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Microwave assisted cycloaddition of benzonitrile oxides to 1-iodobuta-1,3-diynes

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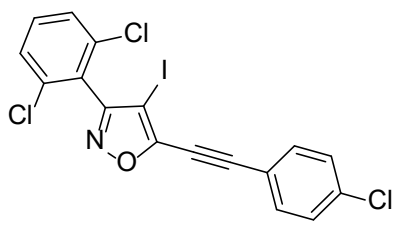
General remarks

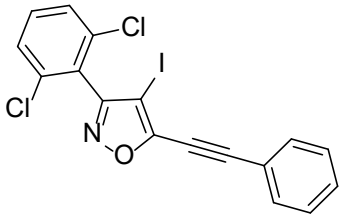
Solvents and reagents used for reactions were purchased from commercial suppliers. Evaporation of solvents and concentration of reaction mixtures were performed in vacuum at 35 °C on a rotary evaporator. ^{1}H and ^{13}C NMR spectra were recorded on Avance 400 at 400 and 100 MHz or Bruker Avance III 500 spectrometers (Bruker, Billerica, USA) at 500 MHz and 126 MHz respectively at 25 °C in $CDCl_3$ without using an internal standard. Chemical shifts are given relative to the residual proton signals of $CDCl_3$, δH 7.26 and δC 77.16. High resolution mass spectra were recorded using electrospray ionization (ESI) in the positive mode on a Bruker microTOF spectrometer (Billerica, USA). The reactions were monitored by thin layer chromatography (TLC) on the plates pre-coated with silica gel 60, F254 (Merck, Darmstadt, Germany), which were visualized with UV. Column chromatography was performed on a Merck Silica gel 60 (0.040—0.063 mm). All syntheses under microwave irradiation were performed in a microwave oven Discover SP in a 10-ml glass reactor. Melting points were measured on a HMK 68/2401 Kofler hot stage apparatus and were uncorrected. The starting iodobutadiynes[S1] and nitrile oxides[S2] were obtained using known procedures. Atom-condensed Fukui functions f(+) and f(–) , global electrophilicity (ω) and nucleophilicity (N) indexes were evaluated for compounds 1a, 1b and 1c in dimethoxyethane. Geometry optimization for all studied species was performed at the b3lyp/(6-31g**, def2TZVP for I) (SMD=dimethoxyethane) level of theory. The optimized geometries were used for the subsequent electron density calculations that were performed at the b3lyp/(6-311++g**, def2TZVP for I) (SMD=dimethoxyethane) level of theory. NBO charges were evaluated to obtain Fukui functions f(+) and f(–). All calculations were done with the Gaussian 09W program package.[S3]

General Procedure for the cycloaddition of stable nitrile oxides

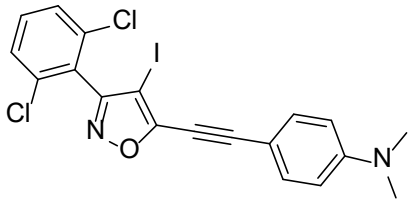
A mixture of 0.25 mmol iodobutadiyne **1** and 0.25 mmol nitrile oxide **2** in 0.5 mL of DME was heated under stirring at 120 °C using microwave irradiation during 1 hour until starting compounds has disappeared (TLC-control). The solvent was removed under reduced pressure and products were purified by column chromatography on silica gel to give the pure product **3**.



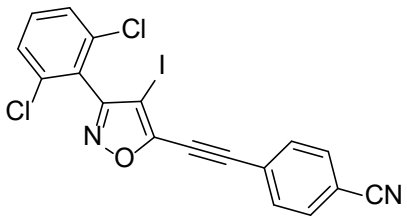
5-((4-Chlorophenyl)ethynyl)-3-(2,6-dichlorophenyl)-4-iodoisoxazole (**3a**). This compound was synthesized according to the general procedure 1-iodobuta-1,3-diyne **1a** (40 mg, 0.14 mmol) and nitrile oxide **2a** (26 mg, 0.14 mmol). Reaction time – 1 h. The crude product was purified by column chromatography (eluent: hexane/benzene = 10:1) to afford a white solid (23 mg, 35% yield): mp 183−184 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (d, J = 8.5 Hz, 2H), 7.49 – 7.38 (m, 5H). 13C NMR (126 MHz, $CDCl_3$) 163.1, 157.5, 136.8, 136.0, 133.5, 132.1, 129.3, 128.3, 127.0, 119.1, 100.7, 76.2 68.2 HRMS (ESI): m/z Calcd. for $C_{17}H_7Cl_3INO$ [$(M+Na)^+$]: 495.8530. Found: 495.8534.



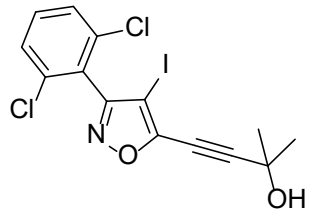
3-(2,6-Dichlorophenyl)-4-iodo-5-(phenylethynyl)isoxazole (**3b**). This compound was synthesized according to the general procedure 1-iodobuta-1,3-diyne **1b** (63 mg, 0.25 mmol) and nitrile oxide **2a** (47 mg, 0.25 mmol). Reaction time – 1 h. The crude product was purified by column chromatography (eluent: hexane/ethyl acetate = 50:1) to afford a beige solid (67 mg, 61% yield): mp 140−141 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 – 7.62 (m, $2H_{Ar}$), 7.50 – 7.37 (m, $6H_{Ar}$). ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.0, 157.8, 136.1, 132.3, 132.0, 130.5, 128.8, 128.3, 127.2, 120.7, 102.0, 75.3, 67.8. HRMS (ESI): m/z Calcd. for $C_{17}H_8Cl_2INO$ [$(M+H)^+$]: 439.9100. Found: 439.9105.



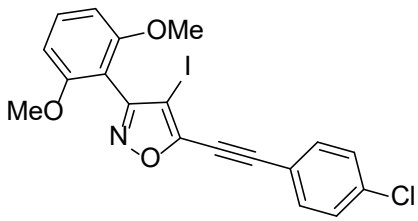
4-((3-(2,6-Dichlorophenyl)-4-iodoisoxazol-5-yl)ethynyl)-N,N-dimethylaniline (**3c**) This compound was synthesized according to the general procedure 1-iodobuta-1,3-diyne **1c** (47 mg, 0.16 mmol) and nitrile oxide **2a** (30 mg, 0.16 mmol). Reaction time – 1 h. The crude product was purified by column chromatography (eluent: hexane/acetone = 20:1) to afford a yellow green solid (34 mg, 44% yield): mp 174−176 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 – 7.29 (m, $5H_{Ar}$), 6.68 (d, *J* = 8.5 Hz, $2H_{Ar}$), 3.04 (s, 6H, CH_3). ^{13}C NMR (126 MHz, $CDCl_3$) δ 162.8, 158.6, 151.4, 136.1, 133.7, 131.9, 128.3, 127.5, 111.8, 106.7, 104.5, 74.2, 66.0, 40.2. HRMS (ESI): m/z Calcd. for $C_{27}H_{29}N_2O_3$ [$(M+H)^+$]: 482.9522. Found: 482.9521.



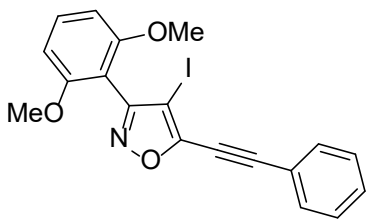
4-((3-(2,6-Dichlorophenyl)-4-iodoisoxazol-5-yl)ethynyl)benzonitrile (**3d**) This compound was synthesized according to the general procedure 1-iodobuta-1,3-diyne **1** (36 mg, 0.13 mmol) and nitrile oxide **2a** (24 mg, 0.13 mmol). Reaction time – 1 h. The crude product was purified by column chromatography (eluent: hexane/ ethyl acetate = 20:1) to afford a beige solid (16 mg, 27% yield): mp 149−151 °C;^{1}H NMR (400 MHz, $CDCl_3$) δ 1H NMR (400 MHz, CDCl3) δ 7.77 – 7.69 (m, $4H_{Ar}$), 7.50 – 7.39 (m, $3H_{Ar}$). ^{13}C NMR (126 MHz, $CDCl_3$) 163.2, 156.9, 136.0, 132.7, 132.5, 132.2, 128.6, 126.8, 125.4, 118.1, 113.8, 99.4, 78.8, 69.3. HRMS (ESI): m/z Calcd. for $C_{27}H_{29}N_2O_3$ [$(M+H)^+$]: 464.9053. Found: 464.9052.



4-(3-(2,6-Dichlorophenyl)-4-iodoisoxazol-5-yl)-2-methylbut-3-yn-2-ol (**3e**). This compound was synthesized according to the general procedure 1-iodobuta-1,3-diyne **1e** (117 mg, 0.50 mmol) and nitrile oxide **2a** (47 mg, 0.25 mmol). Reaction time – 1 h. The crude product was purified by column chromatography (eluent: hexane/acetone = 30:1) to afford a colorless oil (42 mg, 40% yield); ^{1}H NMR (400 MHz, CDCl3) δ 7.49 – 7.36 (m, $3H_{Ar}$), 2.20 – 2.10 (m, 1H, OH), 1.69 (s, 6H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.9, 157.2, 136.0, 132.0, 128.3, 127.0, 106.7, 68.9, 68.1, 65.9, 31.0. HRMS (ESI): m/z Calcd. for $C_{27}H_{29}N_2O_3$ [$(M+H)^+$]: 421.9206. Found: 421.9204.



5-((4-Chlorophenyl)ethynyl)-3-(2,6-dimethoxyphenyl)-4-iodoisoxazole (**3f**). This compound was synthesized according to the general procedure 1-iodobuta-1,3-diyne **1a** (49 mg, 0.171 mmol) and nitrile oxide **2b** (31 mg, 0.171 mmol). Reaction time – 1.5 h. The crude product was purified by column chromatography (eluent: hexane/ ethyl acetate = 10:1) to afford a colorless crystals (27 mg, 34% yield): mp 158−160 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 – 7.50 (m, $2H_{Ar}$), 7.46 – 7.35 (m, $3H_{Ar}$), 6.65 (d, J = 8.4 Hz, $2H_{Ar}$), 3.79 (s, 6H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.5, 158.9, 156.3, 136.4, 133.4, 132.2, 129.2, 119.5, 105.6, 104.1, 99.6, 70.9, 56.1. HRMS (ESI): m/z Calcd. for $C_{19}H_{13}ClINO_3$ [$(M+H)^+$]: 465.9701. Found: 465.9690. Appropriate crystals for X-Ray analysis were obtained from chloroform/hexane solution. Crystallographic data for **3f** have been deposited with the Cambridge Crystallographic Data Centre, no. CCDC 2341764.

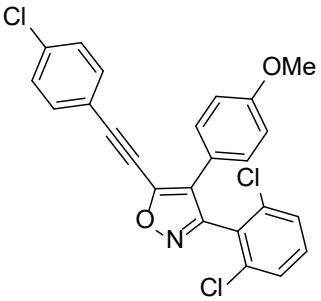


3-(2,6-Dimethoxyphenyl)-4-iodo-5-(phenylethynyl)isoxazole (**3g**). This compound was synthesized according to the general procedure 1-iodobuta-1,3-diyne **1b** (63 mg, 0.25 mmol) and nitrile oxide **2b** (45 mg, 0.25 mmol). Reaction time – 1 h. The crude product was purified by column chromatography (eluent: hexane/

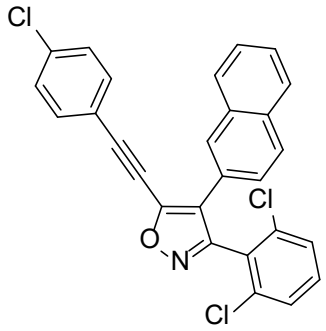
ethyl acetate = 10:1) to afford a beige solid (57 mg, 53% yield): mp 105−106 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 – 7.60 (m, $2H_{Ar}$), 7.46 – 7.37 (m, $4H_{Ar}$), 6.65 (d, J = 8.4 Hz, $2H_{Ar}$), 3.79 (s, 6H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.5, 159.0, 156.6, 132.2, 132.1, 130.1, 128.7, 121.1, 105.7, 104.1, 100.9, 76.0, 70.5, 56.1. HRMS (ESI): m/z Calcd. for $C_{19}H_{14}INO_3$ [(M+H)+]: 432.0091. Found: 432.0092.

General Procure for the Suzuki-Miyaura cross-coupling

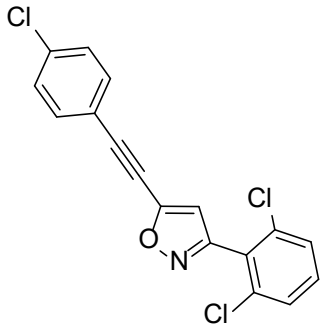
4-Iodoisoxazole **3a** (1 equiv), $ArB(OH)_2$ (2 equiv), K_3PO_4 (2 equiv), and $Pd(PPh_3)_4$ (5 mol %) were placed in a vial. The vial was sealed, and the mixture was evacuated and flushed with Argon several times. 1,4-Dioxane (0.08 M) was added, and the vial with the reaction mixture was placed in a preheated IKA Dry Block Heater (100 °C) and stirred for 4 or16 h (TLC control). After cooling to rt, the reaction mixture was filtered through a pad of silica gel and washed with CH_2Cl_2. Solvents were removed under reduced pressure, and the crude product was purified by column chromatography on silica gel.



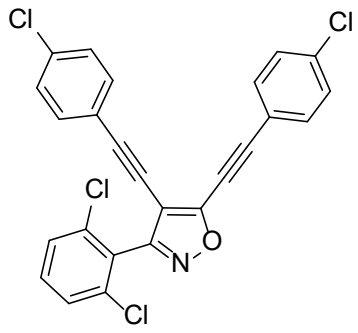
5-((4-Chlorophenyl)ethynyl)-3-(2,6-dichlorophenyl)-4-(4-methoxyphenyl)isoxazole (**5a**). This compound was synthesized according to the general procedure from isoxazole **3a** (40.0 mg, 0.084 mmol) and (4-methoxyphenyl)boronic acid (26 mg, 0.17 mmol). Reaction time – 4 h. The crude product was purified by column chromatography (eluent: hexane/EtOAc = 20:1) to afford colorless oil (19 mg, 50% yield). ^{1}H NMR (400 MHz, $CDCl^3$) δ 7.53 – 7.46 (m, $2H_{Ar}$), 7.43 – 7.33 (m, $5H_{Ar}$), 7.33 – 7.27 (m, $2H_{Ar}$), 6.87 – 6.81 (m, $2H_{Ar}$), 3.79 (s, 3H, CH_3). ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.8, 158.5, 149.8, 136.3, 136.2, 133.2, 131.6, 129.2, 129.1, 128.9, 128.4, 127.9, 123.2, 120.5, 119.7, 114.3, 99.1, 55.4. HRMS (ESI): m/z Calcd. for $C_{27}H_{29}N_2O_3$ [$(M+H)^+$]: 454.0163. Found: 454.0162.



5-((4-Chlorophenyl)ethynyl)-3-(2,6-dichlorophenyl)-4-(naphthalen-2-yl)isoxazole (**5b**). This compound was synthesized according to the general procedure from isoxazole **3a** (30.0 mg, 0.06 mmol) and naphthalen-2-ylboronic acid (22 mg, 0.13 mmol). Reaction time – 16 h. The crude product was purified by column chromatography (eluent: hexane/EtOAc = 20:1) to afford off-white solid (14 mg, 47% yield) mp 151−152 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (s, $1H_{Ar}$), 7.85 – 7.76 (m, $2H_{Ar}$), 7.74 – 7.68 (m, $1H_{Ar}$), 7.52 – 7.44 (m, $5H_{Ar}$), 7.43 – 7.33 (m, 5H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.6, 150.6, 136.4, 136.2, 133.4, 133.2, 133.1, 131.7, 129.2, 128.6, 128.4, 128.3, 127.9, 127.4, 126.8, 126.6, 125.8, 125.3, 123.5, 119.6, 99.4. HRMS (ESI): m/z Calcd. for $C_{27}H_{14}Cl_3NO$ [$(M+Na)^+$]: 496.0033. Found: 496.0053.



5-((4-Chlorophenyl)ethynyl)-3-(2,6-dichlorophenyl)isoxazole (**4**). Off-white solid (5 mg, 25% yield) mp 117−118 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 – 7.50 (m, $2H_{Ar}$), 7.46 – 7.32 (m, $5H_{Ar}$), 6.61 (s, 1H, CH). ^{13}C NMR (101 MHz, CDCl3) δ 159.1, 153.8, 136.5, 135.8, 133.3, 131.5, 129.2, 128.5, 127.8, 119.4, 109.7, 97.9, 76.4. HRMS (ESI): m/z Calcd. for $C_{17}H_8Cl_3NO$ [$(M+H)^+$]: 347.9744. Found: 347.9745.



4,5-bis((4-Chlorophenyl)ethynyl)-3-(2,6-dichlorophenyl)isoxazole (**6**). 4-Iodoisoxazole **3a** (25 mg, 0.053 mmol, 1 equiv), 1-chloro-4-ethynylbenzene (14 mg, 0,105 mmol, 2 equiv), CuI (1.5 mg, 0.0079 mmol, 0.15 equiv), and $Pd(PPh_3)_4$ (3.0 mg, 0.0026 mmol, 5 mol %) and 0.5 ml of abs. DMF were placed in a vial. The vial was sealed, and the mixture was evacuated and flushed with Argon several times. Next, DIPA (59 µl, 42.6 mg, 0.421 mmol, 8 equiv.) was added, with a syringe and the vial with the reaction mixture was placed in a preheated IKA Dry Block Heater (40 °C) and stirred for 30 h (TLC control). After cooling to rt, the reaction mixture was washed by saturated NH_4Cl solution, brine and extracted with ethyl acetate. Combined organic fractions were dried by Na_2SO_4. Solvents were removed under reduced pressure, and the crude product was purified by column chromatography on silica gel (eluent: hexane/CH_2Cl_2 = 20:1) to afford yellow oil (12 mg, 48% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 – 7.55 (m, $2H_{Ar}$), 7.50 – 7.45 (m, $2H_{Ar}$), 7.43 – 7.37 (m, $3H_{Ar}$), 7.32 – 7.26 (m, $4H_{Ar}$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.2, 155.1, 136.8, 136.1, 135.3, 133.5, 133.0, 131.9, 129.3, 128.9, 128.4, 126.4, 120.8, 119.2, 108.2, 101.8, 96.3, 76.0. HRMS (ESI): m/z Calcd. for $C_{25}H_{11}Cl_4NO$ [$(M+Na)^+$]: 505.9460. Found: 505.9462. In addition, 12% of the starting iodoisoxazole **3a** was isolated.

Table S1 Crystal data and structure refinement for **3f**

Empirical formula	$C_{19}H_{13}NO_3ClI$
Formula weight	465.65
Temperature/K	100.0(2)
Crystal system	monoclinic
Space group	$P2_1/n$
a/Å	7.40100(10)
b/Å	14.3259(2)
c/Å	16.9061(2)
α/°	90
β/°	95.3010(10)
γ/°	90
Volume/Å^3	1784.82(4)
Z	4
ρ_{calc}g/cm^3	1.733
μ/mm^{-1}	15.630
F(000)	912.0
Crystal size/mm^3	0.1 × 0.06 × 0.04
Radiation	Cu Kα (λ = 1.54184)
2Θ range for data collection/°	8.104 to 139.93
Index ranges	$-9 \le h \le 9$, $-17 \le k \le 17$, $-20 \le l \le 20$
Reflections collected	13275
Independent reflections	3371 [R_{int} = 0.0501, R_{sigma} = 0.0384]
Data/restraints/parameters	3371/0/228
Goodness-of-fit on F^2	1.083
Final R indexes [I>=2σ (I)]	R_1 = 0.0318, wR_2 = 0.0844
Final R indexes [all data]	R_1 = 0.0337, wR_2 = 0.0856
Largest diff. peak/hole / e Å^{-3}	0.93/-1.27

Table S2 Cartesian atomic coordinates for optimized geometries of **1b**, **2a** and **2b** in dimethoxyethane (b3lyp/(6-31g**, I Def2TZVP) (SMD=dimethoxyethane) level of theory). Nuclear charges of elements are shown in the second column.

Compound	Charge	X	Y	Z
1b				
	6	4.124085	-2.778199	-5.526023
	6	2.965593	-3.129099	-4.837958
	6	5.281583	-2.426388	-4.825316
	1	2.06495	-3.402739	-5.378492
	1	6.182803	-2.154045	-5.367084
	6	2.95459	-3.131632	-3.427057
	6	5.27869	-2.426018	-3.4273
	1	6.176759	-2.153426	-2.880508
	6	4.126934	-2.775262	-2.727221
	1	4.120804	-2.776396	-1.641761
	1	4.124068	-2.779363	-6.612221
	6	1.774955	-3.49045	-2.716739
	6	0.763856	-3.800619	-2.104815
	6	-0.36058	-4.147948	-1.422631
	6	-1.369465	-4.4614	-0.808975
	53	-3.0026	-4.98074	0.191549

2a				
	6	4.113396	-2.780314	-5.522532
	6	2.967396	-3.127292	-4.817685
	6	5.2669	-2.430283	-4.821299
	1	6.164292	-2.159857	-5.367972
	6	2.940203	-3.135339	-3.404599
	6	5.28171	-2.424266	-3.426843
	1	6.178525	-2.152514	-2.882236
	6	4.129563	-2.773246	-2.732931
	1	4.102933	-2.784407	-6.606352
	6	1.767858	-3.493971	-2.690109
	7	0.793378	-3.802037	-2.128105
	8	-0.220847	-4.121799	-1.537041
	17	4.150362	-2.764475	-0.981084
	17	1.520302	-3.566917	-5.702137
2b				
	6	3.947793	-3.628407	-5.292594
	6	2.72504	-3.767388	-4.62795
	6	5.101835	-3.388098	-4.546845
	1	6.049377	-3.279884	-5.066548
	6	2.672506	-3.664504	-3.215716
	6	5.079571	-3.281507	-3.156175
	1	5.996755	-3.094556	-2.612333
	6	3.861142	-3.420355	-2.483656
	1	4.005486	-3.703385	-6.37073
	6	1.433377	-3.800525	-2.53642
	7	0.420629	-3.908766	-1.968134
	8	-0.64539	-4.022661	-1.372784
	8	3.705115	-3.340309	-1.141878
	6	4.854328	-3.068903	-0.335908
	1	5.606626	-3.859997	-0.43022
	1	5.301242	-2.102119	-0.592
	1	4.492282	-3.037974	0.692488
	8	1.537436	-3.998334	-5.234177
	6	1.509836	-4.114262	-6.659336
	1	1.850127	-3.191226	-7.141407
	1	2.120105	-4.956916	-7.002731
	1	0.466211	-4.29504	-6.919744

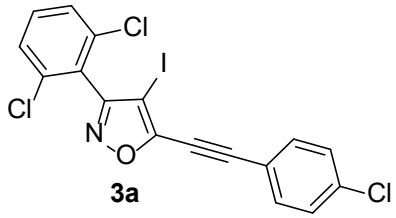
References

S1 A. I. Govdi, N. A. Danilkina, A. V. Ponomarev, I. A. Balova, *J. Org. Chem.* 2019, **84**, 1925.

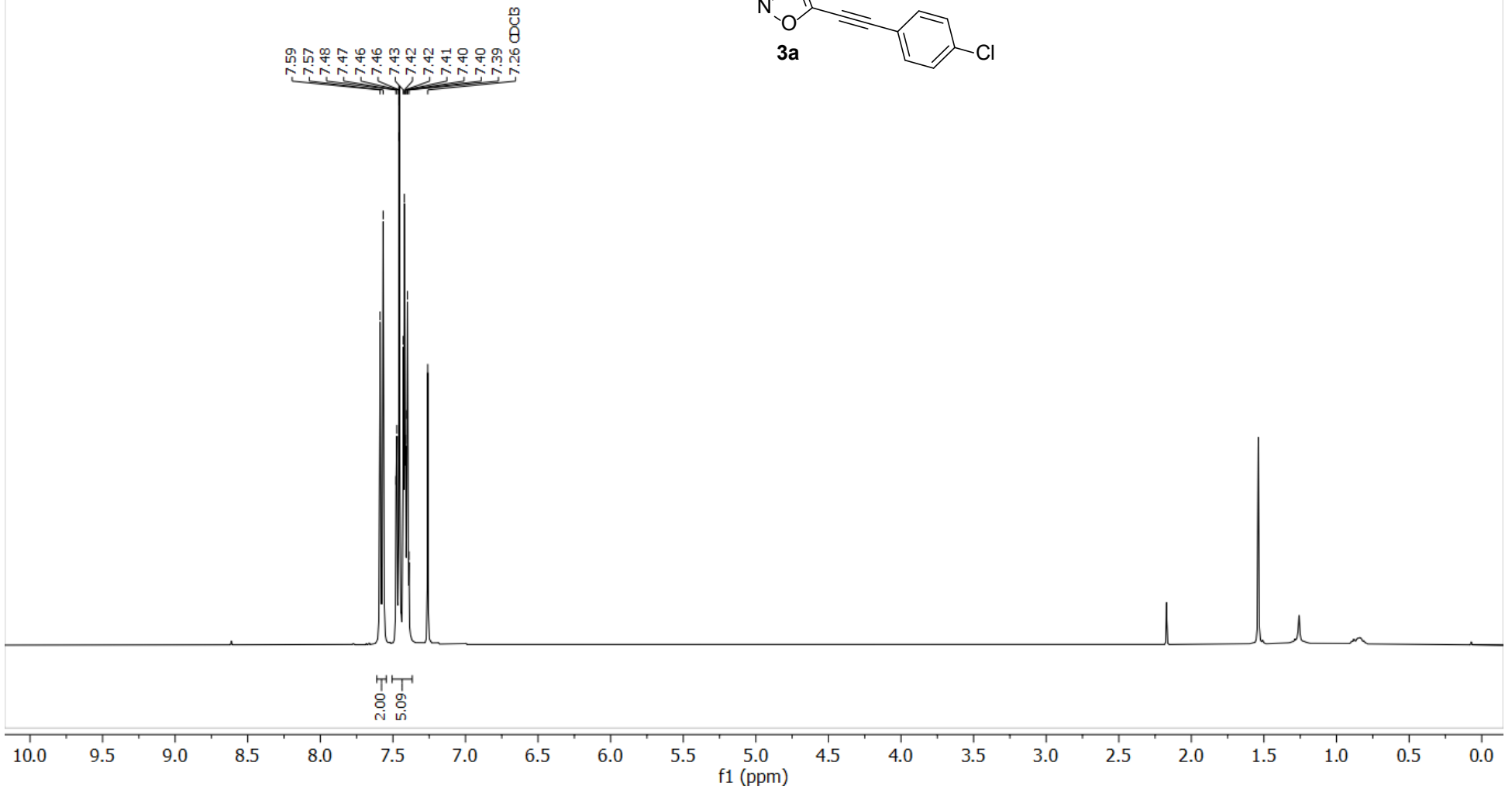
S2 Y. Koyama, Y.-G. Lee, S. Kuroki, T. Takata *Tetrahedron Lett.* 2015, **56**, 7038.

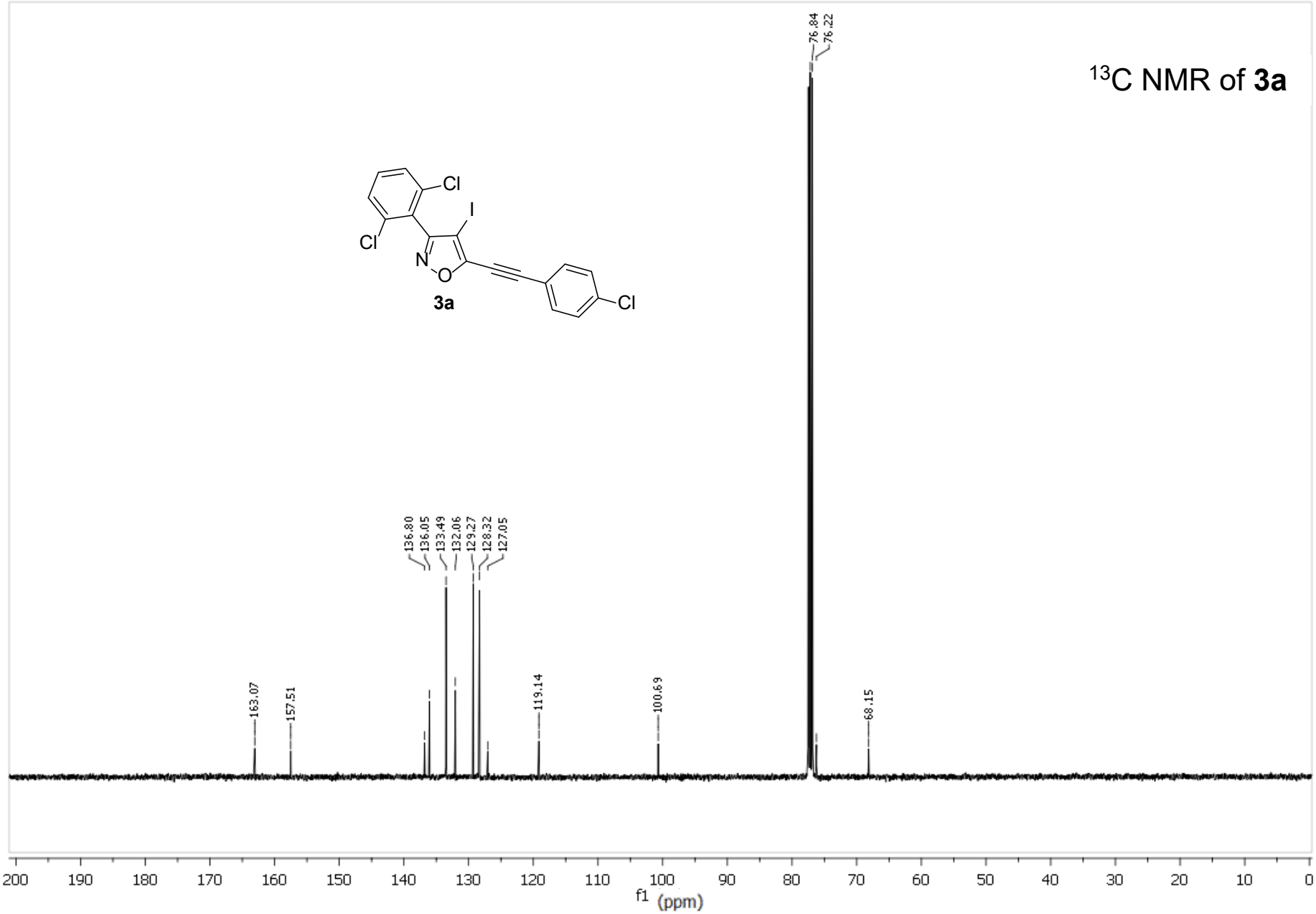
S3 M. J. Frisch, G. W. Trucks, H. B. Schlegel, et al., in: Gaussian 09, Revision C.01, Gaussian, Inc., Wallingford, CT, 2010

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

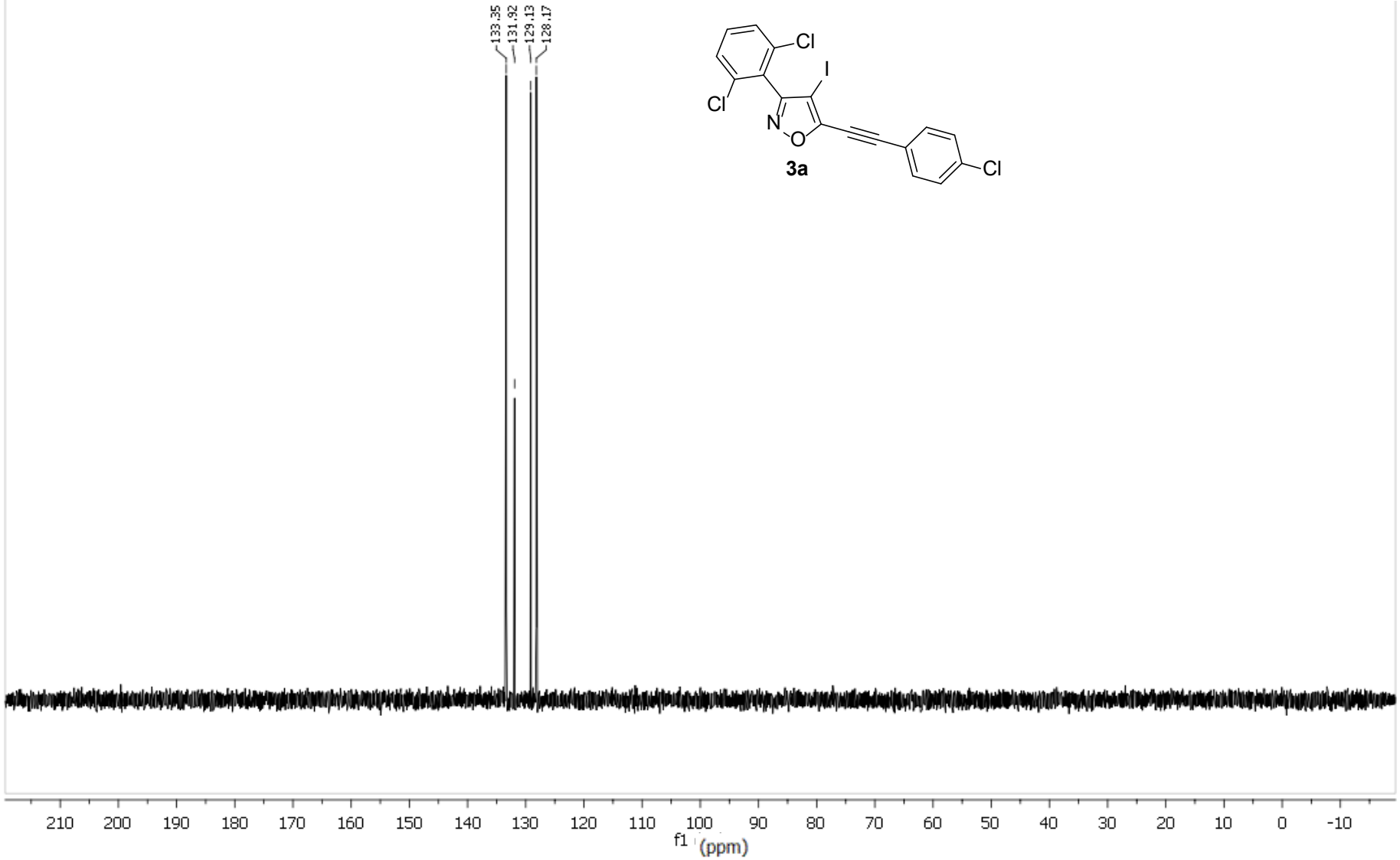


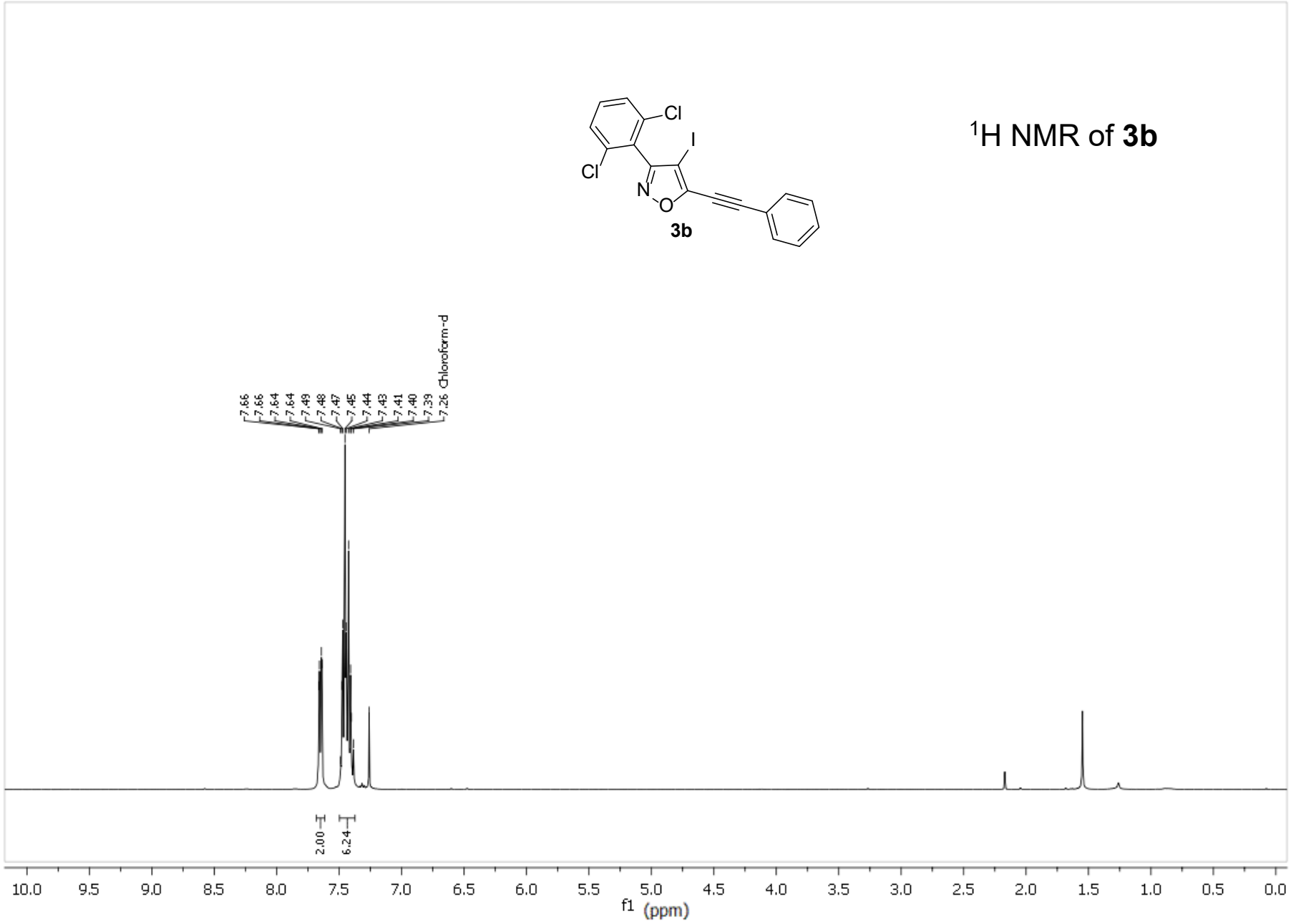
3a



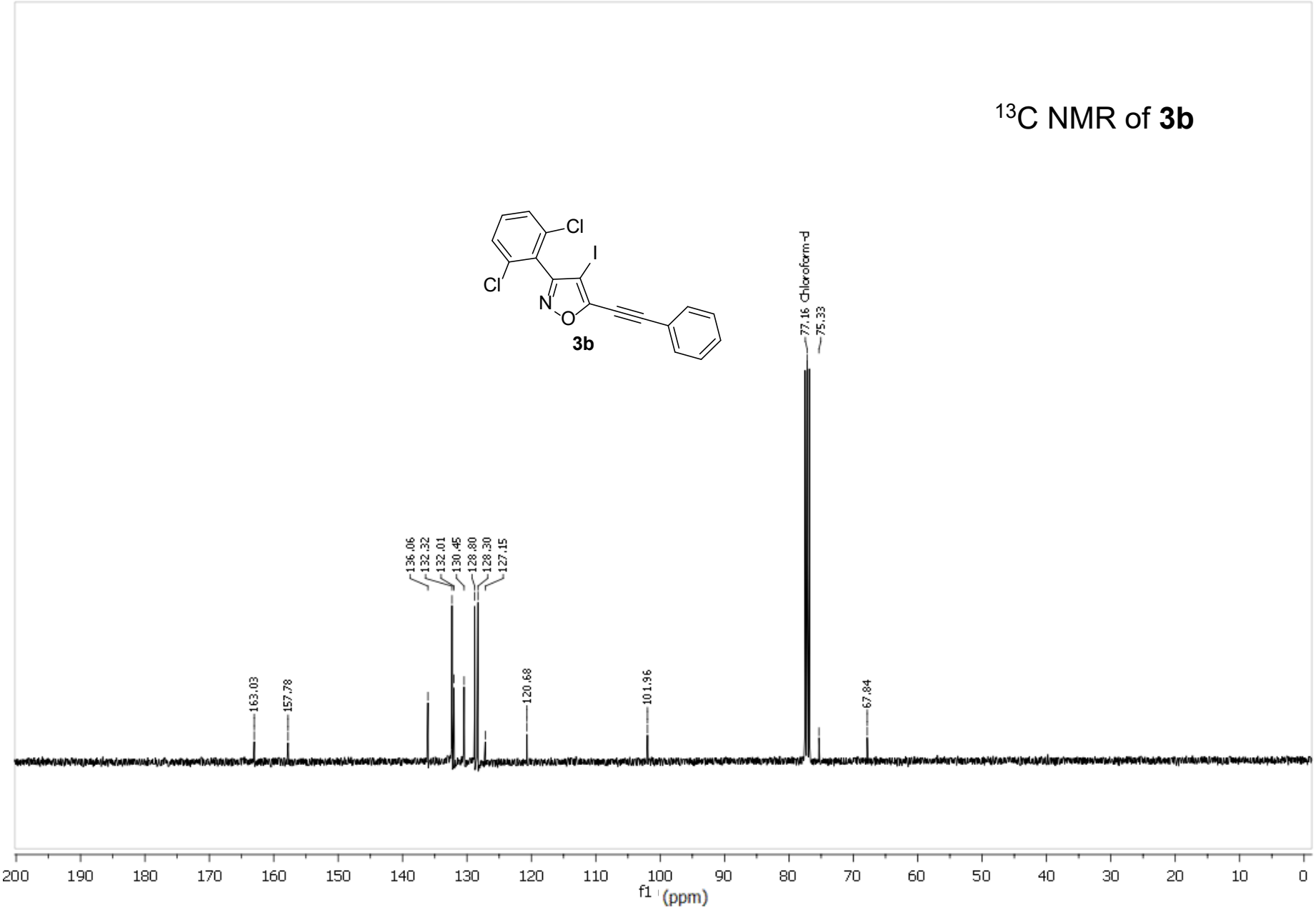

^{13}C NMR of **3a**
Cl
I
Cl
N
O
Cl
3a
76.84
76.22
136.80
136.05
133.49
132.06
129.27
128.32
127.05
163.07
157.51
119.14
100.69
68.15
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

^{13}C dept NMR of **3a**

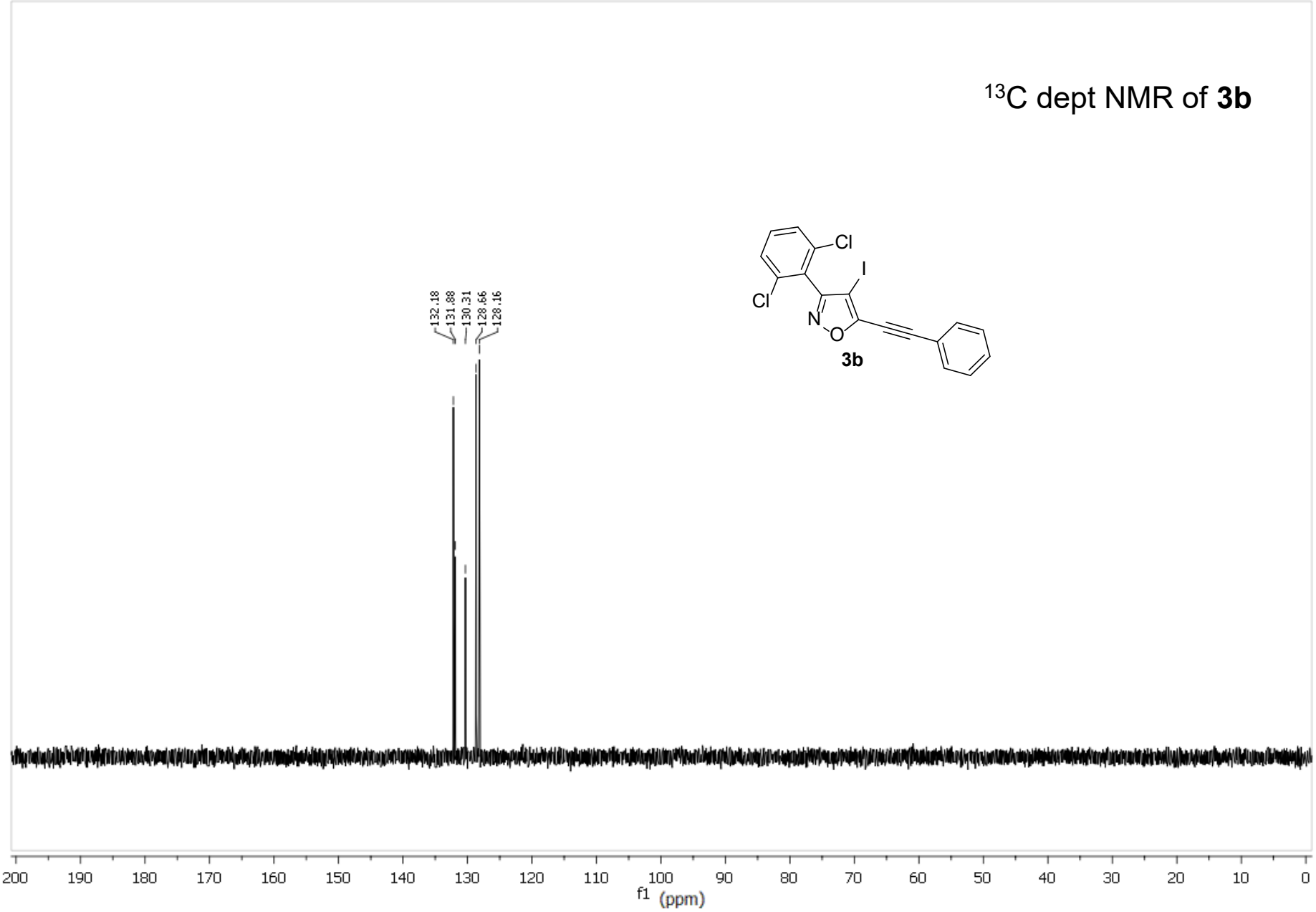



Cl
I
Cl
N
O
3b
^{1}H NMR of **3b**
7.66
7.66
7.64
7.64
7.49
7.48
7.47
7.45
7.44
7.43
7.41
7.40
7.39
7.26
Chloroform-d
2.00
6.24
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

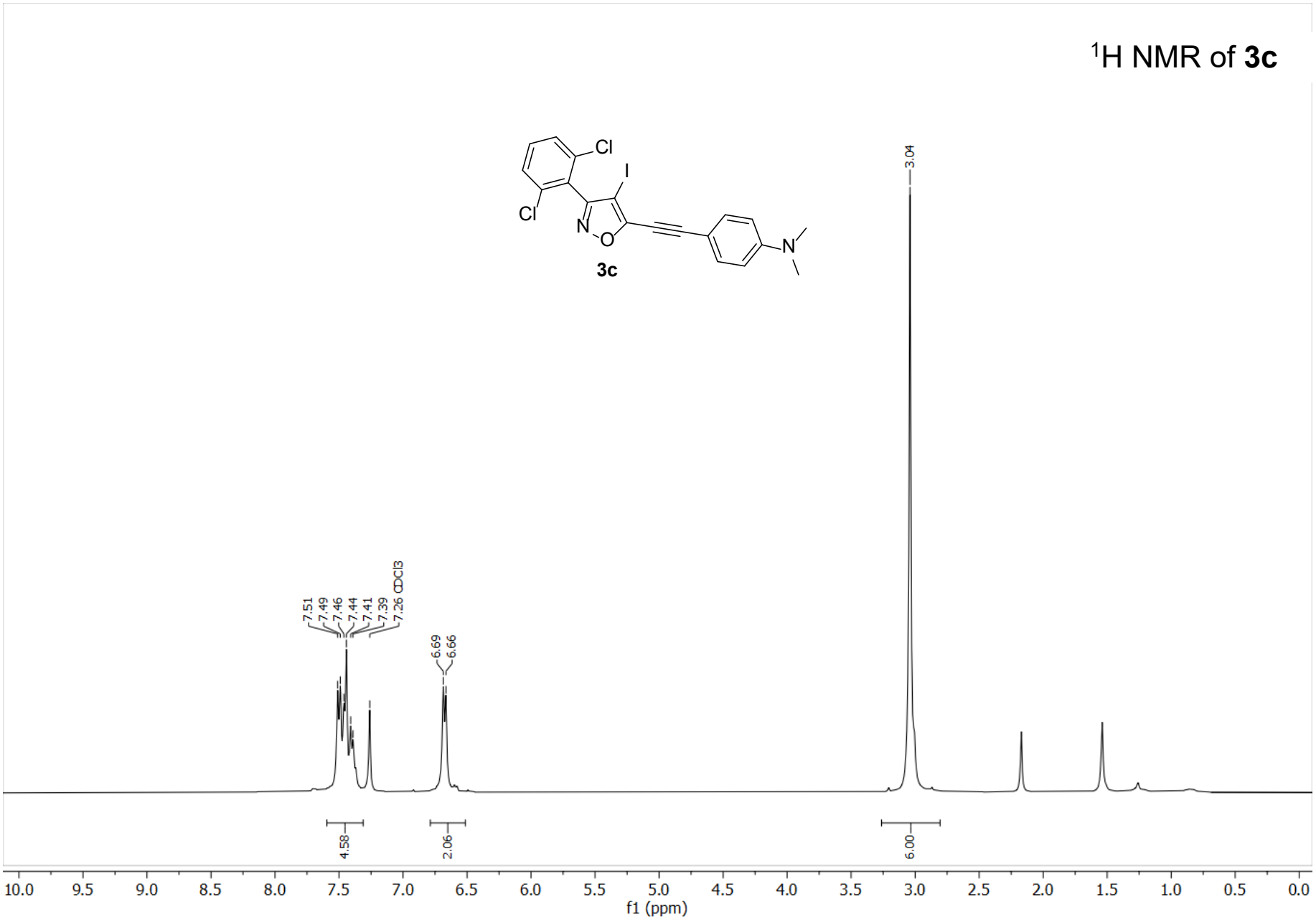
^{13}C NMR of **3b**


Cl
Cl
I
N
O
3b
77.16 Chloroform-d
75.33
136.06
132.32
132.01
130.45
128.80
128.30
127.15
163.03
157.78
120.68
101.96
67.84
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

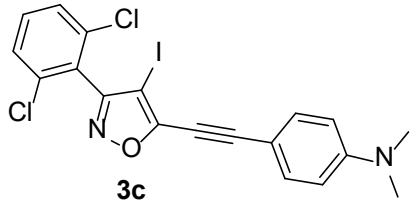
^{13}C dept NMR of **3b**



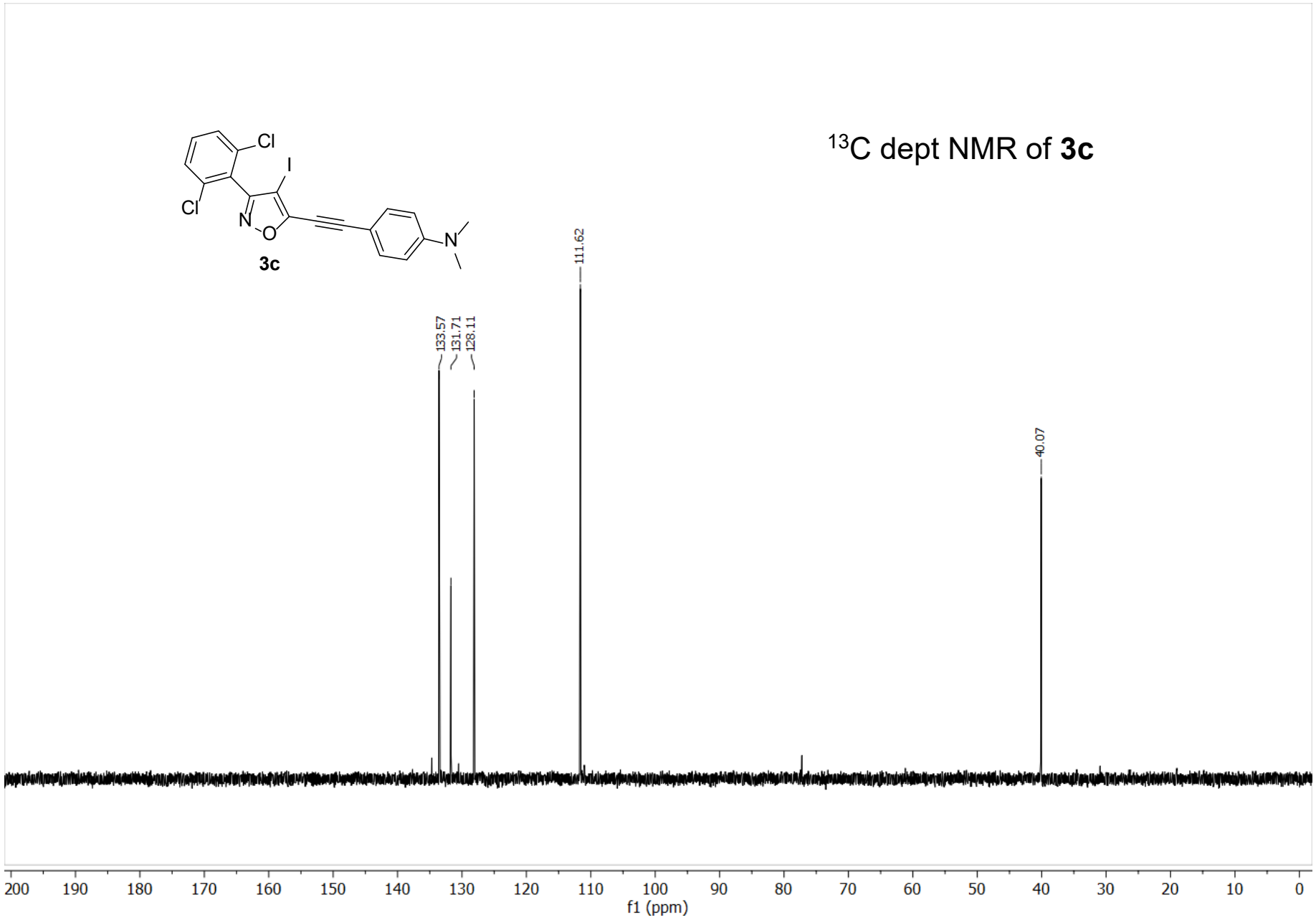
^{1}H NMR of **3c**

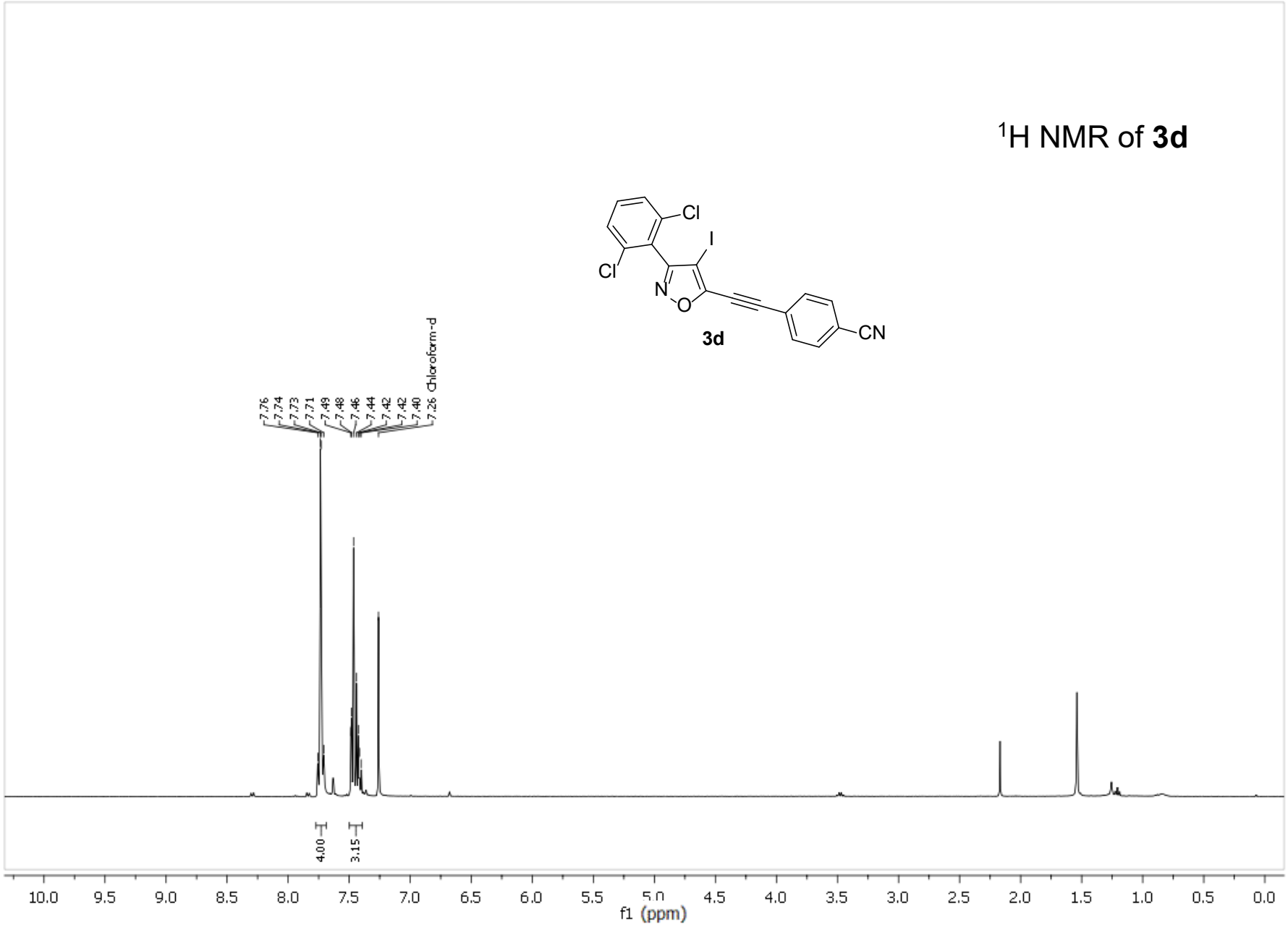

Cl
Cl
I
N
O
N
3c
3.04
7.51
7.49
7.46
7.44
7.41
7.39
7.26 CDCl3
6.69
6.66
4.58
2.06
6.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

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

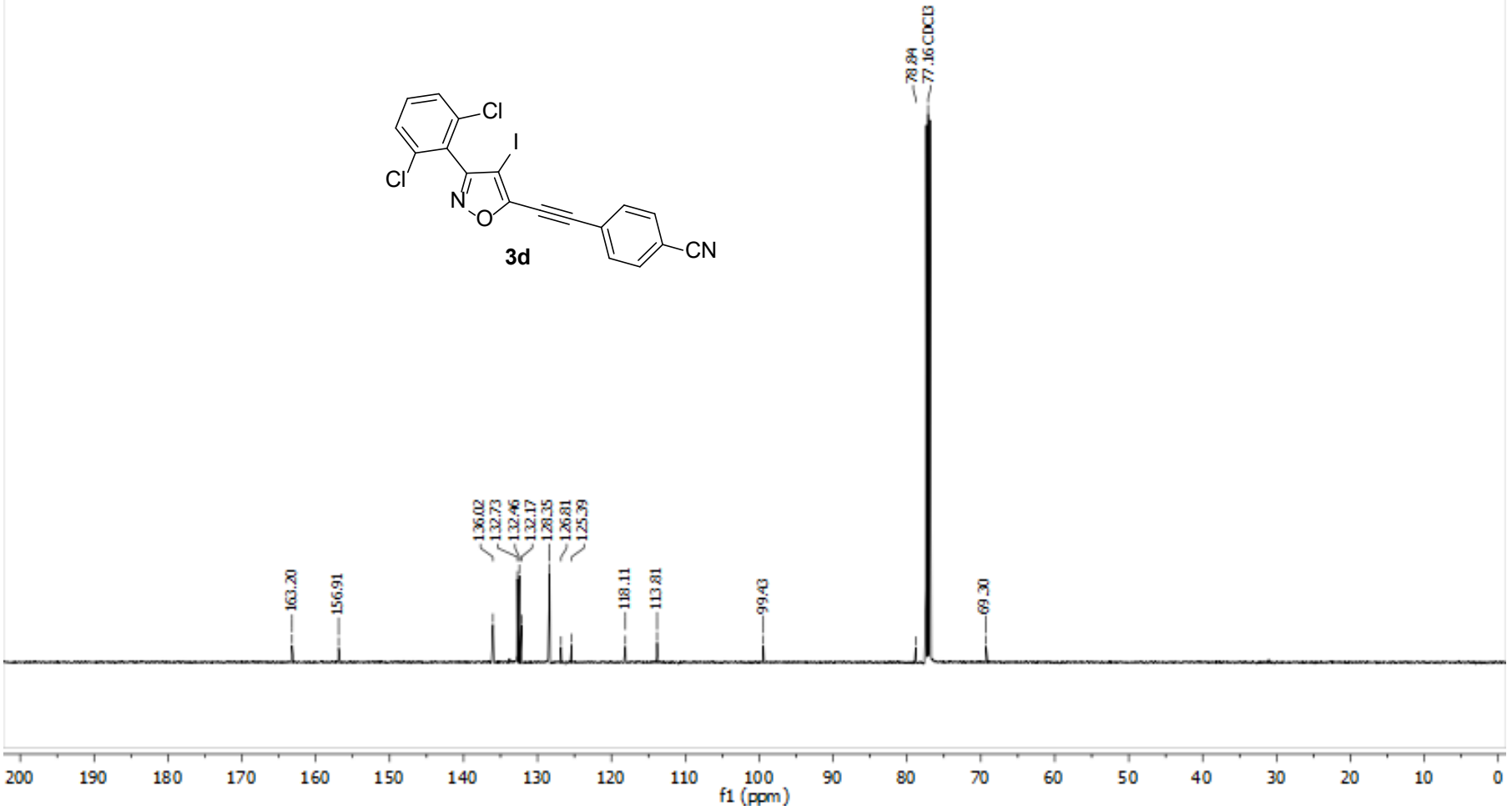


3c

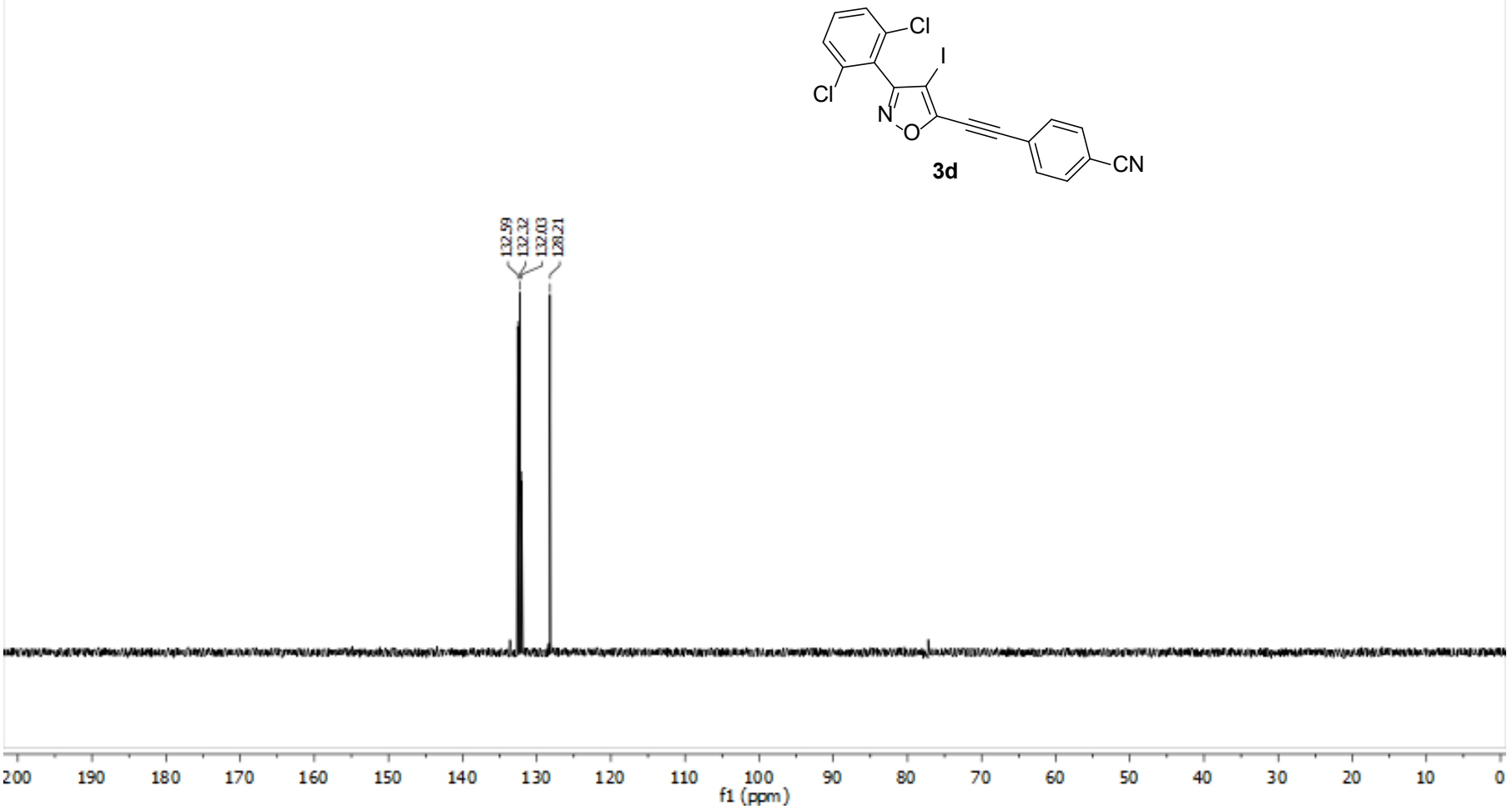

Cl
I
Cl
N
O
N
3c
^{13}C dept NMR of **3c**
133.57
131.71
128.11
111.62
40.07
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

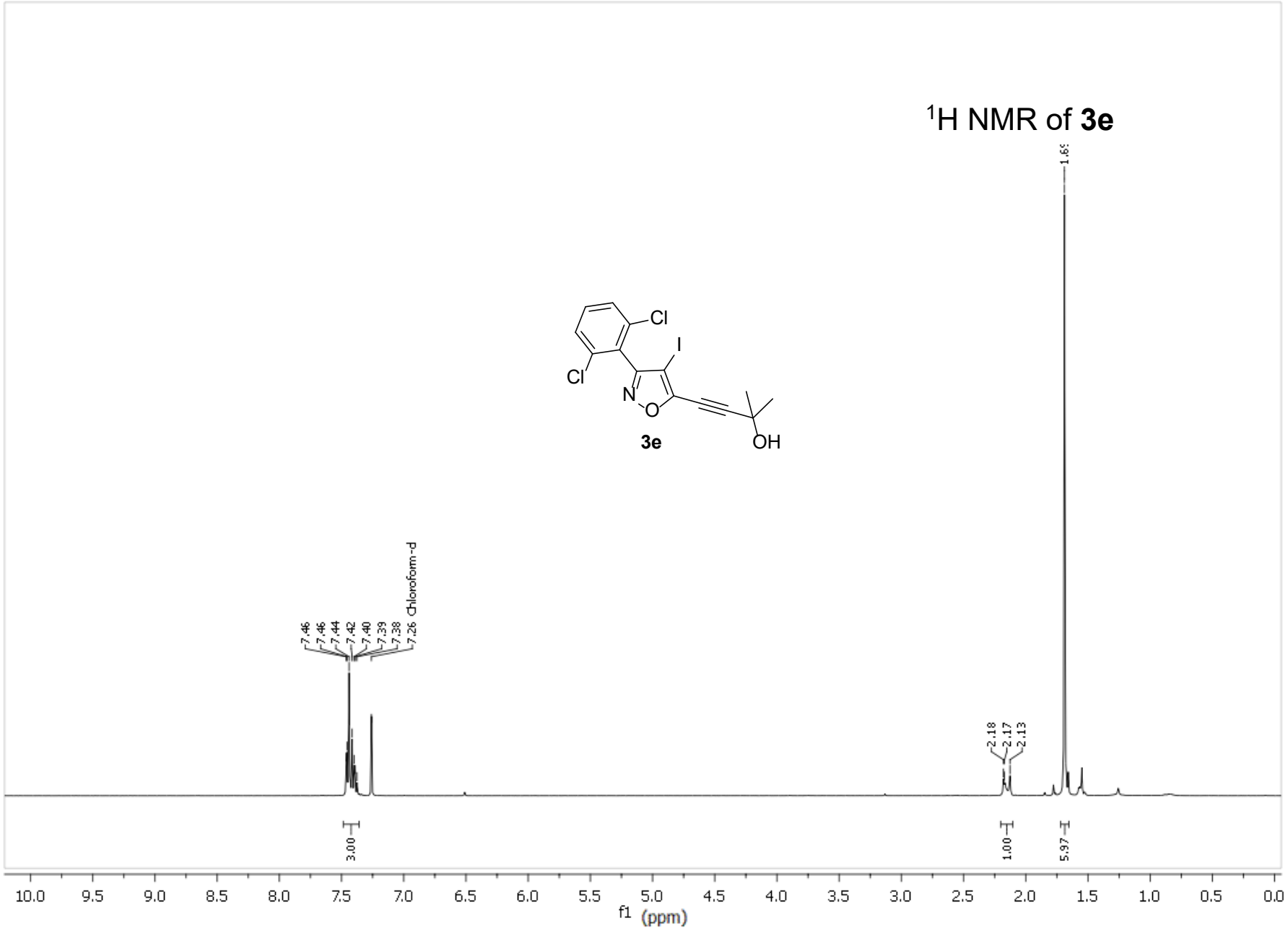

^{1}H NMR of **3d**
Cl
I
Cl
N
O
CN
3d
7.76
7.74
7.73
7.71
7.49
7.48
7.46
7.44
7.42
7.42
7.40
7.26 Chloroform-d
4.00
3.15
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

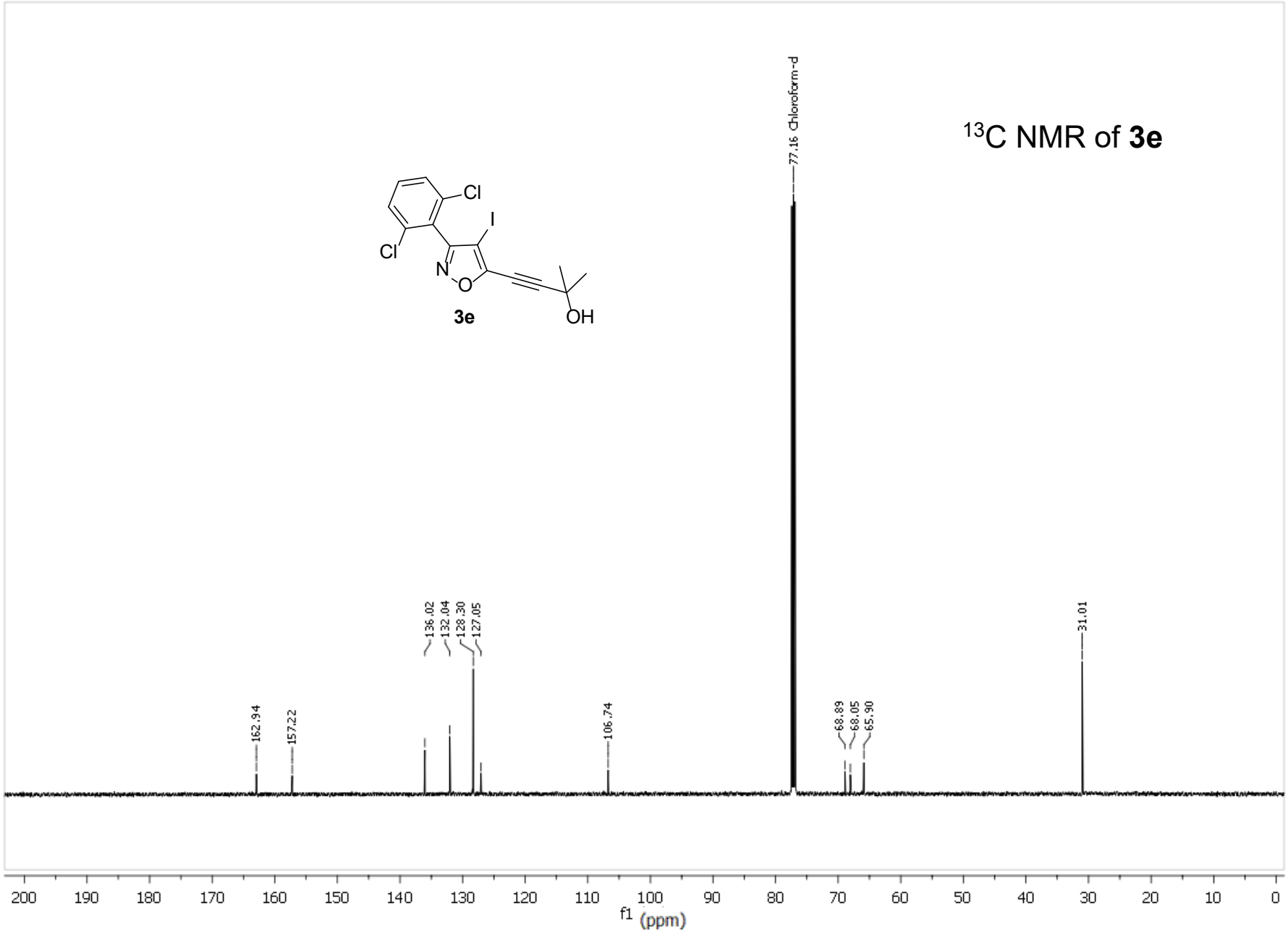
^{13}C NMR of **3d**


Cl
Cl
I
N
O
CN
3d
78.84
77.16 CDCl3
136.02
132.73
132.46
132.17
128.35
126.81
125.39
163.20
156.91
118.11
113.81
99.43
69.30
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

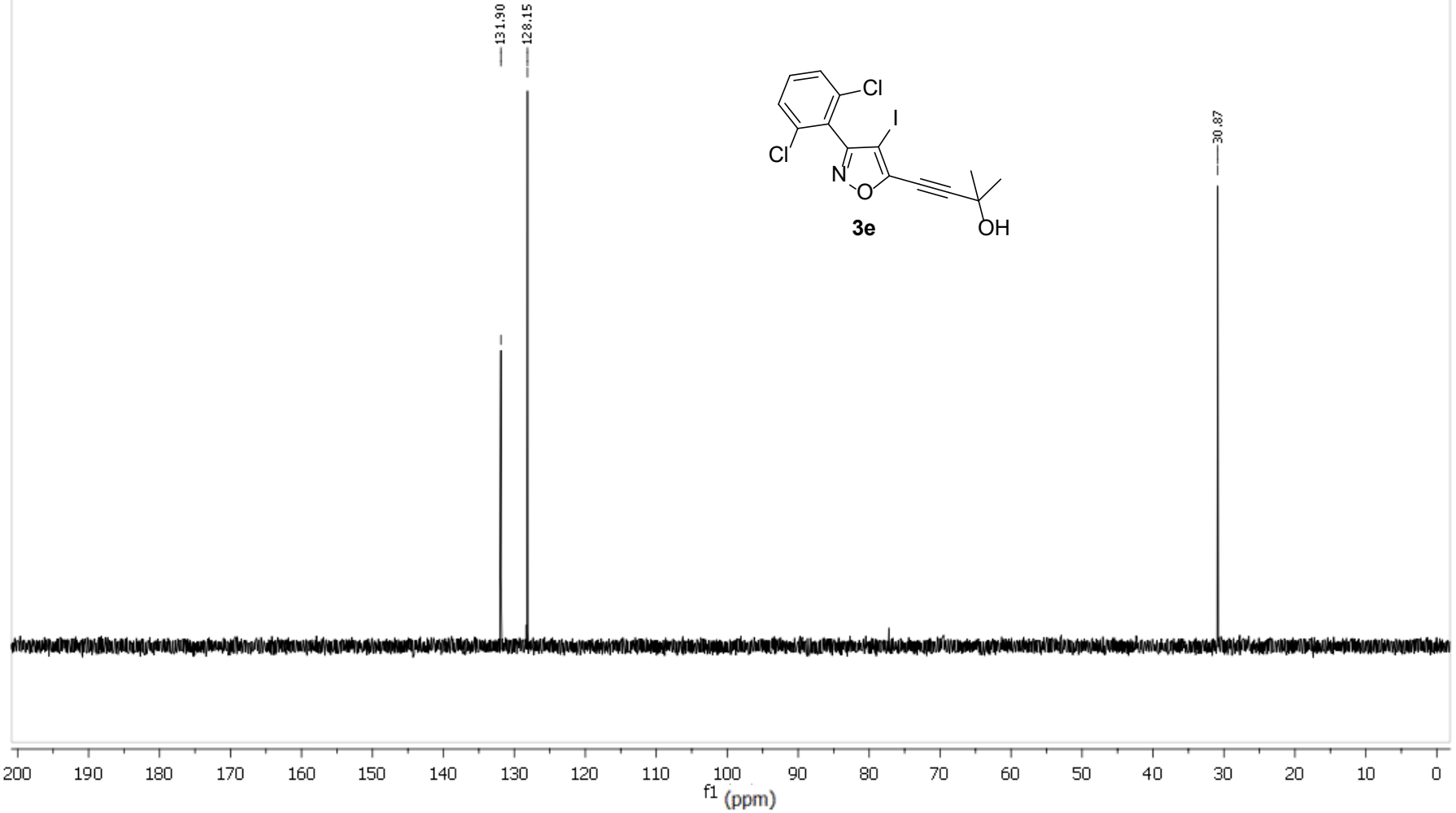
^{13}C dept NMR of **3d**



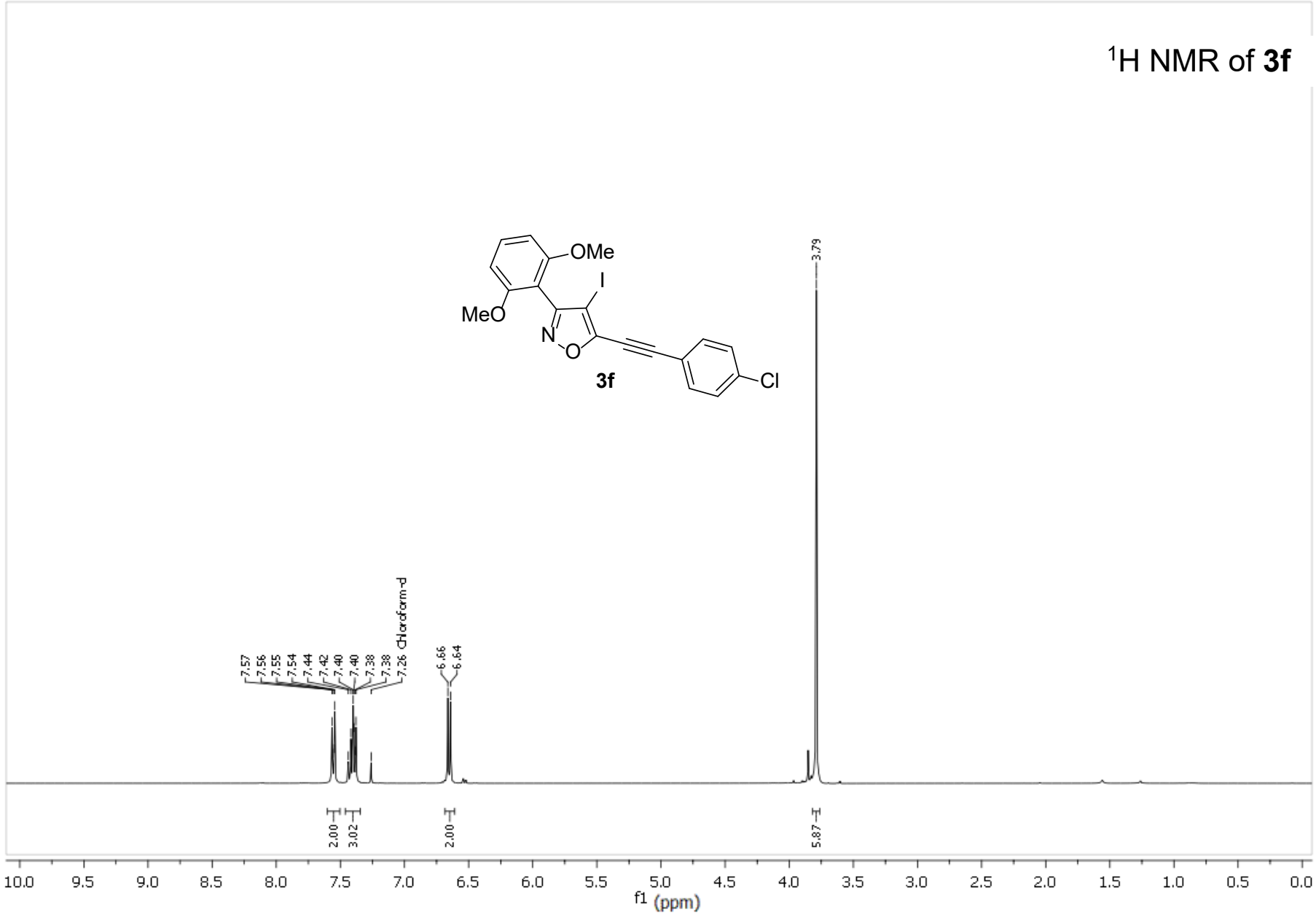

^{1}H NMR of **3e**
Cl
Cl
I
N
O
OH
3e
7.46
7.46
7.44
7.42
7.40
7.39
7.38
7.26
Chloroform-d
2.18
2.17
2.13
3.00
1.00
5.97
f1 (ppm)

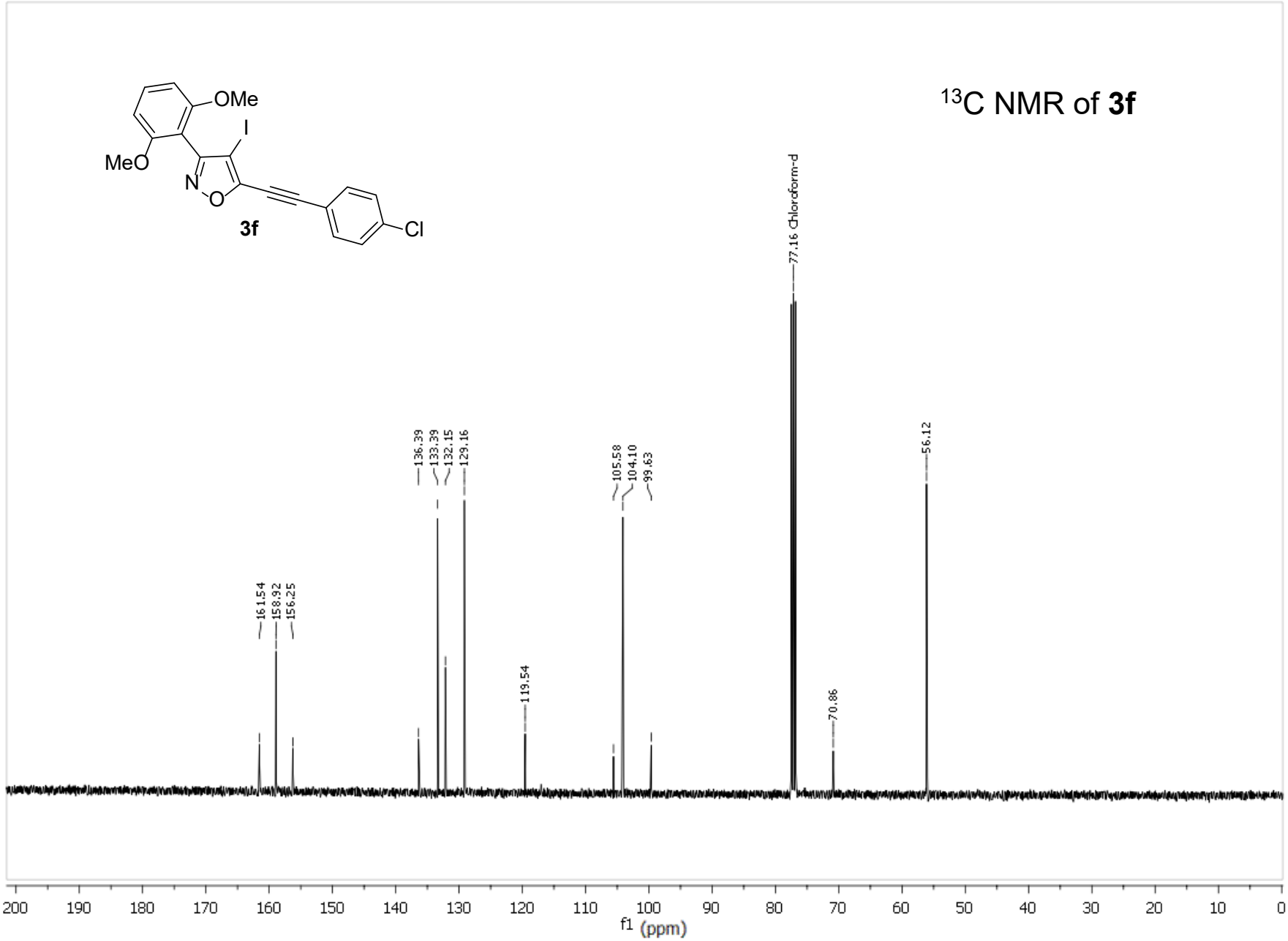

^{13}C NMR of **3e**
Cl
Cl
I
N
O
OH
3e
77.16 Chloroform-d
162.94
157.22
136.02
132.04
128.30
127.05
106.74
68.89
68.05
65.90
31.01
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

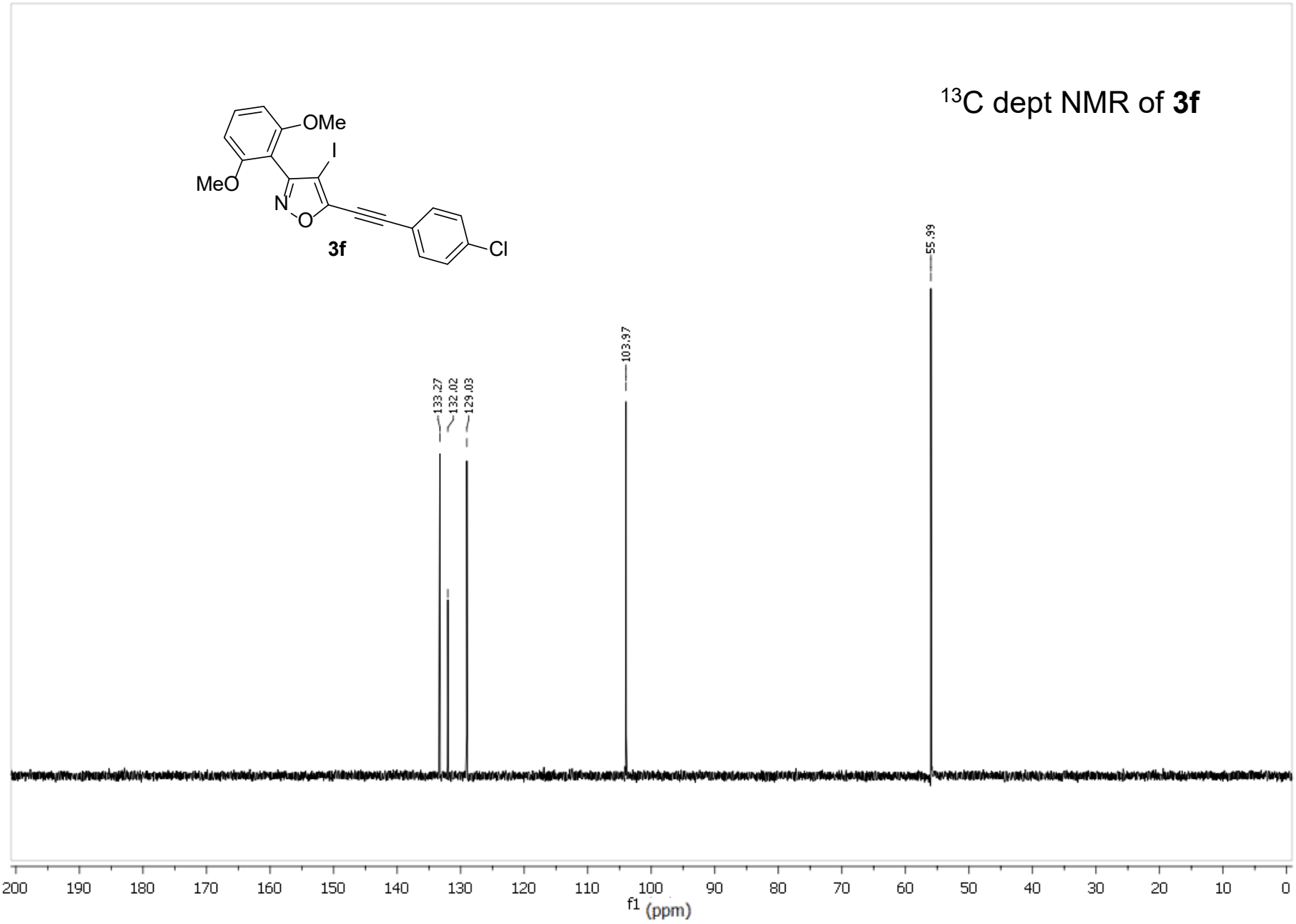
^{13}C dept NMR of **3e**

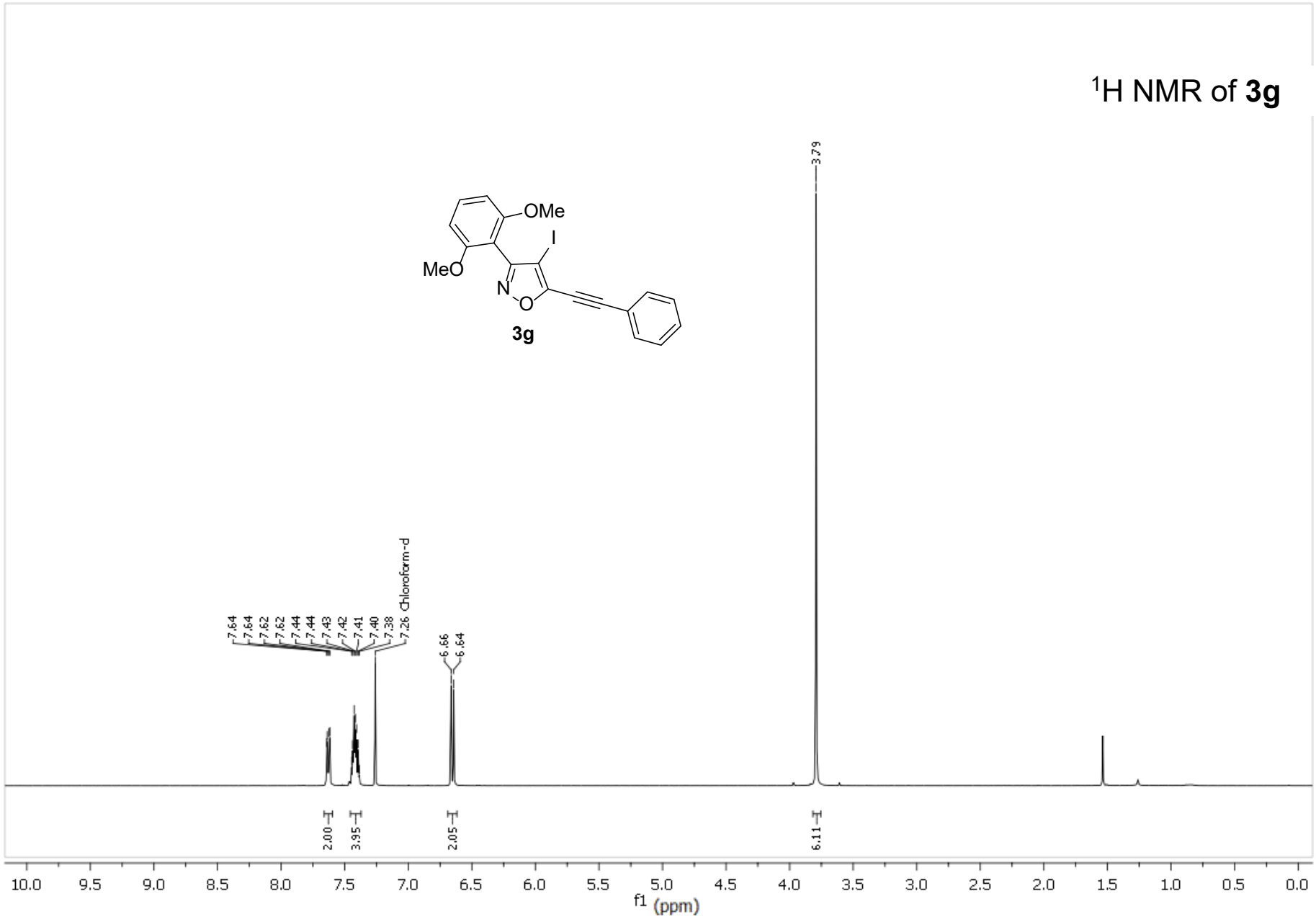


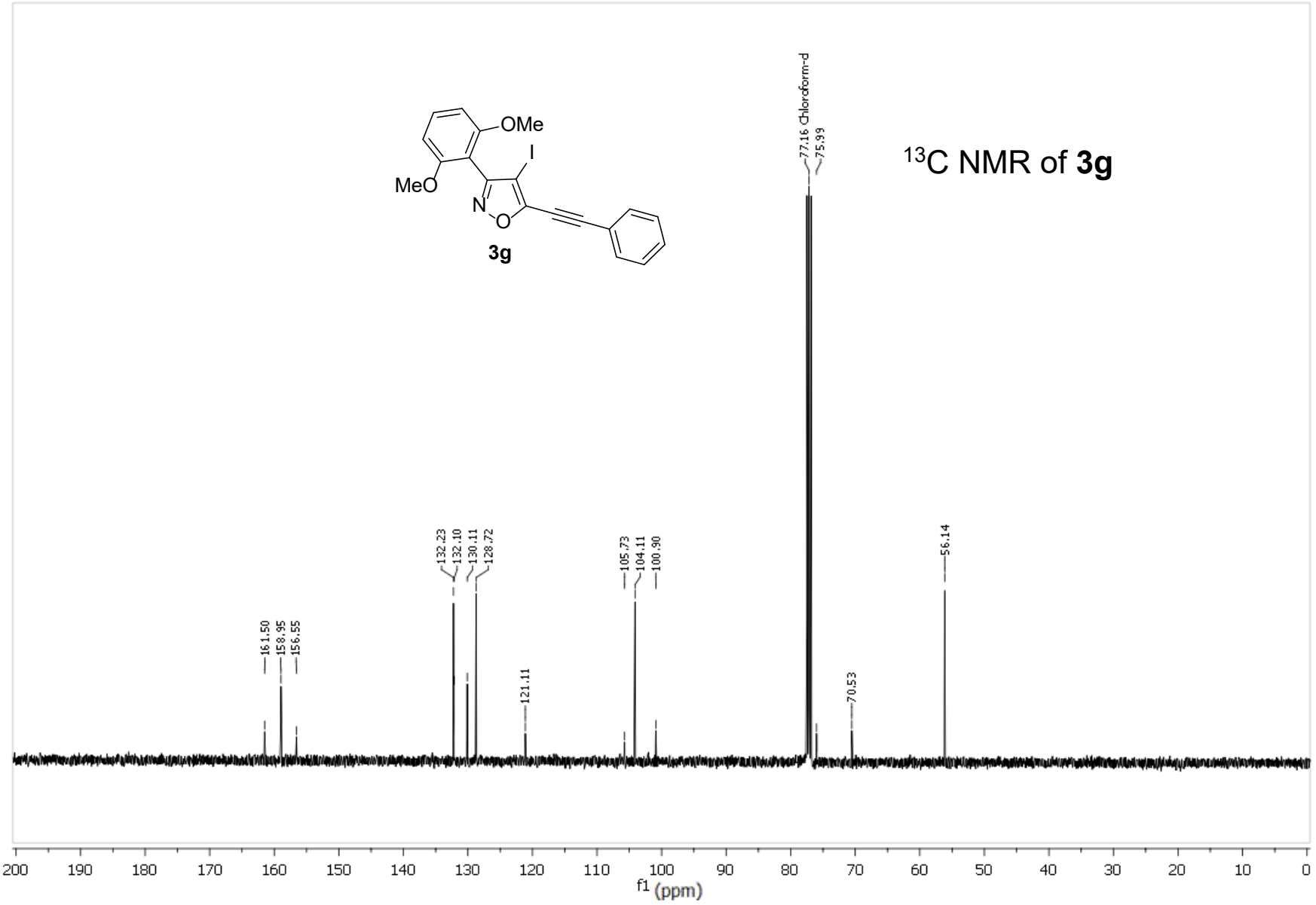
^{1}H NMR of **3f**

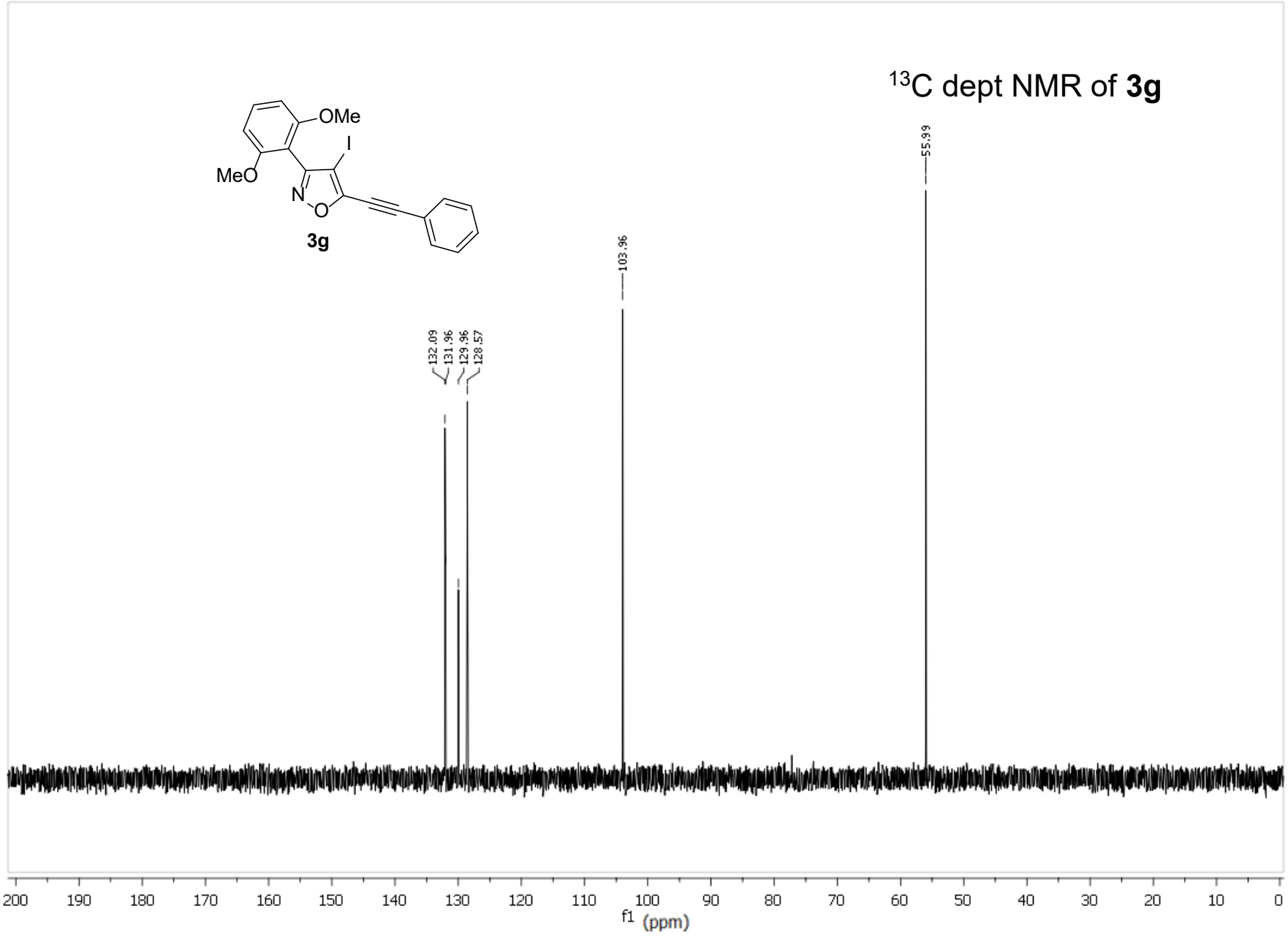

OMe
I
MeO
N
O
3f
Cl
3.79
7.57
7.56
7.55
7.54
7.44
7.42
7.40
7.40
7.38
7.38
7.26 Chloroform-d
6.66
6.64
2.00
3.02
2.00
5.87
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

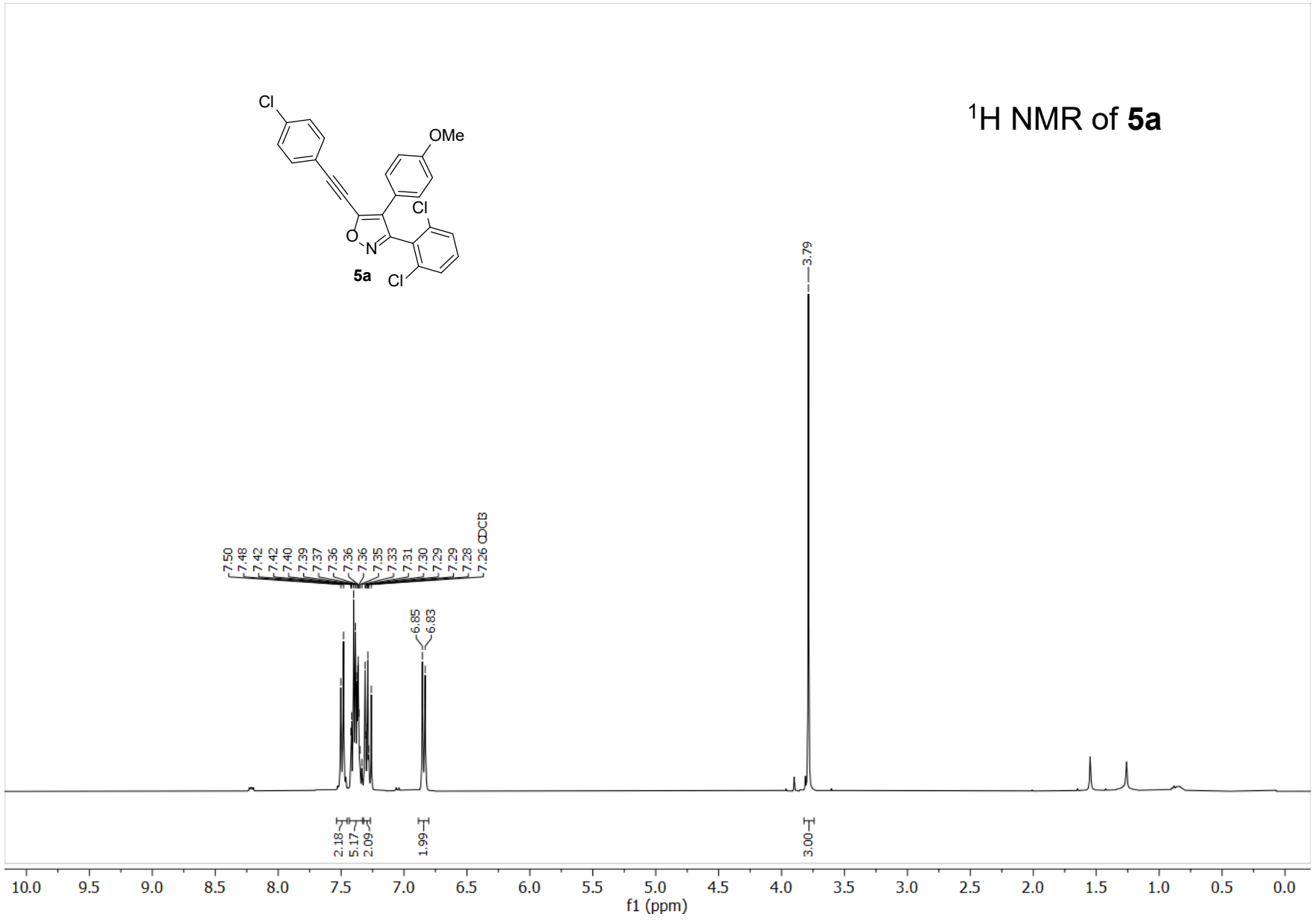

OMe
I
MeO
N
O
3f
Cl
^{13}C NMR of **3f**
77.16 Chloroform-d
136.39
133.39
132.15
129.16
105.58
104.10
99.63
56.12
161.54
158.32
156.25
119.54
70.86
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

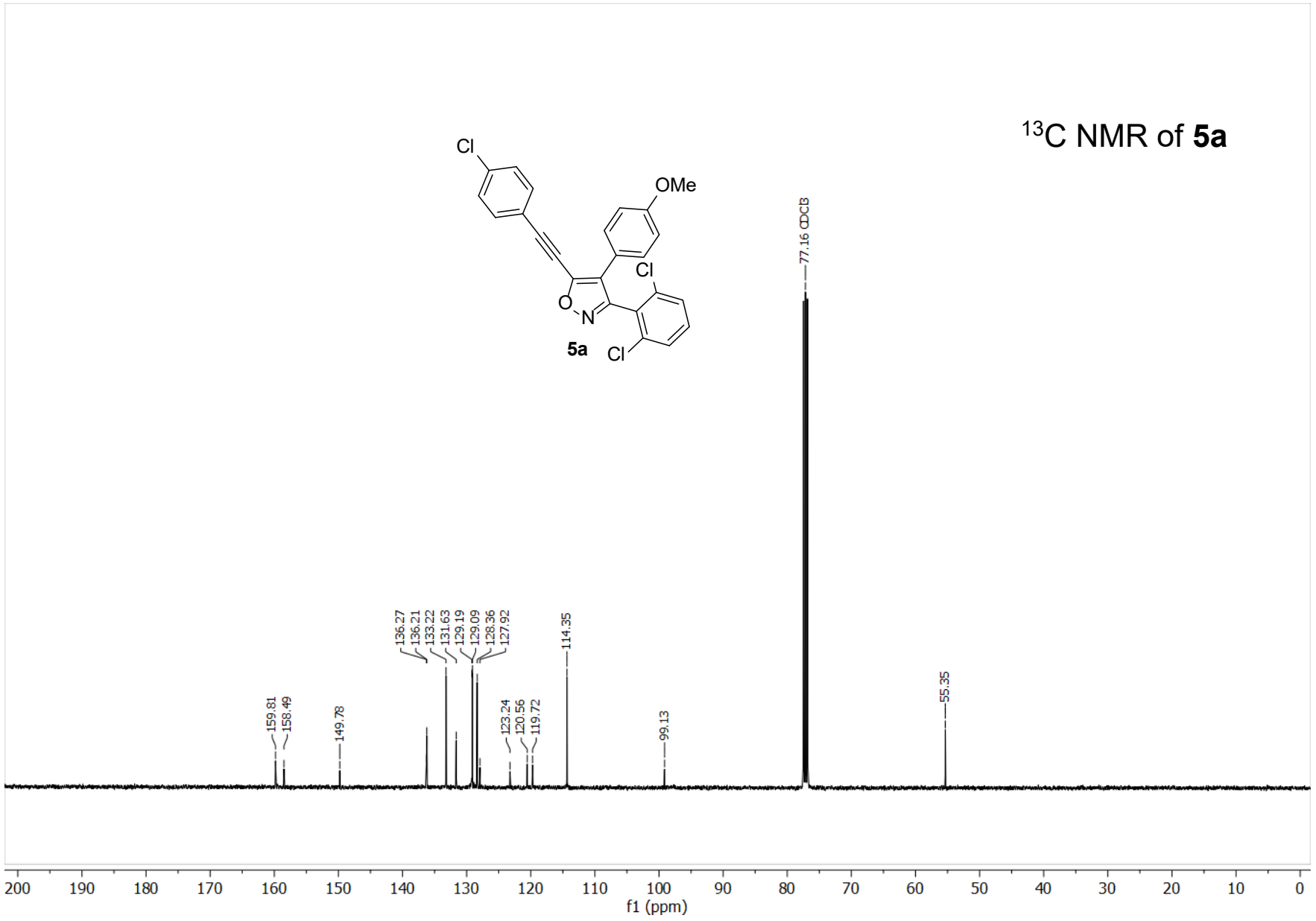

^{13}C dept NMR of **3f**
OMe
I
MeO
N
O
Cl
3f
55.99
103.97
133.27
132.02
129.03
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

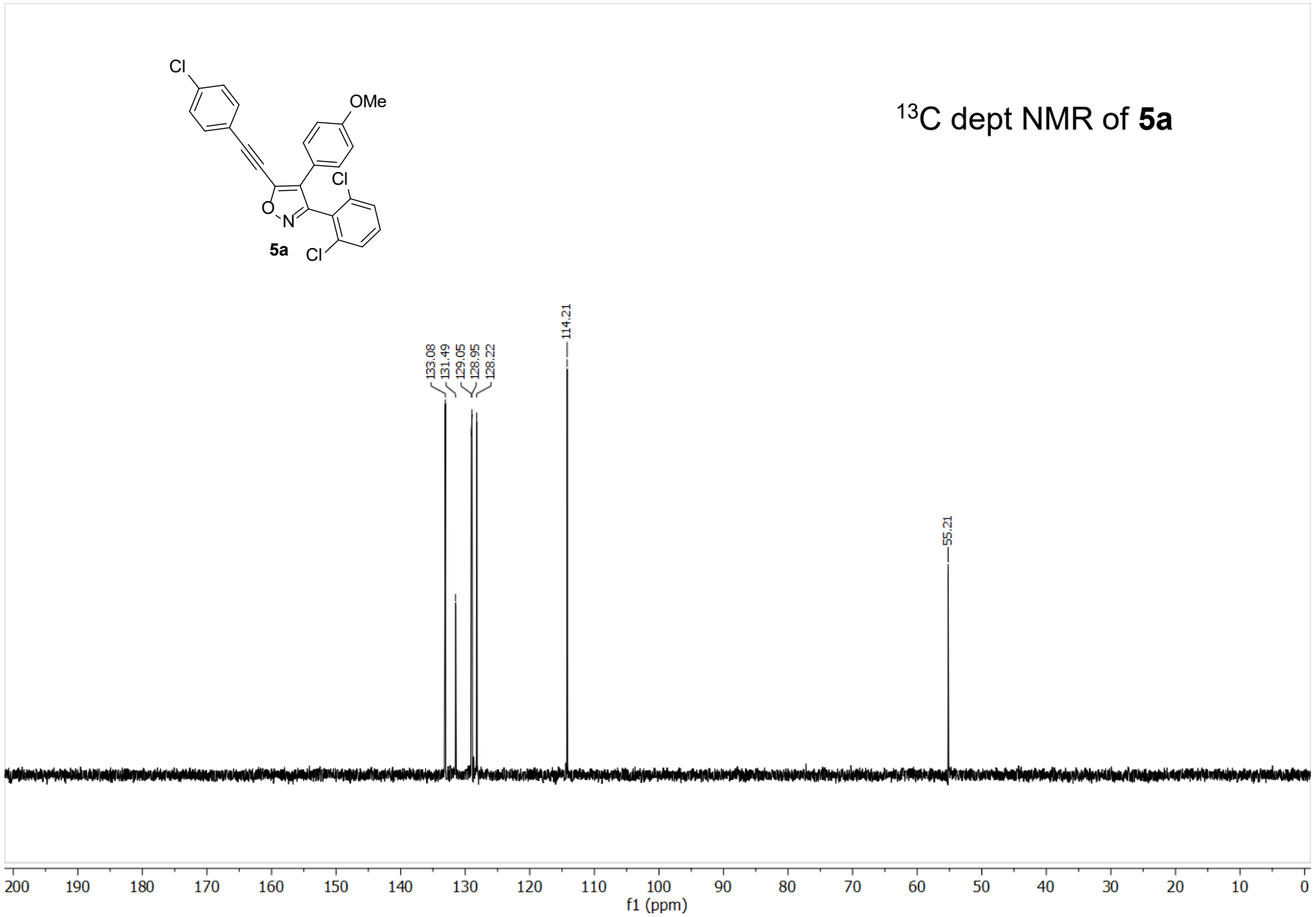

^{1}H NMR of **3g**
OMe
I
MeO
N
O
3g
3.79
Chloroform-d
7.64
7.64
7.62
7.62
7.44
7.44
7.43
7.42
7.41
7.40
7.38
7.26
6.66
6.64
2.00
3.95
2.05
6.11
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


OMe
I
MeO
N
O
3g
77.16 Chloroform-d
75.99
^{13}C NMR of **3g**
132.23
132.10
130.11
128.72
121.11
105.73
104.11
100.90
161.50
158.95
156.55
70.53
56.14
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

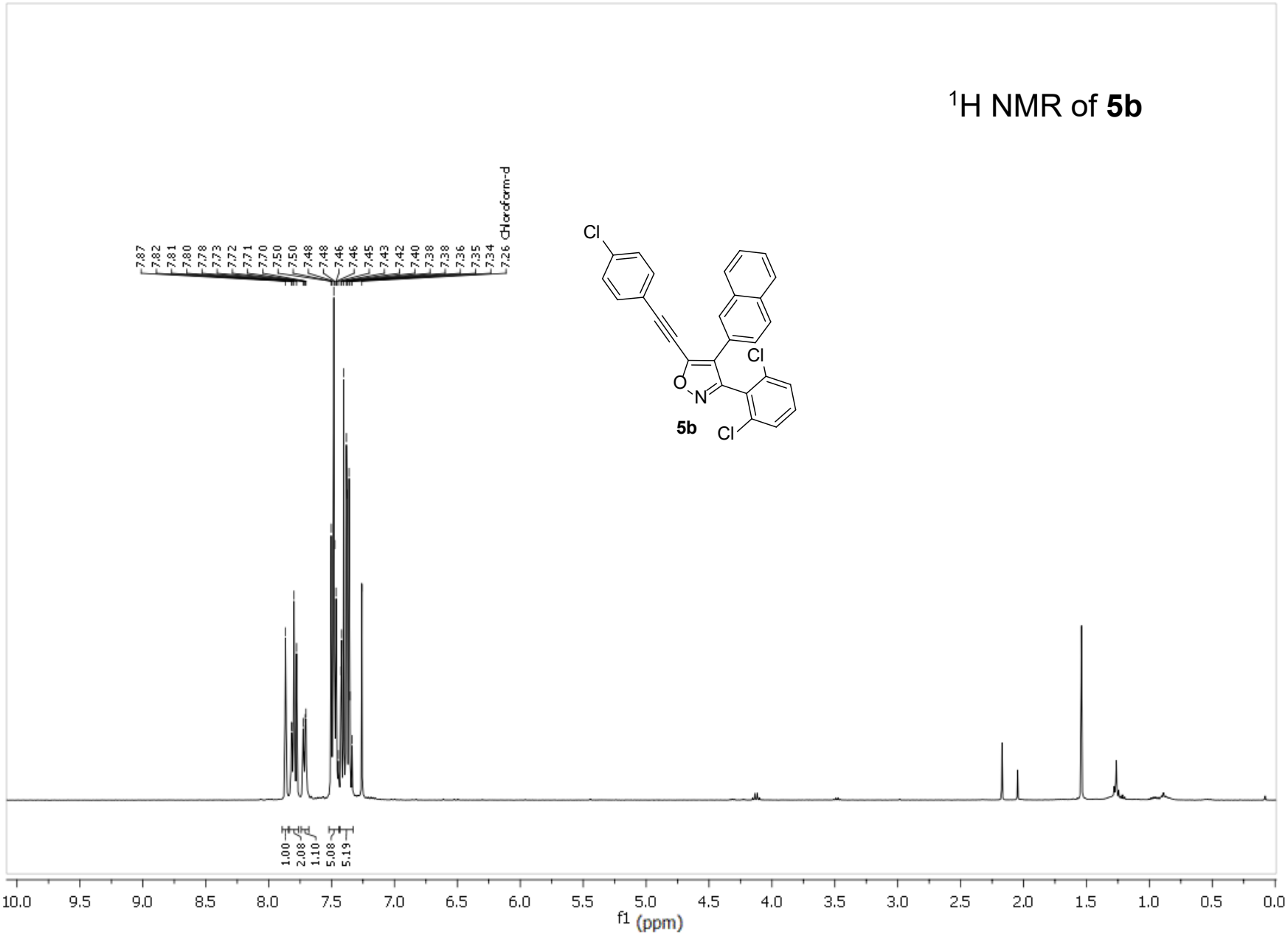

^{13}C dept NMR of **3g**
OMe
I
MeO
N
O
3g
55.99
103.96
132.09
131.96
129.96
128.57
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

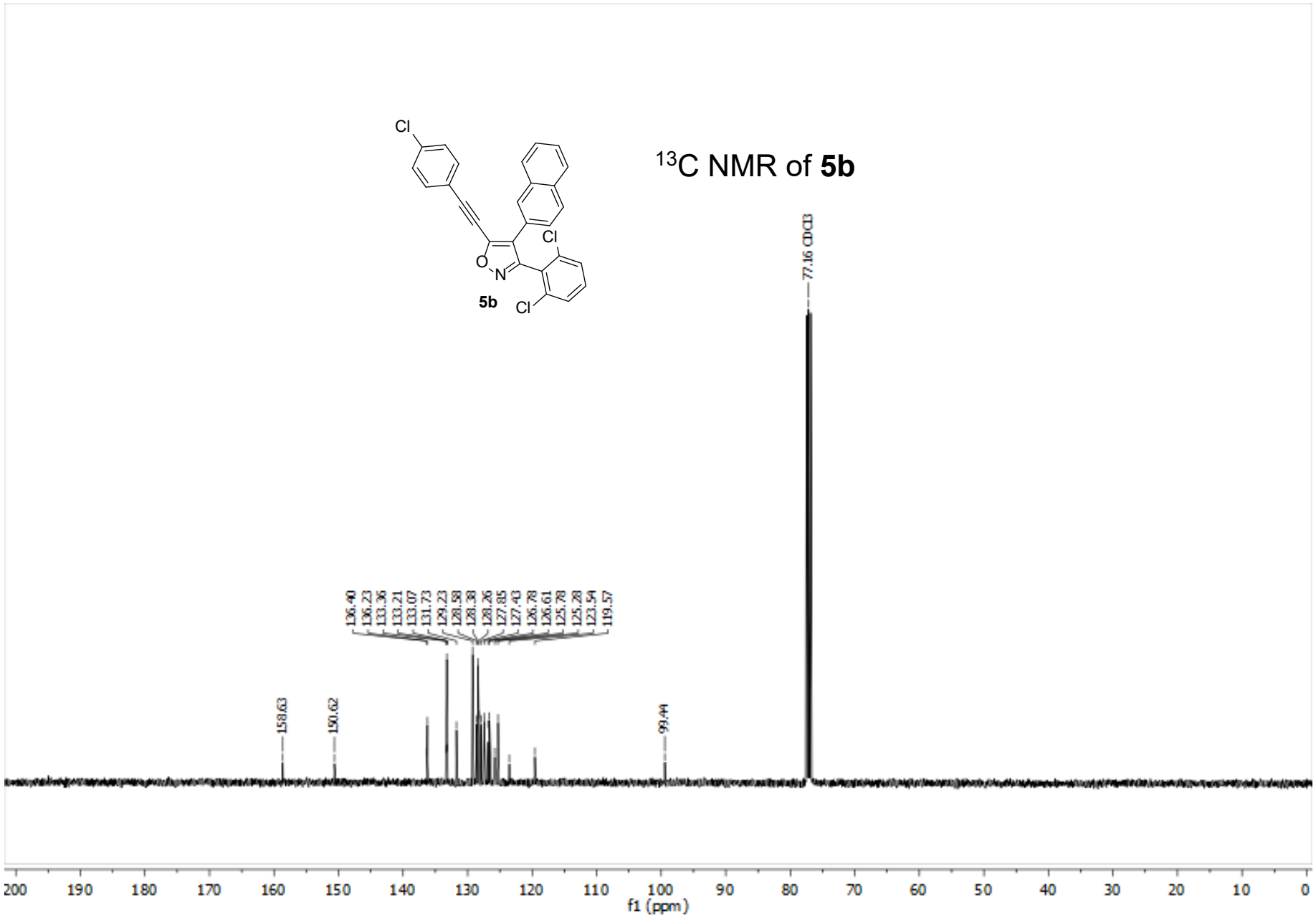

^{1}H NMR of **5a**
Cl
OMe
Cl
O
N
Cl
5a
3.79
7.50
7.48
7.42
7.42
7.40
7.39
7.37
7.36
7.36
7.36
7.35
7.33
7.31
7.30
7.29
7.29
7.28
7.26 CDCl3
6.85
6.83
2.18
5.17
2.09
1.99
3.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


^{13}C NMR of **5a**
Cl
OMe
Cl
O
N
Cl
5a
77.16 CDCl3
159.81
158.49
149.78
136.27
136.21
133.22
131.63
129.19
129.09
128.36
127.92
123.24
120.56
119.72
114.35
99.13
55.35
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

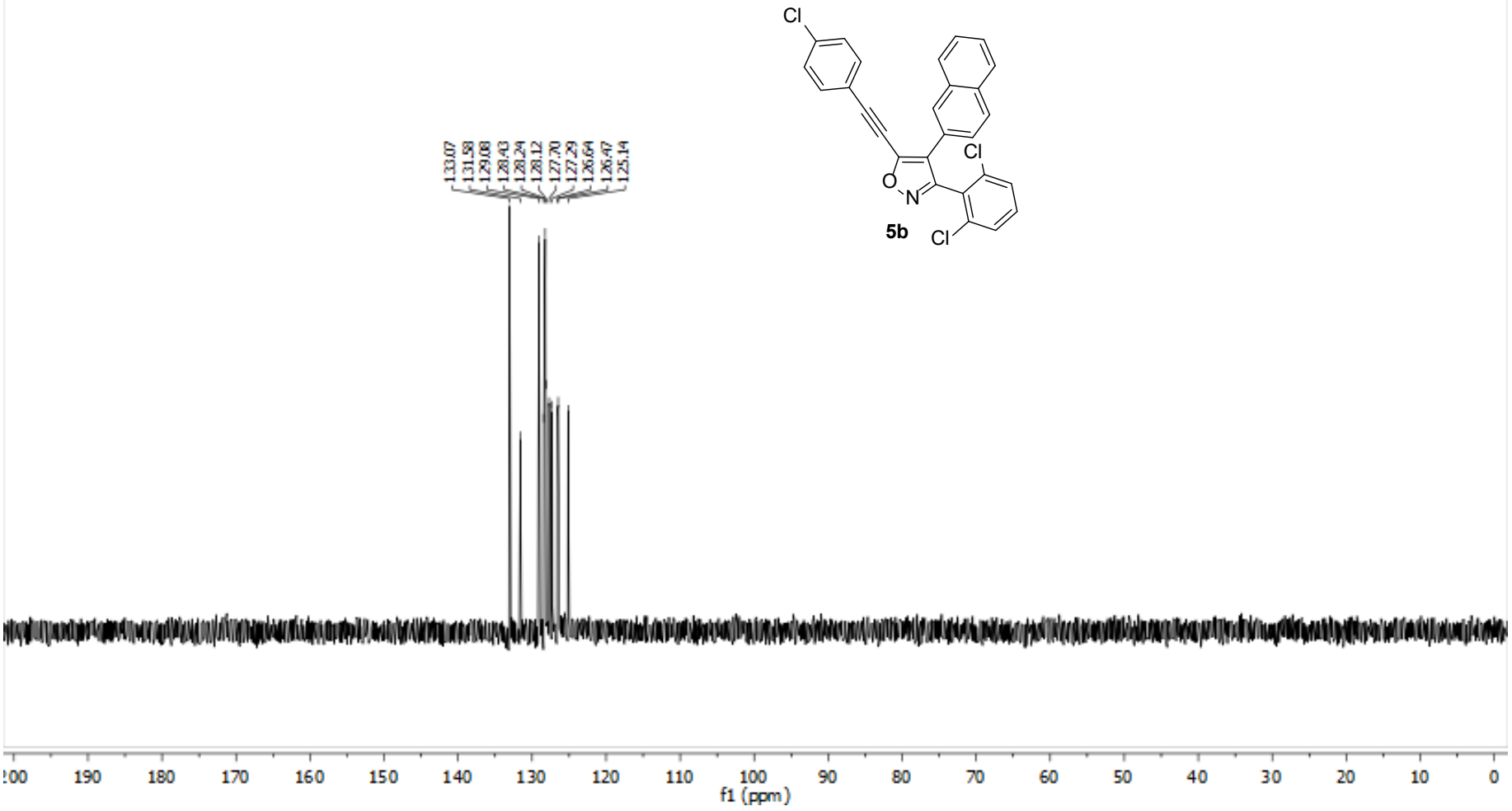


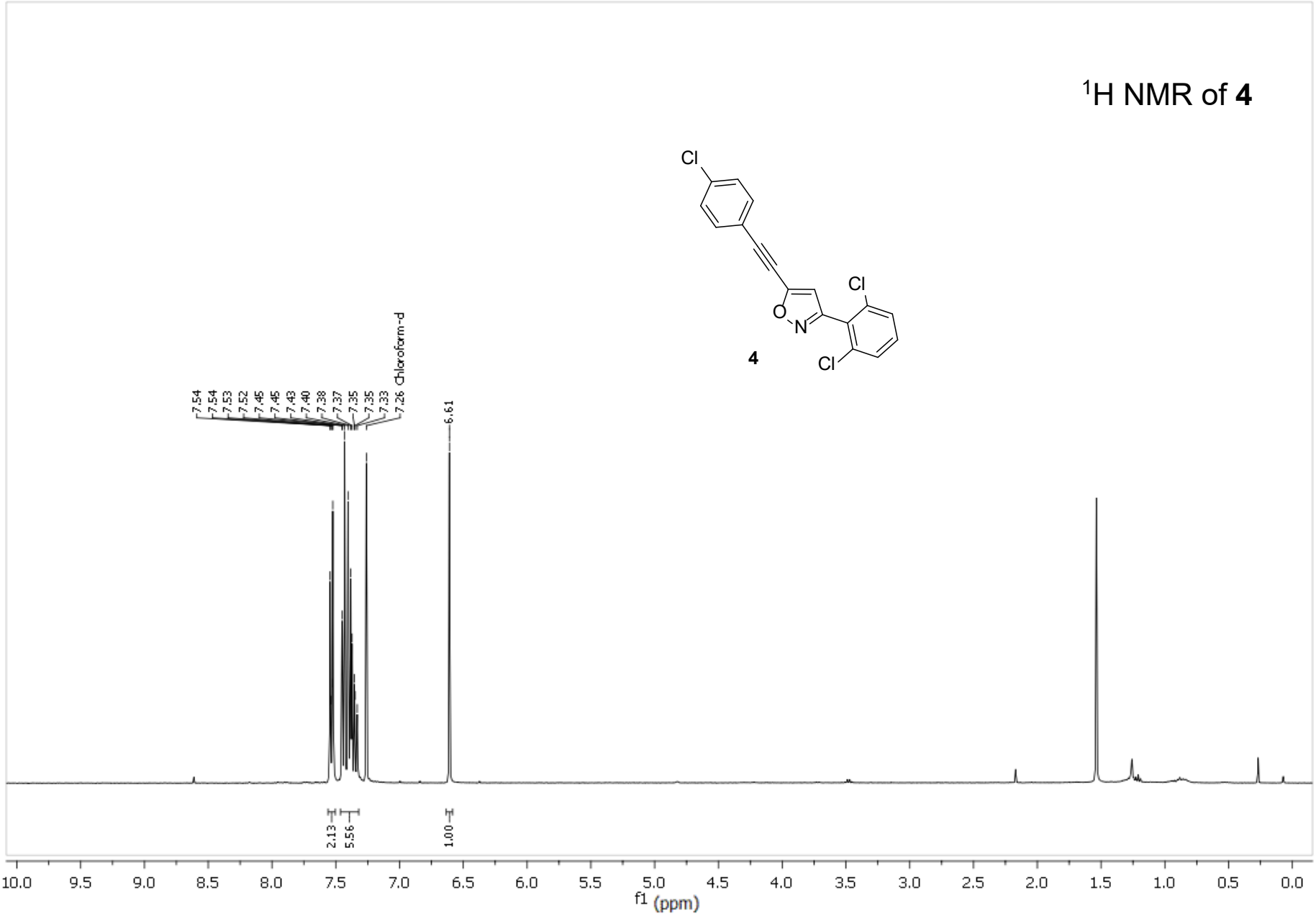
^{13}C dept NMR of **5a**

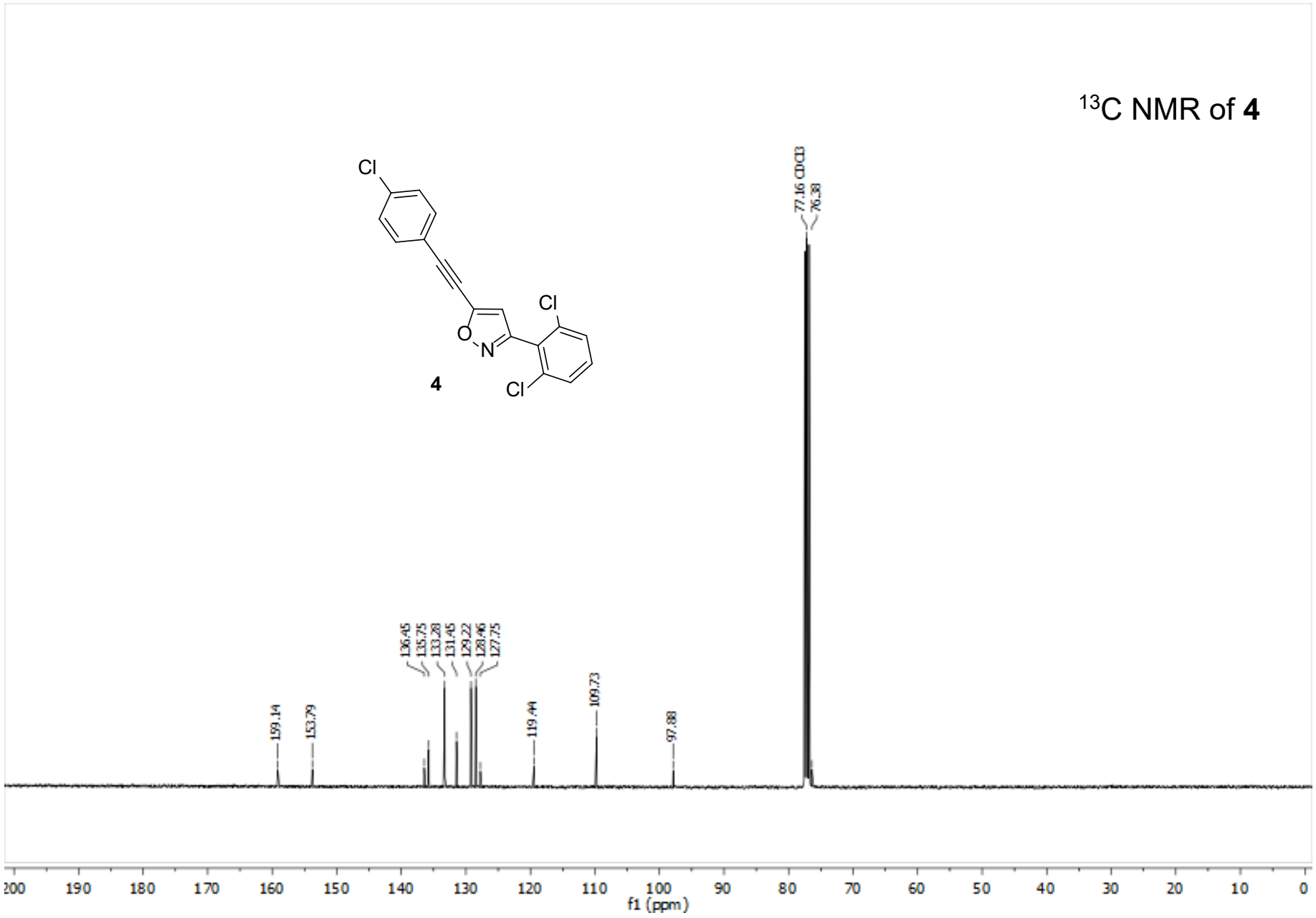

^{1}H NMR of **5b**
7.87
7.82
7.81
7.80
7.78
7.73
7.72
7.71
7.70
7.50
7.50
7.48
7.48
7.46
7.46
7.45
7.43
7.42
7.40
7.38
7.38
7.36
7.35
7.34
7.26
Chloroform-d
Cl
Cl
O
N
Cl
5b
1.00
2.08
1.10
5.08
5.19
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


Cl
Cl
O
N
Cl
5b
^{13}C NMR of **5b**
77.16 CDCl3
136.40
136.23
133.36
133.21
133.07
131.73
129.23
128.58
128.38
128.26
127.85
127.43
126.78
126.61
125.78
125.28
123.54
119.57
158.63
150.62
99.44
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

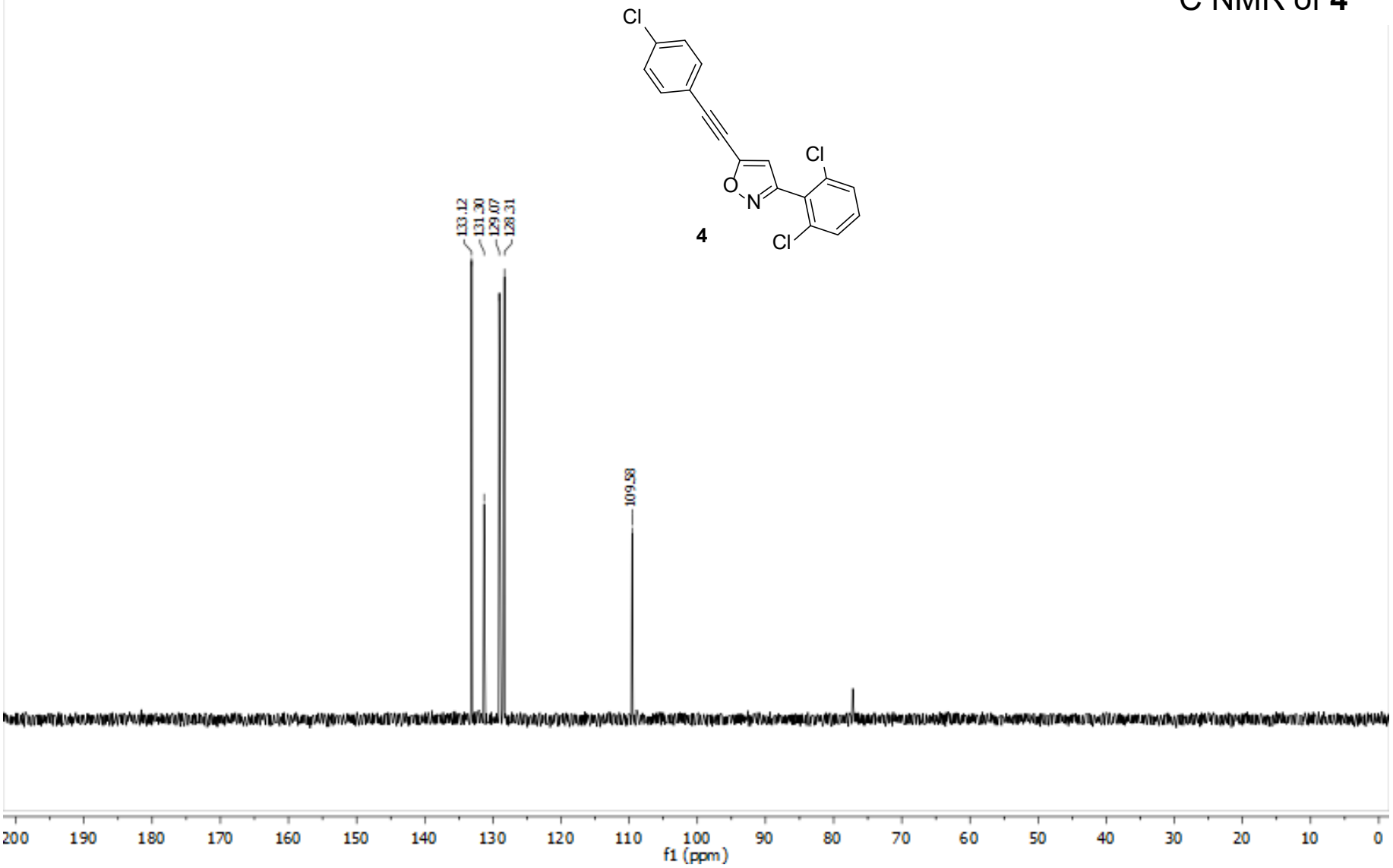
^{13}C dept NMR of **5b**



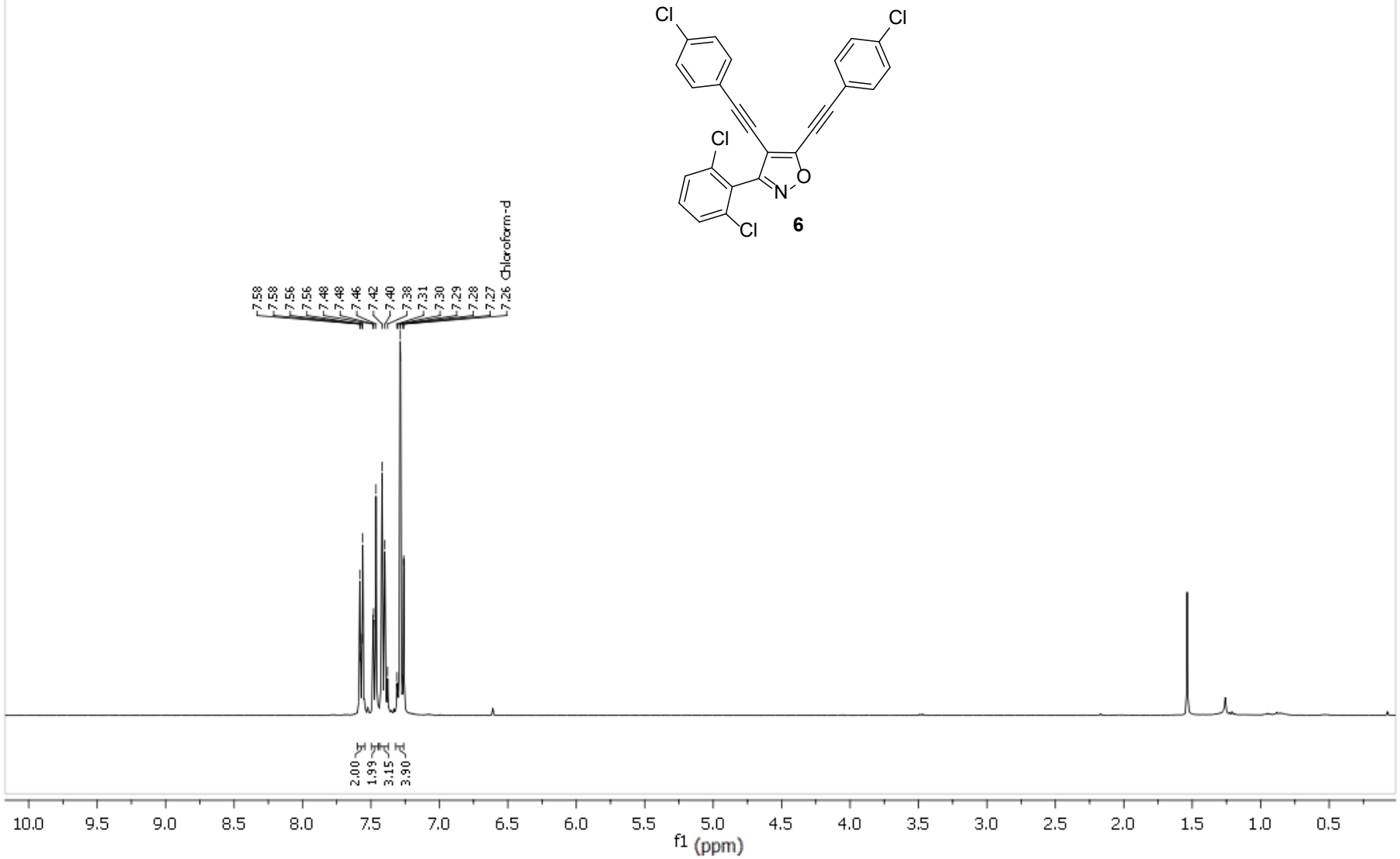

^{1}H NMR of **4**
Cl
Cl
O
N
Cl
4
7.54
7.54
7.53
7.52
7.45
7.45
7.43
7.40
7.38
7.37
7.35
7.35
7.33
7.26 Chloroform-d
6.61
2.13
5.56
1.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

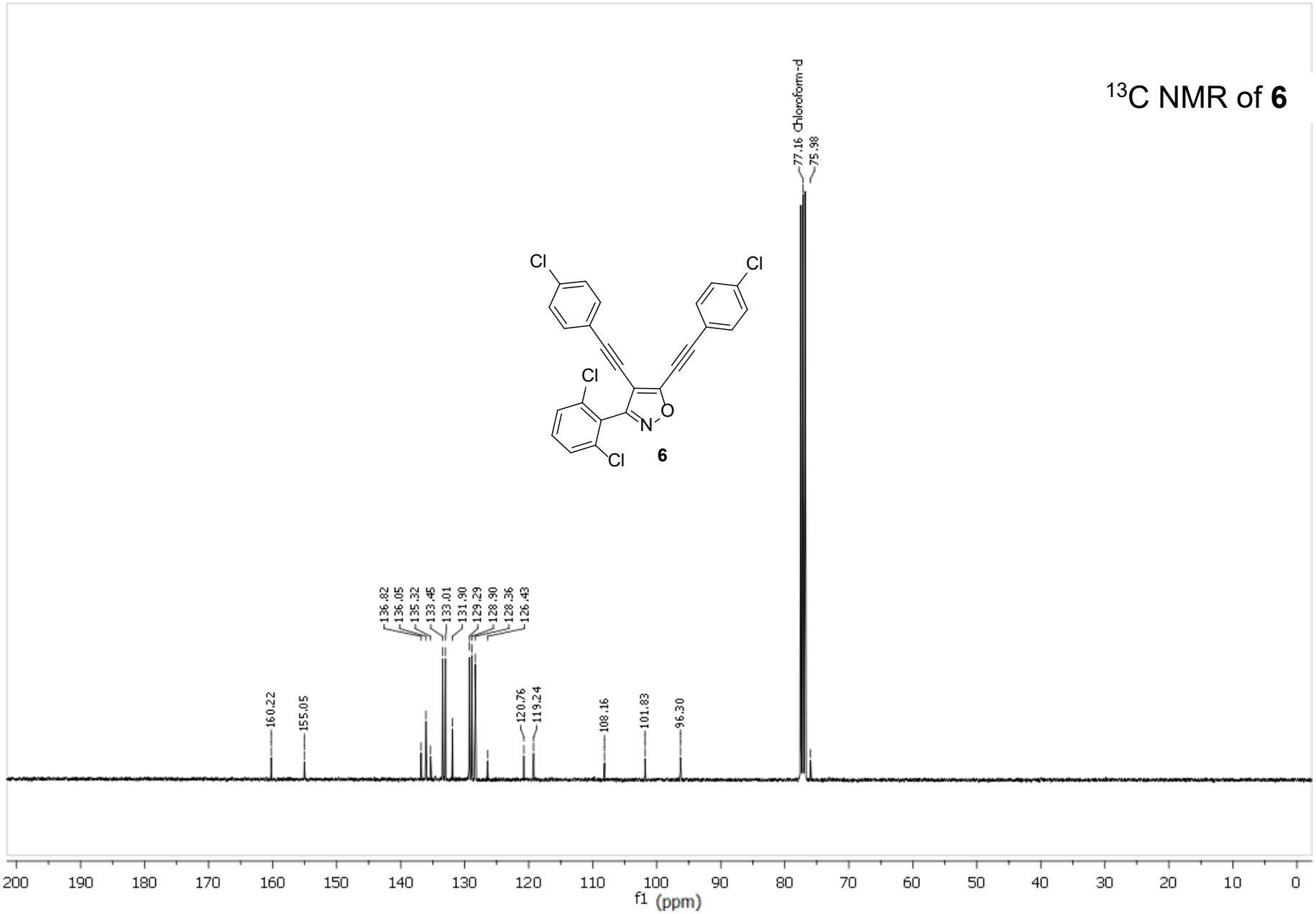

^{13}C NMR of **4**
Cl
O
N
Cl
Cl
4
77.16 CDCl3
76.38
159.14
153.79
136.45
135.75
133.28
131.45
129.22
128.46
127.75
119.44
109.73
97.88
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

^{13}C NMR of **4**


Cl
Cl
O
N
Cl
4
133.12
131.30
129.07
128.31
109.58
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

^{1}H NMR of **6**


Cl
Cl
Cl
Cl
N
O
6
7.58
7.58
7.56
7.56
7.48
7.48
7.46
7.42
7.40
7.38
7.31
7.30
7.29
7.28
7.27
7.26
Chloroform-d
2.00
1.99
3.15
3.90
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)


^{13}C NMR of **6**
77.16 Chloroform-d
75.98
Cl
Cl
Cl
Cl
O
N
6
136.82
136.05
135.32
133.45
133.01
131.90
129.29
128.90
128.36
126.43
160.22
155.05
120.76
119.24
108.16
101.83
96.30
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

^{13}C dept NMR of **6**