SUPPORTING INFORMATION

Copper-Catalyzed 1,2-Aminocyanation of Unactivated Alkenes via Cyano Migration

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I. General Methods

General Information. Glassware was dried either with a propane torch or in an oven at 140 °C for at least 12 h before cooling in a desiccator over Drierite. Optimization and substrate screens were performed in 1-Dram glass vials with Teflon-coated micro stir bars. All other reactions were performed in round-bottom flasks with rubber septa and Teflon-coated stir bars. Reaction mixtures were stirred and heated (if needed) using hot plate with magnetic stirrer. Plastic syringes were used for the transfer of pure solvents, while glass pipets were used for the transfer of crude reaction solutions. Thin-layer chromatography (TLC) was performed using aluminum plates pre-coated with 0.25 mm of 230–400 mesh silica gel impregnated with a fluorescent indicator (254 nm). TLC plates were visualized by exposure to ultraviolet light and/or exposure to either $KMnO_4$ or vanillin stain. Organic solutions were concentrated *in vacuo* using a rotary evaporator. Column chromatography was performed with silica gel (60 Å, standard grade).

Material. Commercial reagents and anhydrous solvents were used as received. Specific anhydrous solvents (Et_2O, CH_2Cl_2, and THF) were obtained from a departmentally-maintained Innovative Technologies solvent purification system. Cyanohydrins and *O*-Benzoylhydroxylamines used as starting materials were prepared according to reported procedures.[1, 2]

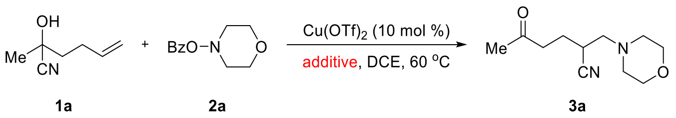
Instrumentation. Nuclear magnetic resonance spectra were recorded at ambient temperature on 400 MHz or 500 MHz spectrometers. All values for proton chemical shifts are reported in parts per million (ppm, δ) and are referenced to the residual protium in $CDCl_3$ (δ 7.26). All values for carbon chemical shifts are reported as total carbons in parts per million (ppm, δ) and referenced to the carbon resonances of $CDCl_3$ (δ 77.0). NMR data are represented as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, m = multiplet, br = broad), coupling constant (Hz), and integration. Infrared spectroscopic data are reported in wavenumbers (cm^{-1}) with selected peaks shown. High-resolution mass spectra were obtained through the Duke University Mass Spectrometry Facility using an Agilent 6224 TOF liquid chromatography-electrospray ionization mass spectrometer.

II. Condition Optimization for 1,2-Aminocyanation

Procedures for optimization screening

To a 1-Dram vial, was added alkene **1a** (26.9 µL, 0.2 mmol, 1.0 equiv), *O*-benzoylhydroxylamine **2a** (82.9 mg, 2.0 equiv), $Cu(OTf)_2$ (7.2 mg, 0.1 equiv), $TsOH·H_2O$ (57.1 mg, 1.5 equiv), and DCE (1.0 mL). The vial was capped and stirred with a Teflon-coated stir bar. The mixture was then stirred and heated until *O*-benzoylhydroxylamine was consumed based on TLC analysis (20% EtOAc–hexanes). The resulting reaction mixture was cooled to room temperature, filtered through activated basic Al_2O_3 (Brockman Grade I, 58–60Å mesh powder) and concentrated *in vacuo* to yield the crude product. To determine yields by ^1H NMR spectroscopy, 0.75 mL $CDCl_3$ was added to the crude reaction mixture, upon which dibromomethane (7.0 µL, 0.2 mmol) was added by 10-µL microsyringe.

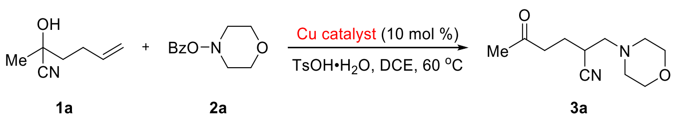
Table S1. Additive screening for aminocyanation.



entry	additive	**3a** (%)[a]
1	-	7
2	PPTS	18
3	Pyridine	ND
4	DIPEA	ND
5	HCOOH	16
6	BzOH	13
7	AcOH	11
8	K_2CO_3	5
9	TfOH	36
10	NaOTf	8
11	$TsOH·H_2O$	49
12	MsOH	33

Reaction conditions: **1a** (0.2 mmol, 1.0 equiv), **2a** (2.0 equiv), $Cu(OTf)_2$ (10 mol %), additive (1.0 equiv), and DCE (1 mL). [a]Yields determined by 400 MHz ^1H NMR spectroscopy with CH_2Br_2 as an internal standard.

Table S2. Copper catalyst screening for aminocyanation.

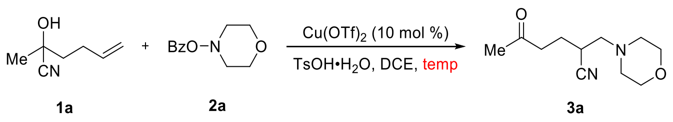


entry	Cu catalyst	**3a** (%)[a]
1	$Cu(OTf)_2$	45
2	$[Cu(OTf)]_2·tol$	27
3	CuOAc	34
4	$Cu(OAc)_2$	41
5	$Cu(eh)_2$	31
6	$Cu(acac)_2$	35

7	CuCl	37
8	$CuCl_2$	28
9	CuBr	34
10	CuF_2	35
11	CuI	30
12	CuCN	39

Reaction conditions: **1a** (0.2 mmol, 1.0 equiv), **2a** (2.0 equiv), Cu catalyst (10 mol %), TsOH·H_2O (1.0 equiv), and DCE (1 mL). [a]Yields determined by 400 MHz ^{1}H NMR spectroscopy with CH_2Br_2 as an internal standard.

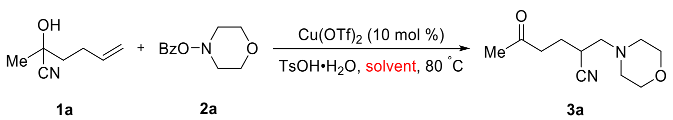
Table S3. Temperature screening for aminocyanation.



entry	temp (°C)	**3a** (%)[a]
1	RT	22
2	40	37
3	60	37
4	80	48
5	100	41

Reaction conditions: **1a** (0.2 mmol, 1.0 equiv), **2a** (2.0 equiv), $Cu(OTf)_2$ (10 mol %), TsOH·H_2O (1.0 equiv), and DCE (1 mL). [a]Yields determined by 500 MHz ^{1}H NMR spectroscopy with CH_2Br_2 as an internal standard.

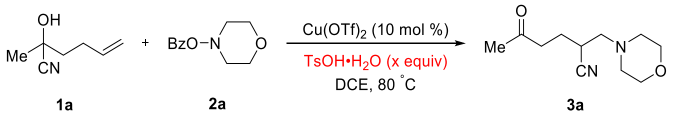
Table S4. Solvent screening for aminocyanation.



entry	solvent	**3a** (%)[a]
1	DCE	48
2	DME	16
3	1,4-Dioxane	25
4	EtOH	16
5	DMF	19
6	MeCN	9
7	THF	7

Reaction conditions: **1a** (0.2 mmol, 1.0 equiv), **2a** (2.0 equiv), $Cu(OTf)_2$ (10 mol %), TsOH·H_2O (1.0 equiv), and solvent (1 mL). [a]Yields determined by 500 MHz ^{1}H NMR spectroscopy with CH_2Br_2 as an internal standard.

Table S5. Additive loading screening for aminocyanation.

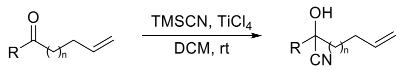


entry	TsOH·H_2O (equiv)	**3a** (%)[a]
1	0.1	15
2	0.5	36
3	1.0	45
4	1.5	59 (61)[b]
5	2.0	51

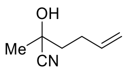
Reaction conditions: **1a** (0.2 mmol, 1.0 equiv), **2a** (2.0 equiv), TsOH·H_2O (x equiv), $Cu(OTf)_2$ (10 mol %), and DCE (1 mL). [a]Yields determined by 500 MHz ^1H NMR spectroscopy with CH_2Br_2 as an internal standard. [b]Isolation yield in parentheses.

III. Compound Characterization of Unsaturated Cyanohydrins

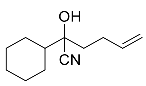
Unsaturated cyanohydrins were prepared following the literature procedure as described below.[1]



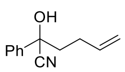
To a stirring solution of ketone (1.0 equiv) in DCM (0.5 M), was added TMSCN (1.2 equiv) and $TiCl_4$ (0.2 equiv) in sequence under N_2. The reaction mixture was allowed to stir at room temperature until the completion of the reaction. To the reaction mixture, was then added a solution of acetonitrile (0.2 M) followed by the same volumn of HCl (2 M). The mixture was stirred at room temperature for 1 h, and then was diluted with water (10 mL/mmol M). The mixture was extracted with EtOAc (10 mL/mmol x 3). The combined organic layers were washed with brine (10 mL/mmol), dried with Na_2SO_4, and filtered. The filtrate was concentrated *in vacuo*. The crude cyanohydrin was purified or used as a crude as below. The isolation yields depend much on the instability of cyanohydrin products, ranging from 9–83% yields.



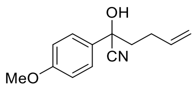
2-Hydroxy-2-methylhex-5-enenitrile (1a). Isolated by flash column chromatography (5% EtOAc–hexanes to 10% EtOAc–hexanes), as a pale-yellow oil. ^1H NMR ($CDCl_3$, 500 MHz): δ 5.87 (ddt, J = 17.0, 10.2, 6.6 Hz, 1H), 5.16 (dd, J = 17.0, 0.9 Hz, 1H), 5.07 (dd, J = 10.2, 0.9 Hz, 1H), 2.67–2.59 (m, 1H), 2.43–2.28 (m, 2H), 1.88 (t, J = 8.0 Hz, 2H), 1.62 (s, 3H); ^{13}C NMR ($CDCl_3$, 126 MHz): δ 136.7, 121.7, 116.4, 68.7, 40.5, 28.7, 27.9; FTIR (thin film): 3435, 2987, 2937, 2242, 1377, 1128, 916 cm^{-1}; HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_7H_{11}NONa^+$ 148.0733; Found: 148.0731.



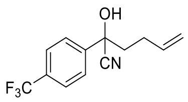
2-Cyclohexyl-2-hydroxyhex-5-enenitrile (1b). Isolated by flash column chromatography (5% EtOAc–hexanes to 10% EtOAc–hexanes), as a pale-yellow oil. ^1H NMR ($CDCl_3$, 500 MHz): δ 5.88 (ddt, J = 17.0, 10.3, 6.7 Hz, 1H), 5.16 (dd, J = 17.0, 1.5 Hz, 1H), 5.07 (dd, J = 10.3, 1.5 Hz, 1H), 2.44 (s, 1H), 2.42–2.31 (m, 2H), 1.97–1.77 (m, 6H), 1.72–1.70 (m, 1H), 1.59 (tt, J = 11.6, 3.0 Hz, 1H), 1.32–1.13 (m, 5H). The spectroscopic data match those reported previously.[3]



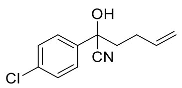
2-Hydroxy-2-phenylhex-5-enenitrile (1c). Obtained as a pale-yellow oil and used as a crude for the 1,2-aminocyanation reaction. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.58–7.56 (m, 2H), 7.45–7.38 (m, 3H), 5.81 (ddt, *J* = 17.1, 10.2, 6.1 Hz, 1H), 5.08 (dd, *J* = 17.1, 1.5 Hz, 1H), 5.02 (dd, *J* = 10.2, 1.5 Hz, 1H), 2.96 (s, 1H), 2.39–2.31 (m, 1H), 2.23–2.14 (m, 2H), 2.13–2.03 (m, 1H). The spectroscopic data match those reported previously.[3]



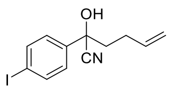
2-Hydroxy-2-(4-methoxyphenyl)hex-5-enenitrile (1d). Isolated by flash column chromatography (5% EtOAc–hexanes to 10% EtOAc–hexanes), as a pale-yellow oil. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.49 (d, *J* = 8.8 Hz , 2H), 6.93 (d, *J* = 8.8 Hz, 2H), 5.80 (ddt, *J* = 16.9, 10.4, 6.4 Hz, 1H), 5.08 (dd, *J* = 16.9, 1.0 Hz, 1H), 5.01 (dd, *J* = 10.4, 1.0 Hz, 1H), 3.83 (s, 3H), 2.86 (s, 1H), 2.36–2.31 (m, 1H), 2.20–2.13 (m, 2 H), 2.08–2.04 (m, 1H). The spectroscopic data match those reported previously.[3]



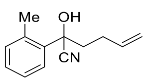
2-Hydroxy-2-(4-(trifluoromethyl)phenyl)hex-5-enenitrile (1e). Obtained as a pale-yellow oil and used as a crude for the 1,2-aminocyanation reaction. ^{1}H NMR ($CDCl_3$, 500 MHz): 7.70 (br s, 4H), 5.81 (ddt, *J* = 17.0, 10.3, 6.6 Hz, 1H), 5.12 (d, *J* = 17.0 Hz, 1H), 5.06 (d, *J* = 10.3 Hz, 1H), 3.14 (br, 1H), 2.40–2.33 (m, 1H), 2.27–2.23 (m, 1H), 2.21–2.06 (m, 2H). The spectroscopic data match those reported previously.[3]



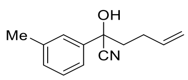
2-(4-Chlorophenyl)-2-hydroxyhex-5-enenitrile (1f). Obtained as a pale-yellow oil and used as a crude for the 1,2-aminocyanation reaction. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.51 (d, *J* = 8.5 Hz, 2H), 7.41 (d, *J* = 8.5 Hz, 2H), 5.80 (ddt, *J* = 17.0, 10.5, 6.1 Hz, 1H), 5.10 (d, *J* = 17.0 Hz, 1H), 5.04 (d, *J* = 10.5 Hz, 1H), 2.39–2.29 (m, 1H), 2.23–2.03 (m, 3H). The spectroscopic data match those reported previously.[3]



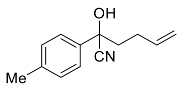
2-Hydroxy-2-(4-iodophenyl)hex-5-enenitrile (1g). Isolated by flash column chromatography (7% EtOAc–hexanes to 10% EtOAc–hexanes), as a pale-yellow solid. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.76 (d, *J* = 8.4 Hz, 2H), 7.30 (d, *J* = 8.4 Hz, 2H), 5.80 (ddt, *J* = 16.9, 10.3, 6.4 Hz, 1H), 5.09 (dd, *J* = 16.9, 1.0 Hz, 1H), 5.04 (dd, *J* = 10.3, 1.0 Hz, 1H), 3.08–2.01 (m, 1H), 2.37–2.30 (m, 1H), 2.23–2.09 (m, 2H), 2.07–2.01 (m, 1H); ^{13}C NMR ($CDCl_3$, 126 MHz): δ 139.5, 138.0, 136.3, 126.8, 120.1, 116.4, 95.1, 74.2, 42.5, 28.7; FTIR (thin film): 3412, 2245, 1485, 1394, 1064, 1006, 917, 821 cm^{-1}. HRMS (ESI) m/z: $[M-(HCN)+H]^+$ Calcd for $C_{11}H_{12}IO^+$ 286.9927; Found: 286.9933. HRMS data of this compound was only obtainable as the fragment ion with the loss of HCN due to its instability. The presence of nitrile and hydroxy group is confirmed by ^{13}C NMR and FTIR.



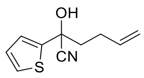
2-Hydroxy-2-(*o*-tolyl)hex-5-enenitrile (1h). Isolated by flash column chromatography (5% EtOAc–hexanes), as a yellow oil. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.61 (d, *J* = 8.0 Hz, 1H), 7.30–7.27 (m, 1H), 7.24–7.22 (m, 2H), 5.84 (ddt, *J* = 17.1, 10.2, 6.5 Hz, 1H), 5.11 (dd, *J* = 17.1, 1.2 Hz, 1H), 5.04 (dd, *J* = 10.2, 1.2 Hz, 1H), 2.91 (s, 1H), 2.58 (s, 3H), 2.41–2.25 (m, 2H), 2.23–2.16 (m, 2H). The spectroscopic data match those reported previously.[3]



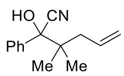
2-Hydroxy-2-(*m*-tolyl)hex-5-enenitrile (1i). Isolated by flash column chromatography (5% EtOAc–hexanes to 10% EtOAc–hexanes), as a yellow oil. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.37–7.35 (m, 2H), 7.31 (t, *J* = 7.5 Hz, 1H), 7.20 (d, *J* = 7.5 Hz, 1H), 5.81 (ddt, *J* = 16.9, 10.2, 6.2 Hz, 1H), 5.08 (dd, *J* = 16.9, 1.5 Hz, 1H), 5.02 (dd, *J* = 10.2, 1.5 Hz, 1H), 2.96–2.92 (m,1H), 2.39 (s, 3H), 2.38–2.30 (m, 1H), 2.23–2.13 (m, 2H), 2.11–2.04 (m, 1H). The spectroscopic data match those reported previously.[3]



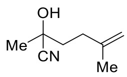
2-Hydroxy-2-(*p*-tolyl)hex-5-enenitrile (1j). Isolated by flash column chromatography (5% EtOAc–hexanes), as a yellow oil. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.44 (d, *J* = 7.9 Hz, 2H), 7.23 (d, *J* = 7.9 Hz, 2H), 5.84–5.75 (m, 1H), 5.07 (d, *J* = 17.1 Hz, 1H), 5.01 (d, *J* = 10.2 Hz, 1H), 2.99 (s, 1H), 2.37 (s, 3H), 2.35–2.30 (m, 1H), 2.17–2.11 (m, 2H), 2.08–2.03 (m, 1H). The spectroscopic data match those reported previously.[3]



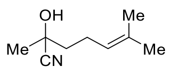
2-Hydroxy-2-(thiophen-2-yl)hex-5-enenitrile (1k). Isolated by flash column chromatography (5% EtOAc–hexanes), as a pale-yellow oil. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.38 (dd, *J* = 5.1, 1.2 Hz, 1H), 7.30 (dd, *J* = 3.7, 1.2 Hz, 1H), 7.02 (dd, *J* = 5.1, 3.7 Hz, 1H), 5.84 (ddt, *J* = 17.0, 10.4, 6.4 Hz, 1H), 5.12 (dd, *J* = 17.0, 1.5 Hz, 1H), 5.05 (dd, *J* = 10.4, 1.5 Hz, 1H), 3.08 (s, 1H), 2.45–2.37 (m, 1H), 2.33–2.16 (m, 3H). The spectroscopic data match those reported previously.[3]



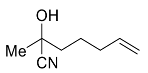
2-Hydroxy-3,3-dimethyl-2-phenylhex-5-enenitrile (1l). Isolated by flash column chromatography (5% EtOAc–hexanes), as a pale-yellow solid. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.56–7.54 (m, 2H), 7.43–7.38 (m, 3H), 5.83 (ddt, *J* = 16.6, 10.7, 7.5 Hz, 1H), 5.12 (d, *J* = 10.7 Hz, 1H), 5.11 (d, *J* = 16.6 Hz, 1H), 2.88 (s, 1H), 2.28 (dd, *J* = 13.5, 7.5 Hz, 1H), 2.21 (dd, *J* = 13.5, 7.5 Hz, 1H), 1.03 (s, 3H), 1.01 (s, 3H). The spectroscopic data match those reported previously.[3]



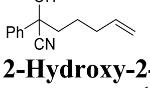
2-Hydroxy-2,5-dimethylhex-5-enenitrile (1m). Isolated by flash column chromatography (3% EtOAc–hexanes to 10% EtOAc–hexanes), as a pale-yellow oil. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 4.81 (s, 2H), 2.93–2.85 (m, 1H), 2.36 (ddd, *J* = 14.6, 10.4, 6.5 Hz, 1H), 2.23 (ddd, *J* = 14.6, 9.8, 5.5 Hz, 1H), 1.97–1.86 (m, 2H), 1.78 (s, 3H), 1.62 (s, 3H); ^{13}C NMR ($CDCl_3$, 126 MHz): δ 144.4, 121.7, 111.5, 68.9, 39.3, 32.6, 27.9, 22.4; FTIR (thin film): 3437, 2938, 2242, 1448, 1377, 1127, 893 cm^{-1}; HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_8H_{14}NO^+$ 140.1070; Found: 140.1067.



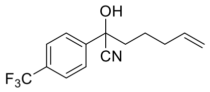
2-Hydroxy-2,6-dimethylhept-5-enenitrile (1n). Isolated by flash column chromatography (1% EtOAc–hexanes to 6% EtOAc–hexanes), as a pale-yellow oil. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 5.16 (t, *J* = 6.8 Hz, 1H), 2.87–2.82 (m, 1H), 2.41–2.34 (m, 1H), 2.25–2.19 (m, 1H), 1,86–1.76 (m, 2H), 1.71 (s, 3H), 1.69 (s, 3H), 1.60 (s, 3H).



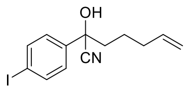
2-Hydroxy-2-methylhept-6-enenitrile (1o). Isolated by flash column chromatography (8% EtOAc–hexanes to 10% EtOAc–hexanes), as a pale-yellow oil. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 5.79 (ddt, *J* = 17.0, 10.3, 6.7 Hz, 1H), 5.05 (dd, *J* = 17.0, 1.7 Hz, 1H), 5.01 (d, *J* = 10.3 Hz, 1H), 2.42–2.36 (m, 1H), 2.14 (q, *J* = 7.1 Hz, 2H), 1.80–1.76 (m, 2H), 1.75–1.52 (m, 2H), 1.61 (s, 3H); ^{13}C NMR ($CDCl_3$, 126 MHz): δ 137.6, 122.0, 115.4, 68.4, 40.9, 33.1, 27.6, 23.3; FTIR (thin film): 3439, 2981, 2948, 2868, 2242, 1377, 914 cm^{-1}; HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_8H_{13}NONa^+$ 162.0889; Found: 162.0886.



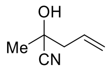
2-Hydroxy-2-phenylhept-6-enenitrile (1p). Isolated by flash column chromatography (8% EtOAc–hexanes), as a yellow oil. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.57 (d, *J* = 7.0 Hz, 2H), 7.42 (m, 3H), 5.74 (ddt, *J* = 16.9, 10.2, 6.7 Hz, 1H), 5.01–4.96 (m, 2H), 2.75 (s, 1H), 2.12–2.04 (m, 3H), 2.02–1.96 (m, 1H), 1.71–1.62 (m, 1H), 1.53–1.44 (m, 1H). The spectroscopic data match those reported previously.[3]



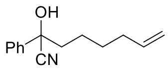
2-Hydroxy-2-(4-(trifluoromethyl)phenyl)hept-6-enenitrile (1q). Isolated by flash column chromatography (7% EtOAc–hexanes to 10% EtOAc–hexanes), as a pale-yellow oil. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.69 (br s, 4H), 5.73 (ddt, *J* = 17.0, 10.3, 6.7 Hz, 1H), 5.00 (dd, *J* = 17.0, 1.5 Hz, 1H), 4.99 (d, *J* = 10.3 Hz, 1H), 3.01 (br, 1H), 2.12–2.04 (m, 3H), 2.02–1.96 (m, 1H), 1.69–1.60 (m, 1H), 1.55–1.46 (m, 1H). The spectroscopic data match those reported previously.[3]



2-Hydroxy-2-(4-iodophenyl)hept-6-enenitrile (1r). Isolated by flash column chromatography (7% EtOAc–hexanes), as a pale-yellow solid. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.76 (d, *J* = 8.5 Hz, 2H), 7.30 (d, *J* = 8.5 Hz, 2H), 5.73 (ddt, *J* = 17.0, 10.3, 6.7 Hz, 1H), 5.00 (dd, *J* = 17.0, 1.5 Hz, 1H), 4.98 (d, *J* = 10.3 Hz, 1H), 2.73 (s, 1H), 2.10–2.02 (m, 3H), 1.98–1.92 (m, 1H), 1.68–1.59 (m, 1H), 1.52–1.43 (m, 1H); ^{13}C NMR ($CDCl_3$, 126 MHz): δ 139.6, 138.0, 137.3, 126.8, 120.2, 115.6, 95.1, 74.2, 42.8, 32.9, 23.4; FTIR (thin film): 3409, 2950, 2929, 2246, 1393, 1064, 1006, 915, 819 cm^{-1}. HRMS (ESI) m/z: [M-(HCN)+H]$^+$ Calcd for $C_{12}H_{14}IO^+$ 301.0084; Found: 301.0092. HRMS data of this compound was only obtainable as the fragment ion with the loss of HCN due to its instability. The presence of nitrile and hydroxy group is confirmed by ^{13}C NMR and FTIR.



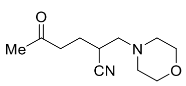
2-Hydroxy-2-methylpent-4-enenitrile (5a). Isolated by flash column chromatography (5% EtOAc–hexanes to 10% EtOAc–hexanes), as a pale-yellow oil. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 5.86 (ddt, *J* = 17.1, 10.2, 7.4 Hz, 1H), 5.29 (d, *J* = 10.2 Hz, 1H), 5.22 (dd, *J* = 17.1, 1.3 Hz, 1H), 3.75 (br, 1H), 2.52 (dd, *J* = 13.9, 6.9 Hz, 1H), 2.47 (dd, *J* = 13.9, 7.8 Hz, 1H), 1.56 (s, 3H); ^{13}C NMR ($CDCl_3$, 126 MHz): δ 130.4, 121.6, 121.5, 67.6, 45.8, 26.8; FTIR (thin film): 3429, 2242, 1376, 1125, 1056, 927, 563 cm^{-1}; HRMS (ESI) m/z: [M+Na]$^+$ Calcd for $C_6H_9NONa^+$ 134.0576; Found: 134.0578.



2-Hydroxy-2-phenyloct-7-enenitrile (5b). Isolated by flash column chromatography (10% EtOAc–hexanes), as a pale-yellow oil. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.56 (d, *J* = 7.6 Hz, 2H), 7.44–7.38 (m, 3H), 5.76 (ddt, *J* = 16.9, 10.3, 6.7 Hz, 1H), 4.98 (d, *J* = 16.9 Hz, 1H), 4.93 (d, *J* = 10.3 Hz, 1H), 2.99–2.82 (m, 1H), 2.11–1.95 (m, 4H), 1.63–1.53 (m, 1H), 1.44–1.38 (m, 3H); ^{13}C NMR ($CDCl_3$, 126 MHz): δ 139.9, 138.2, 129.2, 128.9, 124.9, 120.7, 114.8, 74.7, 43.4, 33.3, 28.4, 23.8; FTIR (thin film): 3415, 2929, 2242, 912, 765, 698 cm^{-1}; HRMS (ESI) m/z: [M+Na]$^+$ Calcd for $C_{14}H_{17}NONa^+$ 238.1202; Found: 238.1205.

IV. 1,2-Aminocyanation Procedure and Product Characterization

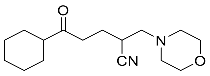
Standard Procedure: To a 1-Dram vial, was added alkene (0.2 mmol, 1.0 equiv), *O*-benzoylhydroxylamine (0.4 mmol, 2.0 equiv), $Cu(OTf)_2$ (7.2 mg, 0.02 mmol, 0.1 equiv), $TsOH·H_2O$ (57.1 mg, 0.3 mmol, 1.5 equiv) and DCE (1.0 mL). The vial was capped and stirred with a Teflon-coated stir bar at 80 ºC until *O*-benzoylhydroxylamine was consumed based on TLC analysis (20% EtOAc–hexanes). The resulting reaction mixture was cooled to room temperature, filtered through activated basic Al_2O_3 (Brockman Grade I, 58–60Å mesh powder). The filtrate was concentrated *in vacuo*, providing the crude reaction mixture. The crude reaction mixture was then purified by silica column chromatography.



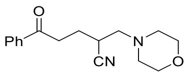
2-(Morpholinomethyl)-5-oxohexanenitrile (3a). Synthesized using standard conditions. Isolated by flash column chromatography (20% EtOAc–hexanes to 100% EtOAc), as a yellow oil (25.7 mg, 61%). ^{1}H NMR

($CDCl_3$, 500 MHz): δ 3.68 (t, *J* = 4.6 Hz, 4H), 2.84 (dddd, *J* = 10.2, 8.1, 6.6, 4.7 Hz, 1H), 2.77–2.66 (m, 2H), 2.60 (dd, *J* = 12.6, 8.1 Hz, 1H), 2.48 (t, *J* = 4.6 Hz, 4H), 2.46 (dd, *J* = 12.6, 8.1 Hz, 1H), 2.16 (s, 3H), 2.00 (dtd, *J* = 12.4, 7.0, 4.7 Hz, 1H), 1.69 (dddd, *J* = 13.9, 10.2, 7.0, 5.5 Hz, 1H); ^{13}C NMR ($CDCl_3$, 126 MHz): δ 206.9, 121.1, 66.7, 59.8, 53.5, 40.1, 30.0, 29.2, 23.8; FTIR (thin film): 2922, 2854, 2214, 1713, 1630, 1114, 866, 712 cm^{-1}; HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{11}H_{19}N_2O_2^+$ 211.1441; Found: 211.1443.

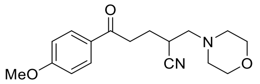
Experimental procedure for the synthesis 3a in a 2 mmol-scale reaction: To a 20-mL vial, was added alkene **1a** (0.27 mL, 2 mmol, 1.0 equiv), *O*-benzoylhydroxylamine **2a** (0.8289 g, 2.0 equiv), $Cu(OTf)_2$ (72.3 mg, 0.1 equiv), TsOH·H_2O (0.5707 g, 1.5 equiv), and DCE (10 mL). The vial was capped and stirred with a Teflon-coated stir bar. The mixture was then stirred and heated until *O*-benzoylhydroxylamine **2a** was consumed based on TLC analysis (20% EtOAc–hexanes). The resulting reaction mixture was cooled to room temperature, filtered through activated basic Al_2O_3 (Brockman Grade I, 58–60Å mesh powder) and concentrated *in vacuo* to yield the crude product. The crude reaction mixture was then purified by silica column chromatography (5% EtOAc–hexanes to 100% EtOAc), providing **3a** as a yellow oil (0.2958 g, 70%).



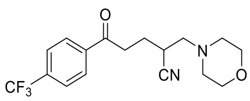
5-Cyclohexyl-2-(morpholinomethyl)-5-oxopentanenitrile (3b). Synthesized using standard conditions. Isolated by flash column chromatography (20% EtOAc–hexanes to 100% EtOAc), as a pale-yellow oil (31.9 mg, 57%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 3.69 (t, *J* = 4.6 Hz, 4H), 2.84 (dddd, *J* = 10.7, 8.2, 6.5, 4.6 Hz, 1H), 2.69 (dd, *J* = 7.8, 6.2 Hz, 2H), 2.60 (dd, *J* = 12.6, 8.2 Hz, 1H), 2.49 (t, *J* = 4.6 Hz, 4H), 2.47 (dd, *J* = 12.6, 6.5 Hz, 1H), 2.34 (tt, *J* = 11.2, 3.4 Hz, 1H), 2.01 (dtd, *J* = 14.0, 7.7, 4.6 Hz, 1H), 1.86–1.76 (m, 4H), 1.71–1.64 (m, 2H), 1.37–1.14 (m, 5H); ^{13}C NMR ($CDCl_3$, 126 MHz): δ 212.5, 121.2, 66. 8, 60.0, 53.6, 50.9, 37.0, 29.3, 28.5, 28.4, 25.7, 25.5 (2C), 23.9; FTIR (thin film): 2928, 2853, 2813, 2240, 1705, 1449, 1116, 866, 730 cm^{-1}; HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{16}H_{27}N_2O_2^+$ 279.2067; Found: 279.2071.



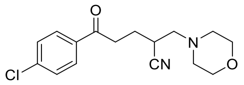
2-(Morpholinomethyl)-5-oxo-5-phenylpentanenitrile (3c). Synthesized using standard conditions. Isolated by flash column chromatography (20% EtOAc–hexanes to 100% EtOAc), as a yellow oil (34.0 mg, 62%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.98 (d, *J* = 7.8 Hz, 2H), 7.60 (t, *J* = 7.5 Hz, 1H), 7.49 (m, 2H), 3.71 (t, *J* = 4.6 Hz, 4H), 3.31–3.19 (m, 2H), 2.98 (dddd, *J* = 10.2, 7.9, 6.8, 4.6 Hz, 1H), 2.69 (dd, *J* = 12.6, 7.9 Hz, 1H), 2.58–2.53 (m, 5H), 2.24 (dtd, *J* = 13.8, 7.6, 4.6 Hz, 1H), 1.93 (dddd, *J* = 13.8, 10.2, 6.7, 5.5 Hz, 1H); ^{13}C NMR ($CDCl_3$, 126 MHz): δ 198.3, 136.4, 133.5, 128.7, 127.9, 121.3, 66.8, 60.0, 53.6, 35.2, 29.4, 24.4; FTIR (thin film): 2855, 2814, 2234, 1684, 1632, 1116 cm^{-1}; HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{16}H_{21}N_2O_2^+$ 273.1598; Found: 273.1605.



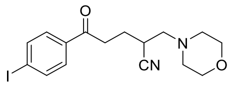
5-(4-Methoxyphenyl)-2-(morpholinomethyl)-5-oxopentanenitrile (3d). Synthesized using standard conditions. Isolated by flash column chromatography (20% EtOAc–hexanes to 100% EtOAc), as a yellow oil (41.0 mg, 52%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.93 (d, *J* = 8.8 Hz, 2H), 6.93 (d, *J* = 8.8 Hz, 2H), 3.86 (s, 3H), 3.69 (t, *J* = 4.7 Hz, 4H), 3.23–3.11 (m, 2H), 2.99–2.93 (m, 1H), 2.66 (dd, *J* = 12.6, 8.1 Hz, 1H), 2.55–2.50 (m, 5H), 2.20 (dtd, *J* = 14.1, 7.6, 4.7 Hz, 1H), 1.92–1.85 (m, 1H); ^{13}C NMR ($CDCl_3$, 126 MHz): δ 196.8, 163.7, 130.2, 129.5, 121.3, 113.8, 66.7, 59.9, 55.4, 53.5, 34.8, 29.4, 24.5; FTIR (thin film): 2937, 2813, 2240, 1673, 1598, 1168, 1114 cm^{-1}; HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{17}H_{23}N_2O_3^+$ 303.1703; Found: 303.1711.



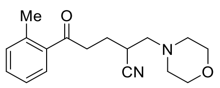
2-(Morpholinomethyl)-5-oxo-5-(4-(trifluoromethyl)phenyl)pentanenitrile (3e). Synthesized using standard conditions. Isolated by flash column chromatography (20% EtOAc–hexanes to 100% EtOAc), as a pale-yellow oil (36.1 mg, 53%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.07 (d, *J* = 8.0 Hz, 2H), 7.74 (d, *J* = 8.0 Hz, 2H), 3.70 (t, *J* = 4.7 Hz, 4H), 3.21–3.20 (m, 2H), 3.00–2.94 (m, 1H), 2.68 (dd, *J* = 12.6, 7.9 Hz, 1H), 2.58–2.52 (m, 5H), 2.27–2.21 (m, 1H), 1.97–1.90 (m, 1H); ^{13}C NMR ($CDCl_3$, 126 MHz): δ 197.3, 139.0, 134.7 (q, $J_{C–F}$ = 32.4 Hz), 128.3, 125.80 (q, $J_{C\text{–}F}$ = 3.6 Hz), 123.4 (q, $J_{C\text{–}F}$ = 272.7 Hz), 120.2, 66.8, 59.9, 53.6, 35.6, 29.3, 24.2; FTIR (thin film): 2816, 2241, 1691, 1323, 1115, 1064 cm^{-1}; HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{17}H_{20}F_3N_2O_2^+$ 341.1471; Found: 341.1472.



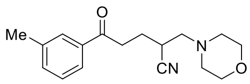
5-(4-Chlorophenyl)-2-(morpholinomethyl)-5-oxopentanenitrile (3f). Synthesized using standard conditions. Isolated by flash column chromatography (20% EtOAc–hexanes to 100% EtOAc), as a yellow oil (31.0 mg, 51%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.90 (d, *J* = 8.5 Hz, 2H), 7.44 (d, *J* = 8.5 Hz, 2H), 3.69 (t, *J* = 4.6 Hz, 4H), 3.26–3.14 (m, 2H), 2.96 (dddd, *J* = 10.3, 8.0, 6.6, 4.7 Hz, 1H), 2.67 (dd, *J* = 12.6, 8.0 Hz, 1H), 2.56–2.52 (m, 5H), 2.22 (dtd, *J* = 13.9, 7.5, 4.7 Hz, 1H), 1.90 (dddd, *J* = 13.9, 10.3, 6.9, 5.6 Hz, 1H); ^{13}C NMR ($CDCl_3$, 126 MHz): δ 197.0, 139.9, 134.6, 129.3, 129.0, 121.2, 66.8, 59.9, 53.6, 35.2, 29.4, 24.2; FTIR (thin film): 2856, 2814, 2241, 1684, 1589, 1115, 1091, 728 cm^{-1}; HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{16}H_{20}ClN_2O_2^+$ 307.1208; Found: 307.1212.



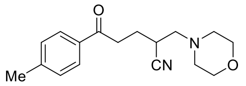
5-(4-Iodophenyl)-2-(morpholinomethyl)-5-oxopentanenitrile (3g). Synthesized using standard conditions. Isolated by flash column chromatography (20% EtOAc–hexanes to 100% EtOAc), as a yellow solid (49.2 mg, 62%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.84 (d, *J* = 8.4 Hz, 2H), 7.66 (d, *J* = 8.4 Hz, 2H), 3.69 (t, *J* = 4.6 Hz, 4H), 3.24–3.12 (m, 2H), 2.95 (dddd, *J* = 10.2, 7.8, 6.6, 4.7 Hz, 1H), 2.67 (dd, *J* = 12.6, 7.8 Hz, 1H), 2.56–2.51 (m, 5H), 2.21 (dtd, *J* = 13.8, 7.5, 4.7 Hz, 1H), 1.90 (dddd, *J* = 13.8, 10.2, 6.9, 5.5 Hz, 1H); ^{13}C NMR ($CDCl_3$, 126 MHz): δ 197.6, 138.0, 135.6, 129.3, 121.2, 101.5, 66.8, 59.9, 53.6, 35.2, 29.4, 24.2; FTIR (thin film): 2834, 2813, 2239, 1682, 1580, 1392, 1114, 1003 cm^{-1}; HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{16}H_{20}IN_2O_2^+$ 399.0564; Found: 399.0570.



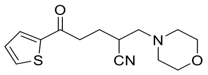
2-(Morpholinomethyl)-5-oxo-5-(*o*-tolyl)pentanenitrile (3h). Synthesized using standard conditions. Isolated by flash column chromatography (20% EtOAc–hexanes to 100% EtOAc), as a yellow oil (34.6 mg, 60%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.68 (d, *J* = 7.5 Hz, 1H), 7.38 (t, *J* = 7.5 Hz, 1H), 7.28–7.24 (m, 2H), 3.70 (t, *J* = 4.6 Hz, 4H), 3.24–3.10 (m, 2H), 2.98–2.92 (m, 1H), 2.67 (dd, *J* = 12.6, 8.1 Hz, 1H), 2.55–2.51 (m, 5H), 2.49 (s, 3H), 2.18 (dtd, *J* = 13.1, 7.6, 4.7 Hz, 1H), 1.88 (ddt, *J* = 13.1, 10.1, 6.2 Hz, 1H); ^{13}C NMR ($CDCl_3$, 126 MHz): δ 202.0, 138.3, 137.0, 132.1, 131.7, 128.6, 125.8, 121.2, 66.8, 60.0, 53.6, 37.9, 29.4, 24.5, 21.4; FTIR (thin film): 2854, 2812, 2240, 1682, 1115, 756 cm^{-1}; HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{17}H_{23}N_2O_2^+$ 287.1754; Found: 287.1762.



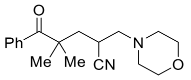
2-(Morpholinomethyl)-5-oxo-5-(*m*-tolyl)pentanenitrile (3i). Synthesized using standard conditions. Isolated by flash column chromatography (20% EtOAc–hexanes to 100% EtOAc), as a yellow oil (35.0 mg, 61%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.76 (s, 1H), 7.76 (d, *J* = 8.0 Hz, 1H), 7.40–7.34 (m, 2H), 3.63 (t, *J* = 4.7 Hz, 4H), 3.27–3.16 (m, 2H), 2.90 (dddd, *J* = 10.3, 8.1, 6.8, 4.7 Hz, 1H), 2.67 (dd, *J* = 12.6, 8.1 Hz, 1H), 2.57–2.52 (m, 5H), 2.41 (s, 3H), 2.22 (dtd, *J* = 13.8, 7.7, 4.7 Hz, 1H), 1.90 (dddd, *J* = 13.8, 10.3, 6.8, 6.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 126 MHz): δ 198.5, 138.5, 136.4, 134.2, 128.5, 128.4, 125.1, 121.3, 66.7, 59.9, 53.6, 35.3, 29.4, 24.4, 21.3; FTIR (thin film): 2855, 2813, 2240, 1681, 1115, 865, 690 cm^{-1}; HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{17}H_{23}N_2O_2^+$ 287.1754; Found: 287.1760.



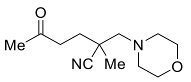
2-(Morpholinomethyl)-5-oxo-5-(*p*-tolyl)pentanenitrile (3j). Synthesized using standard conditions. Isolated by flash column chromatography (20% EtOAc–hexanes to 100% EtOAc), as a yellow oil (35.5 mg, 62%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.86 (d, *J* = 8.2 Hz, 2H), 7.26 (d, *J* = 8.2 Hz, 2H), 3.69 (t, *J* = 4.6 Hz, 4H), 3.26–3.15 (m, 2H), 2.96 (dddd, *J* = 10.2, 8.0, 6.7, 4.7 Hz, 1H), 2.66 (dd, *J* = 12.6, 8.0 Hz, 1H), 2.54 (dd, *J* = 12.6, 6.7 Hz, 1H), 2.53–2.51 (m, 4H), 2.41 (s, 3H), 2.21 (dtd, J = 14.0, 7.6, 4.7 Hz, 1H), 1.84 (dddd, J = 14.0, 10.2, 6.8, 6.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 126 MHz): δ 197.9, 144.3, 133.9, 129.3, 128.0, 121.3, 66.8, 59.9, 53.6, 35.1, 29.4, 24.4, 21.6; FTIR (thin film): 2854, 2812, 2240, 1679, 1607, 1116 cm^{-1}; HRMS (ESI) m/z: [M+H]$^+$ Calcd for $C_{17}H_{23}N_2O_2^+$ 287.1754; Found: 287.1760.



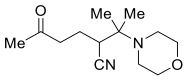
2-(Morpholinomethyl)-5-oxo-5-(thiophen-2-yl)pentanenitrile (3k). Synthesized using standard conditions. Isolated by flash column chromatography (20% EtOAc–hexanes to 100% EtOAc), as a yellow oil (20.4 mg, 37%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.76 (dd, J = 3.8, 1.1 Hz, 1H), 7.66 (dd, J = 4.9, 1.1 Hz, 1H), 7.15 (dd, J = 4.9, 3.8 Hz, 1H), 3.70 (t, J = 4.7 Hz, 4H), 3.25–3.13 (m, 2H), 2.96 (dddd, J = 10.2, 7.9, 6.8, 4.7 Hz, 1H), 2.66 (dd, J = 12.7, 7.9 Hz, 1H), 2.56–2.51 (m, 5H), 2.21 (dtd, J = 13.8, 7.5, 4.7 Hz, 1H), 1.90 (dddt, J = 13.8, 10.2, 6.9, 5.5 Hz, 1H); ^{13}C NMR ($CDCl_3$, 126 MHz): δ 191.2, 143.6, 134.0, 132.2, 128.2, 121.2, 66.8, 59.9, 53.6, 35.8, 29.4, 24.5; FTIR (thin film): 2855, 2815, 2240, 1663, 1416, 1116, 865, 731 cm^{-1}; HRMS (ESI) m/z: [M+H]$^+$ Calcd for $C_{14}H_{19}N_2O_2S^+$ 279.1162; Found: 279.1157.



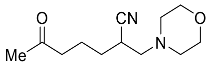
4,4-Dimethyl-2-(morpholinomethyl)-5-oxo-5-phenylpentanenitrile (3l). Synthesized using standard conditions. Isolated by flash column chromatography (20% EtOAc–hexanes to 100% EtOAc), as a yellow oil (41.4 mg, 68%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.68 (d, J = 7.5 Hz, 2H), 7.48 (t, J = 7.3 Hz, 1H), 7.42–7.39 (m, 2H), 3.66–3.59 (m, 4H), 2.69 (dtd, J = 9.8, 7.8, 2.8 Hz, 1H), 2.60 (dd, J = 12.5, 7.8 Hz, 1H), 2.45–2.41 (m, 5H), 2.24 (dd, J = 14.2, 2.8 Hz, 1H), 1.96 (dd, J = 14.2, 9.8 Hz, 1H), 1.48 (s, 3H), 1.42 (s, 3H); ^{13}C NMR ($CDCl_3$, 126 MHz): δ 207.5, 138.1, 131.3, 128.2, 127.8, 122.2, 66.7, 60.9, 53.5, 47.3, 40.3, 27.1, 26.0, 25.4; FTIR (thin film): 2966, 2858, 2240, 2189, 1671, 1115, 703 cm^{-1}; HRMS (ESI) m/z: [M+H]$^+$ Calcd for $C_{18}H_{25}N_2O_2^+$ 301.1911; Found: 301.1918.



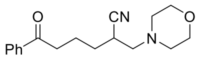
2-Methyl-2-(morpholinomethyl)-5-oxohexanenitrile (3m). Synthesized using standard conditions. Isolated by flash column chromatography (20% EtOAc–hexanes to 100% EtOAc), as a yellow oil (14.4 mg, 32%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 3.69 (t, J = 4.6 Hz, 4H), 2.72 (ddd, J = 15.9, 10.6, 5.3 Hz, 1H), 2.67–2.60 (m, 5H), 2.47 (d, J = 13.8 Hz, 1H), 2.42 (d, J = 13.8 Hz, 1H), 2.19 (s, 3H), 2.02 (ddd, J =14.1, 10.6, 5.3 Hz, 1H), 1.66 (ddd, J = 14.1, 10.6, 5.5 Hz, 1H), 1.28 (s, 3H); ^{13}C NMR ($CDCl_3$, 126 MHz): δ 206.8, 123.8, 67.1, 66.2, 55.3, 39.1, 37.2, 30.8, 30.1, 22.5; FTIR (thin film): 2958, 2855, 2811, 2233, 1716, 1117, 864 cm^{-1}; HRMS (ESI) m/z: [M+H]$^+$ Calcd for $C_{12}H_{21}N_2O_2^+$ 225.1598; Found: 225.1597.



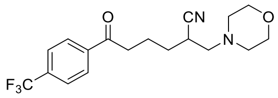
2-(2-Morpholinopropan-2-yl)-5-oxohexanenitrile (3n). Synthesized using standard conditions. Isolated by flash column chromatography (20% EtOAc–hexanes to 100% EtOAc), as a yellow oil (11.4 mg, 24%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 3.69 (t, J = 4.7 Hz, 4H), 2.89 (dd, J = 12.2, 3.7 Hz, 1H), 2.74 (dt, J = 18.7, 5.9 Hz, 1H), 2.66 (ddd, J = 18.7, 9.4, 5.6 Hz, 1H), 2.57–2.49 (m, 4H), 2.24 (dddd, J = 13.9, 9.4, 5.9, 3.7 Hz, 1H), 2.17 (s, 3H), 1.55 (dddd, J = 13.9, 12.3, 5.9, 5.6 Hz, 1H), 1.15 (s, 6H); ^{13}C NMR ($CDCl_3$, 126 MHz): δ 207.5, 121.4, 67.6, 57.8, 46.0, 40.5, 39.9, 30.1, 21.2, 20.4, 19.8; FTIR (thin film): 2967, 2853, 2236, 1714, 1367, 1274, 1118, 977 cm^{-1}; HRMS (ESI) m/z: [M+H]$^+$ Calcd for $C_{13}H_{23}N_2O_2^+$ 239.1754; Found: 239.1756.



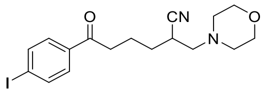
2-(Morpholinomethyl)-6-oxoheptanenitrile (3o). Synthesized using standard conditions. Isolated by flash column chromatography (20% EtOAc–hexanes to 100% EtOAc), as a pale-yellow oil (25.8 mg, 58%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 3.69 (t, J = 4.65 Hz, 4H), 2.71 (tdd, J = 8.5, 6.1, 5.0 Hz, 1H), 2.61 (dd, J = 12.6, 8.5 Hz, 1H), 2.52–2.49 (m, 6H), 2.44 (dd, J = 12.6, 6.1 Hz, 1H), 2.14 (s, 3H), 1.85–1.75 (m, 1H), 1.74–1.52 (m, 3H); ^{13}C NMR ($CDCl_3$, 126 MHz): δ 207.7, 121.4, 66.8, 59.7, 53.7, 42.6, 30.2, 29.9, 29.5, 21.0; FTIR (thin film): 2922, 2854, 2813, 2238, 1714, 1116, 866 cm^{-1}; HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{12}H_{21}N_2O_2^+$ 225.1598; Found: 225.1603.



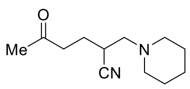
2-(Morpholinomethyl)-6-oxo-6-phenylhexanenitrile (3p). Synthesized using standard conditions. Isolated by flash column chromatography (20% EtOAc–hexanes to 100% EtOAc), as a pale-yellow oil (25.8 mg, 45%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.95 (d, J = 7.3 Hz, 2H), 7.57 (t, J = 7.4 Hz, 1H), 7.48–7.45 (m, 2H), 3.70 (t, J = 4.7 Hz, 4H), 3.05 (t, J = 6.9 Hz, 2H), 2.78 (tdd, J = 8.6, 6.1, 5.0 Hz, 1H), 2.64 (dd, J = 12.7, 8.6 Hz, 1H), 2.54–2.46 (m, 5H), 2.04–1.95 (m, 1H), 1.95–1.87 (m, 1H), 1.79–1.72 (m, 1H), 1.71–1.63 (m, 1H); ^{13}C NMR ($CDCl_3$, 126 MHz): δ 199.1, 136.7, 133.2, 128.6, 127.9, 121.4, 66.8, 59.8, 53.7, 37.6, 30.2, 29.7, 21.5; FTIR (thin film): 2854, 2813, 2239, 1683, 1448, 1116, 691 cm^{-1}; HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{17}H_{23}N_2O_2^+$ 287.1754; Found: 287.1760.



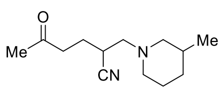
2-(Morpholinomethyl)-6-oxo-6-(4-(trifluoromethyl)phenyl)hexanenitrile (3q). Synthesized using standard conditions. Isolated by flash column chromatography (20% EtOAc–hexanes to 100% EtOAc), as a pale-yellow oil (35.8 mg, 51%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.05 (d, J = 8.2 Hz, 2H), 7.73 (d, J = 8.2 Hz, 2H), 3.70 (t, J = 4.6 Hz, 4H), 3.08 (t, J = 6.9 Hz, 2H), 2.78 (tdd, J = 8.5, 6.2, 5.0 Hz, 1H), 2.65 (dd, J = 12.7, 8.5 Hz, 1H), 2.55–2.47 (m, 5H), 2.06–1.97 (m, 1H), 1.97–1.88 (m, 1H), 1.80–1.73 (m, 1H), 1.72–1.64 (m, 1H); ^{13}C NMR ($CDCl_3$, 126 MHz): 198.0, 139.3, 134.5 (q, J_{C-F} = 32.7 Hz), 128.3, 125.7 (q, J_{C-F} = 3.7 Hz), 123.5 (q, J_{C-F} = 272.8 Hz), 120.3, 66.8, 59.8, 53.7, 37.9, 30.2, 29.6, 21.3; FTIR (thin film): 2857, 2814, 2240, 1691, 1323, 1115, 1065 cm^{-1}; HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{18}H_{22}F_3N_2O_2^+$ 355.1628; Found: 355.1627.



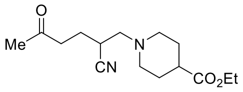
6-(4-Iodophenyl)-2-(morpholinomethyl)-6-oxohexanenitrile (3r). Synthesized using standard conditions. Isolated by flash column chromatography (20% EtOAc–hexanes to 100% EtOAc), as a pale-yellow solid (38.5 mg, 47%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.83 (d, J = 8.5 Hz, 2H), 7.65 (d, J = 8.5 Hz, 2H), 3.70 (t, J = 4.7 Hz, 4H), 3.00 (t, J = 6.9 Hz, 2H), 2.77 (tdd, J = 8.4, 6.1, 5.1 Hz, 1H), 2.64 (dd, J = 12.6, 8.4 Hz, 1H), 2.54–2.46 (m, 5H), 2.03 –1.94 (m, 1H), 1.93–1.85 (m, 1H), 1.78–1.71 (m, 1H), 1.69–1.62 (m, 1H); ^{13}C NMR ($CDCl_3$, 126 MHz): δ 198.3, 138.0, 135.9, 129.3, 121.4, 101.1, 66.8, 59.8, 53.7, 37.5, 30.2, 29.6, 21.3; FTIR (thin film): 2855, 2813, 2241, 1684, 1580, 1115, 728 cm^{-1}; HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{17}H_{22}IN_2O_2^+$ 413.0721; Found: 413.0725.



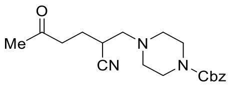
5-Oxo-2-(piperidin-1-ylmethyl)hexanenitrile (4a). Synthesized using standard conditions. Isolated by flash column chromatography (20% EtOAc–hexanes to 100% EtOAc), as a yellow oil (21.4 mg, 51%). ^{1}H NMR ($CDCl_3$, 500 MHz): 2.81 (dddd, J = 10.1, 7.8, 6.6, 4.8 Hz, 1H), 2.73–2.60 (m, 2H), 2.57 (dd, J = 12.7, 7.8 Hz, 1H), 2.42 (dd, J = 12.7, 6.6 Hz, 1H), 2.42 (br, 4H), 2.16 (s, 3H), 1.98 (dtd, J = 14.0, 7.7, 4.8 Hz, 1H), 1.70 (dddd, J = 14.0, 10.1, 7.6, 5.6 Hz, 1H), 1.55 (p, J = 5.6 Hz, 4H), 1.42–1.37 (m, 2H); ^{13}C NMR ($CDCl_3$, 126 MHz): δ 207.0, 121.5, 60.3, 54.6, 40.2, 30.0, 29.4, 25.8, 24.1, 24.0; FTIR (thin film): 2935, 2853, 2803, 2239, 1714, 1161, 1117 cm^{-1}; HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{12}H_{21}N_2O^+$ 209.1648; Found: 209.1651.



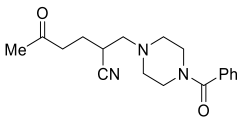
2-((3-Methylpiperidin-1-yl)methyl)-5-oxohexanenitrile (4b). Synthesized using standard conditions. Isolated by flash column chromatography (20% EtOAc–hexanes to 100% EtOAc) as a yellow oil (23.6 mg, 53%, as a mixture of two diastereomers yet dr can't be determined based on ^{1}H NMR). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 2.85–2.60 (m, 6H), 2.57 (ddd, J = 12.7, 7.8, 1.2 Hz, 1H), 2.42 (ddd, J = 12.7, 6.7, 5.0 Hz, 1H), 2.16 (s, 3H), 2.03–1.92 (m, 2H), 1.73–1.58 (m, 5H), 1.56–1.48 (m, 1H), 0.83 (d, J = 5.7 Hz, 3H); ^{13}C NMR ($CDCl_3$, 126 MHz): δ 207.0, 121.5, 62.0, 61.9, 60.0 (2C), 54.1, 54.0, 40.2, 32.6, 31.0, 30.9, 30.0, 29.4 (2C), 25.3, 25.2, 24.0, 19.5; FTIR (thin film): 2928, 2852, 2239, 1715, 1358, 1163, 974 cm^{-1}; HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{13}H_{23}N_2O^+$ 223.1805; Found: 223.1809.



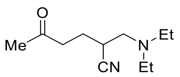
Ethyl 1-(2-cyano-5-oxohexyl)piperidine-4-carboxylate (4c). Synthesized using standard conditions. Isolated by flash column chromatography (20% EtOAc–hexanes to 100% EtOAc), as a yellow oil (27.4 mg, 49%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 4.11 (q, *J* = 7.1 Hz, 2H), 2.85–2.78 (m, 3H), 2.74–2.65 (m, 2H), 2.59 (dd, *J* = 12.7, 7.8 Hz, 1H), 2.46 (dd, *J* = 12.7, 6.7 Hz, 1H), 2.25 (tt, *J* = 11.1, 4.1 Hz, 1H), 2.16 (s, 3H), 2.15–2.09 (m, 2H), 1.99 (dtd, *J* = 15.0, 7.8, 4.9 Hz, 1H), 1.88–1.85 (m, 2H), 1.77–1.65 (m, 3H), 1.23 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR ($CDCl_3$, 126 MHz): δ 206.9, 174.8, 121.3, 60.3, 59.7, 53.1, 52.9, 40.8, 40.2, 30.0, 29.5, 28.1 (2C), 23.9, 14.1; FTIR (thin film): 2946, 2810, 2239, 1716, 1166, 1047 cm^{-1}; HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{15}H_{25}N_2O_3^+$ 281.1860; Found: 281.1865.



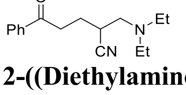
Benzyl 4-(2-cyano-5-oxohexyl)piperazine-1-carboxylate (4d). Synthesized using standard conditions. Isolated by flash column chromatography (20% EtOAc–hexanes to 100% EtOAc), as a yellow oil (21.3 mg, 31%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.37–7.29 (m, 5H), 5.12 (s, 2H), 3.52 (t, *J* = 5.0 Hz, 4H), 2.85 (dddd, *J* = 10.2, 8.1, 6.5, 4.7 Hz, 1H), 2.75–2.67 (m, 2H), 2.63 (dd, *J* = 12.8, 8.1 Hz, 1H), 2.49 (dd, *J* = 12.8, 6.5 Hz, 1H), 2.48 (br, 4H), 2.18 (s, 3H), 2.01 (dtd, *J* = 13.9, 7.7, 4.7 Hz, 1H), 1.70 (dddd, *J* = 13.9, 10.2, 7.0, 5.6 Hz, 1H); ^{13}C NMR ($CDCl_3$, 126 MHz): δ 206.9, 155.1, 136.6, 128.5, 128.0, 127.9, 121.1, 67.1, 59.5, 52.9, 43.7, 40.1, 30.1, 29.5, 23.9; FTIR (thin film): 2924, 2816, 2240, 1696, 1427, 1234, 1123, 698 cm^{-1}; HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{19}H_{26}N_3O_3^+$ 344.1969; Found: 344.1973.



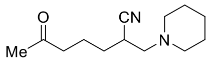
2-((4-Benzoylpiperazin-1-yl)methyl)-5-oxohexanenitrile (4e). Synthesized using standard conditions. Isolated by flash column chromatography (20% EtOAc–hexanes to 100% EtOAc), as a yellow oil (22.1 mg, 35%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.41–7.36 (m, 5H), 3.79 (br, 2H), 3.44 (br, 2H), 2.86 (dddd, *J* = 10.8, 8.2, 6.4, 4.6 Hz, 1H), 2.75–2.63 (m, 3H), 2.52 (br d, 4H), 2.52 (dd, *J* = 12.8, 6.5 Hz, 1H), 2.17 (s, 3H), 2.01 (dtd, *J* = 13.9, 7.7, 4.6 Hz, 1H), 1.70 (dddd, *J* = 13.9, 10.4, 6.8, 5.5 Hz, 1H); ^{13}C NMR ($CDCl_3$, 126 MHz): δ 206.9, 170.3, 135.6, 129.7, 128.5, 127.0, 121.0, 59.4, 53.5, 53.0, 47.5, 42.0, 40.1, 30.0, 29.5, 23.8; FTIR (thin film): 2924, 2816, 2239, 1714, 1628, 1432, 1279, 712 cm^{-1}; HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{18}H_{24}N_3O_2^+$ 314.1863; Found: 314.1859.



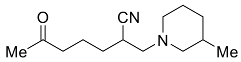
2-((Diethylamino)methyl)-5-oxohexanenitrile (4f). Synthesized using standard conditions. Isolated by flash column chromatography (20% EtOAc–hexanes to 100% EtOAc), as a yellow oil (11.4 mg, 29%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 2.77–2.61 (m, 4H), 2.60–2.53 (m, 5H), 2.17 (s, 3H), 2.05–1.96 (m, 1H), 1.69 (dddd, *J* = 14.0, 9.9, 7.6, 5.5 Hz, 1H), 1.02 (t, *J* = 7.1 Hz, 6H); ^{13}C NMR ($CDCl_3$, 126 MHz): 207.0, 121.6, 55.1, 47.3, 40.4, 30.8, 30.0, 23.9, 11.9; FTIR (thin film): 2970, 2931, 2239, 1716, 1372, 1167, 1068 cm^{-1}; HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{11}H_{21}N_2O^+$ 197.1648; Found:197.1650.



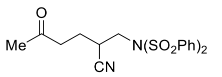
2-((Diethylamino)methyl)-5-oxo-5-phenylpentanenitrile (4g). Synthesized using standard conditions. Isolated by flash column chromatography (20% EtOAc–hexanes to 100% EtOAc), as a yellow oil (17.2 mg, 33%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.97 (d, *J* = 7.3 Hz, 2H), 7.58 (t, *J* = 7.4 Hz, 1H), 7.49–7.46 (m, 2H), 3.29–3.17 (m, 2H), 2.87 (dddd, *J* = 10.2, 8.1, 6.5, 4.6 Hz, 1H), 2.78 (dd, *J* = 13.1, 8.1 Hz, 1H), 2.64–2.54 (m, 5H), 2.20 (dtd, *J* = 14.0, 7.7, 4.6 Hz, 1H), 1.89 (dddd, *J* = 14.0, 10.2, 7.5, 5.4 Hz, 1H), 1.04 (t, *J* = 7.2 Hz, 6H); ^{13}C NMR ($CDCl_3$, 126 MHz): δ 198.4, 136.5, 133.4, 128.7, 128.0, 121.8, 55.1, 47.3, 35.5, 30.8, 24.5, 11.7; FTIR (thin film): 2969, 2929, 2239, 1686, 1449, 1209, 691 cm^{-1}; HRMS (ESI) m/z: [M+H]$^+$ Calcd for $C_{16}H_{23}N_2O^+$ 259.1807; Found: 259.1807.



6-Oxo-2-(piperidin-1-ylmethyl)heptanenitrile (4h). Synthesized using standard conditions. Isolated by flash column chromatography (20% EtOAc–hexanes to 100% EtOAc), as a yellow oil (18.5 mg, 42%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 2.69 (dddd, *J* = 9.1, 7.9, 6.3, 4.9 Hz, 1H), 2.58 (dd, *J* = 12.6, 7.9 Hz, 1H), 2.49 (t, *J* = 7.1 Hz, 2H), 2.43–2.40 (m, 5H), 2.14 (s, 3H), 1.85–1.77 (m, 1H), 1.75–1.61 (m, 2H), 1.58–1.51 (m, 5H), 1.41 (p, *J* = 6.0 Hz, 2H); ^{13}C NMR ($CDCl_3$, 126 MHz): δ 207.8, 121.8, 60.2, 54.7, 42.8, 30.3, 29.9, 29.7, 25.9, 24.1, 21.1; FTIR (thin film): 2931, 2853, 2239, 1714, 1354, 1160, 1117 cm^{-1}; HRMS (ESI) m/z: [M+H]$^+$ Calcd for $C_{13}H_{23}N_2O^+$ 223.1805; Found: 223.1809.

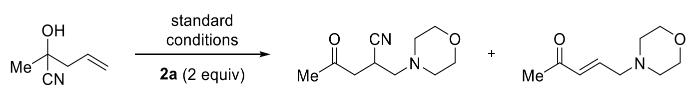


2-((3-Methylpiperidin-1-yl)methyl)-6-oxoheptanenitrile (4i). Synthesized using standard conditions. Isolated by flash column chromatography (20% EtOAc–hexanes to 100% EtOAc), as a pale-yellow oil (24.6 mg, 52%, as a mixture of two diastereomers yet dr can't be determined based on ^{1}H NMR). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 2.78–2.67 (m, 3H), 2.58 (ddd, *J* = 12.7, 8.1, 1.5 Hz, 1H), 2.48 (t, *J* = 7.1 Hz, 2H), 2.41 (ddd, *J* = 12.7, 6.4, 4.3 Hz, 1H), 2.14 (s, 3H), 1.97 (tdd, *J* = 11.1, 5.2, 3.1 Hz, 1H), 1.85– 1.76 (m, 1H), 1.75–1.48 (m, 9H), 0.84 (d, *J* = 6.1 Hz, 3H); ^{13}C NMR ($CDCl_3$, 126 MHz): δ 207.8, 121.8, 62.1, 62.0, 59.9 (2C), 54.1 (2C), 42.8, 32.6, 31.0, 30.9, 30.3 (2C), 29.9, 29.6, 25.3 (2C), 21.1, 19.5; FTIR (thin film): 2927, 2239, 1714, 1358, 1163, 1123, 974 cm^{-1}; HRMS (ESI) m/z: [M+H]$^+$ Calcd for $C_{14}H_{25}N_2O^+$ 237.1961; Found: 237.1965.



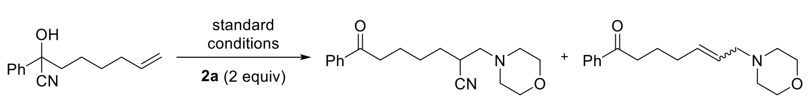
***N*-(2-Cyano-5-oxohexyl)-*N*-(phenylsulfonyl)benzenesulfonamide (4j).** Synthesized using standard conditions. Isolated by flash column chromatography (20% EtOAc–hexanes to 100% EtOAc), as a pale-yellow oil (23.9 mg, 34%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.08 (d, *J* = 7.6 Hz, 4H), 7.69 (t, *J* = 7.5 Hz, 2H), 7.60–7.57 (m, 4H), 4.05 (dd, *J* = 15.3, 8.1 Hz, 1H), 3.67 (dd, *J* = 15.3, 6.8 Hz, 1H), 3.33 (dddd, *J* = 10.2, 8.1, 6.8, 5.0 Hz, 1H), 2.73 (ddd, *J* = 18.4, 7.7, 5.3 Hz, 1H), 2.62 (dt, *J* = 18.4, 7.7 Hz, 1H), 2.17 (s, 3H), 1.95 (dtd, *J* = 14.0, 7.7, 5.0 Hz, 1H), 1.73 (dddd, *J* = 14.0, 10.2, 7.7, 5.3 Hz, 1H); ^{13}C NMR ($CDCl_3$, 126 MHz): δ 206.2, 138.5, 134.4, 129.2, 128.7, 119.1, 48.6, 39.9, 31.6, 29.9, 23.5; FTIR (thin film): 2927, 2244, 1714, 1448, 1372, 1166, 685, 580, 548 cm^{-1}; HRMS (ESI) m/z: [M+H]$^+$ Calcd for $C_{19}H_{20}N_2O_5S_2^+$ 421.0886; Found: 421.0888.

V. 1,2-Aminocyanation Reactions Involving 1,3- and 1,6-Migrations



5a **6a**, trace **7**, 7%

5-Morpholinopent-3-en-2-one (7). Reaction run under standard conditions, from which compound **7** was obtained after a flash column chromatography (70% EtOAc–hexanes to 3% MeOH–DCM) in a mixture containing some impurities. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 6.77 (dt, *J* = 16.1, 6.1 Hz, 1H), 6.22 (d, *J* = 16.1 Hz, 1H), 3.73 (t, *J* = 4.5 Hz, 4H, 3.16 (d, *J* = 6.1 Hz, 1H), 2.48 (br, 4H), 2.27 (s, 3H); FTIR (thin film): 2920, 2851, 1713, 1361,1272, 1116, 867 cm^{-1}; HRMS (ESI) m/z: [M+H]$^+$ Calcd for $C_9H_{16}NO_2^+$ 170.1176; Found: 170.1178.

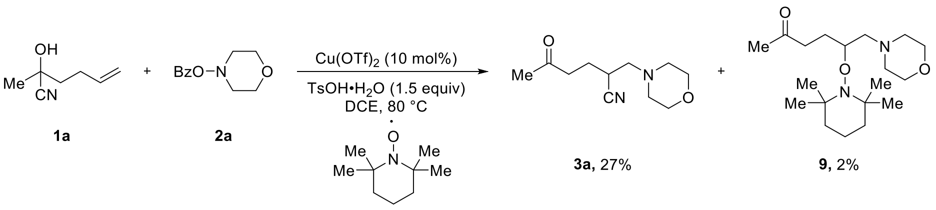


5b **6b**, trace **8**, 36%

7-Morpholino-1-phenylhept-5-en-1-one (8). Reaction run under standard conditions. Isolated by flash column chromatography (30% EtOAc–hexanes to 100% EtOAc), as a pale-yellow oil and mixture (19.7 mg, 36%, E/Z=1:1). ^{1}H NMR ($CDCl_3$, 500 MHz): 7.95–7.93 (m, 4H), 7.57–7.54 (m, 2H), 7.47–7.44 (m, 4H), 5.65–5.57 (m, 2H), 5.54–5.48 (m, 2H), 3.71–3.68 (m, 8H), 3.00–2.93 (m, 8H), 2.42 (br s, 8H), 2.20–2.12 (m, 4H), 1.87–1.80 (m, 4H), ^{13}C NMR ($CDCl_3$, 126 MHz): δ 200.0 (2C), 137.0, 136.9, 135.1, 133.5, 133.0 (2C), 128.6 (2C), 128.0 (2C), 125.7, 125.6, 66.6 (2C), 61.0, 55.3, 53.4, 53.2, 37.7, 37.6, 31.9, 26.9, 23.8, 23.5; FTIR (thin film): 2937, 2854, 2804, 1738, 1686, 1235, 1117, 1044, 733 cm^{-1}; HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{17}H_{24}NO_2^+$ 274.1802; Found: 274.1805.

VI. Mechanistic Studies and Compound Characterization

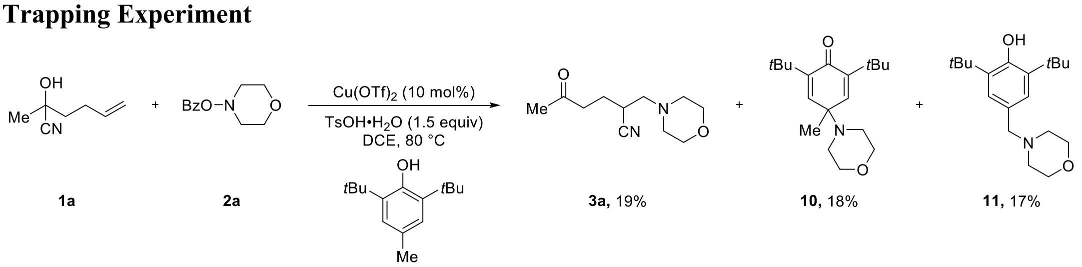
TEMPO Trapping Experiment



To a 1-Dram vial, was added alkene **1a** (53.9 µL, 0.4 mmol, 1.0 equiv), *O*-benzoylhydroxylamine **2a** (165.8 mg, 2.0 equiv), TEMPO (2,2,6,6-tetramethyl-1-piperidinyloxy) (62.5 mg, 1.0 equiv), $Cu(OTf)_2$ (14.5 mg, 0.1 equiv), $TsOH·H_2O$ (114.1 mg, 1.5 equiv), and DCE (2.0 mL). The vial was capped and stirred with a Teflon-coated stir bar. The mixture was then stirred and heated until *O*-benzoylhydroxylamine **2a** was consumed based on TLC analysis (20% EtOAc–hexanes). The resulting reaction mixture was cooled to room temperature, filtered through activated basic Al_2O_3 (Brockman Grade I, 58–60Å mesh powder) and concentrated *in vacuo* to yield the crude product. The crude reaction mixture was then purified by silica column chromatography (30% EtOAc–hexanes to 100% EtOAc).

6-Morpholino-5-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)hexan-2-one (9). Isolated as a pale-yellow oil (3.2 mg, 2%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 3.94–3.89 (m, 1H), 3.70–3.63 (m, 4H), 2.76 (dd, J = 12.6, 4.2 Hz, 1H), 2.56–2.49 (m, 4H), 2.44–2.39 (m, 2H), 2.24 (dd, J = 12.6, 8.4 Hz, 1H), 2.17 (s, 3H), 1.96 (td, J = 7.7, 5.7 Hz, 2H), 1.67 (br, 2H), 1.44 (br, 4H), 1.09 (s, 12H); ^{13}C NMR ($CDCl_3$, 126 MHz): δ 209.2, 78.6, 67.2, 60.9, 59.8, 54.8, 54.6, 40.0, 29.8, 29.4, 26.7, 17.2; FTIR (thin film): 2928, 2852, 2806, 2357, 1717, 1455, 1360, 1119 cm^{-1}; HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{19}H_{37}N_2O_3^+$ 341.2799; Found: 341.2799.

BHT Trapping Experiment



To a 1-Dram vial, was added alkene **1a** (26.9 µL, 0.2 mmol, 1.0 equiv), *O*-benzoylhydroxylamine **2a** (82.9 mg, 2.0 equiv), BHT (2,6-di-*tert*-butyl-4-methylphenol) (44.1 mg, 1.0 equiv), $Cu(OTf)_2$ (7.2 mg, 0.1 equiv), $TsOH·H_2O$ (57.1 mg, 1.5 equiv), and DCE (1.0 mL). The vial was capped and stirred with a Teflon-coated stir bar. The mixture was then stirred and heated until *O*-benzoylhydroxylamine **2a** was consumed based on TLC analysis (20% EtOAc–hexanes). The resulting reaction mixture was cooled to room temperature, filtered through activated basic Al_2O_3 (Brockman Grade I, 58–60Å mesh powder) and concentrated *in vacuo* to yield the crude product. The crude reaction mixture was then purified by silica column chromatography (5% EtOAc–hexanes to 100% EtOAc).

2,6-Di-*tert*-butyl-4-methyl-4-morpholinocyclohexa-2,5-dien-1-one (10). Isolated as a yellow oil (11.0 mg, 18%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 6.54 (s, 2H), 3.70 (t, J = 4.6 Hz, 4H), 2.60 (t, J = 4.6 Hz, 4H), 1.30 (s, 3H), 1.23 (s, 18H); ^{13}C NMR ($CDCl_3$, 126 MHz): δ 186.2, 148.1, 142.9, 67.6, 57.3, 47.0, 35.0, 29.6, 24.6; FTIR (thin film): 2956, 2855, 2816, 1661, 1643, 1118, 880 cm^{-1}; HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{19}H_{32}NO_2^+$ 306.2428; Found: 306.2426.

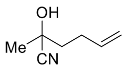
2,6-Di-*tert*-butyl-4-(morpholinomethyl)phenol (11). Isolated as a pale-yellow oil (10.4 mg, 17%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.08 (s, 2H), 5.12 (s, 1H), 3.71 (t, J = 4.7 Hz, 4H), 3.42 (s, 2H), 2.44 (t, J = 4.7 Hz, 4H), 1.44 (s, 18H). The spectroscopic data match those reported previously.[4]

VII. References

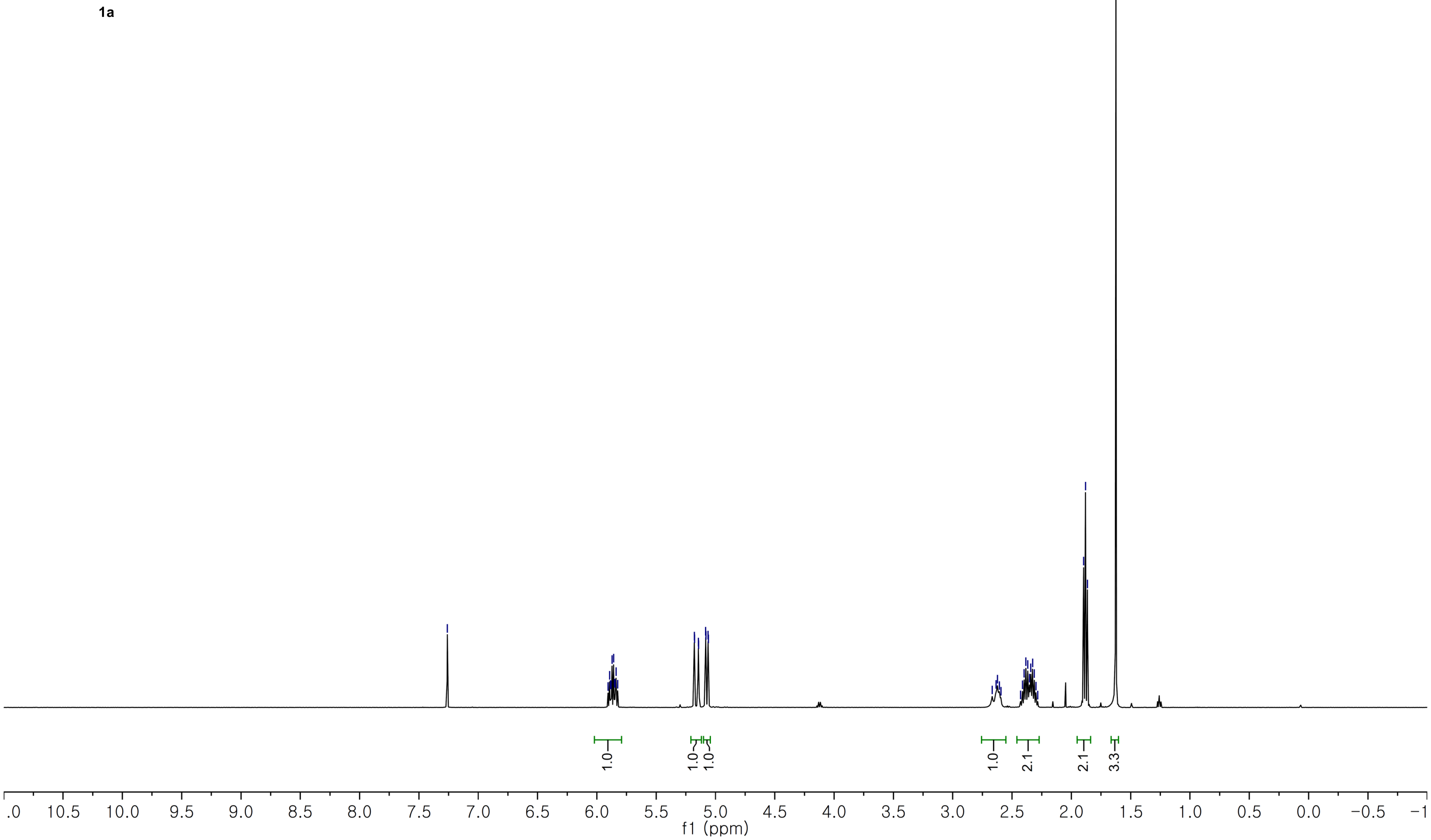
1. Aramini, A.; Sablone, M. R.; Bianchini, G.; Amore, A.; Fanì, M.; Perrone, P.; Dolce, A.; Allegretti, M., Facile One-Pot Preparation of 2-Arylpropionic and Arylacetic Acids from Cyanohydrins by Treatment with Aqueous HI. *Tetrahedron* **2009,** *65* (10), 2015–2021.
2. Berman, A. M.; Johnson, J. S., Copper-Catalyzed Electrophilic Amination of Organozinc Nucleophiles: Documentation of *O*-Benzoyl Hydroxylamines as Broadly Useful $R_2N(^+)$ and $RHN(^+)$ Synthons. *J. Org. Chem.* **2006,** *71* (1), 219–224.
3. Wu, Z.; Ren, R.; Zhu, C., Combination of a Cyano Migration Strategy and Alkene Difunctionalization: The Elusive Selective Azidocyanation of Unactivated Olefins. *Angew. Chem. Int. Ed.* **2016,** *55* (36), 10821–10824.
4. Hemric, B. N.; Chen, A. W.; Wang, Q., Copper-Catalyzed 1,2-Amino Oxygenation of 1,3-Dienes: A Chemo-, Regio-, and Site-Selective Three-Component Reaction with *O*-Acylhydroxylamines and Carboxylic Acids. *ACS Catal.* **2019,** *9* (11), 10070–10076.

VIII. NMR Spectra

^{1}H
500 MHz, $CDCl_3$

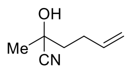


1a

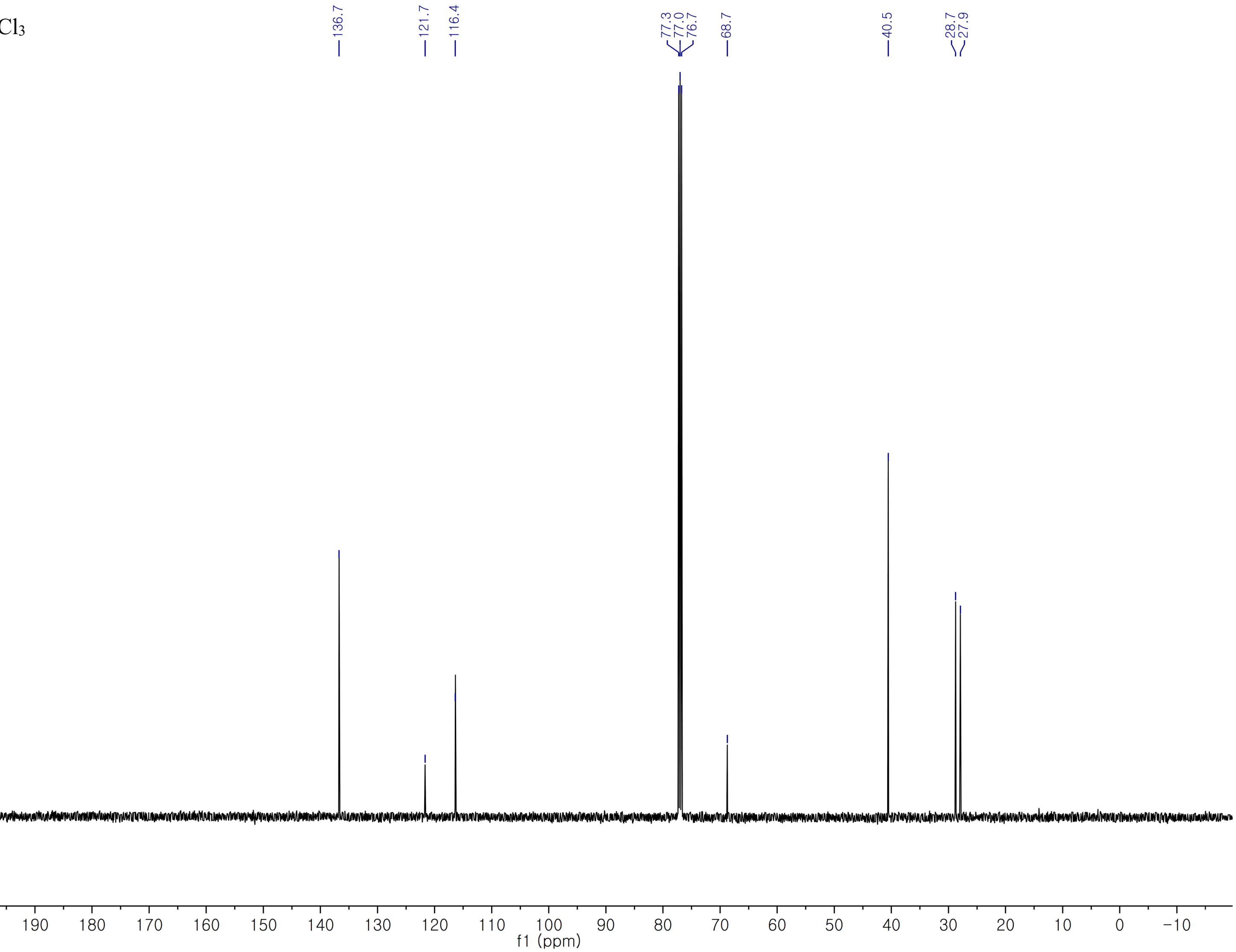


^{13}C

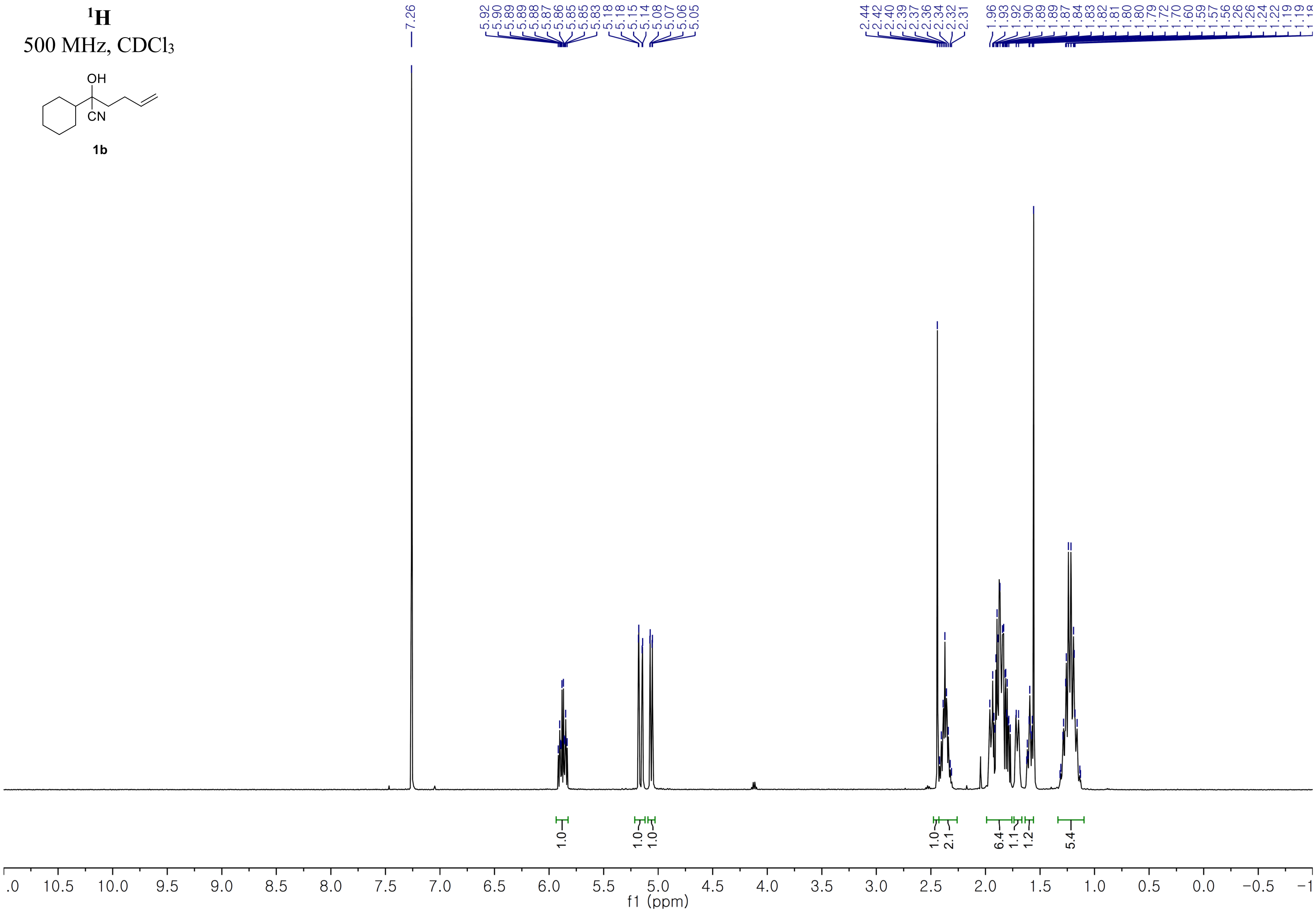
126 MHz, $CDCl_3$



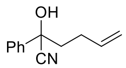
1a



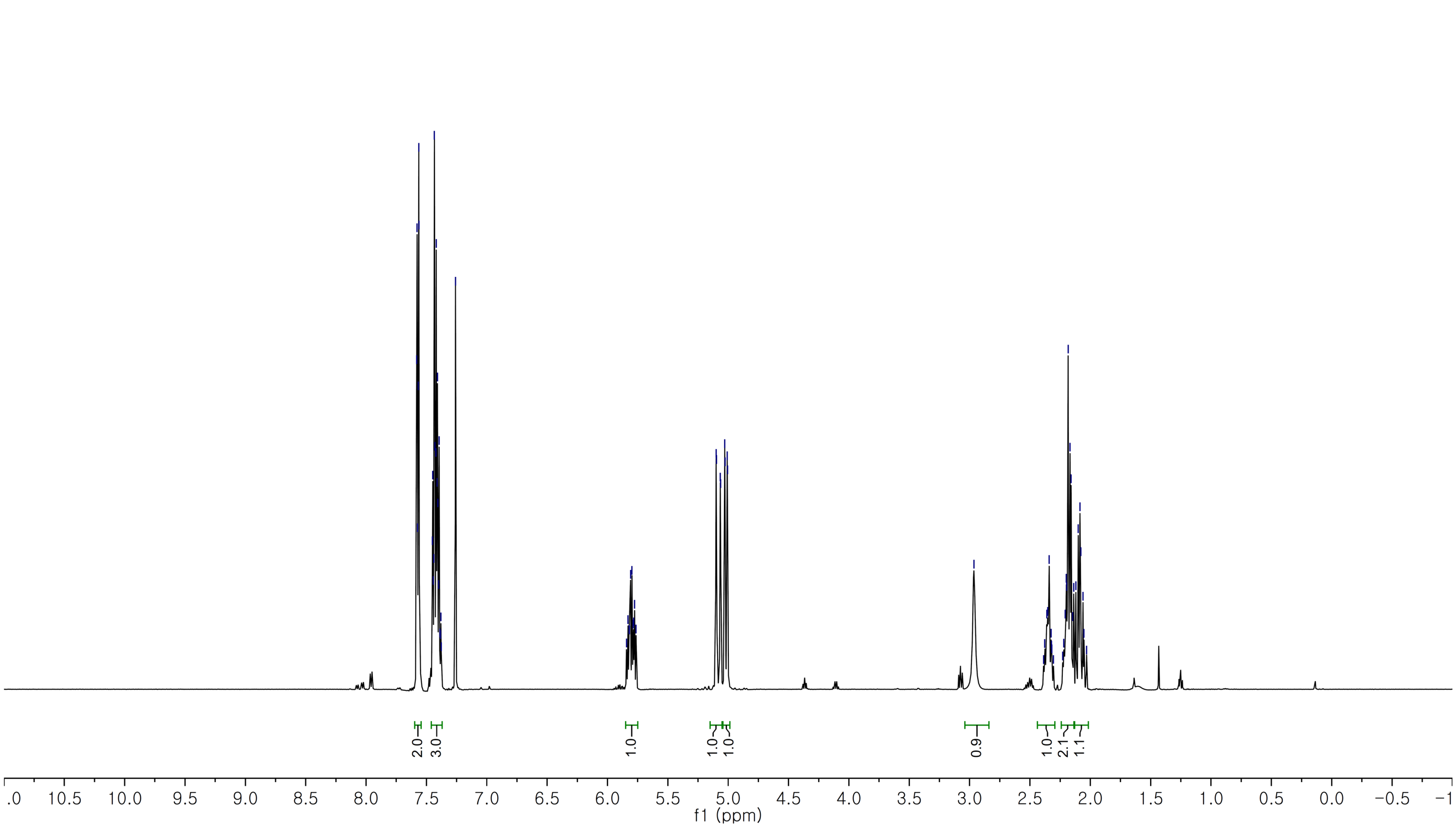
^{1}H
500 MHz, $CDCl_3$



[1]H
500 MHz, $CDCl_3$

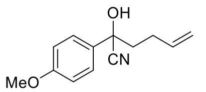


1c

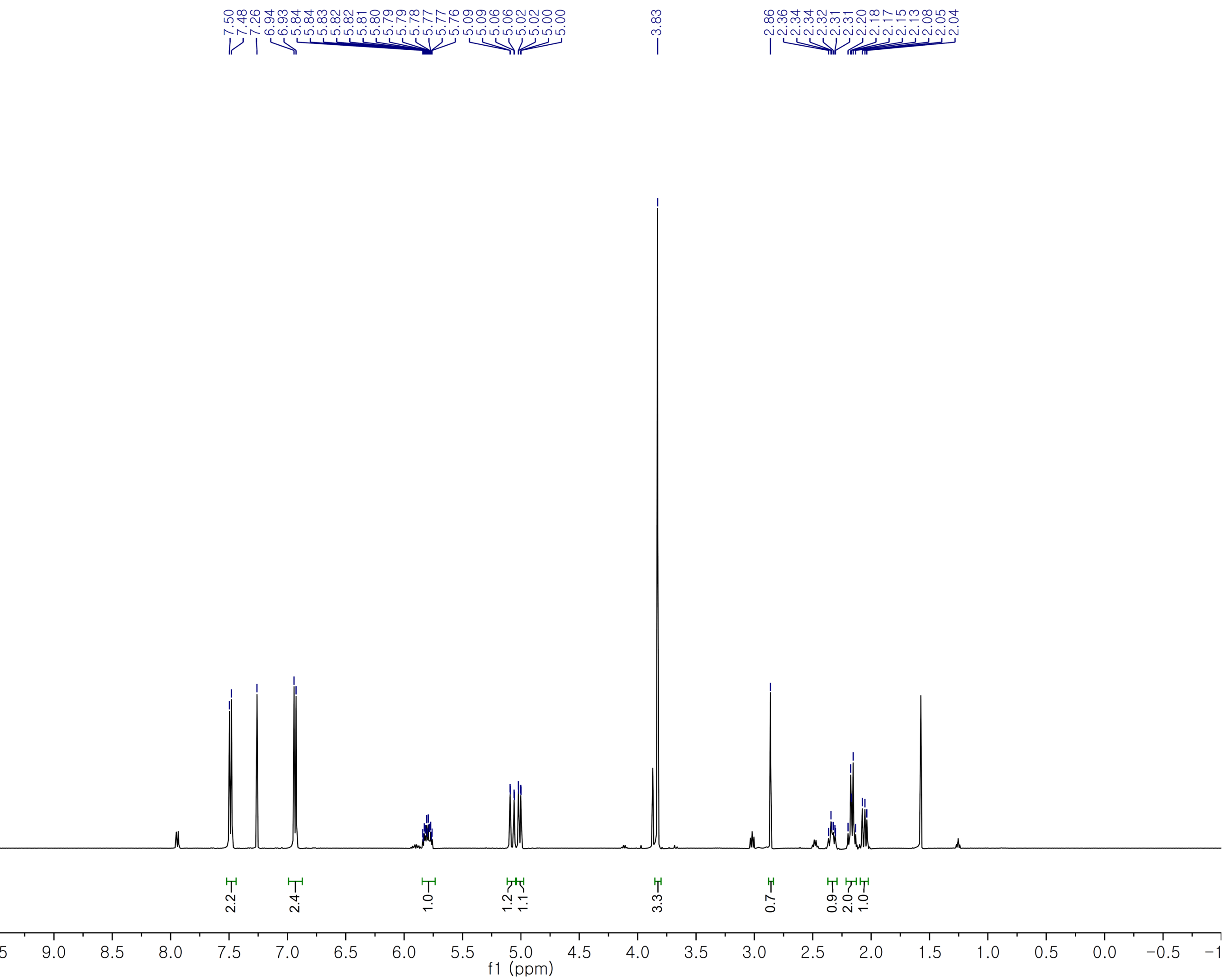


^{1}**H**

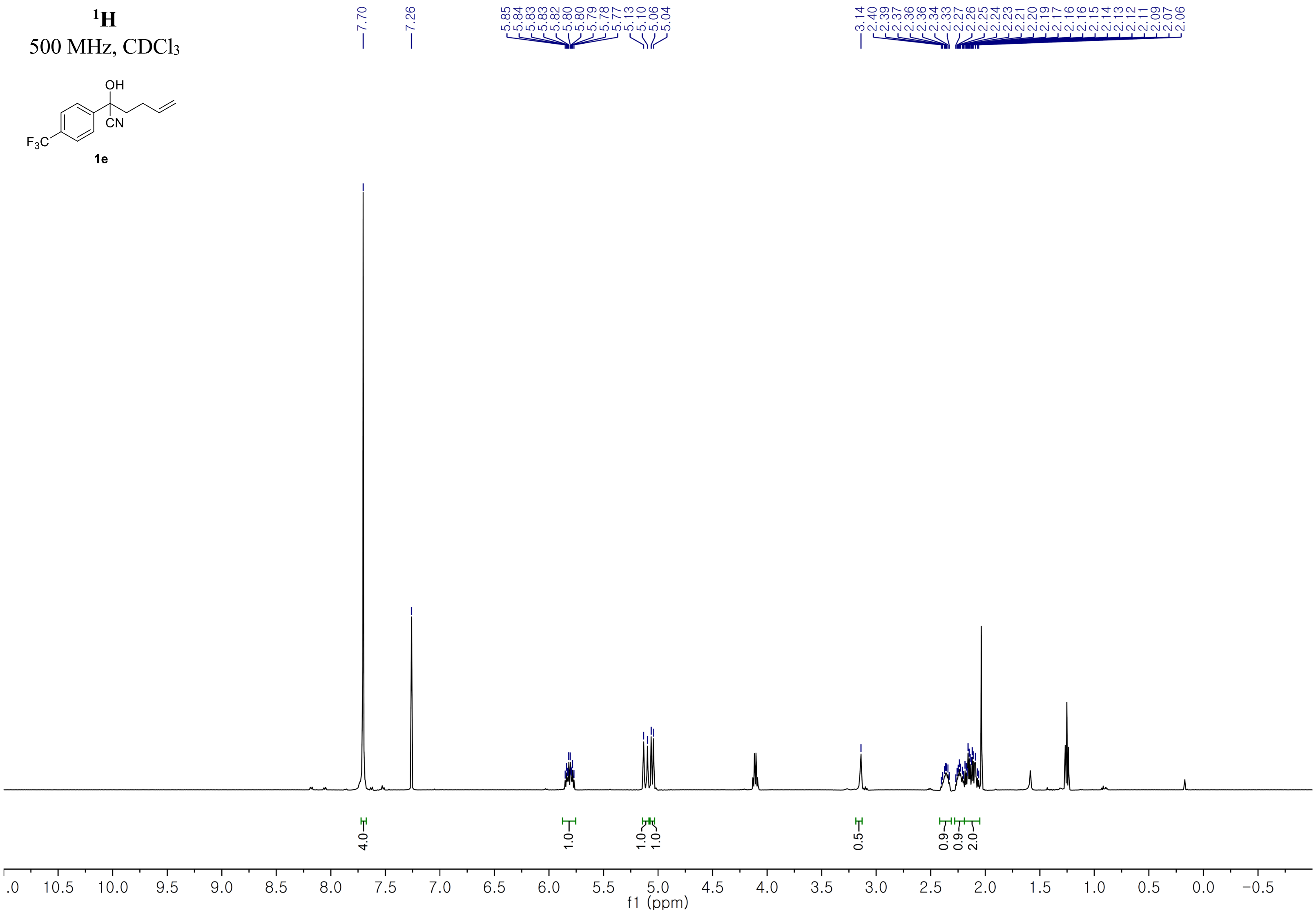
500 MHz, $CDCl_3$



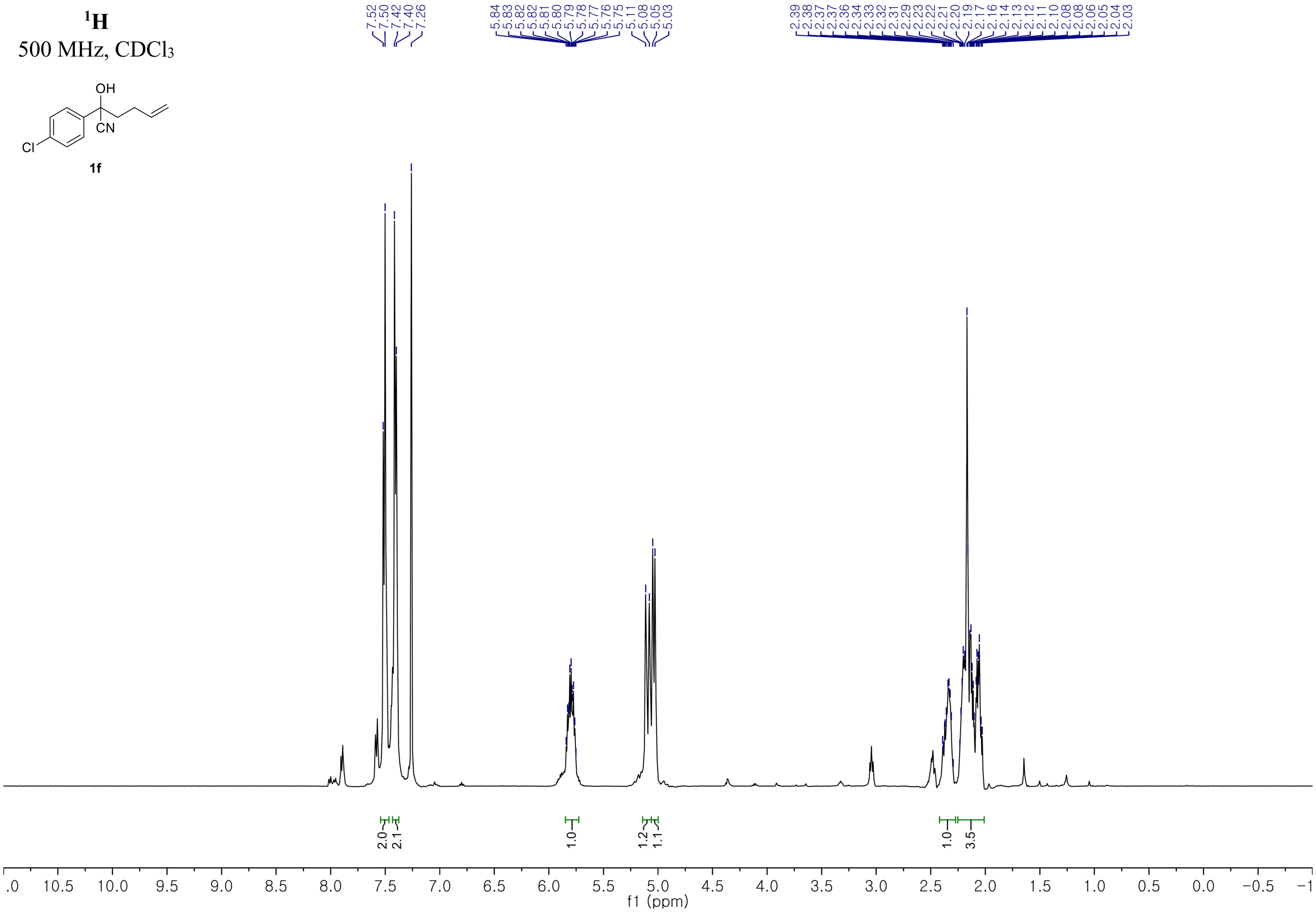
1d



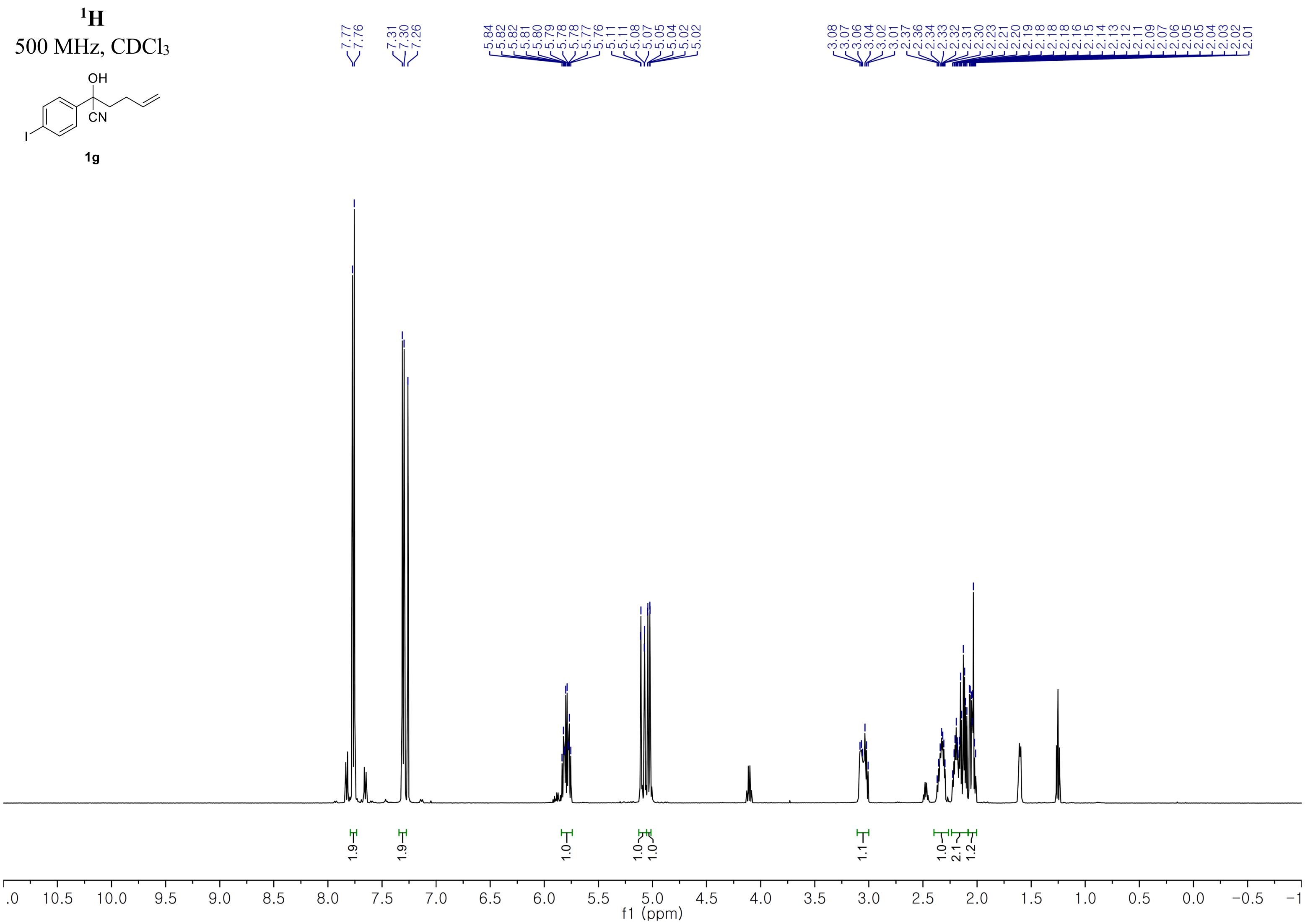
Note: The sample contains ~5% of the ketone precursor due to instability of the cyanohydrin.


^{1}H
500 MHz, $CDCl_3$
OH
CN
F_3C
1e
7.70
7.26
5.85 5.84 5.83 5.83 5.82 5.80 5.80 5.79 5.78 5.77 5.13 5.10 5.06 5.04
3.14 2.40 2.39 2.37 2.36 2.36 2.34 2.33 2.27 2.26 2.25 2.24 2.23 2.21 2.20 2.19 2.17 2.16 2.16 2.15 2.14 2.13 2.12 2.11 2.09 2.07 2.06
4.0
1.0
1.0
1.0
0.5
0.9
0.9
2.0
.0 10.5 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 −0.5
f1 (ppm)

¹H
500 MHz, $CDCl_3$



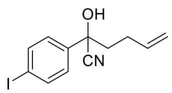
Note: The sample contains ~5% of the ketone precursor due to instability of the cyanohydrin.



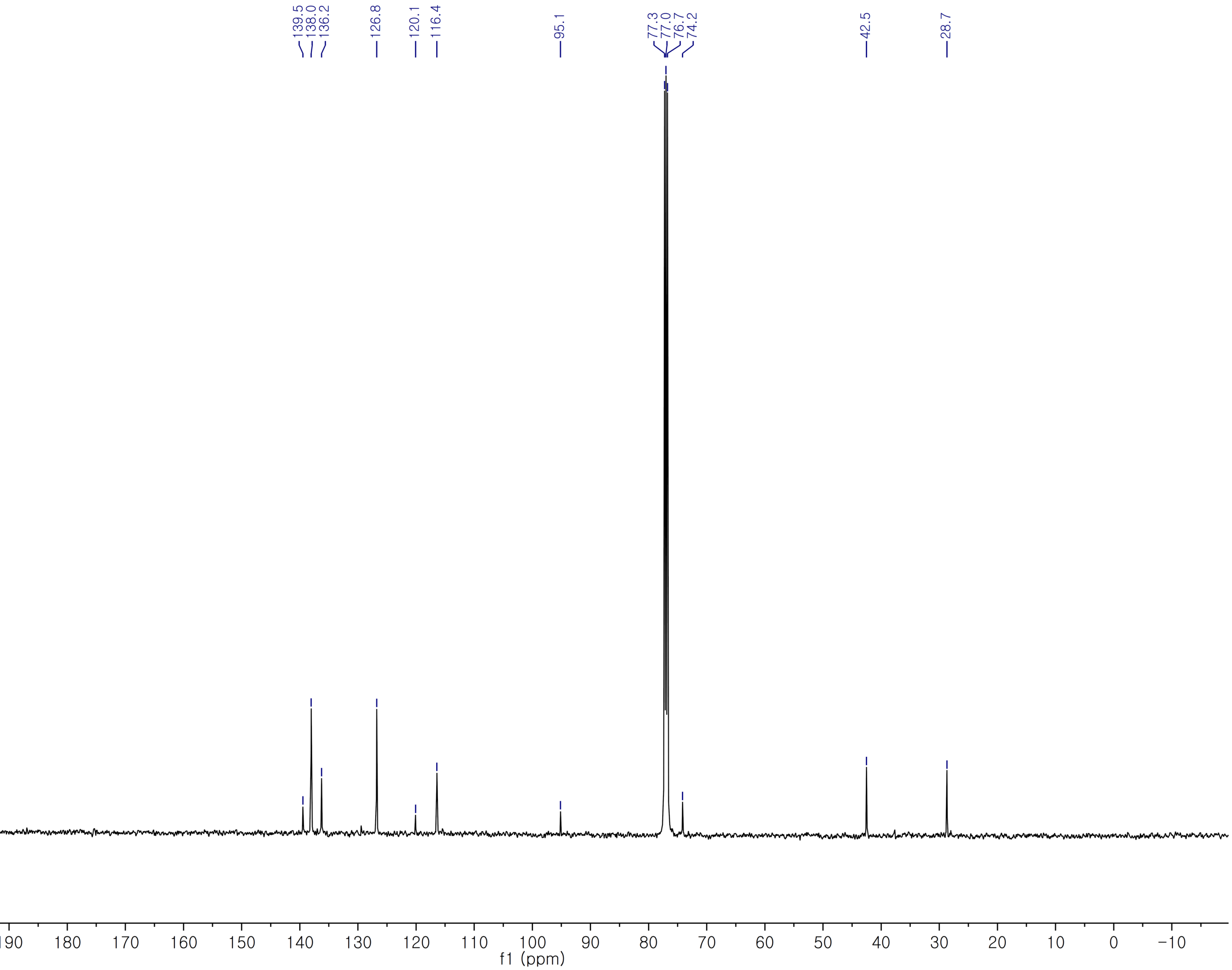
Note: The sample contains ~5% of the ketone precursor due to instability of the cyanohydrin.

^{13}C

126 MHz, $CDCl_3$

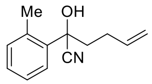


1g

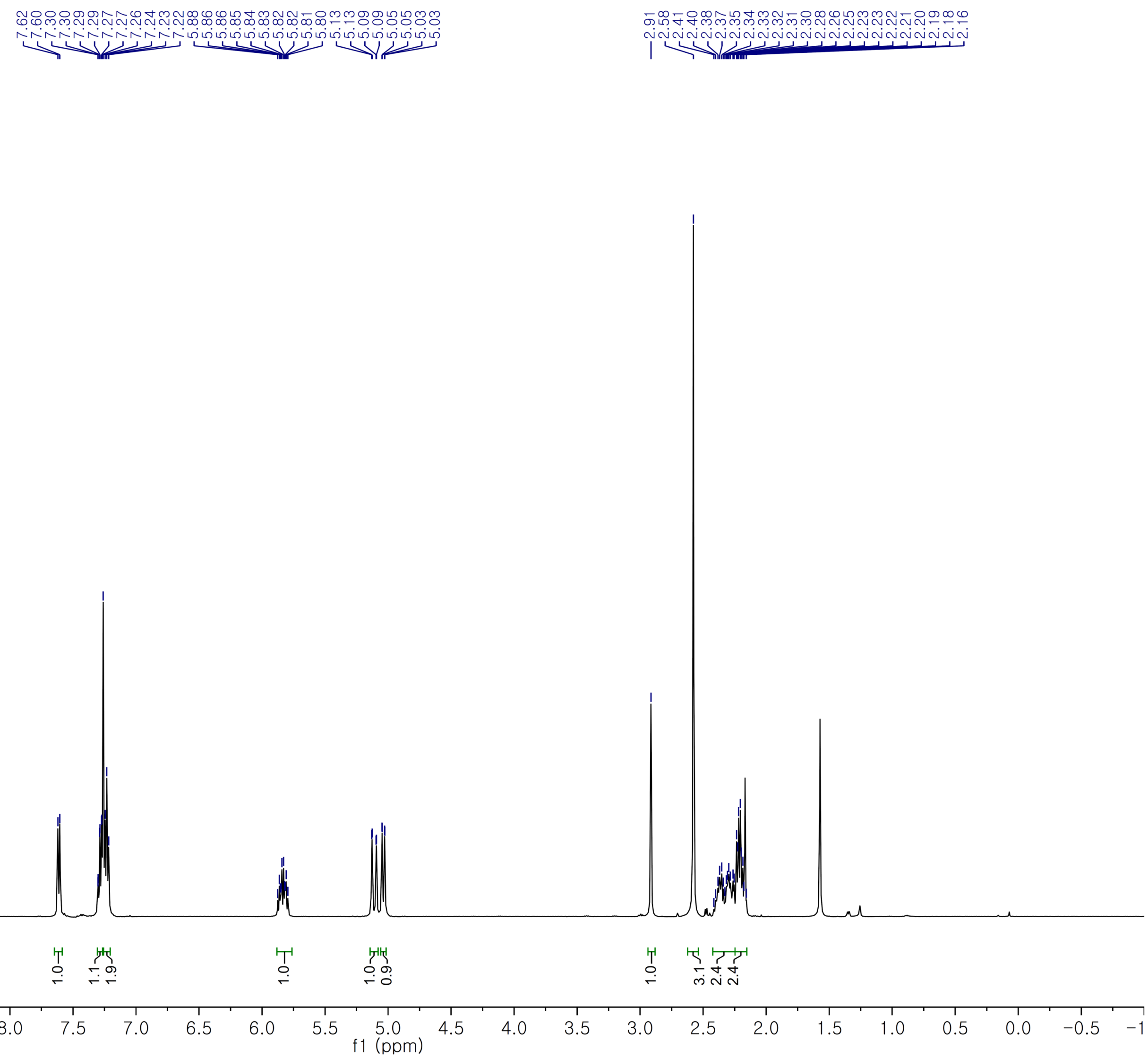


^{1}**H**

500 MHz, $CDCl_3$

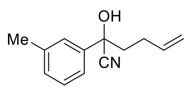


1h

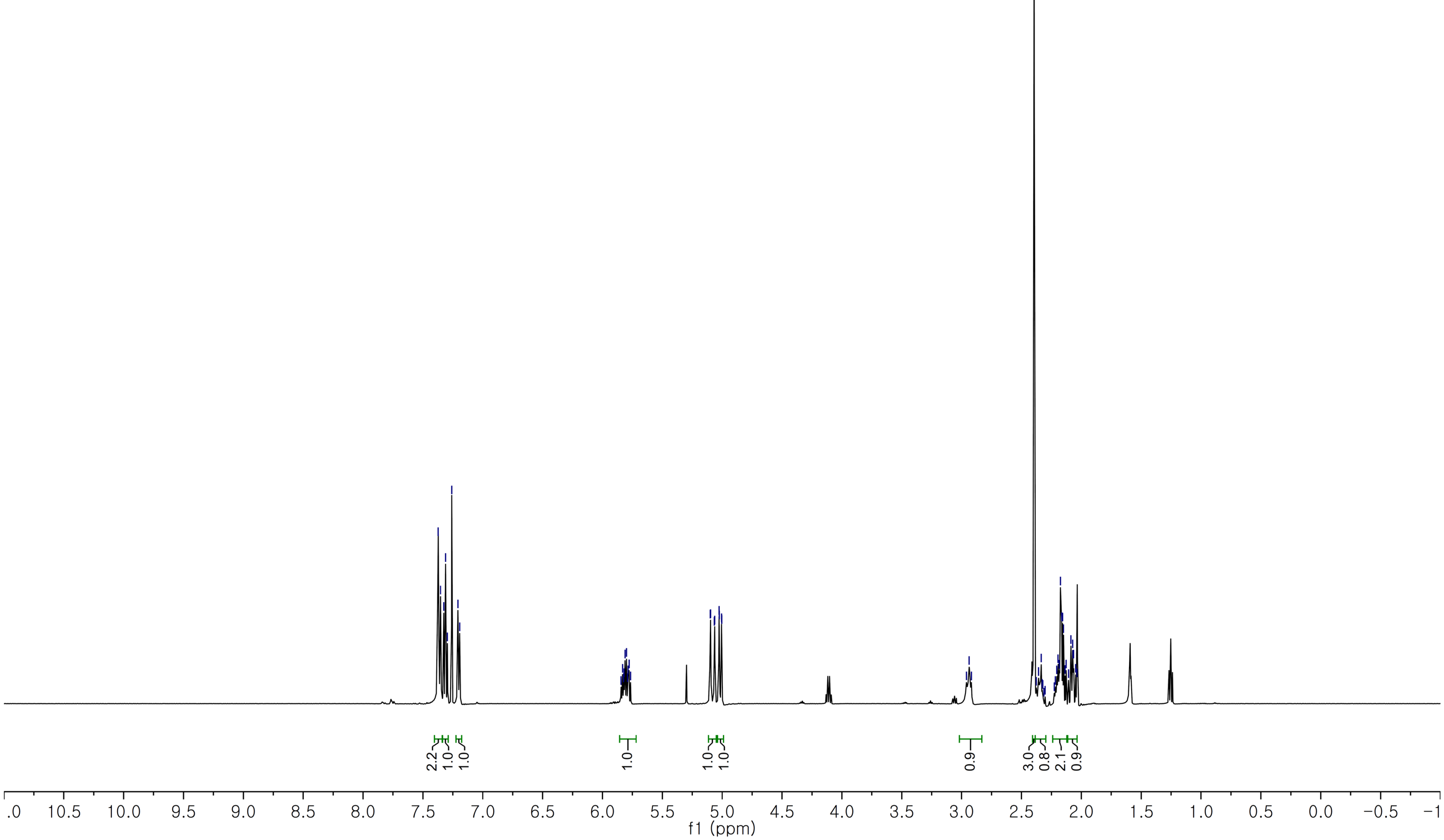


^{1}H

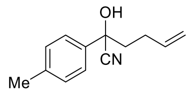
500 MHz, $CDCl_3$



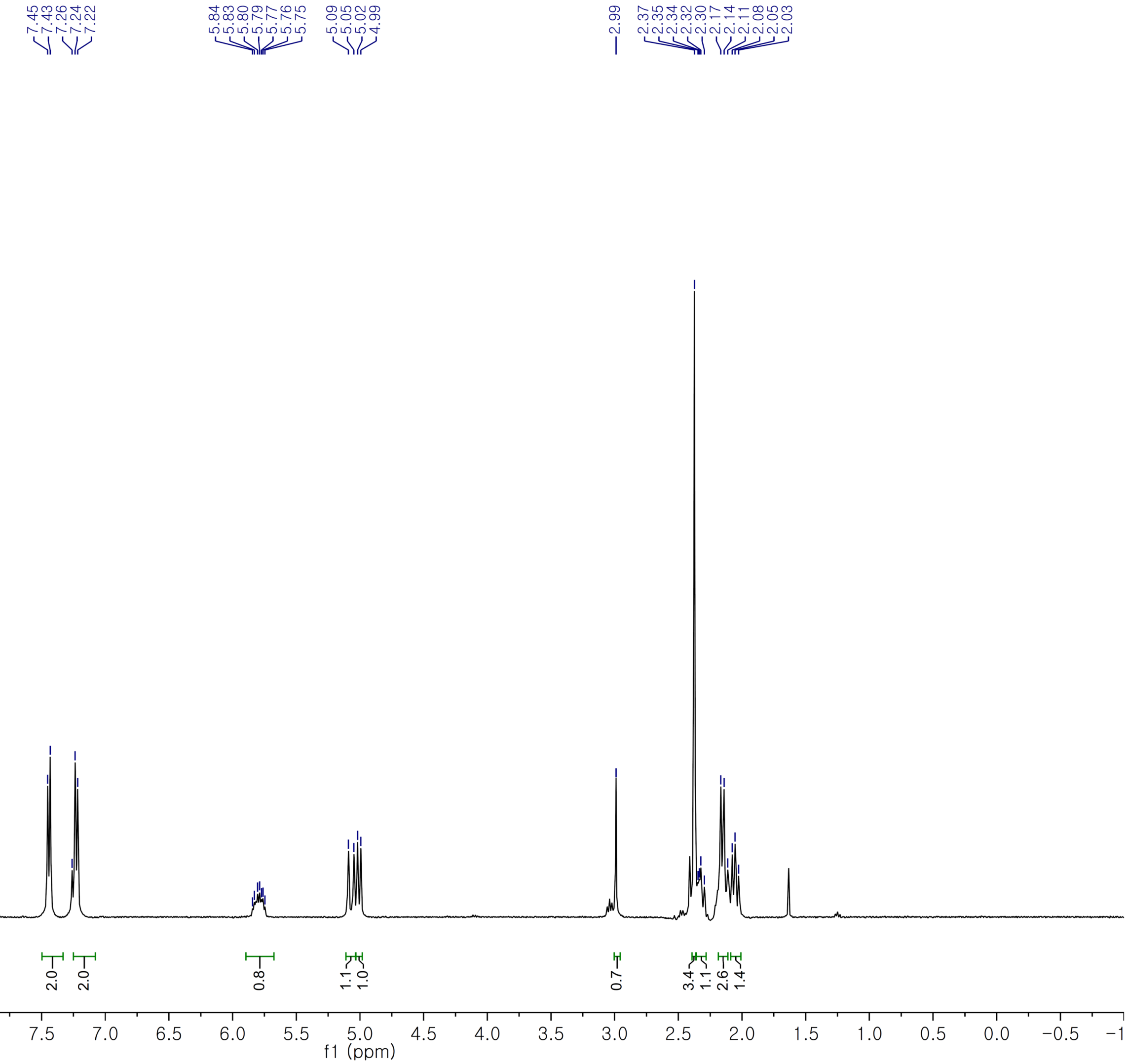
1i



^{1}H
500 MHz, $CDCl_3$

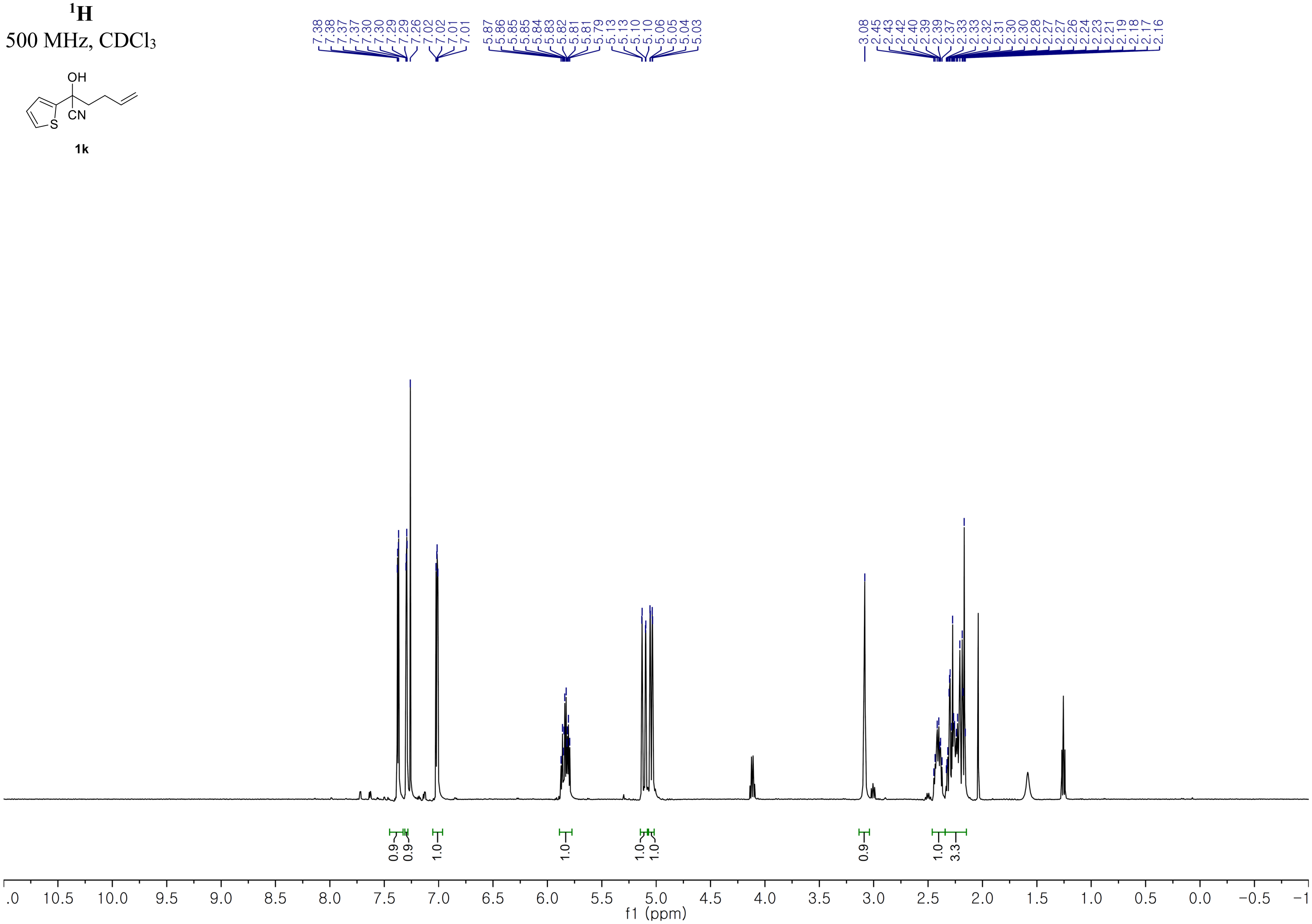


1j



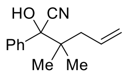
Note: The sample contains ~5% of the ketone precursor due to instability of the cyanohydrin.

^{1}H
500 MHz, $CDCl_3$

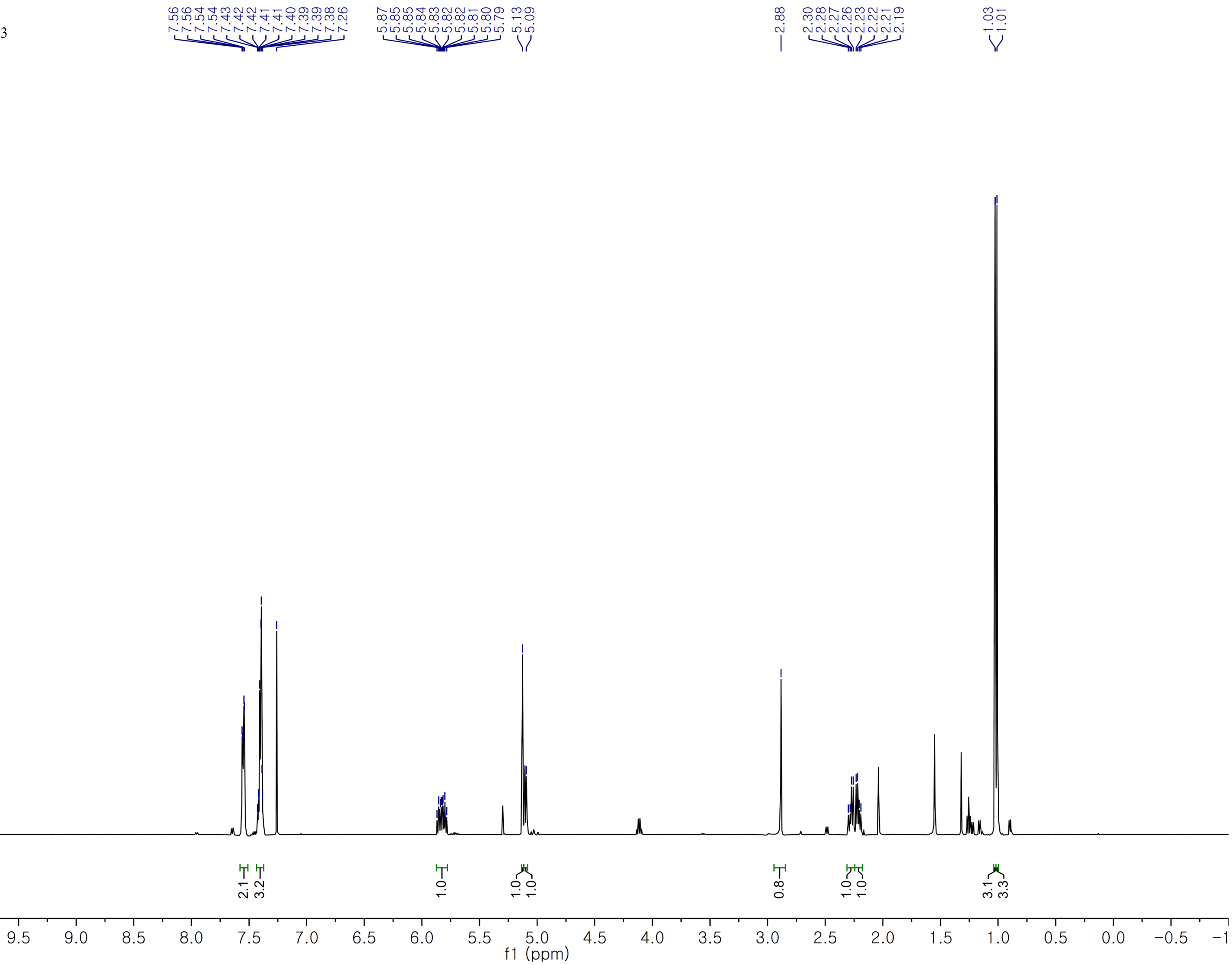


^{1}H

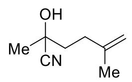
500 MHz, $CDCl_3$



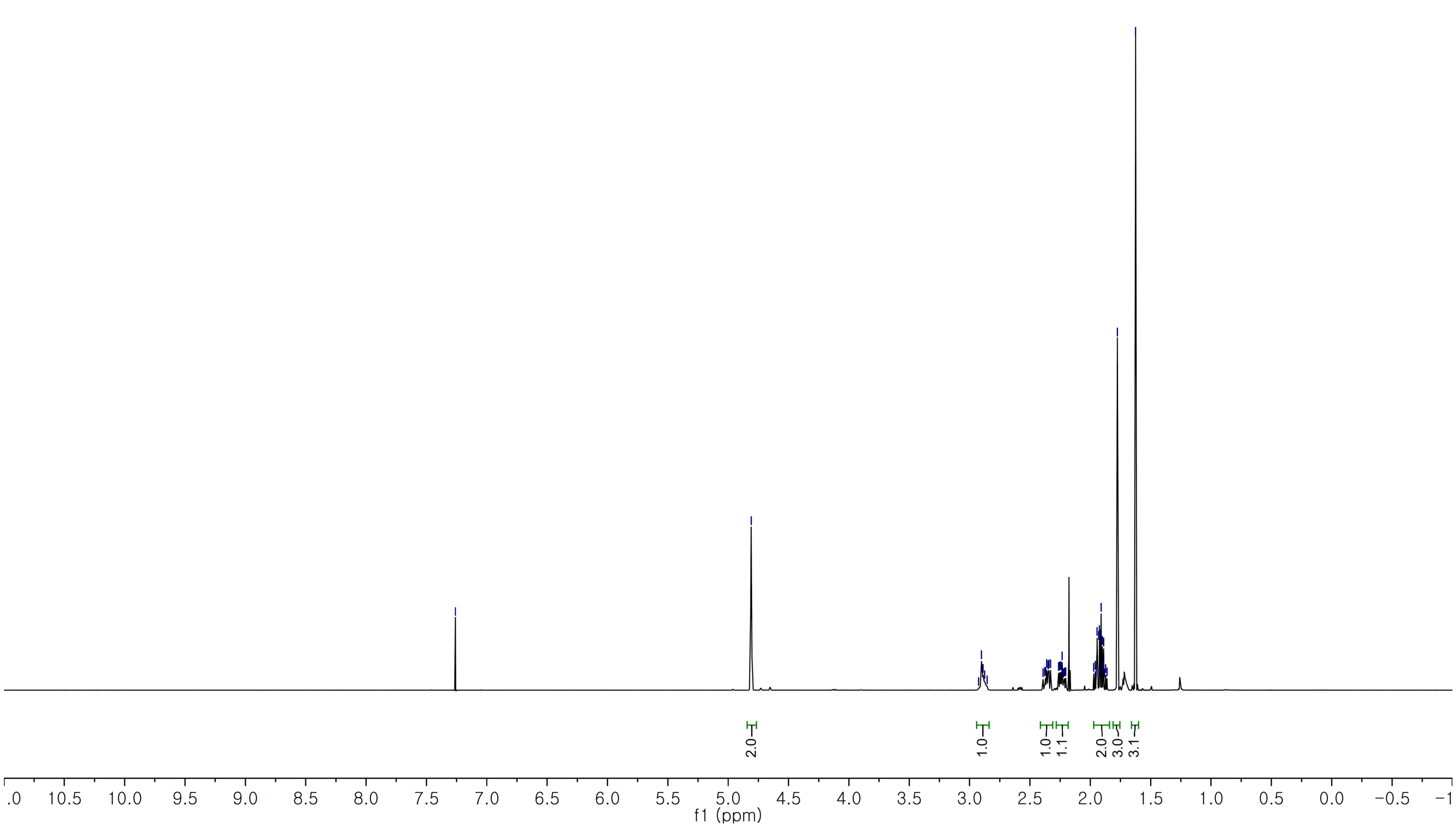
1l



1H
500 MHz, CDCl3

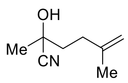


1m

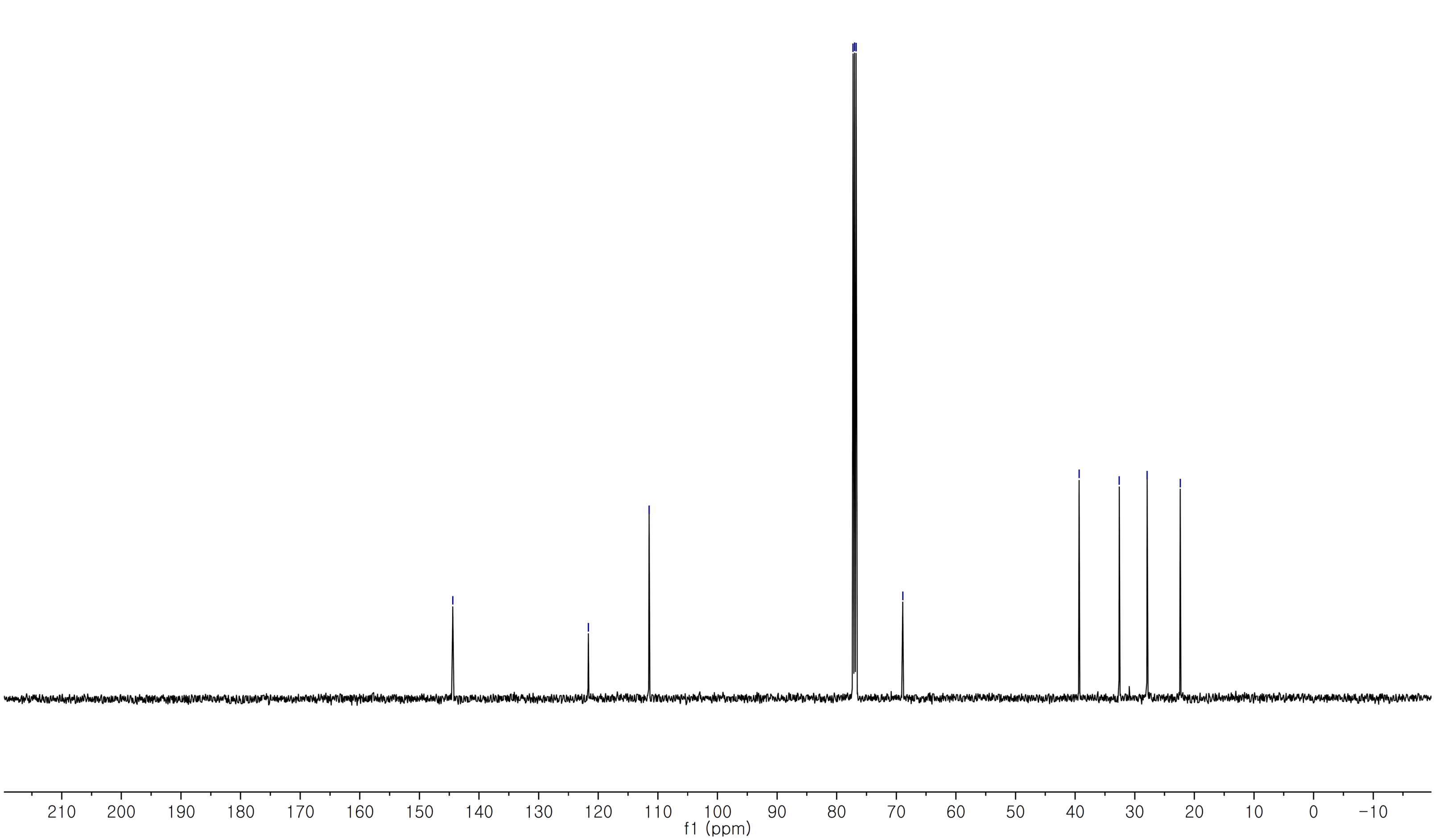


^{13}C

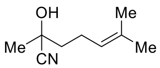
126 MHz, $CDCl_3$



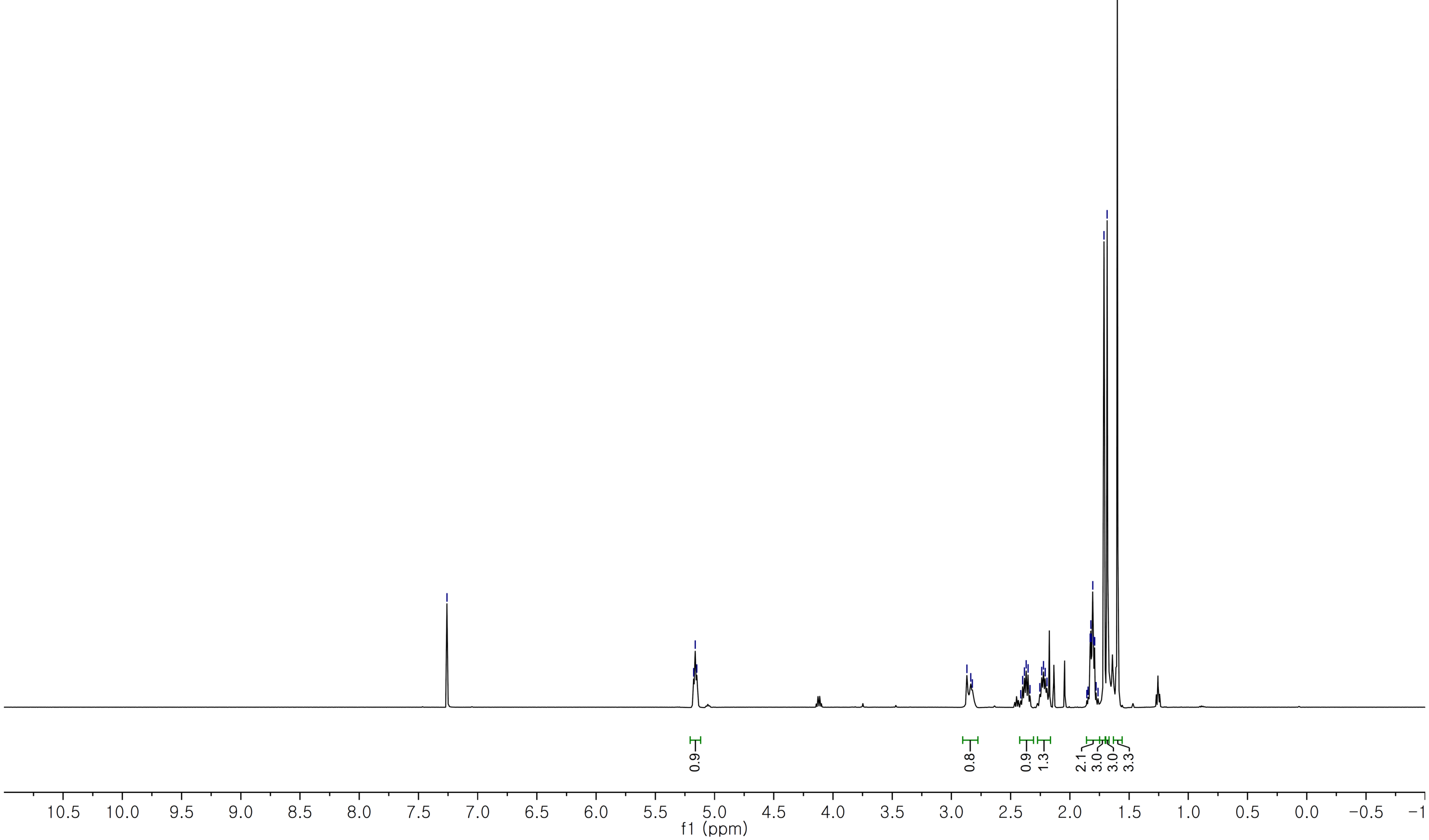
1m

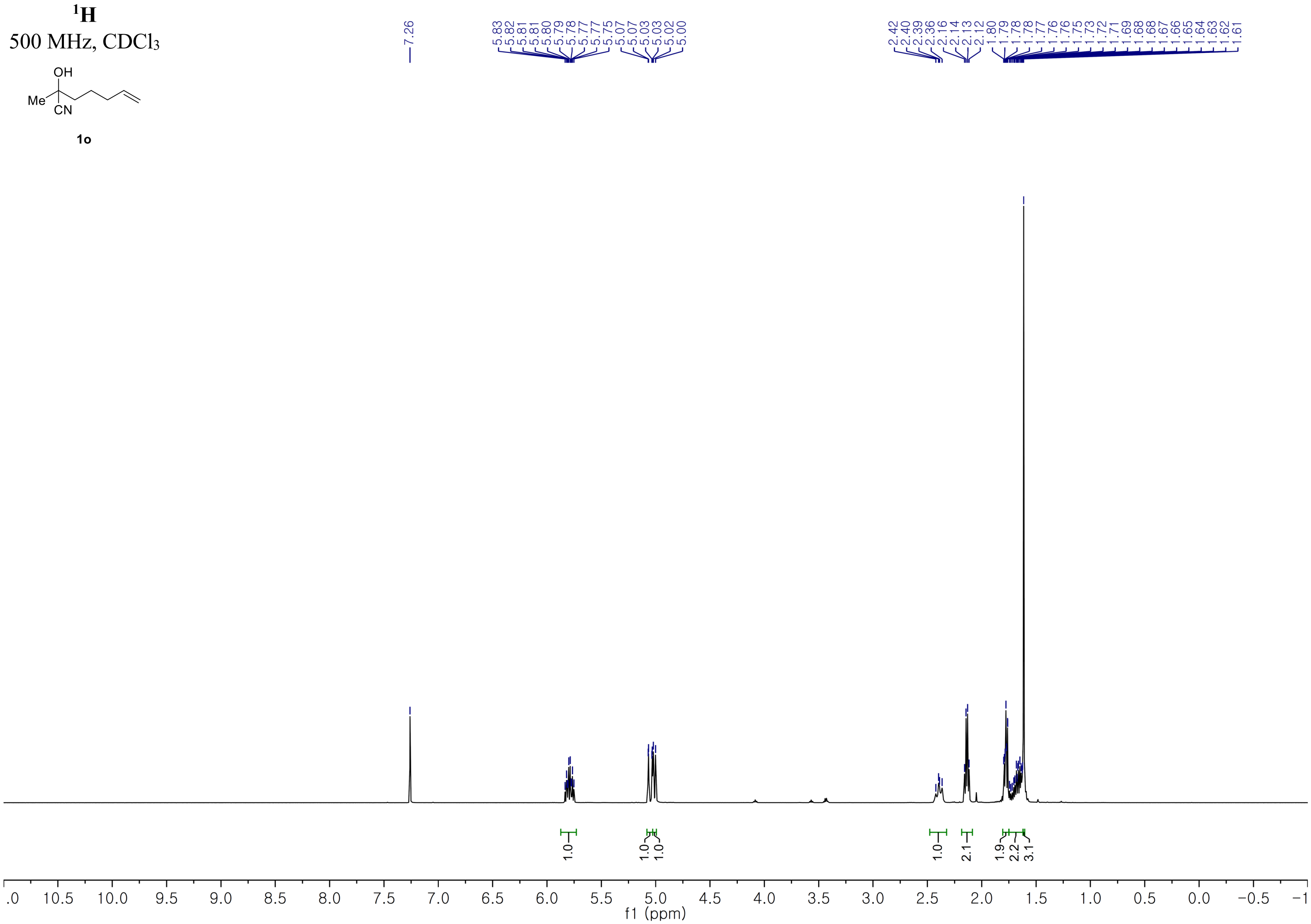


^{1}H
500 MHz, $CDCl_3$



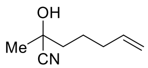
1n



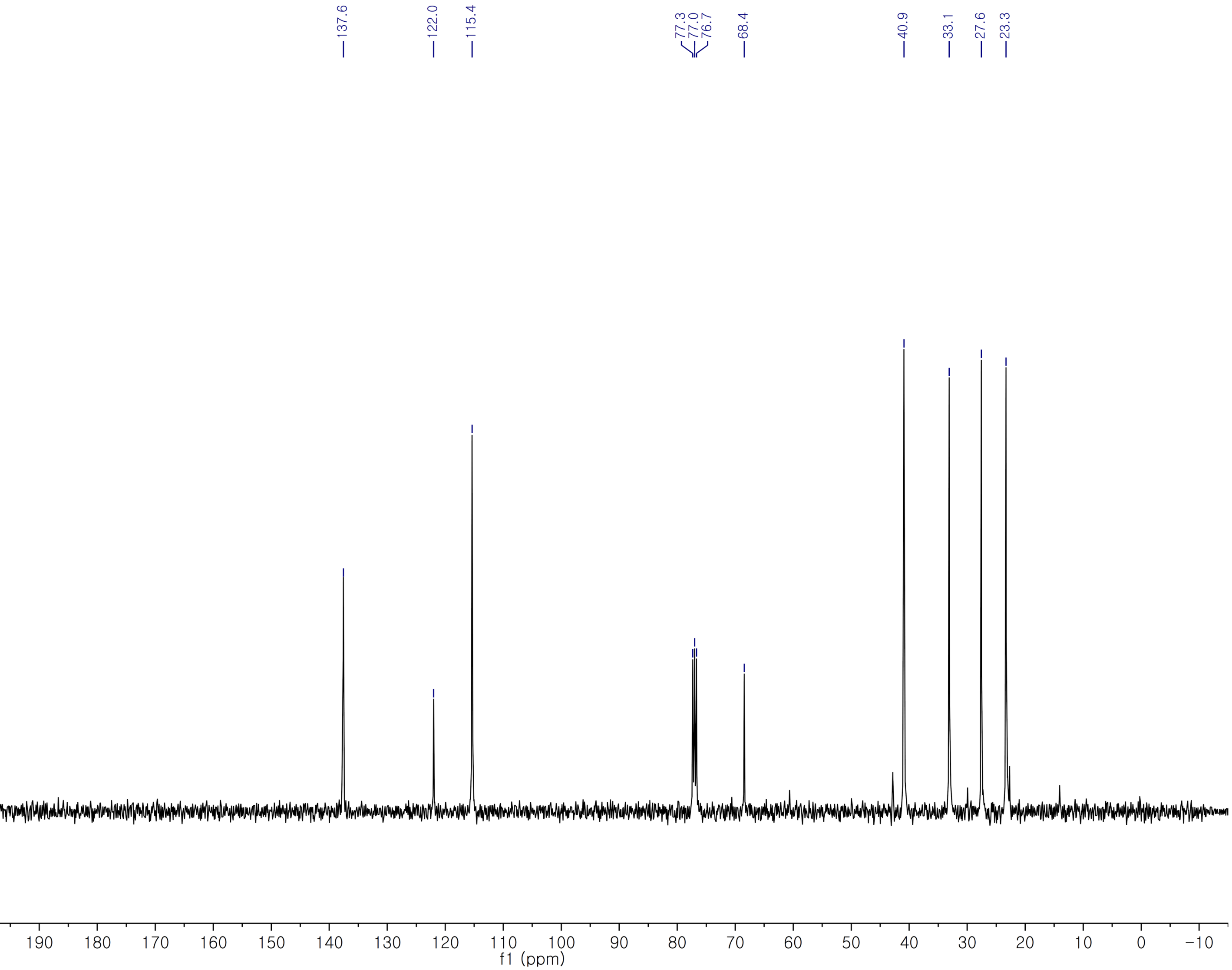


^{1}H
500 MHz, CDCl$_3$
OH
Me
CN
1o
7.26
5.83 5.82 5.81 5.80 5.79 5.78 5.77 5.77 5.75 5.07 5.03 5.03 5.02 5.00
2.42 2.40 2.39 2.36 2.16 2.14 2.13 2.12 1.80 1.79 1.78 1.78 1.77 1.76 1.76 1.75 1.73 1.72 1.71 1.69 1.68 1.68 1.67 1.66 1.65 1.64 1.63 1.62 1.61
1.0 1.0 1.0 1.0 2.1 1.9 2.2 3.1
f1 (ppm)

^{13}C
126 MHz, $CDCl_3$

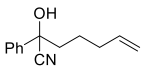


1o

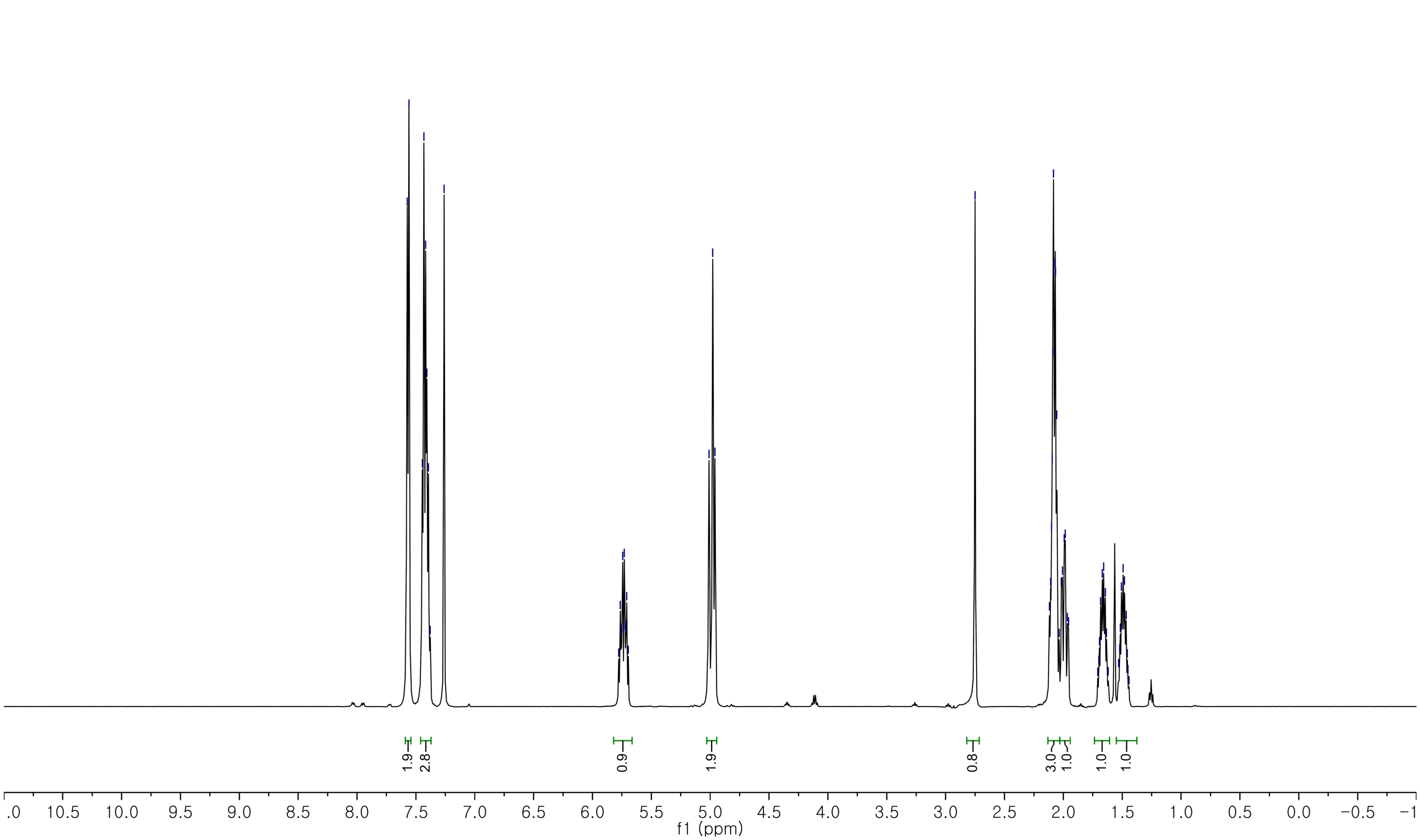


^{1}H

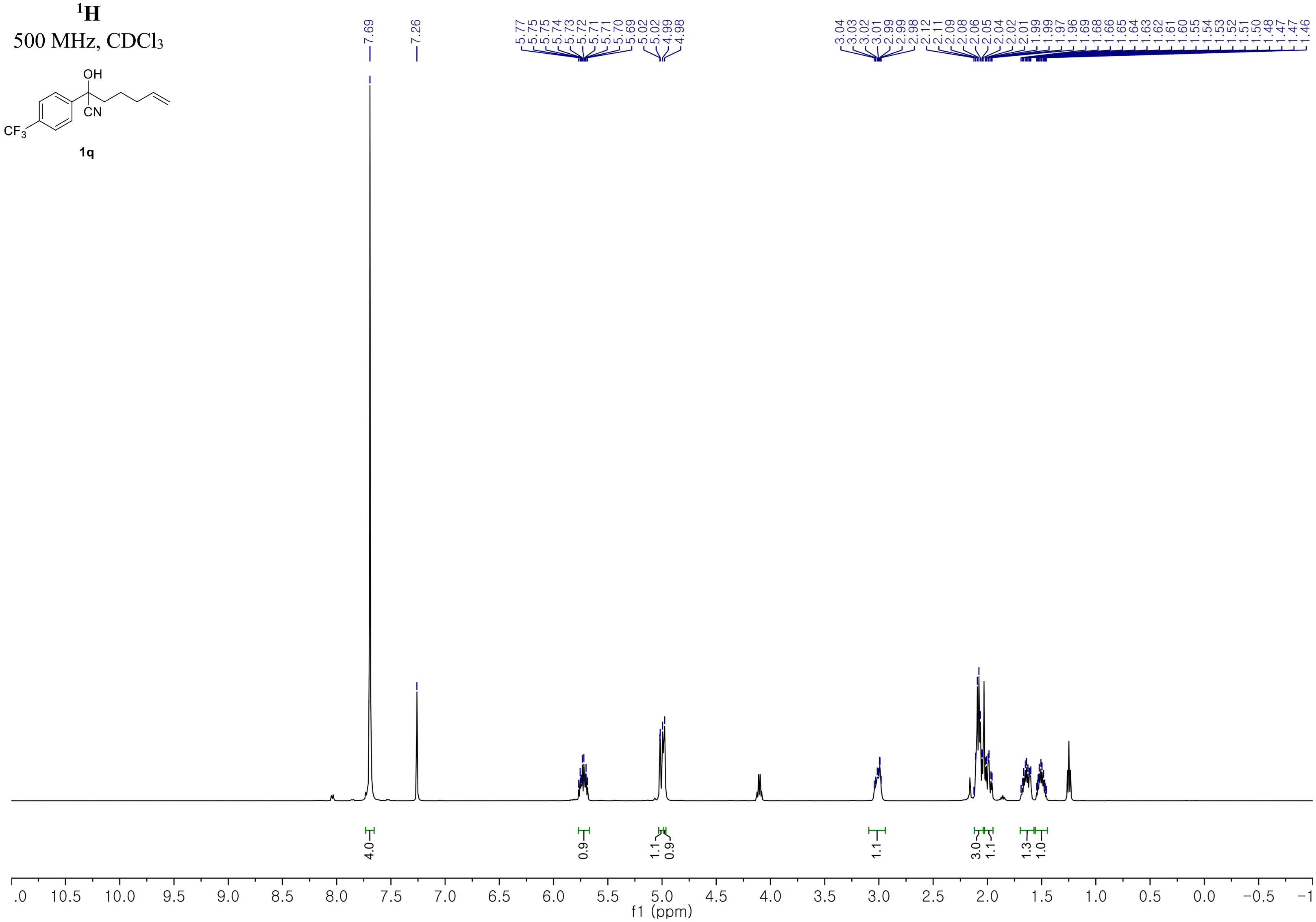
500 MHz, $CDCl_3$



1p

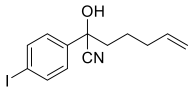


^{1}H
500 MHz, CDCl$_3$

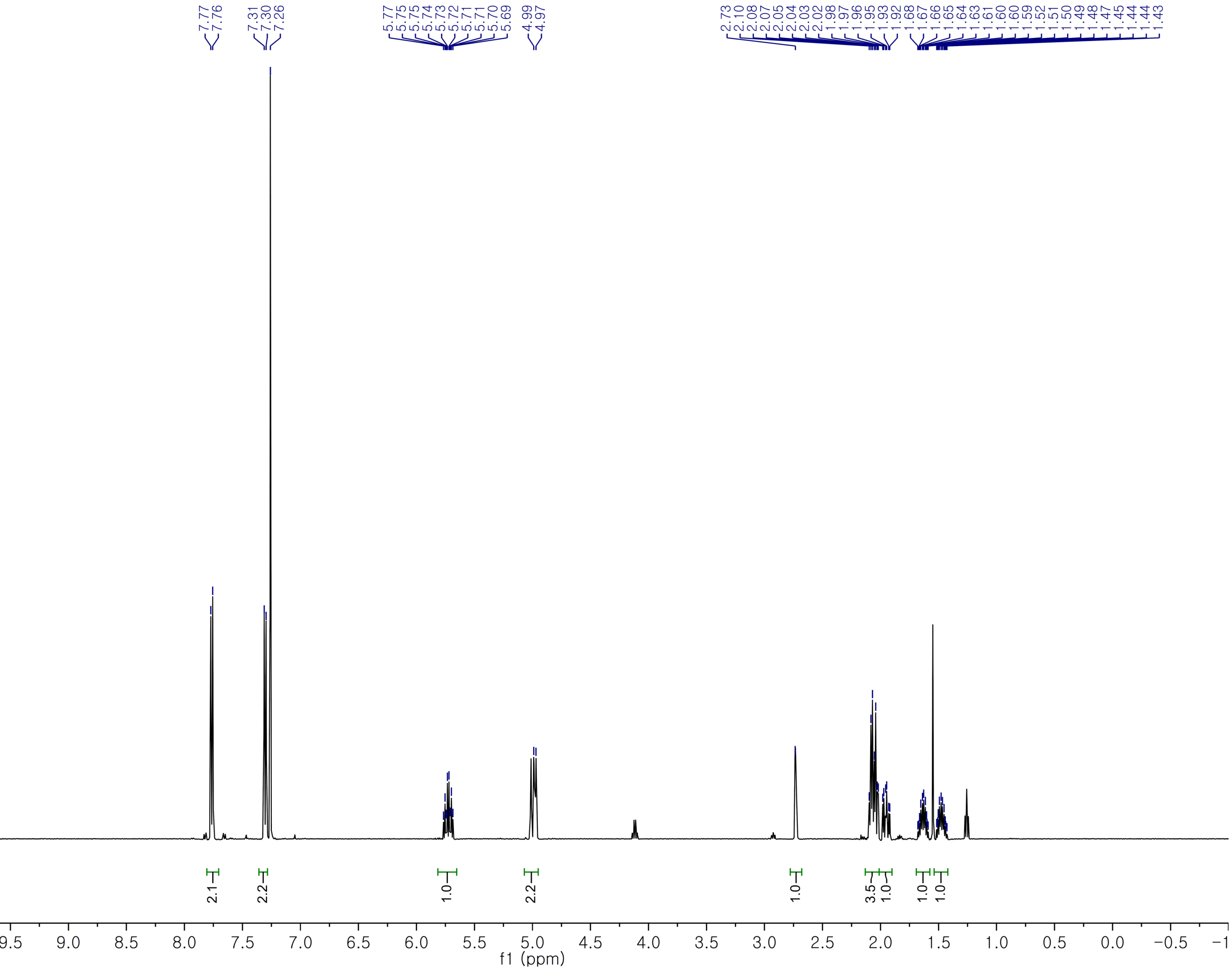


^{1}H

500 MHz, $CDCl_3$

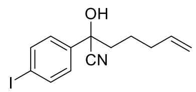


1r

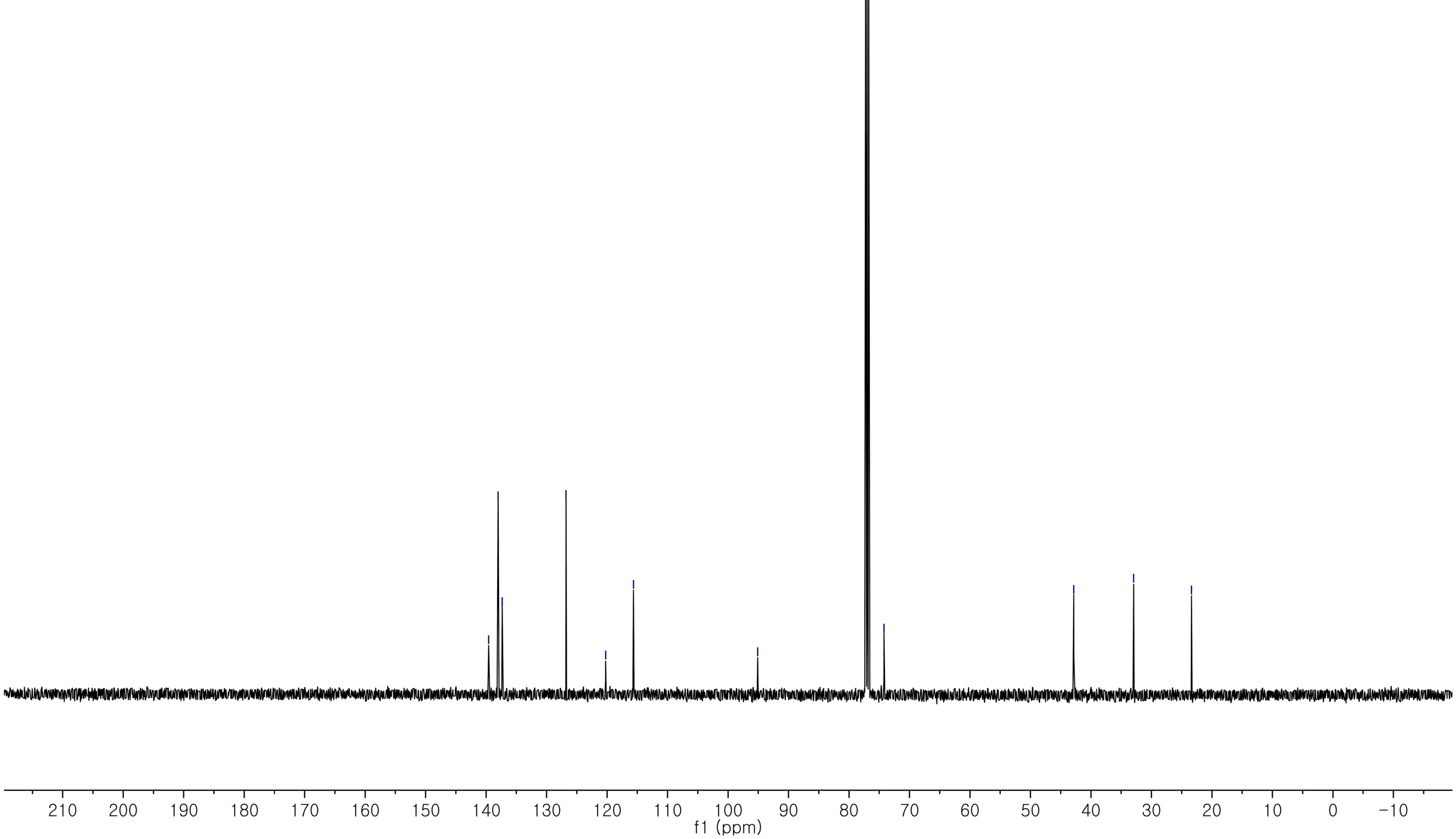


^{13}C

126 MHz, $CDCl_3$

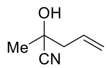


1r

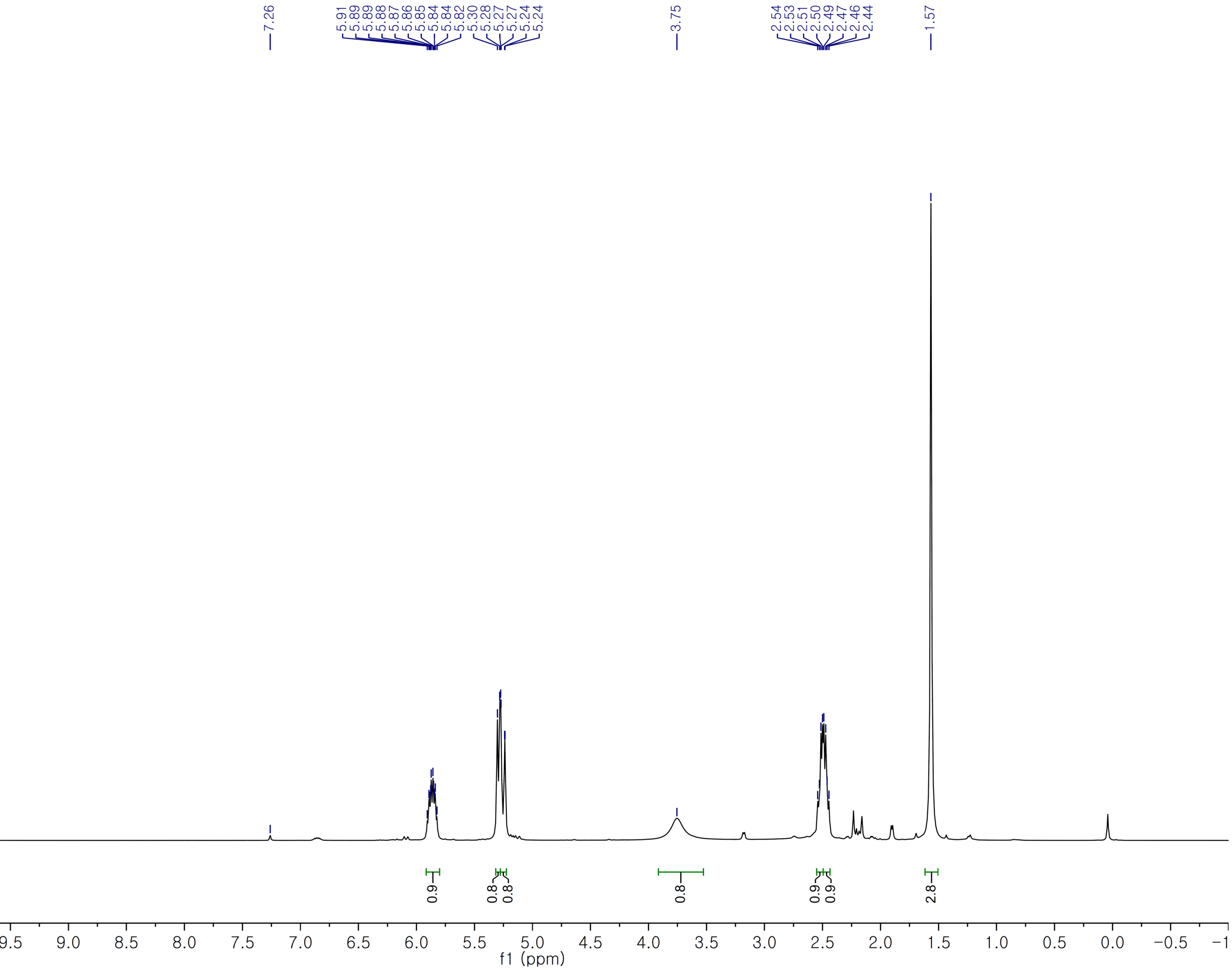


^{1}H

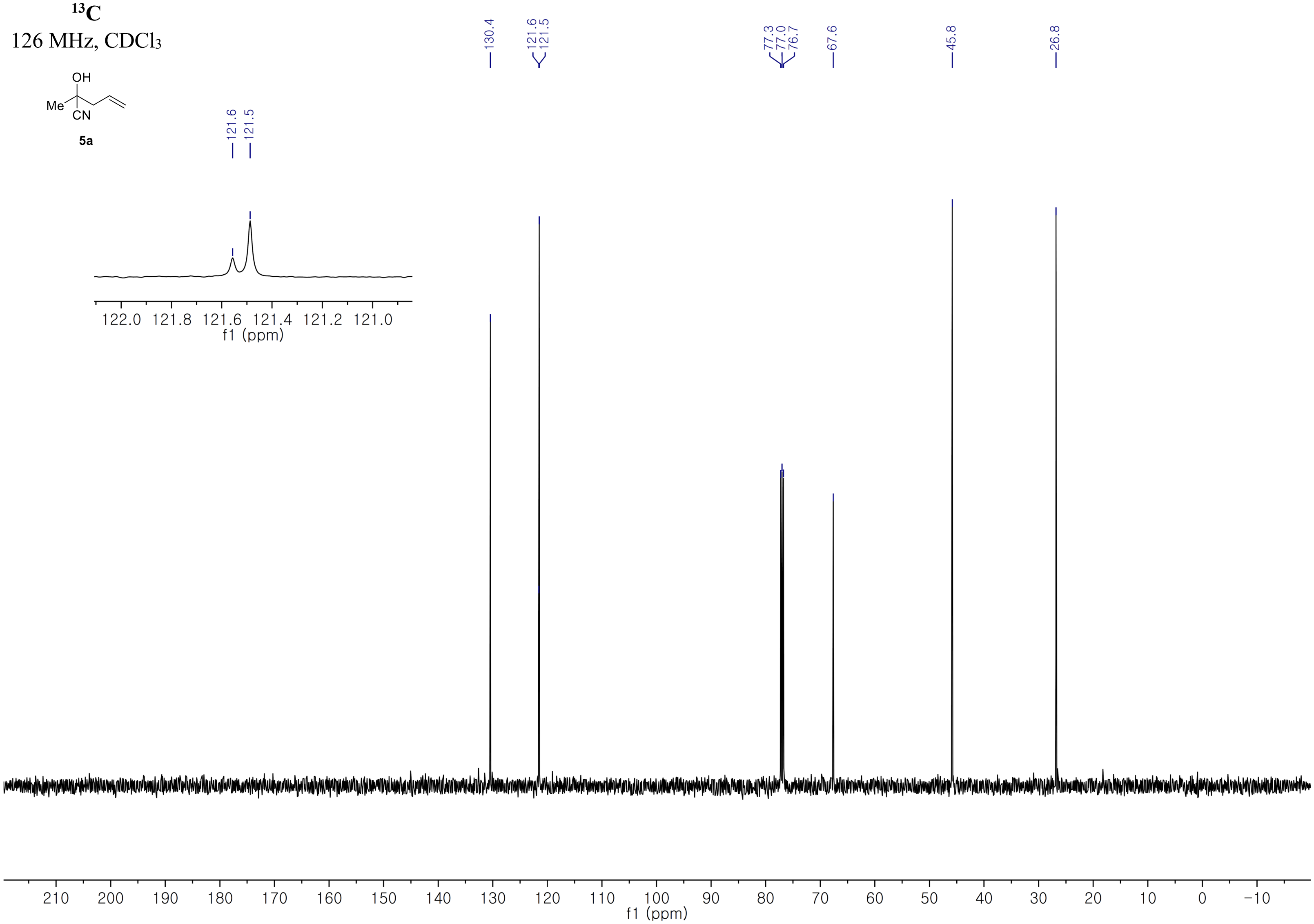
500 MHz, $CDCl_3$



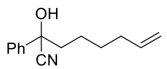
5a



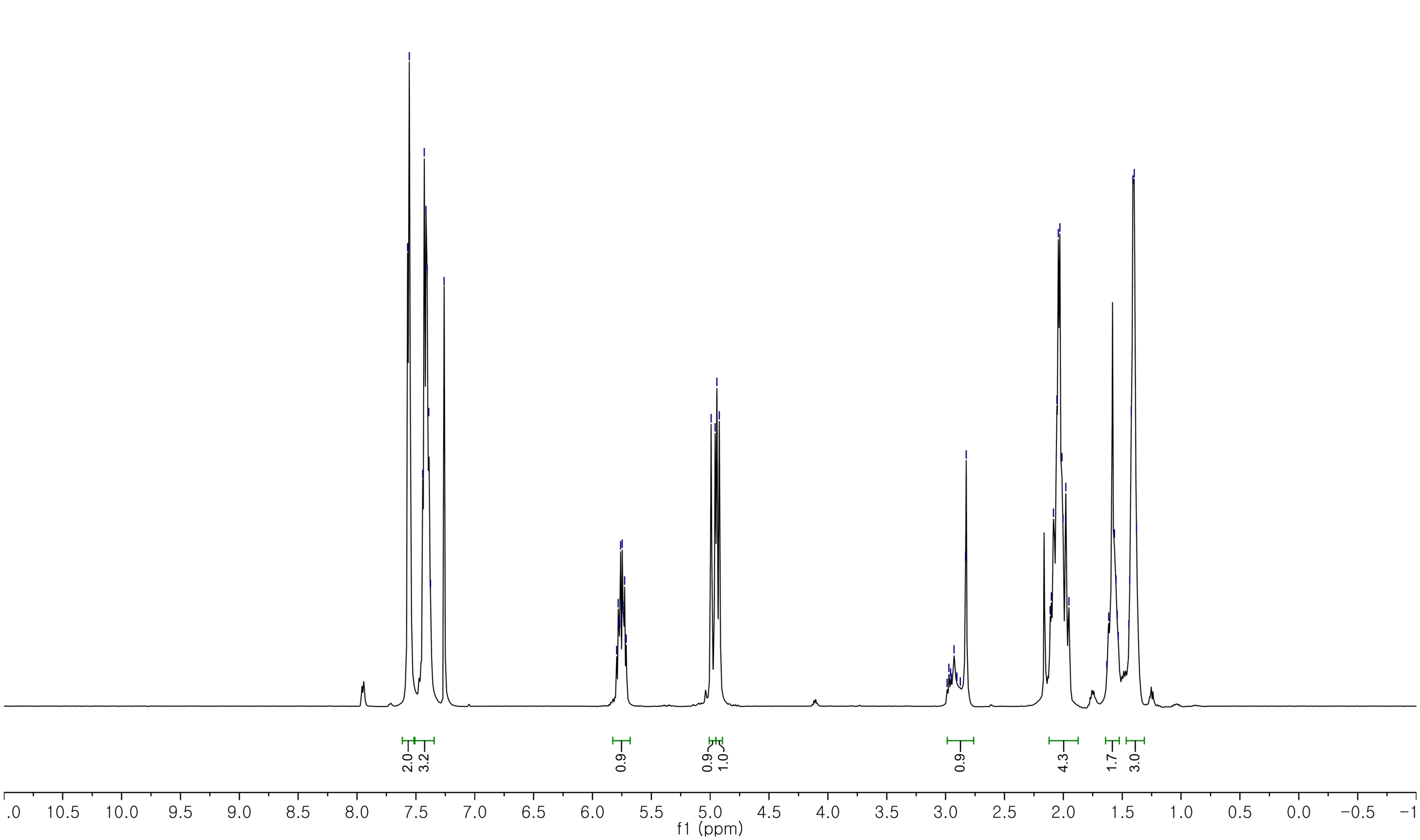
^{13}C
126 MHz, $CDCl_3$



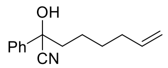
^{1}H
500 MHz, $CDCl_3$



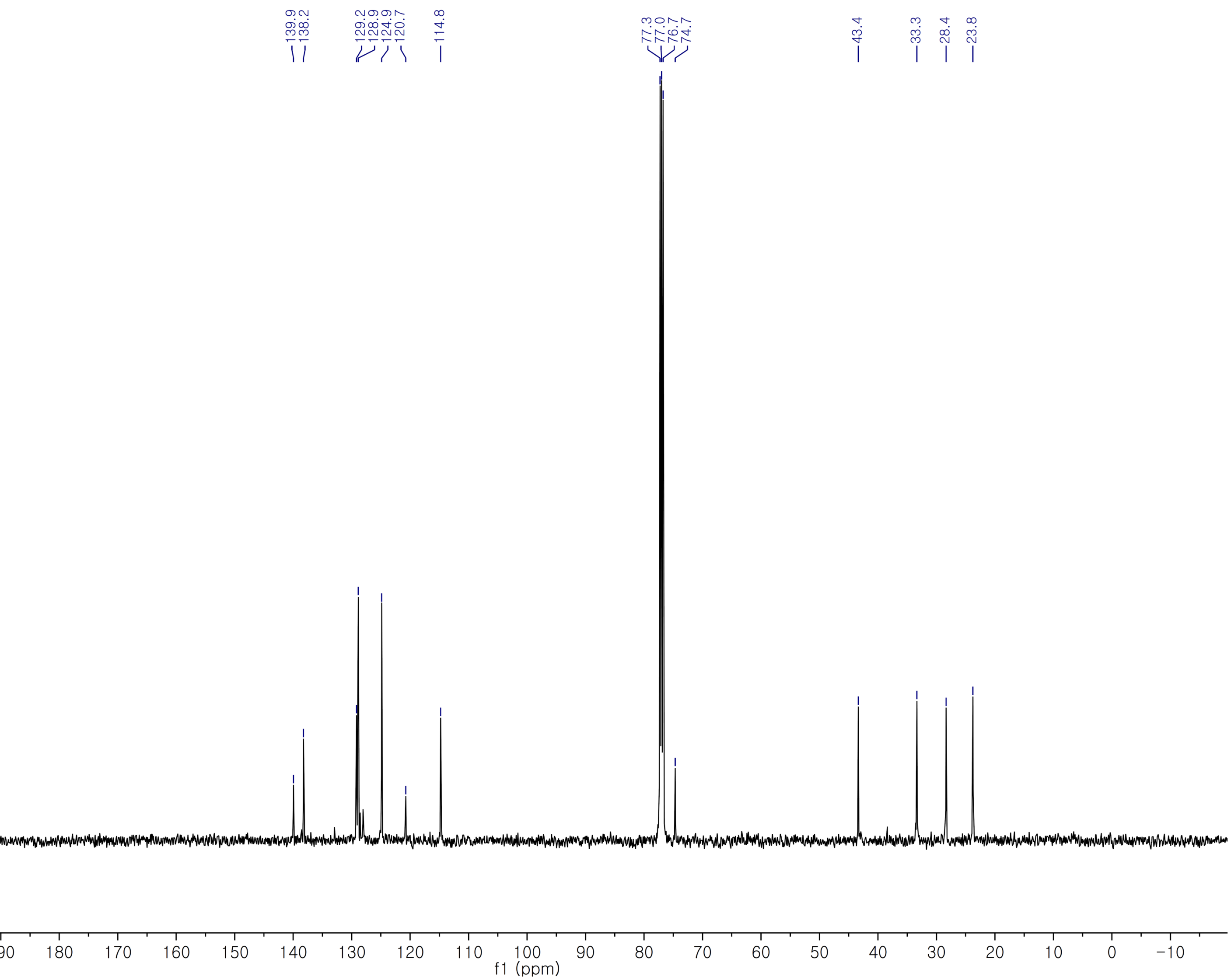
5b



^{13}C
126 MHz, $CDCl_3$

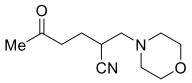


5b

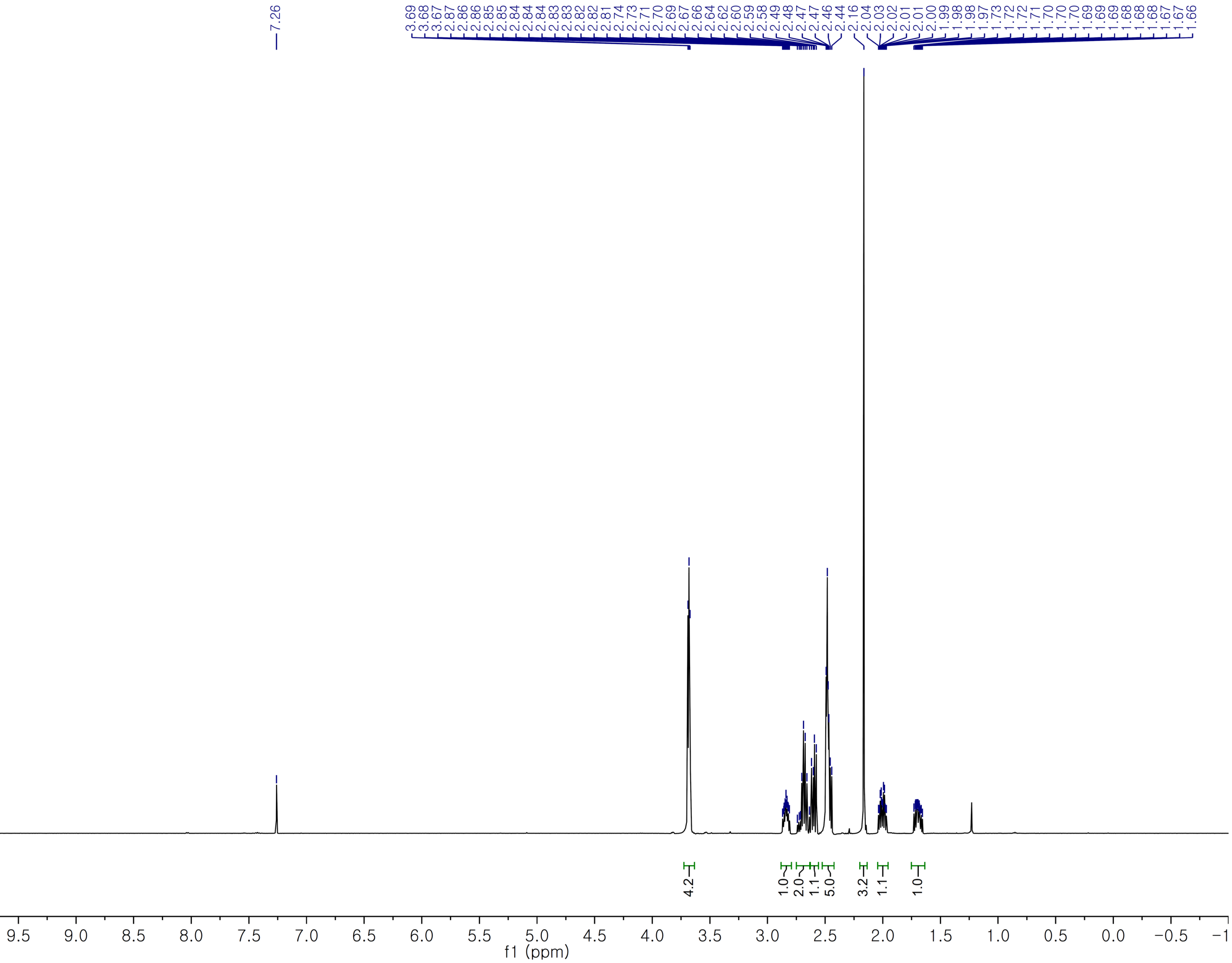


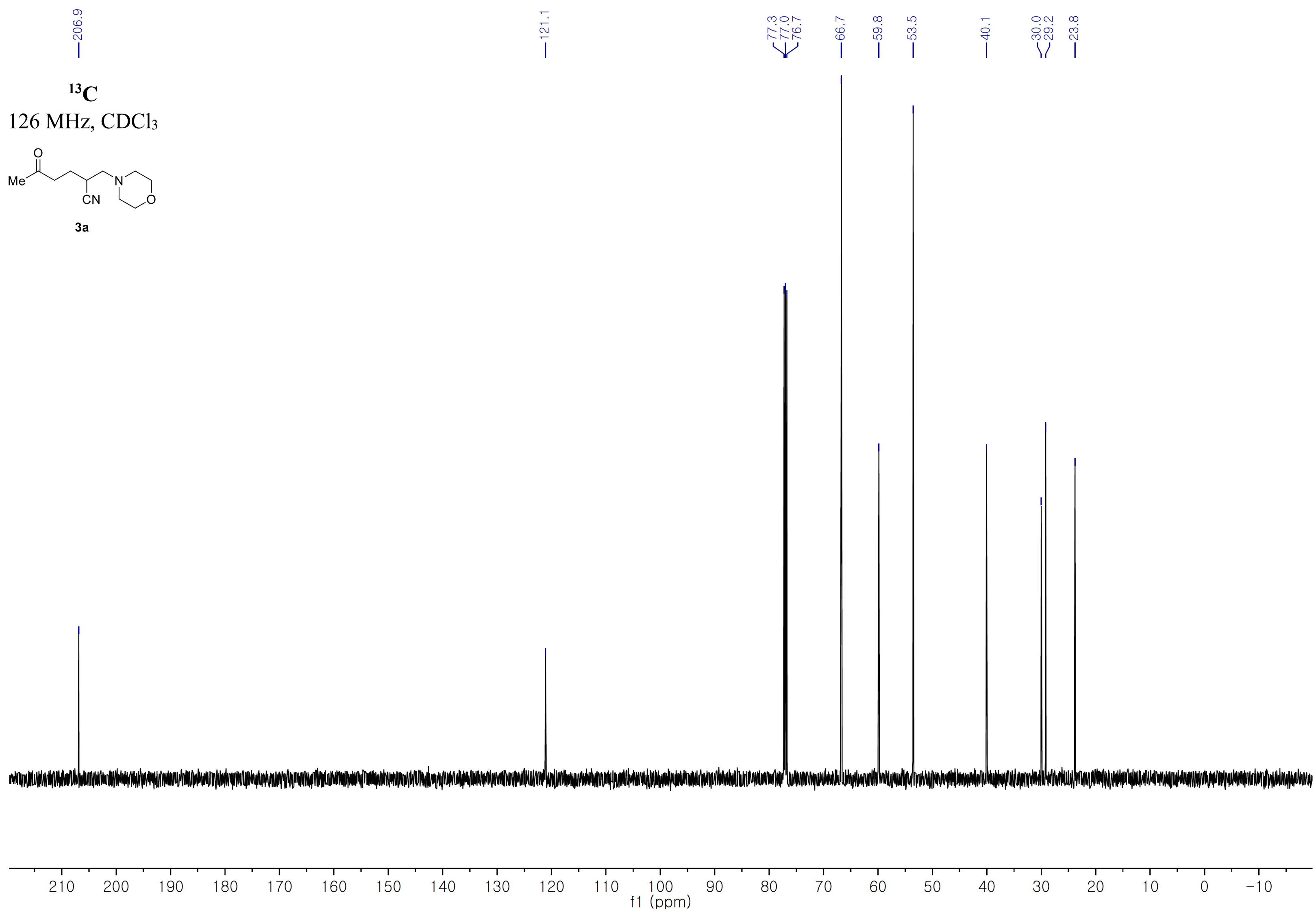
^{1}H

500 MHz, $CDCl_3$



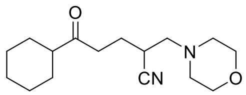
3a



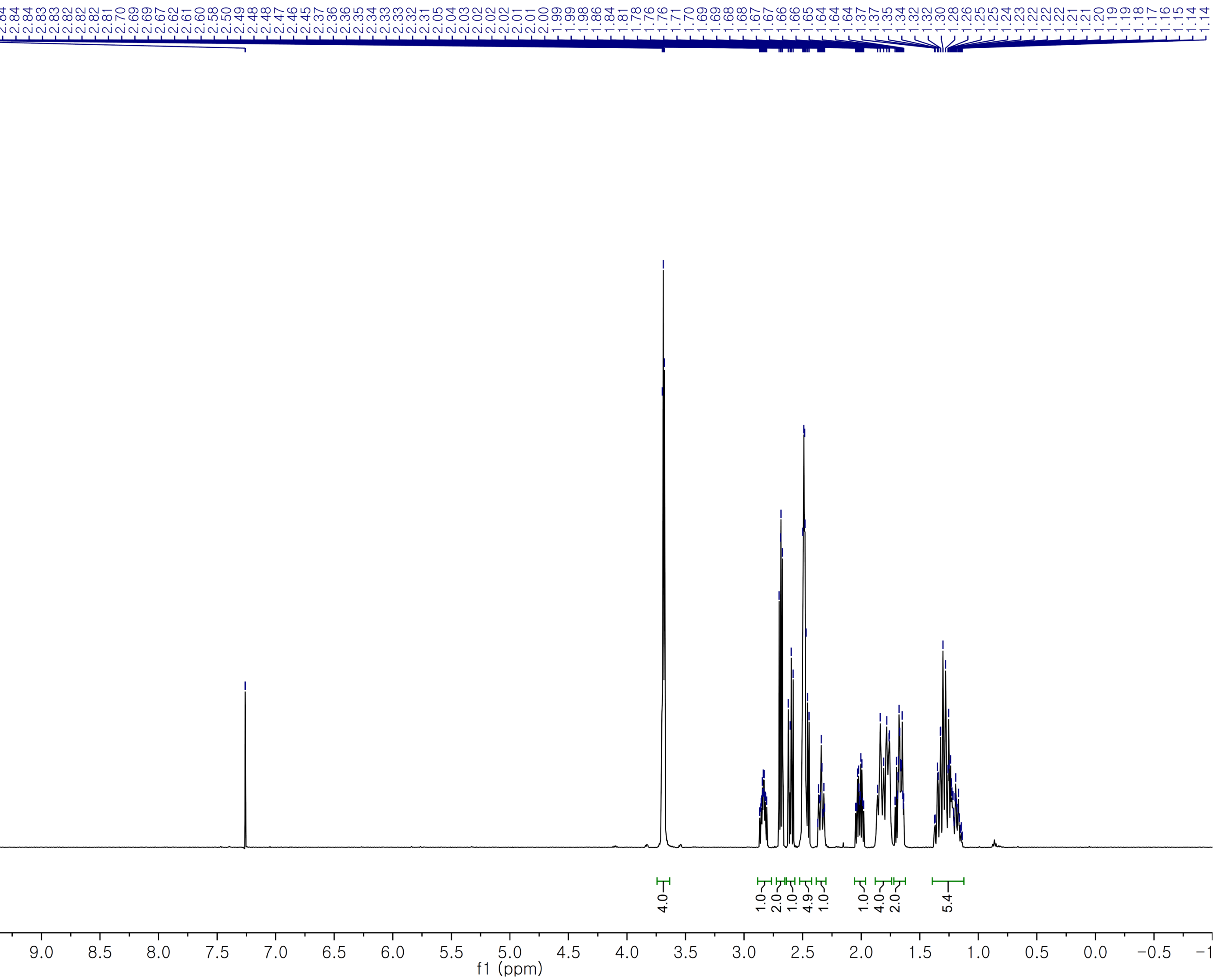

206.9
121.1
77.3
77.0
76.7
66.7
59.8
53.5
40.1
30.0
29.2
23.8
13C
126 MHz, CDCl3
O
Me
CN
N
O
3a
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10
f1 (ppm)

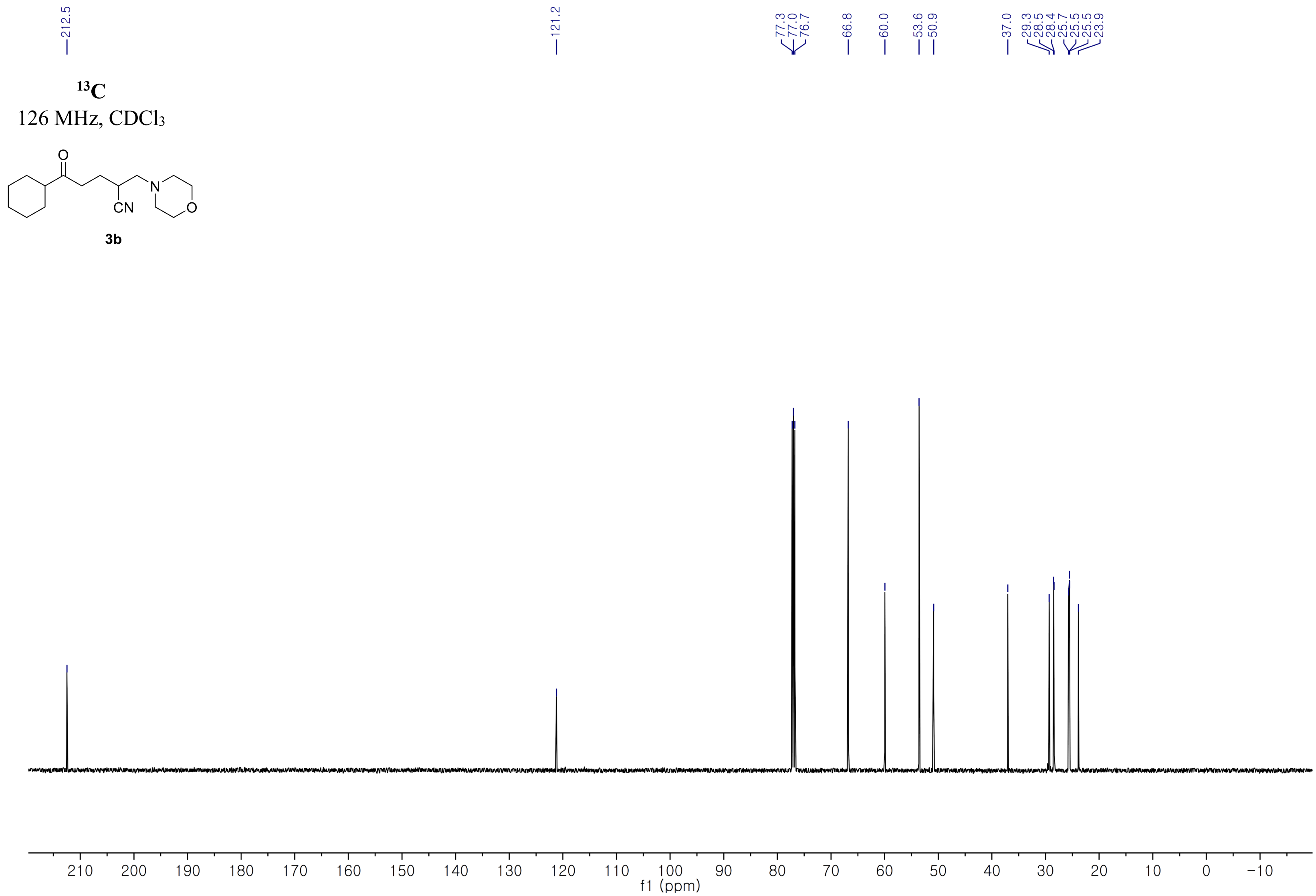
^{1}H

500 MHz, $CDCl_3$



3b

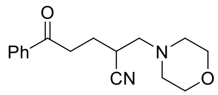




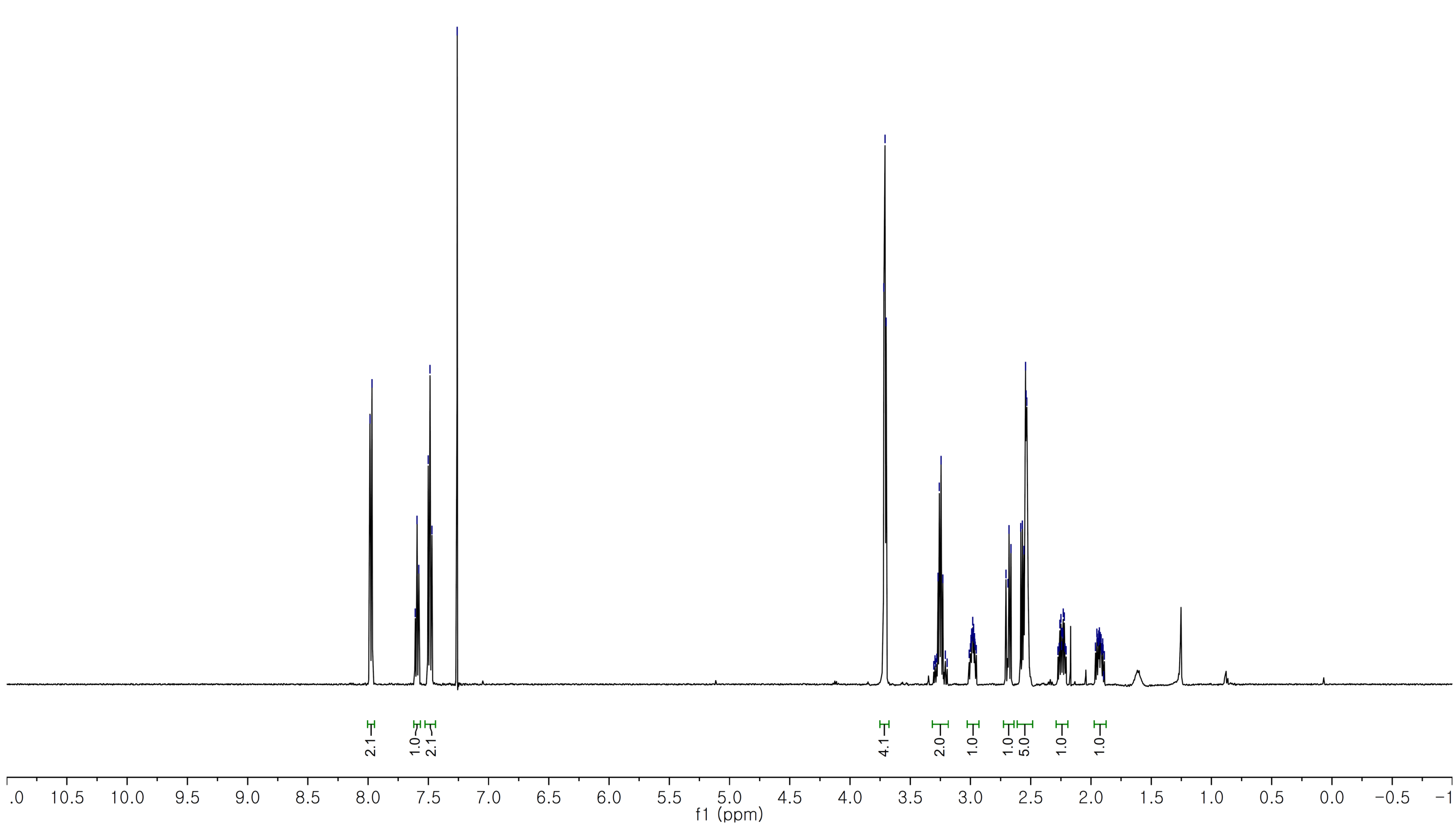
13C
126 MHz, CDCl3
O
CN
N
O
3b
212.5
121.2
77.3
77.0
76.7
66.8
60.0
53.6
50.9
37.0
29.3
28.5
28.4
25.7
25.5
25.5
23.9
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10
f1 (ppm)

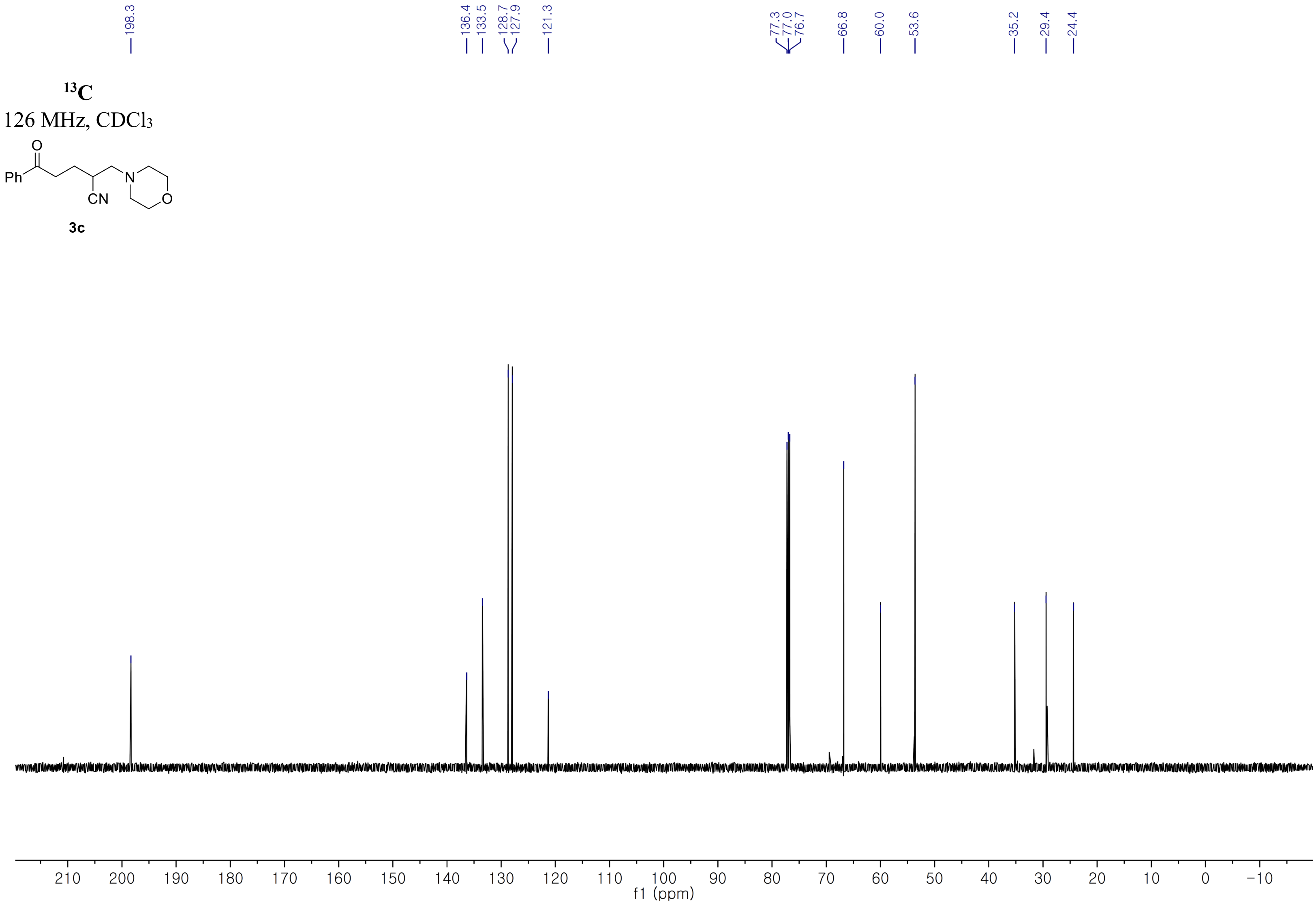
^{1}H

500 MHz, $CDCl_3$



3c

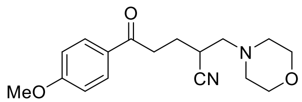




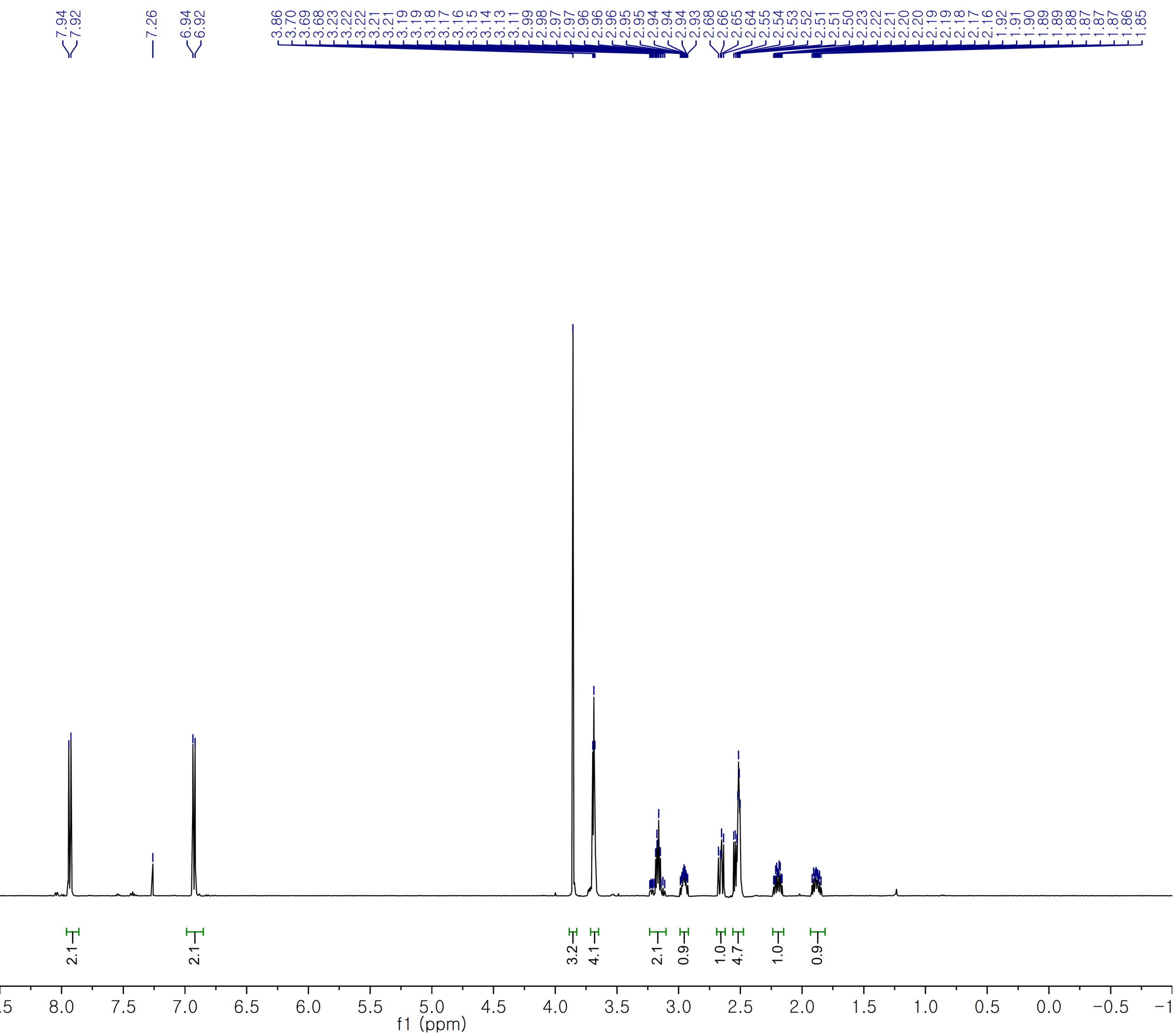
198.3
136.4
133.5
128.7
127.9
121.3
77.3
77.0
76.7
66.8
60.0
53.6
35.2
29.4
24.4
13C
126 MHz, CDCl3
O
Ph
N
O
CN
3c
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10
f1 (ppm)

^{1}H

500 MHz, $CDCl_3$

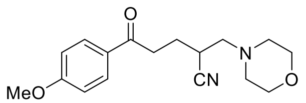


3d

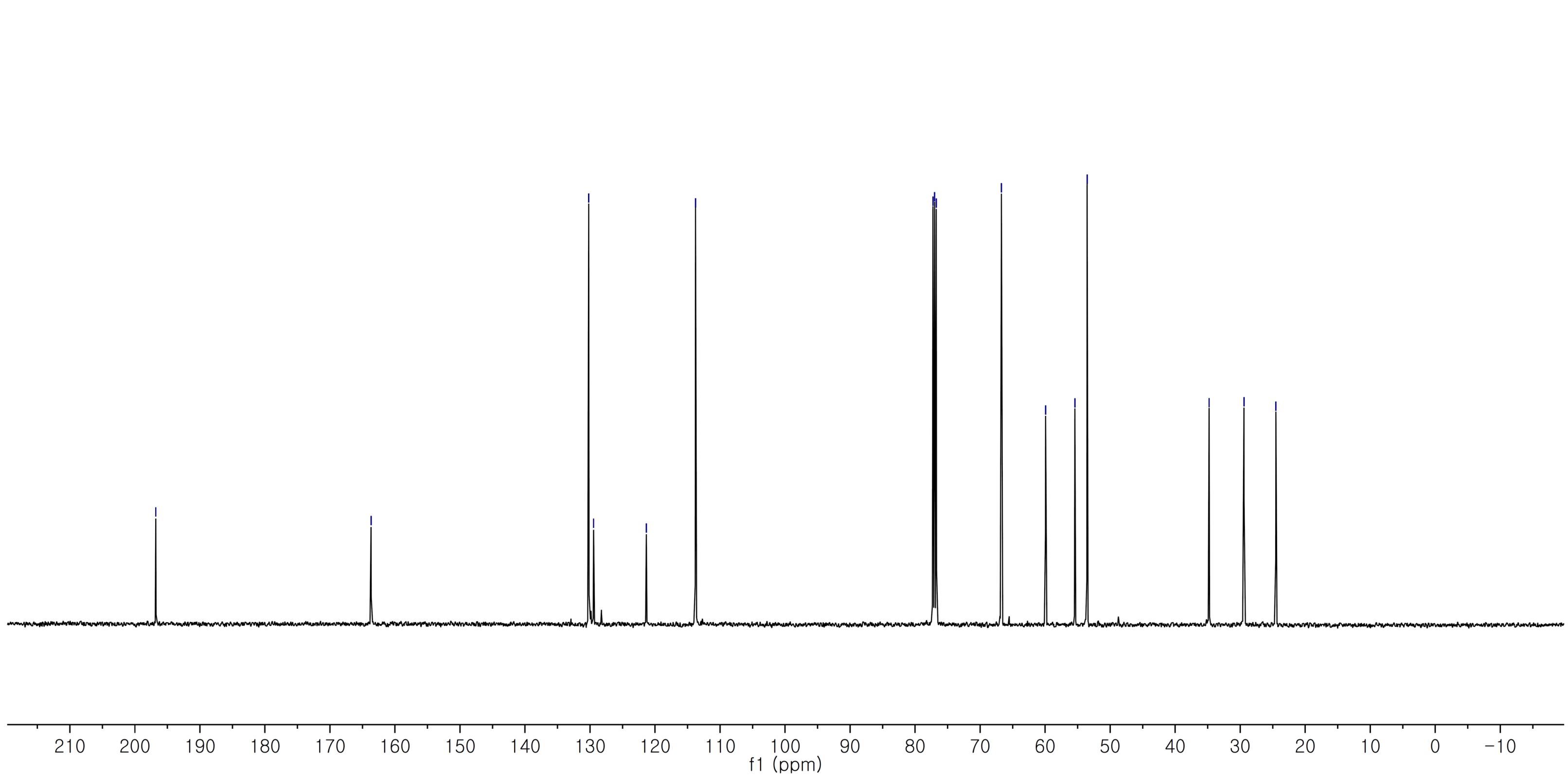


^{13}C

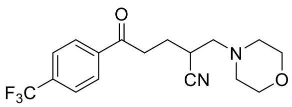
126 MHz, $CDCl_3$



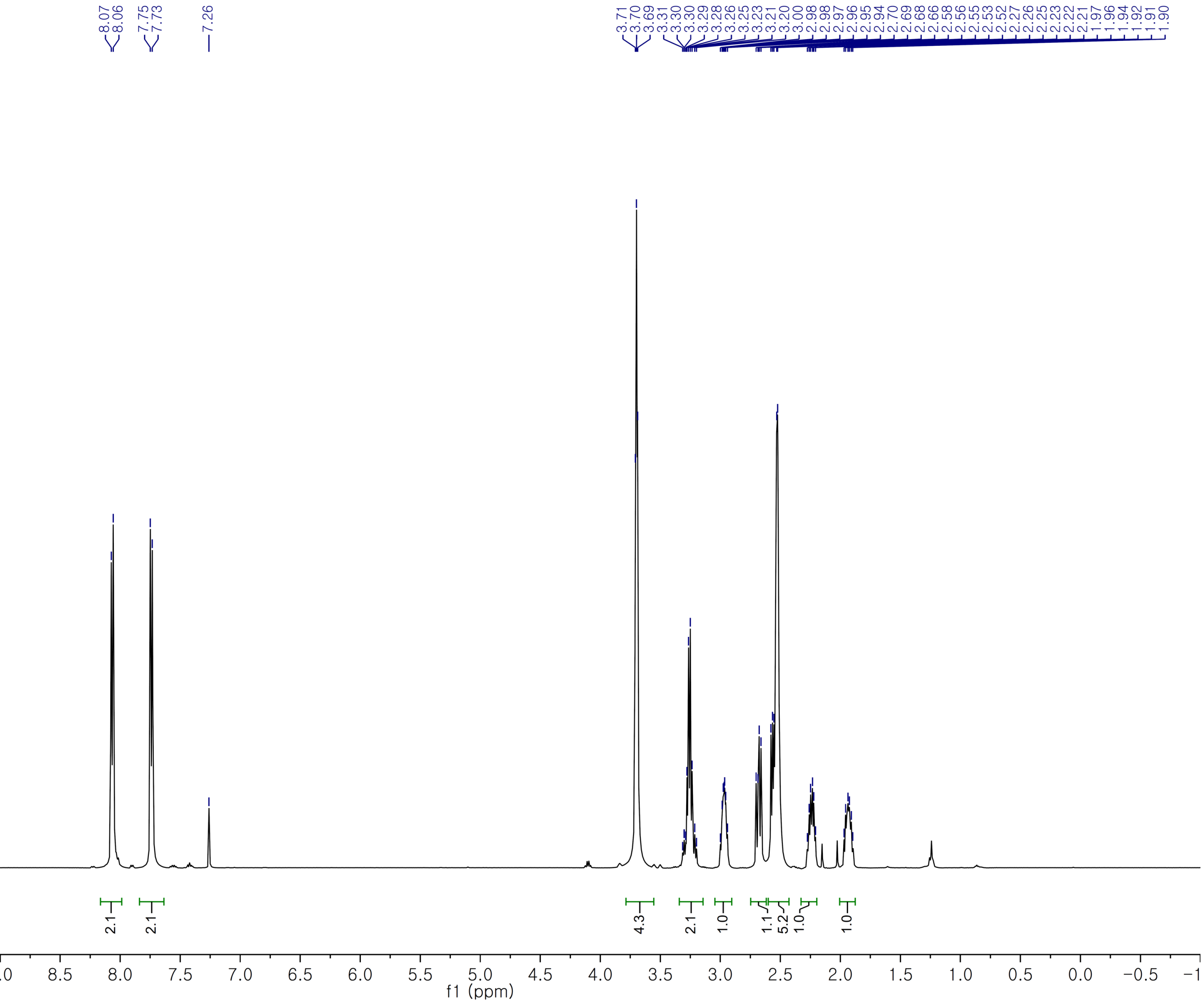
3d

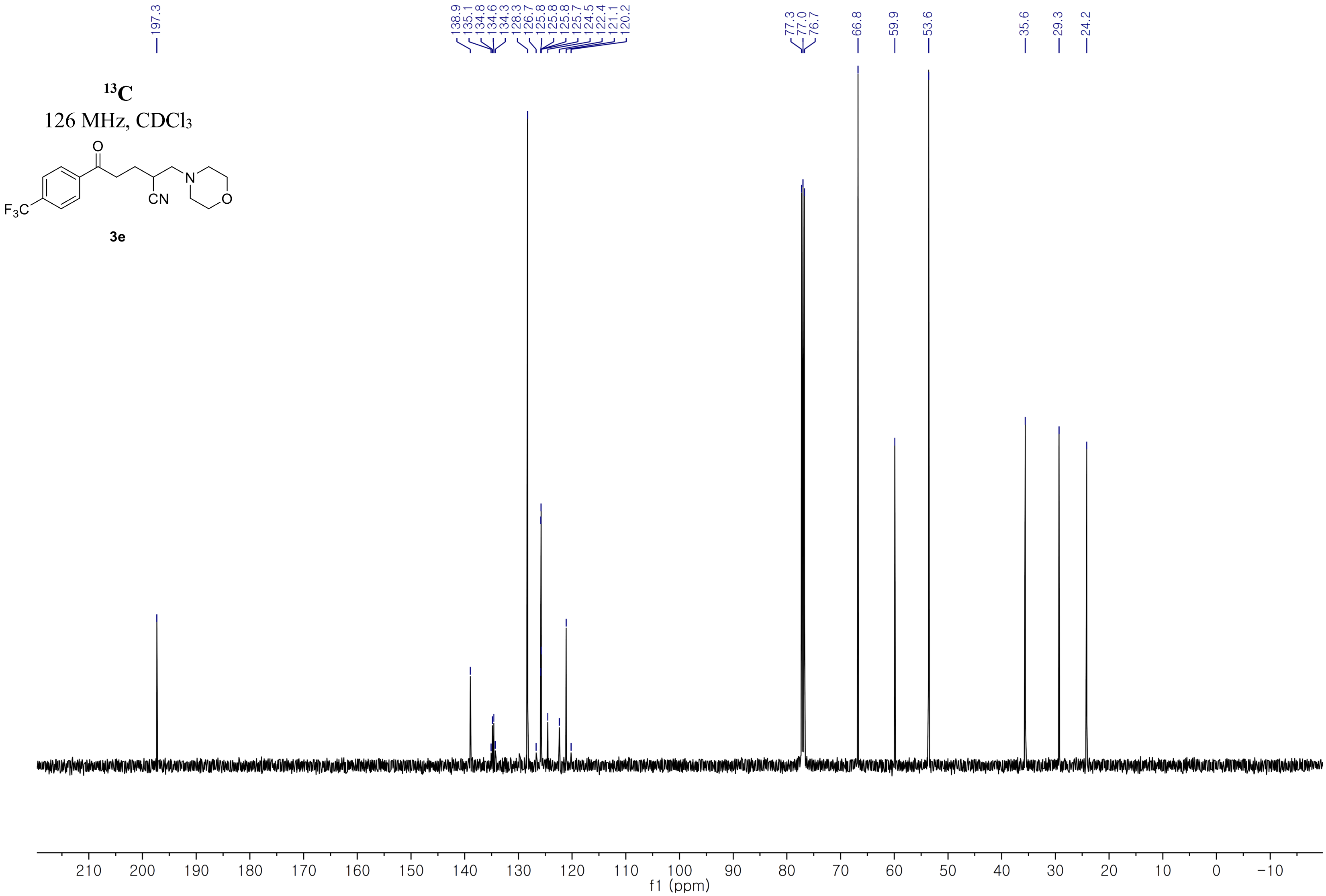


^{1}H
500 MHz, $CDCl_3$



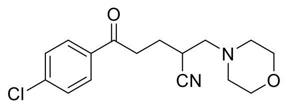
3e



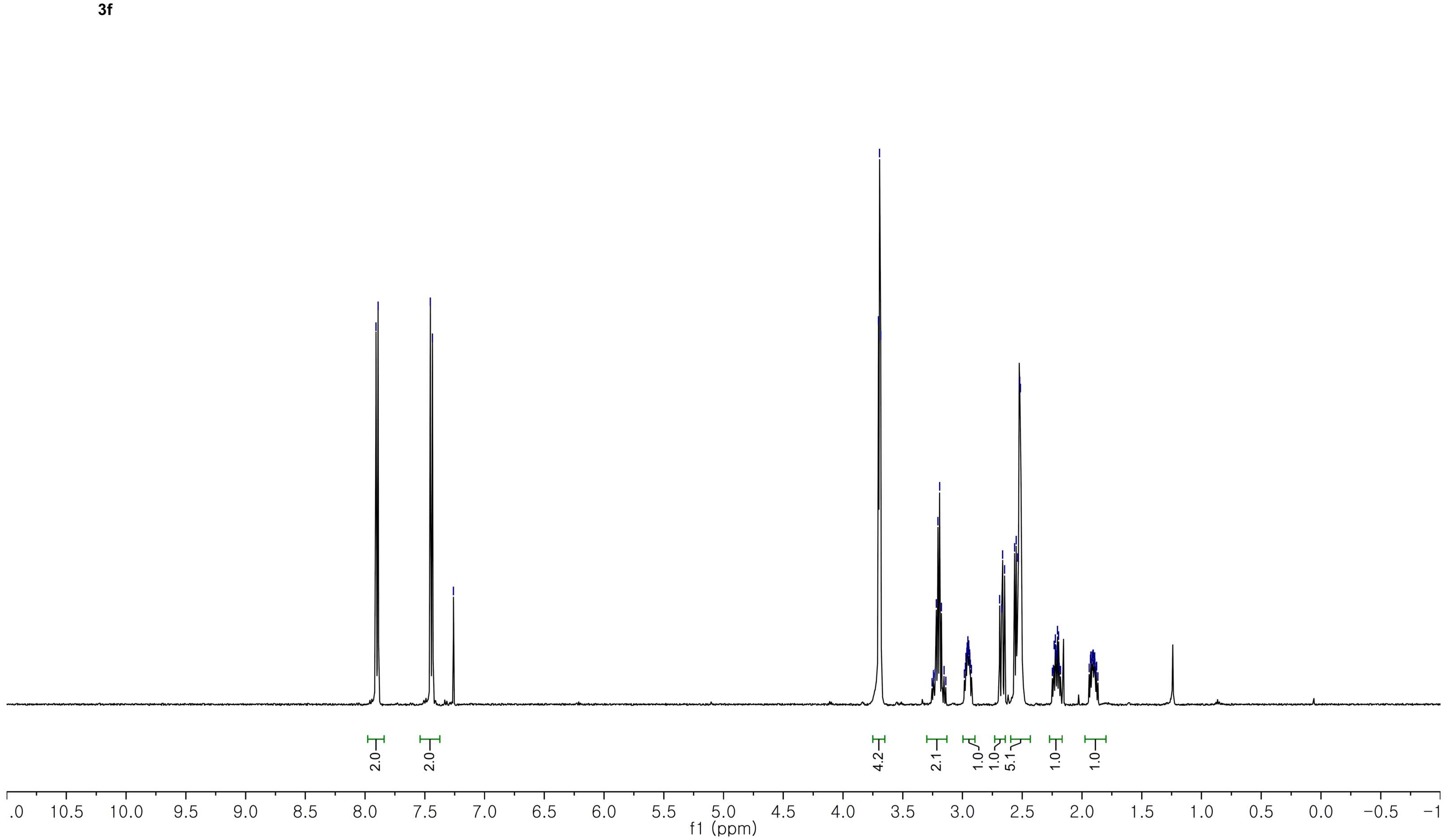

197.3
138.9
135.1
134.8
134.6
134.3
128.3
126.7
125.8
125.8
125.8
125.7
124.5
122.4
121.1
120.2
77.3
77.0
76.7
66.8
59.9
53.6
35.6
29.3
24.2
^{13}C
126 MHz, $CDCl_3$
O
N
CN
O
F_3C
3e
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10
f1 (ppm)

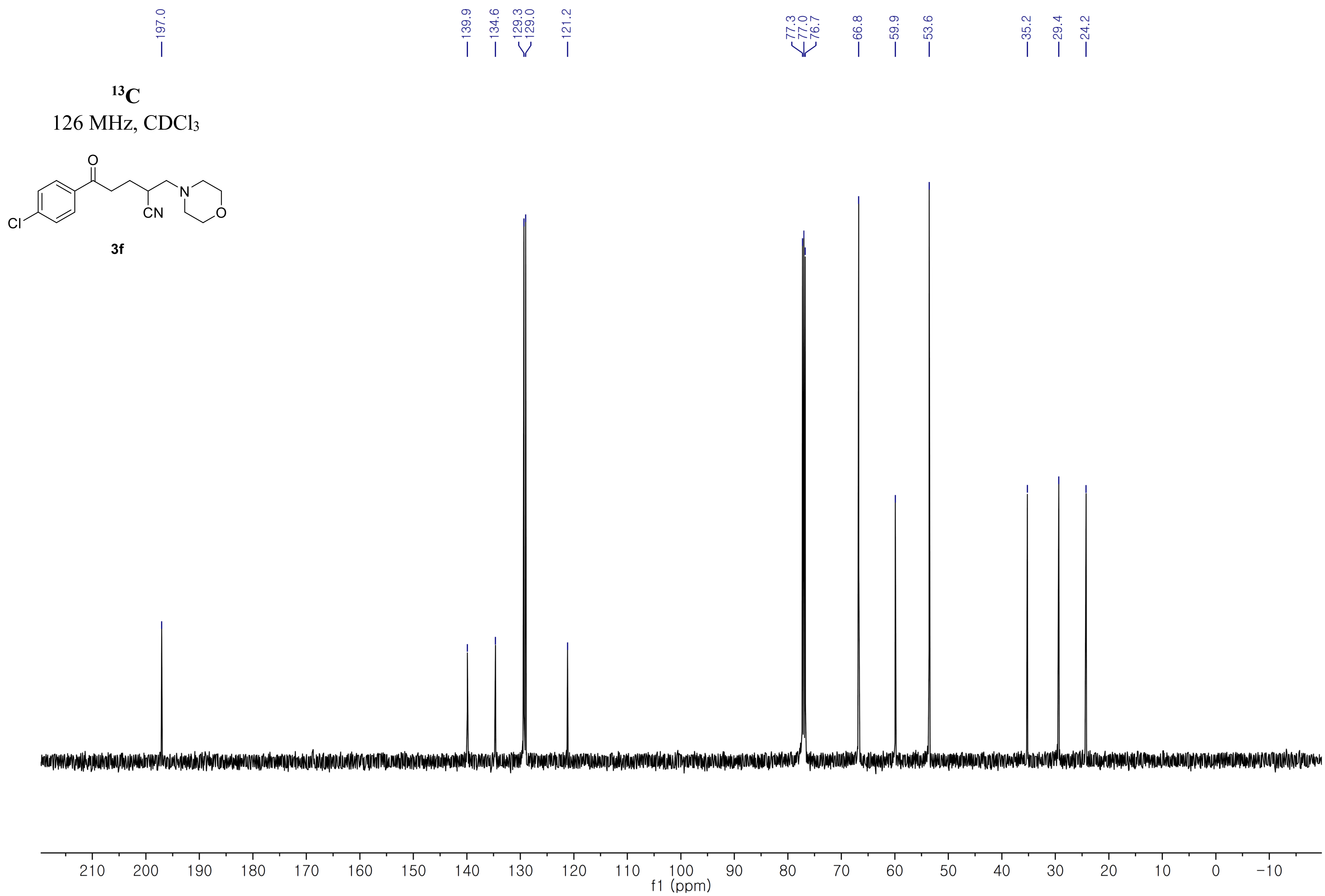
^{1}H

500 MHz, $CDCl_3$

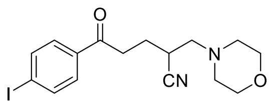


3f

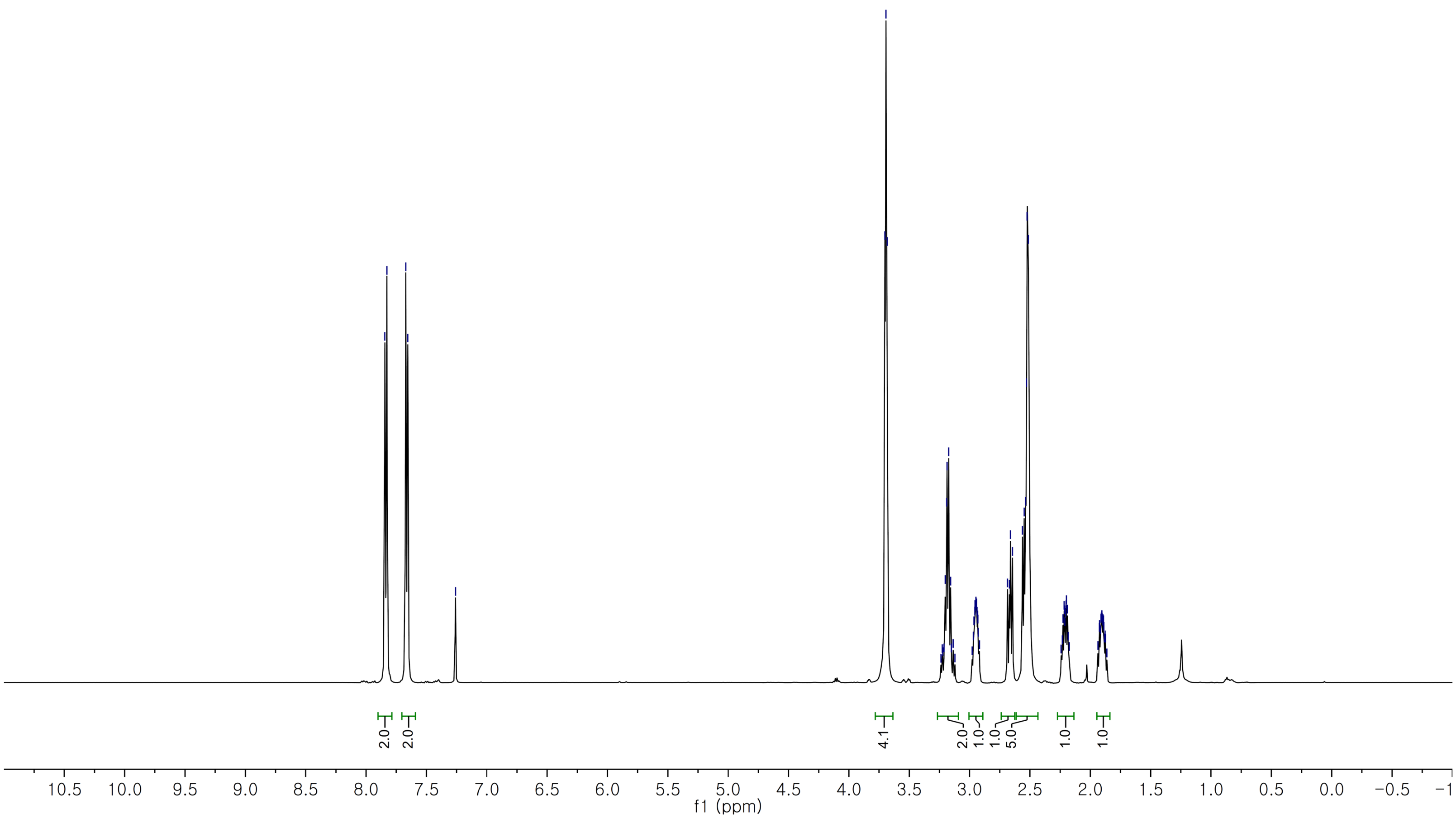


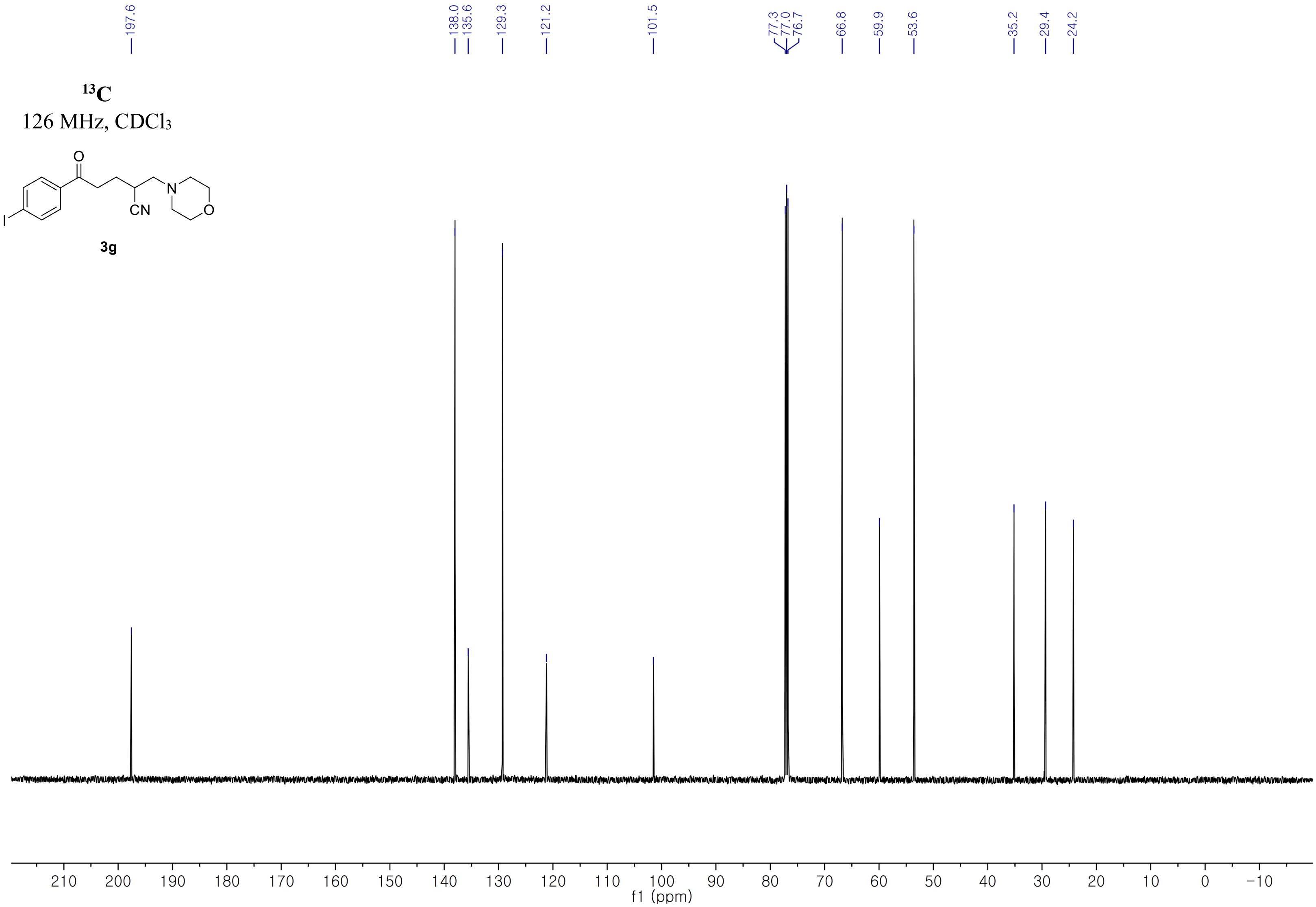

197.0
139.9
134.6
129.3
129.0
121.2
77.3
77.0
76.7
66.8
59.9
53.6
35.2
29.4
24.2
13C
126 MHz, CDCl3
O
Cl
CN
N
O
3f
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10
f1 (ppm)

¹H
500 MHz, $CDCl_3$



3g

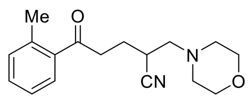




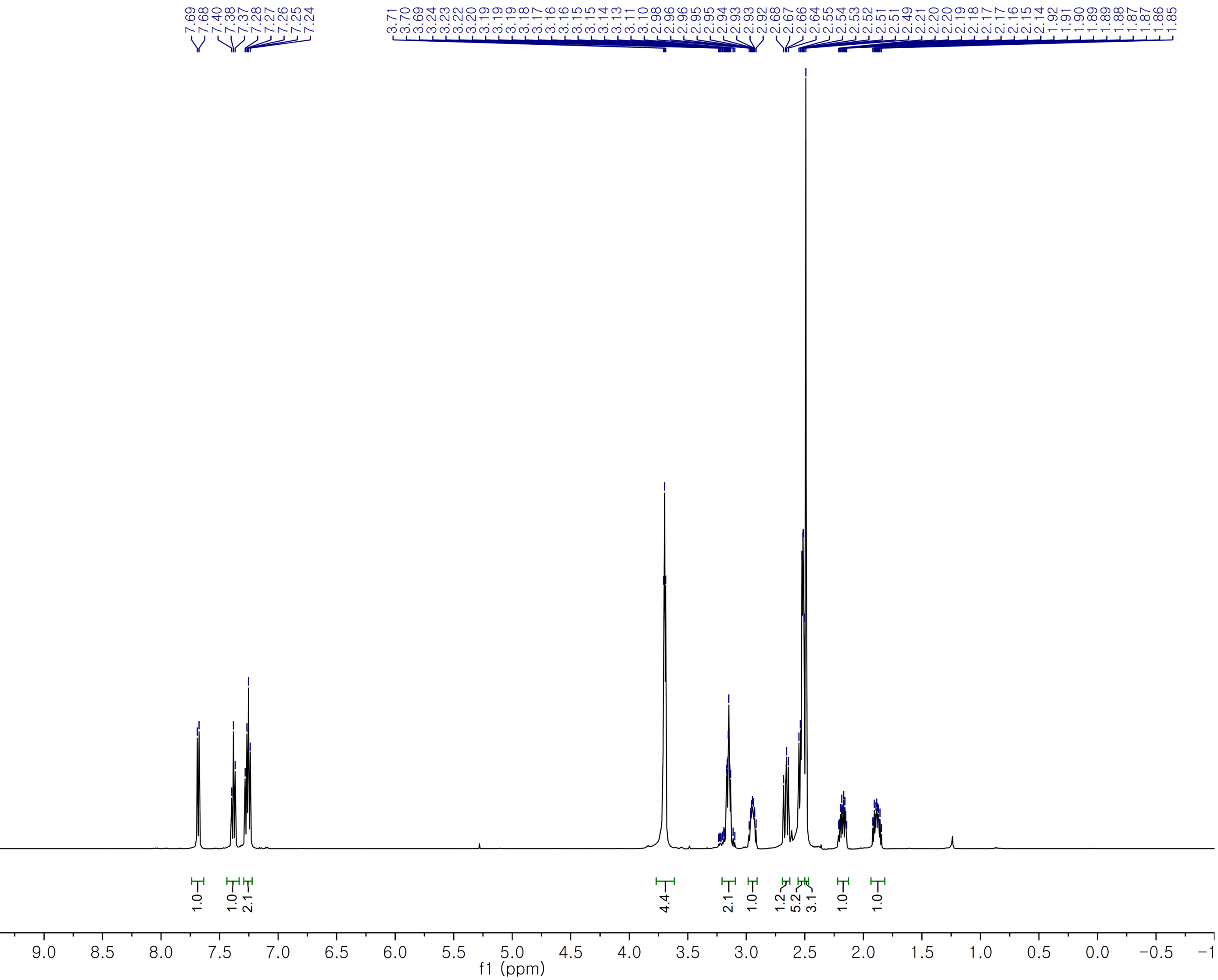
197.6
138.0
135.6
129.3
121.2
101.5
77.3
77.0
76.7
66.8
59.9
53.6
35.2
29.4
24.2
13C
126 MHz, CDCl3
O
I
CN
N
O
3g
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10
f1 (ppm)

^{1}H

500 MHz, $CDCl_3$

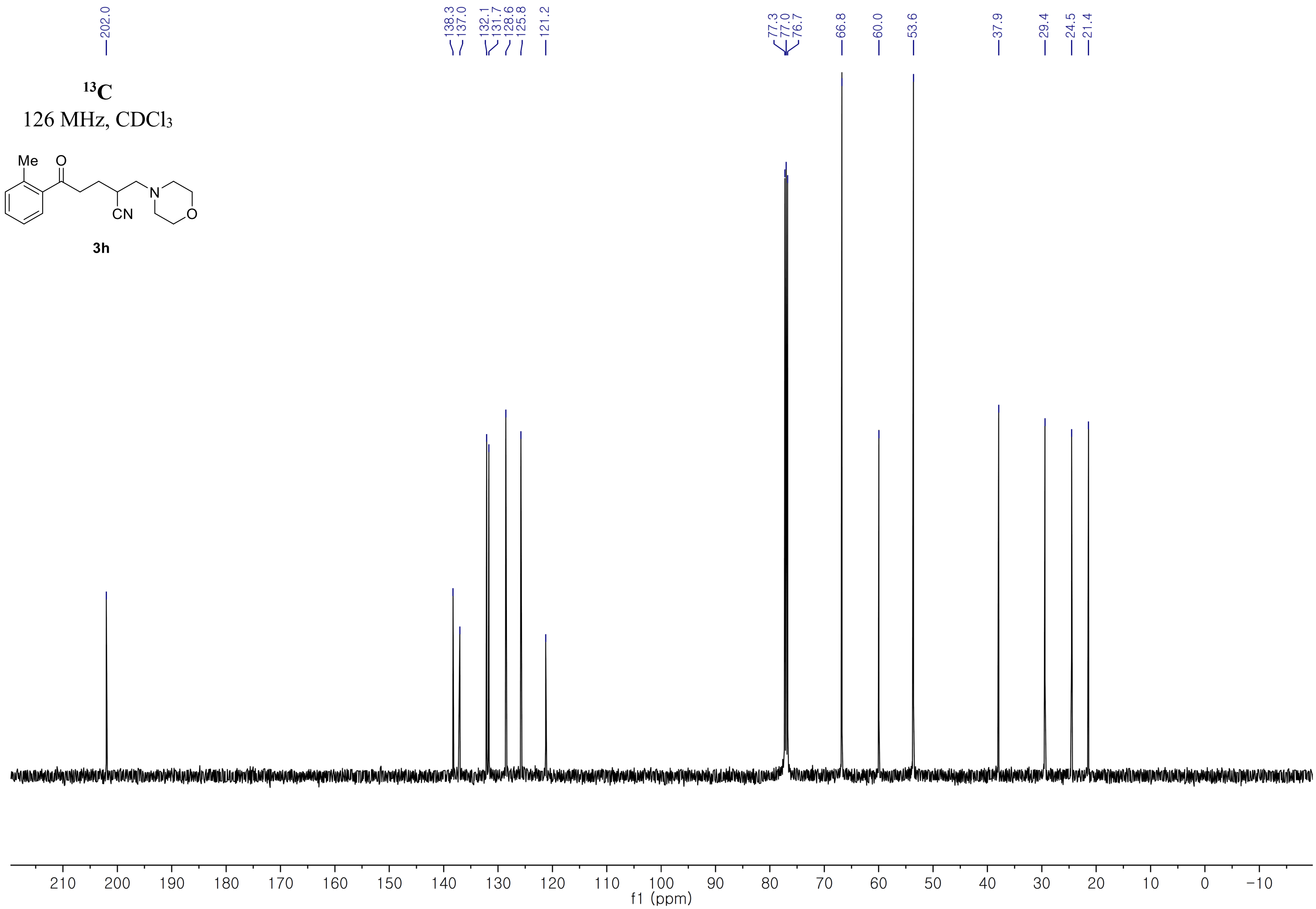


3h

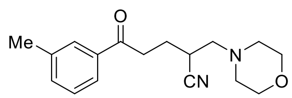


^{13}C
126 MHz, $CDCl_3$

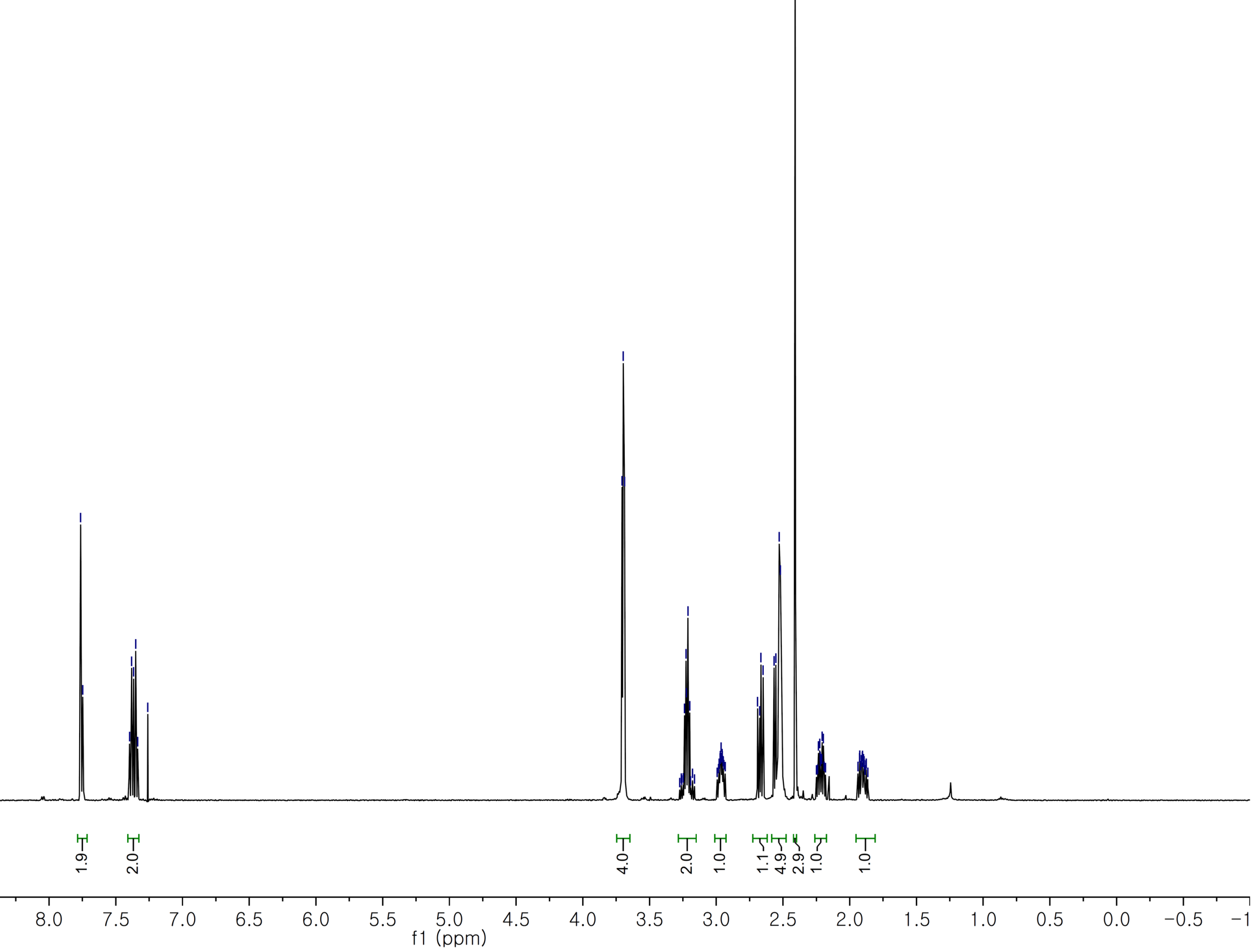
3h



^{1}H
500 MHz, CDCl$_3$



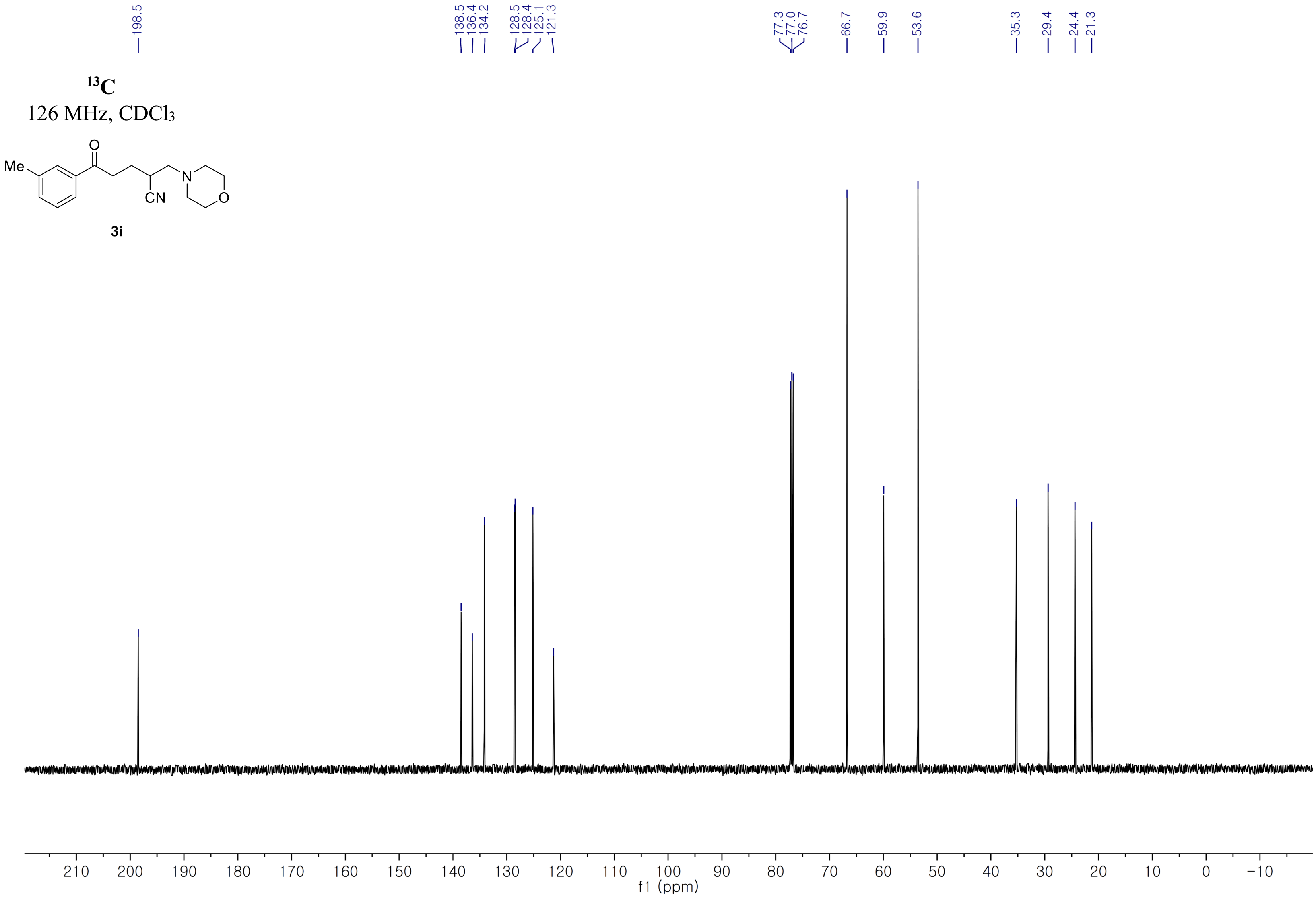
3i



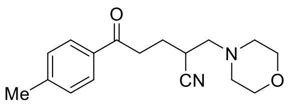
^{13}C

126 MHz, $CDCl_3$

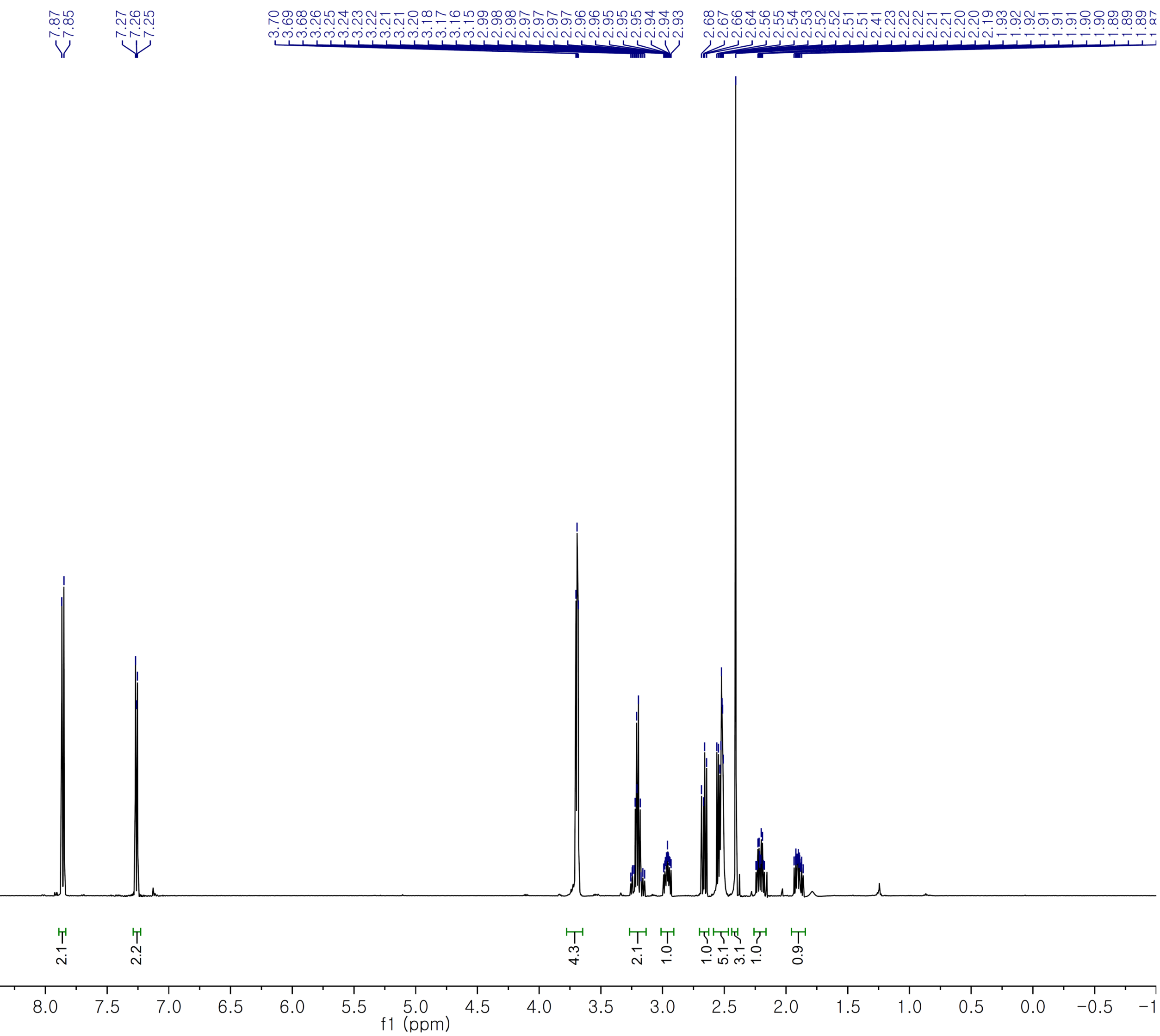
3i

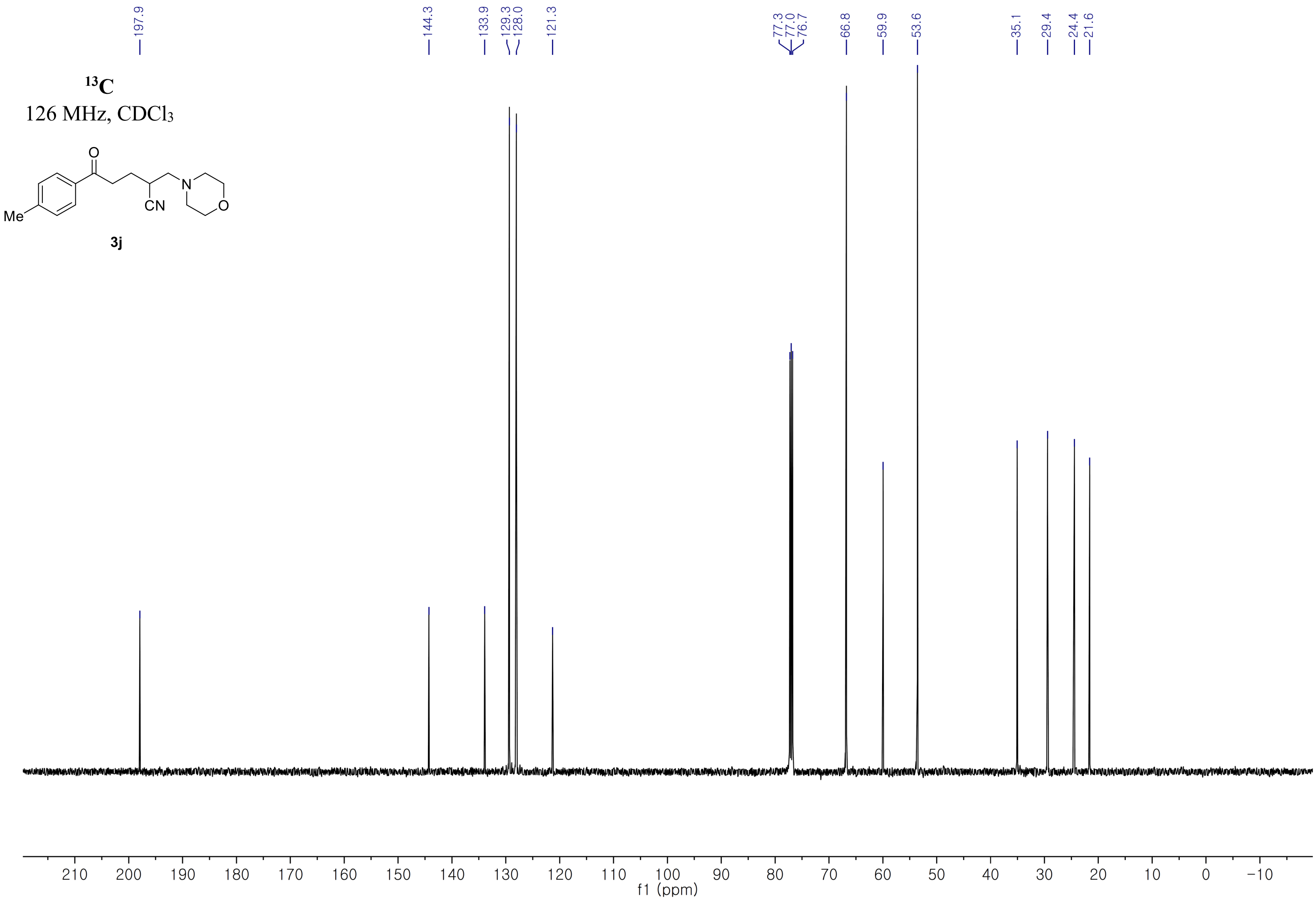


[1]H
500 MHz, $CDCl_3$



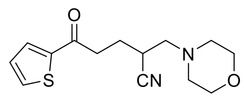
3j



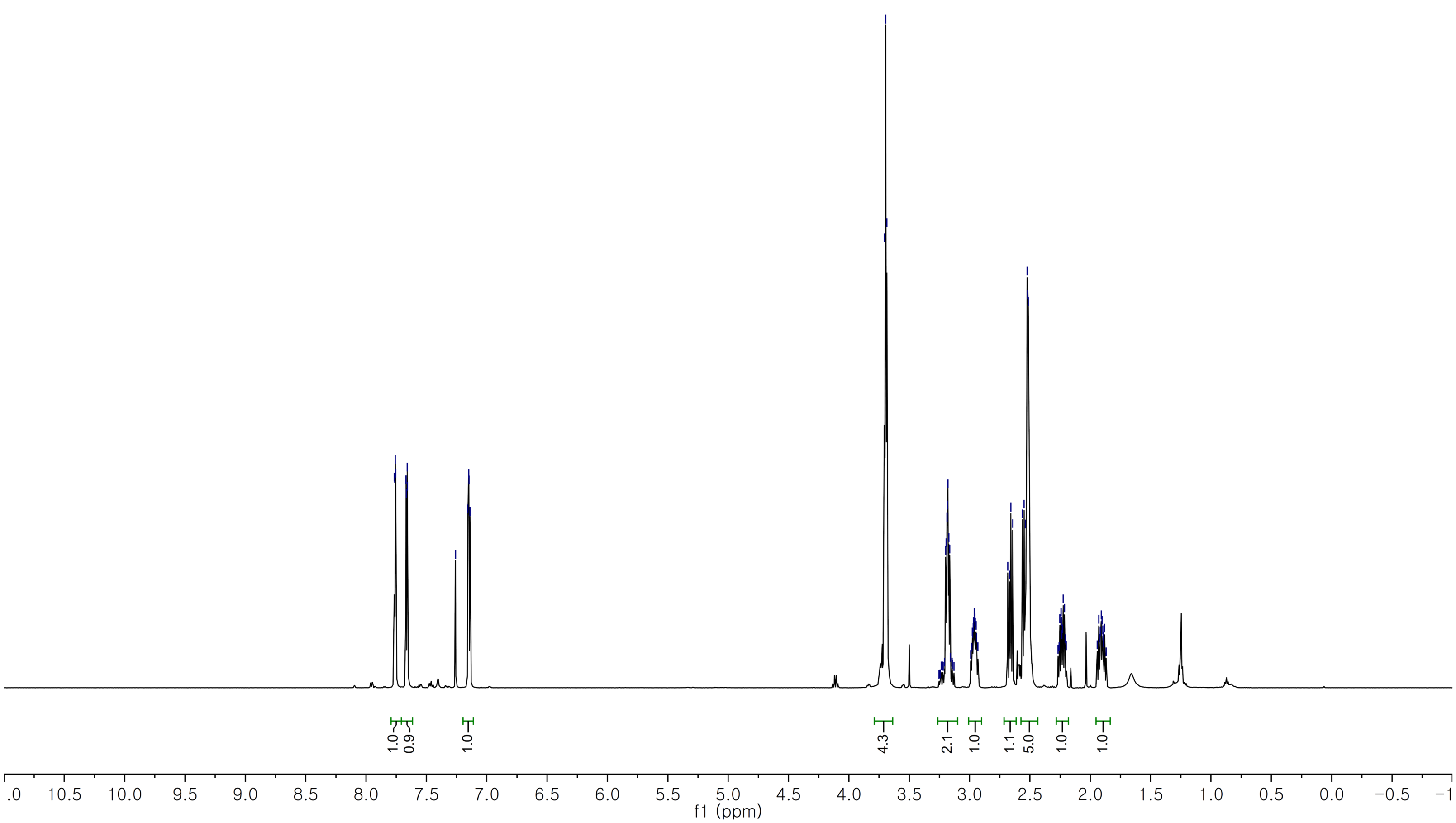


197.9
144.3
133.9
129.3
128.0
121.3
77.3
77.0
76.7
66.8
59.9
53.6
35.1
29.4
24.4
21.6
^{13}C
126 MHz, $CDCl_3$
O
Me
CN
N
O
3j
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10
f1 (ppm)

^{1}H
500 MHz, $CDCl_3$



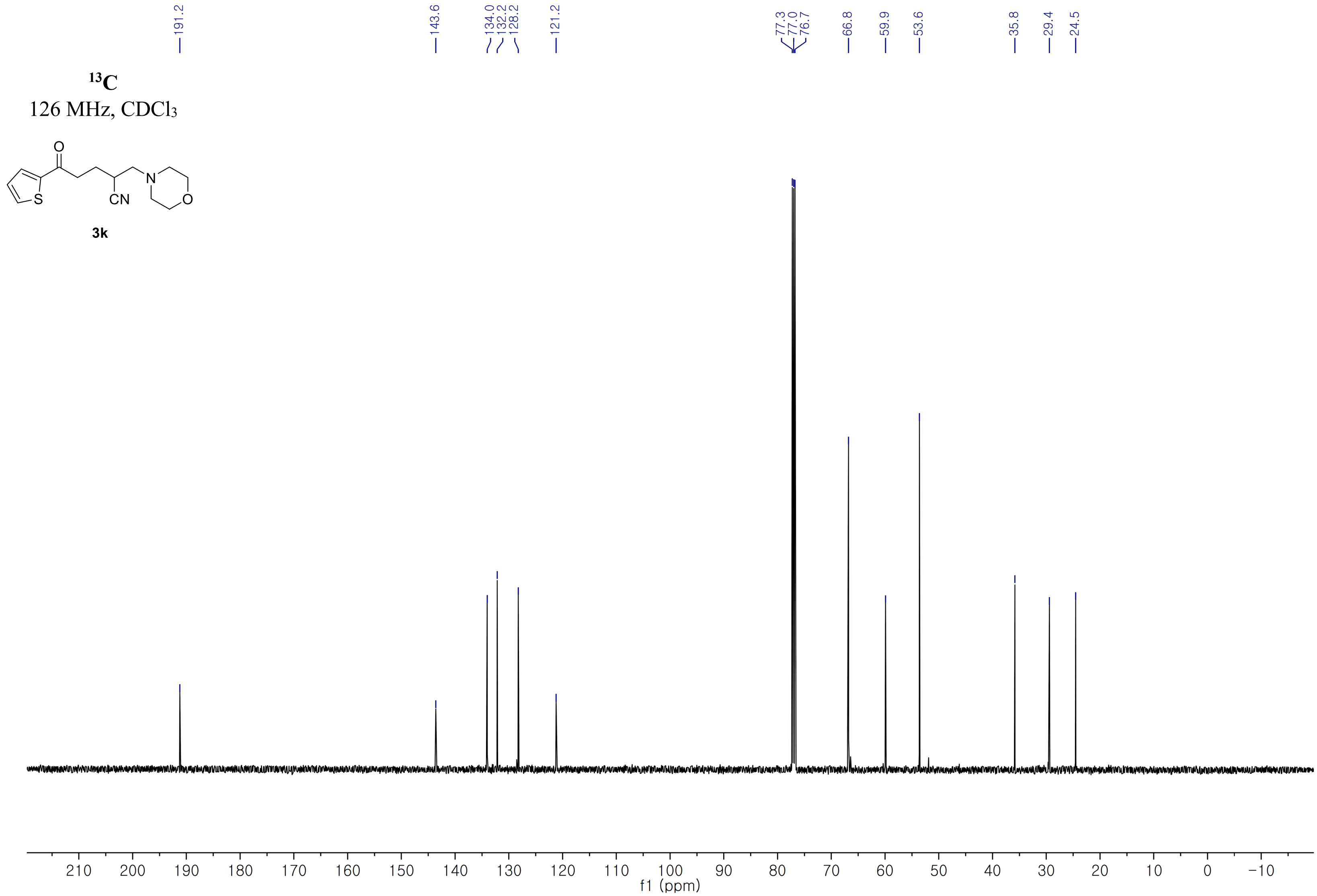
3k



^{13}C

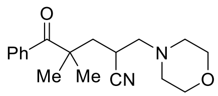
126 MHz, $CDCl_3$

3k

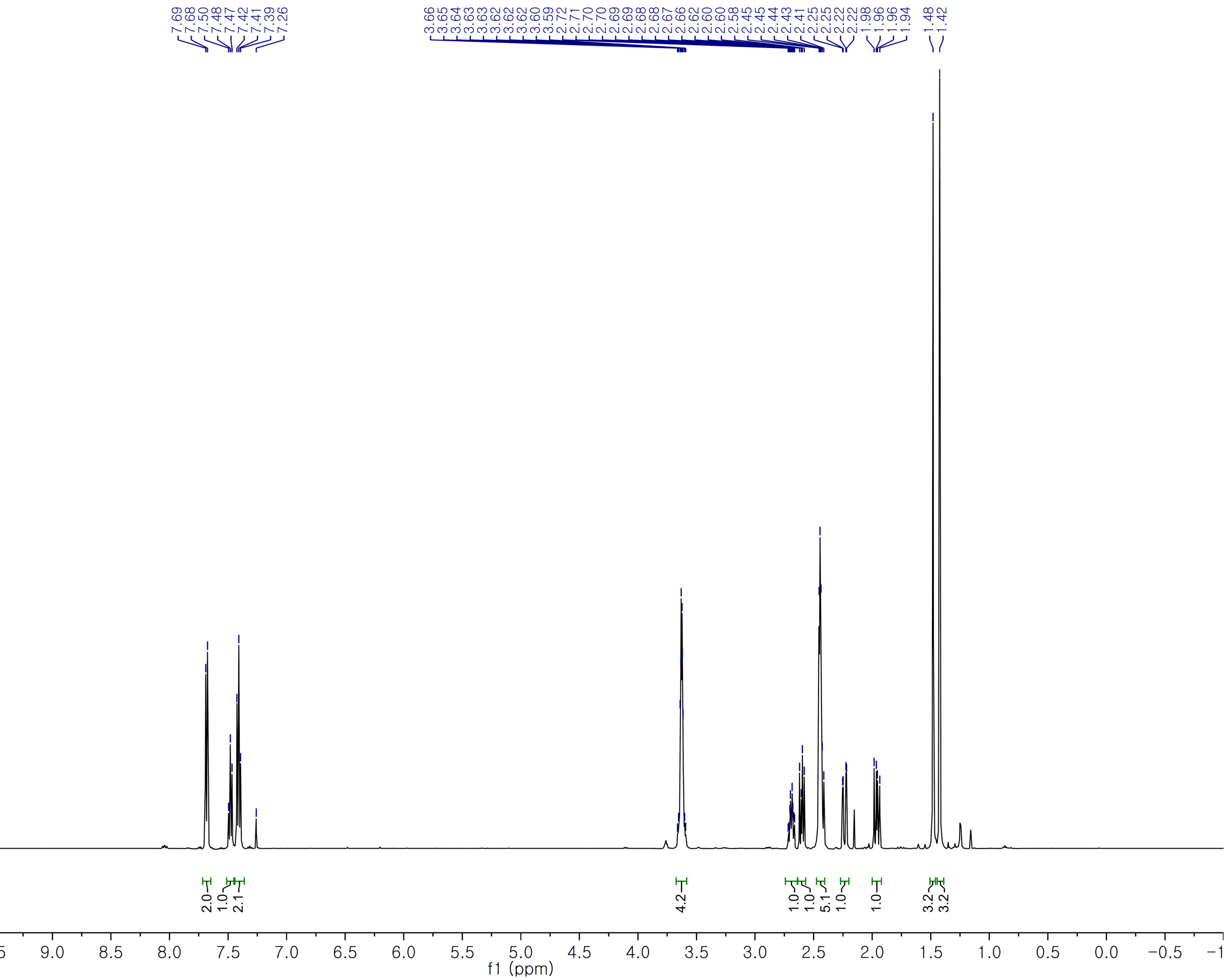


^{1}H

500 MHz, $CDCl_3$

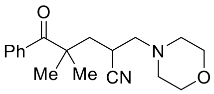


3l

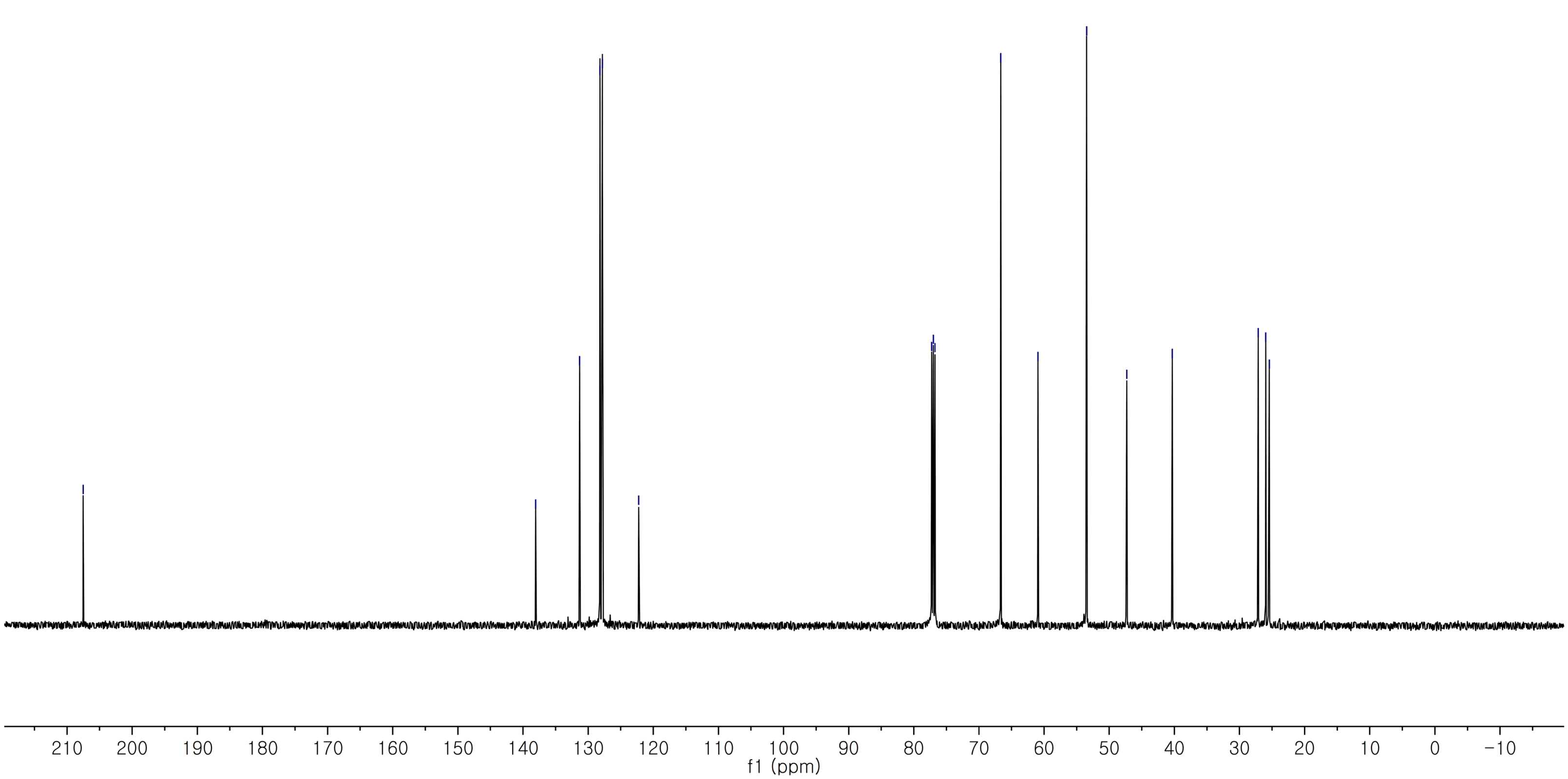


^{13}C

126 MHz, $CDCl_3$

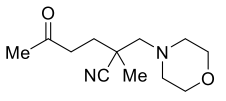


3l

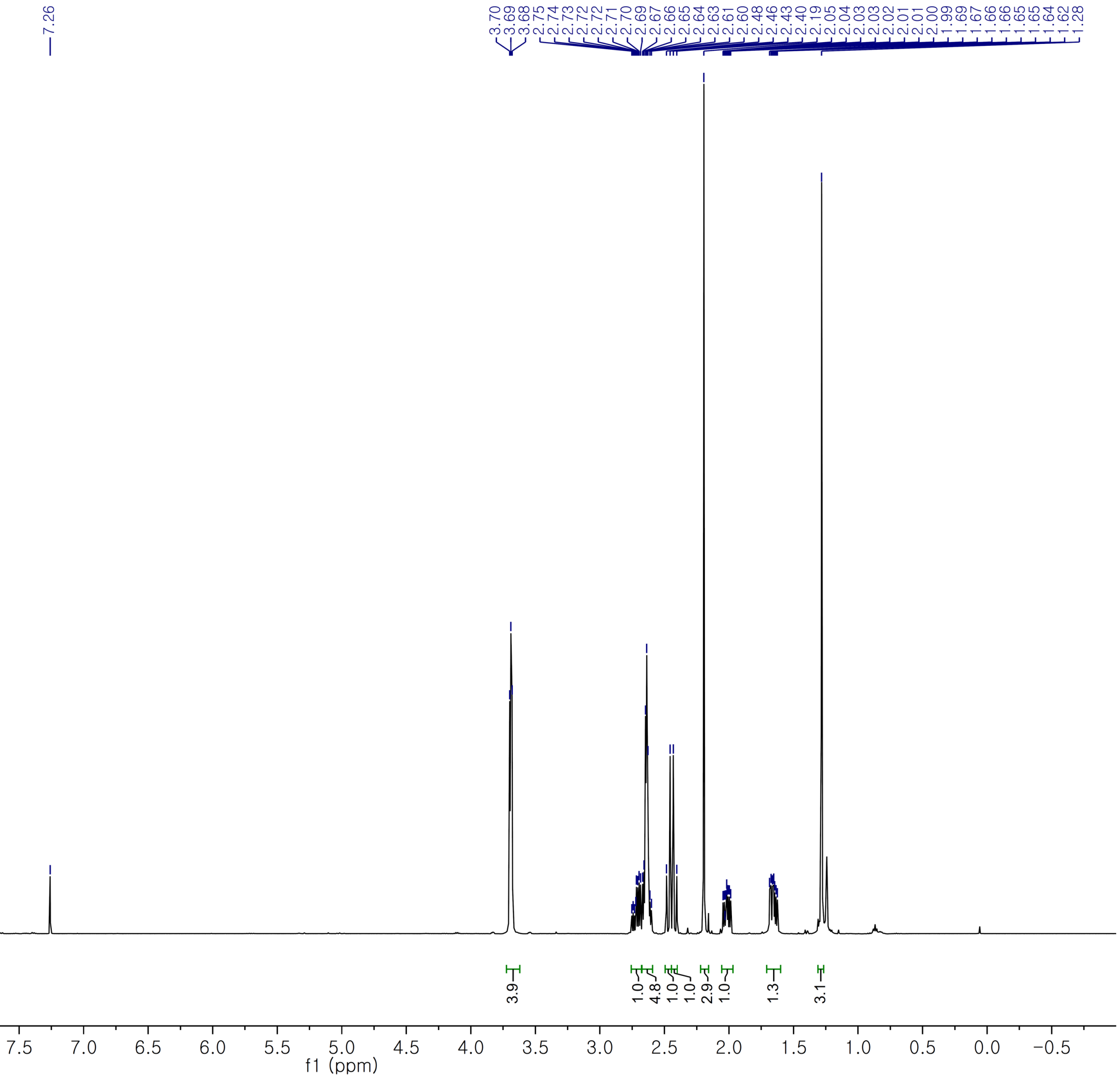


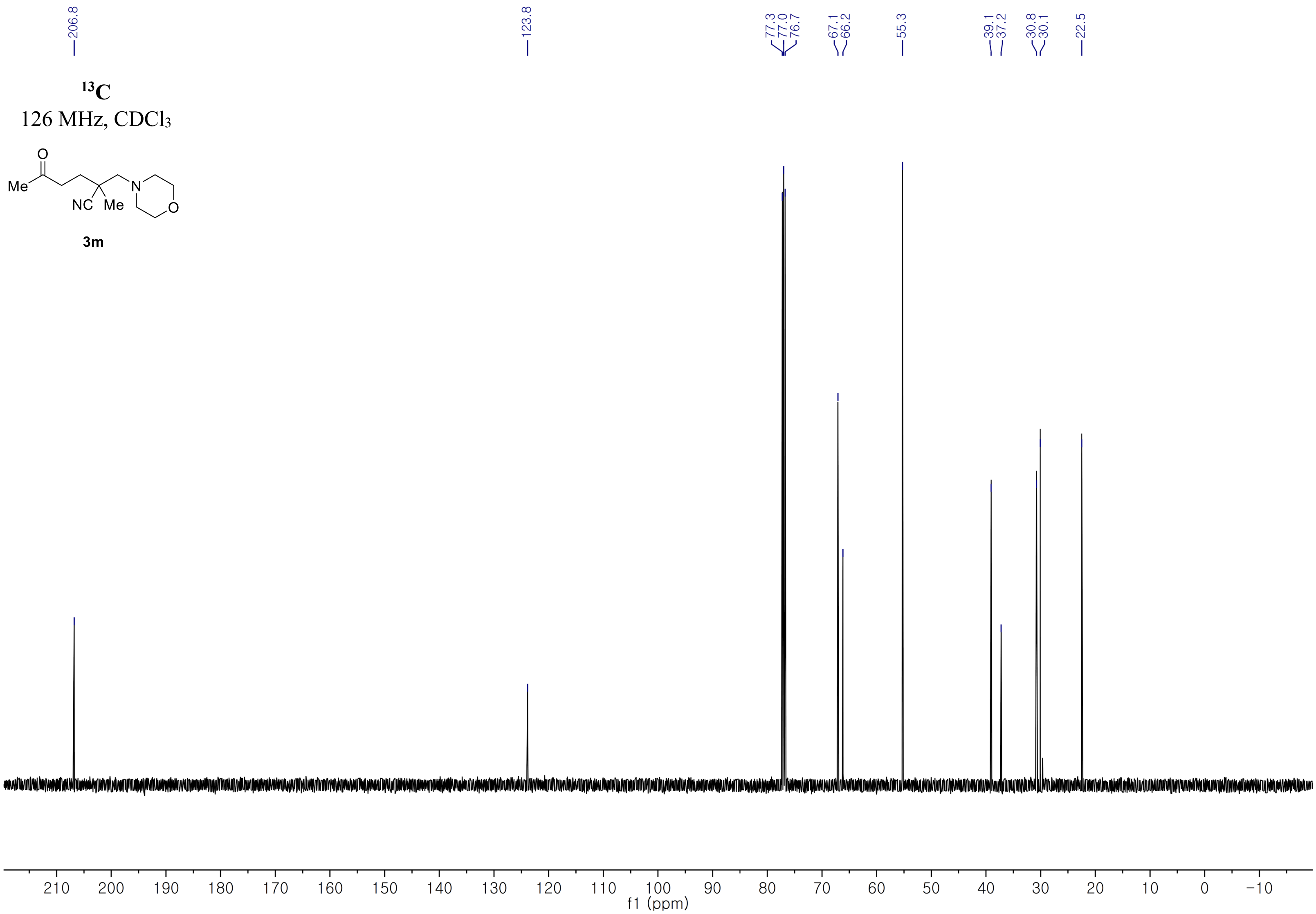
^{1}H

500 MHz, $CDCl_3$



3m

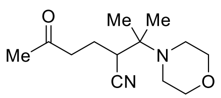




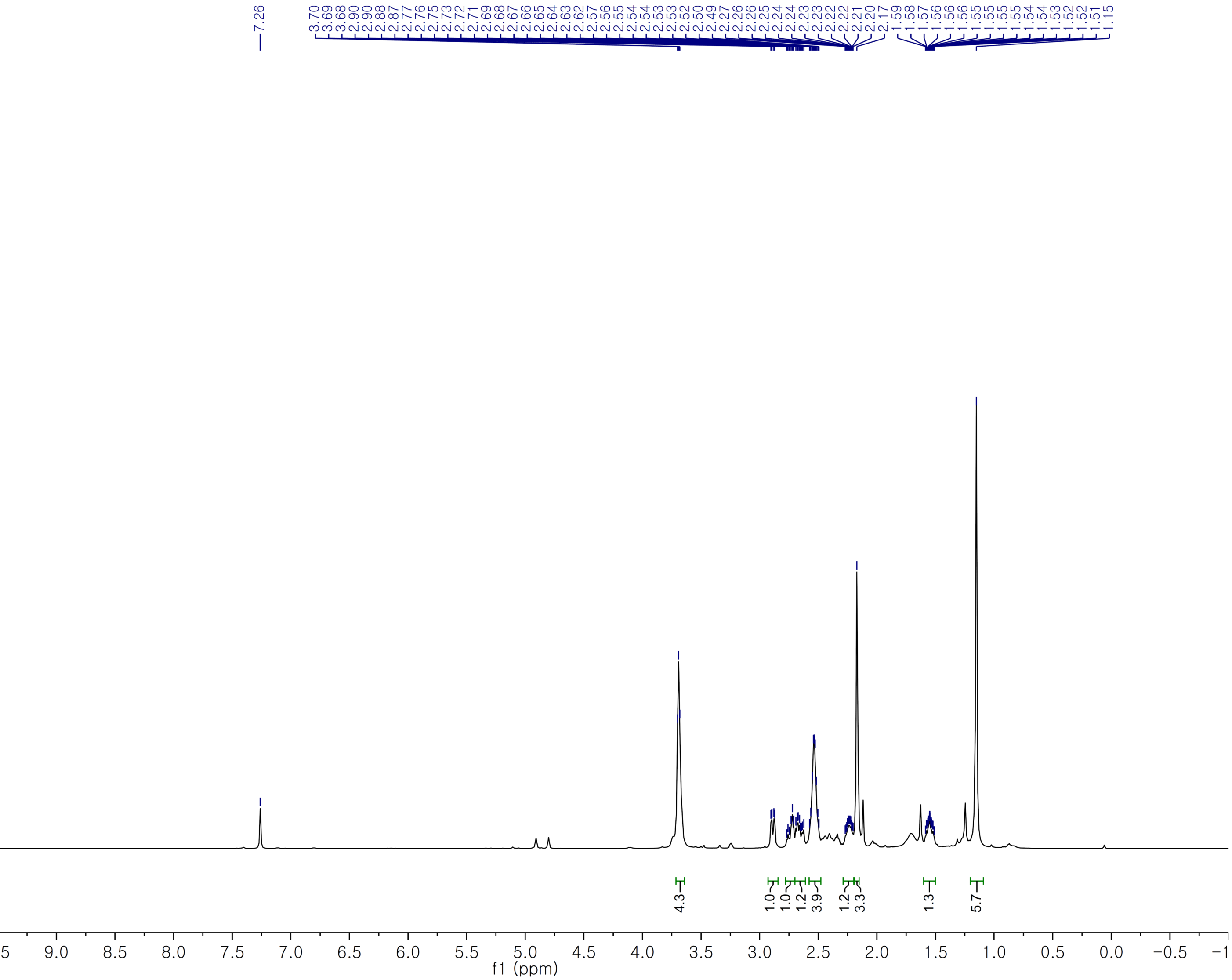
206.8
123.8
77.3
77.0
76.7
67.1
66.2
55.3
39.1
37.2
30.8
30.1
22.5
^{13}C
126 MHz, CDCl$_3$
O
Me
NC
Me
N
O
3m
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10
f1 (ppm)

^{1}H

500 MHz, $CDCl_3$

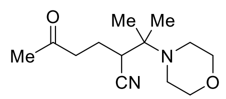


3n

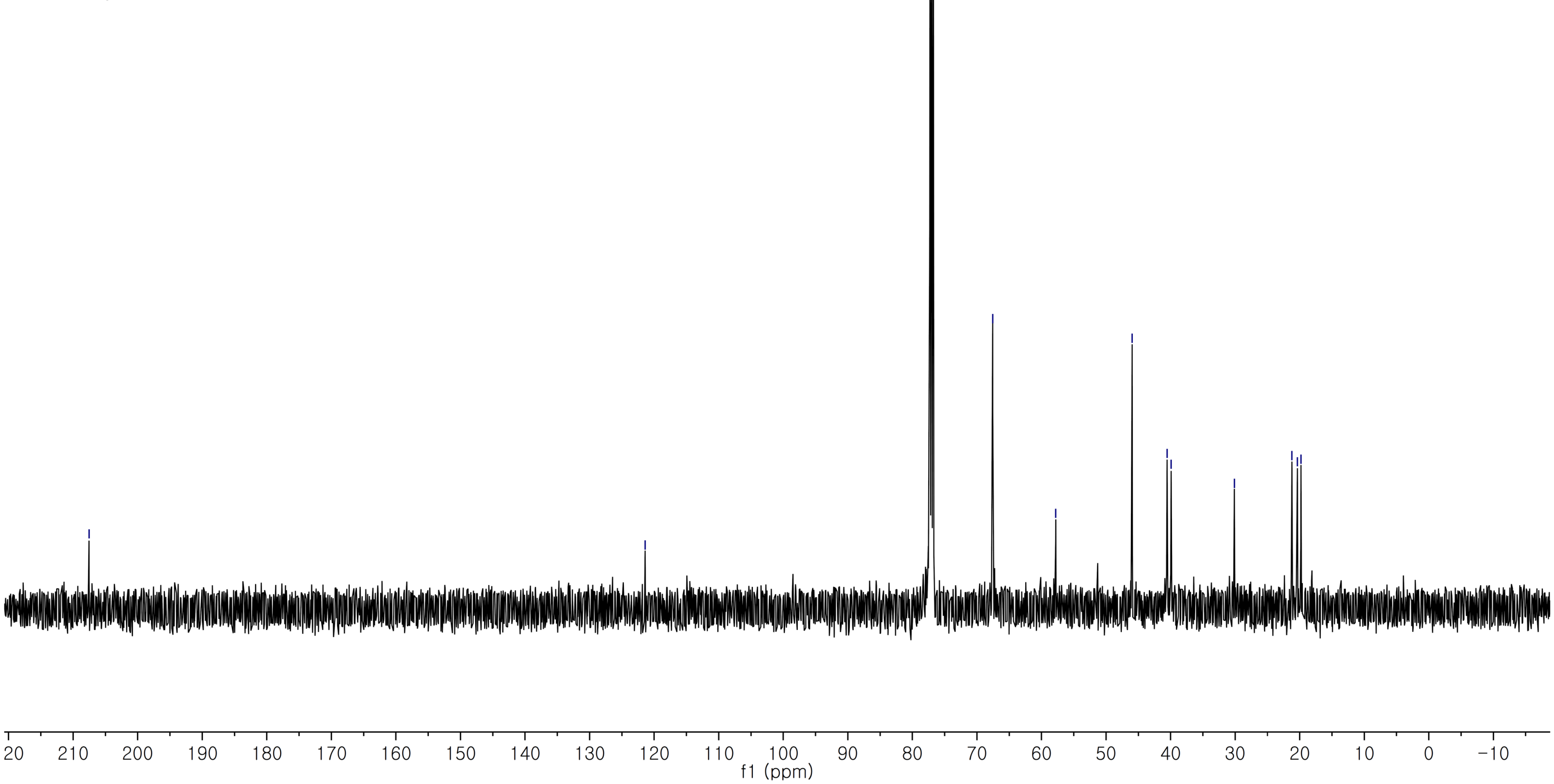


^{13}C

126 MHz, $CDCl_3$

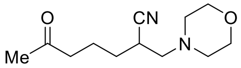


3n

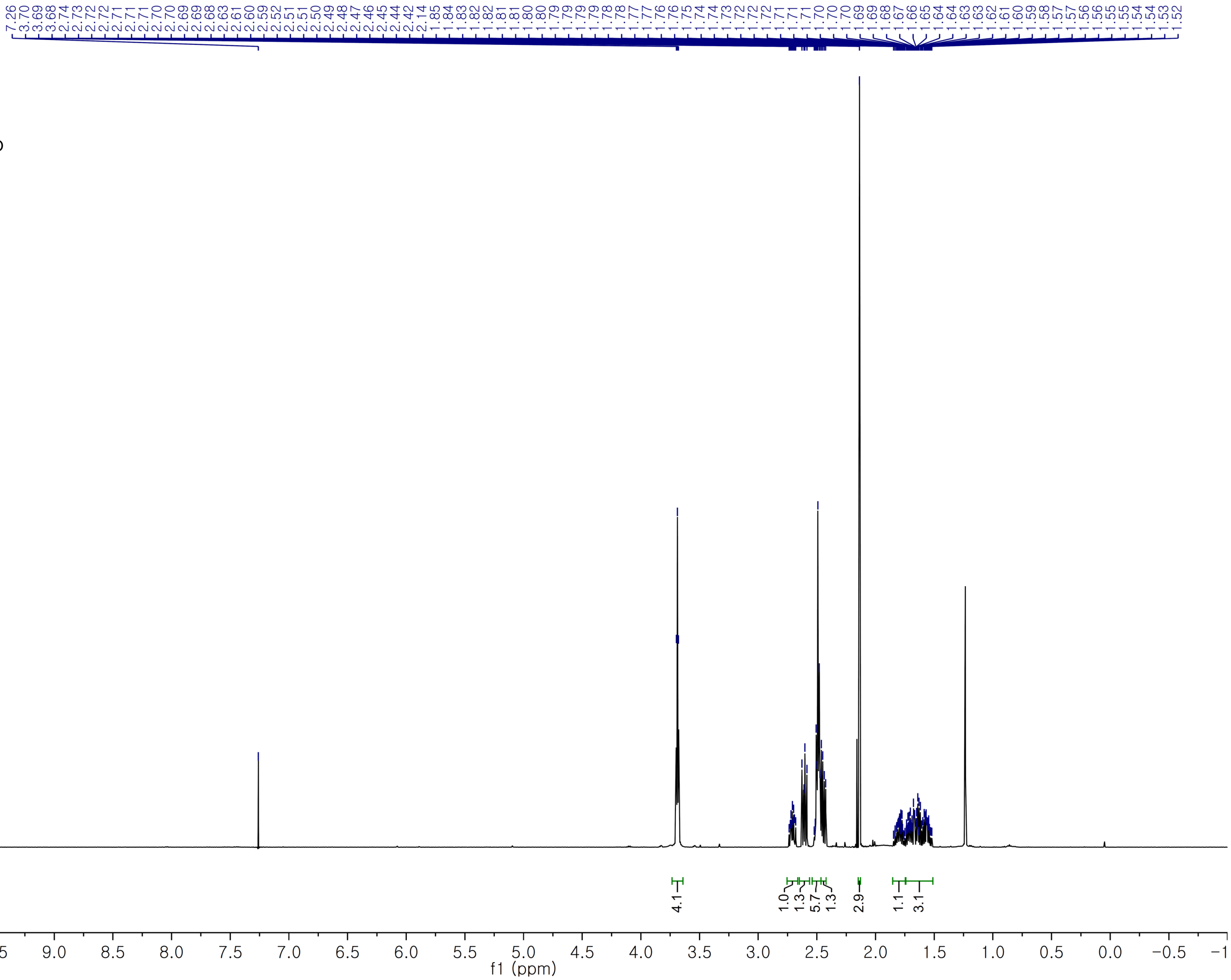


^{1}H

500 MHz, $CDCl_3$

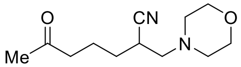


3o

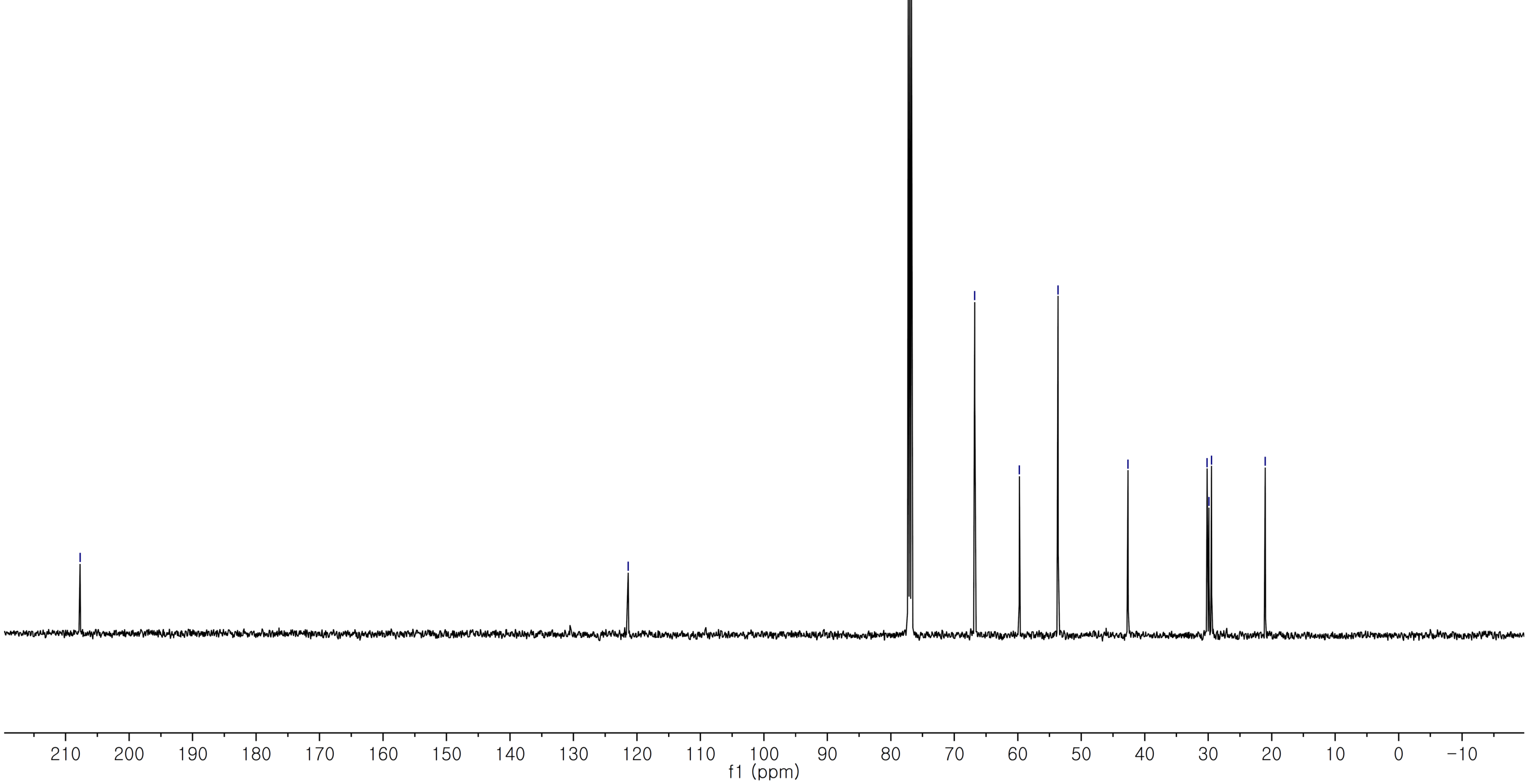


^{13}C

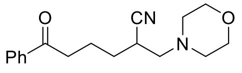
126 MHz, $CDCl_3$



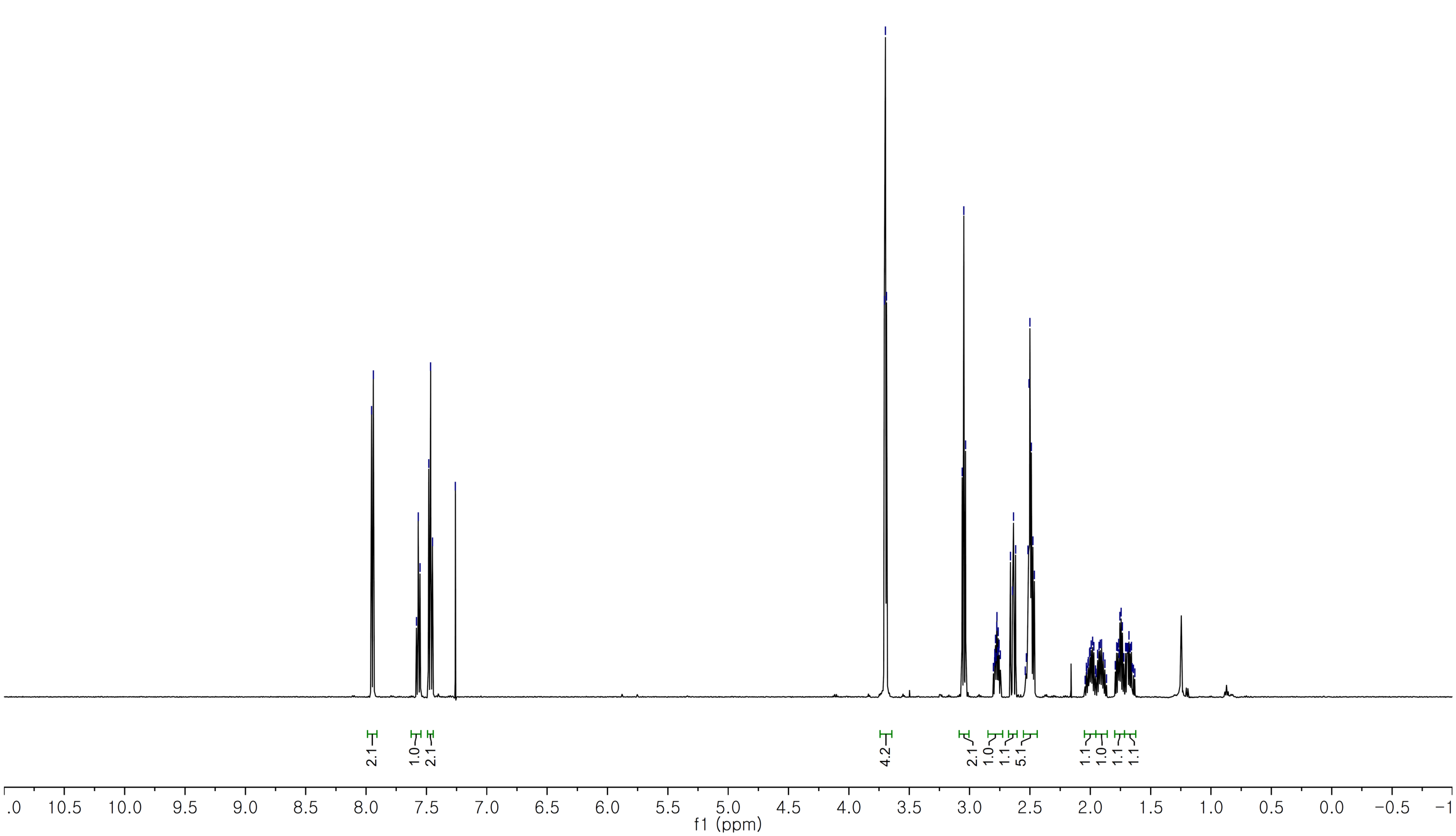
3o



[1]H
500 MHz, $CDCl_3$

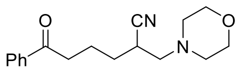


3p

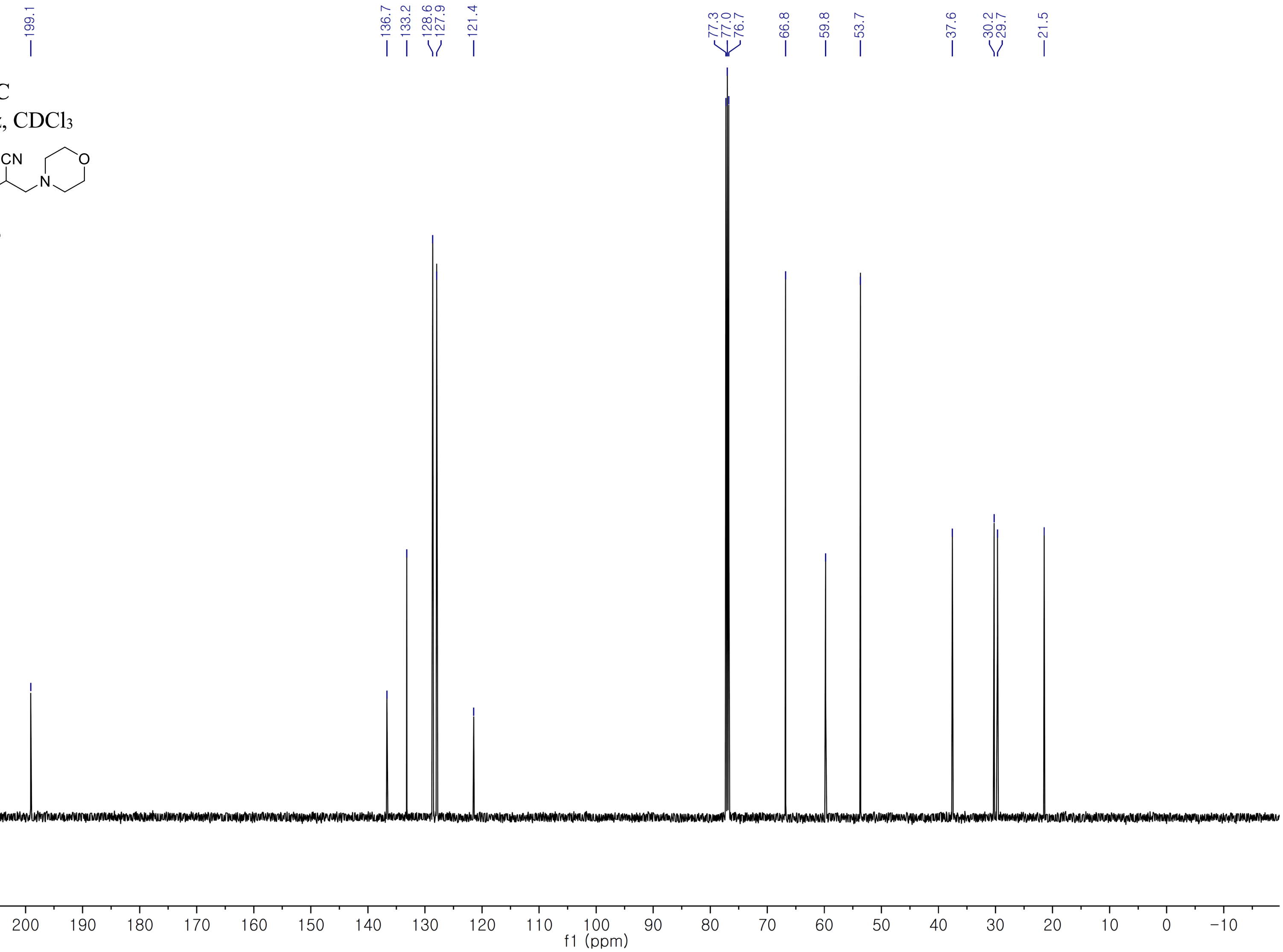


^{13}**C**

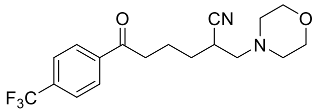
126 MHz, $CDCl_3$



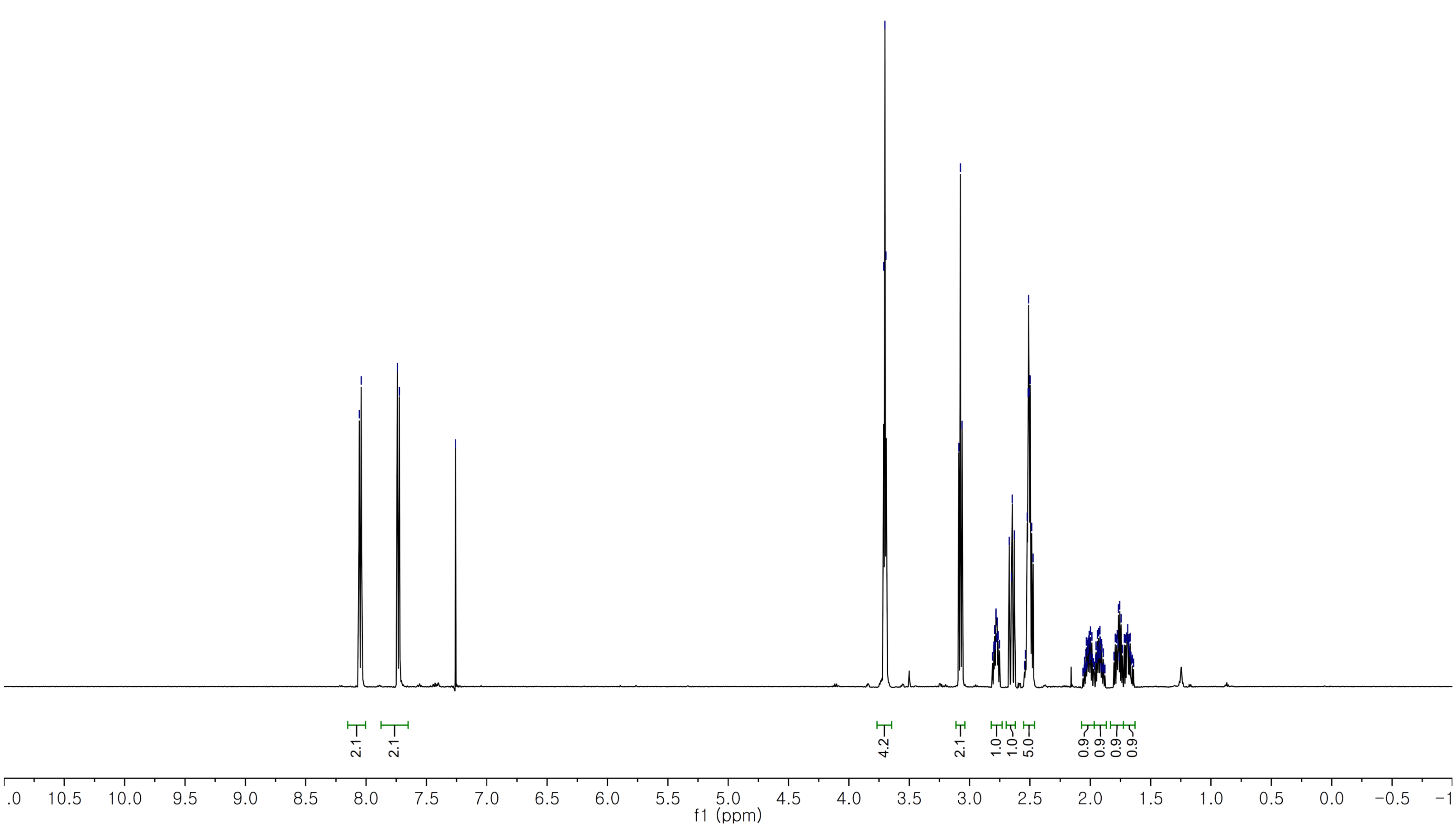
3p



^{1}H
500 MHz, $CDCl_3$

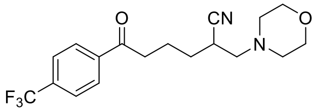


3q

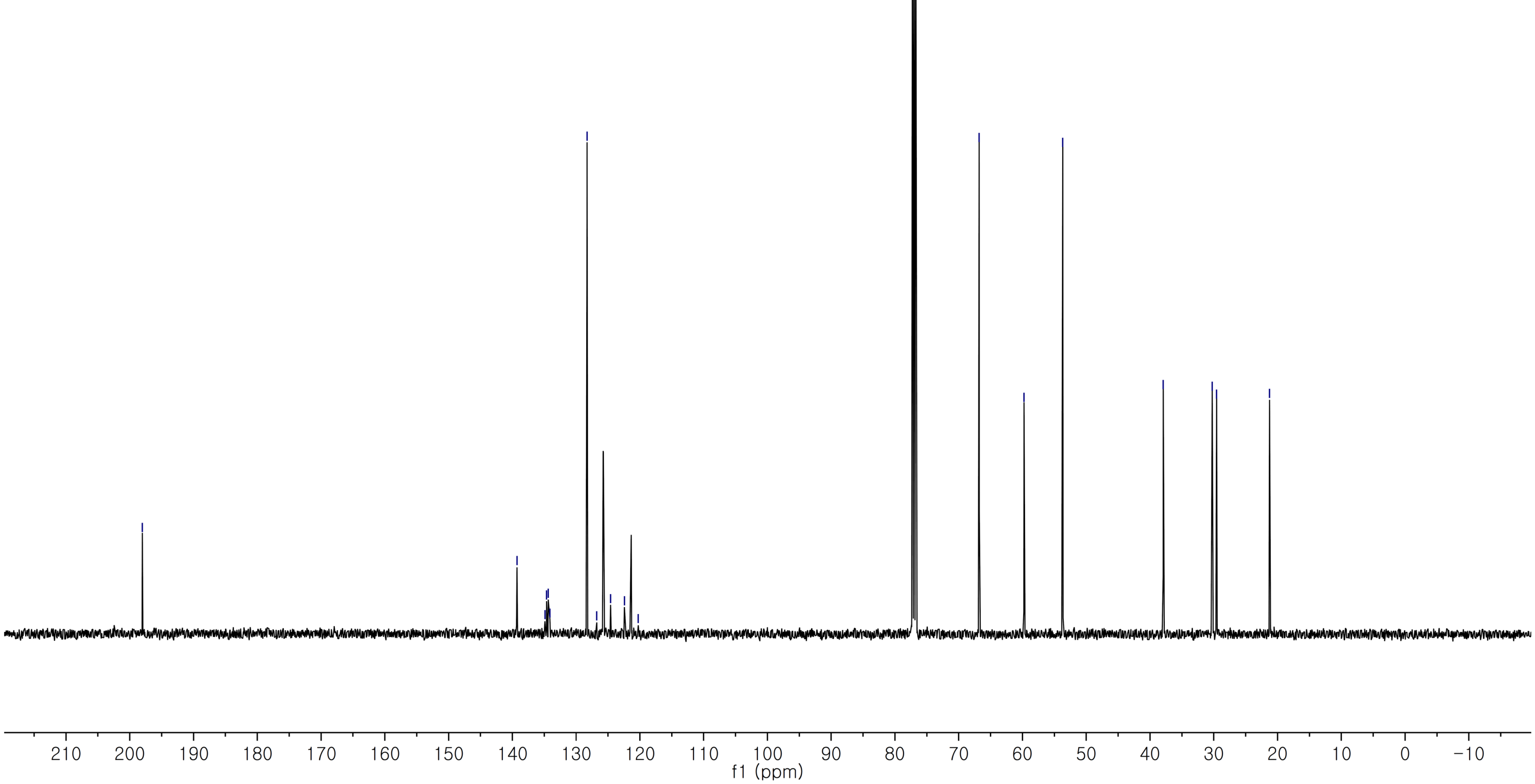


^{13}C

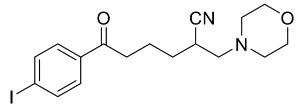
126 MHz, $CDCl_3$



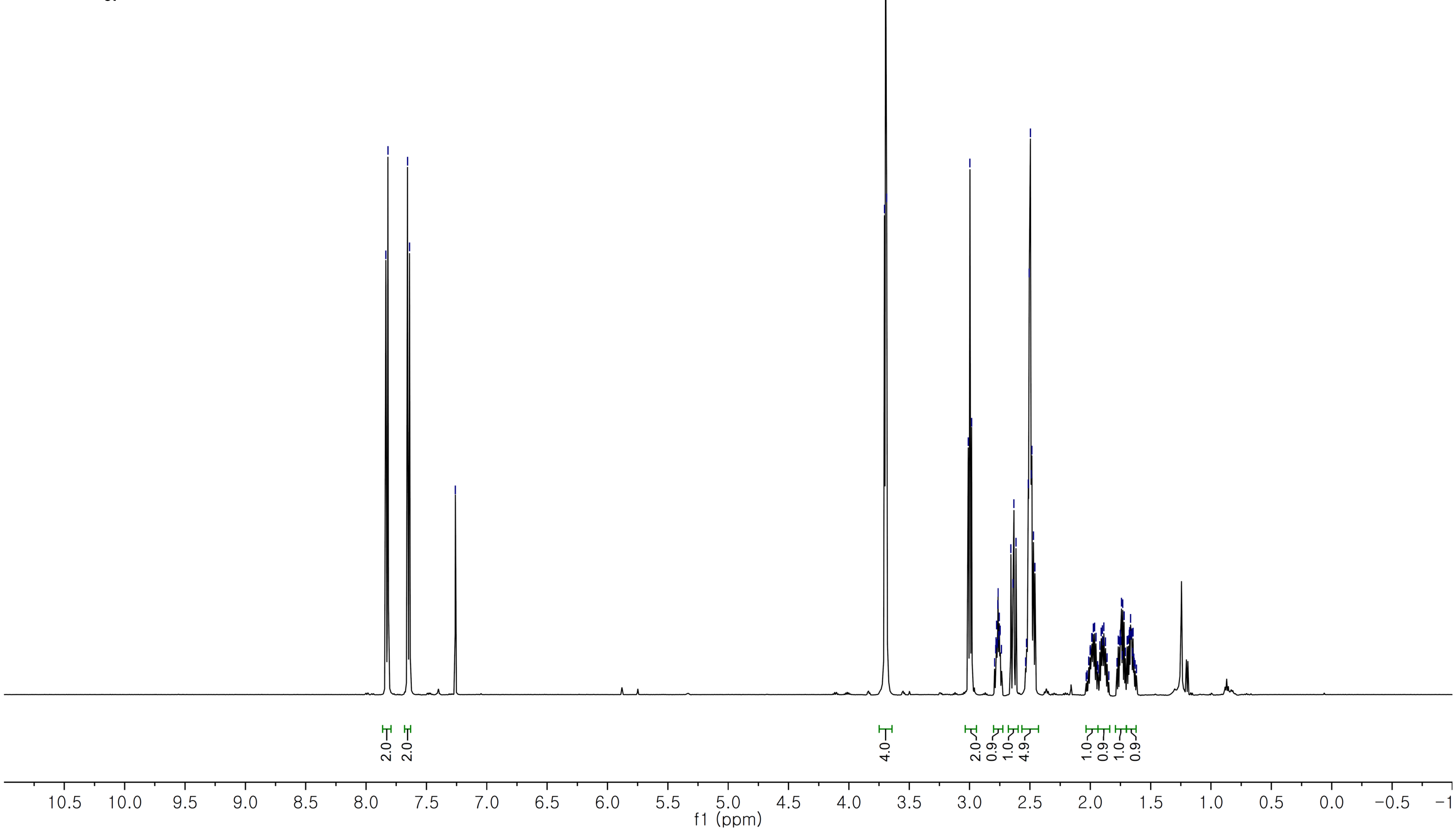
3q



^{1}H
500 MHz, $CDCl_3$

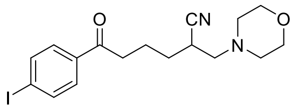


3r

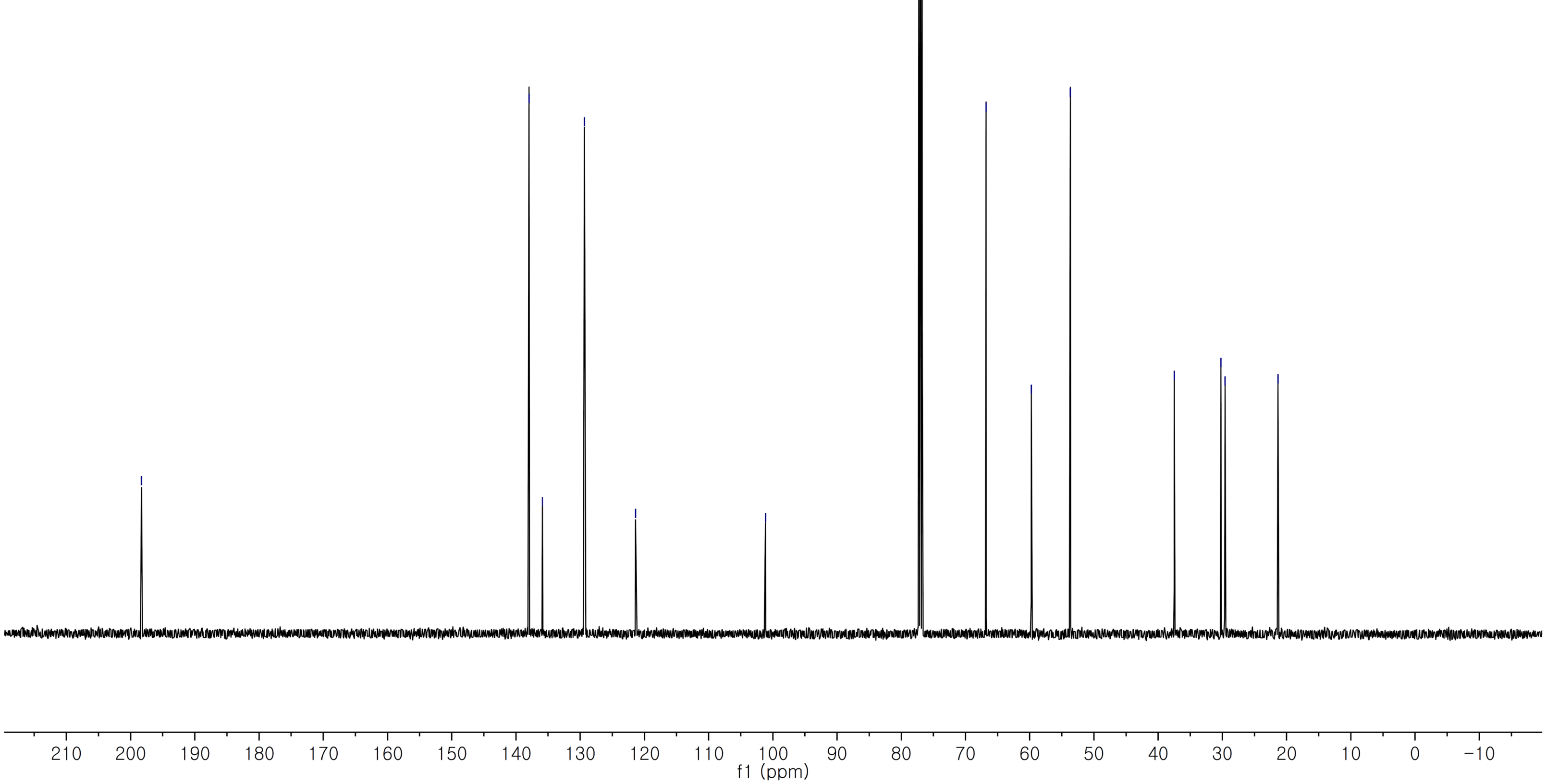


^{13}C

126 MHz, $CDCl_3$

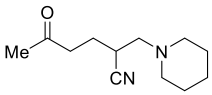


3r

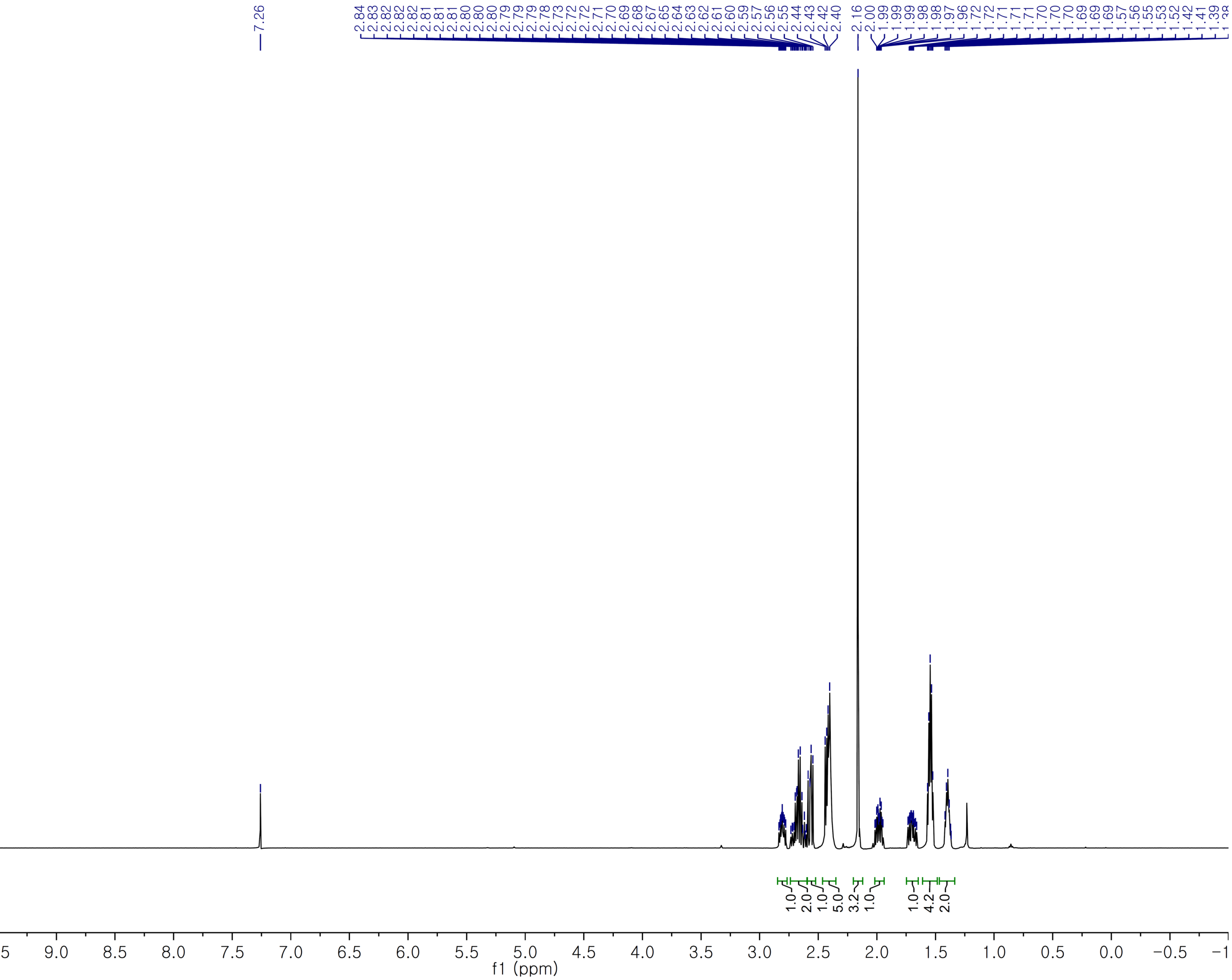


^{1}H

500 MHz, $CDCl_3$

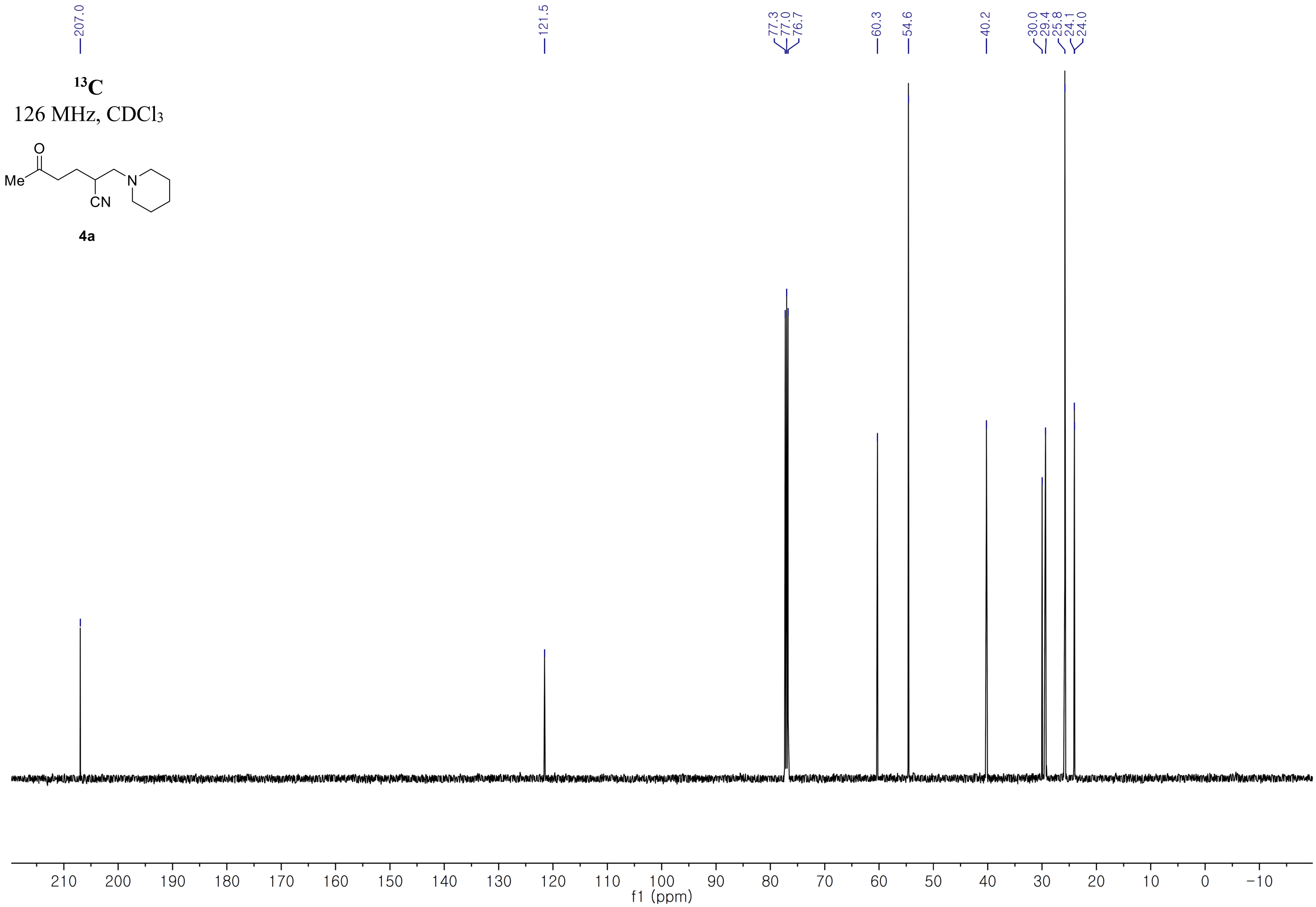


4a



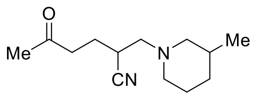
^{13}C

126 MHz, $CDCl_3$

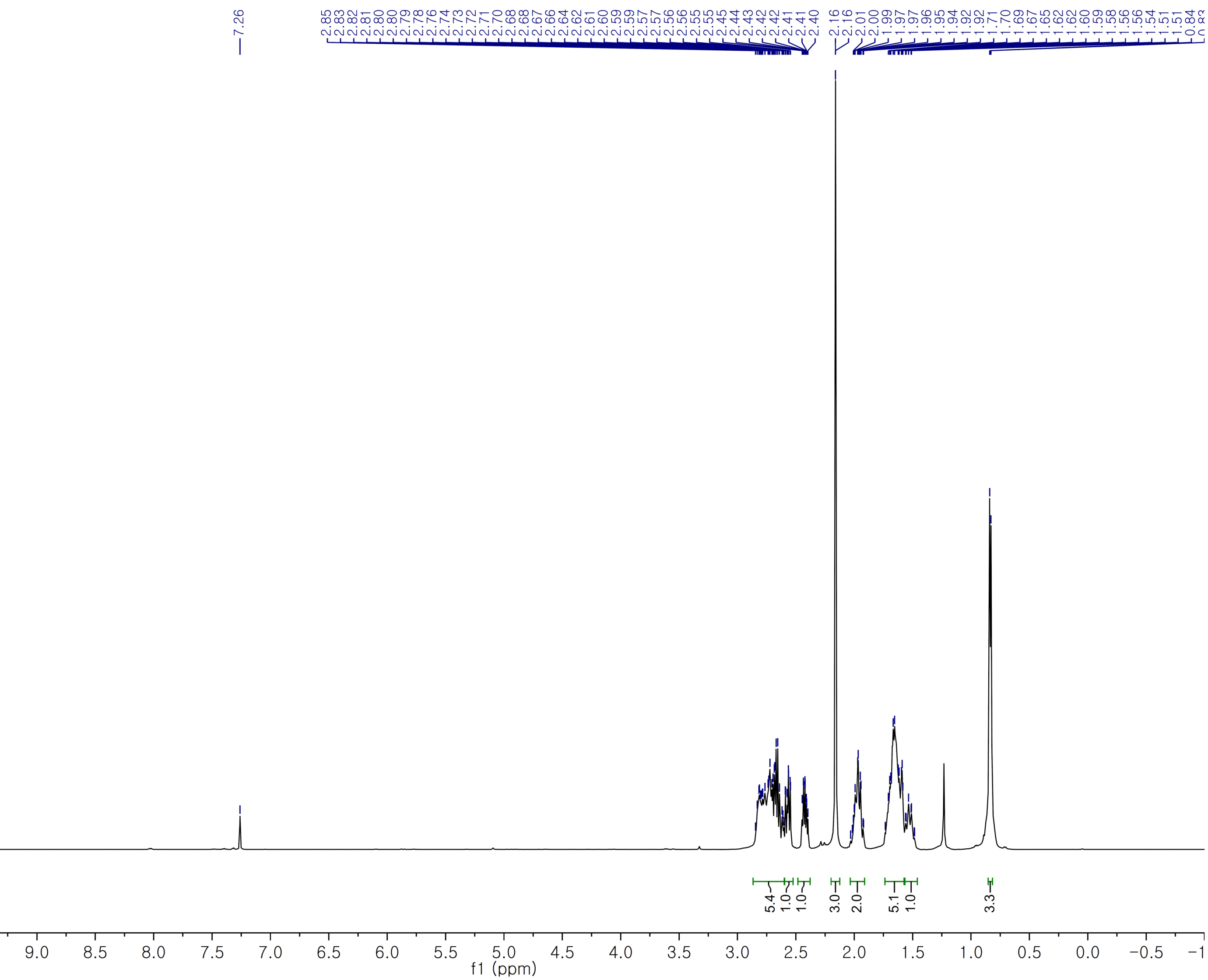


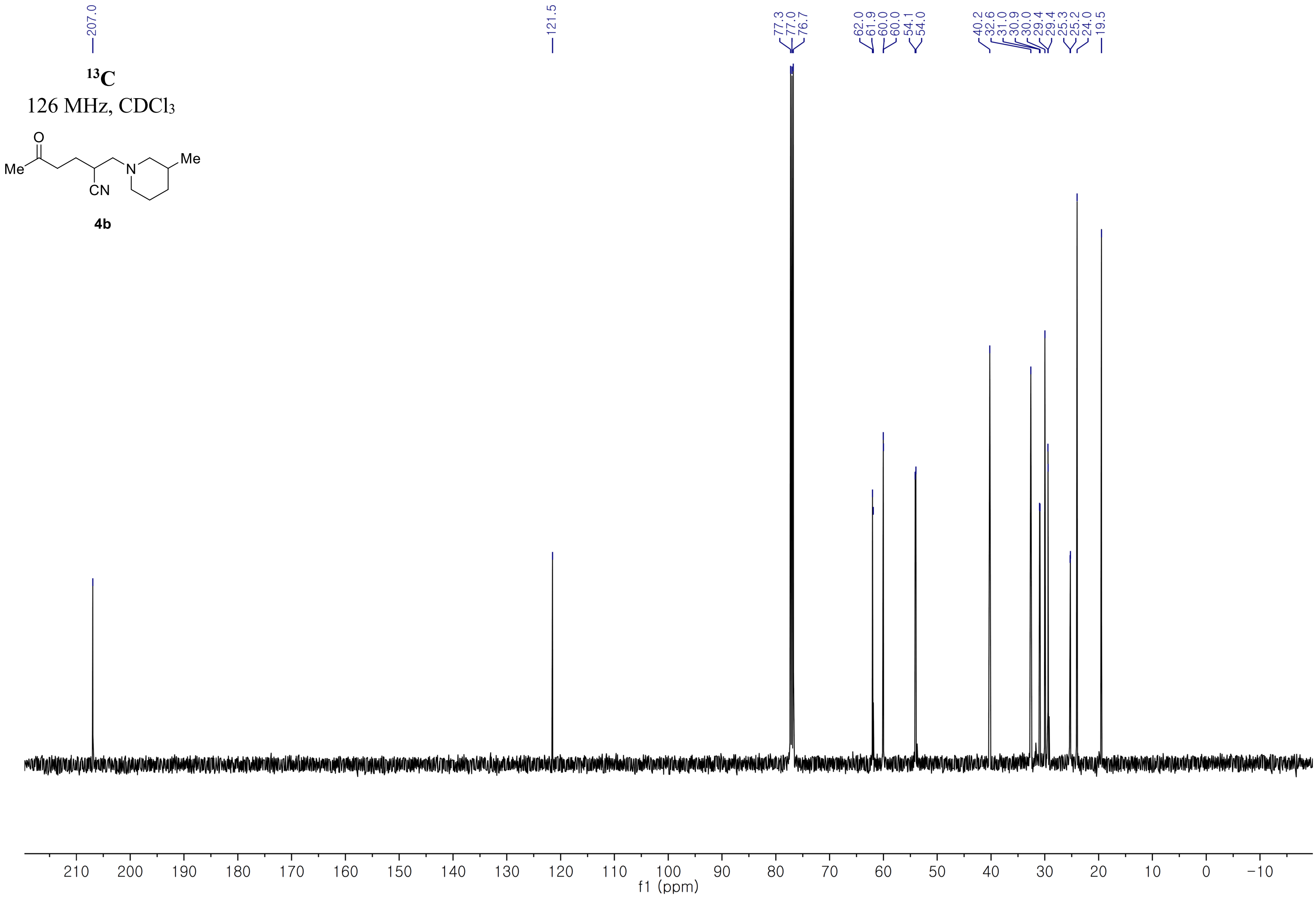
4a

^{1}H
500 MHz, $CDCl_3$



4b

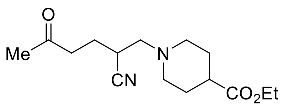




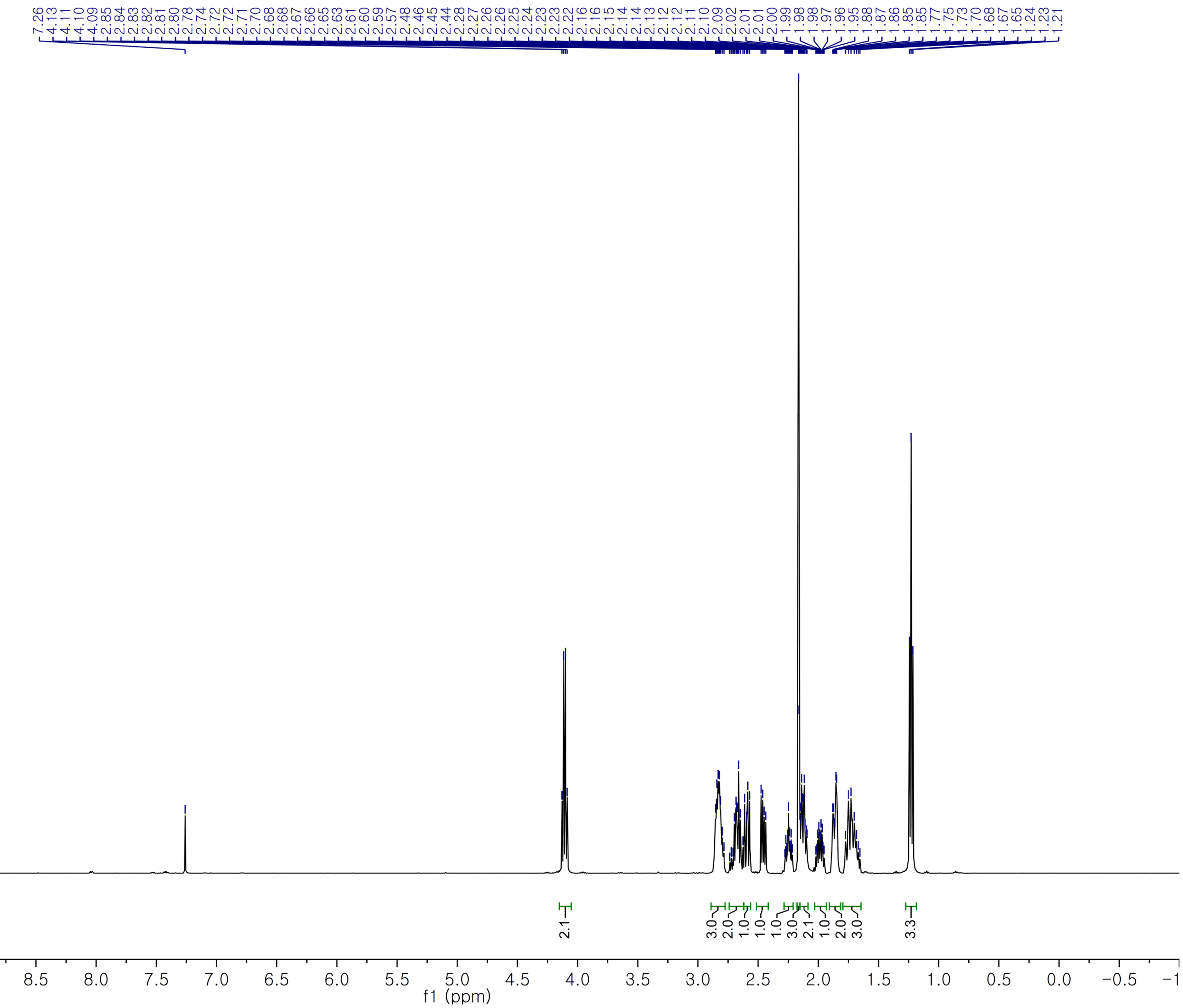
^{13}C
126 MHz, $CDCl_3$

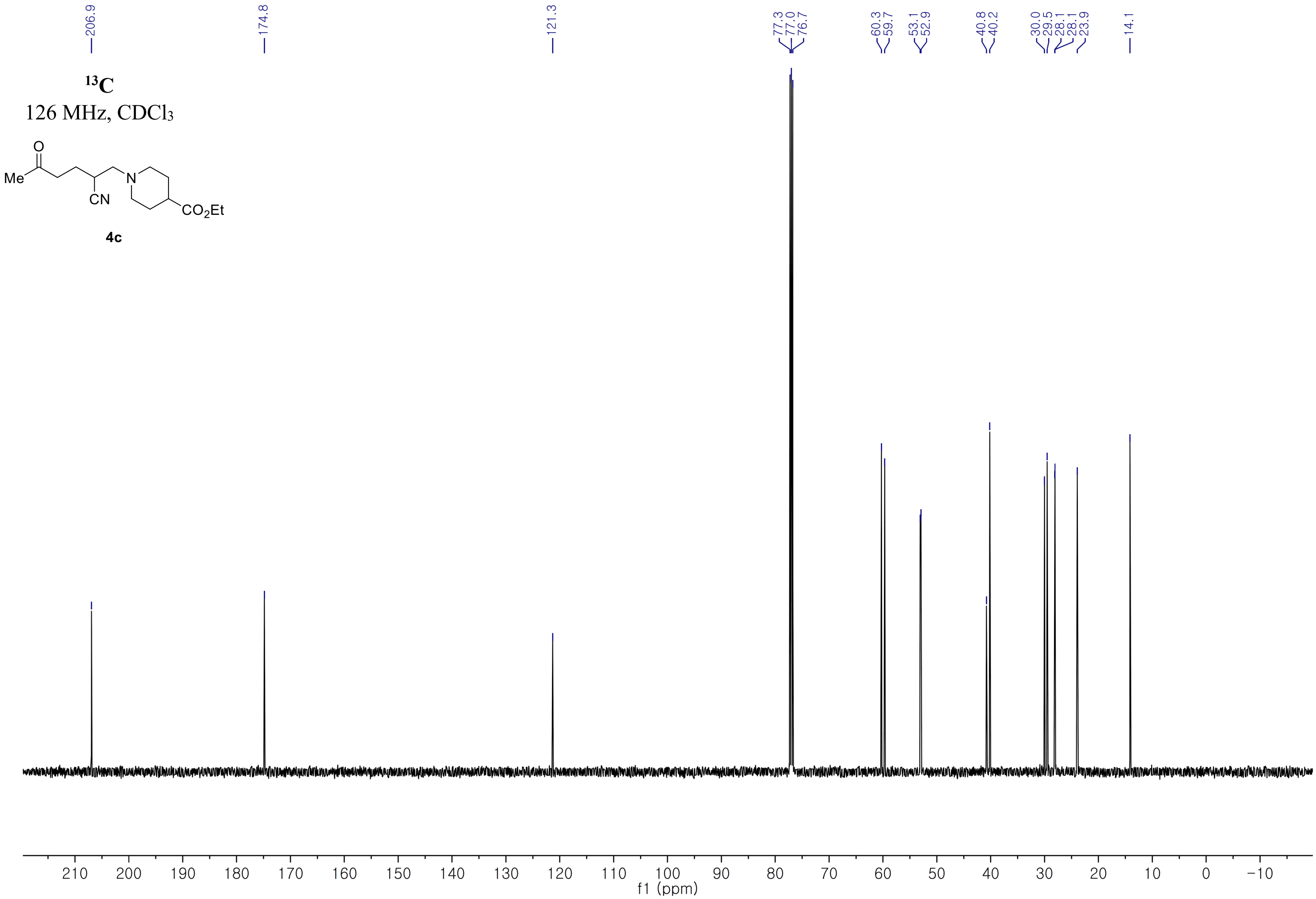
4b

[1]H
500 MHz, CDCl3



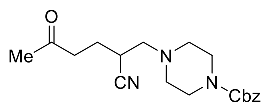
4c



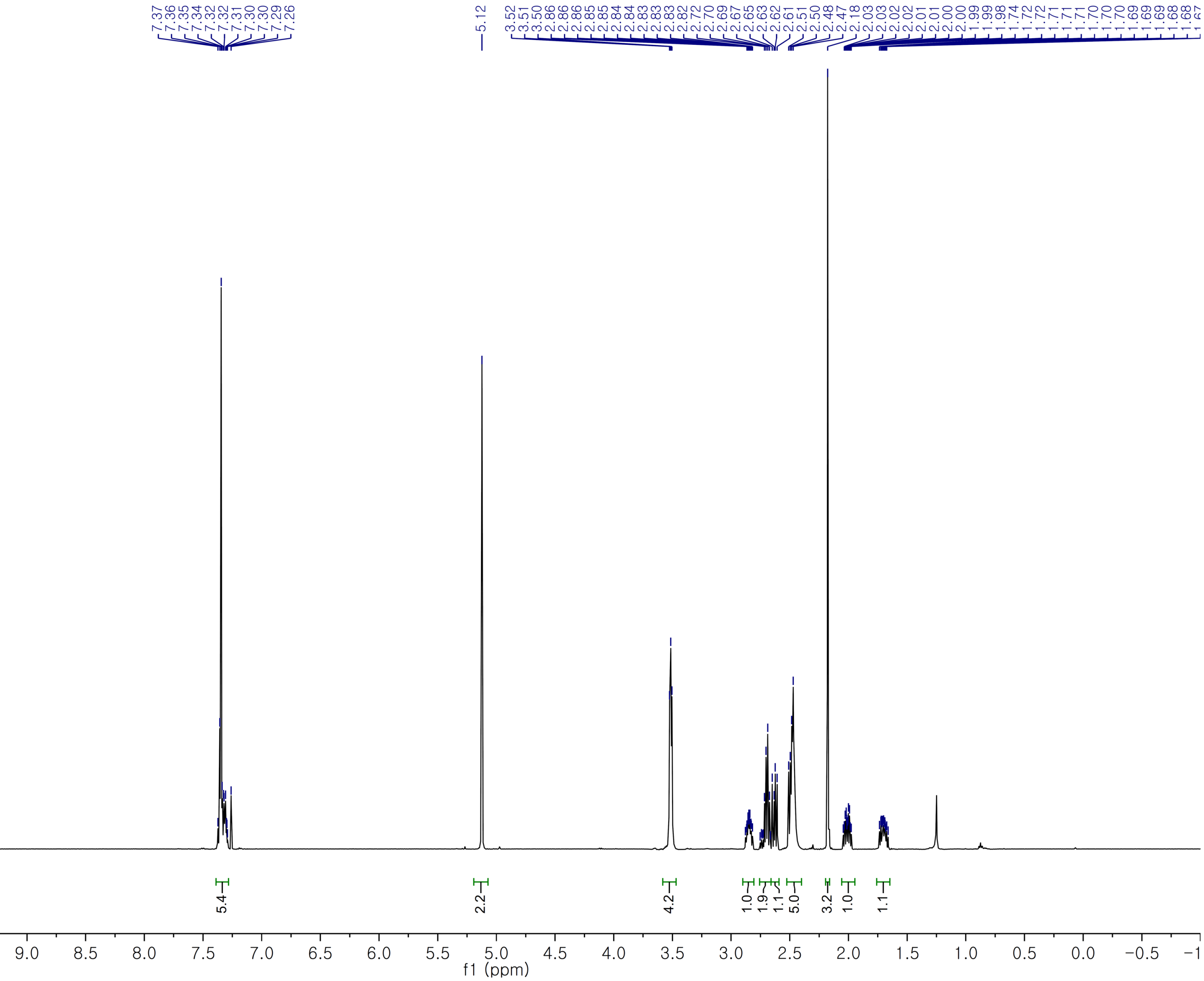

206.9
174.8
121.3
77.3
77.0
76.7
60.3
59.7
53.1
52.9
40.8
40.2
30.0
29.5
28.1
28.1
23.9
14.1
^{13}C
126 MHz, CDCl$_3$
O
Me
N
CN
CO$_2$Et
4c
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
f1 (ppm)

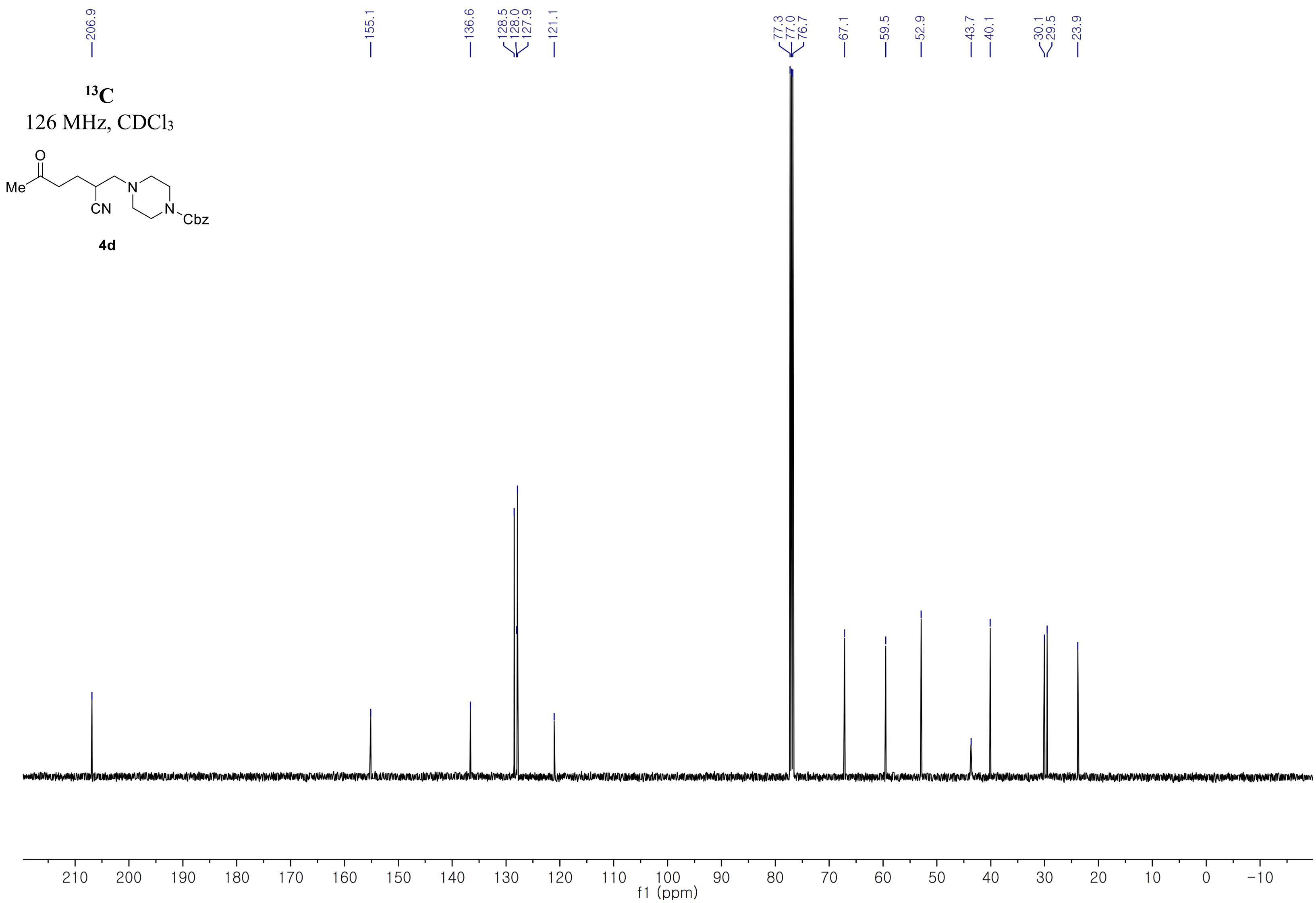
^{1}H

500 MHz, $CDCl_3$

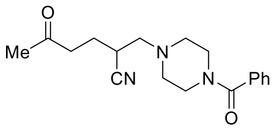


4d

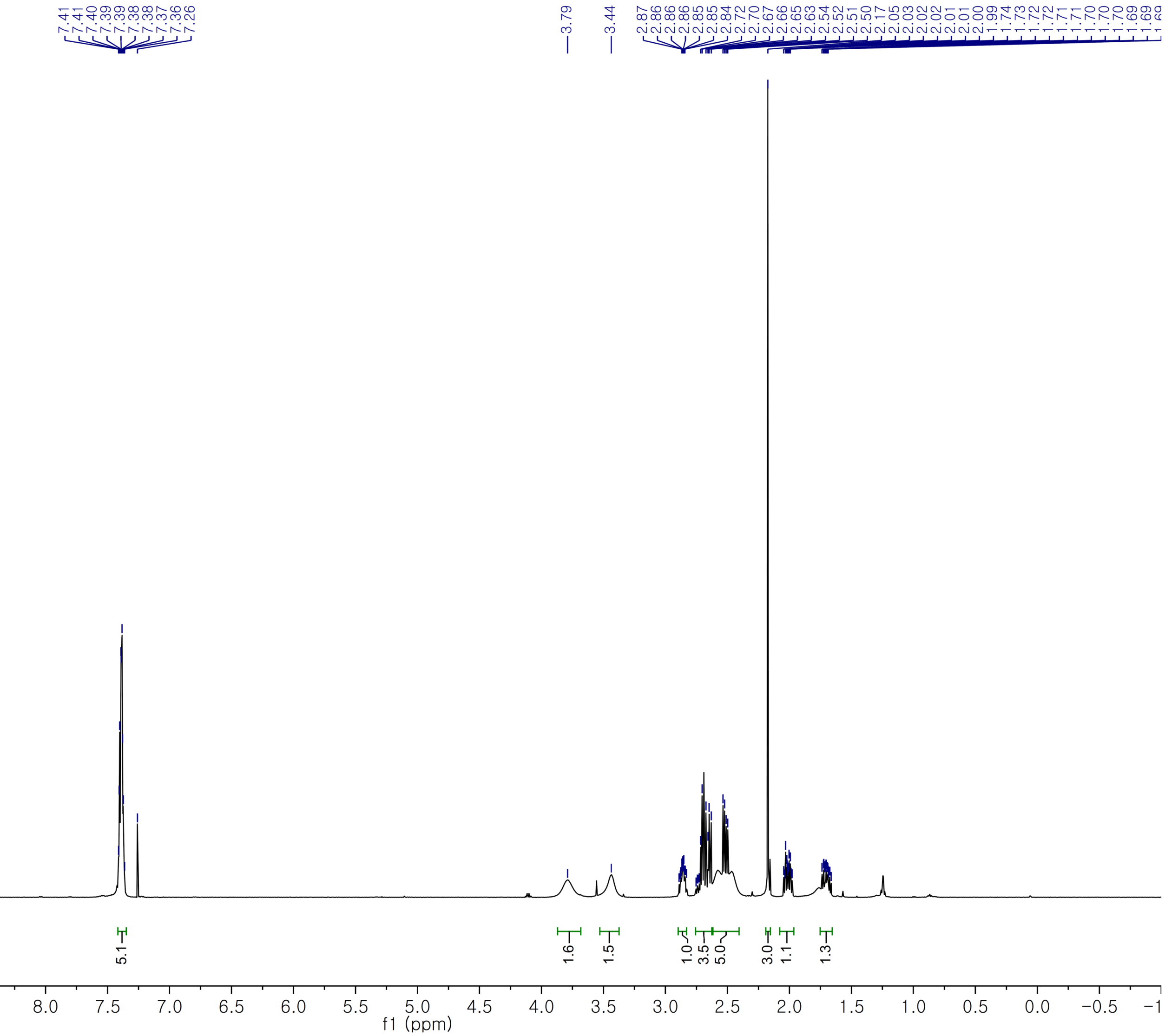


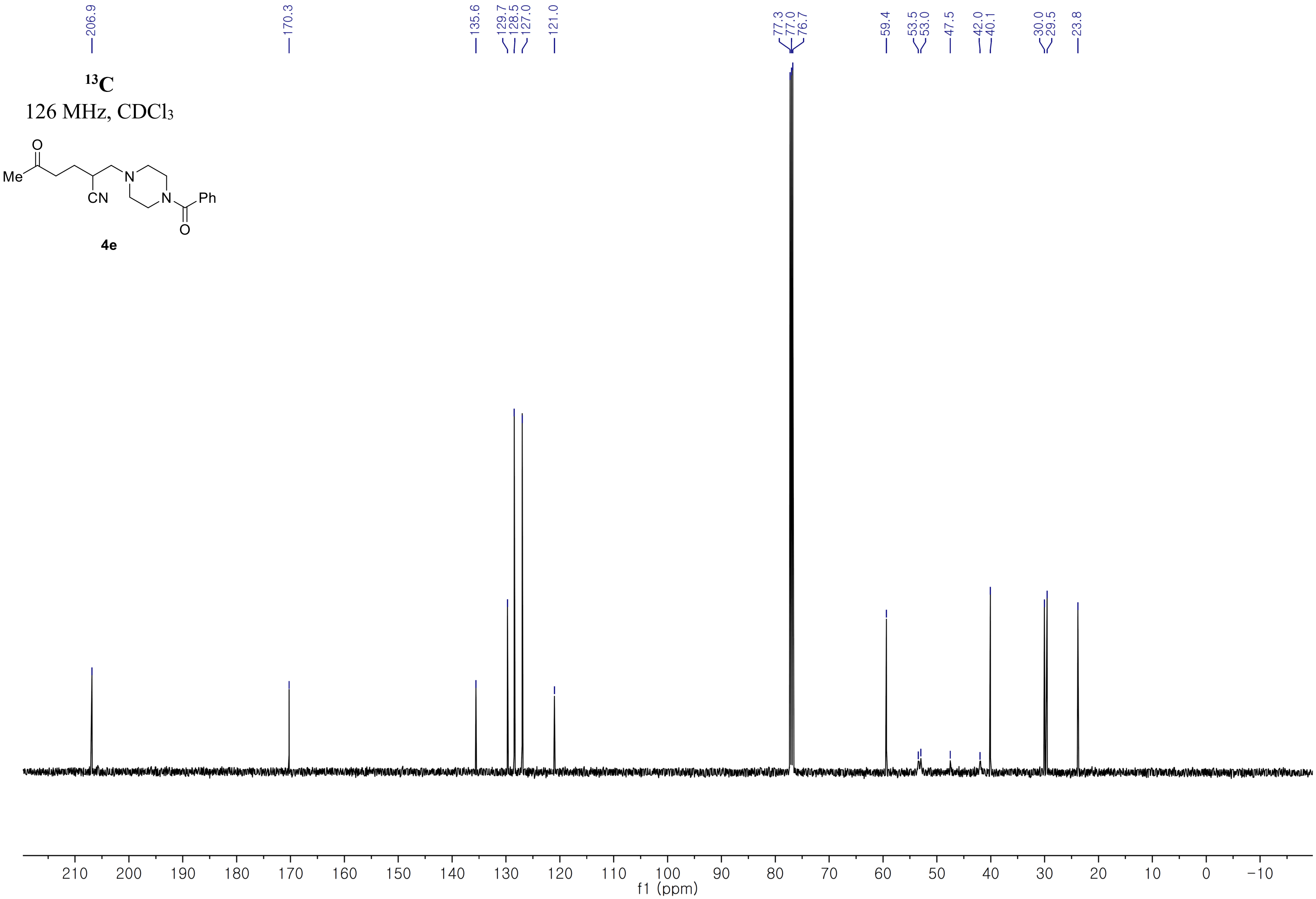

206.9
155.1
136.6
128.5
128.0
127.9
121.1
77.3
77.0
76.7
67.1
59.5
52.9
43.7
40.1
30.1
29.5
23.9
^{13}C
126 MHz, $CDCl_3$
O
Me
CN
N
N
Cbz
4d
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10
f1 (ppm)

^{1}H
500 MHz, $CDCl_3$



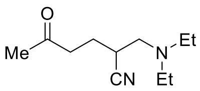
4e



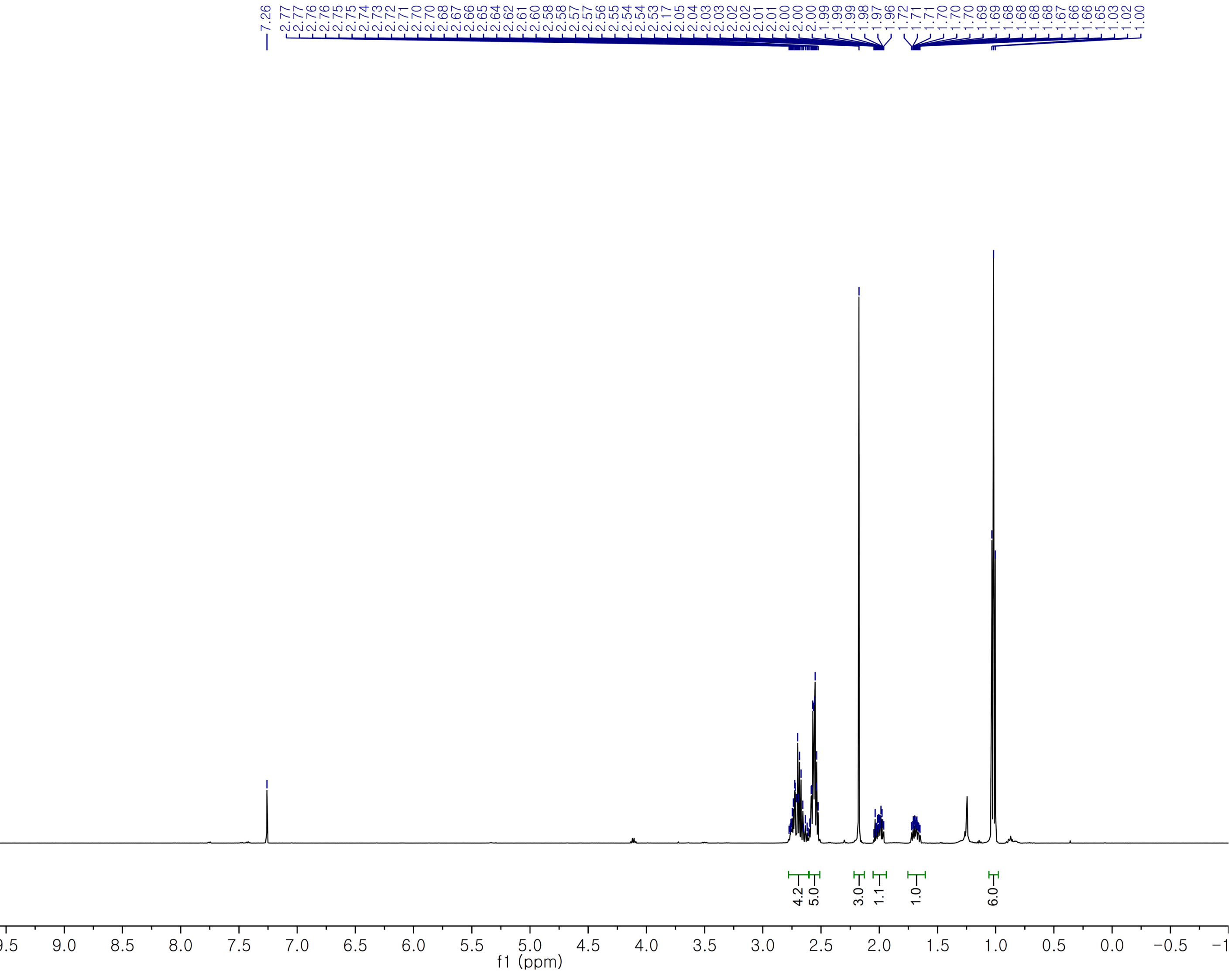


206.9
170.3
135.6
129.7
128.5
127.0
121.0
77.3
77.0
76.7
59.4
53.5
53.0
47.5
42.0
40.1
30.0
29.5
23.8
^{13}C
126 MHz, $CDCl_3$
Me
O
CN
N
N
Ph
O
4e
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10
f1 (ppm)

^{1}**H**
500 MHz, $CDCl_3$

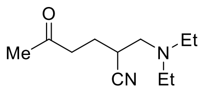


4f

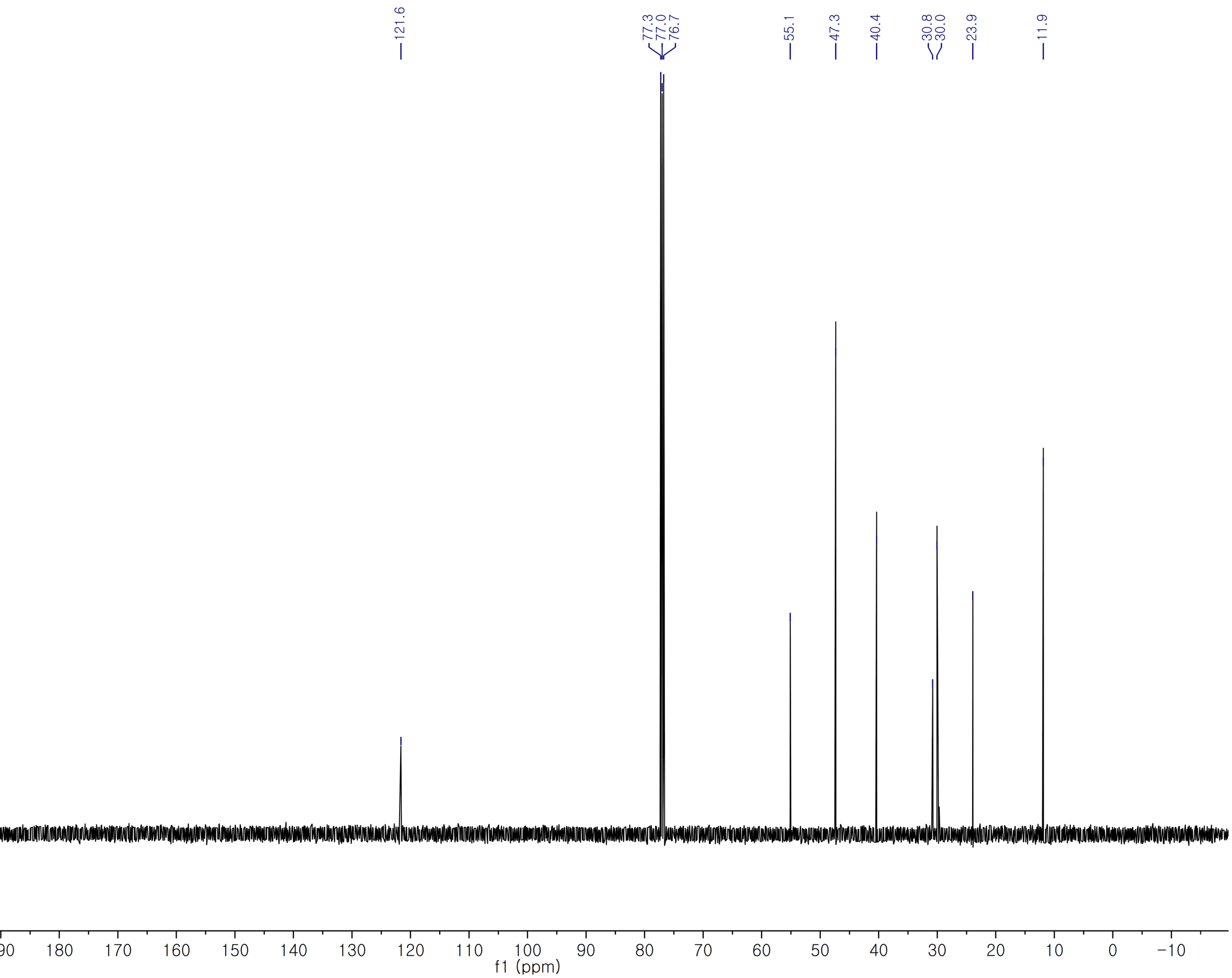


^{13}C

126 MHz, $CDCl_3$

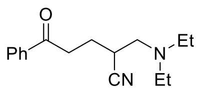


4f

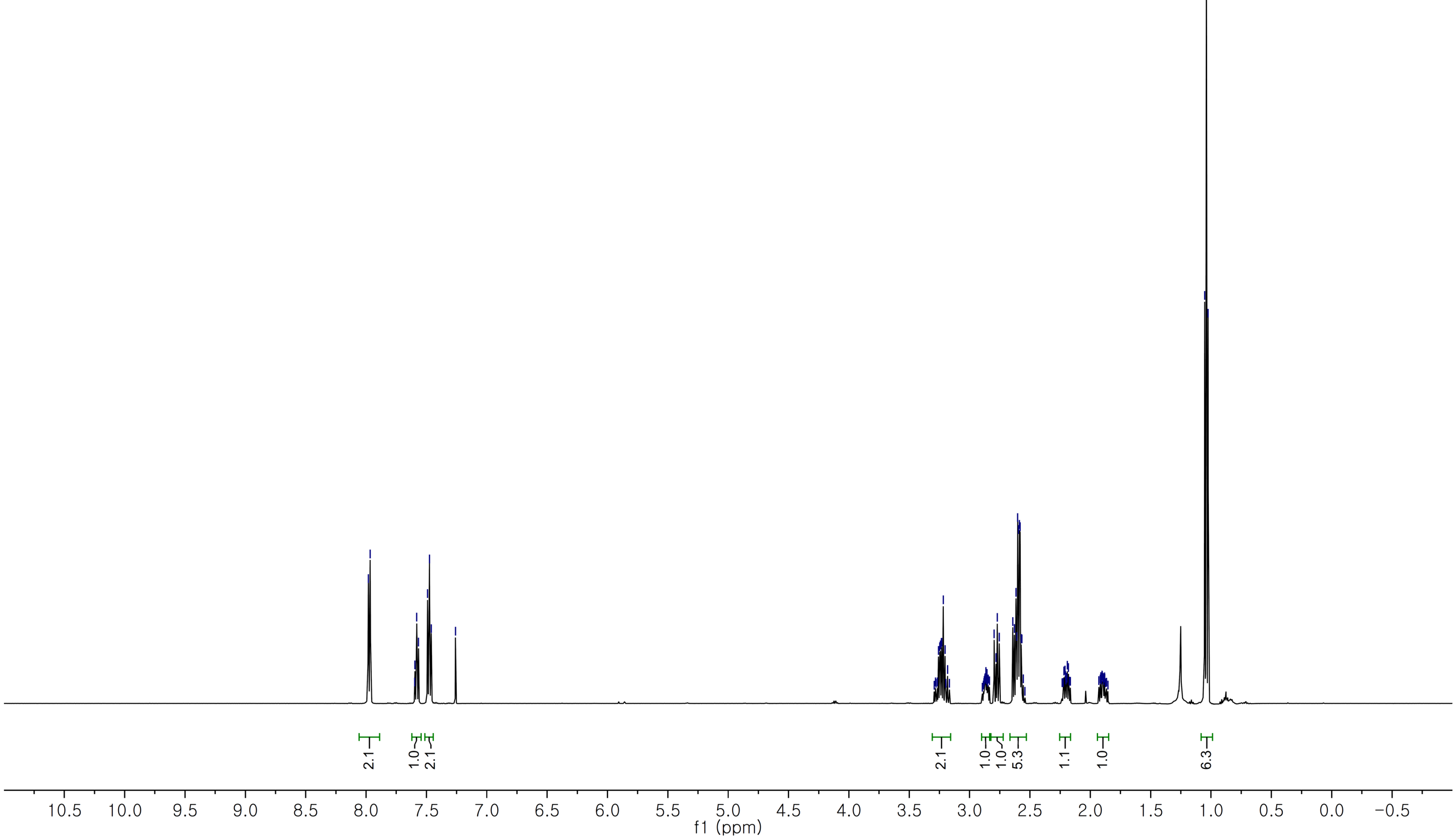


^{1}**H**

500 MHz, $CDCl_3$

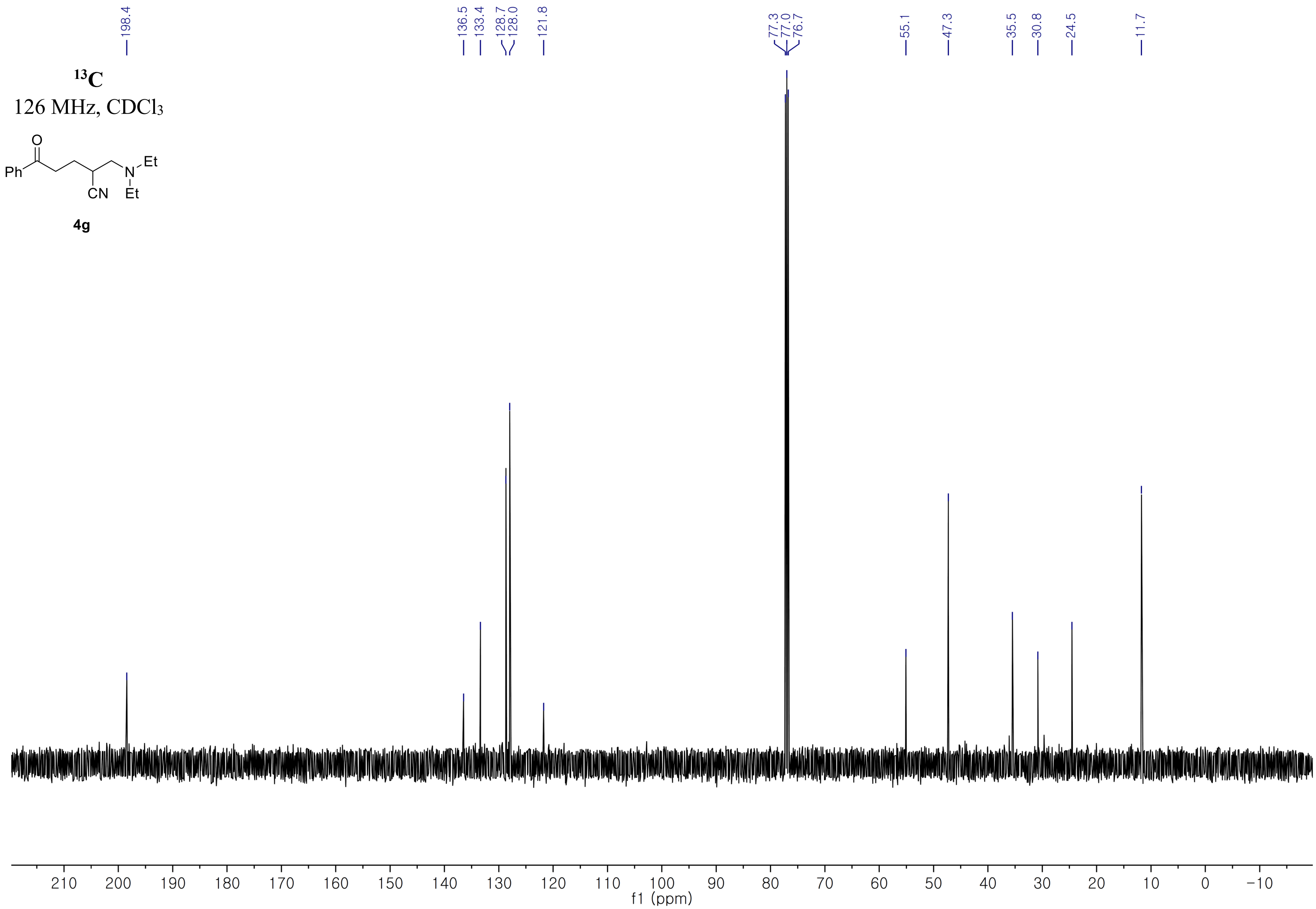


4g



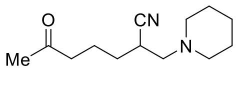
^{13}C

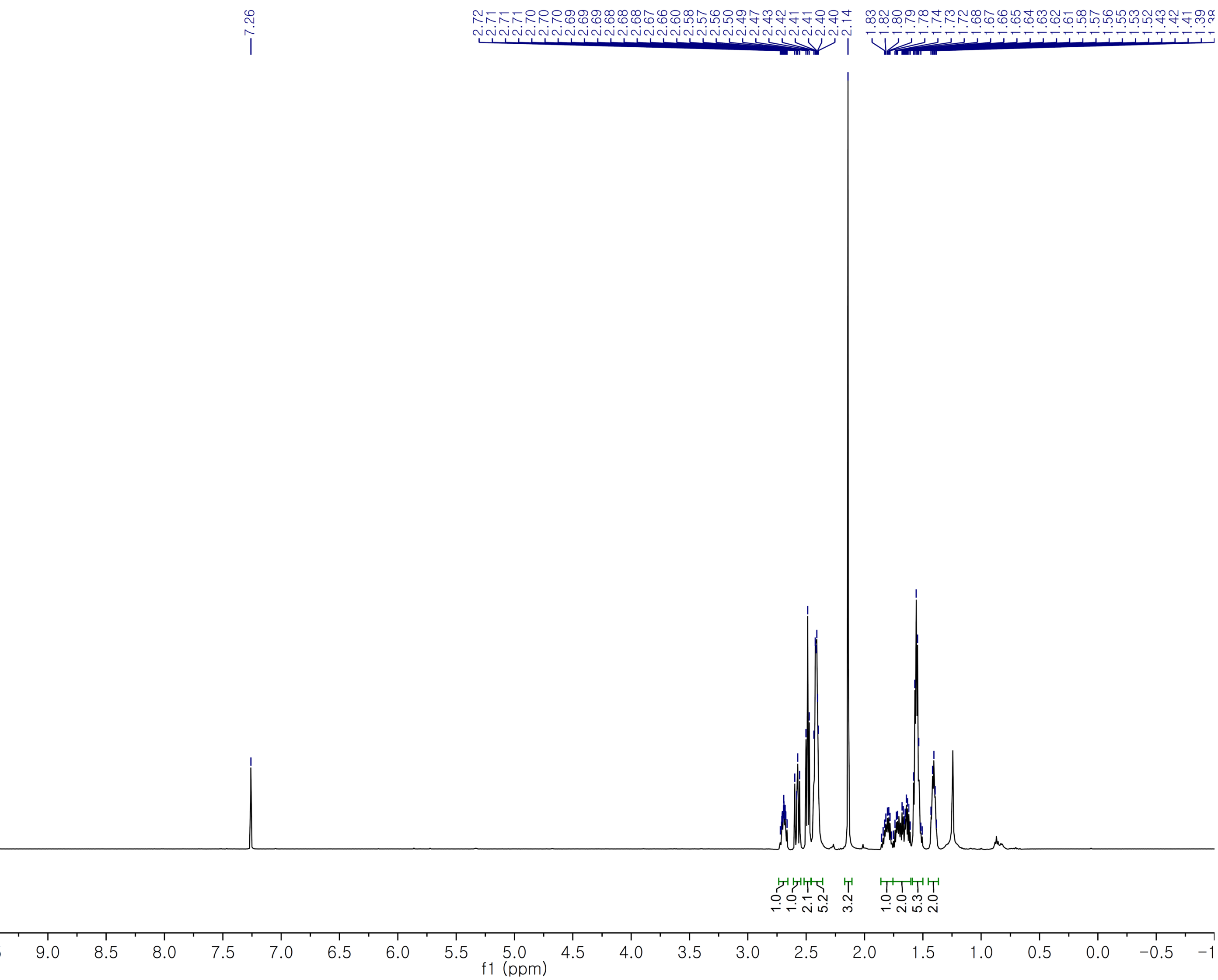
126 MHz, $CDCl_3$

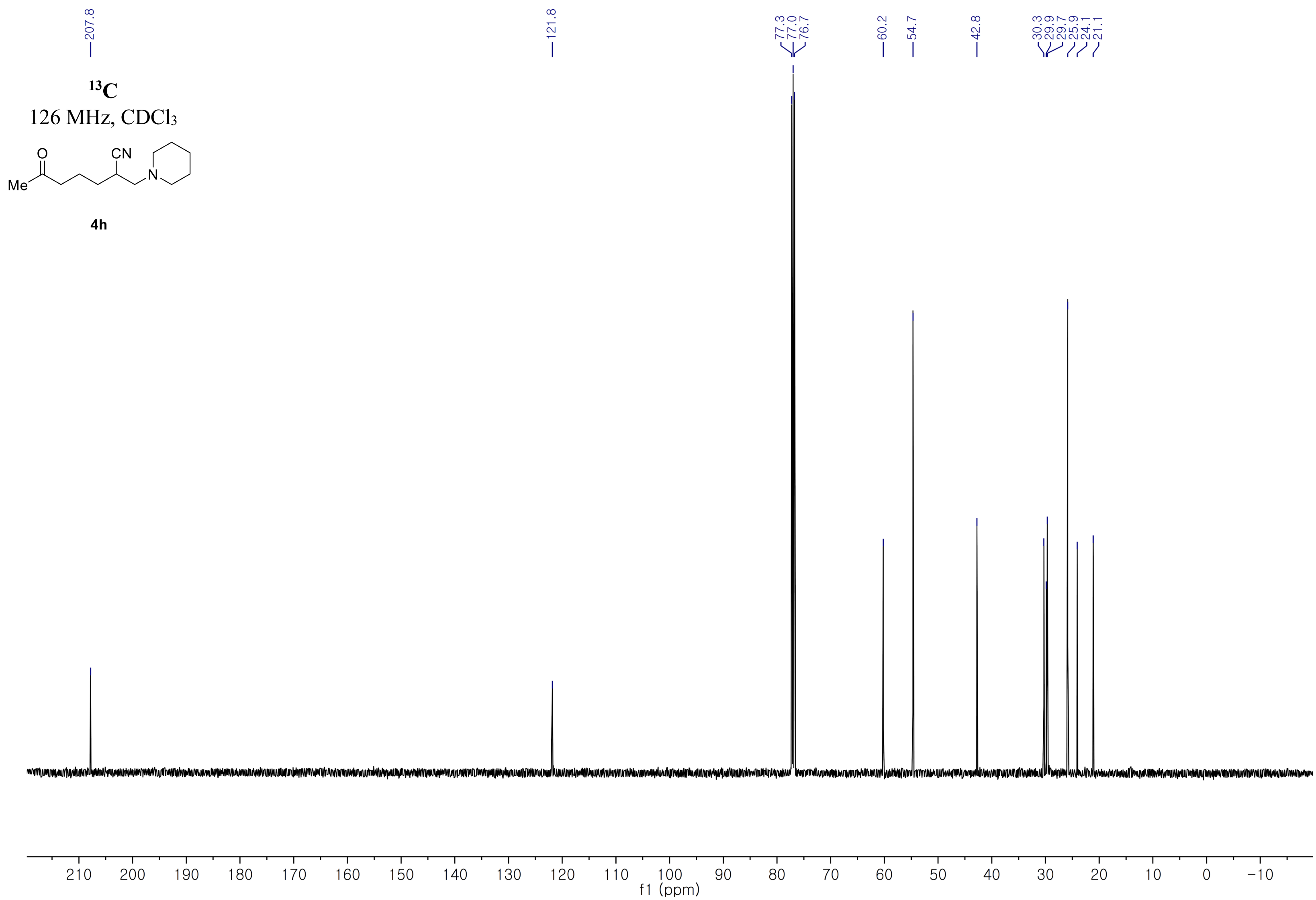


4g

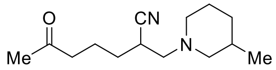
^{1}H
500 MHz, $CDCl_3$



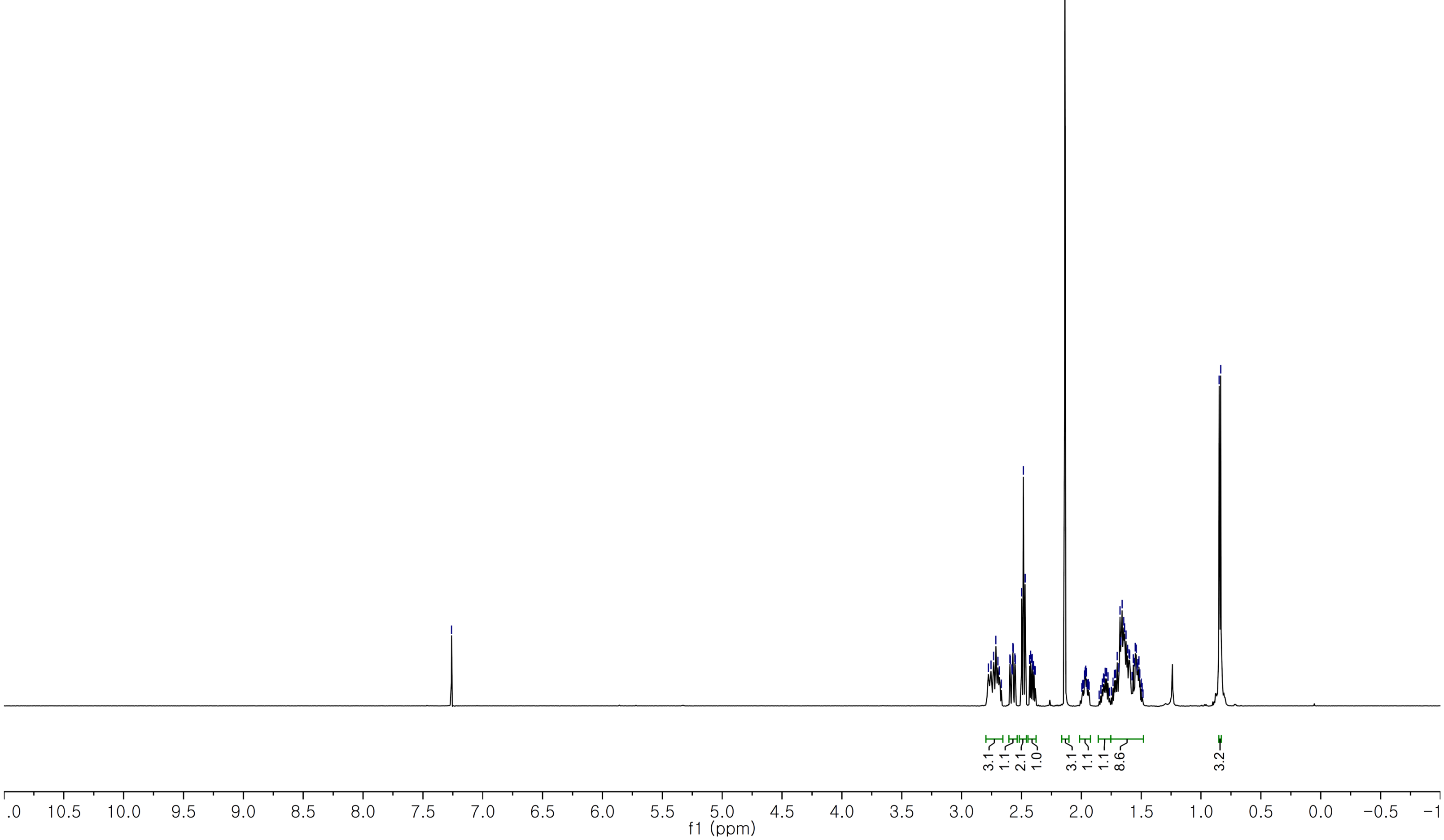



207.8
121.8
77.3
77.0
76.7
60.2
54.7
42.8
30.3
29.9
29.7
25.9
24.1
21.1
^{13}C
126 MHz, CDCl$_3$
O
CN
Me
N
4h
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10
f1 (ppm)

^{1}H
500 MHz, $CDCl_3$

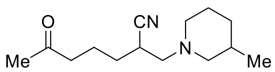


4i

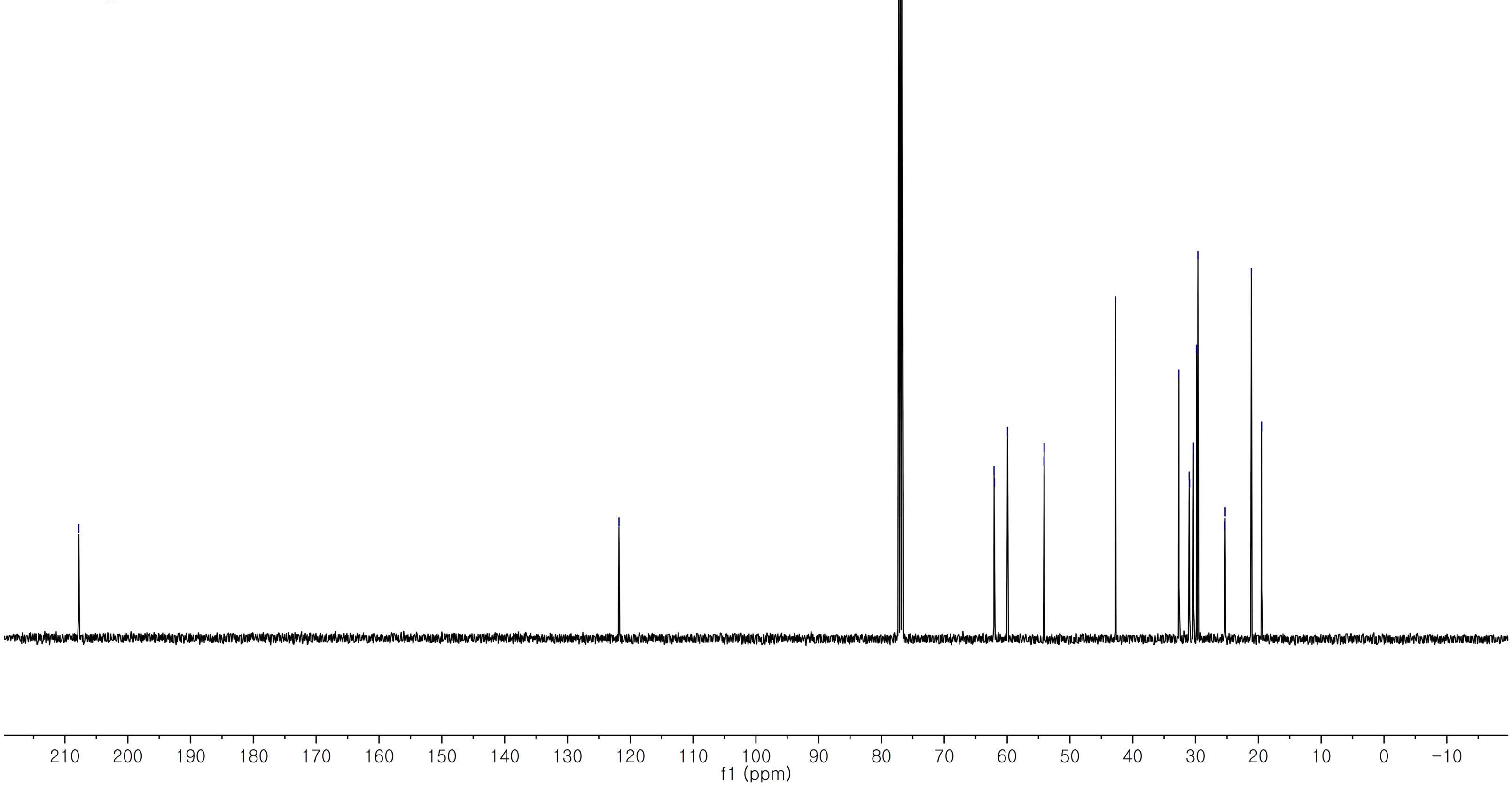


^{13}C

126 MHz, $CDCl_3$

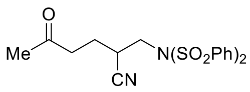


4i

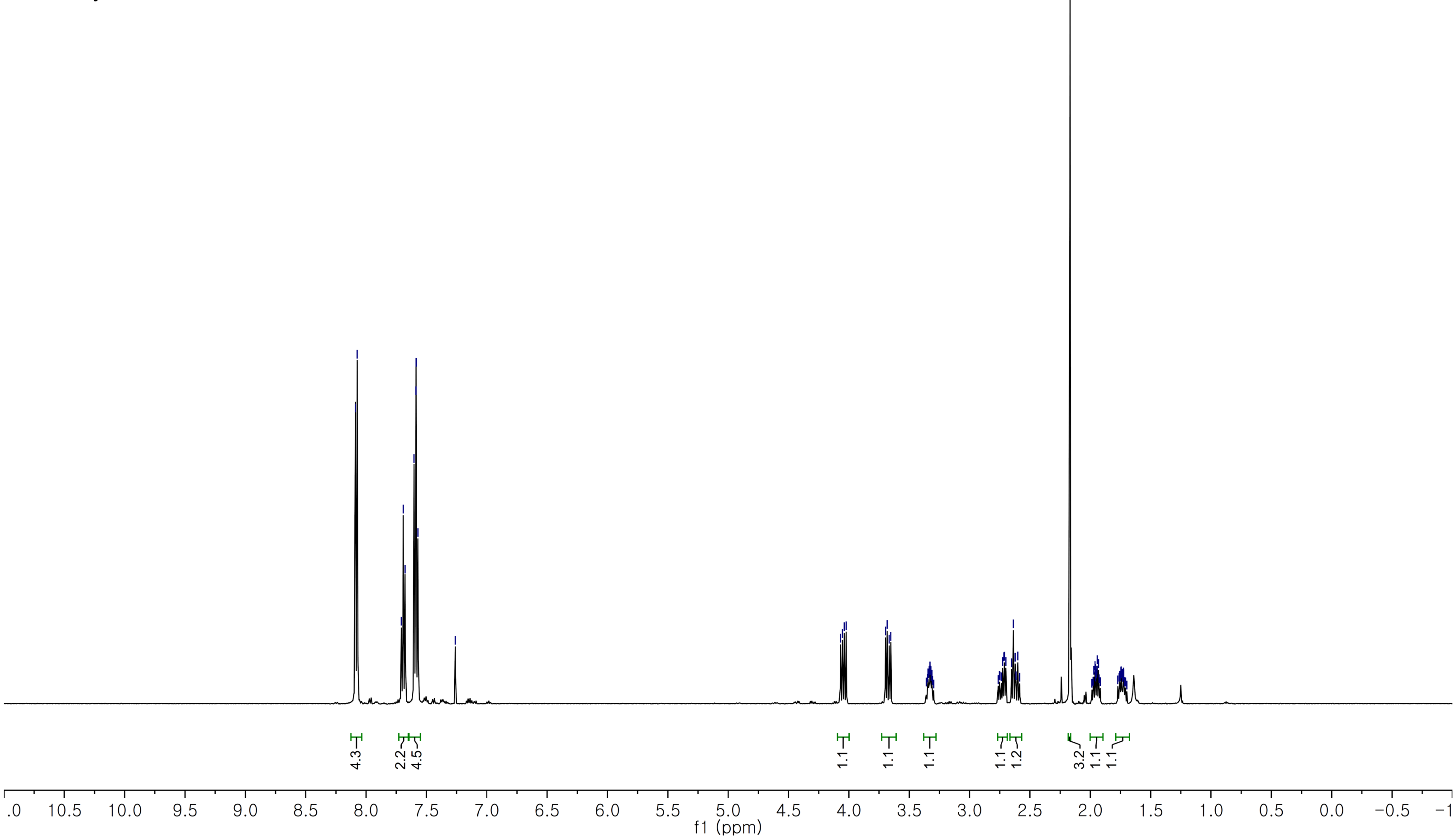


^{1}H

500 MHz, $CDCl_3$

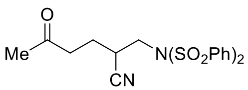


4j

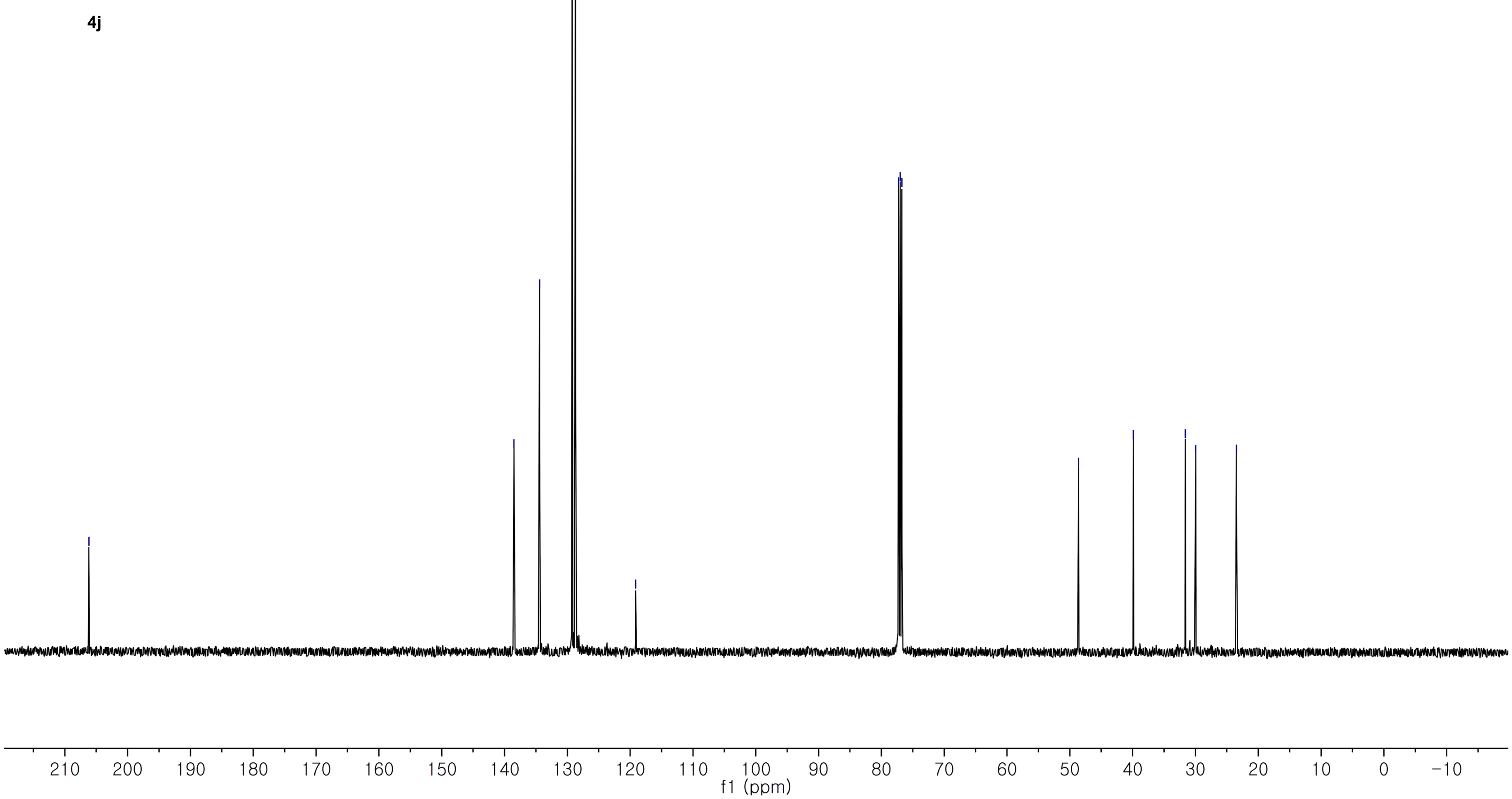


^{13}C

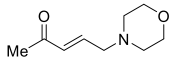
126 MHz, $CDCl_3$



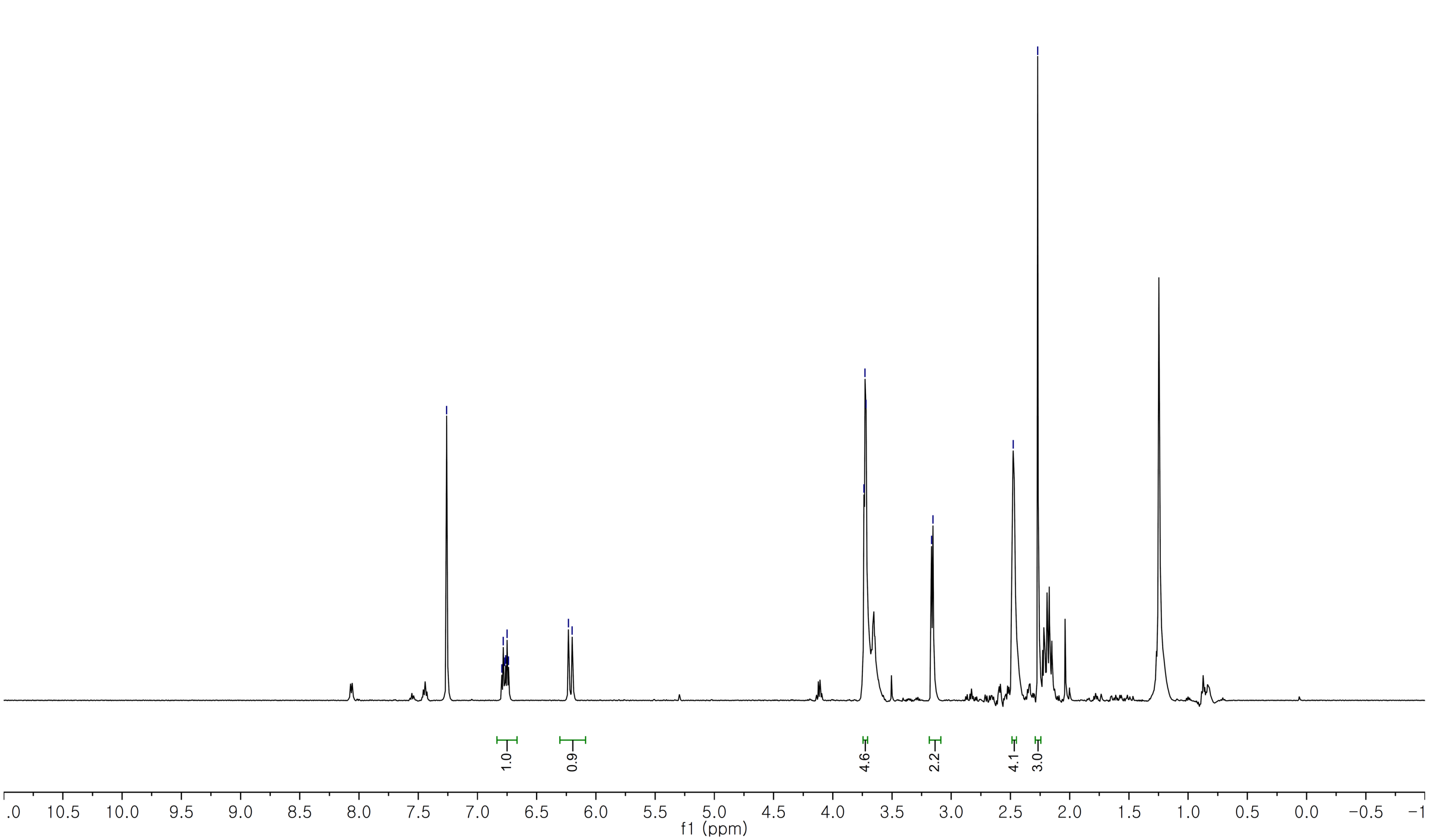
4j



¹H
500 MHz, $CDCl_3$

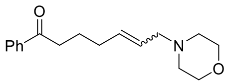


7

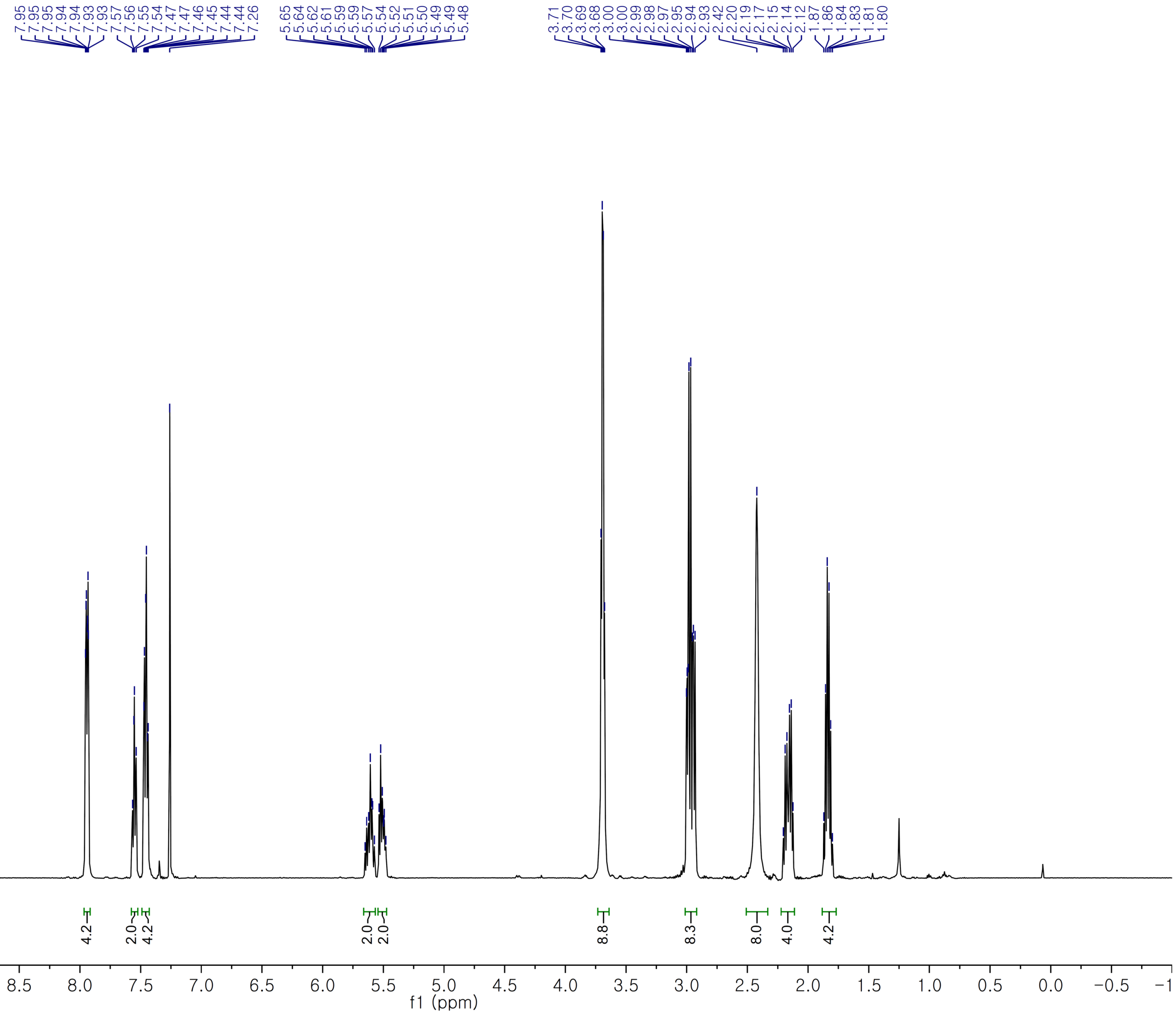


Note: The sample contains ~10% benzoic acid and unknown impurity.

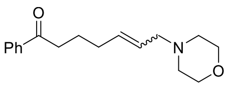
[1]H
500 MHz, CDCl3



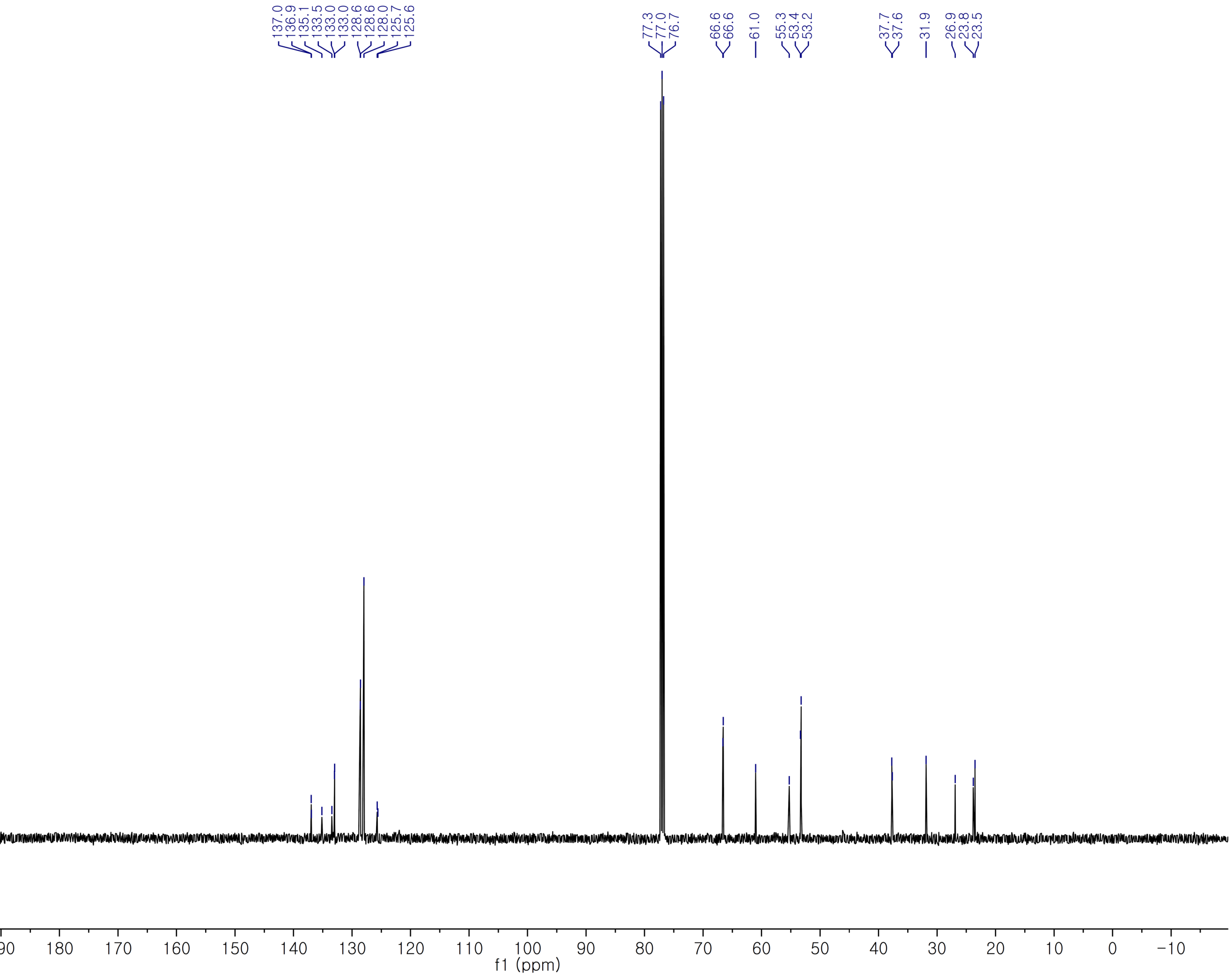
8



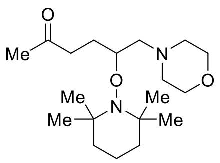
^{13}C
126 MHz, $CDCl_3$



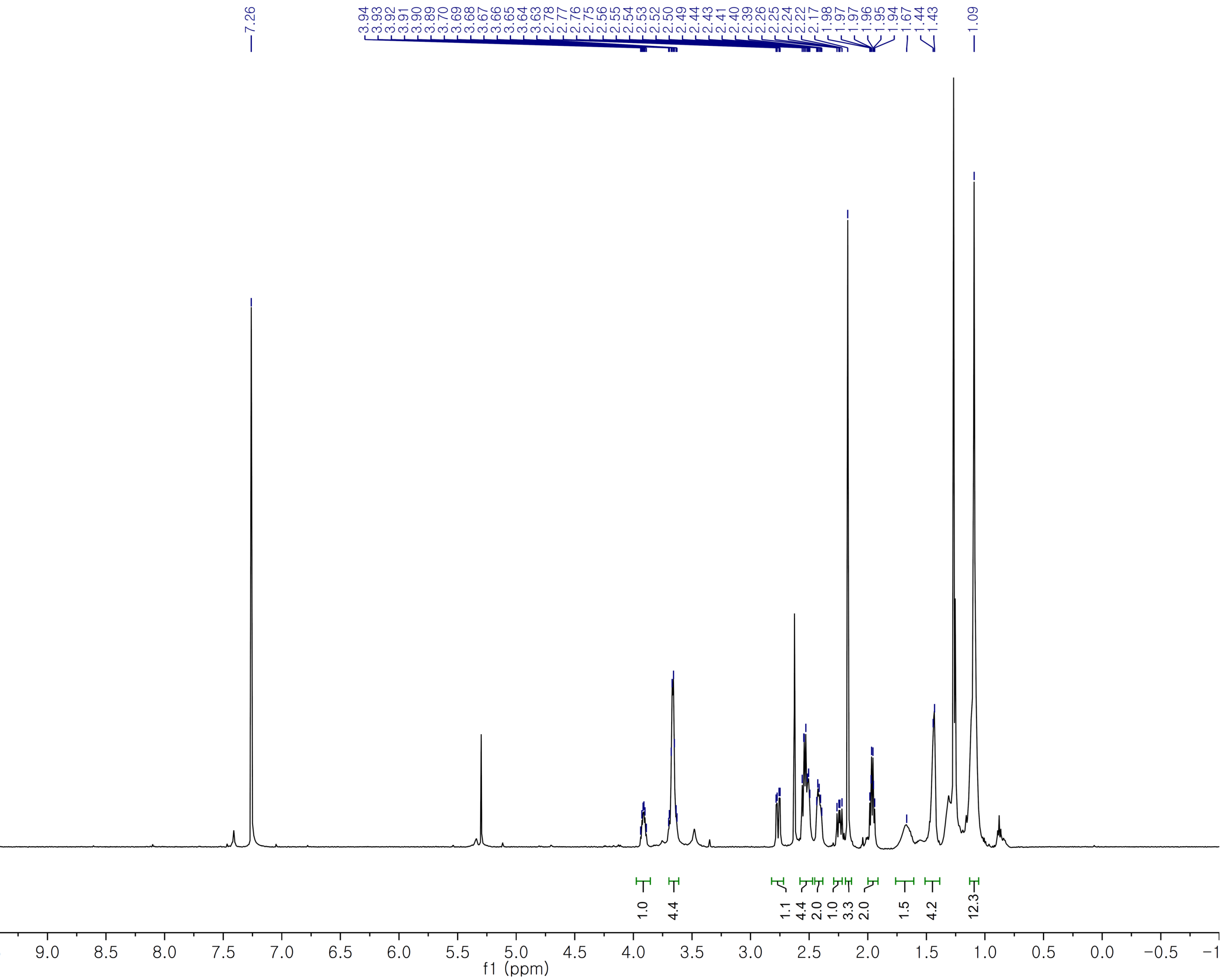
8



^{1}H
500 MHz, $CDCl_3$



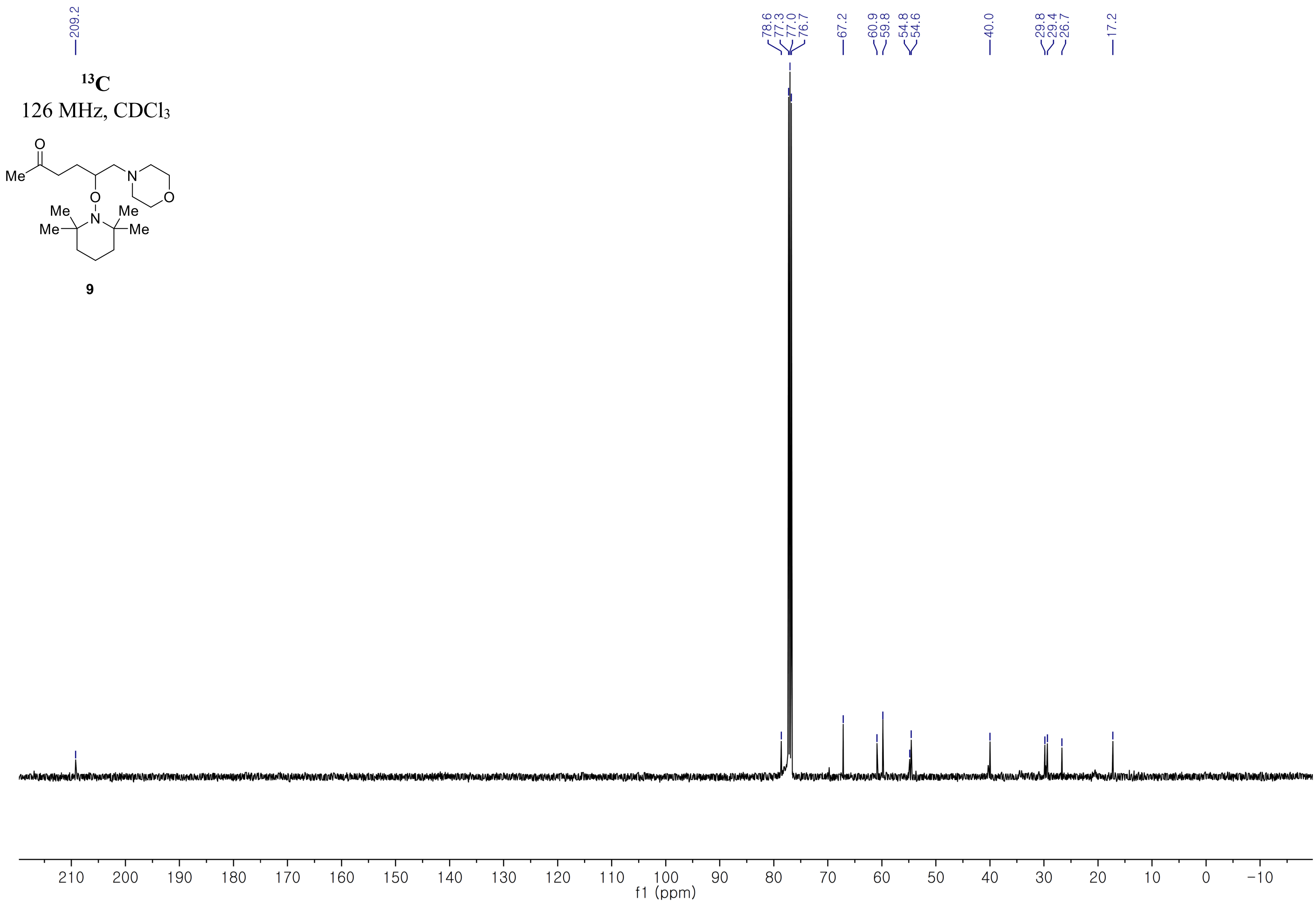
9



Note: The sample contains some grease due to the small quantity of **9**.

^{13}C

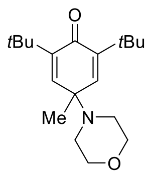
126 MHz, $CDCl_3$



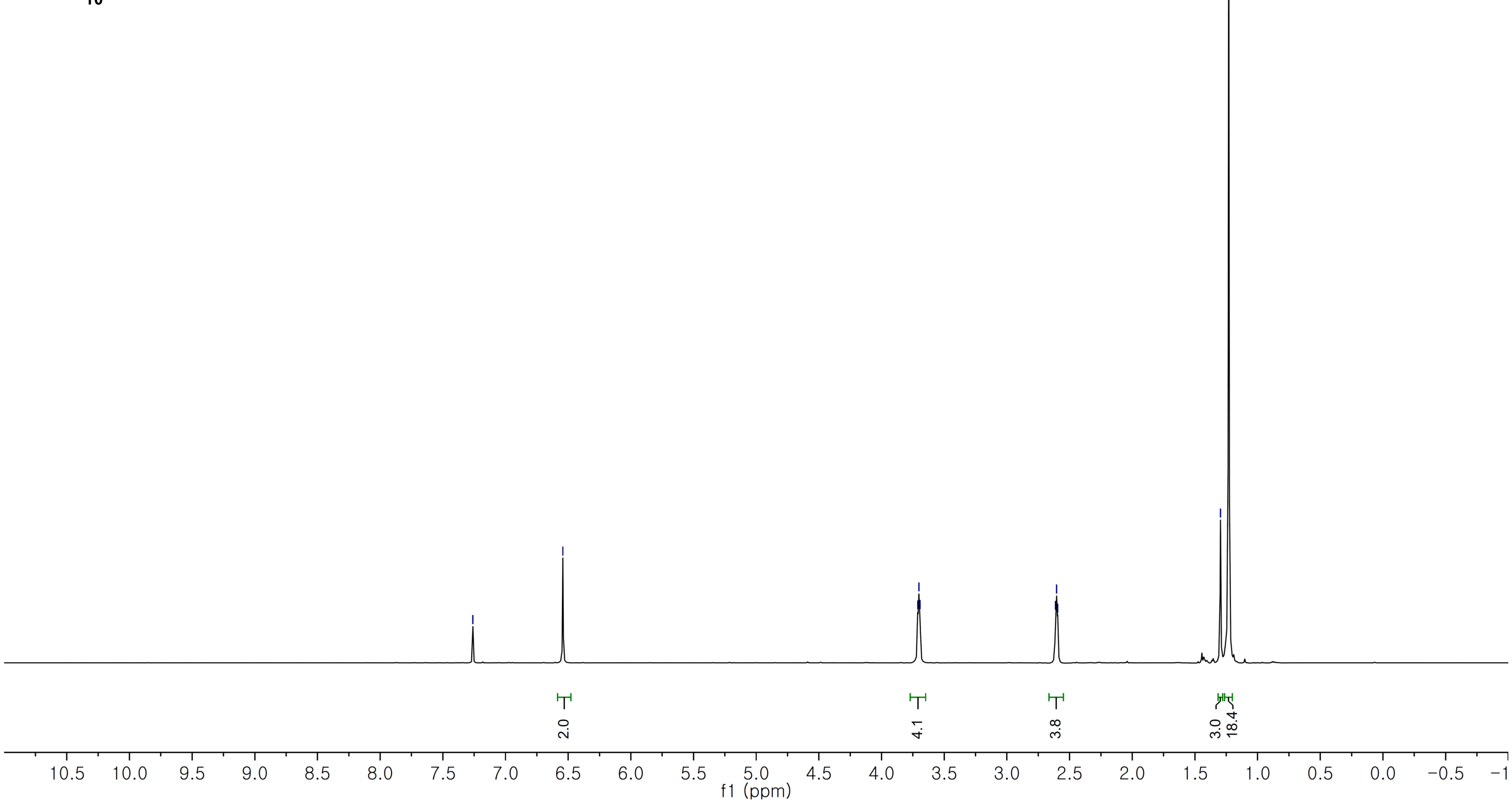
9

[1]H

500 MHz, $CDCl_3$

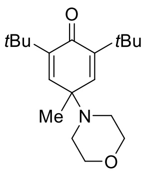


10

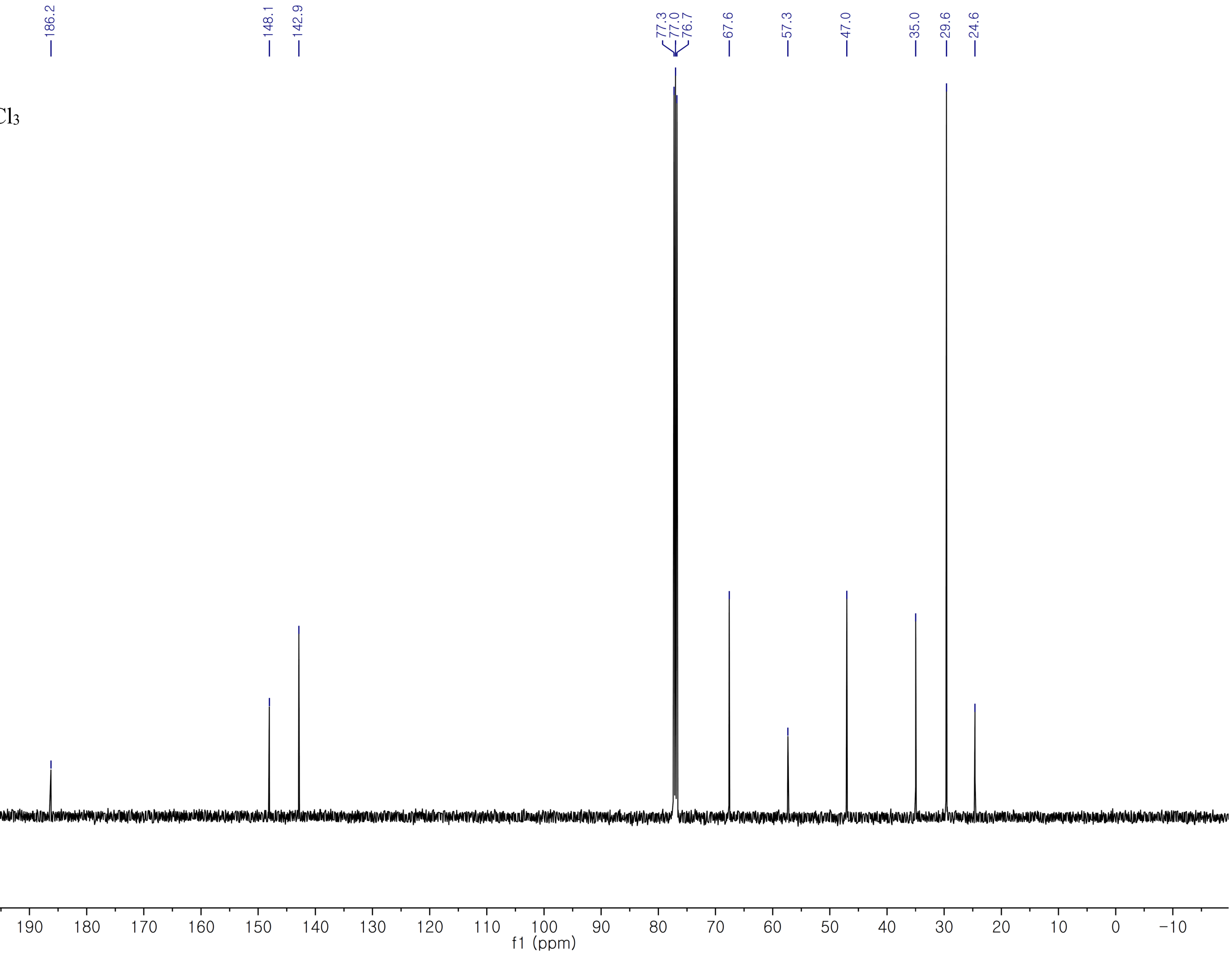


^{13}C

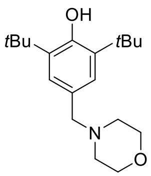
126 MHz, $CDCl_3$



10



[1]H
500 MHz, $CDCl_3$



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