Catalyst-free visible light-promoted defunctionalization of alkyl isocyanides with a hydrosilane through C–N bond cleavage

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Supporting Information

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General Information

The ^{1}H NMR, ^{13}C NMR, and ^{19}F NMR spectra were recorded on a Bruker AC-500 FT spectrometer (500 MHz, 125 MHz, 471 MHz). The chemical shifts of ^{1}H NMR and ^{13}C NMR spectra were referenced internally with tetramethylsilane (δ H 0.00, δ C 0.0) or residual protio solvent signals $CDCl_3$ (δ C 77.2). The chemical shifts of ^{19}F NMR spectra were referenced to external trifluoroacetic acid (δ F -76.2). Chemical shifts (δ) and coupling constants (J) were expressed in ppm and Hz, respectively. The following abbreviations are used in reporting NMR data: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad. High resolution mass spectra (HRMS) were recorded on a LC-TOF spectrometer (Micromass). EI-mass or ESI-mass data were acquired using a Thermo LTQ Orbitrap XL instrument equipped with an EI or ESI source and controlled by Xcalibur software. Melting points are uncorrected.

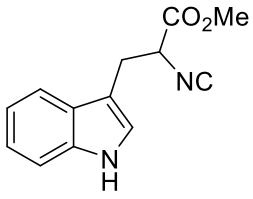
Chemicals were purchased from the Adamas, Energy Chemical, Acros, Accela, Alfa Aesar, and TCI, and used as received.

Abbreviations: Bn = benzyl, Boc = *t*-butyloxycarbonyl, Bu = butyl, DMF = *N*,*N*-dimethylformamide, TEMPO = (2,2,6,6-tetramethylpiperidin-1-yl)oxyl, THF = tetrahydrofuran.

Preparation of Isocyanides

(1) Known Isocyanides

The following isocyanides were prepared according to known procedures.[1-7]



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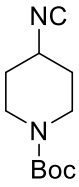

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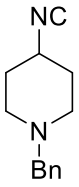

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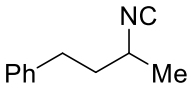

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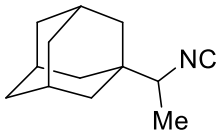

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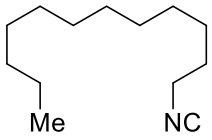

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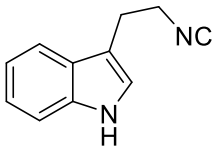

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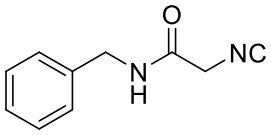

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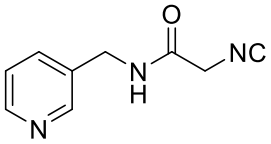

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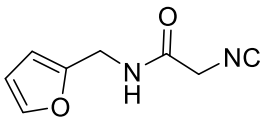

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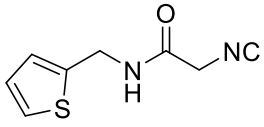

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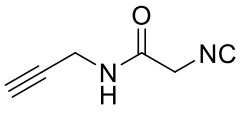

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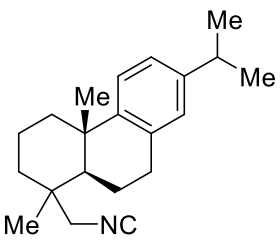

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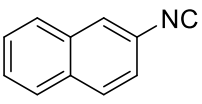
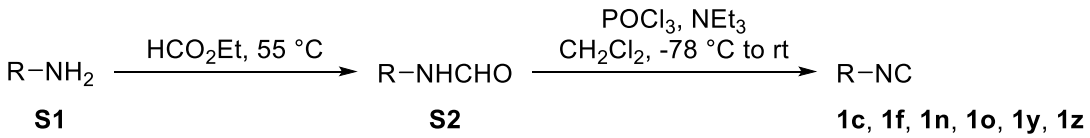


1aa

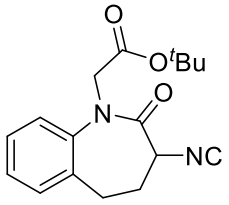
(2) Preparation of Isocyanides **1c**, **1f**, **1n**, **1o**, **1y**, and **1z**



S1 **S2** **1c**, **1f**, **1n**, **1o**, **1y**, **1z**

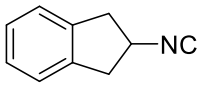
Ethyl formate (3.70 g, 4.02 mL, 50.0 mmol) was slowly added to primary amine **S1** (5.00 mmol) at room temperature. The mixture was heated at 55˚C for 16 h, and cooled to room temperature. Volatiles were removed under reduced pressure to give crude formamide **S2**, which was used in next step without purification.

NEt_3 (2.53 g, 3.47 mL, 25.0 mmol) and $POCl_3$ (997 mg, 606 μL, 6.50 mmol) were added dropwise to a solution of formamide **S2** in dry dichloromethane (20 mL) at -78˚C. The mixture was stirred at -78˚C for 3-4 h, warmed up to room temperature, and stirred for 1 h. The reaction was quenched with ice cold water, extracted with dichloromethane (2 x 20 mL), and washed with brine (20 mL). The organic layer was dried over anhydrous sodium sulfate, and concentrated under reduced pressure. The residue was purified by silica gel chromatography (petroleum ether/ethyl acetate = 15:1 to 2:1 v/v) to give isocyanide **1c**, **1f**, **1n**, **1o**, or **1z**.



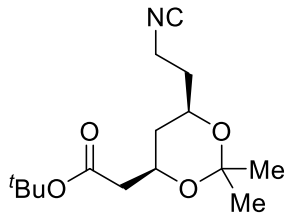
1c

tert-Butyl 2-(3-isocyano-2-oxo-2,3,4,5-tetrahydro-1*H*-benzo[*b*]azepin-1-yl)acetate (**1c**), colorless liquid (707 mg, 47% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34-7.32 (m, 1H), 7.27-7.22 (m, 2H), 7.14 (d, J = 8.0 Hz, 1H), 4.66-4.62 (m, 1H), 4.31-4.29 (m, 2H), 3.41-3.39 (m, 1H), 2.66-2.51 (m, 3H), 1.44 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.3, 165.5, 160.1, 140.1, 134.5, 129.7, 128.5, 127.6, 122.7, 82.5, 54.1, 51.4, 37.2, 28.0, 27.6. HRMS (ESI) m/z: $(M + Na)^+$ Calcd for $C_{17}H_{20}N_2O_3Na^+$ 323.1366; Found 323.1367.



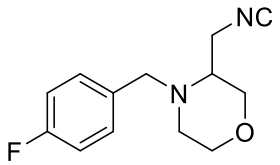
1f

2-Isocyano-2,3-dihydro-1*H*-indene (**1f**), colorless liquid (543 mg, 76% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43 (d, J = 6.5 Hz, 1H), 7.30-7.24 (m, 3H), 5.02-4.99 (m, 1H), 3.10-3.04 (m, 1H), 2.89-2.83 (m, 1H), 2.61-2.55 (m, 1H), 2.31-2.25 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 155.8 (t, J = 4.9 Hz), 142.6, 139.2, 129.1, 127.3, 125.1, 124.1, 57.3 (t, J = 13.2 Hz), 34.5, 30.2. HRMS (ESI) m/z: $(M + Na)^+$ Calcd for $C_{10}H_9NNa^+$ 166.0627; Found 166.0624.



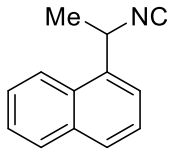
1n

tert-Butyl 2-((4*R*,6*R*)-6-(2-isocyanoethyl)-2,2-dimethyl-1,3-dioxan-4-yl)acetate (**1n**), orange liquid (1.14 g, 80% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.30-4.26 (m, 1H), 4.07-4.03 (m, 1H), 3.59-3.53 (m, 1H), 3.49-3.44 (m, 1H), 2.45-2.41 (m, 1H), 2.33-2.29 (m, 1H), 1.86-1.82 (m, 1H), 1.76-1.73 (m, 1H), 1.61-1.58 (m, 1H), 1.47 (s, 3H), 1.45 (s, 9H), 1.35 (s, 3H), 1.26-1.19 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.1, 156.0 (t, J = 5.6 Hz), 99.0, 80.7, 66.1, 65.0, 53.5, 42.6, 37.6 (t, J = 6.4 Hz), 36.1, 35.4, 30.0, 28.1, 19.6. HRMS (ESI) m/z: $(M + Na)^+$ Calcd for $C_{15}H_{25}NO_4Na^+$ 306.1076; Found 306.1074.



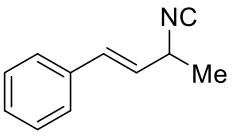
1o

4-(4-Fluorobenzyl)-3-(isocyanomethyl)morpholine (**1o**), brown liquid (995 mg, 85% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28-7.25 (m, 2H), 7.00-6.96 (m, 2H), 3.85-3.81 (m, 1H), 3.70-3.62 (m, 2H), 3.44-3.40 (m, 4H), 2.72 (d, J = 11.5 Hz, 1H), 2.59-2.57 (m, 1H), 2.18-2.13 (m, 1H), 2.00-1.95 (m, J = 10.5 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.4 (d, J = 245.1 Hz), 157.8, 132.8 (d, J = 2.9 Hz), 130.0 **(**d, J = 8.0 Hz*)*, 114.6 (d, J = 4.6 Hz), 71.9, 66.0, 61.5, 54.5, 51.8, 43.7. ^{19}F NMR δ -115.4. HRMS (ESI) m/z: $(M + H)^+$ Calcd for $C_{13}H_{16}N_2OF^+$ 235.1241; Found 235.1244.



1y

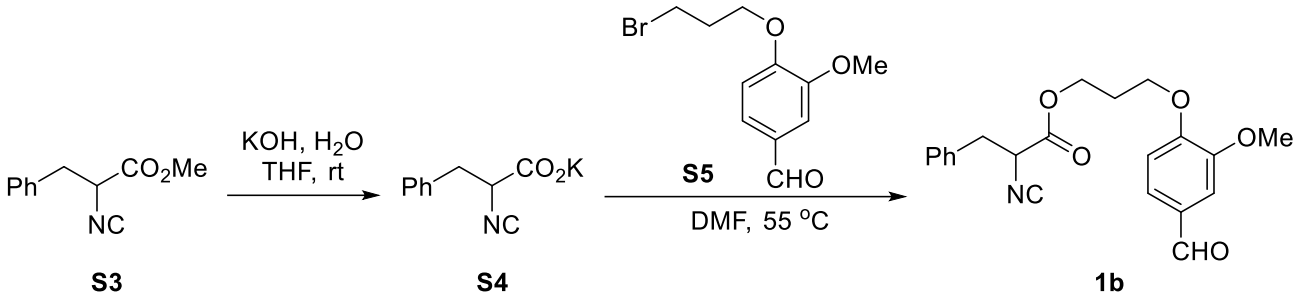
1-(1-Isocyanoethyl)naphthalene (**1y**), brown liquid (480 mg, 53% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.88-7.80 (m, 3H), 7.71 (d, J = 7.5 Hz, 1H*)*, 7.55-7.47 (m, 3H), 5.53 (q, J = 6.5 Hz, 1H*)*, 1.79 (d, J = 7.0 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$*)* δ 156.8 (d, J = 4.5 Hz), 133.9, 129.3, 129.3, 129.1, 126.9, 126.1, 125.6, 123.1, 122.0, 51.1 (d, J = 6.4 Hz), 24.2. HRMS (ESI) m/z: $(M + Na)^+$ Calcd for $C_{13}H_{11}N\ Na^+$ 204.0784; Found 204.0786.



1z

(*E*)-(3-Isocyanobut-1-en-1-yl)benzene (**1z**), colorless liquid (691 mg, 88% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39-7.36 (m, 2H), 7.32-7.29 (m, 1H), 7.24-7.22 (m, 2H), 6.63 (d, J = 16.5 Hz, 1H), 5.69-5.64 (m, 1H), 4.62-4.56 (m, 1H), 1.50-1.48 (m, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 154.9 (t, J = 7.1 Hz), 135.4, 132.3, 129.2, 128.7, 128.5, 127.9, 47.6 (t, J = 6.1 Hz), 23.0. HRMS (EI) m/z: Calcd for $C_{11}H_{11}N$ 157.0891; Found 157.0887

(3) Preparation of Isocyanide **1b**

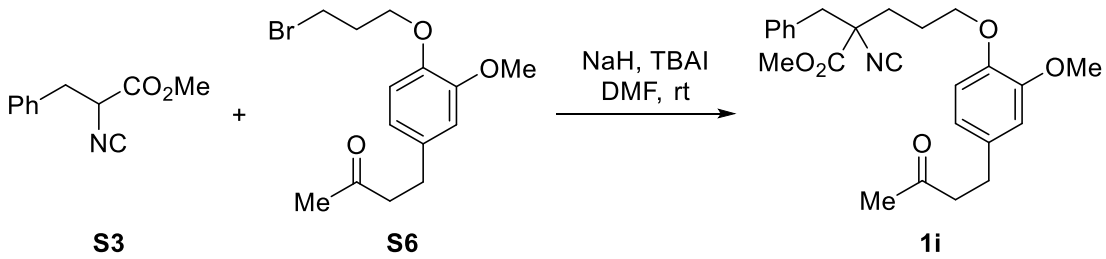


S3 **S4** **1b**

To a solution of isocyanide **S3** (1.90 g, 10.0 mmol)[8] in tetrahydrofuran (15 mL) at room temperature was added a solution of KOH (560 mg, 10.0 mmol) in water (3.0 mL). The mixture was stirred for 5 h, concentrated under reduced pressure, washed with diethyl ether (30 mL), and dried in vacuo to give crude salt **S4**.

To a suspension of salt **S1** in *N*,*N*-dimethylformamide (15.0 mL) was added aldehyde **S5** (1.50 g, 5.50 mmol).[9] The mixture was stirred at 55 °C for 12 h, poured into water (20 mL), and extracted with ethyl acetate (30 mL). The organic layer was washed with brine (3 × 15 mL), dried over anhydrous sodium sulfate, and concentrated under reduced pressure. The residue was purified by silica gel chromatography (petroleum ether/ethyl acetate = 12:1 v/v) to give 3-(4-formyl-2-methoxyphenoxy)propyl 2-isocyano-3-phenylpropanoate (**1b**) as a yellow liquid (1.01 g, 54% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.85 (s, 1H), 7.45-7.41 (m, 2H), 7.32-7.23 (m, 5H), 6.92 (d, J = 8.0 Hz, 1H), 4.50-4.48 (m, 1H), 4.42-4.39 (m, 2H), 4.08-4.06 (m, 2H), 3.90 (s, 3H), 2.27-2.13 (m, 2H), 2.21-2.17 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 190.9, 166.0, 161.0, 153.6, 149.9, 134.3, 130.3, 129.3, 128.8, 127.9, 126.9, 111.7, 109.4, 45.1, 63.3, 58.0, 56.0, 38.9, 28.1. HRMS (ESI) m/z: $(M + Na)^+$ Calcd for $C_{21}H_{21}NO_5Na^+$ 390.1312; Found 390.1314.

(4) Preparation of Isocyanide **1i**

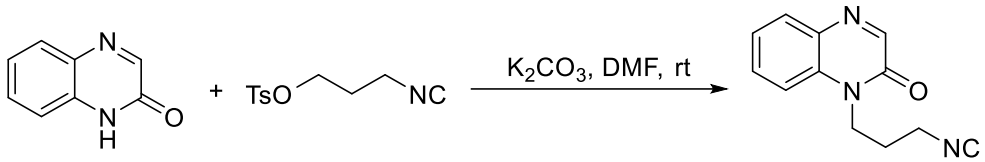


S3 **S6** **1i**

To a solutions of isocyanide **S3** (380 mg, 2.0 mmol) in *N*,*N*-dimethylformamide (5.0 mL) were added NaH (480 mg, 2.2 mmol), ketone **S6** (690 mg, 2.2 mmol), and tetrabutylammonium iodide (73.9 mg, 0.20 mmol). The mixture was stirred at room temperature for 12 h, poured into water (30 mL),

and extracted with ethyl acetate (20 mL). The organic layer was washed with brine (20 mL), dried over anhydrous sodium sulfate, and concentrated under reduced pressure. The residue was purified by silica gel chromatography (petroleum ether/ethyl acetate = 10:1 v/v) to give methyl 2-benzyl-2-isocyano-5-(2-methoxy-4-(3-oxobutyl)phenoxy)pentanoate (**1i**) as a yellow liquid (491 mg, 58% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34-7.30 (m, 3H), 7.26-7.23 (m, 2H), 6.78-6.76 (m, 1H), 6.72-6.68 (m, 2H), 4.01 (t, J = 5.5 Hz, 2H), 3.84 (s, 3H), 3.70 (s, 3H), 3.25 (d, J = 13.5 Hz, 1H), 3.07 (d, J = 13.5 Hz, 1H), 2.84 (t, J = 7.5 Hz, 2H), 2.74 (t, J = 7.5 Hz, 2H), 2.29-2.24 (m, 1H), 2.14 (s, 3H), 2.13-2.01 (m, 2H), 1.83-1.78 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 208.1, 168.8, 160.6, 149.6, 146.4, 134.5, 133.5, 130.1, 128.5, 127.9, 120.2, 114.1, 112.5, 69.2, 68.3, 56.0, 45.4, 44.9, 35.7, 30.2, 29.4, 24.4. HRMS (ESI) m/z: $(M + Na)^+$ Calcd for $C_{25}H_{29}NO_5Na^+$ 446.1938; Found 446.1942.

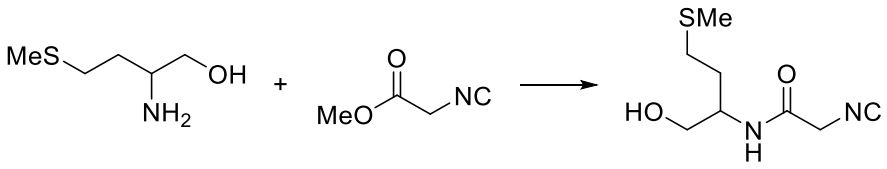
(5) Preparation of Isocyanide **1m**



1m

To a solution of quinoxalinone (292 mg, 2.0 mmol) in *N*,*N*-dimethylformamide (5.0 mL) was added K_2CO_3 (331 mg, 2.4 mmol). The mixture was stirred at room temperature for 10 min, and added dropwise 3-isocyano-1-tosylpropane (576 mg, 2.4 mmol). The mixture was stirred at room temperature for 12 h, quenched with water (25 mL), and extracted with dichloromethane (30 mL). The organic layer was dried over anhydrous sodium sulfate, and concentrated under reduced pressure. The residue was purified by silica gel chromatography (eluent: petroleum ether/ethyl acetate = 2:1 v/v) to give 1-(3-isocyanopropyl)quinoxalin-2(1*H*)-one (**1m**) as a colorless liquid (290 mg, 68% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.31 (s, 1H), 7.92 (dd, J = 8.0, 1.0 Hz, 1H), 7.66-7.63 (m, 1H), 7.43-7.37 (m, 2H), 4.32 (t, J = 7.5 Hz, 2H), 3.59 (t, J = 6.5 Hz, 2H), 2.20-2.16 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.8 (t, J = 5.0 Hz), 154.9, 149.9, 133.6, 132.1, 131.5, 131.1, 124.1, 139.2, 39.5 (t, J = 6.5 Hz), 39.1, 26.9. HRMS (EI) m/z: Calcd for $C_{12}H_{11}N_3O$ 213.0902; Found 213.0897.

(6) Preparation of Isocyanide **1v**

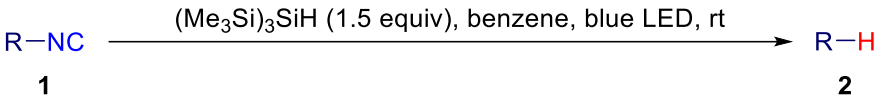


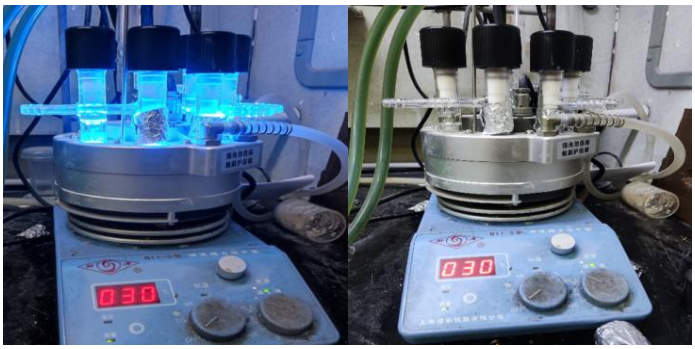
1v

A mixture of 2-amino-4-(methylthio)butan-1-ol (675 mg, 5.0 mmol) and methyl isocyanoacetate (500 mg, 5.0 mmol) was stirred at room temperature for 10 h. The reaction was quenched with water, and the mixture was extracted with ethyl acetate (30 mL). The organic layer was dried over anhydrous sodium sulfate, and concentrated under reduced pressure. The residue was purified by silica gel chromatography (eluent: petroleum ether/ethyl acetate = 1:3 v/v) to give *N*-(1-hydroxy-4-

(methylthio)butan-2-yl)-2-isocyanoacetamide (**1v**) as a yellow solid (930 mg, 92% yield). m.p. 67-68 ˚C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.95 (d, J = 8.0 Hz, 1H), 4.24 (s, 2H), 4.17-4.09 (m, 1H), 3.74-3.66 (m, 2H), 3.06 (s, br, 1H), 2.56 (t, J = 7.0 Hz, 2H) 2.13 (s, 3H), 1.94-1.84 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.1, 161.6, 63.9, 51.4, 45.4, 30.6, 30.1, 15.6. HRMS (ESI) m/z: $(M + Na)^+$ Calcd for $C_8H_{14}N_2O_2SNa^+$ 225.0668; Found 225.0669.

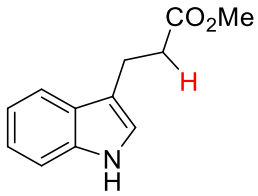
General Procedure for the Defunctionalization Reaction of Alkyl Isocyanides (Scheme 2)





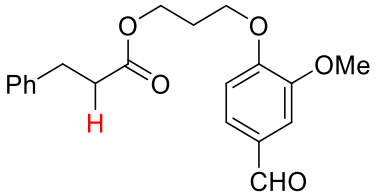
Alkyl isocyanide **1** (0.10 mmol), tris(trimethylsilyl)silane (37.3 mg, 45 μL, 0.15 mmol), and benzene (0.50 mL) were added to a sealed test tube under nitrogen atmosphere. The mixture was stirred at room temperature under blue LED (465 nm, 10 W) irradiation for 2 or 8 h, and purified by silica gel chromatography (petroleum ether/ethyl acetate = 1:0 to 4:1 v/v) to give compound **2**.

Characterization Data for the Products (Scheme 2)



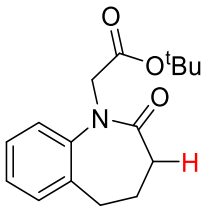
2a

Ethyl 3-(1*H*-indol-3-yl)propanoate (**2a**),[12] colorless liquid **(**20.1 mg, 99% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.02 (s, br, 1H), 7.59 (d, J = 7.0 Hz, 1H), 7.34 (d, J = 7.0 Hz, 1H), 7.20-7.17 (m, 1H), 7.13-7.10 (m, 1H), 6.96 (s, 1H), 3.66 (s, 3H), 3.10 (t, J = 7.5 Hz, 2H), 2.72 (t, J = 7.5 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.0, 136.3, 122.1, 121.5, 119.4, 118.7, 114.9, 111.2, 51.7, 34.8, 20.9.



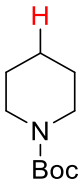
2b

3-(4-Formyl-2-methoxyphenoxy)propyl 3-phenylpropanoate (**2b**), colorless liquid (30.1 mg, 88% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.86 (s, 1H), 7.45-7.41 (m, 2H), 7.28-7.25 (m, 2H), 7.20-7.18 (m, 3H), 6.92 (d, J = 7.0 Hz, 1H), 4.29 (t, J = 6.0 Hz, 2H), 4.09 (t, J = 6.0 Hz, 2H), 3.91 (s, 3H), 2.95 (t, J = 8.0 Hz, 2H), 2.65 (t, J = 8.0 Hz, 2H), 2.20-2.14 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 190.9, 172.9, 153.8, 149.9, 140.4, 130.2, 128.5, 128.3, 126.7, 111.6, 109.4, 85.6, 61.1, 56.0, 35.8, 30.9, 28.4. HRMS (ESI) m/z: $(M + Na)^+$ Calcd for $C_{20}H_{25}O_5Na^+$ 365.1359; Found 365.1364.



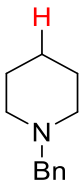
2c

tert-Butyl 2-(2-oxo-2,3,4,5-tetrahydro-1*H*-benzo[*b*]azepin-1-yl)acetate (**2c**), colorless liquid (26.1 mg, 95% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29-7.26 (m, 1H), 7.21 (d, J = 6.0 Hz, 1H), 7.16 (t, J = 7.5 Hz, 1H), 7.12 (t, J = 8.0 Hz, 1H), 4.41 (s, 2H), 3.15-2.80 (m, 2H), 2.34 (t, J = 7.0 Hz, 2H), 2.28-2.12 (m, 2H), 1.43 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.2, 168.3, 142.6, 135.9, 129.5, 127.5, 126.3, 121.9, 81.9, 50.8, 32.9, 29.9, 28.8, 28.0. HRMS (ESI) m/z: $(M + Na)^+$ Calcd for $C_{16}H_{21}NO_3Na^+$ 298.1414; Found 298.1417.



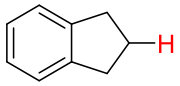
2d

tert-Butyl piperidine-1-carboxylate (**2d**),[16] colorless liquid (16.1 mg, 87% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.37-3.35 (m, 4H), 1.53-1.50 (m, 6H), 1.46 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 154.9, 79.1, 44.6, 28.5, 25.7, 24.5.



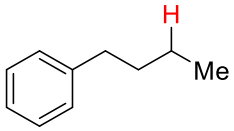
2e

1-Benzylpiperidine (**2e**),[13] colorless liquid (15.4 mg, 88% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33-7.29 (m, 4H), 7.25-7.23 (m, 1H), 3.48 (s, 2H), 2.45-2.34 (m, 4H), 1.60-1.57 (m, 4H), 1.44-1.43 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 140.5, 131.5, 130.3, 129.1, 66.0, 56.6, 28.1, 26.5.



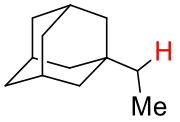
2f

2,3-Dihydro-1*H*-indene (**2f**),[10] colorless liquid (9.5 mg, 80% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.21-7.19 (m, 2H), 7.12-7.10 (m, 2H), 2.89 (t, J = 7.5 Hz, 4H), 2.07-2.01 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 144.4, 126.3, 124.7, 33.2, 25.7.



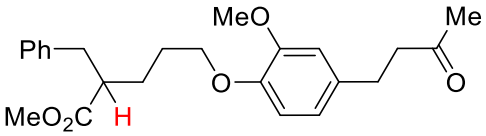
2g

Butylbenzene (**2g**),[19] colorless liquid (9.8 mg, 73% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.25 (t, J = 7.5 Hz, 2H), 7.17-7.14 (m, 3H), 2.60 (t, J = 7.0 Hz, 2H), 1.62-1.56 (m, 2H), 1.37-1.33 (m, 2H), 0.92 (t, J = 7.0 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.0, 128.5, 128.3, 125.7, 35.8, 33.8, 22.5, 14.1.



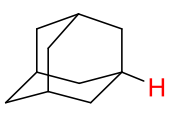
2h

1-Ethyladamantane (**2h**),[19] colorless liquid (15.1 mg, 92% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.95-1.93 (m, 3H), 1.71-1.60 (m, 6H), 1.44-1.43 (m, 6H), 1.08 (q, J = 7.5 Hz, 2H), 0.77 (t, J = 7.5 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 42.0, 37.4, 36.7, 32.2, 38.8, 6.9.



2i

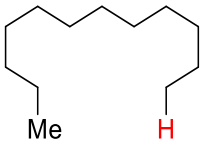
Methyl 2-benzyl-5-(2-methoxy-4-(3-oxobutyl)phenoxy)pentanoate (**2i**), colorless liquid (39.0 mg, 98% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28-7.4 (m, 5H), 6.75-6.67 (m, 3H), 3.97-3.92 (m, 2H), 3.82 (s, 3H), 3.58 (s, 3H), 2.98-2.93 (m, 1H), 2.85-2.72 (m, 6H), 2.13 (s, 3H), 1.86-1.71 (m, 4H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 208.1, 175.8, 149.4, 146.7, 139.2, 134.0, 128.9, 128.4, 126.4, 120.2, 113.5, 112.3, 68.7, 56.0, 51.5, 47.3, 45.4, 38.5, 30.1, 29.4, 28.5, 27.1. HRMS (ESI) m/z: $(M + Na)^+$ Calcd for $C_{24}H_{30}O_5Na^+$ 421.1985; Found 421.1989.



2j

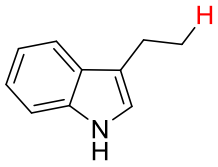
Adamantane (**2j**),[13] white solid (12.9 mg, 95% yield), m.p. 209-210 ^{o}C. ^{1}H NMR (500 MHz,

$CDCl_3$) δ 1.89-1.86 (m, 4H), 1.78-1.73 (m, 12H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 37.8, 28.4.



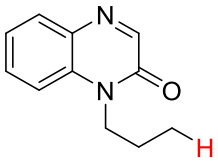
2k

Dodecane (**2k**),[13] colorless liquid (14.3 mg, 84% yield). ^1H NMR (500 MHz, $CDCl_3$) δ 1.33-1.26 (m, 20H), 0.88 (t, J = 7.0 Hz, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 32.0, 29.8, 29.7, 29.4, 22.7, 14.1.



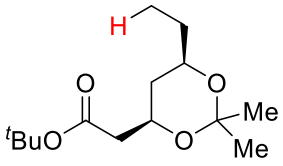
2l

3-Ethyl-1*H*-indole (**2l**),[19] colorless liquid **(**12.6 mg, 87% yield). ^1H NMR (500 MHz, $CDCl_3$) δ 7.88 (s, br, 1H), 7.61 (d, J = 8.0 Hz, 1H), 7.35 (d, J = 8.0 Hz, 1H), 7.19 (t, J = 7.0 Hz, 1H), 7.11 (t, J = 7.0 Hz, 1H), 6.97 (s, 1H), 2.79 (q, J = 7.5 Hz, 2H), 1.34 (t, J = 7.5 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 136.4, 127.4, 1212.9, 120.4, 119.1, 119.0, 118.9, 111.1, 18.4, 14.5.



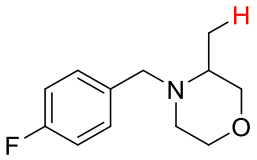
2m

1-Propylquinoxalin-2(1*H*)-one (**2m**),[14] colorless liquid (12.6 mg, 67% yield). ^1H NMR (500 MHz, $CDCl_3$) δ 8.30 (s, 1H), 7.88 (dd, J = 8.5, 1.5 Hz, 1H), 7.61-7.58 (m, 1H), 7.37-7.34 (m, 2H), 4.21 (t, J = 8.0 Hz, 2H), 1.84-1.77 (m, 2H), 1.06 (t, J = 7.5 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 154.8, 150.3, 133.6, 132.4, 131.0, 130.7, 123.6, 113.9, 43.4, 20.6, 11.3



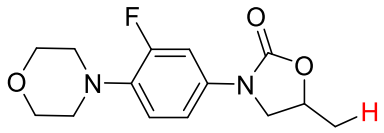
2n

tert-Butyl 2-((4*R*,6*R*)-6-ethyl-2,2-dimethyl-1,3-dioxan-4-yl)acetate (**2n**),[19] colorless liquid (23.7 mg, 92% yield). ^1H NMR (500 MHz, $CDCl_3$) δ 4.27-4.22 (m, 1H), 3.77-3.74 (m, 1H), 2.46-2.31 (m, 2H), 1.58 (dt, J = 12.5 Hz, 2.0 Hz, 1H), 1.55-1.50 (m, 1H), 1.46-1.44 (m, 12H), 1.37 (s, 3H), 1.18-1.10 (m, 1H), 0.90 (t, J = 7.5 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.4, 98.6, 80.5, 70.2, 66.3, 42.8, 36.0, 30.1, 29.2, 28.1, 19.8, 9.4.



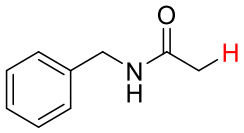
2o

4-(4-Fluorobenzyl)-3-methylmorpholine (**2o**),[19] colorless liquid (20.7 mg, 99% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30-7.27 (m, 2H), 7.00 (d, J = 8.5 Hz, 2H), 3.85-3.83 (m, 1H), 3.69-3.60 (m, 2H), 3.48-3.42 (m, 2H), 2.70-2.62 (m, 2H), 2.16-2.11 (m, 1H), 1.83-1.78 (m, 1H), 1.12 (d, J = 6.0 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.0 (d, J = 243.6 Hz), 133.5, 130.6 (d, J = 8.0 Hz), 115.1 (d, J = 21.0 Hz), 71.8, 66.8, 62.4, 59.9, 52.9, 19.1. ^{19}F NMR (471 MHz, $CDCl_3$) δ -115.5.



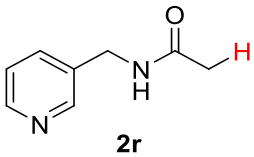
2p

3-(3-Fluoro-4-morpholinophenyl)-5-methyloxazolidin-2-one (**2p**), yellow solid (26.0 mg, 93% yield). m.p. 95-96 ^{o}C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.44 (dd, J = 14.5, 2.5 Hz, 1H), 7.11 (dd, J = 8.5, 1.5 Hz, 1H), 6.93 (t, J = 9.0 Hz, 1H), 4.81-4.75 (m, 1H), 4.08-4.06 (m, 1H), 3.89-3.85 (m, 4H), 3.57 (dd, J = 8.5, 7.5 Hz, 1H), 3.05 (t, J = 5.0 Hz, 4H), 1.53 (d, J = 6.5 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.5, 154.6 (d, J = 25.6 Hz), 136.1, 133.6 (d, J = 10.5 Hz), 118.9, 113.7 (d, J = 3.1 Hz), 107.4 (d, J = 26.0 Hz), 69.6, 67.0, 51.9, 51.08, 51.05. ^{19}F NMR (471 MHz, $CDCl_3$) δ -120.4. HRMS (ESI) m/z: $(M + Na)^+$ Calcd for $C_{14}H_{17}N_2O_3FNa^+$ 303.1115; Found 303.1121.



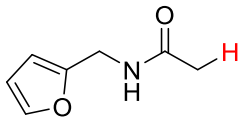
2q

N-Benzylacetamide (**2q**),[11] white solid (13.6 mg, 91% yield). m.p. 59-62 ^{o}C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34 (d, J = 7.5 Hz, 2H), 7.29-7.26 (m, 3H), 5.87 (s, br, 1H), 4.42 (d, J = 6.0 Hz, 2H), 2.02 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.0, 138.2, 128.7, 127.9, 127.6, 43.8, 23.3.



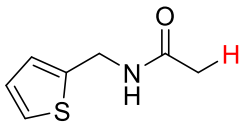
2r

N-(Pyridin-3-ylmethyl)acetamide (**2r**),[11] colorless liquid (11.6 mg, 77% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.52-8.50 (m, 2H), 7.65 (d, J = 7.5 Hz, 1H), 7.29-7.26 (m, 1H), 6.34 (s, br, 1H), 4.44 (d, J = 6.0 Hz, 2H), 2.02 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.3, 149.1, 148.8, 135.8, 134.1, 123.7, 41.1, 23.2.



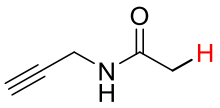
2s

N-(Furan-2-ylmethyl)acetamide (**2s**),[11] colorless liquid (11.3 mg, 81% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36-7.35 (m, 1H), 6.33-6.32 (m, 1H), 6.23 (d, J = 3.0 Hz, 1H), 5.94 (s, br, 1H), 4.43 (d, J = 5.5 Hz, 2H), 2.01 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.9, 151.2, 142.2, 110.5, 107.5, 36.6, 23.2.



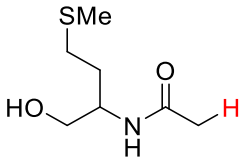
2t

N-(Thiophen-2-ylmethyl)acetamide (**2t**),[11] yellow liquid (11.0 mg, 71% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.21 (d, J = 5.0 Hz, 1H), 6.96-6.94 (m, 2H), 6.01 (s, br, 1H), 4.58 (d, J = 5.5 Hz, 2H), 2.00 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.8, 139.8, 125.9, 125.1, 124.2, 37.3, 22.1.



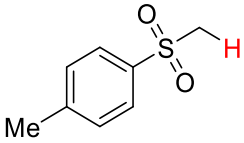
2u

N-(Prop-2-yn-1-yl)acetamide (**2u**),[18] colorless liquid (8.2 mg, 84% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.8 (s, br, 1H), 4.05 (dd, J = 5.5, 2.5 Hz, 2H), 2.24 (t, J = 2.5 Hz, 1H), 2.02 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.8, 79.5, 71.6, 29.3, 23.1.



2v

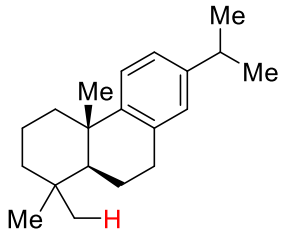
N-(1-Hydroxy-4-(methylthio)butan-2-yl)acetamide (**2v**), colorless liquid (8.3 mg, 47% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.00 (s, br, 1H), 4.08-4.02 (m, 1H), 3.72-3.63 (m, 2H), 2.55 (t, J = 7.5 Hz, 2H), 2.12 (s, 3H), 2.02 (s, 3H), 1.89-1.79 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.9, 64.0, 50.3, 29.7, 29.4, 22.4, 14.6. HRMS (ESI) m/z: $(M + Na)^+$ Calcd for $C_7H_{15}NO_2SNa^+$ 200.0716; Found 200.0718.



2w

1-Methyl-4-(methylsulfonyl)benzene (**2w**),[17] white solid (13.3 mg, 78% yield). m.p. 85-87 ˚C. ^{1}H

NMR (500 MHz, $CDCl_3$) δ 7.83 (d, J = 8.0 Hz, 2H), 7.37 (d, J = 8.0 Hz, 2H), 3.04 (s, 3H), 2.46 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.6, 136.7, 128.9, 126.4, 43.6, 20.6.

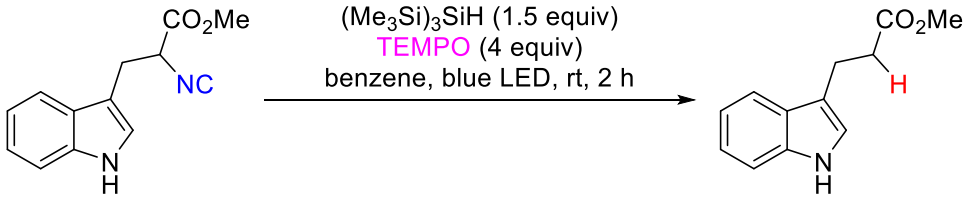


2x

(4a*R*,10a*R*)-7-Isopropyl-1,1,4a-trimethyl-1,2,3,4,4a,9,10,10a-octahydrophenanthrene (**2x**),[17] colorless liquid (22.6 mg, 84% yield). ^1H NMR (500 MHz, $CDCl_3$) δ 7.17 (d, J = 8.0 Hz, 1H), 6.98 (d, J = 8.0 Hz, 1H), 6.89 (s, 1H), 2.94-2.79 (m, 3H), 2.29-2.26 (m, 1H), 1.89-1.85 (m, 1H), 1.76-1.69 (m, 2H), 1.62-1.56 (m, 1H), 1.48-1.33 (m, 4H), 1.22 (d, J = 7.0 Hz, 6H), 1.18 (s, 3H), 0.94 (s, 3H), 0.92 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.6, 145.4, 135.0, 126.8, 124.3, 123.8, 50.4, 41.8, 38.9, 37.6, 33.5, 33.4, 30.5, 24.9, 24.1, 24.0, 21.7, 19.4, 19.1.

Mechanistic Studies (Scheme 3)

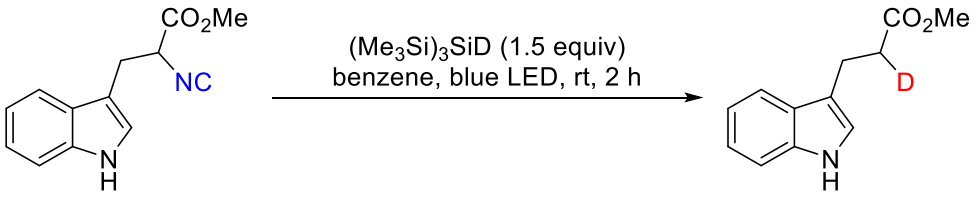
(a) Radical Trapping Experiment (Scheme 3a)



1a **2a**, 0%

Alkyl isocyanide **1a** (24.2 mg, 0.10 mmol), tris(trimethylsilyl)silane (37.3 mg, 45 μL, 0.15 mmol), TEMPO (62.5 mg, 0.40 mmol), and benzene (0.50 mL) were added to a sealed test tube under nitrogen atmosphere. The mixture was stirred at room temperature under blue LED (465 nm, 10 W) irradiation for 2 h. Compound **2a** was not detected by thin-layer chromatography.

(b) Deuterium-Labelling Experiments (Scheme 3b)



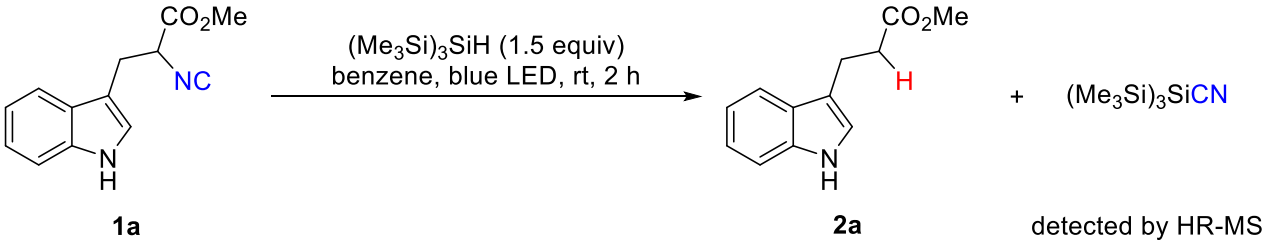
1a

2a-D
H/D < 1:99, 99%

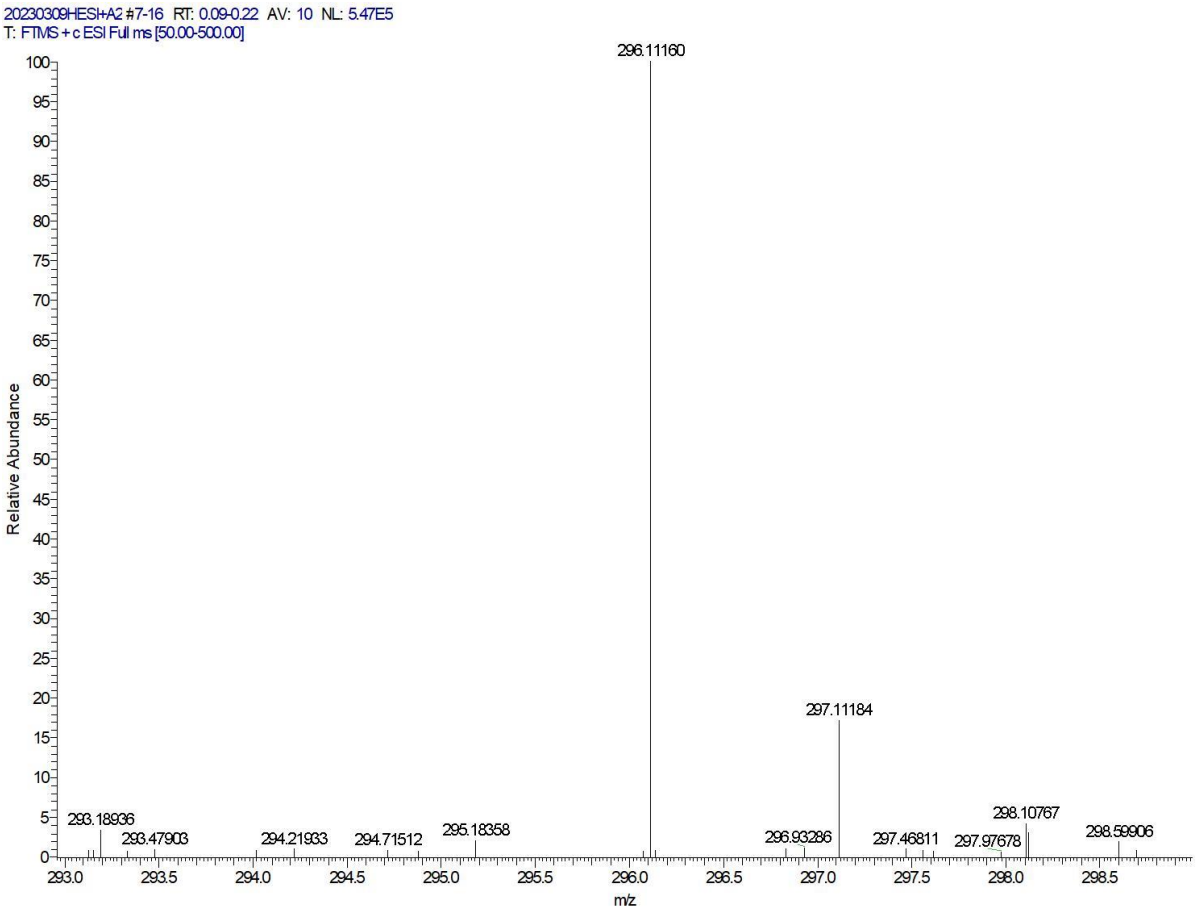
Alkyl isocyanide **1a** (24.2 mg, 0.10 mmol), $(Me_3Si)_3SiD$ (37.5 mg, 45 μL, 0.15 mmol), and benzene (0.50 mL) were added to a sealed test tube under nitrogen atmosphere. The mixture was stirred at room temperature under blue LED (465 nm, 10 W) irradiation for 2 h, and purified by silica gel

chromatography (petroleum ether/ethyl acetate = 5:1 v/v) to give compound **2a-D** (24.0 mg, 99% yield, > 99% deuteration rate). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.99 (s, br, 1H), 7.60 (d, J = 8.0 Hz, 1H), 7.34 (d, J = 8.0 Hz, 1H), 7.19 (t, J = 7.0 Hz, 1H), 7.12 (t, J = 7.0 Hz, 1H), 6.99 (s, 1H), 3.67 (s, 3H), 3.10 (d, J = 8.0 Hz, 2H), 2.74-2.69 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.0, 136.3, 127.2, 122.1, 121.5, 119.4, 118.7, 114.9, 111.2, 51.6, 34.8-34.3 (m), 20.6.

Detection of $(Me_3Si)_3SiCN$ by ESI-MS Analysis

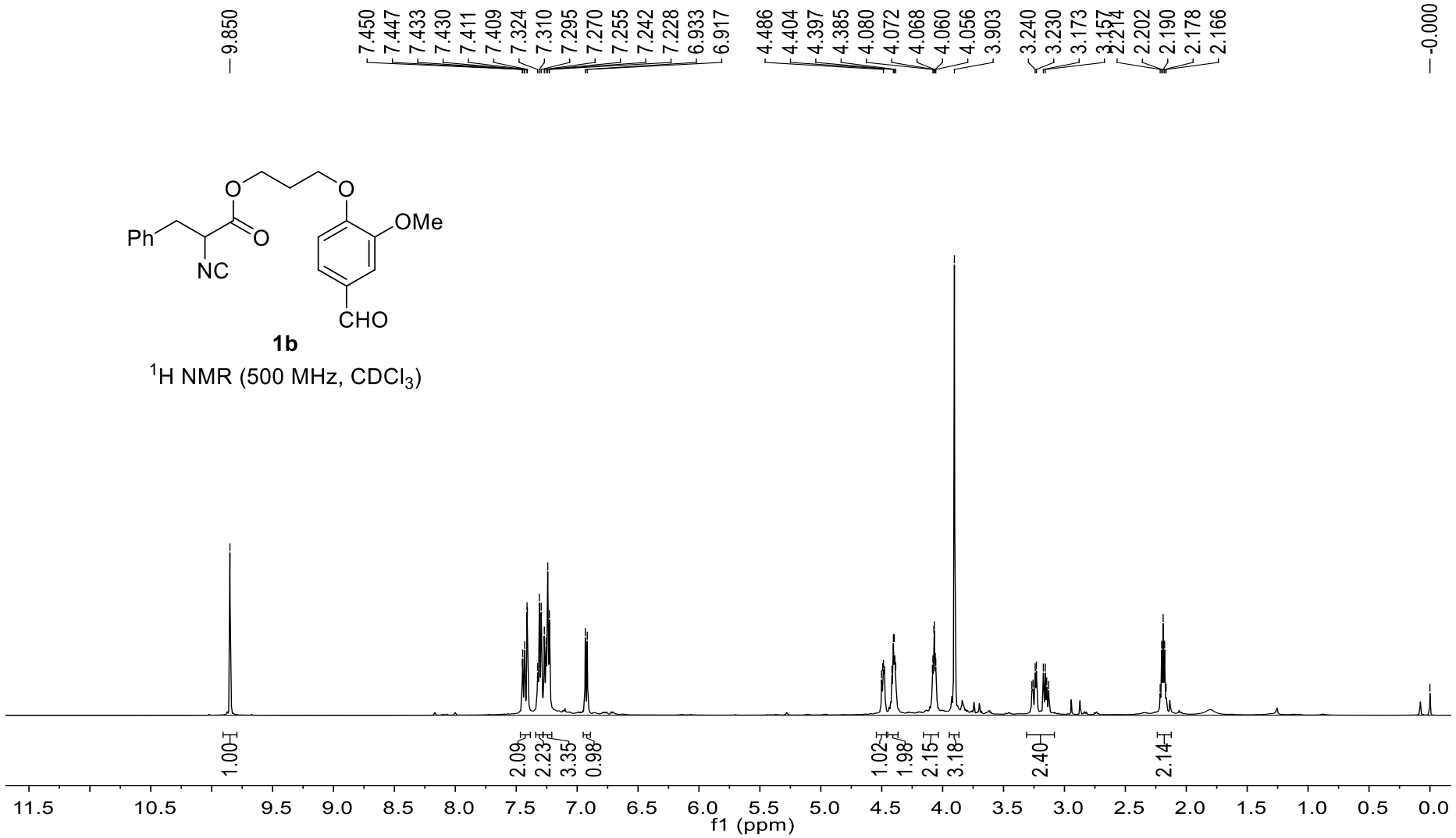


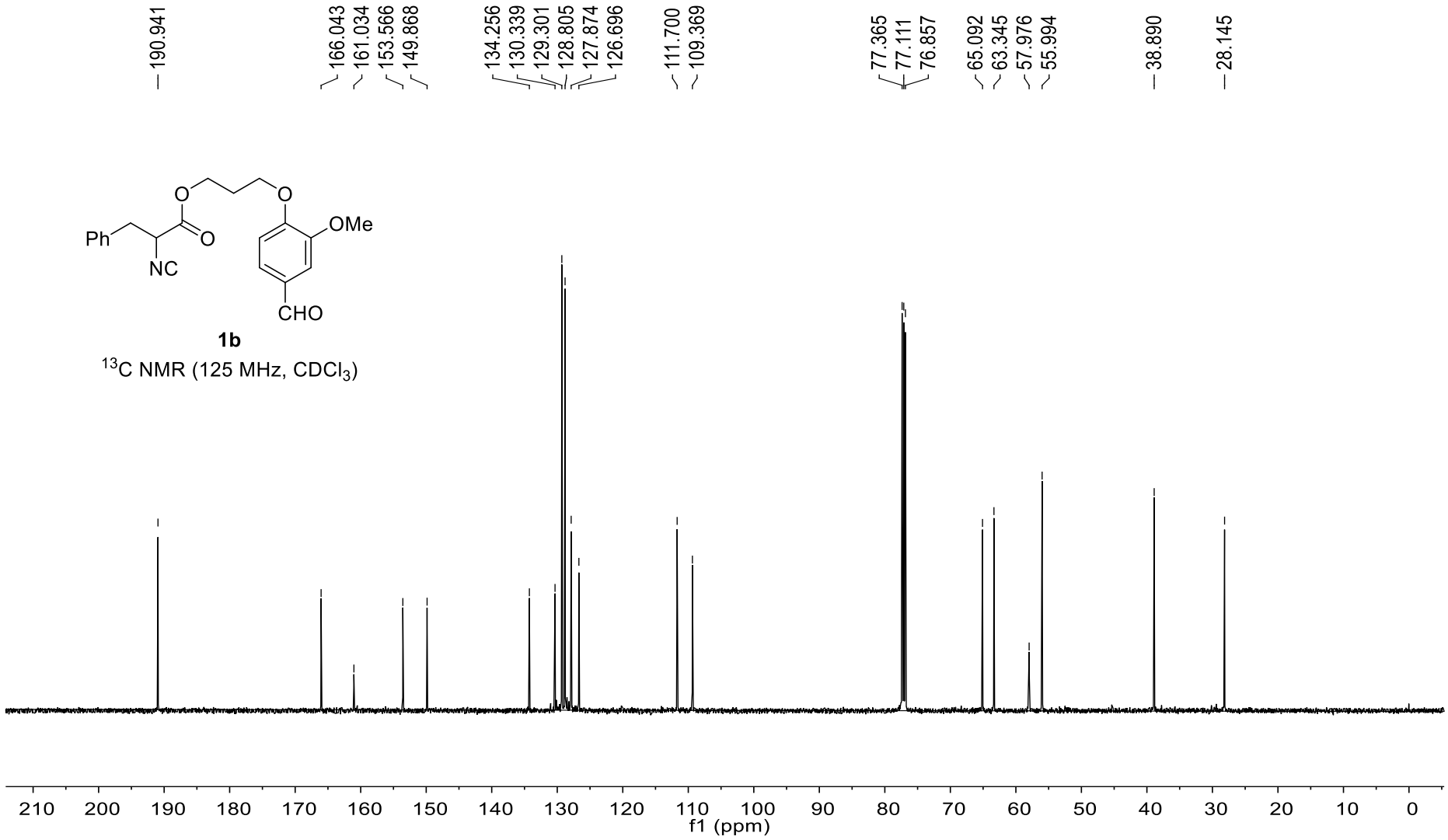
Alkyl isocyanide **1a** (24.2 mg, 0.10 mmol), tris(trimethylsilyl)silane (37.3 mg, 45 μL, 0.15 mmol), and benzene (0.50 mL) were added to a sealed test tube under nitrogen atmosphere. The mixture was stirred at room temperature under blue LED (465 nm, 10 W) irradiation for 2 h. The mixture was subjected to ESI-MS analysis. We tentatively assigned $(Me_3Si)_3SiCN$: HRMS (ESI) m/z: $(M + Na)^+$ Calcd for $C_{10}H_{27}NSi_4Na^+$ 296.1113; Found 296.1116.

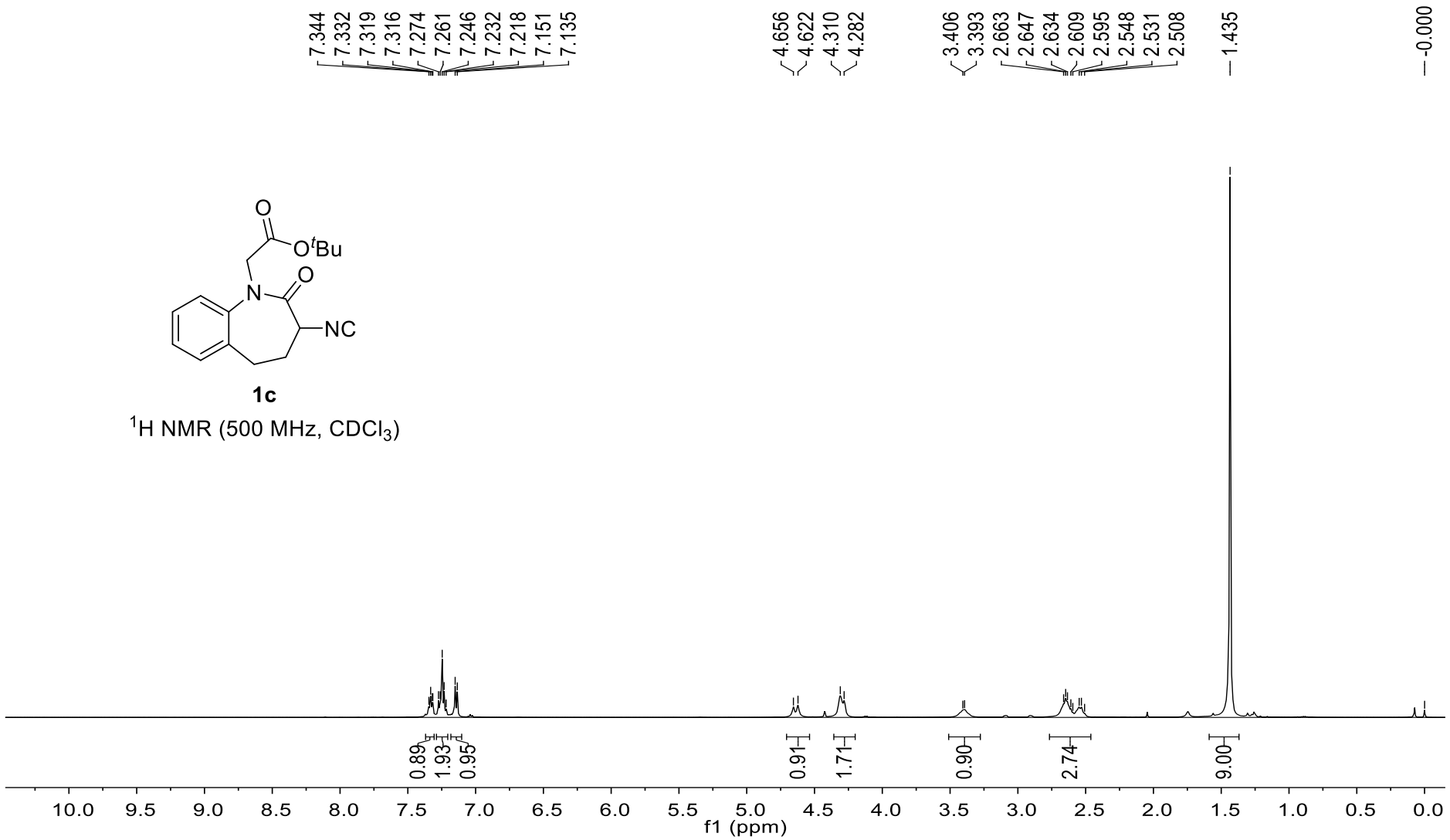


References

1. Y. Si, P. Zhu and S. Zhang, *Org. Lett*., 2020, **22**, 9086-9090.
2. S. Tang, J. Wang, Z. Xiong, Z. Xie, D. Li, J. Huang and Q. Zhu, *Org. Lett*., 2017, **19**, 5577-5580.
3. C. G. Neochoritis and A. Dömling, *Org. Biomol. Chem*., 2014, **12**, 1649-1651.
4. S. Wu, J. Huang, S. Gazzarrini, L. Chen. J. Li, J. Xing, C. Li, L. Chen, C. G. Neochoritis, G. Liao, H. Zhou, A. Dçmling, A. Moroni and W. Wang, *ChemMedChem*, 2015, **10**, 1837-1845.
5. P. Patil, M. A. Moghaddam and A. Dçmling, *Green Chem*., 2020, **22**, 6902-6911.
6. Y. Wang, P. Patil and A. Dömling, *Synthesis*, 2016, **48**, 3701-3712.
7. L. A. Polindara-García and A. Vazquez, *Org. Biomol. Chem*. **2014**, *12*, 7068-7082.
8. J. R. Wolstenhulme, A. Cavell, M. Gredičak, R. W. Driver and M. D. Smith, *Chem. Commun*., 2014, **50**, 13585-13588.
9. E. K. Ryu, Y. S. Choe, K. H. Lee, Y. Choi and B. T. Kim, *J. Med. Chem*., 2006, **49**, 6111-6119.
10. T. Ankner and G. Hilmersson, *Tetrahedron*, 2009, **65**, 10856–10862.
11. A. Alalla, M. M. Khelassi, L. A. Zouioueche and O. Riant, *Synth. Commun*., 2014, **44**, 2364-2376.
12. M. Yasui, H. Fujioka, N. Takeda and M. Ueda, *Org. Lett*., 2022, **24**, 43-47
13. Y. T. Gu, H. F. Yin, M. Wakeling, J. Z. An and R. Martin, *ACS Catal*., 2022, **12**, 1031-1036.
14. D. Chen and W. Bao, *Adv. Synth. Catal*., 2010, **352**, 955-960.
15. S. Park and M. Brookhart, *J. Am. Chem. Soc*., 2012, **134**, 640-653.
16. B. Abadie, D. M. Jardel, G. Pozzi, P. Toullec and J. M. Vincent, *Chem. Eur. J*., 2019, **25**, 16120-16127.
17. K. Liu, Z. Wang, L. Lu, J. Chen, F. Zeng, Y. Lin, Z. Cao, X. Yu and W. He, *Green Chem*., 2021, **23**, 496-500.
18. Z. Zhou, K. Chen and L. He, *Chin. J. Chem*., 2019, **37**, 1223-1228.
19. K. J. Berger, J. L. Driscoll, M. B. Yuan, B. D. Dherange, O. Gutierrez and M. D. Levin, *J. Am. Chem. Soc*., 2021, **143**, 17366-17373.

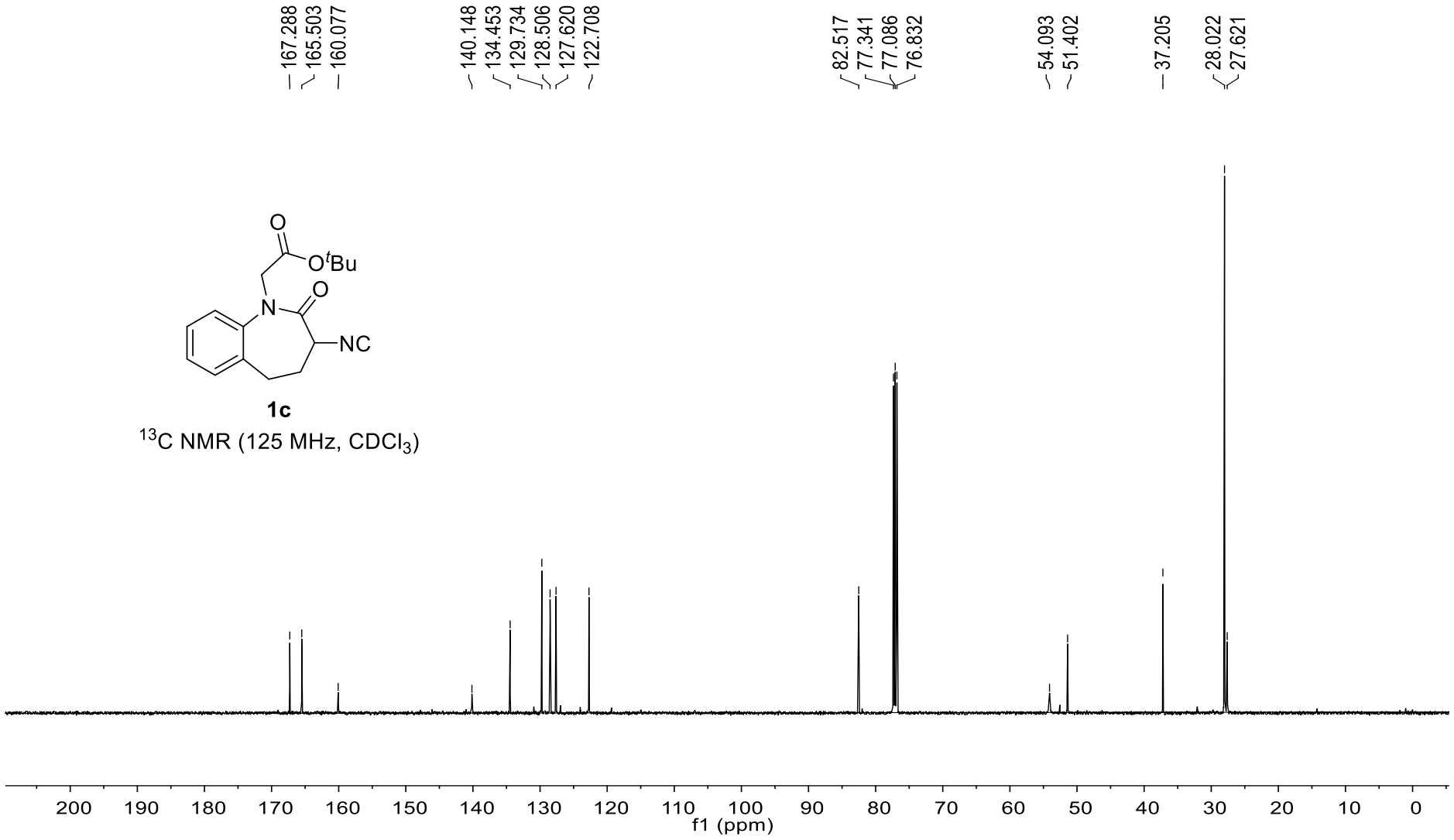

9.850
7.450
7.447
7.433
7.430
7.411
7.409
7.324
7.310
7.295
7.270
7.255
7.242
7.228
6.933
6.917
4.486
4.404
4.397
4.385
4.080
4.072
4.068
4.060
4.056
3.903
3.240
3.230
3.173
3.157
2.214
2.202
2.190
2.178
2.166
-0.000
Ph
NC
O
O
O
O
OMe
CHO
1b
1H NMR (500 MHz, CDCl3)
1.00
2.09
2.23
3.35
0.98
1.02
1.98
2.15
3.18
2.40
2.14
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


190.941
166.043
161.034
153.566
149.868
134.256
130.339
129.301
128.805
127.874
126.696
111.700
109.369
77.365
77.111
76.857
65.092
63.345
57.976
55.994
38.890
28.145
O
O
O
OMe
Ph
NC
CHO
1b
13C NMR (125 MHz, CDCl3)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



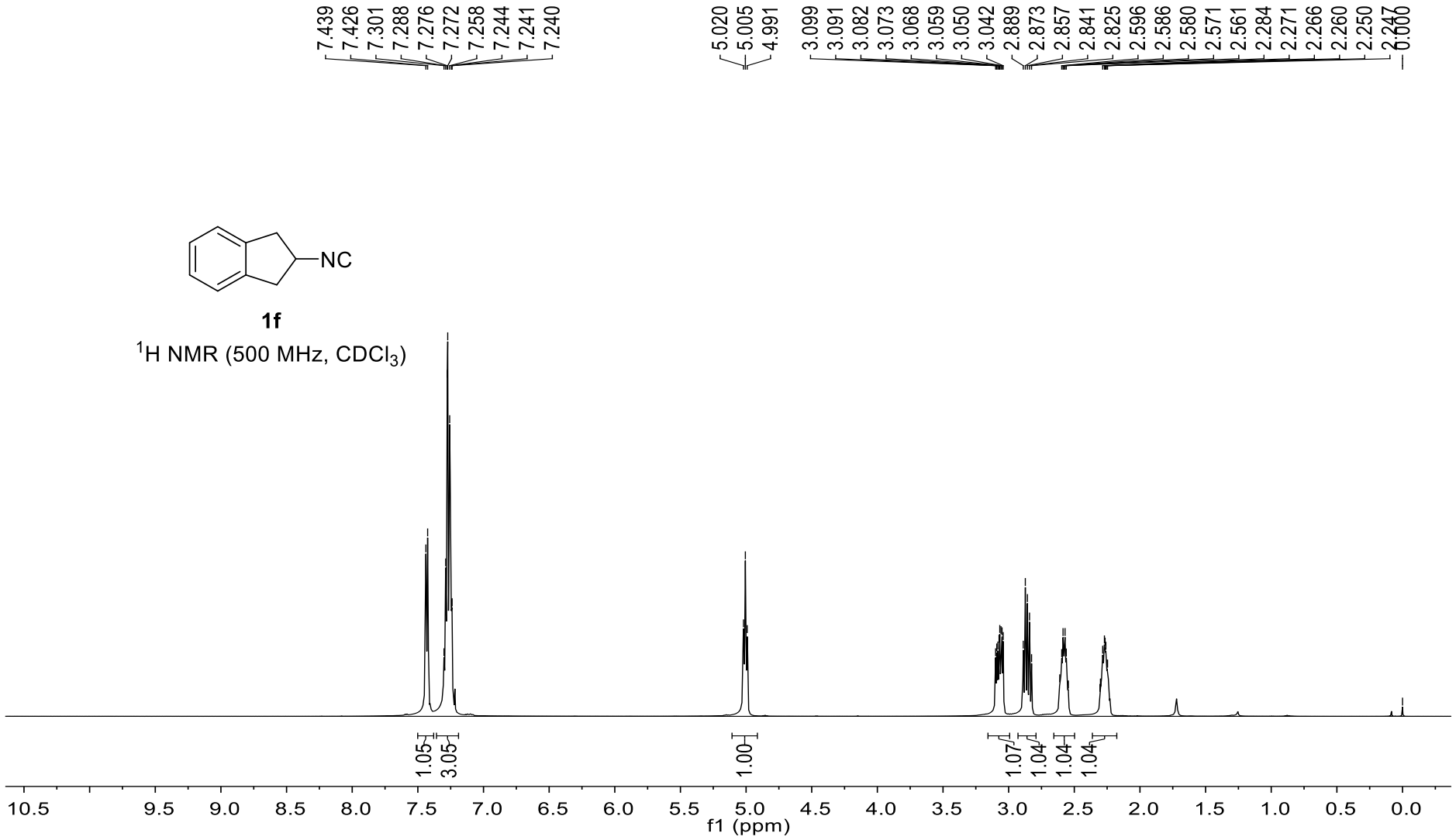
1c

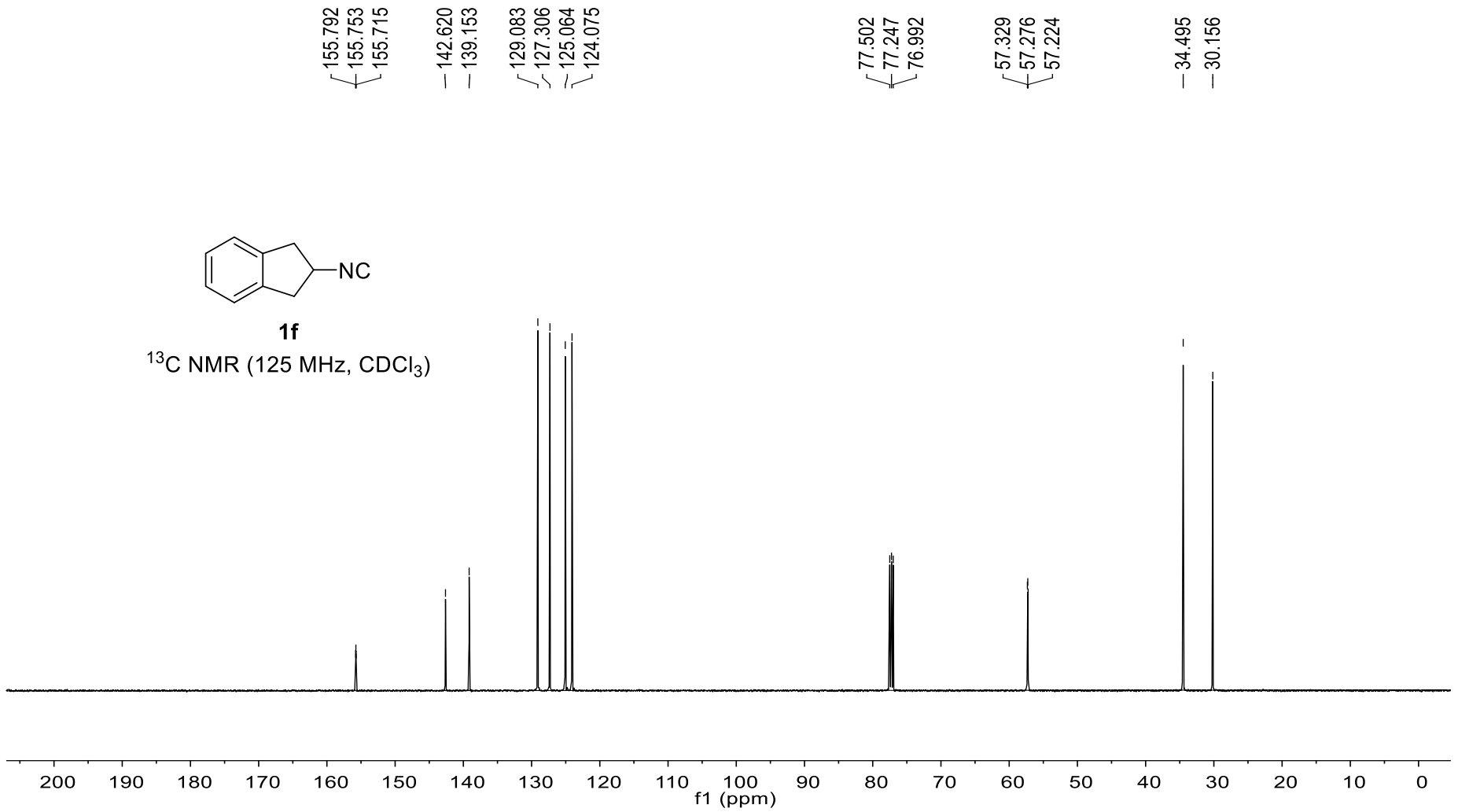
^{1}H NMR (500 MHz, $CDCl_3$)

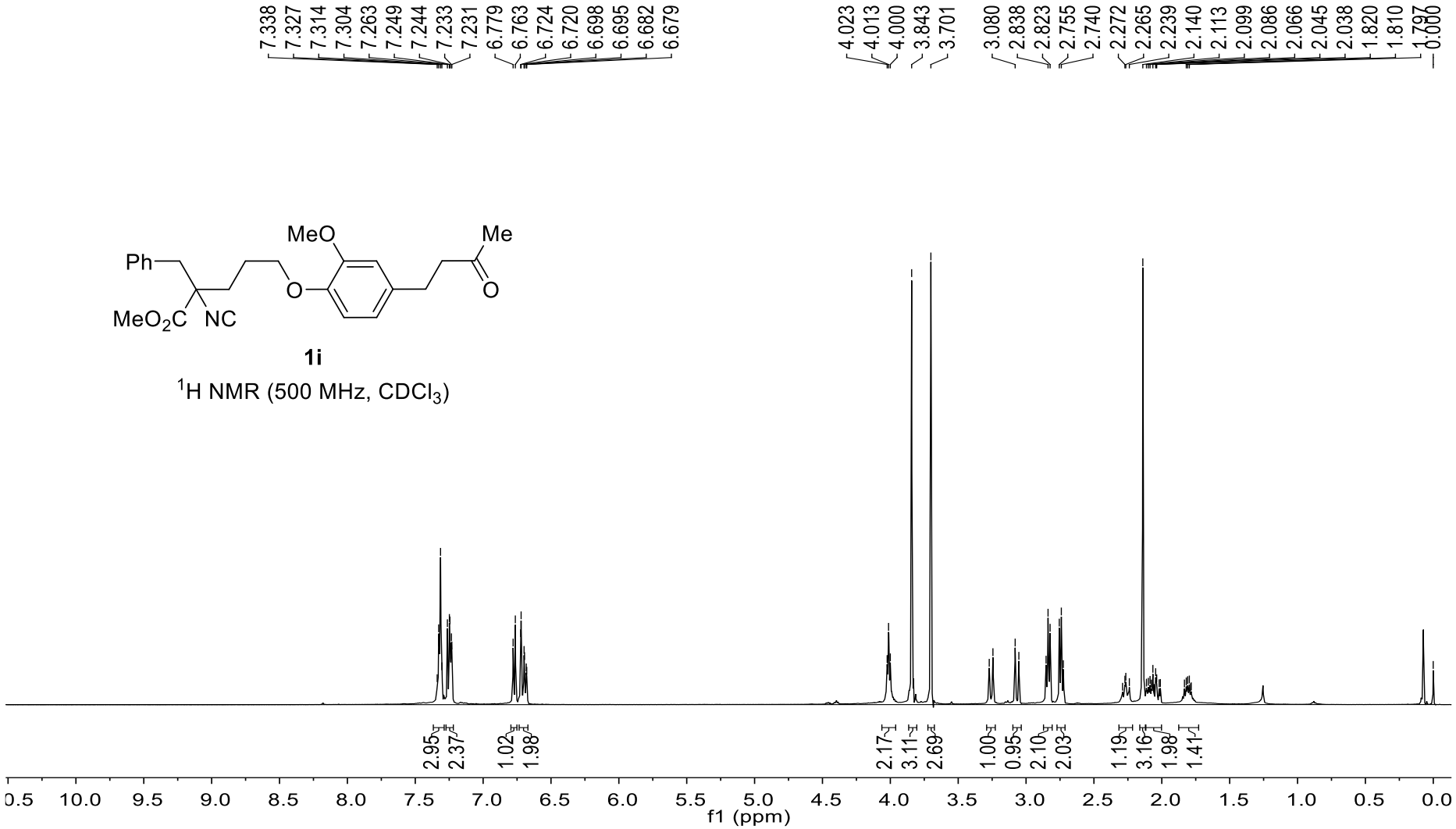


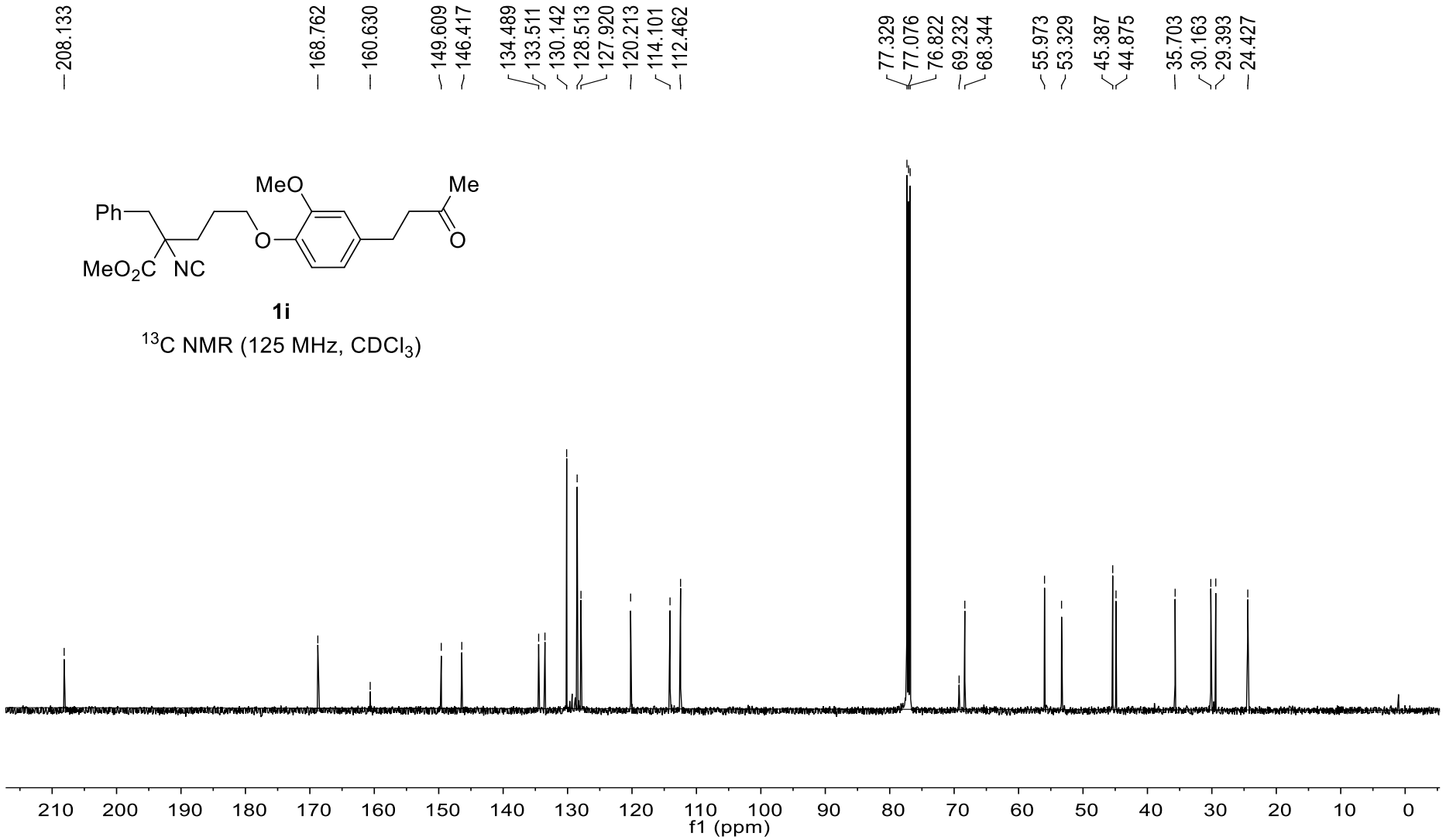
1c

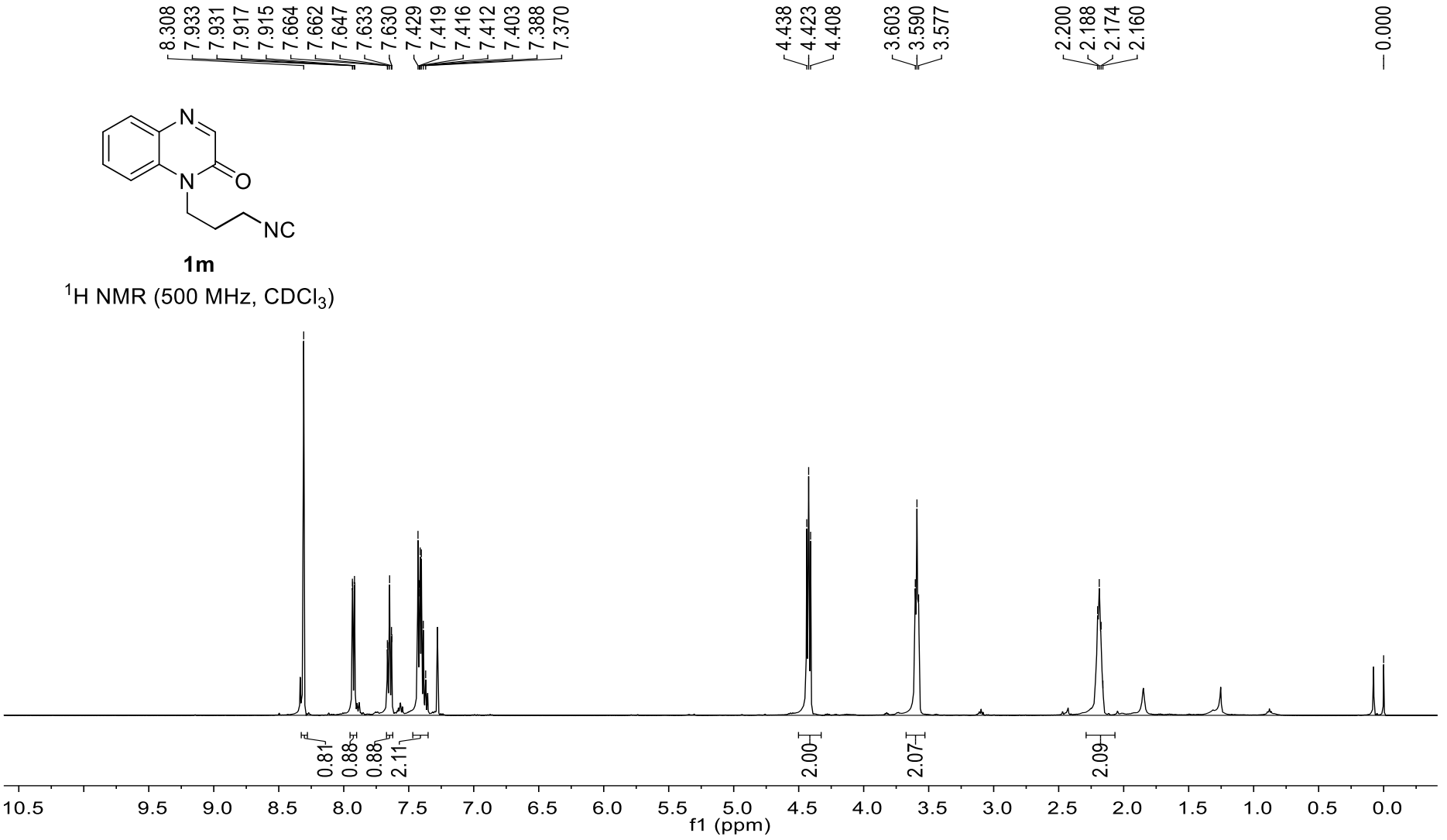
^{13}C NMR (125 MHz, $CDCl_3$)


7.439
7.426
7.301
7.288
7.276
7.272
7.258
7.244
7.241
7.240
5.020
5.005
4.991
3.099
3.091
3.082
3.073
3.068
3.059
3.050
3.042
2.889
2.873
2.857
2.841
2.825
2.596
2.586
2.580
2.571
2.561
2.284
2.271
2.266
2.260
2.250
2.247
0.000
NC
1f
1H NMR (500 MHz, CDCl3)
1.05
3.05
1.00
1.07
1.04
1.04
1.04
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


155.792
155.753
155.715
142.620
139.153
129.083
127.306
125.064
124.075
77.502
77.247
76.992
57.329
57.276
57.224
34.495
30.156
NC
1f
13C NMR (125 MHz, CDCl3)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

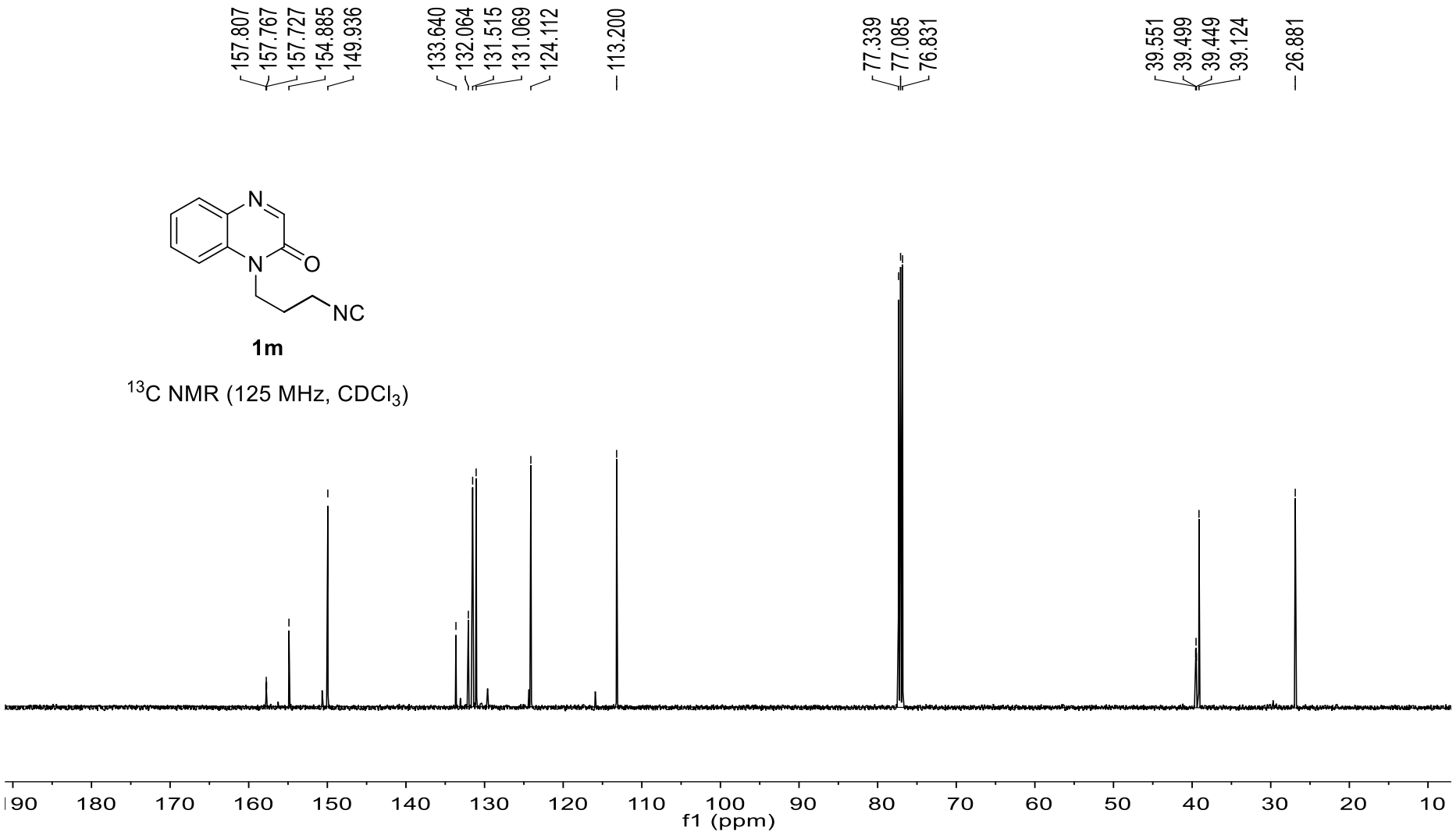

7.338
7.327
7.314
7.304
7.263
7.249
7.244
7.233
7.231
6.779
6.763
6.724
6.720
6.698
6.695
6.682
6.679
4.023
4.013
4.000
3.843
3.701
3.080
2.838
2.823
2.755
2.740
2.272
2.265
2.239
2.140
2.113
2.099
2.086
2.066
2.045
2.038
1.820
1.810
1.797
0.000
MeO
Me
Ph
O
O
MeO2C NC
1i
1H NMR (500 MHz, CDCl3)
2.95
2.37
1.02
1.98
2.17
3.11
2.69
1.00
0.95
2.10
2.03
1.19
3.16
1.98
1.41
f1 (ppm)

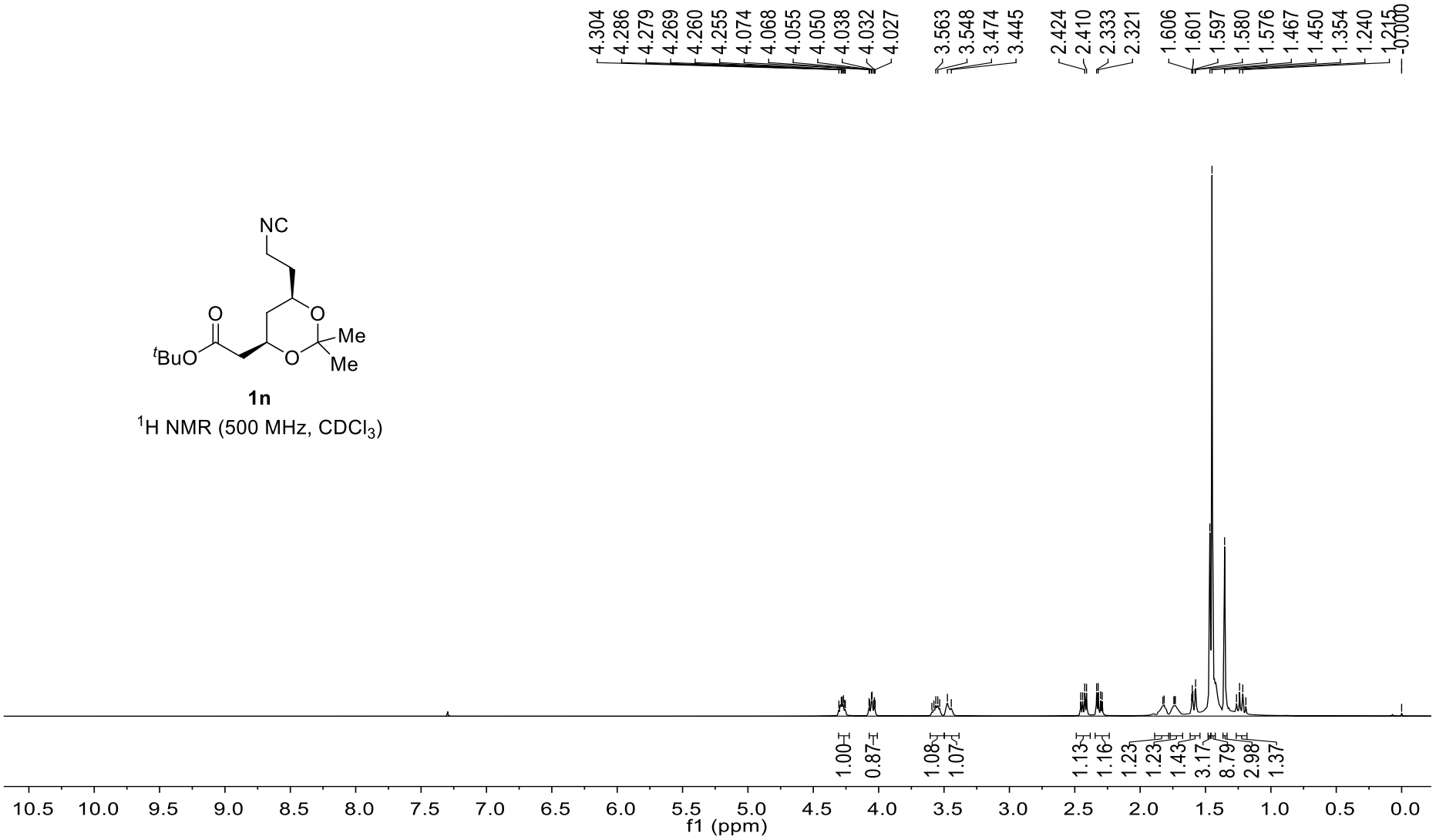

208.133
168.762
160.630
149.609
146.417
134.489
133.511
130.142
128.513
127.920
120.213
114.101
112.462
77.329
77.076
76.822
69.232
68.344
55.973
53.329
45.387
44.875
35.703
30.163
29.393
24.427
MeO
Me
Ph
O
O
MeO2C NC
1i
13C NMR (125 MHz, CDCl3)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



1m

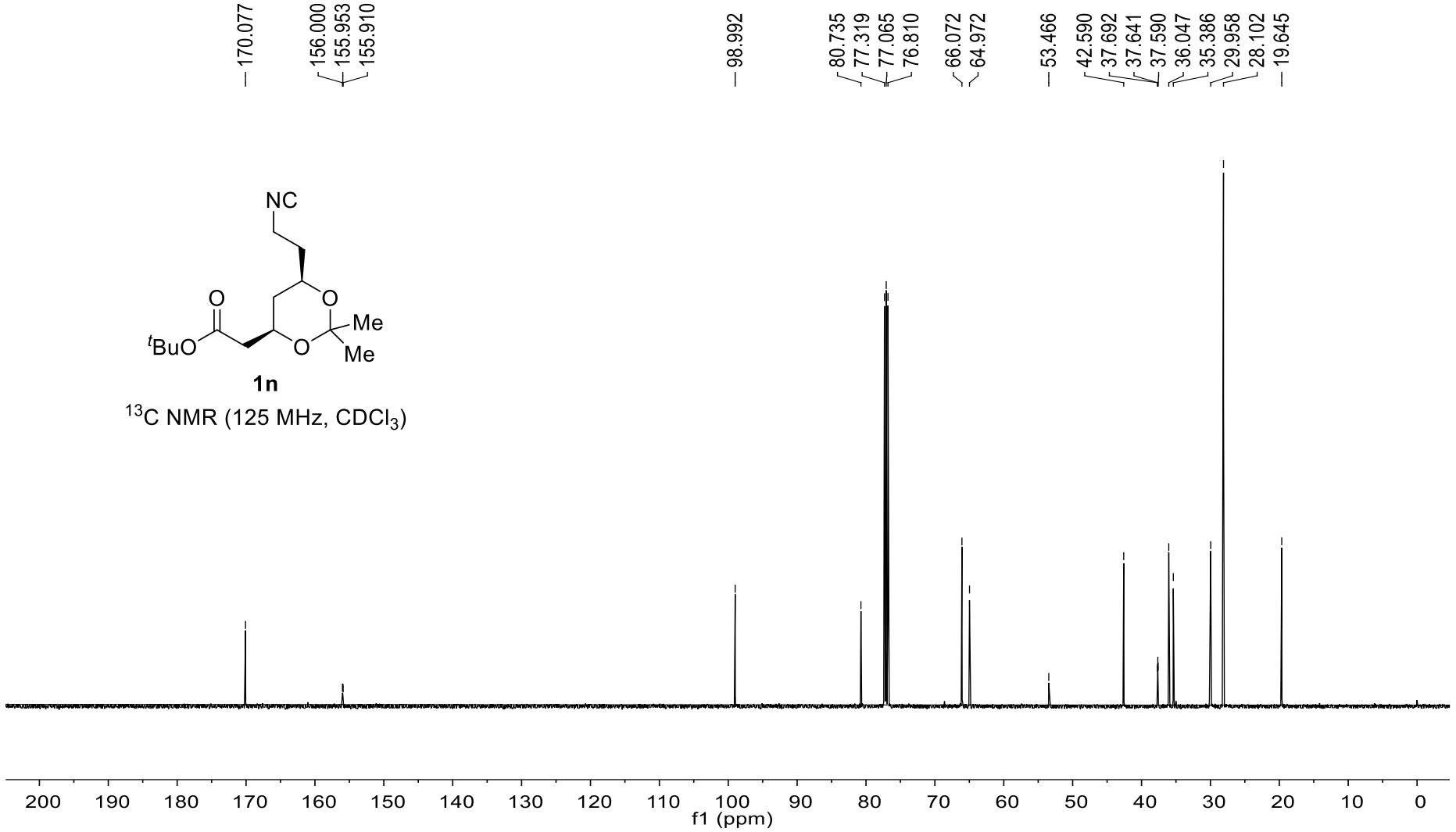
^{1}H NMR (500 MHz, $CDCl_3$)

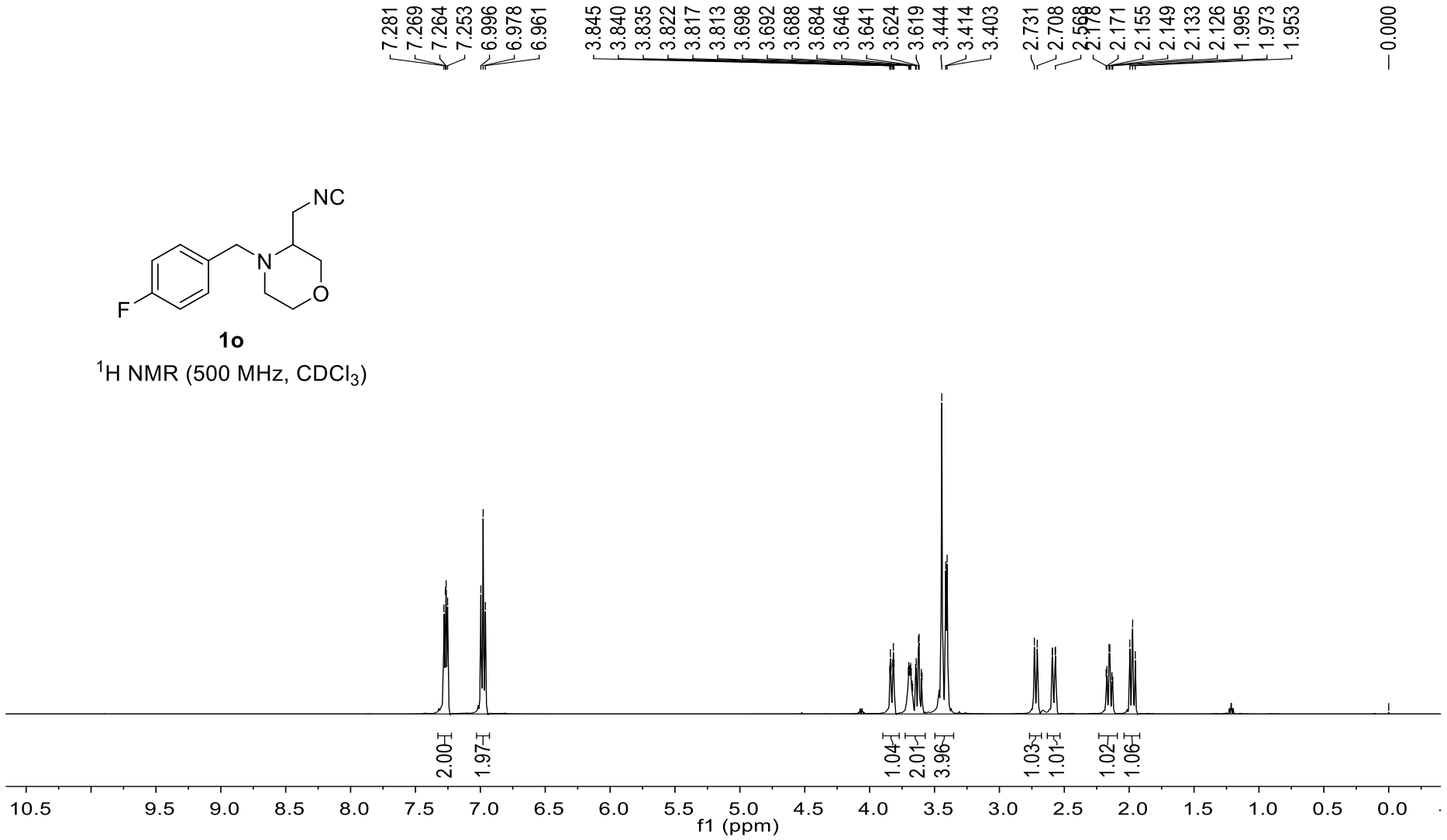

157.807
157.767
157.727
154.885
149.936
133.640
132.064
131.515
131.069
124.112
113.200
77.339
77.085
76.831
39.551
39.499
39.449
39.124
26.881
N
N
O
NC
1m
13C NMR (125 MHz, CDCl3)
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

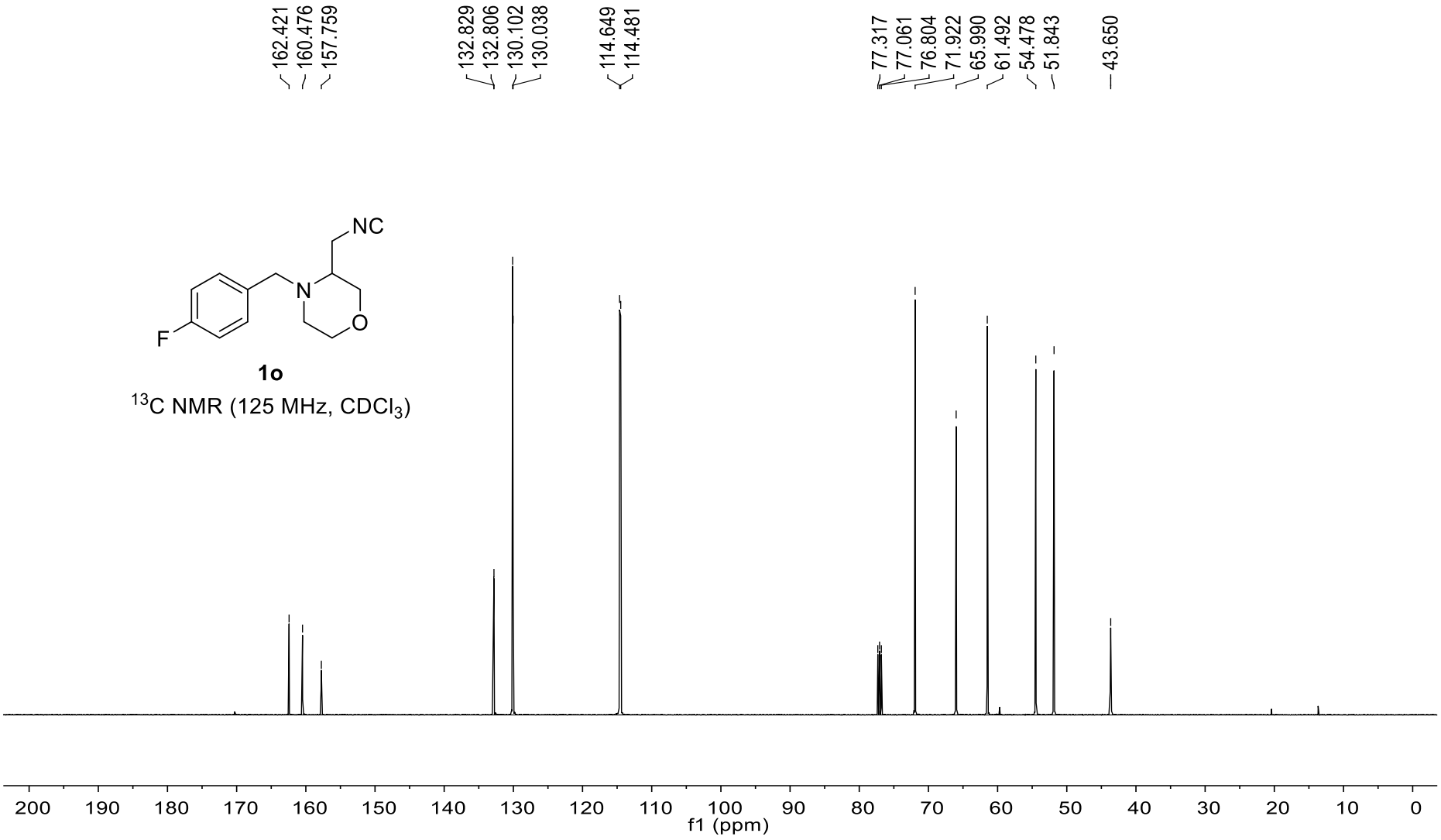


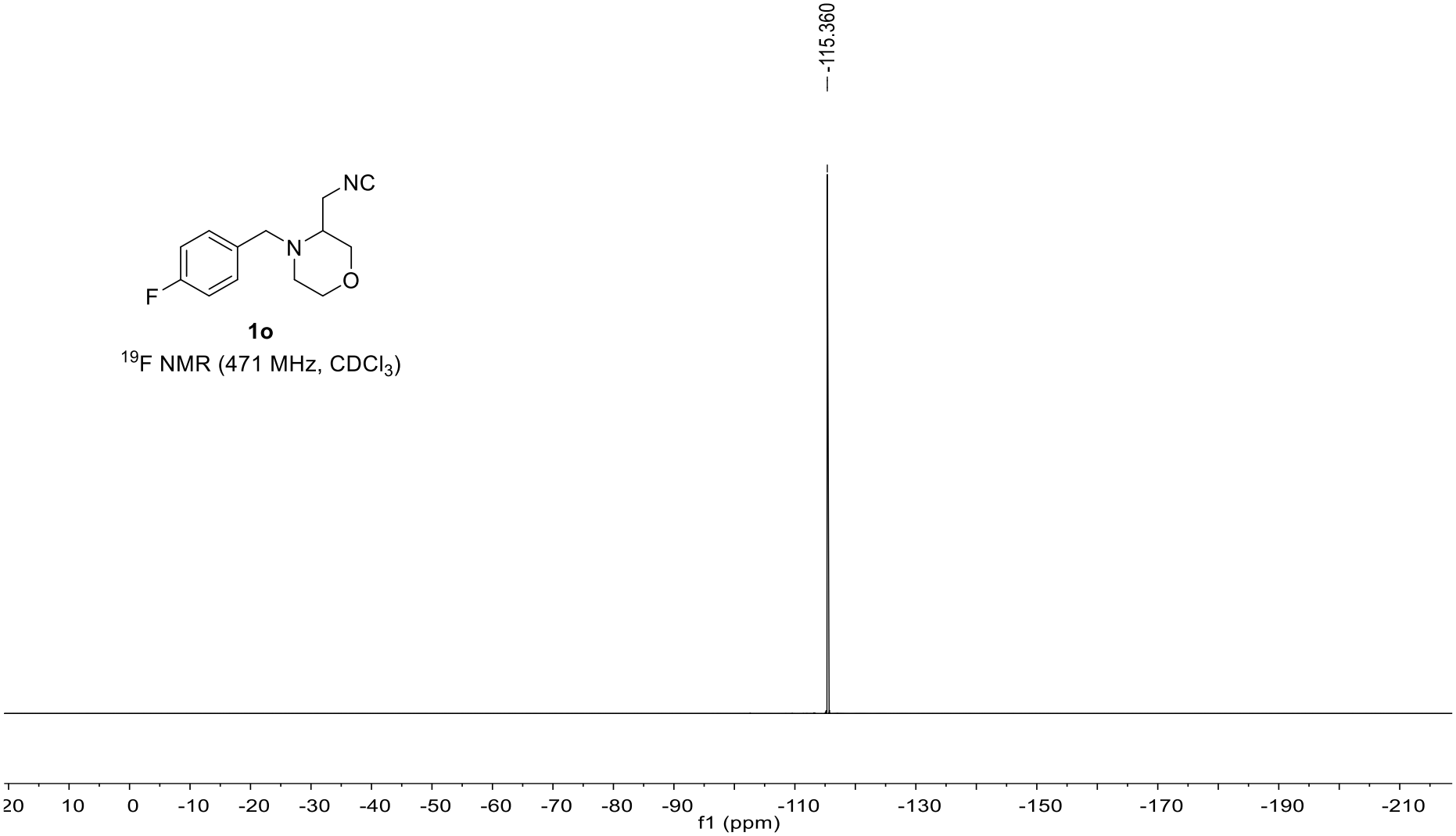
1n

^{1}H NMR (500 MHz, $CDCl_3$)


170.077
156.000
155.953
155.910
98.992
80.735
77.319
77.065
76.810
66.072
64.972
53.466
42.590
37.692
37.641
37.590
36.047
35.386
29.958
28.102
19.645
NC
O
O
Me
tBuO
O
Me
1n
13C NMR (125 MHz, CDCl3)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

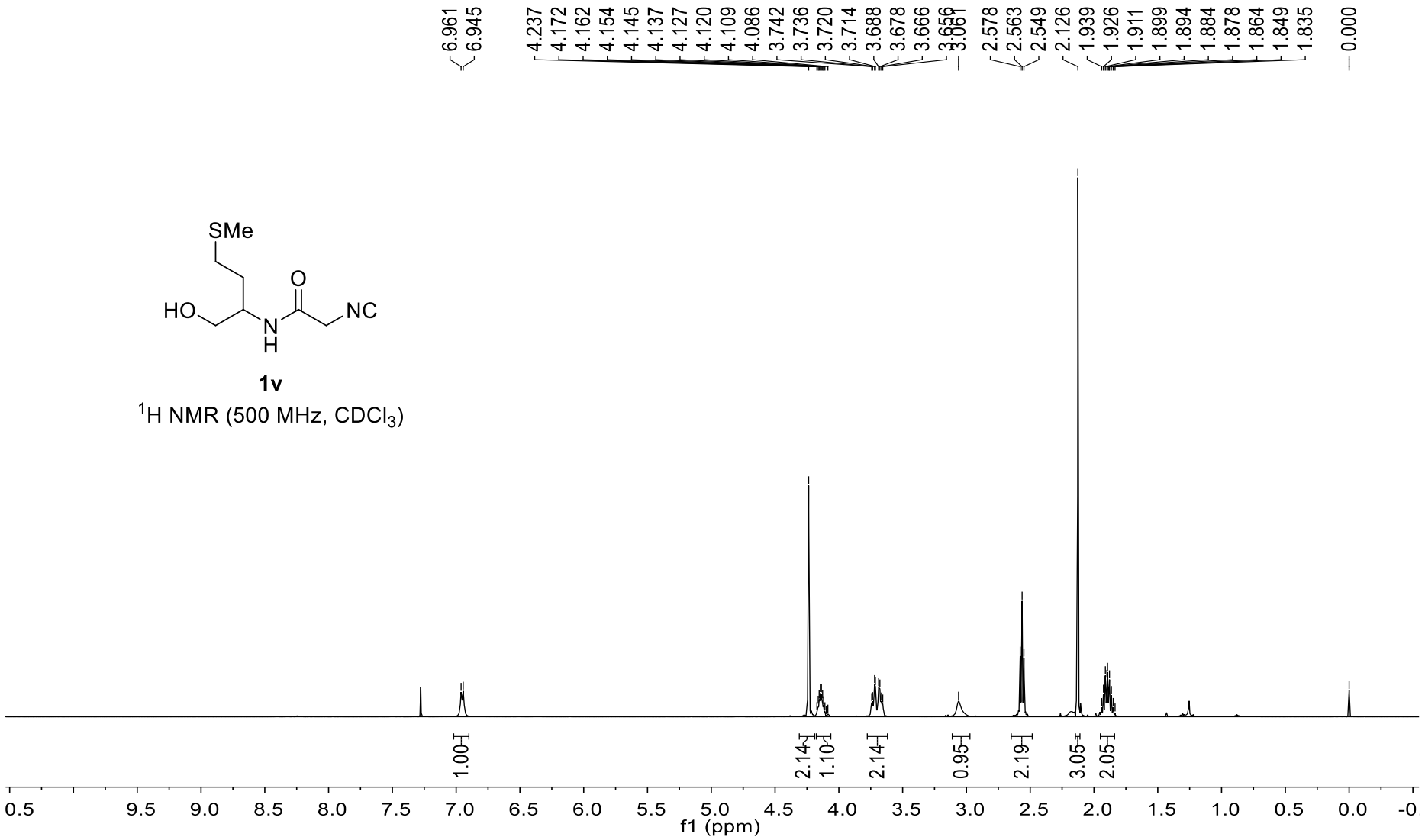

7.281
7.269
7.264
7.253
6.996
6.978
6.961
3.845
3.840
3.835
3.822
3.817
3.813
3.698
3.692
3.688
3.684
3.646
3.641
3.624
3.619
3.444
3.414
3.403
2.731
2.708
2.568
2.178
2.171
2.155
2.149
2.133
2.126
1.995
1.973
1.953
0.000
NC
N
O
F
1o
1H NMR (500 MHz, CDCl3)
2.00
1.97
1.04
2.01
3.96
1.03
1.01
1.02
1.06
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

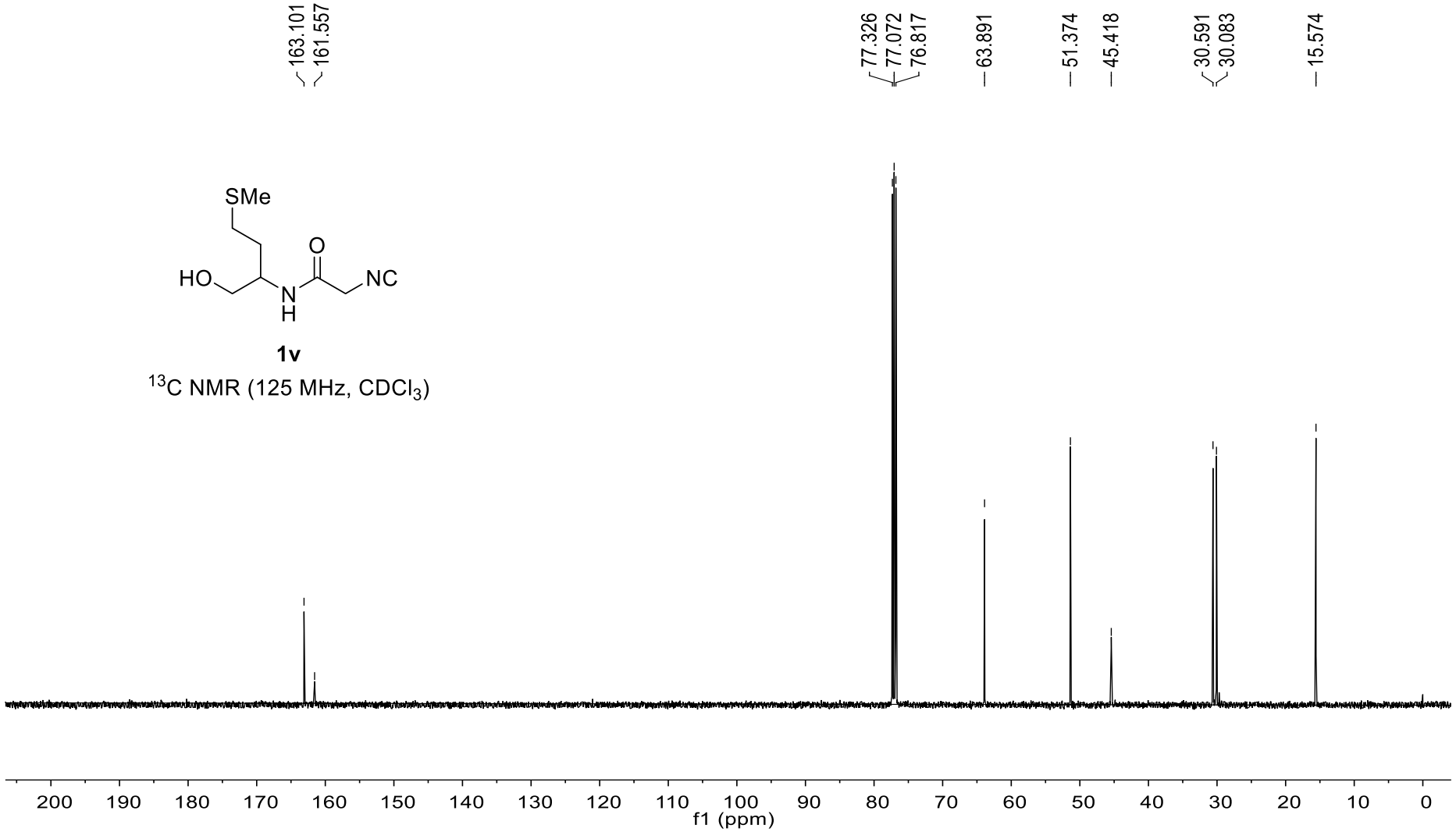

162.421
160.476
157.759
132.829
132.806
130.102
130.038
114.649
114.481
77.317
77.061
76.804
71.922
65.990
61.492
54.478
51.843
43.650
NC
N
O
F
1o
13C NMR (125 MHz, CDCl3)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

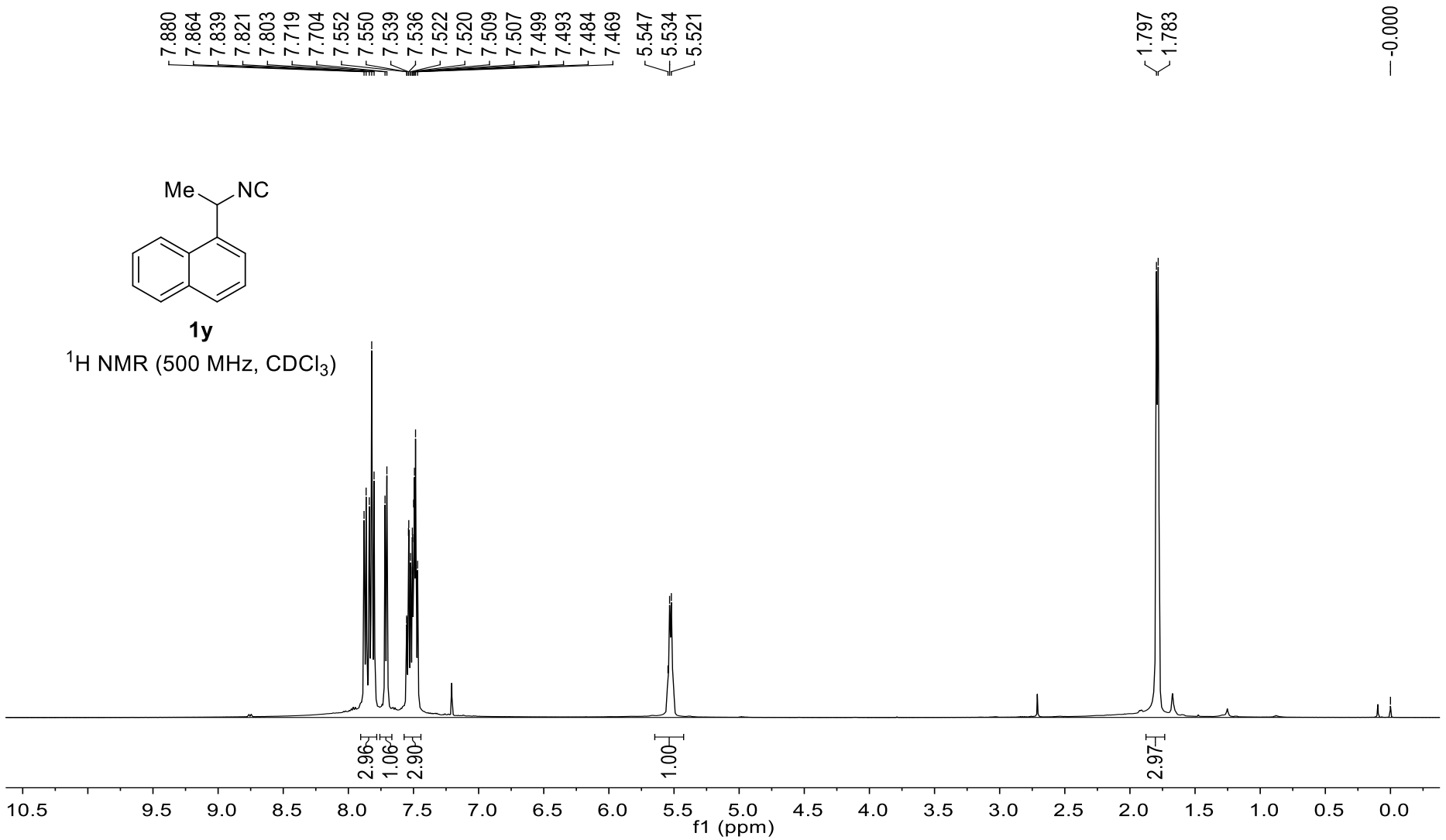


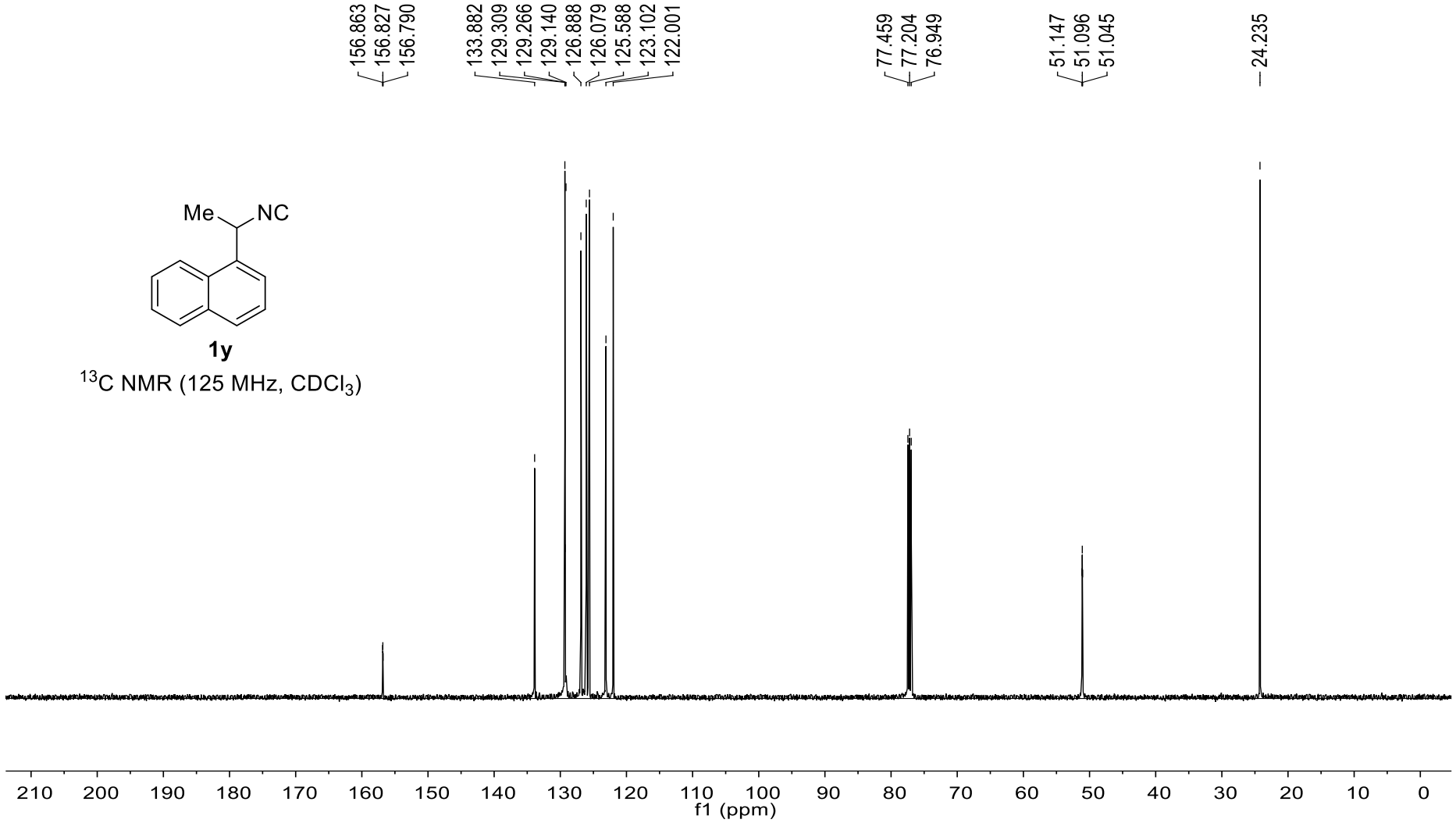
1o

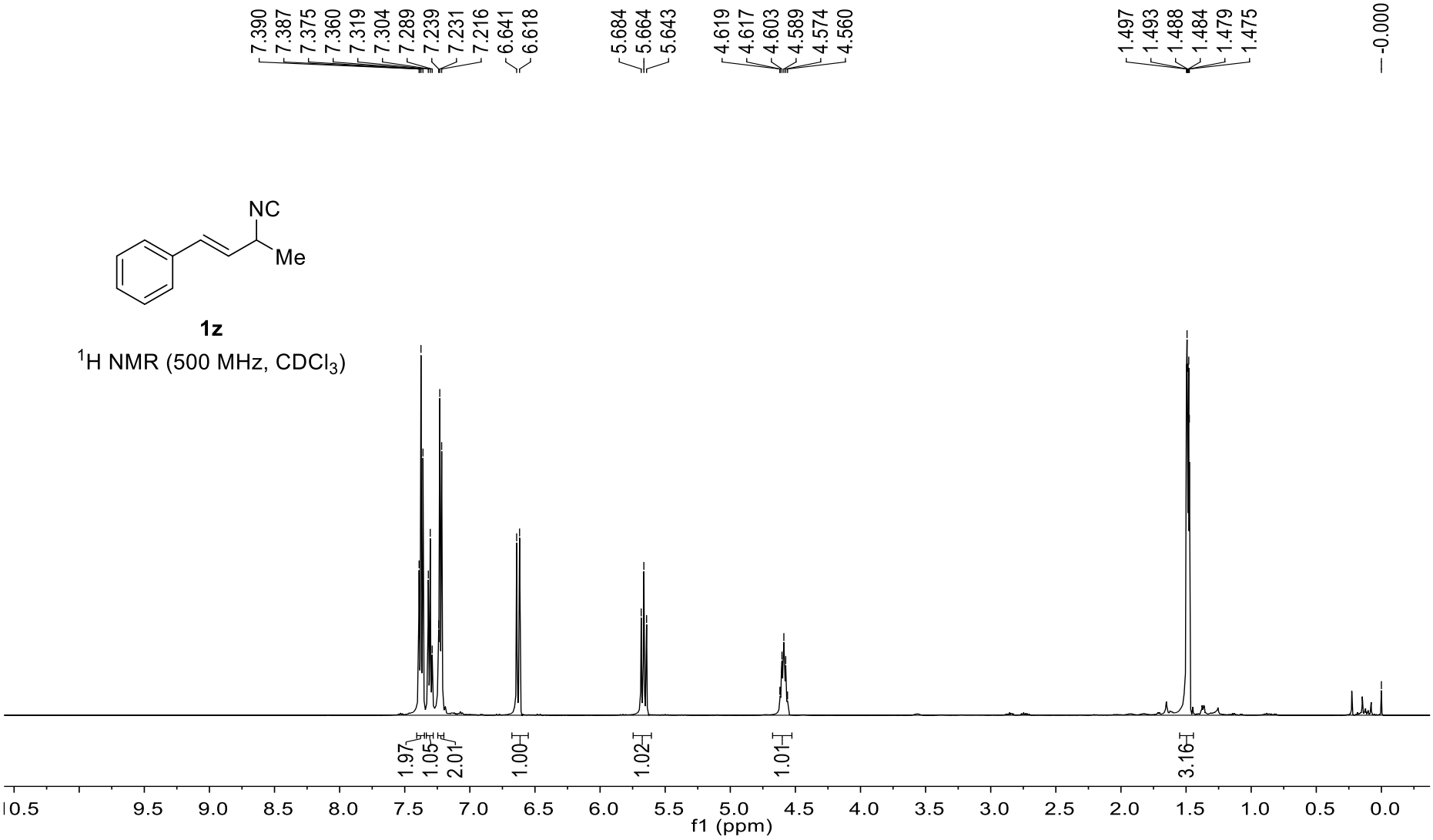
^{19}F NMR (471 MHz, $CDCl_3$)

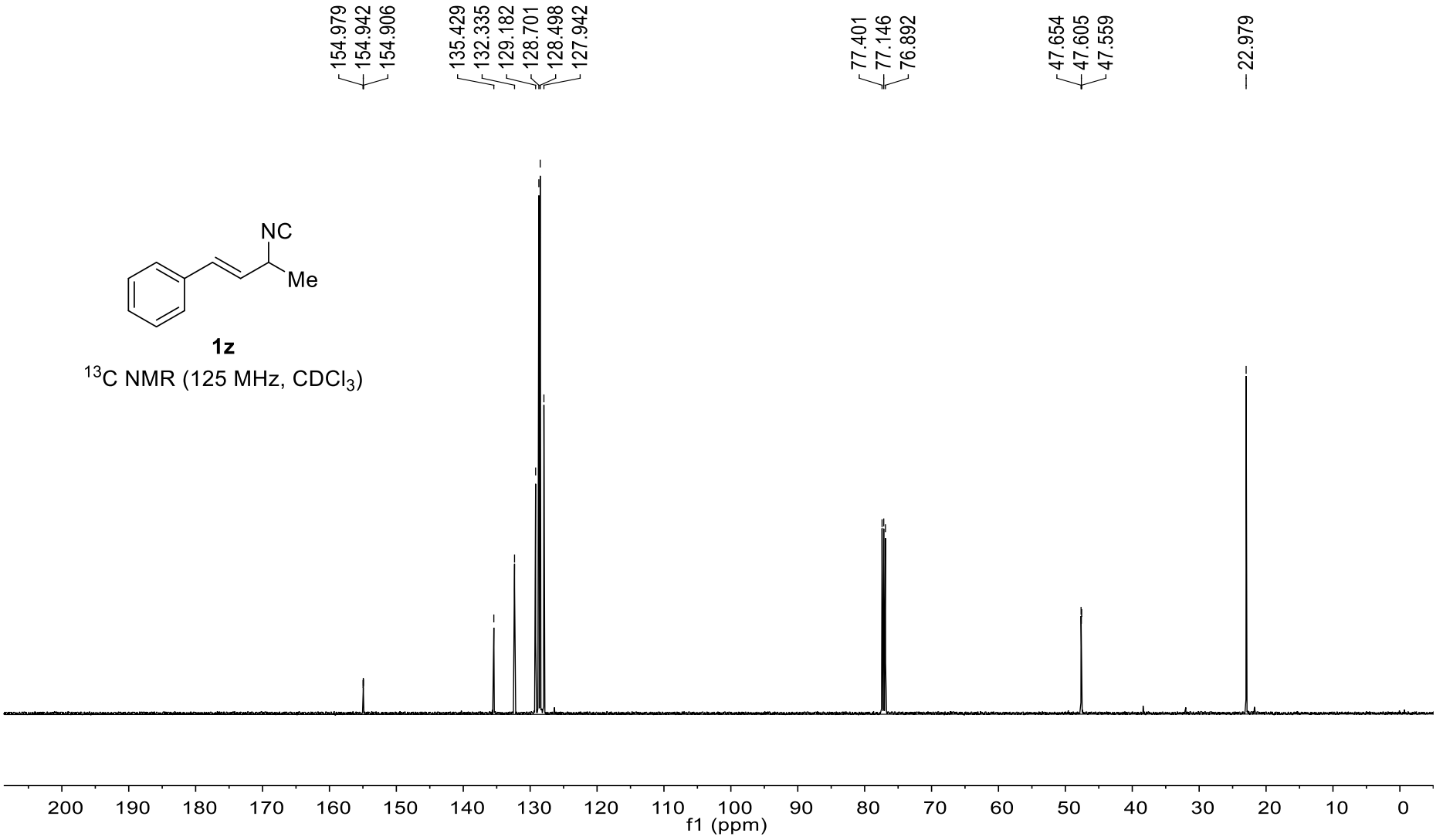

SMe
HO
N
H
O
NC
1v
1H NMR (500 MHz, CDCl3)
6.961
6.945
4.237
4.172
4.162
4.154
4.145
4.137
4.127
4.120
4.109
4.086
3.742
3.736
3.720
3.714
3.688
3.678
3.666
3.656
3.061
2.578
2.563
2.549
2.126
1.939
1.926
1.911
1.899
1.894
1.884
1.878
1.864
1.849
1.835
0.000
1.00
2.14
1.10
2.14
0.95
2.19
3.05
2.05
f1 (ppm)

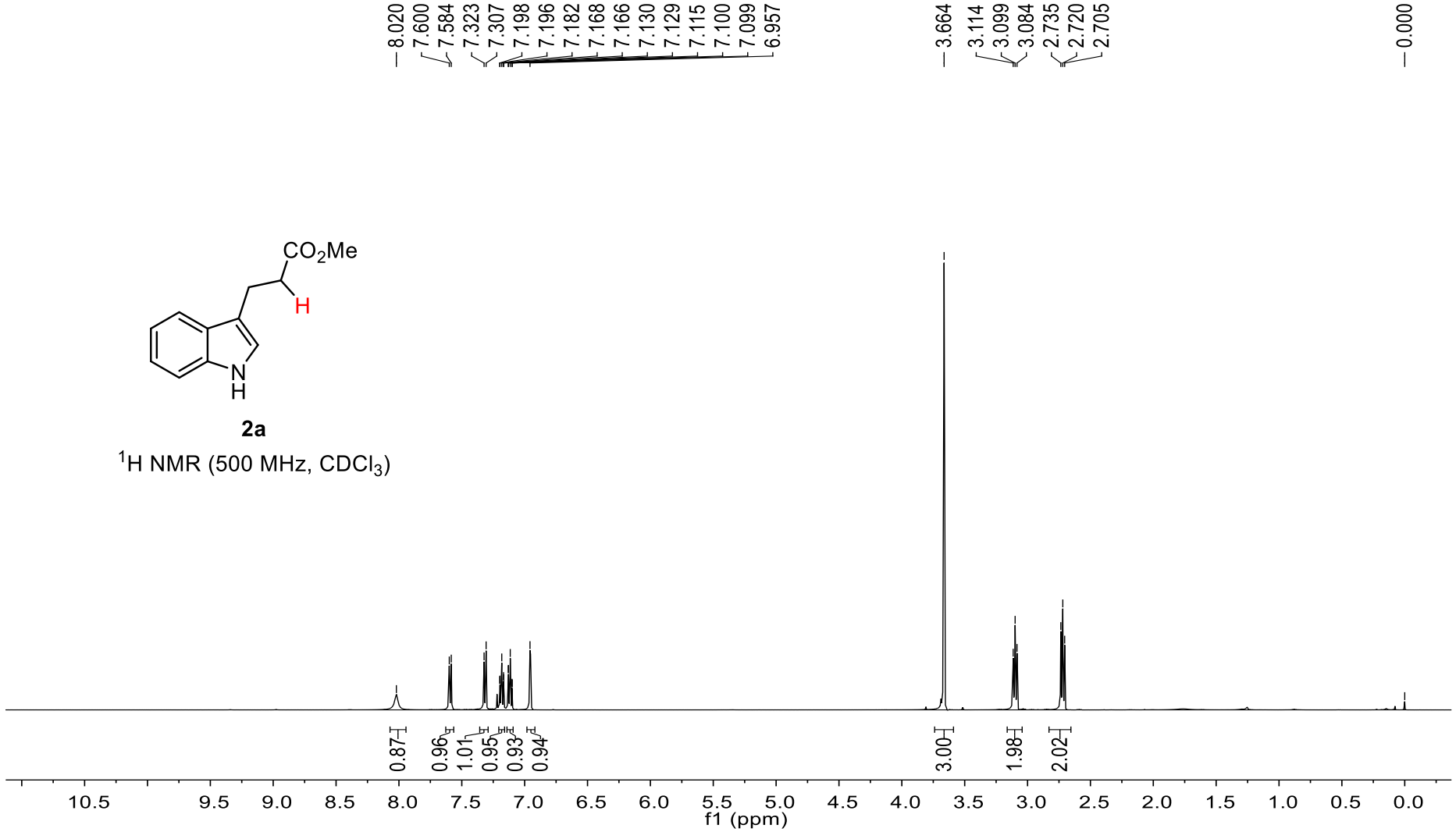

163.101
161.557
77.326
77.072
76.817
63.891
51.374
45.418
30.591
30.083
15.574
SMe
O
HO
N
H
NC
1v
13C NMR (125 MHz, CDCl3)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


7.880
7.864
7.839
7.821
7.803
7.719
7.704
7.552
7.550
7.539
7.536
7.522
7.520
7.509
7.507
7.499
7.493
7.484
7.469
5.547
5.534
5.521
1.797
1.783
-0.000
Me
NC
1y
1H NMR (500 MHz, CDCl3)
2.96
1.06
2.90
1.00
2.97
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


156.863
156.827
156.790
133.882
129.309
129.266
129.140
126.888
126.079
125.588
123.102
122.001
77.459
77.204
76.949
51.147
51.096
51.045
24.235
Me
NC
1y
13C NMR (125 MHz, CDCl3)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

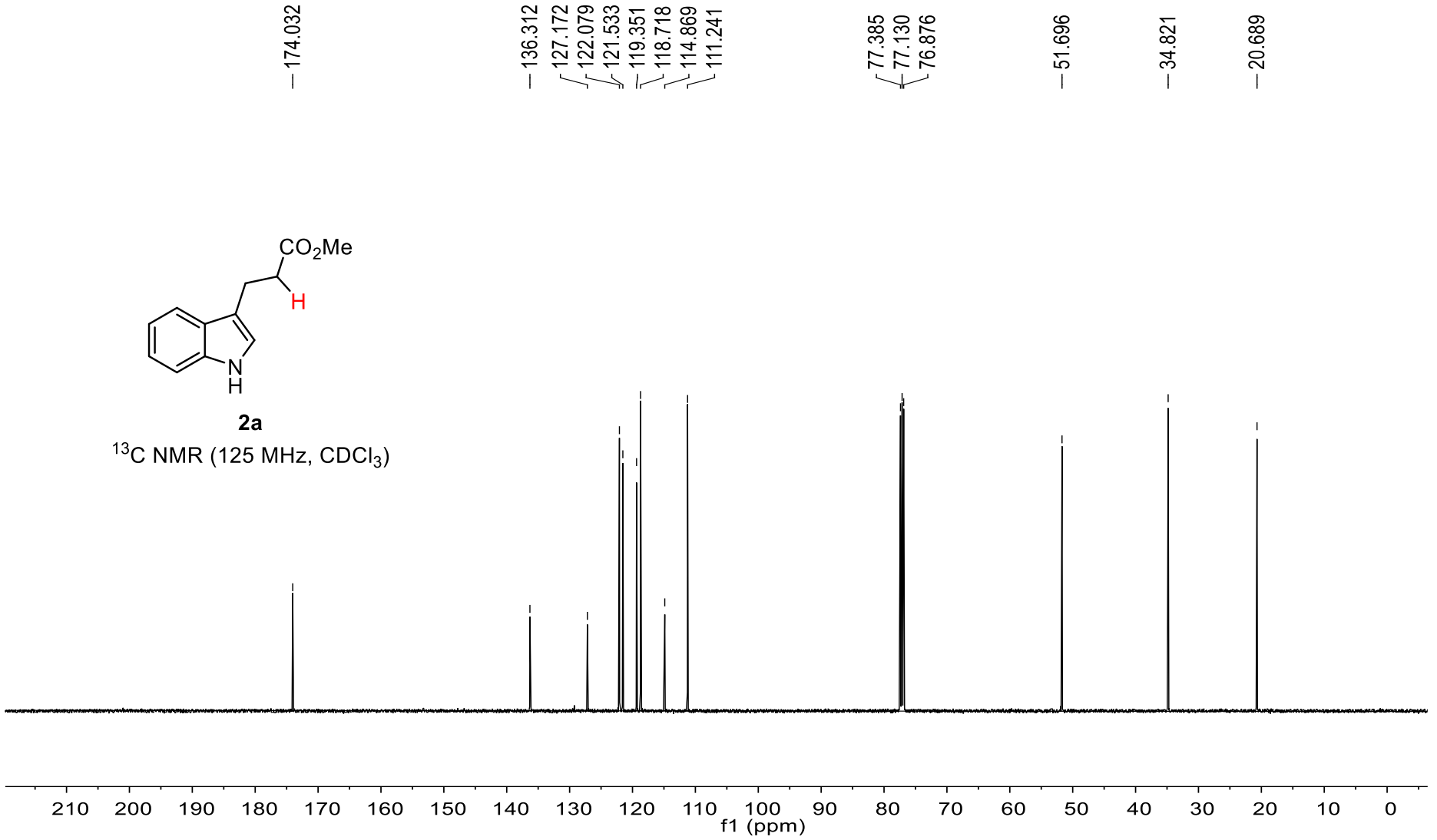

7.390
7.387
7.375
7.360
7.319
7.304
7.289
7.239
7.231
7.216
6.641
6.618
5.684
5.664
5.643
4.619
4.617
4.603
4.589
4.574
4.560
1.497
1.493
1.488
1.484
1.479
1.475
-0.000
NC
Me
1z
1H NMR (500 MHz, CDCl3)
1.97
1.05
2.01
1.00
1.02
1.01
3.16
f1 (ppm)

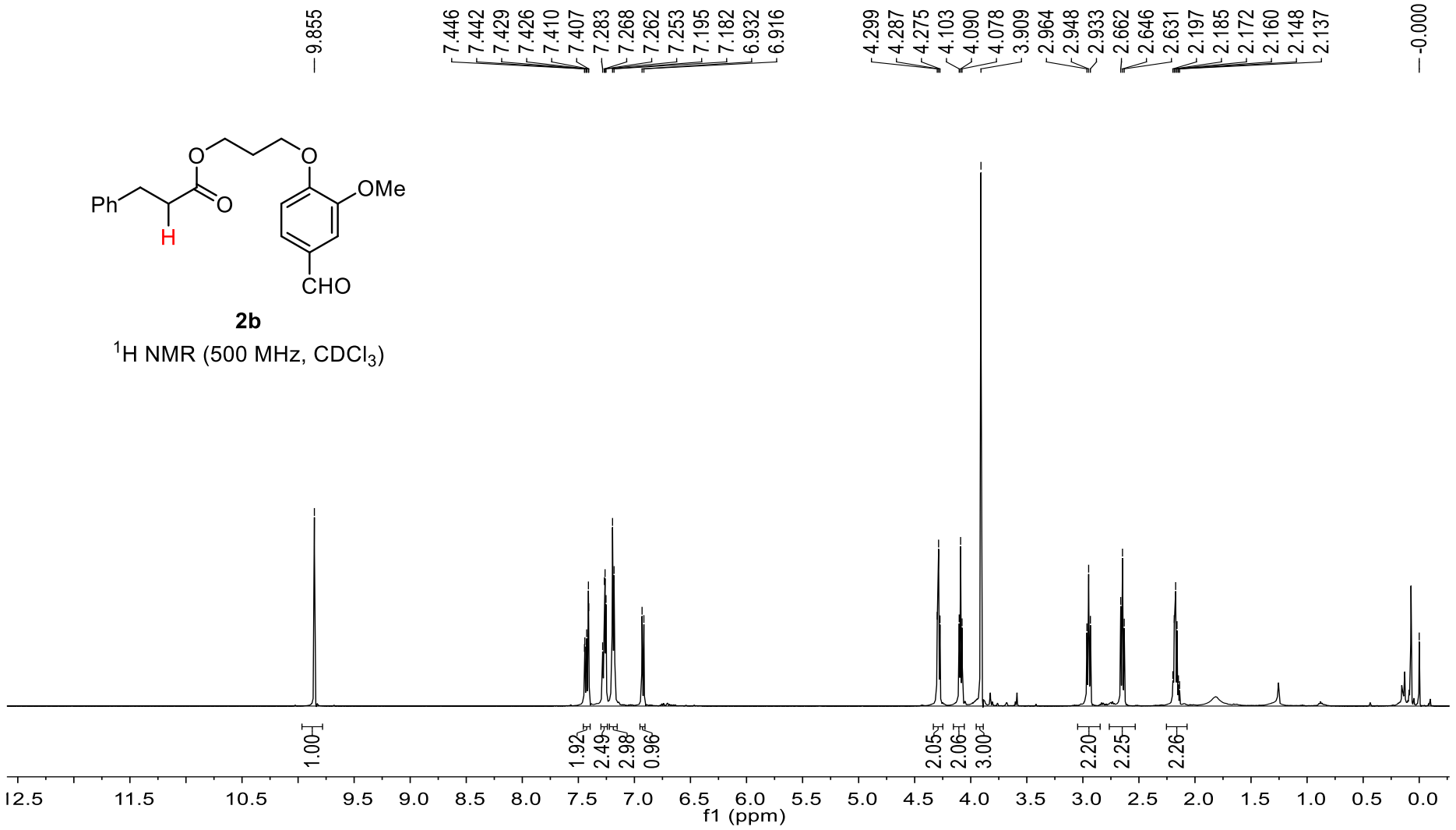

154.979
154.942
154.906
135.429
132.335
129.182
128.701
128.498
127.942
77.401
77.146
76.892
47.654
47.605
47.559
22.979
NC
Me
1z
13C NMR (125 MHz, CDCl3)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

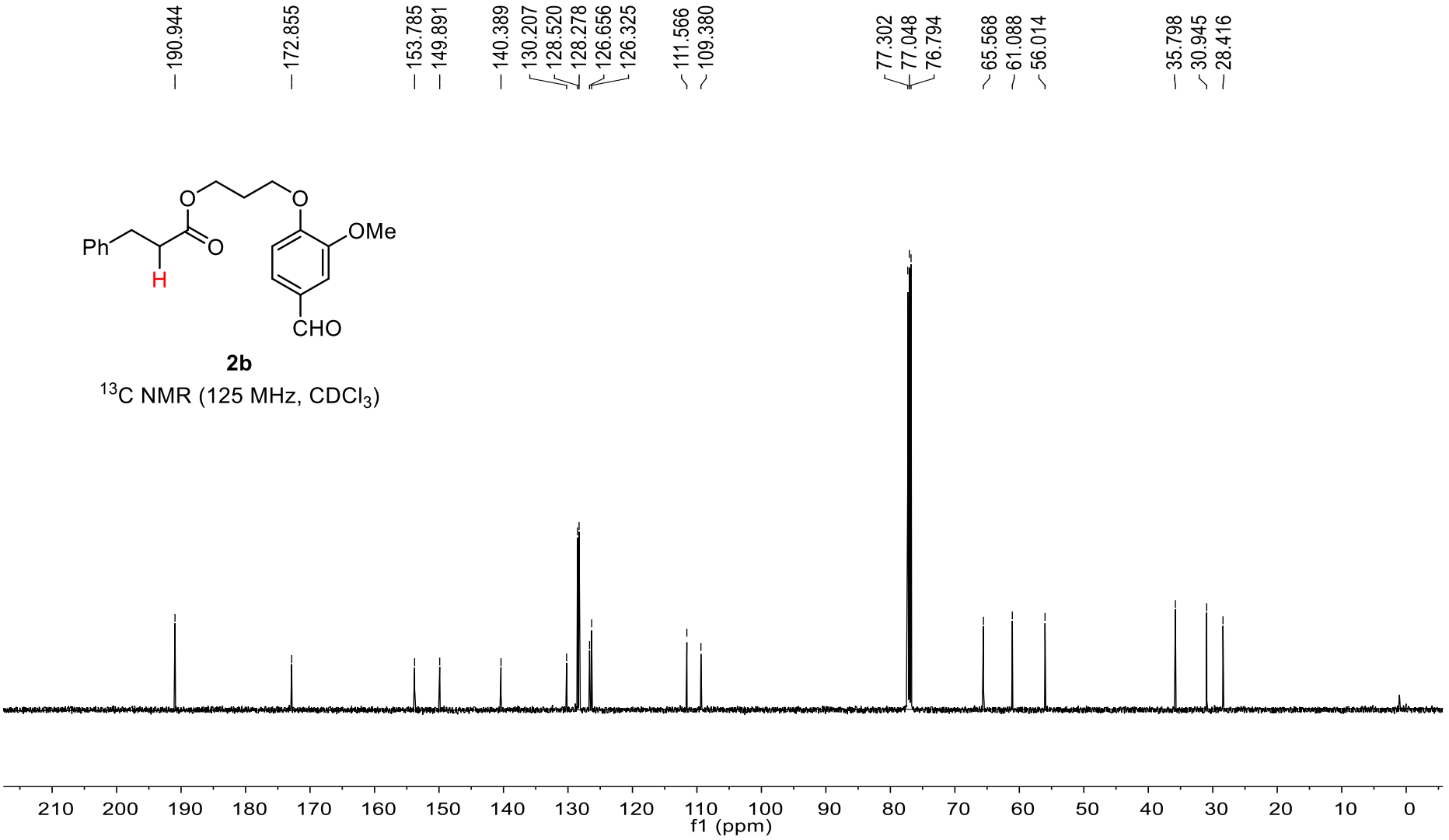


2a

^{1}H NMR (500 MHz, $CDCl_3$)

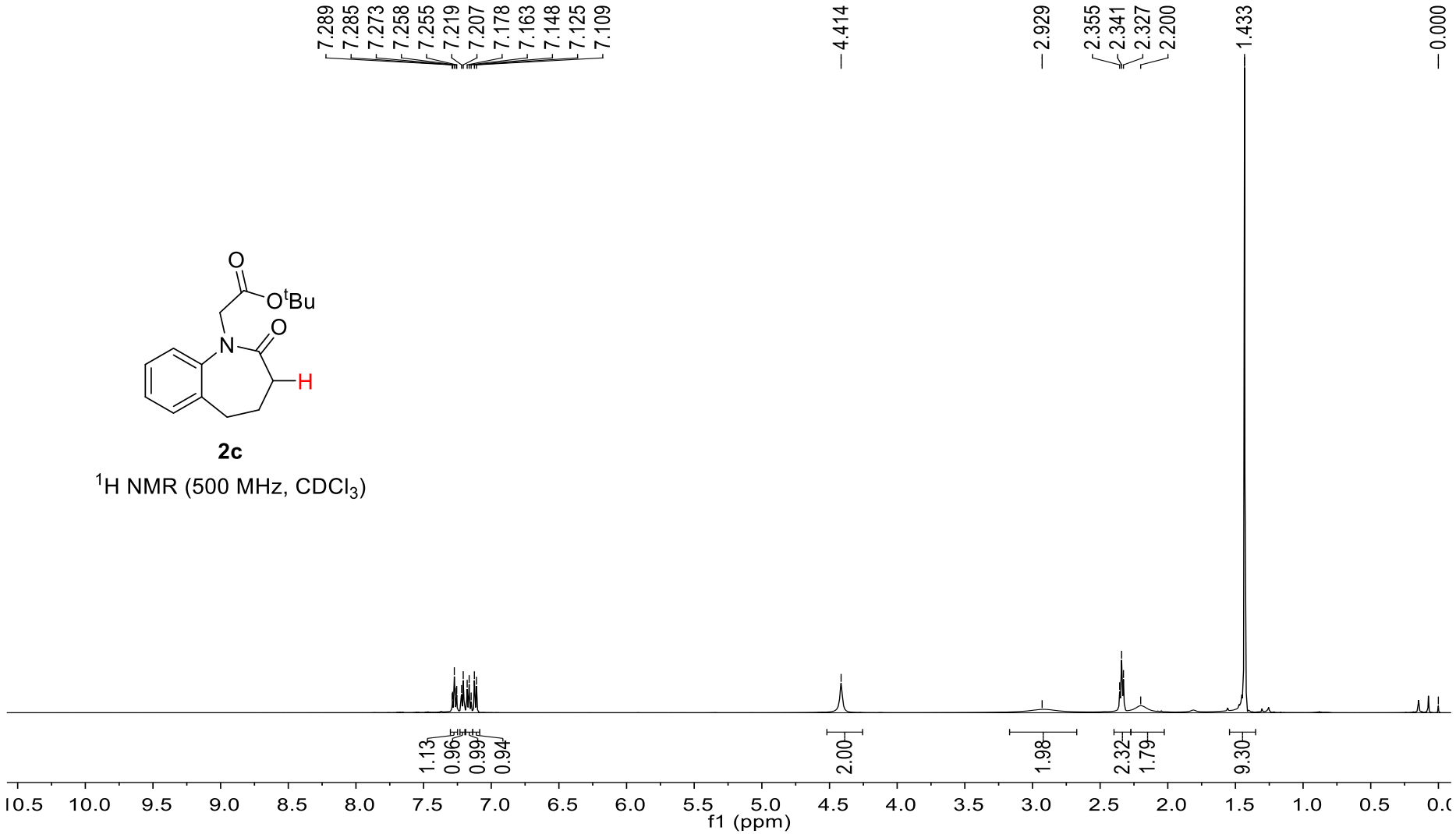

174.032
136.312
127.172
122.079
121.533
119.351
118.718
114.869
111.241
77.385
77.130
76.876
51.696
34.821
20.689
CO2Me
H
N
H
2a
13C NMR (125 MHz, CDCl3)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


9.855
7.446
7.442
7.429
7.426
7.410
7.407
7.283
7.268
7.262
7.253
7.195
7.182
6.932
6.916
4.299
4.287
4.275
4.103
4.090
4.078
3.909
2.964
2.948
2.933
2.662
2.646
2.631
2.197
2.185
2.172
2.160
2.148
2.137
-0.000
O
O
O
Ph
H
OMe
CHO
2b
1H NMR (500 MHz, CDCl3)
1.00
1.92
2.49
2.98
0.96
2.05
2.06
3.00
2.20
2.25
2.26
12.5
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)



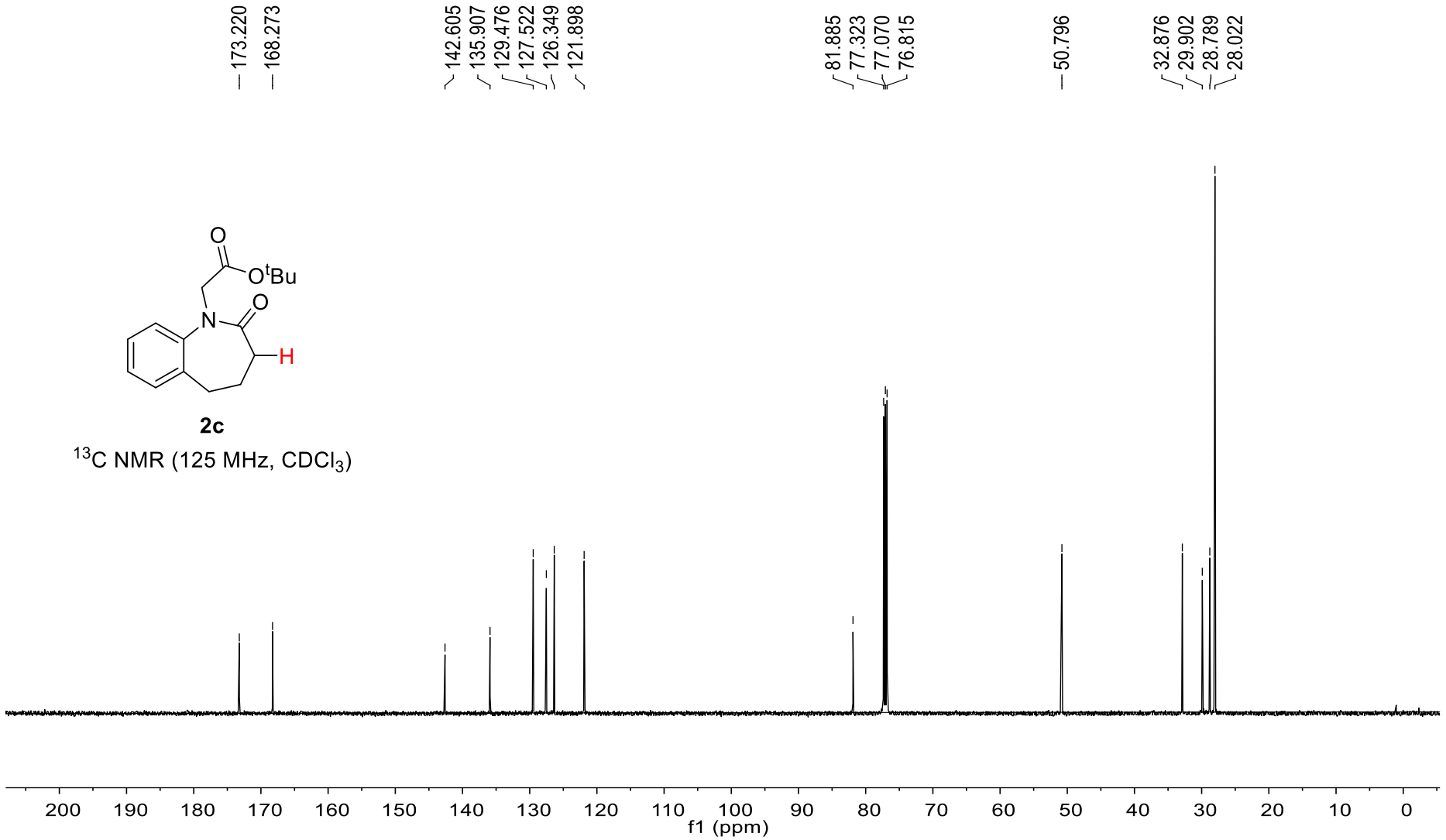
2b

^{13}C NMR (125 MHz, $CDCl_3$)



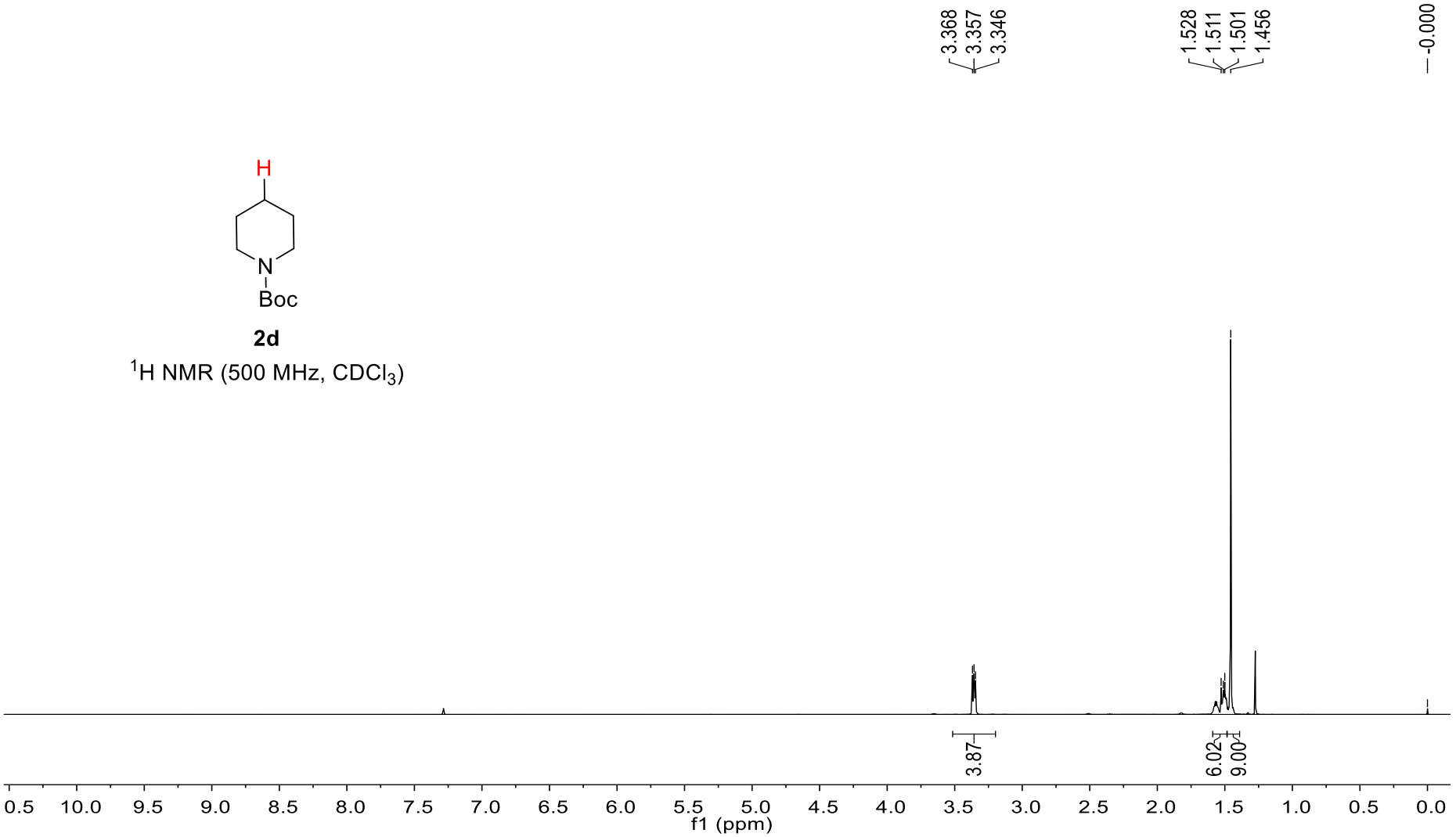
2c

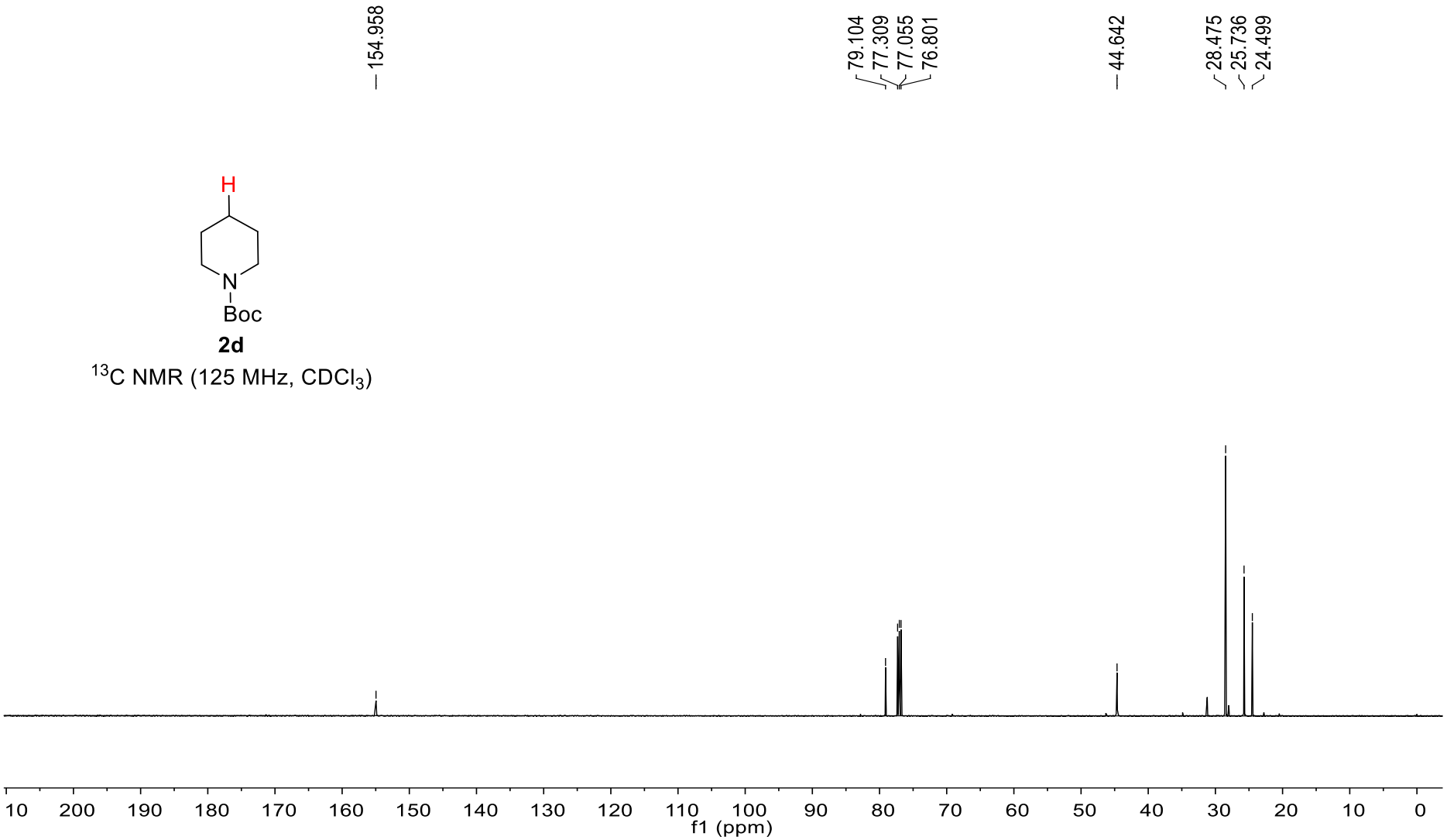
^{1}H NMR (500 MHz, $CDCl_3$)

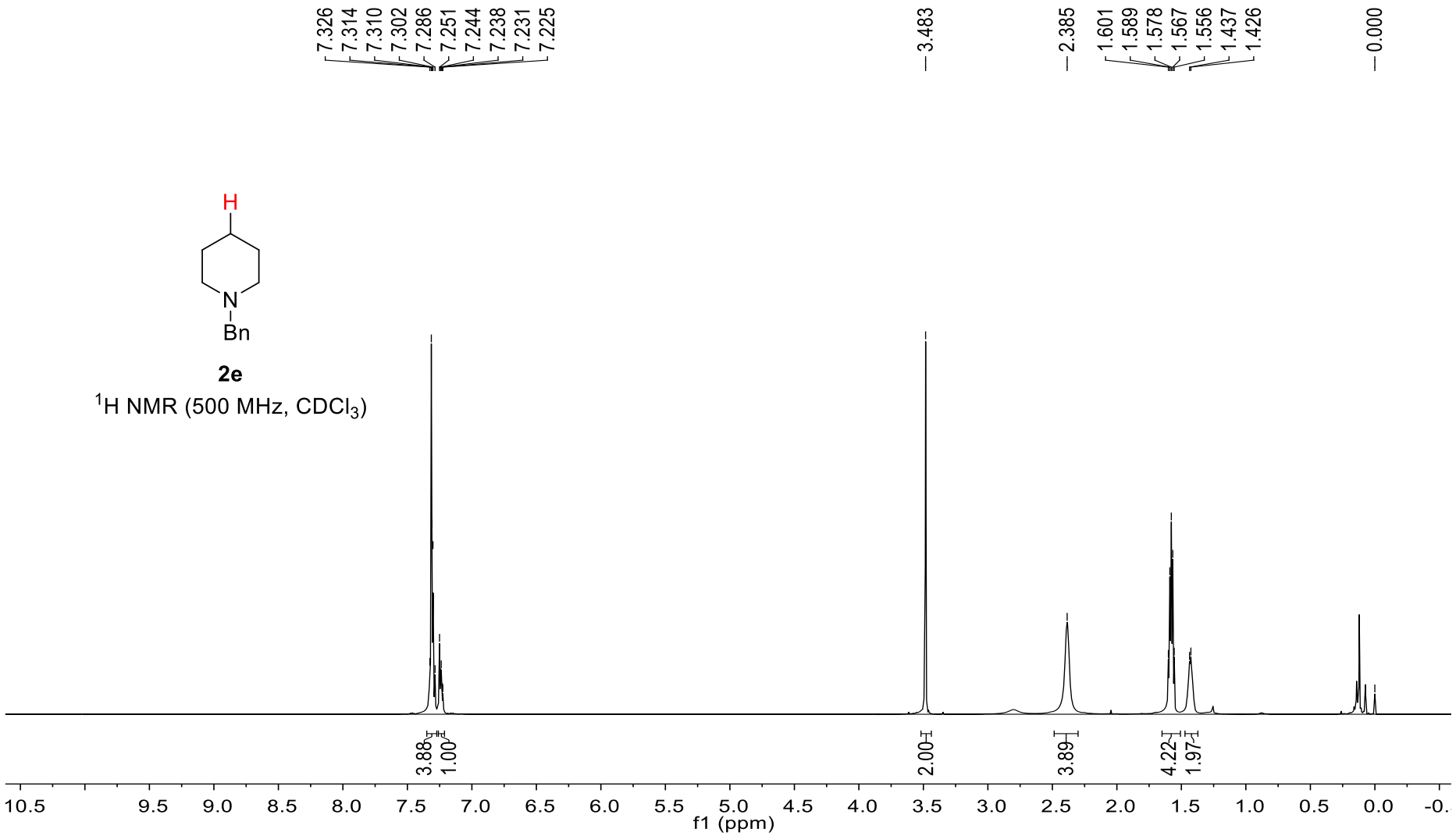


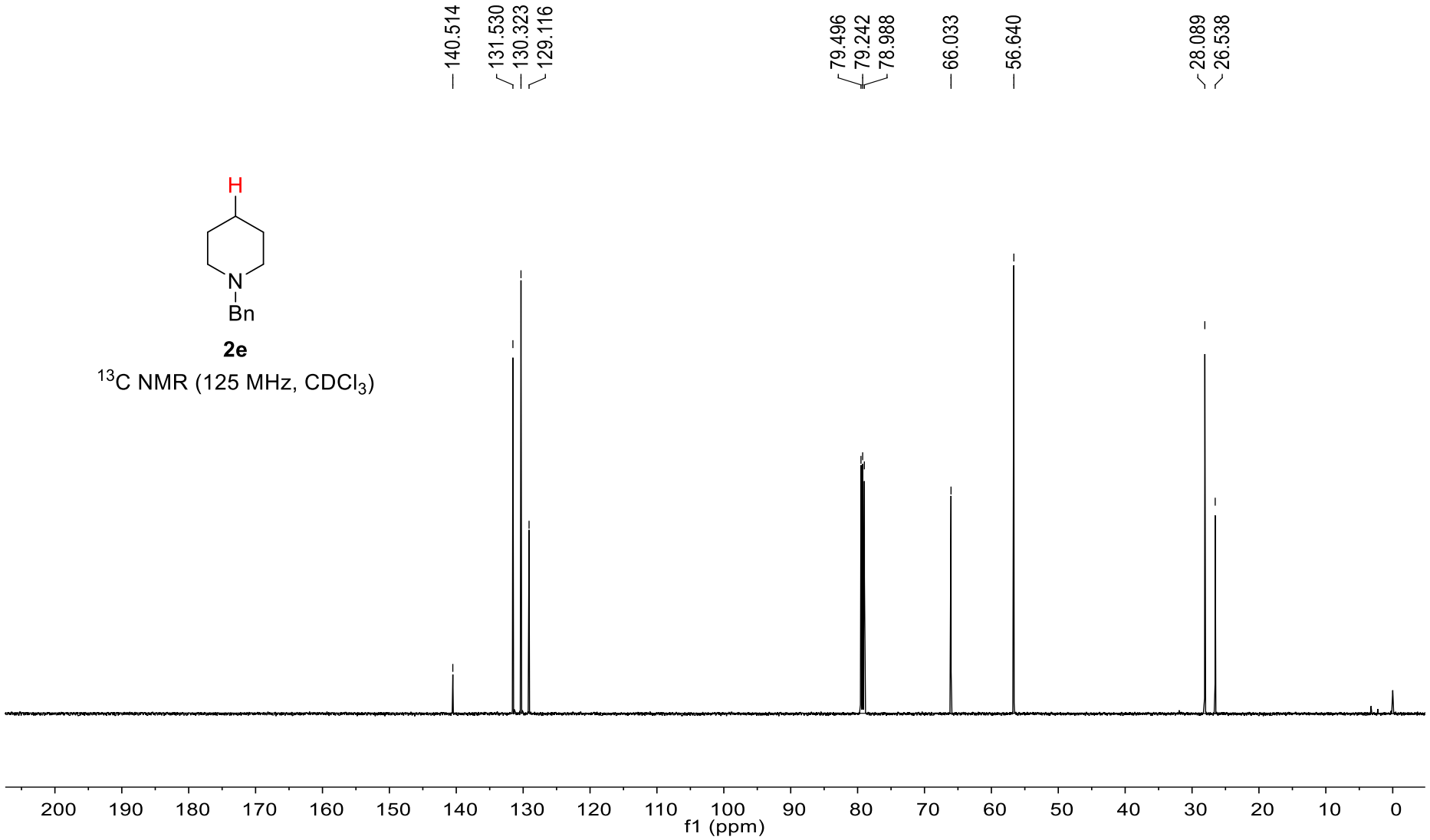
2c

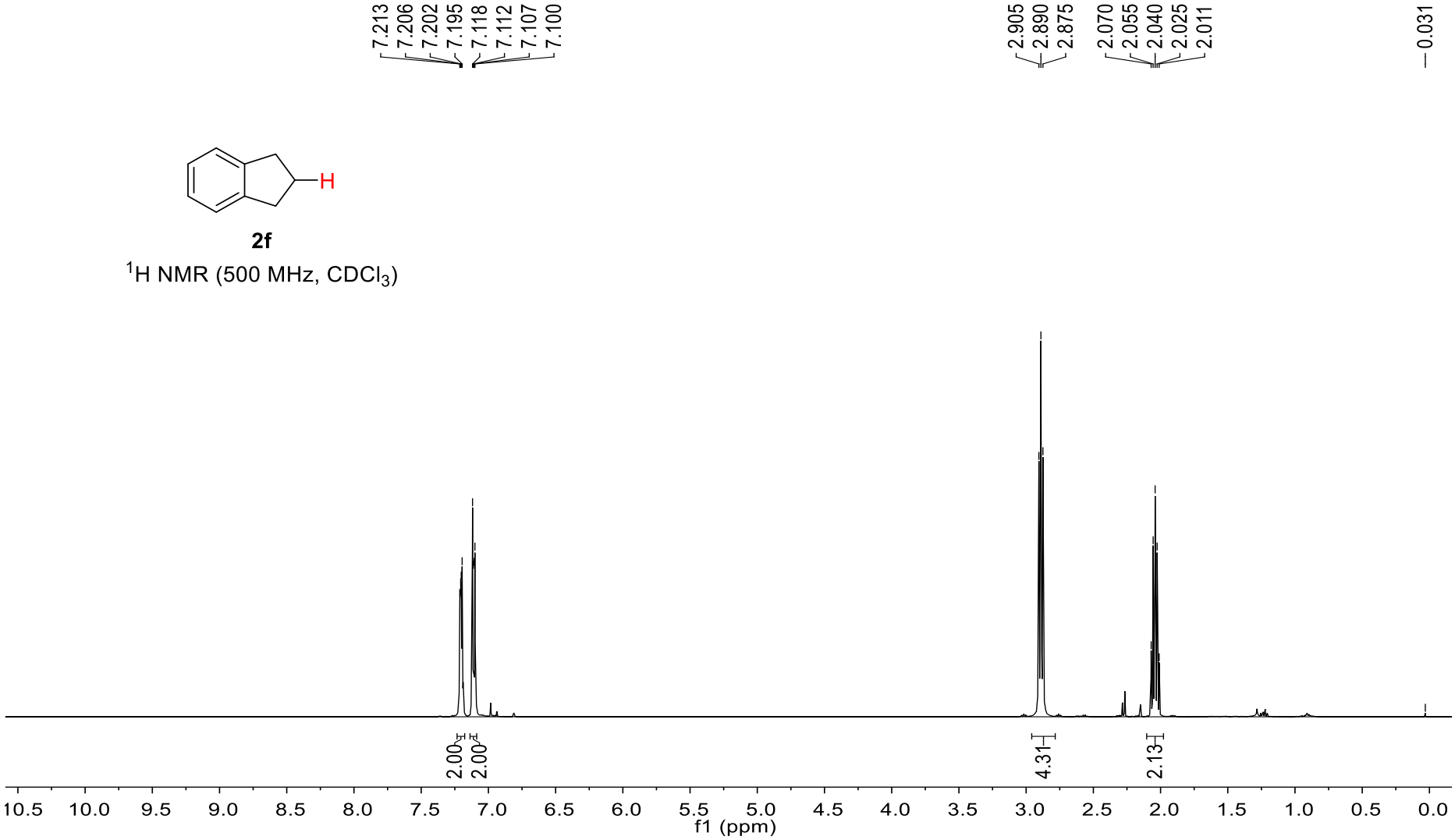
^{13}C NMR (125 MHz, $CDCl_3$)

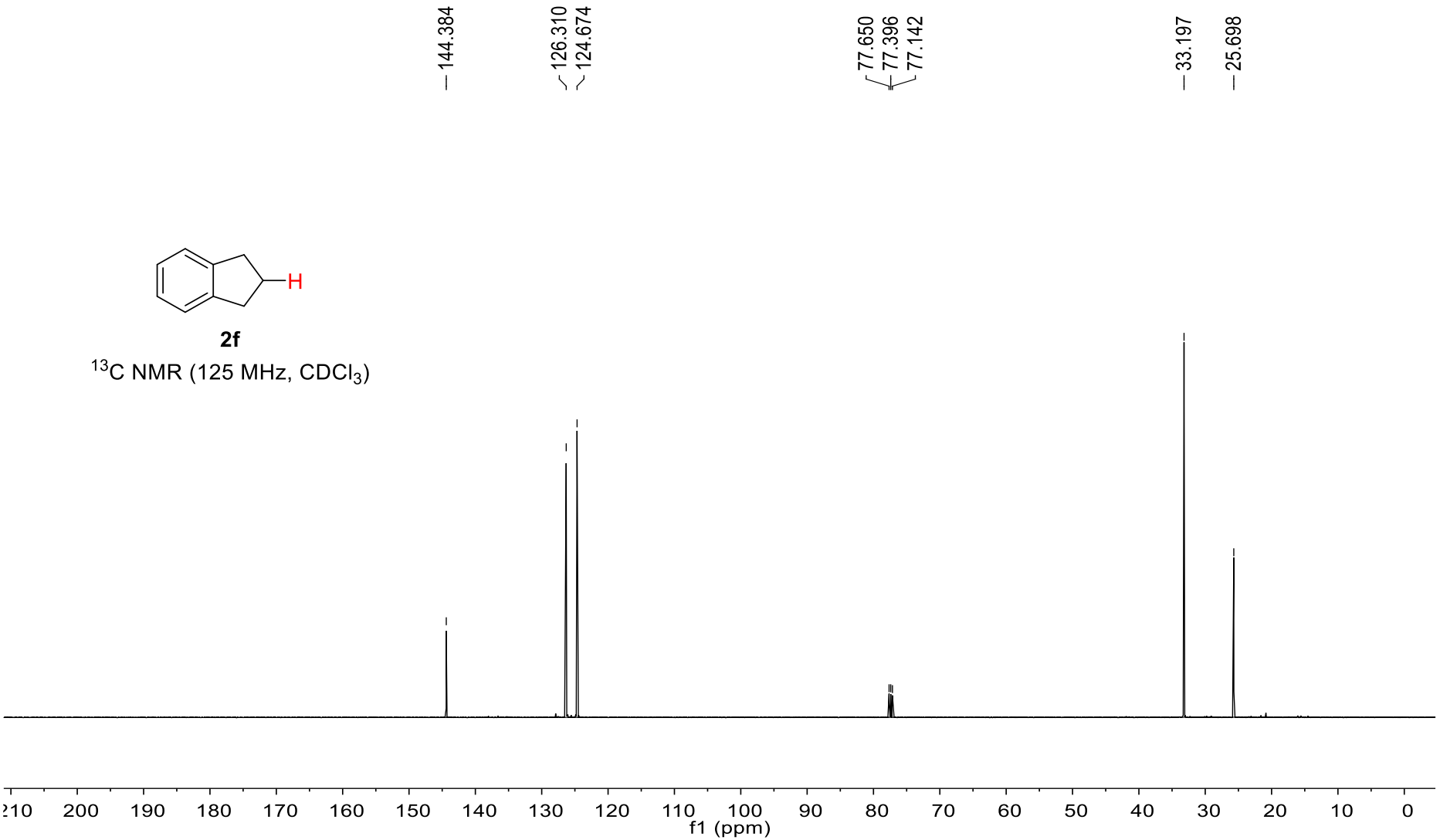

H
N
Boc
2d
1H NMR (500 MHz, CDCl3)
3.368
3.357
3.346
1.528
1.511
1.501
1.456
-0.000
3.87
6.02
9.00
0.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

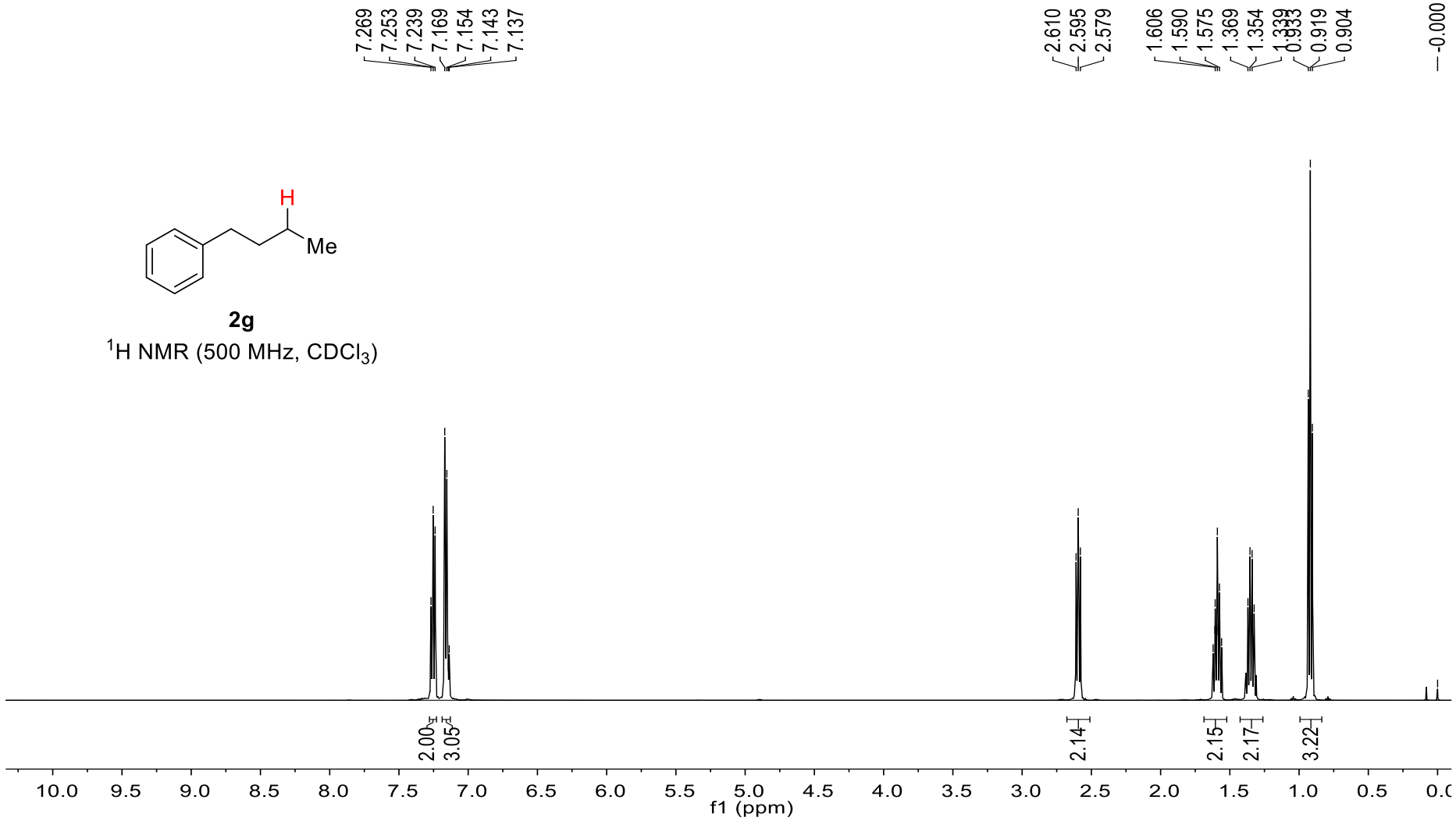

154.958
79.104
77.309
77.055
76.801
44.642
28.475
25.736
24.499
H
N
Boc
2d
13C NMR (125 MHz, CDCl3)
10 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

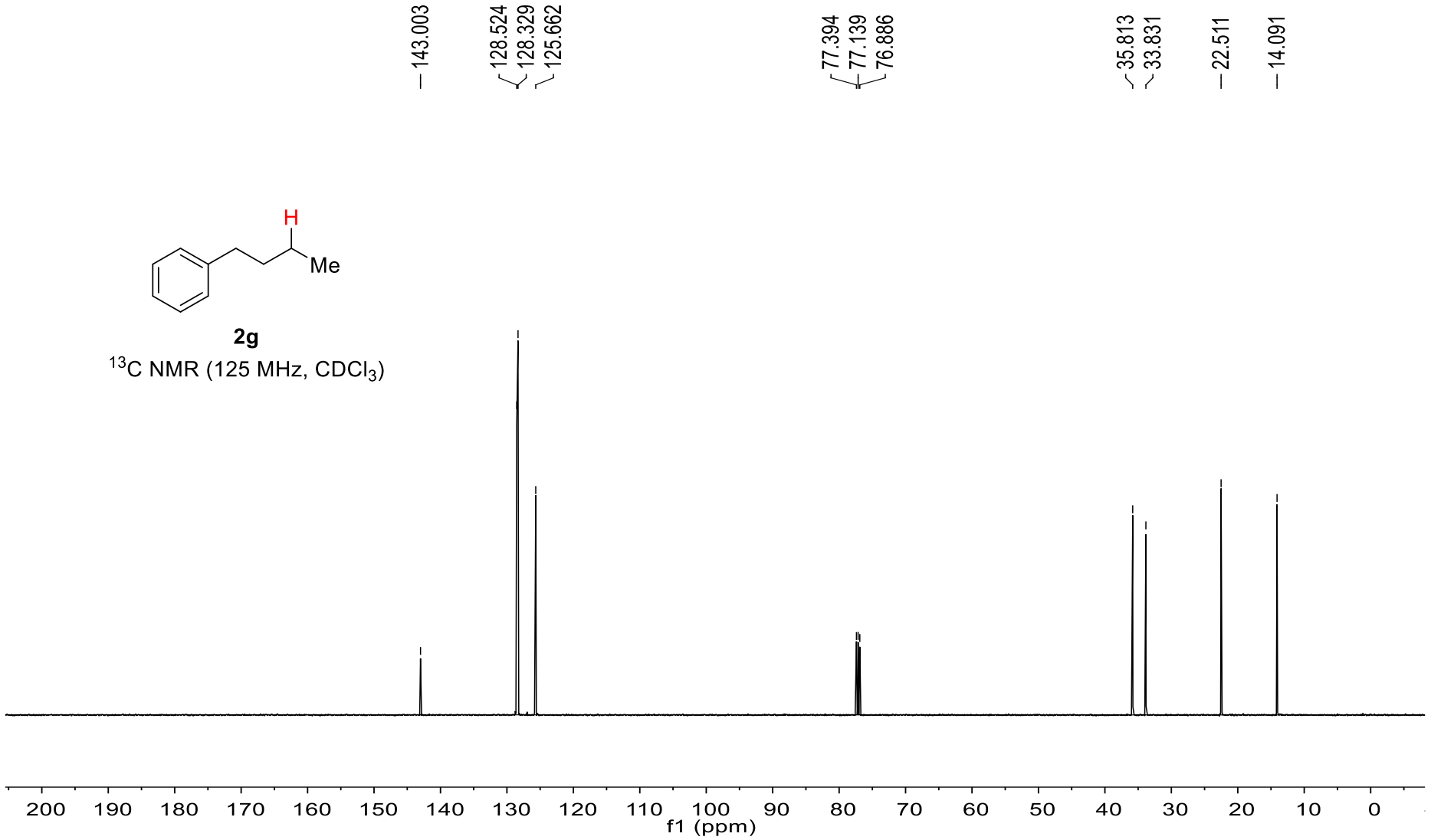

7.326
7.314
7.310
7.302
7.286
7.251
7.244
7.238
7.231
7.225
3.483
2.385
1.601
1.589
1.578
1.567
1.556
1.437
1.426
0.000
H
N
Bn
2e
1H NMR (500 MHz, CDCl3)
3.88
1.00
2.00
3.89
4.22
1.97
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

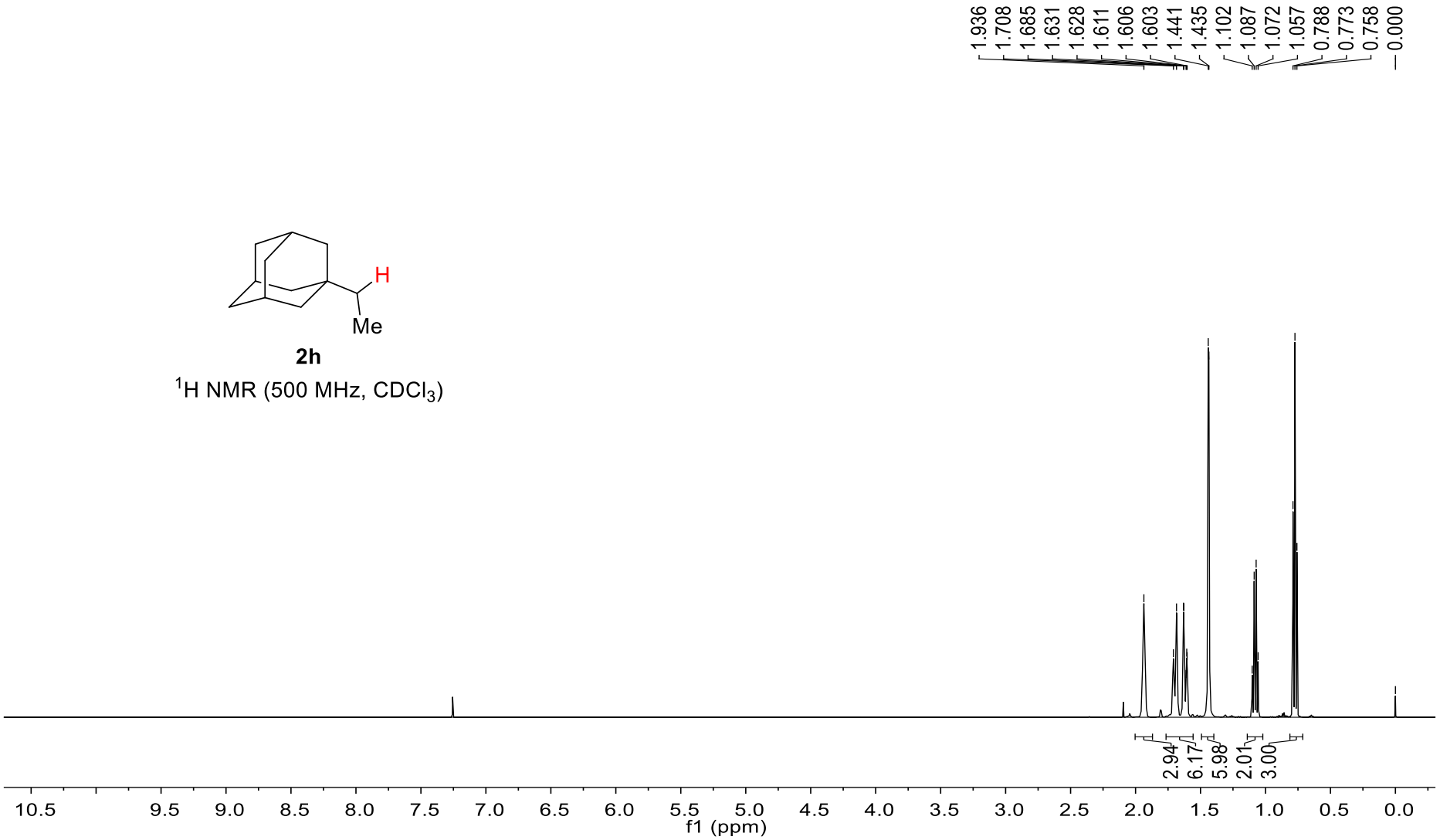

140.514
131.530
130.323
129.116
79.496
79.242
78.988
66.033
56.640
28.089
26.538
H
N
Bn
2e
13C NMR (125 MHz, CDCl3)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

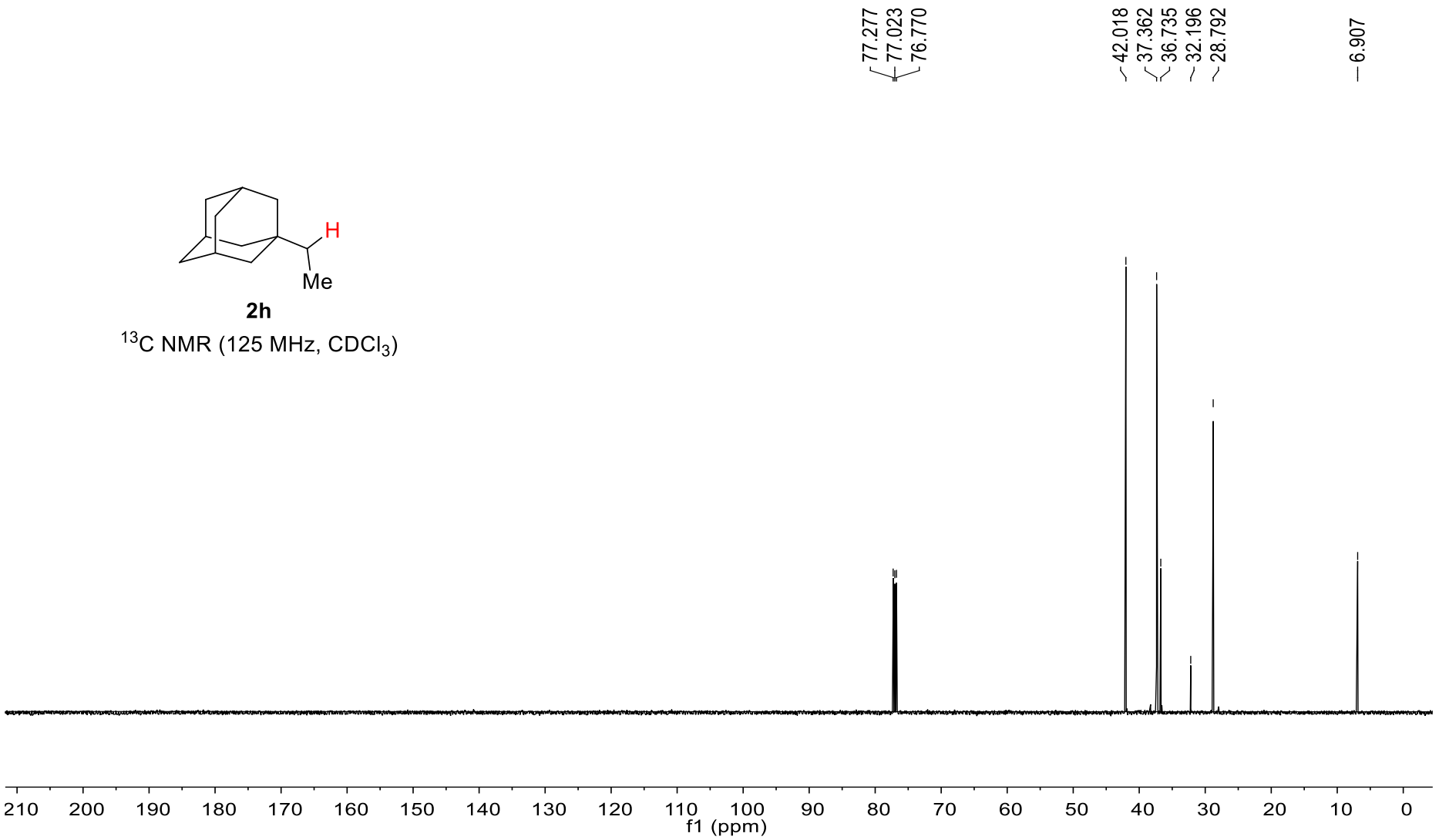

7.213
7.206
7.202
7.195
7.118
7.112
7.107
7.100
2.905
2.890
2.875
2.070
2.055
2.040
2.025
2.011
0.031
H
2f
1H NMR (500 MHz, CDCl3)
2.00
2.00
4.31
2.13
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

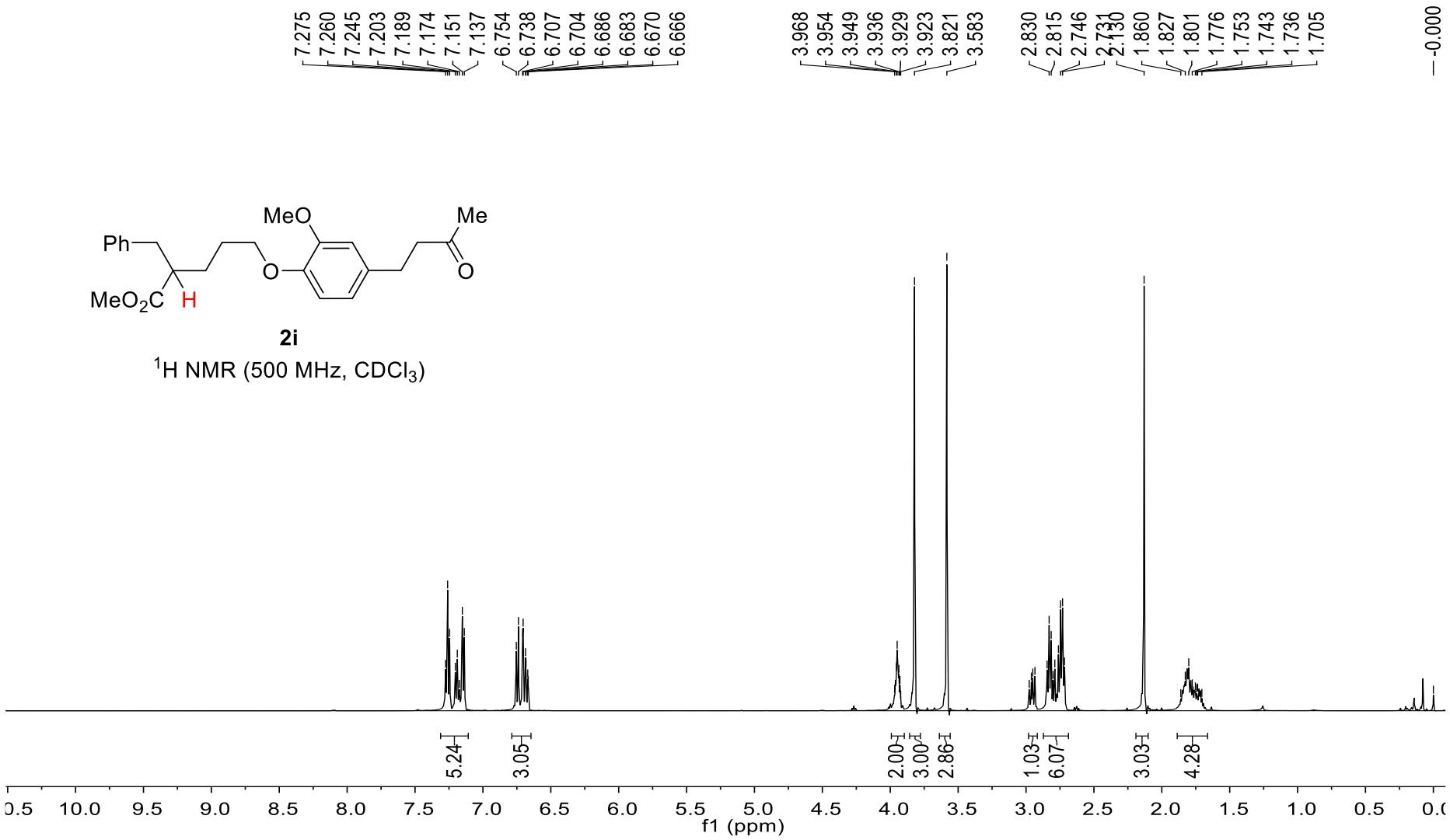

144.384
126.310
124.674
77.650
77.396
77.142
33.197
25.698
H
2f
13C NMR (125 MHz, CDCl3)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

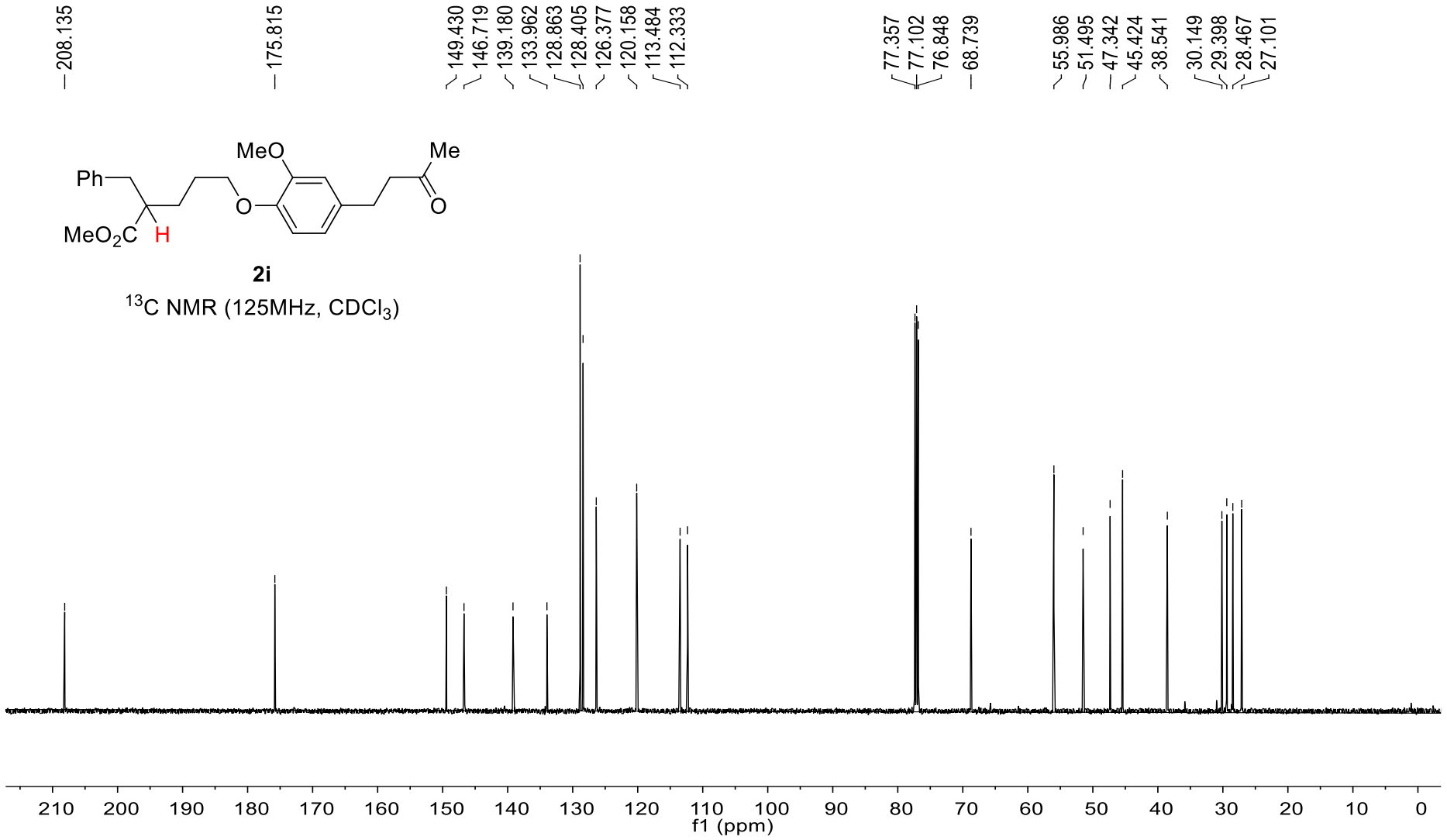

7.269
7.253
7.239
7.169
7.154
7.143
7.137
2.610
2.595
2.579
1.606
1.590
1.575
1.369
1.354
1.339
0.933
0.919
0.904
-0.000
H
Me
2g
1H NMR (500 MHz, CDCl3)
2.00
3.05
2.14
2.15
2.17
3.22
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

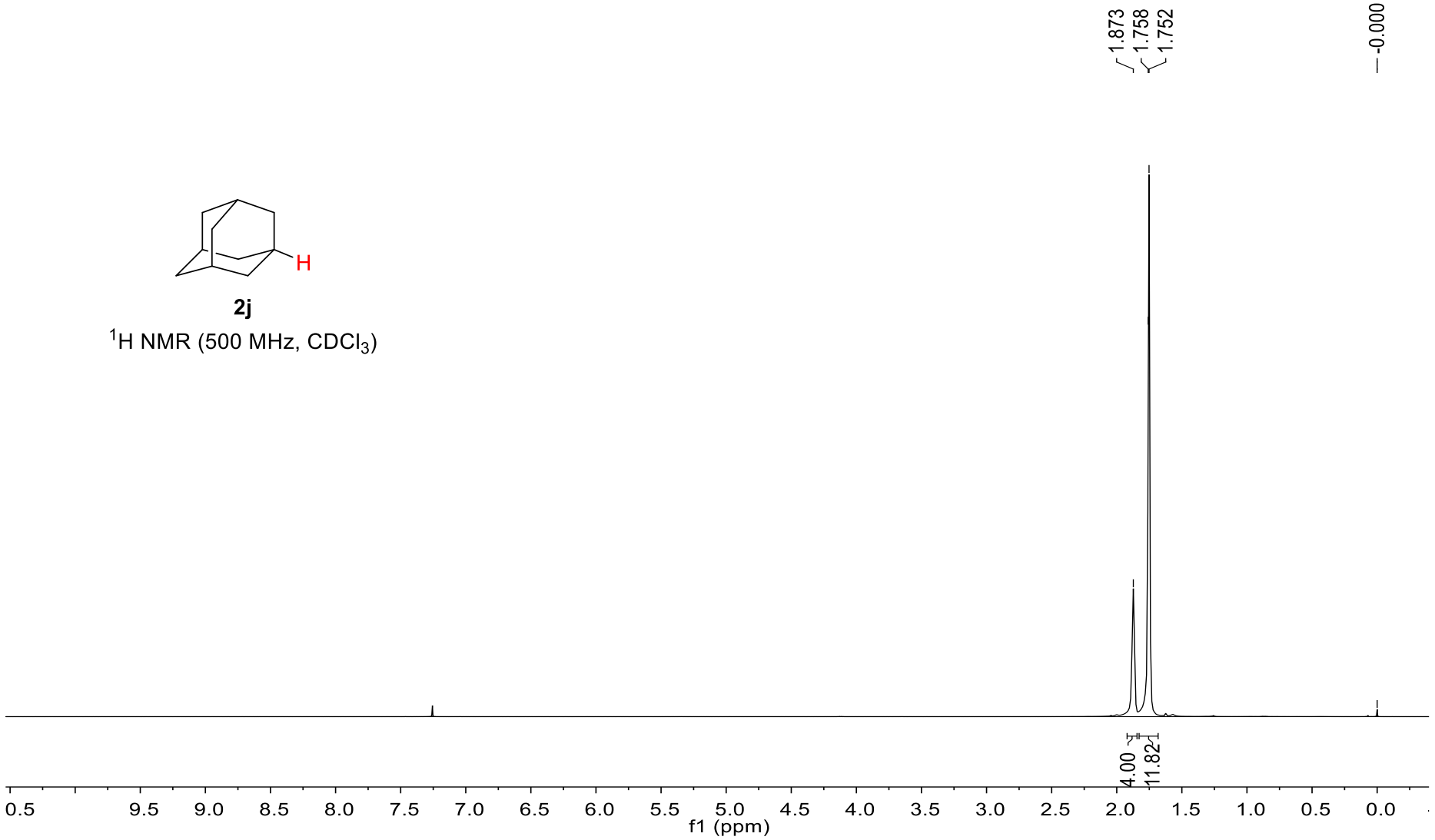

143.003
128.524
128.329
125.662
77.394
77.139
76.886
35.813
33.831
22.511
14.091
H
Me
2g
13C NMR (125 MHz, CDCl3)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

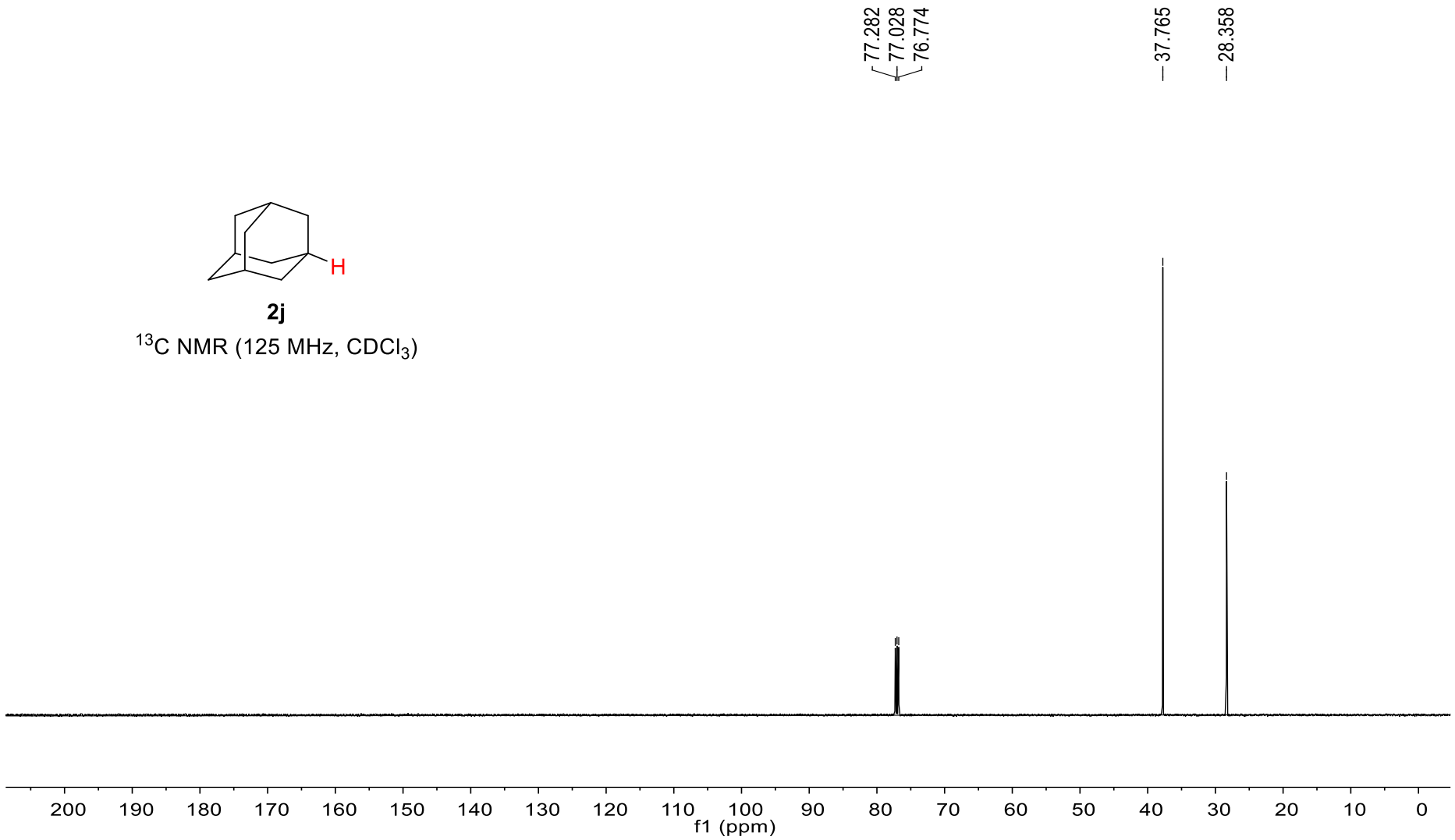

1.936
1.708
1.685
1.631
1.628
1.611
1.606
1.603
1.441
1.435
1.102
1.087
1.072
1.057
0.788
0.773
0.758
0.000
H
Me
2h
1H NMR (500 MHz, CDCl3)
2.94
6.17
5.98
2.01
3.00
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


77.277
77.023
76.770
42.018
37.362
36.735
32.196
28.792
6.907
H
Me
2h
13C NMR (125 MHz, CDCl3)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


7.275
7.260
7.245
7.203
7.189
7.174
7.151
7.137
6.754
6.738
6.707
6.704
6.686
6.683
6.670
6.666
3.968
3.954
3.949
3.936
3.929
3.923
3.821
3.583
2.830
2.815
2.746
2.731
2.130
1.860
1.827
1.801
1.776
1.753
1.743
1.736
1.705
-0.000
MeO
Me
Ph
O
O
MeO2C H
2i
1H NMR (500 MHz, CDCl3)
5.24
3.05
2.00
3.00
2.86
1.03
6.07
3.03
4.28
f1 (ppm)

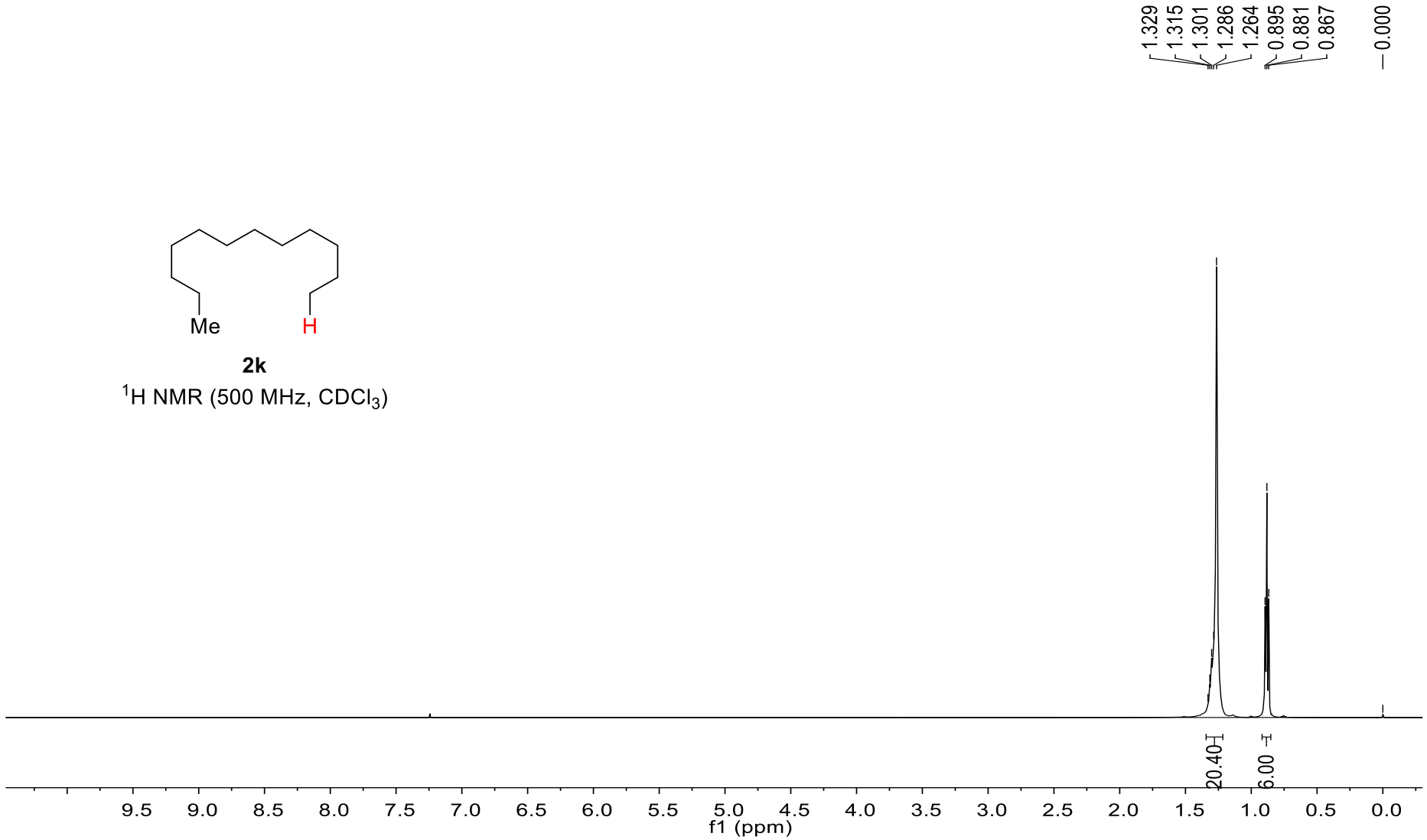

208.135
175.815
149.430
146.719
139.180
133.962
128.863
128.405
126.377
120.158
113.484
112.333
77.357
77.102
76.848
68.739
55.986
51.495
47.342
45.424
38.541
30.149
29.398
28.467
27.101
MeO
Me
Ph
O
O
MeO2C
H
2i
13C NMR (125MHz, CDCl3)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

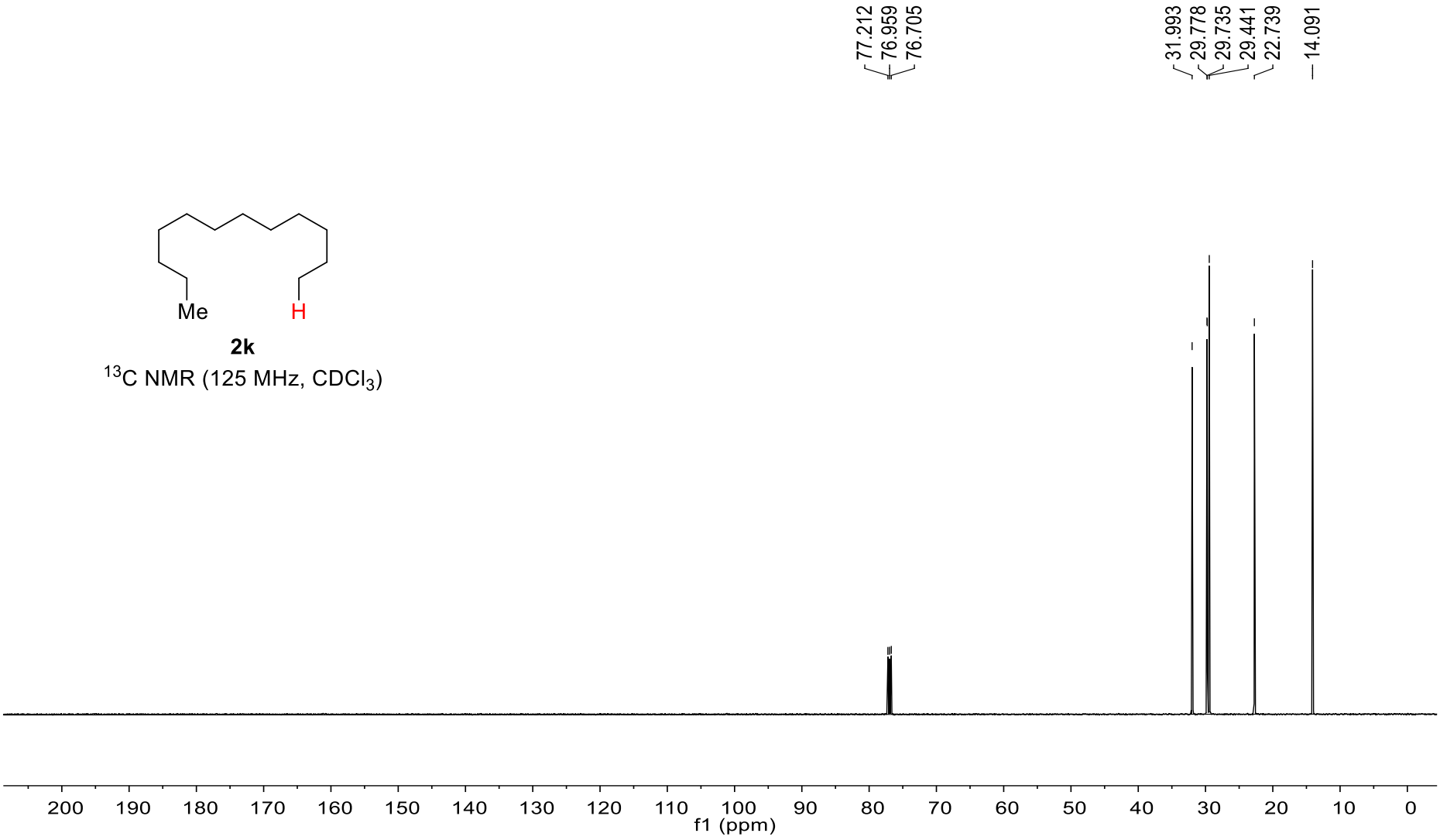

1.873
1.758
1.752
-0.000
H
2j
^{1}H NMR (500 MHz, $CDCl_3$)
4.00
11.82
0.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)



2j

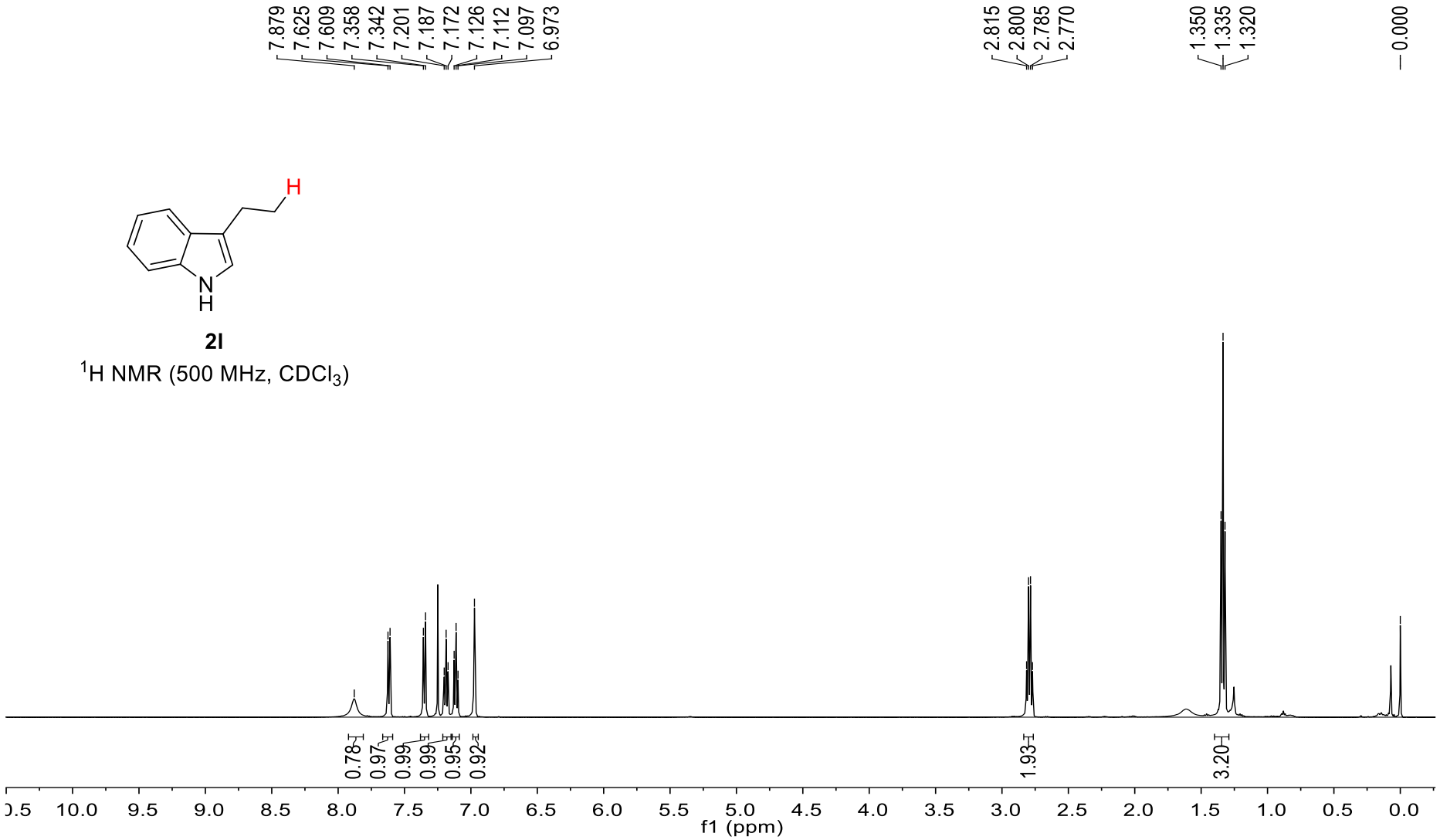
^{13}C NMR (125 MHz, $CDCl_3$)


1.329
1.315
1.301
1.286
1.264
0.895
0.881
0.867
0.000
Me
H
2k
^{1}H NMR (500 MHz, $CDCl_3$)
20.40
6.00
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)



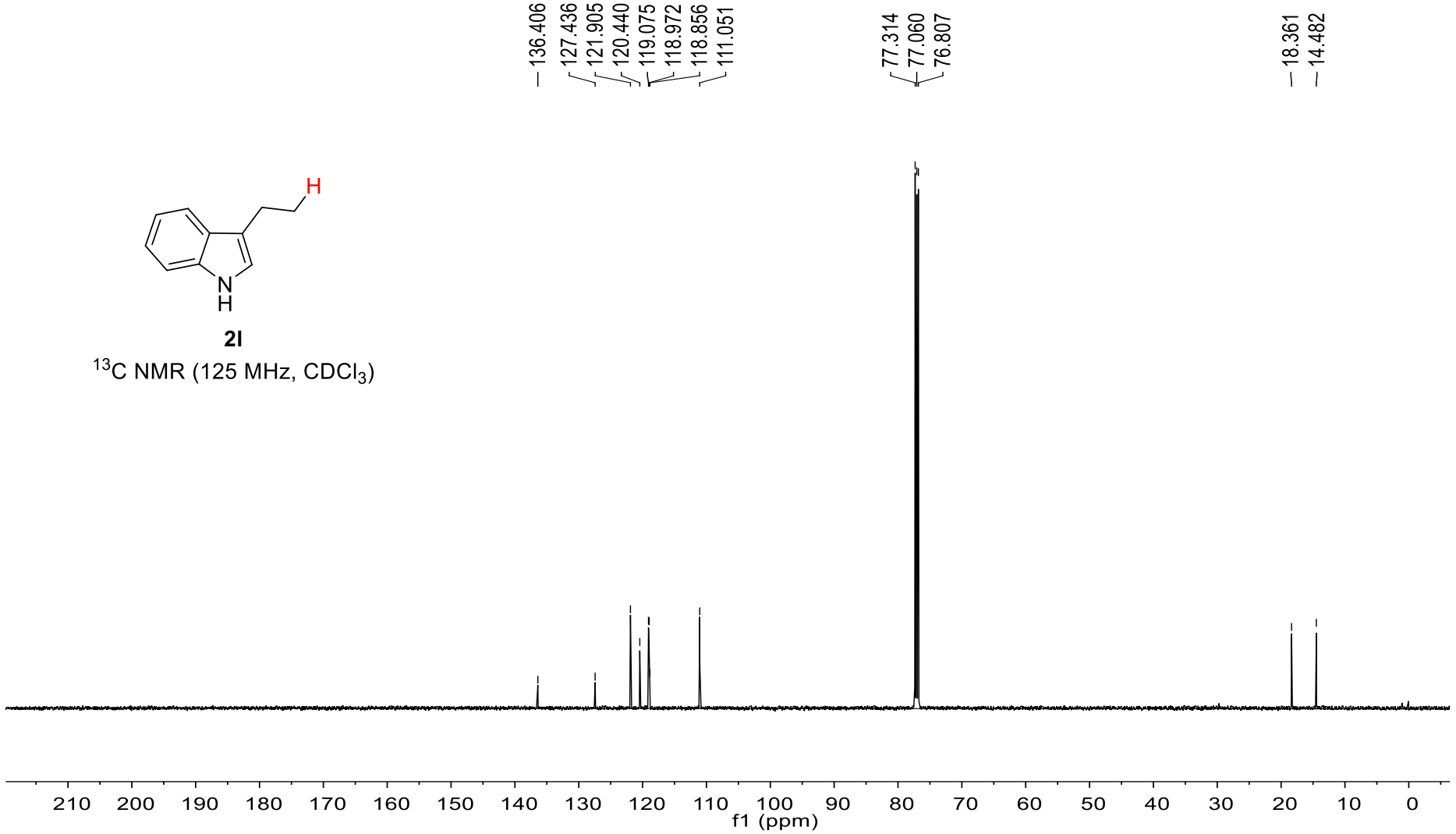
2k

^{13}C NMR (125 MHz, $CDCl_3$)



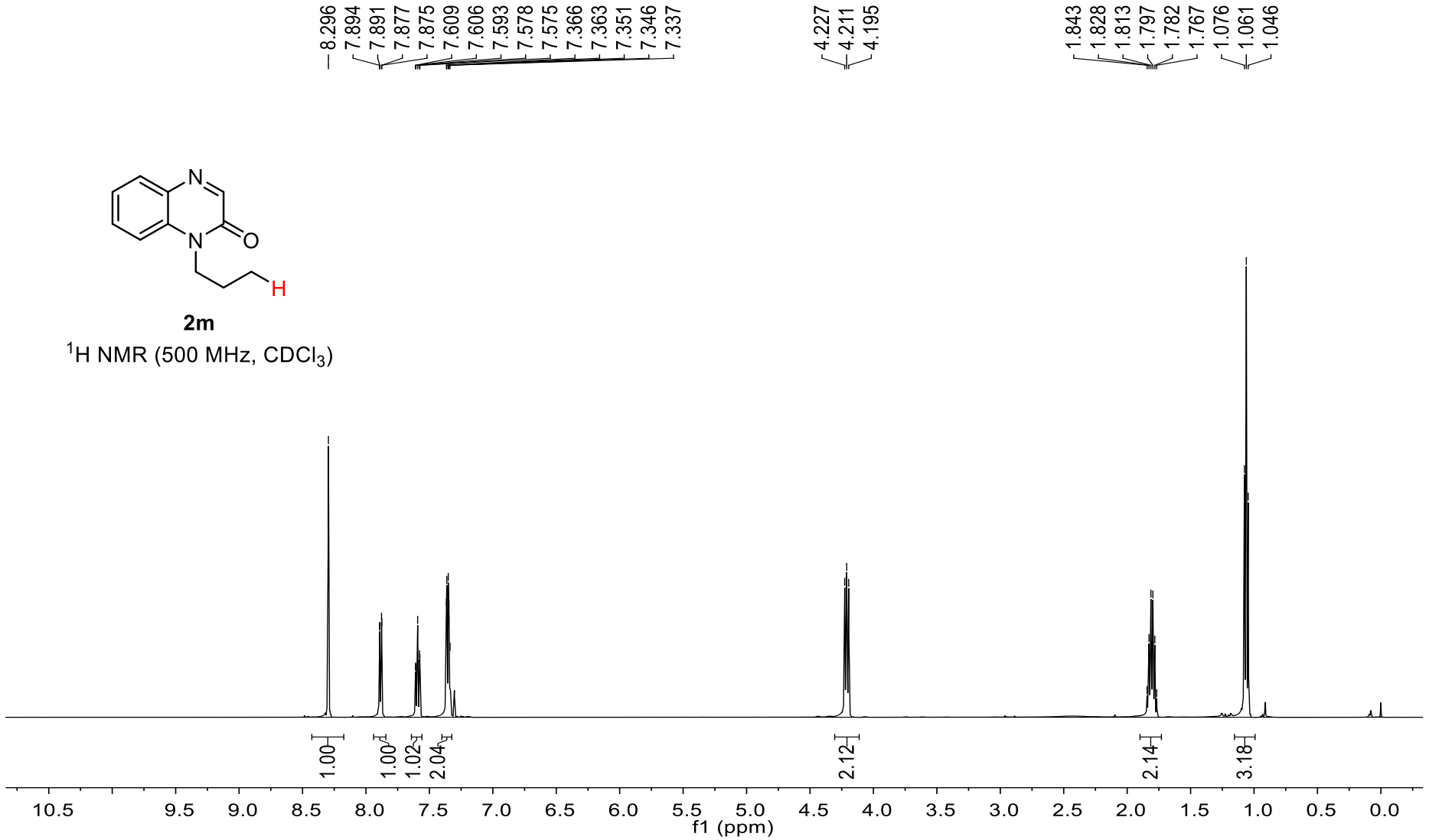
2l

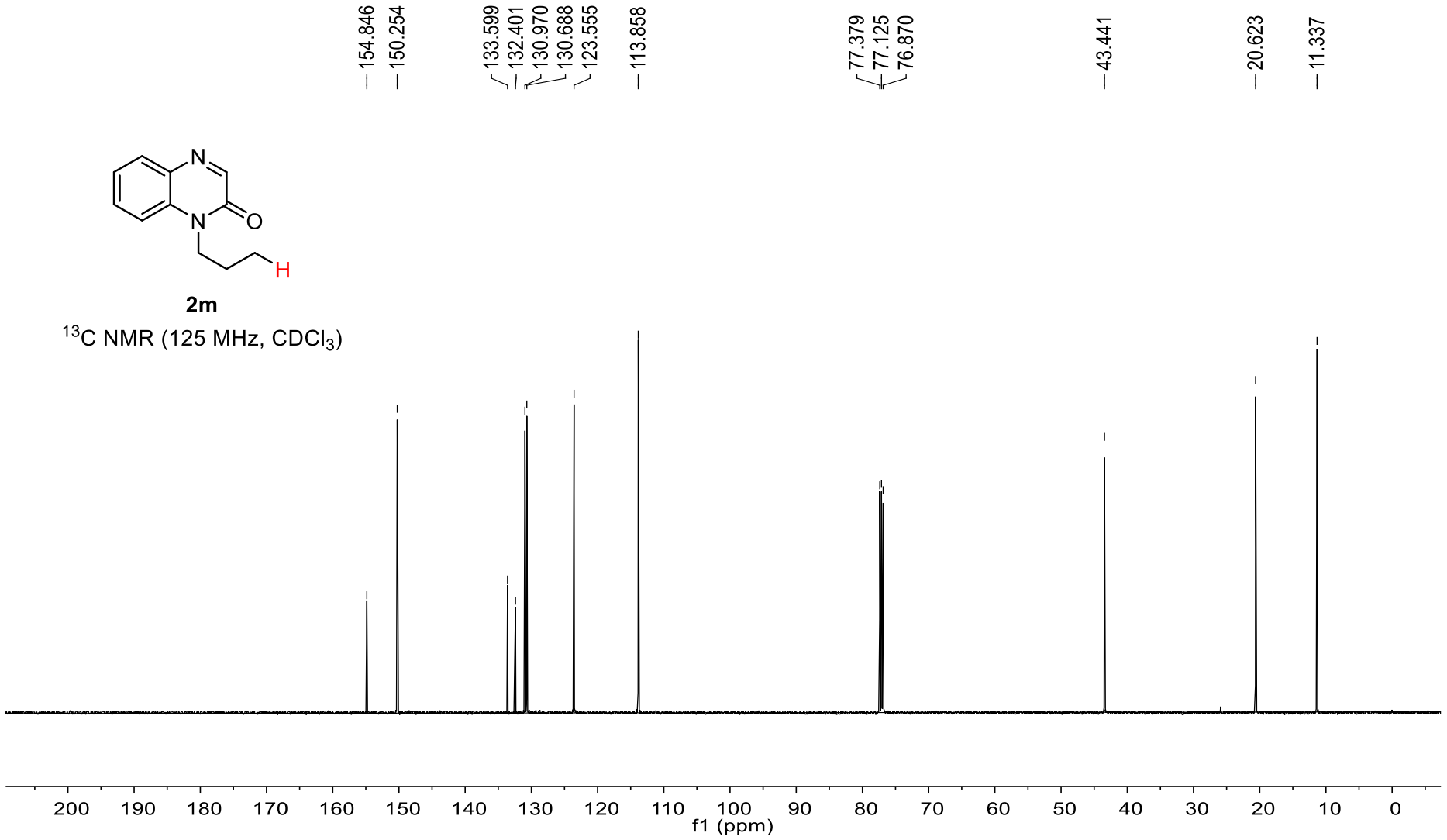
^{1}H NMR (500 MHz, $CDCl_3$)

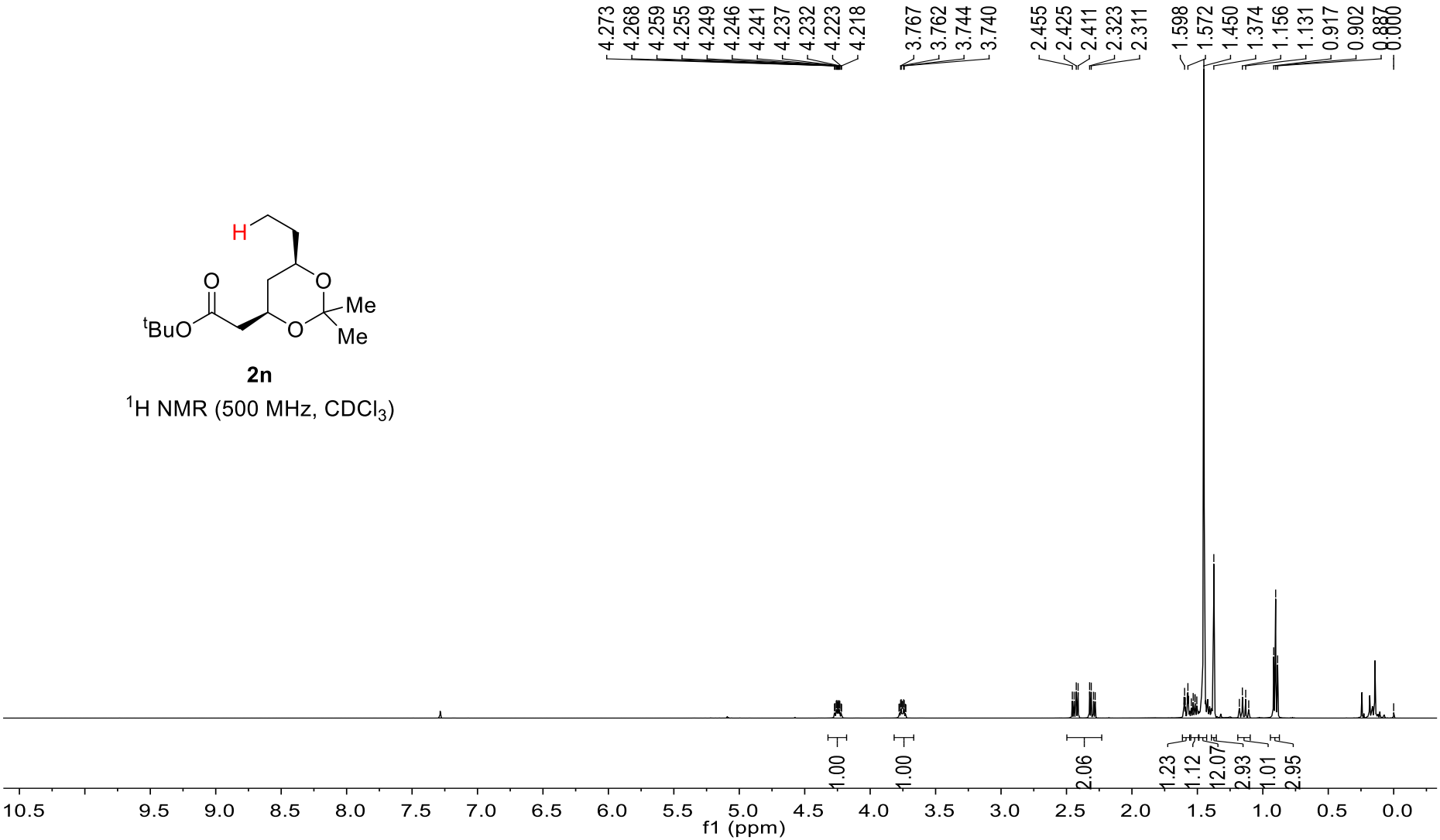


2l

^{13}C NMR (125 MHz, $CDCl_3$)

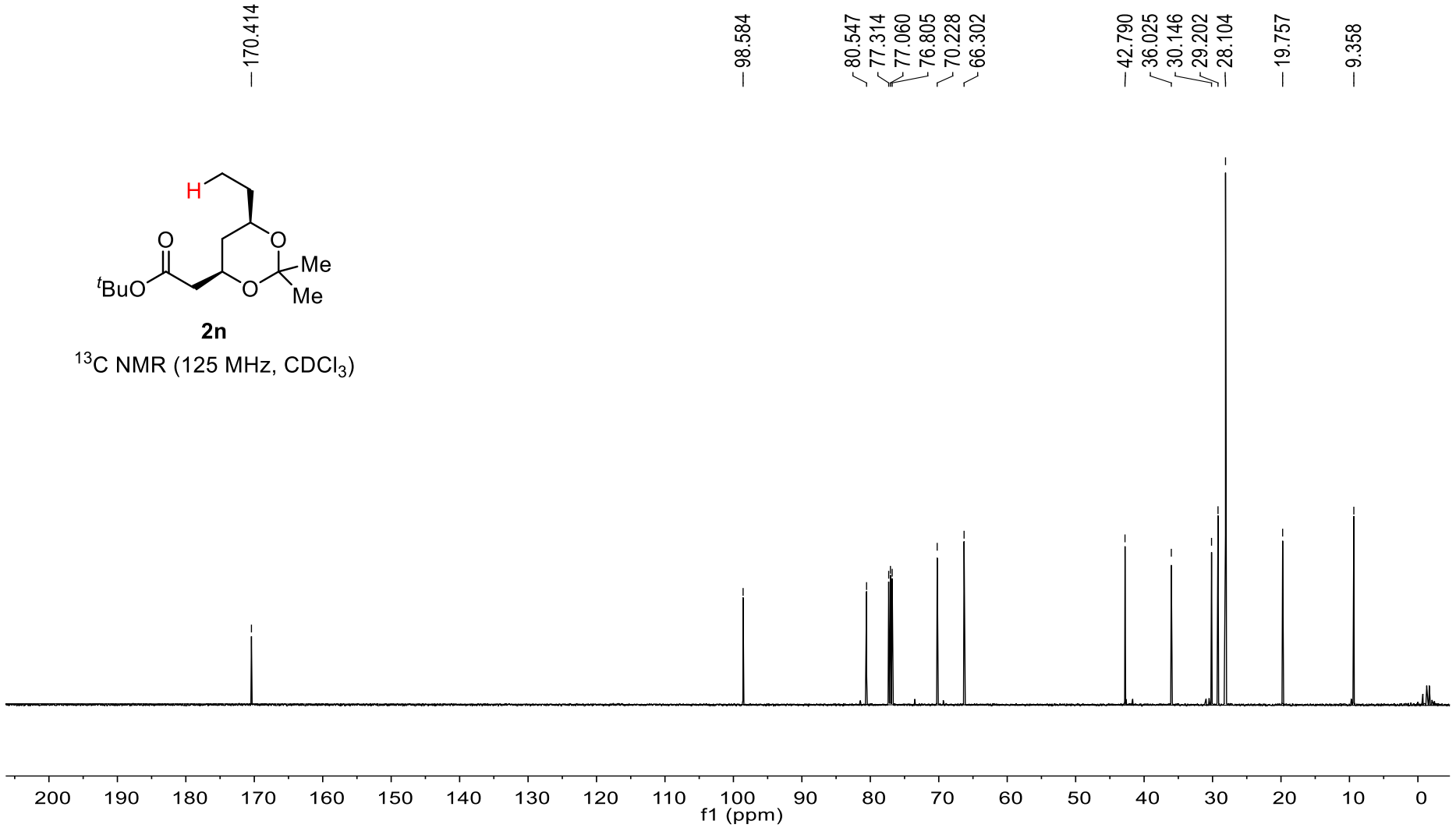

8.296
7.894
7.891
7.877
7.875
7.609
7.606
7.593
7.578
7.575
7.366
7.363
7.351
7.346
7.337
4.227
4.211
4.195
1.843
1.828
1.813
1.797
1.782
1.767
1.076
1.061
1.046
N
N
O
H
2m
1H NMR (500 MHz, CDCl3)
1.00
1.00
1.02
2.04
2.12
2.14
3.18
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

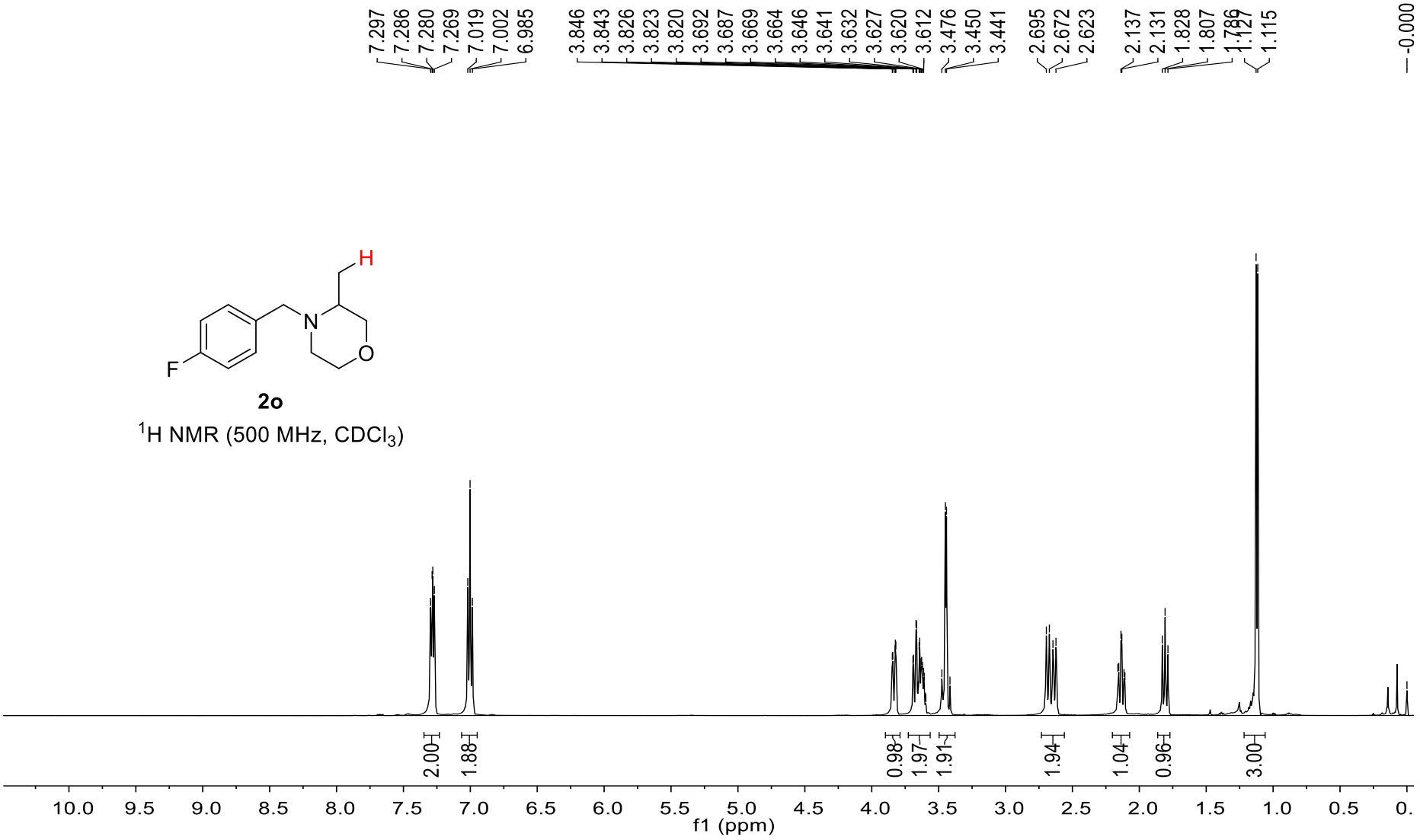

154.846
150.254
133.599
132.401
130.970
130.688
123.555
113.858
77.379
77.125
76.870
43.441
20.623
11.337
N
N
O
H
2m
13C NMR (125 MHz, CDCl3)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

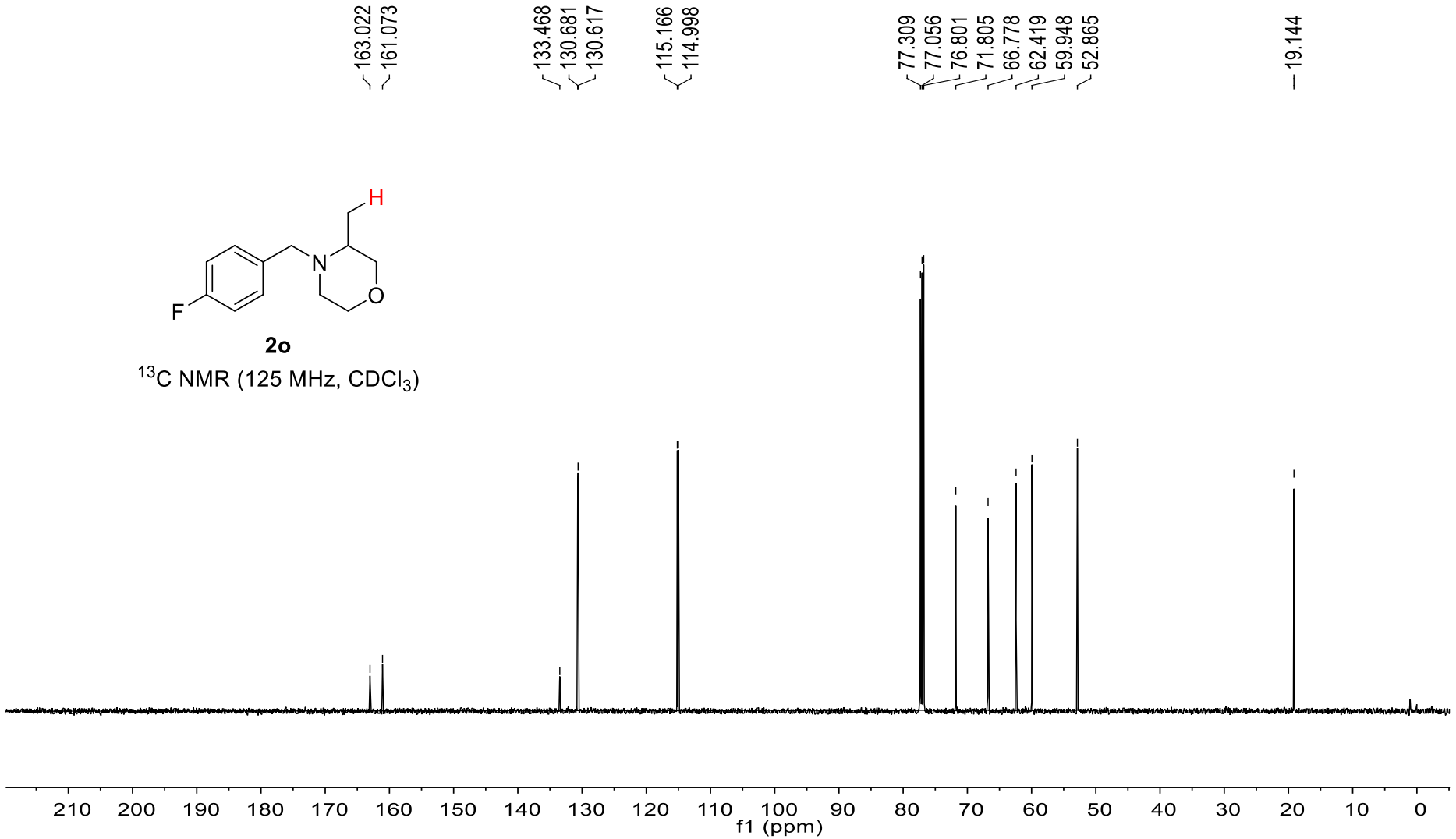


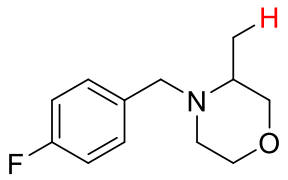
2n

^{1}H NMR (500 MHz, $CDCl_3$)


170.414
98.584
80.547
77.314
77.060
76.805
70.228
66.302
42.790
36.025
30.146
29.202
28.104
19.757
9.358
H
O
O
Me
tBuO
O
Me
2n
13C NMR (125 MHz, CDCl3)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

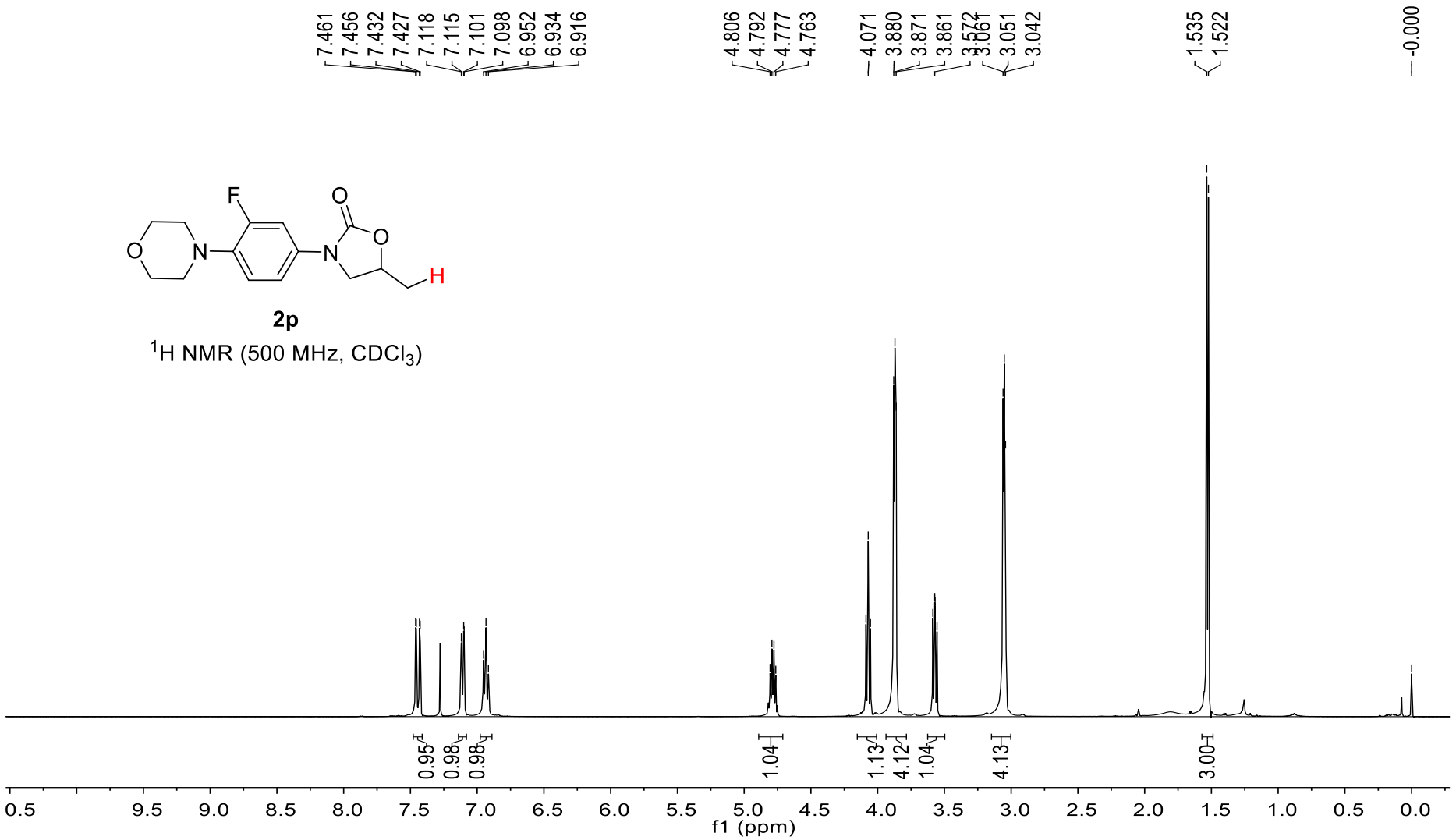

7.297
7.286
7.280
7.269
7.019
7.002
6.985
3.846
3.843
3.826
3.823
3.820
3.692
3.687
3.669
3.664
3.646
3.641
3.632
3.627
3.620
3.612
3.476
3.450
3.441
2.695
2.672
2.623
2.137
2.131
1.828
1.807
1.786
1.127
1.115
-0.000
H
N
O
F
2o
1H NMR (500 MHz, CDCl3)
2.00
1.88
0.98
1.97
1.91
1.94
1.04
0.96
3.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.
f1 (ppm)

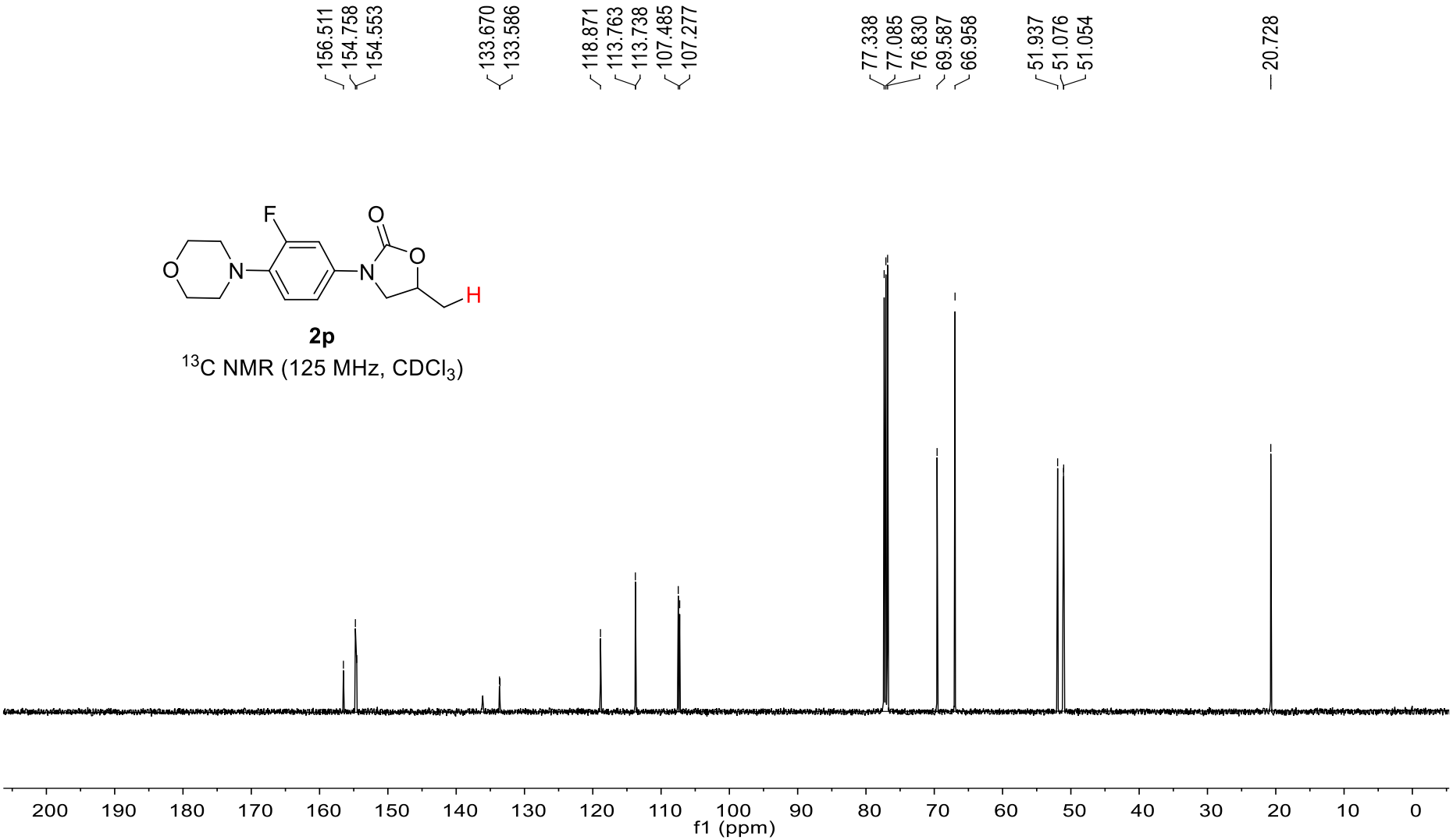

163.022
161.073
133.468
130.681
130.617
115.166
114.998
77.309
77.056
76.801
71.805
66.778
62.419
59.948
52.865
19.144
H
N
O
F
2o
13C NMR (125 MHz, CDCl3)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



2o

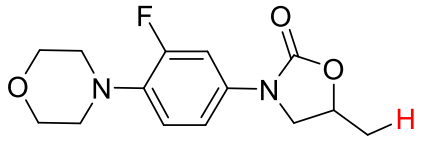
^{19}F NMR (471 MHz, $CDCl_3$)


7.461
7.456
7.432
7.427
7.118
7.115
7.101
7.098
6.952
6.934
6.916
4.806
4.792
4.777
4.763
4.071
3.880
3.871
3.861
3.572
3.061
3.051
3.042
1.535
1.522
-0.000
F
O
O
N
N
O
H
2p
1H NMR (500 MHz, CDCl3)
0.95
0.98
0.98
1.04
1.13
4.12
1.04
4.13
3.00
f1 (ppm)



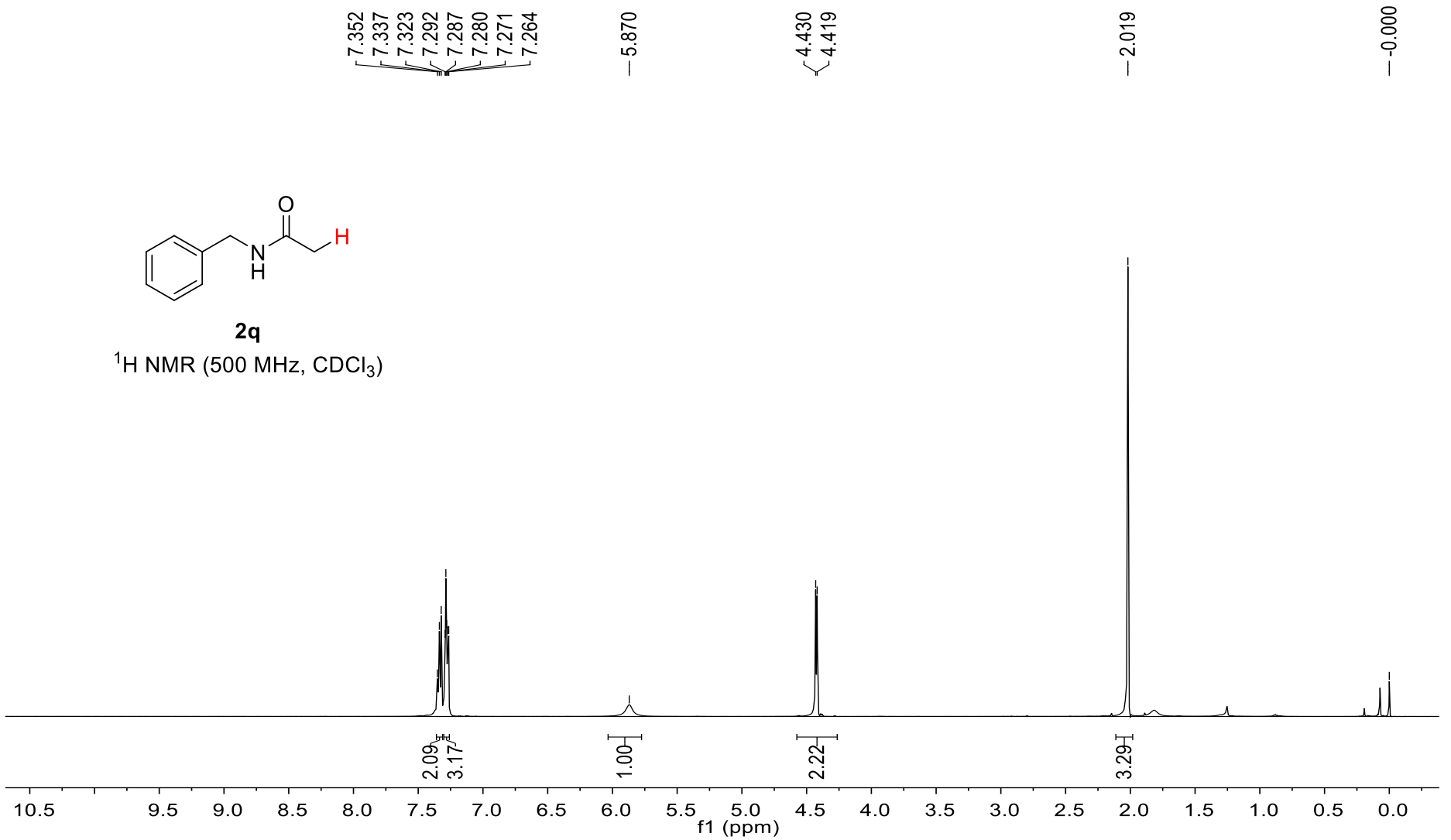
2p

^{13}C NMR (125 MHz, $CDCl_3$)



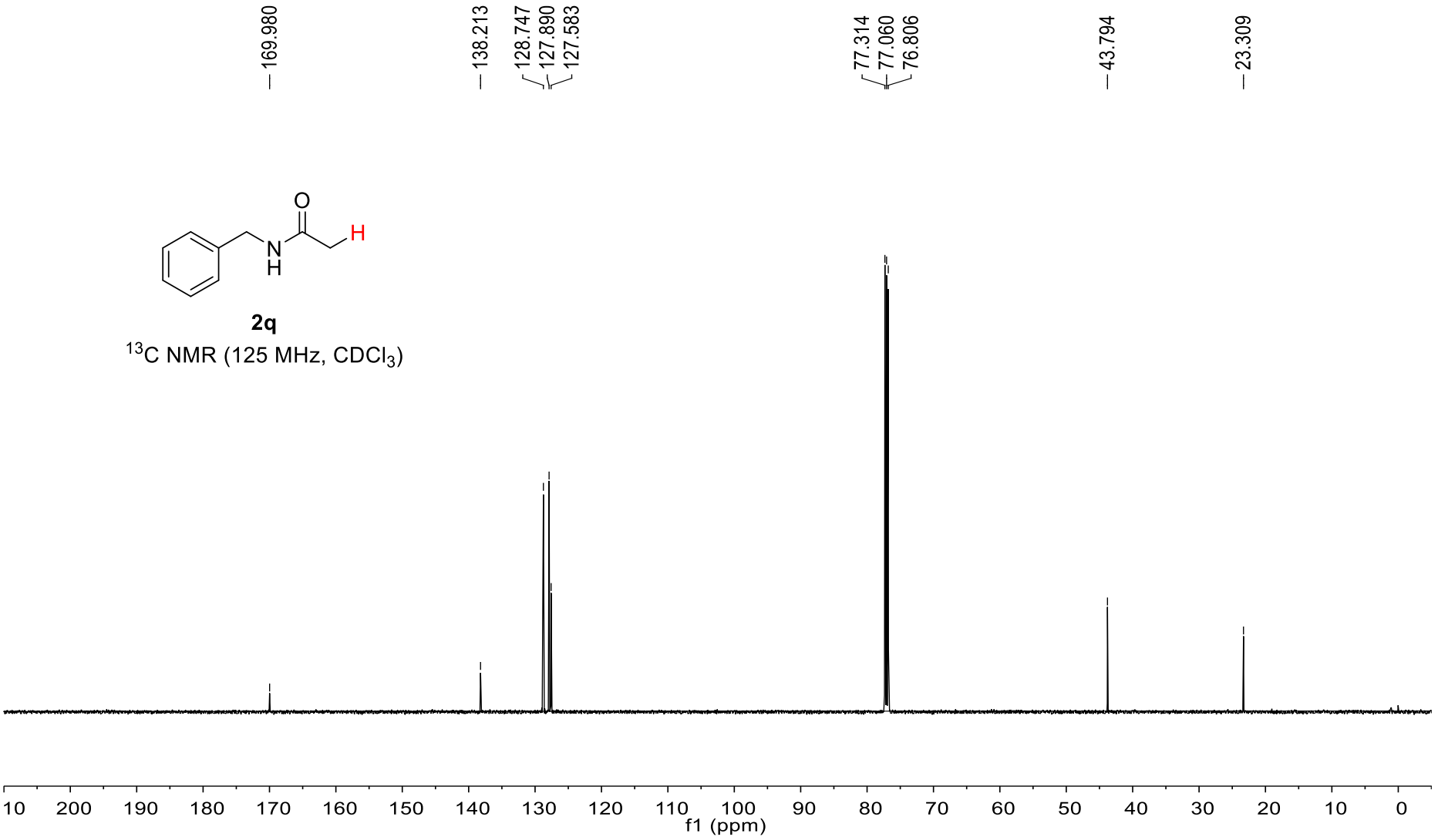
2p

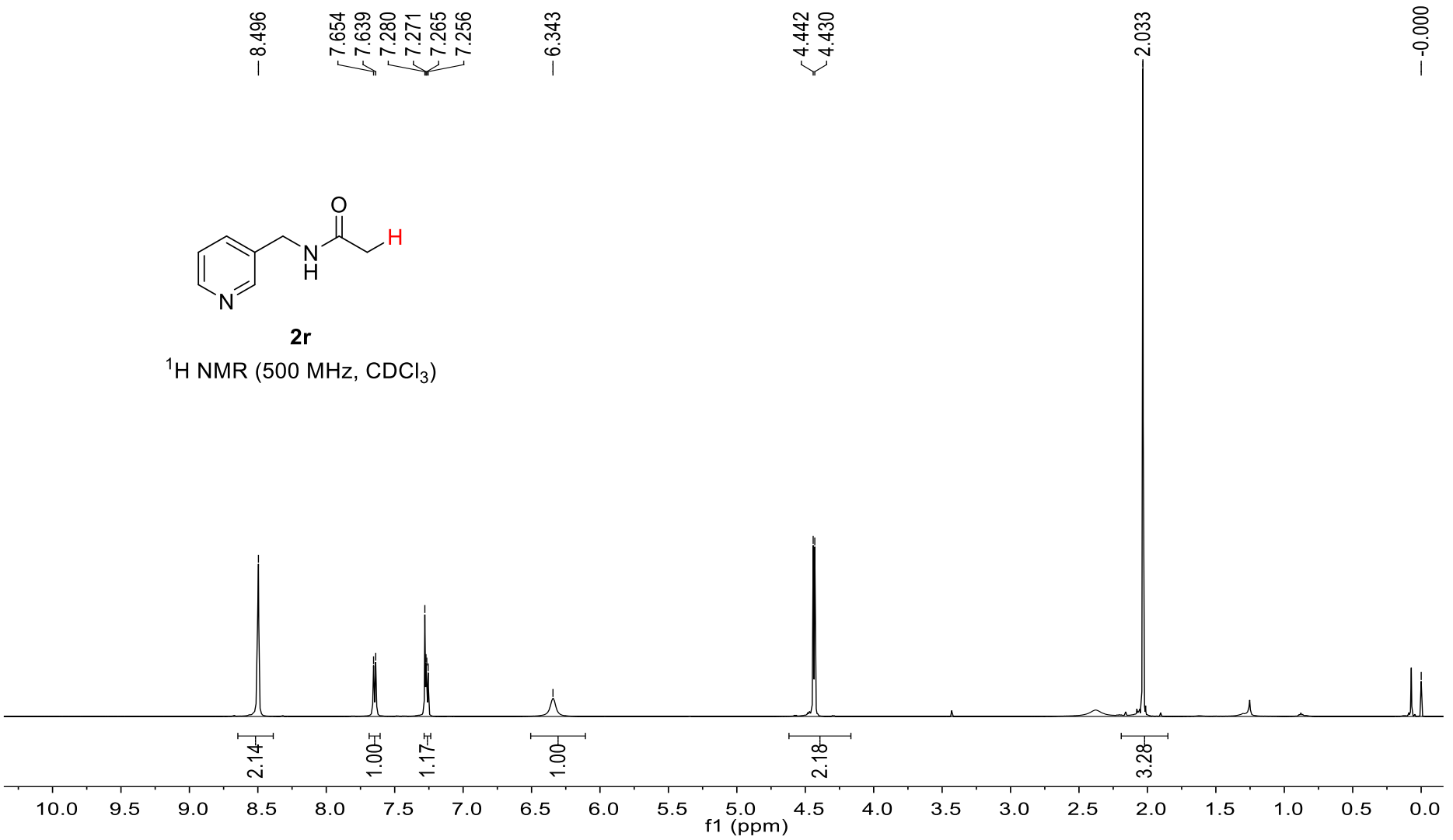
^{19}F NMR (471 MHz, $CDCl_3$)

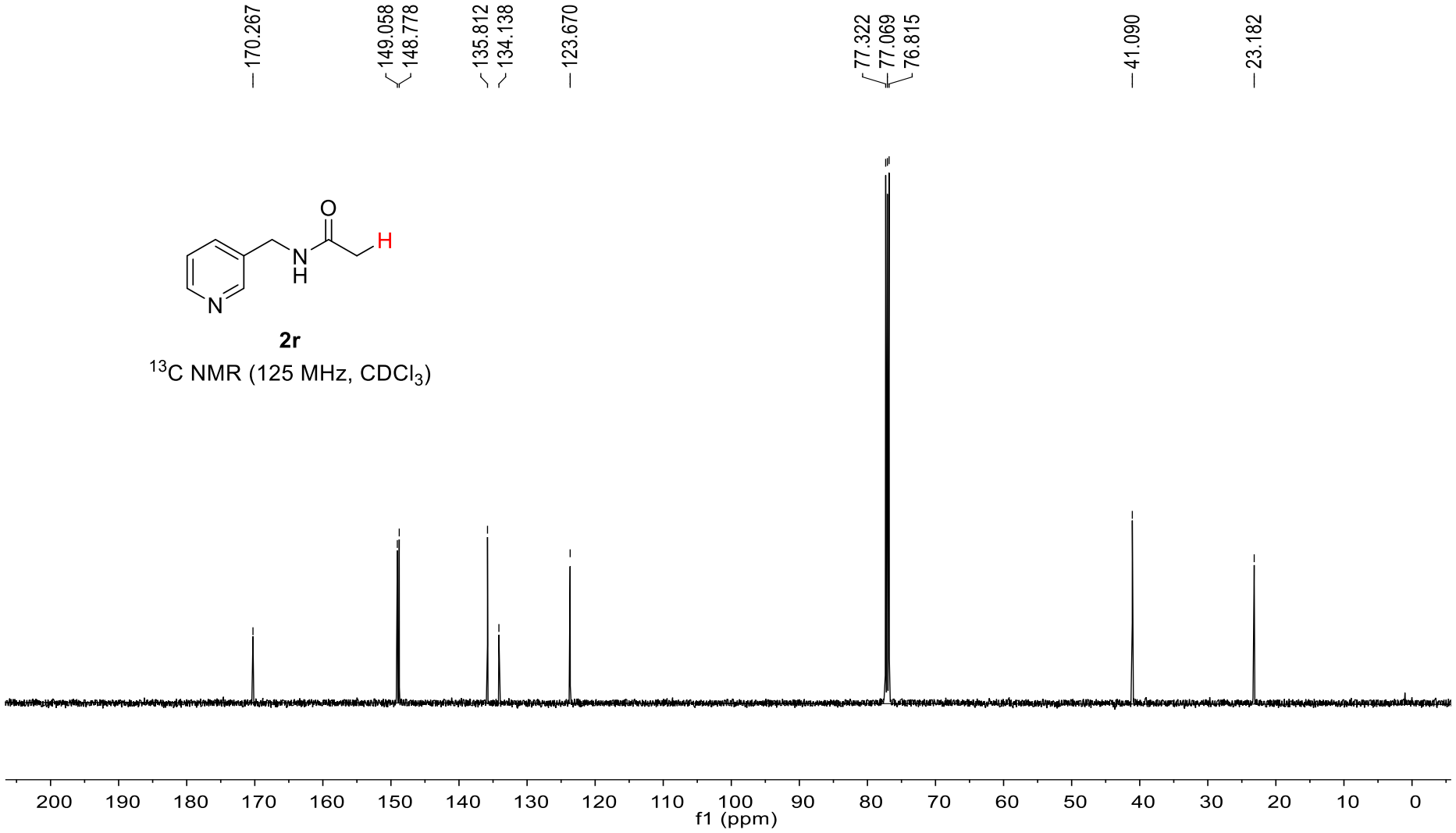


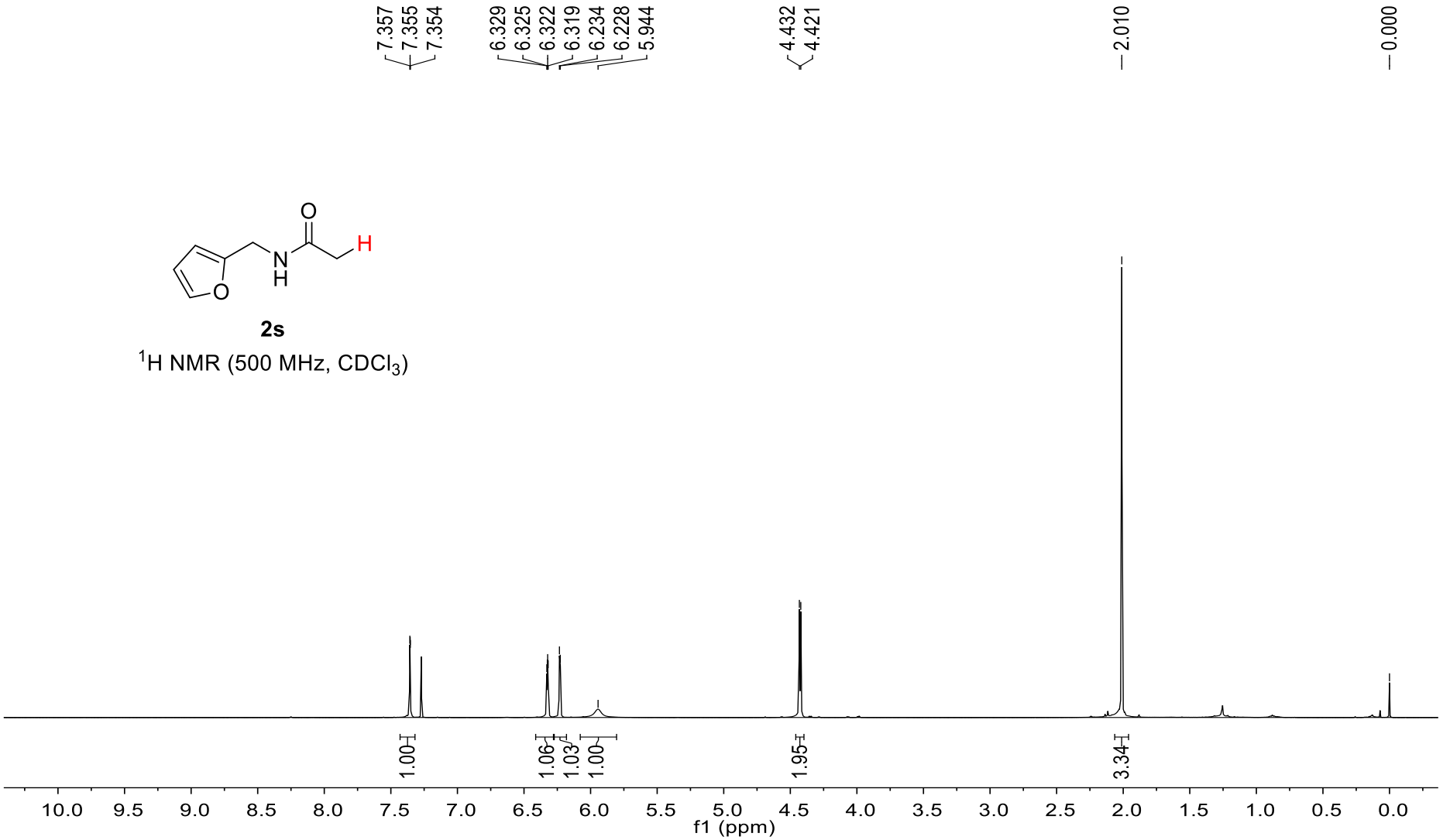
2q

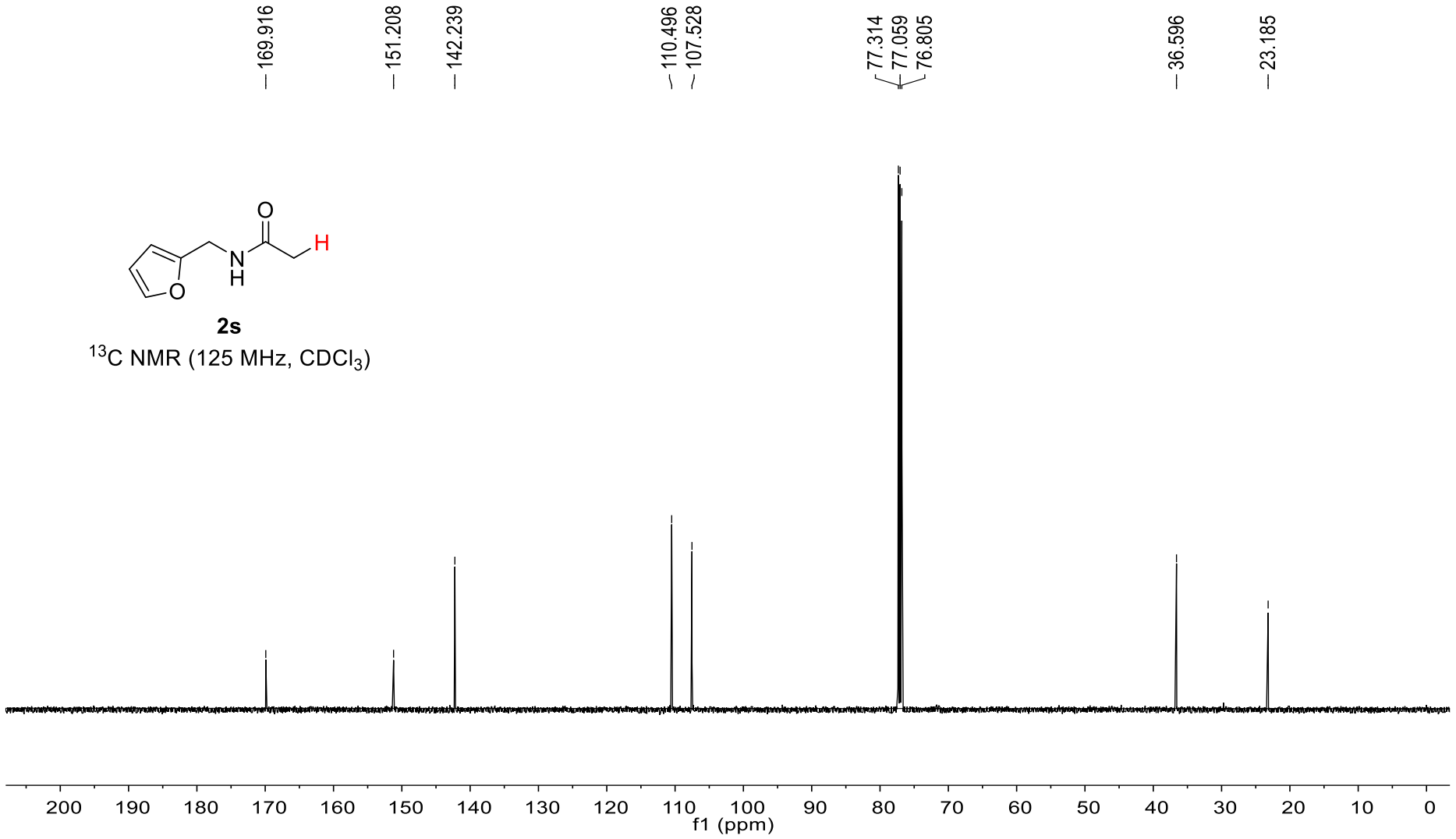
^{1}H NMR (500 MHz, $CDCl_3$)


169.980
138.213
128.747
127.890
127.583
77.314
77.060
76.806
43.794
23.309
O
N
H
H
2q
13C NMR (125 MHz, CDCl3)
10 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


8.496
7.654
7.639
7.280
7.271
7.265
7.256
6.343
4.442
4.430
2.033
-0.000
O
N
H
N
H
2r
^{1}H NMR (500 MHz, $CDCl_3$)
2.14
1.00
1.17
1.00
2.18
3.28
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

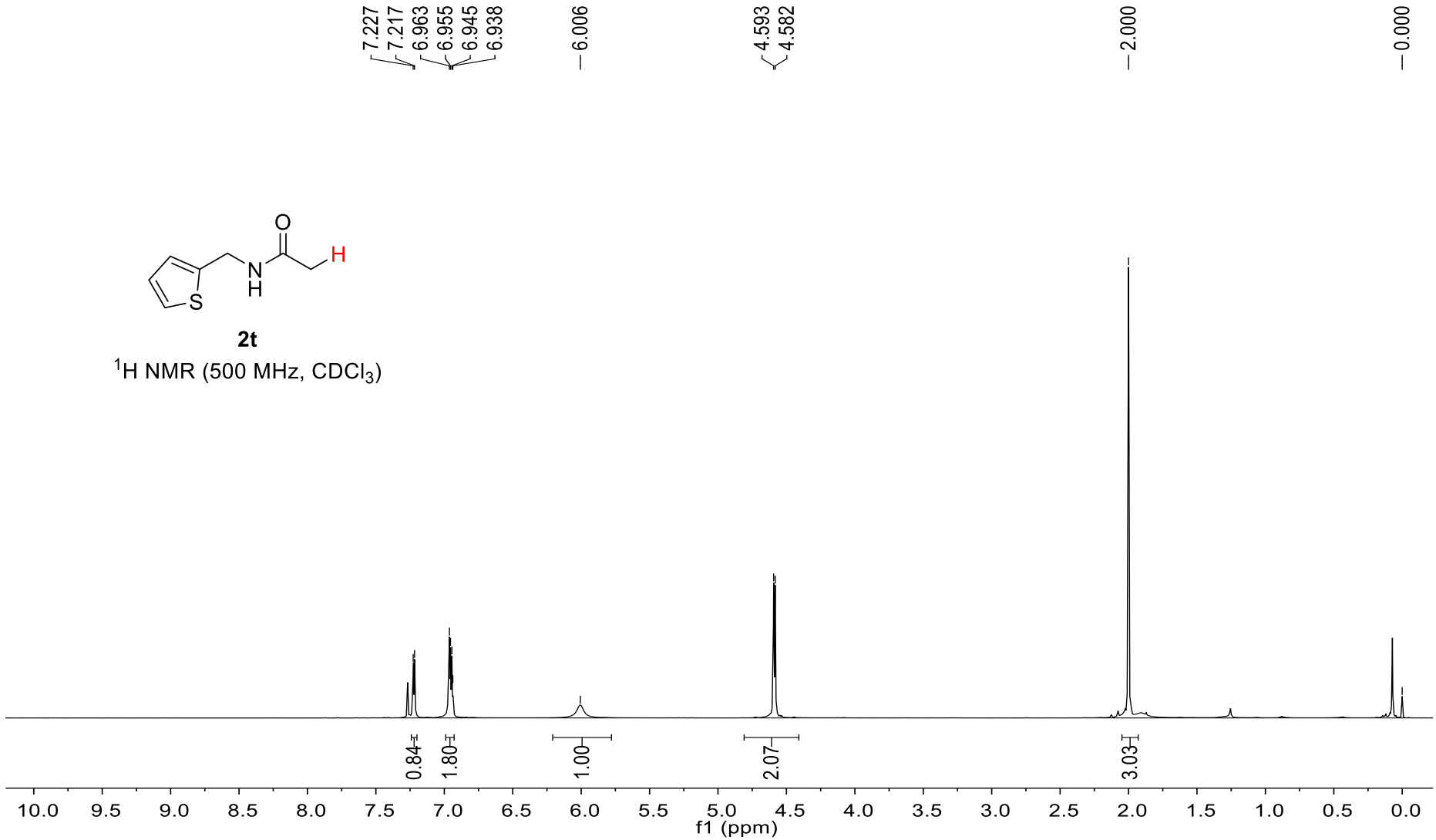

170.267
149.058
148.778
135.812
134.138
123.670
77.322
77.069
76.815
41.090
23.182
O
H
N
H
N
2r
13C NMR (125 MHz, CDCl3)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

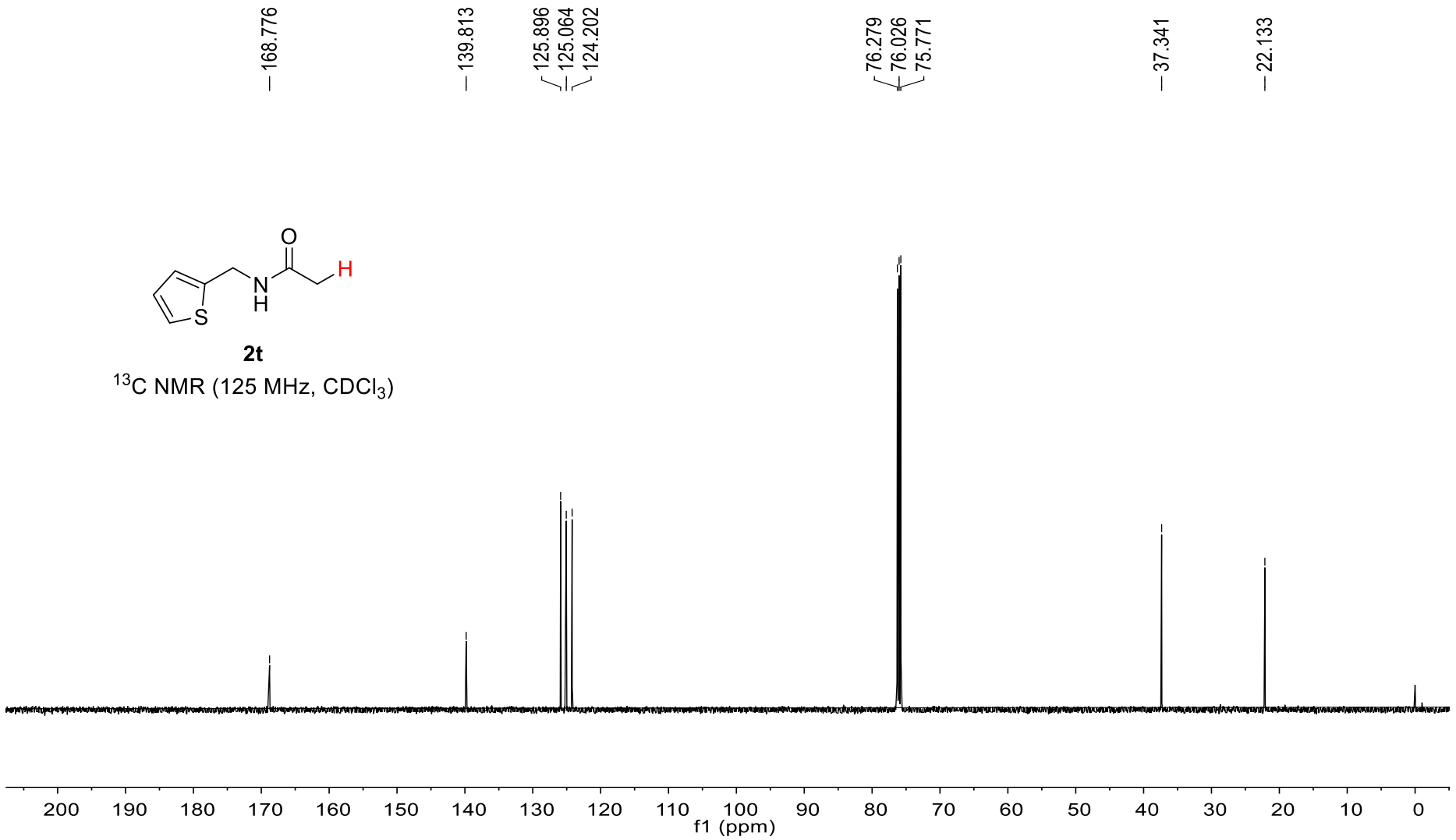

7.357
7.355
7.354
6.329
6.325
6.322
6.319
6.234
6.228
5.944
4.432
4.421
2.010
0.000
O
N
H
H
O
2s
1H NMR (500 MHz, CDCl3)
1.00
1.06
1.03
1.00
1.95
3.34
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

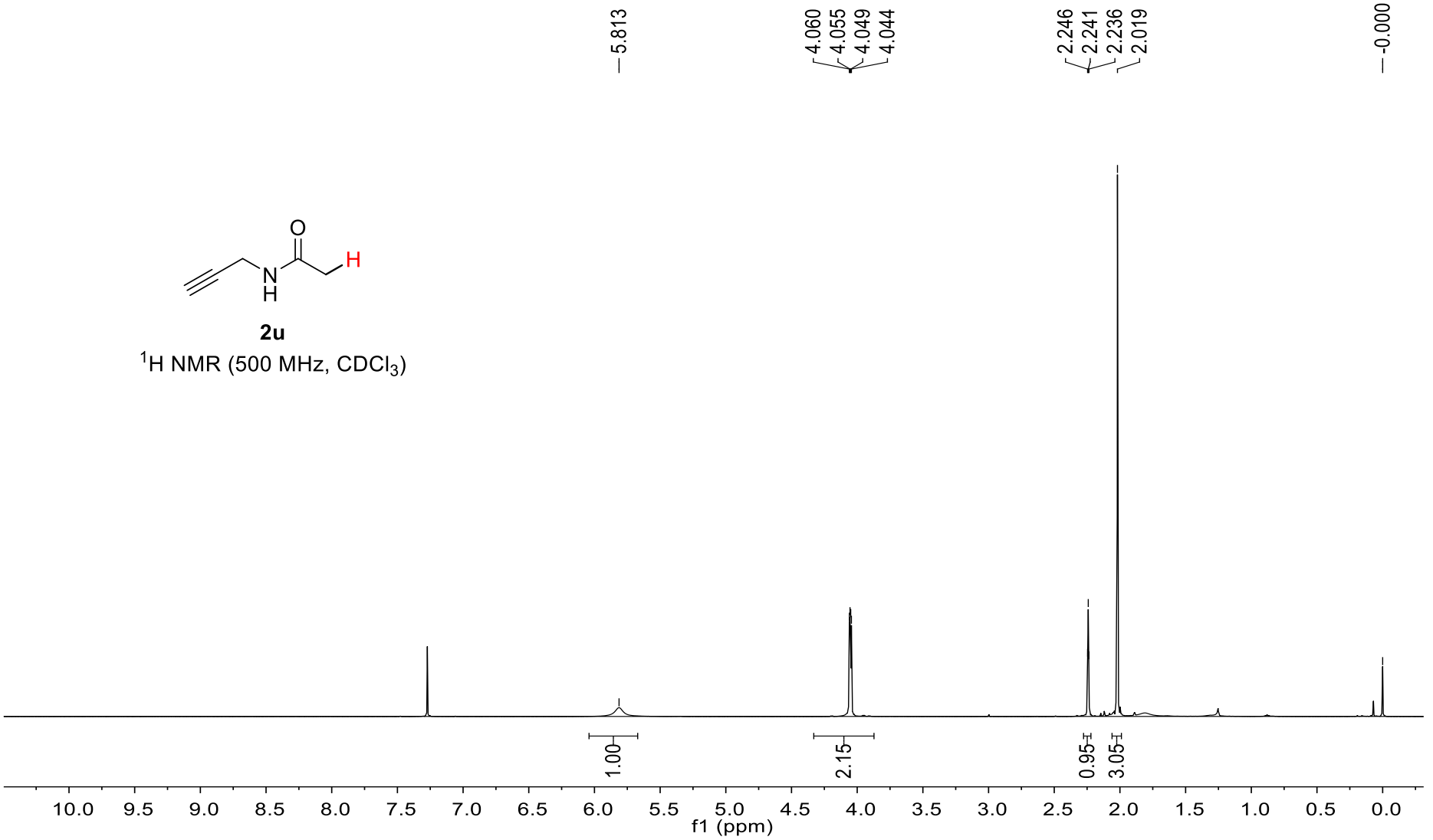


2s

^{13}C NMR (125 MHz, $CDCl_3$)

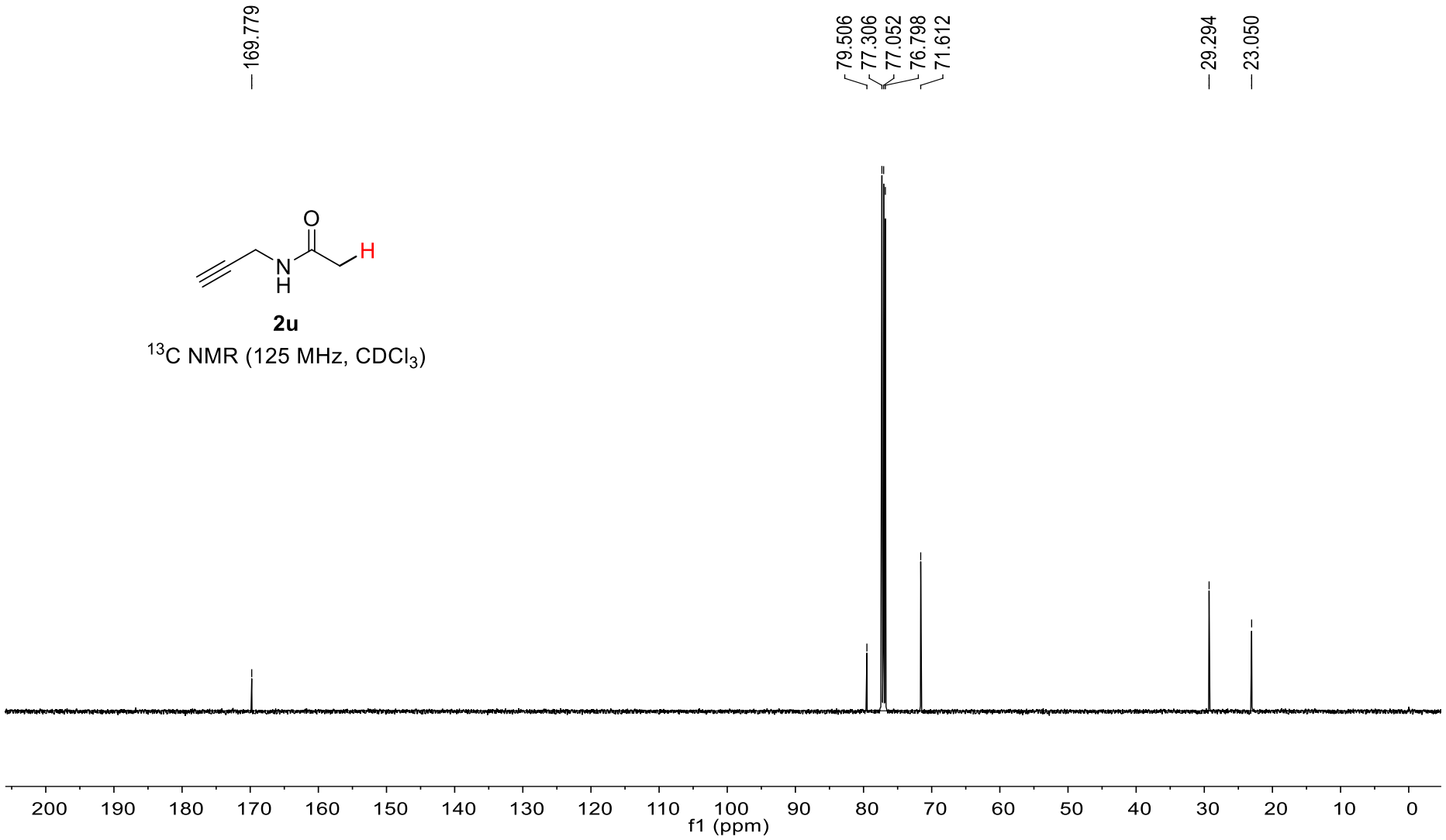

7.227
7.217
6.963
6.955
6.945
6.938
6.006
4.593
4.582
2.000
0.000
O
N
H
S
H
2t
1H NMR (500 MHz, CDCl3)
0.84
1.80
1.00
2.07
3.03
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

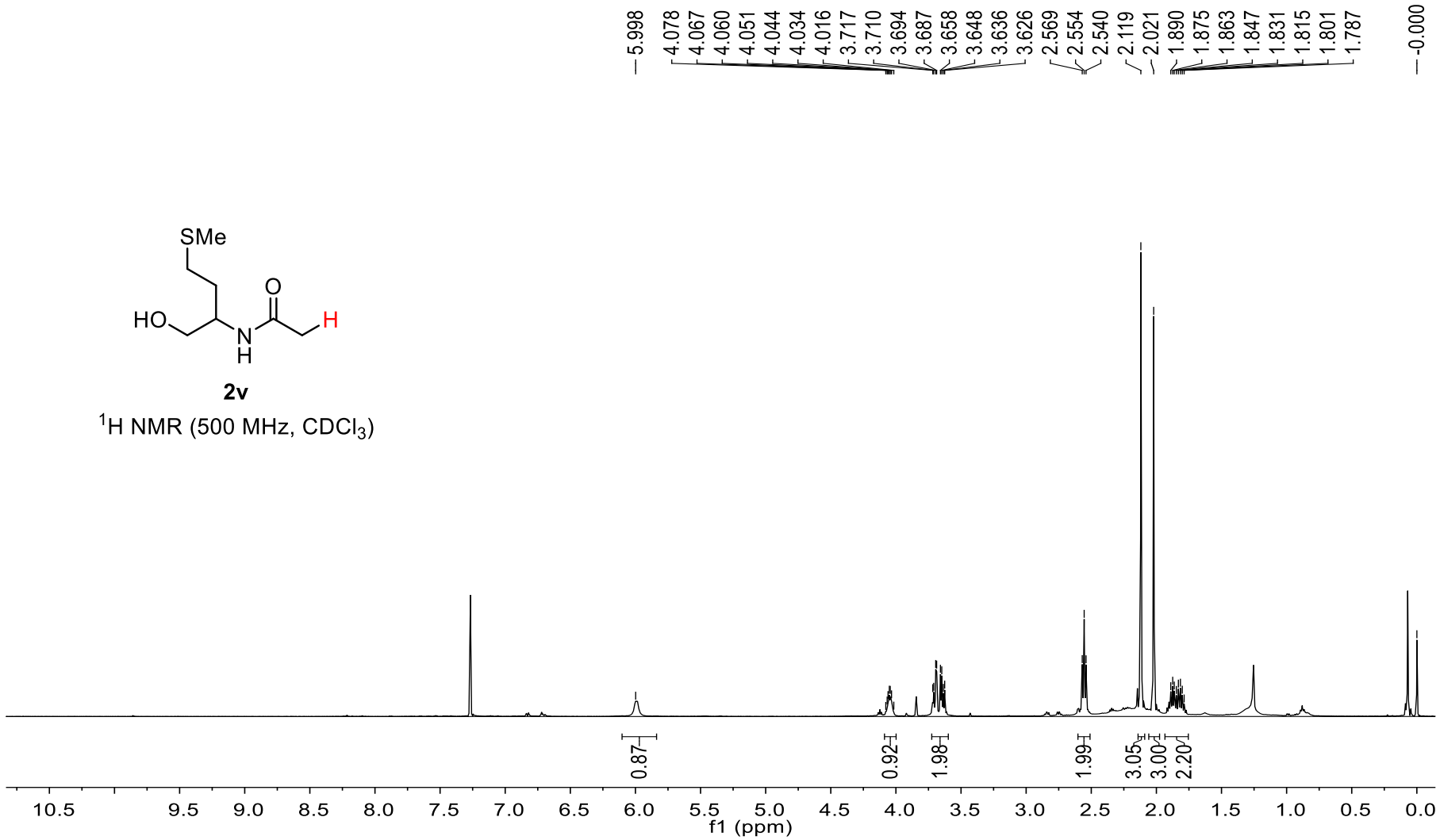

168.776
139.813
125.896
125.064
124.202
76.279
76.026
75.771
37.341
22.133
O
N
H
H
S
2t
13C NMR (125 MHz, CDCl3)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

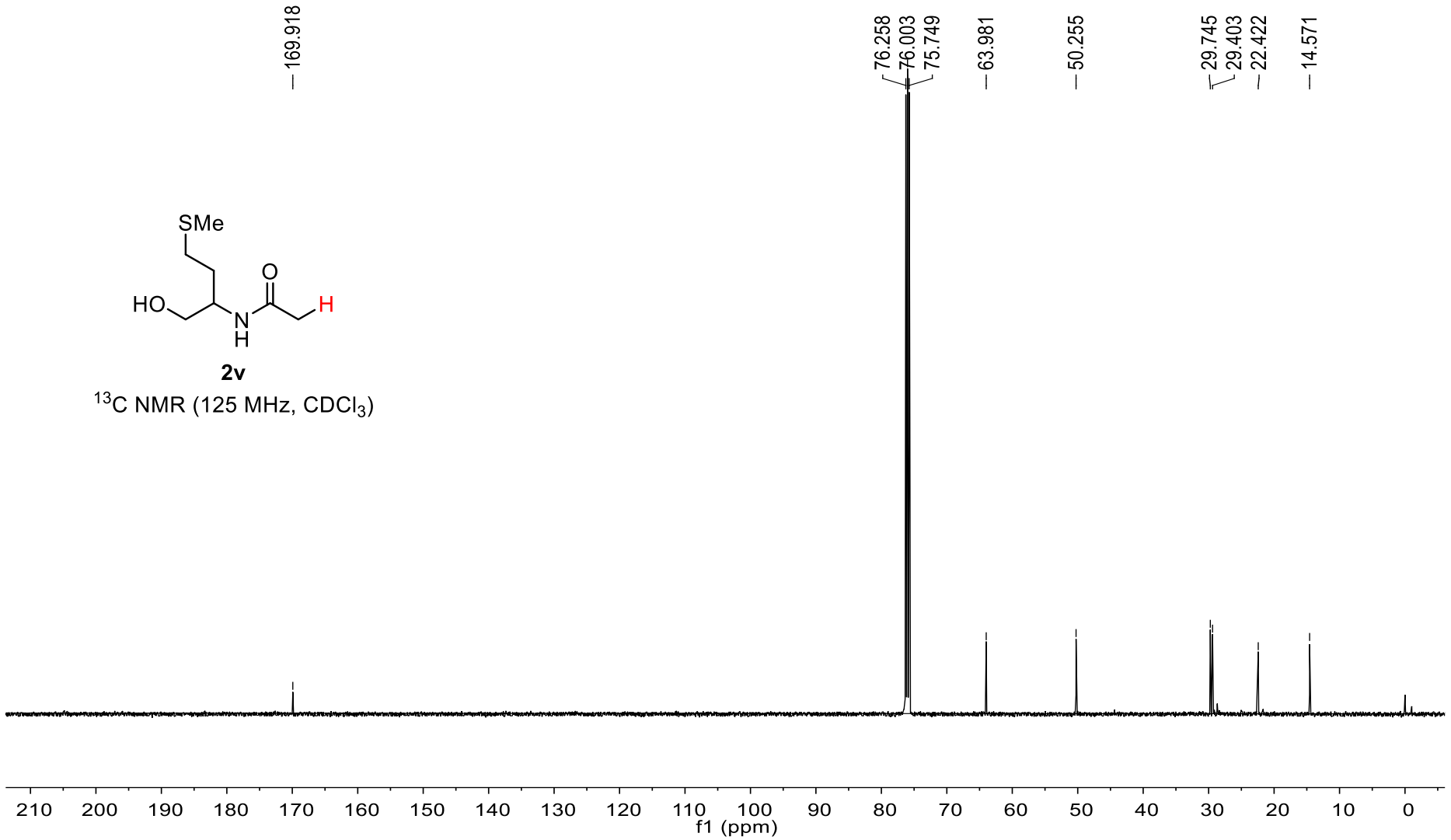


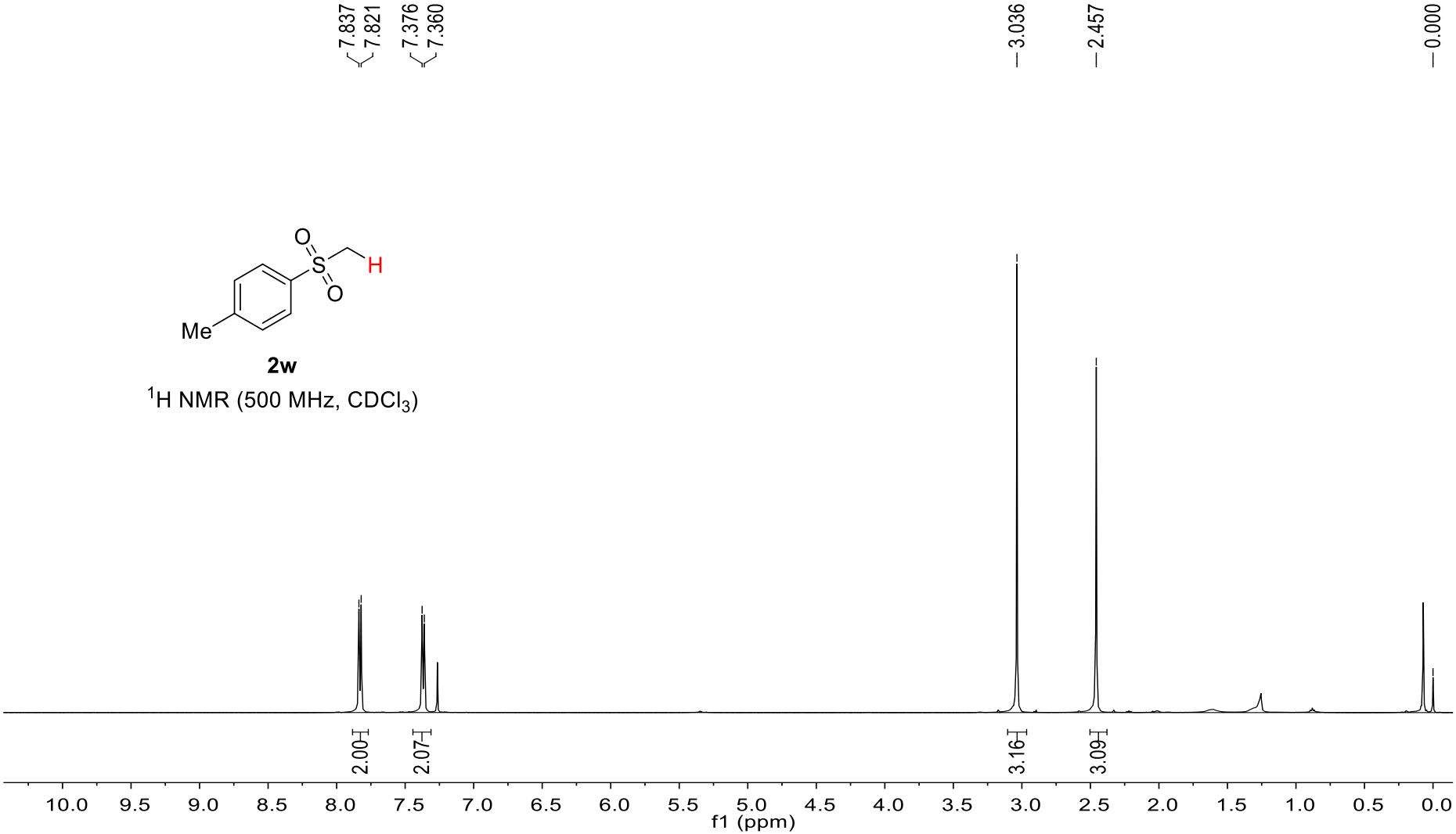
2u

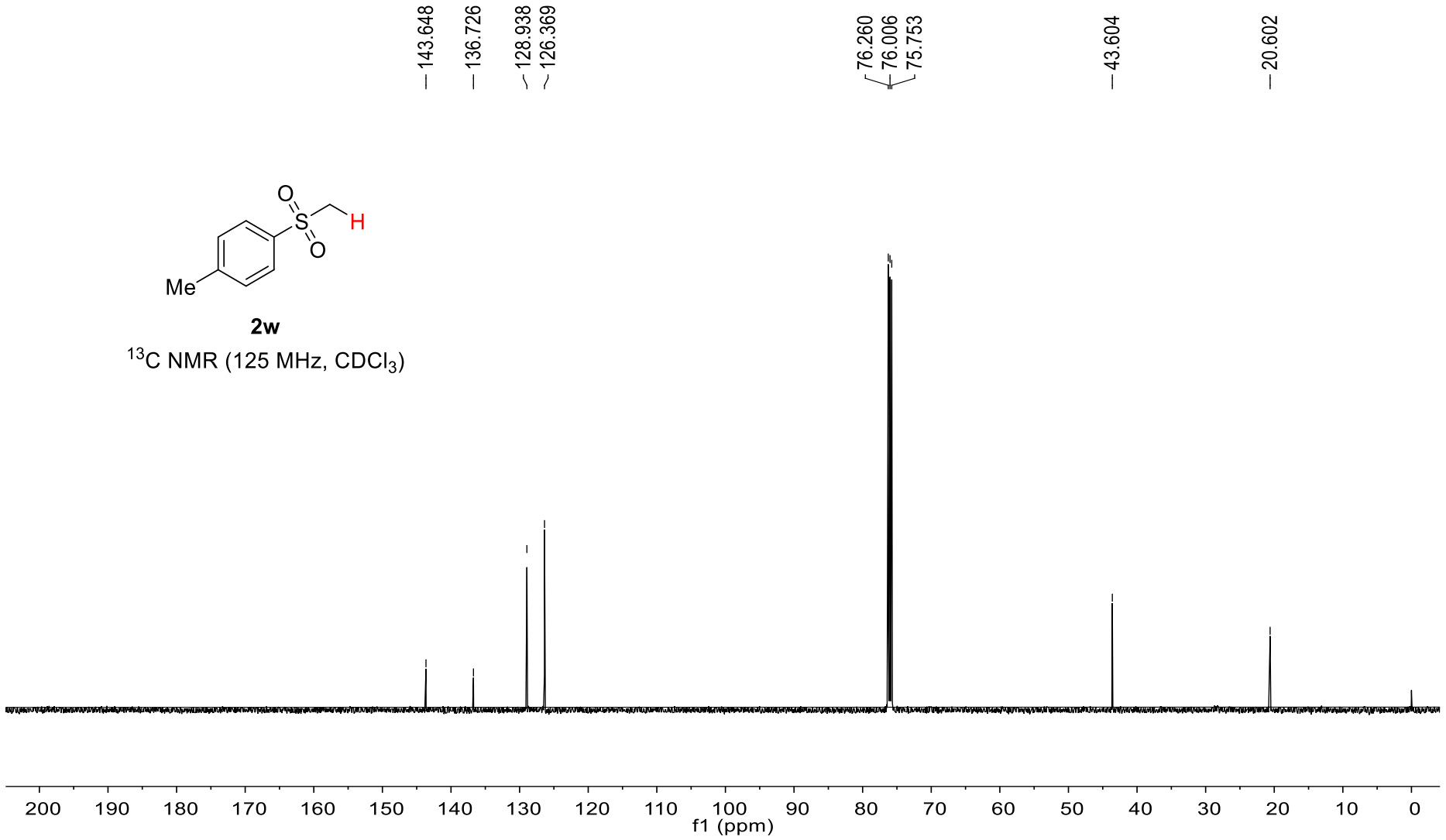
^{1}H NMR (500 MHz, $CDCl_3$)

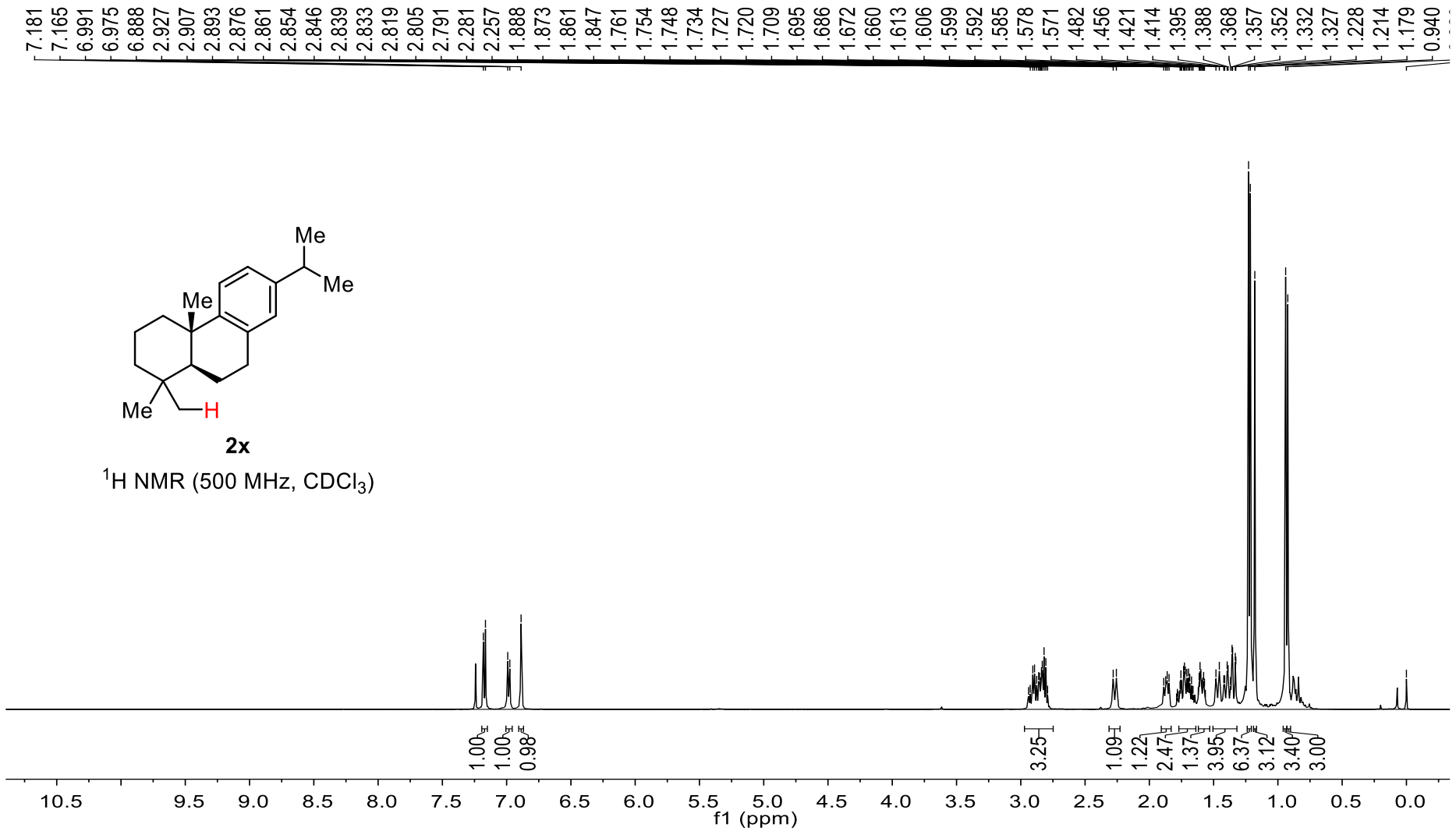

169.779
79.506
77.306
77.052
76.798
71.612
29.294
23.050
O
N
H
H
2u
13C NMR (125 MHz, CDCl3)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

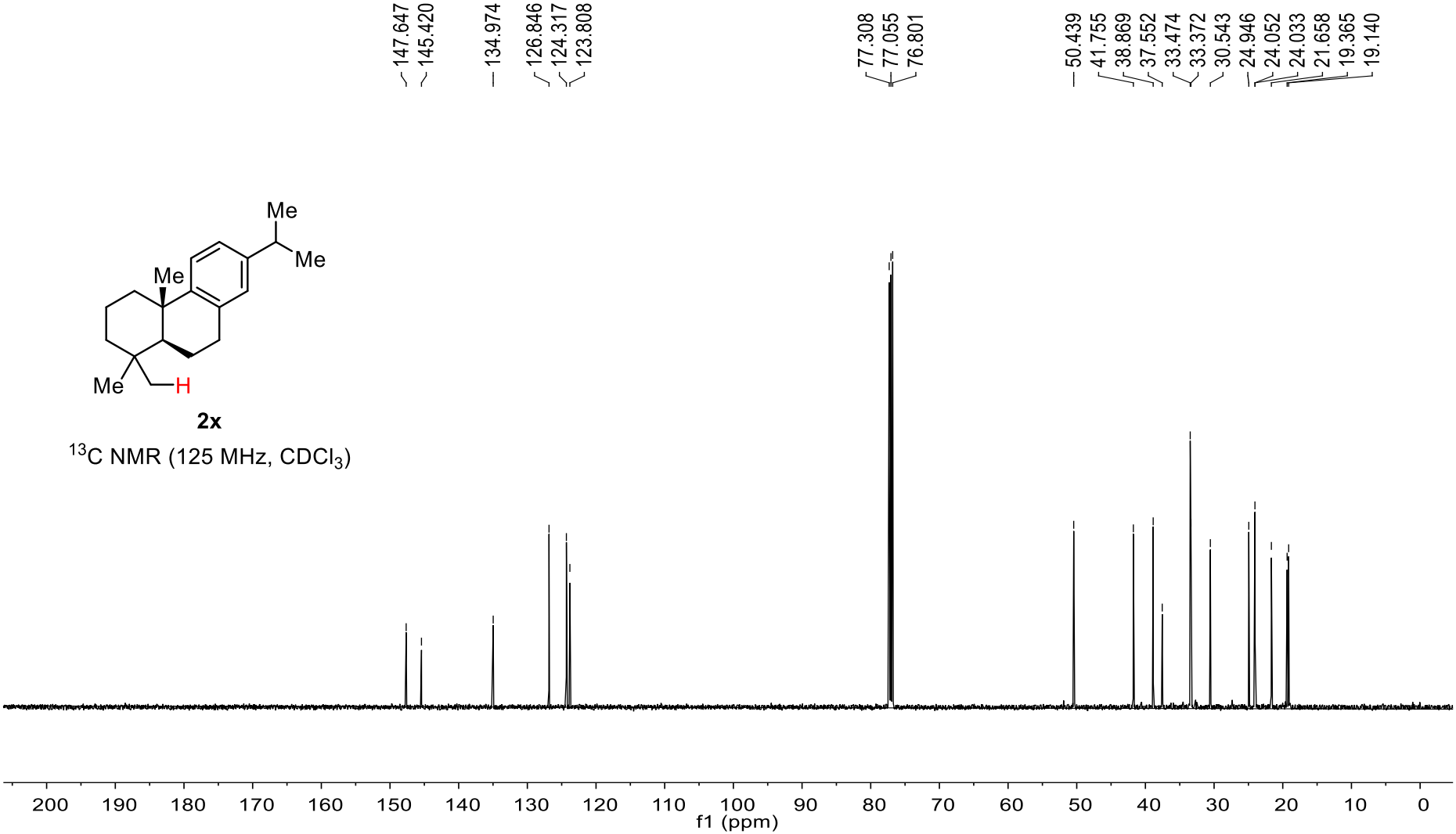

5.998
4.078
4.067
4.060
4.051
4.044
4.034
4.016
3.717
3.710
3.694
3.687
3.658
3.648
3.636
3.626
2.569
2.554
2.540
2.119
2.021
1.890
1.875
1.863
1.847
1.831
1.815
1.801
1.787
-0.000
SMe
HO
N
H
O
H
2v
1H NMR (500 MHz, CDCl3)
0.87
0.92
1.98
1.99
3.05
3.00
2.20
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

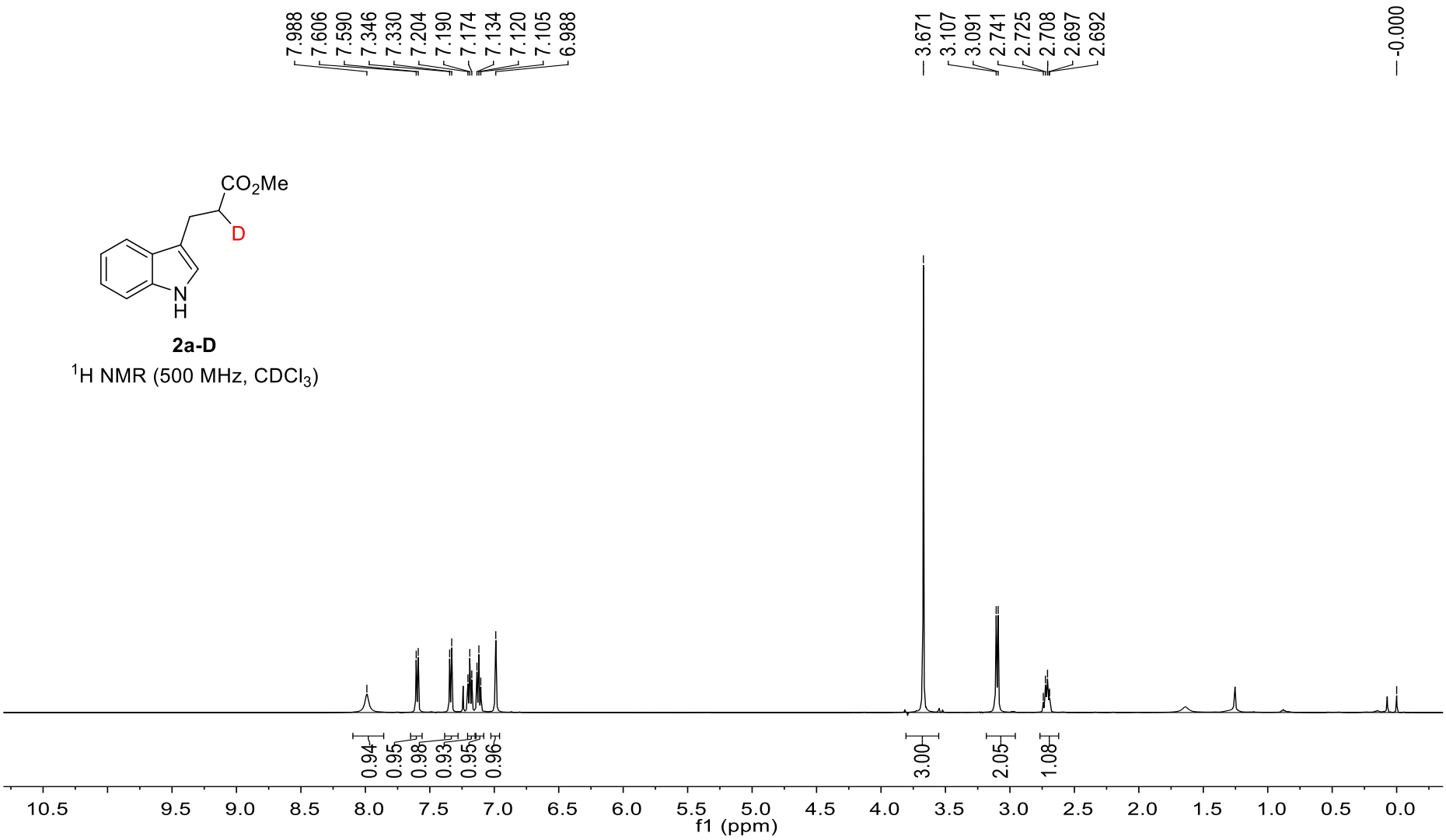

169.918
76.258
76.003
75.749
63.981
50.255
29.745
29.403
22.422
14.571
SMe
O
HO
N
H
H
2v
13C NMR (125 MHz, CDCl3)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

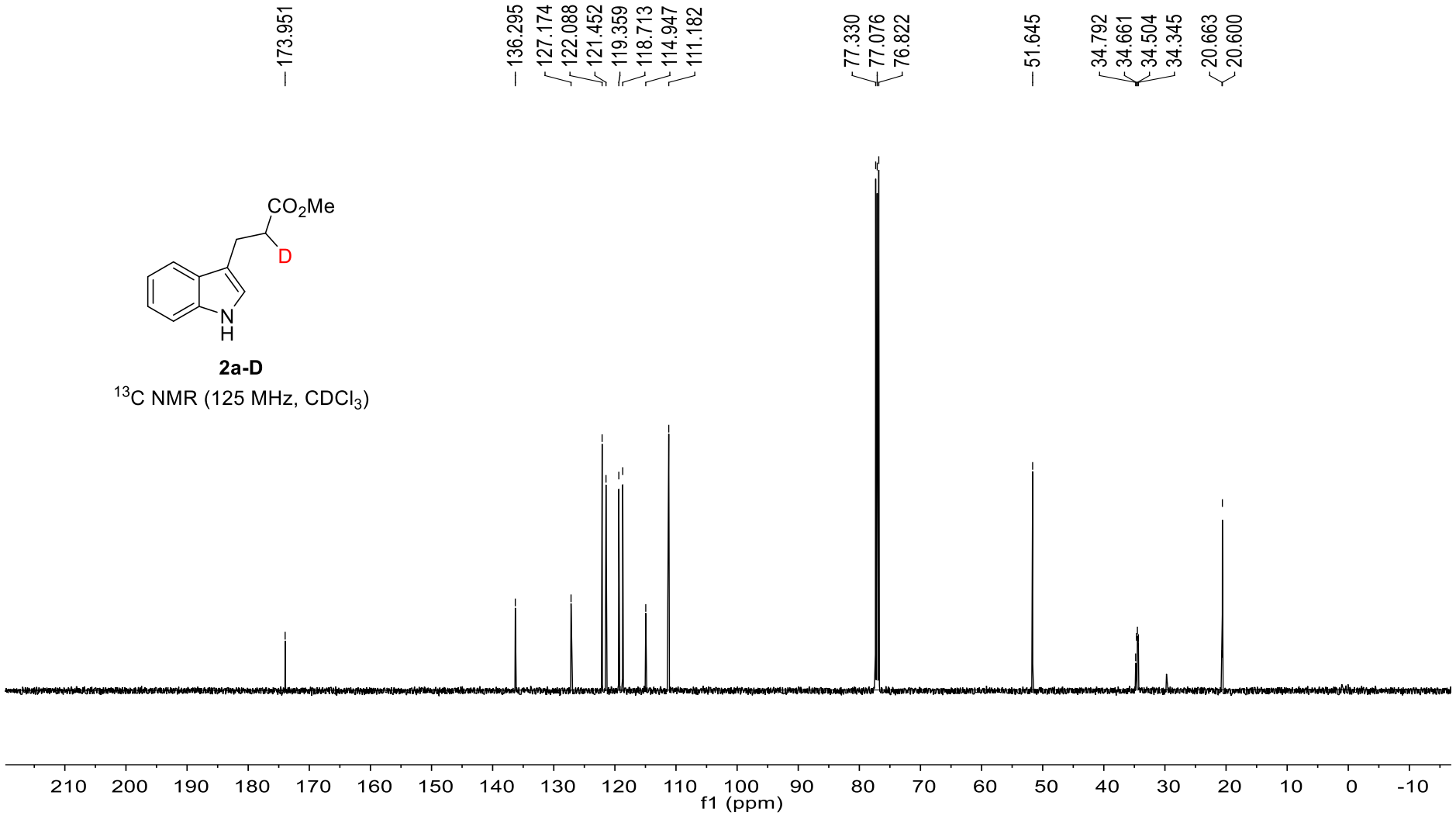

7.837
7.821
7.376
7.360
3.036
2.457
0.000
O
S
O
H
Me
2w
^{1}H NMR (500 MHz, $CDCl_3$)
2.00
2.07
3.16
3.09
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


143.648
136.726
128.938
126.369
76.260
76.006
75.753
43.604
20.602
O
S
O
H
Me
2w
13C NMR (125 MHz, CDCl3)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


7.181
7.165
6.991
6.975
6.888
2.927
2.907
2.893
2.876
2.861
2.854
2.846
2.839
2.833
2.819
2.805
2.791
2.281
2.257
1.888
1.873
1.861
1.847
1.761
1.754
1.748
1.734
1.727
1.720
1.709
1.695
1.686
1.672
1.660
1.613
1.606
1.599
1.592
1.585
1.578
1.571
1.482
1.456
1.421
1.414
1.395
1.388
1.368
1.357
1.352
1.332
1.327
1.228
1.214
1.179
0.940
Me
Me
Me
Me
H
2x
1H NMR (500 MHz, CDCl3)
1.00
1.00
0.98
3.25
1.09
1.22
2.47
1.37
3.95
6.37
3.12
3.40
3.00
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


147.647
145.420
134.974
126.846
124.317
123.808
77.308
77.055
76.801
50.439
41.755
38.869
37.552
33.474
33.372
30.543
24.946
24.052
24.033
21.658
19.365
19.140
Me
Me
Me
Me
H
2x
13C NMR (125 MHz, CDCl3)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


7.988
7.606
7.590
7.346
7.330
7.204
7.190
7.174
7.134
7.120
7.105
6.988
3.671
3.107
3.091
2.741
2.725
2.708
2.697
2.692
-0.000
CO2Me
D
N
H
2a-D
1H NMR (500 MHz, CDCl3)
0.94
0.95
0.98
0.93
0.95
0.96
3.00
2.05
1.08
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


173.951
136.295
127.174
122.088
121.452
119.359
118.713
114.947
111.182
77.330
77.076
76.822
51.645
34.792
34.661
34.504
34.345
20.663
20.600
CO2Me
D
N
H
2a-D
13C NMR (125 MHz, CDCl3)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)