Radical Alkylation and Protonation Induced anti-Markovnikov Hydroalkylation of Unactivated Olefins via Cobalt Catalysis

(Supporting Information)

Shanshan Huang, Xiaoyang Chen, Zhangwenyi Xu, Xiaobao Zeng, Biao Xiong* and Xiaodong Qiu*

Nantong Key Laboratory of Small Molecular Drug Innovation, School of Pharmacy, Nantong University, 9 Seyuan Road, Nantong 226019, China

Email: qiuxiaodong@ntu.edu.cn; hsiung1987@ntu.edu.cn

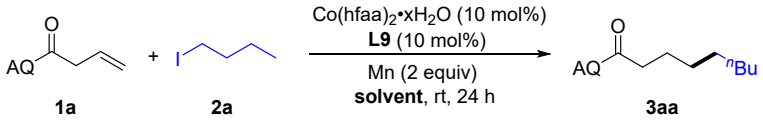
Table of contents

1. General Information.

Unless otherwise noted, all reactions were performed under an nitrogen atmosphere using flame-dried glassware. MeCN, MeOH, DMF, DMA, DMSO, THF and DCE were purchased as anhydrous solvents and were used directly. Toluene was dried and distilled over Na. All new compounds were fully characterized. NMR-spectra were recorded on Bruker ARX-400 MHz spectrometer. ^{1}H NMR spectra data were reported as δ values in ppm relative to chloroform (δ 7.26), methanol (δ 3.30), or DMSO (δ 2.50) if collected in $CDCl_3$, CD_3OD, or DMSO-d^6. ^{13}C NMR spectra data were reported as δ values in ppm relative to chloroform (δ 77.0) methanol (δ 49.0) or DMSO (δ 39.5) if collected in $CDCl_3$ (the carbon attached to B was not observed), CD_3OD, DMSO-d^6. ^{1}H NMR coupling constants were reported in Hz, and multiplicity was indicated as follows: s (singlet); d (doublet); t (triplet); q (quartet); quint (quintet); m (multiplet); dd (doubletof doublets); ddd (doublet of doublet of doublets); dddd (doublet of doublet of doublet of doublets); dt (doublet of triplets); td (triplet of doublets); ddt (doublet of doublet of triplets); dq (doubletof quartets); app (apparent); br (broad). Mass spectra were conducted at Micromass Q-Tof instrument (ESI) and Agilent Technologies 5973N (EI). Metal catalyzed reactions were carried out in flame-dried 25 mL Schlenk tubes with Teflon screw caps under nitrogen and the reactions was heated and reacted on the aluminum alloy heating reaction module. Unless otherwise noted, materials obtained from commercial suppliers were used without further purification.

2. Other optimizations of the reaction conditions

Table S1. Screening of the solvents[a]



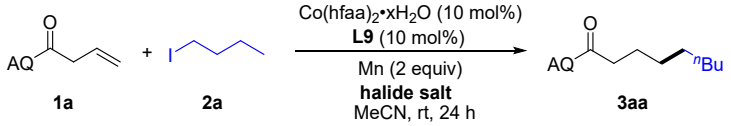
1a **2a** **3aa**

entry	solvent	yield of **3aa** (%)[b]
1	DMF	41
2	DMA	39
3	DMSO	21
4	DCM	trace
5	THF	trace
6	**MeCN**	**47**
7	Acetone	21
8	Ethyl acetate	trace
9	Toluene	n.r.
10	EtOH	n.r.

[a]Reaction conditions: **1a** (0.2 mmol), **2a** (0.4 mmol), $Co(hfaa)_2 \cdot xH_2O$ (0.02 mmol), **L9** (0.02 mmol) and

Mn (0.4 mmol) react at room temperature in 2 mL solvent for 24 h. [b]Isolated yields.

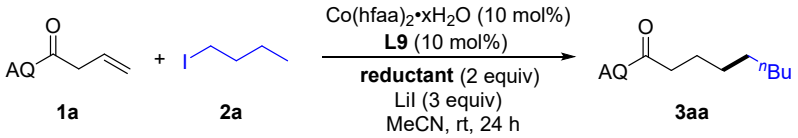
Table S2. Screening of the halide salts[a]



entry	halide salt	yield of **3aa** (%)[b]
1	LiF	48
2	NaF	45
3	LiCl	48
4	NaCl	50
5	KCl	47
6	LiBr	52
7	NaBr	49
8	KBr	48
9	LiI	55
10	NaI	53
11	KI	50
12	$ZnBr_2$	18
13	$MgBr_2$	42
14	$CaCl_2$	21
15[c]	**LiI**	**58**

[a]Reaction conditions: **1a** (0.2 mmol), **2a** (0.4 mmol), $Co(hfaa)_2 \cdot xH_2O$ (0.02 mmol), **L9** (0.02 mmol), Mn (0.4 mmol) and halide salt (0.4 mmol) react at room temperature in 2 mL MeCN for 24 h. [b]Isolated yields. [c]LiI (0.6 mmol) was applied.

Table S3. Screening of the reductants[a]

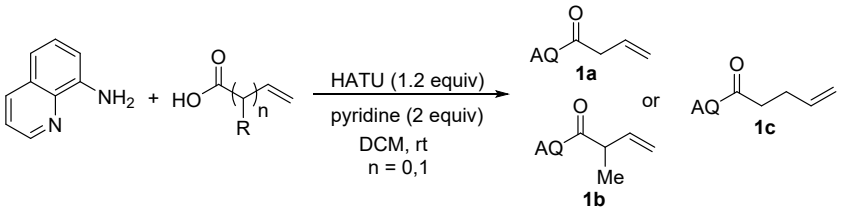


entry	reductant	yield of **3aa** (%)[b]
1	**Mn**	**58**
2	Zn	36
3	Fe	trace
4	Mg	25
5	$ZnEt_2$	trace
6	$LiAlH_4$	trace
7	PMHS	n.d.
8	$(MeO)_3SiH$	n.d.

[a]Reaction conditions: **1a** (0.2 mmol), **2a** (0.4 mmol), $Co(hfaa)_2 \cdot xH_2O$ (0.02 mmol), **L9** (0.02 mmol),

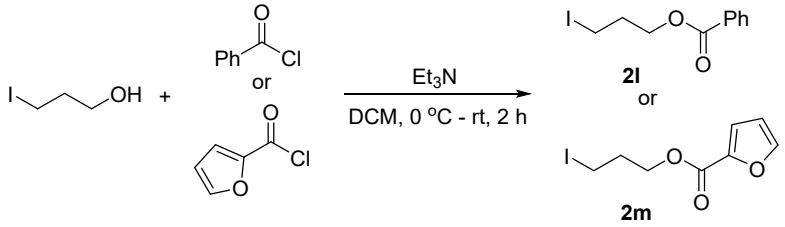
reductant (0.4 mmol) and LiI (0.6 mmol) react at room temperature in 2 mL MeCN for 24 h. [b]Isolated yields. n.d. = not detected.

3. General procedure for the synthesis of unsaturated amides



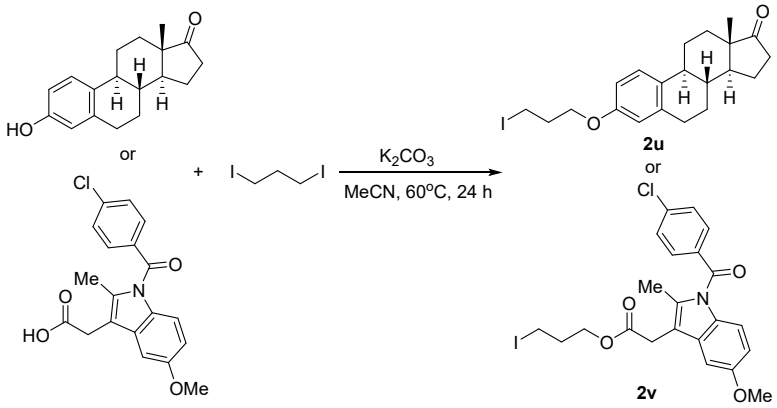
Substrates **1a**-**1c** were synthesised according to the reported procedure.[1] The corresponding alkenyl acid (12 mmol) was charged into a 100 mL round bottom flask containing dichloromethane (30 mL). 8-Aminoquinoline (10 mmol, 1.44 g), pyridine (20 mmol, 1.58 g), and HATU (12 mmol, 4.56 g) were added sequentially, and the reaction was stirred at ambient temperature for 16 h. The residue was dissolved in EtOAc (40 mL), washed with sat. $NaHCO_3$ (2 × 30 mL) and brine (1 × 30 mL), and then purified by silica gel flash column chromatography to yield the corresponding product (mixed solution of petroleum ether and ethyl acetate used as the eluent). **1a** was obtained as a white solid (1.9 g, 90%). **1b** was obtained as a colorless oil (1.97 g, 87%). **1c** was obtained as a colorless oil (2.06 g, 91%).

4. Experimental procedures for the synthesis of alkyl iodides

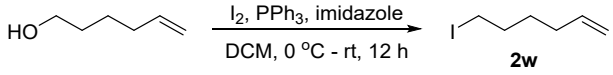


Substrates **2l, 2m** were synthesised according to the reported procedure.[2] 3-Iodopropan-1-ol (10 mmol, 1.86 g) was charged into a 100 mL round bottom flask containing dichloromethane (20 mL). Benzoyl chloride (10.5 mmol, 1.47 g) or furan-2-carbonyl chloride (10.5 mmol, 1.37 g) was added and the mixture was stirred under 0 °C. Triethylamine (11 mmol, 1.11 g) was then added dropwise. After addition of triethylamine, the reaction was stirred under room temperature for 2h. Saturated NH_4Cl aqueous solution (30 mL) was added to the reaction, and the aqueous phase was extracted with ethyl acetate (20 mL x 3). The combined organic phase was dried over anhydrous Na_2SO_4 and filtered to collect the filtrate. The solvent in filtrate was removed under reduced pressure and the crude product was purified through silica gel flash column chromatography (mixed solution of petroleum ether and ethyl acetate used as the eluent). Iodoalkane **2l** was obtained as a colorless oil (2.78 g, 96%) and **2m** was also obtained as a

colorless oil (2.63 g, 94%).

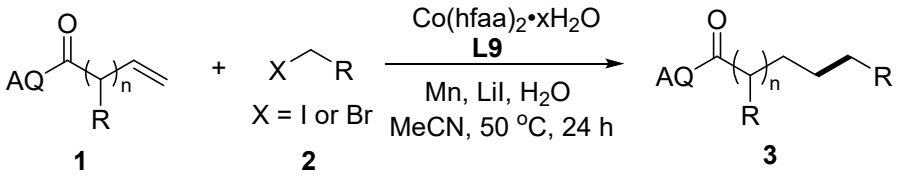


Substrates **2u, 2v** were synthesised according to the reported procedure.[3,4] In a 100 mL round bottom flask was charged with estrone (5 mmol, 1.35 g) or indometacin (5 mmol, 1.78 g) and K_2CO_3 (10 mmol, 1.38 g). Then MeCN (15 mL) and 1,3-diiodopropane (5 mmol, 1.48 g) were added at ambient temperature. The mixture was heated and stirred under 60 °C for 24 h. Then the reaction was quenched by water, and the aqueous phase was extracted with ethyl acetate (20 mL x 3). The combined organic phase was dried over anhydrous Na_2SO_4 and filtered to collect the filtrate. Then the solvent in the filtrate was removed under reduced pressure and the crude product was purified through silica gel flash column chromatography (mixed solution of petroleum ether and ethyl acetate used as the eluent). Iodoalkane **2u** was obtained as a colorless oil (1.33 g, 61%) and **2v** was obtained as a white solid (1.70 g, 65%).



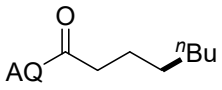
Substrates **2w** was synthesised according to the reported procedure.[5] Add I_2 (13 mmol, 3.3 g) to a stirred solution of PPh_3 (12 mmol, 3.14 g) and imidazole (12 mmol, 0.82 g) in DCM at 0°C. Add alcohol (10 mmol, 1.0 g) dropwise to the mixture. Stir the mixture for 12 hours at room temperature. Wash the mixture with a saturated sodium sulfite solution. Then the solution was dried over anhydrous Na_2SO_4 and filtered to collect the filtrate. Then the solvent in the filtrate was removed under reduced pressure and the crude product was purified through silica gel flash column chromatography (petroleum ether as the eluent) to obtain 6-iodohex-1-ene **2w** (1.99 g, 95%).

5. General procedure for the hydroalkylation of olefins



A flame dried 25 mL Schlenk tube was charged with $Co(hfaa)_2 \cdot xH_2O$ (0.02 mmol, 10.0 mg), **L9** (0.02 mmol, 10.7 mg), **1** (0.2 mmol), Mn (0.4 mmol, 22 mg) and LiI (0.6 mmol, 80.4 mg). The tube was vacuumed and refilled with N_2 three times. MeCN (2.0 mL), H_2O (0.4 mmol, 7.2 mg) and **2** (0.4 mmol) were added to the reaction under N_2 atmosphere. The tube was screwed and the mixture was stirred at 50 °C in an aluminium alloy heating module. After 24 h, the mixture was cooled and transferred to the 25 mL round bottom flask. The solvent was removed under reduced pressure and the crude mixture was purified through silica gel column chromatography with ethyl acetate/petroleum ether as the eluent to provide product **3**.

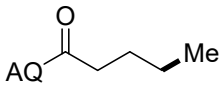
***N*-(quinolin-8-yl)octanamide (3aa)**



3aa

Compound **3aa** was obtained in 78% yield (41.9 mg) as a colorless oil (eluted by EA:PE = 1:10). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.80 (s, 1H), 8.84 – 8.72 (m, 2H), 8.13 (dd, *J* = 8.3, 1.5 Hz, 1H), 7.56 – 7.40 (m, 3H), 2.55 (t, *J* = 7.6 Hz, 2H), 1.81 (p, *J* = 7.6 Hz, 2H), 1.48 – 1.20 (m, 8H), 0.93 – 0.83 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.9, 148.0, 138.2, 136.3, 134.5, 127.8, 127.3, 121.5, 121.2, 116.3, 38.2, 31.6, 29.2, 29.0, 25.6, 22.6, 14.1. The spectroscopic data was consisted with the reported literature.[6]

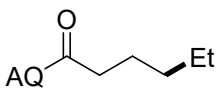
***N*-(quinolin-8-yl)pentanamide (3ab)**



3ab

Compound **3ab** was obtained in 82% yield (37.2 mg) as a colorless oil (eluted by EA:PE = 1:10). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.81 (s, 1H), 8.85 – 8.73 (m, 2H), 8.20 – 8.09 (m, 1H), 7.58 – 7.39 (m, 3H), 2.56 (t, *J* = 7.6 Hz, 2H), 1.80 (p, *J* = 7.6 Hz, 2H), 1.52 – 1.40 (m, 2H), 0.98 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.9, 148.1, 138.2, 136.3, 134.5, 127.9, 127.4, 121.5, 121.3, 116.3, 38.0, 27.7, 22.4, 13.9. The spectroscopic data was consisted with the reported literature.[6]

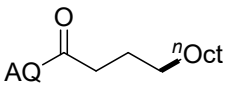
***N*-(quinolin-8-yl)hexanamide (3ac)**



3ac

Compound **3ac** was obtained in 77% yield (37.1 mg) as a colorless oil (eluted by EA:PE = 1:10). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.80 (s, 1H), 8.83 – 8.74 (m, 2H), 8.14 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.57 – 7.39 (m, 3H), 2.56 (t, *J* = 7.6 Hz, 2H), 1.83 (p, *J* = 7.4 Hz, 2H), 1.50 – 1.31 (m, 4H), 0.93 (t, *J* = 6.9 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.9, 148.0, 138.3, 136.3, 134.5, 127.9, 127.4, 121.5, 121.3, 116.3, 38.2, 31.4, 25.3, 22.4, 13.9. The spectroscopic data was consisted with the reported literature.[7]

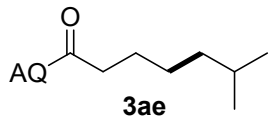
***N*-(quinolin-8-yl)dodecanamide (3ad)**



3ad

Compound **3ad** was obtained in 74% yield (48.1 mg) as a colorless oil (eluted by EA:PE = 1:10). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.81 (s, 1H), 8.84 – 8.75 (m, 2H), 8.20 – 8.09 (m, 1H), 7.57 – 7.40 (m, 3H), 2.56 (t, *J* = 7.6 Hz, 2H), 1.88 – 1.73 (m, 2H), 1.51 – 1.13 (m, 16H), 0.87 (t, *J* = 6.7 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.9, 148.0, 138.3, 136.3, 134.5, 127.9, 127.4, 121.5, 121.3, 116.3, 38.3, 31.9, 29.60, 29.58, 29.5, 29.4, 29.31, 29.28, 25.7, 22.7, 14.1. HRMS (ESI) m/z: $(M+H)^+$ calcd for $C_{21}H_{31}N_2O$, 327.2431; found, 327.2426.

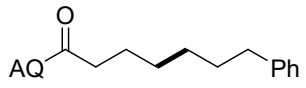
6-Methyl-*N*-(quinolin-8-yl)heptanamide (3ae)



3ae

Compound **3ae** was obtained in 71% yield (38.3 mg) as a colorless oil (eluted by EA:PE = 1:10). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.81 (s, 1H), 8.84 – 8.75 (m, 2H), 8.16 (dd, *J* = 8.3, 1.5 Hz, 1H), 7.57 – 7.41 (m, 3H), 2.64 – 2.49 (m, 2H), 1.81 (p, *J* = 7.6 Hz, 2H), 1.61 – 1.51 (m, 1H), 1.48 – 1.38 (m, 2H), 1.30 – 1.21 (m, 2H), 0.88 (d, *J* = 6.6 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.9, 148.0, 138.3, 136.4, 134.5, 127.9, 127.4, 121.5, 121.3, 116.4, 38.7, 38.3, 27.9, 27.1, 25.9, 22.6. HRMS (ESI) m/z: $(M+H)^+$ calcd for $C_{17}H_{23}N_2O$, 271.1805; found, 271.1800.

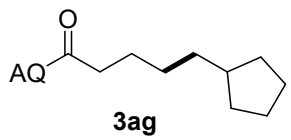
7-Phenyl-*N*-(quinolin-8-yl)heptanamide (3af)



3af

Compound **3af** was obtained in 75% yield (49.7 mg) as a white solid (eluted by EA:PE = 1:10). Melting point: 59.7 – 61.5 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.81 (s, 1H), 8.83 – 8.72 (m, 2H), 8.17 (d, *J* = 8.2 Hz, 1H), 7.60 – 7.39 (m, 3H), 7.31 – 7.23 (m, 2H), 7.21 – 7.11 (m, 3H), 2.66 – 2.49 (m, 4H), 1.82 (p, *J* = 7.4 Hz, 2H), 1.65 (p, *J* = 7.6 Hz, 2H), 1.54 – 1.34 (m, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.8, 148.0, 142.7, 138.3, 136.4, 134.5, 128.4, 128.2, 127.9, 125.6, 121.5, 121.3, 116.4, 38.2, 35.9, 31.3, 29.1, 29.0, 25.6. HRMS (ESI) m/z: $(M+H)^+$ calcd for $C_{22}H_{25}N_2O$, 333.1961; found, 333.1956.

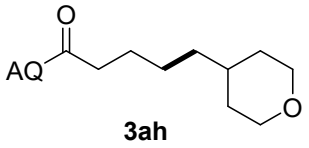
5-Cyclopentyl-*N*-(quinolin-8-yl)pentanamide (3ag)



3ag

Compound **3ag** was obtained in 67% yield (39.6 mg) as a colorless oil (eluted by EA:PE = 1:10). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.81 (s, 1H), 8.83 – 8.74 (m, 2H), 8.14 (dd, *J* = 8.3, 1.4 Hz, 1H), 7.57 – 7.39 (m, 3H), 2.56 (t, *J* = 7.6 Hz, 2H), 1.88 – 1.68 (m, 5H), 1.67 – 1.30 (m, 8H), 1.14 – 0.97 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.9, 148.0, 138.2, 136.3, 134.5, 127.9, 127.4, 121.5, 121.2, 116.3, 40.0, 38.3, 35.9, 32.6, 28.4, 25.9, 25.1. HRMS (ESI) m/z: $(M+H)^+$ calcd for $C_{19}H_{25}N_2O$, 297.1961; found, 297.1957.

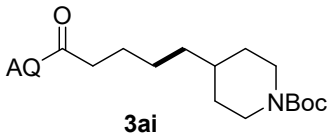
***N*-(quinolin-8-yl)-5-(tetrahydro-2H-pyran-4-yl)pentanamide (3ah)**



3ah

Compound **3ah** was obtained in 69% yield (42.9 mg) as a colorless oil (eluted by EA:PE = 1:10). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.80 (s, 1H), 8.82 – 8.72 (m, 2H), 8.14 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.56 – 7.41 (m, 3H), 3.92 (dd, *J* = 11.3, 3.6 Hz, 2H), 3.33 (t, *J* = 11.7 Hz, 2H), 2.56 (t, *J* = 7.5 Hz, 2H), 1.80 (p, *J* = 7.6 Hz, 2H), 1.62 – 1.53 (m, 2H), 1.52 – 1.38 (m, 3H), 1.35 – 1.18 (m, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.7, 148.0, 138.2, 136.3, 134.4, 127.8, 127.3, 121.5, 121.3, 116.3, 68.0, 38.1, 36.6, 34.7, 33.1, 25.9, 25.7. HRMS (ESI) m/z: $(M+H)^+$ calcd for $C_9H_{25}N_2O$, 313.1911; found, 313.1905.

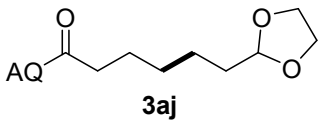
***tert*-Butyl 4-(5-oxo-5-(quinolin-8-ylamino)pentyl)piperidine-1-carboxylate (3ai)**



3ai

Compound **3ai** was obtained in 62% yield (50.9 mg) as a colorless oil (eluted by EA:PE = 1:5). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.81 (s, 1H), 8.79 (t, *J* = 6.0 Hz, 2H), 8.16 (d, *J* = 8.1 Hz, 1H), 7.58 – 7.41 (m, 3H), 4.05 (d, *J* = 28.8 Hz, 2H), 2.76 – 2.46 (m, 4H), 1.80 (p, *J* = 7.5 Hz, 2H), 1.70 – 1.56 (m, 2H), 1.50 – 1.35 (m, 12H), 1.34 – 1.25 (m, 2H), 1.13 – 0.98 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.7, 154.9, 148.0, 138.2, 136.4, 134.4, 127.9, 127.4, 121.5, 121.3, 116.5, 79.1, 43.9, 38.1, 36.2, 35.8, 32.1, 28.4, 26.3, 25.7. HRMS (ESI) m/z: $(M+H)^+$ calcd for $C_{24}H_{34}N_3O_3$, 412.2595; found, 412.2587.

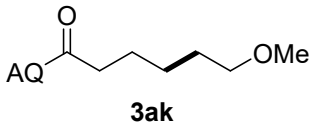
6-(1,3-Dioxolan-2-yl)-*N*-(quinolin-8-yl)hexanamide (3aj)



3aj

Compound **3aj** was obtained in 73% yield (45.6 mg) as a colorless oil (eluted by EA:PE = 1:5). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.80 (s, 1H), 8.83 – 8.69 (m, 2H), 8.14 (dd, *J* = 8.3, 1.4 Hz, 1H), 7.57 – 7.39 (m, 3H), 4.85 (t, *J* = 4.8 Hz, 1H), 4.01 – 3.89 (m, 2H), 3.90 – 3.76 (m, 2H), 2.56 (t, *J* = 7.6 Hz, 2H), 1.83 (p, *J* = 7.4 Hz, 2H), 1.74 – 1.62 (m, 2H), 1.56 – 1.40 (m, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.7, 148.0, 138.2, 136.3, 134.4, 127.8, 127.4, 121.5, 121.3, 116.3, 104.4, 64.8, 38.0, 33.7, 29.1, 25.5, 23.8. HRMS (ESI) m/z: $(M+H)^+$ calcd for $C_{18}H_{23}N_2O_3$, 315.1703; found, 315.1696.

6-Methoxy-*N*-(quinolin-8-yl)hexanamide (3ak)

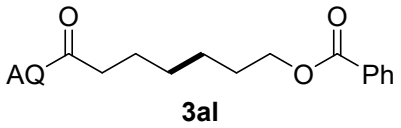


3ak

Compound **3ak** was obtained in 76% yield (41.1 mg) as a colorless oil (eluted by EA:PE = 1:5). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.81 (s, 1H), 8.82 – 8.75 (m, 2H), 8.16 (d, *J* = 7.7 Hz, 1H), 7.57 – 7.41 (m, 3H), 3.39

(t, *J* = 6.5 Hz, 2H), 3.33 (s, 3H), 2.58 (t, *J* = 7.6 Hz, 2H), 1.85 (p, *J* = 7.6 Hz, 2H), 1.71 – 1.60 (m, 2H), 1.56 – 1.42 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.7, 148.0, 138.2, 136.4, 134.5, 127.9, 127.4, 121.5, 121.4, 116.5, 72.6, 58.5, 38.1, 29.4, 25.8, 25.5. HRMS (ESI) m/z: $(M+H)^+$ calcd for $C_{16}H_{21}N_2O_2$, 273.1598; found, 273.1592.

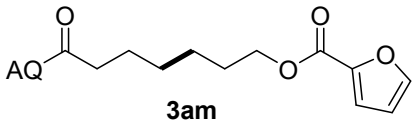
7-Oxo-7-(quinolin-8-ylamino)heptyl benzoate (3al)



3al

Compound **3al** was obtained in 72% yield (54.1 mg) as a white solid (eluted by EA:PE = 1:10). Melting point: 78.9-80.2 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.81 (s, 1H), 8.85 – 8.72 (m, 2H), 8.16 (d, *J* = 8.2 Hz, 1H), 8.04 (d, *J* = 7.3 Hz, 2H), 7.60 – 7.47 (m, 3H), 7.48 – 7.37 (m, 3H), 4.33 (t, *J* = 6.5 Hz, 2H), 2.58 (t, *J* = 7.5 Hz, 2H), 1.91 – 1.75 (m, 4H), 1.62 – 1.44 (m, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.7, 166.6, 148.1, 138.2, 136.4, 134.4, 132.8, 130.4, 129.5, 128.3, 127.9, 127.4, 121.5, 121.3, 116.4, 64.9, 38.0, 28.9, 28.6, 25.9, 25.5. HRMS (ESI) m/z: $(M+H)^+$ calcd for $C_{23}H_{25}N_2O_3$, 377.1860; found, 377.1853.

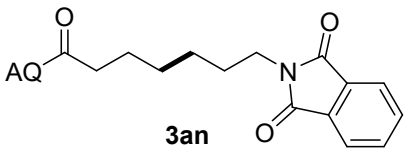
7-Oxo-7-(quinolin-8-ylamino)heptyl furan-2-carboxylate (3am)



3am

Compound **3am** was obtained in 67% yield (48.8 mg) as a colorless oil (eluted by EA:PE = 1:10). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.81 (s, 1H), 8.87 – 8.68 (m, 2H), 8.15 (d, *J* = 8.2 Hz, 1H), 7.62 – 7.39 (m, 4H), 7.16 (d, *J* = 3.4 Hz, 1H), 6.48 (dd, *J* = 3.4, 1.6 Hz, 1H), 4.30 (t, *J* = 6.6 Hz, 2H), 2.57 (t, *J* = 7.4 Hz, 2H), 1.90 – 1.70 (m, 4H), 1.58 – 1.40 (m, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.6, 158.8, 148.1, 146.1, 144.8, 138.3, 136.3, 134.5, 127.9, 127.4, 121.5, 121.3, 117.7, 116.4, 111.7, 64.9, 38.0, 28.9, 28.5, 25.7, 25.4. HRMS (ESI) m/z: $(M+H)^+$ calcd for $C_{21}H_{23}N_2O_4$, 367.1652; found, 367.1648.

7-(1,3-Dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)heptanamide (3an)

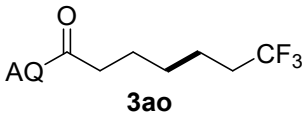


3an

Compound **3an** was obtained in 58% yield (46.4 mg) as a brown solid (eluted by EA:PE = 1:2). Melting point: 123.8-125.5 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.79 (s, 1H), 8.84 – 8.71 (m, 2H), 8.15 (dd, *J* = 8.2, 1.3 Hz, 1H), 7.82 (dt, *J* = 7.5, 3.7 Hz, 2H), 7.69 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.57 – 7.39 (m, 3H), 3.69 (t, *J* = 7.2 Hz, 2H), 2.56 (t, *J* = 7.5 Hz, 2H), 1.84 (dp, *J* = 22.5, 8.5, 7.6 Hz, 2H), 1.71 (q, *J* = 8.5, 8.0 Hz, 3H), 1.45 (dtt, *J* = 20.3, 9.3, 5.7 Hz, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.7, 168.4, 148.1, 138.3, 136.3, 134.5, 133.8, 132.1, 127.9, 127.4, 123.1, 121.5, 121.3, 116.3, 38.0, 37.9, 28.8, 28.5, 26.6, 25.5. The spectroscopic data was consisted

with the reported literature.[8]

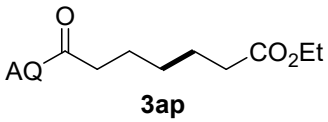
7,7,7-Trifluoro-*N*-(quinolin-8-yl)heptanamide (3ao)



3ao

Compound **3ao** was obtained in 83% yield (51.4 mg) as a white solid (eluted by EA:PE = 1:10). Melting point: 74.1-75.7 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.81 (s, 1H), 8.79 (dd, *J* = 12.3, 5.7 Hz, 2H), 8.17 (d, *J* = 8.3 Hz, 1H), 7.59 – 7.42 (m, 3H), 2.59 (t, *J* = 7.4 Hz, 2H), 2.19 – 2.02 (m, 2H), 1.85 (p, *J* = 7.5 Hz, 2H), 1.70 – 1.59 (m, 2H), 1.52 (p, *J* = 7.5, 7.1 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.3, 148.1, 138.3, 136.4, 134.4, 127.9, 127.4, 127.1 (q, *J* = 276.3 Hz), 121.6, 121.4, 116.4, 37.7, 33.6 (q, *J* = 28.4 Hz), 28.3, 25.1, 21.7 (q, *J* = 3.0 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ -66.4. HRMS (ESI) m/z: $(M+H)^+$ calcd for $C_{16}H_{18}F_3N_2O$, 311.1366; found, 311.1359.

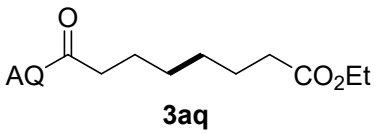
Ethyl 7-oxo-7-(quinolin-8-ylamino)heptanoate (3ap)



3ap

Compound **3ap** was obtained in 82% yield (51.3 mg) as a white solid (eluted by EA:PE = 1:10). Melting point: 49.5-50.7 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.80 (s, 1H), 8.85 – 8.73 (m, 2H), 8.16 (dd, *J* = 8.2, 1.7 Hz, 1H), 7.59 – 7.40 (m, 3H), 4.12 (q, *J* = 7.1 Hz, 2H), 2.57 (t, *J* = 7.6 Hz, 2H), 2.33 (t, *J* = 7.5 Hz, 2H), 1.84 (p, *J* = 7.6 Hz, 2H), 1.71 (p, *J* = 7.5 Hz, 2H), 1.53 – 1.42 (m, 2H), 1.24 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.6, 171.5, 148.1, 138.3, 136.4, 134.5, 127.9, 127.4, 121.5, 121.3, 116.4, 60.2, 37.9, 34.2, 28.7, 25.3, 24.7, 14.2. The spectroscopic data was consisted with the reported literature.[9]

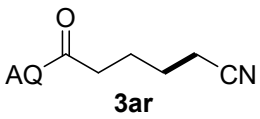
Ethyl 8-oxo-8-(quinolin-8-ylamino)octanoate (3aq)



3aq

Compound **3aq** was synthesised from the reaction of **1a** and **2q**, and was obtained in 74% yield (48.6 mg) as a colorless oil (eluted by EA:PE = 1:10). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.79 (s, 1H), 8.84 – 8.71 (m, 2H), 8.14 (dd, *J* = 8.3, 1.4 Hz, 1H), 7.59 – 7.38 (m, 3H), 4.10 (q, *J* = 7.2 Hz, 2H), 2.55 (t, *J* = 7.5 Hz, 2H), 2.29 (t, *J* = 7.5 Hz, 2H), 1.81 (p, *J* = 7.5 Hz, 2H), 1.64 (p, *J* = 7.5 Hz, 2H), 1.51 – 1.32 (m, 4H), 1.23 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.7, 171.7, 148.0, 138.2, 136.3, 134.4, 127.8, 127.3, 121.5, 121.3, 116.3, 60.1, 38.0, 34.2, 28.84, 28.82, 25.4, 24.7, 14.2. HRMS (ESI) m/z: $(M+H)^+$ calcd for $C_{19}H_{25}N_2O_3$, 329.1860; found, 329.1853.

5-Cyano-*N*-(quinolin-8-yl)pentanamide (3ar)

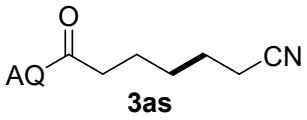


3ar

Compound **3ar** was obtained in 73% yield (37.0 mg) as a white solid (eluted by EA:PE = 1:5). Melting point: 96.4-97.9 °C. ^{1}H NMR (400 MHz,

$CDCl_3$) δ 9.88 (s, 1H), 8.81 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.78 – 8.72 (m, 1H), 8.18 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.59 – 7.51 (m, 2H), 7.47 (dd, *J* = 8.3, 4.2 Hz, 1H), 4.66 – 4.53 (m, 1H), 3.39 – 3.20 (m, 3H), 2.75 – 2.66 (m, 1H), 2.64 – 2.50 (m, 1H), 2.30 – 2.16 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.5, 148.3, 138.2, 136.4, 133.8, 127.9, 127.3, 122.1, 121.7, 118.3, 116.7, 48.7, 35.6, 25.1, 18.3. HRMS (ESI) m/z: $(M+H)^+$ calcd for $C_{15}H_{16}N_3O$, 254.1288; found, 254.1282.

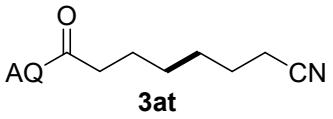
6-Cyano-*N*-(quinolin-8-yl)hexanamide (3as)



3as

Compound **3as** was obtained in 70% yield (37.4 mg) as a colorless oil (eluted by EA:PE = 1:5). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.81 (s, 1H), 8.80 (dd, *J* = 4.2, 1.5 Hz, 1H), 8.76 (dd, *J* = 7.1, 1.5 Hz, 1H), 8.16 (dd, *J* = 8.3, 1.4 Hz, 1H), 7.60 – 7.38 (m, 3H), 2.59 (t, *J* = 7.4 Hz, 2H), 2.37 (t, *J* = 7.1 Hz, 2H), 1.85 (p, *J* = 7.4 Hz, 2H), 1.80 – 1.69 (m, 2H), 1.65 – 1.52 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.1, 148.1, 138.2, 136.4, 134.3, 127.9, 127.3, 121.6, 121.5, 119.6, 116.4, 37.5, 28.2, 25.2, 24.6, 17.0. HRMS (ESI) m/z: $(M+H)^+$ calcd for $C_{16}H_{18}N_3O$, 268.1444; found, 268.1439.

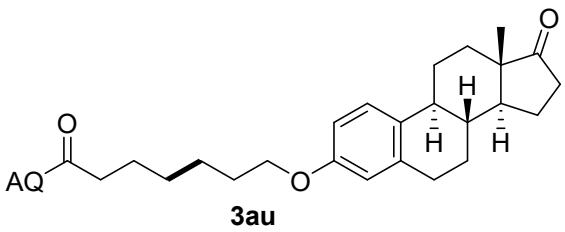
7-Cyano-*N*-(quinolin-8-yl)heptanamide (3at)



3at

Compound **3at** was obtained in 65% yield (36.6 mg) as a colorless oil (eluted by EA:PE = 1:5). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.81 (s, 1H), 8.86 – 8.73 (m, 2H), 8.16 (d, *J* = 8.2 Hz, 1H), 7.59 – 7.40 (m, 3H), 2.58 (t, *J* = 7.4 Hz, 2H), 2.35 (t, *J* = 7.1 Hz, 2H), 1.84 (p, *J* = 7.5 Hz, 2H), 1.69 (p, *J* = 7.0 Hz, 2H), 1.59 – 1.42 (m, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.4, 148.1, 138.2, 136.4, 134.4, 127.9, 127.4, 121.6, 121.4, 119.7, 116.4, 37.8, 28.4, 28.3, 25.2, 17.1. The spectroscopic data was consisted with the reported literature.[10]

7-(((8*R*,9*S*,13*S*,14*S*)-13-Methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6*H*-cyclopenta[*a*]phenanthren-3-yl)oxy)-*N*-(quinolin-8-yl)heptanamide (3au)

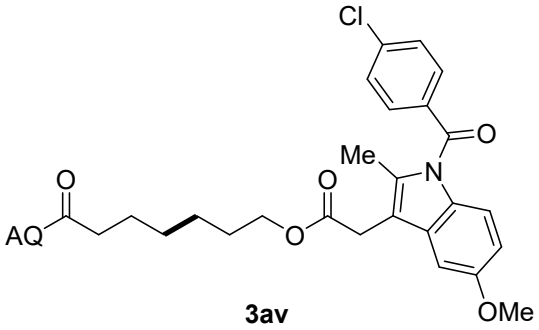


3au

Compound **3au** was obtained in 54% yield (56.6 mg) as a colorless oil (eluted by EA:PE = 1:2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.82 (s, 1H), 8.85 – 8.75 (m, 2H), 8.16 (dd, *J* = 8.2, 1.4 Hz, 1H), 7.57 – 7.41 (m, 3H), 7.17 (d, *J* = 8.6 Hz, 1H), 6.70 (dd, *J* = 8.5, 2.6 Hz, 1H), 6.64 (d, *J* = 2.4 Hz, 1H), 3.93 (t, *J* = 6.5 Hz, 2H), 2.92 – 2.82 (m, 2H), 2.58 (t, *J* = 7.5 Hz, 2H), 2.54 – 2.44 (m, 1H), 2.42 – 2.33 (m, 1H), 2.28 – 2.19 (m, 1H), 2.17 – 2.07 (m, 1H), 2.05 – 1.91 (m, 3H), 1.90 – 1.75 (m, 4H),

1.67 – 1.35 (m, 10H), 0.90 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.7, 157.0, 148.0, 138.2, 137.6, 136.3, 134.4, 131.7, 127.9, 127.4, 126.2, 121.5, 121.3, 116.3, 114.4, 112.0, 67.7, 50.3, 47.9, 43.9, 38.3, 38.0, 35.8, 31.5, 29.6, 29.1, 29.0, 26.5, 25.8, 25.5, 21.5, 13.8. HRMS (ESI) m/z: $(M+H)^+$ calcd for $C_{34}H_{41}N_2O_3$, 525.3112; found, 525.3106.

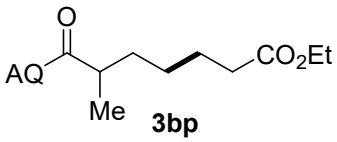
7-Oxo-7-(quinolin-8-ylamino)heptyl 2-(1-(4-chlorobenzoyl)-5-methoxy-2-methyl-1*H*-indol-3-yl)acetate (3av)



3av

Compound **3av** was obtained in 47% yield (57.5 mg) as a colorless oil (eluted by EA:PE = 1:2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.79 (s, 1H), 8.81 – 8.70 (m, 2H), 8.15 (d, *J* = 7.7 Hz, 1H), 7.69 – 7.59 (m, 2H), 7.57 – 7.39 (m, 5H), 6.99 – 6.93 (m, 1H), 6.87 (d, *J* = 9.0 Hz, 1H), 6.67 (dd, *J* = 9.0, 2.1 Hz, 1H), 4.10 (t, *J* = 6.5 Hz, 2H), 3.82 (s, 3H), 3.65 (s, 2H), 2.52 (t, *J* = 7.5 Hz, 2H), 2.38 (s, 3H), 1.83 – 1.72 (m, 2H), 1.71 – 1.59 (m, 2H), 1.48 – 1.32 (m, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.6, 170.9, 168.2, 156.0, 148.0, 139.1, 138.2, 136.4, 135.8, 134.4, 133.9, 131.1, 130.7, 130.6, 129.0, 127.9, 127.4, 121.5, 121.3, 116.4, 114.9, 112.7, 111.6, 101.3, 65.0, 55.6, 37.9, 30.4, 28.8, 28.4, 25.7, 25.4, 13.3. HRMS (ESI) m/z: $(M+H)^+$ calcd for $C_{35}H_{35}ClN_3O_5$, 612.2260; found, 612.2252.

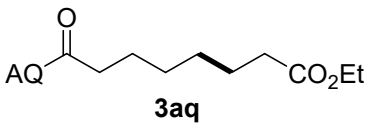
Ethyl 6-methyl-7-oxo-7-(quinolin-8-ylamino)heptanoate (3bp)



3bp

Compound **3bp** was obtained in 66% yield (43.3 mg) as a colorless oil (eluted by EA:PE = 1:10). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.86 (s, 1H), 8.84 – 8.75 (m, 2H), 8.15 (dd, *J* = 8.3, 1.5 Hz, 1H), 7.58 – 7.40 (m, 3H), 4.09 (q, *J* = 7.1 Hz, 2H), 2.66 – 2.55 (m, 1H), 2.29 (t, *J* = 7.5 Hz, 2H), 1.94 – 1.79 (m, 1H), 1.67 (p, *J* = 7.5 Hz, 2H), 1.62 – 1.51 (m, 1H), 1.51 – 1.38 (m, 2H), 1.32 (d, *J* = 6.9 Hz, 3H), 1.21 (t, *J* = 7.1 Hz, 3H). HRMS (ESI) m/z: $(M+H)^+$ calcd for $C_{19}H_{25}N_2O_3$, 329.1860; found, 329.1853.

Ethyl 8-oxo-8-(quinolin-8-ylamino)octanoate (3aq)



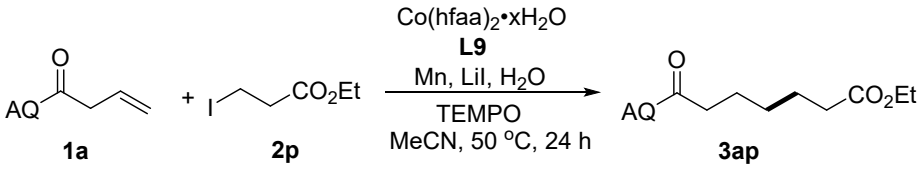
3aq

Compound **3aq** was synthesised from the reaction of **1c** and **2p**, and was obtained in 58% yield (38.1 mg) as a colorless oil (eluted by EA:PE = 1:10). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.79 (s, 1H), 8.82 – 8.73 (m, 2H), 8.14 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.57 – 7.40 (m, 3H),

4.11 (q, *J* = 7.1 Hz, 2H), 2.55 (t, *J* = 7.5 Hz, 2H), 2.29 (t, *J* = 7.5 Hz, 2H), 1.82 (p, *J* = 7.6 Hz, 2H), 1.65 (p, *J* = 7.5 Hz, 2H), 1.51 – 1.34 (m, 4H), 1.23 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.7, 171.7, 148.0, 138.2, 136.3, 134.4, 127.9, 127.4, 121.5, 121.3, 116.3, 60.1, 38.1, 34.2, 28.9, 28.8, 25.4, 24.8, 14.2. HRMS (ESI) m/z: $(M+H)^+$ calcd for $C_{19}H_{25}N_2O_3$, 329.1860; found, 329.1853.

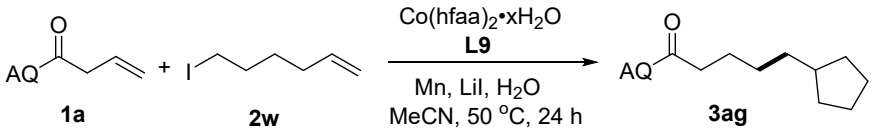
6. Mechanistic studies

6.1. Radical trapping experiment



A flame dried 25 mL Schlenk tube was charged with $Co(hfaa)_2 \cdot xH_2O$ (0.02 mmol, 10.0 mg), **L9** (0.02 mmol, 10.7 mg), **1a** (0.2 mmol, 42.4 mg), Mn (0.4 mmol, 22 mg), LiI (0.6 mmol, 80.4 mg) and tempo (0.6 mmol, 93.6 mg). The tube was vacuumed and refilled with N_2 three times. MeCN (2.0 mL), H_2O (0.4 mmol, 7.2 mg) and **2p** (0.4 mmol, 91.2 mg) were added to the reaction under N_2 atmosphere. The tube was screwed and the mixture was stirred at 50 °C in an aluminium alloy heating module. After 24 h, the mixture was cooled and the reaction result was detected by GC-MS which showed no product **3ap** was generated.

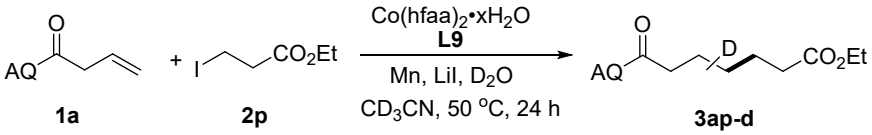
6.2. Radical clock experiment



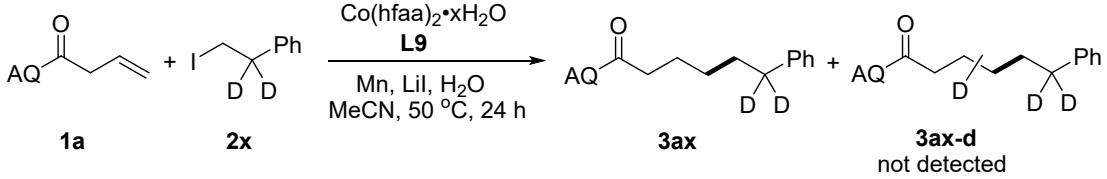
A flame dried 25 mL Schlenk tube was charged with $Co(hfaa)_2 \cdot xH_2O$ (0.02 mmol, 10.0 mg), **L9** (0.02 mmol, 10.7 mg), **1a** (0.2 mmol, 42.4 mg), Mn (0.4 mmol, 22 mg) and LiI (0.6 mmol, 80.4 mg). The tube was vacuumed and refilled with N_2 three times. MeCN (2.0 mL), H_2O (0.4 mmol, 7.2 mg) and **2e** (0.4 mmol, 84.0 mg) were added to the reaction under N_2 atmosphere. The tube was screwed and the mixture was stirred at 50 °C in an aluminium alloy heating module. After 24 h, the mixture was cooled and transferred to the 25 mL round bottom flask. The solvent was removed under reduced pressure and the crude mixture was purified through silica gel column chromatography (EA:PE = 1:10 as the eluent) to provide product **3ag** (33.1 mg, 56%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.81 (s, 1H), 8.84 – 8.73 (m, 2H), 8.14 (dd, *J* = 8.3, 1.4 Hz, 1H), 7.56 – 7.39 (m, 3H), 2.56 (t, *J* = 7.6 Hz, 2H), 1.88 – 1.68

(m, 5H), 1.64 – 1.31 (m, 8H), 1.13 – 0.98 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.9, 148.0, 138.2, 136.3, 134.5, 127.9, 127.4, 121.5, 121.2, 116.3, 40.0, 38.3, 35.9, 32.6, 28.4, 25.9, 25.1.

6.3. Deuteration experiments

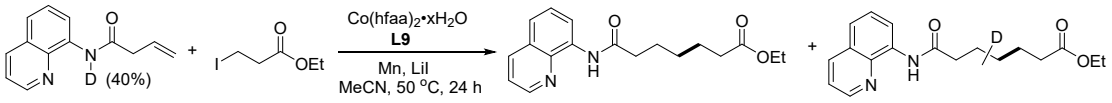


A flame dried 25 mL Schlenk tube was charged with $Co(hfaa)_2 \cdot xH_2O$ (0.02 mmol, 10.0 mg), **L9** (0.02 mmol, 10.7 mg), **1a** (0.2 mmol, 42.4 mg), Mn (0.4 mmol, 22 mg) and LiI (0.6 mmol, 80.4 mg). The tube was vacuumed and refilled with N_2 three times. CD_3CN (2.0 mL), D_2O (0.4 mmol, 8.0 mg) and **2p** (0.4 mmol, 91.2 mg) were added to the reaction under N_2 atmosphere. The tube was screwed and the mixture was stirred at 50 °C in an aluminium alloy heating module. After 24 h, the mixture was cooled and transferred to the 25 mL round bottom flask. The solvent was removed under reduced pressure and the crude mixture was purified through silica gel column chromatography (EA:PE = 1:10 as the eluent) to provide product **3ap-d** (45.9 mg, 73%) as a colorless oil. ^{1}H NMR showed deuteration was scattered on the five carbons in **3ap-d**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.81 (s, 1H), 8.87 – 8.72 (m, 2H), 8.17 (dd, *J* = 8.2, 1.7 Hz, 1H), 7.60 – 7.41 (m, 3H), 4.12 (q, *J* = 7.1 Hz, 2H), 2.58 (t, *J* = 7.5 Hz, 1.84H), 2.33 (t, *J* = 7.5 Hz, 1.82H), 1.85 (p, *J* = 7.6 Hz, 1.80H), 1.71 (p, *J* = 7.5 Hz, 1.90H), 1.54 – 1.38 (m, 1.87H), 1.24 (t, *J* = 7.1 Hz, 3H).



A flame dried 25 mL Schlenk tube was charged with $Co(hfaa)_2 \cdot xH_2O$ (0.02 mmol, 10.0 mg), **L9** (0.02 mmol, 10.7 mg), **1a** (0.2 mmol, 42.4 mg), Mn (0.4 mmol, 22 mg) and LiI (0.6 mmol, 80.4 mg). The tube was vacuumed and refilled with N_2 three times. MeCN (2.0 mL), H_2O (0.4 mmol, 8.0 mg) and **2x** (0.4 mmol, 93.6 mg, synthesized according to the literature report[11]) were added to the reaction under N_2 atmosphere. The tube was screwed and the mixture was stirred at 50 °C in an aluminium alloy heating module. After 24 h, the mixture was cooled and a small sample was tested through GC-MS. Then the mixture was transferred to the 25 mL round bottom flask. The solvent was removed under reduced pressure and the crude mixture was purified through silica gel column chromatography (EA:PE = 1:10 as the eluent) to provide product **3ax** (39.5 mg, 62%) as a white solid. Both GC-MS and ^{1}H NMR results

showed that deuteration was not happened in other carbons. Spectroscopic data of **3ax**: ^{1}H NMR (400 MHz, CDCl3) δ 9.80 (s, 1H), 8.85 – 8.73 (m, 2H), 8.16 (d, *J* = 8.2 Hz, 1H), 7.59 – 7.41 (m, 3H), 7.32 – 7.22 (m, 2H), 7.18 (d, *J* = 7.5 Hz, 3H), 2.56 (t, *J* = 7.5 Hz, 2H), 1.86 (p, *J* = 7.6 Hz, 2H), 1.76 – 1.65 (m, 2H), 1.55 – 1.41 (m, 2H). ^{13}C NMR (101 MHz, CDCl3) δ 171.8, 148.1, 142.5, 138.3, 136.4, 134.5, 128.4, 128.2, 127.9, 127.4, 125.6, 121.6, 121.3, 116.4, 38.1, 31.1, 28.8, 25.5.



A flame dried 25 mL Schlenk tube was charged with $Co(hfaa)_2 \cdot xH_2O$ (0.02 mmol, 10.0 mg), **L9** (0.02 mmol, 10.7 mg), **1a-d** (0.2 mmol, 42.4 mg, 40% deuterated, synthesized according to the literature report[12]), Mn (0.4 mmol, 22 mg) and LiI (0.6 mmol, 80.4 mg). The tube was vacuumed and refilled with N_2 three times. MeCN (2.0 mL) and **2p** (0.4 mmol, 91.2 mg) were added to the reaction under N_2 atmosphere. The tube was screwed and the mixture was stirred at 50 °C in an aluminium alloy heating module. After 24 h, the mixture was cooled and was transferred to the 25 mL round bottom flask. The solvent was removed under reduced pressure and the crude mixture was purified through silica gel column chromatography (EA:PE = 1:10 as the eluent) to provide **3ap** (26.9 mg, 43%) as a white solid. ^{1}H NMR results showed that nearly no deuteration was happened in the carbon chain. Spectroscopic data of **3ap** from the above procedure: ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.81 (s, 1H), 8.79 (dd, *J* = 12.4, 5.7 Hz, 2H), 8.17 (d, *J* = 8.2 Hz, 1H), 7.66 – 7.35 (m, 3H), 4.12 (q, *J* = 7.2 Hz, 2H), 2.58 (t, *J* = 7.5 Hz, 2H), 2.33 (t, *J* = 7.5 Hz, 2H), 1.84 (p, *J* = 7.6 Hz, 2H), 1.71 (p, *J* = 7.5 Hz, 2H), 1.47 (p, *J* = 7.7, 6.9 Hz, 2H), 1.24 (t, *J* = 7.1 Hz, 3H).

7. Reference

1. T. Ishii, Y. Kakeno, K. Nagao, H. Ohmiya, *J. Am. Chem. Soc.* **2019**, *141*, 3854-3858.

2. J.-S. Yang, K. Lu, C.-X. Li, Z.-H. Zhao, F.-M. Zhang, X.-M. Zhang, Y.-Q. Tu. *J. Am. Chem. Soc.* **2023**, *145*, 22122-22134.

3. Y. Li, W. Nie, Z. Chang, J.-W. Wang, X. Lu, Y. Fu, *Nat. Catal.* **2021**, *4*, 901-911.

4. J.-W. Wang, Z. Li, D. Liu, J.-Y. Zhang, X. Lu, Y. Fu, *J. Am. Chem. Soc.* **2023**, *145*, 10411-10421.

5. X.-X. Wang, Y.-T. Xu, Z.-L. Zhang, X. Lu, Y. Fu, *Nat. Commun.* **2022**, *13*, 1890.

6. W. Wu, X. Sang, Y. Liu, G. Fang, H. Wang, W. Hao, *Tetrahedron Lett.* **2023**, *115*, 154316.

7. Y. Huang, X. Lv, H.-R. Tong, W. He, Z. Bai, H. Wang, G. He, G. Chen, *Org. Lett.* **2024**, *26*, 94-99.

8. R. Tomar, D. Bhattacharya, S. A. Babu, *Tetrahedron* **2019**, *75*, 2447-2465.

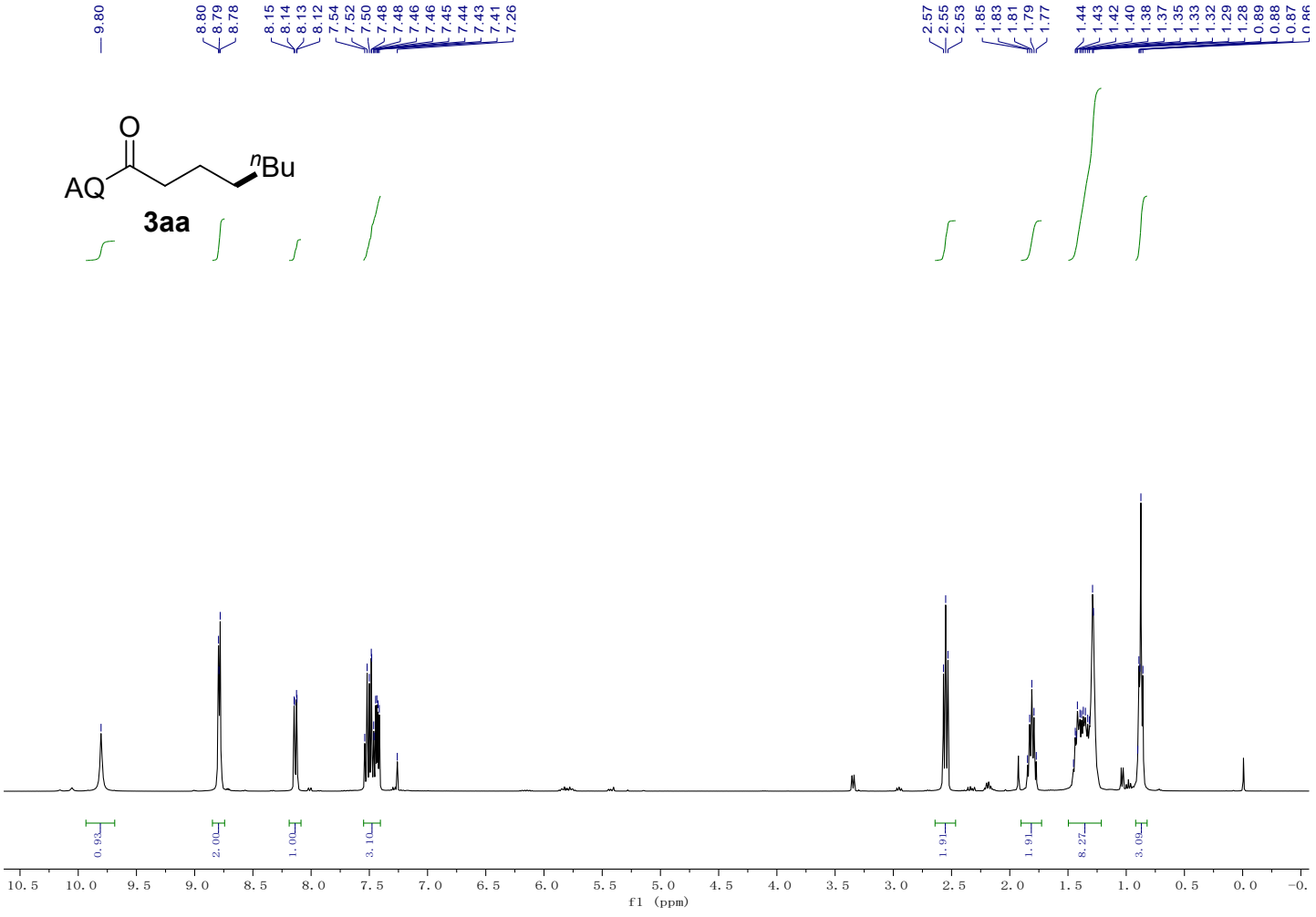
9. X. Zhang, G. Lu, M. Sun, M. Mahankali, Y. Ma, M. Zhang, W. Hua, Y. Hu, Q. Wang, J. Chen, G. He, X. Qi, W. Shen, P. Liu, G. Chen, *Nat. Chem.* **2018**, *10*, 540-548.

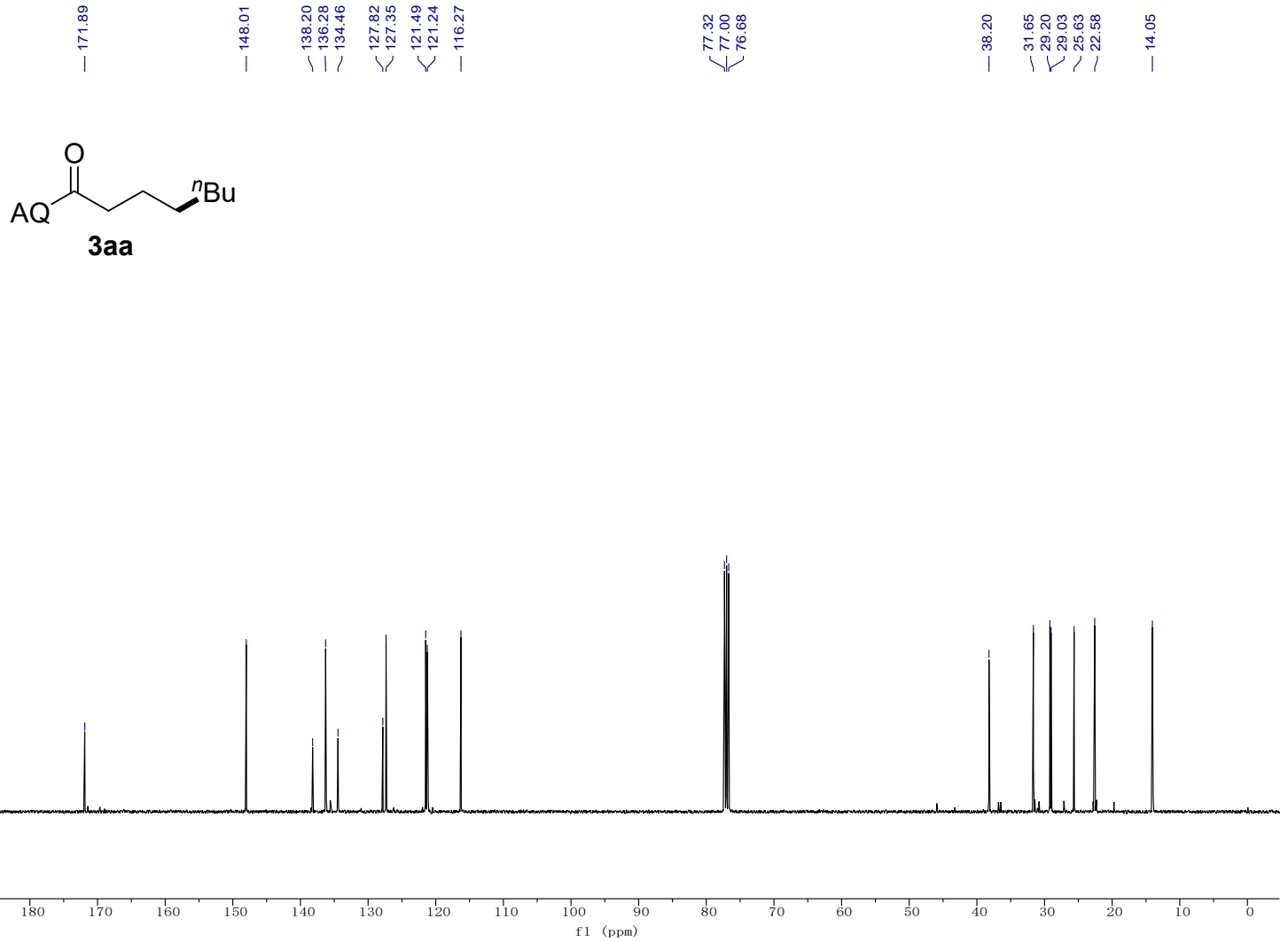
10. D. Yang, H. Huang, M.-H. Li, X.-J. Si, H. Zhang, J.-L. Niu, M.-P. Song, *Org. Lett.* **2020**, *22*, 4333-4338.

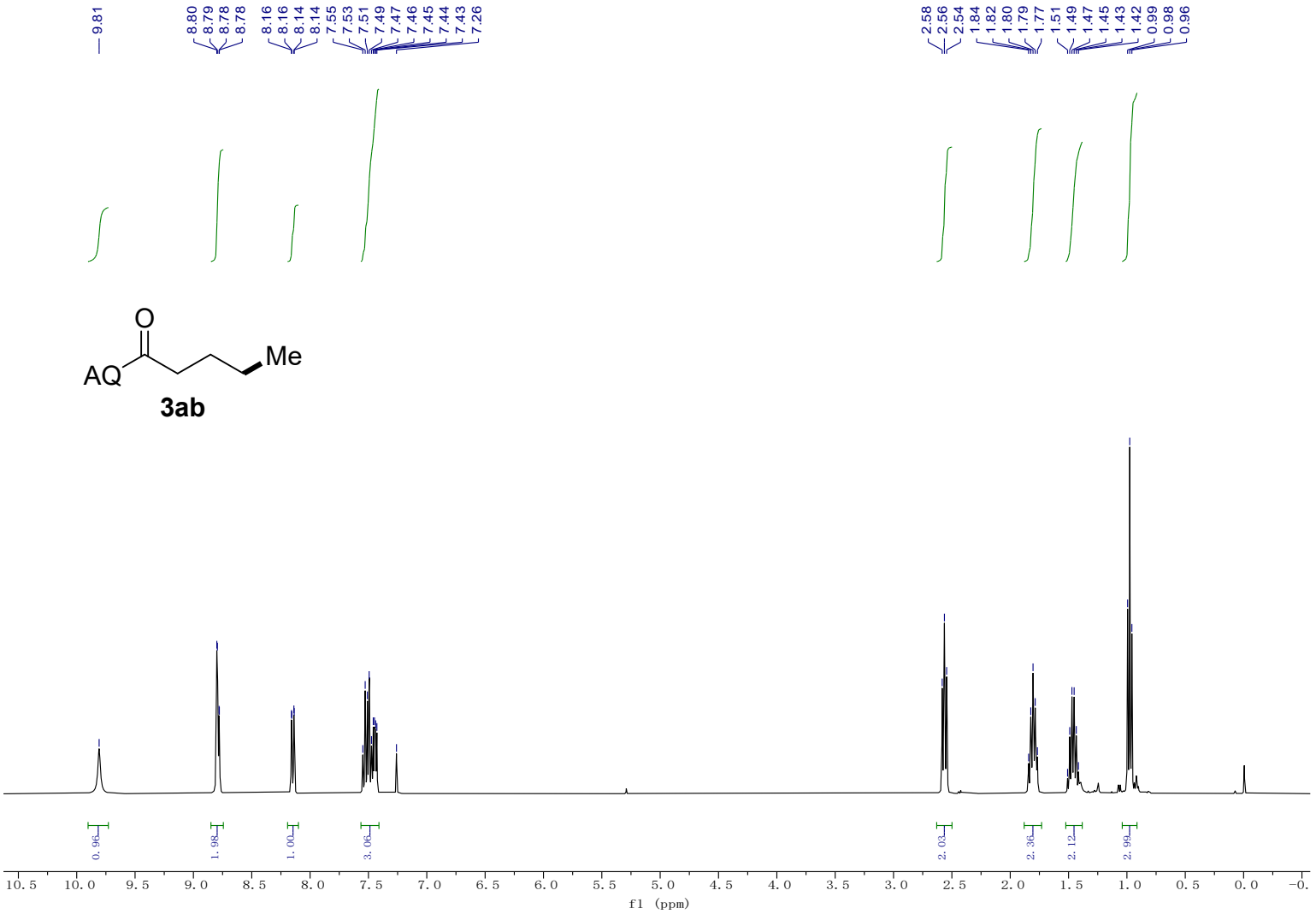
11. B.-Y. Zhao, X.-L. Zhang, R.-L. Guo, M.-Y. Wang, Y.-R. Gao, Y.-Q. Wang, *Org. Lett.* **2021**, *23*, 1216-1221.

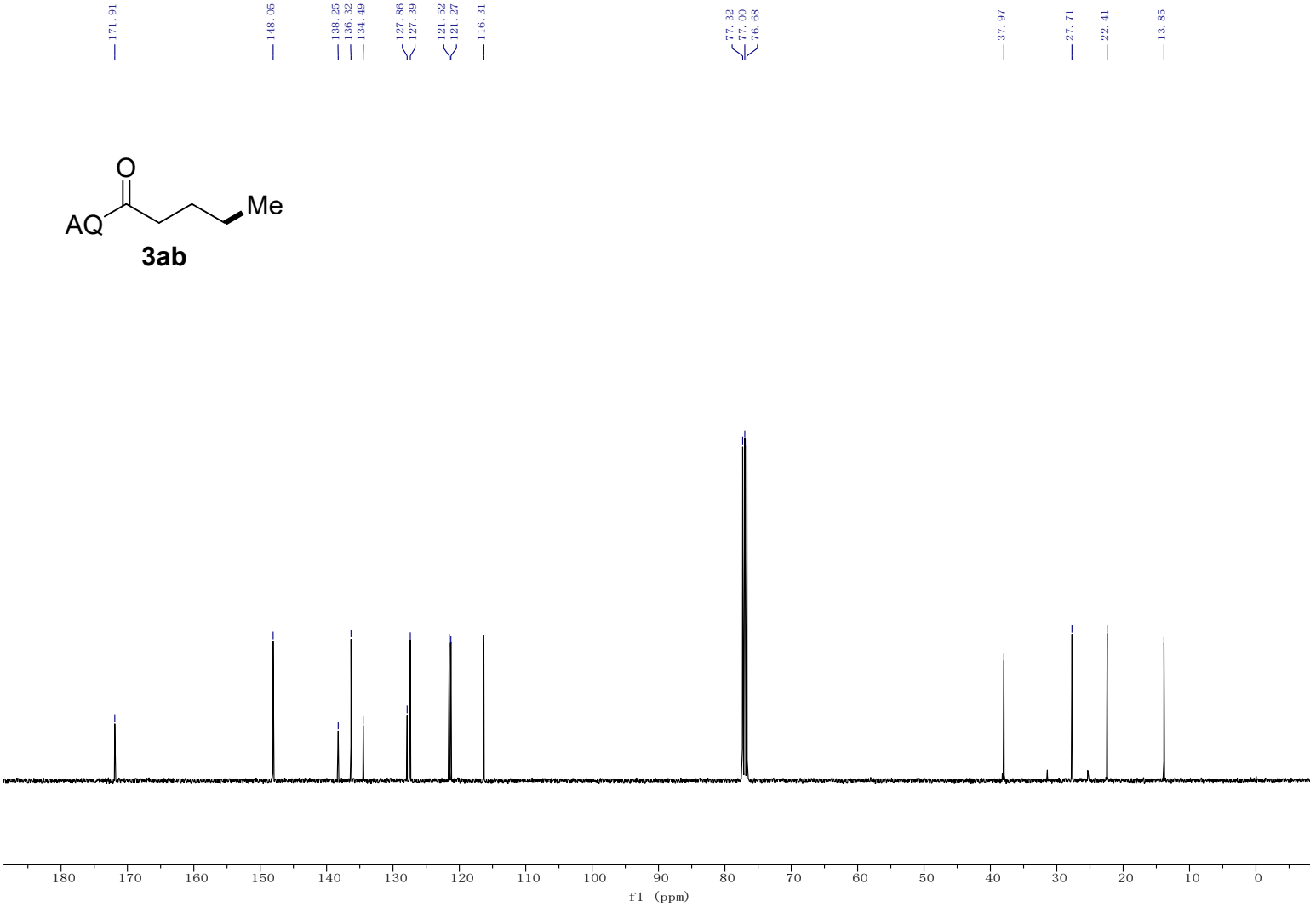
12. T. Shirai, Y. Migitera, R. Nakajima, T. Kumamoto, *J. Org. Chem.* **2024**, *89*, 2787-2793

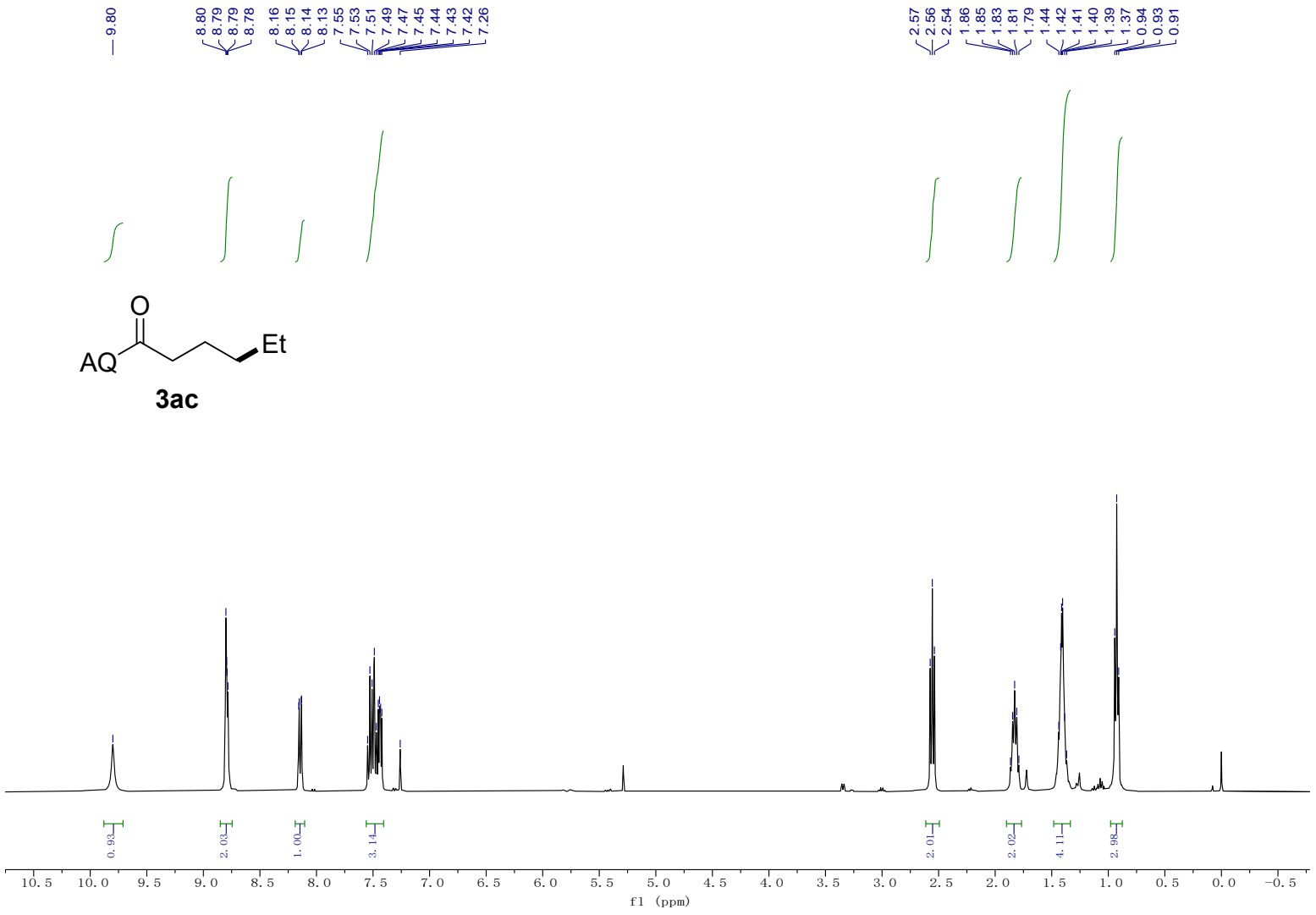
8. Spectroscopic data

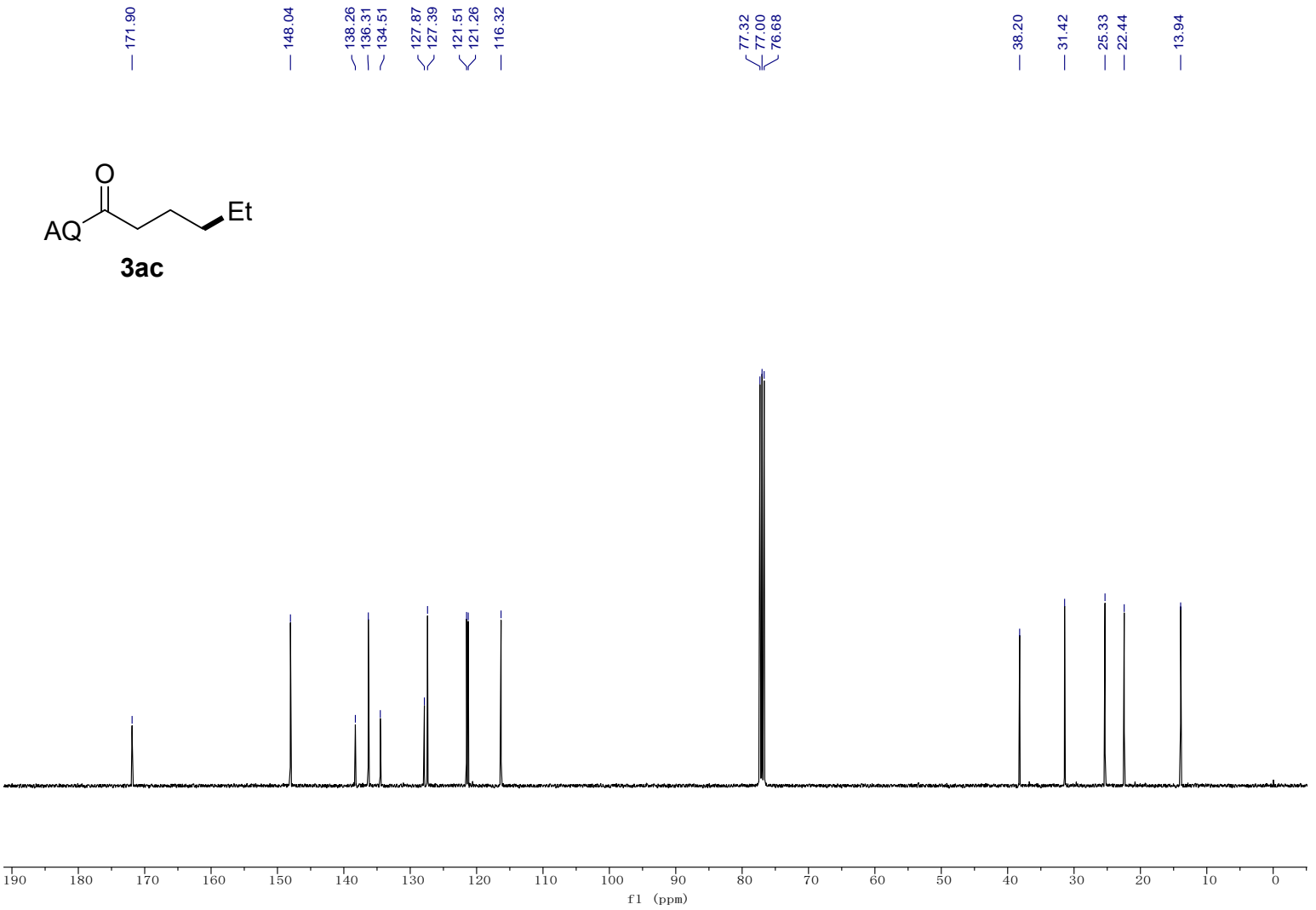


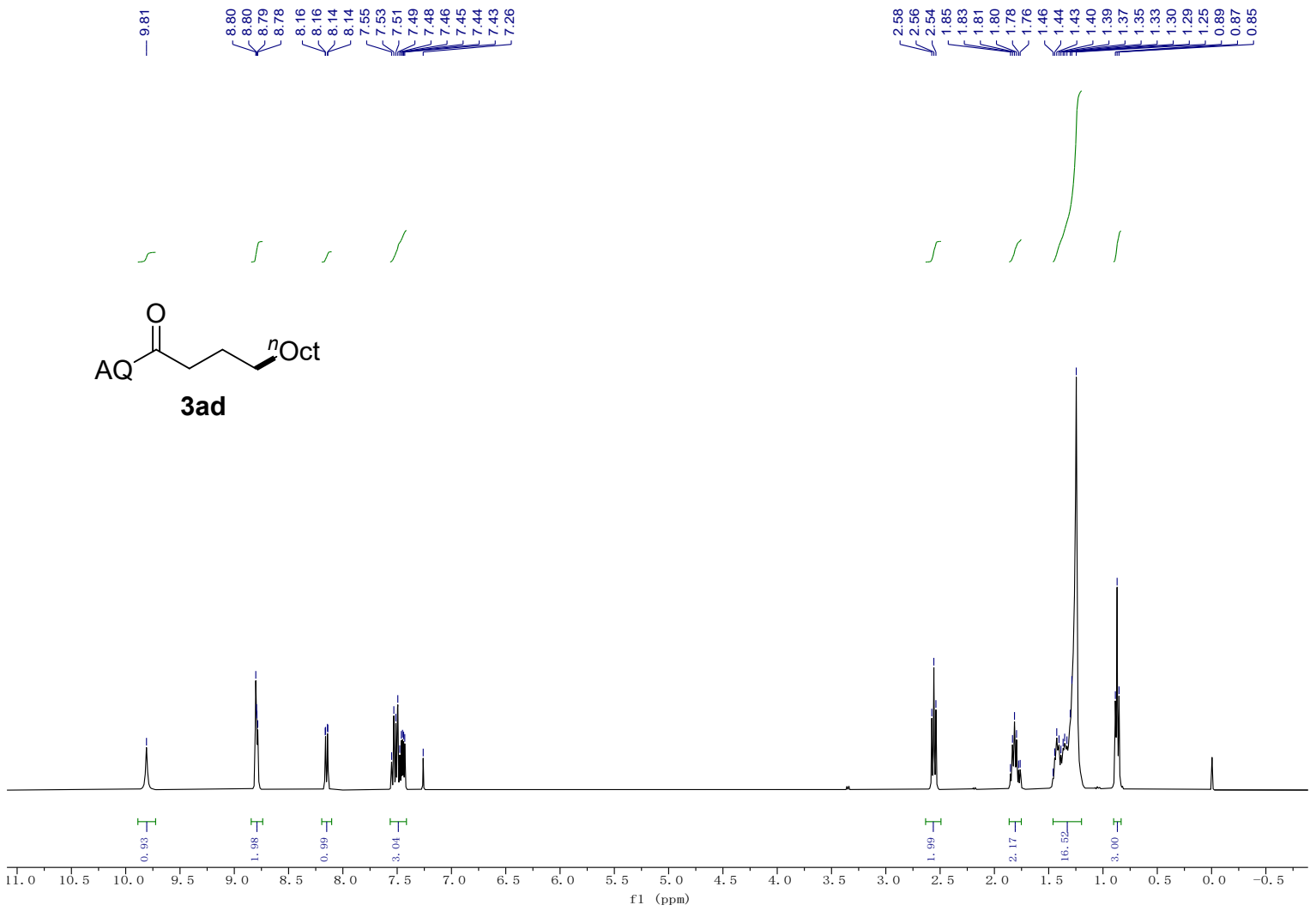

171.89
148.01
138.20
136.28
134.46
127.82
127.35
121.49
121.24
116.27
77.32
77.00
76.68
38.20
31.65
29.20
29.03
25.63
22.58
14.05
O
AQ
nBu
3aa
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

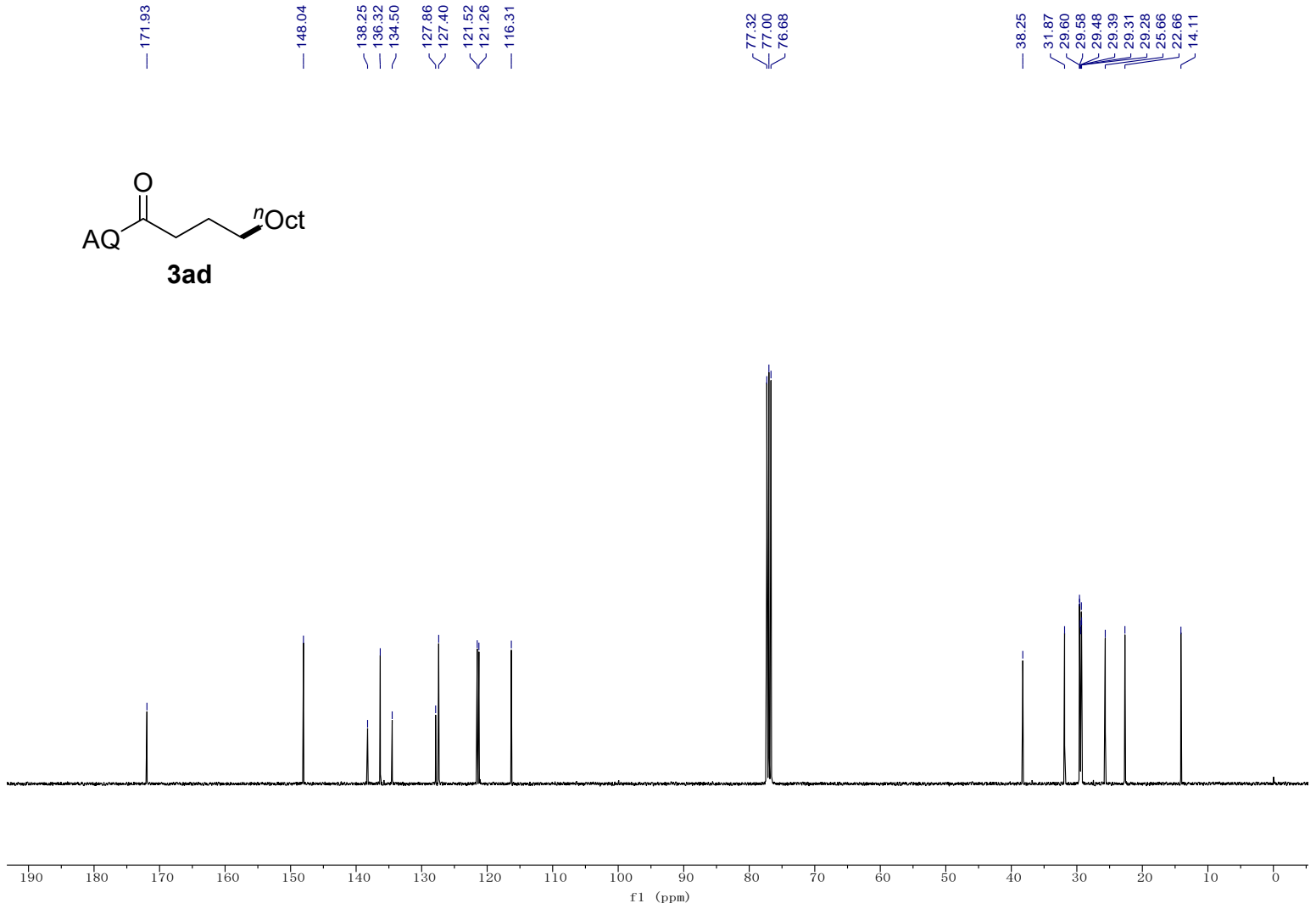

9.81
8.80
8.79
8.78
8.78
8.16
8.16
8.14
8.14
7.55
7.53
7.51
7.49
7.47
7.46
7.45
7.44
7.43
7.26
2.58
2.56
2.54
1.84
1.82
1.80
1.79
1.77
1.51
1.49
1.47
1.45
1.43
1.42
0.99
0.98
0.96
O
AQ
Me
3ab
0.96
1.98
1.00
3.06
2.03
2.36
2.12
2.99
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
−0.
f1 (ppm)

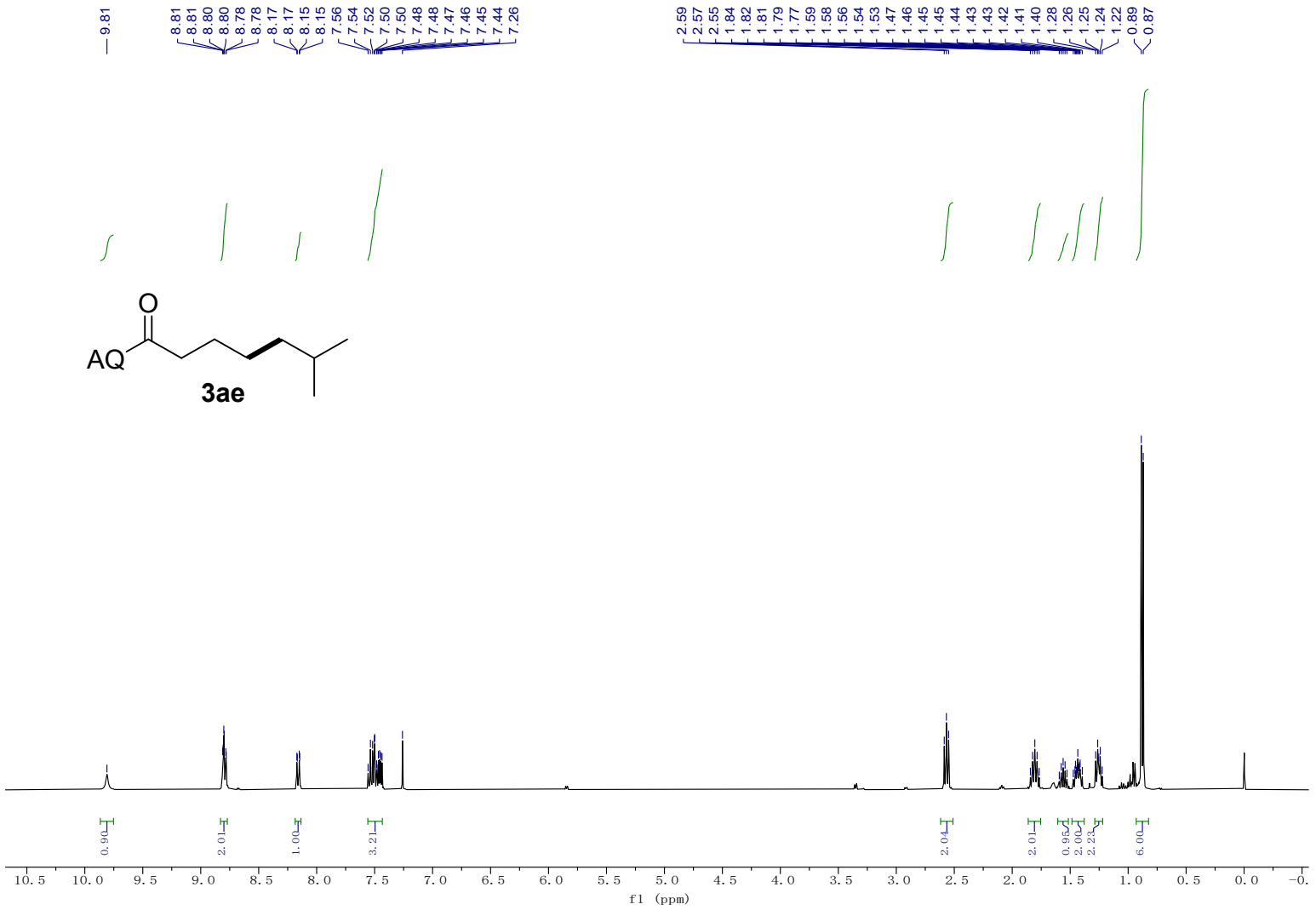

171.91
148.05
138.25
136.32
134.49
127.86
127.39
121.52
121.27
116.31
77.32
77.00
76.68
37.97
27.71
22.41
13.85
O
AQ
Me
3ab
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

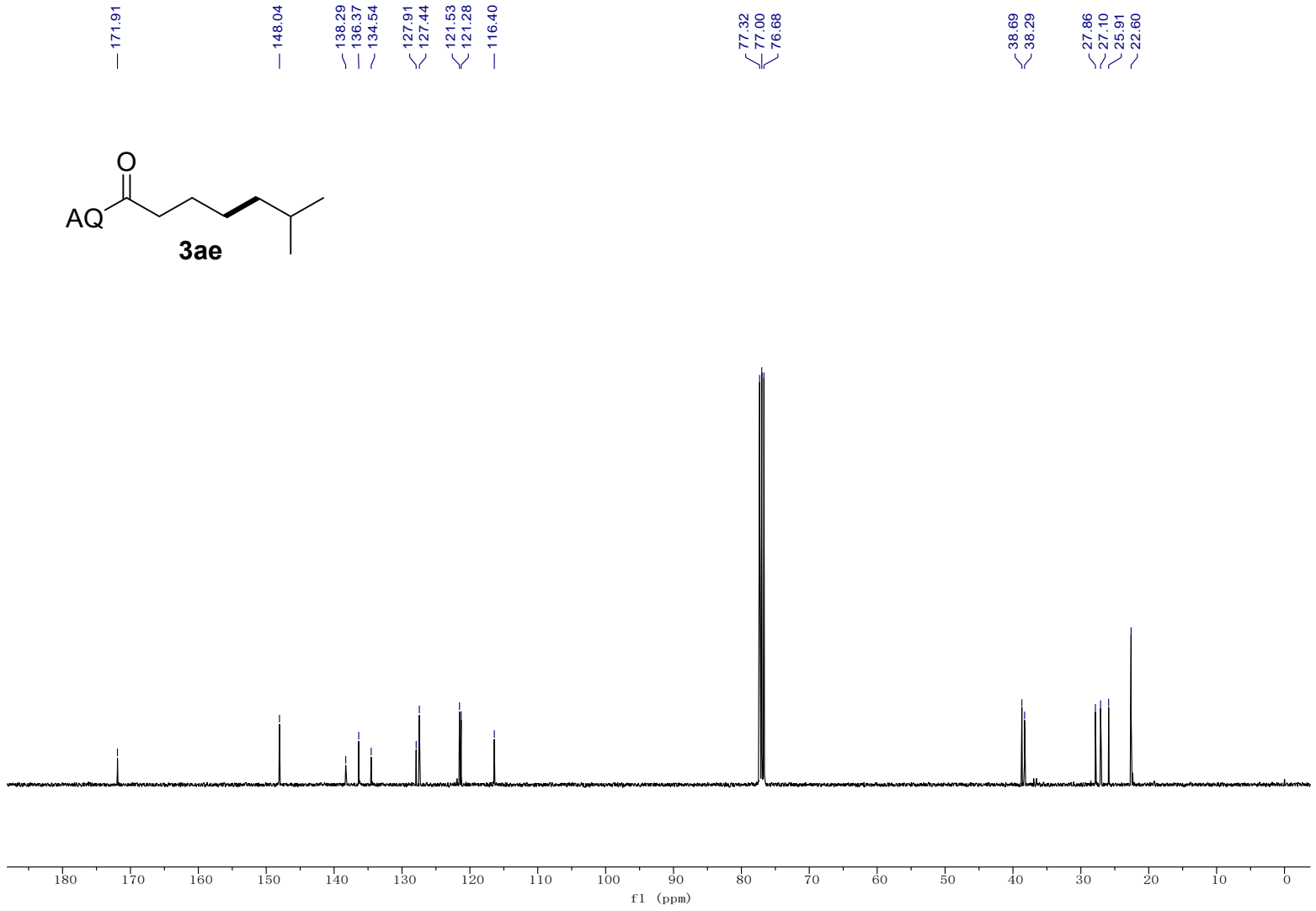

9.80
8.80
8.79
8.79
8.78
8.16
8.15
8.14
8.13
7.55
7.53
7.51
7.49
7.47
7.45
7.44
7.43
7.42
7.26
2.57
2.56
2.54
1.86
1.85
1.83
1.81
1.79
1.44
1.42
1.41
1.40
1.39
1.37
0.94
0.93
0.91
O
AQ
Et
3ac
0.93
2.03
1.00
3.14
2.01
2.02
4.11
2.98
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

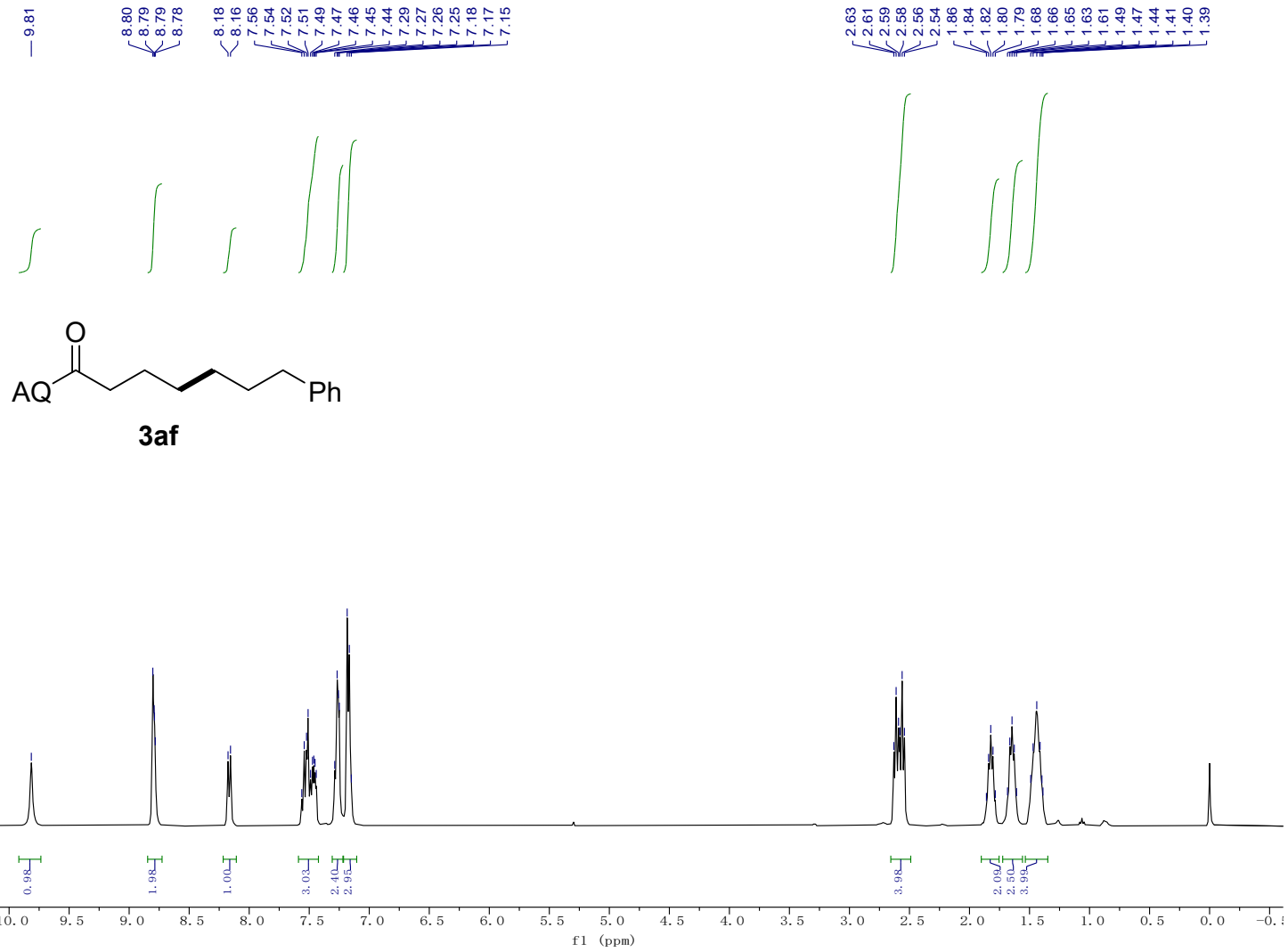

171.90
148.04
138.26
136.31
134.51
127.87
127.39
121.51
121.26
116.32
77.32
77.00
76.68
38.20
31.42
25.33
22.44
13.94
O
AQ
Et
3ac
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


9.81
8.80
8.80
8.79
8.78
8.16
8.16
8.14
8.14
7.55
7.53
7.51
7.49
7.48
7.46
7.45
7.44
7.43
7.26
2.58
2.56
2.54
1.85
1.83
1.81
1.80
1.78
1.76
1.46
1.44
1.43
1.40
1.39
1.37
1.35
1.33
1.30
1.29
1.25
0.89
0.87
0.85
O
AQ
nOct
3ad
0.93
1.98
0.99
3.04
1.99
2.17
16.52
3.00
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 −0.5
f1 (ppm)

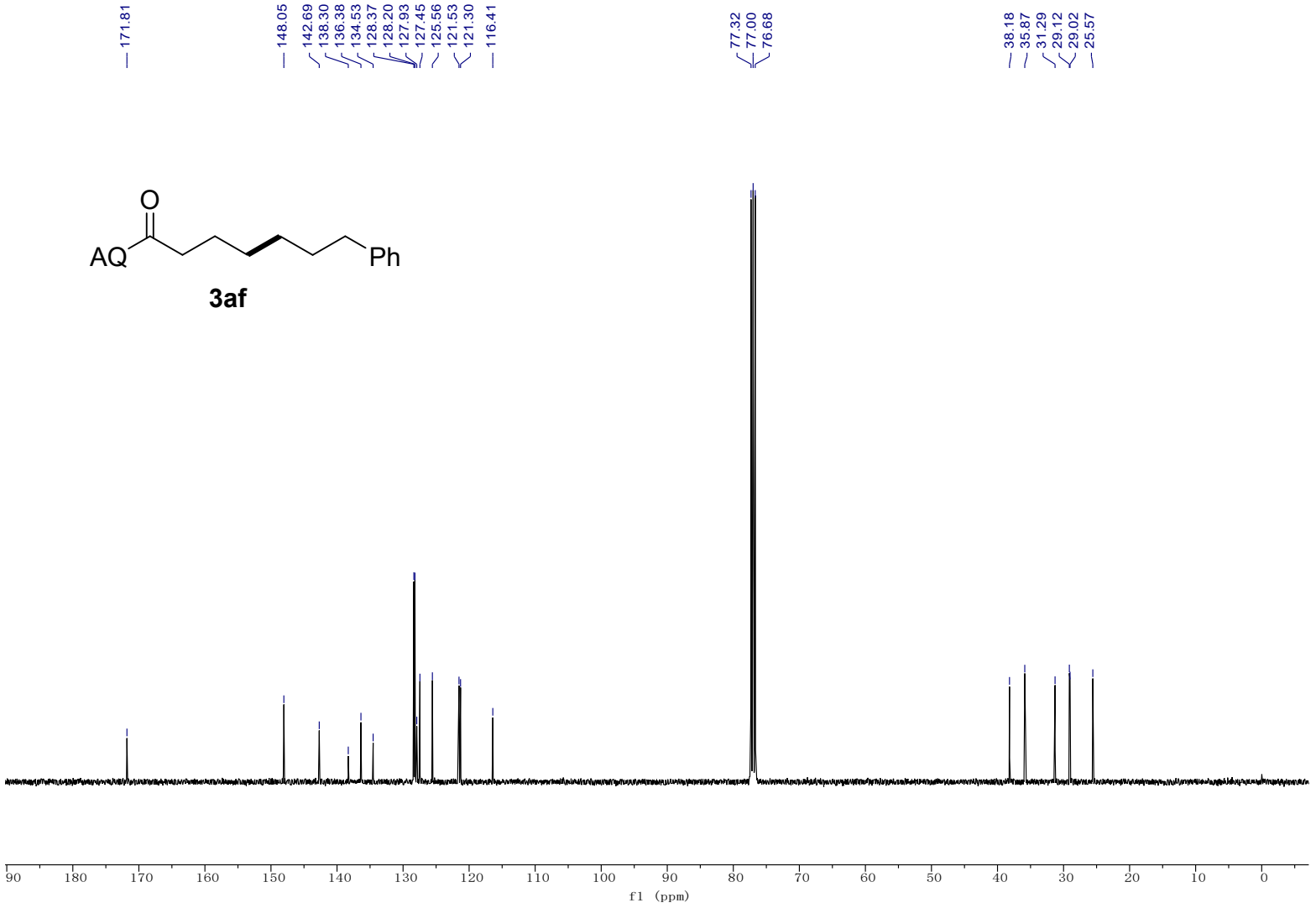

171.93
148.04
138.25
136.32
134.50
127.86
127.40
121.52
121.26
116.31
77.32
77.00
76.68
38.25
31.87
29.60
29.58
29.48
29.39
29.31
29.28
25.66
22.66
14.11
O
AQ
nOct
3ad
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

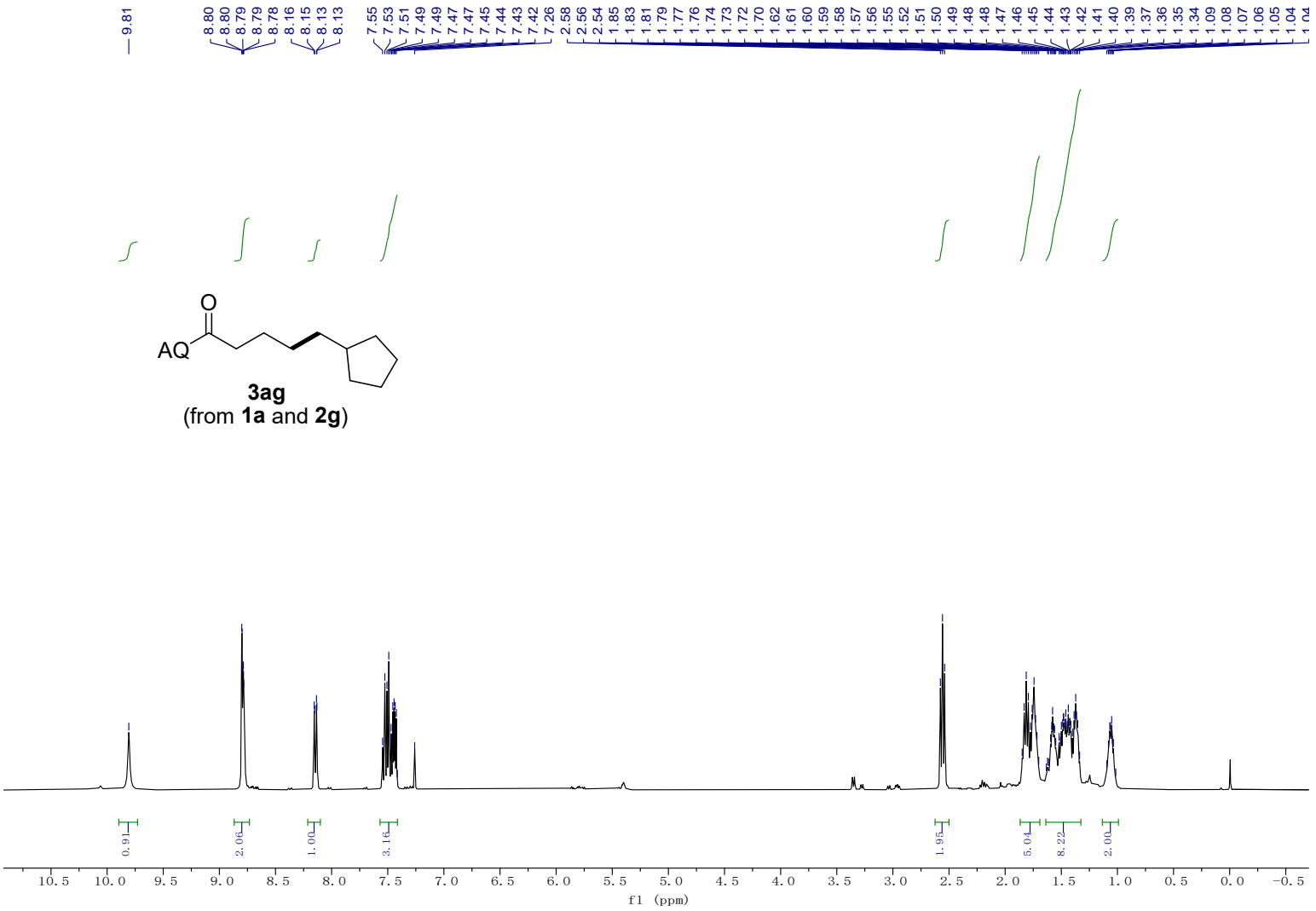

9.81
8.81
8.81
8.80
8.80
8.78
8.78
8.17
8.17
8.15
8.15
7.56
7.54
7.52
7.50
7.50
7.48
7.48
7.47
7.46
7.45
7.44
7.26
2.59
2.57
2.55
1.84
1.82
1.81
1.79
1.77
1.59
1.58
1.56
1.54
1.53
1.47
1.46
1.45
1.45
1.44
1.43
1.43
1.42
1.41
1.40
1.28
1.26
1.25
1.24
1.22
0.89
0.87
O
AQ
3ae
0.90
2.01
1.00
3.21
2.04
2.01
0.95
2.00
2.23
6.00
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)


171.91
148.04
138.29
136.37
134.54
127.91
127.44
121.53
121.28
116.40
77.32
77.00
76.68
38.69
38.29
27.86
27.10
25.91
22.60
O
AQ
3ae
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

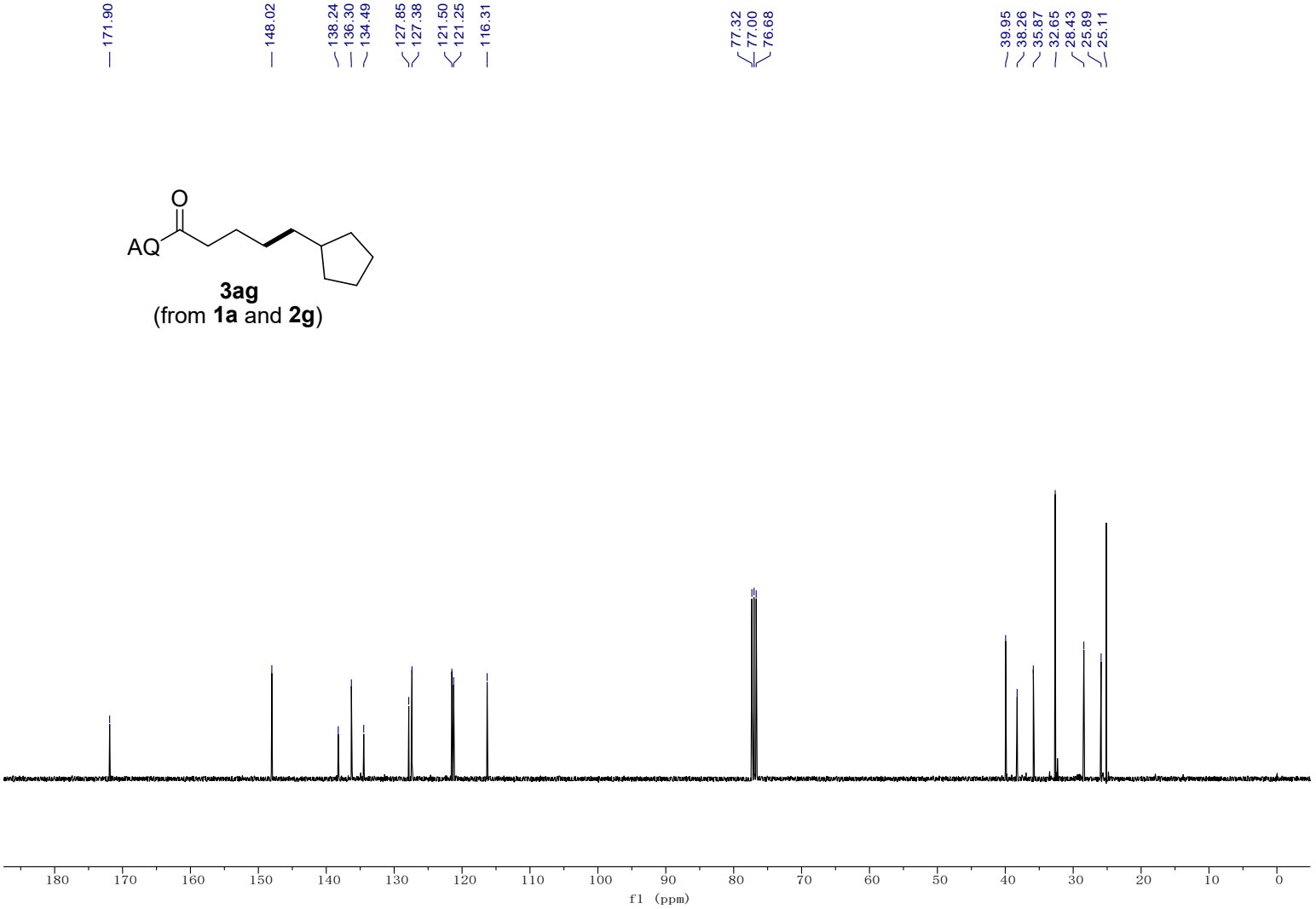

9.81
8.80
8.79
8.79
8.78
8.18
8.16
7.56
7.54
7.52
7.51
7.49
7.47
7.46
7.45
7.44
7.29
7.27
7.26
7.25
7.18
7.17
7.15
2.63
2.61
2.59
2.58
2.56
2.54
1.86
1.84
1.82
1.80
1.79
1.68
1.66
1.65
1.63
1.61
1.49
1.47
1.44
1.41
1.40
1.39
O
AQ
Ph
0.98
1.98
1.00
3.03
2.40
2.95
3.98
2.09
2.50
3.99
f1 (ppm)

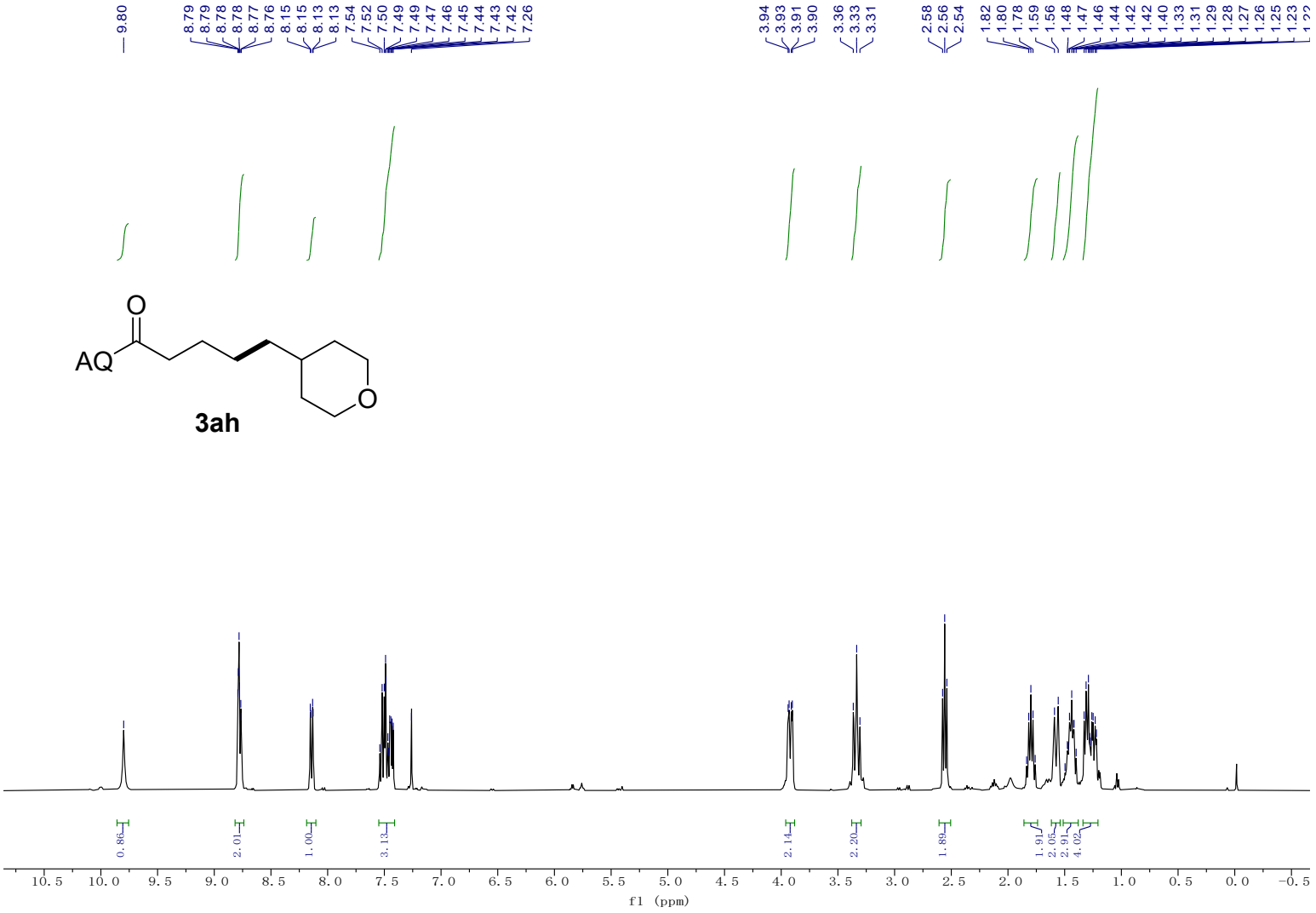
3af

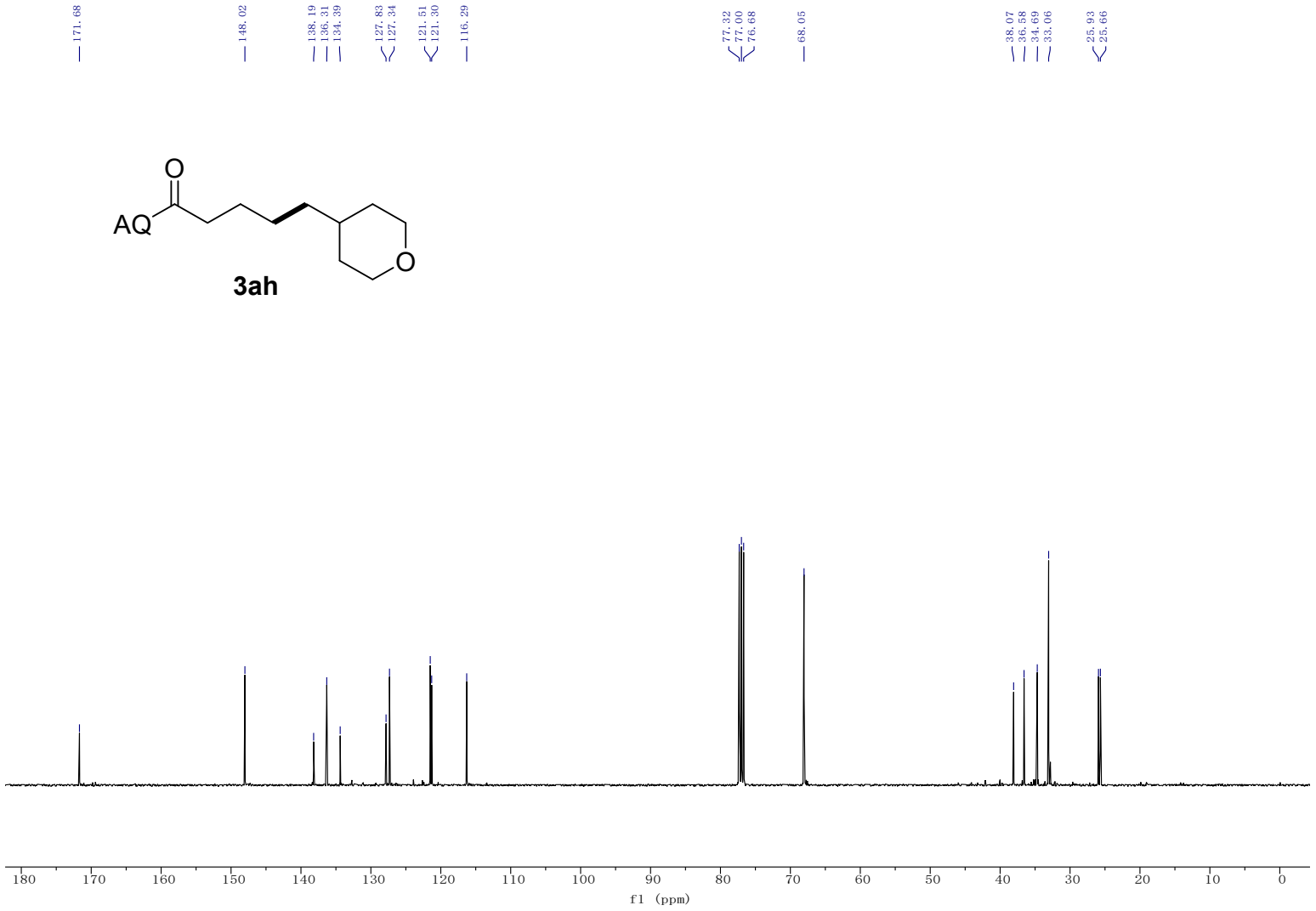

171.81
148.05
142.69
138.30
136.38
134.53
128.37
128.20
127.93
127.45
125.56
121.53
121.30
116.41
77.32
77.00
76.68
38.18
35.87
31.29
29.12
29.02
25.57
O
AQ
Ph
3af
90
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

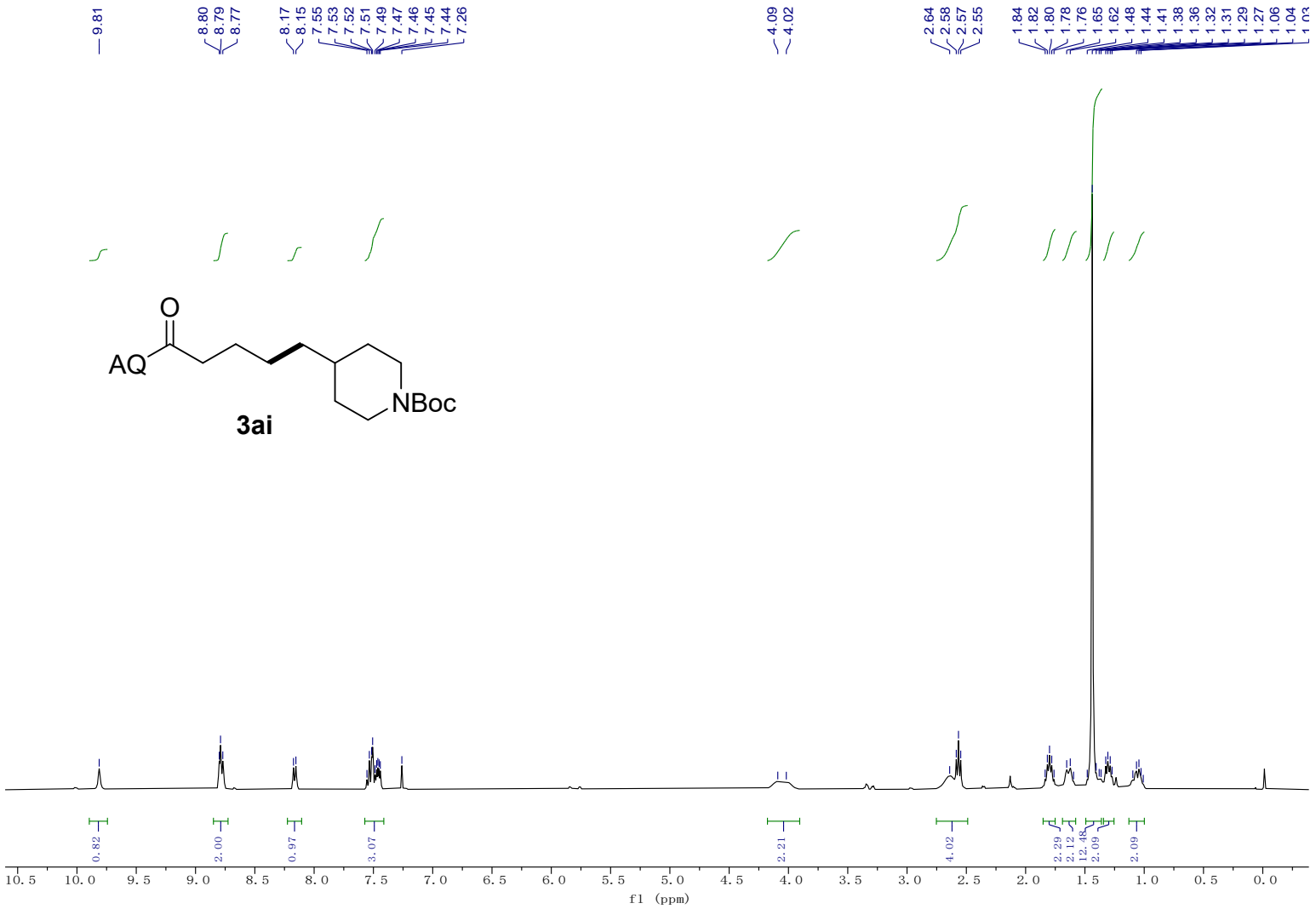


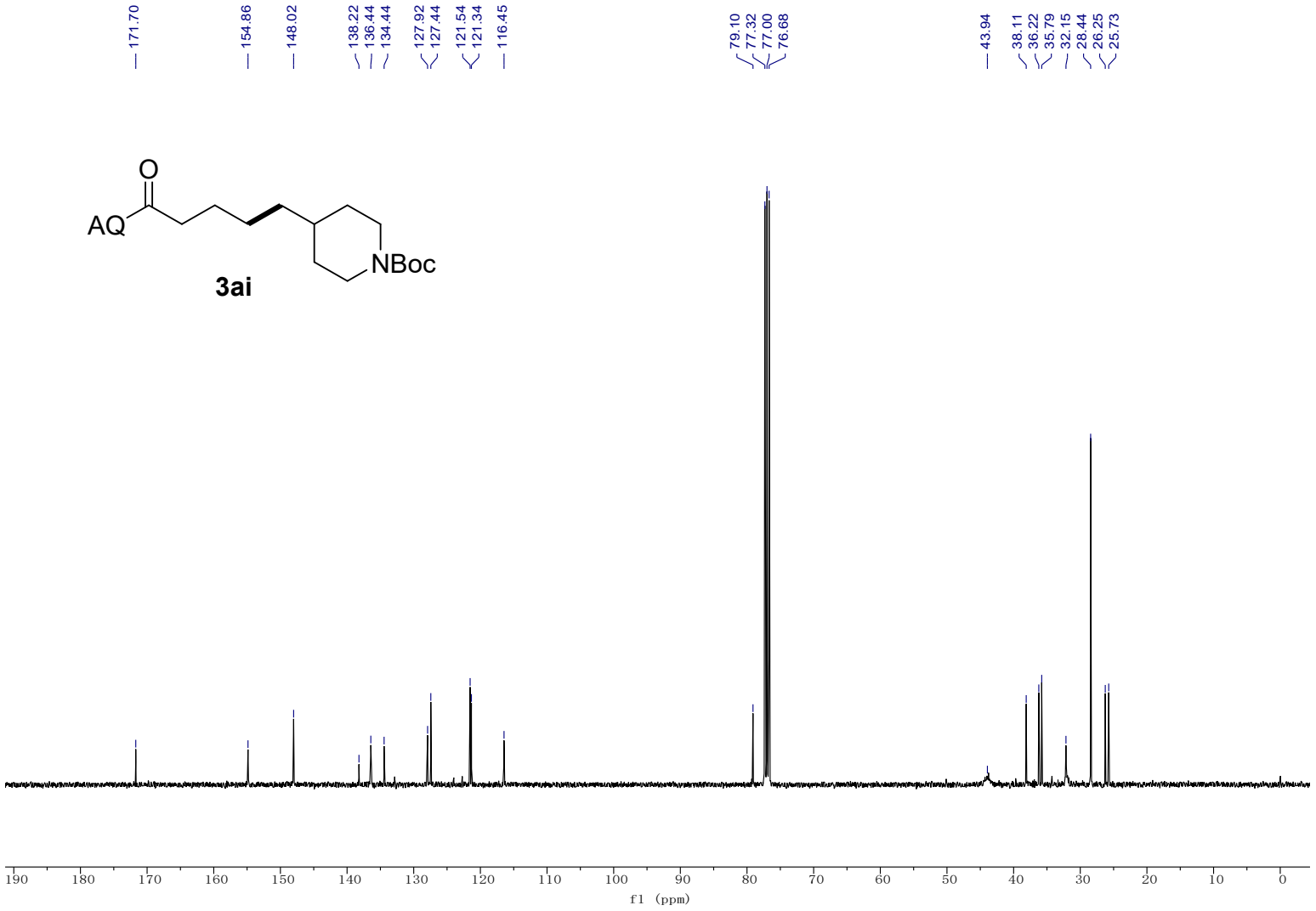
3ag
(from **1a** and **2g**)

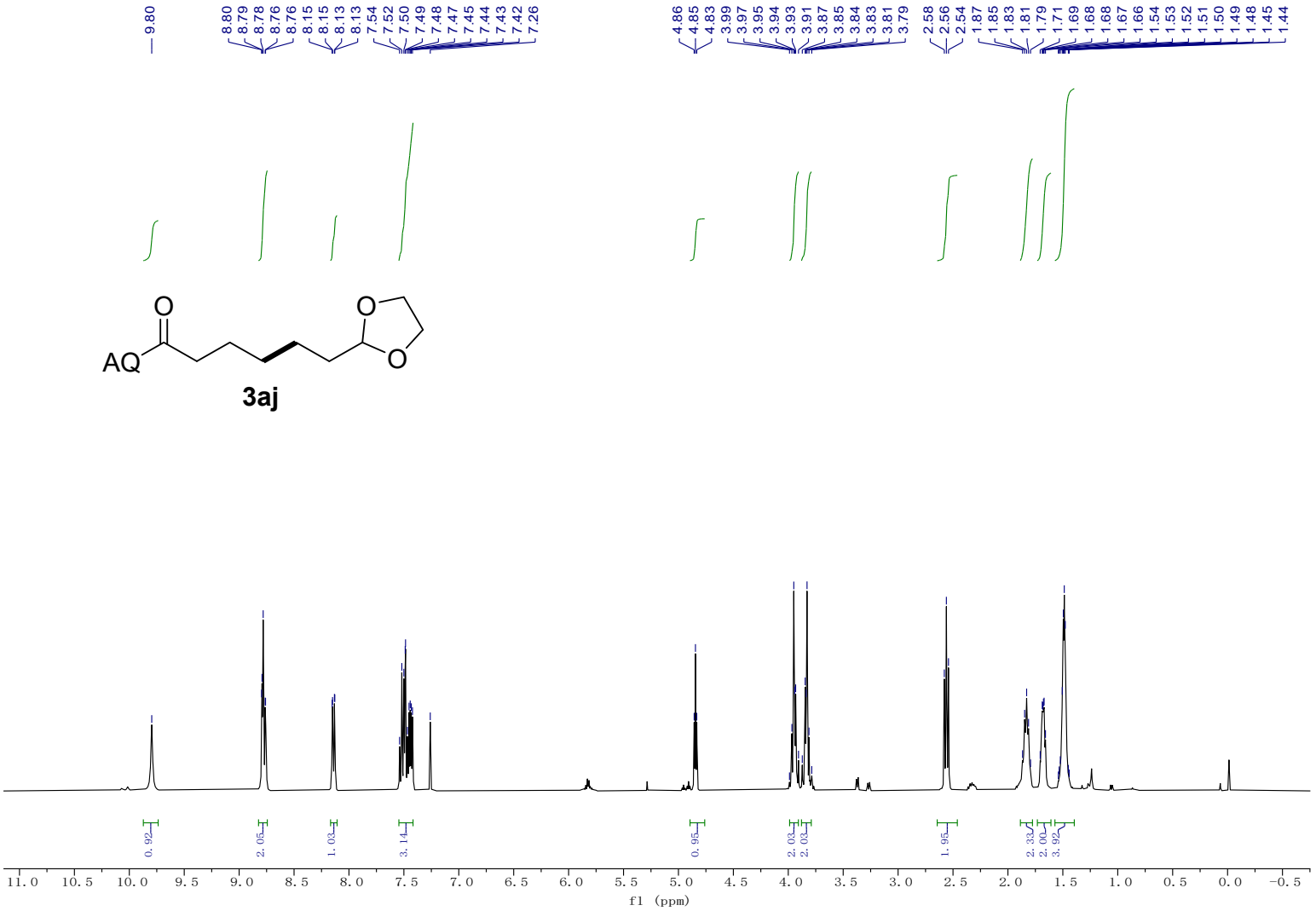

171.90
148.02
138.24
136.30
134.49
127.85
127.38
121.50
121.25
116.31
77.32
77.00
76.68
39.95
38.26
35.87
32.65
28.43
25.89
25.11
O
AQ
3ag
(from 1a and 2g)
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

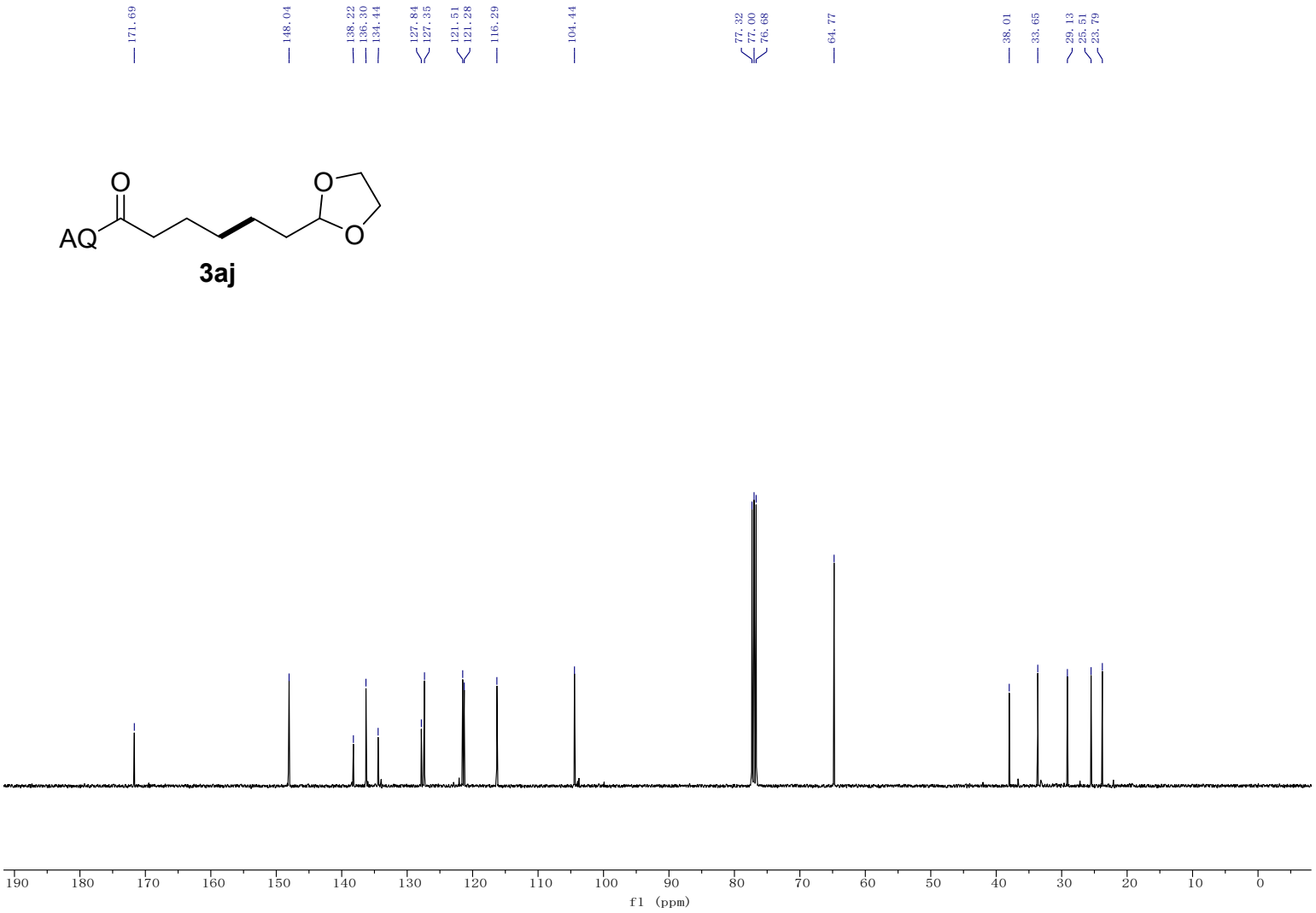

9.80
8.79
8.79
8.78
8.78
8.77
8.76
8.15
8.15
8.13
8.13
7.54
7.52
7.50
7.49
7.49
7.47
7.46
7.45
7.44
7.43
7.42
7.26
3.94
3.93
3.91
3.90
3.36
3.33
3.31
2.58
2.56
2.54
1.82
1.80
1.78
1.59
1.56
1.48
1.47
1.46
1.44
1.42
1.42
1.40
1.33
1.31
1.29
1.28
1.27
1.26
1.25
1.23
O
AQ
O
3ah
0.86
2.01
1.00
3.13
2.14
2.20
1.89
1.91
2.05
2.91
4.02
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
−0.5
f1 (ppm)

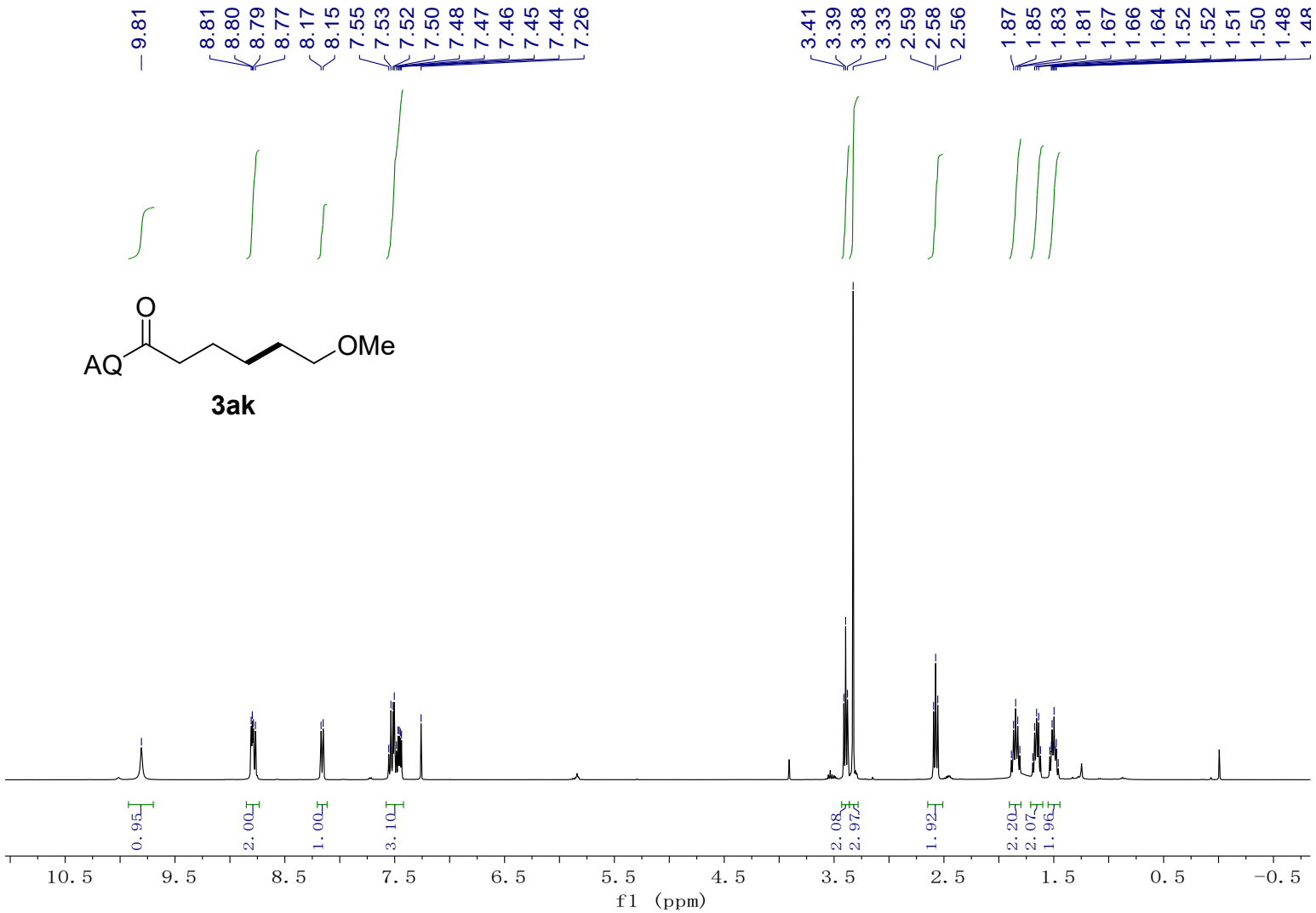

171.68
148.02
138.19
136.31
134.39
127.83
127.34
121.51
121.30
116.29
77.32
77.00
76.68
68.05
38.07
36.58
34.69
33.06
25.93
25.66
O
AQ
O
3ah
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

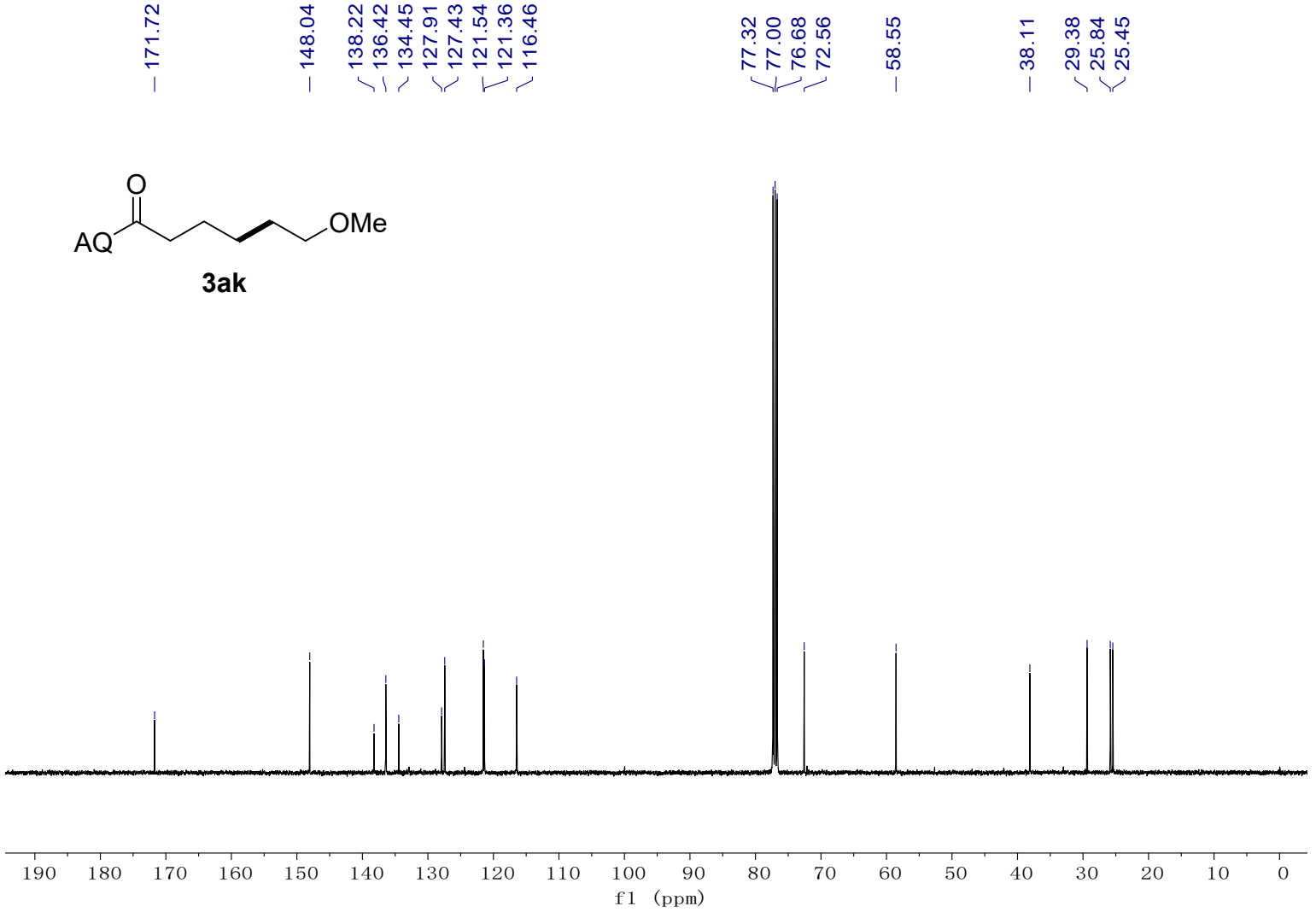

9.81
8.80
8.79
8.77
8.17
8.15
7.55
7.53
7.52
7.51
7.49
7.47
7.46
7.45
7.44
7.26
4.09
4.02
2.64
2.58
2.57
2.55
1.84
1.82
1.80
1.78
1.76
1.65
1.62
1.48
1.44
1.41
1.38
1.36
1.32
1.31
1.29
1.27
1.06
1.04
O
AQ
NBoc
3ai
0.82
2.00
0.97
3.07
2.21
4.02
2.29
2.12
12.48
2.09
2.09
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
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)

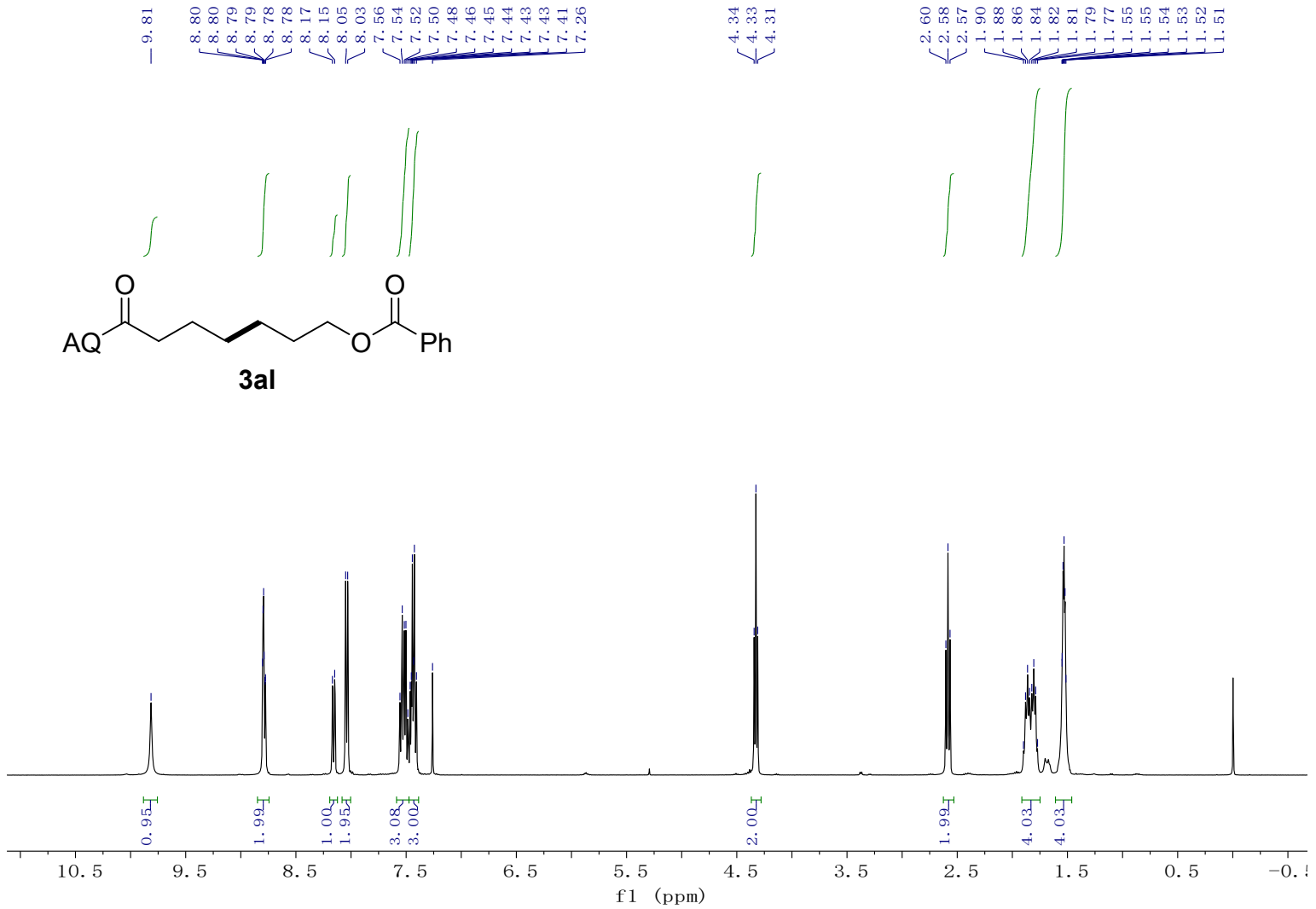

171.70
154.86
148.02
138.22
136.44
134.44
127.92
127.44
121.54
121.34
116.45
79.10
77.32
77.00
76.68
43.94
38.11
36.22
35.79
32.15
28.44
26.25
25.73
O
AQ
NBoc
3ai
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

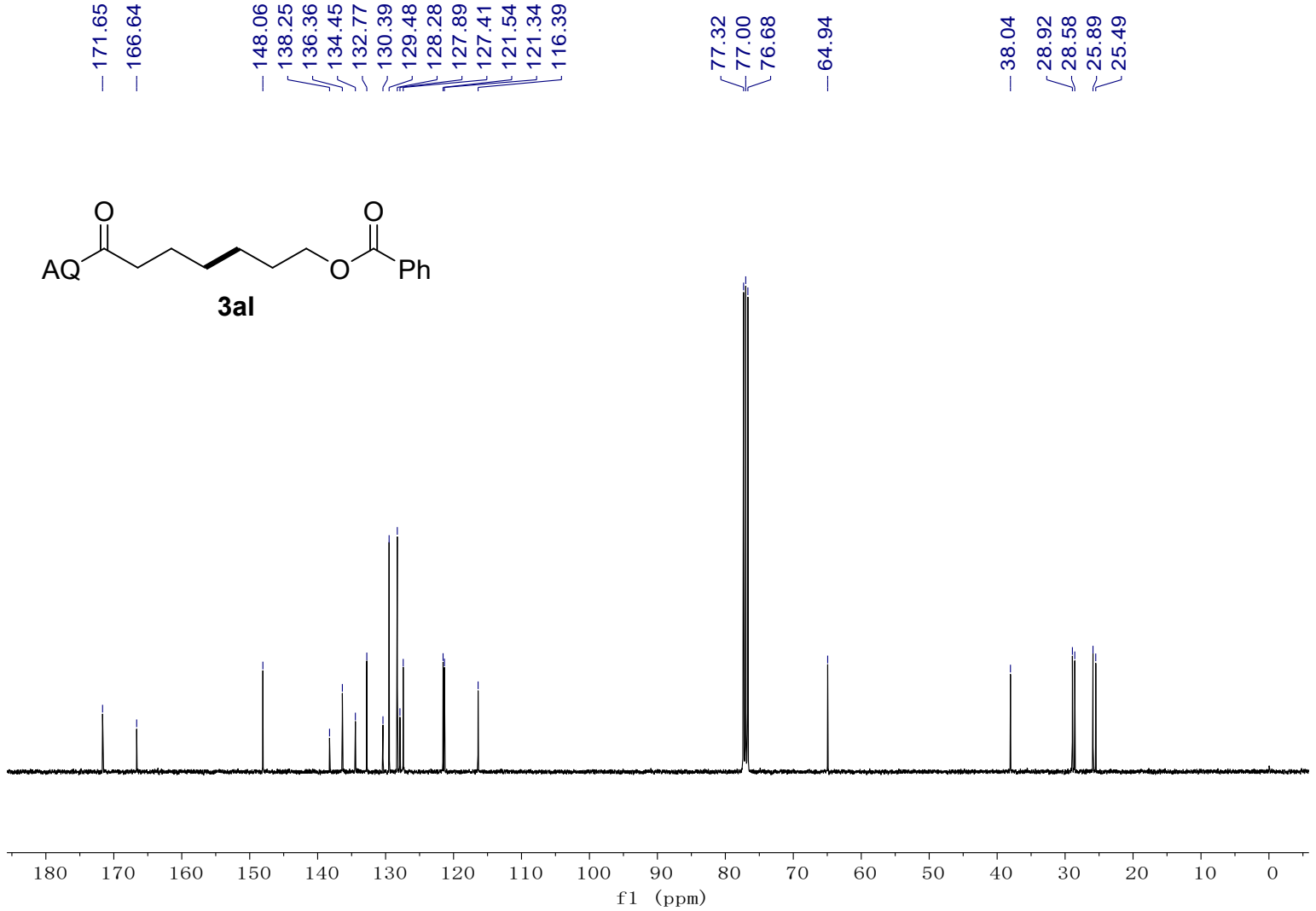

9.80
8.80
8.79
8.78
8.76
8.76
8.15
8.15
8.13
8.13
7.54
7.52
7.50
7.49
7.48
7.47
7.45
7.44
7.43
7.42
7.26
4.86
4.85
4.83
3.99
3.97
3.95
3.94
3.93
3.91
3.87
3.85
3.84
3.83
3.81
3.79
2.58
2.56
2.54
1.87
1.85
1.83
1.81
1.79
1.71
1.69
1.68
1.68
1.67
1.66
1.54
1.53
1.52
1.51
1.50
1.49
1.48
1.45
1.44
O
O
AQ
O
3aj
0.92
2.05
1.03
3.14
0.95
2.03
2.03
1.95
2.33
2.00
3.92
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
−0.5
f1 (ppm)

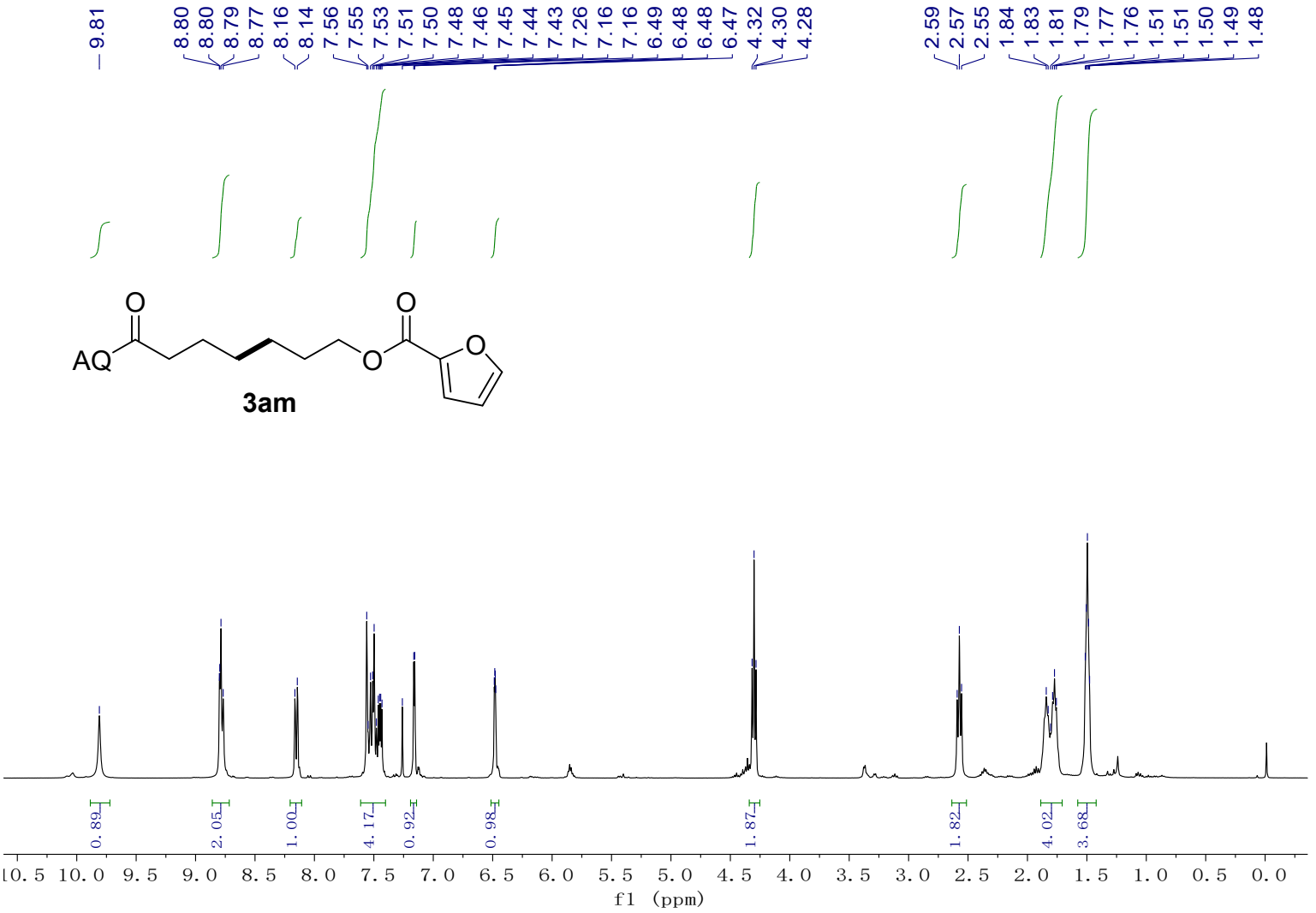

171.69
148.04
138.22
136.30
134.44
127.84
127.35
121.51
121.28
116.29
104.44
77.32
77.00
76.68
64.77
38.01
33.65
29.13
25.51
23.79
O
O
AQ
O
3aj
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

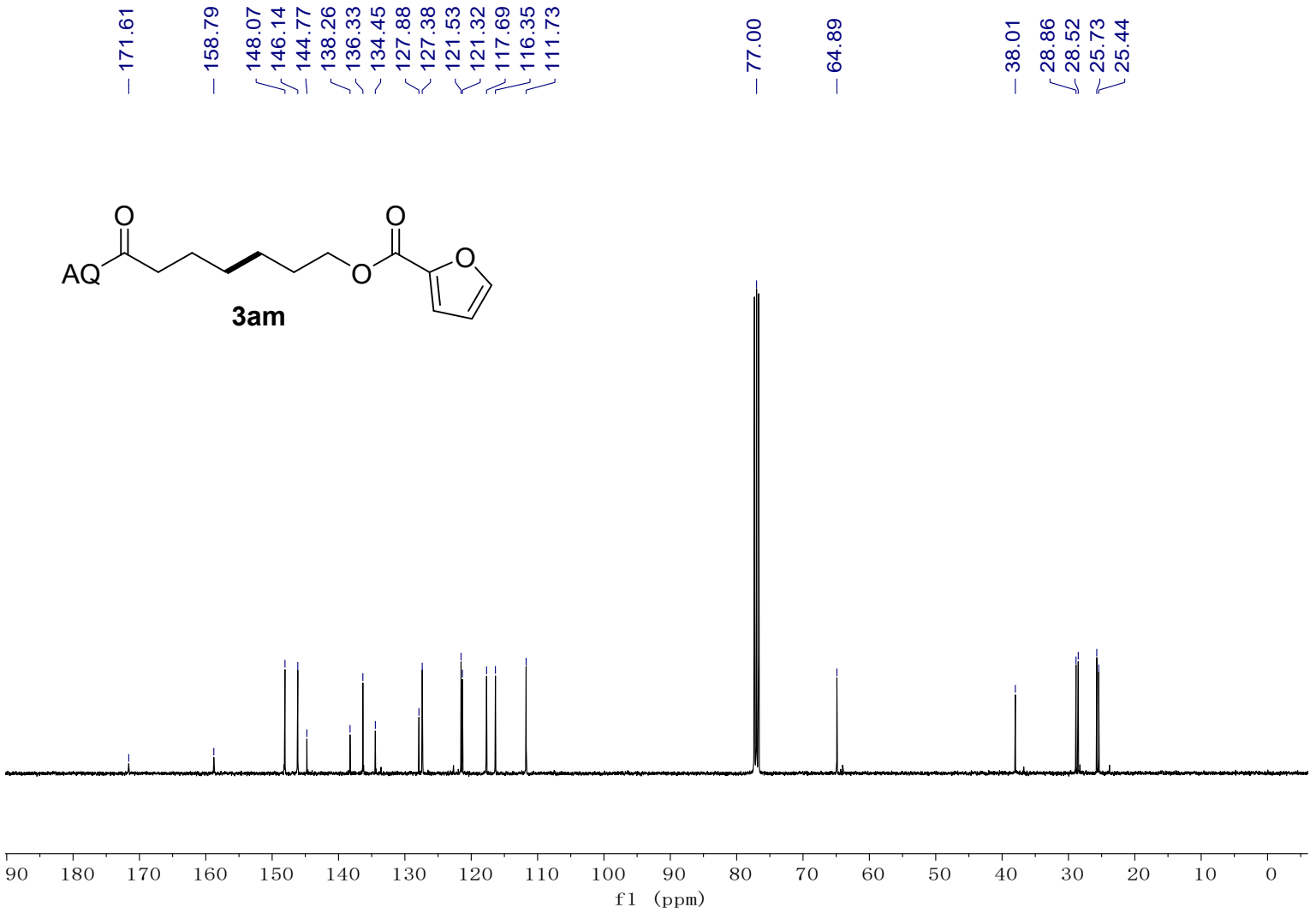

9.81
8.81
8.80
8.79
8.77
8.17
8.15
7.55
7.53
7.52
7.50
7.48
7.47
7.46
7.45
7.44
7.26
3.41
3.39
3.38
3.33
2.59
2.58
2.56
1.87
1.85
1.83
1.81
1.67
1.66
1.64
1.52
1.52
1.51
1.50
1.48
O
AQ
OMe
3ak
0.95
2.00
1.00
3.10
2.08
2.97
1.92
2.20
2.07
1.96
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
−0.5
f1 (ppm)

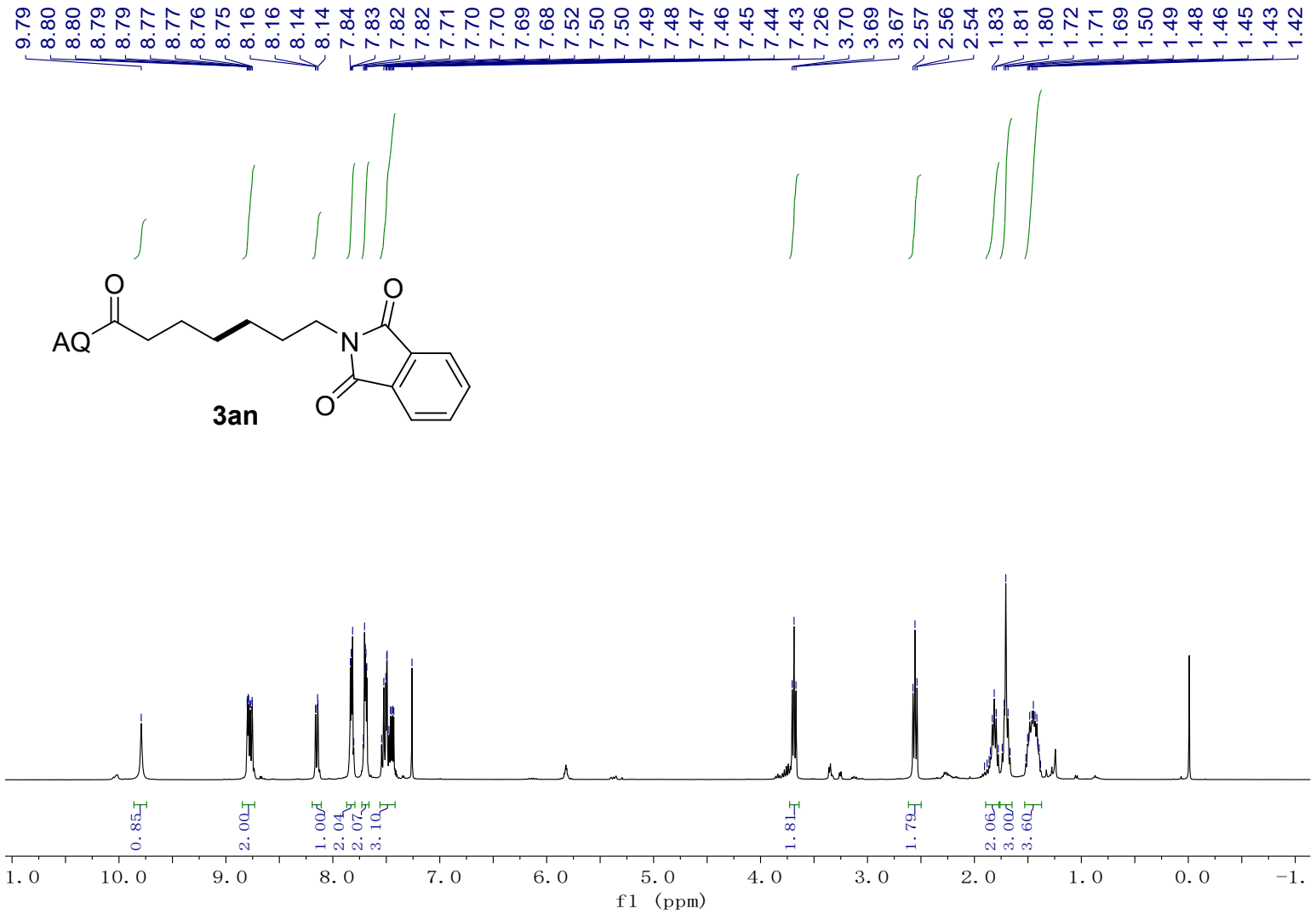

171.72
148.04
138.22
136.42
134.45
127.91
127.43
121.54
121.36
116.46
77.32
77.00
76.68
72.56
58.55
38.11
29.38
25.84
25.45
O
AQ
OMe
3ak
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

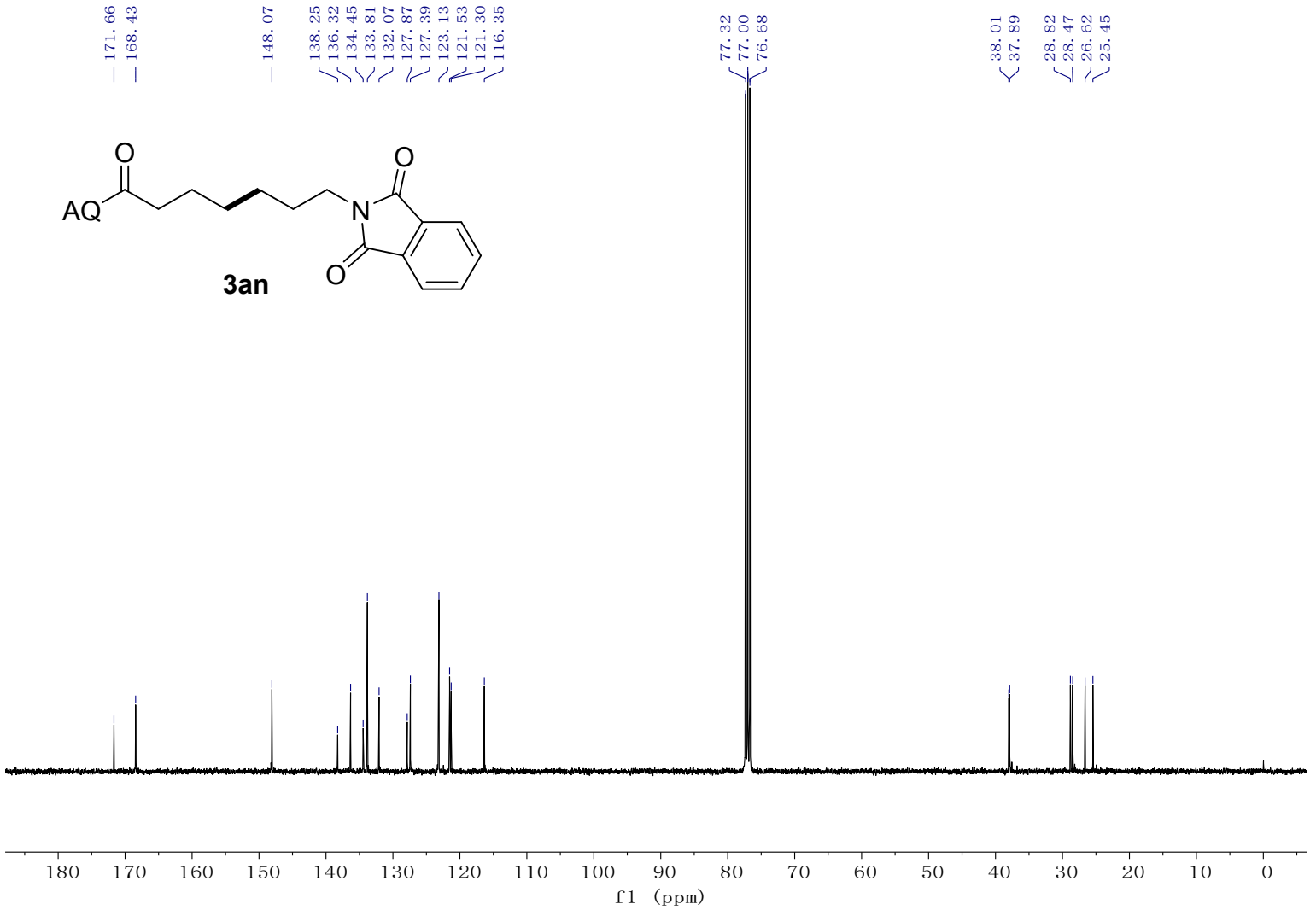

9.81
8.80
8.80
8.79
8.79
8.78
8.78
8.17
8.15
8.05
8.03
7.56
7.54
7.52
7.50
7.48
7.46
7.45
7.44
7.43
7.43
7.41
7.26
4.34
4.33
4.31
2.60
2.58
2.57
1.90
1.88
1.86
1.84
1.82
1.81
1.79
1.77
1.55
1.55
1.54
1.53
1.52
1.51
O
O
AQ
O
Ph
3al
0.95
1.99
1.00
1.95
3.08
3.00
2.00
1.99
4.03
4.03
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
f1 (ppm)

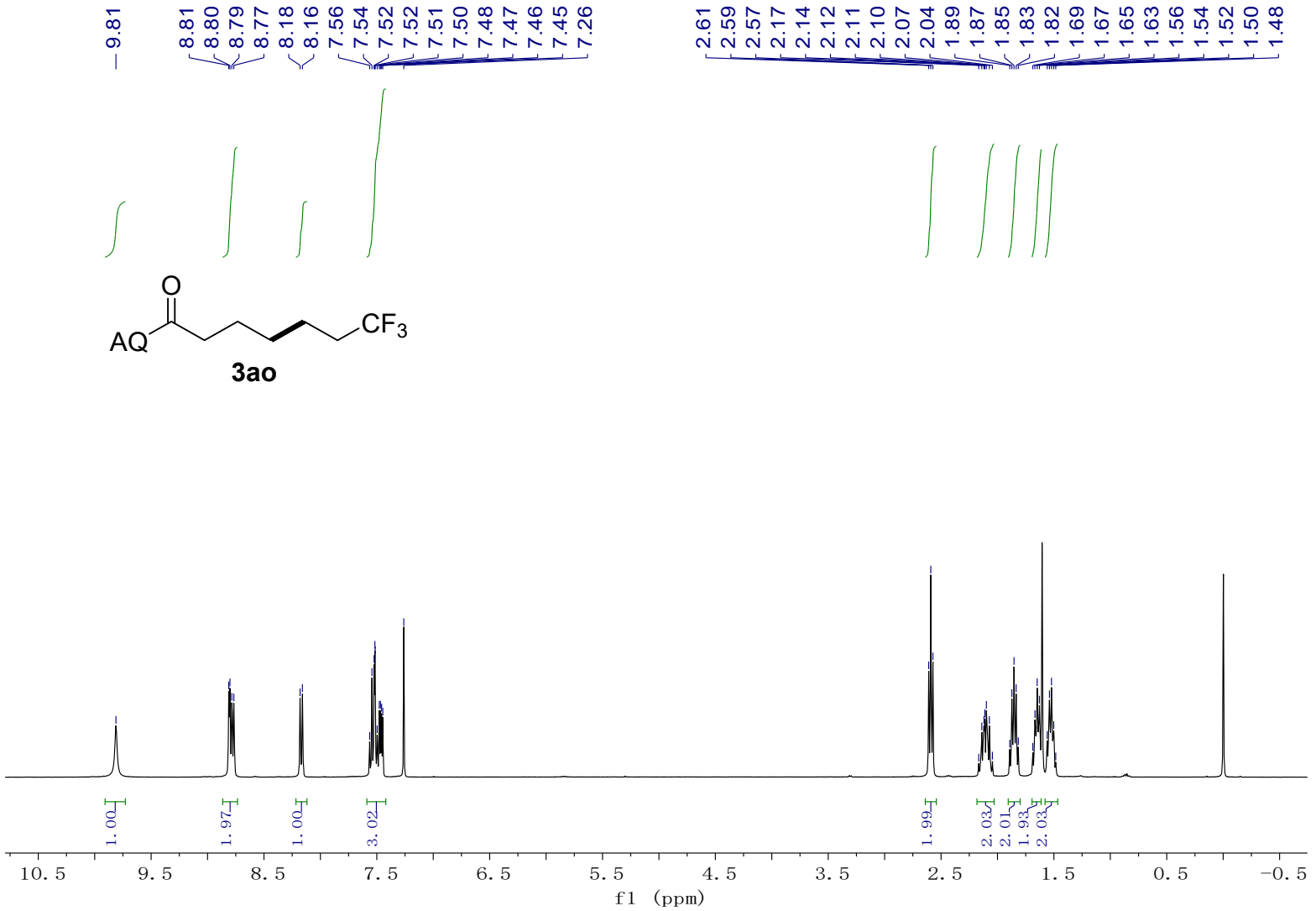

171.65
166.64
148.06
138.25
136.36
134.45
132.77
130.39
129.48
128.28
127.89
127.41
121.54
121.34
116.39
77.32
77.00
76.68
64.94
38.04
28.92
28.58
25.89
25.49
AQ
O
O
O
Ph
3al
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

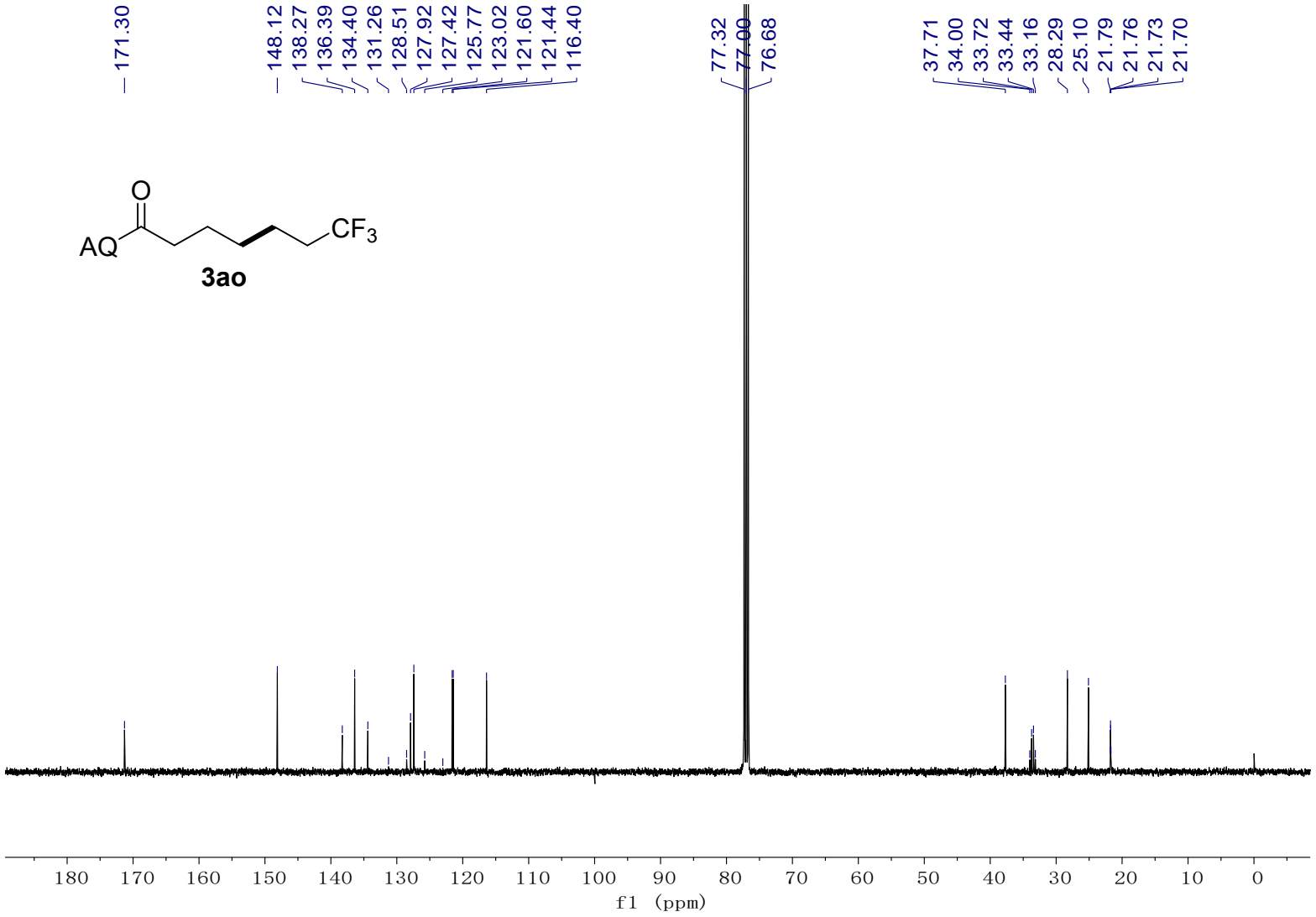

9.81
8.80
8.80
8.79
8.77
8.16
8.14
7.56
7.55
7.53
7.51
7.50
7.48
7.46
7.45
7.44
7.43
7.26
7.16
7.16
6.49
6.48
6.48
6.47
4.32
4.30
4.28
2.59
2.57
2.55
1.84
1.83
1.81
1.79
1.77
1.76
1.51
1.51
1.50
1.49
1.48
AQ
O
O
O
O
3am
0.89
2.05
1.00
4.17
0.92
0.98
1.87
1.82
4.02
3.68
f1 (ppm)

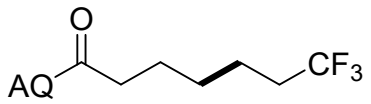

171.61
158.79
148.07
146.14
144.77
138.26
136.33
134.45
127.88
127.38
121.53
121.32
117.69
116.35
111.73
77.00
64.89
38.01
28.86
28.52
25.73
25.44
AQ
O
O
O
O
3am
90 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


9.79
8.80
8.80
8.79
8.79
8.77
8.77
8.76
8.75
8.16
8.16
8.14
8.14
7.84
7.83
7.82
7.82
7.71
7.70
7.70
7.69
7.68
7.52
7.50
7.50
7.49
7.48
7.47
7.46
7.45
7.44
7.43
7.26
3.70
3.69
3.67
2.57
2.56
2.54
1.83
1.81
1.80
1.72
1.71
1.69
1.50
1.49
1.48
1.46
1.45
1.43
1.42
AQ
O
O
N
O
O
3an
0.85
2.00
1.00
2.04
2.07
3.10
1.81
1.79
2.06
3.00
3.60
1.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
−1.
f1 (ppm)

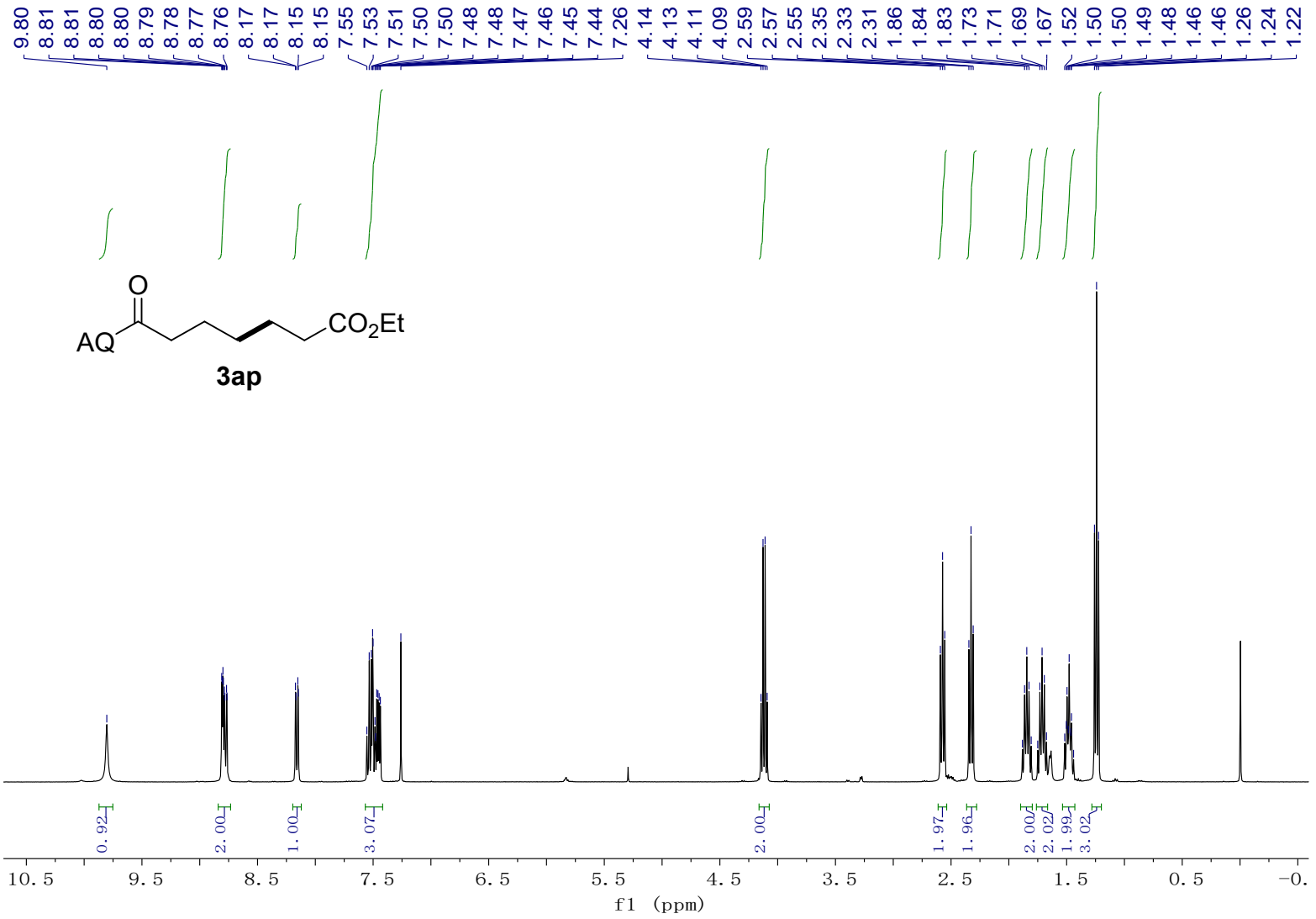

171.66
168.43
148.07
138.25
136.32
134.45
133.81
132.07
127.87
127.39
123.13
121.53
121.30
116.35
77.32
77.00
76.68
38.01
37.89
28.82
28.47
26.62
25.45
AQ
O
O
N
O
O
3an
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

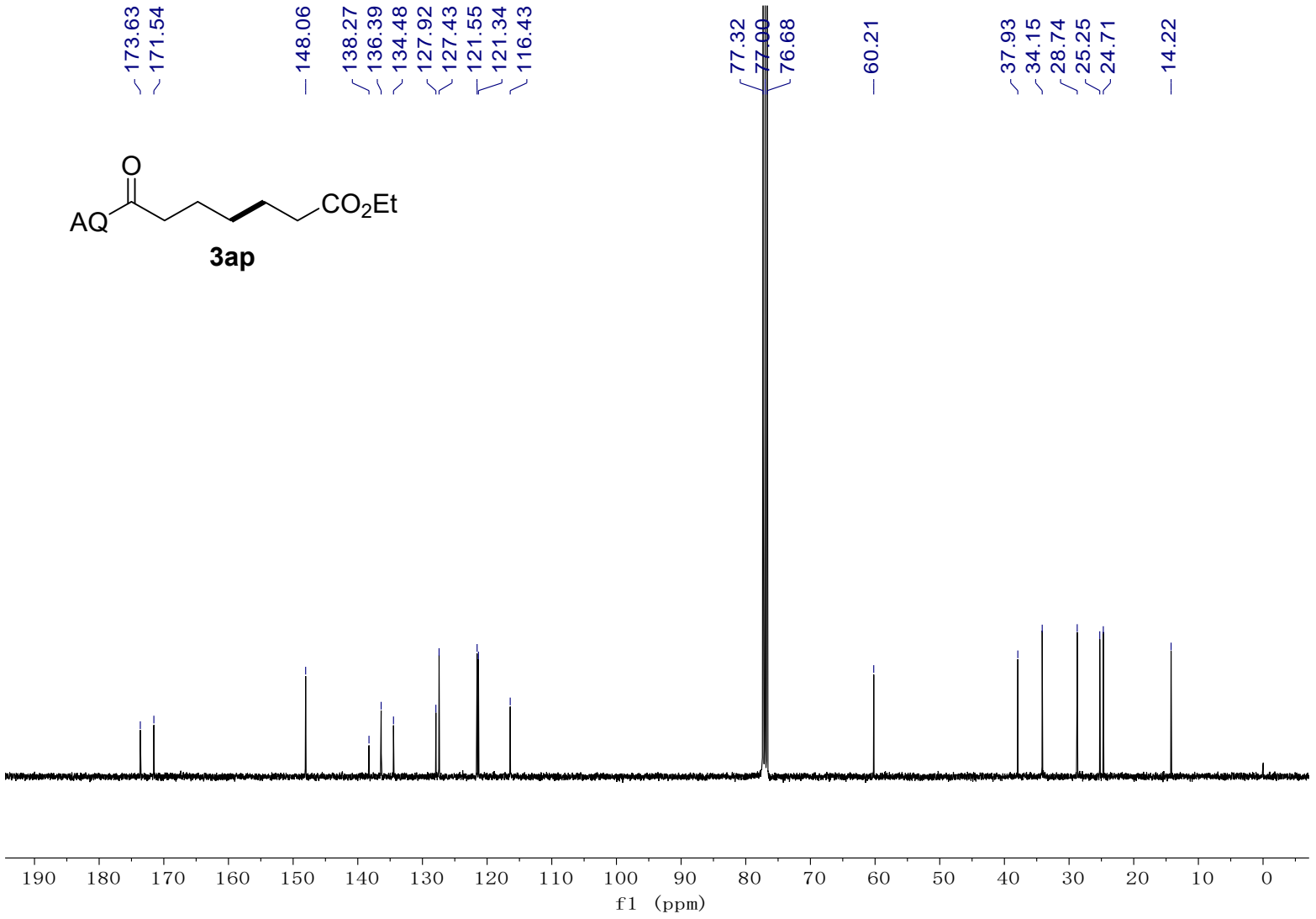

9.81
8.81
8.80
8.79
8.77
8.18
8.16
7.56
7.54
7.52
7.52
7.51
7.50
7.48
7.47
7.46
7.45
7.26
2.61
2.59
2.57
2.17
2.14
2.12
2.11
2.10
2.07
2.04
1.89
1.87
1.85
1.83
1.82
1.69
1.67
1.65
1.63
1.56
1.54
1.52
1.50
1.48
O
AQ
CF3
3ao
1.00
1.97
1.00
3.02
1.99
2.03
2.01
1.93
2.03
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
−0.5
f1 (ppm)

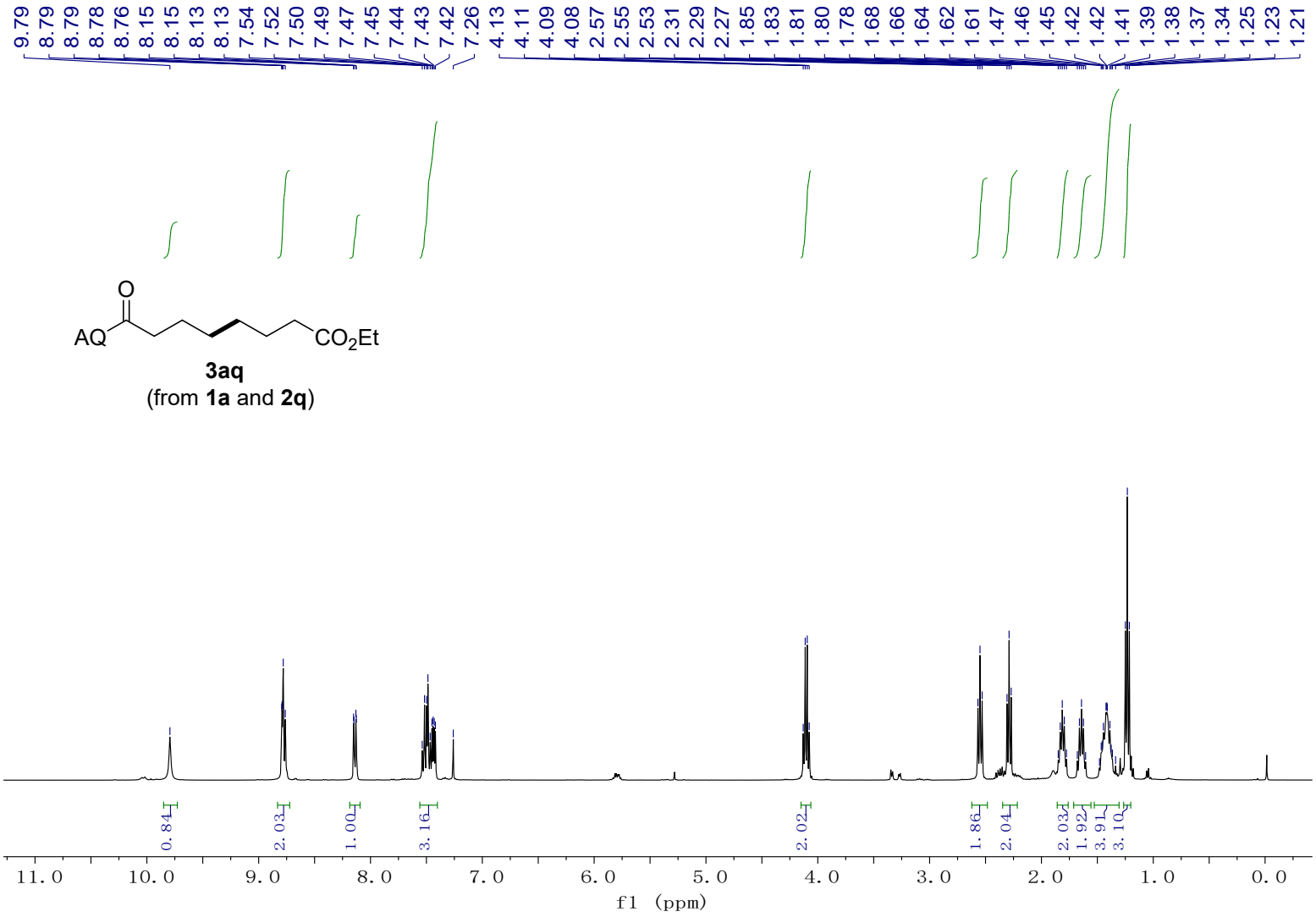

171.30
148.12
138.27
136.39
134.40
131.26
128.51
127.92
127.42
125.77
123.02
121.60
121.44
116.40
77.32
77.00
76.68
37.71
34.00
33.72
33.44
33.16
28.29
25.10
21.79
21.76
21.73
21.70
O
AQ
CF3
3ao
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



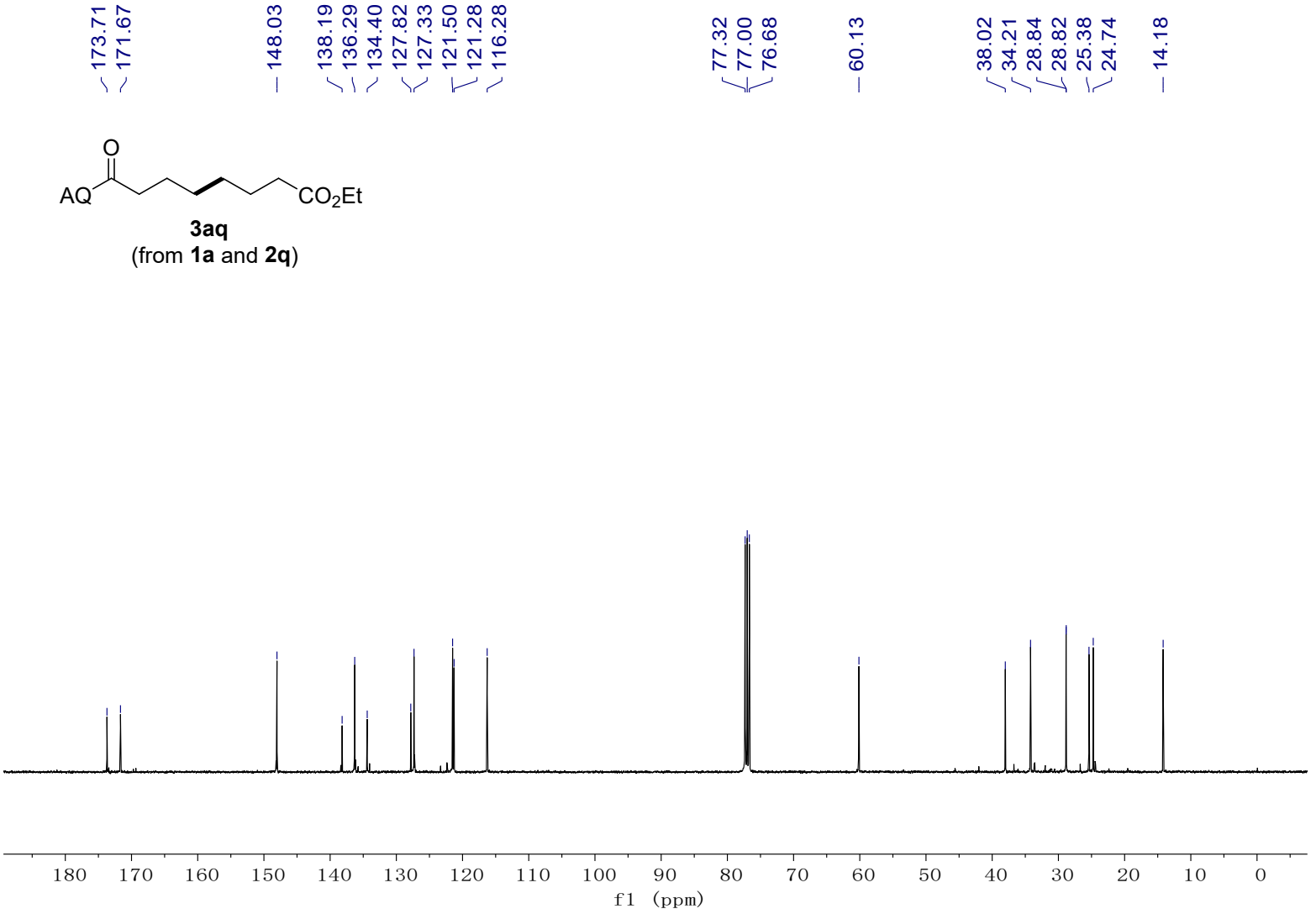
3ao


9.80
8.81
8.81
8.80
8.80
8.79
8.78
8.77
8.76
8.17
8.17
8.15
8.15
7.55
7.53
7.51
7.50
7.50
7.48
7.48
7.47
7.46
7.45
7.44
7.26
4.14
4.13
4.11
4.09
2.59
2.57
2.55
2.35
2.33
2.31
1.86
1.84
1.83
1.73
1.71
1.69
1.67
1.52
1.50
1.50
1.49
1.48
1.46
1.46
1.26
1.24
1.22
O
AQ
CO2Et
3ap
0.92
2.00
1.00
3.07
2.00
1.97
1.96
2.00
2.02
1.99
3.02
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
−0.
f1 (ppm)

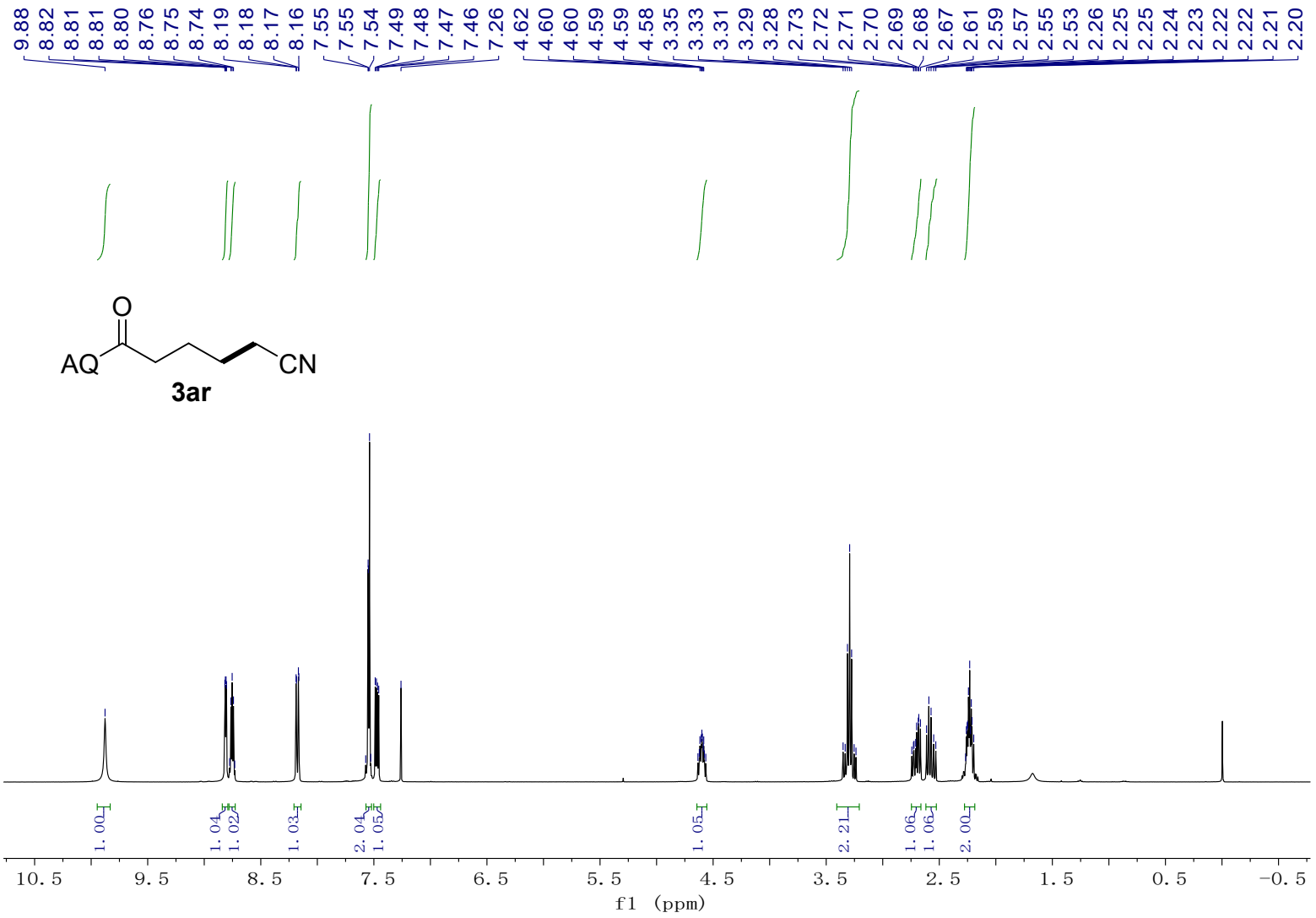

173.63
171.54
148.06
138.27
136.39
134.48
127.92
127.43
121.55
121.34
116.43
77.32
77.00
76.68
60.21
37.93
34.15
28.74
25.25
24.71
14.22
O
AQ
CO2Et
3ap
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

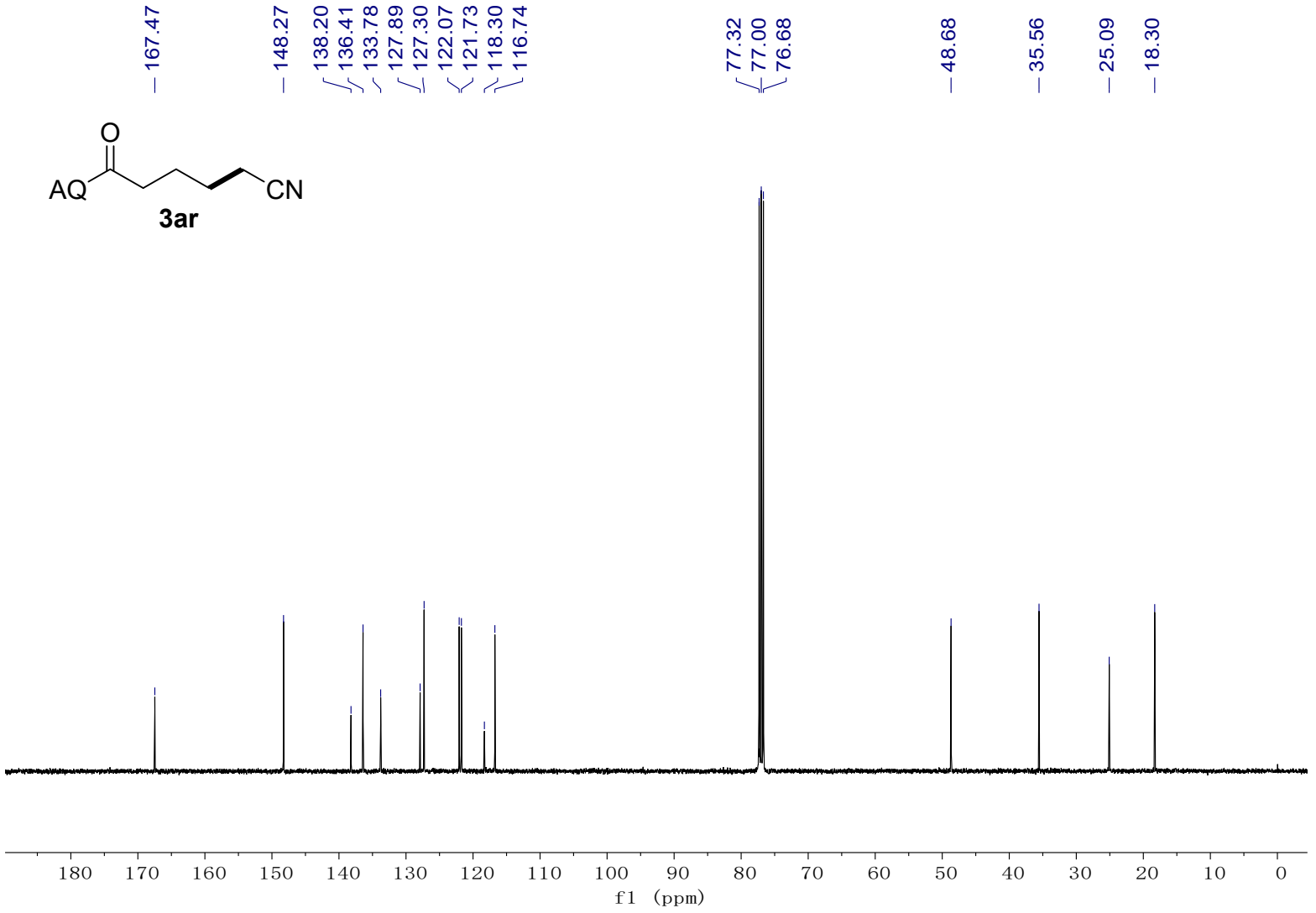


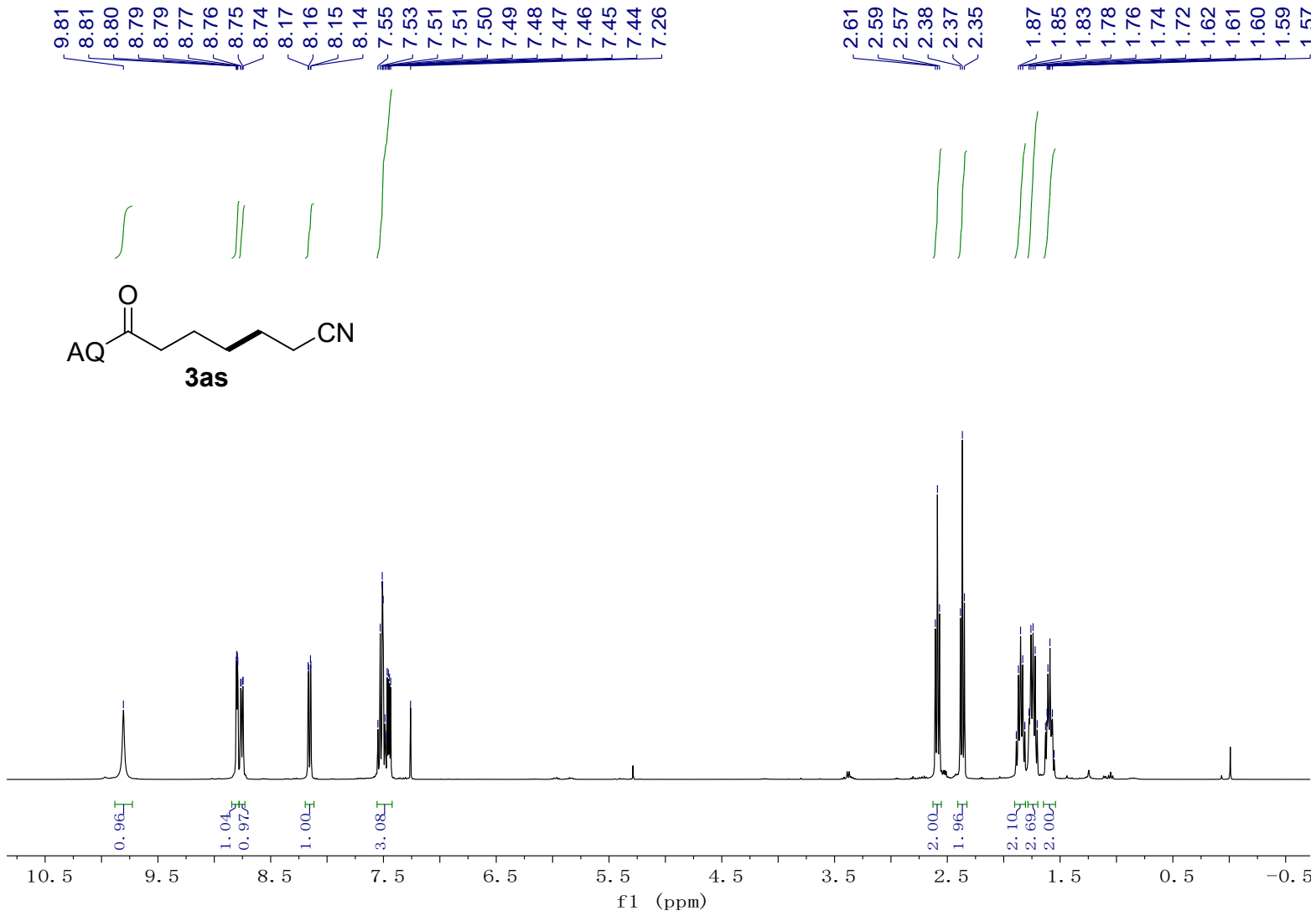
3aq
(from **1a** and **2q**)

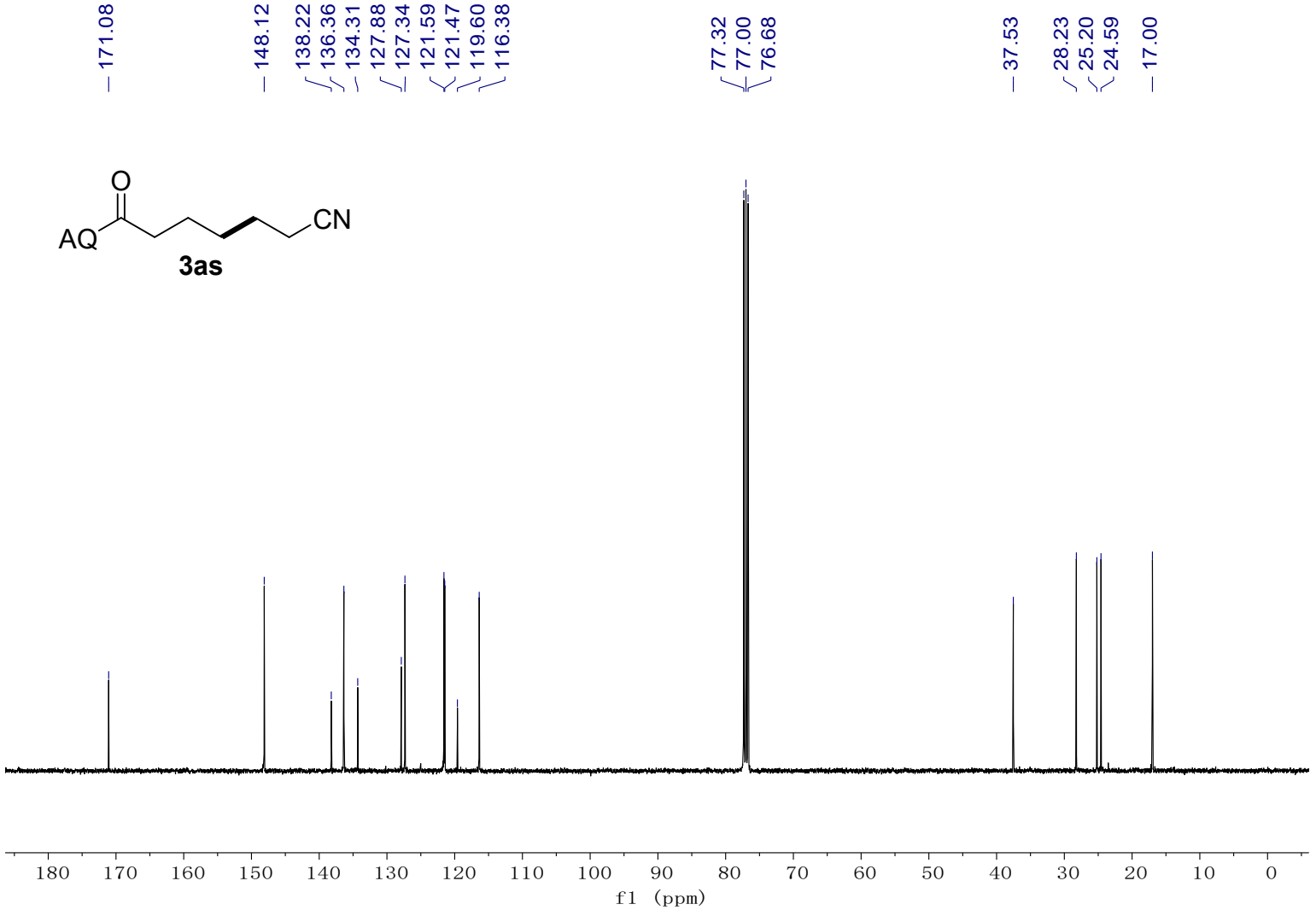


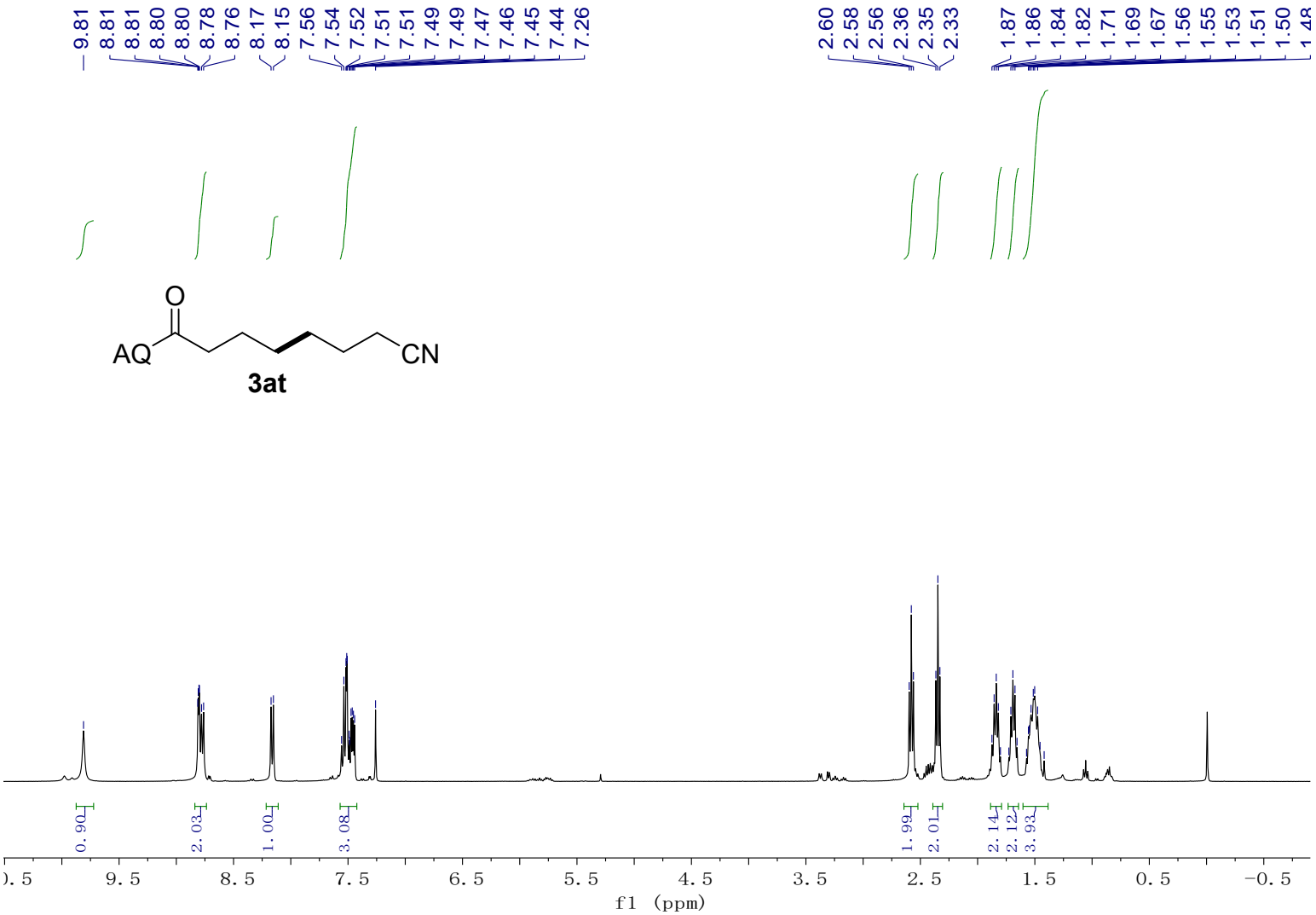
3aq
(from **1a** and **2q**)

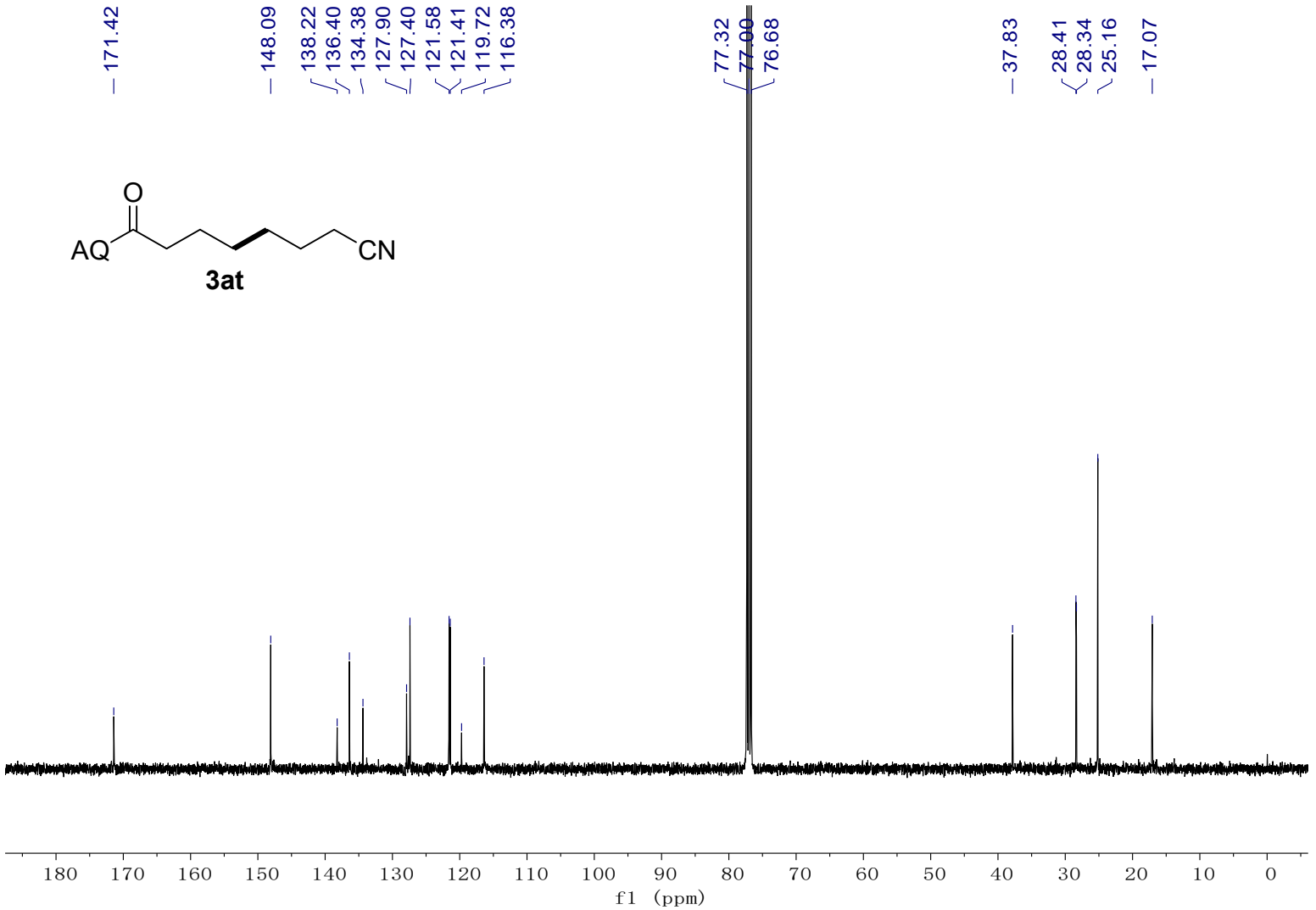

9.88
8.82
8.81
8.81
8.80
8.76
8.75
8.74
8.19
8.18
8.17
8.16
7.55
7.55
7.54
7.49
7.48
7.47
7.46
7.26
4.62
4.60
4.60
4.59
4.59
4.58
3.35
3.33
3.31
3.29
3.28
2.73
2.72
2.71
2.70
2.69
2.68
2.67
2.61
2.59
2.57
2.55
2.53
2.26
2.25
2.25
2.24
2.23
2.22
2.22
2.21
2.20
O
AQ
CN
3ar
1.00
1.04
1.02
1.03
2.04
1.05
1.05
2.21
1.06
1.06
2.00
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
-0.5
f1 (ppm)

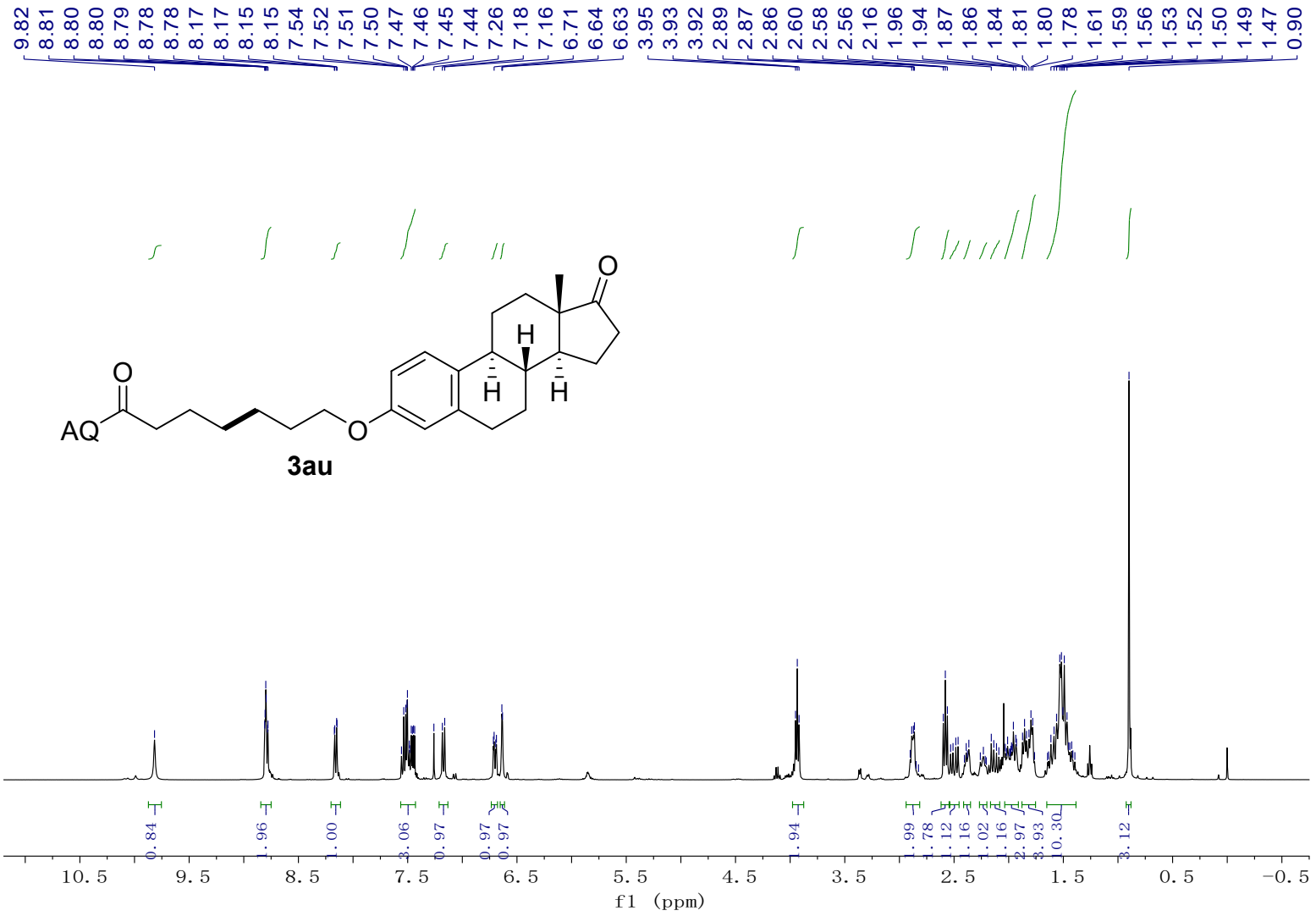

167.47
148.27
138.20
136.41
133.78
127.89
127.30
122.07
121.73
118.30
116.74
77.32
77.00
76.68
48.68
35.56
25.09
18.30
O
AQ
CN
3ar
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

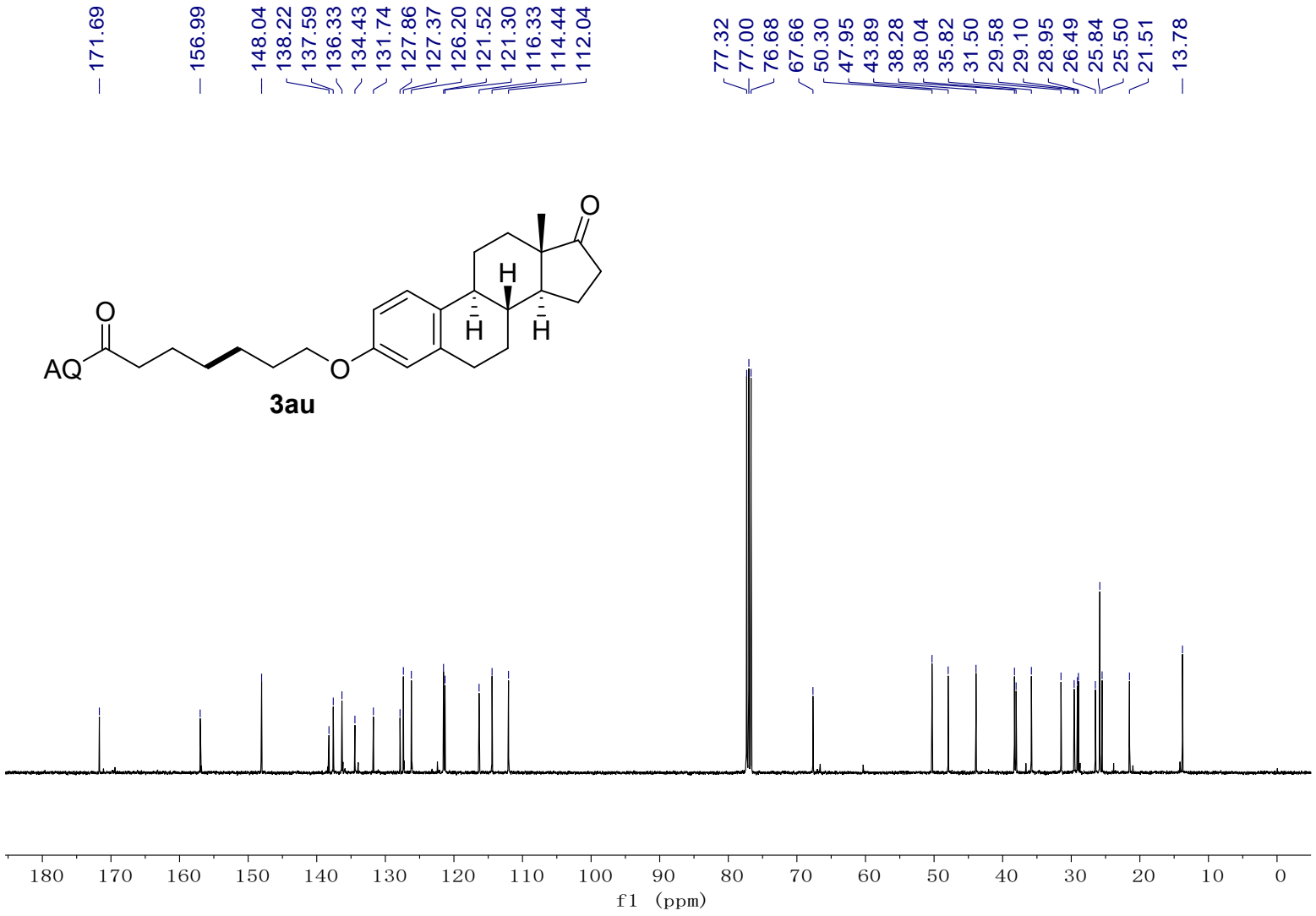

9.81
8.81
8.80
8.79
8.79
8.77
8.76
8.75
8.74
8.17
8.16
8.15
8.14
7.55
7.53
7.51
7.51
7.50
7.49
7.48
7.47
7.46
7.45
7.44
7.26
2.61
2.59
2.57
2.38
2.37
2.35
1.87
1.85
1.83
1.78
1.76
1.74
1.72
1.62
1.61
1.60
1.59
O
AQ
CN
3as
0.96
1.04
0.97
1.00
3.08
2.00
1.96
2.10
2.69
2.00
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
−0.5
f1 (ppm)

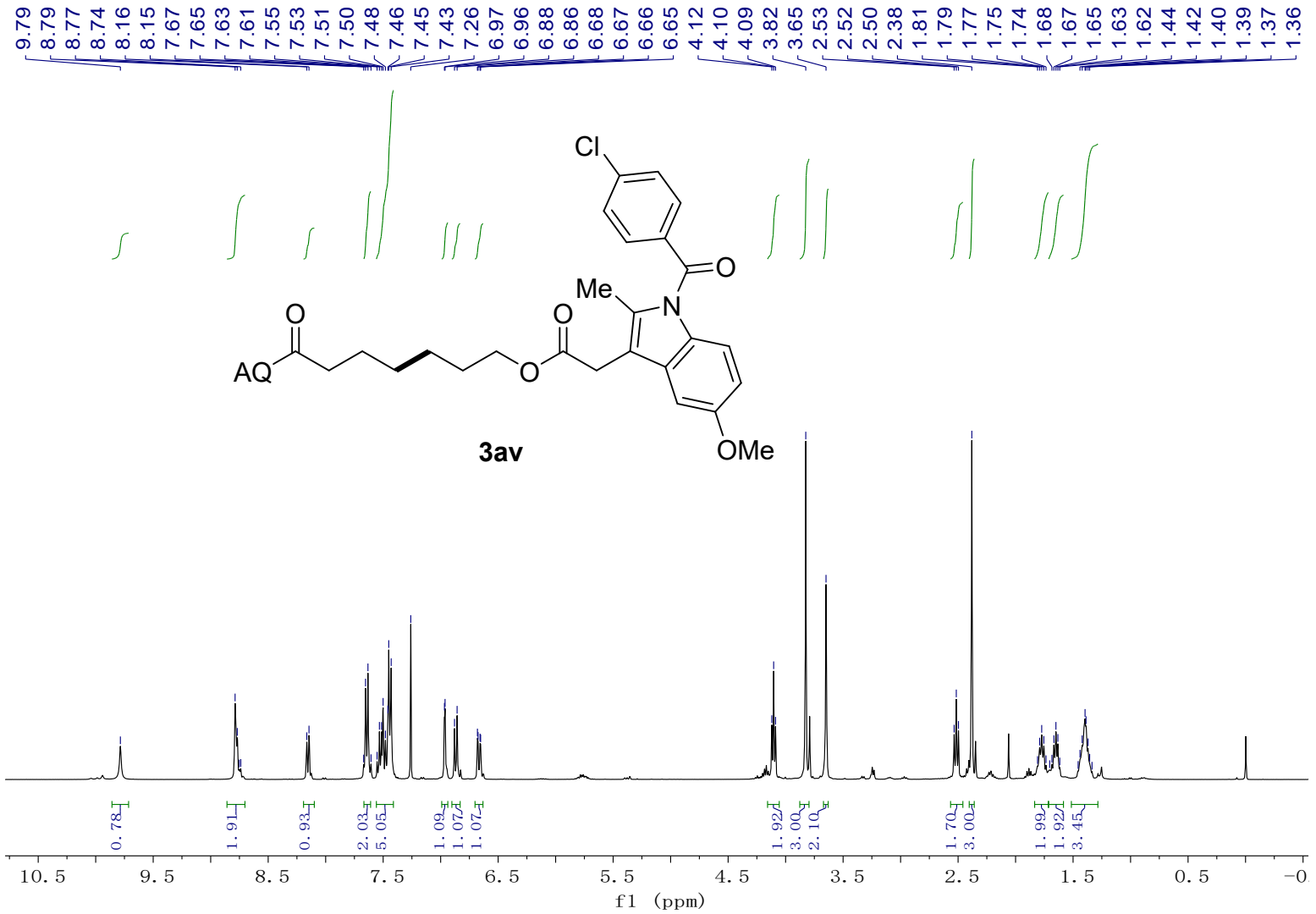

171.08
148.12
138.22
136.36
134.31
127.88
127.34
121.59
121.47
119.60
116.38
77.32
77.00
76.68
37.53
28.23
25.20
24.59
17.00
O
AQ
CN
3as
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

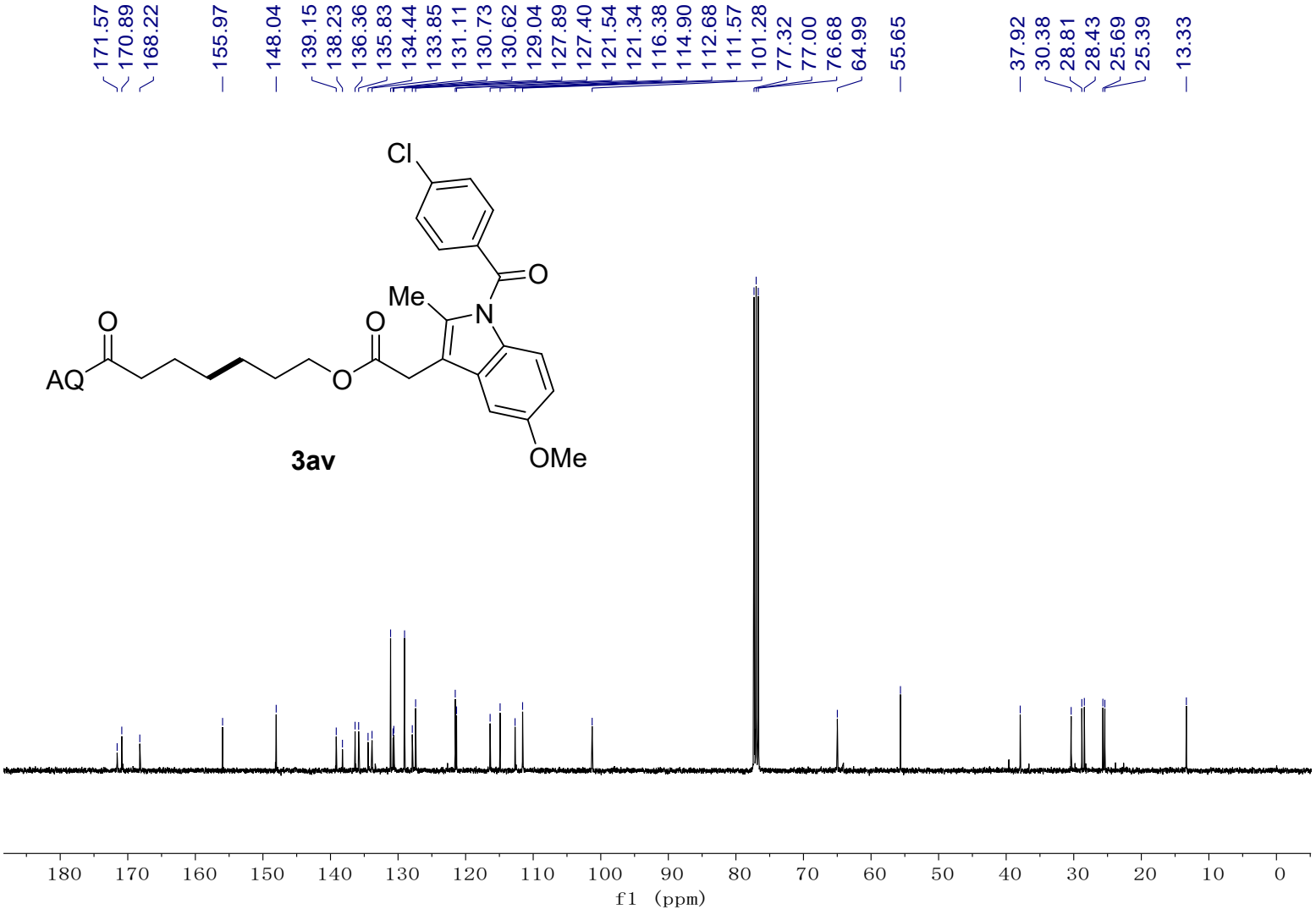

9.81
8.81
8.81
8.80
8.80
8.78
8.76
8.17
8.15
7.56
7.54
7.52
7.51
7.51
7.49
7.49
7.47
7.46
7.45
7.44
7.26
2.60
2.58
2.56
2.36
2.35
2.33
1.87
1.86
1.84
1.82
1.71
1.69
1.67
1.56
1.55
1.53
1.51
1.50
O
AQ
CN
3at
0.90
2.03
1.00
3.08
1.99
2.01
2.14
2.12
3.93
f1 (ppm)

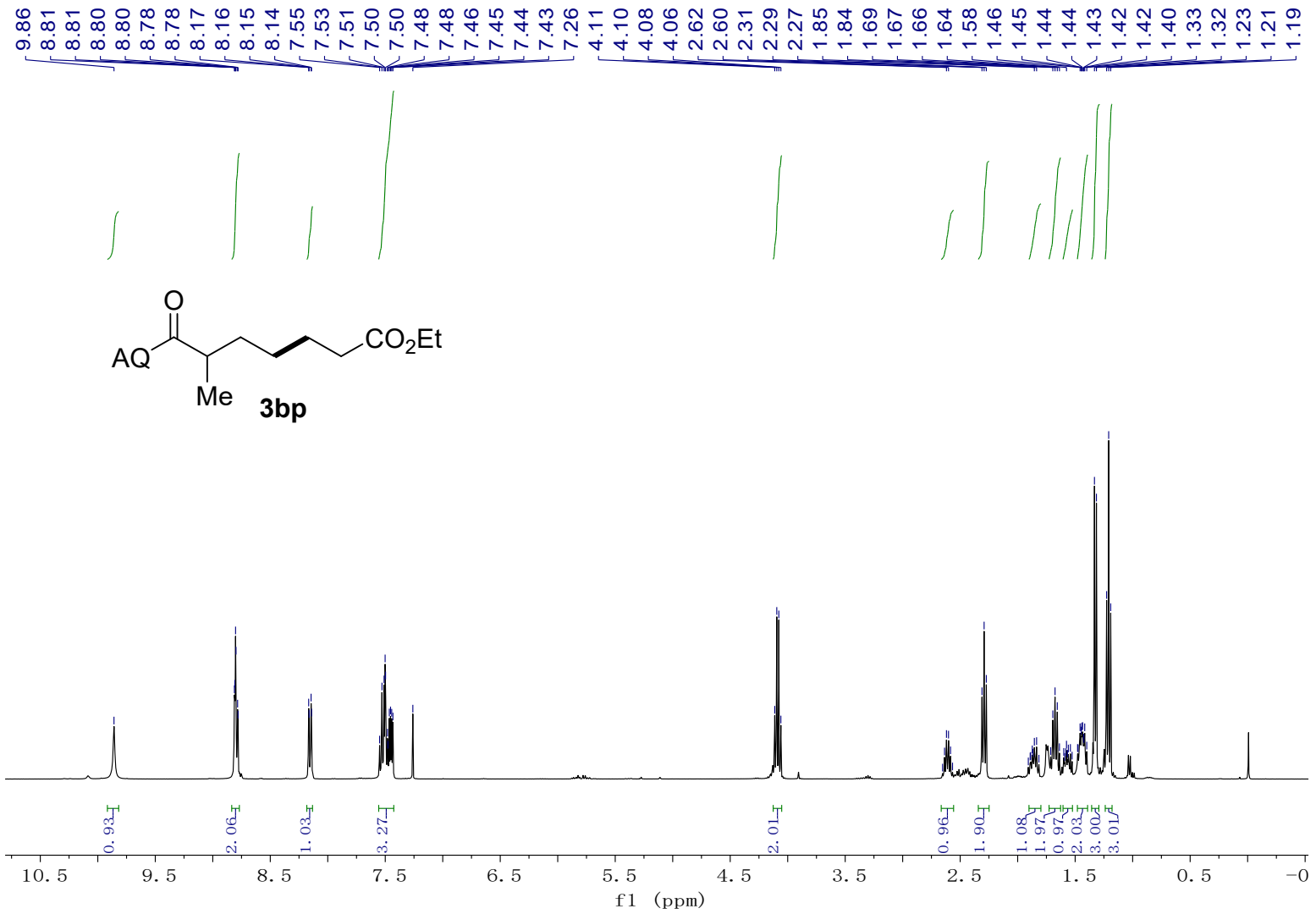

171.42
148.09
138.22
136.40
134.38
127.90
127.40
121.58
121.41
119.72
116.38
77.32
77.00
76.68
37.83
28.41
28.34
25.16
17.07
O
AQ
CN
3at
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

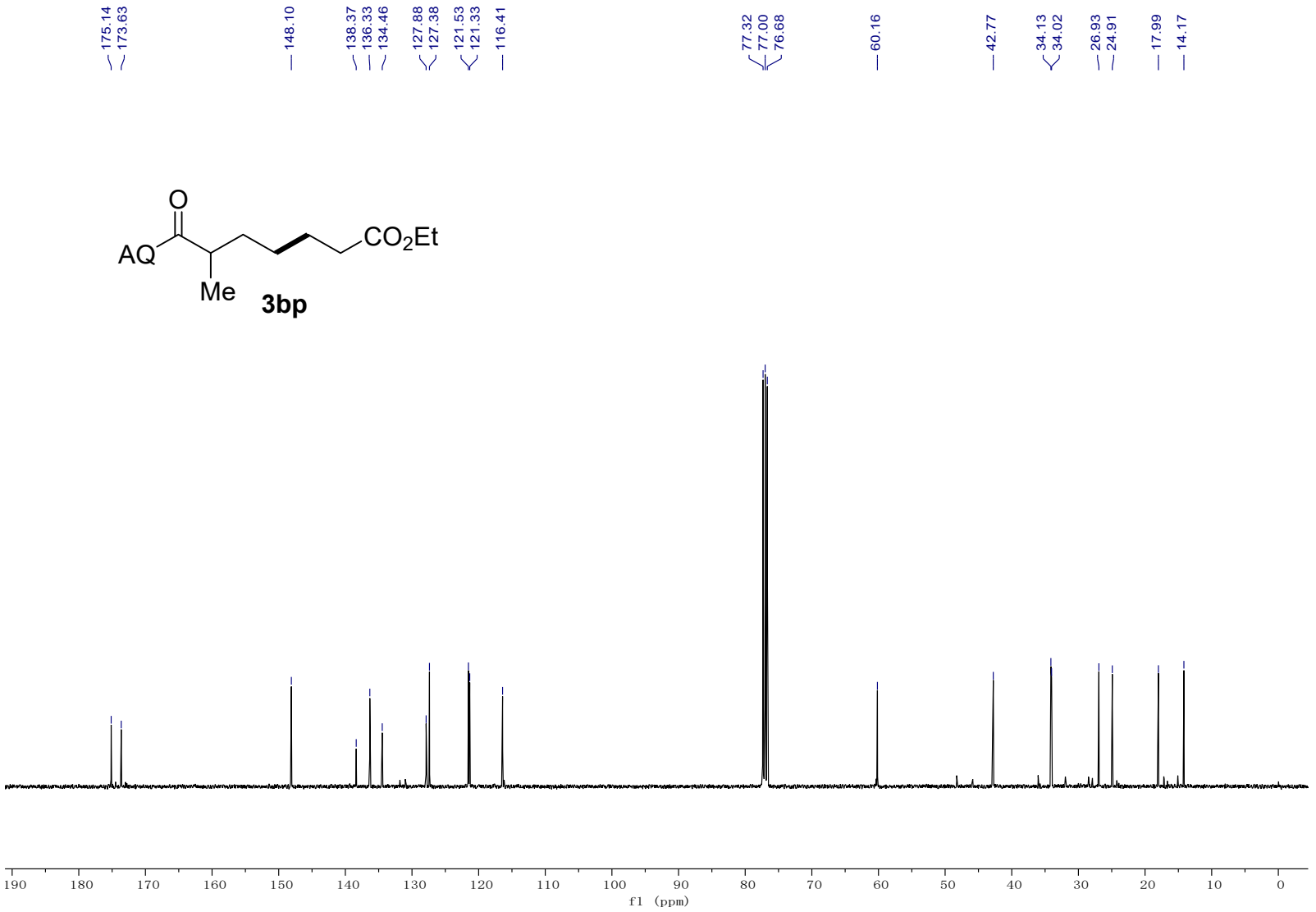

9.82 8.81 8.80 8.80 8.79 8.78 8.78 8.17 8.17 8.15 8.15 7.54 7.52 7.51 7.50 7.47 7.46 7.45 7.44 7.26 7.18 7.16 6.71 6.64 6.63 3.95 3.93 3.92 2.89 2.87 2.86 2.60 2.58 2.56 2.16 1.96 1.94 1.87 1.86 1.84 1.81 1.80 1.78 1.61 1.59 1.56 1.53 1.52 1.50 1.49 1.47 0.90
O
O
AQ
O
H
H
H
O
3au
0.84 1.96 1.00 3.06 0.97 0.97 0.97 1.94 1.99 1.78 1.12 1.16 1.02 1.16 2.97 3.93 10.30 3.12
10.5 9.5 8.5 7.5 6.5 5.5 4.5 3.5 2.5 1.5 0.5 −0.5
f1 (ppm)

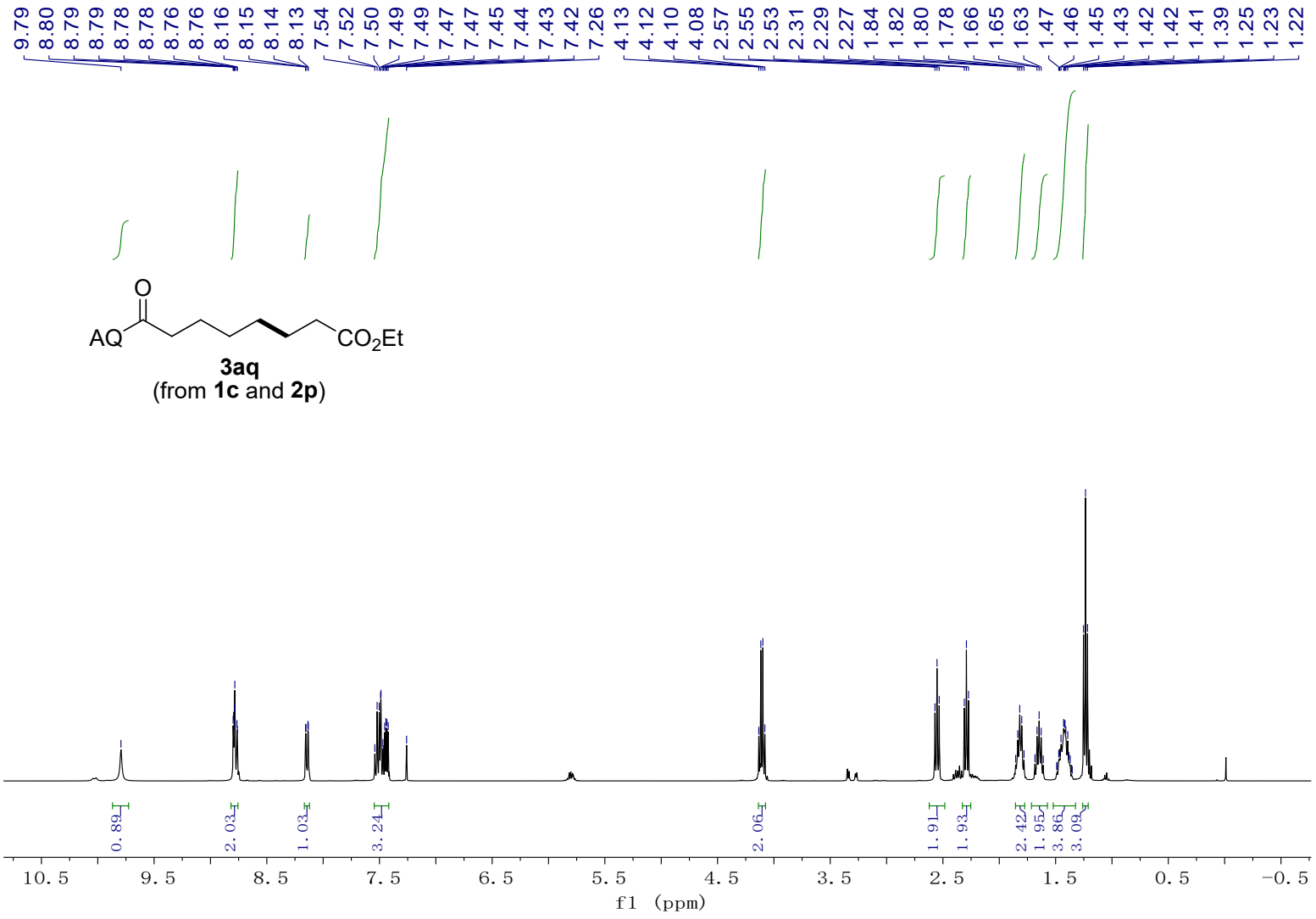

171.69
156.99
148.04
138.22
137.59
136.33
134.43
131.74
127.86
127.37
126.20
121.52
121.30
116.33
114.44
112.04
77.32
77.00
76.68
67.66
50.30
47.95
43.89
38.28
38.04
35.82
31.50
29.58
29.10
28.95
26.49
25.84
25.50
21.51
13.78
O
H
H
H
O
AQ
O
3au
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

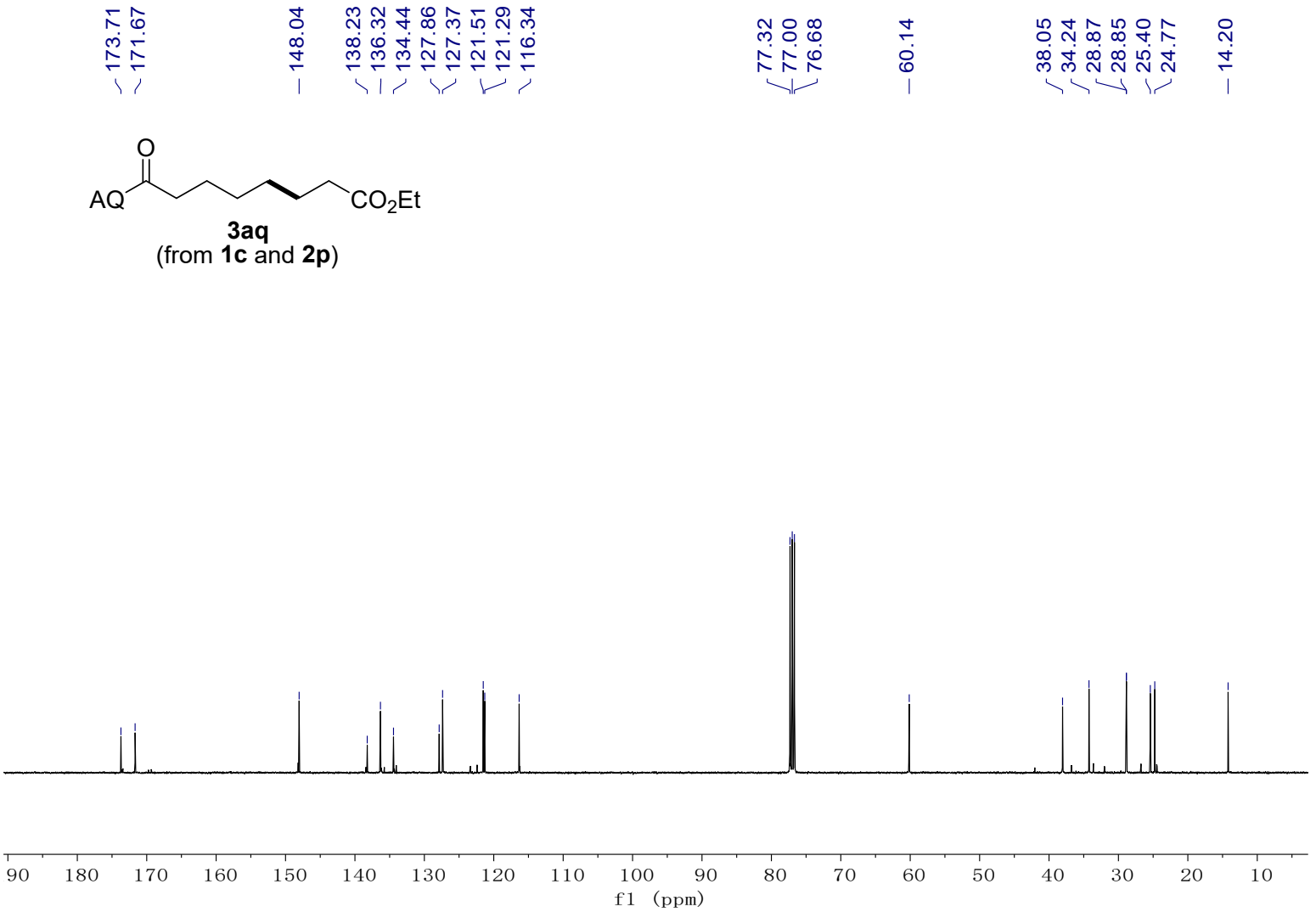

9.79
8.79
8.77
8.74
8.16
8.15
7.67
7.65
7.63
7.61
7.55
7.53
7.51
7.50
7.48
7.46
7.45
7.43
7.26
6.97
6.96
6.88
6.86
6.68
6.67
6.66
6.65
4.12
4.10
4.09
3.82
3.65
2.53
2.52
2.50
2.38
1.81
1.79
1.77
1.75
1.74
1.68
1.67
1.65
1.63
1.62
1.44
1.42
1.40
1.39
1.37
1.36
Cl
O
Me
N
O
O
AQ
O
3av
OMe
0.78
1.91
0.93
2.03
5.05
1.09
1.07
1.07
1.92
3.00
2.10
1.70
3.00
1.99
1.92
3.45
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
−0
f1 (ppm)

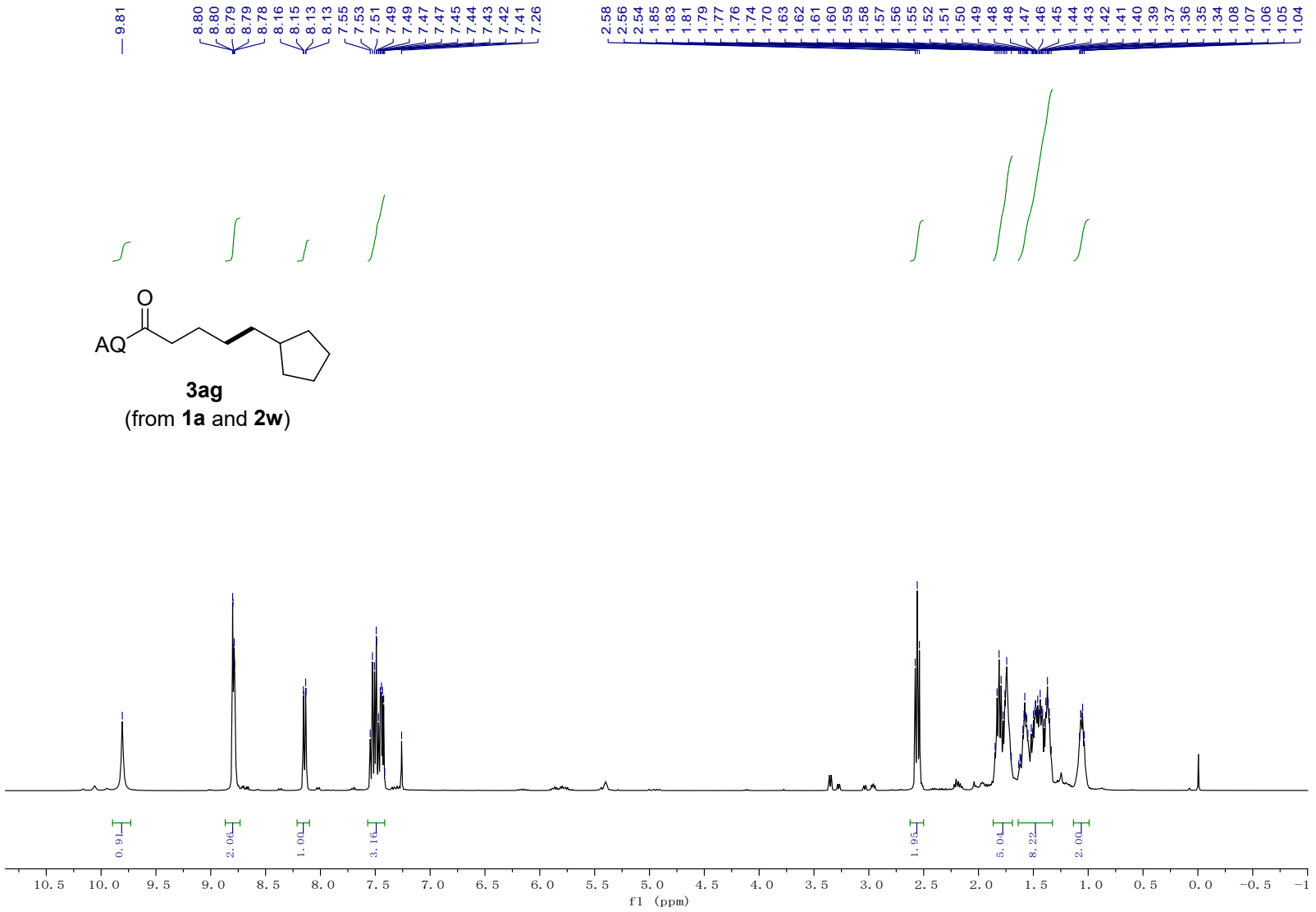

171.57
170.89
168.22
155.97
148.04
139.15
138.23
136.36
135.83
134.44
133.85
131.11
130.73
130.62
129.04
127.89
127.40
121.54
121.34
116.38
114.90
112.68
111.57
101.28
77.32
77.00
76.68
64.99
55.65
37.92
30.38
28.81
28.43
25.69
25.39
13.33
Cl
O
Me
N
O
O
AQ
O
OMe
3av
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


9.86
8.81
8.81
8.80
8.80
8.78
8.78
8.17
8.16
8.15
8.14
7.55
7.53
7.51
7.50
7.50
7.48
7.48
7.46
7.45
7.44
7.43
7.26
4.11
4.10
4.08
4.06
2.62
2.60
2.31
2.29
2.27
1.85
1.84
1.69
1.67
1.66
1.64
1.58
1.46
1.45
1.44
1.44
1.43
1.42
1.42
1.40
1.33
1.32
1.23
1.21
1.19
O
AQ
CO2Et
Me
3bp
0.93
2.06
1.03
3.27
2.01
0.96
1.90
1.08
1.97
0.97
2.03
3.00
3.01
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
−0
f1 (ppm)

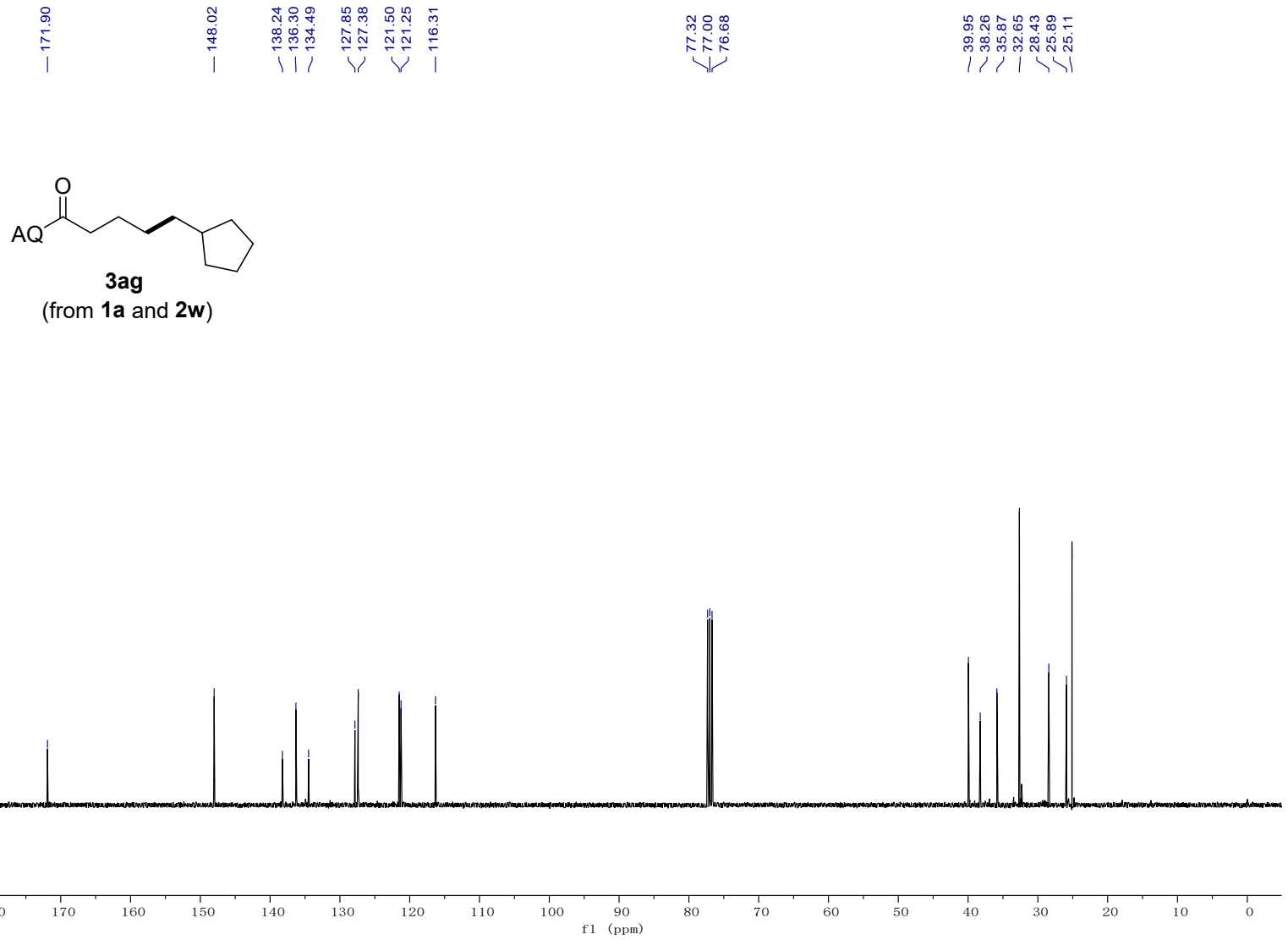

175.14
173.63
148.10
138.37
136.33
134.46
127.88
127.38
121.53
121.33
116.41
77.32
77.00
76.68
60.16
42.77
34.13
34.02
26.93
24.91
17.99
14.17
O
AQ
CO2Et
Me
3bp
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


9.79
8.80
8.79
8.79
8.78
8.78
8.76
8.76
8.16
8.15
8.14
8.13
7.54
7.52
7.50
7.49
7.49
7.47
7.47
7.45
7.44
7.43
7.42
7.26
4.13
4.12
4.10
4.08
2.57
2.55
2.53
2.31
2.29
2.27
1.84
1.82
1.80
1.78
1.66
1.65
1.63
1.47
1.46
1.45
1.43
1.42
1.42
1.41
1.39
1.25
1.23
1.22
O
AQ
CO2Et
3aq
(from 1c and 2p)
0.89
2.03
1.03
3.24
2.06
1.91
1.93
2.42
1.95
3.86
3.09
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
−0.5
f1 (ppm)

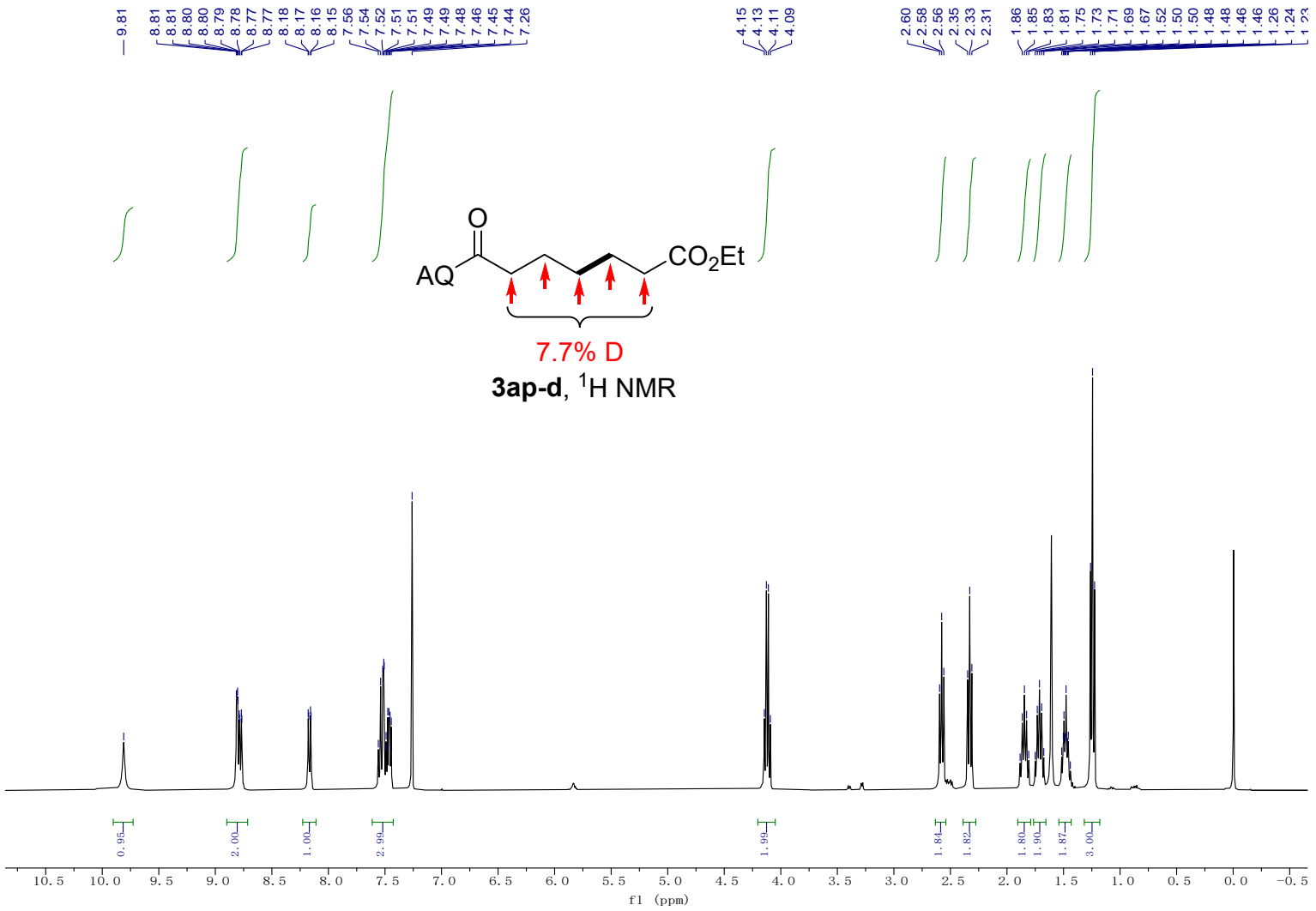

173.71
171.67
148.04
138.23
136.32
134.44
127.86
127.37
121.51
121.29
116.34
77.32
77.00
76.68
60.14
38.05
34.24
28.87
28.85
25.40
24.77
14.20
O
AQ
CO2Et
3aq
(from 1c and 2p)
90 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

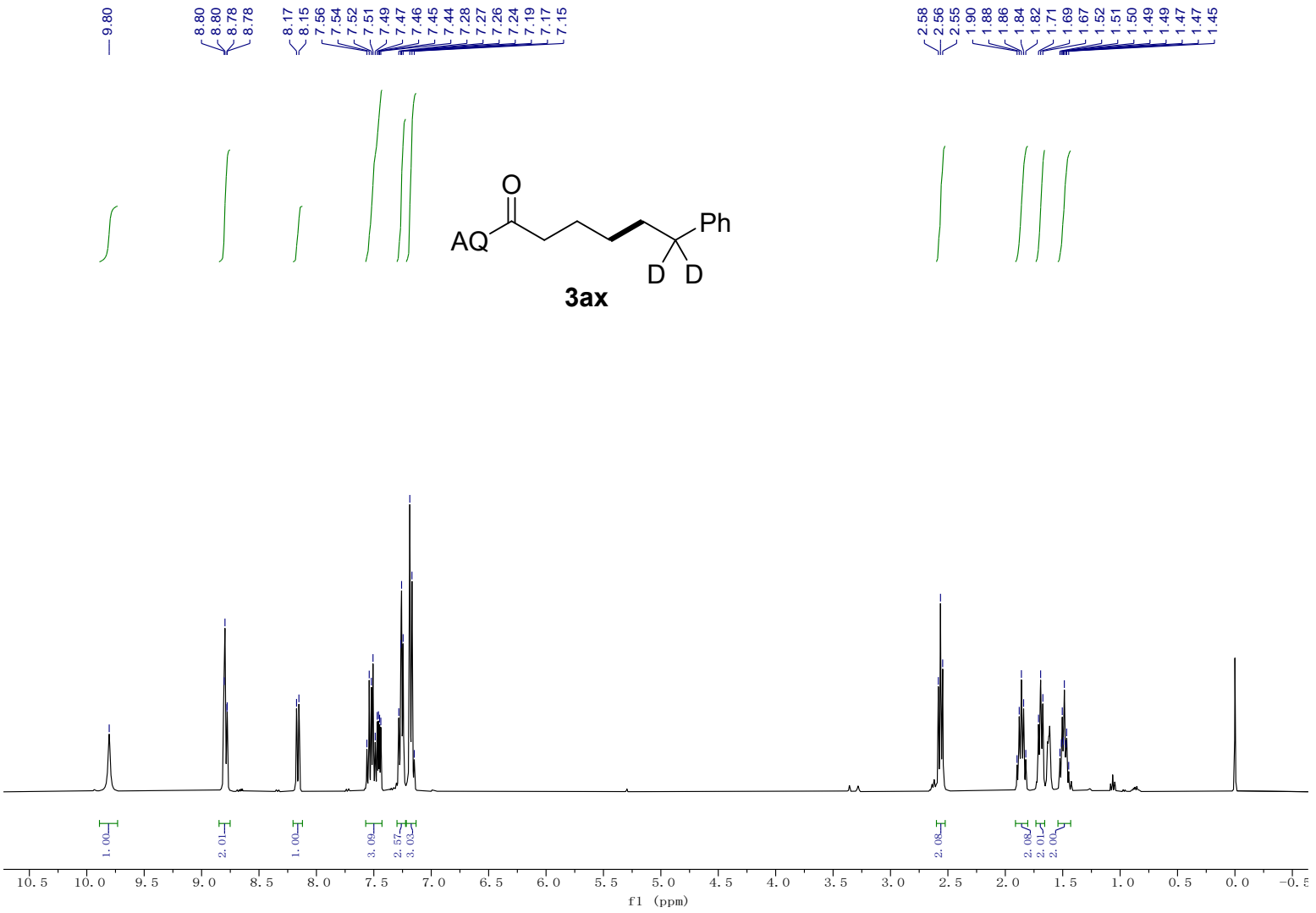


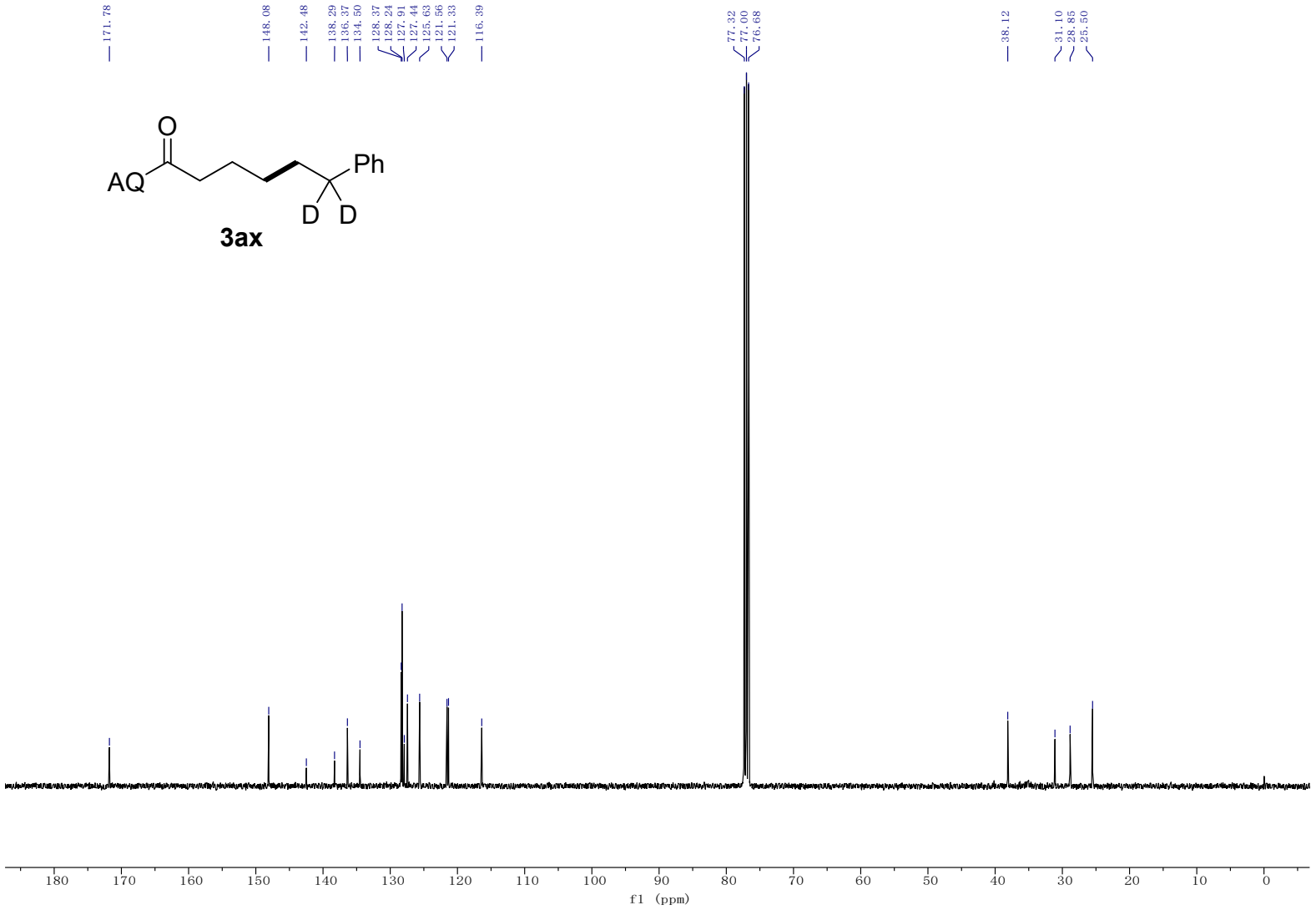
3ag
(from **1a** and **2w**)

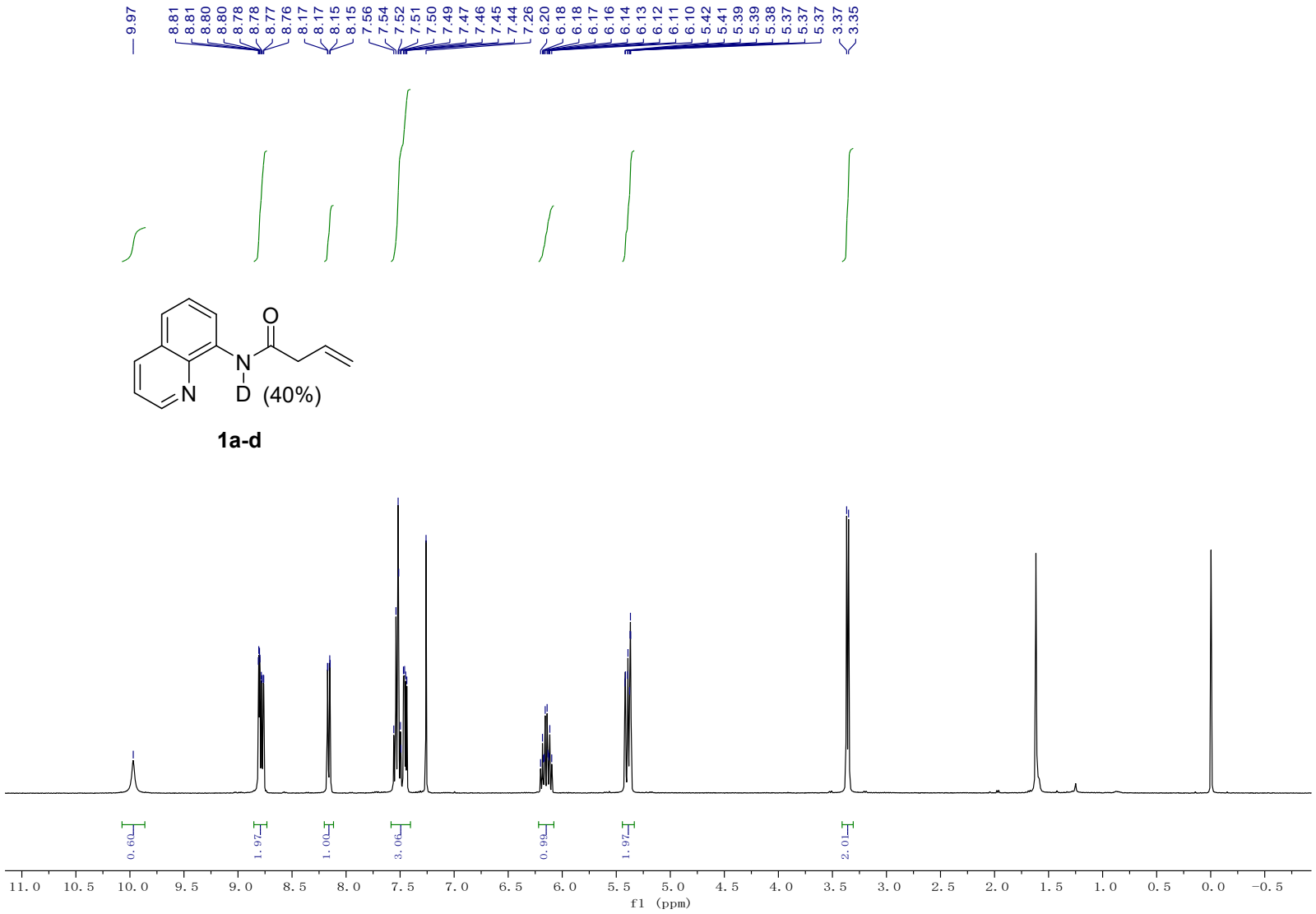


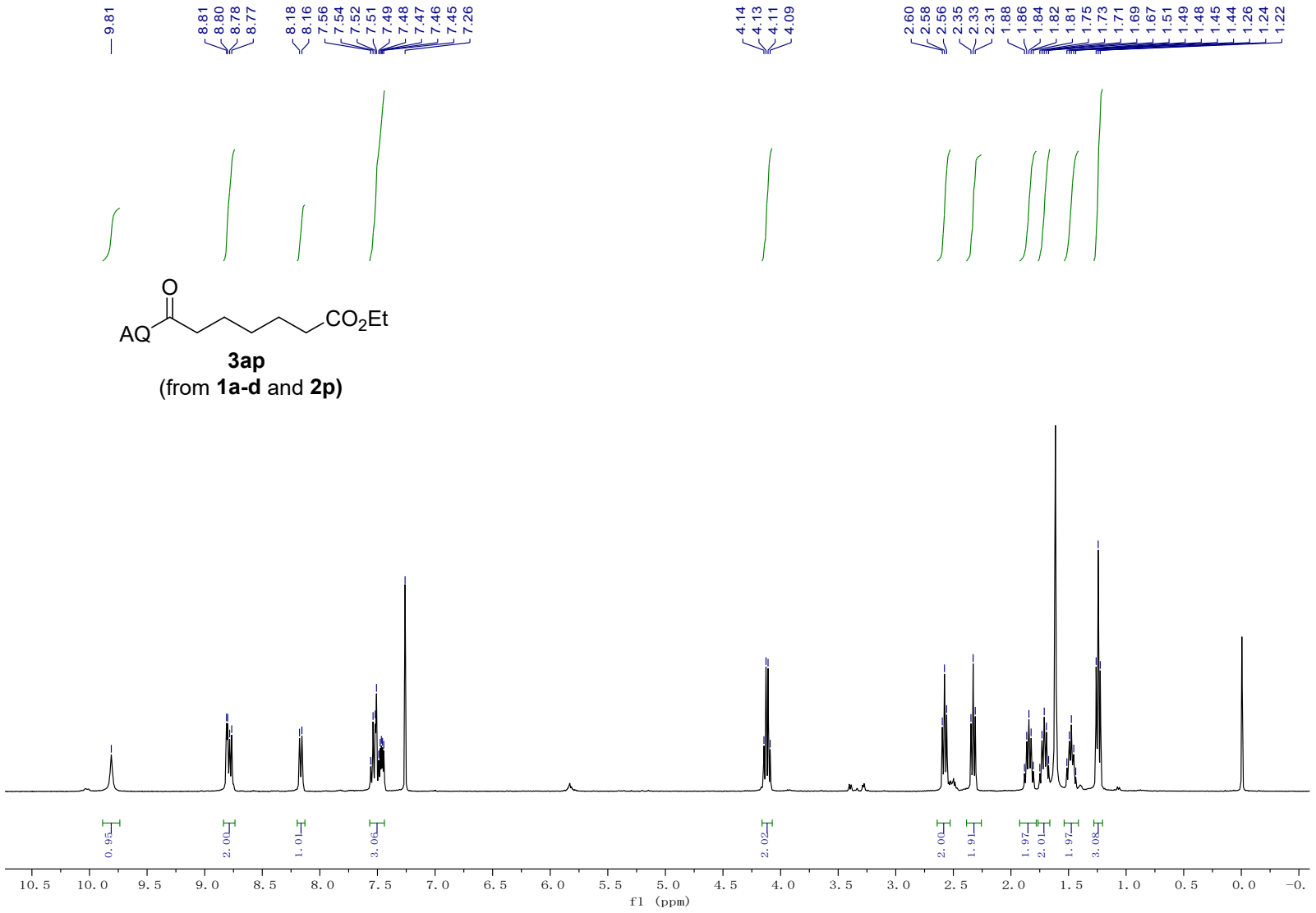
3ag
(from **1a** and **2w**)


9.81
8.81
8.81
8.80
8.80
8.79
8.78
8.77
8.77
8.18
8.17
8.16
8.15
7.56
7.54
7.52
7.51
7.51
7.49
7.49
7.48
7.46
7.45
7.44
7.26
4.15
4.13
4.11
4.09
2.60
2.58
2.56
2.35
2.33
2.31
1.86
1.85
1.83
1.81
1.75
1.73
1.71
1.69
1.67
1.52
1.50
1.50
1.48
1.48
1.46
1.46
1.26
1.24
O
AQ
CO2Et
7.7% D
3ap-d, 1H NMR
0.96
2.00
1.00
2.99
1.99
1.84
1.82
1.88
1.90
1.87
3.00
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)


9.80
8.80
8.80
8.78
8.78
8.17
8.15
7.56
7.54
7.52
7.51
7.49
7.47
7.46
7.45
7.44
7.28
7.27
7.26
7.24
7.19
7.17
7.15
2.58
2.56
2.55
1.90
1.88
1.86
1.84
1.82
1.71
1.69
1.67
1.52
1.51
1.50
1.49
1.49
1.47
1.47
1.45
O
AQ
Ph
D
D
3ax
1.00
2.01
1.00
3.09
2.57
3.03
2.08
2.08
2.01
2.00
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)


171.78
148.08
142.48
138.29
136.37
134.50
128.37
128.24
127.91
127.44
125.63
121.56
121.33
116.39
77.32
77.00
76.68
38.12
31.10
28.85
25.50
O
AQ
Ph
D
D
3ax
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


9.97
8.81
8.81
8.80
8.80
8.78
8.78
8.77
8.76
8.17
8.17
8.15
8.15
7.56
7.54
7.52
7.51
7.50
7.49
7.47
7.46
7.45
7.44
7.26
6.20
6.18
6.18
6.17
6.16
6.14
6.13
6.12
6.11
6.10
5.42
5.41
5.39
5.39
5.38
5.37
5.37
5.37
3.37
3.35
O
N
D (40%)
N
1a-d
0.60
1.97
1.00
3.06
0.99
1.97
2.01
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
−0.5
f1 (ppm)



3ap
(from **1a-d** and **2p)**