Supplementary information

Stereocontrolled Synthesis of Heterocycles from Unactivated Alkynes by Photoredox/Nickel Dual-Catalyzed Cyclization

Bo-Rong Leng, [a,b,†] Feng Yang, [a,†] Jin-Lian Bai, [a] Yu-Wen Huang, [a] Qing-Quan Liu, *[a] Ping Wei, [a] De-Cai Wang, *[a] Yi-Long Zhu *[a]

[a]*Institute of Materia Medica, School of Pharmaceutical Sciences, Nanjing Tech University, Nanjing 211816, P. R. China.*

[b]*College of Life and Health, Nanjing Polytechnic Institute, Nanjing 211816, P. R. China.*

[†]*These authors contributed equally.*

Content

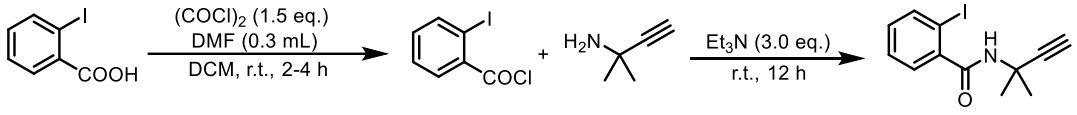
General Information

All glassware was thoroughly oven-dried and all reactions were carried out under nitrogen. Column chromatography was performed with silica gel (200-300 mesh) and used petroleum ether/ethyl acetate as eluents. Thin-layer chromatography (TLC) plates were visualized by exposure to ultraviolet light. ^{1}H NMR and ^{13}C NMR spectra were measured on a Bruker DPX 400 MHz spectrometer in $CDCl_3$ or DMSO-d_6 with chemical shift (δ) given in ppm relative to TMS as internal standard [(s = singlet, d = doublet, m = multiplet), coupling constant (Hz)]. The residual solvent signals were used as references and the chemical shifts were converted to the TMS scale ($CDCl_3$: δ_H = 7.26 ppm, δ_C = 77.00 ppm; DMSO-d_6: δ_H = 2.50 ppm, δ_C = 39.52 ppm). HRMS

(ESI) was performed on a Bruker Apex II mass instrument. X-Ray crystallographic analysis was performed with a Siemens SMART CCD and a Siemens P4 diffractometer.

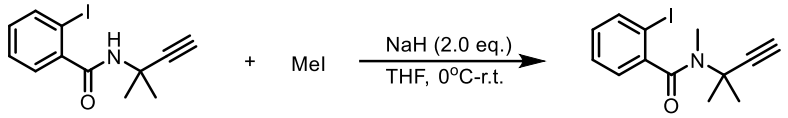
General procedure for the synthesis of substrates 1

2-iodo-N-methyl-N-(2-methylbut-3-yn-2-yl)benzamide **1a** were prepared from the corresponding *o*-iodobenzoic acid and *2-methylbut-3-yn-2-amine*.



S1

Product S1: In a nitrogen-purged, dry flask, introduce *o*-iodobenzoic acid (10 mmol, 1.0 equivalent). Dissolve the acid in 20mL of dichloromethane (DCM) and cool the mixture to 0 °C. Slowly add oxalyl chloride (15 mmol, 1.5 equivalents) dropwise to the cooled solution while stirring. Subsequently, introduce DMF (0.15 mL) to the reaction mixture. Allow the reaction to proceed at room temperature for 2 hours, then add another 0.15 mL of DMF. Monitor for the evolution of carbon dioxide and continue stirring for an additional 2 hours. Once the reaction is complete as indicated by TLC analysis, cool the system to 0 °C and add triethylamine (30 mmol, 3.0 equivalents) and 2-methylbut-3-yn-2-amine (15 mmol, 1.5 equivalents) dropwise with continuous stirring. Stir the reaction mixture overnight at room temperature. After the reaction is complete, quench with a saturated ammonium chloride solution (40 mL), and extract the product with dichloromethane (15 mL × 3). Combine the organic layers and dry them over anhydrous sodium sulfate. Finally, distill the solution under reduced pressure to obtain a white solid crude product, **S1**. The crude product can be used directly in subsequent reactions without the need for further purification.

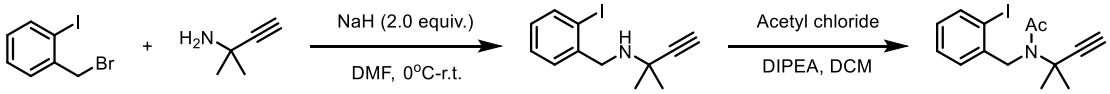


S1 **1a**

Product 1a: Place **S1** (10 mmol) into a 100 mL round-bottom flask and dissolve it in tetrahydrofuran (THF). Slowly introduce sodium hydride (NaH), 60% in mineral oil

(20 mmol, 2.0 equivalents), to the solution at 0 °C. Stir the reaction mixture at 0 °C for 30 minutes to ensure complete dissolution and reaction. Subsequently, add the iodinated alkane (15 mmol, 1.5 equivalents) dropwise to the stirred solution. Monitor the reaction progress using thin-layer chromatography (TLC) to confirm the consumption of the starting material. Once the reaction is complete, quench it with a saturated ammonium chloride aqueous solution. Then, perform a liquid-liquid extraction using ethyl acetate (10 mL × 3). Combine the organic layers and dry the mixture over anhydrous sodium sulfate (Na_2SO_4) to remove any residual water. Finally, purify the crude product through a silica gel column chromatography to isolate the final product, a white solid **1a**.

N-(2-iodobenzyl)-N-(2-methylbut-3-yn-2-yl)acetamide **1a'** were prepared from the corresponding *1-(bromomethyl)-2-iodobenzene* and *2-methylbut-3-yn-2-amine*.



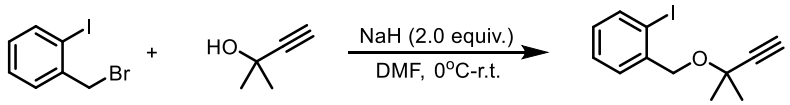
S2 1a'

Product S2: Introduce 2-methylbut-3-yn-2-amine (5 mmol, 1.0 equiv.) into a 100 mL round-bottom flask. Dissolve the compound in 30 mL of *N, N*-dimethylformamide (DMF) and stir the mixture at 0 °C. Gradually add sodium hydride (NaH), 10.0 mmol, 2.0 equivalents, to the flask under a nitrogen atmosphere to prevent oxidation, and continue stirring at 0 °C for 30 minutes. Subsequently, add ortho-iodobenzyl bromide (5.5 mmol, 1.1 equiv.) to the reaction mixture and stir at 0 °C for an additional 15 minutes. Then, allow the reaction to proceed at room temperature with continuous stirring overnight. To assess the completion of the reaction, perform thin-layer chromatography (TLC) analysis. Once the reaction is confirmed complete by TLC, quench it with water and proceed with extraction using ethyl acetate (3 × 30 mL). Separate the organic layer and wash it with a saturated brine solution to remove any inorganic impurities. Dry the organic layer over anhydrous sodium sulfate (Na_2SO_4) to remove residual water. After drying, concentrate the solution under reduced pressure to remove the solvent and obtain the crude product **S2**. This crude product

can be used directly in subsequent reactions without the need for further purification.

Product 1a': In an oven-dried flask, the crude product of S2 (1.0 equiv.) was dissolved in dichloromethane (10 mL) along with *N*, *N*-Diisopropylethylamine (DIPEA, 2.0 equiv.) and 4-Dimethylaminopyridine (DMAP, 0.05 equiv.), and the solution was cooled to 0 °C. Acetyl chloride (1.1 equiv.), pre-dissolved in CH_2Cl_2 (10 mL), was added dropwise to the well-stirred reaction mixture. After stirring at room temperature for 9 hours, the solvent was removed under reduced pressure. The residue was subjected to column chromatography using silica gel and eluted with a mixture of ethyl acetate (EA) and petroleum ether (PE) in a 1:10 ratio to afford the final product **1a'** as a white solid.

iodo-2-(((2-methylbut-3-yn-2-yl)oxy)methyl)benzene **1b'** were prepared from the corresponding *1-(bromomethyl)-2-iodobenzene* and *2-methyl-3-butyne-2-ol*.

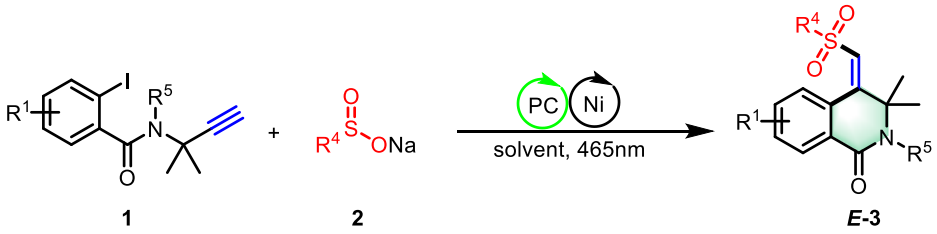


1b'

Introduce 2-methyl-3-butyne-2-ol (5 mmol, 1.0 equiv.) into a 100 mL round-bottom flask. Dissolve the compound in 30 mL of *N*,*N*-dimethylformamide (DMF) and stir the mixture at 0 °C. Gradually add sodium hydride (NaH), 10.0 mmol, 2.0 equivalents, to the flask under a nitrogen atmosphere to prevent oxidation, and continue stirring at 0 °C for 30 minutes. Subsequently, add ortho-iodobenzyl bromide (5.5 mmol, 1.1 equivalents) to the reaction mixture and stir at 0 °C for an additional 15 minutes. Then, allow the reaction to proceed at room temperature with continuous stirring overnight. To assess the completion of the reaction, perform thin-layer chromatography (TLC) analysis. Once the reaction is confirmed complete by TLC, quench it with water and proceed with extraction using ethyl acetate (3 × 30 mL). Separate the organic layer and wash it with a saturated brine solution to remove any inorganic impurities. Dry the organic layer over anhydrous sodium sulfate (Na_2SO_4) to remove residual water. After drying, concentrate the solution under reduced pressure to remove the solvent and obtain the crude product. Further purification of the crude product is achieved

through column chromatography, using an appropriate stationary phase and eluent system, to isolate and yield the target compound **1b'**.

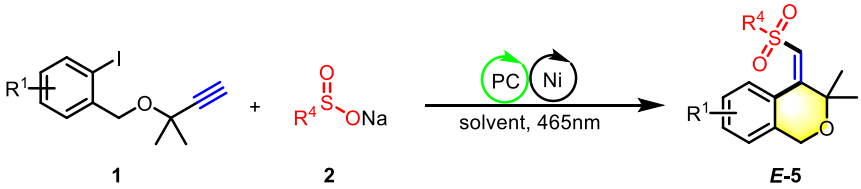
General Procedure for the Synthesis of *(E)-2,3,3-trimethyl-4-(tosylmethylene)-3,4-dihydroisoquinolin-1(2H)-one*



1 **2** ***E*-3**

Under a nitrogen atmosphere, an oven-dried 10 mL Schlenk tube was sequentially charged with the following reagents: *2-iodo-N-methyl-N-(2-methylbut-3-yn-2-yl)benzamide* (**1a**, 0.2 mmol, 1.0 equivalent), *sodium 4-methylbenzenesulfinate* (**2a**, 0.4 mmol, 2.0 equivalents), Na_2-Eosin Y (5 mol%), $NiCl_2 \cdot 6H_2O$ (10 mol%), 4,4'-di-tert-butyl-2,2'-dipyridyl (**L1**, 10 mol%), and dimethyl sulfoxide (DMSO, 2 mL). The mixture was stirred at 25°C for 12 hours under 465 nm blue LED irradiation. The reaction was monitored by thin-layer chromatography (TLC) analysis until the complete consumption of the starting material **1a** was confirmed. Upon completion, the reaction mixture was diluted with water (8 mL) and then extracted with ethyl acetate (10 mL × 3). The combined organic phases were washed with brine (10 mL) to remove any inorganic salts. The organic layer was dried over anhydrous sodium sulfate (Na_2SO_4) to remove residual water, and the solvent was subsequently evaporated under reduced pressure. The crude product was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (PE/EA) as the eluent to yield the desired product **3a**.

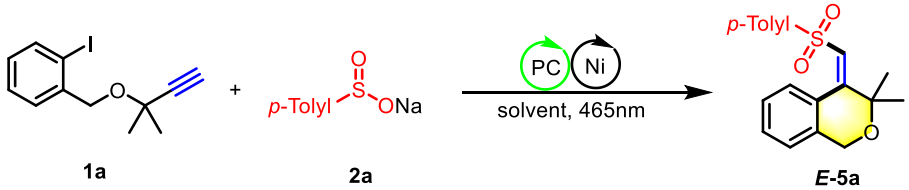
General Procedure for the Synthesis of (*E*)-*N*-(2-methyl-4-(phenylselanyl)-3-(*p*-tolyl)but-3-en-2-yl)acetamide



1 **2** ***E*-5**

Under a nitrogen atmosphere, an oven-dried 10 mL Schlenk tube was sequentially charged with the following reagents: *iodo-2-(((2-methylbut-3-yn-2-yl)oxy)methyl)benzene* (**1b'**, 0.2 mmol, 1.0 equivalent), *sodium 4-methylbenzenesulfinate* (**2a**, 0.4 mmol, 2.0 equivalents), $Ru(bpy)_3Cl_2·6H_2O$ (5 mol%), $NiCl_2·6H_2O$ (10 mol%), 4,4'-di-tert-butyl-2,2'-dipyridyl (**L1**, 10 mol%), and dimethyl sulfoxide (DMSO, 2 mL). The mixture was stirred at 25°C for 12 hours under 465 nm blue LED irradiation. The reaction was monitored by thin-layer chromatography (TLC) analysis until the complete consumption of the starting material **1b'** was confirmed. Upon completion, the reaction mixture was diluted with water (8 mL) and then extracted with ethyl acetate (10 mL × 3). The combined organic phases were washed with brine (10 mL) to remove any inorganic salts. The organic layer was dried over anhydrous sodium sulfate (Na_2SO_4) to remove residual water, and the solvent was subsequently evaporated under reduced pressure. The crude product was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (PE/EA) as the eluent to yield the desired product **5a**.

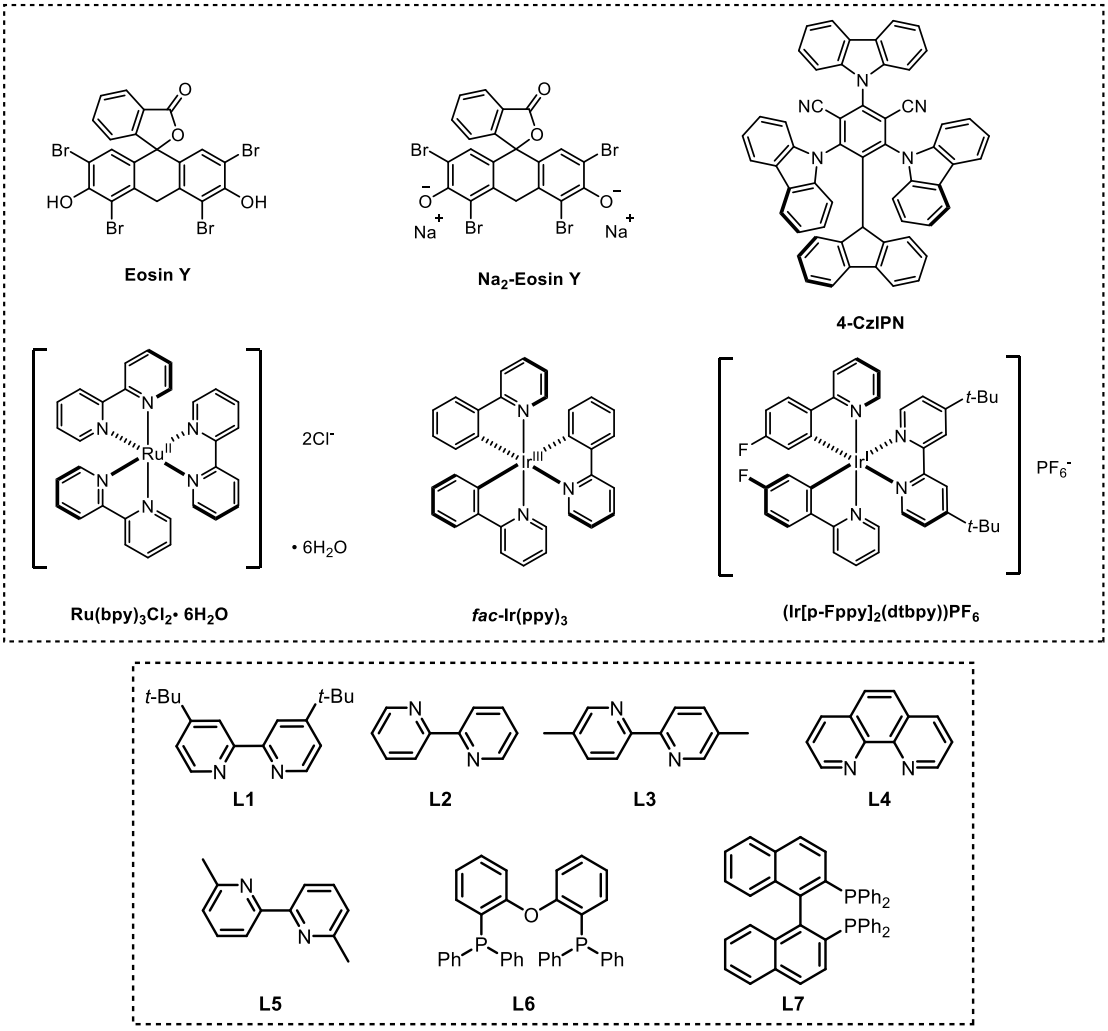
Optimization of the Reaction Conditions for Compound 5a



1a **2a** ***E*-5a**

Entry	Photocatalyst	Catalyst	Ligand	Solvent	Yield

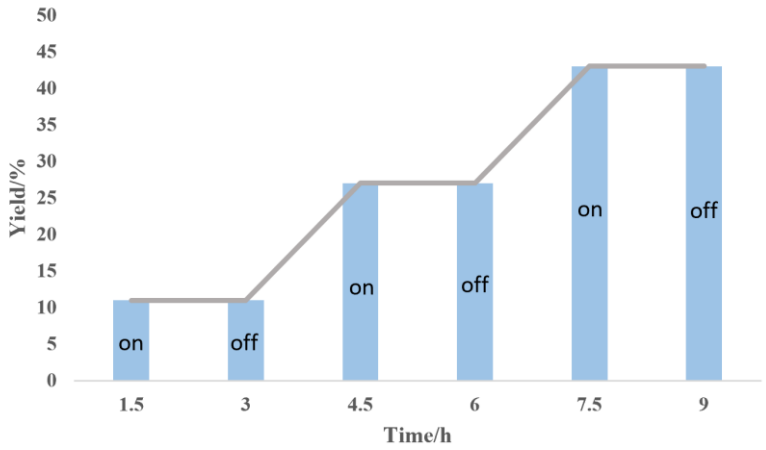
					6a(%)[b]
1	Na_2-Eosin Y	$NiCl_2·6H_2O$	**L1**	DMSO	34
2	Eosin Y	$NiCl_2·6H_2O$	**L1**	DMSO	29
3	4-CzIPN	$NiCl_2·6H_2O$	**L1**	DMSO	26
4	$Ru(bpy)_3Cl_2·6H_2O$	$NiCl_2·6H_2O$	**L1**	DMSO	87
5	*fac*-$Ir(ppy)_3$	$NiCl_2·6H_2O$	**L1**	DMSO	67
6	(Ir[*p*-Fppy]$_2$(dtbpy))PF_6	$NiCl_2·6H_2O$	**L1**	DMSO	39
7	$Ru(bpy)_3Cl_2·6H_2O$	$Ni(OAc)_2·4H_2O$	**L1**	DMSO	43
8	$Ru(bpy)_3Cl_2·6H_2O$	$Ni(PPh_3)_2Cl_2$	**L1**	DMSO	53
9	$Ru(bpy)_3Cl_2·6H_2O$	NiI_2	**L1**	DMSO	39
10	$Ru(bpy)_3Cl_2·6H_2O$	$NiCO_3$	**L1**	DMSO	11
11	$Ru(bpy)_3Cl_2·6H_2O$	$Ni(acac)_2$	**L1**	DMSO	25
12	$Ru(bpy)_3Cl_2·6H_2O$	$NiBr_2$·DME	**L1**	DMSO	64
13	$Ru(bpy)_3Cl_2·6H_2O$	$NiCl_2·6H_2O$	**L2**	DMSO	49
14	$Ru(bpy)_3Cl_2·6H_2O$	$NiCl_2·6H_2O$	**L3**	DMSO	52
15	$Ru(bpy)_3Cl_2·6H_2O$	$NiCl_2·6H_2O$	**L4**	DMSO	71
16	$Ru(bpy)_3Cl_2·6H_2O$	$NiCl_2·6H_2O$	**L5**	DMSO	Trace
17	$Ru(bpy)_3Cl_2·6H_2O$	$NiCl_2·6H_2O$	**L6**	DMSO	20
18	$Ru(bpy)_3Cl_2·6H_2O$	$NiCl_2·6H_2O$	**L7**	DMSO	19
19	$Ru(bpy)_3Cl_2·6H_2O$	$NiCl_2·6H_2O$	**L1**	DMF	83
20	$Ru(bpy)_3Cl_2·6H_2O$	$NiCl_2·6H_2O$	**L1**	DMA	12
21	$Ru(bpy)_3Cl_2·6H_2O$	$NiCl_2·6H_2O$	**L1**	MeCN	N.D.
22	$Ru(bpy)_3Cl_2·6H_2O$	$NiCl_2·6H_2O$	**L1**	EtOH	Trace
23	$Ru(bpy)_3Cl_2·6H_2O$	$NiCl_2·6H_2O$	**L1**	THF	N.D.
24	$Ru(bpy)_3Cl_2·6H_2O$	$NiCl_2·6H_2O$	**L1**	DCM	N.D.



Light/Dark Experiment Procedure

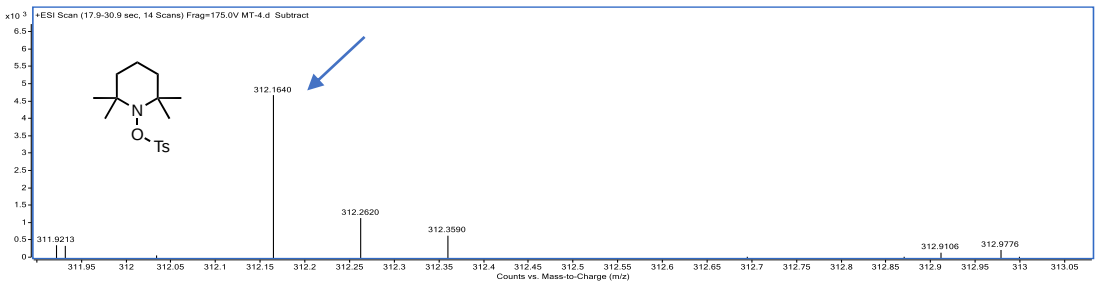
Under a nitrogen atmosphere, an oven-dried 10 mL Schlenk tube was sequentially charged with the following reagents: *2-iodo-N-methyl-N-(2-methylbut-3-yn-2-yl)benzamide* (**1a**, 0.2 mmol, 1.0 equivalent), *sodium 4-methylbenzenesulfinate* (**2a**, 0.4 mmol, 2.0 equivalents), Na_2-Eosin Y (5 mol%), $NiCl_2 \cdot 6H_2O$ (10 mol%), 4,4'-di-tert-butyl-2,2'-dipyridyl (**L1**, 10 mol%), and dimethyl sulfoxide (DMSO, 2 mL). The mixture was stirred at 25°C under 465nm blue LED irradiation. The reaction was conducted in cycles of 1.5 hours of light exposure followed by 1.5 hours in the dark.

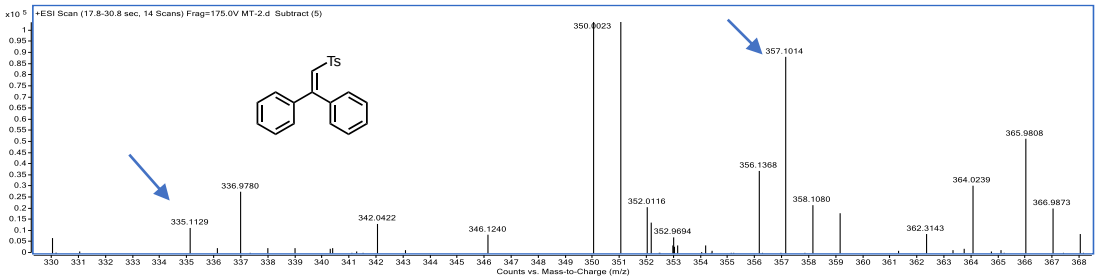
This alternating photochemical and thermal process was continued throughout the reaction period. At the end of each light exposure and dark period, a 50 μL sample was withdrawn using a microsyringe for analysis. The reaction progress and yields were monitored by ^{1}H NMR spectroscopy, employing 1,3,5-trimethoxybenzene as an internal standard. It was observed that yields increased during the periods of irradiation, with no significant yield improvement observed during the dark periods.

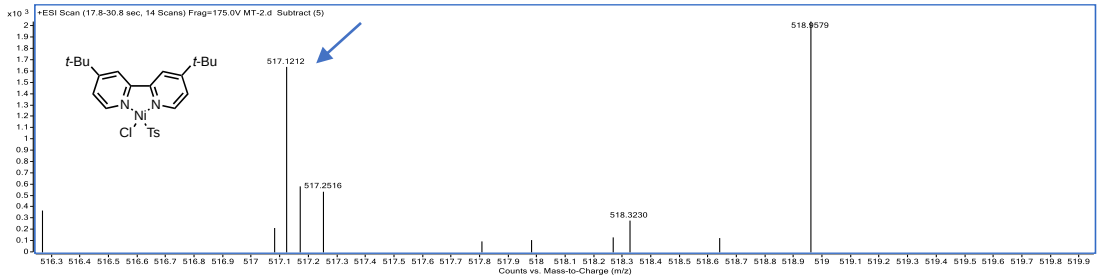


Scheme S1 On/off experiments of **3a**

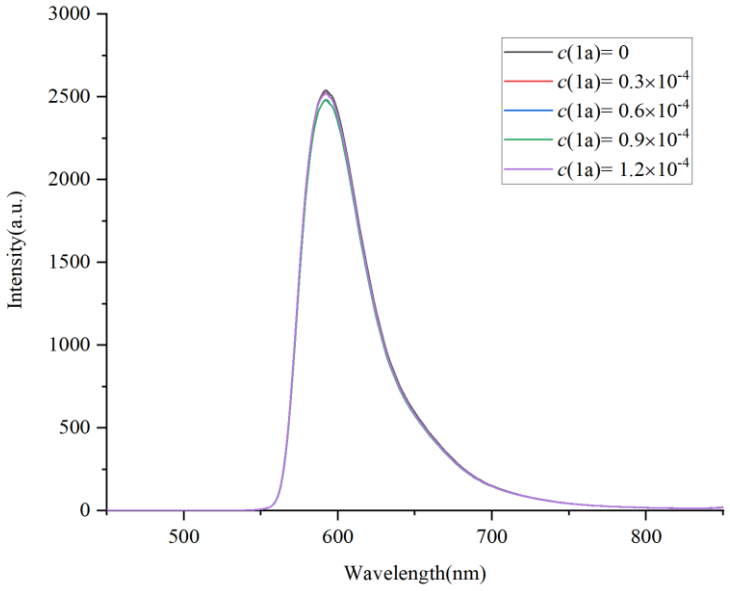
Copies of HRMS Data of radical trapping experiments:



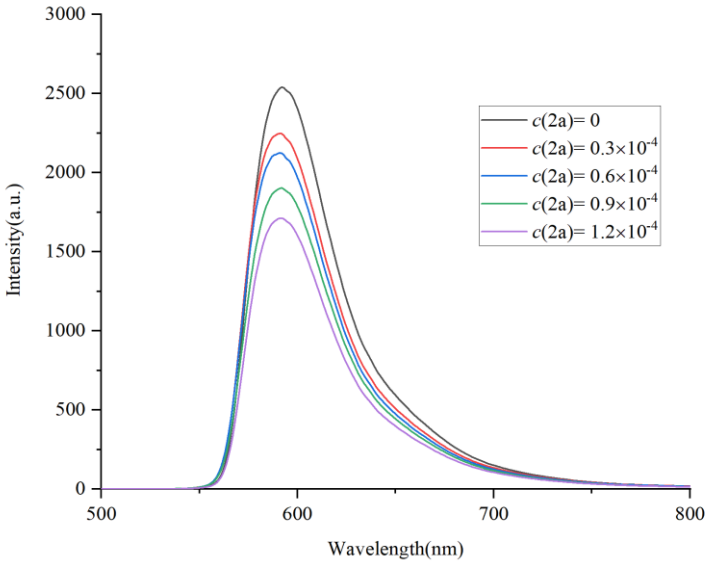




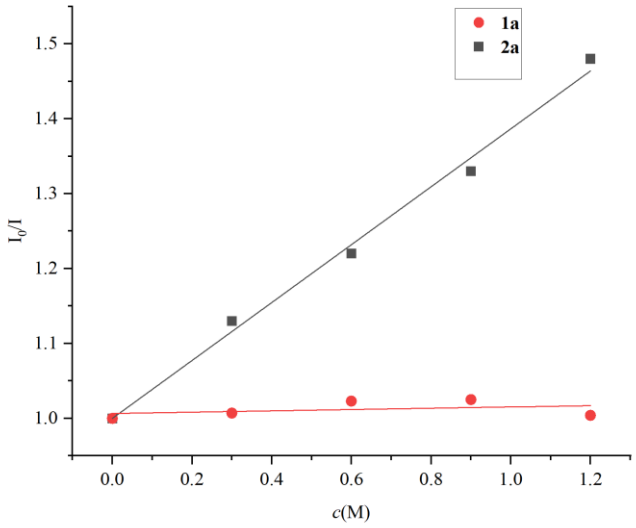
Luminescence Quenching Experiment



(a)



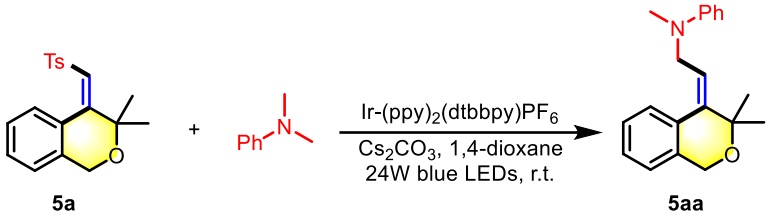
(b)



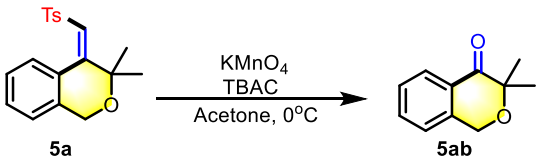
(c)

Scheme S3 (a) Emission spectra of Na_2-Eosin Y in the presence of increasing **1a** concentrations. (b) Emission spectra of Na_2-Eosin Y in the presence of increasing **2a** concentrations. (c) Stern–Volmer plot of I_0/I versus **1a** or **2a** concentration in Na_2-Eosin Y's DMSO solution.

Synthetic applicability

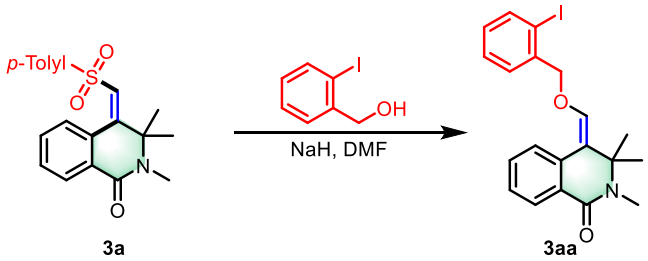


A dry reaction tube, fitted with a Teflon-coated magnetic stir bar, was charged with *(E)-3,3-dimethyl-4-(tosylmethylene)isochromane* **5a** (0.5 mmol, 1.0 equivalent), Ir-(ppy)$_2$(dtbbpy)PF$_6$ (3 mol%), and Cs_2CO_3 (2.0 equivalents). The tube was sealed with a rubber septum, evacuated, and backfilled with argon gas (three cycles). Subsequently, 1,4-dioxane (2.0 mL) was introduced via syringe, and the solution was degassed by argon bubbling for 10 minutes. *N*, *N*-dimethylaniline (1.5 equivalents) was added to the solution via syringe. The reaction mixture was stirred at room temperature for 24 hours under irradiation with a 24 W blue LED lamp. The reaction mixture was then diluted with saturated aqueous $NaHCO_3$ (20 mL), and the layers were allowed to separate. The aqueous phase was further extracted with dichloromethane (DCM, 2×10 mL), and the combined organic extracts were dried over anhydrous Na_2SO_4 and concentrated under vacuum. The crude product was purified by column chromatography on silica gel, using a petroleum ether/ethyl acetate (PE/EA) mixture as the eluent. This yielded the desired product **5aa** as a colorless oil (59% yield, 86.4 mg).



Tetrabutylammonium chloride (TBAC, 1.0 mmol, 2.0 equivalents) and potassium permanganate ($KMnO_4$, 1.0 mmol, 2.0 equivalents) were combined in acetone (2.0 mL). The mixture was stirred at room temperature for 1 hour, then cooled to 0°C. A solution of compound **5a** (0.5 mmol, 1.0 equivalent) in acetone (1.0 mL) was added dropwise over a period of 5 minutes, maintaining the internal temperature at 5°C or

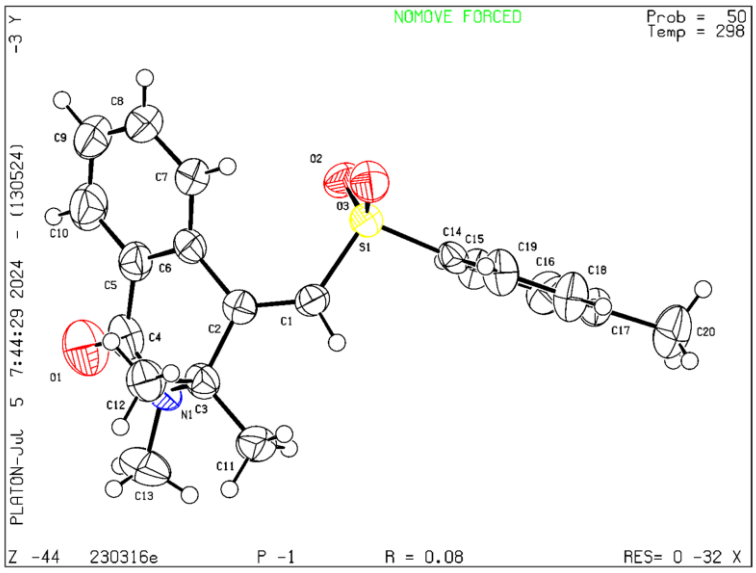
below. After the addition was complete, the mixture was stirred for an additional 6 hours at 0°C until complete consumption of compound **5a** was confirmed by thin-layer chromatography (TLC). To quench the reaction, a saturated aqueous solution of sodium bisulfite ($NaHSO_3$, 10 mL) was added in one portion. The mixture was then filtered through Celite, which was subsequently washed with acetone. The filtrate was concentrated, and the residue was extracted with ethyl acetate (EtOAc). The organic phase was dried over anhydrous sodium sulfate (Na_2SO_4), filtered, and evaporated to dryness. The product was purified by flash column chromatography on silica gel, yielding product **5ab** as a colorless oil (62 mg, 70% yield).



A 25 mL round-bottom flask was charged with 2-iodobenzyl alcohol (1.0 mmol, 2.0 equivalents). The compound was dissolved in *N*, *N*-dimethylformamide (DMF, 2.0 mL) and the mixture was stirred at 0°C. Sodium hydride (NaH, 1.0 mmol, 2.0 equivalents) was gradually added to the flask under a nitrogen atmosphere to prevent oxidation, and stirring was continued at 0°C for 30 minutes. Subsequently, compound **3a** (0.5 mmol, 1.0 equivalent) was added to the reaction mixture and stirred at 0°C for an additional 15 minutes. The reaction was then allowed to proceed at room temperature with continuous stirring overnight. To assess the completion of the reaction, thin-layer chromatography (TLC) analysis was performed. Once the reaction was confirmed complete by TLC, it was quenched with water and extraction was carried out using ethyl acetate (3×30 mL). The organic layer was separated and washed with a saturated brine solution to remove any inorganic impurities. The organic layer was dried over anhydrous sodium sulfate (Na_2SO_4) to remove residual

water. After drying, the solution was concentrated under reduced pressure to remove the solvent and obtain the crude product. The crude product was purified by flash column chromatography on silica gel, yielding product **3aa** as a white solid (104 mg, 48% yield).

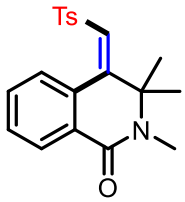
X-ray data of 3a



Accession Code

CCDC 2368219 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via https://www.ccdc.cam.ac.uk/structures/.

General Characterization Data of Products *E*-3, *E*-4 and *E*-5



(E)-2,3,3-trimethyl-4-(tosylmethylene)-3,4-dihydroisoquinolin-1(2H)-one (3a)

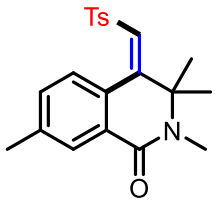
White solid; 50mg, 70% yield; m.p.: 219-220℃.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.06–8.01 (m, 1H), 7.99–7.96 (m, 1H), 7.63 (d,

J = 12.0 Hz, 2H), 7.53–7.45 (m, 2H), 7.19 (d, *J* = 8.0 Hz, 2H), 6.63 (s, 1H), 3.08 (s, 3H), 2.36 (s, 3H), 1.38 (s, 6H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 163.8, 151.4, 144.6, 137.5, 131.0, 130.9, 130.4, 130.3, 129.6, 128.4, 127.7, 127.6, 127.5, 60.4, 27.4, 25.1, 21.6.

HRMS (ESI-TOF) calcd for $C_{20}H_{21}NO_3S[M+Na]^+$: 378.1134; Found: 378.1136.



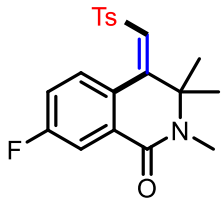
(E)-2,3,3,7-tetramethyl-4-(tosylmethylene)-3,4-dihydroisoquinolin-1(2H)-one (3b)

White solid; 33mg, 45% yield; m.p.: 206-208℃.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.93 (d, *J* = 8.0 Hz, 1H), 7.81 (s, 1H), 7.65 (d, *J* = 8.0 Hz, 2H), 7.32 (d, *J* = 8.0 Hz, 1H), 7.22 (d, *J* = 8.0 Hz, 2H), 6.56 (s, 1H), 3.08 (s, 3H), 2.41 (s, 3H), 2.38 (s, 3H), 1.37 (s, 6H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 164.1, 151.5, 144.5, 141.5, 137.7, 131.8, 130.4, 129.7, 128.2, 128.2, 127.6, 127.6, 126.7, 60.4, 27.5, 25.2, 21.6, 21.5.

HRMS (ESI-TOF) calcd for $C_{21}H_{23}NO_3S[M+Na]^+$: 392.1291; Found 392.1293.



(E)-7-fluoro-2,3,3-trimethyl-4-(tosylmethylene)-3,4-dihydroisoquinolin-1(2H)-one (3c)

White solid; 51mg, 68% yield; m.p.: 181-182℃.

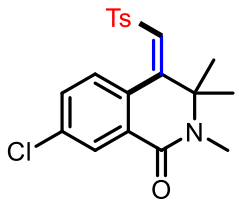
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.08 (dd, *J* = 12.0, 8.0 Hz, 1H), 7.72 – 7.62 (m, 3H), 7.28 – 7.16 (m, 3H), 6.61 (s, 1H), 3.09 (s, 3H), 2.39 (s, 3H), 1.39 (s, 6H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 164.2 (d, *J* = 251.0 Hz), 162.7 (d, *J* = 2.0 Hz), 150.1, 144.8, 137.4, 132.8 (d, *J* = 8.0 Hz), 131.0 (d, *J* = 8.0 Hz), 129.8, 127.6, 127.5, 126.5 (d, *J* = 3.0 Hz), 118.2 (d, *J* = 22.0 Hz), 114.7 (d, *J* = 23.0 Hz), 60.6, 27.6, 25.2,

21.6.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -107.71.

HRMS (ESI-TOF) calcd for $C_{20}H_{20}FNO_3S[M+Na]^+$: 396.1040; Found: 396.1044.



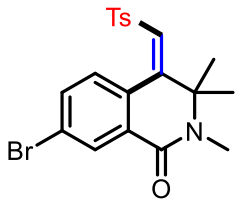
(E)-7-chloro-2,3,3-trimethyl-4-(tosylmethylene)-3,4-dihydroisoquinolin-1(2H)-one (3d)

White solid; 47mg, 61% yield; m.p.: 178-179°C.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.01 (d, *J* = 8.0 Hz, 1H), 7.99 (d, *J* = 2.2 Hz, 1H), 7.67 (d, *J* = 8.0 Hz, 2H), 7.49 (dd, *J* = 8.0, 2.4 Hz, 1H), 7.27 (d, *J* = 4.0 Hz, 2H), 6.62 (s, 1H), 3.09 (s, 3H), 2.41 (s, 3H), 1.39 (s, 6H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 162.7, 149.9, 144.9, 137.4, 137.3, 131.9, 131.1, 130.0, 129.9, 128.7, 128.0, 127.8, 127.6, 60.5, 27.6, 25.2, 21.6.

HRMS (ESI-TOF) calcd for $C_{20}H_{20}ClNO_3S[M+Na]^+$: 412.0745; Found: 412.0748.



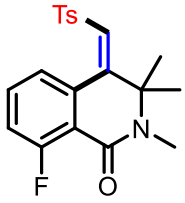
(E)-7-bromo-2,3,3-trimethyl-4-(tosylmethylene)-3,4-dihydroisoquinolin-1(2H)-one (3e)

White solid; 42mg, 48% yield; m.p.: 177-178°C.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.15 (d, *J* = 2.0 Hz, 1H), 7.93 (d, *J* = 8.0 Hz, 1H), 7.70 – 7.61 (m, 3H), 7.27 (d, *J* = 8.0 Hz, 2H), 6.63 (s, 1H), 3.09 (s, 3H), 2.42 (s, 3H), 1.39 (s, 6H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 162.5, 149.9, 145.0, 137.3, 134.0, 131.9, 130.7, 130.0, 129.9, 129.1, 128.1, 127.6, 125.6, 60.4, 27.6, 25.2, 21.7.

HRMS (ESI-TOF) calcd for $C_{20}H_{20}BrNO_3S[M+Na]^+$: 456.0239, Found: 456.0244.



(E)-8-fluoro-2,3,3-trimethyl-4-(tosylmethylene)-3,4-dihydroisoquinolin-1(2H)-one (3f)

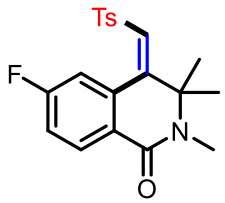
White solid; 27mg, 36% yield; m.p.: 246-247℃.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.80 (d, *J* = 8.0 Hz, 1H), 7.64 (d, *J* = 8.0 Hz, 2H), 7.53 – 7.43 (m, 1H), 7.26 – 7.16 (m, 3H), 6.62 (s, 1H), 3.06 (s, 3H), 2.39 (s, 3H), 1.37 (s, 6H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 160.7 (d, *J* = 262.0 Hz), 160.7 (d, *J* = 4.0 Hz), 150.3 (d, *J* = 3.0 Hz), 144.9, 137.3, 132.7, 132.3 (d, *J* = 9.0 Hz), 129.8, 128.3, 127.6, 126.4 (d, *J* = 4.0 Hz), 119.6 (d, *J* = 23.0 Hz), 116.2 (d, *J* = 5.0 Hz), 59.9, 27.1, 25.0, 21.6.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -113.04.

HRMS (ESI-TOF) calcd for $C_{20}H_{20}FNO_3S[M+Na]^+$: 396.1040; Found 396.1042.



(E)-6-fluoro-2,3,3-trimethyl-4-(tosylmethylene)-3,4-dihydroisoquinolin-1(2H)-one (3g)

White solid; 40mg, 53% yield; m.p.: 208-209℃.

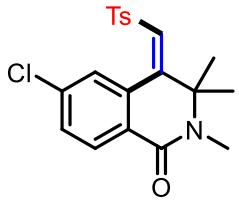
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.98 (dd, *J* = 8.0, 4.0 Hz, 1H), 7.76 (dd, *J* = 8.0, 2.4 Hz, 1H), 7.65 (d, *J* = 8.0 Hz, 2H), 7.22 (d, *J* = 8.0 Hz, 2H), 7.18 – 7.09 (m, 1H), 6.70 (s, 1H), 3.08 (s, 3H), 2.36 (s, 3H), 1.40 (s, 6H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ163.7 (d, *J* = 251.0 Hz), 162.9, 149.8 (d, *J* = 2.0 Hz), 144.8, 137.1, 132.5 (d, *J* = 10.0 Hz), 130.4 (d, *J* = 9.0 Hz), 129.7, 129.0, 127.5, 124.8 (d, *J* = 3.0 Hz), 117.7 (d, *J* = 22.0 Hz), 117.4 (d, *J* = 24.0 Hz), 60.4, 27.4,

25.1, 21.6.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -106.79.

HRMS (ESI-TOF) calcd for $C_{20}H_{20}FNO_3S[M+Na]^+$: 396.1040; Found 396.1044.



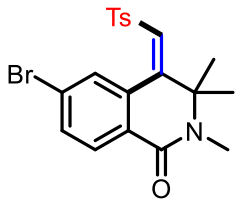
(E)-6-chloro-2,3,3-trimethyl-4-(tosylmethylene)-3,4-dihydroisoquinolin-1(2H)-one (3h)

White solid; 40mg, 51% yield; m.p.: 220-222℃.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.96 (d, *J* = 2.0 Hz, 1H), 7.87 (d, *J* = 8.0 Hz, 1H), 7.63 (d, *J* = 8.0 Hz, 2H), 7.39 (dd, *J* = 8.0, 2.0 Hz, 1H), 7.20 (d, *J* = 8.0 Hz, 2H), 6.74 (s, 1H), 3.08 (s, 3H), 2.35 (s, 3H), 1.41 (s, 6H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 162.9, 149.6, 144.8, 137.3, 136.8, 131.6, 130.7, 130.0, 129.6, 129.4, 129.2, 127.6, 126.7, 60.5, 27.5, 25.1, 21.6.

HRMS (ESI-TOF) calcd for $C_{20}H_{20}ClNO_3S[M+Na]^+$: 412.0745; Found 412.0748.



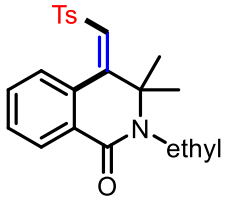
(E)-6-bromo-2,3,3-trimethyl-4-(tosylmethylene)-3,4-dihydroisoquinolin-1(2H)-one (3i)

White solid; 38mg, 44% yield; m.p.: 227-228℃.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.10 (d, *J* = 4.0 Hz, 1H), 7.78 (d, *J* = 8.0 Hz, 1H), 7.63 (d, *J* = 8.0 Hz, 2H), 7.55 (dd, *J* = 8.0, 2.0 Hz, 1H), 7.19 (d, *J* = 8.0 Hz, 2H), 6.75 (s, 1H), 3.08 (s, 3H), 2.34 (s, 3H), 1.41 (s, 6H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 163.0, 149.5, 144.8, 136.8, 133.7, 132.8, 131.8, 129.6, 129.5, 129.3, 127.7, 127.1, 125.9, 60.5, 27.5, 25.1, 21.6.

HRMS (ESI-TOF) calcd for $C_{20}H_{20}BrNO_3S[M+Na]^+$: 456.0239; Found 456.0244.



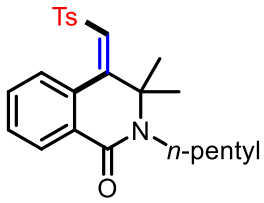
(E)-2-ethyl-3,3-dimethyl-4-(tosylmethylene)-3,4-dihydroisoquinolin-1(2H)-one (3j)

White solid; 35mg, 48% yield; m.p.: 157-158℃.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.06 – 7.92 (m, 2H), 7.65 – 7.60 (m, 2H), 7.54 – 7.44 (m, 2H), 7.19 (d, *J* = 8.0 Hz, 2H), 6.62 (s, 1H), 3.63 (q, *J* = 8.0 Hz, 2H), 2.36 (s, 3H), 1.43 (s, 6H), 1.22 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 163.5, 152.1, 144.6, 137.5, 131.0, 130.9, 130.5, 130.3, 129.6, 128.7, 127.5, 127.5, 127.2, 60.6, 37.1, 26.3, 21.6, 15.6.

HRMS (ESI-TOF) calcd for $C_{21}H_{23}NO_3S[M+Na]^+$: 392.1291; Found 392.1294.



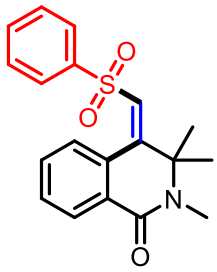
(E)-3,3-dimethyl-2-pentyl-4-(tosylmethylene)-3,4-dihydroisoquinolin-1(2H)-one (3k)

White solid; 28mg, 34% yield; m.p.: 121-122℃.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.05 – 7.88 (m, 2H), 7.61 (d, *J* = 8.0 Hz, 2H), 7.52 – 7.44 (m, 2H), 7.19 (d, *J* = 8.0 Hz, 2H), 6.62 (s, 1H), 3.56 – 3.47 (m, 2H), 2.36 (s, 3H), 1.62 – 1.54 (m, 2H), 1.42 (s, 6H), 1.39 – 1.24 (m, 4H), 0.90 (m, 3H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 163.7, 152.2, 144.5, 137.5, 131.0, 130.9, 130.5, 130.3, 129.6, 128.7, 127.6, 127.5, 127.2, 60.6, 42.5, 30.0, 29.4, 26.2, 22.4, 21.6, 14.1.

HRMS (ESI-TOF) calcd for $C_{24}H_{29}NO_3S[M+Na]^+$: 434.1760; Found 434.1762.



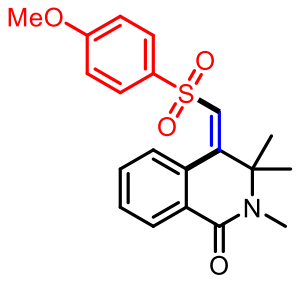
(E)-2,3,3-trimethyl-4-((phenylsulfonyl)methylene)-3,4-dihydroisoquinolin-1(2H)-one (3l)

White solid; 38mg, 56% yield; m.p.: 207-208℃.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.06 – 7.99 (m, 1H), 8.00 – 7.93 (m, 1H), 7.74 (d, *J* = 4.0 Hz, 2H), 7.55 – 7.44 (m, 3H), 7.40 (t, *J* = 8.0 Hz, 2H), 6.65 (s, 1H), 3.09 (s, 3H), 1.39 (s, 6H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 163.7, 151.9, 140.3, 133.6, 131.1, 131.0, 130.3, 130.3, 129.0, 128.4, 127.7, 127.5, 127.4, 60.4, 27.4, 25.1.

HRMS (ESI-TOF) calcd for $C_{19}H_{19}NO_3S[M+Na]^+$: 364.0978; Found 364.0981.



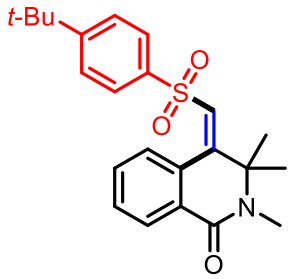
(E)-4-(((4-methoxyphenyl)sulfonyl)methylene)-2,3,3-trimethyl-3,4-dihydroisoquinolin-1(2H)-one (3m)

White solid; 56mg, 75% yield; m.p.: 188-189℃.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.07 – 8.02 (m, 1H), 8.00 – 7.95 (m, 1H), 7.67 (d, *J* = 8.0 Hz, 2H), 7.55 – 7.45 (m, 2H), 6.85 (d, *J* = 8.0 Hz, 2H), 6.64 (s, 1H), 3.81 (s, 3H), 3.08 (s, 3H), 1.38 (s, 6H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 163.8, 163.6, 151.0, 131.9, 131.0, 130.9, 130.4, 130.3, 129.8, 128.4, 128.0, 127.7, 114.2, 60.4, 55.7, 27.4, 25.1.

HRMS (ESI-TOF) calcd for $C_{20}H_{21}NO_4S[M+Na]^+$: 394.1083; Found 394.1088.



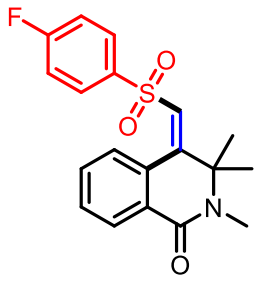
(E)-4-(((4-(tert-butyl)phenyl)sulfonyl)methylene)-2,3,3-trimethyl-3,4-dihydroisoquinolin-1(2H)-one (3n)

White solid; 51mg, 64% yield; m.p.: 207-208℃.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.03 – 7.96 (m, 1H), 7.98 – 7.92 (m, 1H), 7.65 (d, *J* = 8.0 Hz, 2H), 7.52 – 7.42 (m, 2H), 7.39 (d, *J* = 8.0 Hz, 2H), 6.65 (s, 1H), 3.09 (s, 3H), 1.40 (s, 6H), 1.28 (s, 9H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 163.8, 157.5, 151.3, 137.2, 131.0, 130.8, 130.4, 130.3, 128.4, 127.7, 127.6, 127.4, 126.0, 60.4, 35.2, 31.0, 27.4, 25.1.

HRMS (ESI-TOF) calcd for $C_{23}H_{27}NO_3S[M+Na]^+$: 420.1604; Found 420.1605.



(E)-4-(((4-fluorophenyl)sulfonyl)methylene)-2,3,3-trimethyl-3,4-dihydroisoquinolin-1(2H)-one (3o)

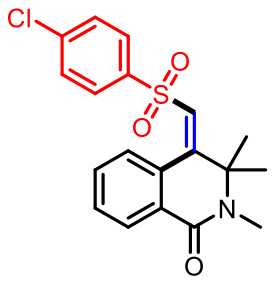
White solid; 32mg, 45% yield; m.p.: 186-187℃.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.05 – 7.94 (m, 2H), 7.79 – 7.70 (m, 2H), 7.55 – 7.46 (m, 2H), 7.12 – 7.01 (m, 2H), 6.64 (s, 1H), 3.09 (s, 3H), 1.40 (s, 6H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 165.6 (d, *J* = 255.0 Hz), 163.6, 152.2, 136.3 (d, *J* = 3.0 Hz), 131.1 (d, *J* = 4.0 Hz), 130.5, 130.4, 130.2, 130.2, 128.4, 127.8, 127.4, 116.3 (d, *J* = 22.0 Hz), 60.4, 27.4, 25.1.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -103.24.

HRMS (ESI-TOF) calcd for $C_{19}H_{18}FNO_3S[M+Na]^+$: 382.0884; Found 382.0886.



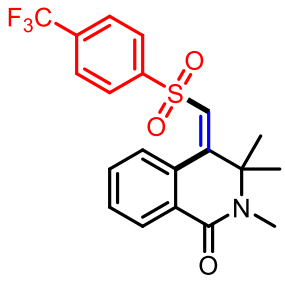
(E)-4-(((4-chlorophenyl)sulfonyl)methylene)-2,3,3-trimethyl-3,4-dihydroisoquinolin-1(2H)-one (3p)

White solid; 49mg, 65% yield; m.p.: 182-183℃.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.04 – 7.96 (m, 2H), 7.67 (d, *J* = 8.0 Hz, 2H), 7.56 – 7.47 (m, 2H), 7.37 (d, *J* = 8.0 Hz, 2H), 6.61 (s, 1H), 3.09 (s, 3H), 1.40 (s, 6H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 163.7, 152.5, 140.3, 138.8, 131.2, 131.1, 130.2, 130.2, 129.4, 129.0, 128.4, 127.8, 127.0, 60.4, 27.5, 25.1.

HRMS (ESI-TOF) calcd for $C_{19}H_{18}ClNO_3S[M+Na]^+$: 398.0588; Found 398.0591.



(E)-2,3,3-trimethyl-4-(((4-(trifluoromethyl)phenyl)sulfonyl)methylene)-3,4-dihydroisoquinolin-1(2H)-one (3q)

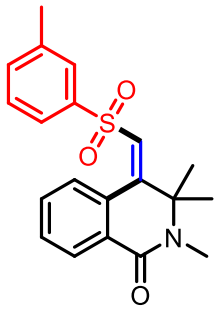
White solid; 29mg, 35% yield; m.p.: 200-201℃.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.03 – 7.93 (m, 2H), 7.87 (d, *J* = 8.0 Hz, 2H), 7.67 (d, *J* = 8.0 Hz, 2H), 7.55 – 7.46 (m, 2H), 6.62 (s, 1H), 3.10 (s, 3H), 1.41 (s, 6H).

^{19}F NMR (376 MHz, Chloroform-*d*) δ -63.30.

^{13}C NMR (100 MHz, Chloroform-*d*) δ 163.5, 153.3, 143.8, 135.2 (d, *J* = 33.2 Hz), 131.3, 131.2, 130.1 (d, *J* = 3.0 Hz), 128.4, 128.1, 127.9, 126.5, 126.2 (q, *J* = 4.0 Hz), 123.0 (d, *J* = 273.0 Hz), 60.5, 27.5, 25.1.

HRMS (ESI-TOF) calcd for $C_{20}H_{18}F_3NO_3S[M+Na]^+$: 432.0852; Found 432.0855.



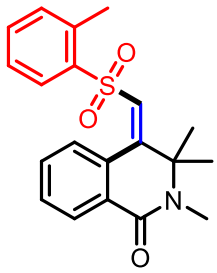
(E)-2,3,3-trimethyl-4-((m-tolylsulfonyl)methylene)-3,4-dihydroisoquinolin-1(2H)-one (3r)

White solid; 38mg, 53% yield; m.p.: 186-188℃.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.05–8.01 (m, 1H), 7.99–7.93 (m, 1H), 7.57–7.45 (m, 4H), 7.34–7.28 (m, 2H), 6.63 (s, 1H), 3.09 (s, 3H), 2.33 (s, 3H), 1.39 (s, 6H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 163.8, 151.7, 140.2, 139.3, 134.3, 131.0, 130.9, 130.4, 130.3, 129.0, 128.4, 128.0, 127.7, 127.6, 124.6, 60.4, 27.4, 25.1, 21.2.

HRMS (ESI-TOF) calcd for $C_{20}H_{21}NO_3S[M+Na]^+$: 378.1134; Found 378.1136.



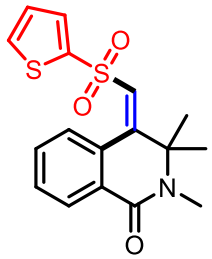
(E)-2,3,3-trimethyl-4-((o-tolylsulfonyl)methylene)-3,4-dihydroisoquinolin-1(2H)-one (3s)

White solid; 59mg, 83% yield; m.p.: 134-135℃.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.07–7.88 (m, 3H), 7.55–7.40 (m, 2H), 7.38–7.31 (m, 1H), 7.20 (t, *J* = 8.0 Hz, 1H), 7.14 (d, *J* = 8.0 Hz, 1H), 6.69 (s, 1H), 3.12 (s, 3H), 2.43 (s, 3H), 1.43 (s, 6H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 163.8, 151.6, 138.1, 137.4, 133.5, 132.5, 131.1, 130.9, 130.2, 129.7, 129.4, 128.0, 127.7, 127.5, 126.0, 60.5, 27.4, 25.1, 20.3.

HRMS (ESI-TOF) calcd for $C_{20}H_{21}NO_3S[M+Na]^+$: 378.1134; Found 378.1136.



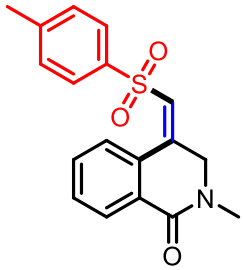
(E)-2,3,3-trimethyl-4-((thiophen-2-ylsulfonyl)methylene)-3,4-dihydroisoquinolin-1(2H)-one (3t)

White solid; 24mg, 34% yield; m.p.: 171-172℃.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.08–8.03 (m, 1H), 8.03–7.99 (m, 1H), 7.58 (dd, *J* = 4.0, 1.2 Hz, 1H), 7.56–7.52 (m, 2H), 7.49 (dd, *J* = 4.0, 1.6 Hz, 1H), 6.96 (dd, *J* = 8.0, 4.0 Hz, 1H), 6.76 (s, 1H), 3.10 (s, 3H), 1.41 (s, 6H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 163.7, 152.1, 141.5, 134.2, 134.1, 131.1, 130.3, 130.3, 128.5, 128.1, 127.8, 127.4, 60.4, 27.4, 25.1.

HRMS (ESI-TOF) calcd for $C_{17}H_{17}NO_3S_2[M+Na]^+$: 370.0542; Found 370.0549.



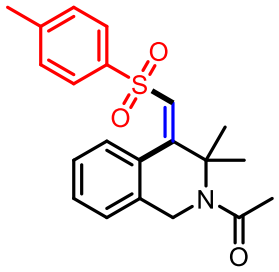
(E)-2-methyl-4-(tosylmethylene)-3,4-dihydroisoquinolin-1(2H)-one (3u)

White solid; 37mg, 56% yield; m.p.: 208-209℃.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.41 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.61 (d, *J* = 8.4 Hz, 2H), 7.56-7.49 (m, 1H), 7.47-7.41 (m, 1H), 7.38 (d, *J* = 8.4 Hz, 1H), 7.21 (d, *J* = 8.0 Hz, 2H), 6.96 (s, 1H), 4.38 (s, 2H), 3.53 (s, 3H), 2.37 (s, 3H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 162.1, 145.1, 136.0, 135.5, 135.1, 132.1, 129.7, 128.7, 128.1, 127.0, 125.7, 122.7, 103.9, 56.8, 37.1, 21.6.

HRMS (ESI-TOF) calcd for $C_{17}H_{18}NO_3S[M+Na]^+$: 350.0821; Found 350.0829.



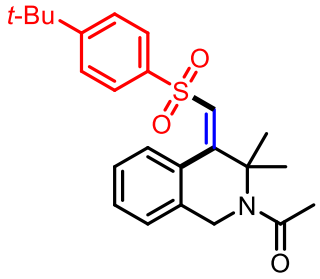
(E)-1-(3,3-dimethyl-4-(tosylmethylene)-3,4-dihydroisoquinolin-2(1H)-yl)ethan-1-one (4a)

White solid; 61mg, 82% yield; mp: 167-168℃.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.85-7.79 (m, 1H), 7.46 (d, *J* = 8.0 Hz, 2H), 7.40 – 7.33 (m, 2H), 7.12 (d, *J* = 8.0 Hz, 2H), 7.07-7.00 (m, 1H), 6.71 (s, 1H), 3.96 (s, 2H), 2.34 (s, 3H), 2.11 (s, 3H), 1.60 (s, 6H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 168.8, 156.7, 144.1, 138.1, 134.7, 131.6, 130.7, 130.2, 129.3, 127.7, 127.5, 127.3, 123.8, 62.7, 48.4, 25.1, 24.2, 21.5.

HRMS (ESI-TOF) calcd for $C_{21}H_{23}NO_3S[M+Na]^+$: 392.1291; Found 392.1294.



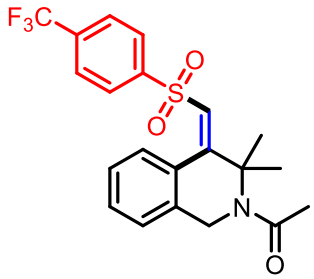
(E)-1-(4-(((4-(tert-butyl)phenyl)sulfonyl)methylene)-3,3-dimethyl-3,4-dihydroisoquinolin-2(1H)-yl)ethan-1-one (4b)

White solid; 50mg, 61% yield; mp: 141-142℃.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.81 (d, *J* = 8.0 Hz, 1H), 7.50 (d, *J* = 8.0 Hz, 2H), 7.39 – 7.30 (m, 4H), 6.98 (d, *J* = 8.0 Hz, 1H), 6.75 (s, 1H), 3.93 (s, 2H), 2.11 (s, 3H), 1.62 (s, 6H), 1.27 (s, 9H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 168.8, 156.9, 156.6, 137.7, 134.7, 131.6, 130.7, 130.2, 127.9, 127.5, 127.1, 125.6, 123.8, 62.7, 48.4, 35.1, 31.0, 25.1, 24.2.

HRMS (ESI-TOF) calcd for $C_{24}H_{29}NO_3S[M+Na]^+$: 434.1760; Found 434.1764.



(E)-1-(3,3-dimethyl-4-(((4-(trifluoromethyl)phenyl)sulfonyl)methylene)-3,4-dihydroisoquinolin-2(1H)-yl)ethan-1-one (4c)

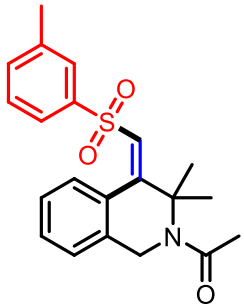
White solid; 46mg, 54% yield; mp: 140-141℃.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.84-7.78 (m, 1H), 7.66 (d, *J* = 8.0 Hz, 2H), 7.55 (d, *J* = 8.0 Hz, 2H), 7.41 – 7.34 (m, 2H), 7.04-6.97 (m, 1H), 6.76 (s, 1H), 3.89 (s, 2H), 2.10 (s, 3H), 1.62 (s, 6H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 168.8, 158.7, 144.2, 134.8, 134.6 (d, *J* = 33.4 Hz), 131.2, 130.7 (d, *J* = 7.9 Hz), 127.8, 127.6, 127.0, 125.6 (d, *J* = 3.7 Hz), 123.9, 123.3 (q, *J* = 271.2 Hz), 62.8, 48.3, 25.1, 24.2.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -63.30.

HRMS (ESI-TOF) calcd for $C_{21}H_{20}F_3NO_3S[M+Na]^+$: 446.1008; Found 446.1013.



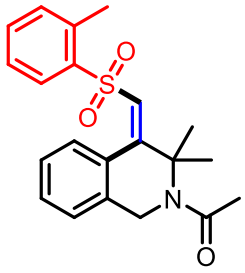
(E)-1-(3,3-dimethyl-4-((m-tolylsulfonyl)methylene)-3,4-dihydroisoquinolin-2(1H)-yl)ethan-1-one (4d)

Yellow solid; 58mg, 78% yield; m.p.: 132-133℃.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.84 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.44 – 7.27 (m, 4H), 7.26 – 7.17 (m, 2H), 7.03 (d, *J* = 8.0 Hz, 1H), 6.75 (s, 1H), 3.93 (s, 2H), 2.27 (s, 3H), 2.11 (s, 3H), 1.62 (s, 6H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 168.8, 157.1, 140.6, 138.8, 134.8, 133.8, 131.5, 130.7, 130.2, 128.6, 127.8, 127.7, 127.4, 124.3, 123.9, 62.7, 48.4, 25.1, 24.2, 21.1.

HRMS (ESI-TOF) calcd for $C_{21}H_{23}NO_3S[M+Na]^+$: 392.1291; Found 392.1294.



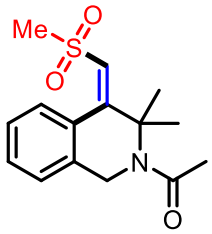
(E)-1-(3,3-dimethyl-4-((o-tolylsulfonyl)methylene)-3,4-dihydroisoquinolin-2(1H)-yl)ethan-1-one (4e)

Colorless oil; 27mg, 36% yield.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.81 (d, *J* = 8.4 Hz, 1H), 7.65 (d, *J* = 8.0 Hz, 1H), 7.38-7.29 (m, 3H), 7.17 (d, *J* = 7.6 Hz, 1H), 7.07 (t, *J* = 8.0 Hz, 1H), 6.99 (d, *J* = 6.4 Hz, 1H), 6.75 (s, 1H), 4.00 (s, 2H), 2.56 (s, 3H), 2.13 (s, 3H), 1.65 (s, 6H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 168.8, 157.0, 138.8, 136.9, 134.7, 133.1, 132.0, 131.3, 130.7, 130.2, 129.2, 127.5, 127.3, 125.9, 123.9, 62.8, 48.4, 25.1, 24.3, 20.4.

HRMS (ESI-TOF) calcd for $C_{21}H_{23}NO_3S[M+Na]^+$: 392.1291; Found 392.1294.



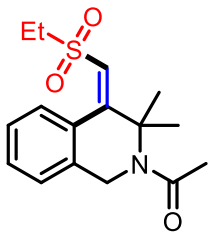
(E)-1-(3,3-dimethyl-4-((methylsulfonyl)methylene)-3,4-dihydroisoquinolin-2(1H)-yl)ethan-1-one (4f)

White solid; 44mg, 75% yield; mp: 148-149°C.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.83 (dd, *J* = 6.8, 1.2 Hz, 1H), 7.45 – 7.38 (m, 2H), 7.28-7.22 (m, 1H), 6.61 (s, 1H), 4.25 (s, 2H), 2.67 (s, 3H), 2.16 (s, 3H), 1.65 (s, 6H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 168.9, 156.9, 135.1, 131.4, 130.6, 130.1, 128.0, 126.4, 124.6, 62.9, 48.5, 42.9, 25.2, 24.3.

HRMS (ESI-TOF) calcd for $C_{15}H_{19}NO_3S[M+Na]^+$: 316.0978; Found 316.0981.



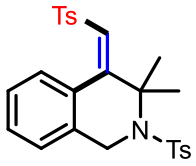
(E)-1-(4-((ethylsulfonyl)methylene)-3,3-dimethyl-3,4-dihydroisoquinolin-2(1H)-yl)ethan-1-one (4g)

White solid; 33mg, 53% yield; mp: 149-150℃.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.89-7.84 (m, 1H), 7.45 – 7.38 (m, 2H), 7.27-7.22 (m, 1H), 6.50 (s, 1H), 4.26 (s, 2H), 2.76 (q, *J* = 8.0 Hz, 2H), 2.17 (s, 3H), 1.66 (s, 6H), 1.20 (t, *J* = 8.0 Hz, 3H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 168.9, 157.7, 134.9, 131.4, 130.6, 130.2, 127.8, 124.5, 124.0, 63.0, 49.0, 48.6, 25.2, 24.3, 7.0.

HRMS (ESI-TOF) calcd for $C_{16}H_{21}NO_3S[M+Na]^+$: 330.1134; Found 330.1139.



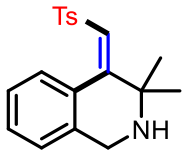
(E)-3,3-dimethyl-2-tosyl-4-(tosylmethylene)-1,2,3,4-tetrahydroisoquinoline (4h)

White solid; 46mg, 48% yield; mp: 177-179℃.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.82-7.72 (m, 1H), 7.47 (d, *J* = 8.0 Hz, 2H), 7.43 (d, *J* = 8.0j Hz, 2H), 7.30 – 7.27 (m, 2H), 7.13 (d, *J* = 8.0 Hz, 2H), 7.10 (d, *J* = 8.0 Hz, 2H), 6.94-6.89 (m, 1H), 6.63 (s, 1H), 4.11 (s, 2H), 2.34 (s, 3H), 2.33 (s, 3H), 1.58 (s, 6H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 155.2, 144.2, 143.1, 139.2, 137.8, 135.2, 131.0, 130.6, 130.1, 129.5, 129.3, 128.0, 127.3, 127.2, 126.7, 124.3, 64.0, 47.6, 27.1, 21.5, 21.4.

HRMS (ESI-TOF) calcd for $C_{26}H_{27}NO_4S_2[M+Na]^+$: 504.1274; Found 504.1276.



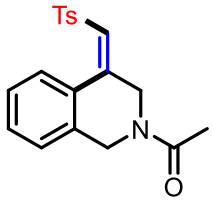
(E)-3,3-dimethyl-4-(tosylmethylene)-1,2,3,4-tetrahydroisoquinoline (4i)

Yellow solid; 38mg, 58% yield; mp: 166-167℃.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.96 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.75 – 7.69 (m, 2H), 7.35 (td, J = 7.6, 1.2 Hz, 1H), 7.30 – 7.22 (m, 3H), 7.03 (dd, J = 7.6, 1.2 Hz, 1H), 6.39 (s, 1H), 3.97 (s, 2H), 2.41 (s, 3H), 1.24 (s, 6H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 155.8, 143.9, 139.0, 137.8, 132.4, 130.5, 129.6, 129.3, 127.3, 125.7, 124.7, 122.6, 55.0, 44.6, 26.5, 21.6.

HRMS (ESI-TOF) calcd for $C_{19}H_{21}NO_2S[M+Na]^+$: 350.1185; Found 350.1188.



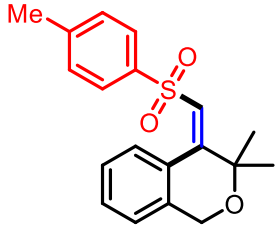
(E)-1-(4-(tosylmethylene)-3,4-dihydroisoquinolin-2(1H)-yl)ethan-1-one (4j)

Colorless oil; 54mg, 79% yield.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.21-8.08 (m, 1H), 7.80 – 7.70 (m, 2H), 7.47 – 7.24 (m, 4H), 7.22 – 7.16 (m, 1H), 6.56-6.47 (m, 1H), 4.65 (d, J = 19.2 Hz, 2H), 4.22 (d, J = 48.0 Hz, 2H), 2.42 (d, J = 10.0 Hz, 3H), 2.14 (d, J = 30.0 Hz, 3H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 169.4, 144.7, 142.9, 138.1, 135.2, 134.1, 131.3, 131.0, 129.9, 127.9, 127.6, 126.9, 125.6, 52.6, 48.4, 44.6, 21.6.

HRMS (ESI-TOF) calcd for $C_{19}H_{19}NO_3S[M+Na]^+$: 364.0978; Found 364.0979.



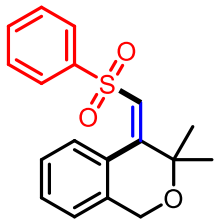
(E)-3,3-dimethyl-4-((phenylsulfonyl)methylene)isochromane (5a)

White solid; 57mg, 87% yield; mp: 129-130℃.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.06 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.70 (d, *J* = 8.0 Hz, 2H), 7.37 – 7.27 (m, 2H), 7.22 (d, *J* = 8.0 Hz, 2H), 7.03 (dd, *J* = 7.6, 1.2 Hz, 1H), 6.42 (s, 1H), 4.64 (s, 2H), 2.38 (s, 3H), 1.35 (s, 6H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 152.4, 144.1, 138.4, 137.2, 132.1, 130.4, 129.6, 127.8, 127.4, 126.4, 124.9, 123.6, 75.6, 63.8, 26.4, 21.6.

HRMS (ESI-TOF) calcd for $C_{19}H_{20}O_3S[M+Na]^+$: 351.1025; Found 351.1028.



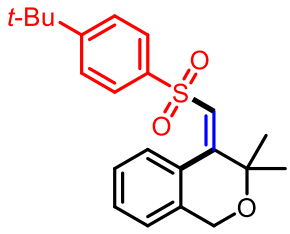
(E)-3,3-dimethyl-4-((phenylsulfonyl)methylene)isochromane (5b)

White solid; 33mg, 52% yield; mp: 140-141℃.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.05 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.82 – 7.80 (m, 2H), 7.53 – 7.49 (m, 1H), 7.43 – 7.39 (m, 2H), 7.39 – 7.34 (m, 1H), 7.33-7.27 (m, 1H), 7.03 (d, *J* = 8.0 Hz, 1H), 6.45 (s, 1H), 4.62 (s, 2H), 1.35 (s, 6H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 152.9, 141.2, 137.2, 133.2, 132.0, 130.5, 128.9, 127.8, 127.4, 126.4, 124.7, 123.6, 75.6, 63.8, 26.3.

HRMS (ESI-TOF) calcd for $C_{18}H_{18}O_3S[M+Na]^+$: 337.0869; Found 337.0871.



(E)-4-(((4-(tert-butyl)phenyl)sulfonyl)methylene)-3,3-dimethylisochromane (5c)

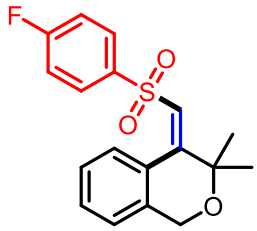
White solid; 36mg, 48% yield; mp: 118-119℃.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.04 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.78-7.72 (m, 2H), 7.48-7.43 (m, 2H), 7.39-7.33 (m, 1H), 7.33-7.29 (m, 1H), 7.01 (dd, *J* = 7.6, 1.2 Hz, 1H), 6.44 (s, 1H), 4.64 (s, 2H), 1.36 (s, 6H), 1.29 (s, 9H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 157.0, 152.3, 138.1, 137.2, 132.0, 130.4, 127.9,

127.3, 126.4, 125.9, 125.0, 123.5, 75.6, 63.8, 35.2, 31.0, 26.4.

HRMS (ESI-TOF) calcd for $C_{22}H_{26}O_3S[M+Na]^+$: 393.1495; Found 393.1498.



(E)-4-(((4-fluorophenyl)sulfonyl)methylene)-3,3-dimethylisochromane (5d)

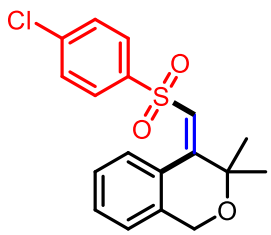
White solid; 41mg, 61% yield; mp: 116-117℃.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.03 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.87 – 7.78 (m, 2H), 7.40-7.34 (m, 1H), 7.33 – 7.27 (m, 1H), 7.13-7.06 (m, 2H), 7.02 (dd, *J* = 7.6, 1.2 Hz, 1H), 6.46 (s, 1H), 4.62 (s, 2H), 1.35 (s, 6H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 165.4 (d, *J* = 254.0 Hz), 153.2, 137.2, 137.1 (d, *J* = 4.0 Hz), 131.9, 130.6, 130.3 (d, *J* = 9.0 Hz), 127.7, 126.4, 124.7, 123.7, 116.1 (d, *J* = 22.0 Hz), 75.6, 63.8, 26.3.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -104.10.

HRMS (ESI-TOF) calcd for $C_{18}H_{17}FO_3S[M+Na]^+$: 355.0775 Found 355.0777.



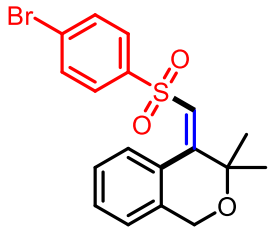
(E)-4-(((4-chlorophenyl)sulfonyl)methylene)-3,3-dimethylisochromane (5e)

White solid; 41mg, 59% yield; mp: 122-123℃.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.02 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.79 – 7.72 (m, 2H), 7.42 – 7.38 (m, 2H), 7.37 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.33-7.28 (m, 1H), 7.05 (d, *J* = 8.0 Hz, 1H), 6.44 (s, 1H), 4.63 (s, 2H), 1.35 (s, 6H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 153.5, 139.8, 139.7, 137.2, 131.9, 130.7, 129.2, 128.9, 127.6, 126.4, 124.3, 123.7, 75.6, 63.8, 26.3.

HRMS (ESI-TOF) calcd for $C_{18}H_{17}ClO_3S[M+Na]^+$: 371.0479; Found 371.0481.



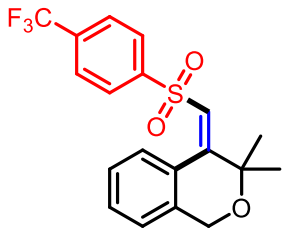
(E)-4-(((4-bromophenyl)sulfonyl)methylene)-3,3-dimethylisochromane (5f)

White solid; 37mg, 47% yield; mp: 124-125℃.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.02 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.67 – 7.64 (m, 2H), 7.56 – 7.54 (m, 2H), 7.39 – 7.35 (m, 1H), 7.29 – 7.27 (m, 1H), 7.03 (dd, *J* = 7.6, 1.2 Hz, 1H), 6.41 (s, 1H), 4.64 (s, 2H), 1.36 (s, 6H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 153.5, 140.2, 137.2, 132.2, 131.9, 130.7, 129.0, 128.4, 127.6, 126.4, 124.2, 123.7, 75.6, 63.8, 26.3.

HRMS (ESI-TOF) calcd for $C_{18}H_{17}BrO_3S[M+Na]^+$: 414.9974; Found 414.9975.



(E)-3,3-dimethyl-4-(((4-(trifluoromethyl)phenyl)sulfonyl)methylene)isochromane (5g)

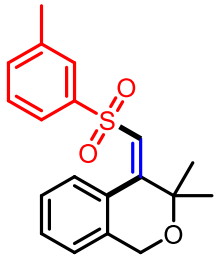
White solid; 28mg, 37% yield; mp: 132-133℃.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.00 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.92 (d, *J* = 8.0 Hz, 2H), 7.67 (d, *J* = 8.0 Hz, 2H), 7.44-7.35 (m, 1H), 7.34 – 7.29 (m, 1H), 7.02 (d, *J* = 8.0 Hz, 1H), 6.43 (s, 1H), 4.63 (s, 2H), 1.37 (s, 6H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 154.3, 144.6, 137.3, 134.8 (d, *J* = 5.8 Hz), 131.9, 130.8, 128.0, 127.6, 126.5, 126.0 (q, *J* = 4.0 Hz), 123.8 (d, *J* = 4.0 Hz), 123.1 (q, *J* = 272.0 Hz), 75.6, 63.8, 26.2.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -63.23.

HRMS (ESI-TOF) calcd for $C_{19}H_{17}F_3O_3S[M+Na]^+$: 405.0743; Found 405.0745.



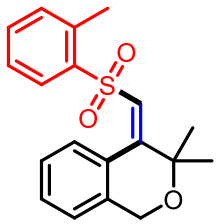
(E)-3,3-dimethyl-4-((m-tolylsulfonyl)methylene)isochromane (5h)

White solid; 36mg, 54% yield; m.p.: 96-97℃.

^{1}H NMR (400 MHz, Chloroform-*d*) 8.08 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.70-7.60 (m, 2H), 7.39 – 7.29 (m, 4H), 7.08 – 7.01 (m, 1H), 6.46 (s, 1H), 4.65 (s, 2H), 2.37 (s, 3H), 1.38 (s, 6H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 152.6, 141.1, 139.1, 137.2, 134.0, 132.0, 130.4, 128.8, 127.8, 126.3, 124.9, 124.5, 123.6, 75.6, 63.8, 26.4, 21.2.

HRMS (ESI-TOF) calcd for $C_{19}H_{20}O_3S[M+Na]^+$: 351.1025; Found 351.1028.



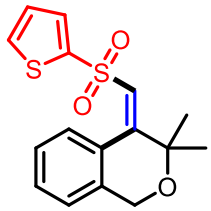
(E)-3,3-dimethyl-4-((o-tolylsulfonyl)methylene)isochromane (5i)

Colorless oil; 28mg, 42% yield.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.03 (d, *J* = 8.0 Hz, 1H), 7.98 (d, *J* = 8.0 Hz, 1H), 7.39-7.33 (m, 1H), 7.32-7.26 (m, 1H), 7.22 (t, *J* = 7.6 Hz, 2H), 7.17 (d, *J* = 8.0 Hz, 1H), 6.98 (d, *J* = 7.6 Hz, 1H), 6.45 (s, 1H), 4.65 (s, 2H), 2.53 (s, 3H), 1.38 (s, 6H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 152.5, 139.0, 137.5, 136.9, 133.3, 132.3, 132.0, 130.4, 129.3, 127.5, 126.3, 126.0, 124.6, 123.5, 75.5, 63.8, 26.2, 20.4.

HRMS (ESI-TOF) calcd for $C_{19}H_{20}O_3S[M+Na]^+$: 351.1025; Found 351.1028.



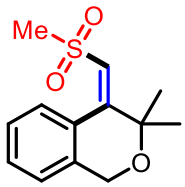
(E)-3,3-dimethyl-4-((thiophen-2-ylsulfonyl)methylene)isochromane (5j)

White solid; 25mg, 39% yield; mp: 88-89℃.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.06 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.59 – 7.55 (m, 2H), 7.44-7.38 (m, 1H), 7.37 – 7.30 (m, 1H), 7.09 (d, *J* = 8.0 Hz, 1H), 7.02 (dd, *J* = 5.0, 3.8 Hz, 1H), 6.55 (s, 1H), 4.65 (s, 2H), 1.38 (s, 6H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 153.0, 142.5, 137.4, 133.7, 133.5, 132.1, 130.6, 127.7, 127.3, 126.4, 125.4, 123.7, 75.7, 63.9, 26.4.

HRMS (ESI-TOF) calcd for $C_{16}H_{16}O_3S_2[M+Na]^+$: 343.0433; Found 343.0435.



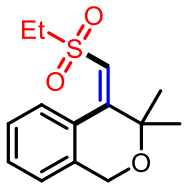
(E)-3,3-dimethyl-4-((methylsulfonyl)methylene)isochromane (5k)

White solid; 27mg, 53% yield; mp: 136-137℃.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.14 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.47-7.40 (m, 1H), 7.36 – 7.32 (m, 1H), 7.13 (dd, *J* = 7.6, 1.2 Hz, 1H), 6.42 (s, 1H), 4.76 (s, 2H), 2.87 (s, 3H), 1.42 (s, 6H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 152.7, 137.5, 131.3, 130.8, 127.8, 126.9, 124.4, 124.1, 75.5, 63.7, 42.7, 26.2.

HRMS (ESI-TOF) calcd for $C_{13}H_{16}O_3S[M+Na]^+$: 275.0712; Found 275.0715.



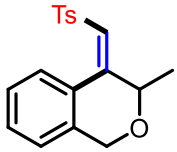
(E)-4-((ethylsulfonyl)methylene)-3,3-dimethylisochromane (5l)

White solid; 20mg, 36% yield; mp: 105-106℃.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.14 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.47-7.41 (m, 1H), 7.40-7.33 (m, 1H), 7.13 (d, *J* = 8.0 Hz, 1H), 6.30 (s, 1H), 4.76 (s, 2H), 2.95 (q, *J* = 7.6 Hz, 2H), 1.43 (s, 6H), 1.26 (t, *J* = 8.0 Hz, 3H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 153.6, 137.4, 131.5, 130.7, 127.9, 126.8, 124.0, 122.0, 75.7, 63.8, 48.8, 26.3, 7.1.

HRMS (ESI-TOF) calcd for $C_{14}H_{18}O_3S[M+Na]^+$: 289.0869; Found 289.0872.



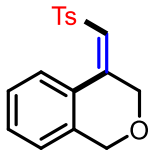
(E)-3-methyl-4-(tosylmethylene)isochromane (5m)

White solid; 31mg, 48% yield; mp: 91-92℃.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.15 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.83-7.75 (m, 2H), 7.42-7.37 (m, 1H), 7.36-7.31 (m, 1H), 7.26 (d, *J* = 8.0 Hz, 2H), 7.05 (dd, *J* = 7.2, 1.2 Hz, 1H), 6.35 (d, *J* = 1.2 Hz, 1H), 4.73 (q, *J* = 16.0 Hz, 2H), 4.40 (q, *J* = 4.0 Hz, 1H), 2.39 (s, 3H), 1.34 (d, *J* = 8.0 Hz, 3H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 148.2, 144.3, 138.3, 136.7, 131.8, 130.6, 129.7, 127.6, 127.5, 126.5, 125.2, 123.9, 74.5, 66.4, 21.6, 19.3.

HRMS (ESI-TOF) calcd for $C_{18}H_{18}O_3S[M+Na]^+$: 337.0869; Found 337.0869.



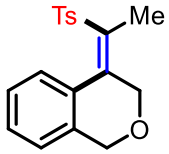
(E)-4-(tosylmethylene)isochromane (5n)

White solid; 37mg, 61% yield; mp: 131-132℃.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.35 (d, *J* = 8.0 Hz, 1H), 7.84 (d, *J* = 8.4 Hz, 2H), 7.44-7.37 (m, 1H), 7.37-7.34 (m, 1H), 7.32 (d, *J* = 8.0 Hz, 2H), 7.08 (d, *J* = 7.6 Hz, 1H), 6.32 (s, 1H), 4.83 (s, 2H), 4.34 (s, 3H), 2.43 (s, 3H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 144.5, 143.0, 138.4, 136.8, 131.6, 131.0, 129.8, 127.5, 127.4, 126.6, 125.8, 124.2, 71.7, 68.6, 21.6.

HRMS (ESI-TOF) calcd for $C_{17}H_{16}O_3S[M+Na]^+$: 323.0712; Found 323.0717.



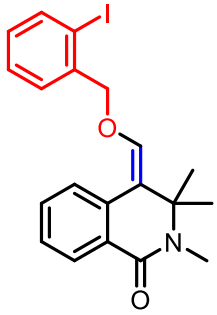
(E)-4-(1-tosylethylidene)isochromane (5p)

Colorless oil; 6mg, 9% yield.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.16 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.77 (d, *J* = 8.4 Hz, 2H), 7.71 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.62-7.56 (m, 1H), 7.51-7.41 (m, 1H), 7.32-7.26 (m, 2H), 4.88 (s, 2H), 4.10 (q, *J* = 2.0 Hz, 2H), 2.41 (s, 3H), 1.85 (t, *J* = 2.4 Hz, 3H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 144.1, 138.4, 138.0, 137.9, 133.6, 129.7, 129.4, 128.8, 127.7, 127.6, 120.0, 116.5, 67. 6, 58.6, 21.6, 3.64.

HRMS (ESI-TOF) calcd for $C_{18}H_{18}O_3S[M+Na]^+$: 337.0869; Found 337.0878.



(E)-4-(((2-iodobenzyl)oxy)methylene)-2,3,3-trimethyl-3,4-dihydroisoquinolin-1(2H)-one (3aa)

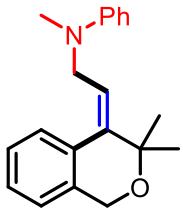
White solid; 104mg, 48% yield; mp: 120-121℃.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.14 (dd, J = 7.6, 1.6 Hz, 1H), 8.01 (dd, J = 7.6, 1.2 Hz, 1H), 7.87 (d, J = 7.6 Hz, 1H), 7.49 (td, J = 7.6, 1.2 Hz, 1H), 7.39-7.36 (m, 2H), 7.34 (td, J = 7.6, 1.2 Hz, 1H), 7.08-6.99 (m, 1H), 6.60 (s, 1H), 4.98 (s, 2H), 3.15 (s, 3H), 1.44 (s, 6H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 164.8, 142.8, 139.4, 139.0, 133.4, 131.2, 129.7,

128.6, 128.5, 128.1, 127.9, 127.7, 126.9, 117.1, 96.9, 79.1, 57.6, 27.5, 25.7.

HRMS (ESI-TOF) calcd for $C_{20}H_{20}INO_2[M+Na]^+$: 456.0431; Found 456.0437.



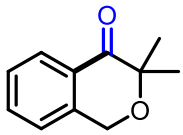
(E)-N-(2-(3,3-dimethylisochroman-4-ylidene)ethyl)-N-methylaniline (5aa)

Colorless oil; 86mg, 59% yield.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.37-7.31 (m, 2H), 7.30-7.28 (m, 1H), 7.28-7.23 (m, 2H), 7.22-7.17 (m, 1H), 6.77 (t, J = 7.2 Hz, 1H), 6.72 (d, J = 7.6 Hz, 2H), 5.70 (t, J = 6.0 Hz, 1H), 4.74 (s, 2H), 4.31 (d, J = 5.6 Hz, 2H), 2.94 (s, 3H), 1.42 (s, 6H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 149.4, 141.8, 137.5, 131.9, 129.2, 129.1, 127.4, 126.4, 124.2, 122.3, 116.8, 113.0, 75.7, 63.7, 52.1, 38.3, 27.3.

HRMS (ESI-TOF) calcd for $C_{20}H_{23}NO[M+Na]^+$: 316.1672; Found 316.1677.



3,3-dimethylisochroman-4-one (5ab)

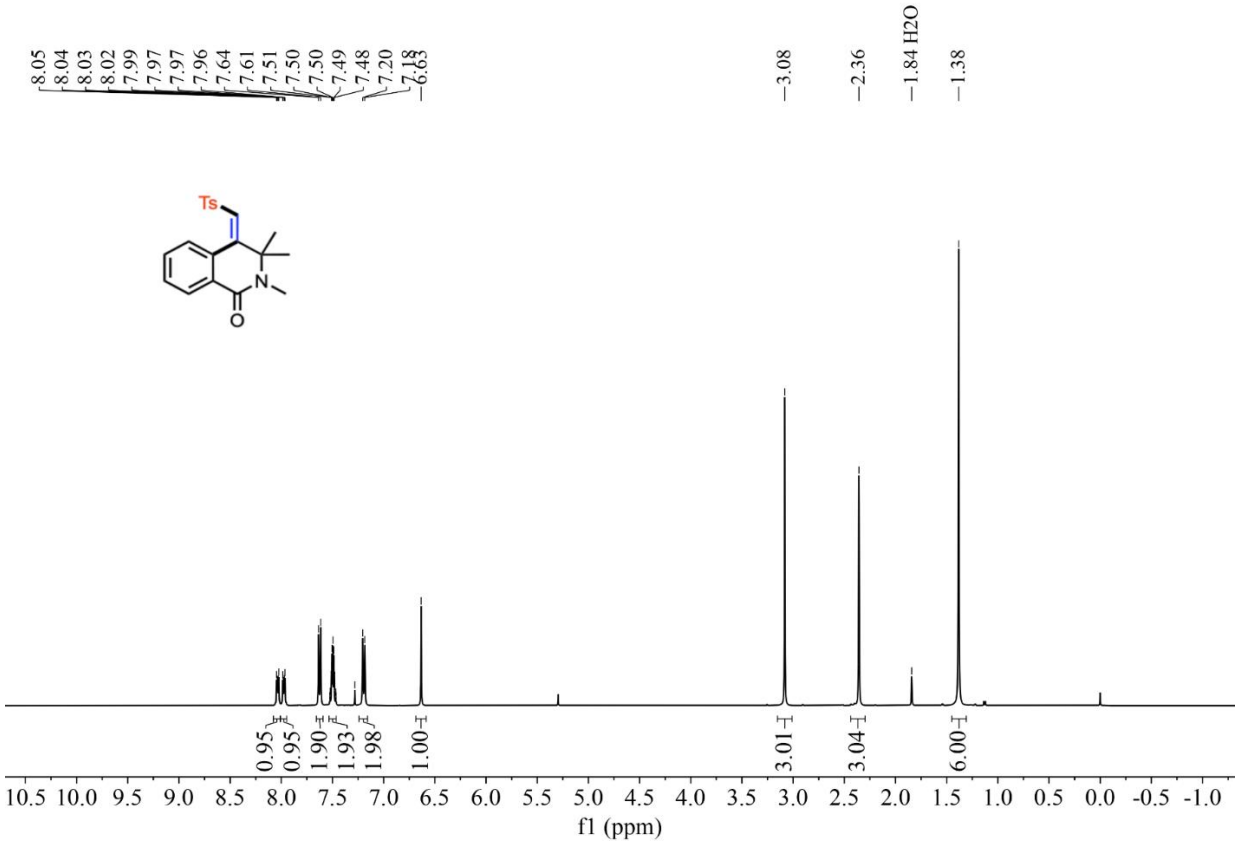
Colorless oil; 62mg, 70% yield.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.06 (d, J = 7.6 Hz, 1H), 7.55 (td, J = 7.6, 1.6 Hz, 1H), 7.45-7.37 (m, 1H), 7.19 (d, J = 7.6 Hz, 1H), 4.95 (s, 2H), 1.49 (s, 6H).

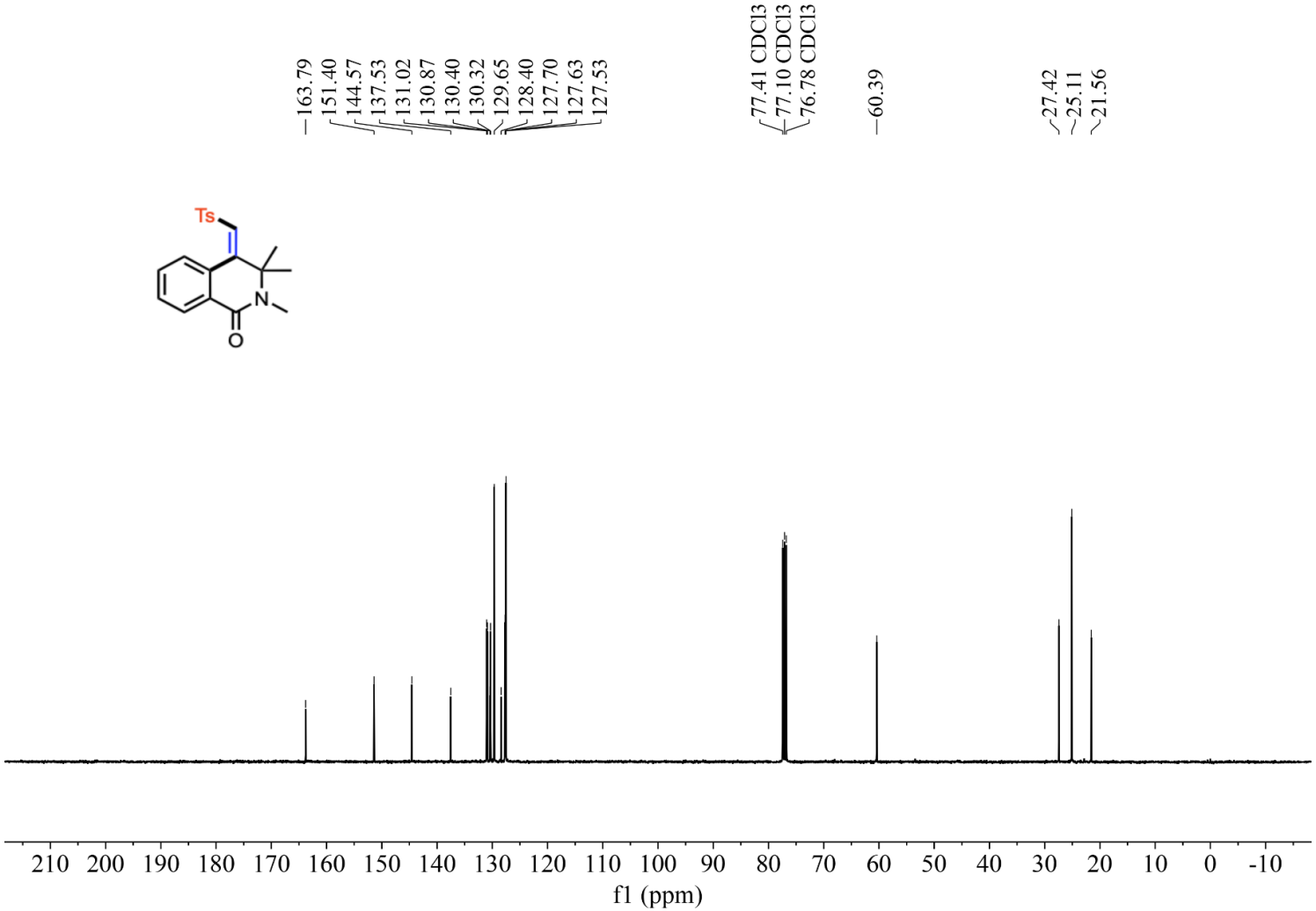
^{13}C NMR (100 MHz, Chloroform-*d*) δ 197.8, 141.6, 133.69, 128.1, 127.6, 127.3, 124.1, 78.9, 61.7, 22.7.

HRMS (ESI-TOF) calcd for $C_{11}H_{12}O_2[M+Na]^+$: 199.0730; Found 199.0734.

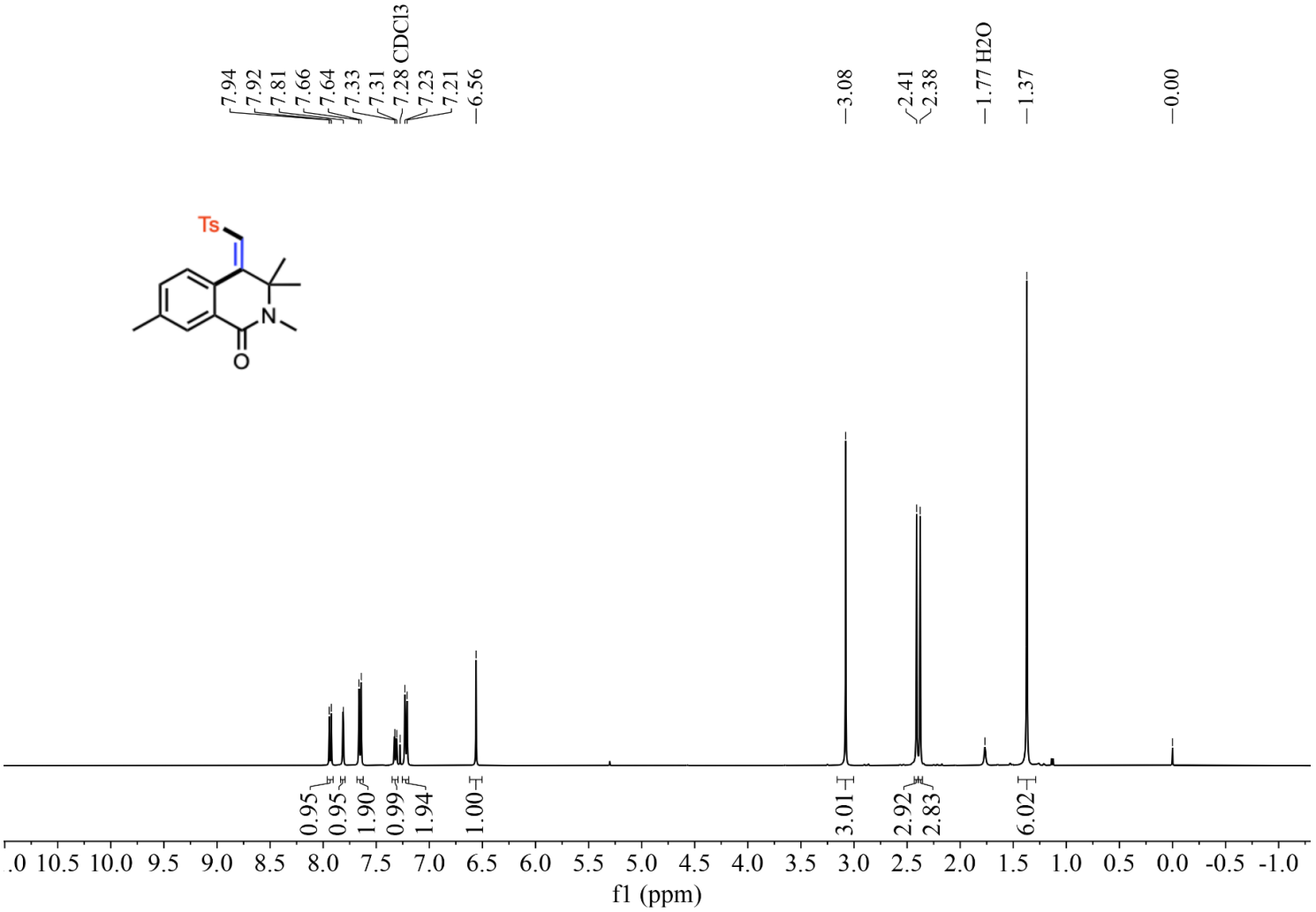
Spectra



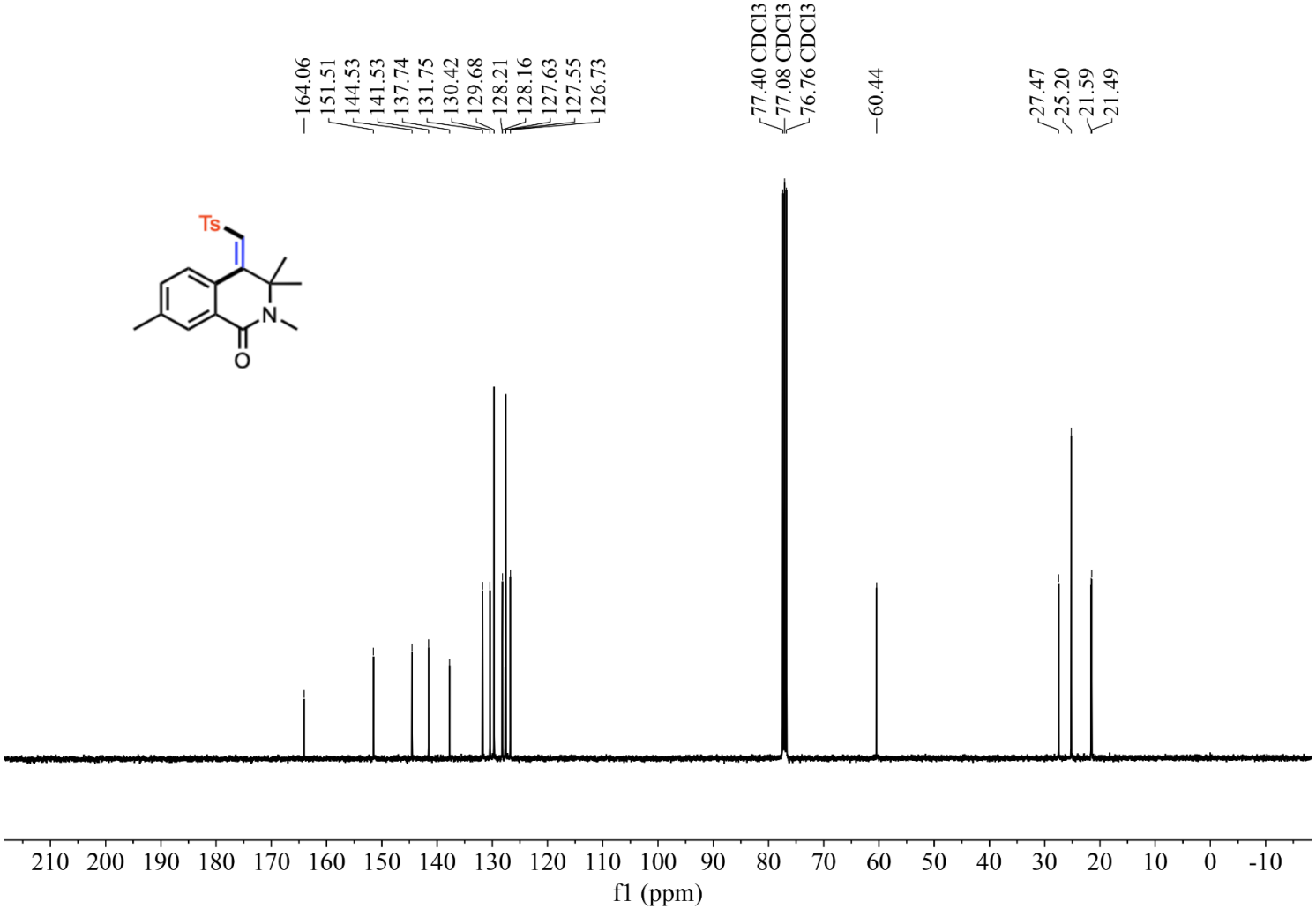
^{1}H spectrum of **3a**



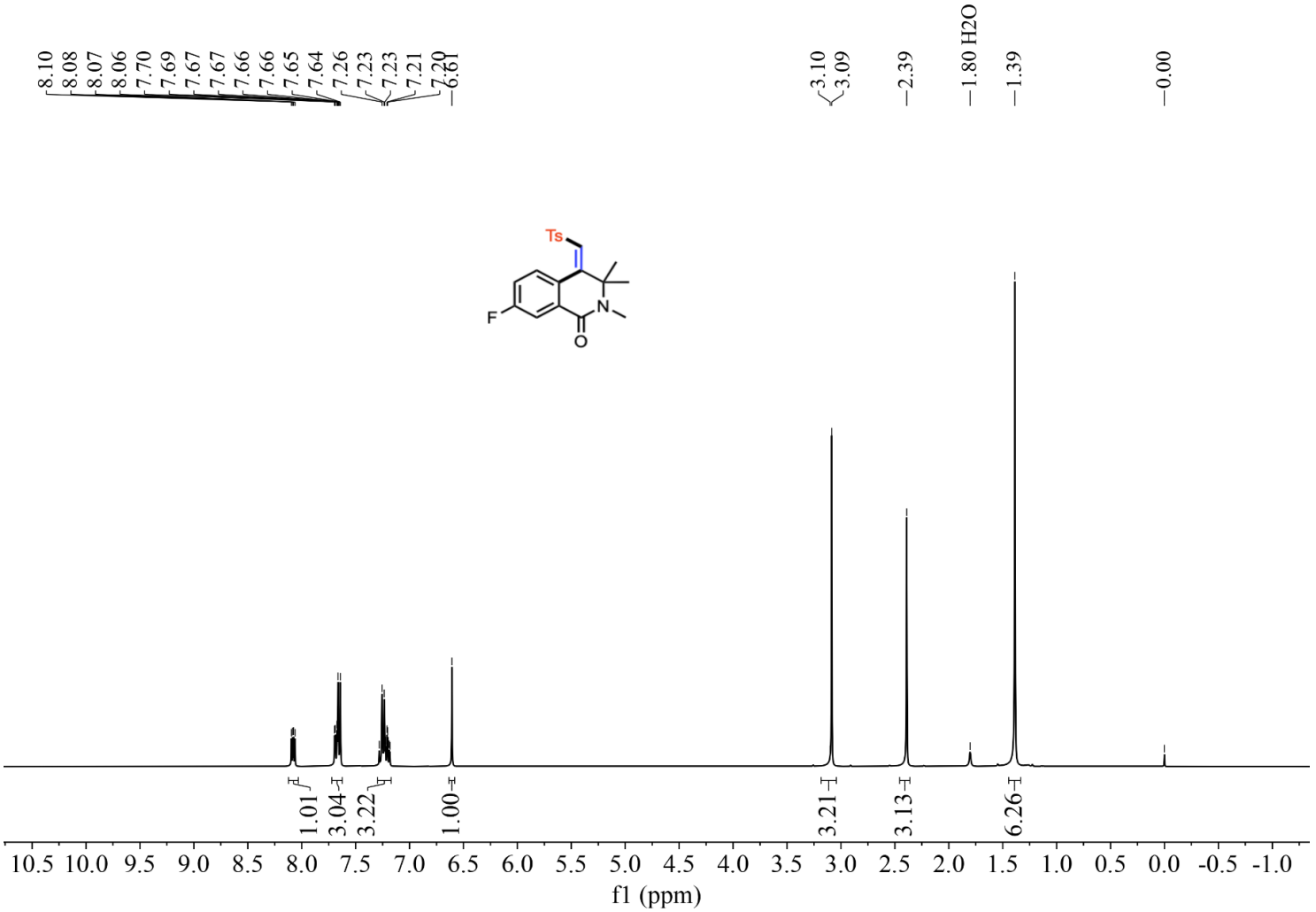
^{13}C spectrum of **3a**



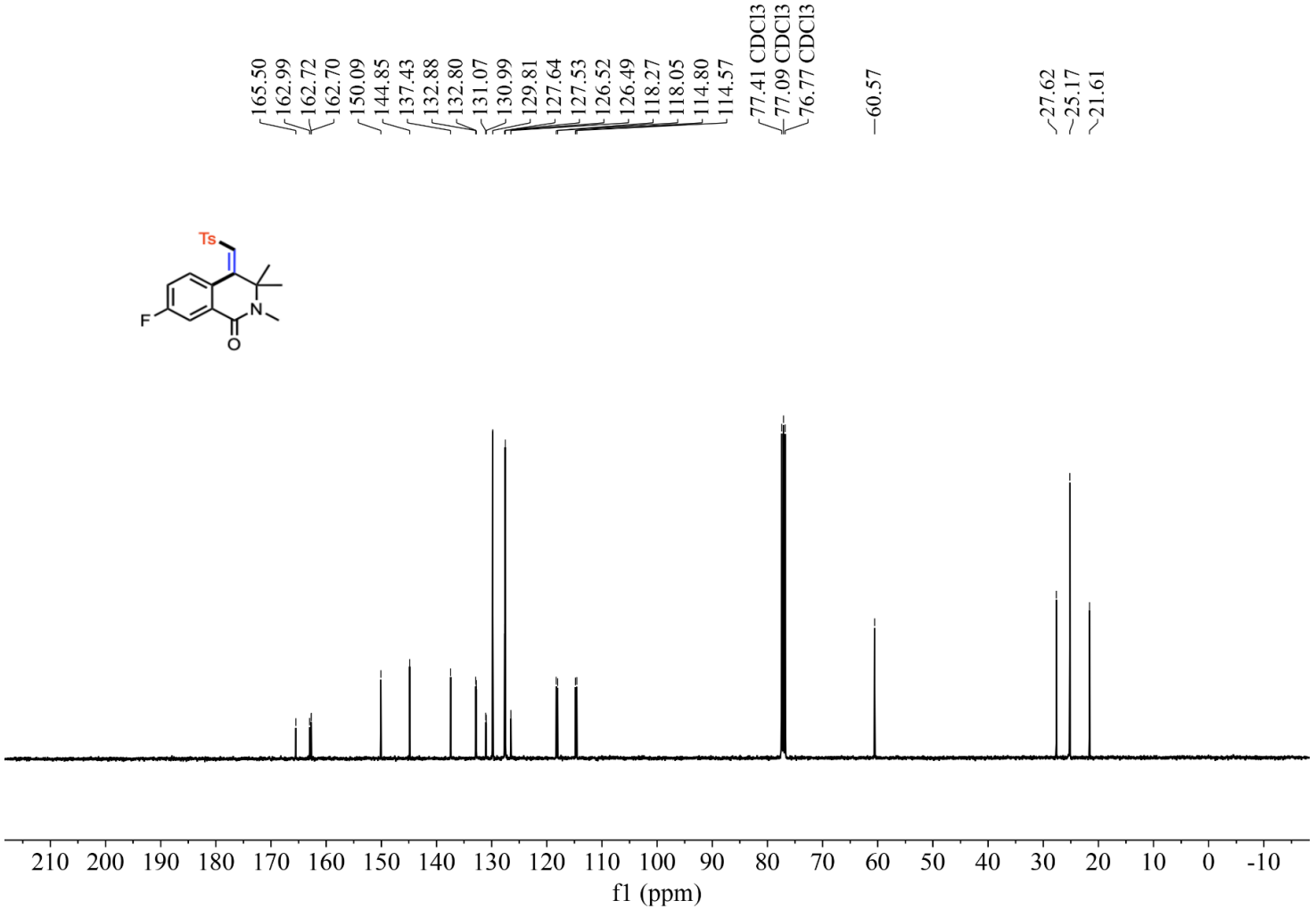
^{1}H spectrum of **3b**



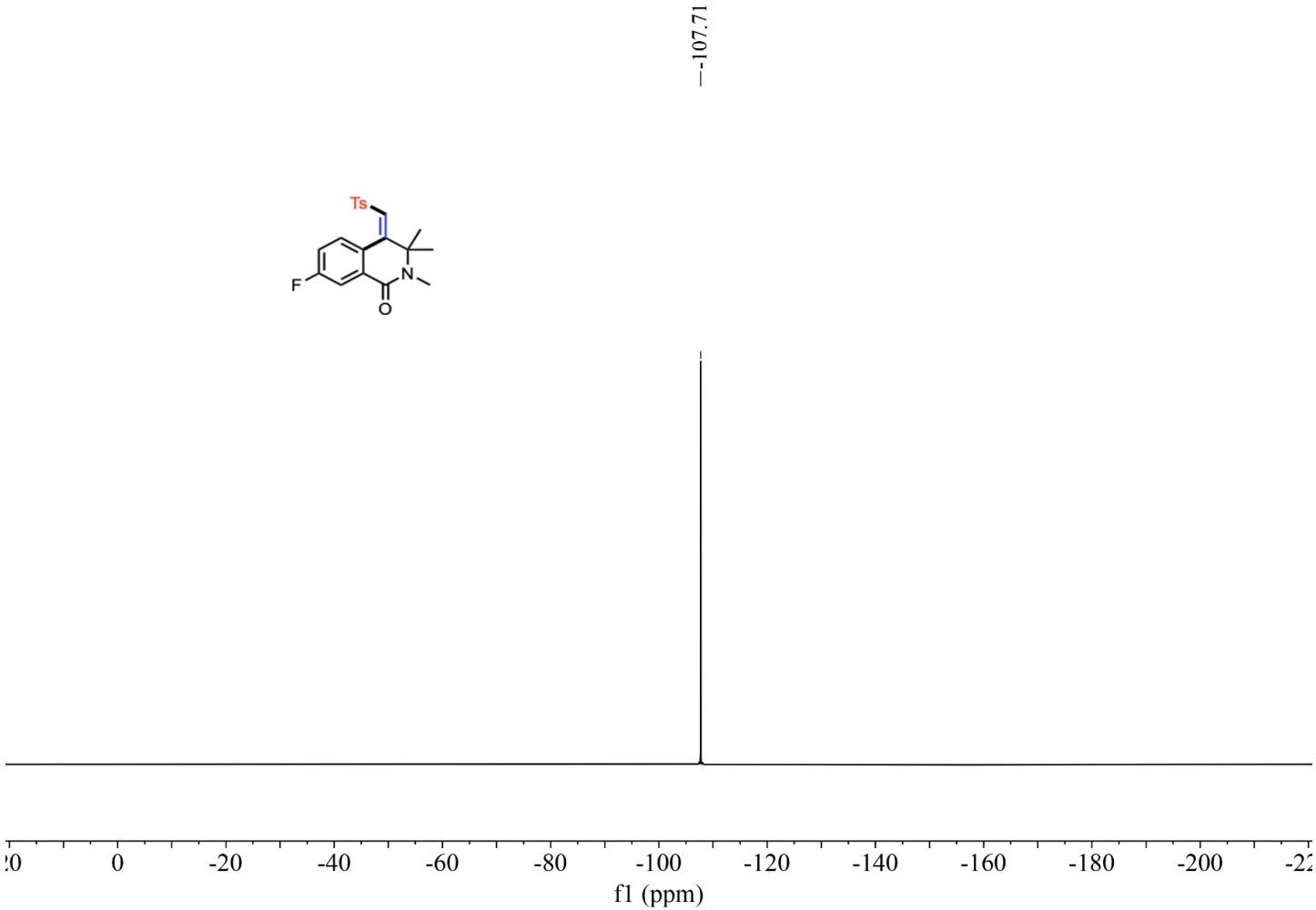
^{13}C spectrum of **3b**



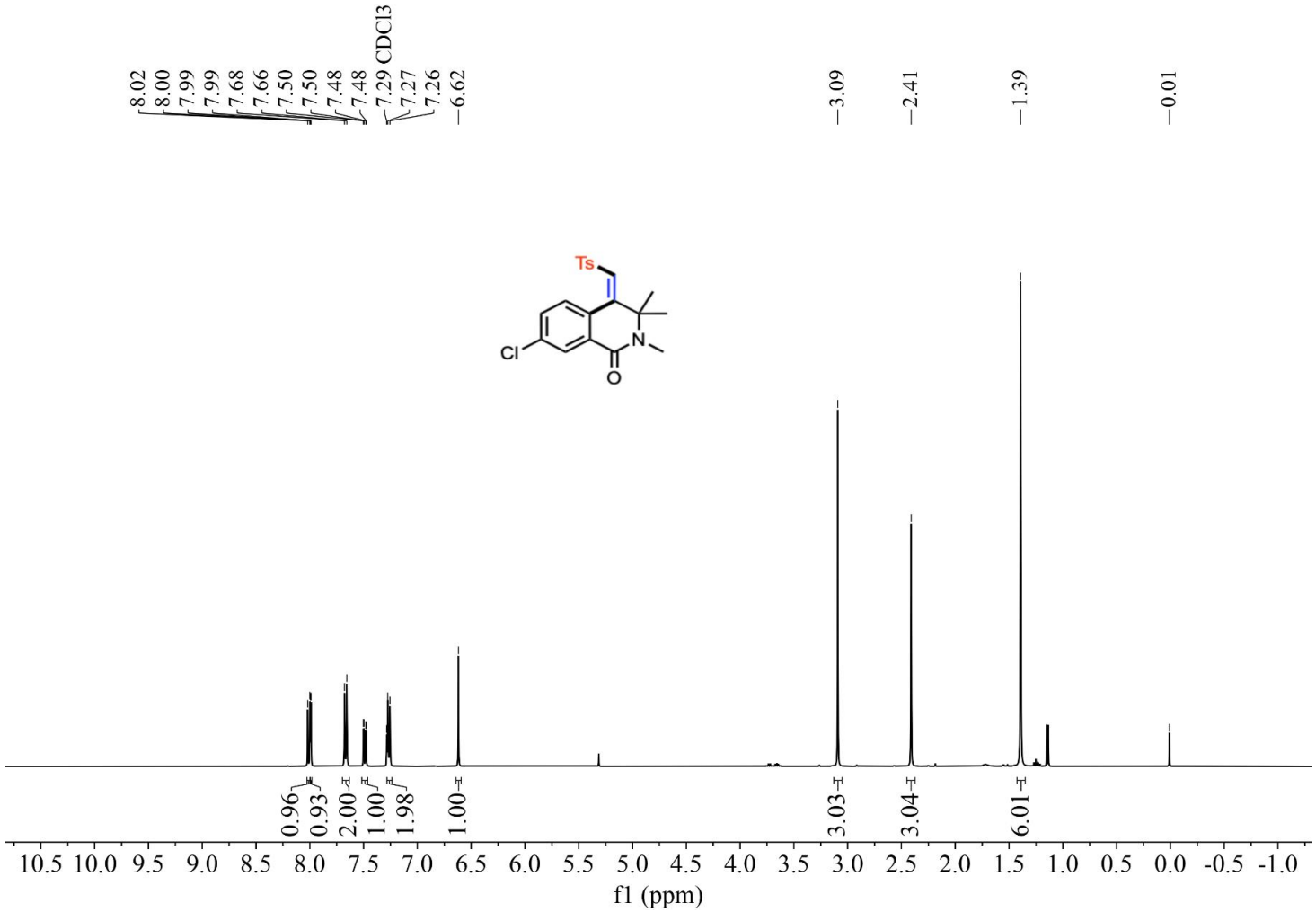
^{1}H spectrum of **3c**



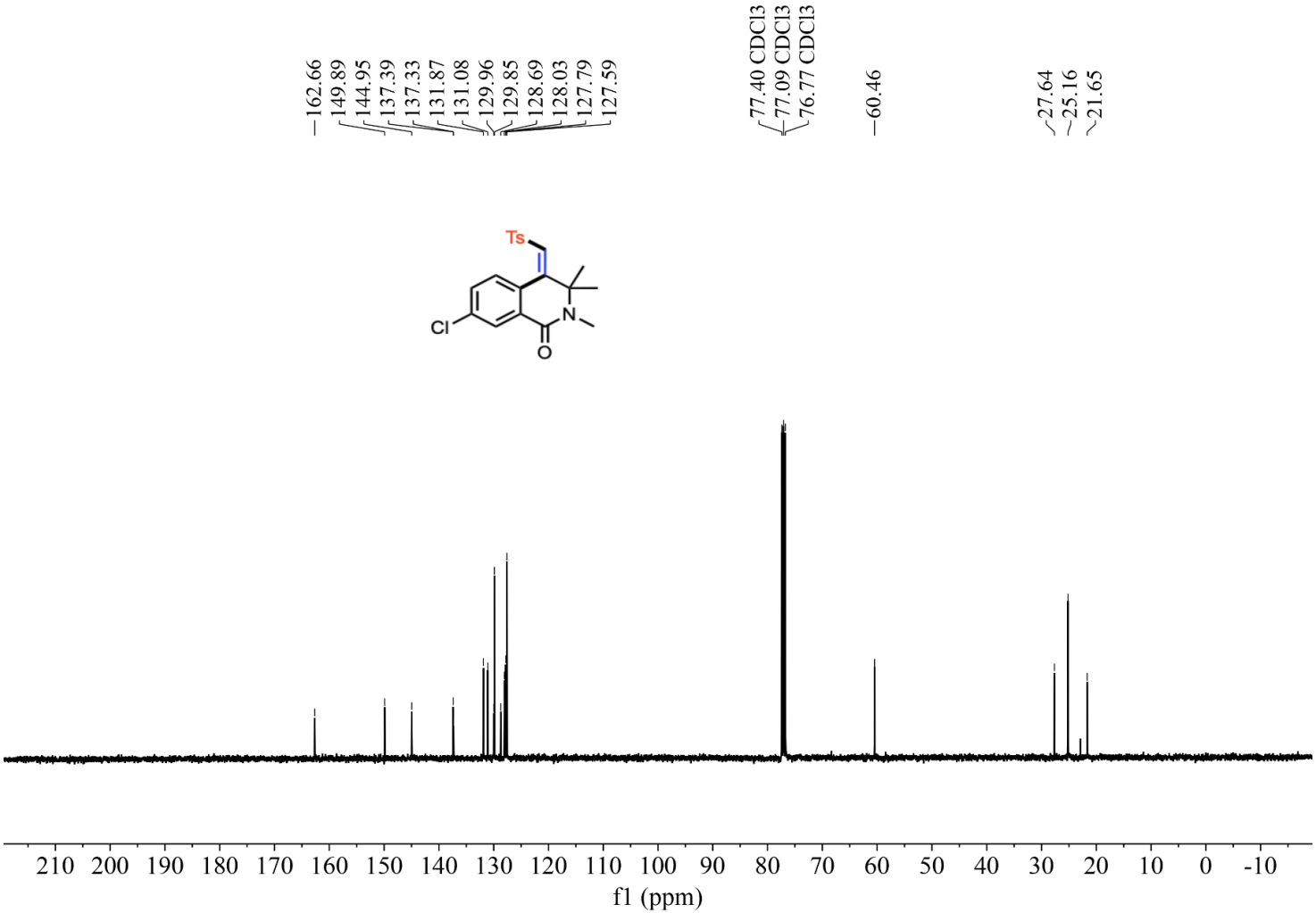
^{13}C spectrum of **3c**



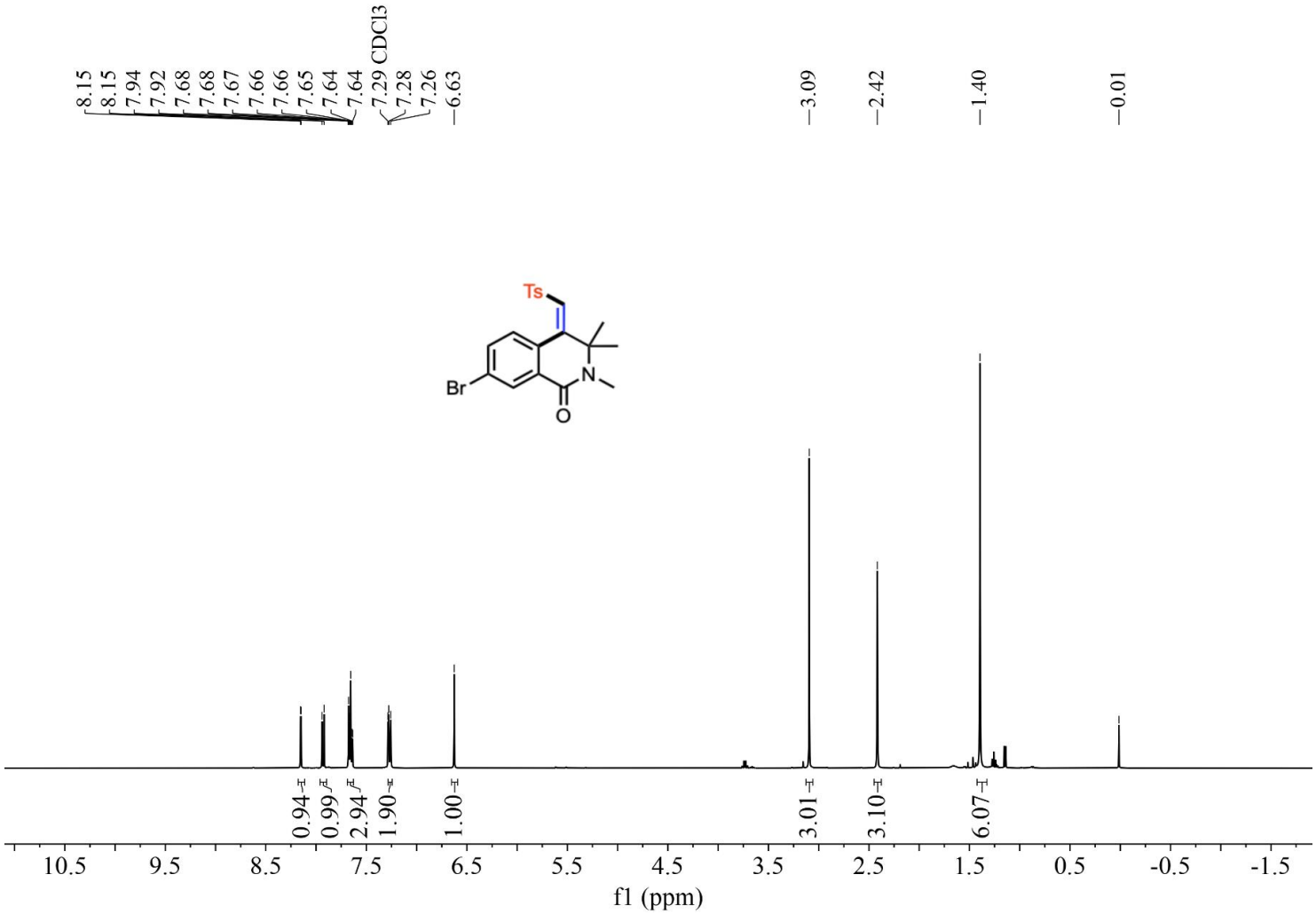
^{19}F spectrum of **3c**



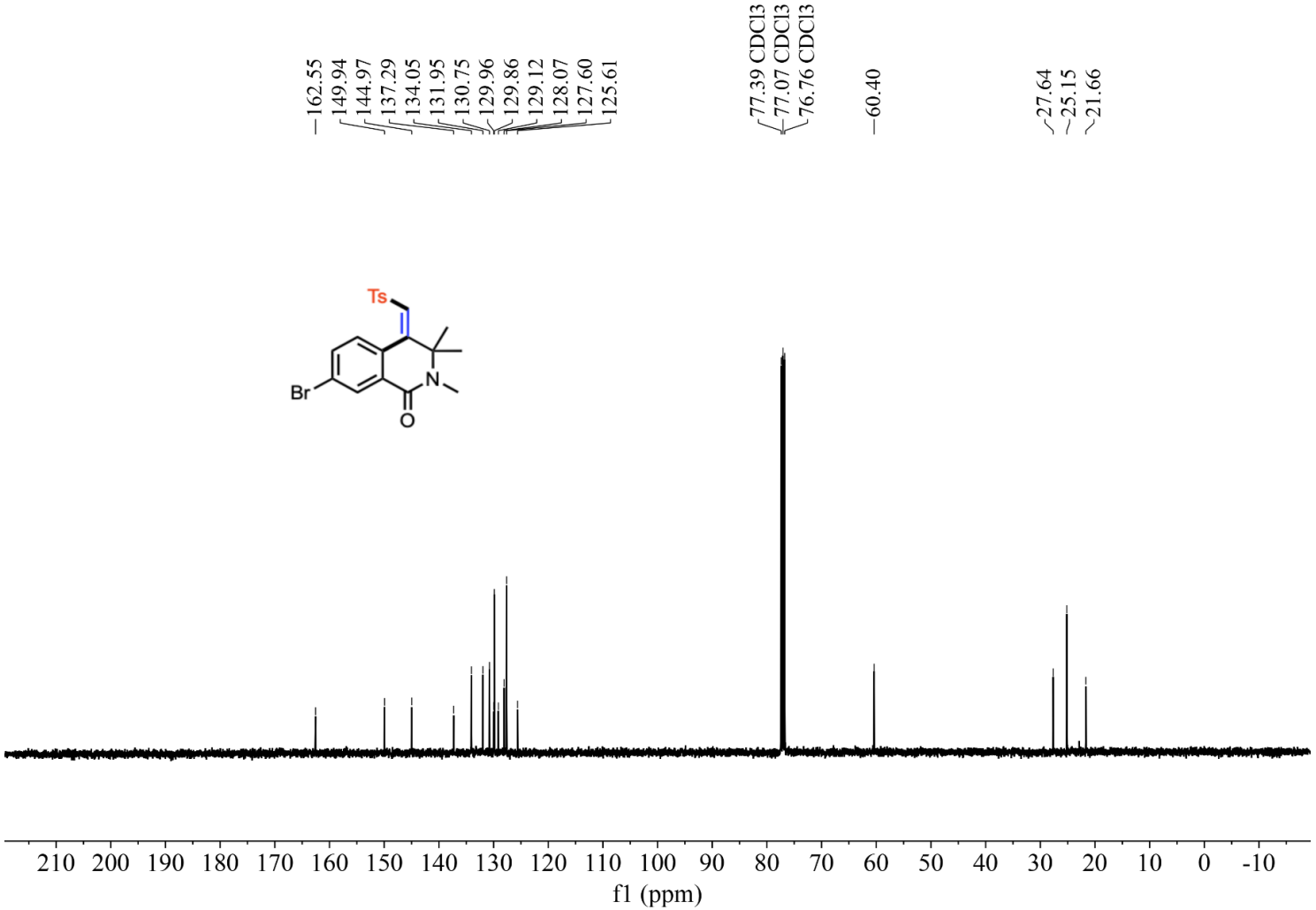
^{1}H spectrum of **3d**



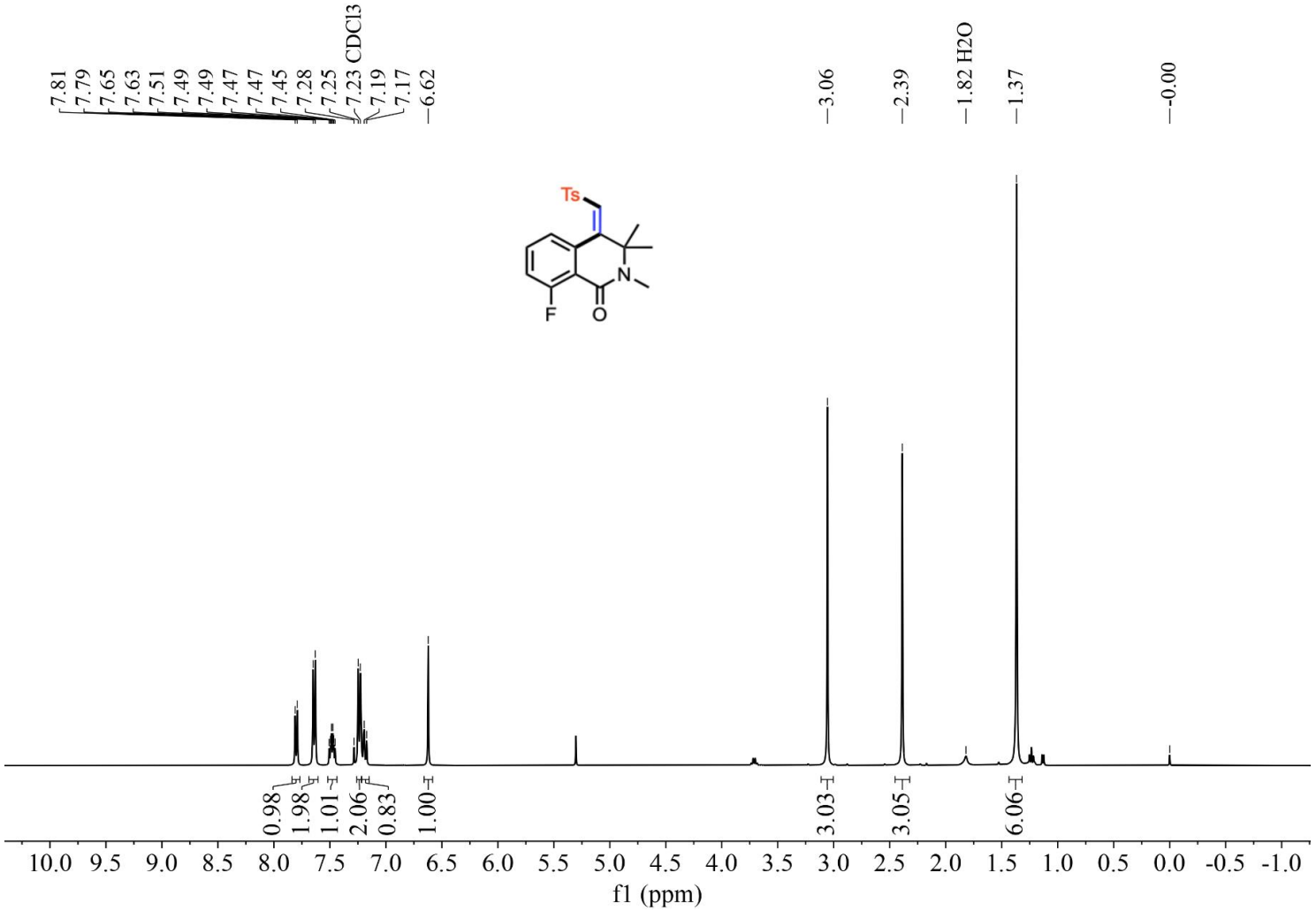
^{13}C spectrum of **3d**



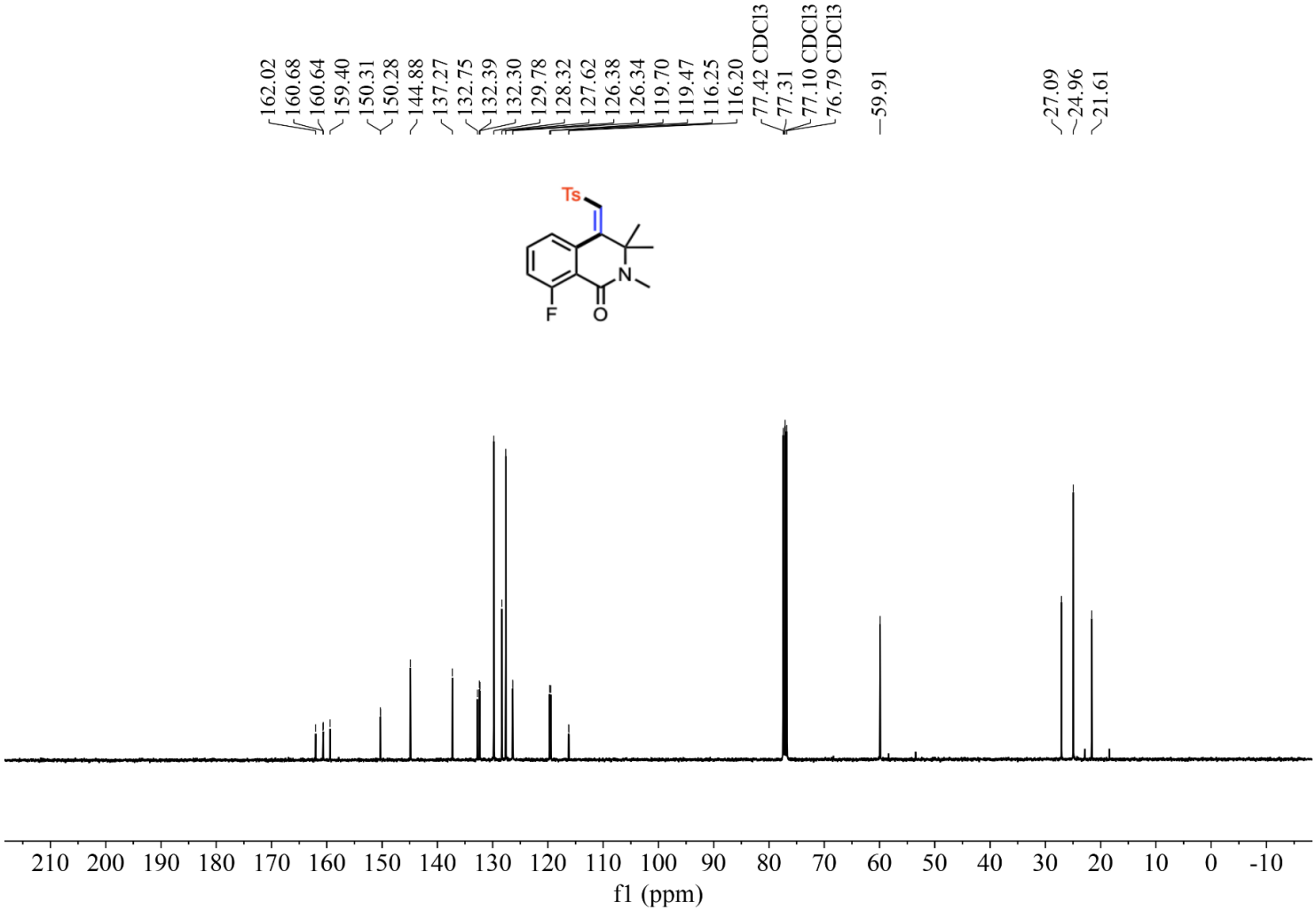
^{1}H spectrum of **3e**



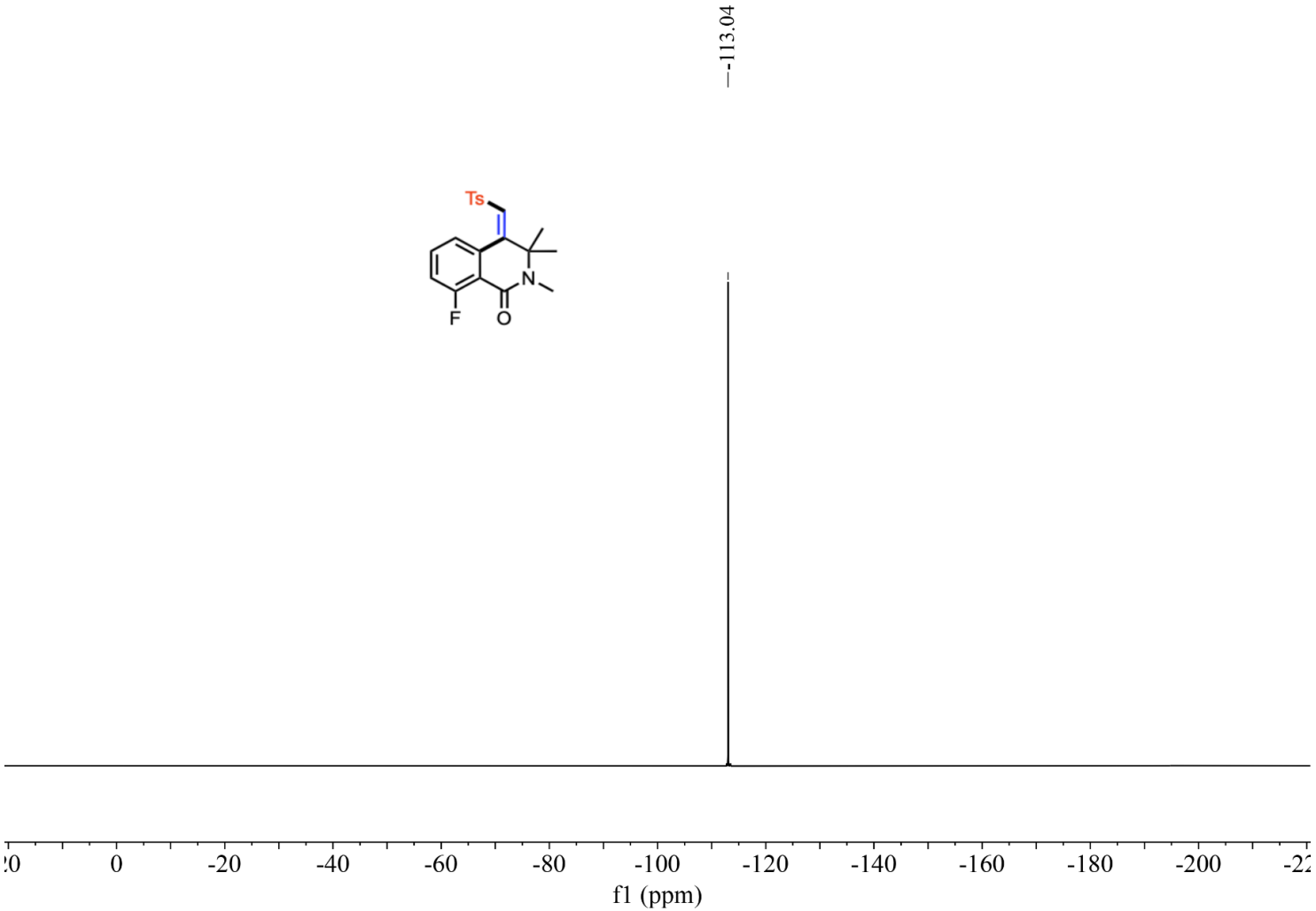
^{13}C spectrum of **3e**



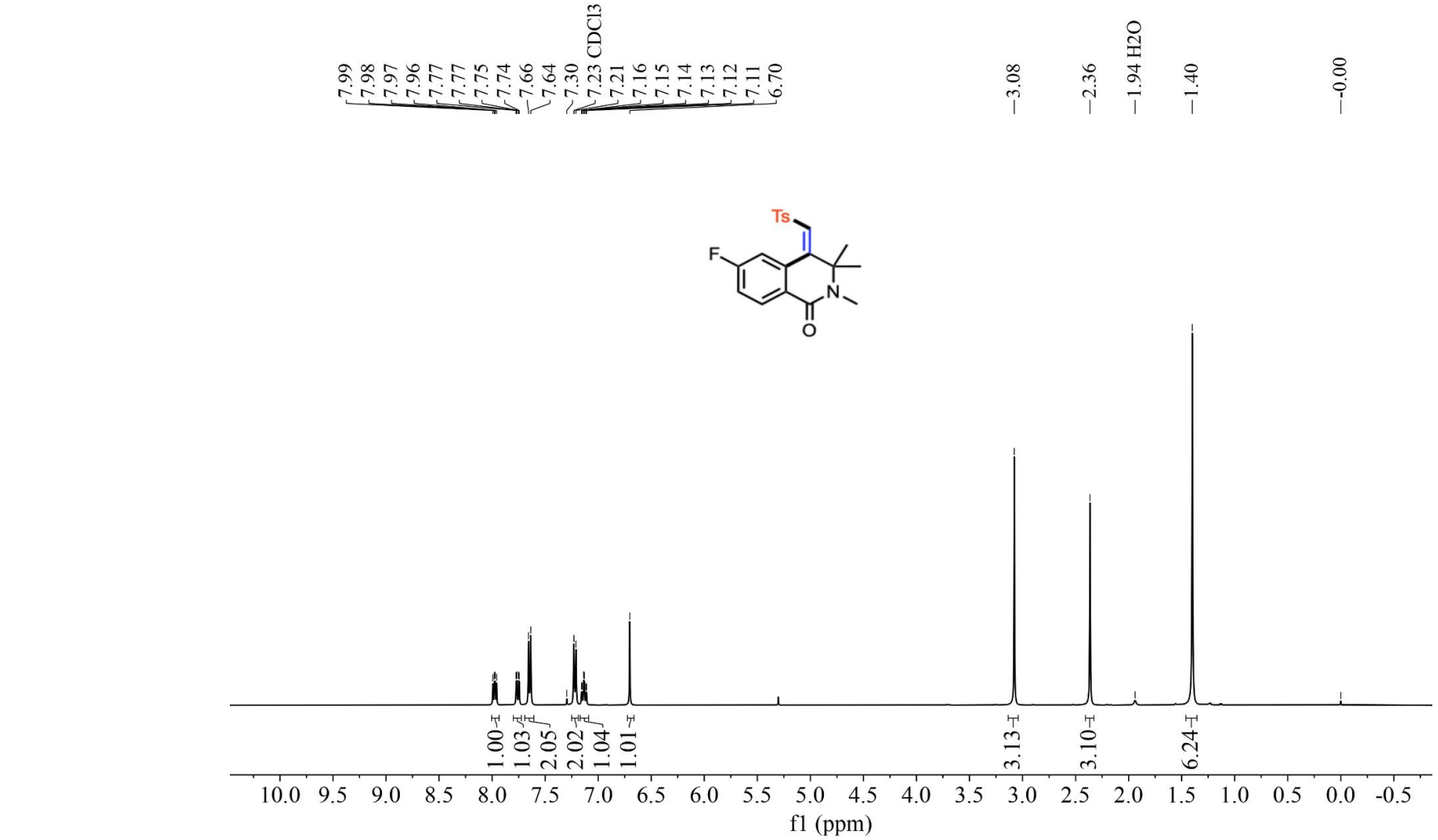
^{1}H spectrum of **3f**



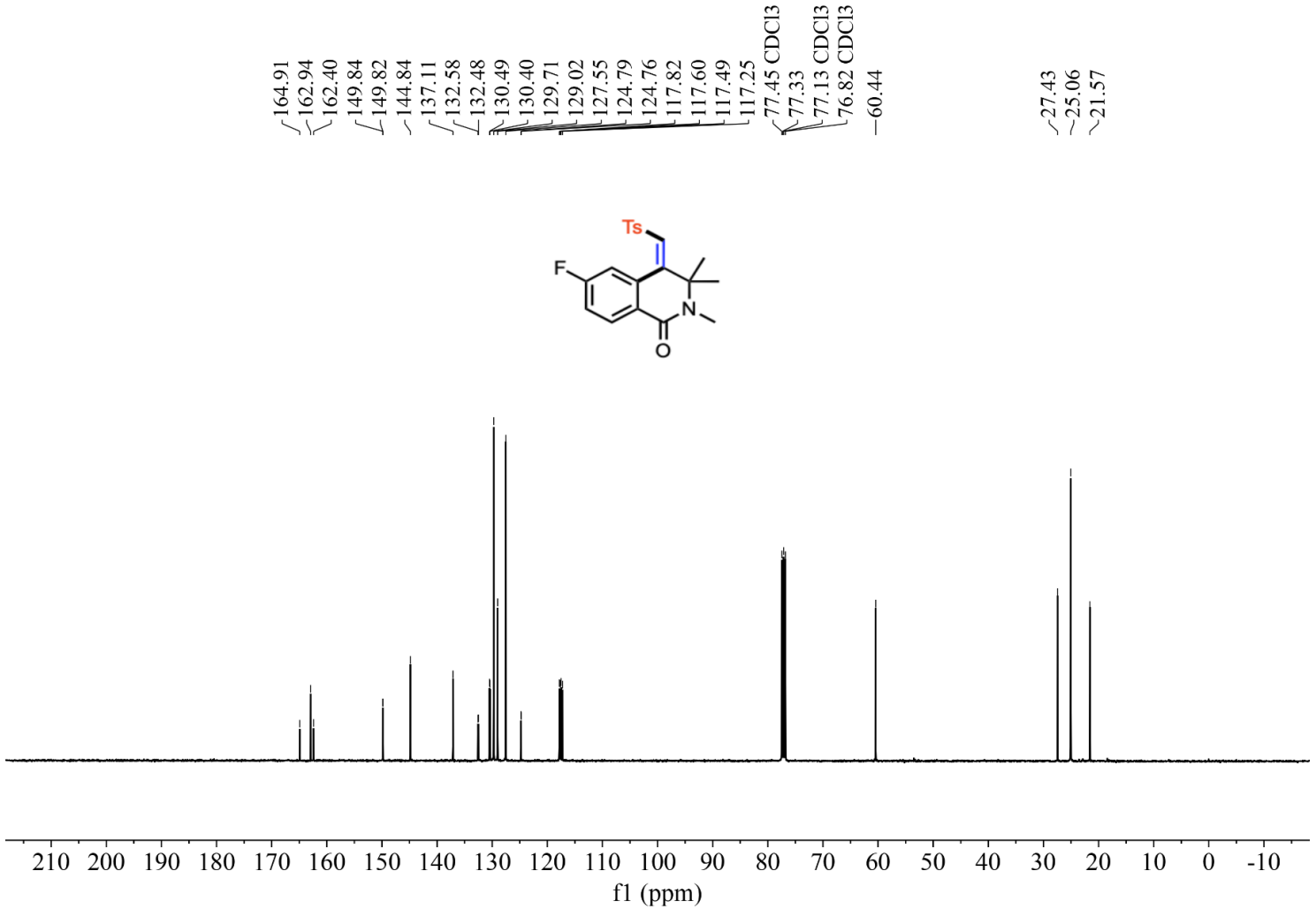
^{13}C spectrum of **3f**



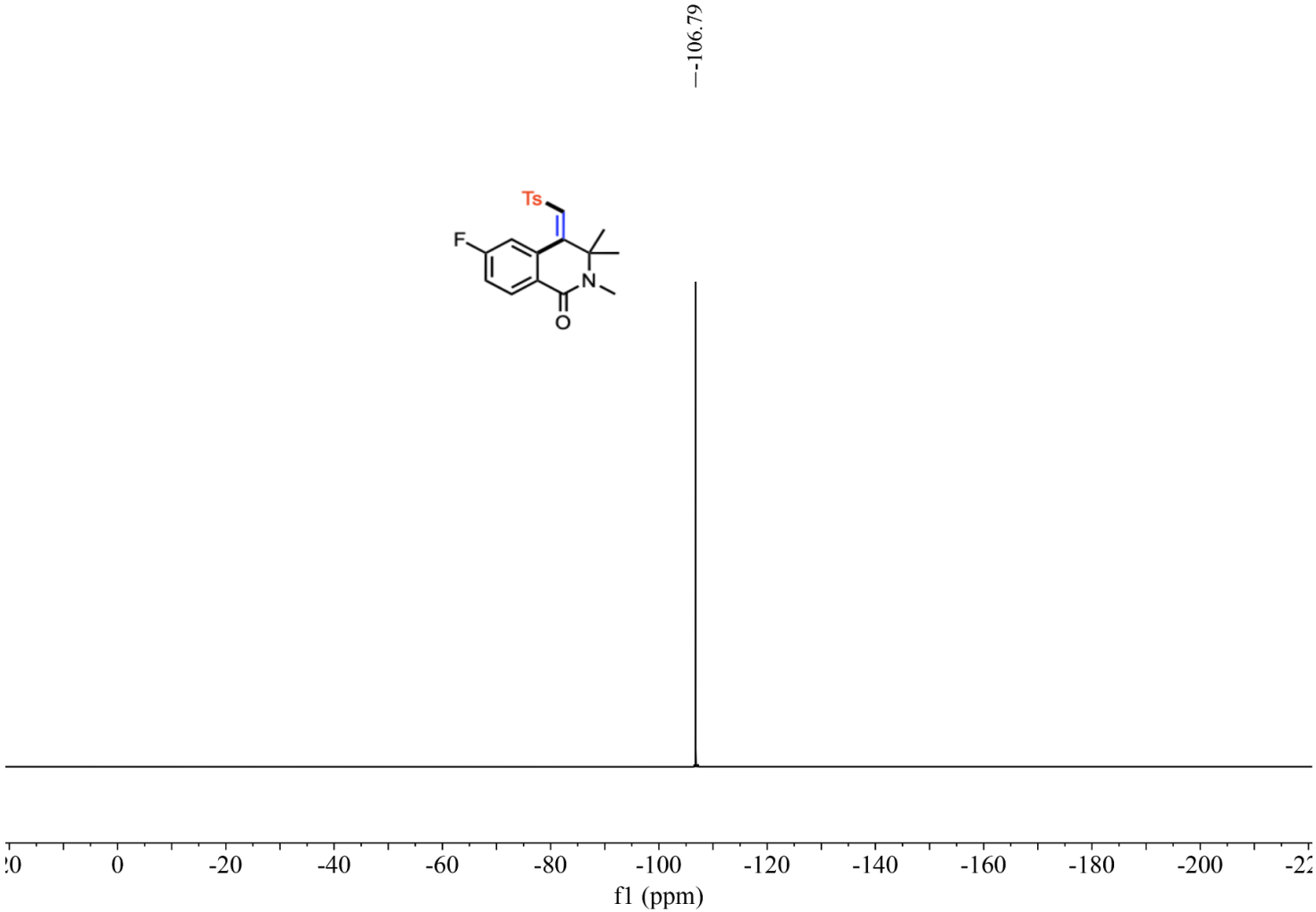
^{19}F spectrum of **3f**



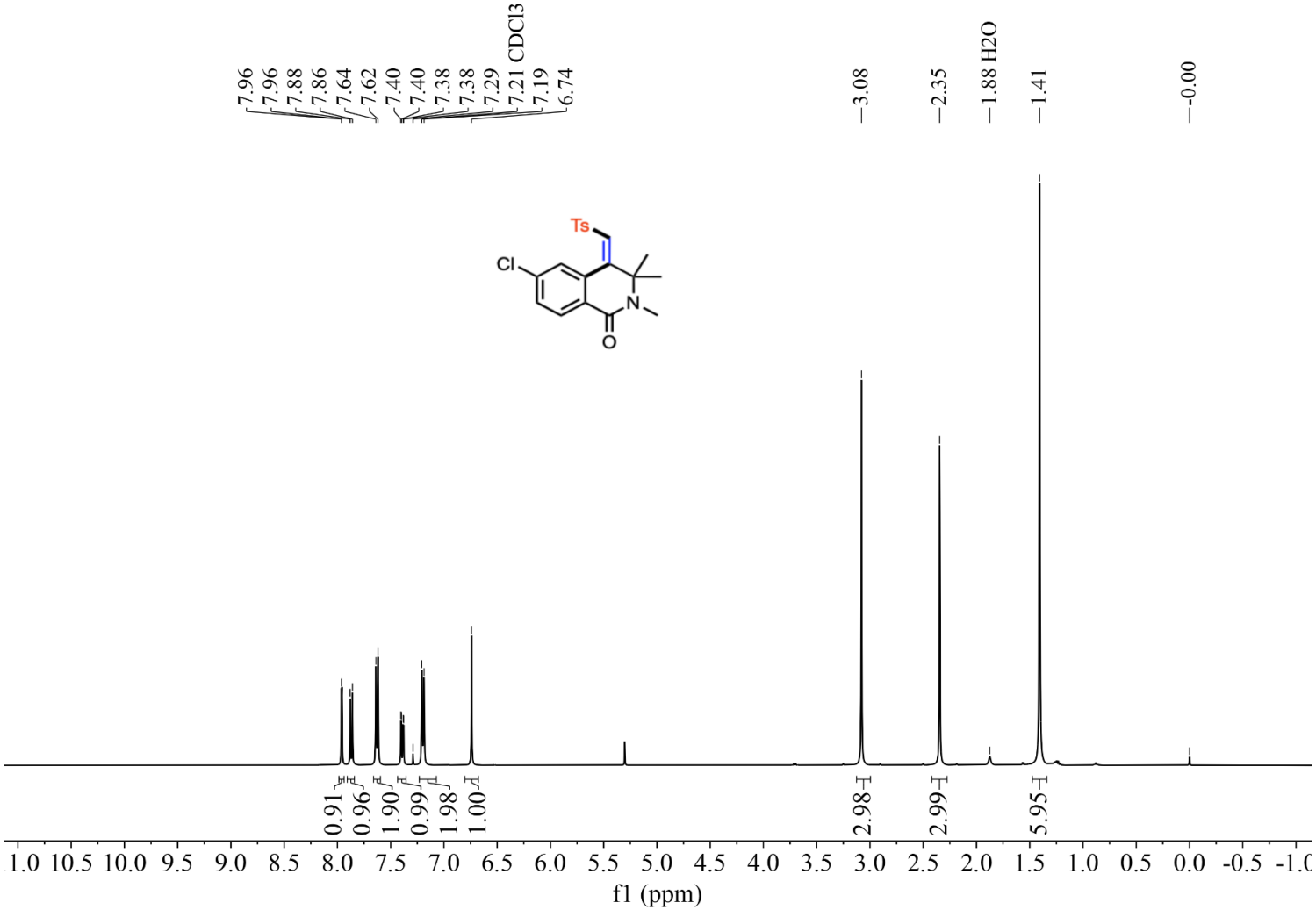
^{1}H spectrum of **3g**



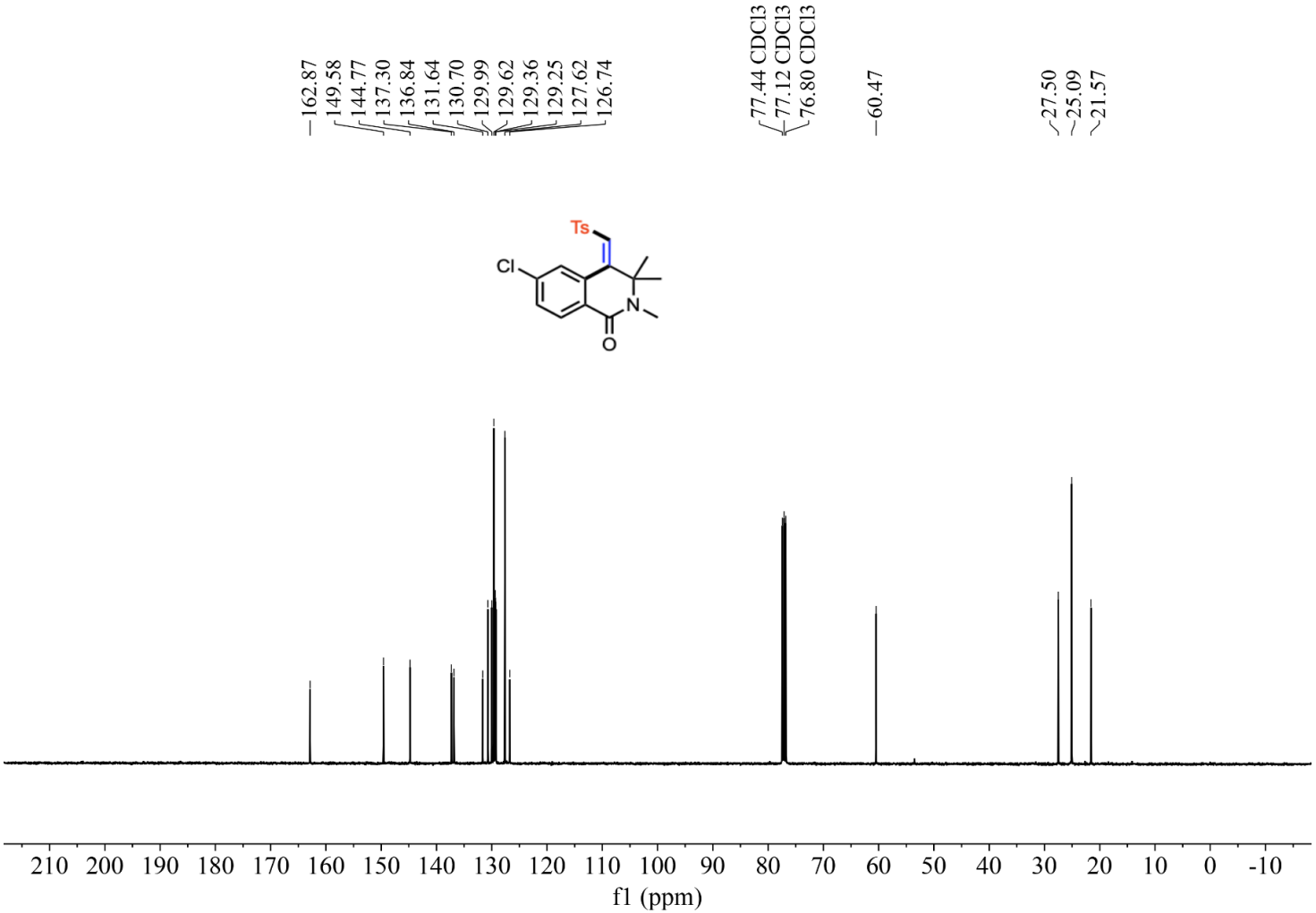
^{13}C spectrum of **3g**



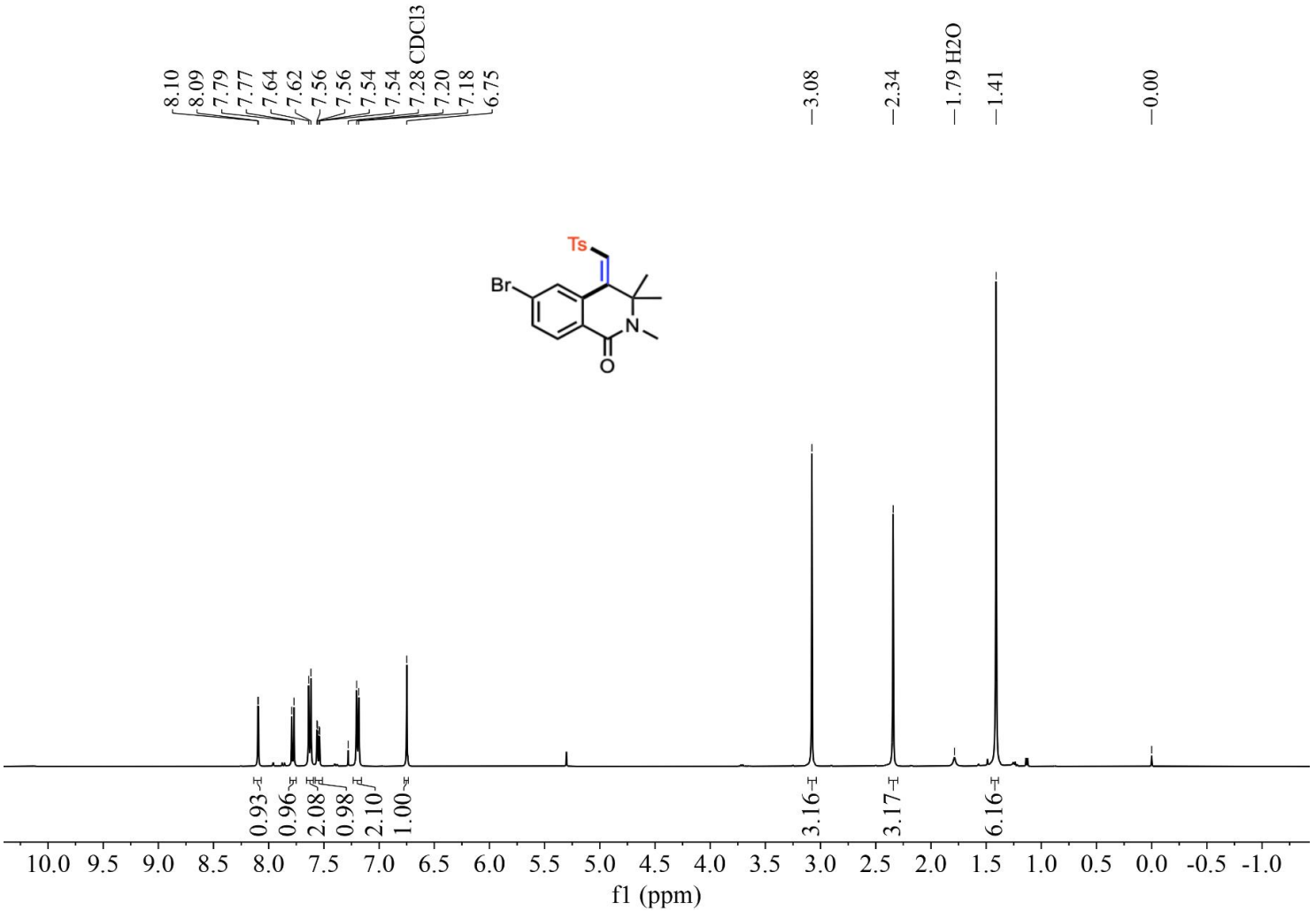
^{19}F spectrum of **3g**



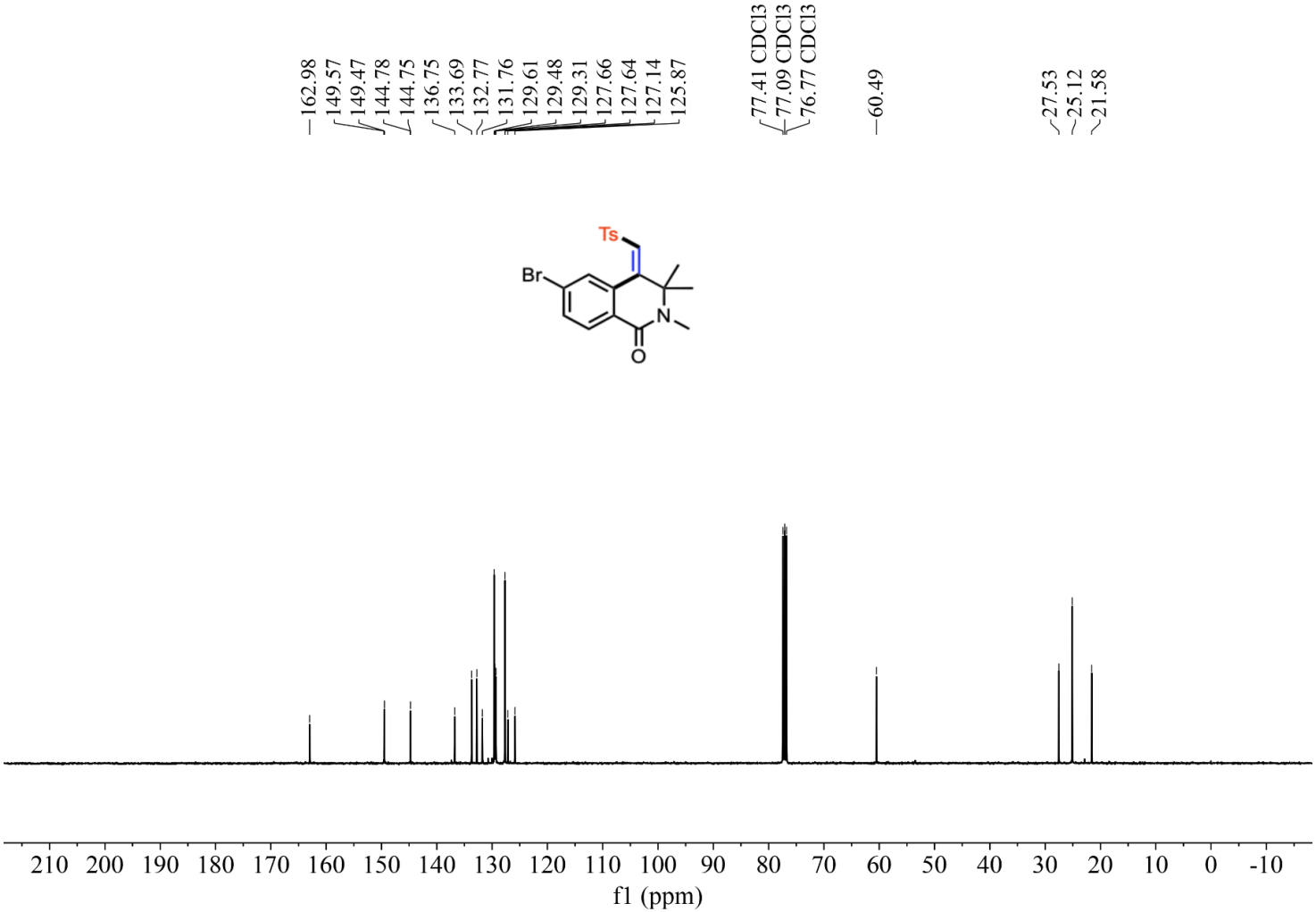
^{1}H spectrum of **3h**



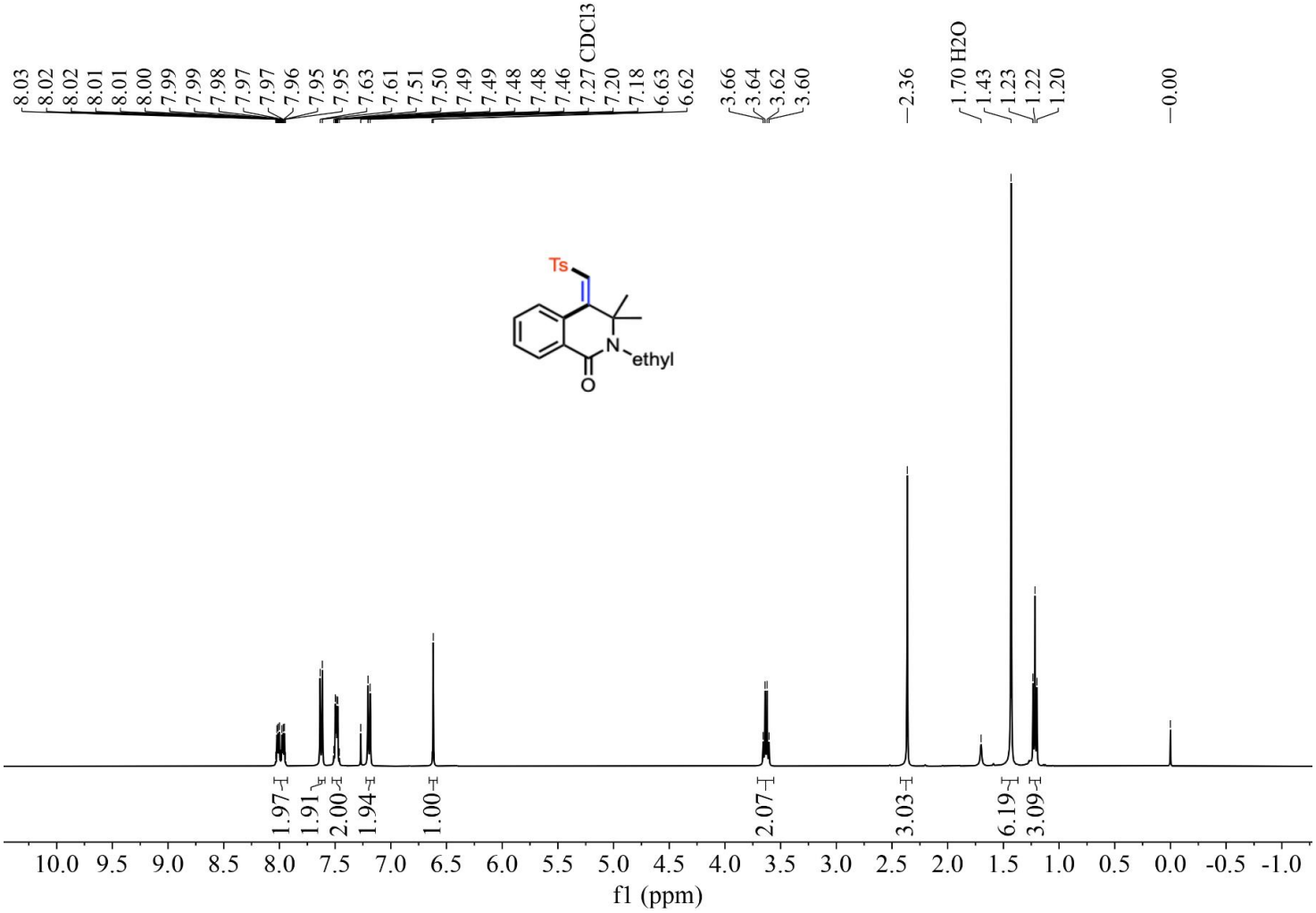
^{13}C spectrum of **3h**



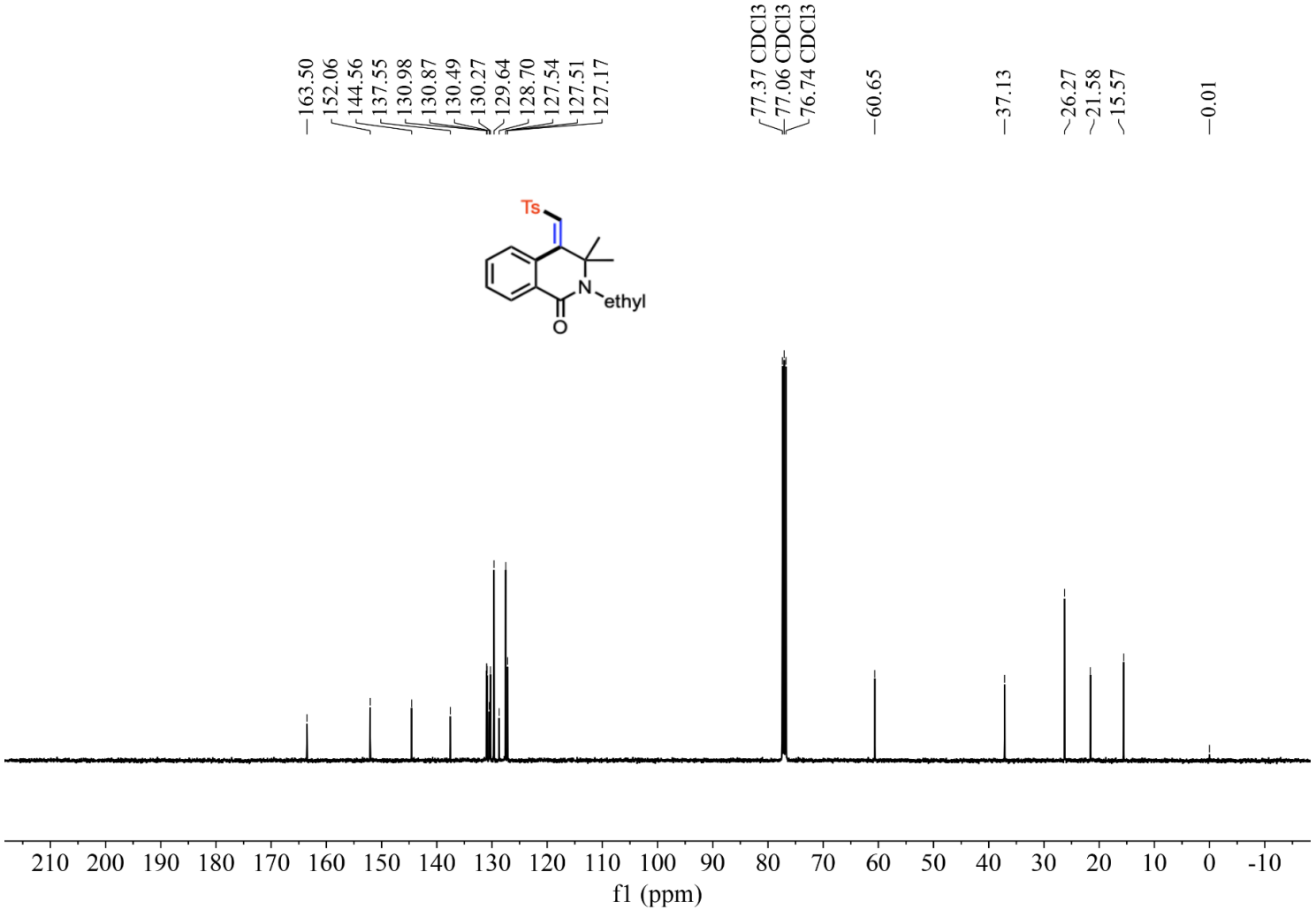
^{1}H spectrum of **3i**



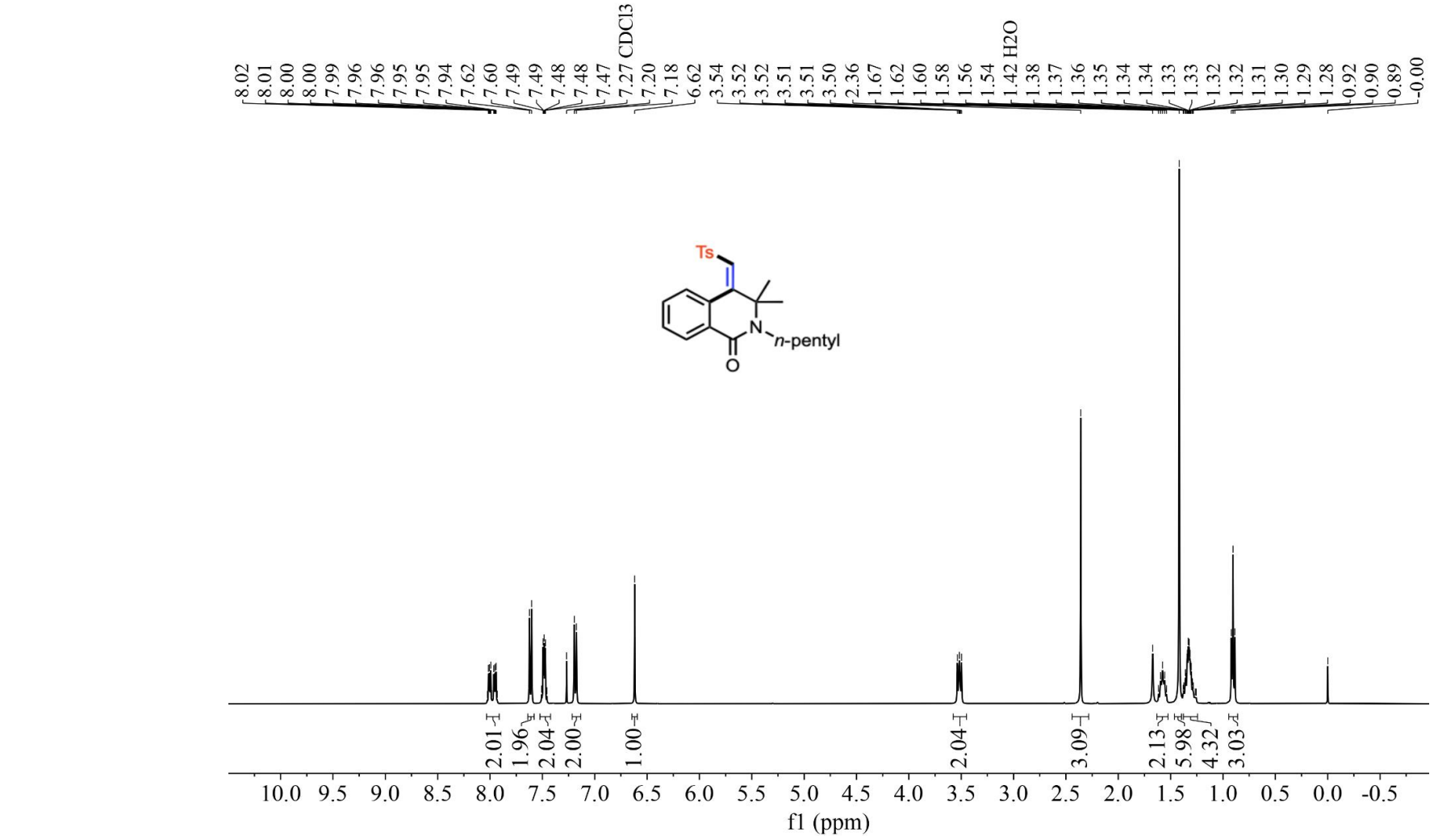
^{13}C spectrum of **3i**



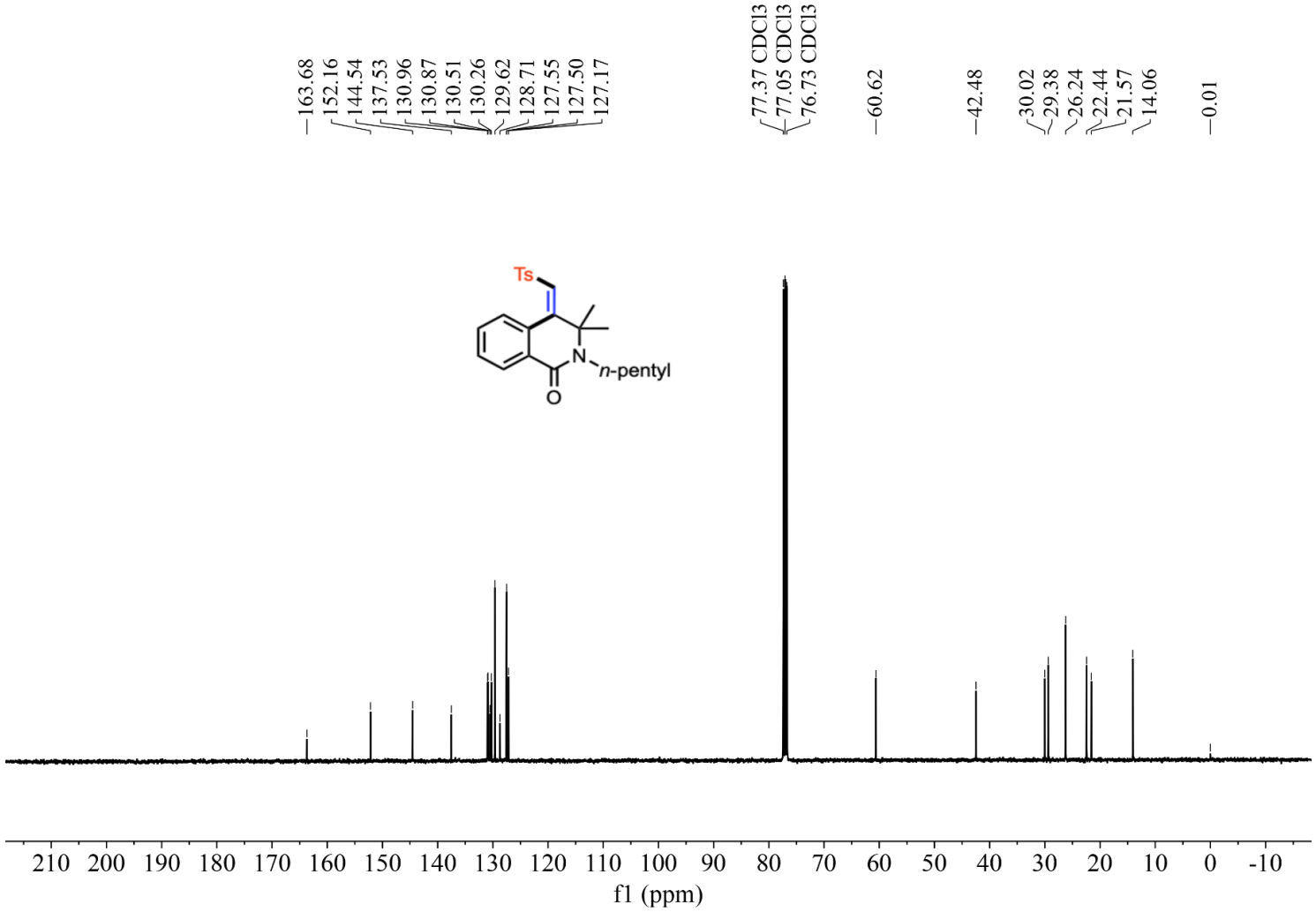
^{1}H spectrum of **3j**



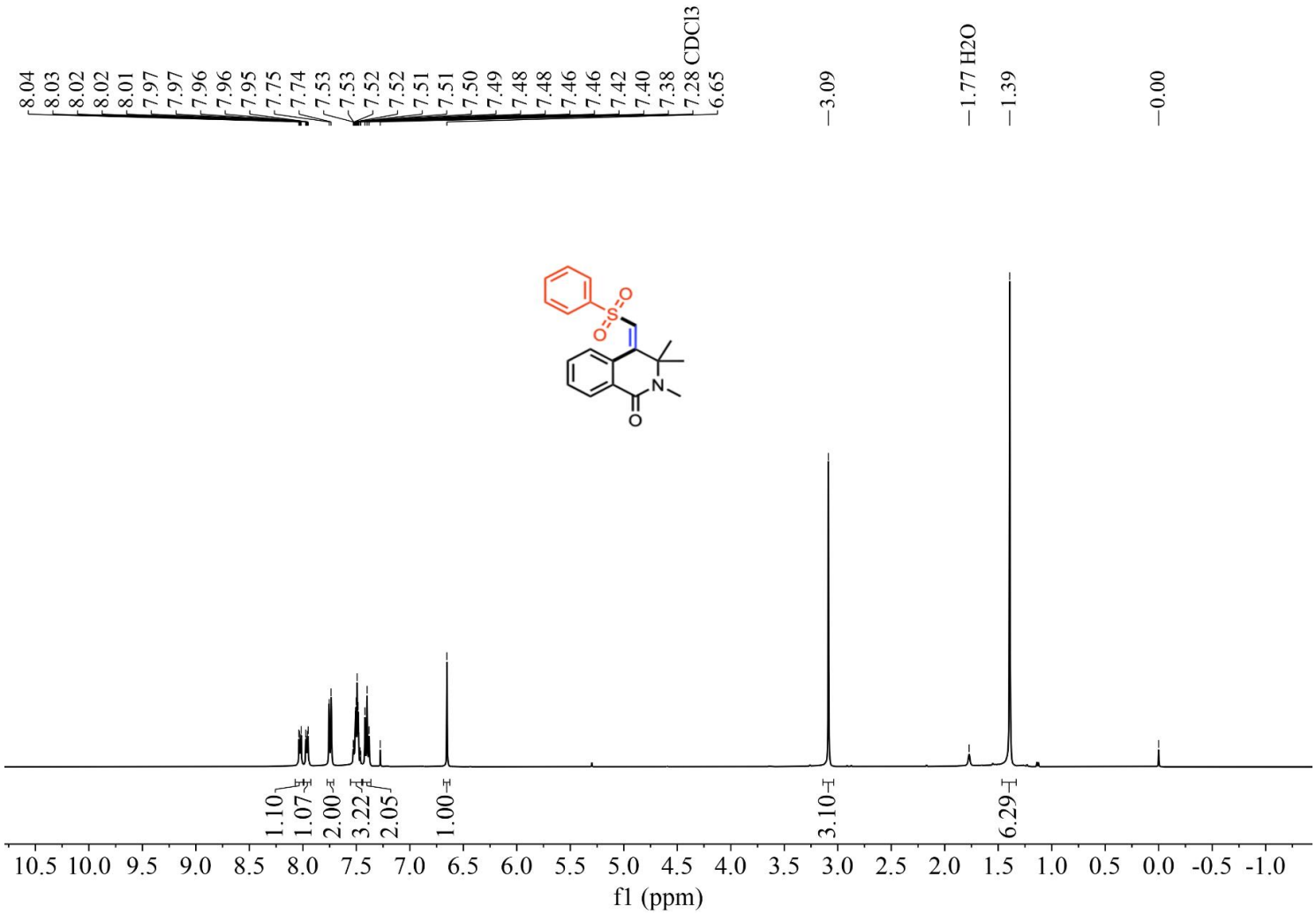
^{13}C spectrum of **3j**



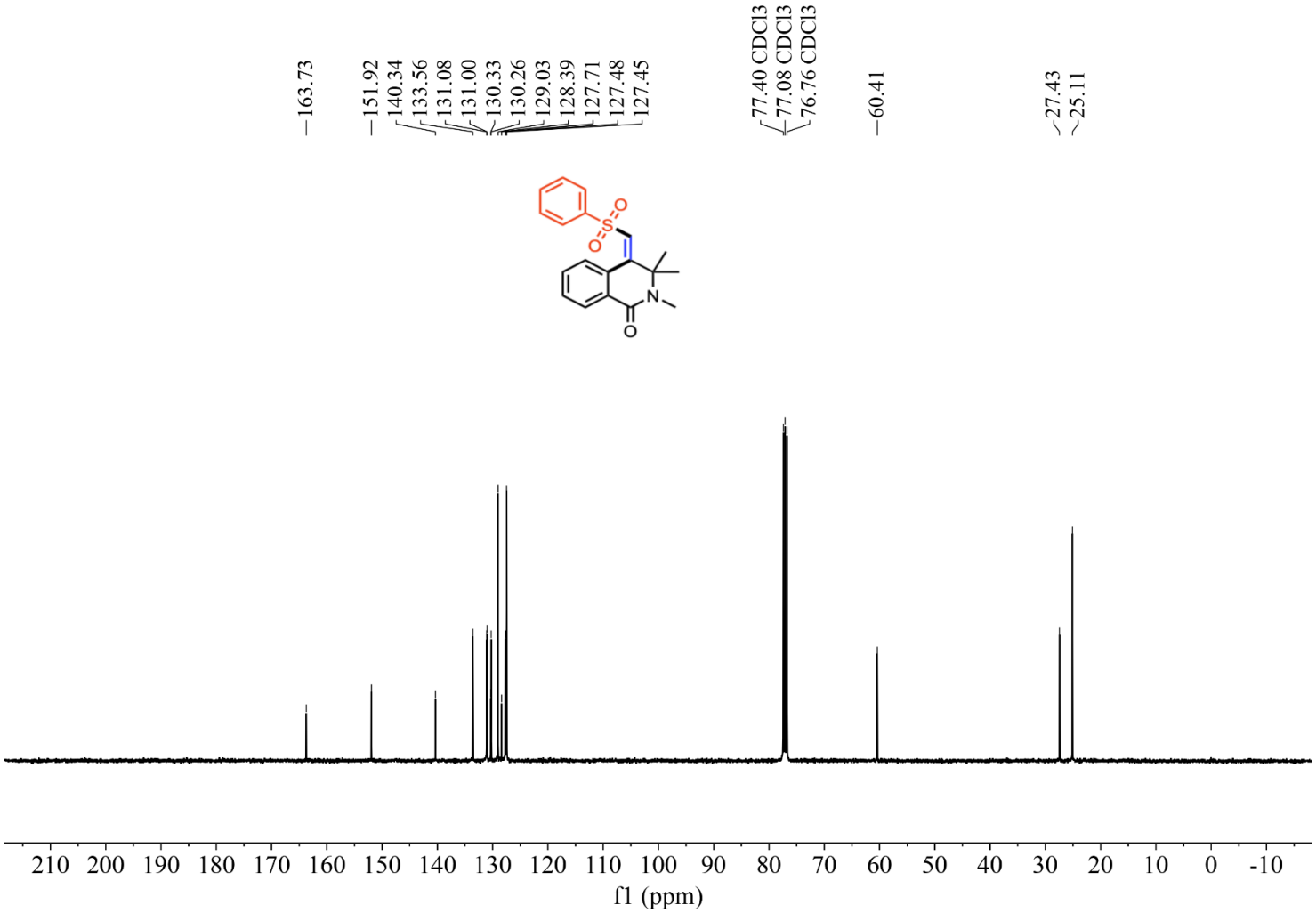
^{1}H spectrum of **3k**



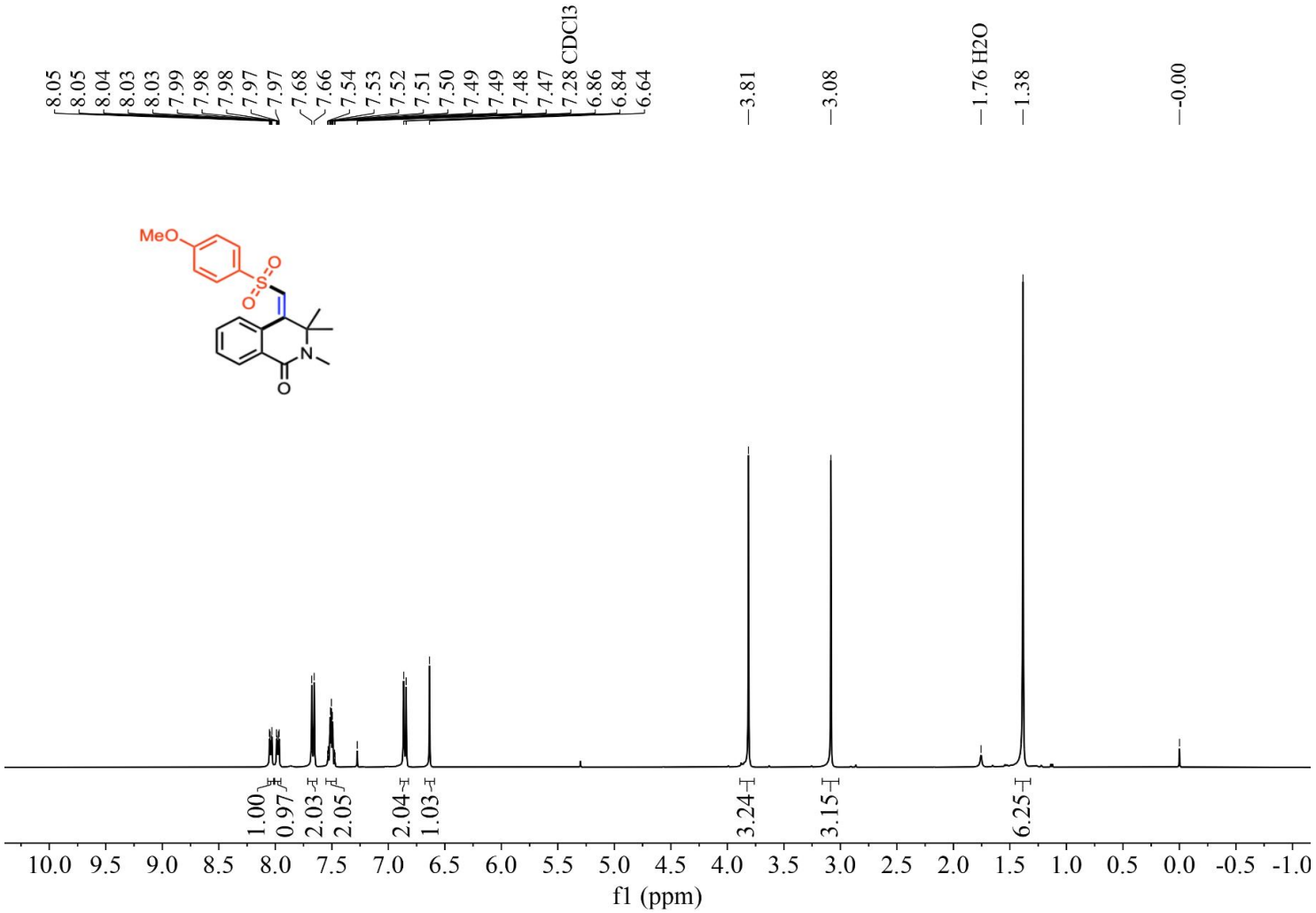
^{13}C spectrum of **3k**



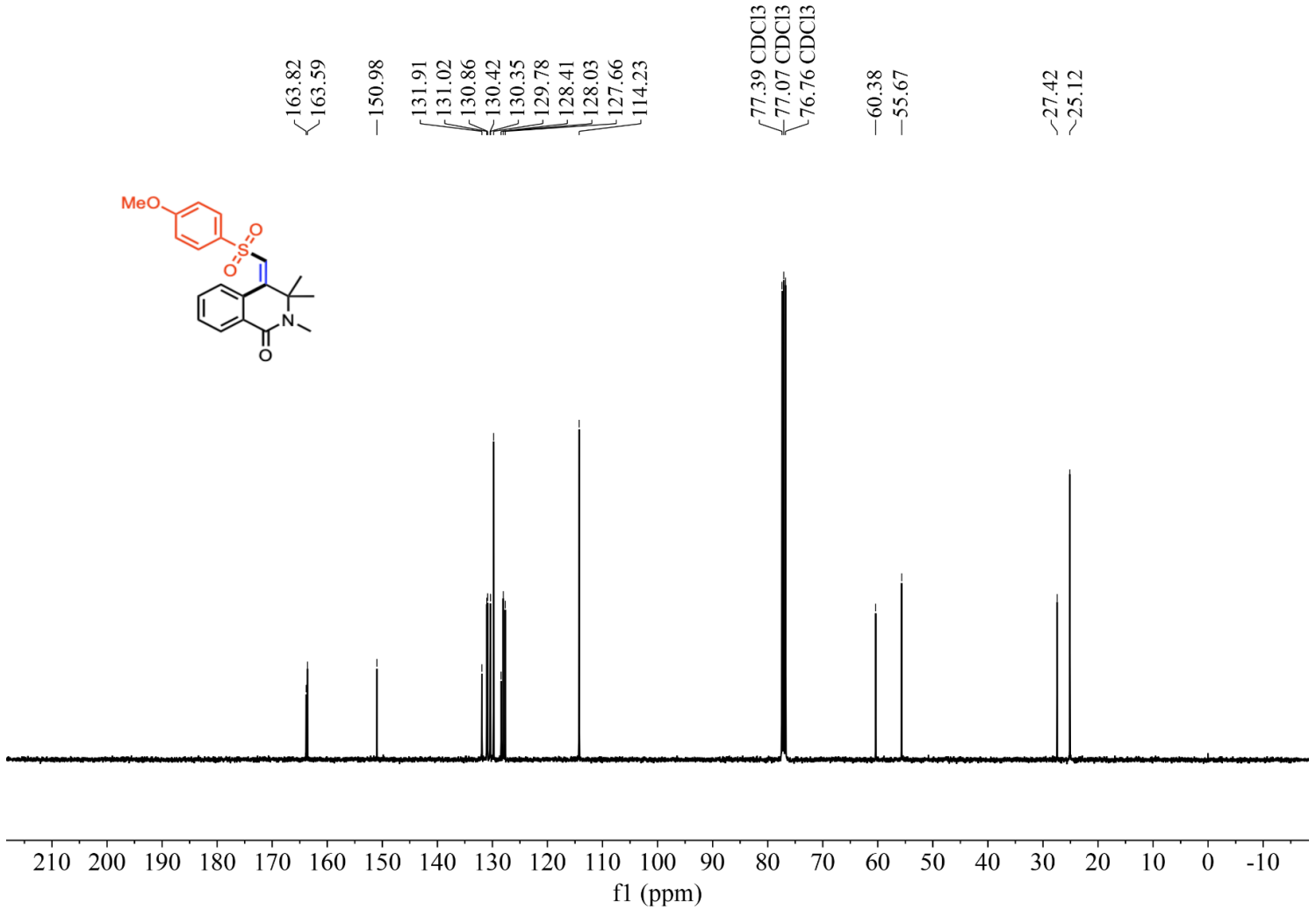
^{1}H spectrum of **3l**



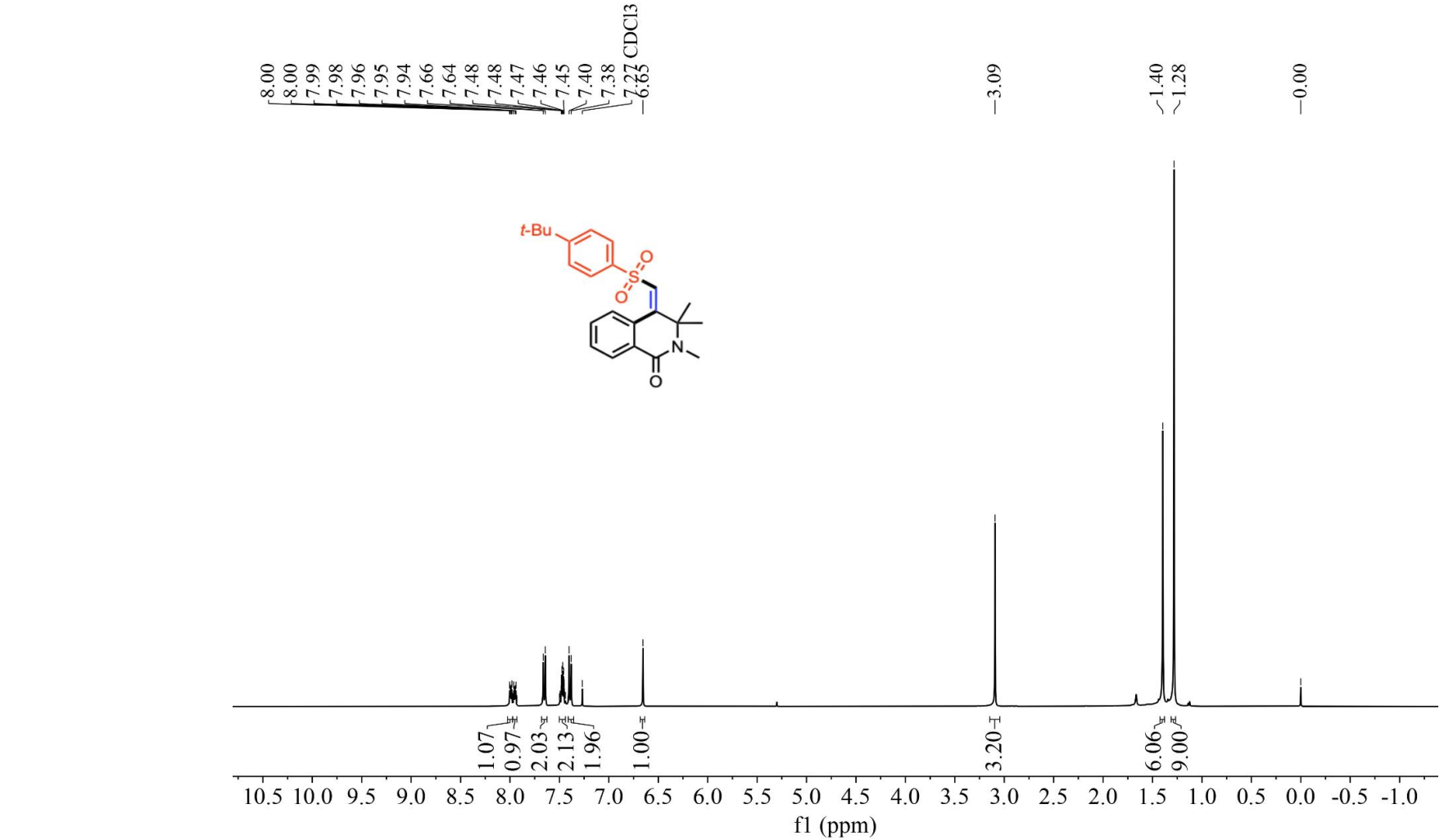
^{13}C spectrum of **3l**



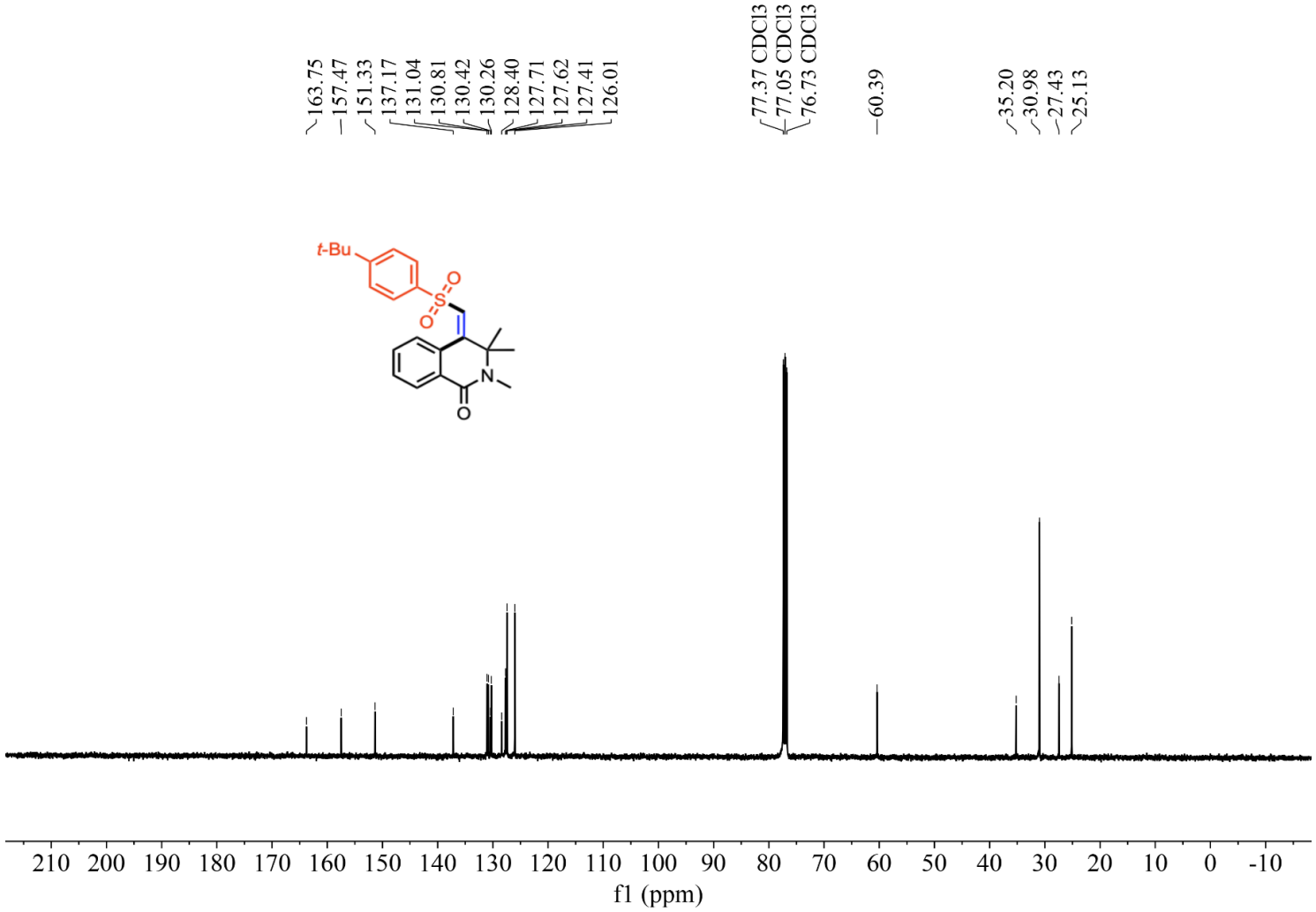
^{1}H spectrum of **3m**



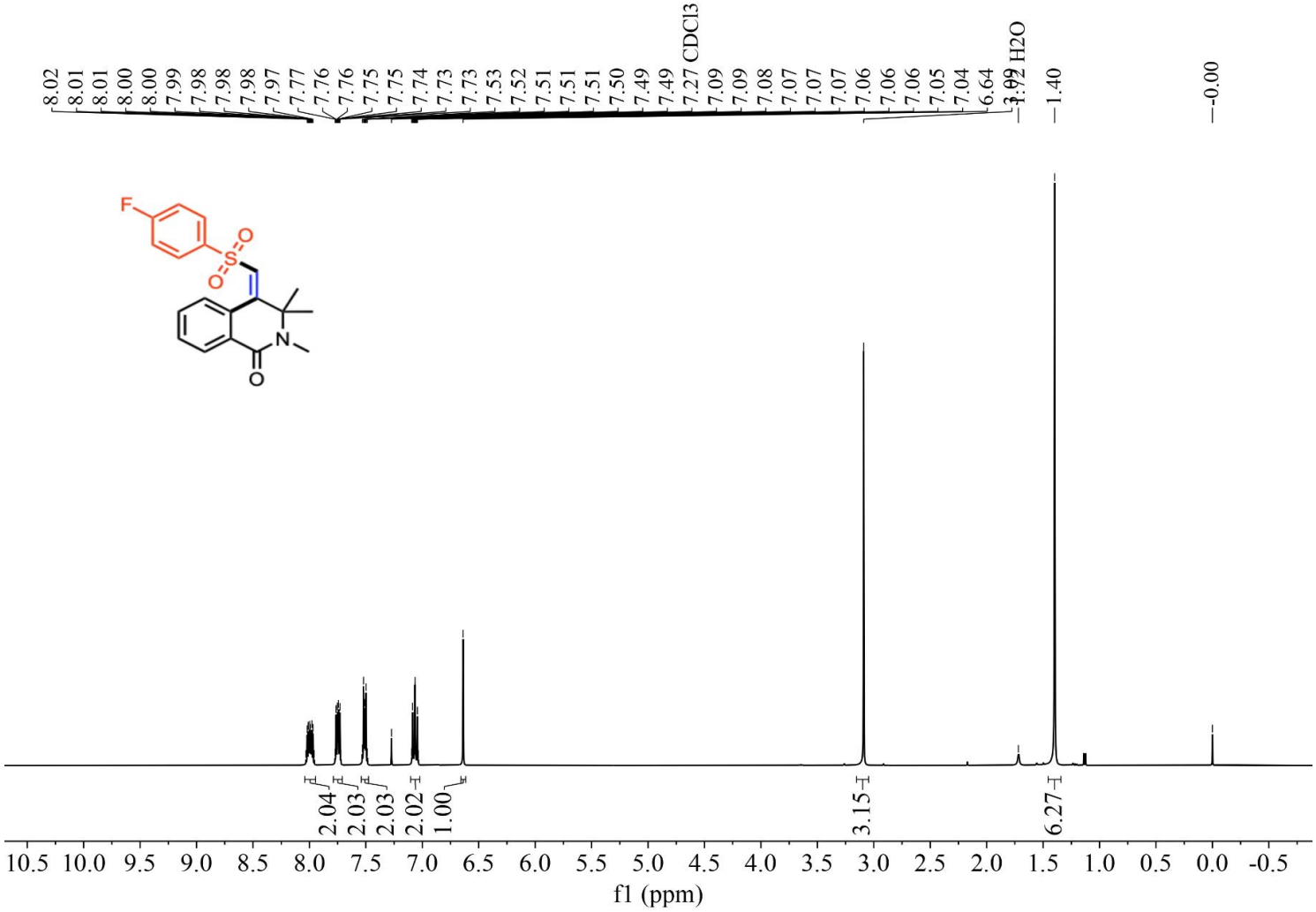
^{13}C spectrum of **3m**



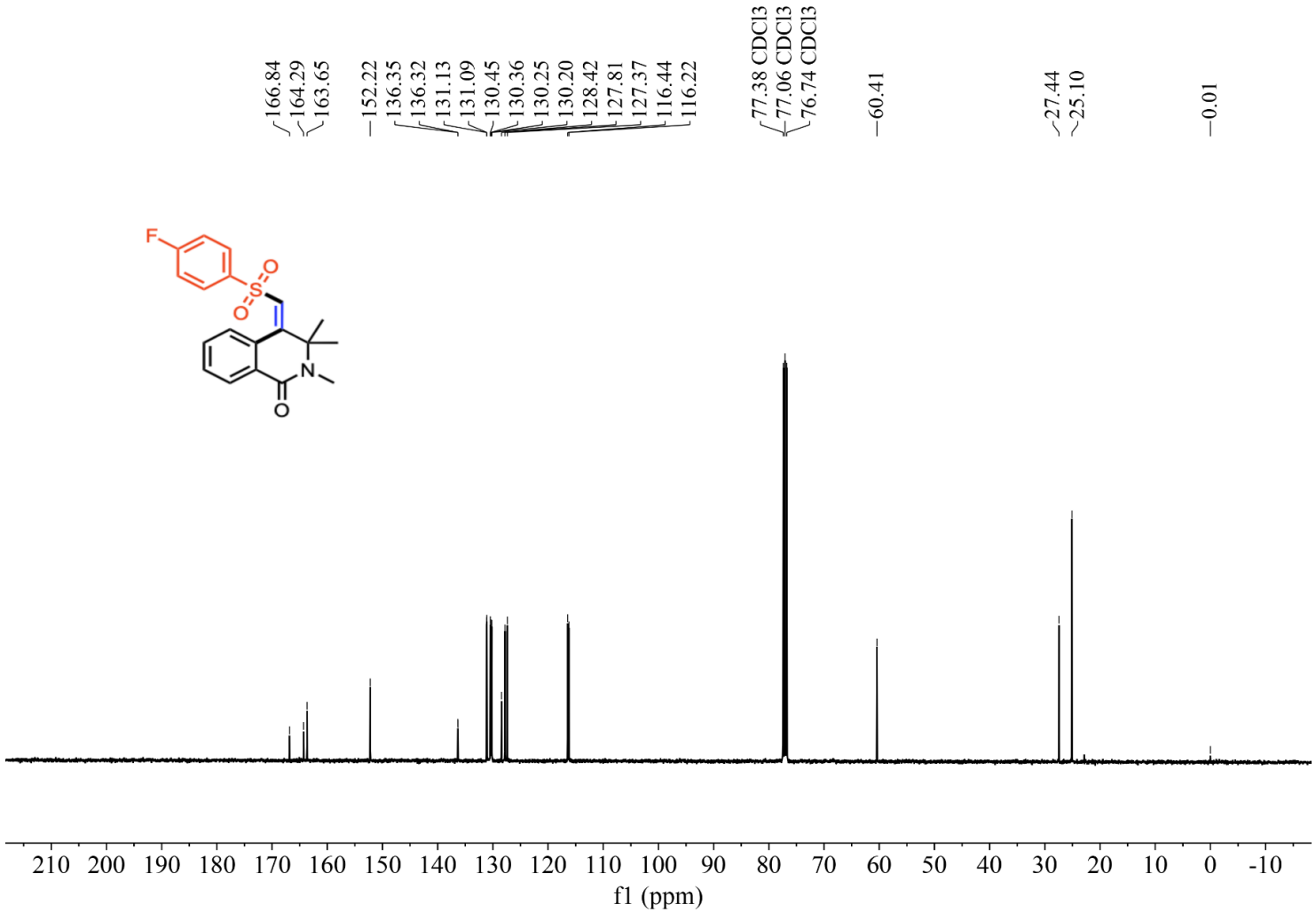
^{1}H spectrum of **3n**



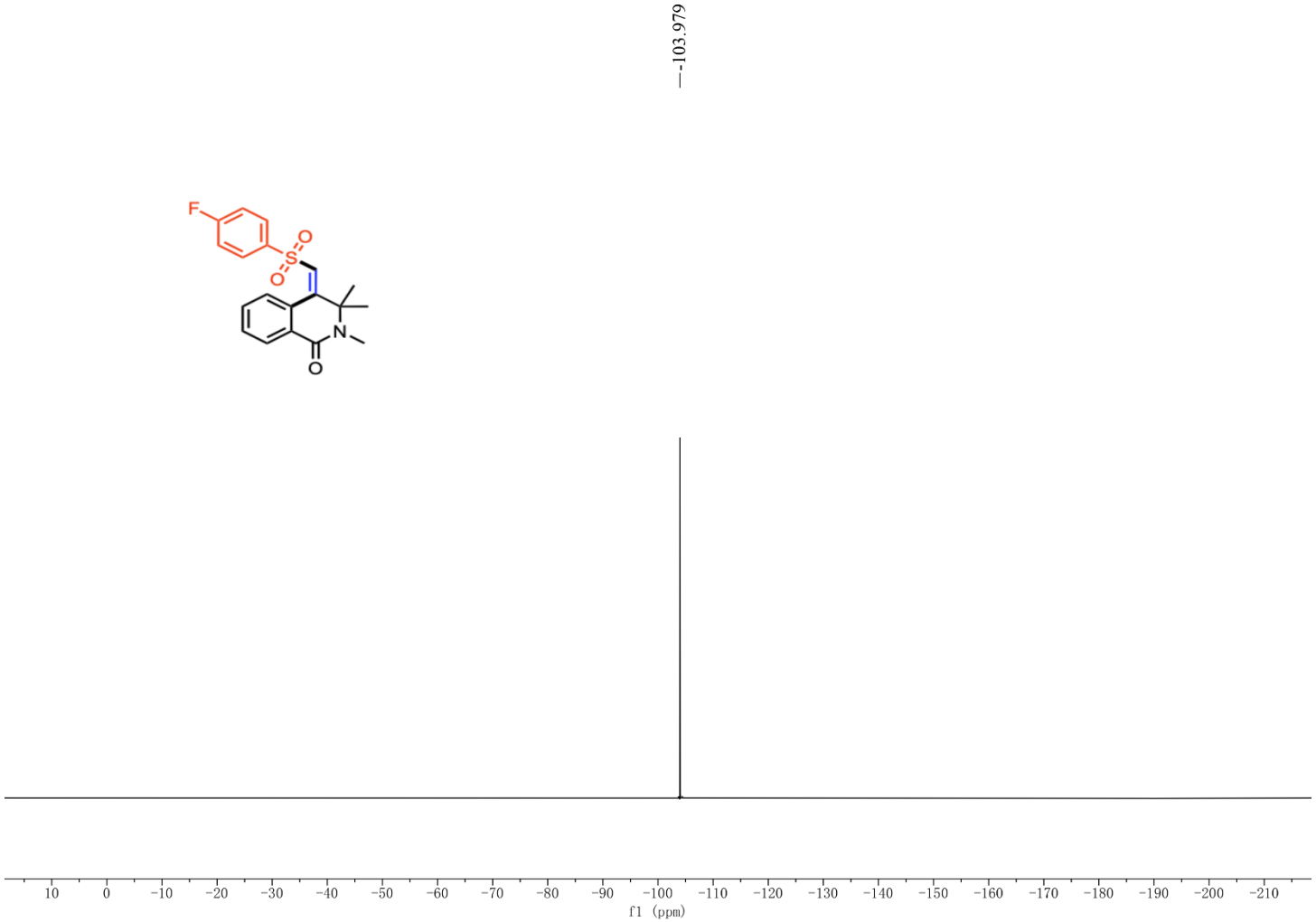
^{13}C spectrum of **3n**



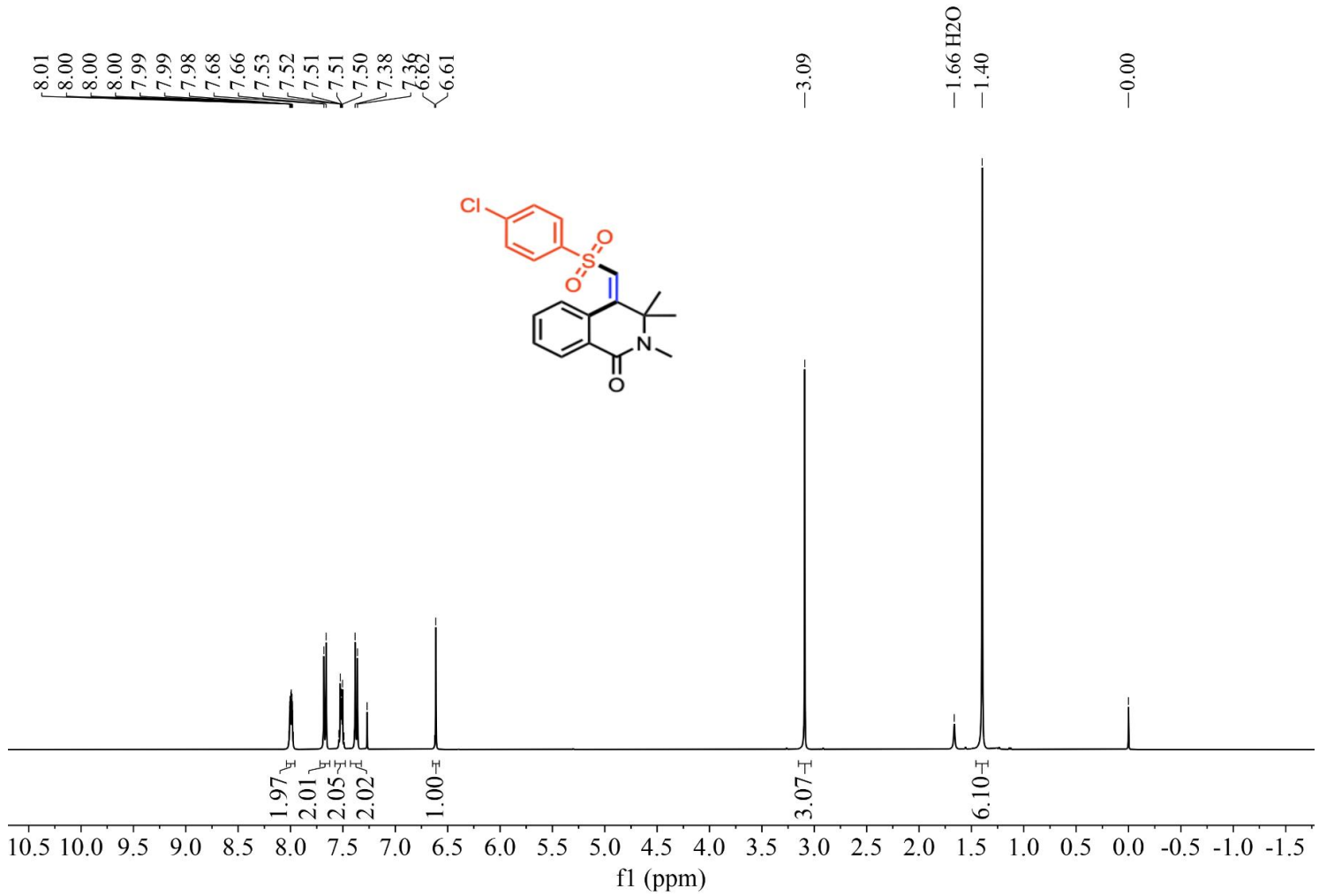
^{1}H spectrum of **3o**



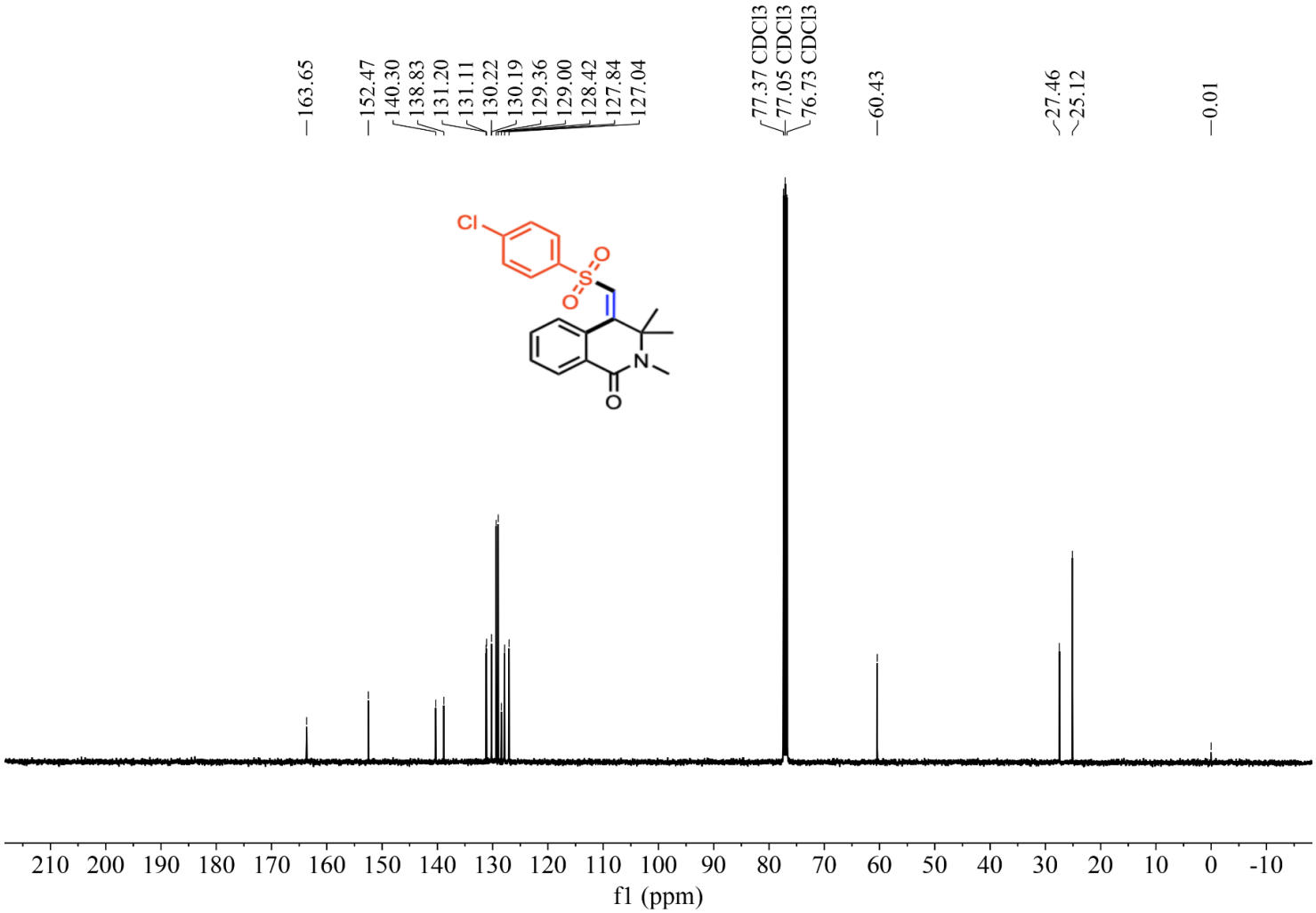
^{13}C spectrum of **3o**



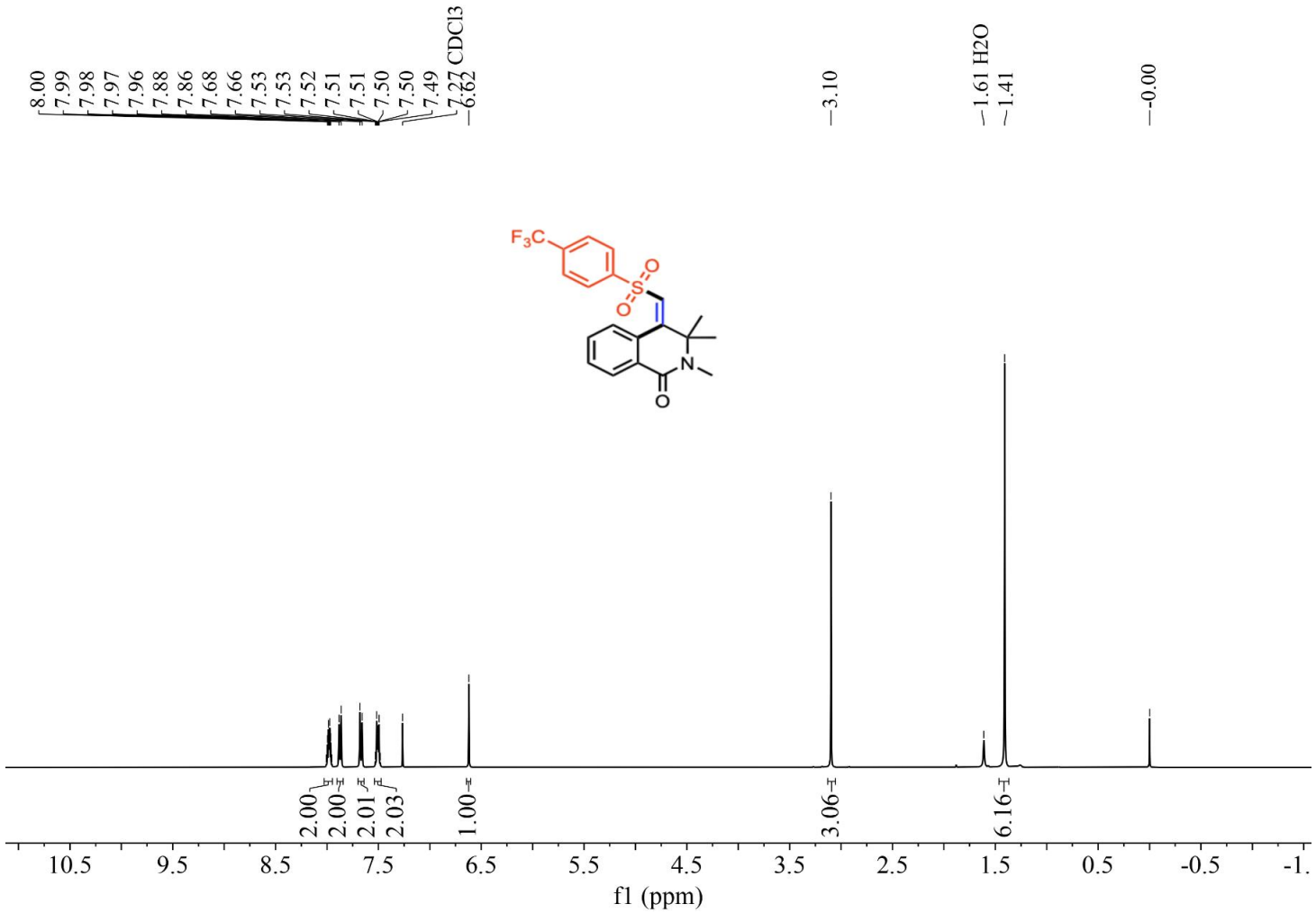
^{19}F spectrum of **3o**



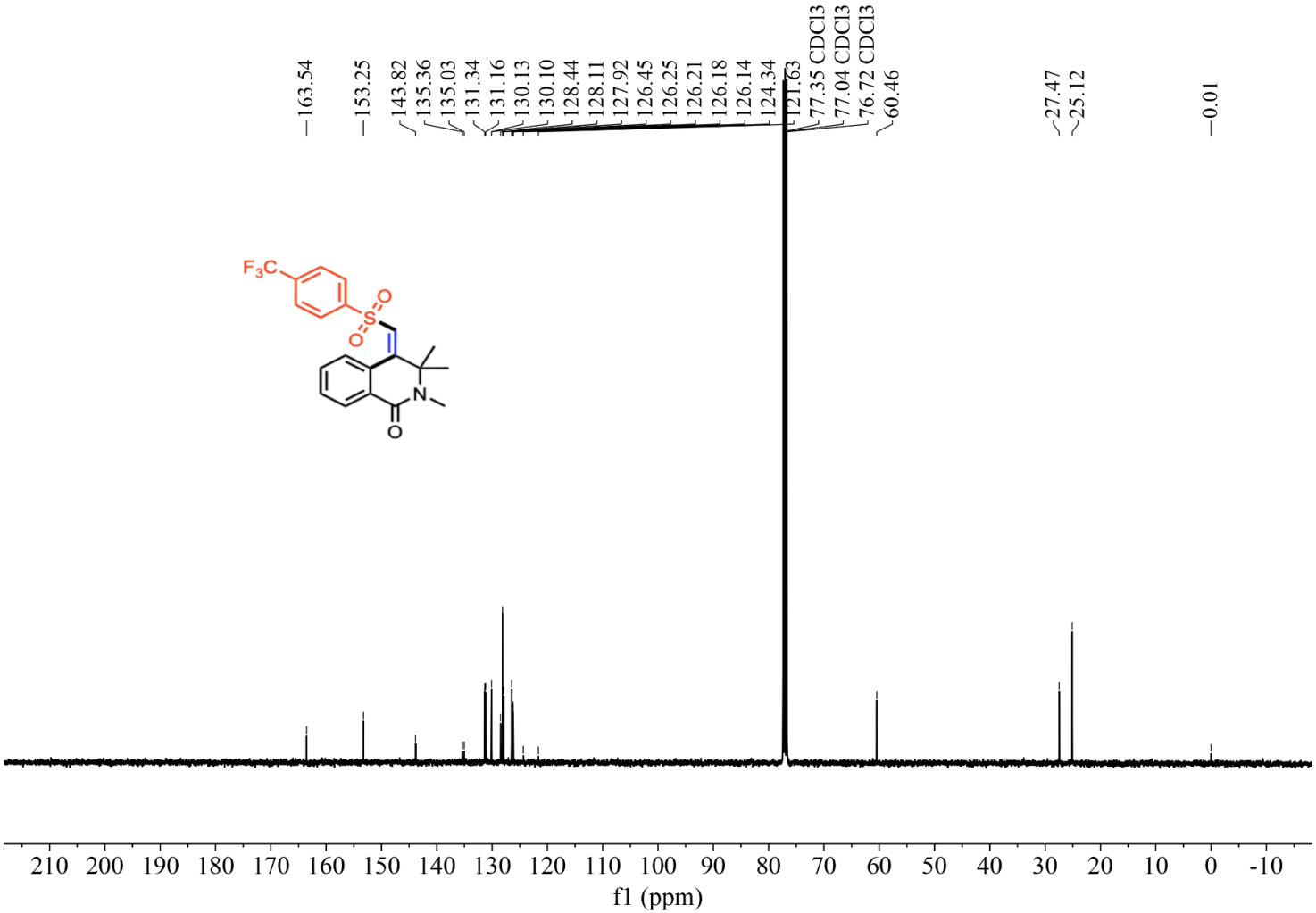
^{1}H spectrum of **3p**



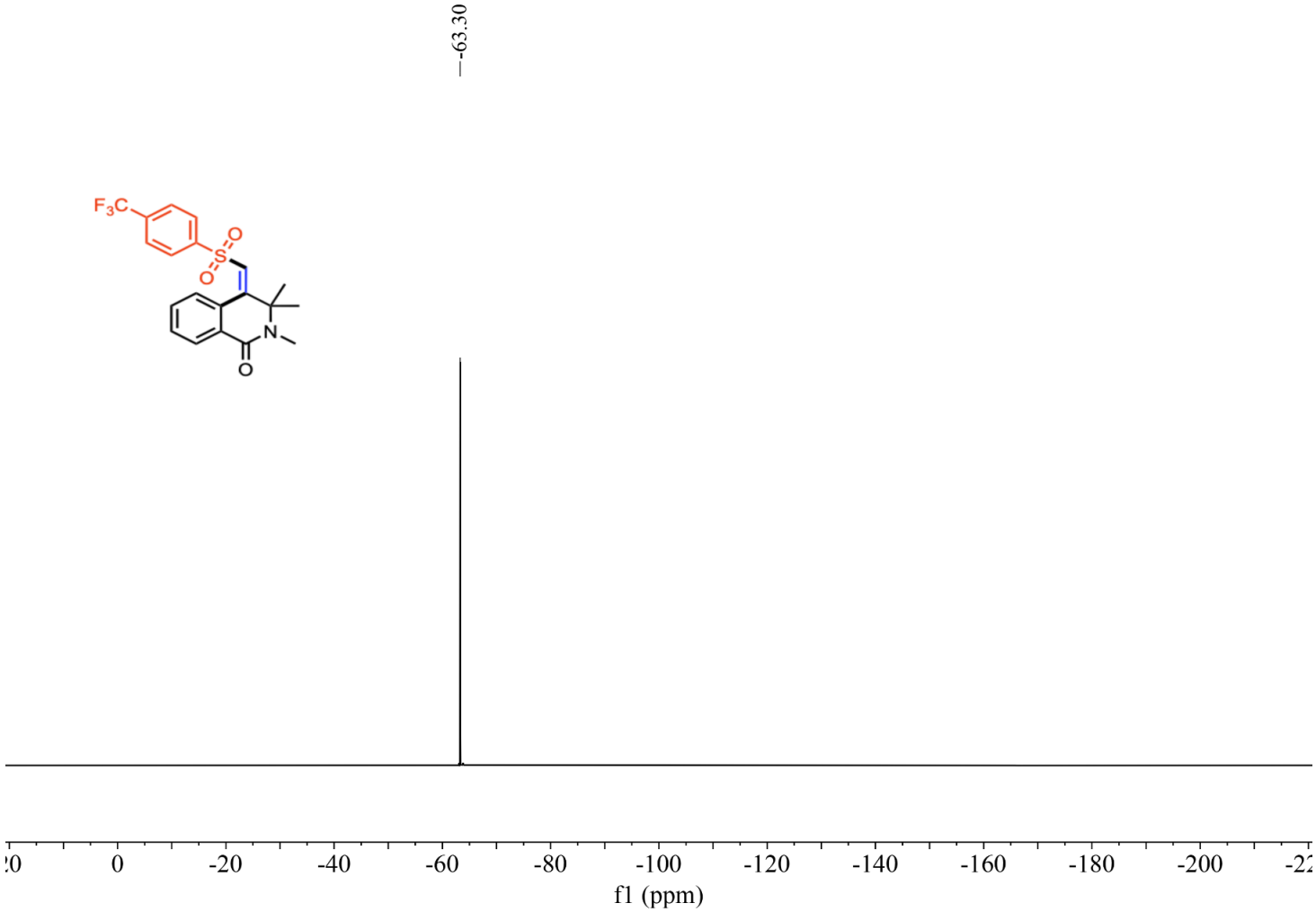
^{13}C spectrum of **3p**



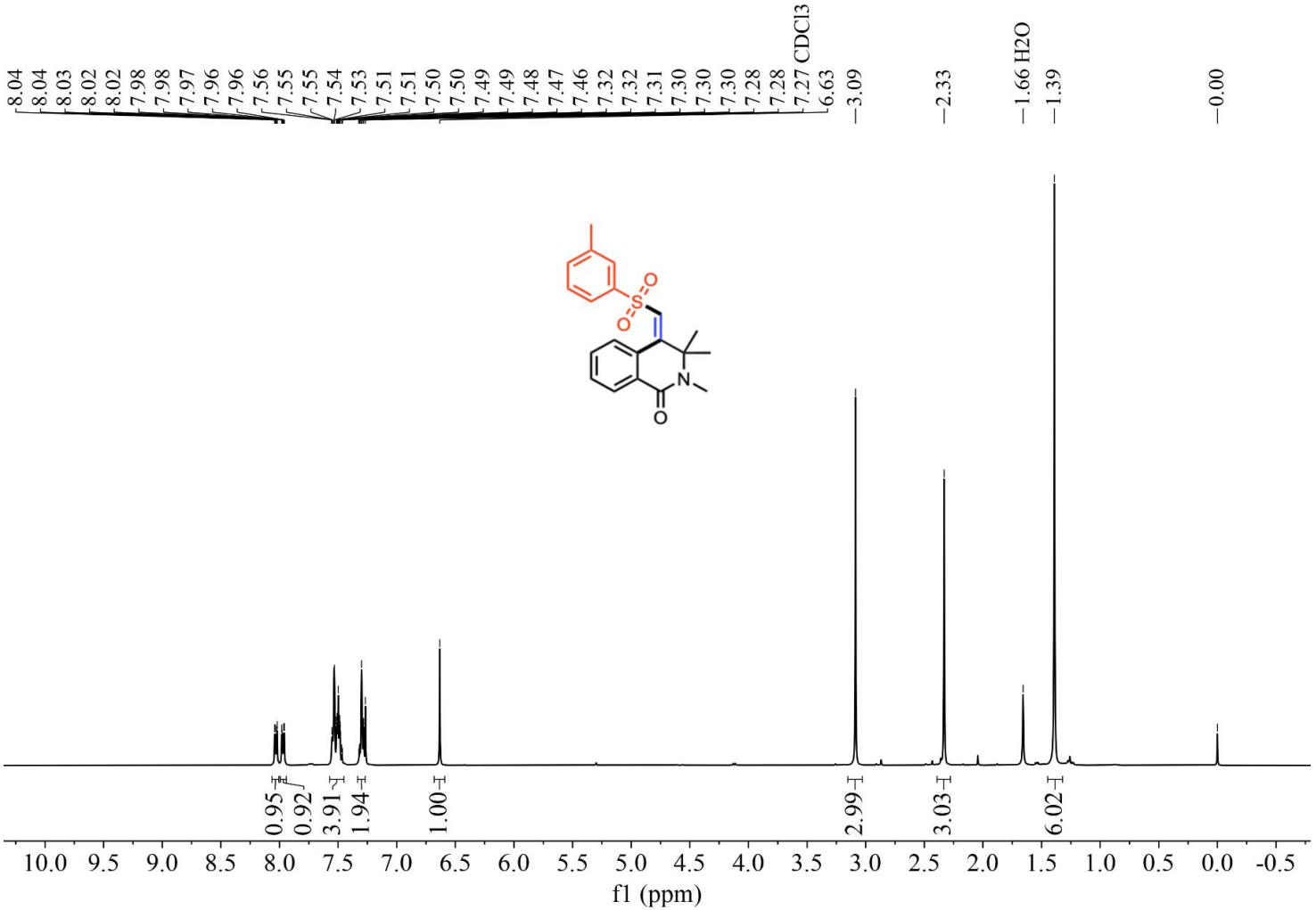
^{1}H spectrum of **3q**



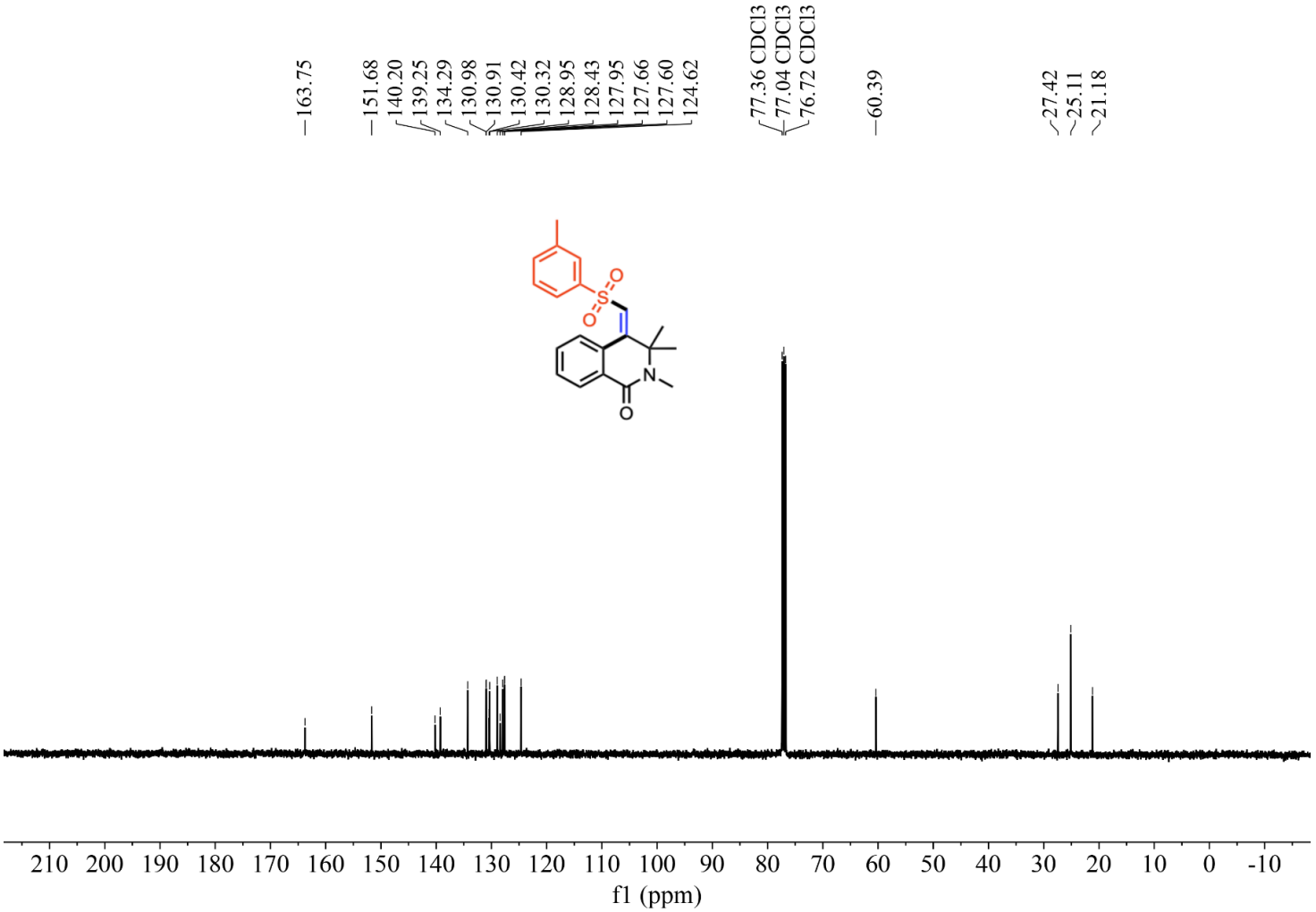
^{13}C spectrum of **3q**



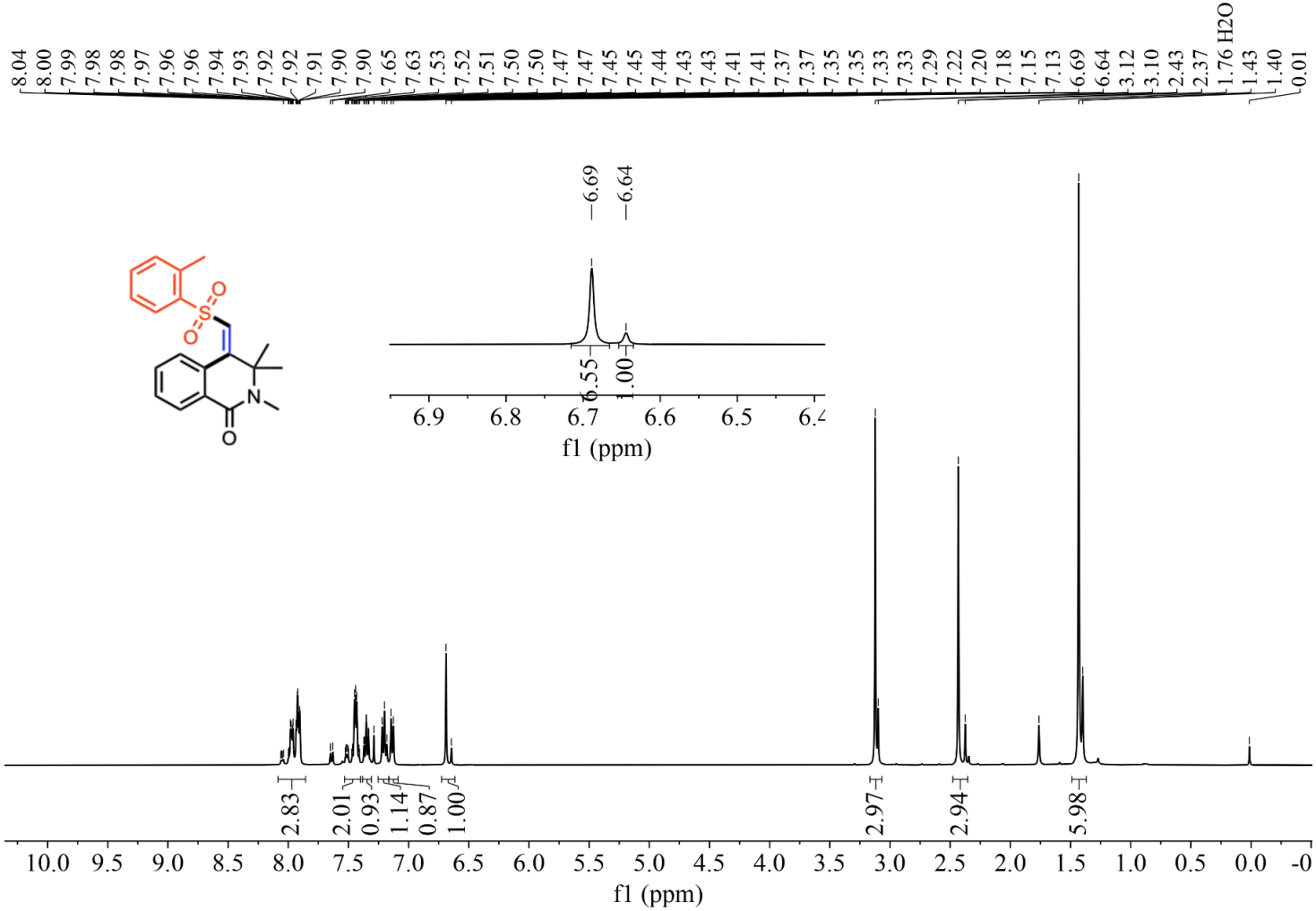
^{19}F spectrum of **3q**



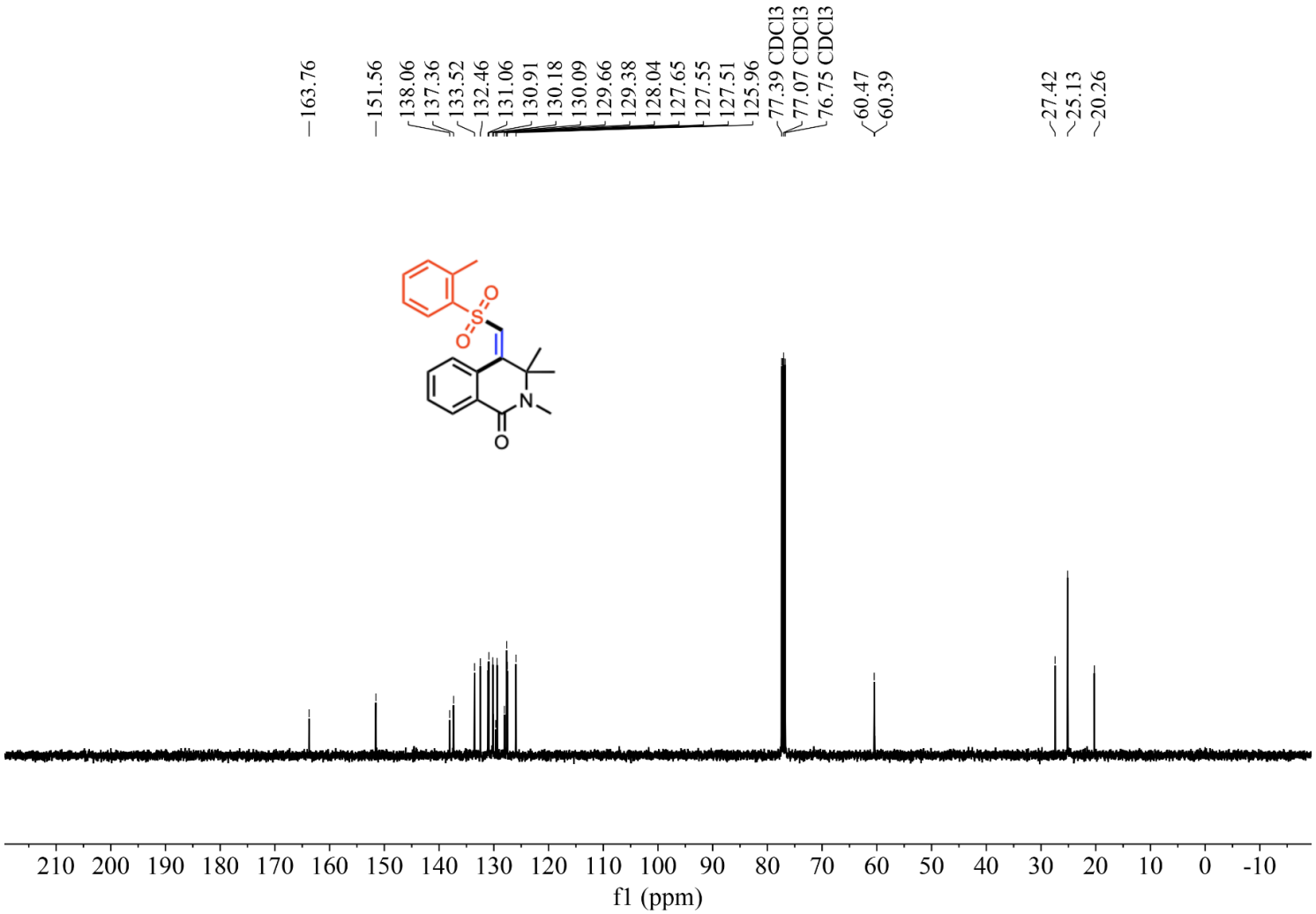
^{1}H spectrum of **3r**



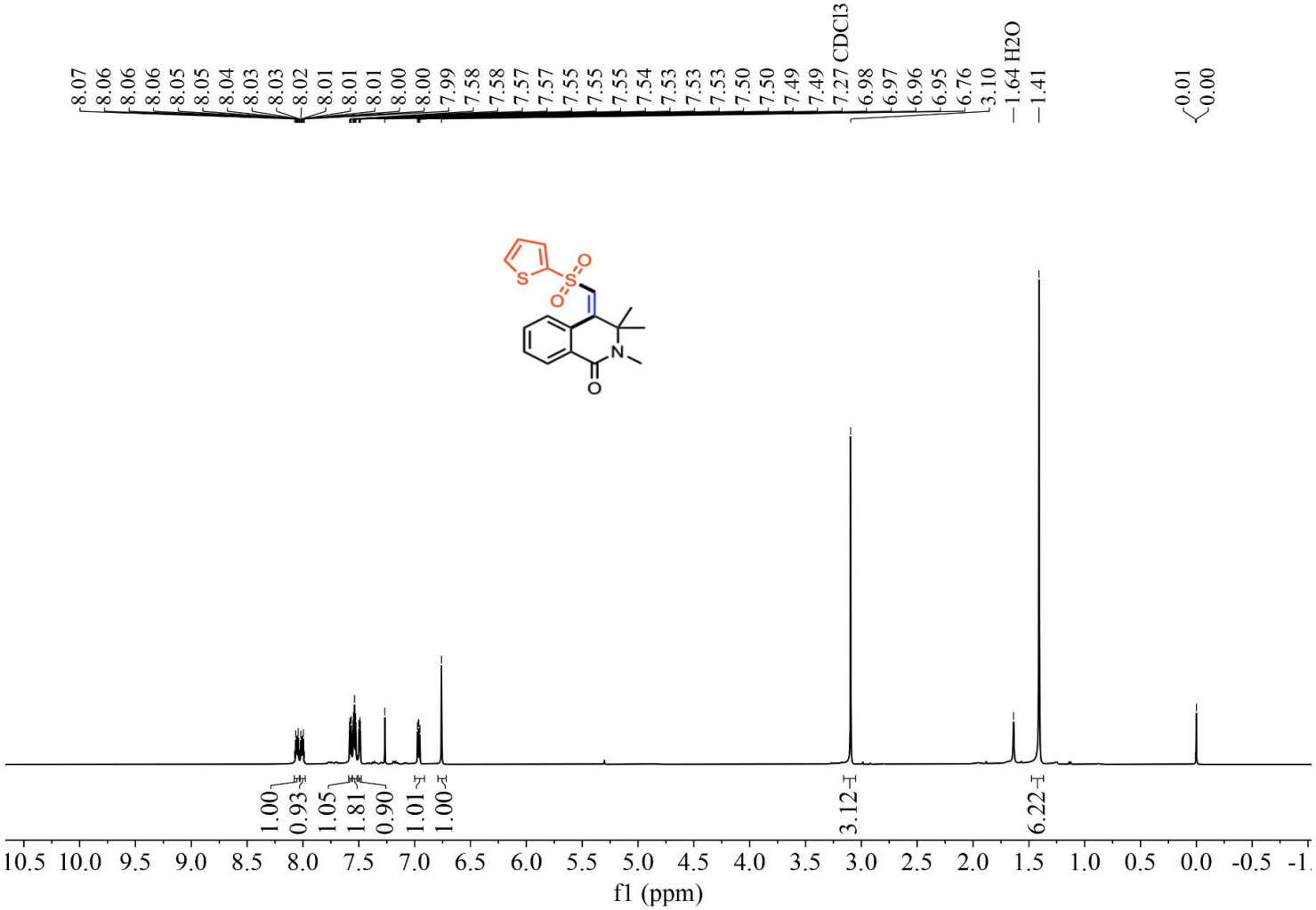
^{13}C spectrum of **3r**



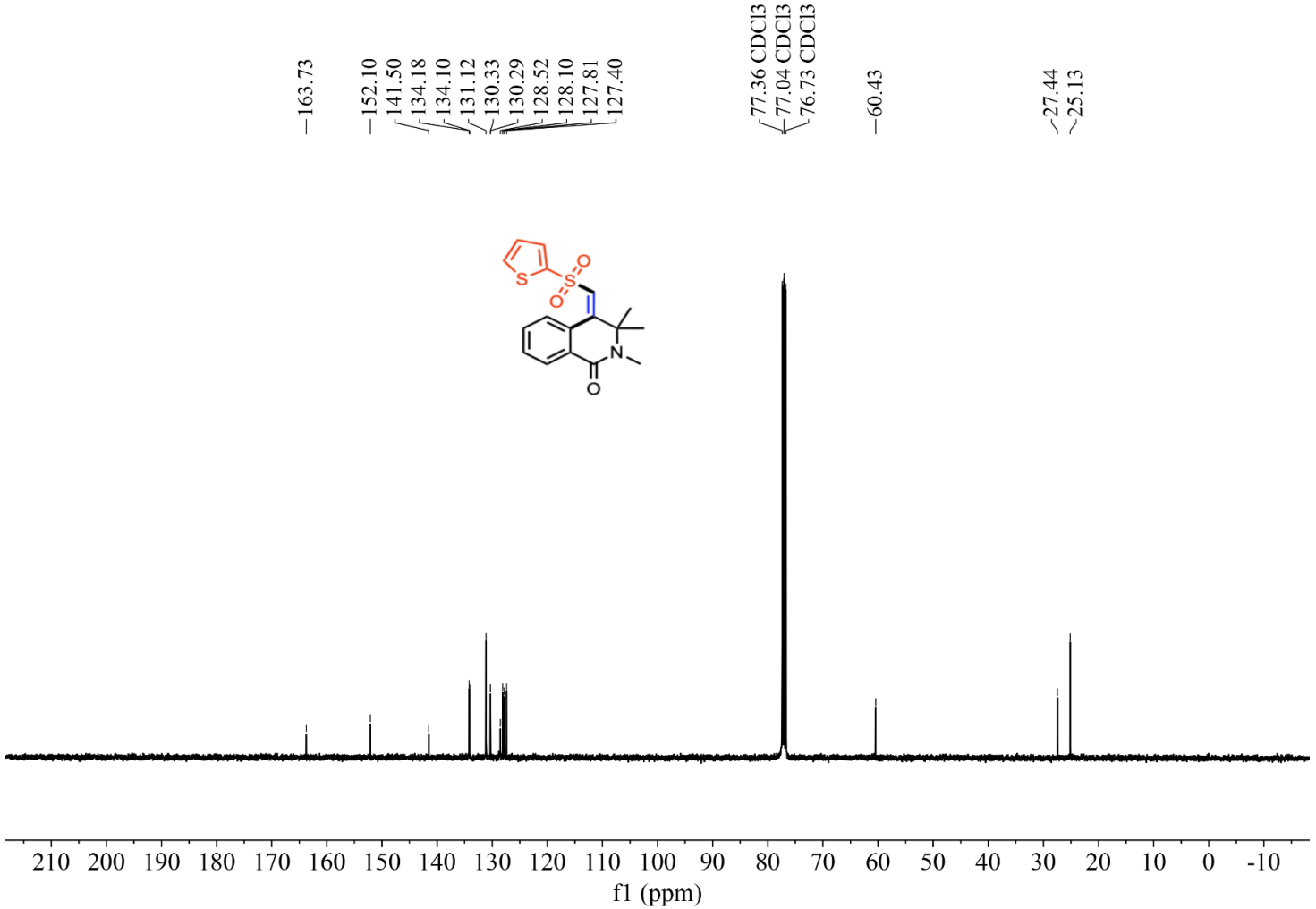
^{1}H spectrum of **3s**



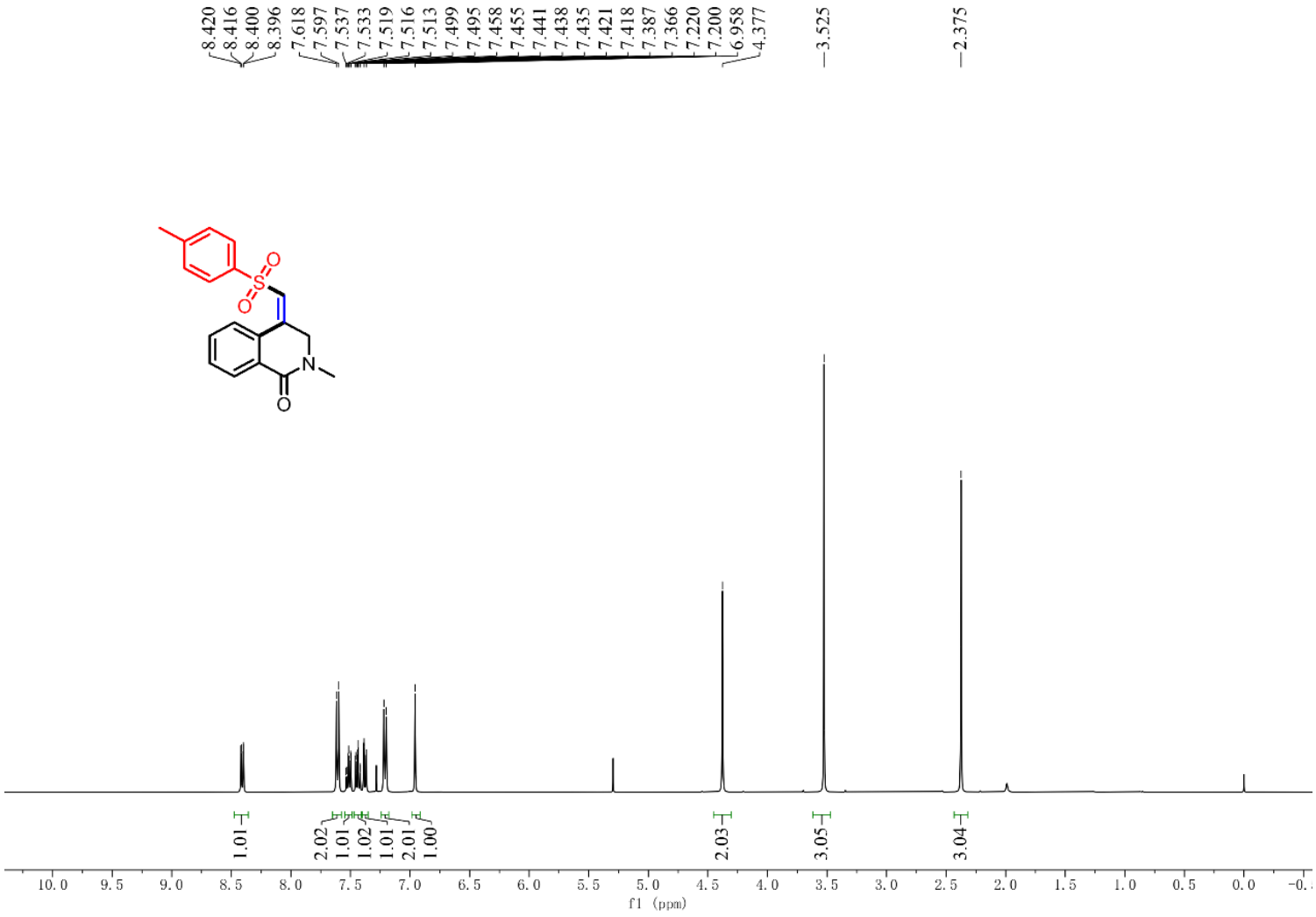
^{13}C spectrum of **3s**



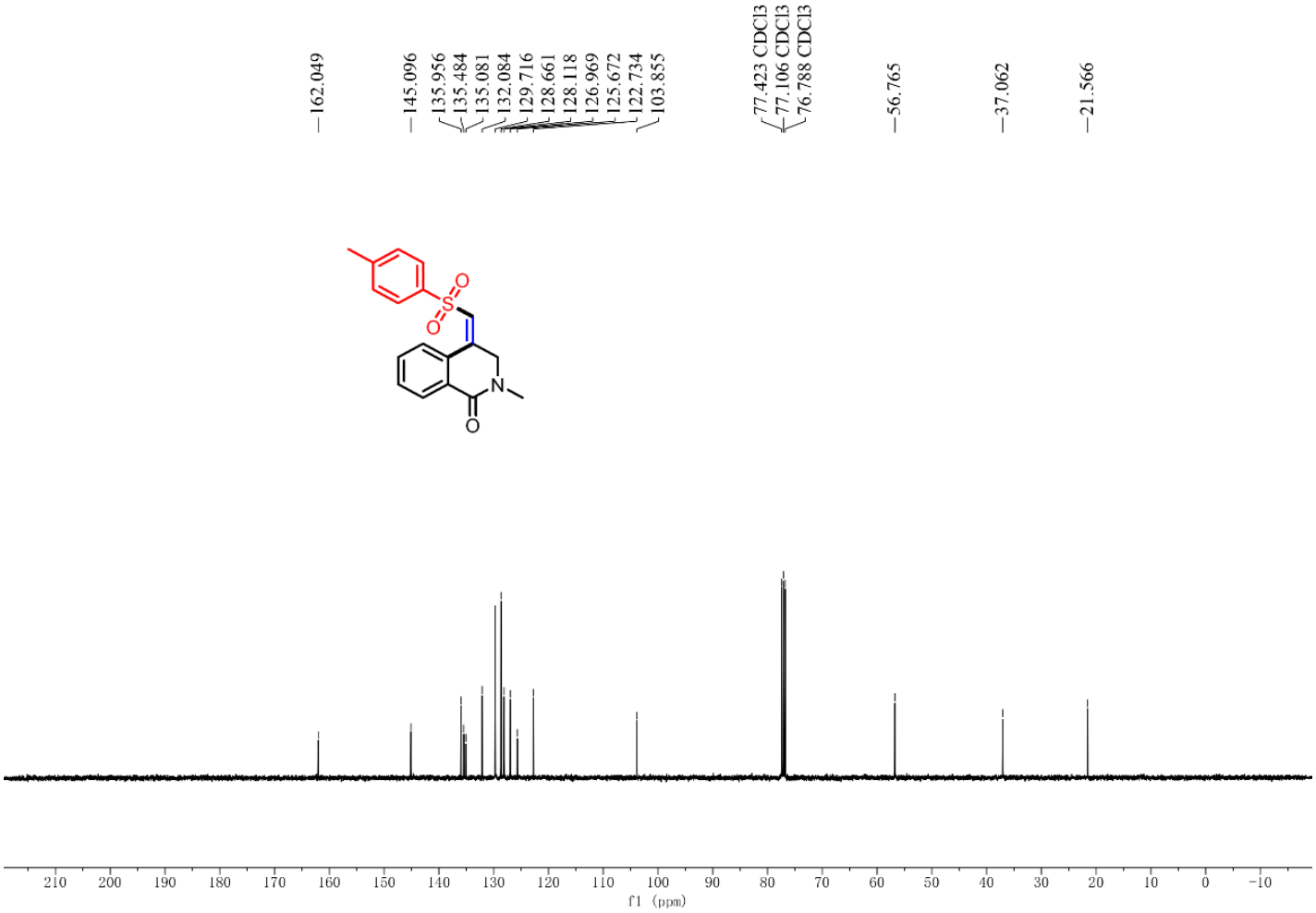
^{1}H spectrum of **3t**



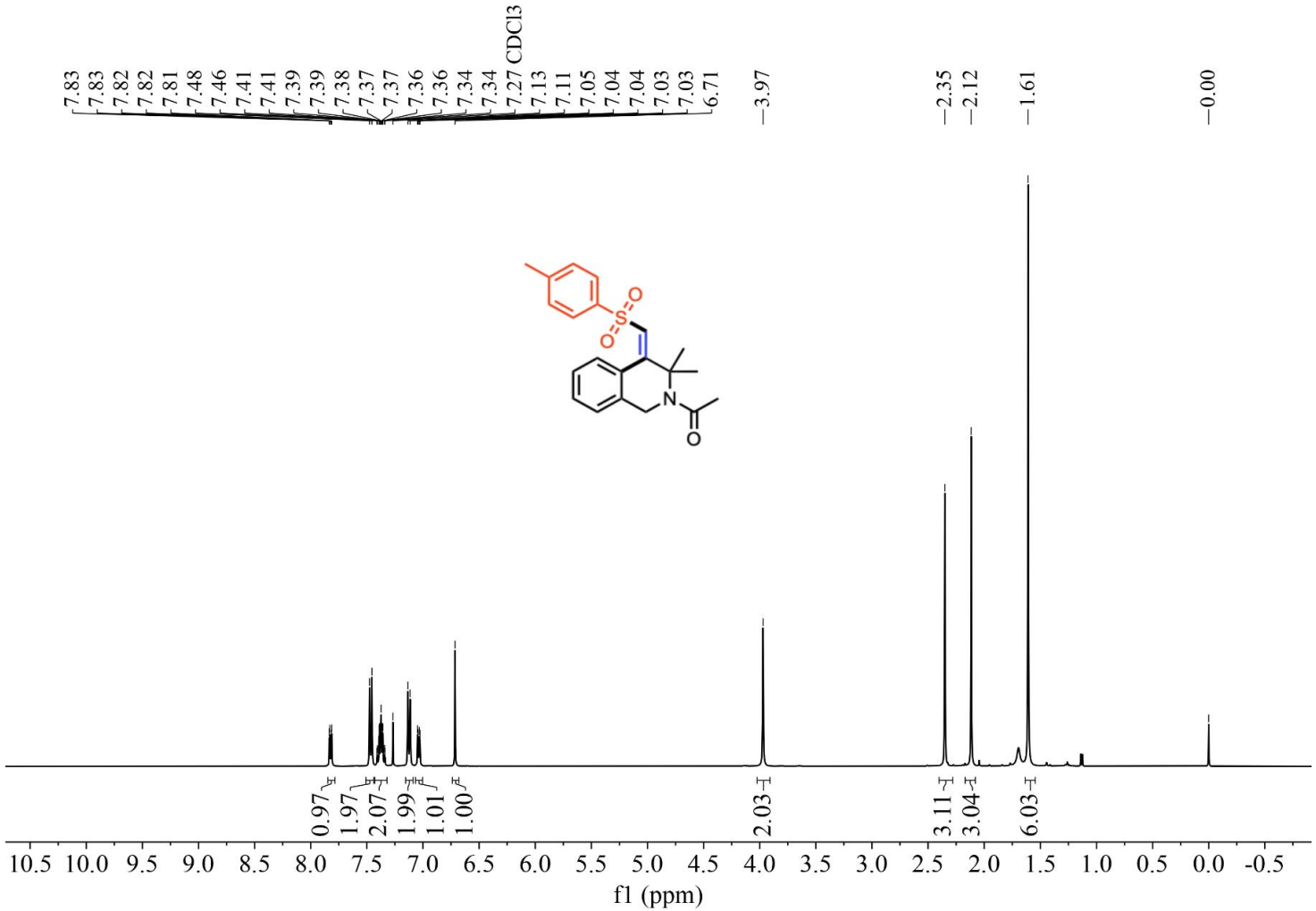
^{13}C spectrum of **3t**



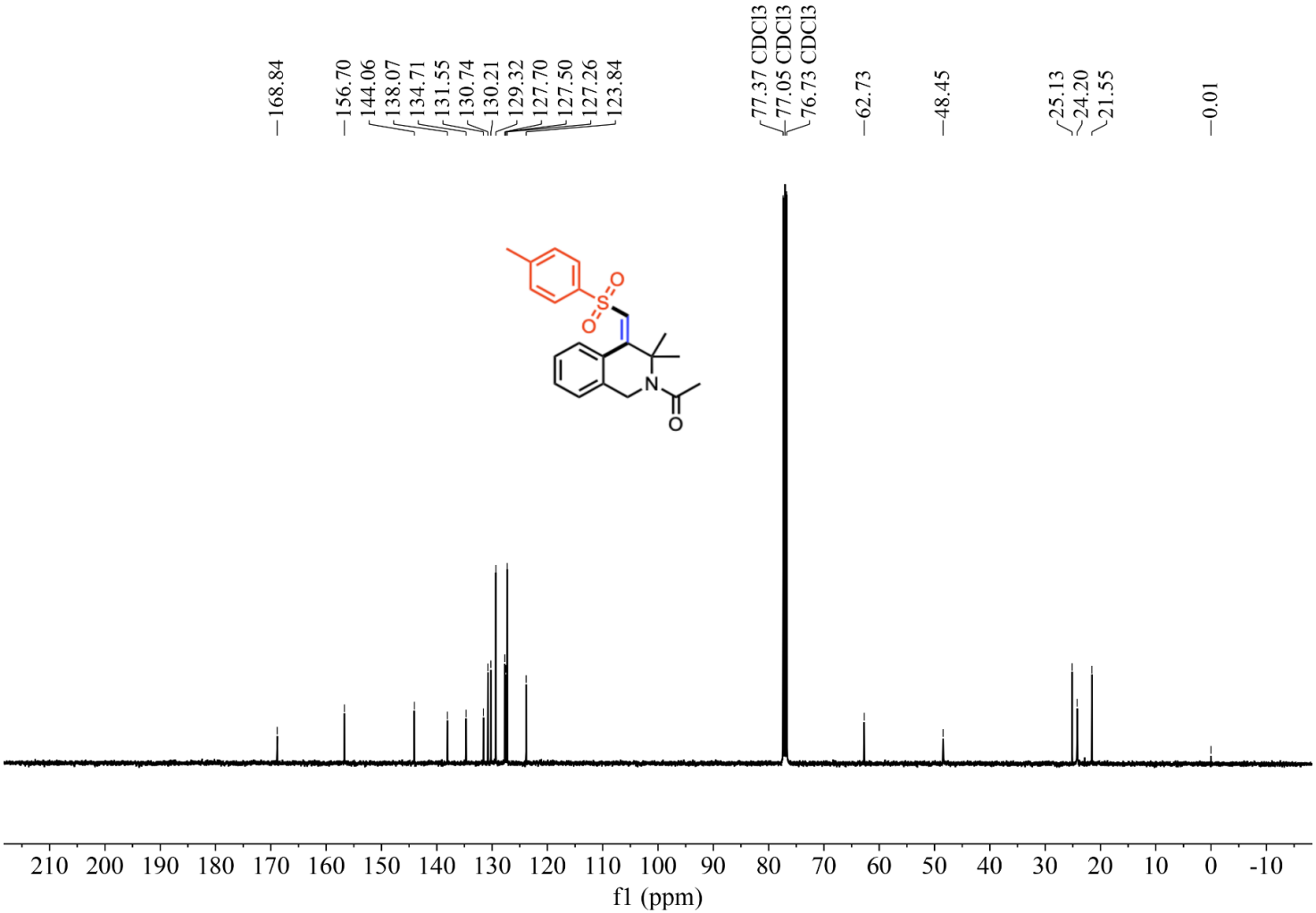
^{1}H spectrum of **3u**



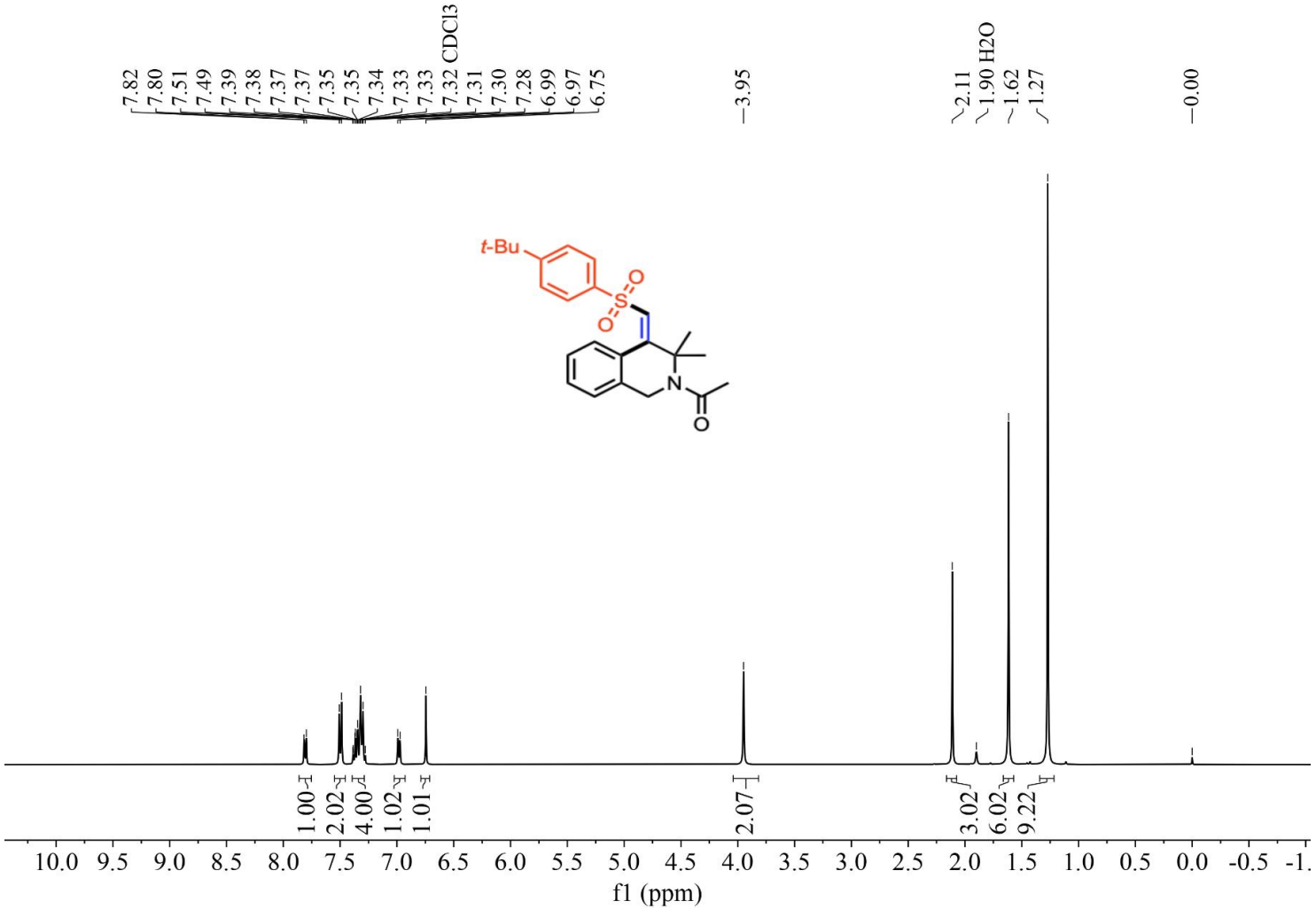
^{13}C spectrum of **3u**



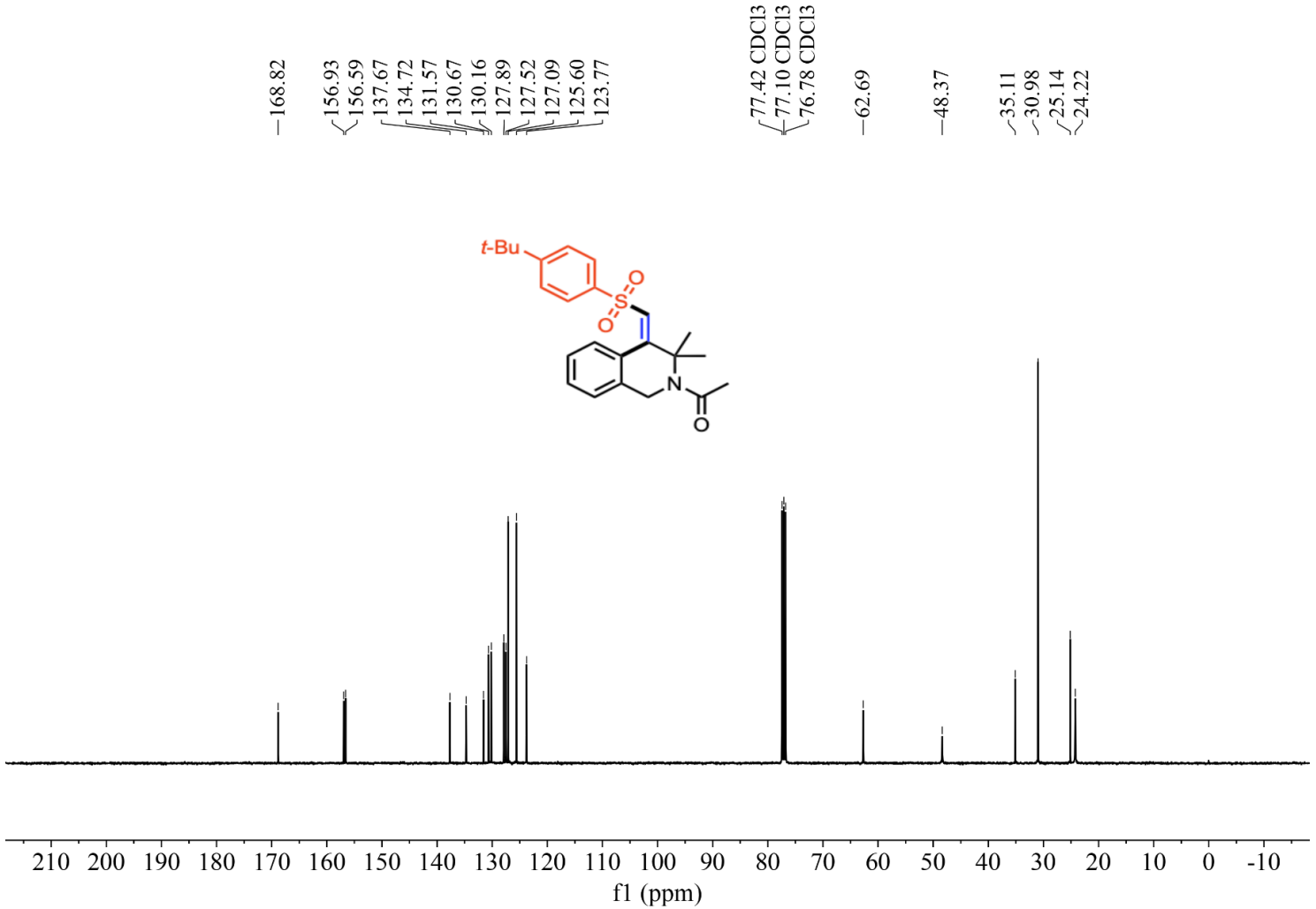
^{1}H spectrum of **4a**



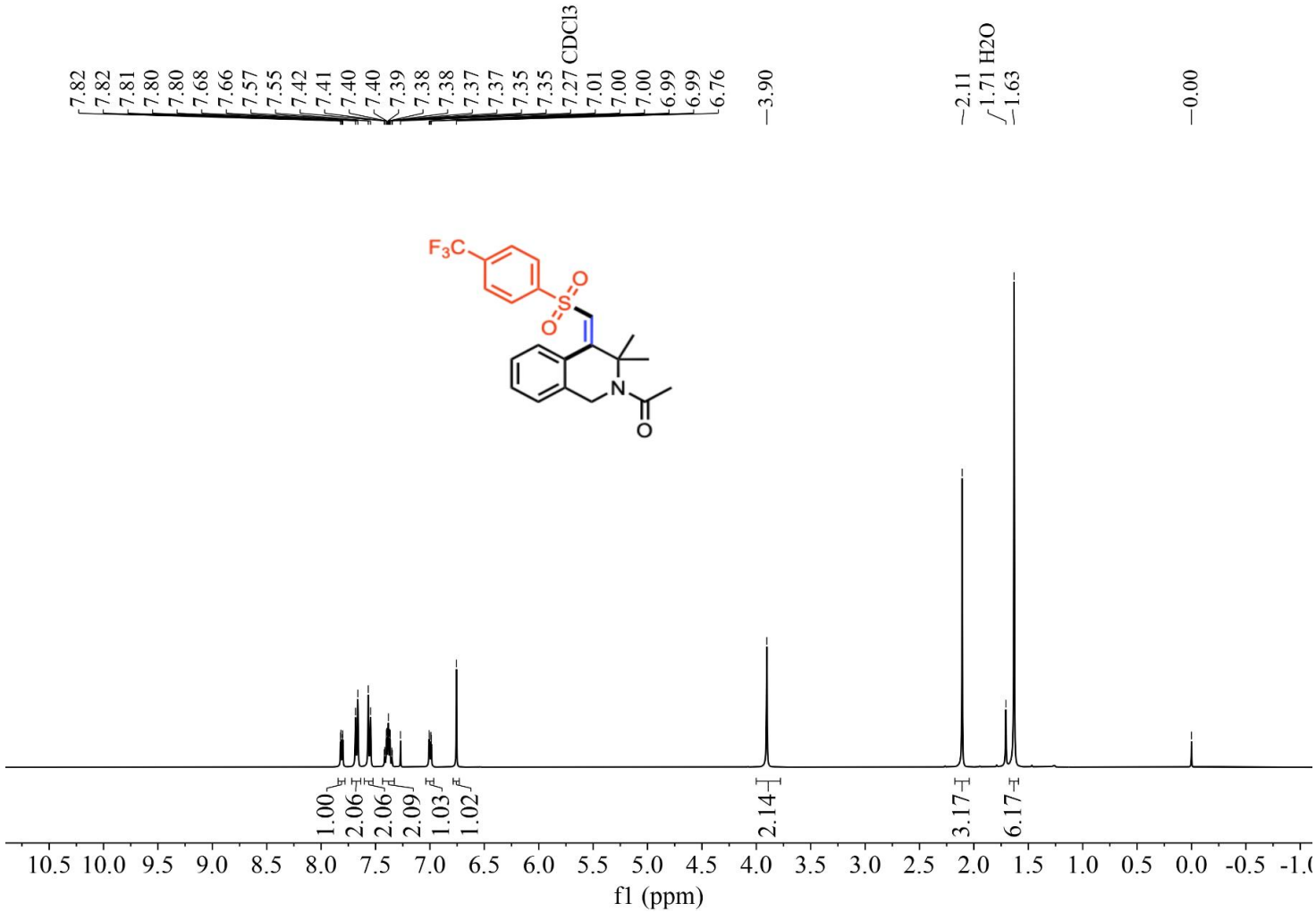
^{13}C spectrum of **4a**



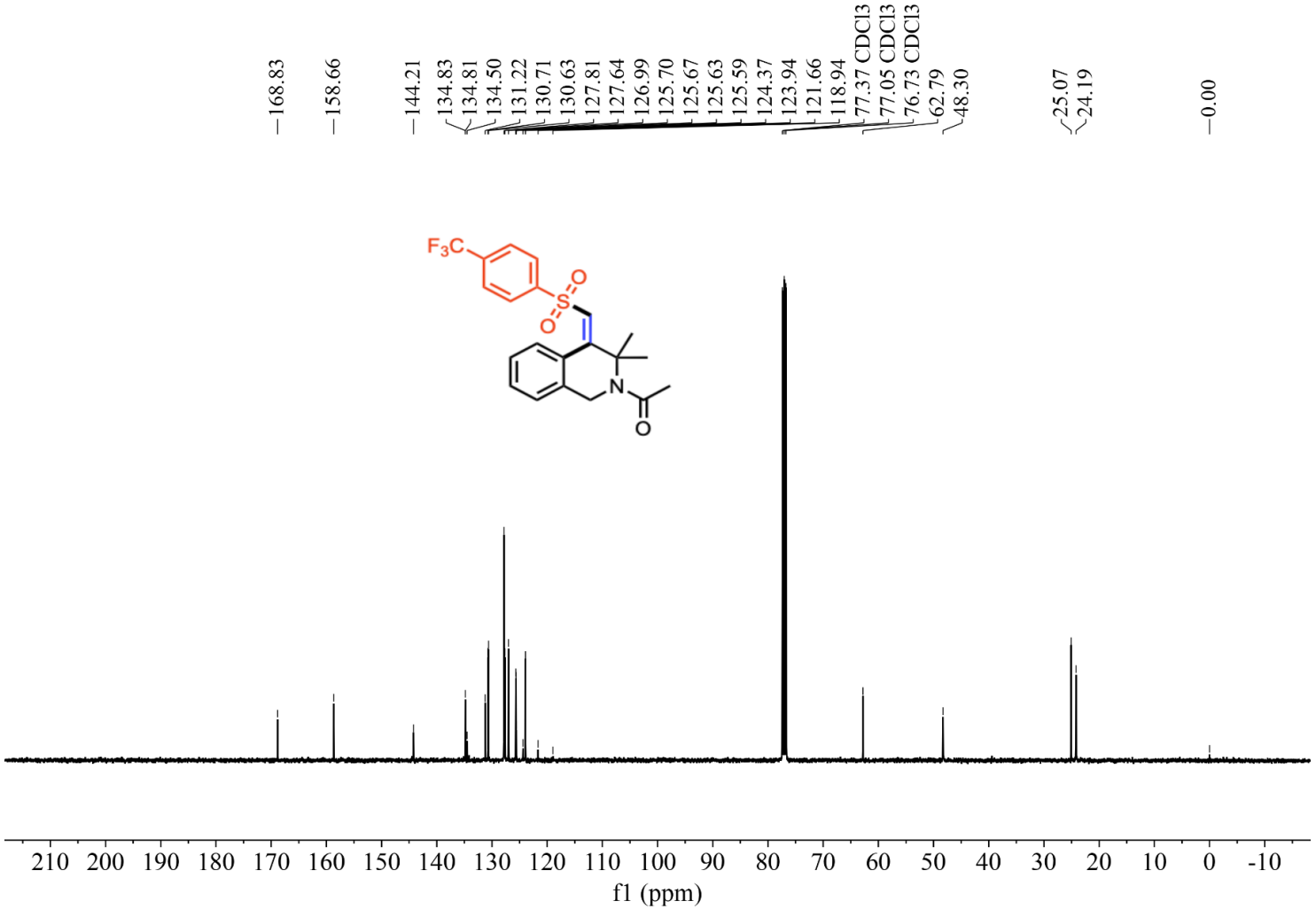
^{1}H spectrum of **4b**



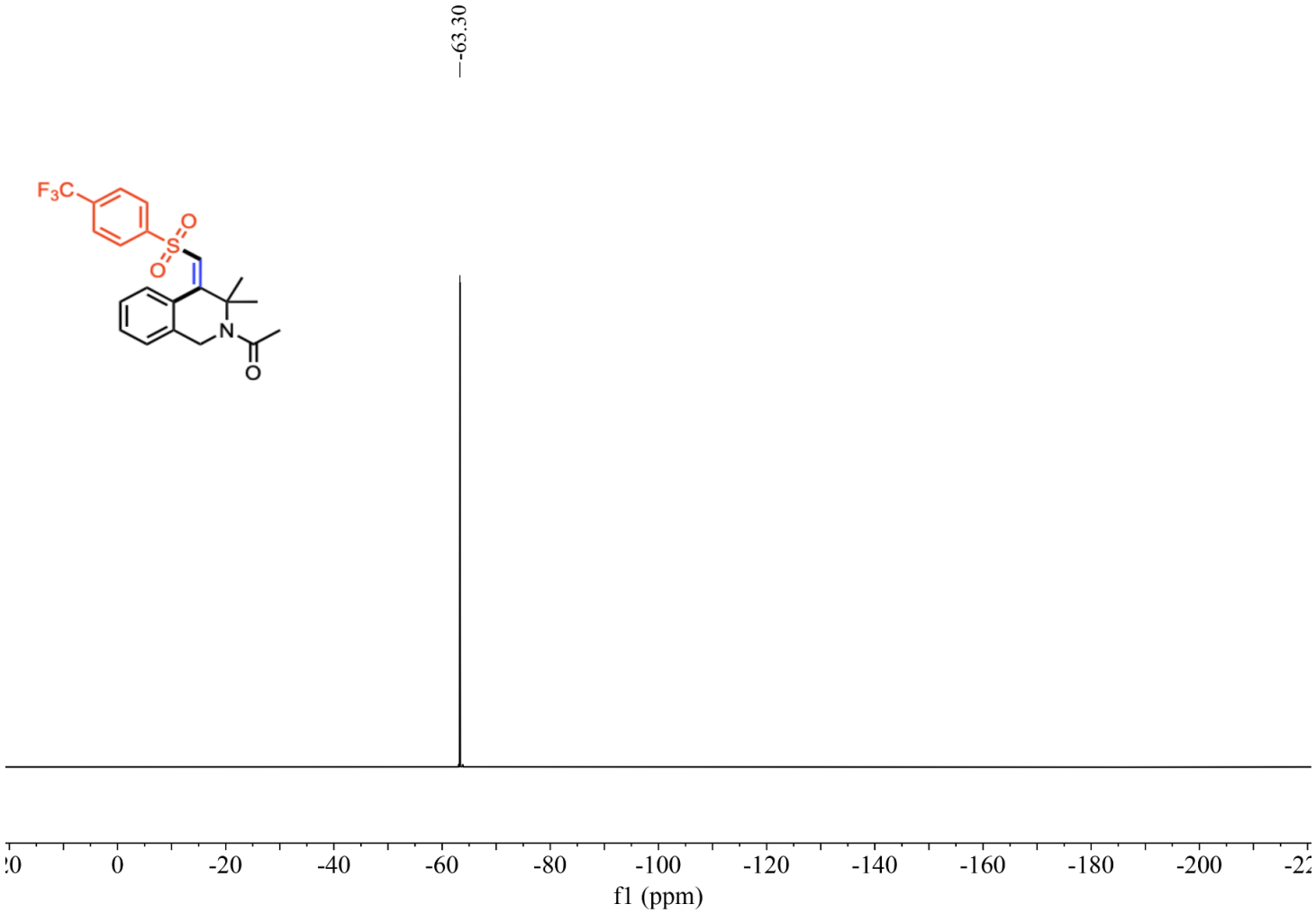
^{13}C spectrum of **4b**



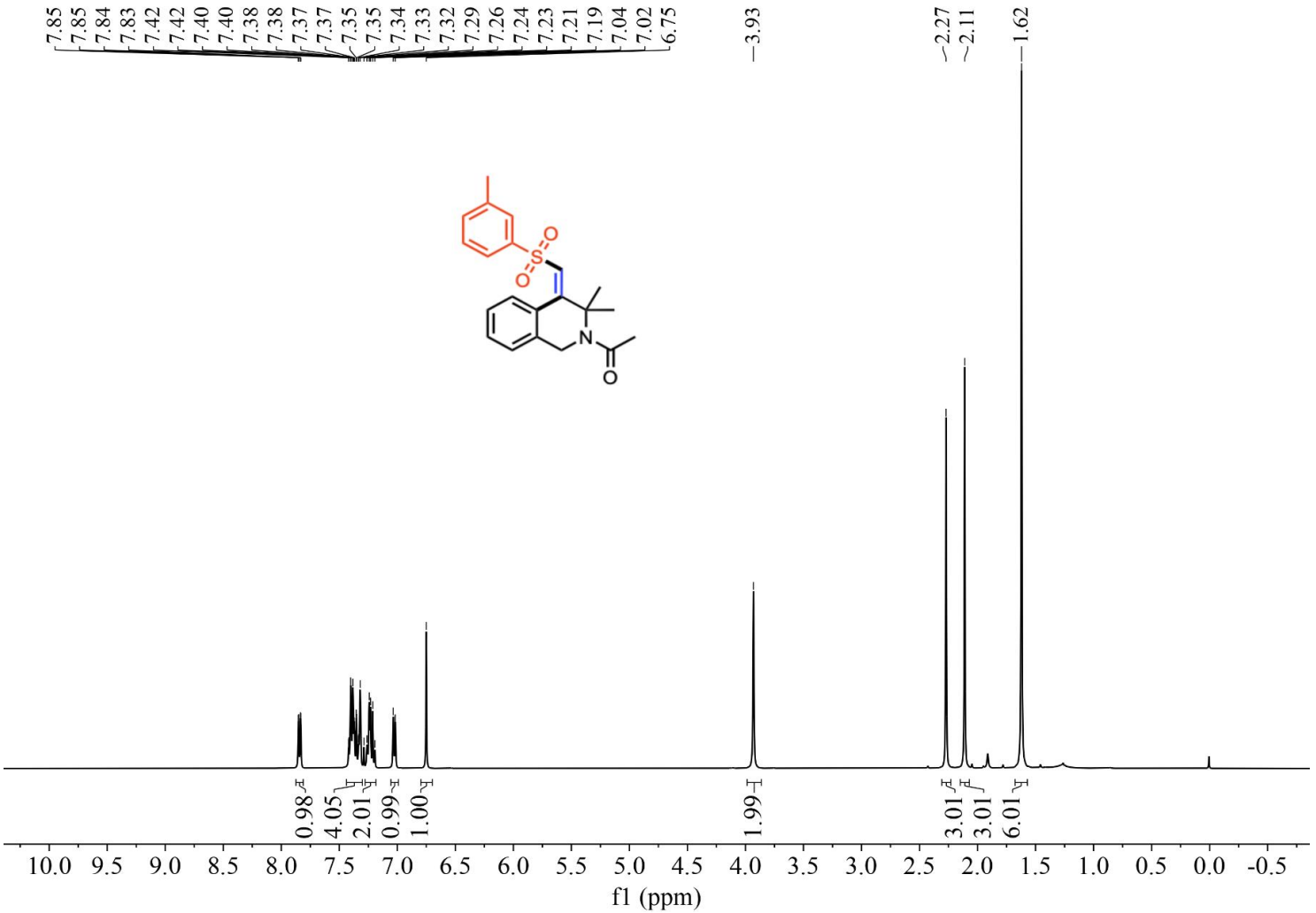
^{1}H spectrum of **4c**



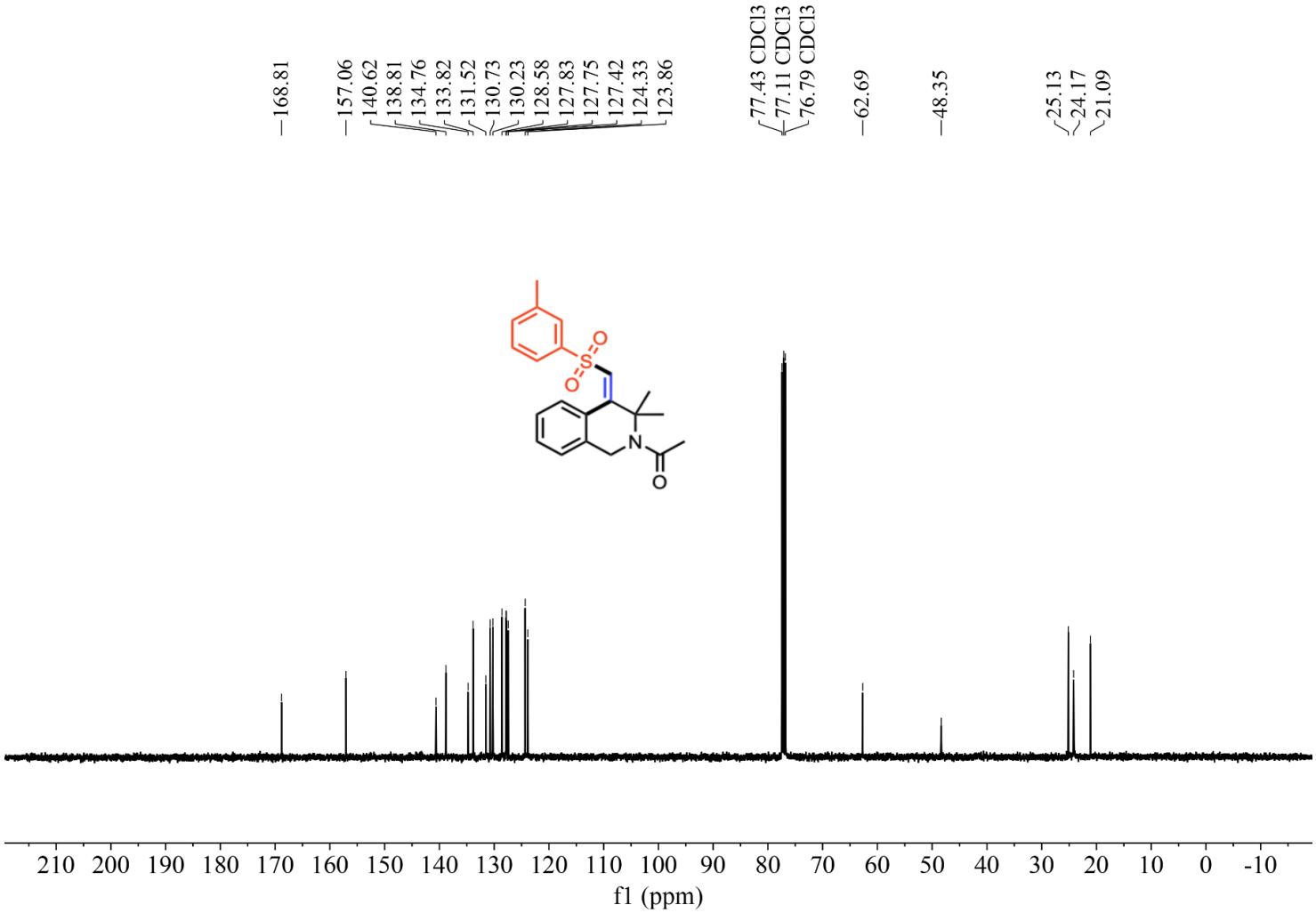
^{13}C spectrum of **4c**



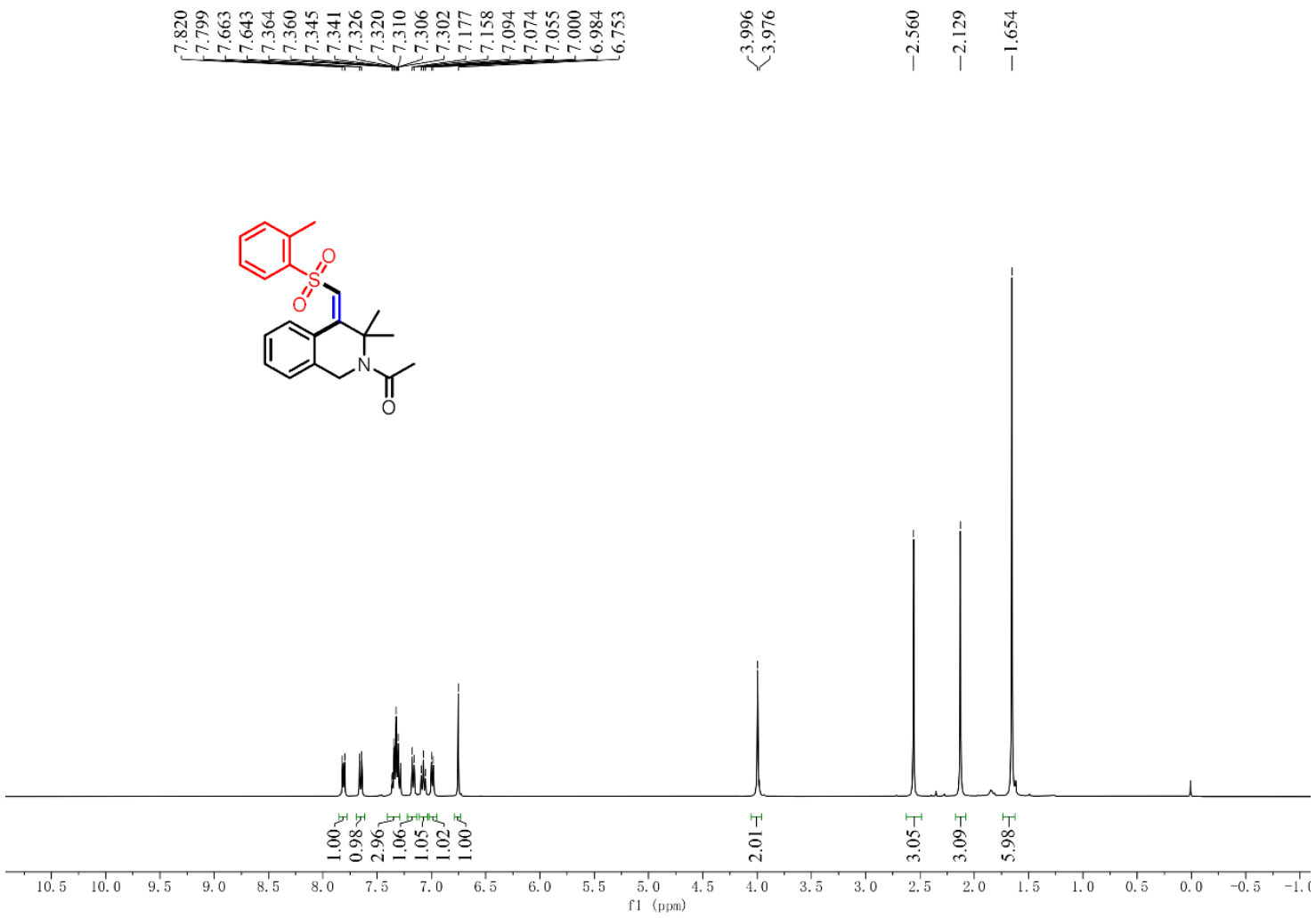
^{19}F spectrum of **4c**



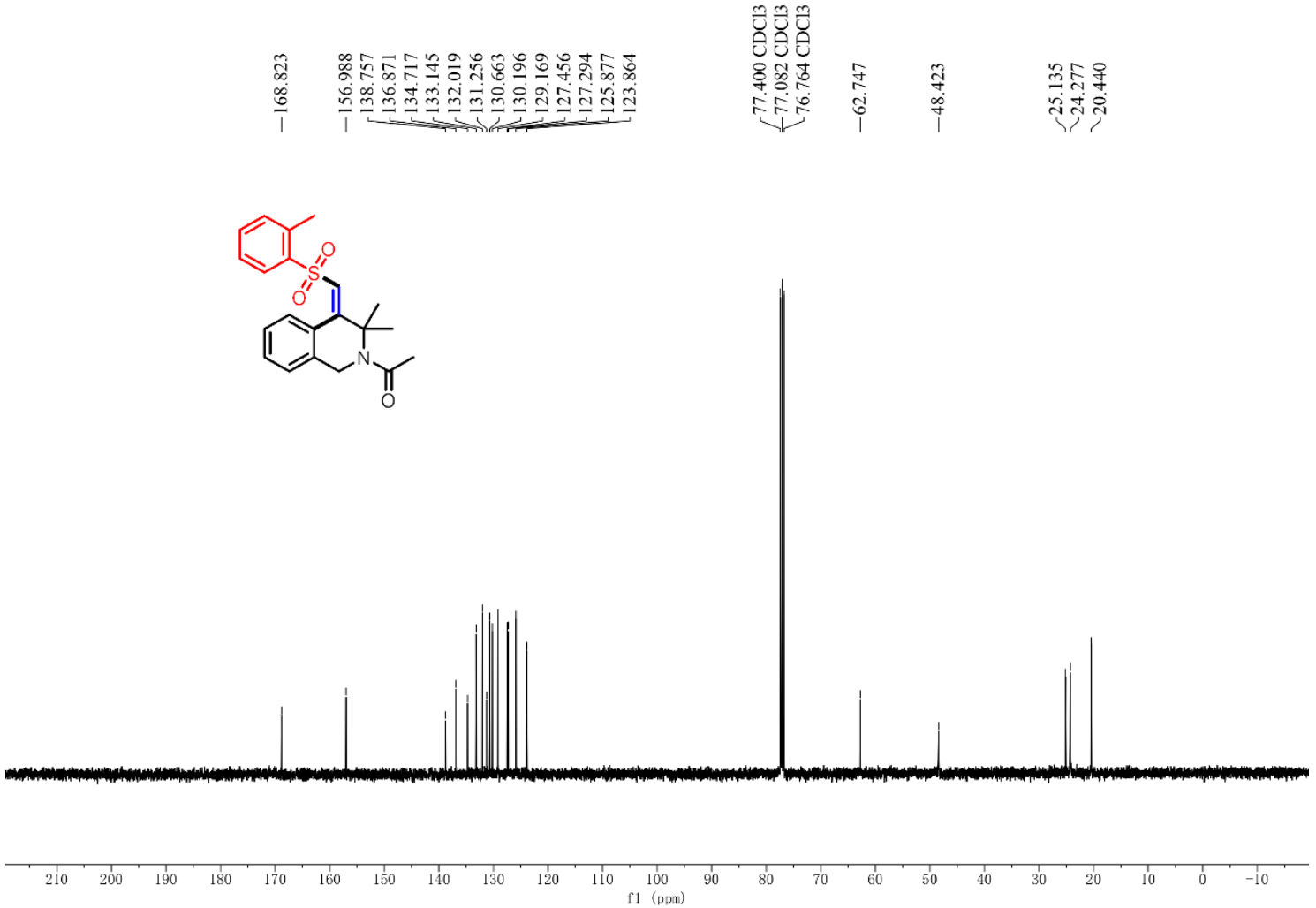
^{1}H spectrum of **4d**



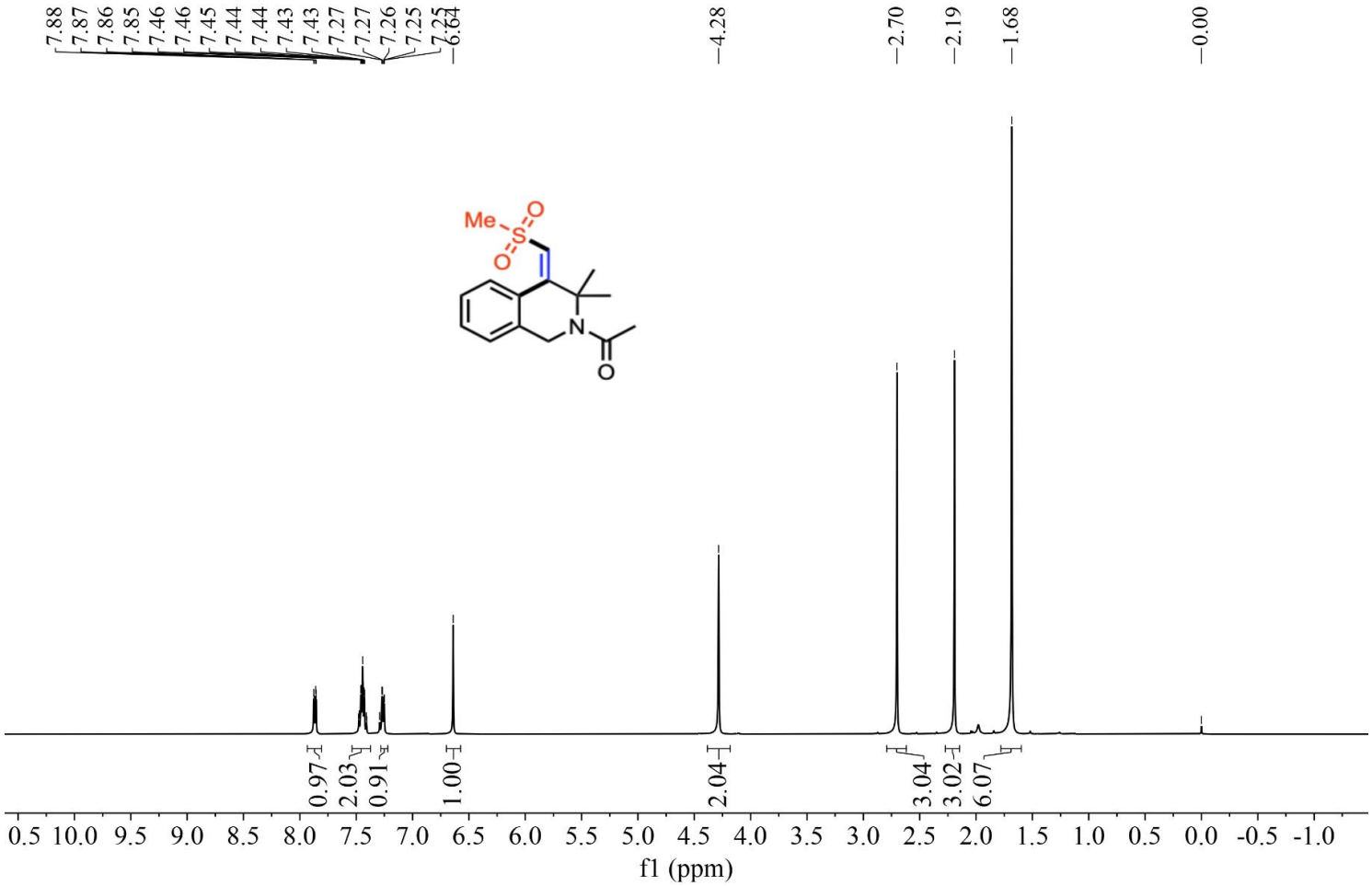
^{13}C spectrum of **4d**



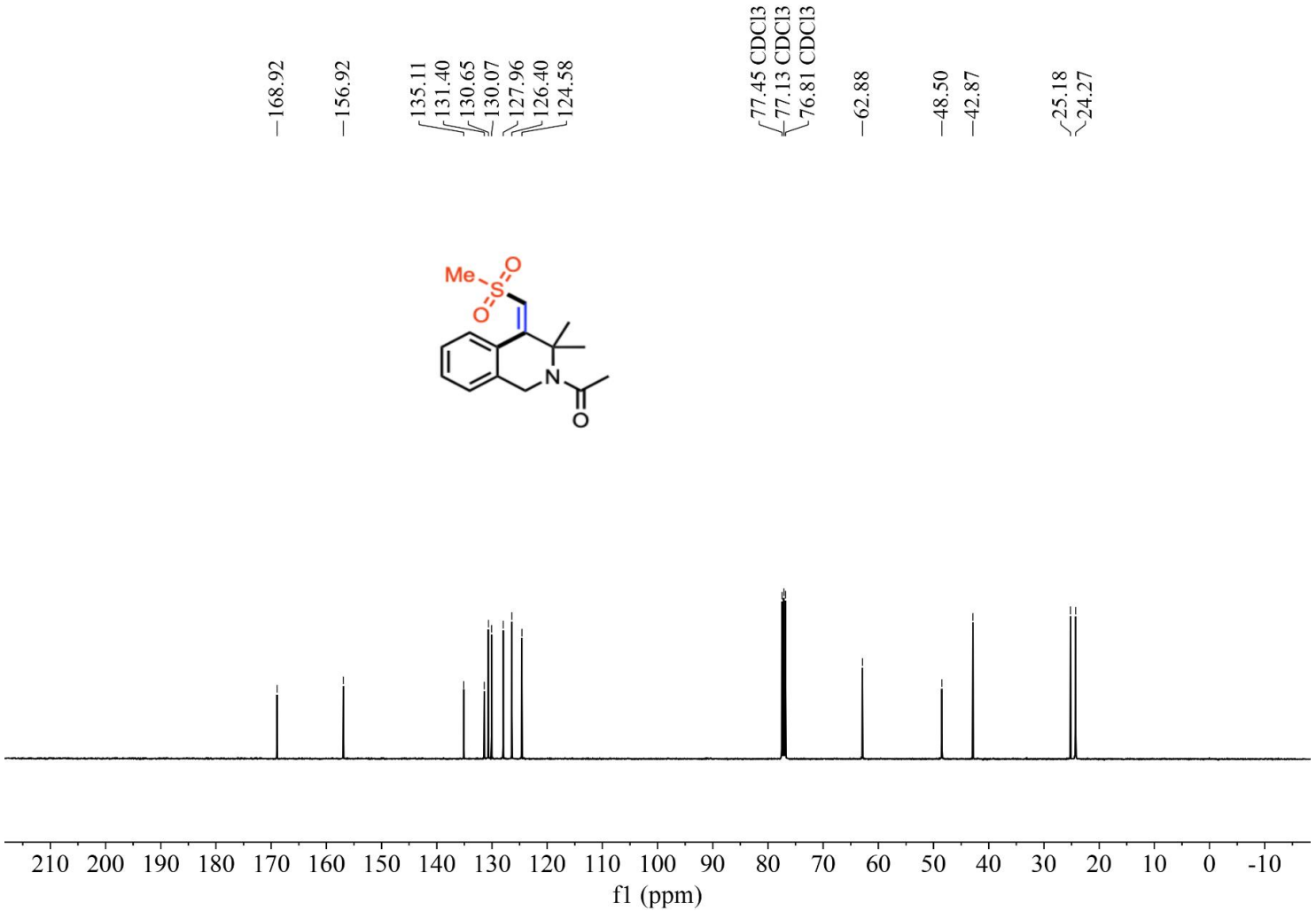
^{1}H spectrum of **4e**



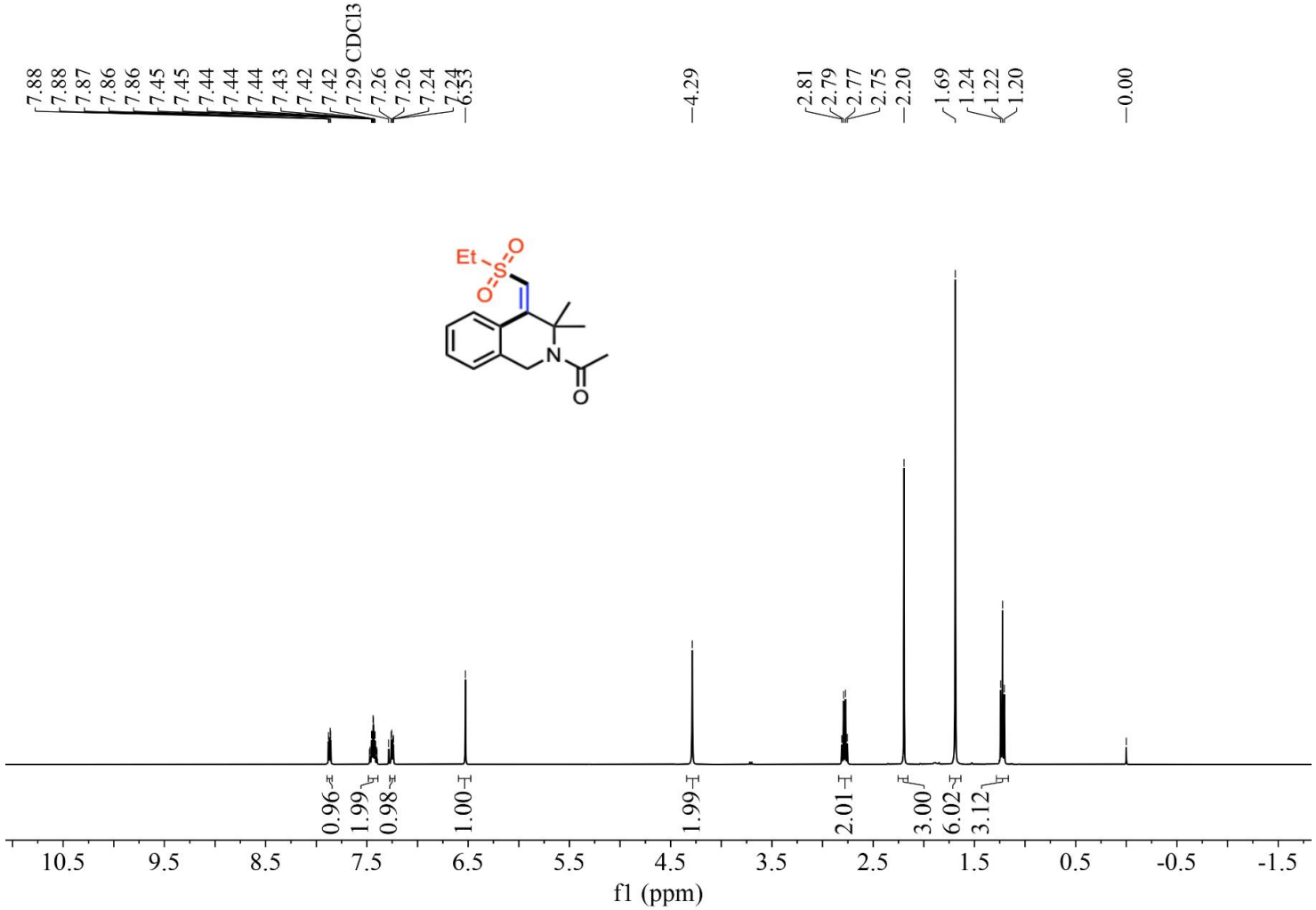
^{13}C spectrum of **4e**



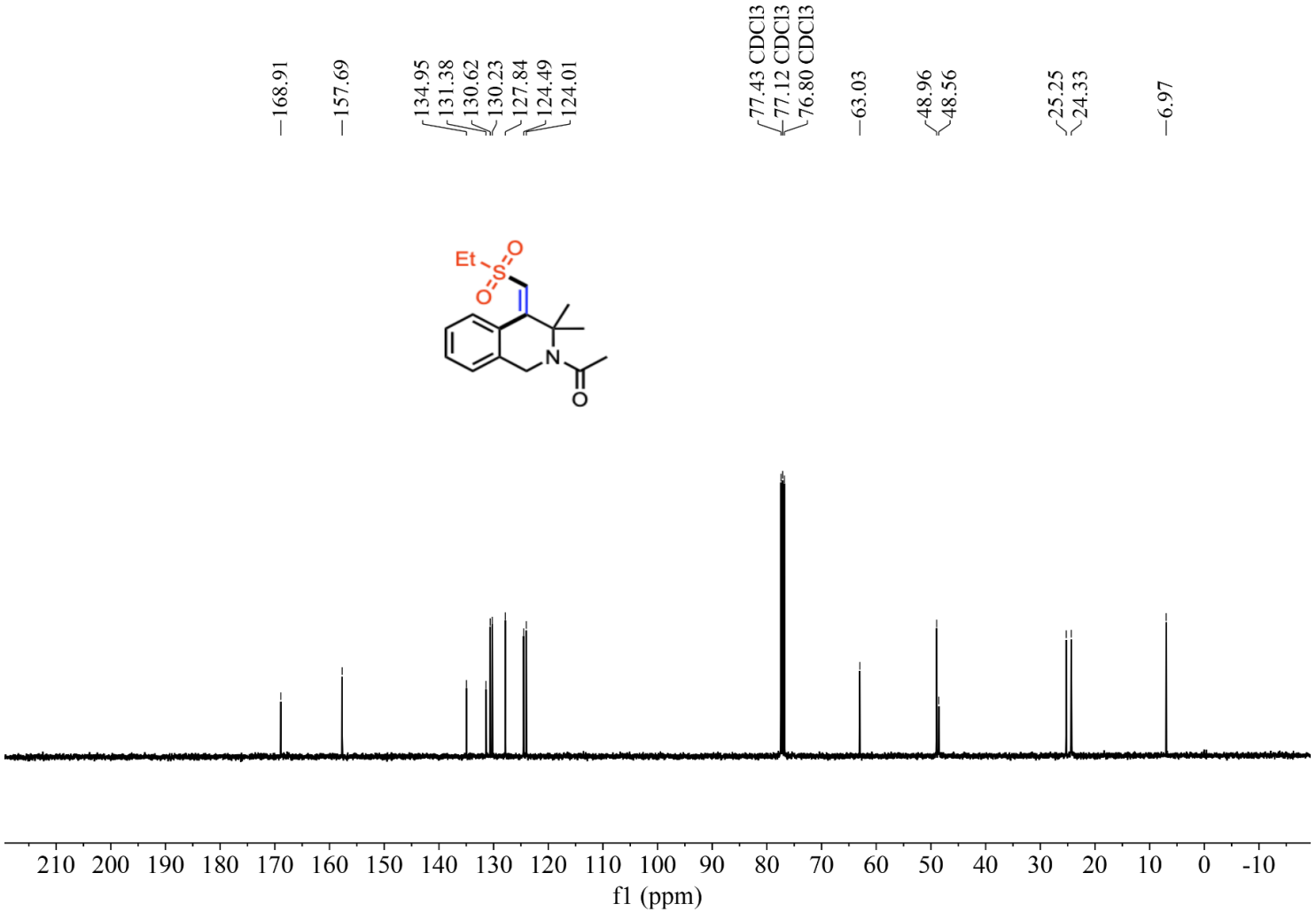
^{1}H spectrum of **4f**



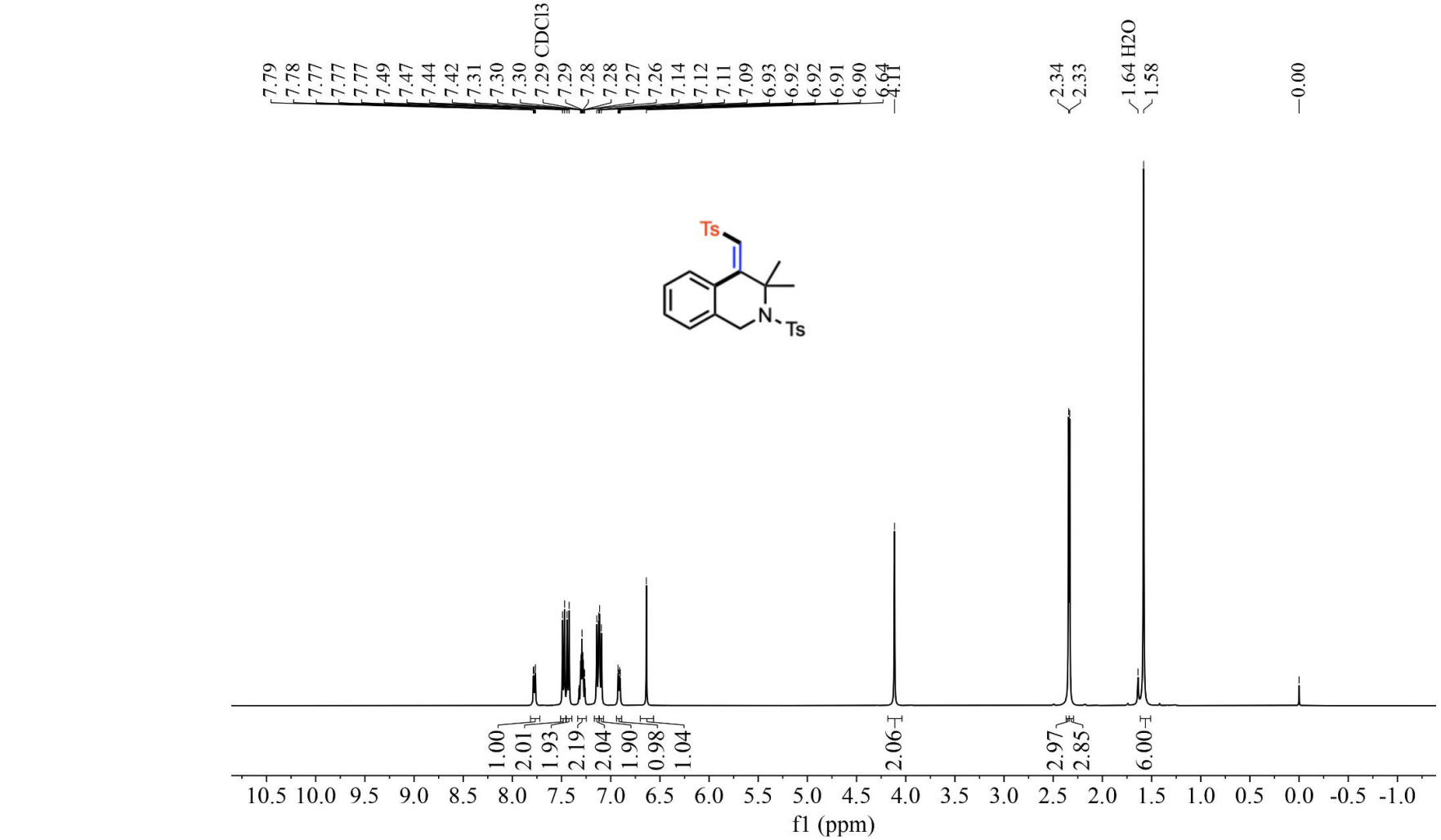
^{13}C spectrum of **4f**



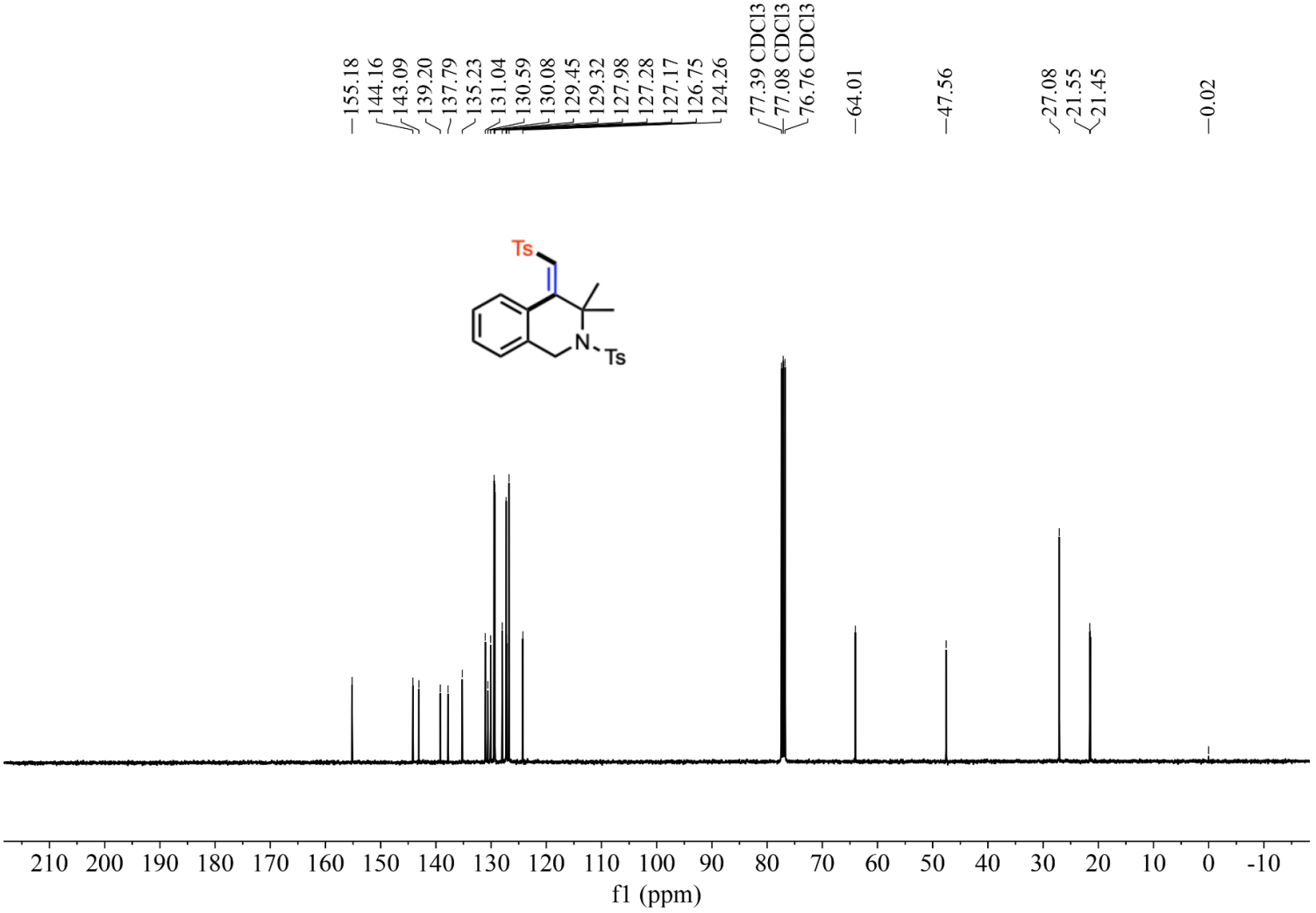
^{1}H spectrum of **4g**



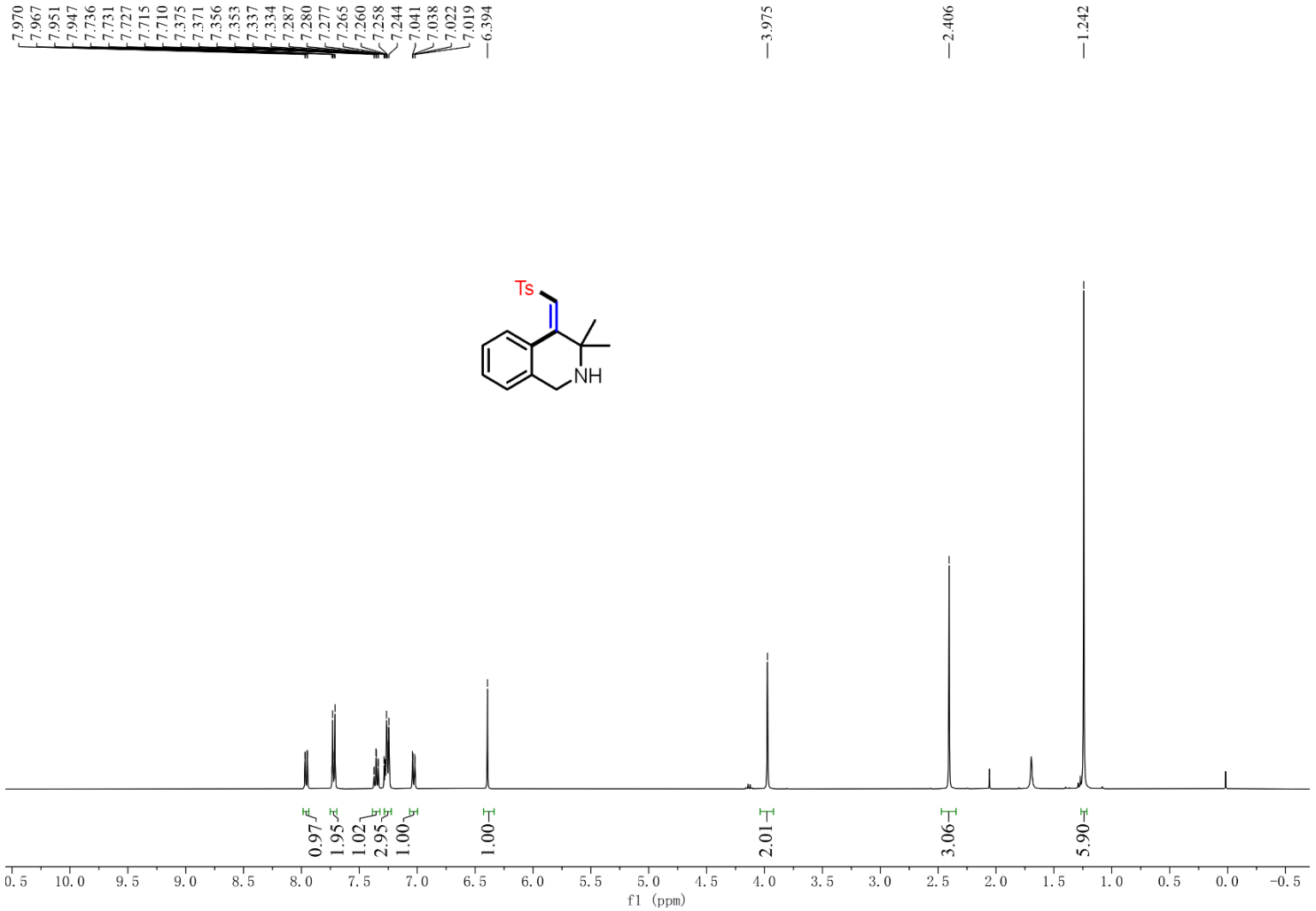
^{13}C spectrum of **4g**



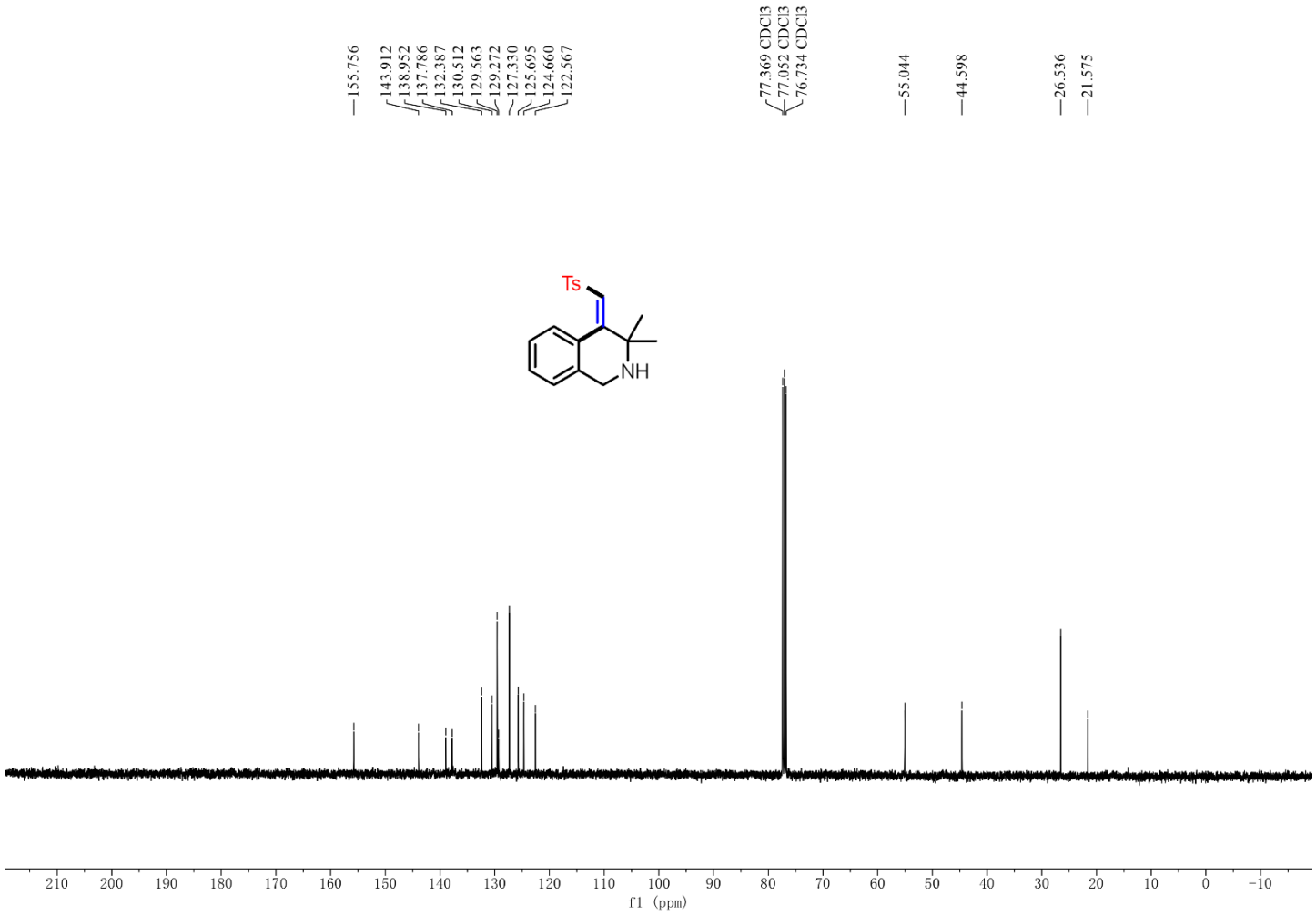
^{1}H spectrum of **4h**



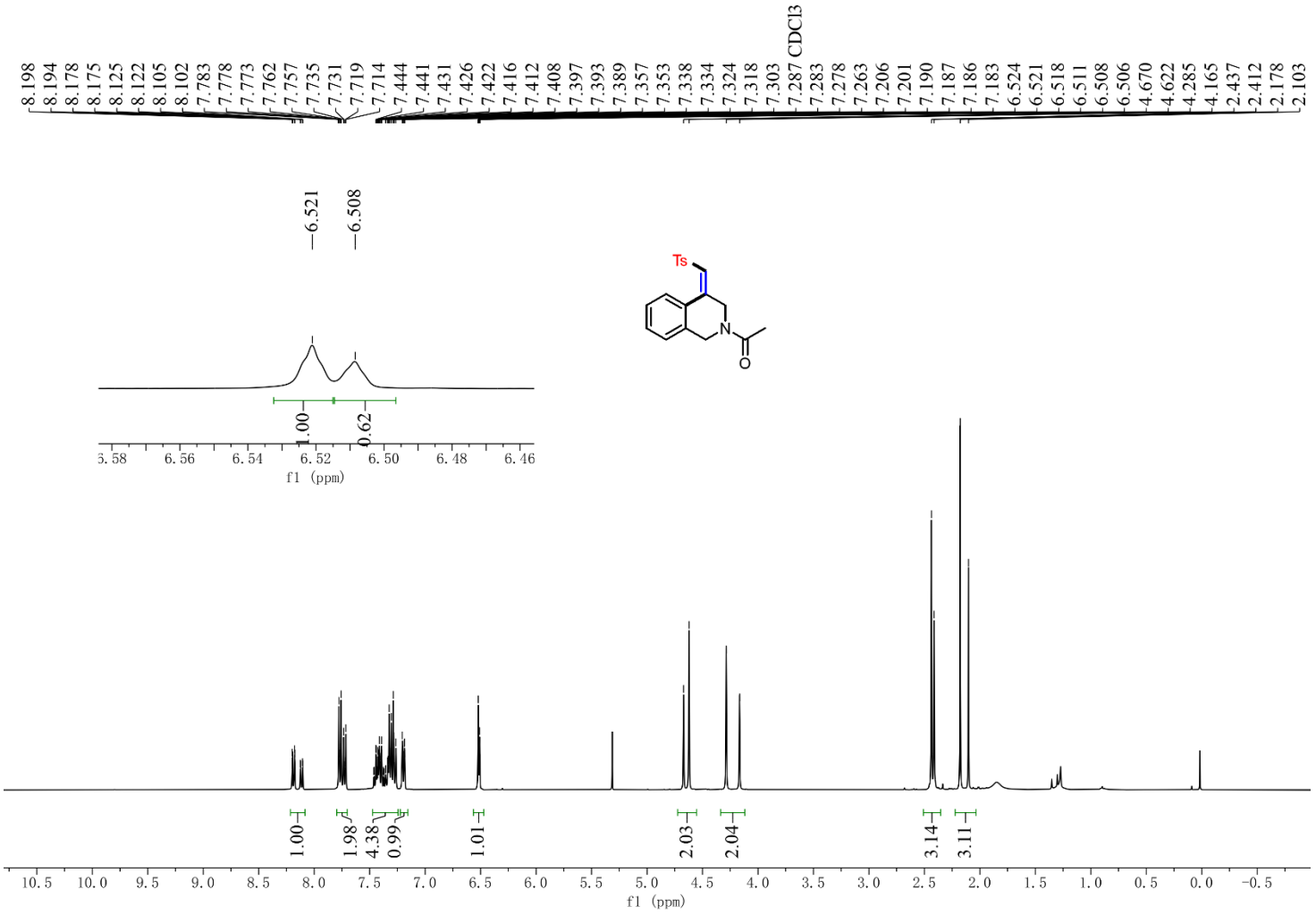
^{13}C spectrum of **4h**



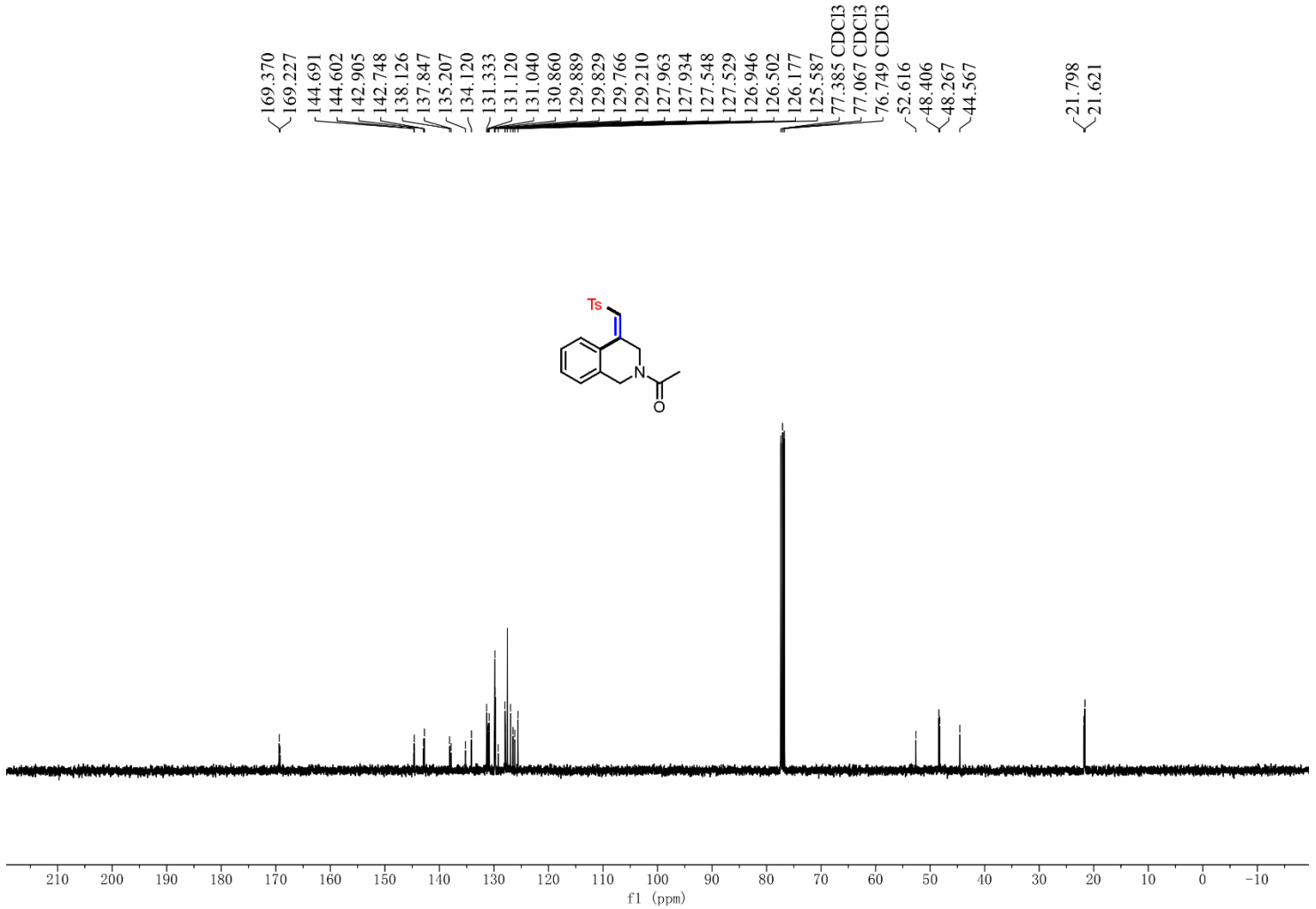
^{1}H spectrum of **4i**



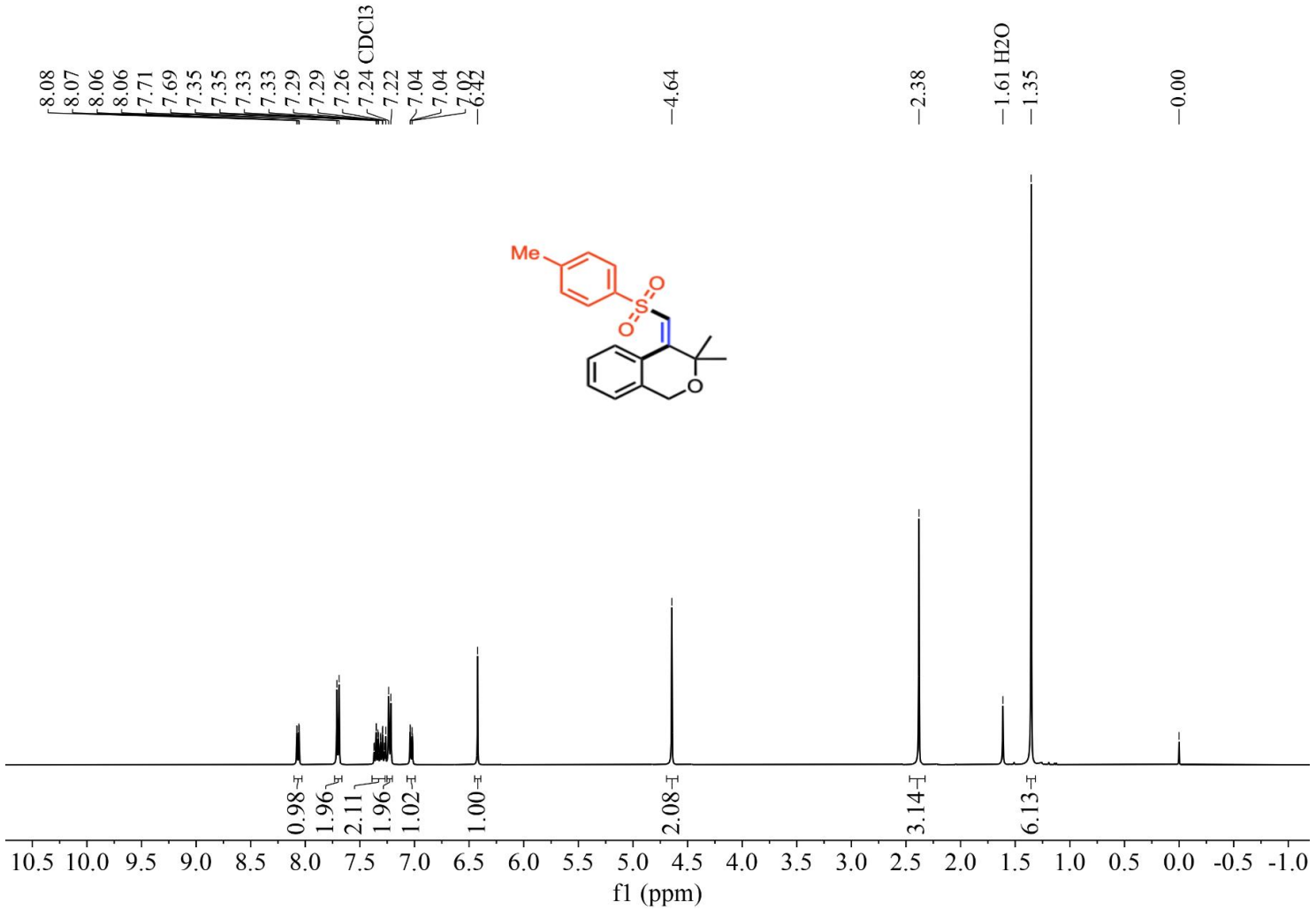
^{13}C spectrum of **4i**



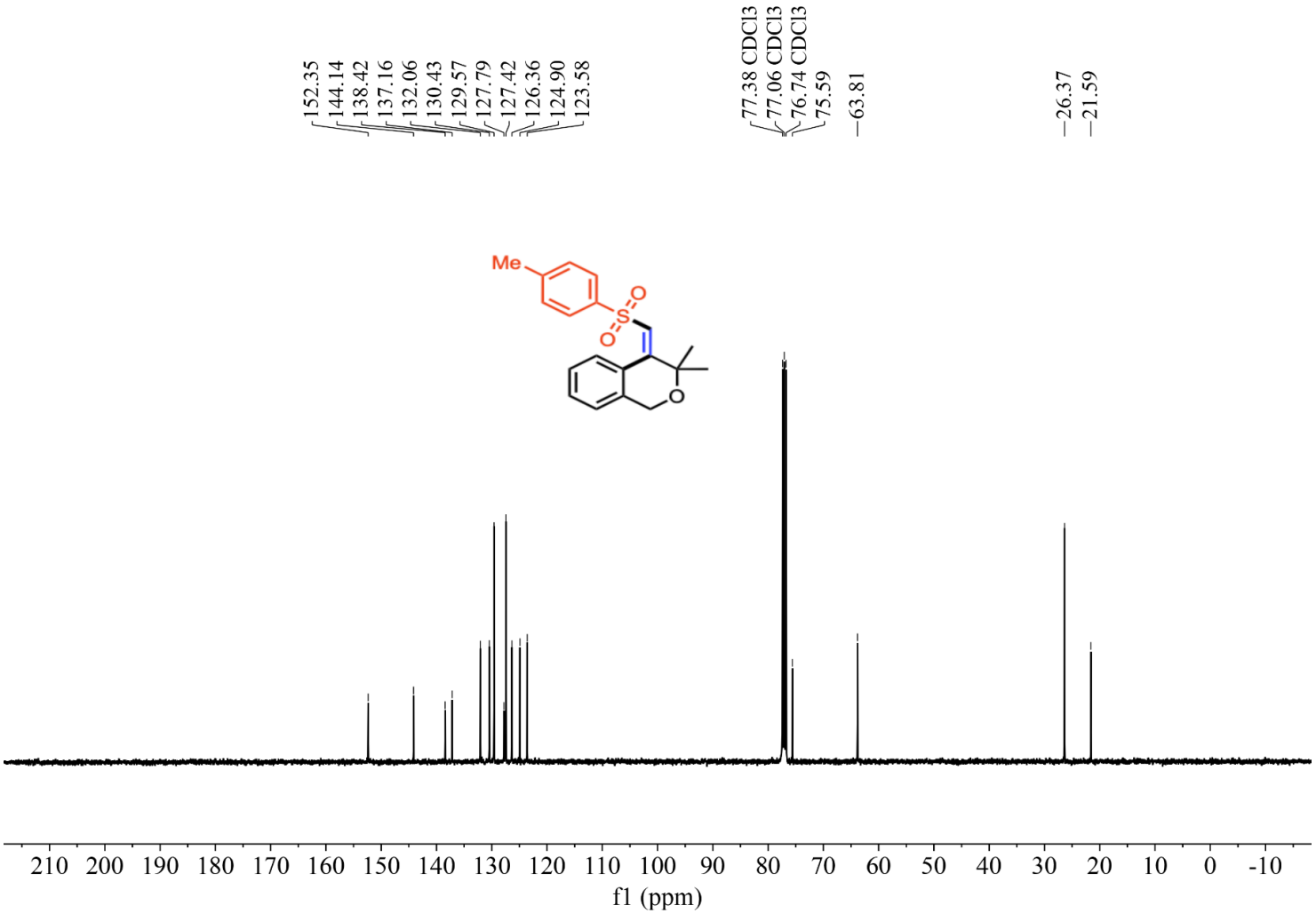
^{1}H spectrum of **4j**



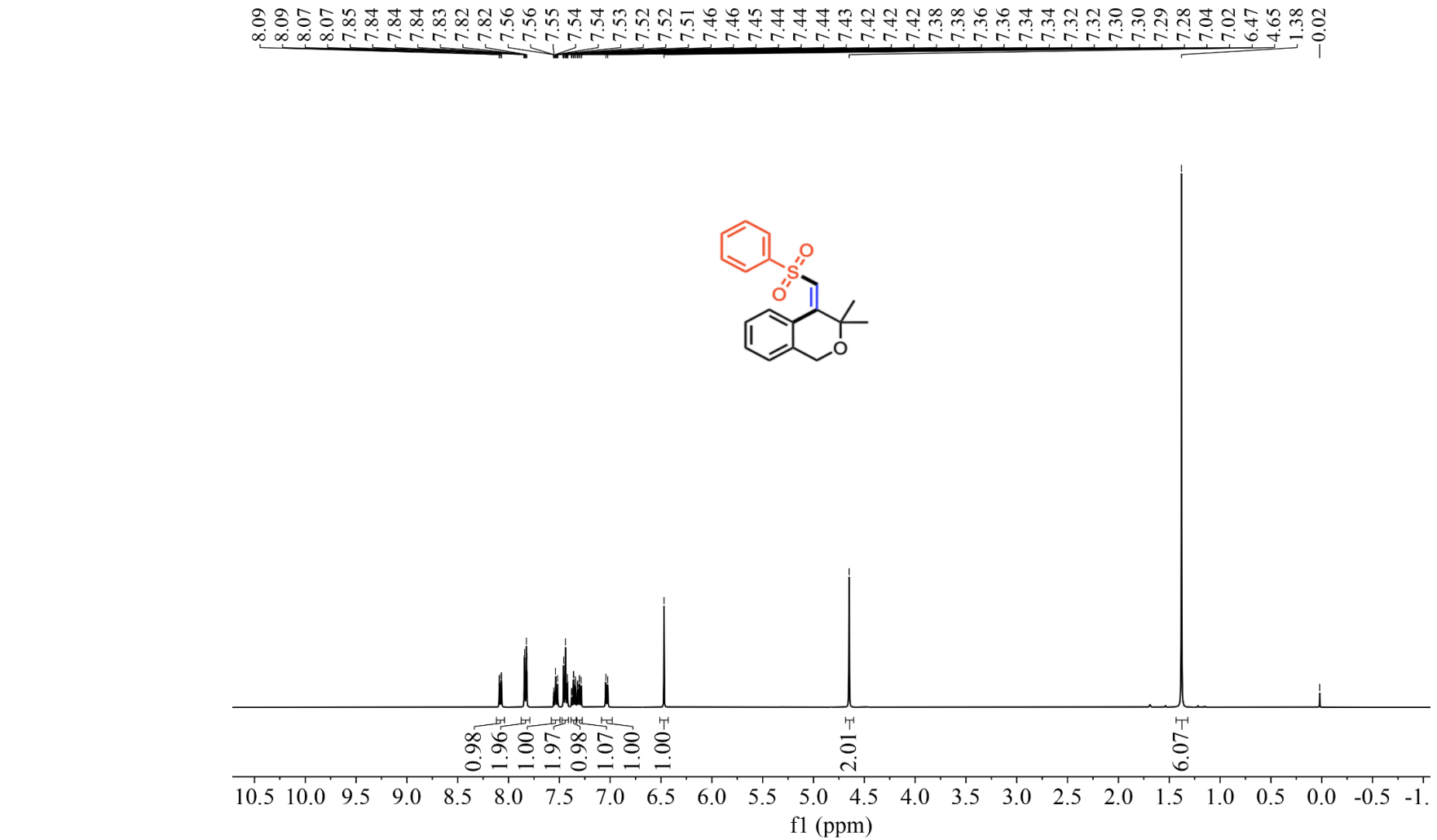
^{13}C spectrum of **4j**



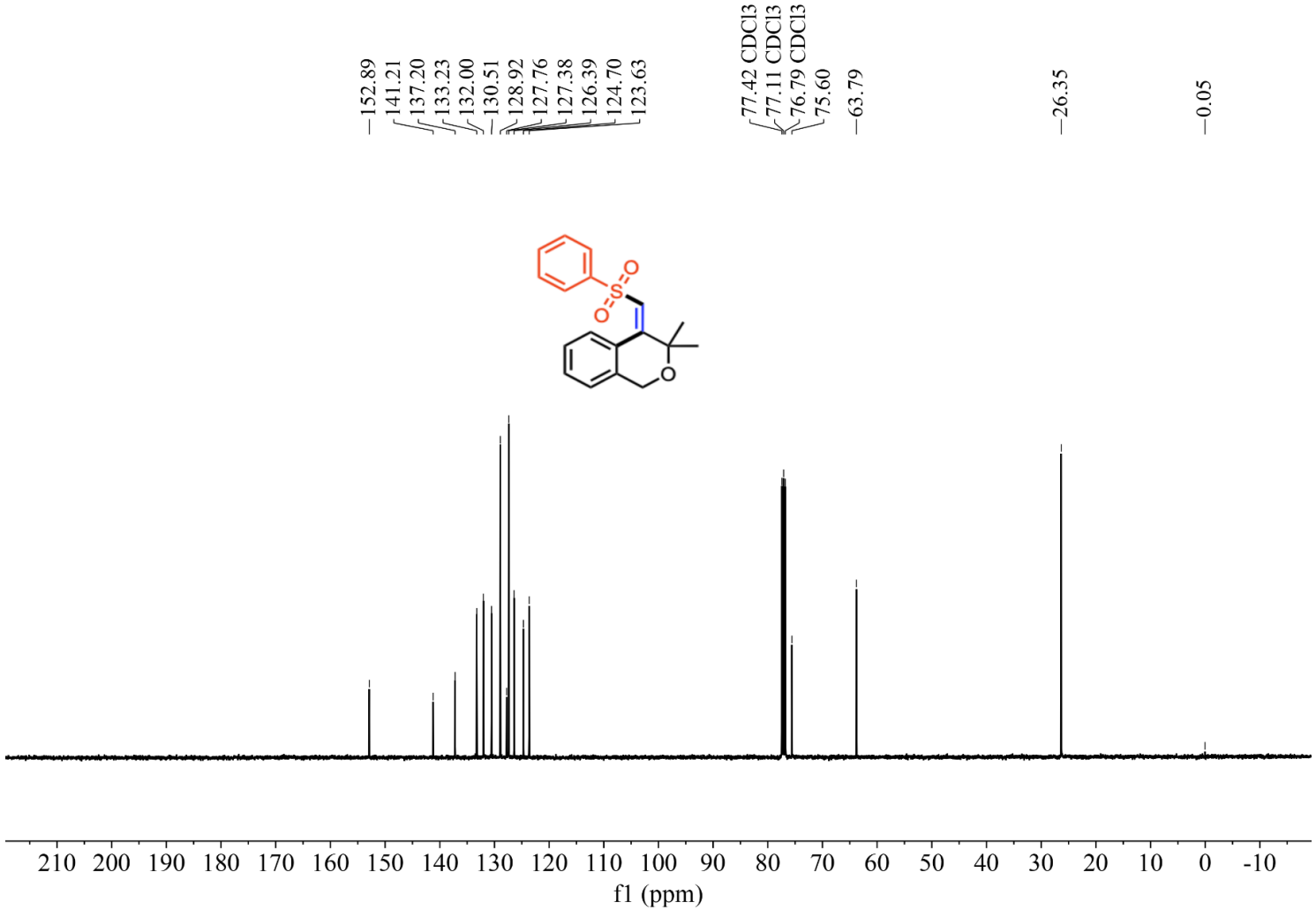
^{1}H spectrum of **5a**



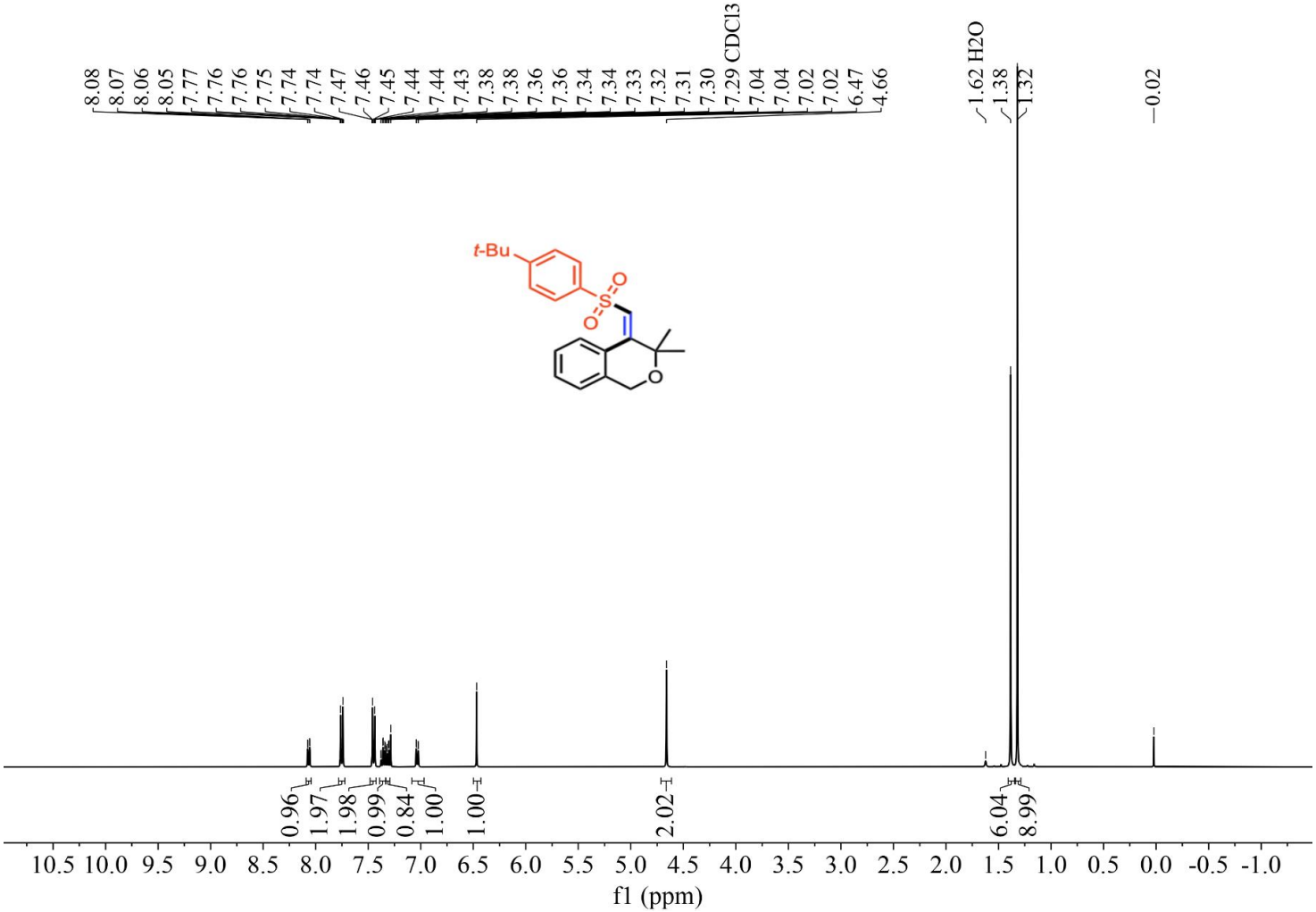
^{13}C spectrum of **5a**



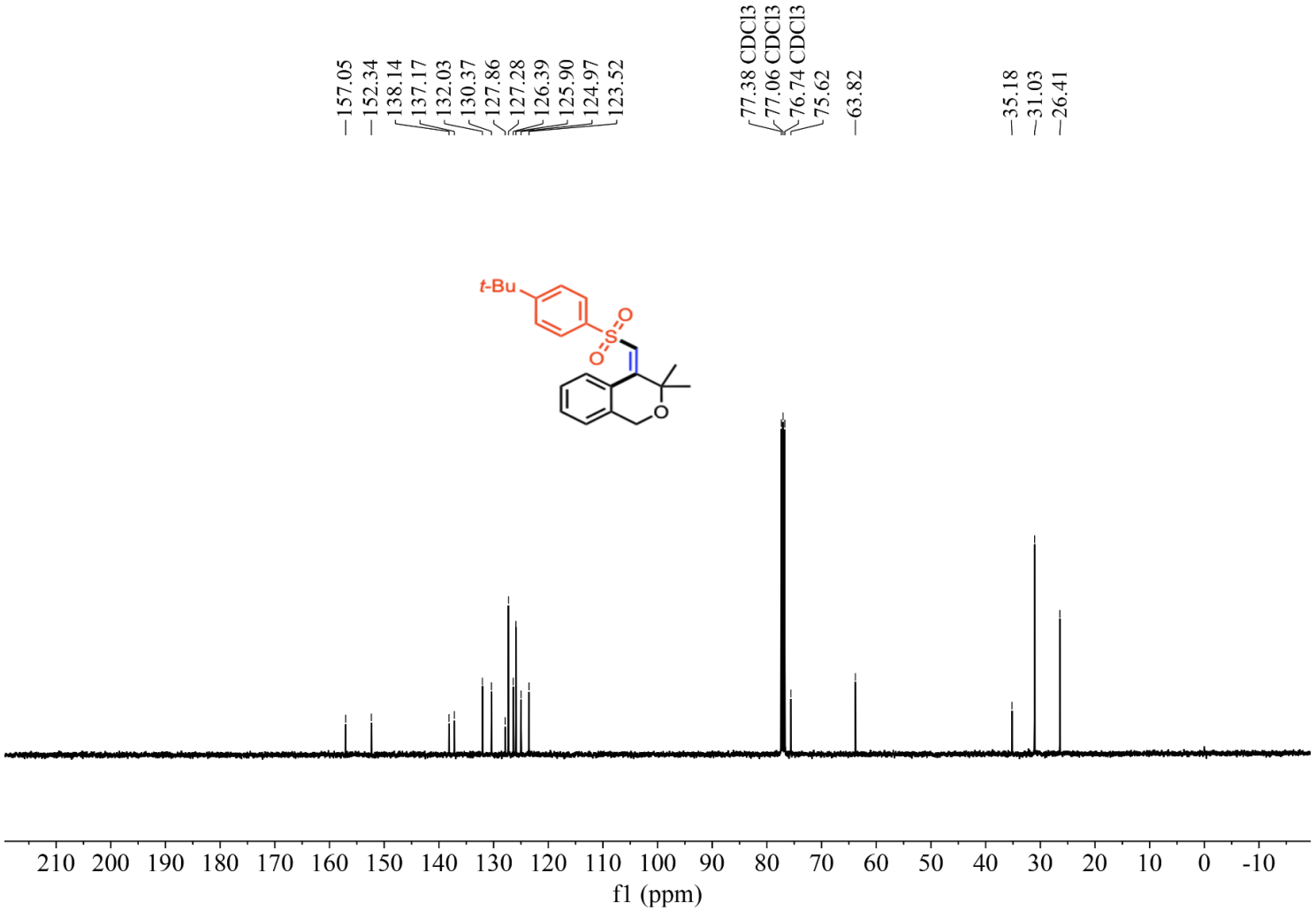
^{1}H spectrum of **5b**



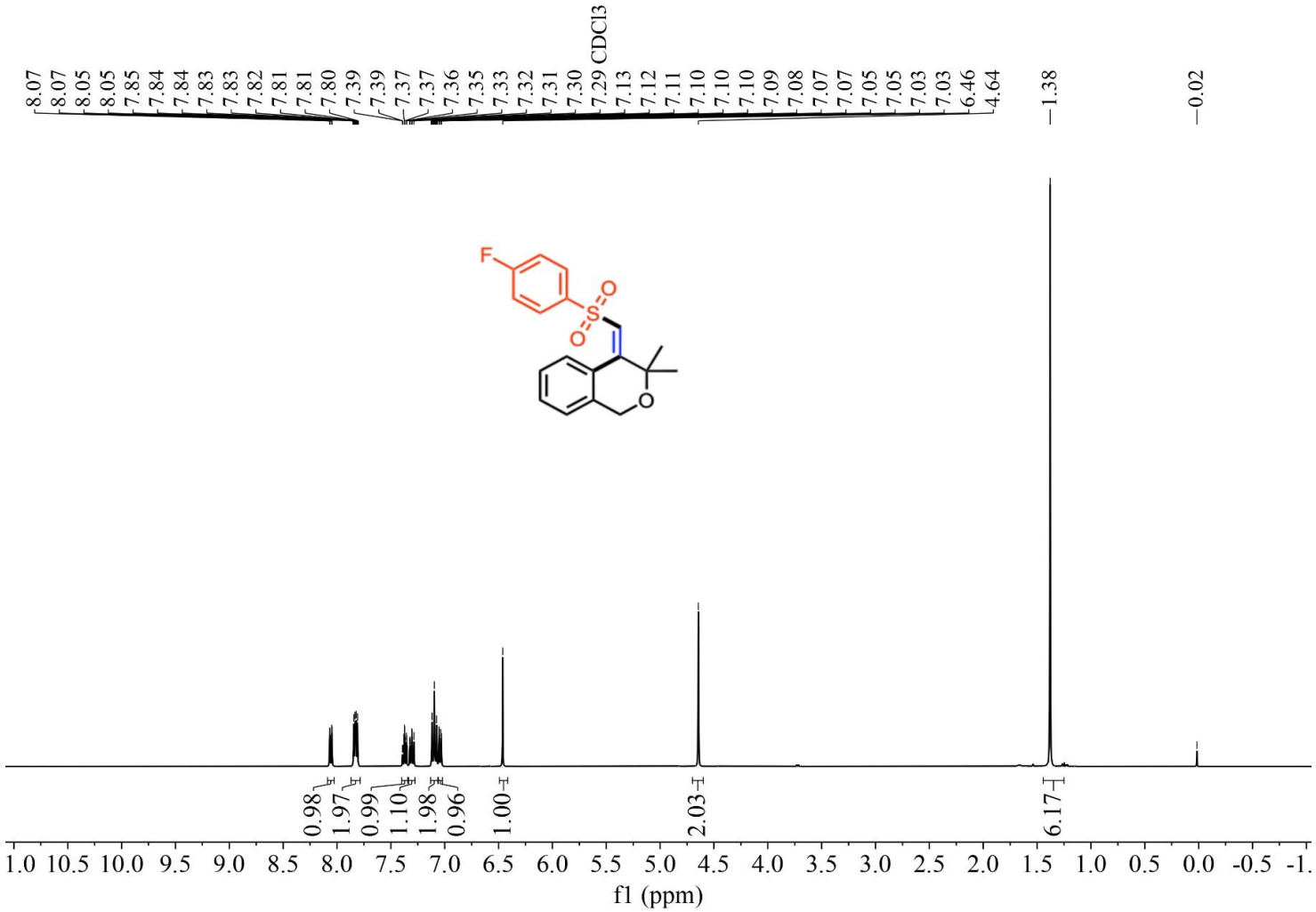
^{13}C spectrum of **5b**



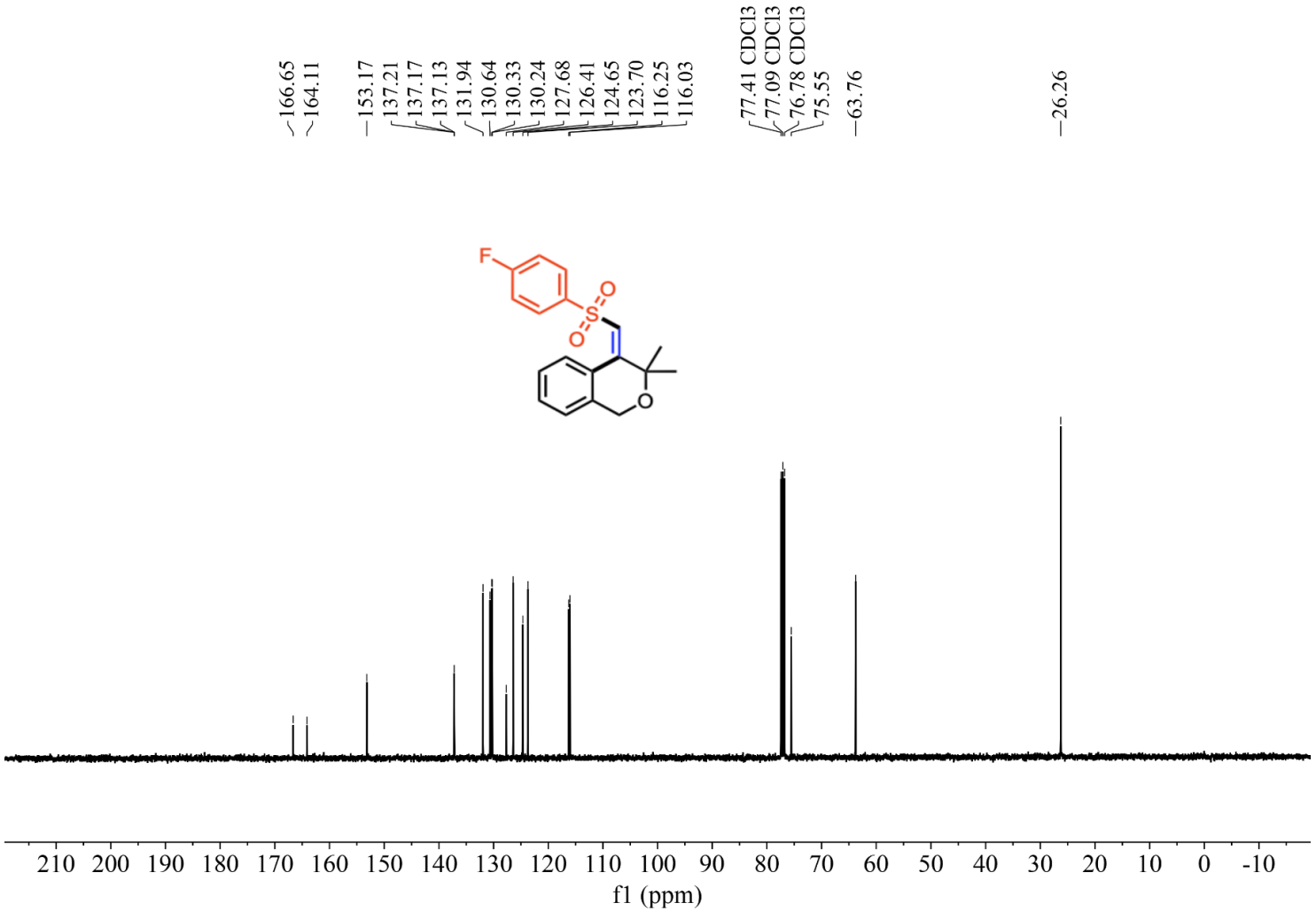
^{1}H spectrum of **5c**



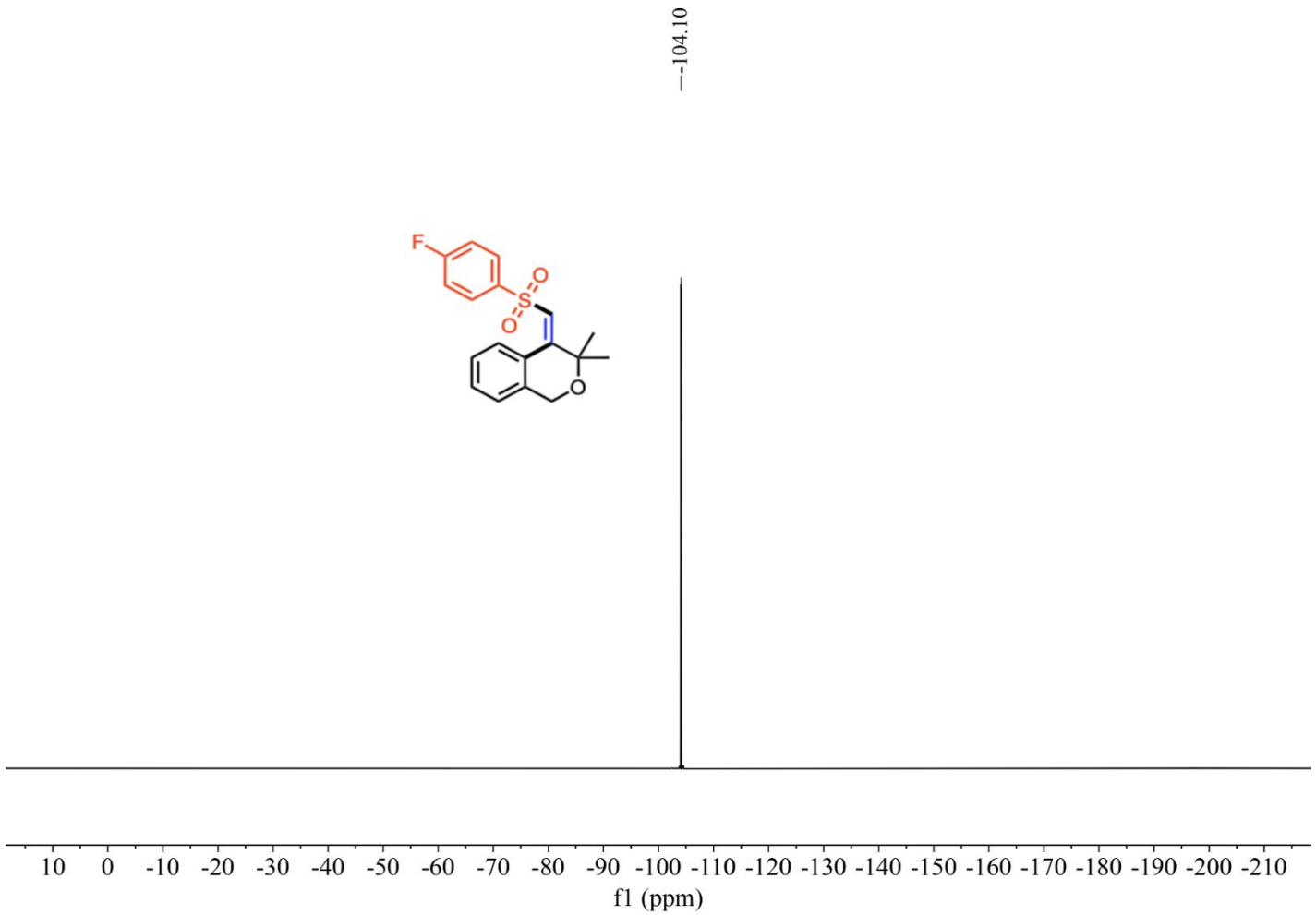
^{13}C spectrum of **5c**



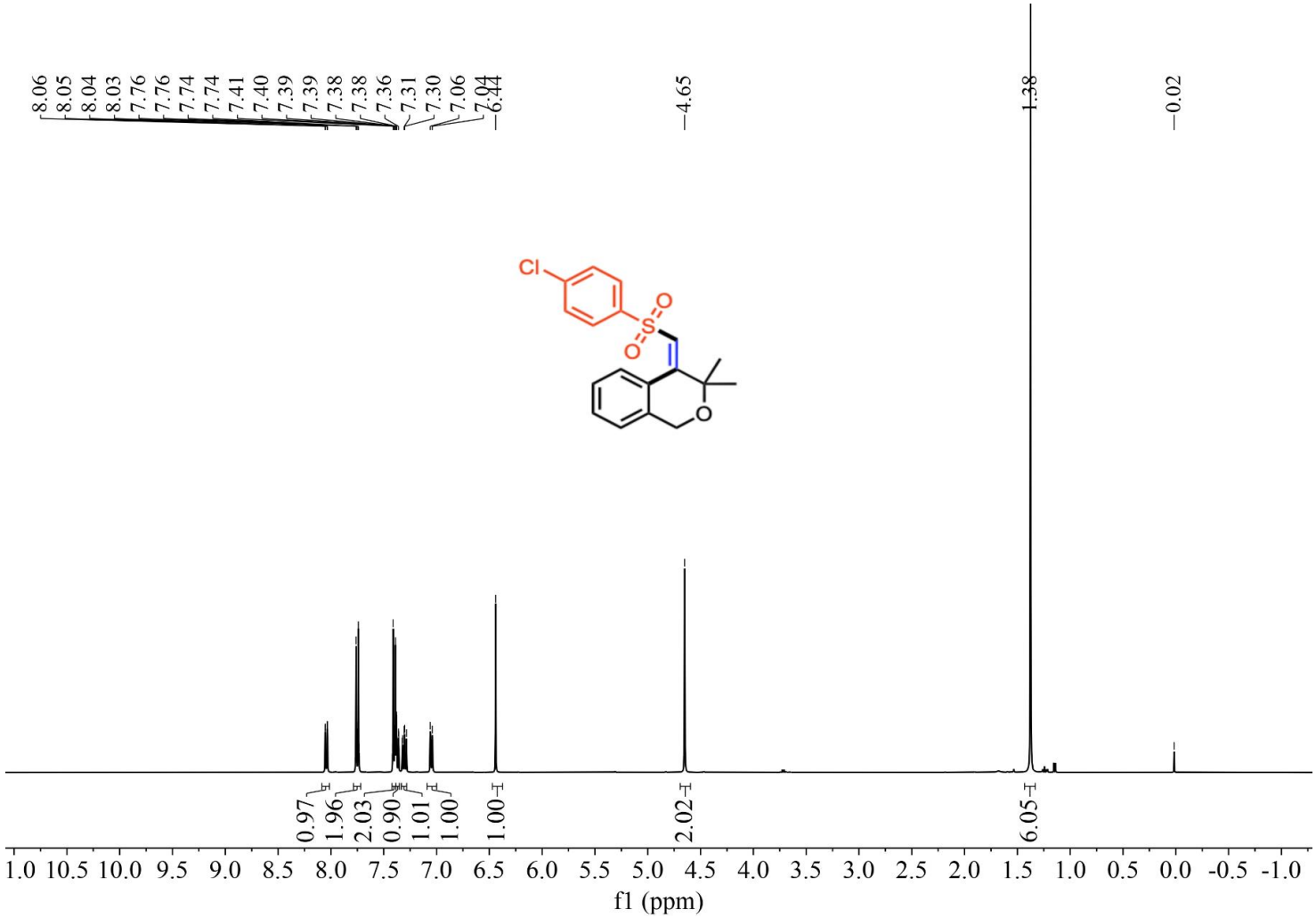
^{1}H spectrum of **5d**



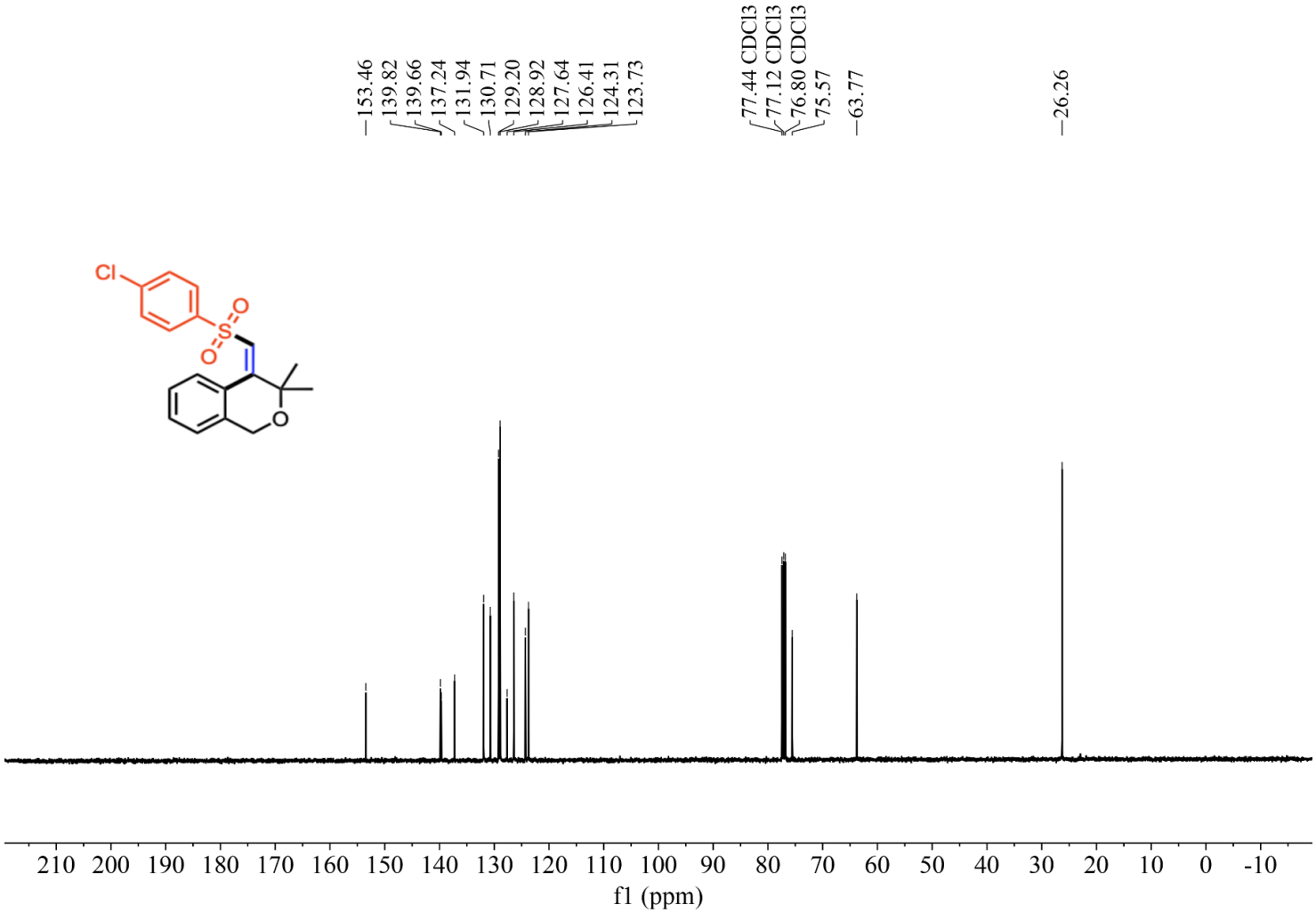
^{13}C spectrum of **5d**



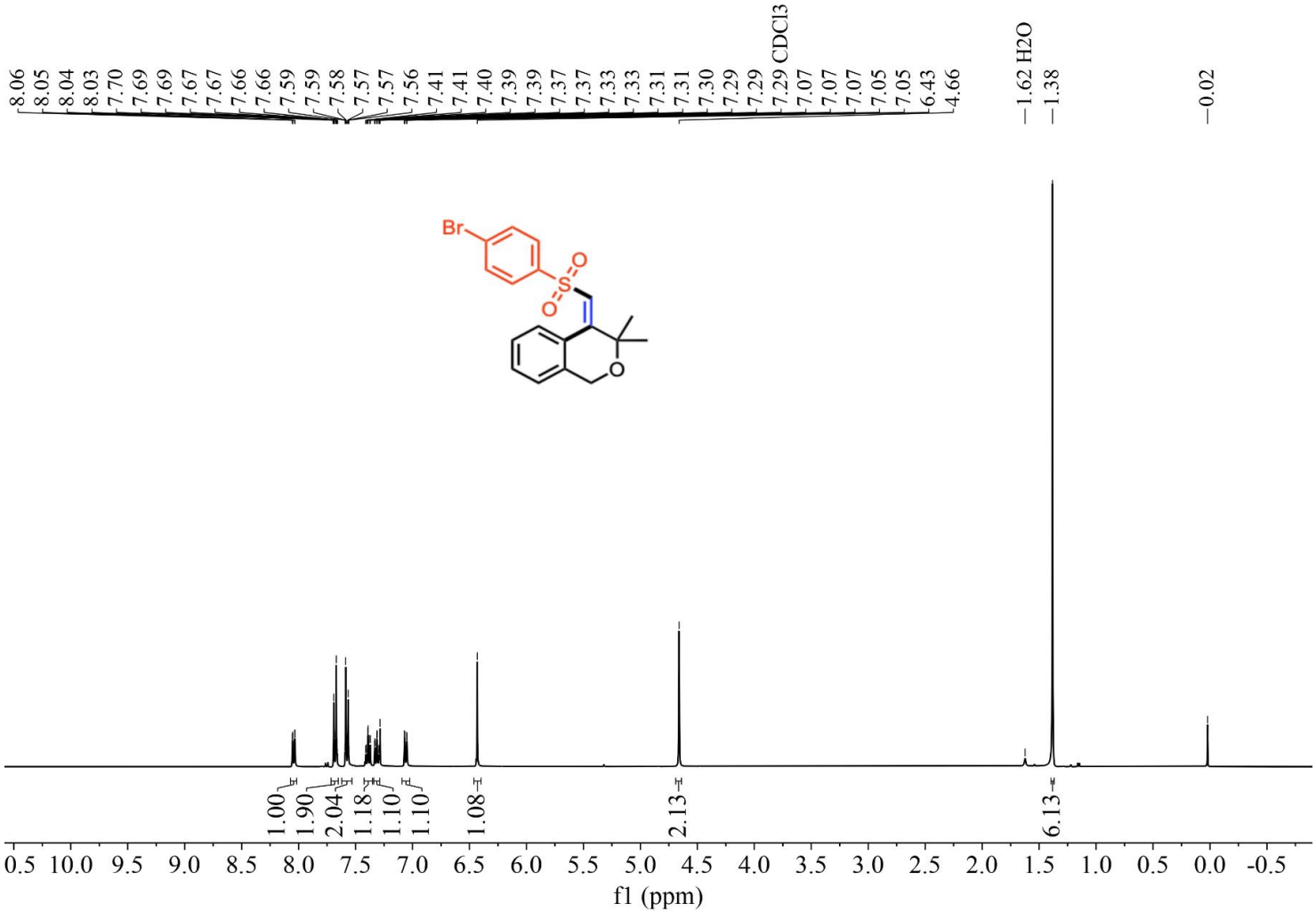
^{19}F spectrum of **5d**



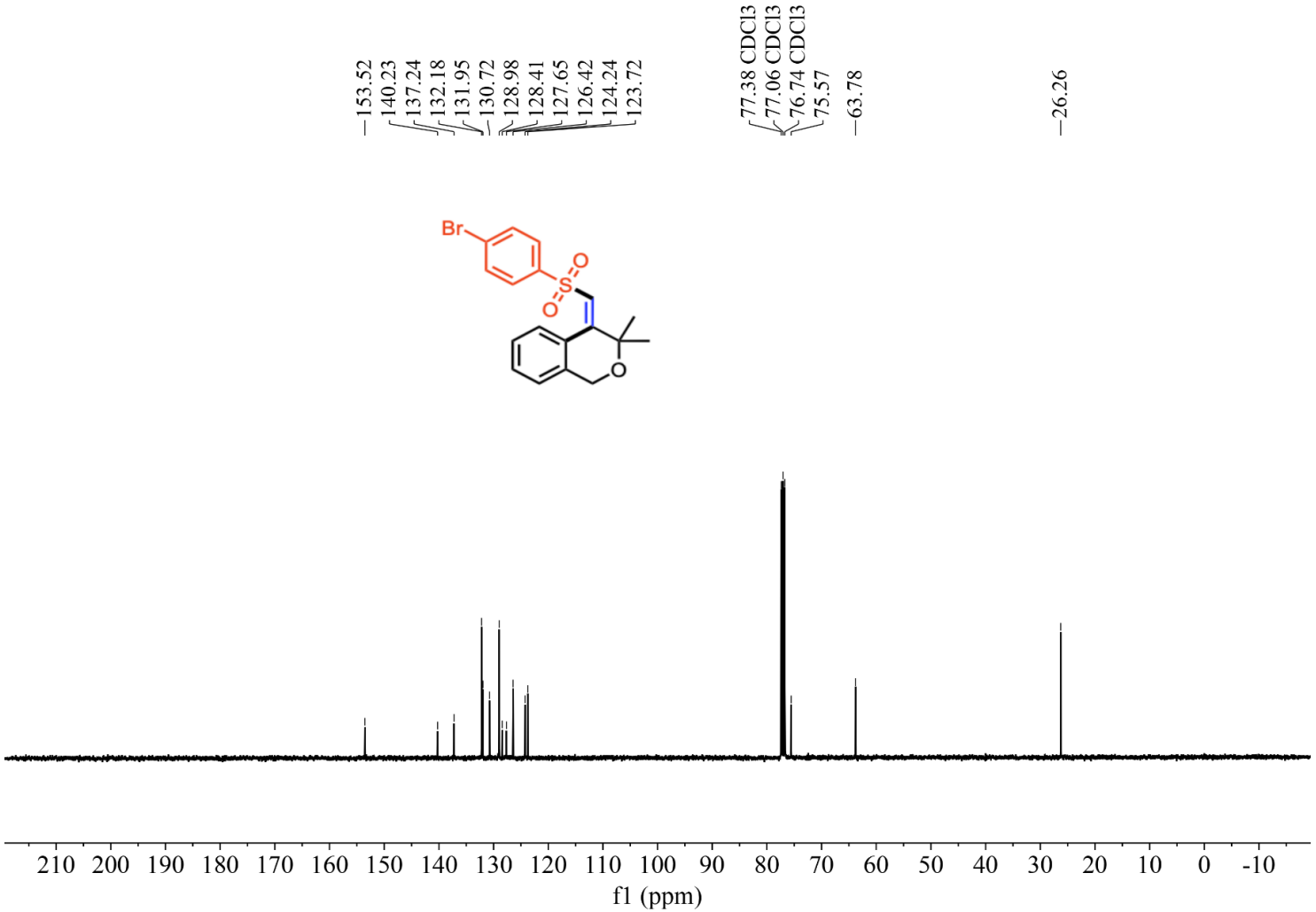
^{1}H spectrum of **5e**



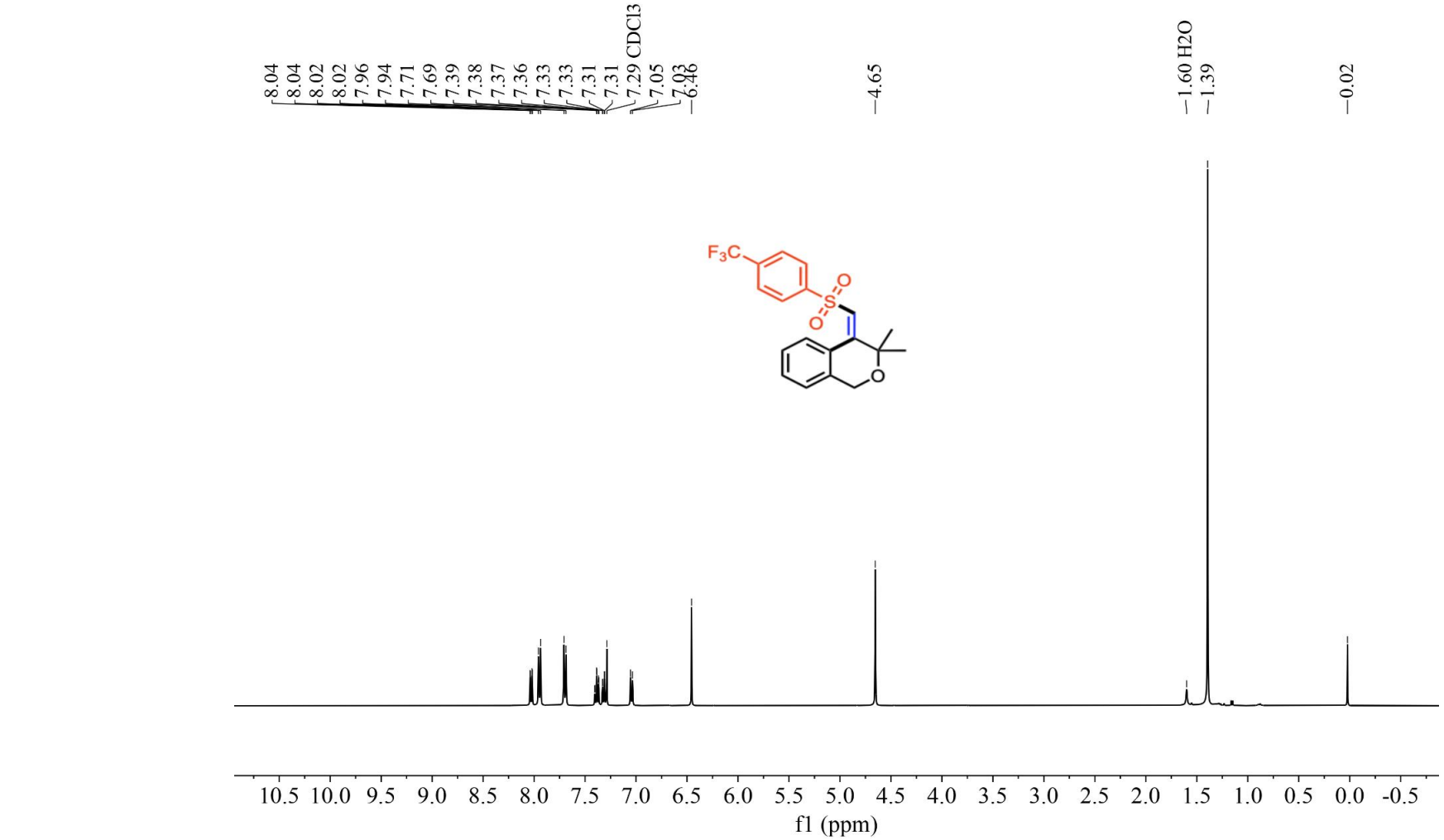
^{13}C spectrum of **5e**



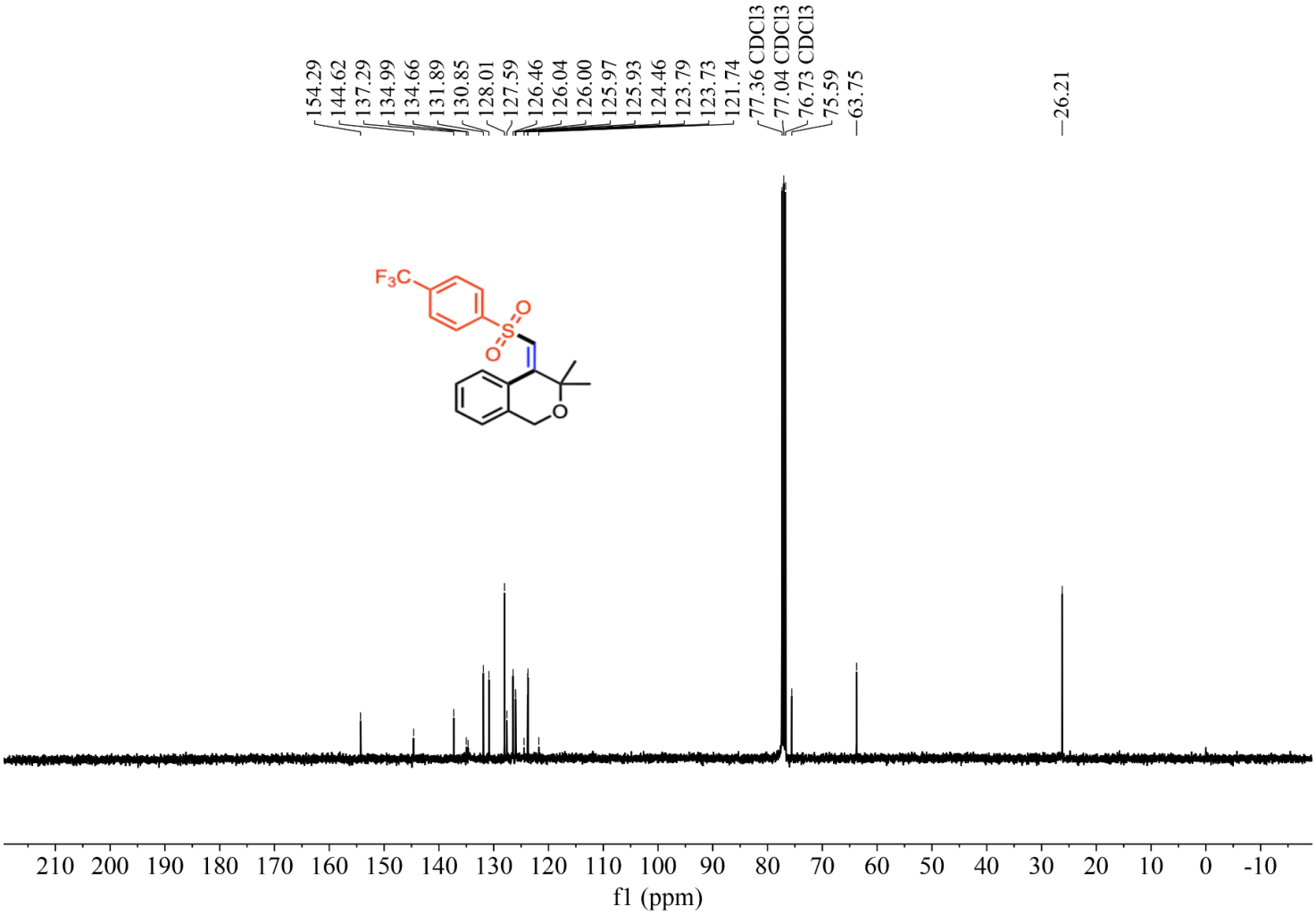
^{1}H spectrum of **5f**



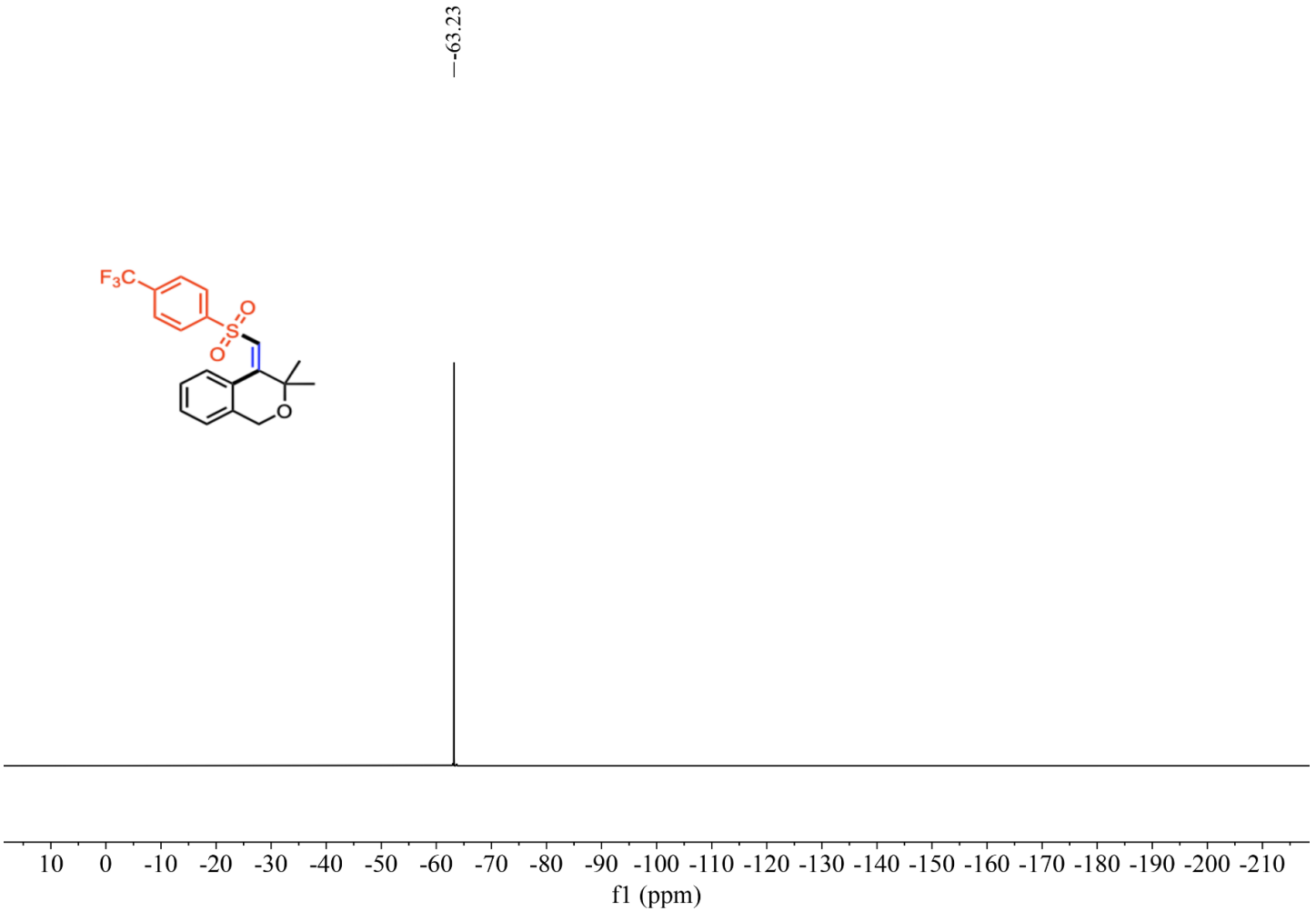
^{13}C spectrum of **5f**



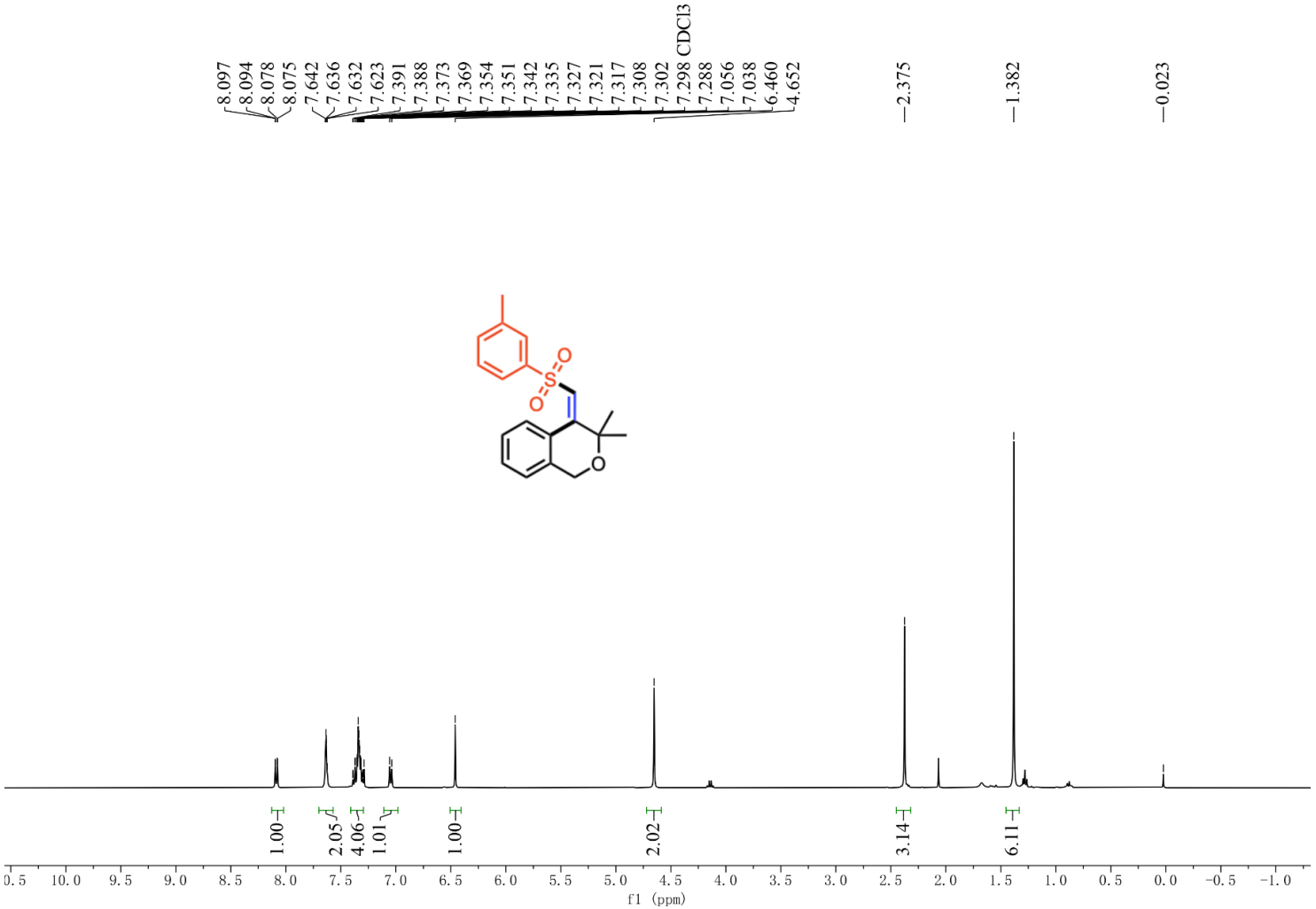
^{1}H spectrum of **5g**



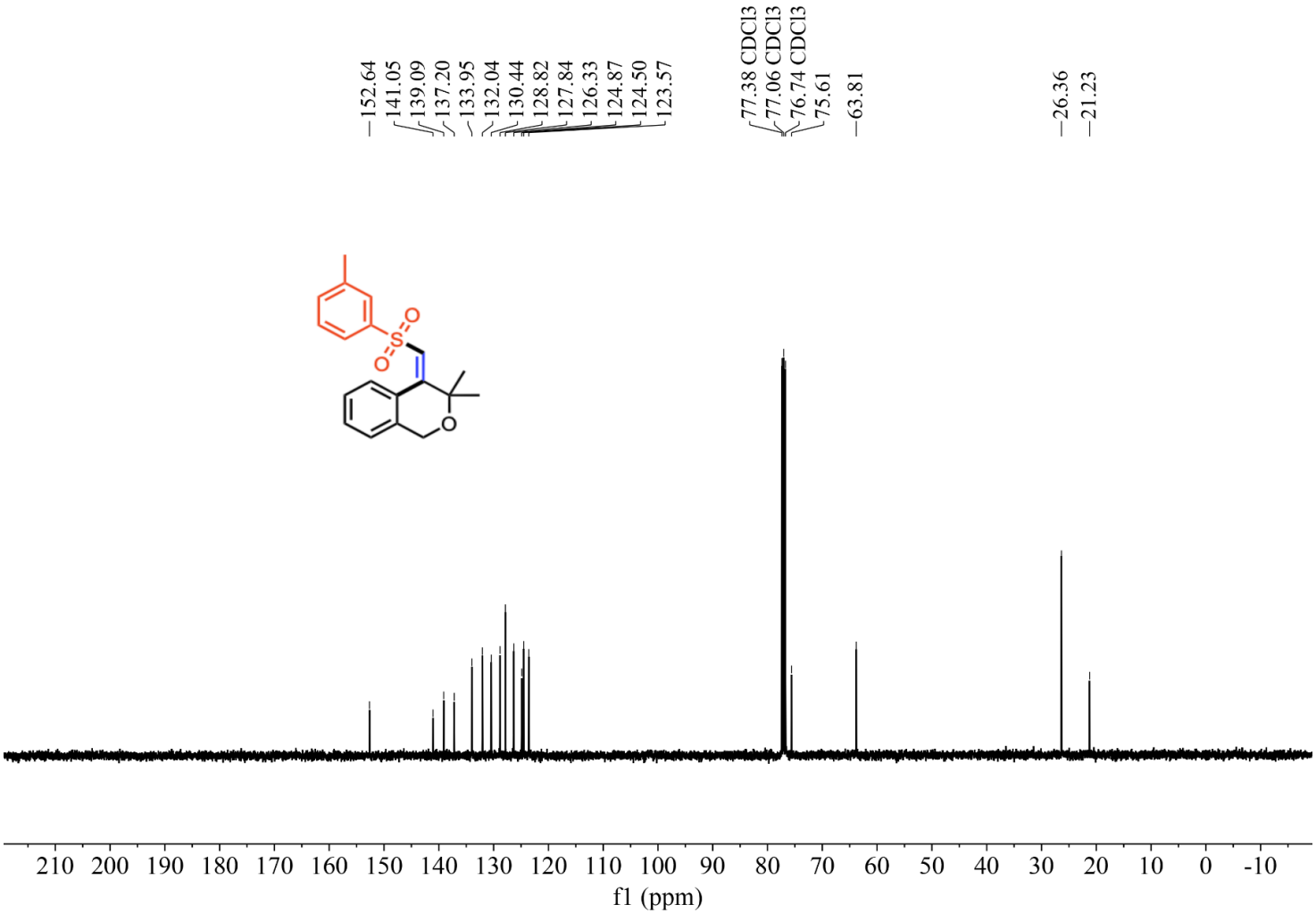
^{13}C spectrum of **5g**



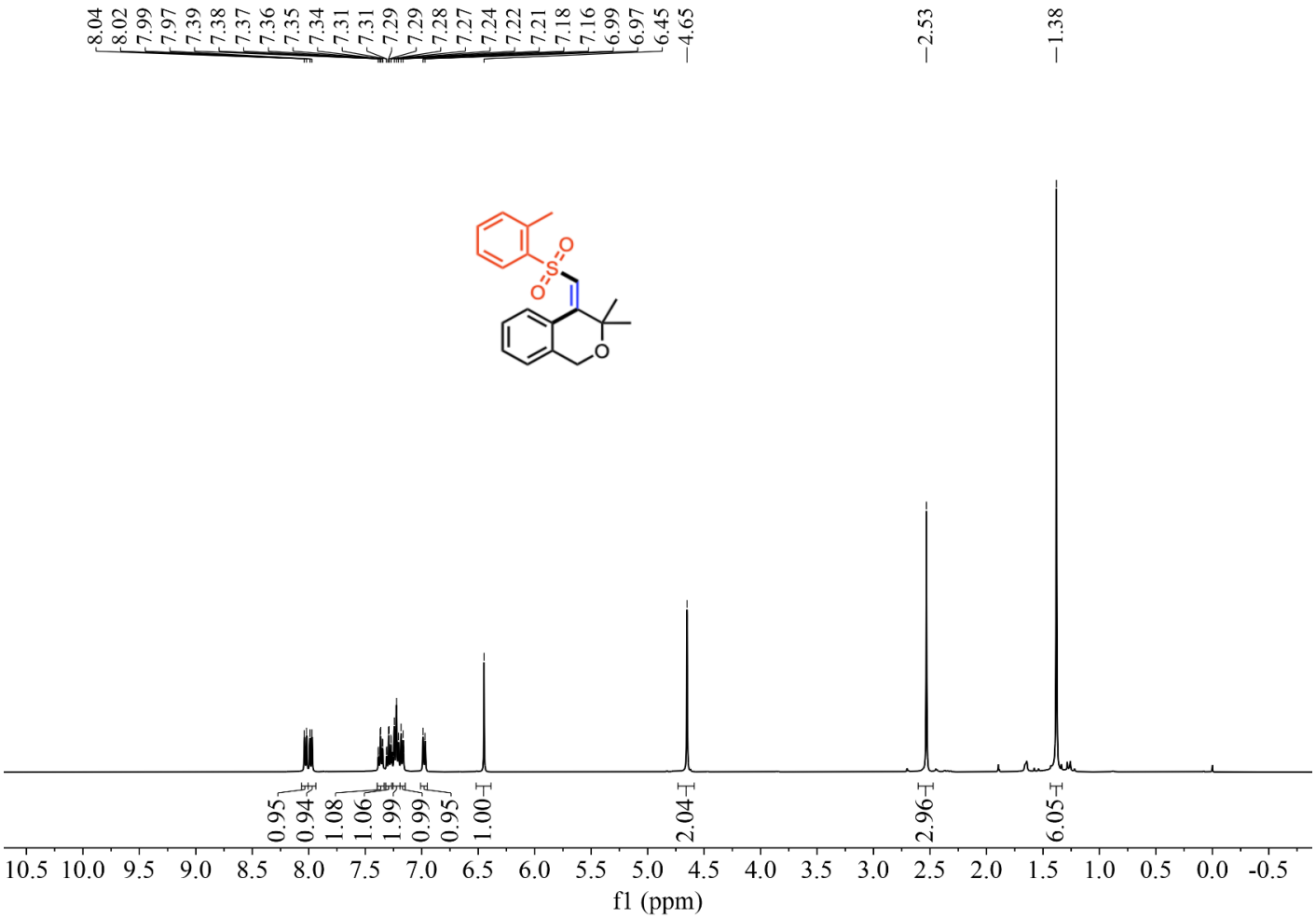
^{19}F spectrum of **5g**



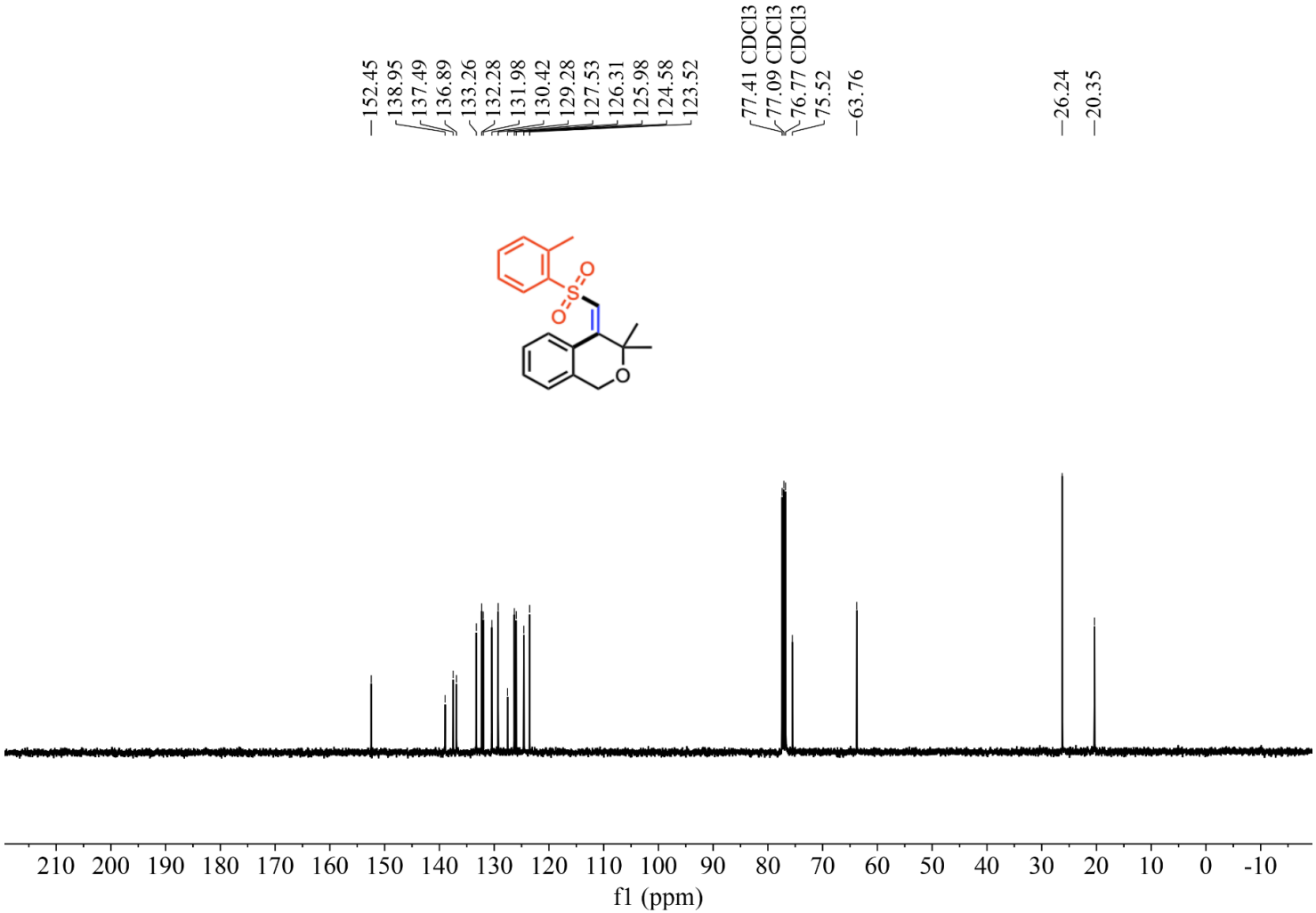
^{1}H spectrum of **5h**



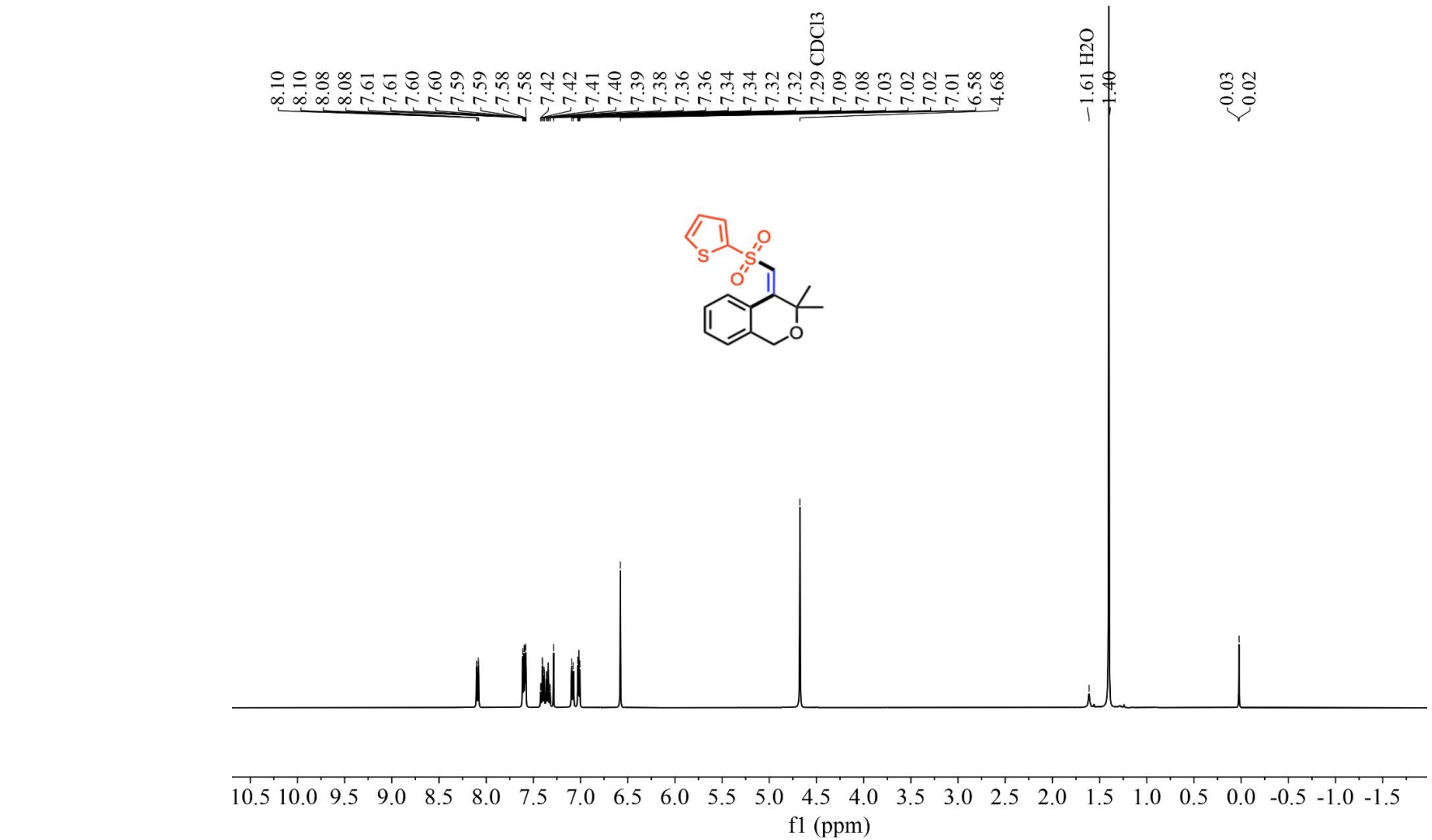
^{13}C spectrum of **5h**



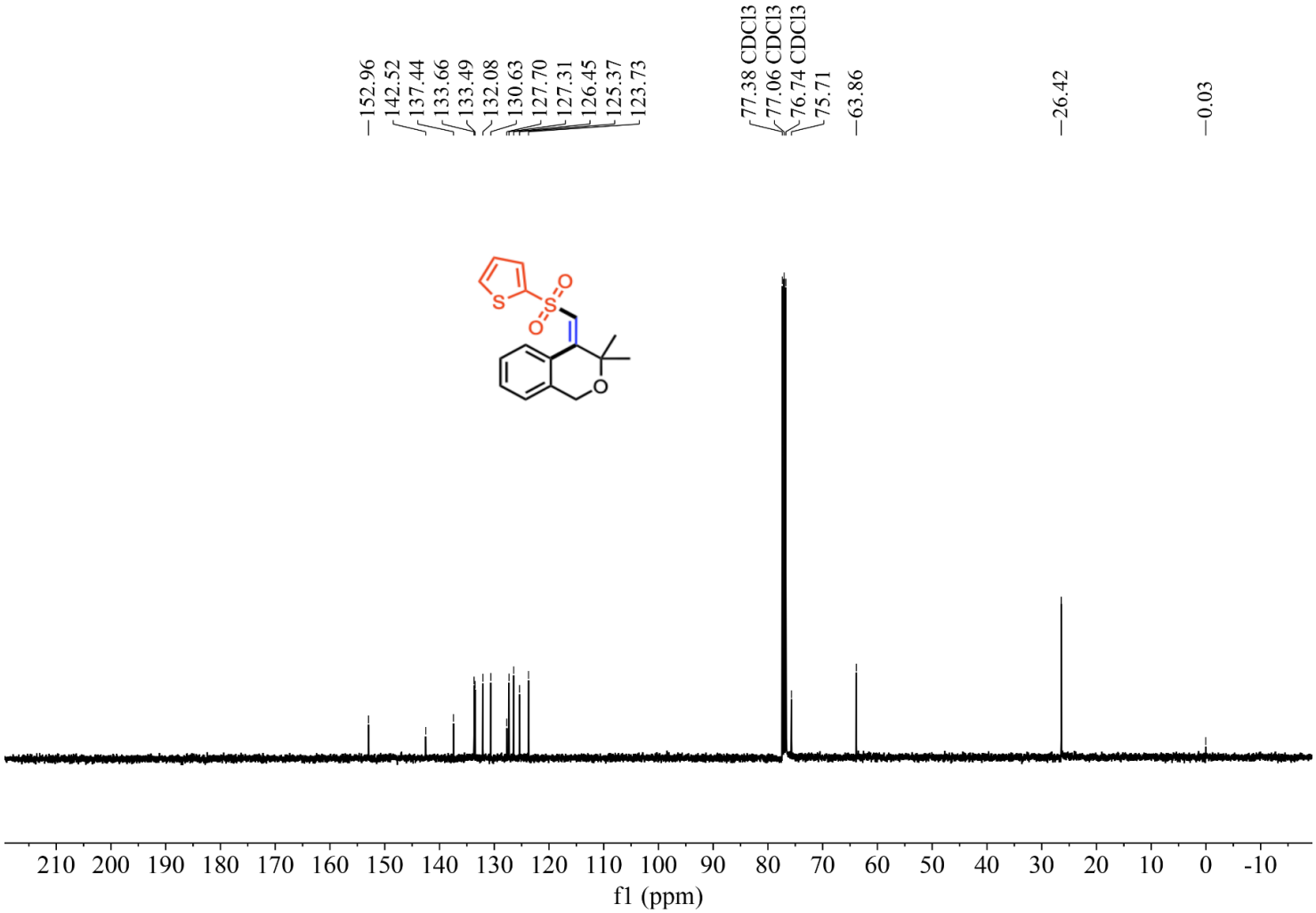
^{1}H spectrum of **5i**



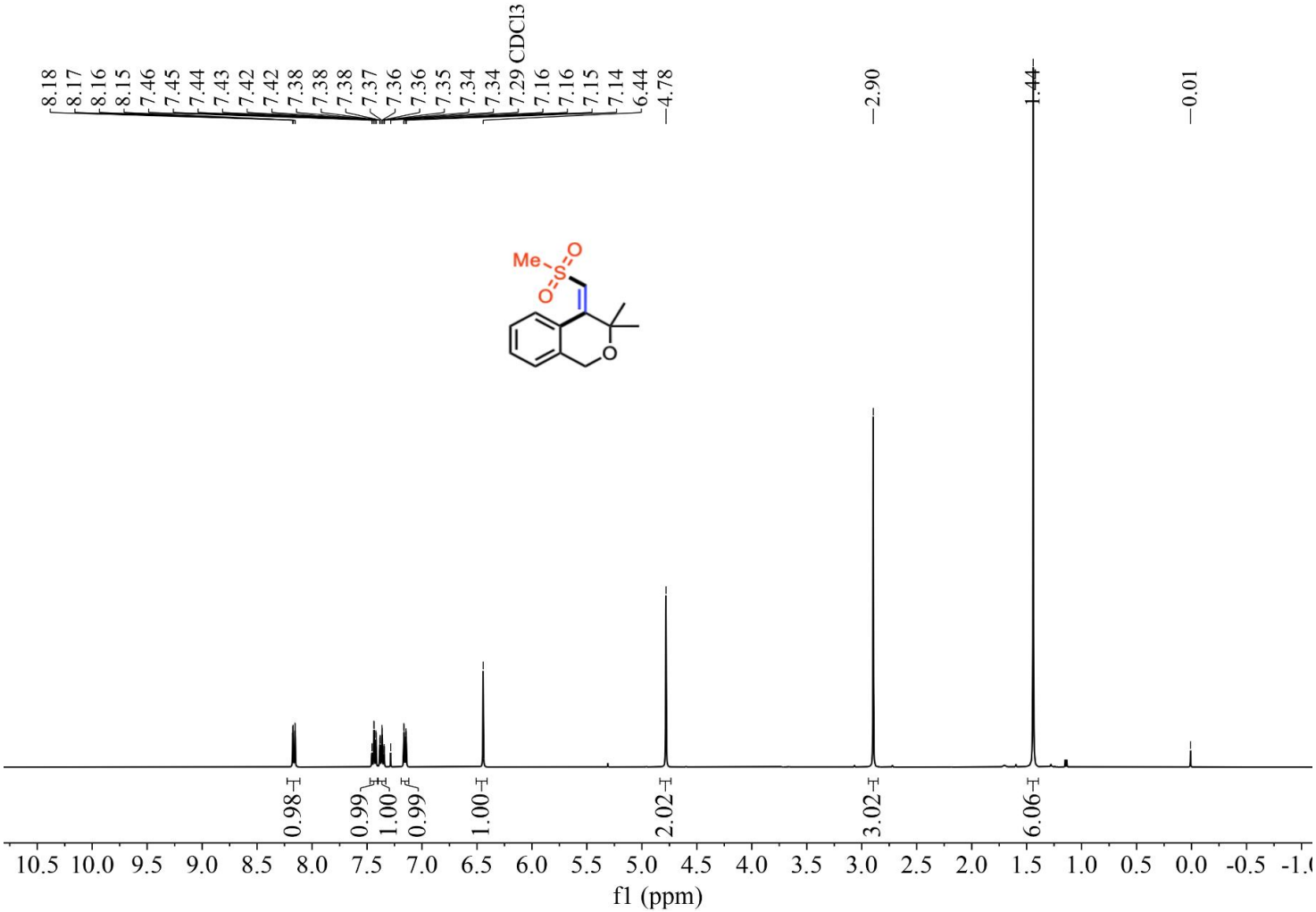
^{13}C spectrum of **5i**



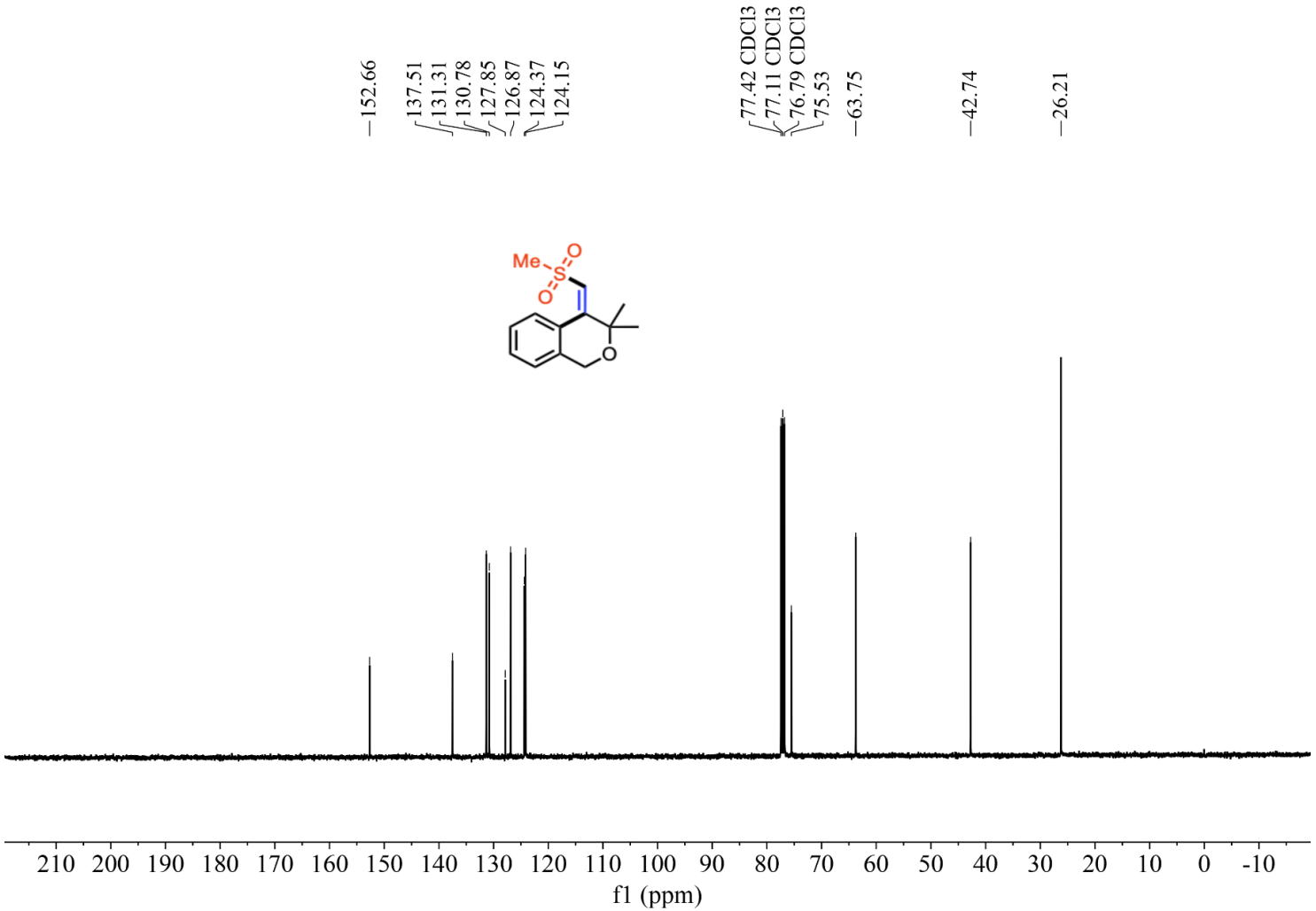
^{1}H spectrum of **5j**



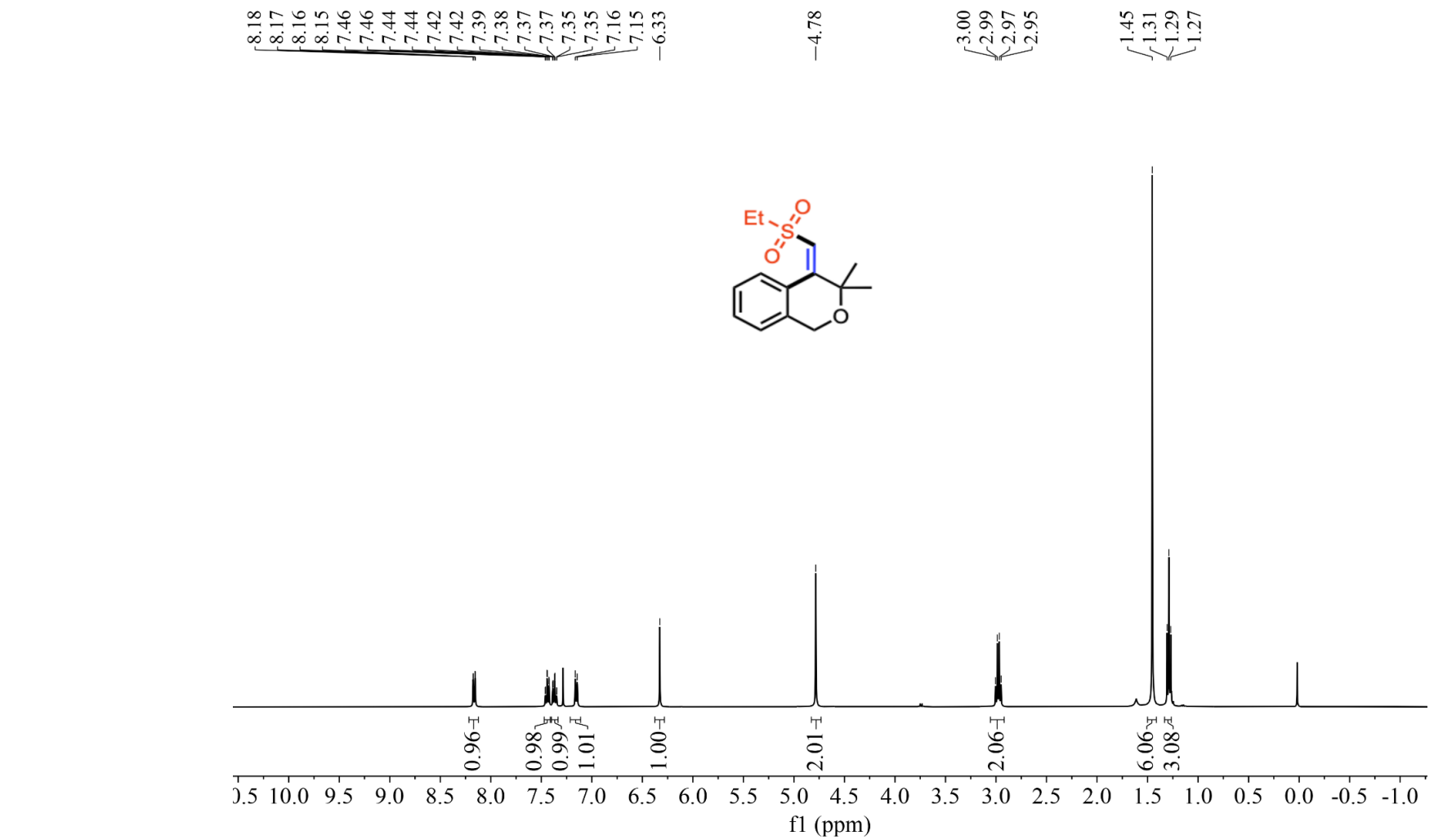
^{13}C spectrum of **5j**



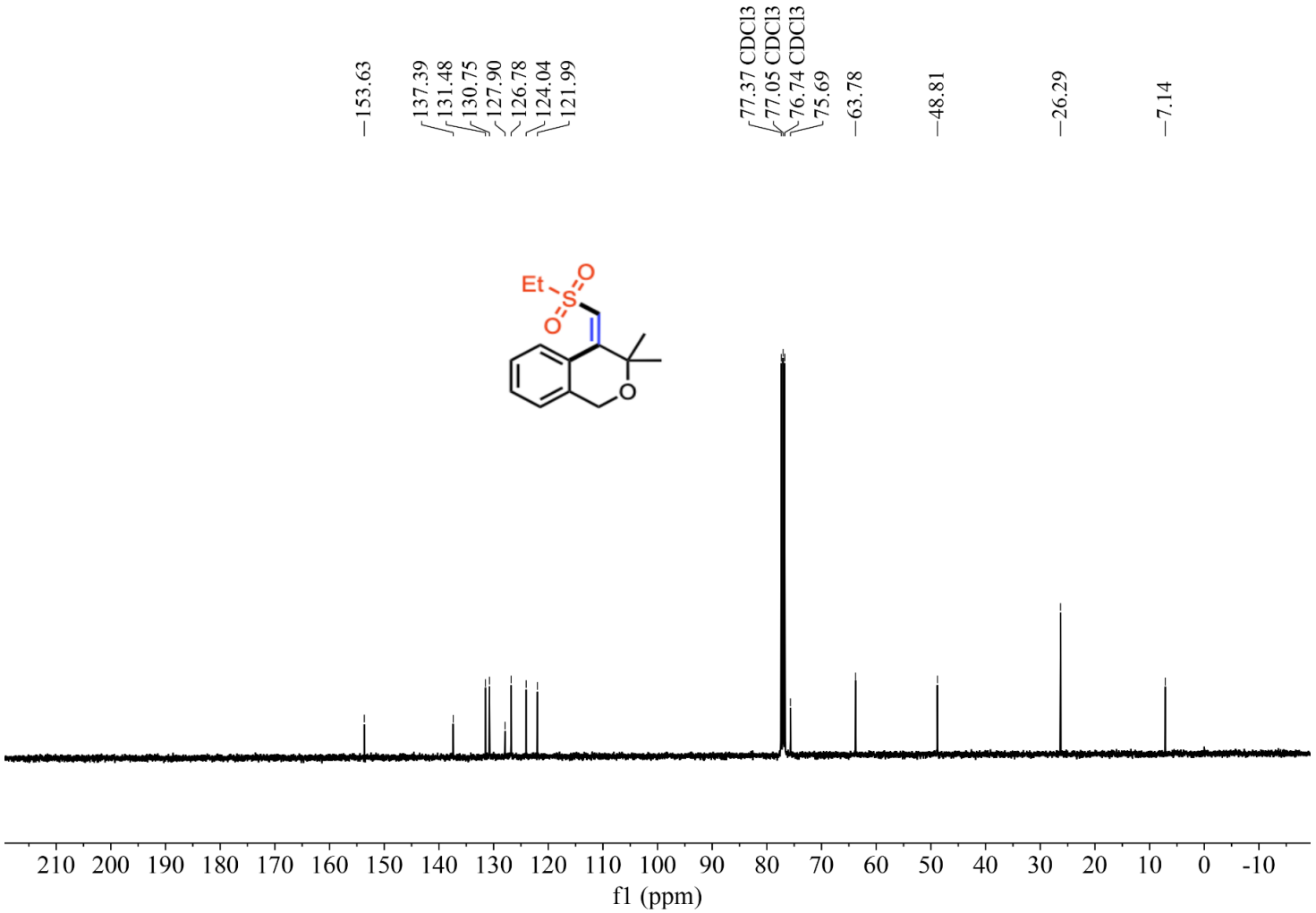
^{1}H spectrum of **5k**



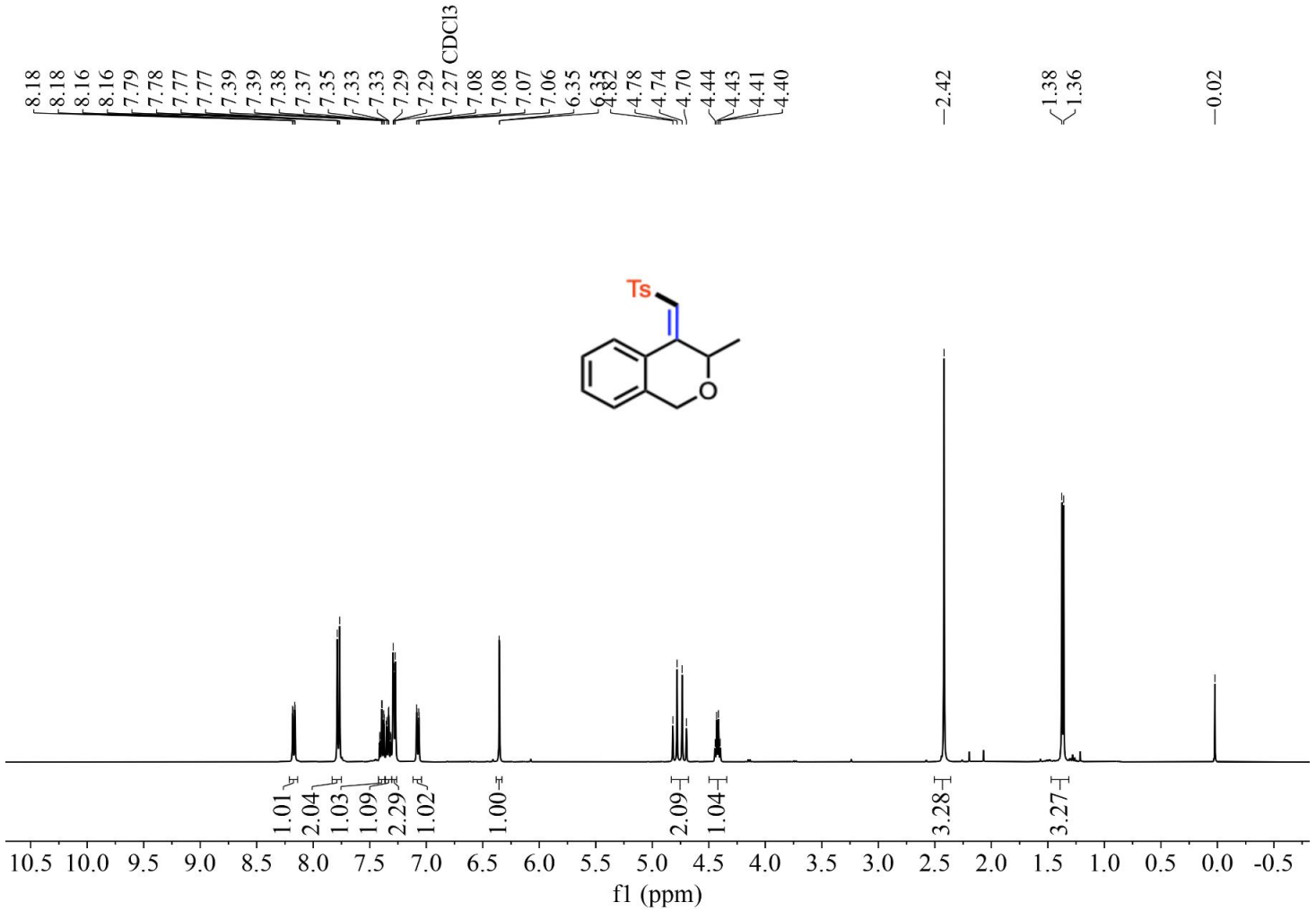
^{13}C spectrum of **5k**



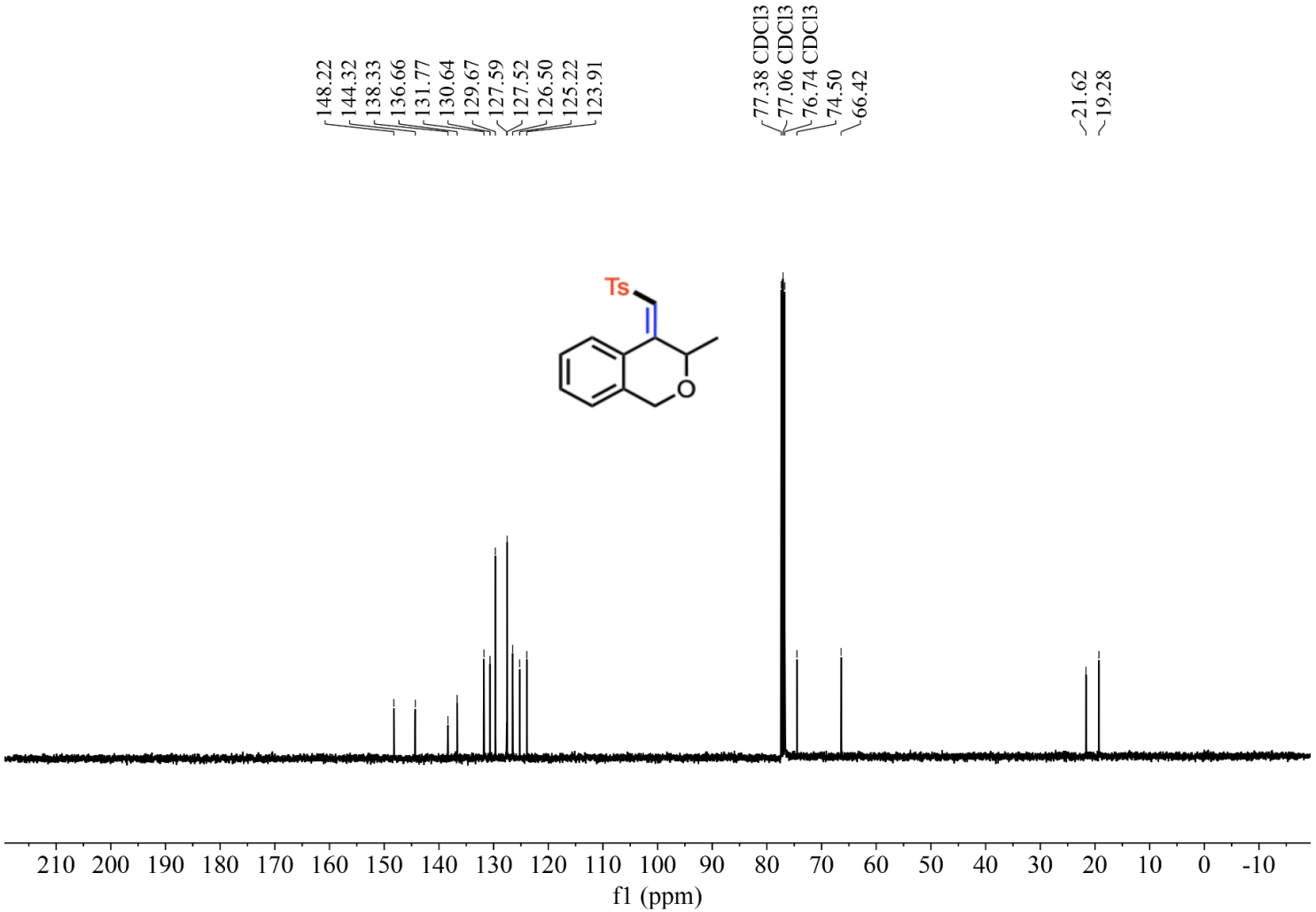
^{1}H spectrum of **5l**



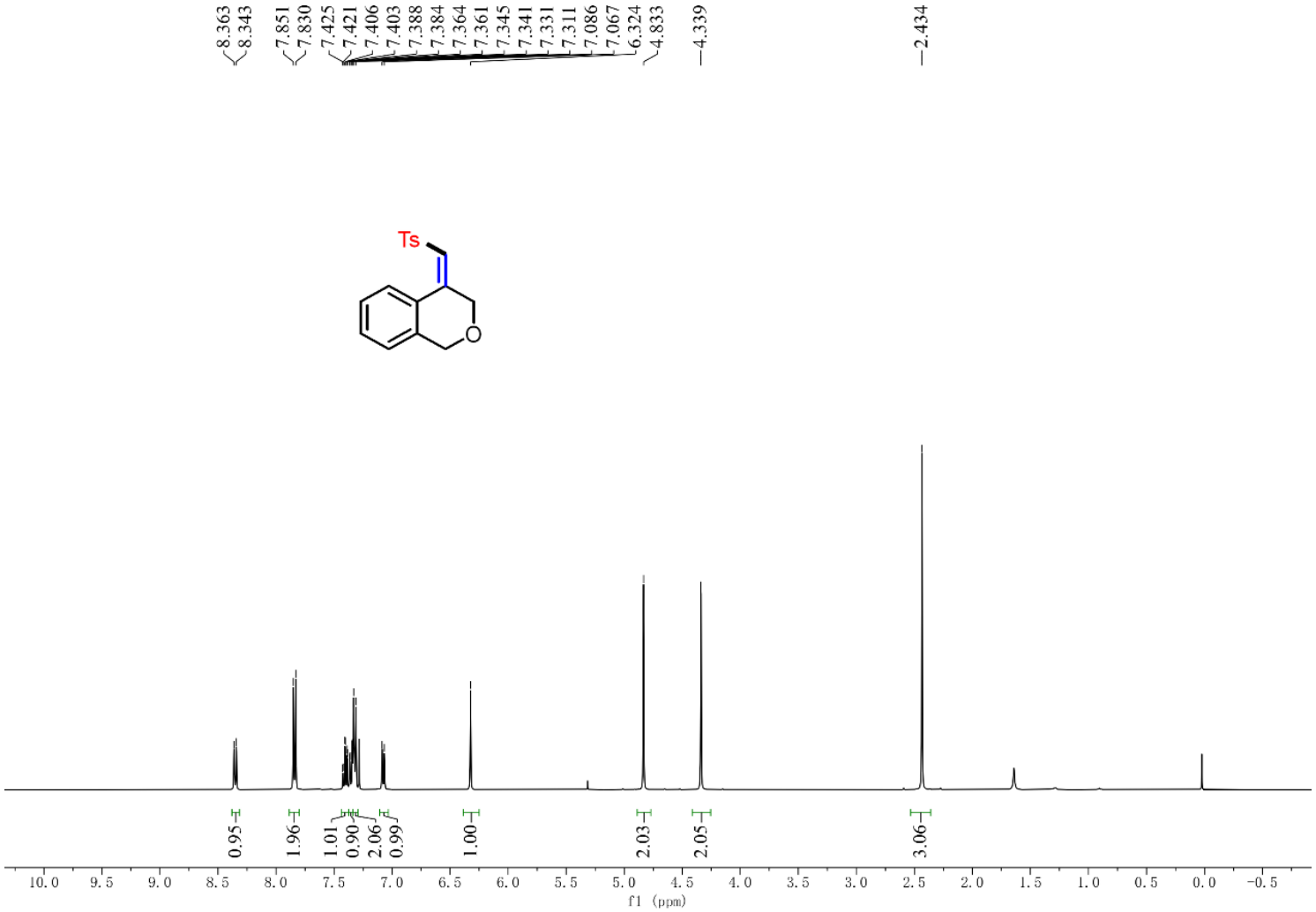
^{13}C spectrum of **5l**



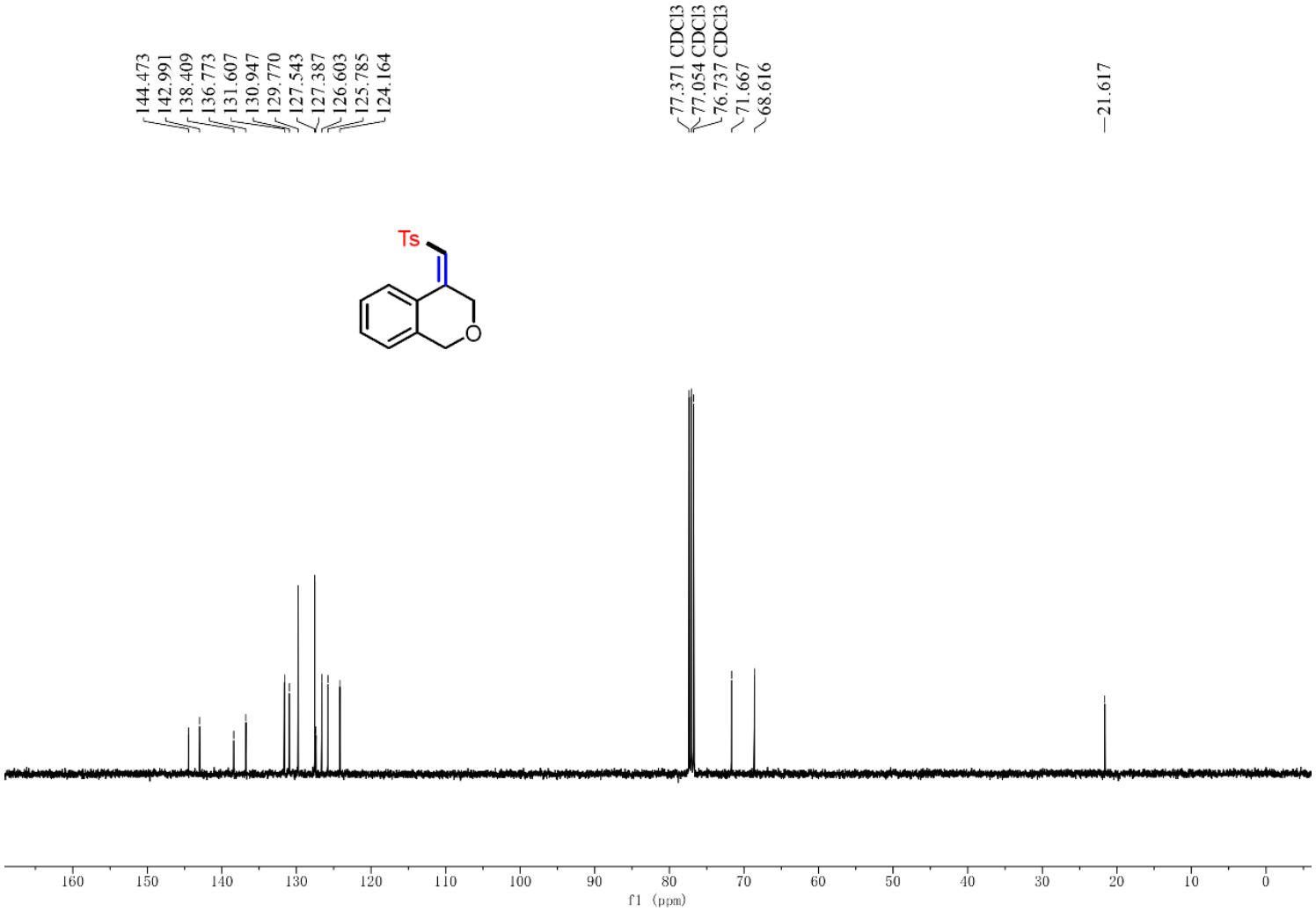
^{1}H spectrum of **5m**



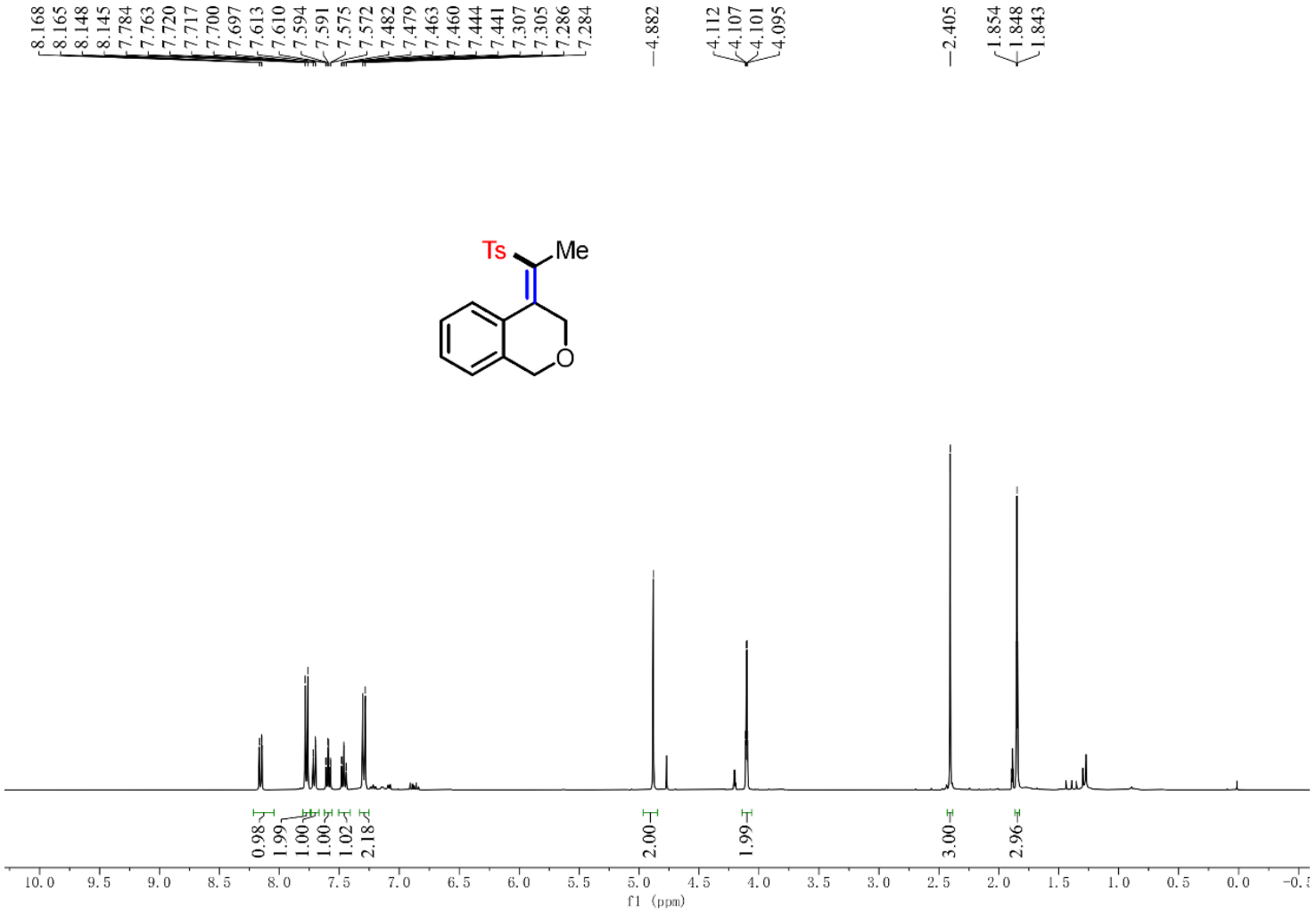
^{13}C spectrum of **5m**



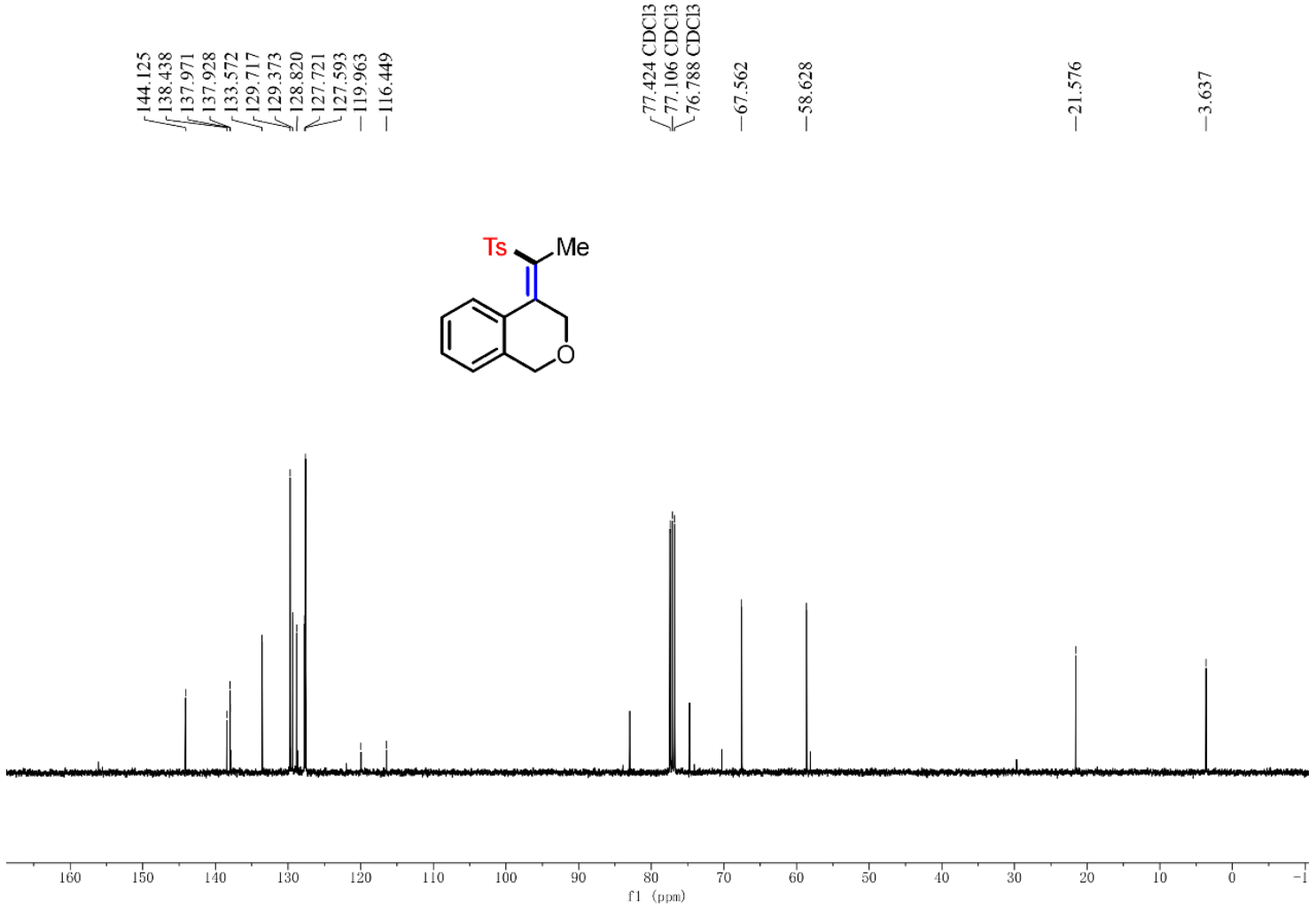
^{1}H spectrum of **5n**



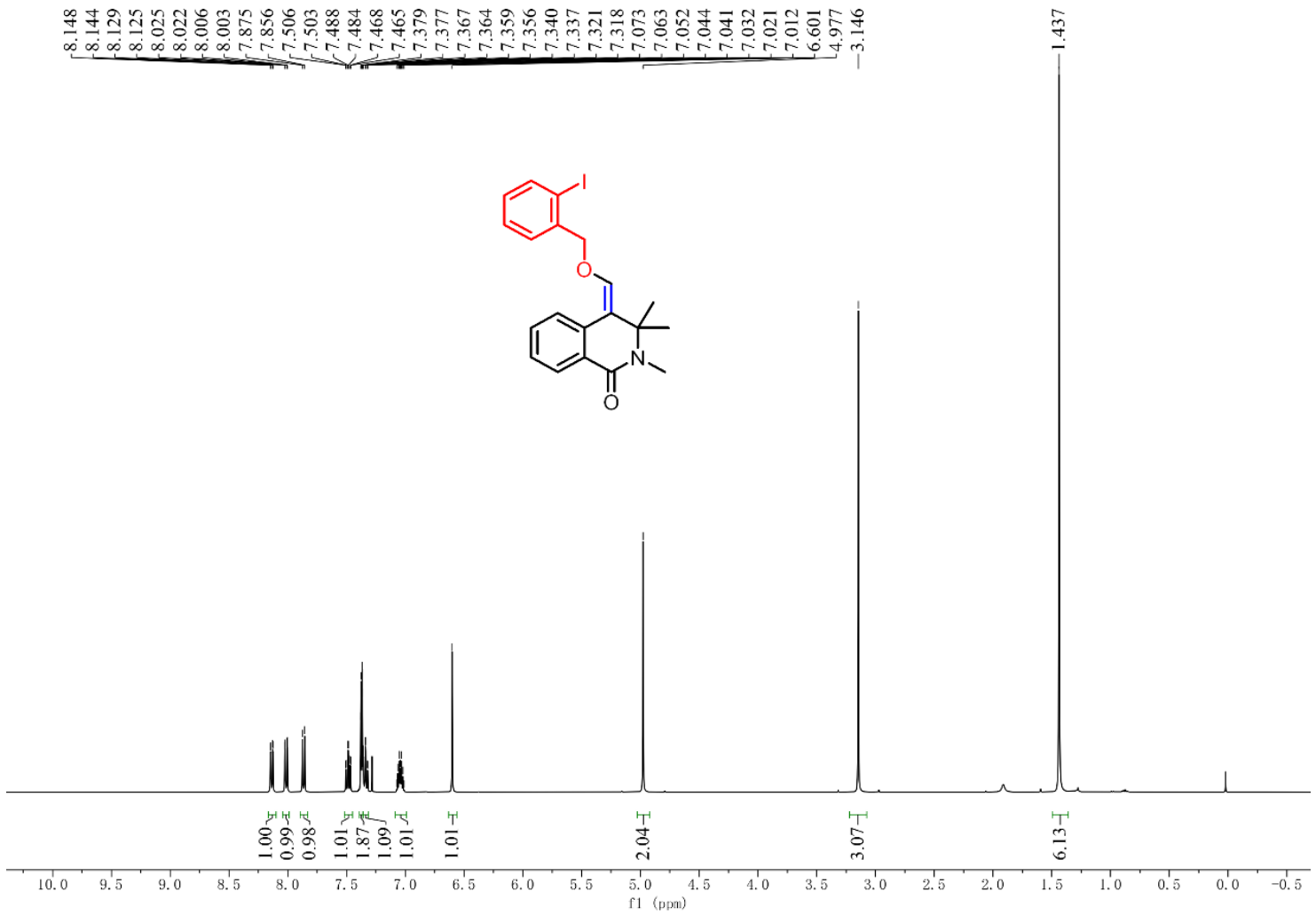
^{13}C spectrum of **5n**



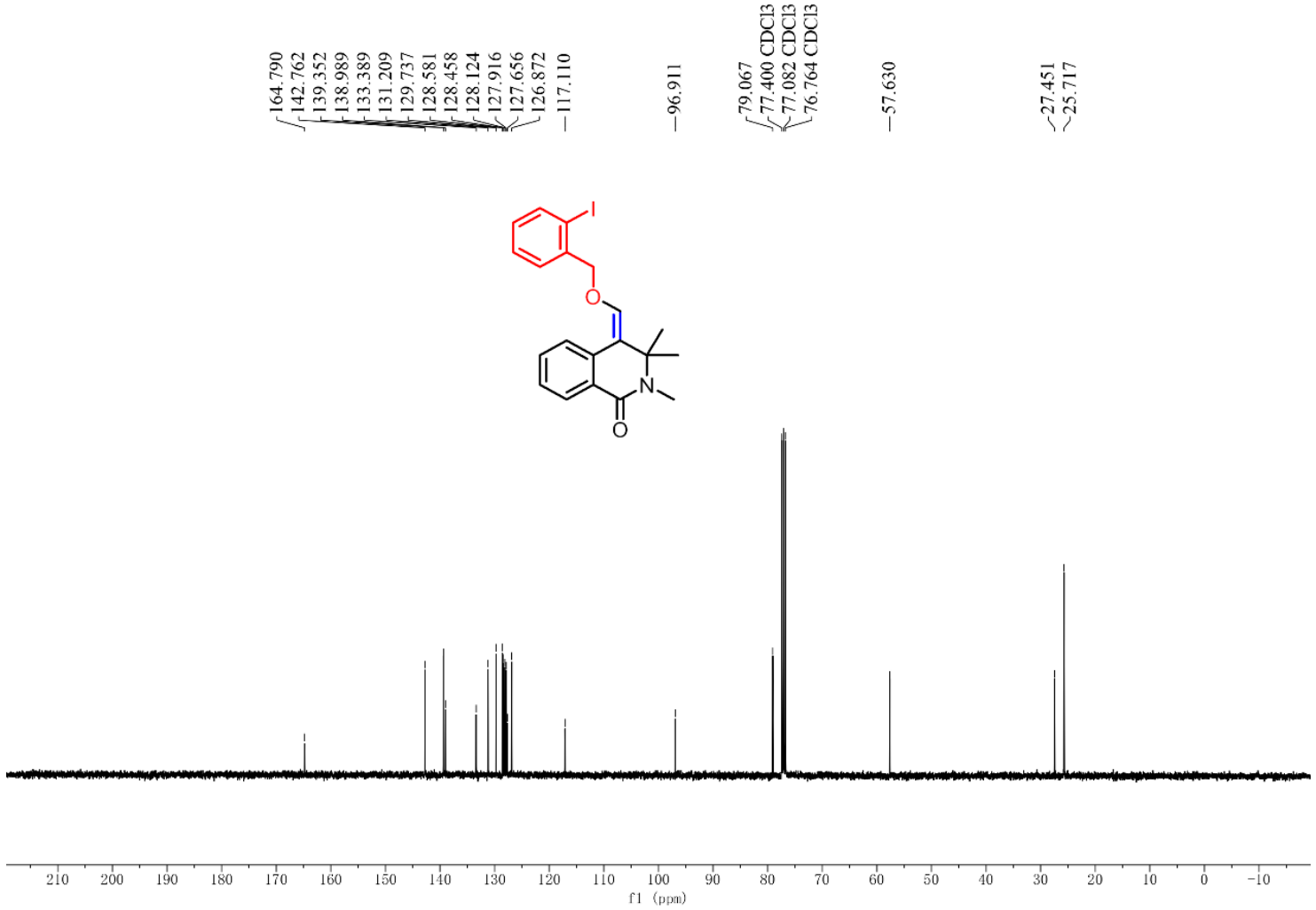
^{1}H spectrum of **5p**



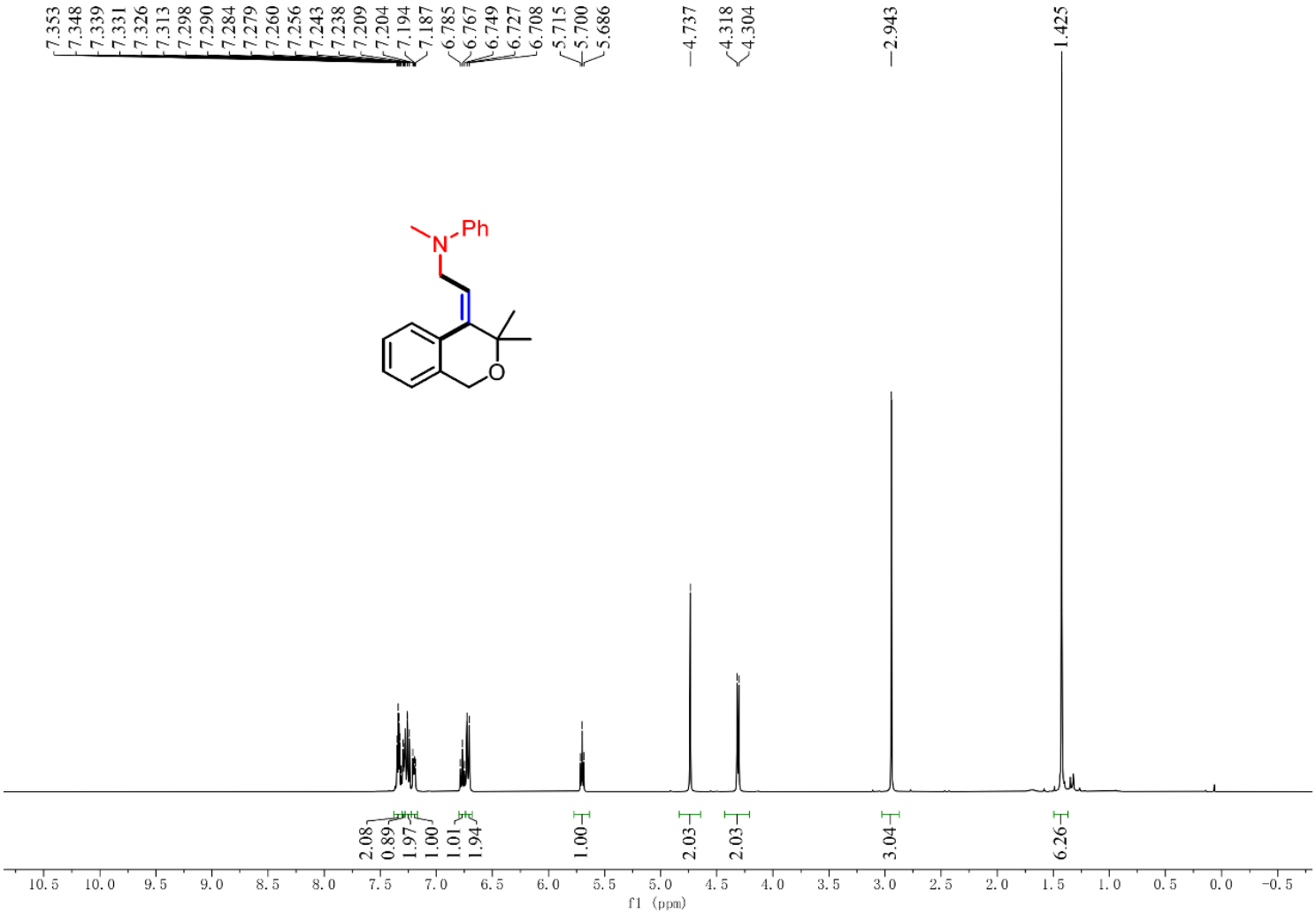
^{13}C spectrum of **5p**



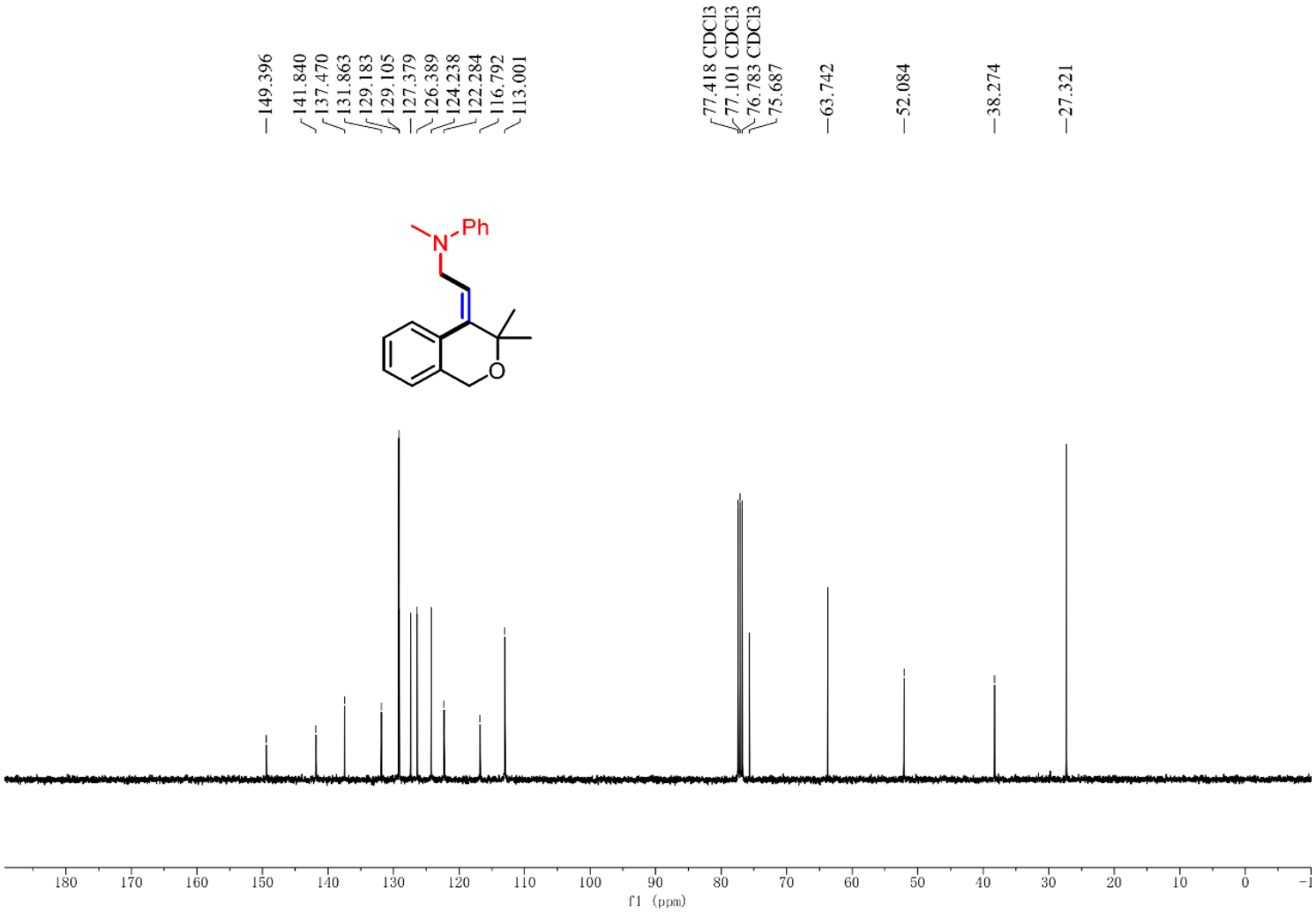
^{1}H spectrum of **3aa**



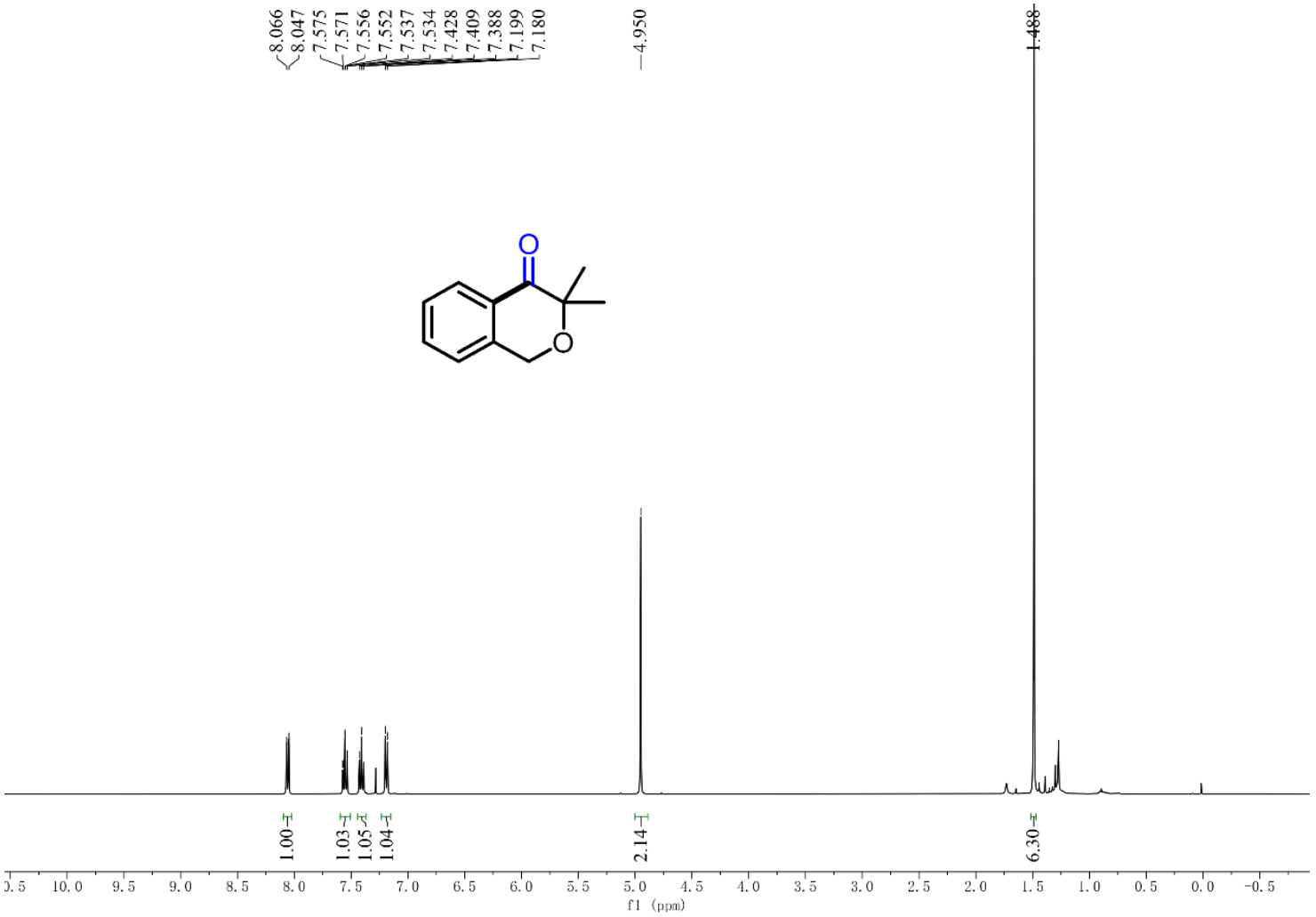
^{13}C spectrum of **3aa**



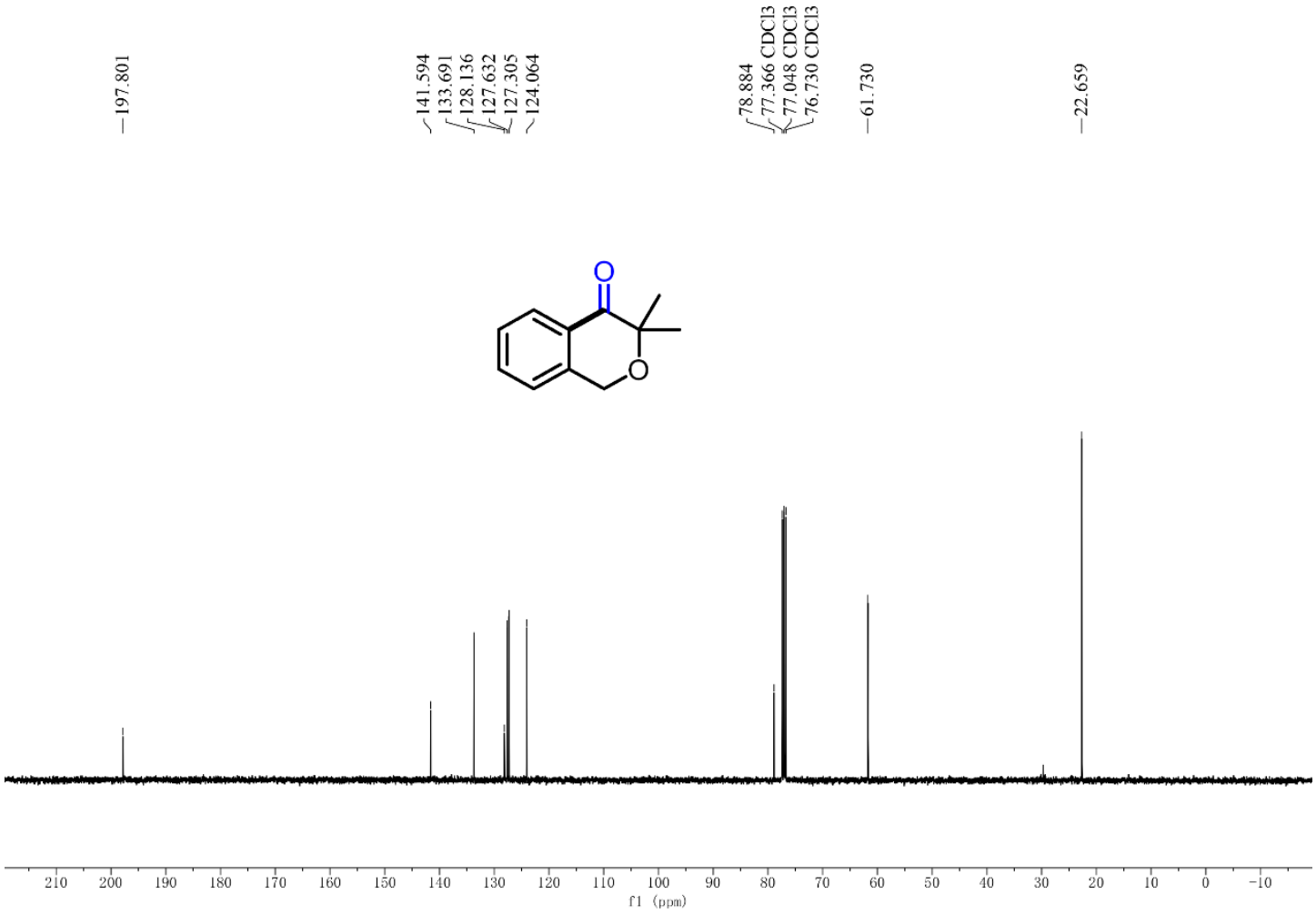
^{1}H spectrum of **5aa**



^{13}C spectrum of **5aa**



^{1}H spectrum of **5ab**



^{13}C spectrum of **5ab**