2954, 2865, 2227, 1472, 1226, 1133, 1034, 823.

Synthesis of compound 3w on 5.0 mmol scale

Scheme S9. Synthesis of compound **3w** on 5.0 mmol scale

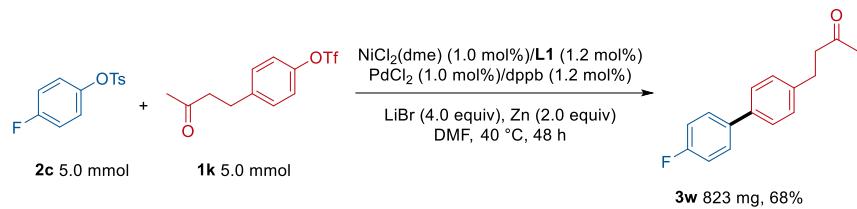


Figure S3. Compound **3w** isolated from the reaction.

Procedure for synthesis of compound 3w on 5.0 mmol scale

The following procedures were conducted in a N₂ filled glovebox for convenience. Nickel and palladium catalyst stock solutions were prepared following *general procedure for optimization studies* (page S4) using **L1** (18.5 mg, 0.060 mmol) as the amine ligand and dppb (25.6 mg, 0.060 mmol) as the phosphine ligand.

Catalytic Reaction Setup

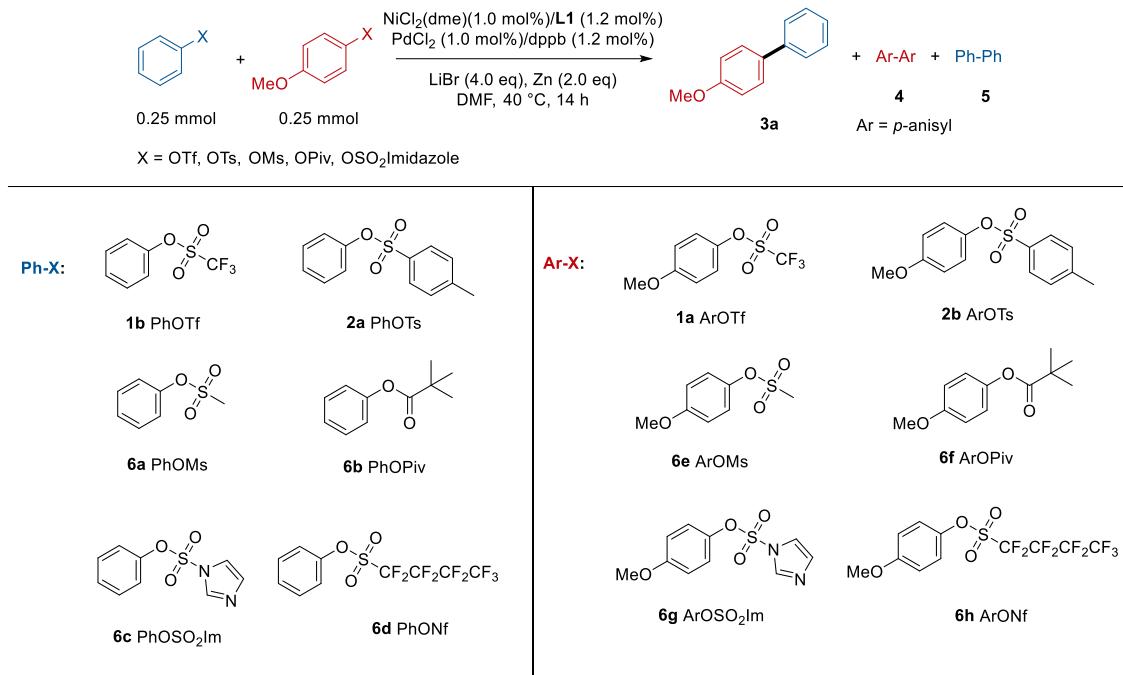
An oven-dried 100 mL Schlenk tube equipped with a PTFE-coated stir-bar was charged sequentially with **1k** (1480 mg, 5.00 mmol, 1.00 equiv), **2c** (1330 mg, 5.00 mmol, 1.00 equiv), LiBr (1740 mg, 20.0 mmol, 4.00 equiv), and Zn flake (650 mg, 10.0 mmol, 2.00 equiv). (*Attention: zinc flake instead of zinc powder was used as the reductant.*) Nickel catalyst stock solution (2.0 mL for 1.0 mol%), palladium catalyst stock solution (2.0 mL for 1.0 mol%) were added, followed by additional DMF (11.0 mL). The reaction tube was sealed with a PTFE valve plug, removed from glovebox, and the reaction mixture was stirred (1000 rpm) at rt for 20 min. The reaction tube was then placed into a 40 °C oil bath and stirred (1000 rpm) for 48 h.

Isolation and purification

When the reaction was judged complete (GC analysis), the reaction mixture was cooled to rt, diluted with ethyl acetate (50 mL), filtered through a short plug of silica gel (3.0 cm × 3.0 cm), and the vessel and silica gel were washed with extra portions of ethyl acetate (50 mL × 4). The combined filtrate was poured into a 500 mL separatory funnel and washed with brine (50 mL × 3). The ethyl acetate layer was set aside while the aqueous layer was washed further with ethyl acetate (50 mL × 3). The combined organic layers were dried over anhydrous MgSO₄, the resulting mixture was filtered to remove the MgSO₄, and the filtrate was concentrated by rotary evaporation. The crude material was purified by flash chromatography on silica gel (hexanes/ethyl acetate = 100/1 to 10/1) to afford the desired product (822.6 mg, 68%) as a white solid. ¹H NMR (500 MHz, CDCl₃, TMS) δ 7.50 (dd, *J* = 8.5, 5.4 Hz, 2 H), 7.44 (d, *J* = 7.9 Hz, 2 H), 7.23 (d, *J* = 7.8 Hz, 2 H), 7.09 (t, *J* = 8.6 Hz, 2 H), 2.92 (t, *J* = 7.6 Hz, 2 H), 2.77 (t, *J* = 7.6 Hz, 2 H), 2.14 (s, 3 H); ¹³C{¹H} NMR (125 MHz, CDCl₃) δ 207.8, 162.5 (d, *J* = 246.1 Hz), 140.3, 138.2, 137.2 (d, *J* = 3.3 Hz), 128.9, 128.6 (d, *J* = 8.0 Hz), 127.2, 115.7 (d, *J* = 21.4 Hz), 45.1, 30.2, 29.4; ¹⁹F{¹H} NMR (376 MHz, CDCl₃) δ -115.94 ppm. Characterization data matched those obtained from 0.50 mmol scale reactions (see page S35).

4.2 Cross-Electrophile Couplings Between Selected Phenol Derivatives

Scheme S10. Cross-electrophile couplings between selected phenol derivatives



Procedure for cross-electrophile couplings between selected phenol derivatives

The following procedures were conducted in a nitrogen filled glovebox for convenience. Nickel and palladium catalyst stock solutions were prepared following *general procedure for optimization studies* (page S4) using **L1** (18.5 mg, 0.060 mmol) as the amine ligand and dppb (25.6 mg, 0.060 mmol) as the phosphine ligand. Catalytic reactions were setup following *general procedure for optimization studies* (page S4) using **Ph-X** (0.25 mmol, 1.0 equiv) and **Ar-X** (0.25 mmol, 1.0 equiv; Ar = *p*-anisyl) as starting materials, 1.0 mol% $\text{NiCl}_2(\text{dme})/\text{L1}$ and 1.0 mol% $\text{PdCl}_2/\text{dppb}$ as catalysts, LiBr (87 mg, 1.0 mmol, 4.0 equiv) as additive, and Zn (33 mg, 0.50 mmol, 2.0 equiv) as reductant at 40°C (as in Scheme S10). GC analyses were conducted following *general procedure for optimization studies* (page S4).

Table S3. Yields of **3a** in cross-electrophile couplings between selected phenol derivatives (Ar = *p*-anisyl).^a

3a (%)	Ph-OTf	Ph-OTs	Ph-OMs	Ph-OPiv	Ph-ONf	Ph-OSO ₂ Im
Ar-OTf	55	76	19	0	0	47
Ar-OTs	66	36	3	0	0	11
Ar-OMs	13	0	0	0	0	0
Ar-OPiv	0	0	0	0	0	0
Ar-ONf	0	0	0	0	0	0
Ar-OSO ₂ Im	63	41	5	0	0	34

^aGC yields using dodecane as an internal standard.

Table S4. Yields of biaryls in cross-electrophile couplings between selected phenol derivatives (Ar = *p*-anisyl).^a

4 (%)/ 3a (%)/ 5 (%)	Ph-OTf	Ph-OTs	Ph-OMs	Ph-OPiv	Ph-ONf	Ph-OSO ₂ Im
Ar-OTf	22/55/23	12/76/13	37/19/0	0/0/0	0/0/0	24/47/23
Ar-OTs	2/66/22	20/36/25	8/3/0	0/0/0	0/0/0	35/11/33
Ar-OMs	0/13/31	0/0/22	0/0/2	0/0/0	0/0/0	0/0/34
Ar-OPiv	0/0/17	0/0/0	0/0/0	0/0/0	0/0/0	0/0/41
Ar-ONf	0/0/0	0/0/0	0/0/0	0/0/0	0/0/0	0/0/0
Ar-OSO ₂ Im	13/63/16	25/41/15	48/5/1	0/0/0	0/0/0	31/34/33

^aGC yields using dodecane as an internal standard.

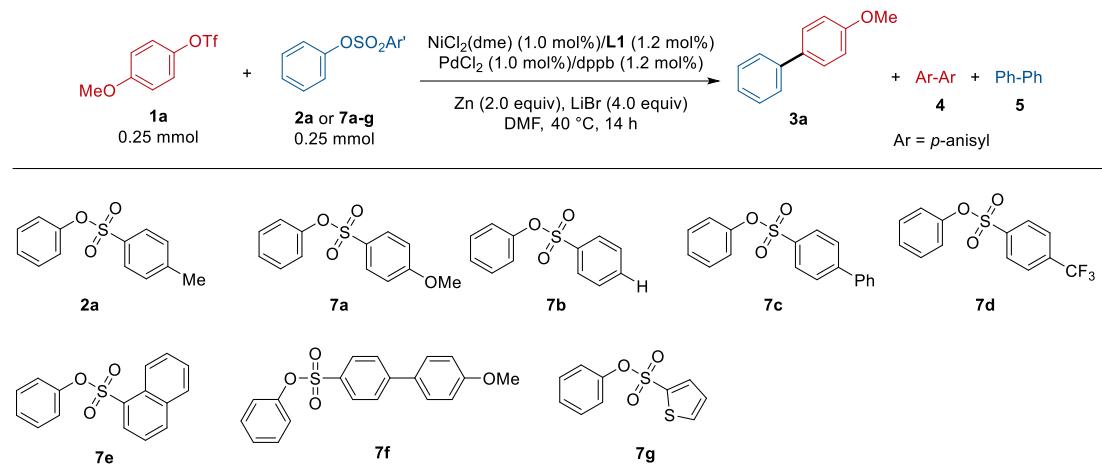
Table S5. Yields of recovered phenol derivatives after the reactions (Ar = *p*-anisyl).^a

Ar-X (%)/ Ph-X (%)	Ph-OTf	Ph-OTs	Ph-OMs	Ph-OPiv	Ph-ONf	Ph-OSO ₂ Im
Ar-OTf	0/0	0/0	0/62	42/86	99/20	0/0
Ar-OTs	0/0	0/0	34/58	94/88	91/17	0/0
Ar-OMs	65/0	82/25	85/87	92/90	89/18	67/0
Ar-OPiv	84/0	93/70	93/92	87/89	93/22	83/0
Ar-ONf	15/91	17/95	14/93	24/88	42/43	52/X ^b
Ar-OSO ₂ Im	0/0	0/0	0/54	X ^b /92	X ^b /33	0/0

^aGC yields using dodecane as an internal standard. ^bThe yields (shown as X in entries 5 and 6) of Ph-OSO₂Im (**6c**) or Ar-OSO₂Im (**6g**) after the reactions cannot be determined by GC due to their decomposition at high temperatures. However, no GC signals from the decompositions of them could be observed if they were fully consumed after reactions. This was used as the standard to determine if they were fully consumed.

4.3 Cross-Electrophile Couplings of *p*-Anisyl Triflate (1a) with Selected Aryl Arenesulfonate Esters

Scheme S11. Cross-electrophile couplings of **1a** with selected aryl arenesulfonate esters



Procedure for cross-electrophile couplings of **1a** with selected aryl arenesulfonate esters

The following procedures were conducted in a N₂ filled glovebox for convenience. Nickel and palladium catalyst stock solutions were prepared following *general procedure for optimization studies* (page S4) using **L1** (18.5 mg, 0.060 mmol) as the amine ligand and dppb (25.6 mg, 0.060 mmol) as the phosphine ligand. Catalytic reactions were setup following *general procedure for optimization studies* (page S4) using **1a** (0.25 mmol, 1.0 equiv) and **2a** or **7a-g** (0.25 mmol, 1.0 equiv) as starting materials, 1.0 mol% NiCl₂(dme)/**L1** and 1.0 mol% PdCl₂/dppb as catalysts, LiBr (87 mg, 1.0 mmol, 4.0 equiv) as additive, and Zn (33 mg, 0.50 mmol, 2.0 equiv) as reductant at 40 °C (as in Scheme S11). GC analyses were conducted following *general procedure for optimization studies* (page S4).

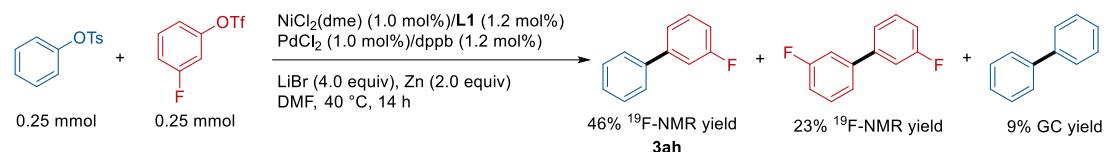
Table S6. Yields of **3a**, **4** and **5** in cross-electrophile couplings of **1a** with selected aryl arenesulfonate esters^a

entry	Ar'	3a (%)	4 (%)	5 (%)
1	4-methylphenyl, 2a	76	12	13
2	<i>p</i> -anisyl, 7a	80	11	10
3	phenyl, 7b	30	13	18
4	1,1'-biphenyl-4-yl, 7c	42	19	6
5	4-trifluoromethylphenyl, 7d	5	37	10
6	1-naphthyl, 7e	30	22	3
7	4'-methoxy-1,1'-biphenyl-4-yl, 7f	74	10	6
8	2-thiophenyl, 7g	0	0	0

^aGC yields using dodecane as an internal standard.

4.4 Hammett Constants of Substituents on Selected Aryl Triflates and Aryl Tosylates and Their Influence on the Yield of Cross-Coupled Product

Scheme S12. Cross-electrophile coupling of phenyl tosylate with 3-fluorophenyl triflate^{a,b,c}



^a4-Trifluoromethyl-1,1'-biphenyl was used as an internal standard for ¹⁹F-NMR. ^bDodecane was used as an internal standard for GC analysis. ^cReaction was set up according to *general procedure for optimization studies* (page S4).

Table S7. The relationship of Hammett constants of substituents on aryl triflates and yields of products

product	aryl substitution	σ^a	yield (%) ^b
3a	<i>p</i> -OMe	$\sigma_p = -0.27$	72
3b	<i>p</i> -H	$\sigma_p = 0$	62
3e	<i>m</i> -OMe	$\sigma_m = 0.12$	57
3i	<i>m</i> -NMe ₂	$\sigma_m = -0.16$	67
3k	<i>p</i> -OMe	$\sigma_p = -0.27$	57
3r	<i>p</i> -OMe	$\sigma_p = -0.27$	82
3u	<i>p</i> -OMe	$\sigma_p = -0.27$	57
3ac	<i>p</i> -OMe	$\sigma_p = -0.27$	64
3ah	<i>m</i> -F	$\sigma_m = 0.34$	46 ^c

^aData source: *Chem. Rev.* **1991**, *91*, 165–195. ^bIsolated yields on 0.50 mmol scale. ^c¹⁹F NMR yield.

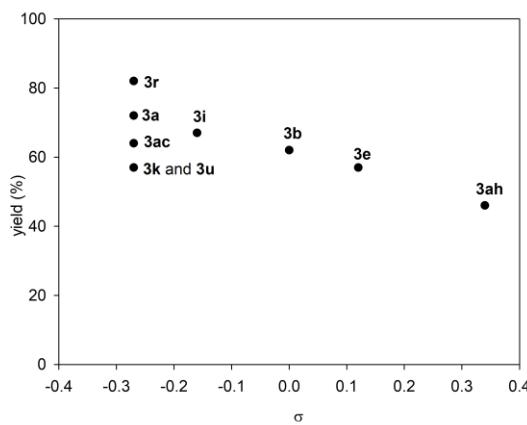
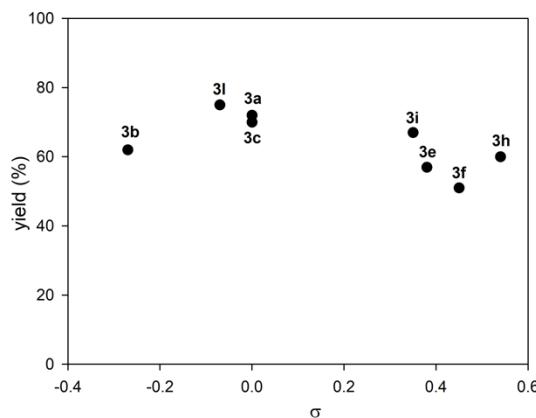


Figure S4. The relationship of Hammett constants of substituents on aryl triflates and yields of products.

Table S8. The relationship of Hammett constants of aryl substituents on tosylates and yields of products

product	aryl substitution	σ^a	yield (%) ^b
3a	<i>p</i> -H	$\sigma_p = 0$	72
3b	<i>p</i> -OMe	$\sigma_p = -0.27$	62
3c	<i>p</i> -H	$\sigma_p = 0$	70
3e	<i>m</i> -COMe	$\sigma_m = 0.38$	57
3f	<i>p</i> -COOMe	$\sigma_p = 0.45$	51
3h	<i>p</i> -CF ₃	$\sigma_p = 0.54$	60
3i	<i>p</i> -OCF ₃	$\sigma_p = 0.35$	67
3l	<i>m</i> -Me	$\sigma_m = -0.07$	75

^aData source: *Chem. Rev.* **1991**, *91*, 165–195. ^bIsolated yields on 0.50 mmol scale.

**Figure S5.** The relationship of Hammett constants of aryl substituents on tosylates and yields of products.**Table S9.** The relationship of the difference in Hammett constants ($\Delta\sigma = \sigma_{\text{OTs}} - \sigma_{\text{OTf}}$) of substituents on aryl triflates and tosylates and yields of products

product	substitution on aryl	substitution on aryl	$\Delta\sigma^a$	yield (%) ^b
	tosylate	triflate		
3a	<i>p</i> -H	<i>p</i> -OMe	0.27	72
3b	<i>p</i> -OMe	<i>p</i> -H	-0.27	62
3e	<i>m</i> -COMe	<i>m</i> -OMe	0.26	57
3i	<i>p</i> -OCF ₃	<i>m</i> -NMe ₂	0.51	67
3k	<i>p</i> -Cl	<i>p</i> -OMe	0.50	57
3ah	<i>p</i> -H	<i>m</i> -F	-0.34	46 ^c

^aData source: *Chem. Rev.* **1991**, *91*, 165–195. ^bIsolated yields on 0.50 mmol scale. ^c¹⁹F NMR yield.

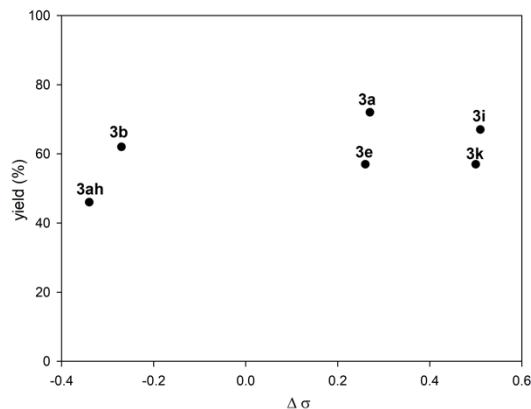
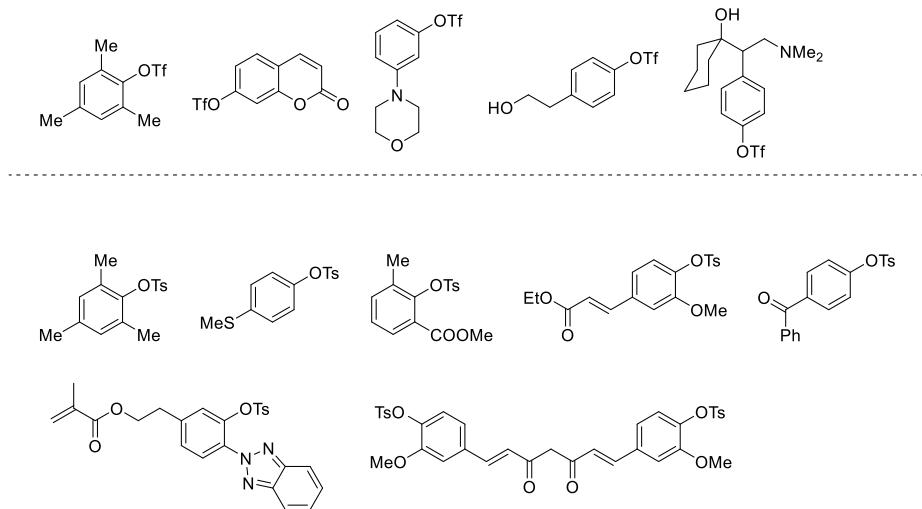


Figure S6. The relationship of the difference in Hammett constants ($\Delta\sigma = \sigma_{\text{OTs}} - \sigma_{\text{OTf}}$) of substituents on aryl triflates and tosylates and yields of products

4.5 Aryl Sulfonate Esters That Are Not Suitable for Nickel and Palladium Multimetallic Conditions

In the substrate scope studies, we found that some aryl sulfonate esters were not successful. Reactions of these aryl triflates with phenyl tosylate (**2a**) and reactions of these aryl tosylates with *p*-anisyl triflate (**1a**) were attempted under standard reaction conditions on 0.25 mmol scale, but no product or only trace amount of product was observed by GC or SFC-MS analysis.

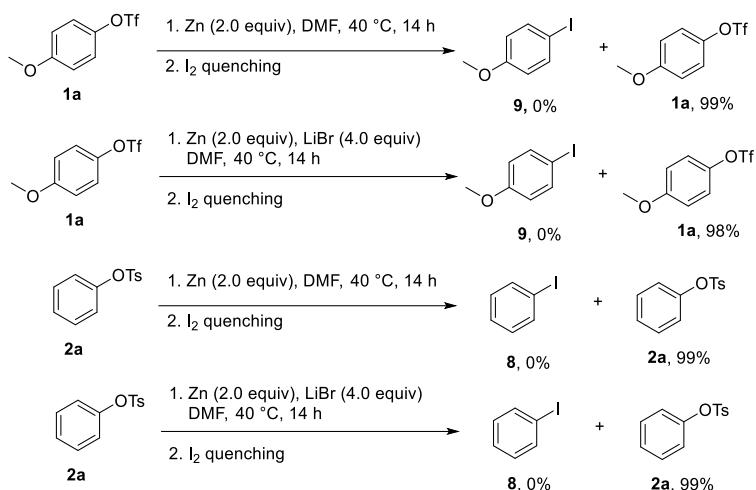
Scheme S13. Aryl sulfonate esters that failed to couple under standard conditions



5. Mechanistic Studies

5.1 Background Reactions of Zn with *p*-Anisyl Triflate (1a) and Phenyl Tosylate (2a)

Scheme S14. Control reactions of **1a** and **2a** with zinc, with and without LiBr^a



^aGC yields using 1,3,5-trimethoxybenzene as an internal standard.

Preparation of I₂ and LiCl quenching solution^{40, 55}

In a N₂ filled glovebox, LiCl (127 mg, 3.00 mmol) and THF (6.0 mL) were added to an oven-dried scintillation vial equipped with a PTFE-coated stir-bar. The solution was stirred at rt overnight until all solids were dissolved, resulting in a 0.5 M solution of LiCl. In a separate scintillation vial was weighed I₂ (254 mg, 1.00 mmol), and 4 mL of the 0.5 M solution of LiCl was added. The resulting brown solution was stirred at rt for 1 hour before being used.

Procedure for reactions of Zn with **1a** and **2a** in DMF at 40 °C

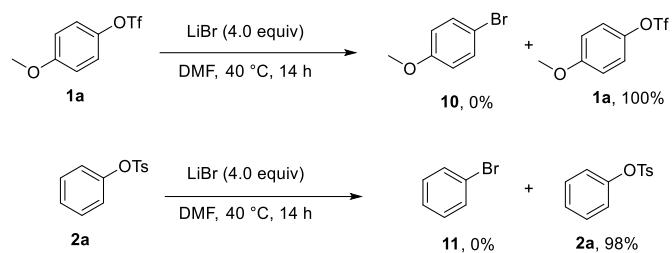
In a N₂ filled glovebox, an oven-dried 1-dram vial fitted with a PTFE-coated stir-bar was charged sequentially with **1a** (64 mg, 0.25 mmol, 1.0 equiv) or **1b** (62 mg, 0.25 mmol, 1.0 equiv), Zn (33 mg, 0.50 mmol, 2.0 equiv), LiBr (0 or 87 mg, 1.0 mmol, 4.0 equiv), and 1,3,5-trimethoxybenzene (15-20 mg) as an internal standard. DMF (1.0 mL) was added before the vial was capped with a screw cap fitted with a PTFE-faced silicone septum. The reaction mixture was stirred (1250 rpm) in a reaction block set to 40 °C in the glovebox for 14 h. A 100 μ L aliquot of the reaction mixture was transferred into another 1-dram vial equipped with a PTFE-coated stir-bar. Iodine-LiCl solution (200 μ L, 0.05 mmol) was added using a pipette before the vial was capped with a screw cap fitted with a PTFE-faced silicone septum. The quenched mixture was stirred at rt in the glovebox for 20 min before the vial was removed from the glovebox. The mixture was diluted with ethyl acetate (2 mL) and filtered through a 2-cm silica gel plug in a Pasteur pipette. The resulting filtrate was collected in a GC vial. The sample was analyzed by GC and the yields were

determined based on the peak area of the analyte compared to 1,3,5-trimethoxybenzene as an internal standard.

Results: Neither of the starting materials were consumed and no aryl iodides were formed, confirming that zinc does not react with aryl tosylates or triflates to form arylzinc reagents without a catalyst.

5.2 Background Reactions of LiBr with *p*-Anisyl Triflate (**1a**) and Phenyl Tosylate (**2a**)

Scheme S15. Reactions of LiBr with **1a** and **2a** in DMF at 40 °C



^aGC yields using 1,3,5-trimethoxybenzene as an internal standard.

Procedure for reactions of LiBr with **1a** and **2a** in DMF at 40 °C

In a N₂ filled glovebox, an oven-dried 1-dram vial equipped with a PTFE-coated stir-bar was charged sequentially with **1a** (64 mg, 0.25 mmol, 1.0 equiv) or **1b** (62 mg, 0.25 mmol, 1.0 equiv), LiBr (87 mg, 1.0 mmol, 4.0 equiv), and 1,3,5-trimethoxybenzene (15–20 mg) as an internal standard. DMF (1.0 mL) was added before the vial was capped with a screw cap fitted with a PTFE-faced silicone septum. The vial was removed from the glovebox, and the mixture was stirred (1250 rpm) in a reaction block set to 40 °C for 14 h. A 100 μ L aliquot of the reaction mixture was removed, diluted with ethyl acetate (2 mL), and filtered through a 2-cm silica gel plug in a Pasteur pipette. The resulting filtrate was collected in a GC vial. The sample was analyzed by GC and the yields were determined based on the peak area of the analyte compared to 1,3,5-trimethoxybenzene as an internal standard.

Results: No conversion of the aryl sulfonate esters to aryl bromides was observed.

5.3 Iodine Quenching Experiments for Reactions of *p*-Anisyl Triflate (1a) with Phenyl Tosylate (2a) in the Presence of Nickel and/or Palladium Catalysts

General procedure for iodine quenching experiments

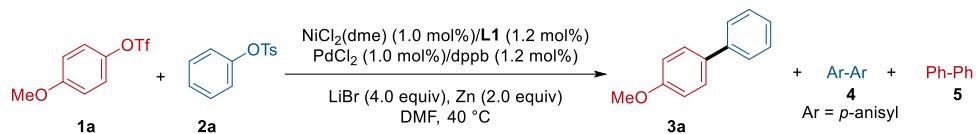
The following procedures were conducted in a N₂ filled glovebox for convenience. Nickel and palladium catalyst stock solutions were prepared following *general procedure for optimization studies* (page S4) using **L1** (18.5 mg, 0.060 mmol) as the amine ligand and dppb (25.6 mg, 0.060 mmol) as the phosphine ligand. Reactions were setup following *general procedure for optimization studies* (page S4) using **1a** (64 mg, 0.25 mmol, 1.0 equiv) and **1b** (62 mg, 0.25 mmol, 1.0 equiv) as starting materials, 0 or 1.0 mol% NiCl₂(dme)/**L1** and 0, 1.0, or 5.0 mol% PdCl₂/dppb as catalysts, LiBr (87 mg, 1.0 mmol, 4.0 equiv) as additive, and Zn (33 mg, 0.50 mmol, 2.0 equiv) as reductant at 40 °C.

Iodine quenching and GC analysis

At 0, 20, 40, 60, 120, 180, 300 and 420 min, a 25 μ L aliquot of the reaction mixture was removed and transferred into another 1-dram vial fitted with a PTFE-coated stir-bar. Iodine-LiCl solution (200 μ L, 0.05 mmol) was added using a pipette before the vial was capped with a screw cap fitted with a PTFE-faced silicone septum. The quenched mixture was stirred at rt in the glovebox for 20 min, and the vial was removed from the glovebox. The quenched mixture was diluted with ethyl acetate (2 mL) and filtered through a 2-cm silica gel plug in a Pasteur pipette. The resulting filtrate was collected in a GC vial. The sample was analyzed by GC and the yields were determined based on the peak area of the analyte compared to 1,3,5-trimethoxybenzene as an internal standard. Concentrations lower than 2.5×10^{-4} M (lower limit of detection) were recorded as 0.

5.3.1 Iodine Quenching Experiments for the Reaction of *p*-Anisyl Triflate (1a**) with Phenyl Tosylate (**2a**) under Standard Conditions (Condition A)**

Table S10. Concentrations of **1a**, **2a**, **3a**, **4** and **5** in Condition A^a



time (min)	[1a] (M)	[2a] (M)	[3a] (M)	[4] (M)	[5] (M)
0	0.250	0.250	0	0	0
20	0.245	0.245	0.002	0	0
40	0.242	0.238	0.005	0.002	0.002
60	0.232	0.225	0.010	0.003	0.005
120	0.190	0.162	0.050	0.010	0.015
180	0.108	0.095	0.105	0.020	0.020
300	0.015	0.020	0.178	0.030	0.022
420	0	0	0.185	0.032	0.025

^aConcentrations determined by GC analysis using 1,3,5-trimethoxybenzene as an internal standard.

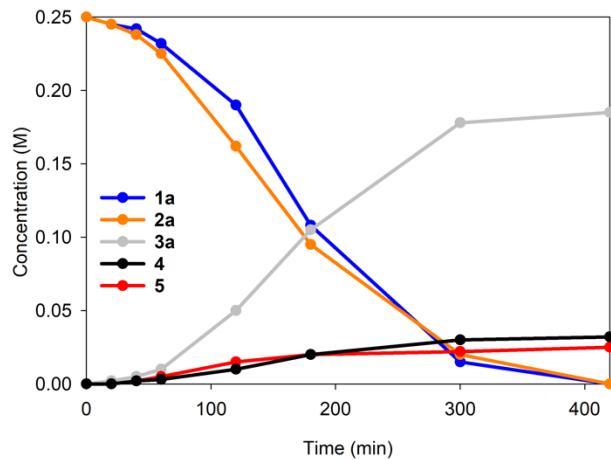
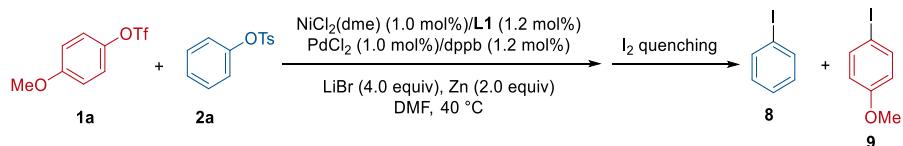


Figure S7. Plot of the concentrations of **1a** (Ar-OTf), **2a** (Ph-OTs), **3a** (Ph-Ar), **4** (Ar-Ar) and **5** (Ph-Ph) in Condition A over time. Ar = *p*-anisyl.

Table S11. Concentrations of **8** and **9** and the [aryl iodide]/[Ni] ratios from iodine quenching experiments in Condition A^a



time(min)	[8] (M)	[8]/[Ni]	[9] (M)	[9]/[Ni]
0	0	0	0	0
20	0	0	0.0016	0.64
40	0.0007	0.27	0.0025	1.00
60	0.0019	0.76	0.0019	0.76
120	0.0011	0.44	0.0026	1.04
180	0.0049	1.95	0.0024	0.96
300	0.0051	2.02	0.0026	1.04
420	0.0026	1.04	0	0

^aConcentrations determined by GC analysis using 1,3,5-trimethoxybenzene as an internal standard.

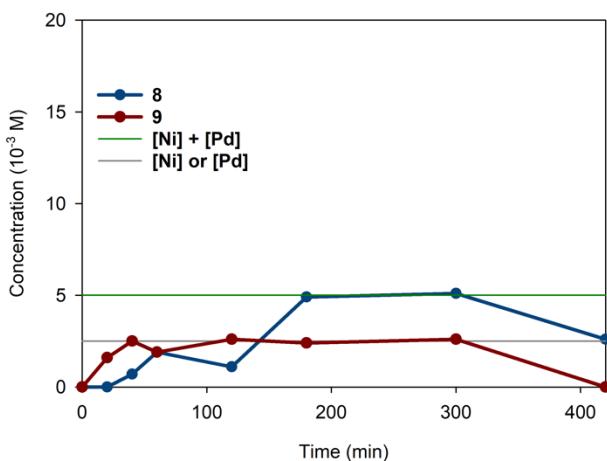
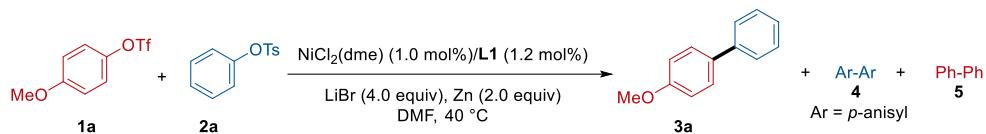


Figure S8. Plot of concentrations of iodobenzene (**8**) and *p*-iodoanisole (**9**) from iodine-quenched aliquots of Condition A over time.

5.3.2 Iodine Quenching Experiments for the Reaction of *p*-Anisyl Triflate (1a**) with Phenyl Tosylate (**2a**) under Ni-Only Conditions (Condition B)**

Table S12. Concentrations of **1a**, **2a**, **3a**, **4** and **5** in Condition B^a



time(min)	[1a] (M)	[2a] (M)	[3a] (M)	[4] (M)	[5] (M)
0	0.250	0.250	0	0	0
20	0.247	0.250	0	0	0
40	0.241	0.248	0.005	0	0.004
60	0.236	0.234	0.008	0.001	0.006
120	0.188	0.174	0.040	0.006	0.015
180	0.120	0.103	0.088	0.015	0.024
300	0.031	0.069	0.132	0.029	0.028
420	0	0	0.145	0.032	0.031

^aConcentrations determined by GC analysis using 1,3,5-trimethoxybenzene as an internal standard.

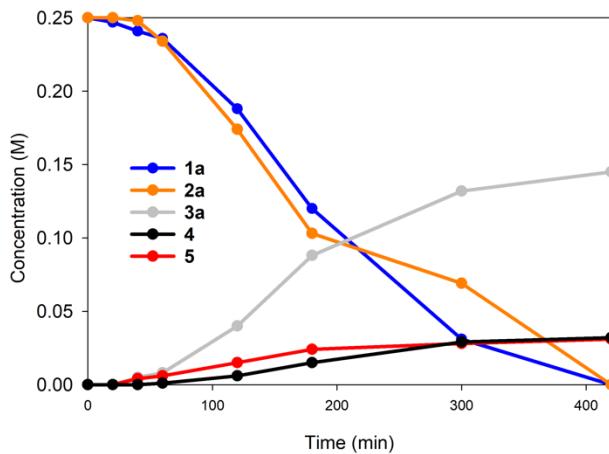
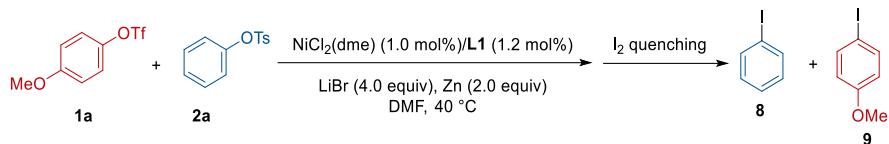


Figure S9. Plot of the concentrations of **1a** (Ar-OTf), **2a** (Ph-OTs), **3a** (Ph-Ar), **4** (Ar-Ar) and **5** (Ph-Ph) in Condition B over time. Ar = *p*-anisyl.

Table S13. Concentrations of **8** and **9** and the [aryl iodide]/[Ni] ratios from iodine quenching experiments in Condition B^a



time(min)	[8] (M)	[8]/[Ni]	[9] (M)	[9]/[Ni]
0	0	0	0	0
20	0	0	0	0
40	0.00086	0.34	0	0
60	0.00094	0.37	0	0
120	0.0035	1.40	0	0
180	0.0046	1.83	0.00030	0.12
300	0.0182	7.28	0.0043	1.72
420	0.0244	9.76	0.0152	6.08

^aConcentrations determined by GC analysis using 1,3,5-trimethoxybenzene as an internal standard.

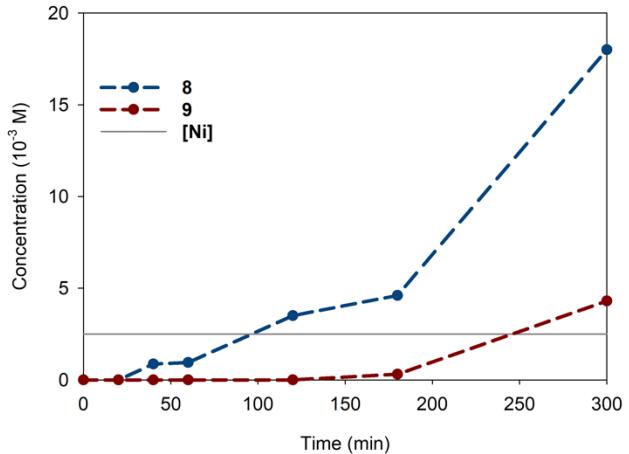


Figure S10. Plot of concentrations of iodobenzene (**8**) and *p*-iodoanisole (**9**) from iodine-quenched aliquots of Condition B over time.

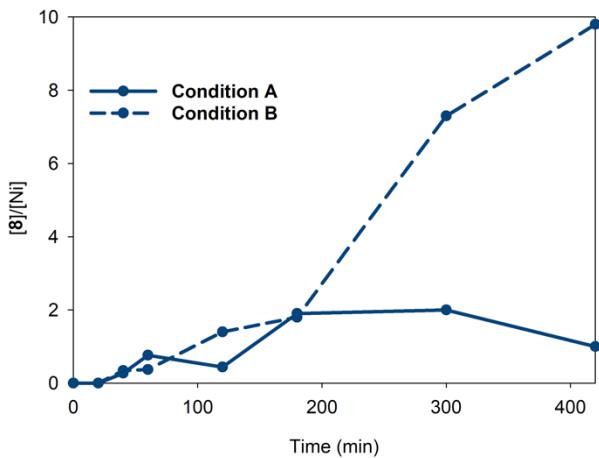
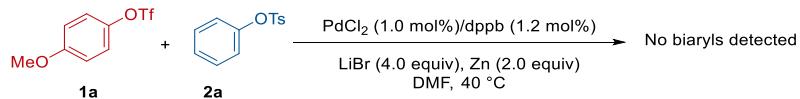


Figure S11. Plot of $[8]/[Ni]$ ratios from iodine-quenched aliquots of Condition A and B over time.

5.3.3 Iodine Quenching Experiments for the Reaction of *p*-Anisyl Triflate (**1a**) with Phenyl Tosylate (**2a**) under Pd-Only Conditions (Condition C)

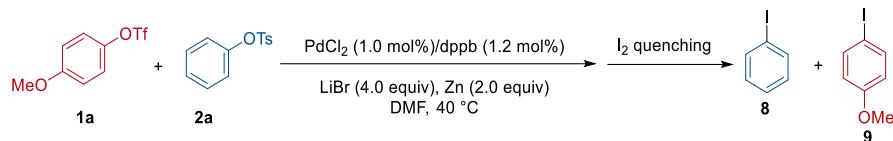
Table S14. Concentrations of **1a**, **2a**, **3a** (Ph-Ar), **4** (Ar-Ar) and **5** (Ph-Ph) in Condition C (Ar = *p*-anisyl)^a



time(min)	[1a] (M)	[2a] (M)	[3a] (M)	[4] (M)	[5] (M)
0	0.250	0.256	0	0	0
20	0.250	0.256	0	0	0
40	0.252	0.247	0	0	0
60	0.249	0.250	0	0	0
120	0.242	0.250	0	0	0
180	0.244	0.249	0	0	0
300	0.240	0.252	0	0	0
420	0.240	0.246	0	0	0

^aConcentrations determined by GC analysis using 1,3,5-trimethoxybenzene as an internal standard.

Table S15. Concentrations of **8** and **9** and the [aryl iodide]/[Pd] ratios from iodine quenching experiments of Condition C^a



time(min)	[8] (M)	[8]/[Pd]	[9] (M)	[9]/[Pd]
0	0	0	0	0
20	0	0	0.0023	0.92
40	0	0	0.0027	1.01
60	0	0	0.0025	1.00
120	0	0	0.0023	0.92
180	0	0	0.0015	0.60
300	0	0	0.0021	0.84
420	0	0	0.0019	0.72

^aConcentrations determined by GC analysis using 1,3,5-trimethoxybenzene as an internal standard.

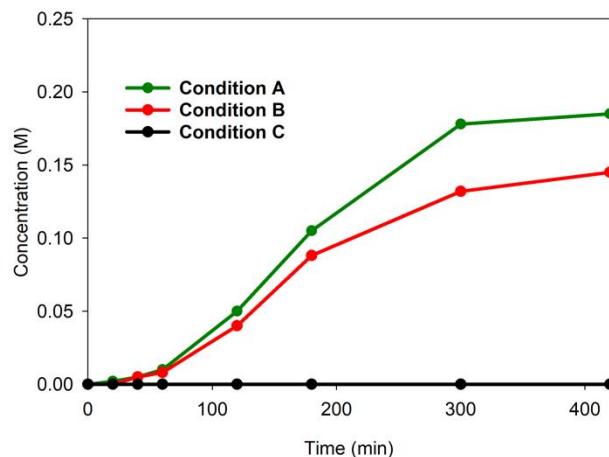
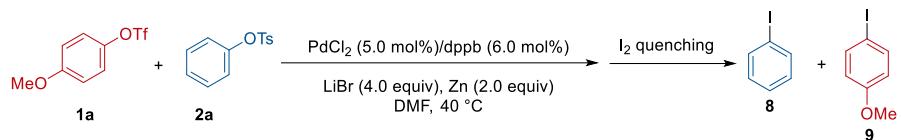


Figure 12. Plot of concentration of **3a** in Condition A (Ni + Pd), Condition B (Ni-only) and Condition C (Pd-only) over time.

5.3.4 Iodine Quenching Experiments for the Reaction of *p*-Anisyl Triflate (1a) with Phenyl Tosylate (2a) under Pd-Only Conditions (Condition D)

Table S16. Concentrations of **8** and **9** and the [aryl iodide]/[Pd] ratios from iodine quenching experiments of Condition D^{a,b}



time(min)	[8] (M)	[8]/[Pd]	[9] (M)	[9]/[Pd]
0	0	0	0	0
20	0	0	0.0019	0.15
40	0	0	0.0104	0.83
60	0	0	0.0111	0.89
120	0	0	0.0116	0.93
180	0	0	0.0100	0.80
300	0	0	0.0113	0.90
420	0	0	0.0092	0.72

^aConcentrations determined by GC analysis using 1,3,5-trimethoxybenzene as an internal standard.

^bUntil 420 min, no formation of biaryls or consumption of **2a** was observed. Only trace amount of **1a** was consumed.

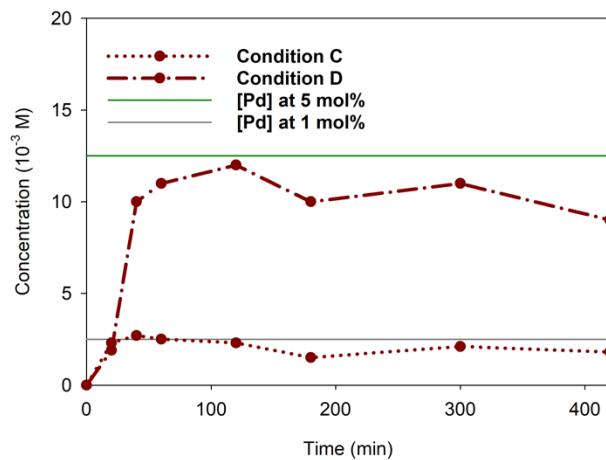


Figure S13. Plot of concentration of *p*-iodoanisole (**9**) from iodine-quenched aliquots of Condition C and Condition D over time.

5.4 Competitive Oxidative Additions of *p*-Anisyl Triflate (**1a**) and Phenyl Tosylate (**2a**) to **(L1)Ni⁰(cod)**

Procedure

In a N₂ filled glovebox, an oven-dried 1-dram vial equipped with a PTFE-coated stir-bar was charged with Ni(COD)₂ (13.8 mg, 0.050 mmol) and 4,4'-diphenyl-2,2'-bipyridine (15.4 mg, 0.050 mmol). DMF (1.0 mL) was then added. The vial was capped with a screw cap fitted with a PTFE-faced silicone septum, and the mixture was stirred (1000 rpm) at rt in the glovebox for 6 h. To the resulting dark blue solution was added **1a** (38 mg, 0.15 mmol), **2a** (37 mg, 0.15 mmol) and 1,3,5-trimethoxybenzene (16.5 mg) as an internal standard. The reaction vial was re-capped with a screw cap fitted with a PTFE-faced silicone septum, and the mixture was heated in a reaction block set to 40 °C with stirring (1250 rpm). At 5, 10, 20 and 30 min, a 50 μ L aliquot of the reaction mixture was transferred into another 1-dram vial. The vial was capped with a screw cap fitted with a PTFE-faced silicone septum and removed from the glovebox. The aliquot was then diluted with ethyl acetate (2 mL) and filtered through a 2-cm silica gel plug in a Pasteur pipette. The resulting filtrate was collected in a GC vial. The sample was analyzed by GC and the yields were determined based on the peak area of the analyte compared to 1,3,5-trimethoxybenzene as an internal standard. For the calculations in Table S14, **1a** and **2a** were used as limiting reagents and the theoretical yield is 0.15 mmol.

Table S17. Oxidative additions of **1a** and **2a** to **(L1)Ni⁰(cod)** in DMF at 40 °C^a

time(min)	1a consumption (%)	2a consumption (%)	ratio of consumption of 2a/1a	Consumption of 1a vs Consumption of 2a		
				3a (%)	4 (%)	5 (%)
5	11	32	2.91	7	1	12
10	10	34	3.40	9	1	15
20	12	38	3.17	9	1	14
30	12	38	3.17	9	1	15
average ratio of consumption of 2a/1a = 3.2 ± 0.2						

^aGC yields using 1, 3, 5-trimethoxybenzene as an internal standard.

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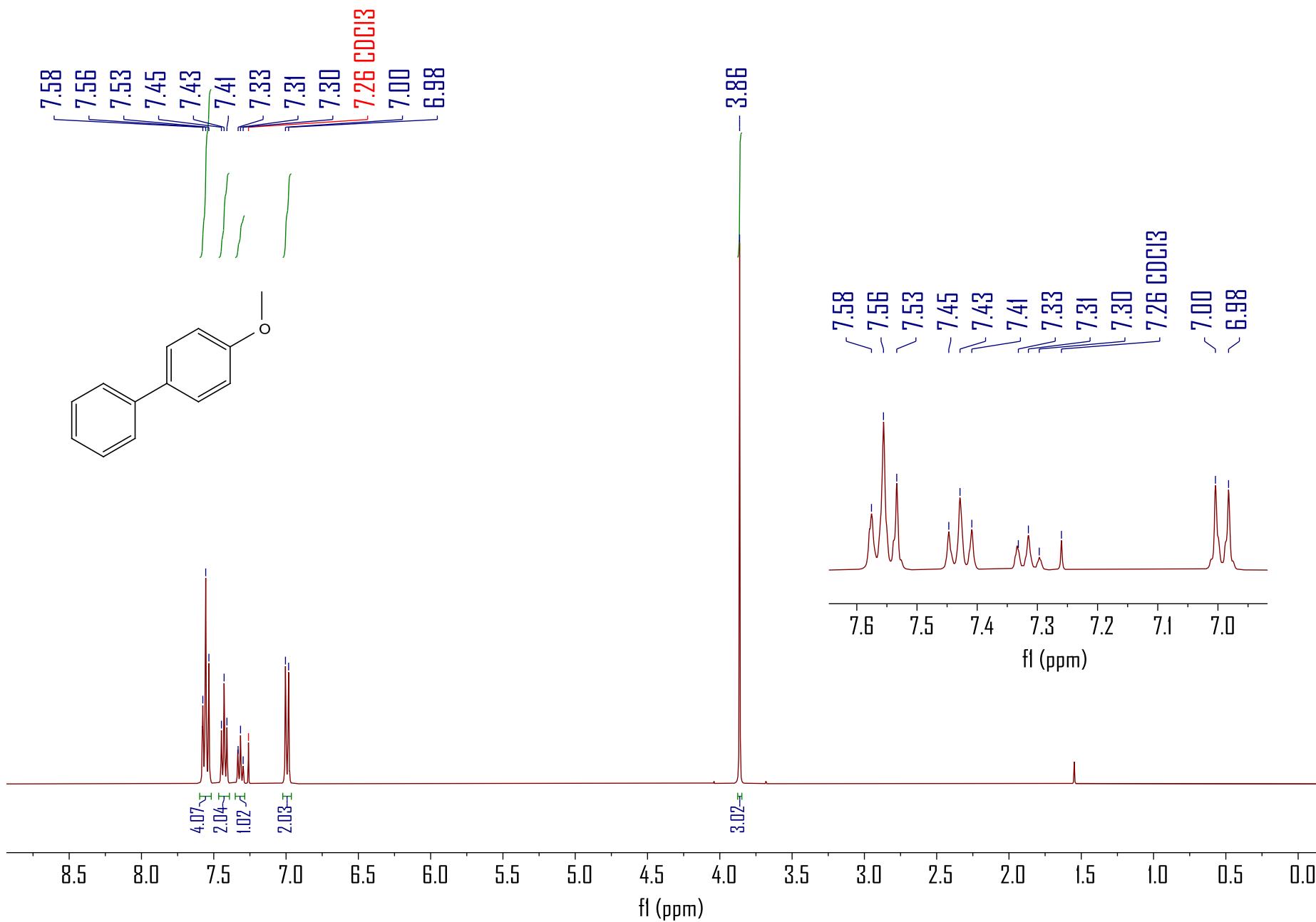
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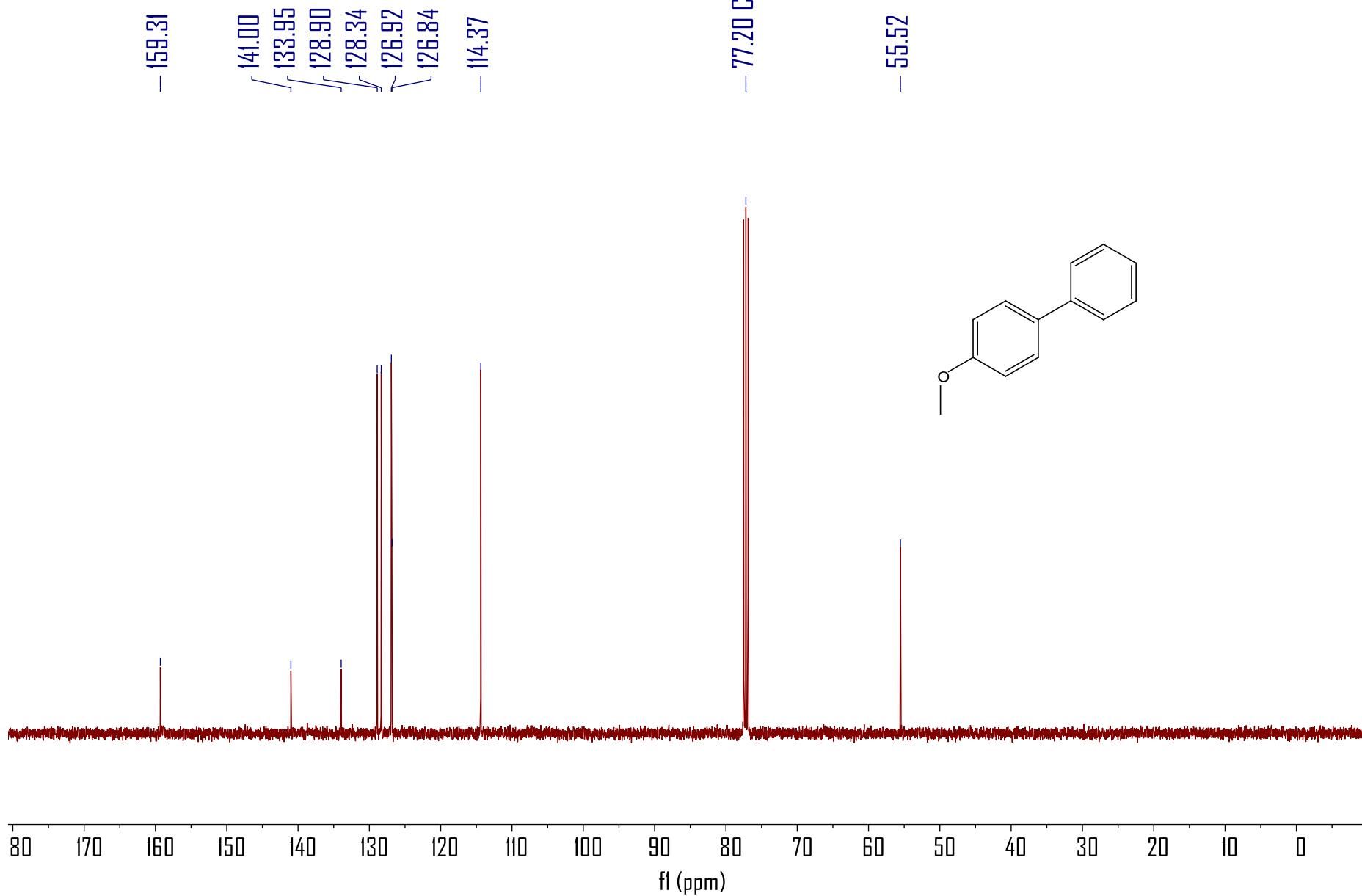
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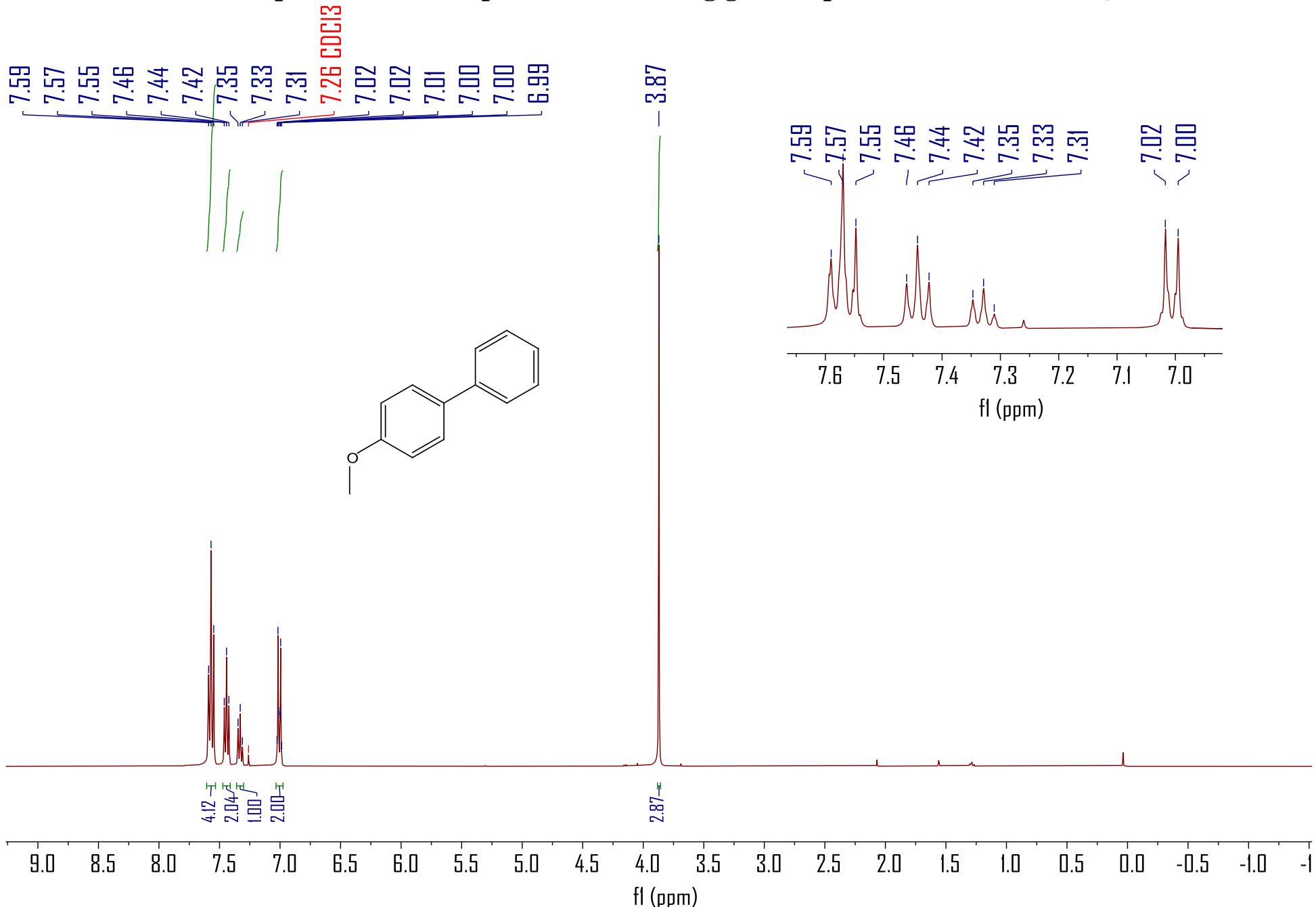
^1H NMR spectrum for compound 3a following general procedure A (400 MHz, CDCl_3)



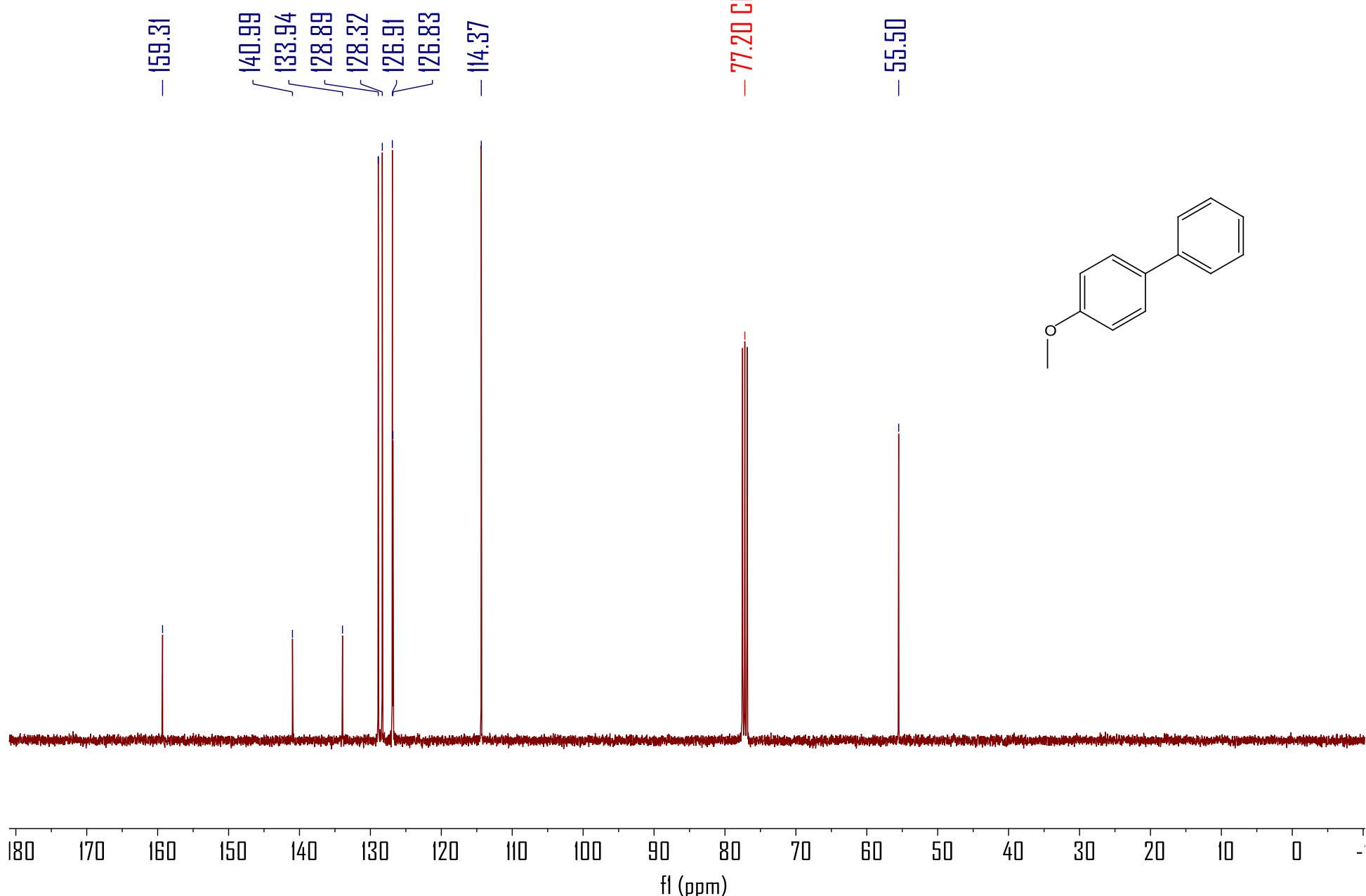
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum for compound 3a following general procedure A (100 MHz, CDCl_3)



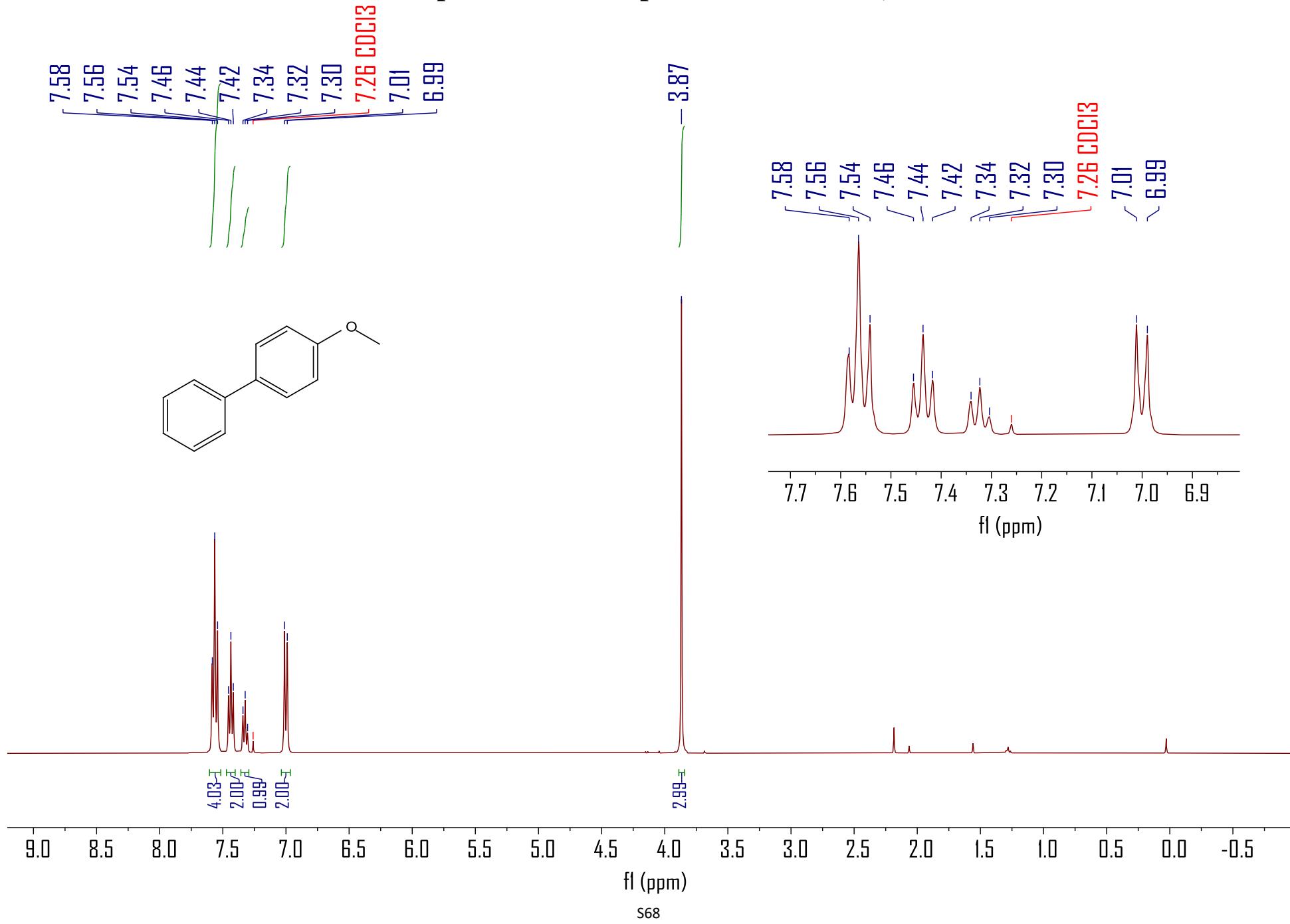
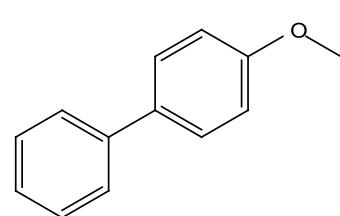
^1H NMR spectrum for compound 3a following general procedure B (400 MHz, CDCl_3)



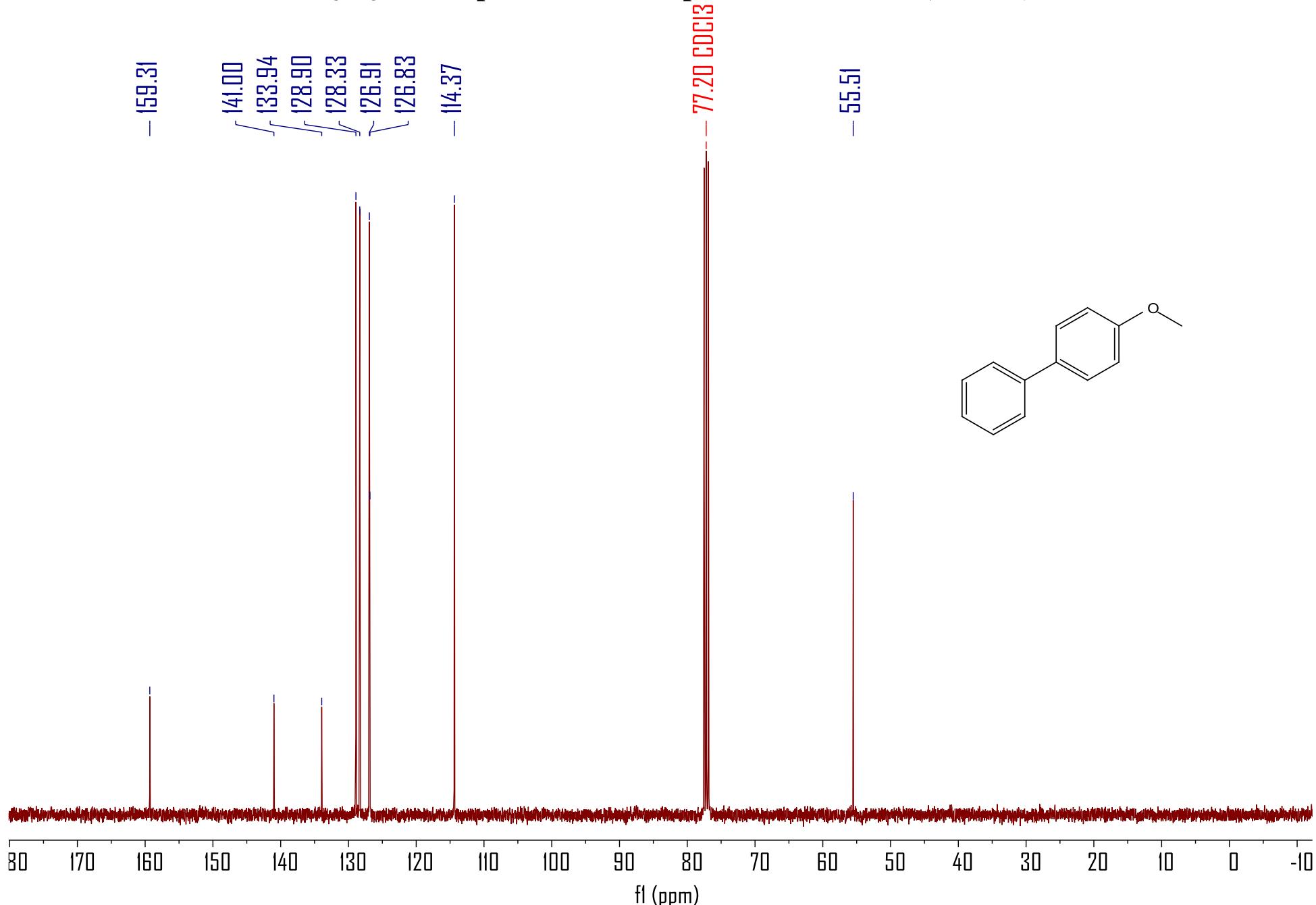
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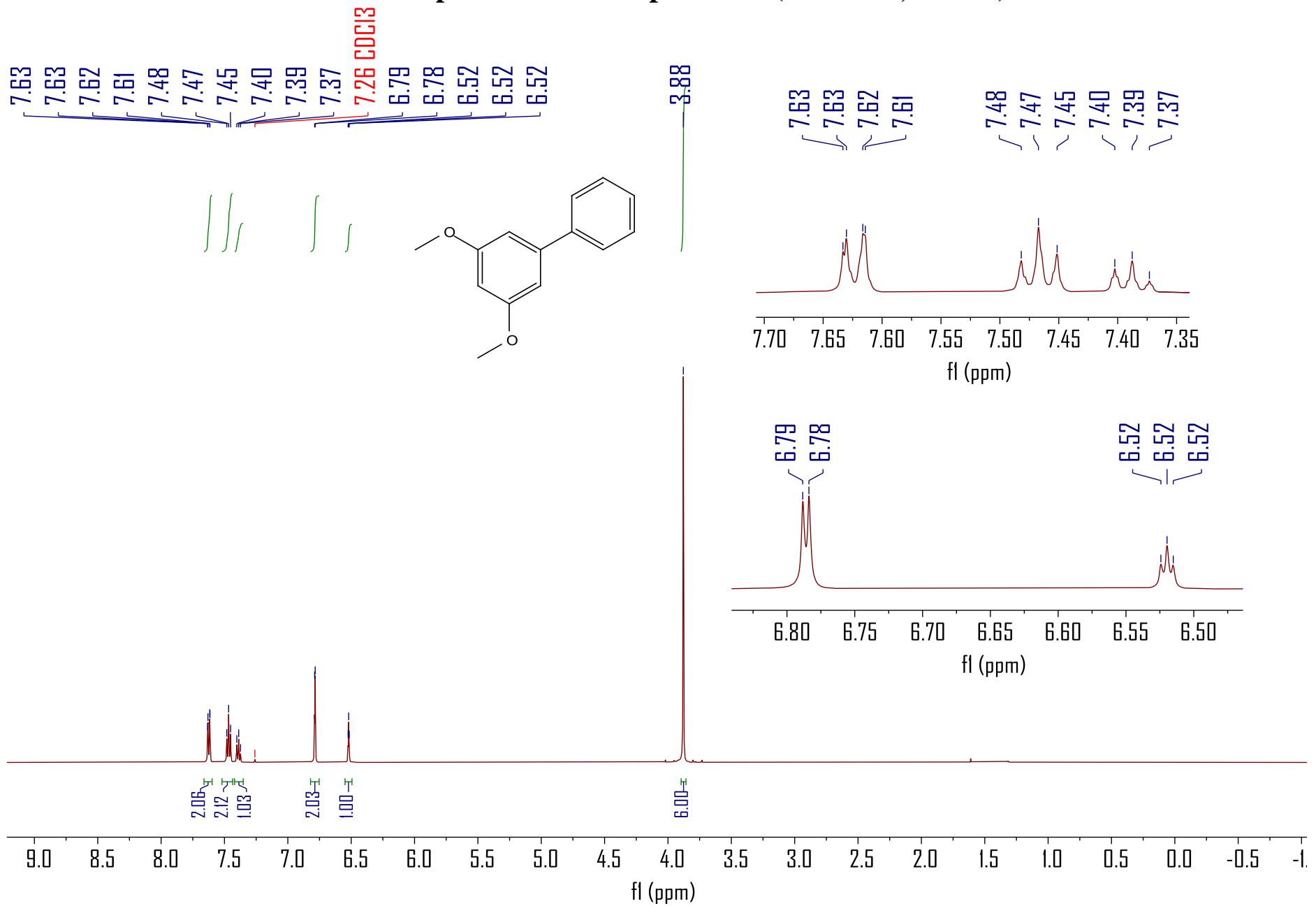
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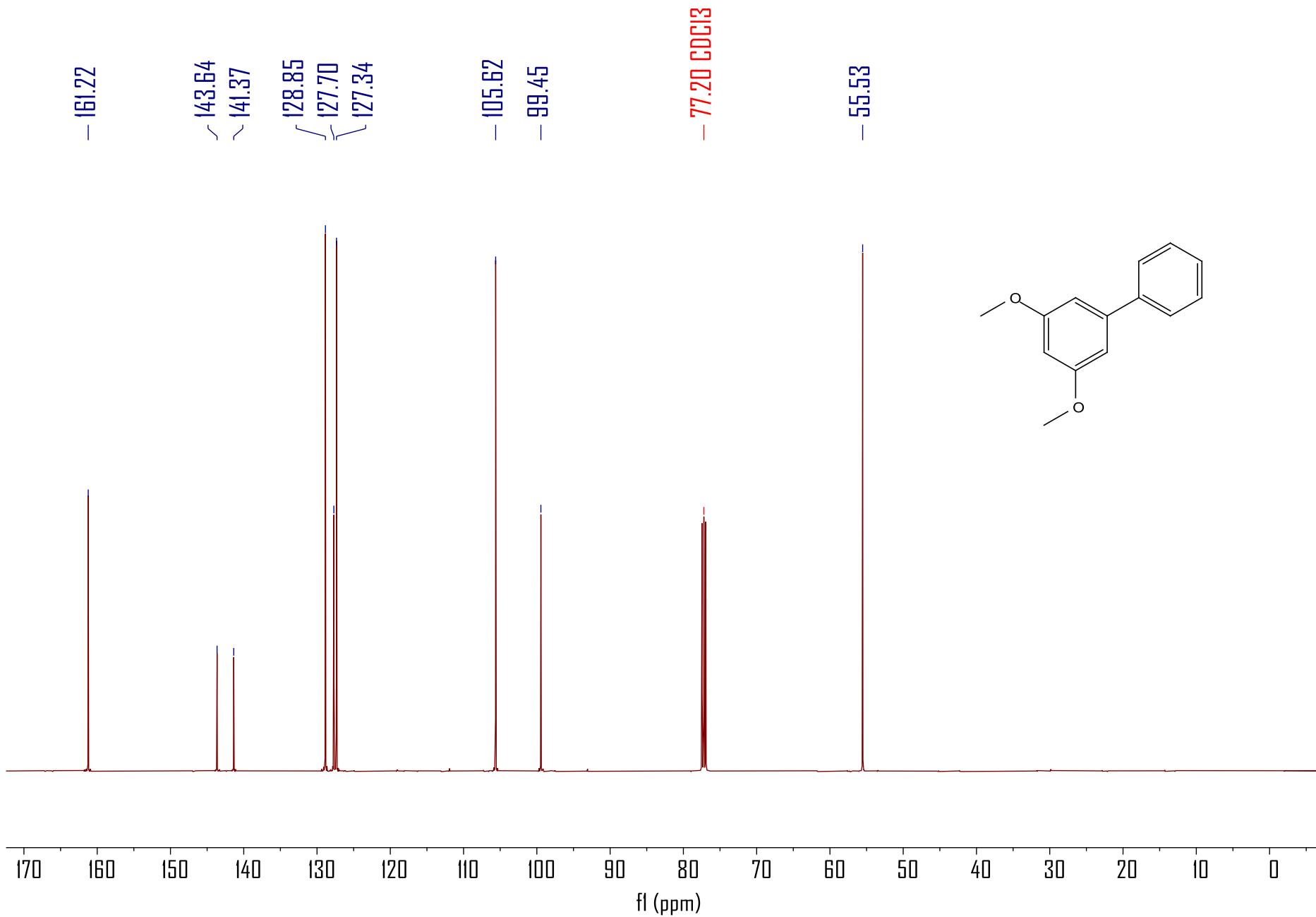
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum for compound 3b (100 MHz, CDCl_3)



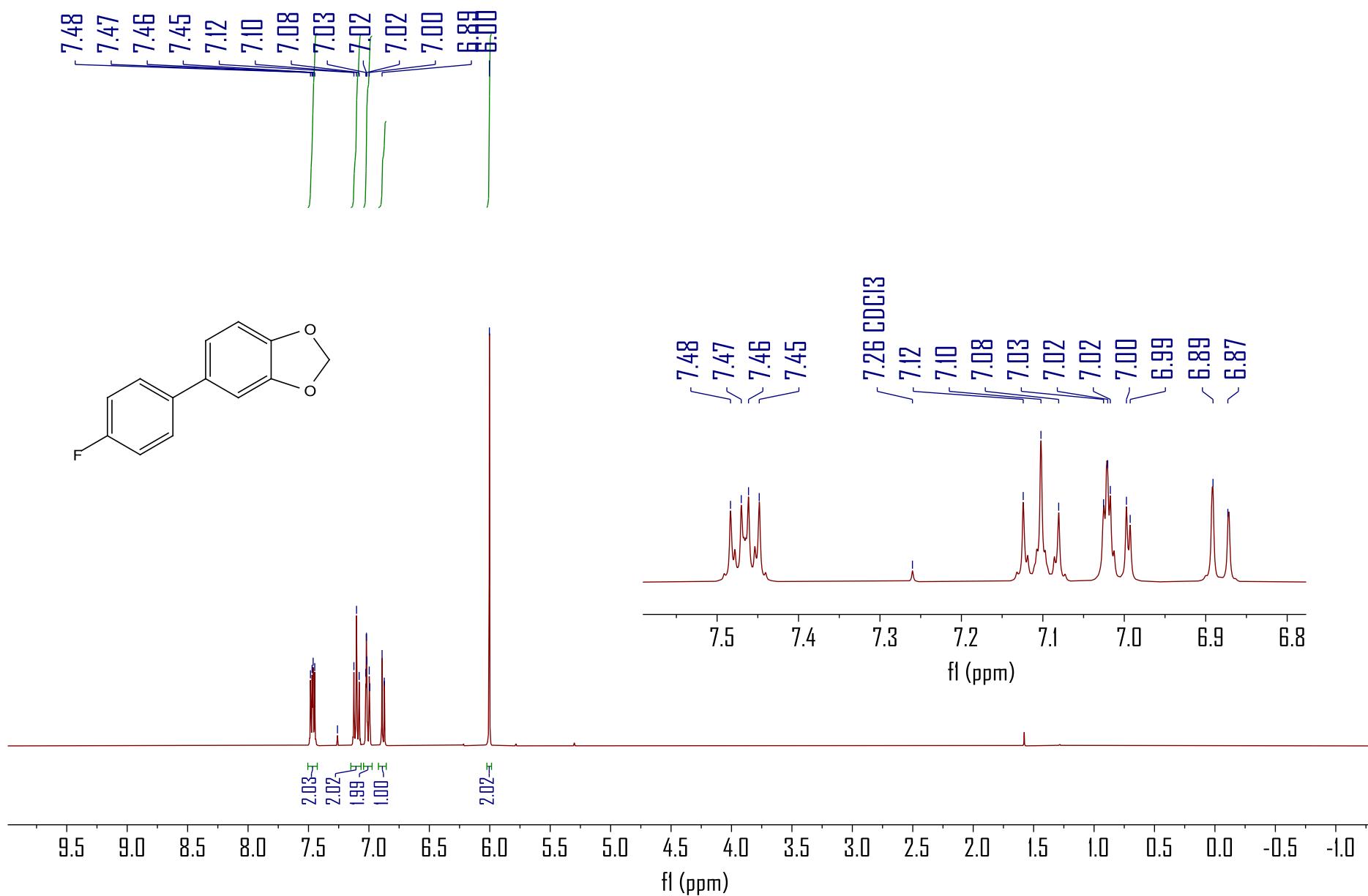
^1H NMR spectrum for compound 3c (500 MHz, CDCl_3)



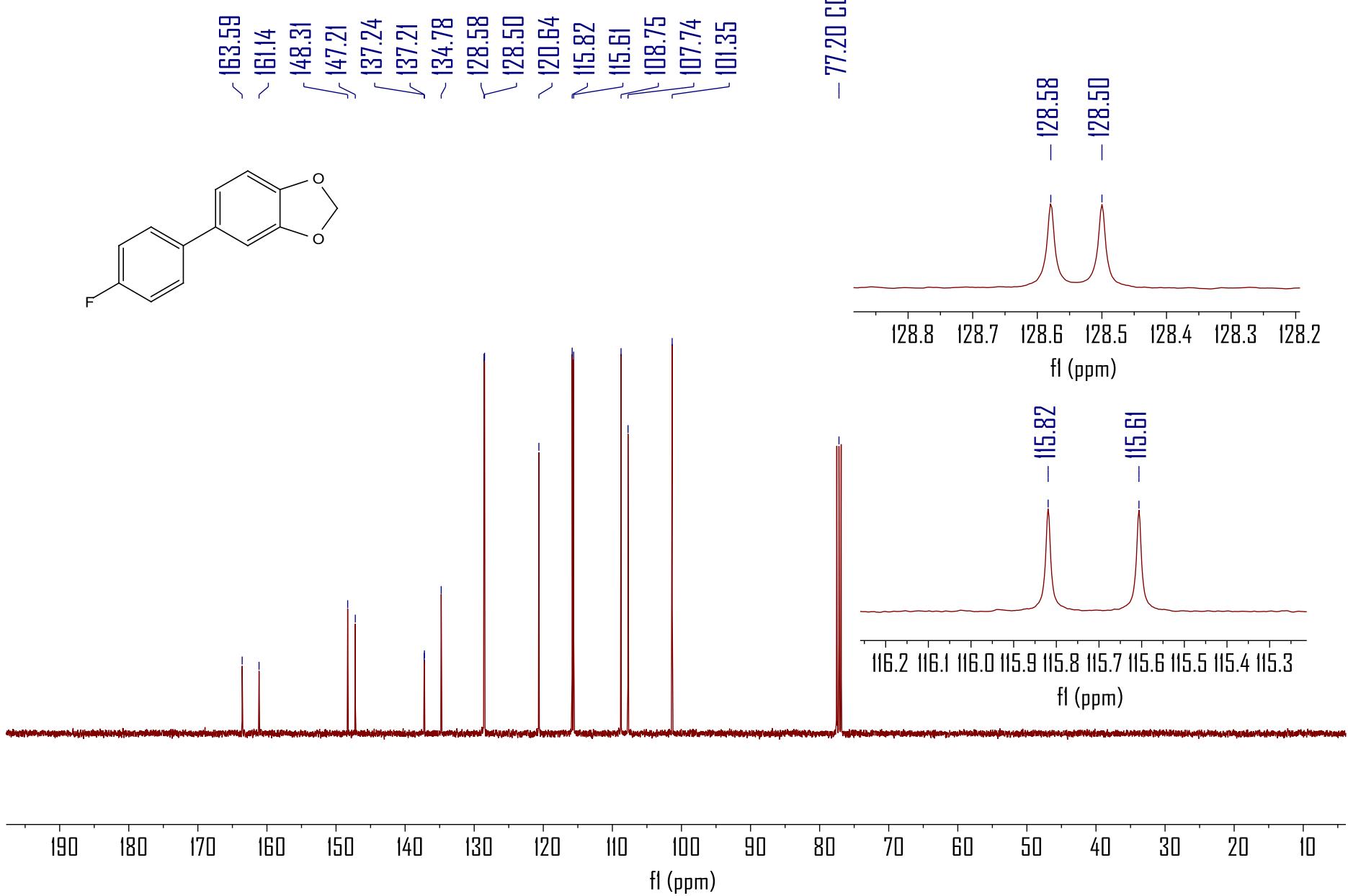
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum for compound 3c (125 MHz, CDCl_3)



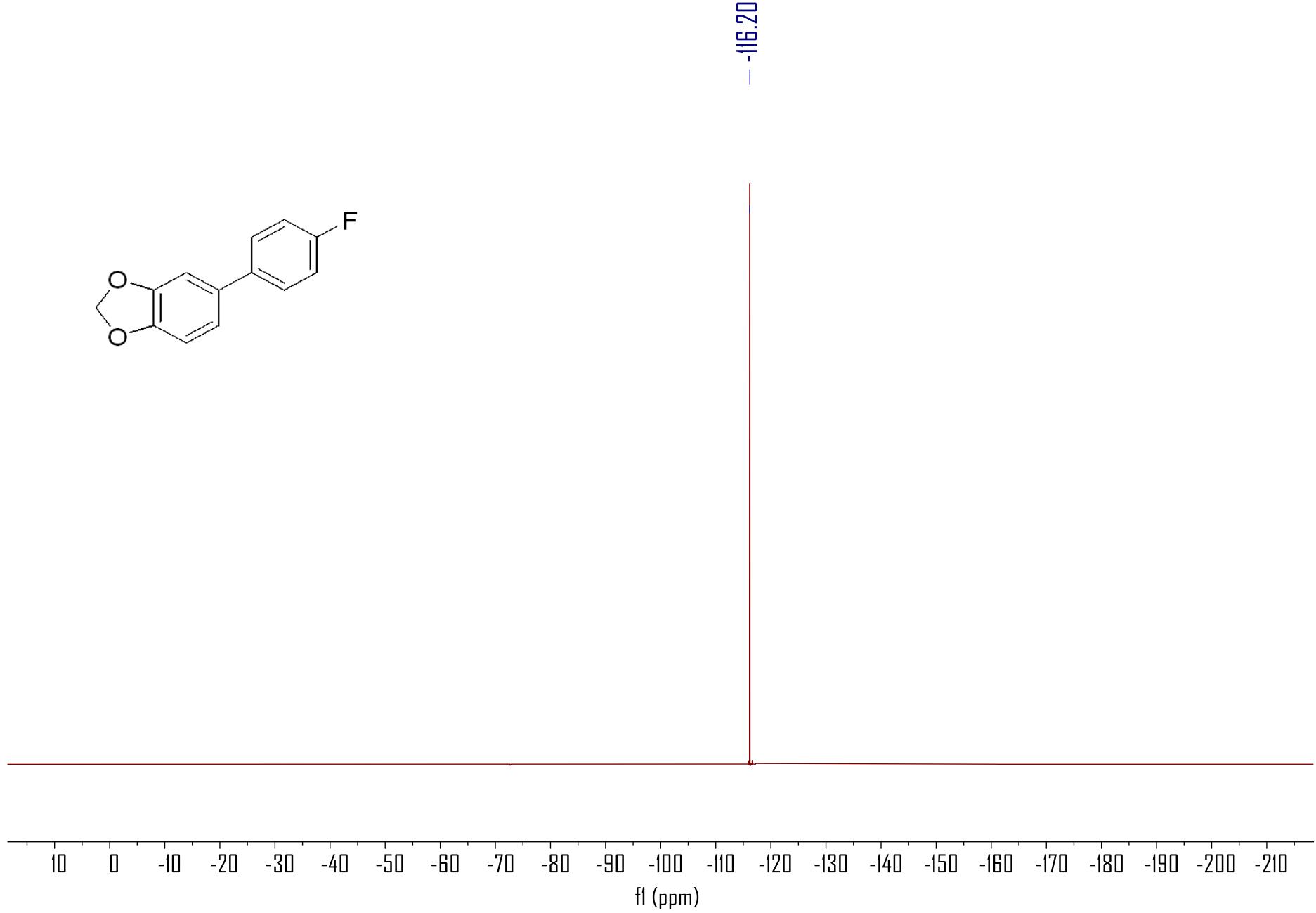
^1H NMR spectrum for compound 3d following general procedure A (400 MHz, CDCl_3)



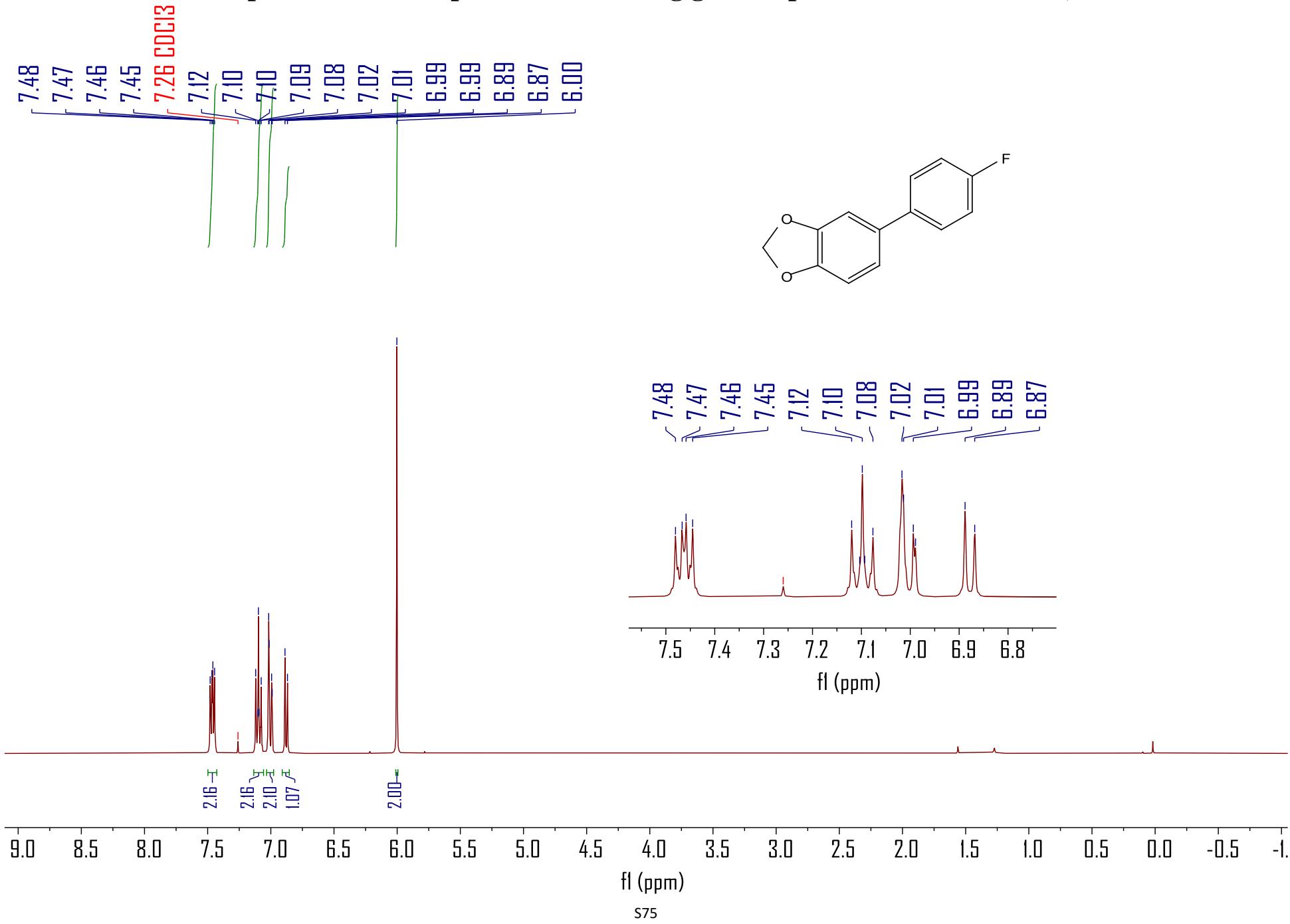
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum for compound 3d following general procedure A (100 MHz, CDCl_3)



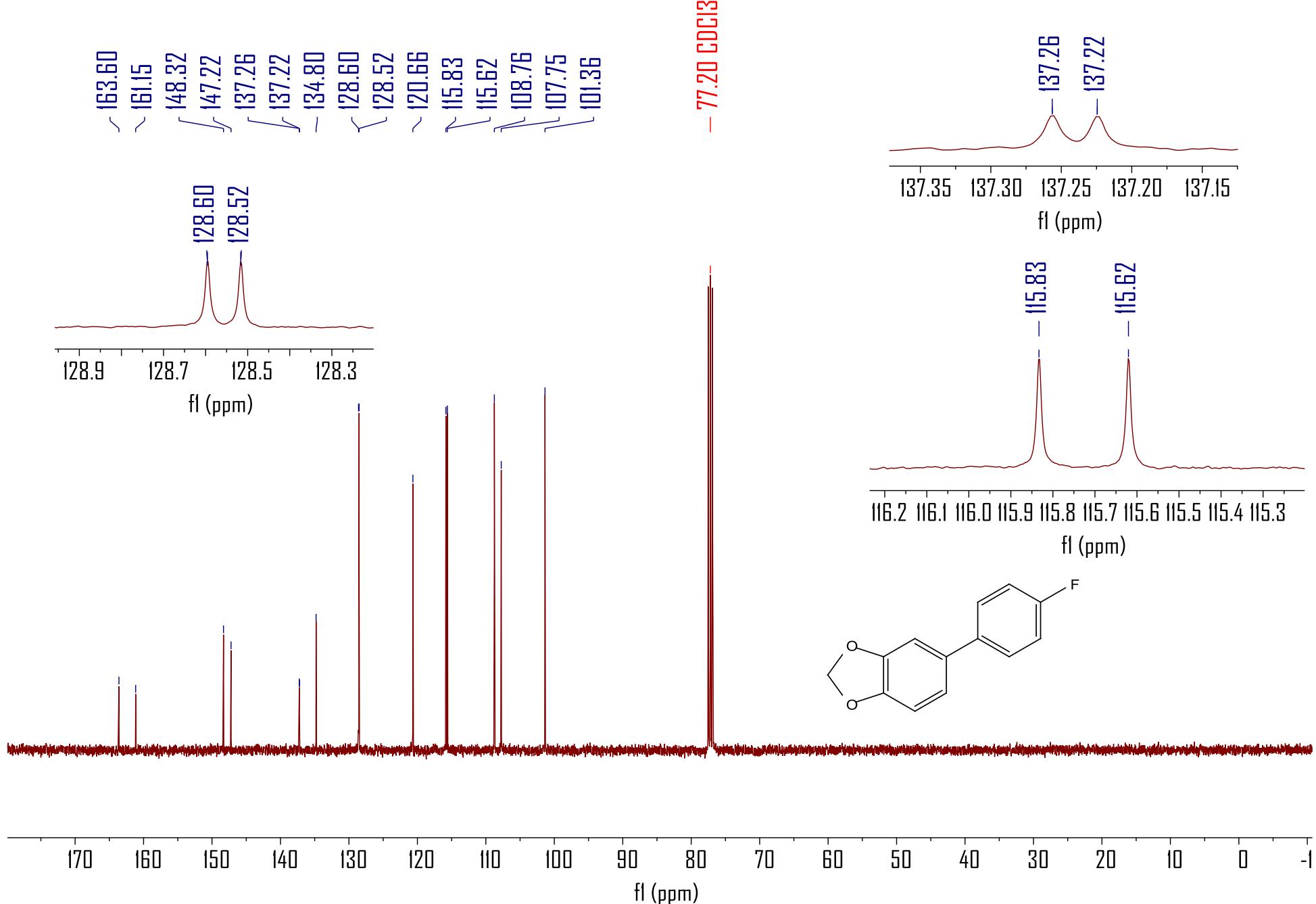
$^{19}\text{F}\{^1\text{H}\}$ NMR spectrum for compound 3d following general procedure A (376 MHz, CDCl_3)



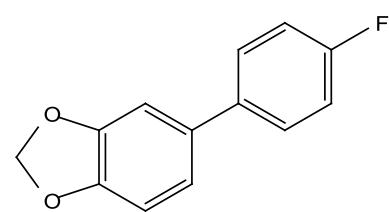
^1H NMR spectrum for compound 3d following general procedure B (400 MHz, CDCl_3)



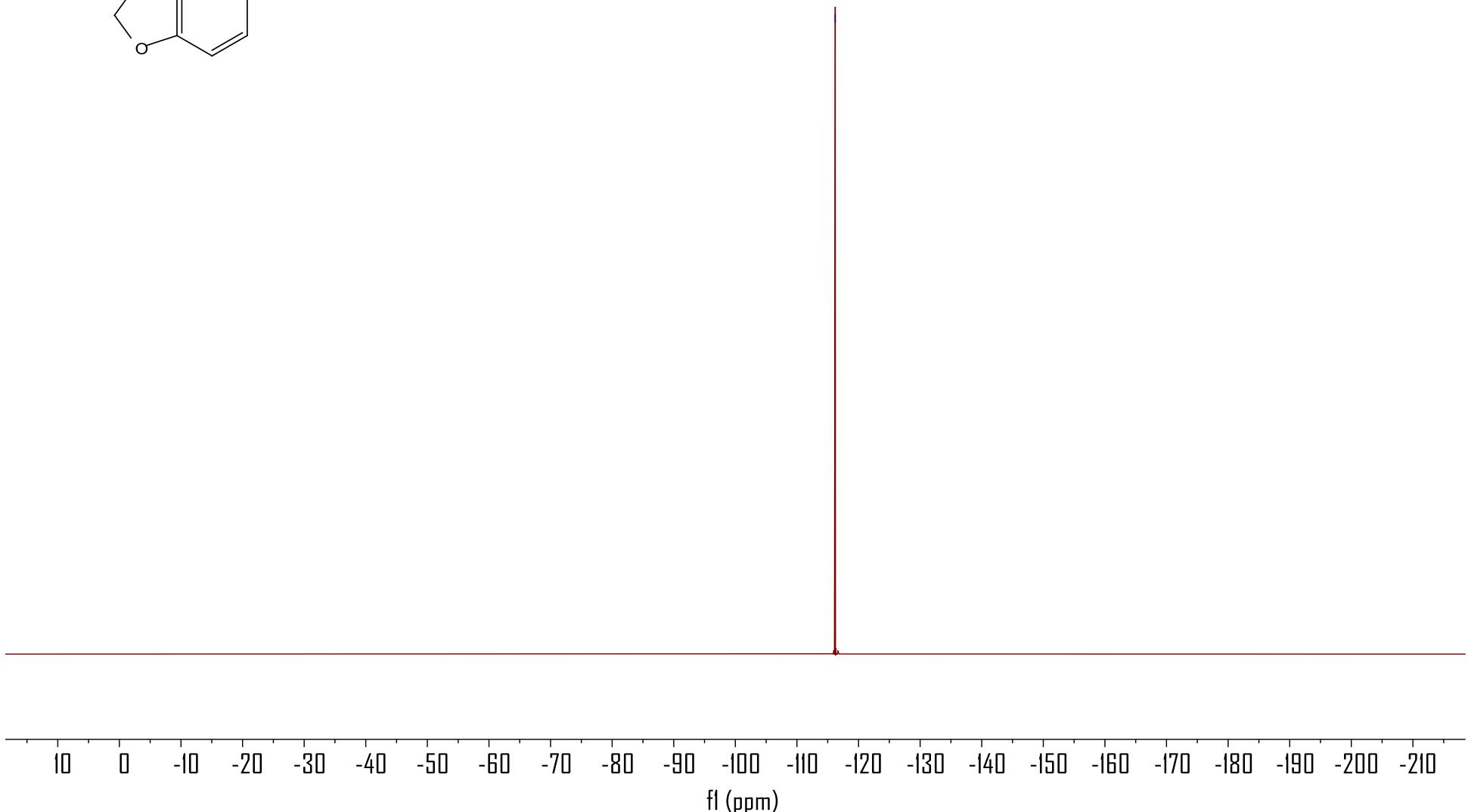
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum for compound 3d following general procedure B (100 MHz, CDCl_3)



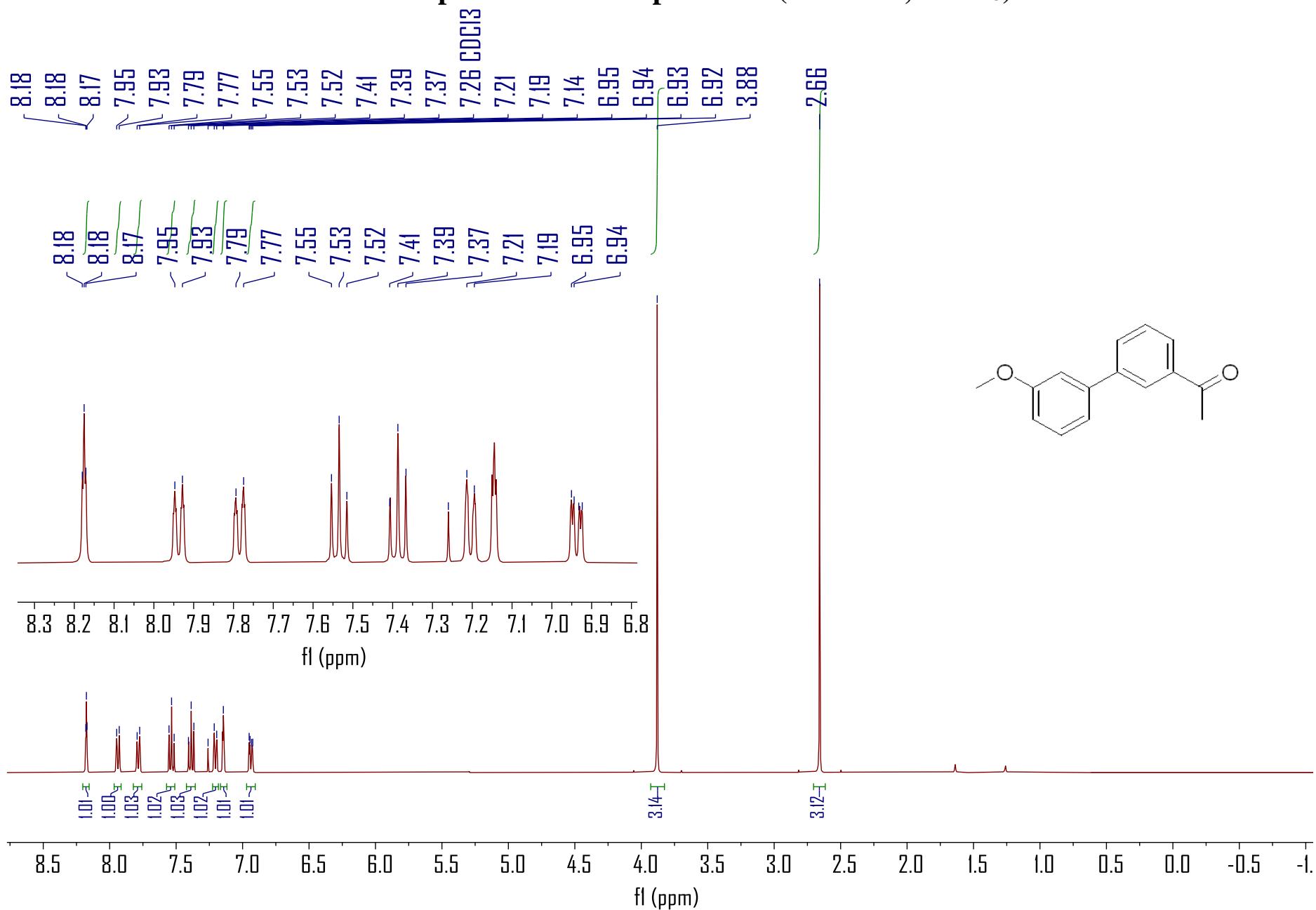
$^{19}\text{F}\{^1\text{H}\}$ NMR spectrum for compound 3d following general procedure B (376 MHz, CDCl_3)



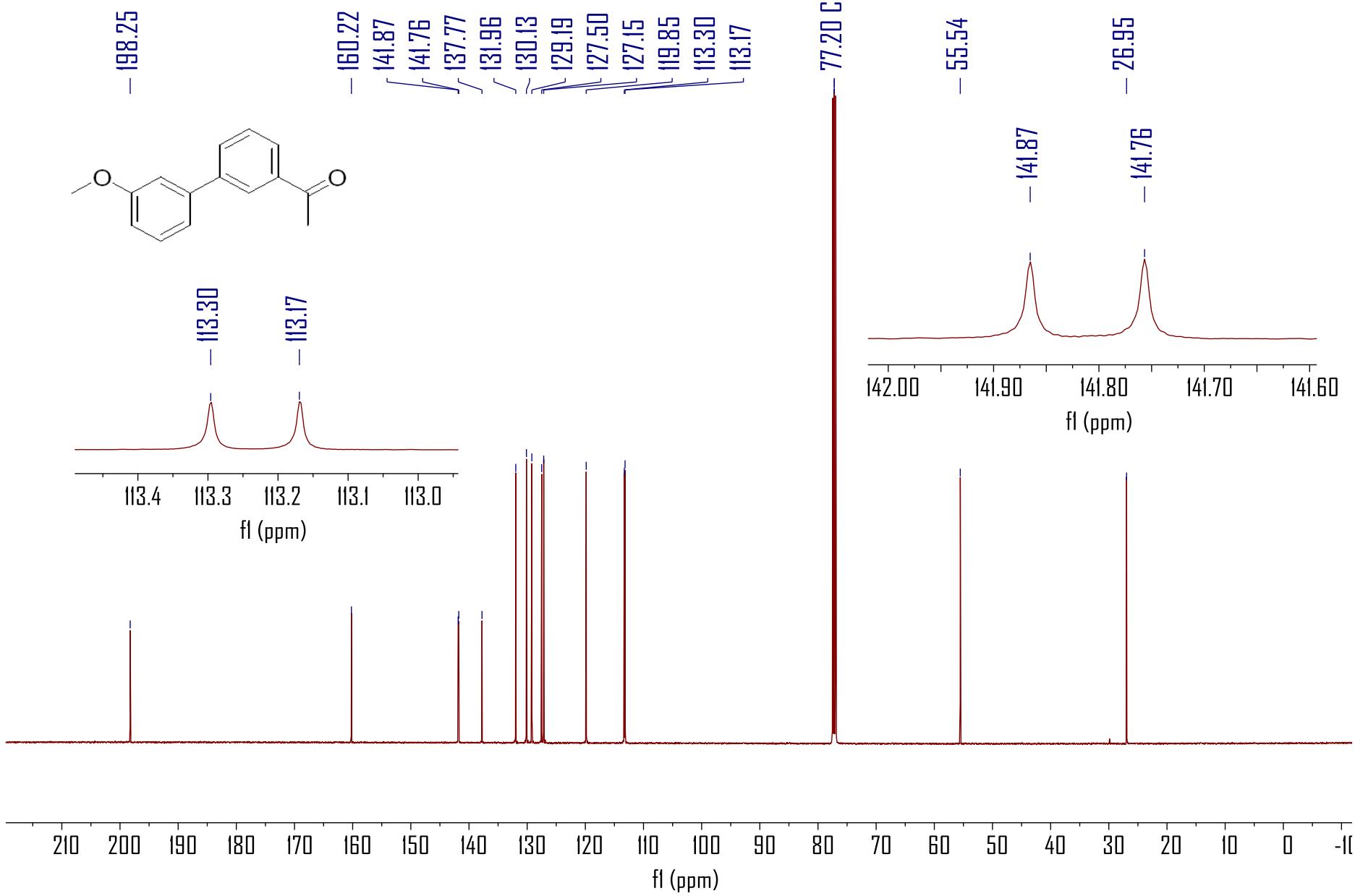
-116.22



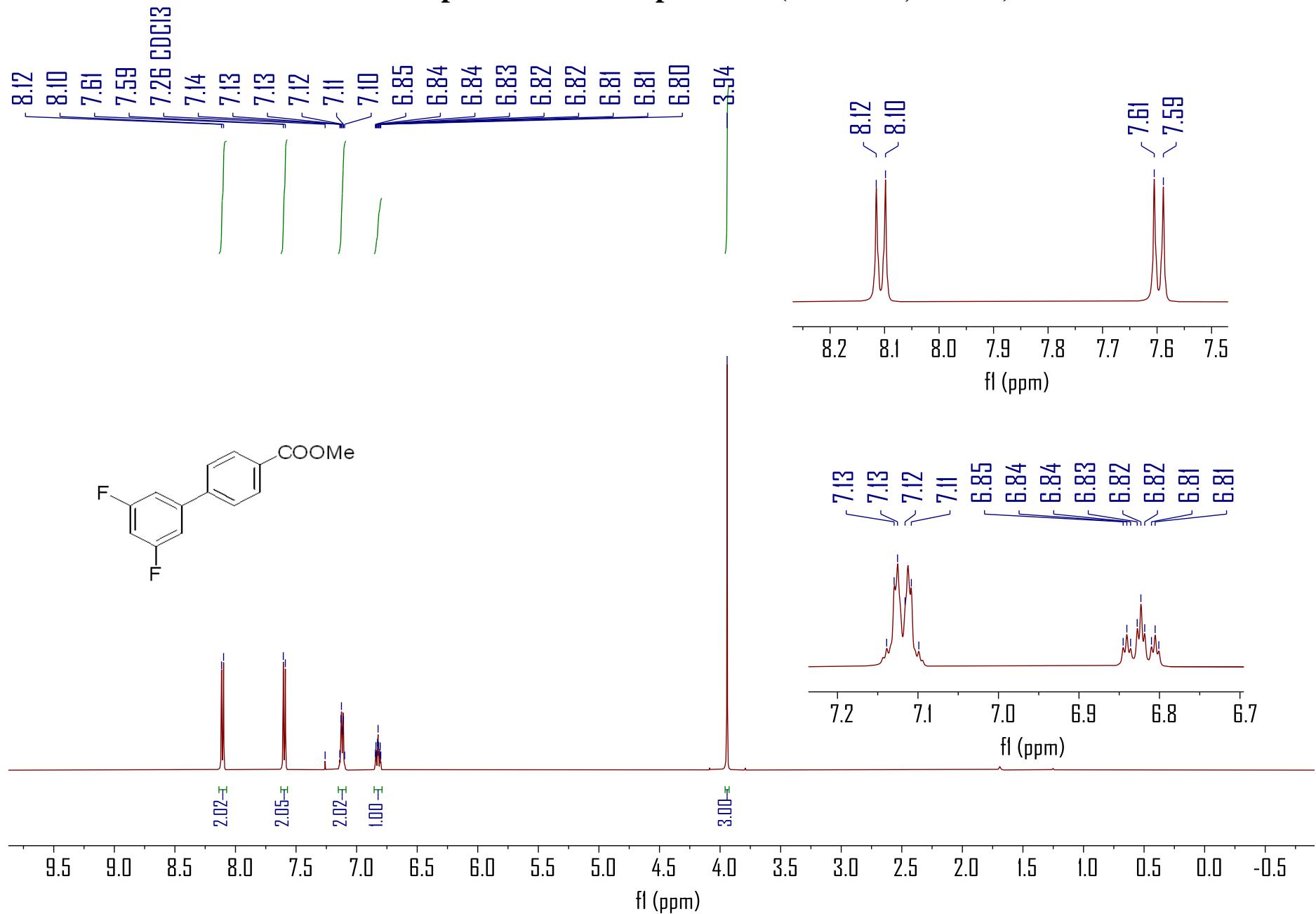
¹H NMR spectrum for compound 3e (400 MHz, CDCl₃)



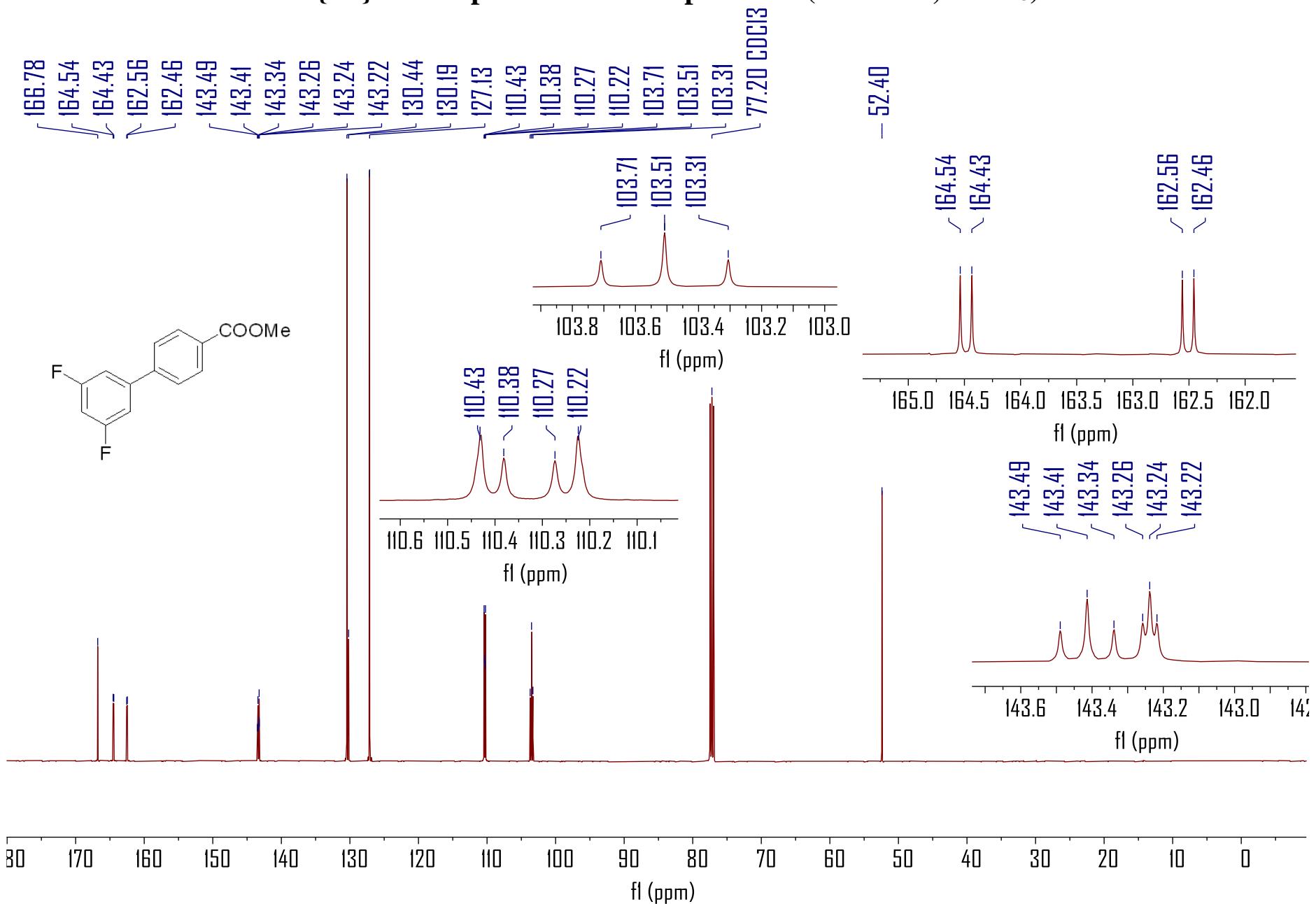
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum for compound 3e (125 MHz, CDCl_3)



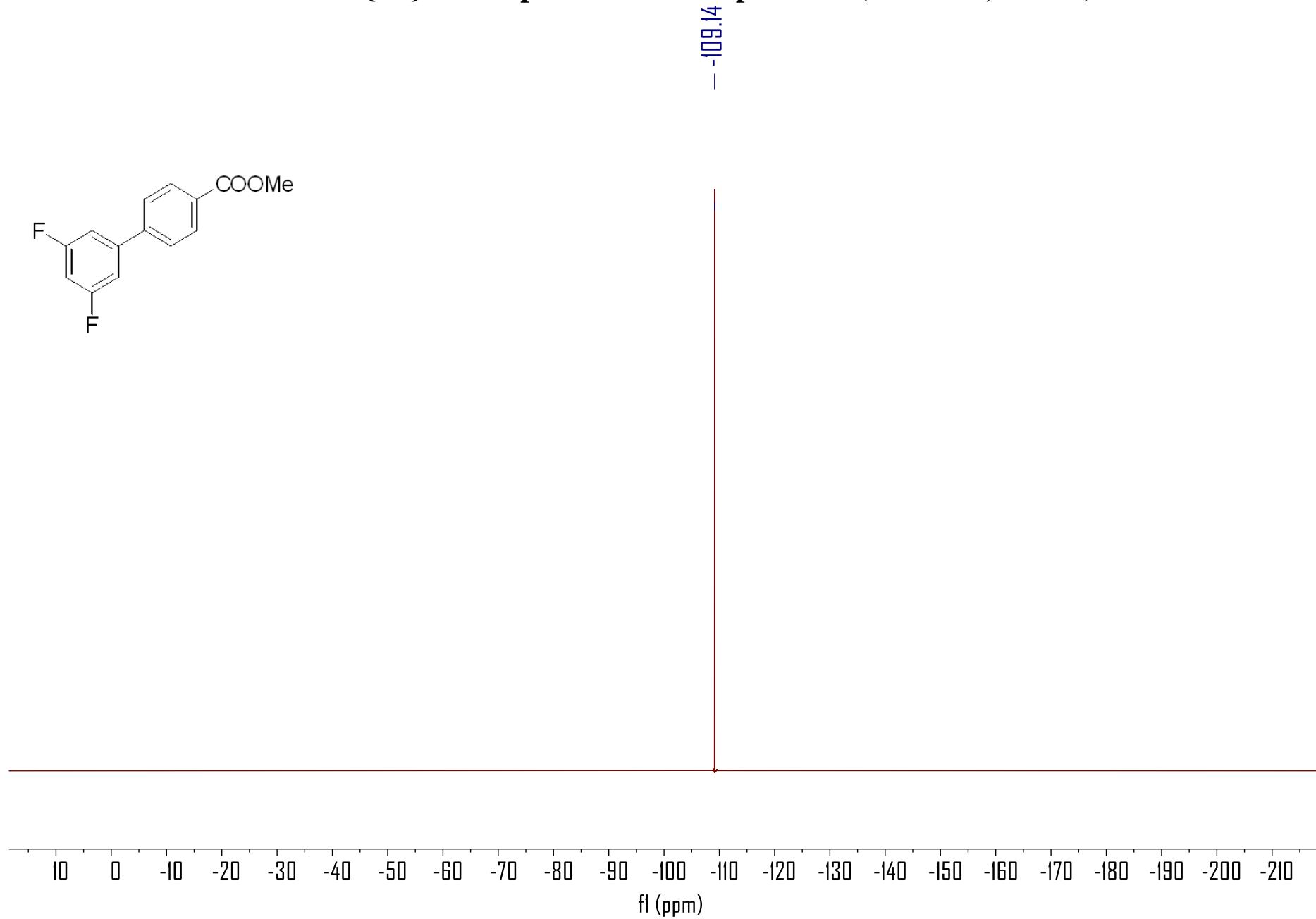
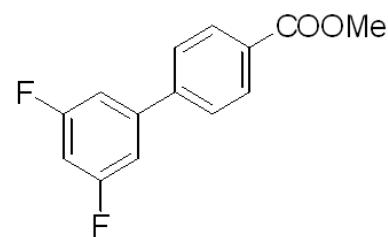
¹H NMR spectrum for compound 3f (500 MHz, CDCl₃)



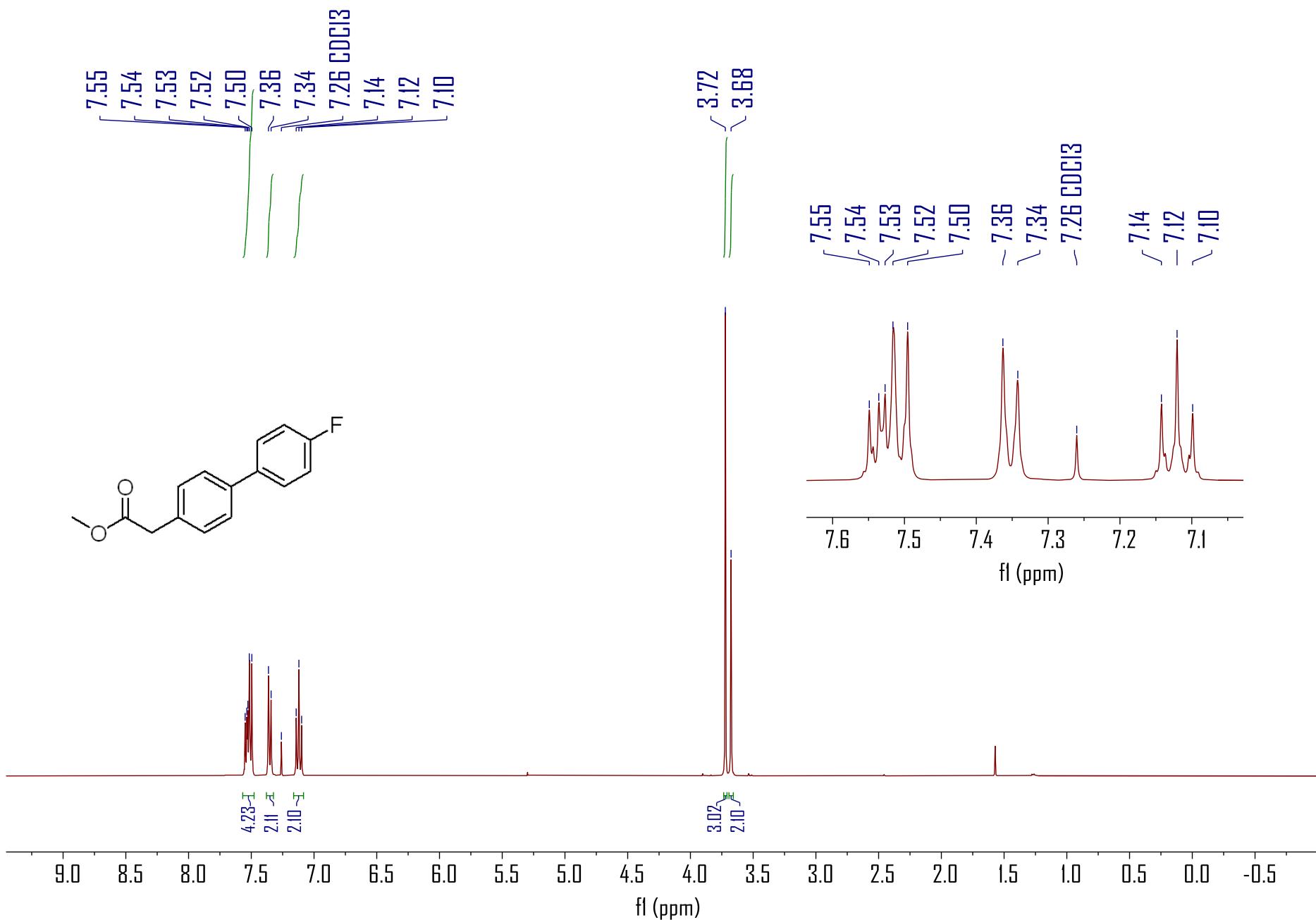
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum for compound 3f (125 MHz, CDCl_3)



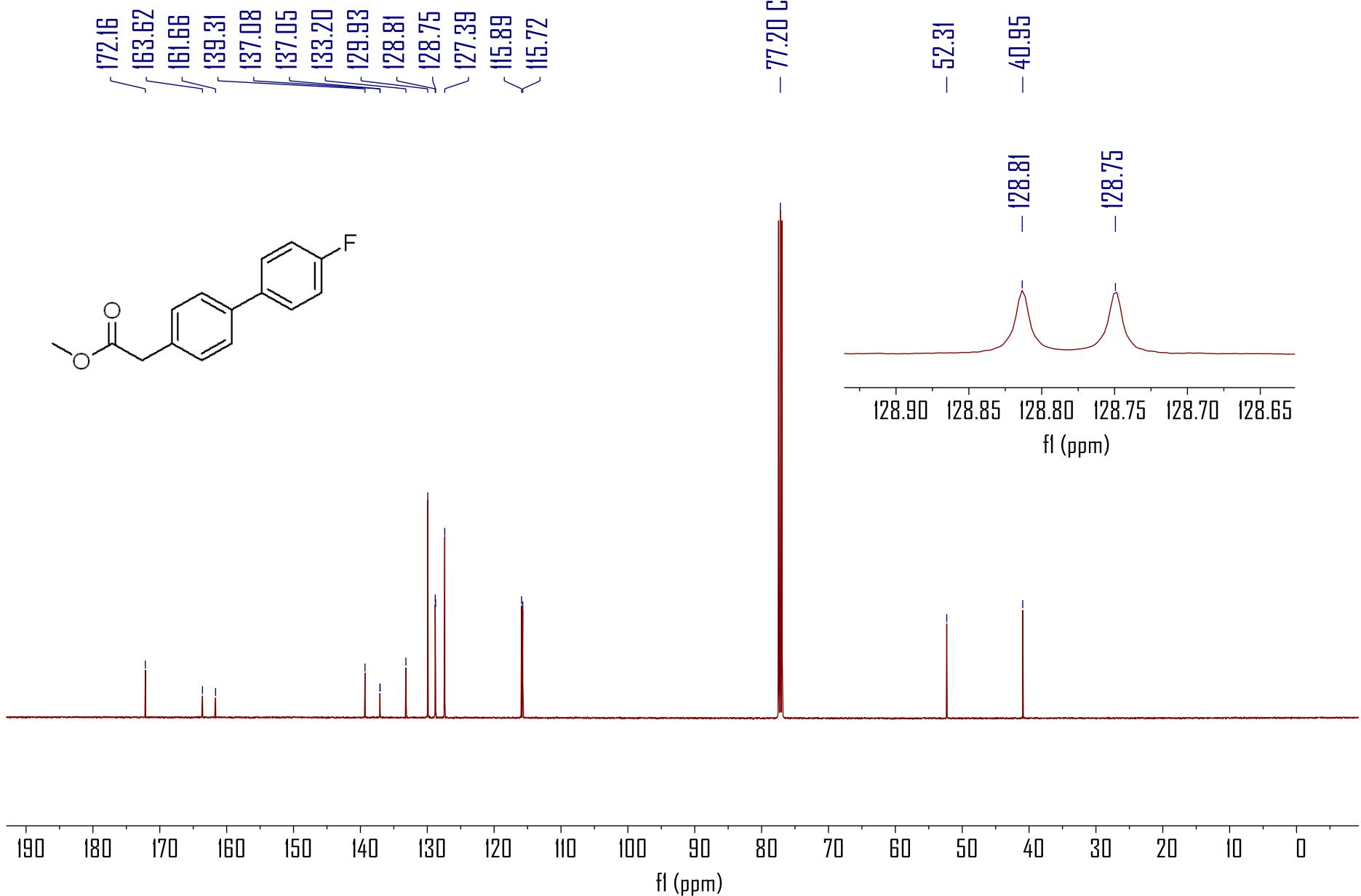
$^{19}\text{F}\{^1\text{H}\}$ NMR spectrum for compound 3f (376 MHz, CDCl_3)



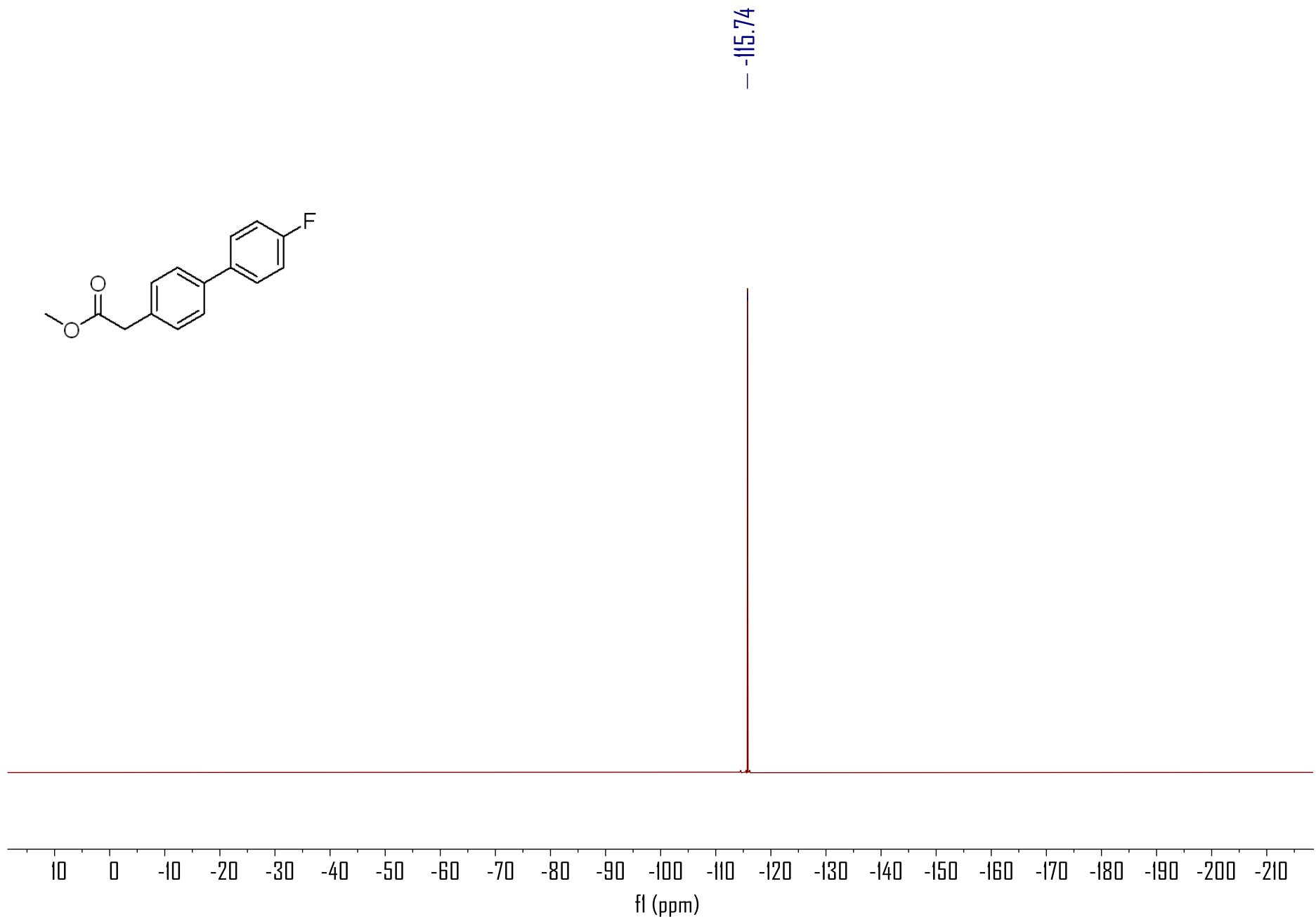
^1H NMR spectrum for compound 3g (400 MHz, CDCl_3)



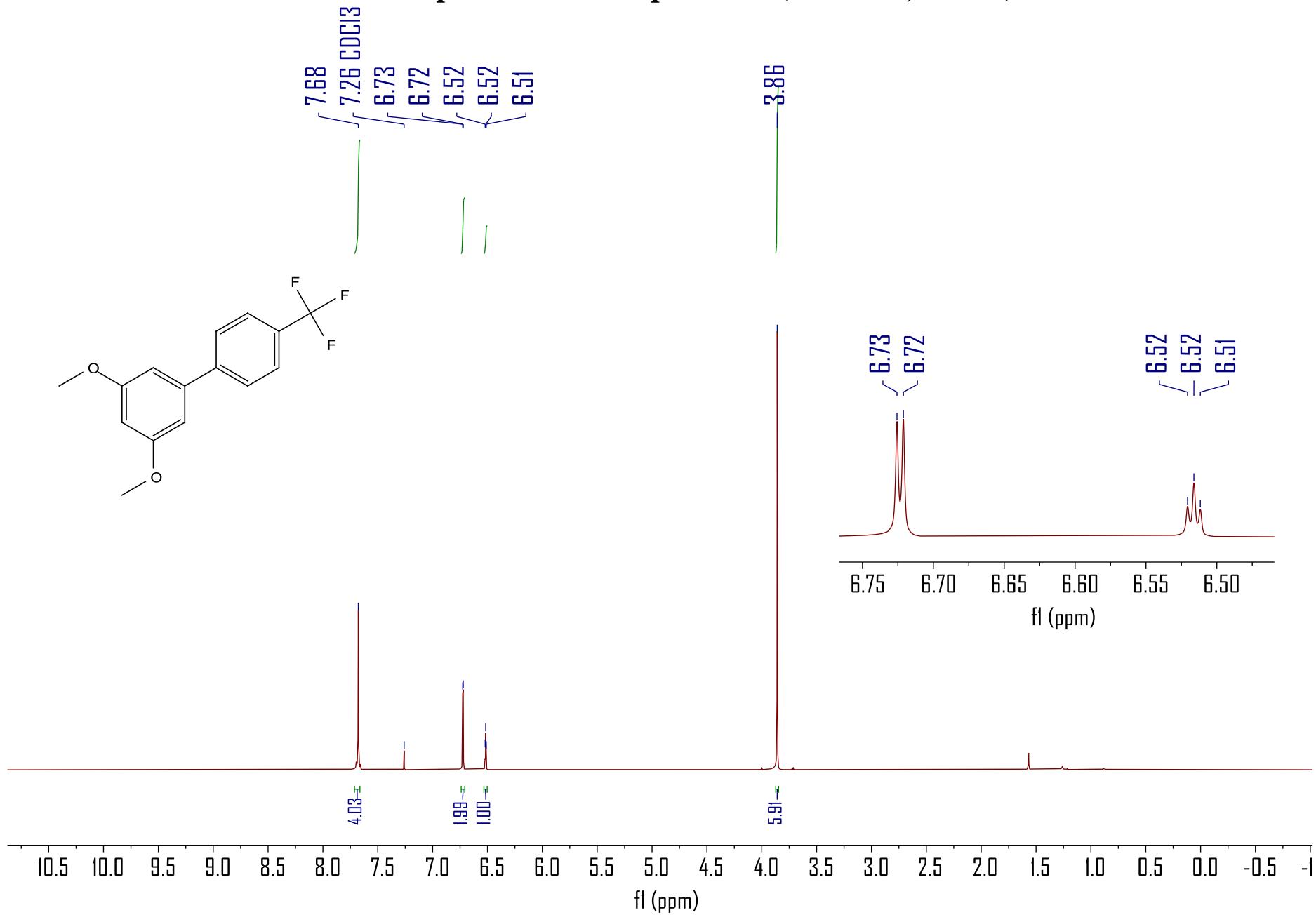
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum for compound 3g (125 MHz, CDCl_3)



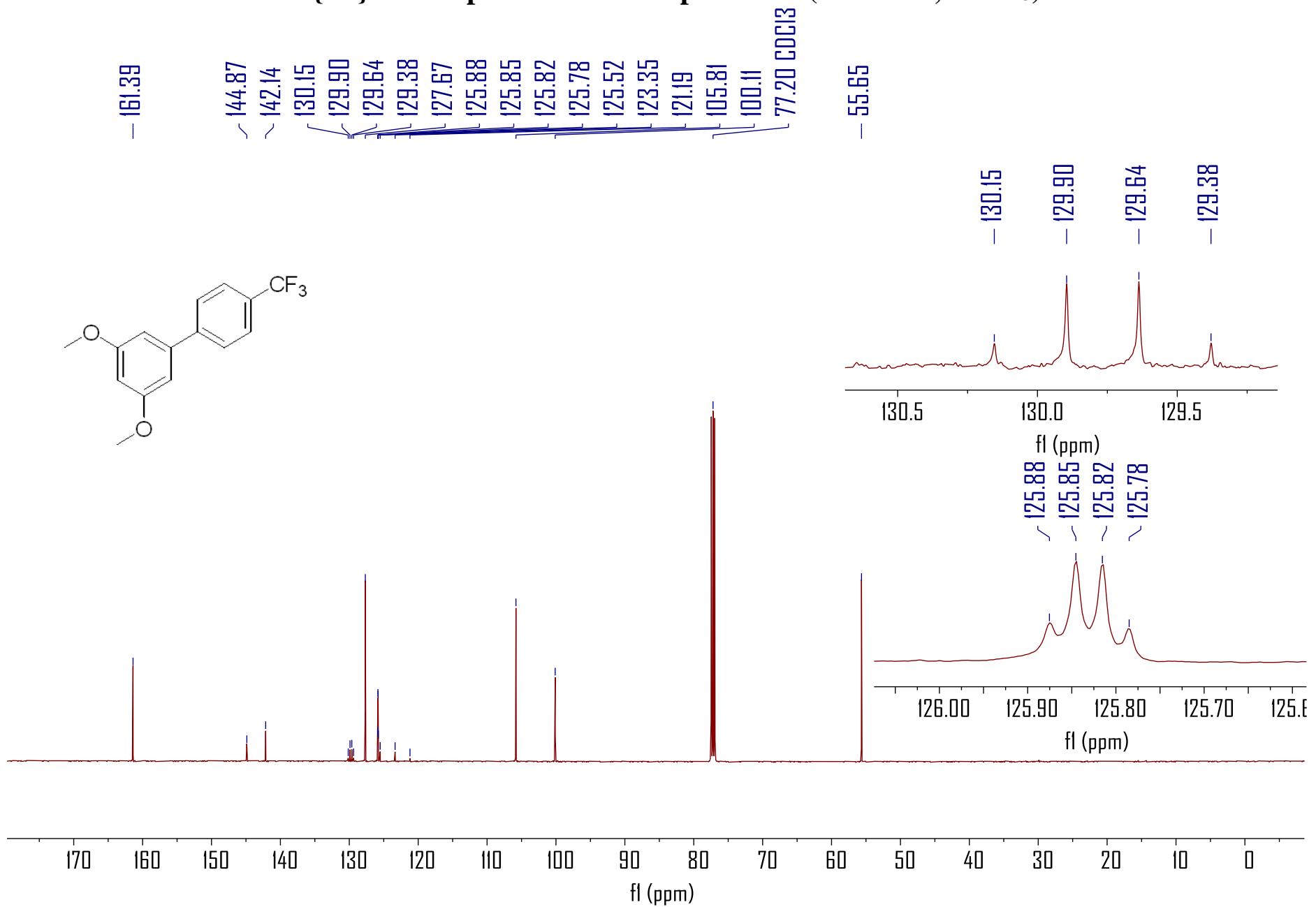
$^{19}\text{F}\{^1\text{H}\}$ NMR spectrum for compound 3g (376 MHz, CDCl_3)



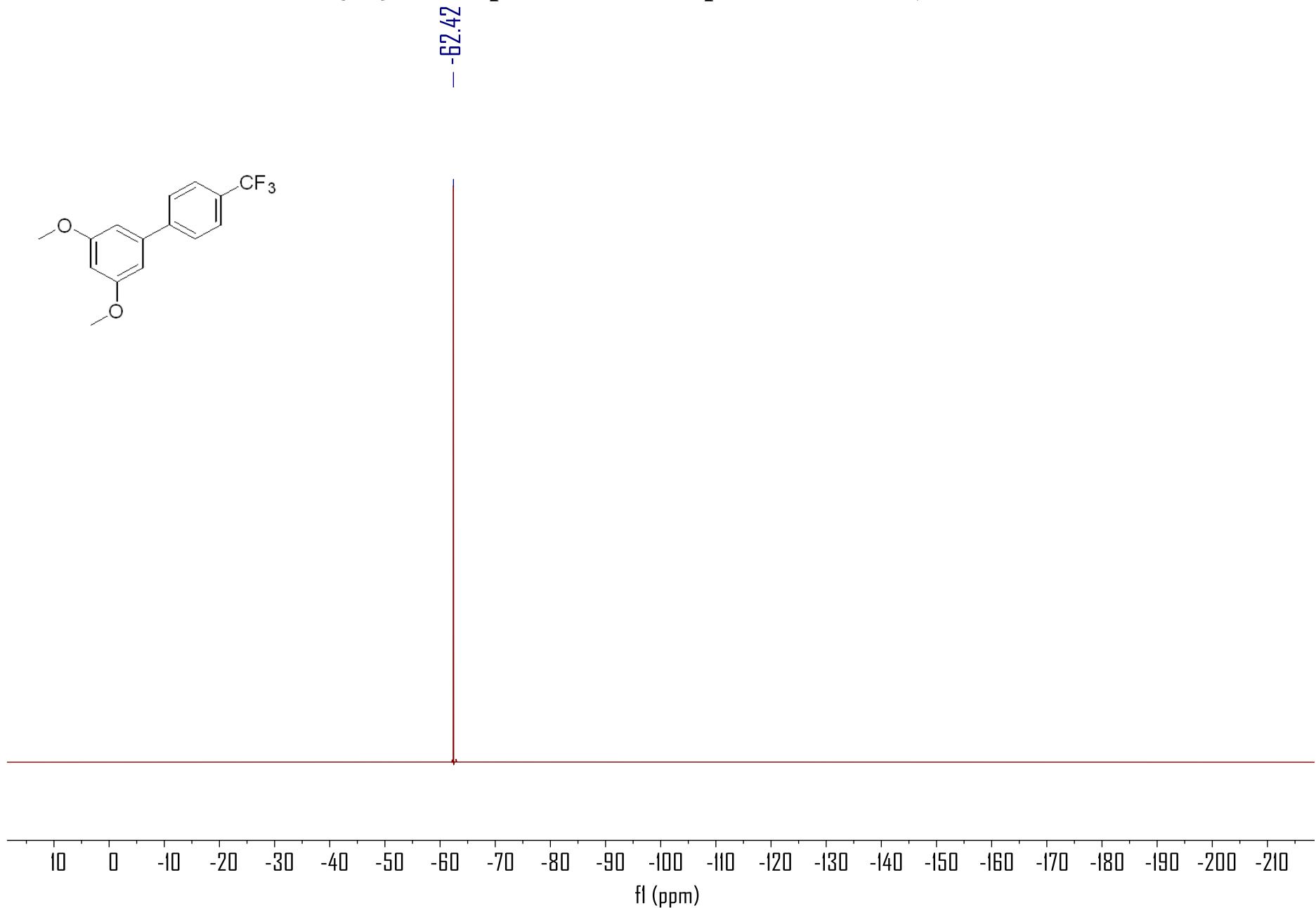
¹H NMR spectrum for compound 3h (500 MHz, CDCl₃)



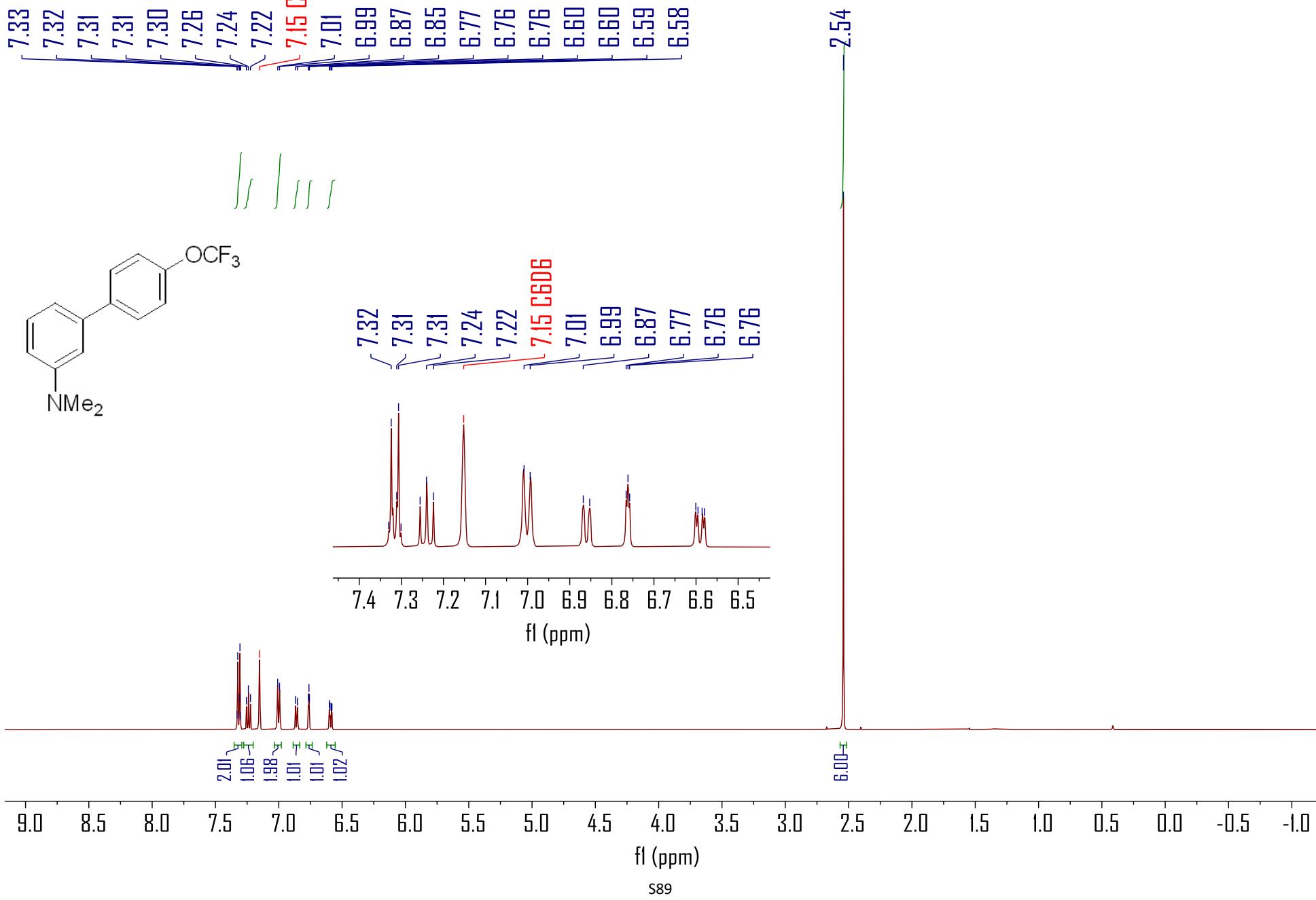
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum for compound 3h (125 MHz, CDCl_3)



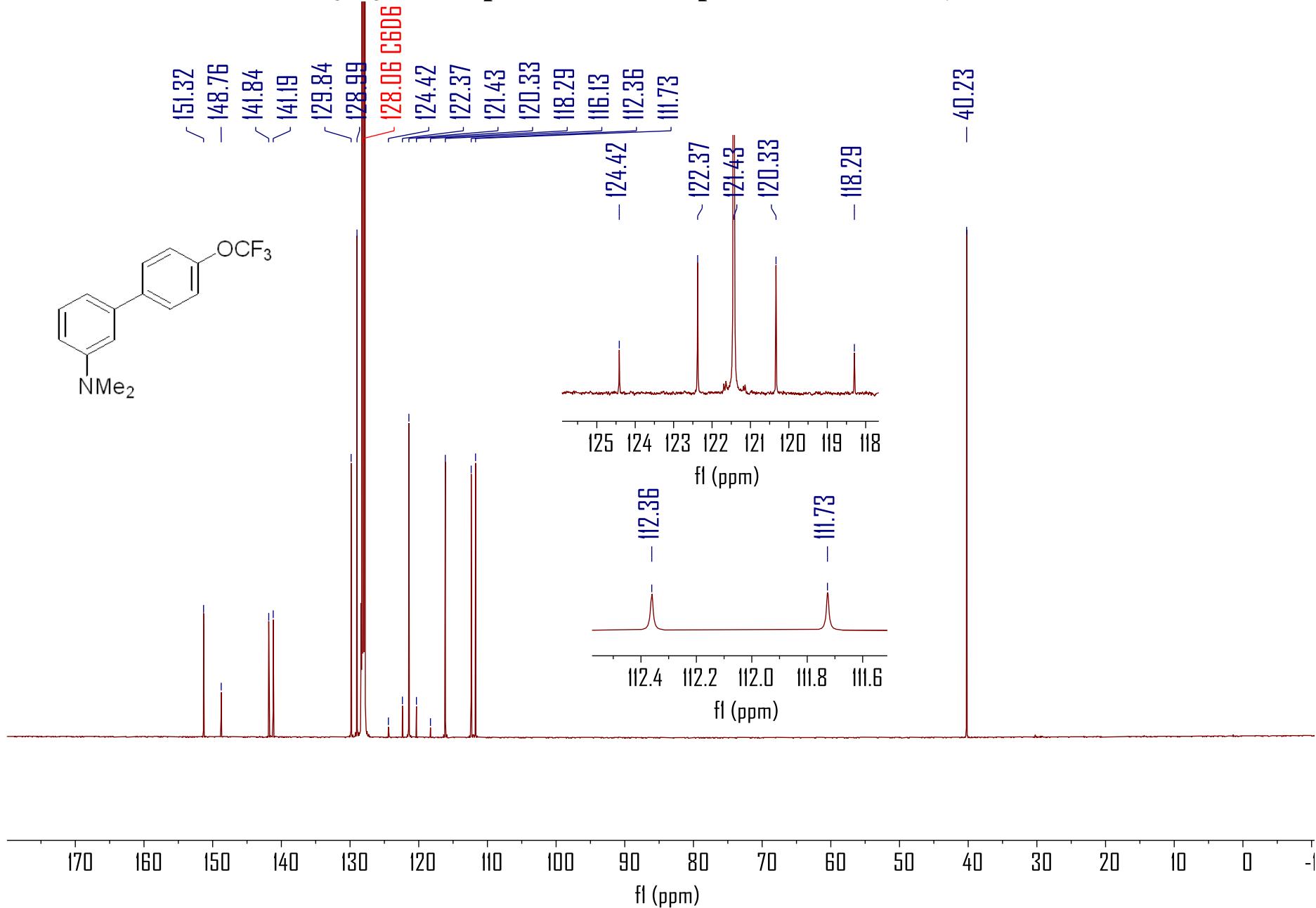
$^{19}\text{F}\{^1\text{H}\}$ NMR spectrum for compound 3h (376M, CDCl_3)



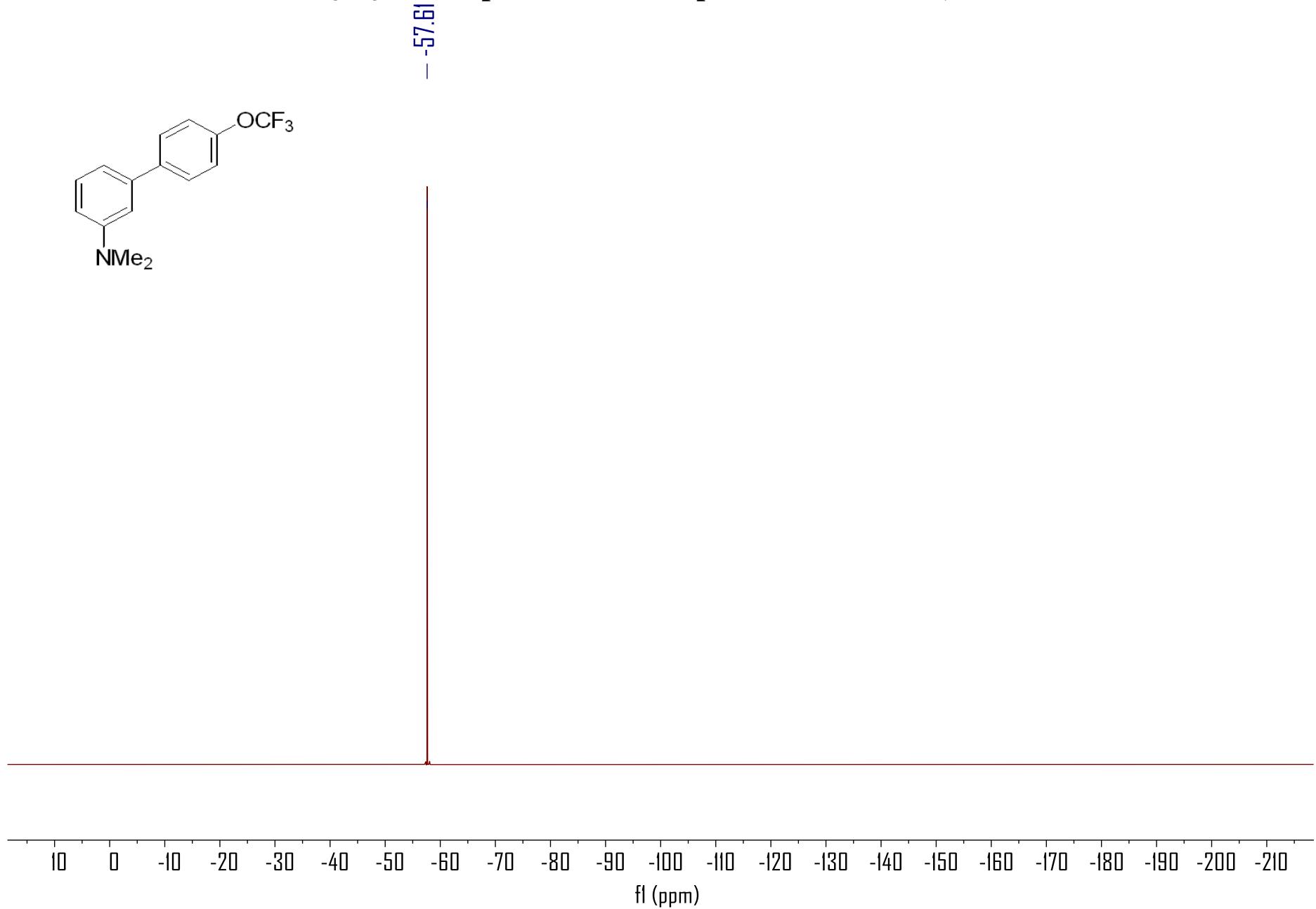
¹H NMR spectrum for compound 3i (500 MHz, C₆D₆)



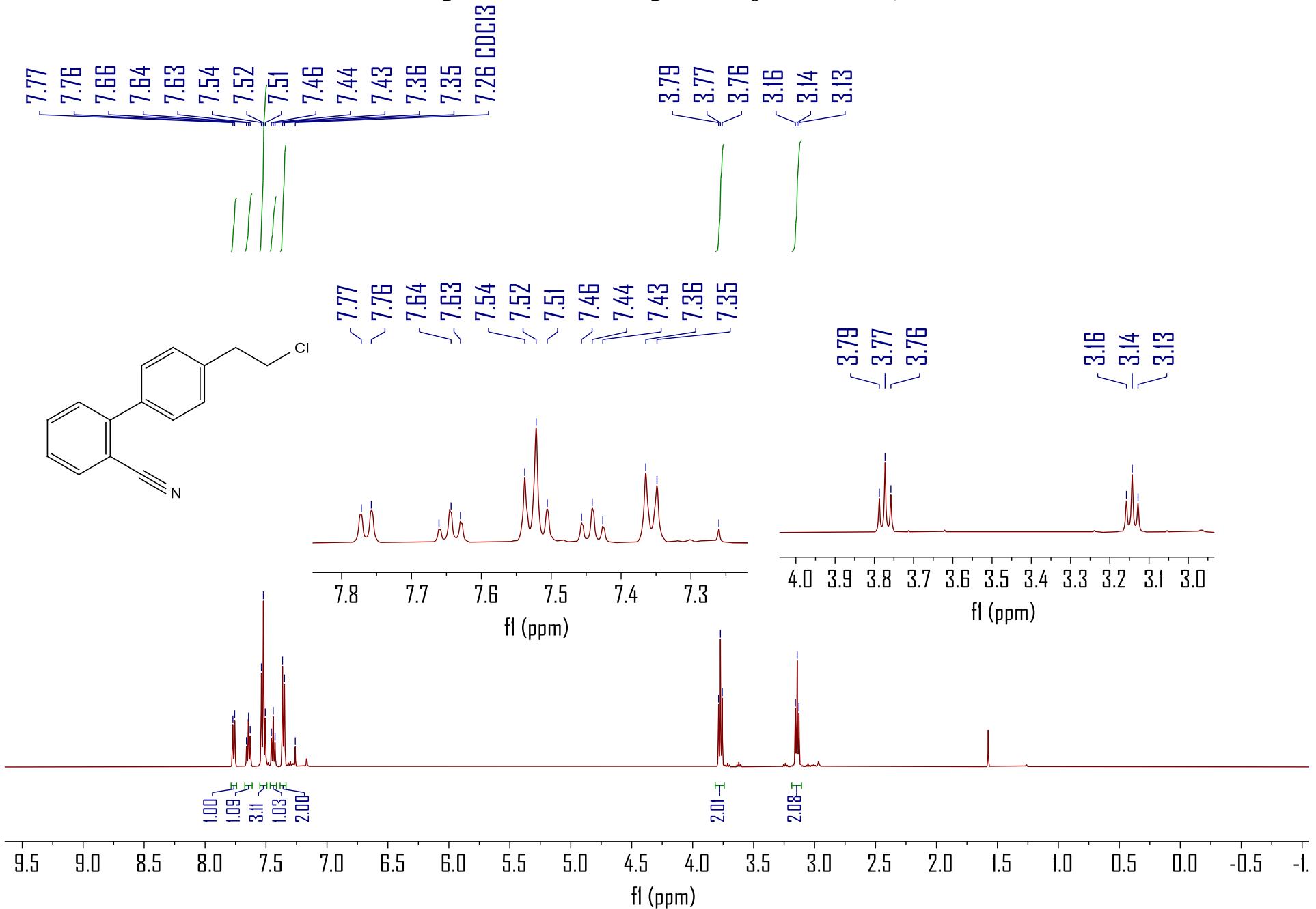
¹³C{¹H} NMR spectrum for compound 3i (125 MHz, C₆D₆)



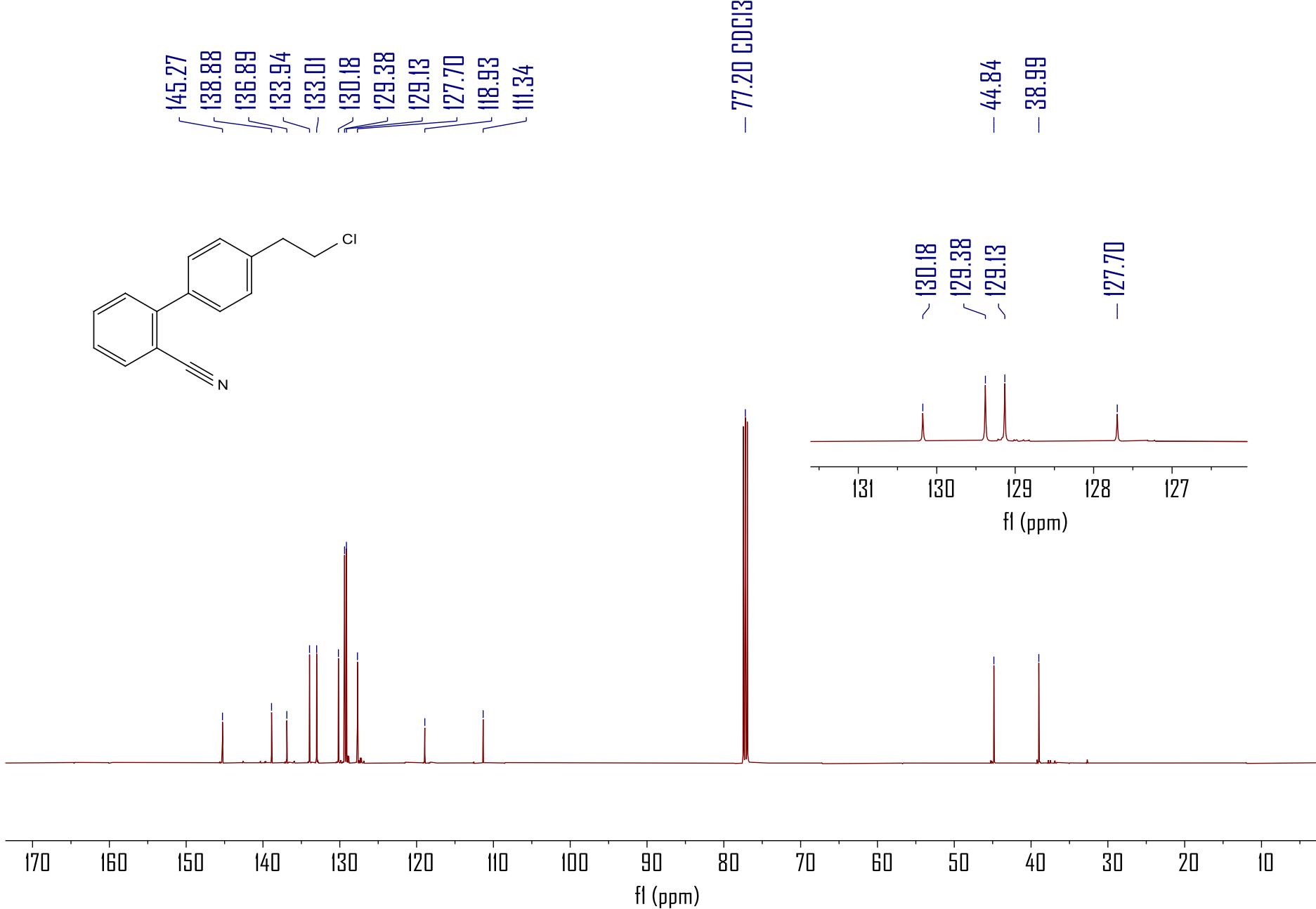
¹⁹F{¹H} NMR spectrum for compound 3i (376 MHz, C₆D₆)



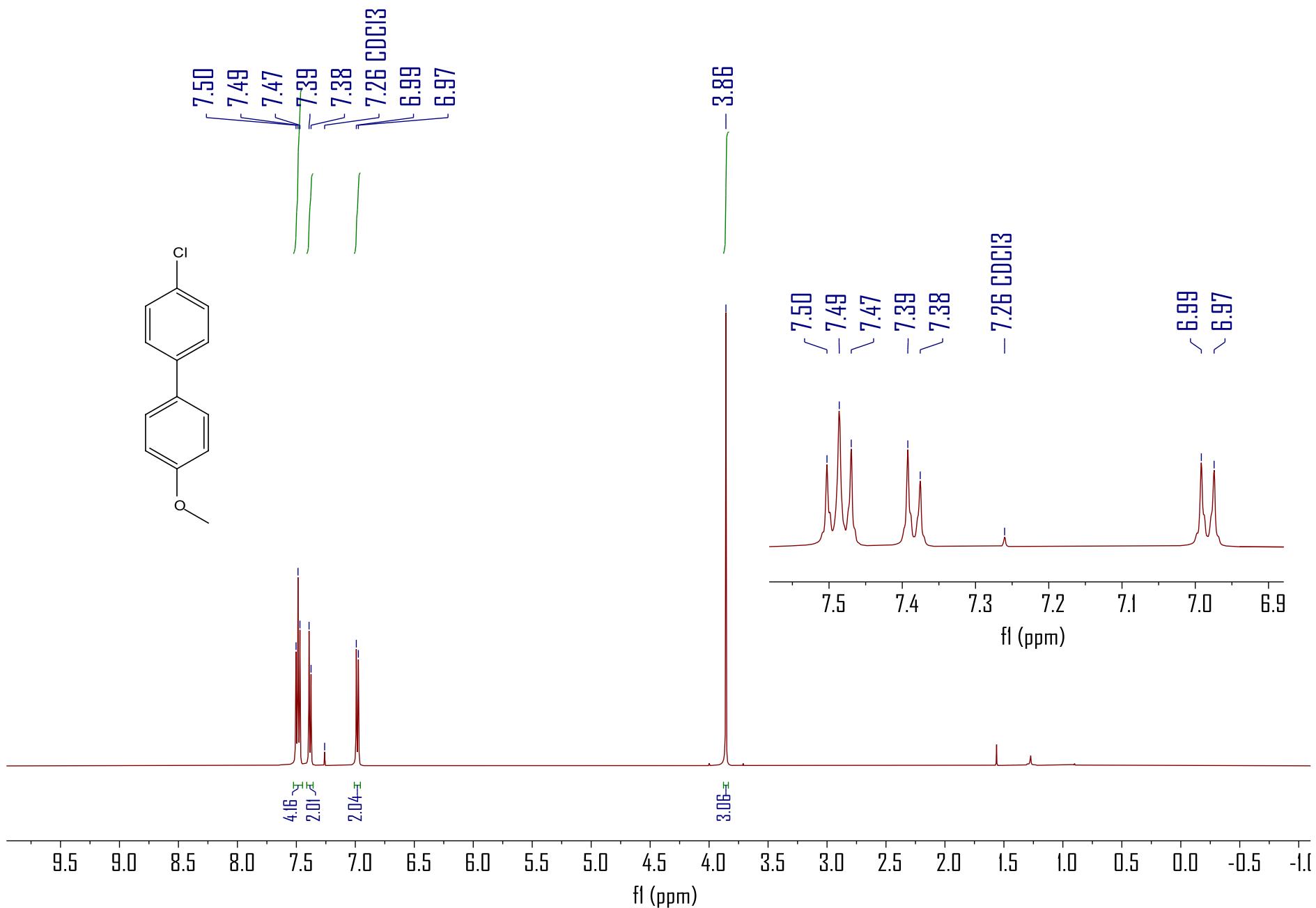
¹H NMR spectrum for compound 3j (500 MHz, CDCl₃)



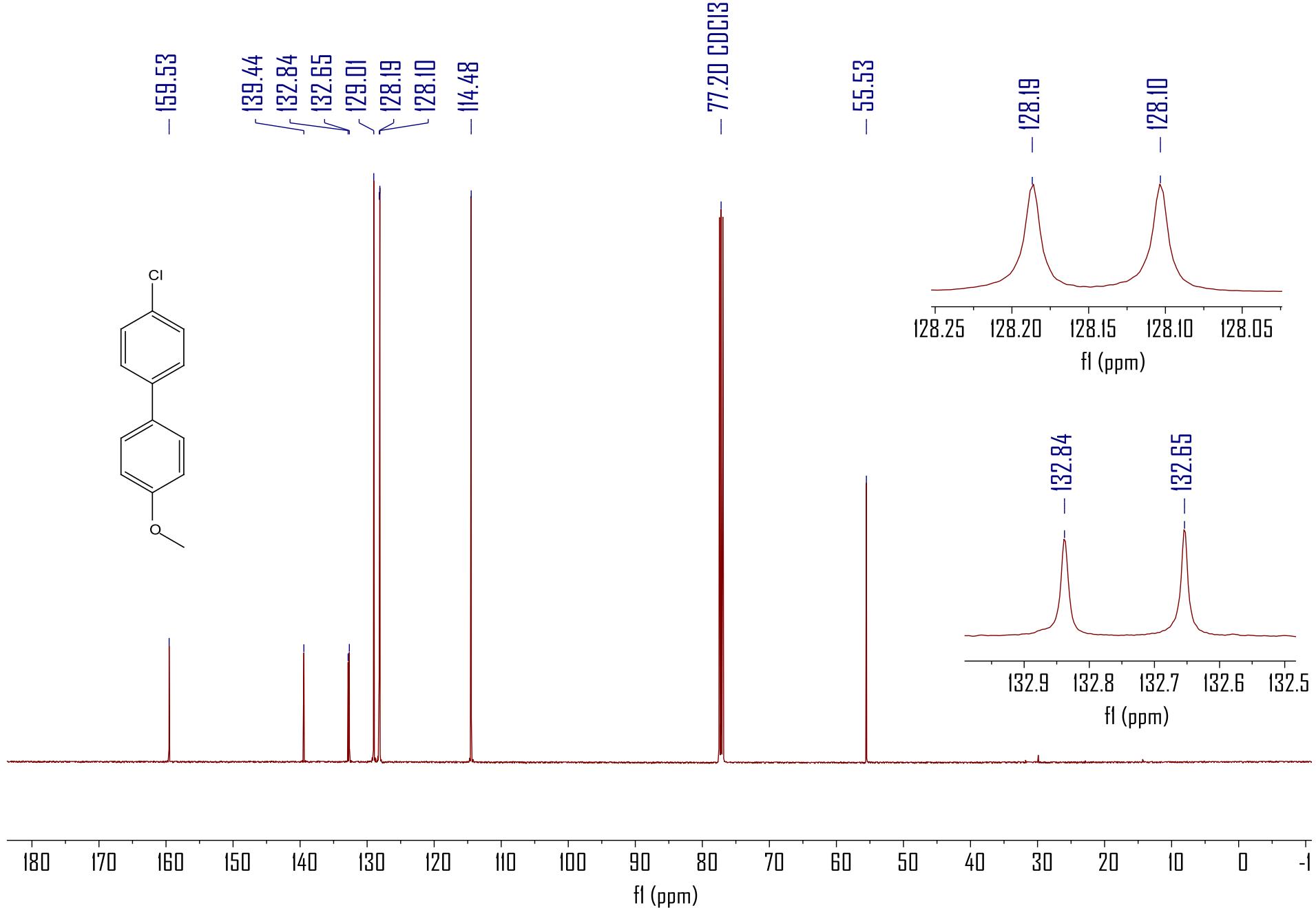
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum for compound 3j (125 MHz, CDCl_3)



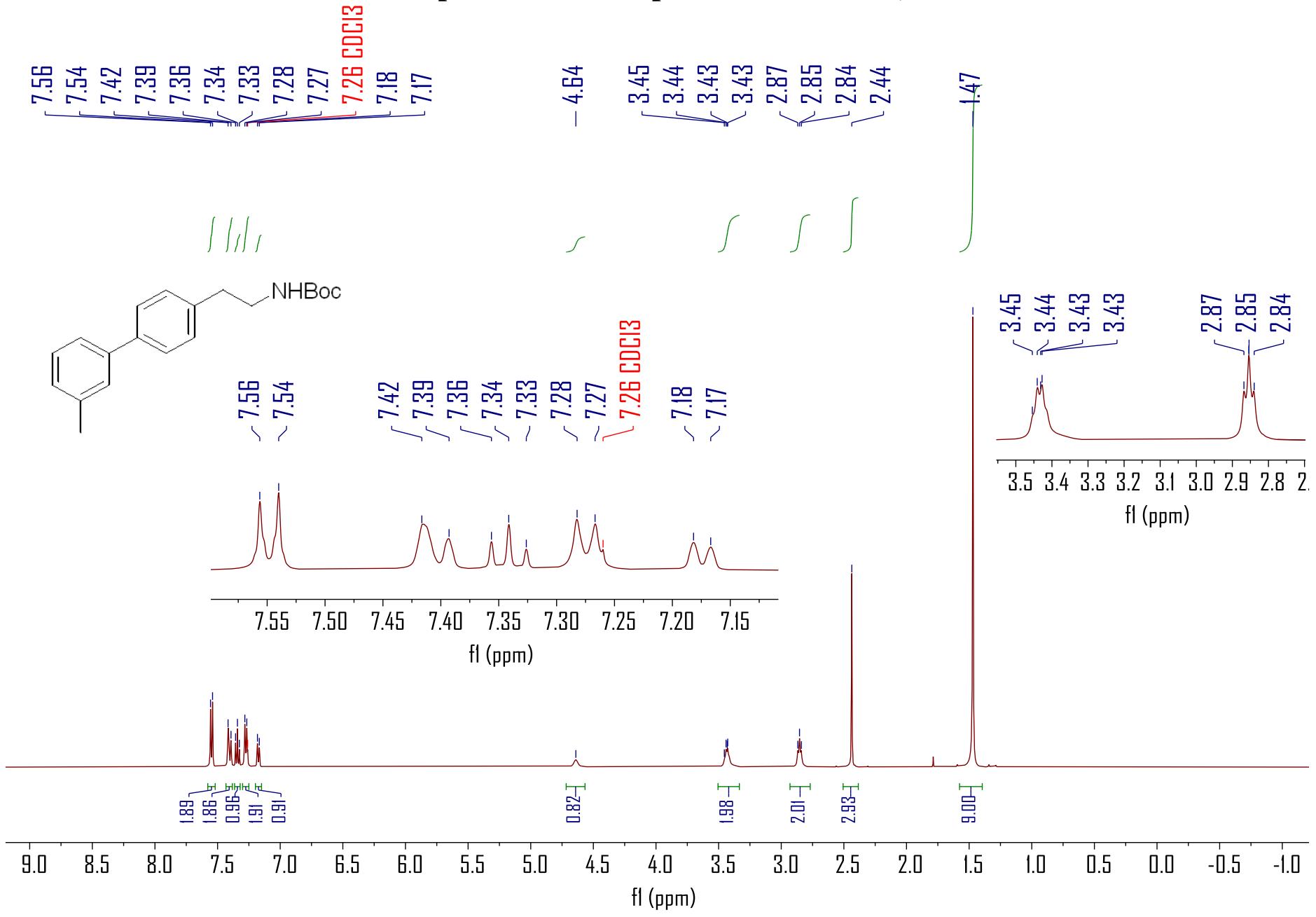
^1H NMR spectrum for compound 3k (500 MHz, CDCl_3)



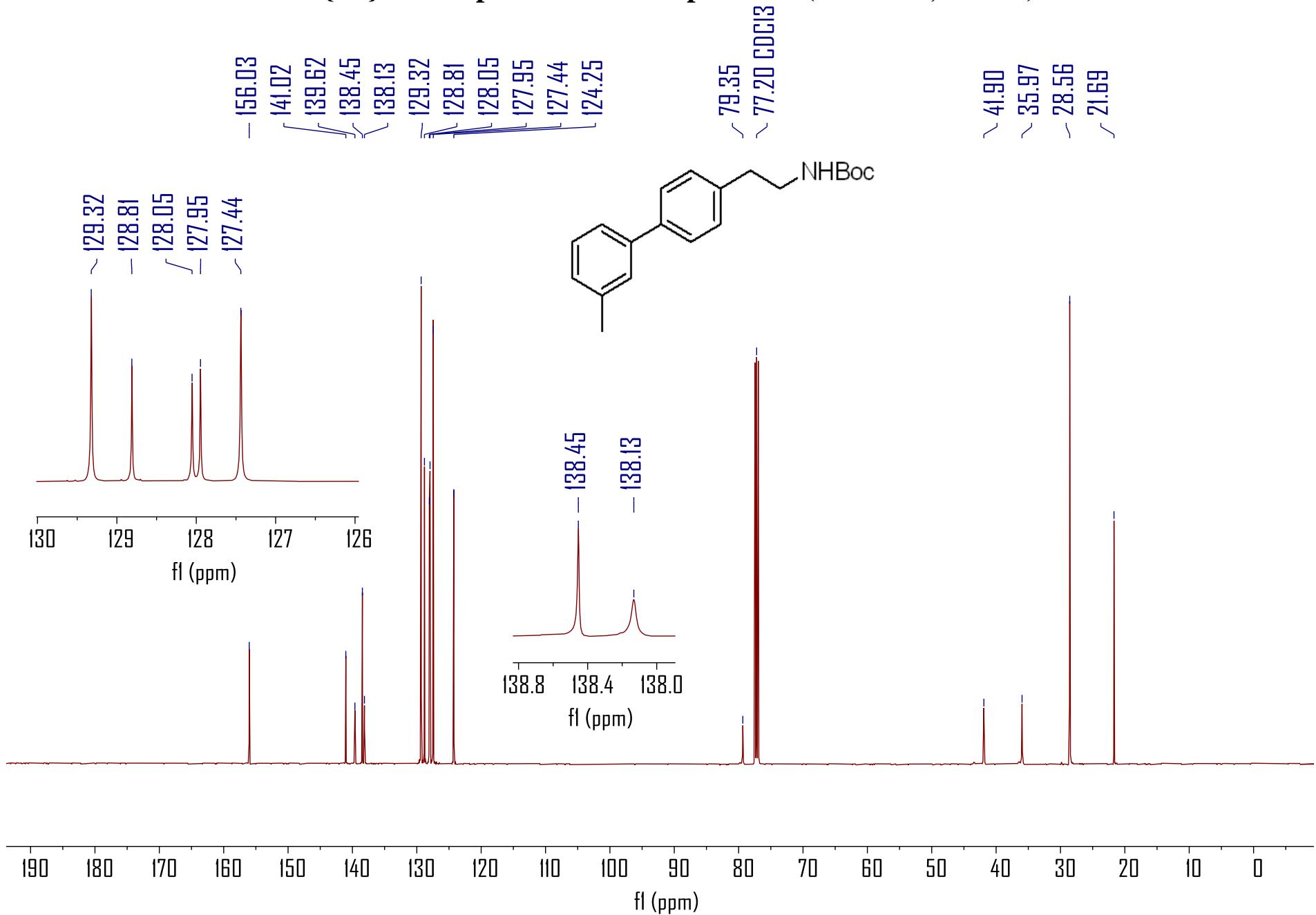
^{13}C NMR spectrum for compound 3k (125 MHz, CDCl_3)



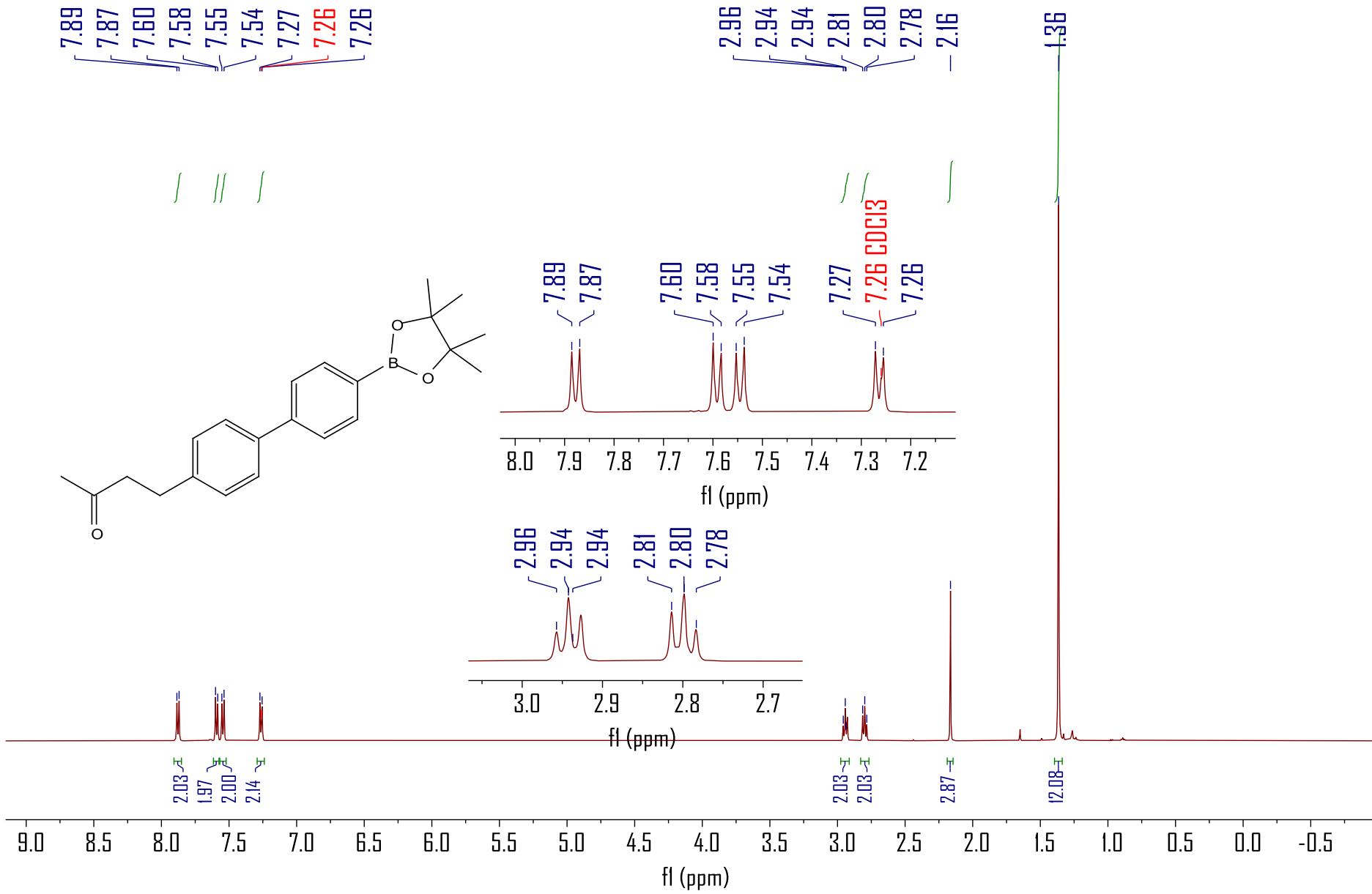
¹H NMR spectrum for compound 3l (500 MHz, CDCl₃)



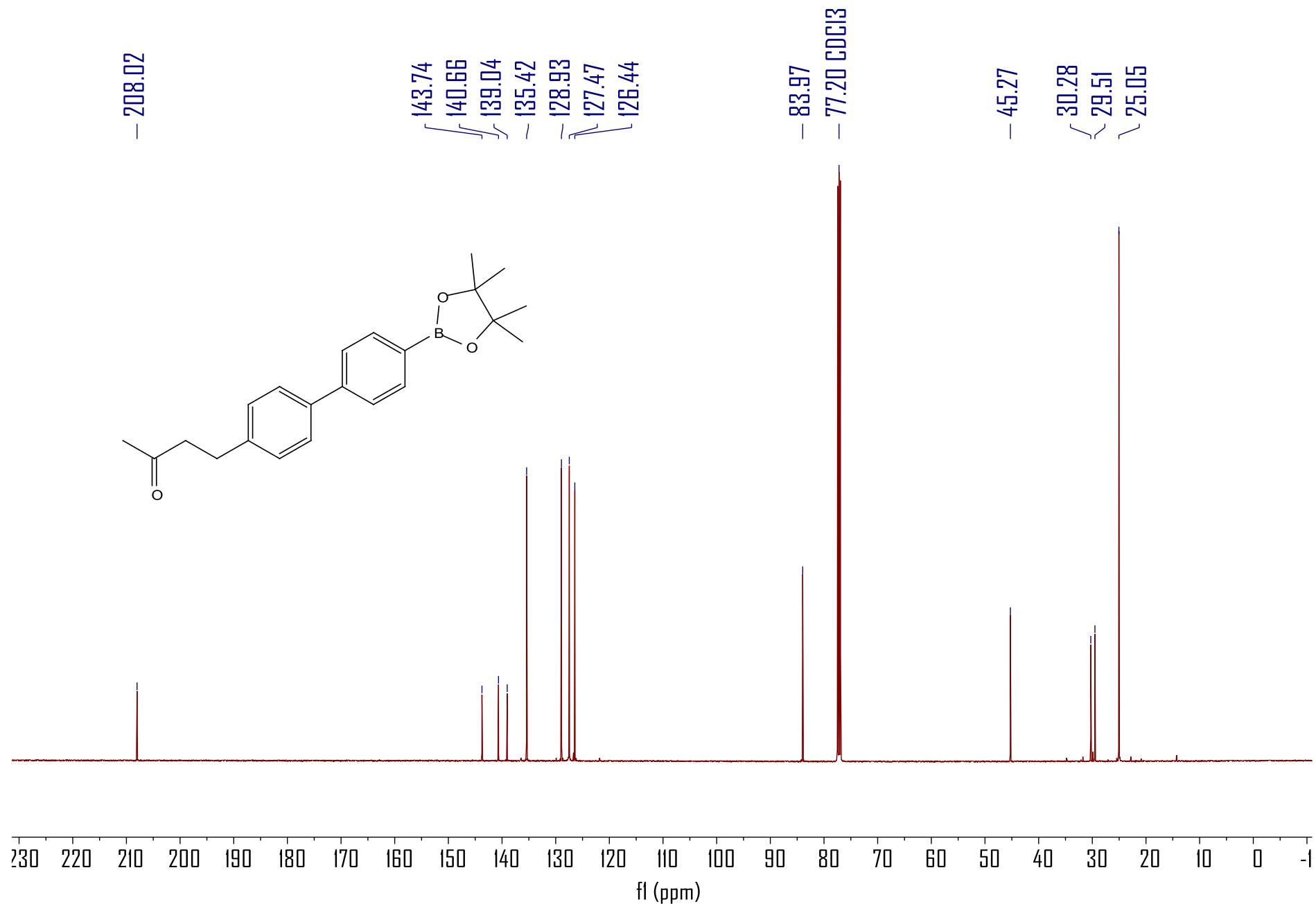
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum for compound 3l (125 MHz, CDCl_3)



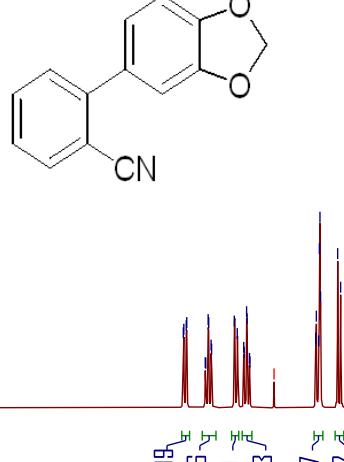
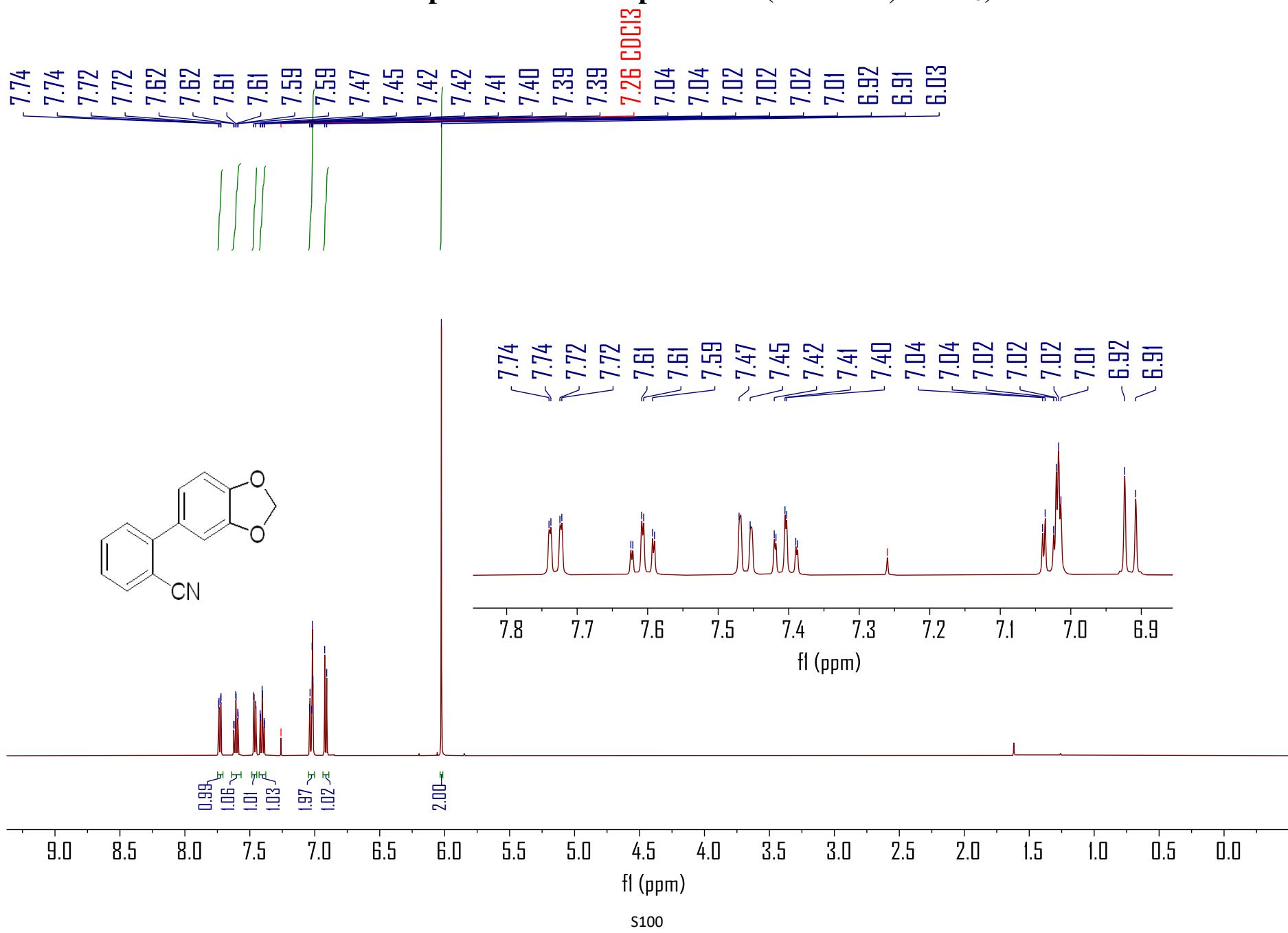
¹H NMR spectrum for compound 3m (500 MHz, CDCl₃)



$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum for compound 3m (125 MHz, CDCl_3)

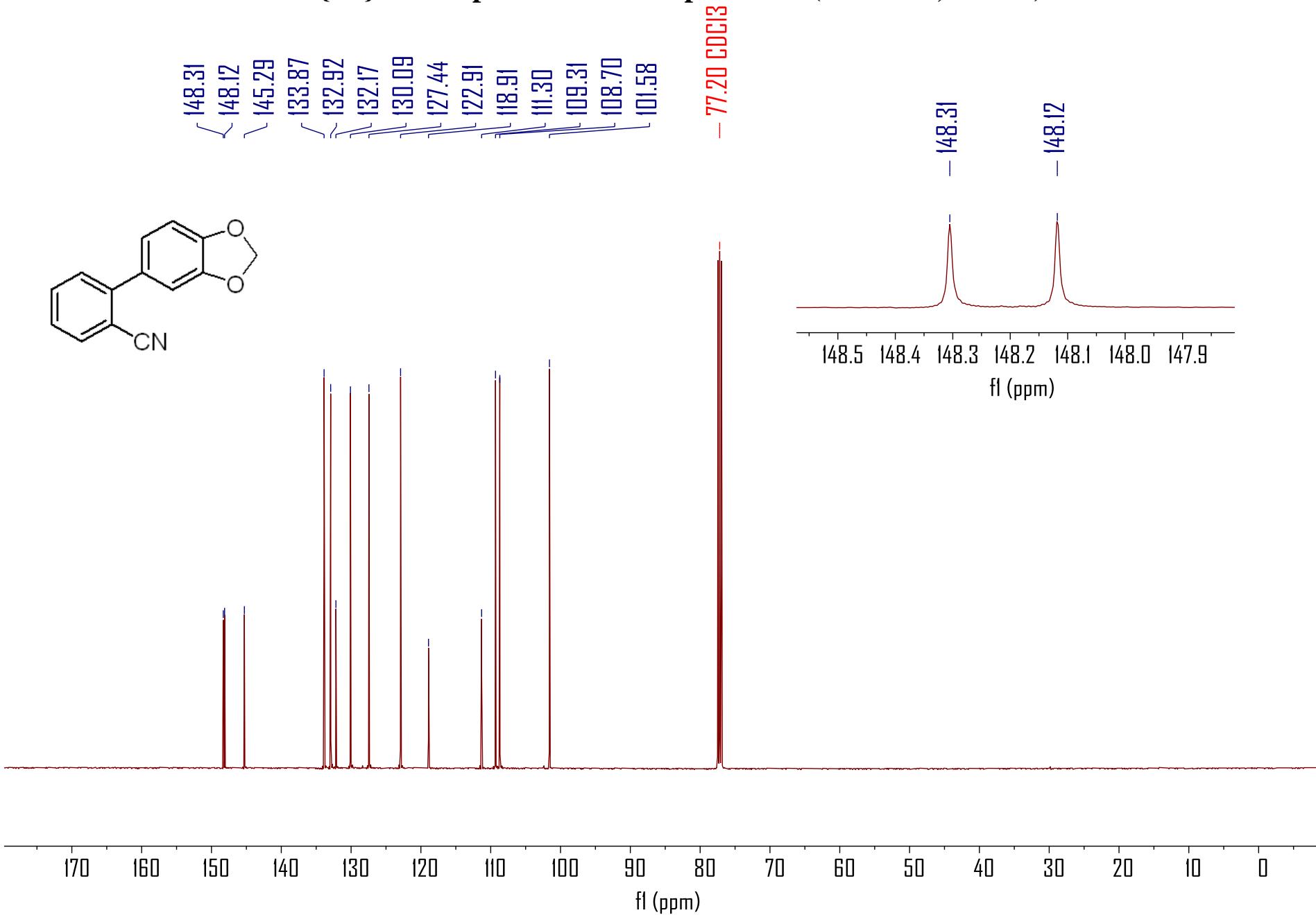


^1H NMR spectrum for compound 3n (500 MHz, CDCl_3)

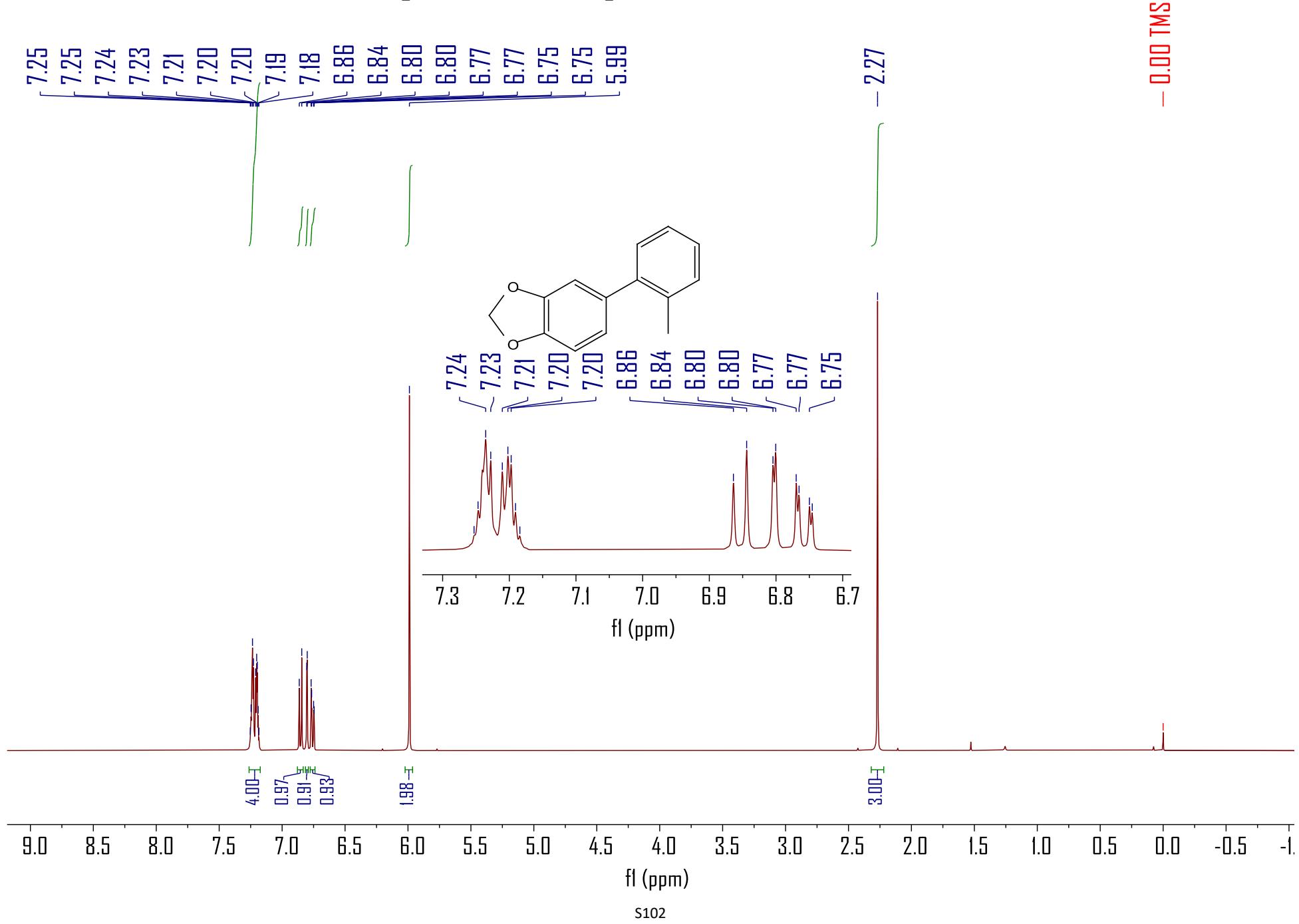


S100

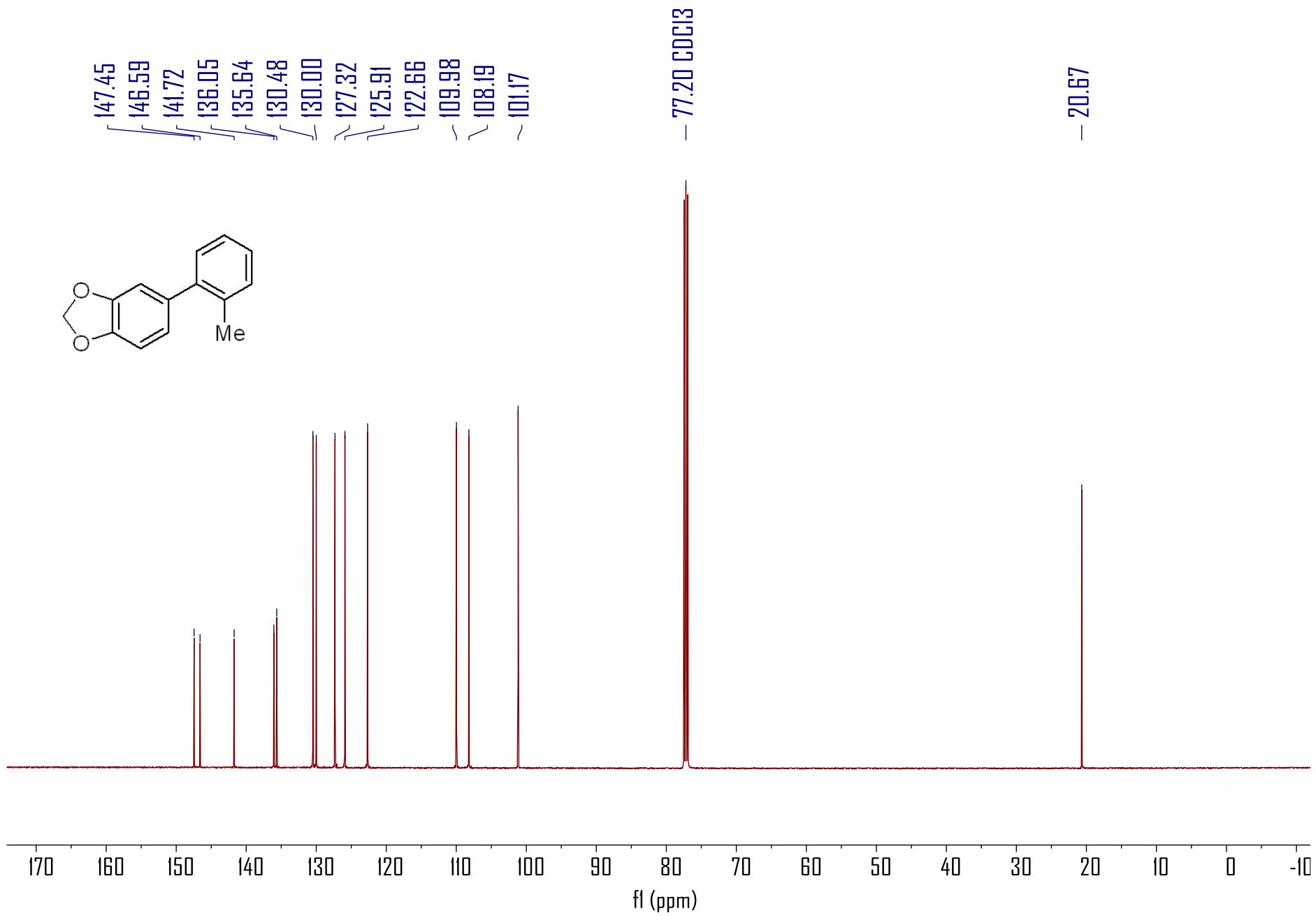
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum for compound 3n (125 MHz, CDCl_3)



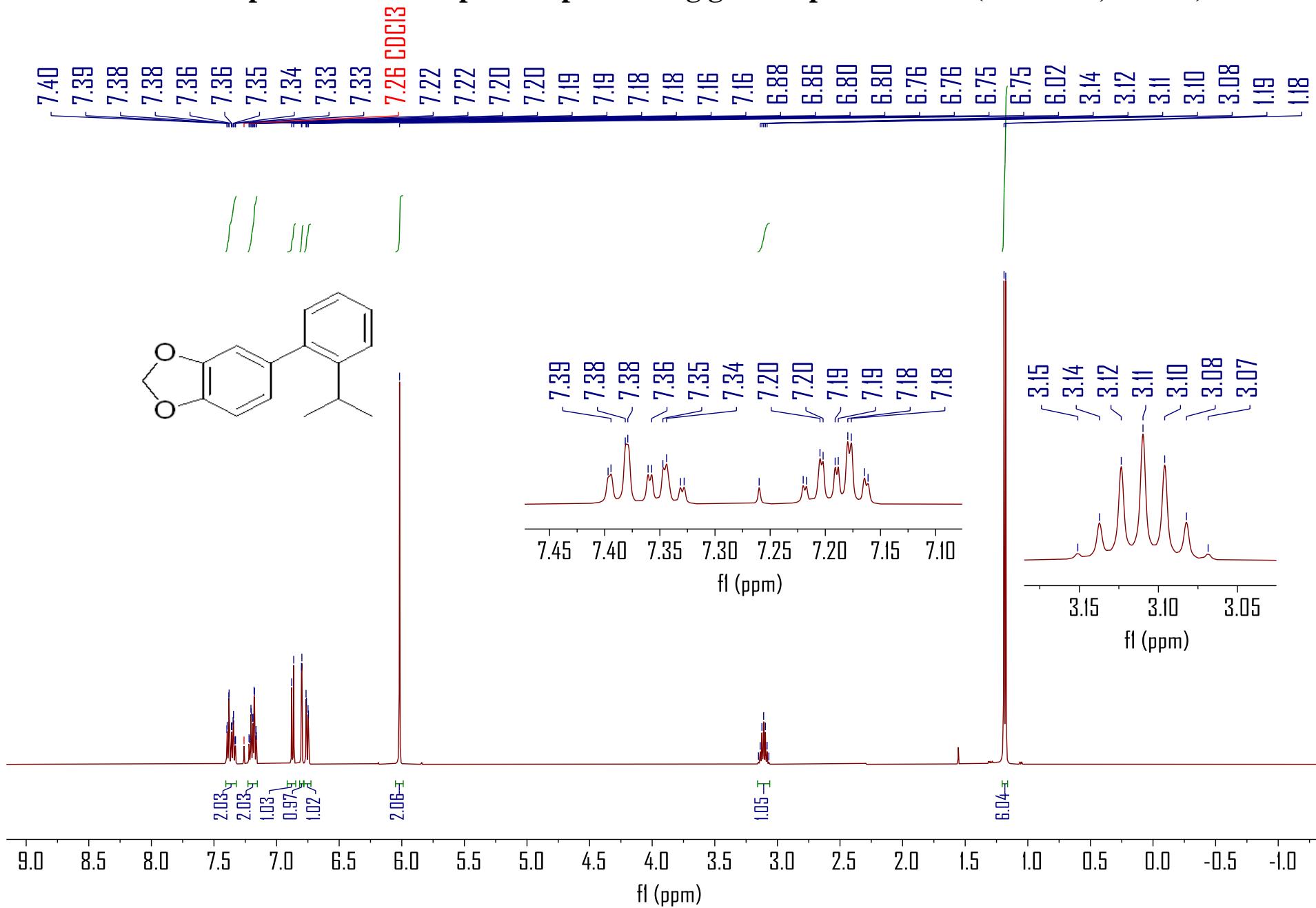
^1H NMR spectrum for compound 3o (400 MHz, CDCl_3 , TMS)



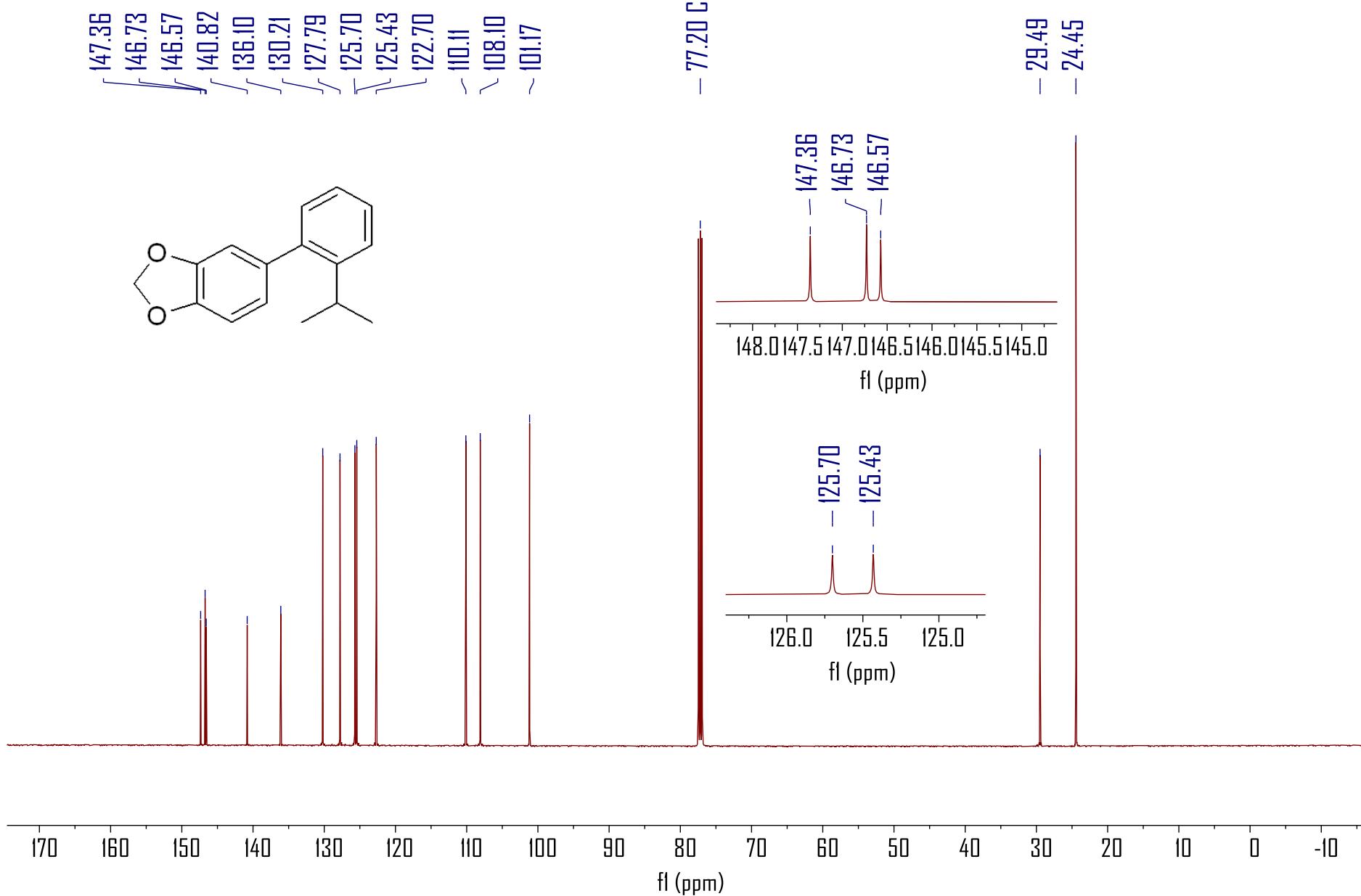
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum for compound 3o (125 MHz, CDCl_3)



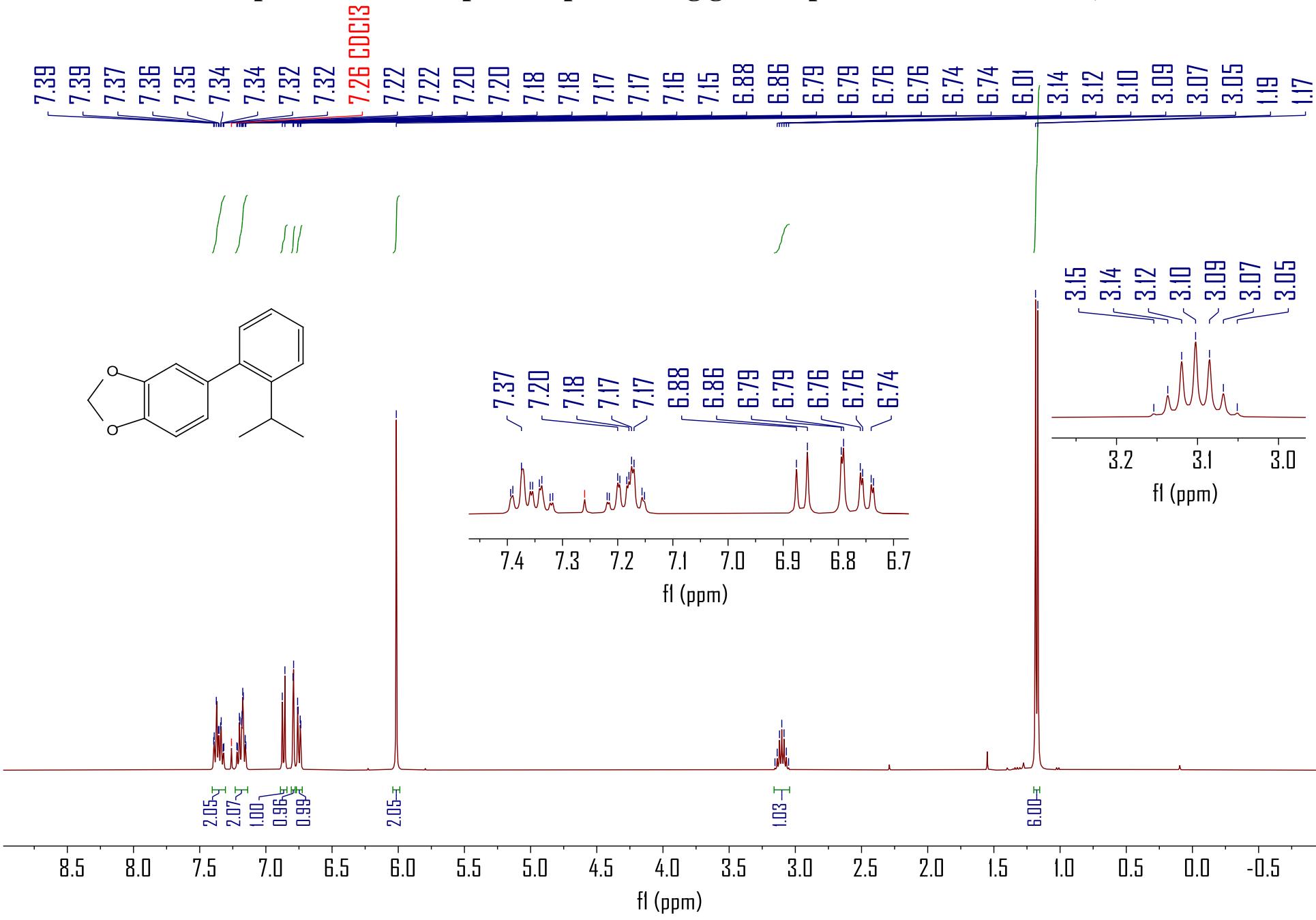
¹H NMR spectrum for compound 3p following general procedure A (500 MHz, CDCl₃)



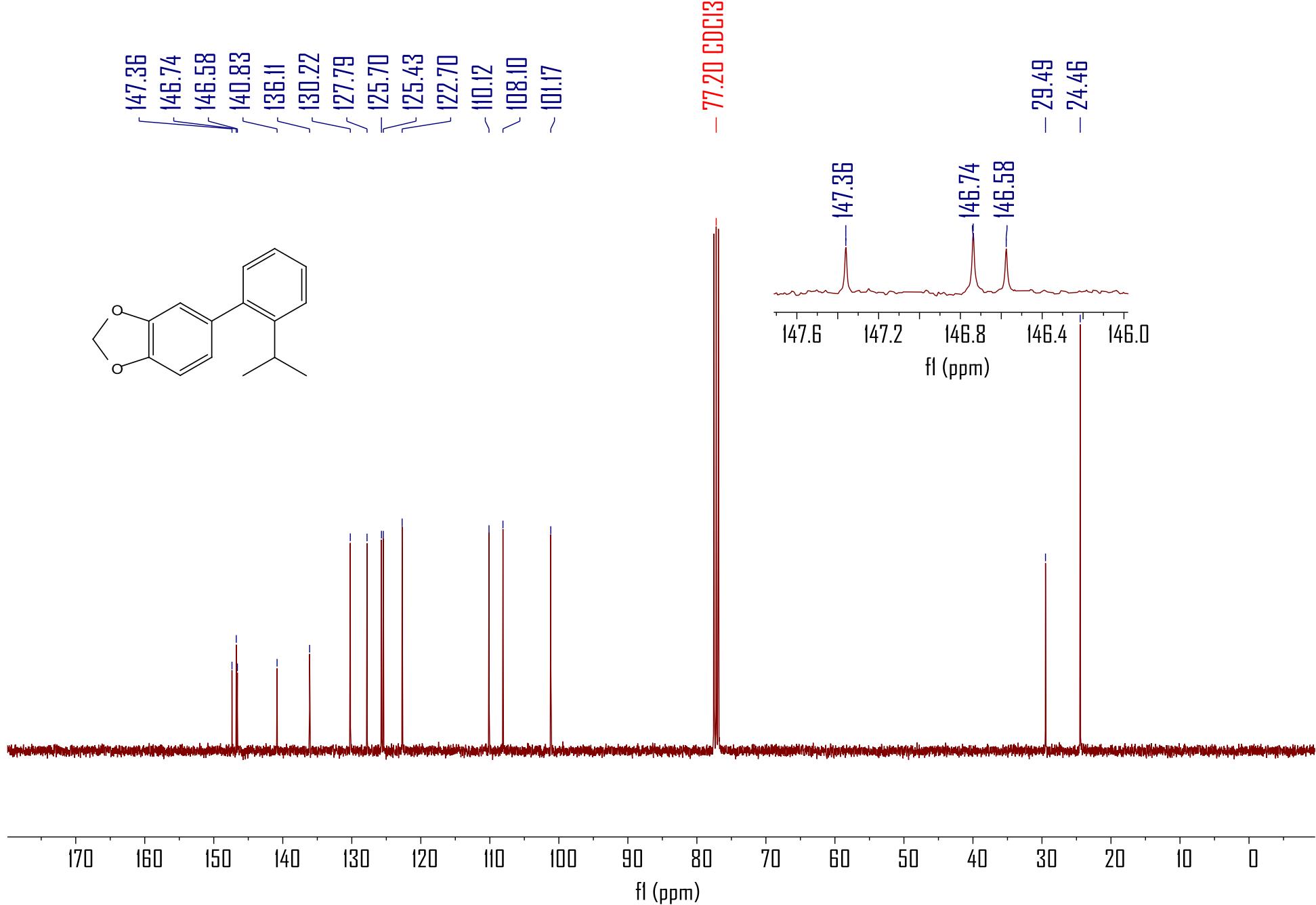
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum for compound 3p following general procedure A (125 MHz, CDCl_3)



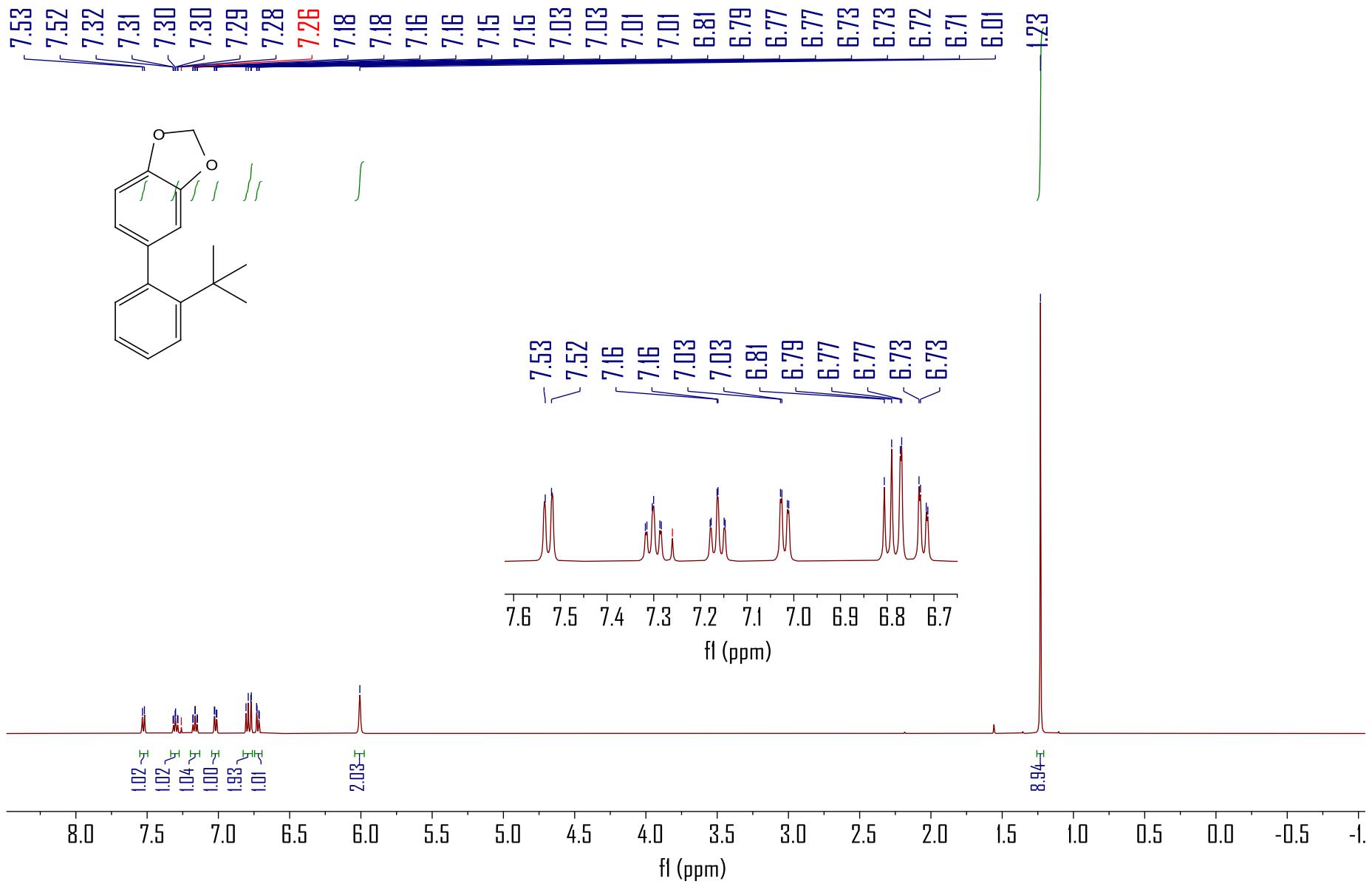
¹H NMR spectrum for compound 3p following general procedure B (400 MHz, CDCl₃)



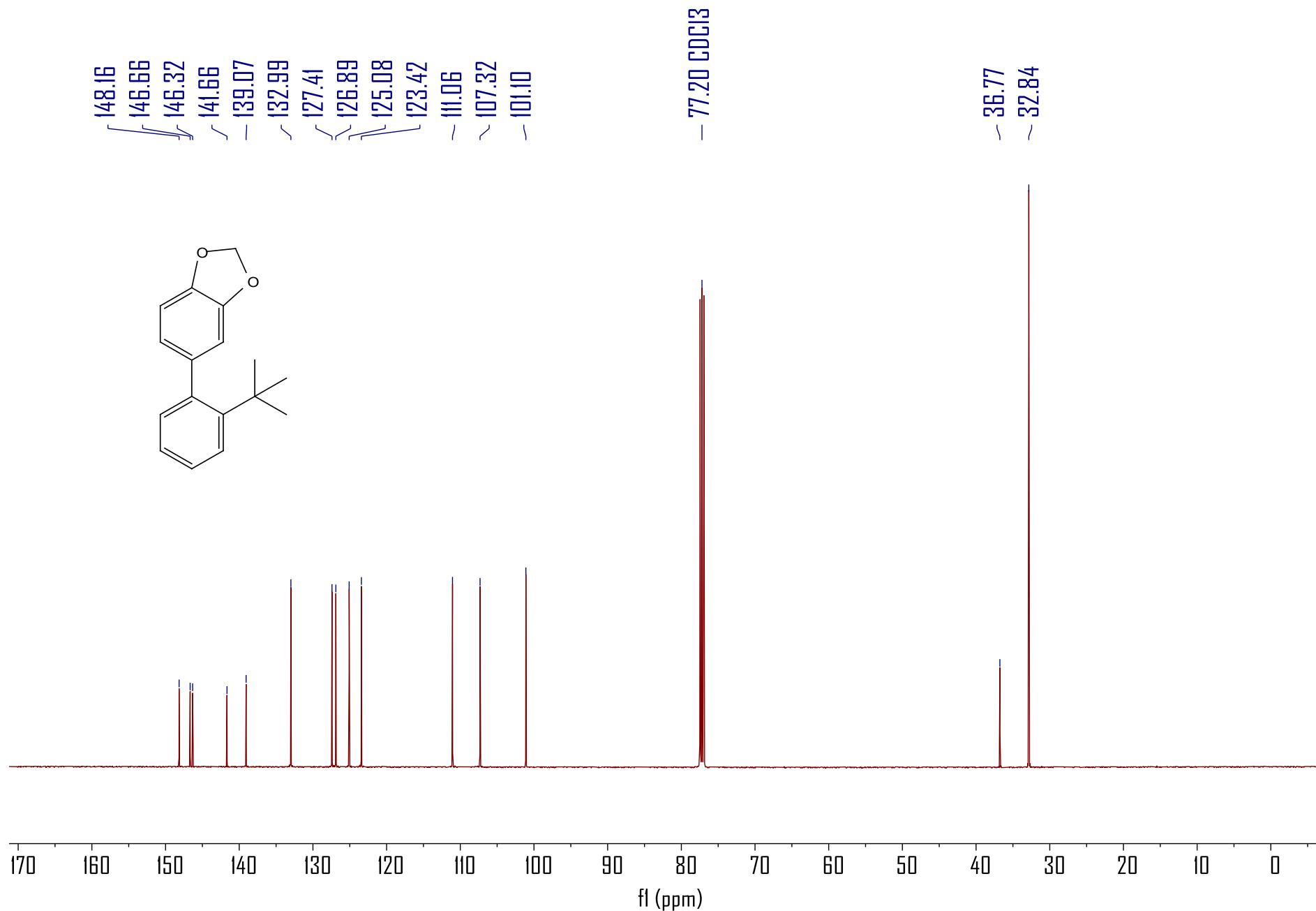
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum for compound 3p following general procedure B (100 MHz, CDCl_3)



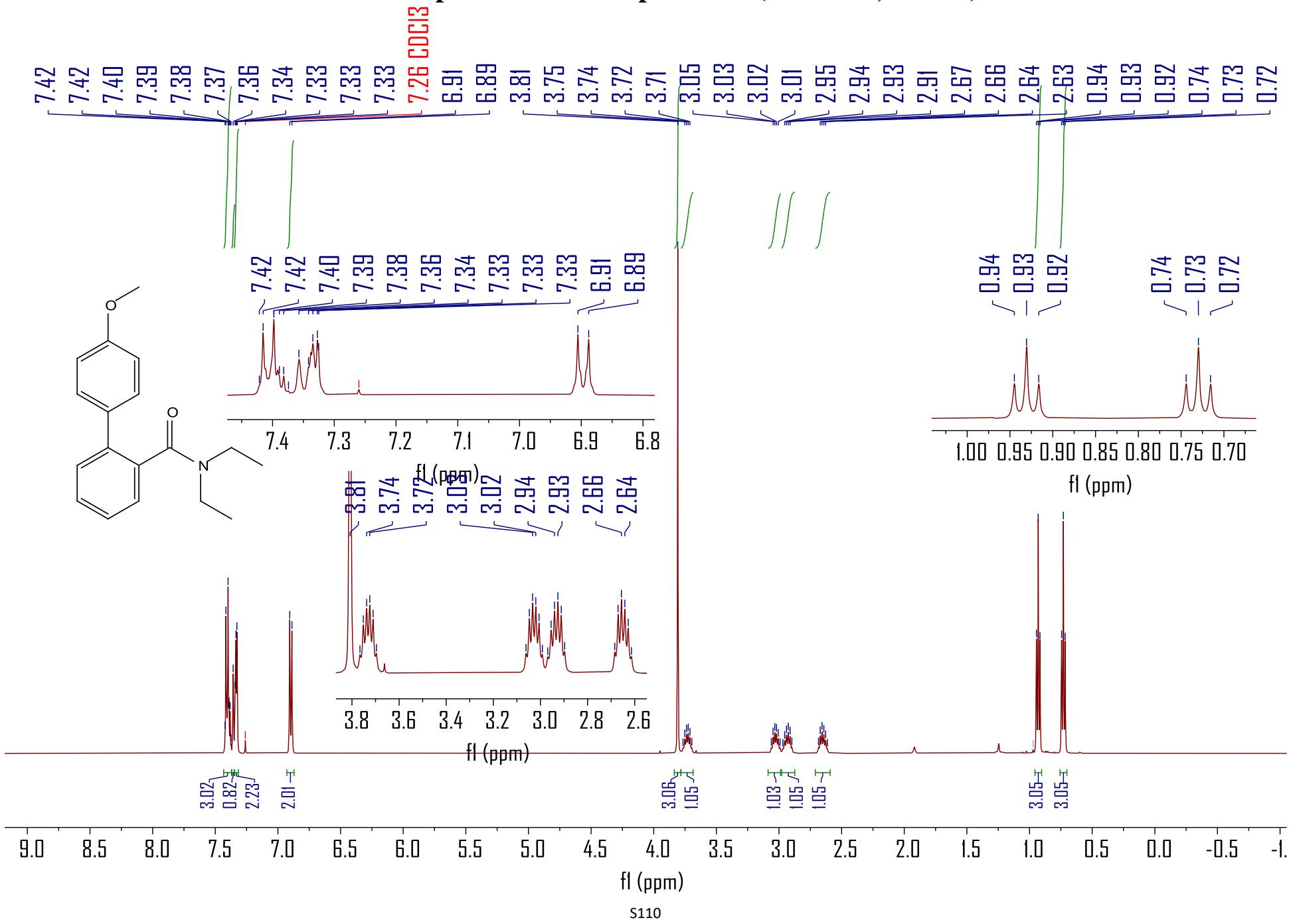
¹H NMR spectrum for compound 3q (500 MHz, CDCl₃)



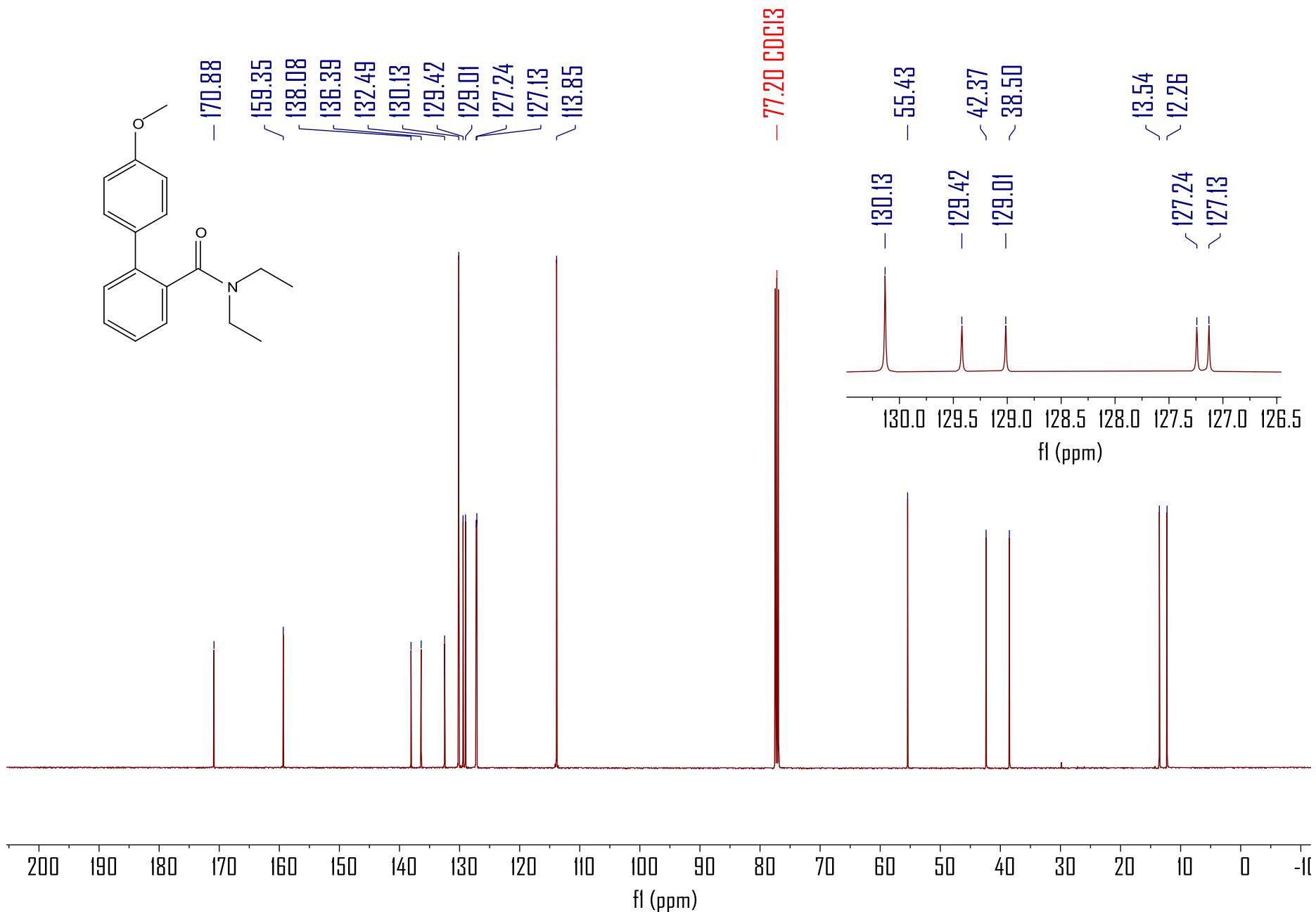
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum for compound 3q (125 MHz, CDCl_3)



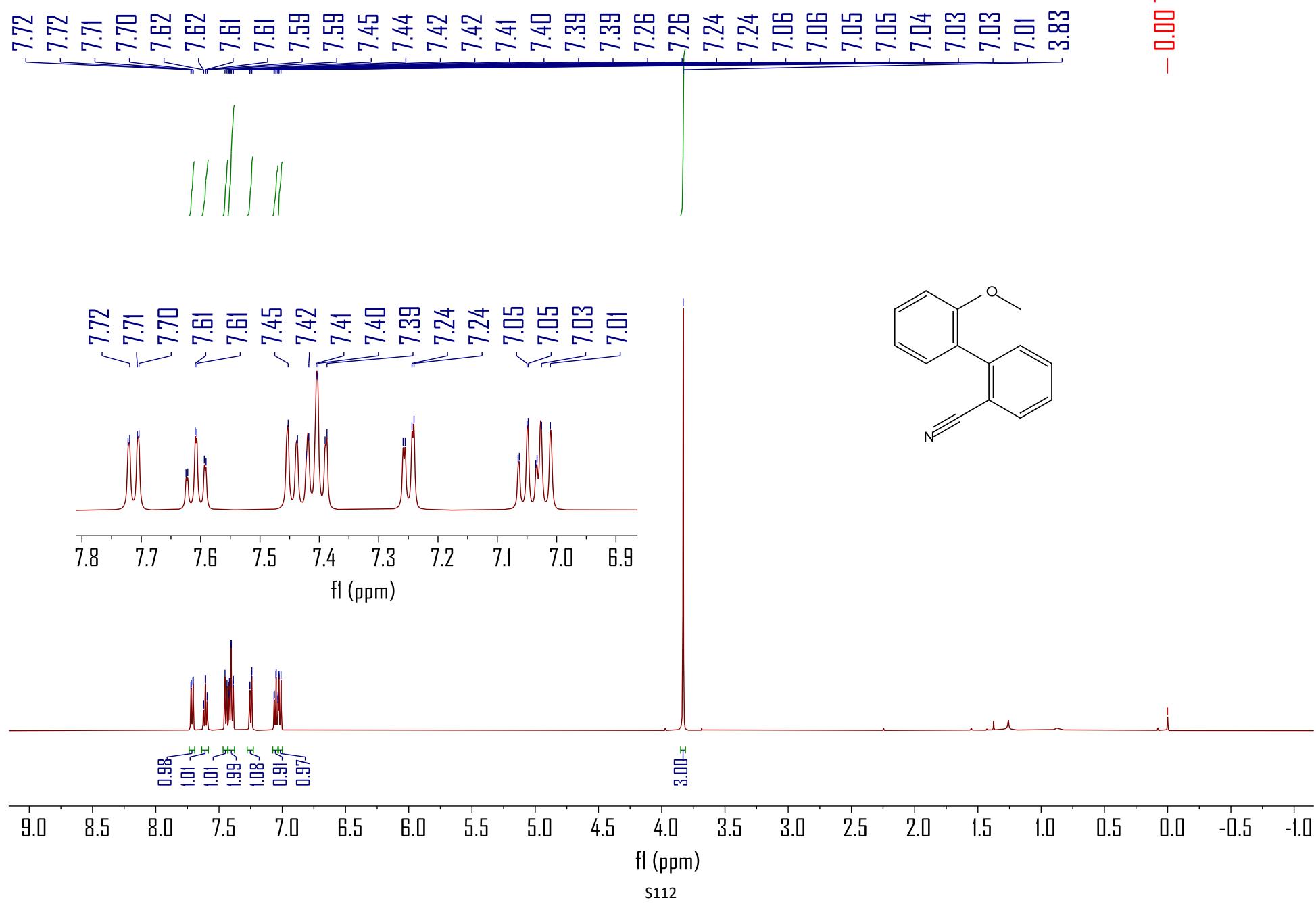
¹H NMR spectrum for compound 3r (500 MHz, CDCl₃)



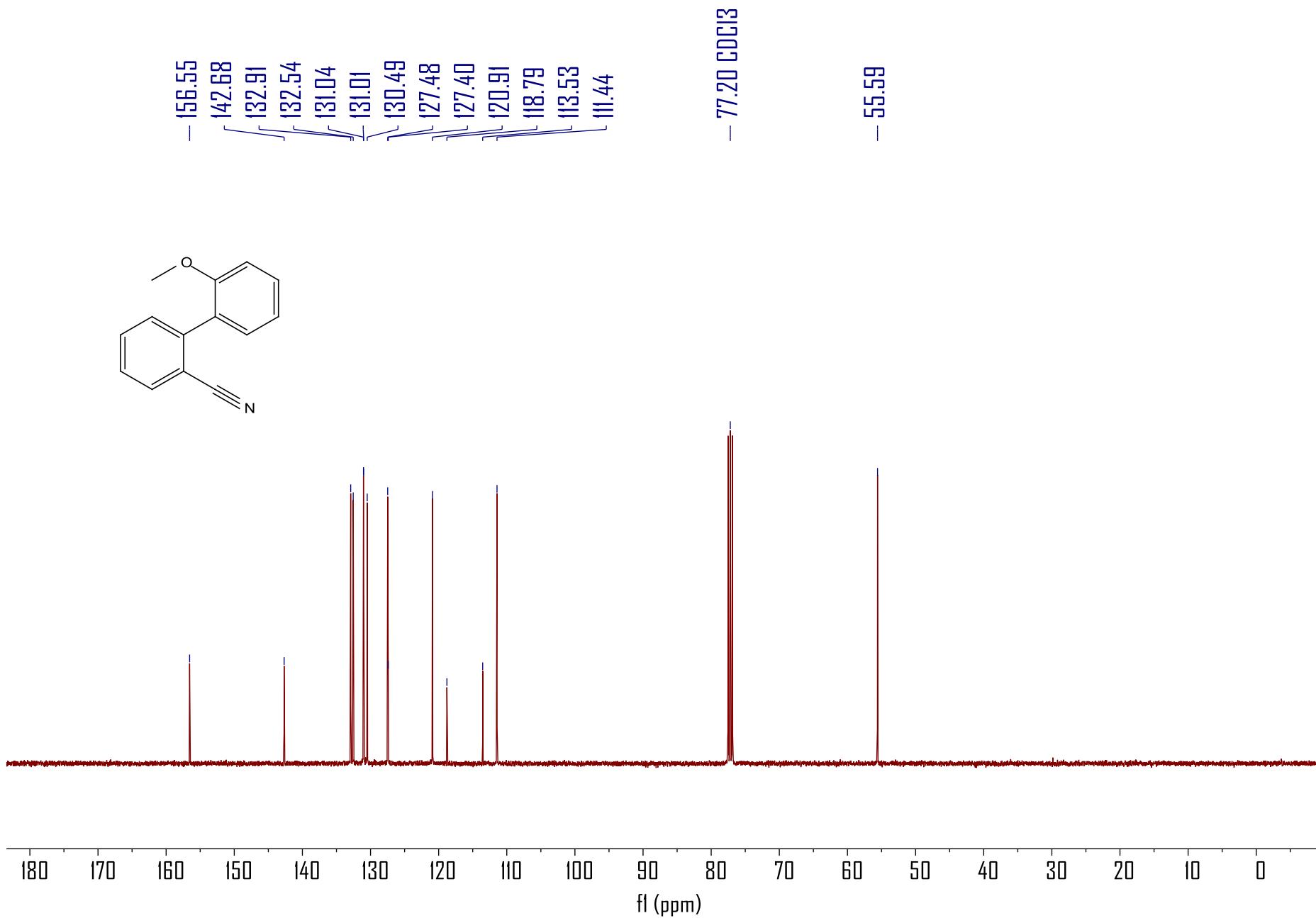
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum for compound 3r (125 MHz, CDCl_3)



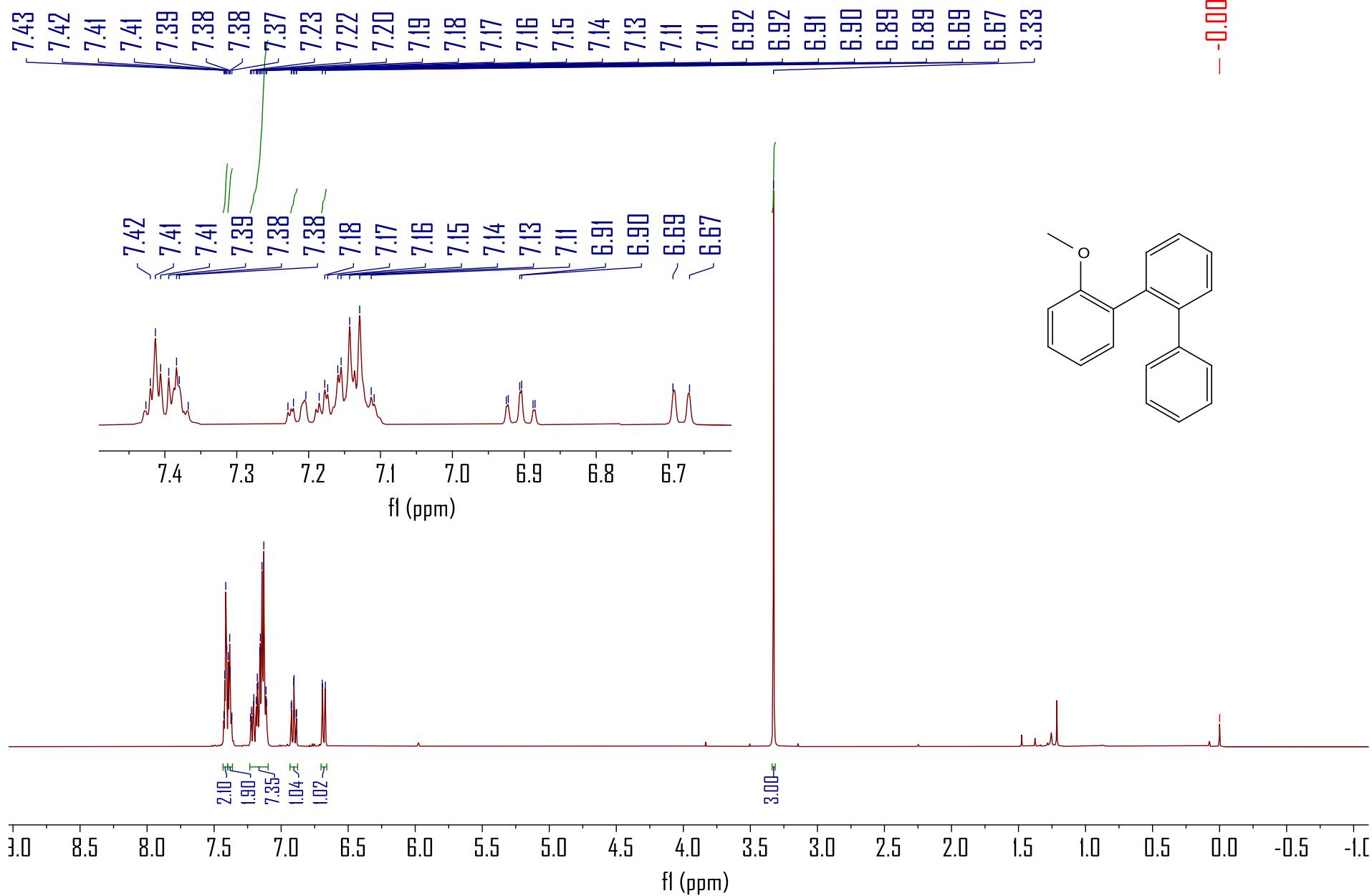
^1H NMR spectrum for compound 3s (500 MHz, CDCl_3 , TMS)



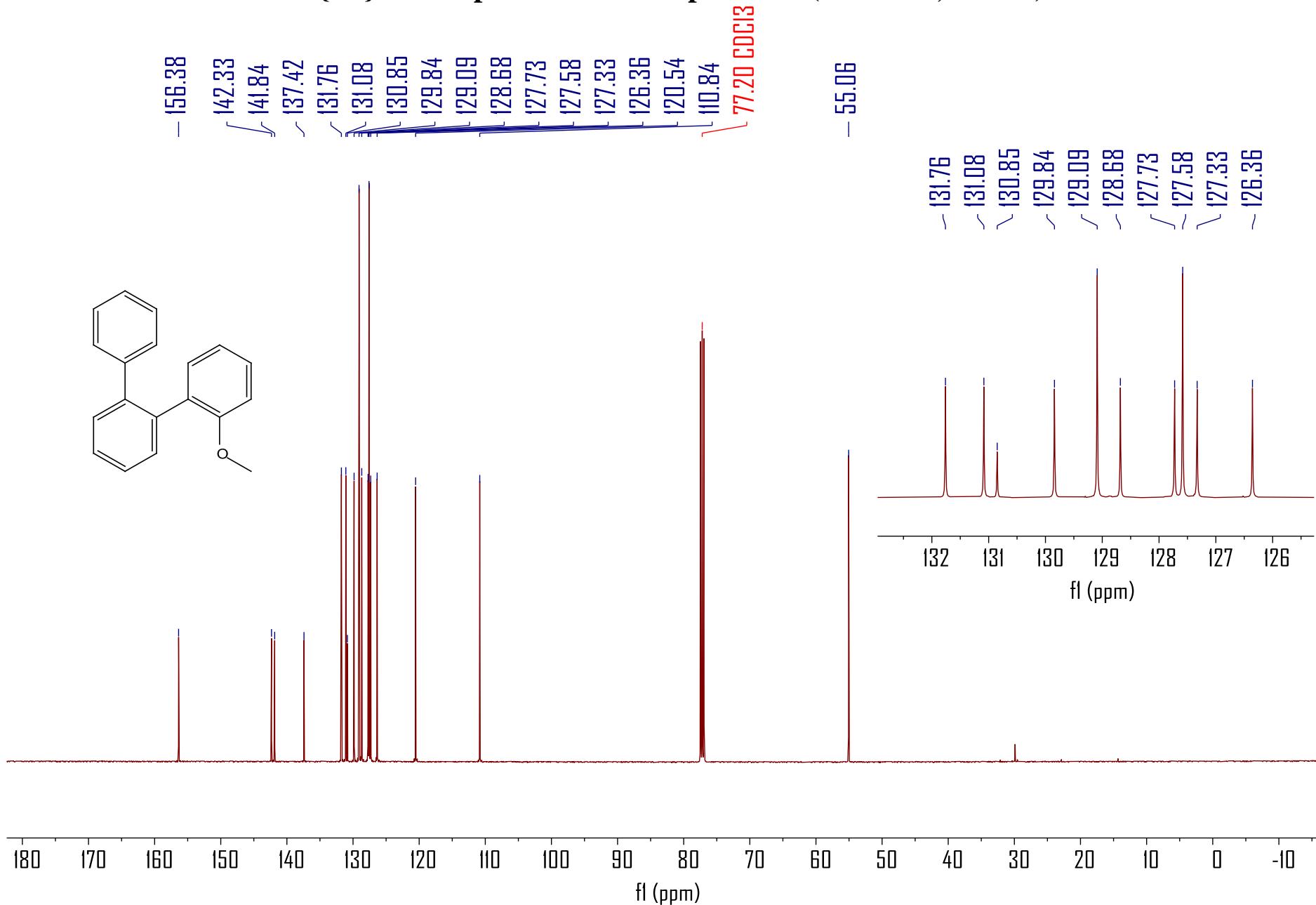
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum for compound 3s (100 MHz, CDCl_3)



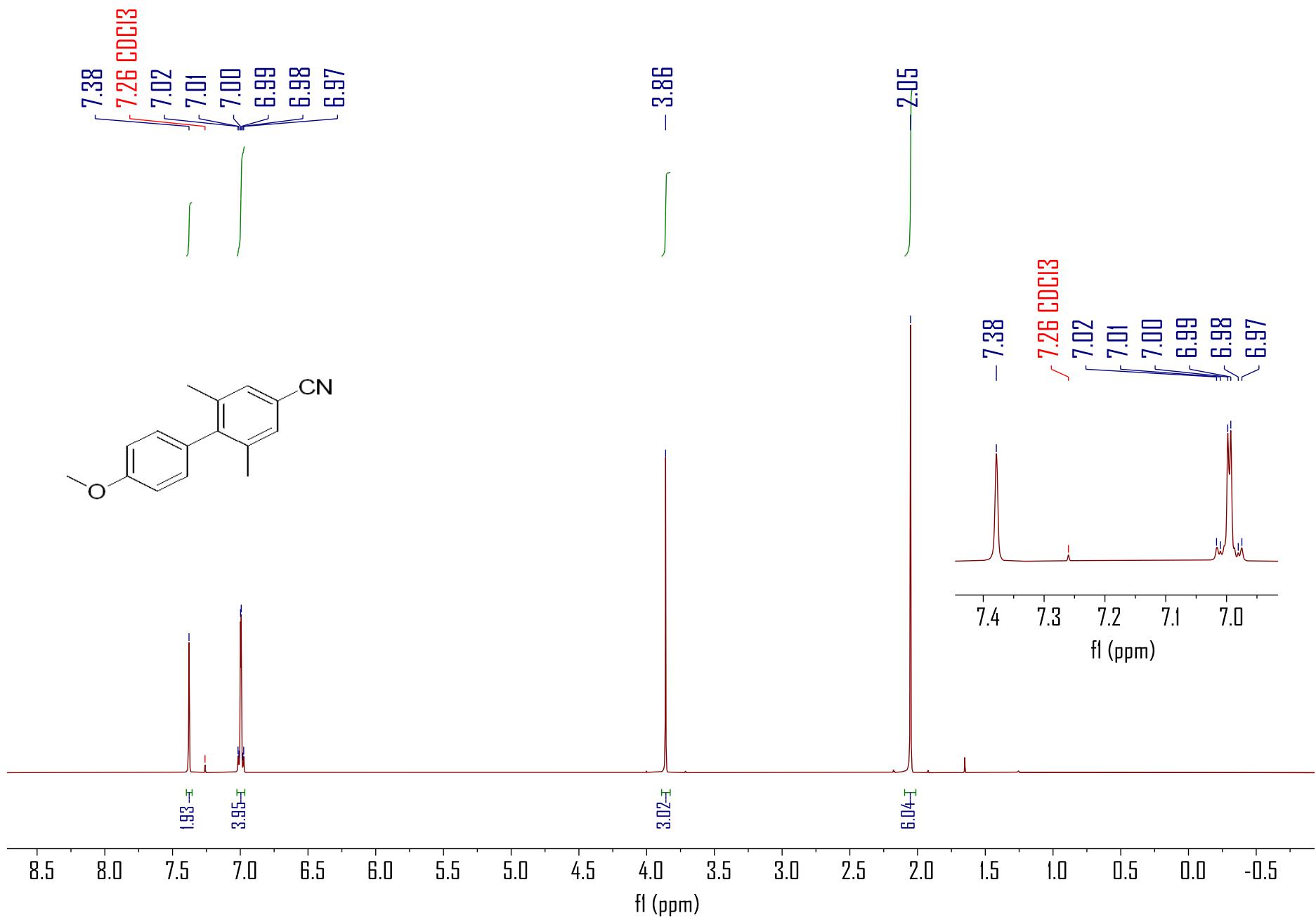
¹H NMR spectrum for compound 3t (400 MHz, CDCl₃, TMS)



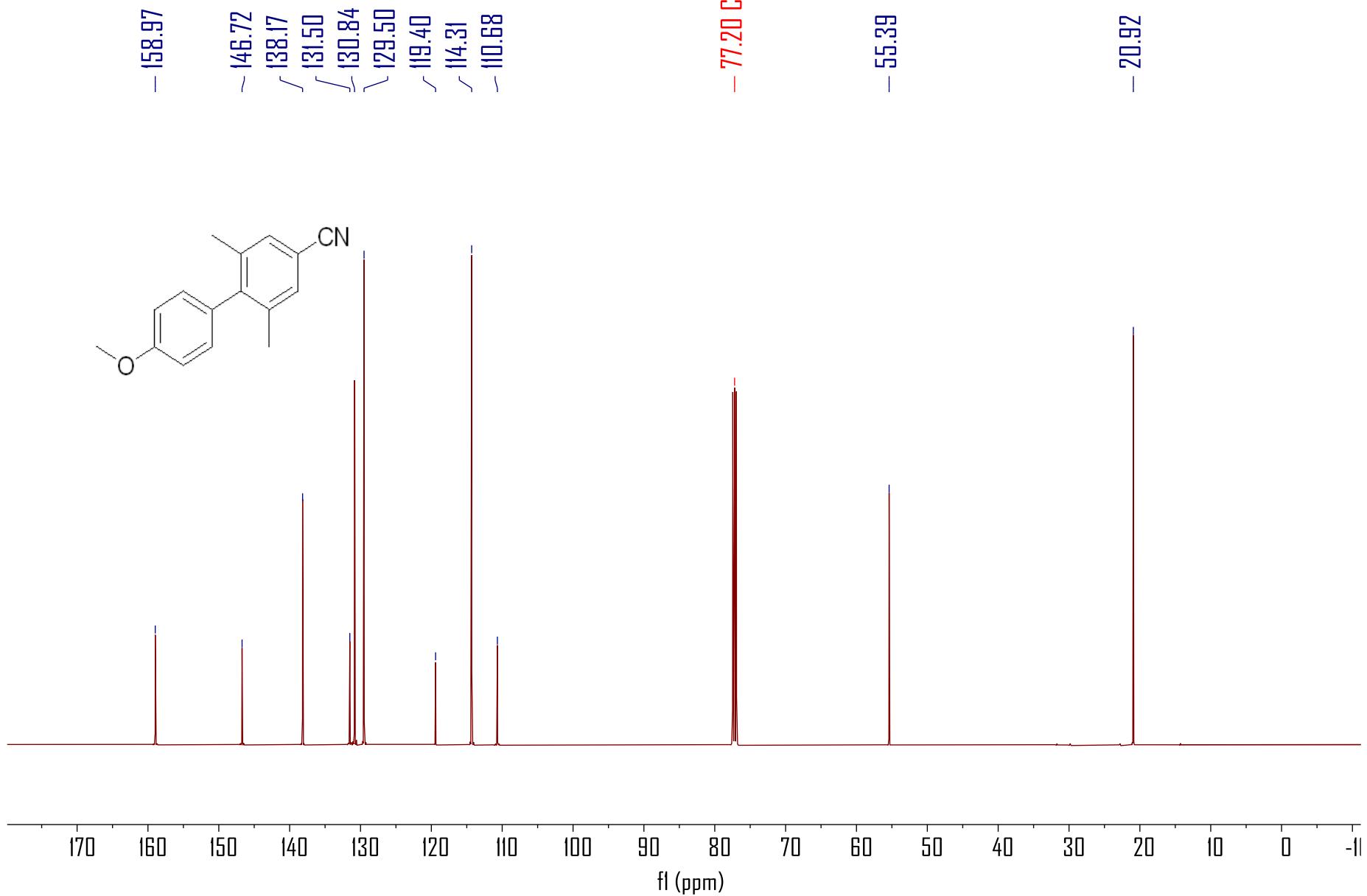
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum for compound 3t (125 MHz, CDCl_3)



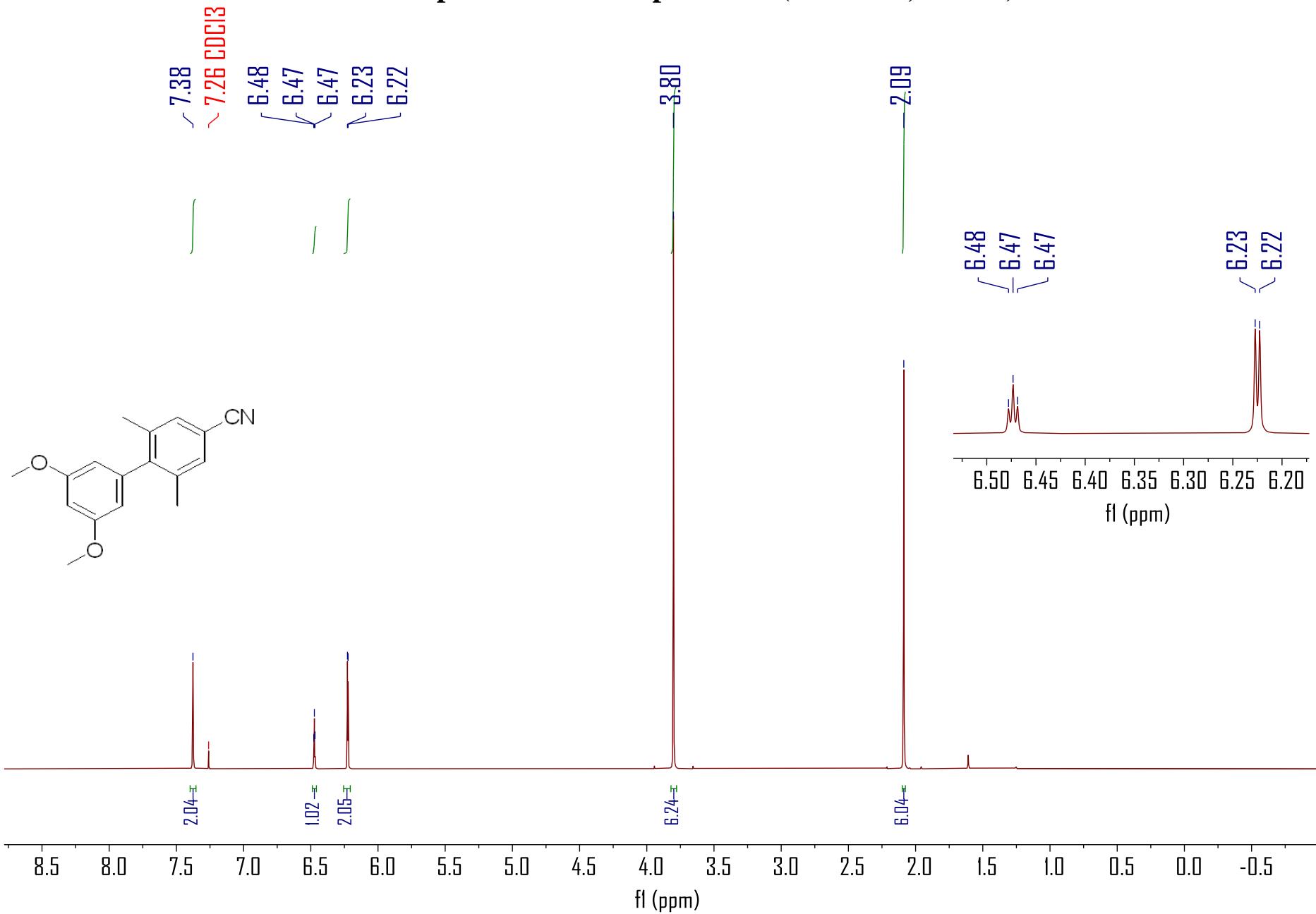
^1H NMR spectrum for compound 3u (500 MHz, CDCl_3)



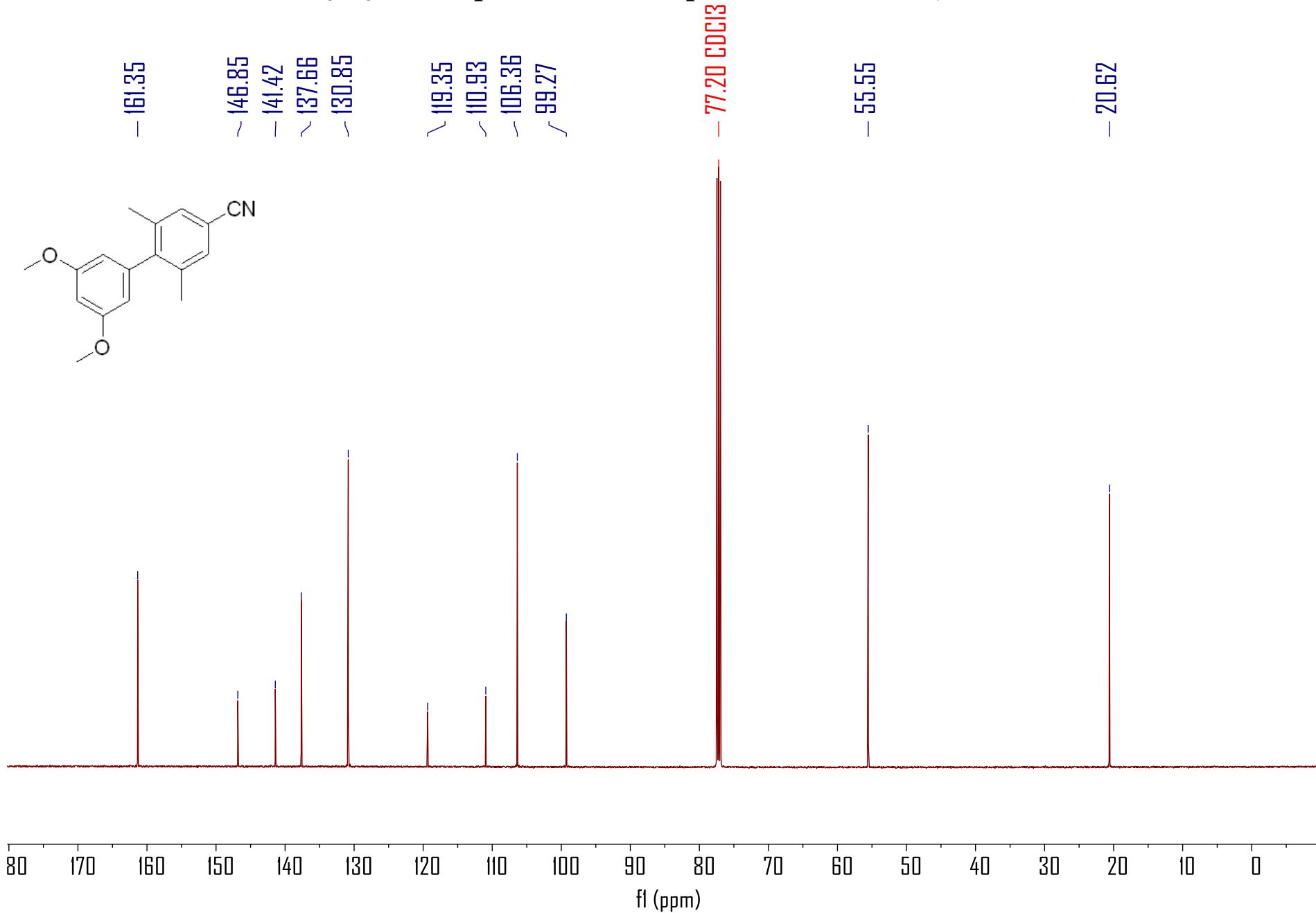
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum for compound 3u (125 MHz, CDCl_3)



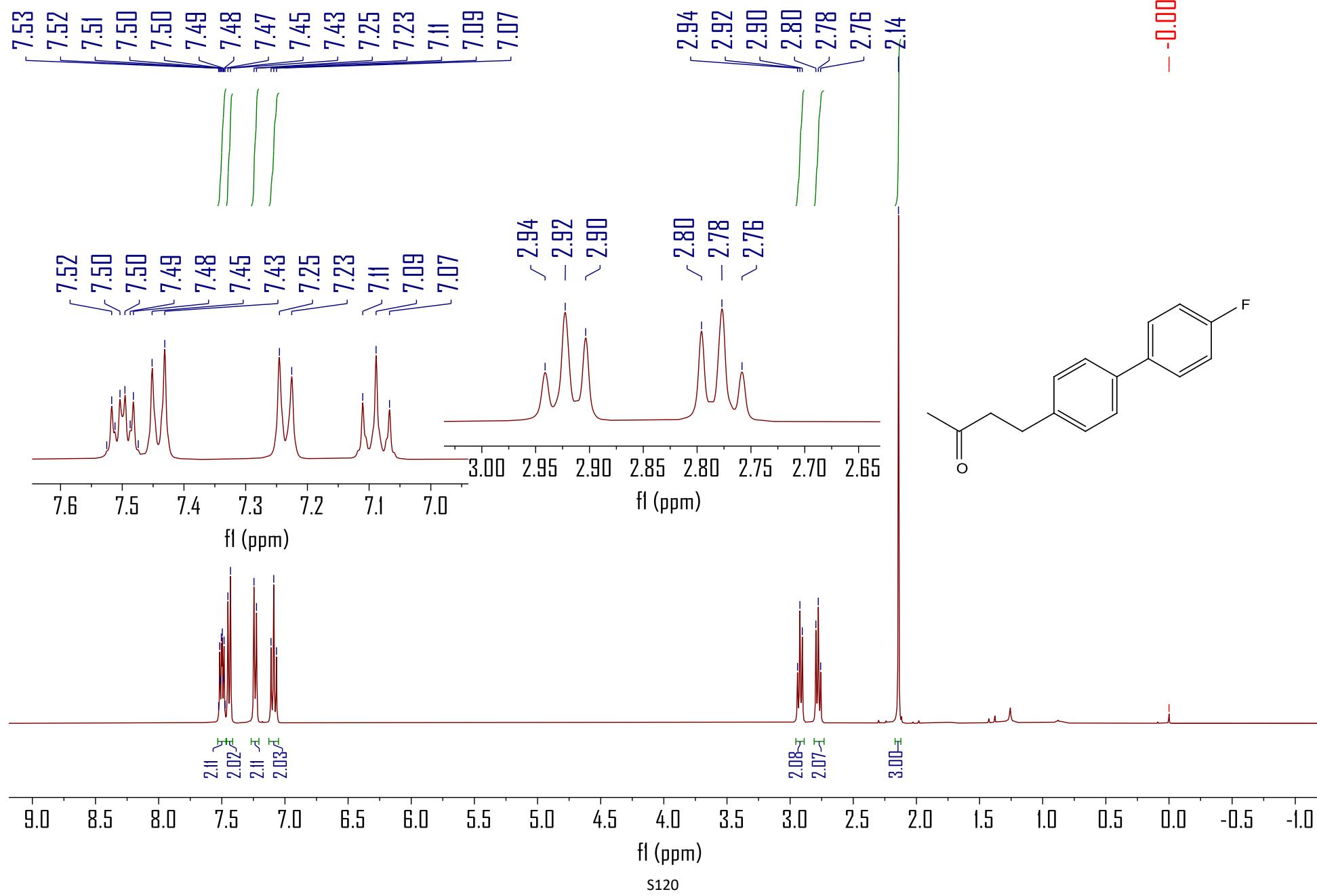
^1H NMR spectrum for compound 3v (500 MHz, CDCl_3)



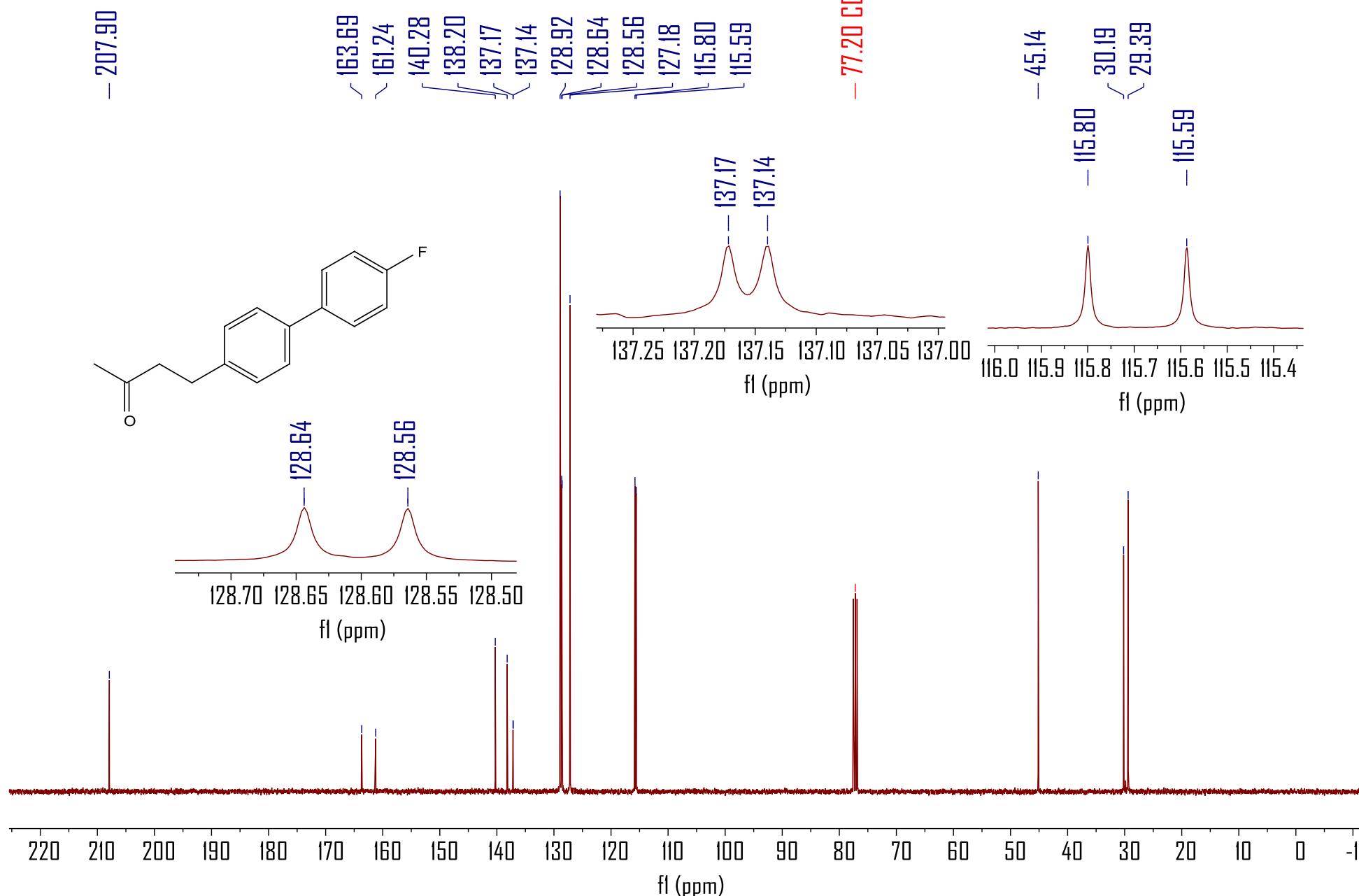
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum for compound 3v (125 MHz, CDCl_3)



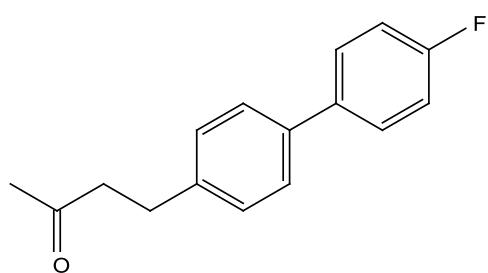
¹H NMR spectrum for compound 3w following general procedure A (400 MHz, CDCl₃, TMS)



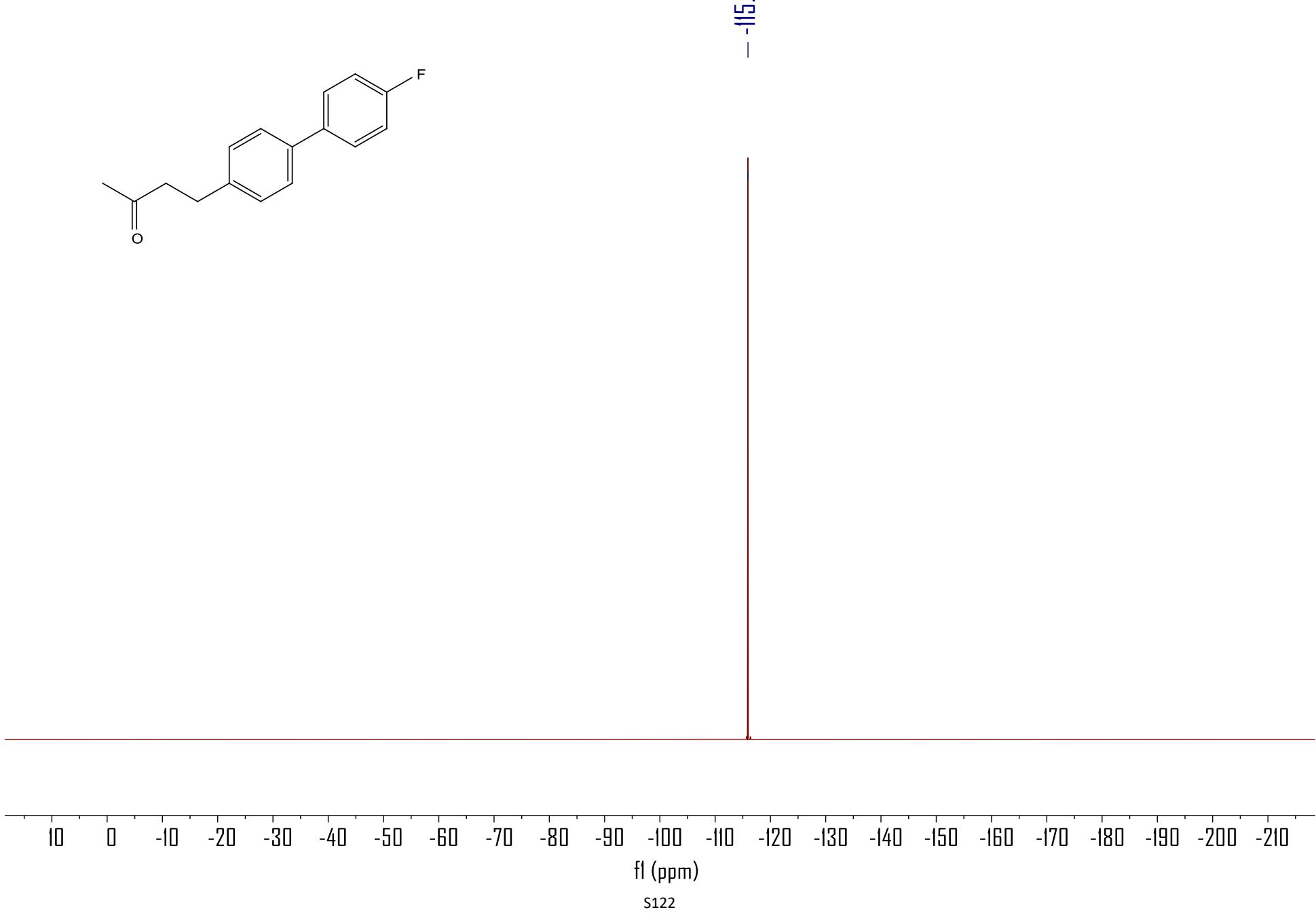
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum for compound 3w following general procedure A (100 MHz, CDCl_3)



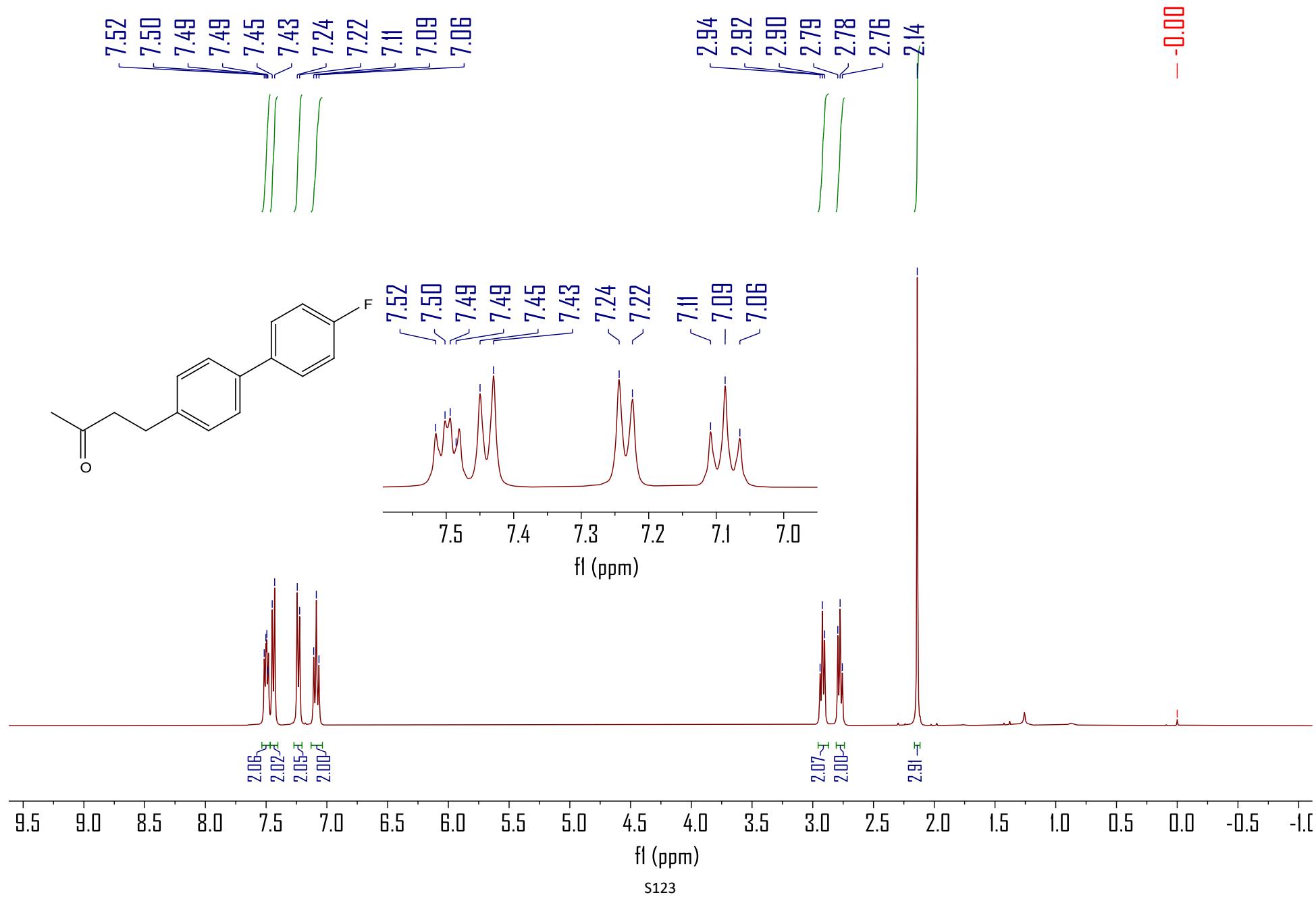
$^{19}\text{F}\{^1\text{H}\}$ NMR spectrum for compound 3w following general procedure A (376 MHz, CDCl_3)



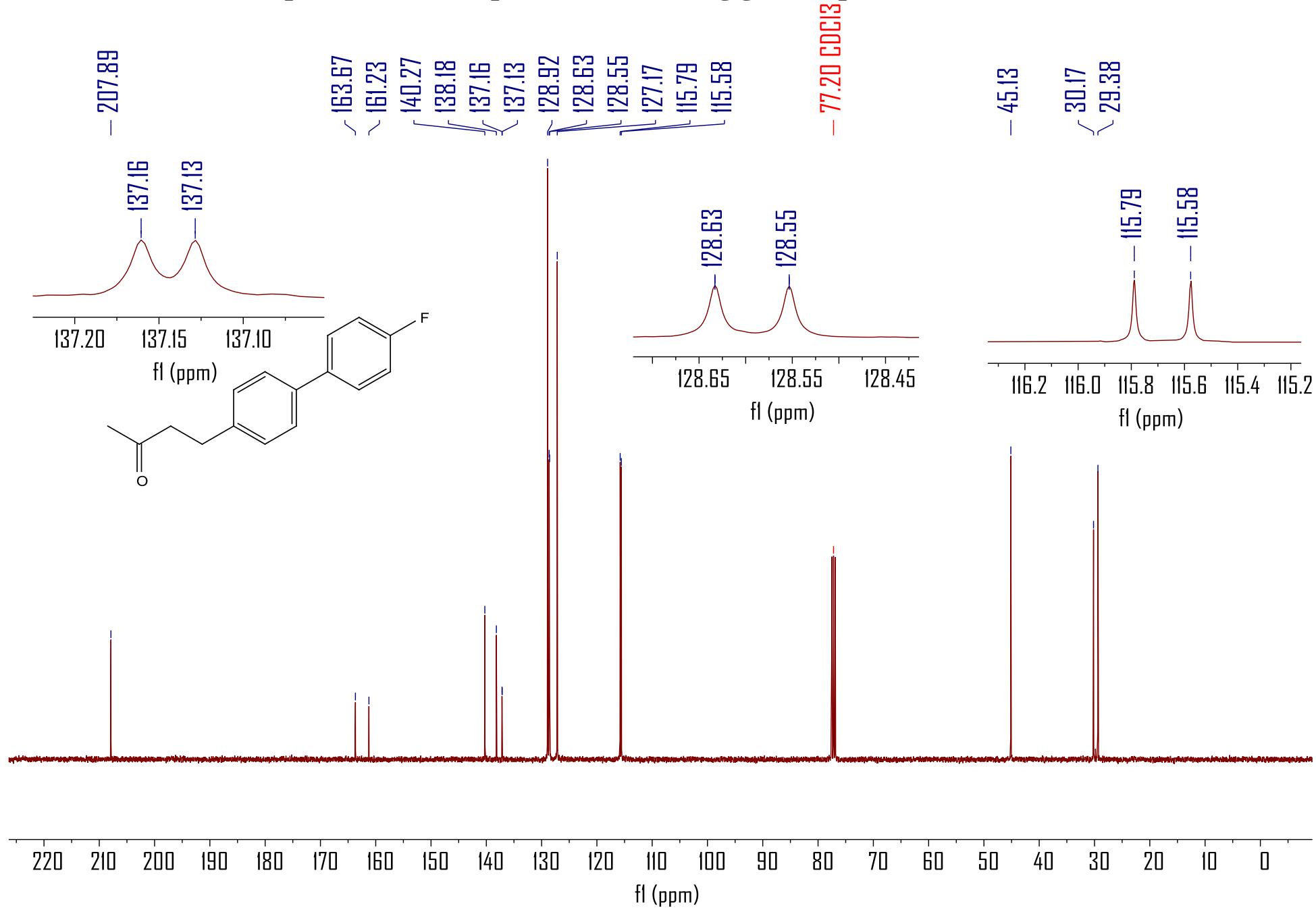
-115.94



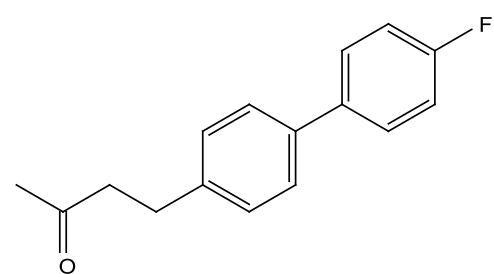
¹H NMR spectrum for compound 3w following general procedure B (400 MHz, CDCl₃, TMS)



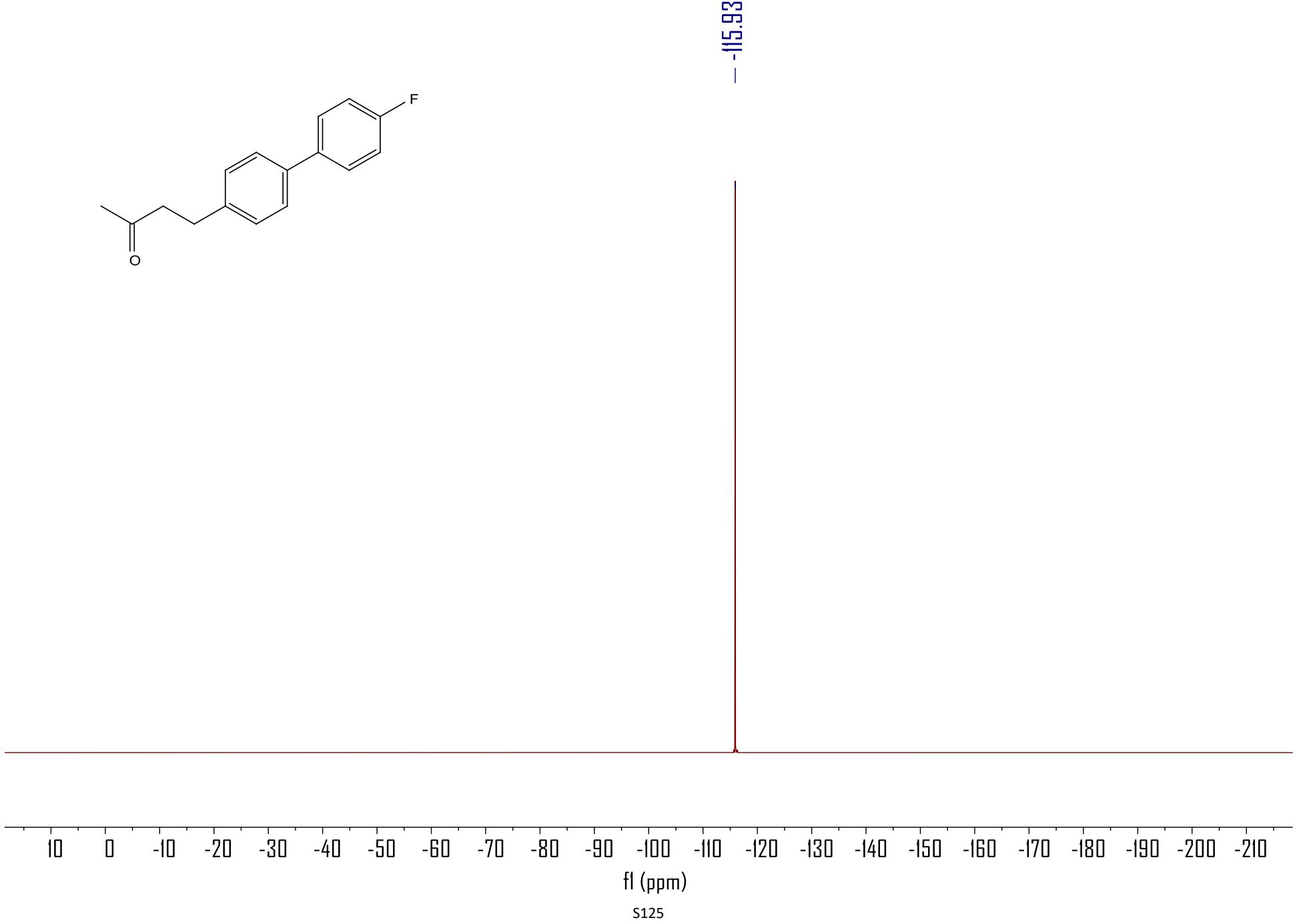
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum for compound 3w following general procedure B (100 MHz, CDCl_3)



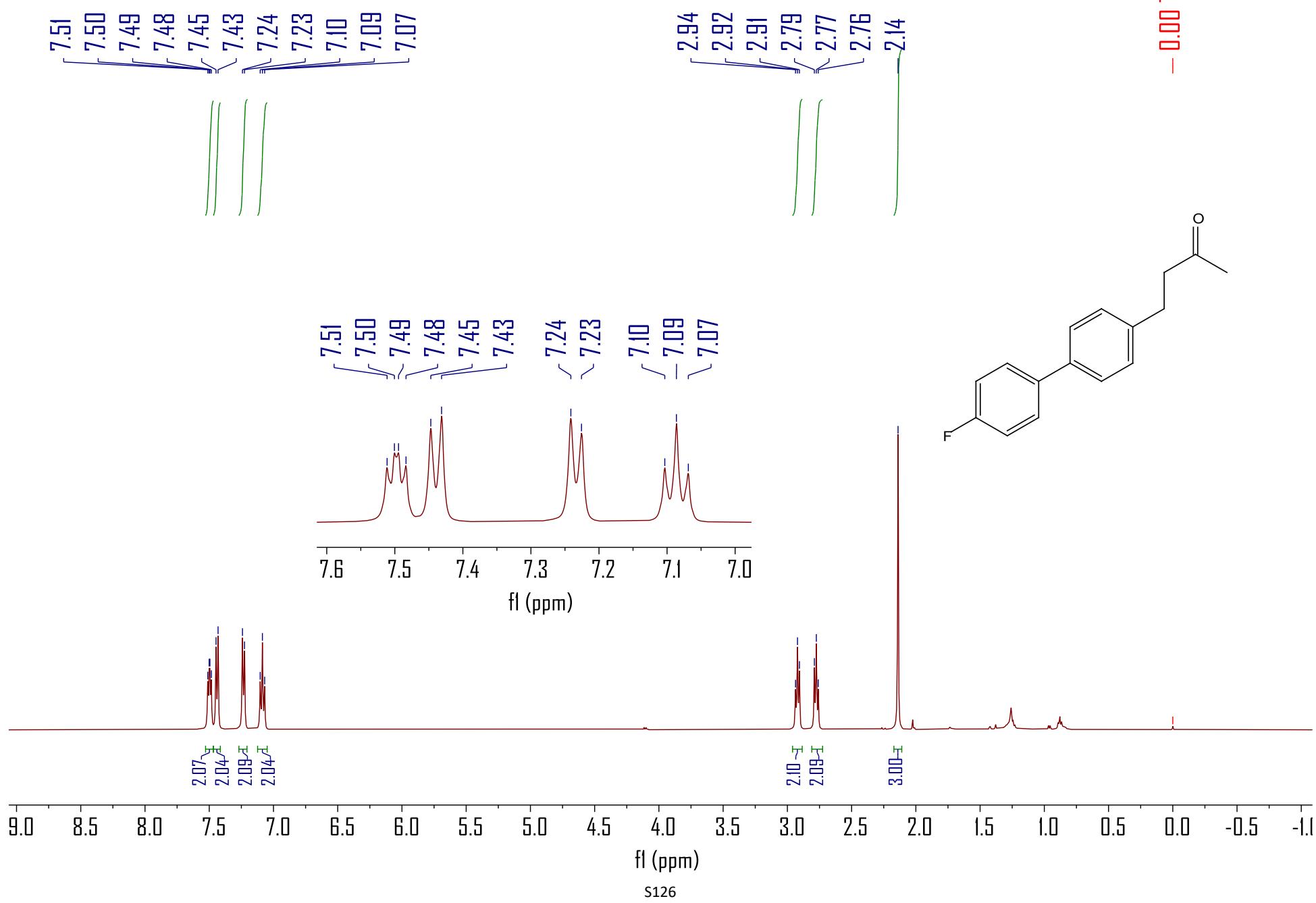
$^{19}\text{F}\{^1\text{H}\}$ NMR spectrum for compound 3w following general procedure B (376 MHz, CDCl_3)



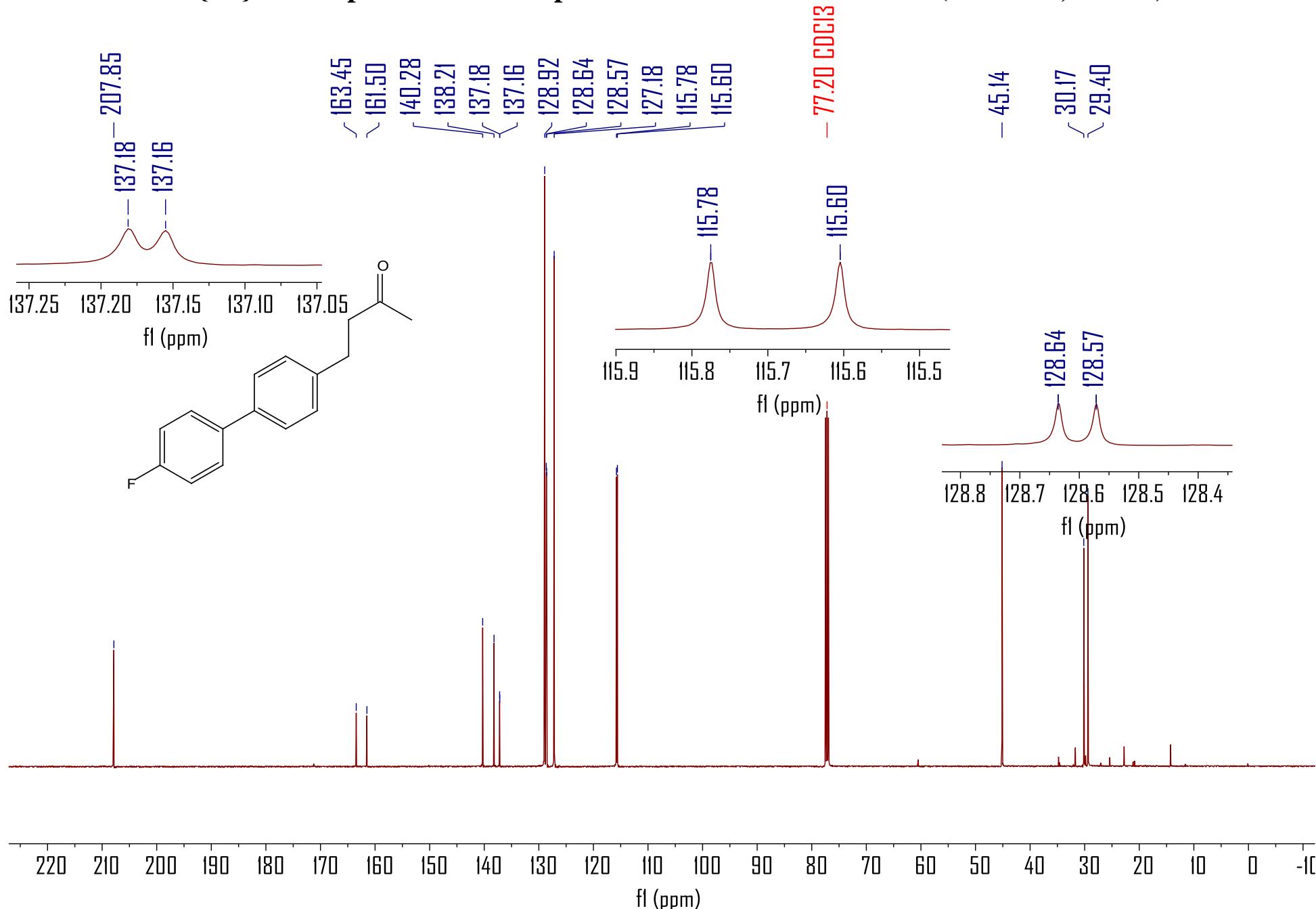
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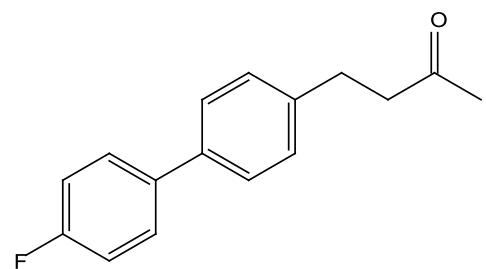
¹H NMR spectrum for compound 3w from 5.0 mmol scale (500 MHz, CDCl₃, TMS)



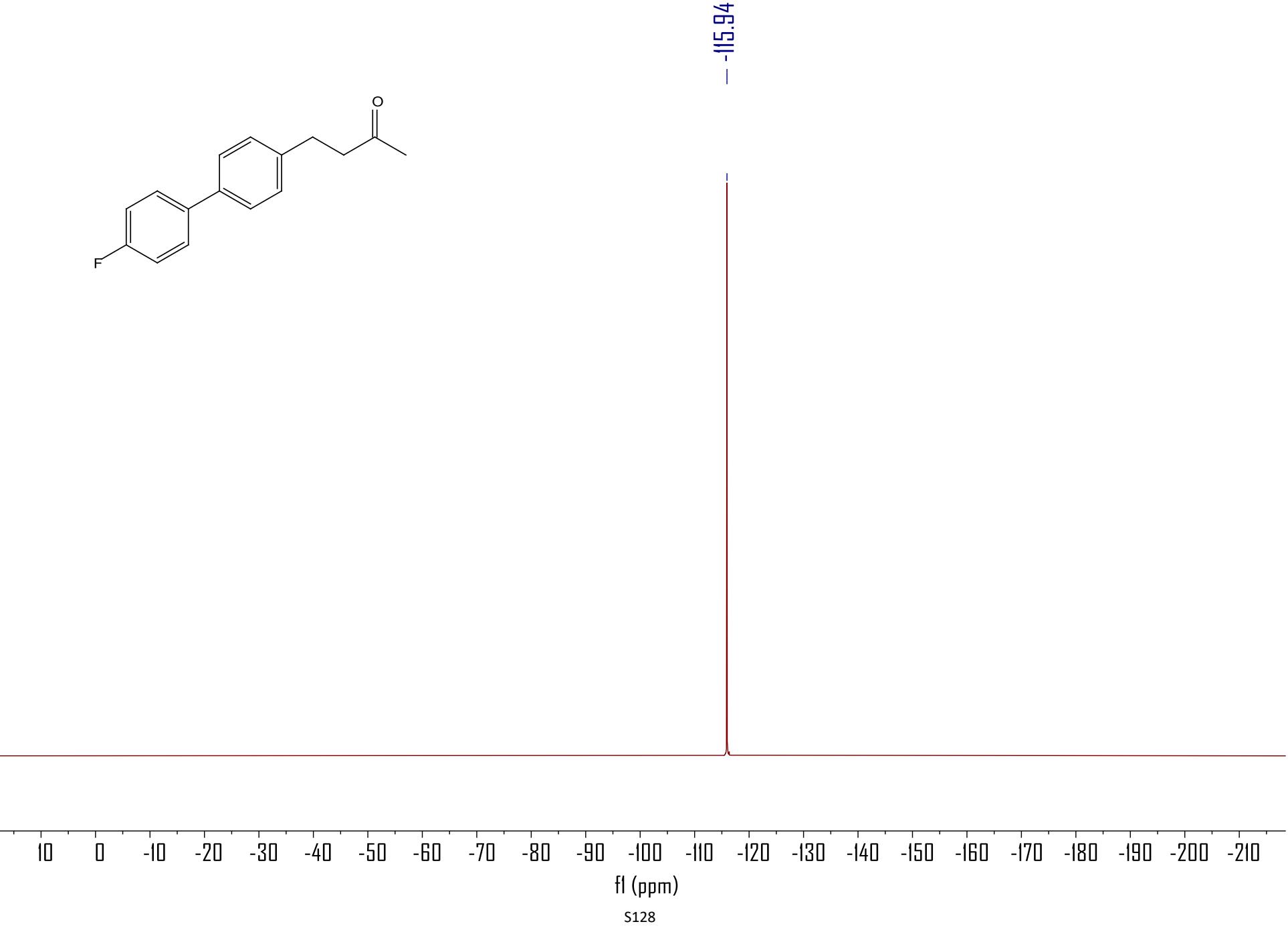
¹³C{¹H} NMR spectrum for compound 3w from 5.0 mmol scale (125 MHz, CDCl₃)



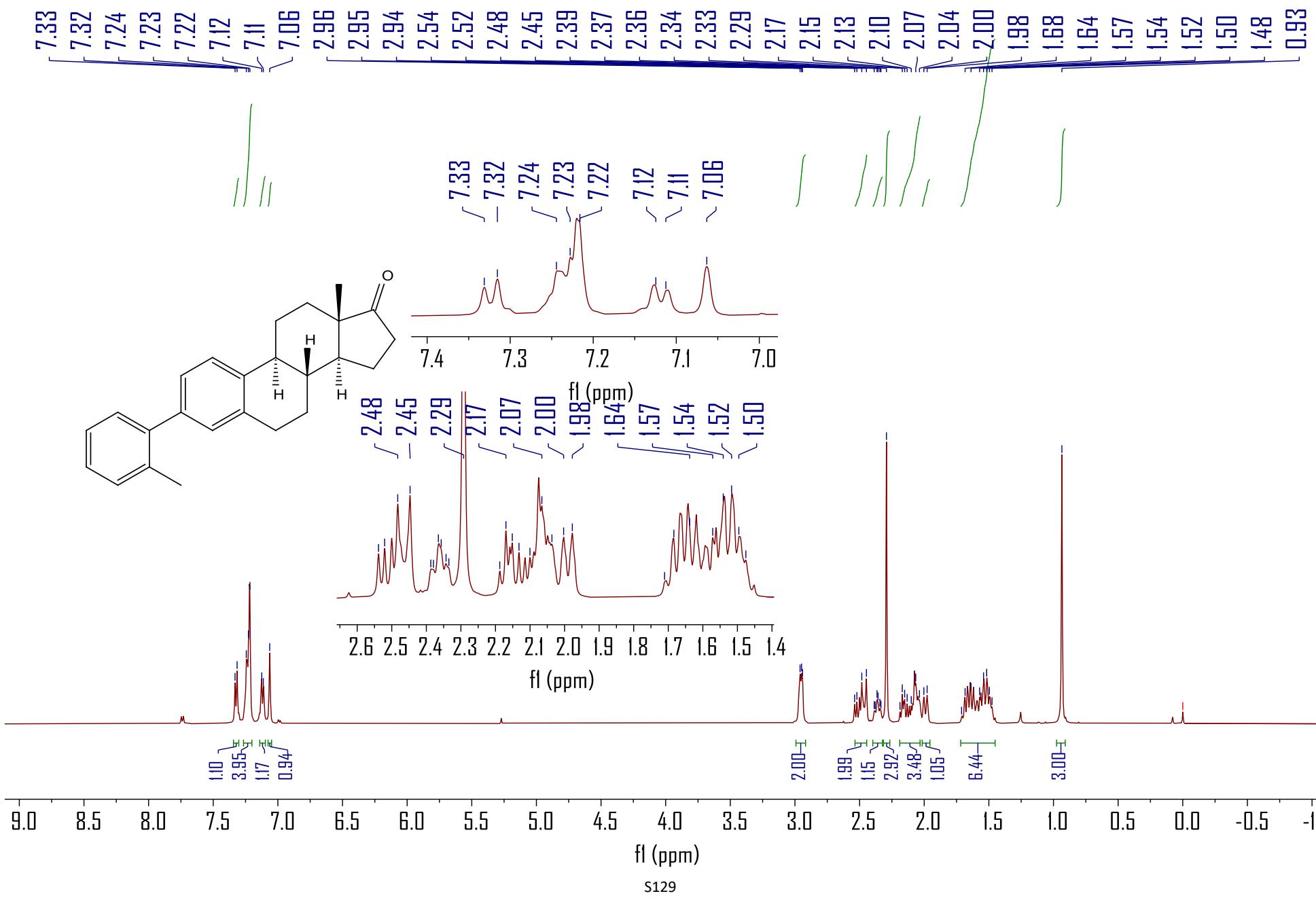
$^{19}\text{F}\{^1\text{H}\}$ NMR spectrum for compound 3w from 5.0 mmol scale (376 MHz, CDCl_3)



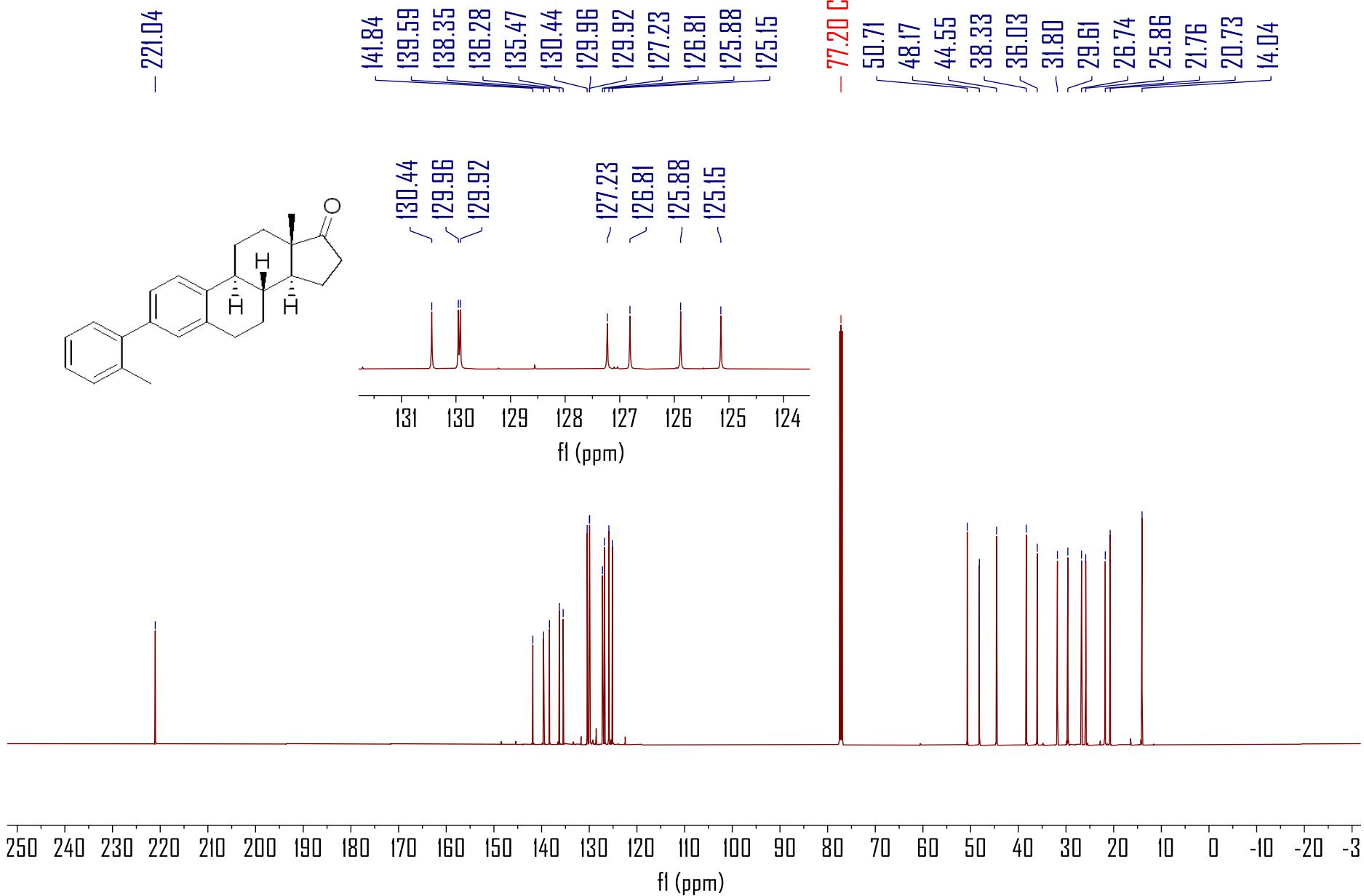
-115.94



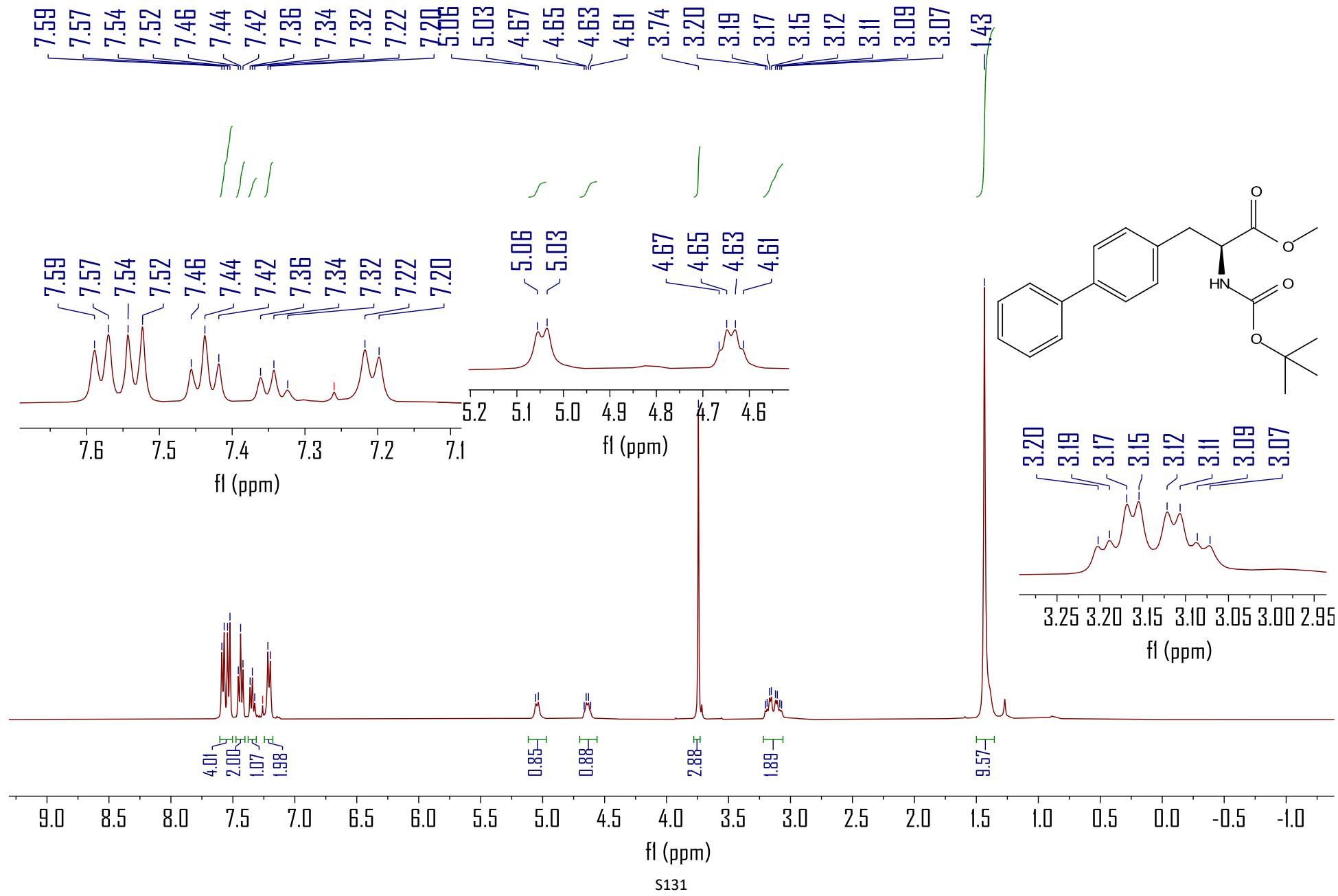
¹H NMR spectrum for compound 3x (500 MHz, CDCl₃, TMS)



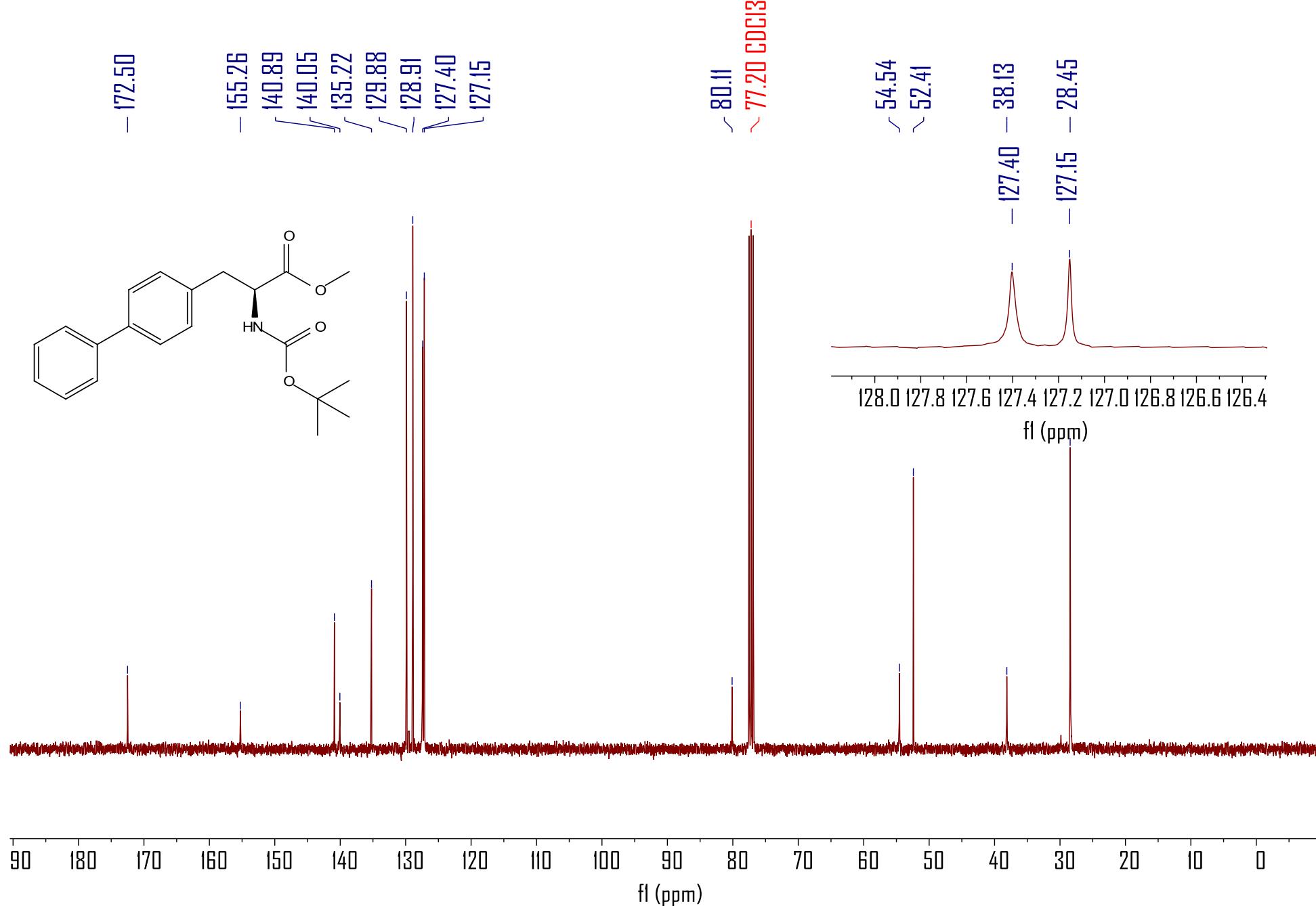
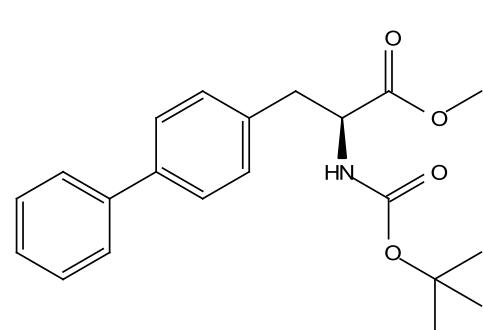
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum for compound 3x (125 MHz, CDCl_3)



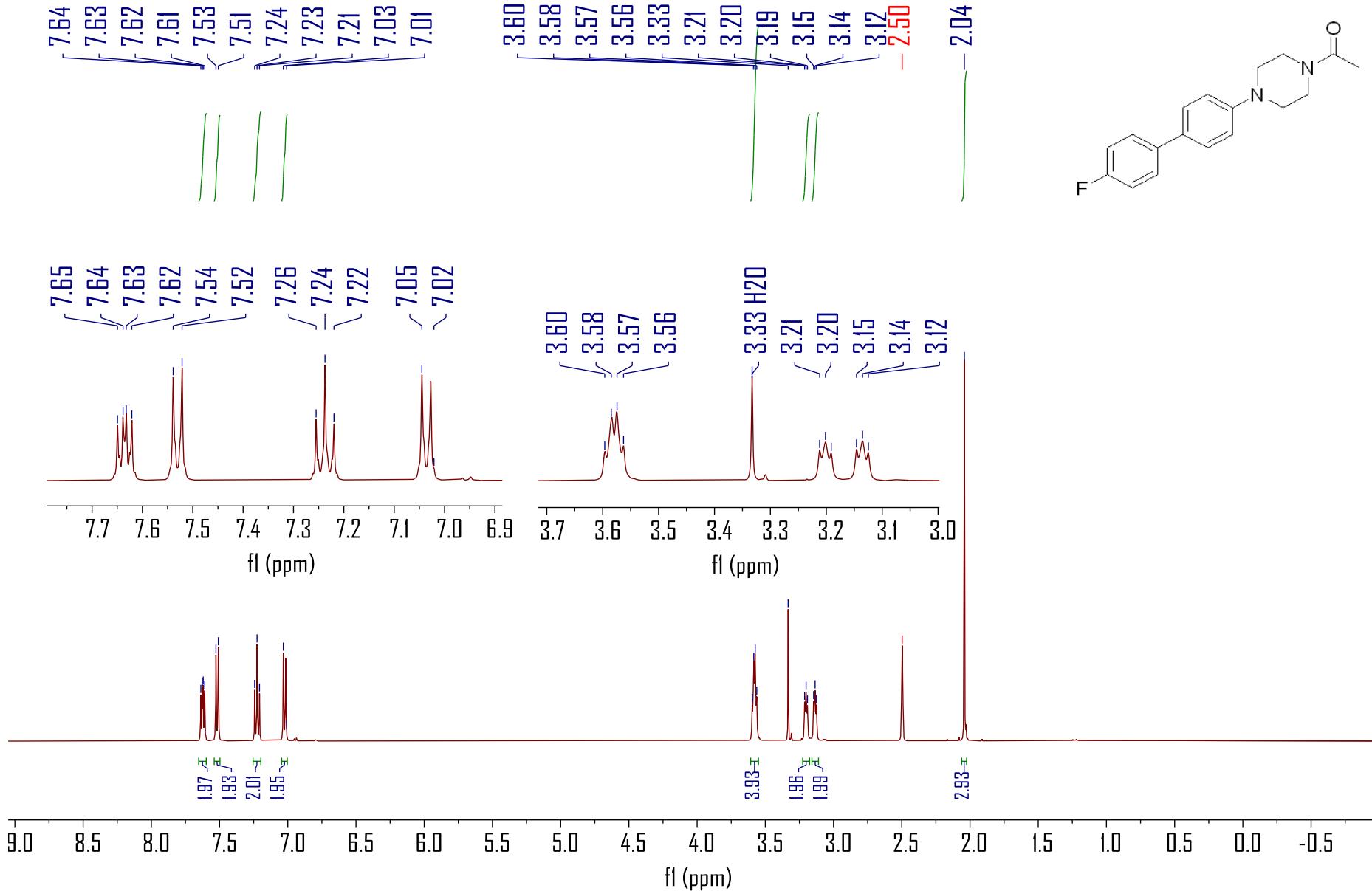
¹H NMR spectrum for compound 3y (400 MHz, CDCl₃)



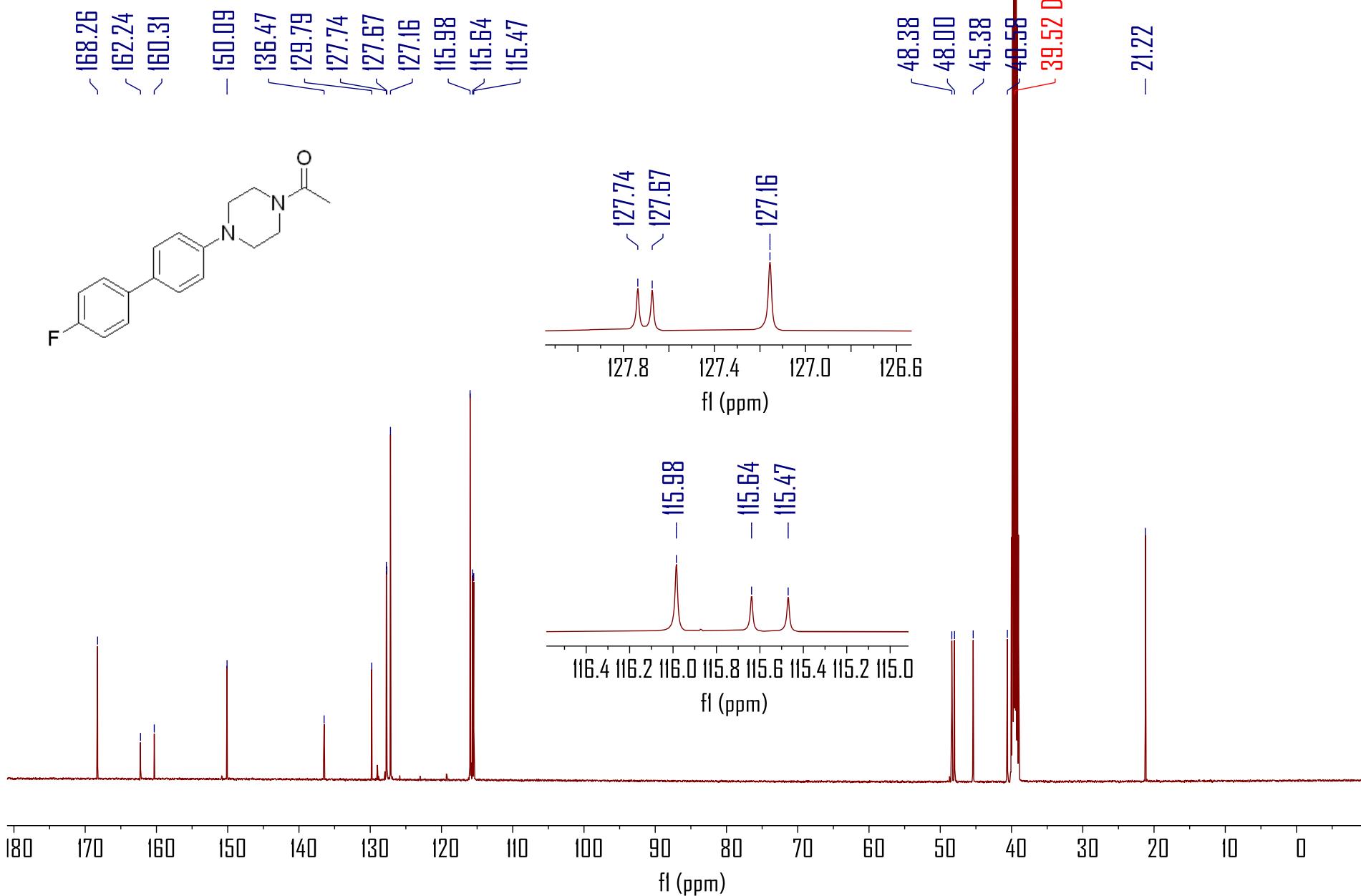
¹³C{¹H} NMR spectrum for compound 3y (100 MHz, CDCl₃)



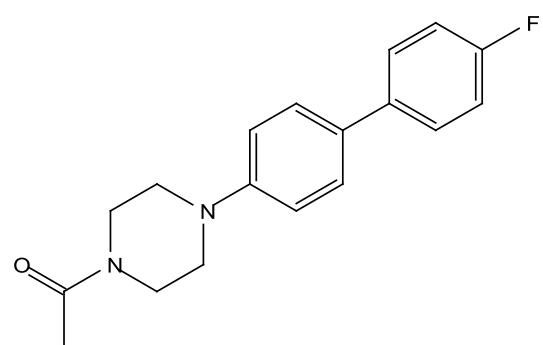
¹H NMR spectrum for compound 3z (500 MHz, DMSO-d₆)



$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum for compound 3z (DMSO-d₆, 125 MHz)



$^{19}\text{F}\{^1\text{H}\}$ NMR spectrum for compound 3z (DMSO- d_6 , 376 MHz)

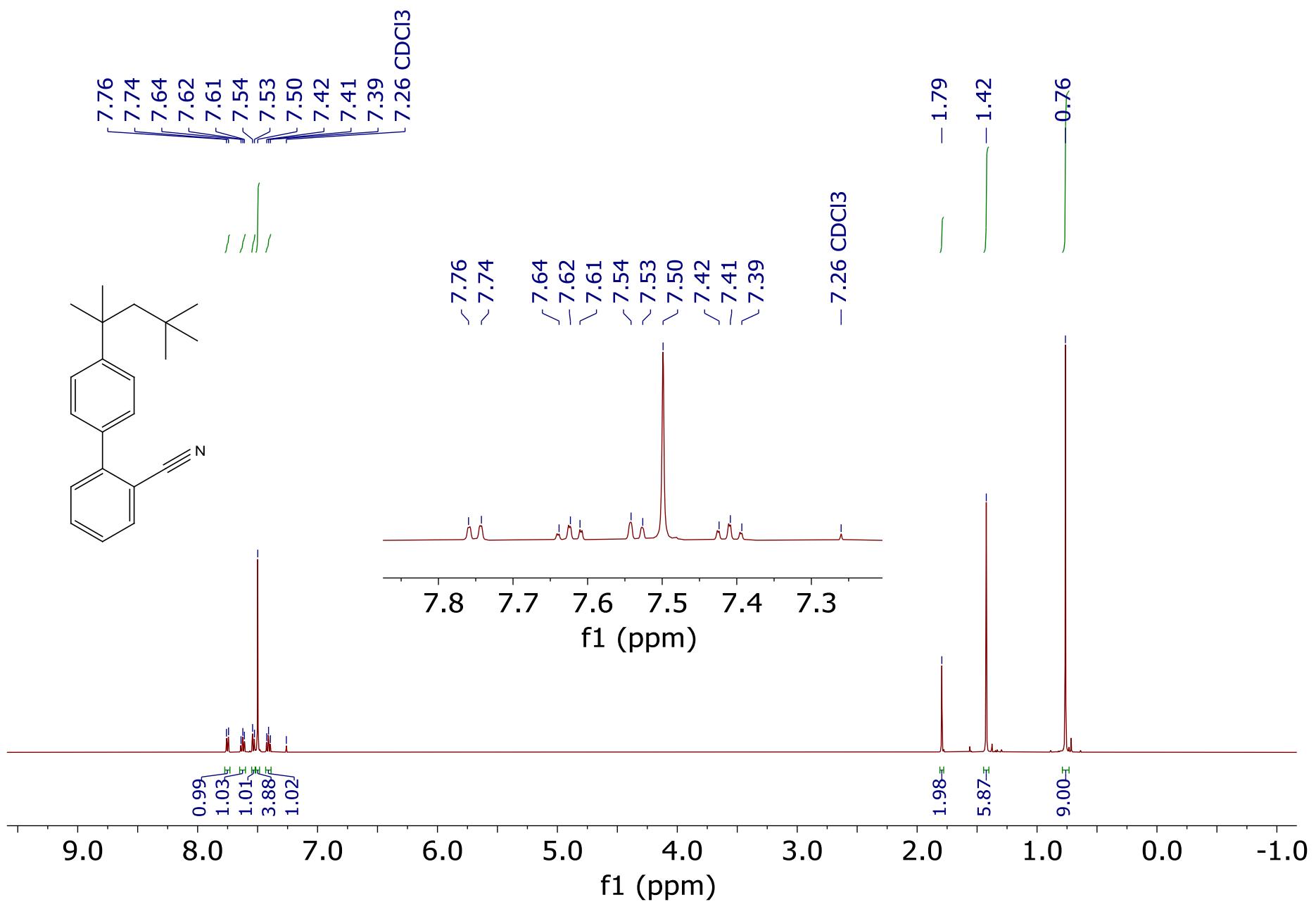


-116.94

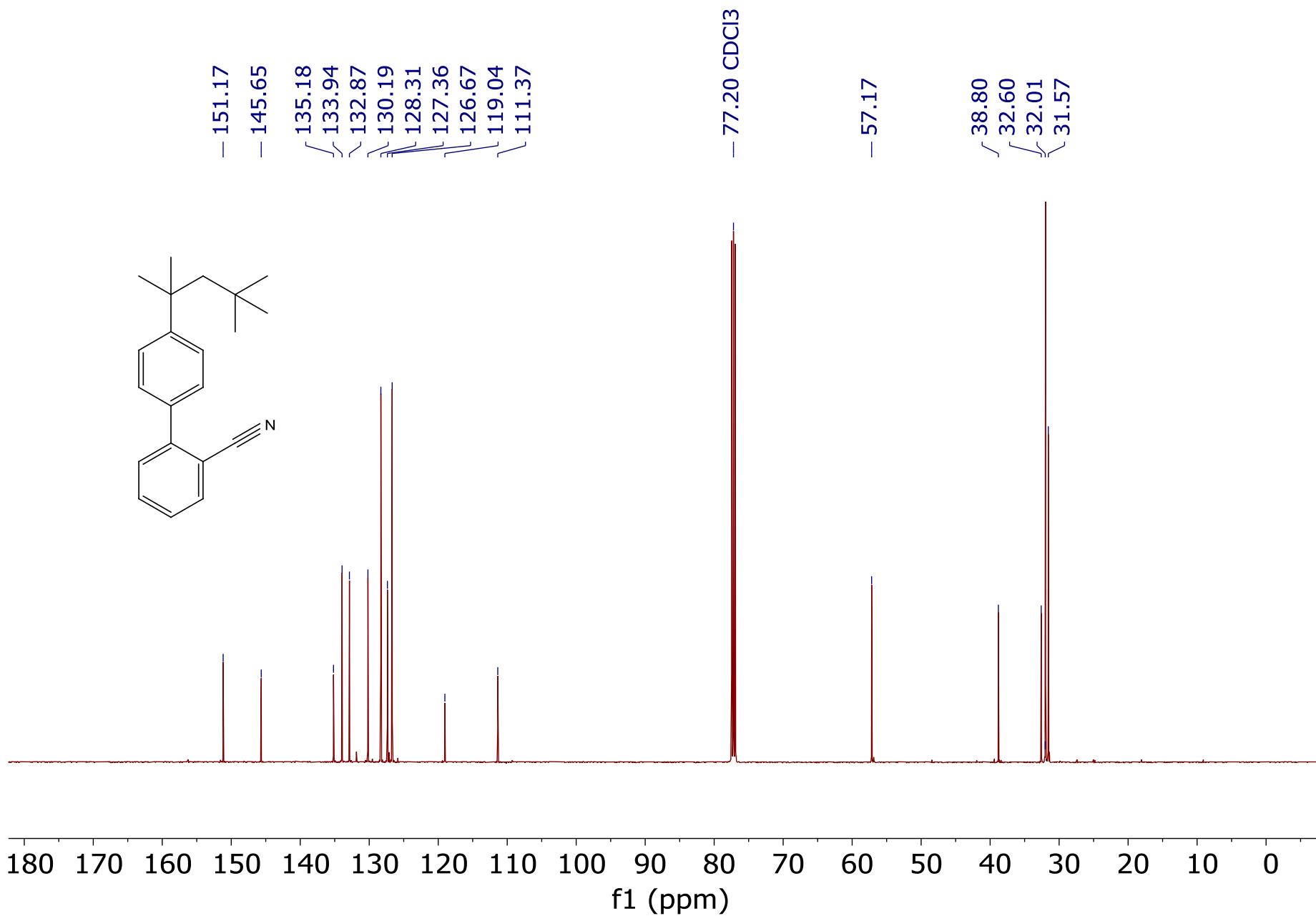
f_1 (ppm)

S135

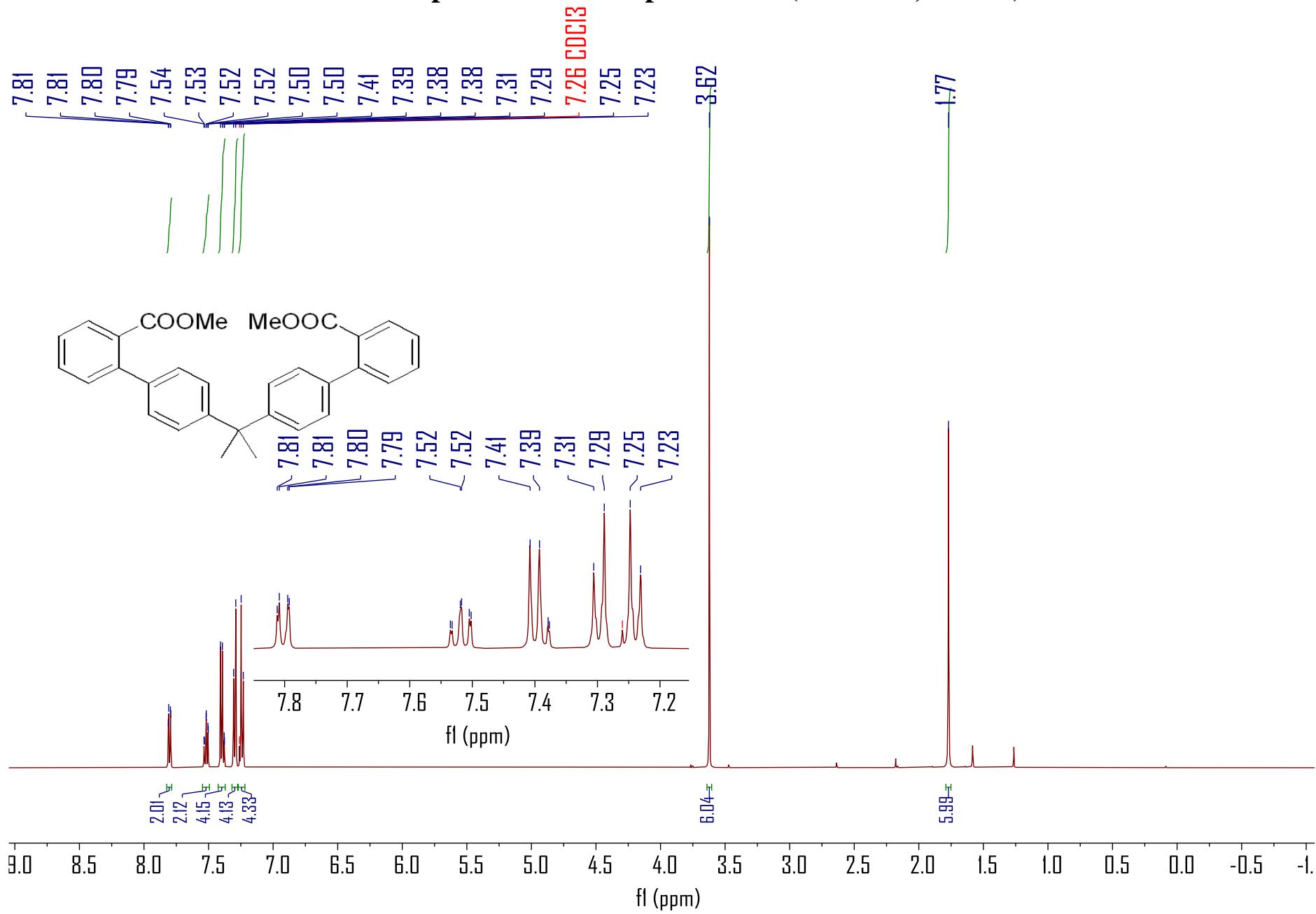
¹H NMR spectrum for compound 3aa (500 MHz, CDCl₃)



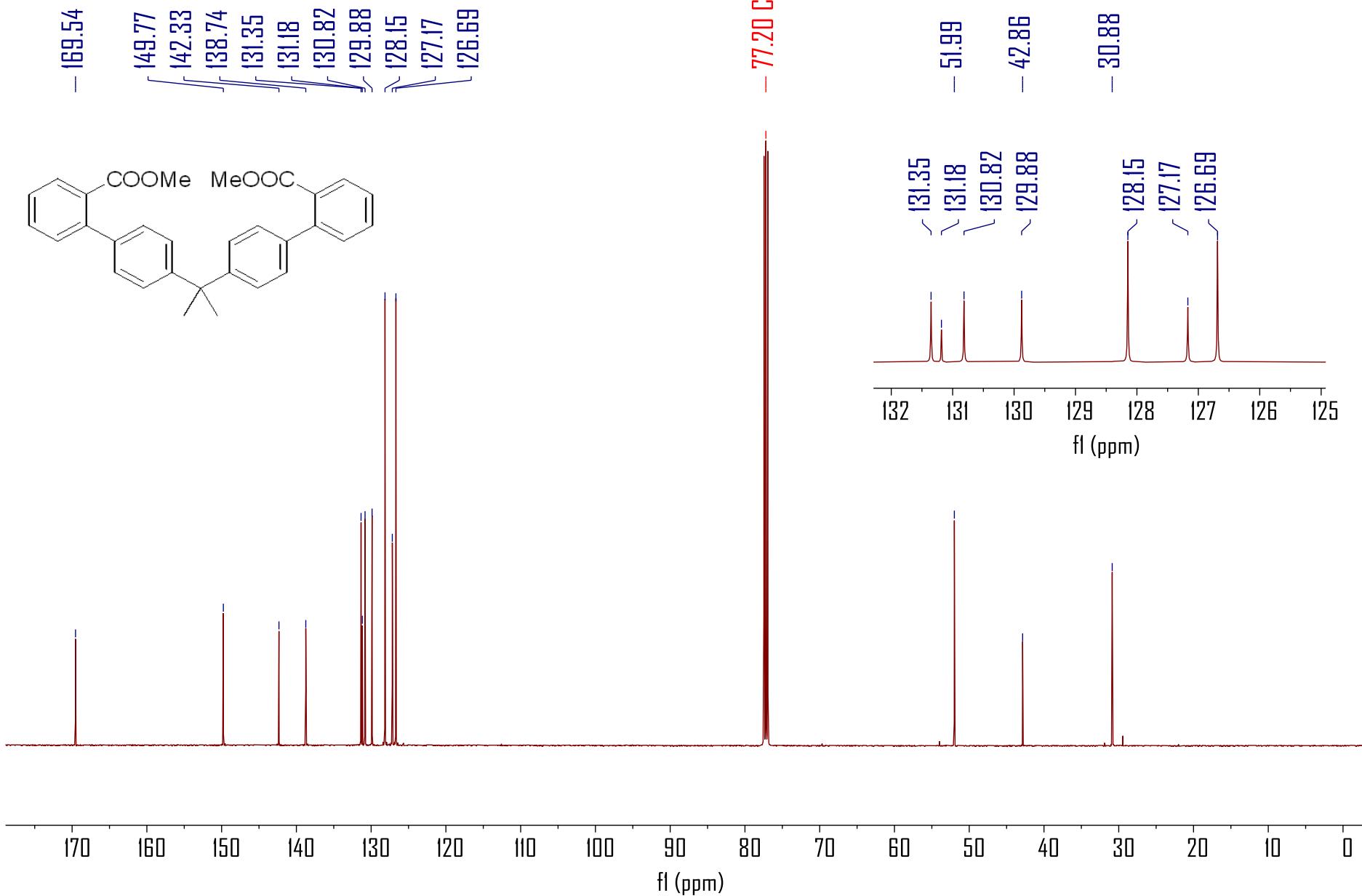
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum for compound 3aa (125 MHz, CDCl_3)



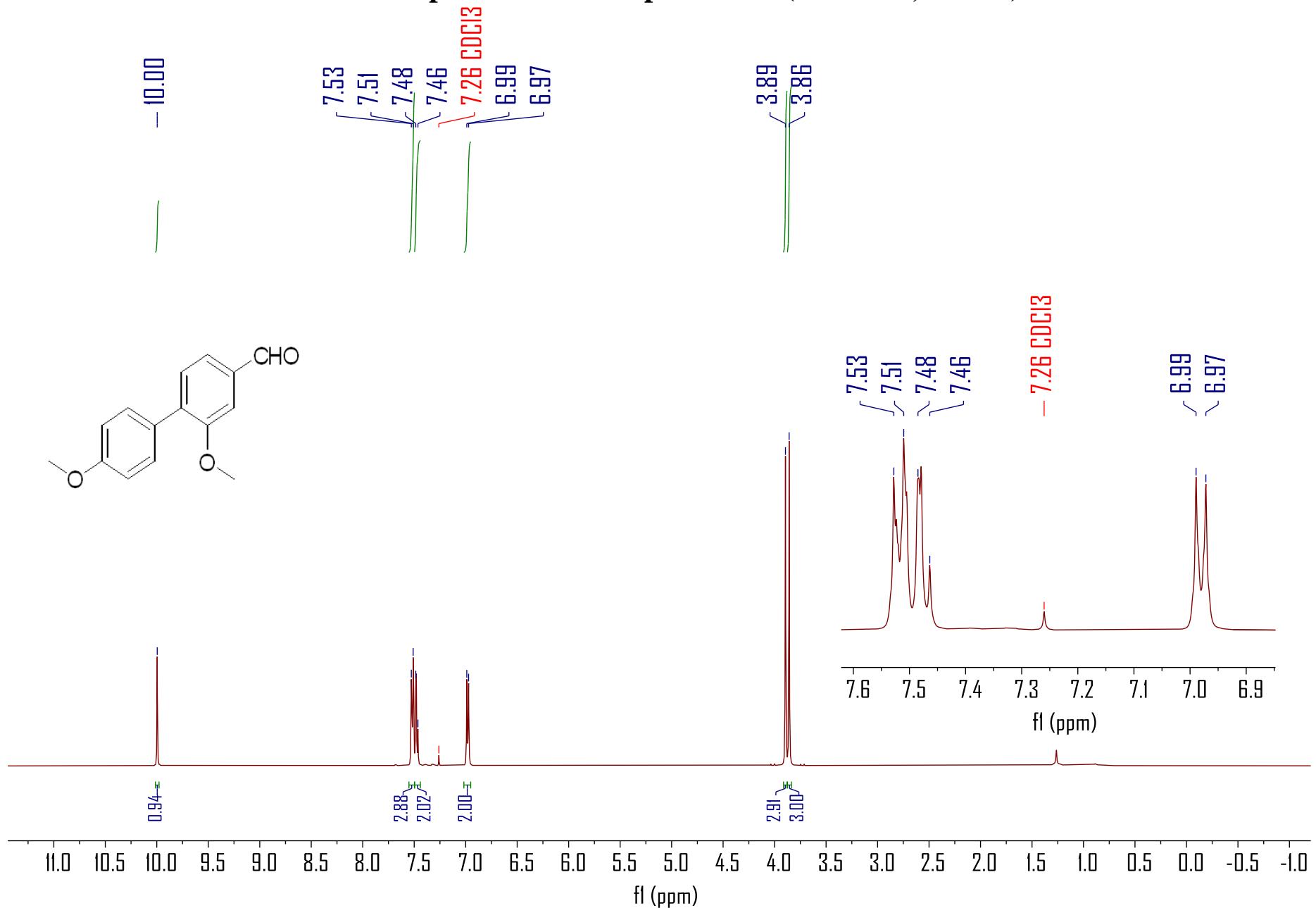
¹H NMR spectrum for compound 3ab (500 MHz, CDCl₃)



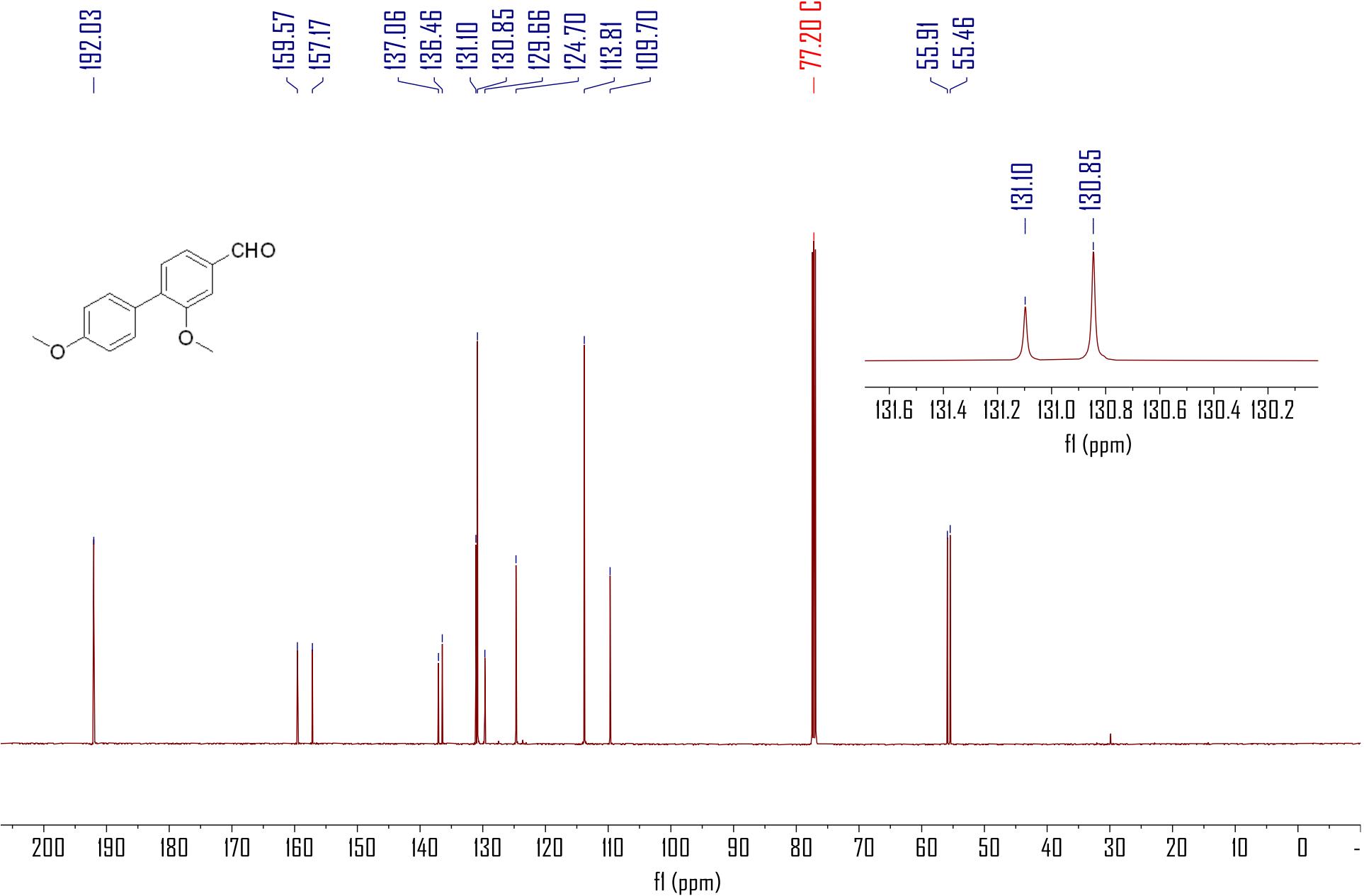
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum for compound 3ab (125 MHz, CDCl_3)



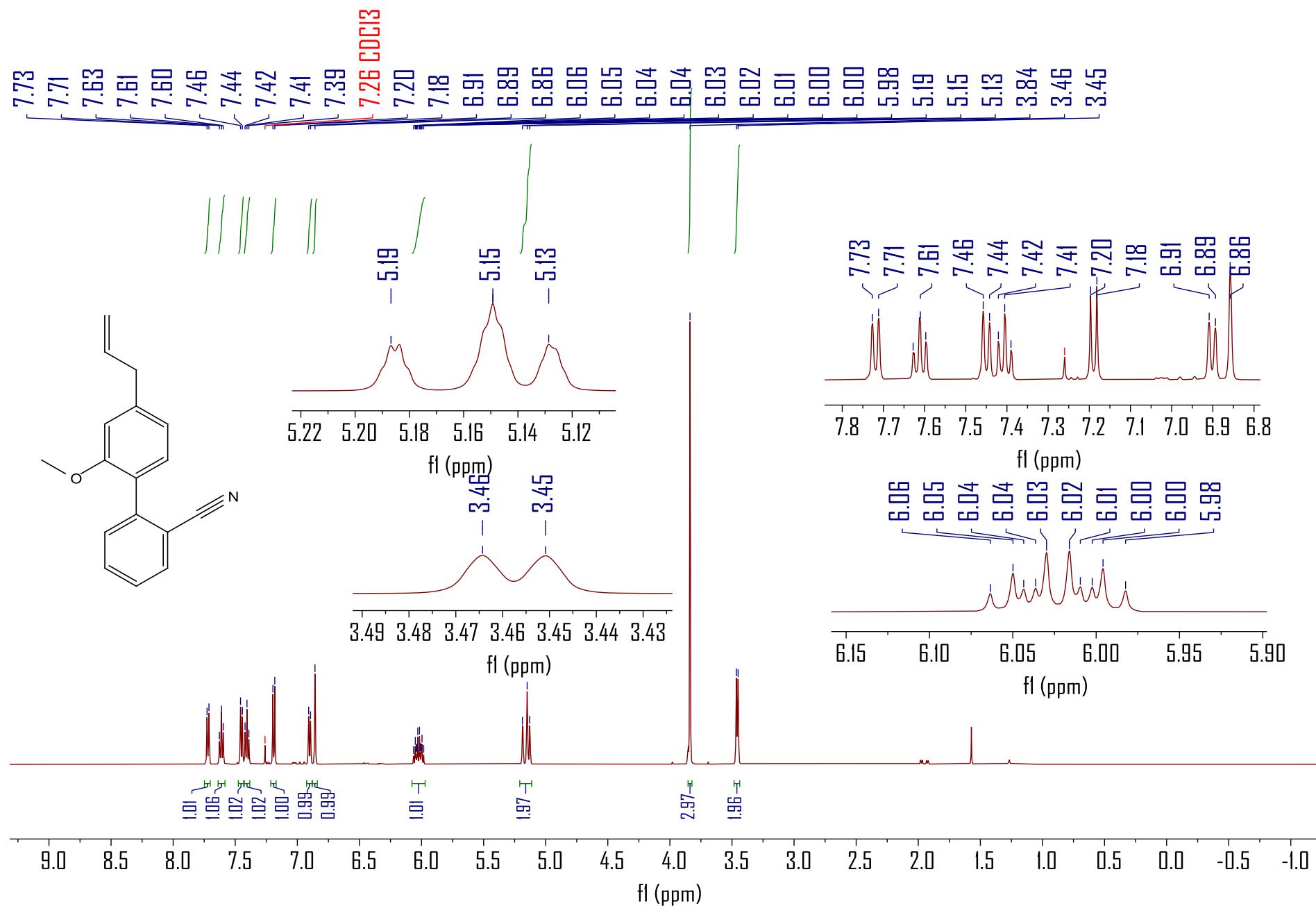
¹H NMR spectrum for compound 3ac (500 MHz, CDCl₃)



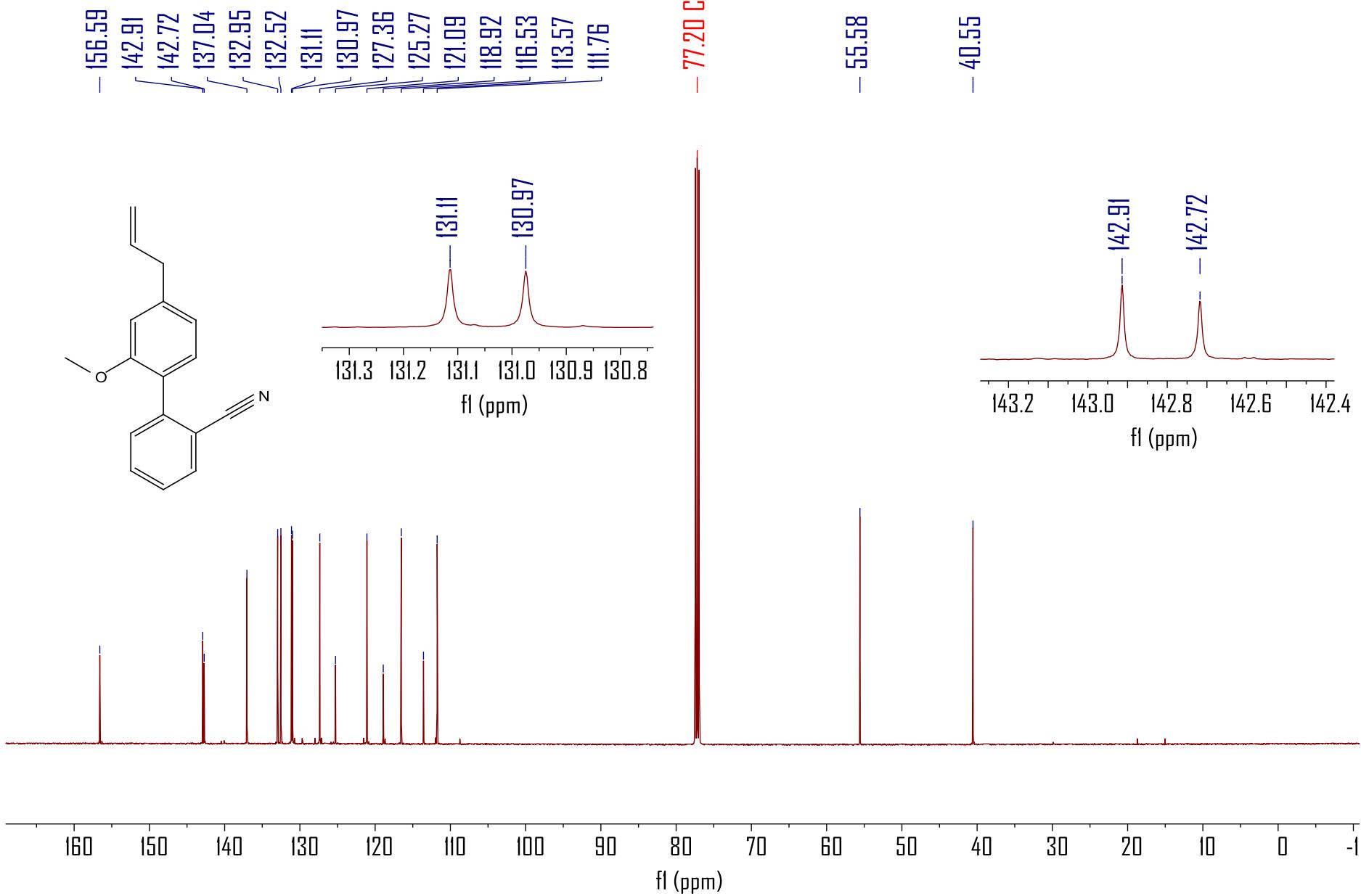
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum for compound 3ac (125 MHz, CDCl_3)



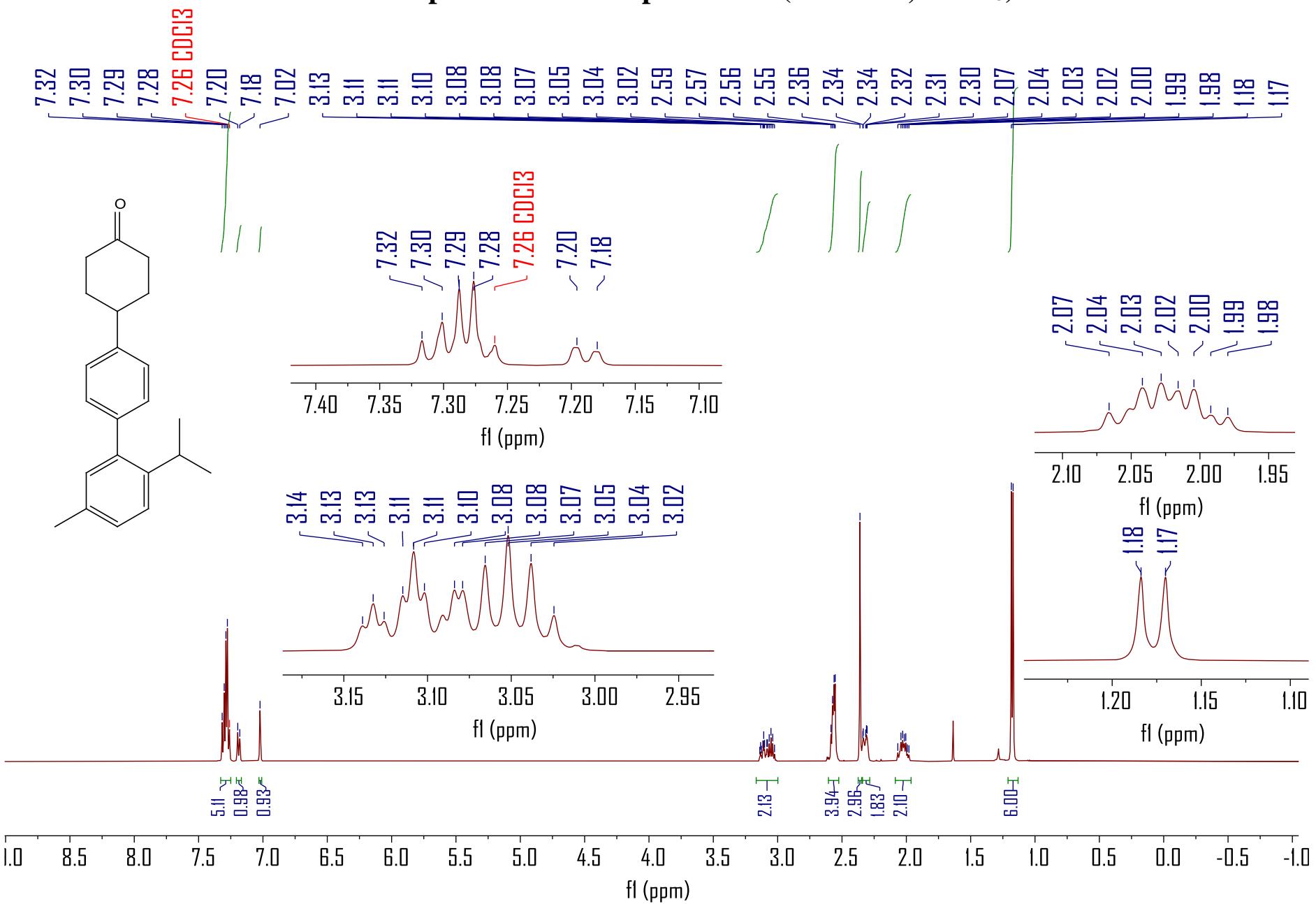
¹H NMR spectrum for compound 3ad (500 MHz, CDCl₃)



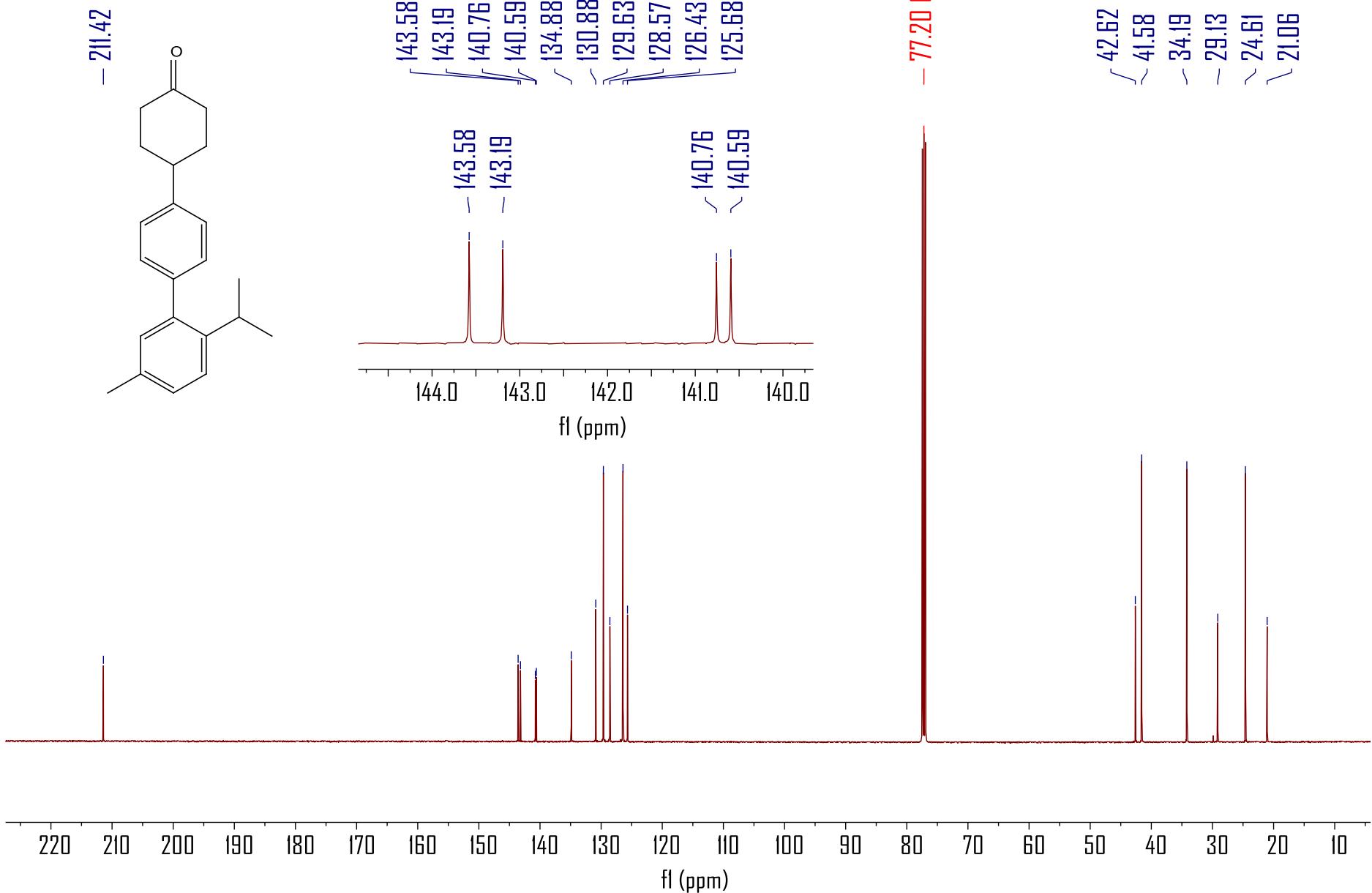
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum for compound 3ad (125 MHz, CDCl_3)



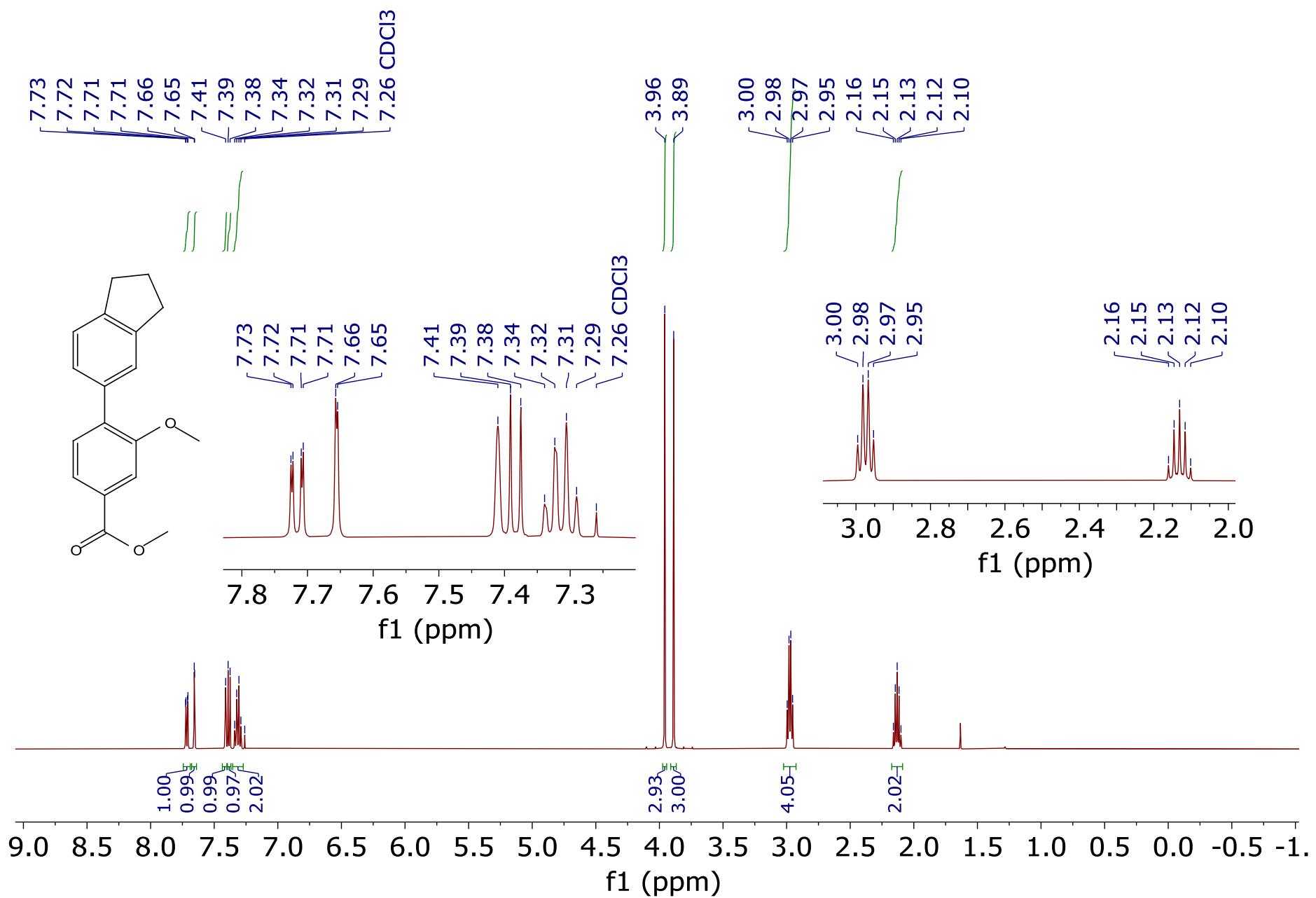
¹H NMR spectrum for compound 3ae (500 MHz, CDCl₃)



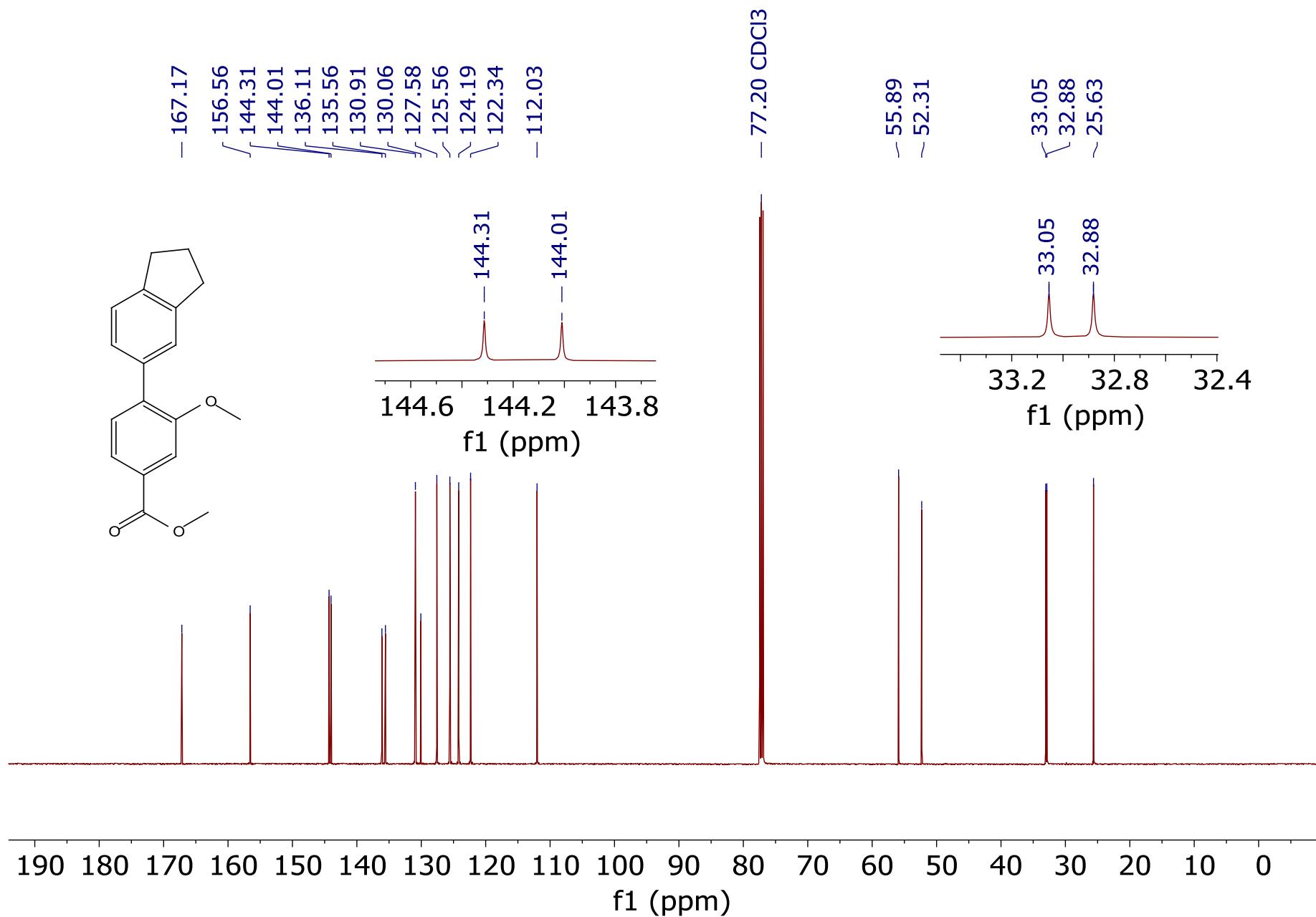
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum for compound 3ae (125 MHz, CDCl_3)



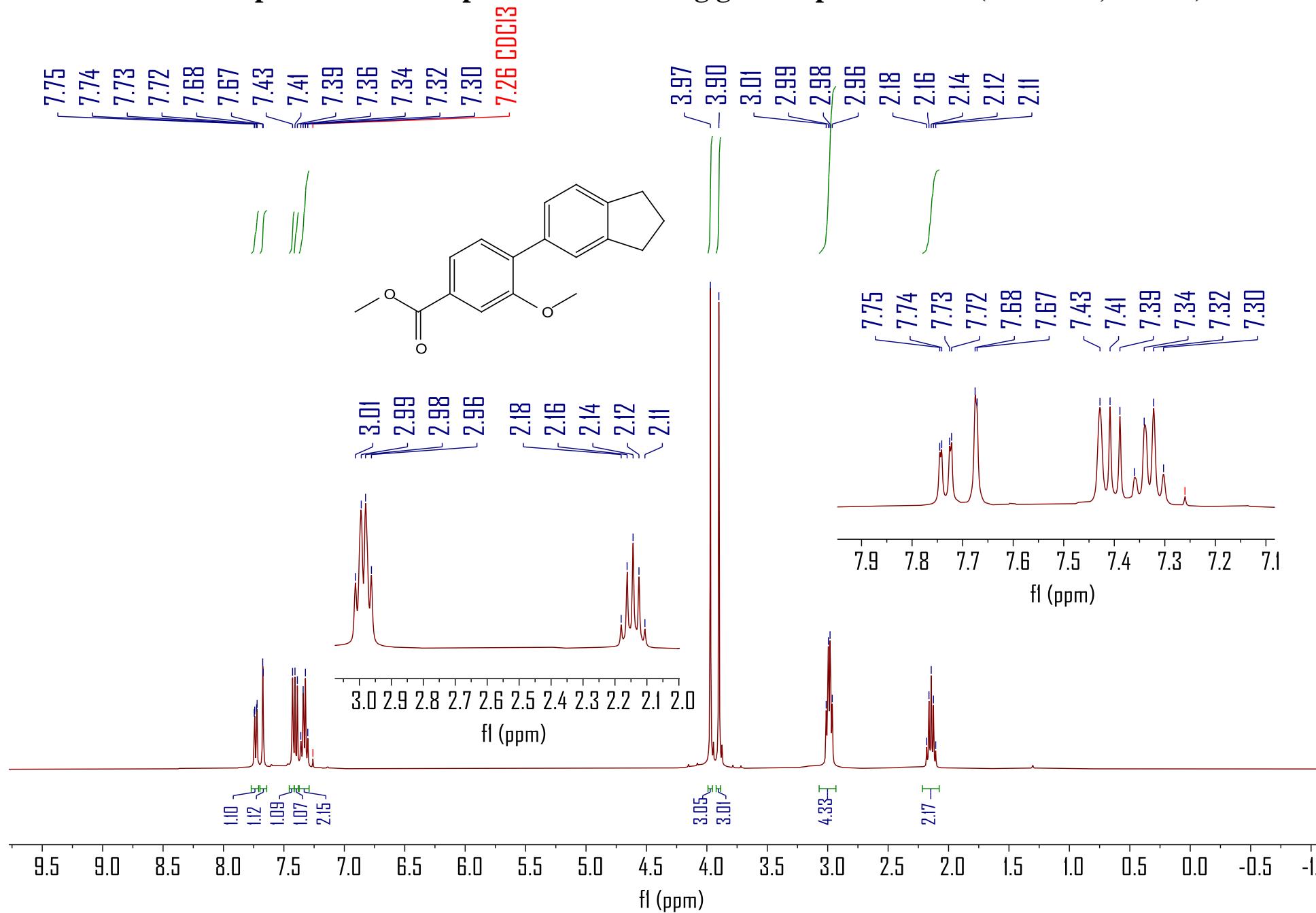
^1H NMR spectrum for compound 3af following general procedure A (500 MHz, CDCl_3)



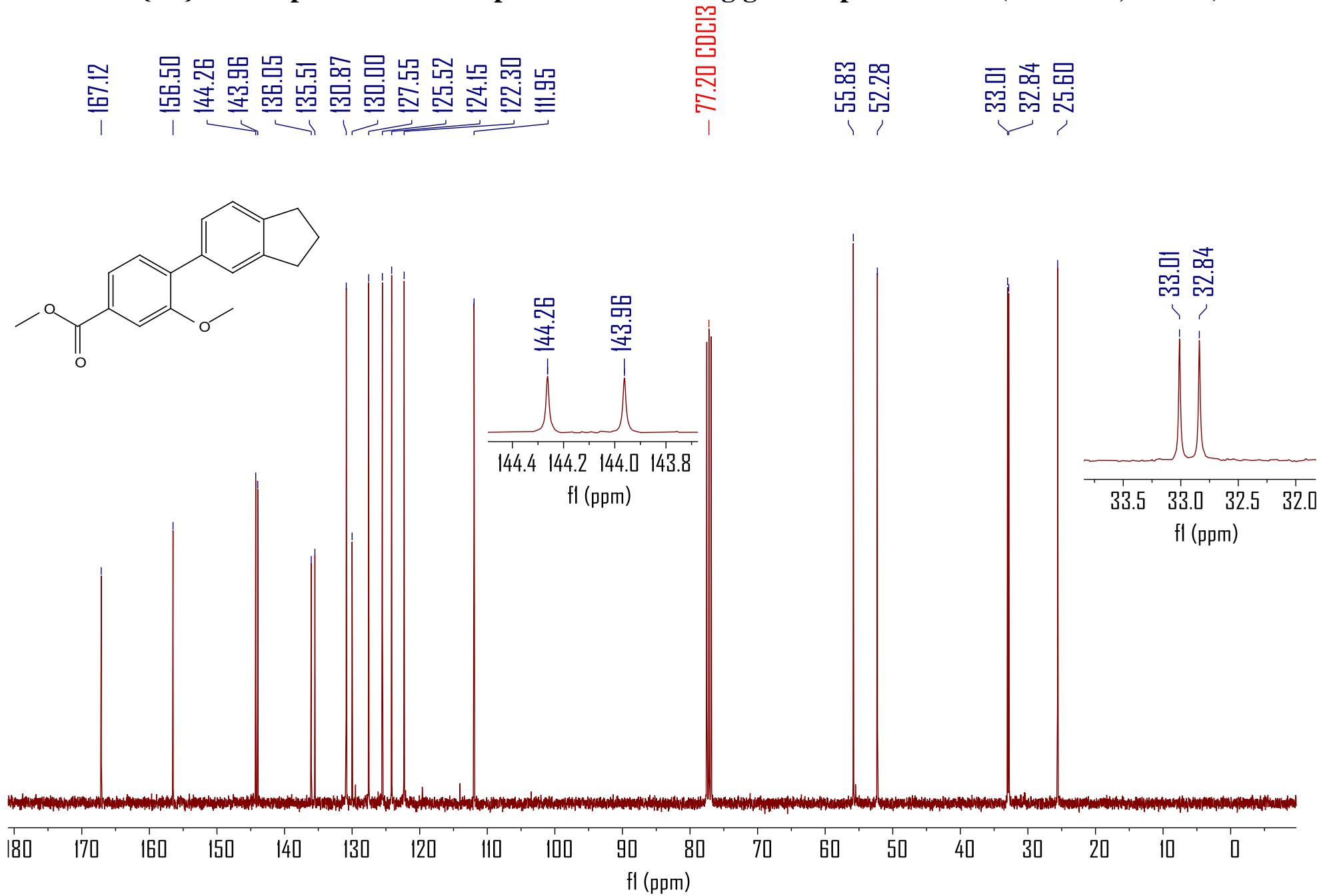
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum for compound 3af following general procedure A (125 MHz, CDCl_3)



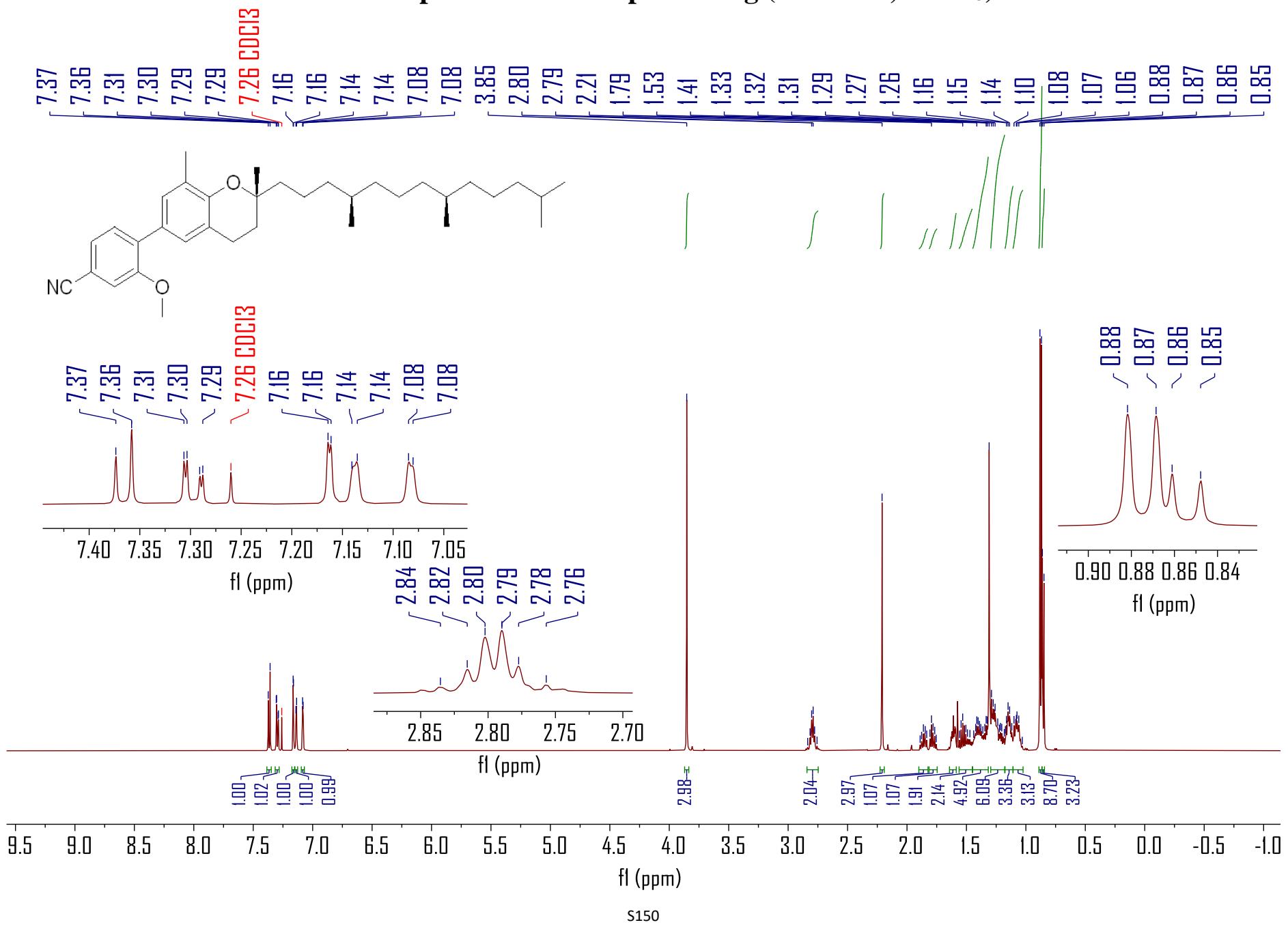
¹H-NMR spectrum for compound 3af following general procedure B (400 MHz, CDCl₃)



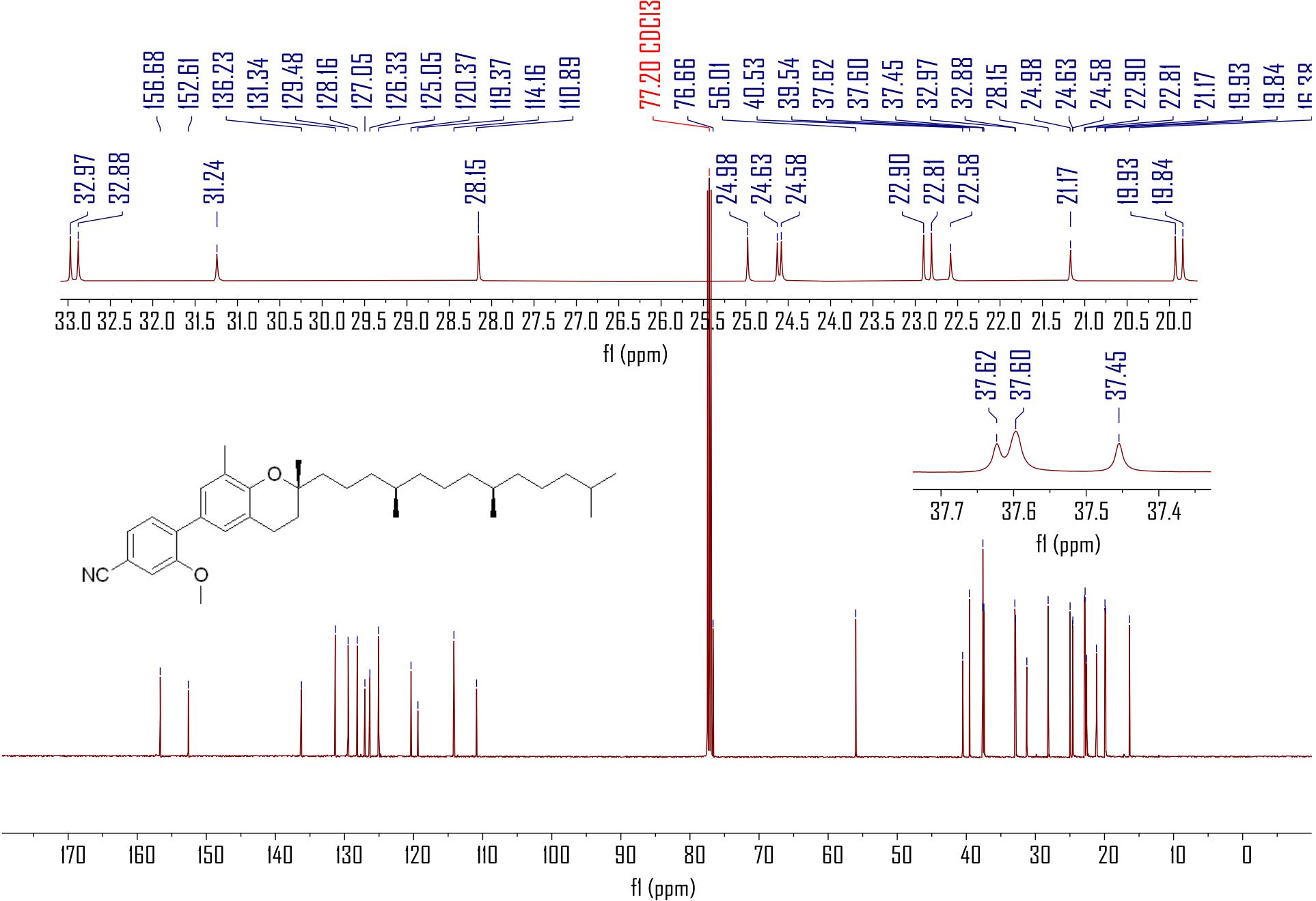
$^{13}\text{C}\{^1\text{H}\}$ -NMR spectrum for compound 3af following general procedure B (100 MHz, CDCl_3)



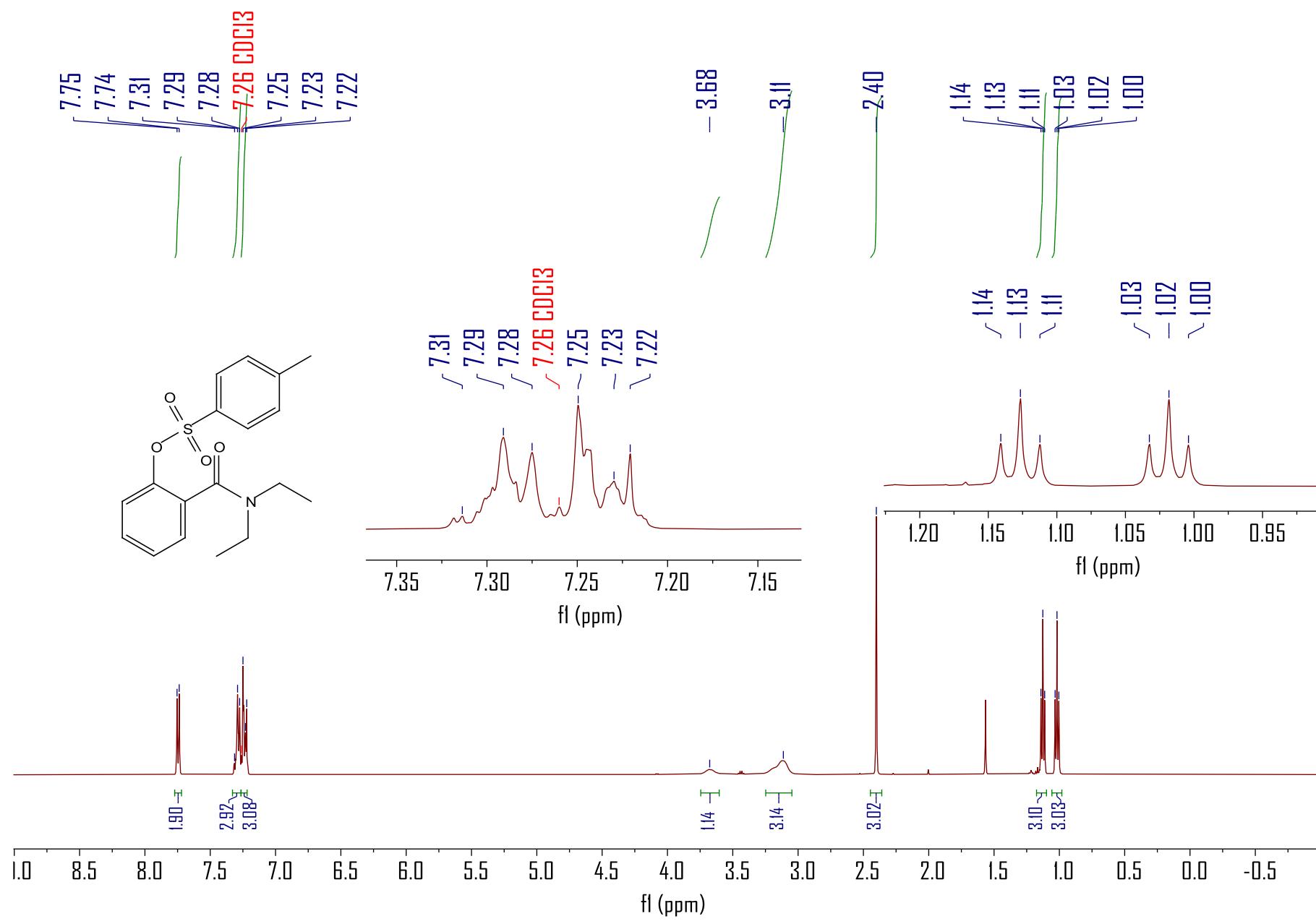
¹H NMR spectrum for compound 3ag (500 MHz, CDCl₃)



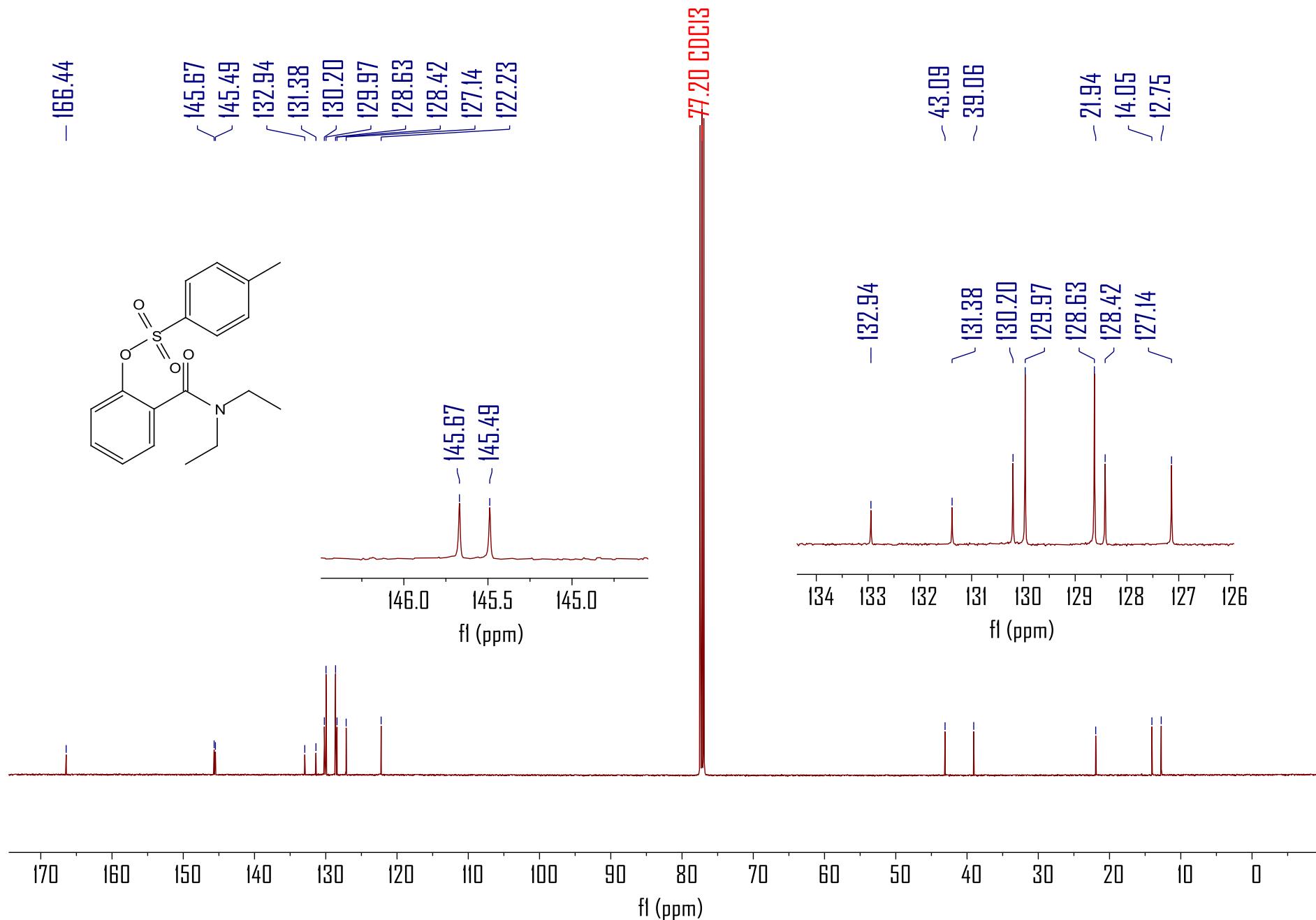
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum for compound 3ag (125 MHz, CDCl_3)



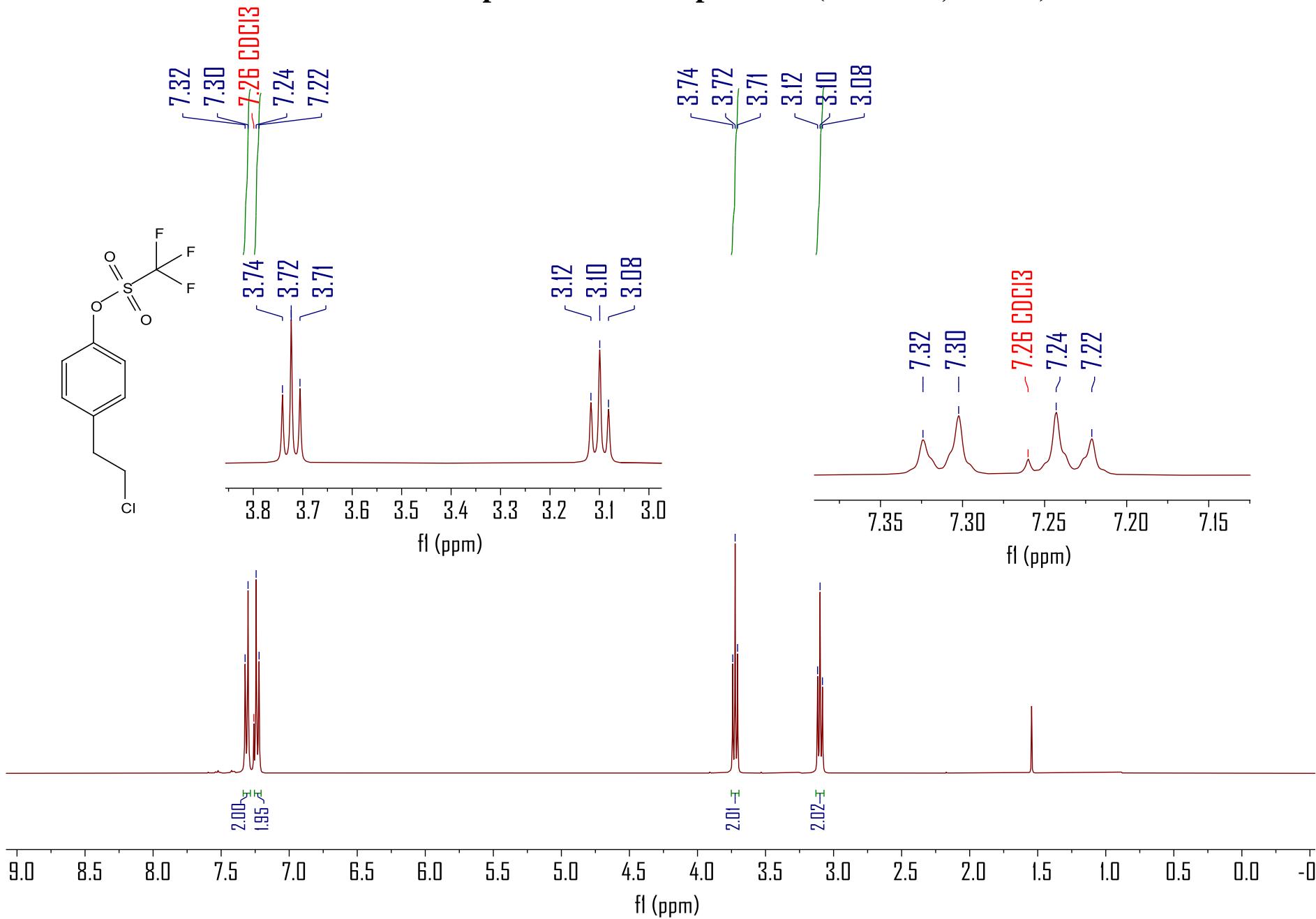
^1H NMR spectrum for compound 2o (500 MHz, CDCl_3)



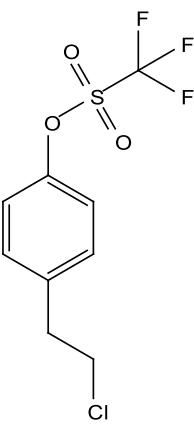
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum for compound 2o (125 MHz, CDCl_3)



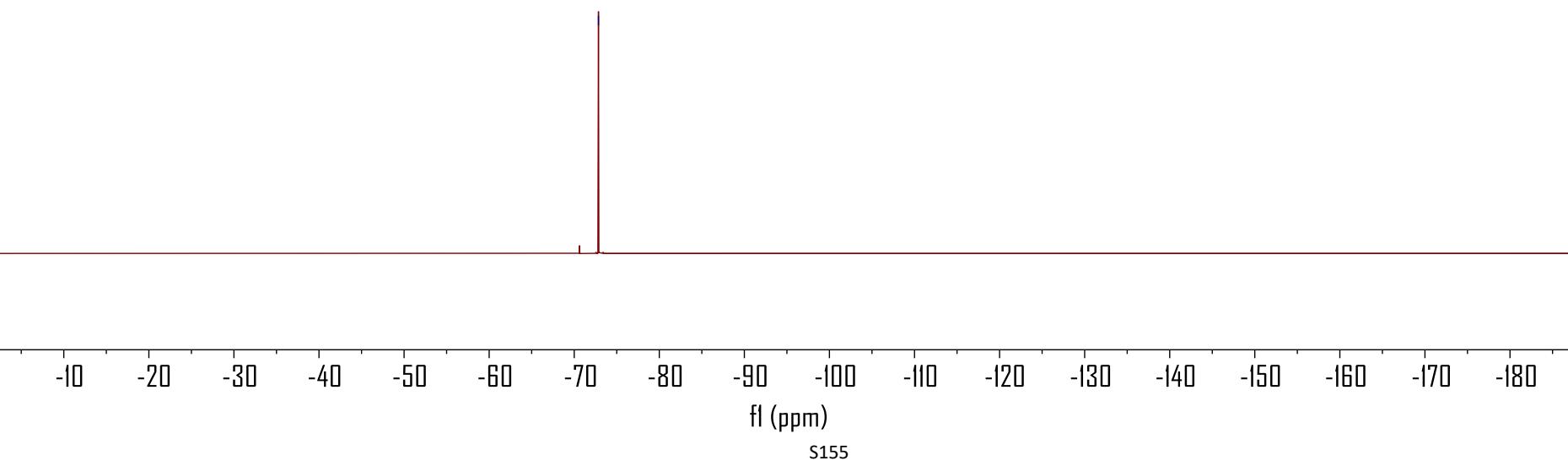
¹H NMR spectrum for compound 1i (400 MHz, CDCl₃)



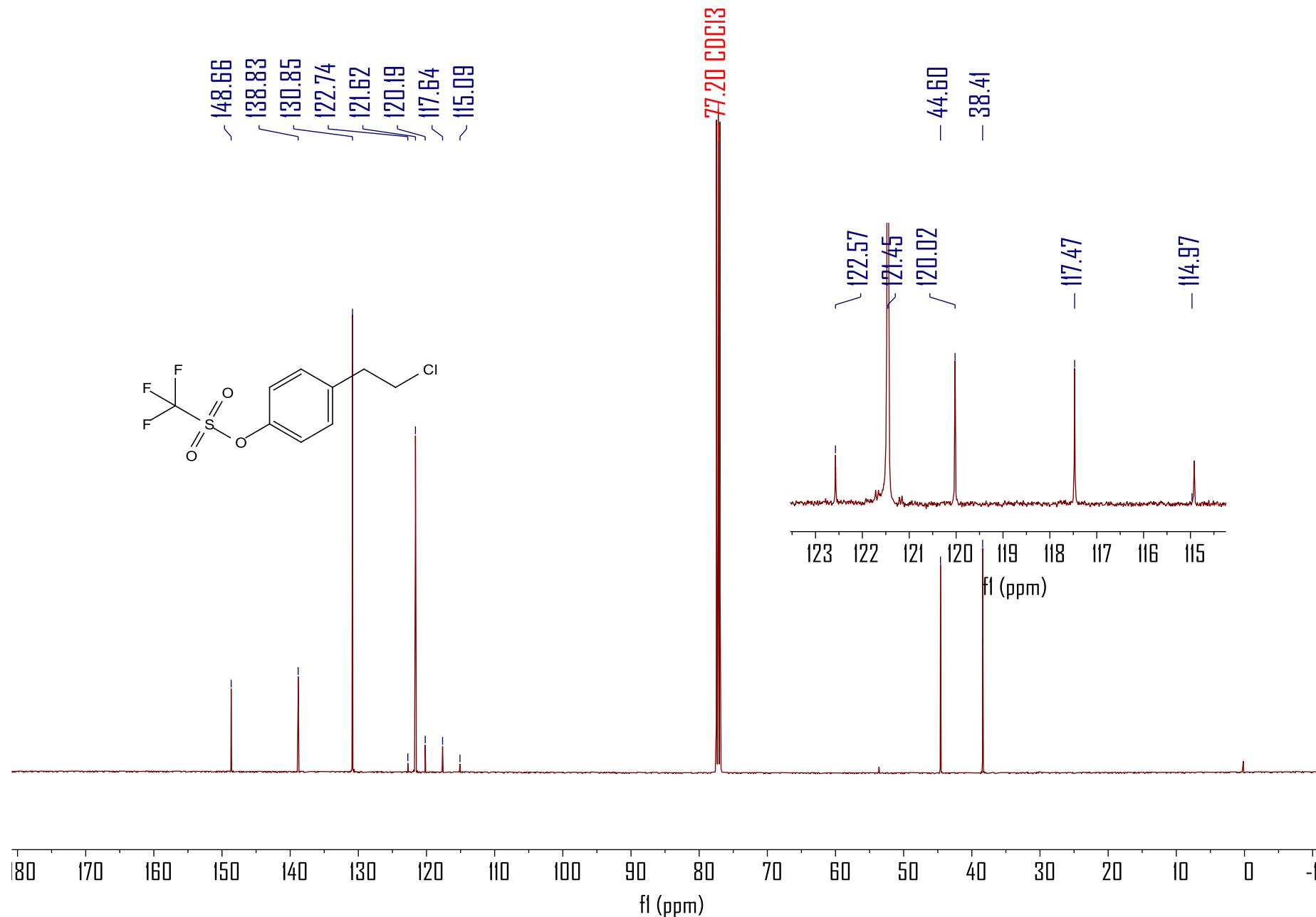
$^{19}\text{F}\{^1\text{H}\}$ NMR spectrum for compound 1i (376 MHz, CDCl_3)



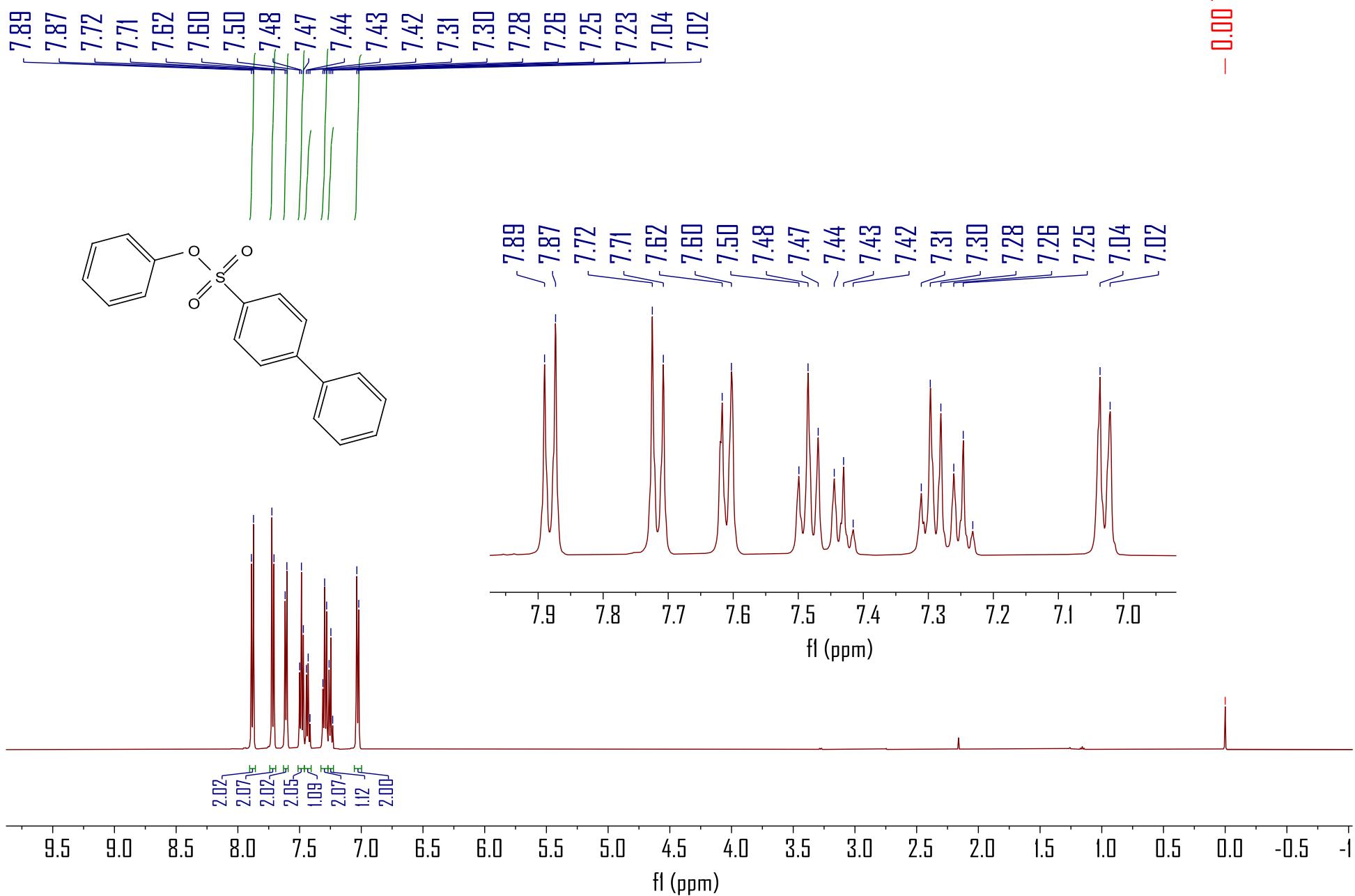
-72.85



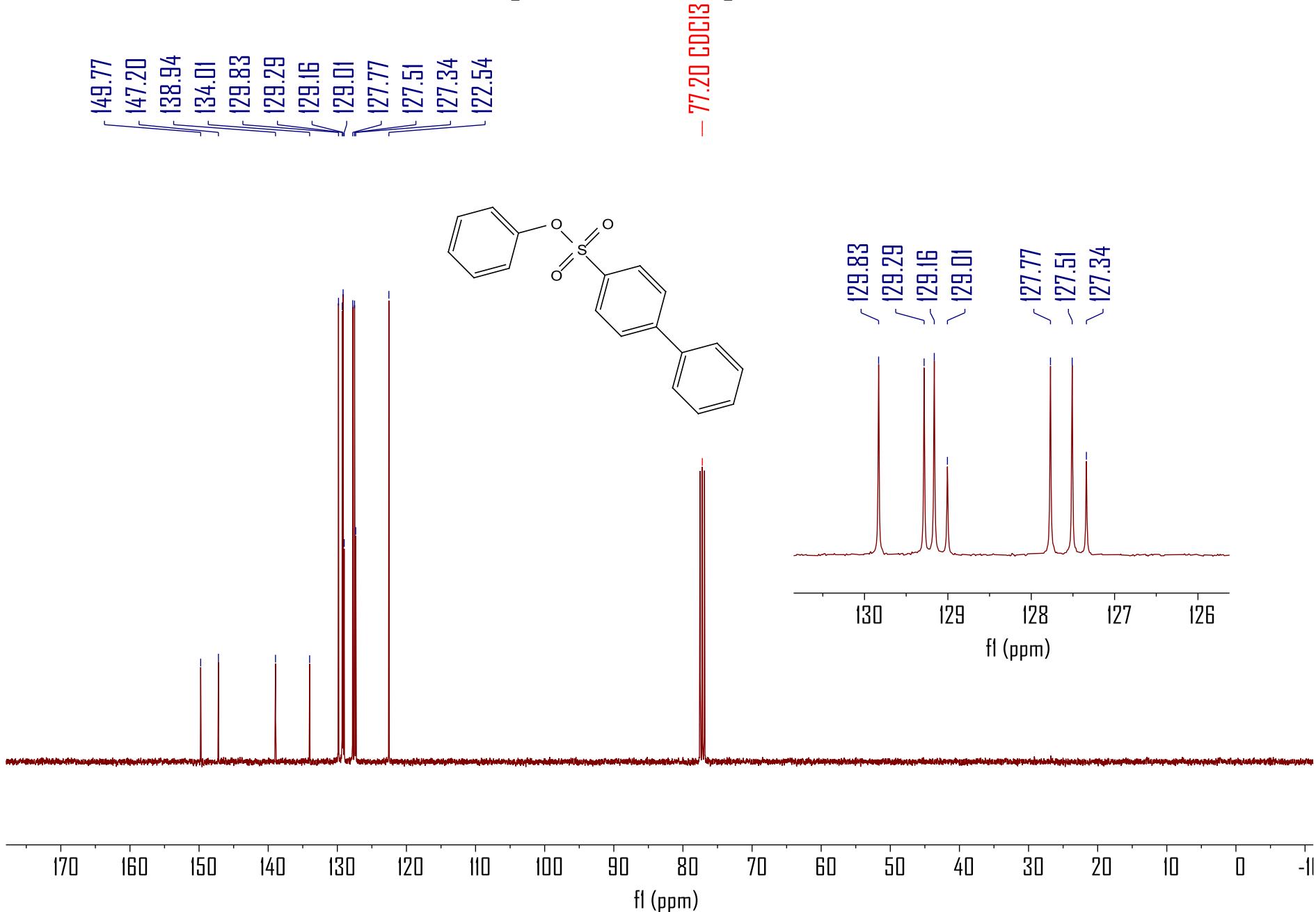
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum for compound 1i (125 MHz, CDCl_3)



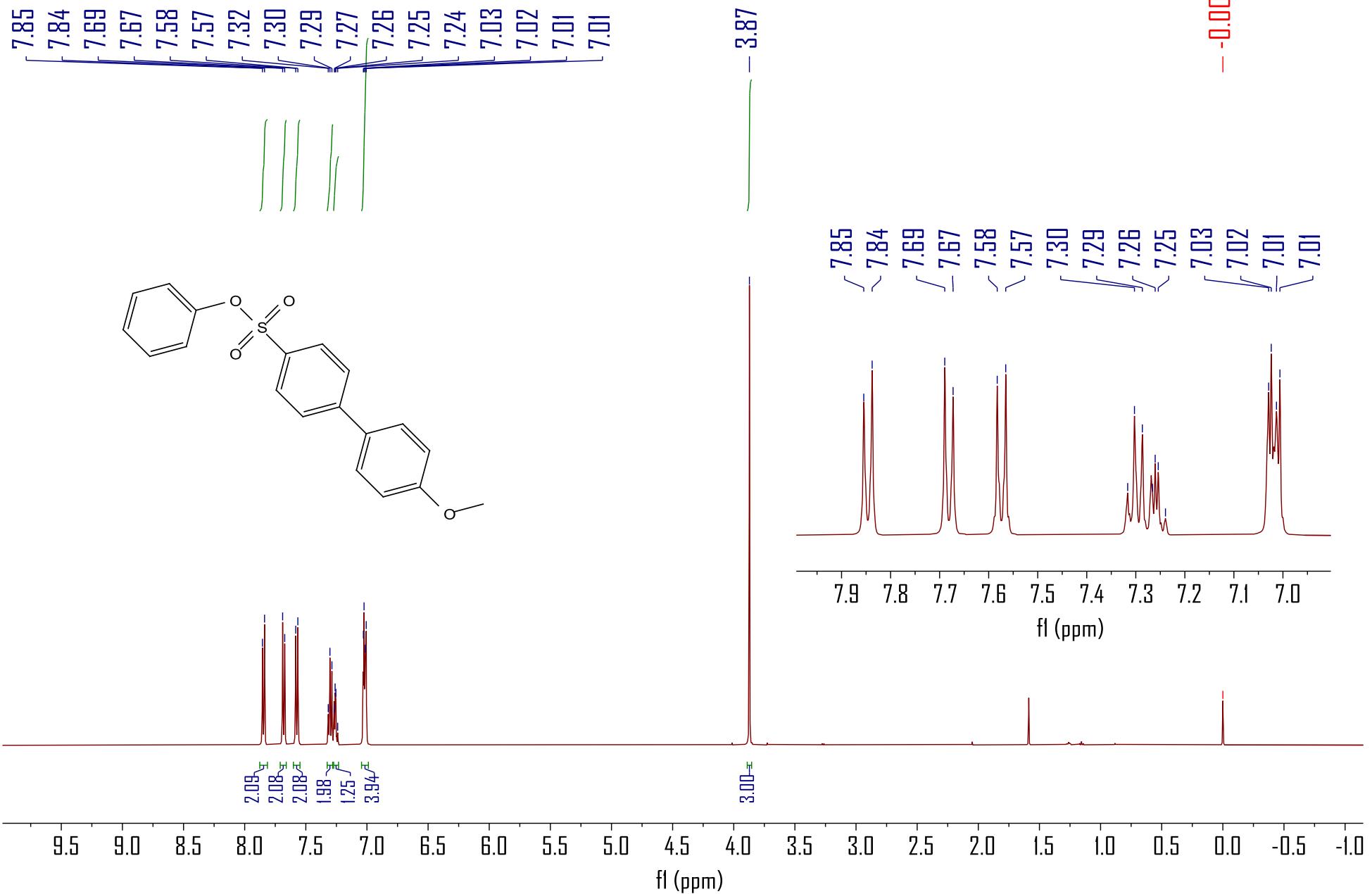
^1H NMR spectrum for compound 7c (500 MHz, CDCl_3 , TMS)



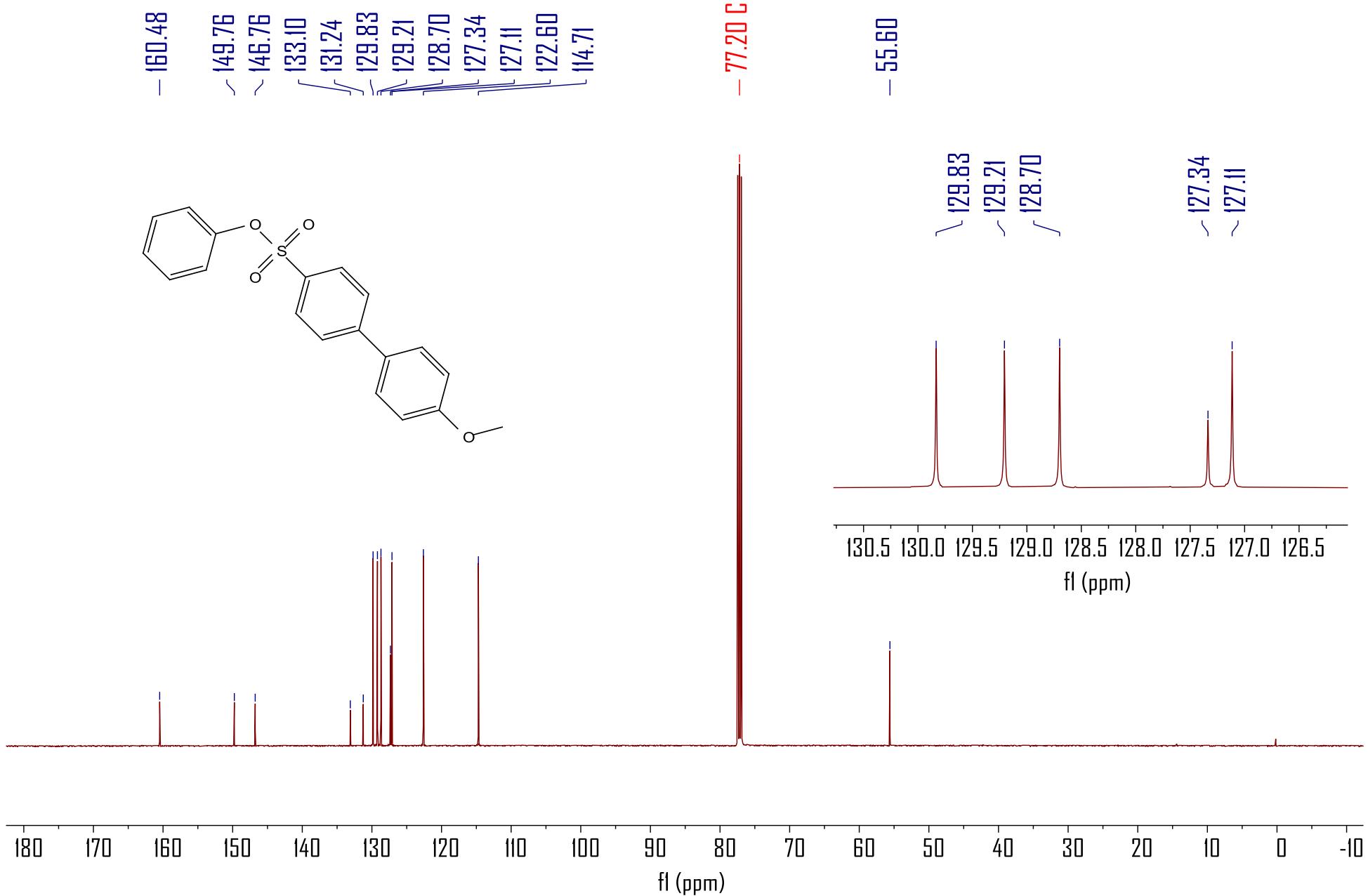
$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum for compound 7c (100 MHz, CDCl_3)



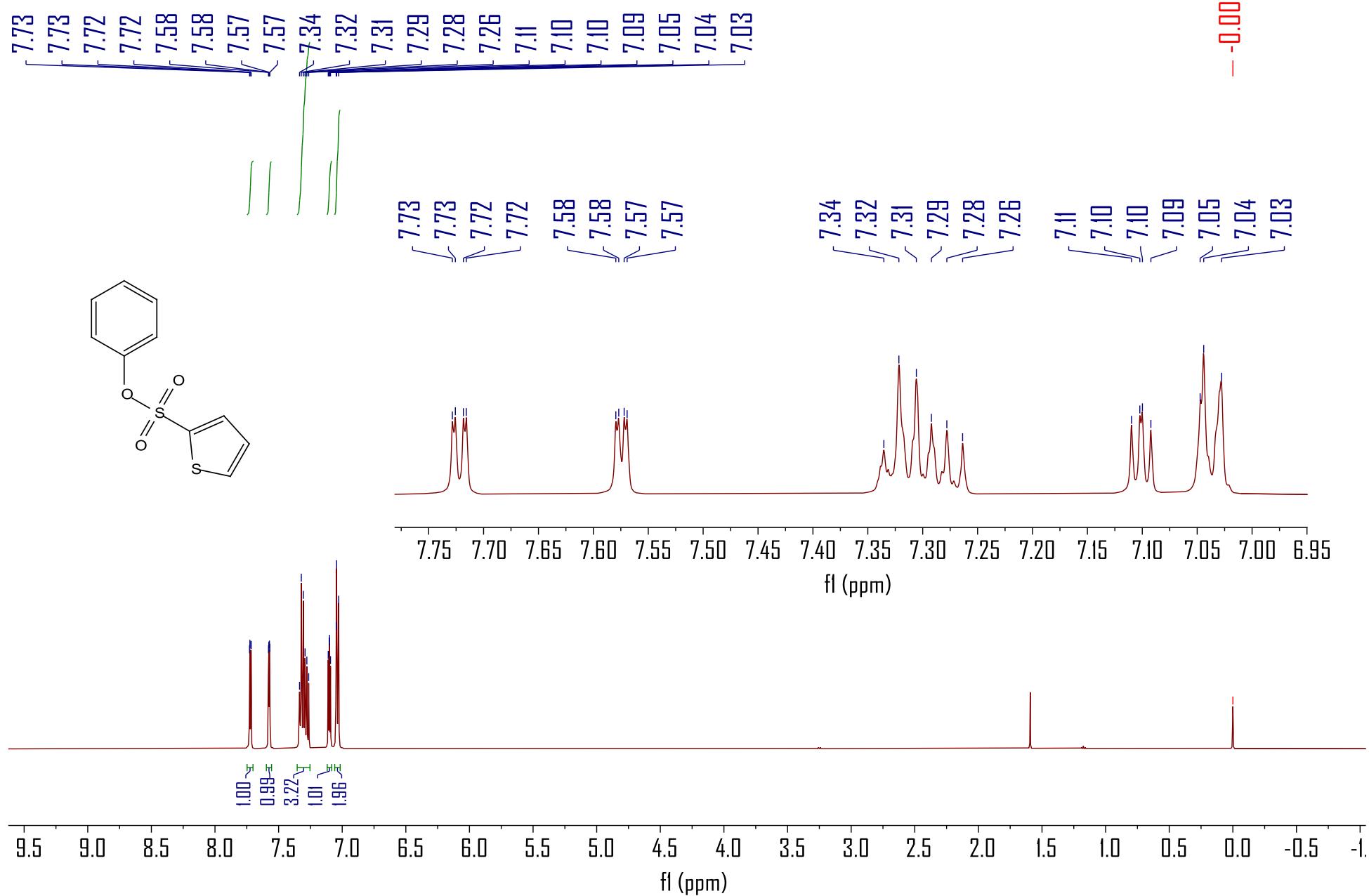
^1H NMR spectrum for compound 7f (500 MHz, CDCl_3 , TMS)



$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum for compound 7f (125 MHz, CDCl_3)



¹H NMR spectrum for compound 7g (500 MHz, CDCl₃, TMS)



$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum for compound 7g (125 MHz, CDCl_3)

