Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Supporting Information

Palladium-Catalyzed Oxidative C=C bonds Cleavage with Molecular Oxygen: One-Pot Synthesis of Quinazolinones from 2-Amino Benzamides and Alkenes

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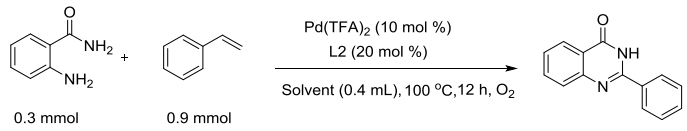
1. General Information

Unless otherwise noted, materials were purchased from commercial suppliers and used without further purification. All the solvents were treated according to general methods. Melting points are uncorrected and recorded on Digital Melting Point Apparatus WRS-1B. ^{1}H NMR and ^{13}C NMR spectra were measured on a 500 MHz Bruker spectrometer (500 MHz for ^{1}H and 125 MHz for ^{13}C) or 400 MHz Bruker spectrometer (400 MHz for ^{1}H and 100 MHz for ^{13}C), using DMSO-d_6 or PYRIDINE-d_5 as the solvent with tetramethylsilane (TMS) as the internal standard at room temperature. Chemical shifts are given in δ relative to TMS, the coupling constants J are given in Hz. High-resolution mass spectra were recorded on an ESI-Q-TOF mass spectrometer. Column chromatography was performed using EM silica gel 60 (300-400 mesh).

2. Experimental Section

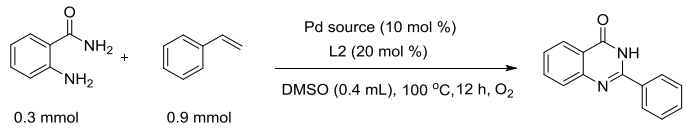
2.1 Optimization of Reaction Conditions

Table S1: Solvent Optimization



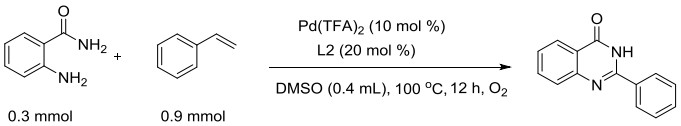
entry	solvent	yield (%)
1	1,2-DCE	NR
2	CH_3OH	NR
3	PhCl	Trace
4	toluene	Trace
5	THF	12
6	2-MeTHF	Trace
7	dioxane	NR
8	DME	NR
9	DMF	Trace
10	DMA	47
11	NMA	Trace
12	DMSO	85
13	NMP	Trace
14	DMI	31
15	CH_3CN	NR
16	HOAc	Trace
17	H_2O	Trace

Table S2: Catalyst optimization

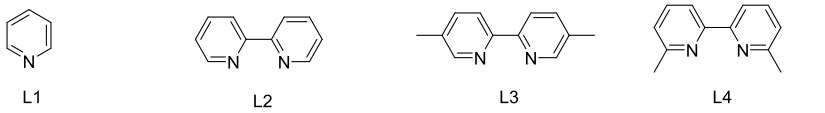


entry	Pd catalyst	yield (%)
1	$PdCl_2$	Trace
2	$Pd(TFA)_2$	85
3	$[Pd(allyl)Cl]_2$	Trace
4	$Pd(OAc)_2$	64
5	$PdBr_2$	Trace
6	$Pd_2(dba)_3$	Trace
7	$Pd(acac)_2$	Trace
8	$PdCl_2(CH_3CN)_2$	NR
9	$Pd(PPh_3)_4$	NR
10	$PdCl_2(PPh_3)_2$	NR
11	$Pd(CH_3CN)_4BF_4$	NR

Table S3：Ligand optimization



entry	ligand	yield (%)
1	L1	NR
2	L2	85
3	L3	38
4	L4	Trace
5	L5	67
6	L6	70
7	L7	Trace
8	L8	48
9	L9	60
10	L10	35
11	L11	23
12	L12	52
13	L13	NR
14	L14	NR
15	L15	NR
16	L16	NR
17	L17	NR
18	L18	NR
19	L19	NR
20	L20	NR
21	L21	NR
22	L22	NR
23	L23	NR
24	L24	NR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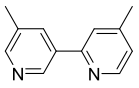
L2

L3

L4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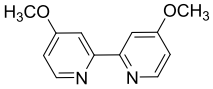
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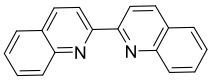
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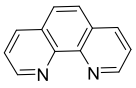
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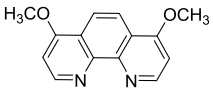
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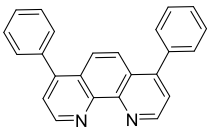
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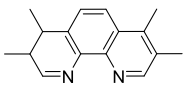
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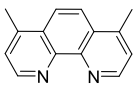
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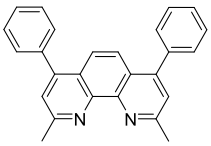
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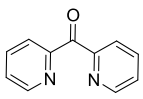
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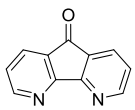
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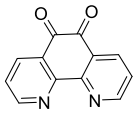
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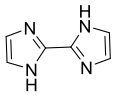
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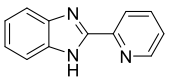
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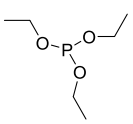
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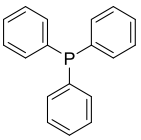
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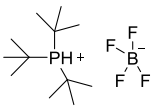
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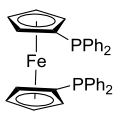
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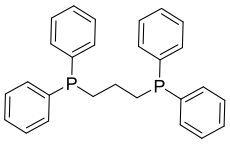
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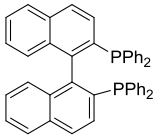
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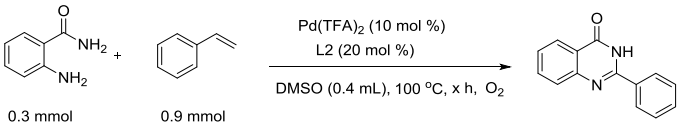
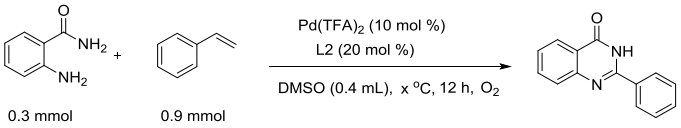
Table S4: Optimization of Time



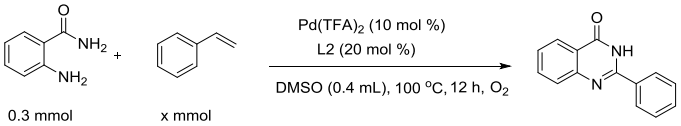
entry	Time (h)	yield (%)
1	6	23
2	9	67
3	12	85
4	15	81
5	18	78
6	21	75
7	24	74
8	36	50

Table S5: Optimization of Temperature



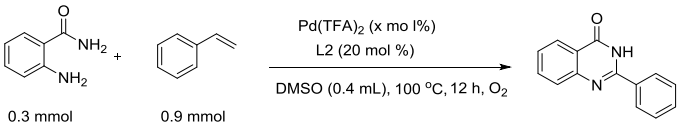
entry	temperature (°C)	yield (%)
1	80	60
2	85	69
3	90	74
4	95	83
5	100	85
6	105	76
7	110	71
8	115	68
9	120	65

Table S6: Optimization of Olefin amount



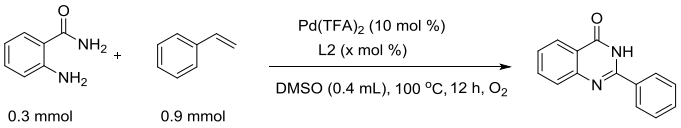
entry	olefin (x mmol)	yield (%)
1	0.6	62
2	0.9	85
3	1.2	74
4	1.5	50
5	1.8	32

Table S7: Optimization of Catalyst amount



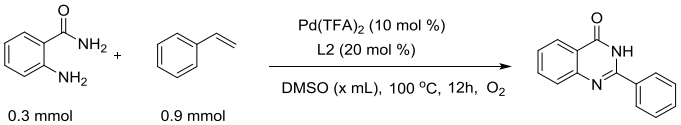
entry	Pd (x mol%)	yield (%)
1	5	70
2	10	85
3	20	62
4	30	45

Table S8: Optimization of Ligand amount



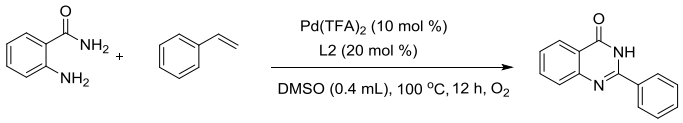
entry	ligand (x mol%)	yield (%)
1	10	28
2	12	40
3	14	58
4	16	69
5	18	77
6	20	85
7	22	83

Table S9: Optimization of Solvent amount



entry	DMSO (x mL)	yield (%)
1	0.2	48
2	0.3	62
3	0.4	85
4	0.5	78
5	0.6	72
6	0.7	67
7	0.8	61
8	0.9	54
9	1.0	50

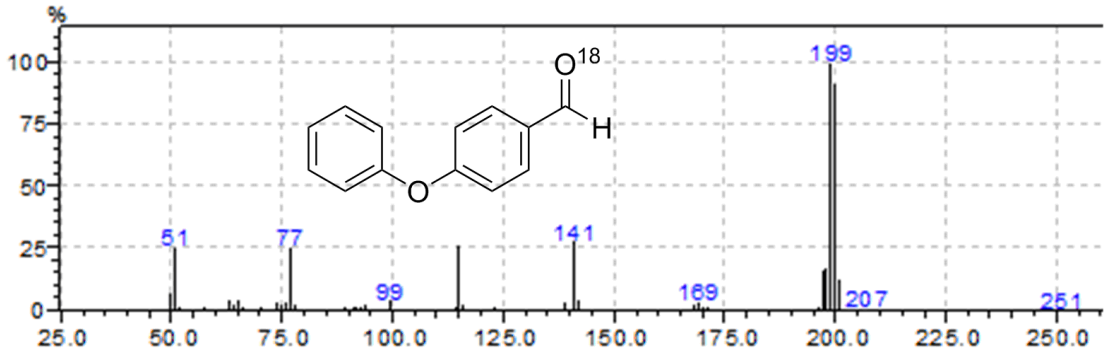
2.2 General Procedure for the Palladium Catalyzed Synthesis of Quinazolines



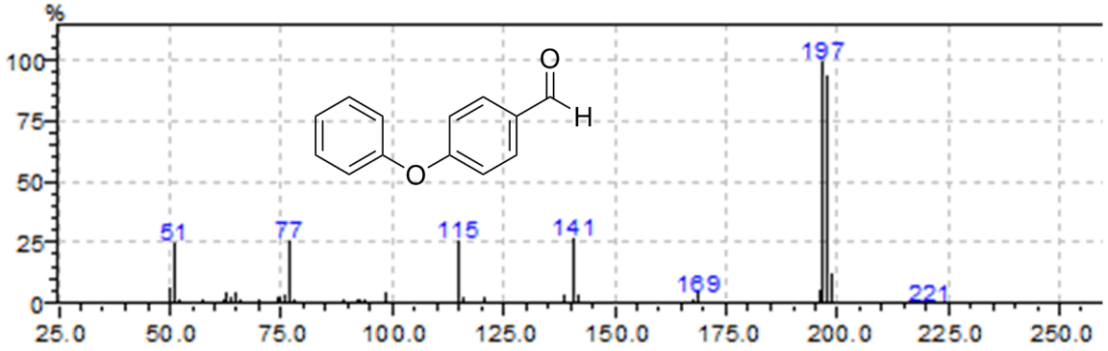
In a 25 mL Schlenk tube equipped with a stir bar were placed 2-Amino Benzamides (0.3 mmol), $Pd(TFA)_2$ (10 mol %) and bpy (20 mol %). The tube was evacuated and refilled with O_2 three times. Styrene (0.9 mmol) and DMSO (0.4 mL) were added. The reaction mixture was stirred at 100 ^oC for 12 h. After it was cooled, the reaction mixture was diluted with 10 mL of methylene chloride, and filtered through a pad of silica gel, followed by washing the pad of silica gel with the same solvent (20 mL). The filtrate was washed with water (3×15 mL). The organic phase was dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was then purified by flash chromatography on silica gel to provide the corresponding product.

3. ^{18}O Labeling Experiments

3.1 The GC-MS data in the presence of $^{18}O_2$

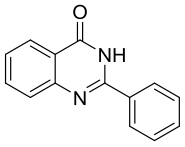


3.2 The GC-MS data in the presence of $H_2{}^{18}O$



4. Analytical Data for All Products

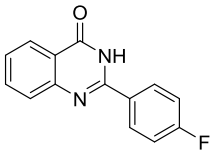
2-phenylquinazolin-4(3H)-one[1]



3a

Following the general procedure, using 8/1 methylene chloride/ethyl acetate as the eluant to afford white soild (85% yield). **^{1}H NMR** (500 MHz, DMSO-d_6) δ 12.53 (s, 1H), 8.19 (d, J = 7.5 Hz, 2H), 8.16 (d, J = 8.0 Hz, 1H), 7.85-7.82 (m, 1H), 7.74 (d, J = 8.0 Hz, 1H), 7.59-7.50 (m, 4H); **^{13}C NMR** (125 MHz, DMSO-d_6) δ 162.2, 152.3, 148.6, 134.5, 132.7, 131.3, 128.5, 127.7, 127.3, 126.5, 125.8, 120.9.

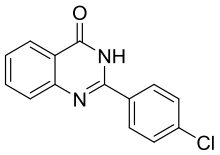
2-(4-fluorophenyl)quinazolin-4(3H)-one[3]



3b

Following the general procedure, using 8/1 methylene chloride/ethyl acetate as the eluant to afford white soild (78% yield). **^{1}H NMR** (500 MHz, DMSO-d_6) δ 12.56 (s, 1H), 8.25 (dd, J = 5.5, 9.0 Hz, 2H), 8.15 (d, J = 8.0 Hz, 1H), 7.85-7.82 (m, 1H), 7.73 (d, J = 8.0 Hz, 1H), 7.53-7.50 (m, 1H), 7.40-7.37 (m, 2H); **^{13}C NMR** (125 MHz, DMSO-d_6) δ 163.6 (d, $J_{C\text{-}F}$ = 348.8 Hz), 163.0, 151.4, 148.5, 134.5, 130.3 (d, $J_{C\text{-}F}$ = 8.8 Hz), 129.2, 127.3, 126.5, 125.8, 120.8, 115.5 (d, $J_{C\text{-}F}$ = 21.3 Hz).

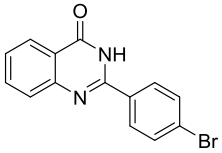
2-(4-chlorophenyl)quinazolin-4(3H)-one[1]



3c

Following the general procedure, using 8/1 methylene chloride/ethyl acetate as the eluant to afford white soild (76% yield). **^{1}H NMR** (500 MHz, DMSO-d_6) δ 12.62 (s, 1H), 8.20 (d, *J* = 8.0 Hz, 2H), 8.15 (d, *J* = 7.5 Hz, 1H), 7.86-7.83 (m, 1H), 7.74 (d, *J* = 8.0 Hz, 1H), 7.62 (d, *J* = 8.5 Hz, 2H), 7.55-7.52 (m, 1H); **^{13}C NMR** (125 MHz, DMSO-d_6) δ 162.1, 151.3, 148.5, 136.2, 134.6, 131.5, 129.6, 128.6, 127.4, 126.7, 125.8, 121.0.

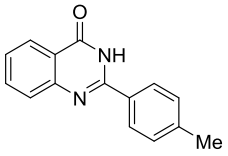
2-(4-bromophenyl)quinazolin-4(3H)-one[3]



3d

Following the general procedure, using 8/1 methylene chloride/ethyl acetate as the eluant to afford white soild (70% yield). **^{1}H NMR** (500 MHz, DMSO-d_6) δ 12.60 (s, 1H), 8.16 (d, *J* = 8.0 Hz, 1H), 8.13 (d, *J* = 8.5 Hz, 2H), 7.86-7.83 (m, 1H), 7.77-7.74 (m, 3H), 7.55-7.52 (m, 1H); **^{13}C NMR** (125 MHz, DMSO-d_6) δ 162.1, 151.4, 148.5, 134.6, 131.9, 131.5, 129.7, 127.5, 126.7, 125.8, 125.1, 121.0.

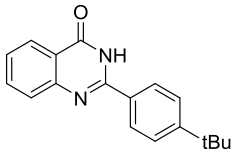
2-(p-tolyl)quinazolin-4(3H)-one[2]



3e

Following the general procedure, using 8/1 methylene chloride/ethyl acetate as the eluant to afford white soild (83% yield). **^{1}H NMR** (500 MHz, DMSO-d_6) δ 12.45 (s, 1H), 8.14 (d, *J* = 8.0 Hz, 1H), 8.10 (d, *J* = 8.0 Hz, 2H), 7.83-7.80 (m, 1H), 7.72 (d, *J* = 8.0 Hz, 1H), 7.51-7.49 (m, 1H), 7.35 (d, *J* = 8.0 Hz, 2H), 2.39 (s, 3H); **^{13}C NMR** (125 MHz, DMSO-d_6) δ 162.2, 152.2, 148.7, 141.4, 134.4, 129.9, 129.1, 127.6, 127.2, 126.3, 125.8, 120.8, 20.9.

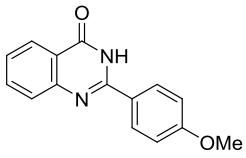
2-(4-(tert-butyl)phenyl)quinazolin-4(3H)-one[5]



3f

Following the general procedure, using 8/1 methylene chloride/ethyl acetate as the eluant to afford white soild (82% yield). **^{1}H NMR** (500 MHz, DMSO-d_6) δ 12.46 (s, 1H), 8.16-8.13 (m, 3H), 7.84-7.81 (m, 1H), 7.73 (d, *J* = 8.0 Hz, 1H), 7.55 (d, *J* = 8.5 Hz, 2H) , 7.52-7.49 (m, 1H), 1.32 (s, 9H); **^{13}C NMR** (125 MHz, DMSO-d_6) δ 162.1, 154.2, 152.1, 148.8, 134.4, 129.9, 127.5, 127.4, 126.3, 125.8, 125.3, 120.9, 34.6, 30.8.

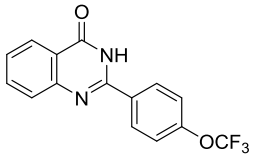
2-(4-methoxyphenyl)quinazolin-4(3H)-one[3]



3g

Following the general procedure, using 8/1 methylene chloride/ethyl acetate as the eluant to afford white soild (79% yield). **^{1}H NMR** (500 MHz, DMSO-d_6) δ 12.41 (s, 1H), 8.19 (d, *J* = 9.0 Hz, 2H), 8.13 (d, *J* = 7.0 Hz, 1H), 7.83-7.80 (m, 1H), 7.70 (d, *J* = 8.0 Hz, 1H), 7.50-7.47 (m, 1H), 7.09 (d, *J* = 9.0 Hz, 2H), 3.85 (s, 3H); **^{13}C NMR** (125 MHz, DMSO-d_6) δ 162.3, 161.8, 151.9, 148.8, 134.4, 129.4, 127.1, 126.0, 125.7, 124.8, 120.6, 113.9, 55.4.

2-(4-(trifluoromethoxy)phenyl)quinazolin-4(3H)-one[4]

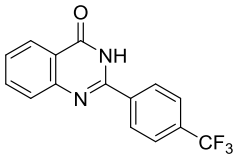


3h

Following the general procedure, using 8/1 methylene chloride/ethyl acetate as the eluant to afford white soild (68% yield). **^{1}H NMR** (500 MHz, DMSO-d_6) δ 12.65 (s, 1H), 8.30 (d, *J* = 9.0 Hz, 2H), 8.16 (d, *J* = 7.5 Hz, 1H), 7.87-7.84 (m, 1H), 7.75 (d, *J* =

8.0 Hz, 1H), 7.56-7.53 (m, 3H); **^{13}C NMR** (125 MHz, DMSO-d_6) δ 162.1, 151.2, 150.4, 148.5, 134.6, 131.8, 130.0, 127.4, 126.7, 125.8, 120.8, 120.5, 119.9 (d, $J_{C\text{-}F}$ = 252.5 Hz), 101.2.

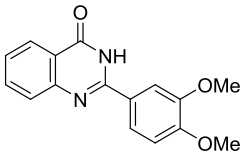
2-(4-(trifluoromethyl)phenyl)quinazolin-4(3H)-one[4]



3i

Following the general procedure, using 8/1 methylene chloride/ethyl acetate as the eluant to afford white soild (60% yield). **^{1}H NMR** (500 MHz, DMSO-d_6) δ 12.74 (s, 1H), 8.37 (d, J = 8.0 Hz, 2H), 8.17 (d, J = 8.0 Hz, 1H), 7.92 (d, J = 8.0 Hz, 1H), 7.88-7.85 (m, 1H), 7.78 (d, J = 8.0 Hz, 1H), 7.57-7.54 (m, 1H); **^{13}C NMR** (125 MHz, DMSO-d_6) δ 162.1, 149.8 (d, $J_{C\text{-}F}$ = 357.5 Hz), 136.6, 134.6, 131.0 (q, $J_{C\text{-}F}$ =32.5 Hz), 128.7, 127.5, 127.0, 125.8, 125.4 (q, $J_{C\text{-}F}$ = 3.8 Hz), 121.2.

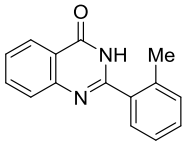
2-(3,4-dimethoxyphenyl)quinazolin-4(3H)-one[10]



3j

Following the general procedure, using 8/1 methylene chloride/ethyl acetate as the eluant to afford white soild (70% yield). **^{1}H NMR** (500 MHz, DMSO-d_6) δ 12.43 (s, 1H), 8.13 (d, J = 7.0 Hz, 1H), 7.88-7.86 (m, 1H), 7.83-7.79 (m, 2H), 7.71 (d, J = 8.0 Hz, 1H), 7.50-7.47 (m, 1H), 7.11 (d, J = 8.5 Hz, 1H), 3.89 (s, 3H), 3.85 (s, 3H); **^{13}C NMR** (125 MHz, DMSO-d_6) δ 162.3, 151.8, 151.6, 148.8, 148.5, 134.4, 127.2, 126.0, 125.8, 124.7, 121.1, 120.6, 111.4, 110.7, 55.6, 55.6.

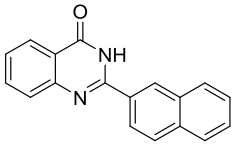
2-(o-tolyl)quinazolin-4(3H)-one[2]



3k

Following the general procedure, using 8/1 methylene chloride/ethyl acetate as the eluant to afford white soild (80% yield). **^{1}H NMR** (500 MHz, DMSO-d_6) δ 12.43 (s, 1H), 8.17 (d, *J* = 8.0 Hz, 1H), 7.85-7.82 (m, 1H), 7.69 (d, *J* = 8.0 Hz, 1H), 7.55-7.50 (m, 2H), 7.44-7.41 (m, 1H), 7.35-7.31 (m, 2H), 2.39 (s, 3H); **^{13}C NMR** (125 MHz, DMSO-d_6) δ 161.7, 154.3, 148.7, 136.0, 134.3, 134.2, 130.4, 129.8, 129.0, 127.3, 126.5, 125.7, 125.6, 120.9, 19.5.

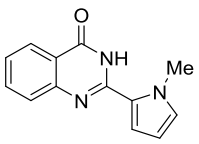
2-(naphthalen-2-yl)quinazolin-4(3H)-one[5]



3l

Following the general procedure, using 8/1 methylene chloride/ethyl acetate as the eluant to afford white soild (71% yield). **^{1}H NMR** (500 MHz, DMSO-d_6) δ 12.66 (s, 1H), 8.82 (s, 1H), 8.31 (d, *J* = 7.0 Hz, 1H), 8.19 (d, *J* = 7.5 Hz, 1H), 8.08-8.05 (m, 2H), 8.01 (d, *J* = 7.0 Hz, 1H), 7.88-7.85 (m, 1H), 7.80 (d, *J* = 9.0 Hz, 1H), 7.66-7.61 (m, 2H), 7.56-7.53 (m, 1H); **^{13}C NMR** (125 MHz, DMSO-d_6) δ 162.2, 152.2, 148.7, 134.6, 134.1, 132.2, 129.9, 128.9, 128.1, 128.0, 127.8, 127.6, 127.5, 126.8, 126.6, 125.8, 124.4, 121.0.

2-(1-methyl-1H-pyrrol-2-yl)quinazolin-4(3H)-one

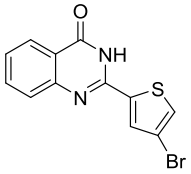


3m

Following the general procedure, using 8/1 methylene chloride/ethyl acetate as the eluant to afford white soild (53% yield), mp: 211-212 ^{o}C. **^{1}H NMR** (500 MHz,

DMSO-d_6) δ 12.03 (s, 1H), 8.09 (d, J = 7.5 Hz, 1H), 7.77-7.74 (m, 1H), 7.61 (d, J = 8.0 Hz, 1H), 7.43-7.40 (m, 1H), 7.22 (d, J = 2.5 Hz, 1H), 7.09 (s, 1H), 6.15-6.14 (m, 1H), 4.07 (s, 3H); **^{13}C NMR** (125 MHz, DMSO-d_6) δ 161.9, 148.8, 146.7, 134.4, 130.0, 126.9, 125.7, 125.5, 123.9, 120.4, 114.7, 107.6, 37.4. **HRMS** (ESI) calcd for $C_{13}H_{11}N_3O$ $[M+H]^+$: 226.0980, found: 226.0985.

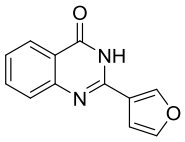
2-(4-bromothiophen-2-yl)quinazolin-4(3H)-one



3n

Following the general procedure, using 10/1 methylene chloride/ethyl acetate as the eluant to afford yellow soild (40% yield), mp: 303-304 ^{o}C. **^{1}H NMR** (500 MHz, DMSO-d_6) δ 12.68 (s, 1H), 8.23 (s, 1H), 8.13 (d, J = 7.0 Hz, 1H) , 7.99 (s, 1H), 7.83-7.80 (m, 1H), 7.66 (d, J = 8.0 Hz, 1H), 7.52-7.50 (m, 1H); **^{13}C NMR** (125 MHz, DMSO-d_6) δ 161.5, 148.2, 146.5, 138.5, 134.7, 131.1, 129.6, 127.0, 126.7, 126.0, 121.0, 109.3. **HRMS** (ESI) calcd for $C_{12}H_7BrN_2OS$ $[M+H]^+$: 306.9540, found: 306.9547.

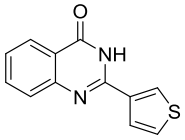
2-(furan-3-yl)quinazolin-4(3H)-one[5]



3o

Following the general procedure, using 10/1 methylene chloride/ethyl acetate as the eluant to afford white soild (52% yield). **^{1}H NMR** (500 MHz, DMSO-d_6) δ 12.40 (s, 1H), 8.13 (s, 1H), 8.12 (d, J = 8.0 Hz, 1H), 7.85 (s, 1H) 7.81-7.79 (m, 1H), 7.66 (d, J = 8.0 Hz, 1H), 7.50-7.47 (m, 1H), 7.16 (d, J = 1.0 Hz, 1H); **^{13}C NMR** (125 MHz, DMSO-d_6) δ 161.8, 148.8, 147.2, 145.0, 144.6, 134.5, 127.0, 126.2, 125.8, 121.4, 120.9, 109.0.

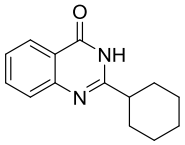
2-(thiophen-3-yl)quinazolin-4(3H)-one[5]



3p

Following the general procedure, using 10/1 methylene chloride/ethyl acetate as the eluant to afford yellow soild (58% yield). **^{1}H NMR** (500 MHz, DMSO-d_6) δ 12.46 (s, 1H), 8.60 (d, *J* = 1.5 Hz, 1H), 8.13 (d, *J* = 7.0 Hz, 1H), 7.88 (d, *J* = 4.5 Hz, 1H), 7.83-7.80 (m, 1H), 7.72-7.69 (m, 2H), 7.51-7.48 (m, 1H); **^{13}C NMR** (125 MHz, DMSO-d_6) δ 162.0, 148.8, 148.3, 135.4, 134.5, 128.6, 127.2, 127.2, 127.0, 126.3, 125.8, 120.9.

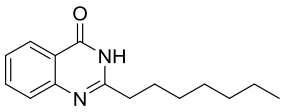
2-cyclohexylquinazolin-4(3H)-one[5]



3q

Following the general procedure, using 8/1 methylene chloride/ethyl acetate as the eluant to afford white soild (37% yield). **^{1}H NMR** (500 MHz, DMSO-d_6) δ 12.07 (s, 1H), 8.07 (d, *J* = 7.5 Hz, 1H), 7.76-7.73 (m, 1H), 7.59 (d, *J* = 8.0 Hz, 1H), 7.44 (d, *J* = 7.5 Hz, 1H), 2.59-2.55 (m, 1H), 1.91-1.89 (m, 4H), 1.68-1.55 (m, 3H), 1.33-1.17 (m, 3H); **^{13}C NMR** (125 MHz, DMSO-d_6) δ 161.8, 160.7, 148.9, 134.1, 126.9, 125.8, 125.6, 120.9, 42.8, 30.1, 25.4, 25.3.

2-heptylquinazolin-4(3H)-one[5]

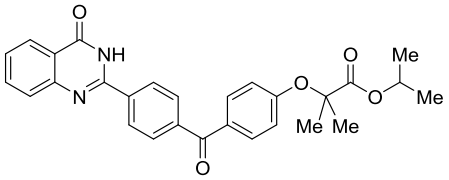


3r

Following the general procedure, using 8/1 methylene chloride/ethyl acetate as the

eluant to afford white soild (45% yield). **^{1}H NMR** (500 MHz, DMSO-d_6) δ 11.59 (s, 1H), 8.28 (d, J = 7.5 Hz, 1H)，7.79-7.76 (m, 1H), 7.72 (d, J = 7.5 Hz, 1H), 7.48-7.46 (m, 1H), 2.80 (t, J = 7.5 Hz, 2H), 1.92-1.86 (m, 2H), 1.49-1.43 (m, 8H), 0.87 (t, J = 6.5 Hz, 3H); **^{13}C NMR** (125 MHz, DMSO-d_6) δ 161.8, 157.5, 148.9, 134.1, 126.7, 125.8, 125.6, 120.7, 34.4, 31.0, 28.4, 28.3, 26.7, 22.0, 13.8.

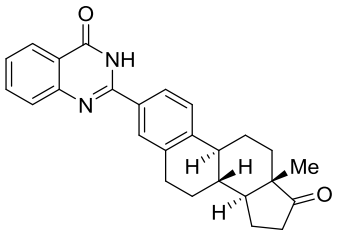
isopropyl 2-methyl-2-(4-(4-(4-oxo-3,4-dihydroquinazolin-2-yl)benzoyl)phenoxy)propanoate



3s

Following the general procedure, using 8/1 methylene chloride/ethyl acetate as the eluant to afford white soild (58% yield), mp: 149-150 ºC. **^{1}H NMR** (500 MHz, DMSO-d_6) δ 12.70 (s, 1H), 8.33 (d, J = 8.0 Hz, 2H), 8.17 (d, J = 8.0 Hz, 1H), 7.87-7.81 (m, 3H), 7.78-7.75 (m, 3H), 7.56-7.53 (m, 1H), 6.92 (d, J = 9.0 Hz, 2H), 5.01-4.96 (m, 1H), 1.61 (s, 6H), 1.16 (s, 3H) 1.15 (s, 3H); **^{13}C NMR** (125 MHz, DMSO-d_6) δ 193.7, 172.0, 162.1, 159.3, 151.5, 148.5, 139.8, 135.6, 134.6, 131.8, 129.6, 129.2, 127.8, 127.5, 126.8, 125.8, 121.1, 117.2, 79.1, 68.9, 25.0, 21.1. **HRMS** (ESI) calcd for $C_{28}H_{26}N_2O_5$ $[M+H]^+$: 471.1920, found: 471.1932.

2-((8R,9S,13S,14S)-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-3-yl)quinazolin-4(3H)-one

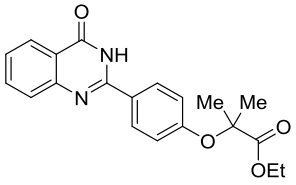


3t

Following the general procedure, using 8/1 methylene chloride/ethyl acetate as the

eluant to afford white soild (46% yield), mp: 315-316 °C. **^{1}H NMR** (500 MHz, PYRIDINE-d_5) δ 13.52 (s, 1H), 8.63 (d, *J* = 7.5 Hz, 1H), 8.35 (d, *J* = 8.5 Hz, 1H), 8.21 (s, 1H), 8.06 (d, *J* = 8.0 Hz, 1H), 7.82-7.79 (m, 1H), 7.56 (d, *J* = 8.5 Hz, 1H), 7.50-7.47 (m, 1H), 2.92-2.91 (m, 2H), 2.49-2.43 (m, 1H), 2.31-2.29 (m, 1H), 2.22 (t, *J* = 10.5 Hz, 2H), 2.00-1.98 (m, 1H), 1.88-1.82 (m, 2H), 1.54-1.43 (m, 4H), 1.36-1.32 (m, 2H), 0.85 (s, 3H); **^{13}C NMR** (100 MHz, PYRIDINE-d_5) δ 218.4, 162.5, 152.9, 149.4, 143.1, 136.6, 133.8, 130.9, 128.2, 127.3, 125.9, 125.7, 125.4, 124.9, 121.5, 49.6, 47.1, 43.9, 37.1, 35.0, 31.2, 28.7, 25.6, 24.9, 20.8, 12.9. **HRMS** (ESI) calcd for $C_{26}H_{26}N_2O_2$ $[M+H]^+$: 399.2072, found: 399.2075.

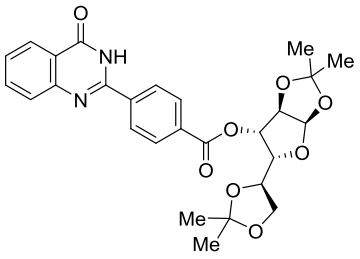
2,3-diphenylquinazolin-4(3H)-one



3u

Following the general procedure, using 8/1 methylene chloride/ethyl acetate as the eluant to afford white soild (69% yield), mp 167-168 °C. **^{1}H NMR** (500 MHz, DMSO-d_6) δ 12.40 (s, 1H), 8.13 (d, *J* = 8.0 Hz, 3H), 7.82-7.79 (m, 1H), 7.69 (d, *J* = 8.0 Hz, 1H), 7.50-7.47 (m, 1H), 6.90 (d, *J* = 8.0 Hz, 2H), 4.19 (q, *J* = 6.5 Hz, 2H), 1.60 (s, 6H), 1.17 (t, *J* = 7.0 Hz, 3H); **^{13}C NMR** (125 MHz, DMSO-d_6) δ 172.8, 162.1, 157.8, 151.7, 148.8, 134.4, 129.2, 127.2, 126.1, 125.8, 125.7, 120.7, 117.7, 78.9, 61.2, 25.0, 13.8. **HRMS** (ESI) calcd for $C_{20}H_{20}N_2O_4$ $[M+H]^+$: 353.1501, found: 353.1507.

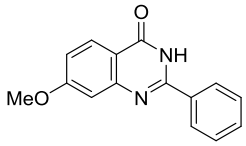
4-(4-oxo-3,4-dihydroquinazolin-2-yl)phenyl(3aR,5S,6S,6aR)-5-((R)-2,2-dimethyl-1,3-dioxolan-4-yl)-2,2-dimethyltetrahydrofuro[2,3-d][1,3]dioxole-6-carboxylate



3v

Following the general procedure, using 8/1 methylene chloride/ethyl acetate as the eluant to afford white soild (60% yield), mp: 245-246 ^{o}C. **^{1}H NMR** (500 MHz, DMSO-d_6) δ 12.70 (s, 1H), 8.33 (d, *J* = 8.0 Hz, 2H), 8.18 (d, *J* = 8.0 Hz, 1H), 8.11 (d, *J* = 8.5 Hz, 2H), 7.88-7.85 (m, 1H), 7.78 (d, *J* = 8.0 Hz, 1H), 7.58-7.55 (m, 1H), 6.02 (d, *J* = 3.5 Hz, 1H), 5.32 (d, *J* = 2.5 Hz, 1H), 4.76 (d, *J* = 3.5 Hz, 1H), 4.40 (dd, *J* = 6.5, 12.5 Hz, 1H), 4.27 (dd, *J* = 2.0, 7.0 Hz, 1H), 4.08 (m, 1H), 3.96 (dd, *J* = 6.5, 12.5 Hz, 1H), 1.48 (s, 3H), 1.34 (s, 3H), 1.28 (s, 3H), 1.21 (s, 3H); **^{13}C NMR** (125 MHz, DMSO-d_6) δ 164.1, 162.0, 151.3, 148.4, 137.3, 134.6, 131.1, 129.4, 128.2, 127.6, 127.0, 125.8, 121.1, 111.3, 108.4, 104.7, 82.6, 79.1, 76.6, 72.1, 66.2, 26.5, 26.4, 25.9, 25.0. **HRMS** (ESI) calcd for $C_{27}H_{28}N_2O_8$ $[M+H]^+$: 509.1924, found: 509.1930.

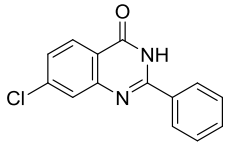
7-methoxy-2-phenylquinazolin-4(3H)-one[1]



4a

Following the general procedure, using 8/1 methylene chloride/ethyl acetate as the eluant to afford white soild (87% yield). **^{1}H NMR** (500 MHz, DMSO-d_6) δ 12.41 (s, 1H), 8.17 (d, *J* = 8.0 Hz, 2H), 8.05 (d, *J* = 9.0 Hz, 1H), 7.60-7.53 (m, 3H), 7.18 (s, 1H), 7.09 (d, *J* = 7.0 Hz, 1H), 3.91 (s, 3H); **^{13}C NMR** (125 MHz, DMSO-d_6) δ 164.2, 161.7, 152.9, 150.9, 132.7, 131.3, 128.5, 127.7, 127.4, 116.1, 114.4, 108.5, 55.7.

7-chloro-2-phenylquinazolin-4(3H)-one[1]

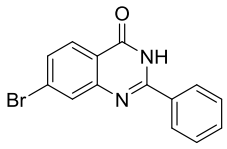


4b

Following the general procedure, using 8/1 methylene chloride/ethyl acetate as the eluant to afford white soild (73% yield). **^{1}H NMR** (500 MHz, DMSO-d_6) δ 12.66 (s,

1H), 8.18-8.16 (m, 2H), 8.13 (d, *J* = 8.5 Hz, 1H), 7.78-7.77 (m, 1H), 7.62-7.52 (m, 4H); **^{13}C NMR** (125 MHz, DMSO-d_6) δ 161.7, 153.8, 149.8, 139.1, 132.4, 131.6, 129.2, 128.5, 127.8, 126.7, 126.4, 119.8.

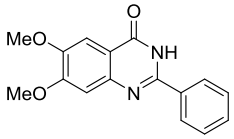
7-bromo-2-phenylquinazolin-4(3H)-one[11]



4c

Following the general procedure, using 8/1 methylene chloride/ethyl acetate as the eluant to afford white soild (70% yield). **^{1}H NMR** (500 MHz, DMSO-d_6) δ 12.66 (s, 1H), 8.18 (d, *J* = 7.5 Hz, 2H), 7.94 (s, 1H), 7.67 (d, *J* = 8.5 Hz, 1H), 7.62-7.54 (m, 3H); **^{13}C NMR** (125 MHz, DMSO-d_6) δ 161.7, 153.7, 149.8, 132.3, 131.6, 129.6, 129.4, 128.5, 128.0, 127.8, 127.8, 120.0.

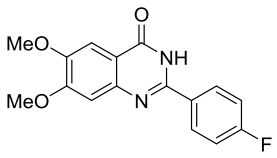
6,7-dimethoxy-2-phenylquinazolin-4(3H)-one[1]



4d

Following the general procedure, using 8/1 methylene chloride/ethyl acetate as the eluant to afford white soild (92% yield). **^{1}H NMR** (500 MHz, DMSO-d_6) δ 12.43 (s, 1H), 8.16 (d, *J* = 7.0 Hz, 2H), 7.58-7.52 (m, 3H), 7.48 (s, 1H), 7.21 (s, 1H), 3.98 (s, 3H), 3.89 (s, 3H); **^{13}C NMR** (125 MHz, DMSO-d_6) δ 161.5, 154.7, 150.8, 148.6, 144.8, 132.8, 131.0, 128.5, 127.4, 114.0, 108.2, 105.0, 55.9, 55.7.

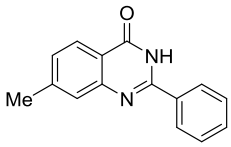
2-(4-fluorophenyl)-6,7-dimethoxyquinazolin-4(3H)-one[6]



4e

Following the general procedure, using 8/1 methylene chloride/ethyl acetate as the eluant to afford white soild (83% yield). **^{1}H NMR** (500 MHz, DMSO-d_6) δ 12.42 (s, 1H), 8.24-8.21 (m, 2H), 7.48 (s, 1H), 7.39-7.35 (m, 2H), 7.20 (s, 1H), 3.93 (s, 3H), 3.89 (s, 3H); **^{13}C NMR** (125 MHz, DMSO-d_6) δ 163.2 (d, $J_{C\text{-}F}$ = 393.8 Hz), 162.8, 154.7, 150.0, 148.6, 144.7, 129.9 (d, $J_{C\text{-}F}$ = 8.8 Hz), 129.4, 115.5 (d, $J_{C\text{-}F}$ = 21.3 Hz), 113.8, 108.1, 105.0, 99.4, 55.9, 55.7.

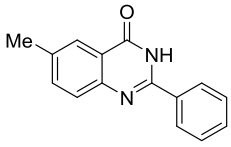
7-methyl-2-phenylquinazolin-4(3H)-one[4]



4f

Following the general procedure, using 8/1 methylene chloride/ethyl acetate as the eluant to afford white soild (81% yield). **^{1}H NMR** (500 MHz, DMSO-d_6) δ 12.44(s, 1H), 8.17 (d, J = 7.0 Hz, 2H), 8.03 (d, J = 8.0 Hz, 1H), 7.58-7.52 (m, 4H), 7.32 (d, J = 8.0 Hz, 1H), 2.46 (s, 3H); **^{13}C NMR** (125 MHz, DMSO-d_6) δ 162.1, 152.3, 148.7, 144.9, 132.8, 131.2, 128.5, 127.9, 127.6, 127.0, 125.6, 118.5, 21.3.

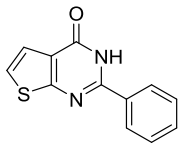
6-methyl-2-phenylquinazolin-4(3H)-one[2]



4g

Following the general procedure, using 8/1 methylene chloride/ethyl acetate as the eluant to afford white soild (67% yield). **^{1}H NMR** (500 MHz, DMSO-d_6) δ 12.46 (s, 1H), 8.17 (d, J = 7.5 Hz, 2H), 7.96 (s, 1H), 7.67-7.64 (m, 2H), 7.59-7.53 (m, 3H), 2.46 (s, 3H); **^{13}C NMR** (125 MHz, DMSO-d_6) δ 162.1, 151.4, 146.6, 136.2, 135.7, 132.7, 131.1, 128.5, 127.5, 127.2, 125.1, 120.6, 20.7.

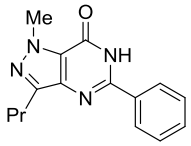
2-phenylthieno[3,2-d]pyrimidin-4(3H)-one



4h

Following the general procedure, using 8/1 methylene chloride/ethyl acetate as the eluant to afford white soild (60% yield), mp: 280-281 ºC. **^{1}H NMR** (500 MHz, DMSO-d_6) δ 12.70 (s, 1H), 8.21 (d, J = 5.5 Hz, 1H), 8.13 (d, J = 7.5 Hz, 2H), 7.60-7.52 (m, 3H), 7.47 (d, J = 5.0 Hz, 1H); **^{13}C NMR** (125 MHz, DMSO-d_6) δ 158.4, 157.8, 154.2, 135.2, 132.5, 131.2, 128.5, 127.7, 125.3, 121.2. **HRMS** (ESI) calcd for $C_{12}H_8N_2OS$ $[M+H]^+$: 229.0435, found 229.0442.

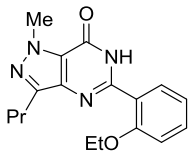
1-methyl-5-phenyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one[8]



4i

Following the general procedure, using 8/1 methylene chloride/ethyl acetate as the eluant to afford white soild (70% yield). **^{1}H NMR** (500 MHz, DMSO-d_6) δ 12.39 (s, 1H), 8.07 (d, J = 6.5 Hz, 2H), 7.55-7.50 (m, 3H), 4.15 (s, 3H), 2.80 (t, J = 7.5 Hz, 2H), 1.81-1.74 (m, 2H), 0.95 (t, J = 7.0 Hz, 3H); **^{13}C NMR** (125 MHz, DMSO-d_6) δ 154.5, 150.0, 144.9, 137.8, 132.9, 130.5, 128.4, 127.4, 124.3, 37.7, 27.1, 21.5, 13.7.

5-(2-methoxyphenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one[13]

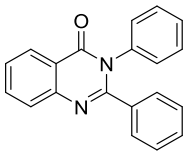


4j

Following the general procedure, using 8/1 methylene chloride/ethyl acetate as the eluan tto afford white soild (64% yield). **^{1}H NMR** (500 MHz, DMSO-d_6) δ 11.95 (s, 1H), 7.66 (d, J = 7.5 Hz, 1H), 7.49-7.46 (m, 1H), 7.14 (d, J = 8.0 Hz, 1H), 7.07-7.04

(m, 1H), 4.15 (s, *3*H), 4.12 (t, *J* = 7.0 Hz, 2H), 2.77 (t, *J* = 7.5 Hz, 2H), 1.78-1.70 (m, 2H), 1.33 (t, *J* = 7.0 Hz, 3H), 0.93 (t, *J* = 7.5 Hz, 3H); **^{13}C NMR** (125 MHz, DMSO-d_6) δ 156.4, 153.6, 149.5, 144.8, 137.9, 131.7, 130.3, 124.1, 122.5, 120.4, 112.8, 64.0, 37.7, 27.1, 21.6, 14.4, 13.7.

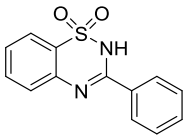
2,3-diphenylquinazolin-4(3H)-one[7]



4k

Following the general procedure, using 8/1 methylene chloride/ethyl acetate as the eluant to afford white soild (78% yield). **^{1}H NMR** (500 MHz, DMSO-d_6) δ 8.21 (d, *J* = 8.0 Hz, 1H), 7.92-7.89 (m, 1H), 7.77 (d, *J* = 8.5 Hz, 1H), 7.61 (d, *J* = 7.5 Hz, 1H), 7.38 (d, *J* = 7.0 Hz, 2H), 7.33-7.29 (m, 4H), 7.27-7.21 (m, 4H); **^{13}C NMR** (125 MHz, DMSO-d_6) δ 161.3, 155.1, 147.2, 137.7, 135.5, 134.7, 129.4, 128.8, 128.8, 128.5, 128.0, 127.4, 127.3, 127.1, 126.4, 120.7.

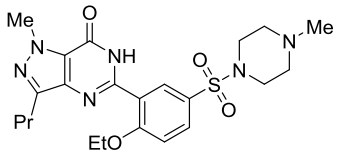
3-phenyl-2H-benzo[e][1,2,4]thiadiazine 1,1-dioxide[12]



4l

Following the general procedure, using 8/1 methylene chloride/ethyl acetate as the eluant to afford white soild (72% yield). **^{1}H NMR** (500 MHz, DMSO-d_6) δ 12.20 (s, 1H), 8.06-8.04 (m, 2H), 7.87-7.86 (m, 1H), 7.75-7.69 (m, 2H), 7.65-7.62 (m, 3H), 7.52-7.49 (m, 1H); **^{13}C NMR** (125 MHz, DMSO-d_6) δ 154.8, 135.5, 133.0, 132.7, 131.8, 128.8, 128.2, 126.6, 123.2, 121.5, 118.4.

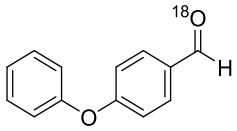
Sildenafil[13]



4m

Following the general procedure, using 8/1 methylene chloride/ethyl acetate as the eluant to afford white soild (90% yield). **^{1}H NMR** (500 MHz, DMSO-d_6) δ 12.20 (s, 1H), 7.85-7.82 (m, 2H), 7.37 (d, J = 8.5 Hz, 1H), 4.23-4.20 (m, 2H), 4.16 (s, 3H), 2.90 (s, 4H), 2.77 (t, J = 7.5 Hz, 2H), 2.36 (s, 4H), 2.14 (s, 3H), 2.24 (s, 2H), 1.77-1.70 (m, 2H), 1.33 (t, J = 7.0 Hz, 3H), 0.93 (t, J = 7.0 Hz, 3H); **^{13}C NMR** (125 MHz, DMSO-d_6) δ 159.8, 153.6, 148.1, 144.9, 137.7, 131.3, 129.8, 126.4, 124.3, 123.6, 113.2, 64.8, 53.4, 45.6, 45.2, 37.7, 27.1, 21.5, 14.1, 13.7.

4-phenoxy(benzaldehyde-^{18}O)



4m

Following the general procedure, using 20/1 petroleum ether/ethyl acetate as the eluant to afford white liquid (91% yield). **^{1}H NMR** (500 MHz, DMSO-d_6) δ 9.92 (s, 1H), 7.93-7.91 (m, 2H), 7.49-7.46 (m, 2H), 7.28-7.25 (m, 1H), 7.16-7.14 (d, J = 7.5 Hz, 2H) 7.12-7.10 (m, 2H); **^{13}C NMR** (125 MHz, DMSO-d_6) δ 191.3, 162.3, 154.7, 131.9, 131.2, 130.3, 124.9, 120.1, 117.4. **HRMS** (ESI) calcd for $C_{13}H_{10}O^{18}O$ $[M+H]^+$: 201.0801, found: 201.0793.

Reference

[1] M. Kumar, Richa, S. Sharma, V. Bhatt and N. Kumar, *Adv. Synth. Catal*., 2015, **357**, 2862.

[2] W. Lin, W. Wu, M. Selvaraju and C. Sun, *Org*. *Chem. Front*., 2017, **4**, 392.

[3] S. Parua, S. Das, R. Sikari, S. Sinha and N.-D. Paul, *J. Org. Chem*., 2017, **82**, 7165.

[4] K. Upadhyaya, R.-K. Thakur, S.-K. Shukla and R.-T. Tripathi, *J. Org. Chem*., 2016, **81**, 5046.

[5] M. Sharif, J. Opalach, P. Langer, M. Beller and X. Wu, *RSC Adv*., 2014, **4***,* 8.

[6] G. Schwan, G. Barbar Asskar, N. Höfgen, L. Kubicova, U. Funke, U. Egerland, M. Zahn, K. Nieber, M. Scheunemann, N. Sträter, P. Brus and D. Briel, *ChemMedChem*., 2014, **9**, 1476.

[7] D. Zhao, T. Wang, and J. Li. *Chem. Commun*., 2014, **50**, 6471.

[8] S. Mohammed, R.-A. Vishwakarma and S.-B. Bharate, *J. Org. Chem*., 2015, **80**, 6915.

[9] M.-R. Yadav, F. Grande, B.-S. Chouhan, P.-P. Naik, R. Giridhar, A. Garofalo and N. Neamati, *Eur. J. Med. Chem*., 2012, **48**, 231.

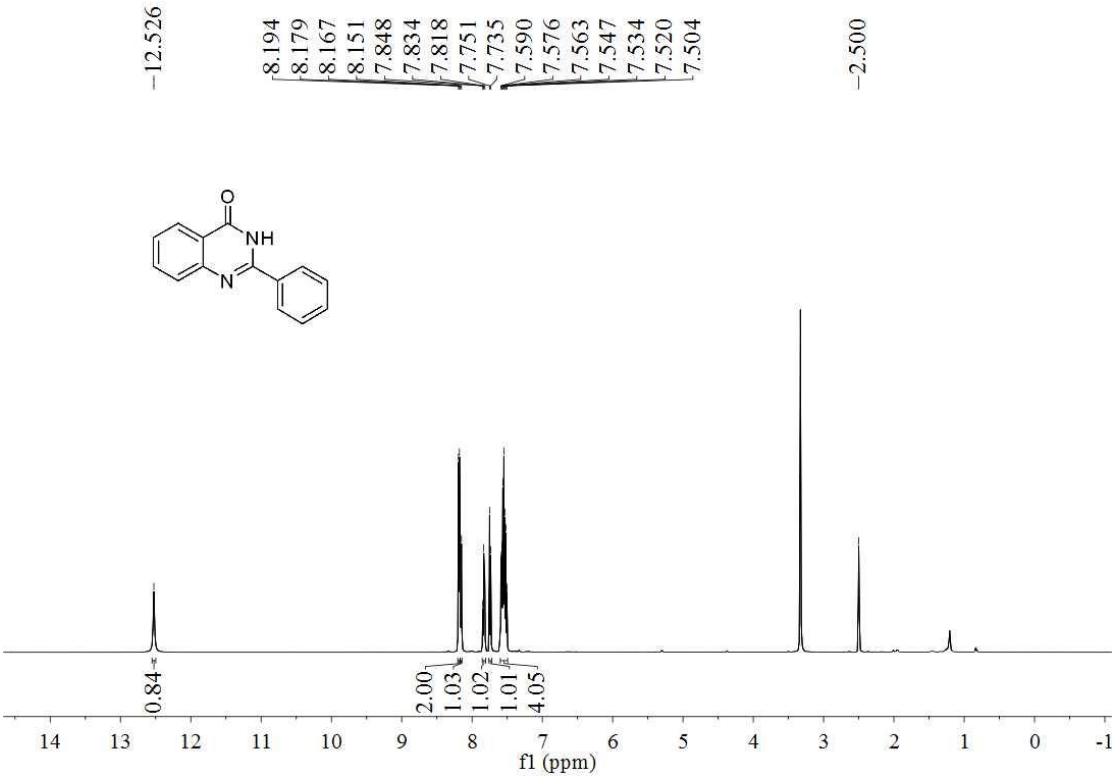
[10] F. Wang, H. Wang, Q. Wang, S. Yu, and X. Li, *Org. Lett*., 2016, **18***,* 1306.

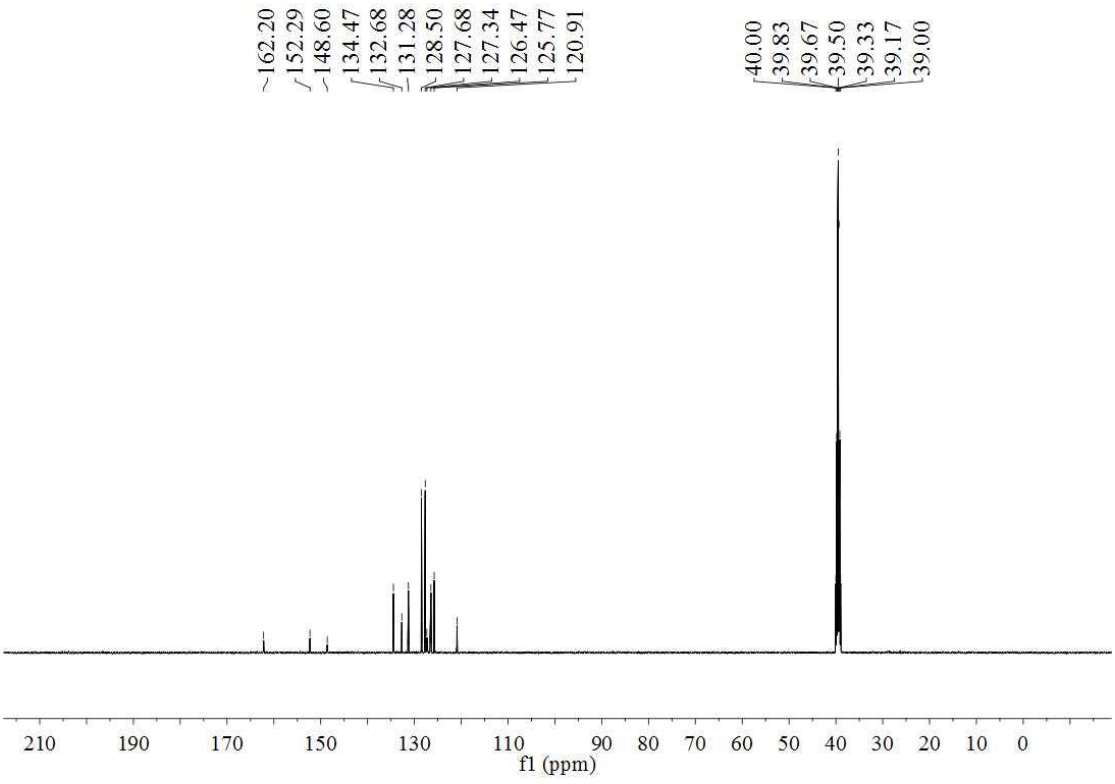
[11] F. Jia, Z. Zhou, C. Xu, Y. Wu and A. Wu, *Org. Lett*., 2016, **18**, 2942.

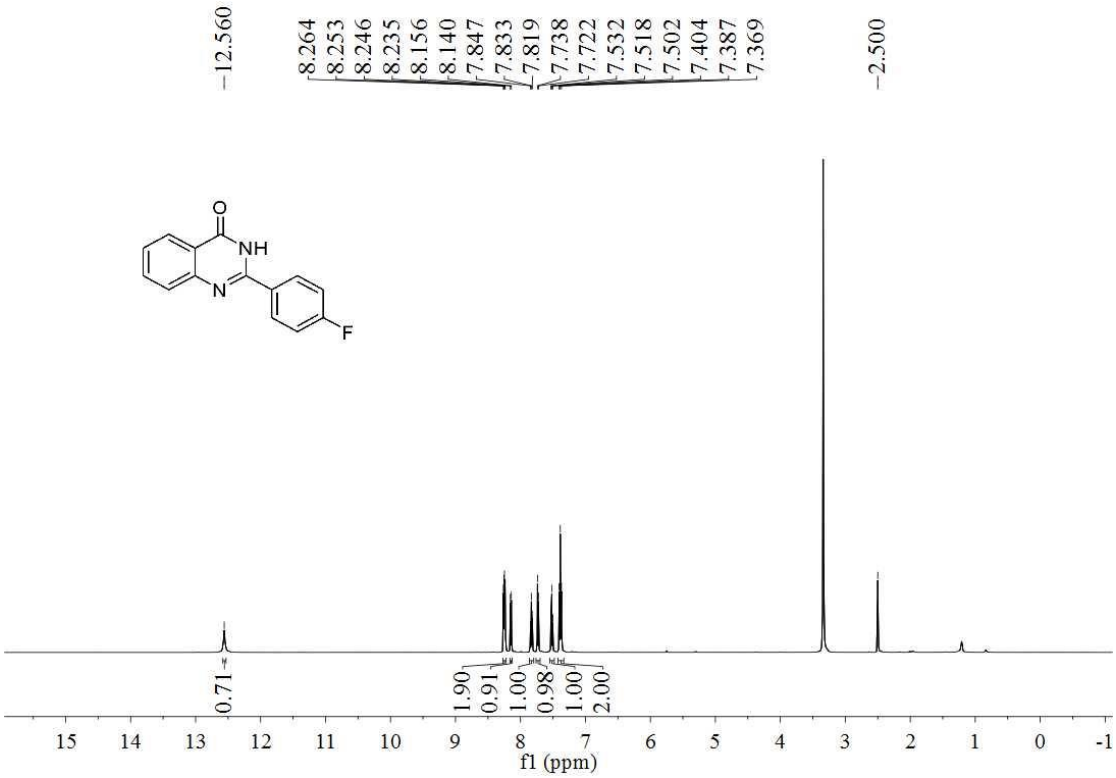
[12] D. Wang, X. Li, X, Y. Zhao and J. Chen, *Synth Commun*., 2016, **4**, 351.

[13] J. K. Laha, K. V. Pate, K. S. S. Tummalapalli and N. Dayal, *Chem. Commun*., 2016, **52**, 10245.

5. NMR Spectra for All Products



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7.738
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7.532
7.518
7.502
7.404
7.387
7.369
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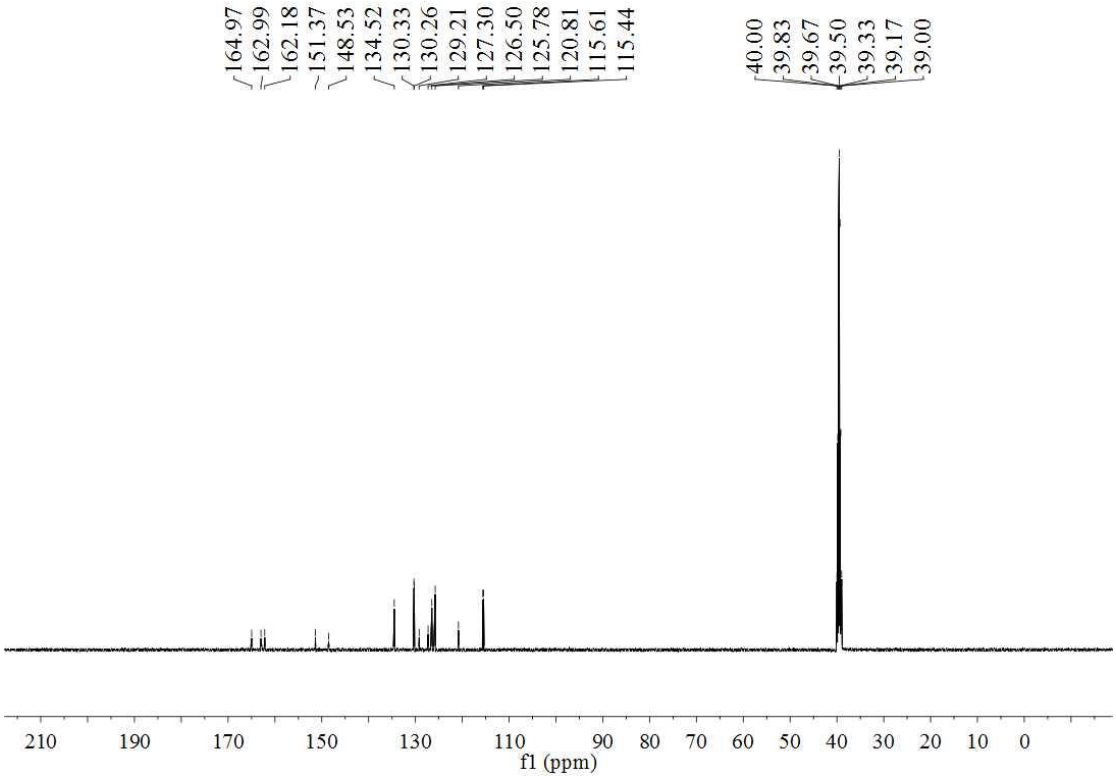
O
NH
N
F
0.71
1.90
0.91
1.00
0.98
1.00
2.00
f1 (ppm)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134.52
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130.26
129.21
127.30
126.50
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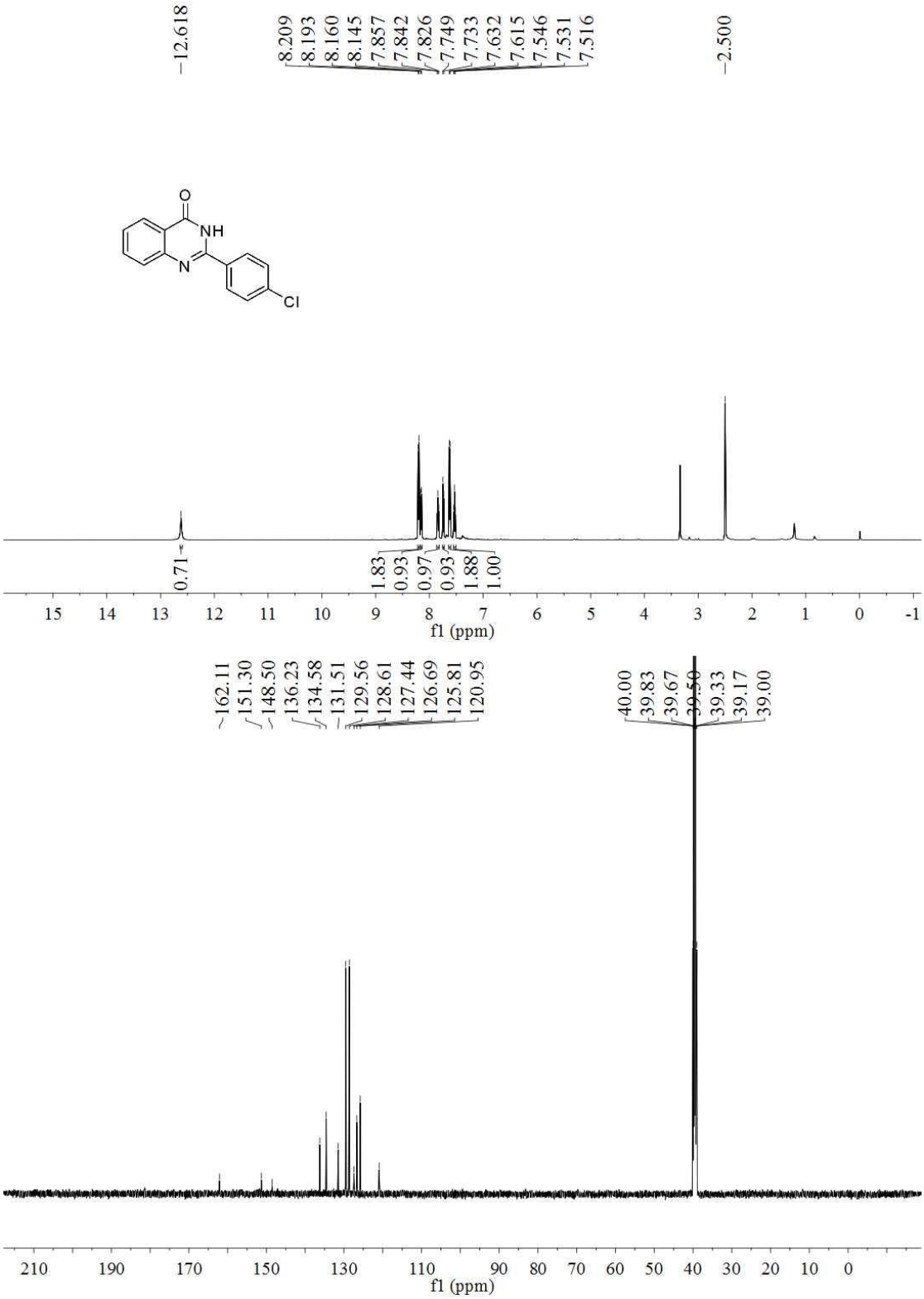
39.50
39.33
39.17
39.00
f1 (ppm)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7.733
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7.615
7.546
7.531
7.516
2.500
O
NH
N
Cl
0.71
1.83
0.93
0.97
0.93
1.88
1.00
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1
f1 (ppm)
162.11
151.30
148.50
136.23
134.58
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127.44
126.69
125.81
120.95
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39.17
39.00
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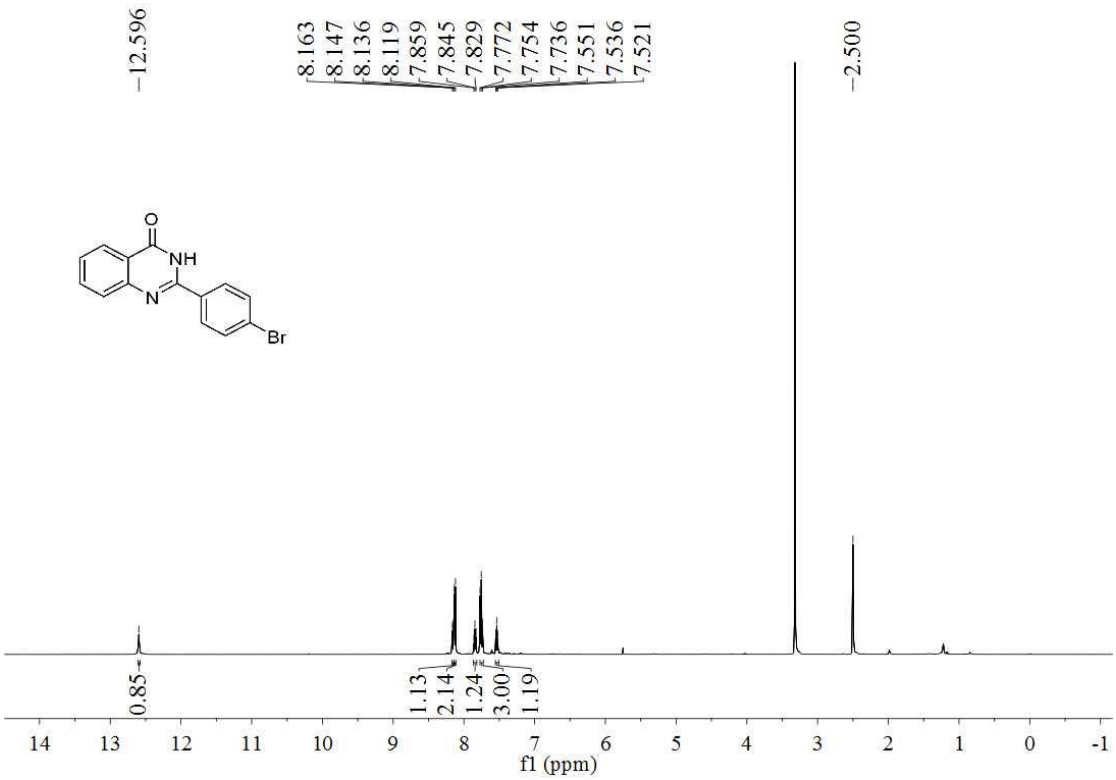
f1 (ppm)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7.829
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7.551
7.536
7.521
2.500
O
NH
N
Br
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2.14
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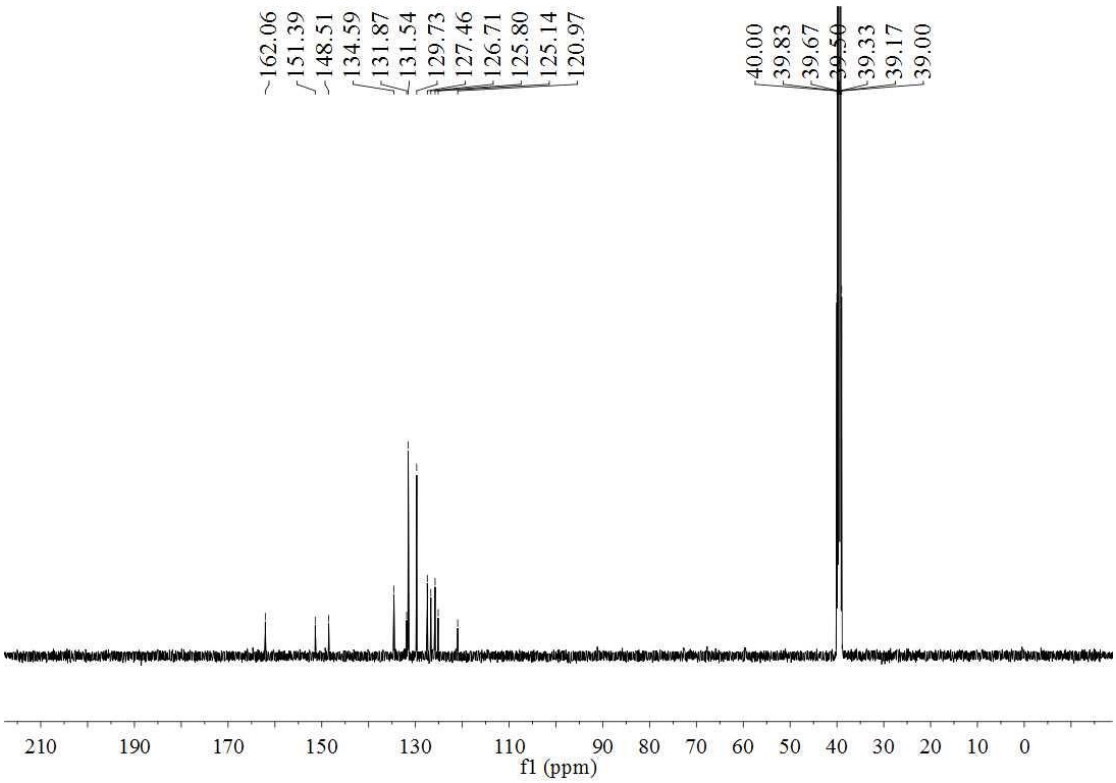
3.00
1.19
14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1
f1 (ppm)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39.67
39.50
39.33
39.17
39.00
210 190 170 150 130 110 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


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8.136
8.105
8.089
7.834
7.819
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7.728
7.712
7.514
7.499
7.485
7.354
7.338
2.500
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NH
N
Me
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0.92
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0.99
1.04
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f1 (ppm)
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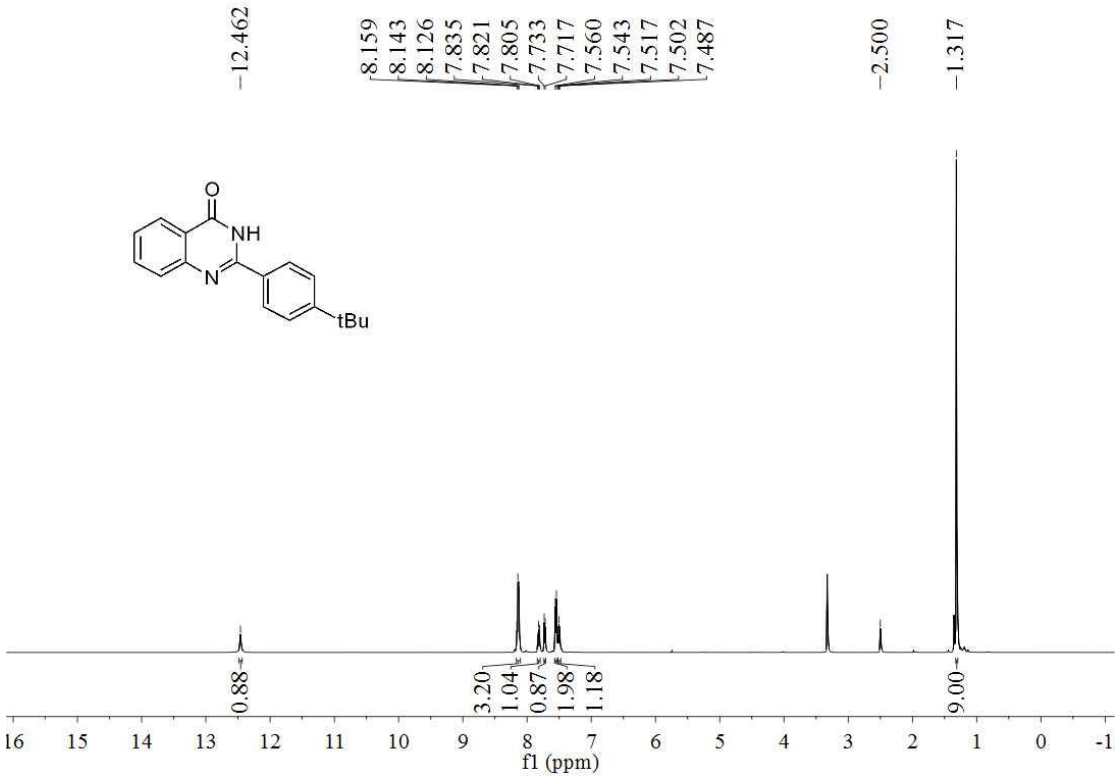
f1 (ppm)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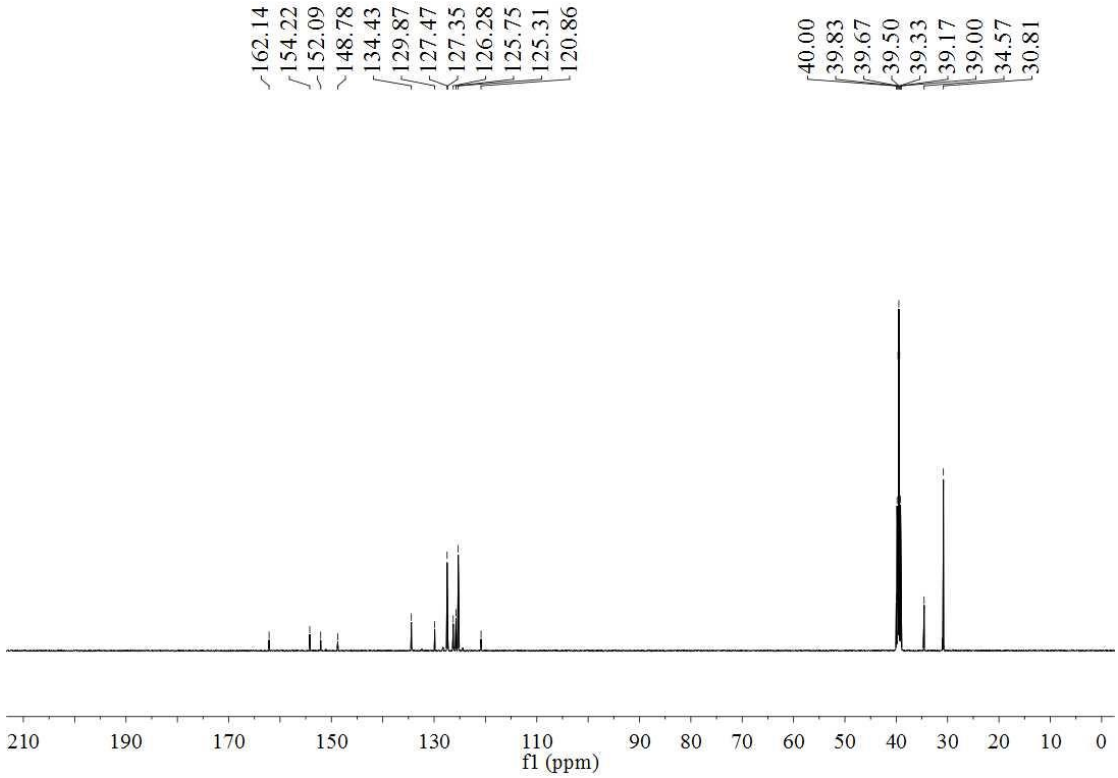
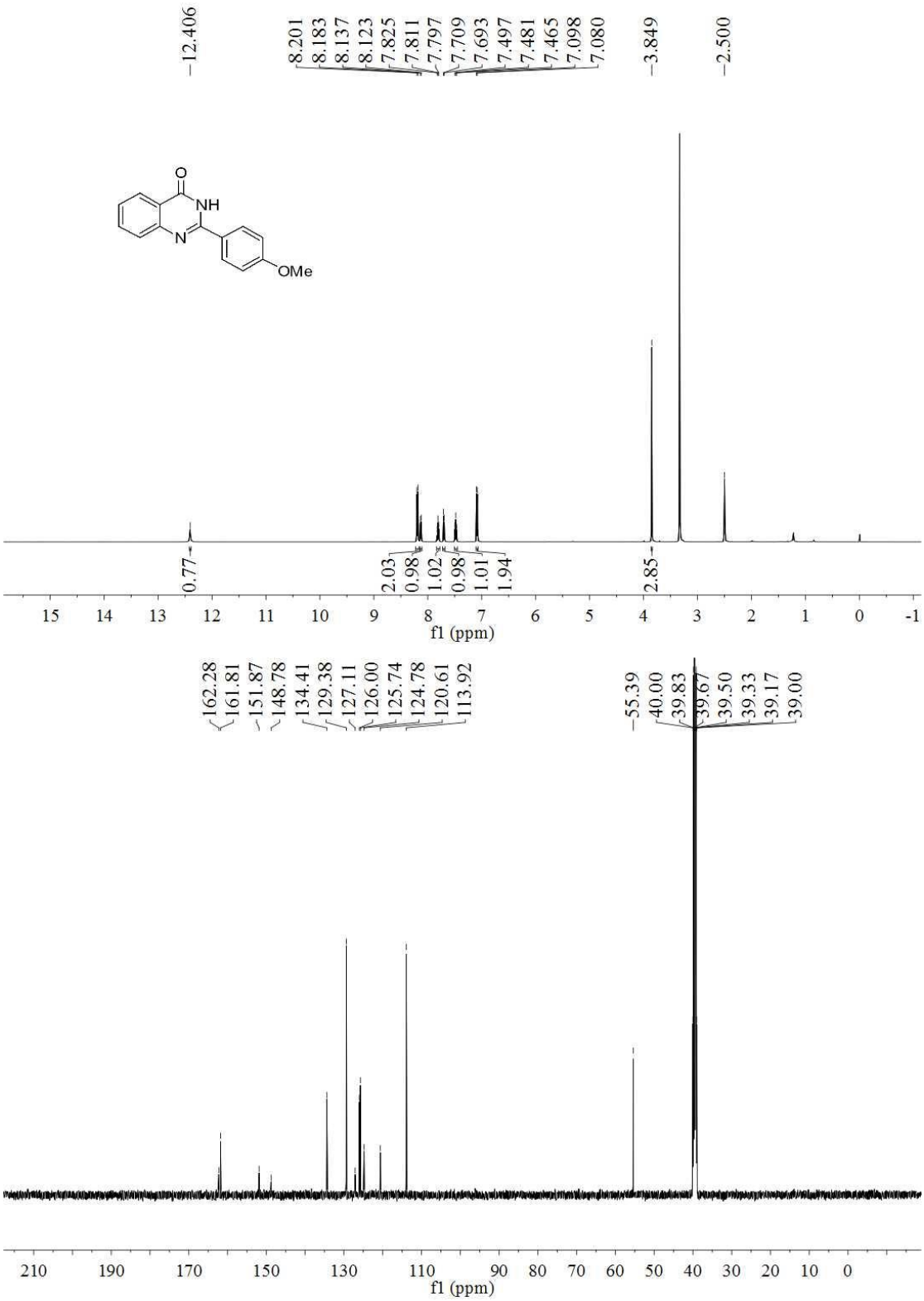
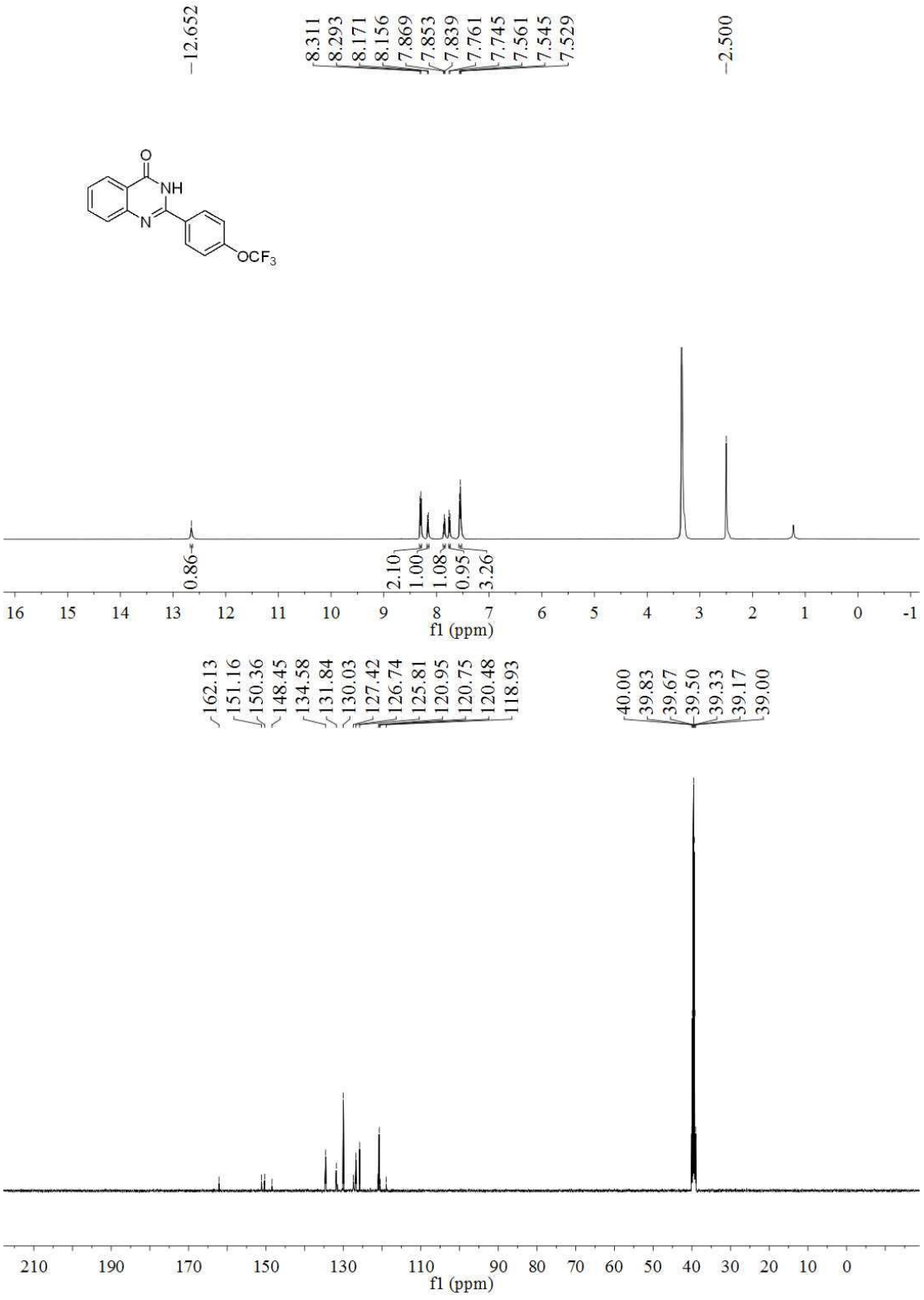
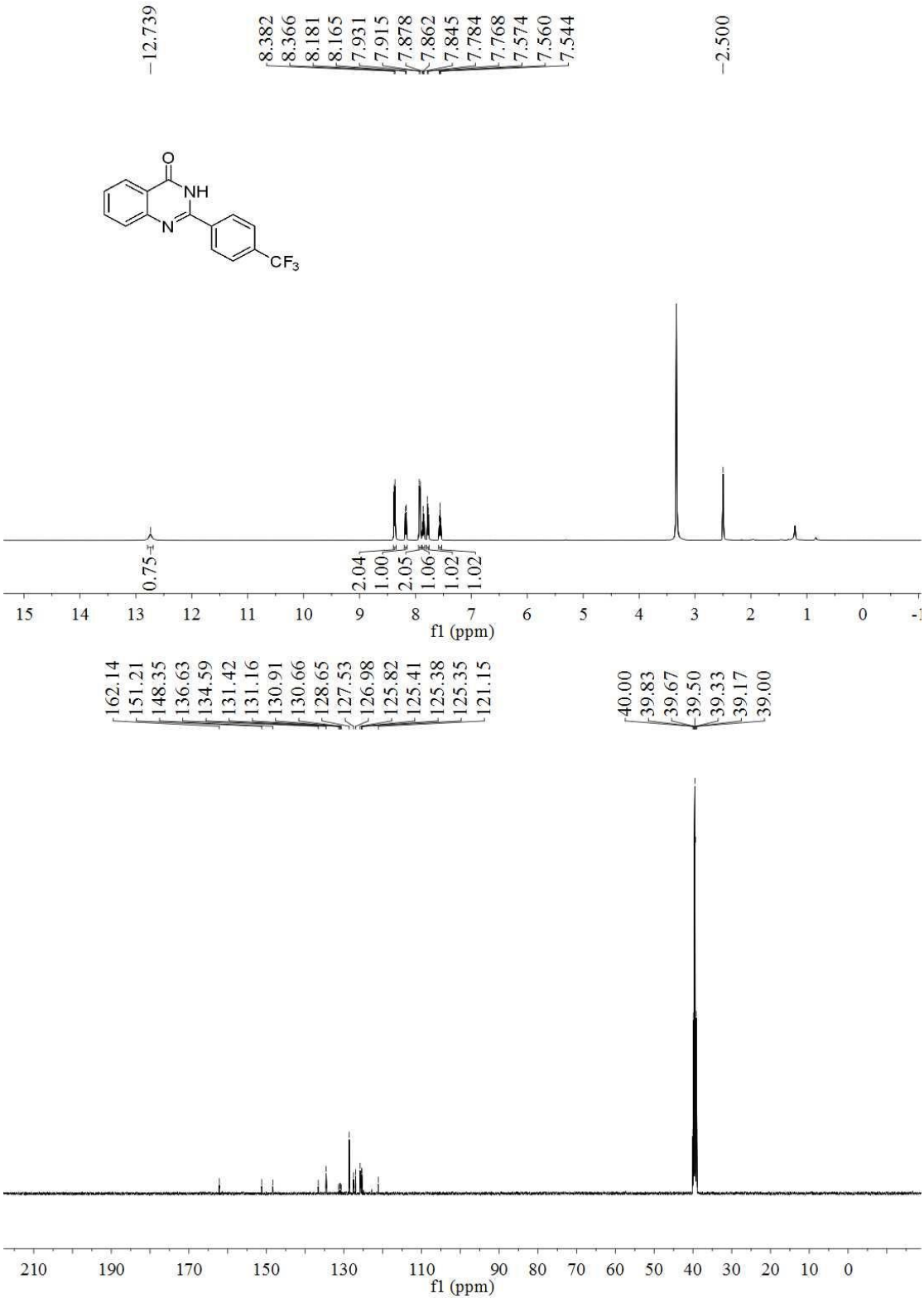
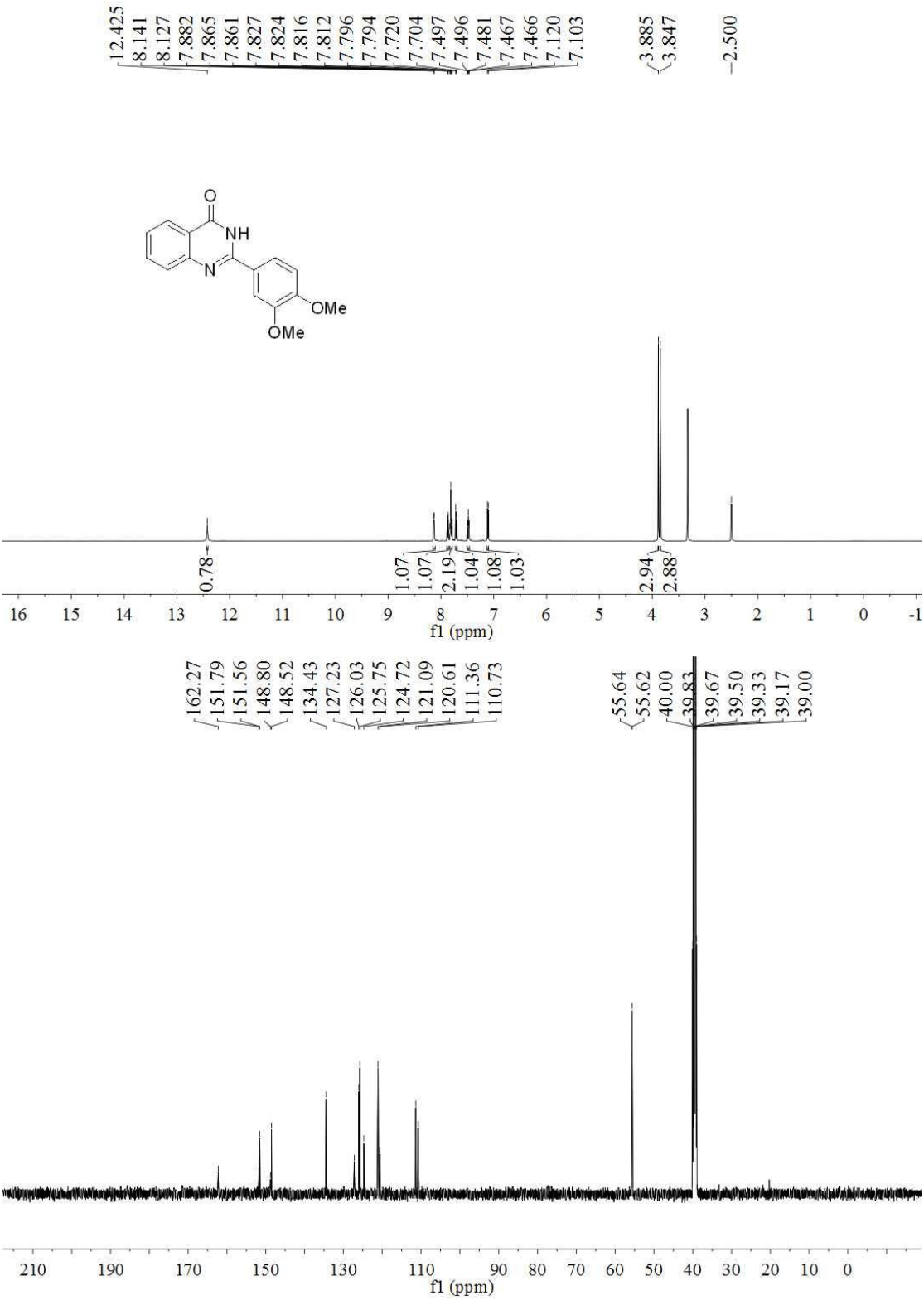
7.487
2.500
1.317
O
NH
N
tBu
0.88
3.20
1.04
0.87
1.98
1.18
9.00
f1 (ppm)

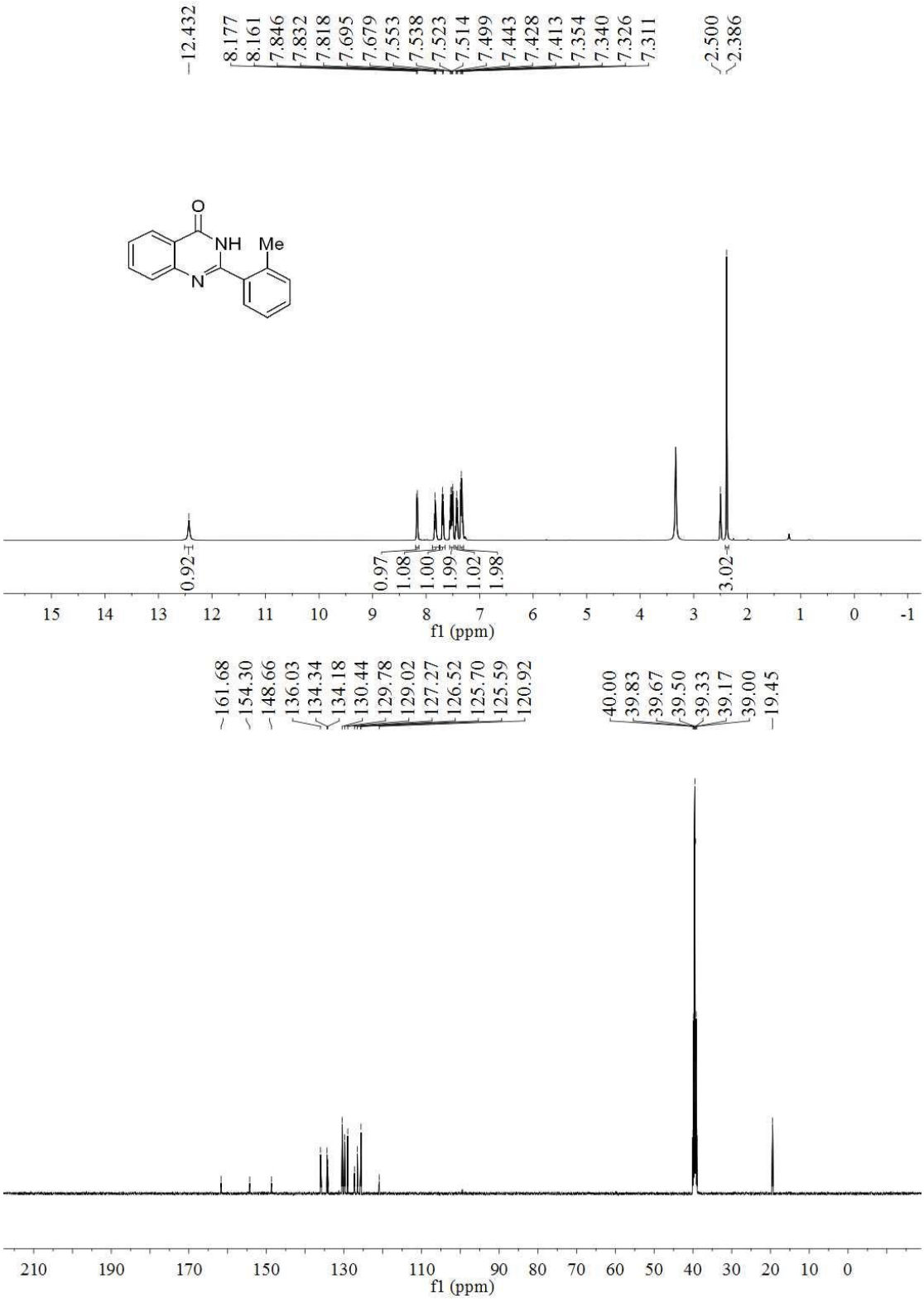

162.14
154.22
152.09
148.78
134.43
129.87
127.47
127.35
126.28
125.75
125.31
120.86
40.00
39.83
39.67
39.50
39.33
39.17
39.00
34.57
30.81
f1 (ppm)


12.406
8.201
8.183
8.137
8.123
7.825
7.811
7.797
7.709
7.693
7.497
7.481
7.465
7.098
7.080
3.849
2.500
O
NH
N
OMe
0.77
2.03
0.98
1.02
0.98
1.01
1.94
2.85
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1
f1 (ppm)
162.28
161.81
151.87
148.78
134.41
129.38
127.11
126.00
125.74
124.78
120.61
113.92
55.39
40.00
39.83
39.67
39.50
39.33
39.17
39.00
210 190 170 150 130 110 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

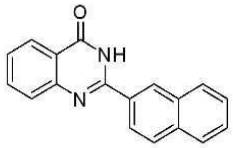

12.652
8.311
8.293
8.171
8.156
7.869
7.853
7.839
7.761
7.745
7.561
7.545
7.529
2.500
O
NH
N
OCF3
0.86
2.10
1.00
1.08
0.95
3.26
f1 (ppm)
162.13
151.16
150.36
148.45
134.58
131.84
130.03
127.42
126.74
125.81
120.95
120.75
120.48
118.93
40.00
39.83
39.67
39.50
39.33
39.17
39.00
f1 (ppm)

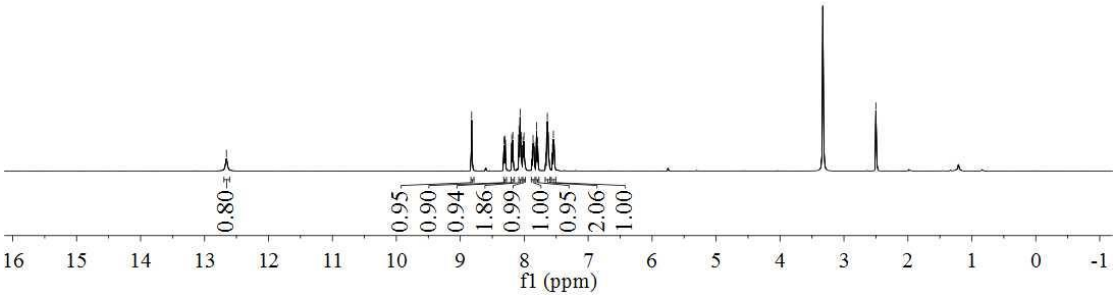

12.739
8.382
8.366
8.181
8.165
7.931
7.915
7.878
7.862
7.845
7.784
7.768
7.574
7.560
7.544
2.500
O
NH
N
CF3
0.75
2.04
1.00
2.05
1.06
1.02
1.02
f1 (ppm)
162.14
151.21
148.35
136.63
134.59
131.42
131.16
130.91
130.66
128.65
127.53
126.98
125.82
125.41
125.38
125.35
121.15
40.00
39.83
39.67
39.50
39.33
39.17
39.00
f1 (ppm)

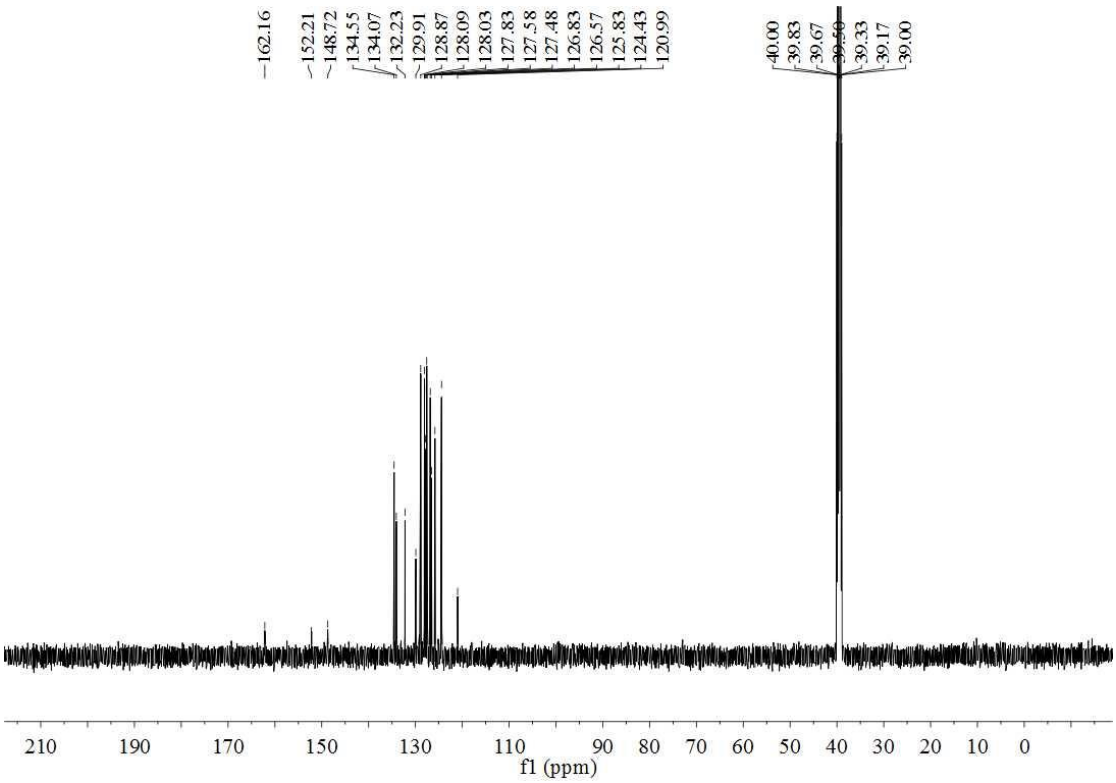

12.425
8.141
8.127
7.882
7.865
7.861
7.827
7.824
7.816
7.812
7.796
7.794
7.720
7.704
7.497
7.496
7.481
7.467
7.466
7.120
7.103
3.885
3.847
2.500
O
NH
N
OMe
OMe
0.78
1.07
1.07
2.19
1.04
1.08
1.03
2.94
2.88
f1 (ppm)
162.27
151.79
151.56
148.80
148.52
134.43
127.23
126.03
125.75
124.72
121.09
120.61
111.36
110.73
55.64
55.62
40.00
39.83
39.67
39.50
39.33
39.17
39.00
f1 (ppm)

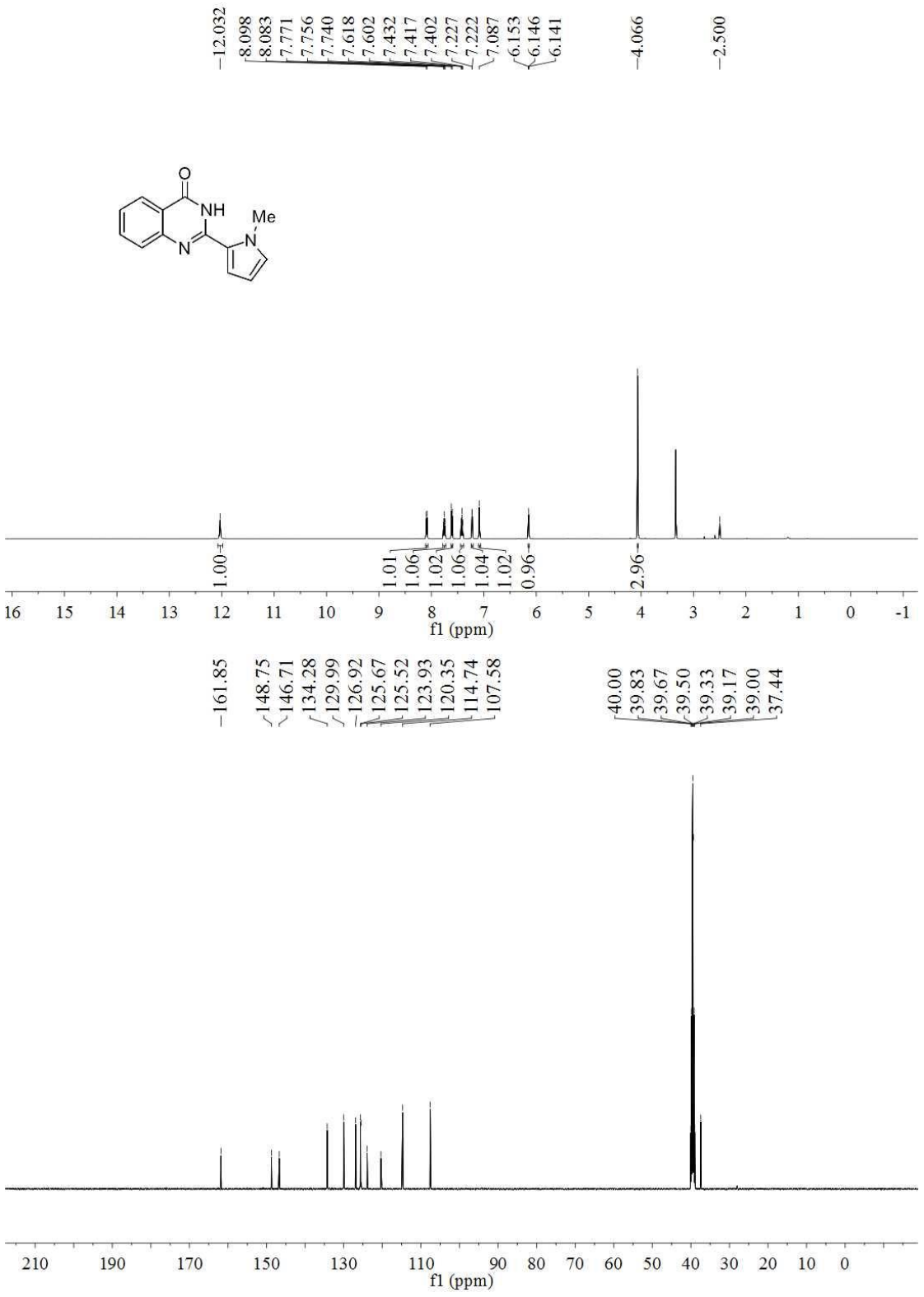

12.432
8.177
8.161
7.846
7.832
7.818
7.695
7.679
7.553
7.538
7.523
7.514
7.499
7.443
7.428
7.413
7.354
7.340
7.326
7.311
2.500
2.386
O
NH
Me
N
0.92
0.97
1.08
1.00
1.99
1.02
1.98
3.02
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1
f1 (ppm)
161.68
154.30
148.66
136.03
134.34
134.18
130.44
129.78
129.02
127.27
126.52
125.70
125.59
120.92
40.00
39.83
39.67
39.50
39.33
39.17
39.00
19.45
210 190 170 150 130 110 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

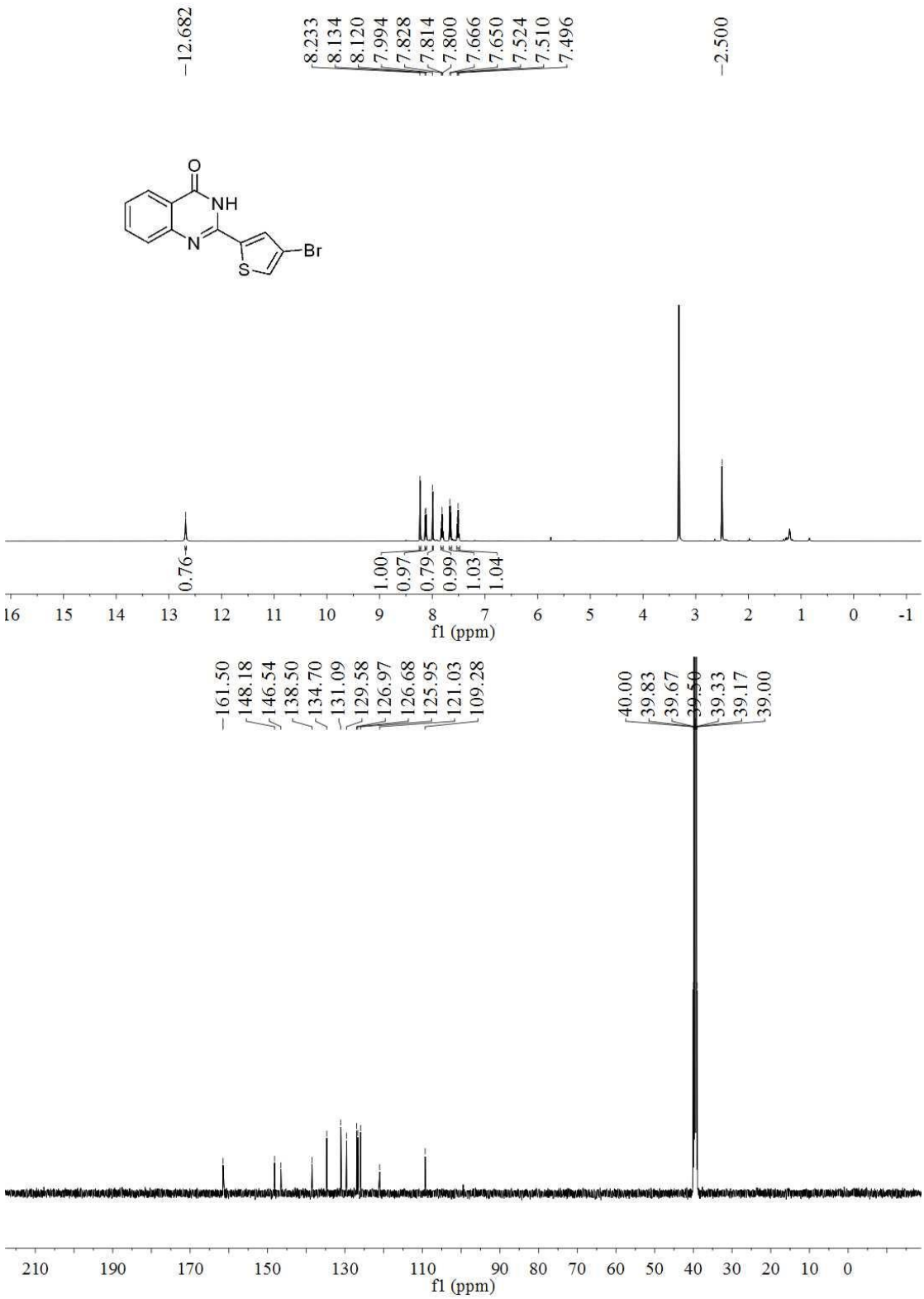

12.657
8.822
8.315
8.301
8.194
8.179
8.081
8.064
8.055
8.051
8.019
8.005
7.877
7.863
7.849
7.807
7.791
7.663
7.652
7.649
7.643
7.638
7.634
7.627
7.625
7.614
7.558
7.544
7.528
2.500

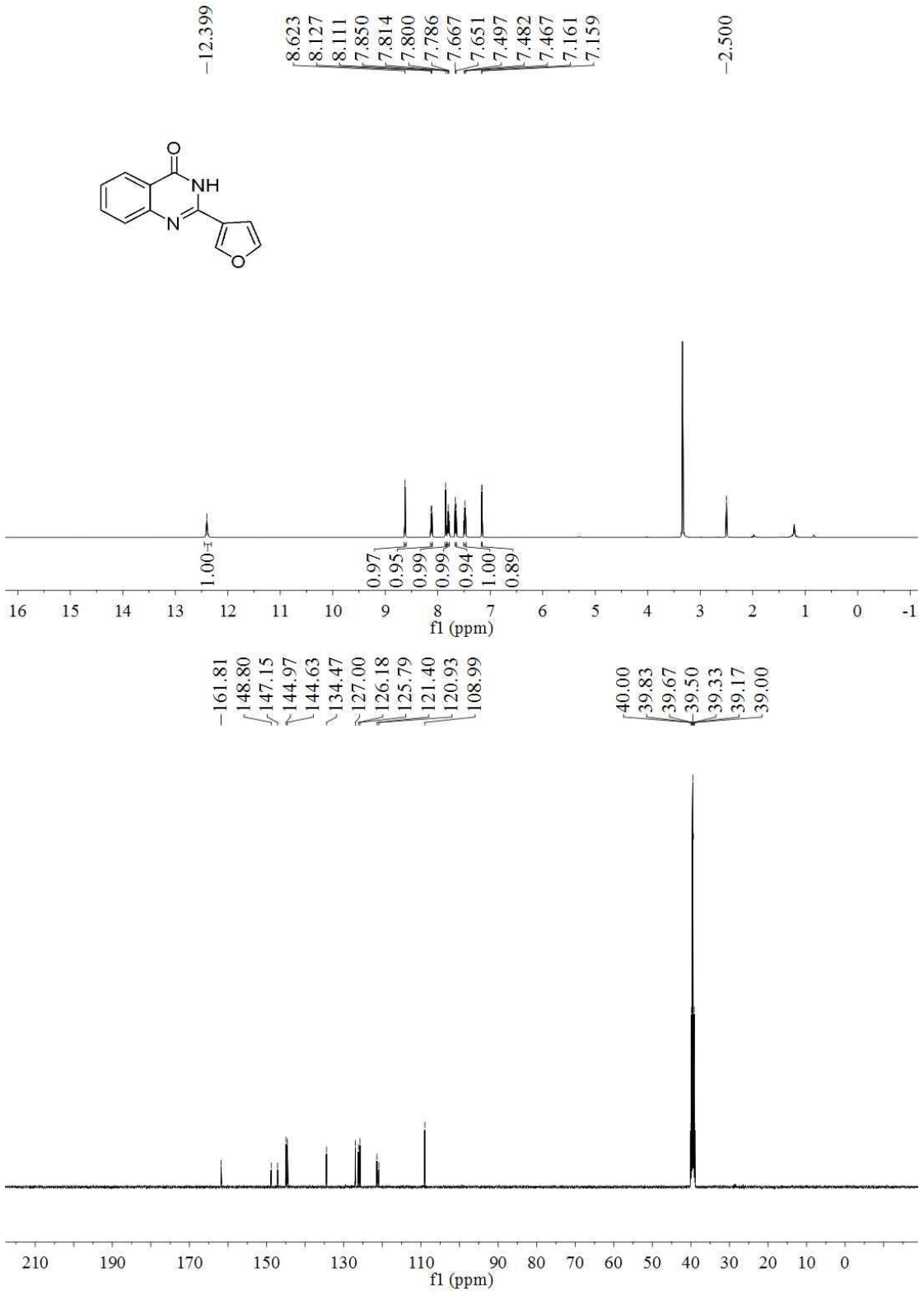

O
NH
N

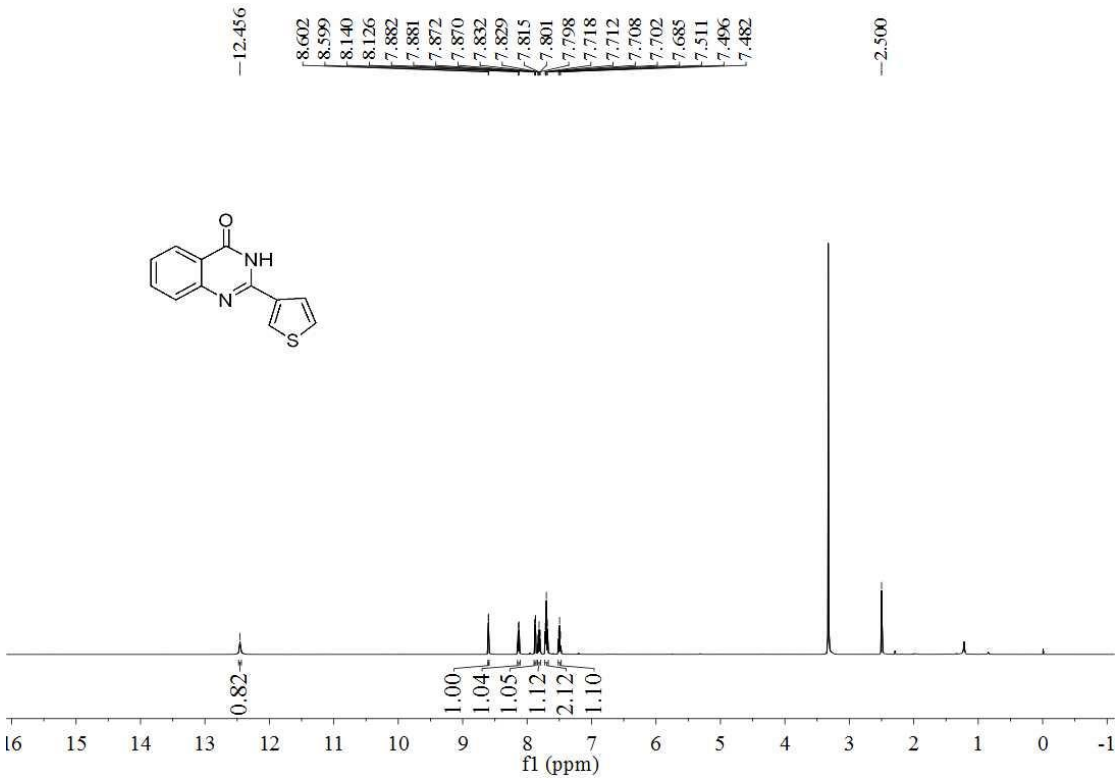

0.80
0.95
0.90
0.94
1.86
0.99
1.00
0.95
2.06
1.00
16 15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1
f1 (ppm)

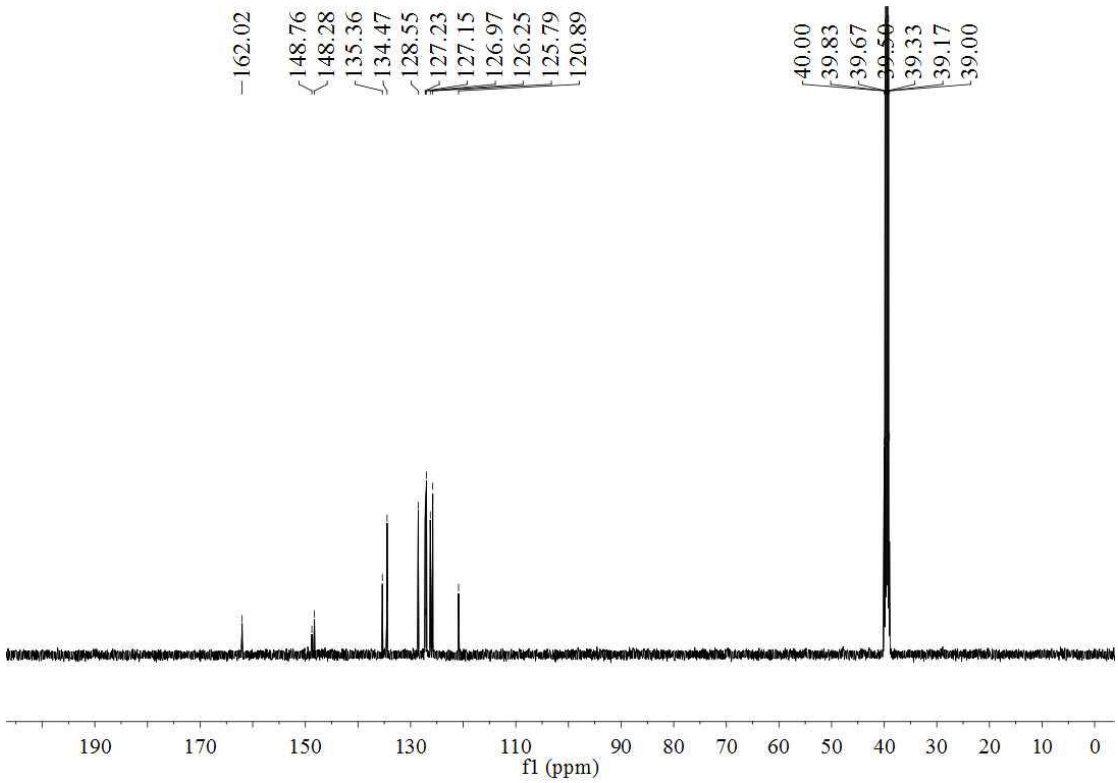

162.16
152.21
148.72
134.55
134.07
132.23
129.91
128.87
128.09
128.03
127.83
127.58
127.48
126.83
126.57
125.83
124.43
120.99
40.00
39.83
39.67
39.50
39.33
39.17
39.00
210 190 170 150 130 110 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


12.032
8.098
8.083
7.771
7.756
7.740
7.618
7.602
7.432
7.417
7.402
7.227
7.222
7.087
6.153
6.146
6.141
4.066
2.500
O
NH
Me
N
N
1.00
1.01
1.06
1.02
1.06
1.04
1.02
0.96
2.96
f1 (ppm)
161.85
148.75
146.71
134.28
129.99
126.92
125.67
125.52
123.93
120.35
114.74
107.58
40.00
39.83
39.67
39.50
39.33
39.17
39.00
37.44
f1 (ppm)

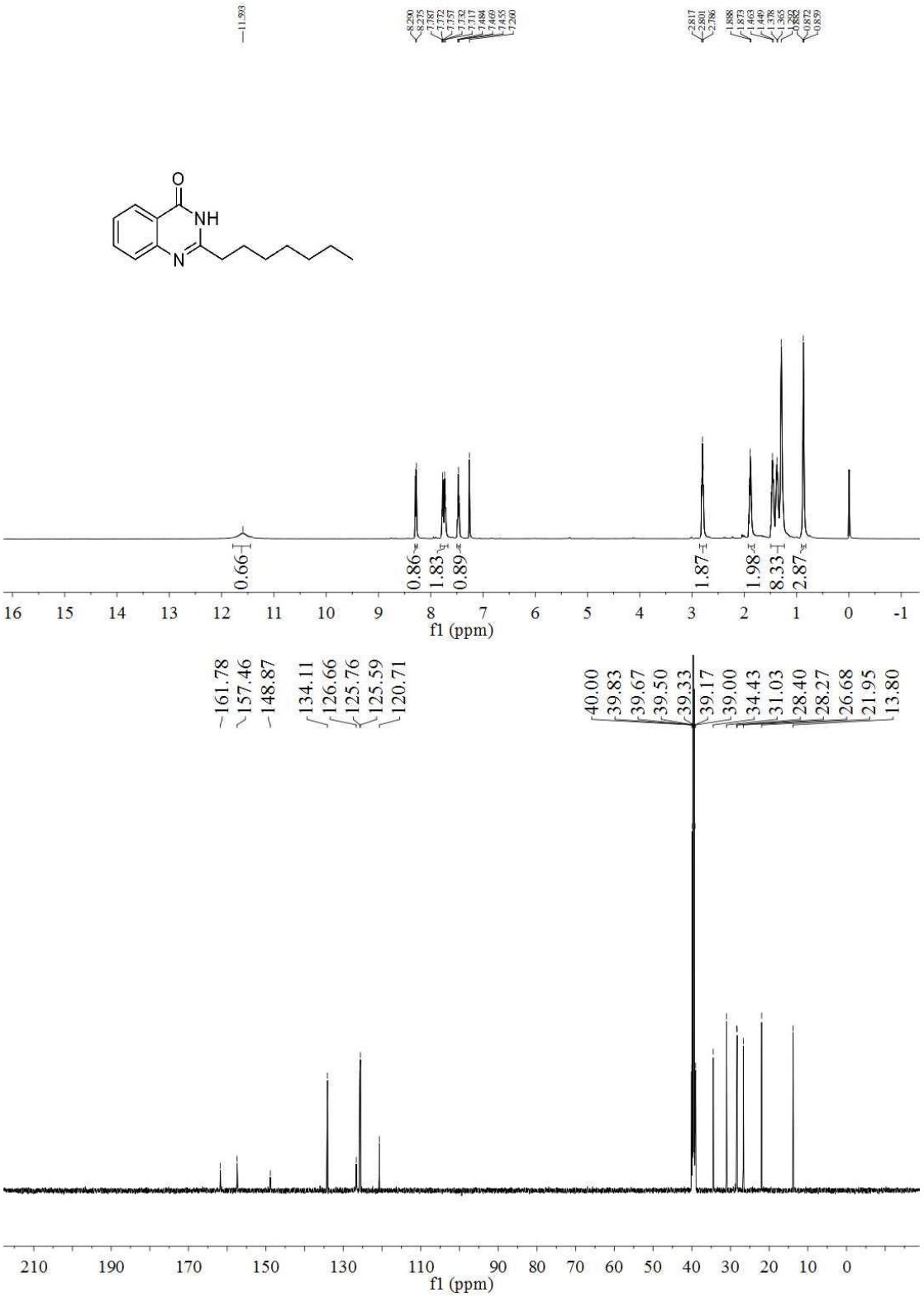

12.682
8.233
8.134
8.120
7.994
7.828
7.814
7.800
7.666
7.650
7.524
7.510
7.496
2.500
O
NH
N
S
Br
0.76
1.00
0.97
0.79
0.99
1.03
1.04
f1 (ppm)
161.50
148.18
146.54
138.50
134.70
131.09
129.58
126.97
126.68
125.95
121.03
109.28
40.00
39.83
39.67
39.50
39.33
39.17
39.00
f1 (ppm)

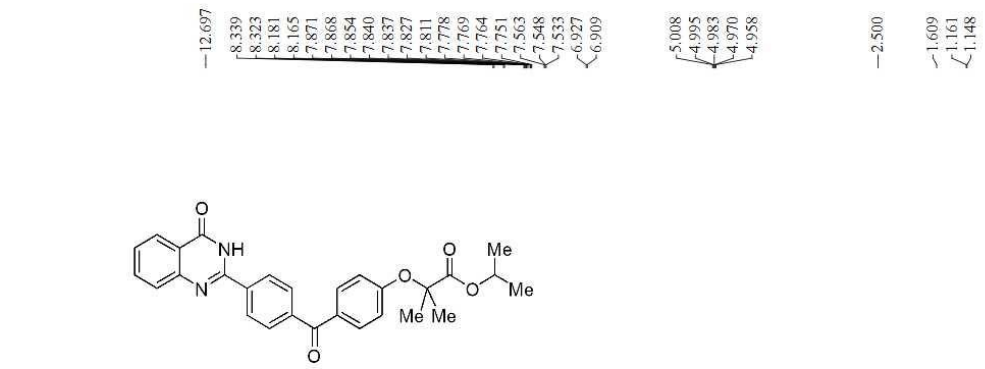

12.399
8.623
8.127
8.111
7.850
7.814
7.800
7.786
7.667
7.651
7.497
7.482
7.467
7.161
7.159
2.500
NH
N
O
1.00
0.97
0.95
0.99
0.99
0.94
1.00
0.89
f1 (ppm)
161.81
148.80
147.15
144.97
144.63
134.47
127.00
126.18
125.79
121.40
120.93
108.99
40.00
39.83
39.67
39.50
39.33
39.17
39.00
f1 (ppm)


12.456
8.602
8.599
8.140
8.126
7.882
7.881
7.872
7.870
7.832
7.829
7.815
7.801
7.798
7.718
7.712
7.708
7.702
7.685
7.511
7.496
7.482
2.500
O
NH
N
S
0.82
1.00
1.04
1.05
1.12
2.12
1.10
f1 (ppm)


162.02
148.76
148.28
135.36
134.47
128.55
127.23
127.15
126.97
126.25
125.79
120.89
40.00
39.83
39.67
39.50
39.33
39.17
39.00
f1 (ppm)


12.063
8.076
8.061
7.763
7.748
7.734
7.592
7.576
7.450
7.436
7.421
2.588
2.566
2.543
2.500
1.994
1.880
1.798
1.765
1.674
1.652
1.610
1.586
1.562
1.540
1.327
1.304
1.279
1.251
1.220
1.197
1.165
O
NH
N
0.85
0.84
0.87
0.85
0.91
0.97
4.08
3.28
3.38
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1
f1 (ppm)
161.83
160.66
148.90
134.11
126.90
125.79
125.57
120.91
42.77
40.00
39.83
39.67
39.50
39.33
39.17
39.00
30.12
25.43
25.27
210 190 170 150 130 110 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


11.593
8.290
8.275
7.797
7.772
7.757
7.732
7.317
7.484
7.469
7.455
7.200
2.817
2.801
2.786
1.888
1.873
1.463
1.449
1.378
1.365
1.282
0.872
0.859
O
NH
N
0.66
0.86
1.83
0.89
1.87
1.98
8.33
2.87
16 15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1
f1 (ppm)
161.78
157.46
148.87
134.11
126.66
125.76
125.59
120.71
40.00
39.83
39.67
39.50
39.33
39.17
39.00
34.43
31.03
28.40
28.27
26.68
21.95
13.80
210 190 170 150 130 110 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


12.697
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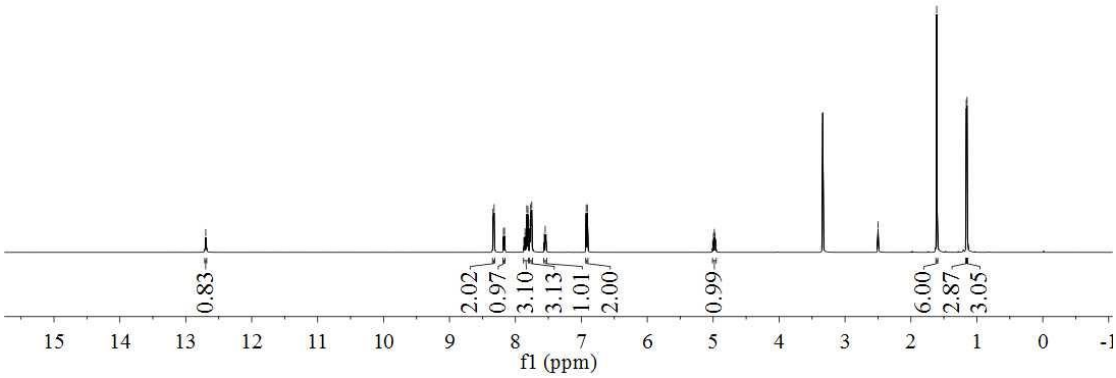
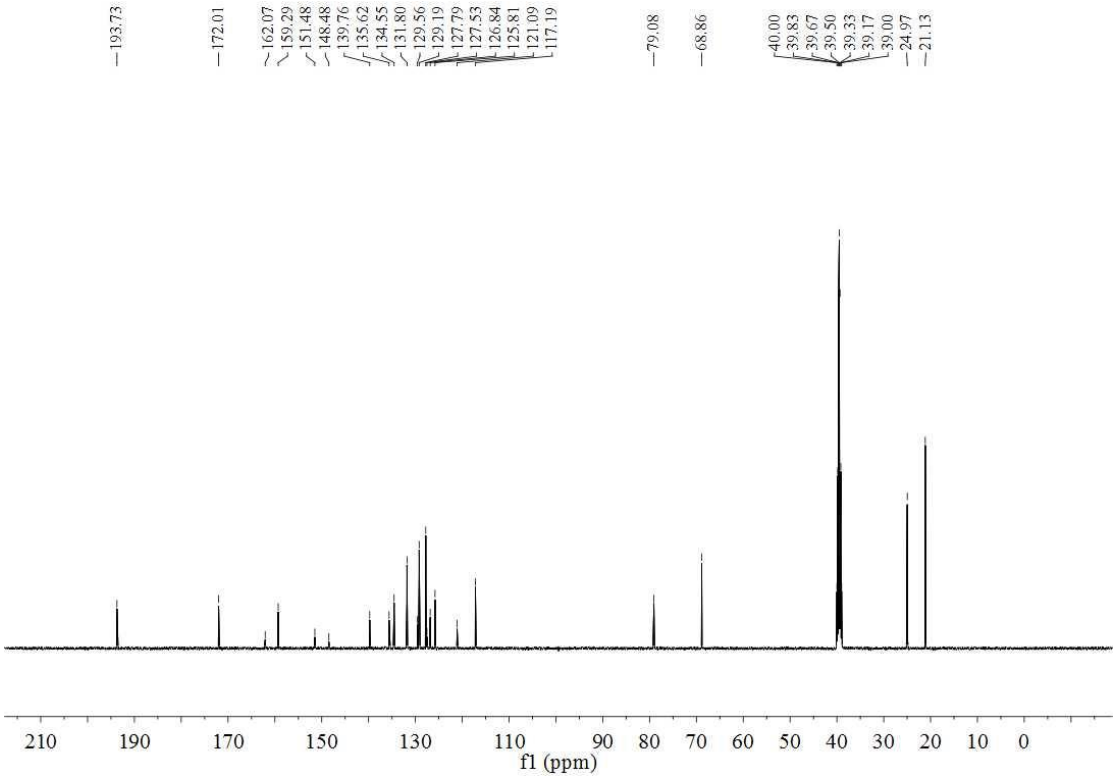
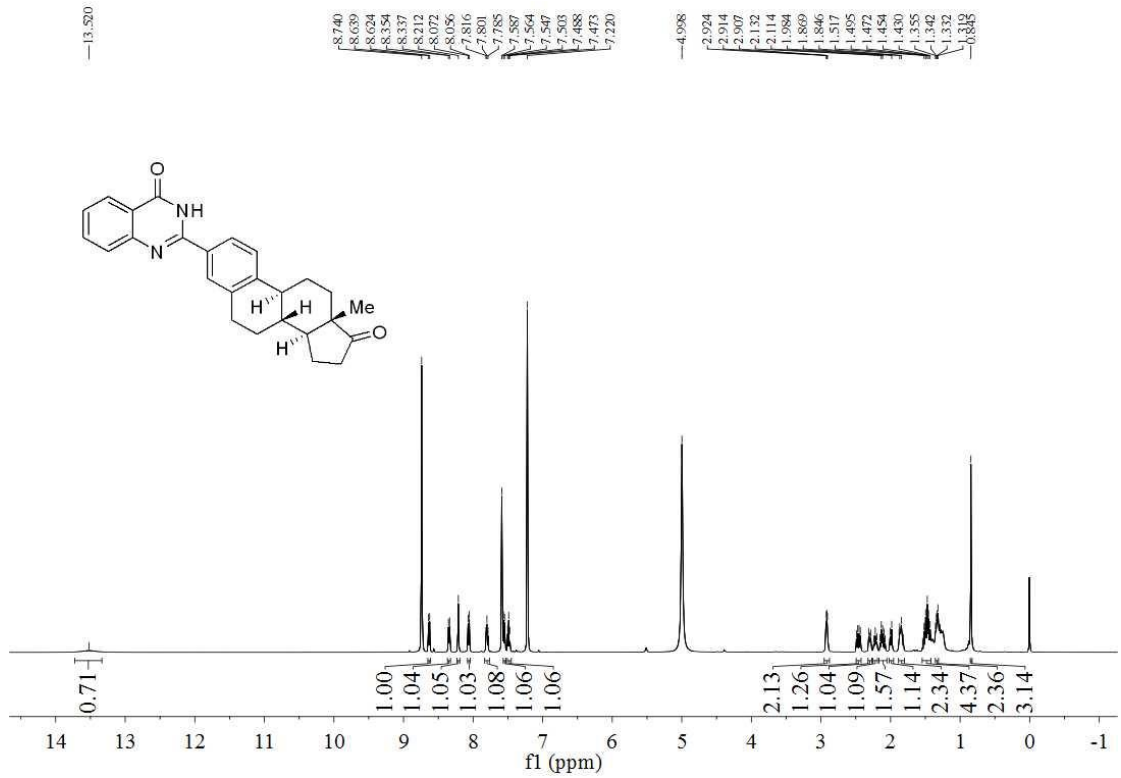
8.323
8.181
8.165
7.871
7.868
7.854
7.840
7.837
7.827
7.811
7.778
7.769
7.764
7.751
7.563
7.548
7.533
6.927
6.909
5.008
4.995
4.983
4.970
4.958
2.500
1.609
1.161
1.148
O
NH
N
O
O
Me
O
Me
Me Me
O


0.83
2.02
0.97
3.10
3.13
1.01
2.00
0.99
6.00
2.87
3.05
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1
f1 (ppm)


193.73
172.01
162.07
159.29
151.48
148.48
139.76
135.62
134.55
131.80
129.56
129.19
127.79
127.53
126.84
125.81
121.09
117.19
79.08
68.86
40.00
39.83
39.67
39.50
39.33
39.17
39.00
24.97
21.13
210 190 170 150 130 110 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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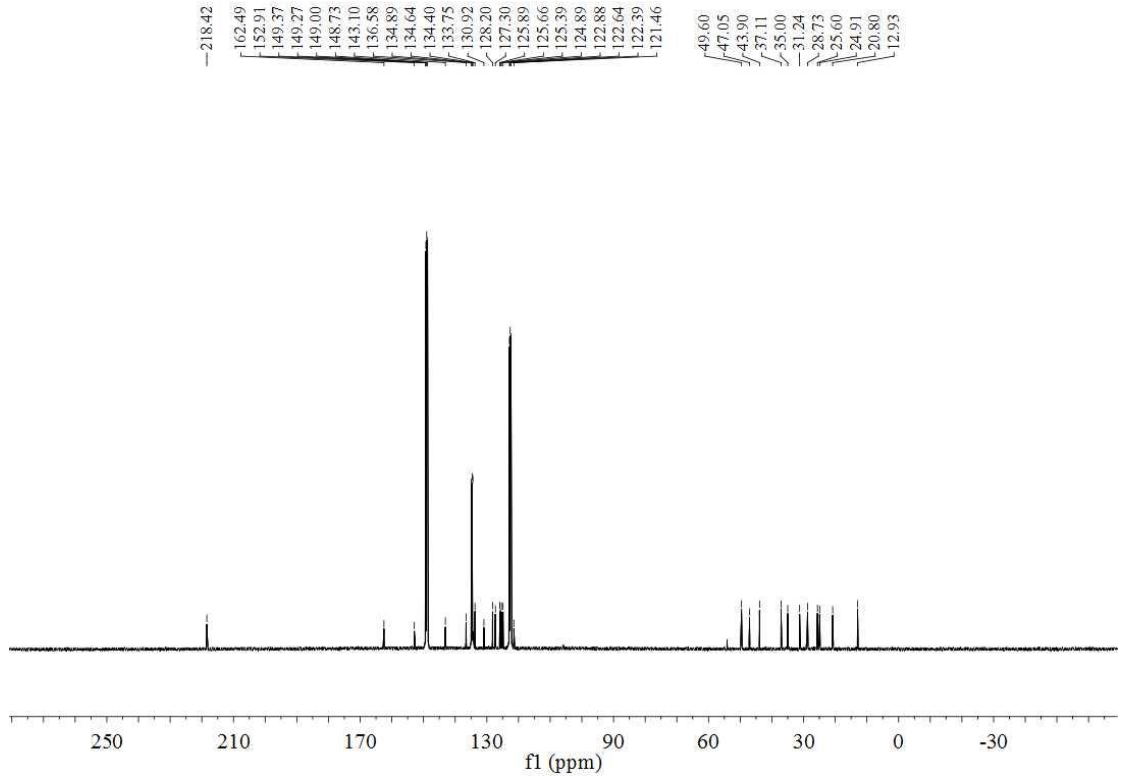
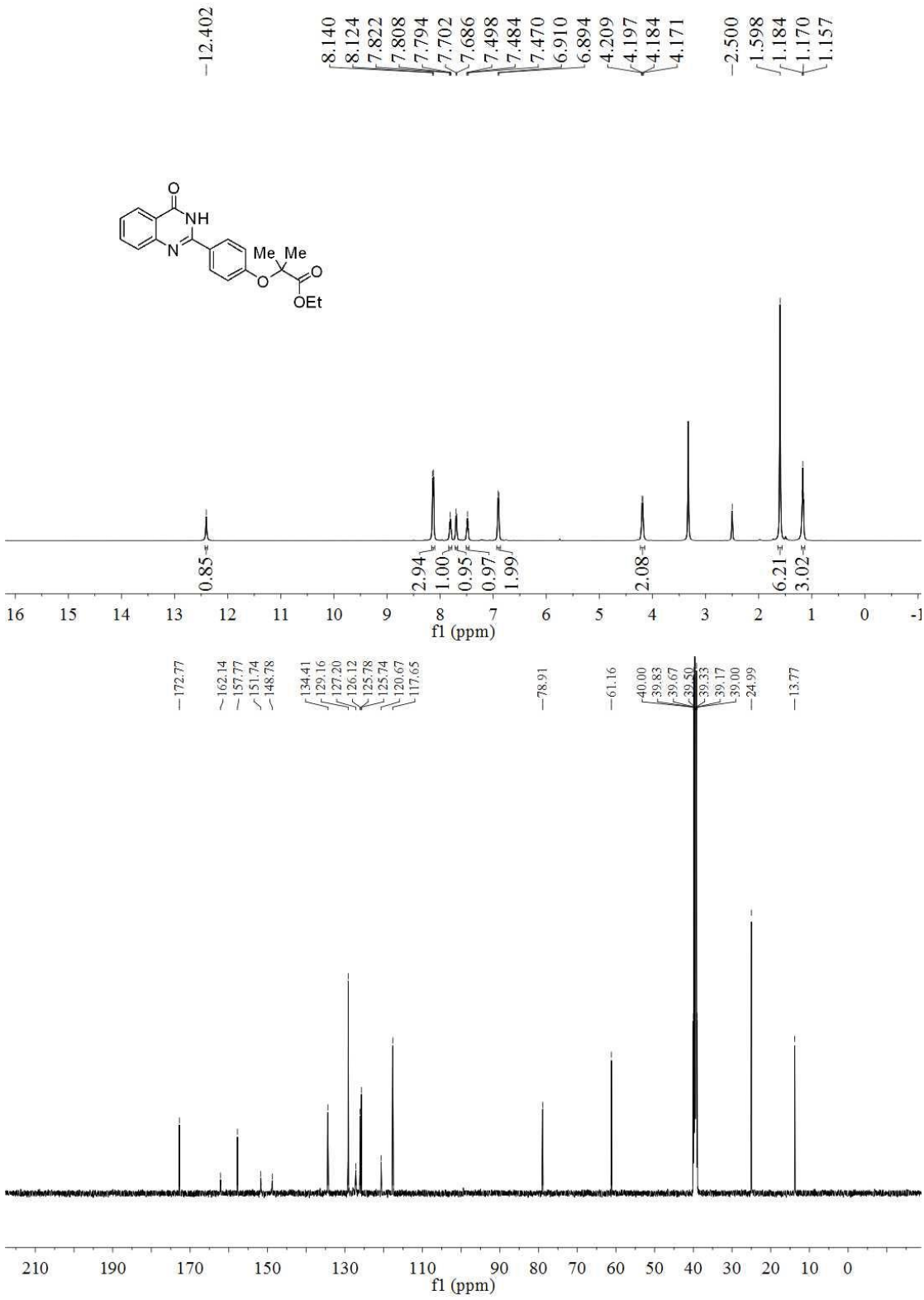
8.639
8.624
8.354
8.337
8.212
8.072
8.056
7.816
7.801
7.785
7.587
7.564
7.547
7.503
7.488
7.473
7.220
4.998
2.924
2.914
2.907
2.132
2.114
1.984
1.869
1.846
1.517
1.495
1.472
1.454
1.430
1.355
1.342
1.332
0.848
NH
N
O
H
H
Me
H
O
0.71
1.00
1.04
1.05
1.03
1.08
1.06
1.06
2.13
1.26
1.04
1.09
1.57
1.14
2.34
4.37
2.36
3.14
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
f1 (ppm)


218.42
162.49
152.91
149.37
149.27
149.00
148.73
143.10
136.58
134.89
134.64
134.40
133.75
130.92
128.20
127.30
125.89
125.66
125.39
124.89
122.88
122.64
122.39
121.46
49.60
47.05
43.90
37.11
35.00
31.24
28.73
25.60
24.91
20.80
12.93
250
210
170
130
90
60
30
0
-30
f1 (ppm)


12.402
8.140
8.124
7.822
7.808
7.794
7.702
7.686
7.498
7.484
7.470
6.910
6.894
4.209
4.197
4.184
4.171
2.500
1.598
1.184
1.170
1.157
NH
N
O
Me
Me
O
O
OEt
0.85
2.94
1.00
0.95
0.97
1.99
2.08
6.21
3.02
f1 (ppm)
172.77
162.14
157.77
151.74
148.78
134.41
129.16
127.20
126.12
125.78
125.74
120.67
117.65
78.91
61.16
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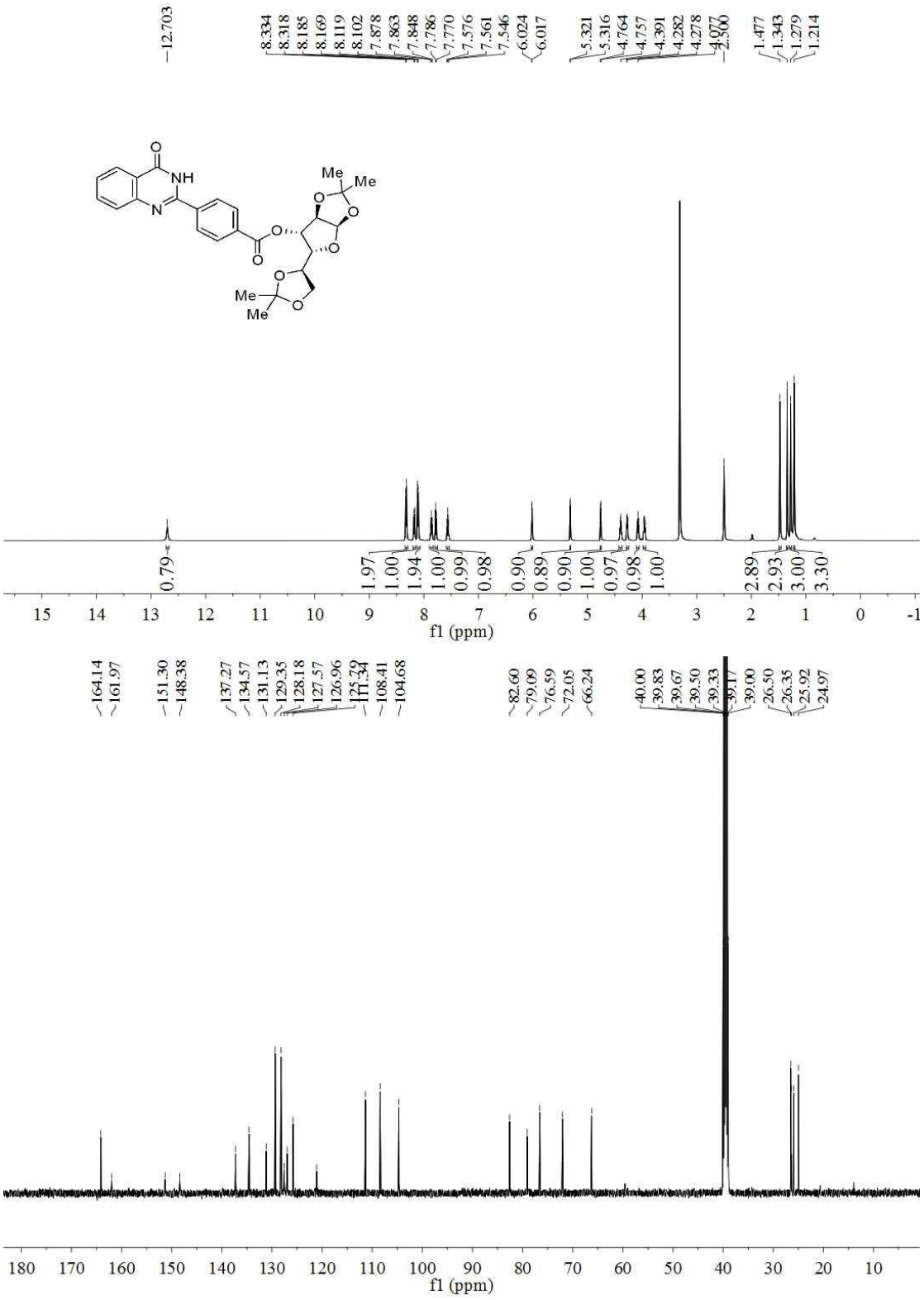
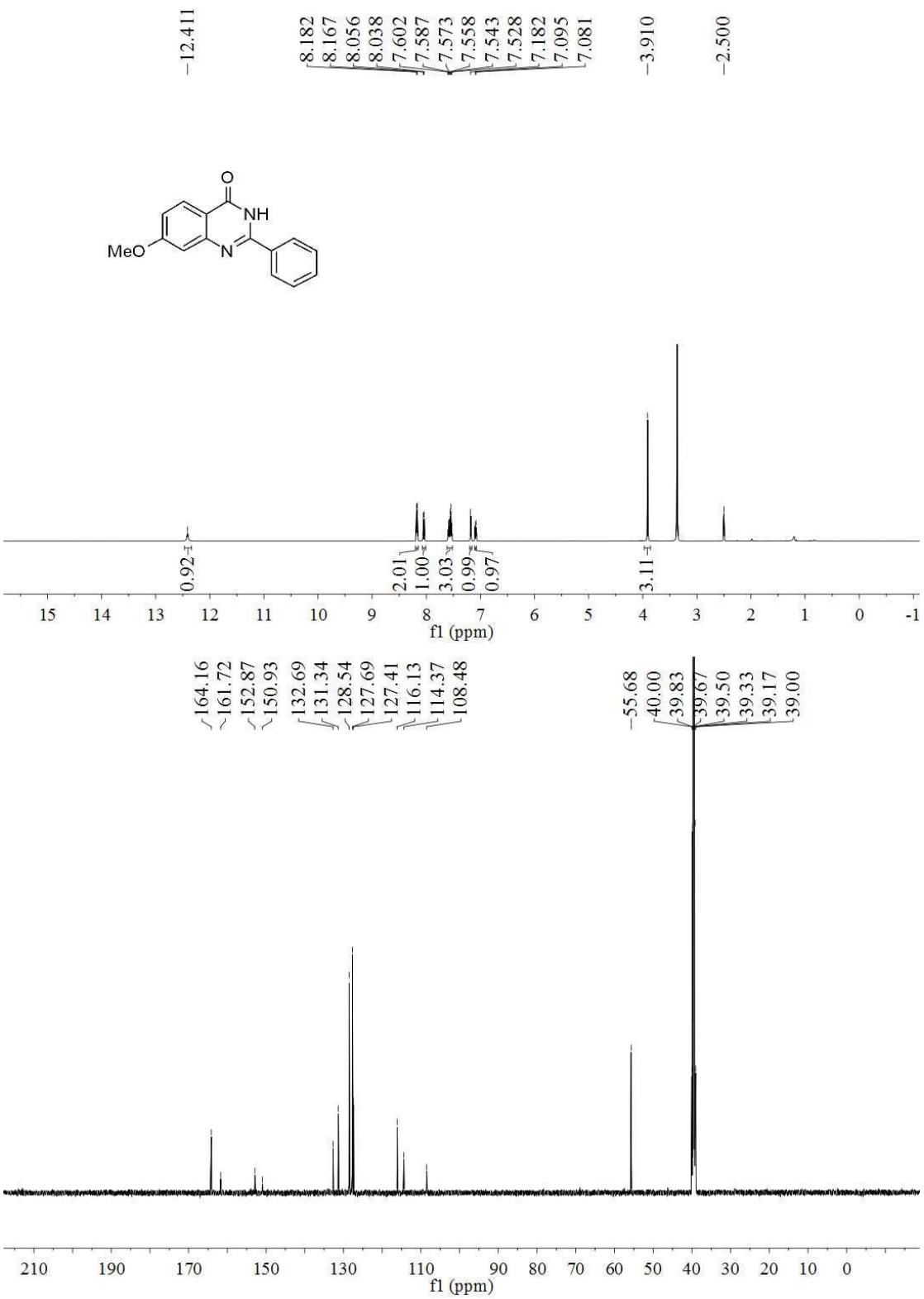
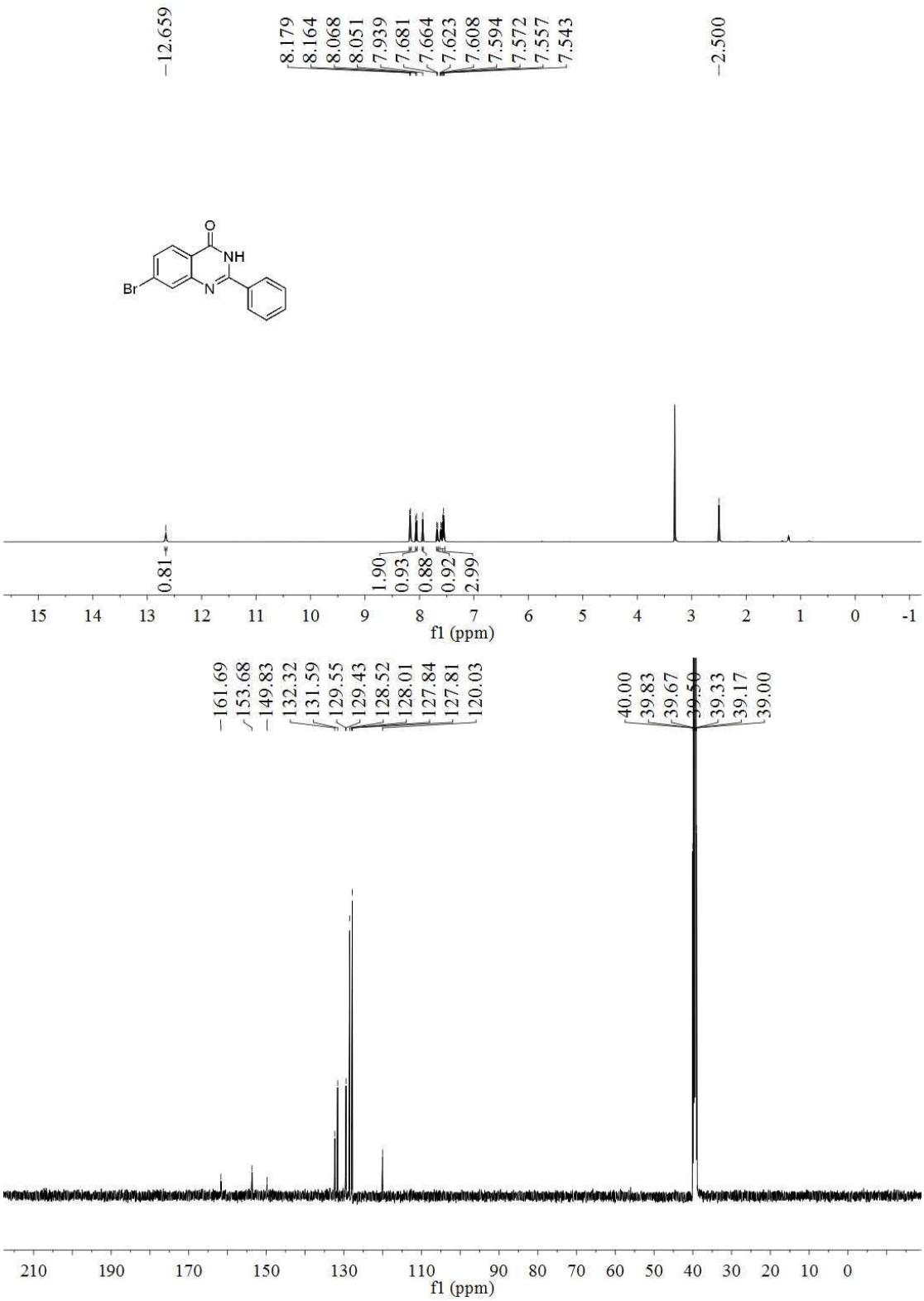
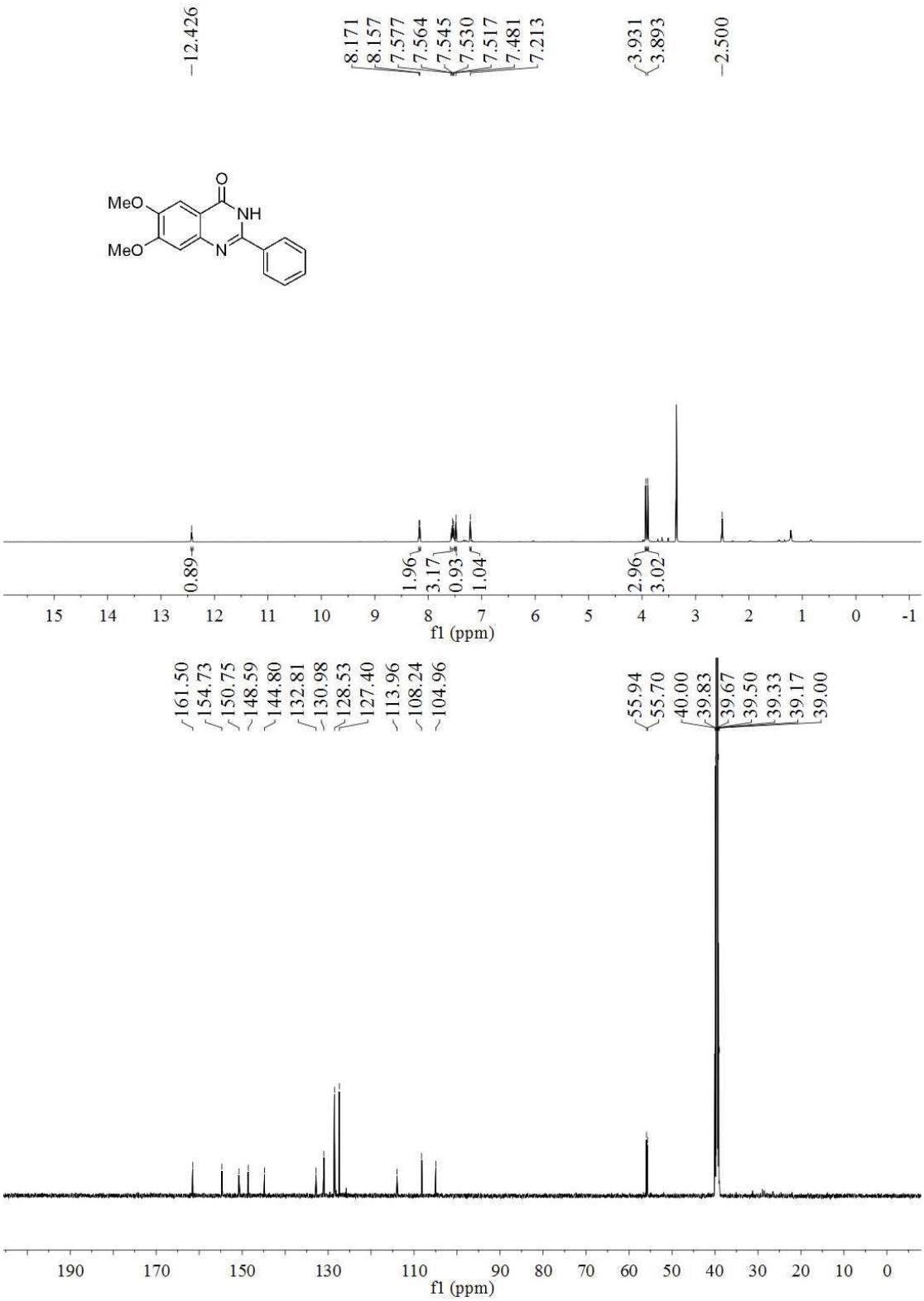
39.83
39.67
39.50
39.33
39.17
39.00
24.99
13.77
f1 (ppm)

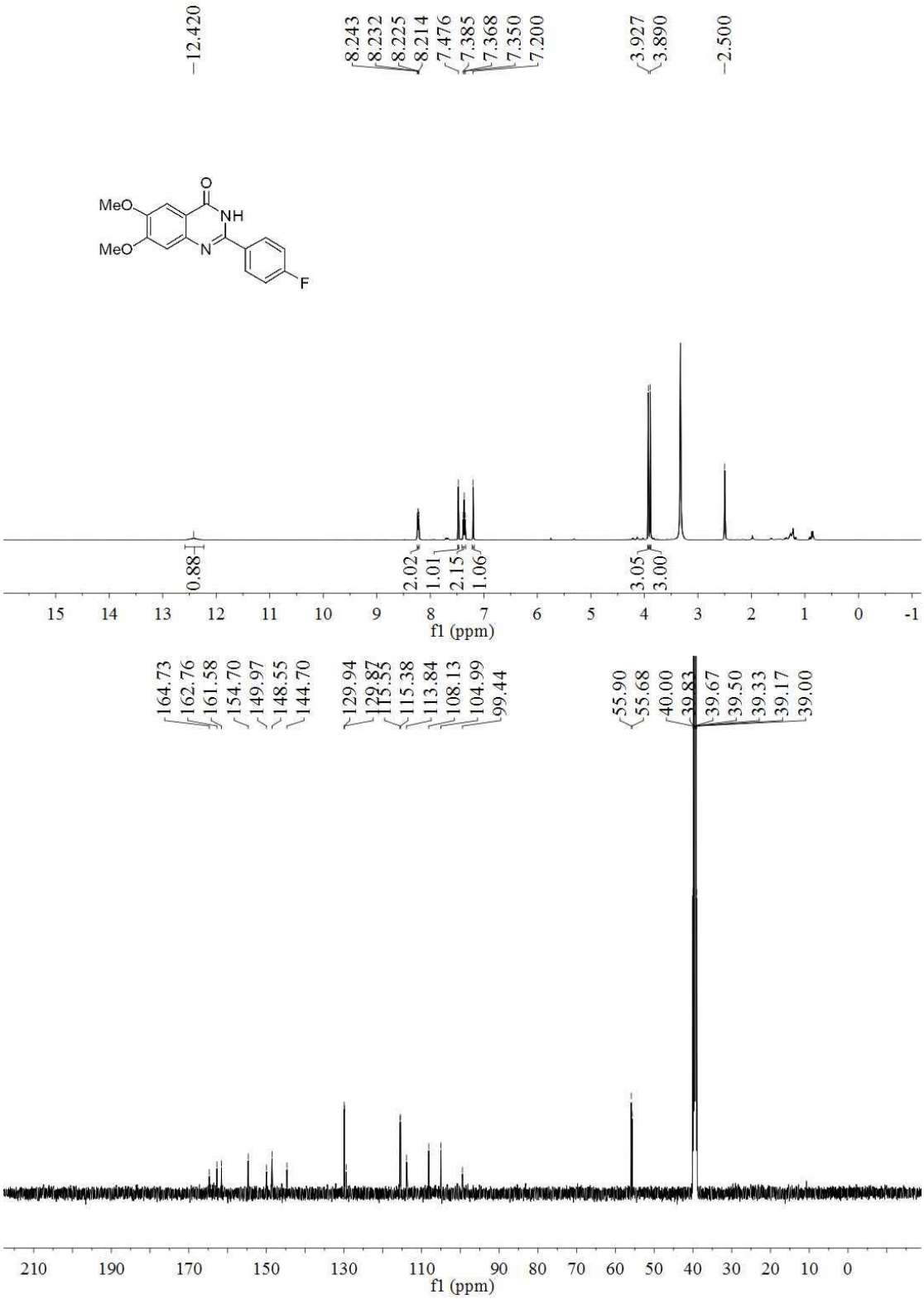

12.703
8.334
8.318
8.185
8.169
8.119
8.102
7.878
7.863
7.848
7.786
7.770
7.576
7.561
7.546
6.024
6.017
5.321
5.316
4.764
4.757
4.391
4.282
4.278
4.077
2.500
1.477
1.343
1.279
1.214
NH
N
O
Me
Me
Me
Me
0.79
1.97
1.00
1.94
1.00
0.99
0.98
0.90
0.89
0.90
1.00
0.97
0.98
1.00
2.89
2.93
3.00
3.30
f1 (ppm)
164.14
161.97
151.30
148.38
137.27
134.57
131.13
129.35
128.18
127.57
126.96
125.29
111.34
108.41
104.68
82.60
79.09
76.59
72.05
66.24
40.00
39.83
39.67
39.50
39.33
39.17
39.00
26.50
26.35
25.92
24.97
f1 (ppm)

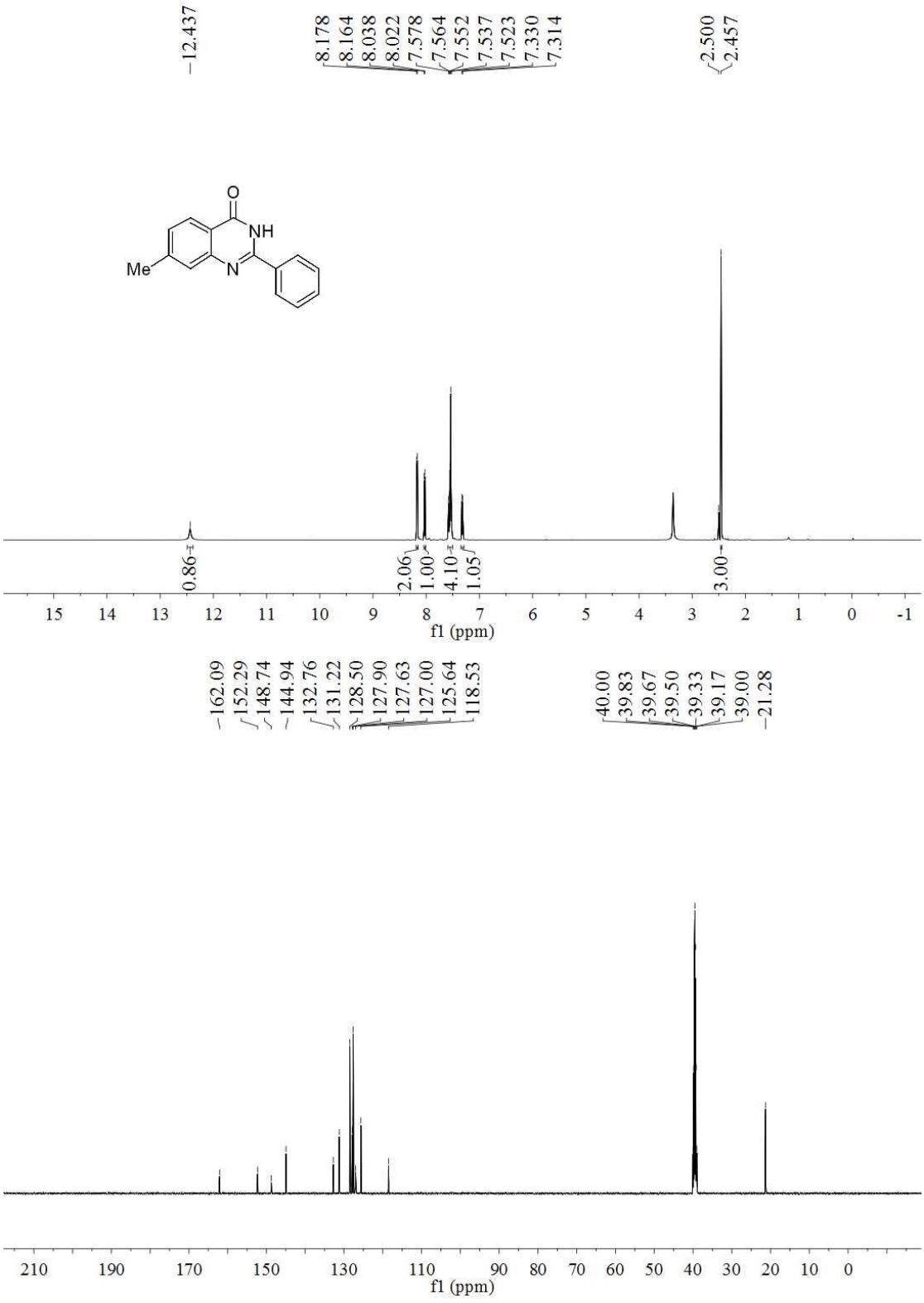

12.411
8.182
8.167
8.056
8.038
7.602
7.587
7.573
7.558
7.543
7.528
7.182
7.095
7.081
3.910
2.500
O
NH
MeO
N
0.92
2.01
1.00
3.03
0.99
0.97
3.11
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1
f1 (ppm)
164.16
161.72
152.87
150.93
132.69
131.34
128.54
127.69
127.41
116.13
114.37
108.48
55.68
40.00
39.83
39.67
39.50
39.33
39.17
39.00
210 190 170 150 130 110 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

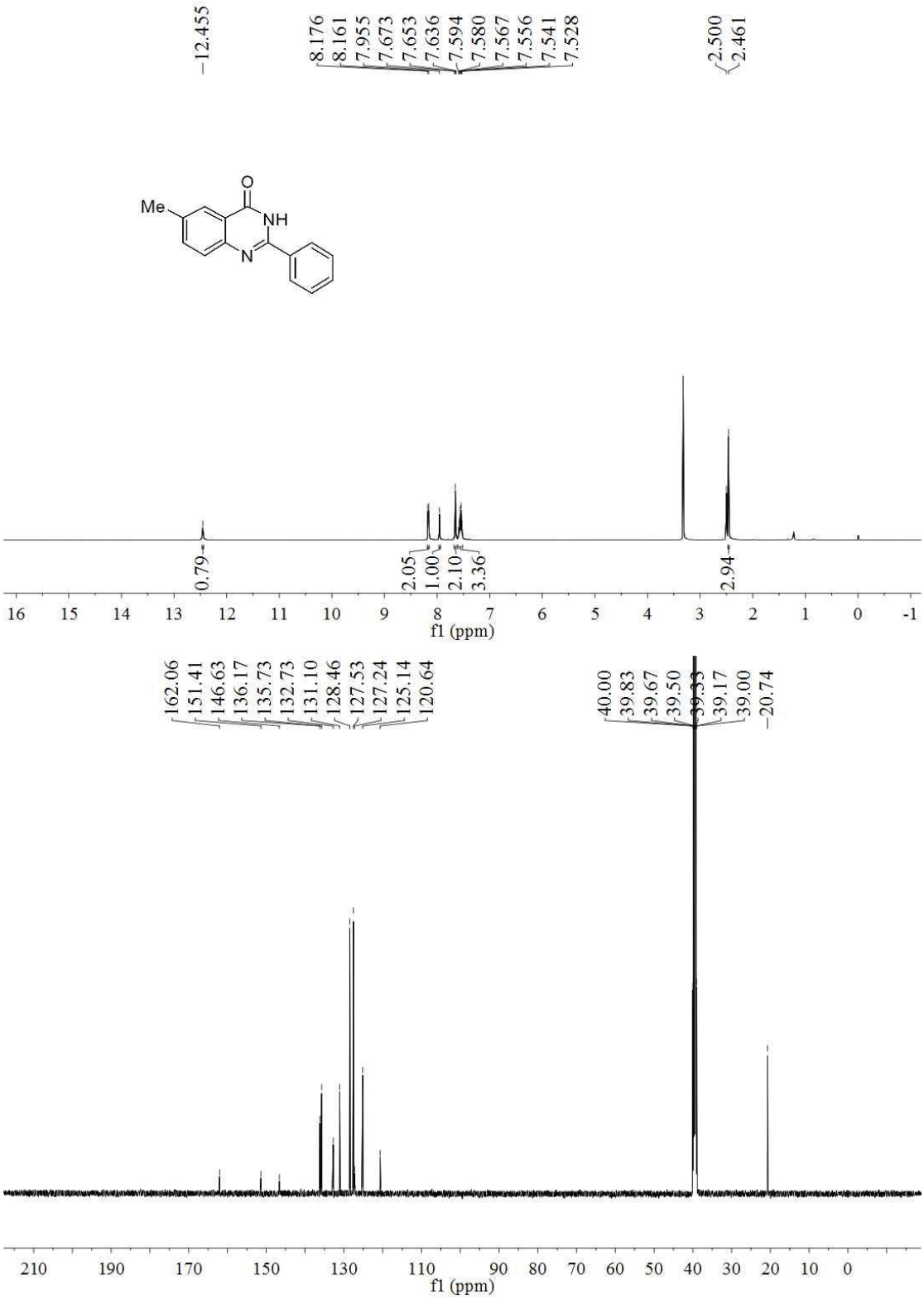

12.664
8.176
8.162
8.159
8.140
8.123
7.774
7.771
7.617
7.603
7.588
7.566
7.550
7.542
7.538
7.525
7.521
2.500
O
NH
Cl
N
0.72
1.83
0.94
0.77
3.96
f1 (ppm)
161.66
153.80
149.79
139.07
132.38
131.60
129.15
128.54
127.84
126.67
126.44
119.75
40.00
39.83
39.67
39.50
39.33
39.17
39.00
f1 (ppm)

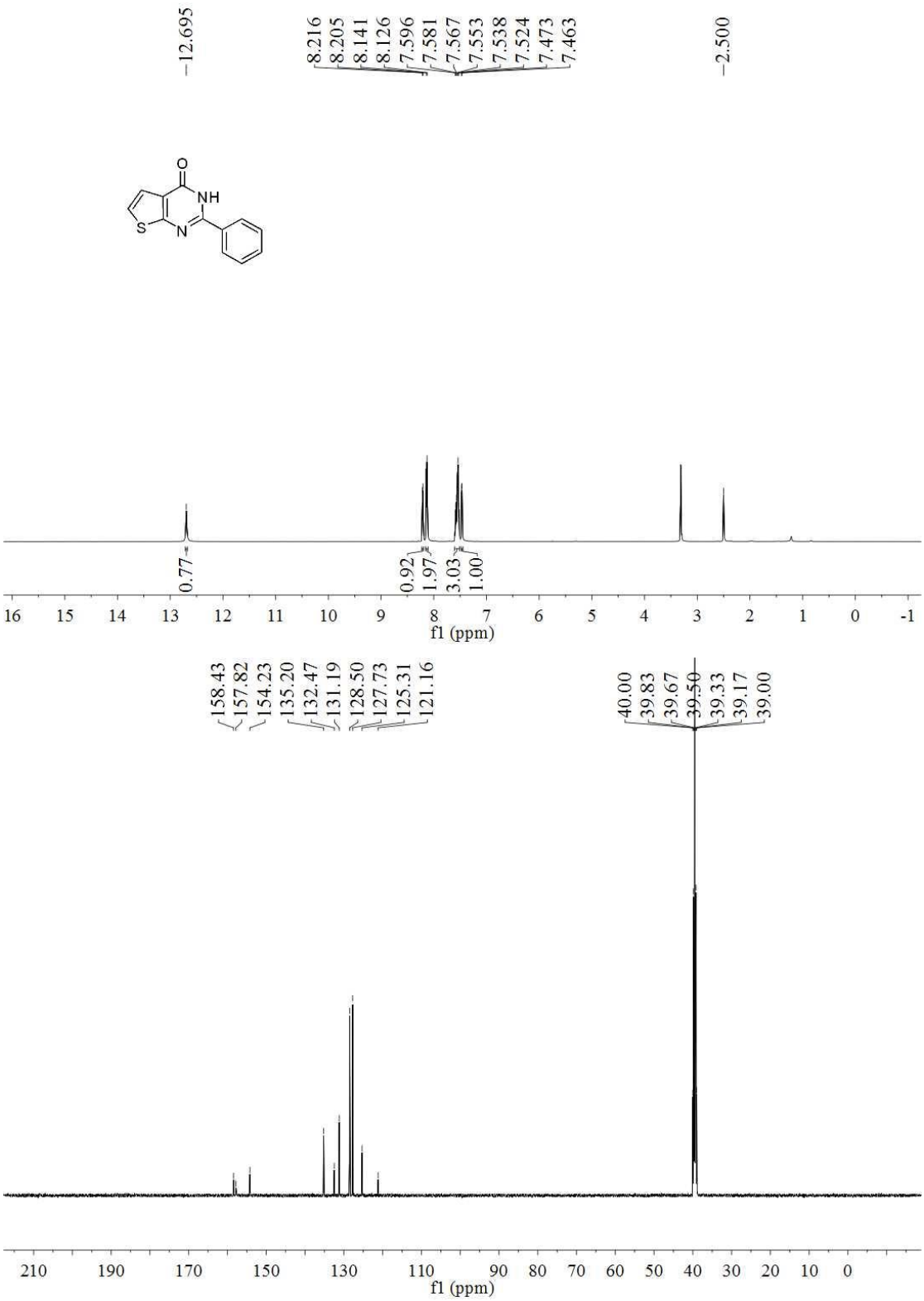

12.659
8.179
8.164
8.068
8.051
7.939
7.681
7.664
7.623
7.608
7.594
7.572
7.557
7.543
2.500
O
NH
Br
N
0.81
1.90
0.93
0.88
0.92
2.99
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1
f1 (ppm)
161.69
153.68
149.83
132.32
131.59
129.55
129.43
128.52
128.01
127.84
127.81
120.03
40.00
39.83
39.67
39.50
39.33
39.17
39.00
210 190 170 150 130 110 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

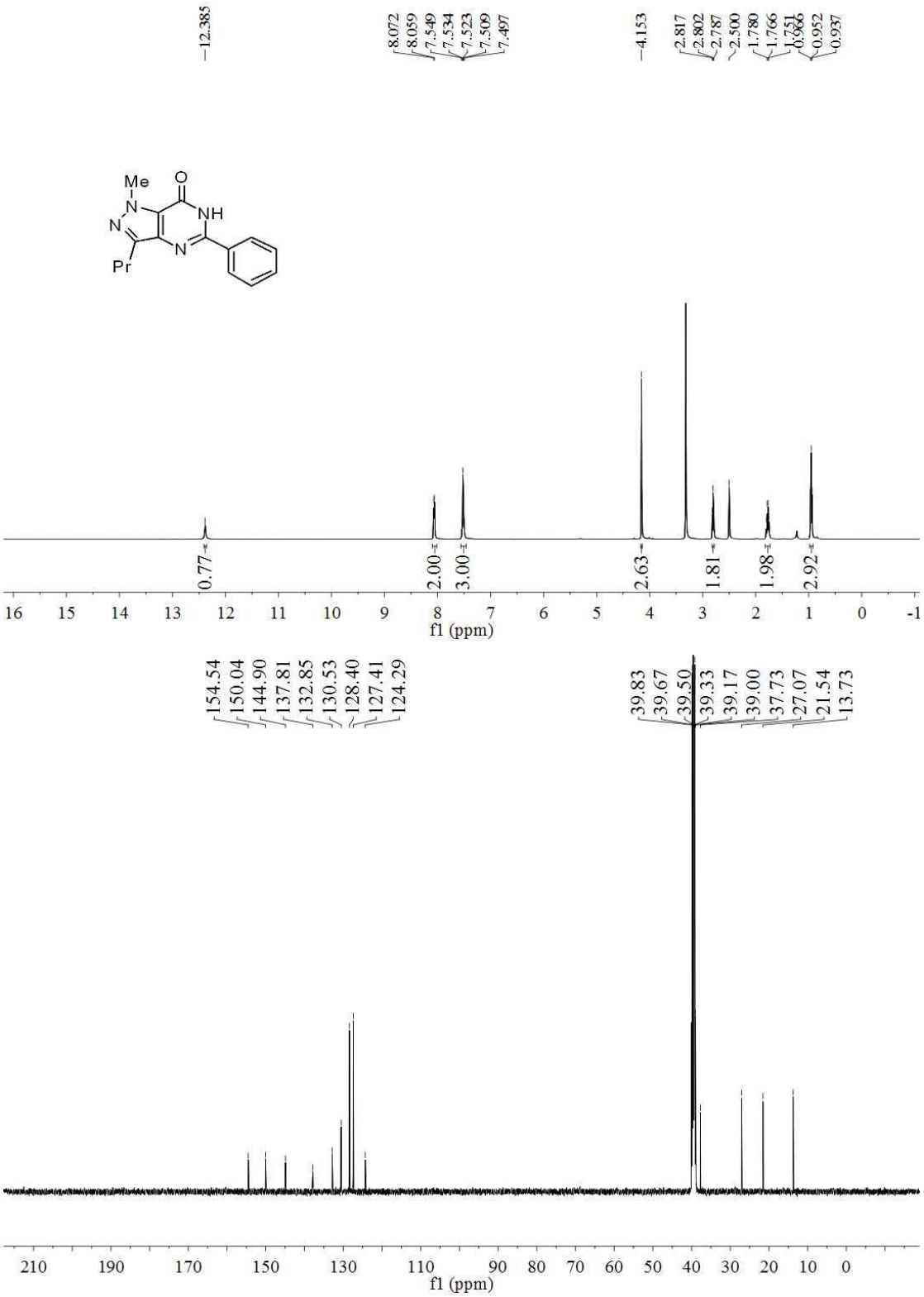

12.426
8.171
8.157
7.577
7.564
7.545
7.530
7.517
7.481
7.213
3.931
3.893
2.500
MeO
MeO
O
NH
N
0.89
1.96
3.17
0.93
1.04
2.96
3.02
f1 (ppm)
161.50
154.73
150.75
148.59
144.80
132.81
130.98
128.53
127.40
113.96
108.24
104.96
55.94
55.70
40.00
39.83
39.67
39.50
39.33
39.17
39.00
f1 (ppm)

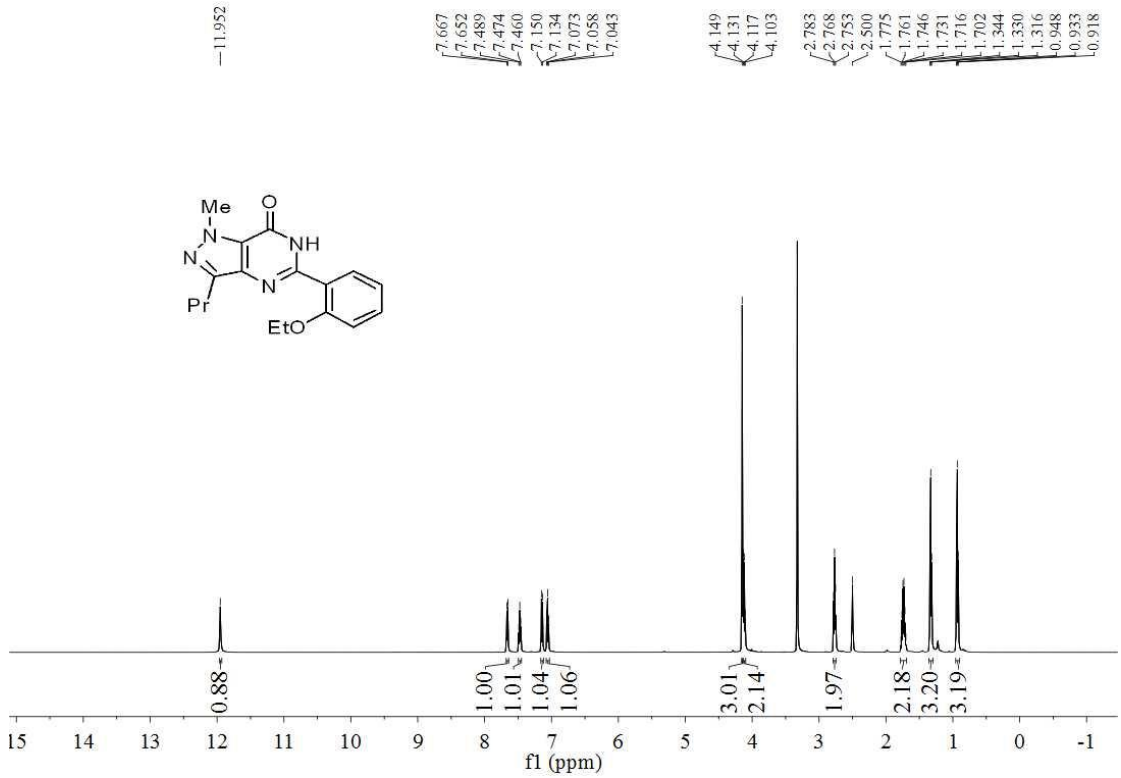

12.420
8.243
8.232
8.225
8.214
7.476
7.385
7.368
7.350
7.200
3.927
3.890
2.500
MeO
MeO
NH
N
O
F
0.88
2.02
1.01
2.15
1.06
3.05
3.00
f1 (ppm)
164.73
162.76
161.58
154.70
149.97
148.55
144.70
129.94
129.87
115.55
115.38
113.84
108.13
104.99
99.44
55.90
55.68
40.00
39.83
39.67
39.50
39.33
39.17
39.00
f1 (ppm)

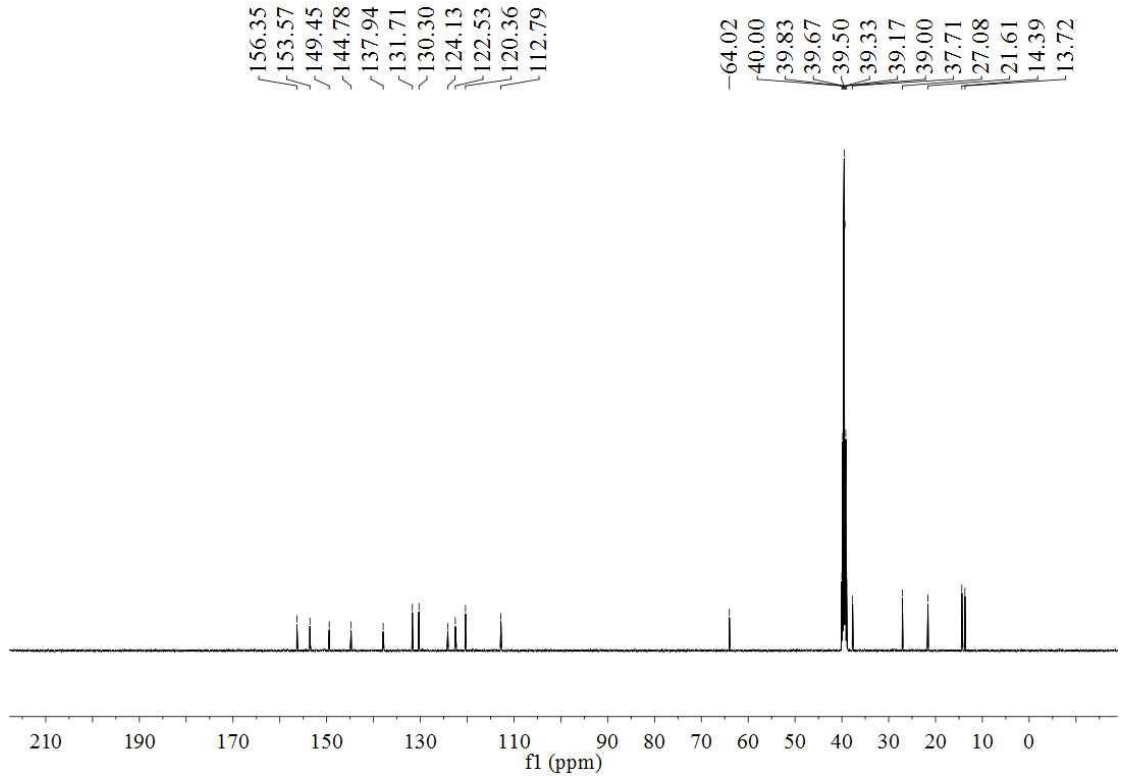

12.437
8.178
8.164
8.038
8.022
7.578
7.564
7.552
7.537
7.523
7.330
7.314
2.500
2.457
O
NH
Me
N
0.86
2.06
1.00
4.10
1.05
3.00
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1
f1 (ppm)
162.09
152.29
148.74
144.94
132.76
131.22
128.50
127.90
127.63
127.00
125.64
118.53
40.00
39.83
39.67
39.50
39.33
39.17
39.00
21.28
210 190 170 150 130 110 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

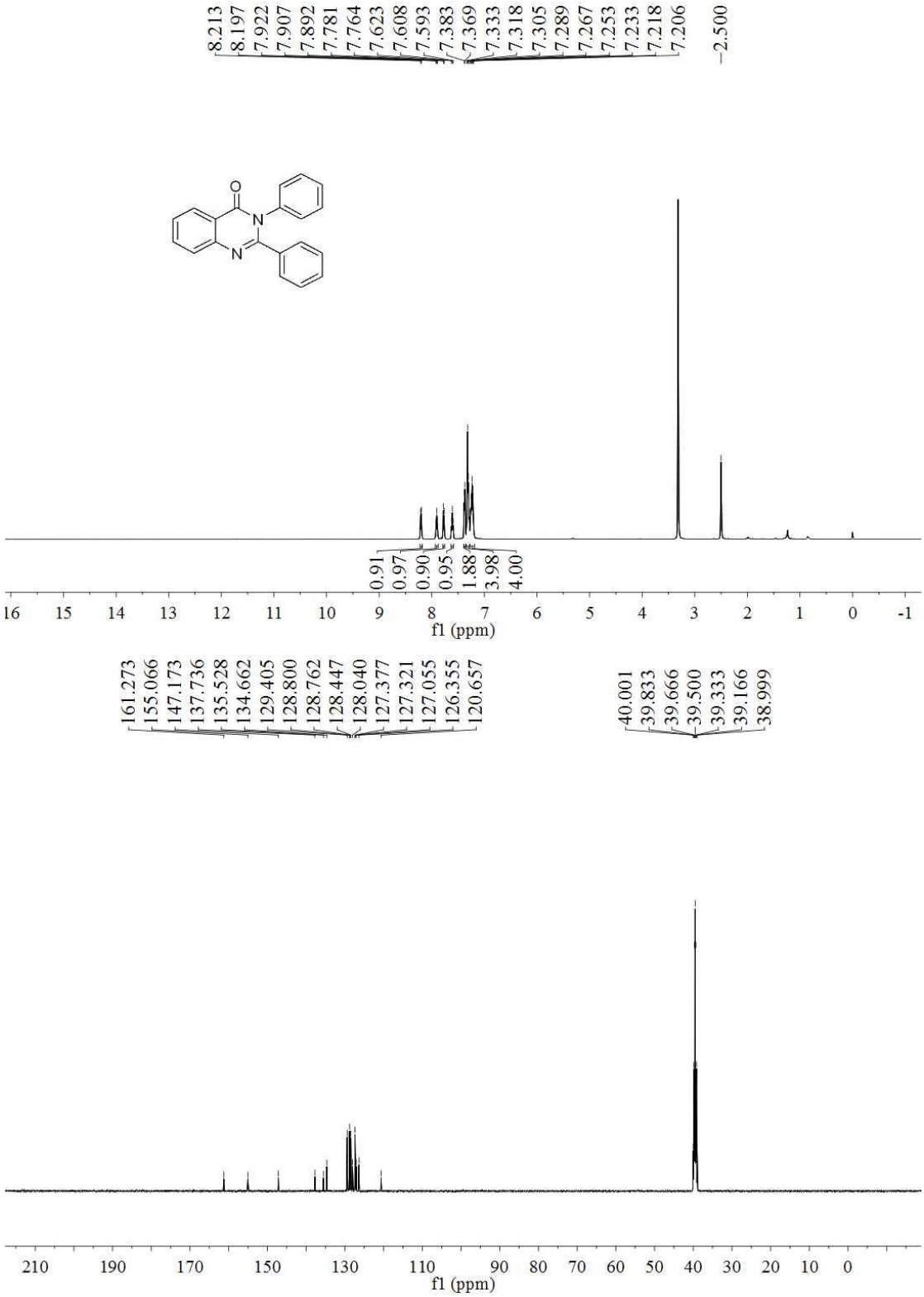

12.455
8.176
8.161
7.955
7.673
7.653
7.636
7.594
7.580
7.567
7.556
7.541
7.528
2.500
2.461
O
Me
NH
N
0.79
2.05
1.00
2.10
3.36
2.94
f1 (ppm)
162.06
151.41
146.63
136.17
135.73
132.73
131.10
128.46
127.53
127.24
125.14
120.64
40.00
39.83
39.67
39.50
39.33
39.17
39.00
20.74
f1 (ppm)

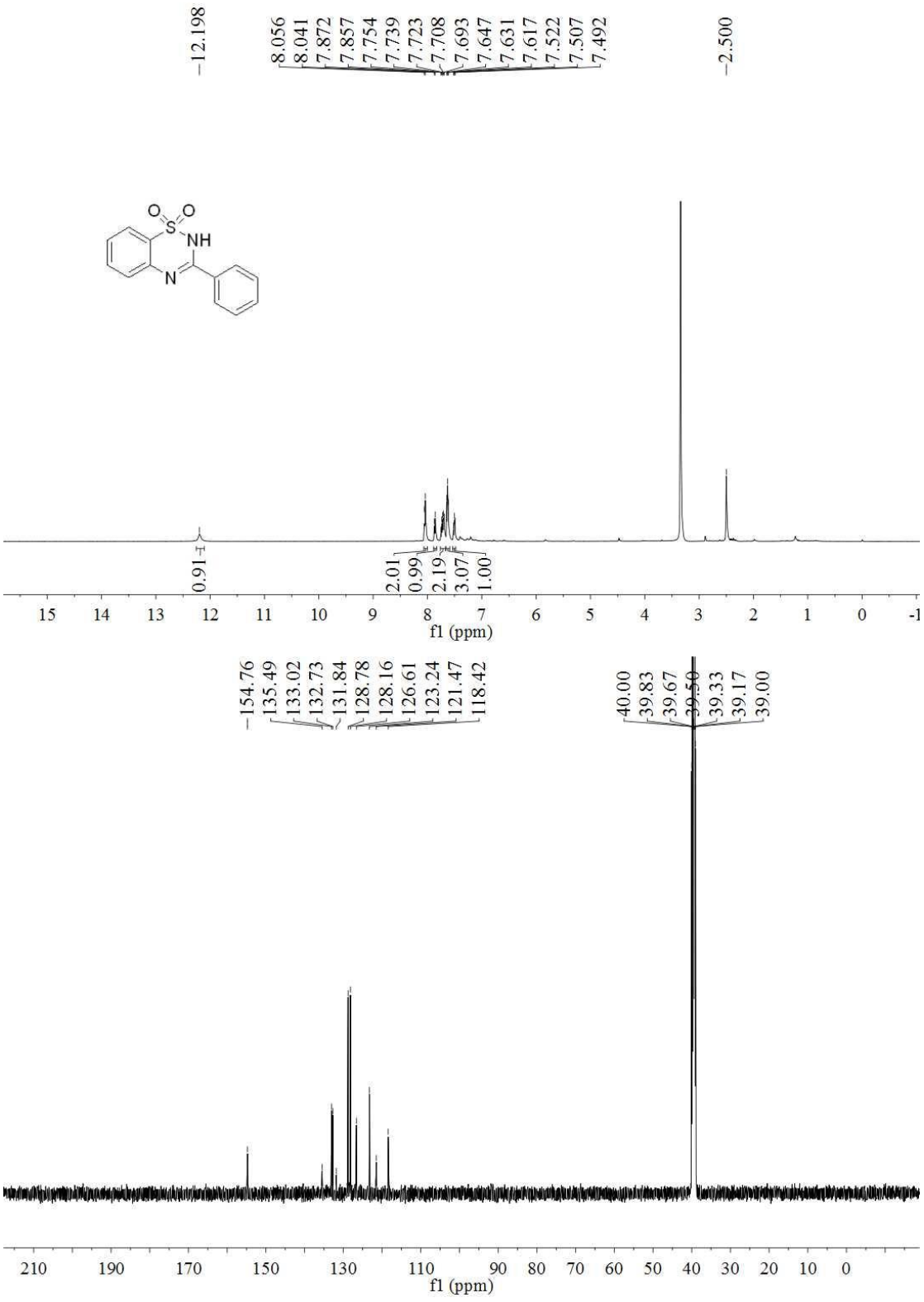

12.695
8.216
8.205
8.141
8.126
7.596
7.581
7.567
7.553
7.538
7.524
7.473
7.463
2.500
O
NH
S
N
0.77
0.92
1.97
3.03
1.00
f1 (ppm)
158.43
157.82
154.23
135.20
132.47
131.19
128.50
127.73
125.31
121.16
40.00
39.83
39.67
39.50
39.33
39.17
39.00
f1 (ppm)

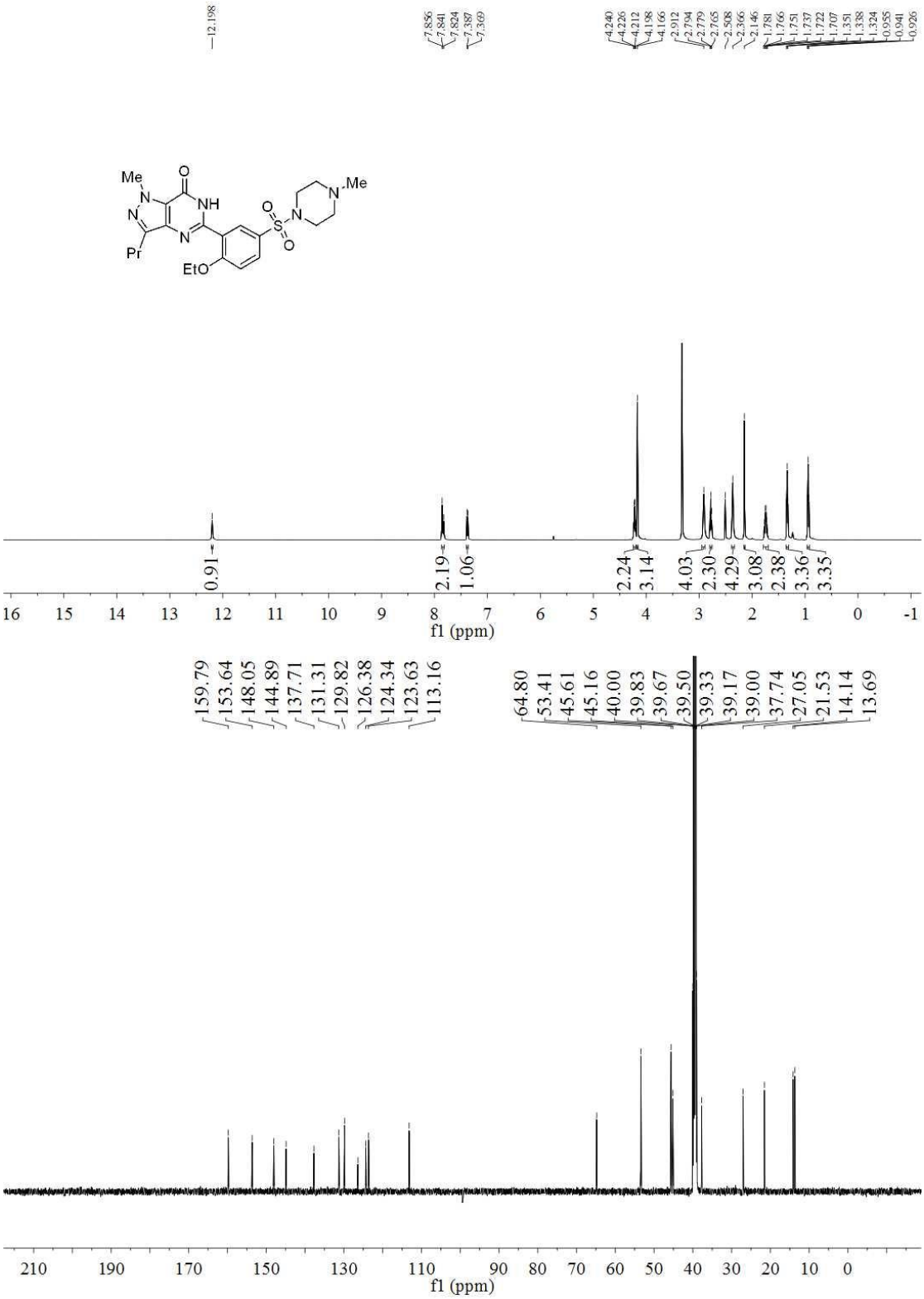

12.385
8.072
8.059
7.549
7.534
7.523
7.509
7.497
4.153
2.817
2.802
2.787
2.500
1.780
1.766
1.751
0.966
0.952
0.937
Me
O
NH
N
N
Pr
0.77
2.00
3.00
2.63
1.81
1.98
2.92
f1 (ppm)
154.54
150.04
144.90
137.81
132.85
130.53
128.40
127.41
124.29
39.83
39.67
39.50
39.33
39.17
39.00
37.73
27.07
21.54
13.73
f1 (ppm)

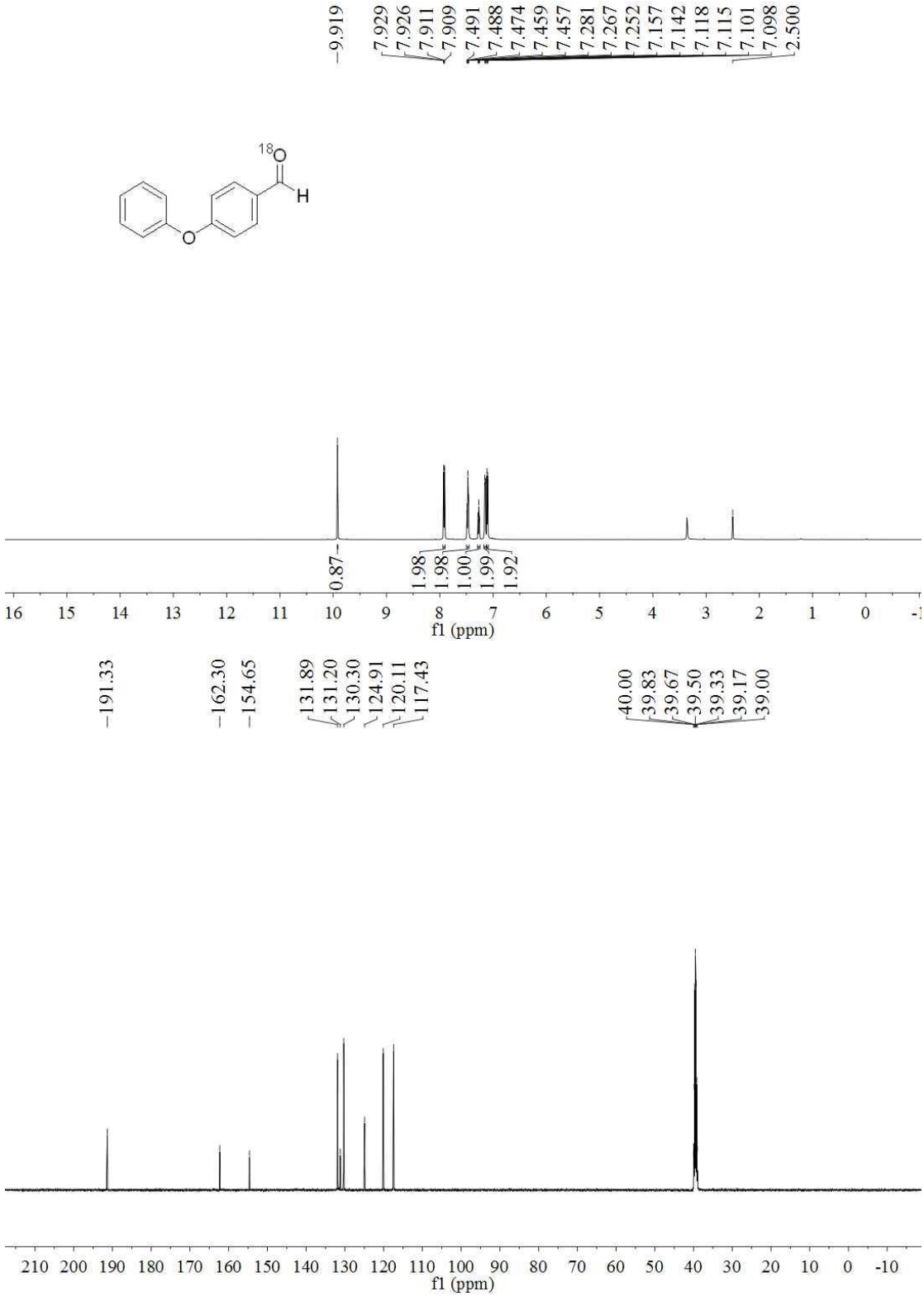

11.952
7.667
7.652
7.489
7.474
7.460
7.150
7.134
7.073
7.058
7.043
4.149
4.131
4.117
4.103
2.783
2.768
2.753
2.500
1.775
1.761
1.746
1.731
1.716
1.702
1.344
1.330
1.316
0.948
0.933
0.918
Me
O
NH
N
N
N
Pr
EtO
0.88
1.00
1.01
1.04
1.06
3.01
2.14
1.97
2.18
3.20
3.19
f1 (ppm)


156.35
153.57
149.45
144.78
137.94
131.71
130.30
124.13
122.53
120.36
112.79
64.02
40.00
39.83
39.67
39.50
39.33
39.17
39.00
37.71
27.08
21.61
14.39
13.72
f1 (ppm)

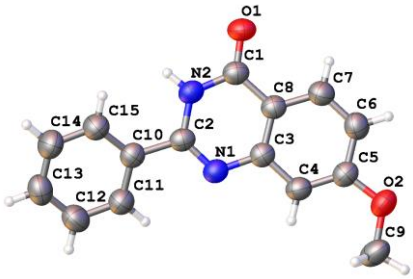

8.213
8.197
7.922
7.907
7.892
7.781
7.764
7.623
7.608
7.593
7.383
7.369
7.333
7.318
7.305
7.289
7.267
7.253
7.233
7.218
7.206
2.500
O
N
N
0.91
0.97
0.90
0.95
1.88
3.98
4.00
f1 (ppm)
161.273
155.066
147.173
137.736
135.528
134.662
129.405
128.800
128.762
128.447
128.040
127.377
127.321
127.055
126.355
120.657
40.001
39.833
39.666
39.500
39.333
39.166
38.999
f1 (ppm)


12.198
8.056
8.041
7.872
7.857
7.754
7.739
7.723
7.708
7.693
7.647
7.631
7.617
7.522
7.507
7.492
2.500
NH
0.91
2.01
0.99
2.19
3.07
1.00
f1 (ppm)
154.76
135.49
133.02
132.73
131.84
128.78
128.16
126.61
123.24
121.47
118.42
40.00
39.83
39.67
39.50
39.33
39.17
39.00
f1 (ppm)


12.198
7.856
7.841
7.824
7.387
7.369
4.240
4.226
4.212
4.198
4.166
2.912
2.794
2.779
2.765
2.508
2.366
2.146
1.781
1.766
1.751
1.737
1.722
1.707
1.351
1.338
1.324
0.955
0.941
0.926
Me
N
O
NH
N
N
Me
O
S
O
N
Pr
EtO
0.91
2.19
1.06
2.24
3.14
4.03
2.30
4.29
3.08
2.38
3.36
3.35
f1 (ppm)
159.79
153.64
148.05
144.89
137.71
131.31
129.82
126.38
124.34
123.63
113.16
64.80
53.41
45.61
45.16
40.00
39.83
39.67
39.50
39.33
39.17
39.00
37.74
27.05
21.53
14.14
13.69
f1 (ppm)


9.919
7.929
7.926
7.911
7.909
7.491
7.488
7.474
7.459
7.457
7.281
7.267
7.252
7.157
7.142
7.118
7.115
7.101
7.098
2.500
18O
H
O
0.87
1.98
1.98
1.00
1.99
1.92
f1 (ppm)
191.33
162.30
154.65
131.89
131.20
130.30
124.91
120.11
117.43
40.00
39.83
39.67
39.50
39.33
39.17
39.00
f1 (ppm)

6. X-ray Crystallographic study for 4a



CCDC: 1821030

Empirical formula	$C_{15}H_{12}N_2O_2$	
Formula weight	252.27	
Temperature	296 K	
Crystal system	Monoclinic	
Space group	P2	
Unit cell dimensions	a = 15.8271(7) Å	α =90 °
	b= 4.3272(2) Å	β =103.280(4) °
	c = 18.7126(9) Å	γ =90 °
Volume	1247.30(10) $Å^3$	
Z	4	
ρ	1.343 calcg/cm^3	
μ	0.475 mm^{-1}	
F(000)	528.0	
Crystal size	0.15 × 0.03 × 0.02 mm^3	
Radiation	GaKα (λ = 1.34139)	
The range for data collection	9.992 to 110.134 °	
Index ranges	-16≤h≤19, -5≤k≤5, -21≤l≤22	
Reflections collected	7675	
Independent reflections	2363 [Rint = 0.0601, Rsigma = 0.0627]	
Data/restraints/parameters	2363/0/173	
Goodness-of-fit on F^2	0.996	
Final R indexes [I>=2σ (I)]	R1 = 0.0567, wR2 = 0.1448	
Final R indexes [all data]	R1 = 0.1056, wR2 = 0.1815	
Largest diff. peak/hole	0.17 and -0.21 e.$Å^{-3}$	