Redox-neutral rhodium(III)-catalyzed divergent synthesis of tetrasubstituted 1,3-enynes and alkynylated benzofurans

Supporting Information

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General Information

If not otherwise specified, the reagents were obtained from commercial sources and used directly without purification. Heating source: all the reactions that require heating were carried out in an oil bath. Analytical thin-layer chromatography (TLC): HSGF 254 (0.15-0.2 mm thickness). Detection under UV light at 254 nm. Column chromatography: separations were carried out on silica gel FCP 200-300. Yields refer to isolated compounds. Melting point apparatus: a micro melting point apparatus, values are uncorrected. Nuclear magnetic resonance (NMR) apparatus: a Brucker 400, 500 or 600 MHz instrument. Chemical shifts (δ) are given in ppm. Proton coupling patterns were recorded as singlet (s), doublet (d), triplet (t), quartet (q), and multiplet (m). HRMS (high-resolution mass) were measured on a Thermo Scientific LTQ Orbitrap Discovery (Bremen, Germany). The linear ion trap (LTQ) part of the hybrid MS system was equipped with electrospray ionization (ESI) probe and operated in both positive and negative ion modes.

Preparation of the Starting Materials

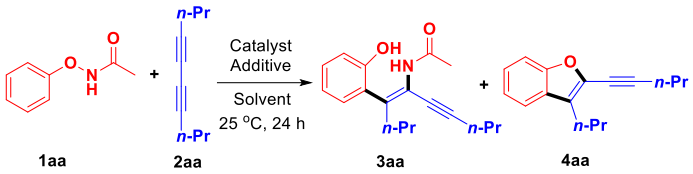
All the *N*-phenoxyacetamides were prepared according to the literature procedure and their characterization data were in accordance with the published ones.[1]

Except for deca-4,6-diyne, which was obtained from commercial sources and used directly without purification, all the 1,3-diynes used in this work were prepared according to the literature procedure and their characterization data were in accordance with the published ones.[2-11]

Preparation of $[D]_5$-1aa

$[D]_5$-1aa was synthesized from Phenyl-d_5-boronic acid following the reported method and the characterization data match published data.[1]

Table S1 Optimization of the reaction conditions[a]



1aa 2aa 3aa 4aa

Entry	Catalyst	Additive	Solvent	Yield of **3aa** (%)[b]	Yield of **4aa** (%)[b]
1	[Cp*Co(CO)I_2]	CsOAc	MeOH	trace	0
2	[Cp*RhCl$_2$]$_2$	CsOAc	DCE	<10	32
3	[Cp*RhCl$_2$]$_2$	CsOAc	THF	14	29
4	[Cp*RhCl$_2$]$_2$	CsOAc	Acetone	<10	28
5	[Cp*RhCl$_2$]$_2$	CsOAc	EtOH	37	<10
6	[Cp*RhCl$_2$]$_2$	Cu(OAc)$_2$	MeOH	50	trace
7	[Cp*RhCl$_2$]$_2$	K_2CO_3	MeOH	65	0
8	[Cp*RhCl$_2$]$_2$	$NaHCO_3$	MeOH	74	0
9	[Cp*RhCl$_2$]$_2$	CsF	MeOH	69	trace
10	[Cp*RhCl$_2$]$_2$	Cu(OAc)$_2$	CH_2Cl_2	0	trace
11	[Cp*RhCl$_2$]$_2$	Na_2CO_3	CH_2Cl_2	10	19
12	[Cp*RhCl$_2$]$_2$	K_2CO_3	CH_2Cl_2	15	19
13	[Cp*RhCl$_2$]$_2$	KF	CH_2Cl_2	15	27

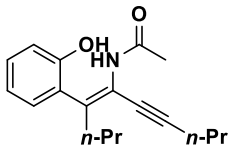
14	$[Cp^*RhCl_2]_2$	CsF	CH_2Cl_2	15	<10
15	$[Cp^*RhCl_2]_2$	—	MeOH	35	0
16	—	$Zn(OAc)_2$	MeOH	0	0
17	$[Cp^*RhCl_2]_2$	—	CH_2Cl_2	0	0
18	—	$NaOPiv·H_2O$	CH_2Cl_2	0	0

[a] Reaction conditions: **1aa** (0.25 mmol), **2aa** (0.275 mmol), catalyst (5 mol%), additive (0.25 mmol), solvent (4.0 mL), 25 °C, 24 h. [b] Isolated yields.

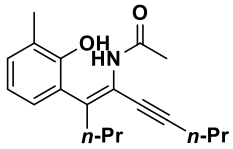
General Procedure for the Rhodium-Catalyzed C–H Alkenylation/Directing Group Migration between *N*-phenoxyacetamides and 1,3-Diynes

To a mixture of *N*-phenoxyacetamides **1** (0.25 mmol), $[Cp^*RhCl_2]_2$ (5 mol%) and $Zn(OAc)_2$ (0.25 mmol) in a 25 mL Schlenk tube was added a solution of 1,3-diynes **2** (0.275 mmol) in MeOH (4.0 mL). Then the tube was capped with septa, and the resulting mixture was stirred at 25 °C for 24 h. After removal of the solvent, the residue was purified by flash chromatography on silica gel to provide the desired products **3**.

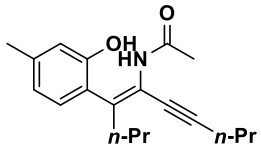
Characterization Data of Products 3



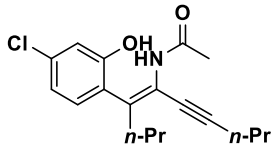
(*Z*)-*N*-(4-(2-hydroxyphenyl)dec-4-en-6-yn-5-yl)acetamide (3aa): The reaction mixture was subjected directly to flash chromatography (DCM/EtOAc: 35/1→DCM/EtOAc: 15/1) on silica gel to provide the product as a white amorphous solid (61.7 mg, yield 86%), mp 121-122 °C. ^{1}H NMR (600 MHz, DMSO-d_6) δ 9.42 (s, 1H), 8.49 (s, 1H), 7.09-7.05 (m, 1H), 6.91 (d, J = 7.5 Hz, 1H), 6.82 (d, J = 8.2 Hz, 1H), 6.74-6.70 (m, 1H), 2.62 (t, J = 7.4 Hz, 2H), 2.34 (t, J = 6.9 Hz, 2H), 1.64 (s, 3H), 1.55-1.48 (m, 2H), 1.26-1.17 (m, 2H), 0.99 (t, J = 7.3 Hz, 3H), 0.82 (t, J = 7.3 Hz, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 167.9, 154.0, 142.4, 129.6, 128.4, 125.2, 118.6, 115.6, 115.0, 91.6, 78.6, 35.2, 22.5, 21.7, 20.8, 13.7, 13.3; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{18}H_{24}NO_2$ 286.1802; Found 286.1804.



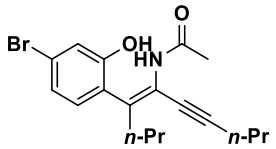
(*Z*)-*N*-(4-(2-hydroxy-3-methylphenyl)dec-4-en-6-yn-5-yl)acetamide (3ab): The reaction mixture was subjected directly to flash chromatography (DCM/EtOAc: 35/1→DCM/EtOAc: 15/1) on silica gel to provide the product as a white amorphous solid (50.3 mg, yield 67%), mp 175-176 °C. ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.59 (s, 1H), 8.05 (s, 1H), 6.98 (d, J = 7.1 Hz, 1H), 6.77-6.66 (m, 2H), 2.59 (t, J = 7.7 Hz, 2H), 2.35 (t, J = 7.3 Hz, 2H), 2.16 (s, 3H), 1.65 (s, 3H), 1.56-1.49 (m, 2H), 1.27-1.18 (m, 2H), 1.00 (t, J = 7.4 Hz, 3H), 0.84 (t, J = 7.6 Hz, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 168.6, 151.6, 143.0, 129.8, 127.1, 126.1, 125.0, 119.0, 115.4, 91.8, 78.6, 48.6, 35.7, 22.4, 21.7, 20.7, 16.6, 13.7, 13.3; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{19}H_{26}NO_2$ 300.1958; Found 300.1953.



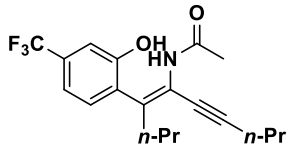
(*Z*)-*N*-(4-(2-hydroxy-4-methylphenyl)dec-4-en-6-yn-5-yl)acetamide (3ac): The reaction mixture was subjected directly to flash chromatography (DCM/EtOAc: 35/1→DCM/EtOAc: 15/1) on silica gel to provide the product as a white amorphous solid (61.4 mg, yield 82%), mp 181-182 °C. ^{1}H NMR (600 MHz, DMSO-d_6) δ 9.36 (s, 1H), 8.47 (s, 1H), 6.79 (d, J = 7.6 Hz, 1H), 6.63 (s, 1H), 6.54 (d, J = 7.7 Hz, 1H), 2.61 (t, J = 7.4 Hz, 2H), 2.33 (t, J = 6.9 Hz, 2H), 2.19 (s, 3H), 1.65 (s, 3H), 1.55-1.46 (m, 2H), 1.25-1.15 (m, 2H), 0.99 (t, J = 7.5 Hz, 3H), 0.81 (t, J = 7.3 Hz, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 167.9, 153.9, 142.3, 137.8, 129.5, 122.2, 119.5, 116.2, 114.9, 91.6, 78.7, 35.3, 22.6, 21.8, 20.9, 20.8, 20.8, 13.7, 13.3; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{19}H_{26}NO_2$ 300.1958; Found 300.1963.



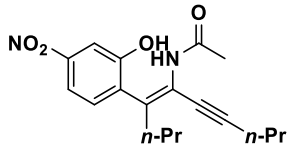
(*Z*)-*N*-(4-(4-chloro-2-hydroxyphenyl)dec-4-en-6-yn-5-yl)acetamide (3ad): The reaction mixture was subjected directly to flash chromatography (DCM/EtOAc: 35/1→DCM/EtOAc: 15/1) on silica gel to provide the product as a white amorphous solid (60.4 mg, yield 76%), mp 180-181 °C. ^{1}H NMR (600 MHz, DMSO-d_6) δ 9.97 (s, 1H), 8.59 (s, 1H), 6.88 (d, J = 8.1 Hz, 1H), 6.83 (s, 1H), 6.77 (d, J = 8.4 Hz, 1H), 2.59 (t, J = 7.4 Hz, 2H), 2.33 (t, J = 6.9 Hz, 2H), 1.65 (s, 3H), 1.56-1.46 (m, 2H), 1.25-1.16 (m, 2H), 0.98 (t, J = 7.5 Hz, 3H), 0.82 (t, J = 7.3 Hz, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 168.0, 155.2, 141.3, 132.1, 131.1, 124.4, 118.5, 115.6, 115.3, 92.1, 78.5, 34.9, 22.6, 21.7, 20.8, 13.7, 13.4; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{18}H_{23}ClNO_2$ 320.1412; Found 320.1415.



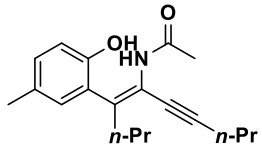
(*Z*)-*N*-(4-(4-bromo-2-hydroxyphenyl)dec-4-en-6-yn-5-yl)acetamide (3ae): The reaction mixture was subjected directly to flash chromatography (DCM/EtOAc: 35/1→DCM/EtOAc: 15/1) on silica gel to provide the product as a white amorphous solid (67.0 mg, yield 74%), mp 181-182 °C. ^{1}H NMR (600 MHz, DMSO-d_6) δ 9.97 (s, 1H), 8.58 (s, 1H), 6.98 (s, 1H), 6.90 (d, J = 8.4 Hz, 1H), 6.82 (d, J = 8.3 Hz, 1H), 2.59 (t, J = 7.3 Hz, 2H), 2.33 (t, J = 6.9 Hz, 2H), 1.65 (s, 3H), 1.55-1.47 (m, 2H), 1.25-1.15 (m, 2H), 0.98 (t, J = 7.3 Hz, 3H), 0.81 (t, J = 7.3 Hz, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 168.0, 155.4, 141.3, 131.4, 124.8, 121.3, 120.5, 118.2, 115.5, 92.1, 78.5, 34.9, 22.5, 21.7, 20.8, 13.7, 13.4; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{18}H_{23}BrNO_2$ 364.0907; Found 364.0911.



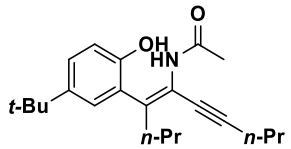
(*Z*)-*N*-(4-(2-hydroxy-4-(trifluoromethyl)phenyl)dec-4-en-6-yn-5-yl)acetamide (3af): The reaction mixture was subjected directly to flash chromatography (DCM/EtOAc: 35/1→DCM/EtOAc: 15/1) on silica gel to provide the product as a yellow amorphous solid (62.5 mg, yield 71%), mp 145-146 °C. ^{1}H NMR (600 MHz, DMSO-d_6) δ 10.16 (s, 1H), 8.65 (s, 1H), 7.12-7.04 (m, 3H), 2.63 (t, J = 7.5 Hz, 2H), 2.35 (t, J = 6.7 Hz, 2H), 1.64 (s, 3H), 1.55-1.48 (m, 2H), 1.24-1.15 (m, 2H), 0.99 (t, J = 7.3 Hz, 3H), 0.83 (t, J = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 168.0, 154.7, 141.0, 130.8, 129.8,128.8 (q, C-F, $^2J_{C\text{-}F}$ = 34.6 Hz), 124.2 (q, C-F, $^1J_{C\text{-}F}$ = 268.6 Hz), 116.0, 115.0, 111.8, 92.4, 78.3, 34.8, 22.5, 21.7, 20.8, 13.6, 13.3; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{19}H_{23}F_3NO_2$ 354.1675; Found 354.1678.



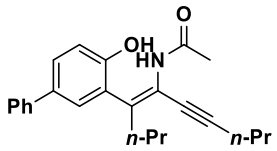
(*Z*)-*N*-(4-(2-hydroxy-4-nitrophenyl)dec-4-en-6-yn-5-yl)acetamide (3ag): The reaction mixture was subjected directly to flash chromatography (DCM/EtOAc: 35/1→DCM/EtOAc: 15/1) on silica gel to provide the product as a yellow amorphous solid (59.5 mg, yield 72%), mp 182-183 °C. ^{1}H NMR (600 MHz, DMSO-d_6) δ 9.73 (s, 1H), 8.61 (s, 1H), 7.10 (d, J = 8.5, 2.7 Hz, 1H), 6.91 (s, 1H), 6.82 (d, J = 8.5 Hz, 1H), 2.60 (t, J = 7.5 Hz, 2H), 2.34 (t, J = 6.8 Hz, 2H), 1.66 (s, 3H), 1.56-1.47 (m, 2H), 1.27-1.18 (m, 2H), 0.99 (t, J = 7.3 Hz, 3H), 0.83 (t, J = 7.3 Hz, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 168.0, 153.2, 141.2, 128.9, 128.0, 127.1, 121.9, 117.1, 115.7, 92.2, 78.4, 35.0, 22.4, 21.7, 20.7, 13.6, 13.3; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{18}H_{23}N_2O_4$ 331.1652; Found 331.1654.



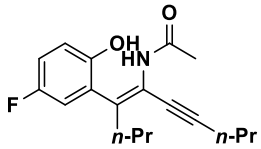
(*Z*)-*N*-(4-(2-hydroxy-5-methylphenyl)dec-4-en-6-yn-5-yl)acetamide (3ah): The reaction mixture was subjected directly to flash chromatography (DCM/EtOAc: 35/1→DCM/EtOAc: 15/1) on silica gel to provide the product as a white amorphous solid (60.1 mg, yield 80%), mp 140-141 °C. ^{1}H NMR (600 MHz, DMSO-d_6) δ 9.24 (s, 1H), 8.46 (s, 1H), 6.90-6.85 (m, 1H), 6.75-6.69 (m, 2H), 2.61 (t, J = 7.4 Hz, 2H), 2.33 (t, J = 6.8 Hz, 2H), 2.14 (s, 3H), 1.65 (s, 3H), 1.56-1.47 (m, 2H), 1.28-1.17 (m, 2H), 0.99 (t, J = 7.3 Hz, 3H), 0.82 (t, J = 7.3 Hz, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 167.9, 151.7, 142.0, 129.8, 128.9, 126.9, 124.9, 115.5, 115.0, 91.6, 78.6, 35.5, 22.6, 21.8, 20.9, 20.8, 20.2, 13.7, 13.3; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{19}H_{26}NO_2$ 300.1958; Found 300.1965.



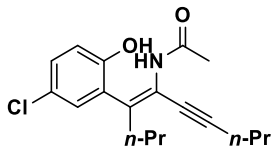
(*Z*)-*N*-(4-(5-(tert-butyl)-2-hydroxyphenyl)dec-4-en-6-yn-5-yl)acetamide (3ai): The reaction mixture was subjected directly to flash chromatography (DCM/EtOAc: 35/1→DCM/EtOAc: 15/1) on silica gel to provide the product as a white amorphous solid (67.5 mg, yield 79%), mp 126-127 °C. ^{1}H NMR (600 MHz, DMSO-d_6) δ 9.27 (s, 1H), 8.58 (s, 1H), 7.06 (m, 1H), 6.95 (d, J = 2.6 Hz, 1H), 6.72 (d, J = 8.6 Hz, 1H), 2.64 (t, J = 7.6 Hz, 2H), 2.33 (t, J = 6.8 Hz, 2H), 1.63 (s, 3H), 1.56-1.47 (m, 2H), 1.27-1.22 (m, 2H), 1.17 (s, 9H), 0.99 (t, J = 7.4 Hz, 3H), 0.82 (t, J = 7.4 Hz, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 168.2, 151.7, 144.2, 140.4, 126.8, 125.0, 124.3, 115.0, 114.8, 91.6, 78.9, 34.9, 33.6, 31.4, 22.5, 21.8, 20.9, 20.8, 13.7, 13.3; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{22}H_{32}NO_2$ 342.2428; Found 342.2433.



(*Z*)-*N*-(4-(4-hydroxy-[1,1'-biphenyl]-3-yl)dec-4-en-6-yn-5-yl)acetamide (3aj): The reaction mixture was subjected directly to flash chromatography (DCM/EtOAc: 35/1→DCM/EtOAc: 15/1) on silica gel to provide the product as a white amorphous solid (71.8 mg, yield 79%), mp 120-121 °C. ^{1}H NMR (600 MHz, DMSO-d_6) δ 9.65 (s, 1H), 8.67 (s, 1H), 7.52 (d, J = 7.6 Hz, 2H), 7.44-7.37 (m, 3H), 7.30-7.21 (m, 2H), 6.91 (d, J = 8.4 Hz, 1H), 2.68 (t, J = 7.5 Hz, 2H), 2.35 (t, J = 6.8 Hz, 2H), 1.67 (s, 3H), 1.58-1.48 (m, 2H), 1.32-1.21 (m, 2H), 1.00 (t, J = 7.3 Hz, 3H), 0.84 (t, J = 7.3 Hz, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 168.2, 153.9, 143.1, 140.2, 130.5, 128.9, 127.98, 126.8, 126.4, 125.9, 125.6, 116.1, 115.2, 91.8, 78.7, 35.1, 22.6, 21.8, 20.9, 20.8, 13.7, 13.3; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{24}H_{28}NO_2$ 362.2115; Found 362.2120.

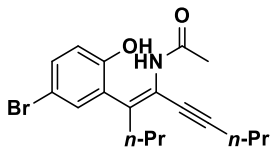


(*Z*)-*N*-(4-(5-fluoro-2-hydroxyphenyl)dec-4-en-6-yn-5-yl)acetamide (3ak): The reaction mixture was subjected directly to flash chromatography (DCM/EtOAc: 35/1→DCM/EtOAc: 15/1) on silica gel to provide the product as a white amorphous solid (59.1 mg, yield 78%), mp 138-139 °C. ^{1}H NMR (600 MHz, DMSO-d_6) δ 9.46 (s, 1H), 8.62 (s, 1H), 6.92-6.87 (m, 1H), 6.82-6.77 (m, 1H), 6.73-6.70 (m, 1H), 2.62 (t, J = 7.4 Hz, 2H), 2.34 (t, J = 6.9 Hz, 2H), 1.66 (s, 3H), 1.56-1.48 (m, 2H), 1.28-1.17 (m, 2H), 0.98 (t, J = 7.3 Hz, 3H), 0.83 (t, J = 7.4 Hz, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 168.1, 155.0 (d, C-F, $^1J_{C\text{-}F}$ = 234.1 Hz), 150.4, 141.5, 126.4 (d, C-F, $^3J_{C\text{-}F}$ = 7.6 Hz), 116.3 (d, C-F, $^3J_{C\text{-}F}$ = 8.4 Hz), 115.6 (d, C-F, $^2J_{C\text{-}F}$ = 22.2 Hz),115.6, 114.7 (d, C-F, $^2J_{C\text{-}F}$ = 22.8 Hz), 92.2, 78.4, 35.1, 22.5, 21.7, 20.8, 13.6, 13.3; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{18}H_{23}FNO_2$ 304.1707; Found 304.1712.

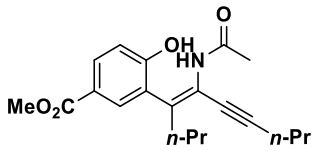


(*Z*)-*N*-(4-(5-chloro-2-hydroxyphenyl)dec-4-en-6-yn-5-yl)acetamide (3al): The reaction mixture

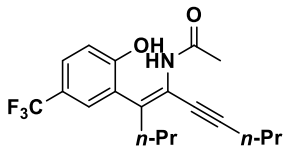
was subjected directly to flash chromatography (DCM/EtOAc: 35/1→DCM/EtOAc: 15/1) on silica gel to provide the product as a yellow amorphous solid (56.6 mg, yield 71%), mp 180-181 °C. ^{1}H NMR (600 MHz, DMSO-d_6) δ 10.50 (s, 1H), 8.69 (s, 1H), 7.70-7.56 (m, 1H), 7.62-7.59 (m, 1H), 7.14 (d, J = 8.6 Hz, 1H), 2.64 (t, J = 7.3 Hz, 2H), 2.36 (t, J = 6.9 Hz, 2H), 1.64 (s, 3H), 1.56-1.49 (m, 2H), 1.26-1.18 (m, 2H), 0.99 (t, J = 7.5 Hz, 3H), 0.83 (t, J = 7.3 Hz, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 167.8, 155.0, 147.3, 140.2, 133.3, 130.7, 116.4, 113.4, 109.8, 92.9, 78.1, 34.7, 22.5, 21.6, 20.7, 13.6, 13.3; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{18}H_{23}ClNO_2$ 320.1412; Found 320.1415.



(*Z*)-*N*-(4-(5-bromo-2-hydroxyphenyl)dec-4-en-6-yn-5-yl)acetamide (3am): The reaction mixture was subjected directly to flash chromatography (DCM/EtOAc: 35/1→DCM/EtOAc: 15/1) on silica gel to provide the product as a white amorphous solid (69.0 mg, yield 76%), mp 190-191 °C. ^{1}H NMR (600 MHz, DMSO-d_6) δ 9.78 (s, 1H), 8.64 (s, 1H), 7.25-7.20 (m, 1H), 7.04-7.01 (m, 1H), 6.77 (d, J = 8.6 Hz, 1H), 2.60 (t, J = 7.5 Hz, 2H), 2.34 (t, J = 6.8 Hz, 2H), 1.66 (s, 3H), 1.55-1.46 (m, 2H), 1.27-1.17 (m, 2H), 0.98 (t, J = 7.3 Hz, 3H), 0.83 (t, J = 7.3 Hz, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 168.1, 153.6, 141.2, 131.8, 130.9, 127.6, 117.7, 115.7, 109.5, 92.3, 78.4, 34.9, 22.6, 21.7, 20.8, 13.7, 13.3; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{18}H_{23}BrNO_2$ 364.0907; Found 364.0911.

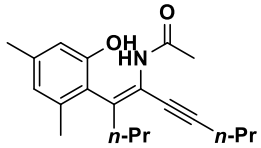


methyl (*Z*)-3-(5-acetamidodec-4-en-6-yn-4-yl)-4-hydroxybenzoate (3an): The reaction mixture was subjected directly to flash chromatography (DCM/EtOAc: 25/1→DCM/EtOAc: 5/1) on silica gel to provide the product as a brown amorphous solid (58.8 mg, yield 68%), mp 130-131 °C. ^{1}H NMR (600 MHz, DMSO-d_6) δ 10.38 (s, 1H), 8.61 (s, 1H), 7.75-7.66 (m, 1H), 7.57-7.51 (m, 1H), 6.89 (d, J = 8.7 Hz, 1H), 3.76 (s, 3H), 2.61 (t, J = 7.4 Hz, 2H), 2.35 (t, J = 6.9 Hz, 2H), 1.61 (s, 3H), 1.54-1.49 (m, 2H), 1.25-1.16 (m, 2H), 0.99 (t, J = 7.3 Hz, 3H), 0.83 (t, J = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 167.8, 166.1, 158.9, 141.0, 131.6, 130.2, 125.4, 119.9, 115.8, 115.6, 92.2, 78.4, 51.7, 35.0, 22.4, 21.7, 20.8, 13.7, 13.4; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{20}H_{26}NO_4$ 344.1856; Found 344.1861.

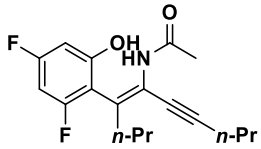


(*Z*)-*N*-(4-(2-hydroxy-5-(trifluoromethyl)phenyl)dec-4-en-6-yn-5-yl)acetamide (3ao): The reaction mixture was subjected directly to flash chromatography (DCM/EtOAc: 35/1→DCM/EtOAc: 15/1) on silica gel to provide the product as a white amorphous solid (58.6 mg,

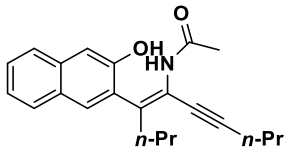
yield 66%), mp 151-152 °C. ^{1}H NMR (600 MHz, DMSO-d_6) δ 10.39 (s, 1H), 8.71 (s, 1H), 7.44-7.41 (m, 1H), 7.22-7.19 (m, 1H), 6.97 (d, J = 8.5 Hz, 1H), 2.64 (t, J = 7.5 Hz, 2H), 2.35 (t, J = 6.9 Hz, 2H), 1.61 (s, 3H), 1.56-1.47 (m, 2H), 1.26-1.18 (m, 2H), 0.99 (t, J = 7.5 Hz, 3H), 0.83 (t, J = 7.4 Hz, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 168.2, 157.7, 141.8, 127.0, 125.7,124.8 (q, C-F, $^1J_{C\text{-}F}$ = 269.9 Hz), 116.0,119.0 (q, C-F, $^2J_{C\text{-}F}$ = 31.9 Hz), 92.5, 78.4, 34.6, 22.3, 21.7, 20.8, 20.8, 13.6, 13.3; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{19}H_{23}F_3NO_2$ 354.1675; Found 354.1677.



(*Z*)-*N*-(4-(2-hydroxy-4,6-dimethylphenyl)dec-4-en-6-yn-5-yl)acetamide (3ap): The reaction mixture was subjected directly to flash chromatography (DCM/EtOAc: 35/1→DCM/EtOAc: 20/1) on silica gel to provide the product as a yellow viscous oil (37.1 mg, yield 47%). ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.82 (s, 1H), 8.24 (s, 1H), 6.42 (s, 1H), 6.40 (s, 1H), 2.52-2.40 (m, 2H), 2.30 (t, J = 6.8 Hz, 2H), 2.11 (s, 3H), 1.94 (s, 3H), 1.62 (s, 3H), 1.54-1.44 (m, 2H), 1.26-1.12 (m, 2H), 0.96 (t, J = 7.5 Hz, 3H), 0.81 (t, J = 7.6 Hz, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 167.8, 154.0, 139.7, 136.6, 136.5, 122.3, 121.5, 116.0, 113.7, 91.6, 78.1, 36.3, 22.6, 21.7, 20.8, 20.7, 19.2, 14.3, 13.3; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{20}H_{28}NO_2$ 314.2115; Found 314.2117.

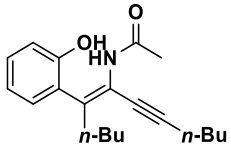


(*Z*)-*N*-(4-(2,4-difluoro-6-hydroxyphenyl)dec-4-en-6-yn-5-yl)acetamide (3aq): The reaction mixture was subjected directly to flash chromatography (DCM/EtOAc: 35/1→DCM/EtOAc: 15/1) on silica gel to provide the product as a white amorphous solid (68.5 mg, yield 85%), mp 147-148 °C. ^{1}H NMR (600 MHz, DMSO-d_6) δ 10.30 (s, 1H), 8.56 (s, 1H), 6.60-6.52 (m, 1H), 6.49-6.40 (m, 1H), 2.57-2.51 (m, 2H), 2.34 (t, J = 7.0 Hz, 2H), 1.66 (s, 3H), 1.58-1.47 (m, 2H), 1.29-1.17 (m, 2H), 0.99 (t, J = 7.2 Hz, 3H), 0.83 (t, J = 7.3 Hz, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 167.2, 161.76 (dd, C-F, $^1J_{C\text{-}F}$ = 242.8 Hz), 160.0 (dd, C-F, $^1J_{C\text{-}F}$ = 242.8 Hz), 157.00 (dd, C-F, $^3J_{C\text{-}F}$ = 10.9 Hz), 132.84, 117.78, 110.04 (t, C-F, $^2J_{C\text{-}F}$ = 19.6 Hz), 98.72 (t, C-F, $^2J_{C\text{-}F}$ = 23.4 Hz), 94.29 (t, C-F, $^2J_{C\text{-}F}$ = 27.1 Hz), 92.6, 77.9, 34.8, 22.6, 21.7, 20.8, 13.7, 13.4; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{18}H_{22}F_2NO_2$ 322.1613; Found 322.1619.

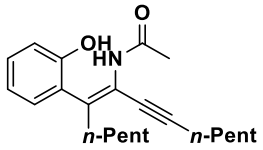


(Z)-N-(4-(3-hydroxynaphthalen-2-yl)dec-4-en-6-yn-5-yl)acetamide (3ar): The reaction mixture was subjected directly to flash chromatography (DCM/EtOAc: 35/1→DCM/EtOAc: 15/1) on silica gel to provide the product as a brown amorphous solid (60.2 mg, yield 72%), mp 137-138 °C. ^{1}H NMR (600 MHz, DMSO-d_6) δ 9.84 (s, 1H), 8.61 (s, 1H), 7.67 (d, J = 8.3 Hz, 1H), 7.64 (d, J = 8.3 Hz, 1H), 7.49-7.45 (m, 1H), 7.38-7.33 (m, 1H), 7.27-7.20 (m, 1H), 7.16-7.13 (m, 1H), 2.70 (t, J =

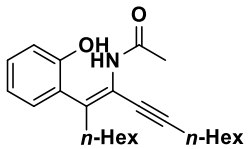
7.5 Hz, 2H), 2.37 (t, *J* = 6.9 Hz, 2H), 1.60 (s, 3H), 1.57-1.50 (m, 2H), 1.28-1.21 (m, 2H), 1.01 (t, *J* = 7.3 Hz, 3H), 0.85 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (150 MHz, DMSO-*d*$_6$) δ 168.0, 153.1, 142.0, 133.9, 128.6, 128.3, 127.6, 127.4, 126.0, 125.6, 122.8, 115.5, 109.0, 92.1, 78.6, 35.6, 22.5, 21.8, 20.8, 13.7, 13.35; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{22}H_{26}NO_2$ 336.1958; Found 336.1964.



(*Z*)-*N*-(5-(2-hydroxyphenyl)dodec-5-en-7-yn-6-yl)acetamide (3as): The reaction mixture was subjected directly to flash chromatography (DCM/EtOAc: 35/1→DCM/EtOAc: 15/1) on silica gel to provide the product as a brown viscous oil (50.3 mg, yield 64%). ^{1}H NMR (600 MHz, DMSO-*d*$_6$) δ 9.44 (s, 1H), 8.49 (s, 1H), 7.11-7.03 (m, 1H), 6.89 (d, *J* = 7.5 Hz, 1H), 6.82 (d, *J* = 8.1 Hz, 1H), 6.75-6.69 (m, 1H), 2.63 (t, *J* = 7.6 Hz, 2H), 2.36 (t, *J* = 6.6 Hz, 2H), 1.63 (s, 3H), 1.50-1.45 (m, 2H), 1.44-1.39 (m, 2H), 1.28-1.21 (m, 2H), 1.20-1.14 (m, 2H), 0.90 (t, *J* = 7.1 Hz, 3H), 0.80 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, DMSO-*d*$_6$) δ 168.0, 154.0, 142.8, 129.7, 128.4, 125.2, 118.6, 115.6, 114.8, 91.7, 78.5, 32.9, 30.3, 29.8, 22.5, 21.9, 21.4, 18.5, 13.8, 13.5; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{20}H_{28}NO_2$ 314.2115; Found 314.2121.

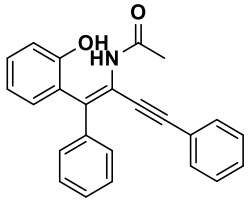


(*Z*)-*N*-(6-(2-hydroxyphenyl)tetradec-6-en-8-yn-7-yl)acetamide (3at): The reaction mixture was subjected directly to flash chromatography (DCM/EtOAc: 35/1→DCM/EtOAc: 15/1) on silica gel to provide the product as a yellow amorphous solid (74.2 mg, yield 87%), mp 109-110 °C. ^{1}H NMR (600 MHz, DMSO-*d*$_6$) δ 9.41 (s, 1H), 8.47 (s, 1H), 7.10-7.03 (m, 1H), 6.90 (d, *J* = 7.5 Hz, 1H), 6.82 (d, *J* = 8.1 Hz, 1H), 6.75-6.68 (m, 1H), 2.65-2.61 (m, 2H), 2.35 (t, *J* = 6.9 Hz, 2H), 1.63 (s, 3H), 1.53-1.47 (m, 2H), 1.45-1.36 (m, 2H), 1.35-1.27 (m, 2H), 1.26-1.15 (m, 6H), 0.89 (t, *J* = 7.2 Hz, 3H), 0.81-0.78 (m, 3H); ^{13}C NMR (150 MHz, DMSO-*d*$_6$) δ 167.9, 154.0, 142.7, 129.6, 128.4, 125.2, 118.5, 115.6, 114.8, 91.7, 78.4, 33.1, 30.9, 30.5, 27.9, 27.1, 22.5, 21.9, 21.9, 21.7, 18.7, 13.8; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{22}H_{32}NO_2$ 342.2428; Found 342.2428.

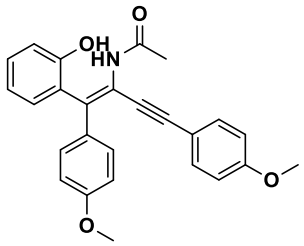


(*Z*)-*N*-(7-(2-hydroxyphenyl)hexadec-7-en-9-yn-8-yl)acetamide (3au): The reaction mixture was subjected directly to flash chromatography (DCM/EtOAc: 35/1→DCM/EtOAc: 15/1) on silica gel to provide the product as a brown viscous oil (80.7 mg, yield 87%). ^{1}H NMR (600 MHz, DMSO-*d*$_6$) δ 9.40 (s, 1H), 8.46 (s, 1H), 7.12-7.01 (m, 1H), 6.90 (d, *J* = 7.6 Hz, 1H), 6.82 (d, *J* = 8.2 Hz, 1H), 6.75-6.68 (m, 1H), 2.69-2.58 (m, 2H), 2.38-2.32 (m, 2H), 1.64 (s, 3H), 1.53-1.46 (m, 2H), 1.46-1.39 (m, 2H), 1.32-1.25 (m, 4H), 1.26-1.11 (m, 8H), 0.93-0.84 (m, 3H), 0.84-0.78 (m, 3H); ^{13}C NMR (150 MHz, DMSO-*d*$_6$) δ 167.8, 154.0, 142.7, 129.6, 128.3, 125.2, 118.5, 115.6, 114.8, 91.7, 78.5,

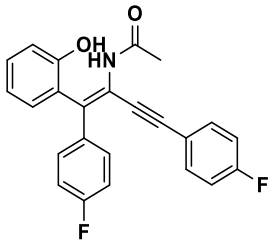
33.2, 31.1, 30.9, 28.4, 28.2, 28.0, 27.4, 22.5, 22.1, 22.0, 18.8, 13.9, 13.8; HRMS (ESI) m/z: [M + H]$^+$ Calcd for $C_{24}H_{36}NO_2$ 370.2741; Found 370.2745.



(*Z*)-*N*-(1-(2-hydroxyphenyl)-1,4-diphenylbut-1-en-3-yn-2-yl)acetamide (3av): The reaction mixture was subjected directly to flash chromatography (DCM/EtOAc: 35/1→DCM/EtOAc: 5/1) on silica gel to provide the product as a yellow amorphous solid (55.7 mg, yield 63%), mp 118-119 ^{o}C. ^{1}H NMR (600 MHz, DMSO-d_6) δ 9.49 (s, 1H), 8.94 (s, 1H), 7.44-7.39 (m, 2H), 7.38-7.31 (m, 5H), 7.31-7.26 (m, 1H), 7.25-7.20 (m, 2H), 7.18-7.12 (m, 1H), 6.98 (d, J = 7.6 Hz, 1H), 6.85 (d, J = 8.3 Hz, 1H), 6.82-6.76 (m, 1H), 1.78 (s, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 168.1, 154.5, 141.8, 139.9, 130.9, 130.6, 129.4, 129.3, 128.7, 128.6, 127.5, 126.0, 122.6, 118.7, 116.0, 115.6, 90.1, 88.6, 22.7; HRMS (ESI) m/z: [M + H]$^+$ Calcd for $C_{24}H_{20}NO_2$ 354.1489; Found 354.1493.

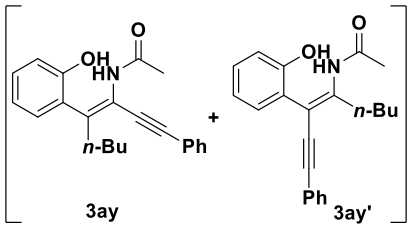


(*Z*)-*N*-(1-(2-hydroxyphenyl)-1,4-bis(4-methoxyphenyl)but-1-en-3-yn-2-yl)acetamide (3aw): The reaction mixture was subjected directly to flash chromatography (DCM/EtOAc: 35/1→DCM/EtOAc: 15/1) on silica gel to provide the product as a brown viscous oil (43.7 mg, yield 42%). ^{1}H NMR (600 MHz, DMSO-d_6) δ 9.39 (s, 1H), 8.82 (s, 1H), 7.42-7.33 (m, 2H), 7.28-7.21 (m, 2H), 7.18-7.09 (m, 1H), 6.98-6.92 (m, 3H), 6.92-6.88 (m, 2H), 6.87-6.83 (m, 1H), 6.81-6.75 (m, 1H), 3.76 (s, 3H), 3.75 (s, 3H), 1.74 (s, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 168.0, 159.4, 158.7, 154.5, 140.8, 132.5, 132.0, 130.6, 129.0, 126.4, 118.7, 115.9, 114.6, 114.4, 112.9, 90.0, 87.6, 55.3, 55.1, 22.7; HRMS (ESI) m/z: [M + H]$^+$ Calcd for $C_{26}H_{24}NO_4$ 414.1700; Found 414.1704.



(*Z*)-*N*-(1,4-bis(4-fluorophenyl)-1-(2-hydroxyphenyl)but-1-en-3-yn-2-yl)acetamide (3ax): The reaction mixture was subjected directly to flash chromatography (DCM/EtOAc: 35/1→DCM/EtOAc: 15/1) on silica gel to provide the product as a brown viscous oil (45.9 mg, yield 47%). ^{1}H NMR (600 MHz, DMSO-d_6) δ 9.48 (s, 1H), 8.96 (s, 1H), 7.50-7.38 (m, 2H), 7.35-7.28 (m, 2H), 7.26-7.20 (m, 2H), 7.20-7.11 (m, 3H), 7.03-6.96 (m, 1H), 6.90-6.82 (m, 1H), 6.83-6.76 (m, 1H), 1.78 (s, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 168.1, 161.6 (d, C-F, $^1J_{C\text{-}F}$ = 244.6

Hz), 161.5 (d, C-F, $^{1}J_{C\text{-}F}$ = 244.6 Hz), 154.5, 140.6, 136.2, 133.2 (d, C-F, $^{3}J_{C\text{-}F}$ = 8.6 Hz), 131.3 (d, C-F, $^{3}J_{C\text{-}F}$ = 7.8 Hz), 130.5, 129.4, 125.8, 118.8, 116.1 (d, C-F, $^{2}J_{C\text{-}F}$ = 21.8 Hz), 116.0, 115.6, 114.4 (d, C-F, $^{2}J_{C\text{-}F}$ = 21.5 Hz), 89.2, 88.0, 22.7; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{24}H_{18}F_2NO_2$ 390.1300; Found 390.1303.



3ay:3ay' = 5.7:1, 72% yield

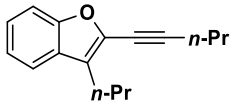
The reaction mixture was subjected directly to flash chromatography (DCM/EtOAc: 35/1→DCM/EtOAc: 15/1) on silica gel to provide an inseparable mixture of **3ay** and **3ay'** (**3ay**:**3ay'** = 5.7:1) as a white amorphous solid (60.0 mg, yield 72%).

(*Z*)-*N*-(4-(2-hydroxyphenyl)-1-phenyloct-3-en-1-yn-3-yl)acetamide (3ay): ^{1}H NMR (600 MHz, DMSO-d_6) δ 9.52 (s, 1H), 8.64 (s, 1H), 7.44–7.34 (m, 5H), 7.12–7.05 (m, 1H), 6.94 (d, J = 7.5 Hz, 1H), 6.84 (d, J = 8.2 Hz, 1H), 6.77–6.69 (m, 1H), 2.74 (t, J = 7.3 Hz, 2H), 1.68 (s, 3H), 1.30–1.26 (m, 2H), 1.26–1.18 (m, 2H), 0.81 (t, J = 7.0 Hz, 3H).; ^{13}C NMR (150 MHz, DMSO-d_6) δ 168.1, 154.0, 144.6, 130.9, 129.5, 129.1, 128.7, 128.4, 124.8, 122.7, 118.6, 115.7, 114.5, 90.6, 87.5, 33.0, 29.7, 22.5, 21.7, 13.8; HRMS (ESI) m/z: $[M - H]^-$ Calcd for $C_{22}H_{24}NO_2$ 332.1651; Found 332.1652.

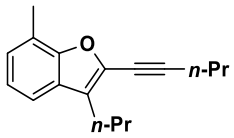
General Procedure for the Rhodium-Catalyzed [3+2] Annulation between *N*-phenoxyacetamides and 1,3-Diynes

To a mixture of *N*-phenoxyacetamides **1** (0.25 mmol), $[Cp^*RhCl_2]_2$ (5 mol%) and $NaOPiv{\cdot}H_2O$ (0.25 mmol) in a 25 mL Schlenk tube was added a solution of 1,3-diynes **2** (0.275 mmol) in CH_2Cl_2 (4.0 mL). Then the tube was capped with septa, and the resulting mixture was stirred at 25 °C or 40 °C as indicated in Table 3 for 24 h. After removal of the solvent, the residue was purified by flash chromatography on silica gel to provide the desired products **4**.

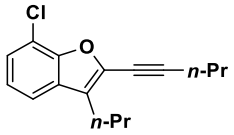
Characterization Data of Products 4



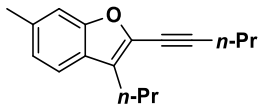
2-(pent-1-yn-1-yl)-3-propylbenzofuran (4aa): The reaction mixture was subjected directly to flash chromatography (Petroleum) on silica gel to provide the product as a colorless viscous oil (35.5 mg, yield 63%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.51 (d, J = 7.7 Hz, 1H), 7.41 (d, J = 8.3 Hz, 1H), 7.33-7.27 (m, 1H), 7.25-7.19 (m, 1H), 2.74 (t, J = 7.4 Hz, 2H), 2.52 (t, J = 6.9 Hz, 2H), 1.80-1.73 (m, 2H), 1.73-1.66 (m, 2H), 1.10 (t, J = 7.5 Hz, 3H), 1.00 (t, J = 7.3 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 154.3, 136.6, 128.6, 125.0, 124.0, 122.6, 119.8, 111.2, 98.9, 71.1, 26.2, 22.7, 22.1, 21.8, 14.1, 13.6; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{16}H_{19}O$ 227.1430; Found 227.1428.



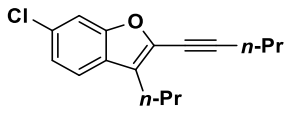
7-methyl-2-(pent-1-yn-1-yl)-3-propylbenzofuran (4ab): The reaction mixture was subjected directly to flash chromatography (Petroleum) on silica gel to provide the product as a yellow viscous oil (24.2 mg, yield 40%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.33 (d, J = 7.5 Hz, 1H), 7.14-7.11 (m, 1H), 7.10-7.08 (m, 1H), 2.71 (t, J = 7.2 Hz, 2H), 2.54-2.51 (m, 2H), 2.50 (s, 3H), 1.77-1.72 (m, 2H), 1.72-1.65 (m, 2H), 1.09 (t, J = 7.6 Hz, 3H), 0.98 (t, J = 14.5 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 153.3, 136.3, 128.1, 126.0, 124.4, 122.7, 121.5, 117.2, 98.7, 71.3, 26.4, 22.7, 22.1, 21.9, 15.2, 14.1, 13.7; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{17}H_{21}O$ 241.1587; Found 241.1584.



7-chloro-2-(pent-1-yn-1-yl)-3-propylbenzofuran (4ac): The reaction mixture was subjected directly to flash chromatography (Petroleum) on silica gel to provide the product as a colorless viscous oil (26.1 mg, yield 40%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.38 (d, J = 7.8 Hz, 1H), 7.30-7.27 (m, 1H), 7.18-7.11 (m, 1H), 2.70 (t, J = 7.5 Hz, 2H), 2.50 (t, J = 7.0 Hz, 2H), 1.75-1.70 (m, 2H), 1.70-1.65 (m, 2H), 1.08 (t, J = 7.5 Hz, 3H), 0.97 (t, J = 7.5 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 145.0, 137.6, 130.3, 125.1, 124.4, 123.6, 118.3, 116.7, 99.8, 70.6, 26.3, 22.6, 22.0, 21.9, 14.0, 13.7; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{16}H_{18}ClO$ 261.1041; Found 261.1045.

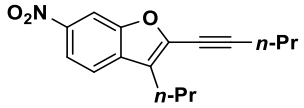


6-methyl-2-(pent-1-yn-1-yl)-3-propylbenzofuran (4ad): The reaction mixture was subjected directly to flash chromatography (Petroleum) on silica gel to provide the product as a brown viscous oil (27.5 mg, yield 46%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.37 (d, J = 7.8 Hz, 1H), 7.20 (s, 1H), 7.04 (d, J = 8.1 Hz, 1H), 2.70 (t, J = 7.4 Hz, 2H), 2.50 (t, J = 7.1 Hz, 2H), 2.46 (s, 3H), 1.76-1.71 (m, 2H), 1.71-1.66 (m, 2H), 1.09 (t, J = 7.5 Hz, 3H), 0.97 (t, J = 7.4 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 154.7, 136.0, 135.4, 126.1, 124.1, 124.0, 119.3, 111.5, 98.6, 71.2, 26.3, 22.7, 22.1, 21.8, 21.8, 14.1, 13.7; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{17}H_{21}O$ 241.1587; Found 241.1585.

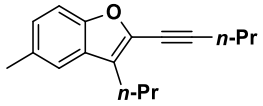


6-chloro-2-(pent-1-yn-1-yl)-3-propylbenzofuran (4ae): The reaction mixture was subjected directly to flash chromatography (Petroleum) on silica gel to provide the product as a yellow viscous oil (27.4 mg, yield 42%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.44-7.34 (m, 2H), 7.23-7.14 (m, 1H), 2.68 (t, J = 7.5 Hz, 2H), 2.50 (t, J = 7.0 Hz, 2H), 1.73-1.69 (m, 2H), 1.69-1.65 (m, 2H), 1.08 (t, J = 7.6 Hz, 3H), 0.96 (t, J = 7.3 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 154.2, 137.3, 131.0, 127.3, 123.7, 123.4, 120.3, 111.7, 99.6, 70.7, 26.1, 22.6, 22.0, 21.8, 14.0, 13.7; HRMS (ESI) m/z: $[M + H]^+$ Calcd for

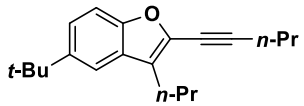
$C_{16}H_{18}ClO$ 261.1041; Found 261.1044.



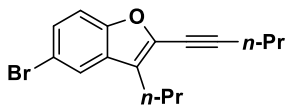
6-nitro-2-(pent-1-yn-1-yl)-3-propylbenzofuran (4af): The reaction mixture was subjected directly to flash chromatography (Petroleum/EtOAc: 70/1→Petroleum /EtOAc: 40/1) on silica gel to provide the product as a red viscous oil (33.3 mg, yield 49%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.26 (d, *J* = 2.0 Hz, 1H), 8.17-8.11 (m, 1H), 7.56 (d, *J* = 8.9 Hz, 1H), 2.72 (t, *J* = 7.5 Hz, 2H), 2.53 (t, *J* = 6.9 Hz, 2H), 1.77-1.71 (m, 2H), 1.71-1.66 (m, 2H), 1.09 (t, *J* = 7.3 Hz, 3H), 0.97 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 152.8, 145.5, 141.8, 134.6, 124.0, 119.5, 118.5, 107.5, 101.9, 70.3, 26.0, 22.6, 21.8, 14.0, 13.6; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{16}H_{18}NO_3$ 272.1281; Found 272.1283.



5-methyl-2-(pent-1-yn-1-yl)-3-propylbenzofuran (4ag): The reaction mixture was subjected directly to flash chromatography (Petroleum) on silica gel to provide the product as a colorless viscous oil (34.6 mg, yield 58%). ^{1}H NMR (600 MHz, DMSO-d_6) δ 7.36 (s, 1H), 7.32 (d, *J* = 8.5 Hz, 1H), 7.13-7.09 (m, 1H), 2.62 (t, *J* = 7.3 Hz, 2H), 2.50-2.46 (m, 2H), 2.36 (s, 3H), 1.66-1.61 (m, 2H), 1.59-1.54 (m, 2H), 0.98 (t, *J* = 7.6 Hz, 3H), 0.87 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 151.9, 135.7, 132.0, 127.8, 126.7, 123.4, 119.6, 110.6, 99.2, 70.9, 25.5, 22.0, 21.4, 20.9, 20.8, 13.7, 13.2; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{17}H_{21}O$ 241.1587; Found 241.1583.

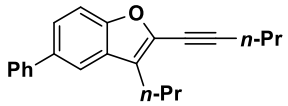


5-(tert-butyl)-2-(pent-1-yn-1-yl)-3-propylbenzofuran (4ah): The reaction mixture was subjected directly to flash chromatography (Petroleum) on silica gel to provide the product as a colorless viscous oil (37.1 mg, yield 53%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.50-7.46 (m, 1H), 7.40-7.35 (m, 1H), 7.35-7.31 (m, 1H), 2.74 (t, *J* = 7.3 Hz, 2H), 2.52 (t, *J* = 7.2 Hz, 2H), 1.81-1.73 (m, 2H), 1.73-1.67 (m, 2H), 1.40 (s, 9H), 1.10 (t, *J* = 7.4 Hz, 3H), 1.02 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 152.5, 145.7, 136.7, 128.2, 124.1, 123.1, 115.7, 110.5, 98.6, 71.3, 34.8, 32.0, 26.2, 22.7, 22.1, 21.8, 14.1, 13.7; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{20}H_{27}O$ 283.2056; Found 283.2060.

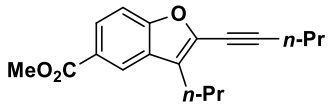


5-bromo-2-(pent-1-yn-1-yl)-3-propylbenzofuran (4ai): The reaction mixture was subjected directly to flash chromatography (Petroleum) on silica gel to provide the product as a yellow viscous oil (36.9 mg, yield 48%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.62 (d, *J* = 2.2 Hz, 1H), 7.40-7.36 (m, 1H), 7.27 (s, 1H), 2.68 (t, *J* = 7.3 Hz, 2H), 2.51 (t, *J* = 7.2 Hz, 2H), 1.76-1.71 (m, 2H), 1.71-1.66 (m, 2H), 1.09 (t, *J* = 7.5 Hz, 3H), 0.98 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 153.0, 137.8, 130.6,

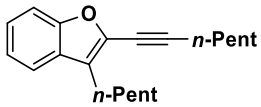
127.9, 123.4, 122.4, 115.8, 112.7, 99.7, 70.7, 26.1, 22.6, 22.0, 21.8, 14.0, 13.6; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{16}H_{18}BrO$ 305.0536; Found 305.0533.



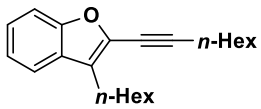
2-(pent-1-yn-1-yl)-5-phenyl-3-propylbenzofuran (4aj): The reaction mixture was subjected directly to flash chromatography (Petroleum) on silica gel to provide the product as a red viscous oil (34.0 mg, yield 45%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.67 (s, 1H), 7.62 (d, *J* = 7.5 Hz, 2H), 7.56-7.49 (m, 1H), 7.50-7.41 (m, 3H), 7.40-7.32 (m, 1H), 2.76 (t, *J* = 7.7 Hz, 2H), 2.53 (t, *J* = 7.0 Hz, 2H), 1.83-1.75 (m, 2H), 1.74-1.67 (m, 2H), 1.10 (t, *J* = 7.5 Hz, 3H), 1.01 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 153.9, 141.8, 137.2, 136.5, 129.1, 128.9, 127.6, 127.0, 124.8, 124.2, 118.3, 111.3, 99.1, 71.1, 26.3, 22.7, 22.1, 21.9, 14.1, 13.7; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{22}H_{23}O$ 303.1743; Found 303.1739.



methyl 2-(pent-1-yn-1-yl)-3-propylbenzofuran-5-carboxylate (4ak): The reaction mixture was subjected directly to flash chromatography (Petroleum/EtOAc: 50/1→Petroleum /EtOAc: 25/1) on silica gel to provide the product as a brown viscous oil (31.8 mg, yield 45%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.22 (s, 1H), 8.00 (d, *J* = 8.7 Hz, 1H), 7.39 (d, *J* = 8.3 Hz, 1H), 3.93 (s, 3H), 2.73 (t, *J* = 7.6 Hz, 2H), 2.50 (t, *J* = 7.2 Hz, 2H), 1.78-1.71 (m, 2H), 1.71-1.65 (m, 2H), 1.08 (t, *J* = 7.5 Hz, 3H), 0.98 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.4, 156.9, 138.0, 128.7, 126.8, 125.1, 124.3, 122.2, 111.0, 99.8, 70.6, 52.2, 26.1, 22.7, 22.0, 21.8, 14.0, 13.6; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{18}H_{21}O_3$ 285.1485; Found 285.1485.

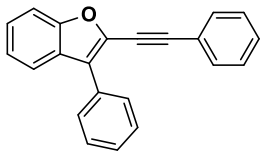


2-(hept-1-yn-1-yl)-3-pentylbenzofuran (4al): The reaction mixture was subjected directly to flash chromatography (Petroleum) on silica gel to provide the product as a colorless viscous oil (41.4 mg, yield 59%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.50 (d, *J* = 8.0 Hz, 1H), 7.40 (d, *J* = 8.2 Hz, 1H), 7.31-7.27 (m, 1H), 7.24-7.19 (m, 1H), 2.74 (t, *J* = 7.6 Hz, 2H), 2.52 (t, *J* = 7.2 Hz, 2H), 1.75-1.69 (m, 2H), 1.68-1.62 (m, 2H), 1.52-1.44 (m, 2H), 1.42-1.38 (m, 2H), 1.38-1.35 (m, 4H), 0.94 (t, *J* = 7.2 Hz, 3H), 0.90 (t, *J* = 6.9 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 154.3, 136.4, 128.6, 125.0, 124.2, 122.6, 119.8, 111.2, 99.2, 70.9, 31.6, 31.2, 29.0, 28.3, 24.1, 22.6, 22.4, 19.8, 14.2, 14.1; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{20}H_{27}O$ 283.2056; Found 283.2062.

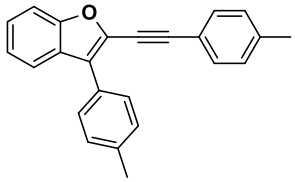


3-hexyl-2-(oct-1-yn-1-yl)benzofuran (4am): The reaction mixture was subjected directly to flash chromatography (Petroleum) on silica gel to provide the product as a colorless viscous oil (42.6 mg,

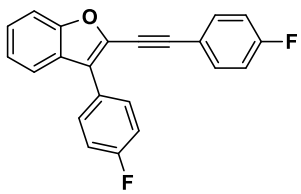
yield 55%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.55-7.46 (m, 1H), 7.42-7.36 (m, 1H), 7.32-7.27 (m, 1H), 7.25-7.18 (m, 1H), 2.74 (t, *J* = 7.6 Hz, 2H), 2.53 (t, *J* = 7.1 Hz, 2H), 1.75-1.68 (m, 2H), 1.68-1.62 (m, 2H), 1.54-1.46 (m, 2H), 1.39-1.30 (m, 10H), 0.92 (t, *J* = 7.0 Hz, 3H), 0.91-0.87 (m, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 154.3, 136.4, 128.6, 125.0, 124.2, 122.6, 119.8, 111.2, 99.2, 70.9, 31.7, 31.5, 29.3, 29.2, 28.7, 28.5, 24.2, 22.8, 22.7, 19.9, 14.3, 14.2; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{22}H_{31}O$ 311.2369; Found 311.2373.



3-phenyl-2-(phenylethynyl)benzofuran (4an): The reaction mixture was subjected directly to flash chromatography (Petroleum) on silica gel to provide the product as a colorless viscous oil (19.2 mg, yield 26%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.37 (d, *J* = 8.1 Hz, 2H), 7.78 (d, *J* = 7.6 Hz, 1H), 7.66 (d, *J* = 7.2 Hz, 2H), 7.62–7.47 (m, 3H), 7.47–7.38 (m, 4H), 7.40–7.32 (m,2H); ^{13}C NMR (150 MHz, $CDCl_3$); δ 156.4, 153.7, 131.7, 130.3, 130.1, 129.3, 128.8, 128.6, 128.6, 126.2, 125.5, 123.5, 120.5, 111.3, 99.4, 96.9, 81.3; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{22}H_{15}O$ 295.1118; Found 295.1123.



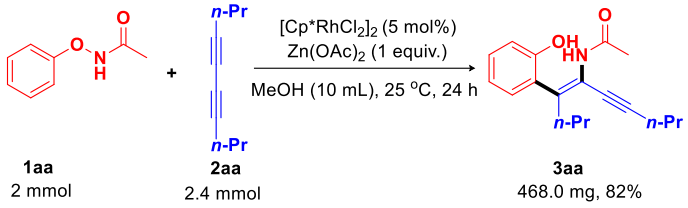
3-(p-tolyl)-2-(p-tolylethynyl)benzofuran (4ao): The reaction mixture was subjected directly to flash chromatography (Petroleum) on silica gel to provide the product as a colorless viscous oil (15.9 mg, yield 20%). ^{1}H NMR (600 MHz, $CDCl_3$) 8.27 (d, *J* = 8.2 Hz, 2H), 7.80–7.73 (m, 1H), 7.58–7.50 (m, 3H), 7.38–7.30 (m, 4H), 7.24 (d, *J* = 8.0 Hz, 2H), 2.45 (s, 3H), 2.43 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 156.6, 153.5, 139.4, 138.6, 131.5, 130.1, 129.5, 129.3, 127.6, 126.1, 125.1, 123.4, 120.5, 120.3, 111.2, 98.7, 96.8, 80.8, 21.6; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{24}H_{19}O$ 323.1431; Found 323.1433.



3-(4-fluorophenyl)-2-((4-fluorophenyl)ethynyl)benzofuran (4ap): The reaction mixture was subjected directly to flash chromatography (Petroleum) on silica gel to provide the product as a colorless viscous oil (20.3 mg, yield 25%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.35–8.27 (m, 2H), 7.73 (dd, *J* = 7.2, 1.7 Hz, 1H), 7.64–7.55 (m, 2H), 7.52 (d, *J* = 7.8 Hz, 1H), 7.40–7.29 (m, 2H), 7.22–7.16 (m, 2H), 7.15–7.09 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$)) δ 163.3 (d, C-F, $^{1}J_{C\text{-}F}$ = 252.0 Hz), 162.8 (d, C-F, $^{1}J_{C\text{-}F}$ = 248.6 Hz), 155.6, 153.6, 133.5 (d, C-F, $^{3}J_{C\text{-}F}$ = 8.3 Hz), 129.9, 128.1 (d, C-F, $^{3}J_{C\text{-}F}$ = 8.5 Hz), 126.6 (d, C-F, $^{4}J_{C\text{-}F}$ = 2.9 Hz), 125.5, 123.6, 120.4, 119.4 (d, C-F, $^{4}J_{C\text{-}F}$ = 4.0 Hz),

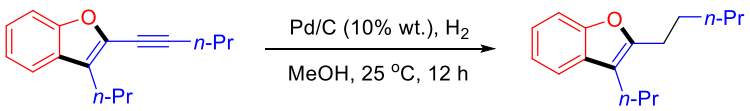
116.0 (d, C-F, $^2J_{C\text{-}F}$ = 22.2 Hz), 115.9 (d, C-F, $^2J_{C\text{-}F}$ = 21.8 Hz), 111.3, 98.8, 95.7, 80.8; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{22}H_{13}F_2O$ 331.0929; Found 331.0930.

Procedure for the Synthetic Applications



1aa 2 mmol　　**2aa** 2.4 mmol　　**3aa** 468.0 mg, 82%

To a mixture of **1aa** (2 mmol), $[Cp^*RhCl_2]_2$ (5 mol%) and $Zn(OAc)_2$ (2 mmol) in a 25 mL Schlenk tube was added a solution of deca-4,6-diyne **2aa** (2.4 mmol) in MeOH (10.0 mL). Then the tube was capped with septa, and the resulting mixture was stirred at 25 °C for 24 h. After removal of the solvent, the residue was purified by flash chromatography (DCM/EtOAc: 25/1→DCM/EtOAc: 10/1) on silica gel to provide the desired product **3aa** as a white amorphous solid (468.0 mg, yield 82%).



4aa　　**5aa**, 84%

A mixture of **4aa** (30.0 mg) and 10 mg Pd/C (10% w.t) in MeOH (6.0 mL) was stirred under H_2 at 25 °C for 12 h. After filtration and removal of the solvents in *vacuo*, the residue was purified by flash chromatography (Petroleum) on silica gel to give the desired product **5aa** as a colorless viscous oil (25.6 mg, 84% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.48–7.44 (m, 1H), 7.41–7.37 (m, 1H), 7.22–7.15 (m, 2H), 2.75–2.69 (m, 2H), 2.61–2.56 (m, 2H), 1.75–1.69 (m, 2H), 1.69–1.63 (m, 2H), 1.39–1.32 (m, 4H), 0.96 (t, J = 7.3 Hz, 3H), 0.90 (t, J = 6.7 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$); δ 154.8, 154.0, 130.0, 122.9, 121.9, 119.0, 114.2, 110.7, 31.6, 28.2, 26.4, 25.7, 23.2, 22.5, 14.1, 14.1; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{16}H_{23}O$ 231.1749; Found 231.1749.

Inhibition Rates of Selected Compounds Against Human Cancer Cell Lines

Table S2 Inhibition rates of selected compounds against human cancer cell line A549 at the concentration of 10 uM

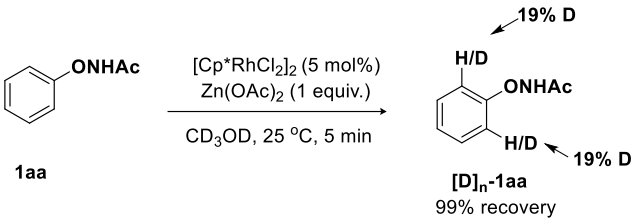
Compound	Inhibition Rate (%)
3aa	14.32
3ac	18.22
3ad	11.40
3ae	9.11
3ag	16.92
3ai	17.07
3am	12.08
3aq	29.20
3at	20.35

Table S3 Inhibition rates of selected compounds against human cancer cell line HL-60 at the concentration of 10 uM

Compound	Inhibition Rate (%)
3ac	25.83
3aj	7.03
3ao	32.99
3av	8.31

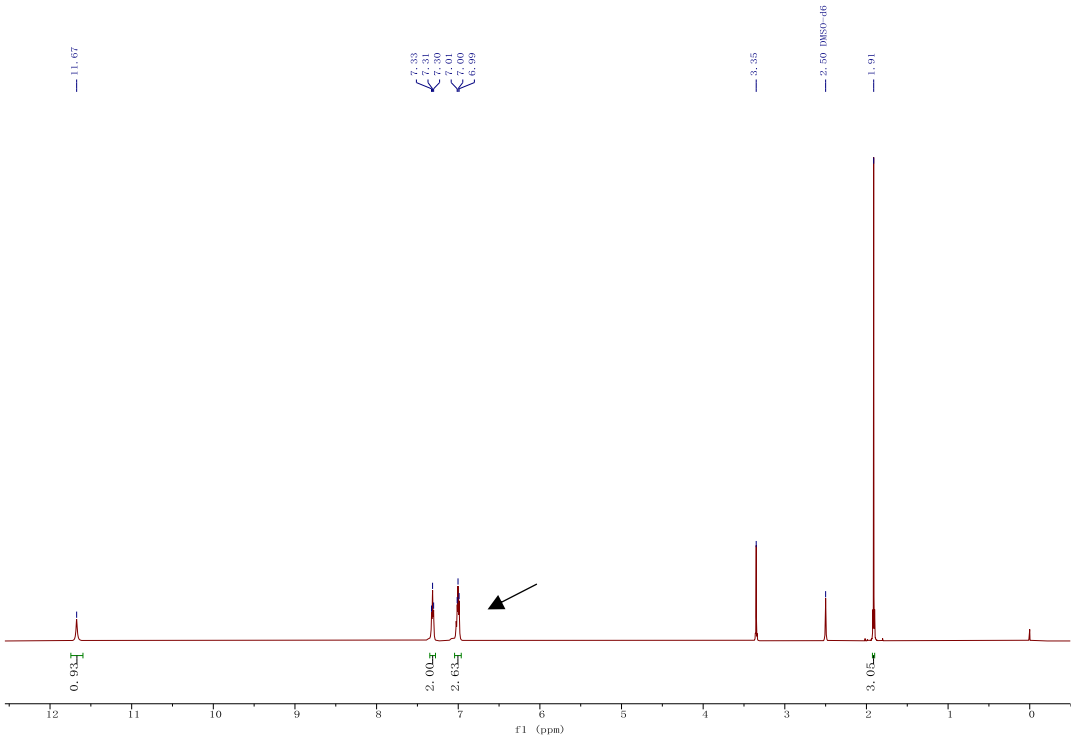
Mechanistic Experiments

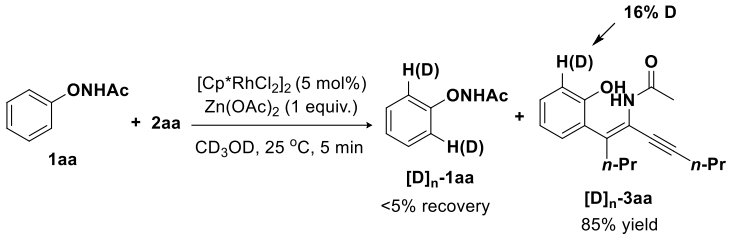
Deuterium Incorporation Experiments



To a mixture of **1aa** (0.25 mmol), $[Cp^*RhCl_2]_2$ (5 mol%), $Zn(OAc)_2$ (0.25 mmol) in a 25 mL Schlenk tube was added CD_3OD (4.0 mL). Then the tube was capped with septa, and the resulting mixture was stirred at 25 °C for 5 minutes. After removal of the solvent, the residue was purified by flash chromatography (DCM/EtOAc: 25/1→DCM/EtOAc: 10/1) on silica gel to give the product **$[D]_n$-1aa** (37.4 mg, 99% yield). *Found H/D exchange occurred at the ortho-position (19% D).*

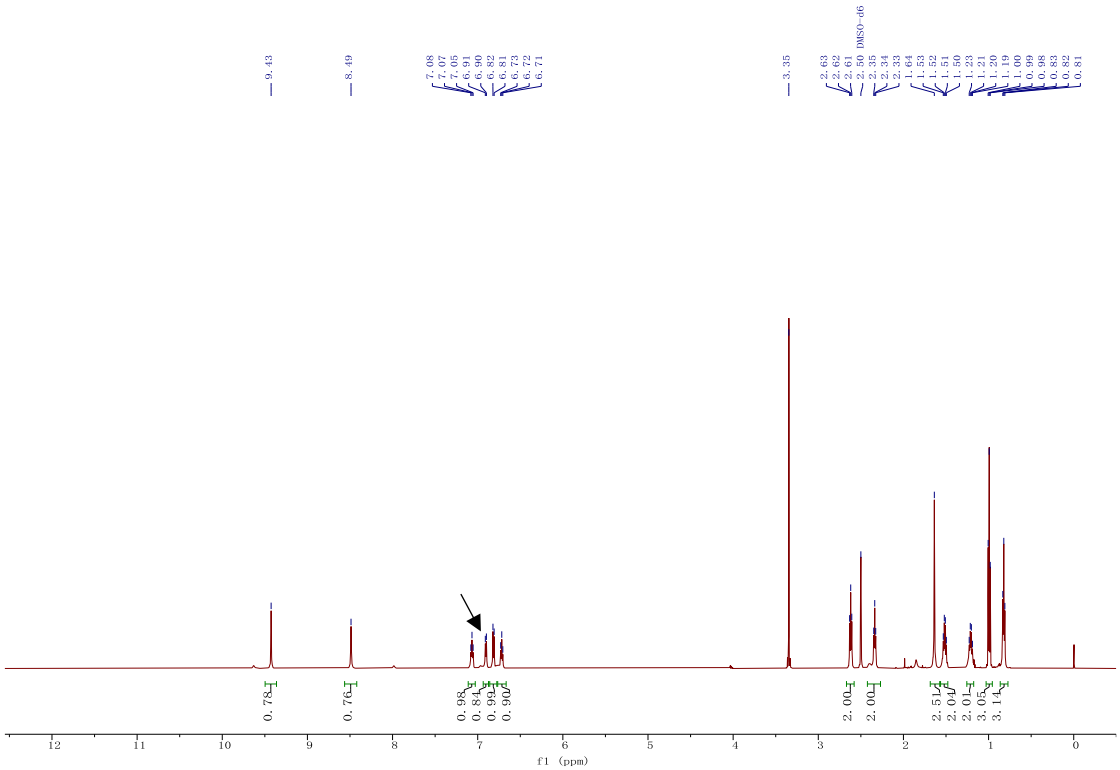
^{1}H NMR of product **$[D]_n$-1aa** of this reaction





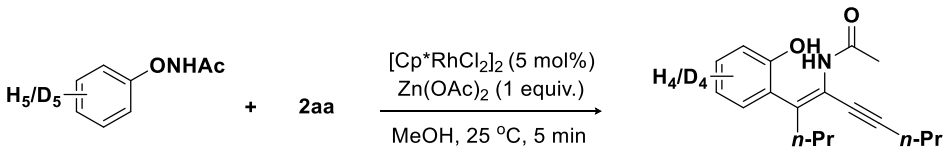
To a mixture of **1aa** (0.25 mmol), $[Cp^*RhCl_2]_2$ (5 mol%), $Zn(OAc)_2$ (0.25 mmol) in a 25 mL Schlenk tube was added a solution of **2aa** (0.275 mmol) in CD_3OD (4.0 mL). Then the tube was capped with septa, and the resulting mixture was stirred at 25 °C for 5 minutes. After that, the reaction was quenched with water (20 mL) and extracted with ethyl acetate (10 mL x 3). The combined organic layers were washed with brine and dried with Na_2SO_4. After filtration and removal of the solvents in *vacuo*, the residue was purified by flash chromatography (DCM/EtOAc: 35/1→DCM/EtOAc: 15/1) on silica gel to give the product **$[D]_n$-3aa** (60.7 mg, 85% yield). *Found H/D exchange occurred at the ortho-position (16% D).*

^{1}H NMR of product **$[D]_n$-3aa** of this reaction.



Determination of the KIE

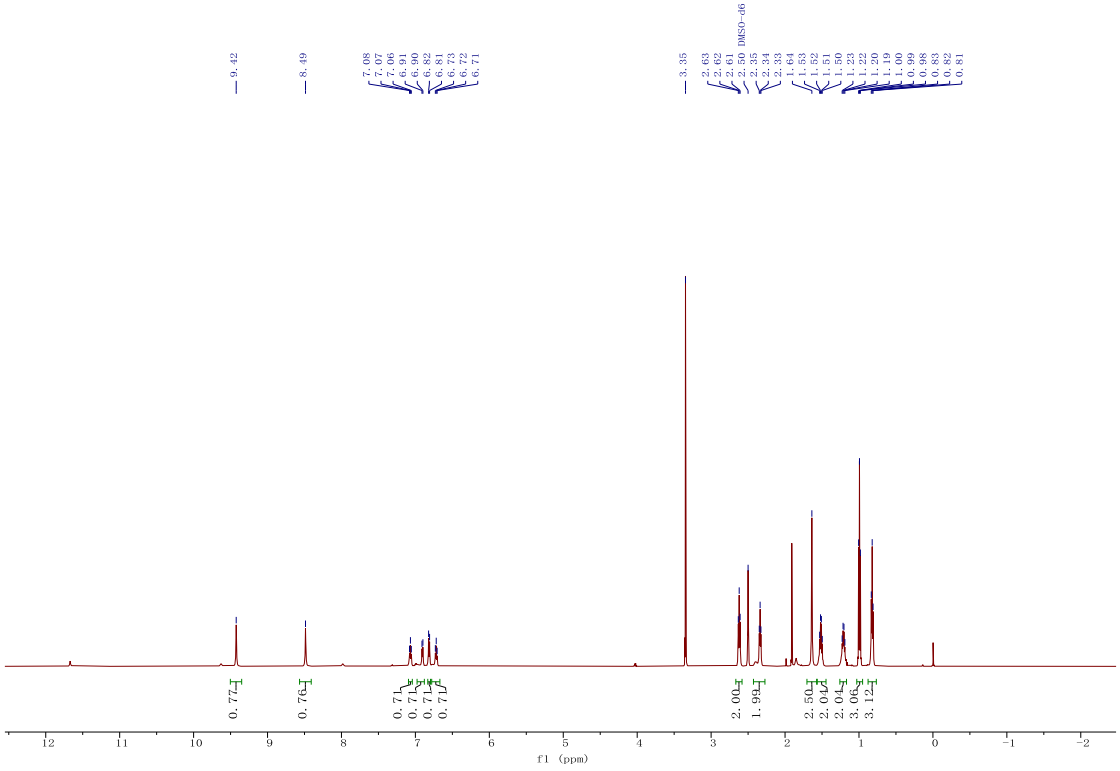
The Intermolecular Competition Experiment



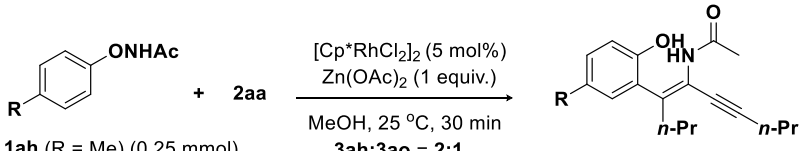
1aa:[D]$_5$-1aa = 1:1

3aa:[D]$_4$-3aa

To a mixture of **1aa** (0.25 mmol), **[D]$_5$-1aa** (0.25 mmol), [Cp*RhCl$_2$]$_2$ (5 mol%), Zn(OAc)$_2$ (0.25 mmol) in a 25 mL Schlenk tube was added a solution of **2aa** (0.275 mmol) in MeOH (4.0 mL). Then the tube was capped with septa, and the resulting mixture was stirred at 25 °C for 5 minutes. After that, the reaction was quenched with water (20 mL) and extracted with ethyl acetate (10 mL x 3). The combined organic layers were washed with brine and dried with Na_2SO_4. After filtration and removal of the solvents in *vacuo*, the residue was purified by flash chromatography (DCM/EtOAc: 35/1→DCM/EtOAc: 15/1) on silica gel to give a mixture of products **3aa** and **[D]$_4$-3aa**. The mixture was analyzed by ^{1}H NMR. *A kinetic isotopic effect of this reaction was determined to be k_H/k_D = 2.45 (0.71/0.29)*.



Competition Experiments between **1ah** and **1ao**

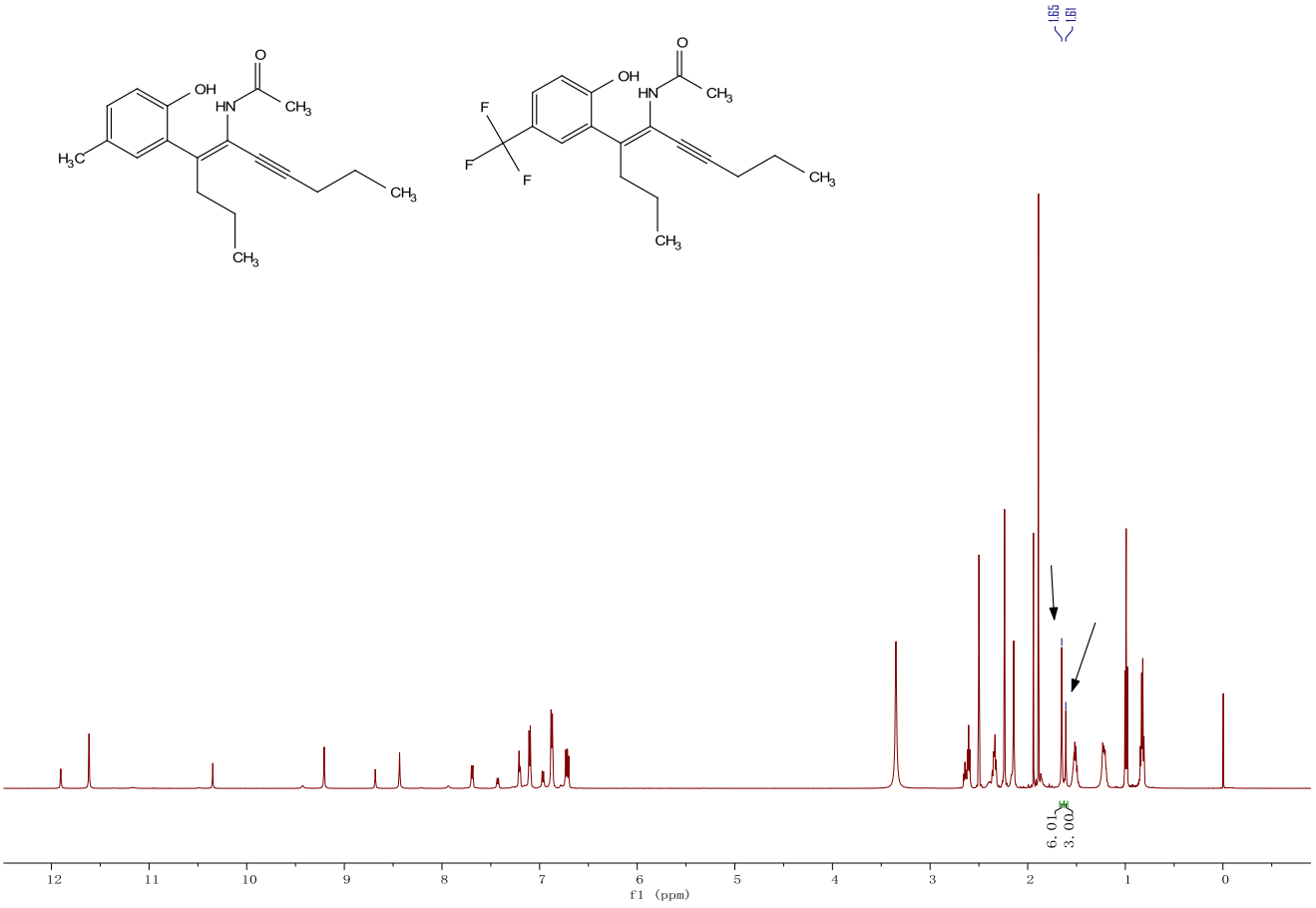


1ah (R = Me) (0.25 mmol)
1ao (R = CF_3) (0.25 mmol)

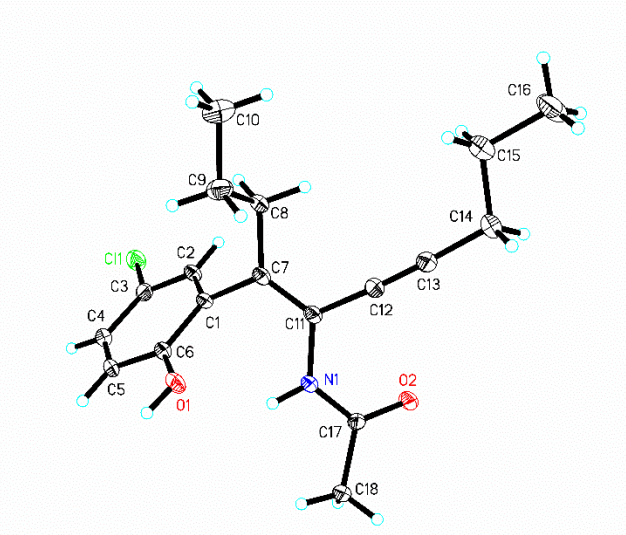
3ah (R = Me)
3ao (R = CF_3)

To a mixture of **1ah** (0.25 mmol), **1ao** (0.25 mmol), [Cp*RhCl$_2$]$_2$ (5 mol%), Zn(OAc)$_2$ (0.25 mmol)

in a 25 mL Schlenk tube was added a solution of **2aa** (0.25 mmol) in MeOH (4.0 mL). Then the tube was capped with septa, and the resulting mixture was stirred at 25 °C for 30 minutes. After that, the reaction was quenched with water (20 mL) and extracted with ethyl acetate (10 mL x 3). The combined organic layers were washed with brine and dried with Na_2SO_4. After filtration and removal of the solvents in *vacuo*, the residue was purified by flash chromatography (DCM/EtOAc: 35/1→DCM/EtOAc: 15/1) on silica gel to give a crude mixture of products **3ah** and **3ao**. The ratio of **3ah**/**3ao** was determined to be 2/1 by ^{1}HNMR integration (see below).



X-ray Data of Compound 3al (Deposition Data: CCDC 2201175) (ellipsoid contour at 30% probability level)



A suitable crystal of compound **3al** was obtained by slowly volatilizing a solution of **3al** in chloroform and methanol at ambient temperature. A colorless crystal of **3al** was mounted on a glass fiber at a random orientation. The data were collected by a diffractometer Rigaku Oxford Diffraction Supernova Dual Source, Cu at Zero equipped with an AtlasS2 CCD using Cu Kα radiation (1.54178 Å) by using a ω scan mode. The structures were solved by direct methods using Olex2 software, and the non-hydrogen atoms were located from the trial structure and then refined anisotropically with XL using a full-matrix least squares procedure based on F^2. The weighted R factor, wR and goodness-of-fit S values were obtained based on F^2. The hydrogen atom positions were fixed geometrically at the calculated distances and allowed to ride on the parent atoms.

Table S4 Crystal data and structure refinement for compound **3al**

Identification code	**3al**
Empirical formula	$C_{18}H_{22}ClNO_2$
Formula weight	319.81
Temperature/K	150.00(10)
Crystal system	monoclinic
Space group	$P2_1/c$
a/Å	17.3131(9)
b/Å	8.5318(4)
c/Å	11.6113(4)
α/°	90
β/°	94.377(4)
γ/°	90
Volume/Å^3	1710.13(13)
Z	4
ρ_{calc}g/cm^3	1.242
μ/mm^{-1}	2.024
F(000)	680.0
Crystal size/mm^3	0.13 × 0.12 × 0.1

Radiation	Cu Kα (λ = 1.54184)
2Θ range for data collection/°	5.12 to 143.64
Index ranges	$-21 \le h \le 20$, $-10 \le k \le 10$, $-9 \le l \le 14$
Reflections collected	8611
Independent reflections	3275 [R_{int} = 0.0642, R_{sigma} = 0.0763]
Data/restraints/parameters	3275/0/203
Goodness-of-fit on F^2	1.057
Final R indexes [I>=2σ (I)]	R_1 = 0.0703, wR_2 = 0.1770
Final R indexes [all data]	R_1 = 0.0996, wR_2 = 0.1931
Largest diff. peak/hole / e Å^{-3}	0.96/-0.30

Crystal structure determination of 3al

Crystal Data for $C_{18}H_{22}ClNO_2$ (M =319.81 g/mol): monoclinic, space group $P2_1/c$ (no. 14), a = 17.3131(9) Å, b = 8.5318(4) Å, c = 11.6113(4) Å, β = 94.377(4)°, V = 1710.13(13) Å^3, Z = 4, T = 150.00(10) K, μ(Cu Kα) = 2.024 mm^{-1}, *Dcalc* = 1.242 g/cm^3, 8611 reflections measured ($5.12° \le 2\Theta \le 143.64°$), 3275 unique ($R_{int}$ = 0.0642, R_{sigma} = 0.0763) which were used in all calculations. The final R_1 was 0.0703 ($I > 2\sigma(I)$) and wR_2 was 0.1931 (all data).

CCDC 2201175 contains the supplementary crystallographic data for compound **3al**. These data can be also obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

References

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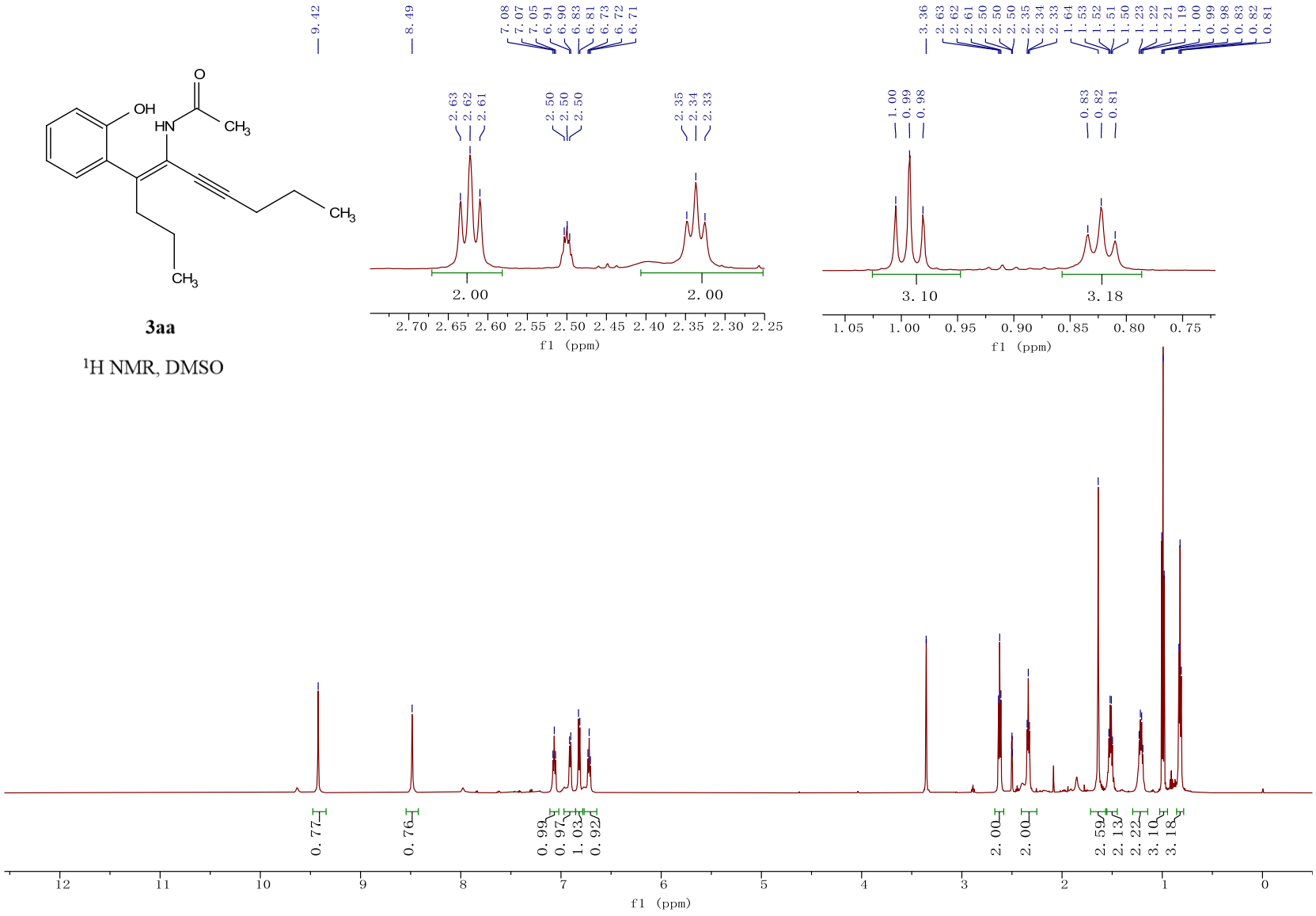
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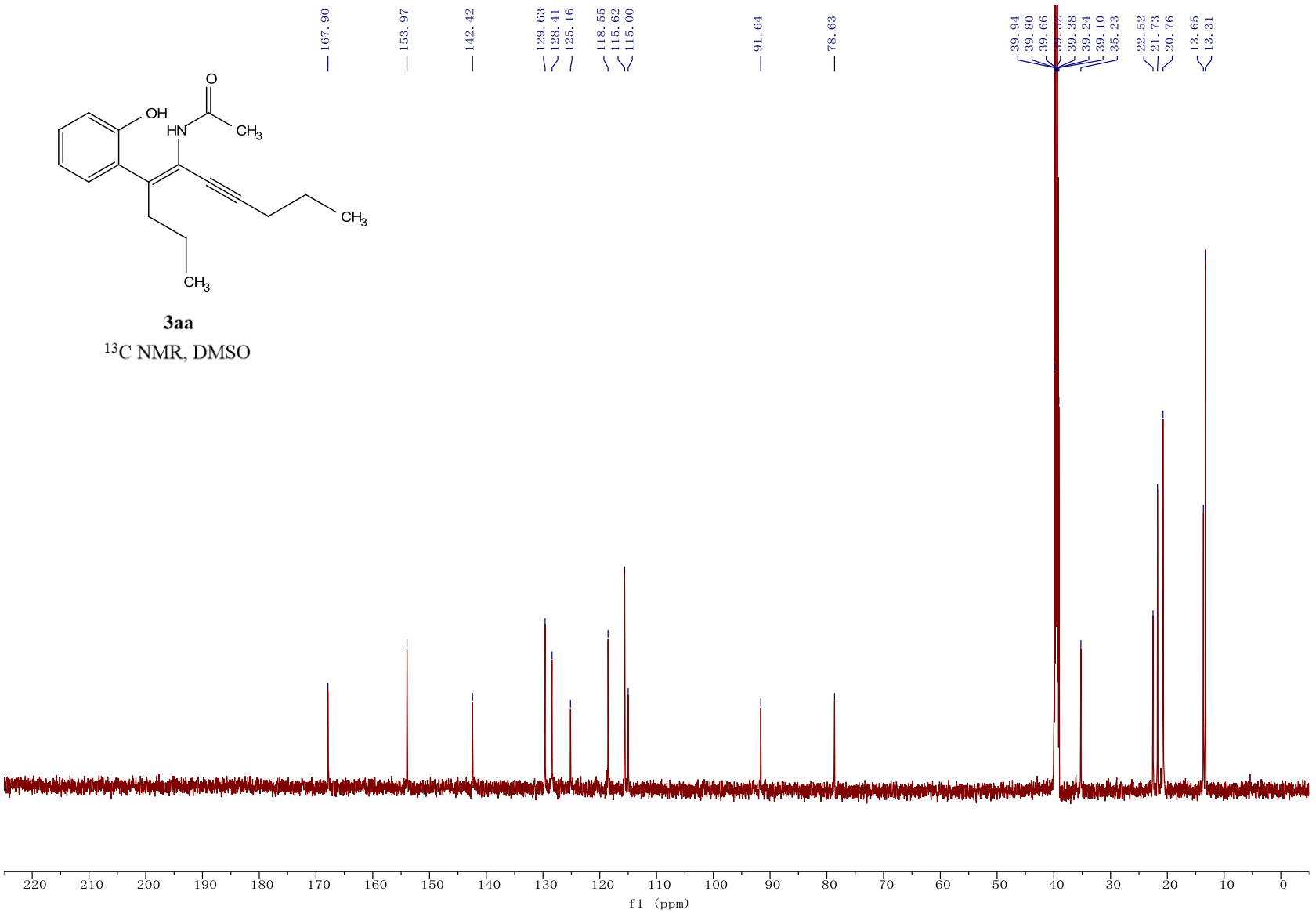
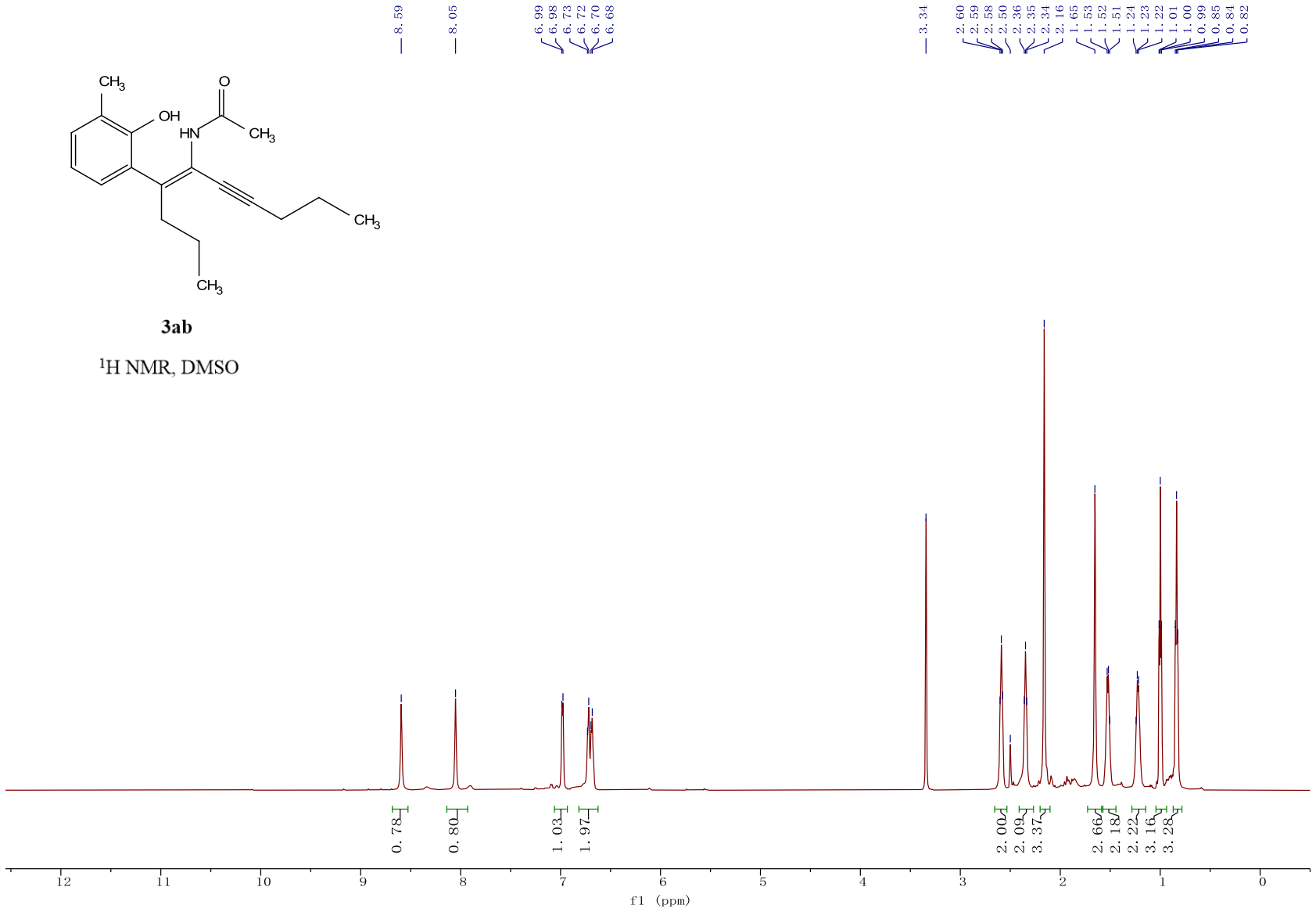
HN
O
CH3
CH3
CH3
3aa
1H NMR, DMSO
f1 (ppm)



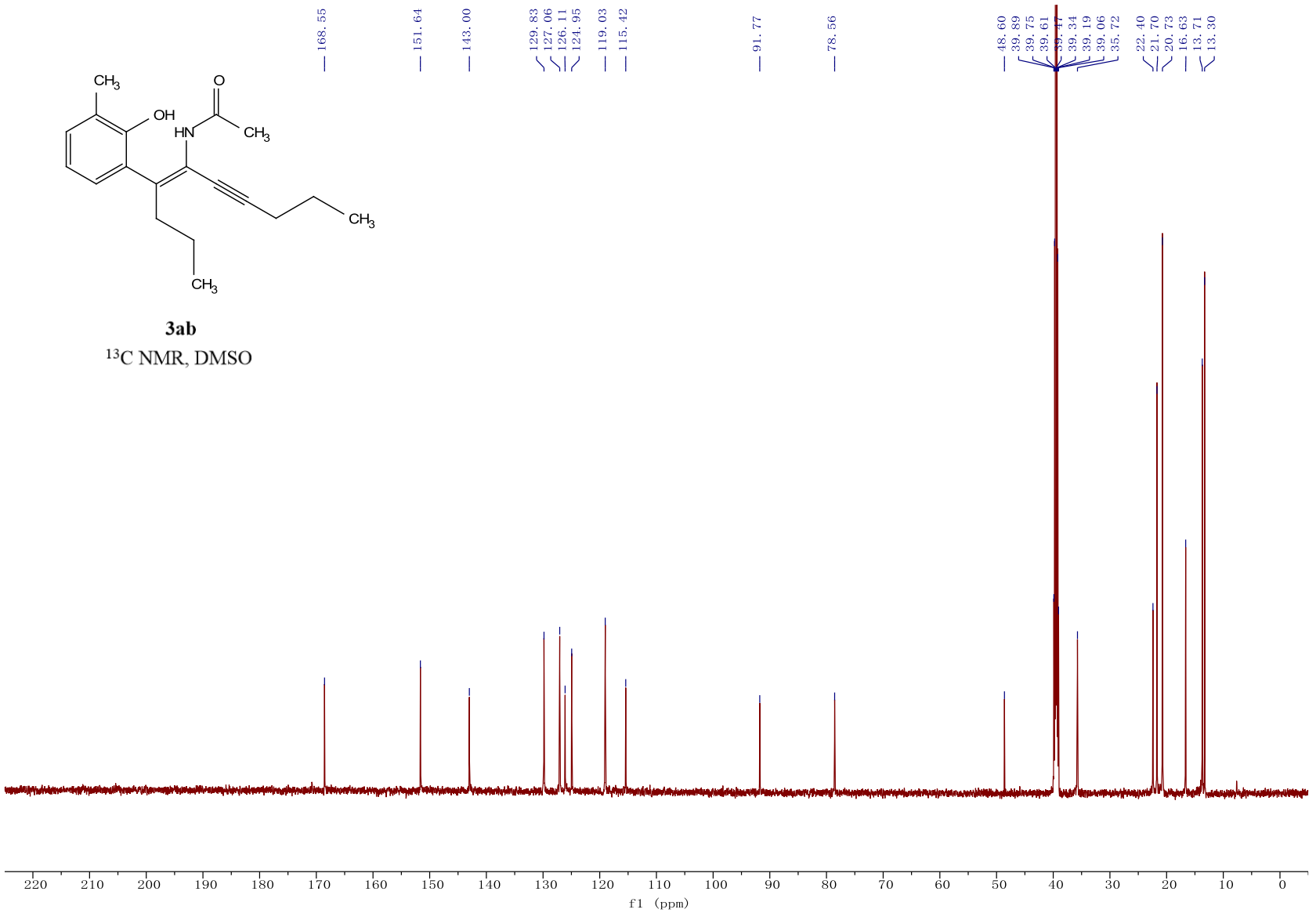
3aa

^{13}C NMR, DMSO



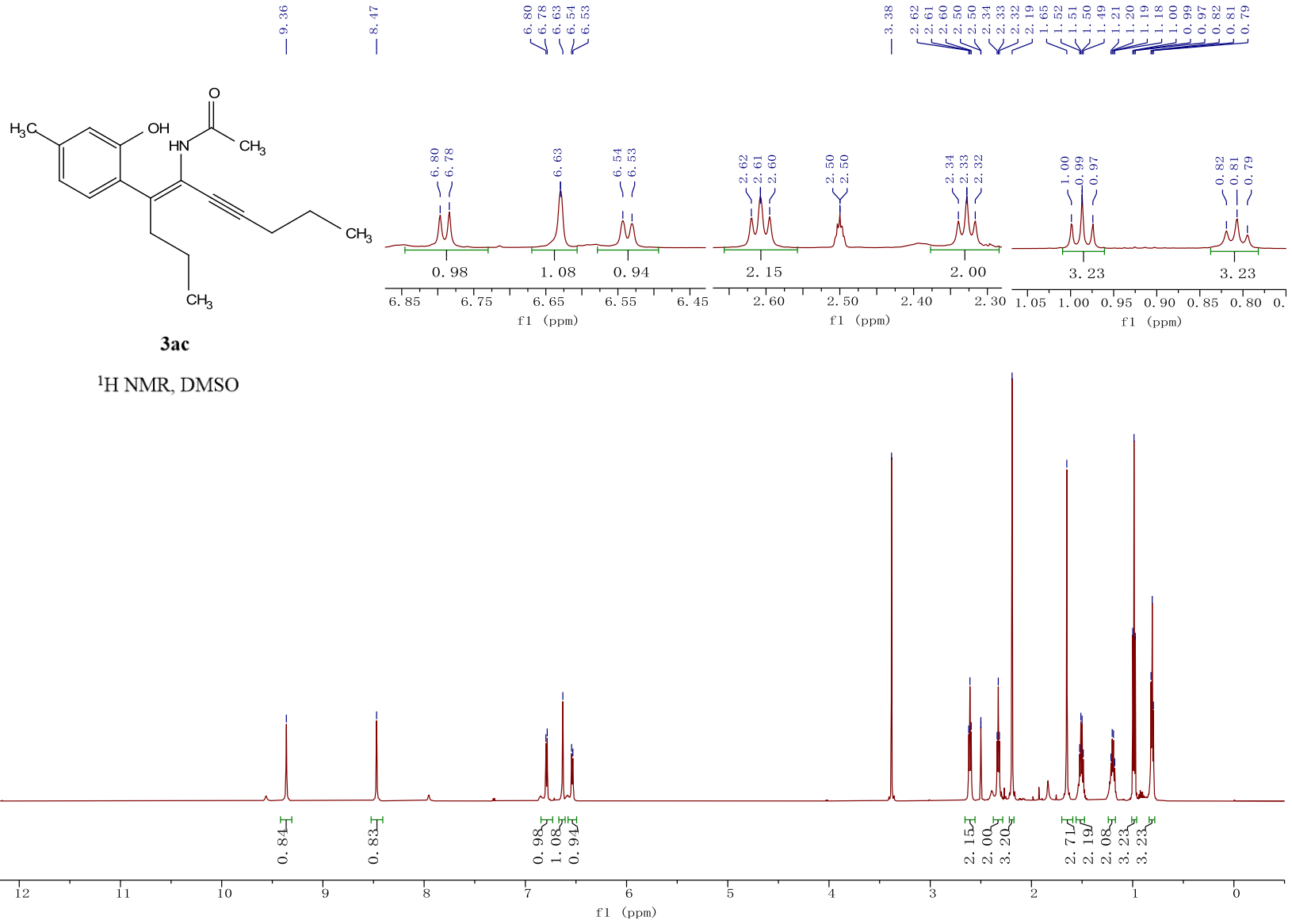
3ab

^{1}H NMR, DMSO



3ab

^{13}C NMR, DMSO



3ac

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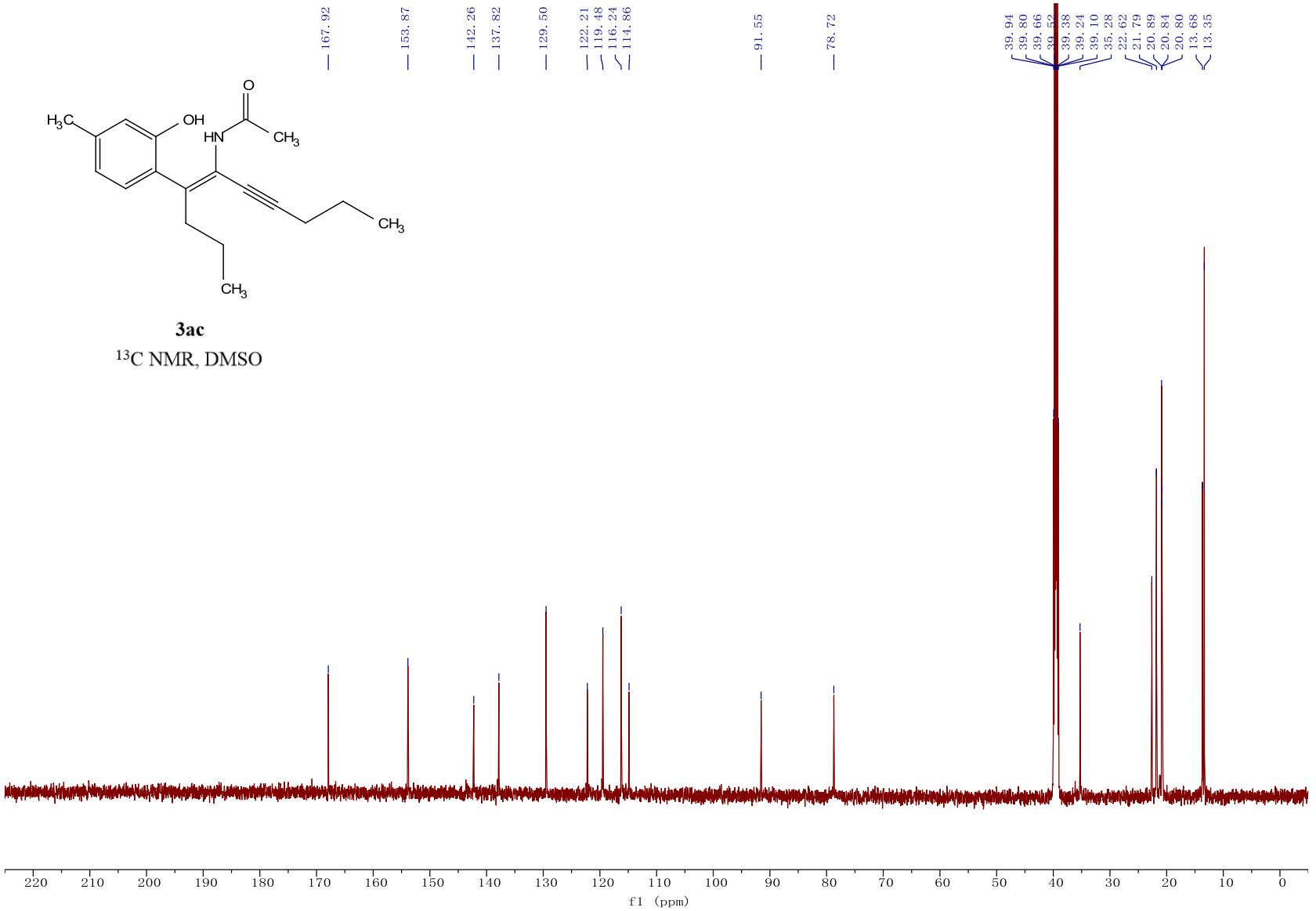

3ac

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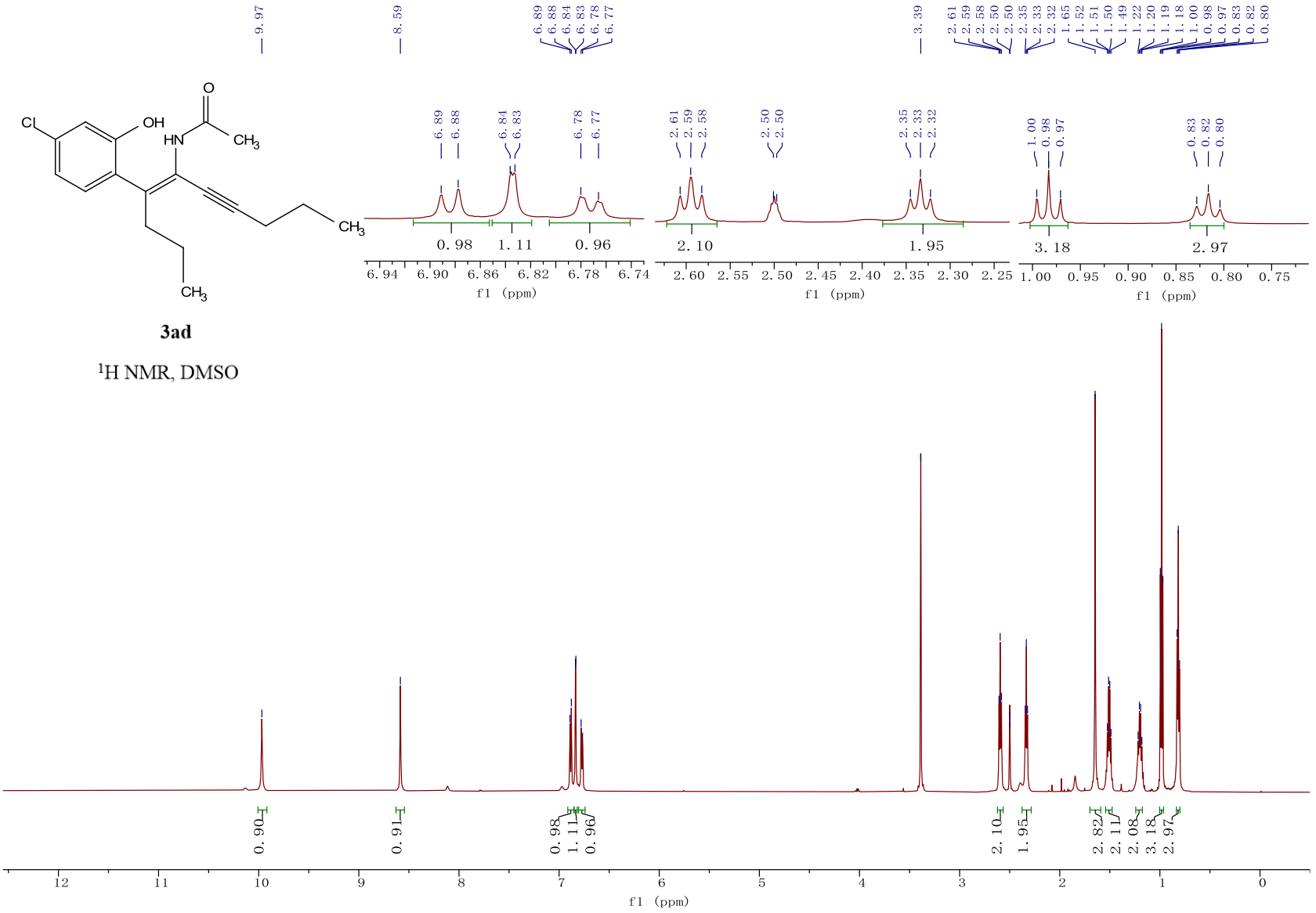
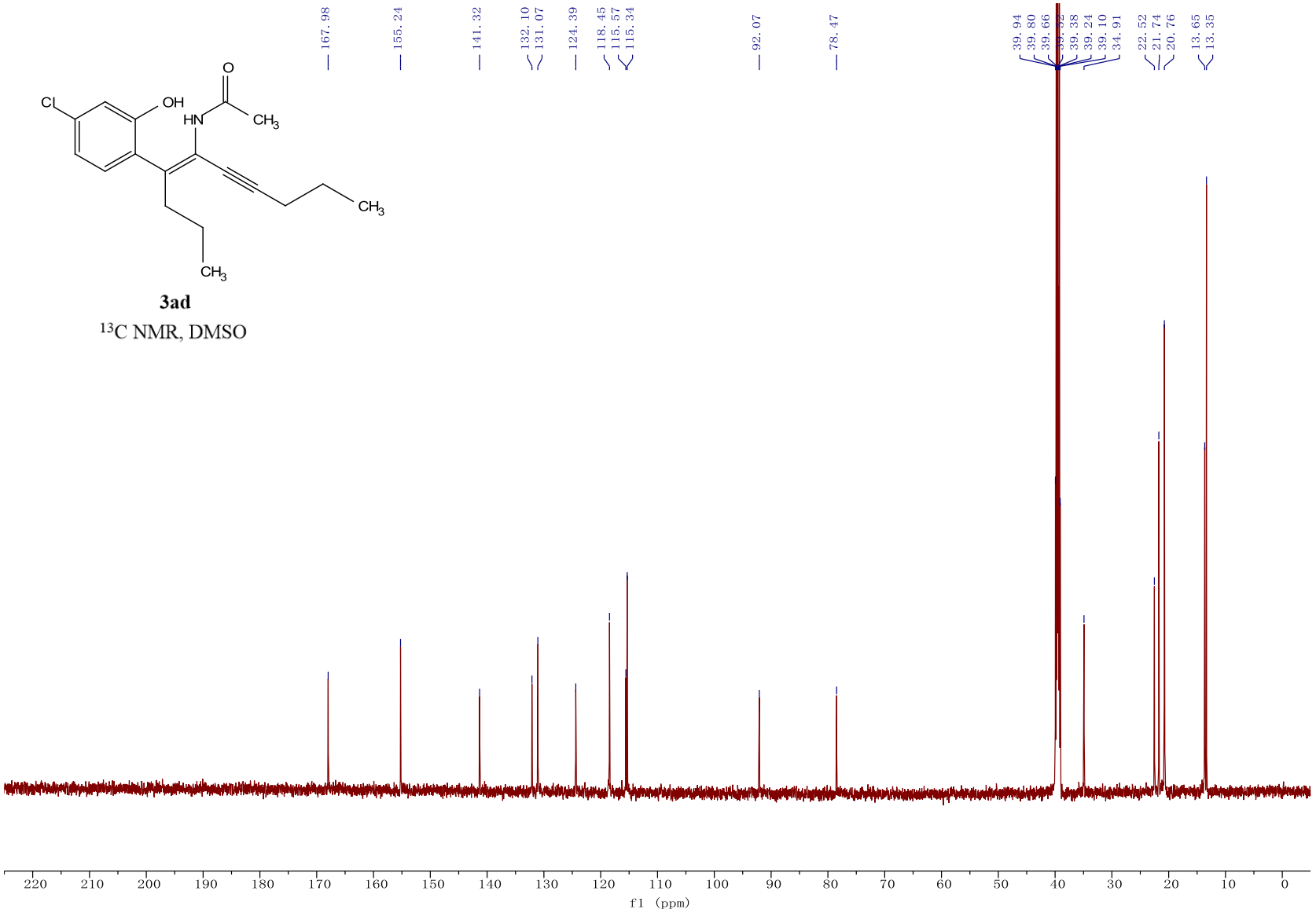


3ad

^{1}H NMR, DMSO



3ad

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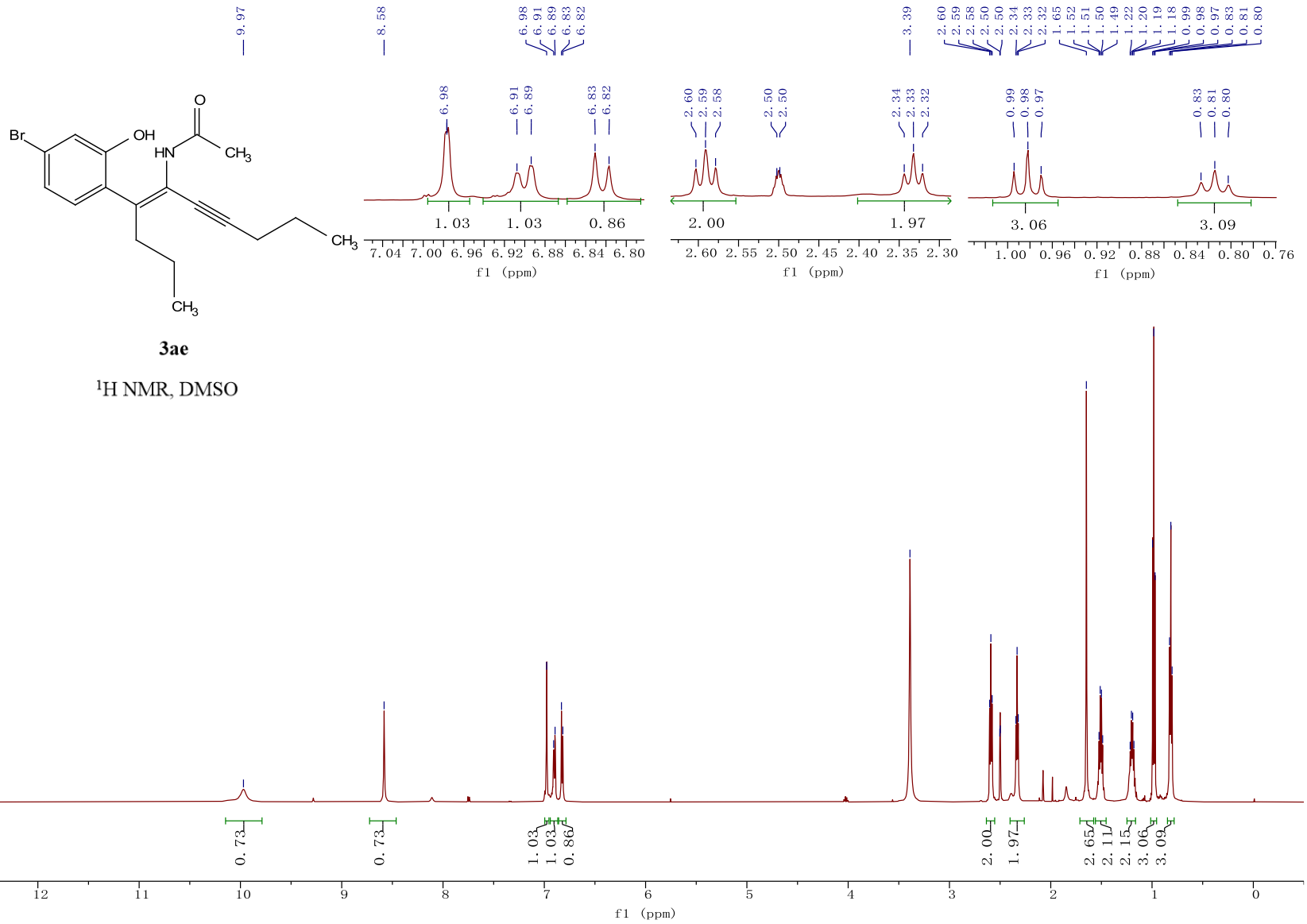
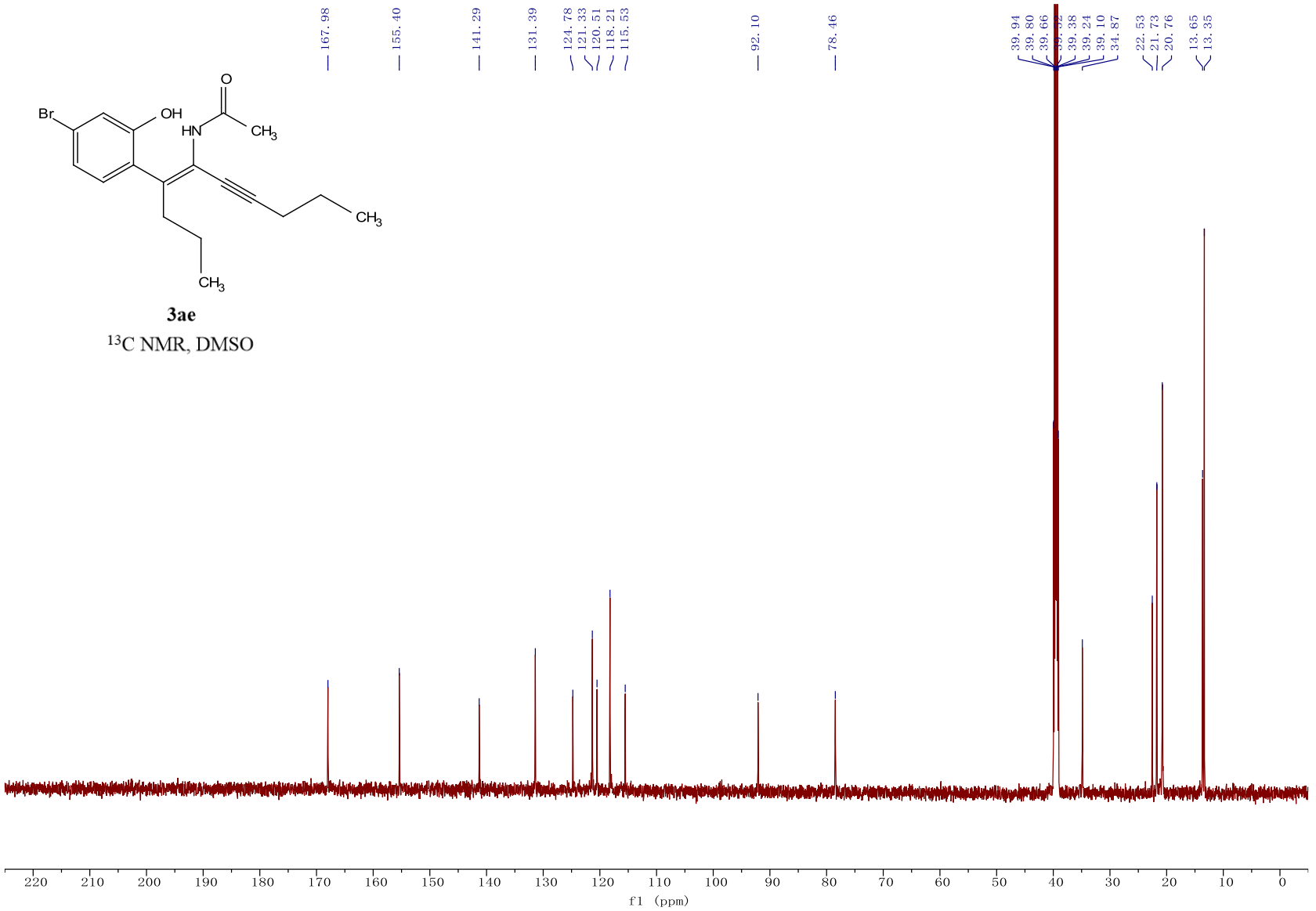


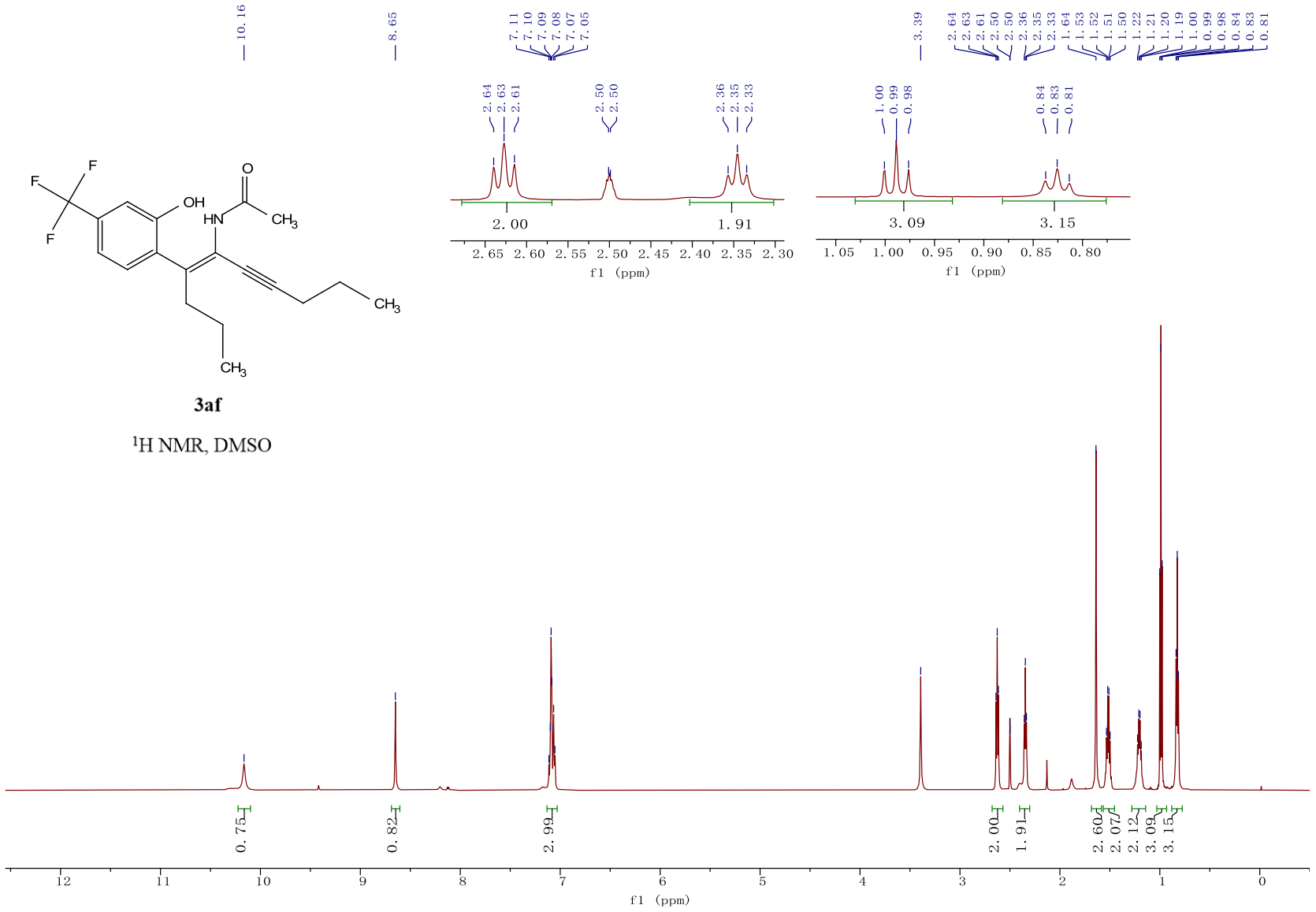
3ae

^{1}H NMR, DMSO



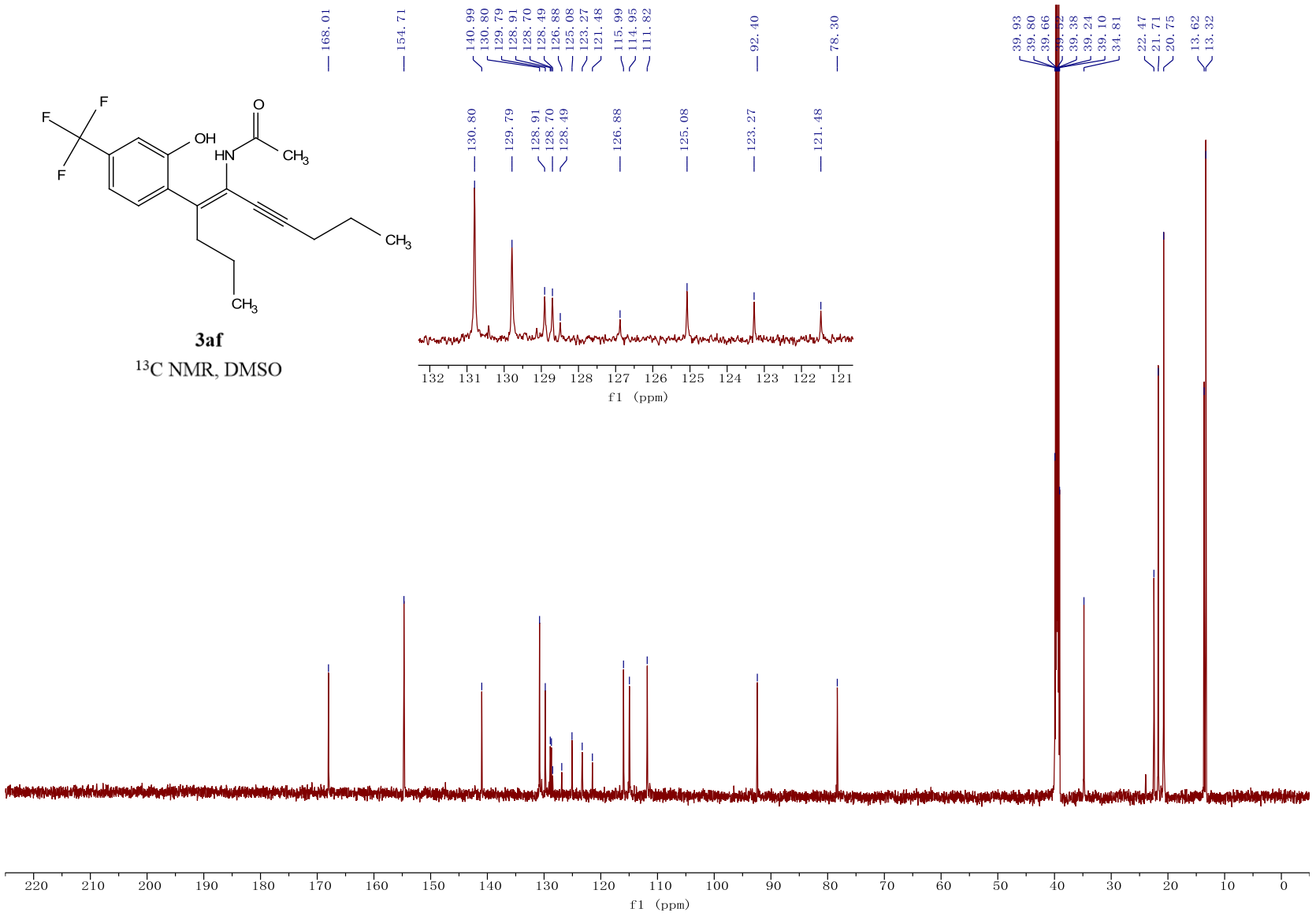
3ae

^{13}C NMR, DMSO



3af

^{1}H NMR, DMSO


F
F
F
OH
HN
O
CH3
CH3
CH3
3af
13C NMR, DMSO
168.01
154.71
140.99
130.80
129.79
128.91
128.70
128.49
126.88
125.08
123.27
121.48
115.99
114.95
111.82
92.40
78.30
39.93
39.80
39.66
39.52
39.38
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39.10
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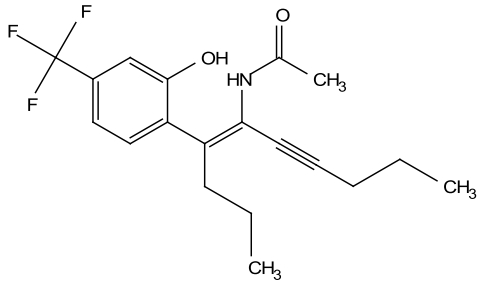
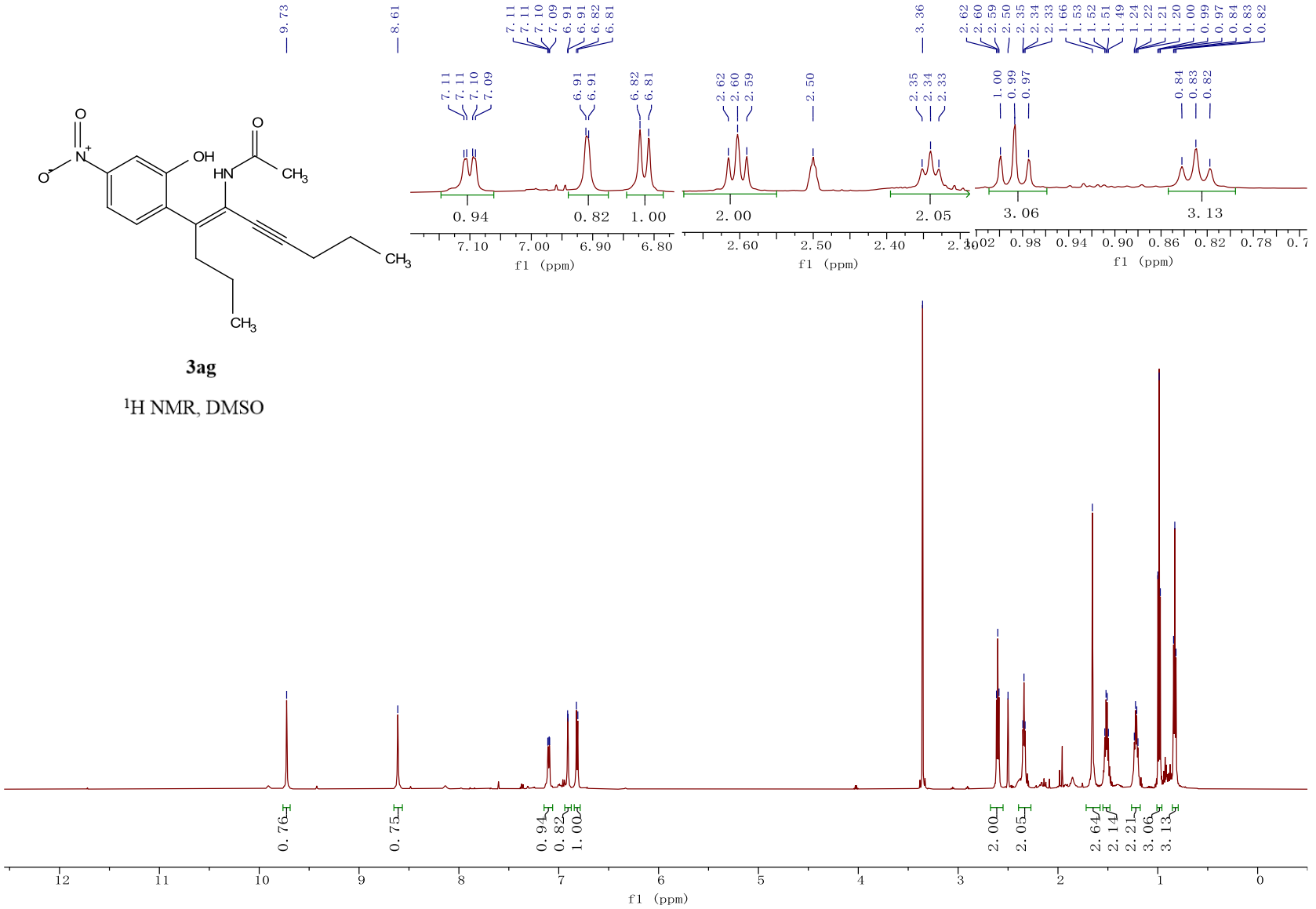
20.75
13.62
13.32
f1 (ppm)
f1 (ppm)



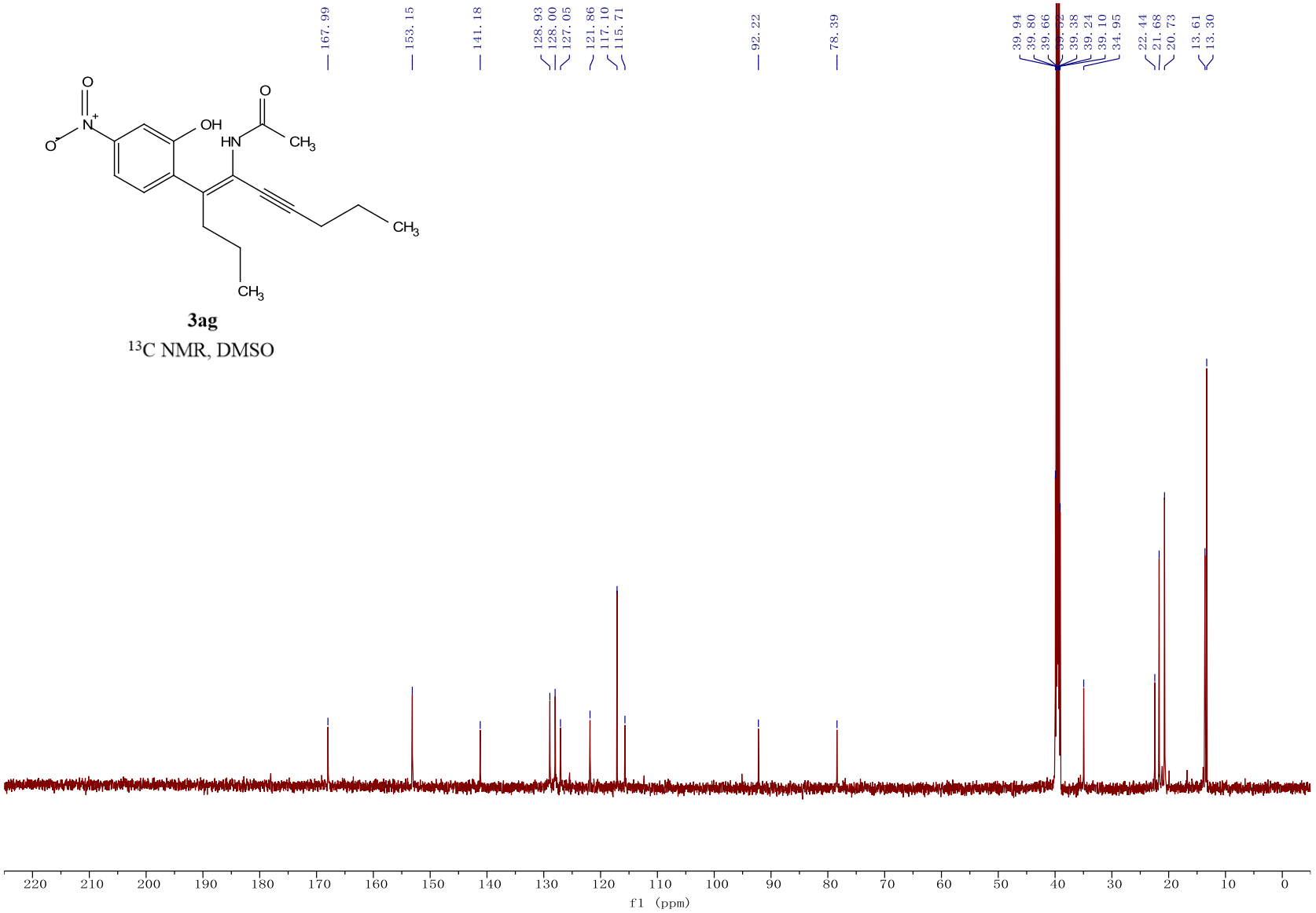
3af

^{19}F NMR, DMSO



3ag

^{1}H NMR, DMSO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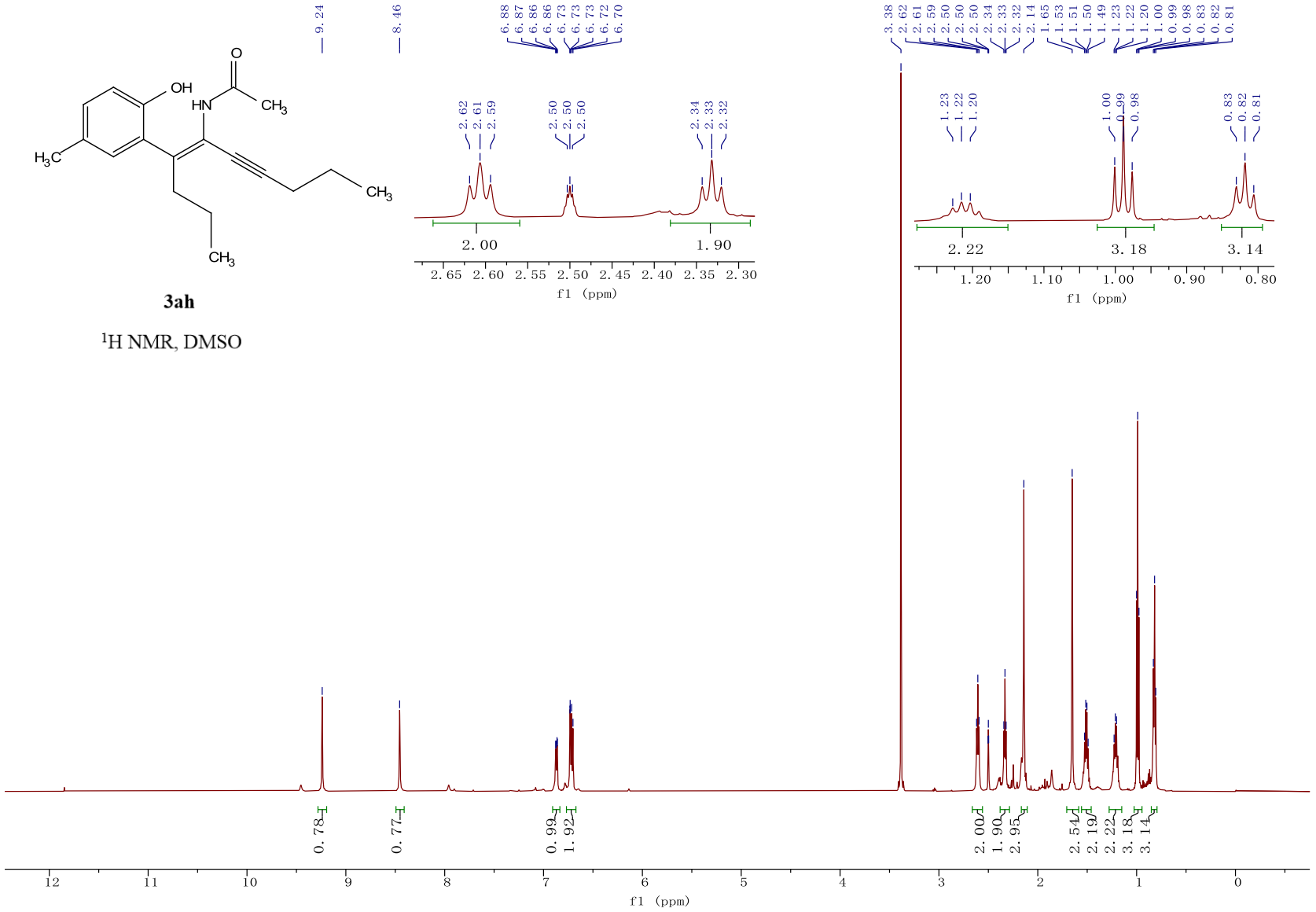
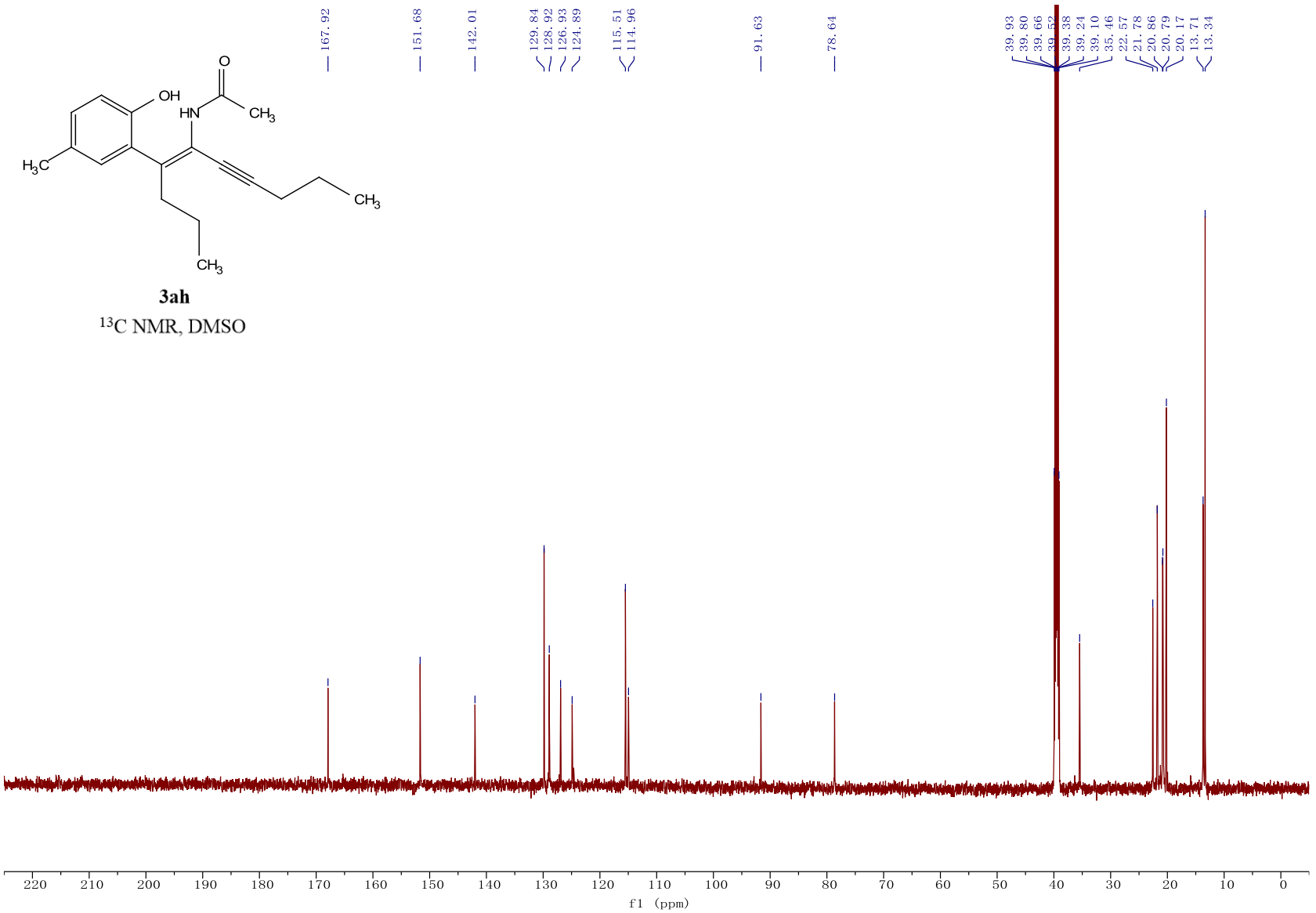
78.39
39.94
39.80
39.66
39.52
39.38
39.24
39.10
34.95
22.44
21.68
20.73
13.61
13.30
O
N+
O-
OH
HN
O
CH3
CH3
CH3
3ag
13C NMR, DMSO
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



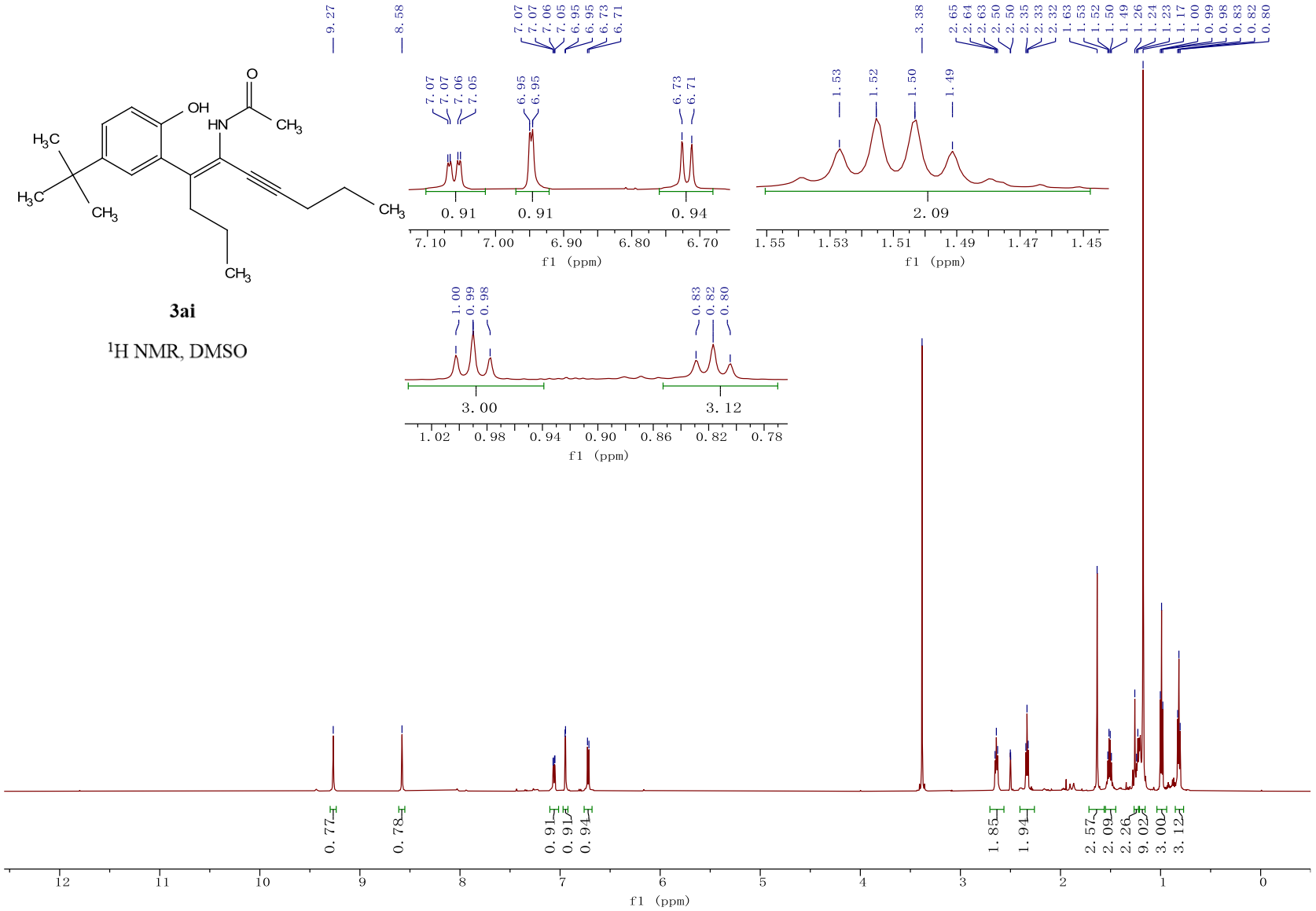
3ah

^{1}H NMR, DMSO



3ah

^{13}C NMR, DMSO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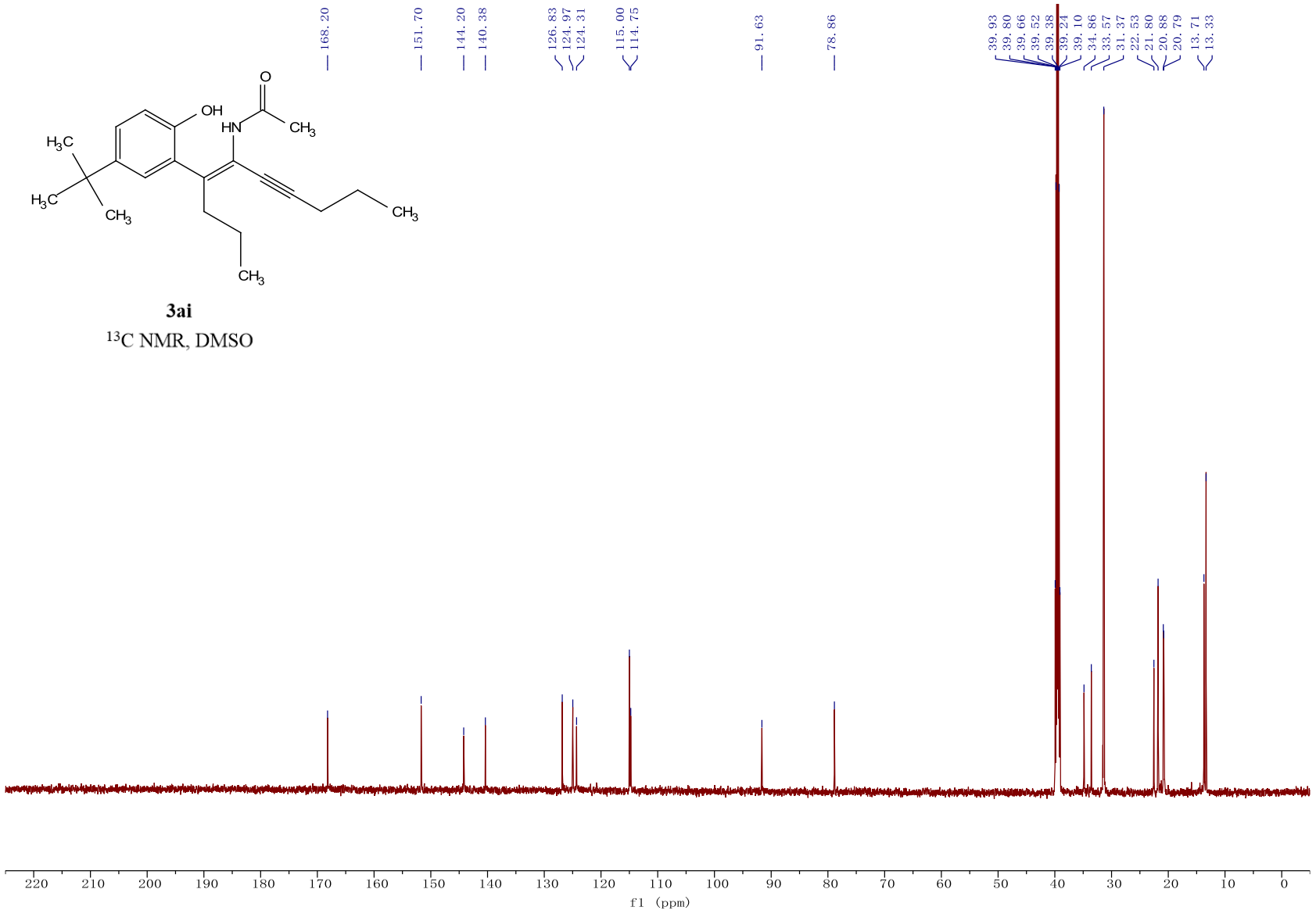
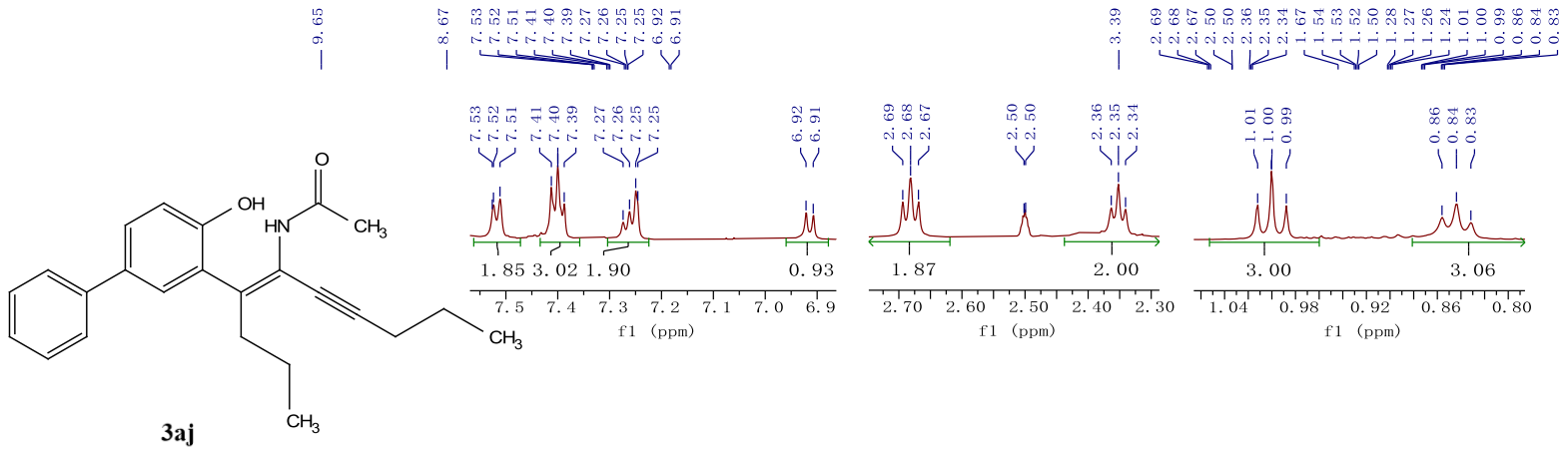
HN
O
CH3
H3C
H3C
CH3
CH3
CH3
3ai
1H NMR, DMSO
f1 (ppm)



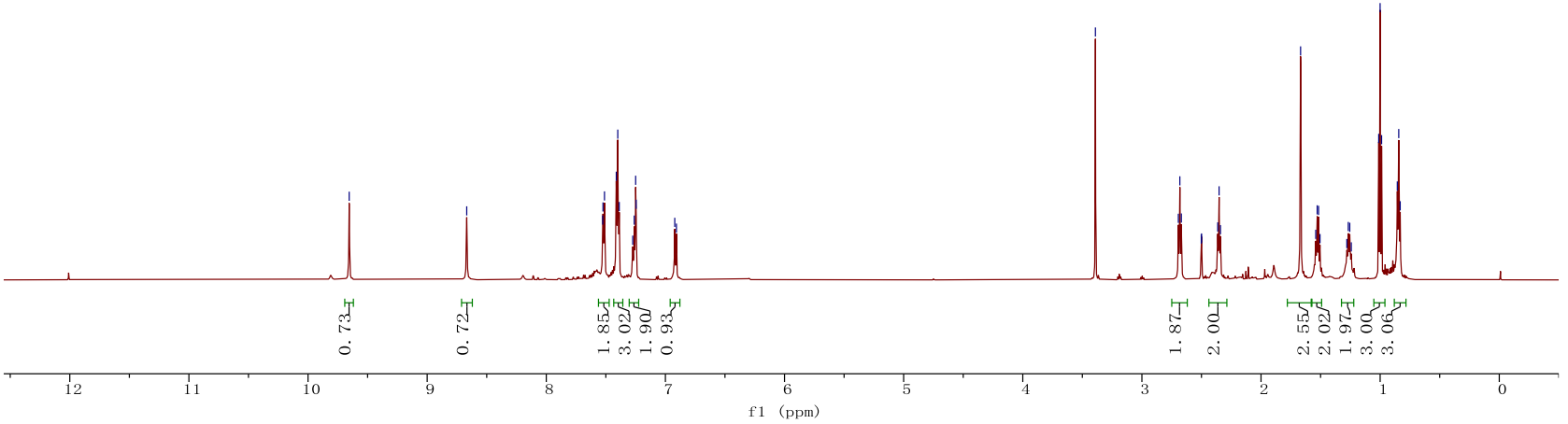
3ai

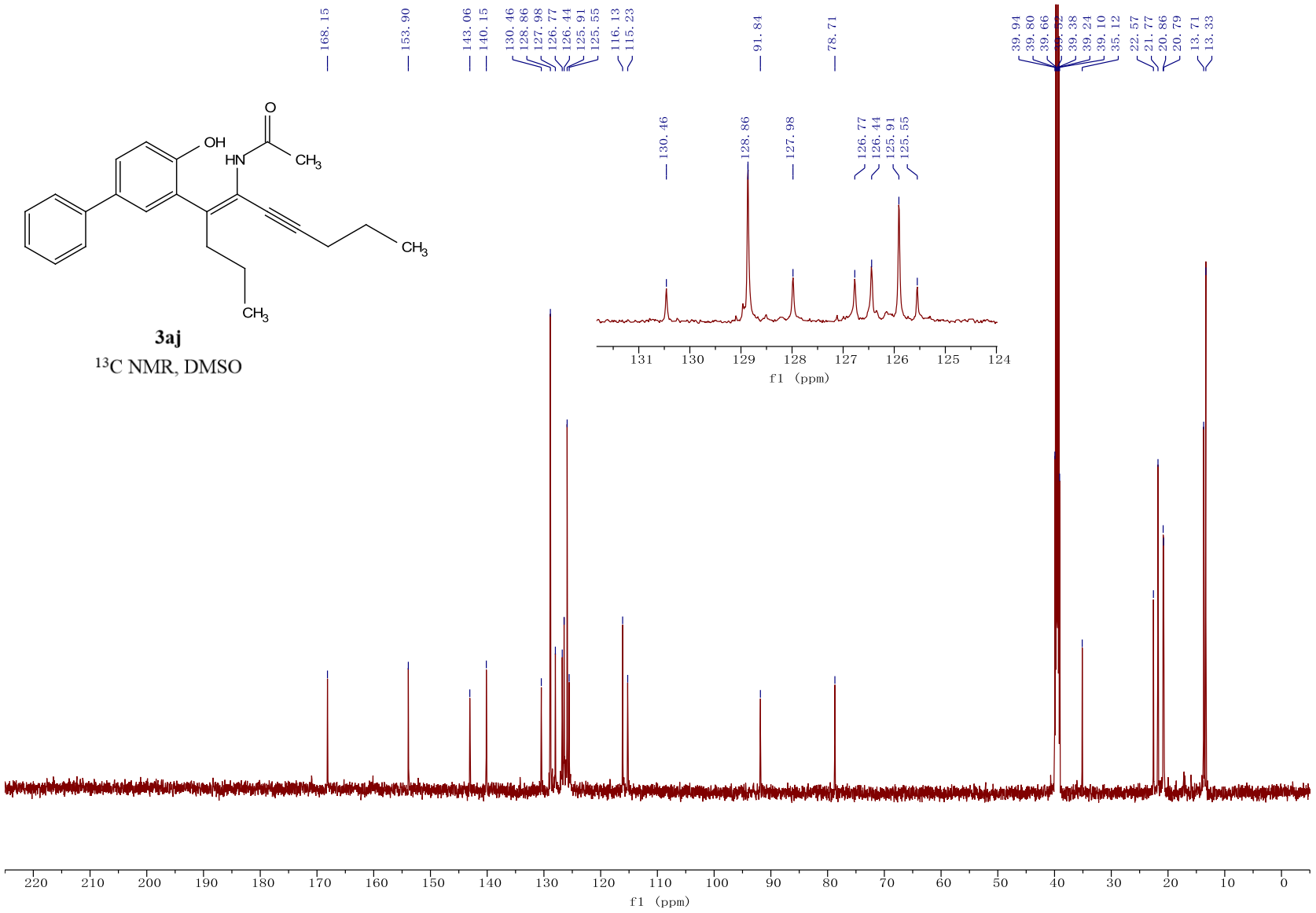
^{13}C NMR, DMSO



3aj

^{1}H NMR, DMSO

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153.90
143.06
140.15
130.46
128.86
127.98
126.77
126.44
125.91
125.55
116.13
115.23
91.84
78.71
39.94
39.80
39.66
39.38
39.24
39.10
35.12
22.57
21.77
20.86
20.79
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HN
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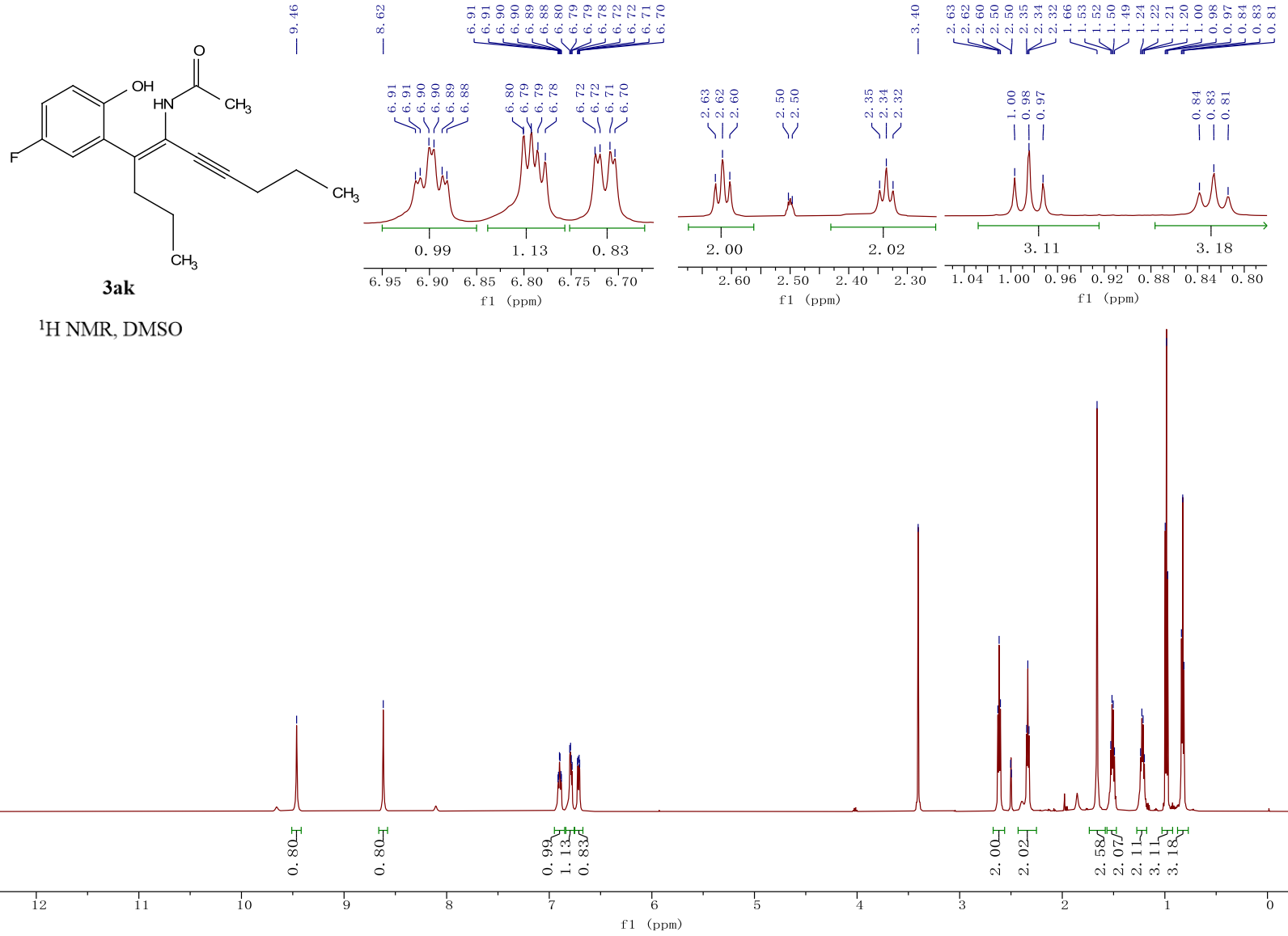
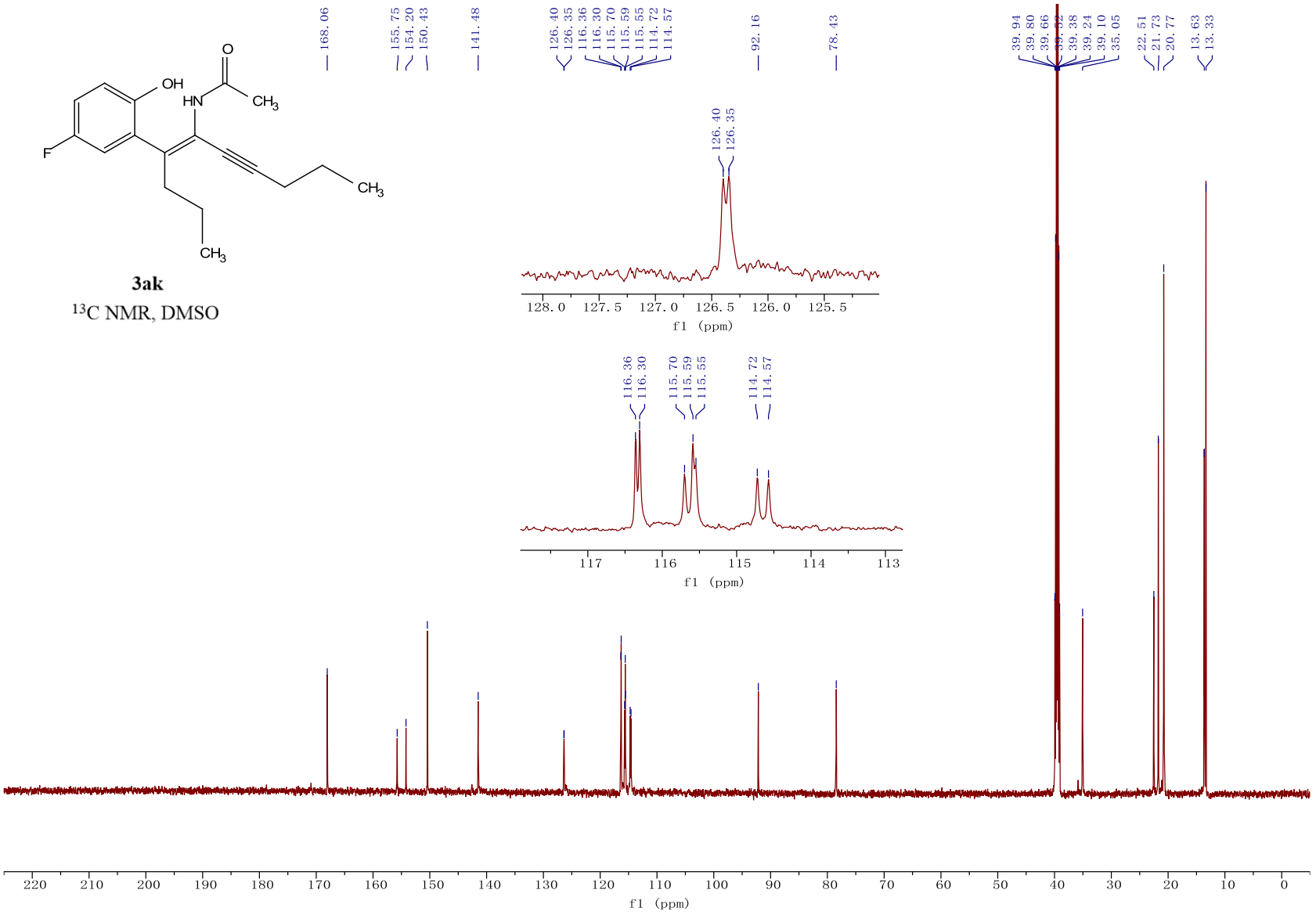
CH3
CH3
CH3
3aj
13C NMR, DMSO
f1 (ppm)


O
OH
HN
CH3
F
CH3
CH3
3ak
1H NMR, DMSO
f1 (ppm)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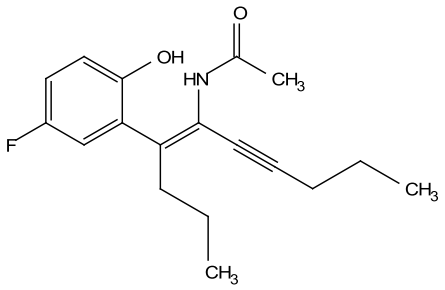
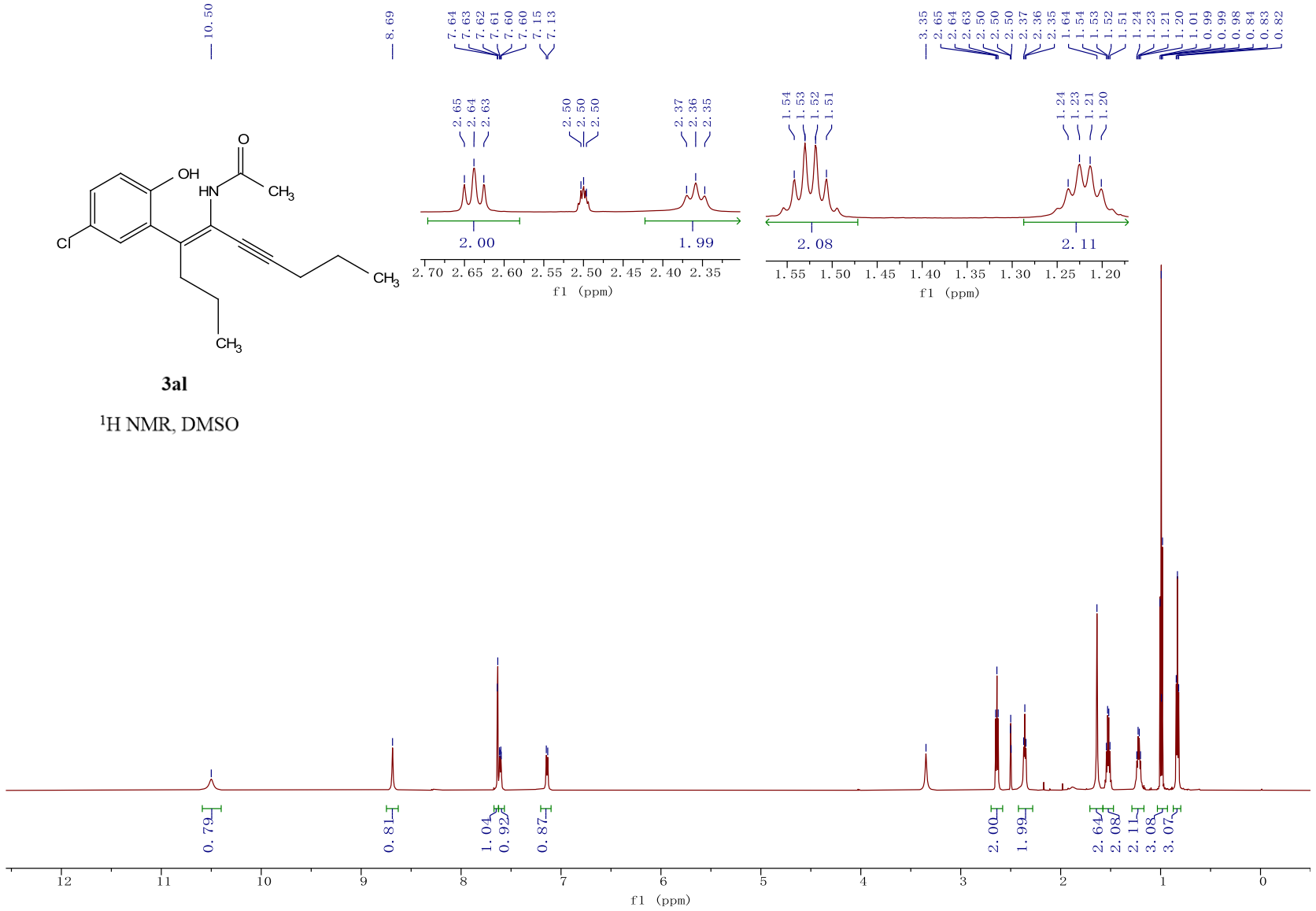
155.75
154.20
150.43
141.48
126.40
126.35
116.36
116.30
115.70
115.59
115.55
114.72
114.57
92.16
78.43
39.94
39.80
39.66
39.52
39.38
39.24
39.10
35.05
22.51
21.73
20.77
13.63
13.33
O
OH
HN
CH3
F
CH3
CH3
3ak
13C NMR, DMSO
f1 (ppm)
f1 (ppm)
f1 (ppm)



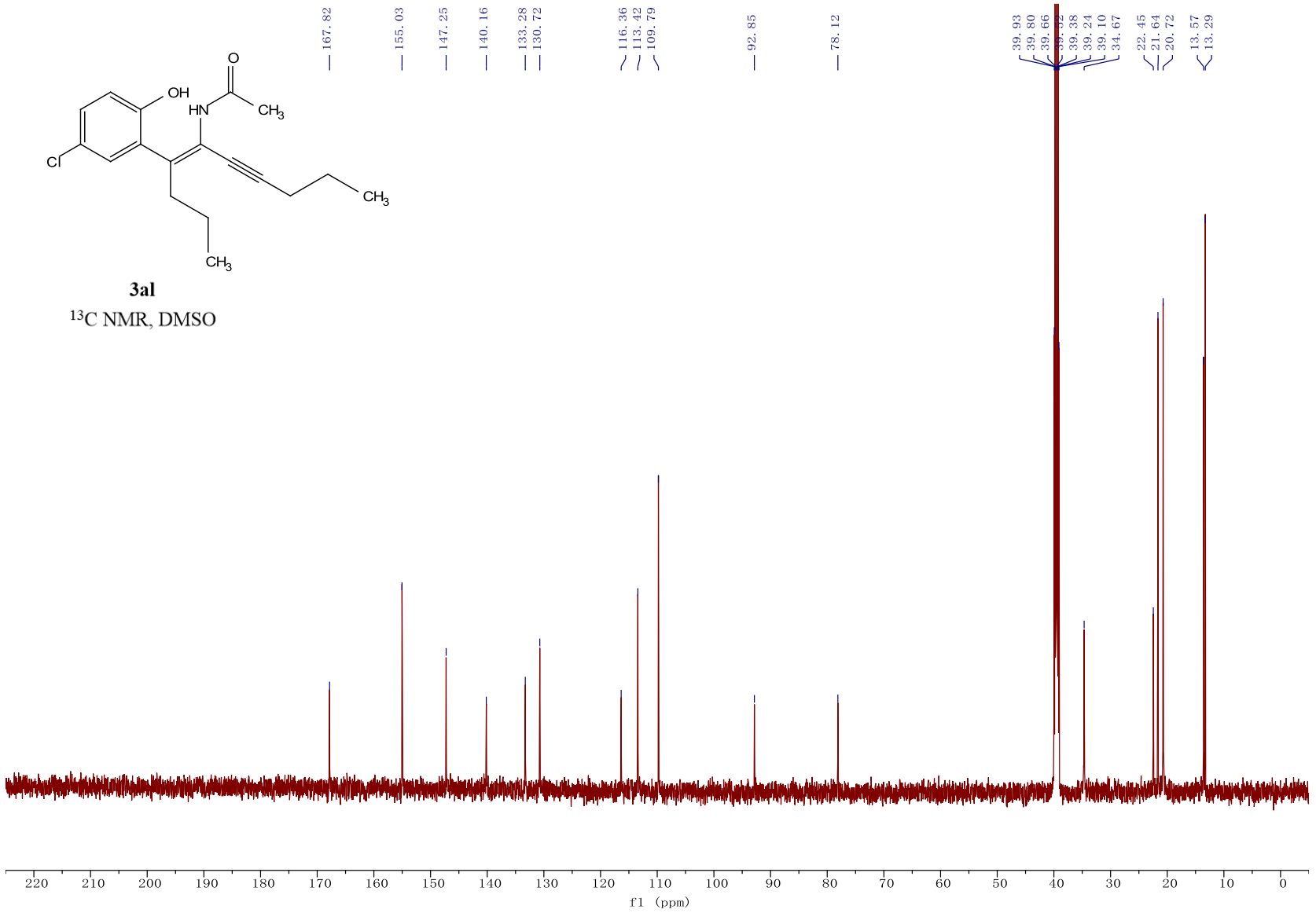
3ak

^{19}F NMR, DMSO



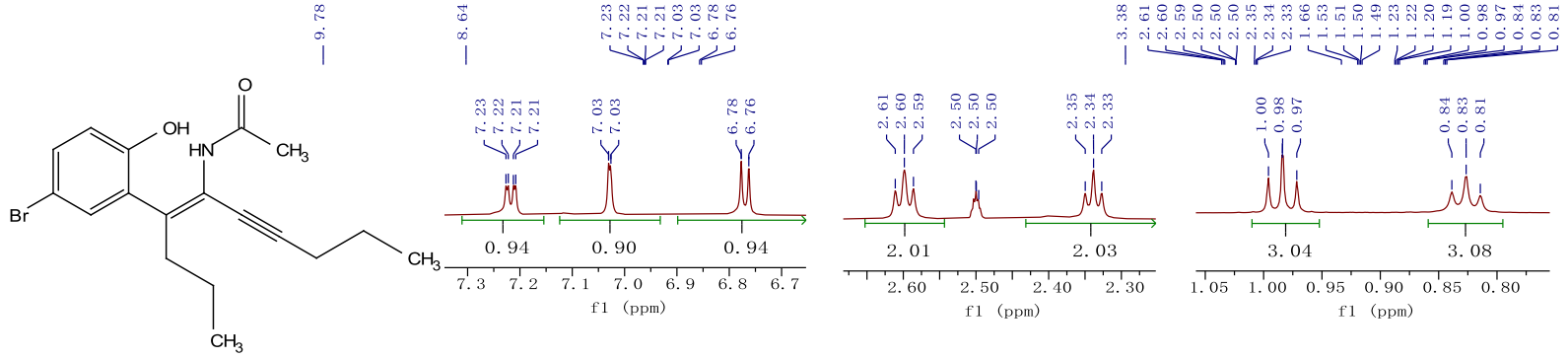
3al

^{1}H NMR, DMSO



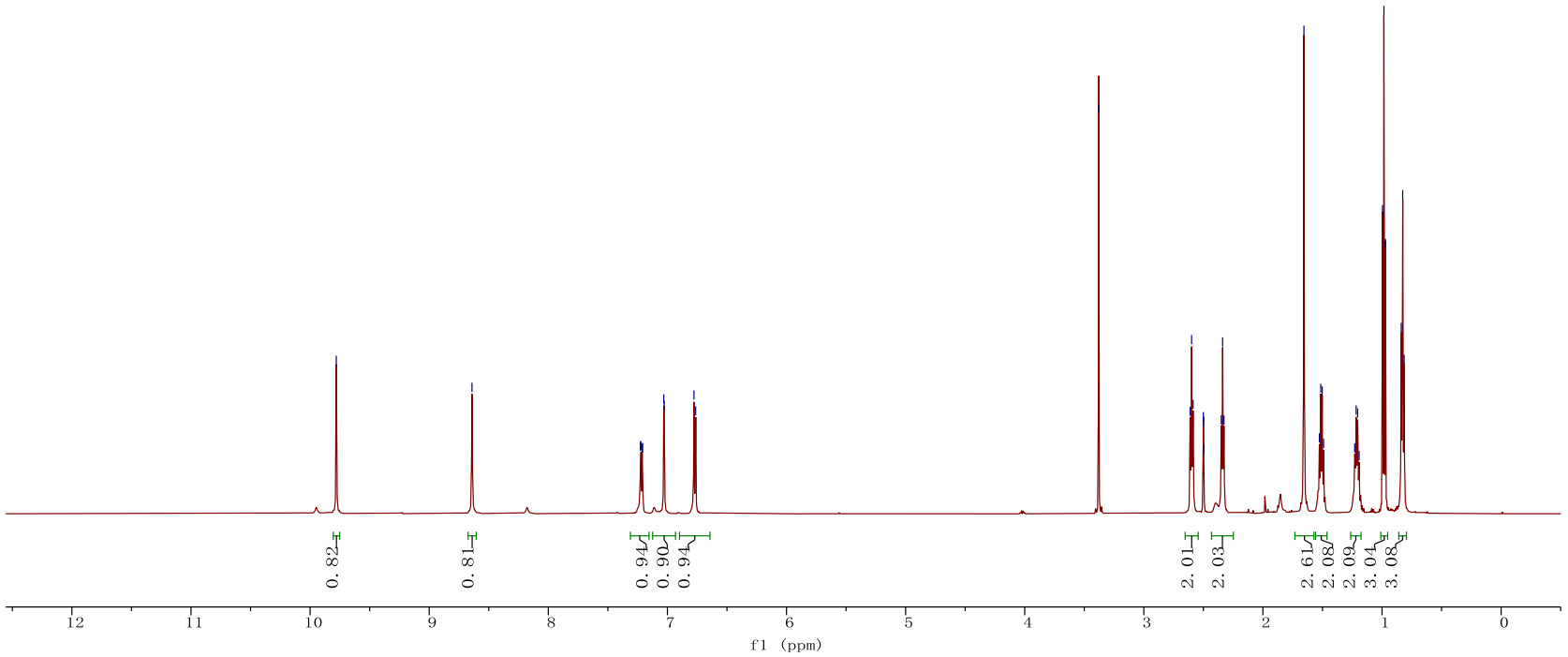
3al

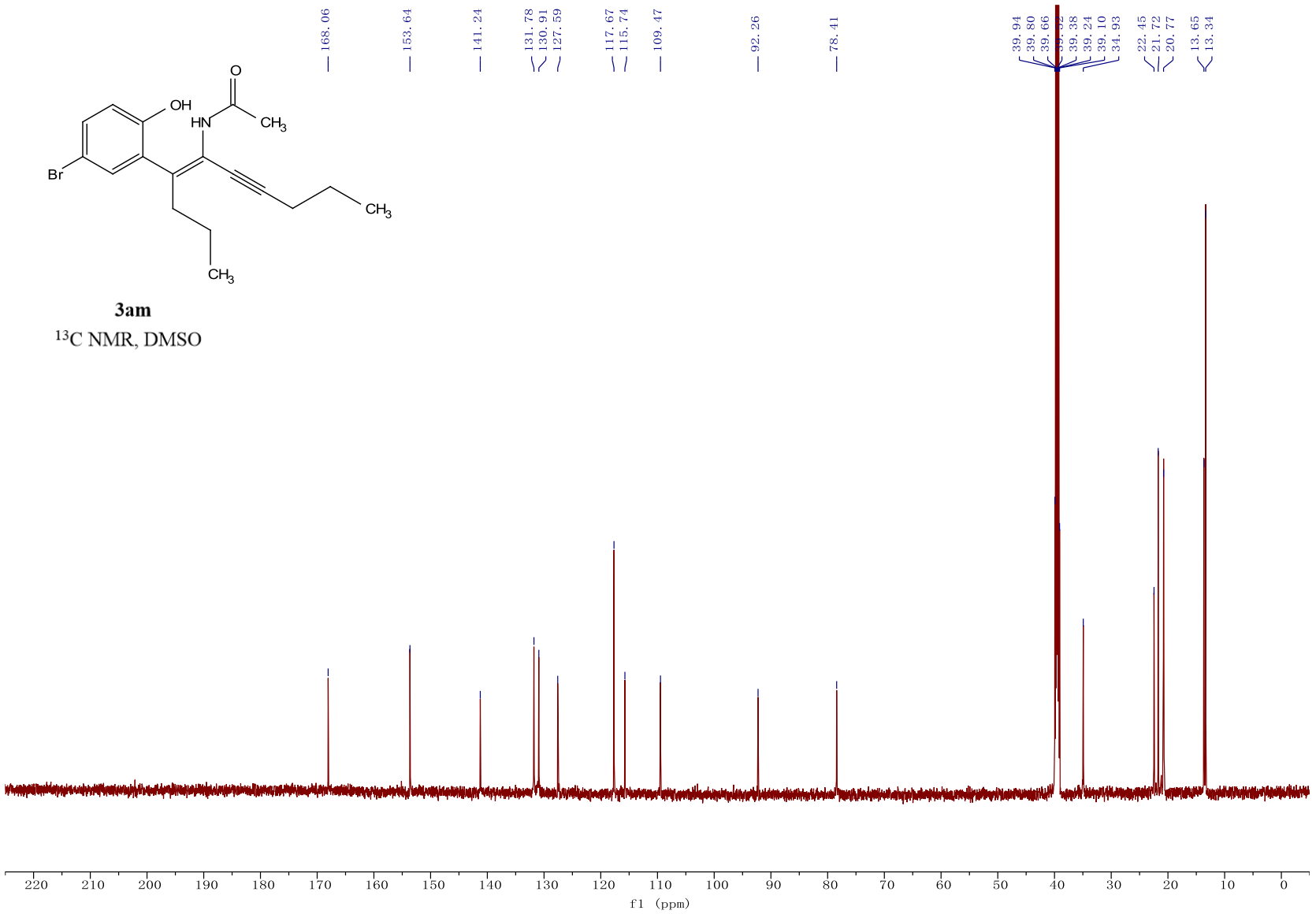
^{13}C NMR, DMSO



3am

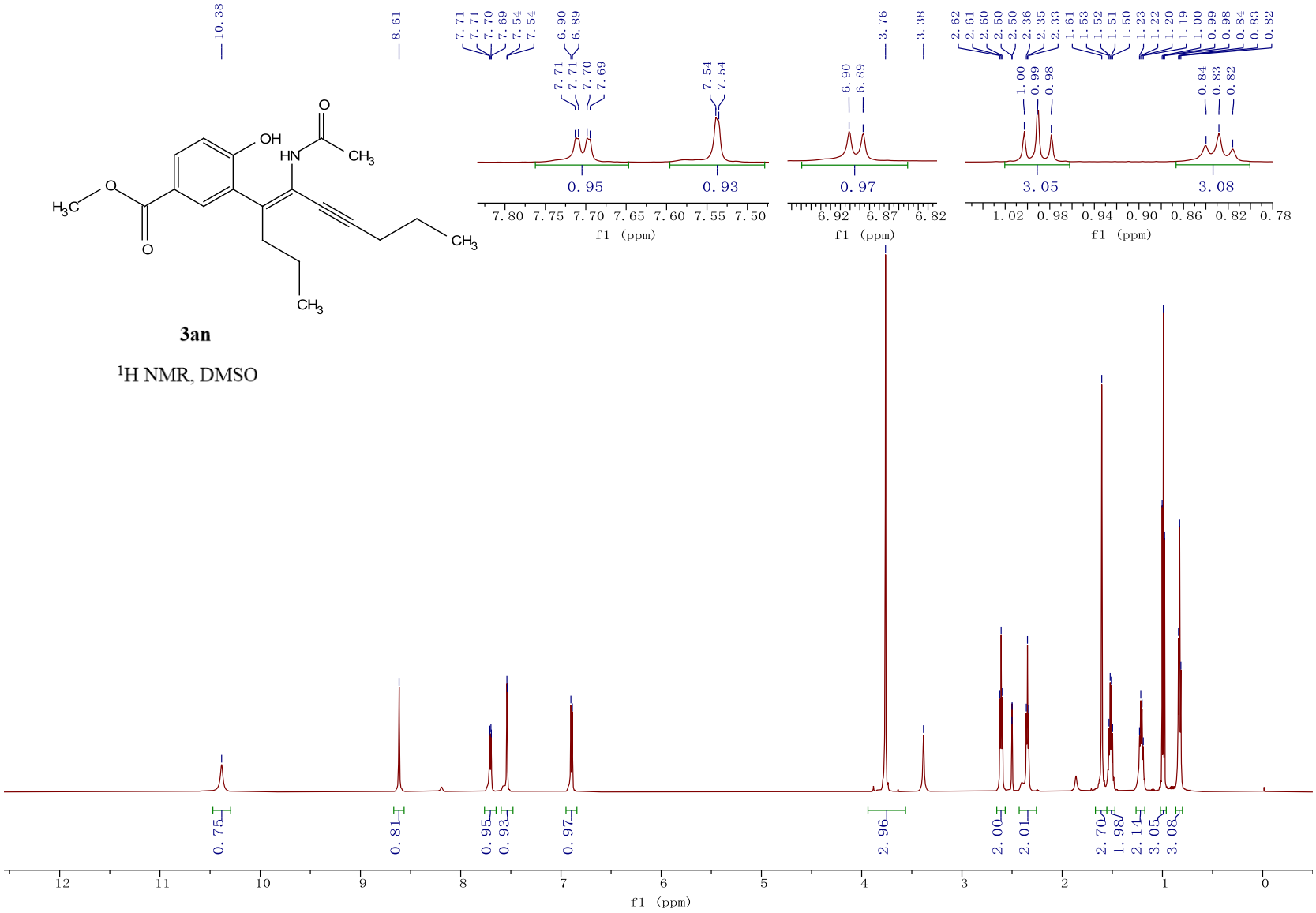
^{1}H NMR, DMSO





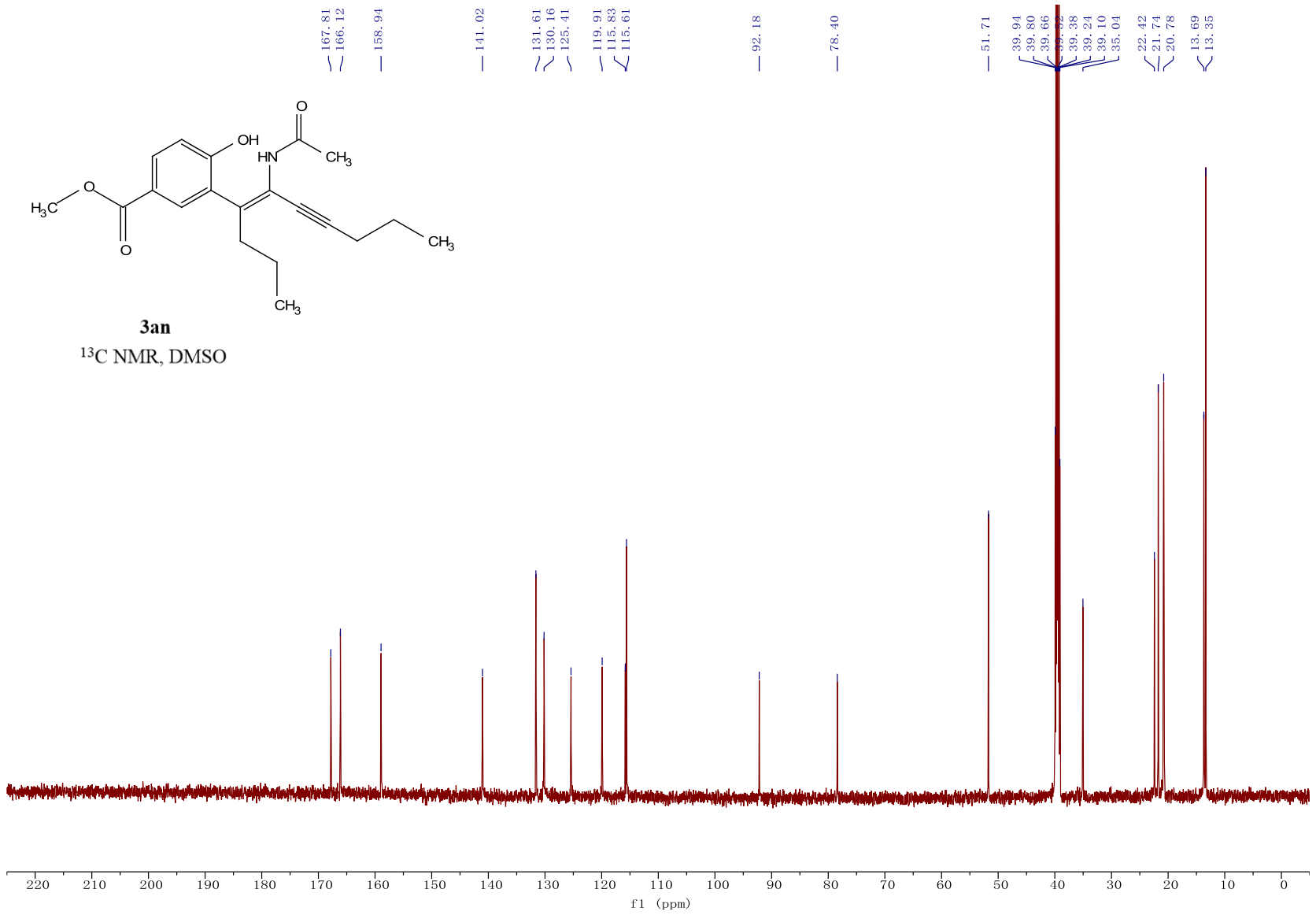
3am

^{13}C NMR, DMSO



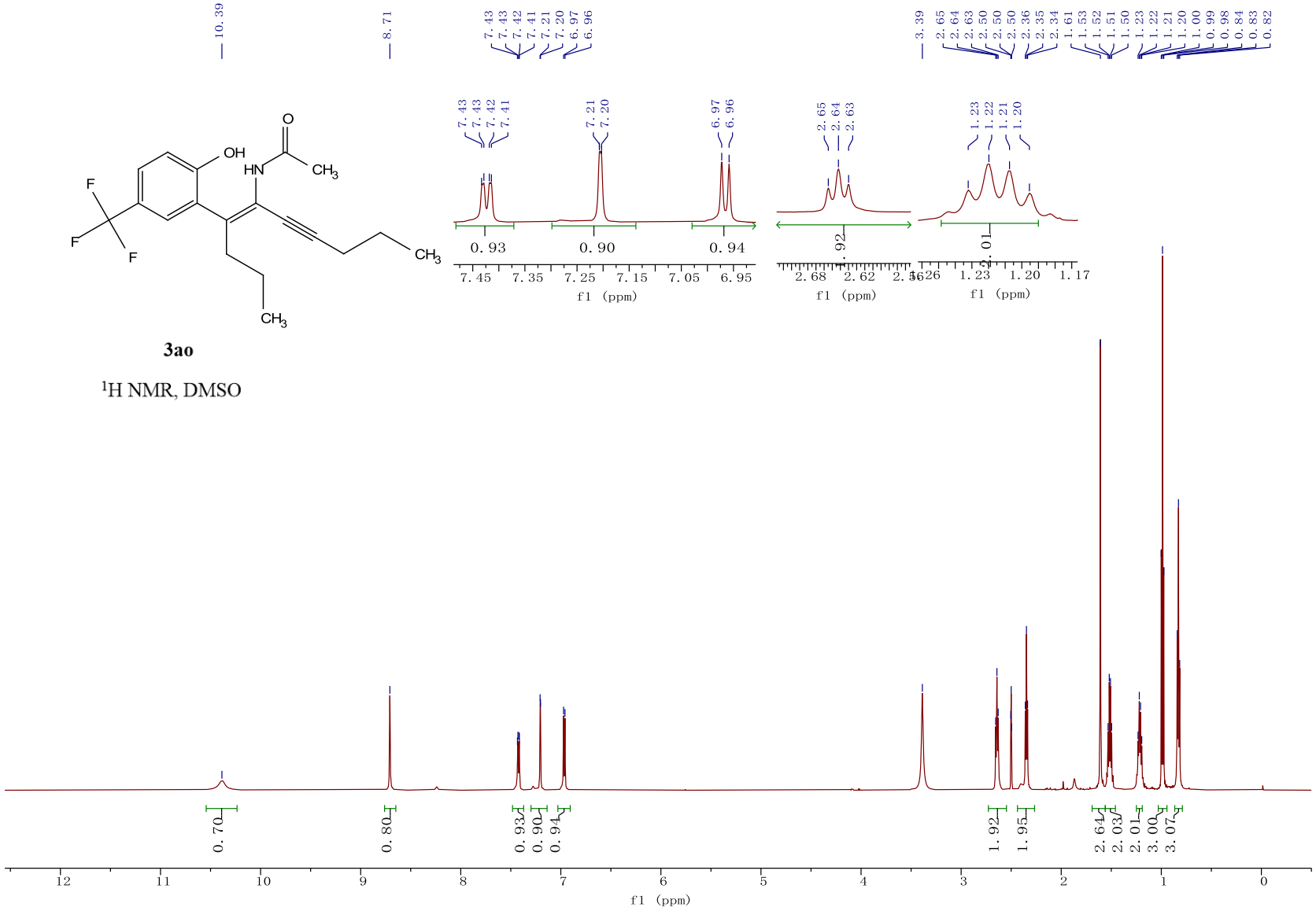
3an

^{1}H NMR, DMSO



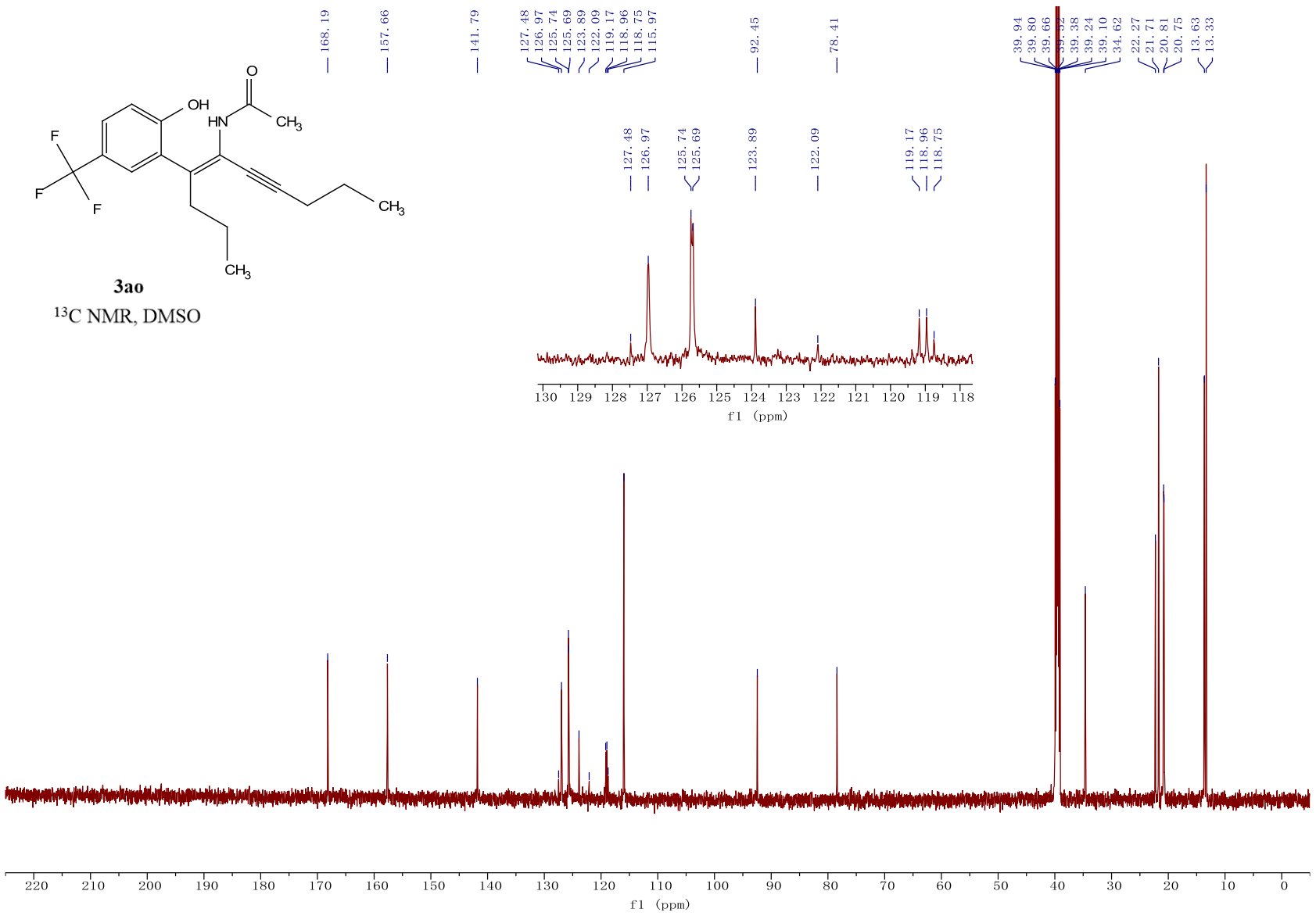
3an

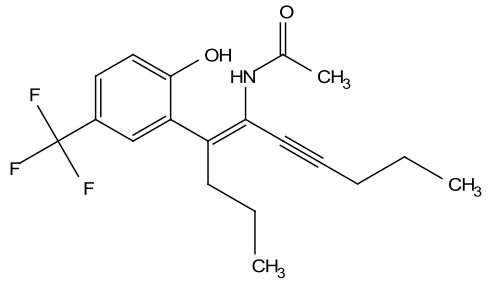
^{13}C NMR, DMSO



3ao

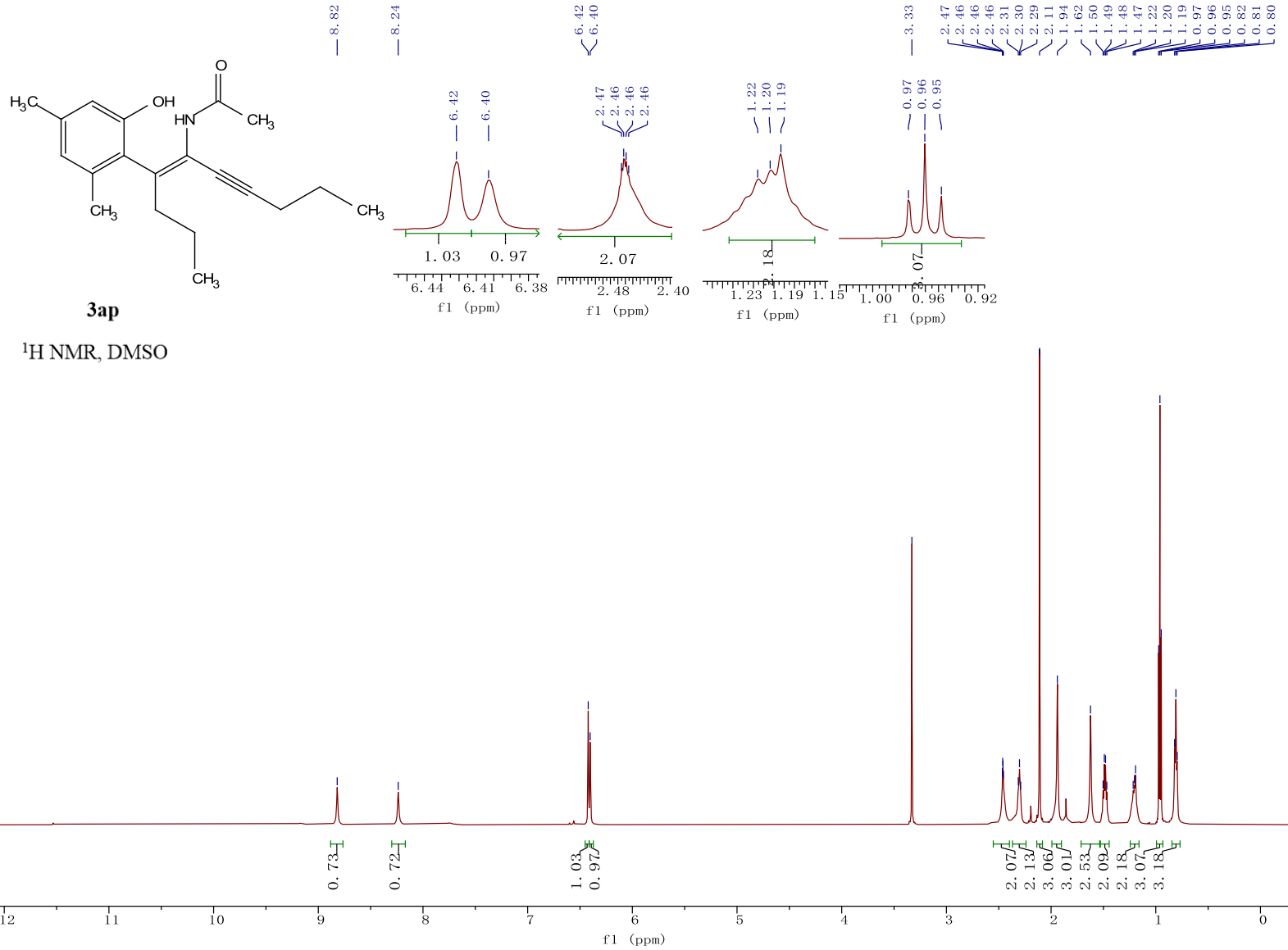
^{1}H NMR, DMSO


168.19
157.66
141.79
127.48
126.97
125.74
125.69
123.89
122.09
119.17
118.96
118.75
115.97
92.45
78.41
39.94
39.80
39.66
39.52
39.38
39.24
39.10
34.62
22.27
21.71
20.81
20.75
13.63
13.33
O
OH
HN
CH3
F
F
F
CH3
CH3
3ao
13C NMR, DMSO
f1 (ppm)
f1 (ppm)



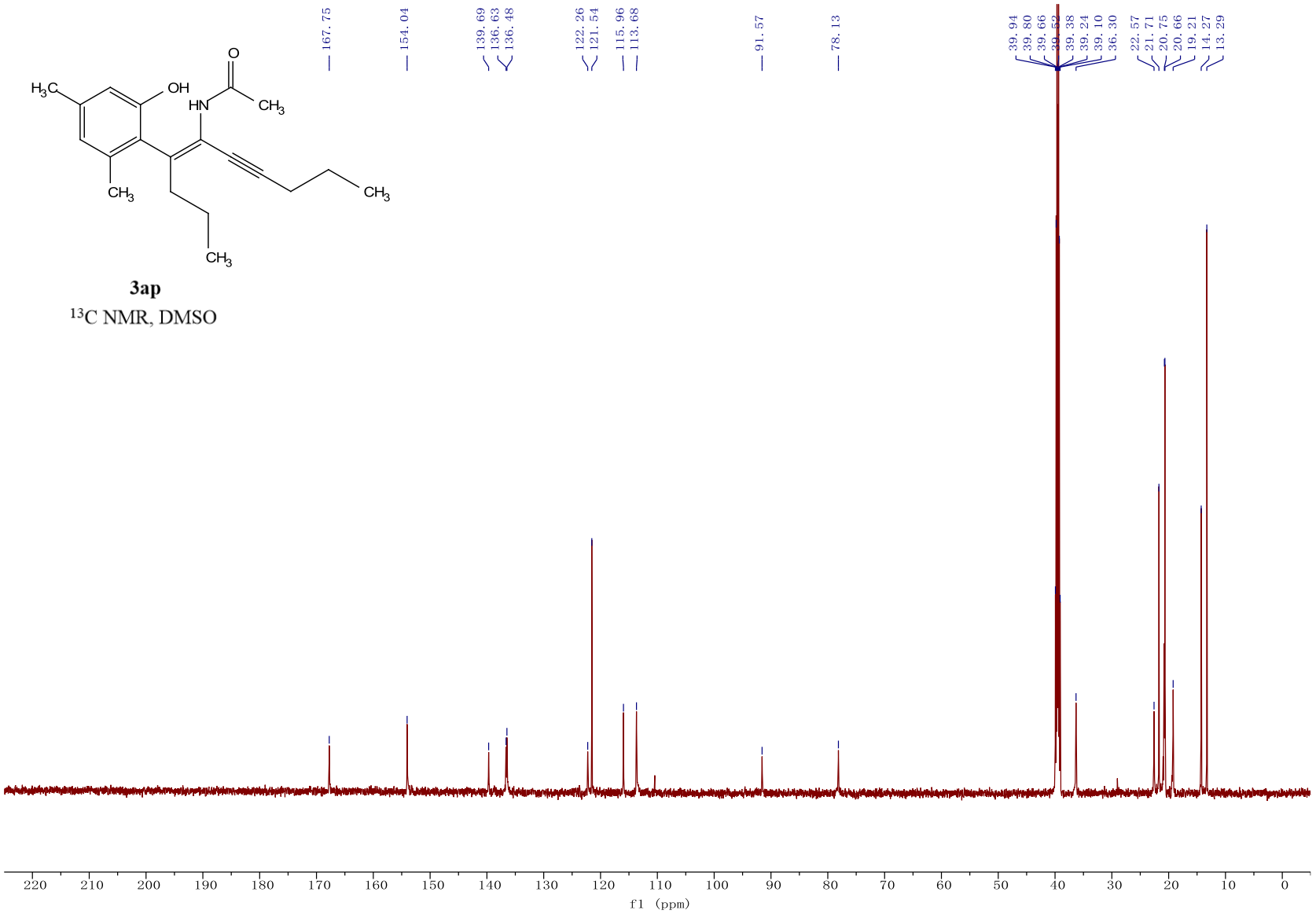
3ao

^{19}F NMR, DMSO



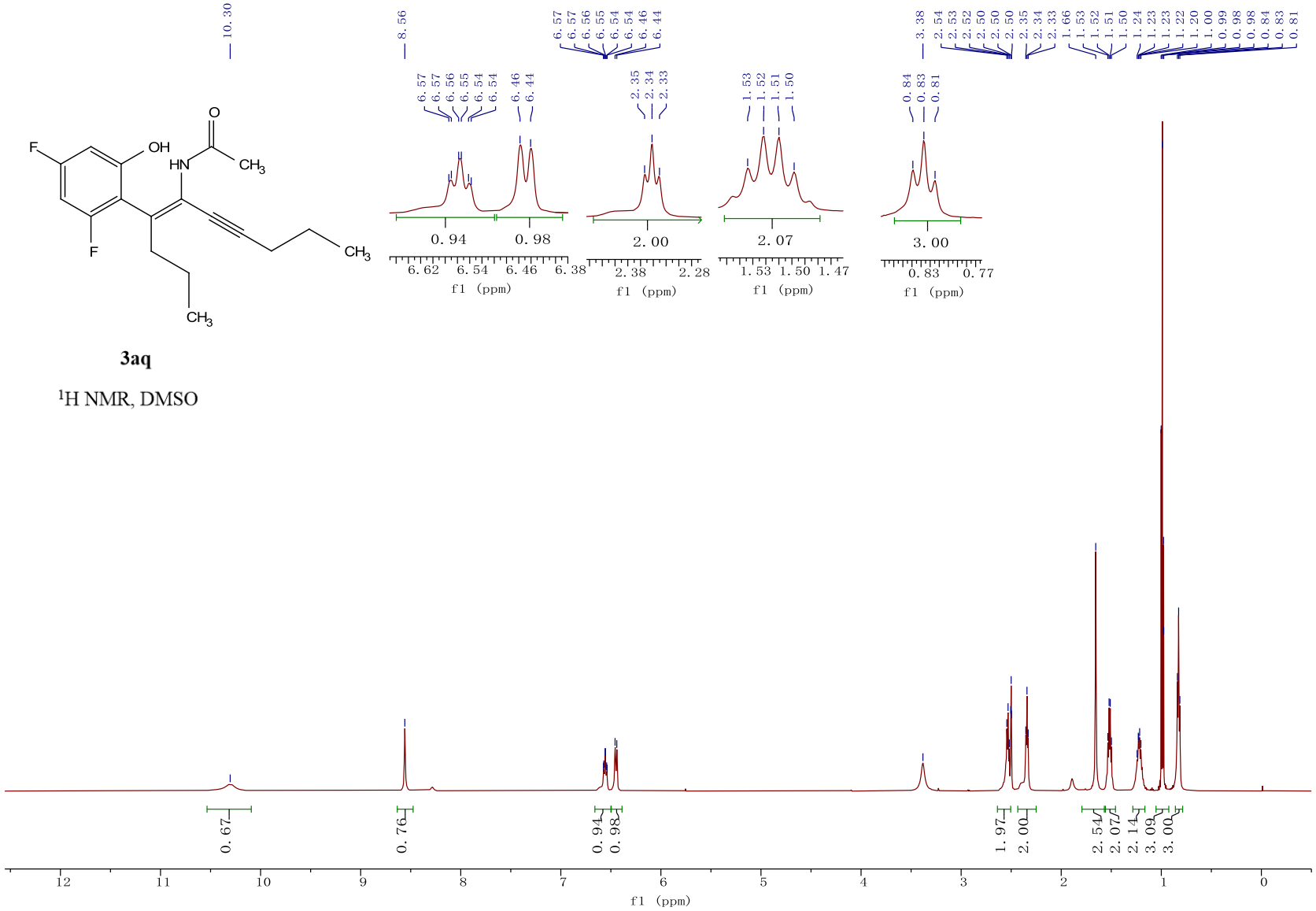
3ap

^{1}H NMR, DMSO



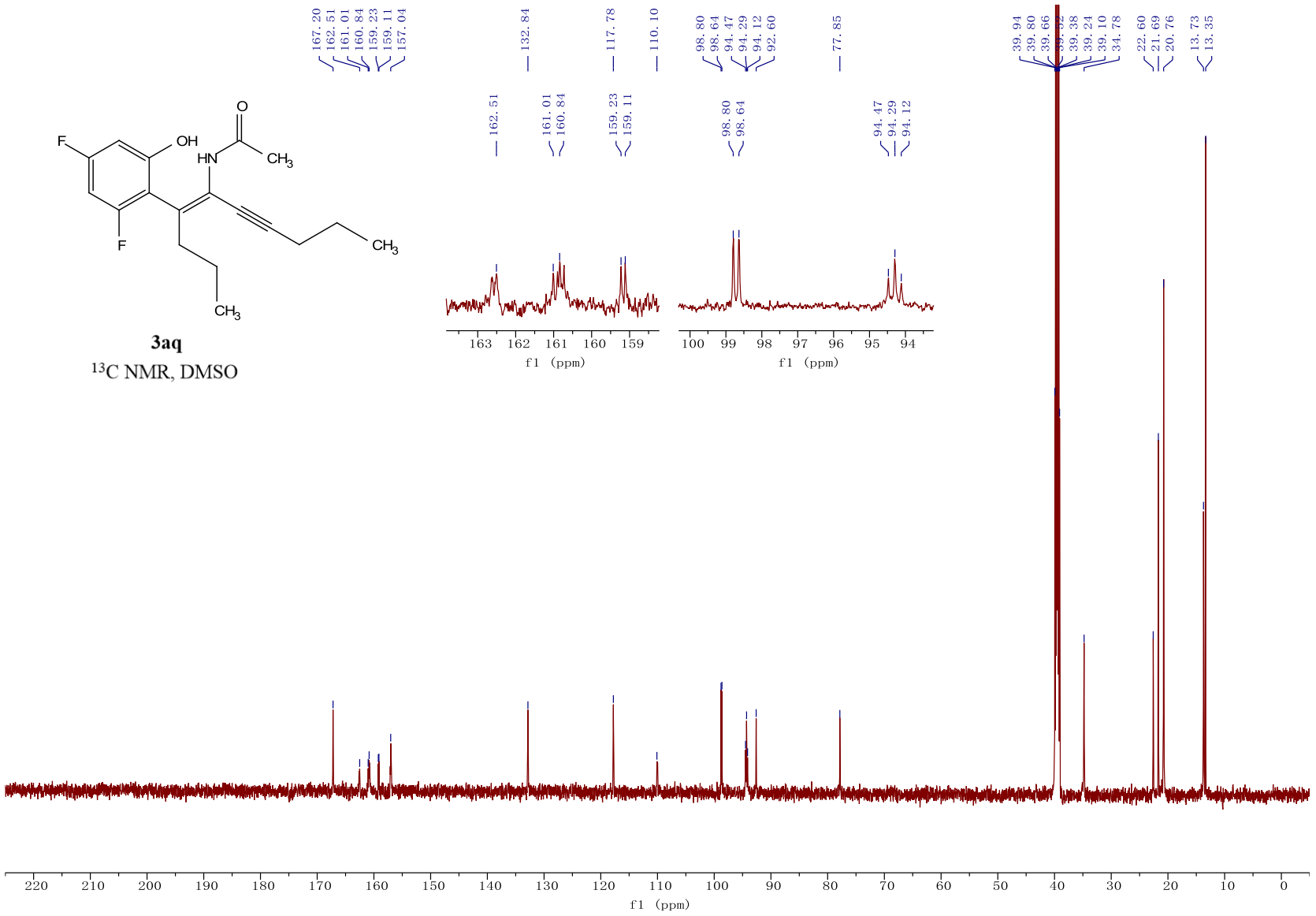
3ap

^{13}C NMR, DMSO



3aq

^{1}H NMR, DMSO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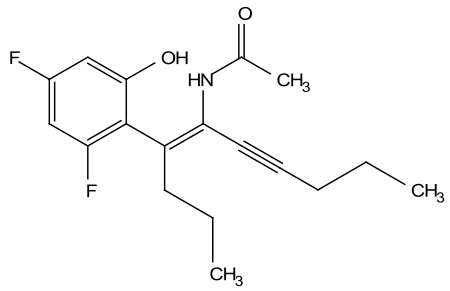
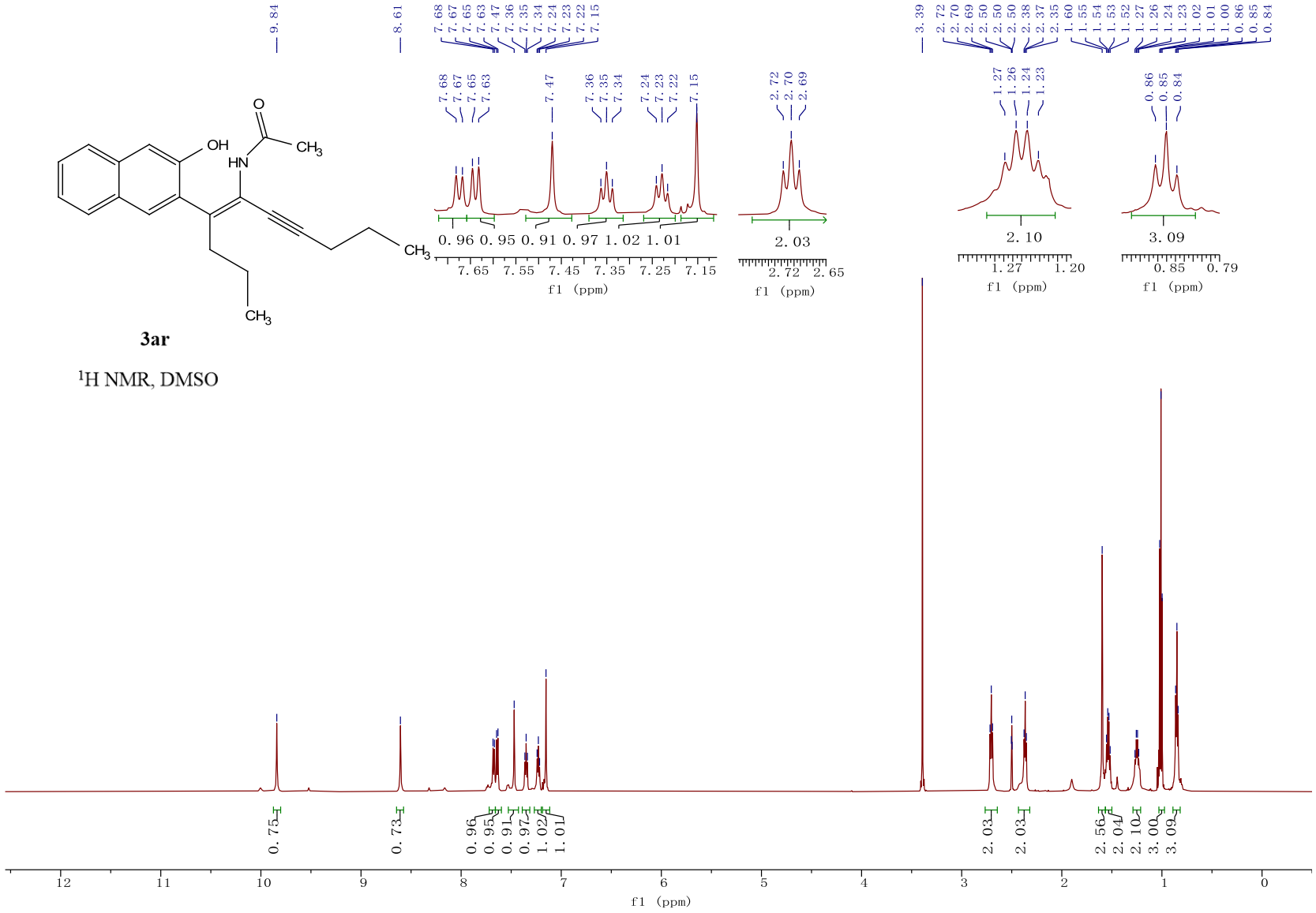
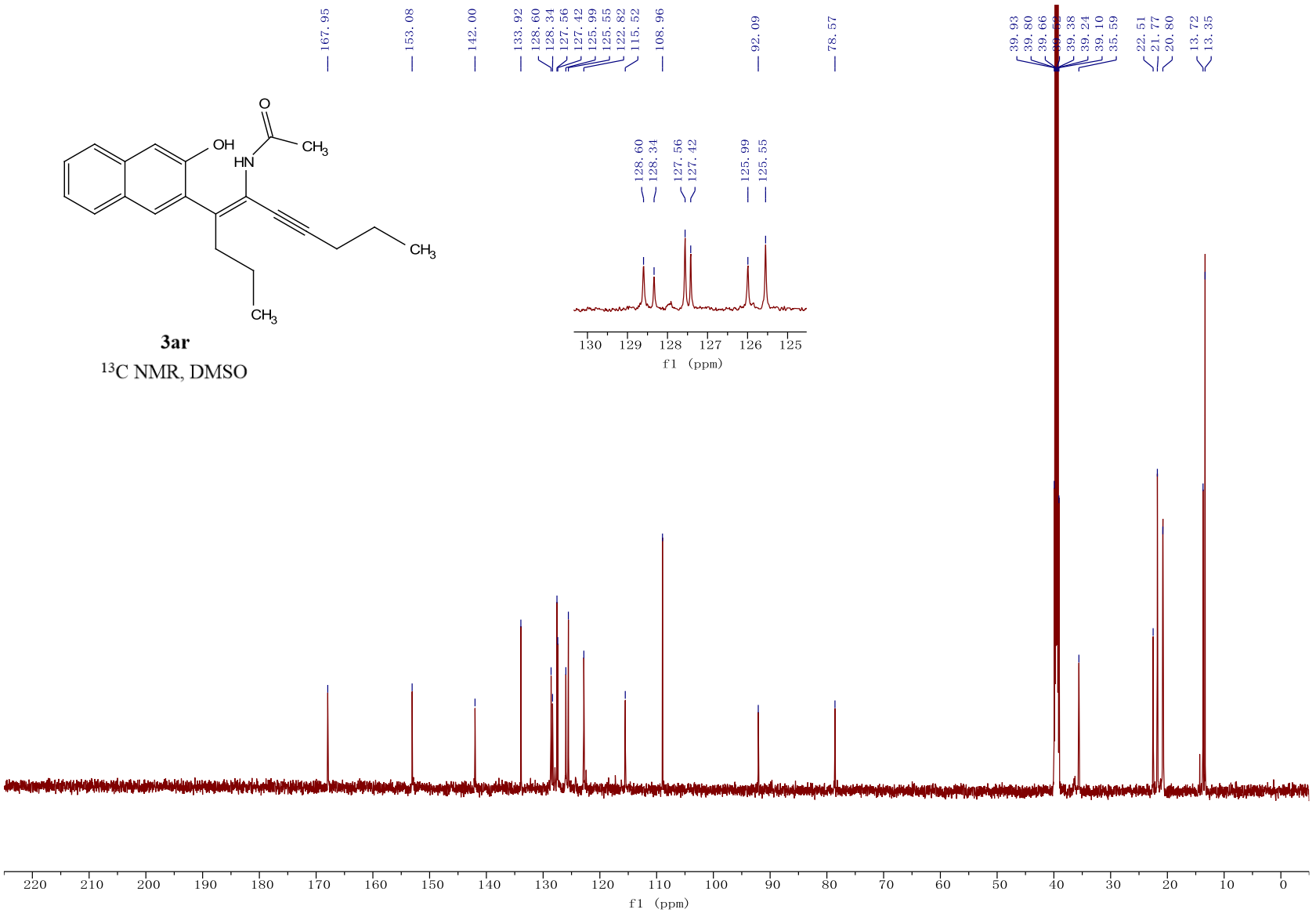
162.51
161.01
160.84
159.23
159.11
157.04
132.84
117.78
110.10
98.80
98.64
94.47
94.29
94.12
92.60
77.85
39.94
39.80
39.66
39.52
39.38
39.24
39.10
34.78
22.60
21.69
20.76
13.73
13.35
F
OH
HN
O
CH3
F
CH3
CH3
3aq
13C NMR, DMSO
162.51
161.01
160.84
159.23
159.11
98.80
98.64
94.47
94.29
94.12
163 162 161 160 159
f1 (ppm)
100 99 98 97 96 95 94
f1 (ppm)
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



3aq

^{19}F NMR, DMSO


OH
HN
O
CH3
CH3
CH3
3ar
1H NMR, DMSO
9.84
8.61
7.68 7.67 7.65 7.63 7.47 7.36 7.35 7.34 7.24 7.23 7.22 7.15
0.96 0.95 0.91 0.97 1.02 1.01
2.72 2.70 2.69
2.03
3.39
2.72 2.70 2.69 2.50 2.38 2.37 2.35 1.60 1.55 1.54 1.53 1.52 1.27 1.26 1.24 1.23 1.02 1.01 1.00 0.86 0.85 0.84
1.27 1.26 1.24 1.23
2.10
0.86 0.85 0.84
3.09
f1 (ppm)
0.75 0.73 0.96 0.95 0.91 0.97 1.02 1.01 2.03 2.03 2.56 2.04 2.10 3.00 3.09


167.95
153.08
142.00
133.92
128.60
128.34
127.56
127.42
125.99
125.55
122.82
115.52
108.96
92.09
78.57
39.93
39.80
39.66
39.52
39.38
39.24
39.10
35.59
22.51
21.77
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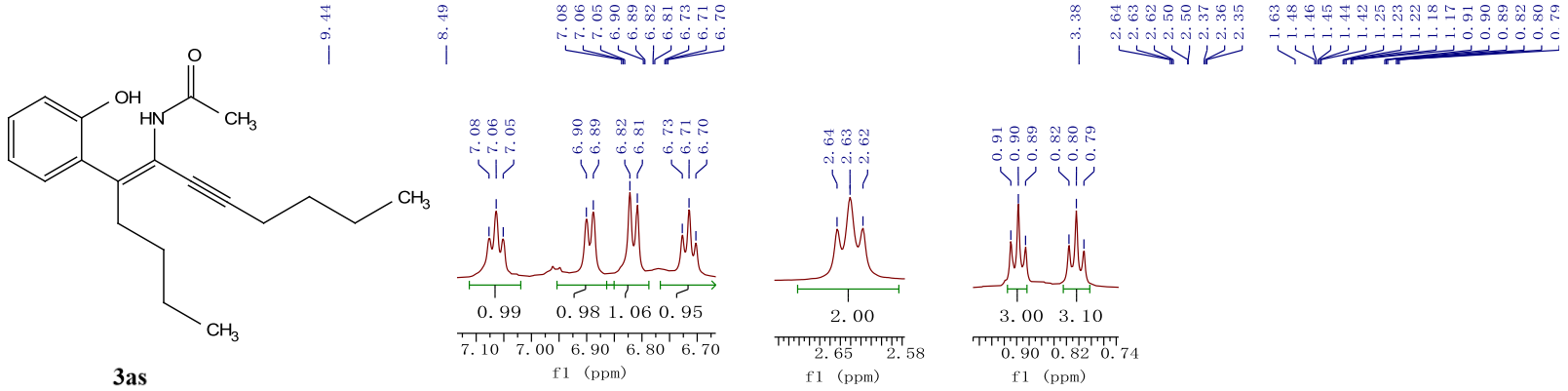
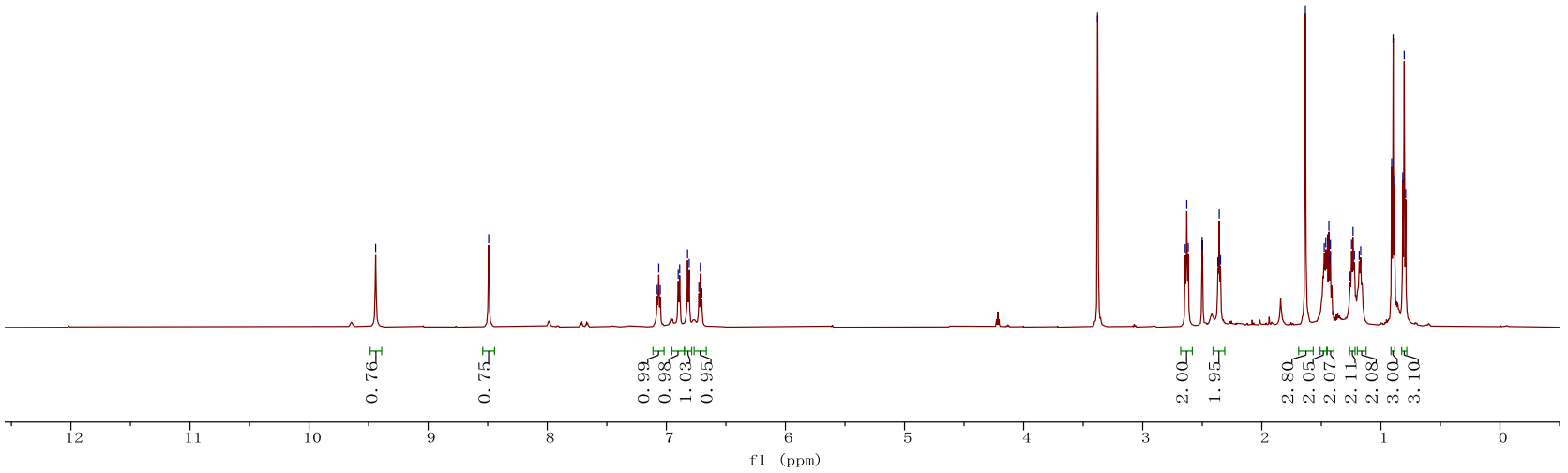
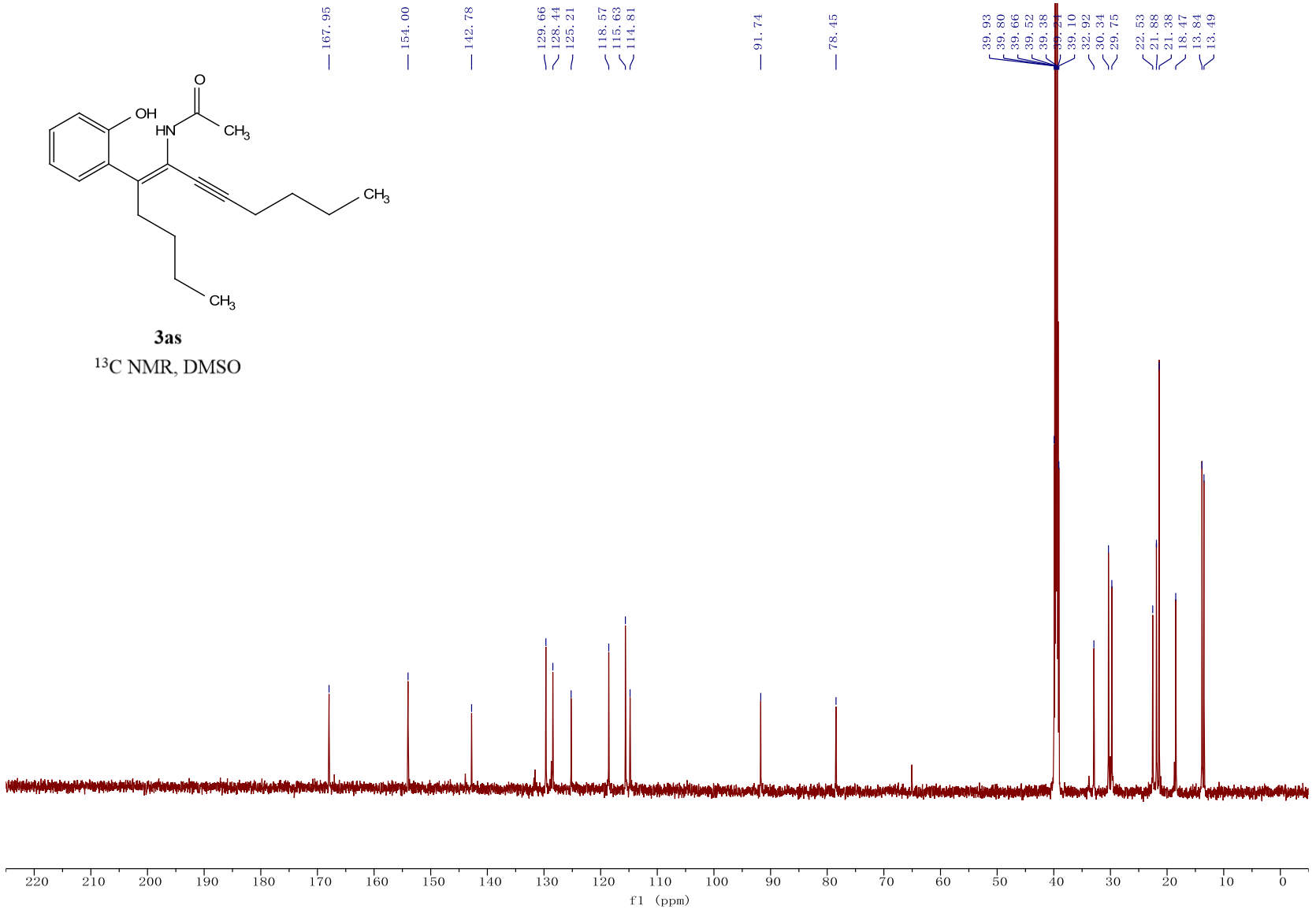
OH
HN
O
CH3
CH3
CH3
3ar
13C NMR, DMSO
f1 (ppm)
f1 (ppm)



3as

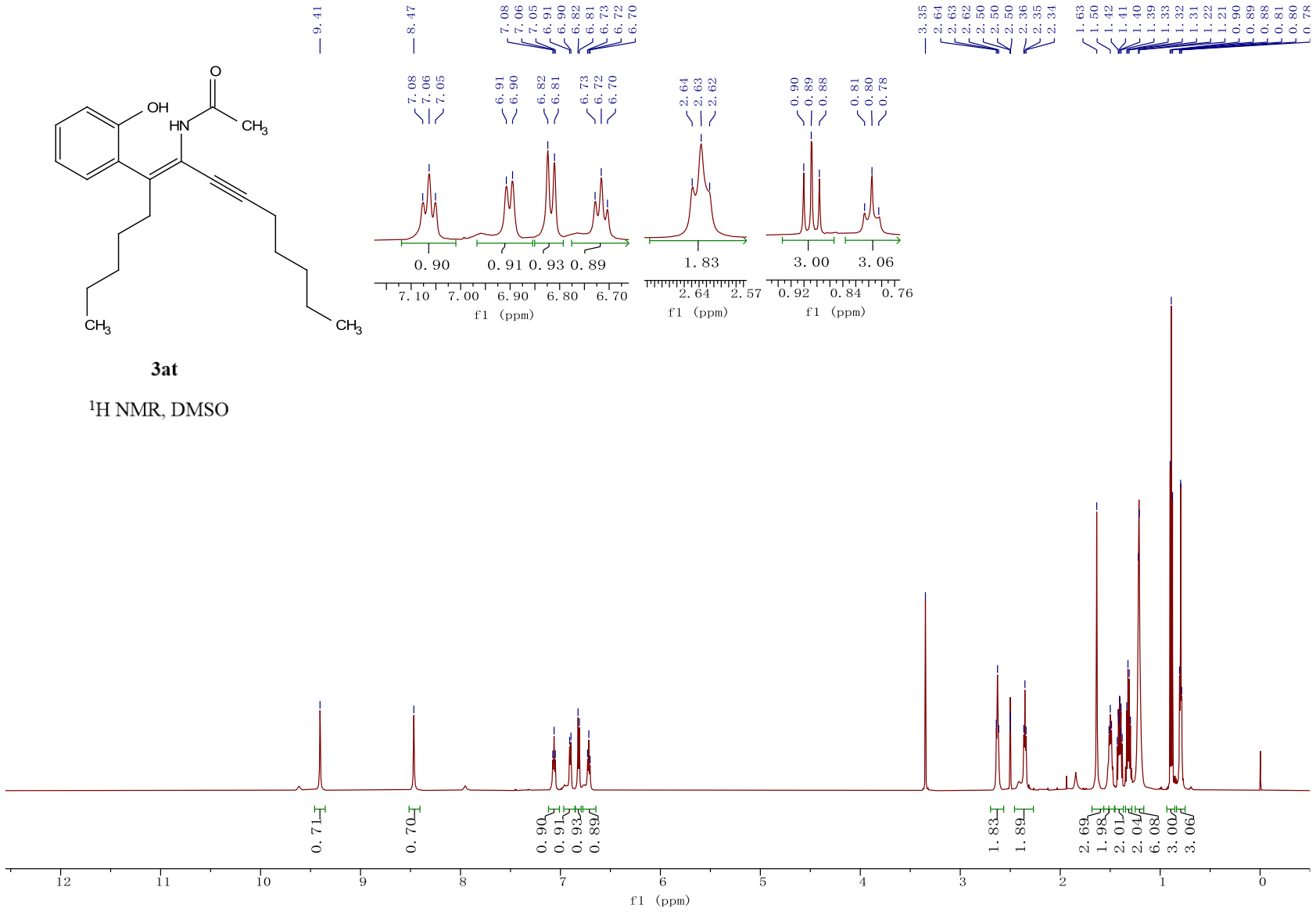
^{1}H NMR, DMSO





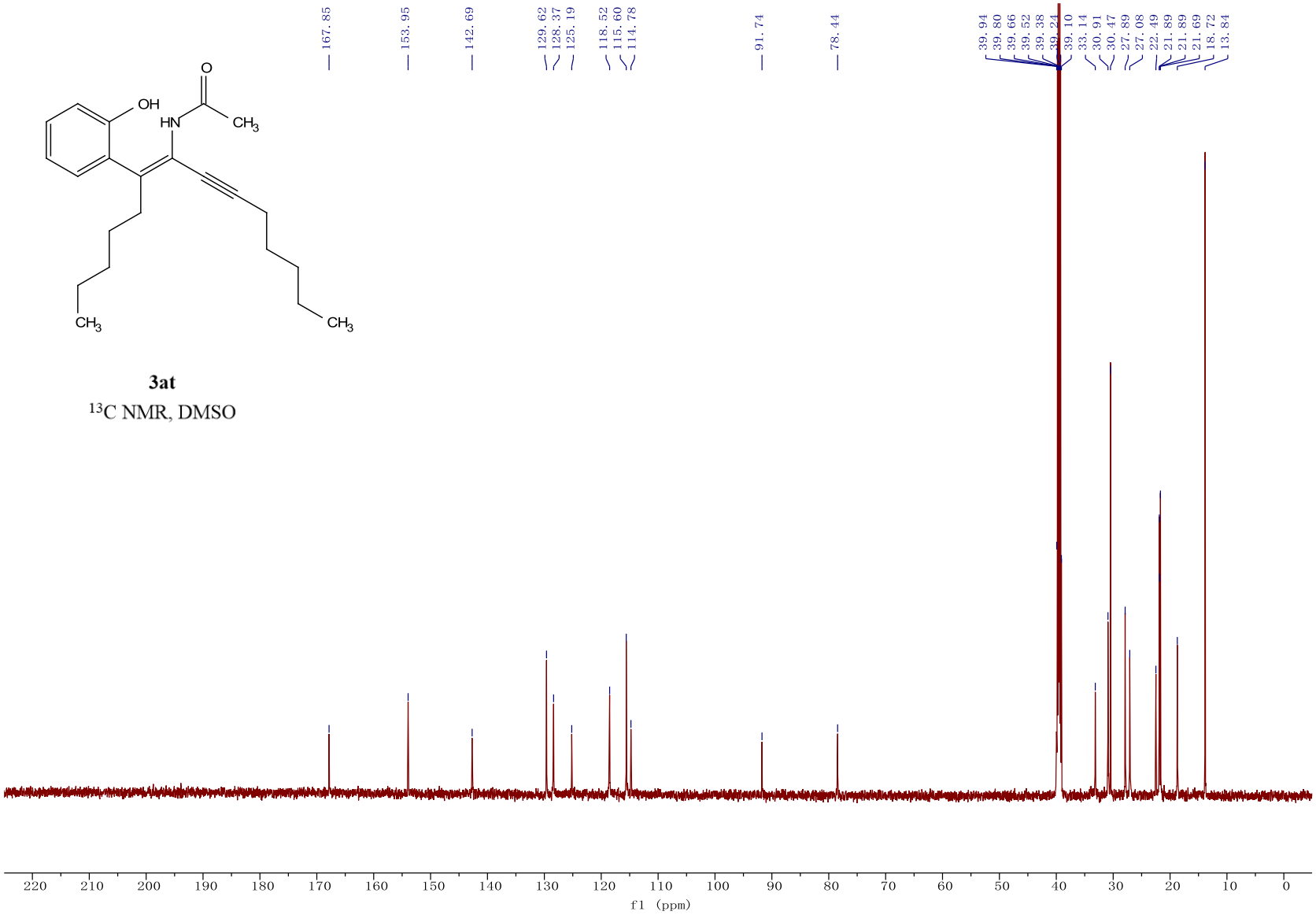
3as

^{13}C NMR, DMSO



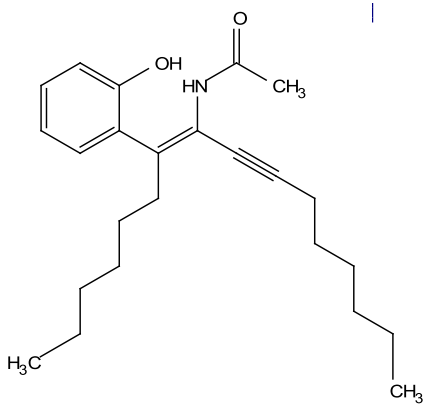
3at

^{1}H NMR, DMSO



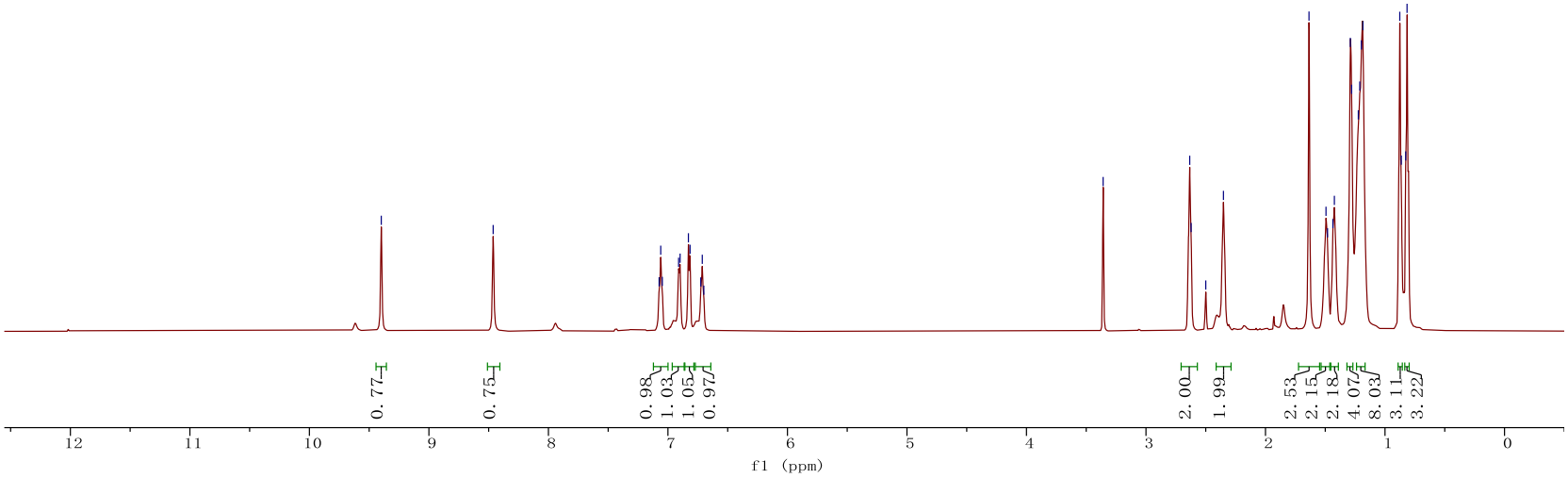
3at

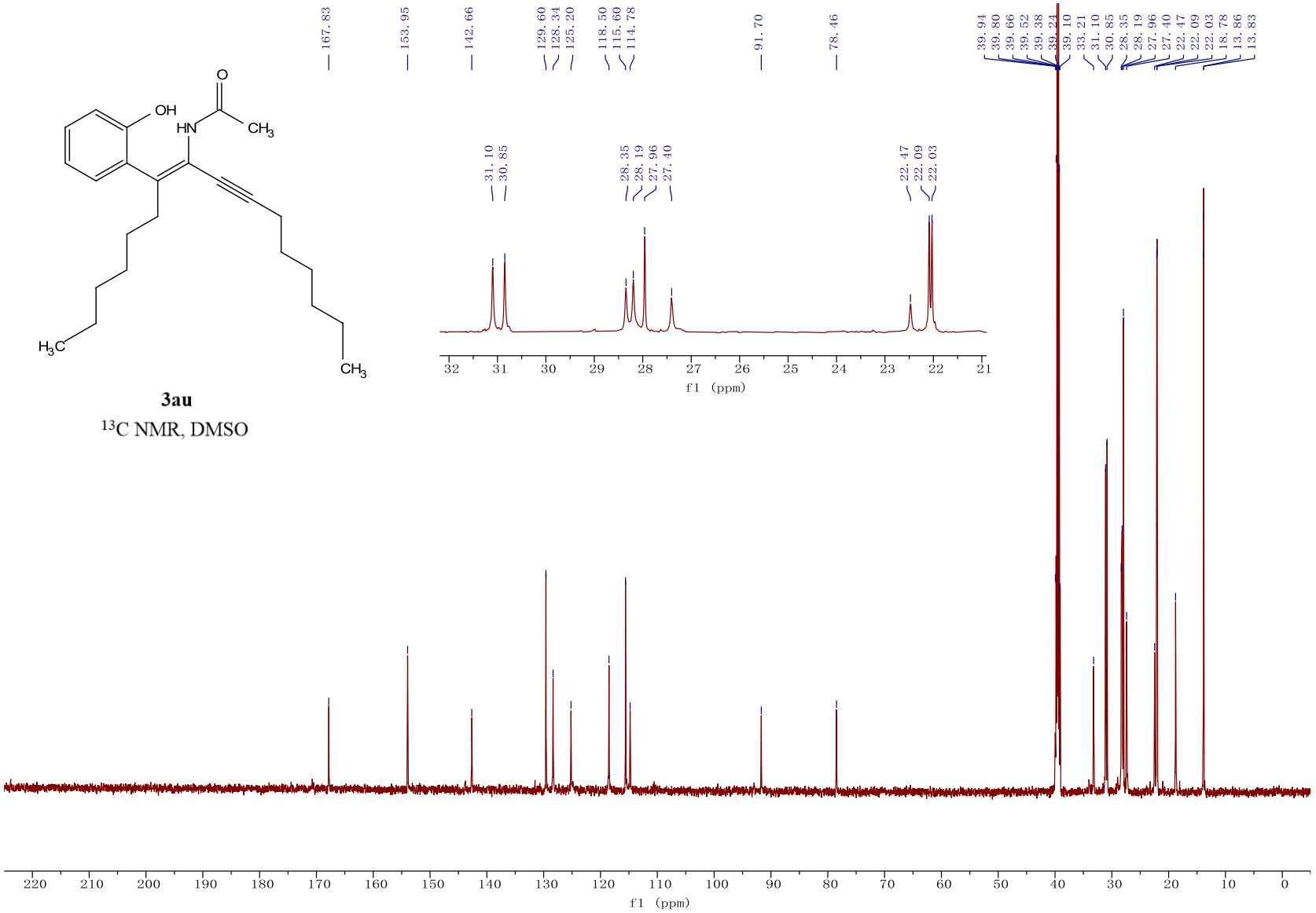
^{13}C NMR, DMSO



3au

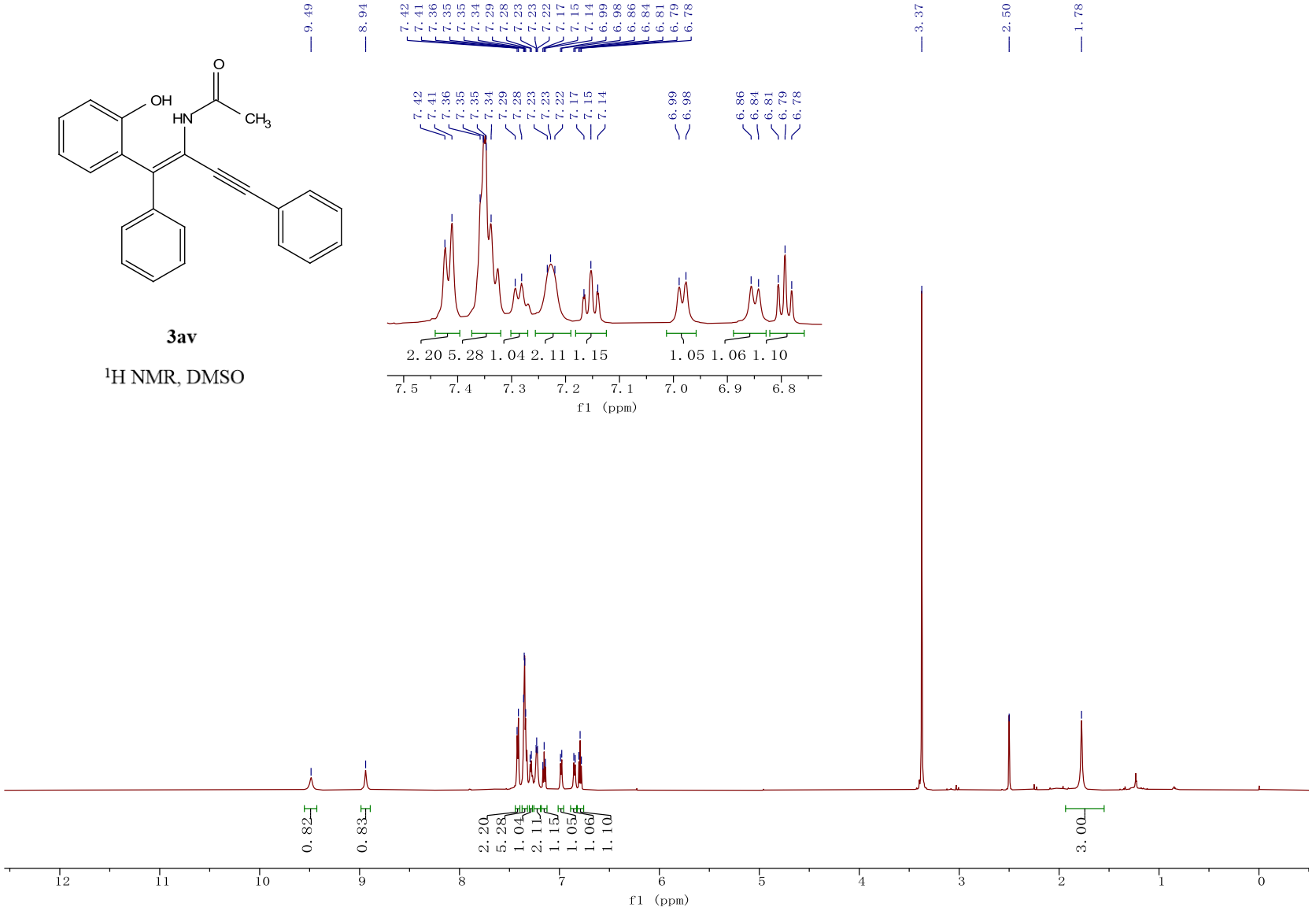
^{1}H NMR, DMSO





3au

^{13}C NMR, DMSO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8.94
7.42
7.41
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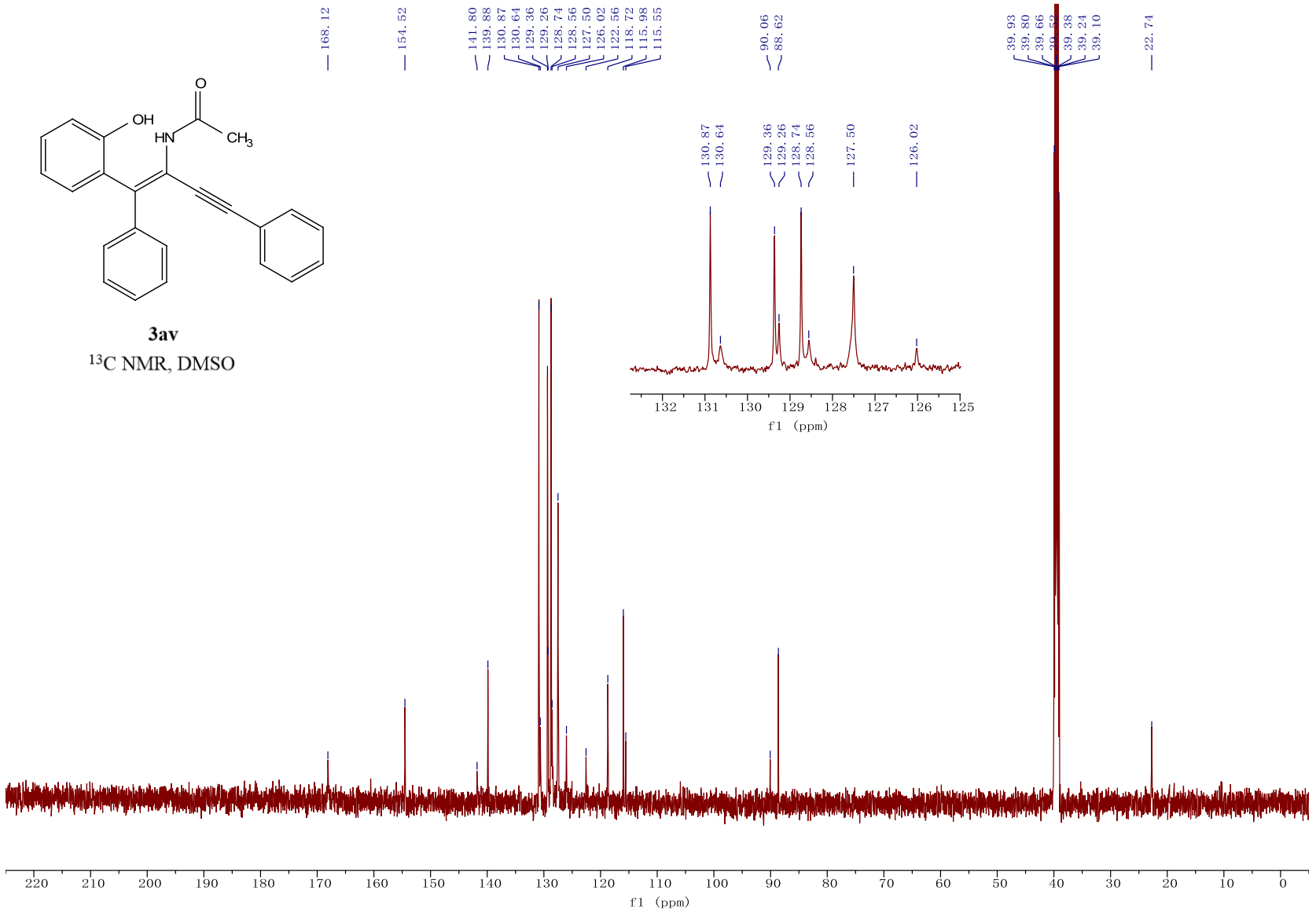
7.35
7.34
7.29
7.28
7.23
7.23
7.22
7.17
7.15
7.14
6.99
6.98
6.86
6.84
6.81
6.79
6.78
3.37
2.50
1.78
OH
HN
O
CH3
3av
1H NMR, DMSO
2.20 5.28 1.04 2.11 1.15
1.05 1.06 1.10
f1 (ppm)
0.82
0.83
2.20
5.28
1.04
2.11
1.15
1.05
1.06
1.10
3.00
f1 (ppm)


OH
HN
O
CH3
3av
13C NMR, DMSO
168.12
154.52
141.80
139.88
130.87
130.64
129.36
129.26
128.74
128.56
127.50
126.02
122.56
118.72
115.98
115.55
90.06
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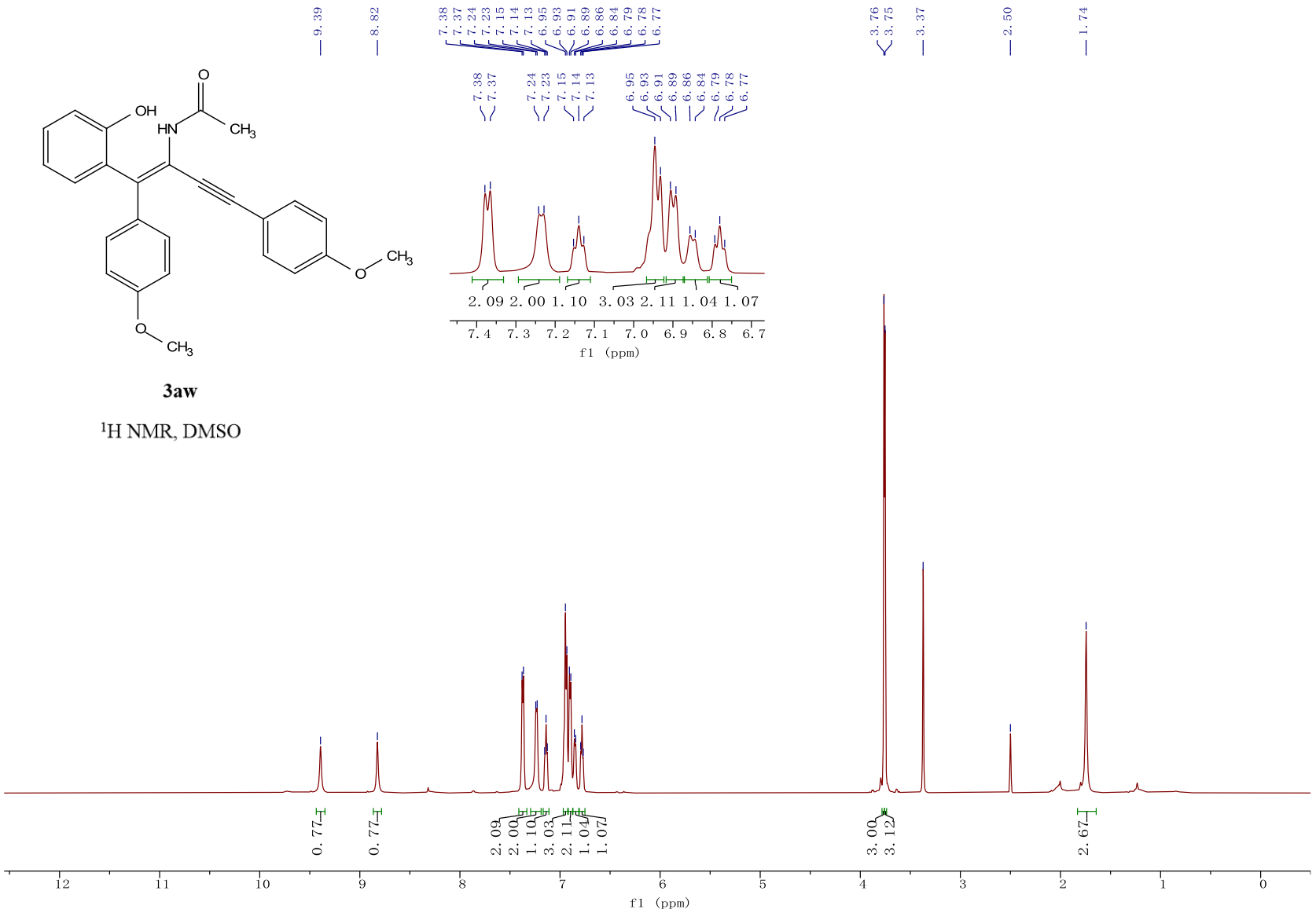
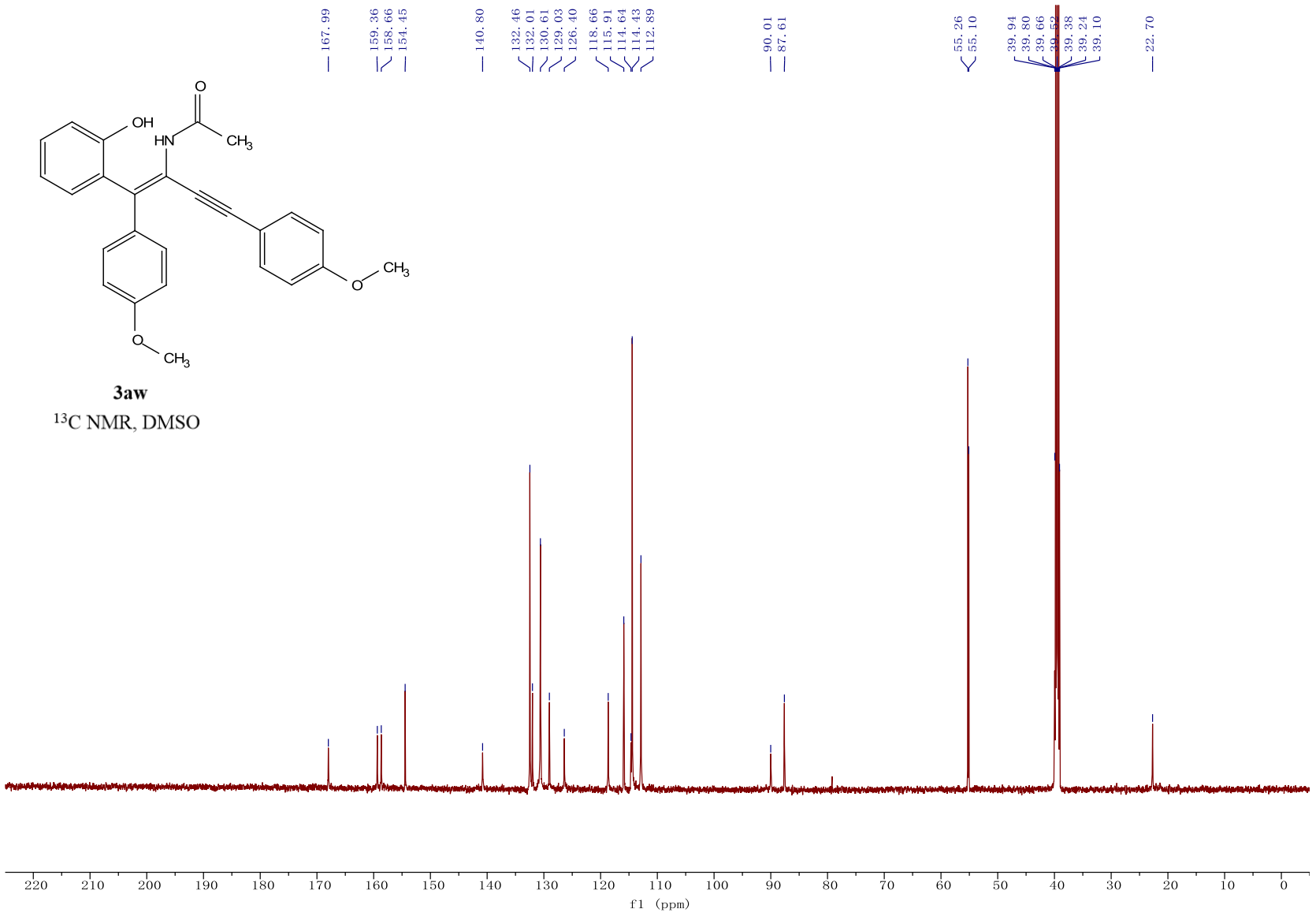
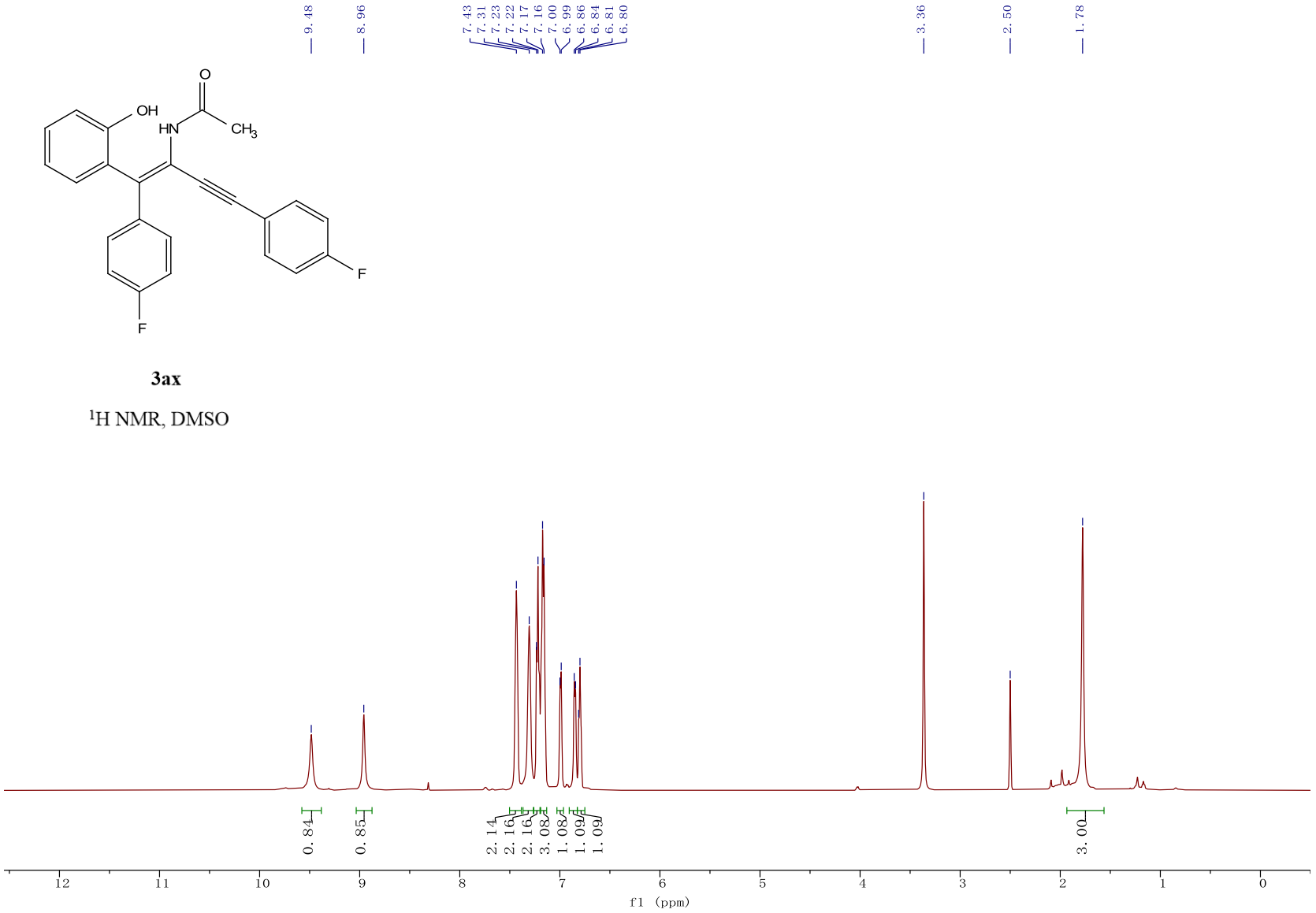
39.93
39.80
39.66
39.52
39.38
39.24
39.10
22.74
f1 (ppm)



3aw

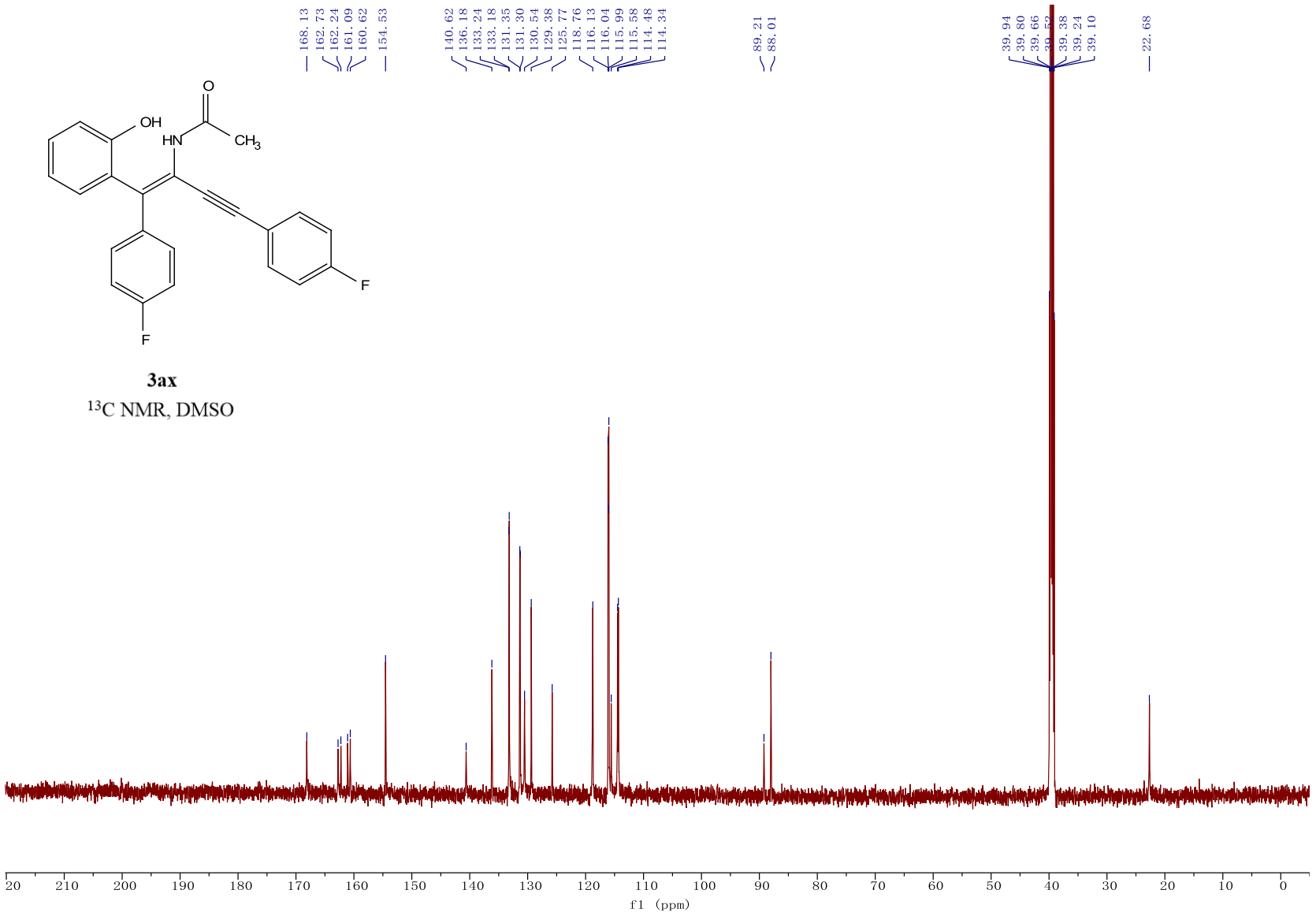
^{1}H NMR, DMSO


167.99
159.36
158.66
154.45
140.80
132.46
132.01
130.61
129.03
126.40
118.66
115.91
114.64
114.43
112.89
90.01
87.61
55.26
55.10
39.94
39.80
39.66
39.52
39.38
39.24
39.10
22.70
OH
HN
O
CH3
O
CH3
O
CH3
3aw
13C NMR, DMSO
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



3ax

^{1}H NMR, DMSO


168.13
162.73
162.24
161.09
160.62
154.53
140.62
136.18
133.24
133.18
131.35
131.30
130.54
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125.77
118.76
116.13
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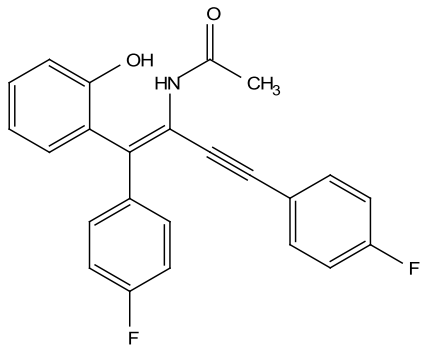
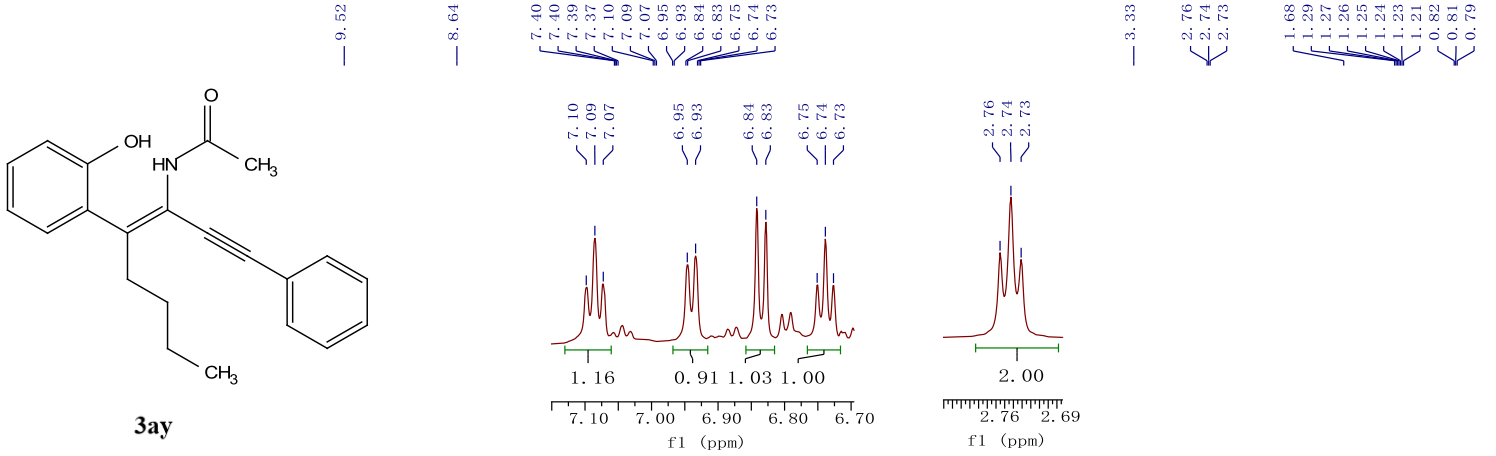
88.01
39.94
39.80
39.66
39.52
39.38
39.24
39.10
22.68
O
OH
HN
CH3
F
F
3ax
13C NMR, DMSO
20
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



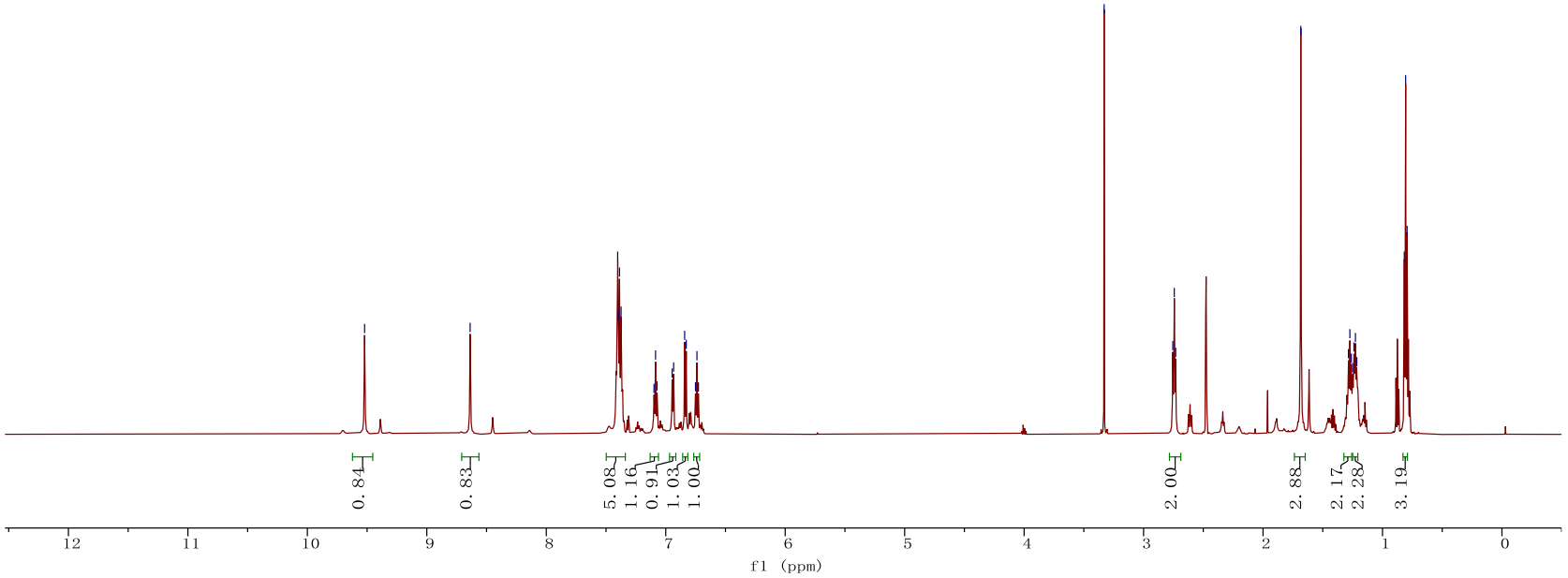
3ax

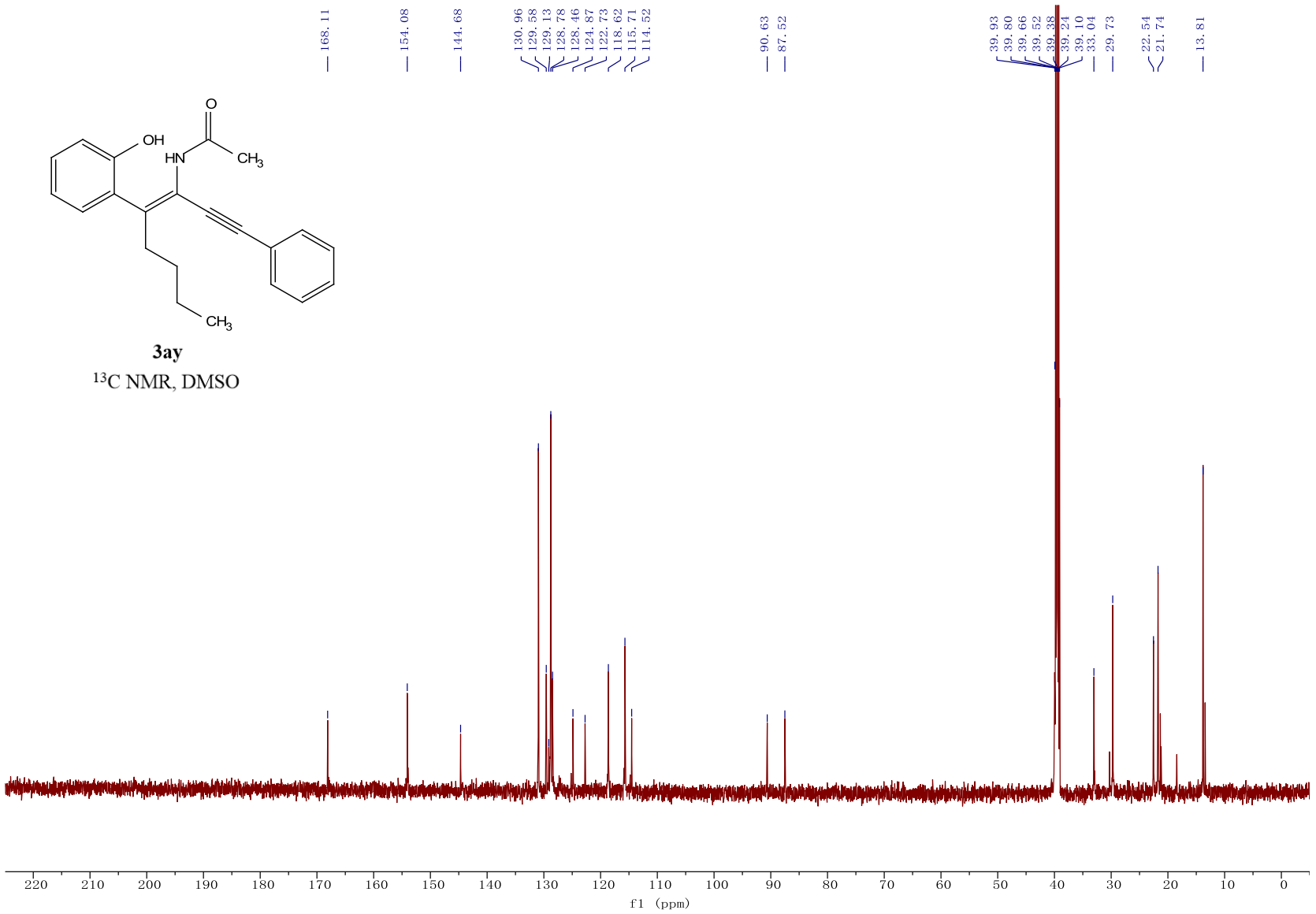
^{19}F NMR, DMSO



3ay

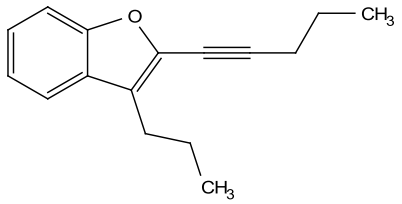
^{1}H NMR, DMSO





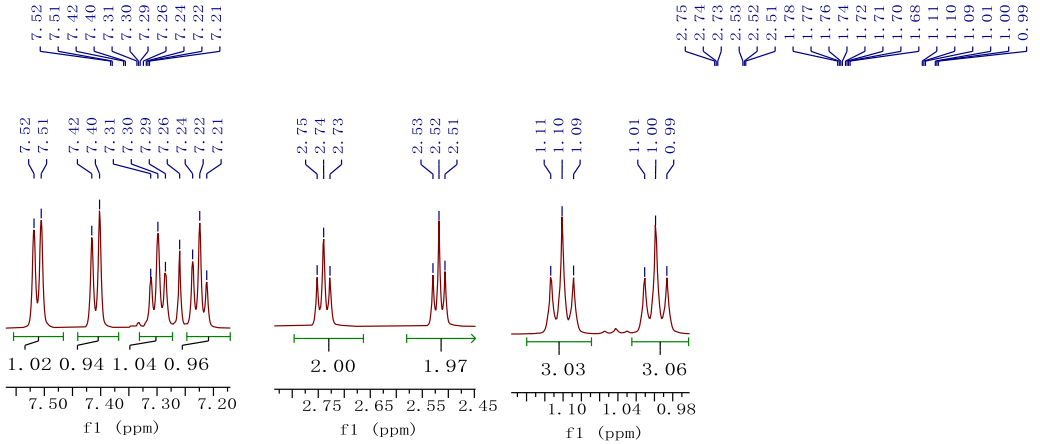
3ay

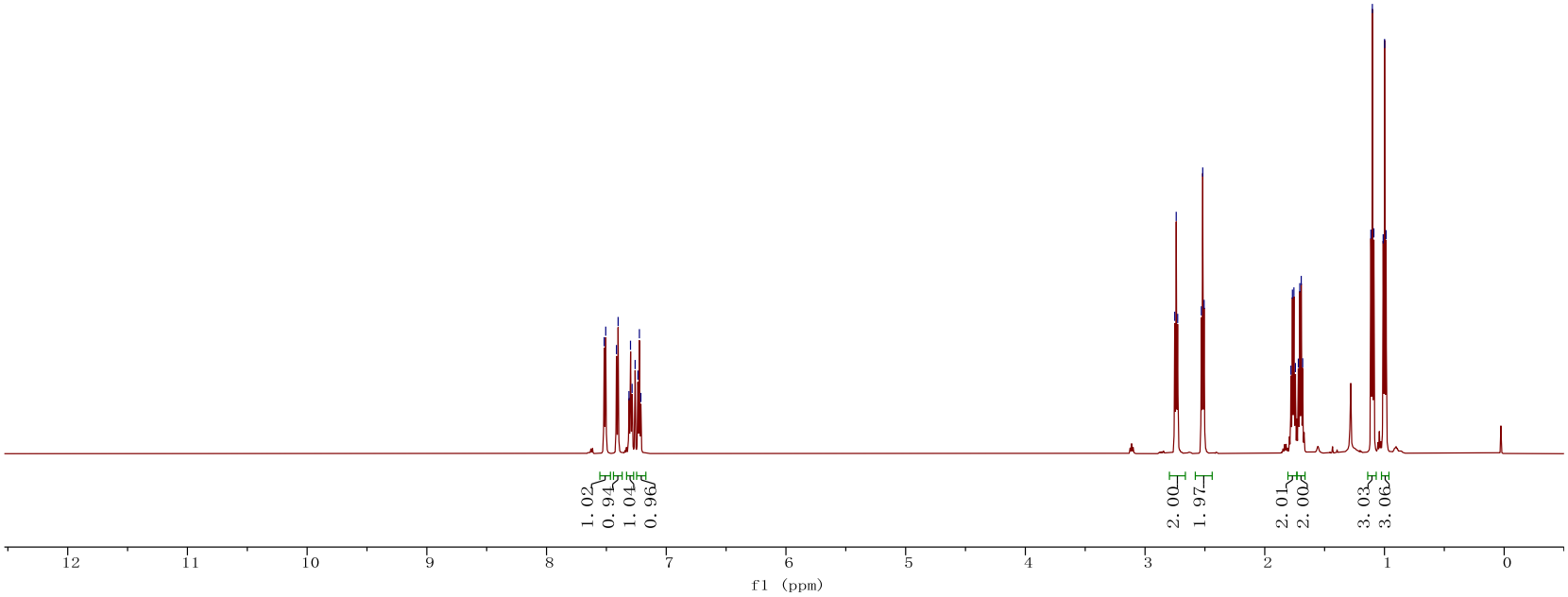
^{13}C NMR, DMSO

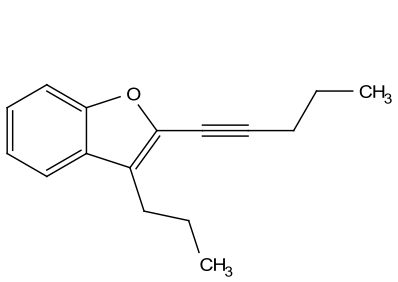


4aa

^{1}H NMR, $CDCl_3$

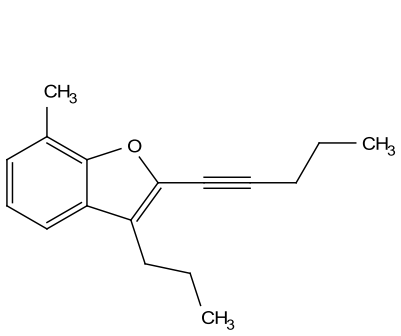






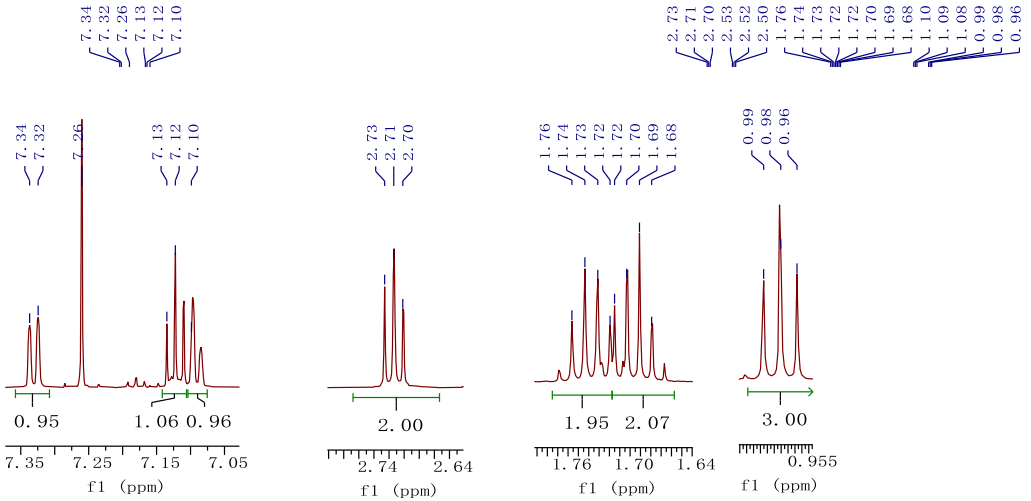
4aa

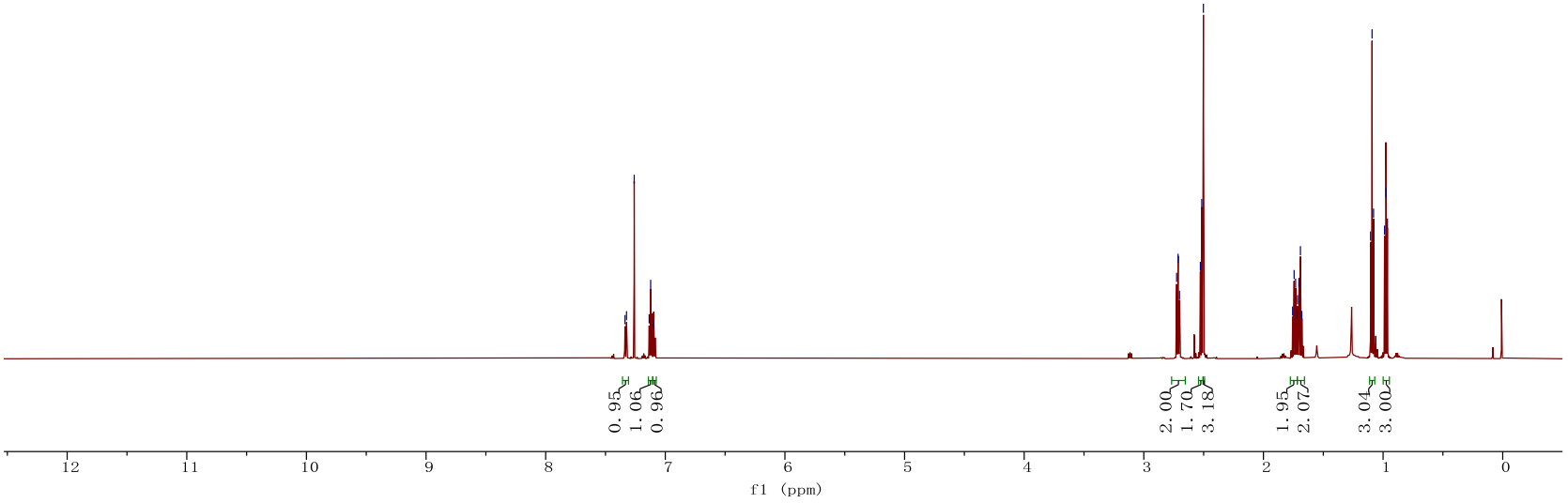
^{13}C NMR, $CDCl_3$

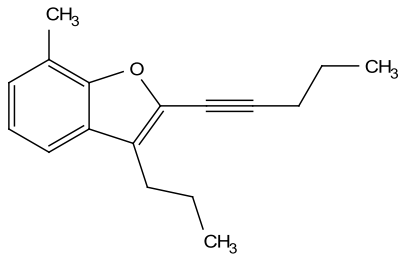


4ab

^{1}H NMR, $CDCl_3$

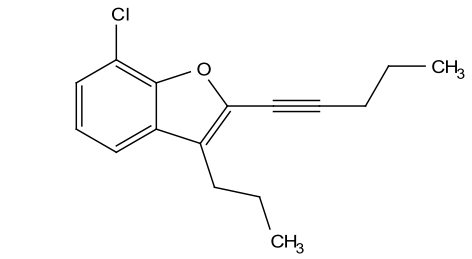






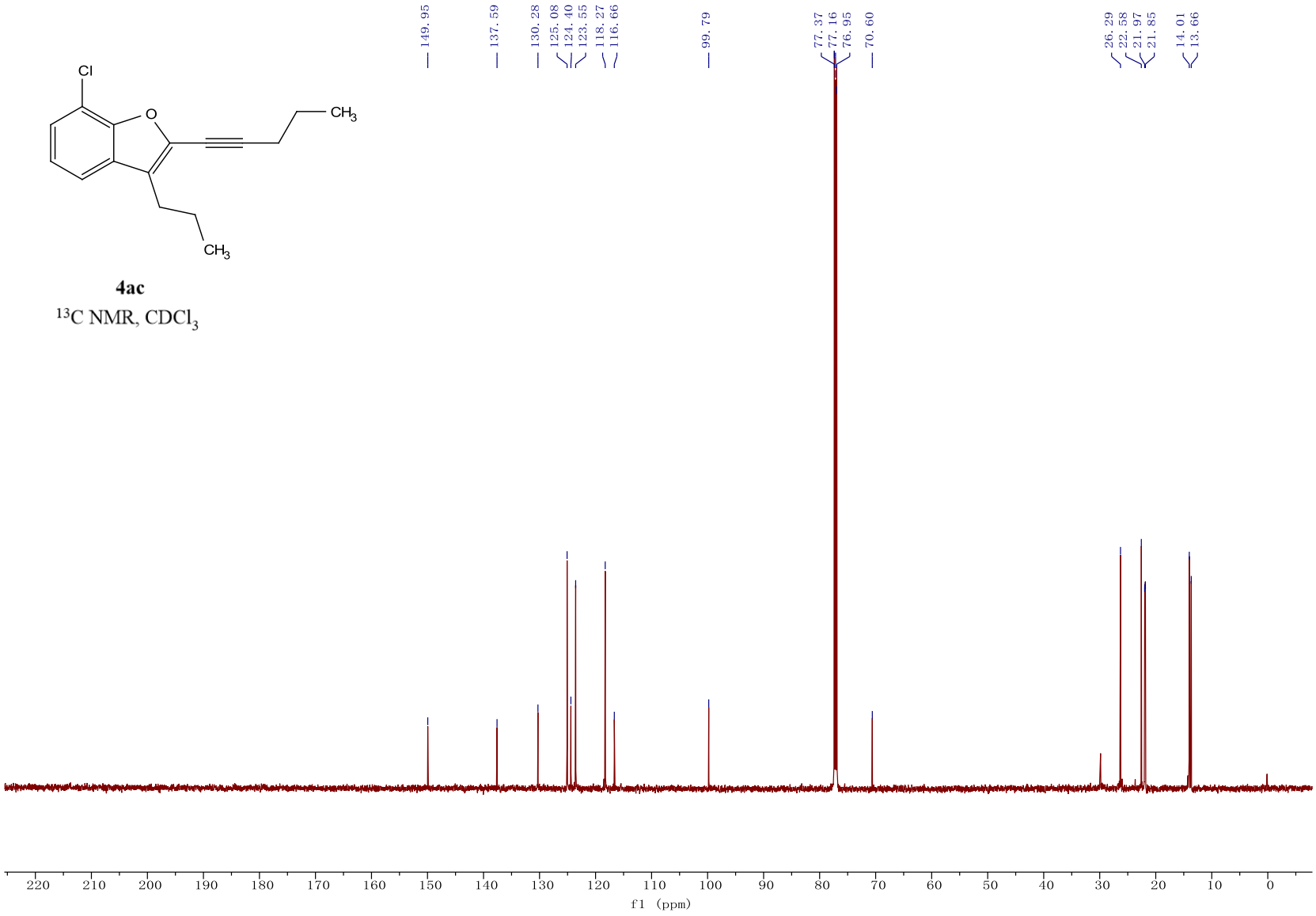
4ab

^{13}C NMR, $CDCl_3$



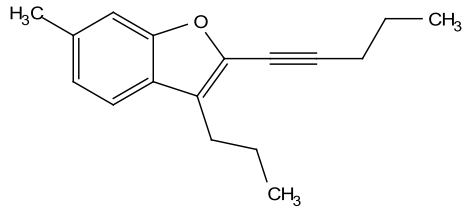
4ac

^{1}H NMR, $CDCl_3$



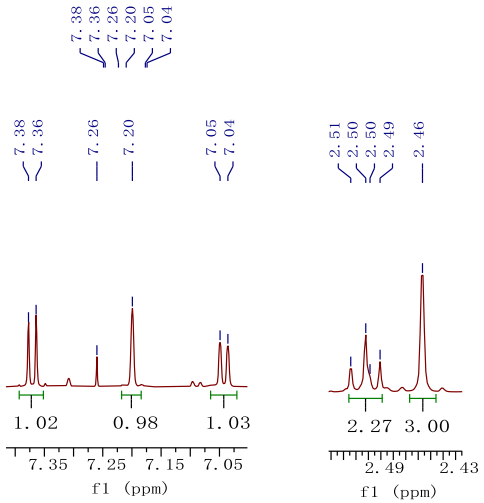
4ac

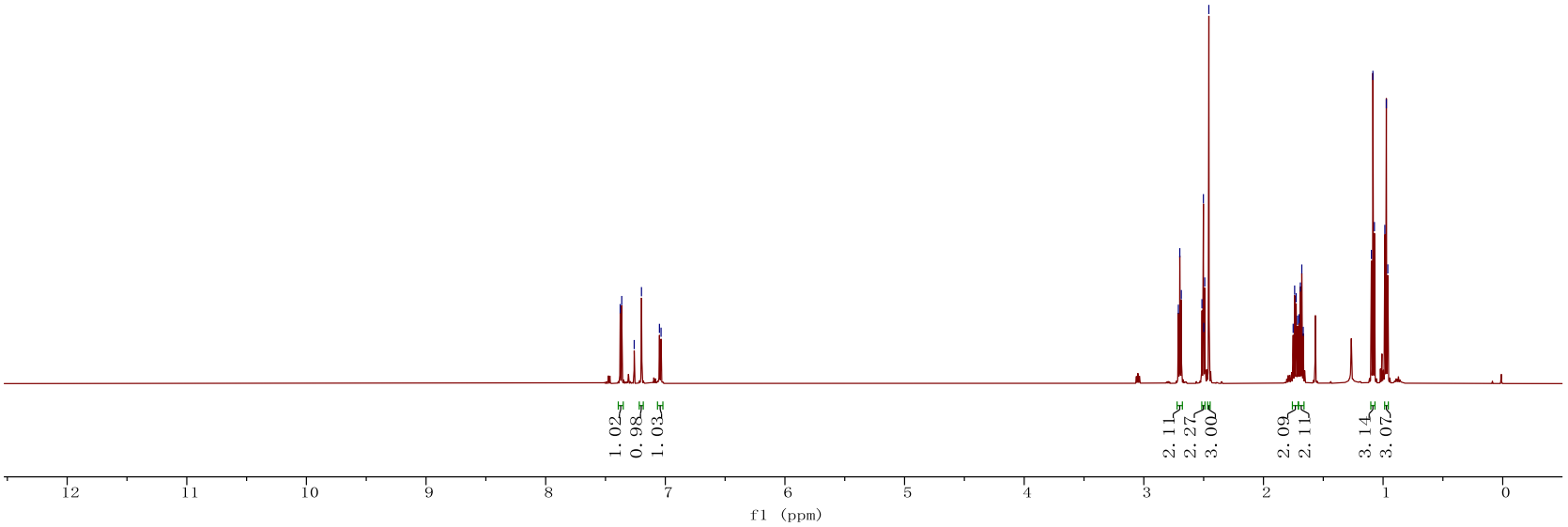
^{13}C NMR, $CDCl_3$

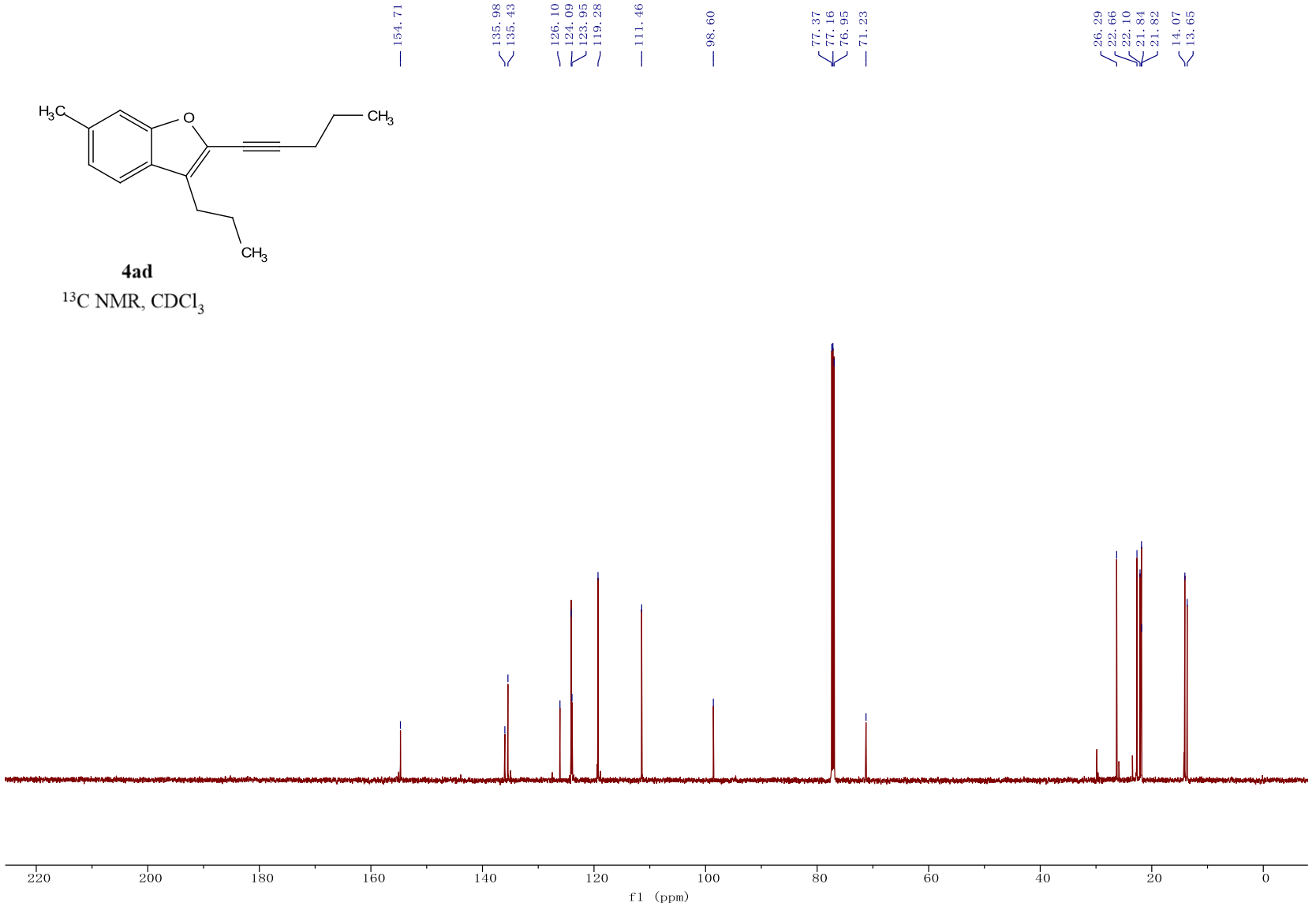


4ad

^{1}H NMR, $CDCl_3$

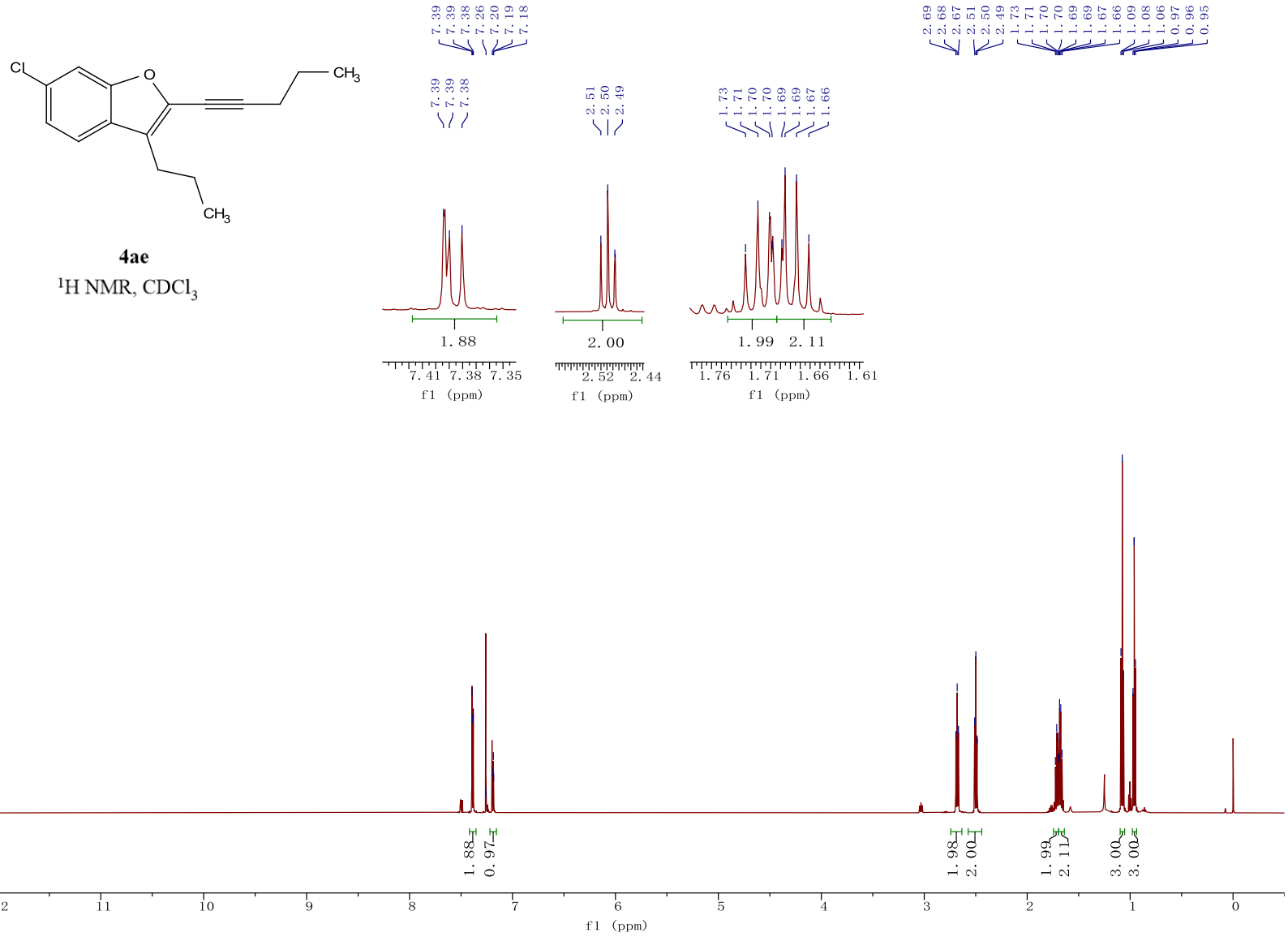


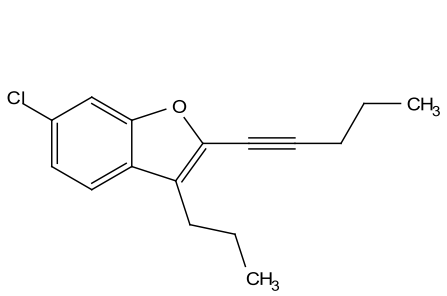




4ad

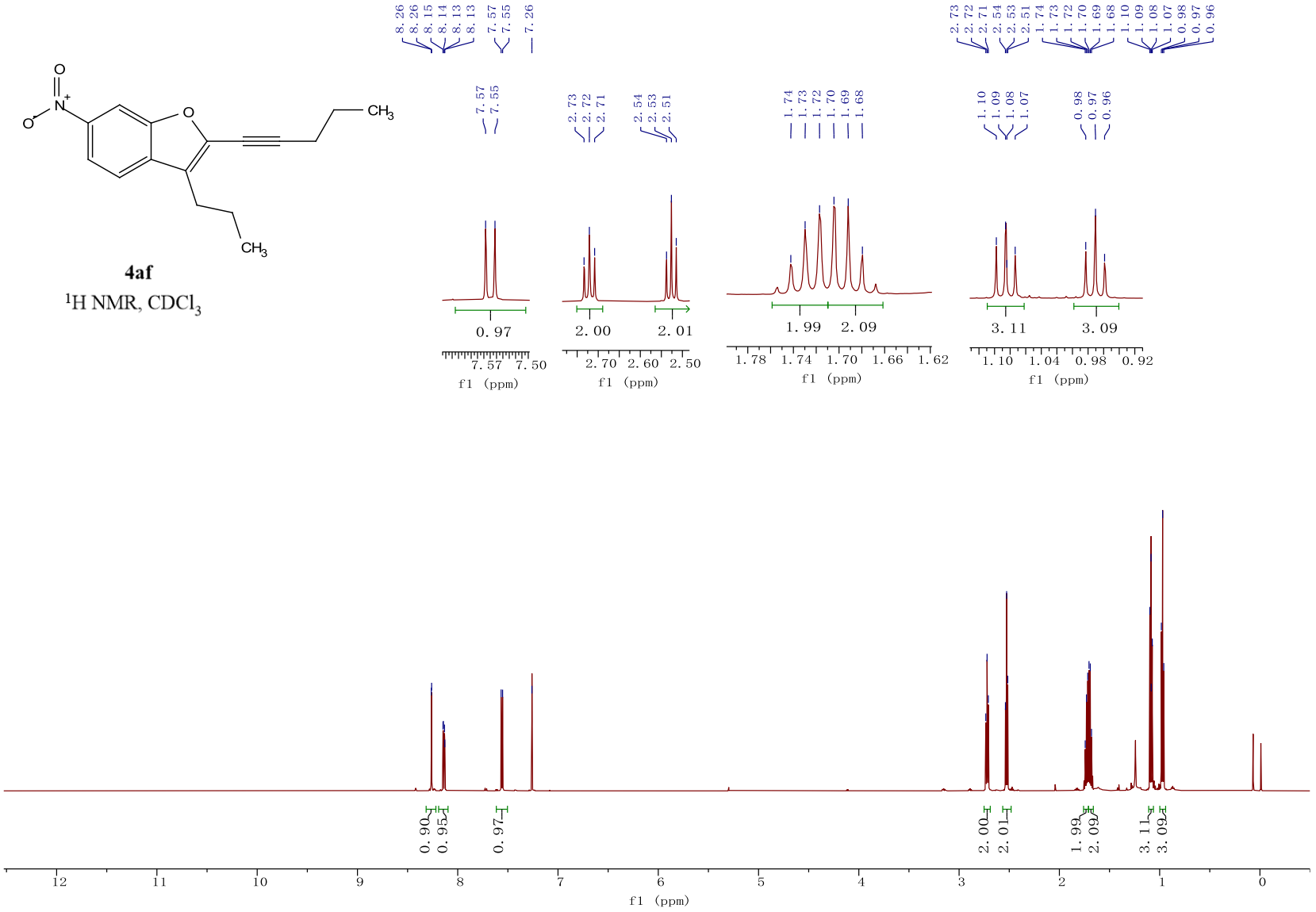
^{13}C NMR, $CDCl_3$

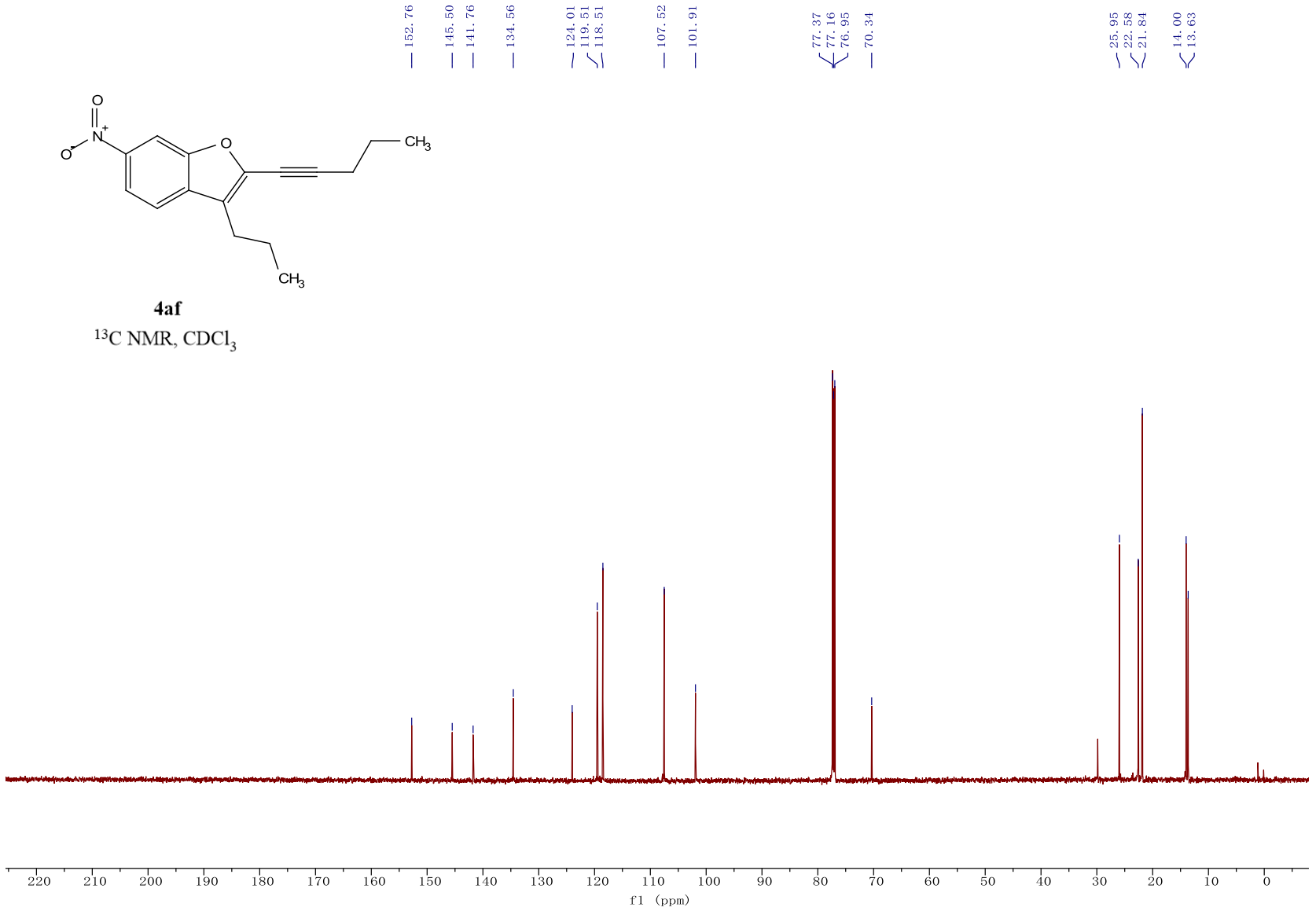

Cl
O
CH3
CH3
4ae
1H NMR, CDCl3
7.39
7.39
7.38
7.26
7.20
7.19
7.18
2.69
2.68
2.67
2.51
2.50
2.49
1.73
1.71
1.70
1.70
1.69
1.69
1.67
1.66
1.09
1.08
1.06
0.97
0.96
0.95
1.88
2.00
1.99
2.11
7.41 7.38 7.35
2.52 2.44
1.76 1.71 1.66 1.61
f1 (ppm)
1.88
0.97
1.98
2.00
1.99
2.11
3.00
3.00
12 11 10 9 8 7 6 5 4 3 2 1 0
f1 (ppm)



4ae

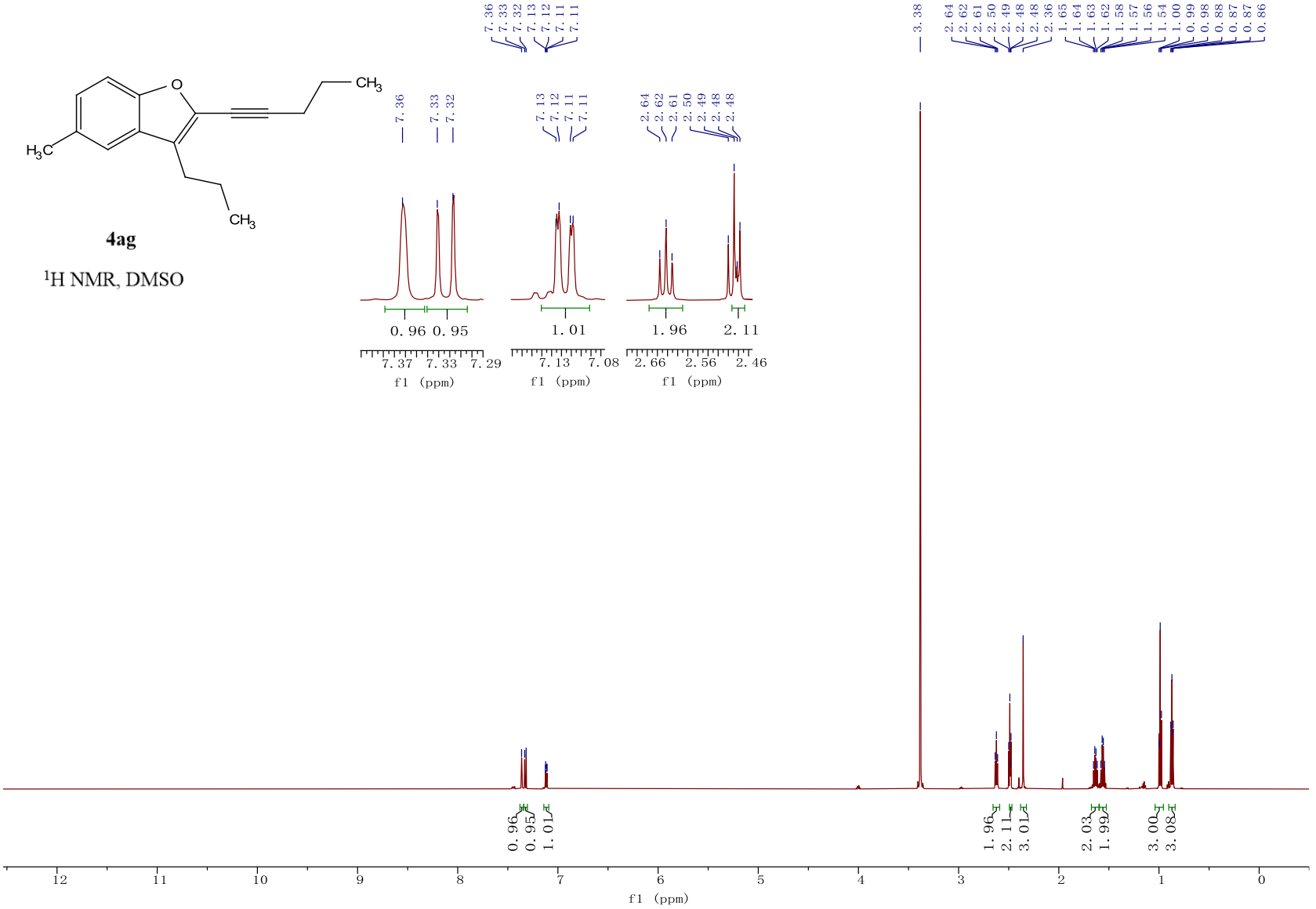
^{13}C NMR, $CDCl_3$

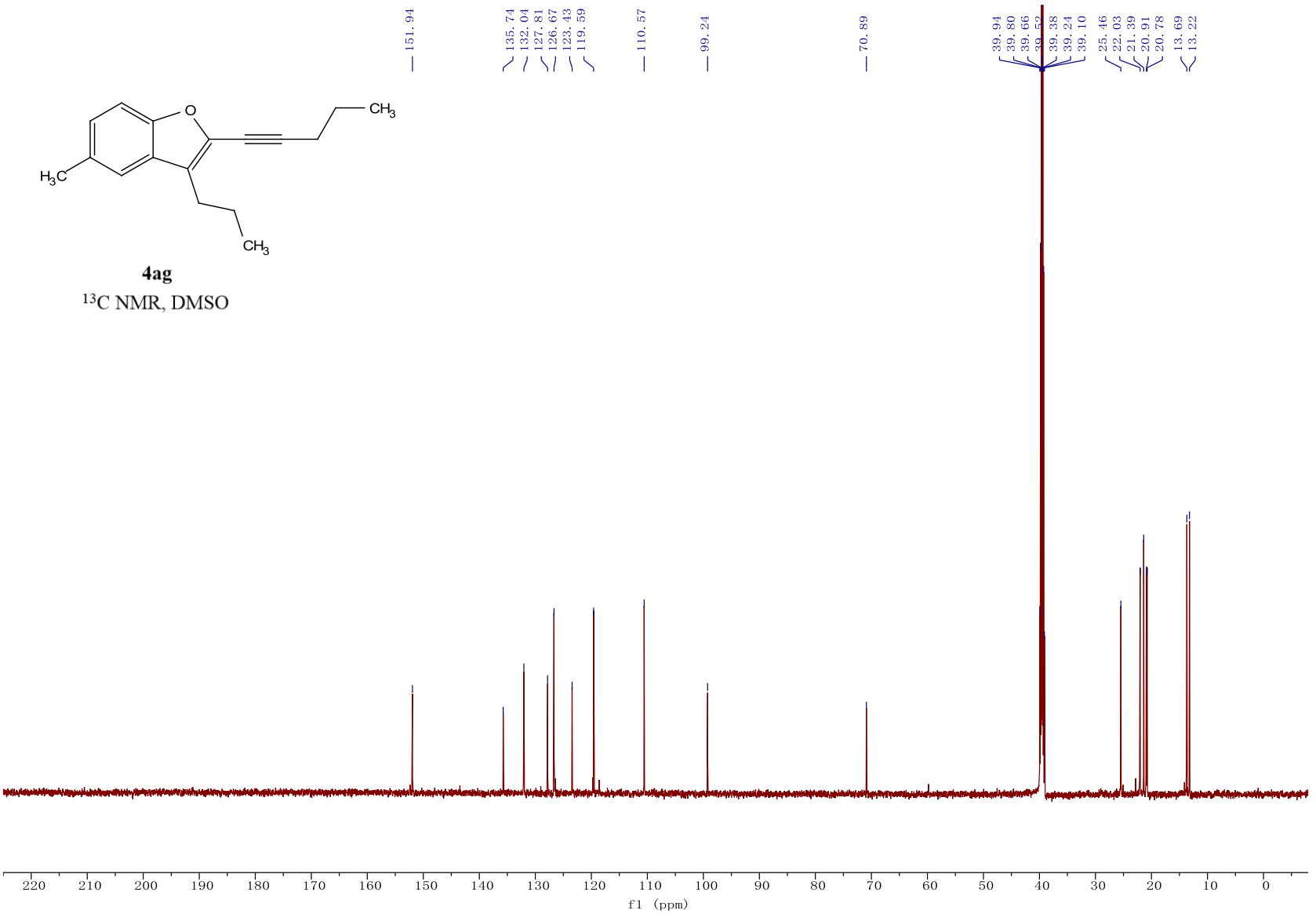

4af
1H NMR, CDCl3
8.26
8.26
8.15
8.14
8.13
8.13
7.57
7.55
7.26
2.73
2.72
2.71
2.54
2.53
2.51
1.74
1.73
1.72
1.70
1.69
1.68
1.10
1.09
1.08
1.07
0.98
0.97
0.96
0.97
2.00
2.01
1.99
2.09
3.11
3.09
f1 (ppm)
0.90
0.95
0.97
2.00
2.01
1.99
2.09
3.11
3.09



4af

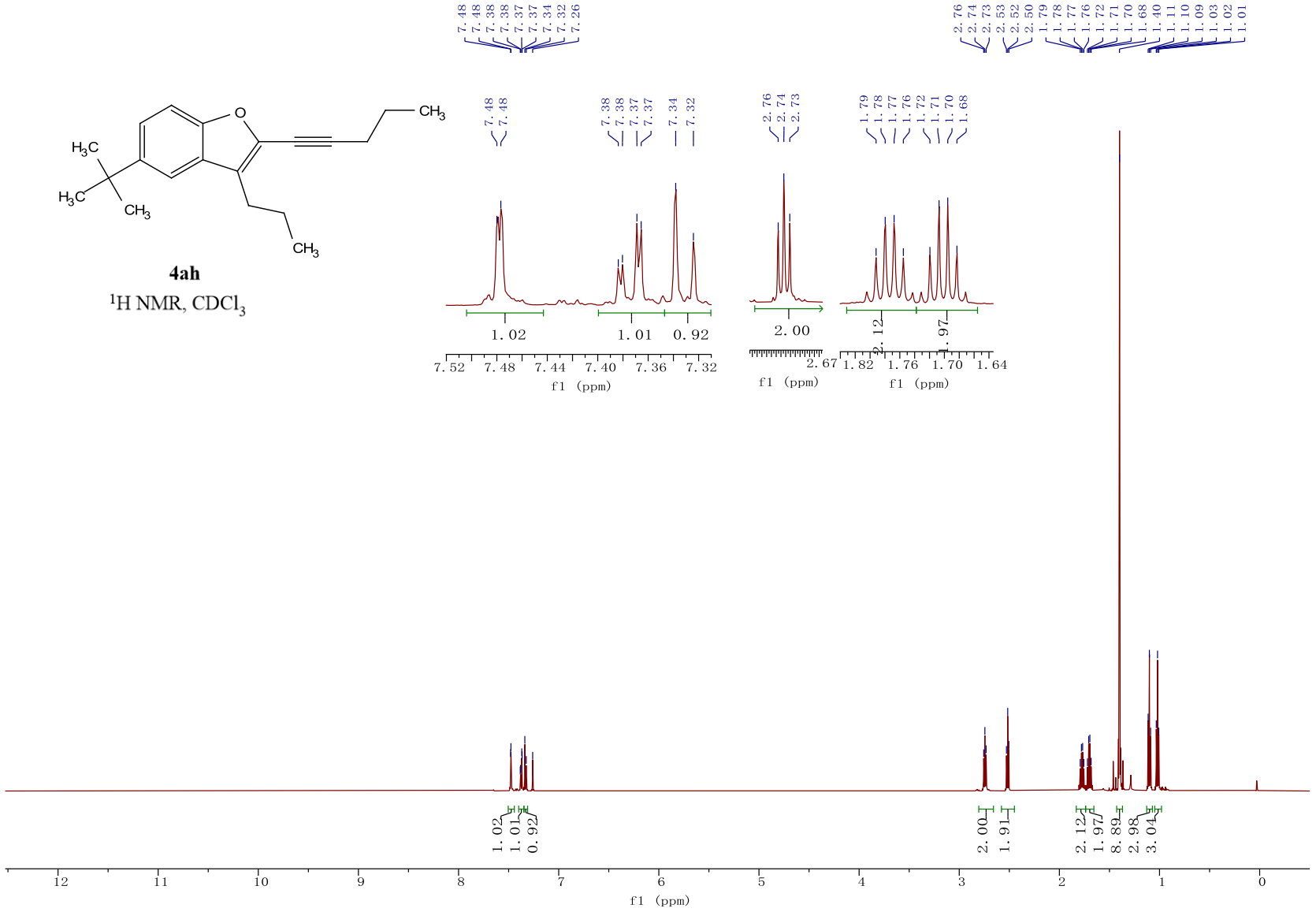
^{13}C NMR, $CDCl_3$

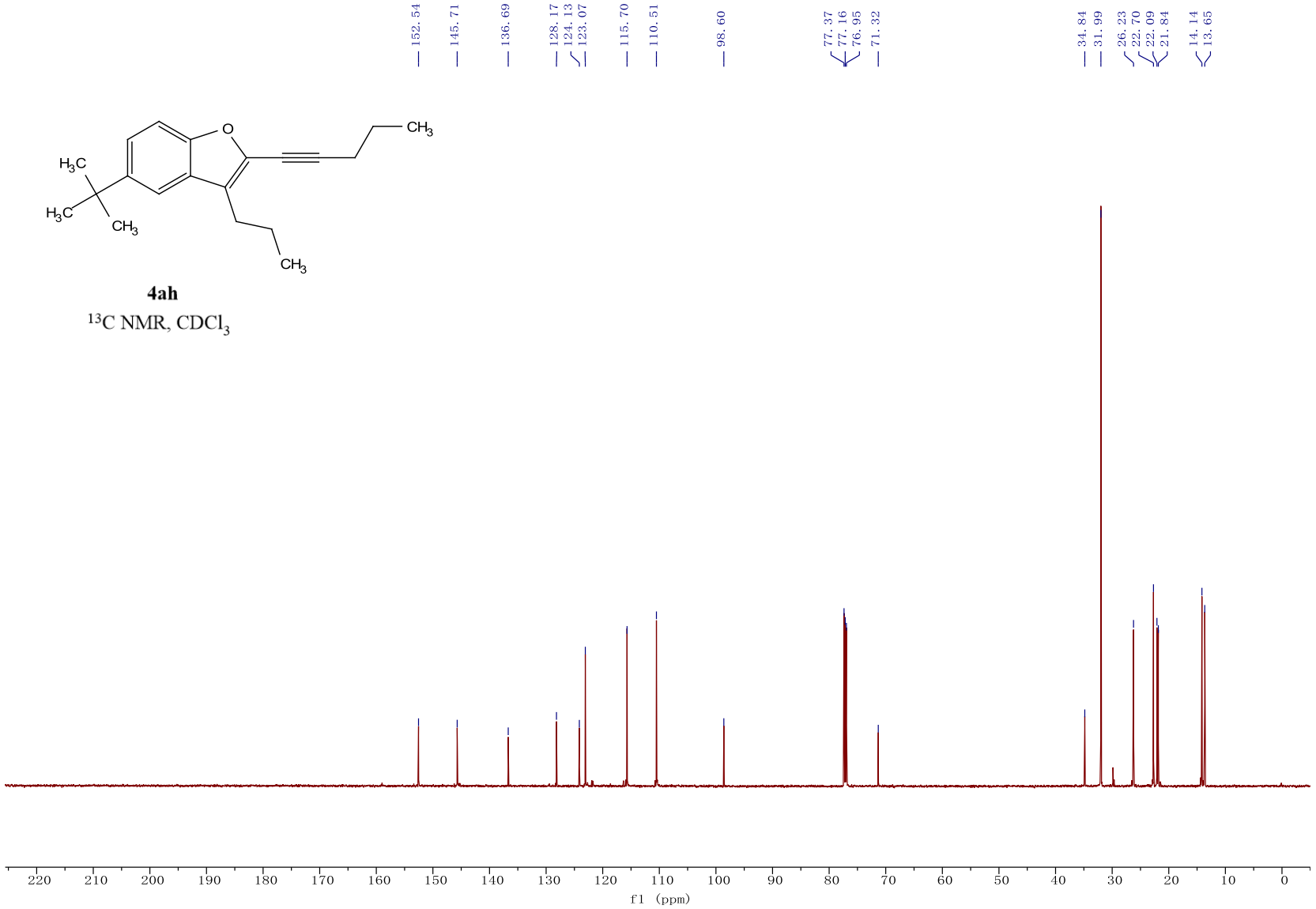

4ag
1H NMR, DMSO
7.36
7.33
7.32
7.13
7.12
7.11
7.11
3.38
2.64
2.62
2.61
2.50
2.49
2.48
2.48
2.36
1.65
1.64
1.63
1.62
1.58
1.57
1.56
1.54
1.00
0.99
0.98
0.88
0.87
0.87
0.86
0.96 0.95
1.01
1.96
2.11
f1 (ppm)
1.96
2.11
3.01
2.03
1.99
3.00
3.08

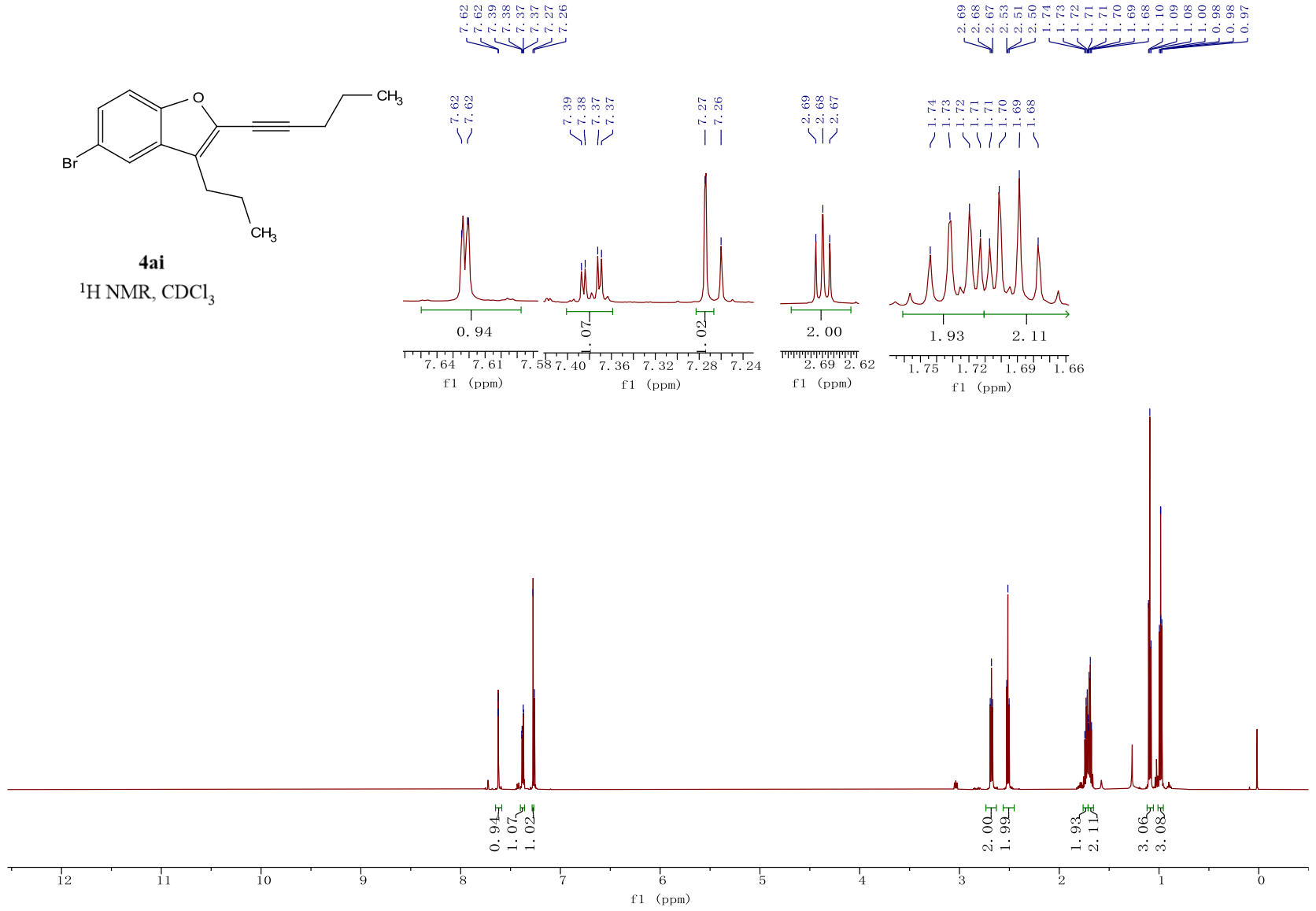


4ag

^{13}C NMR, DMSO

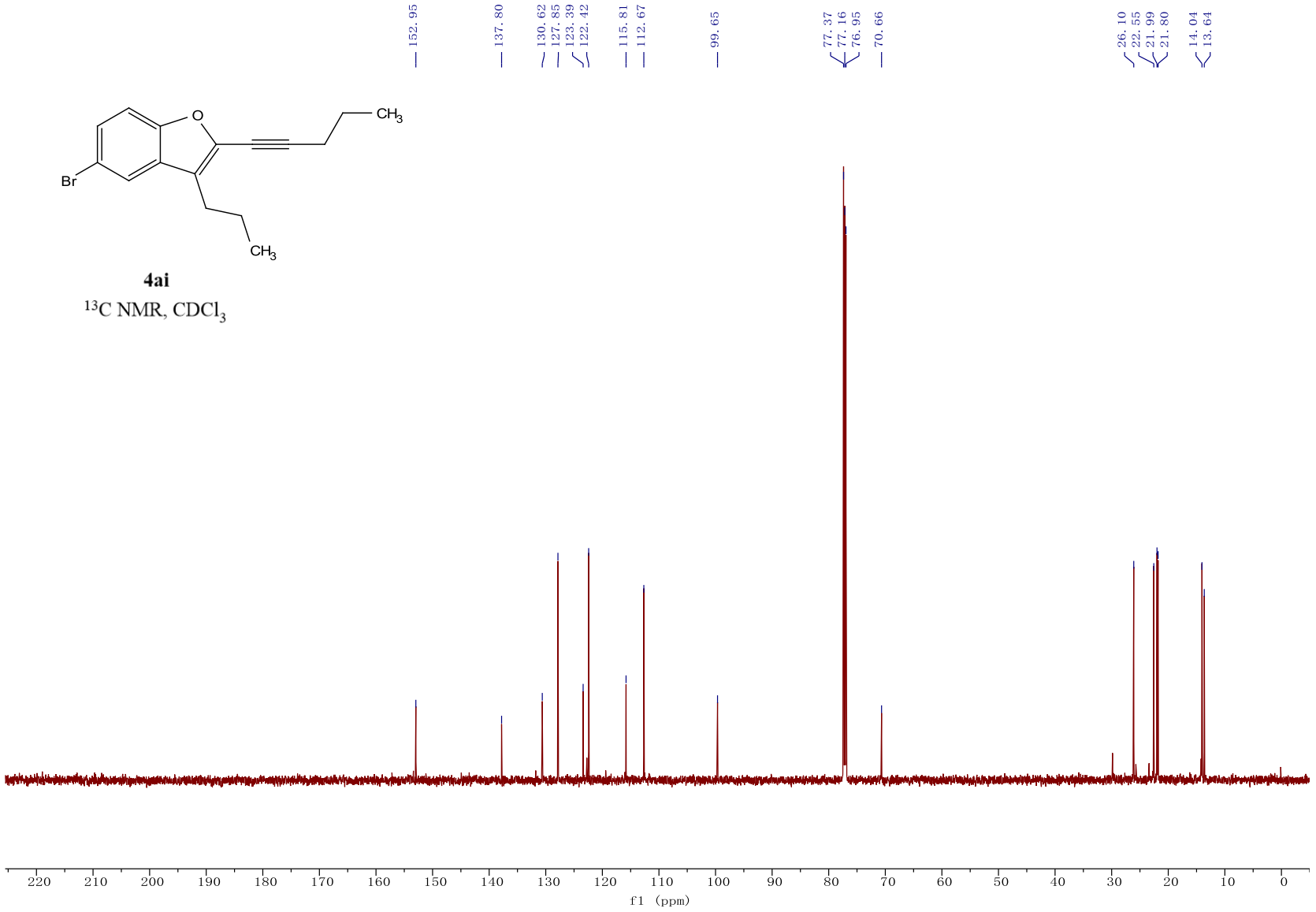

4ah
1H NMR, CDCl3
f1 (ppm)


152.54
145.71
136.69
128.17
124.13
123.07
115.70
110.51
98.60
77.37
77.16
76.95
71.32
34.84
31.99
26.23
22.70
22.09
21.84
14.14
13.65
O
H3C
H3C
CH3
CH3
CH3
4ah
13C NMR, CDCl3
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



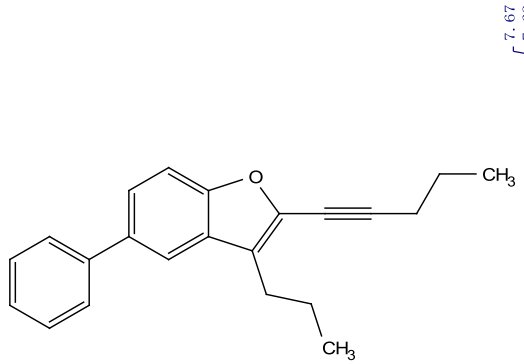
4ai

^{1}H NMR, $CDCl_3$



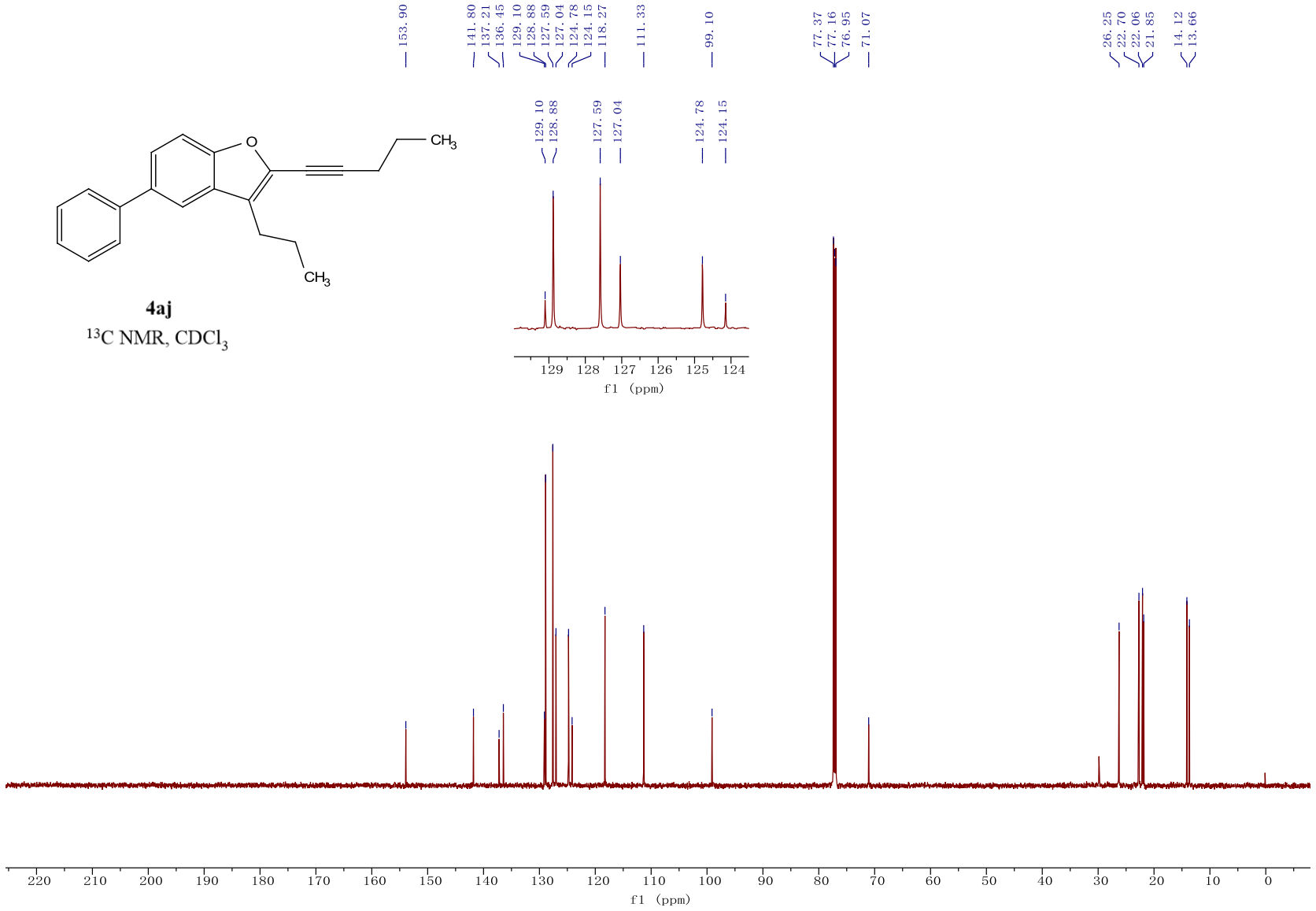
4ai

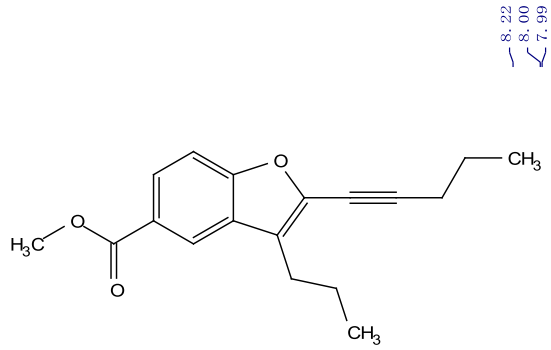
^{13}C NMR, $CDCl_3$



4aj

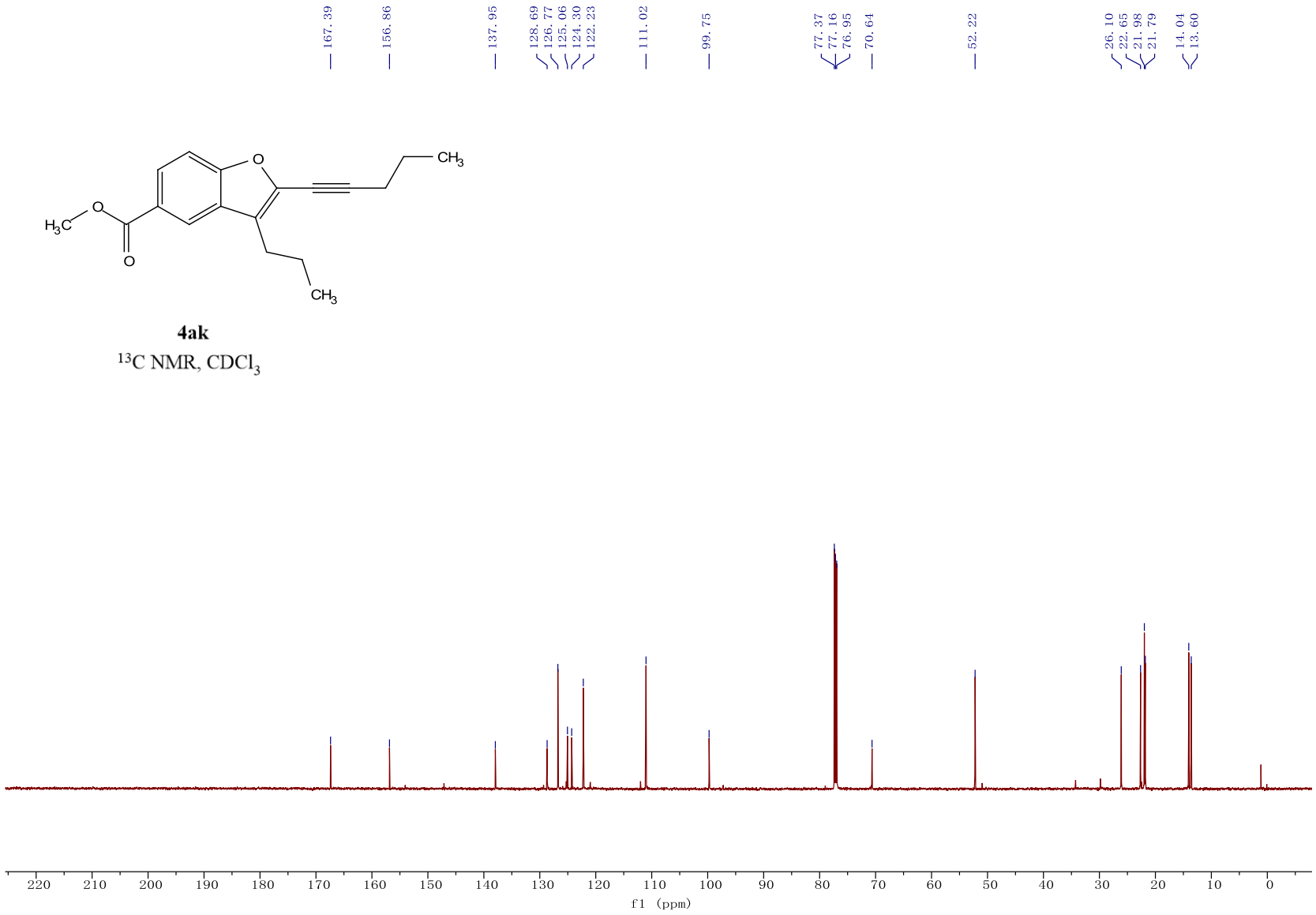
^{1}H NMR, $CDCl_3$


153.90
141.80
137.21
136.45
129.10
128.88
127.59
127.04
124.78
124.15
118.27
111.33
99.10
77.37
77.16
76.95
71.07
26.25
22.70
22.06
21.85
14.12
13.66
O
CH3
CH3
4aj
13C NMR, CDCl3
f1 (ppm)
f1 (ppm)



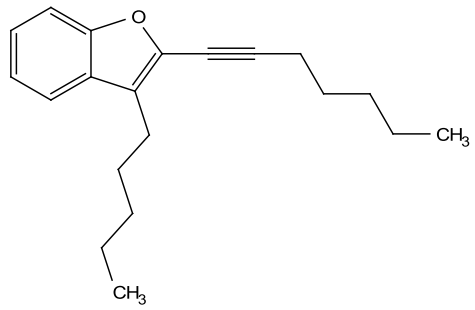
4ak

^{1}H NMR, $CDCl_3$



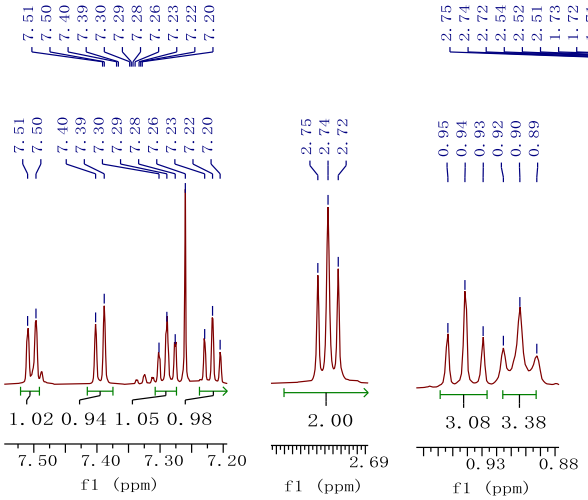
4ak

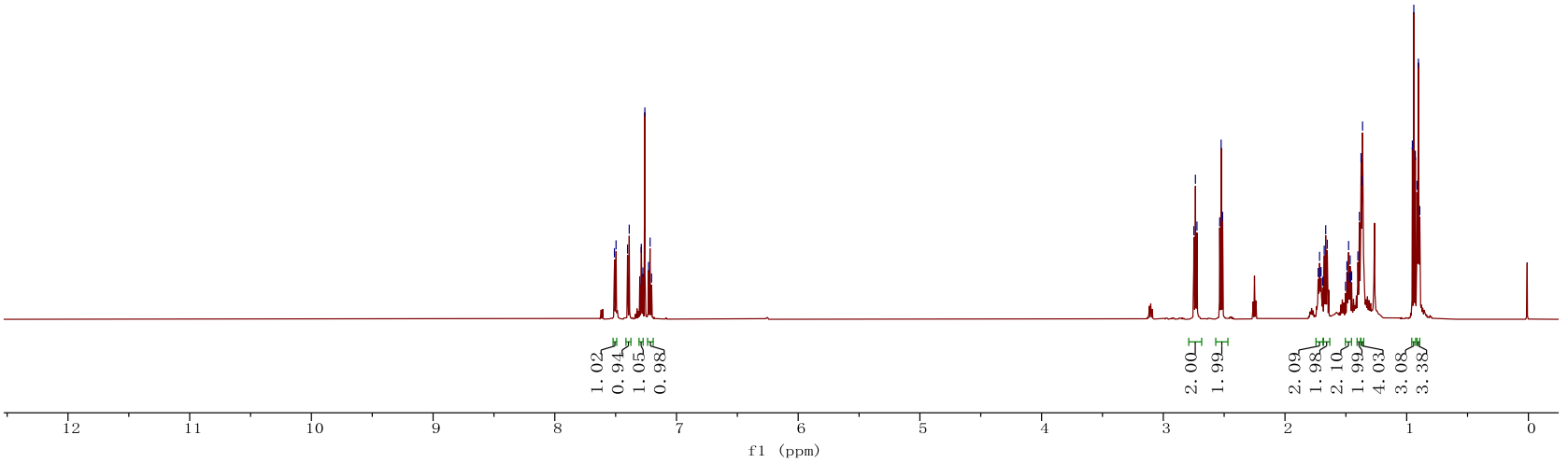
^{13}C NMR, $CDCl_3$

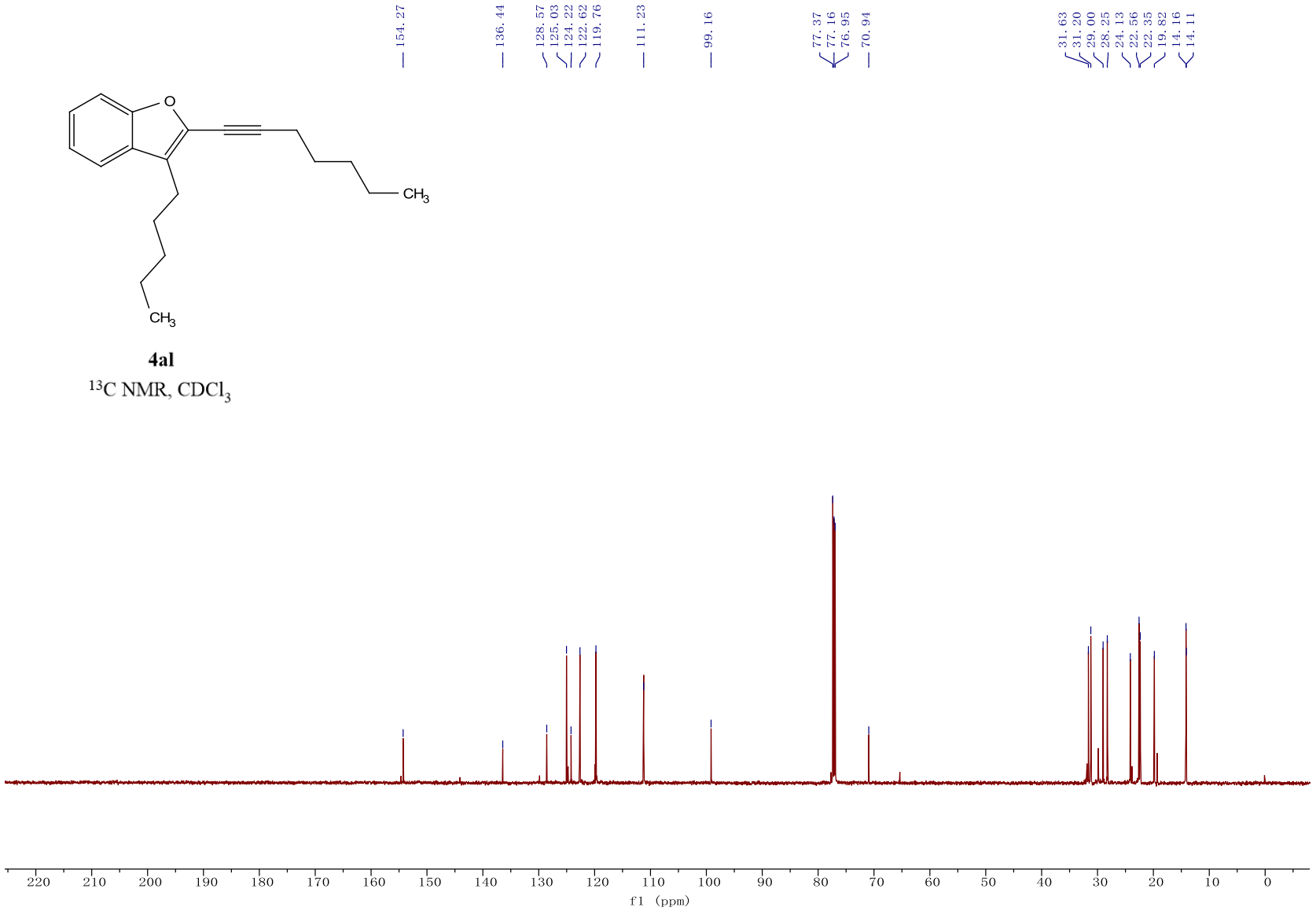


4al

^{1}H NMR, $CDCl_3$

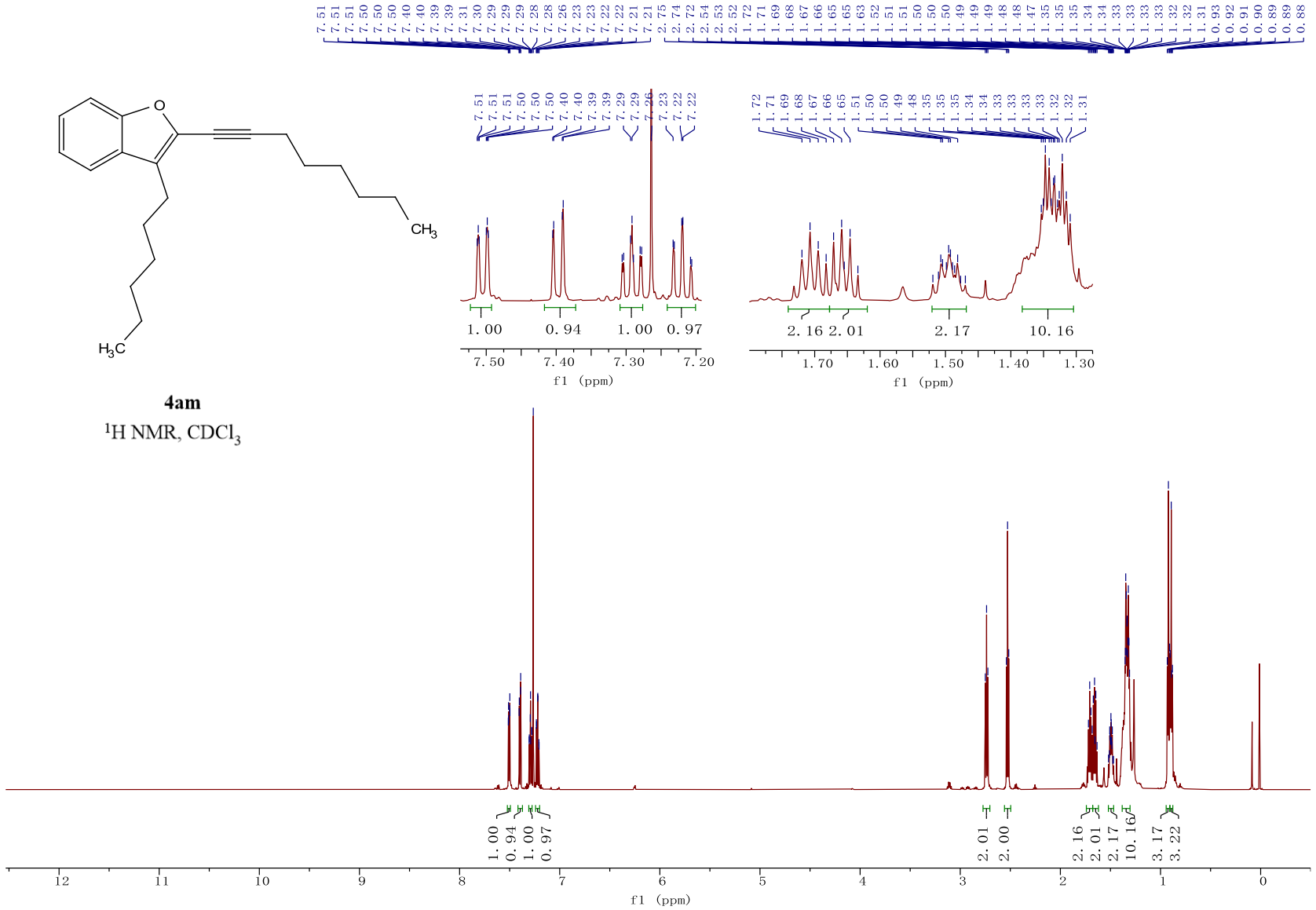






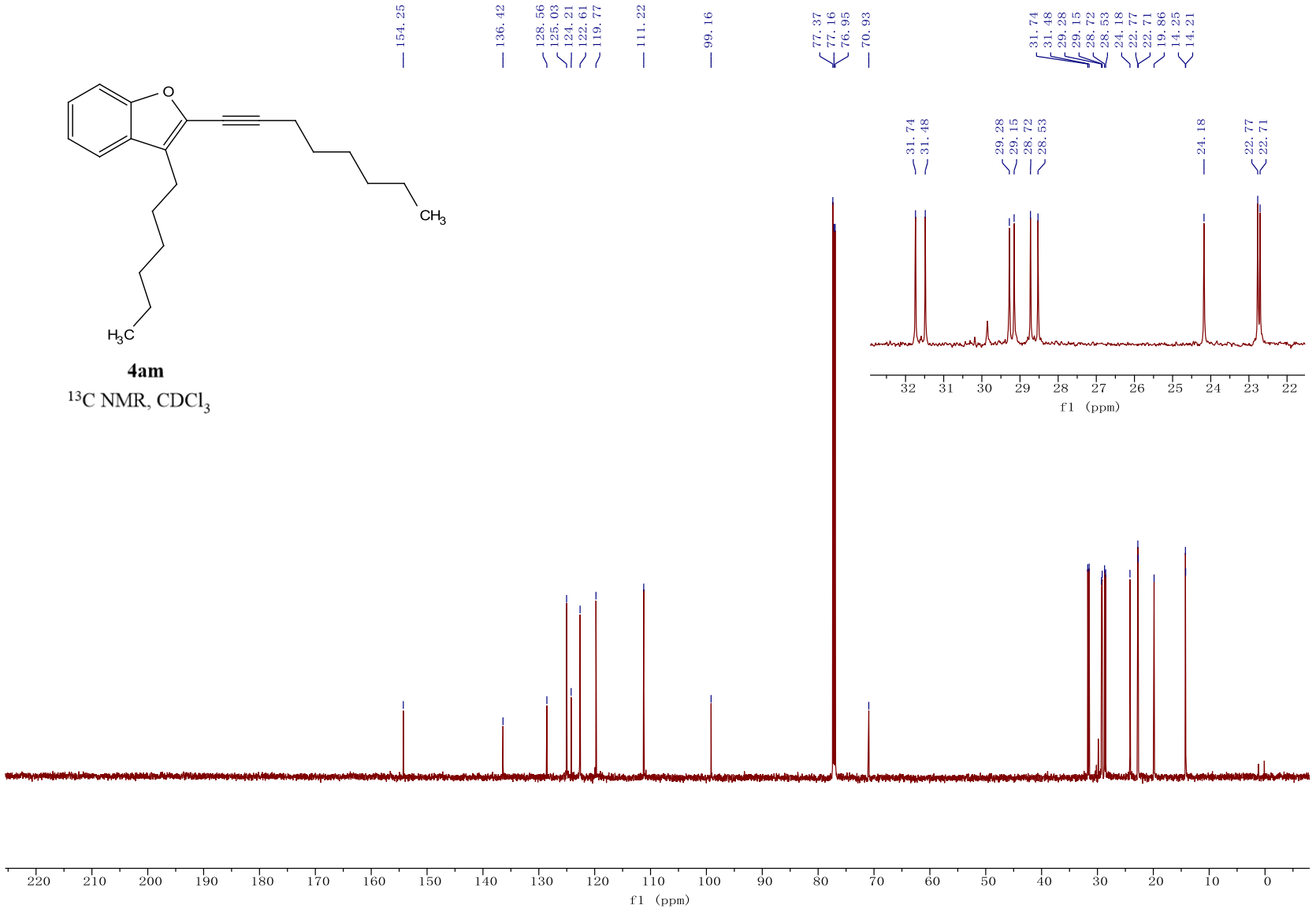
4al

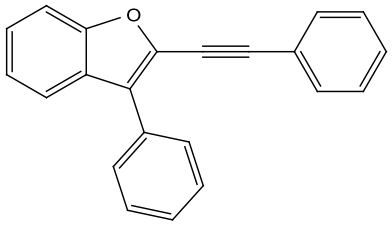
^{13}C NMR, $CDCl_3$



4am

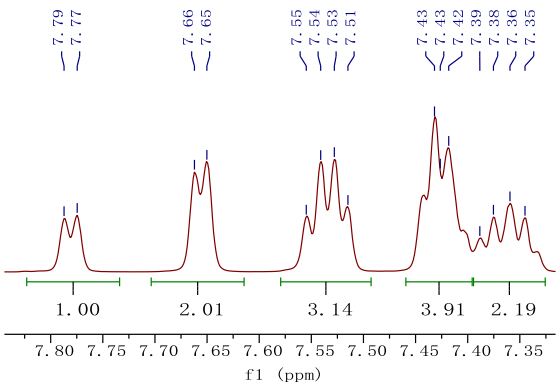
^{1}H NMR, $CDCl_3$

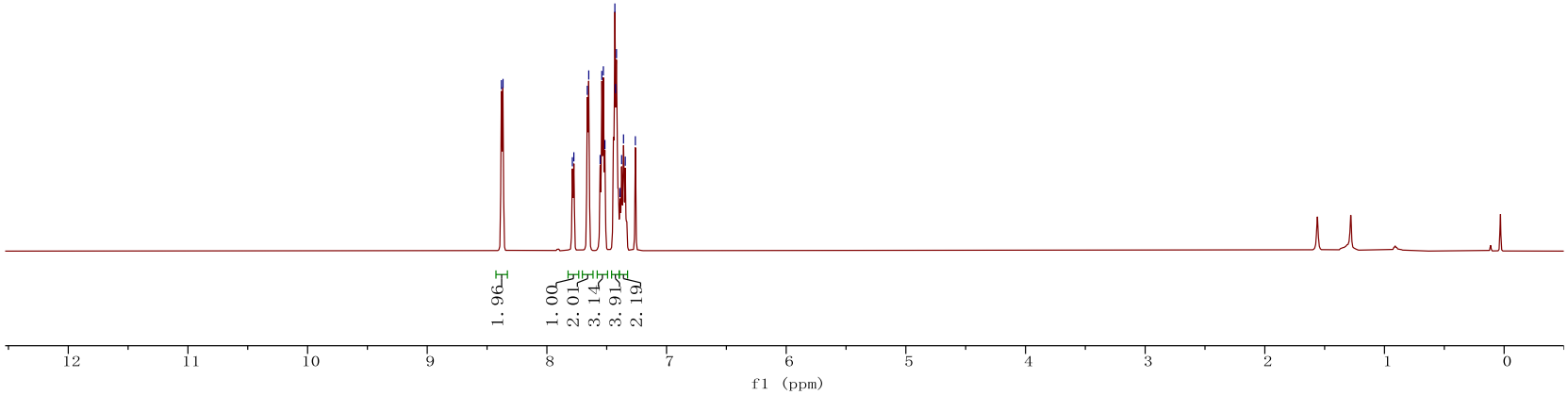

154.25
136.42
128.56
125.03
124.21
122.61
119.77
111.22
99.16
77.37
77.16
76.95
70.93
31.74
31.48
29.28
29.15
28.72
28.53
24.18
22.77
22.71
19.86
14.25
14.21
O
CH3
H3C
4am
13C NMR, CDCl3
f1 (ppm)

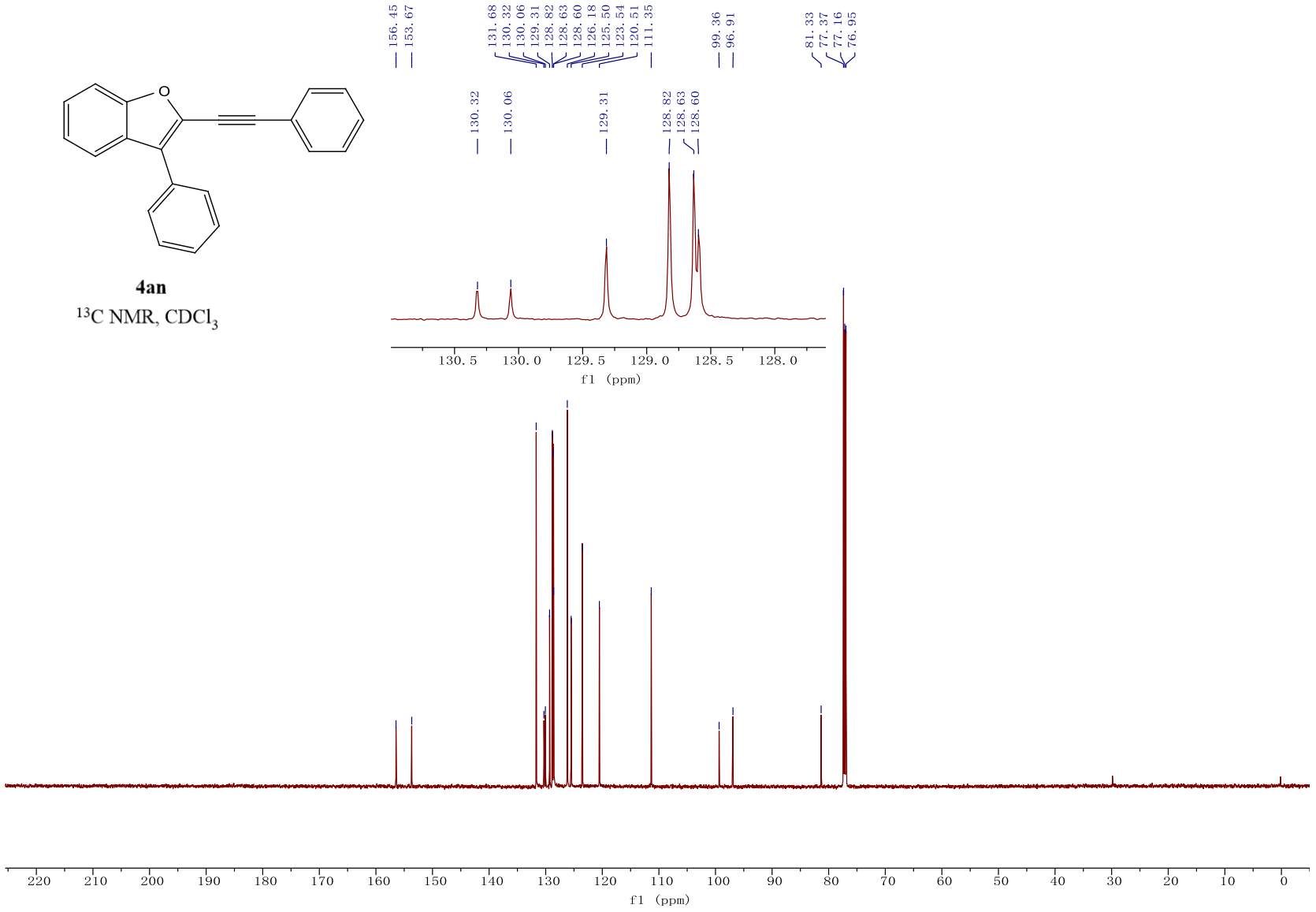


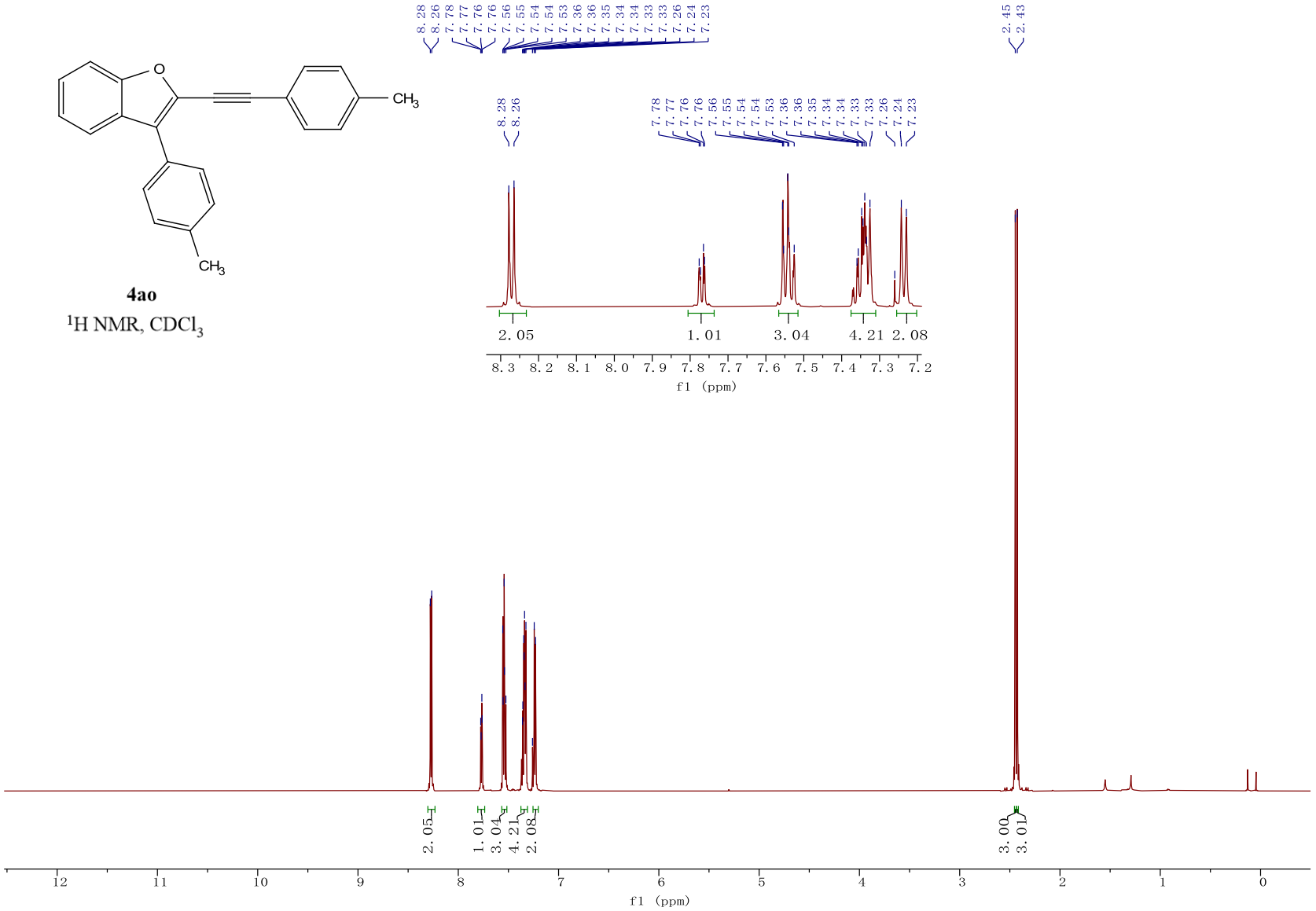
4an

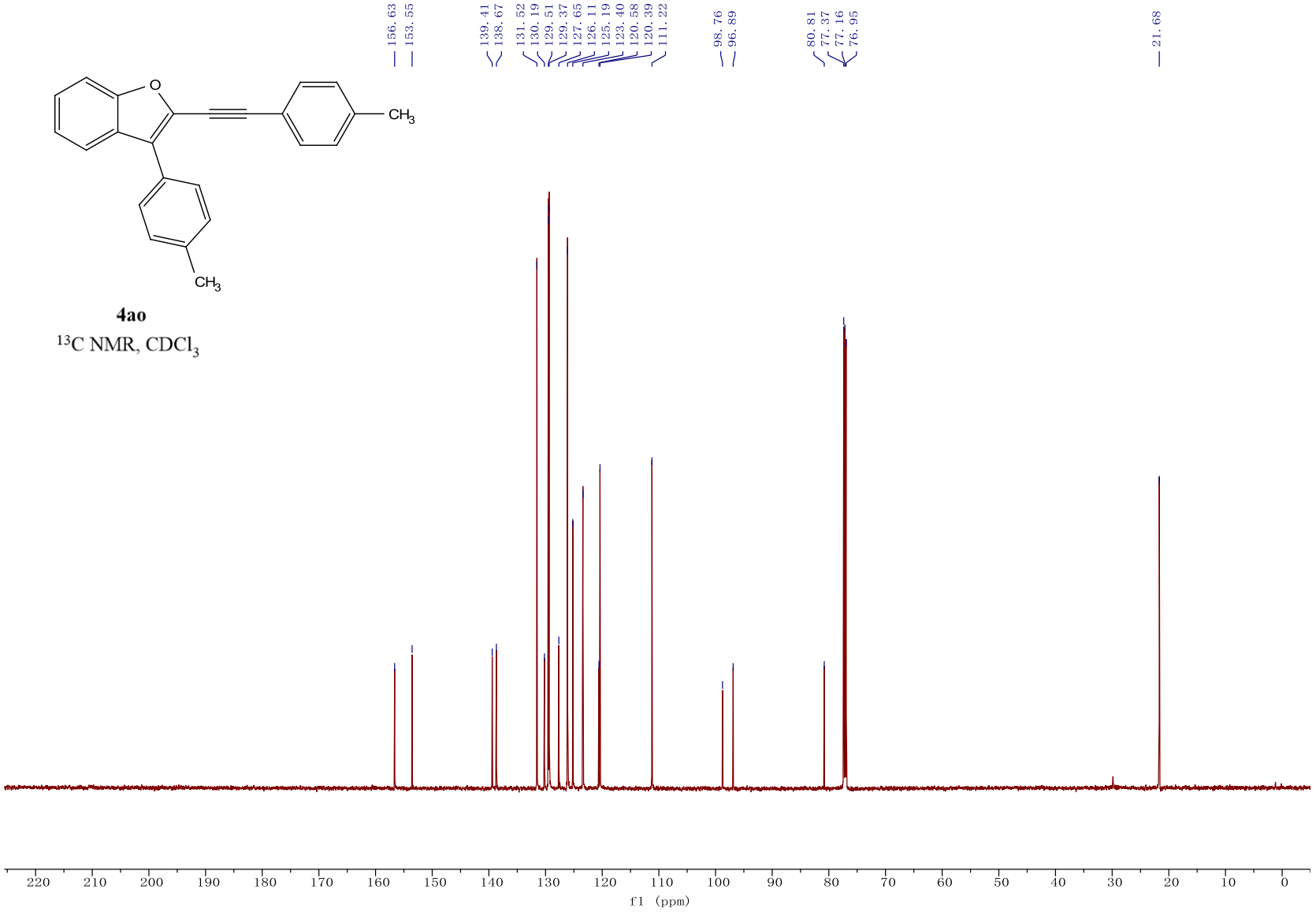
^{1}H NMR, $CDCl_3$

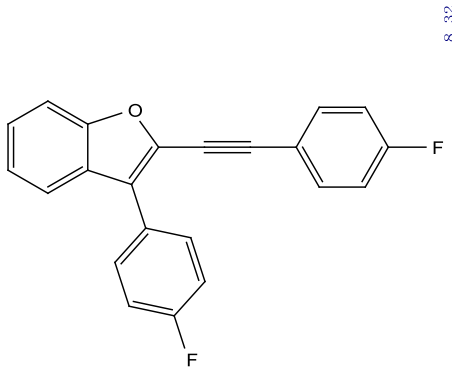





156.45
153.67
131.68
130.32
130.06
129.31
128.82
128.63
128.60
126.18
125.50
123.54
120.51
111.35
99.36
96.91
81.33
77.37
77.16
76.95
O
4an
13C NMR, CDCl3
130.32
130.06
129.31
128.82
128.63
128.60
130.5
130.0
129.5
129.0
128.5
128.0
f1 (ppm)
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

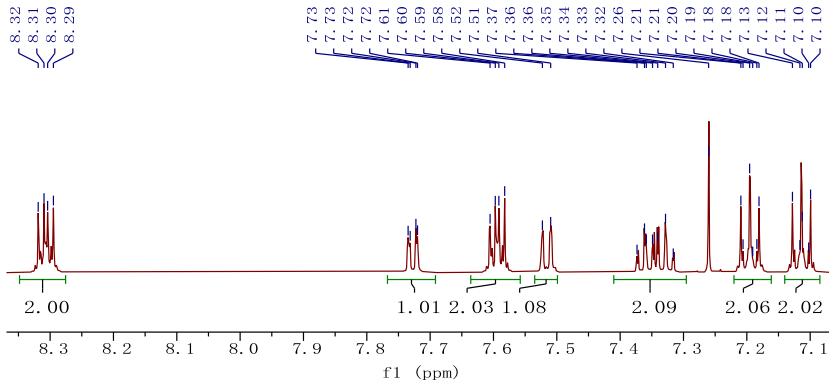

8.28
8.26
7.78
7.77
7.76
7.76
7.56
7.55
7.54
7.54
7.53
7.36
7.35
7.34
7.34
7.33
7.33
7.26
7.24
7.23
2.45
2.43
O
CH3
CH3
4ao
1H NMR, CDCl3
2.05
1.01
3.04
4.21
2.08
3.00
3.01
f1 (ppm)

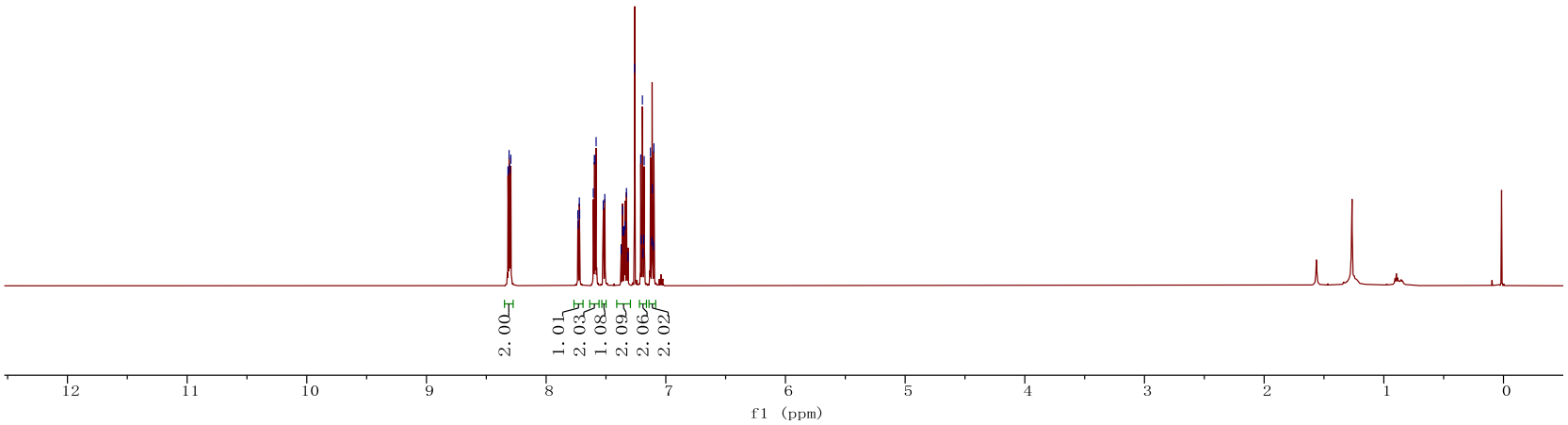

156.63
153.55
139.41
138.67
131.52
130.19
129.51
129.37
127.65
126.11
125.19
123.40
120.58
120.39
111.22
98.76
96.89
80.81
77.37
77.16
76.95
21.68
O
CH3
CH3
4ao
13C NMR, CDCl3
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

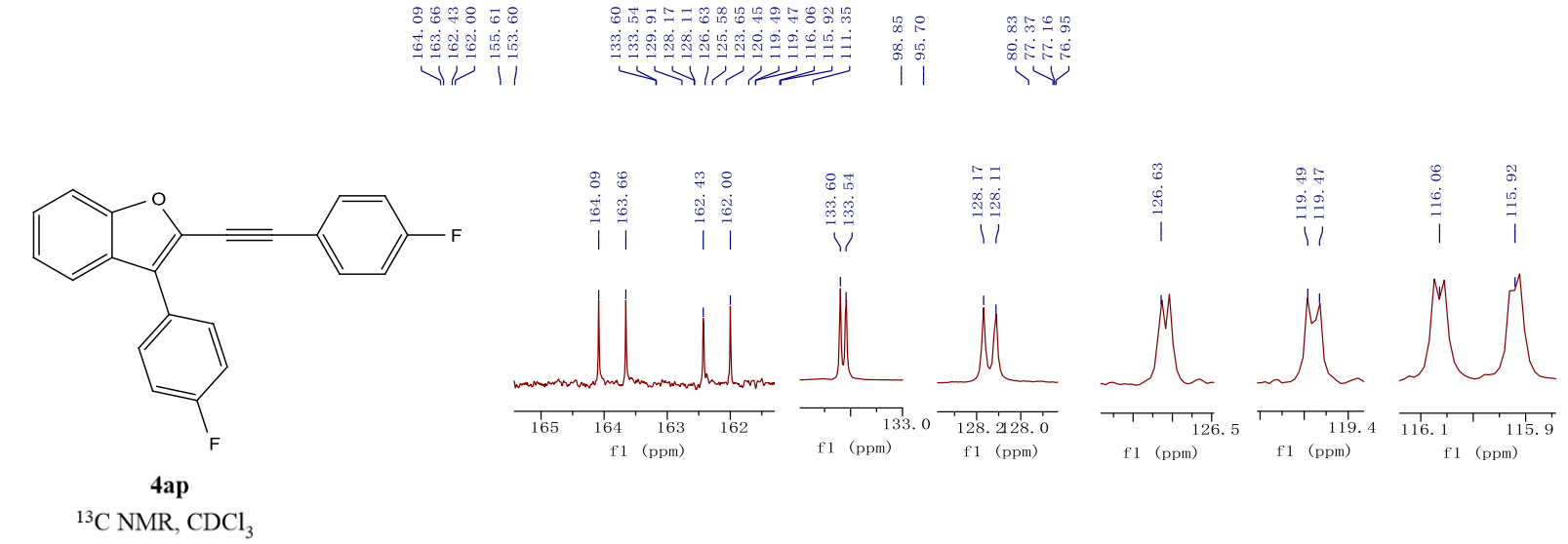


4ap

^{1}H NMR, $CDCl_3$

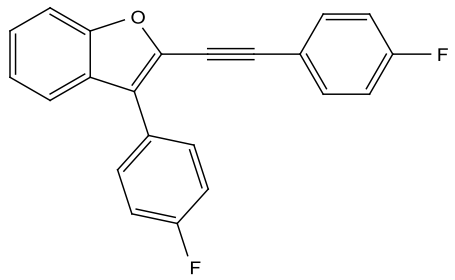






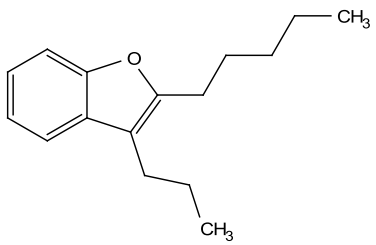
4ap

^{13}C NMR, $CDCl_3$



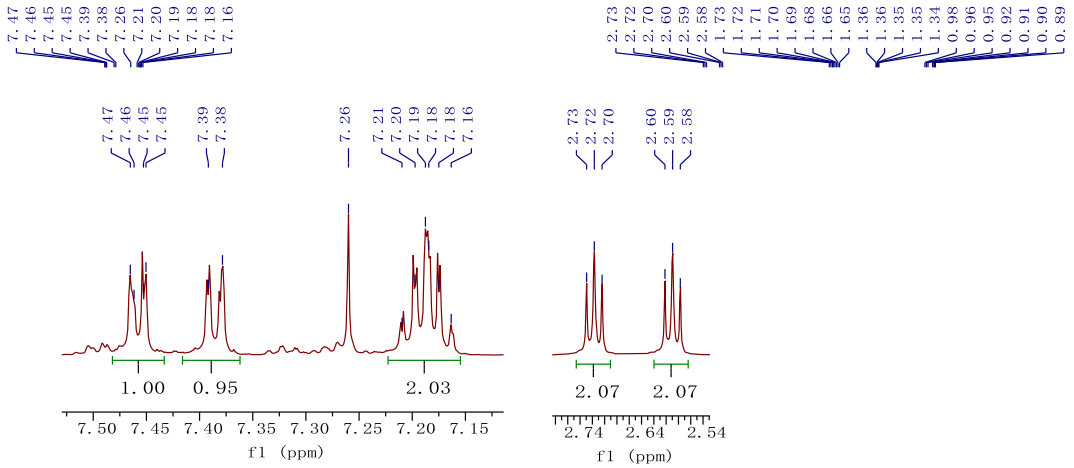
4ap

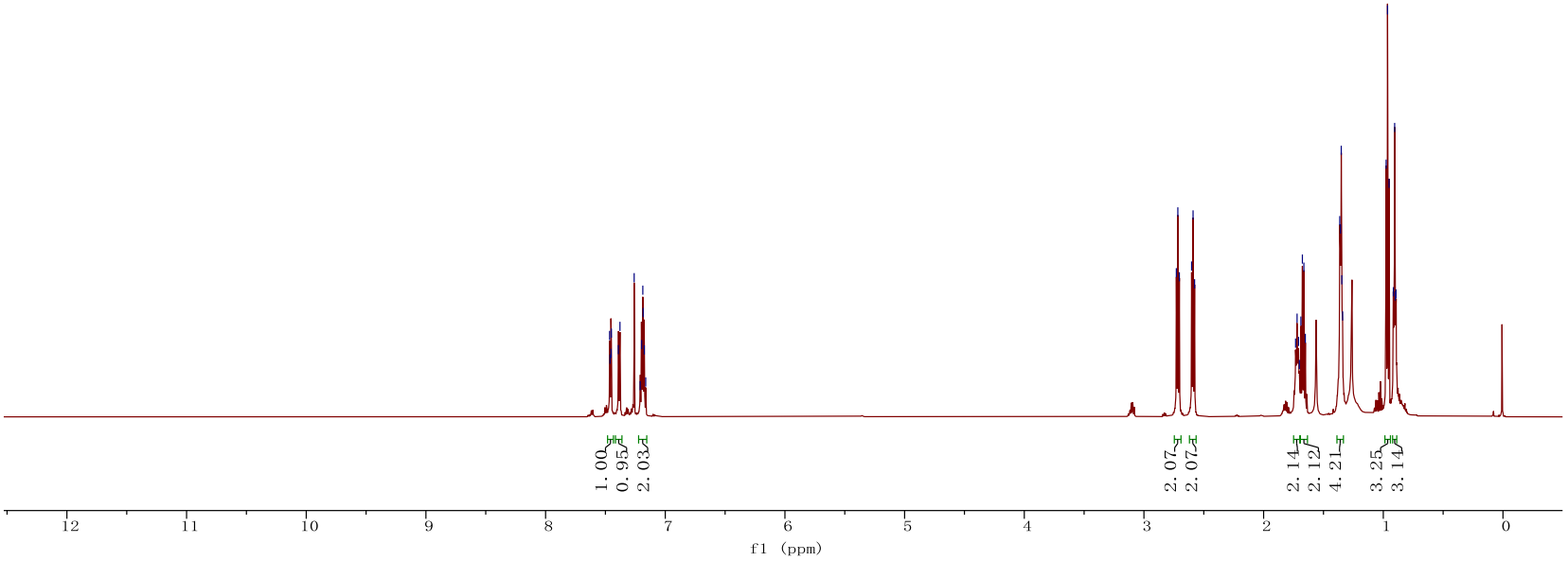
^{19}F NMR, $CDCl_3$

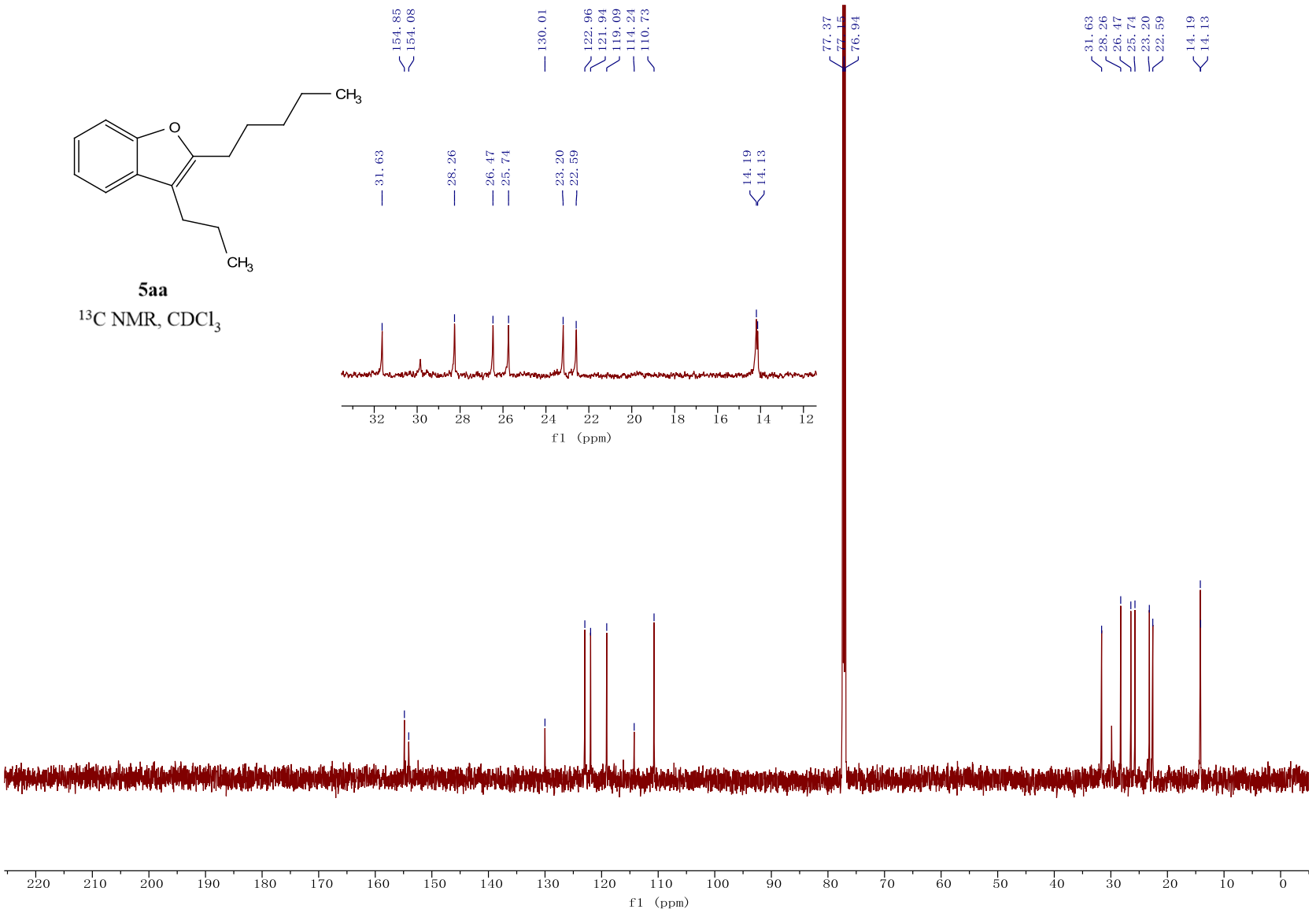


5aa

^{1}H NMR, $CDCl_3$






154.85
154.08
130.01
122.96
121.94
119.09
114.24
110.73
77.37
77.15
76.94
31.63
28.26
26.47
25.74
23.20
22.59
14.19
14.13
CH3
O
CH3
5aa
13C NMR, CDCl3
f1 (ppm)
f1 (ppm)