

Supporting Information

Programmed Sequential Additions to Halogenated Mucononitriles

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Supporting Information

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I. General Information

Reaction setup and reagent purification: All reactions were carried out under a nitrogen atmosphere in flame-dried glassware using standard Schlenk techniques unless otherwise stated. Reactions that were extremely moisture and oxygen sensitive reactions were performed within a Vigor glove box (box atmospheric pressure ranged from 3–5 atm, moisture and oxygen ranged from 0.10–0.20 ppm and 0.01 and 0.02 ppm respectively). All reagents were purchased from commercial sources and were used as received unless otherwise noted. *N*-methyl-1-(naphthalen-2-yl)methanamine HCl,¹ diethyl 2-cinnamylmalonate,² diethyl 2-(furan-2-ylmethyl)malonate,³ and diethyl 2-((1*H*-indol-3-yl)methyl)malonate⁴ were prepared according to previously reported procedures and spectral data matched those reported.

Solvents: Toluene, tetrahydrofuran, dichloromethane, diethyl ether, acetonitrile, and triethylamine were purified using a GlassContour solvent purification system purchased from Pure Process Technologies. Other solvents (hexanes and pentanes) were purified by refluxing over activated 3 Å molecular sieves (beads) for 1 hour and stored as such under a balloon filled with Ar. Anhydrous 1,2-dichloroethane and 1,4-dioxane were purchased from Acros and Dri-Solv, respectively, and were used without purification.

Chromatography: Analytical thin layer chromatography (TLC) was performed on SiliaPlate glass backed silica gel plates (250 mm thickness, 60 Å, F-254 indicator) purchased from Silicycle and visualized using ultraviolet light (254 and 200 nm) and stained with KMNO₄, *p*-anisaldehyde, cerium molybdate, ceric ammonium nitrate, vanillin, or ninhydrin following reported procedures.⁵ Flash column chromatography was performed with SiliaFlash silica gel 60 Å, 230–400 mesh (40–63 mm) purchased from Silicycle according to the literature procedure.

Melting points: All melting points were measured on powdered solids using a Mel-Temp II capillary melting point device and are uncorrected unless otherwise stated.

Nuclear Magnetic Resonance Characterization: ¹H NMR and ¹³C NMR spectra were recorded on a Bruker AV Neo-400 (equipped with a Prodigy cryoprobe), Bruker AV III NanoBay-400, Bruker AV III-500, Bruker AV Neo-600 (equipped with a CryoQNP probe) or Bruker AV III-600 MHz spectrometer (100, 125, or 150 MHz for ¹³C NMR). All spectra were recorded in deuterated chloroform (CDCl₃) with residual chloroform (δ = 7.26 ppm for ¹H NMR and 77.16 for ¹³C NMR) as the internal standard and are reported in parts per million (ppm). Abbreviations for the signal couplings are as follows: s, singlet; d, doublet; t, triplet; q, quartet; quin, quintet; sex, sextet; sept, septet; and m, multiplet. Coupling constants were taken from the spectra directly and are uncorrected. Structural and stereochemical assignments were also made based on analysis of ¹³C APT, 2-D ¹H-¹H COSY and ¹H-¹H NOESY, ¹H-¹³C HSQC and ¹H-¹³C HMBC experiments. All diastereomeric ratios were determined by ¹H NMR analysis of an aliquot from the crude reaction mixture. Yields refer to isolated yields of compounds estimated to be ≥ 95% pure as determined by ¹H NMR analysis unless otherwise noted.

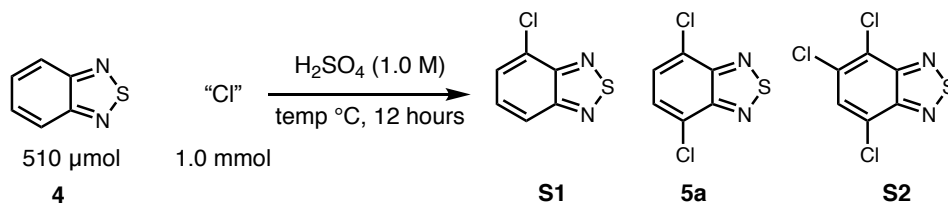
Infrared Spectroscopy Characterization: Infrared (IR) spectra were collected on a Thermo Scientific Nicolet iS 5 FT-IR. Compounds were analyzed as thin films or as solids on the diamond surface. Spectra are reported in frequency of absorption in cm⁻¹. Only selected references are reported.

Mass spectrometry: High-resolution mass spectra (HRMS) determinations were performed by the mass spectral facility at the University of North Carolina at Chapel Hill. Samples were analyzed with a Q Exactive HF-X (ThermoFisher, Bremen, Germany) mass spectrometer for APCI and ESI, on a ThermoFisher GC Exactive with an Electron Ionization (EI) source using an Orbitrap detector.

II. General chlorination procedure – General Procedure A

A flame-dried 4 mL vial equipped with a magnetic Teflon®-coated stir bar was charged with 2,1,3-benzothiadiazole (**4**) (68.0 mg, 511 μ mol, 1.00 equiv), H₂SO₄ (500 μ L, 510 μ mol, 1.00 equiv), chlorinating reagent (1.00 mmol, 2.00 equiv) portionwise over 1–2 minutes. The mixture was stirred opened to air for 12 hours at 45 °C and the solid dissolved upon heating. The solution was cooled to 0 °C, and quenched with cold aqueous saturated sodium bicarbonate (ca. 12 mL, until bubbling subsided). The mixture was extracted with ethyl acetate (3 x 2 mL), dried over Na₂SO₄, filtered and concentrated to give off-white/yellow solid, which was analyzed by ¹H NMR.

Optimization of Chlorination of Benzothiadiazole

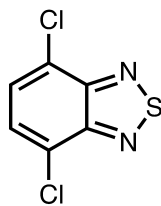


entry	"Cl"	°C	result
1	DCDMH	45 °C	44% 5a , 6% S2
2	NCS	45 °C	19% 4 , 17% S1
3	Palau'Chlor	45 °C	32% 4
4	Chlorox® Bleach	45 °C	31% 4 , 17% S1
5	DCDMH	75 °C	25% 5a , 38% S2
6	DCDMH	25 °C	25% 4 , 25% S1
7	DCDMH + 2 mL 1,2-DCE	45 °C	31% 5a , 4% S2

^a ¹H NMR yields determined using mesitylene as an internal standard

^b DCDMH = 1,3-dichloro-5,5-dimethylhydantoin

III. Preparation and Characterization of 3a and 3b



4,7-Dichlorobenzo[c][1,2,5]thiadiazole (5a). A flame-dried 500 mL Erlenmeyer flask equipped with a magnetic Teflon®-coated stir bar was cooled then charged with benzothiadiazole (**4**) (13.6 g, 100 mmol, 1.00 equiv), H₂SO₄ (200 mL, 500 mM), and 1,3-dichloro-5,5-dimethylhydantoin (39.4 g, 200 mmol, 2.00 equiv) portionwise over 10 minutes. The mixture was stirred opened to air for 12 hours at 45 °C and the solid dissolved upon heating. The solution was cooled to room temperature then poured over roughly 500 g of crushed ice in a 1 L Erlenmeyer flask. Upon warming to 23 °C, the solids were collected in a Büchner funnel using coarse porosity filter paper, and the filter cake was washed with 200 mL of water. Once dry, the solid residue was recrystallized from hot ethanol to afford the title compound as colorless needles (9.68 g, 47%, 47.2 mmol).

R_f (91:9 hexanes:ethyl acetate) = 0.79.

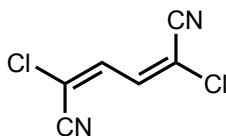
m.p. 178–180 °C (ethanol).

¹H NMR (600 MHz, CDCl₃) δ 7.58 (s, 2H).

¹³C NMR (151 MHz, CDCl₃) δ 152.5, 128.6, 125.0.

IR *v*_{max} (film) 3085, 3051, 2951, 2922, 1717, 1510 cm⁻¹.

HRMS (APCI) *m/z*: [M+H]⁺ Calcd for C₆H₃Cl₂N₂S 204.9394; Found 204.9391.



(2E,4E)-2,5-Dichlorohexa-2,4-dienedinitrile (3a). A flame-dried 1 L round bottomed flask equipped with a magnetic Teflon®-coated stir bar was cooled under a stream of nitrogen and charged with 4,7-dichlorobenzo[c][1,2,5]thiadiazole (**5a**) (10.3 g, 50.0 mmol, 1.00 equiv) and ethanol (250 mL, 0.20 M), and the flask was placed in an ice bath. To the stirred solution was added sodium borohydride (14.2 g, 375 mmol, 7.50 equiv) portionwise over the course of 1 hour, after which the flask was allowed to warm to room temperature. After 18 hours the solvent was removed in vacuo and crude residue was taken up in ethyl acetate (300 mL) then saturated aqueous sodium bicarbonate solution (200 mL) was carefully added. The mixture was placed in a separatory funnel and the aqueous layer was separated then extracted with ethyl acetate (2 x 100 mL), then the combined organic extracts were washed with brine and dried over

Na₂SO₄ then filtered. The solvent was removed in vacuo and the crude residue was dried under high-vacuum overnight and carried forward without further purification. To an oven-dried 500 mL round bottomed flask was added lead (IV) tetraacetate (44.3 g, 100 mmol, 2.00 equiv), 100 mL of anhydrous toluene, and a magnetic Teflon®-coated stir bar. The flask was heated to 60 °C in an oil bath with stirring, then equipped with a slow-addition funnel. To the addition funnel was added the crude *ortho*-phenylenediamine intermediate in 150 mL of anhydrous toluene, and the solution was added dropwise over the course of 15 minutes. The reaction mixture was heated to 60 °C for 2 hours, then was cooled to room temperature and filtered over Celite® and rinsed with dichloromethane. To the mixture was added saturated aqueous sodium bicarbonate solution (200 mL), and the material was extracted with dichloromethane (2 x 100 mL) in a separatory funnel, then the combined organic layers were washed with brine, dried over Na₂SO₄, and filtered. The solvent was removed in vacuo and the crude residue was recrystallized from hot toluene to afford the title compound as a pale yellow crystalline solid (2.75 g, 32%, 16.0 mmol).

m.p. 161–163 °C.

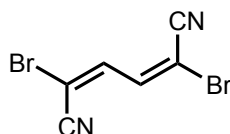
R_f (90:10 hexanes:ethyl acetate) = 0.57.

¹H NMR (600 MHz, CDCl₃) δ 7.27 (s, 2H).

¹³C NMR (151 MHz, CDCl₃) δ 137.7, 112.5, 111.1.

IR (ATR) 3039, 2225, 1522 cm⁻¹.

HRMS (APCI) m/z: [M]⁺ Calcd for C₆H₂Cl₂N₂ 171.9595; Found 171.9591.



(2E,4E)-2,5-Dibromohexa-2,4-dienedinitrile (3b). A flame-dried 1 L round bottomed flask equipped with a magnetic Teflon®-coated stir bar was cooled under a stream of nitrogen and charged with 4,7-dibromobenzo[c][1,2,5]thiadiazole (**5b**) (14.7 g, 50.0 mmol, 1.00 equiv) and ethanol (250 mL, 0.20 M), and the flask was placed in an ice bath. To the stirred solution was added sodium borohydride (14.2 g, 375 mmol, 7.50 equiv) portionwise over the course of 1 hour, after which the flask was allowed to warm to room temperature. After 18 hours the solvent was removed in vacuo and the crude residue was taken up in ethyl acetate (300 mL) then saturated aqueous sodium bicarbonate solution (200 mL) was carefully added. The mixture was placed in a separatory funnel and the aqueous layer was separated then extracted with ethyl acetate (2 x 100 mL), then the combined organic extracts were washed with brine and dried over Na₂SO₄ then filtered. The solvent was removed in vacuo and the crude residue was dried under high-vacuum

overnight and carried forward without further purification. To an oven-dried 500 mL round bottomed flask was added lead (IV) tetraacetate (44.3 g, 100 mmol, 2.00 equiv), 100 mL of anhydrous toluene, and a magnetic Teflon®-coated stir bar. The flask was heated to 60 °C in an oil bath with stirring, then equipped with a slow-addition funnel. To the addition funnel was added the crude *ortho*-phenylenediamine intermediate in 150 mL of anhydrous toluene, and the solution was added dropwise over the course of 15 minutes. The reaction mixture was heated to 60 °C for 2 hours, then was cooled to room temperature and filtered over Celite® and rinsed with dichloromethane. To the mixture was added saturated aqueous sodium bicarbonate solution (200 mL), and the material was extracted with dichloromethane (2 x 100 mL) in a separatory funnel, then the combined organic layers were washed with brine, dried over Na₂SO₄, and filtered. The solvent was removed in vacuo and the crude residue was recrystallized from hot toluene to afford the title compound as a pale yellow crystalline solid (7.22 g, 55%, 27.5 mmol).

m.p. 179–181 °C.

R_f (90:10 hexanes:ethyl acetate) = 0.54.

¹H NMR (600 MHz, CDCl₃) δ 7.44 (s, 2H).

¹³C NMR (151 MHz, CDCl₃) δ 142.3, 113.5, 96.5.

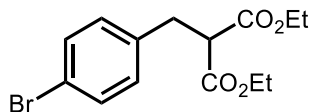
IR (ATR) 3041, 2216, 1543 cm⁻¹.

HRMS (APCI) m/z: [M]⁺ Calcd for C₆H₂Br₂N₂ 259.8585; Found 259.8581.

IV. Preparation and Characterization of Substrates

General procedure for malonate synthesis – General Procedure B.

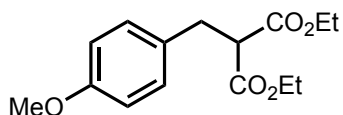
A flame dried 50 mL 1 neck round bottomed flask equipped with a magnetic Teflon®-coated stir bar and septum and charged with the appropriate malonate (1.00 equiv), and ethanol (20 mL, 0.50 M). The appropriate aldehyde (1.00 equiv), acetic acid (0.100 equiv), and piperidine (0.100 equiv) were added and the flask was equipped with a condenser, placed in an oil bath, and the solution was stirred 100 °C for 14 hours. The solution was cooled to room temperature and concentrated *in vacuo* to yield colorless oil. The crude oil was dissolved in ethanol (0.68 M). The solution was cooled to 0 °C and sodium borohydride (1.10 equiv) was added. The mixture was stirred for 1 hour at 25 °C until TLC suggested full conversion. The mixture was quenched with water (5 mL) and extracted with ethyl acetate (3 x 10 mL). The organic layer was dried with Na₂SO₄, and concentrated *in vacuo*, to yield a colorless oil. The crude material was purified *via* column chromatography on silica gel.



Diethyl 2-(4-bromobenzyl)malonate (S3). The title compound was prepared using 4-(bromo)benzaldehyde (925 mg, 5.00 mmol, 1.00 equiv) following General procedure B and the crude residue was purified by column chromatography on silica gel using 91:9 hexanes:ethyl acetate as the eluent affording the title compound as a colorless oil (1.23 g, 75%, 3.75 mmol).

R_f (91:9 hexanes:ethyl acetate) = 0.39.

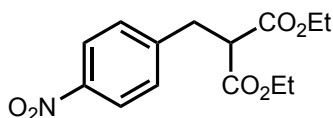
$^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.42 (d, J = 8.4 Hz, 2H), 7.10 (d, J = 8.4 Hz, 2H), 4.18 (q, J = 7.1 Hz, 4H), 3.62 (t, J = 7.8 Hz, 1H), 3.19 (d, J = 7.8 Hz, 2H), 1.24 (t, J = 7.1 Hz, 6H). Spectrum matches previously published data.⁶



Diethyl 2-(4-methoxybenzyl)malonate (S4). The title compound was prepared using 4-(methoxy)benzaldehyde (608 μL , ρ = 1.12 g/mL, 5.00 mmol, 1.00 equiv) following General procedure B and the crude residue was purified by column chromatography on silica gel using 89:11 hexanes:ethyl acetate as the eluent affording the title compound as a colorless oil (785 mg, 56%, 2.81 mmol).

R_f (91:9 hexanes:ethyl acetate) = 0.32.

$^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.12 (d, J = 8.7 Hz, 2H), 6.80 (d, J = 8.7, 2H), 4.15 (q, J = 7.1 Hz, 4H), 3.77 (s, 3H), 3.60 (t, J = 7.8 Hz, 1H), 3.15 (d, J = 7.8 Hz, 2H), 1.21 (t, J = 7.1 Hz, 6H). Spectrum matches previously published data.⁷

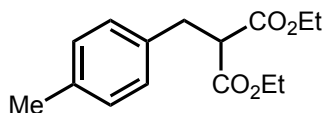


Diethyl 2-(4-nitrobenzyl)malonate (S5). The title compound was prepared using 4-(nitro)benzaldehyde (756 mg, 5.00 mmol, 1.00 equiv) following General procedure B and the crude residue was purified by column chromatography on silica gel using 83:17 hexanes:ethyl acetate as the eluent affording the title compound as a colorless solid (957 mg, 65%, 3.25 mmol).

R_f (91:9 hexanes:ethyl acetate) = 0.22.

mp. 51–53 $^{\circ}\text{C}$ (CDCl_3).

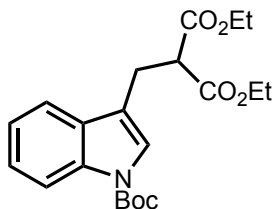
¹H NMR (400 MHz, CDCl₃) δ 8.18 (d, *J* = 8.8 Hz, 2H), 7.40 (d, *J* = 8.8 Hz, 2H), 4.20 (q, *J* = 7.1 Hz, 4H), 3.68 (t, *J* = 7.8 Hz, 1H), 3.34 (d, *J* = 7.8 Hz, 2H), 1.25 (t, *J* = 7.1 Hz, 6H). Spectrum matches previously published data.⁶



Diethyl 2-(4-nitrobenzyl)malonate (S6). The title compound was prepared using 4-(methyl)benzaldehyde (590 μL, ρ = 1.02 g/mL, 5.00 mmol, 1.00 equiv) following General procedure B and the crude residue was purified by column chromatography on silica gel using 91:9 hexanes:ethyl acetate as the eluent affording the title compound as a colorless oil (1.05 g, 80%, 4.02 mmol).

R_f (91:9 hexanes:ethyl acetate) = 0.43.

¹H NMR (400 MHz, CDCl₃) δ 7.11 (s, 4H), 4.18 (q, *J* = 7.1 Hz, 4H), 3.64 (t, *J* = 7.8 Hz, 1H), 3.20 (d, *J* = 7.8 Hz, 2H), 2.33 (s, 3H), 1.24 (t, *J* = 7.1 Hz, 6H). Spectrum matches previously published data.⁷



Diethyl 2-((1-(*tert*-butoxycarbonyl)-1*H*-indol-3-yl)methyl)malonate (S7). To a 250 mL round-bottomed flask was added diethyl 2-((1*H*-indol-3-yl)methyl)malonate (5.78 g, 20.0 mmol) in 100 mL of dichloromethane at 25 °C. To the stirred reaction mixture was added di-*tert*-butyl pyrocarbonate (5.24 g, 24.0 mmol), then 4-(dimethylamino)pyridine (244 mg, 2.00 mmol) and the solution was stirred at room temperature for 18 h, after which the solvent was concentrated *in vacuo* and the crude residue was purified *via* column chromatography on silica gel using 98:2 to 95:5 hexanes:ethyl acetate as the eluent to afford the title compound as a colorless oil (7.42 g, 95%, 19.1 mmol).

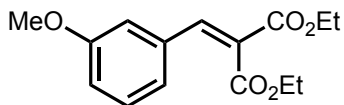
R_f (95:5 hexanes:ethyl acetate) = 0.13.

¹H NMR (600 MHz, CDCl₃) δ 8.11 (s, 1H), 7.54 (d, *J* = 7.8 Hz, 1H), 7.47–7.36 (m, 1H), 7.31 (m, 1H), 7.25 (m, 1H), 4.18 (q, *J* = 7.2 Hz, 4H), 3.75 (t, *J* = 7.7 Hz, 1H), 3.31 (d, *J* = 7.7 Hz, 2H), 1.65 (s, 9H), 1.23 (t, *J* = 7.2 Hz, 6H).

¹³C NMR (151 MHz, CDCl₃) δ 169.1, 124.6, 123.7, 122.6, 118.9, 117.0, 115.4, 83.7, 61.7, 52.2, 28.3, 24.3, 14.2.

IR (ATR) 2979, 2953, 1727, 1452, 1367, 1239, 1153, 1048, 857, 746 cm⁻¹.

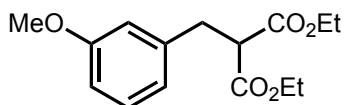
HRMS (APCI) m/z : $[M+H]^+$ Calcd for $C_{17}H_{20}NO_6$ 334.1291; Found 334.1284 (note: Calcd and observed masses are reflective of the carbamic acid without the *tert*-butyl group).



Diethyl 2-(3-methoxybenzylidene)malonate (S8). A flame dried 50 mL 1 neck round bottomed flask equipped with a magnetic Teflon®-coated stir bar and septum and charged with diethyl malonate (1.5 mL, ρ = 1.05 g/mL, 9.8 mmol, 1.0 equiv), and ethanol (20 mL, 0.5 M). *meta*-Anisaldehyde (1.2 mL, ρ = 1.117 g/mL, 9.8 mmol, 1.0 equiv), acetic acid (60 μ L, ρ = 1.05 g/mL, 1.0 mmol, 0.10 equiv), and piperidine (100 μ L, ρ = 0.862 g/mL, 1.0 mmol, 0.10 equiv) were added. The flask was equipped with a reflux condenser and the solution was stirred 100 °C for 14 hours. The solution was then cooled to room temperature and concentrated *in vacuo* to yield colorless oil. The crude material was purified *via* column chromatography on silica gel using 95:5 hexanes:ethyl acetate as the eluent to afford the title compound as a colorless oil (1.9 g, 68%, 6.8 mmol).

R_f (95:5 hexanes:ethyl acetate) = 0.12.

1H NMR (400 MHz, $CDCl_3$) δ 7.70 (s, 1H), 7.33–7.23 (m, 2H), 7.04 (d, J = 7.7 Hz, 1H), 6.99 (t, J = 2.1 Hz, 1H), 6.94 (dd, J = 8.2, 2.6 Hz, 1H), 4.36–4.28 (m, 4H), 3.80 (s, 3H), 1.35–1.28 (m, 6H). Spectra matches previously published data.⁸



Diethyl 2-(3-methoxybenzyl)malonate (S9). A 20 mL vial equipped with a septum and magnetic Teflon®-coated stir bar charged with diethyl 2-(3-methoxybenzylidene)malonate (**S8**) (1.9 g, 6.8 mmol, 1.0 equiv) and ethanol (10 mL, 0.68 M). The solution was cooled to 0 °C and sodium borohydride (0.28 g, 7.5 mmol, 1.1 equiv) was added. The solution was stirred for 1 hour at 25 °C until TLC suggested full conversion. The mixture was quenched with water (5 mL) and extracted with ethyl acetate (3 x 10 mL). The organic layer was dried with Na_2SO_4 , and concentrated *in vacuo*, to yield a colorless oil. The crude material was purified *via* column chromatography on silica gel using 90:10 hexanes:ethyl acetate as the eluent. This procedure afforded the title compound as a colorless oil (1.1 g, 58%, 3.9 mmol).

R_f (90:10 hexanes:ethyl acetate) = 0.28.

¹H NMR (400 MHz, CDCl₃) δ 7.19 (t, *J* = 8.2 Hz, 1H), 6.83–6.71 (m, 3H), 4.17 (q, *J* = 7.2 Hz, 4H), 3.78 (s, 3H), 3.64 (dd, *J* = 8.5, 7.1 Hz, 1H), 3.19 (d, *J* = 7.9 Hz, 2H), 1.22 (t, *J* = 7.1 Hz, 6H). Spectra matches previously published data.⁷

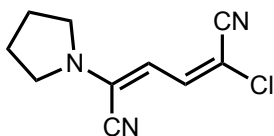
V. Preparation and Characterization of Amine Addition Products

1) General procedure for the addition of amine nucleophiles to bis(2-haloacrylonitrile) – General Procedure C.

To a 4 mL dram vial equipped with magnetic Teflon®-coated stir bar was added bis(2-chloroacrylonitrile) (**3a**) (34.6 mg, 200 μmol, 1.00 equiv) or bis(2-bromoacrylonitrile) (**3b**) (52.4 mg, 0.2 mmol, 1.00 equiv). The vials were capped then evacuated and backfilled with N₂, then THF (0.6 mL, 0.33 M) was added. The stirred homogeneous solution was charged with an amine (700 μmol, 3.50 equiv), and the reaction was stirred at 23 °C for 1 hour. The solvent was then removed *in vacuo* and the products were isolated by silica gel flash column chromatography.

2) General procedure for the addition of amine hydrochloride nucleophiles to bis(2-haloacrylonitrile) – General Procedure D.

To a 4 mL dram vial equipped with magnetic Teflon®-coated stir bar was added bis(2-chloroacrylonitrile) (**3a**) (34.6 mg, 200 μmol, 1.00 equiv) or bis(2-bromoacrylonitrile) (**3b**) (52.4 mg, 0.2 mmol, 1.00 equiv). To the vial was then added cesium carbonate (326 mg, 1.00 mmol, 5.00 equiv) and amine hydrochloride salt (0.7 mmol, 3.50 equiv). The vials were capped then evacuated and placed under N₂, then THF (2.00 mL, 0.1 M) was added, and the reaction was stirred at 23 °C for 18–24 hours. Deionized water (2.00 mL) was added, and the mixture was extracted with ethyl acetate (3 x 1.0 mL) then the combined organic layers were washed with brine. The combined organic layers were dried over Na₂SO₄ then the solvent was removed *in vacuo* and the products were isolated by silica gel flash column chromatography.



(2E,4E)-2-Chloro-5-(pyrrolidin-1-yl)hexa-2,4-dienedinitrile (7a): The title compound was prepared from bis(2-chloroacrylonitrile) (**3a**) (172 mg, 1.00 mmol, 1.00 equiv) and pyrrolidine (57.5 μL, ρ = 0.866 g/mL, 700 μmol, 3.50 equiv) following General Procedure C, on 1.00 mmol scale. The crude material was purified *via* column chromatography on silica gel using 91:9 hexanes:ethyl acetate as the eluent to afford the title compound as a yellow solid (191 mg, 92%, 184 μmol).

R_f (83:17 hexanes:ethyl acetate) = 0.39.

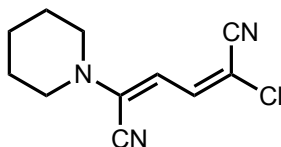
m.p. 113–115°C (CDCl₃).

¹H NMR (600 MHz, CDCl₃) δ 7.25 (d, *J* = 12.2 Hz, 1H), 5.59 (d, *J* = 12.2 Hz, 1H), 3.46–3.40 (m, 4H), 2.06–2.01 (m, 4H).

¹³C NMR (151 MHz, CDCl₃) δ 142.5, 126.5, 115.5, 112.8, 103.7, 94.1, 49.9, 25.3.

IR (ATR) 3046, 2977, 2865, 2235, 2197, 1579, 1558 cm⁻¹.

HRMS (APCI) *m/z*: [M]⁺ Calcd for C₁₀H₁₀ClN₃ 207.0563; Found 207.0558.



(2*E*,4*E*)-2-Chloro-5-(piperidin-1-yl)hexa-2,4-dienedinitrile (8a): The title compound was prepared from bis(2-chloroacrylonitrile) (**3a**) and piperidine (69.1 μL, ρ = 0.862 g/mL, 700 μmol, 3.50 equiv) following General Procedure C. The crude residue was purified *via* column chromatography on silica gel using 91:9 hexanes:ethyl acetate as the eluent to afford the title compound as a yellow solid (42.2 mg, 95%, 190 μmol).

R_f (83:17 hexanes:ethyl acetate) = 0.46.

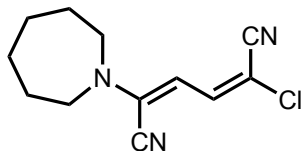
m.p. 69–71 °C (CDCl₃).

¹H NMR (600 MHz, CDCl₃) δ 7.27 (d, *J* = 12.1 Hz, 1H), 5.88 (d, *J* = 12.1 Hz, 1H), 3.37–3.33 (m, 4H), 1.70–1.64 (m, 6H).

¹³C NMR (151 MHz, CDCl₃) δ 142.8, 129.7, 115.3, 112.7, 105.7, 96.1, 49.7, 25.2, 23.8.

IR (ATR) 2941, 2857, 2226, 2204, 1574, 1553 cm⁻¹.

HRMS (APCI) *m/z*: Calcd for C₁₁H₁₂ClN₃ [M]⁺: 221.0720; Found 221.0716.



(2*E*,4*E*)-2-(Azepan-1-yl)-5-chlorohexa-2,4-dienedinitrile (9a): The title compound was prepared from bis(2-chloroacrylonitrile) (**3a**) and azepane (78.9 μL, ρ = 0.880 g/mL, 700 μmol, 3.50 equiv) following General Procedure C. The crude residue was purified *via* column chromatography on silica gel using 91:9

hexanes:ethyl acetate as the eluent to afford the title compound as a yellow oil that solidified on standing (43.5 mg, 92%, 184 μ mol).

R_f (83:17 hexanes:ethyl acetate) = 0.43.

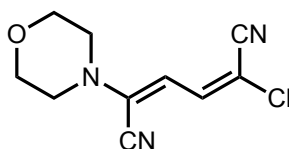
m.p. 55–57 °C (CDCl₃).

¹H NMR (600 MHz, CDCl₃) δ 7.25 (d, J = 12.1 Hz, 1H), 5.73 (d, J = 12.1 Hz, 1H), 3.50–3.46 (m, 4H), 1.83–1.77 (m, 4H), 1.62–1.58 (m, 4H).

¹³C NMR (151 MHz, CDCl₃) δ 143.1, 129.1, 115.6, 112.6, 103.1, 94.2, 51.8, 27.8, 27.1.

IR (ATR) 2928, 2856, 2229, 2202, 1572, 1551 cm⁻¹.

HRMS (APCI) m/z : [M]⁺ Calcd for C₁₂H₁₄ClN₃ 235.0876; Found 235.0871.



(2E,4E)-2-Chloro-5-morpholinohexa-2,4-dienedinitrile (10a): The title compound was prepared from bis(2-chloroacrylonitrile) (**3a**) and morpholine (60.4 μ L, ρ = 1.01 g/mL, 700 μ mol, 3.50 equiv) following General Procedure C. The crude residue was purified *via* column chromatography on silica gel using 83:17 hexanes:ethyl acetate as the eluent to afford the title compound as a yellow solid (40.1 mg, 90%, 180 μ mol).

R_f (83:17 hexanes:ethyl acetate) = 0.25.

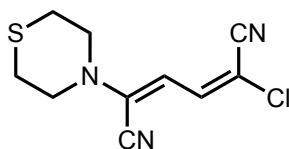
m.p. 147–149 °C (CDCl₃).

¹H NMR (600 MHz, CDCl₃) δ 7.27 (d, J = 12.1 Hz, 1H), 5.94 (d, J = 12.1 Hz, 1H), 3.79 (t, J = 4.8 Hz, 4H), 3.31 (t, J = 4.8 Hz, 4H).

¹³C NMR (151 MHz, CDCl₃) δ 141.9, 129.8, 114.7, 112.3, 107.4, 98.6, 65.8, 48.3.

IR (ATR) 2984, 2904, 2883, 2226, 2211, 1591, 1553 cm⁻¹.

HRMS (APCI) m/z : [M]⁺ Calcd for C₁₀H₁₀ClN₃O 223.0512; Found 223.0509.



(2E,4E)-2-Chloro-5-(4-methylpiperazin-1-yl)hexa-2,4-dienedinitrile (11a): The title compound was prepared from bis(2-chloroacrylonitrile) (**3a**) and thiomorpholine (70.1 μ L, ρ = 1.03 g/mL, 700 μ mol, 3.50

equiv) following General Procedure C. The crude residue was purified *via* column chromatography on silica gel using 83:17 hexanes:ethyl acetate as the eluent to afford the title compound as a yellow oil that solidified on standing (42.7 mg, 90% 180 μ mol).

R_f (83:17 hexanes:ethyl acetate) = 0.45.

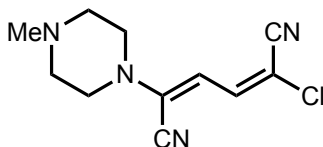
m.p. 108–110 °C (CDCl₃).

¹H NMR (600 MHz, CDCl₃) δ 7.27 (d, *J* = 12.0 Hz, 1H), 5.91 (d, *J* = 12.0 Hz, 1H), 3.74–3.70 (m, 4H), 2.72–2.68 (m, 4H).

¹³C NMR (151 MHz, CDCl₃) δ 142.2, 128.4, 114.9, 112.4, 106.9, 97.6, 51.3, 26.4.

IR (ATR) 3071, 2920, 2852, 2229, 2205, 1574, 1551 cm⁻¹.

HRMS (APCI) *m/z*: [M]⁺ Calcd for C₁₀H₁₀ClN₃S 239.0284; Found 239.0279.



(2E,4E)-2-Chloro-5-(4-oxopiperidin-1-yl)hexa-2,4-dienedinitrile (12a): The title compound was prepared from bis(2-chloroacrylonitrile) (**3a**) and 1-methylpiperazine (77.7 μ L, ρ = 0.903 g/mL, 700 μ mol, 3.50 equiv) following General Procedure C. The crude residue was purified *via* column chromatography on silica gel using 99:1 dichloromethane:methanol as the eluent to afford the title compound as a yellow solid (46.5 mg, 98%, 196 μ mol).

R_f (50:50 hexanes:ethyl acetate) = 0.12.

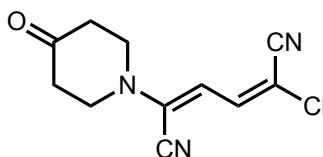
m.p. 139–141 °C (CDCl₃).

¹H NMR (600 MHz, CDCl₃) δ 7.27 (d, *J* = 12.0 Hz, 1H), 5.91 (d, *J* = 12.0 Hz, 1H), 3.39–3.33 (m, 4H), 2.55–2.46 (m, 4H), 2.34 (s, 3H).

¹³C NMR (151 MHz, CDCl₃) δ 142.3, 129.5, 114.9, 112.5, 106.8, 97.6, 53.7, 48.1, 45.9.

IR (ATR) 3056, 2934, 2805, 2222, 2210, 1745, 1582, 1552 cm⁻¹.

HRMS (APCI) *m/z*: [M+H]⁺ Calcd for C₁₁H₁₃ClN₄ 236.0829; Found 236.0823.



(2E,4E)-2-Chloro-5-(dimethylamino)hexa-2,4-dienedinitrile (13a): The title compound was prepared from bis(2-chloroacrylonitrile) (**3a**) and 4-piperidone hydrochloride (94.9 mg, 700 μ mol, 3.50 equiv) following General Procedure D. The crude residue was purified *via* column chromatography on silica gel using 75:25 hexanes:ethyl acetate as the eluent to afford the title compound as a yellow solid (30.9 mg, 66%, 132 μ mol).

R_f (75:25 hexanes:ethyl acetate) = 0.36.

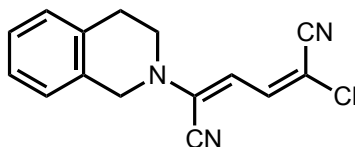
m.p. 113–115 °C (CDCl₃).

¹H NMR (600 MHz, CDCl₃) δ 7.28 (d, *J* = 12.0 Hz, 1H), 5.96 (d, *J* = 12.0 Hz, 1H), 3.73 (t, *J* = 6.3 Hz, 4H), 2.61 (t, *J* = 6.3 Hz, 4H).

¹³C NMR (151 MHz, CDCl₃) δ 204.6, 141.9, 128.1, 114.7, 107.34, 98.4, 47.0, 40.0.

IR (ATR) 2920, 2228, 2206, 1721, 1579, 1557 cm⁻¹.

HRMS (APCI) *m/z*: [M]⁺ Calcd for C₁₁H₁₀ClN₃O 235.0512; Found 235.0507.



(2E,4E)-2-chloro-5-(3,4-dihydroisoquinolin-2(1H)-yl)hexa-2,4-dienedinitrile (14a): The title compound was prepared from bis(2-chloroacrylonitrile) (**3a**) and 1,2,3,4-tetrahydroisoquinoline (88.8 μ L, ρ = 1.05 g/mL, 700 μ mol, 3.50 equiv) following General Procedure C. The crude residue was purified *via* column chromatography on silica gel using 50:50 hexanes:dichloromethane as the eluent to afford the title compound as a yellow solid (46.1 mg, 86%, 172 μ mol).

R_f (83:17 hexanes:ethyl acetate) = 0.54.

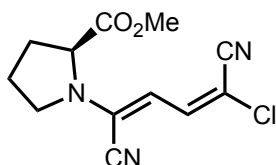
m.p. 113–115 °C (CDCl₃).

¹H NMR (600 MHz, CDCl₃) δ 7.30 (d, *J* = 12.0 Hz, 1H), 7.29–7.24 (m, 2H), 7.21–7.17 (m, 2H), 5.92 (d, *J* = 12.0 Hz, 1H), 4.47 (s, 2H), 3.72 (t, *J* = 5.9 Hz, 2H), 2.99 (t, *J* = 5.9 Hz, 2H).

¹³C NMR (151 MHz, CDCl₃) δ 142.5, 133.7, 131.0, 128.9, 128.6, 127.6, 127.1, 126.4, 115.2, 112.6, 105.1, 96.4, 49.7, 47.0, 28.8.

IR (ATR) 3056, 2919, 2853, 2227, 2207, 1576, 1553 cm⁻¹.

HRMS (APCI) *m/z*: [M]⁺ Calcd for C₁₅H₁₂ClN₃ 269.0720; Found 269.0717.



(2E,4E)-2-Chloro-5-thiomorpholinohexa-2,4-dienedinitrile (15a): The title compound was prepared from bis(2-chloroacrylonitrile) (**3a**) and *L*-proline methyl ester hydrochloride (116 mg, 700 μ mol, 3.50 equiv) following General Procedure D. The crude residue was purified *via* column chromatography on silica gel using 80:20 hexanes:ethyl acetate as the eluent to afford the title compound as a yellow oil (24.7 mg, 47%, 94 μ mol).

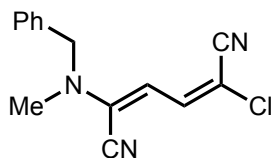
R_f (50:50 hexanes:ethyl acetate) = 0.62.

¹H NMR (600 MHz, CDCl₃) δ 7.20 (d, *J* = 12.1 Hz, 1H), 5.70 (d, *J* = 12.1 Hz, 1H), 4.43 (dd, *J* = 8.5, 2.6 Hz, 1H), 3.79 (s, 3H), 3.57–3.51 (m, 1H), 3.44–3.38 (m, 1H), 2.36–2.28 (m, 1H), 2.26–2.20 (m, 1H), 2.13–2.04 (m, 2H).

¹³C NMR (151 MHz, CDCl₃) δ 171.5, 141.9, 125.7, 114.9, 112.4, 105.7, 96.2, 62.5, 52.9, 49.5, 30.3, 23.4.

IR (ATR) 2955, 2876, 2234, 2206, 1744, 1582, 1559 cm⁻¹.

HRMS (APCI) *m/z*: [M]⁺: Calcd for C₁₂H₁₂ClN₃O₂ 265.0618; Found 265.0617.



(2E,4E)-2-(Benzyl(methyl)amino)-5-chlorohexa-2,4-dienedinitrile (16a): The title compound was prepared from bis(2-chloroacrylonitrile) (**3a**) and *N*-methylbenzylamine (90.3 μ L, ρ = 0.939 g/mL, 700 μ mol, 3.50 equiv) following General Procedure C. The crude residue was purified *via* column chromatography on silica gel using 91:9 hexanes:ethyl acetate as the eluent to afford of the title compound as a yellow/orange oil (44.3 mg, 86%, 172 μ mol).

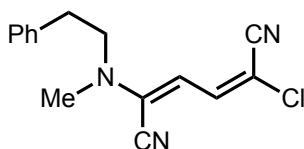
R_f (83:17 hexanes:ethyl acetate) = 0.46.

¹H NMR (600 MHz, CDCl₃) δ 7.44–7.32 (m, 3H), 7.28 (d, *J* = 12.1 Hz, 1H), 7.25–7.17 (m, 2H), 5.80 (d, *J* = 12.1 Hz, 1H), 4.60 (s, 2H), 2.92 (s, 3H).

¹³C NMR (151 MHz, CDCl₃) δ 142.6, 135.2, 129.3 (two peaks), 128.6, 127.5, 115.1, 112.8, 105.3, 96.1, 58.2, 37.9.

IR (ATR) 3065, 3030, 2928, 2230, 2205, 1577, 1558 cm⁻¹.

HRMS (APCI) m/z : $[M]^+$ Calcd for $C_{14}H_{12}ClN_3$ 257.0720; Found 257.0718.



(2E,4E)-2-Chloro-5-(methyl(phenethyl)amino)hexa-2,4-dienedinitrile (17a): The title compound was prepared from bis(2-chloroacrylonitrile) (**3a**) and *N*-methylphenethylamine (102 μ L, ρ = 0.930 g/mL, 700 μ mol, 3.50 equiv) following General Procedure C. The crude residue was purified *via* column chromatography on silica gel using 91:9 hexanes:ethyl acetate as the eluent to afford of the title compound as a yellow solid (51.3 mg, 94%, 188 μ mol).

R_f (83:17 hexanes:ethyl acetate) = 0.38.

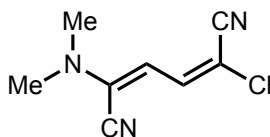
m.p. 77–79 °C (CDCl₃).

¹H NMR (600 MHz, CDCl₃) δ 7.35–7.31 (m, 2H), 7.29–7.25 (m, 1H), 7.20 (d, J = 12.1 Hz, 1H), 7.19–7.16 (m, 2H), 5.66 (d, J = 12.1 Hz, 1H), 3.67 (t, J = 7.2 Hz, 2H), 2.89 (t, J = 7.2 Hz, 2H), 2.89 (s, 3H).

¹³C NMR (151 MHz, CDCl₃) δ 142.6, 137.3, 129.1, 129.0, 128.9, 127.3, 115.3, 112.4, 104.5, 95.5, 56.7, 38.6, 34.9.

IR (ATR) 3064, 3027, 2937, 2230, 2203, 1577, 1558 cm⁻¹.

HRMS (APCI) m/z : $[M]^+$ Calcd for $C_{15}H_{14}ClN_3$ 271.0876; Found 271.0875.



((1E,3E)-Methyl-4-chloro-1,4-dicyanobuta-1,3-dien-1-yl)-L-prolinate (18a): The title compound was prepared from bis(2-chloroacrylonitrile) (**3a**) and dimethylamine hydrochloride (57.1 mg, 700 μ mol, 3.50 equiv) following General Procedure D. The crude residue was purified *via* column chromatography on silica gel using 83:17 hexanes:ethyl acetate as the eluent to afford the title compound as a yellow solid (31.9 mg, 88%, 176 μ mol).

R_f (83:17 hexanes:ethyl acetate) = 0.23.

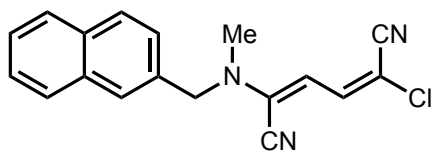
m.p. 99–101 °C (CDCl₃).

¹H NMR (600 MHz, CDCl₃) 7.22 (d, J = 12.1 Hz, 1H), 5.70 (d, J = 12.1 Hz, 1H), 3.06 (s, 6H).

¹³C NMR (151 MHz, CDCl₃) δ 142.6 129.7, 115.3, 112.5, 104.6, 95.4, 40.9.

IR (ATR) 2923, 2231, 2207, 1590, 1565 cm^{-1} .

HRMS (APCI) m/z : $[M]^+$ Calcd for $\text{C}_8\text{H}_8\text{ClN}_3$ 181.0407; Found 181.0401.



(2E,4E)-2-Chloro-5-(methyl(naphthalen-2-ylmethyl)amino)hexa-2,4-dienedinitrile (19a): The title compound was prepared from bis(2-chloroacrylonitrile) (**3a**) and *N*-methyl-1-(naphthalen-2-yl)methanamine (145 mg, 700 μmol , 3.50 equiv) following General Procedure D. The crude residue was purified *via* column chromatography on silica gel using 91:9 hexanes:ethyl acetate as the eluent to afford the title compound as a yellow/orange crystalline solid (57.5 mg, 93%, 186 μmol).

R_f (83:17 hexanes:ethyl acetate) = 0.40.

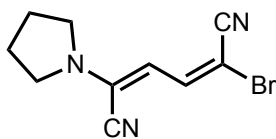
m.p. 128–130 $^{\circ}\text{C}$ (CDCl_3).

^1H NMR (600 MHz, CDCl_3) 7.89–7.83 (m, 3H), 7.65 (s, 1H), 7.55–7.50 (m, 2H), 7.32–7.29 (m, 1H), 7.31 (d, J = 12.0 Hz, 1H), 5.92 (d, J = 12.0 Hz, 1H), 4.76 (s, 2H), 2.96 (s, 3H).

^{13}C NMR (151 MHz, CDCl_3) δ 142.6, 133.4, 133.2, 132.6, 129.4, 129.3, 128.0, 127.9, 126.9, 126.8, 126.7, 124.9, 115.1, 112.8, 105.4, 96.3, 58.5, 37.9.

IR (ATR) 3055, 2923, 2853, 2229, 2205, 1579, 1559 cm^{-1} .

HRMS (APCI) m/z : $[M]^+$ Calcd for $\text{C}_{18}\text{H}_{14}\text{ClN}_3$ 307.0876; Found 307.0871.



(2E,4E)-2-Bromo-5-(pyrrolidin-1-yl)hexa-2,4-dienedinitrile (7b): The title compound was prepared from bis(2-bromoacrylonitrile) (**3b**) (260 mg, 1 mmol, 1 equiv) and pyrrolidine (57.5 μL , ρ = 0.866 g/mL, 700 μmol , 3.50 equiv) following General Procedure C, on 1.00 mmol scale. The crude residue was purified *via* column chromatography on silica gel using 91:9 hexanes:ethyl acetate as the eluent to afford of the title compound as a yellow solid (223 mg, 88%, 176 μmol).

R_f (83:17 hexanes:ethyl acetate) = 0.35.

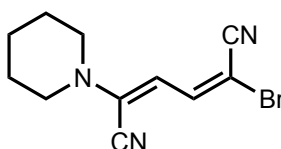
m.p. 90–92 $^{\circ}\text{C}$ (CDCl_3).

¹H NMR (600 MHz, CDCl₃) δ 7.35 (d, *J* = 12.2 Hz, 1 H), 5.59 (d, *J* = 12.2 Hz, 1 H), 3.45–3.37 (m, 4 H), 2.06–2.02 (m, 4 H).

¹³C NMR (151 MHz, CDCl₃) δ 146.0, 126.6, 116.2, 112.9, 105.1, 77.6, 49.9, 25.2.

IR (ATR) 3046, 2975, 2866, 2236, 2191, 1583, 1553 cm⁻¹.

HRMS (APCI) *m/z*: [M+H]⁺ Calcd for C₁₀H₁₀BrN₃ 252.0136; Found 252.0130.



(2*E*,4*E*)-2-Bromo-5-(piperidin-1-yl)hexa-2,4-dienedinitrile (8b): The title compound was prepared from bis(2-bromoacrylonitrile) (**3b**) and piperidine (69.1 μL, ρ = 0.862 g/mL, 700 μmol, 3.50 equiv) following General Procedure C. The crude residue was purified *via* column chromatography on silica gel using 91:9 hexanes:ethyl acetate as the eluent to afford the title compound as a yellow solid (49.5 mg, 93%, 186 μmol).

R_f (83:17 hexanes:ethyl acetate) = 0.44.

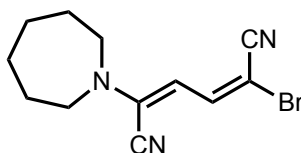
m.p. 83–85 °C (CDCl₃).

¹H NMR (600 MHz, CDCl₃) δ 7.43 (d, *J* = 12.1 Hz, 1H), 5.87 (d, *J* = 12.1 Hz, 1H), 3.36–3.32 (m, 4H), 1.80 (m, 4H), 1.68–1.65 (m, 4H).

¹³C NMR (151 MHz, CDCl₃) δ 146.3, 129.7, 115.8, 112.8, 106.9, 79.8, 49.7, 25.1, 23.8.

IR (ATR) 2939, 2855, 2226, 2198, 1568, 1550 cm⁻¹.

HRMS (APCI) *m/z*: [M+H]⁺ Calcd for C₁₁H₁₂BrN₃ 266.0293; Found 266.0285.



(2*E*,4*E*)-2-(Azepan-1-yl)-5-bromohexa-2,4-dienedinitrile (9b): The title compound was prepared from bis(2-bromoacrylonitrile) (**3b**) and azepane (78.9 μL, ρ = 0.880 g/mL, 700 μmol, 3.50 equiv) following General Procedure C. The crude residue was purified *via* column chromatography on silica gel using 12:1 hexanes:ethyl acetate as the eluent to afford the title compound as a yellow oil that solidified on standing (51.4 mg, 92%, 184 μmol).

R_f (83:17 hexanes:ethyl acetate) = 0.42.

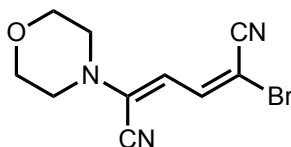
m.p. 52–54 °C (CDCl₃).

¹H NMR (600 MHz, CDCl₃) δ 7.41 (d, *J* = 12.1 Hz, 1H), 5.72 (d, *J* = 12.1 Hz, 1H), 3.49–3.45 (m, 4H), 1.82–1.77 (m, 4 H), 1.62–1.57 (m, 4H).

¹³C NMR (151 MHz, CDCl₃) δ 146.4, 129.1, 116.2, 112.7, 104.5, 77.9, 51.9, 27.8, 27.1.

IR (ATR) 2928, 2856, 2227, 2197, 1567 cm⁻¹.

HRMS (APCI) *m/z*: [M+H]⁺ Calcd for C₁₂H₁₄BrN₃ 280.0449; Found 280.0443.



(2E,4E)-2-Bromo-5-morpholinohexa-2,4-dienedinitrile (10b): The title compound was prepared from bis(2-bromoacrylonitrile) (**3b**) and morpholine (60.4 μL, ρ = 1.01 g/mL, 700 μmol, 3.50 equiv) following General Procedure C. The crude residue was purified *via* column chromatography on silica gel using 83:17 hexanes:ethyl acetate as the eluent to afford the title compound as a yellow solid (53.2 mg, 99%, 198 μmol).

R_f (83:17 hexanes:ethyl acetate) = 0.23.

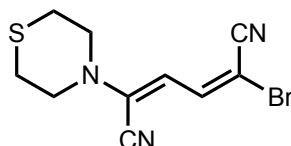
m.p. 124–126 °C (CDCl₃).

¹H NMR (600 MHz, CDCl₃) δ 7.44 (d, 12.0 Hz, 1H), 5.93 (d, 12.0 Hz, 1H), 3.81–3.76 (m, 4H), 3.33–3.29 (m, 4H).

¹³C NMR (151 MHz, CDCl₃) δ 145.4, 129.7, 115.4, 112.4, 108.6, 82.4, 65.8, 48.2.

IR (ATR) 2967, 2922, 2881, 2854, 2223, 2205, 1742, 1584, 1548 cm⁻¹.

HRMS (APCI) *m/z*: [M+H]⁺ Calcd for C₁₀H₁₁BrN₃O 268.0085; Found 268.0079.



(2E,4E)-2-Bromo-5-thiomorpholinohexa-2,4-dienedinitrile (11b): The title compound was prepared from bis(2-bromoacrylonitrile) (**3b**) and thiomorpholine (70.1 μL, ρ = 1.03 g/mL, 700 μmol, 3.50 equiv) following General Procedure C. The crude residue was purified *via* column chromatography on silica gel using 83:17 hexanes:ethyl acetate as the eluent to afford of the title compound as a yellow oil (55.3 mg, 97%, 194 μmol).

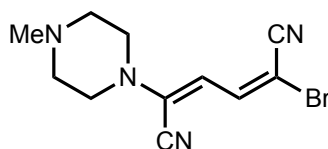
R_f (83:17 hexanes:ethyl acetate) = 0.41.

¹H NMR (600 MHz, CDCl₃) δ 7.43 (d, *J* = 12.0 Hz, 1H), 5.90 (d, *J* = 12.0 Hz, 1H), 3.74–3.70 (m, 4H), 2.72–2.69 (m, 4H).

¹³C NMR (151 MHz, CDCl₃) δ 145.6, 128.3, 115.4, 112.3, 108.1, 81.4, 51.2, 26.3.

IR (ATR) 3065, 2933, 2805, 2222, 2206, 1580, 1552 cm⁻¹.

HRMS (APCI) *m/z*: [M+H]⁺ Calcd for C₁₀H₁₀BrN₃S 283.9857; Found 283.9854.



(2E,4E)-2-Bromo-5-(4-methylpiperazin-1-yl)hexa-2,4-dienedinitrile (12b): The title compound was prepared from bis(2-bromoacrylonitrile) (**3b**) and 1-methylpiperazine (77.7 μL, ρ = 0.903 g/mL, 700 μmol, 3.50 equiv) following General Procedure C. The crude residue was purified *via* column chromatography on silica gel using 99:1 dichloromethane:methanol as the eluent to afford the title compound as a yellow solid (52.2 mg, 93%, 186 μmol).

R_f (50:50 hexanes:ethyl acetate) = 0.12.

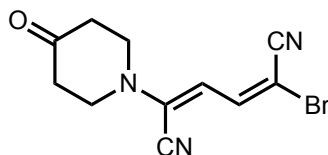
m.p. 137–139 °C (CDCl₃).

¹H NMR (600 MHz, CDCl₃) δ 7.42 (d, *J* = 12.0 Hz, 1H), 5.89 (d, *J* = 12.0 Hz, 1H), 3.37–3.32 (m, 4H), 2.52–2.47 (m, 4H), 2.33 (s, 3H).

¹³C NMR (151 MHz, CDCl₃) δ 145.8, 129.5, 115.5, 112.6, 108.0, 81.3, 53.9, 48.3, 46.0.

IR (ATR) 2940, 2848, 2799, 2229, 2201, 1573 cm⁻¹.

HRMS (APCI) *m/z*: [M+H]⁺ Calcd for C₁₁H₁₃BrN₄ 281.0402; Found 281.0398.



(2E,4E)-2-Bromo-5-(4-oxopiperidin-1-yl)hexa-2,4-dienedinitrile (13b): The title compound was prepared from bis(2-bromoacrylonitrile) (**3b**) and 4-piperidone hydrochloride (94.9 mg, 700 μmol, 3.50 equiv) following General Procedure D. The crude residue was purified *via* column chromatography on silica gel using 75:25 hexanes:ethyl acetate as the eluent to afford the title compound as a yellow solid (48.6 mg, 87%, 174 μmol).

R_f (75:25 hexanes:ethyl acetate) = 0.31.

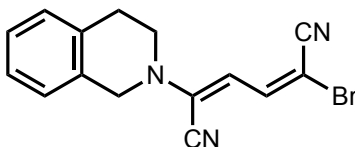
m.p. 96–98 °C (CDCl₃).

¹H NMR (600 MHz, CDCl₃) 7.45 (d, *J* = 11.9 Hz, 1H), 5.95 (d, *J* = 11.9 Hz, 1H), 3.73 (t, *J* = 6.3 Hz, 4H), 2.62 (t, *J* = 6.3 Hz, 4H).

¹³C NMR (151 MHz, CDCl₃) δ 204.4, 145.3, 128.0, 115.2, 112.3, 108.5, 82.4, 46.9, 39.7.

IR (ATR) 2958, 2922, 2853, 2228, 2200, 1719, 1572, 1554 cm⁻¹.

HRMS (APCI) *m/z*: [M+H]⁺ Calcd for C₁₁H₁₀BrN₃O 280.0085; Found 280.0080.



(2E,4E)-2-bromo-5-(3,4-dihydroisoquinolin-2(1H)-yl)hexa-2,4-dienedinitrile (14b): The title compound was prepared from bis(2-bromoacrylonitrile) (**3b**) and 1,2,3,4-tetrahydroisoquinoline (88.8 μL, ρ = 1.05 g/mL, 700 μmol, 3.50 equiv) following General Procedure C. The crude residue was purified *via* column chromatography on silica gel using 50:50 hexanes:dichloromethane as the eluent to afford the title compound as a yellow solid (58.3 mg, 93%, 186 μmol).

R_f (83:17 hexanes:ethyl acetate) = 0.53.

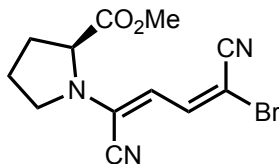
m.p. 91 °C (decomp.) (CDCl₃).

¹H NMR (600 MHz, CDCl₃) δ 7.47 (d, *J* = 12.0 Hz, 1H), 7.29–7.17 (m, 4H), 5.90 (d, *J* = 12. Hz, 1H), 4.46 (s, 2H), 3.71 (t, *J* = 5.9 Hz, 2H), 2.99 (t, *J* = 5.9 Hz, 2H).

¹³C NMR (151 MHz, CDCl₃) δ 145.9, 133.6, 130.8, 128.7, 128.5, 127.5, 127.0, 126.3, 115.7, 112.5, 106.3, 80.0, 49.6, 46.9, 28.6.

IR (ATR) 3062, 3027, 2921, 2852, 2228, 2200, 1735, 1569, 1552 cm⁻¹.

HRMS (APCI) *m/z*: [M+H]⁺ Calcd for C₁₅H₁₃BrN₃ 314.0293; Found 314.0290.



((1E,3E)-Methyl-4-bromo-1,4-dicyanobuta-1,3-dien-1-yl)-L-prolinate (15b): The title compound was prepared from bis(2-bromoacrylonitrile) (**3b**) and *L*-proline methyl ester hydrochloride (116 mg, 700 μmol,

3.50 equiv) following General Procedure D. The crude residue was purified *via* column chromatography on silica gel using 80:20 hexanes:ethyl acetate as the eluent to afford the title compound as a yellow/orange oil (24.7 mg, 40%, 80 μ mol).

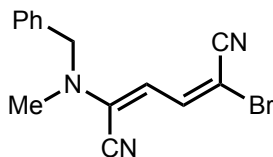
R_f (50:50 hexanes:ethyl acetate) = 0.60.

¹H NMR (600 MHz, CDCl₃) δ 7.37 (d, J = 12.1 Hz, 1H), 5.70 (d, J = 12.1 Hz, 1H), 4.41 (dd, J = 8.6, 2.7 Hz, 1H), 3.79 (s, 3H), 3.55–3.50 (m, 1H), 3.42–3.36 (m, 1H), 2.36–2.28 (m, 1H), 2.26–2.20 (m, 1H), 2.12–2.04 (m, 2H).

¹³C NMR (151 MHz, CDCl₃) δ 171.6, 145.6, 126.0, 115.6, 112.7, 107.3, 80.2, 62.7, 53.0, 49.7, 30.4, 23.6.

IR (ATR) 2954, 2232, 2200, 1742, 1577 cm⁻¹.

HRMS (APCI) m/z : [M+H]⁺ Calcd for C₁₂H₁₂BrN₃O₂ 310.0191; Found 310.0187.



(2E,4E)-2-(Benzyl(methyl)amino)-5-bromohepta-2,4-dienedinitrile (16b): The title compound was prepared from bis(2-bromoacrylonitrile) (**3b**) and *N*-methylbenzylamine (90.3 μ L, ρ = 0.939 g/mL, 700 μ mol, 3.50 equiv) following General Procedure C. The crude residue was purified *via* column chromatography on silica gel using 91:9 hexanes:ethyl acetate as the eluent to afford of the title compound as a yellow/orange oil (51.1 mg, 85%, 170 μ mol).

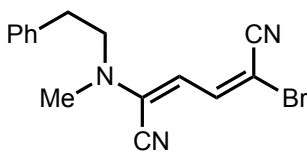
R_f (83:17 hexanes:ethyl acetate) = 0.45.

¹H NMR (600 MHz, CDCl₃) δ 7.45 (d, J = 12.1 Hz, 1H), 7.41–7.37 (m, 2H), 7.36–7.33 (m, 1H), 7.22–7.19 (m, 2H), 5.79 (d, J = 12.1 Hz, 1H), 4.60 (s, 2H), 2.90 (s, 3H).

¹³C NMR (151 MHz, CDCl₃) δ 146.1, 135.1, 129.3, 129.3, 128.6, 127.5, 115.8, 112.8, 106.6, 79.9, 58.3, 37.9.

IR (ATR) 3029, 2926, 2230, 2199, 1572 cm⁻¹.

HRMS (APCI) m/z : [M+H]⁺ Calcd for C₁₄H₁₃BrN₃ 302.0293; Found 302.0291.



(2E,4E)-2-Bromo-5-(methyl(phenethyl)amino)hexa-2,4-dienedinitrile (17b): The title compound was prepared from bis(2-bromoacrylonitrile) (**3b**) and *N*-methylphenethylamine (102 μ L, ρ = 0.930 g/mL, 700 μ mol, 3.50 equiv) following General Procedure C. The crude residue was purified *via* column chromatography on silica gel using 91:9 hexanes:ethyl acetate as the eluent to afford of the title compound as a yellow solid (53.8 mg, 85%, 170 μ mol).

R_f (83:17 hexanes:ethyl acetate) = 0.35.

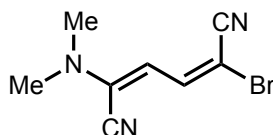
m.p. 76–78 °C (CDCl₃).

¹H NMR (600 MHz, CDCl₃) δ 7.35 (d, J = 12.1 Hz, 1H), 7.34–7.31 (m, 2H), 7.29–7.25 (m, 1H), 7.19–7.16 (m, 2H), 5.66 (d, J = 12.1 Hz, 1H), 3.66 (t, J = 7.3 Hz, 2H), 2.89 (t, J = 7.3 Hz, 2H), 2.88 (s, 3H).

¹³C NMR (151 MHz, CDCl₃) δ 146.1, 137.2, 129.0, 129.0, 128.9, 127.2, 115.9, 112.5, 105.8, 79.2, 56.7, 38.6, 34.8.

IR (ATR) 3026, 2931, 2230, 2198, 1575 cm⁻¹.

HRMS (APCI) m/z : [M+H]⁺ Calcd for C₁₅H₁₅BrN₃ 316.0449; Found 316.0447.



(2E,4E)-2-Bromo-5-(dimethylamino)hexa-2,4-dienedinitrile (18b): The title compound was prepared from bis(2-bromoacrylonitrile) (**3b**) and dimethylamine hydrochloride (57.1 mg, 700 μ mol, 3.50 equiv) following General Procedure D. The crude residue was purified *via* column chromatography on silica gel using 83:17 hexanes:ethyl acetate as the eluent to afford of the title compound as a yellow solid (40.4 mg, 89%, 178 μ mol).

R_f (83:17 hexanes:ethyl acetate) = 0.22.

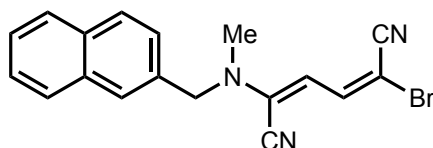
m.p. 116–118 °C (CDCl₃).

¹H NMR (600 MHz, CDCl₃) δ 7.38 (d, J = 12.1 Hz, 1H), 5.69 (d, J = 12.1 Hz, 1H), 3.05 (s, 3H).

¹³C NMR (151 MHz, CDCl₃) δ 146.1, 129.8, 115.9, 112.6, 105.9, 79.2, 41.0.

IR (ATR) 3068, 3021, 2923, 2856, 2229, 2200, 1584 cm⁻¹.

HRMS (APCI) m/z : [M+H]⁺ Calcd for C₈H₈BrN₃ 225.9980; Found 225.9977.



(2E,4E)-2-Bromo-5-(methyl(naphthalen-2-ylmethyl)amino)hexa-2,4-dienedinitrile (19b): The title compound was prepared from bis(2-bromoacrylonitrile) (**3b**) and *N*-methyl-1-(naphthalen-2-yl)methanamine (145 mg, 700 μ mol, 3.50 equiv) following General Procedure D. The crude residue was purified *via* column chromatography on silica gel using 91:9 hexanes:ethyl acetate as the eluent to afford the title compound as a yellow/orange crystalline solid (62.0 mg, 88%, 176 μ mol).

R_f (83:17 hexanes:ethyl acetate) = 0.39.

m.p. 92–94 °C (CDCl₃).

¹H NMR (600 MHz, CDCl₃) δ 7.90–7.82 (m, 3H), 7.65 (s, 1H), 7.55–7.50 (m, 2H), 7.47 (d, *J* = 12.1 Hz, 1H), 7.30 (dd, *J* = 8.4, 1.9 Hz, 1H), 5.84 (d, *J* = 12.1 Hz, 1H), 4.75 (s, 2H), 2.94 (s, 3H).

¹³C NMR (151 MHz, CDCl₃) δ 146.0, 133.3, 133.2, 132.5, 129.3, 127.94, 127.89, 126.8, 126.71, 126.65, 124.9, 115.7, 112.9, 106.6, 80.0, 58.4, 37.9.

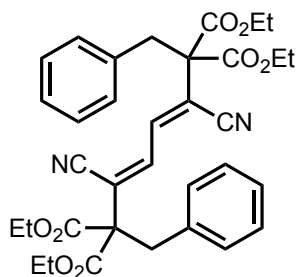
IR (ATR) 3055, 2924, 2853, 2229, 2200, 1741, 1574 cm⁻¹.

HRMS (APCI) *m/z*: [M+H]⁺ Calcd for C₁₈H₁₅BrN₃ 352.0449; Found 352.0445.

VI. Preparation and Characterization of Malonate Additions Products

General procedure for the addition of malonate nucleophiles to bis(2-haloacrylonitrile) – General Procedure E.

To a 4 mL dram vial equipped with magnetic Teflon®-coated stir bar under N₂ was added the appropriate malonate derivative (600 μ mol, 3.00 equiv) followed by 0.50 mL of anhydrous THF. NaH (24.0 mg, 60% mineral oil dispersion, 600 μ mol, 3.00 equiv) was then added and the reaction mixture was stirred until effervescence halted. To the stirred solution was added a solution of bis(2-bromoacrylonitrile) (**3b**) (52.4 mg, 200 μ mol, 1.00 equiv) in 1.50 mL of anhydrous THF (0.2 M) and the reactions were stirred at 23 °C until the conclusion of the reaction as determined by TLC. The solvent was then concentrated *in vacuo* and the products by silica gel flash column chromatography.



(3Z,5Z)-Tetraethyl-3,6-dicyano-1,8-diphenylocta-3,5-diene-2,2,7,7-tetracarboxylate (20a): The title compound was prepared from diethyl 2-benzylmalonate (142 μL , $\rho = 1.06 \text{ g/mL}$, 600 μmol , 3.00 equiv) following General Procedure E. The crude residue was purified *via* column chromatography on silica gel using 91:9 hexanes:ethyl acetate as the eluent to afford the title compound as a colorless solid (101 mg, 84%, 168 μmol).

R_f (83:17 hexanes:ethyl acetate) = 0.17.

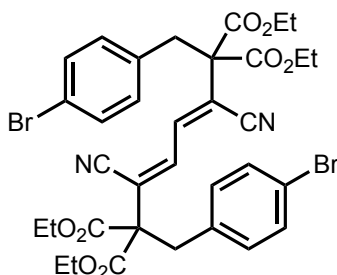
m.p. 76–78 °C (CDCl_3).

^1H NMR (600 MHz, CDCl_3) δ 7.27–7.24 (m, 8H), 7.13–7.10 (m, 4H), 4.25 (q, $J = 7.1 \text{ Hz}$, 8H), 3.54 (s, 4H), 1.26 (t, $J = 7.1 \text{ Hz}$, 12H).

^{13}C NMR (151 MHz, CDCl_3) δ 167.2, 141.9, 134.1, 130.4, 128.6, 127.9, 119.5, 114.6, 63.1, 62.9, 40.7, 14.0.

IR (ATR) 2982, 2938, 2215, 1737, 1454 cm^{-1} .

HRMS (APCI) m/z : $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{34}\text{H}_{37}\text{N}_2\text{O}_8$ 601.2550; Found 601.2549.



(3Z,5Z)-Tetraethyl-1,8-bis(4-bromophenyl)-3,6-dicyano-octa-3,5-diene-2,2,7,7-tetracarboxylate

(20b): The title compound was prepared from diethyl 2-(4-bromobenzyl)malonate (198 mg, 600 μmol , 3.00 equiv) following General Procedure E. The crude residue was purified *via* column chromatography on silica gel using 91:9 hexanes:ethyl acetate as the eluent to afford of the title compound as a colorless crystalline solid (130 mg, 86%, 172 μmol).

R_f (83:17 hexanes:ethyl acetate) = 0.26.

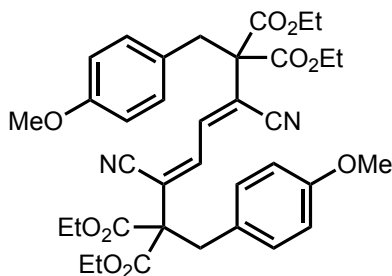
m.p. 88–90 °C (CDCl₃).

¹H NMR (600 MHz, CDCl₃) 7.40 (d, *J* = 7.4 Hz, 4 H), 7.30 (s, 2 H), 7.03 (d, *J* = 7.4 Hz, 4 H), 4.32–4.22 (m, 8 H), 3.49 (s, 4 H), 1.27 (t, *J* = 7.2 Hz, 12 H).

¹³C NMR (151 MHz, CDCl₃) δ 167.0, 141.6, 133.1, 132.2, 131.7, 122.1, 119.8, 114.6, 63.3, 62.7, 40.0, 14.0.

IR (ATR) 2982, 2938, 2216, 1736, 1487 cm⁻¹.

HRMS (APCI) *m/z*: [M+H]⁺ Calcd for C₃₄H₃₄Br₂N₂O₈ 757.0760; Found 757.0758.



(3Z,5Z)-Tetraethyl-3,6-dicyano-1,8-bis(4-methoxyphenyl)octa-3,5-diene-2,2,7,7-tetracarboxylate

(20c): The title compound was prepared from diethyl 2-(4-methoxybenzyl)malonate (168 mg, 600 μmol, 3.00 equiv) following General Procedure E. The crude residue was purified *via* column chromatography on silica gel using 83:17 hexanes:ethyl acetate as the eluent to afford the title compound as a colorless oil (123 mg, 93%, 186 μmol).

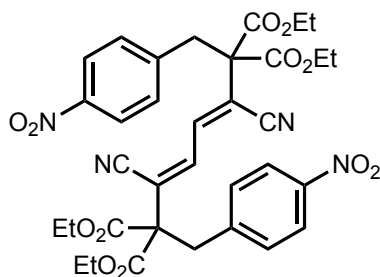
R_f (83:17 hexanes:ethyl acetate) = 0.09.

¹H NMR (600 MHz, CDCl₃) δ 7.26 (s, 2 H), 7.04 (d, *J* = 8.7 Hz, 4H), 6.80 (d, *J* = 8.7 Hz, 4H), 4.27 (q, *J* = 7.2 Hz, 8H), 3.78 (s, 6H), 1.49 (s, 4H), 1.27 (t, *J* = 7.2 Hz, 12H).

¹³C NMR (151 MHz, CDCl₃) δ 167.2, 159.2, 141.9, 131.5, 125.9, 119.5, 114.7, 114.0, 63.0 (two peaks), 55.3, 40.0, 14.0.

IR (ATR) 2982, 2937, 2837, 2215, 1737, 1611, 1513 cm⁻¹.

HRMS (APCI) *m/z*: [M+H]⁺ Calcd for C₃₆H₄₁N₂O₁₀ 661.2761; Found 661.2764.



(3Z,5Z)-Tetraethyl-3,6-dicyano-1,8-bis(4-nitrophenyl)octa-3,5-diene-2,2,7,7-tetracarboxylate (20d):

The title compound was prepared from diethyl 2-(4-nitrobenzyl)malonate (177 mg, 600 μmol , 3.00 equiv) following General Procedure E. The crude residue was purified *via* column chromatography on silica gel using 80:20 hexanes:ethyl acetate as the eluent to afford of the title compound as a pale yellow crystalline solid (105 mg, 76%, 152 μmol).

R_f (83:17 hexanes:ethyl acetate) = 0.09.

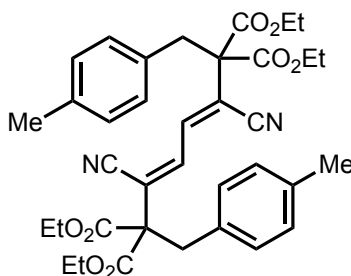
m.p. 118–120 °C (CDCl_3).

¹H NMR (600 MHz, CDCl_3) 8.14 (d, J = 8.7 Hz, 4 H), 7.37 (d, J = 8.7 Hz, 4 H), 7.28 (s, 2 H), 4.33–4.23 (m, 8 H), 3.62 (s, 4 H), 1.26 (t, J = 7.3 Hz, 12 H).

¹³C NMR δ 166.6, 147.6, 141.8, 141.4, 131.5, 123.7, 119.9, 114.4, 63.6, 62.5, 40.2, 13.9.

IR (ATR) 2984, 2217, 1734, 1606, 1520 cm^{-1} .

HRMS (APCI) m/z : $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{34}\text{H}_{35}\text{N}_4\text{O}_{12}$ 691.2251; Found 691.2250.



(3Z,5Z)-Tetraethyl-3,6-dicyano-1,8-di-p-tolylocta-3,5-diene-2,2,7,7-tetracarboxylate (20e): The title compound was prepared from diethyl 2-(4-methylbenzyl)malonate (159 mg, 600 μmol , 3.00 equiv) following General Procedure E. The crude residue was purified *via* column chromatography on silica gel using 91:9 hexanes:ethyl acetate as the eluent to afford the title compound as a colorless oil (105 mg, 84%, 168 μmol).

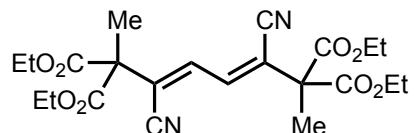
R_f (83:17 hexanes:ethyl acetate) = 0.24.

¹H NMR (600 MHz, CDCl₃) δ 7.25 (s, 2 H), 7.07 (d, *J* = 7.9 Hz, 4 H), 7.00 (d, *J* = 8.1 Hz, 4 H), 4.31–4.22 (m, 8 H), 3.51 (s, 4 H), 2.31 (s, 6 H), 1.28 (t, *J* = 7.2 Hz, 12 H).

¹³C NMR (151 MHz, CDCl₃) δ 167.2, 142.0, 137.6, 130.9, 130.3, 129.3, 119.3, 114.7, 63.0, 62.9, 40.3, 21.3, 14.0.

IR (ATR) 2982, 2937, 2214, 1737, 1515, 1445 cm⁻¹.

HRMS (APCI) *m/z*: [M+H]⁺ Calcd for C₃₆H₄₁N₂O₈ 629.2863; Found 629.2865.



(3Z,5Z)-Tetraethyl-3,6-dicyano-octa-3,5-diene-2,2,7,7-tetracarboxylate (21): The title compound was prepared from diethyl 2-methylmalonate (102 μL, ρ = 1.02 g/mL, 600 μmol, 3.00 equiv) following General Procedure E. The crude residue was purified *via* column chromatography on silica gel using 89:11 hexanes:ethyl acetate as the eluent to afford the title compound as a colorless oil (64.9 mg, 72%, 144 μmol).

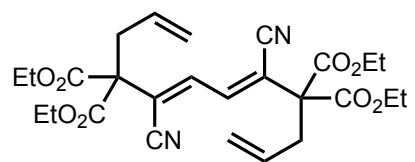
R_f (83:17 hexanes:ethyl acetate) = 0.28.

¹H NMR (600 MHz, CDCl₃) δ 7.24 (s, 2H), 4.29 (q, *J* = 7.1 Hz, 8H), 1.77 (s, 6H), 1.31 (t, *J* = 7.1 Hz, 12H).

¹³C NMR (151 MHz, CDCl₃) δ 168.2, 139.1, 121.5, 114.8, 63.2, 57.8, 20.6, 14.0.

IR (ATR) 2984, 2940, 2229, 1731, 1448 cm⁻¹.

HRMS (APCI) *m/z*: [M+H]⁺ Calcd for C₂₂H₂₉N₂O₈ 449.1924; Found 449.1919.



(5Z,7Z)-Tetraethyl-5,8-dicyano-dodeca-1,5,7,11-tetraene-4,4,9,9-tetracarboxylate (22): The title compound was prepared from diethyl 2-allylmalonate (118 μL, ρ = 1.02 g/mL, 600 μmol, 3.00 equiv) following General Procedure E. The crude residue was purified *via* column chromatography on silica gel using 91:9 hexanes:ethyl acetate as the eluent to afford the title compound as a colorless oil, (74.9 mg, 75%, 150 μmol).

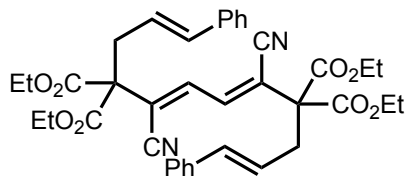
R_f (83:17 hexanes:ethyl acetate) = 0.31.

¹H NMR (600 MHz, CDCl₃) δ 7.41 (s, 2H), 5.74 (ddd, *J* = 17.0, 10.1, 7.5 Hz, 2H), 5.24 (d, *J* = 17.0 Hz, 2H), 5.19 (d, *J* = 10.1 Hz, 2H), 4.29 (q, *J* = 7.1 Hz, 8H), 2.97 (d, *J* = 7.5 Hz, 4H), 1.31 (t, *J* = 7.1 Hz, 12H).

^{13}C NMR (151 MHz, CDCl_3) δ 167.2, 141.0, 130.8, 121.2, 119.9, 114.9, 63.1, 61.3, 38.7, 14.1.

IR (ATR) 2983, 2938, 2217, 1733, 1445 cm^{-1} .

HRMS (APCI) m/z : $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{26}\text{H}_{33}\text{N}_2\text{O}_8$ 501.2237; Found 501.2228.



(1E,5Z,7Z,11E)-Tetraethyl-5,8-dicyano-1,12-diphenyldodeca-1,5,7,11-tetraene-4,4,9,9-

tetracarboxylate (23): The title compound was prepared from diethyl 2-cinnamylmalonate (166 mg, 600 μmol , 3.00 equiv) following General Procedure E. The crude residue was purified *via* column chromatography on silica gel using 91:9 hexanes:ethyl acetate as the eluent to afford of the title compound as a pale yellow oil (127 mg, 98%, 196 μmol).

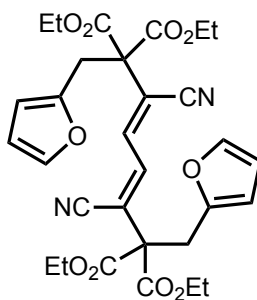
R_f (83:17 hexanes:ethyl acetate) = 0.21.

^1H NMR (600 MHz, CDCl_3) δ 7.44 (s, 2H), 7.33–7.21 (m, 10H), 6.56 (d, J = 15.8 Hz, 2H), 6.11 (dd, J = 15.8, 7.3 Hz, 2H), 4.29 (q, J = 7.1 Hz, 8H), 3.13 (d, J = 7.3 Hz, 4H), 1.28 (t, J = 7.1 Hz, 12H).

^{13}C NMR (151 MHz, CDCl_3) δ 167.2, 141.0, 136.7, 135.8, 128.7, 127.9, 126.6, 122.0, 120.1, 115.0, 63.2, 61.7, 38.3, 14.1.

IR (ATR) 2981, 2937, 2220, 1733, 1447 cm^{-1} .

HRMS (APCI) m/z : $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{38}\text{H}_{41}\text{N}_2\text{O}_8$ 653.2863; Found 653.2858.



(3Z,5Z)-Tetraethyl-3,6-dicyano-1,8-di(furan-2-yl)octa-3,5-diene-2,2,7,7-tetracarboxylate (24) The title compound was prepared from diethyl 2-(furan-2-ylmethyl)malonate (144 mg, 600 μmol , 3.00 equiv) following General Procedure E. The crude residue was purified *via* column chromatography on silica gel using 83:17 hexanes:ethyl acetate as the eluent to afford the title compound as a colorless oil (86.4 mg, 74%, 148 μmol).

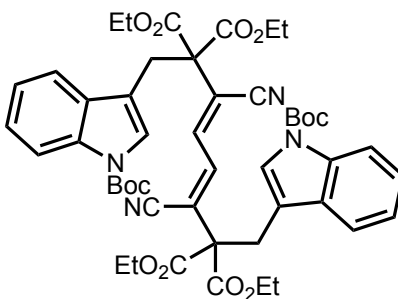
R_f (83:17 hexanes:ethyl acetate) = 0.10.

¹H NMR (600 MHz, CDCl₃) δ 7.31 (s, 2H), 7.30 (d, *J* = 1.9 Hz, 2H), 6.28 (dd, *J* = 3.0, 1.9 Hz, 2H), 6.17 (d, *J* = 3.0 Hz, 2H), 4.31 (q, *J* = 7.2 Hz, 8H), 3.60 (s, 4H), 1.30 (t, *J* = 7.2 Hz, 12H).

¹³C NMR (151 MHz, CDCl₃) δ 166.9, 148.2, 142.6, 141.5, 119.2, 114.4, 110.7, 110.2, 63.3, 61.7, 33.3, 14.0.

IR (ATR) 2984, 2939, 2217, 1736, 1504, 1445 cm⁻¹.

HRMS (APCI) *m/z*: [M+H]⁺ Calcd for C₃₀H₃₃N₂O₁₀ 581.2135; Found 581.2133.



(3Z,5Z)-Tetraethyl-1,8-bis(1-(*tert*-butoxycarbonyl)-1H-indol-3-yl)-3,6-dicyano-octa-3,5-diene-2,2,7,7-tetracarboxylate (25): The title compound was prepared from diethyl 2-((1-(*tert*-butoxycarbonyl)-1H-indol-3-yl)methyl)malonate (234 mg, 600 μmol, 3.00 equiv) following General Procedure E. The crude residue was purified *via* column chromatography on silica gel using 91:9 hexanes:ethyl acetate as the eluent to afford the title compound as a pale yellow powder (146 mg 83%, 166 μmol).

R_f (83:17 hexanes:ethyl acetate) = 0.17.

m.p. 139–141 °C (CDCl₃).

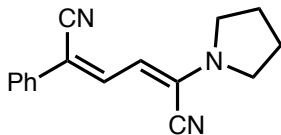
¹H NMR (600 MHz, CDCl₃) δ 8.09 (s, 2H), 7.49 (s, 2H), 7.45 (d, *J* = 7.9 Hz, 2H), 7.36 (s, 2H), 7.30–7.26 (m, 2H), 7.21–7.18 (m, 2H), 4.20 (q, *J* = 7.1 Hz, 8H), 3.65–3.61 (m, 4H), 1.21 (t, *J* = 7.1 Hz, 12H).

¹³C NMR (151 MHz, CDCl₃) δ 167.2, 149.6, 141.5, 130.8, 125.7, 124.6, 122.6, 120.1, 118.8, 115.4, 114.7, 113.1, 84.0, 63.2, 62.2, 30.2, 28.3, 13.9.

IR (ATR) 2980, 2936, 2214, 1730, 1451 cm⁻¹.

HRMS (APCI) *m/z*: [M+H]⁺ Calcd for C₄₈H₅₄N₄O₁₂ 879.3816; Found 879.3817.

VII. Preparation and Characterization of Functionalization of 7a and 7b Products



(2Z,4E)-2-Phenyl-5-(pyrrolidin-1-yl)hexa-2,4-dienedinitrile (28). **(From Cl compound)** A flame-dried 4 mL dram vial equipped with a septum cap and a magnetic Teflon®-coated stir bar was charged with (2E,4E)-2-chloro-5-(pyrrolidin-1-yl)hexa-2,4-dienedinitrile (**7a**) (48.8 mg, 200 μ mol, 1.00 equiv). Phenylboronic acid (48.8 mg, 0.400 mmol, 2.00 equiv), Bis(dibenzylideneacetone)palladium(0) (5.70 mg, 9.90 μ mol, 5.0 mol%), BrettPhos (21.0 mg, 39.0 μ mol, 20.0 mol%), cesium carbonate (130.0 mg, 400 μ mol, 2.00 equiv) were added, followed by 1,4-dioxane (1 mL, 0.2 M). The vial was heated to 60 °C in an Al heating block and stirred for 12 hours. The mixture was cooled to room temperature and quenched with water (2 mL), and extracted with ethyl acetate (3 x 2 mL). The organic layer was dried with Na₂SO₄, and concentrated *in vacuo*, to yield a brown solid. The crude residue was purified *via* column chromatography on silica gel using 90:10 hexanes:ethyl acetate as the eluent. This procedure afforded the title compound as an orange solid (37.2 mg, 75%, 149 μ mol). The compound was obtained as a 10:1 mixture of diastereomers as judged by ¹H NMR analysis. Data are for the major isomer.

(From Br compound) A flame-dried 4 mL dram vial equipped with a septum cap and a magnetic Teflon®-coated stir bar was charged with (2E,4E)-2-bromo-5-(pyrrolidin-1-yl)hexa-2,4-dienedinitrile (**7b**) (48.8 mg, 200 μ mol, 1.00 equiv). Phenylboronic acid (48.8 mg, 400 μ mmol, 2.00 equiv), Bis(dibenzylideneacetone)palladium(0) (5.70 mg, 9.90 μ mol, 5.0 mol%), BrettPhos (21.0 mg, 39.0 μ mol, 20.0 mol%), cesium carbonate (130.0 mg, 400 μ mol, 2.00 equiv) were added, followed by 1,4-dioxane (1.0 mL, 0.20 M). The vial was heated to 60 °C in an Al heating block and stirred for 12 hours. The mixture was cooled to room temperature and quenched with water (2 mL), extracted with ethyl acetate (3 x 2 mL). The organic layer was dried with Na₂SO₄, and concentrated *in vacuo*, to yield a brown solid. The crude residue was purified *via* column chromatography on silica gel using 90:10 hexanes:ethyl acetate as the eluent. This procedure afforded the title compound of as an orange solid (42.6 mg, 86%, 171 μ mol). The compound was obtained as a 10:1 mixture of diastereomers as judged by ¹H NMR analysis. Data are for the major isomer.

m.p. 177–179 °C (CDCl₃).

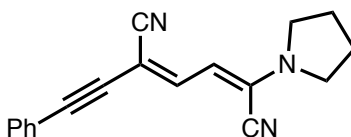
R_f (90:10 hexanes:ethyl acetate) = 0.26.

¹H NMR (600 MHz, CDCl₃) δ 7.59–7.49 (m, 3H), 7.42–7.32 (m, 2H), 7.32–7.24 (m, 1H), 6.01 (d, *J* = 12.0 Hz, 1H), 3.51–3.40 (m, 4H), 2.08–1.99 (m, 4H).

^{13}C NMR (151 MHz, CDCl_3) δ 138.0, 133.9, 129.0, 128.0, 126.2, 125.0, 118, 113.4, 107.5, 106.2, 49.8, 25.3.

IR (ATR) 2979, 2954, 2923, 2853, 2225, 2201, 1603, 1576 cm^{-1} .

HRMS (ESI^+) m/z : $[\text{M}^+]$ Calcd for $\text{C}_{16}\text{H}_{15}\text{N}_3$ 249.1266; Found 249.1265.



(2Z,4E)-2-(Phenylethynyl)-5-(pyrrolidin-1-yl)hexa-2,4-dienedinitrile (29). (From **Cl** compound) A flame-dried 4 mL vial equipped with a septum cap and a magnetic Teflon®-coated stir bar was charged with (2E,4E)-2-chloro-5-(pyrrolidin-1-yl)hexa-2,4-dienedinitrile (**7a**) (41.4 mg, 199 μmol , 1.00 equiv). Tetrakis(triphenylphosphine)palladium(0) (16.2 mg, 14.0 μmol , 7.00 mol%) and copper (I) iodide (4.60 mg, 24.0 μmol , 12.0 mol%) were added followed by 1,4-dioxane (2.0 mL, 0.10 M). Phenylacetylene (100 μL , ρ = 0.930 g/mL, 920 μmol , 4.60 equiv) and triethylamine (120 μL , ρ = 0.725 g/mL, 880 μmol , 4.60 equiv) were added and the vial was heated to 60 $^{\circ}\text{C}$ in an Al heating block and stirred for 12 hours. The mixture was cooled to room temperature and concentrated to yield brown oil. The crude residue was purified *via* column chromatography on silica gel using 90:10 hexanes:ethyl acetate as the eluent. This procedure afforded the title compound as a brown oil (36.7 mg, 67%, 134 μmol). The compound was obtained as a 4:1 mixture of diastereomers as judged by ^1H NMR analysis. Data are for the major isomer.

(From Br compound) A flame-dried 4 mL vial equipped with a septum cap and a magnetic Teflon®-coated stir bar was charged with (2E,4E)-2-bromo-5-(pyrrolidin-1-yl)hexa-2,4-dienedinitrile (**7b**) (23.7 mg, 94.4 μmol , 1.00 equiv). Tetrakis(triphenylphosphine)palladium(0) (8.20 mg, 8.20 μmol , 7.00 mol%) and copper (I) iodide (3.10 mg, 12.0 μmol , 12 mol%) were added followed by 1,4-dioxane (1.0 mL, 0.10 M). Phenylacetylene (50.0 μL , ρ = 0.930 g/mL, 460 μmol , 4.6 equiv) and triethylamine (60 μL , ρ = 0.725 g/mL, 440 μmol , 4.60 equiv) were added and the vial was heated to 60 $^{\circ}\text{C}$ in an Al heating block and stirred for 12 hours. The mixture was cooled to room temperature and concentrated to yield brown oil. The crude residue was purified *via* column chromatography on silica gel using 90:10 hexanes:ethyl acetate as the eluent. This procedure afforded the title compound as a brown oil (22.2 mg, 86%, 81.3 μmol). The compound was obtained as a 4:1:1 mixture of isomers (product isomerizes on silica gel) as judged by ^1H NMR analysis. Data are for the major isomer.

R_f (90:10 hexanes:ethyl acetate) = 0.10.

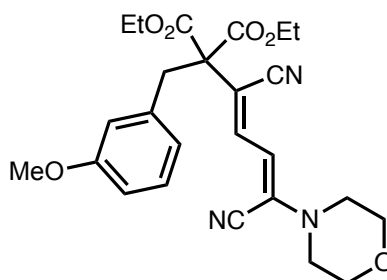
^1H NMR (400 MHz, CDCl_3) δ 7.47–7.43 (m, 2H), 7.37 (d, J = 12.4 Hz, 1H), 7.35–7.31 (m, 3H), 5.90 (d, J = 12.4 Hz, 1H), 3.51 (d, J = 6.4 Hz, 4H), 2.09–2.02 (m, 4H).

^{13}C NMR (151 MHz, CDCl_3) δ 147.8, 131.4, 128.6, 128.4, 126.8, 122.4, 116.4, 112.8, 106.4, 92.6, 86.4, 85.0, 50.0, 25.2.

IR (ATR) 2954, 2923, 2854, 2362, 2226, 2207, 2032, 1568 cm^{-1} .

HRMS (APCI) m/z : $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{18}\text{H}_{16}\text{N}_3$ 274.1344; Found 274.1338.

VIII. Preparation and Characterization of Interrupted Addition to **3b** Products



2-((1Z,3E)- Diethyl -1,4-dicyano-4-morpholinobuta-1,3-dien-1-yl)-2-(3-methoxybenzyl)malonate (26). A flame dried 4 mL vial equipped with a septum cap, and magnetic Teflon®-coated stir bar was charged with diethyl 2-(3-methoxybenzyl)malonate (**S9**) (67.0 mg, 240 μmol , 1.20 equiv), THF (0.50 mL), and sodium hydride (60% in mineral oil, 10.0 mg, 250 μmol , 1.30 equiv). To the mixture (2*E*,4*E*)-2,5-dibromohexa-2,4-dienedinitrile (**3b**) (52.4 mg, 198 μmol , 1.00 equiv) in THF (0.50 mL) was added and stirred at 25 $^{\circ}\text{C}$ for 35 minutes. Morpholine (200 μL , ρ = 1.01 g/mL, 2.00 mmol, 10.0 equiv) was added, and the reaction stirred at 25 $^{\circ}\text{C}$ for 12 hours. The mixture was concentrated to yield an orange oil. The crude residue was purified *via* column chromatography on silica gel using 70:30 hexanes:ethyl acetate as the eluent. This procedure afforded the title compound as a yellow solid (75.4 mg, 82%, 161 μmol).

m.p. 92–95 $^{\circ}\text{C}$ (CDCl_3).

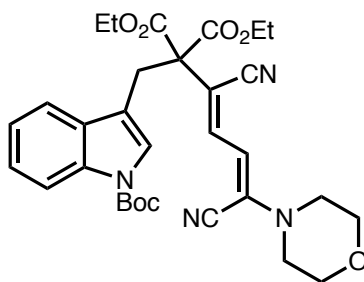
R_f (70:30 hexanes:ethyl acetate) = 0.18.

^1H NMR (600 MHz, CDCl_3) δ 7.27–7.20 (m, 1H), 7.17 (t, J = 7.9 Hz, 1H), 6.81–6.70 (m, 3H), 6.14 (d, J = 11.7 Hz, 1H), 4.30–4.19 (m, 4H), 3.78–3.71 (m, 7H), 3.52 (s, 2H), 3.29 (dd, J = 5.9, 4.0 Hz, 4H), 1.26 (t, J = 7.1 Hz, 6H).

^{13}C NMR (151 MHz, CDCl_3) δ 168.0, 159.4, 143.9, 136.1, 130.3, 129.3, 122.6, 116.8, 116.1, 112.8, 112.4, 109.8, 106.7, 65.7, 62.6, 61.9, 55.2, 48.2, 40.6, 13.9.

IR (ATR) 2978, 2936, 2903, 2856, 2229, 2203, 1733, 1583, 1564 cm^{-1} .

HRMS (ESI^+) m/z : $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{25}\text{H}_{30}\text{N}_3\text{O}_6$ 468.2135; Found 468.2123.



Diethyl 2-((1-(*tert*-butoxycarbonyl)-1*H*-indol-3-yl)methyl)-2-((1*Z*,3*E*)-1,4-dicyano-4-morpholinobuta-1,3-dien-1-yl)malonate (27). A flame dried 4 mL vial equipped with a septum cap, and magnetic Teflon®-coated stir bar was charged with diethyl 2-((1-(*tert*-butoxycarbonyl)-1*H*-indol-3-yl)methyl)malonate (**S7**) (93.0 mg, 240 μ mol, 1.20 equiv), THF (0.50 mL), sodium hydride (60% in mineral oil, 10.0 mg, 250 μ mol, 1.30 equiv). (2*E*,4*E*)-2,5-dibromohexa-2,4-dienedinitrile (**3b**) (52.4 mg, 200 μ mol, 1.00 equiv) in THF (0.50 mL) was added to the mixture and the mixture stirred at 25 °C for 40 minutes. Morpholine (0.20 mL, ρ = 1.01 g/mL, 2.00 mmol, 10.0 equiv) was then added, and the reaction stirred at 25 °C for 5 hours. The mixture was concentrated *in vacuo* to yield orange oil. The crude residue was purified *via* column chromatography on silica gel using 80:20 hexanes:ethyl acetate as the eluent. This procedure afforded the title compound as an orange low melting solid (82.1 mg, 71%, 142 μ mol).

m.p. 48–51 °C (CDCl₃).

R_f (70:30 hexanes:ethyl acetate) = 0.38.

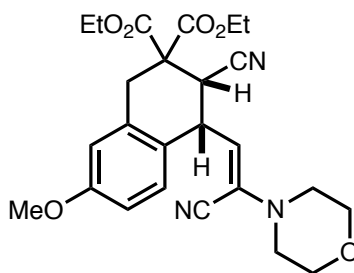
¹H NMR (600 MHz, CDCl₃) δ 8.07 (s, 1H), 7.51–7.43 (m, 2H), 7.30–7.15 (m, 3H), 6.08 (d, *J* = 11.7 Hz, 1H), 4.25–4.14 (m, 4H), 3.77–3.71 (m, 4H), 3.63 (s, 2H), 3.28–3.21 (m, 4H), 1.65 (s, 9H), 1.22 (t, *J* = 7.1 Hz, 6H).

¹³C NMR (151 MHz, CDCl₃) δ 168.1, 149.6, 144.0, 134.9, 131.0, 130.3, 125.2, 124.4, 122.4, 118.9, 116.8, 115.2, 113.7, 112.2, 109.7, 106.6, 83.7, 65.7, 62.7, 61.4, 48.2, 29.9, 28.2, 13.8.

IR (ATR) 3055, 2980, 2935, 2860, 2227, 2204, 1731, 1585, 1563 cm⁻¹.

HRMS (ESI⁺) *m/z*: [M+H⁺] Calcd for C₃₁H₃₇N₄O₇ 577.2663; Found 577.2649.

IX. Preparation and Characterization of Annulation Reaction Products



(3*S*,4*R*)- Diethyl-3-cyano-4-((*E*)-2-cyano-2-morpholinovinyl)-7-methoxy-3,4-dihydronaphthalene-2,2(1*H*)-dicarboxylate (30). A flame dried 4 mL vial equipped with a magnetic Teflon®-coated stir bar was charged with 2-((1*Z*,3*E*)- diethyl -1,4-dicyano-4-morpholinobuta-1,3-dien-1-yl)-2-(3-methoxybenzyl)malonate (**26**, 59.8 mg, 128 μ mol, 1.00 equiv) aluminum trichloride (15.5 mg, 116 μ mol, 0.90 equiv) and 1,2-dichloroethane (1.0 mL, 0.10 M). The reaction was heated to 60 °C in an Al heating block and stirred for 2 hours. The reaction was basified with saturated sodium bicarbonate (2.0 mL), ammonium hydroxide (0.50 mL) and extracted with dichloromethane (3 x 2.0 mL). The organic layer was dried with Na₂SO₄, and concentrated *in vacuo* to yield a brown oil as a 75:25 ratio of diastereomers. The crude residue was purified *via* column chromatography on silica gel using 80:20 to 70:30 hexanes:ethyl acetate as the eluent. This procedure afforded the two diastereomers (52.9 mg, 88%, 113.3 μ mol) as described below:

Data for the major diastereomer:

pale yellow oil (40.1 mg, 67%, 85.9 μ mol)

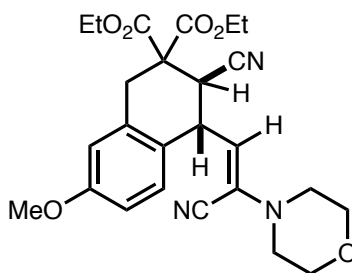
R_f (70:30 hexanes:ethyl acetate) = 0.37.

¹H NMR (600 MHz, CDCl₃) δ 6.97 (dd, *J* = 8.4, 1.0 Hz, 1H), 6.78–6.72 (m, 2H), 5.35 (d, *J* = 10.0 Hz, 1H), 4.37–4.26 (m, 3H), 4.26–4.21 (m, 1H), 4.19 (dd, *J* = 10.8, 7.1 Hz, 1H), 4.12 (dd, *J* = 10.1, 5.4 Hz, 1H), 3.94 (dd, *J* = 5.4, 1.7 Hz, 1H), 3.79 (d, *J* = 1.7 Hz, 7H), 3.69–3.62 (m, 1H), 3.39 (dd, *J* = 17.2, 1.5 Hz, 1H), 3.08 (q, *J* = 5.1 Hz, 4H), 1.33 (t, *J* = 7.1 Hz, 3H), 1.24 (t, *J* = 7.1 Hz, 3H).

¹³C NMR (151 MHz, CDCl₃) δ 167.9, 166.9, 159.1, 133.7, 129.1, 128.5, 124.3, 117.7, 117.3, 113.8, 113.62, 113.57, 66.0, 63.2, 62.9, 55.32, 55.30, 48.9, 38.9, 37.6, 31.8, 14.0, 13.8.

IR (ATR) 2979, 2906, 2838, 2243, 2225, 1734, 1610, 1577, 1502 cm⁻¹.

HRMS (APCI) *m/z*: [M+H]⁺ Calcd for C₂₅H₃₀N₃O₆ 468.2135; Found 468.2125.



(3*S*,4*S*)-Diethyl-3-cyano-4-((*E*)-2-cyano-2-morpholinovinyl)-7-methoxy-3,4-dihydronaphthalene-2,2(1*H*)-dicarboxylate (S10).

Data for the minor diastereomer:

pale yellow oil (12.8 mg, 21%, 27.4 μ mol)

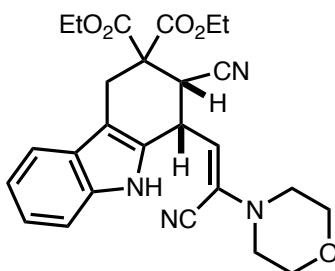
R_f (70:30 hexanes:ethyl acetate) = 0.11.

$^1\text{H NMR}$ (600 MHz, CDCl_3) δ 7.00 (dd, J = 8.6, 1.0 Hz, 1H), 6.76 (dd, J = 8.7, 2.7 Hz, 1H), 6.65 (d, J = 2.6 Hz, 1H), 5.00 (d, J = 10.3 Hz, 1H), 4.35–4.21 (m, 5H), 4.17 (t, J = 10.7 Hz, 2H), 3.82–3.73 (m, 7H), 3.56 (d, J = 16.5 Hz, 1H), 3.29 (d, J = 11.4 Hz, 1H), 3.18–3.11 (m, 1H), 3.06 (q, J = 4.6 Hz, 4H), 1.33 (td, J = 7.1, 1.6 Hz, 6H).

$^{13}\text{C NMR}$ (151 MHz, CDCl_3) δ 169.2, 167.2, 159.2, 133.0, 129.5, 125.0, 118.0, 117.0, 113.69, 113.68, 66.0, 63.0, 62.9, 55.6, 55.3, 48.9, 40.8, 38.7, 35.8, 14.0, 13.8.

IR (ATR) 3057, 2964, 2922, 2855, 2247, 2226, 1730, 1610, 1583, 1502 cm^{-1} .

HRMS (APCI) m/z : $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{25}\text{H}_{30}\text{N}_3\text{O}_6$ 468.2135; Found 468.2126.



1*R*,2*S*- Diethyl -2-cyano-1-((*E*)-2-cyano-2-morpholinovinyl)-1,2,4,9-tetrahydro-3*H*-carbazole-3,3-dicarboxylate (31). A flame dried 4 mL vial equipped with a magnetic Teflon®-coated stir bar was charged with diethyl 2-((1-(*tert*-butoxycarbonyl)-1*H*-indol-3-yl)methyl)-2-((1*Z*,3*E*)-1,4-dicyano-4-morpholinobuta-1,3-dien-1-yl)malonate (**27**). (52.7 mg, 910 μ mol, 1.0 equiv) and 1,2-dichloroethane (1.0 mL, 0.10 M). The mixture was charged with trifluoroacetic acid (50 μ L, ρ = 1.49 g/mL, 650 μ mol, 7.00 equiv), and reaction stirred at 25 $^{\circ}\text{C}$ for 14 hours. The mixture was quenched with saturated sodium

bicarbonate (2 mL), ammonium hydroxide (0.5 mL) and extracted with dichloromethane (3 x 2 mL). The organic layer was dried with Na₂SO₄, and concentrated *in vacuo* to yield brown oil as a 62:38 ratio of diastereomers. The crude residue was purified *via* column chromatography on silica gel using 80:20 to 70:30 hexanes:ethyl acetate as the eluent. This procedure afforded the combined diastereomers (26.6 mg 61%, 55.9 μ mol) as described below:

Data for the major diastereomer:

orange solid (9.9 mg, 22%, 20.8 μ mol),

m.p. 72–75 °C (CDCl₃).

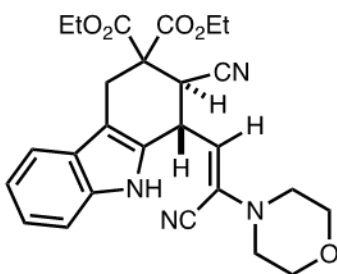
¹H NMR (600 MHz, CDCl₃) δ 7.77 (s, 1H), 7.56 (d, *J* = 7.8 Hz, 1H), 7.31 (d, *J* = 8.1 Hz, 1H), 7.22–7.16 (m, 1H), 7.16–7.11 (m, 1H), 5.37 (d, *J* = 10.3 Hz, 1H), 4.56–4.53 (m, 1H), 4.40–4.26 (m, 2H), 4.25–4.14 (m, 2H), 4.11 (dd, *J* = 5.6, 1.1 Hz, 1H), 3.82–3.77 (m, 4H), 3.73–3.63 (m, 1H), 3.37 (dd, *J* = 16.4, 2.6 Hz, 1H), 3.13 (td, *J* = 4.5, 2.8 Hz, 4H), 1.36 (t, *J* = 7.1 Hz, 3H), 1.21 (t, *J* = 7.1 Hz, 3H).

¹³C NMR (151 MHz, CDCl₃) 167.9, 167.0, 136.5, 129.2, 129.2, 127.0, 122.8, 120.1, 118.8, 117.5, 113.2, 112.7, 110.9, 108.1, 66.0, 63.1, 63.0, 56.8, 48.7, 38.1, 35.6, 24.5, 14.2, 13.9.

R_f (70:30 hexanes:ethyl acetate) = 0.22.

IR (ATR) 3385, 2977, 2923, 2854, 2226, 2203, 1733, 1680, 1613, 1537 cm⁻¹.

HRMS (APCI) *m/z*: [M+H⁺] Calcd for C₂₆H₂₉N₄O₅ 477.2138; Found 477.2125.



1R,2R- Diethyl -2-cyano-1-((E)-2-cyano-2-morpholinovinyl)-1,2,4,9-tetrahydro-3H-carbazole-3,3-dicarboxylate (S11)

Data for the minor diastereomer:

orange solid (6.7 mg, 15%, 14.0 μ mol)

m.p. 122–125 °C (CDCl₃).

¹H NMR (600 MHz, CDCl₃) δ 7.81 (s, 1H), 7.48 (d, *J* = 7.9 Hz, 1H), 7.31 (d, *J* = 8.1 Hz, 1H), 7.20 (t, *J* = 8.2 Hz, 1H), 7.12 (d, *J* = 8.9 Hz, 1H), 5.00 (d, *J* = 10.3 Hz, 1H), 4.55–4.47 (m, 1H), 4.38–4.29 (m, 3H),

4.25–4.17 (m, 1H), 3.80 (t, $J = 4.9$ Hz, 4H), 3.76 (dd, $J = 15.7, 1.3$ Hz, 2H), 3.42 (d, $J = 10.5$ Hz, 1H), 3.17–3.07 (m, 4H), 1.36 (t, $J = 7.1$ Hz, 3H), 1.30 (t, $J = 7.1$ Hz, 3H).

^{13}C NMR (151 MHz, CDCl_3) δ 169.4, 167.3, 136.4, 129.7, 129.5, 126.6, 123.0, 120.2, 118.6, 117.8, 113.3, 113.1, 111.0, 107.3, 65.9, 63.1, 62.8, 56.8, 48.7, 39.2, 38.0, 28.1, 14.0, 13.8.

R_f (70:30 hexanes:ethyl acetate) = 0.11.

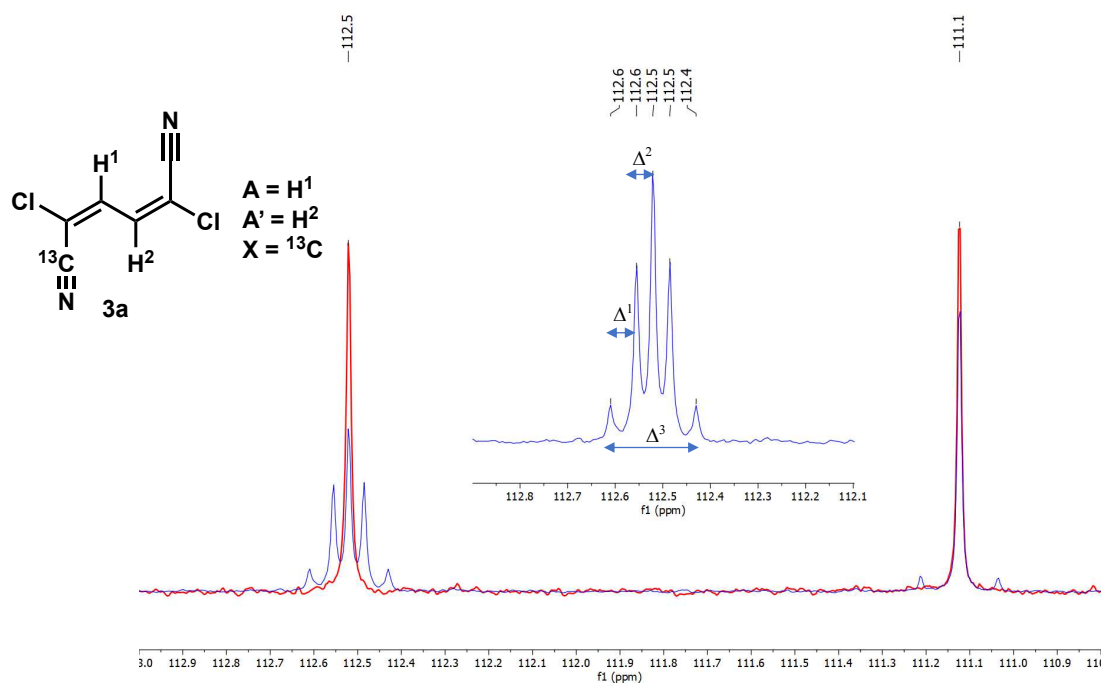
IR (ATR) 3371, 3057, 2971, 2922, 2852, 2226, 2206, 1733, 1680, 1614 cm^{-1} .

HRMS (APCI) m/z : $[\text{M}+\text{H}^+]$ Calcd for $\text{C}_{26}\text{H}_{29}\text{N}_4\text{O}_5$ 477.2138; Found 477.2129.

Note: The remaining mass balance is accounted for in mixed fractions of the two diastereomers (10.0 mg, 22%, 21.0 μmol).

X. Descriptions of Stereochemical Assignments

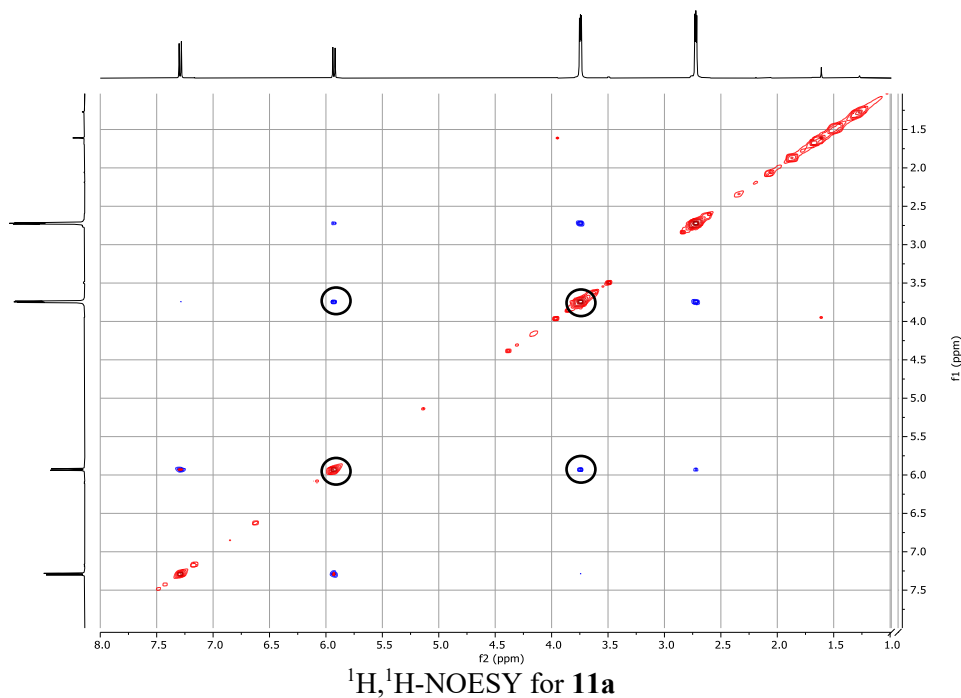
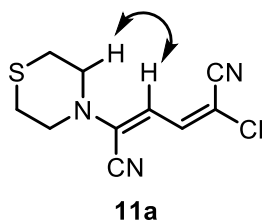
The geometry of diene **3a** was determined by analysis of the ^1H coupled ^{13}C NMR spectrum. The relative stereochemistry of products **11a**, **30**, **S10**, **31**, **S11** was assigned on the basis of ^1H NMR nOe studies. The data for these studies is provided below, along with the key nOe signals.

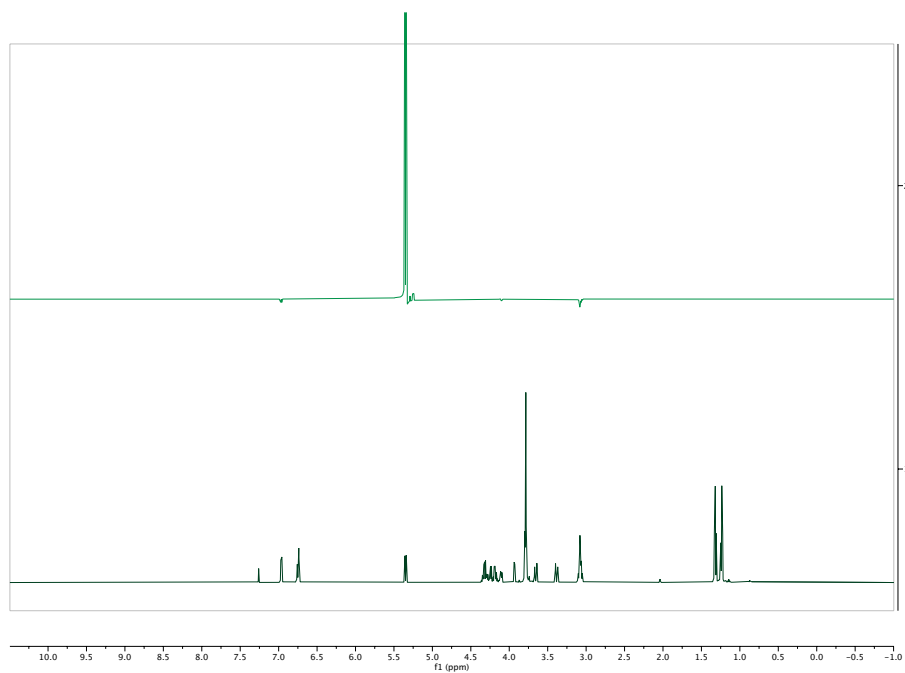
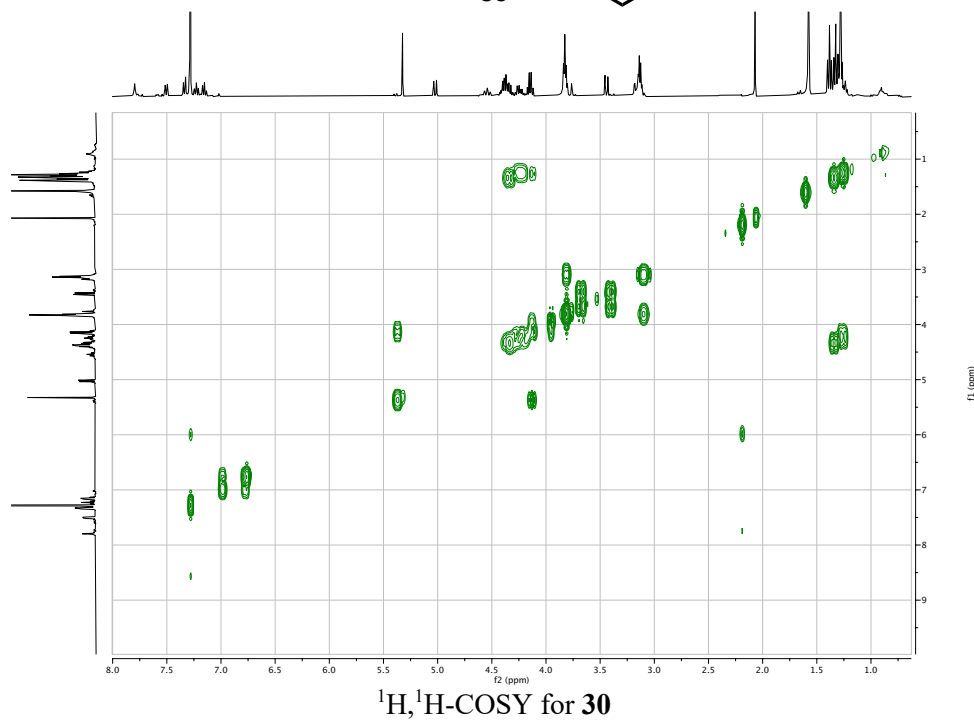
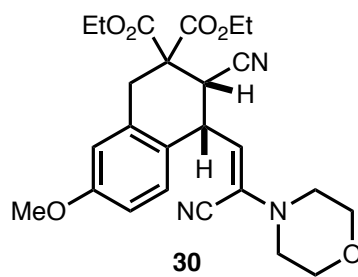


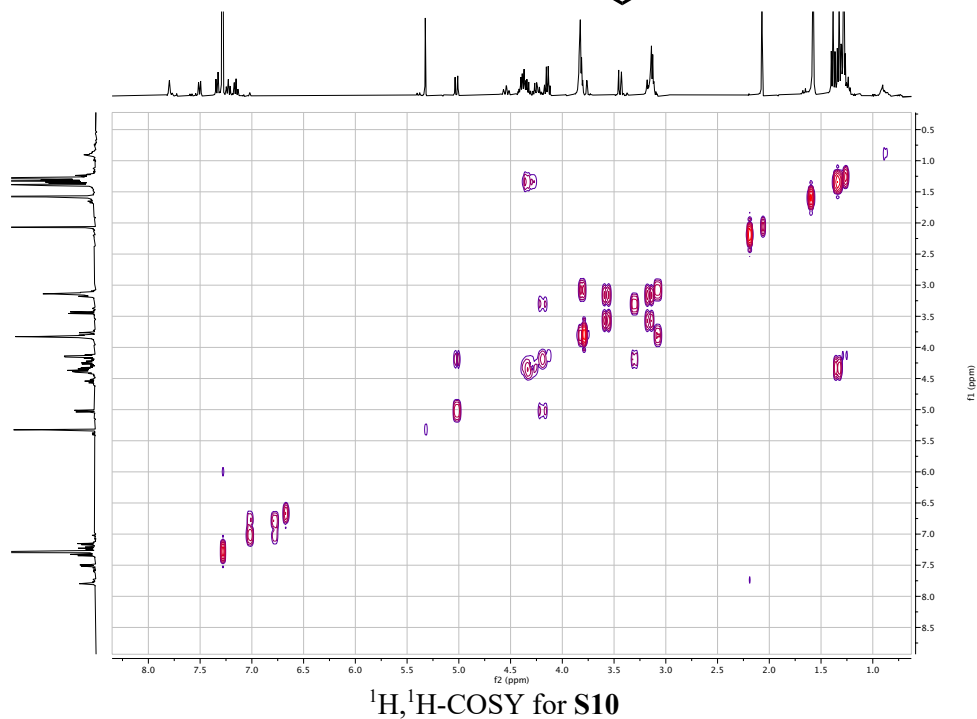
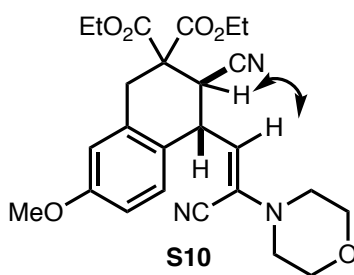
CDCl_3 151 MHz (14.5 mg **3a** in 0.70 mL CDCl_3). ^1H decoupled ^{13}C spectrum shown in red. ^1H coupled ^{13}C spectrum shown in blue.

The 2nd order coupling pattern for the resonance at 112.5 ppm (nitrile resonance) was simulated in SpinWorks⁹ software using the following parameters: $J_{AX} = +13$ Hz, $J_{A'X} = -2$ Hz, $J_{AA'} = +12$ Hz, 2 Hz linewidth. Where A, A' and X are defined for **3a** as shown above. This J -value is in accord with a *trans*-relationship between ¹H and the nitrile group.¹⁰

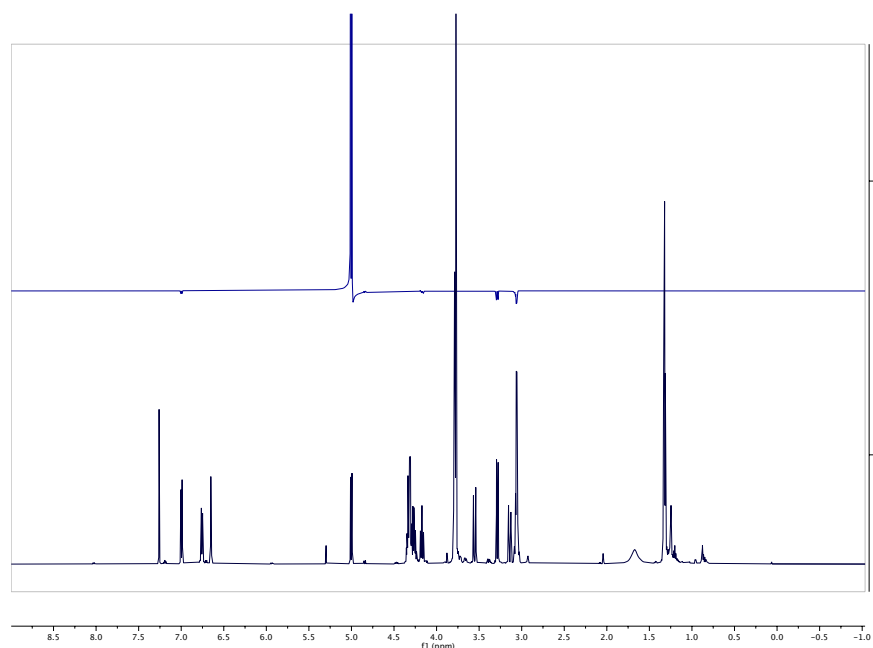
MEASURED FROM SPECTRUM	CALCULATED IN SPINWORKS
$\Delta^3 = 27.2$ Hz	$\Delta^3 = 27$ Hz
$\Delta^2 = 6.0$ Hz	$\Delta^2 = 5.5$ Hz
$\Delta^1 = 7.6$ Hz	$\Delta^1 = 8.4$ Hz



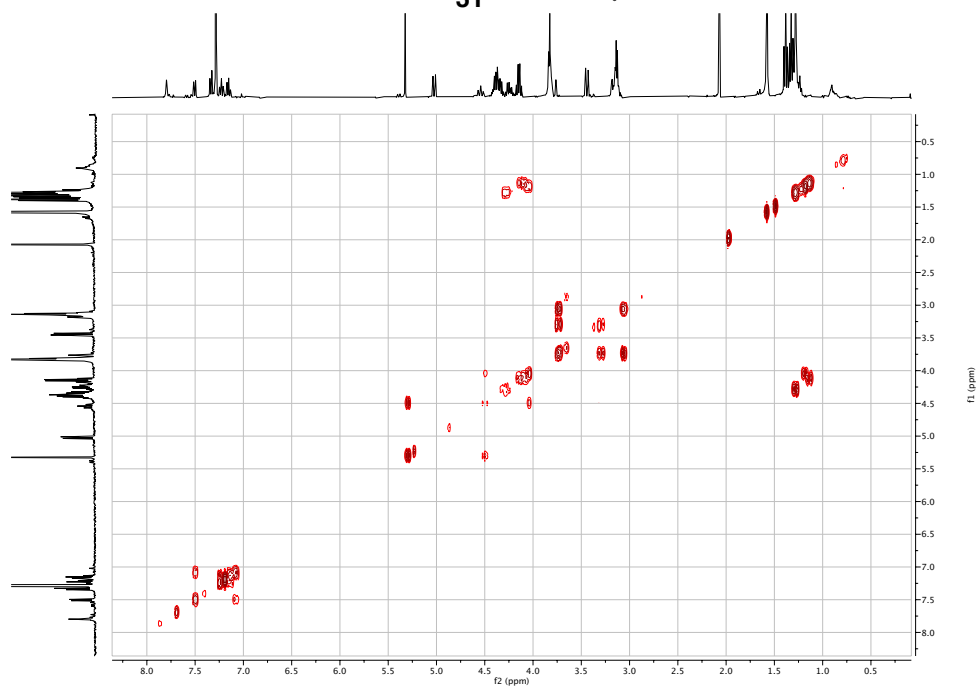
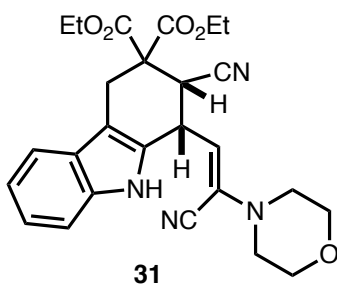




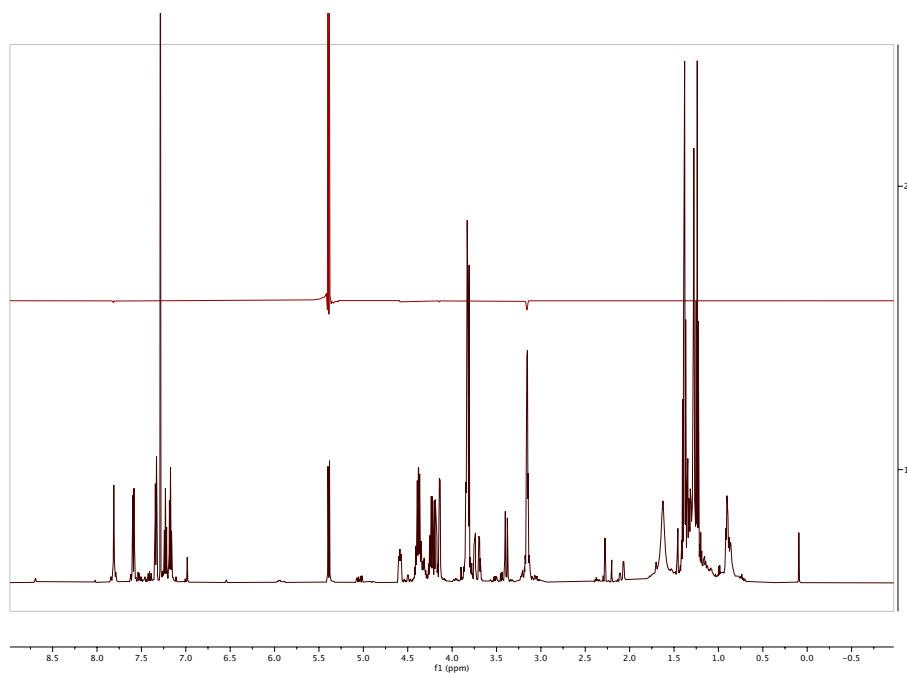
$^1\text{H}, ^1\text{H}$ -COSY for **S10**



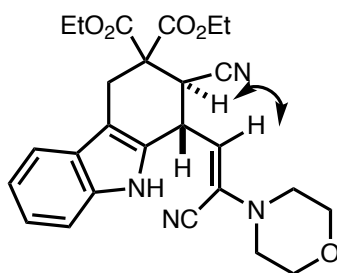
1D NOE for **S10** irradiating peak at 5.00 ppm. Correlation seen with peak at 3.29 ppm, indicating they are on the same side of the cyclohexane.



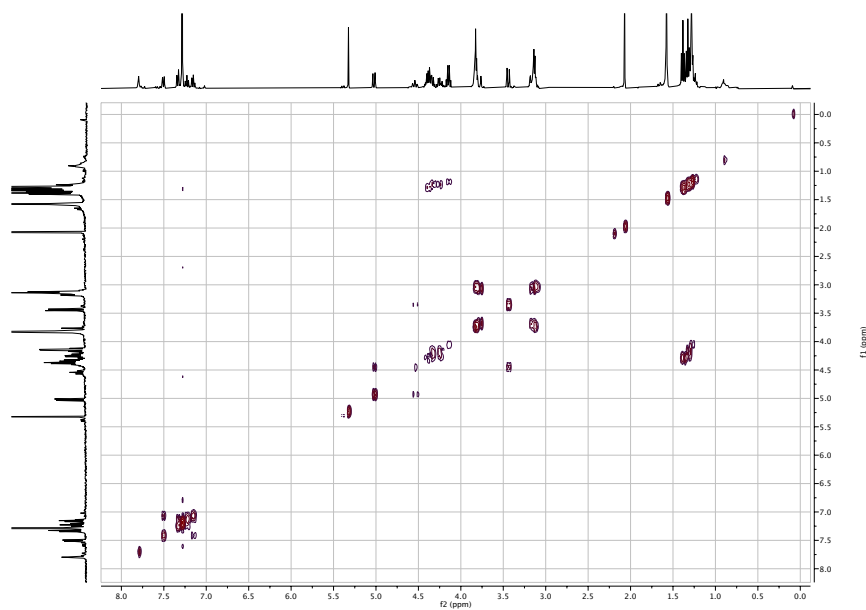
$^1\text{H}, ^1\text{H}$ -COSY for **31**



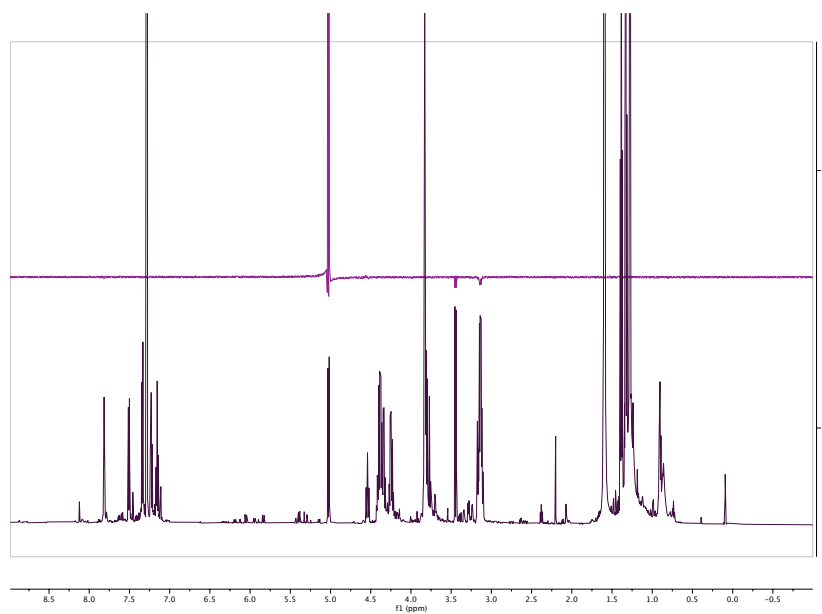
1D NOE for **31** irradiating peak at 5.39 ppm. No correlations observed



S11



$^1\text{H}, ^1\text{H}$ -COSY for S11



1D NOE for **S11** irradiating peak at 5.01 ppm. Correlation seen with peak at 3.43 ppm, indicating they are on the same side of the cyclohexane.

XI. X-ray Data for 3a and 19a

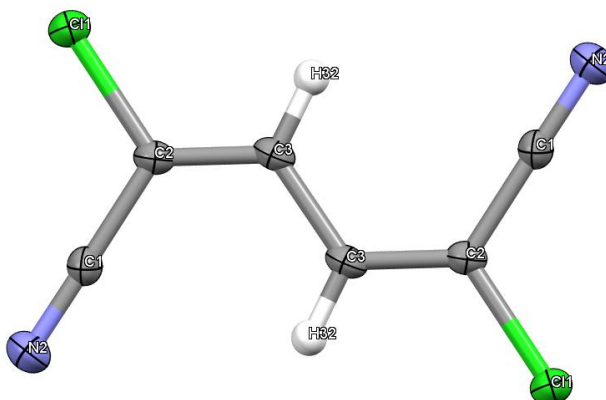


Figure S1: Molecular structure for **3a** (50% probability level shown).

X-ray quality crystals were grown by placing an uncapped 1 dram vial containing a 1.0 mL solution of compound **3a** dissolved in ethyl acetate into a scintillation vial containing 2.0 mL of hexanes and allowing vapor diffusion to occur for 48 hours. A colorless crystal (approximate dimensions 0.200 x 0.200 x 0.200 mm³) was placed onto the tip of MiTeGen and mounted on a Bruker SMART Apex II diffractometer and measured at 150 K.

Data collection

A preliminary set of cell constants was calculated from reflections harvested from three sets of 12 frames. These initial sets of frames were oriented such that orthogonal wedges of reciprocal space were surveyed. This produced initial orientation matrices determined from 140 reflections. The data collection was carried out using Cu K α radiation (graphite monochromator) with a frame time of 10 seconds and a detector distance of 4.0 cm. A randomly oriented region of reciprocal space was surveyed to achieve complete data with a redundancy of 4. Sections of frames were collected with 0.50° steps in ω and ϕ scans. Data to a resolution of 0.84 Å were considered in the reduction. Final cell constants were calculated from the xyz centroids of 690 strong reflections from the actual data collection after integration (SAINT). The intensity data were corrected for absorption (SADABS). Please refer to Table 1 for additional crystal and refinement information.

Structure solution and refinement

The space group P -1 was determined based on intensity statistics and systematic absences. The structure was solved using Superflip3 and refined (full-matrix-least squares) using the Oxford University Crystals for Windows system. The charge-flipping solution provided most non-hydrogen atoms from the E-map. Full-matrix least squares / difference Fourier cycles were performed, which located the remaining non-hydrogen atoms. All non-hydrogen atoms were refined with anisotropic displacement parameters. The

hydrogen atoms were placed in ideal positions and refined with individual relative isotropic displacement parameters.

Table S1. Crystal data and structure refinement for Compound **3a**.

Empirical formula	C ₆ H ₂ Cl ₂ N ₂	
Formula weight	173.00	
Crystal color, shape, size	colorless plate fragment, 0.200 x 0.200 x 0.200 mm ³	
Temperature	150 K	
Wavelength	1.54178 Å	
Crystal system, space group	Triclinic, P -1	
Unit cell dimensions	a = 5.0796(2) Å	a = 73.366(2)°.
	b = 6.0612(2) Å	b = 69.663(2)°.
	c = 6.6441(2) Å	g = 71.280(2)°.
Volume	178.113(11) Å ³	
Z	1	
Density (Calcd)	1.613 Mg/m ³	
Absorption coefficient	7.505 mm ⁻¹	
F(000)	86.0	
Data collection		
Diffractometer	Bruker Apex Kappa Duo, Bruker	
Theta range for data collection	7.251 to 72.318°.	
Index ranges	-6 ≤ h ≤ 6, -7 ≤ k ≤ 7, -8 ≤ l ≤ 8	
Reflections collected	3043	
Independent reflections	690 [R(int) = 0.026]	
Observed Reflections	689	
Solution and Refinement		
Absorption correction	multi-scan	
Max. and min. transmission	0.22 and 0.22	
Solution	Direct methods	
Refinement method	Full-matrix least-squares on F ²	
Weighting scheme	w = 1/[σ ² (Fo ²) + (AP) ² + BP], with	
	P = A × max(Fo ² , 0) + C Fc ² , A = 0.034, B = 0.088, C =	
	0.667	
Data / restraints / parameters	688 / 0 / 46	
Goodness-of-fit on F ²	1.0000	
Final R indices [I > 2σ(I)]	R1 = 0.0257, wR2 = 0.0653	
R indices (all data)	R1 = 0.0257, wR2 = 0.0653	
Largest diff. peak and hole	0.20 and -0.29 e.Å ⁻³	

Table S2. Atomic coordinates and equivalent isotropic displacement parameters (\AA^2)
for compound **3a**. $U(\text{eq})$ is defined as one third of the trace of the orthogonalized U^{ij} tensor.

Label	x	y	z	$U_{\text{iso/eqiv}}$
Cl1	0.10209(7)	0.09722(6)	0.19329(5)	0.0238
N2	0.3108(3)	0.2939(3)	0.5714(2)	0.0291
C1	0.3042(3)	0.2921(3)	0.4015(2)	0.0195
C2	0.2939(3)	0.2882(2)	0.1895(2)	0.0182
C3	0.4195(3)	0.4194(2)	0.0030(2)	0.0189
H32	0.4011(3)	0.4030(2)	-0.1290(2)	0.0224

Table S3. Bond lengths [Å] and angles [°] for compound **3a**.

Cl1-C2	1.7263(14)Å	N2-Cl1	1.144(2)Å
C1-C2	1.4349(19)Å	C2-C3	1.337(2)Å
C3-C3 2	1.447(3)Å	C3-H32	0.949Å
N2-C1-C2	179.41(16)°	Cl1-C2-C1	114.13(11)°
Cl1-C2-C3	121.85(11)°	C1-C2-C3	124.02(13)°
C2-C3-C3 2	122.54(15)°	C2-C3-H32	117.469°
C3 2-C3-H32	119.992°		

Table S4. Anisotropic displacement parameters (Å²) for compound **3a**. The anisotropic displacement factor exponent takes the form: $-2\pi^2 [h^2 a^{*2} U^{11} + \dots + 2 h k a^* b^* U^{12}]$

Label	U ₁₁	U ₂₂	U ₃₃	U ₂₃	U ₁₃	U ₁₂
Cl1	0.0285(2)	0.0262(2)	0.0225(2)	0.00450(15)	0.00824(16)	0.01334(17)
N2	0.0367(8)	0.0360(8)	0.0189(6)	-0.0053(5)	-0.0074(6)	-0.0152(6)
C1	0.0212(7)	0.0206(7)	0.0170(7)	-0.0029(5)	-0.0031(5)	-0.0085(6)
C2	0.0194(7)	0.0194(7)	0.0183(7)	-0.0065(5)	-0.0065(5)	-0.0043(6)
C3	0.0216(7)	0.0213(7)	0.0158(7)	-0.0073(5)	-0.0066(5)	-0.0033(6)

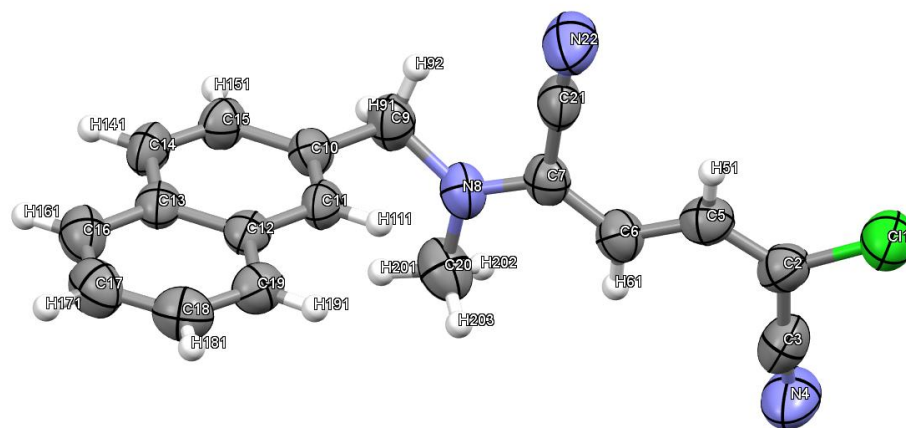


Figure S2: Molecular structure for **19a** (50% probability level shown).

X-ray quality crystals were grown by placing an uncapped 1 dram vial containing a 1.0 mL solution of compound **19a** dissolved in ethyl acetate into a scintillation vial containing 2.0 mL of hexanes and allowing vapor diffusion to occur for 24 hours. A yellow crystal (approximate dimensions 0.200 x 0.300 x 0.300 mm³) was placed onto the tip of MiTeGen and mounted on a Bruker SMART Apex II diffractometer and measured at 293 K.

Data collection

A preliminary set of cell constants was calculated from reflections harvested from three sets of 12 frames. These initial sets of frames were oriented such that orthogonal wedges of reciprocal space were surveyed. This produced initial orientation matrices determined from 140 reflections. The data collection was carried out using Cu K α radiation (graphite monochromator) with a frame time of 10 seconds and a detector distance of 4.0 cm. A randomly oriented region of reciprocal space was surveyed to achieve complete data with a redundancy of 4. Sections of frames were collected with 0.50° steps in ω and ϕ scans. Data to a resolution of 0.84 Å were considered in the reduction. Final cell constants were calculated from the xyz centroids of 2591 strong reflections from the actual data collection after integration (SAINT). The intensity data were corrected for absorption (SADABS). Please refer to Table 5 for additional crystal and refinement information.

Structure solution and refinement

The space group P2₁/n was determined based on intensity statistics and systematic absences. The structure was solved using Superflip3 and refined (full-matrix-least squares) using the Oxford University Crystals for Windows system. The charge-flipping solution provided most non-hydrogen atoms from the E-map. Full-matrix least squares / difference Fourier cycles were performed, which located the remaining non-hydrogen atoms. All non-hydrogen atoms were refined with anisotropic displacement parameters. The hydrogen atoms were placed in ideal positions and refined with individual relative isotropic displacement

parameters.

Table S5. Crystal data and structure refinement for Compound **19a**.

Empirical formula	C ₁₈ H ₁₄ Cl ₁₁ N ₃	
Formula weight	307.78	
Crystal color, shape, size	yellow block fragment, 0.200 x 0.300 x 0.300 mm ³	
Temperature	293 K	
Wavelength	1.54178 Å	
Crystal system, space group	Monoclinic, P2 ₁ /n	
Unit cell dimensions	a = 10.1156(4) Å	a = 90°.
	b = 10.7151(4) Å	b = 102.223(2)°.
	c = 14.7073(6) Å	g = 90°.
Volume	1557.98(11) Å ³	
Z	4	
Density (Calcd)	1.312 Mg/m ³	
Absorption coefficient	2.153 mm ⁻¹	
F(000)	640	
Data collection		
Diffractometer	Bruker Apex Kappa Duo, Bruker	
Theta range for data collection	4.863 to 72.452°.	
Index ranges	-9 ≤ h ≤ 11, -9 ≤ k ≤ 13, -15 ≤ l ≤ 13	
Reflections collected	7948	
Independent reflections	2591 [R(int) = 0.0209]	
Observed Reflections	2580	
Solution and Refinement		
Absorption correction	multi-scan	
Max. and min. transmission	0.52 and 0.65	
Solution	Direct methods	
Refinement method	Full-matrix least-squares on F ²	
Weighting scheme	w = 1 / [s ² (F ²) + (AP) ² + 1.18P], where P = (max(Fo ² , 0) + 2Fc ²)/3, A = 0.11, B = 1.18	
Data / restraints / parameters	2580 / 93 / 255	
Goodness-of-fit on F ²	1.002	
Final R indices [I > 2σ(I)]	R1 = 0.0667, wR2 = 0.1909	
R indices (all data)	R1 = 0.0667, wR2 = 0.1909	
Largest diff. peak and hole	0.40 and -0.42 e.Å ⁻³	

Table S6. Atomic coordinates and equivalent isotropic displacement parameters (\AA^2)
for compound **19a**. $U(\text{eq})$ is defined as one third of the trace of the orthogonalized U^{ij} tensor.

Atom	<i>x</i>	<i>y</i>	<i>z</i>	$U_{\text{iso/equiv.}}$
Cl(1)	0.84333(9)	0.56992(9)	0.56245(7)	0.0839
C(2)	0.6798(3)	0.6162(3)	0.5628(2)	0.0625
C(3)	0.6290(4)	0.7225(4)	0.5038(3)	0.0762
N(4)	0.6024(3)	0.8022(4)	0.4607(3)	0.0985
C(5)	0.6048(3)	0.5575(3)	0.6163(2)	0.0603
C(6)	0.4728(3)	0.5893(3)	0.6232(2)	0.0588
C(7)	0.4073(3)	0.5350(2)	0.6856(2)	0.0534
N(8)	0.2819(2)	0.5651(2)	0.69591(19)	0.0607
C(9)	0.2235(3)	0.5204(3)	0.7725(2)	0.0653
C(10)	0.1042(3)	0.4335(2)	0.7419(2)	0.0516
C(11)	0.0986(3)	0.3511(2)	0.6709(2)	0.0509
C(12)	-0.0131(3)	0.2706(2)	0.64242(18)	0.0482
C(13)	-0.1215(3)	0.2763(2)	0.68919(19)	0.0514
C(14)	-0.1123(3)	0.3612(3)	0.7641(2)	0.0563
C(15)	-0.0036(3)	0.4372(3)	0.7892(2)	0.0564
C(16)	-0.2350(3)	0.1974(3)	0.6598(2)	0.0655
C(17)	-0.2390(4)	0.1175(3)	0.5877(3)	0.0731
C(18)	-0.1316(4)	0.1099(3)	0.5426(2)	0.0682
C(19)	-0.0210(3)	0.1851(3)	0.5678(2)	0.0588
C(20)	0.2054(3)	0.6582(3)	0.6351(3)	0.0746
C(21)	0.4747(3)	0.4368(3)	0.7450(2)	0.0624
N(22)	0.5296(3)	0.3587(3)	0.7898(3)	0.0919

Table S7. Bond lengths [Å] and angles [°] for compound **19a**.

Cl(1)-C(2)	1.728(3)	C(12)-C(13)	1.414(4)
C(2)-C(3)	1.458(5)	C(12)-C(19)	1.418(4)
C(2)-C(5)	1.357(4)	C(13)-C(14)	1.417(4)
C(3)-N(4)	1.064(4)	C(13)-C(16)	1.417(4)
C(5)-C(6)	1.403(4)	C(14)-C(15)	1.356(4)
C(5)-H(51)	0.927(17)	C(14)-H(141)	0.933(17)
C(6)-C(7)	1.370(4)	C(15)-H(151)	0.919(17)
C(6)-H(61)	0.935(17)	C(16)-C(17)	1.358(5)
C(7)-N(8)	1.348(4)	C(16)-H(161)	0.927(18)
C(7)-C(21)	1.444(4)	C(17)-C(18)	1.391(5)
N(8)-C(9)	1.459(4)	C(17)-H(171)	0.915(18)
N(8)-C(20)	1.450(4)	C(18)-C(19)	1.364(4)
C(9)-C(10)	1.516(4)	C(18)-H(181)	0.916(18)
C(9)-H(91)	0.966(18)	C(19)-H(191)	0.926(18)
C(9)-H(92)	0.962(17)	C(20)-H(201)	0.965(18)
C(10)-C(11)	1.359(4)	C(20)-H(202)	0.953(18)
C(10)-C(15)	1.412(4)	C(20)-H(203)	0.951(18)
C(11)-C(12)	1.413(4)	C(21)-N(22)	1.134(4)
C(11)-H(111)	0.912(17)		
Cl(1)-C(2)-C(3)	116.0(2)	C(13)-C(12)-C(19)	118.8(3)
Cl(1)-C(2)-C(5)	121.5(3)	C(12)-C(13)-C(14)	118.4(2)
C(3)-C(2)-C(5)	122.5(3)	C(12)-C(13)-C(16)	119.2(3)
C(2)-C(3)-N(4)	174.2(4)	C(14)-C(13)-C(16)	122.4(3)
C(2)-C(5)-C(6)	126.0(3)	C(13)-C(14)-C(15)	120.9(3)
C(2)-C(5)-H(51)	118.2(12)	C(13)-C(14)-H(141)	119.5(12)
C(6)-C(5)-H(51)	115.8(12)	C(15)-C(14)-H(141)	119.6(12)
C(5)-C(6)-C(7)	123.3(3)	C(10)-C(15)-C(14)	121.0(3)
C(5)-C(6)-H(61)	114.9(12)	C(10)-C(15)-H(151)	119.1(12)

C(7)-C(6)-H(61)	121.8(12)	C(14)-C(15)-H(151)	119.9(12)
C(6)-C(7)-N(8)	125.0(3)	C(13)-C(16)-C(17)	120.2(3)
C(6)-C(7)-C(21)	118.8(3)	C(13)-C(16)-H(161)	119.1(12)
N(8)-C(7)-C(21)	116.2(3)	C(17)-C(16)-H(161)	120.8(12)
C(7)-N(8)-C(9)	123.6(3)	C(16)-C(17)-C(18)	120.8(3)
C(7)-N(8)-C(20)	119.2(3)	C(16)-C(17)-H(171)	119.3(12)
C(9)-N(8)-C(20)	116.9(3)	C(18)-C(17)-H(171)	119.9(12)
N(8)-C(9)-C(10)	113.6(3)	C(17)-C(18)-C(19)	120.9(3)
N(8)-C(9)-H(91)	108.9(13)	C(17)-C(18)-H(181)	120.6(12)
C(10)-C(9)-H(91)	107.8(13)	C(19)-C(18)-H(181)	118.5(12)
N(8)-C(9)-H(92)	109.0(13)	C(12)-C(19)-C(18)	120.1(3)
C(10)-C(9)-H(92)	107.8(13)	C(12)-C(19)-H(191)	120.6(12)
H(91)-C(9)-H(92)	109.8(15)	C(18)-C(19)-H(191)	119.4(12)
C(9)-C(10)-C(11)	121.9(3)	N(8)-C(20)-H(201)	110.6(15)
C(9)-C(10)-C(15)	119.1(3)	N(8)-C(20)-H(202)	109.8(15)
C(11)-C(10)-C(15)	119.1(3)	H(201)-C(20)-H(202)	109.7(16)
C(10)-C(11)-C(12)	121.7(3)	N(8)-C(20)-H(203)	110.6(15)
C(10)-C(11)-H(111)	120.1(11)	H(201)-C(20)-H(203)	107.3(16)
C(12)-C(11)-H(111)	118.2(11)	H(202)-C(20)-H(203)	108.7(16)
C(11)-C(12)-C(13)	118.9(2)	C(7)-C(21)-N(22)	178.0(4)
C(11)-C(12)-C(19)	122.3(3)		

Table S8. Anisotropic displacement parameters (\AA^2) for compound **19a**. The anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2 a^{*2}U^{11} + \dots + 2 h k a^* b^* U^{12}]$.

Label	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
C11	0.0739(6)	0.0904(6)	0.0911(7)	0.0183(5)	0.0259(5)	0.0054(4)
C2	0.0711(19)	0.0621(16)	0.0548(18)	0.0034(14)	0.0148(15)	-0.0090(14)
C3	0.077(2)	0.082(2)	0.077(2)	0.0035(19)	0.0347(19)	-0.0092(18)
N4	0.086(2)	0.105(2)	0.110(3)	0.053(2)	0.0324(19)	0.0244(18)
C5	0.0686(19)	0.0537(15)	0.0569(18)	0.0022(13)	0.0096(14)	-0.0040(13)
C6	0.0554(17)	0.0566(15)	0.0640(19)	-0.0020(13)	0.0118(14)	-0.0058(12)
C7	0.0498(15)	0.0508(13)	0.0589(17)	-0.0077(12)	0.0099(13)	-0.0104(11)
N8	0.0499(14)	0.0591(14)	0.0740(18)	-0.0005(11)	0.0153(12)	-0.0046(10)
C9	0.0545(17)	0.077(2)	0.066(2)	-0.0153(16)	0.0169(15)	-0.0050(14)
C10	0.0462(14)	0.0557(14)	0.0527(17)	0.0003(12)	0.0101(12)	0.0042(11)
C11	0.0433(13)	0.0565(14)	0.0558(17)	0.0035(12)	0.0172(12)	0.0050(10)
C12	0.0489(14)	0.0443(12)	0.0515(16)	0.0080(11)	0.0111(12)	0.0074(10)
C13	0.0491(14)	0.0485(13)	0.0572(17)	0.0111(11)	0.0126(12)	0.0048(10)
C14	0.0528(16)	0.0591(15)	0.0637(18)	0.0045(13)	0.0271(14)	0.0062(12)
C15	0.0563(17)	0.0603(16)	0.0564(17)	-0.0043(13)	0.0206(14)	0.0063(12)
C16	0.0556(17)	0.0623(16)	0.081(2)	0.0086(16)	0.0192(15)	-0.0038(13)
C17	0.067(2)	0.0620(17)	0.086(2)	0.0016(17)	0.0068(18)	-0.0148(14)
C18	0.081(2)	0.0532(16)	0.067(2)	-0.0060(14)	0.0075(17)	-0.0024(14)
C19	0.0665(18)	0.0537(14)	0.0583(18)	0.0010(13)	0.0175(14)	0.0076(12)
C20	0.0612(18)	0.0588(17)	0.101(3)	0.0002(17)	0.0110(18)	0.0011(14)
C21	0.0477(16)	0.0686(18)	0.074(2)	0.0037(15)	0.0207(15)	-0.0060(13)
N22	0.0738(19)	0.095(2)	0.110(3)	0.037(2)	0.0270(18)	0.0089(17)

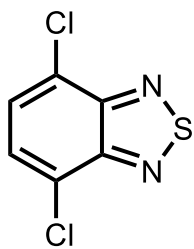
Table S9. Hydrogen coordinates and displacement parameters (\AA^2) for compound **19a**.

Label	<i>x</i>	<i>y</i>	<i>z</i>	$U_{\text{iso/equiv}}$
H51	0.6433(18)	0.4909(14)	0.6527(10)	0.0721(19)
H61	0.4331(18)	0.6531(14)	0.5833(10)	0.0710(19)
H91	0.193(2)	0.5913(18)	0.8029(16)	0.0775(19)
H92	0.292(2)	0.476(2)	0.8159(15)	0.0781(19)
H111	0.1678(17)	0.3469(13)	0.6401(10)	0.0606(19)
H141	-0.1819(17)	0.3646(14)	0.7968(11)	0.0674(19)
H151	-0.0003(17)	0.4937(14)	0.8366(10)	0.0679(19)
H161	-0.3061(17)	0.2013(14)	0.6905(11)	0.0786(19)
H171	-0.3140(18)	0.0687(14)	0.5683(11)	0.0884(19)
H181	-0.1327(18)	0.0529(14)	0.4960(11)	0.0820(19)
H191	0.0475(17)	0.1808(14)	0.5351(11)	0.0701(19)
H201	0.115(2)	0.665(3)	0.646(2)	0.112(2)
H202	0.250(3)	0.7369(19)	0.645(2)	0.1115(19)
H203	0.197(3)	0.635(2)	0.5717(14)	0.112(2)

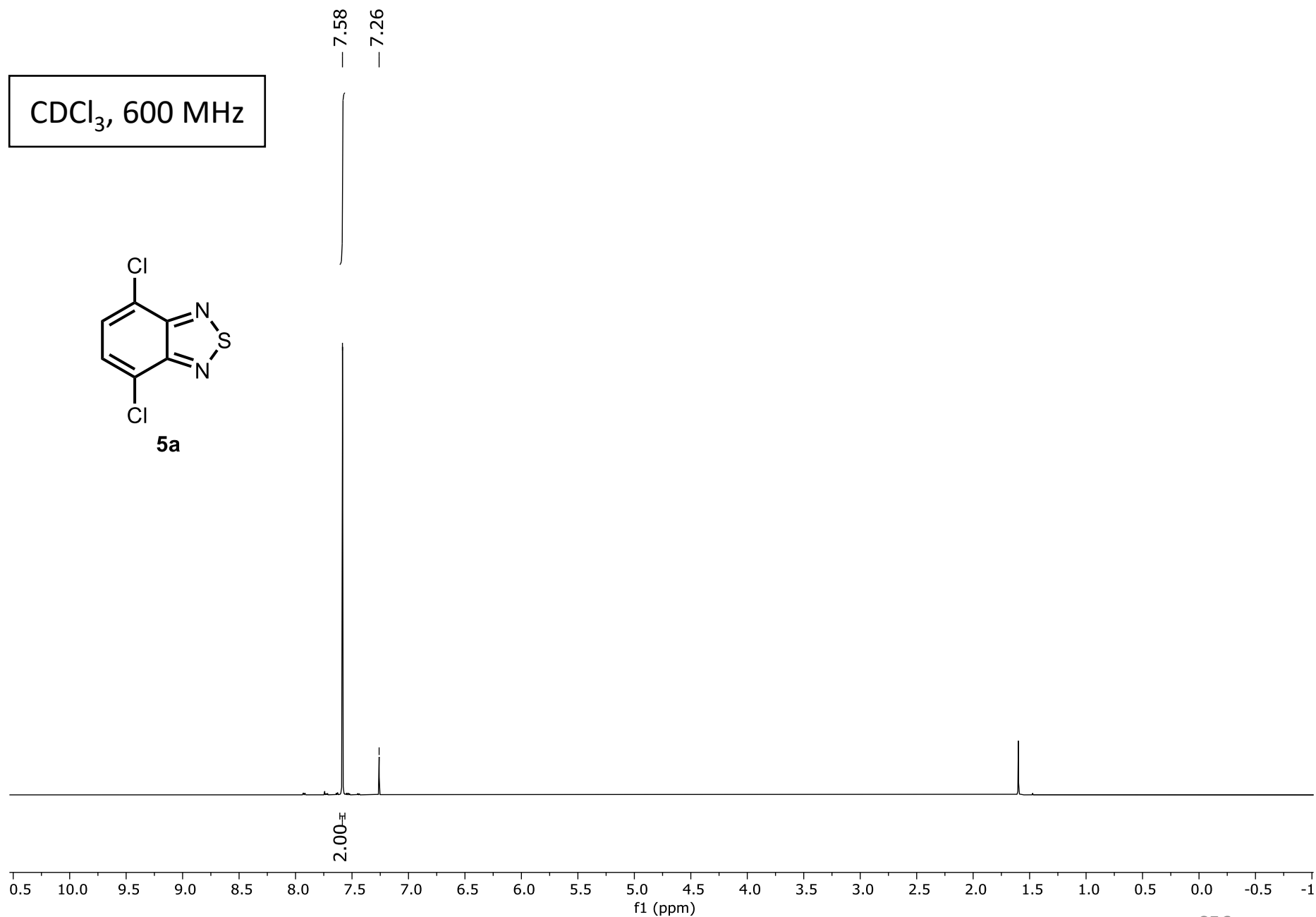
XII. References

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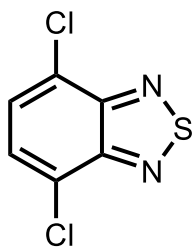
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5a



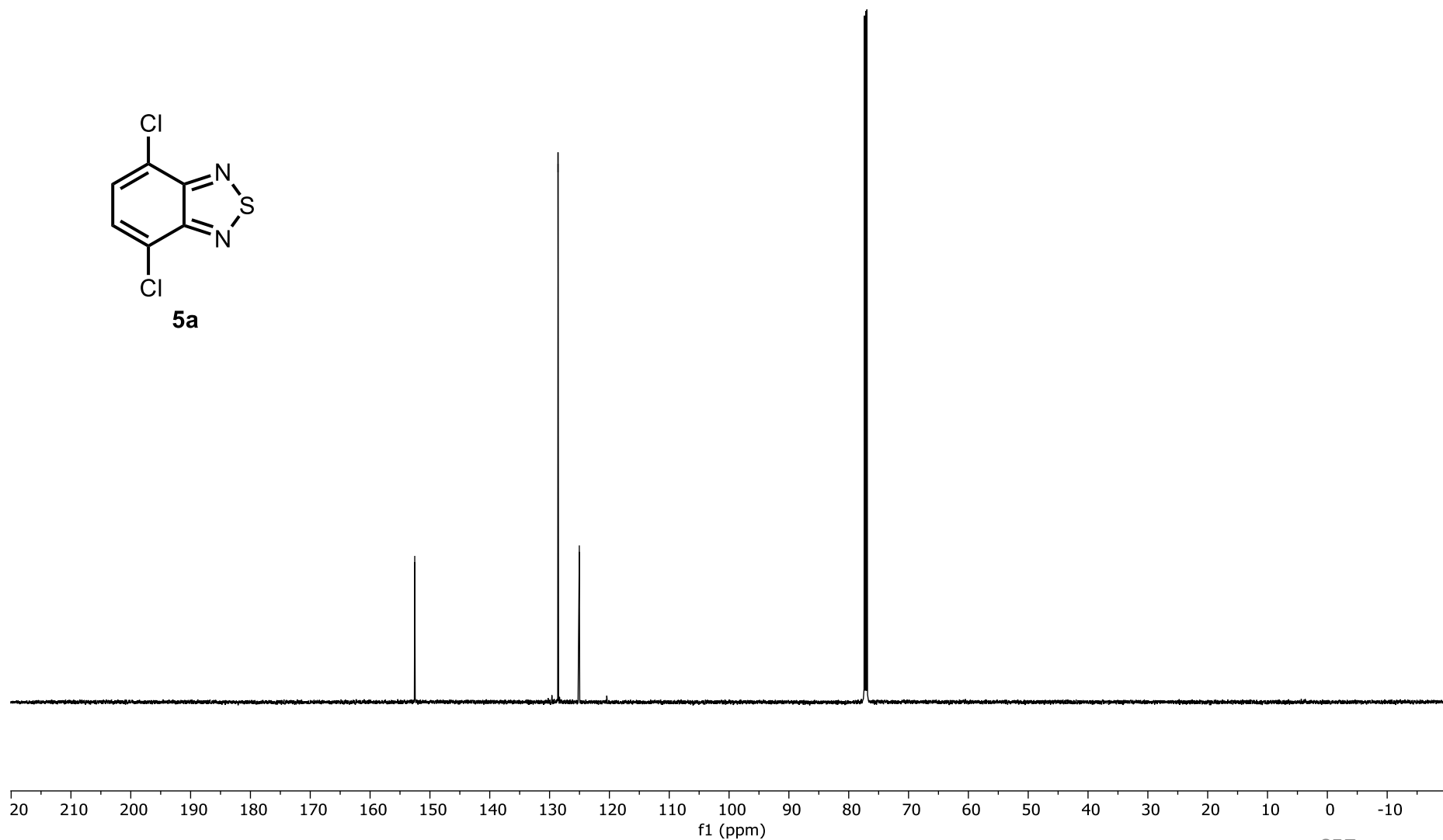
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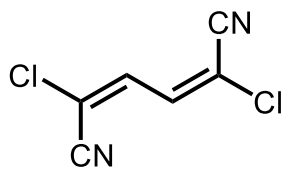
5a

— 152.5

— 128.6
— 125.0



CDCl₃, 600 MHz



3a

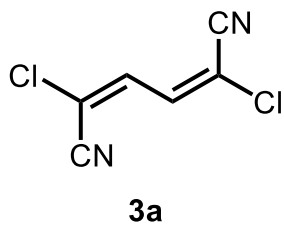
7.27
7.26

2.00

f1 (ppm)

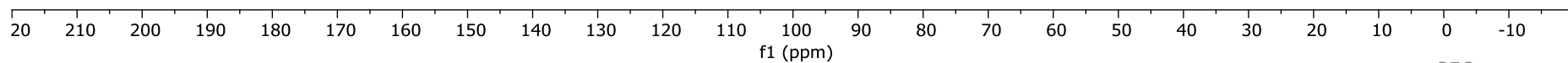
S58

CDCl₃, 151 MHz

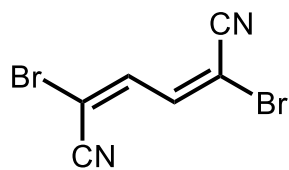


— 137.7

~ 112.5
~ 111.1



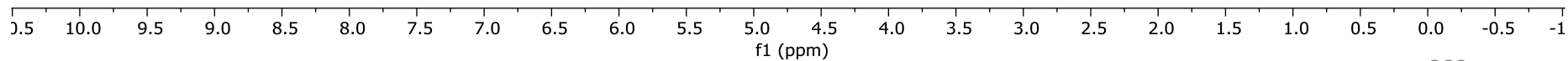
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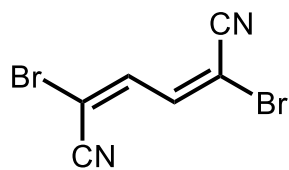
3b

7.44
7.26

2.00



CDCl₃, 151 MHz

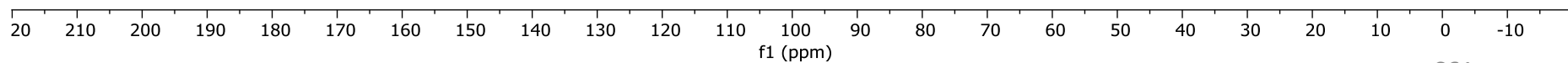


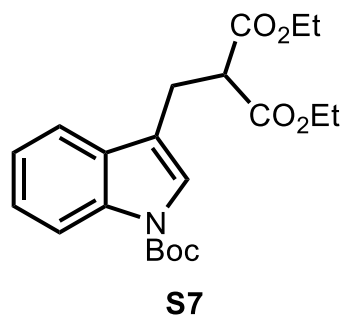
3b

— 142.34

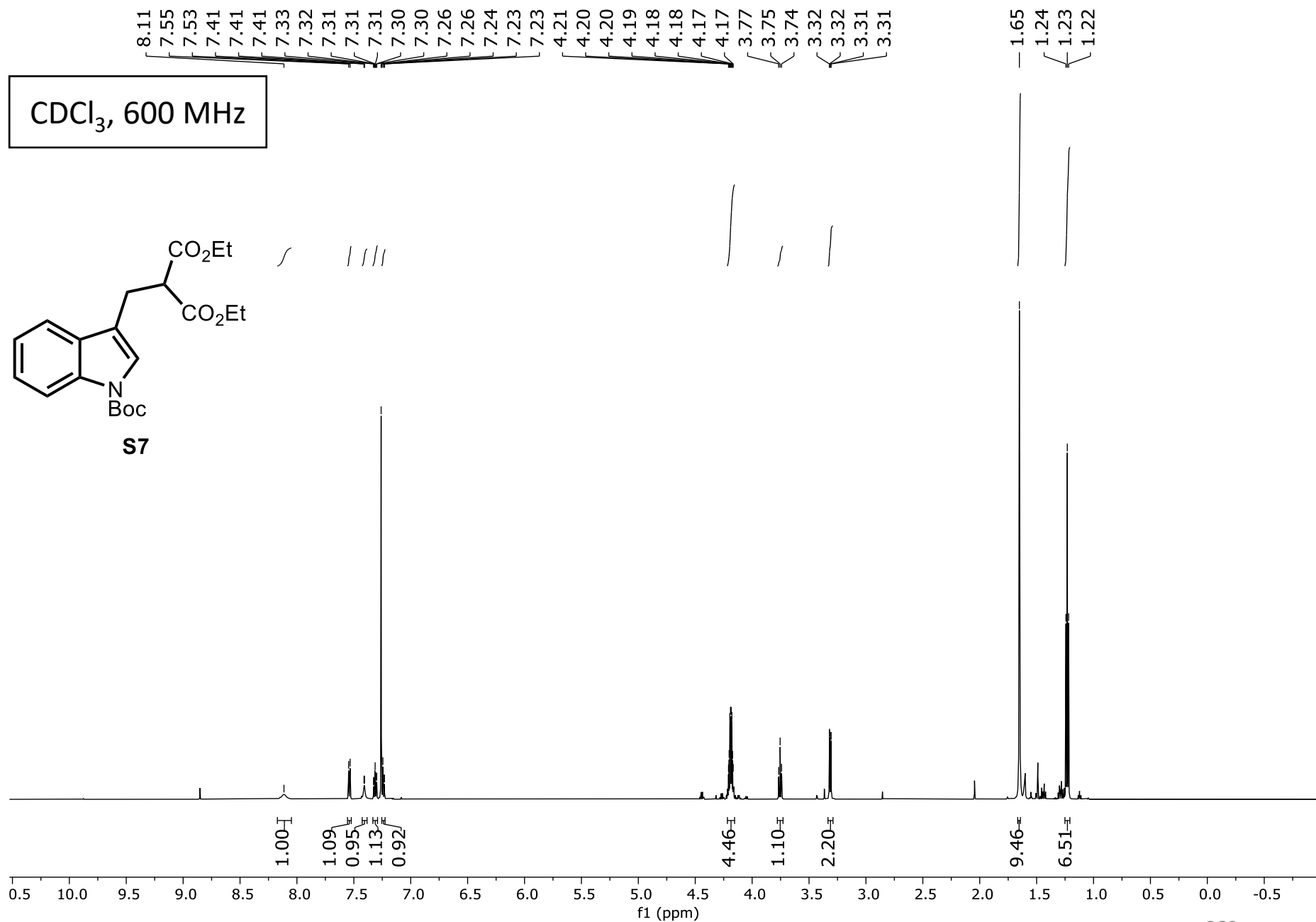
— 113.49

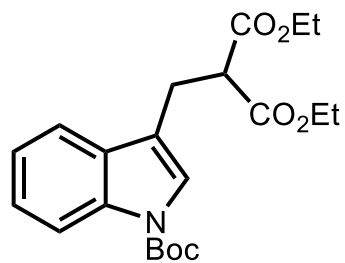
— 96.47





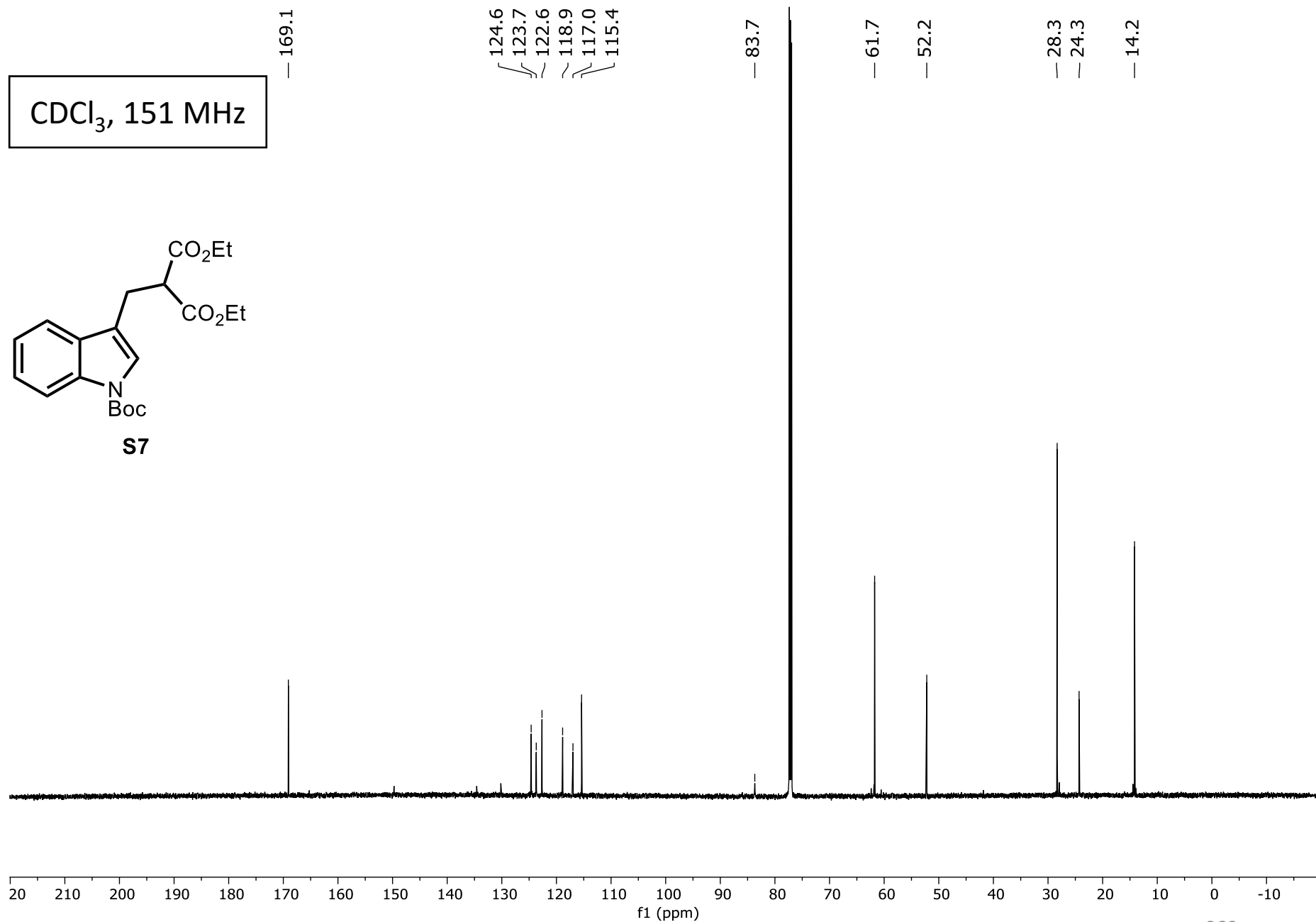
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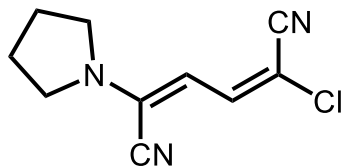
S7

CDCl₃, 151 MHz

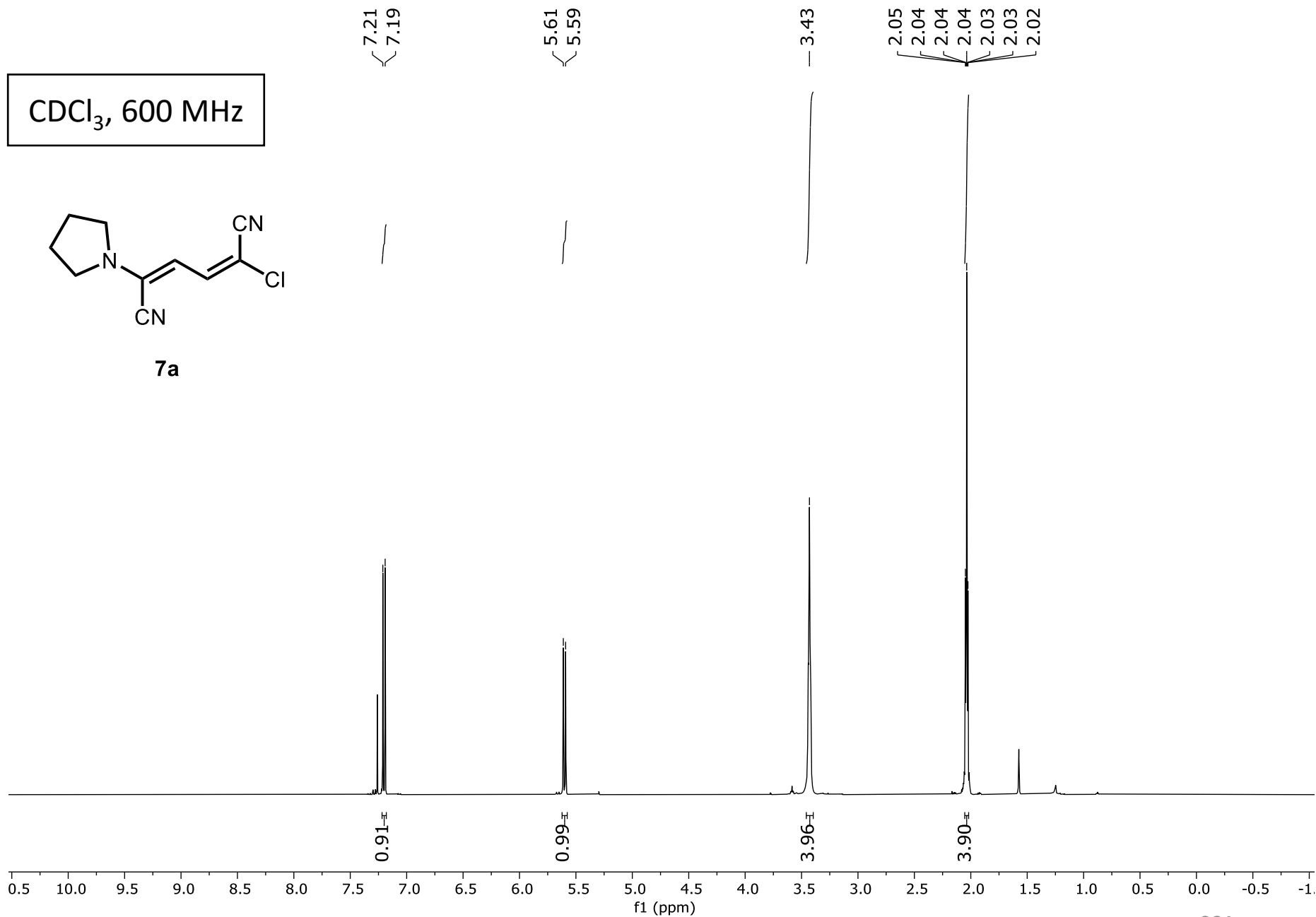


S63

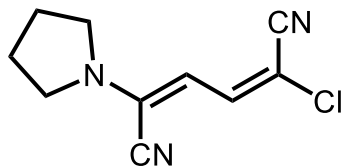
CDCl₃, 600 MHz



7a



CDCl₃, 151 MHz



7a

— 142.5

— 126.5

~ 115.5

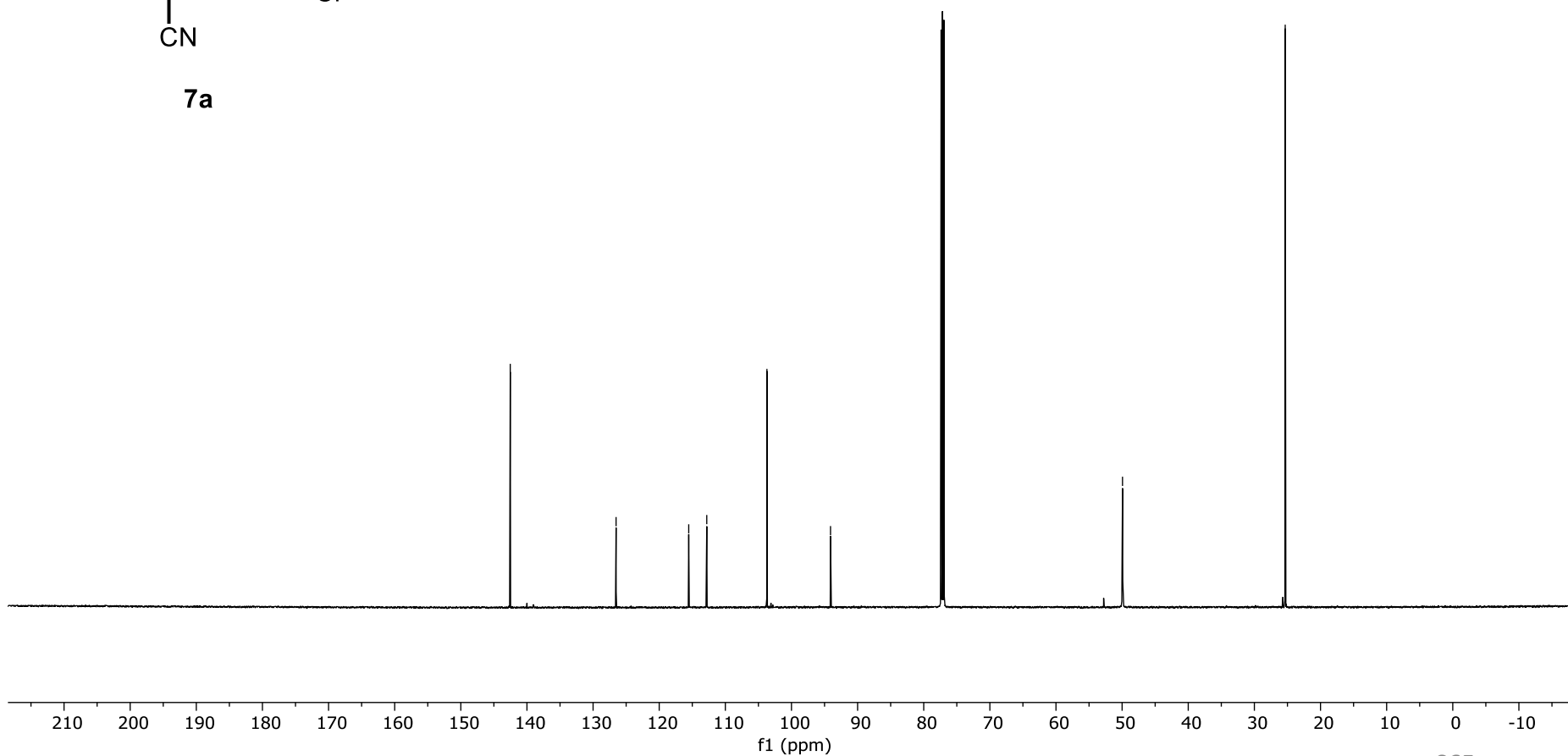
~ 112.8

— 103.7

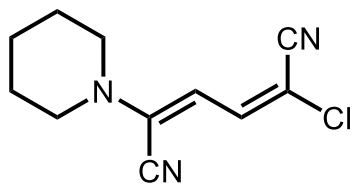
— 94.1

— 49.9

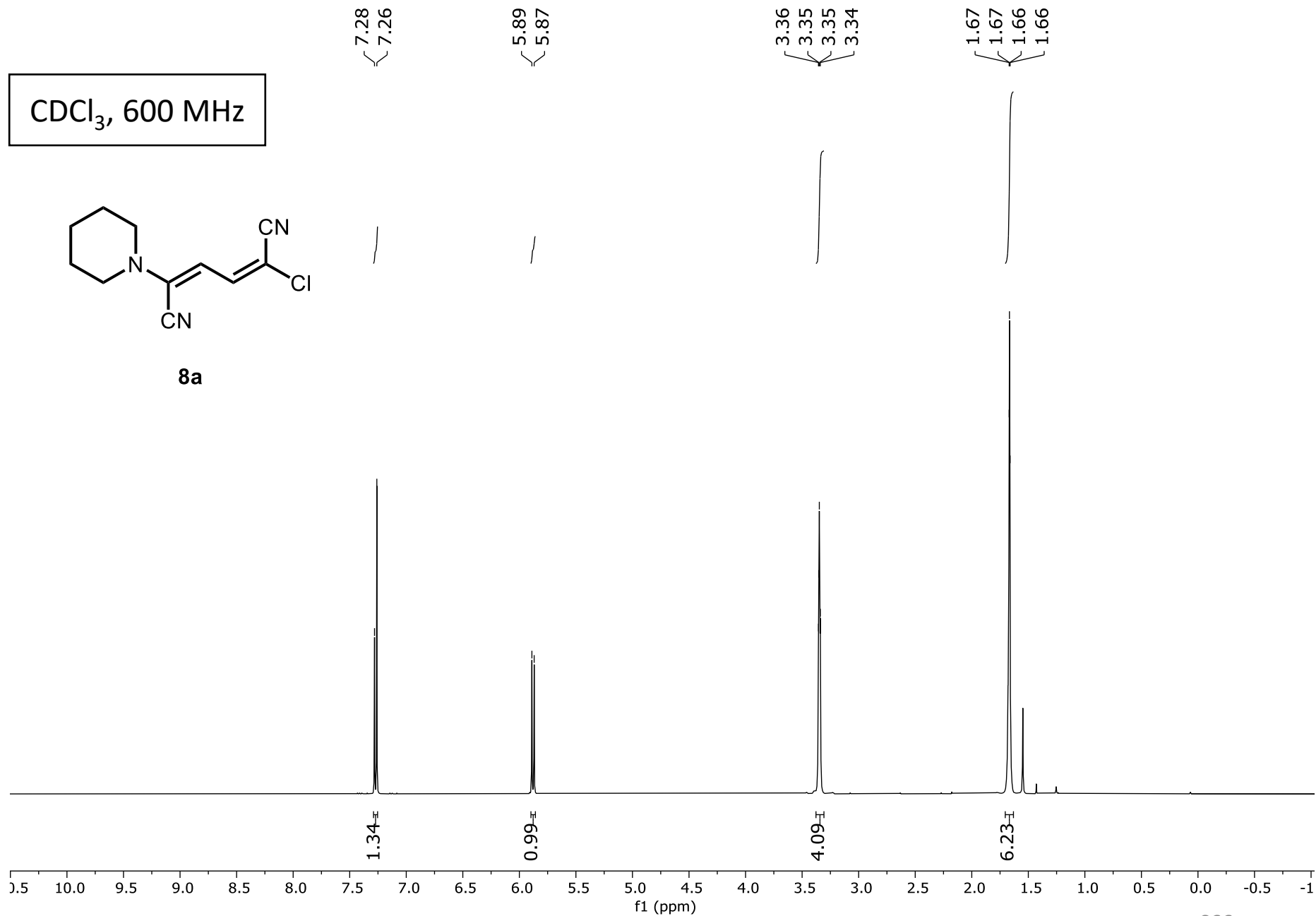
— 25.3



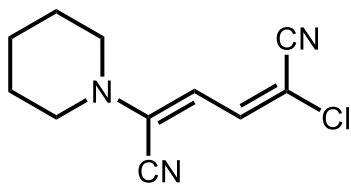
CDCl₃, 600 MHz



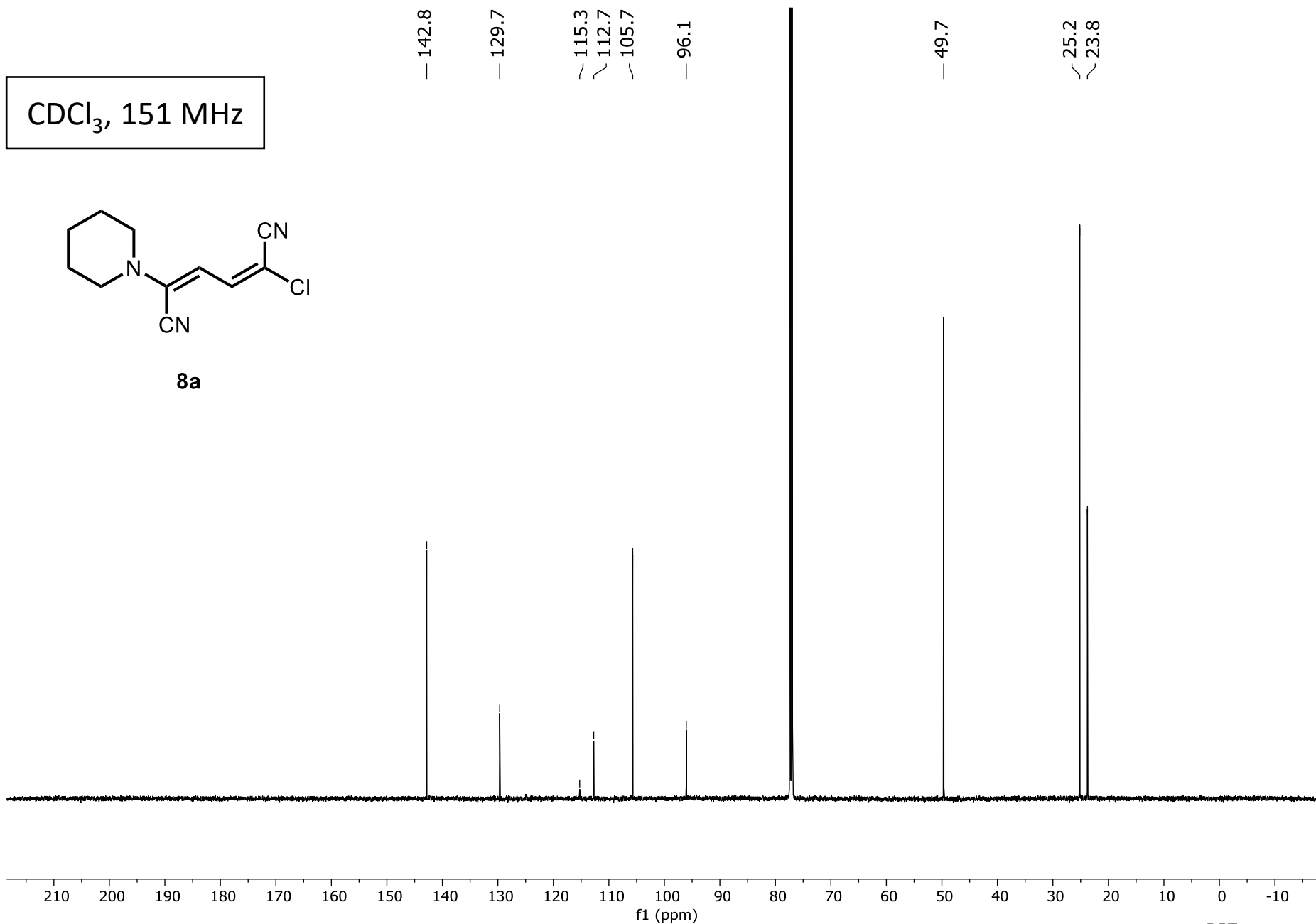
8a



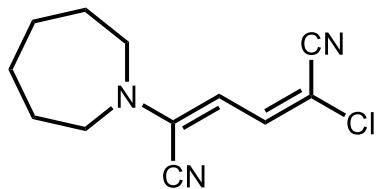
CDCl₃, 151 MHz



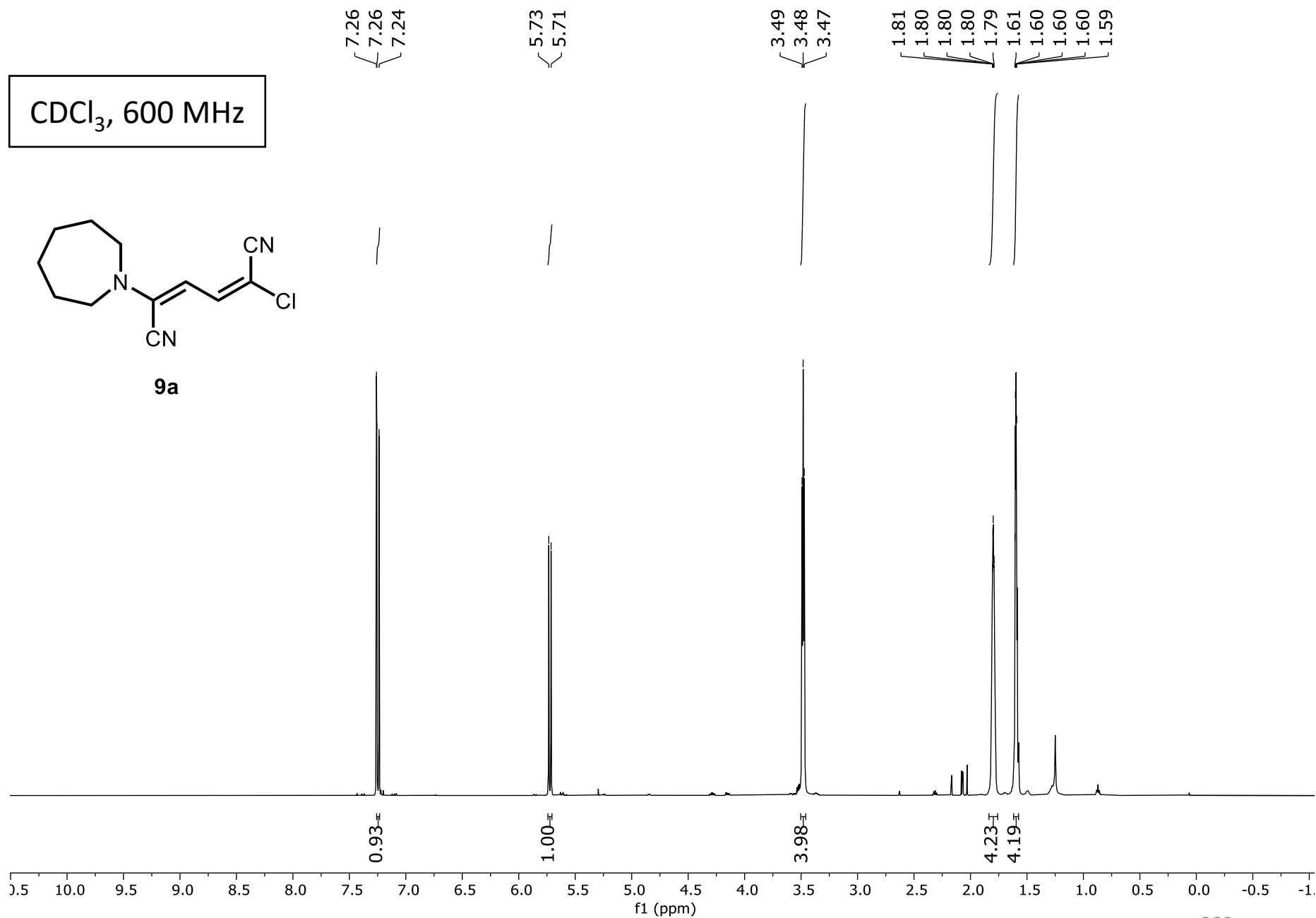
8a



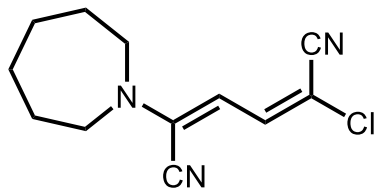
CDCl₃, 600 MHz



9a



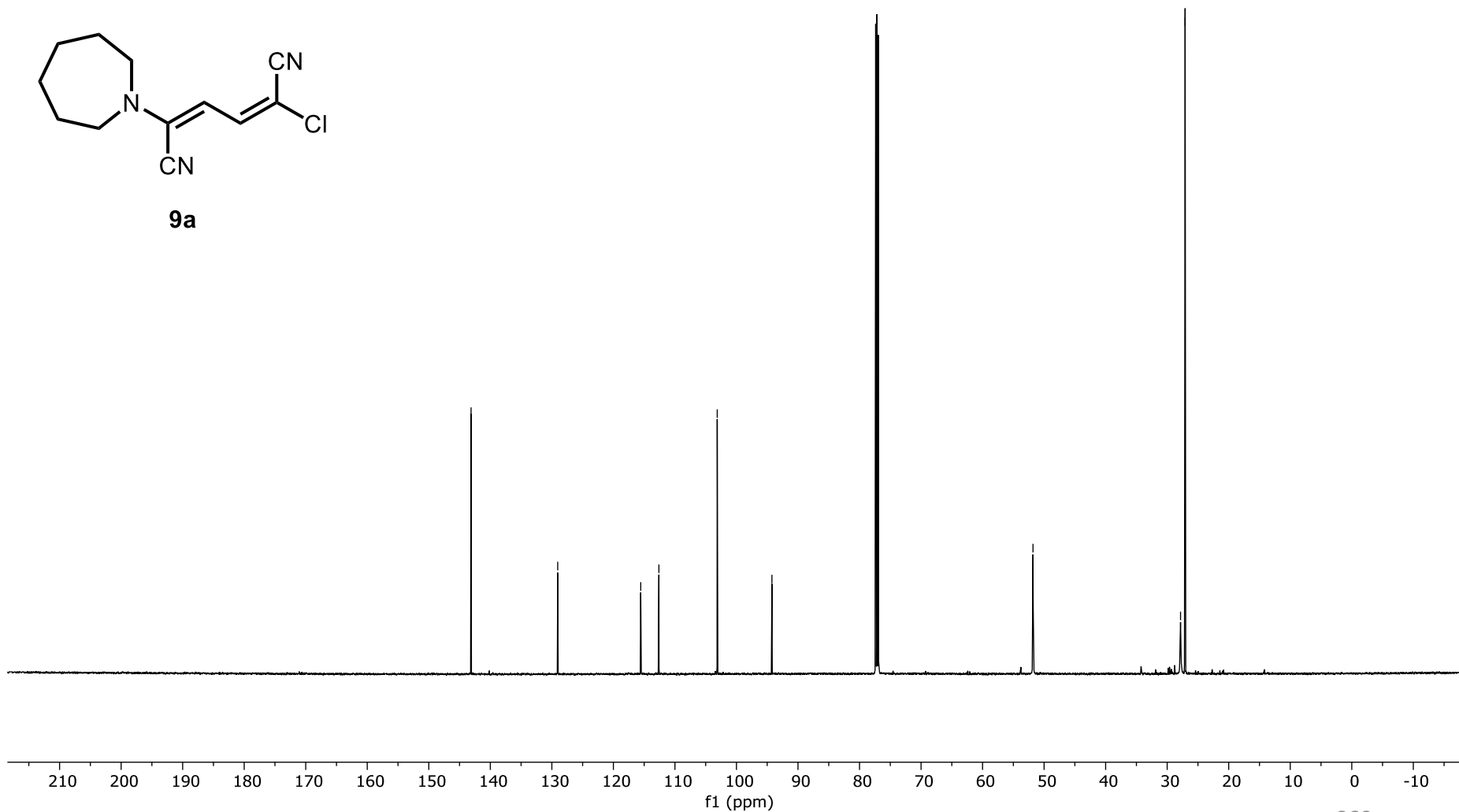
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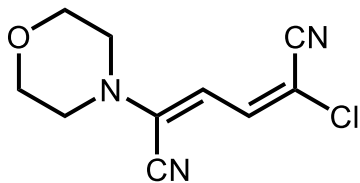
9a

— 143.1
— 129.0
~ 115.6
~ 112.6
— 103.1
— 94.2

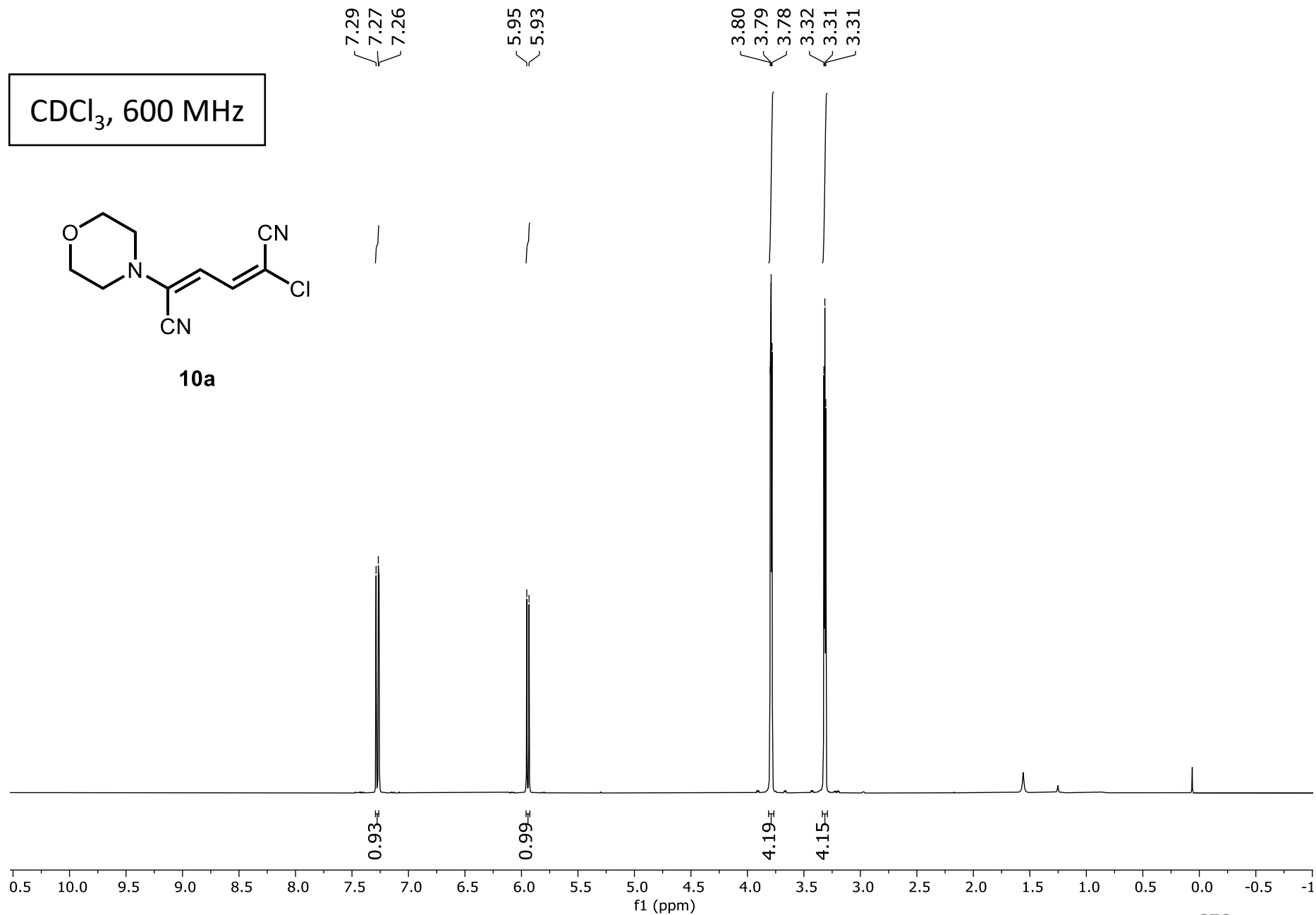
— 51.8
~ 27.8
~ 27.1



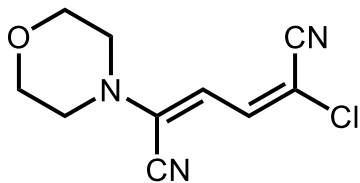
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10a

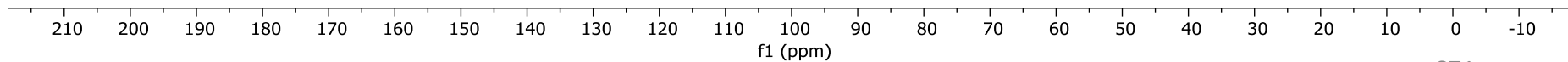


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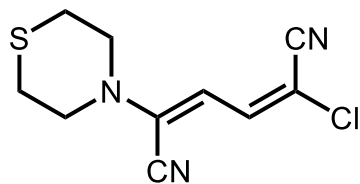


10a

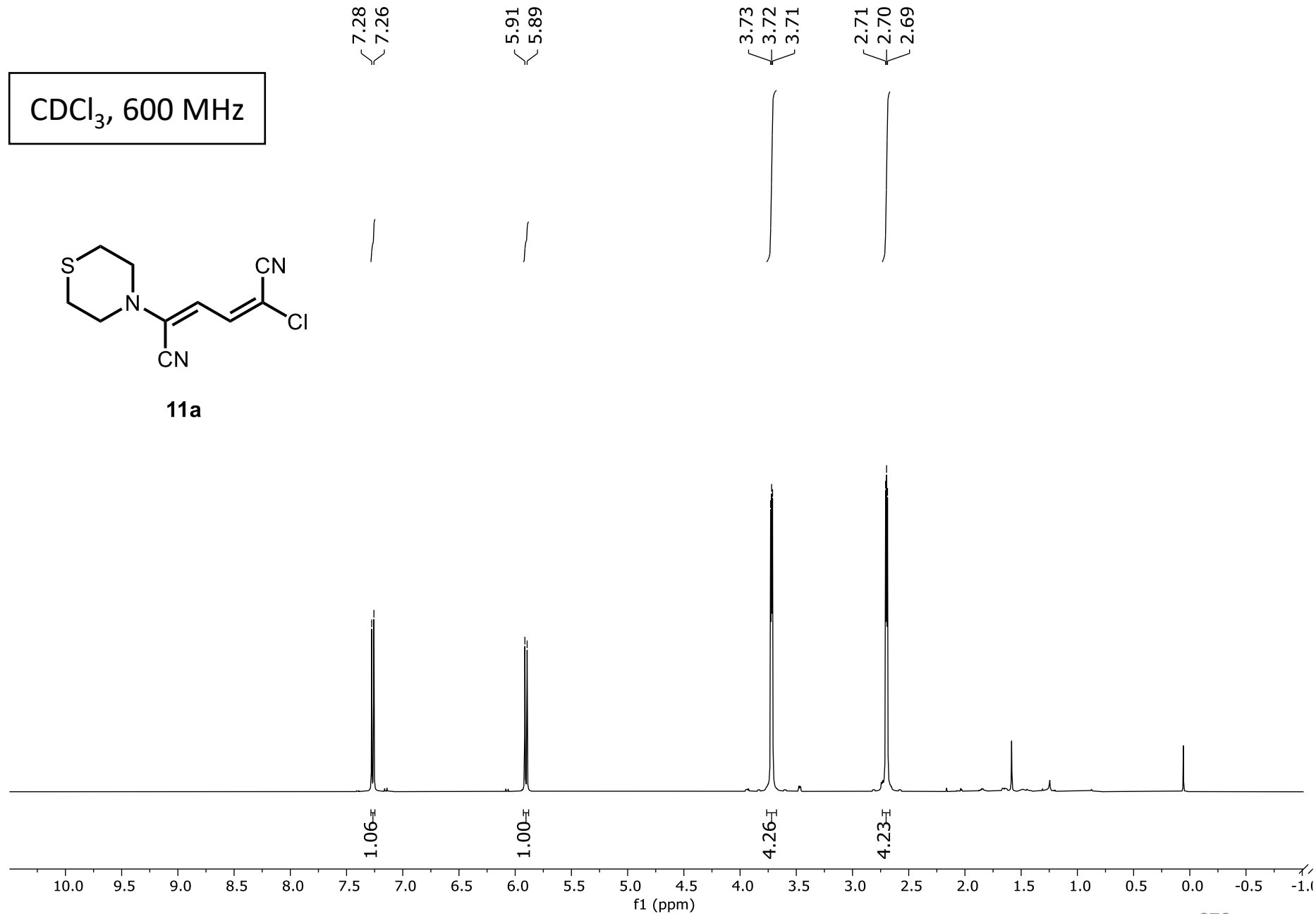
— 141.9
— 129.7
~ 114.7
~ 112.3
~ 107.4
— 98.6
— 65.8
— 48.3



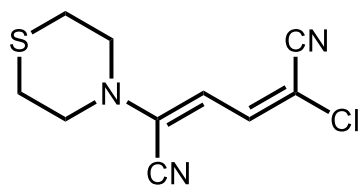
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11a



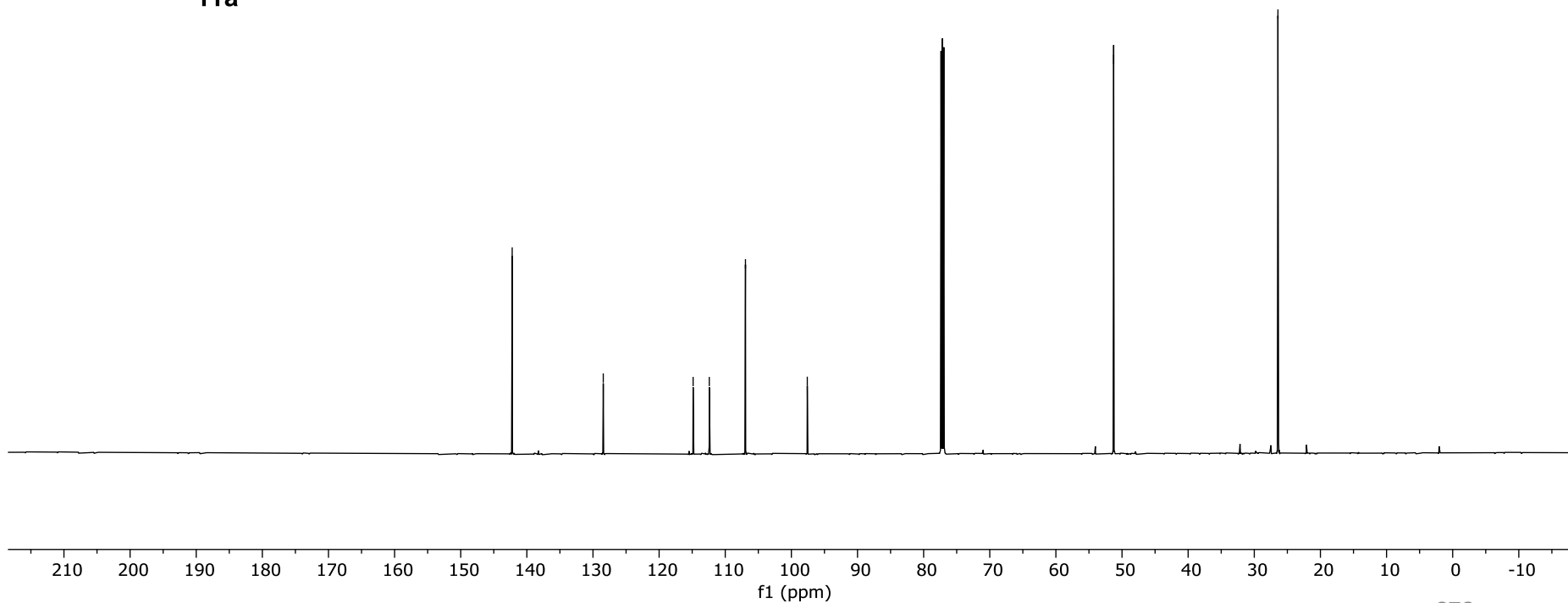
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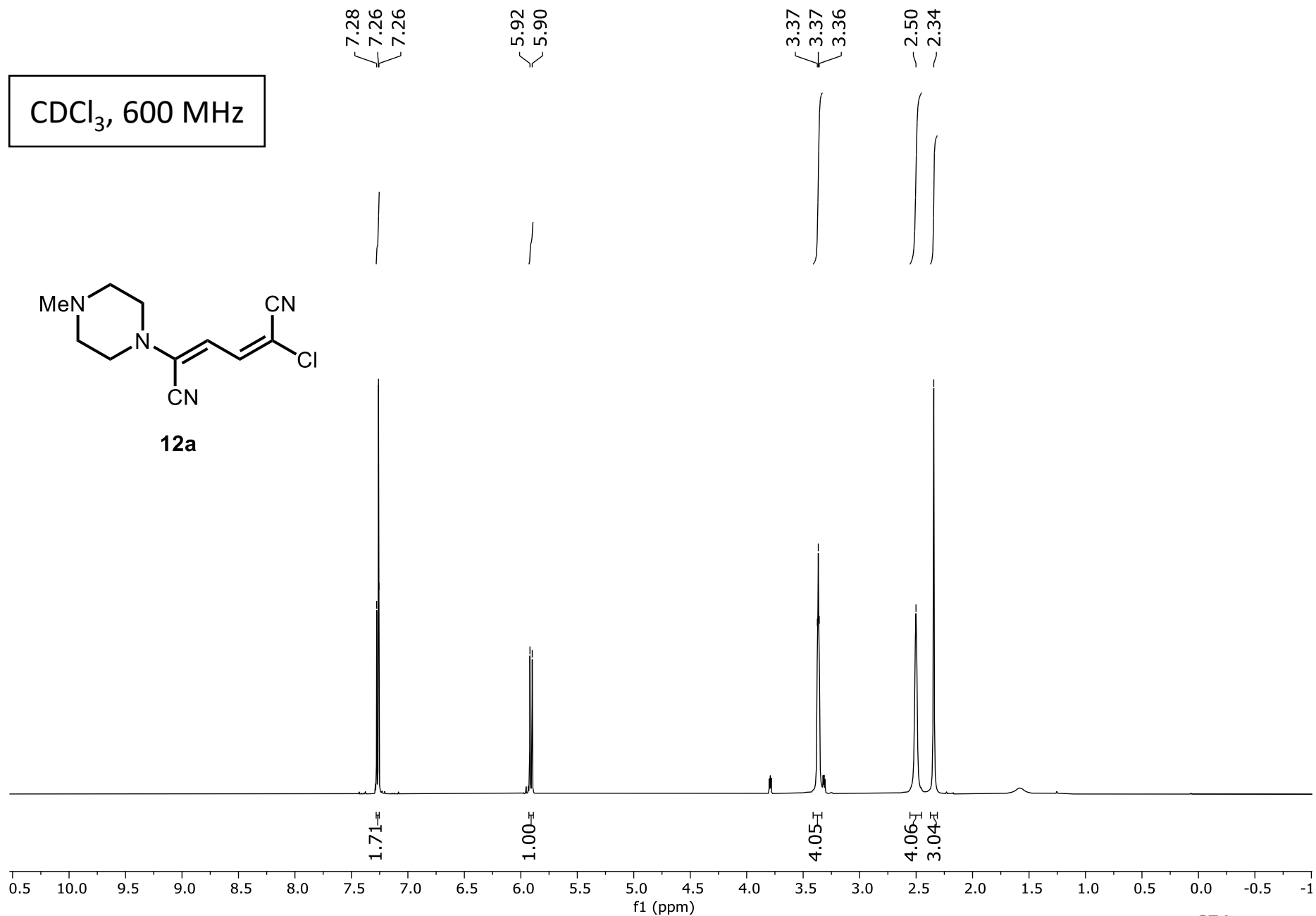
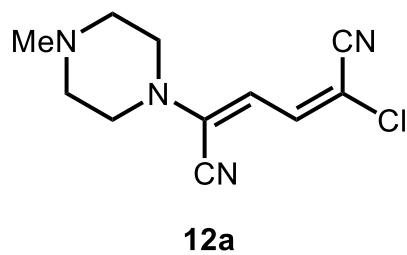
11a

— 142.2
— 128.4
— 114.9
— 112.4
— 106.9
— 97.6

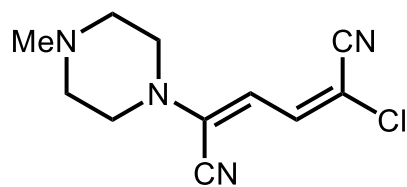
— 51.3
— 26.4



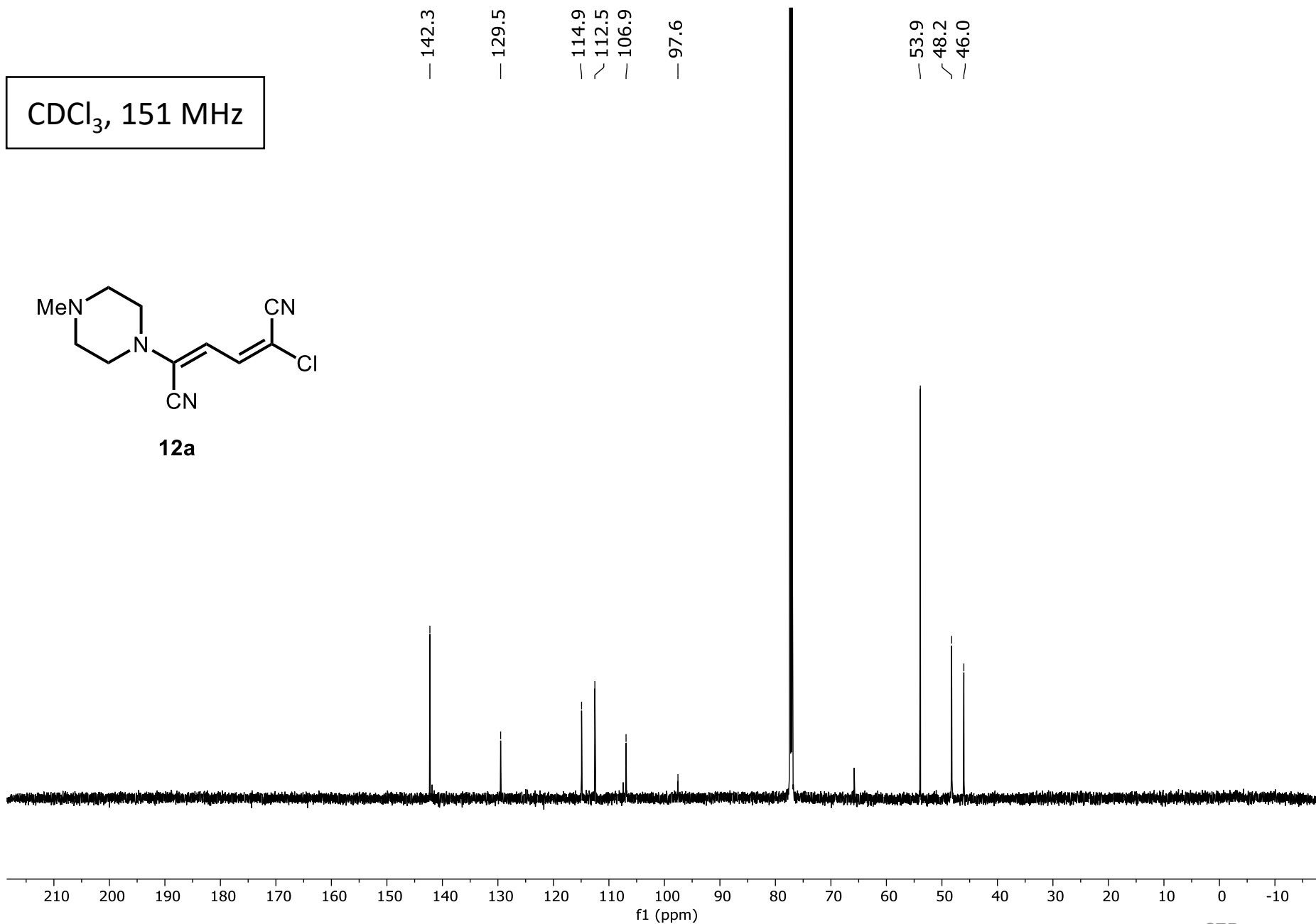
CDCl₃, 600 MHz



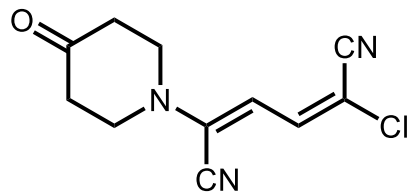
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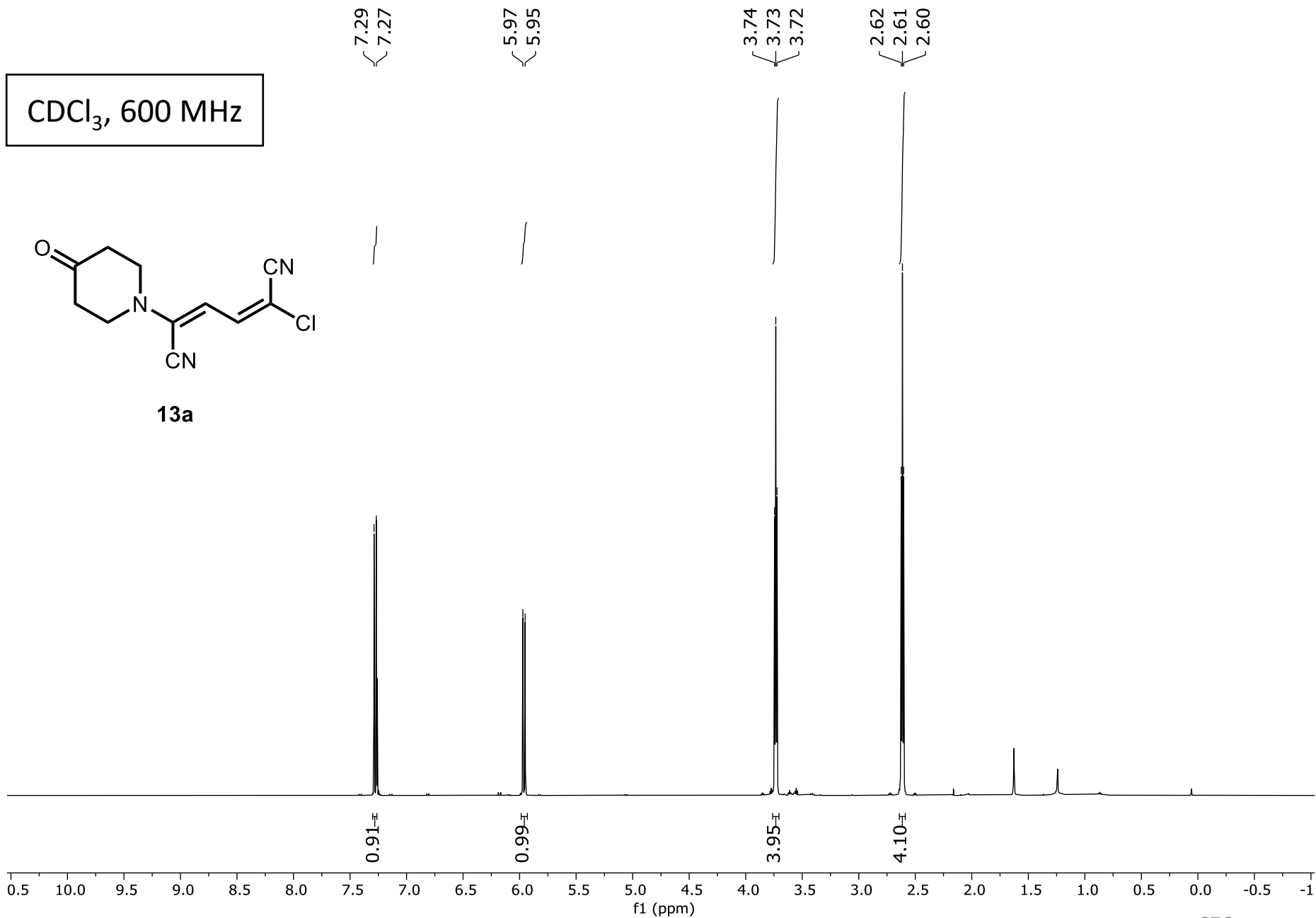
12a

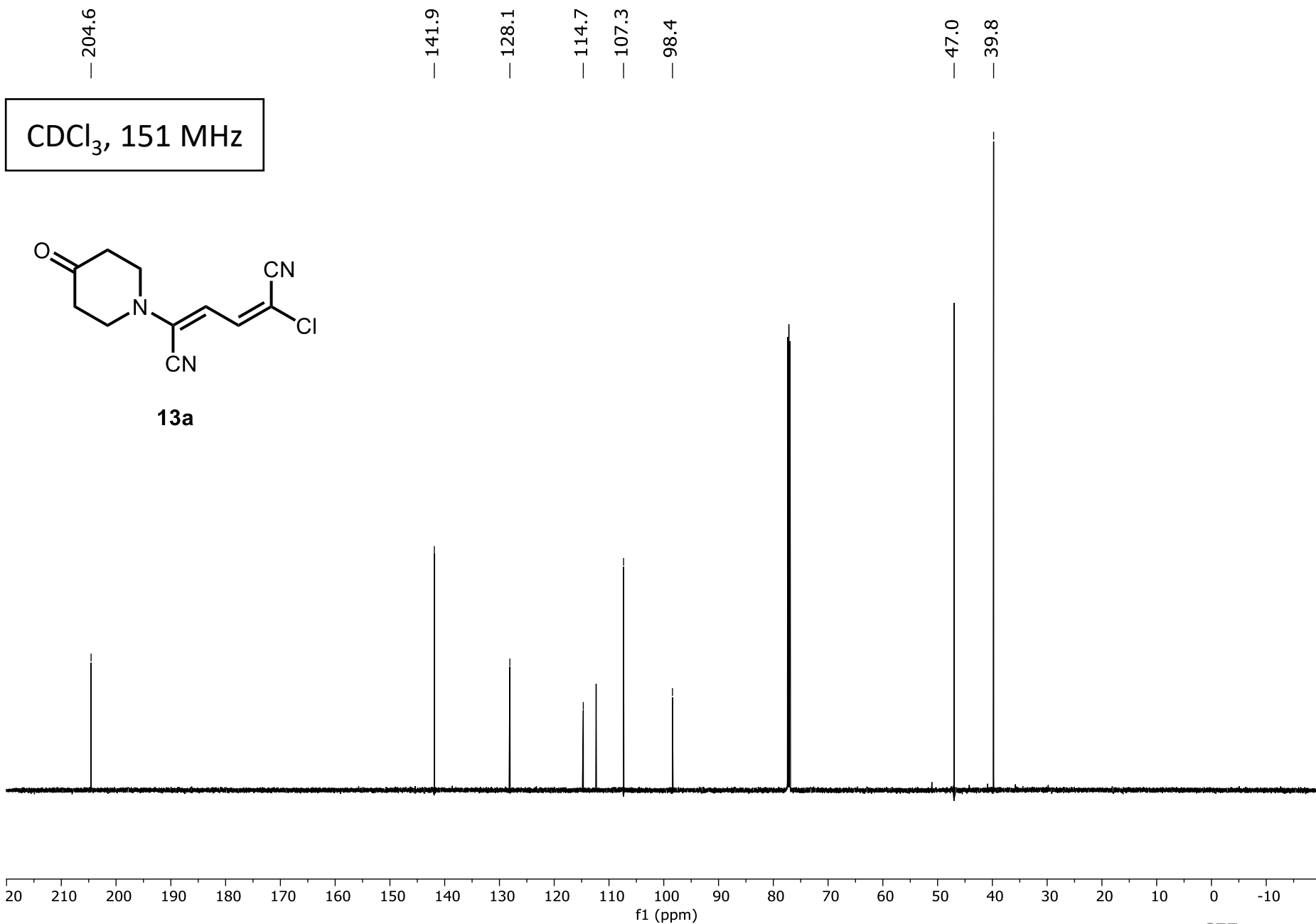


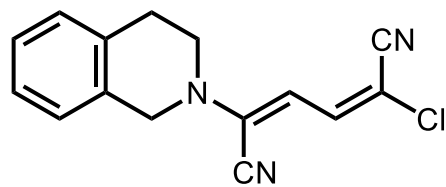
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13a

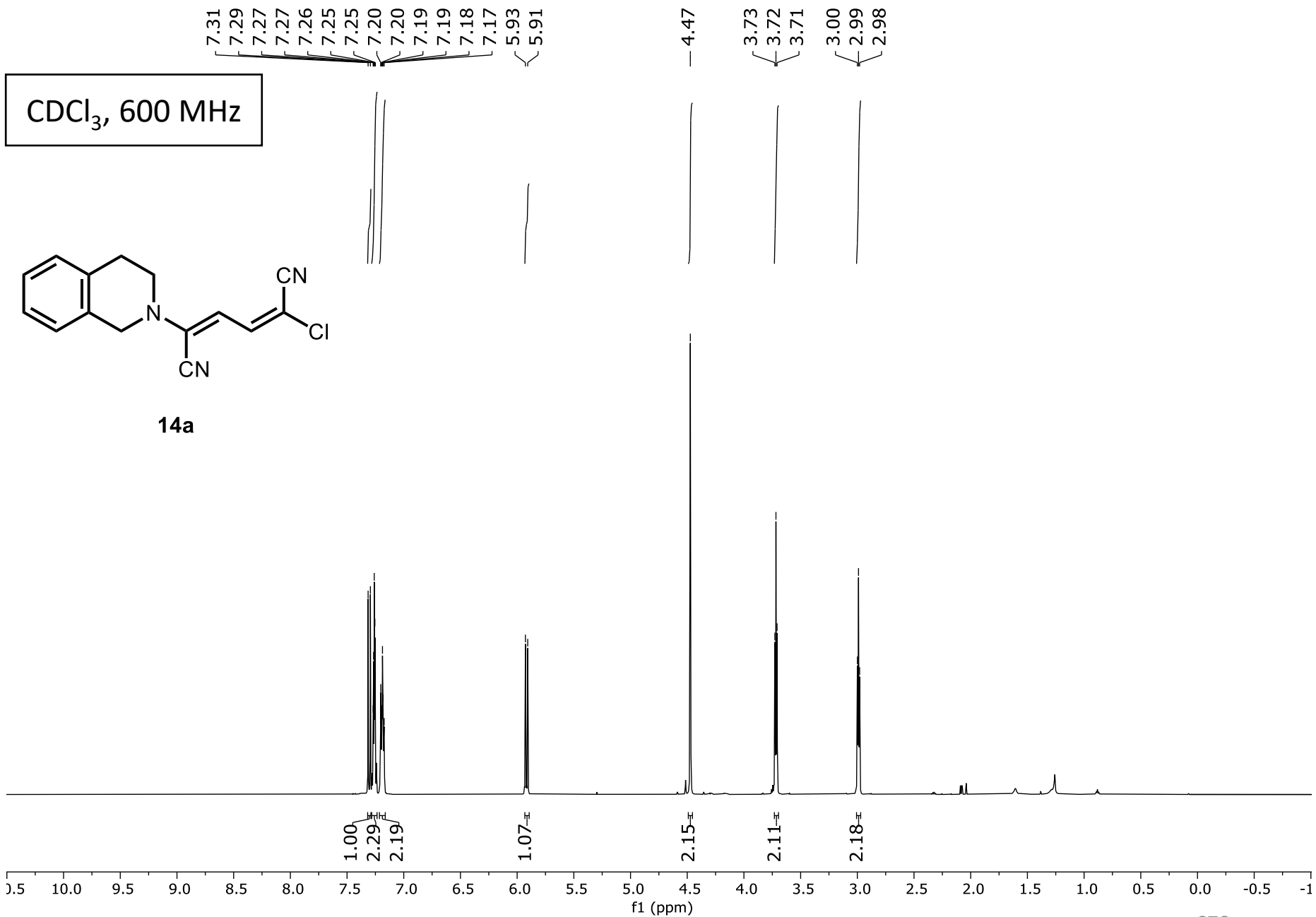




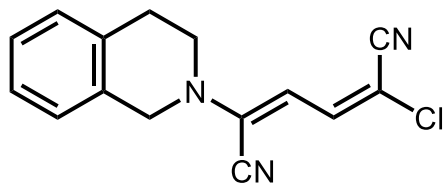


14a

CDCl₃, 600 MHz



CDCl₃, 151 MHz

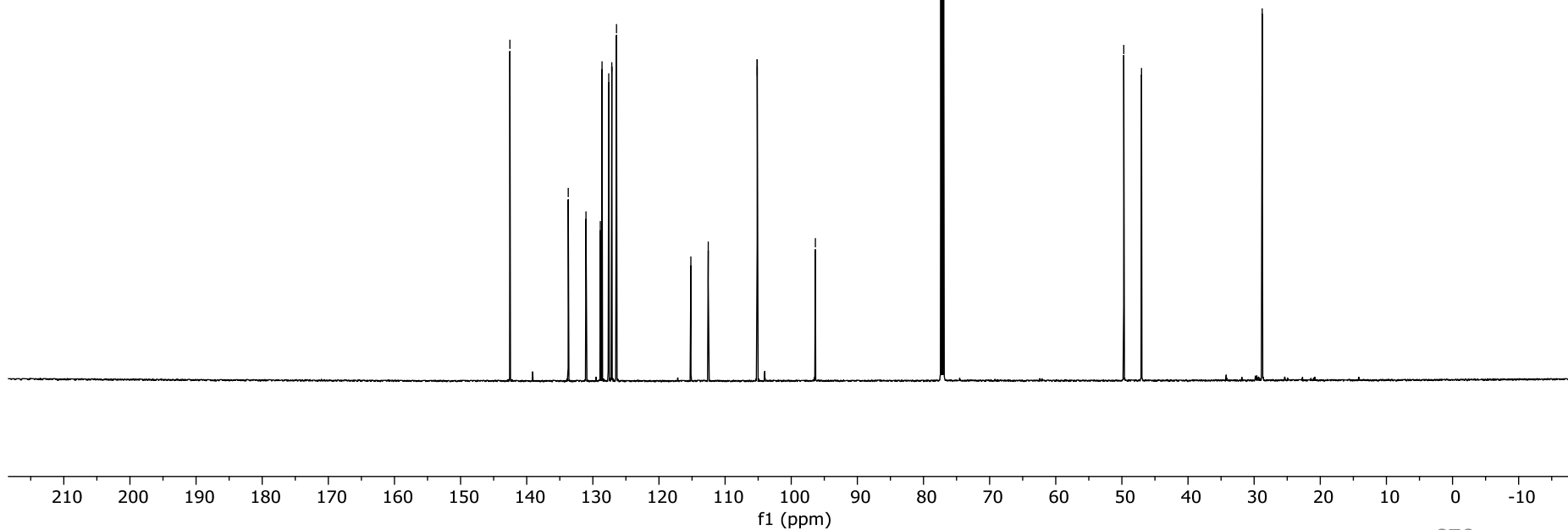


14a

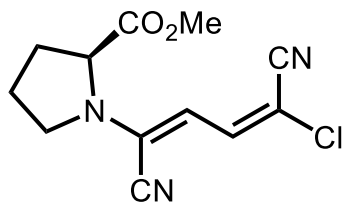
142.5
133.7
131.0
128.9
128.6
127.6
127.1
126.4
~115.2
~112.5
~105.1
— 96.3

~49.7
~47.0

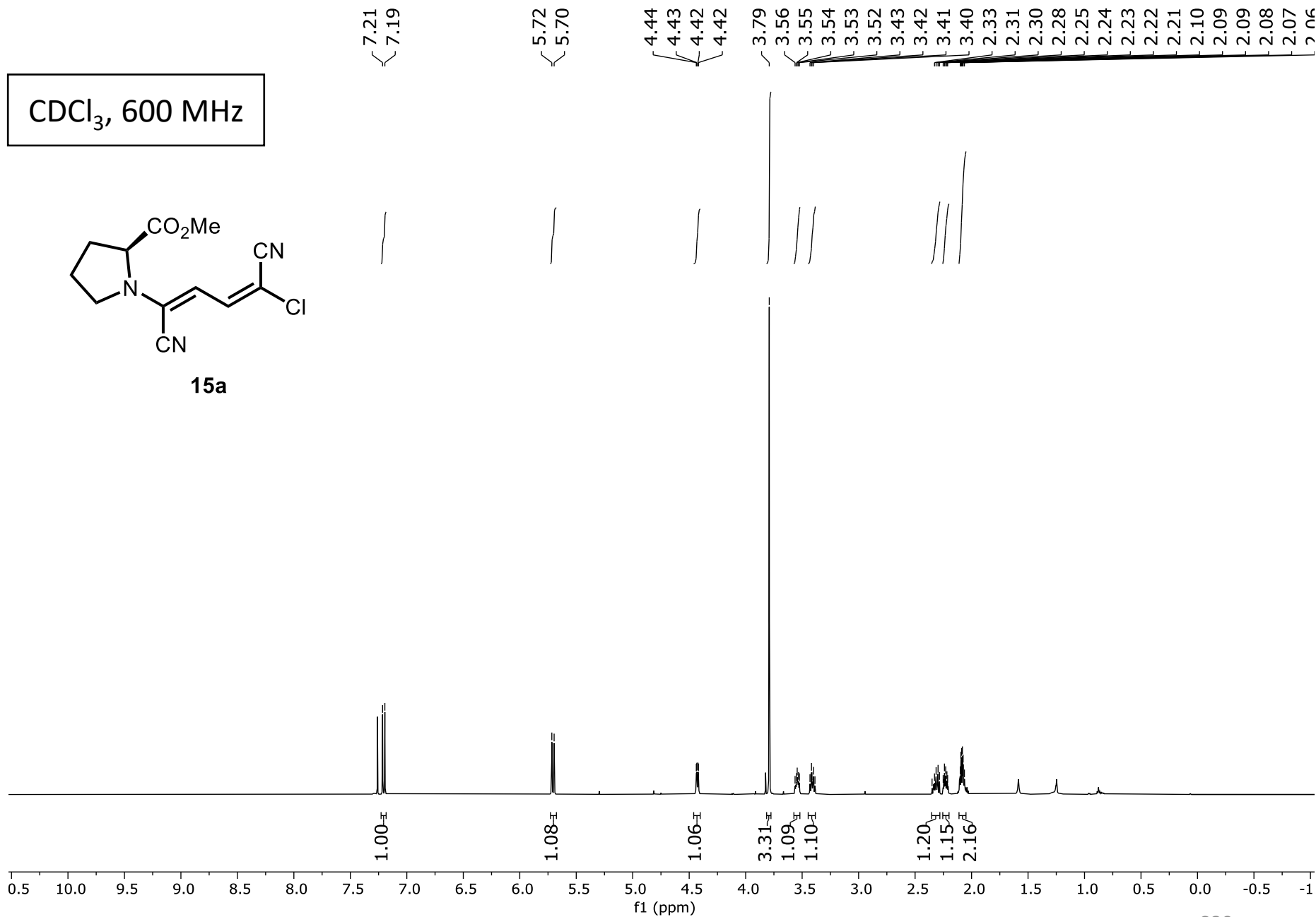
— 28.8



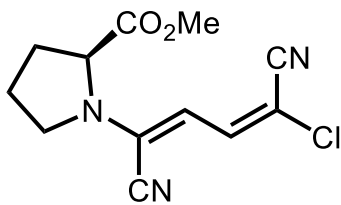
CDCl₃, 600 MHz



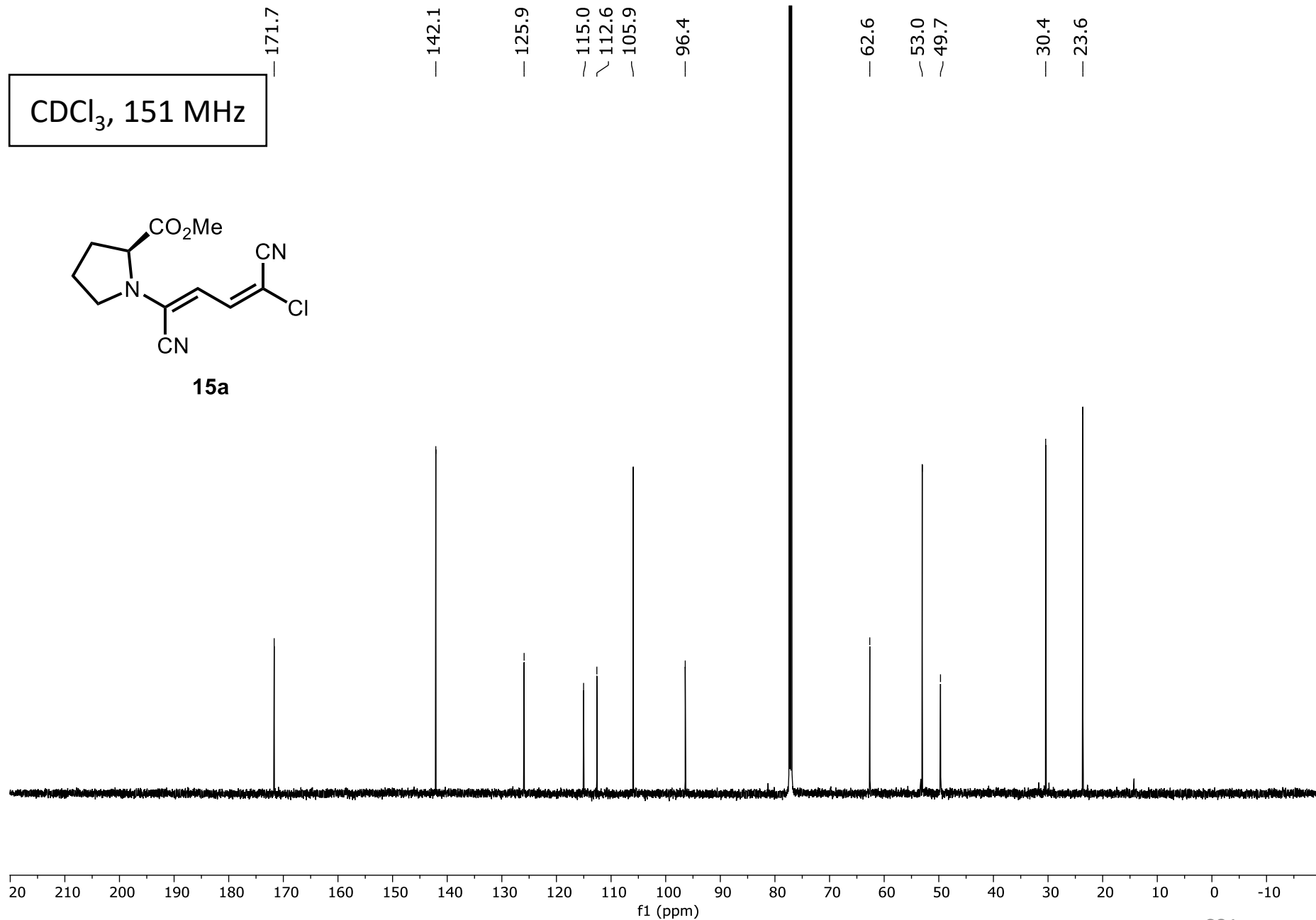
15a

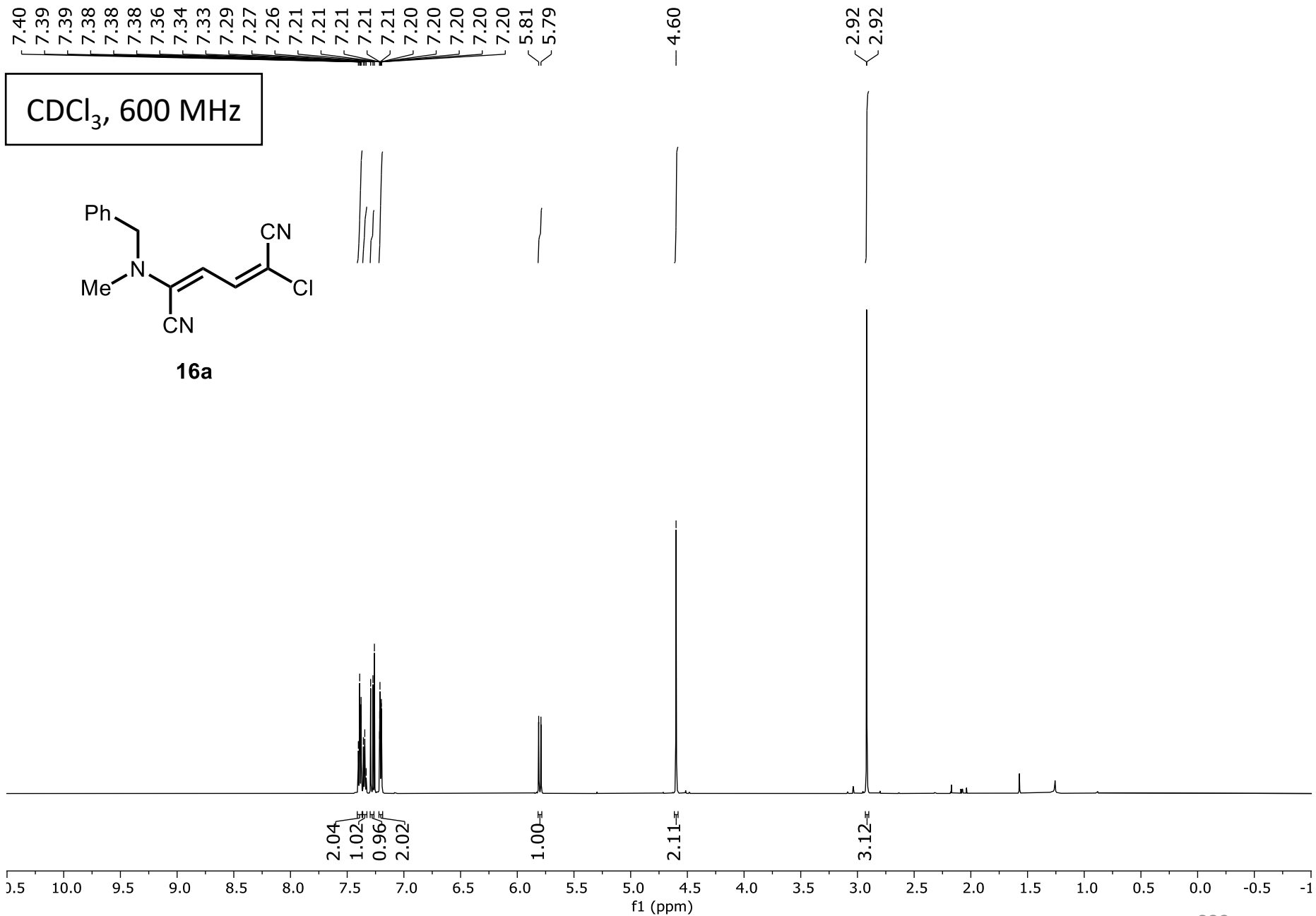


CDCl₃, 151 MHz

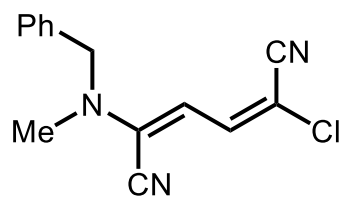


15a



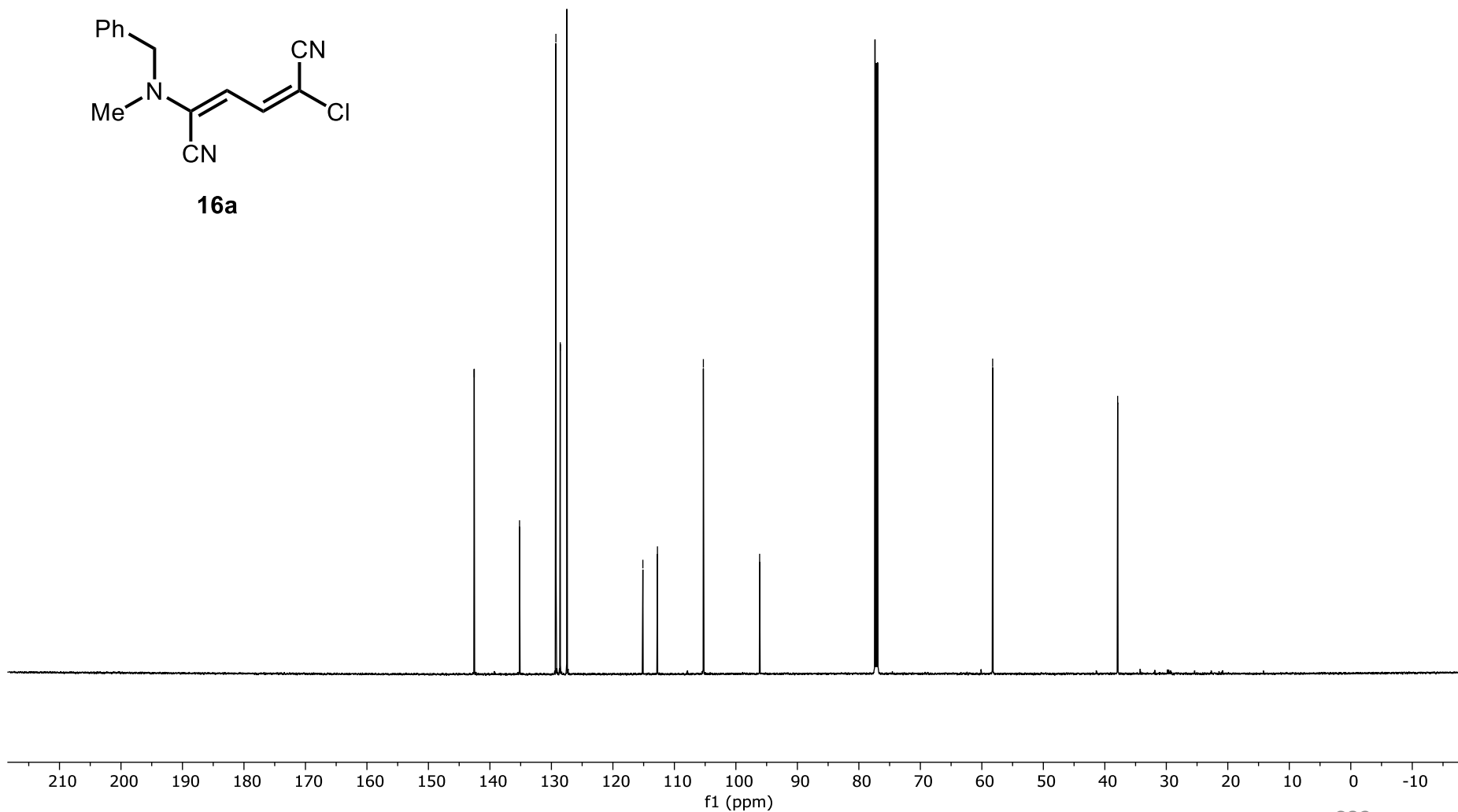


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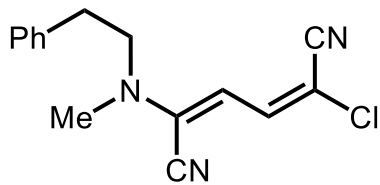


16a

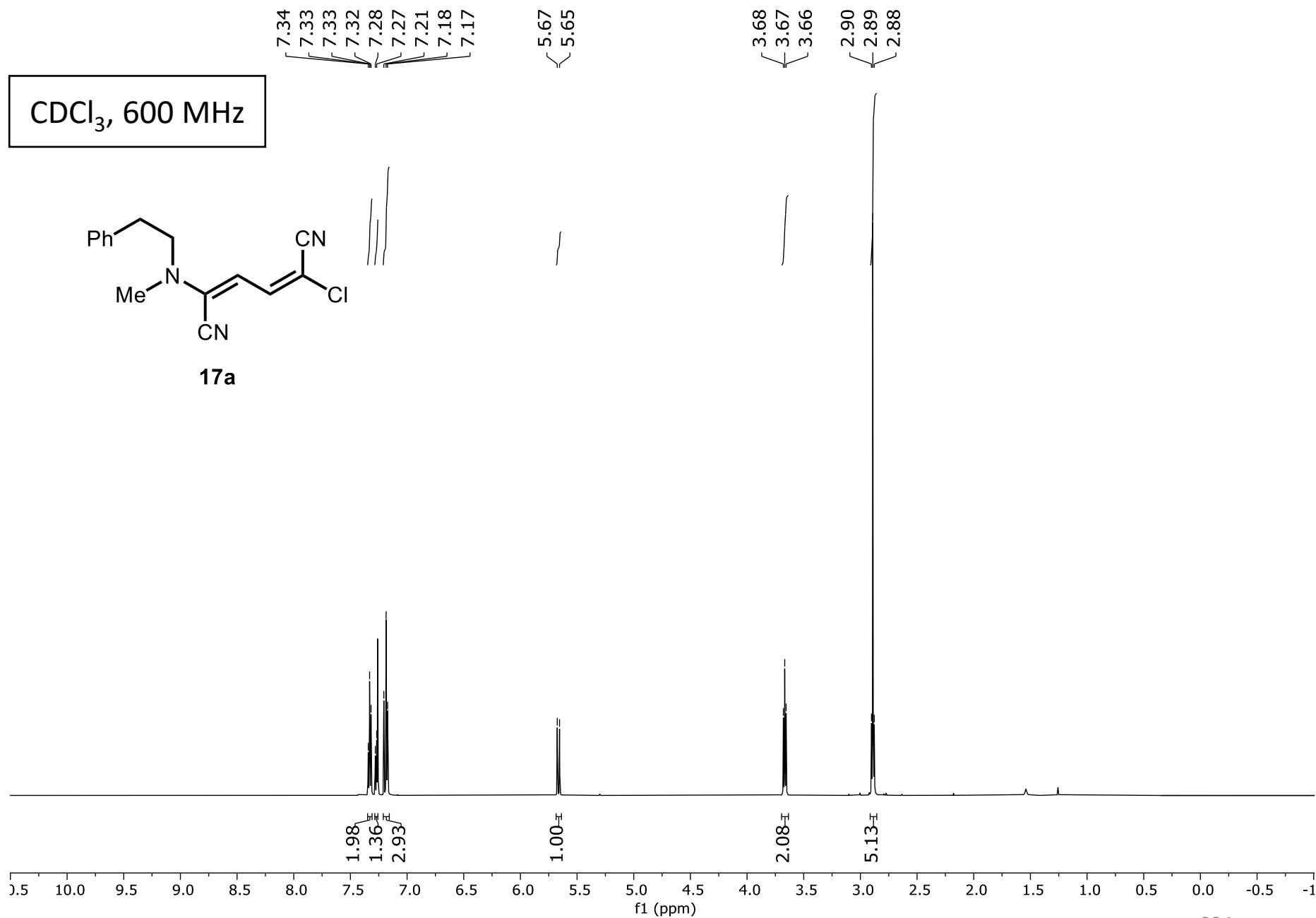
142.6
135.2
129.3
128.6
127.5
115.1
112.8
105.3
96.1
58.2
37.9



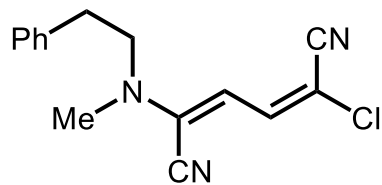
CDCl₃, 600 MHz



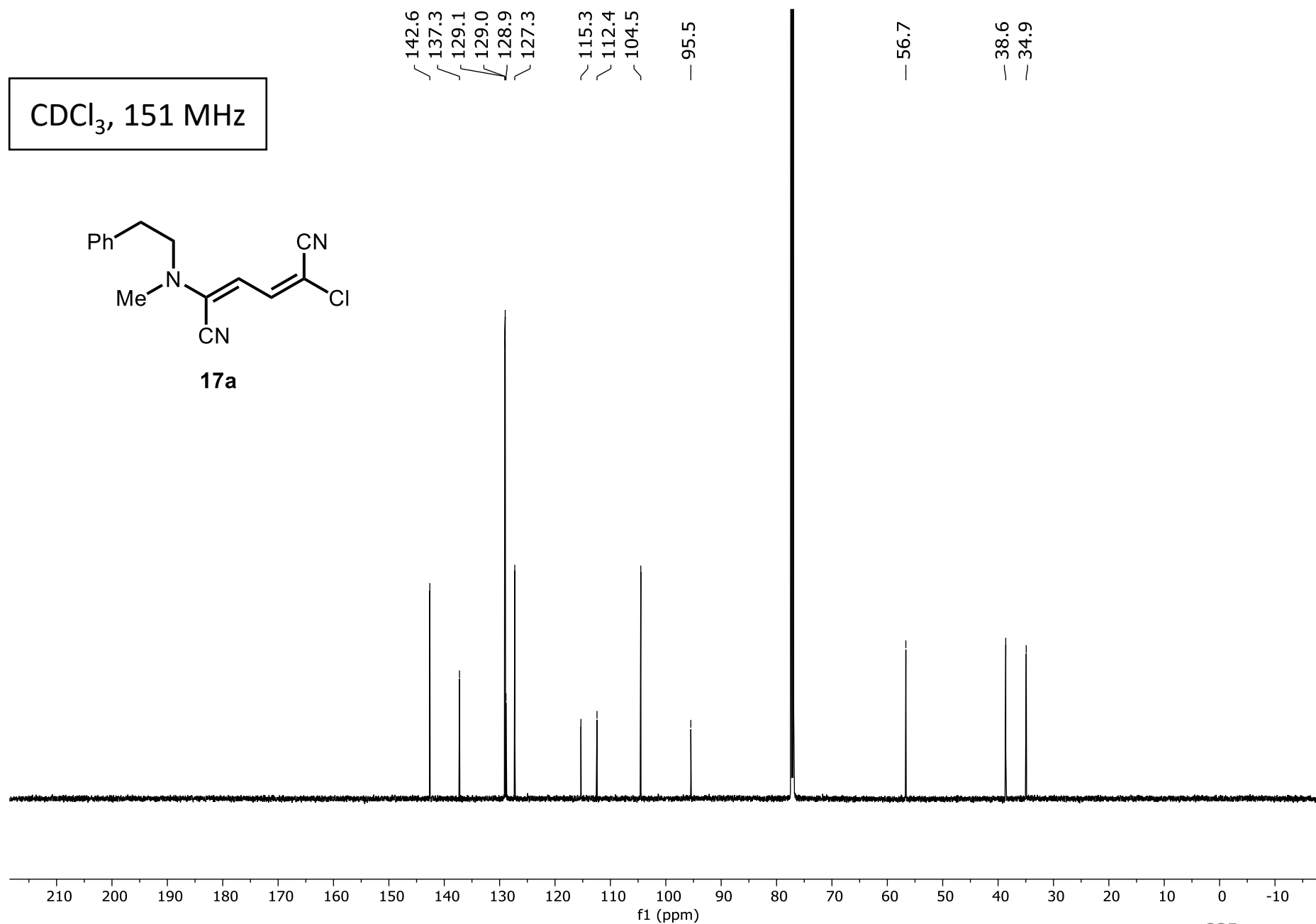
17a



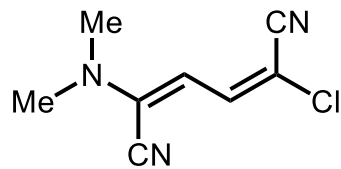
CDCl₃, 151 MHz



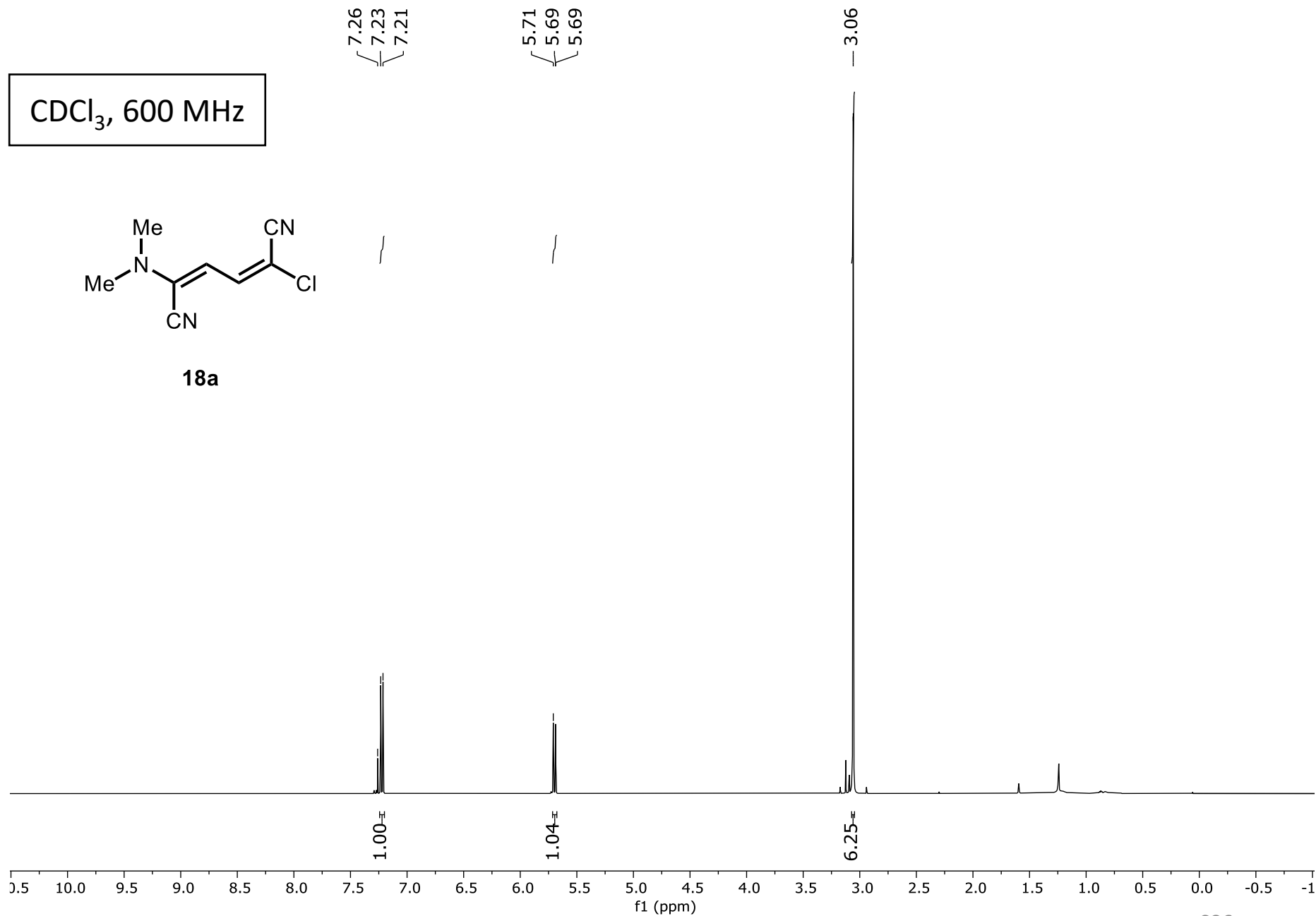
17a



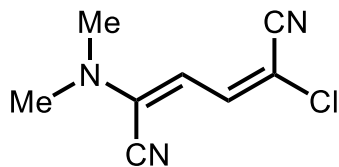
CDCl₃, 600 MHz



18a



CDCl₃, 151 MHz



18a

— 142.6

— 129.7

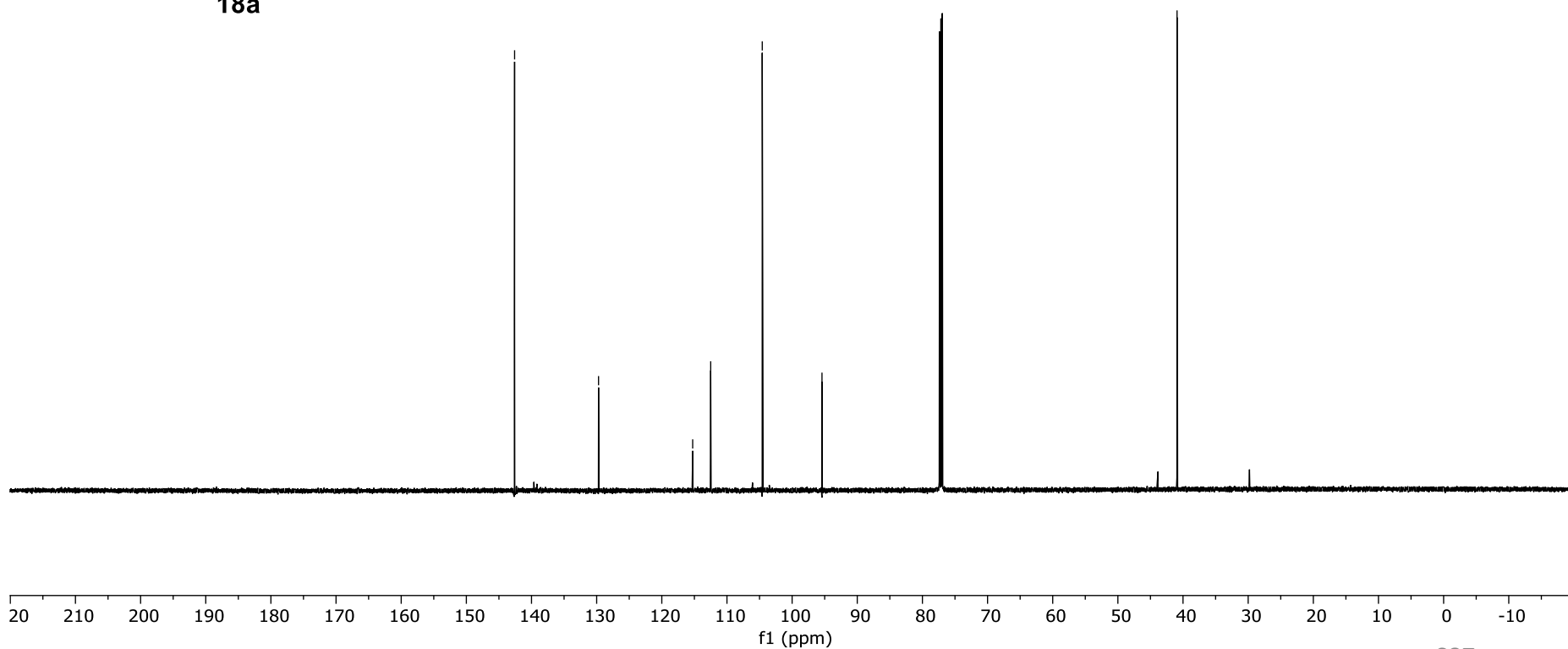
~ 115.3

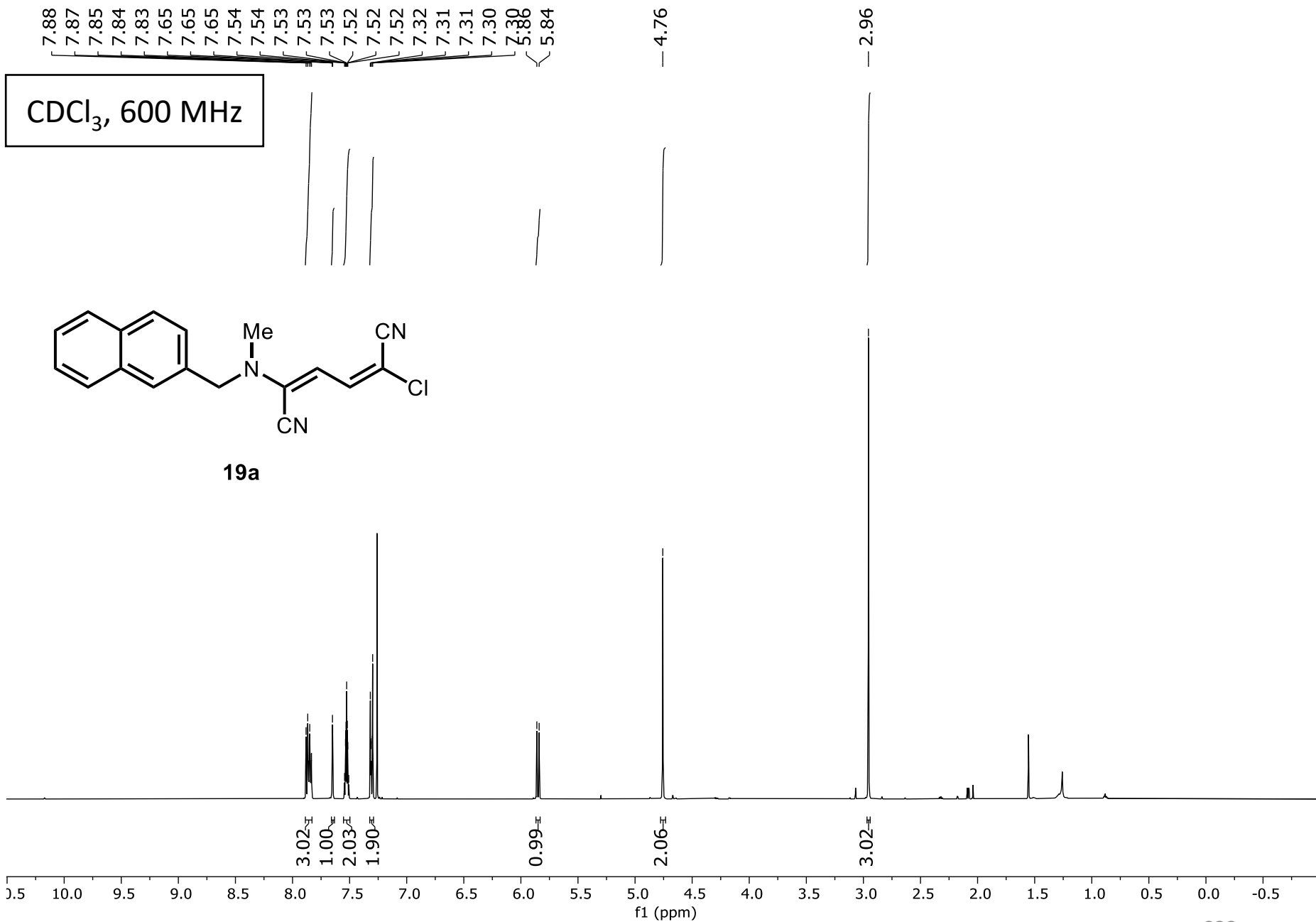
~ 112.5

~ 104.6

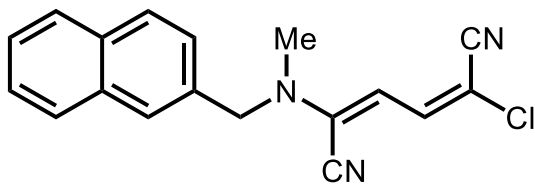
— 95.4

— 40.9

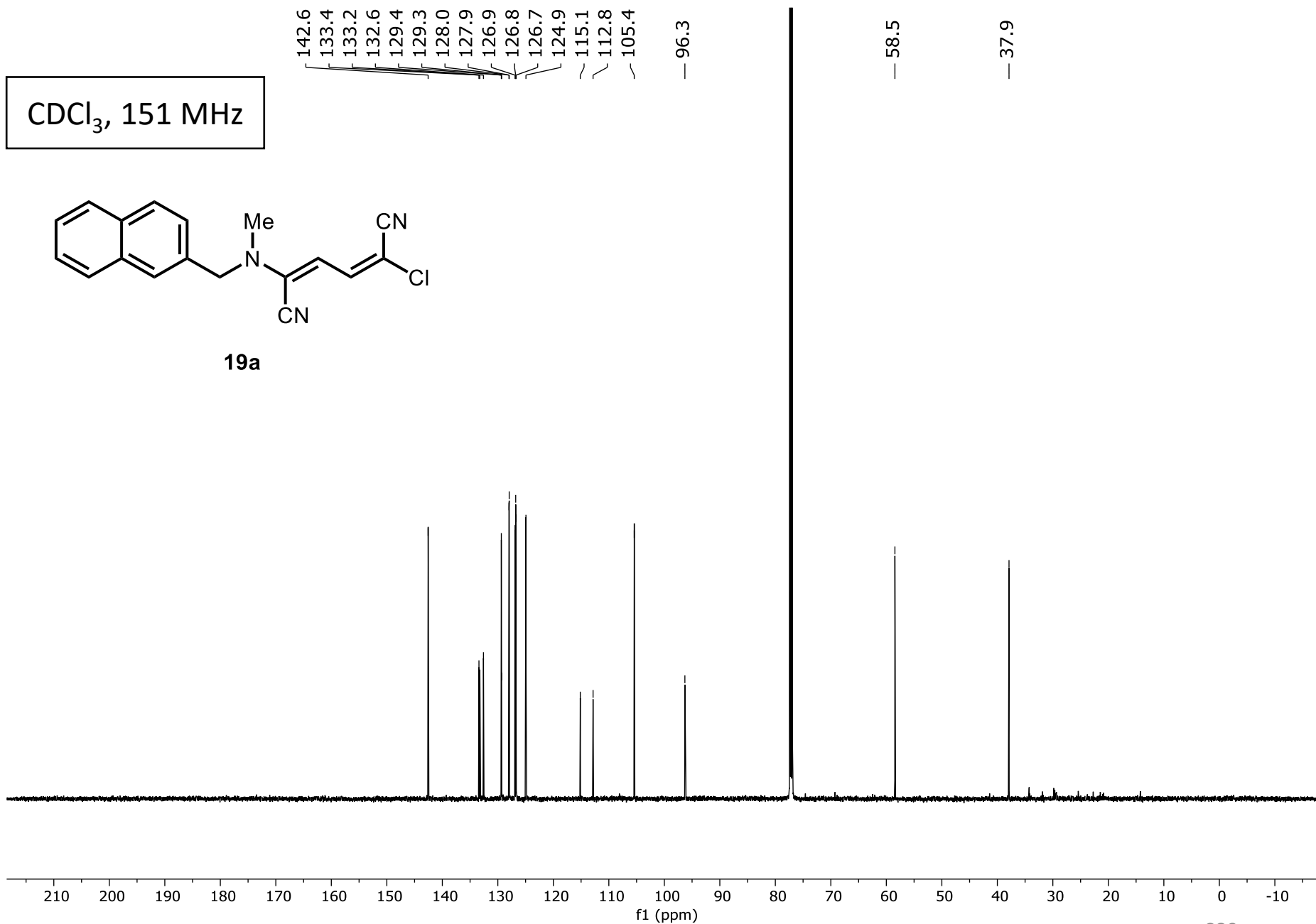




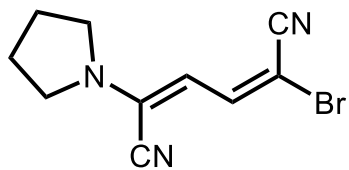
CDCl₃, 151 MHz



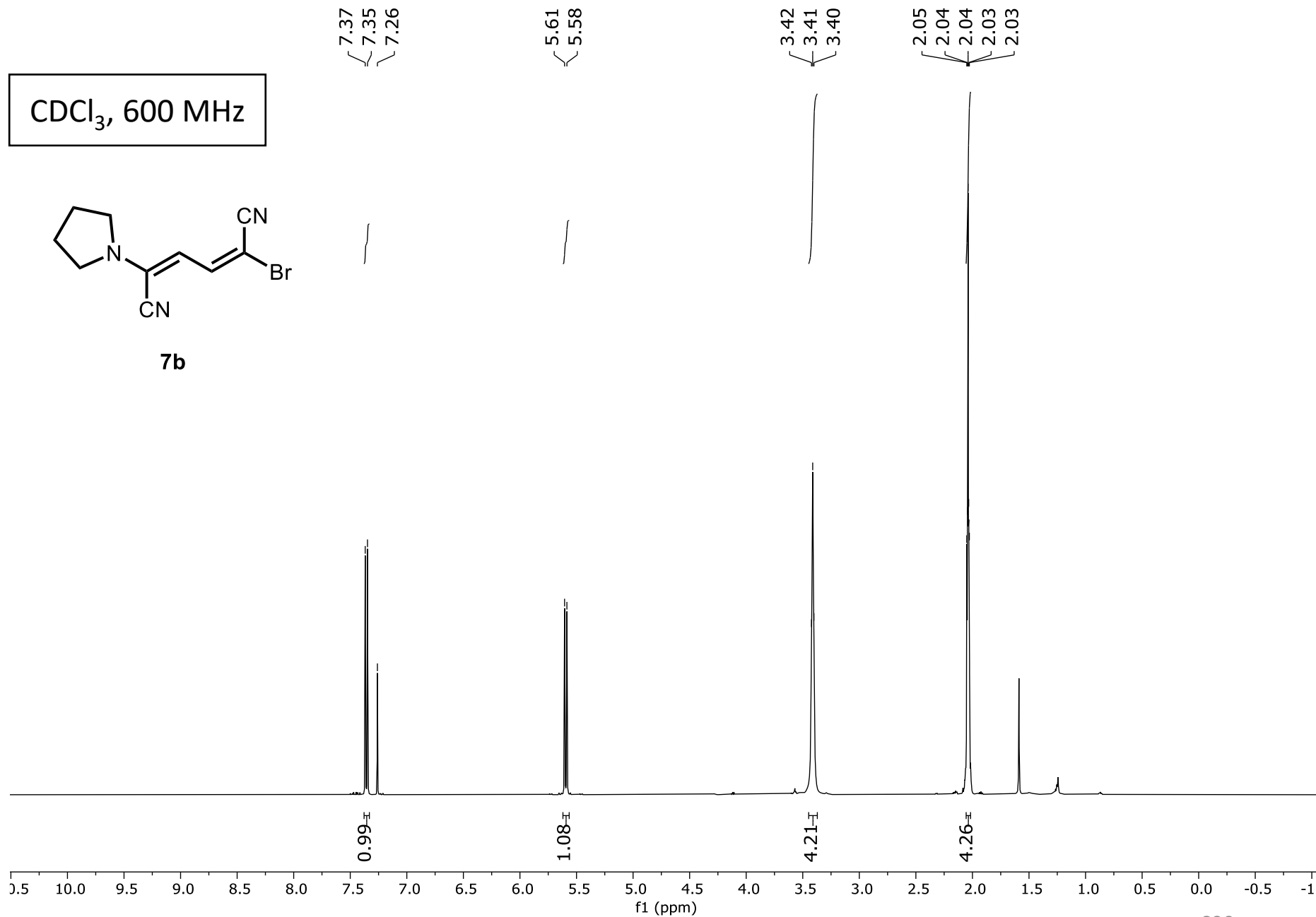
19a



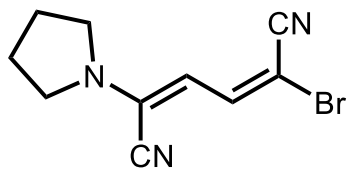
CDCl₃, 600 MHz



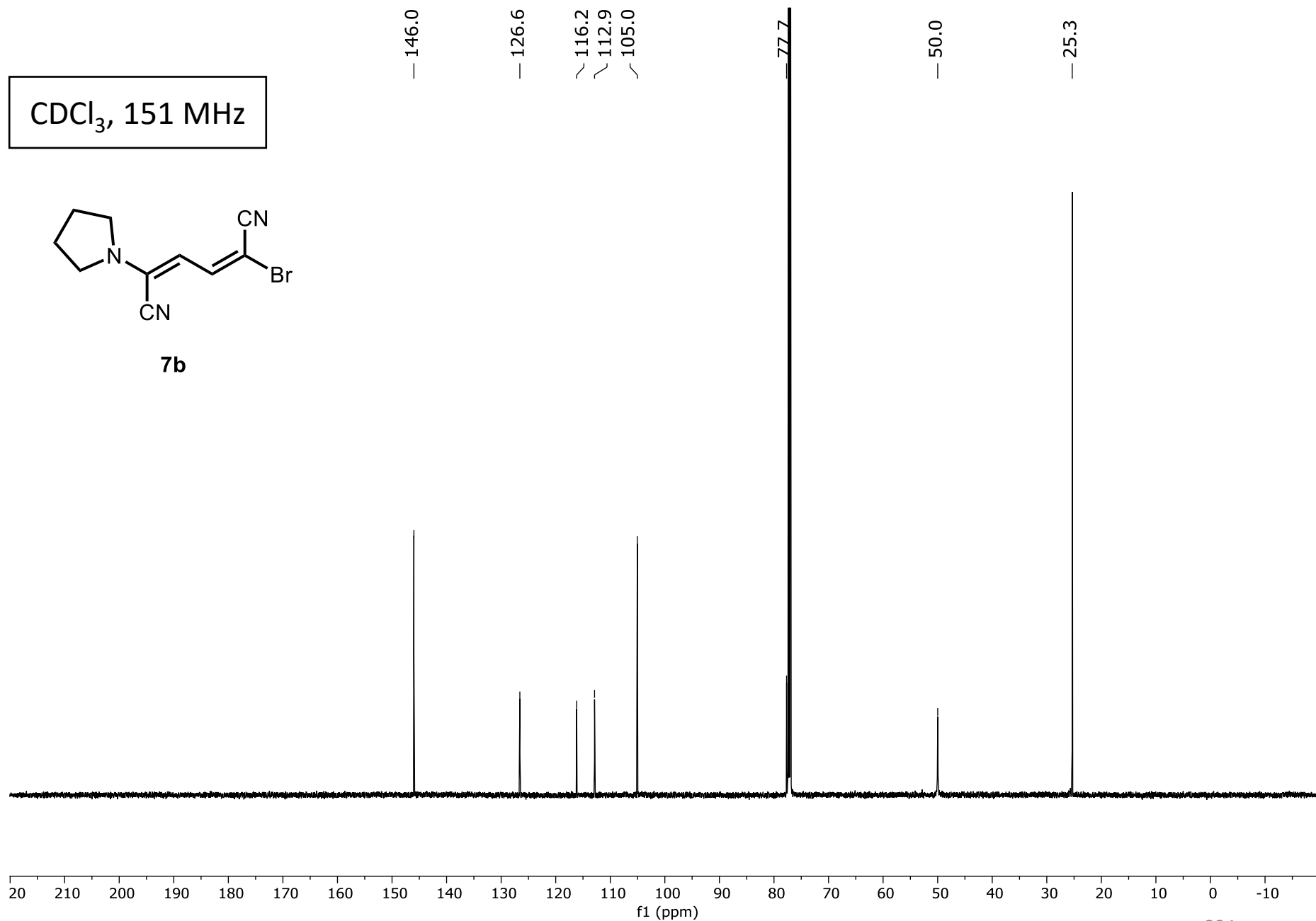
7b



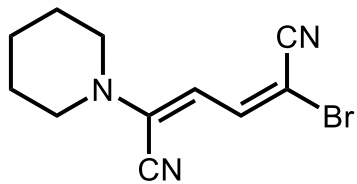
CDCl₃, 151 MHz



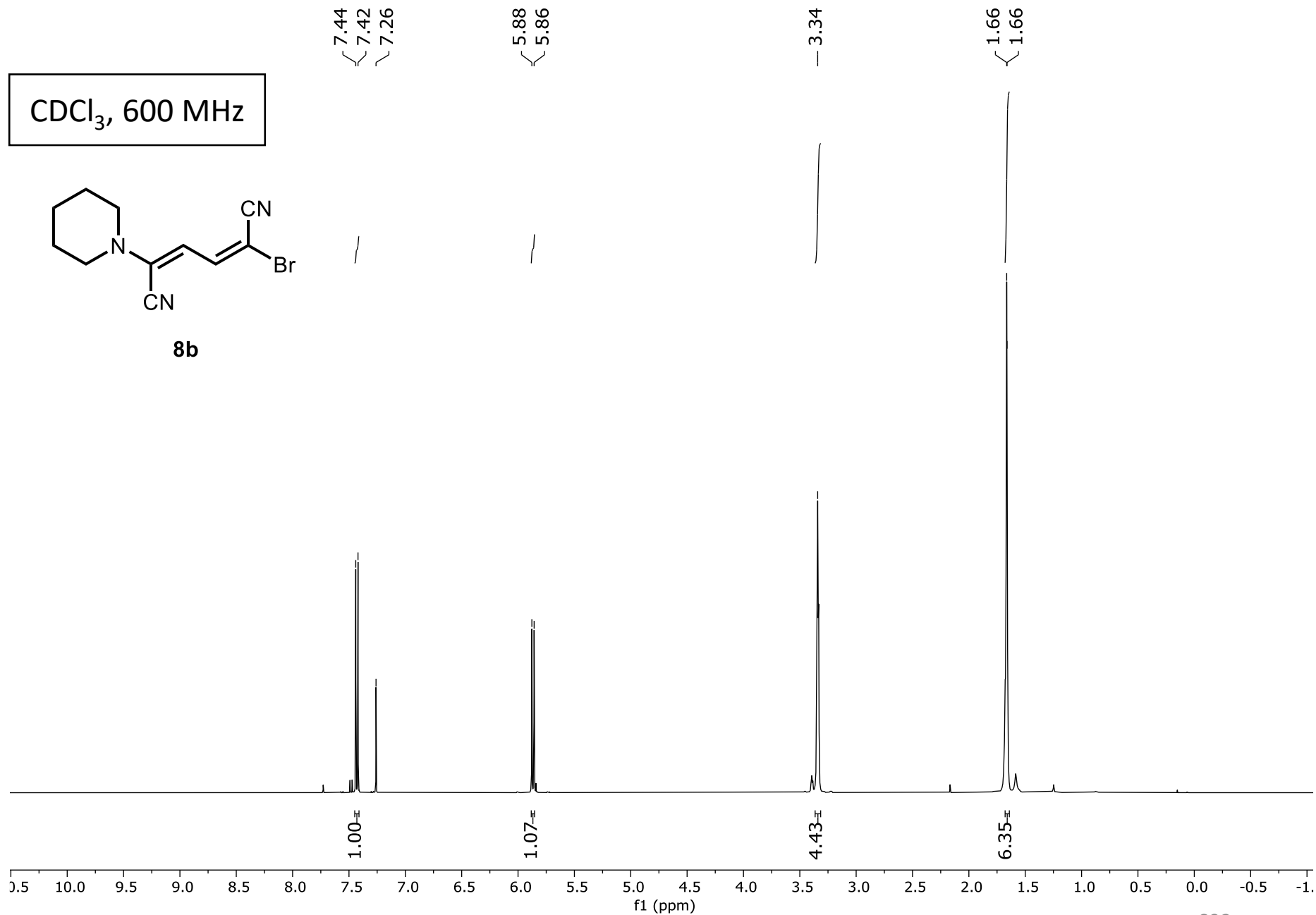
7b



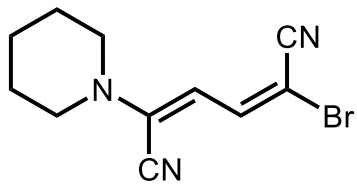
CDCl₃, 600 MHz



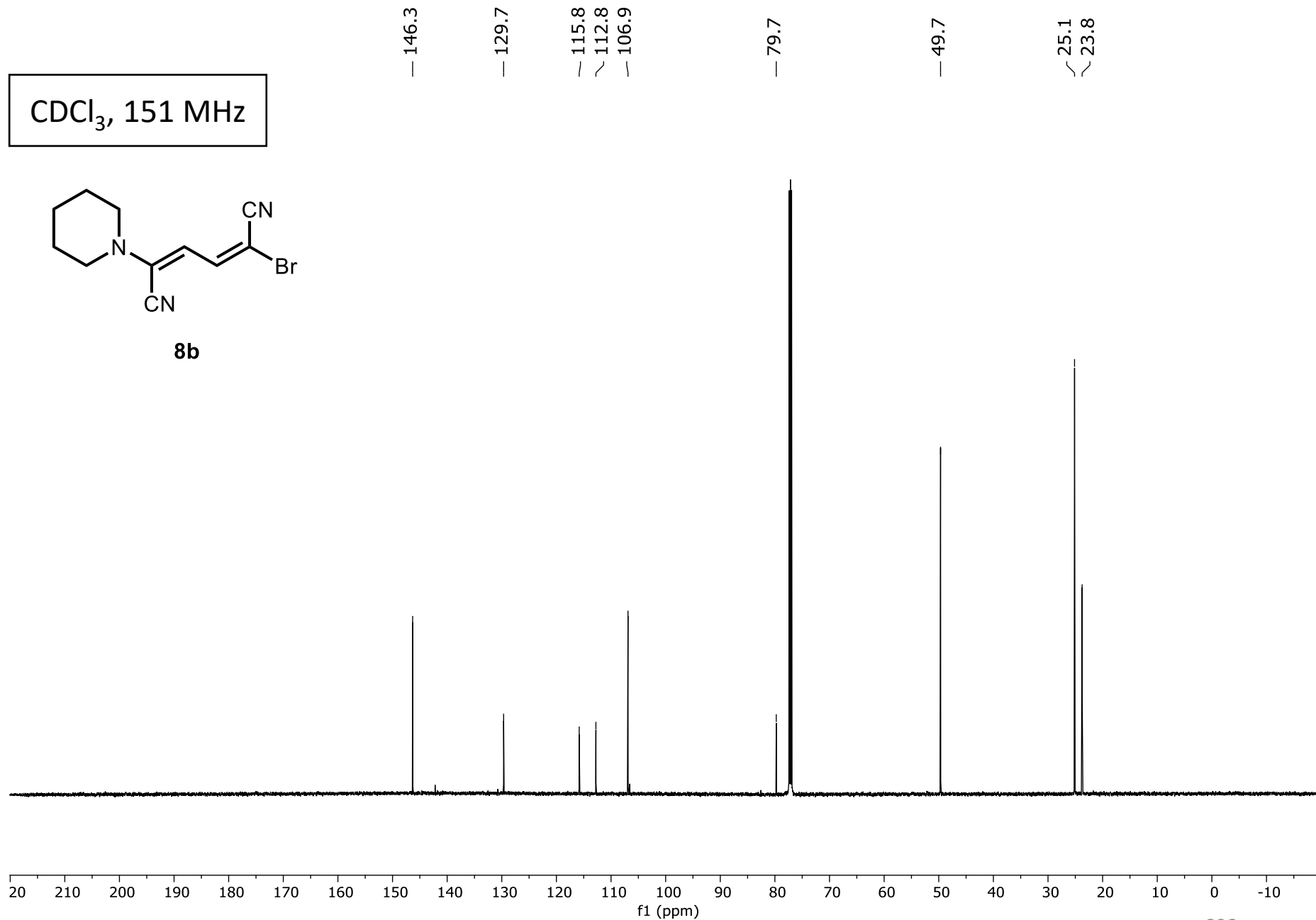
8b



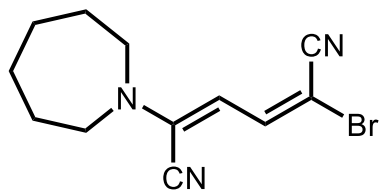
CDCl₃, 151 MHz



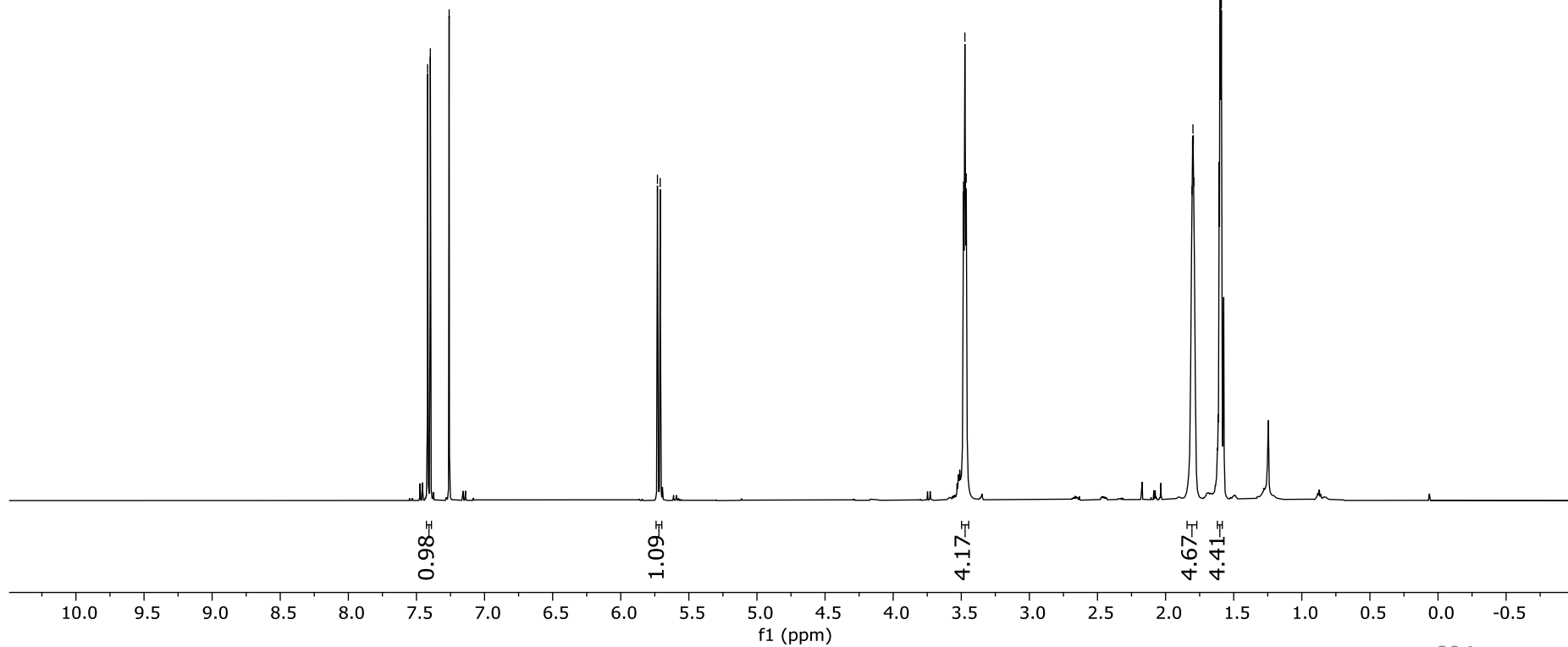
8b



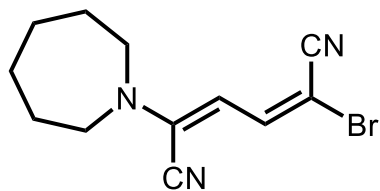
CDCl₃, 600 MHz



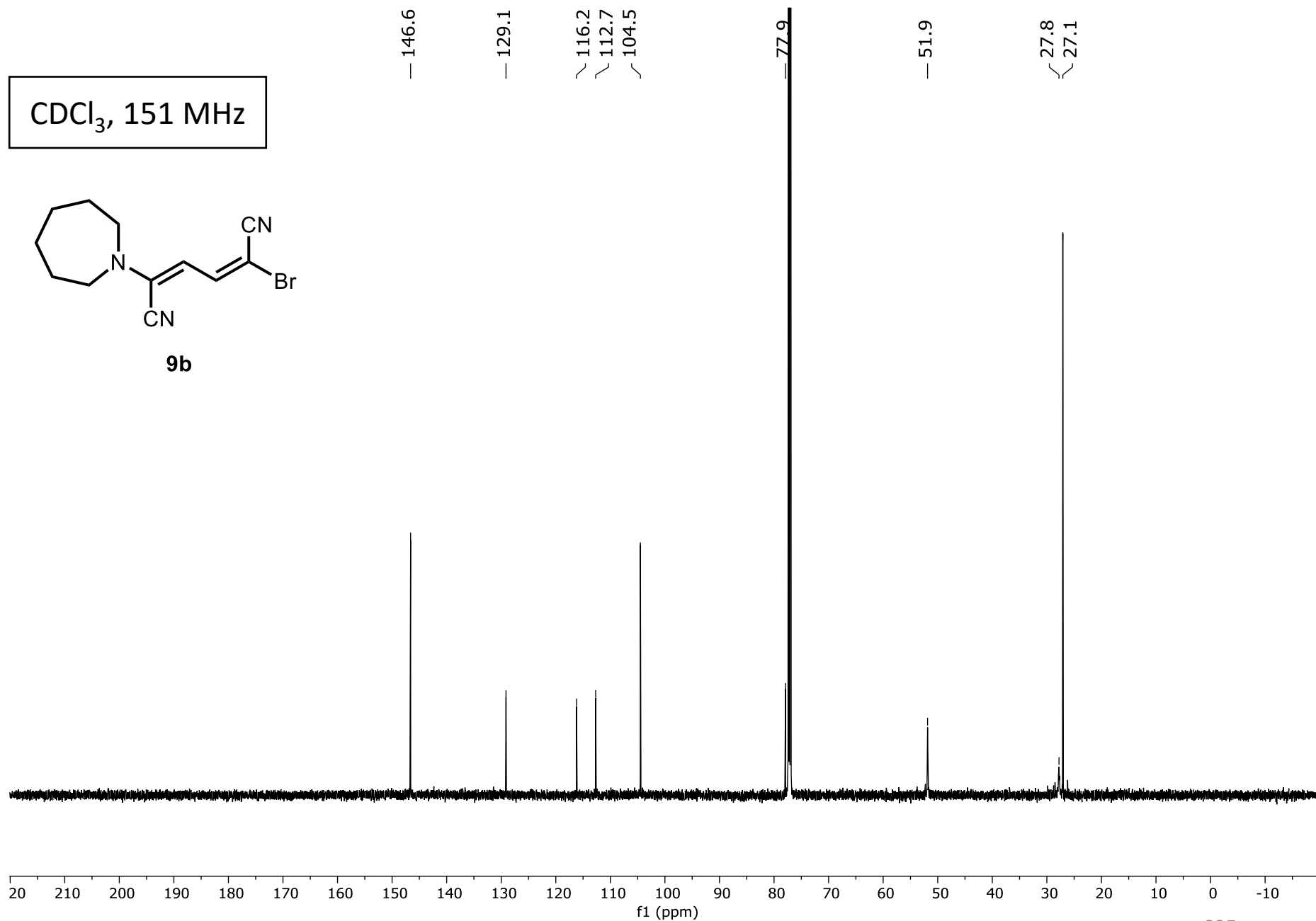
9b



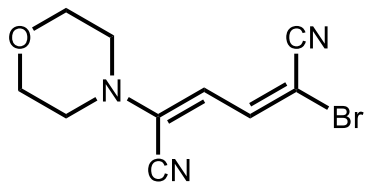
CDCl₃, 151 MHz



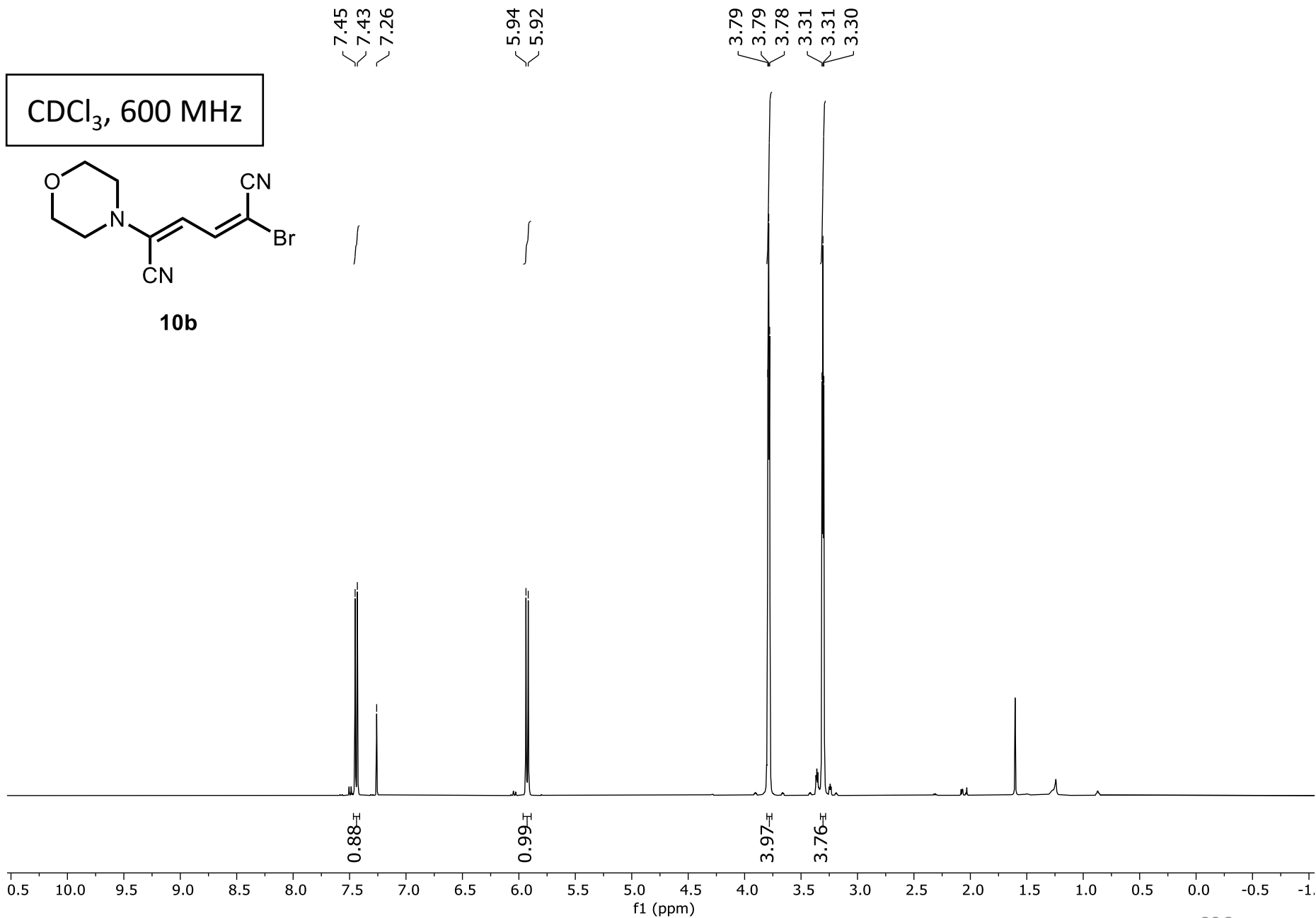
9b



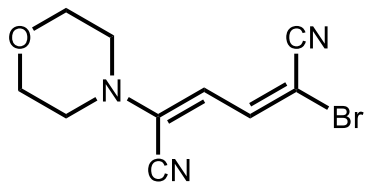
CDCl₃, 600 MHz



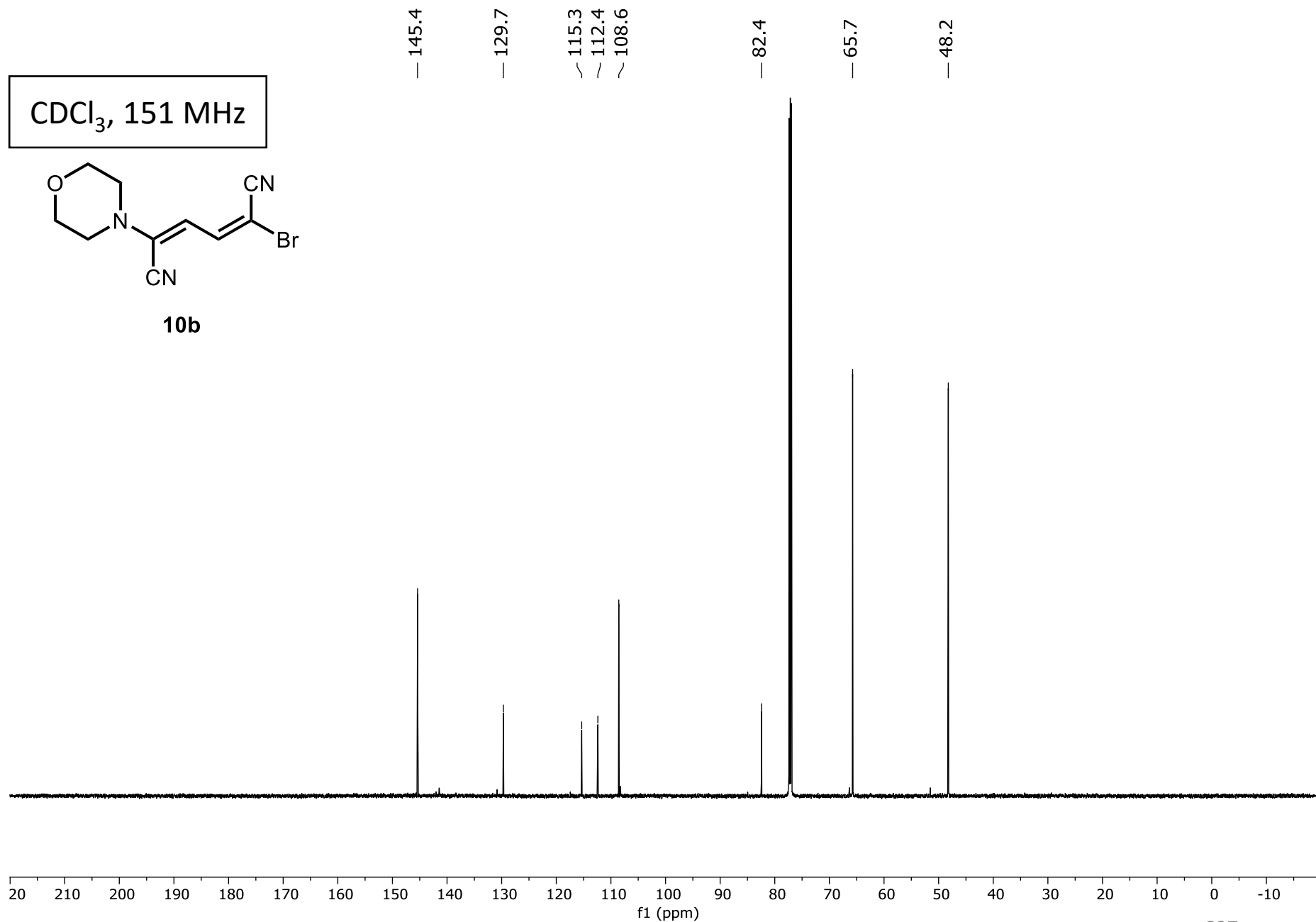
10b



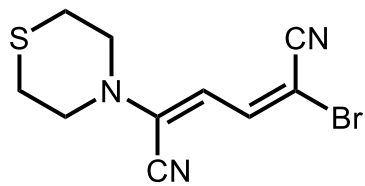
CDCl₃, 151 MHz



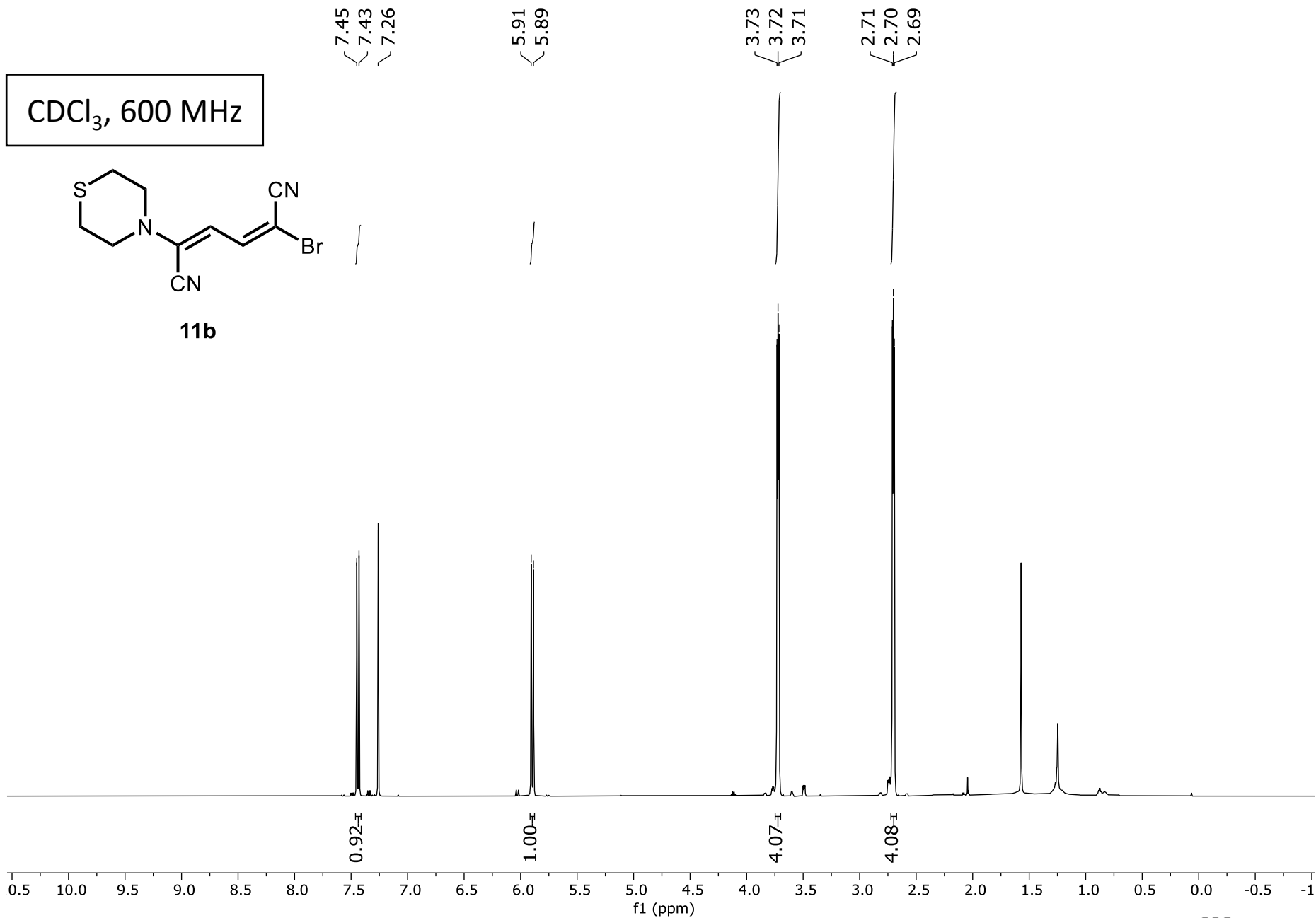
10b



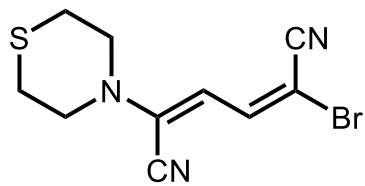
CDCl₃, 600 MHz



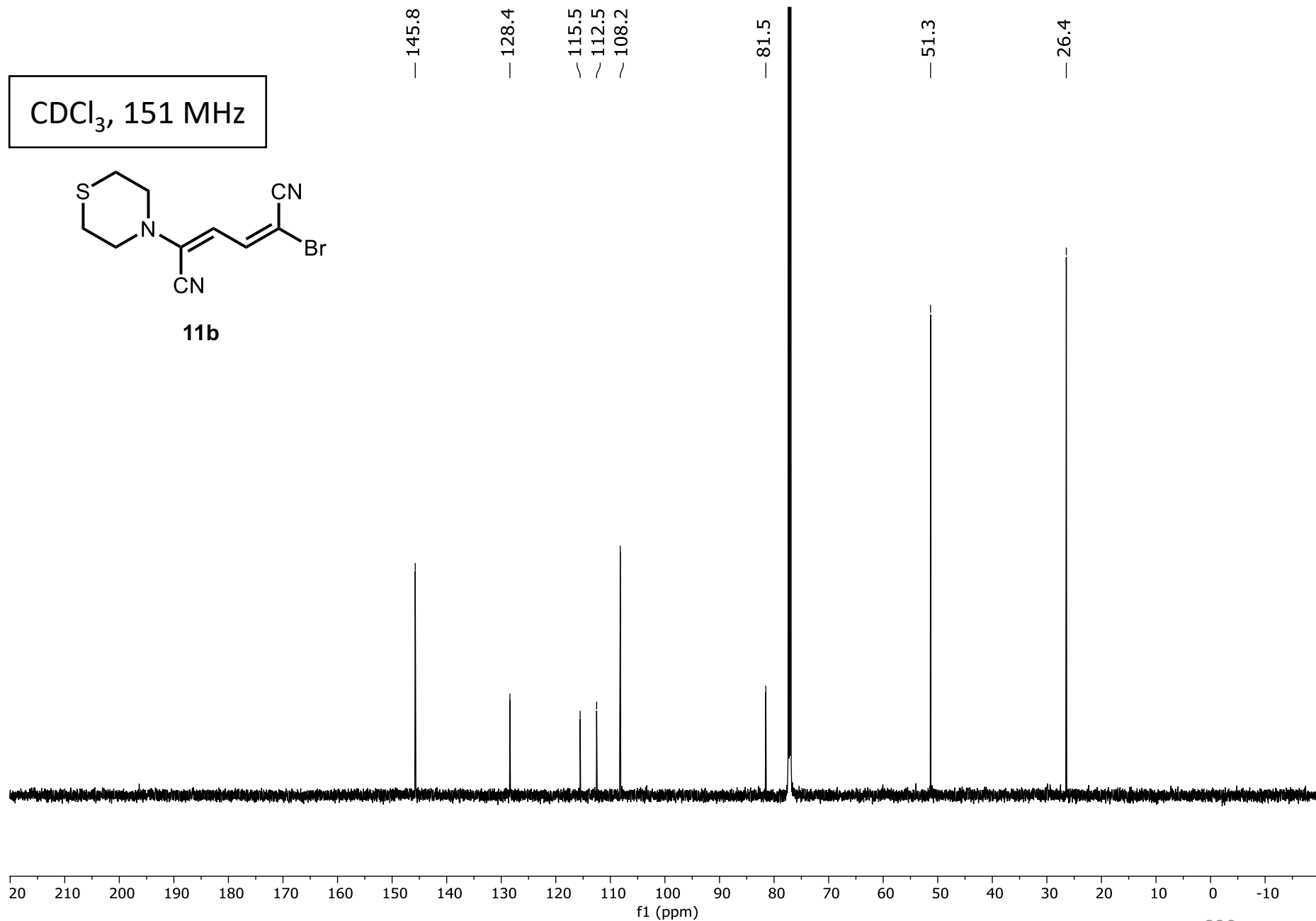
11b



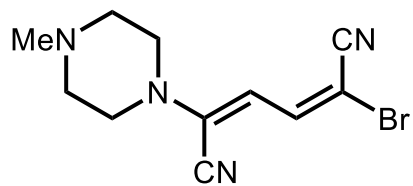
CDCl₃, 151 MHz



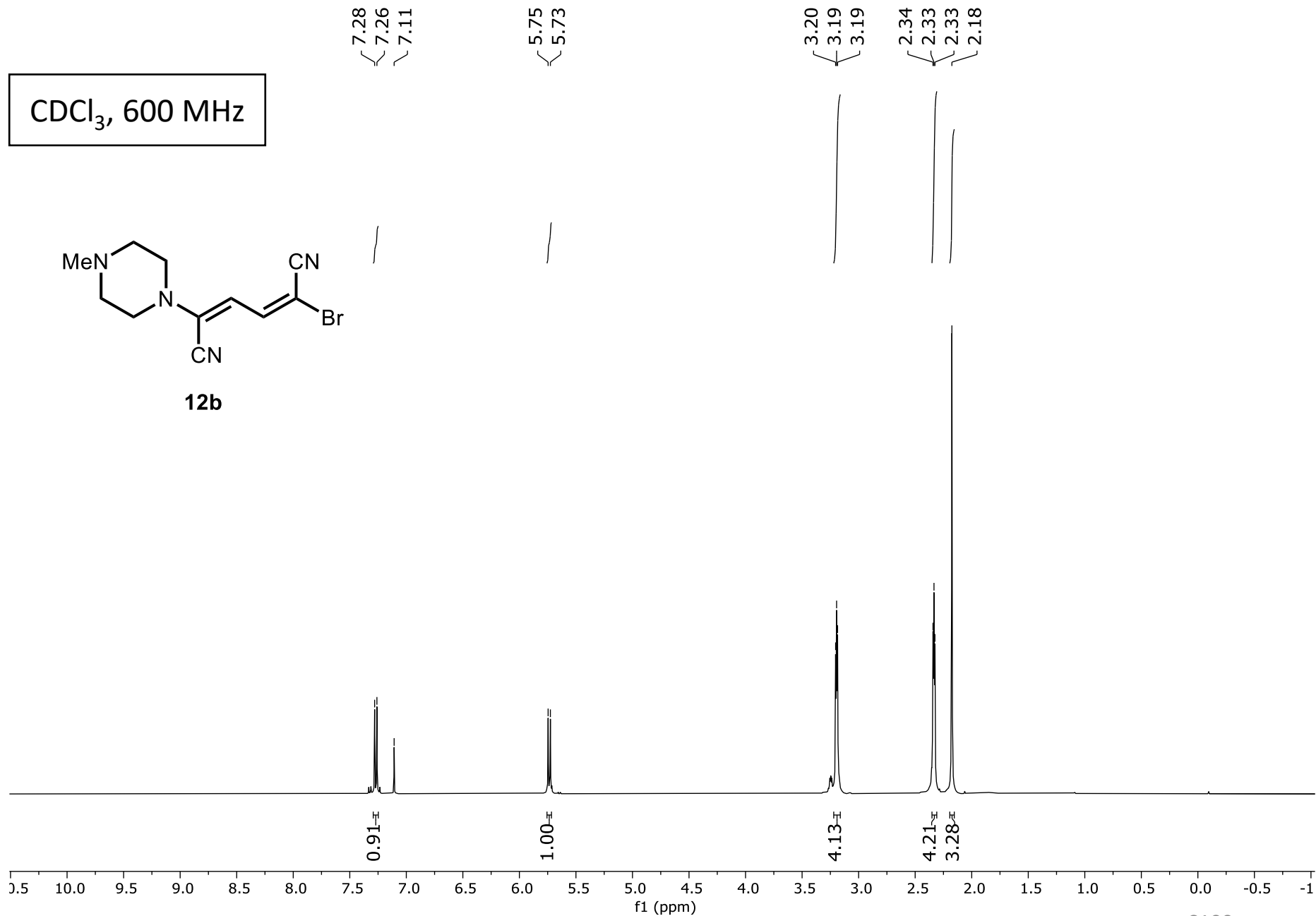
11b



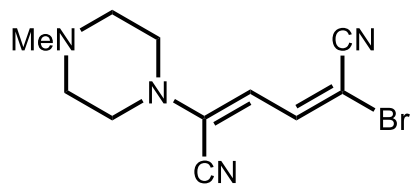
CDCl₃, 600 MHz



12b



CDCl₃, 151 MHz



12b

— 145.8

— 129.5

~ 115.5

~ 112.6

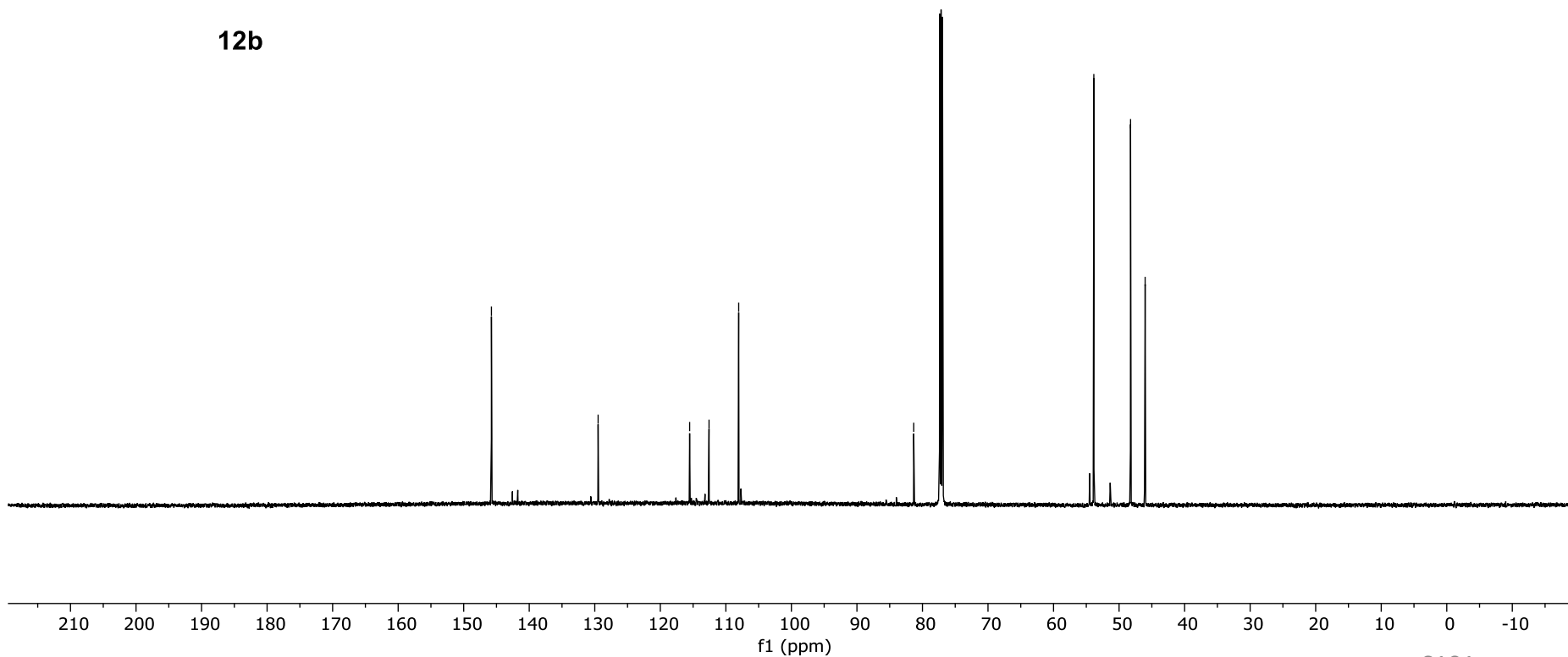
~ 108.0

— 81.3

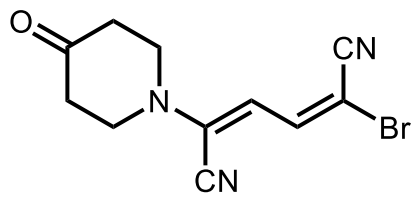
~ 53.9

~ 48.2

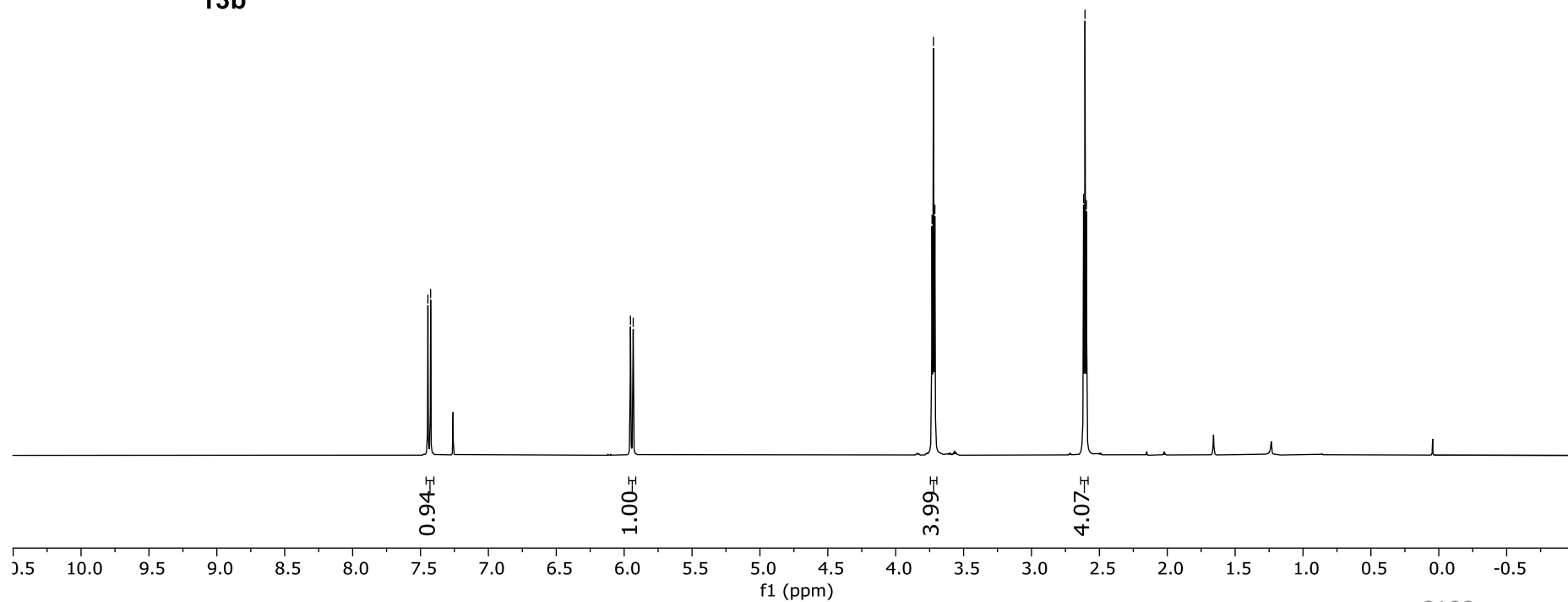
~ 46.0



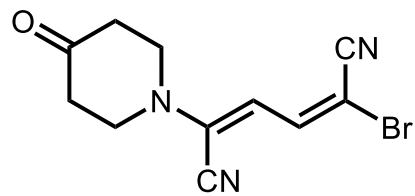
CDCl₃, 600 MHz



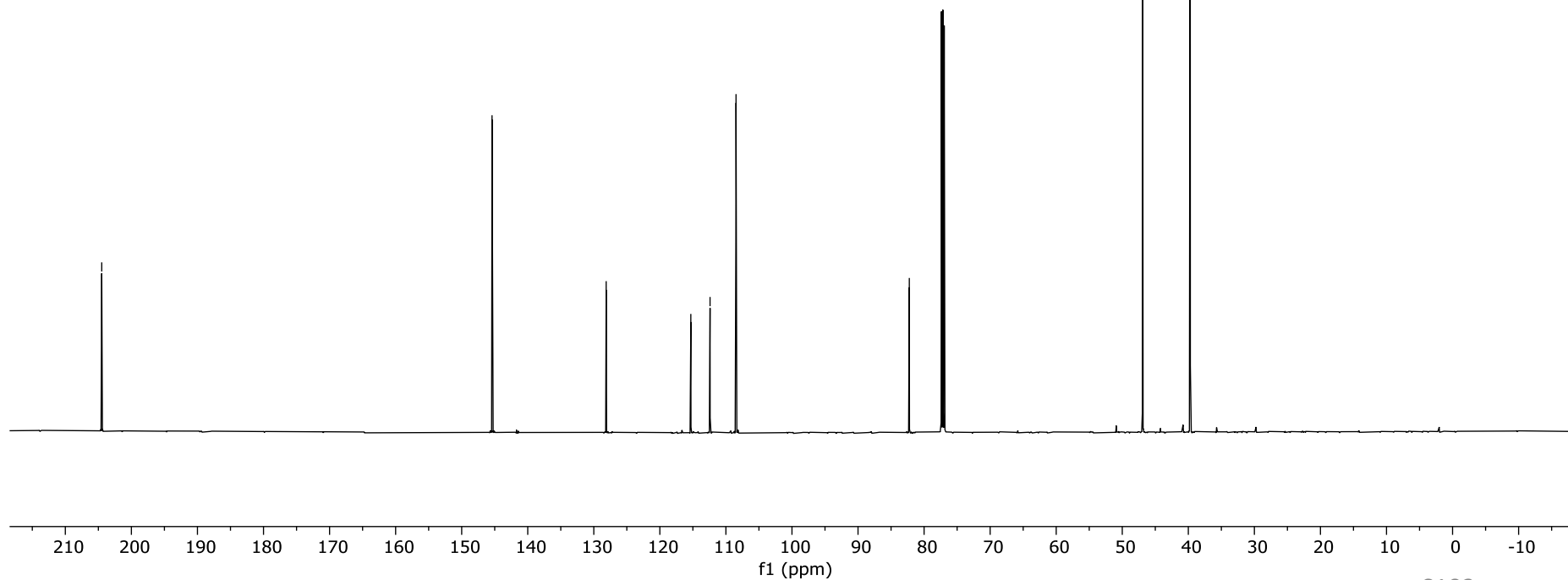
13b



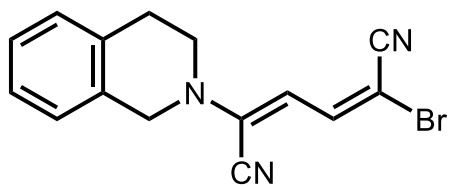
CDCl₃, 151 MHz



13b

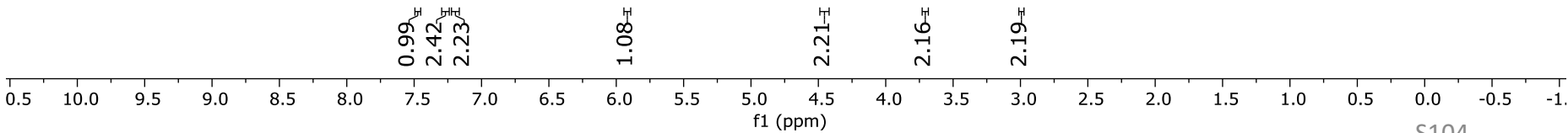


CDCl₃, 600 MHz

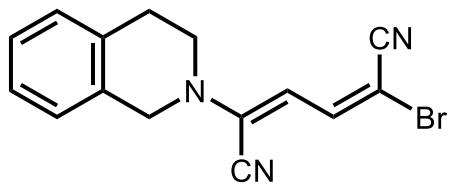


14b

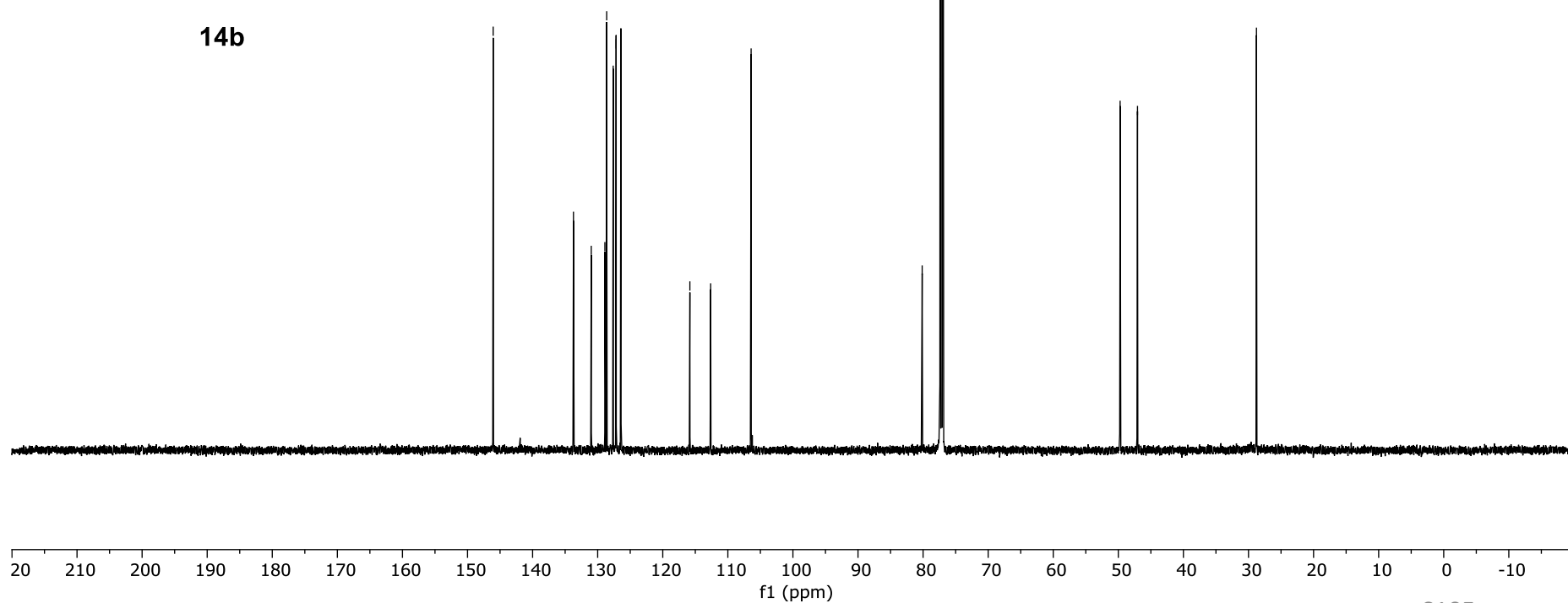
7.48
7.46
7.27
7.27
7.26
7.26
7.21
7.20
7.20
7.20
7.19
7.19
7.18
5.92
5.90
— 4.46
3.72
3.71
3.70
3.00
2.99
2.98



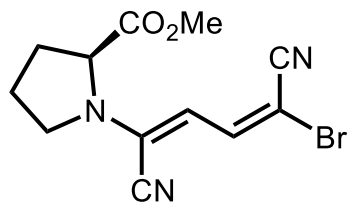
CDCl₃, 151 MHz



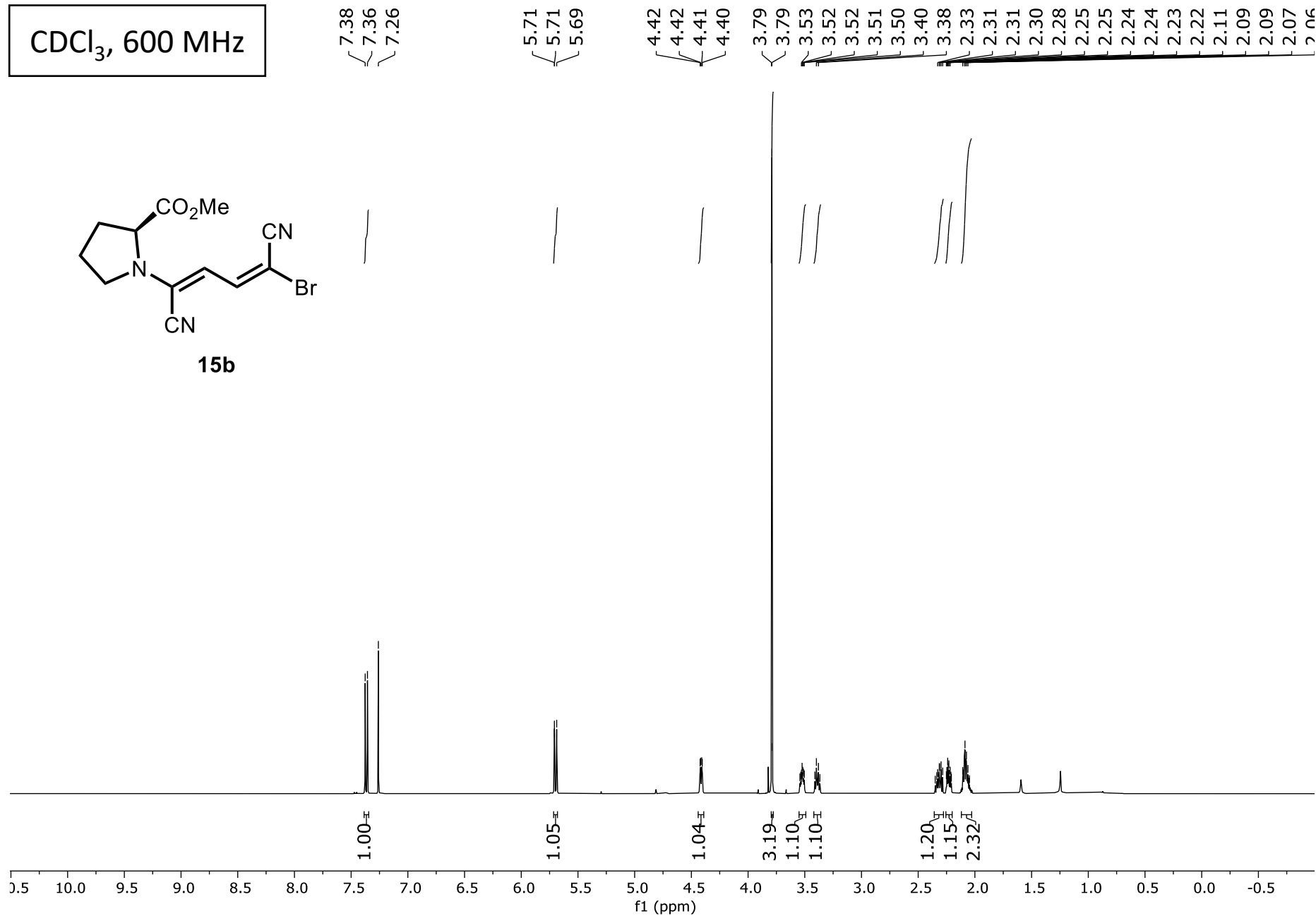
14b



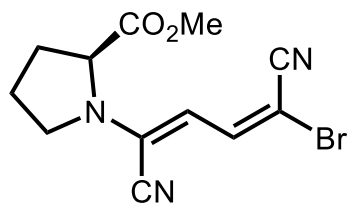
CDCl₃, 600 MHz



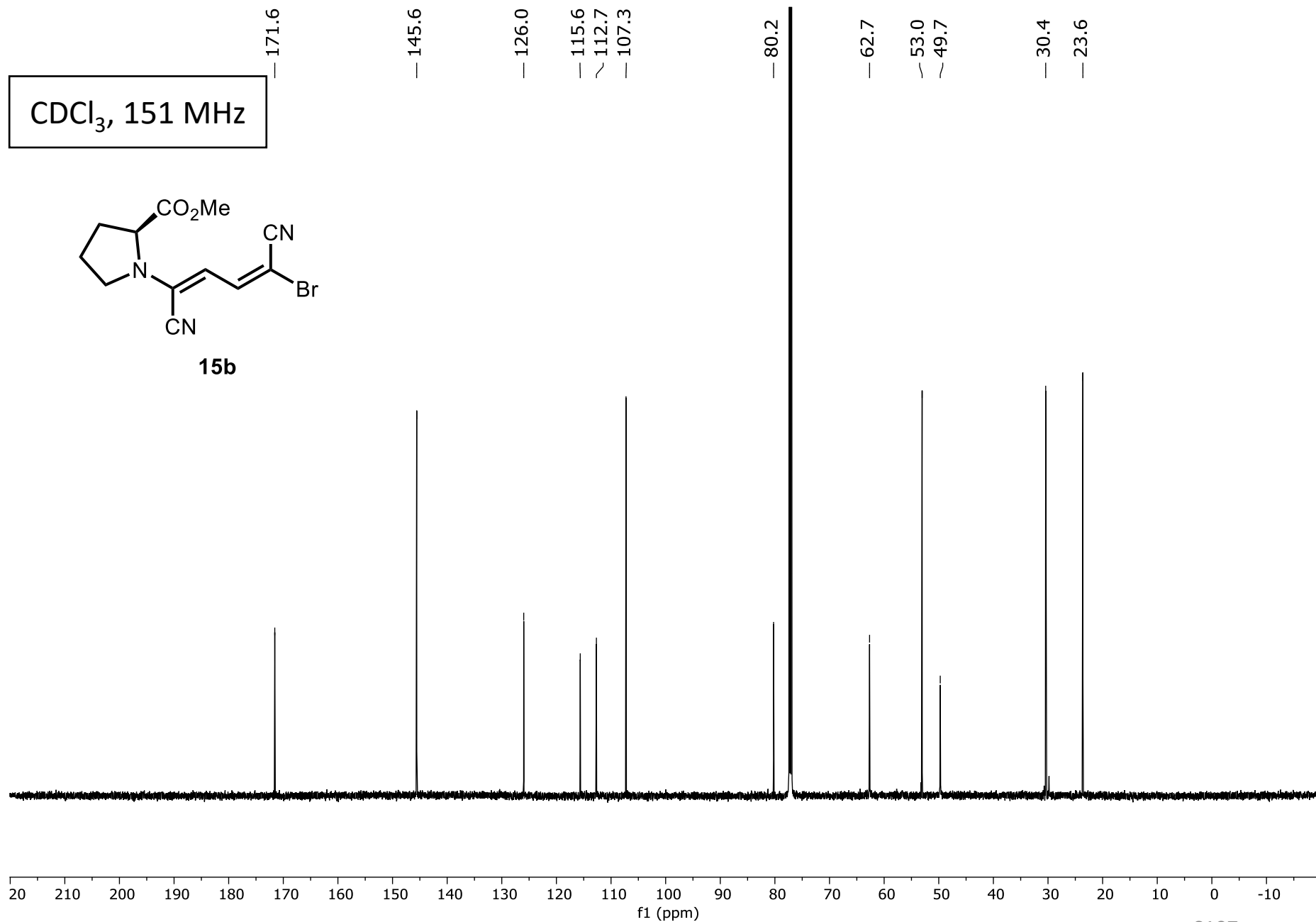
15b

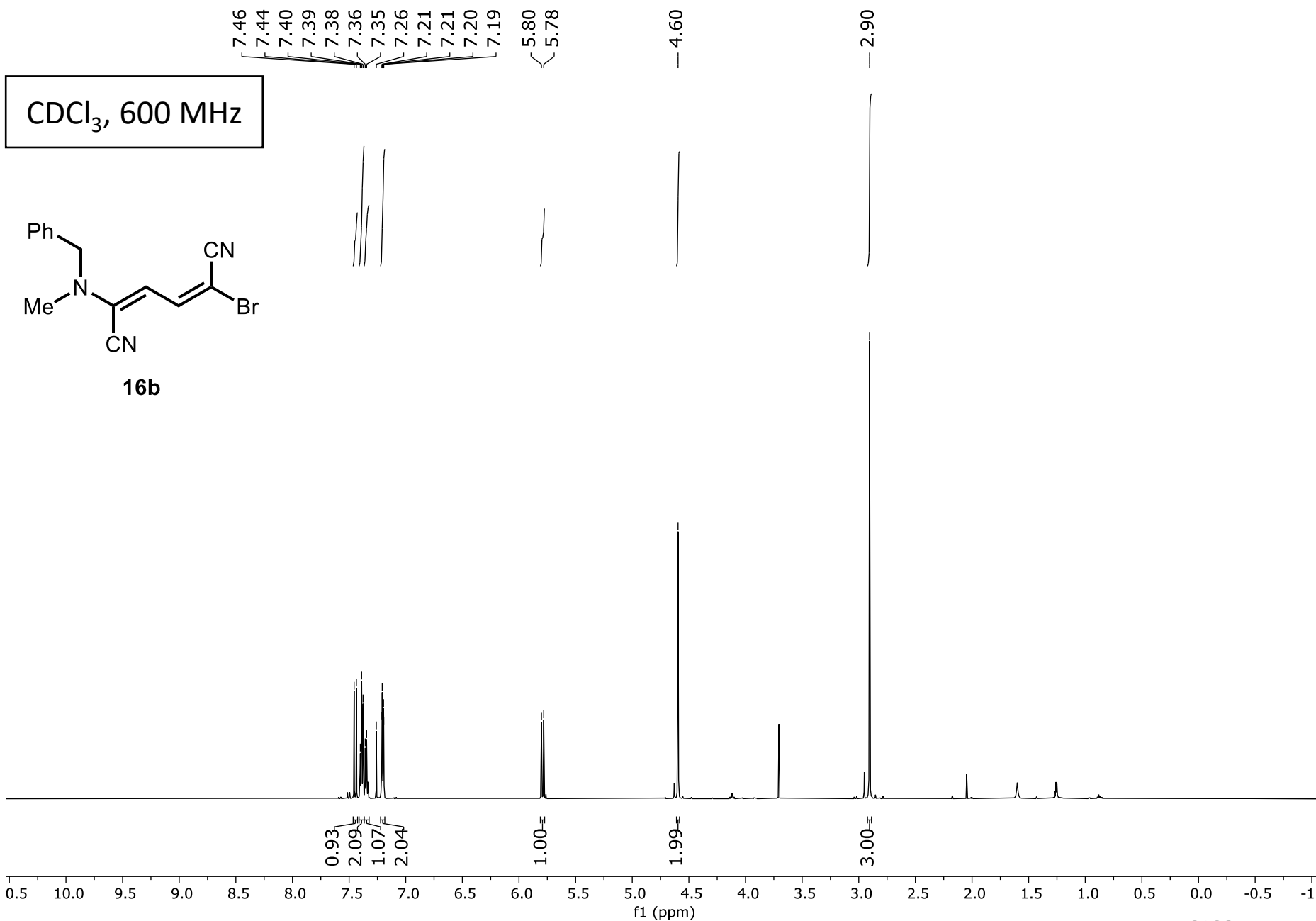


CDCl₃, 151 MHz

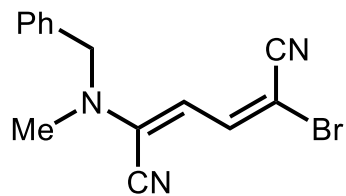


15b

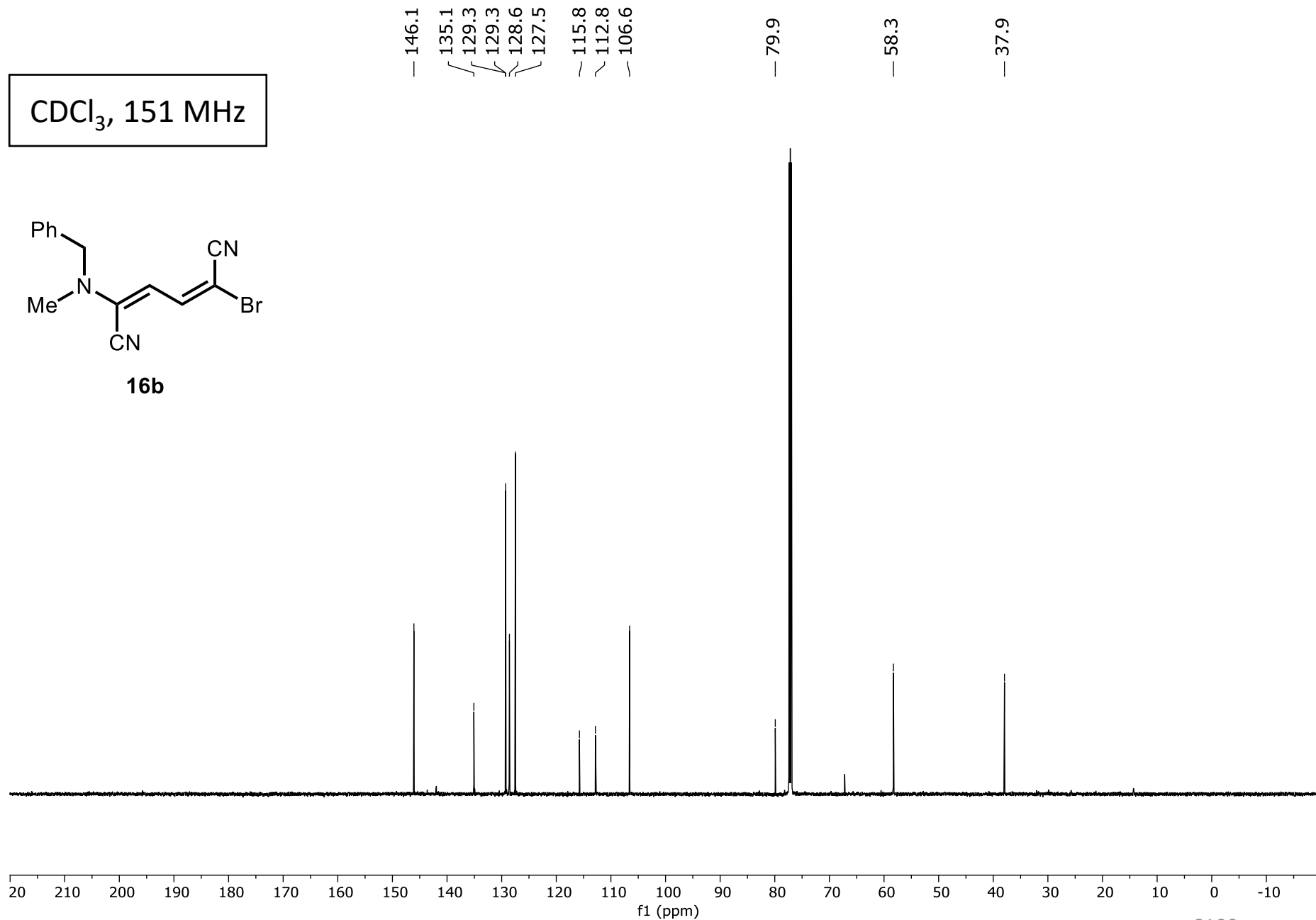




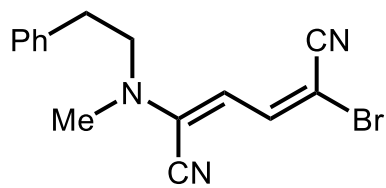
CDCl₃, 151 MHz



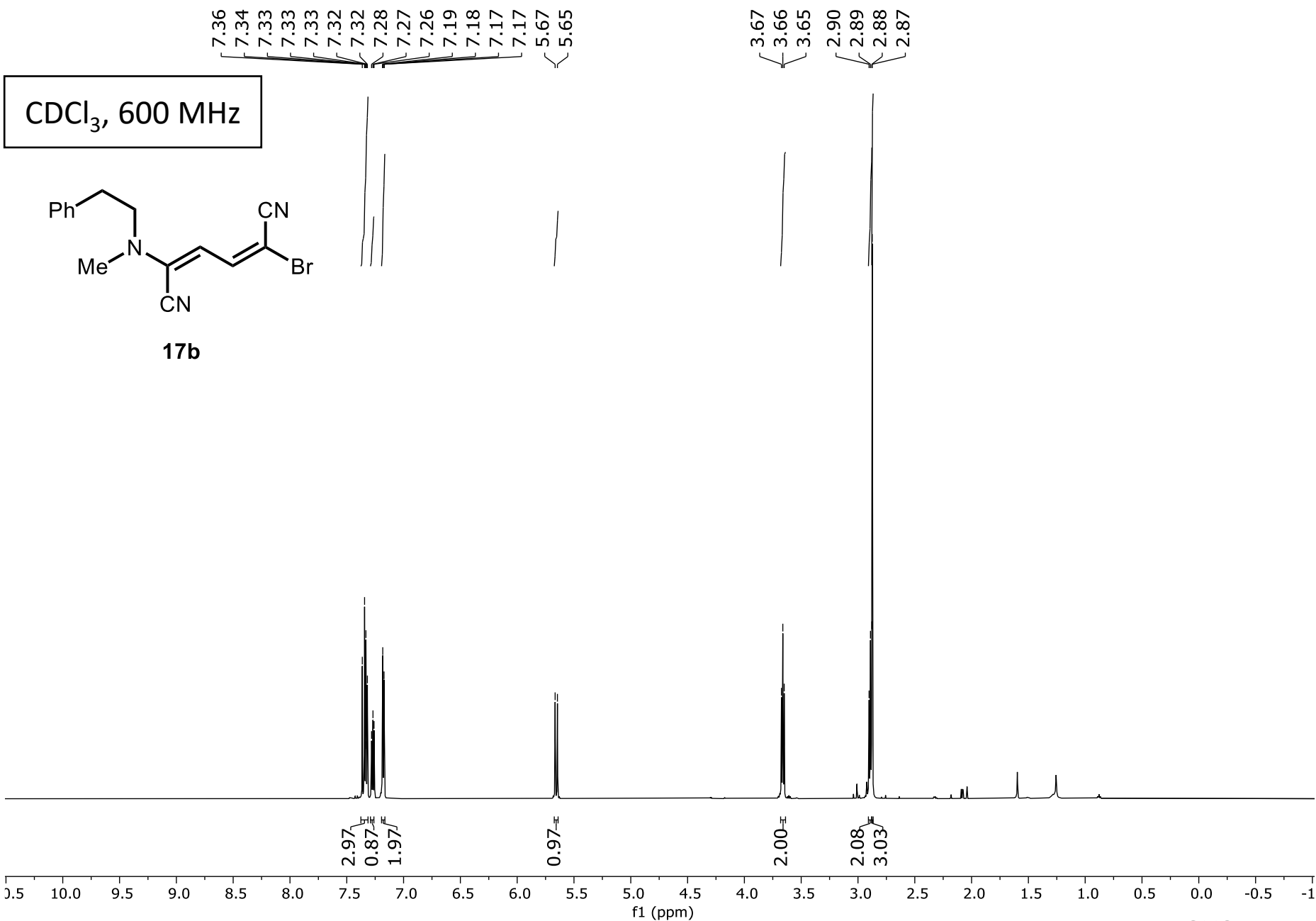
16b



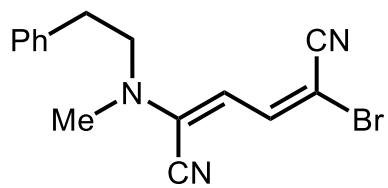
CDCl₃, 600 MHz



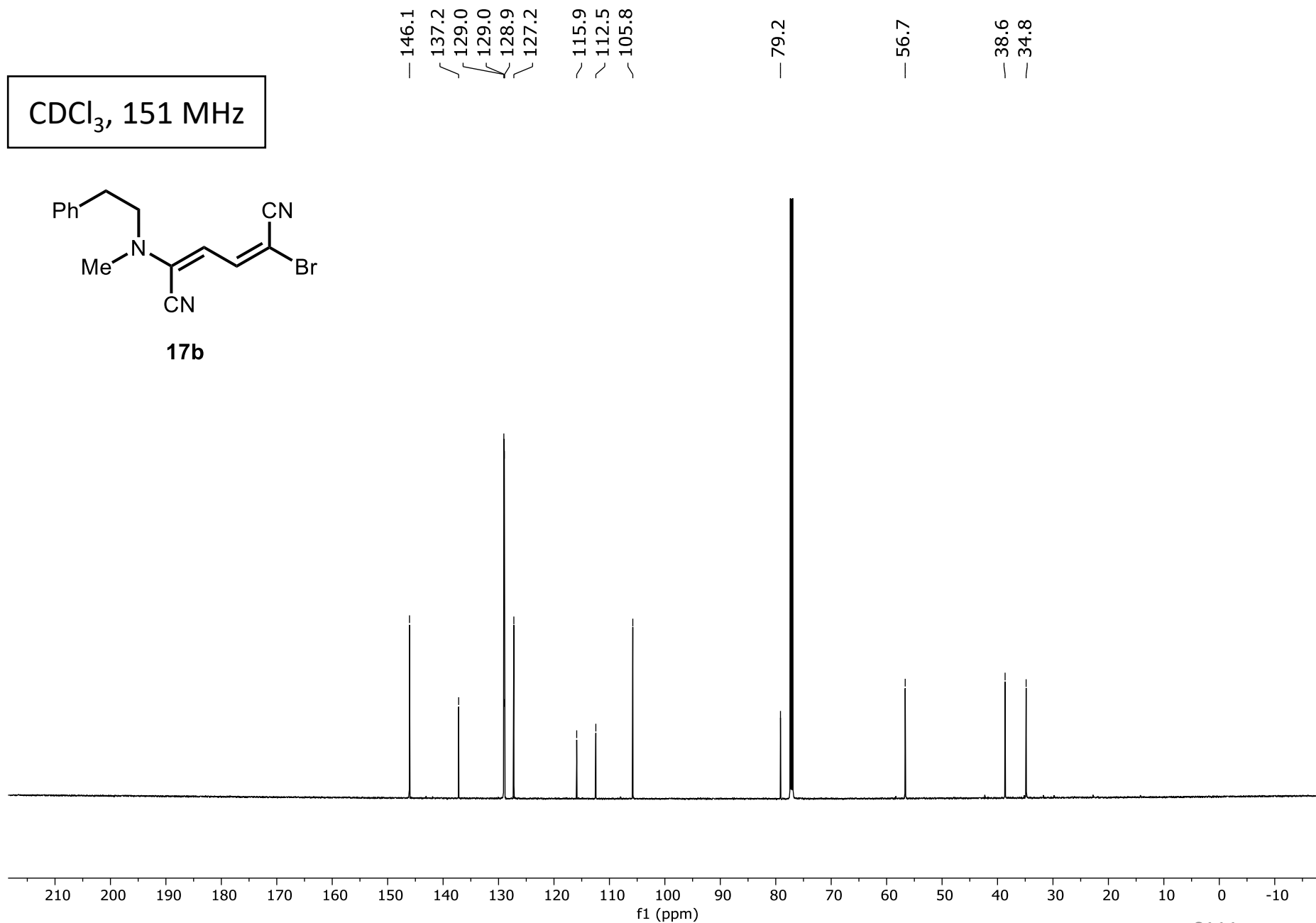
17b



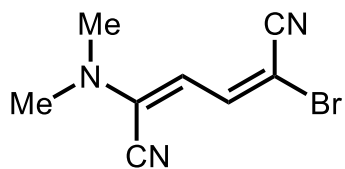
CDCl₃, 151 MHz



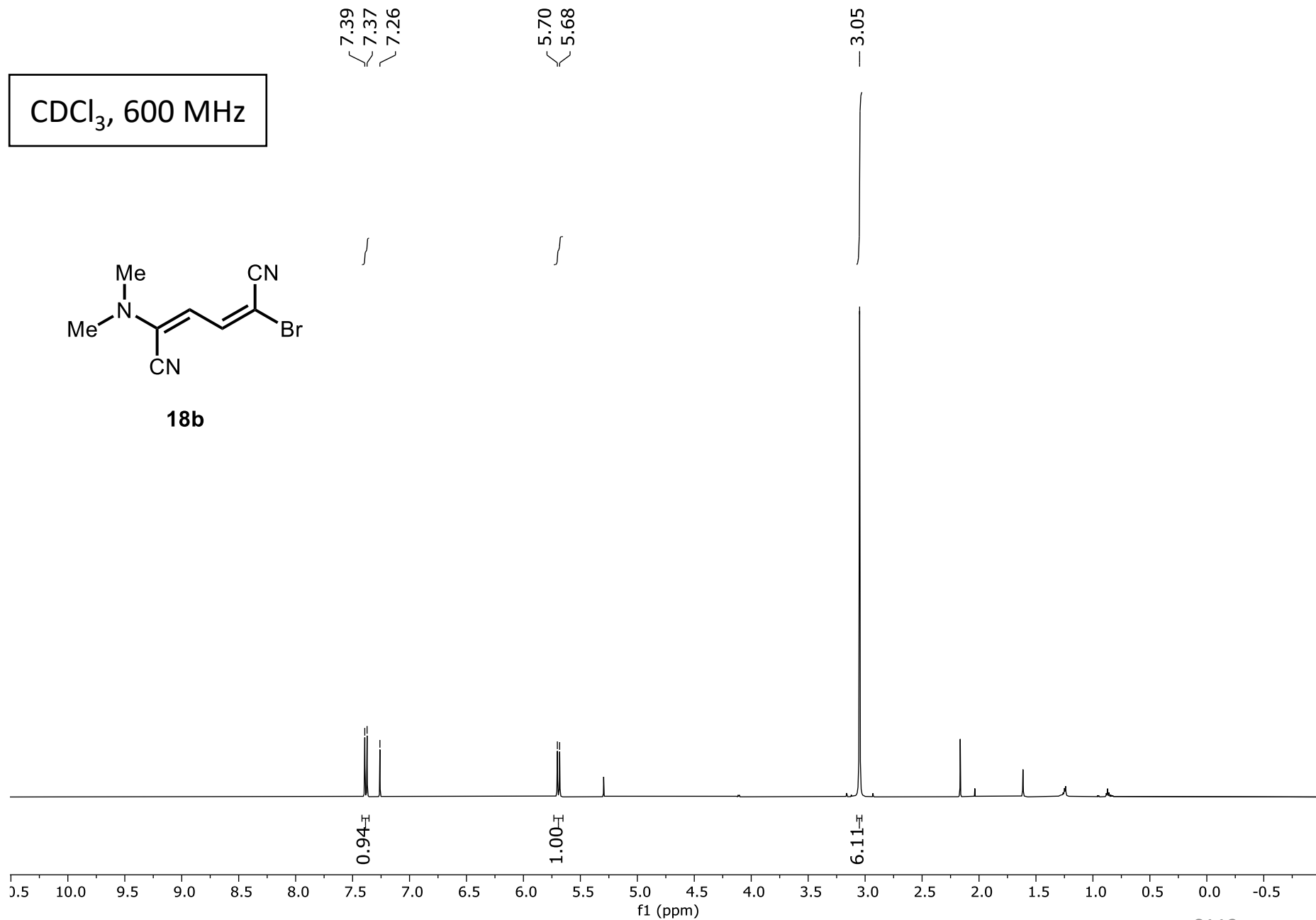
17b



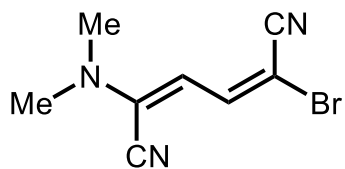
CDCl₃, 600 MHz



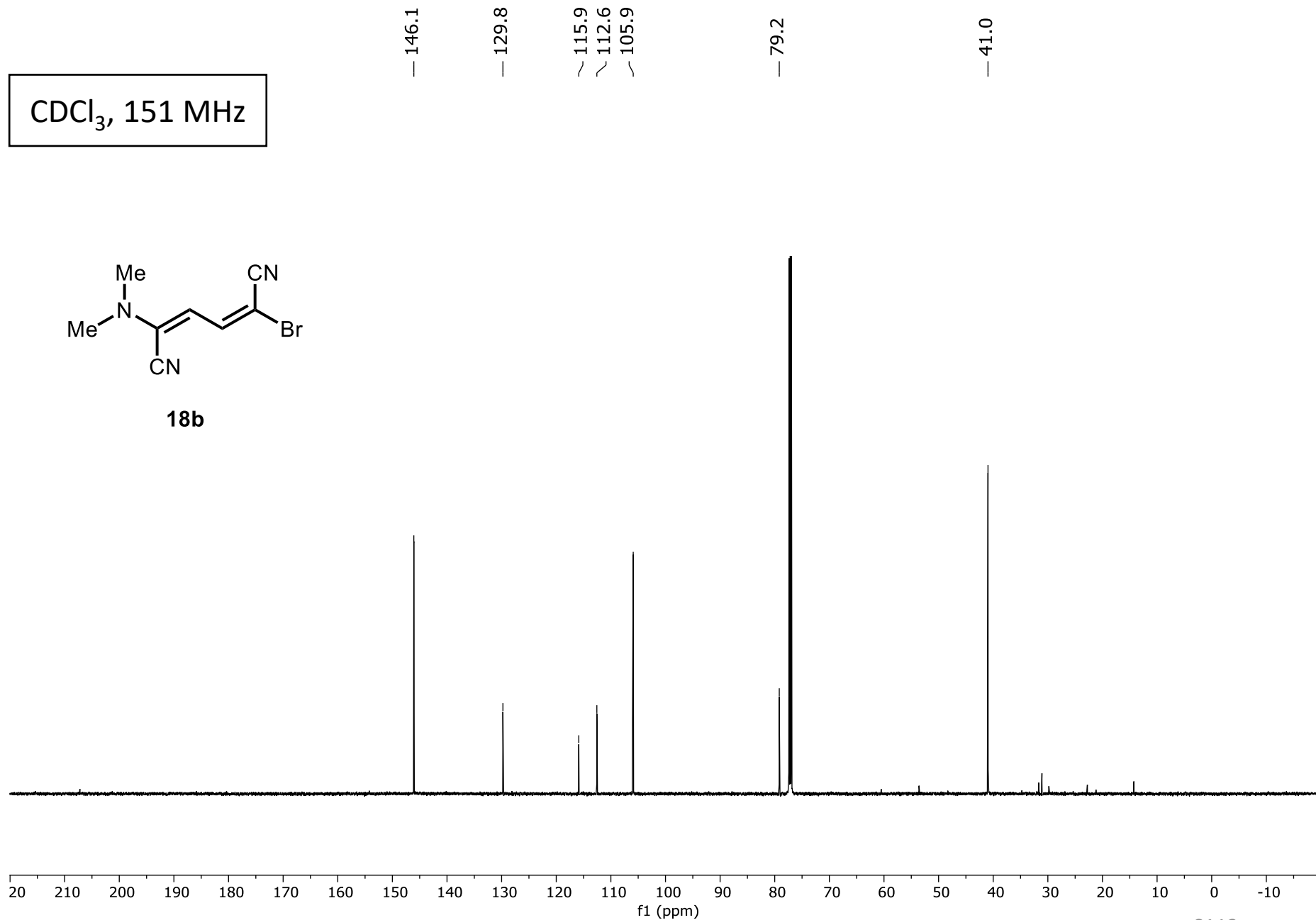
18b

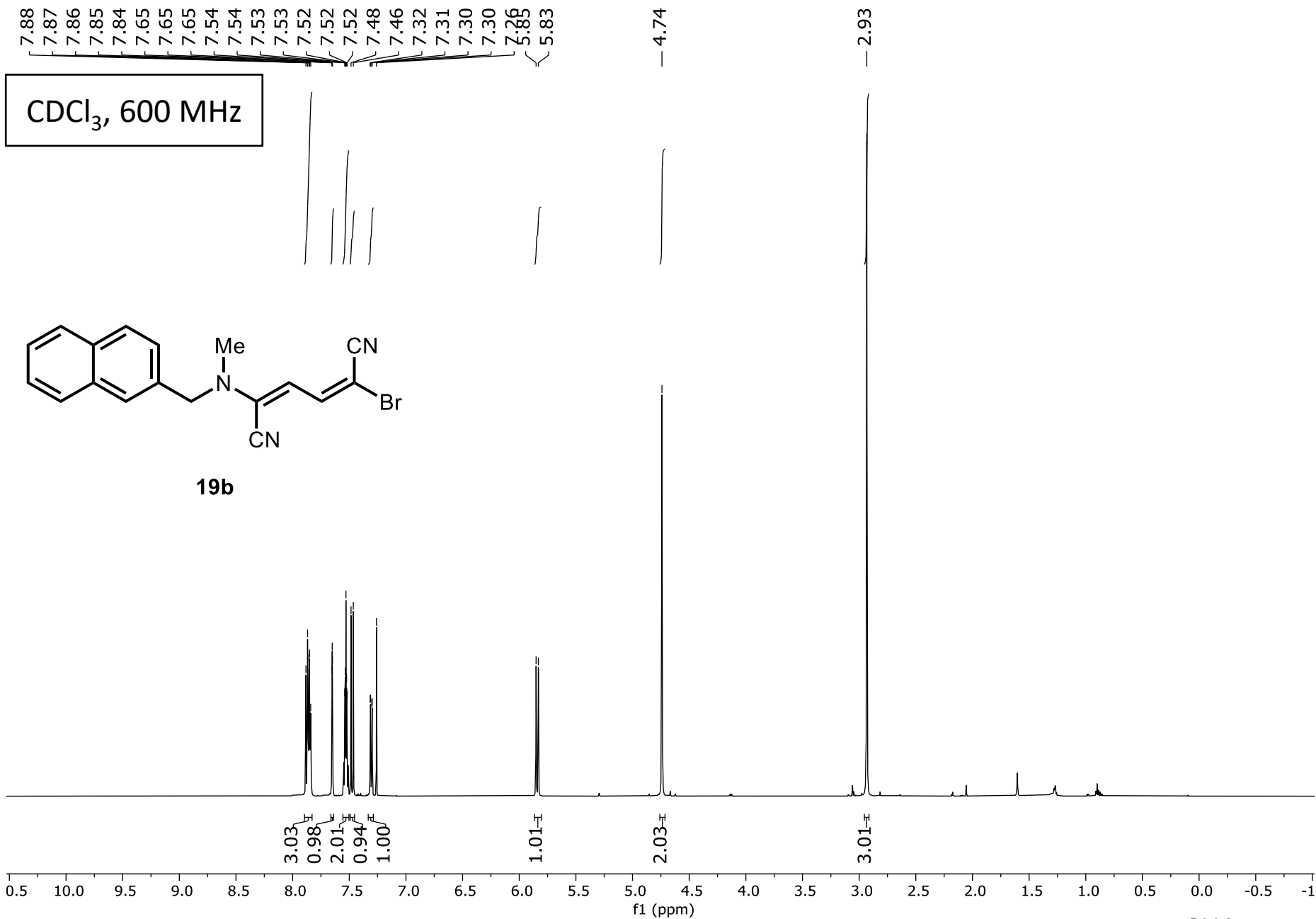


CDCl₃, 151 MHz

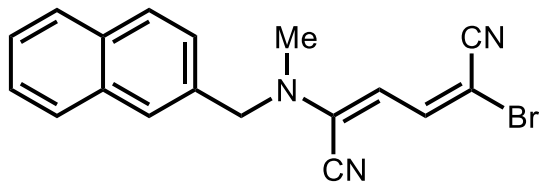


18b

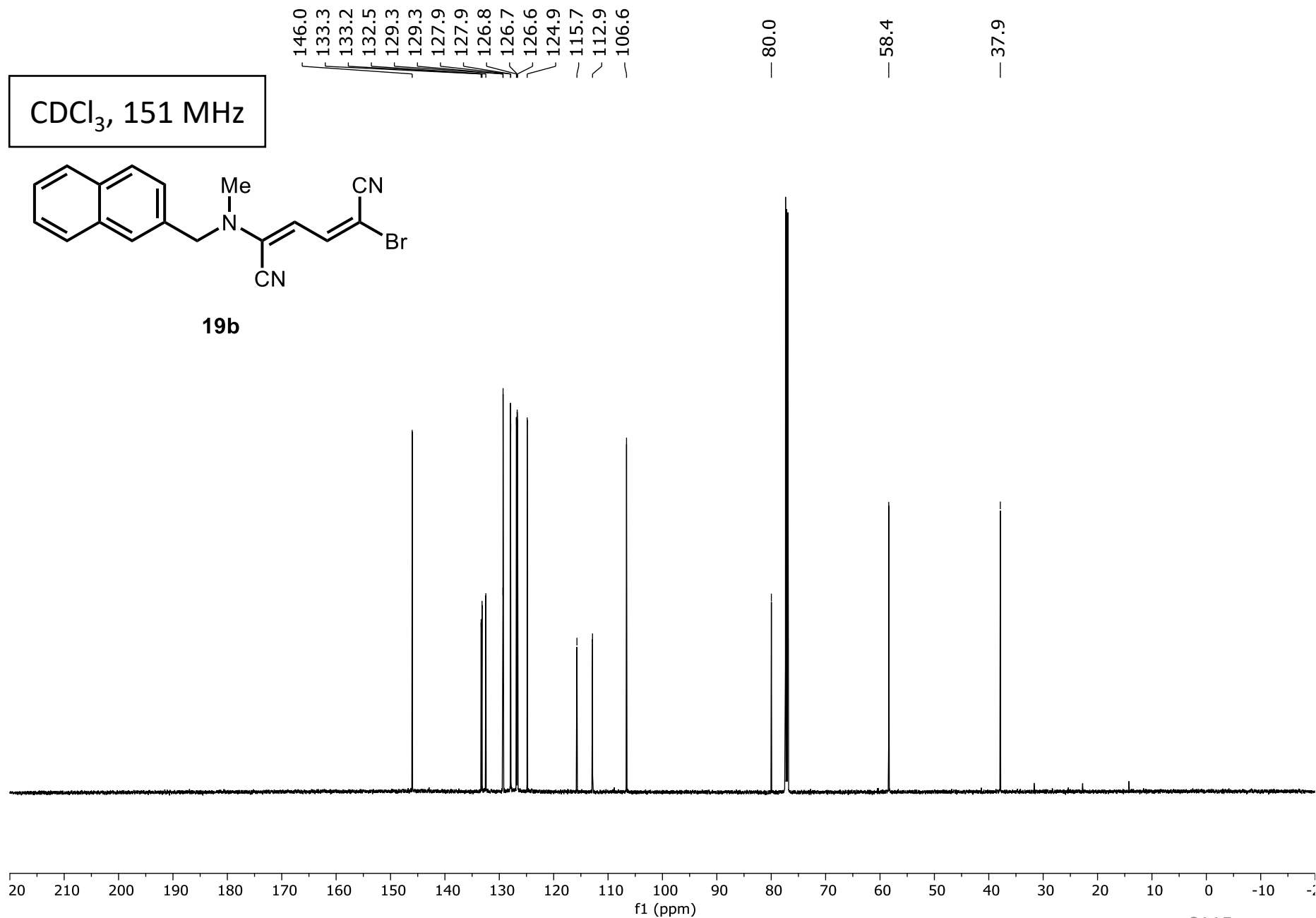




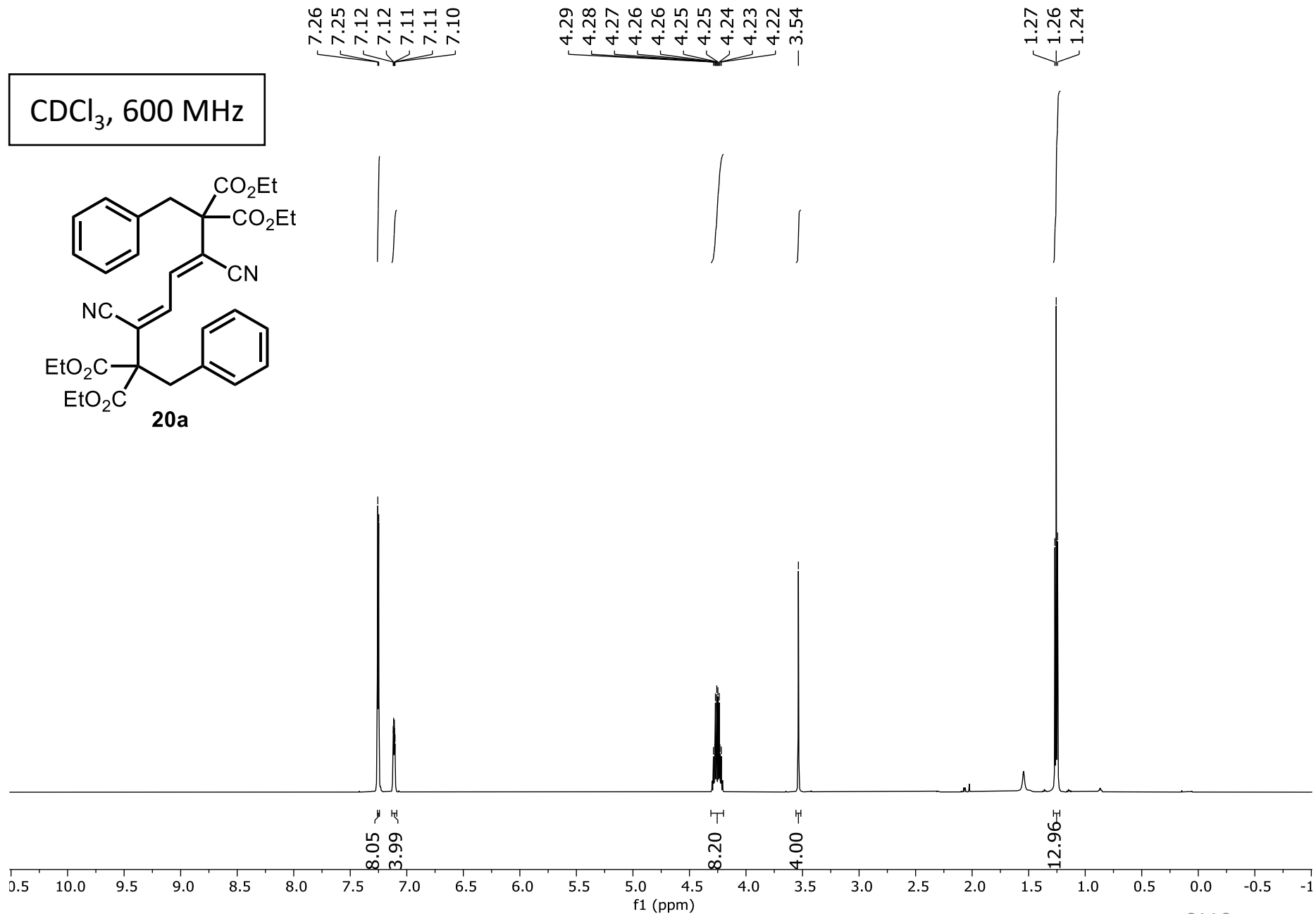
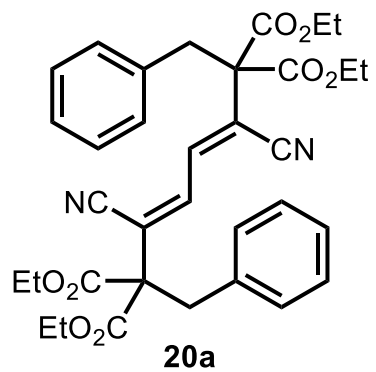
CDCl₃, 151 MHz



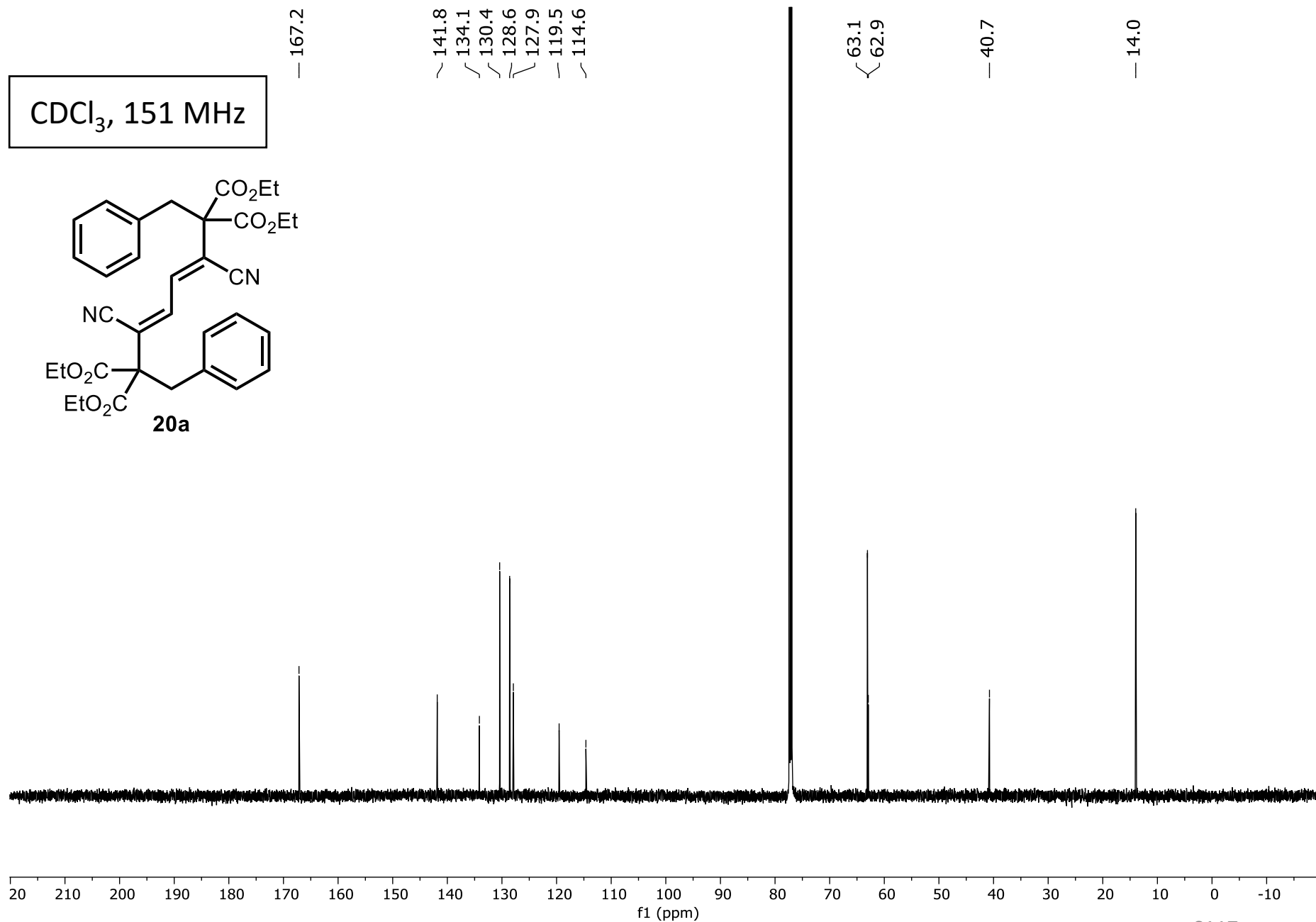
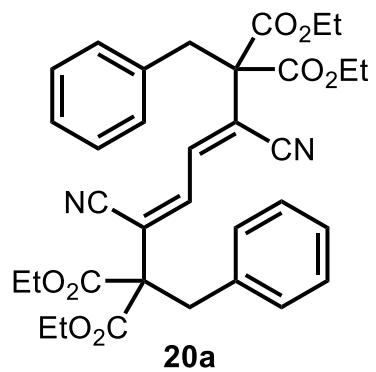
19b



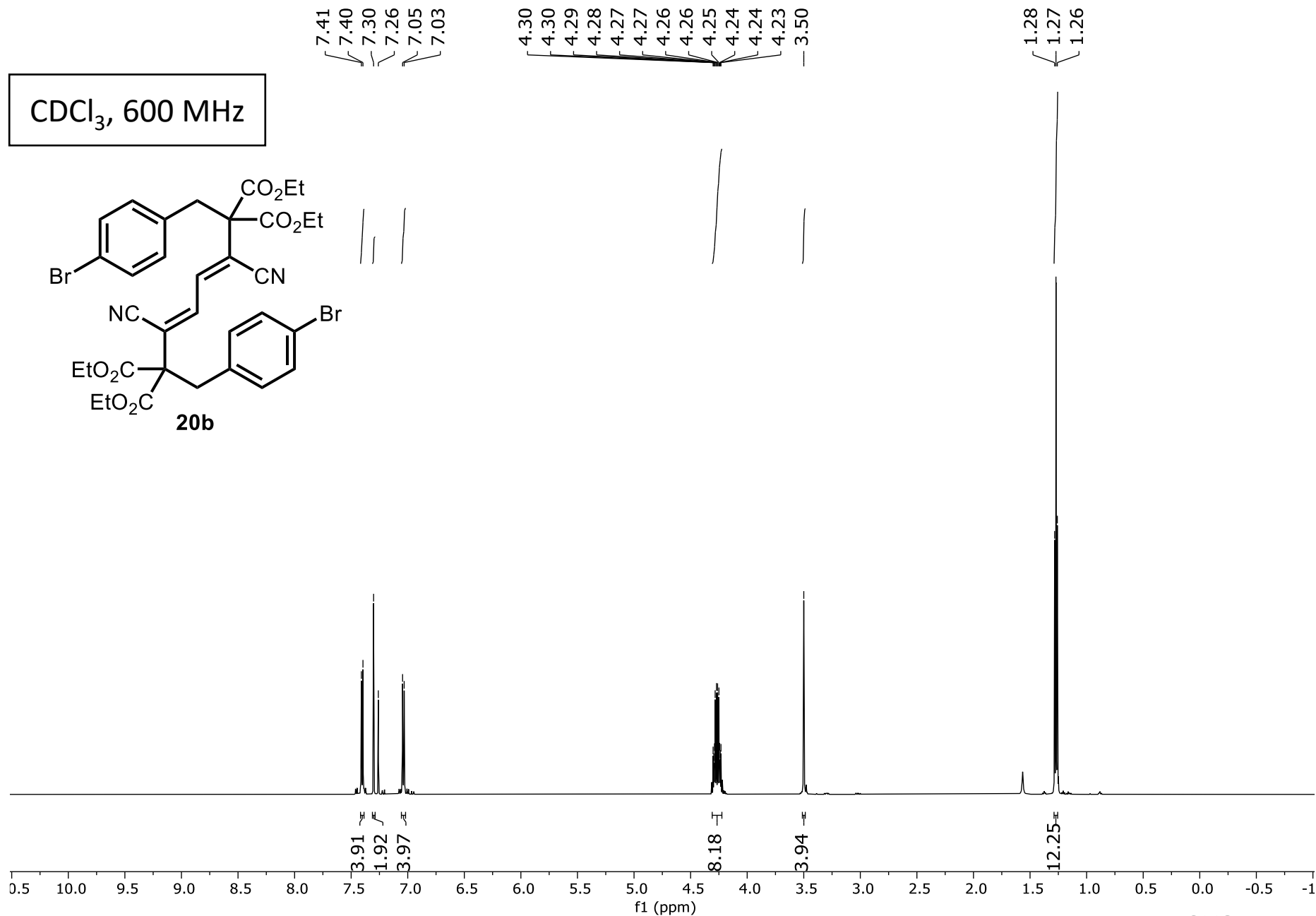
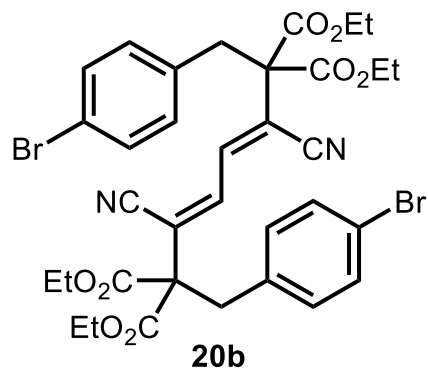
CDCl₃, 600 MHz



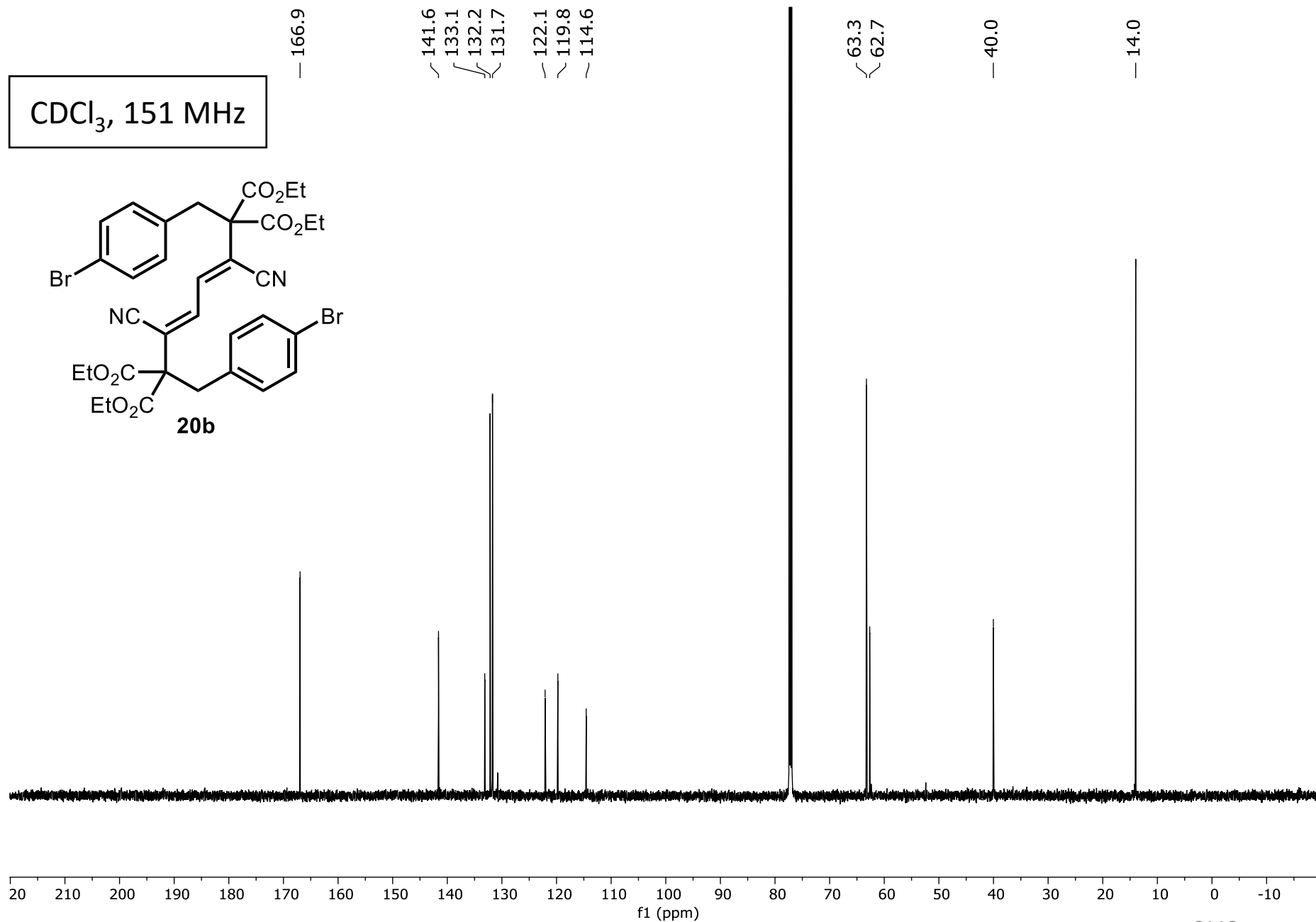
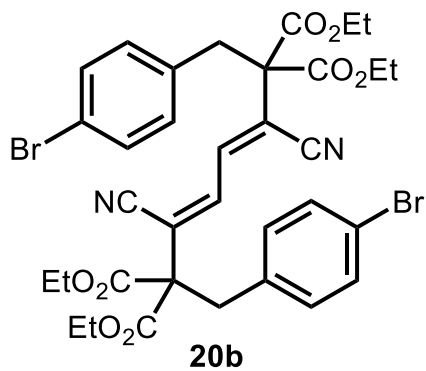
CDCl₃, 151 MHz



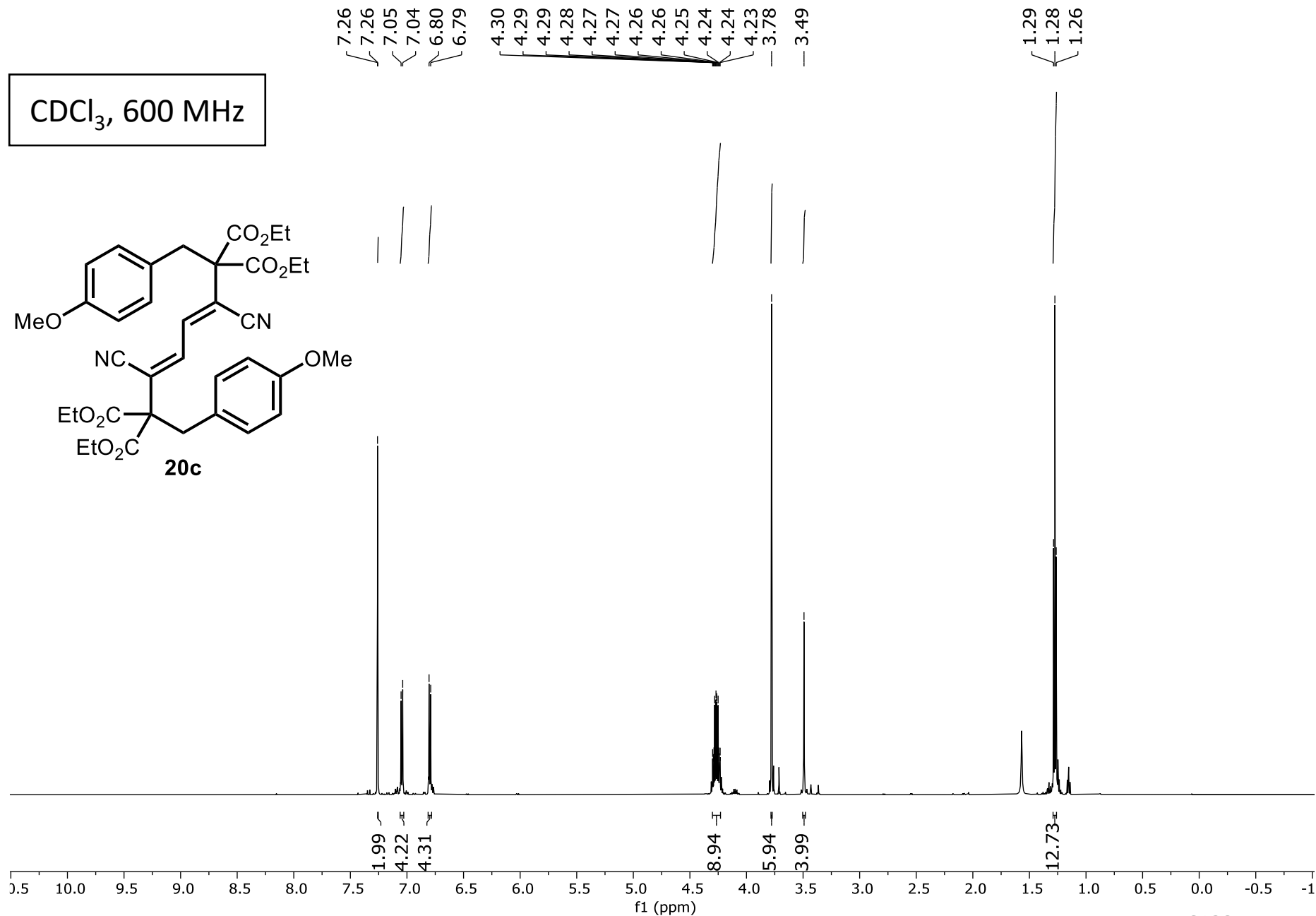
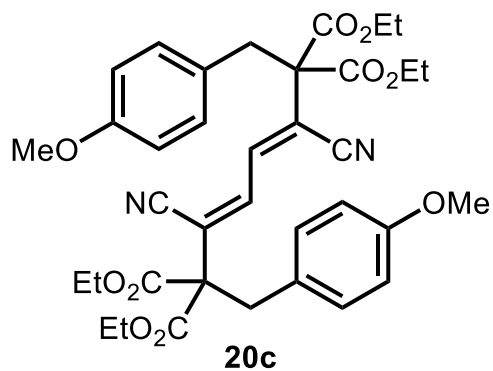
CDCl₃, 600 MHz



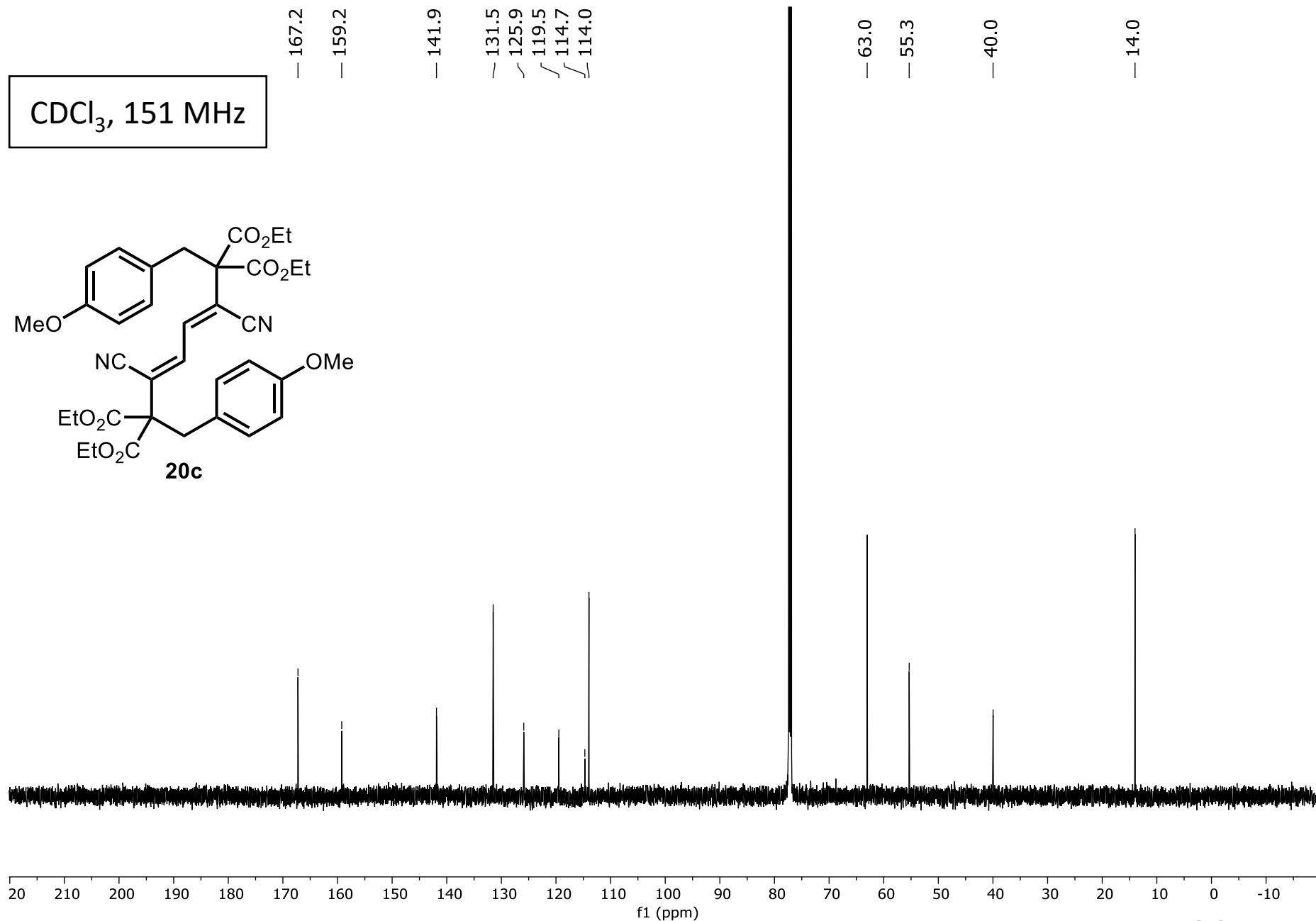
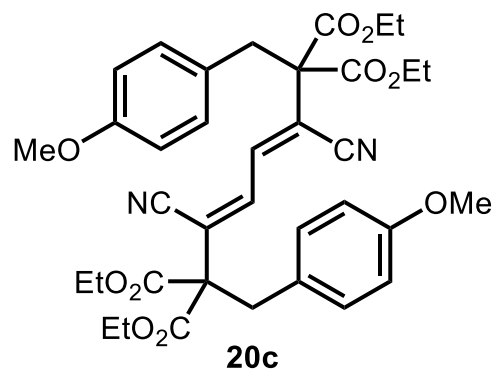
CDCl₃, 151 MHz



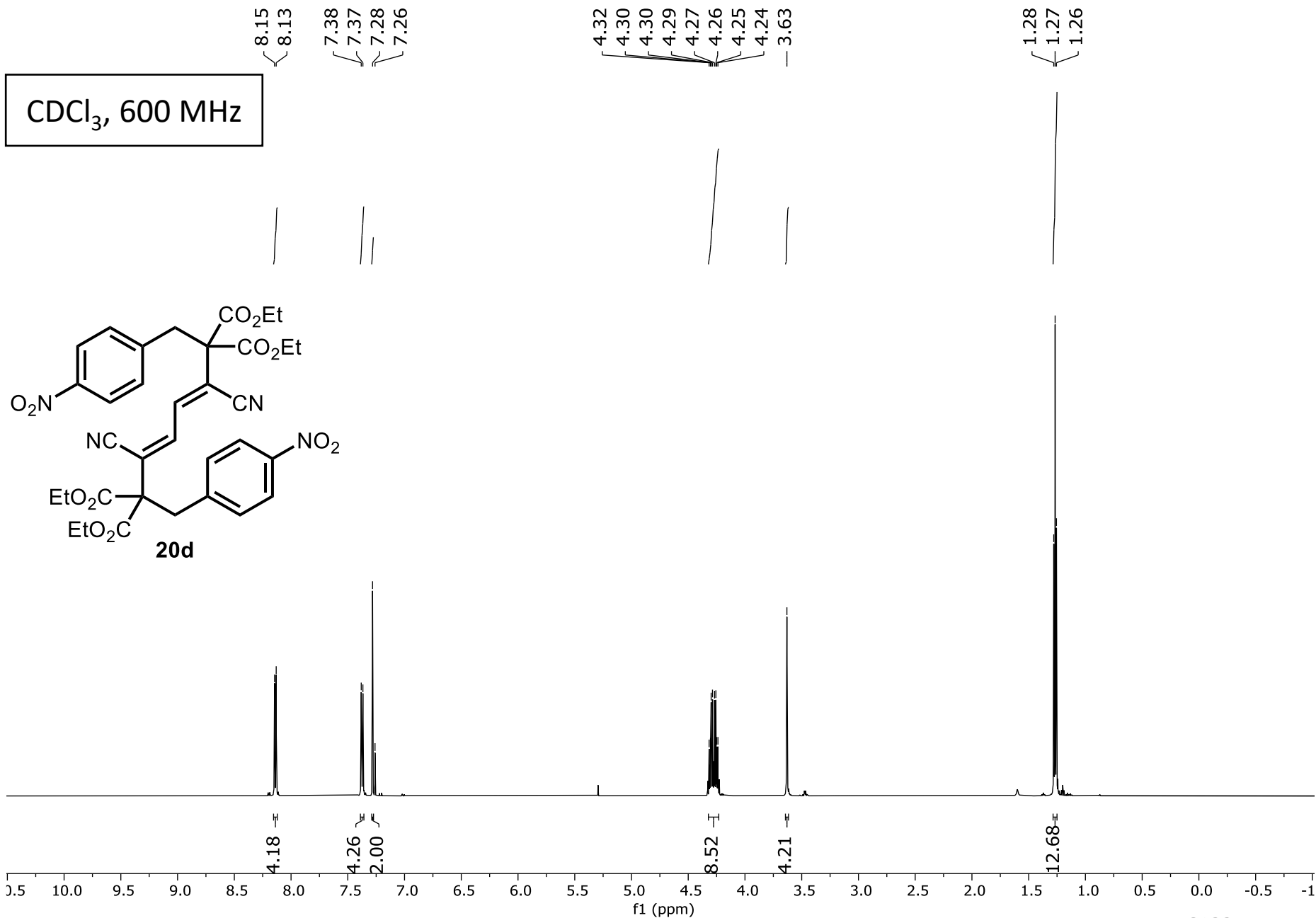
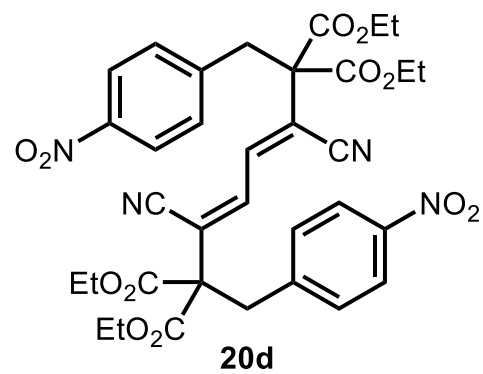
CDCl₃, 600 MHz



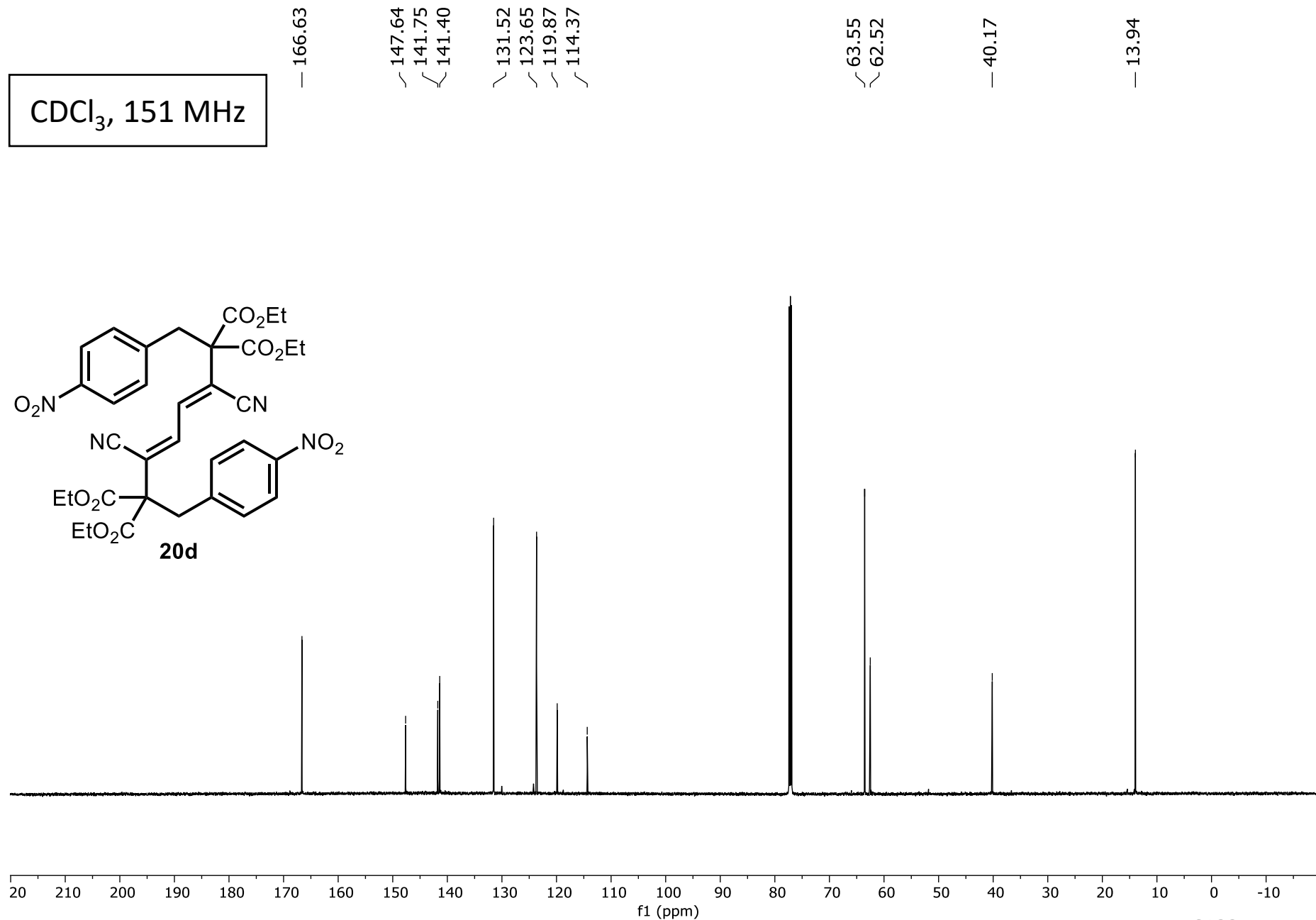
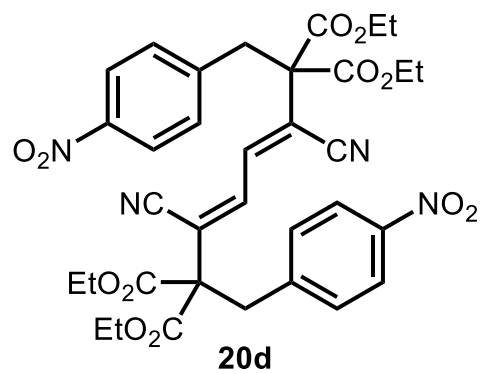
CDCl₃, 151 MHz



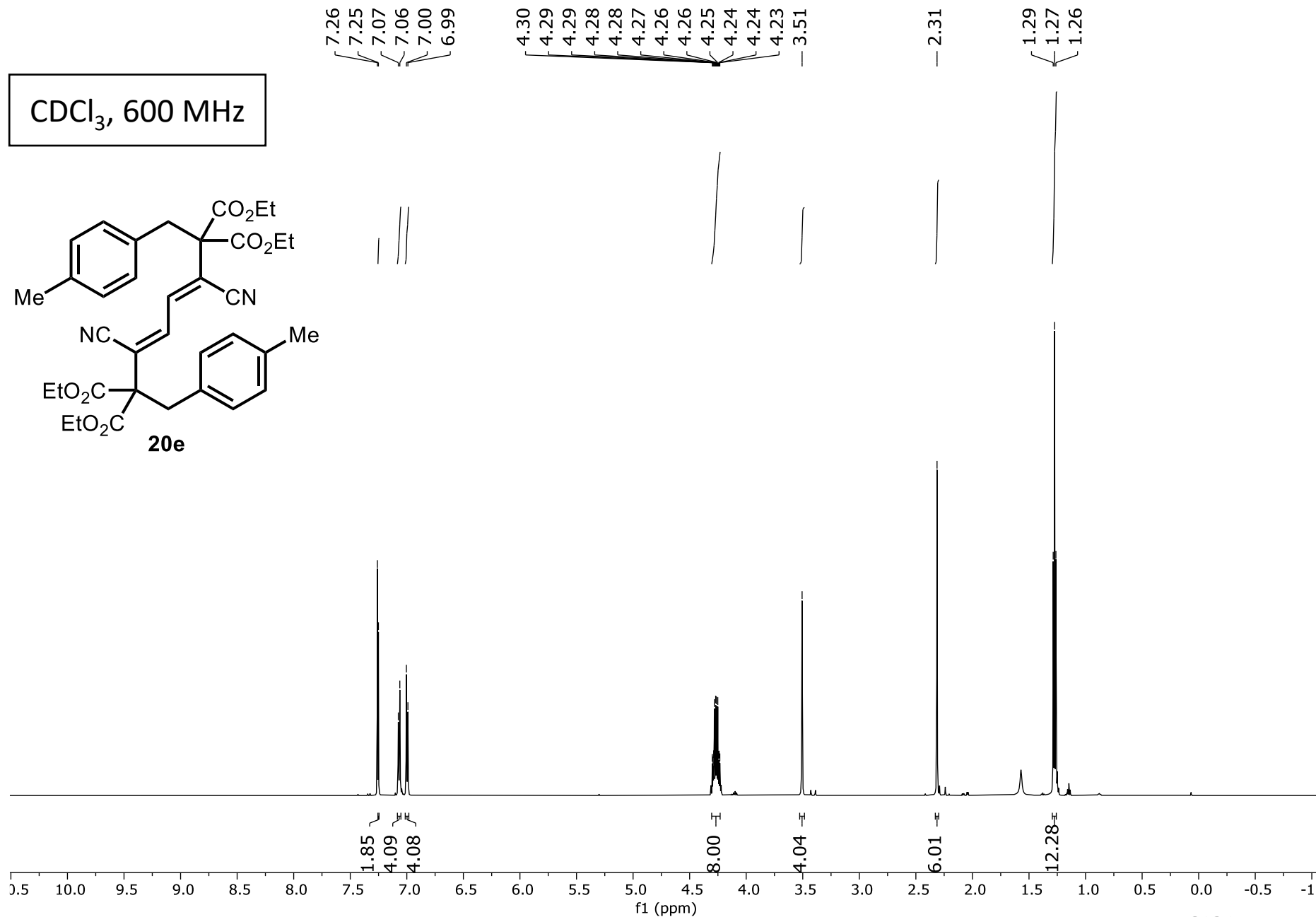
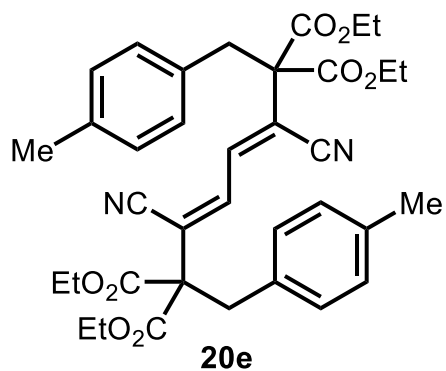
CDCl₃, 600 MHz



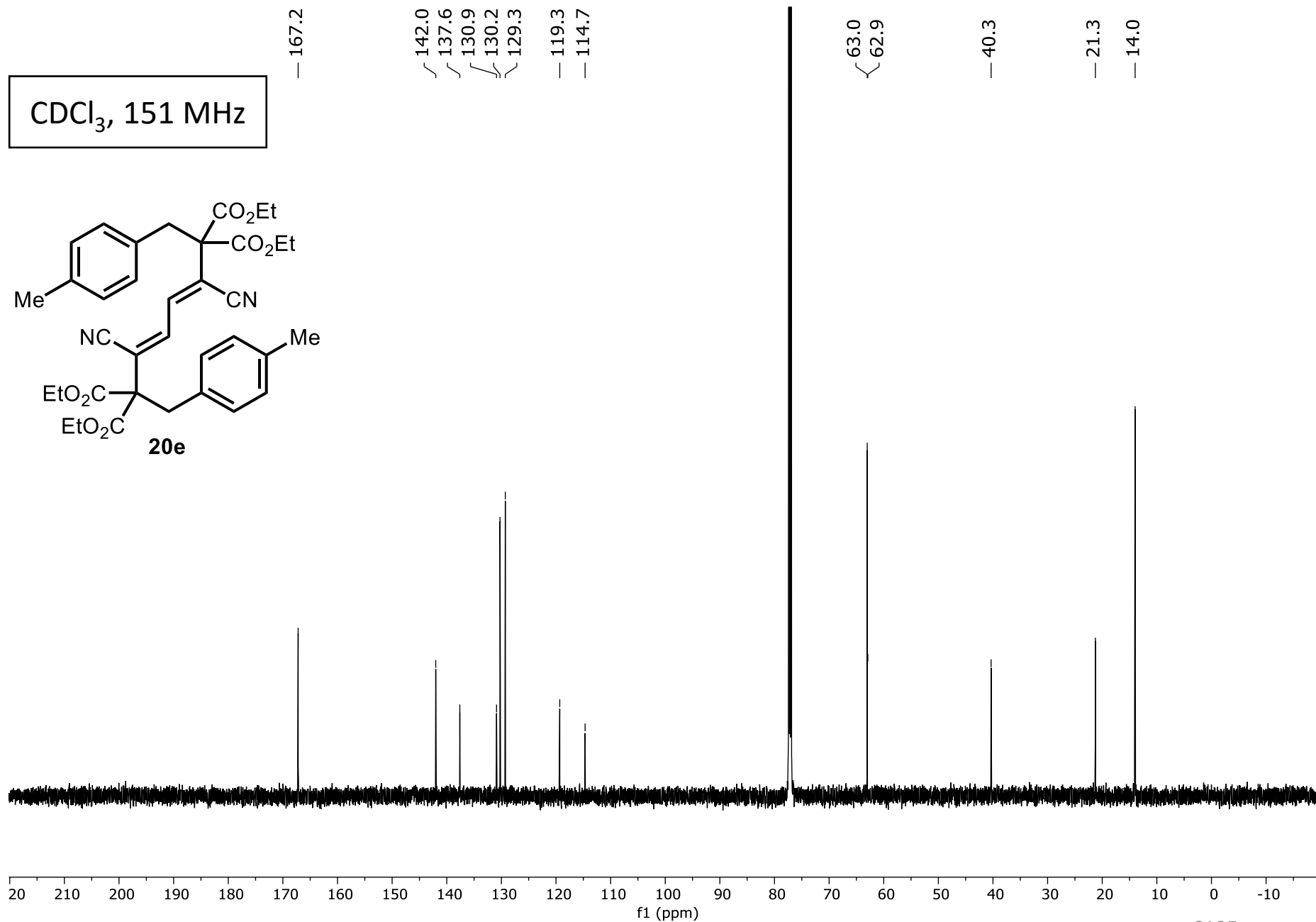
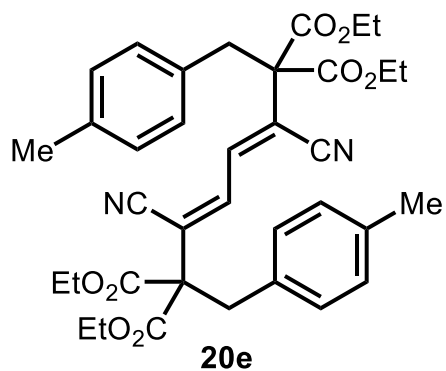
CDCl₃, 151 MHz



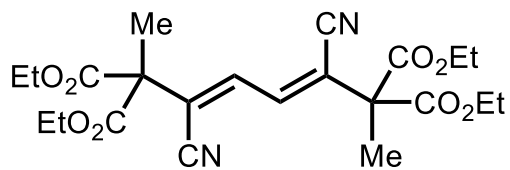
CDCl₃, 600 MHz



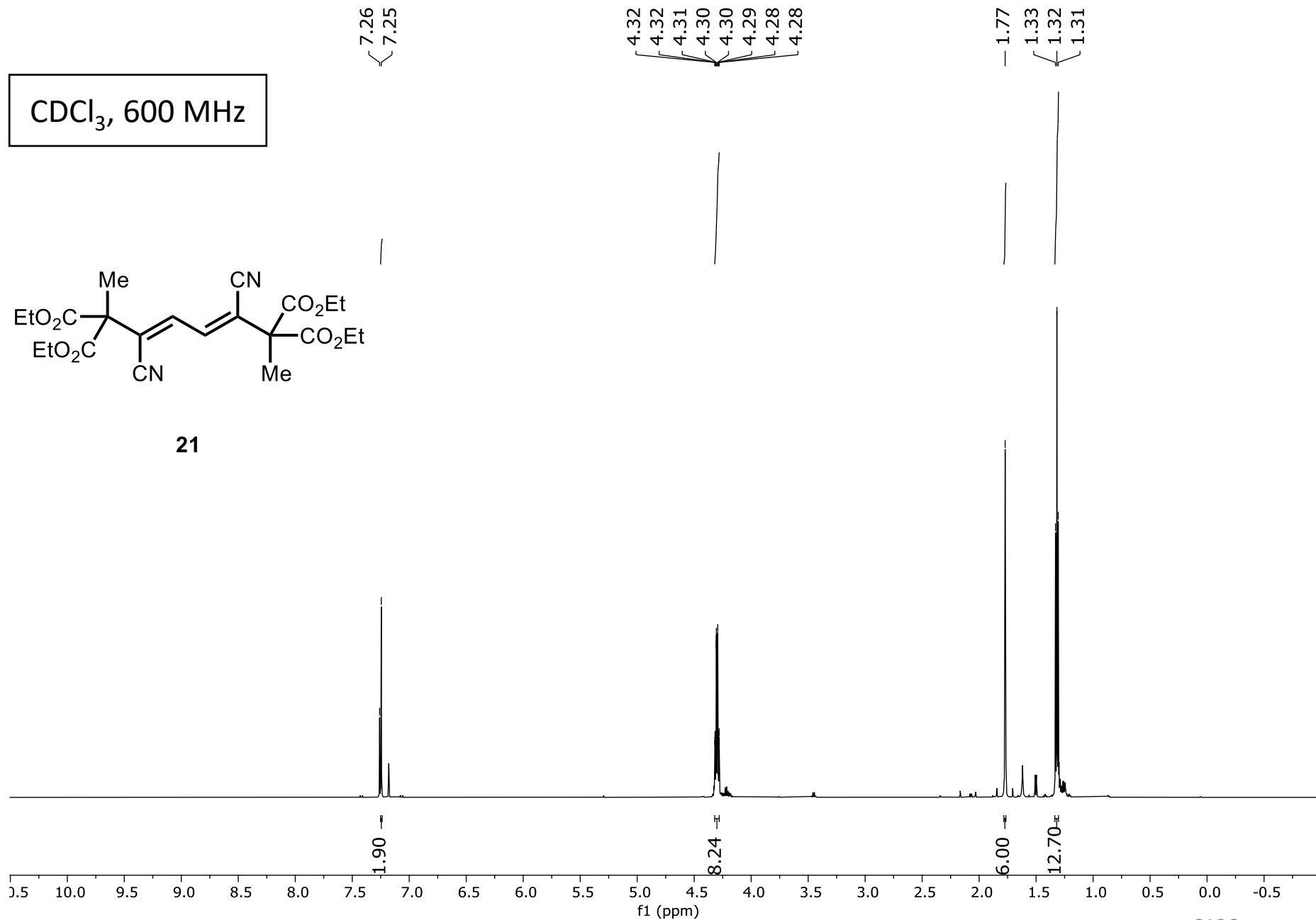
CDCl₃, 151 MHz



CDCl₃, 600 MHz



21



CDCl₃, 151 MHz

— 168.1

— 139.1

— 121.5

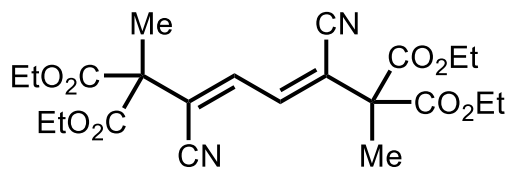
— 114.7

— 63.2

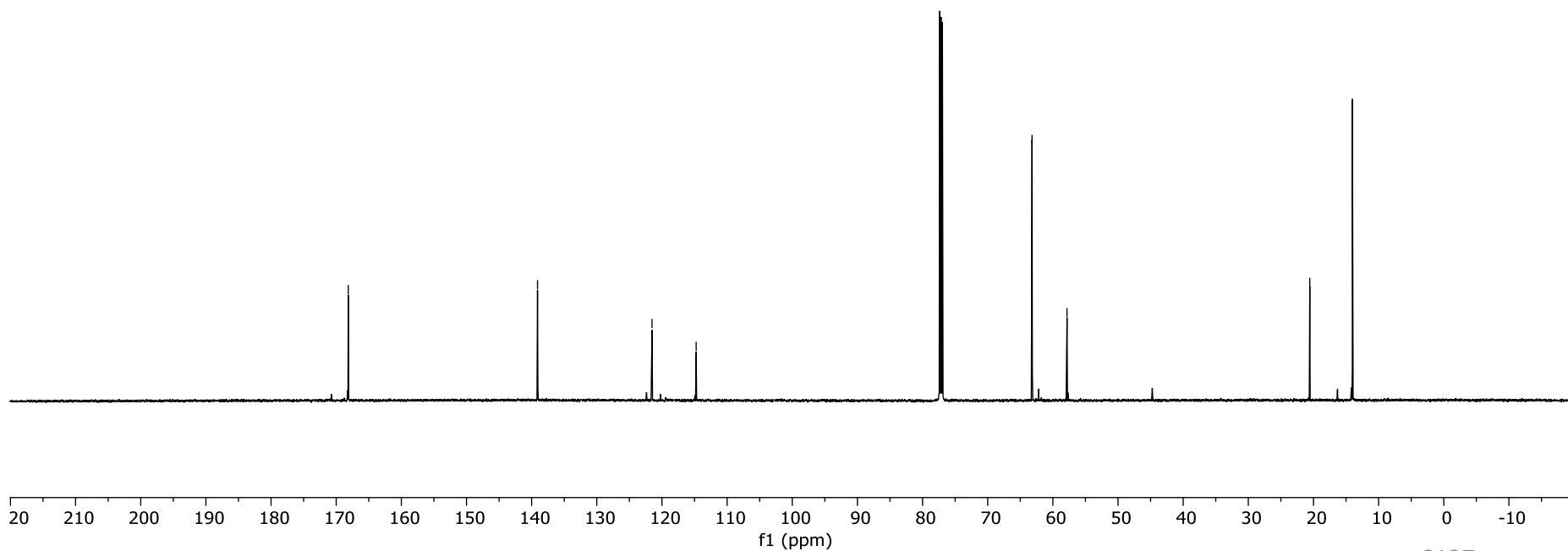
— 57.8

— 20.6

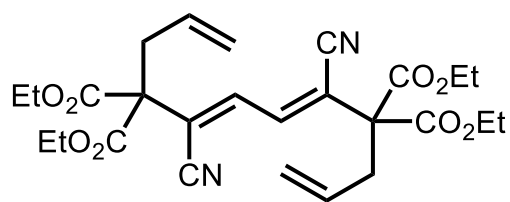
— 14.0



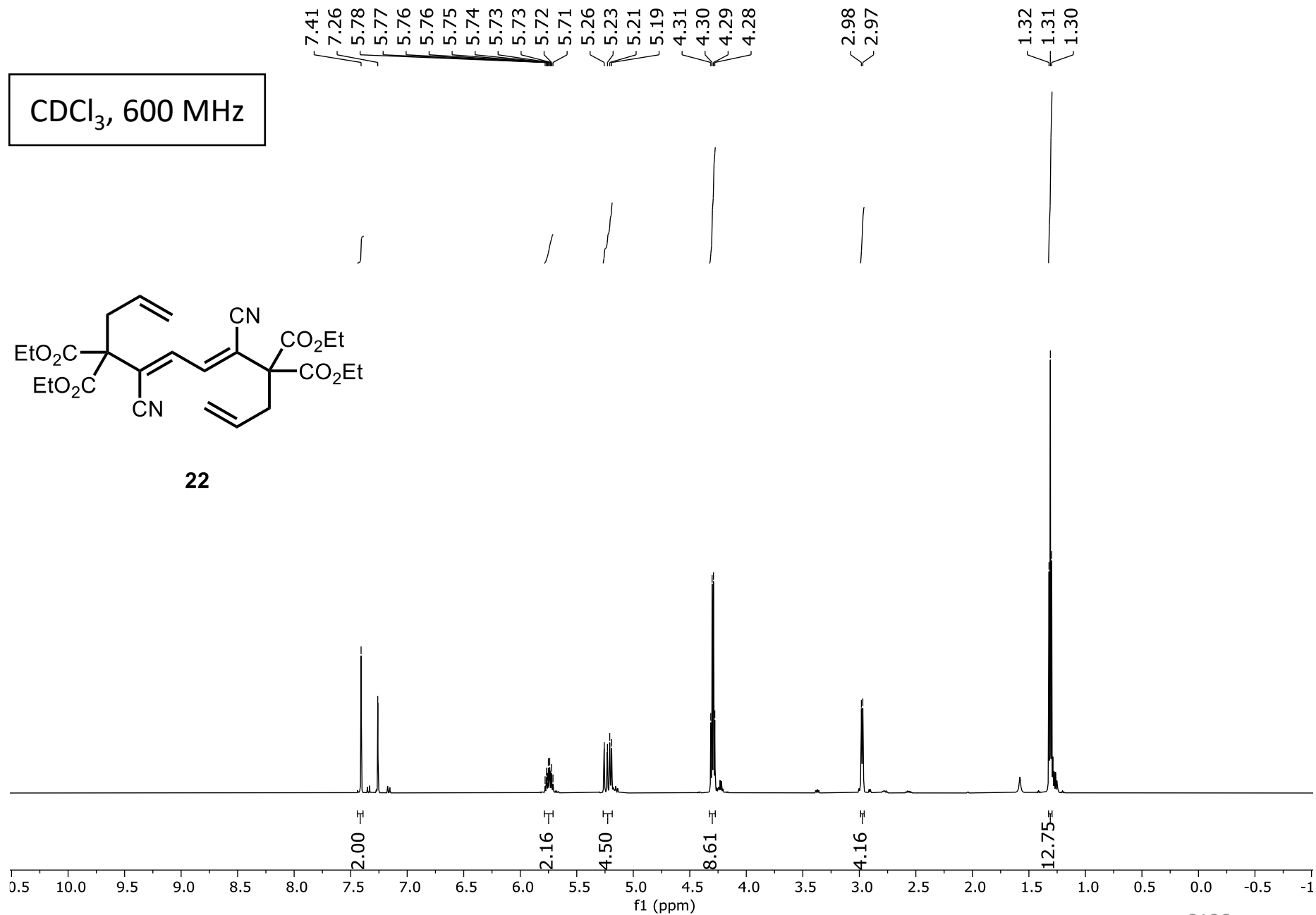
21



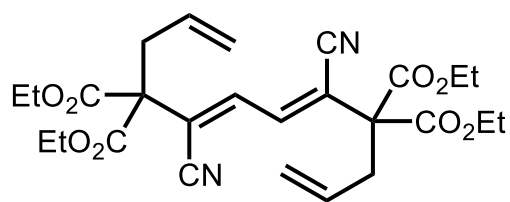
CDCl₃, 600 MHz



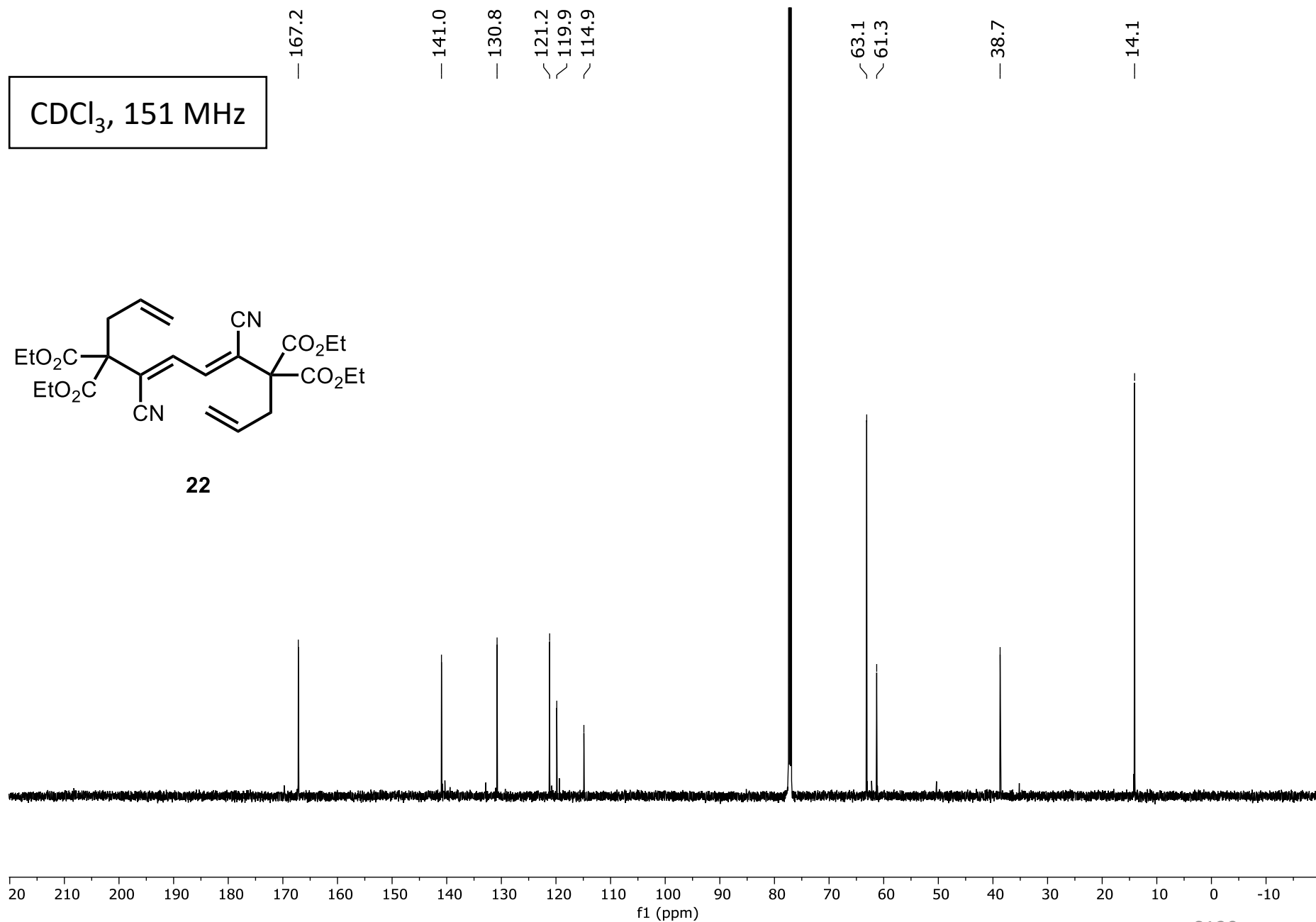
22

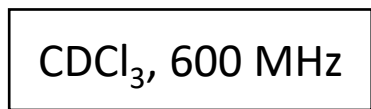


CDCl₃, 151 MHz

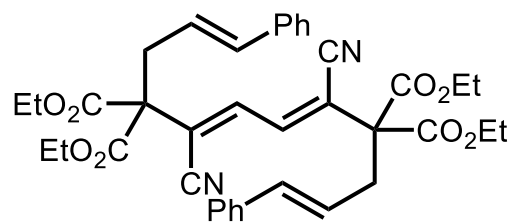


22

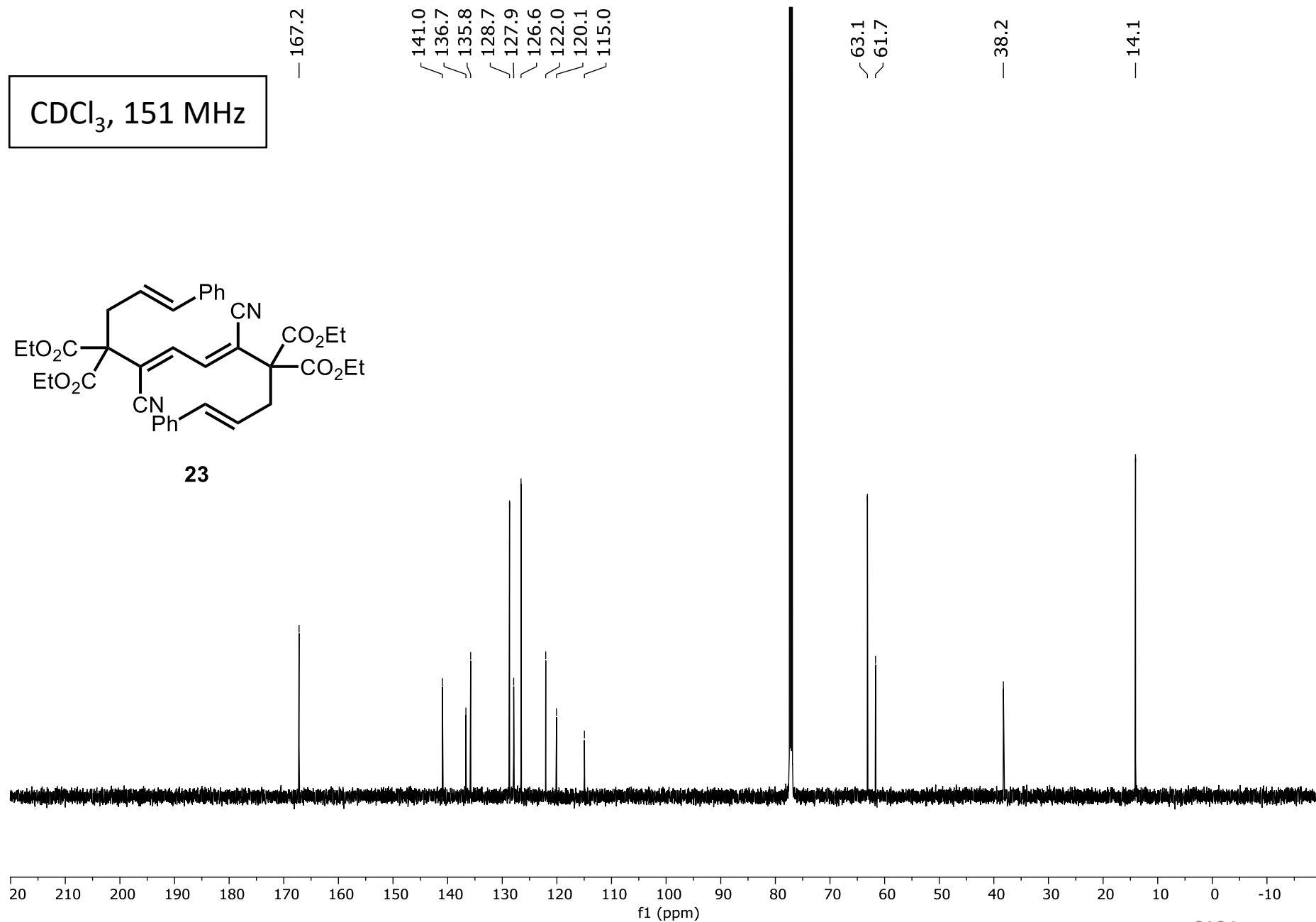




CDCl₃, 151 MHz

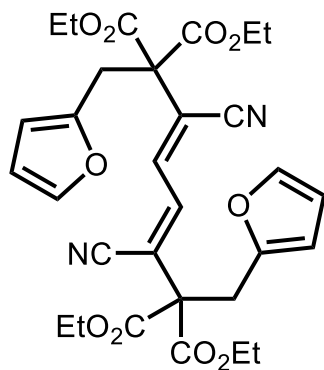


23

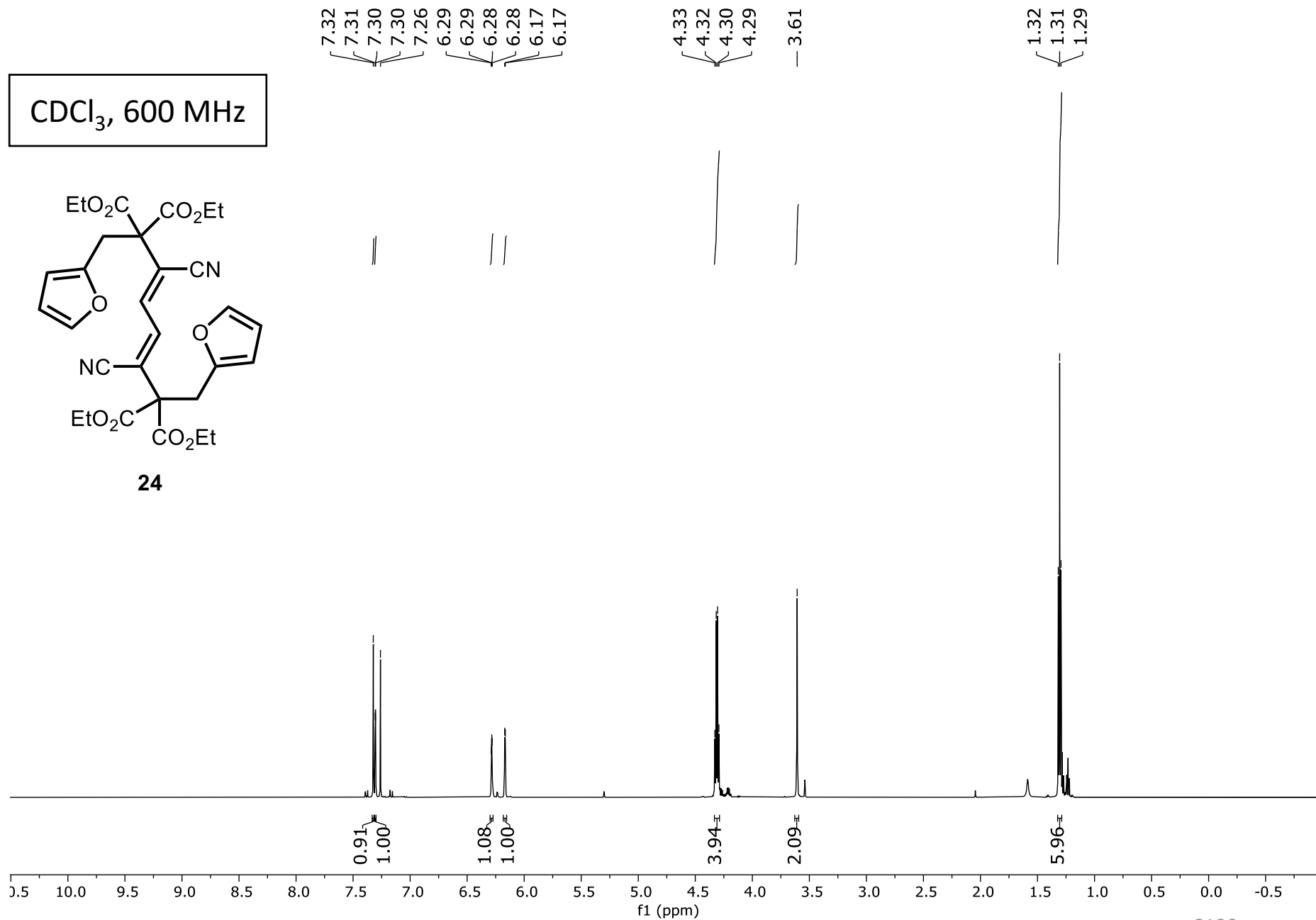


S131

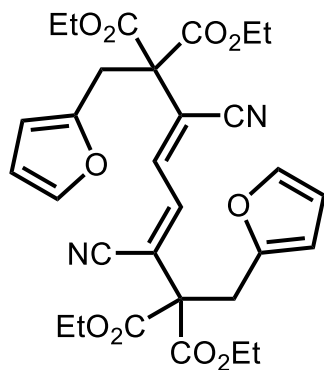
CDCl₃, 600 MHz



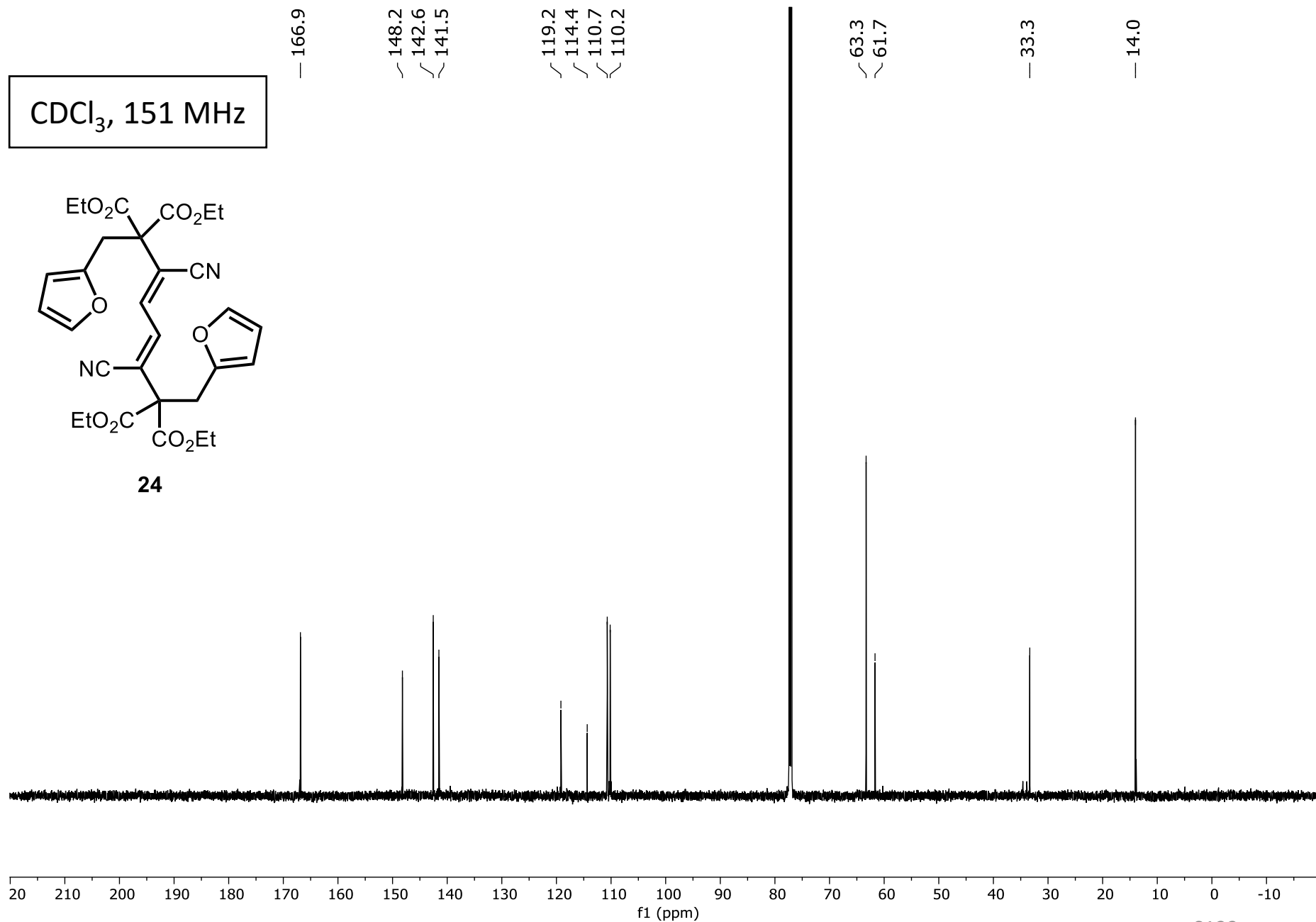
24

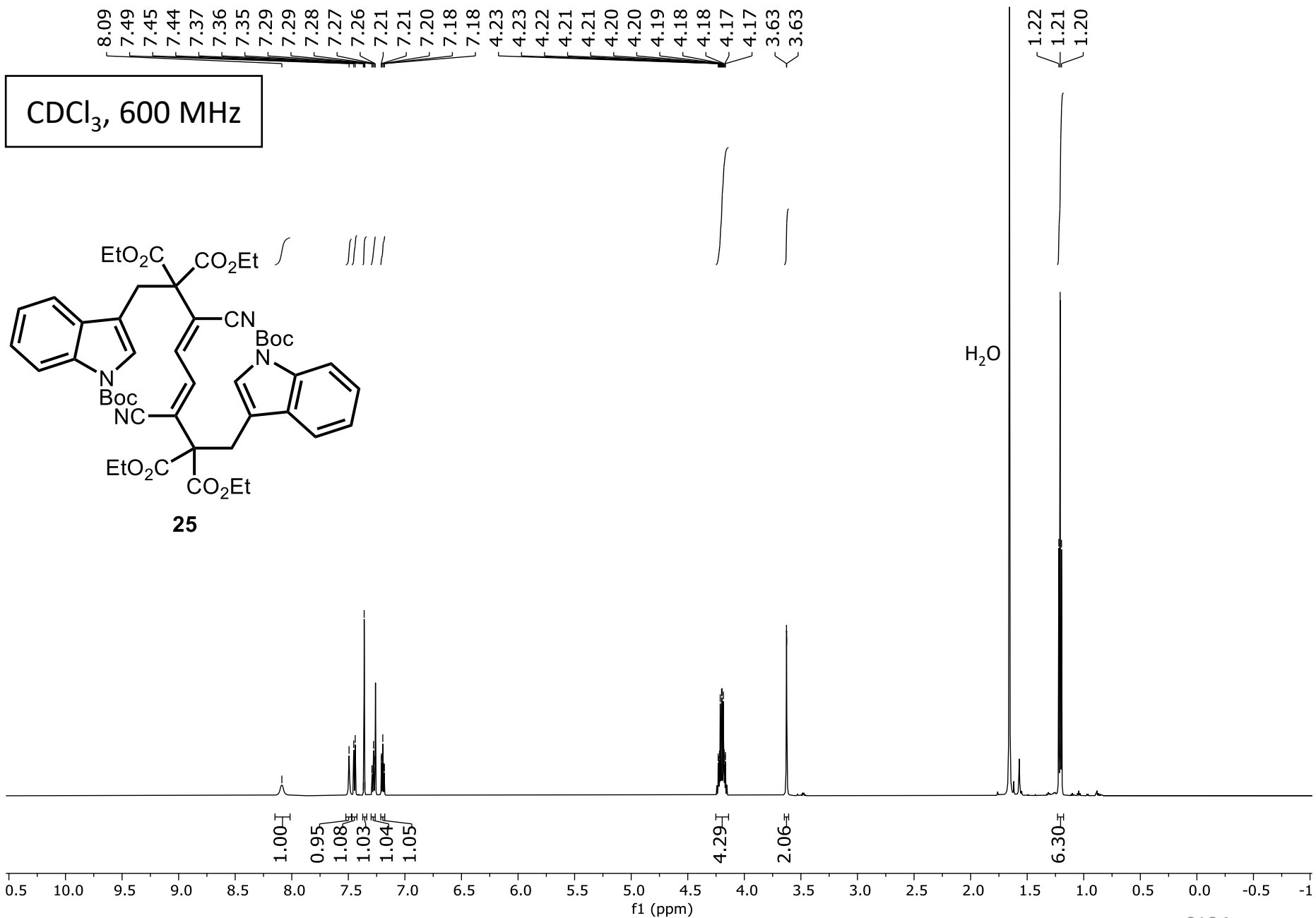


CDCl₃, 151 MHz

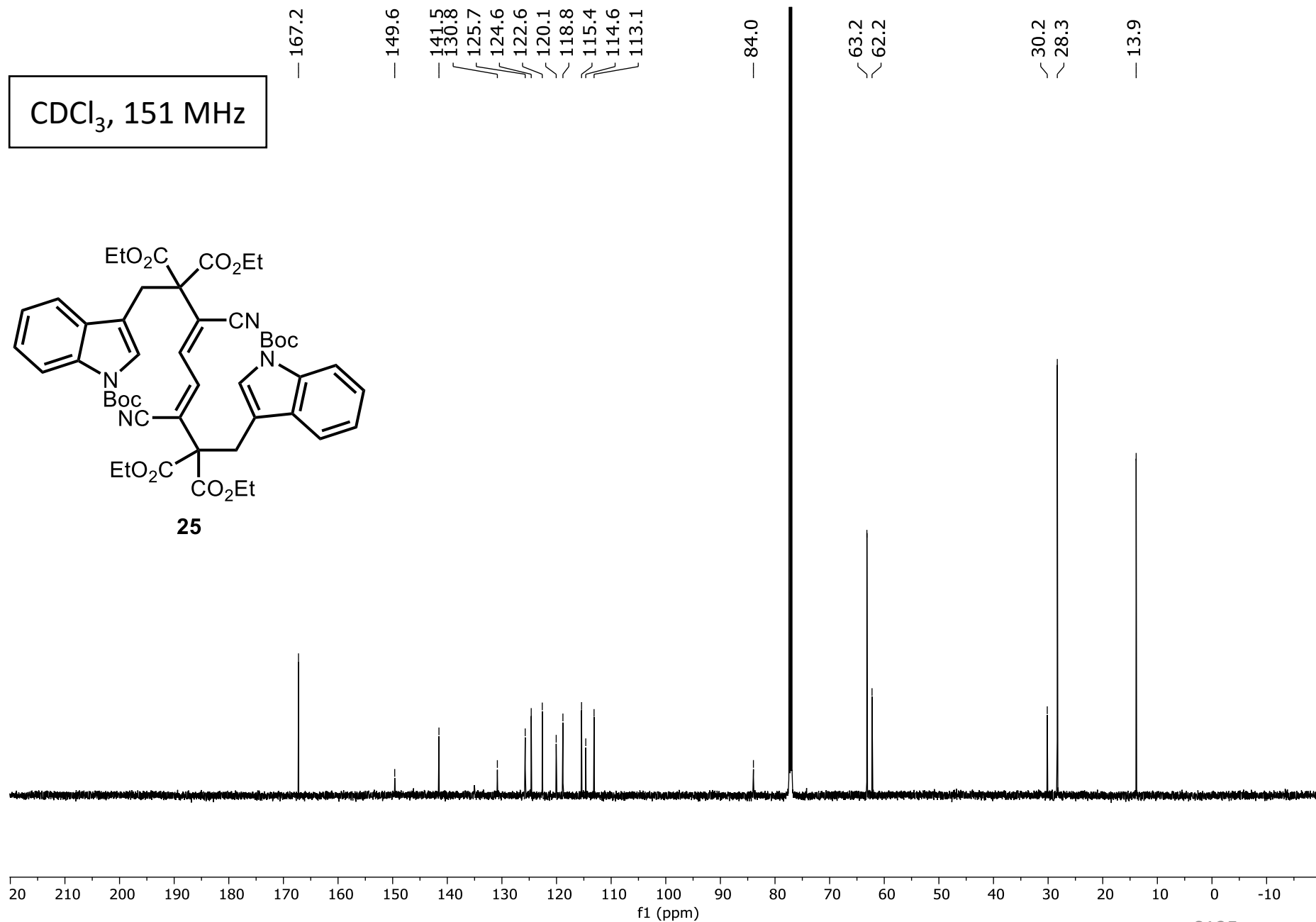
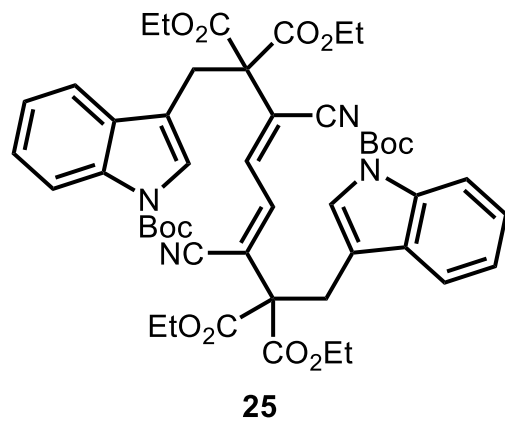


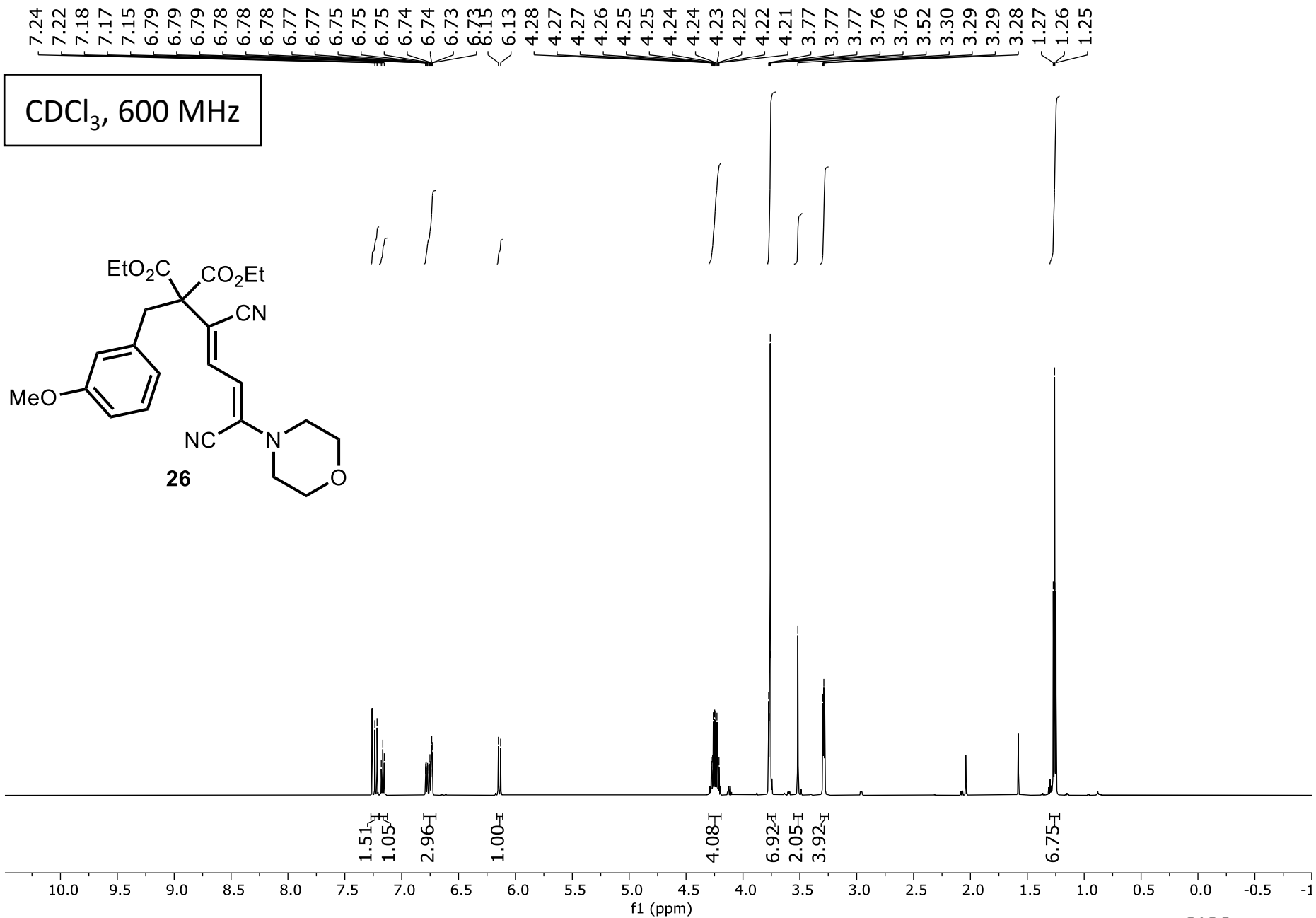
24



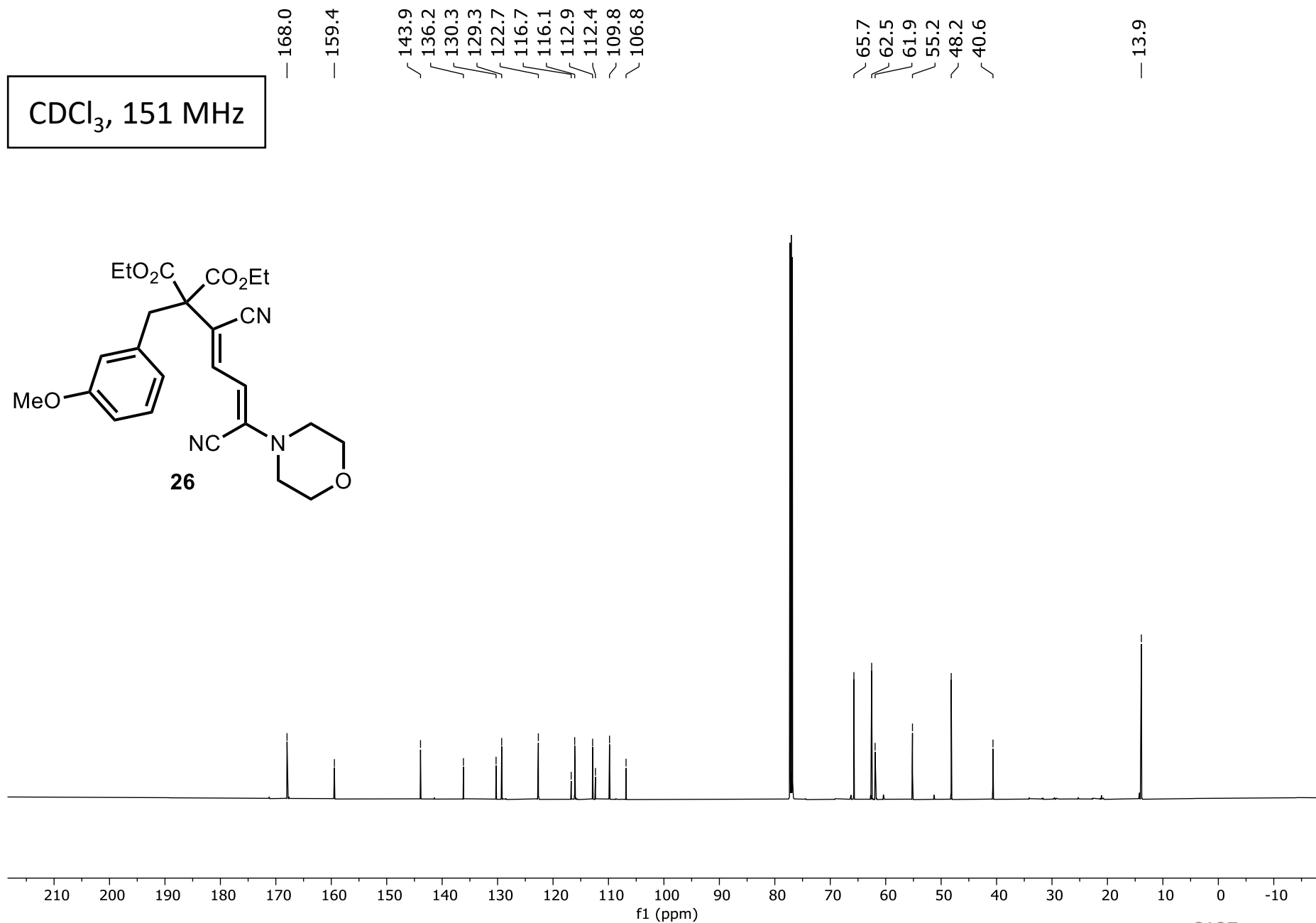
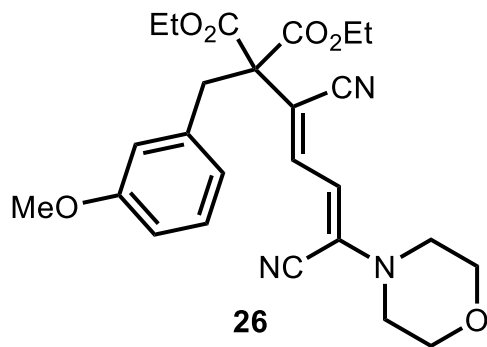


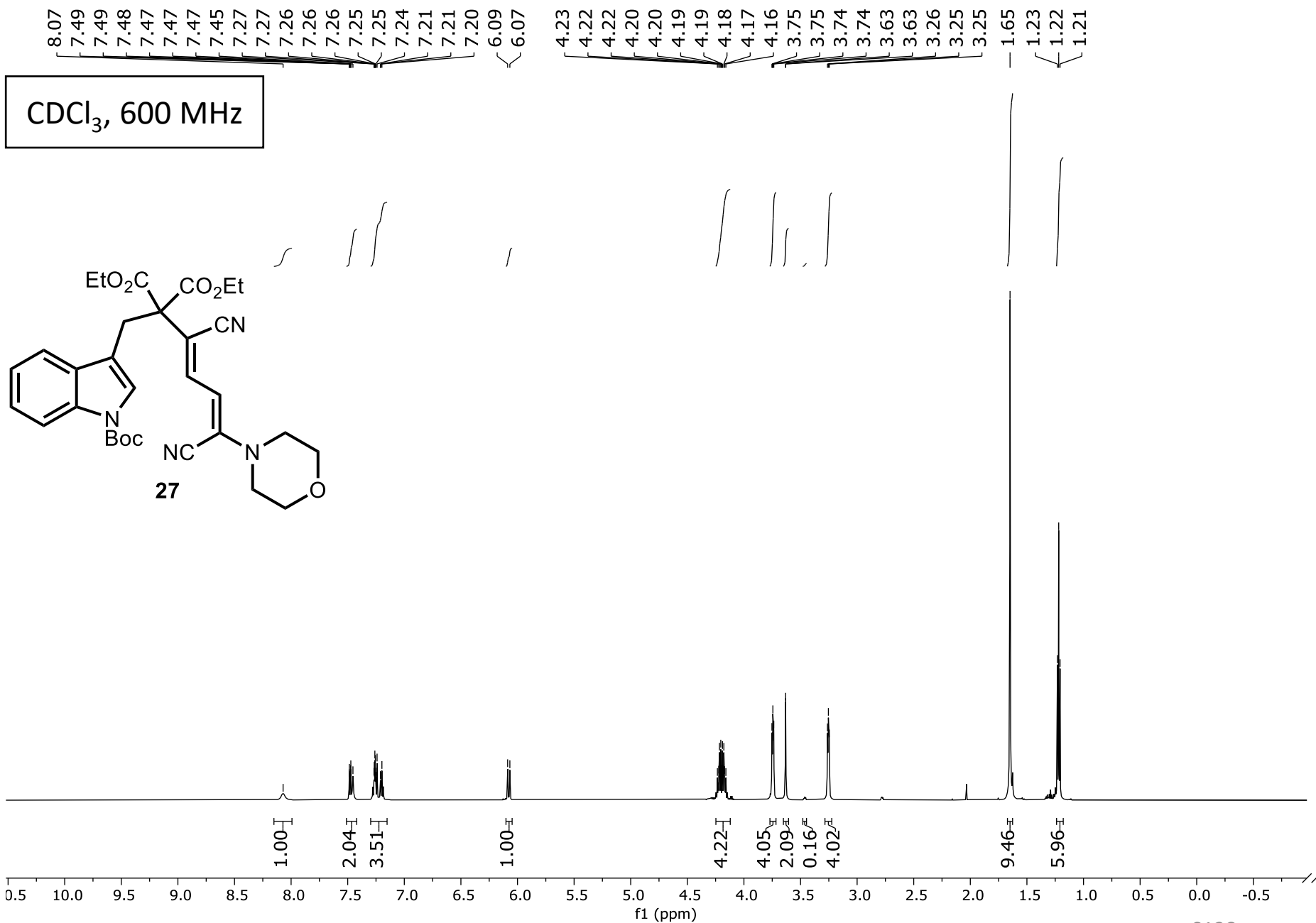
CDCl₃, 151 MHz



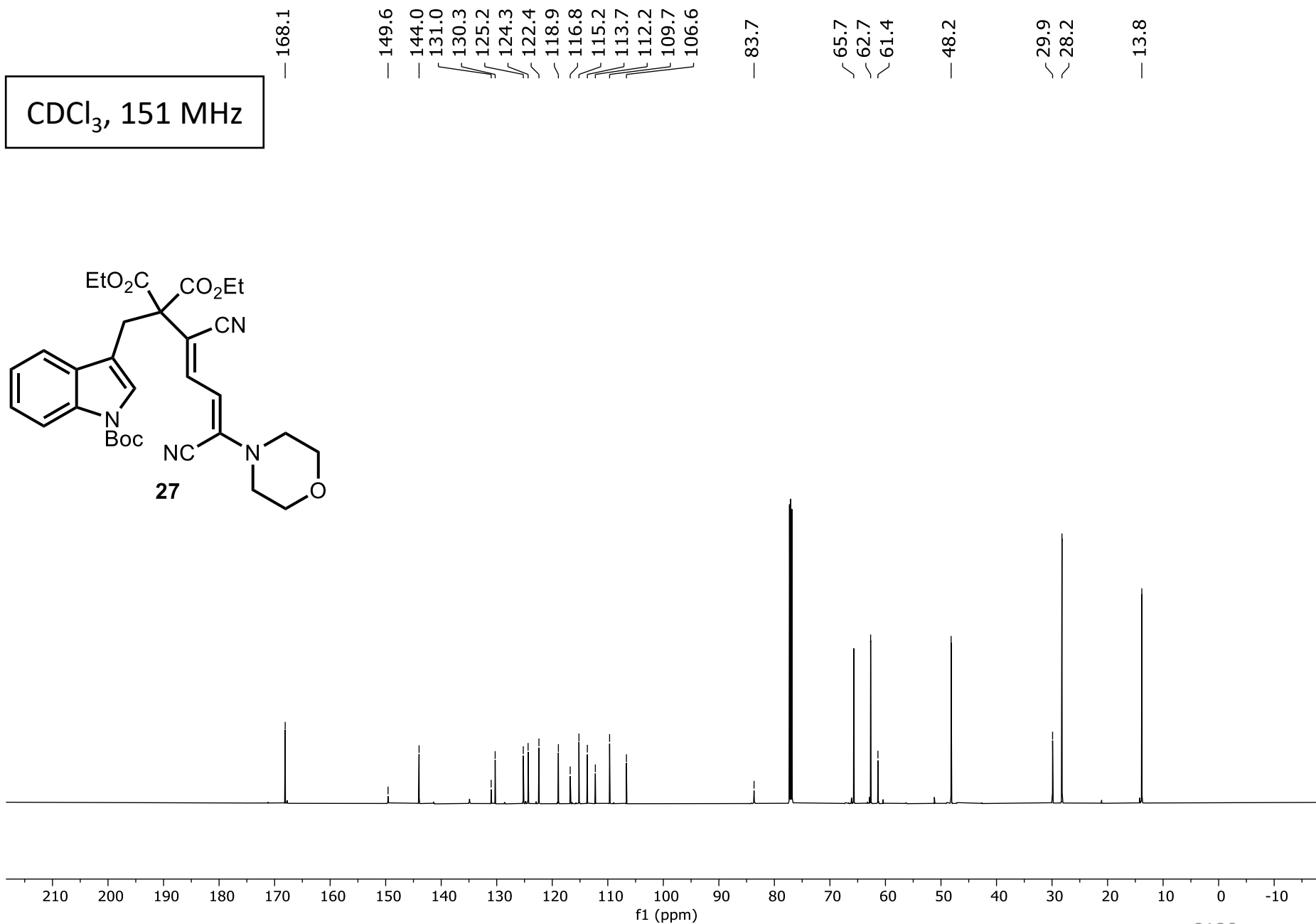
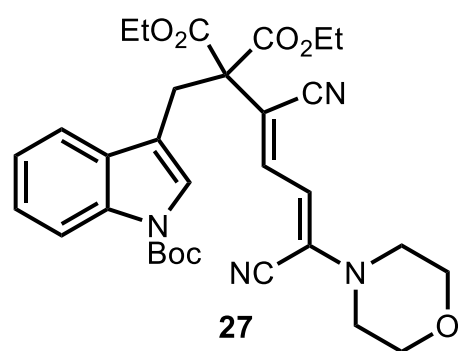


CDCl₃, 151 MHz

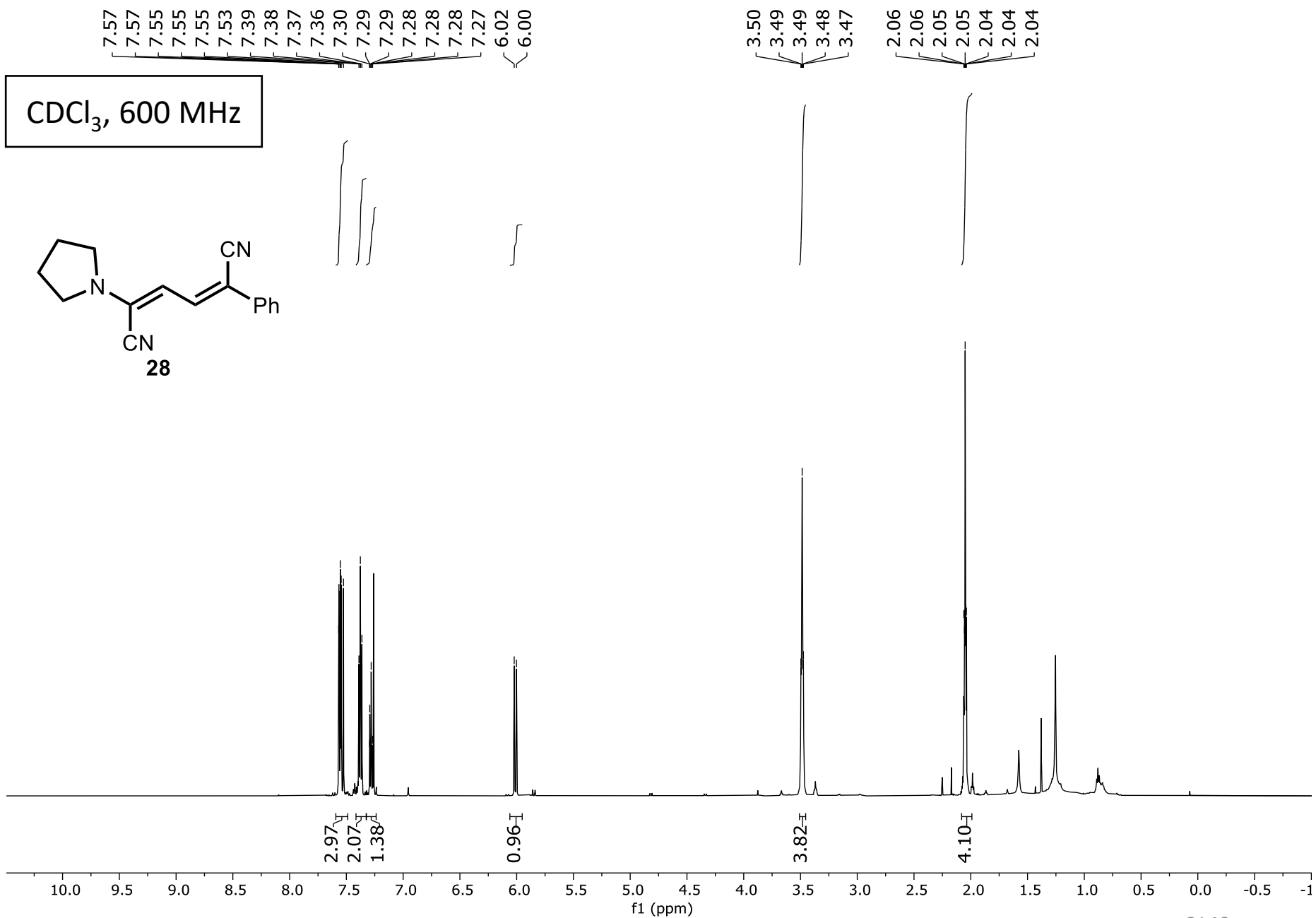
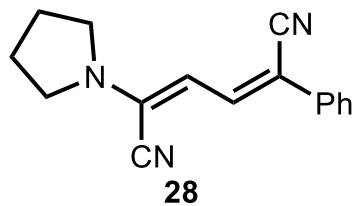




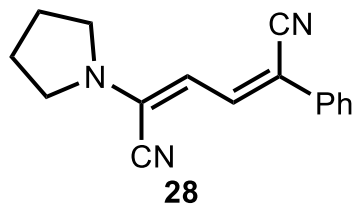
CDCl₃, 151 MHz



CDCl₃, 600 MHz



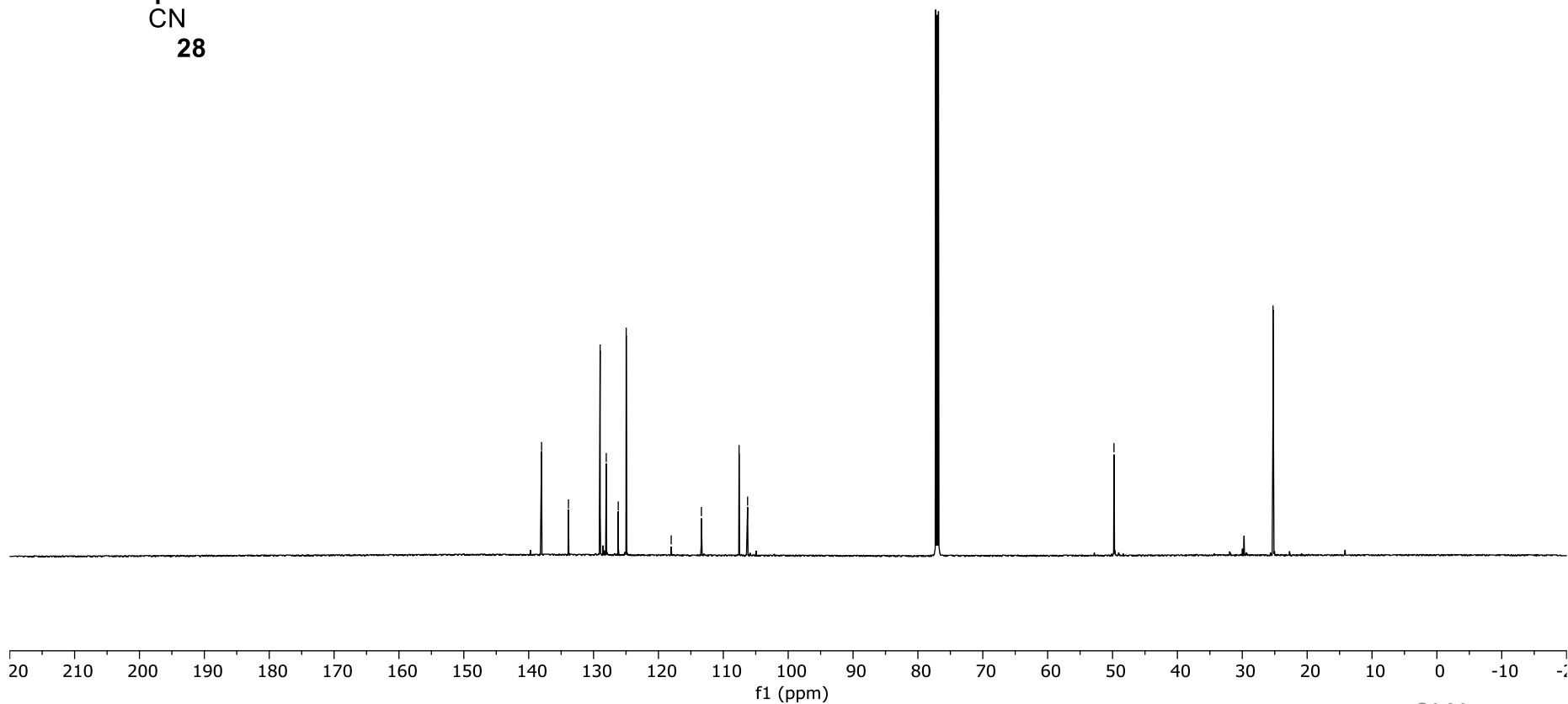
CDCl₃, 151 MHz

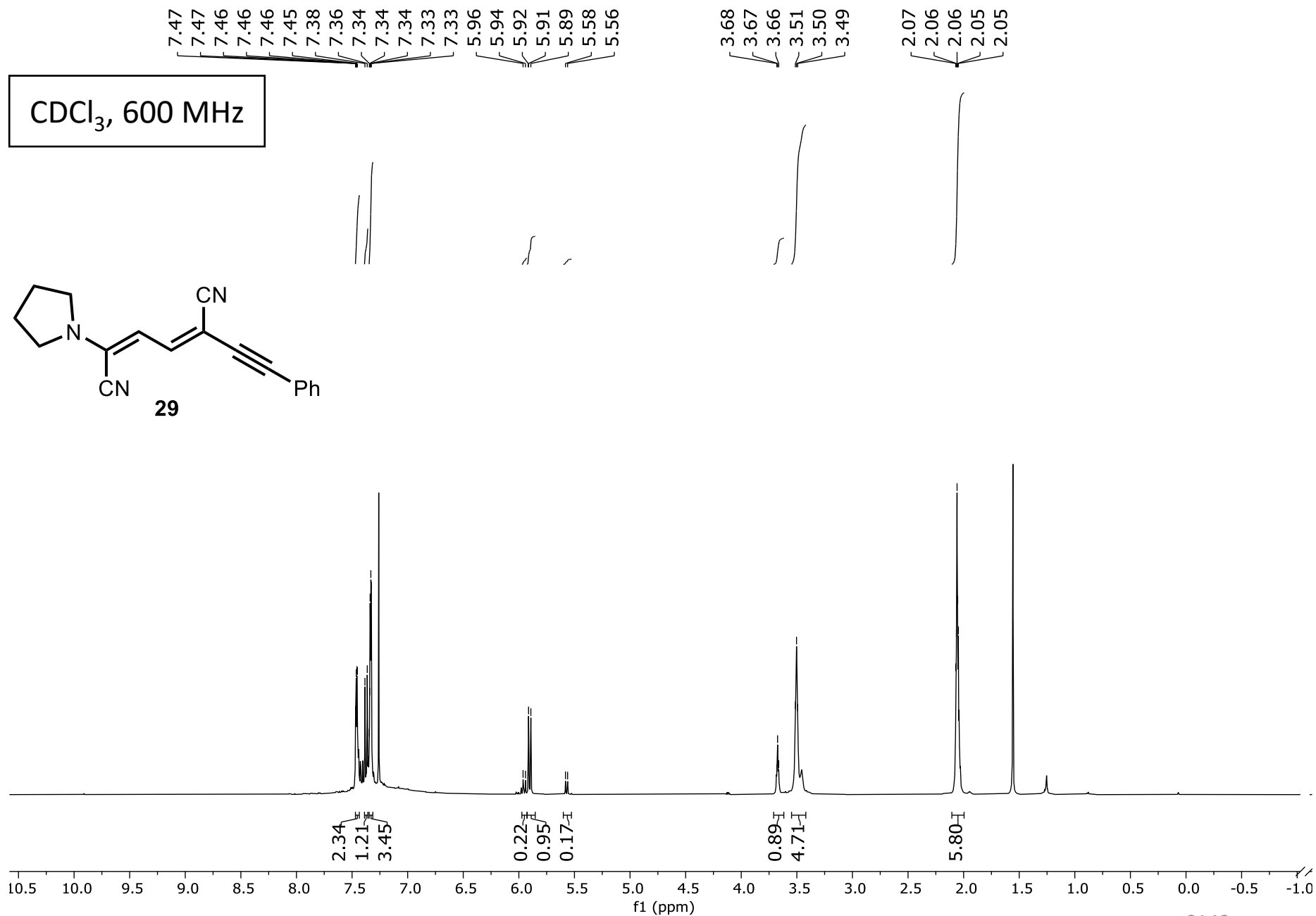
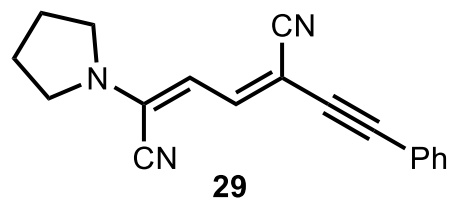


138.0
133.9
129.0
128.0
126.2
125.0
118.0
113.4
107.6
106.3

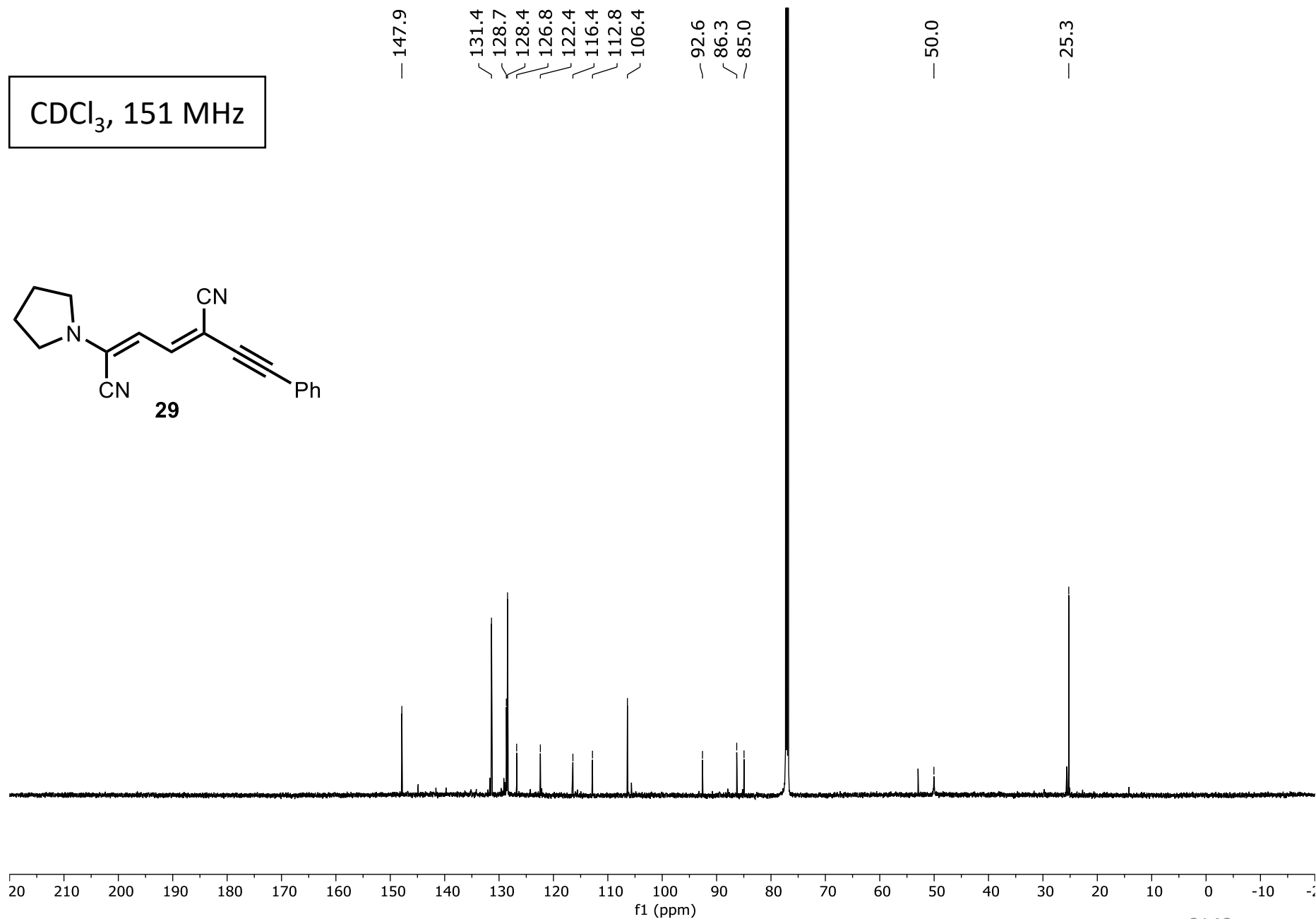
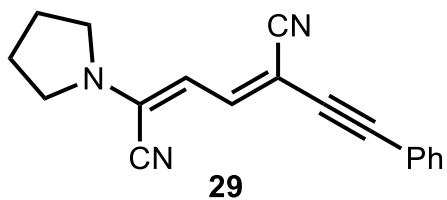
— 49.8

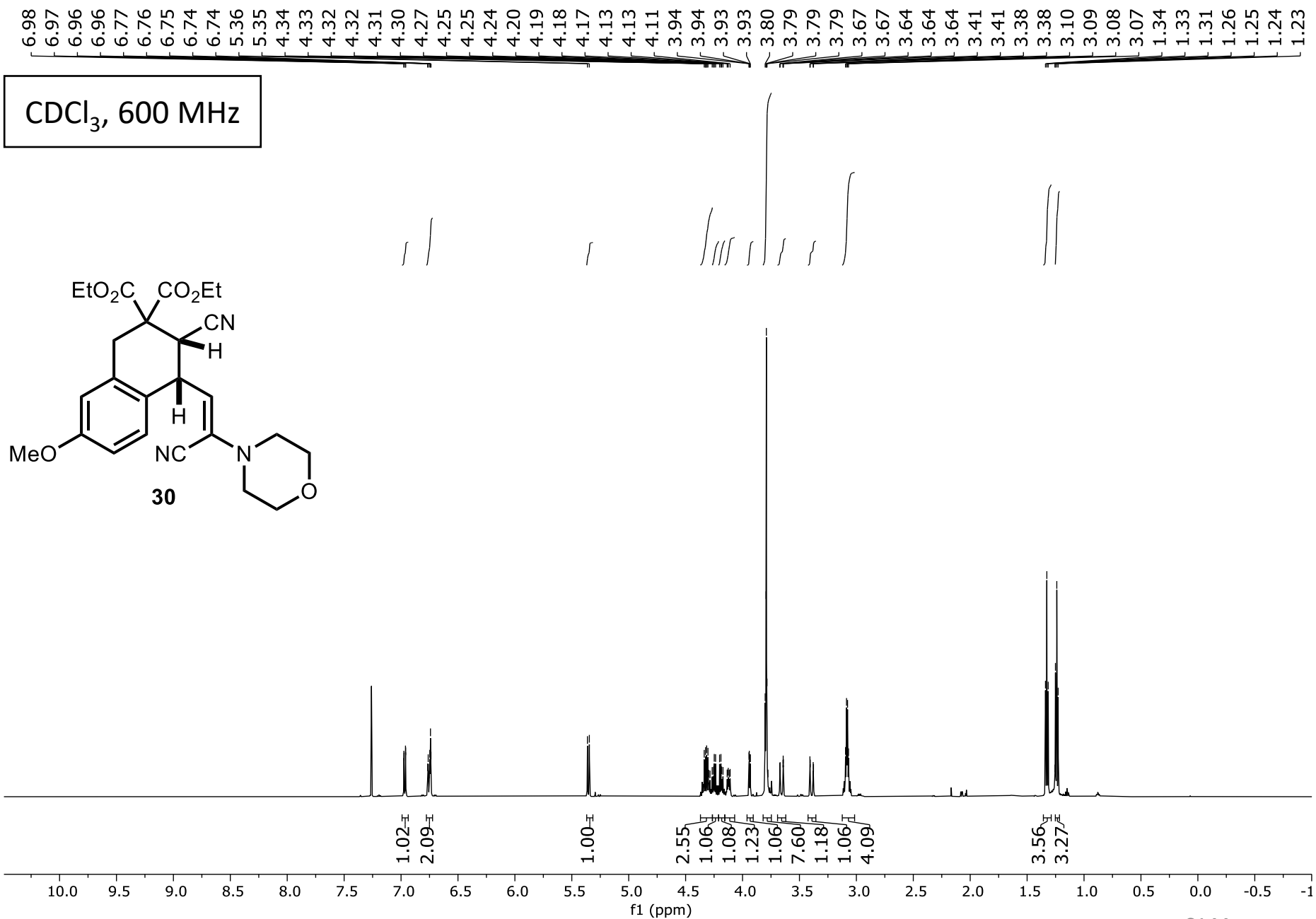
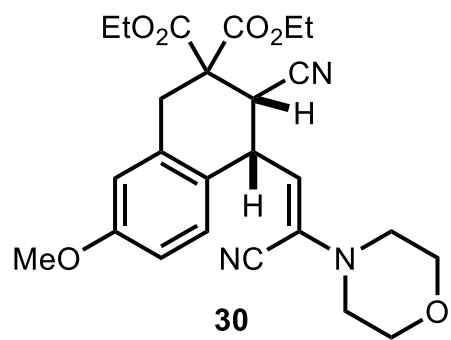
— 25.3



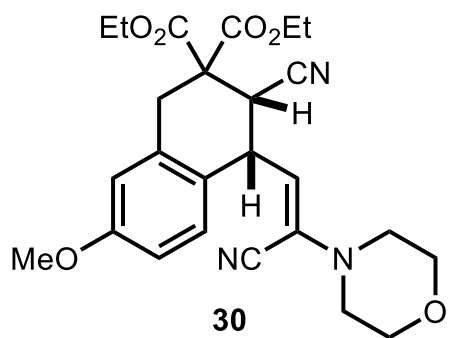


CDCl₃, 151 MHz

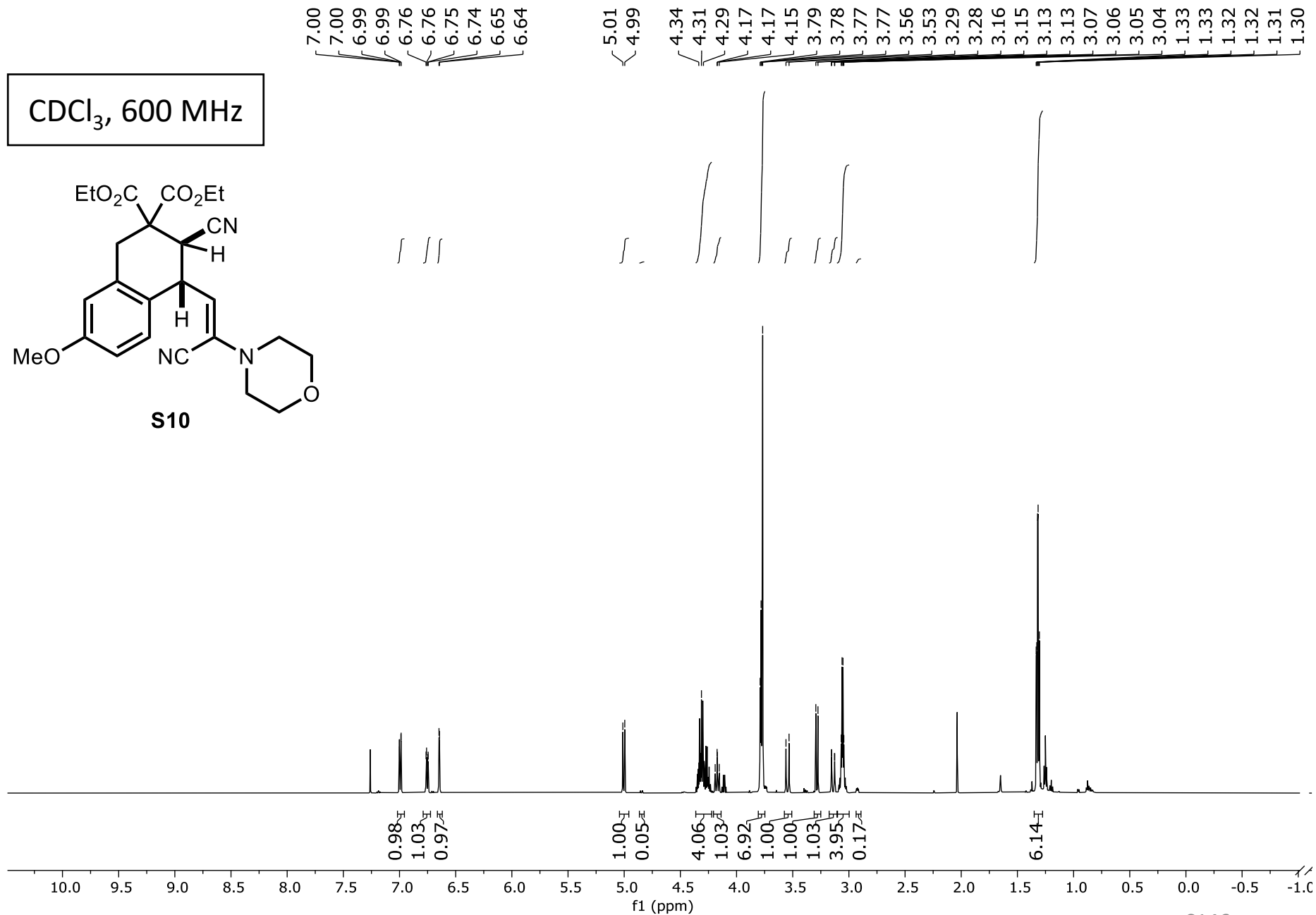
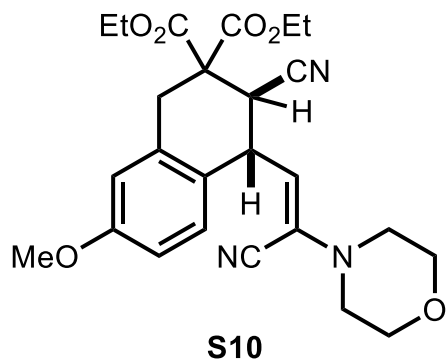




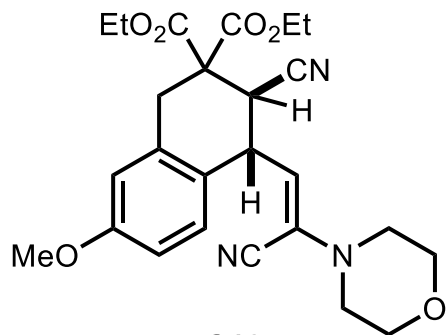
CDCl₃, 151 MHz



CDCl₃, 600 MHz



CDCl₃, 151 MHz

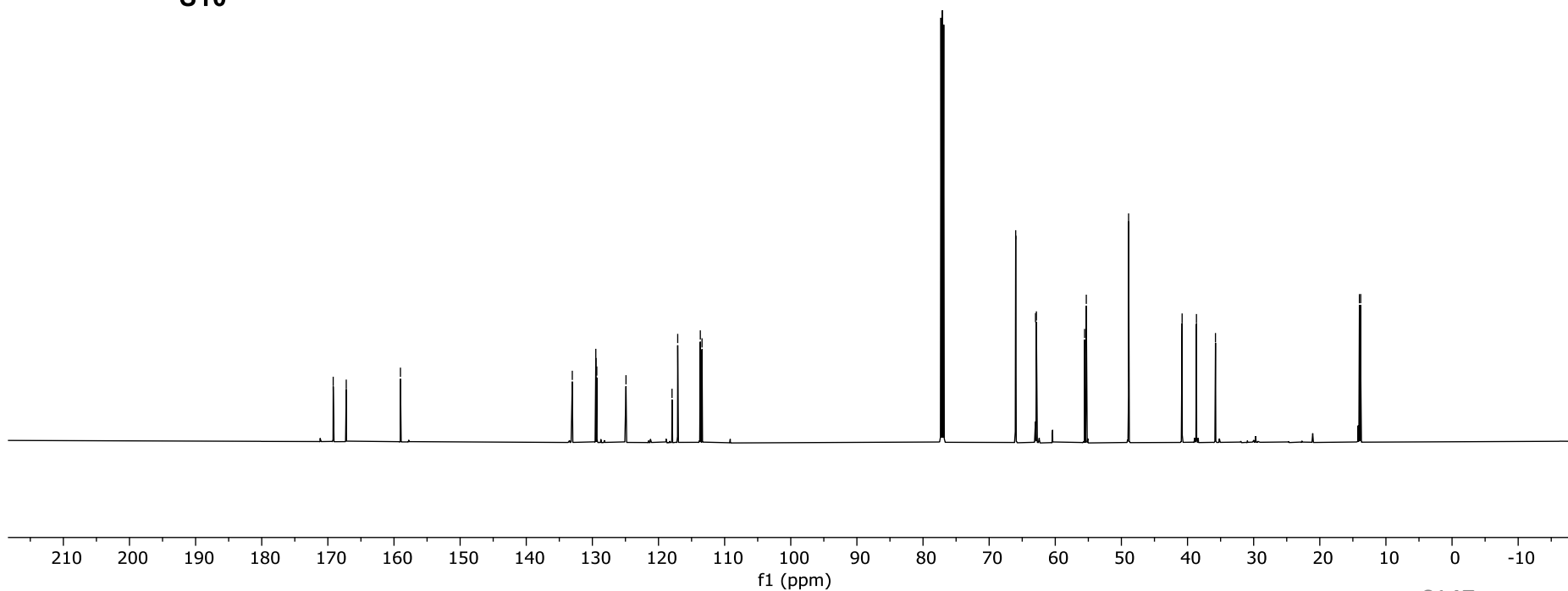


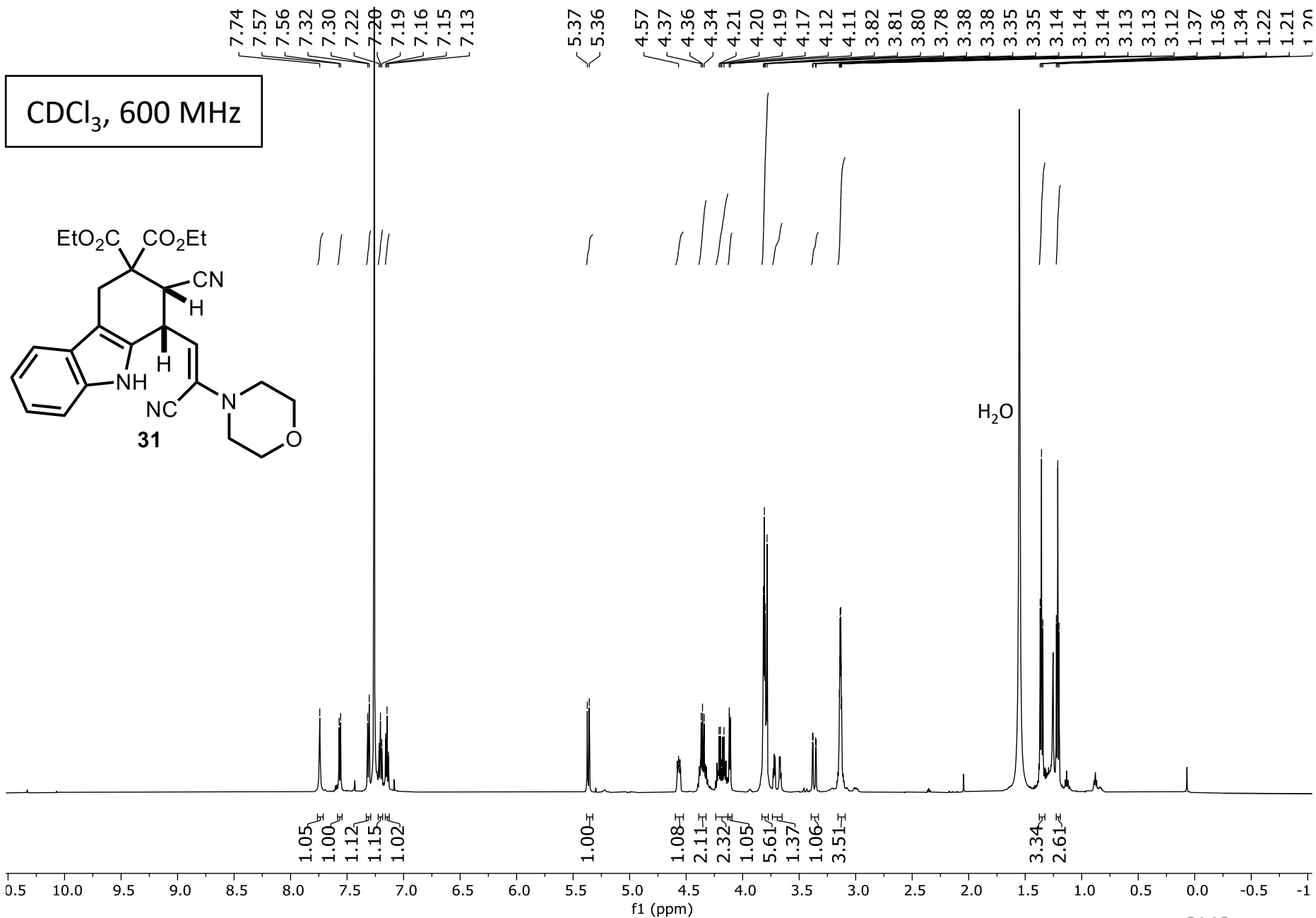
169.2
167.2
159.0

133.0
129.5
129.3
124.9
118.0
117.1
113.7
113.7
113.4

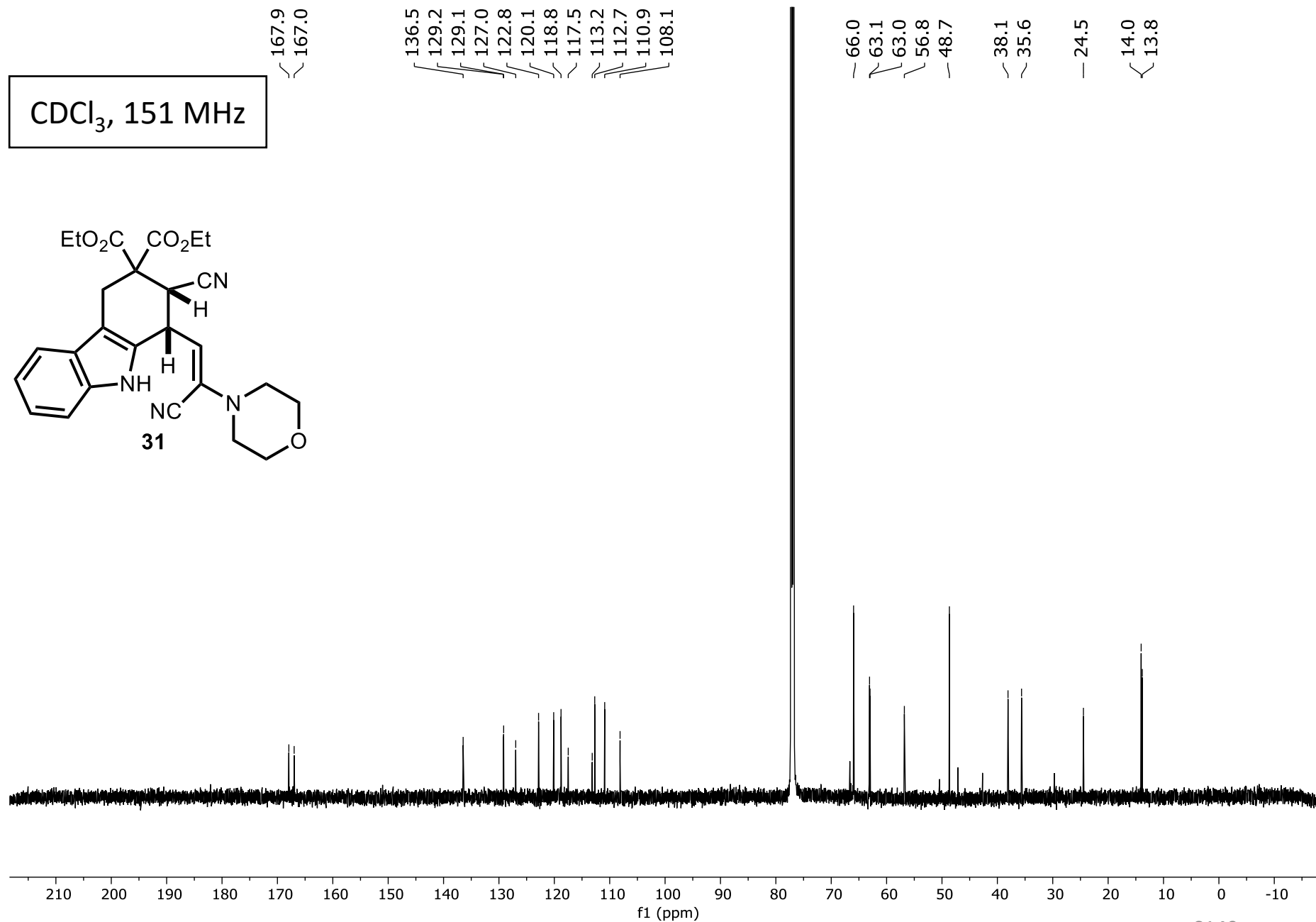
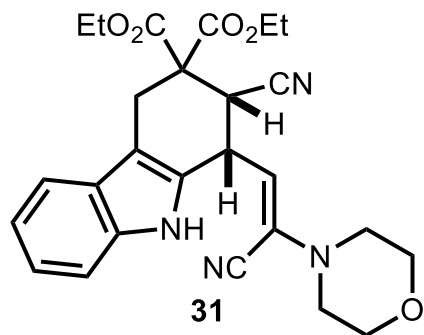
66.0
63.0
62.9
55.6
55.3
48.9
40.8
38.6
35.8

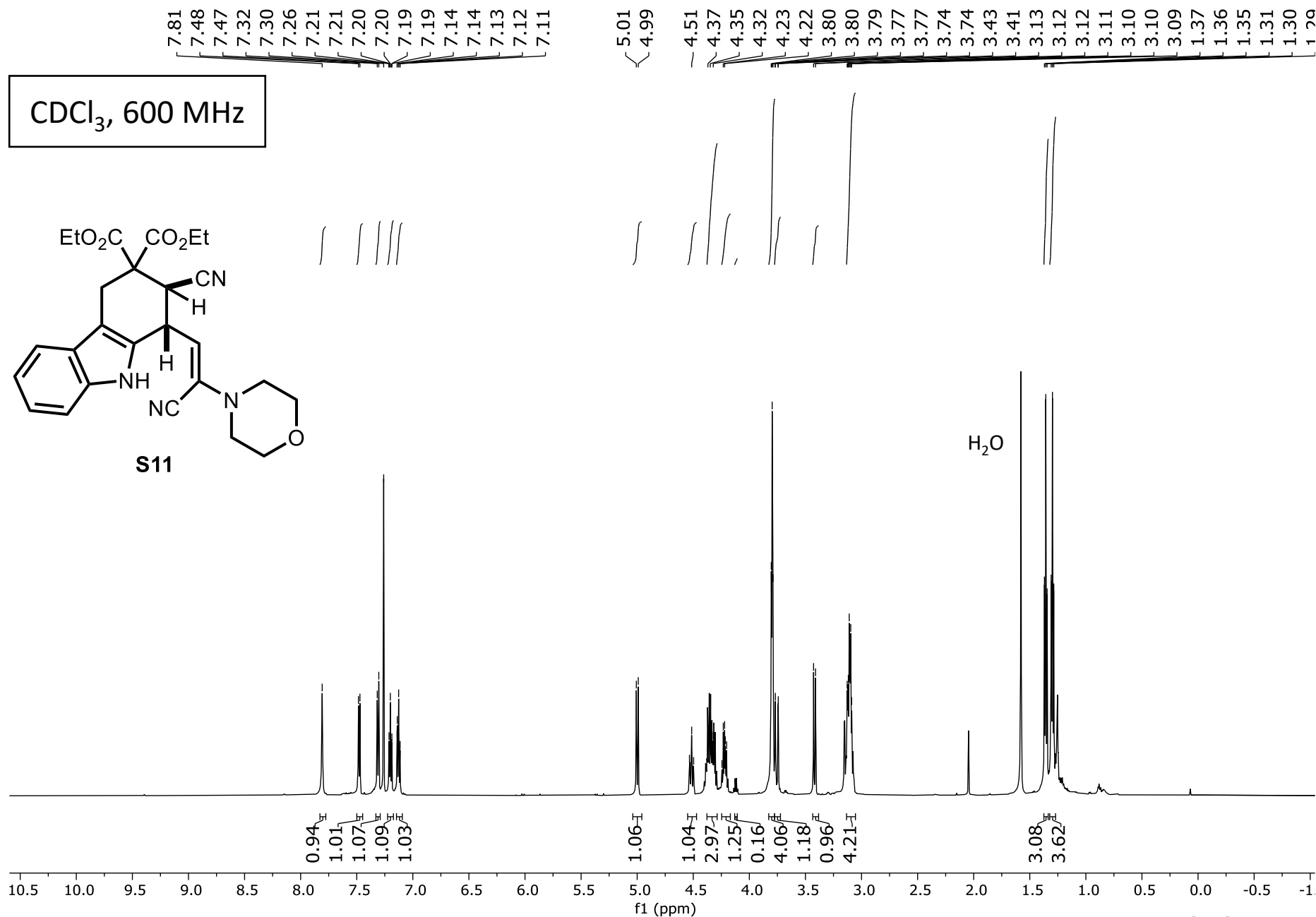
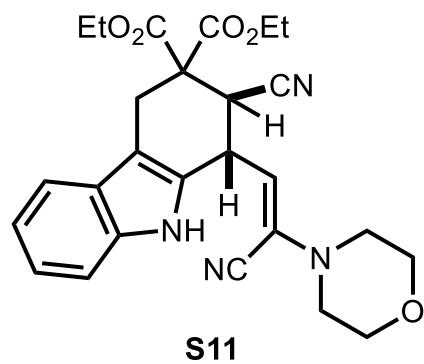
14.0
13.8





CDCl₃, 151 MHz





CDCl₃, 151 MHz

