Palladium-Catalyzed Aerobic Intramolecular Aminoacetoxylation of Alkenes Enabled by Catalytic Nitrate

Jiaming Li, Robert H. Grubbs* and Brian M. Stoltz*

The Warren and Katharine Schlinger Laboratory for Chemistry and Chemical Engineering, Division of Chemistry and Chemical Engineering, California Institute of Technology, Pasadena, California, 91125, United States

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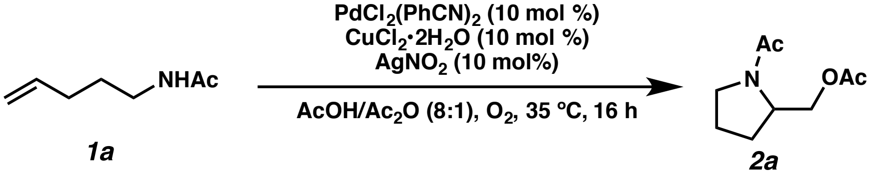
Materials and Methods

Commercial reagents and metal salts were obtained from Sigma-Aldrich, TCI, Combi-Blocks, Alfa Aesar and used without further purification. ^{1}H and ^{13}C NMR spectra were recorded on a Varian 500 MHz, Varian 400 MHz or a Varian 300 MHz spectrometer. High-resolution mass spectra were provided by the California Institute of Technology Mass Spectrometry Facility, using JEOL JMS-600H High Resolution Mass Spectrometer. Gas chromatography data was obtained using an Agilent 6850 FID gas chromatograph equipped with a HP-5 (5%-phenyl)-methylpolysiloxane capillary column (Agilent). Response factors relative to the internal standard tridecane were collected for the substrate N-(pent-4-en-1-yl)acetamide (**1a**), and the product (1-acetylpyrrolidin-2-yl)methyl acetate (**2a**) following literature procedures.[1]

Selected Optimization Experiments

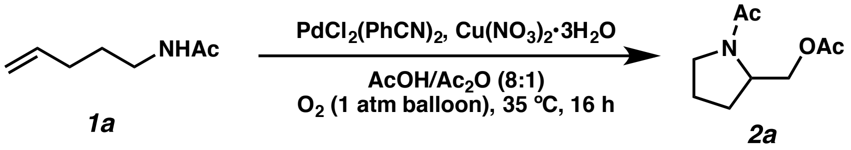
Table S1. Initial Control Experiment from Standard Diacetoxylation Conditions



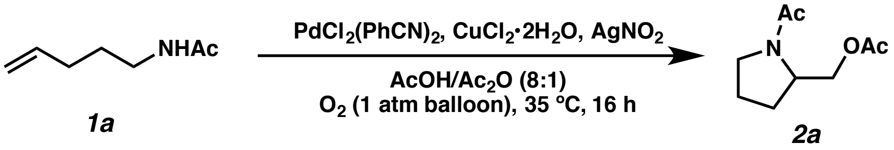
entry	conditions	conversion (%)	yield (%)[a]
1	no change	100	50
2	no $AgNO_2$	99	0
3	no $CuCl_2$	97	34
4	no $CuCl_2$, $AgNO_2$	86	0
5	no O_2	15	2

Observed by-product:

Table S2. Catalysts Ratio Studies



entry	$PdCl_2(PhCN)_2$ (mol%)	$Cu(NO_3)_2•3H_2O$ (mol%)	yield (%)[a]
1	5	5	51
2	5	7.5	52
3	5	10	52
4	10	5	17



entry	$PdCl_2(PhCN)_2$ (mol%)	$CuCl_2•2H_2O$ (mol%)	$AgNO_2$ (mol%)	yield (%)[a]
5	5	5	5	26
6	5	5	10	52

[a] Yields are determined by GC analysis with tridecane as an internal standard in Table S1 and S2.

General Experimental Procedures

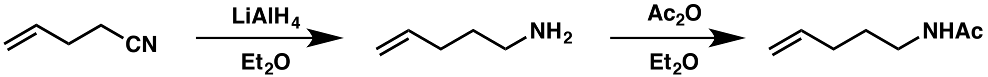
General procedure A for isolation scale (0.5 mmol) aminoacetoxylation of alkenes:

$PdCl_2(PhCN)_2$ (0.025 mmol, 9.6 mg), $Cu(NO_3)_2 \cdot 3H_2O$ (0.025 mmol, 6.0 mg) and alkene substrate (0.5 mmol) were weighed into a 50 mL flame-dried round bottom flask (14/20 neck) with a stir bar. The flask was sparged with oxygen (1 atm) from an oxygen balloon, through a vacuum adapter (14/20). AcOH (9.0 mL) and Ac_2O (1.5 mL) were premixed in a separated vial and sparged with oxygen (through needle and oxygen balloon) for 2 minutes. The oxygenated solvent mixture was then transferred into the flask *via* syringe. The reaction was then allowed to stir at 23 °C for 16 h under an atmosphere of oxygen (1 atm balloon). The solvent was removed under reduced pressure. Dichloromethane (20 mL) was then added and the resulting mixture was washed with saturated $NaHCO_3$ (20 mL). The aqueous layer was extracted with dichloromethane (2 × 20 mL) and the combined organic layer was dried over $MgSO_4$. The solvent was removed under reduced pressure and the crude mixture was purified by silica gel chromatography.

General procedure B for analytical scale (0.2 mmol) aminoacetoxylation of 1a:

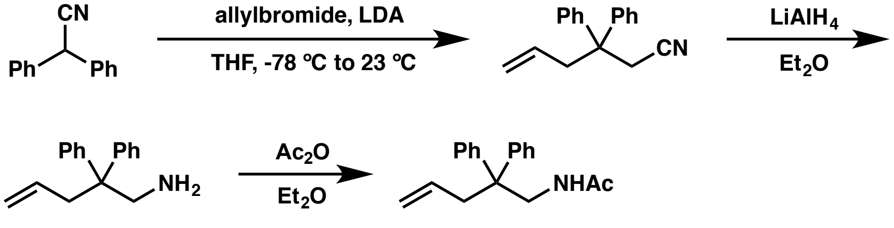
$PdCl_2(PhCN)_2$ (0.01 mmol, 3.8 mg), $Cu(NO_3)_2 \cdot 3H_2O$ (0.01 mmol, 2.4 mg) and alkene substrate (0.5 mmol) were weighed into a 2-dram screw-cap vial charged with a stir bar. The vial was sparged with oxygen (1 atm balloon) for 45 seconds. AcOH (3.6 mL), Ac_2O (0.6 mL) and tridecane (0.00246 mmol, 6 µL) were subsequently added *via* syringe. The solution was saturated with oxygen by an additional 45 seconds of sparging. The reaction was then allowed to stir at 23 °C for 16 h under an atmosphere of oxygen (balloon). Next, an aliquot (*ca.* 0.2 mL) was injected into a 2 mL vial containing an estimated 1 mL of premixed EtOAc/pyridine solution (3:1) to quench the reaction. The resulting solution was subjected to GC analysis to determine yield.

Substrate Synthesis and Characterization Data



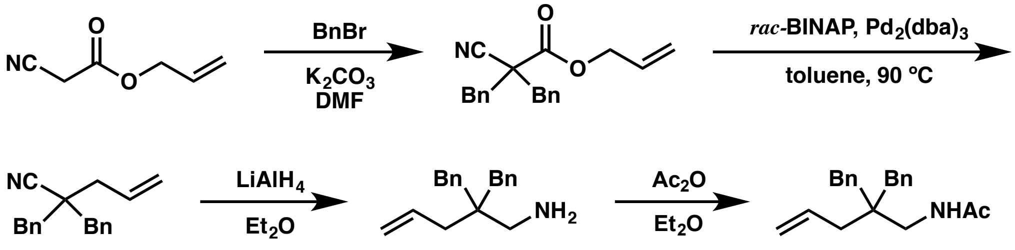
1a

N-(pent-4-en-1-yl)acetamide (1a): Prepared according to the literature procedure from 4-pentenitrile[2] as a colorless oil (1.34 g, 52% yield over 2 steps). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.59 (bs, 1H), 5.73 (ddt, J = 16.9, 10.1, 6.6 Hz, 1H), 5.10 – 4.82 (m, 2H), 3.17 (td, J = 7.3, 5.8 Hz, 2H), 2.02 (m, 2H), 1.91 (s, 3H), 1.54 (ddd, J = 14.7, 7.9, 6.8 Hz, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.4, 137.7, 115.0, 39.1, 31.0, 28.6, 23.1; HRMS (FAB+) *m/z* calc'd for $C_7H_{14}NO$ $[M+H]^+$: 128.1075, found: 128.1077.



1b

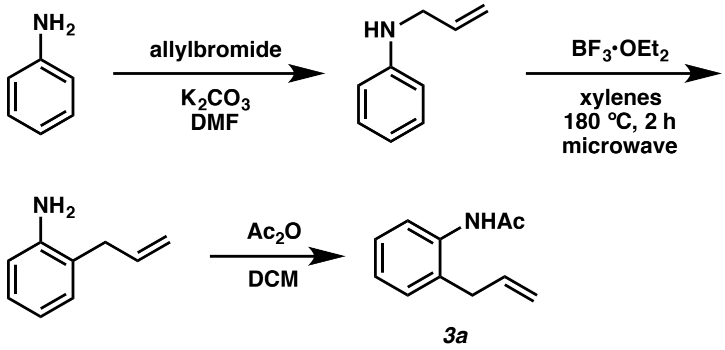
N-(2,2-diphenylpent-4-enyl)acetamide (1b): Synthesized according to literature procedure[3] as a white solid (3.03 g, 54% yield over 3 steps). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33 (dd, J = 8.2, 7.0 Hz, 4H), 7.28 – 7.24 (m, 2H), 7.22 – 7.19 (m, 4H), 5.45 (ddt, J = 16.7, 10.4, 7.1 Hz, 1H), 5.06 (bs, 1H), 5.03 – 4.96 (m, 2H), 3.99 (d, J = 5.8 Hz, 2H), 2.87 (dt, J = 7.2, 1.2 Hz, 2H), 1.87 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.9, 145.2, 133.6, 128.3, 128.0, 126.6, 118.7, 50.2, 46.0, 42.1, 23.4; HRMS (FAB+) *m/z* calc'd for $C_{19}H_{22}NO$ $[M+H]^+$: 280.1701, found 280.1702.



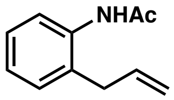
1c

N-(2,2-dibenzylpent-4-en-1-yl)acetamide (1c): 2,2-dibenzyl-4-pentenenitrile could be prepared from allyl 2-cyanoacetate according to the literature procedure[4] as a colorless liquid (1.13 g, 72% yield). Then, $LiAlH_4$ (0.9 g, 23 mmol) was weighed into a flame-dried flask, and the flask was exchanged with vacuum/argon 3 times. 100 mL Et_2O was added to flask through cannula transfer. 2,2-dibenzyl-4-pentenenitrile (1.13 g, 4.3 mmol) was dissolved into 10 mL Et_2O and added *via* syringe. The reaction was stirred overnight and quenched with water and 1M NaOH solution. After the grey color of suspension turned white completely, the reaction mixture was filtered through celite. The filtrate was dried over Na_2SO_4 and concentrated *in vacuo* without purification. Then the crude 2,2-dibenzylpent-4-en-1-amine was dissolved into 50 mL Et_2O and acetic anhydride (1.2 mL, 12.9 mmol) was added. After 3 h, the reaction mixture was washed with saturate $NaHCO_3$ solution (20 mL), and then the aqueous layer was extracted with EtOAc (2 × 20 mL). The combined organic layers was concentrated *in vacuo* and purified by silica gel chromatography (50% EtOAc in hexanes). Product **1c** was obtained as a colorless oil (976 mg, 74% yield over last two steps). ^1H NMR (500 MHz, $CDCl_3$) δ 7.35 – 7.30 (m, 4H), 7.30 – 7.25 (m, 2H), 7.23 – 7.20 (m, 4H), 6.01 (ddt, J = 17.3, 10.2, 7.2 Hz, 1H), 5.24 – 5.13 (m, 2H), 5.02 (bs, 1H), 3.27 (d, J = 5.9 Hz, 2H), 2.76 – 2.66 (m, 4H), 2.16 (dt, J = 7.2, 1.4 Hz, 2H), 1.74 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.8, 137.8, 134.5, 130.6, 128.3, 126.6, 118.8, 45.7, 43.4, 41.4, 39.4, 23.3 (one quaternary carbon signal unresolved); HRMS (FAB+) *m/z* calc'd for $C_{21}H_{26}NO$ $[M+H]^+$: 308.2014, found 308.2013.

General procedure C: synthesis of *o*-allylaniline derivatives 3a, 3b, 3d, 3e

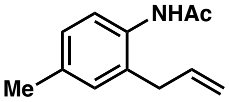


N-allylanilines can be prepared from the literature procedure.[5] In a 5 mL microwave tube, a solution of N-allylaniline (665 mg, 5 mmol) in 4 mL xylenes was added boron trifluoride etherate (0.7 mL, 5,5 mmol) under an argon atmosphere. Then the microwave tubes was sealed and heated to 180 °C in the microwave reactor for 2 h. After cooling down to room temperature, the reaction mixture was poured into 2 M NaOH solution (10 mL), and extracted with EtOAc (10 mL × 2). The combined organic layers were dried over $MgSO_4$, and concentrated *in vacuo*. The crude *o*-allylaniline was dissolved in DCM (30 mL) and acetic anhydride (1.4 mL, 15 mmol) was added dropwise. After reacting 2 h in room temperature, the reaction mixture was poured into saturated $NaHCO_3$ and extracted with EtOAc (2 × 30 mL). The combined organic layers was dried over $MgSO_4$. The solvent was removed by rotary evaporation, and the residue was purified by column chromatography (30% EtOAc in hexanes).



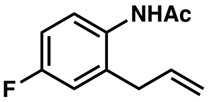
3a

N-(2-allylphenyl)acetamide (3a): Prepared according to General Procedure C as a white solid (257 mg, 44% yield over 2 steps). ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.86 (dd, J = 8.3, 4.0 Hz, 1H), 7.32 – 7.26 (m, 1H), 7.20 (dd, J = 7.7, 1.6 Hz, 1H), 7.14 (t, J = 7.4 Hz, 1H), 6.00 (ddt, J = 16.6, 11.4, 6.2 Hz, 1H), 5.25 – 5.08 (m, 2H), 3.41 (d, J = 6.0, 2H), 2.17 (s, 3H); ^{13}C NMR (126 MHz, CDCl$_3$) δ 168.4, 136.4, 136.0, 130.2, 130.0, 127.5, 125.4, 123.9, 116.6, 37.0, 24.3; HRMS (FAB+) *m/z* calc'd for $C_{11}H_{14}NO$ [M+H]$^+$: 176.1075, found: 176.1083.



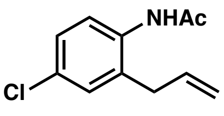
3b

N-(2-allyl-4-methylphenyl)acetamide (3b): Prepared according to General Procedure C from the corresponding N-allyl-4-methylaniline as a white solid (342 mg, 36% yield over 2 steps). ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.66 (d, J = 8.1 Hz, 1H), 7.18 (bs, 1H), 7.08 (dd, J = 8.2, 2.1 Hz, 1H), 7.01 (d, J = 2.0 Hz, 1H), 5.98 (ddt, J = 16.5, 10.1, 6.1 Hz, 1H), 5.23 – 5.07 (m, 2H), 3.36 (dd, J = 6.2, 1.8 Hz, 2H), 2.33 (s, 3H), 2.16 (s, 3H); ^{13}C NMR (126 MHz, CDCl$_3$) δ 168.3, 136.5, 135.2, 133.3, 130.8, 130.3, 128.0, 124.2, 116.3, 36.9, 24.2, 20.9; HRMS (FAB+) *m/z* calc'd for $C_{12}H_{16}NO$ [M+H]$^+$: 190.1232, found 190.1233.



3d

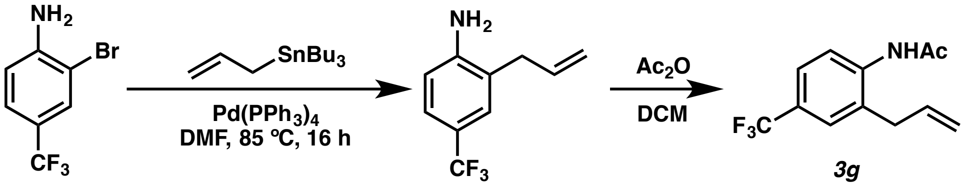
***N*-(2-allyl-4-fluorophenyl)acetamide (3d):** Prepared according to General Procedure C from the corresponding N-allyl-4-fluoroaniline as a white solid (425 mg, 44% yield over 2 steps). ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.72 (dd, J = 8.9, 5.4 Hz, 1H), 7.12 (bs, 1H), 6.97 (td, J = 8.4, 3.0 Hz, 1H), 6.93 (dd, J = 9.1, 3.0 Hz, 1H), 5.97 (ddt, J = 17.2, 10.1, 6.1 Hz, 1H), 5.26 – 5.08 (m, 2H), 3.37 (dt, J = 6.1, 1.7 Hz, 2H), 2.18 (s, 3H); ^{13}C NMR (126 MHz, CDCl$_3$) δ 168.4, 160.1 (d, J = 244.7 Hz), 135.5, 133.2 (d, J = 7.4 Hz), 131.7 (d, J = 2.6 Hz), 126.1 (d, J = 8.4 Hz), 117.1, 116.7 (d, J = 22.8 Hz), 114.0 (d, J = 22.1 Hz), 36.7, 24.1; HRMS (FAB+) *m/z* calc'd for $C_{11}H_{13}NOF$ [M+H]$^+$: 194.0981, found 194.0977.



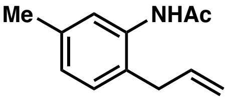
3e

***N*-(2-allyl-4-chlorophenyl)acetamide (3e):** Prepared according to General Procedure C from the corresponding N-allyl-4-chloroaniline as a white solid (442 mg, 42% yield over 2 steps). ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.90 – 7.73 (m, 1H), 7.28 (bs, 1H), 7.25 – 7.22 (m, 1H), 7.18 (m, 1H), 6.00 – 5.90 (m, 1H), 5.26 – 5.09 (m, 2H), 3.36 (dt, J = 6.4, 1.9 Hz, 2H), 2.16 (s, 3H); ^{13}C NMR (126 MHz, CDCl$_3$) δ 168.3, 135.4, 134.6, 131.7, 130.3, 130.0, 127.4, 125.0, 117.2, 36.6, 24.3; HRMS (FAB+) *m/z* calc'd for $C_{11}H_{13}NOCl$ $[M+H]^+$: 210.0686, found 210.0683.

General procedure D: synthesis of *o*-allyl aniline derivatives[6]

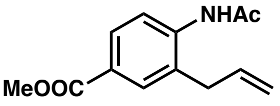


4-Amino-3-bromobenzotrifluoride (960 mg, 4 mmol) dissolved in dry DMF (10 mL) was added allyltributyltin (1.50 mL, 4.8 mmol) under argon at room temperature. Pd(PPh$_3$)$_4$ (457 mg, 0.39 mmol) were then added and the reaction mixture was stirred at 85 °C for 16 h. The reaction mixture was then cooled down to room temperature and diluted with water (10 mL). The aqueous layer was extracted with Et$_2$O (3 × 10 mL). The combined organic layers were dried over MgSO$_4$, filtered and concentrated under reduced pressure. Purification by flash column chromatography gave 2-allyl-4-(trifluoromethyl)aniline (685 mg, 85% yield) as yellow oil. Then 2-allyl-4-(trifluoromethyl)aniline was dissolved in DCM (30 mL) and acetic anhydride (1.0 mL, 10.2 mmol) was added dropwise. After reacting 2 h in room temperature, the reaction mixture was poured into saturated NaHCO$_3$ and extracted with EtOAc (2 × 30 mL). The combined organic layers were dried over MgSO$_4$. The solvent was removed by rotary evaporation, and the residue was purified by column chromatography (30% EtOAc in hexanes).



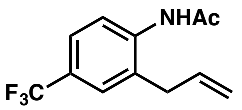
3c

N-(2-allyl-5-methylphenyl)acetamide (3c): Prepared according to General Procedure D from the corresponding 2-bromo-5-methylaniline as a white solid (605 mg, 80% yield over 2 steps). ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.68 (m, 1H), 7.23 (bs, 1H), 7.08 (d, J = 7.7 Hz, 1H), 6.96 – 6.94 (m, 1H), 5.98 (ddt, J = 16.5, 10.1, 6.1 Hz, 1H), 5.21 – 5.07 (m, 2H), 3.36 (dt, J = 6.3, 1.7 Hz, 2H), 2.35 (s, 3H), 2.16 (s, 3H); ^{13}C NMR (126 MHz, CDCl$_3$) δ 168.4, 137.2, 136.7, 135.8, 130.0, 127.1, 126.2, 124.5, 116.3, 36.6, 24.3, 21.2; HRMS (FAB+) *m/z* calc'd for $C_{12}H_{16}NO$ $[M+H]^+$: 190.1232, found 190.1237.



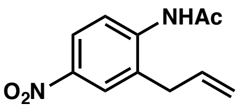
3f

Methyl 4-acetamido-3-allylbenzoate (3f): Prepared according to General Procedure D from the corresponding methyl 4-amino-3-bromobenzoate as a white solid (451 mg, 48% yield over 2 steps). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.15 – 8.09 (m, 1H), 7.95 – 7.91 (m, 1H), 7.87 (bs, 1H), 7.57 – 7.50 (m, 1H), 5.97 (tdt, J = 11.1, 10.1, 6.0 Hz, 1H), 5.28 – 5.10 (m, 2H), 3.90 (s, 3H), 3.45 – 3.43 (m, 2H), 2.17 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.3, 166.7, 140.6, 135.6, 131.7, 129.2, 128.1, 126.0, 121.9, 117.3, 52.1, 36.9, 24.6; HRMS (FAB+) *m/z* calc'd for $C_{13}H_{16}NO_3$ $[M+H]^+$: 234.1130, found 234.1122.



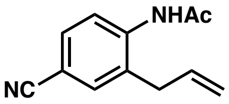
3g

N-(2-allyl-4-(trifluoromethyl)phenyl)acetamide (3g): Prepared according to General Procedure D as a white solid (583 mg, 60% yield over 2 steps). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.10 (d, J = 8.5 Hz, 1H), 7.51 (dd, J = 8.5, 2.2 Hz, 1H), 7.44 (d, J = 2.2 Hz, 1H), 5.97 (ddt, J = 17.3, 10.1, 6.1 Hz, 1H), 5.29 – 5.12 (m, 2H), 3.44 (dt, J = 6.1, 1.7 Hz, 2H), 2.18 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.5, 139.3, 135.2, 129.4, 127.1 (q, J = 4.2 Hz), 126.7 (q, J = 32.6 Hz), 124.6 (q, J = 3.8 Hz), 124.0 (q, J = 272 Hz), 122.9, 117.6, 36.7, 24.4; HRMS (FAB+) *m/z* calc'd for $C_{12}H_{13}NOF_3$ $[M+H]^+$: 244.0949, found 244.0952.



3h

N-(2-allyl-4-nitrophenyl)acetamide (3h): Prepared according to General Procedure D from the corresponding 2-bromo-4-nitroaniline as a white solid (183 mg, 21% yield over 2 steps). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.35 (d, J = 9.1 Hz, 1H), 8.16 (dd, J = 9.0, 2.7 Hz, 1H), 8.10 (d, J = 2.7 Hz, 1H), 7.57 (bs, 1H), 6.00 (ddt, J = 16.5, 10.1, 6.1 Hz, 1H), 5.42 – 5.08 (m, 2H), 3.51 (dt, J = 6.1, 1.8 Hz, 2H), 2.22 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.3, 143.6, 142.3, 134.5, 128.4, 125.6, 123.5, 121.6, 118.3, 36.8, 24.8; HRMS (FAB+) *m/z* calc'd for $C_{11}H_{13}N_2O_3$ $[M+H]^+$: 221.0926, found 221.0919.

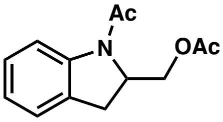


3i

***N*-(2-allyl-4-cyanophenyl)acetamide (3i):** Prepared according to General Procedure D from the corresponding 4-amino-3-bromobenzonitrile as a white solid (460 mg, 58% yield over 2 steps). ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.23 (d, J = 8.5 Hz, 1H), 7.56 (dd, J = 8.5, 1.9 Hz, 1H), 7.51 (bs, 1H), 7.48 (d, J = 1.9 Hz, 1H), 5.97 (ddt, J = 16.8, 10.1, 6.1 Hz, 1H), 5.40 – 5.03 (m, 2H), 3.43 (dt, J = 6.1, 1.8 Hz, 2H), 2.20 (s, 3H); ^{13}C NMR (126 MHz, CDCl$_3$) δ 168.3, 140.5, 134.7, 133.9, 131.8, 128.9, 122.4, 118.8, 118.1, 107.6, 36.5, 24.7; HRMS (FAB+) *m/z* calc'd for $C_{12}H_{13}N_2O$ $[M+H]^+$: 201.1028, found 201.1022.

Product characterization

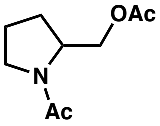
Mixture of rotamer may occur in most products. A representative VT-NMR experiment was conducted on the product **4a**. At 75 °C in DMSO solvent, only one rotamer is predominantly appeared in ^{1}H NMR and the characterization data is shown below.



4a

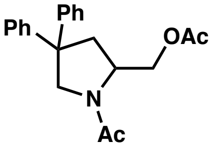
(1-acetylindolin-2-yl)methyl acetate (4a): Prepared according to the general procedure A to provide **4a** (102 mg, 87% yield) as a colorless oil. When the reaction was conducted under air (Table 3, entry 2), an air balloon was used instead of oxygen balloon, which provide **4a** (94 mg, 80% yield) as a colorless oil. ^{1}H NMR (400 MHz, DMSO, 75 °C) δ 7.77 (bs, 1H), 7.23 (d, J = 7.4 Hz, 1H), 7.14 (t, J = 7.8 Hz, 1H), 6.99 (t, J = 7.4 Hz, 1H), 4.82 – 4.74 (m, 1H), 4.08 (d, J = 5.7 Hz, 2H), 3.33 (dd, J = 16.3, 9.2 Hz, 1H), 2.83 (d, J = 16.3 Hz, 1H), 2.26 (s, 3H), 1.87 (s, 3H); ^{13}C NMR (126 MHz, CDCl$_3$) mixture of rotamers, chemical shifts reported are from major rotamer δ 170.7, 168.7, 141.9, 129.7, 127.7, 124.8, 124.2, 118.1, 64.9, 58.5, 32.1, 23.4, 20.7; HRMS (FAB+) *m/z* calc'd for $C_{13}H_{16}NO_3$ $[M+H]^+$: 234.1130, found 234.1127.

For ^{1}H and ^{13}C NMR characterization of the rest of compounds, chemical shifts of only the major rotamer are reported. In ^{1}H and ^{13}C NMR spectra of products, only the major rotamer peaks are integrated.



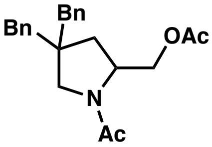
2a

(1-acetylpyrrolidin-2-yl)methyl acetate (2a) : Prepared according to the general procedure A to provide **2a** (64 mg, 69% yield) as a colorless liquid. ^{1}H NMR (500 MHz, CDCl$_3$) mixture of rotamers, chemical shifts reported are from the major rotamer δ 4.32 (tt, J = 7.4, 3.7 Hz, 1H), 4.15 (dd, J = 10.8, 3.9 Hz, 1H) 4.09 (dd, J = 10.8, 6.8 Hz, 1H), 3.50 – 3.37 (m, 2H), 2.03 (s, 3H), 2.03 (s, 3H) (two overlapped singlets), 1.96 – 1.88 (m, 3H) 1.86 – 1.81 (m, 1H); ^{13}C NMR (126 MHz, CDCl$_3$) δ 170.8, 169.7, 63.8, 55.2, 47.9, 27.5, 24.0, 21.9, 20.9; HRMS (FAB+) *m/z* calc'd for $C_9H_{16}NO_3$ [M+H]$^+$: 186.1130, found 186.1134.



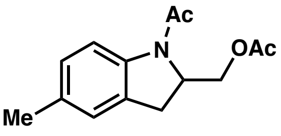
2b

(1-acetyl-4,4-diphenylpyrrolidin-2-yl)methyl acetate (2b): Prepared according to the general procedure A to provide **2b** (126 mg, 75% yield) as a white solid. ^{1}H NMR (500 MHz, DMSO, 23 °C) mixture of rotamers, chemical shifts reported are from major rotamer δ 7.46 – 7.43 (m, 2H), 7.38 – 7.35 (m, 2H), 7.33 – 7.28 (m, 4H), 7.19 (ddt, J = 9.0, 7.9, 1.4 Hz, 2H), 4.68 (dd, J = 11.2, 2.0 Hz, 1H), 4.23 (dd, J = 10.6, 3.5 Hz, 1H), 4.06 (dd, J = 10.6, 6.3 Hz, 1H), 3.92 (dd, J = 10.0, 6.7, 1H), 3.82 (d, J = 11.2 Hz, 1H), 3.12 (ddd, J = 13.0, 7.1, 1.9 Hz, 1H), 2.30 (dd, J = 13.0, 9.2 Hz, 1H), 2.03 (s, 3H), 2.00 (s, 3H); ^{13}C NMR (126 MHz, CDCl$_3$) δ 170.8, 169.3, 145.2, 144.6, 128.8, 128.7, 126.8, 126.8, 126.6, 126.2, 64.1, 58.5, 55.0, 53.2, 40.1, 23.1, 20.9; HRMS (FAB+) *m/z* calc'd for $C_{21}H_{24}NO_3$ [M+H]$^+$: 338.1756, found 338.1757.



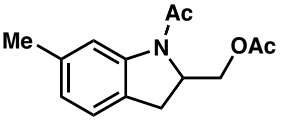
2c

(1-acetyl-4,4-dibenzylpyrrolidin-2-yl)methyl acetate (2c): Prepared according to the general procedure A to provide **2c** (152 mg, 83% yield) as a white solid. ^{1}H NMR (500 MHz, CDCl$_3$) mixture of rotamers, chemical shifts reported are from major rotamer δ 7.38 – 7.22 (m, 6H), 7.19 – 7.09 (m, 4H), 4.33 (dd, J = 11.1, 4.1 Hz, 1H), 4.29 – 4.20 (m, 1H), 4.17 (dd, J = 11.1, 2.5 Hz, 1H), 3.31 (dd, J = 10.5, 1.6 Hz, 1H), 3.18 (d, J = 10.5 Hz, 1H), 2.80 (s, 2H), 2.69 (s, 2H), 2.03 (s, 3H), 1.93 – 1.89 (m, 1H), 1.79 (dd, J = 13.1, 9.1 Hz, 1H), 1.72 (s, 3H); ^{13}C NMR (126 MHz, CDCl$_3$) δ 170.8, 169.3, 137.5, 137.1, 130.8, 130.3, 128.4, 128.3, 126.9, 126.6, 63.6, 55.0, 54.6, 45.7, 43.9, 41.8, 35.0, 23.2, 20.6; HRMS (FAB+) *m/z* calc'd for $C_{23}H_{28}NO_3$ [M+H]$^+$: 366.2069, found 366.2053.



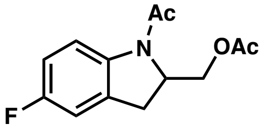
4b

(1-acetyl-5-methylindolin-2-yl)methyl acetate (4b): Prepared according to the general procedure A to provide **4b** (110 mg, 89% yield) as a colorless oil. ^{1}H NMR (500 MHz, CDCl$_3$) mixture of rotamers, chemical shifts reported are from major rotamer δ 7.98 (d, J = 8.1 Hz, 1H), 7.01 (m, 2H), 4.61 (m, 1H), 4.25 – 4.08 (m, 2H), 3.35 (dd, J = 16.1, 8.8 Hz, 1H), 2.83 (d, J = 16.0 Hz, 1H), 2.35 (s, 3H), 2.32 (s, 3H), 2.06 (s, 3H); ^{13}C NMR (126 MHz, CDCl$_3$) δ 170.7, 168.4, 139.6, 133.8, 129.8, 128.1, 125.4, 117.8, 64.8, 58.6, 32.0, 23.3, 21.0, 20.8; HRMS (FAB+) *m/z* calc'd for $C_{14}H_{18}NO_3$ [M+H]$^+$: 248.1287, found 248.1280.



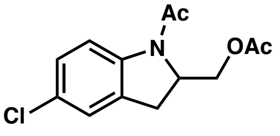
4c

(1-acetyl-6-methylindolin-2-yl)methyl acetate (4c): Prepared according to the general procedure A to provide **4c** (118 mg, 95% yield) as a colorless oil. ^{1}H NMR (500 MHz, CDCl$_3$) mixture of rotamers, chemical shifts reported are from major rotamer δ 7.95 (s, 1H), 7.06 (d, J = 7.6 Hz, 1H), 6.85 (d, J = 7.5 Hz, 1H), 4.60 (m, 1H), 4.19 (dd, J = 11.8, 6.2 Hz, 2H), 3.31 (dd, J = 16.1, 8.8 Hz, 1H), 2.81 (d, J = 15.9 Hz, 1H), 2.35 (s, 3H), 2.34 (s, 3H), 2.04 (s, 3H); ^{13}C NMR (126 MHz, CDCl$_3$) δ 170.7, 168.6, 142.0, 137.6, 126.8, 124.9, 124.4, 118.8, 64.8, 58.8, 31.7, 23.4, 21.6, 20.7; HRMS (FAB+) *m/z* calc'd for $C_{14}H_{18}NO_3$ [M+H]$^+$: 248.1287, found 248.1280.



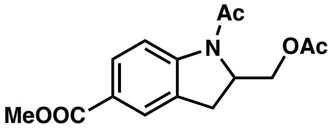
4d

(1-acetyl-5-fluoroindolin-2-yl)methyl acetate (4d). Prepared according to the general procedure A to provide **4d** (110 mg, 88% yield) as a colorless oil. ^{1}H NMR (500 MHz, CDCl$_3$) mixture of rotamers, chemical shifts reported are from major rotamer δ 8.05 (dd, J = 8.4, 4.9 Hz, 1H), 6.97 – 6.83 (m, 2H), 4.63 (m, 1H), 4.20 (dd, J = 11.2, 5.9 Hz, 2H), 3.37 (dd, J = 16.4, 8.9 Hz, 1H), 2.86 (d, J = 16.3 Hz, 1H), 2.34 (s, 3H), 2.03 (s, 3H); ^{13}C NMR (126 MHz, CDCl$_3$) δ 170.6, 168.4, 159.5 (d, J = 243.0 Hz), 134.2 (d, J = 2.7 Hz), 131.8 (d, J = 8.5 Hz), 121.7 (d, J = 7.8 Hz), 115.5 (d, J = 22.3 Hz), 112.0 (d, J = 24.8 Hz), 64.7, 58.8, 32.0, 23.1, 20.7; HRMS (FAB+) *m/z* calc'd for $C_{13}H_{15}NO_3F$ [M+H]$^+$: 252.1036, found 252.1037.



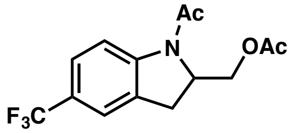
4e

(1-acetyl-5-chloroindolin-2-yl)methyl acetate (4e). Prepared according to the general procedure A to provide **4e** (107 mg, 80% yield) as a yellow oil. ^{1}H NMR (500 MHz, CDCl$_3$) mixture of rotamers, chemical shifts reported are from major rotamer δ 8.03 (d, J = 8.5 Hz, 1H), 7.18 – 7.15 (m, 2H), 4.63 (m, 1H), 4.19 (dd, J = 11.4, 5.8 Hz, 2H), 3.35 (dd, J = 16.4, 8.9 Hz, 1H), 2.86 (d, J = 16.3 Hz, 1H), 2.35 (s, 3H), 2.03 (s, 3H); ^{13}C NMR (126 MHz, CDCl$_3$) δ 170.6, 168.7, 140.7, 131.7, 129.0, 127.6, 124.9, 118.9, 64.7, 58.7, 31.9, 23.2, 20.7; HRMS (FAB+) *m/z* calc'd for $C_{13}H_{15}NO_3Cl$ [M+H]$^+$: 268.0740, found 268.0738.



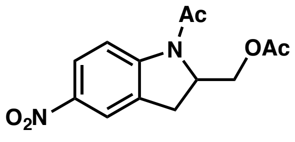
4f

methyl 2-(acetoxymethyl)-1-acetylindoline-5-carboxylate (4f). Prepared according to the general procedure A to provide **4f** (95 mg, 65% yield) as a colorless oil. ^{1}H NMR (500 MHz, CDCl$_3$) mixture of rotamers, chemical shifts reported are from major rotamer δ 8.13 (s, 1H), 7.93 – 7.90 (m, 1H), 7.86 (s, 1H), 4.67 (m, 1H), 4.18 (m, 2H), 3.88 (s, 3H), 3.37 (m, 1H), 2.92 (d, J = 16.1 Hz, 1H), 2.39 (s, 3H), 2.00 (s, 3H); ^{13}C NMR (126 MHz, CDCl$_3$) δ 170.6, 169.0, 166.6, 146.0, 130.1, 126.2, 125.8, 117.2, 114.0, 64.7, 58.9, 52.0, 31.8, 23.5, 20.6; HRMS (FAB+) *m/z* calc'd for $C_{15}H_{18}NO_5$ [M+H]$^+$: 292.1185, found 292.1183.



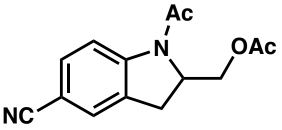
4g

(1-acetyl-5-(trifluoromethyl)indolin-2-yl)methyl acetate (4g). Prepared according to the general procedure A to provide **4g** (88 mg, 58% yield) as a colorless oil. ^{1}H NMR (500 MHz, CDCl$_3$) mixture of rotamers, chemical shifts reported are from major rotamer δ 8.21 (s, 1H), 7.58 – 7.39 (m, 2H), 4.69 (m, J = 8.5 Hz, 1H), 4.23 (m, 2H), 3.41 (m, 1H), 2.96 (d, J = 16.3 Hz, 1H), 2.41 (s, 3H), 2.04 (s, 3H) ^{13}C NMR (126 MHz, CDCl$_3$) δ 170.6, 169.0, 144.8, 130.5, 125.4, 123.1, 121.8, 117.7, 64.6, 58.8, 31.9, 23.4, 20.6 (C–F coupling constants unresolved and one quaternary carbon signal unresolved); HRMS (FAB+) *m/z* calc'd for $C_{14}H_{15}NO_3F_3$ [M+H]$^+$: 302.1004, found 302.1011.



4h

(1-acetyl-5-nitroindolin-2-yl)methyl acetate (4h). Prepared according to the general procedure A to provide **4h** (41 mg, 30% yield) as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) mixture of rotamers, chemical shifts reported are from major rotamer δ 8.24 (s, 1H), 8.17 (dd, J = 8.8, 2.4 Hz, 1H), 8.09 (m, 1H), 4.78 (s, 1H), 4.24 (dd, J = 11.8, 5.1 Hz, 2H), 3.46 (dd, J = 16.5, 9.2 Hz, 1H), 3.03 (d, J = 16.5 Hz, 1H), 2.44 (s, 3H), 2.02 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.6, 169.2, 147.4, 143.9, 124.7, 120.6, 117.3, 64.6, 59.2, 31.6, 23.5, 20.6 (one quaternary carbon signal unresolved); HRMS (FAB+) *m/z* calc'd for $C_{13}H_{15}N_2O_5$ $[M+H]^+$: 279.0981, found 279.0975.



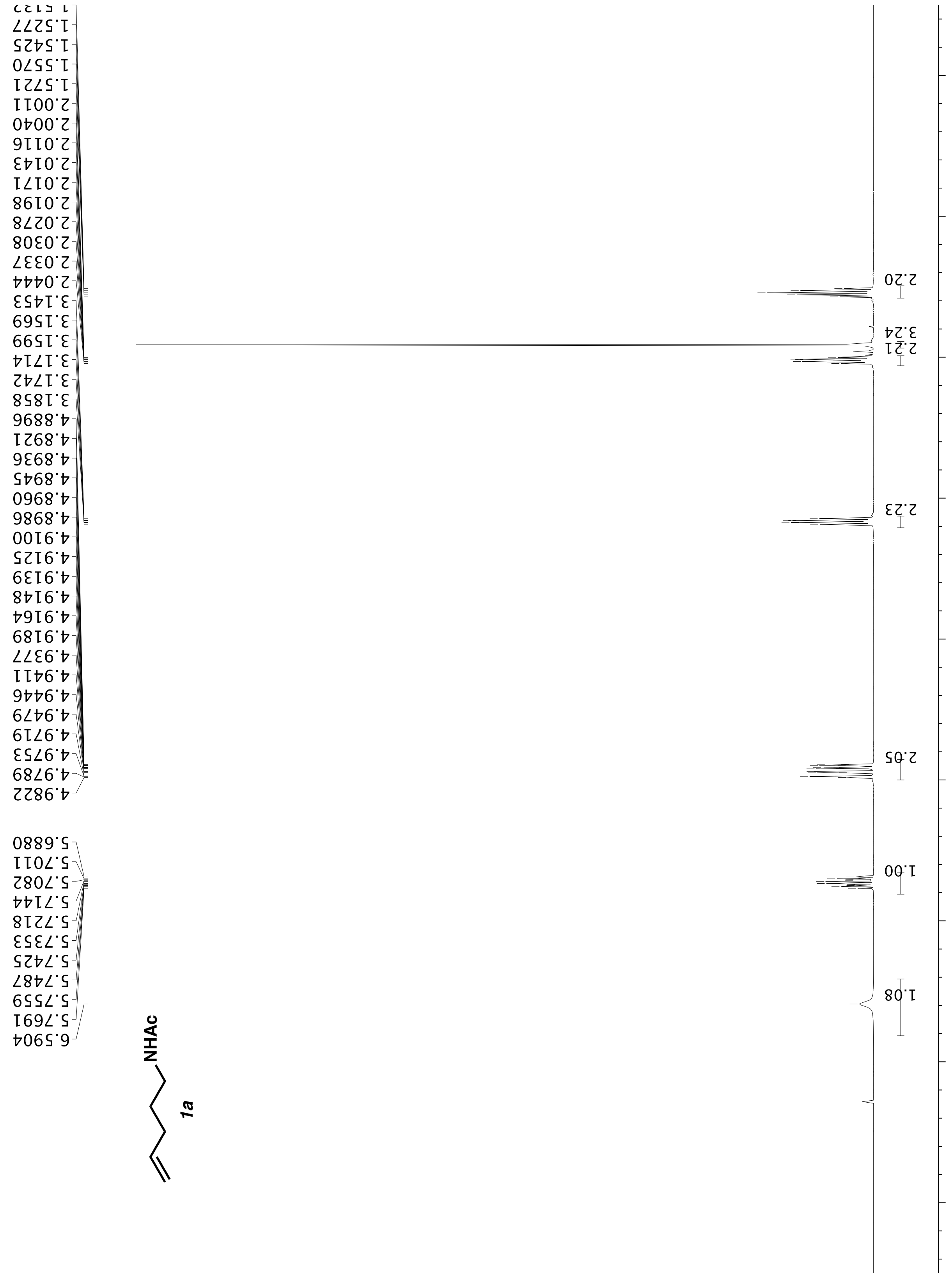
4i

(1-acetyl-5-cyanoindolin-2-yl)methyl acetate (4i). Prepared according to the general procedure A to provide **4i** (41 mg, 32% yield) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) mixture of rotamers, chemical shifts reported are from major rotamer δ 8.22 (s, 1H), 7.59 – 7.52 (m, 1H), 7.48 (s, 1H), 4.71 (m, 1H), 4.22 (d, J = 9.1 Hz, 2H), 3.42 (d, J = 15.1 Hz, 1H), 2.97 (d, J = 16.4 Hz, 1H), 2.41 (s, 3H), 2.02 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.6, 169.2, 145.8, 132.8, 128.4, 119.0, 118.1, 107.0, 64.6, 58.7, 31.7, 23.6, 20.6 (one quaternary carbon signal unresolved); HRMS (FAB+) *m/z* calc'd for $C_{14}H_{15}N_2O_3$ $[M+H]^+$: 259.1083, found 259.1089.

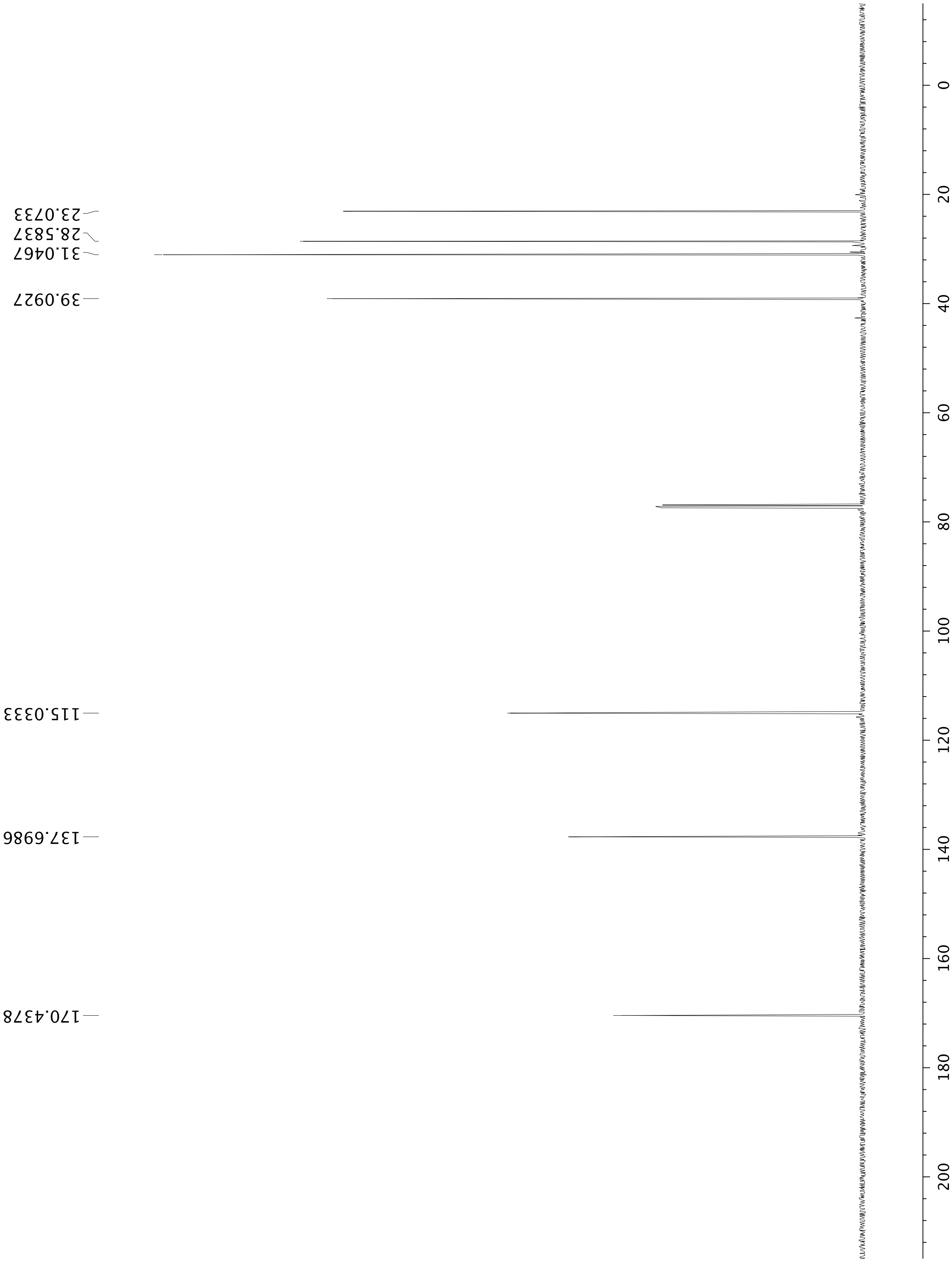
Notes & References

(1) Ritter, T.; Heil, A.; Wenzel, A. G.; Funk, T. W.; Grubbs, R. H. *Organometallics* **2006**, *25*, 5740–5745.
(2) Bertrand, M. B.; Wolfe, J. P. *Tetrahedron* **2005**, *61*, 6447–6459.
(3) Liu, G.-Q.; Li, W.; Li, Y.-M. *Adv. Synth. Catal.* **2013**, *355*, 395–402.
(4) Recio, A., III; Tunge, J. A. *Org. Lett.* **2009**, *11*, 5630–5633.
(5) Yip, K.-T.; Yang, M.; Law, K.-L.; Zhu, N.-Y.; Yang, D. *J. Am. Chem. Soc.* **2006**, *128*, 3130–3131.
(6) Brucelle, F.; Renaud, P. *Org. Lett.* **2012**, *14*, 3048–3051.

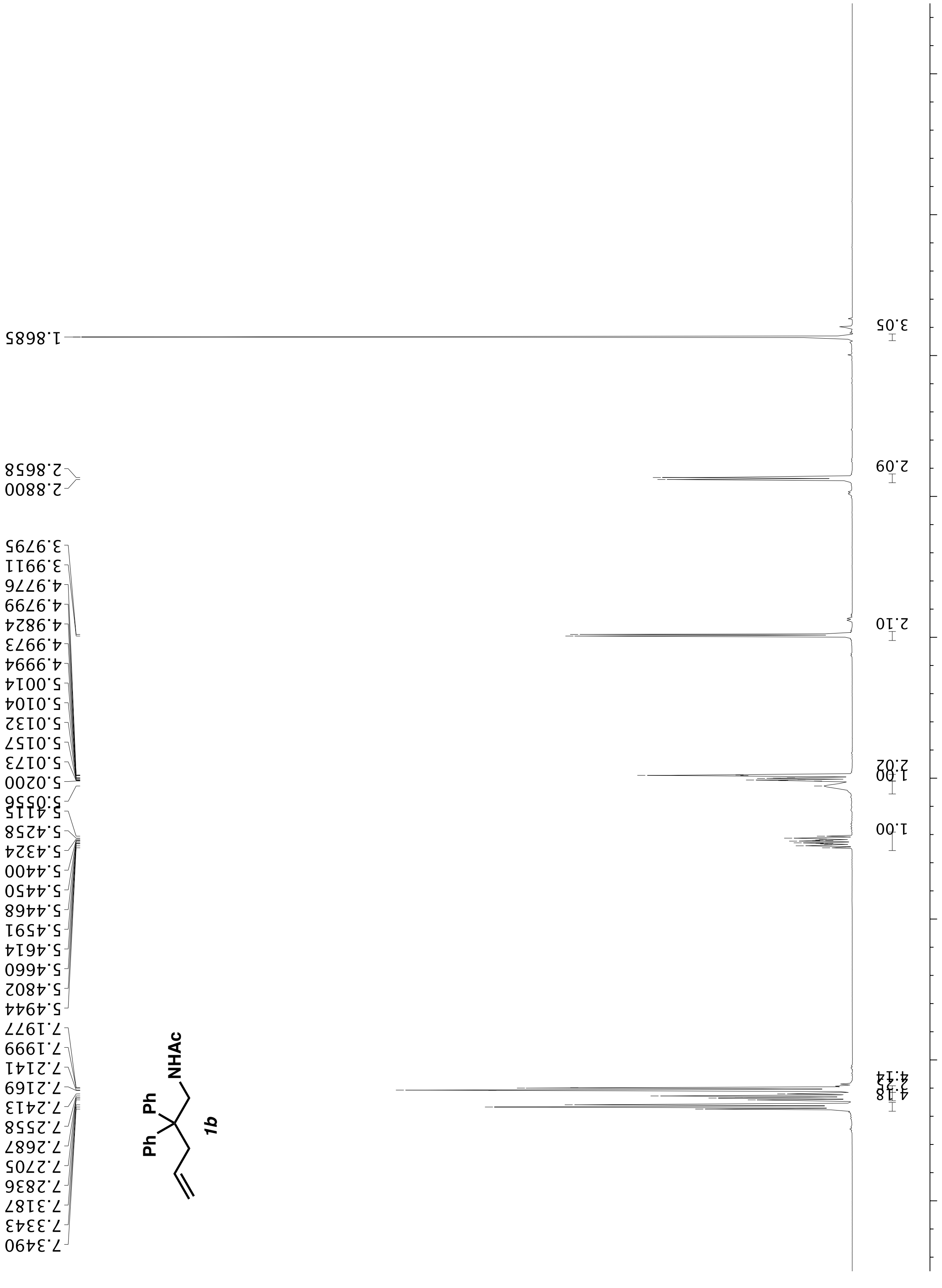
^{1}H and ^{13}C NMR Spectra



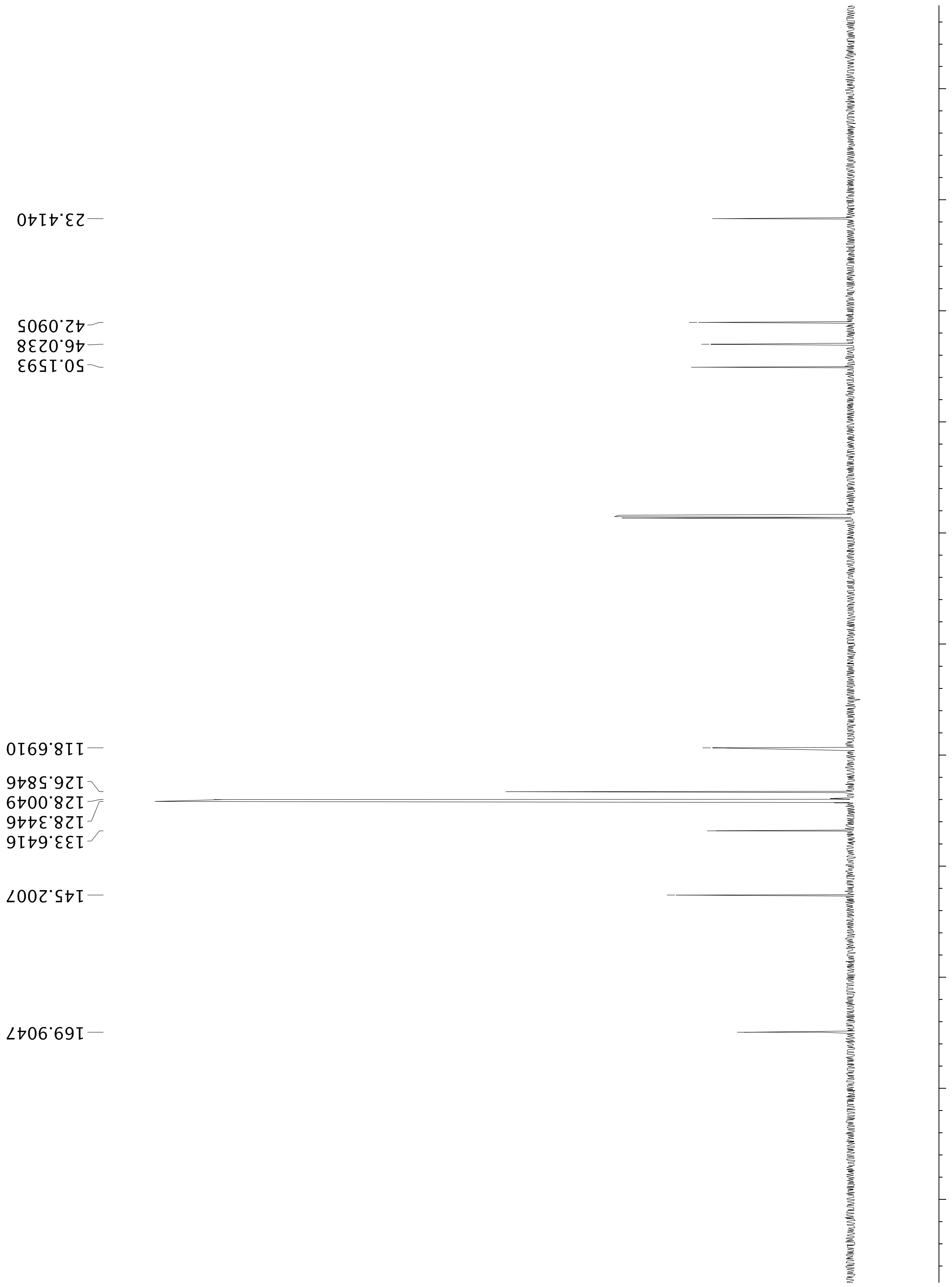
^{1}H NMR (500 MHz, CDCl$_3$) of compound **1a**.



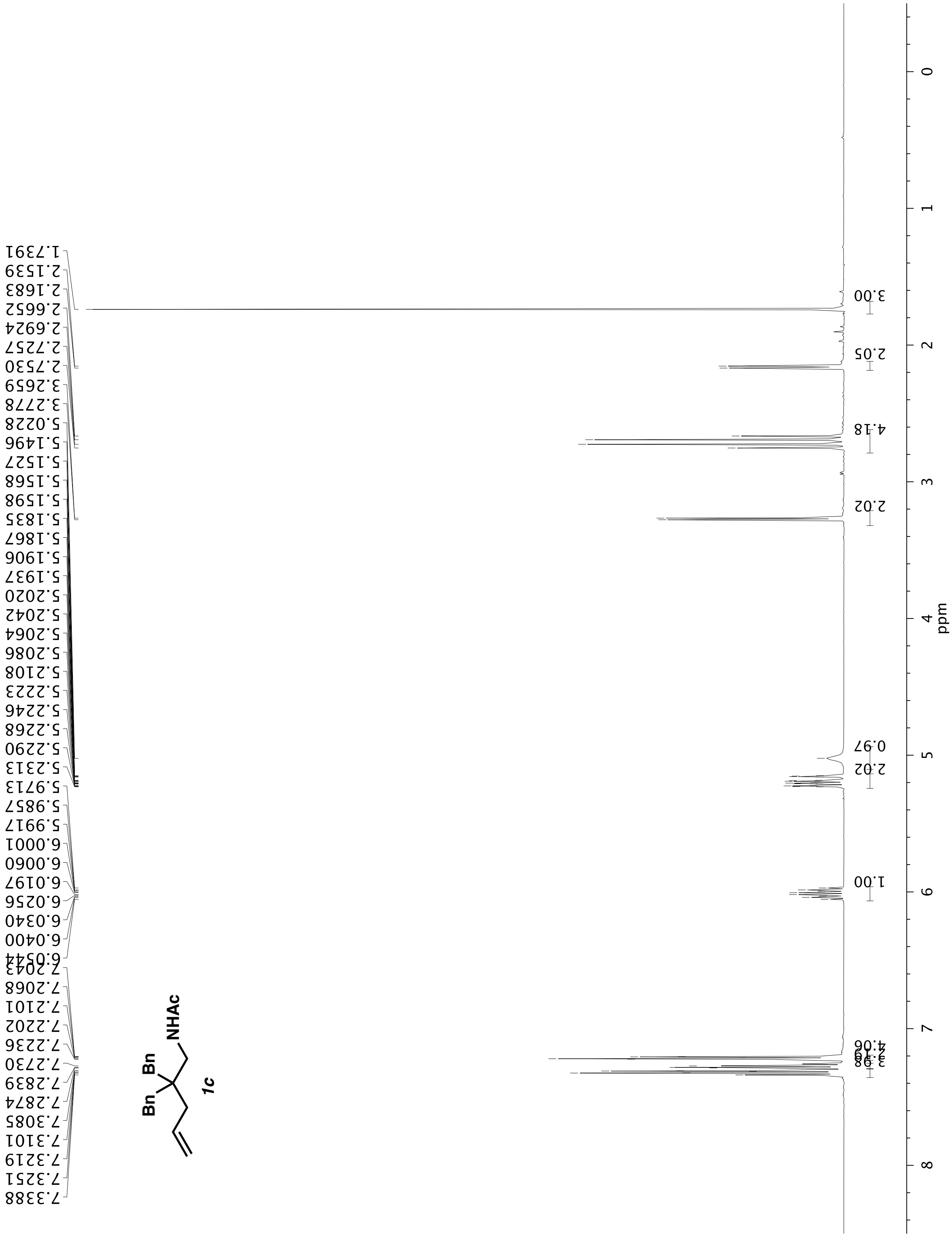
^{13}C NMR (126 MHz, CDCl$_3$) of compound **1a**.



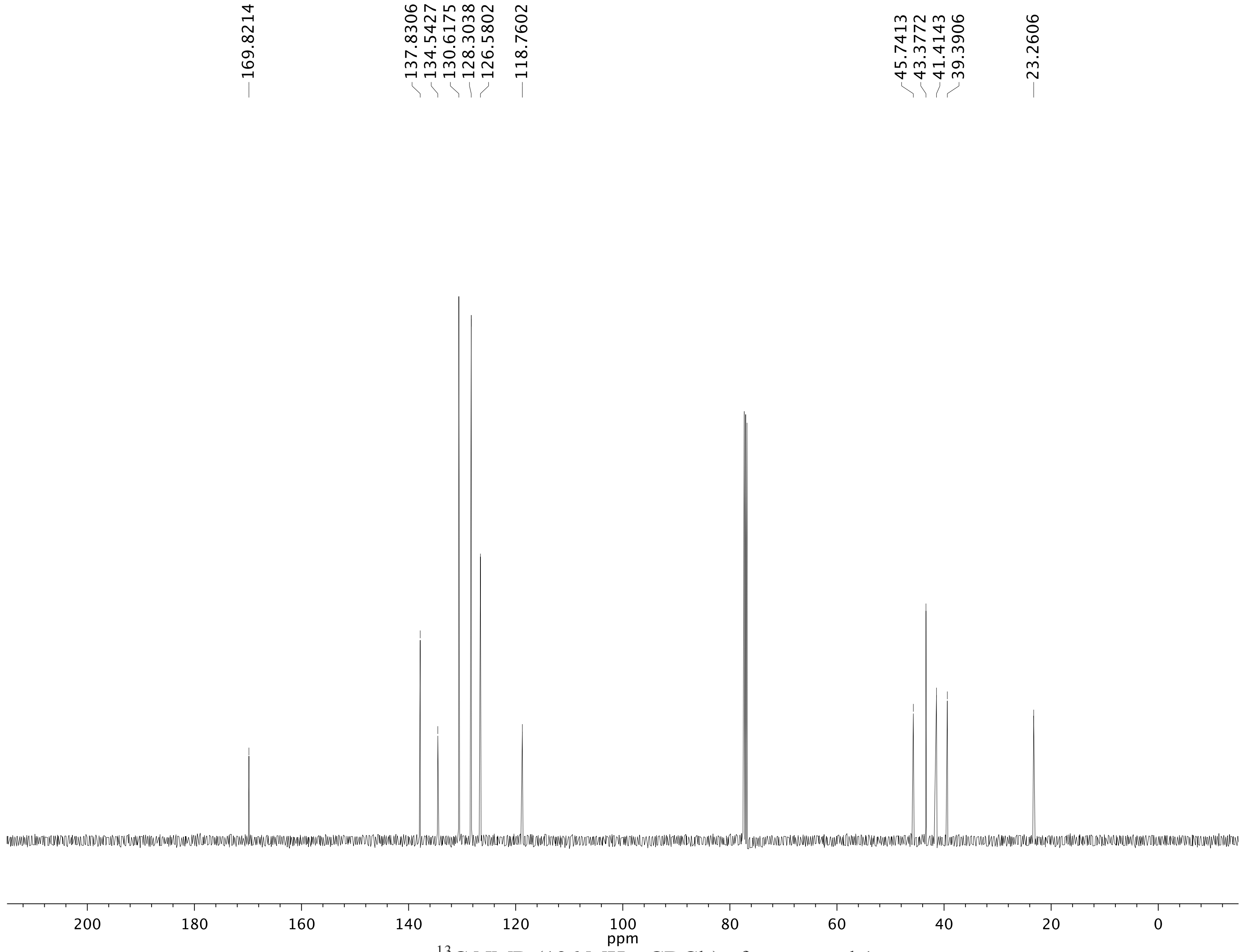
^{1}H NMR (500 MHz, CDCl$_3$) of compound **1b**.



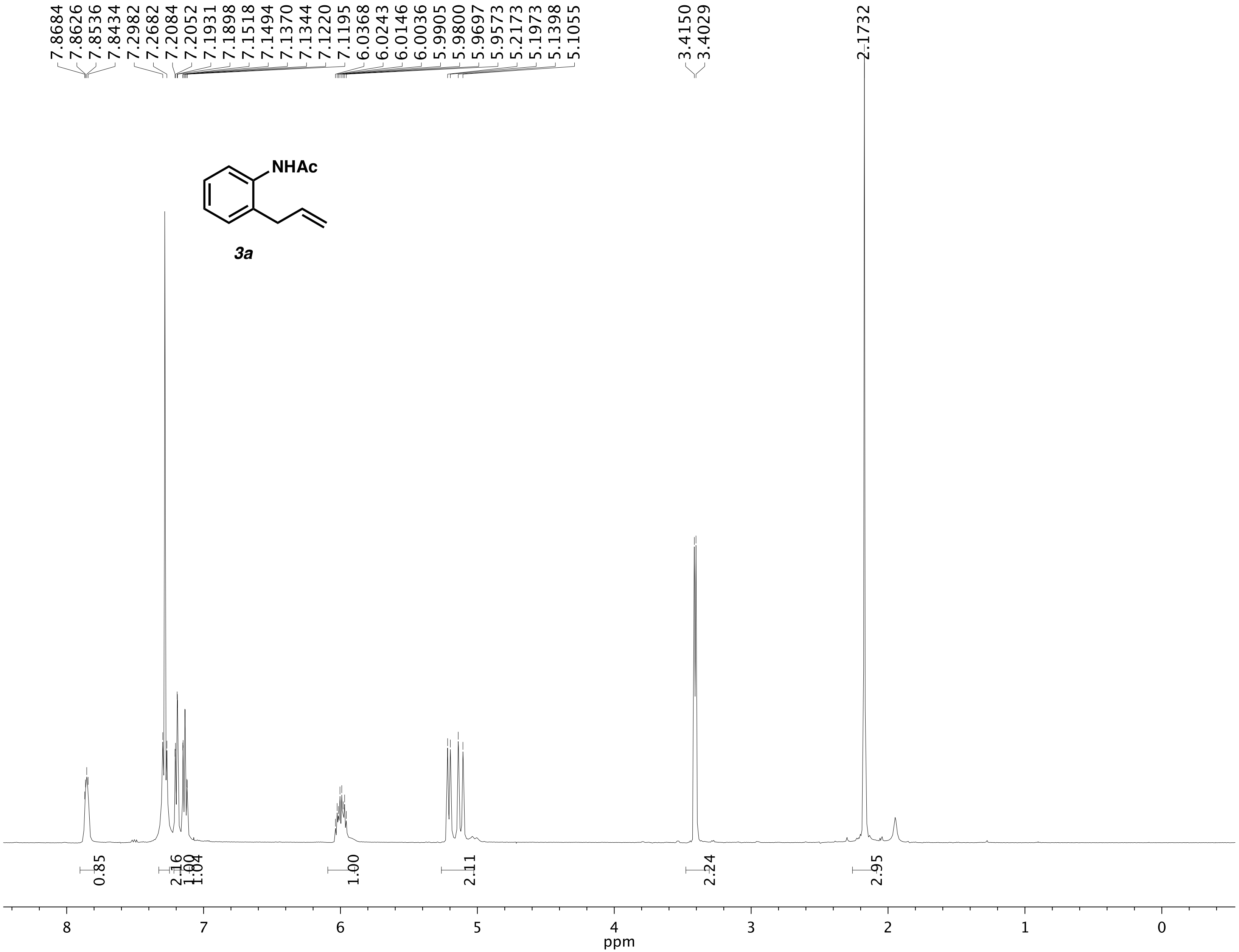
^{13}C NMR (126 MHz, CDCl$_3$) of compound **1b**.



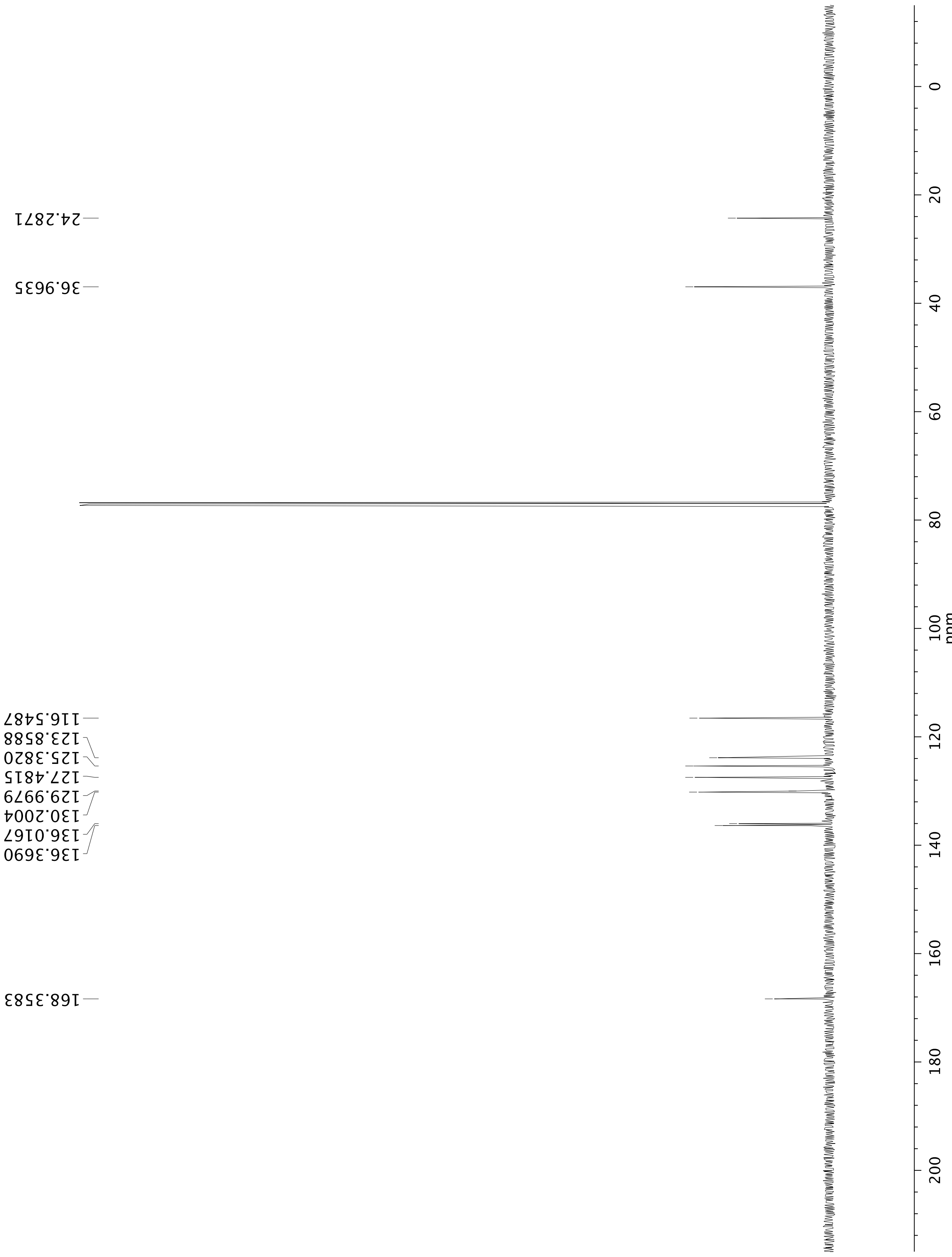
^{1}H NMR (500 MHz, CDCl$_3$) of compound **1c**.



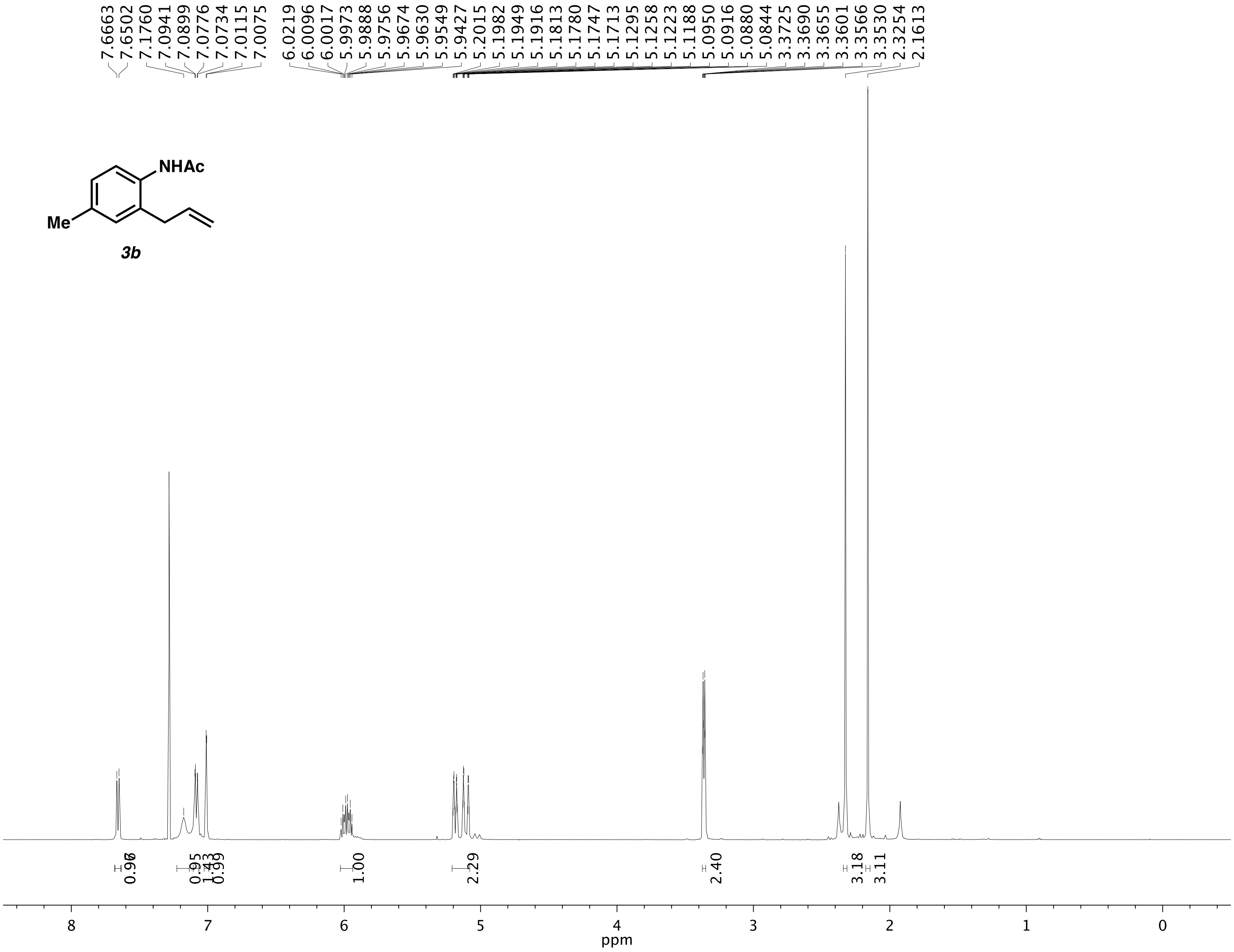
^{13}C NMR (126 MHz, CDCl$_3$) of compound **1c**.



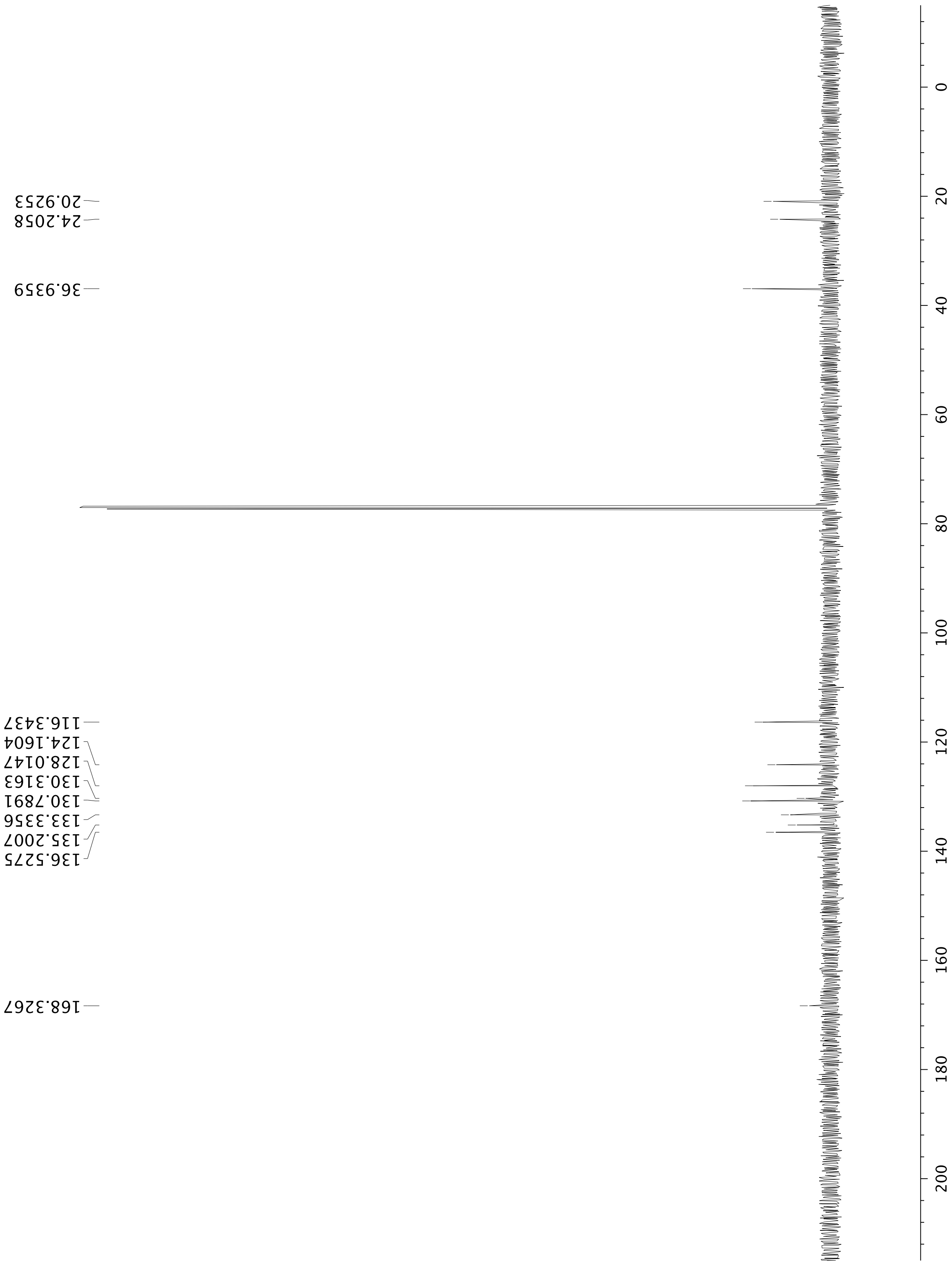
^{1}H NMR (500 MHz, CDCl$_3$) of compound **3a**.



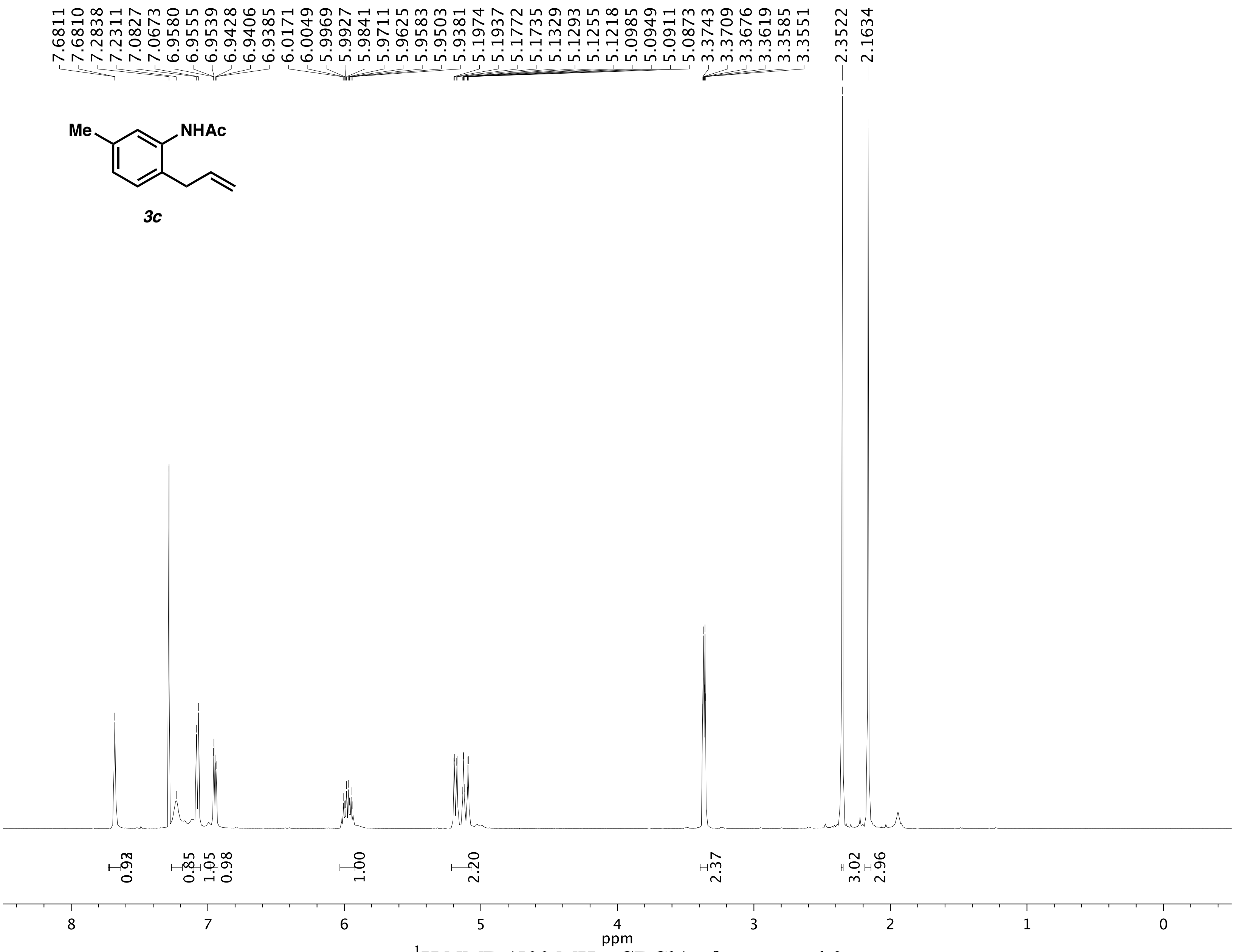
^{13}C NMR (126 MHz, CDCl$_3$) of compound **3a**.



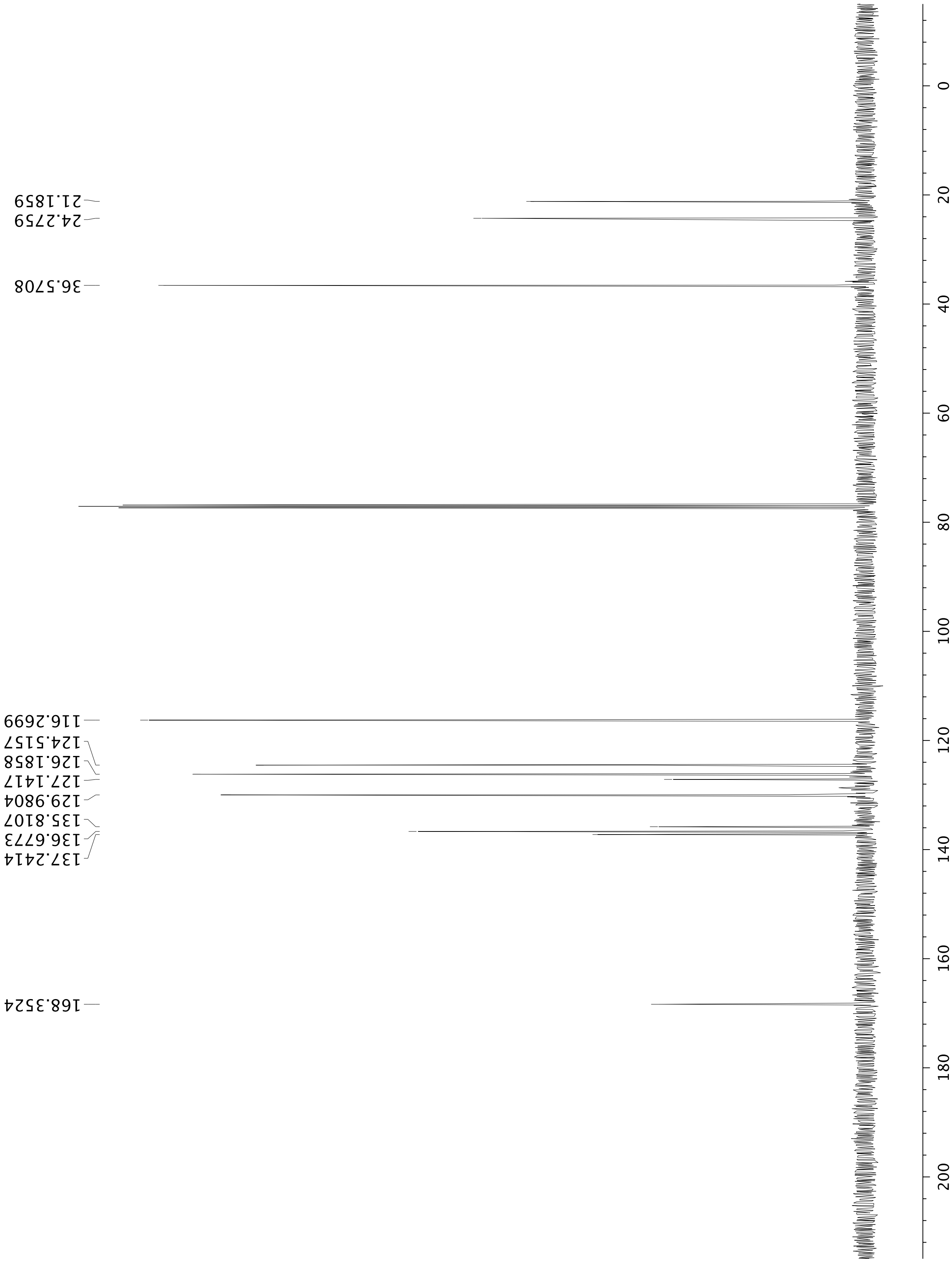
^{1}H NMR (500 MHz, CDCl$_3$) of compound **3b**.



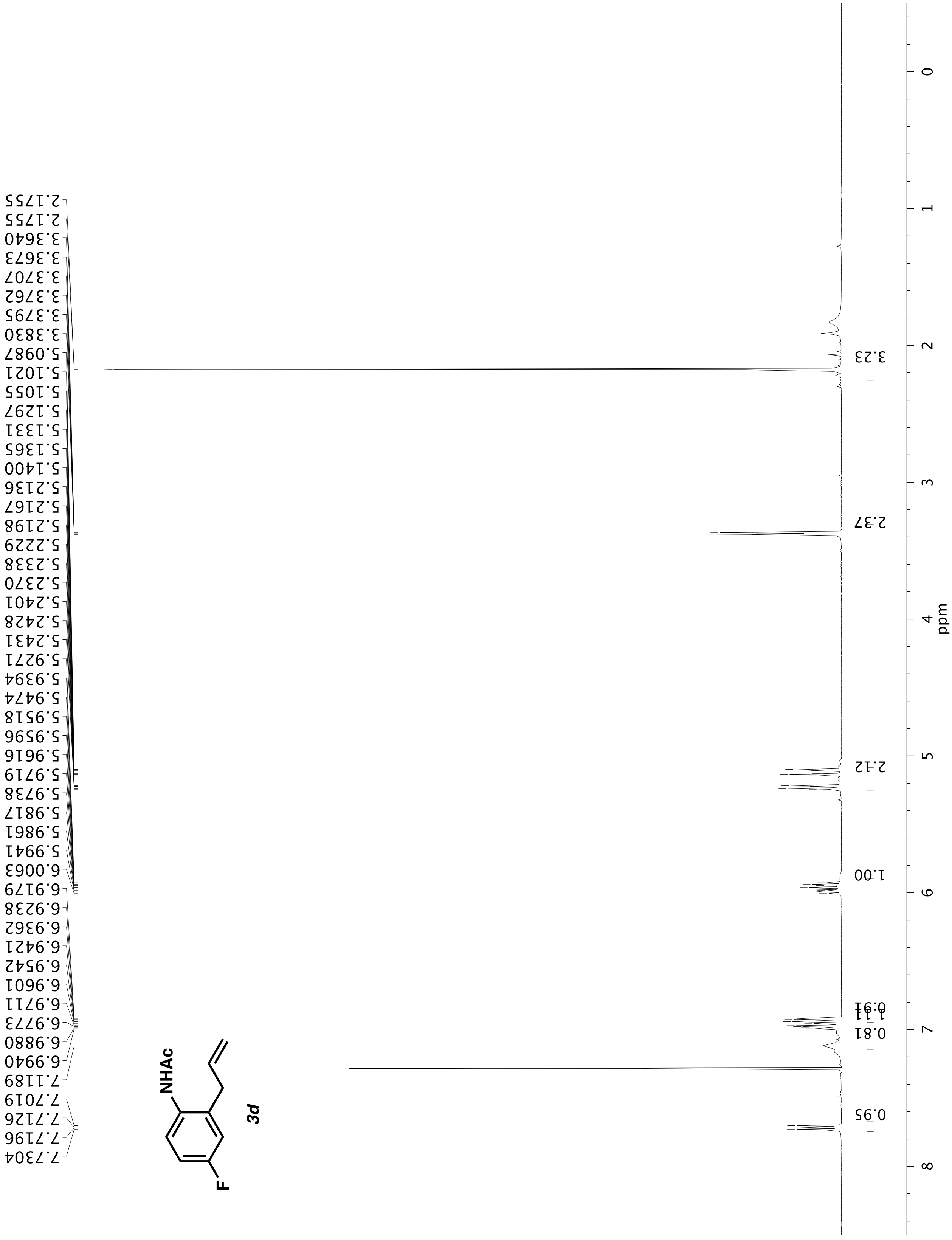
^{13}C NMR (126 MHz, CDCl$_3$) of compound **3b**.



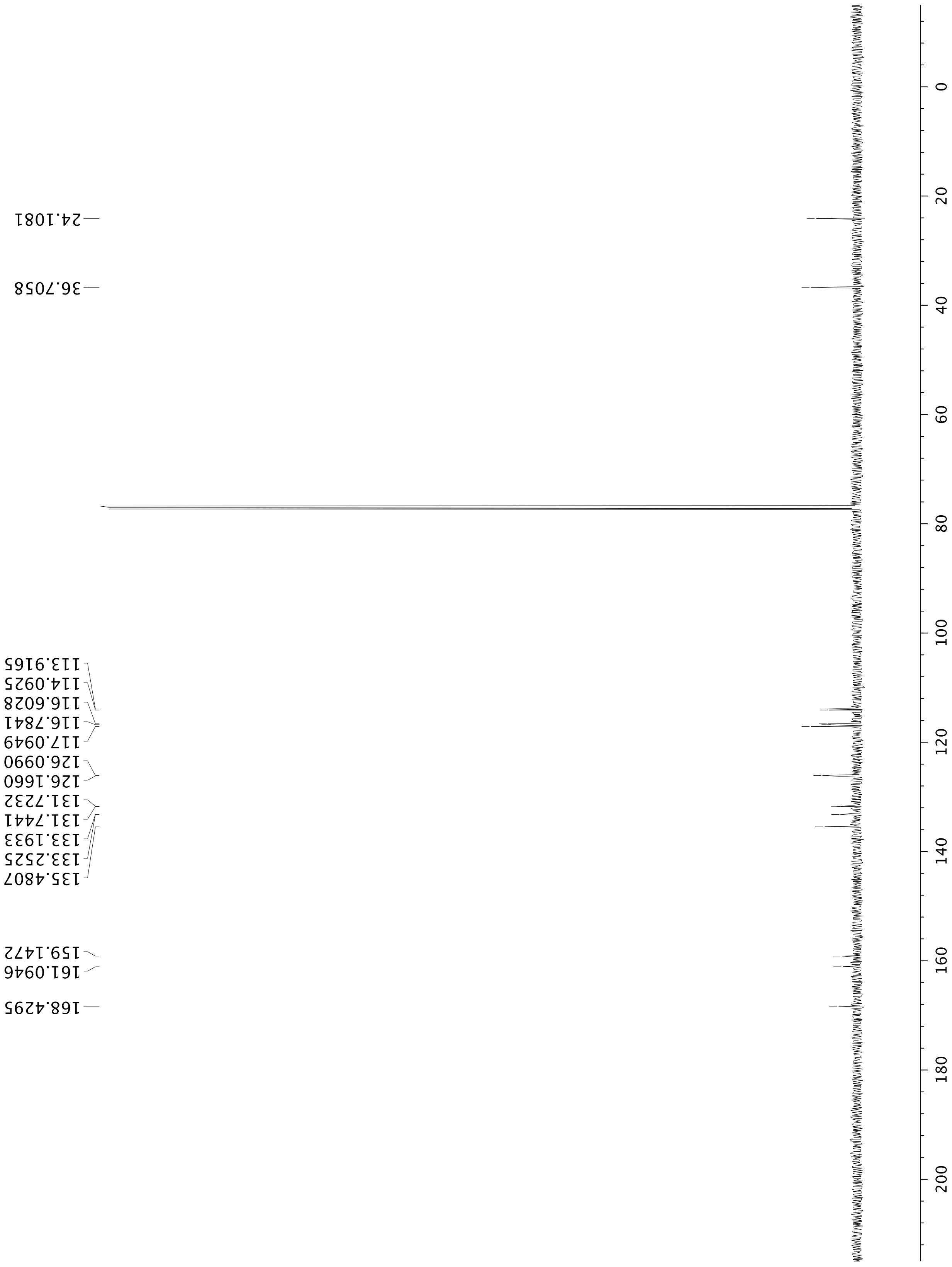
^{1}H NMR (500 MHz, CDCl$_3$) of compound **3c**



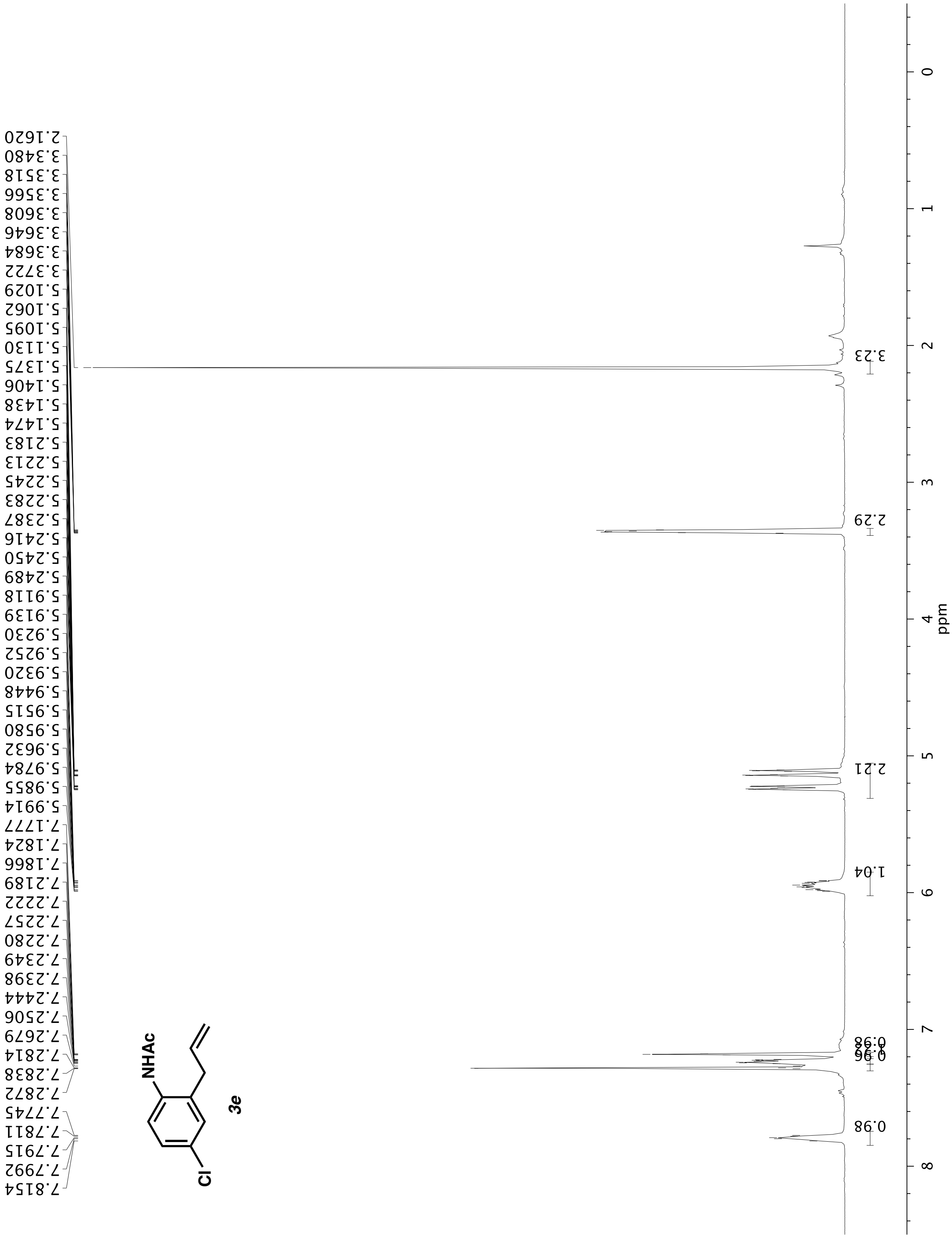
^{13}C NMR (126 MHz, CDCl$_3$) of compound **3c**.



^{1}H NMR (500 MHz, CDCl$_3$) of compound **3d**.

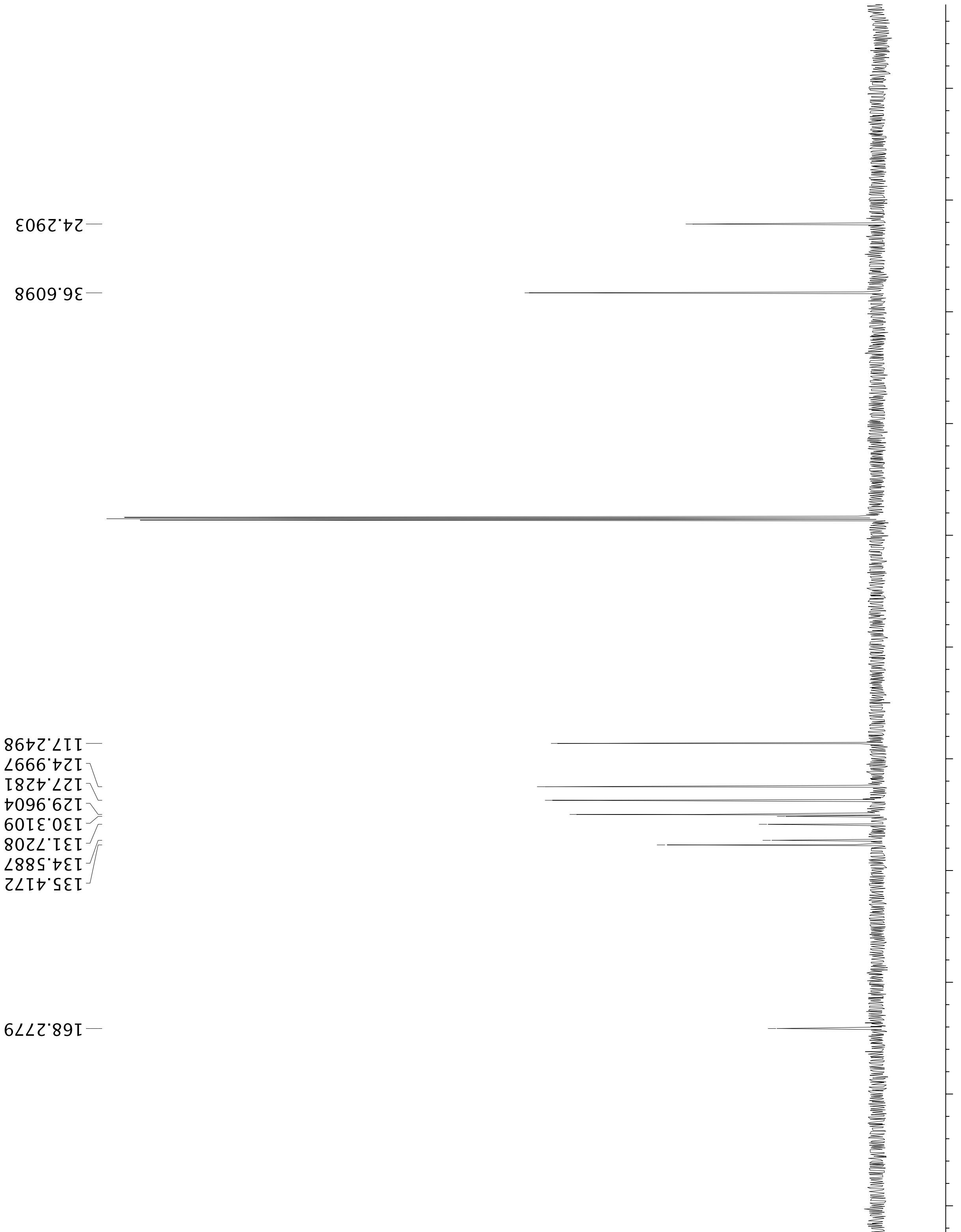


^{13}C NMR (126 MHz, CDCl$_3$) of compound **3d**.

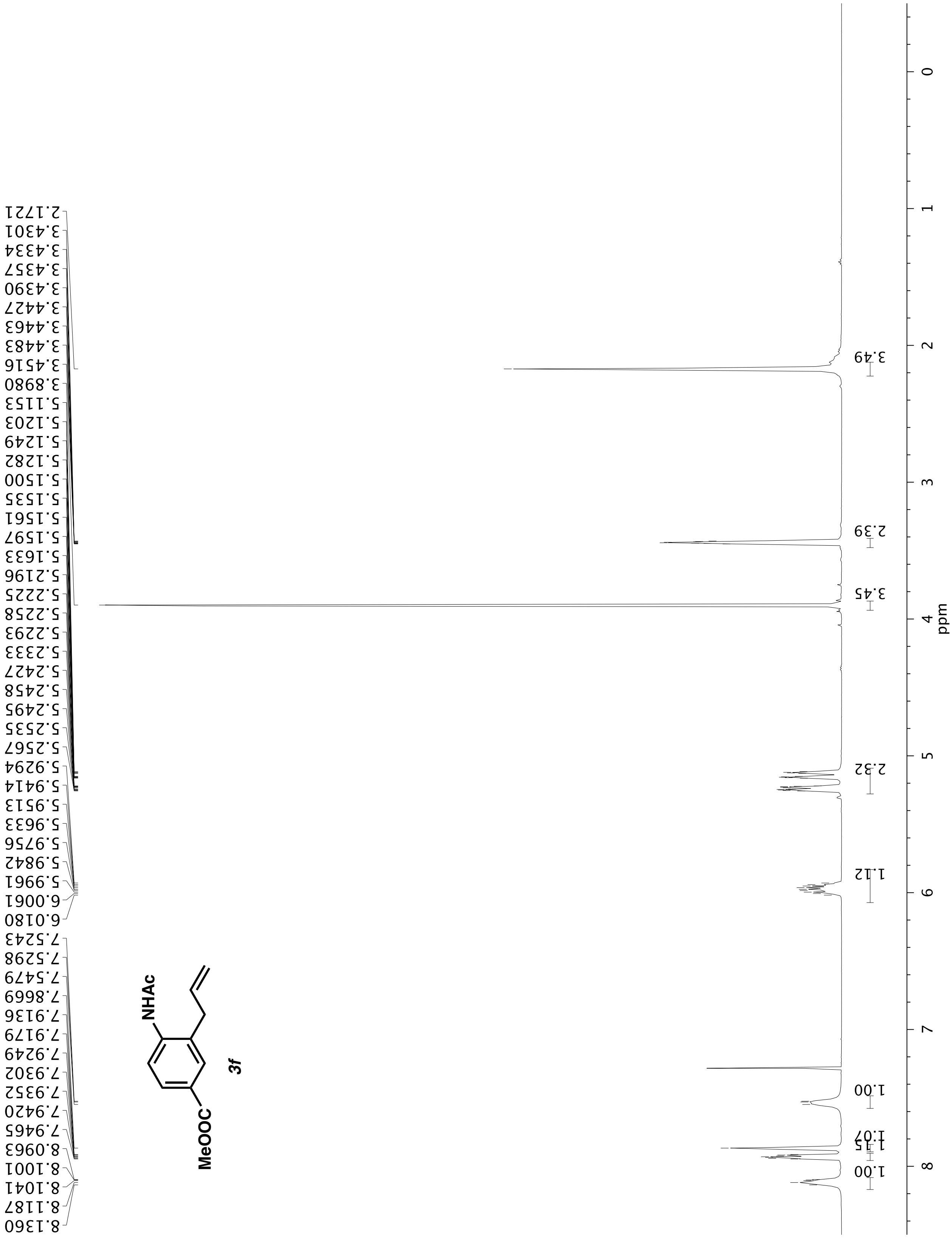


3e

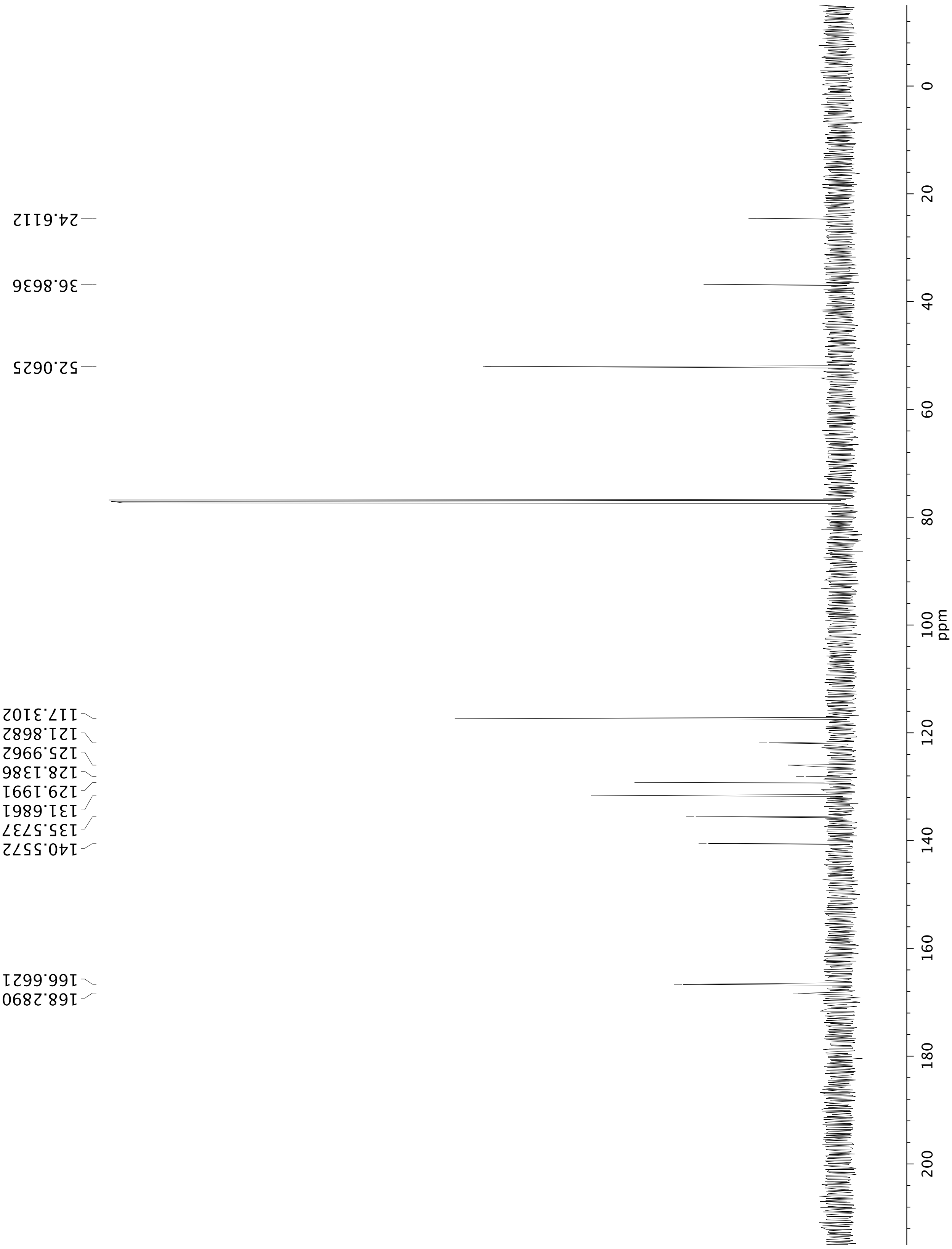
^{1}H NMR (500 MHz, CDCl$_3$) of compound **3e**.



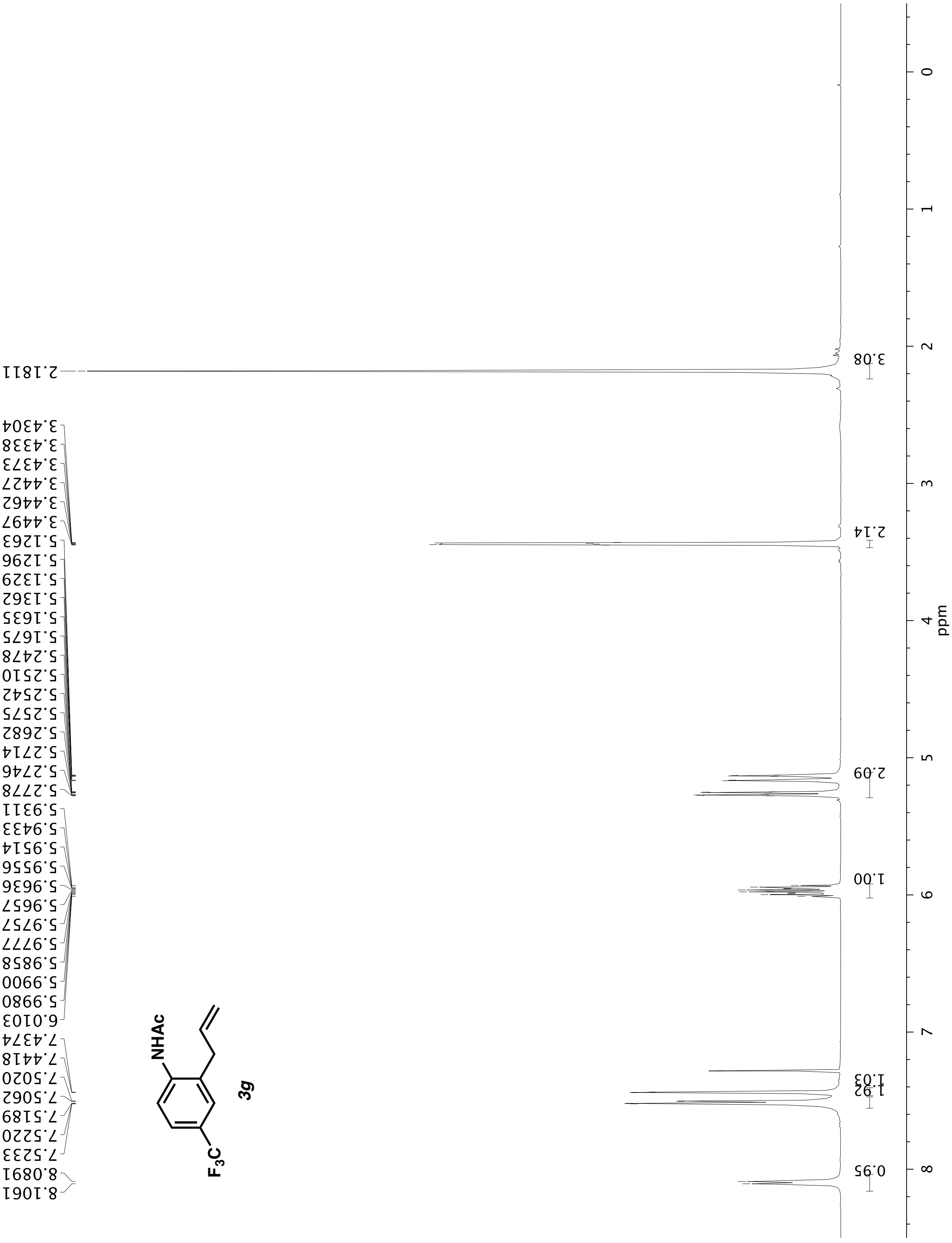
^{13}C NMR (126 MHz, CDCl$_3$) of compound **3e**.



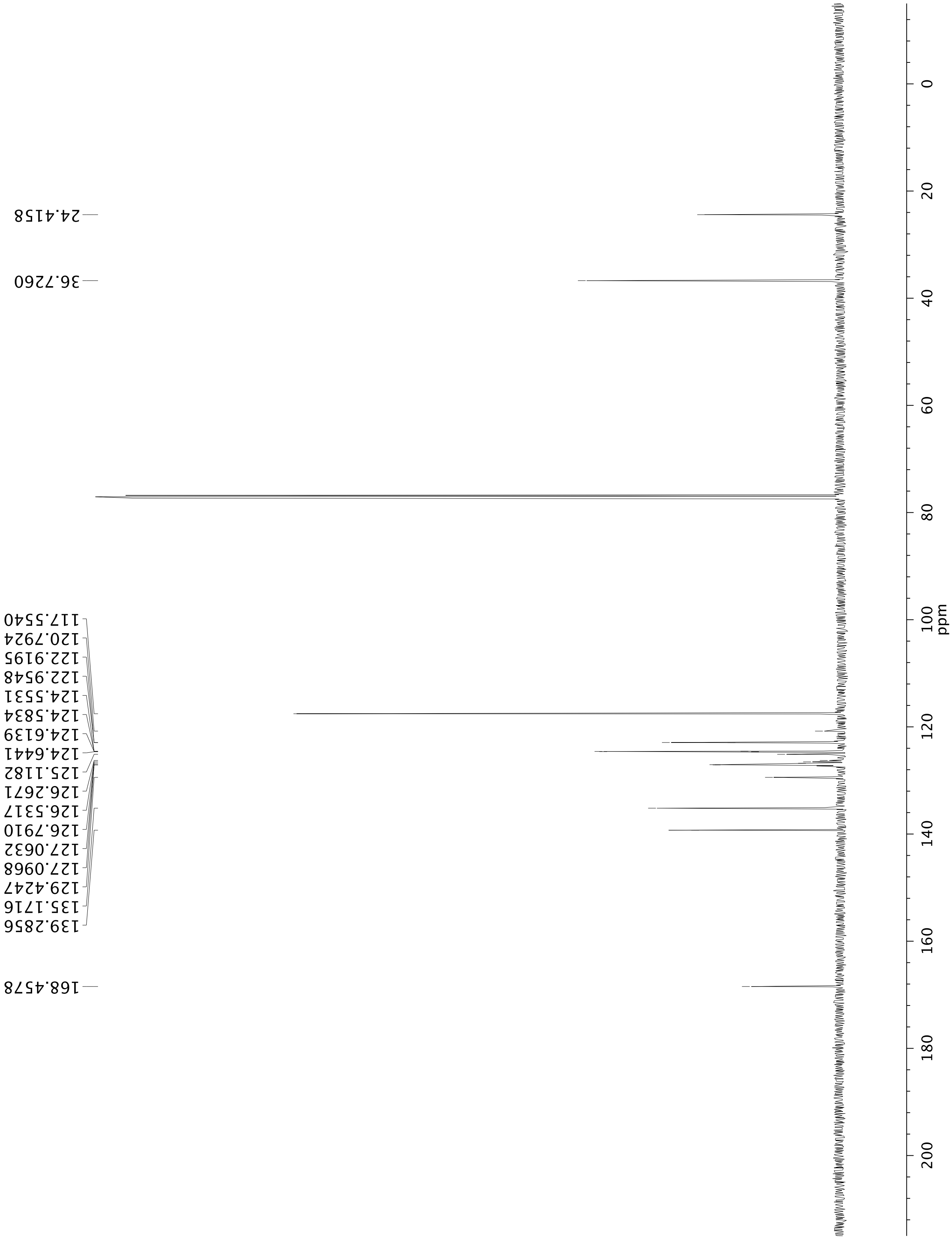
^{1}H NMR (500 MHz, $CDCl_3$) of compound **3f**.



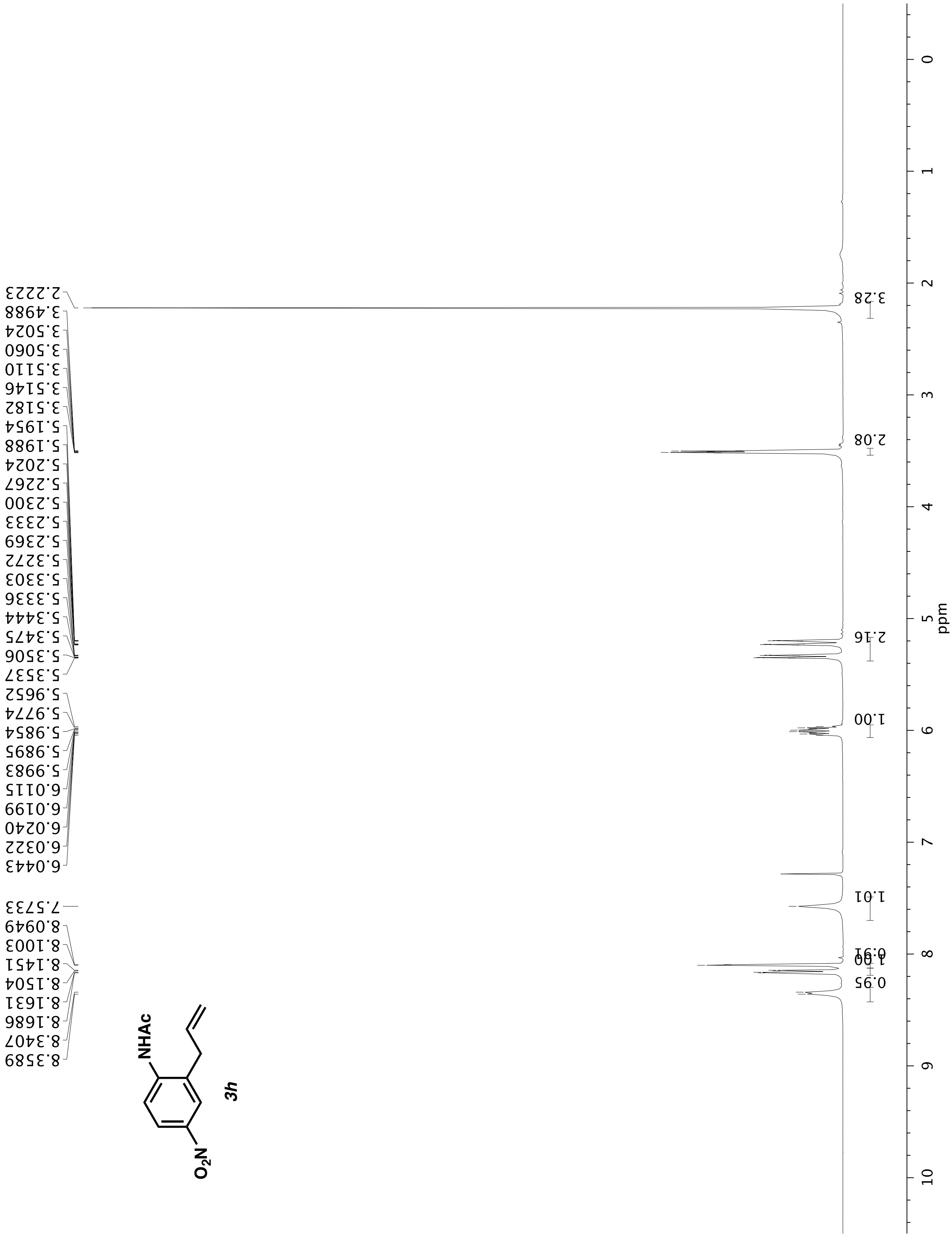
^{13}C NMR (126 MHz, CDCl$_3$) of compound **3f**.



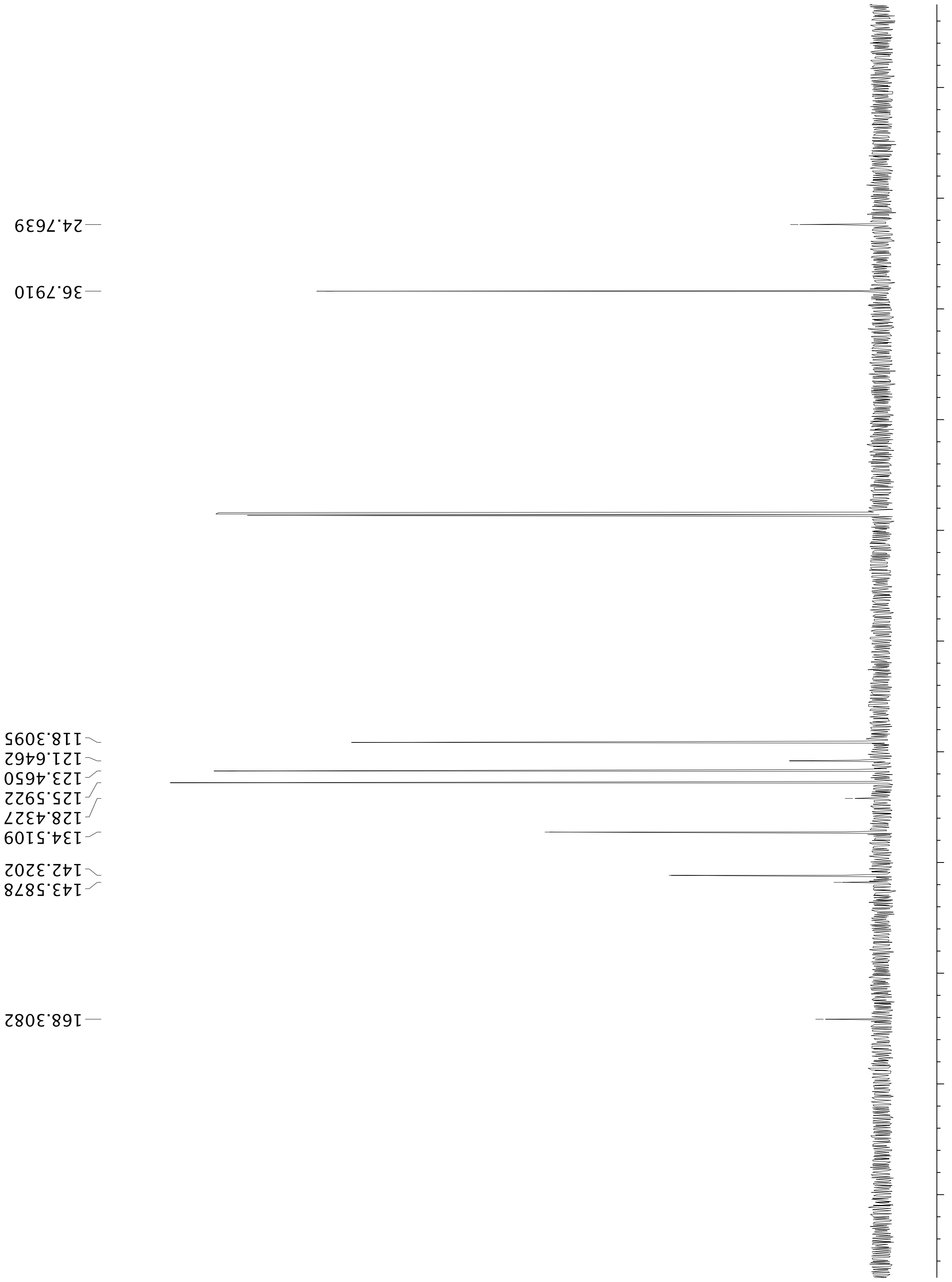
^{1}H NMR (500 MHz, CDCl$_3$) of compound **3g**.



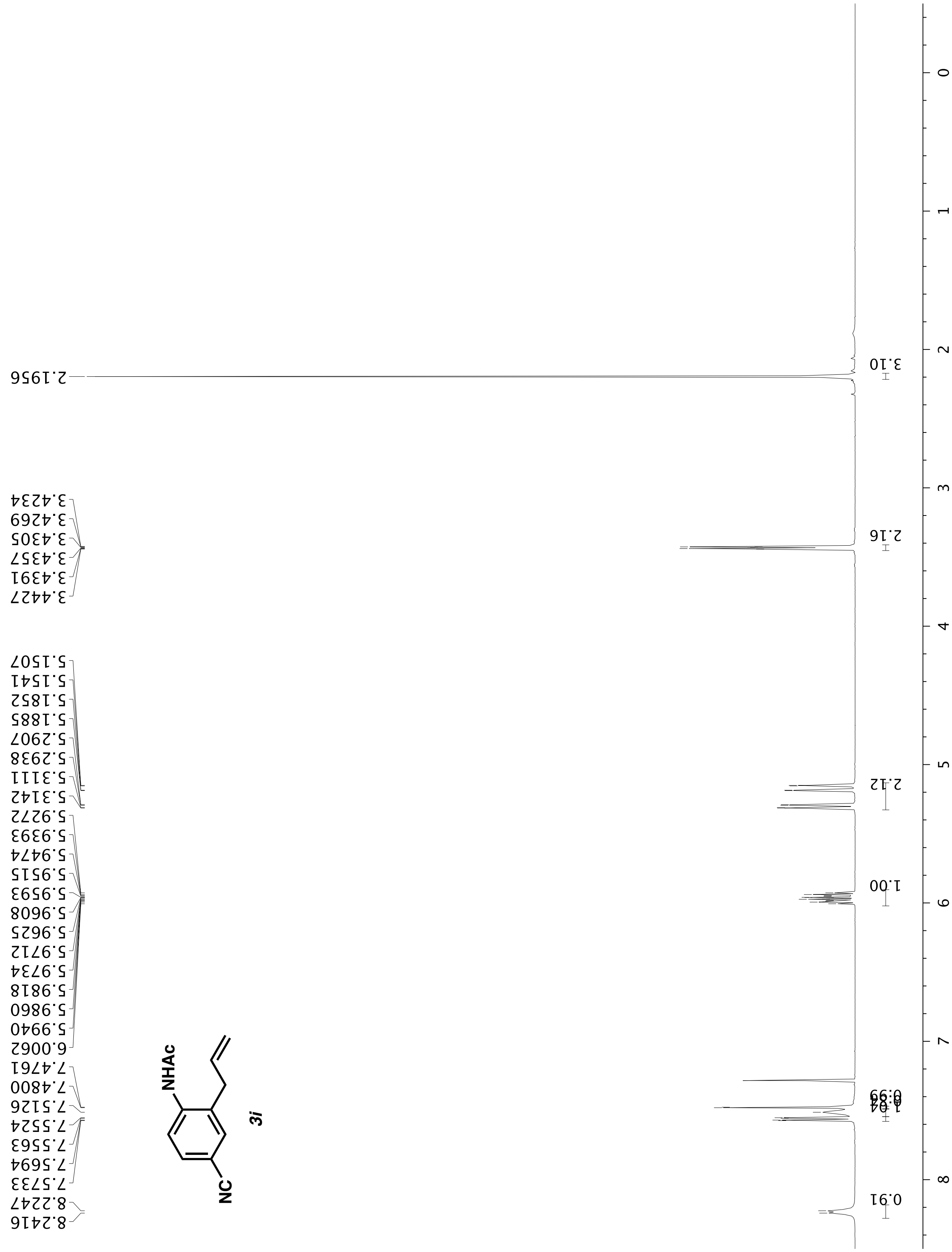
^{13}C NMR (126 MHz, $CDCl_3$) of compound **3g**.



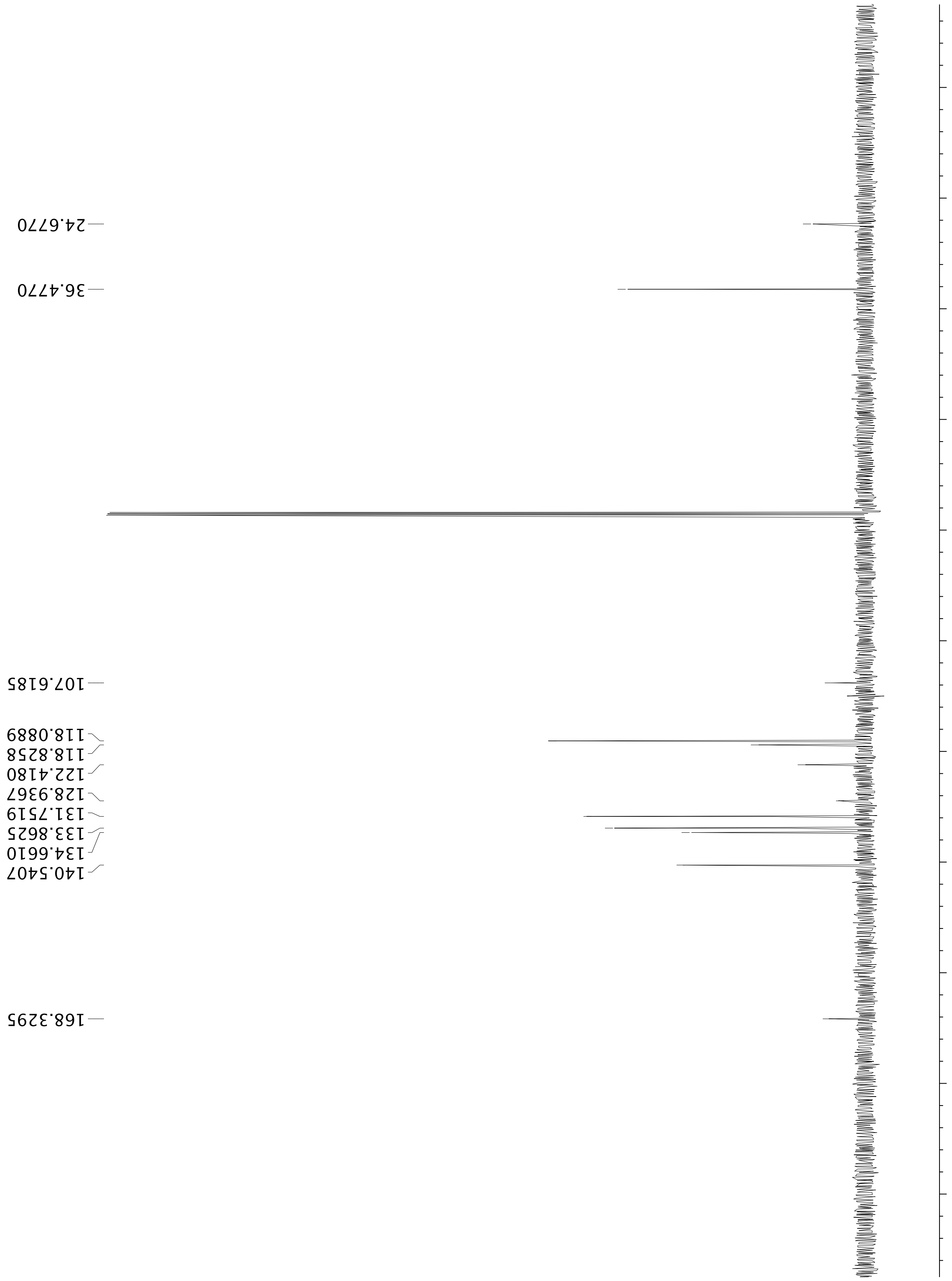
^{1}H NMR (500 MHz, CDCl$_3$) of compound **3h**.



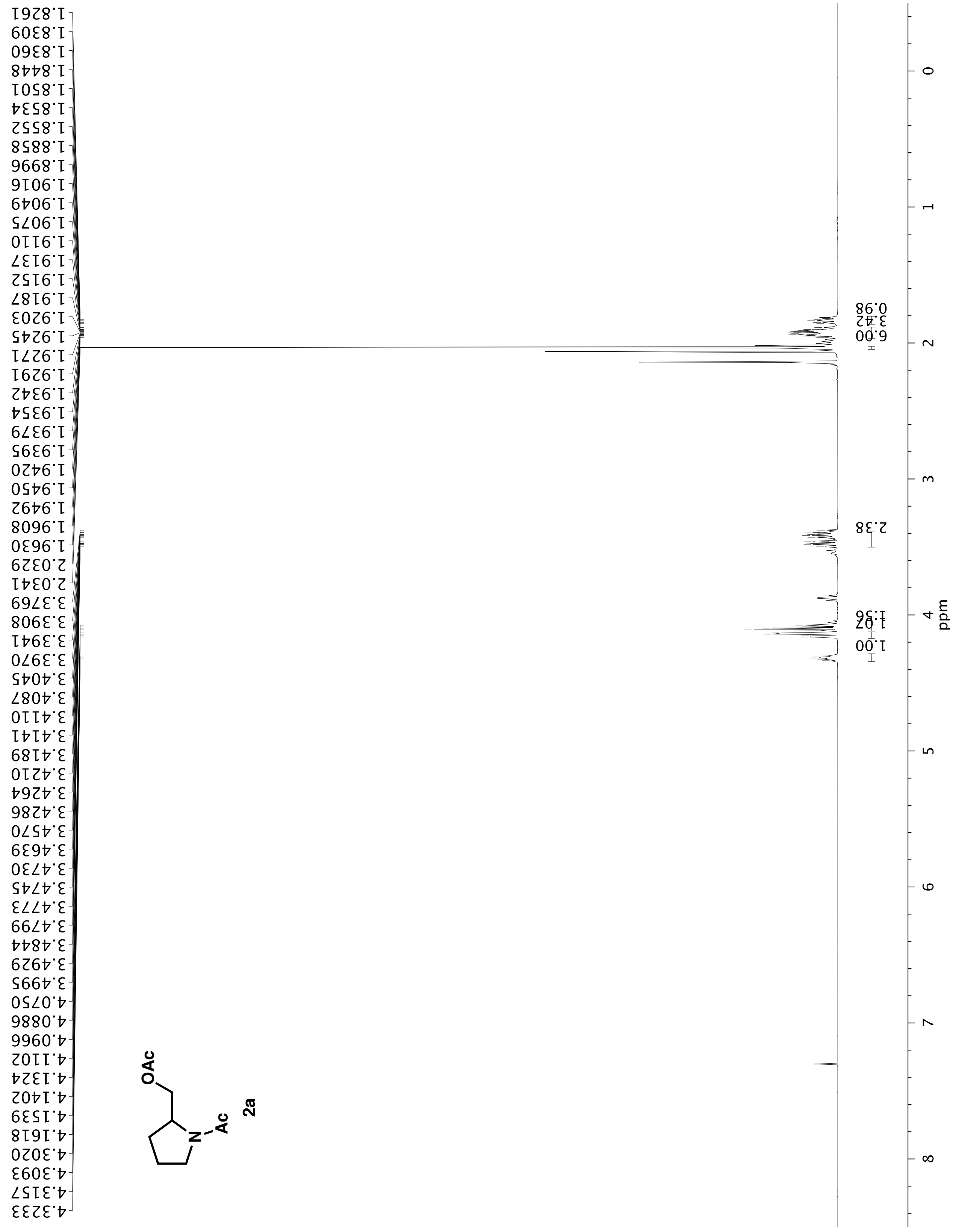
^{13}C NMR (126 MHz, CDCl$_3$) of compound **3h**.



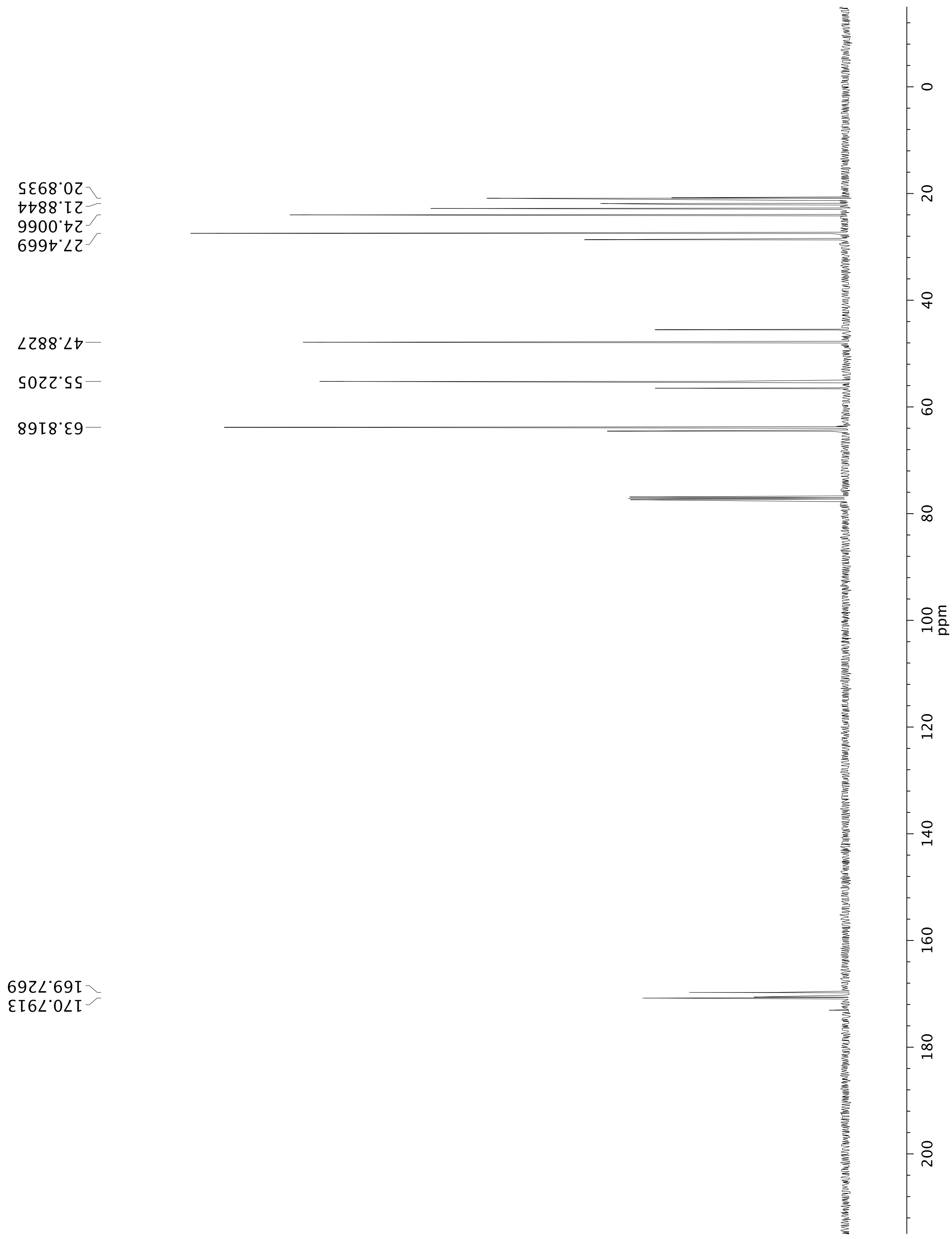
^{1}H NMR (500 MHz, CDCl$_3$) of compound **3i**.



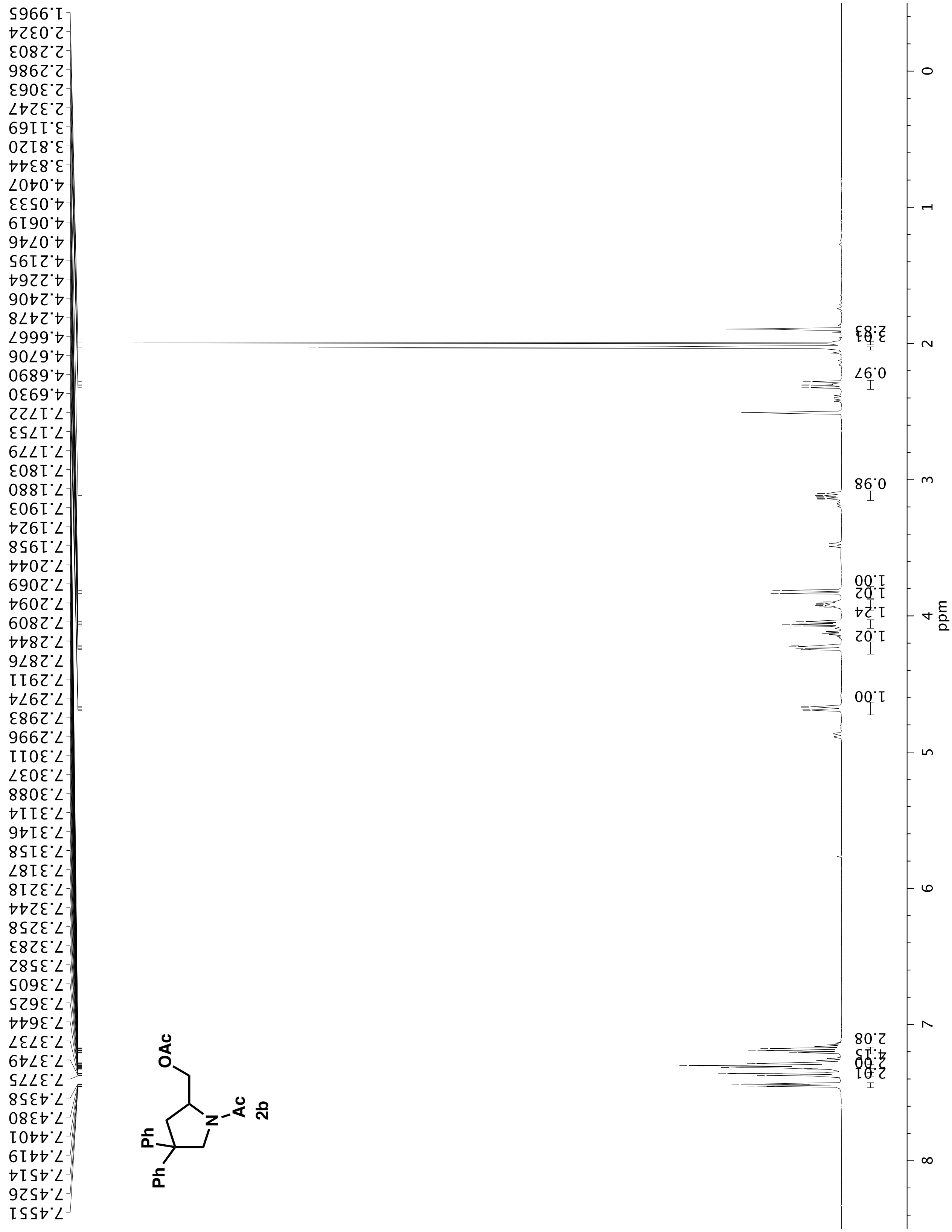
^{13}C NMR (126 MHz, CDCl$_3$) of compound **3i**.



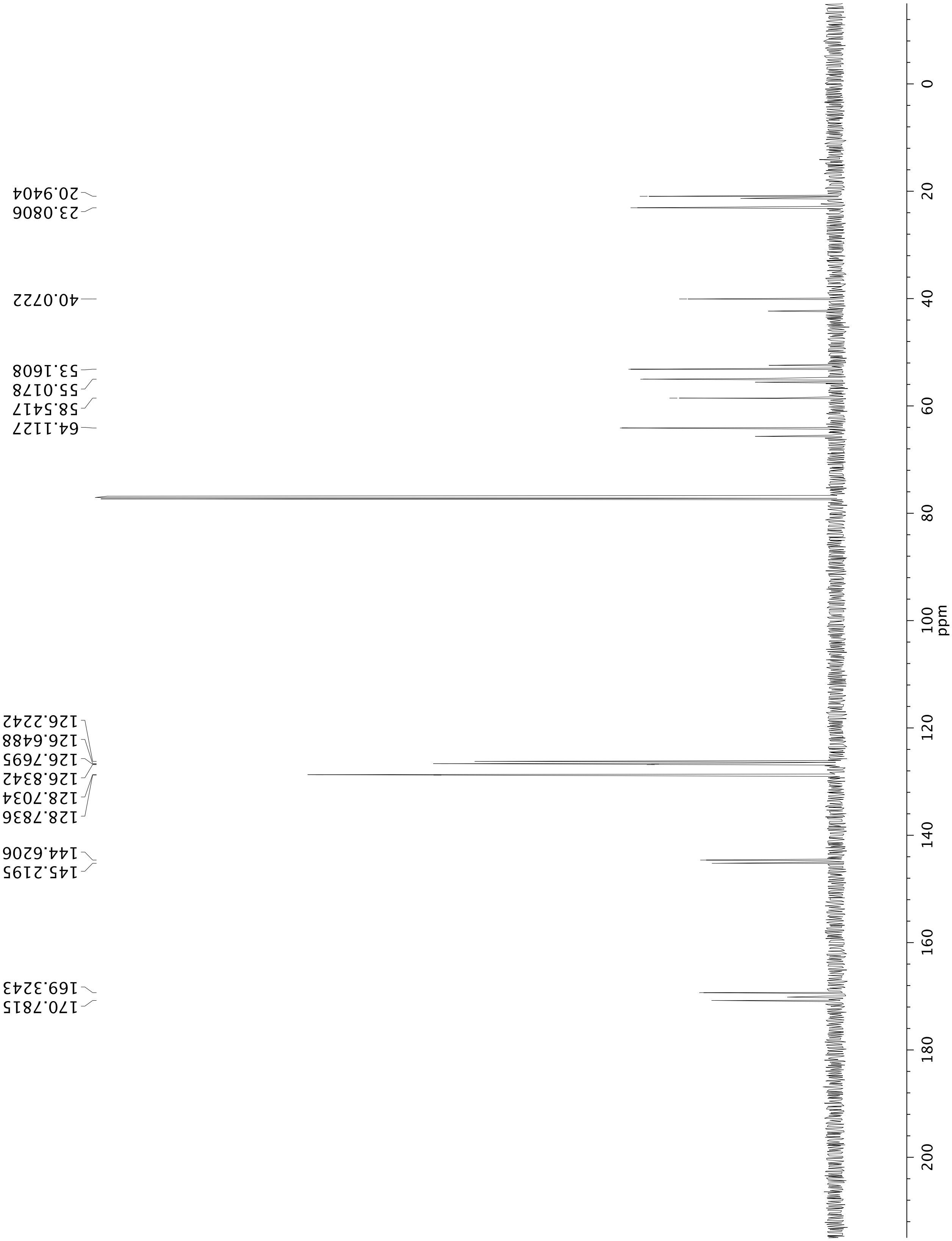
^{1}H NMR (500 MHz, CDCl$_3$) of compound **2a**.



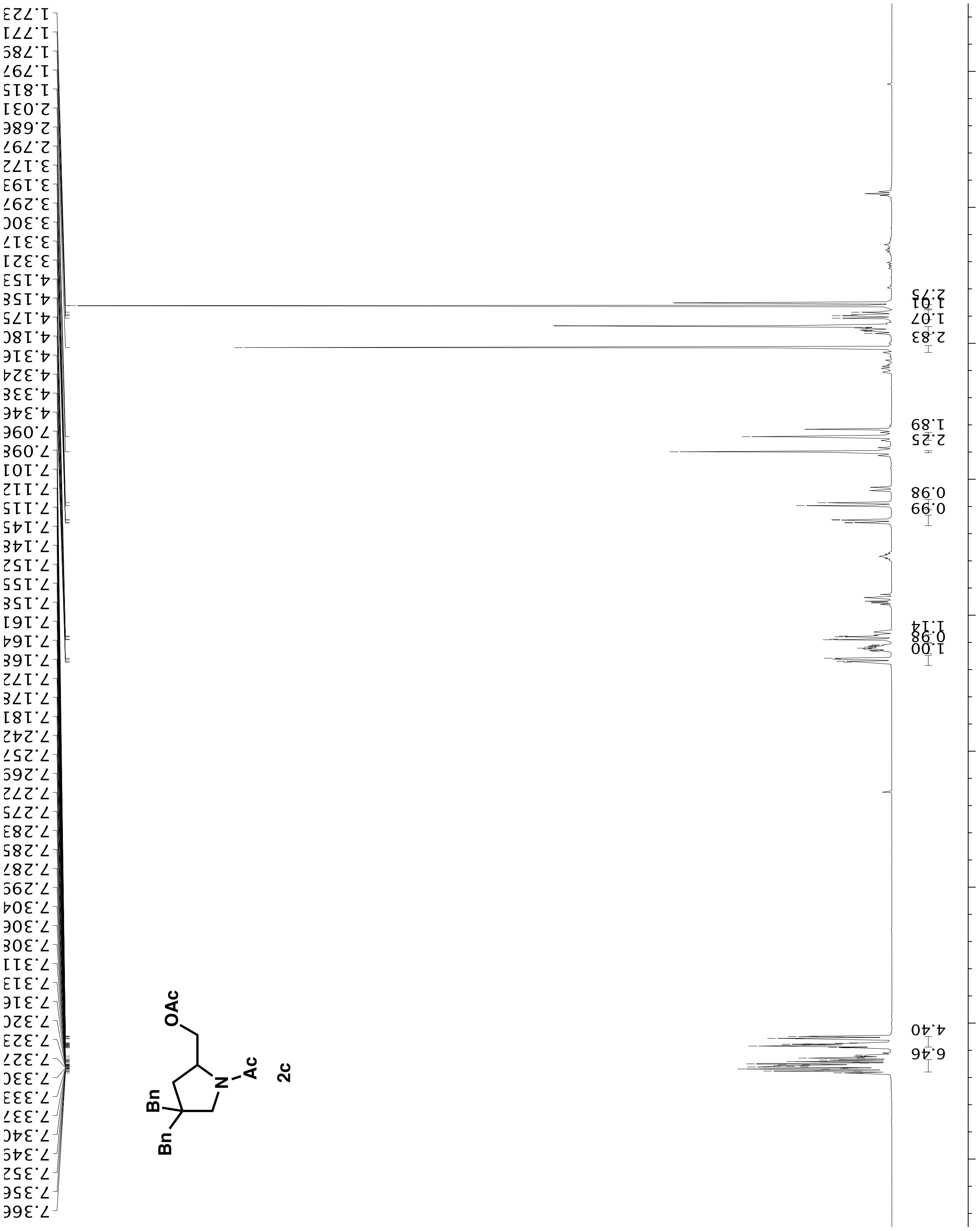
^{13}C NMR (126 MHz, CDCl$_3$) of compound **2a**.



^{1}H NMR (500 MHz, DMSO) of compound **2b**.

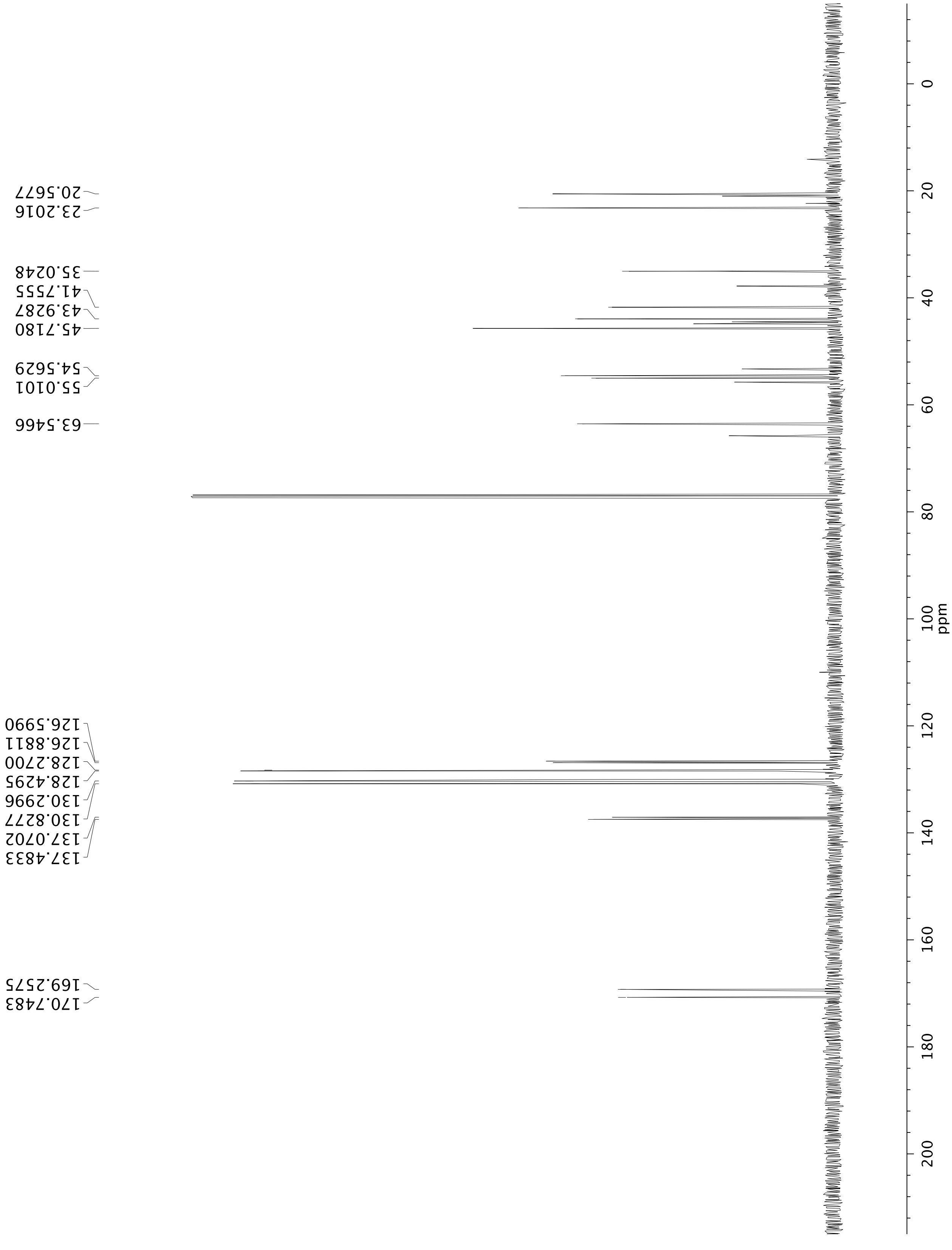


^{13}C NMR (126 MHz, $CDCl_3$) of compound **2b**.

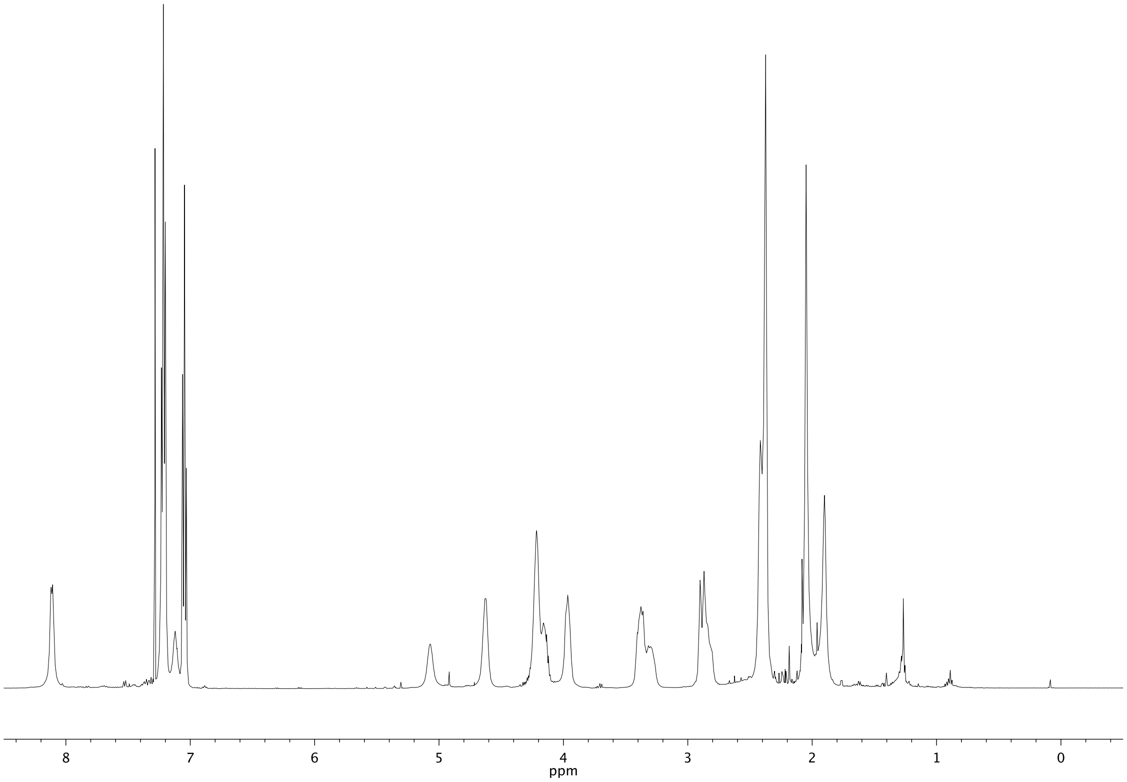


2c

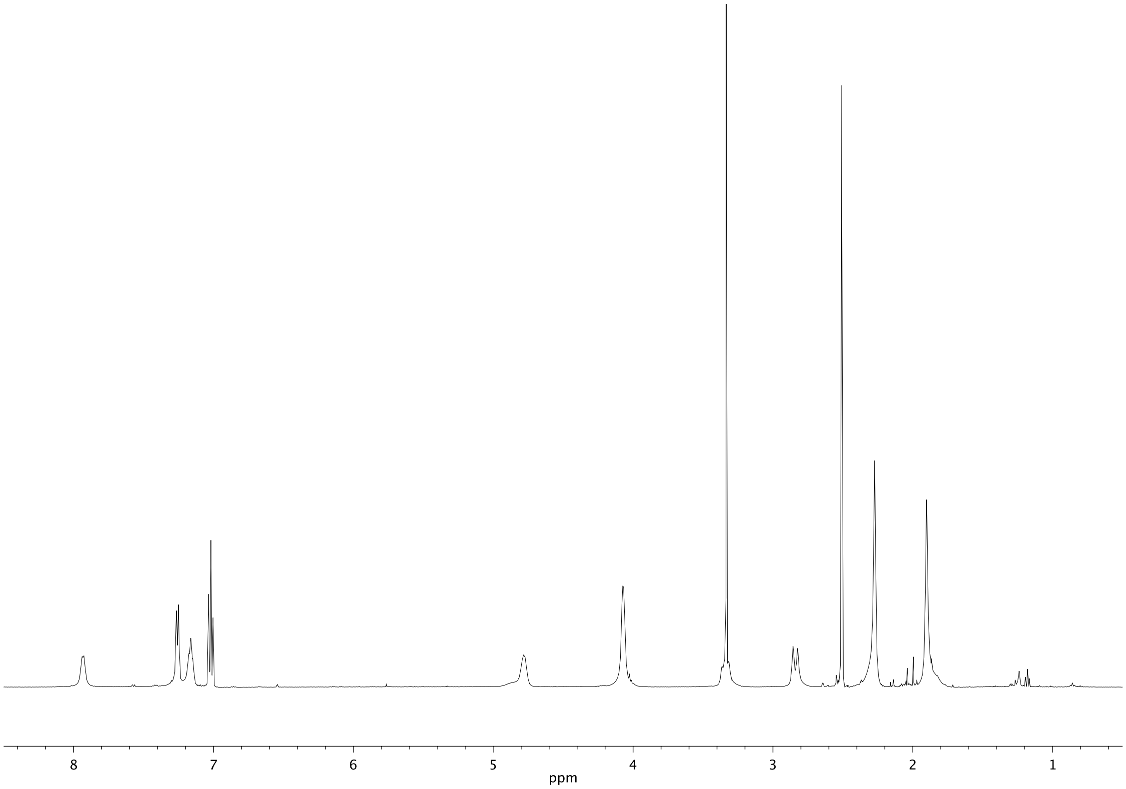
^{1}H NMR (500 MHz, CDCl$_3$) of compound **2c**.



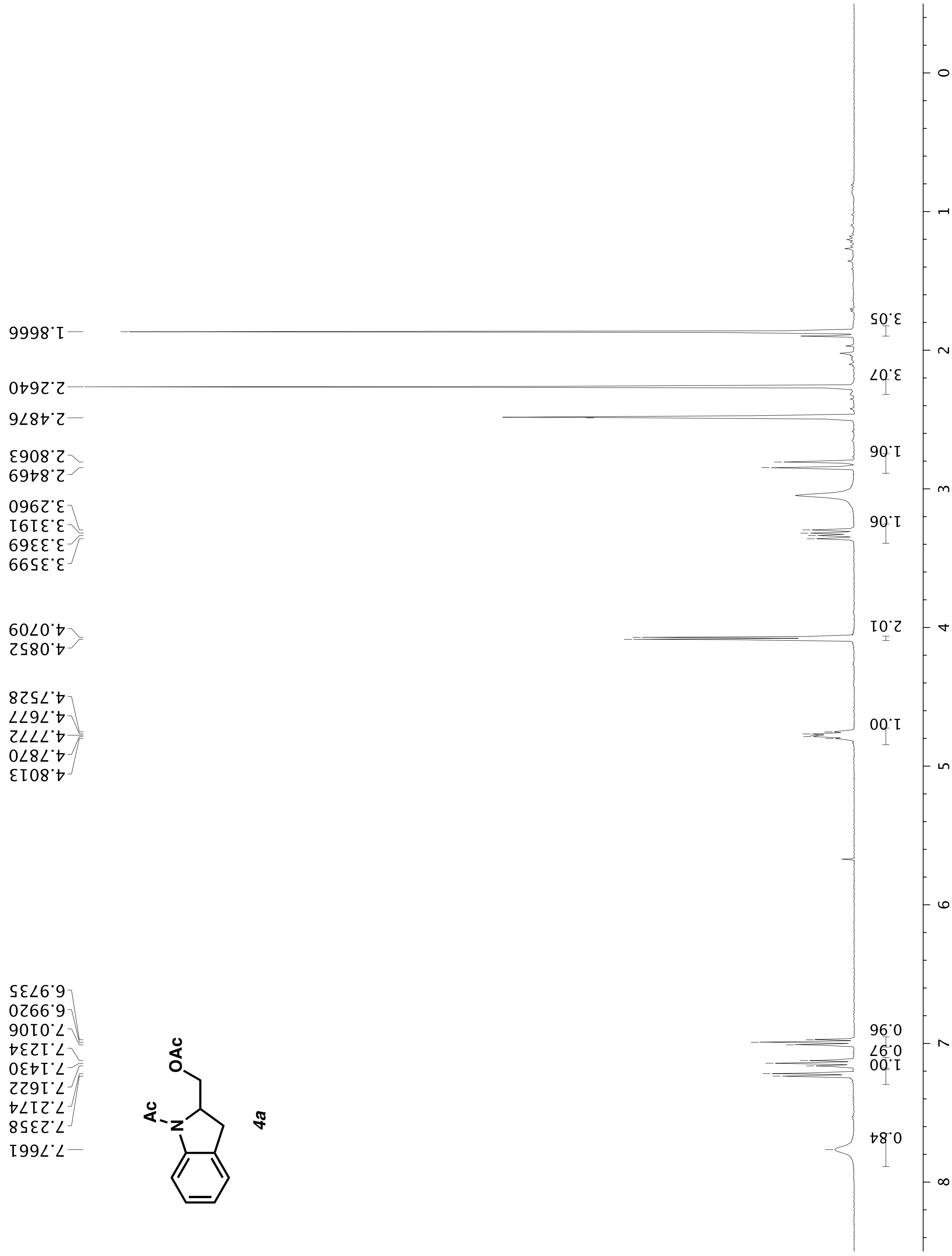
^{13}C NMR (126 MHz, CDCl$_3$) of compound **2c**.



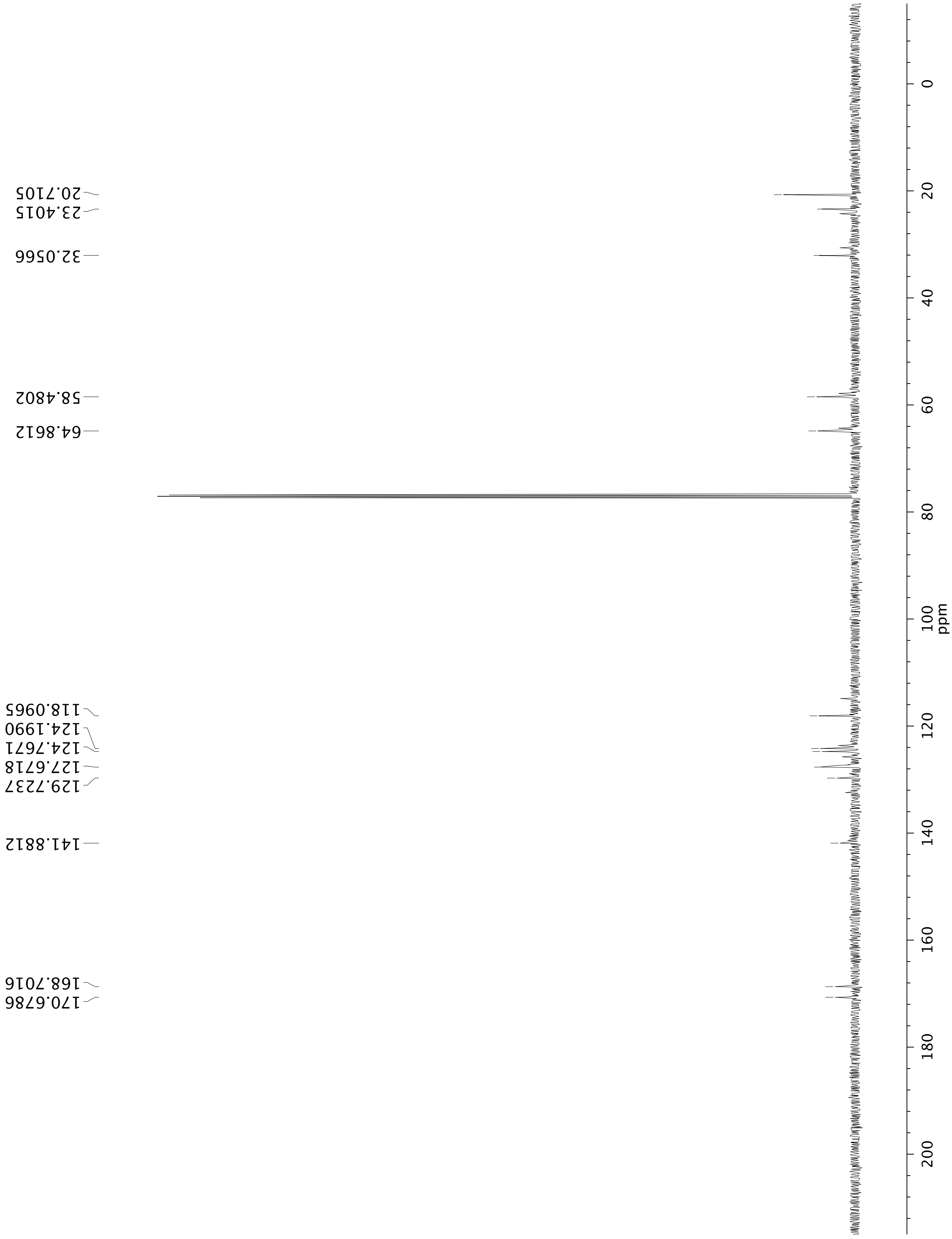
^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC) of compound **4a**.



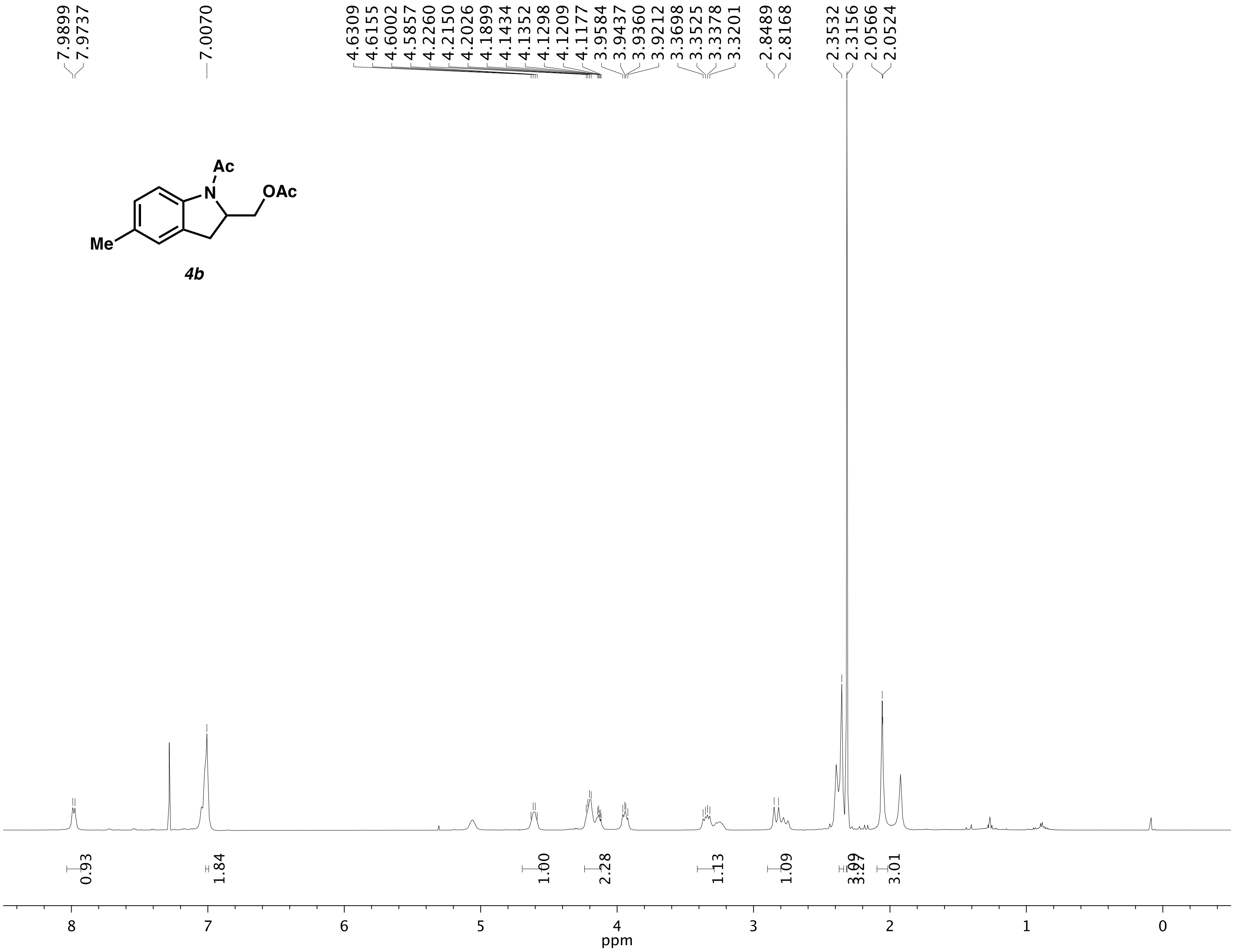
^{1}H NMR (500 MHz, DMSO, 23 ºC) of compound **4a**.



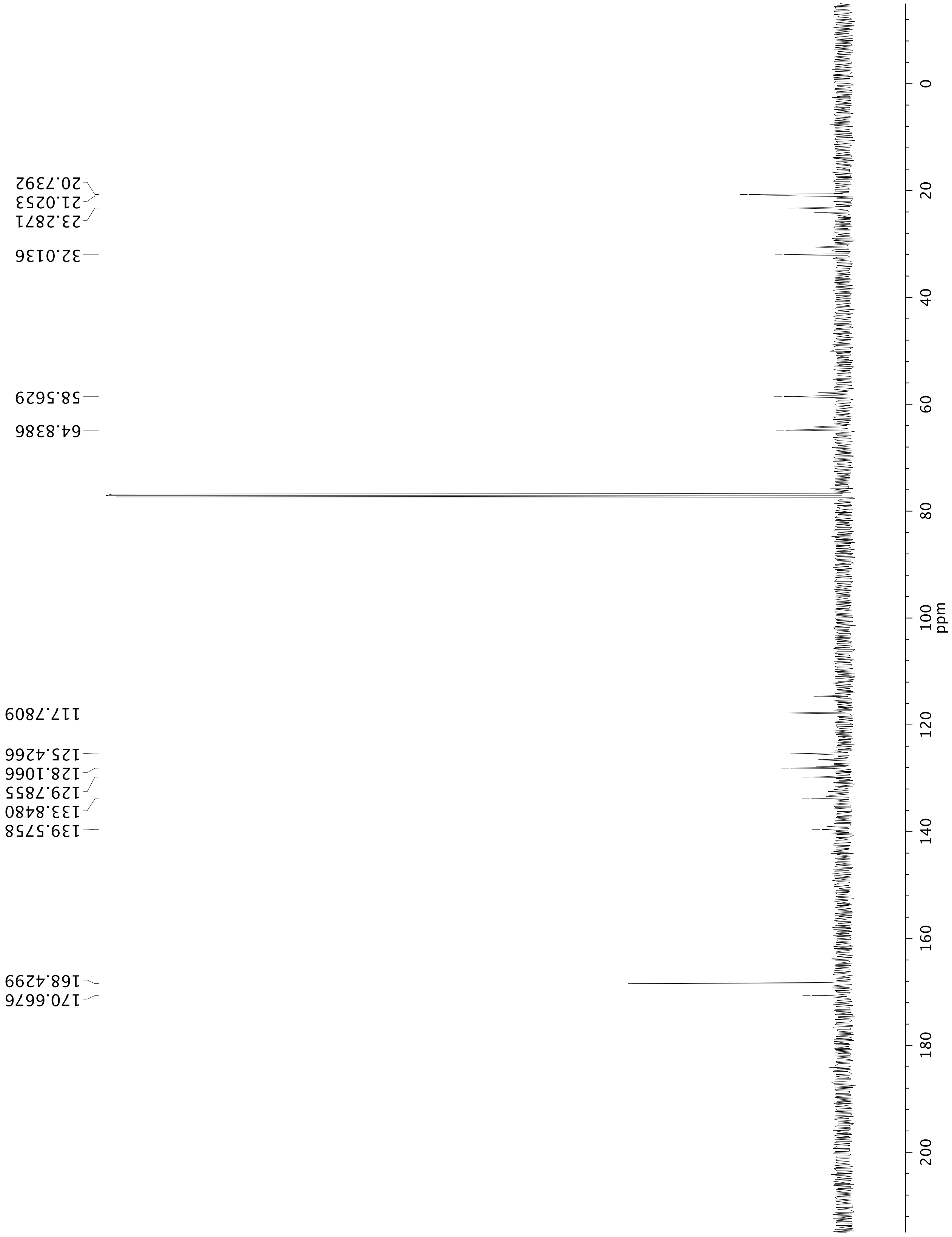
^{1}H NMR (500 MHz, DMSO, 75 °C) of compound **4a**.



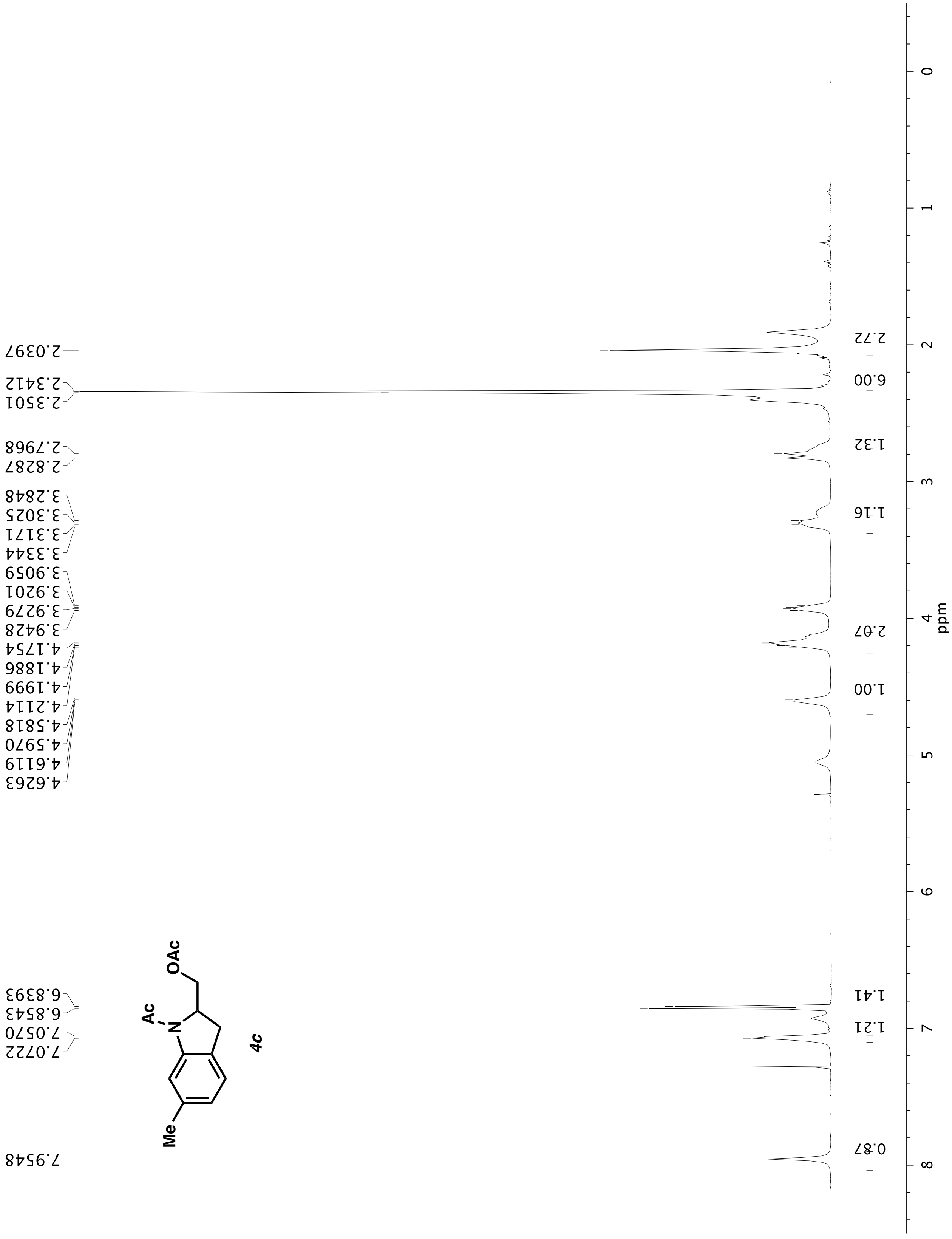
^{13}C NMR (126 MHz, CDCl$_3$) of compound **4a**.



^{1}H NMR (500 MHz, CDCl$_3$) of compound **4b**.

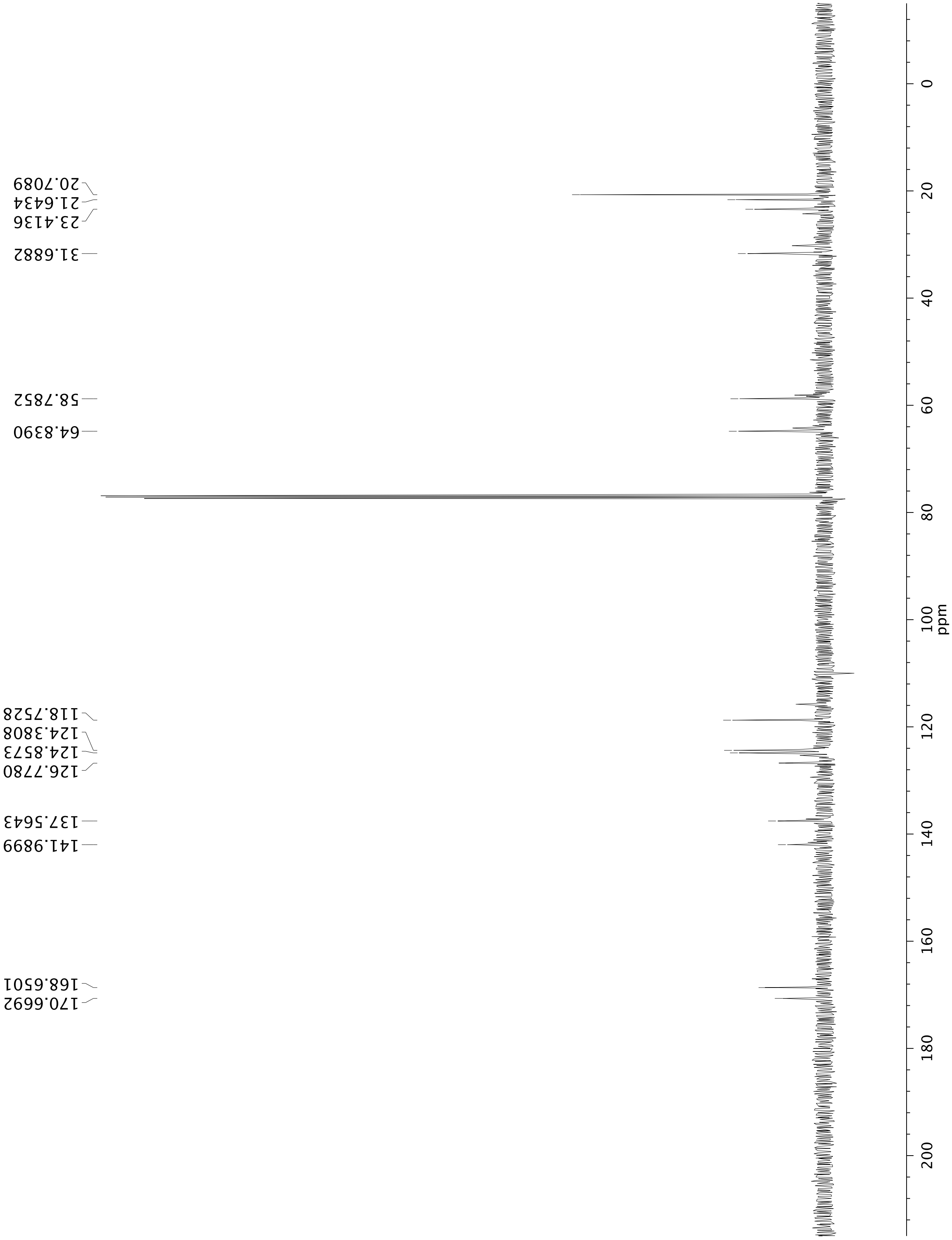


^{13}C NMR (126 MHz, CDCl$_3$) of compound **4b**.

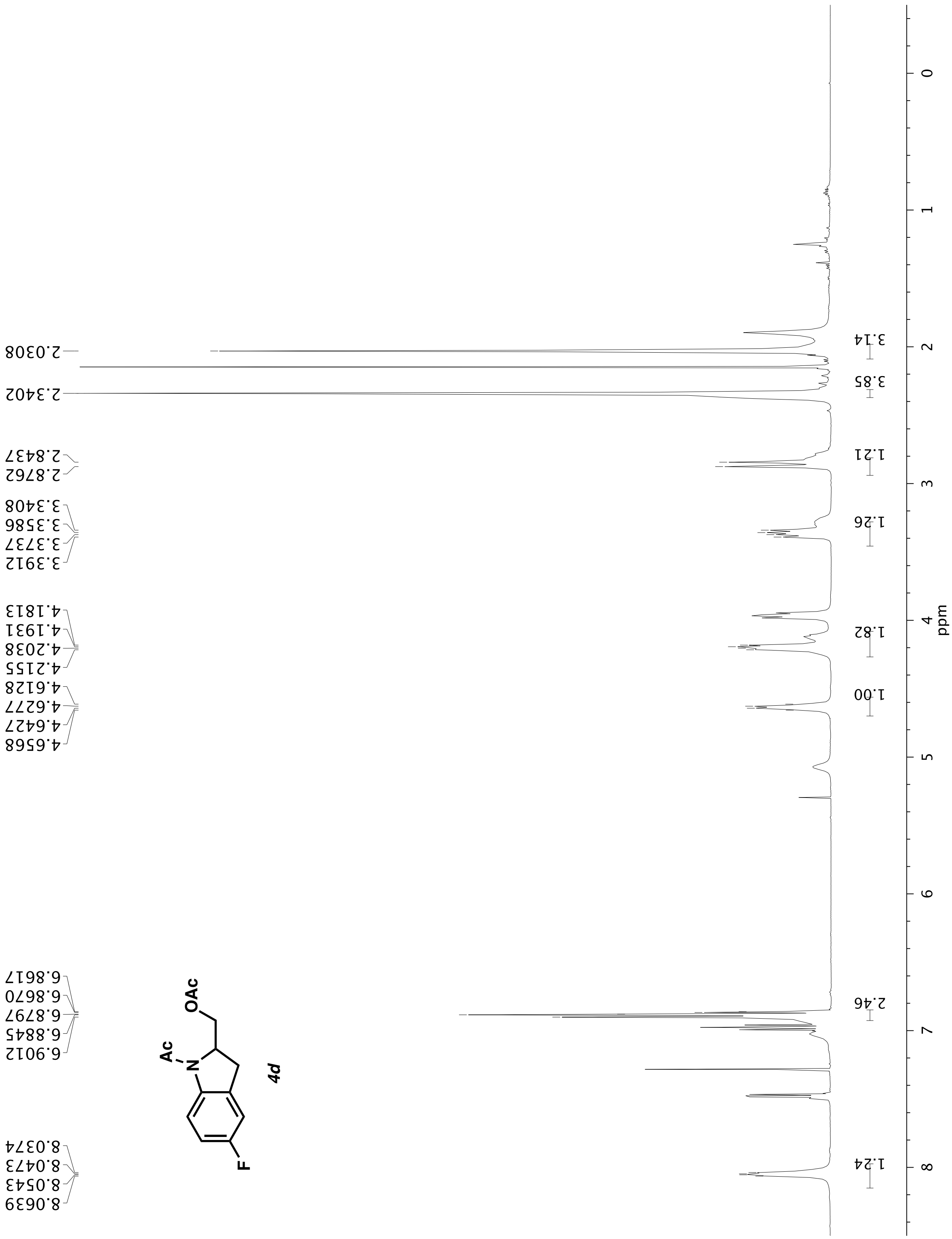


4c

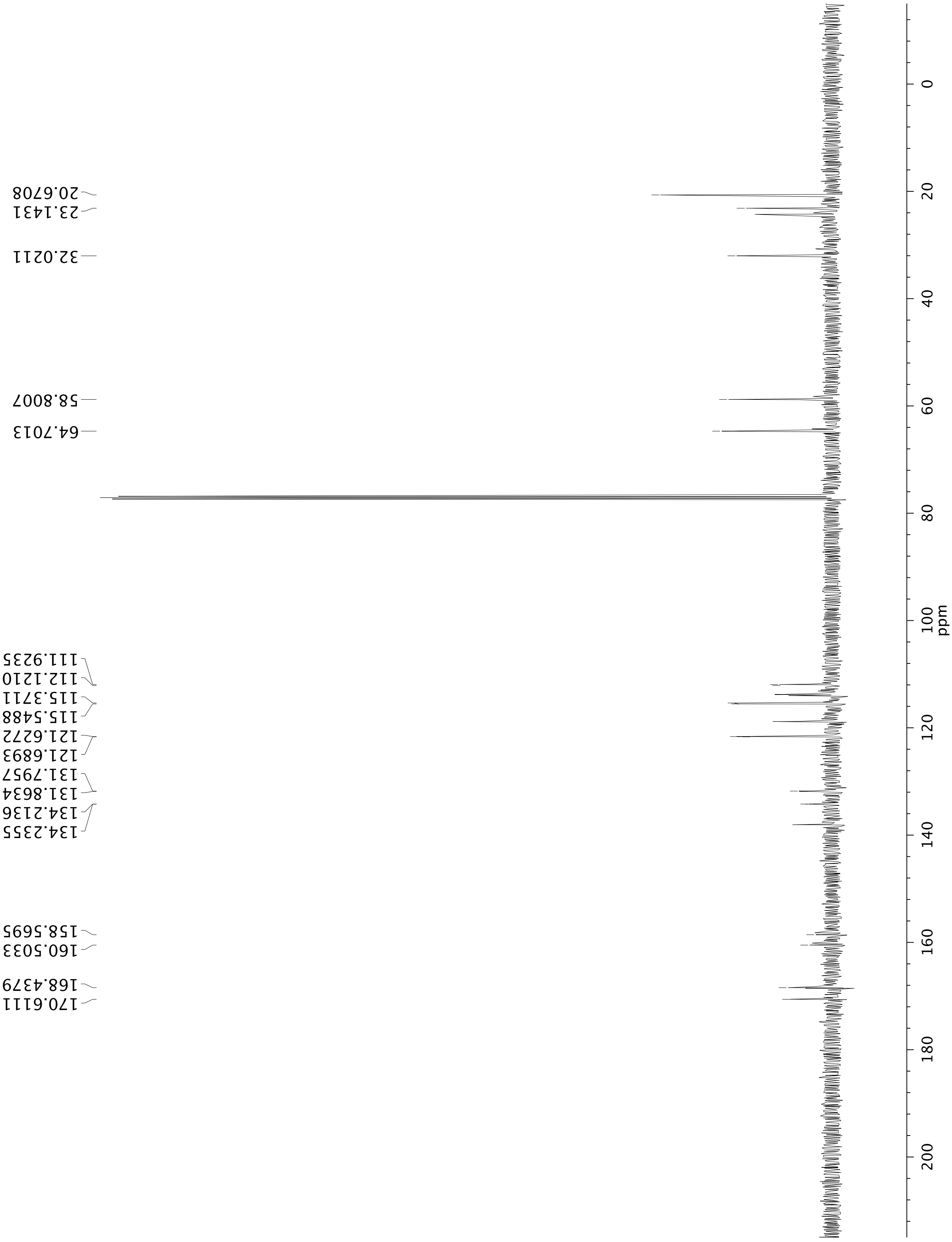
^{1}H NMR (500 MHz, CDCl$_3$) of compound **4c**.



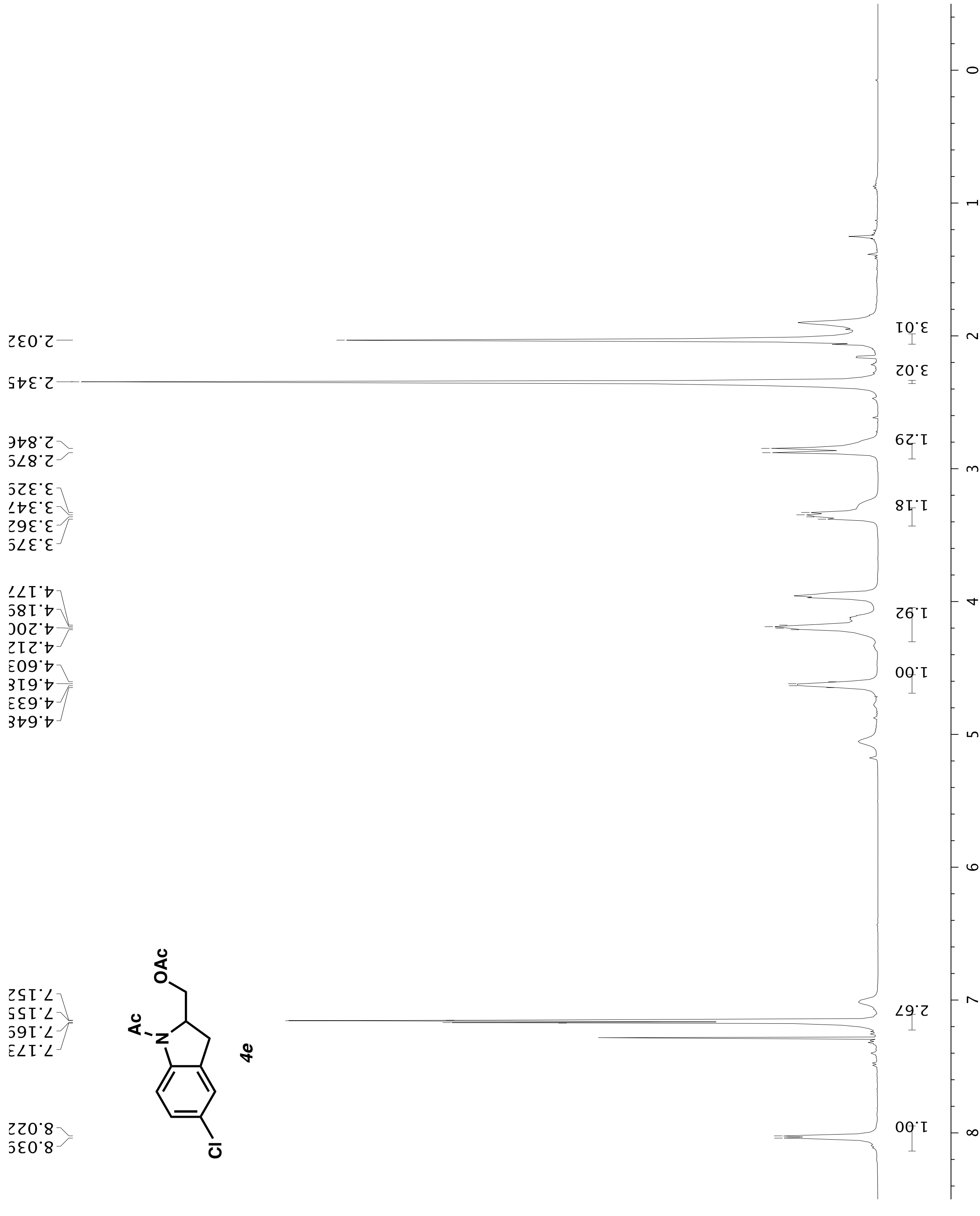
^{13}C NMR (126 MHz, CDCl$_3$) of compound **4c**.



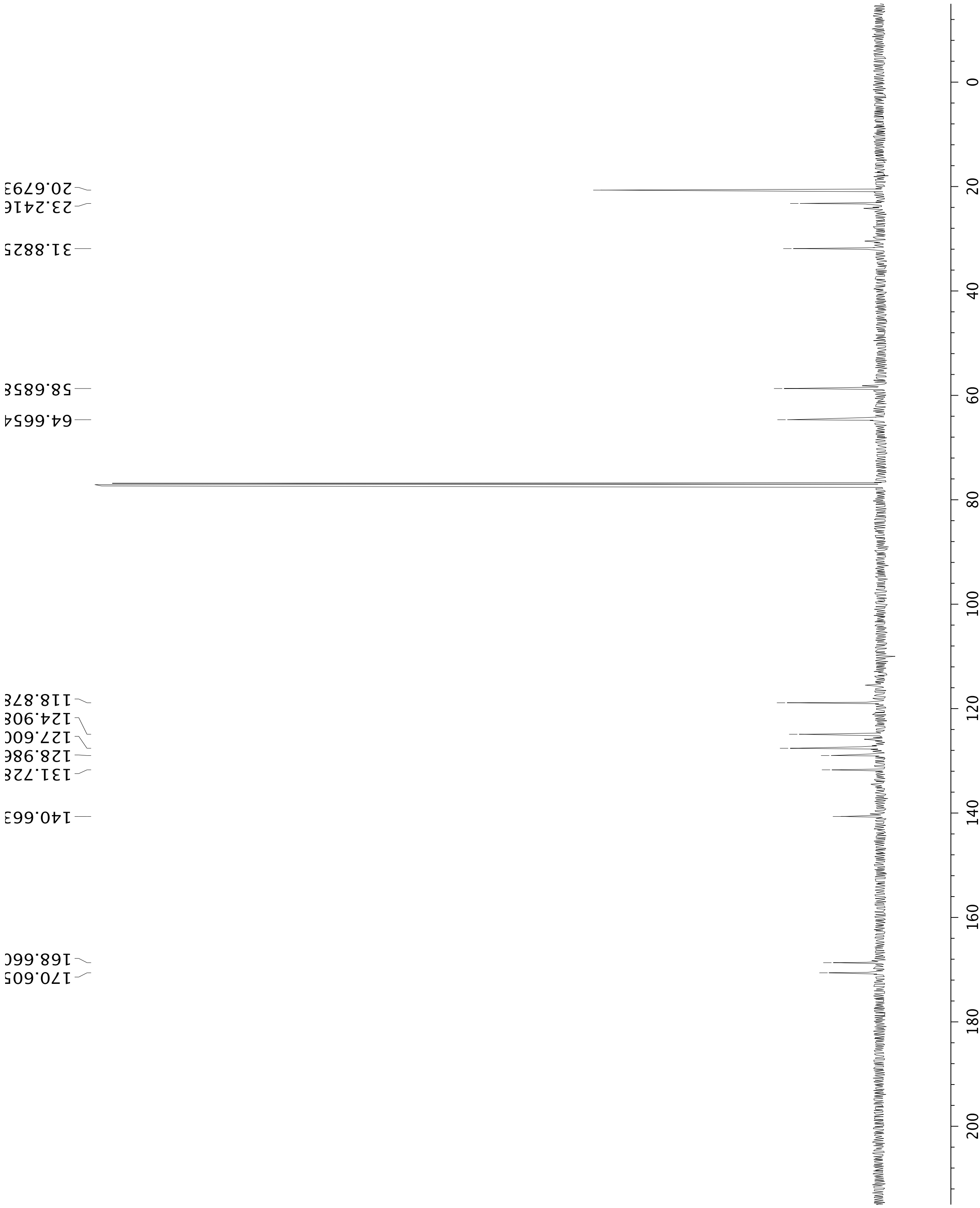
^{1}H NMR (500 MHz, CDCl$_3$) of compound **4d**.



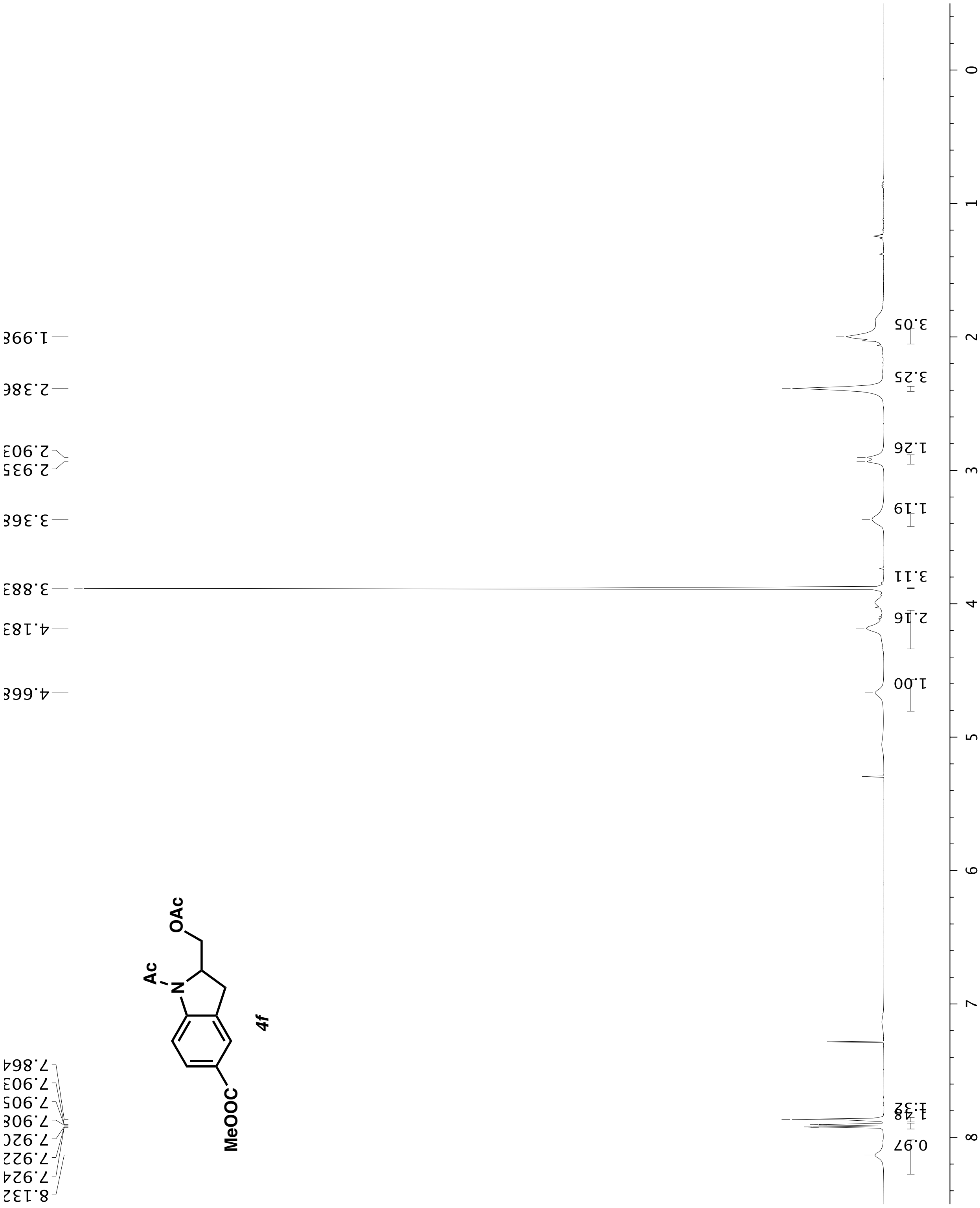
^{13}C NMR (126 MHz, CDCl$_3$) of compound **4d**.



^{1}H NMR (500 MHz, CDCl$_3$) of compound **4e**.

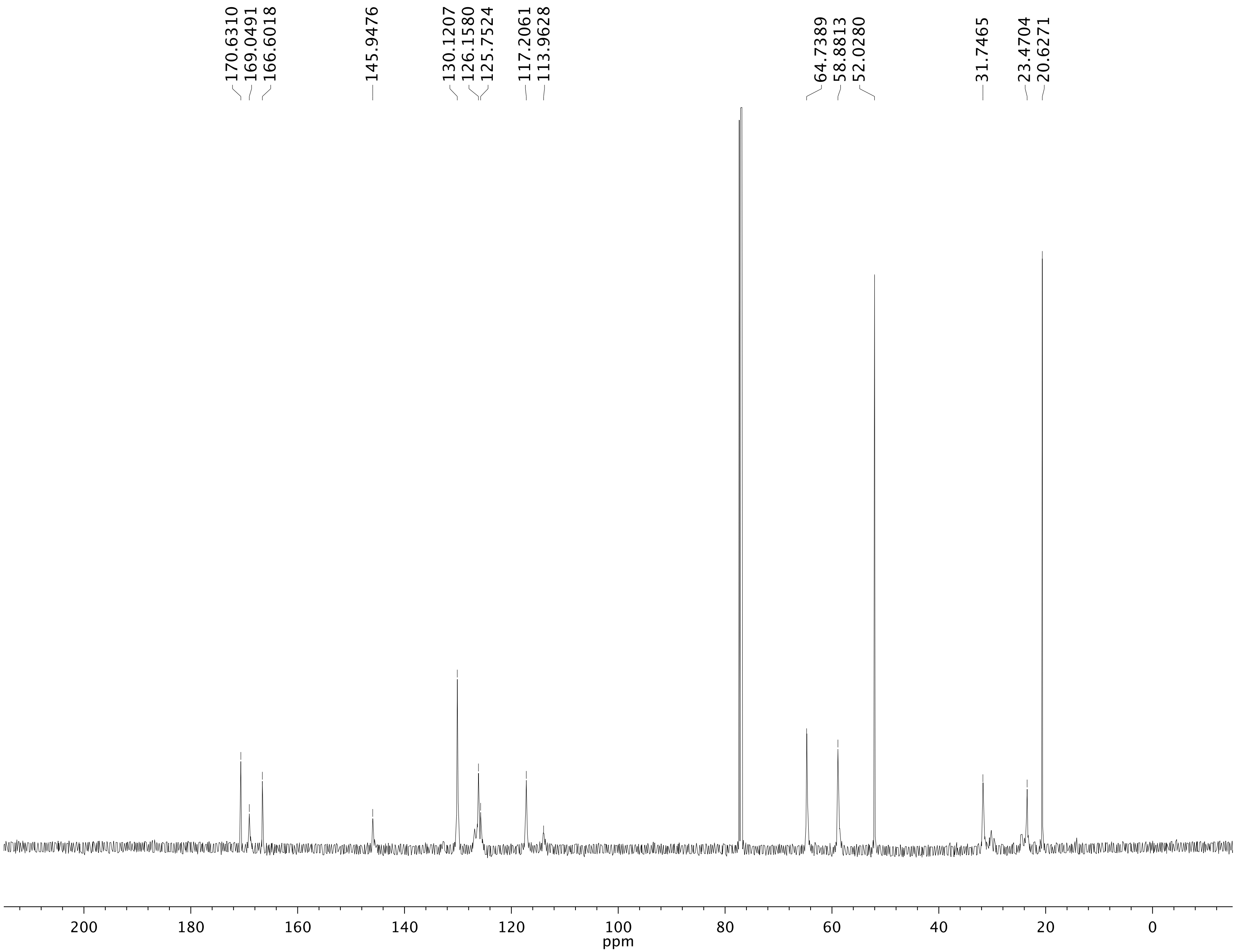


^{13}C NMR (126 MHz, $CDCl_3$) of compound **4e**.

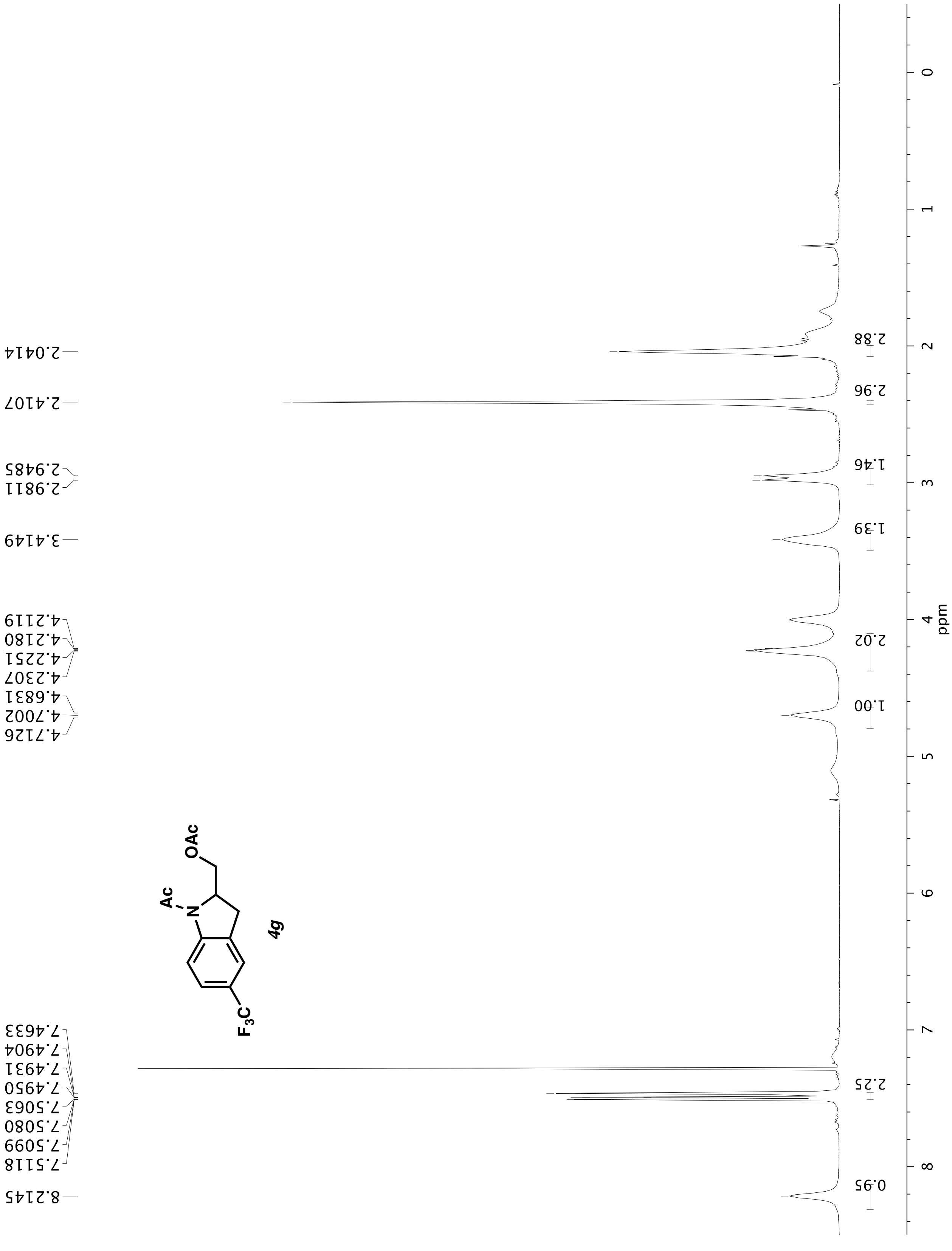


4f

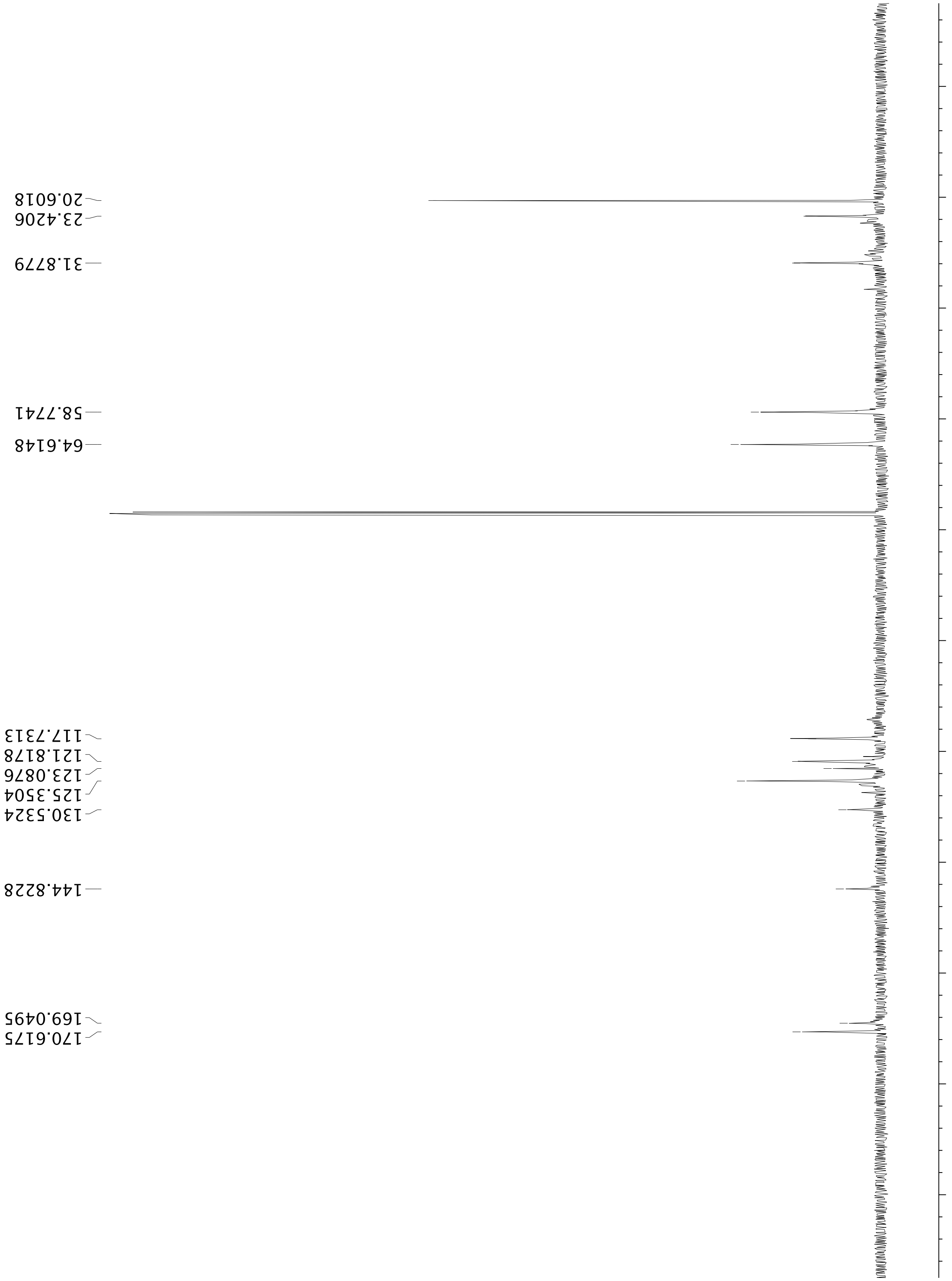
^{1}H NMR (500 MHz, CDCl$_3$) of compound **4f**.



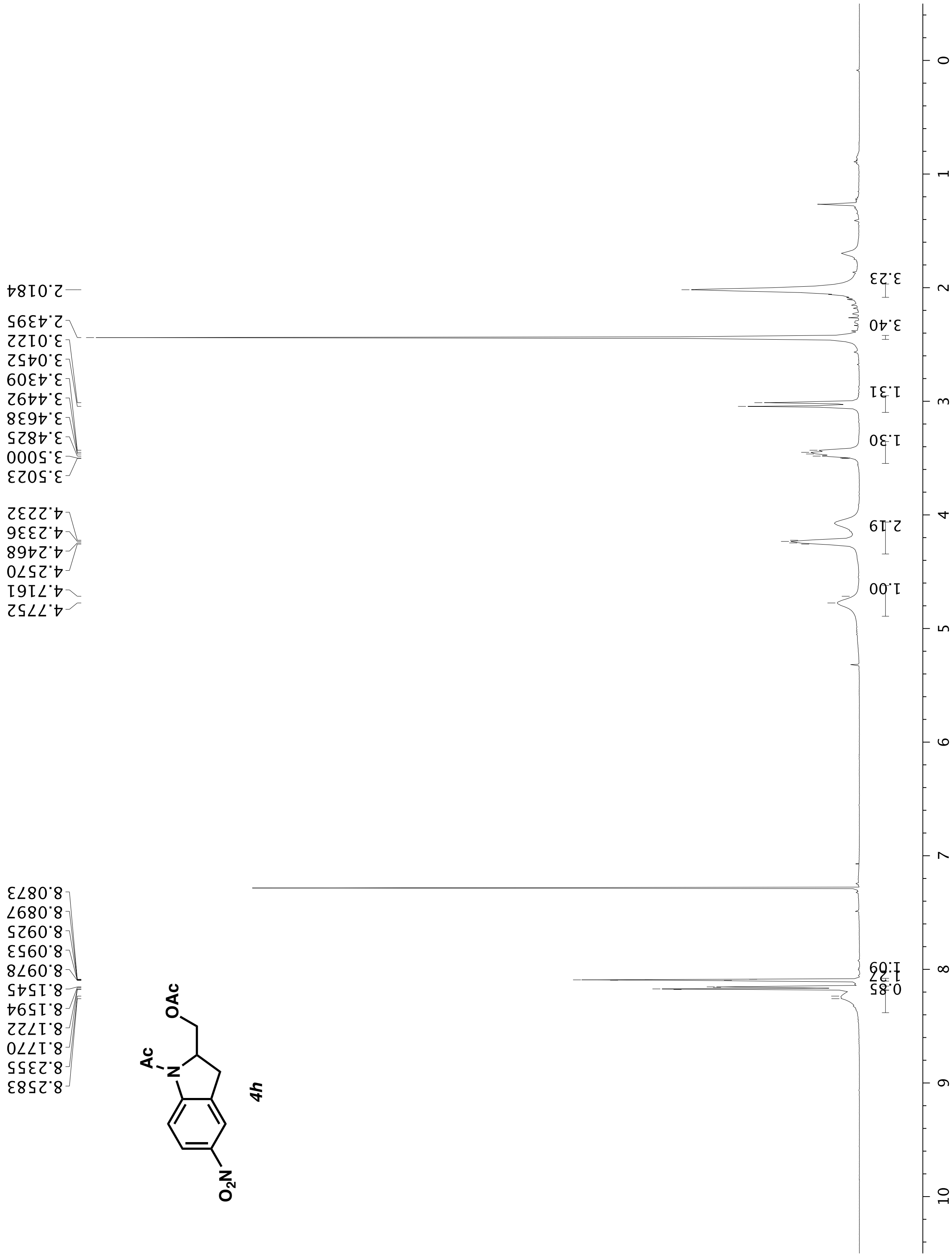
^{13}C NMR (126 MHz, CDCl$_3$) of compound **4f**.



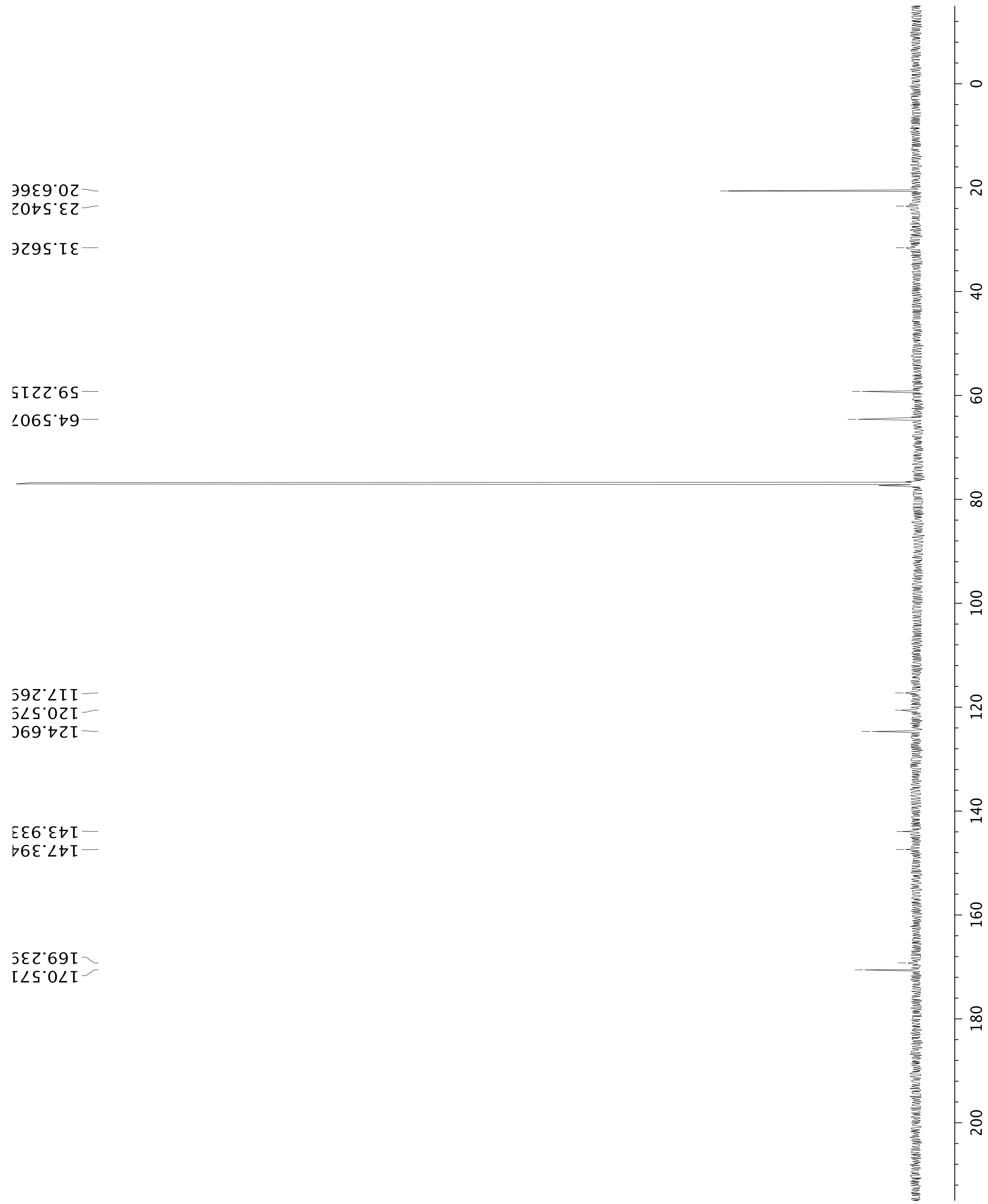
^{1}H NMR (500 MHz, $CDCl_3$) of compound **4g**.



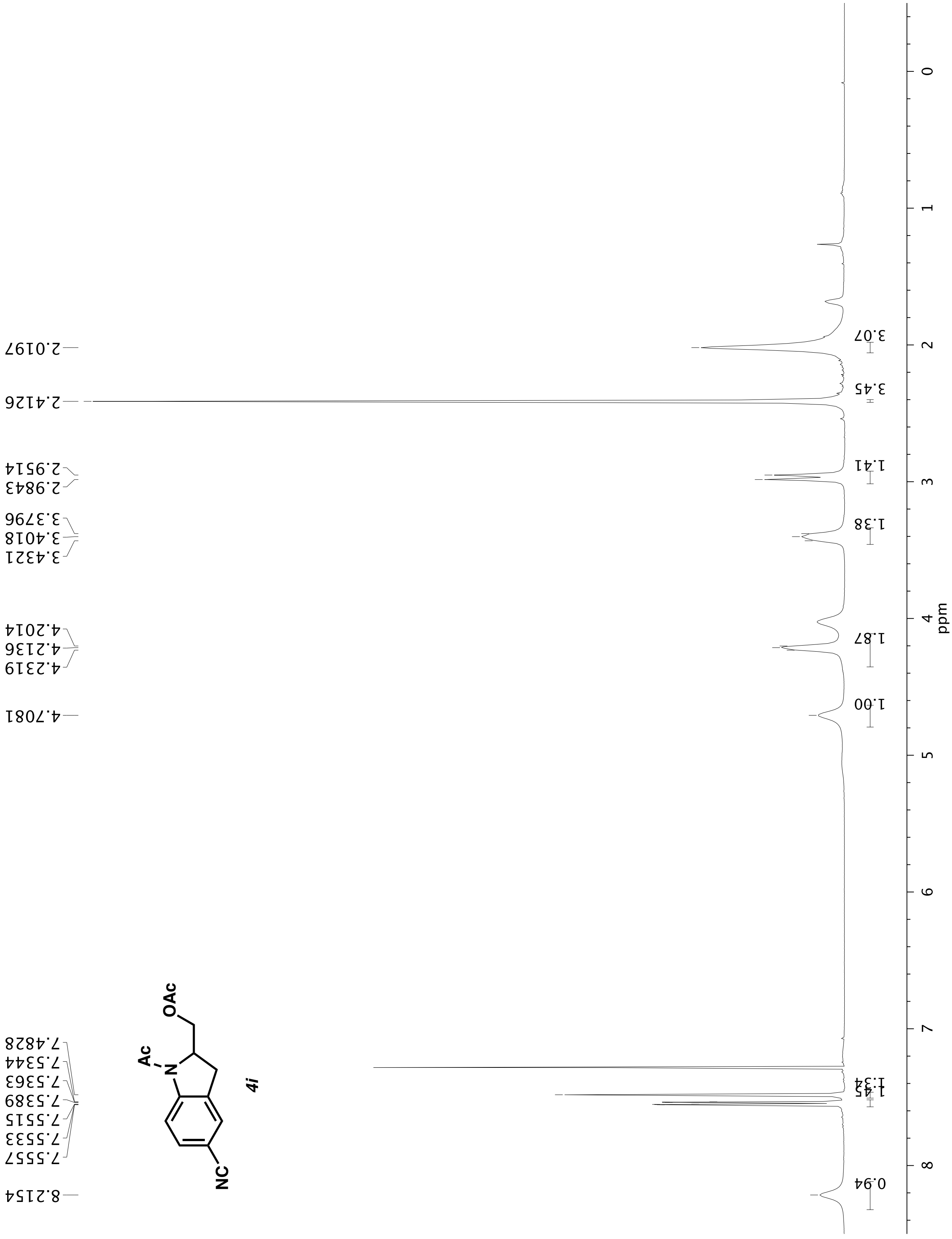
^{13}C NMR (126 MHz, CDCl$_3$) of compound **4g**.



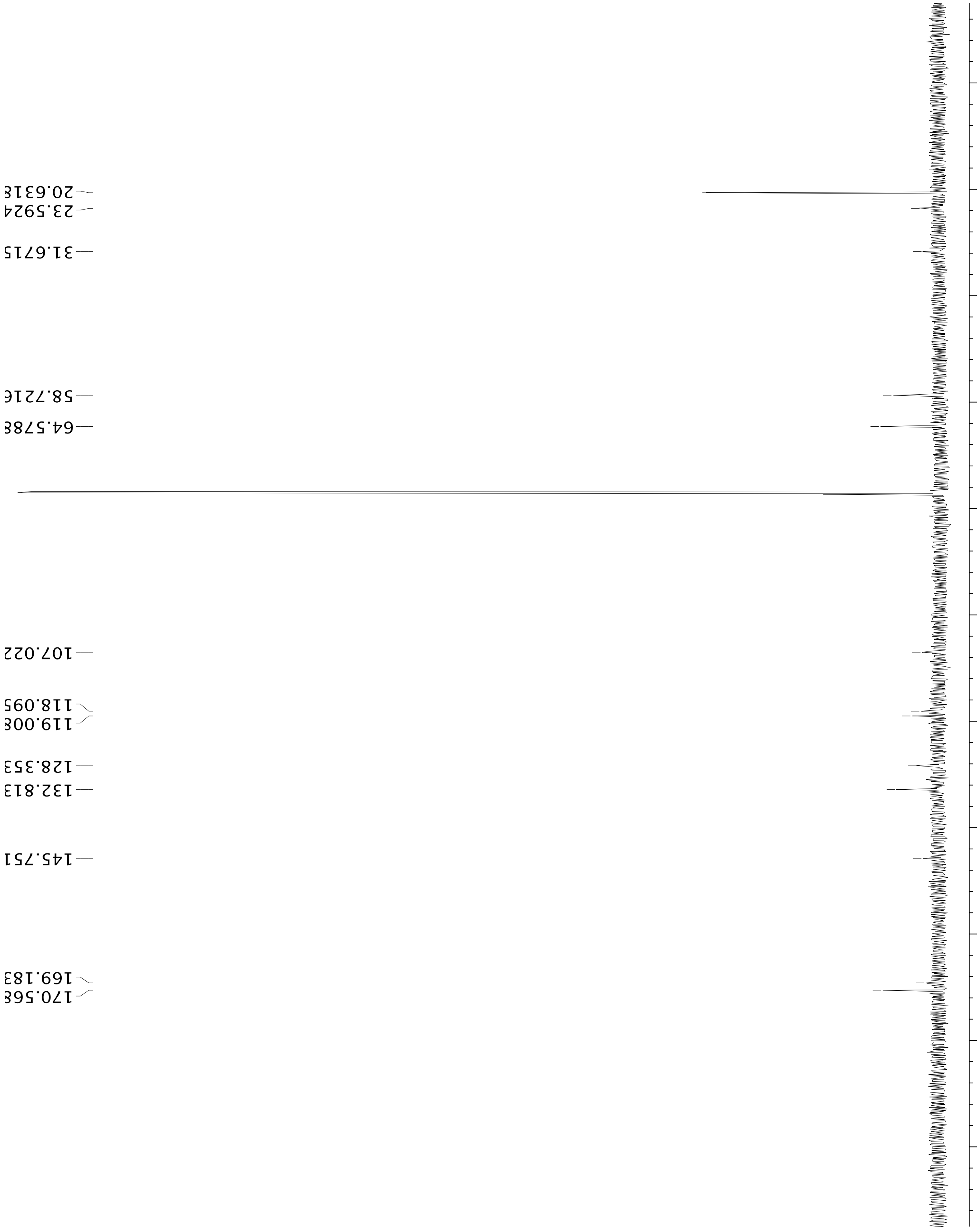
^{1}H NMR (500 MHz, $CDCl_3$) of compound **4h**.



^{13}C NMR (126 MHz, CDCl$_3$) of compound **4h**.



^{1}H NMR (500 MHz, CDCl$_3$) of compound **4i**.



^{13}C NMR (126 MHz, $CDCl_3$) of compound **4i**.