Supporting information for:

Orally bioavailable quinoxaline inhibitors of 15-prostaglandin dehydrogenase (15-PGDH) promote tissue repair and regeneration

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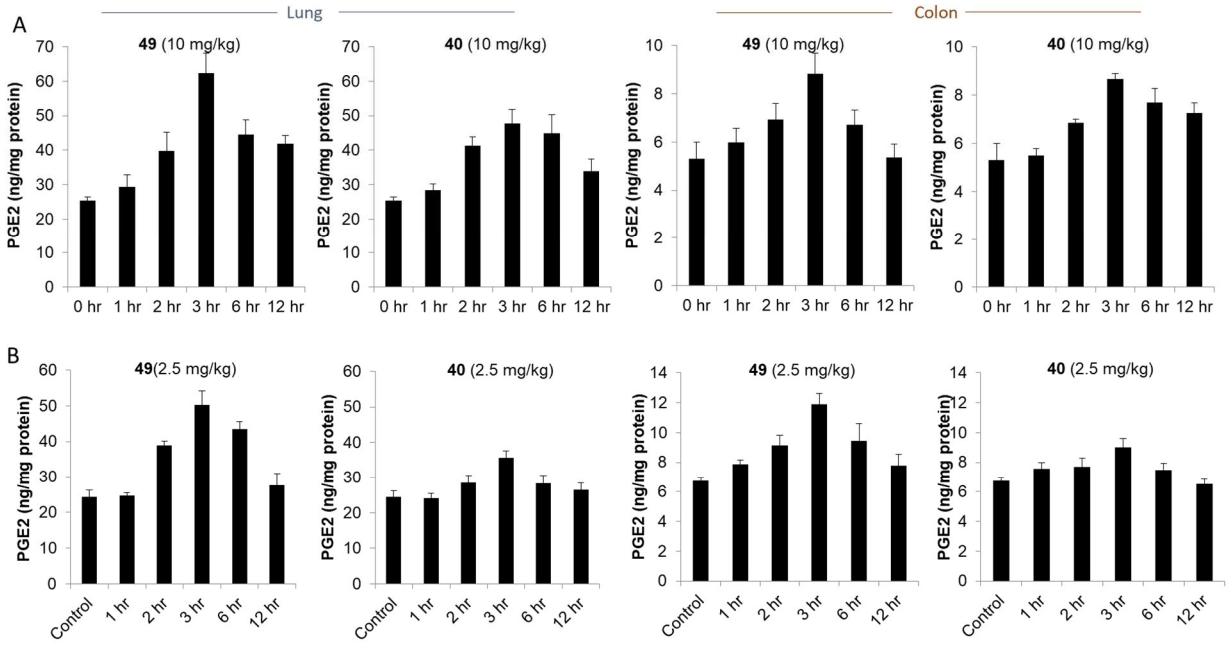


Figure S1. Elevation of PGE2 levels in colon and lung in female C57Bl/6 mice following a 10 (A) or 2.5 (B) mg/kg IP dose of the indicated compound.

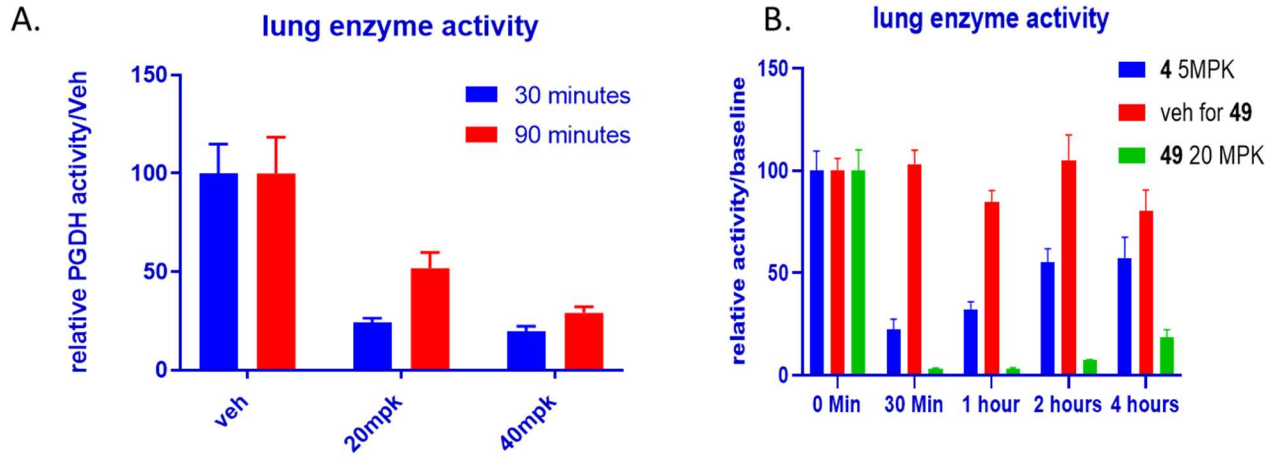


Figure S2. A. Inhibition of 15-PGDH enzymatic activity in the mouse lung following a 20 or 40 mg/kg oral dose of **49**. B. Time course of inhibition of 15-PGDH enzyme activity in the mouse lung following IP delivery of **4** or **49**.

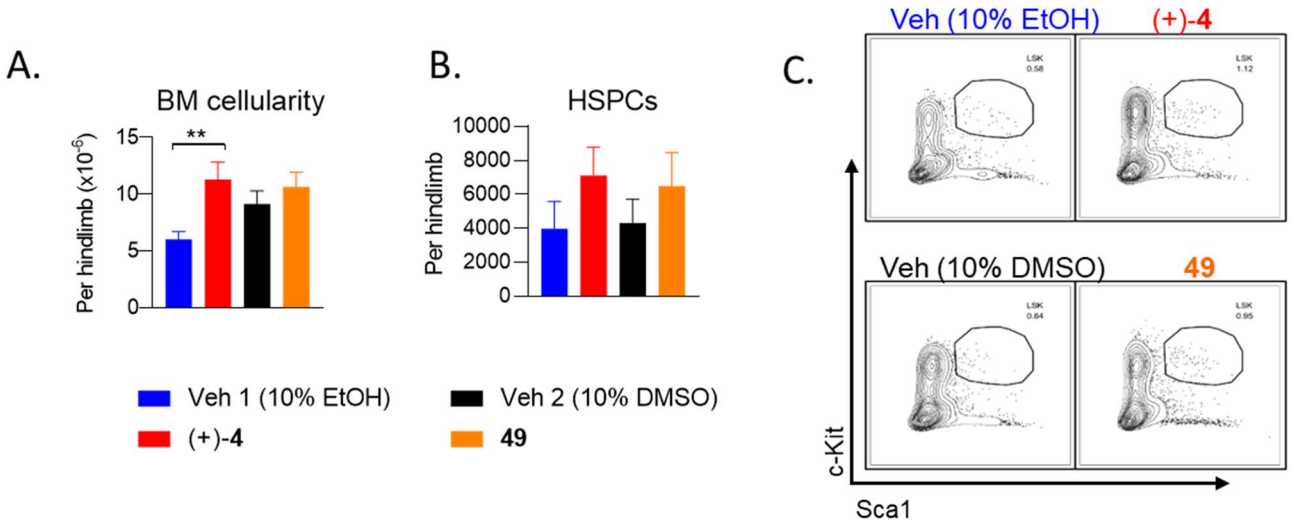


Figure S3. A. Bone marrow cellularity at day 20 (n = 8 – 10). B. Hematopoetic stem and progenitor cells (LSK positive cells) at day 20 (n = 9 – 14). *P < 0.05, **P < 0.005. C. Representative plots depicting hematopoietic stem and progenitor cell (HSPC) identification (gated plot area) among BM hematopoietic lineage negative cells by Sca1 (x-axis) and c-Kit (y-axis) staining in mice treated as indicated, 21 days post-transplantation. A-C experimental outline: Mice were irradiated at day -1 and dosing with vehicle or drug was initiated. (+)-4 was dosed in vehicle 1 (10% EtOH, 5% cremophor EL, 85% D5W, pH 7.4. 49 was dosed in vehicle 2 (10% DMSO, 25% PEG 400, 1% Tween-80, 64% D5W, pH 7.6). On day 0, 10^6 bone marrow cells were injected IV and drug or vehicle administration was continued twice daily.

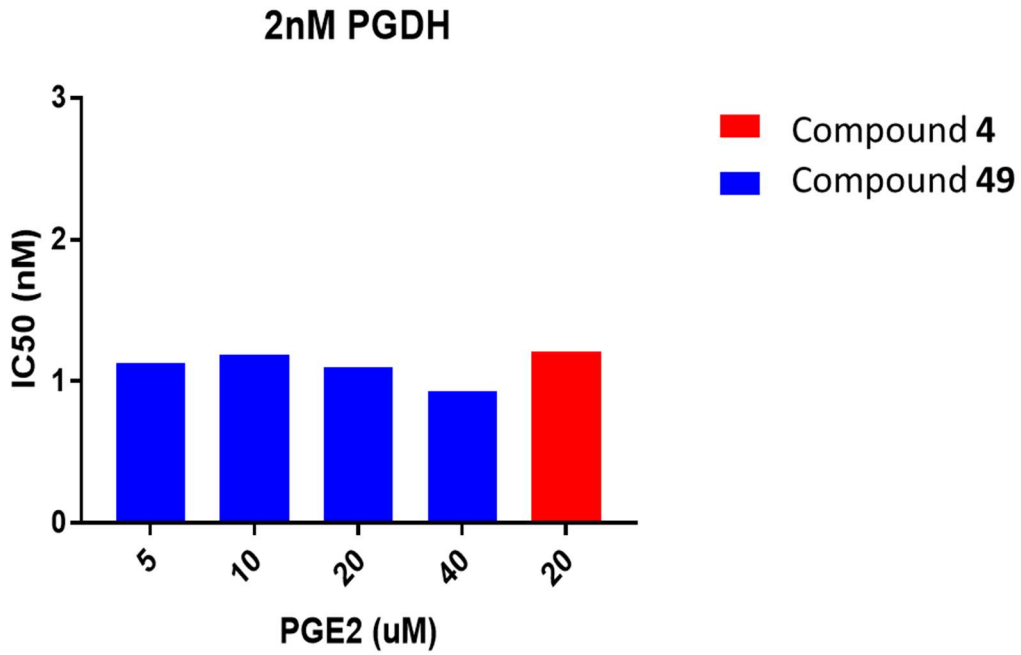
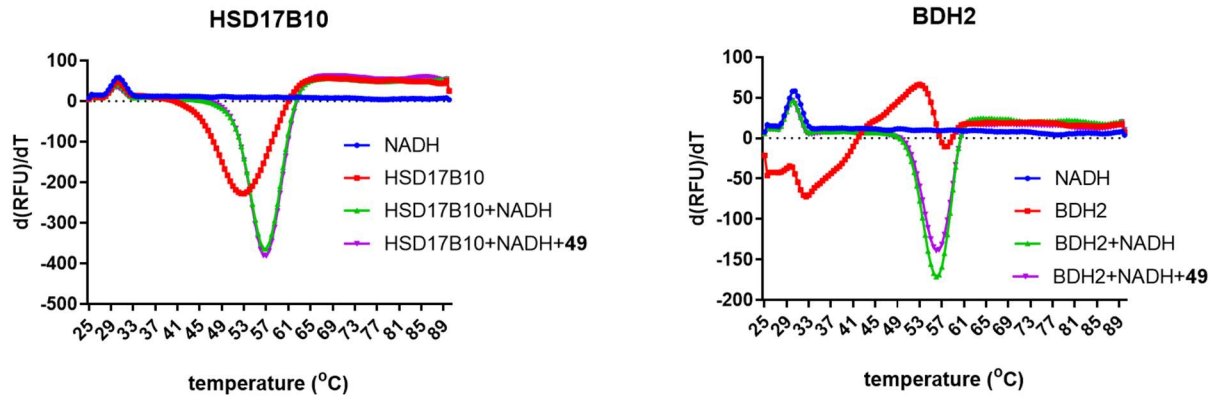


Figure S4. IC50 values for two inhibitors of 15-PGDH (2 nM enzyme) in the presence of the indicated substrate (PGE2) concentration.



	Melting Point (°C)		
	Enzyme	Enzyme+NADH	Enzyme+NADH+49
15-PGDH	**47**	**50.5**	**71**
HSD17B10	**53**	**57**	**57**
BDH2	**32.5**	**56**	**56.5**

Figure S5: 49 binds 15-PGDH but not HSD17B10 or BDH2 as judged by melting point. 10uM of **49**, 0.25ug of human PGDH, HSD17B10 or BDH2, NADH 125uM, HSD17B10 and BDH2 were purchased from SydLabs. Data for 15-PGDH from main text.

Table S1. Antibodies used in the identification and quantification of hematopoietic stem and precursor cells.

Antibody	Clone	Manufacturer
CD45R/B220	RA3-6B2	BD Pharmingen
CD11b	M1/70	BD Pharmingen
CD3e	500A2	BD Pharmingen
Ly-6G and Ly-6C	RB6-8C5	BD Pharmingen
TER-119	TER-119	BD Pharmingen
Ly-6A/E (Sca-1)	D7	Invitrogen
CD117 (c-Kit)	2B8	Invitrogen

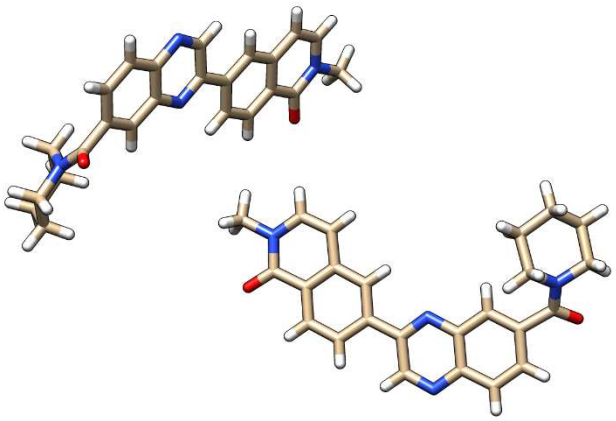


Figure S6. X-ray crystal structure of **49** showing 2 molecules in the unit cell. CCDC 2179639

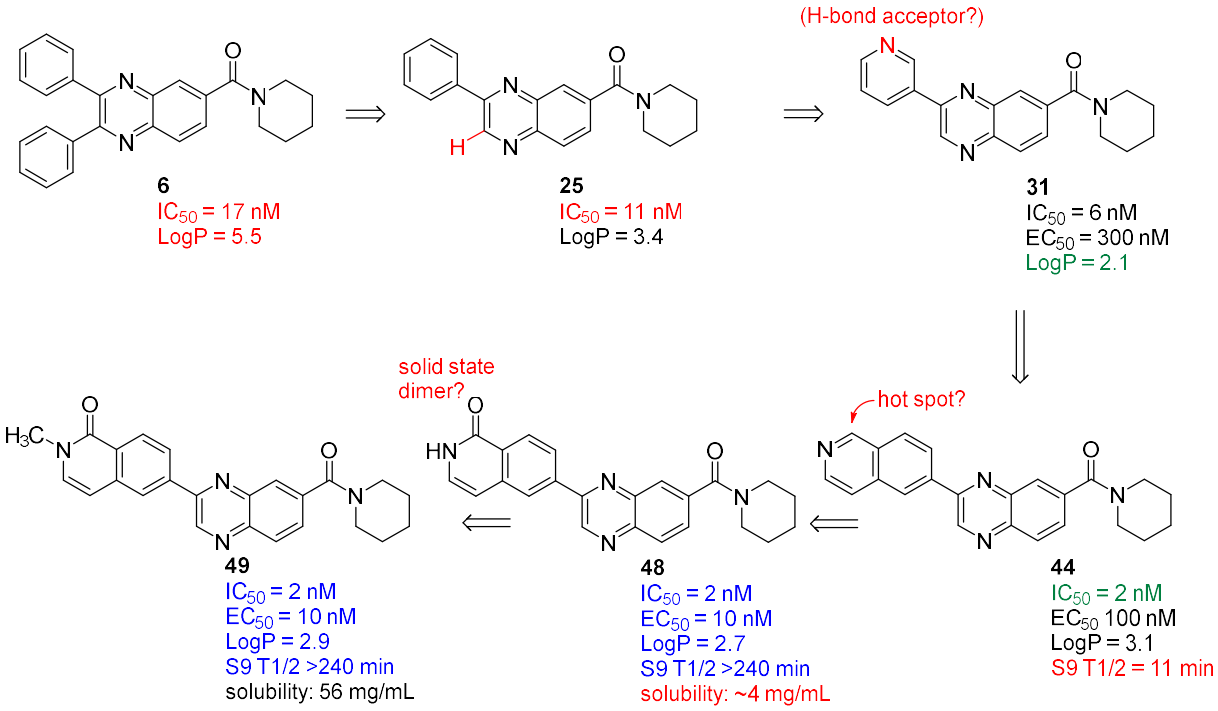
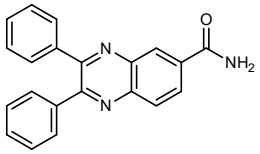
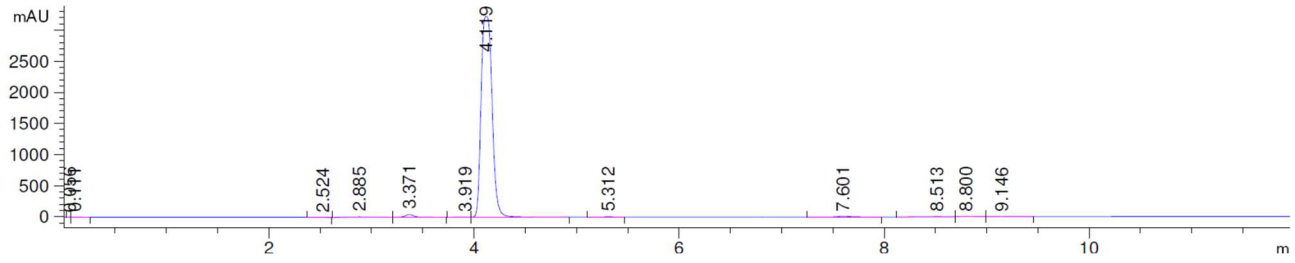


Figure S7. Compound progression from initial hit to potent, stable lead 49.

Representative HPLC Traces (254 nM absorbance)

Compound 9





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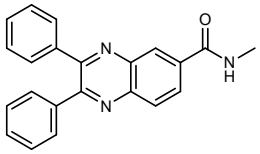

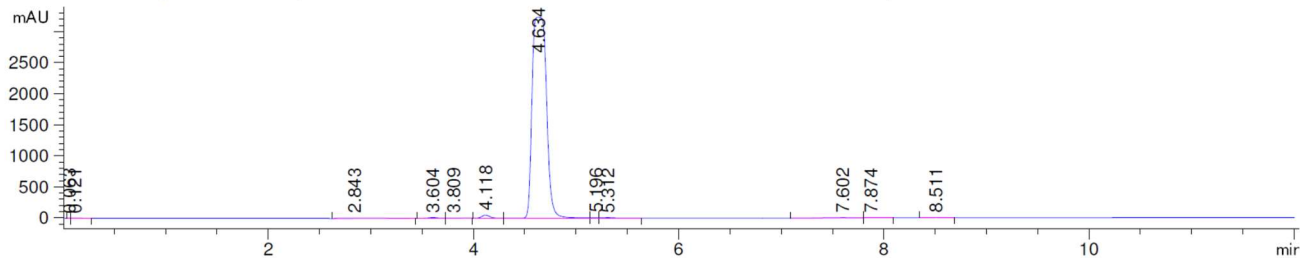

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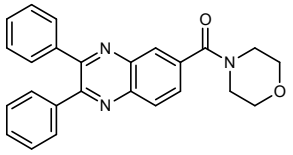

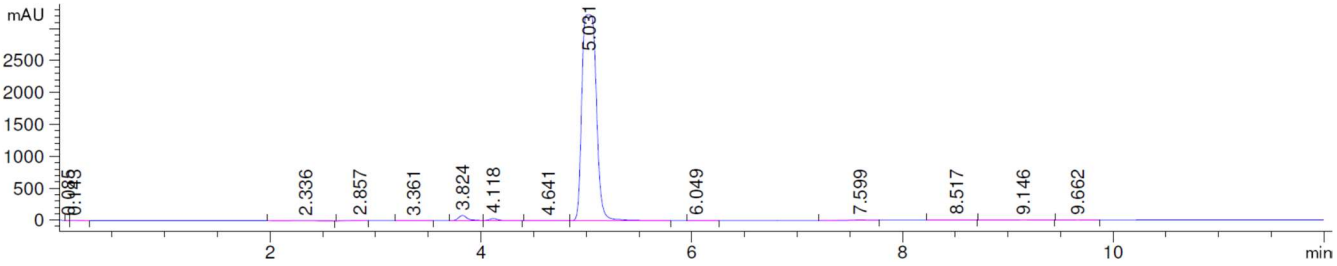

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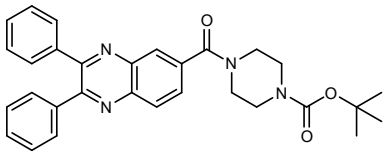

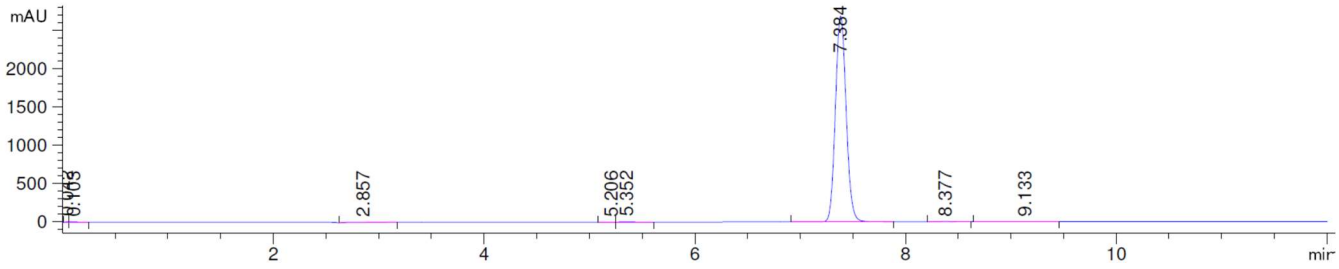

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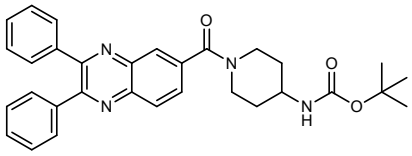

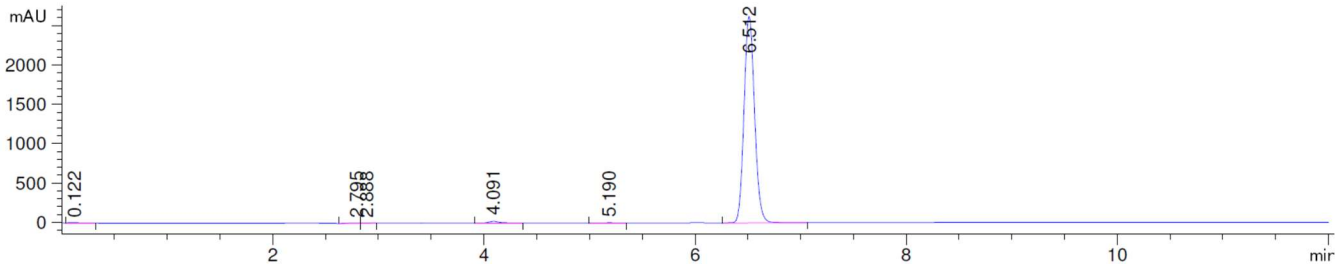

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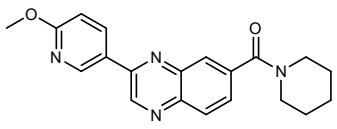

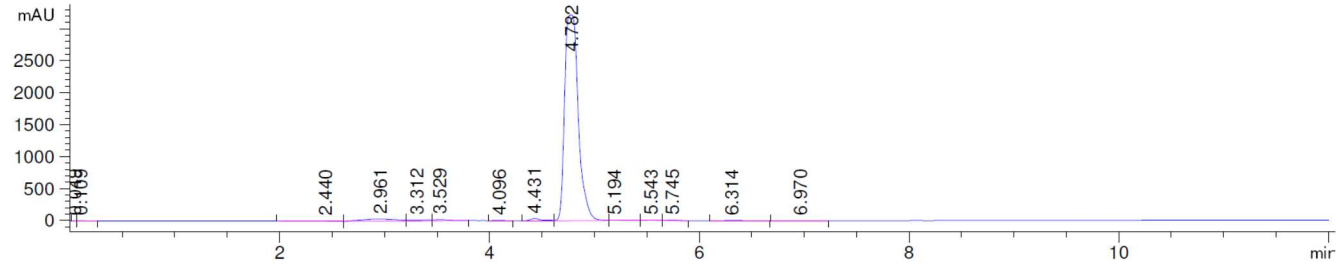

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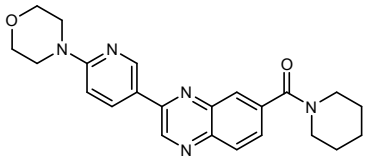

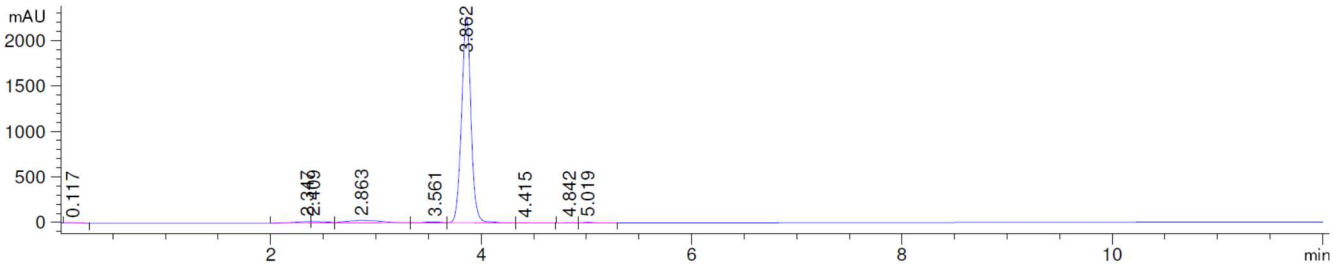

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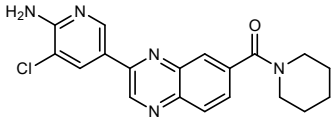

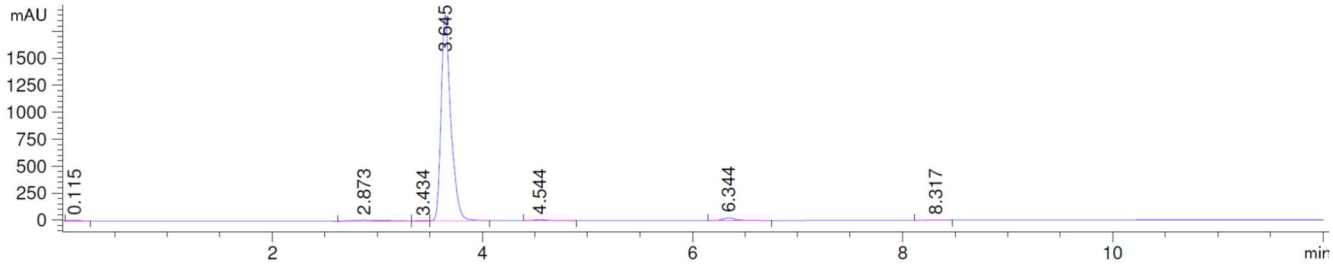

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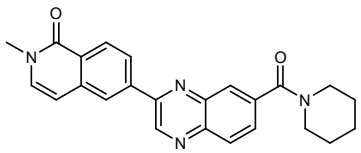

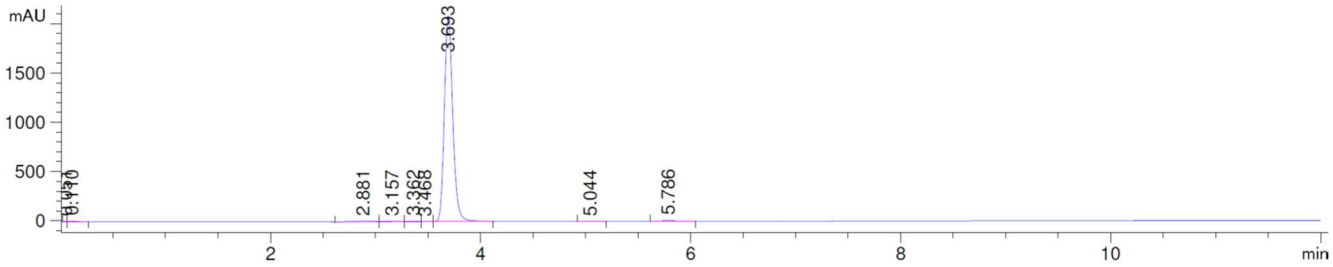

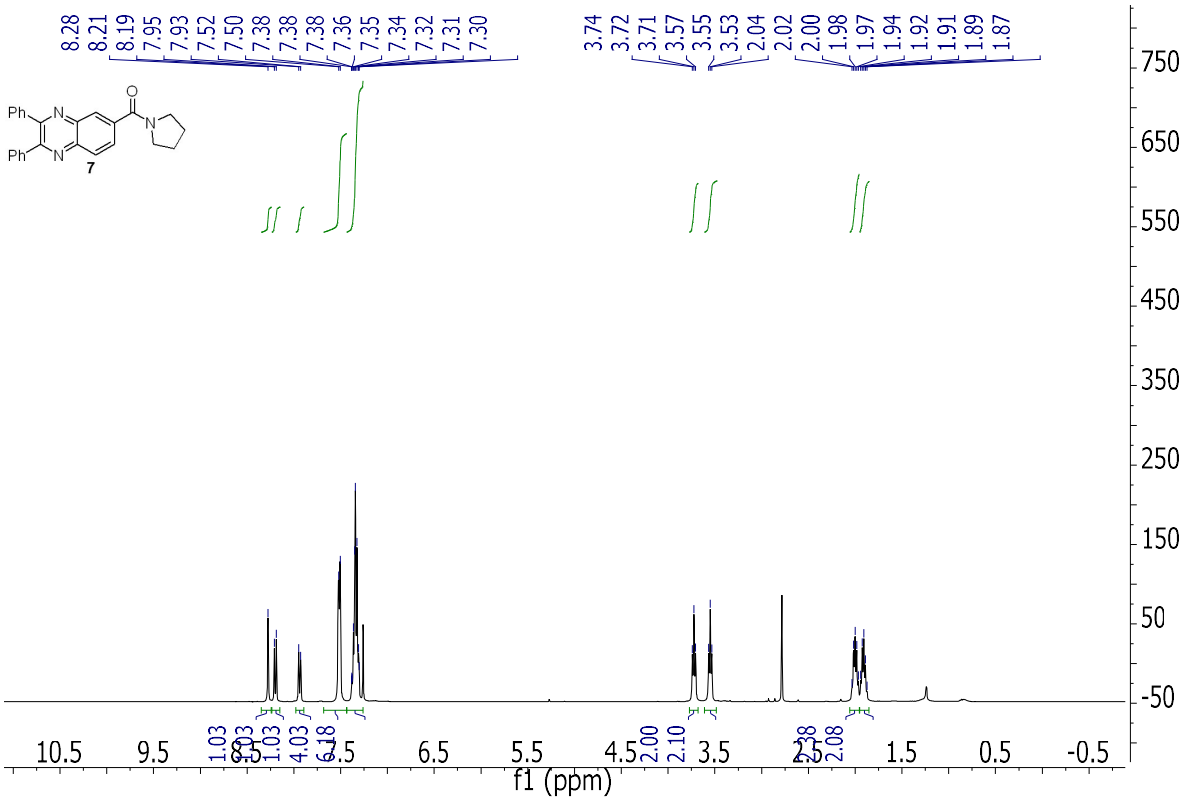
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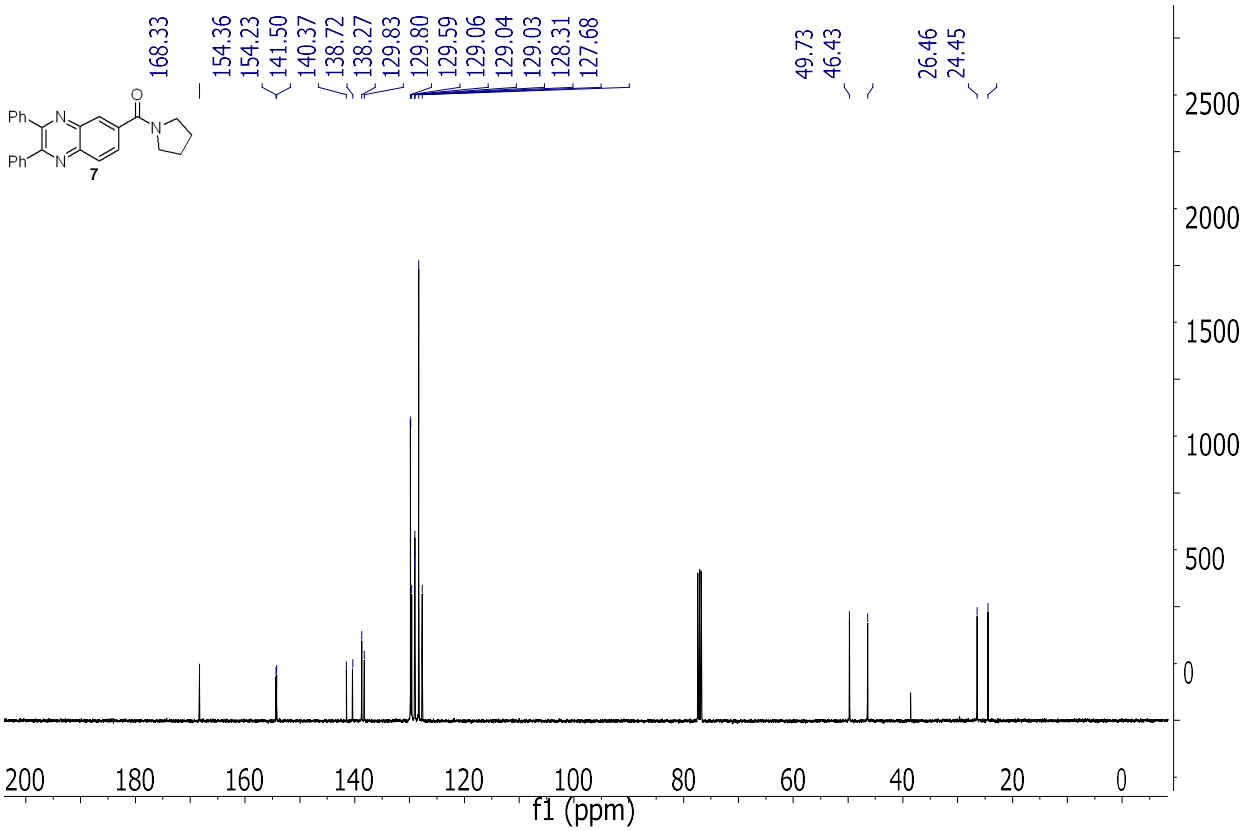
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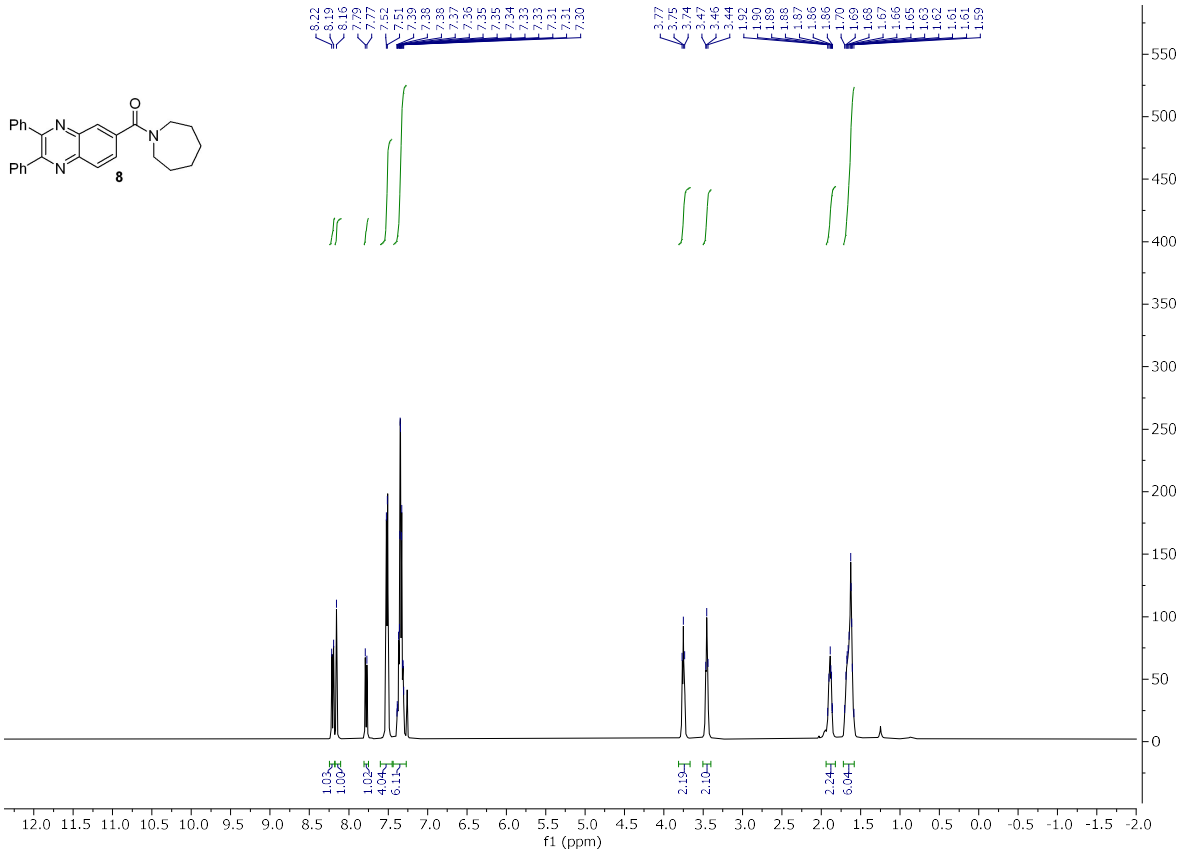
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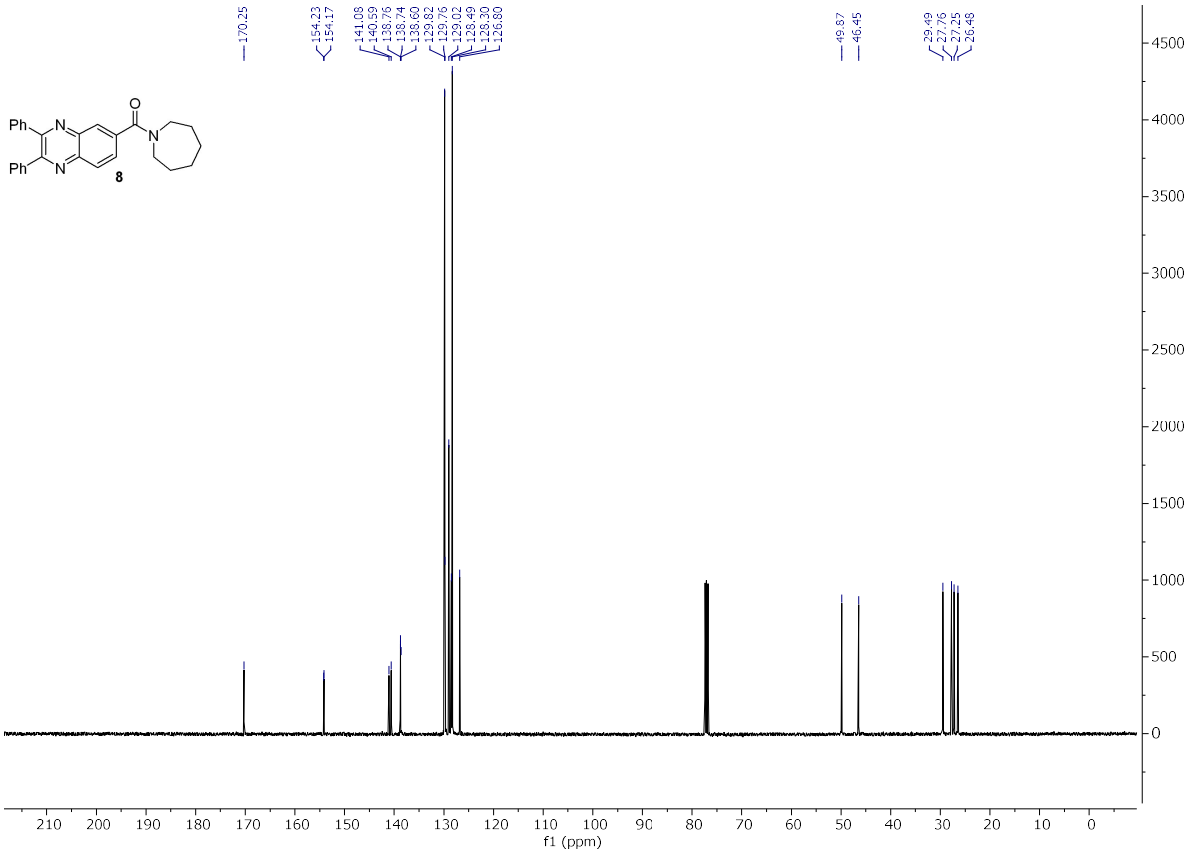
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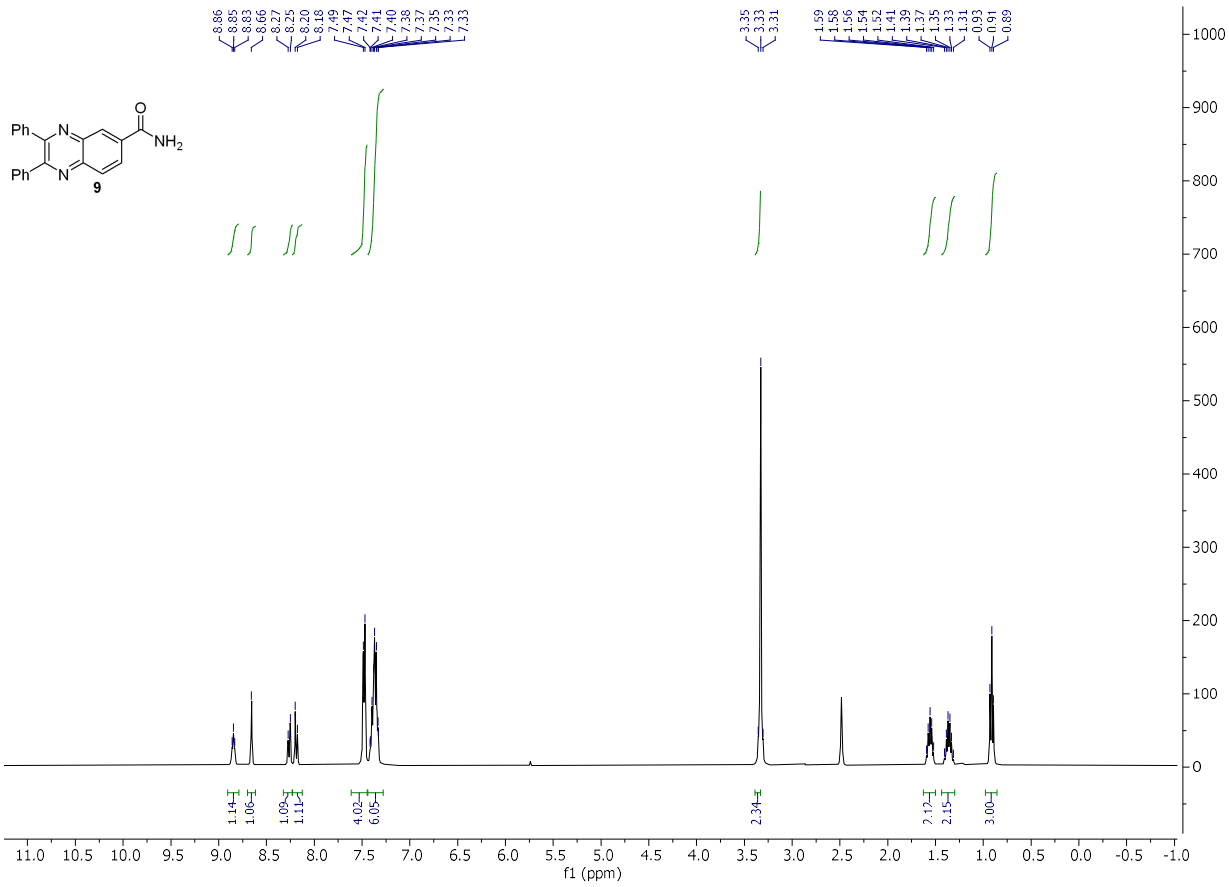
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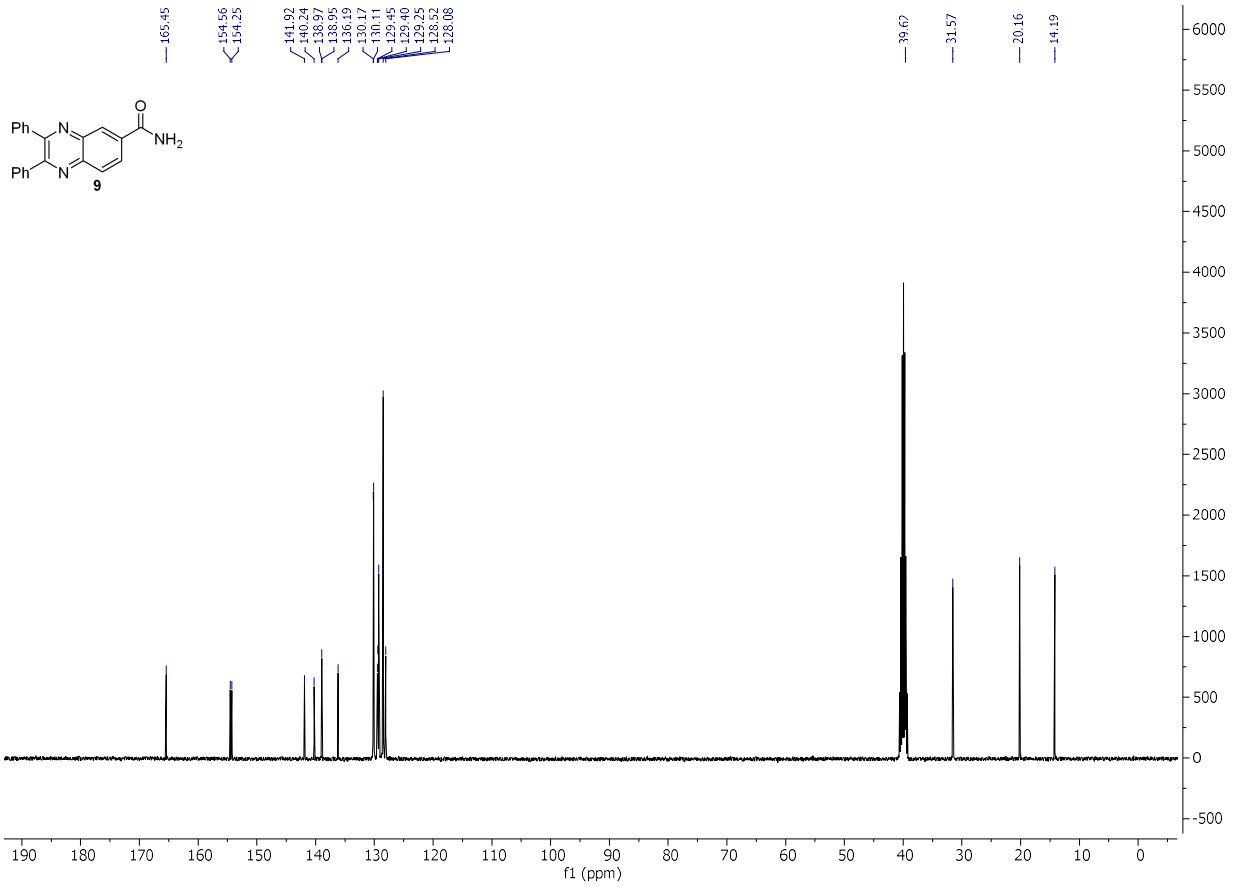
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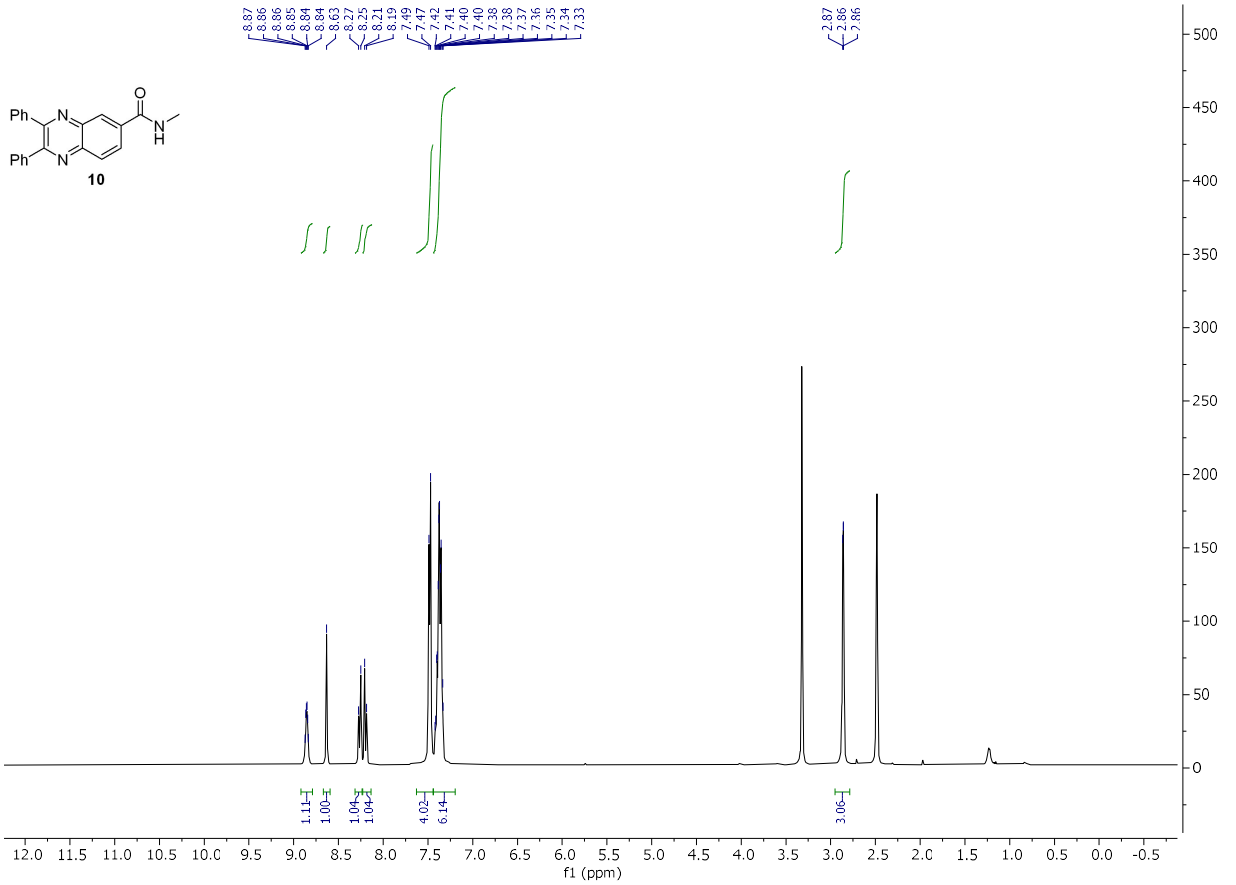
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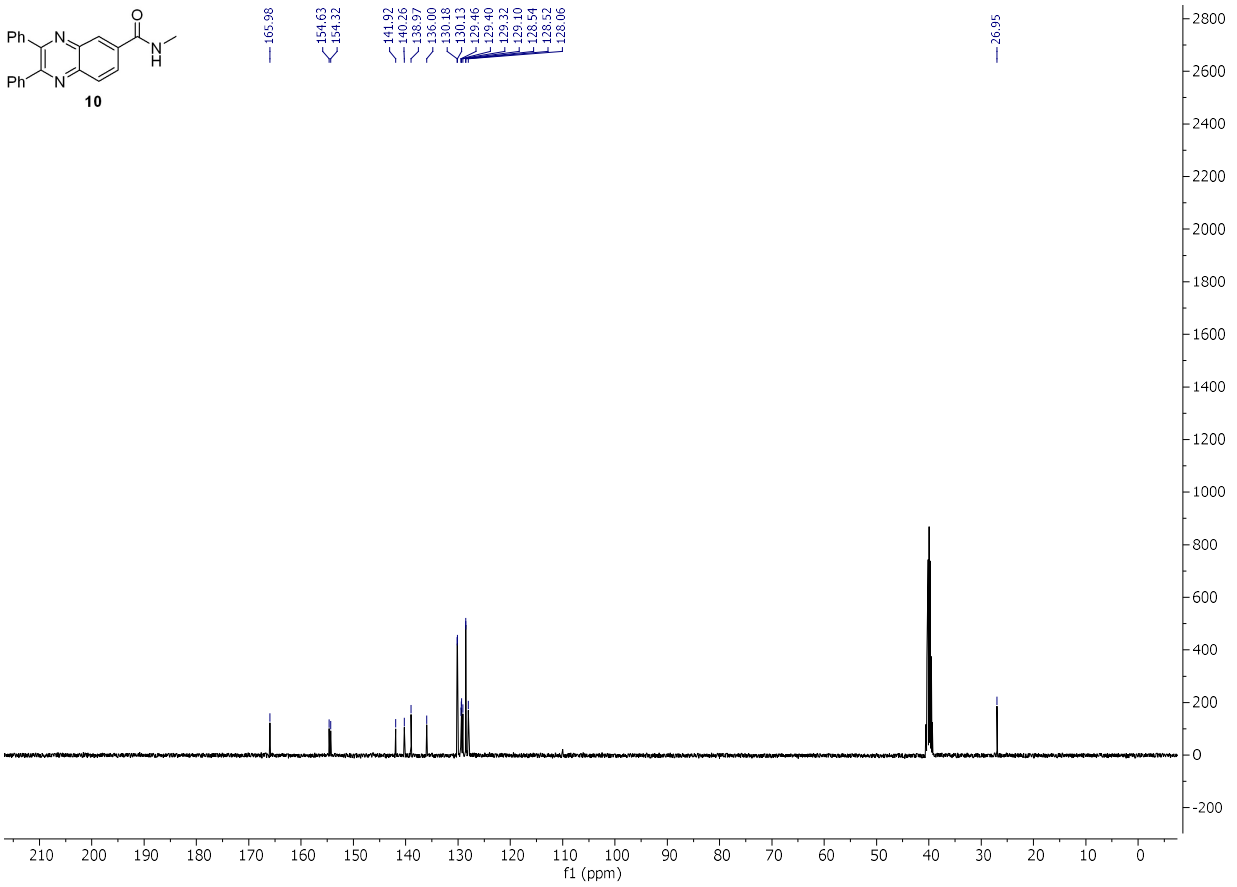
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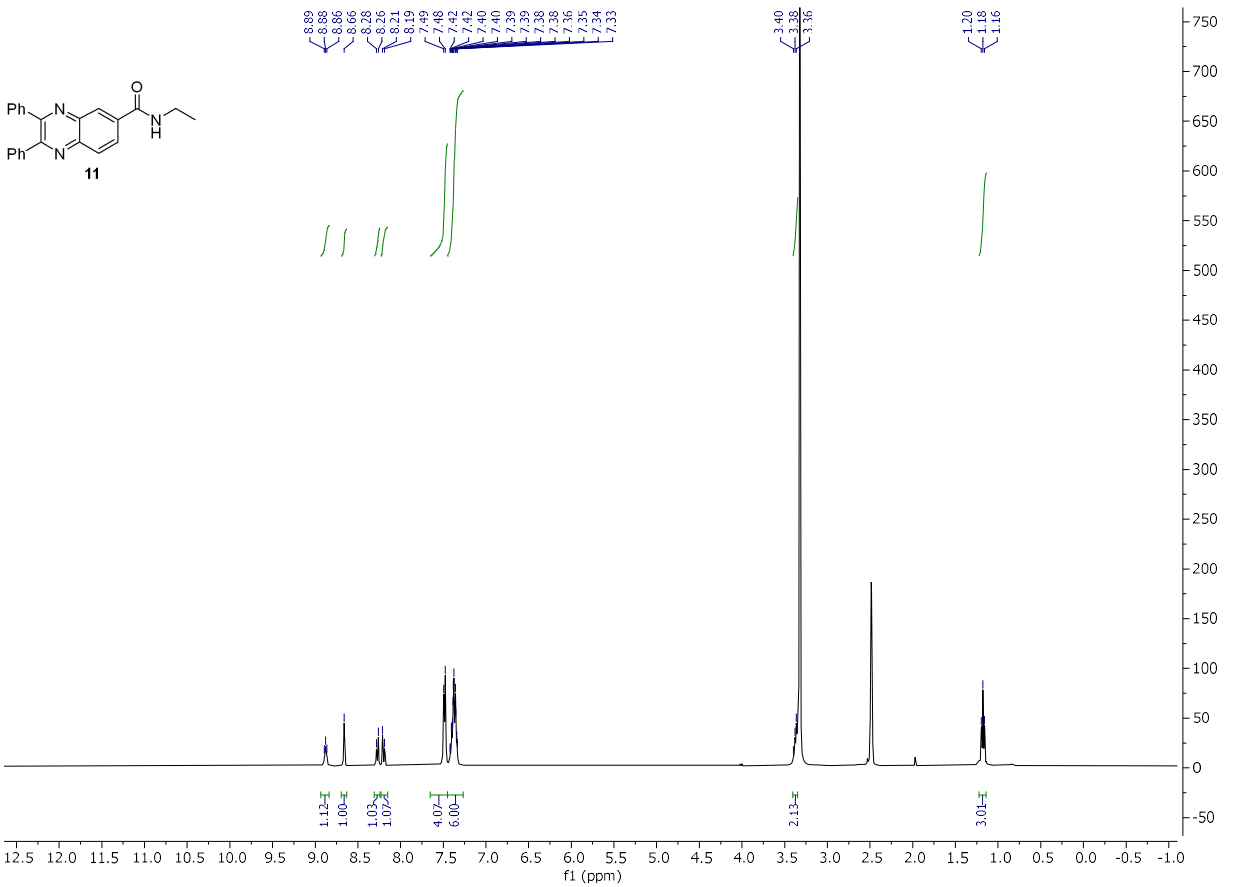
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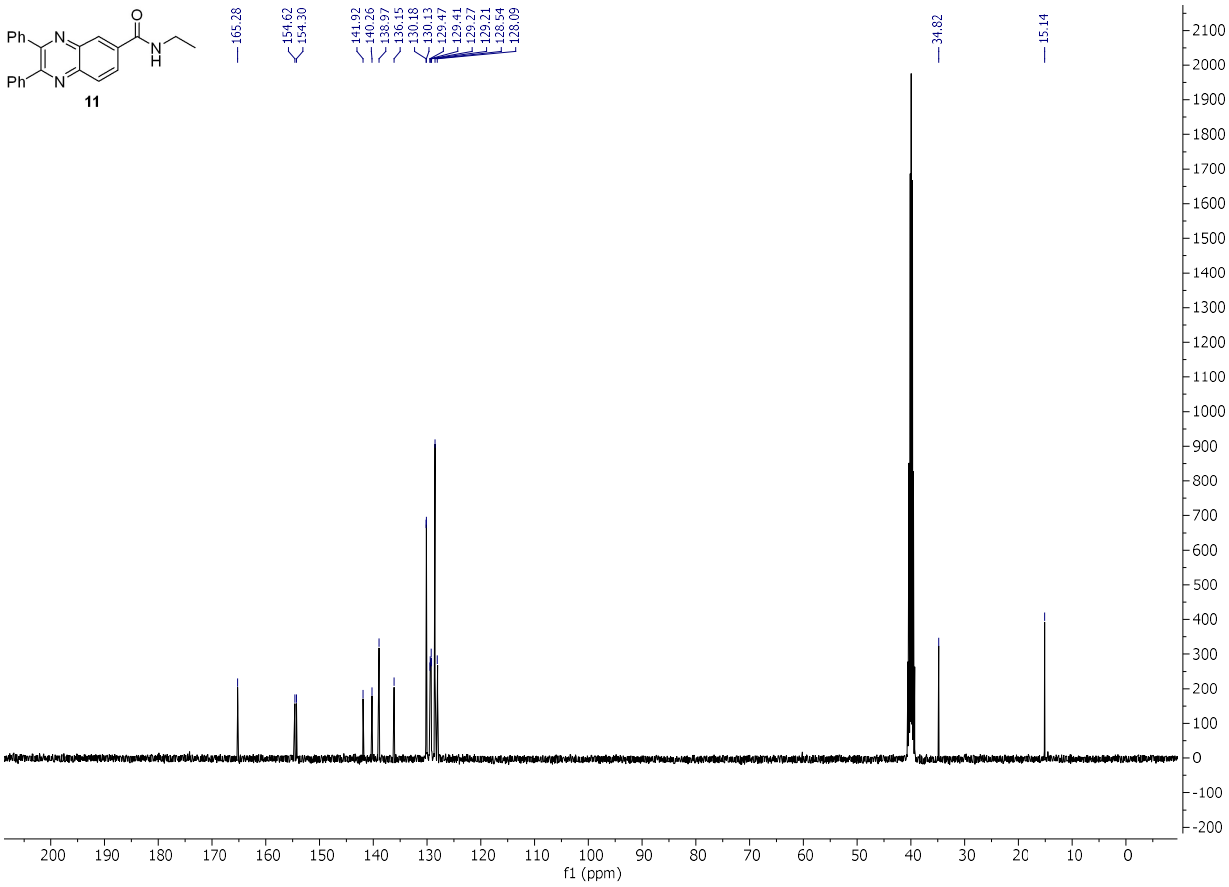
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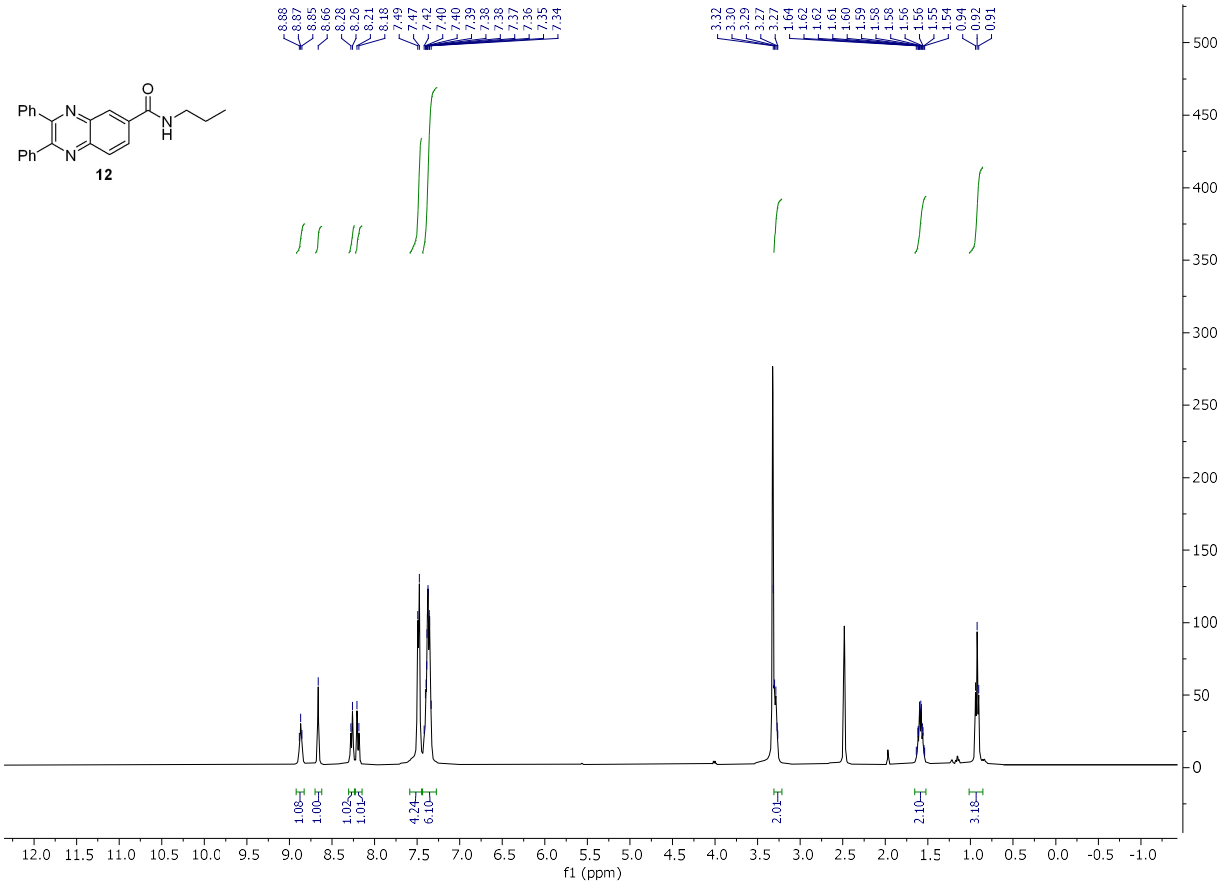
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1.62
1.61
1.60
1.59
1.58
1.58
1.56
1.56
1.55
1.54
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1.02
1.01
4.24
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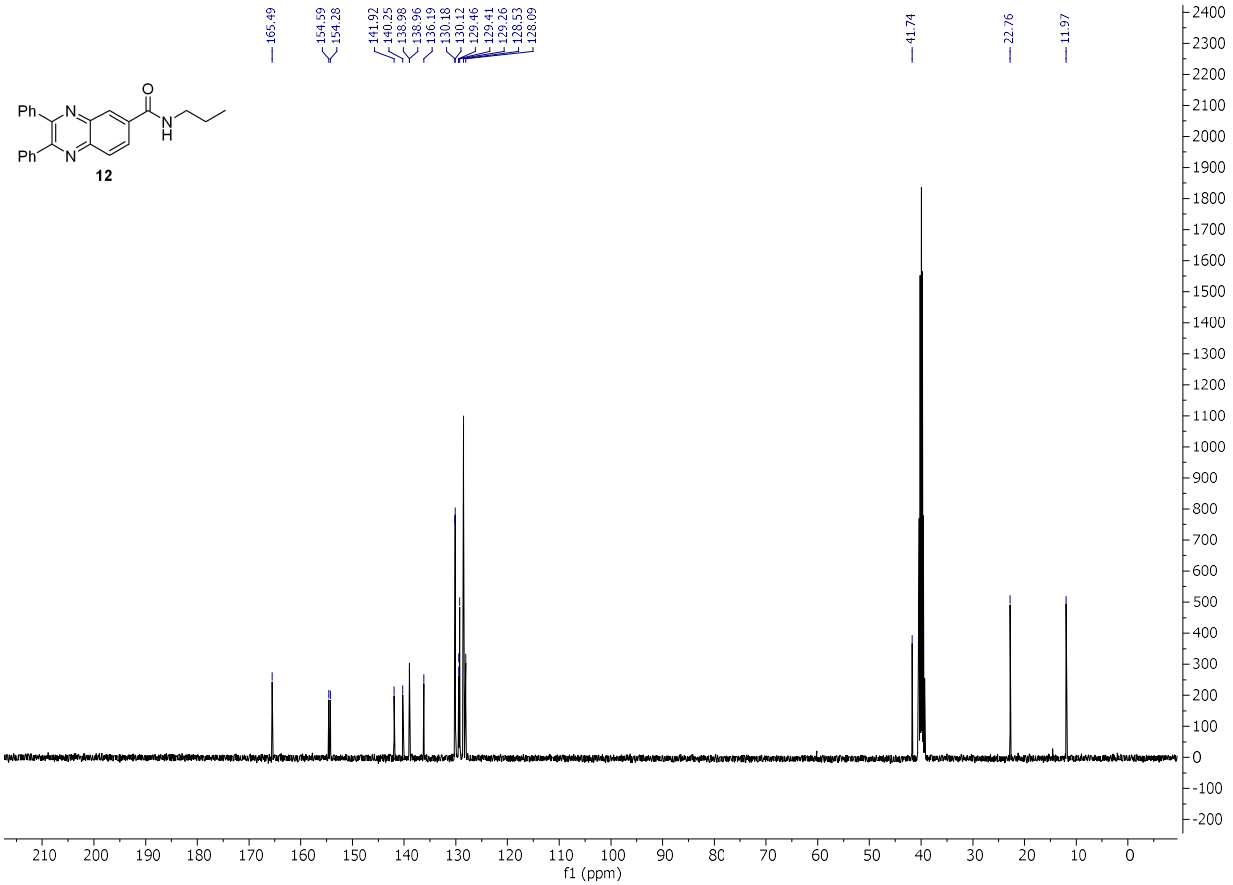
2.01
2.10
3.18
f1 (ppm)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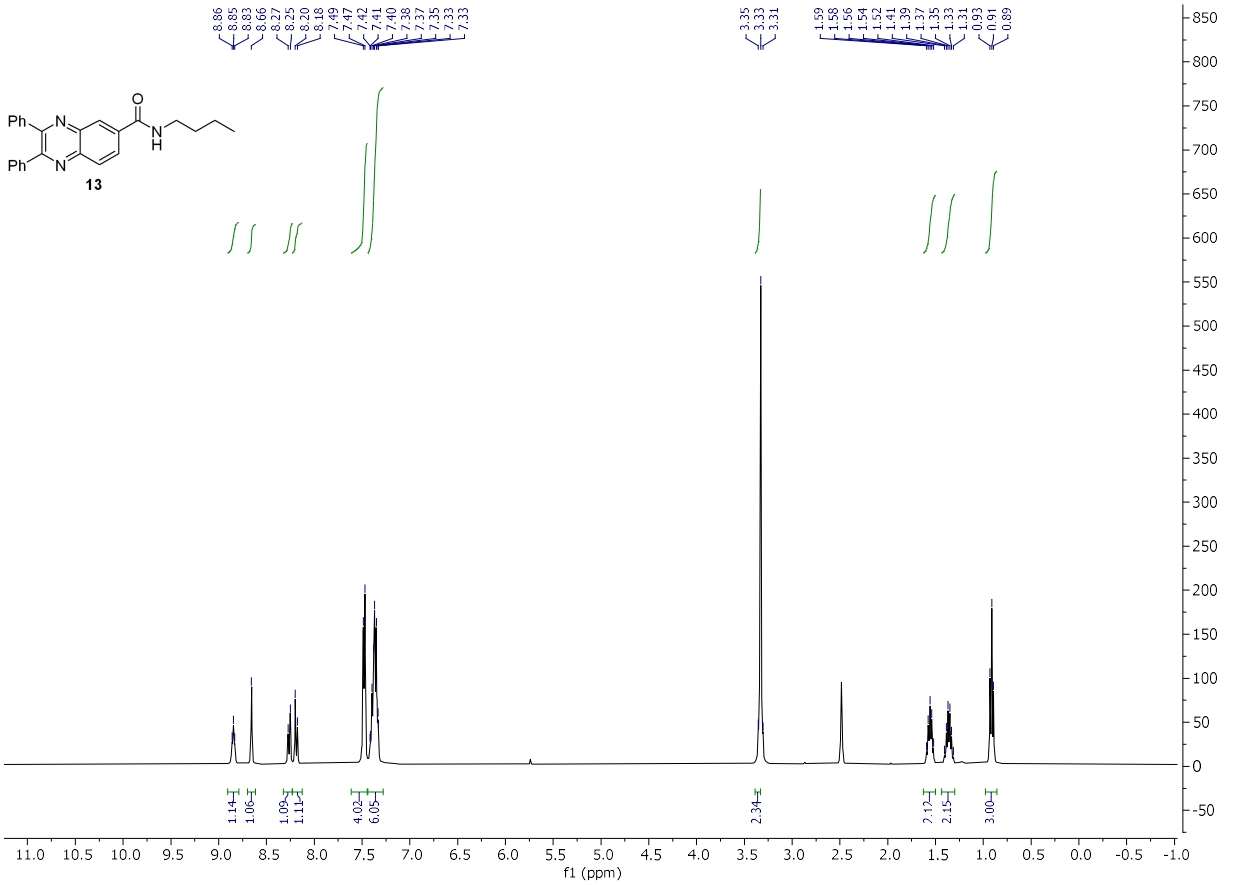
N
H
12
f1 (ppm)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7.38
7.37
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7.33
7.33
3.35
3.33
3.31
1.59
1.58
1.56
1.54
1.52
1.41
1.39
1.37
1.35
1.33
1.31
0.93
0.91
0.89
Ph
Ph
N
N
O
N
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4.02
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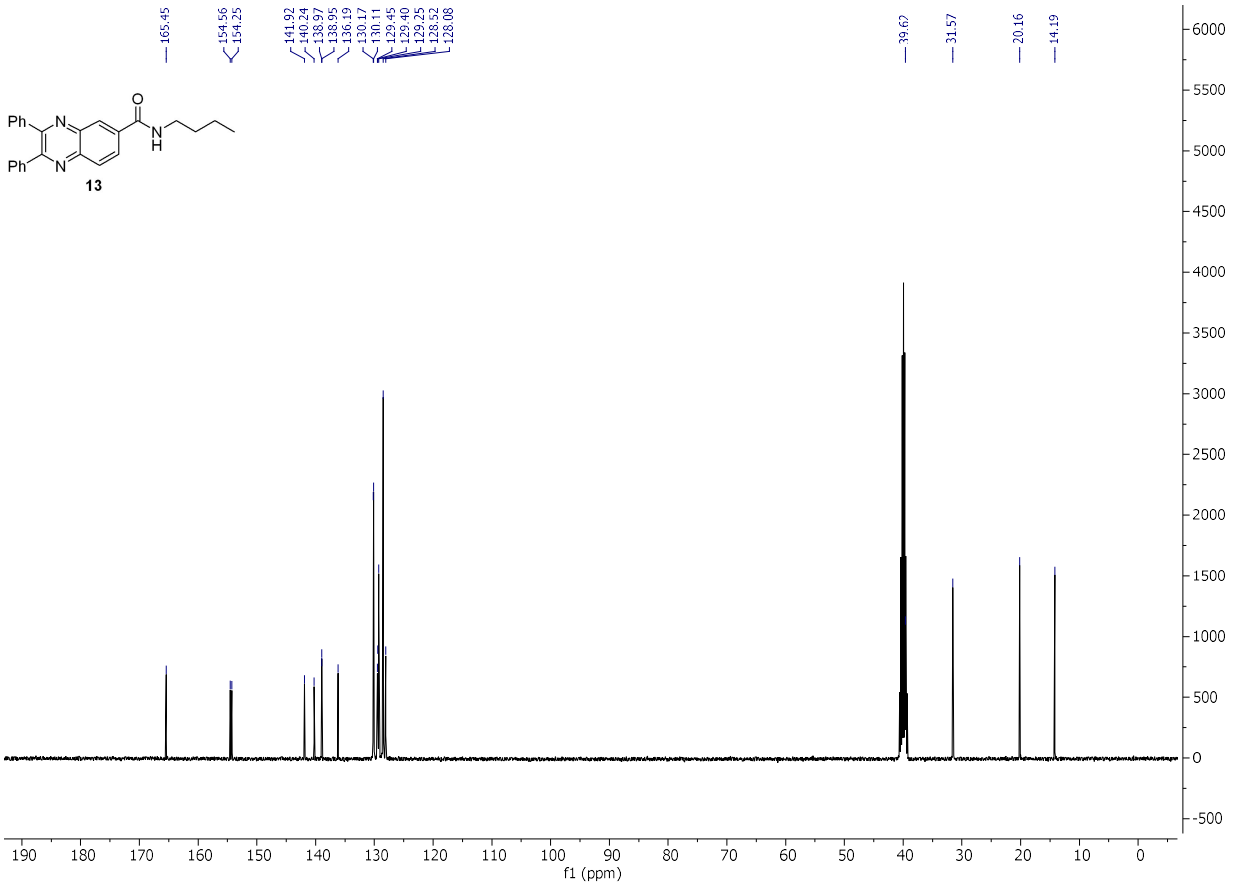
3.00
f1 (ppm)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136.19
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130.11
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129.40
129.25
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31.57
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14.19
Ph
Ph
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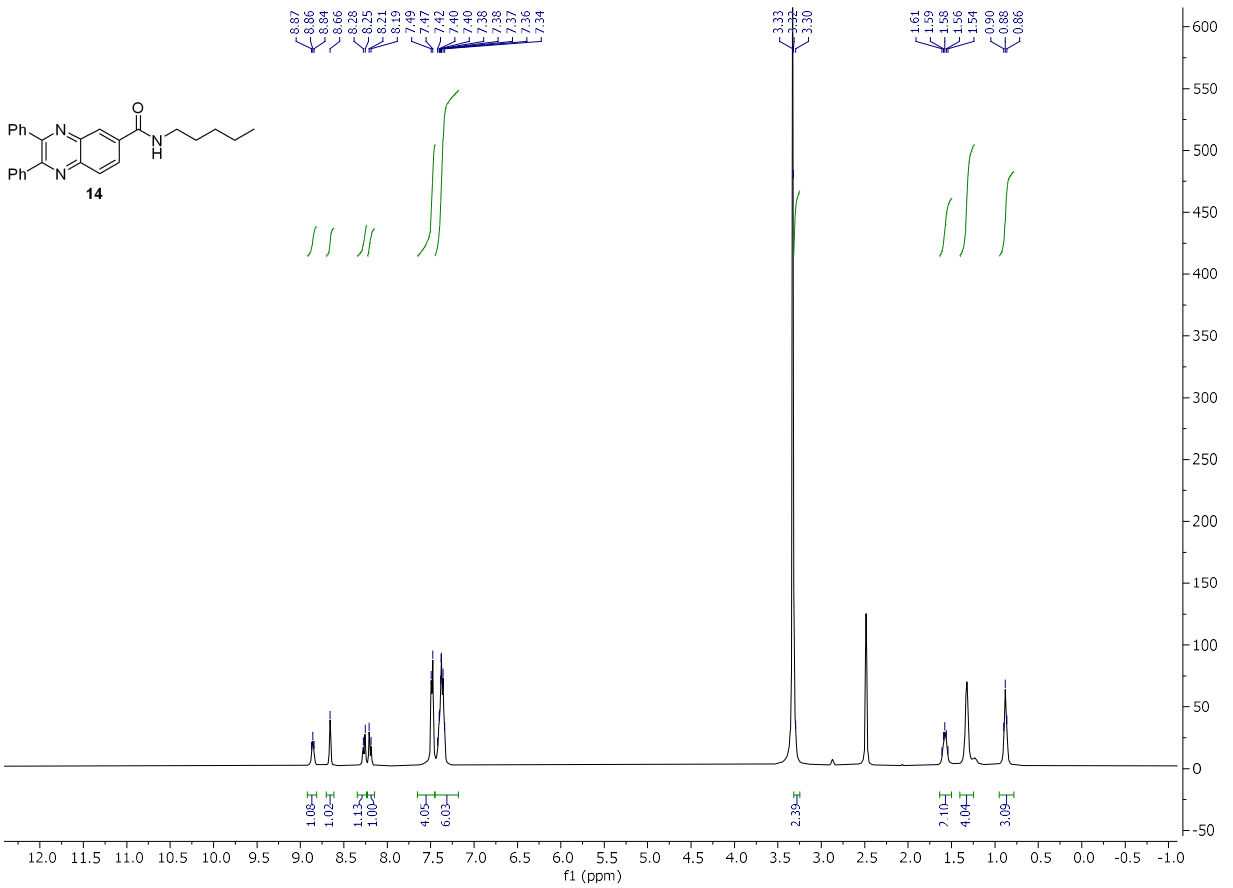
N
O
N
H
13
f1 (ppm)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7.47
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7.38
7.38
7.37
7.36
7.34
3.33
3.32
3.30
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1.59
1.58
1.56
1.54
0.90
0.88
0.86
1.08
1.02
1.13
1.00
4.05
6.03
2.39
2.10
4.04
3.09
Ph
Ph
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N
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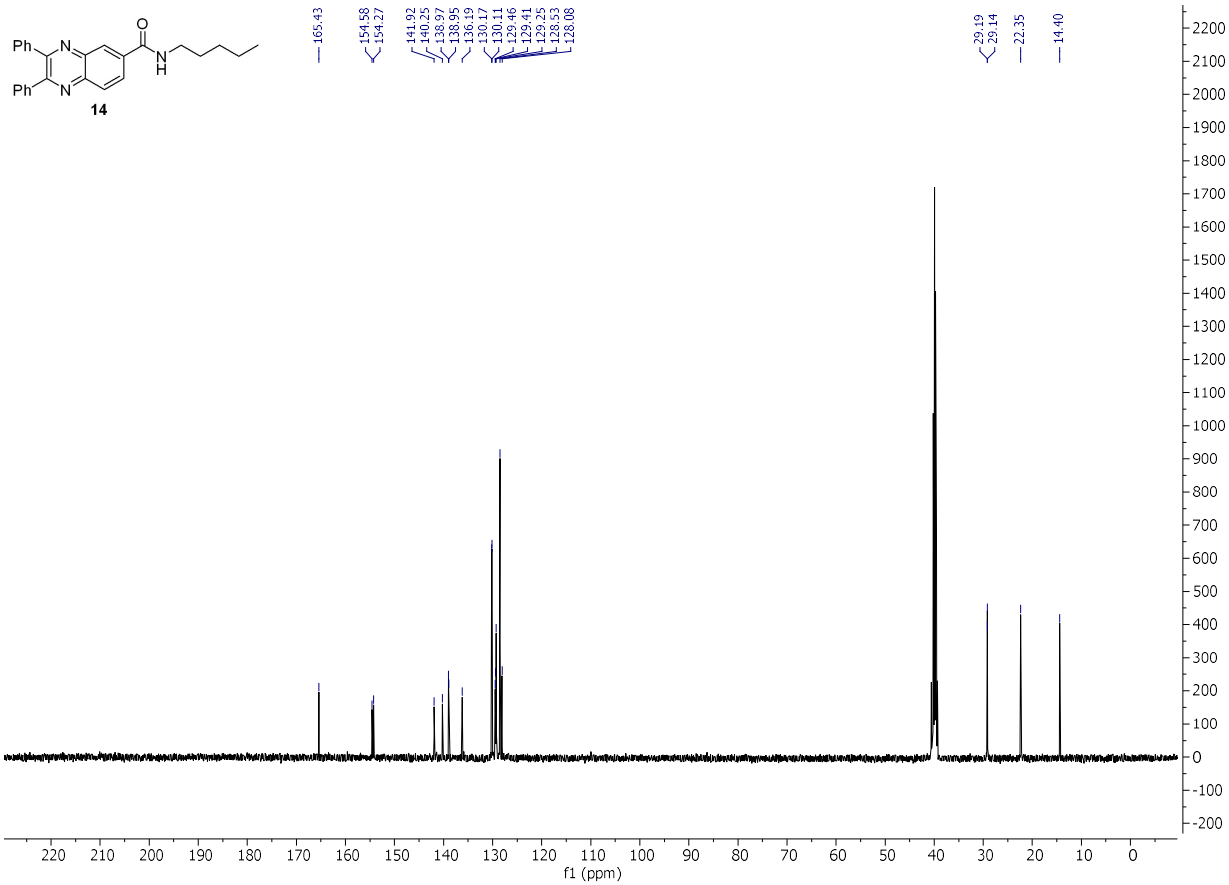
N
H
14
f1 (ppm)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138.95
136.19
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129.41
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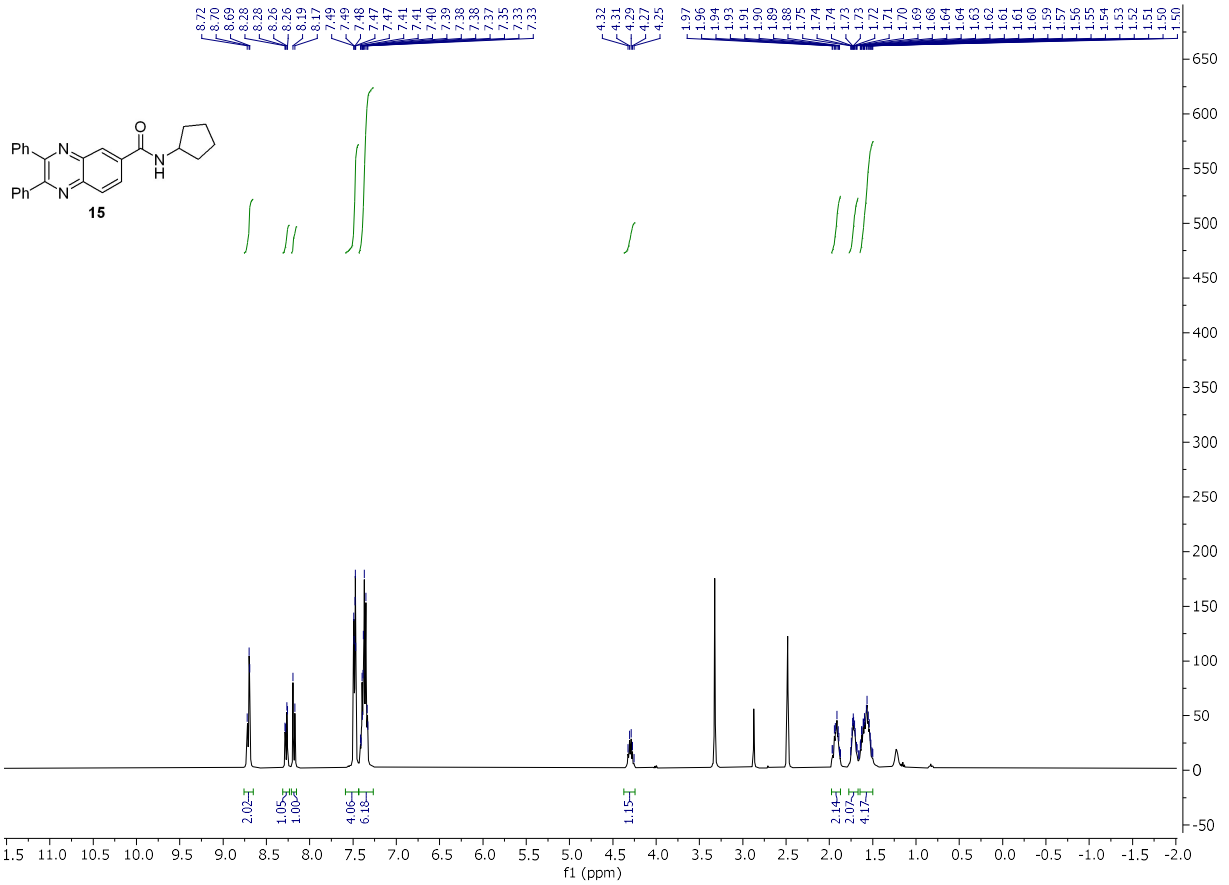
128.53
128.08
29.19
29.14
22.35
14.40
f1 (ppm)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8.28
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8.17
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7.49
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7.47
7.47
7.41
7.41
7.40
7.39
7.38
7.38
7.37
7.35
7.33
7.33
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4.31
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4.27
4.25
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1.96
1.94
1.93
1.91
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1.75
1.74
1.74
1.73
1.73
1.72
1.71
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1.69
1.68
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1.64
1.63
1.62
1.61
1.61
1.60
1.59
1.57
1.56
1.55
1.54
1.53
1.52
1.51
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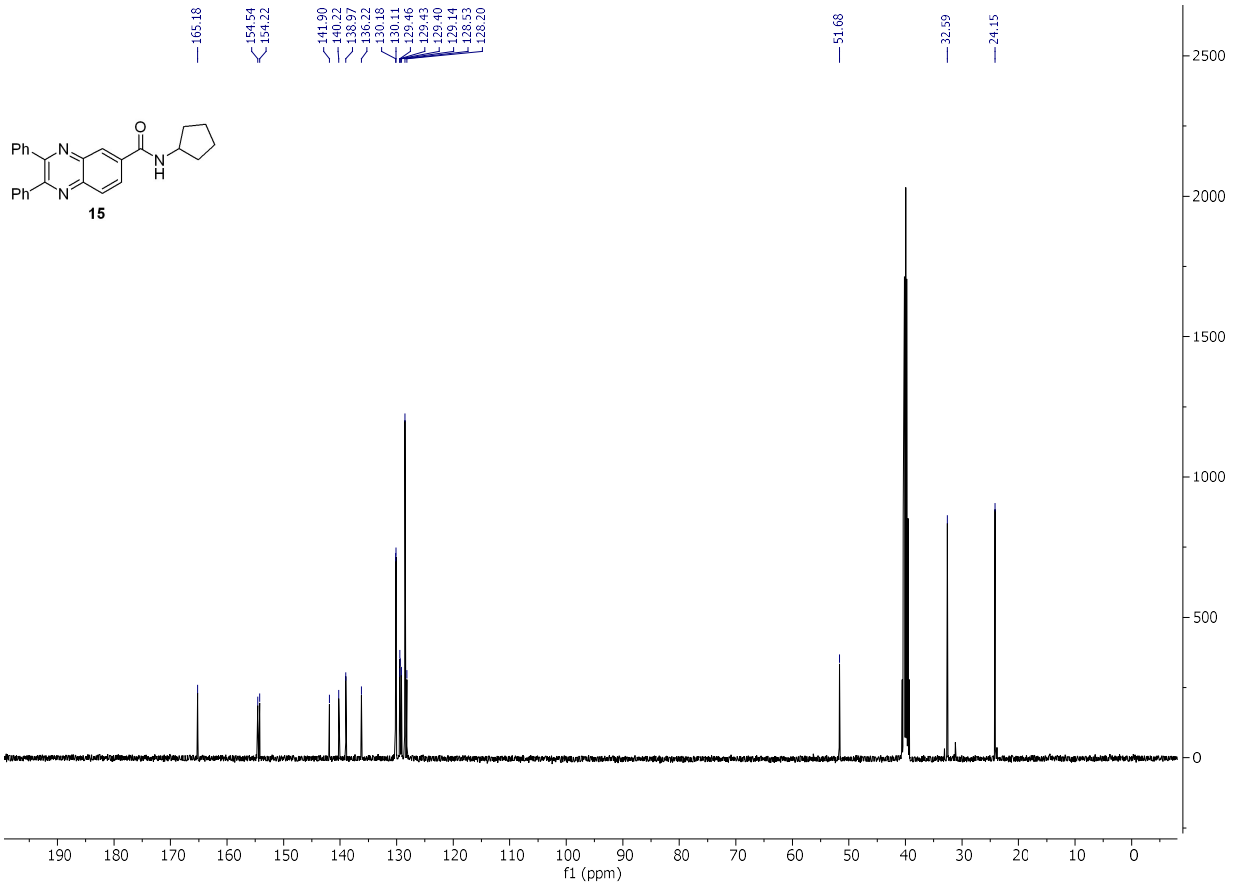
2.14
2.07
4.17
f1 (ppm)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140.22
138.97
136.22
130.18
130.11
129.46
129.43
129.40
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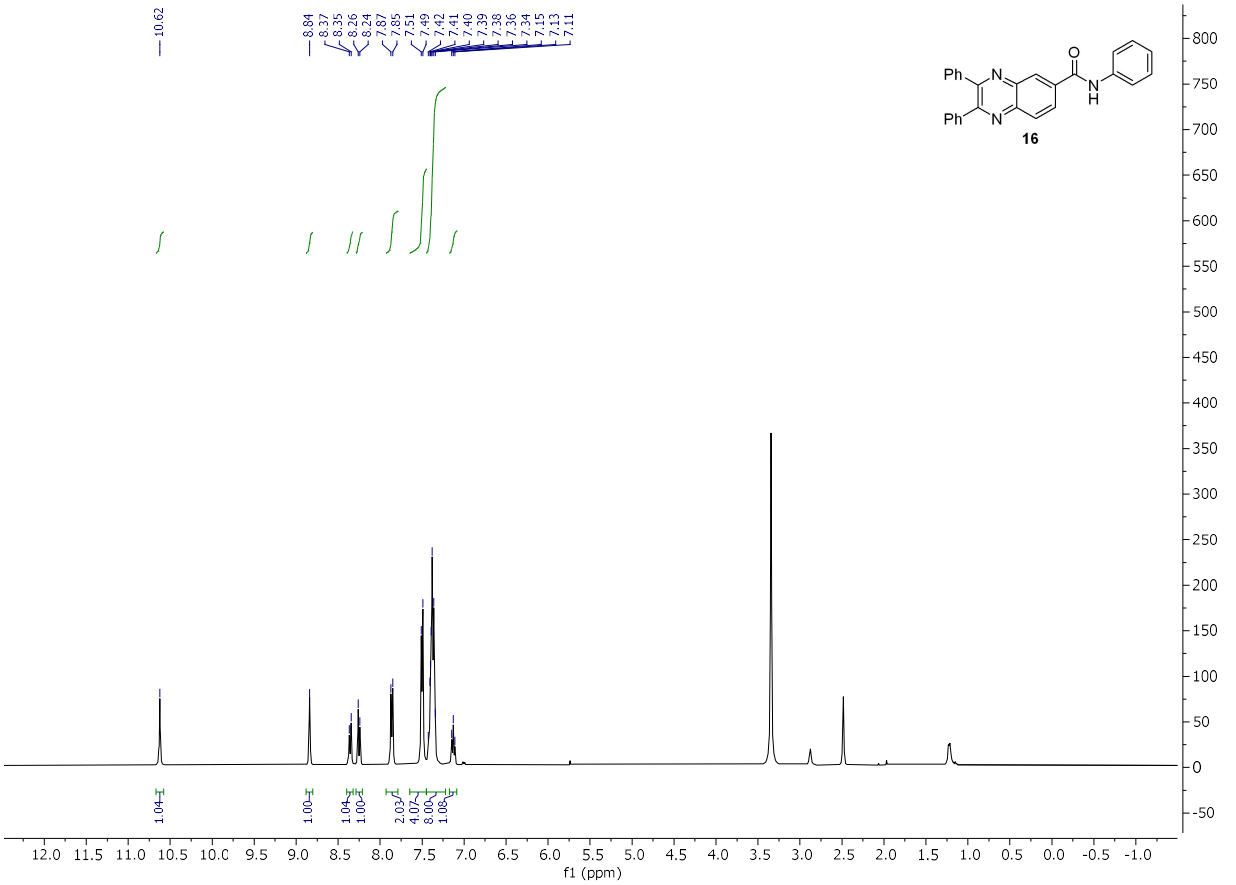
128.53
128.20
51.68
32.59
24.15
Ph
Ph
N
N
O
N
H
15
f1 (ppm)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8.84
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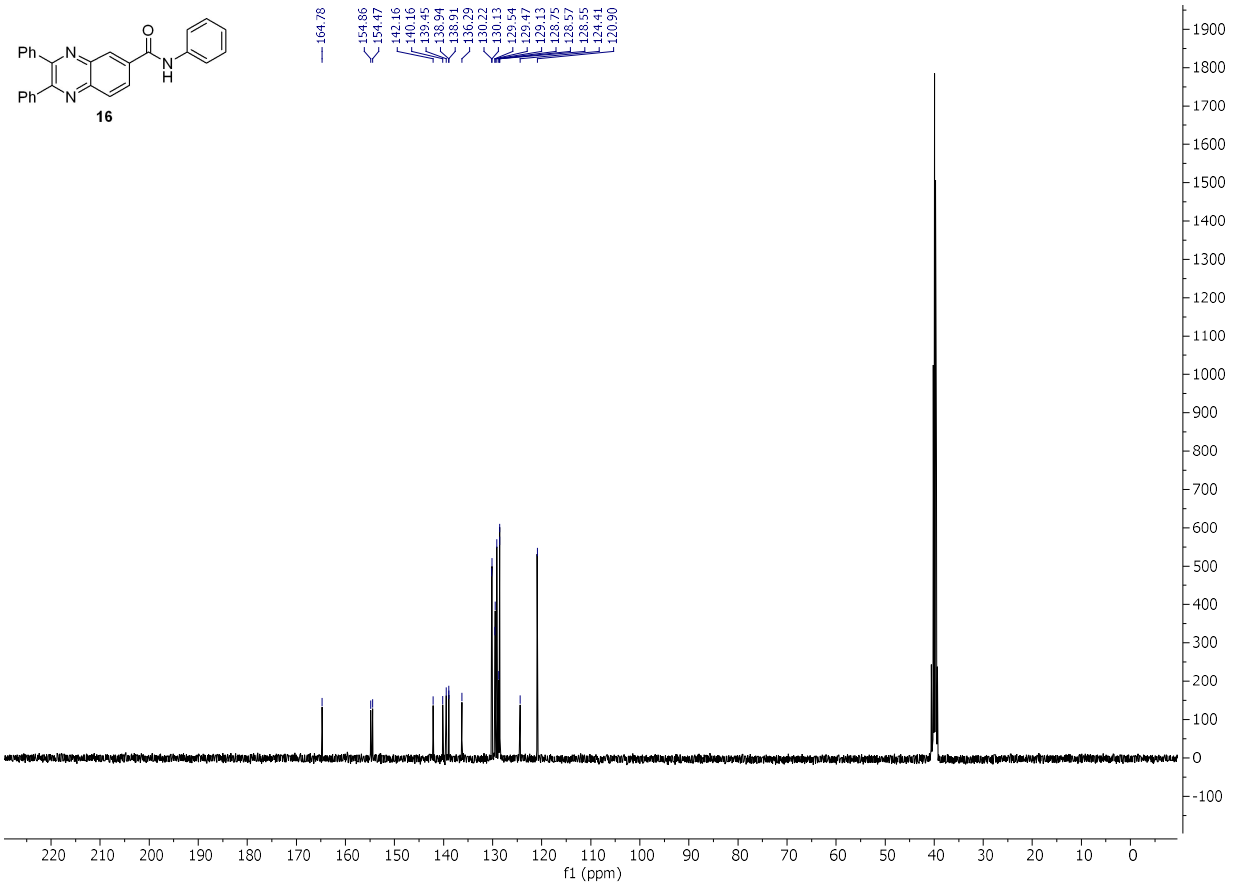
8.24
7.87
7.85
7.51
7.49
7.42
7.41
7.40
7.39
7.38
7.36
7.34
7.15
7.13
7.11
Ph
Ph
N
N
O
N
H
16
1.04
1.00
1.04
1.00
2.03
4.07
8.00
1.08
f1 (ppm)


Ph
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N
H
Ph
N
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154.47
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140.16
139.45
138.94
138.91
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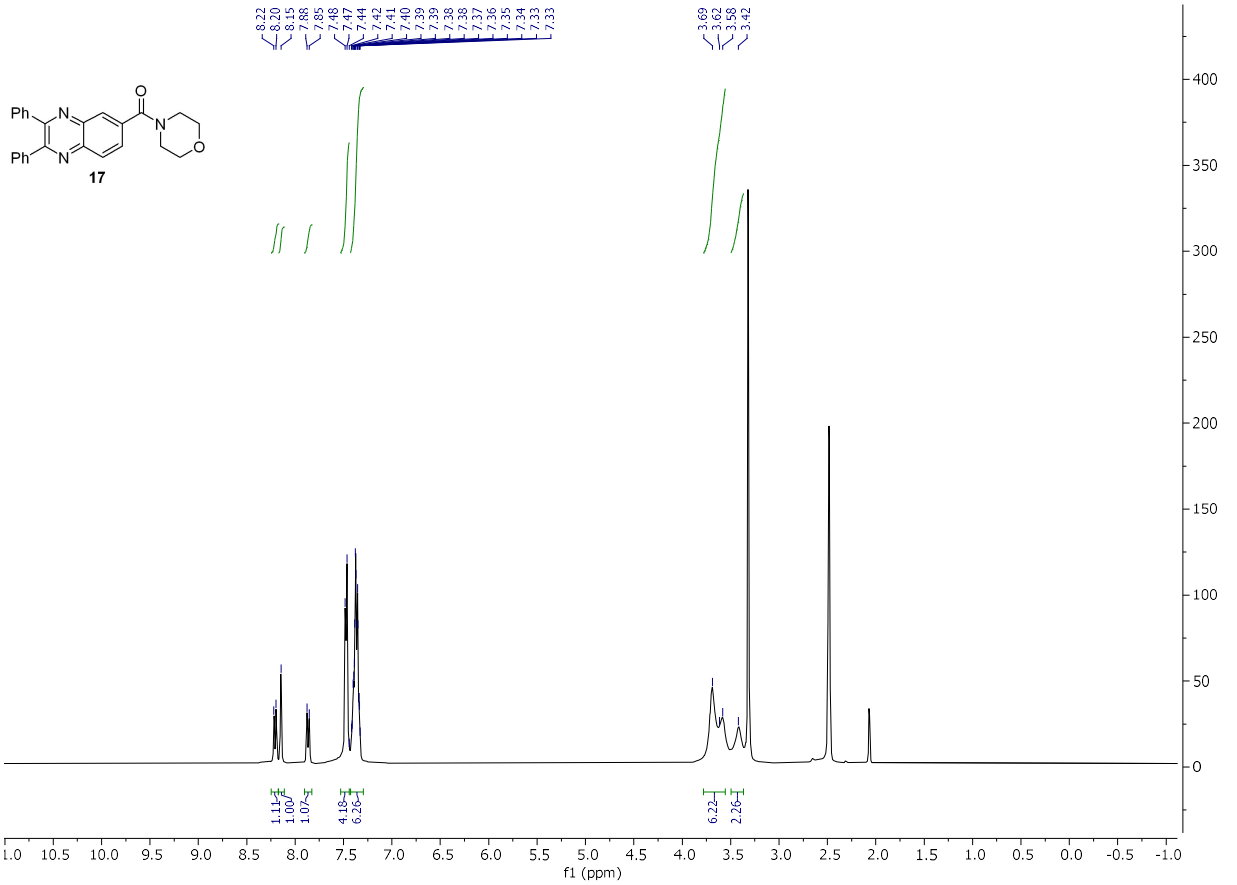
129.47
129.13
128.75
128.57
128.55
124.41
120.90
f1 (ppm)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O
N
O
Ph
N
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8.22
8.20
8.15
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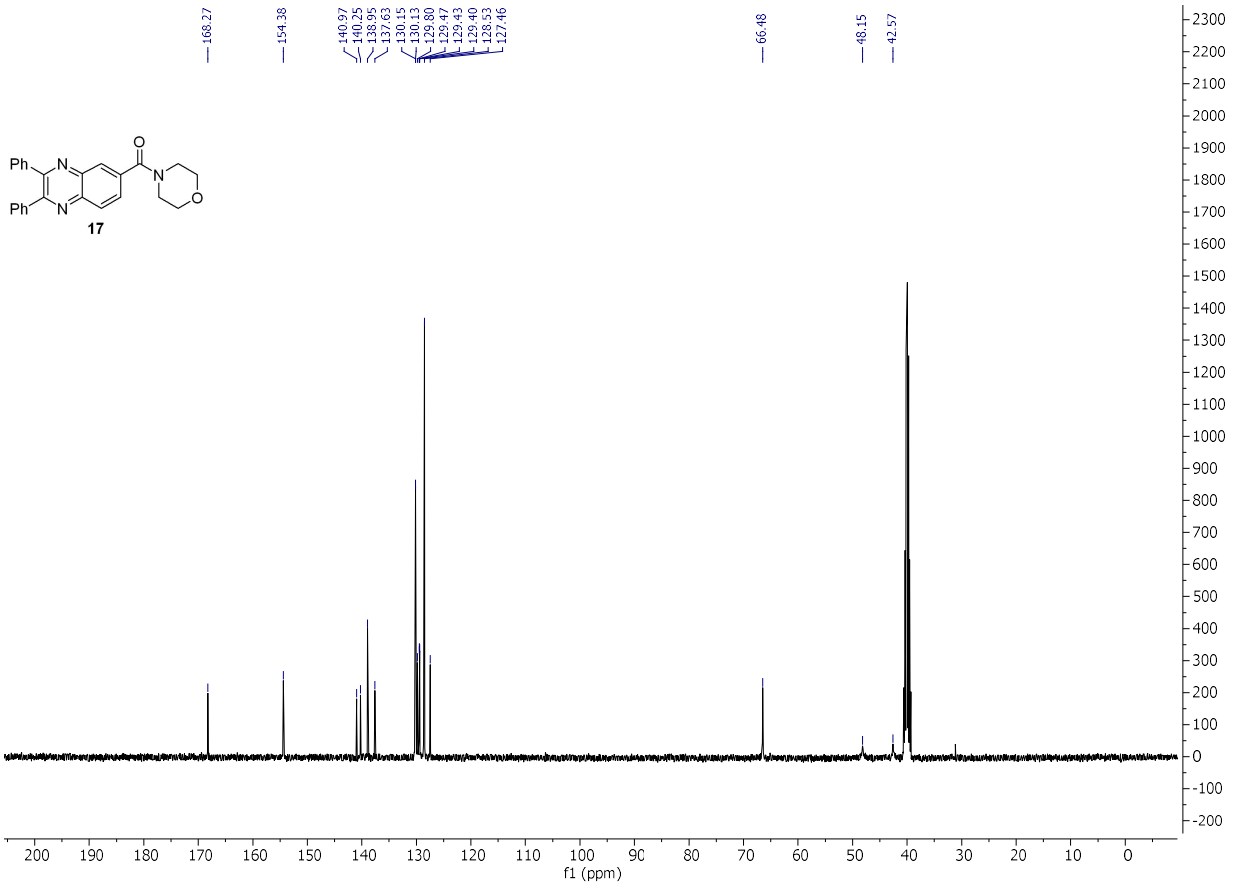
7.85
7.48
7.47
7.44
7.42
7.41
7.40
7.39
7.39
7.38
7.38
7.37
7.36
7.35
7.34
7.33
7.33
3.69
3.62
3.58
3.42
1.11
1.00
1.07
4.18
6.26
6.22
2.26
f1 (ppm)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130.15
130.13
129.80
129.47
129.43
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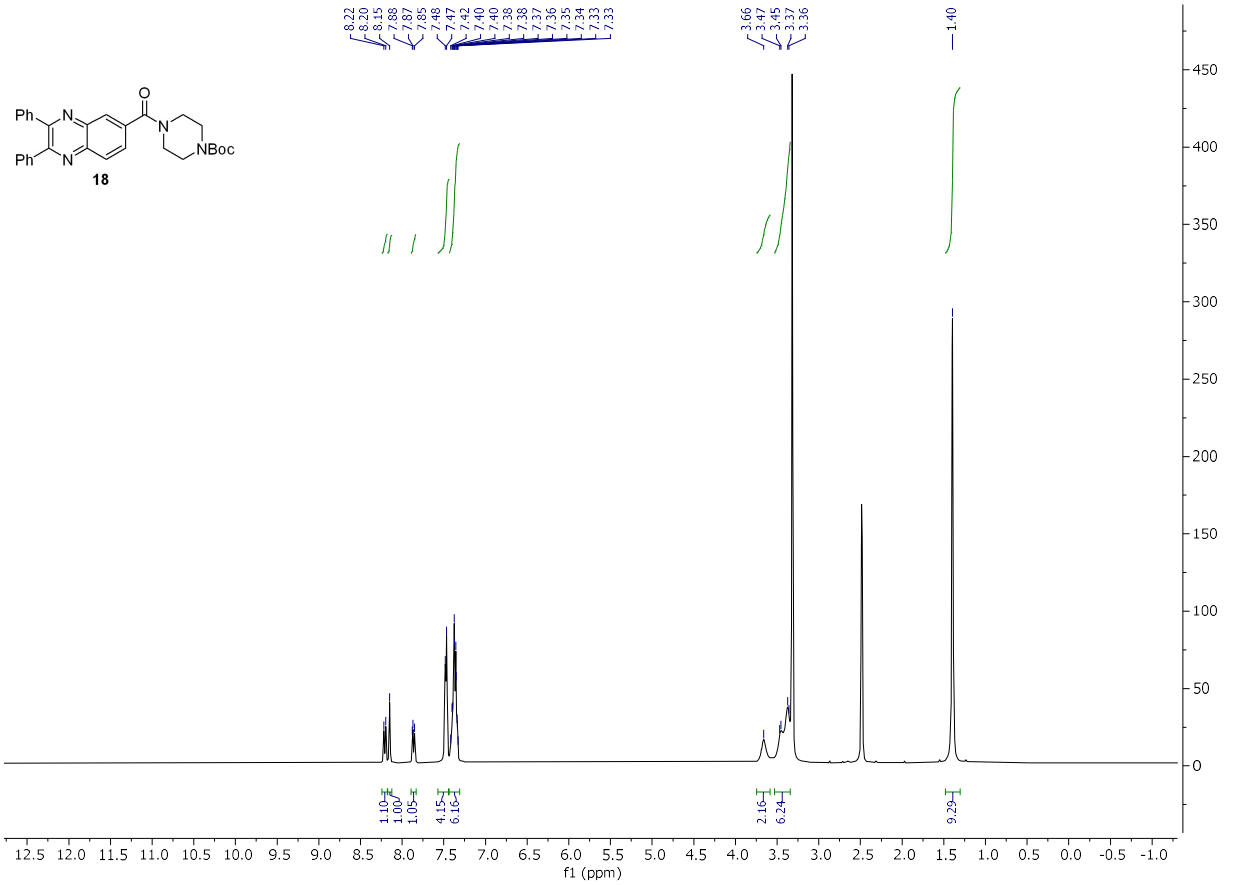
128.53
127.46
66.48
48.15
42.57
Ph
Ph
N
N
O
N
O
17
f1 (ppm)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7.85
7.48
7.47
7.42
7.40
7.40
7.38
7.38
7.37
7.36
7.35
7.34
7.33
7.33
3.66
3.47
3.45
3.37
3.36
1.40
Ph
Ph
N
N
O
N
NBoc
18
1.10
1.00
1.05
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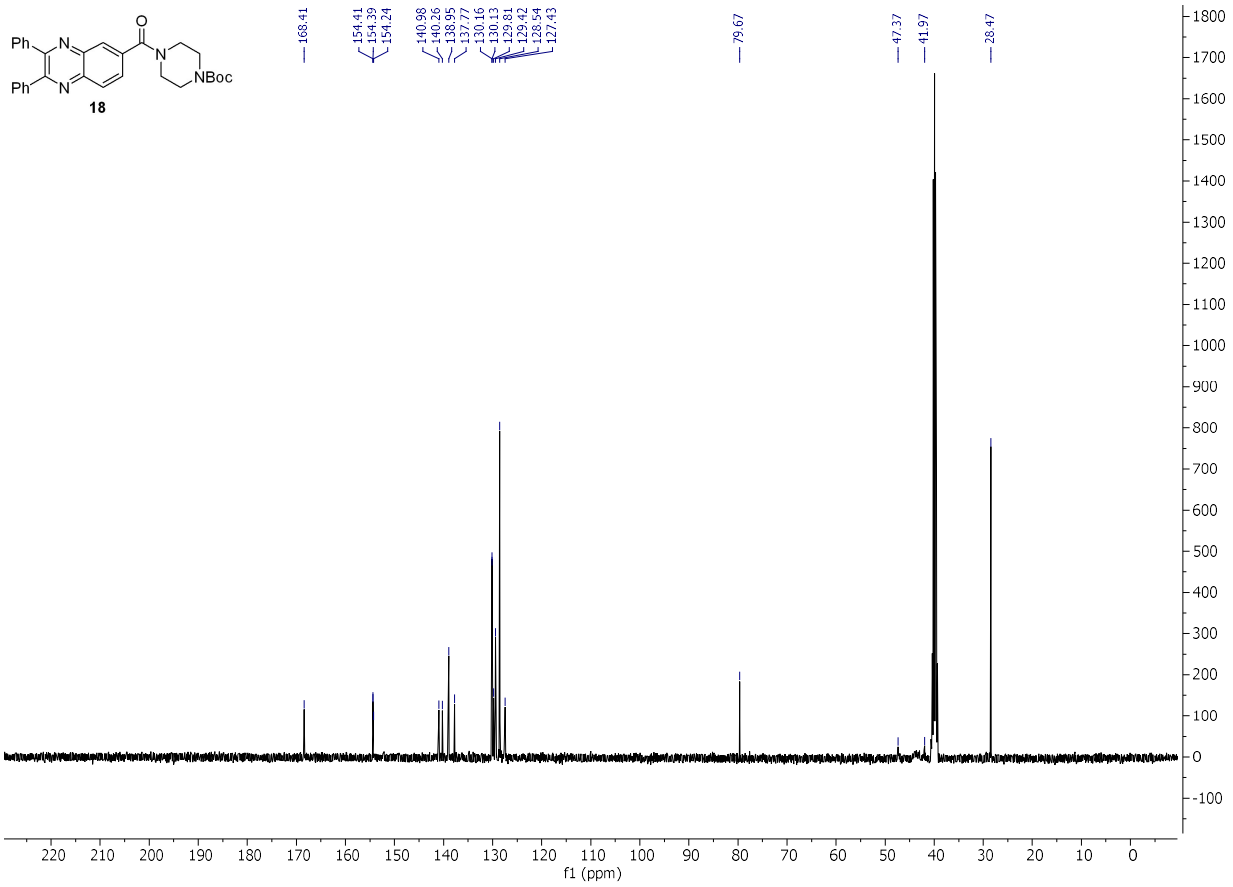
2.16
6.24
9.29
f1 (ppm)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129.42
128.54
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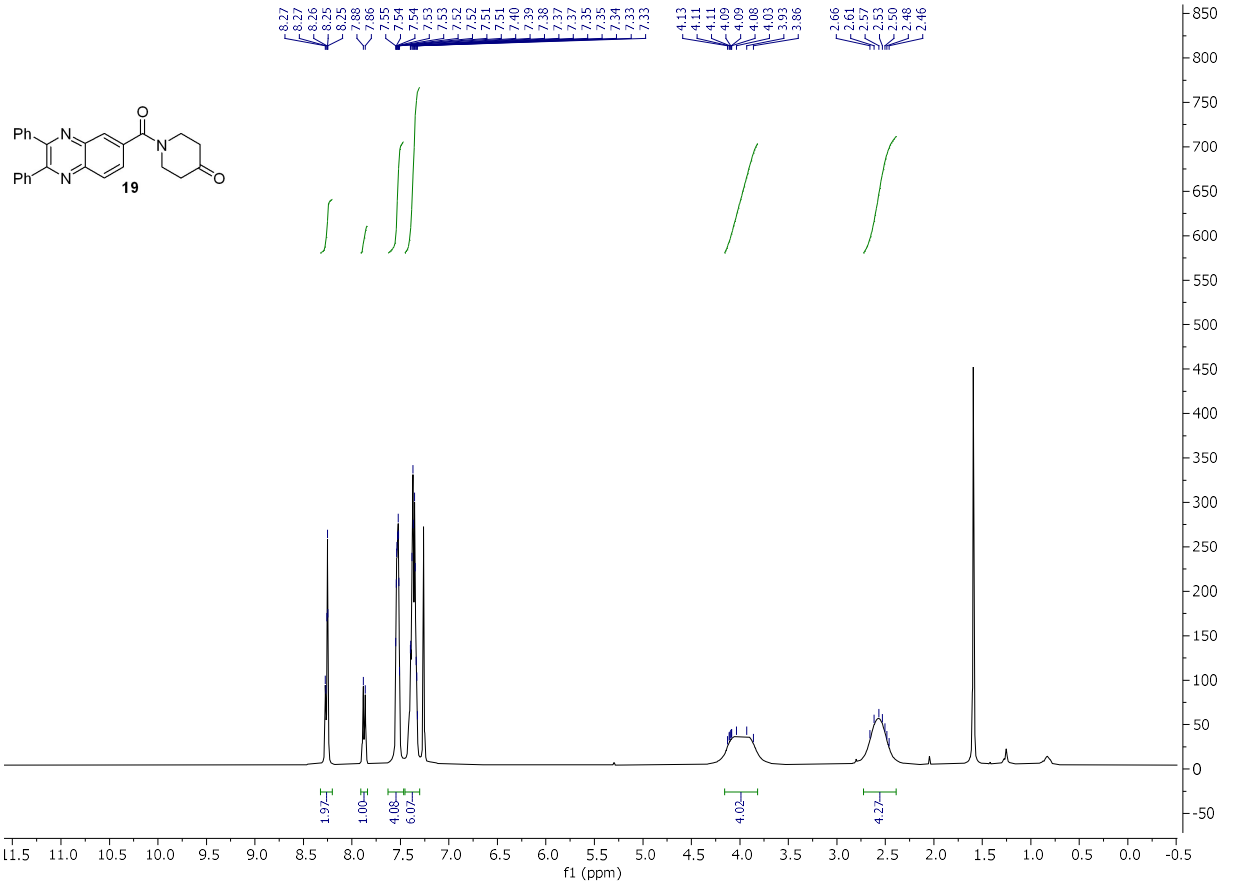
79.67
47.37
41.97
28.47
f1 (ppm)


19
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7.55
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7.53
7.52
7.52
7.51
7.51
7.40
7.39
7.38
7.37
7.37
7.35
7.35
7.34
7.33
7.33
4.13
4.11
4.11
4.09
4.09
4.08
4.03
3.93
3.86
2.66
2.61
2.57
2.53
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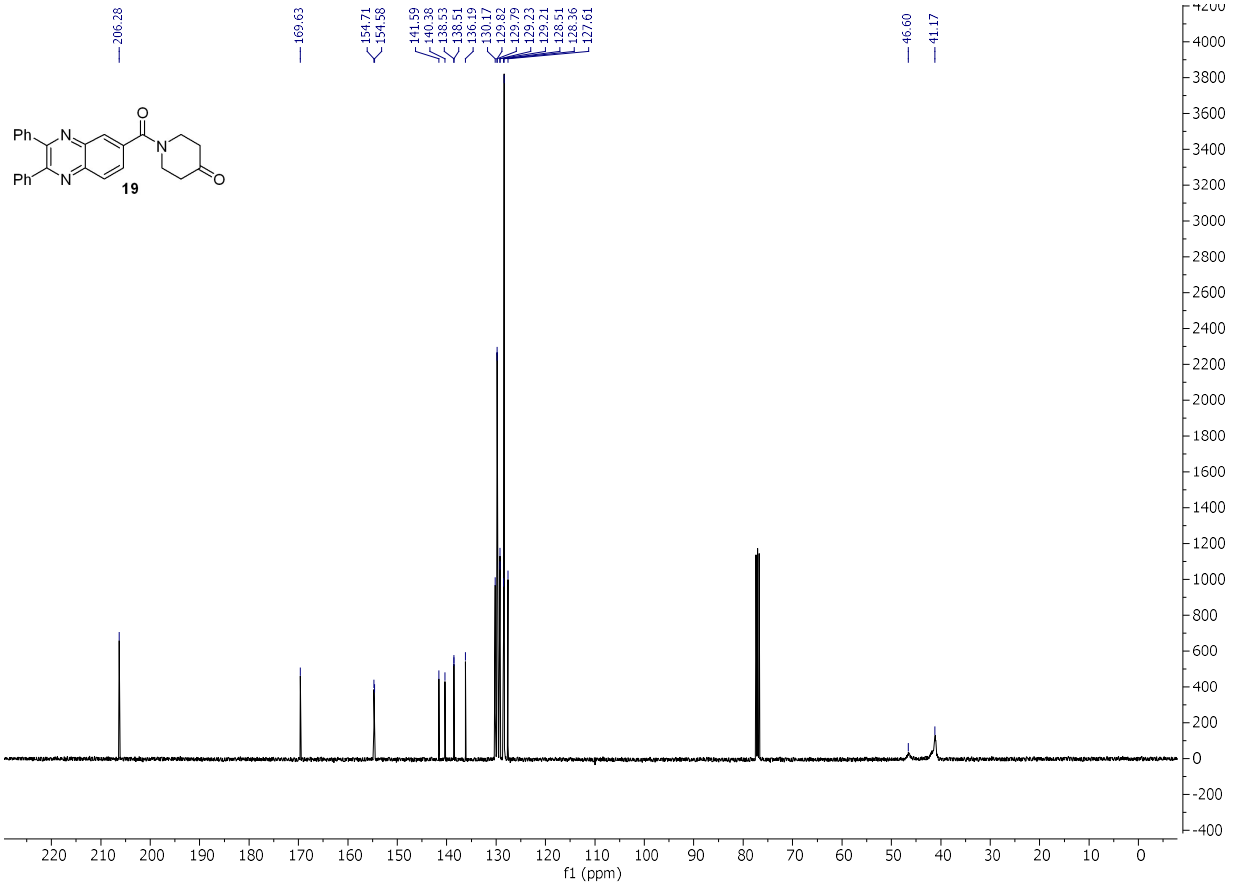
2.48
2.46
1.97
1.00
4.08
6.07
4.02
4.27
f1 (ppm)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130.17
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129.79
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128.36
127.61
46.60
41.17
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Ph
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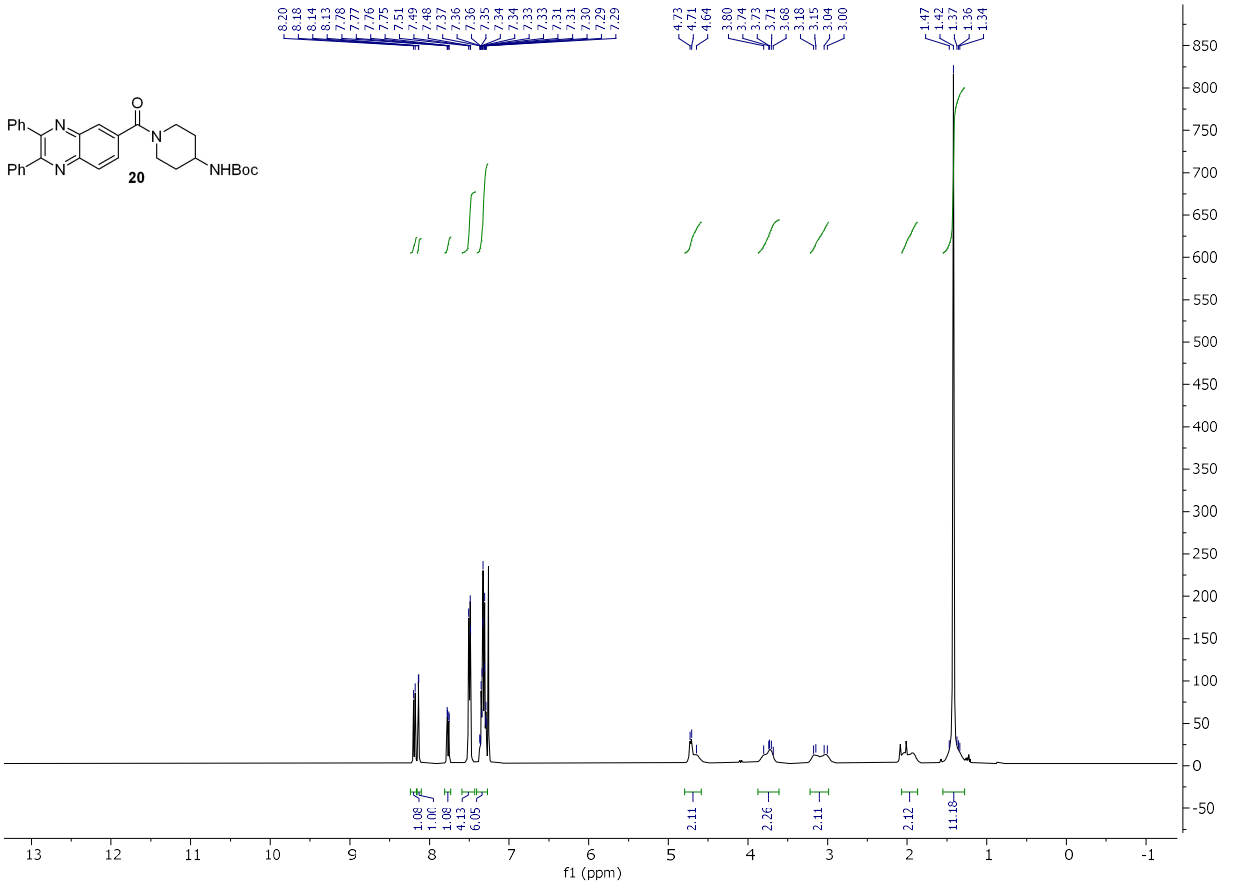
N
O
O
19
f1 (ppm)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7.37
7.36
7.36
7.35
7.34
7.34
7.33
7.33
7.31
7.31
7.30
7.29
7.29
4.73
4.71
4.64
3.80
3.74
3.73
3.71
3.68
3.18
3.15
3.04
3.00
1.47
1.42
1.37
1.36
1.34
Ph
Ph
N
N
O
N
NHBoc
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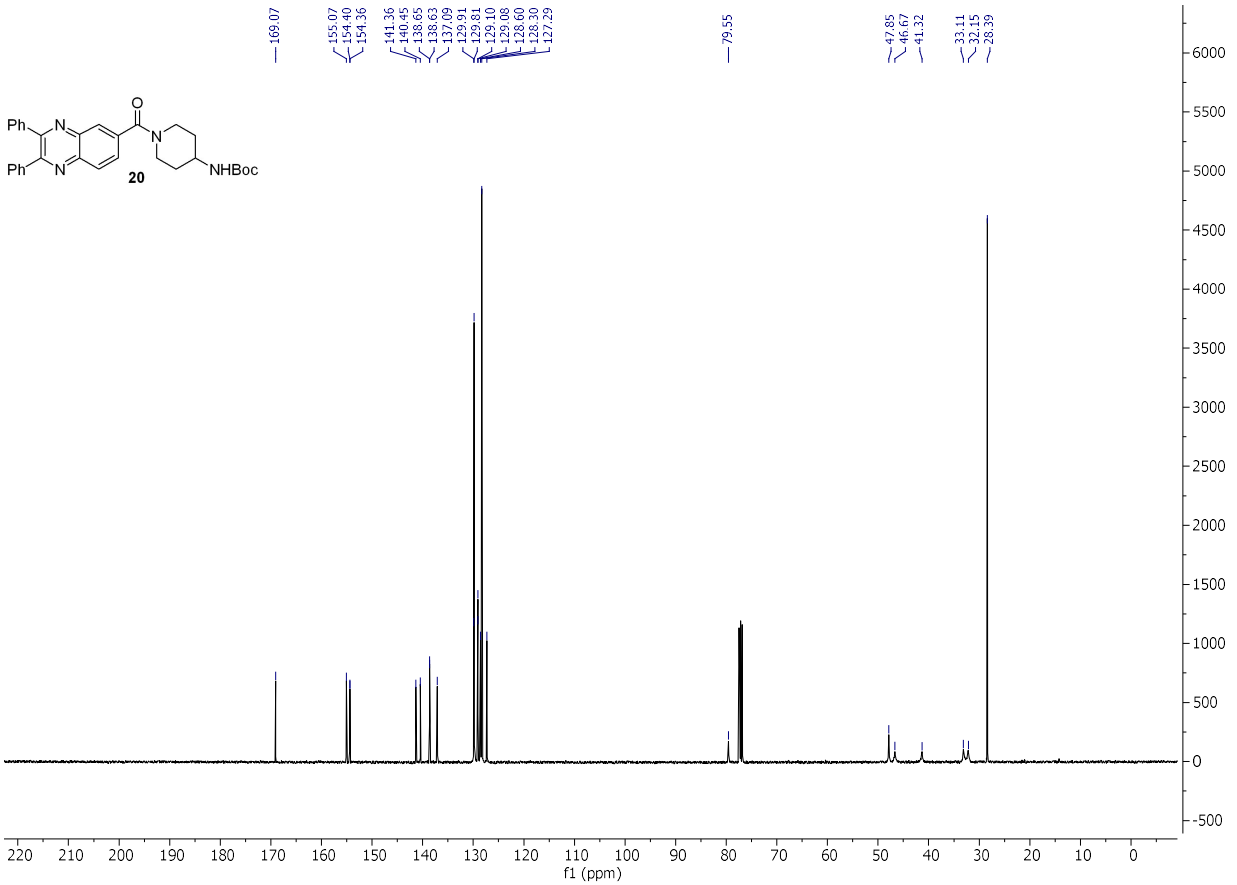
2.11
2.26
2.11
2.12
11.18
f1 (ppm)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129.81
129.10
129.08
128.60
128.30
127.29
79.55
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46.67
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33.11
32.15
28.39
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Ph
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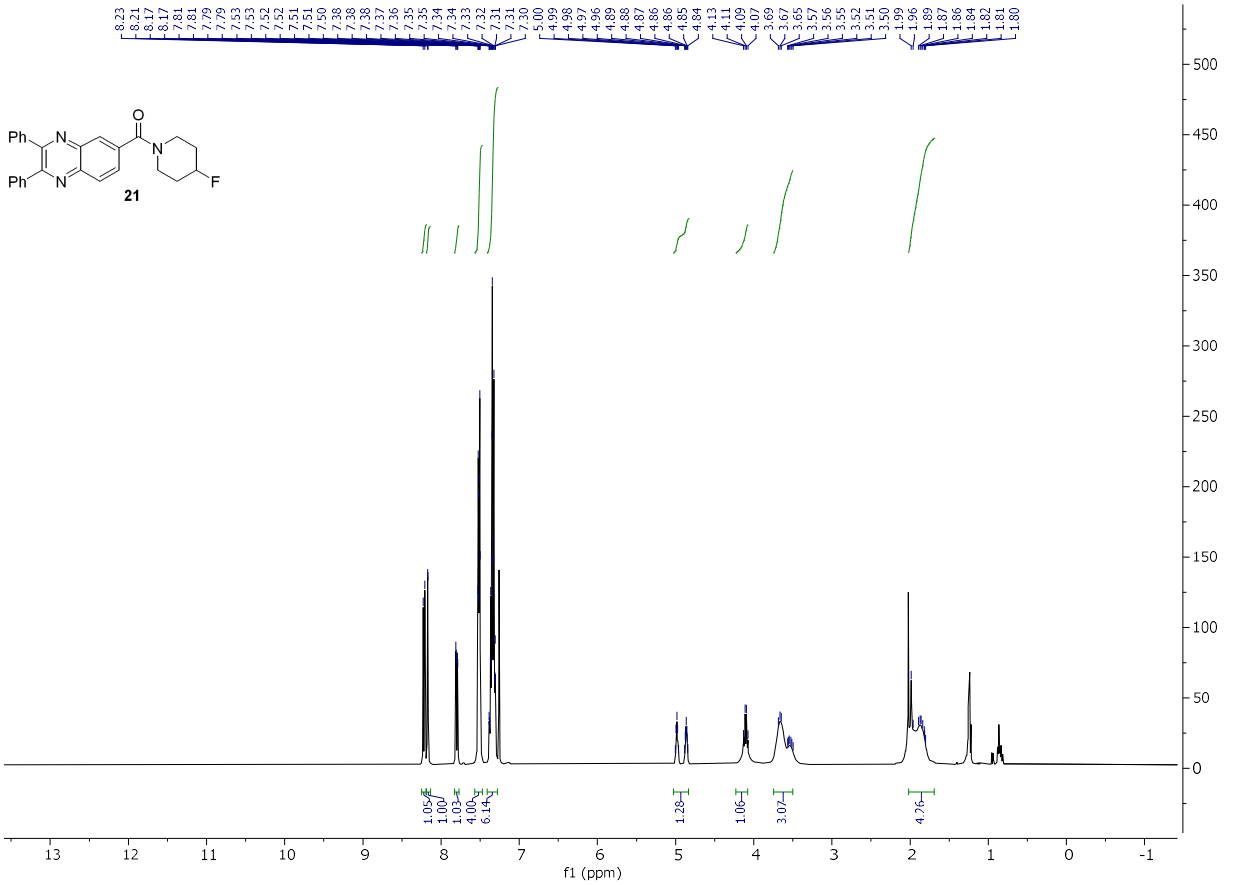
N
O
N
NHBoc
20
f1 (ppm)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7.52
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7.30
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4.97
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4.87
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4.85
4.84
4.13
4.11
4.09
4.07
3.69
3.67
3.65
3.57
3.56
3.55
3.52
3.51
3.50
1.99
1.96
1.89
1.87
1.86
1.84
1.82
1.81
1.80
Ph
Ph
N
N
O
N
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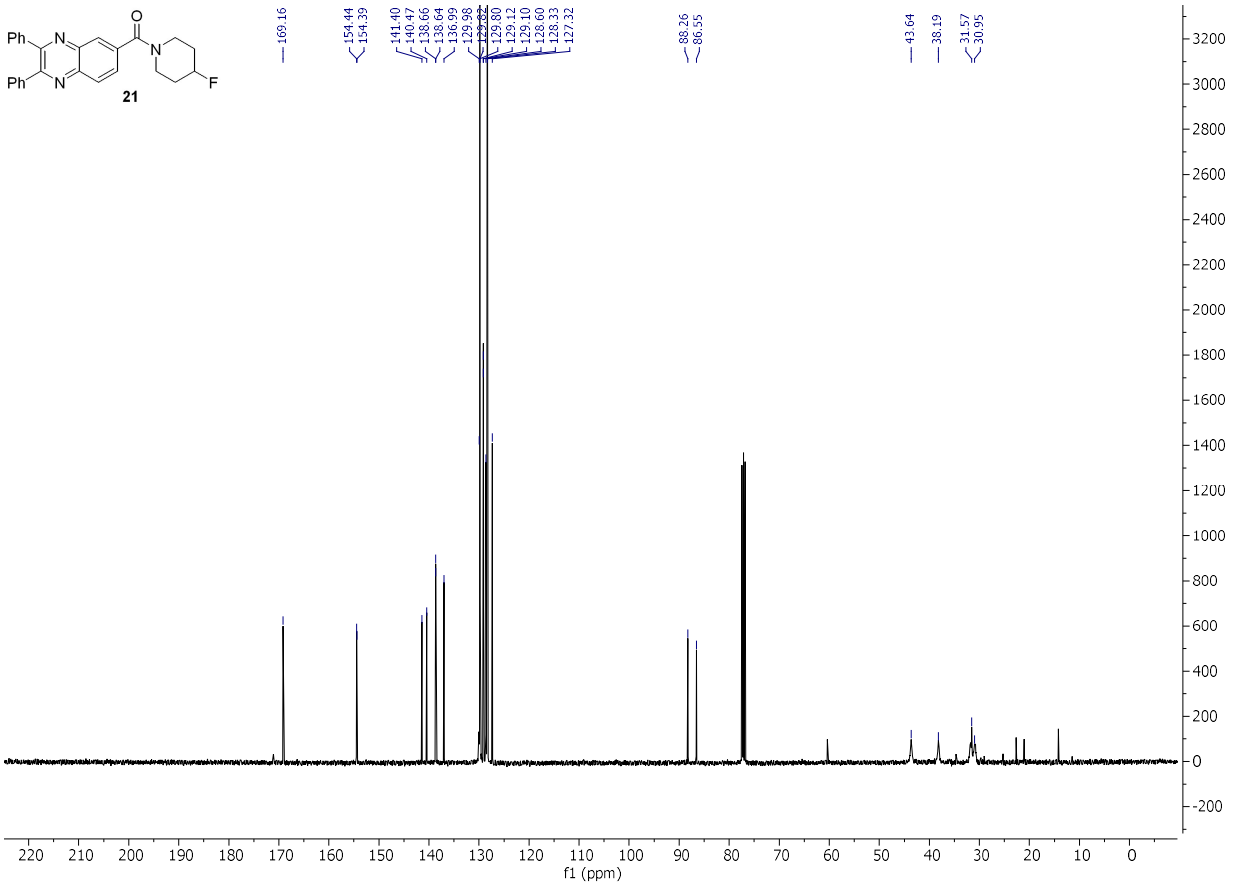
1.00
1.03
4.00
6.14
1.28
1.06
3.07
4.76
f1 (ppm)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O
N
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140.47
138.66
138.64
136.99
129.98
129.80
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128.33
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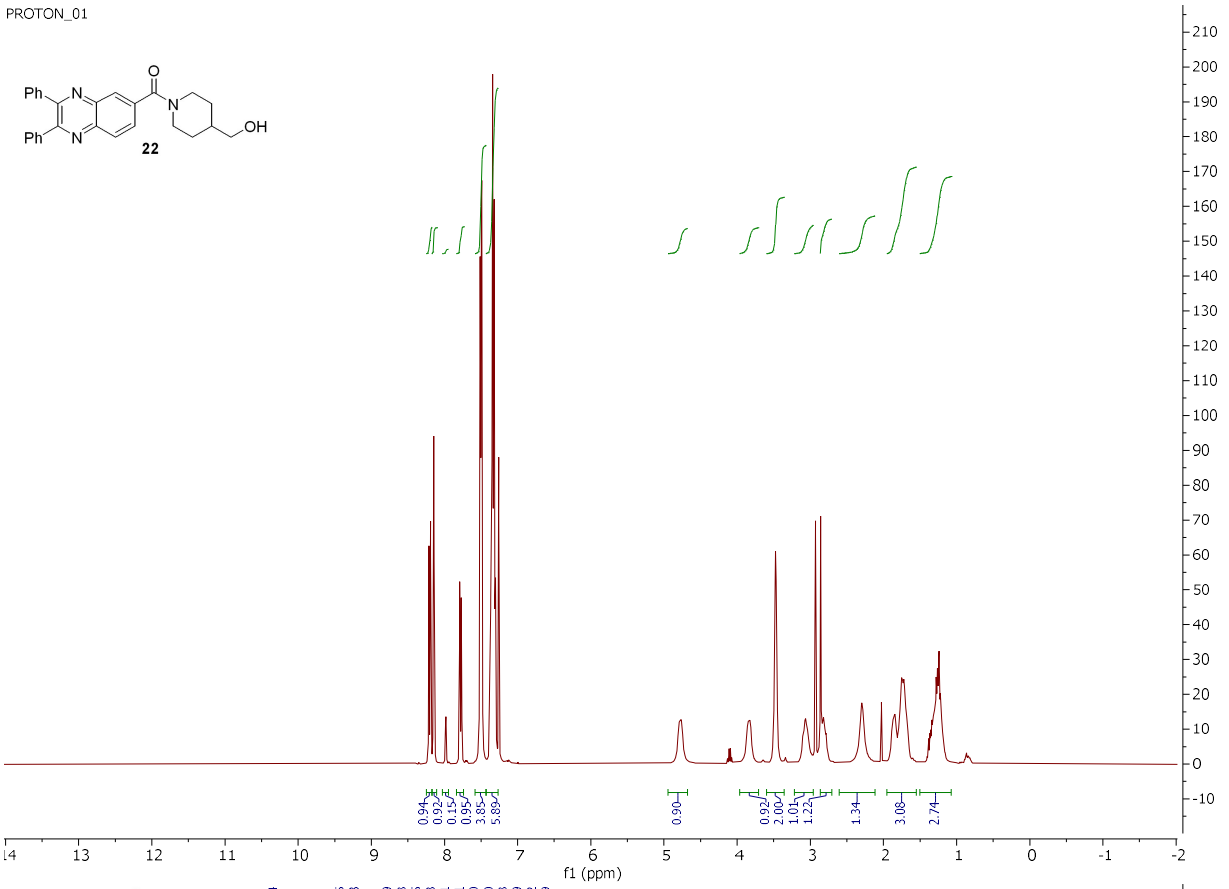
88.26
86.55
43.64
38.19
31.57
30.95
f1 (ppm)


PROTON_01
Ph
Ph
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O
N
OH
22
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0.92
0.15
0.95
3.85
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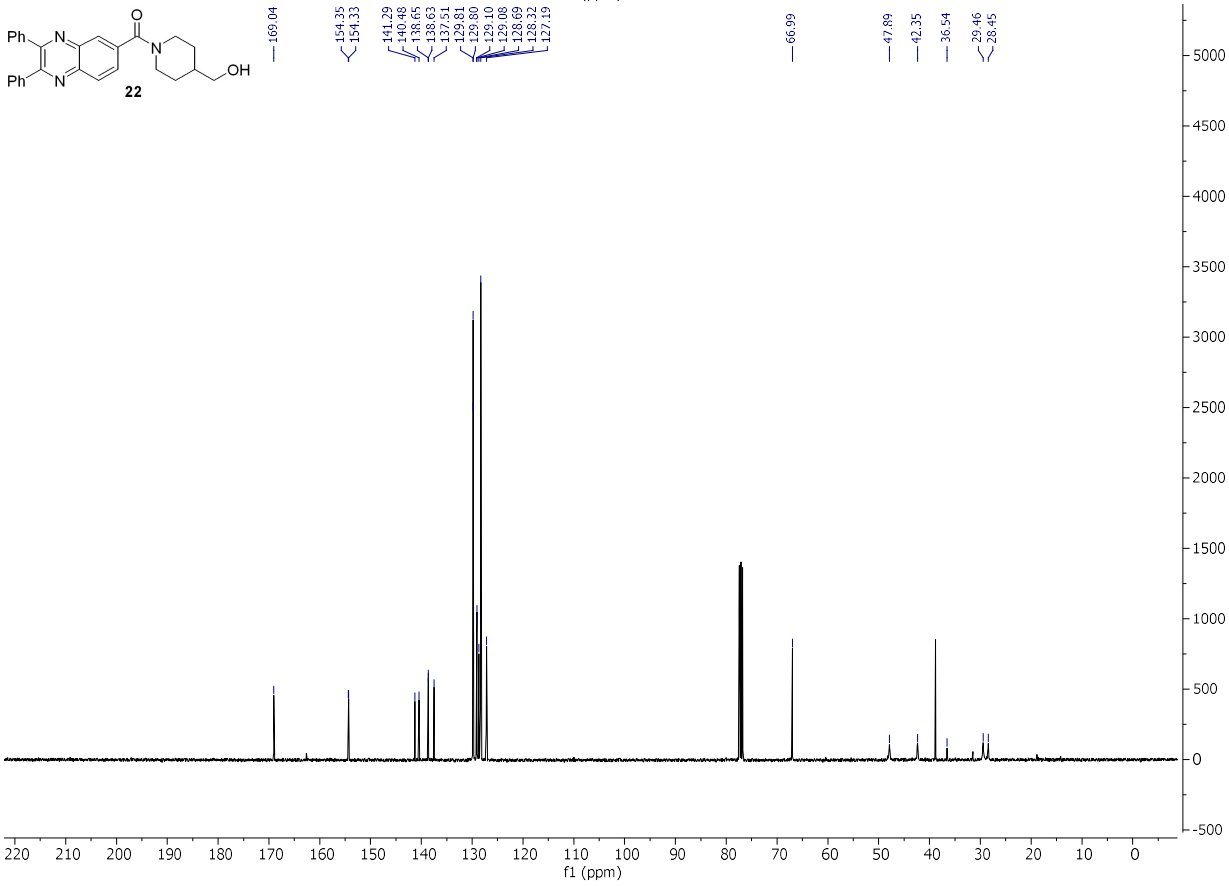
0.90
0.92
2.00
1.01
1.22
1.34
3.08
2.74
f1 (ppm)


Ph
Ph
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N
O
N
OH
22
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154.33
141.29
140.48
138.65
138.63
137.51
129.81
129.80
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129.08
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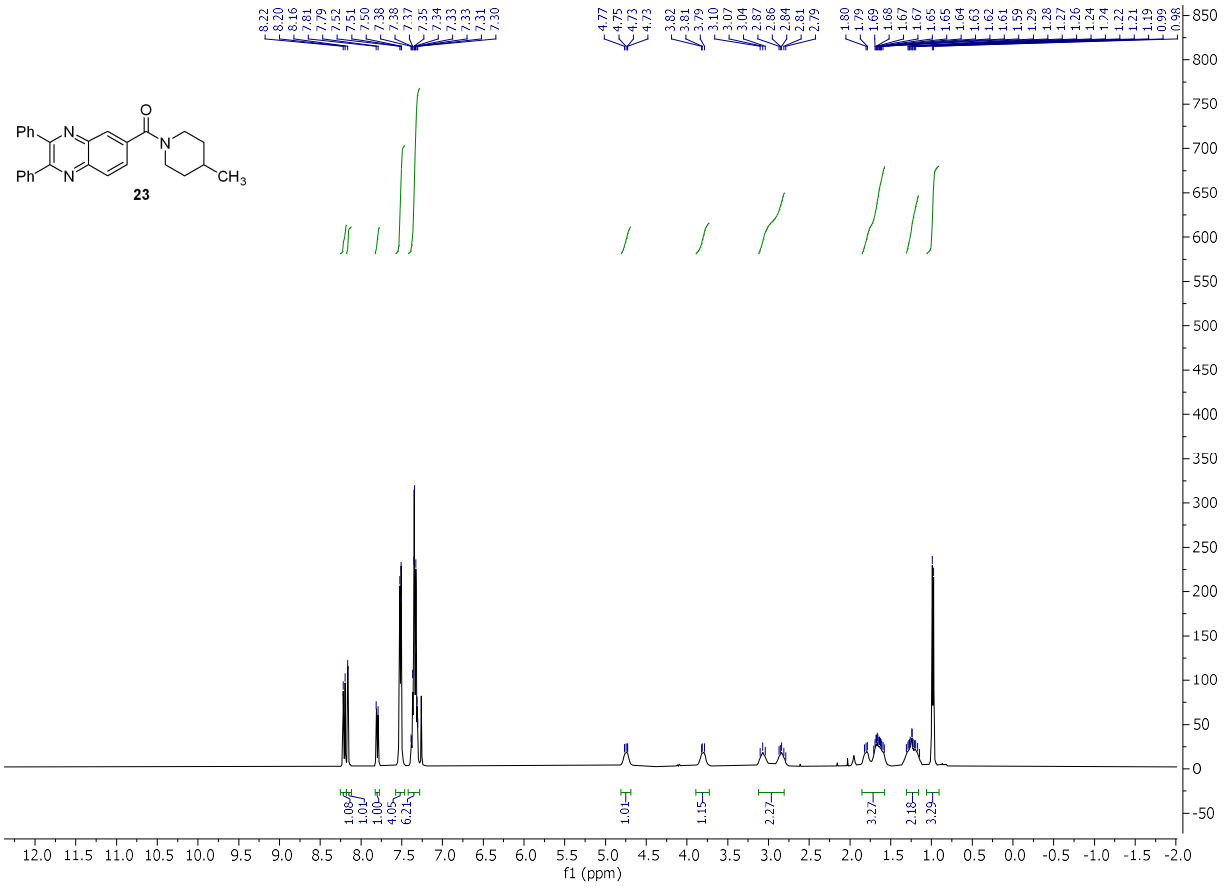
128.32
127.19
66.99
47.89
42.35
36.54
29.46
28.45
f1 (ppm)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O
N
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7.52
7.51
7.50
7.38
7.38
7.37
7.35
7.34
7.33
7.33
7.31
7.30
4.77
4.75
4.73
4.73
3.82
3.81
3.79
3.10
3.07
3.04
2.87
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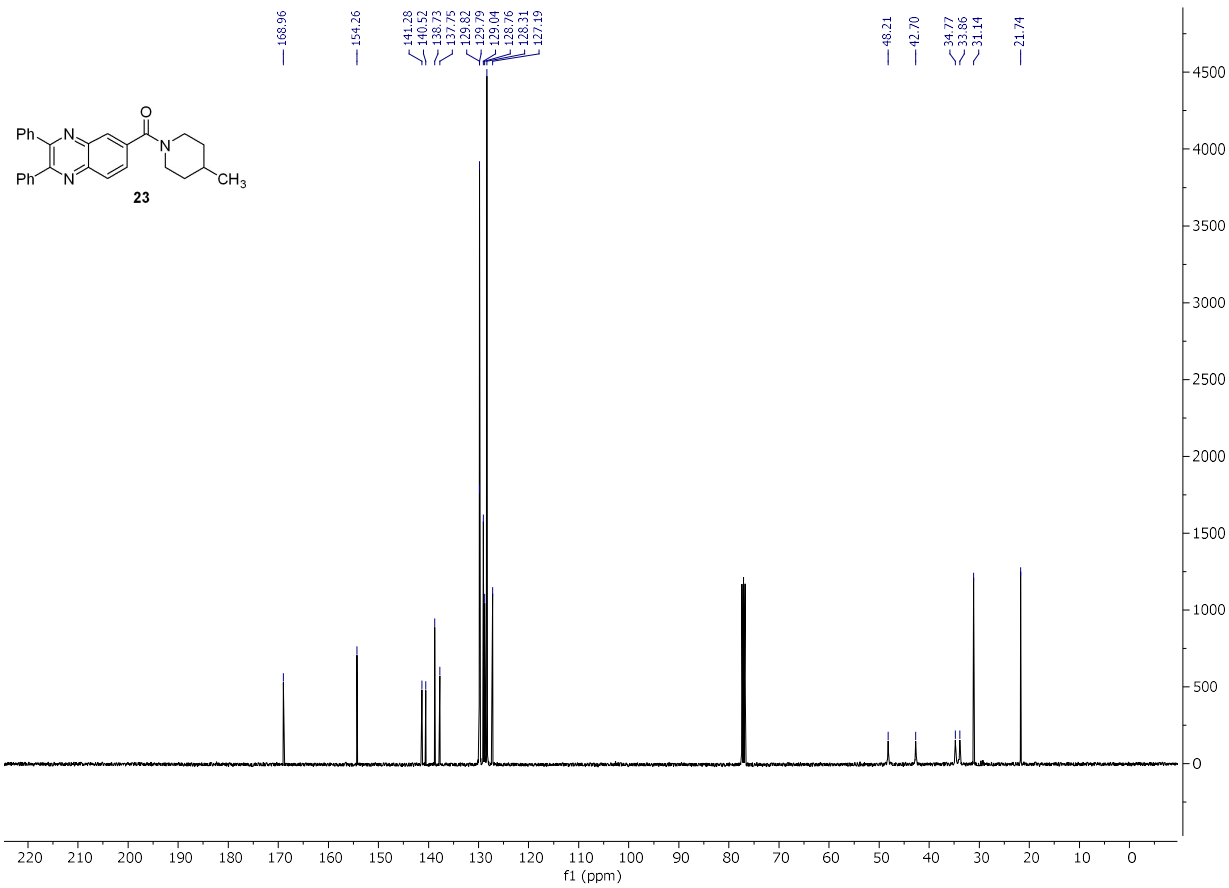
1.62
1.61
1.59
1.29
1.28
1.27
1.26
1.24
1.14
1.22
1.21
1.19
0.98
0.96
1.08
1.01
1.00
4.05
6.24
1.01
1.15
2.27
3.27
2.18
3.29
f1 (ppm)


Ph
Ph
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N
O
N
CH3
23
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138.73
137.75
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128.31
127.19
48.21
42.70
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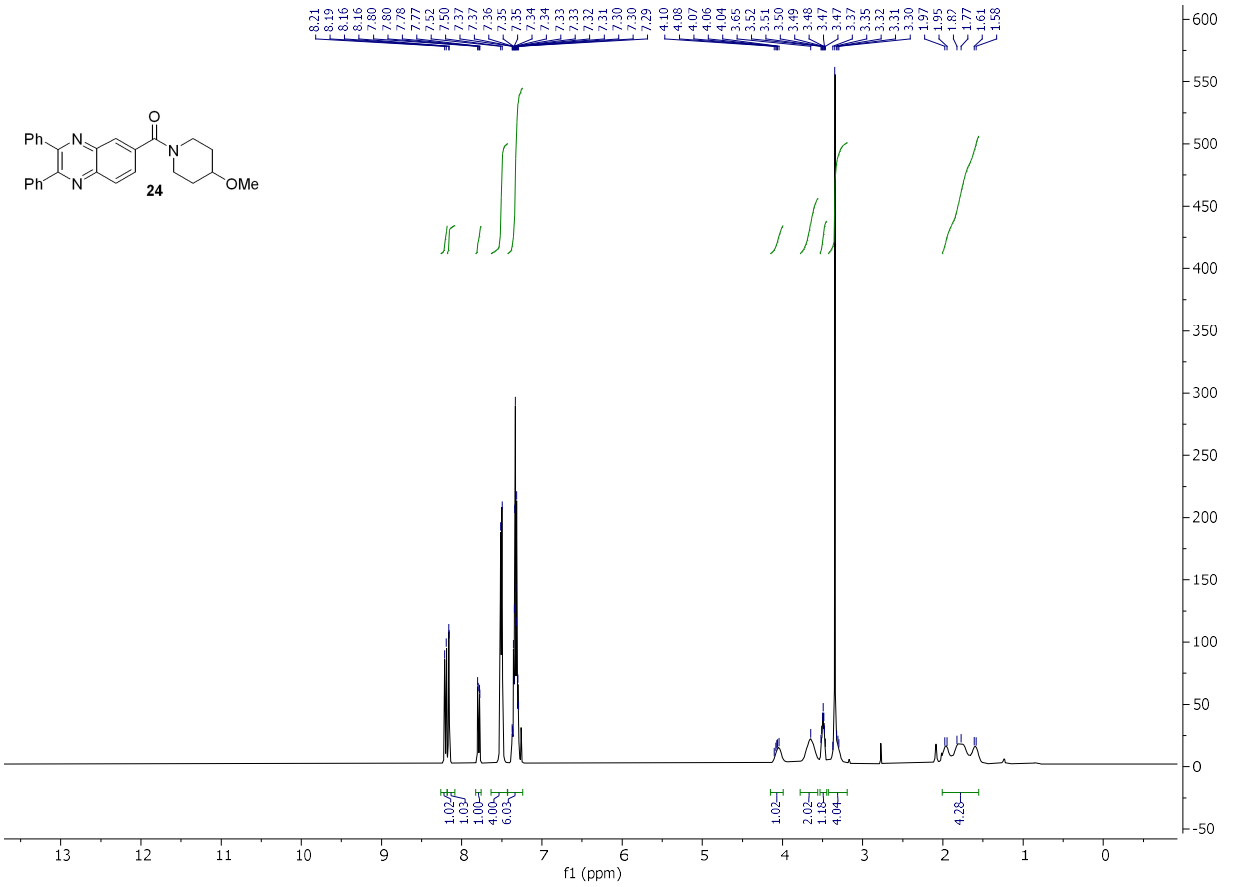
33.86
31.14
21.74
f1 (ppm)


Ph
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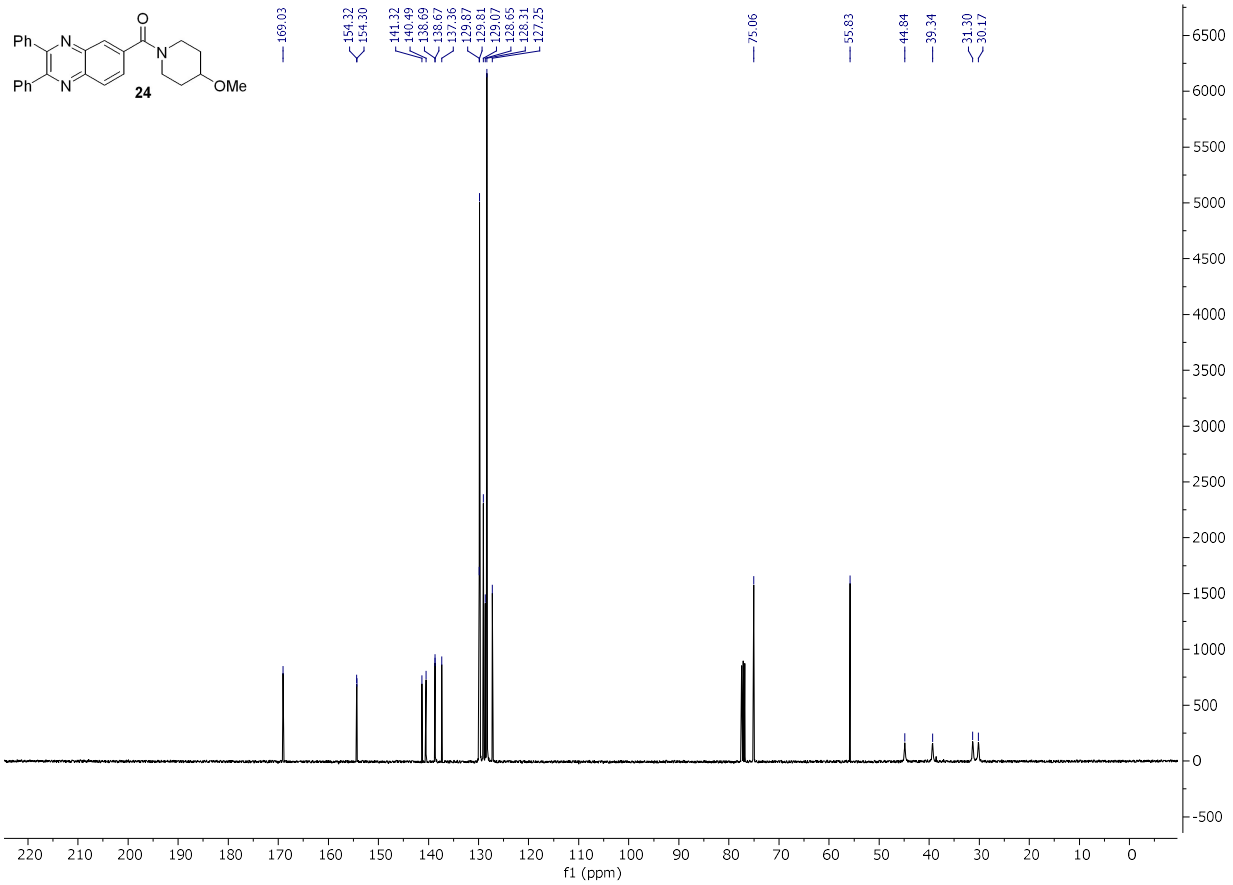
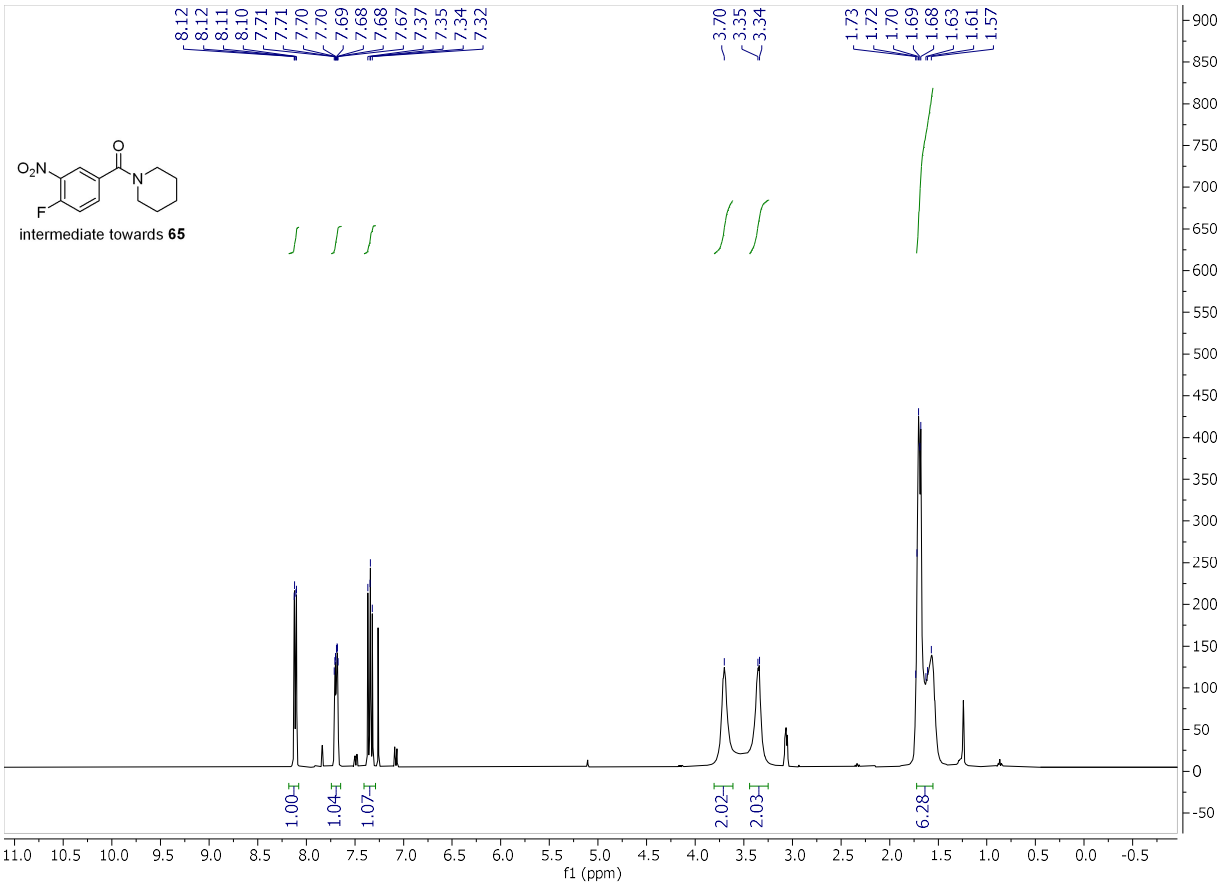
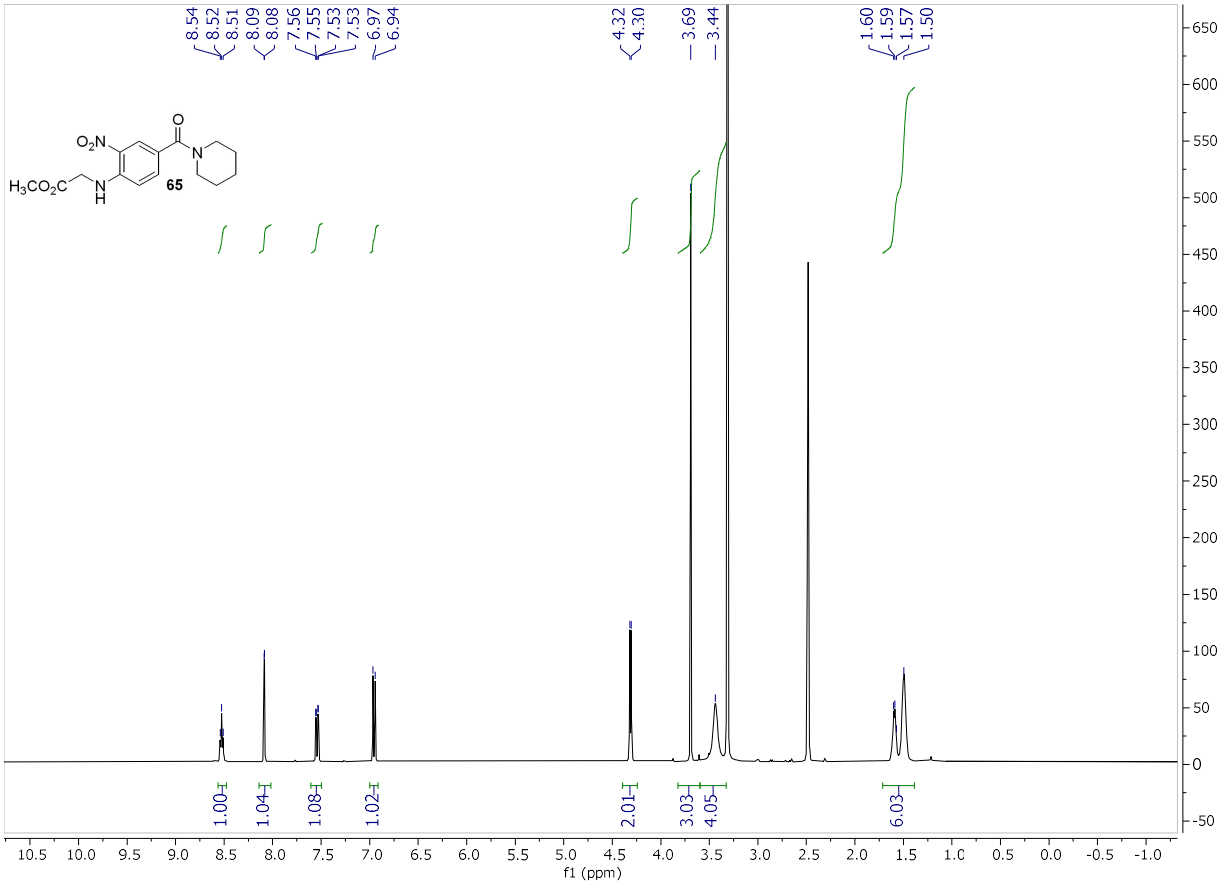
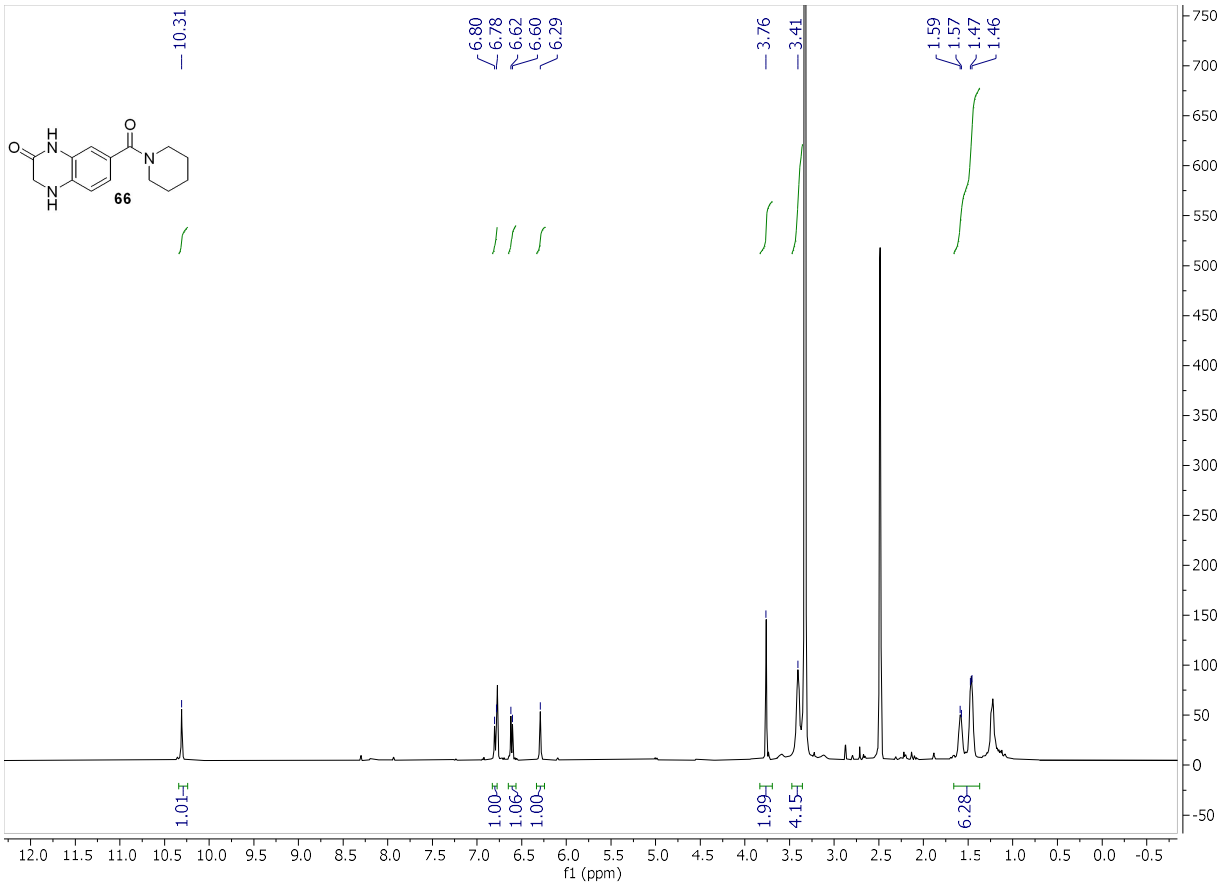
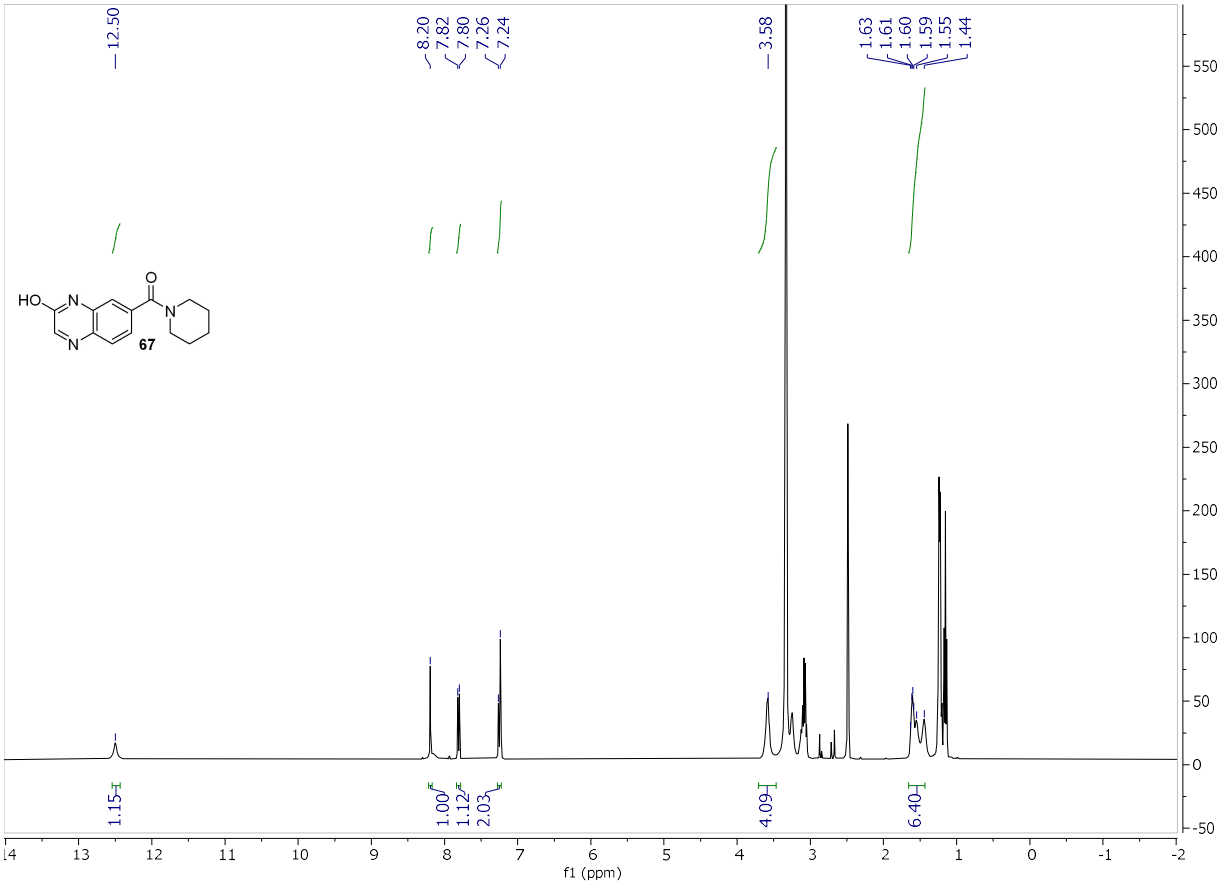
Ph
N
O
N
OMe
24
f1 (ppm)

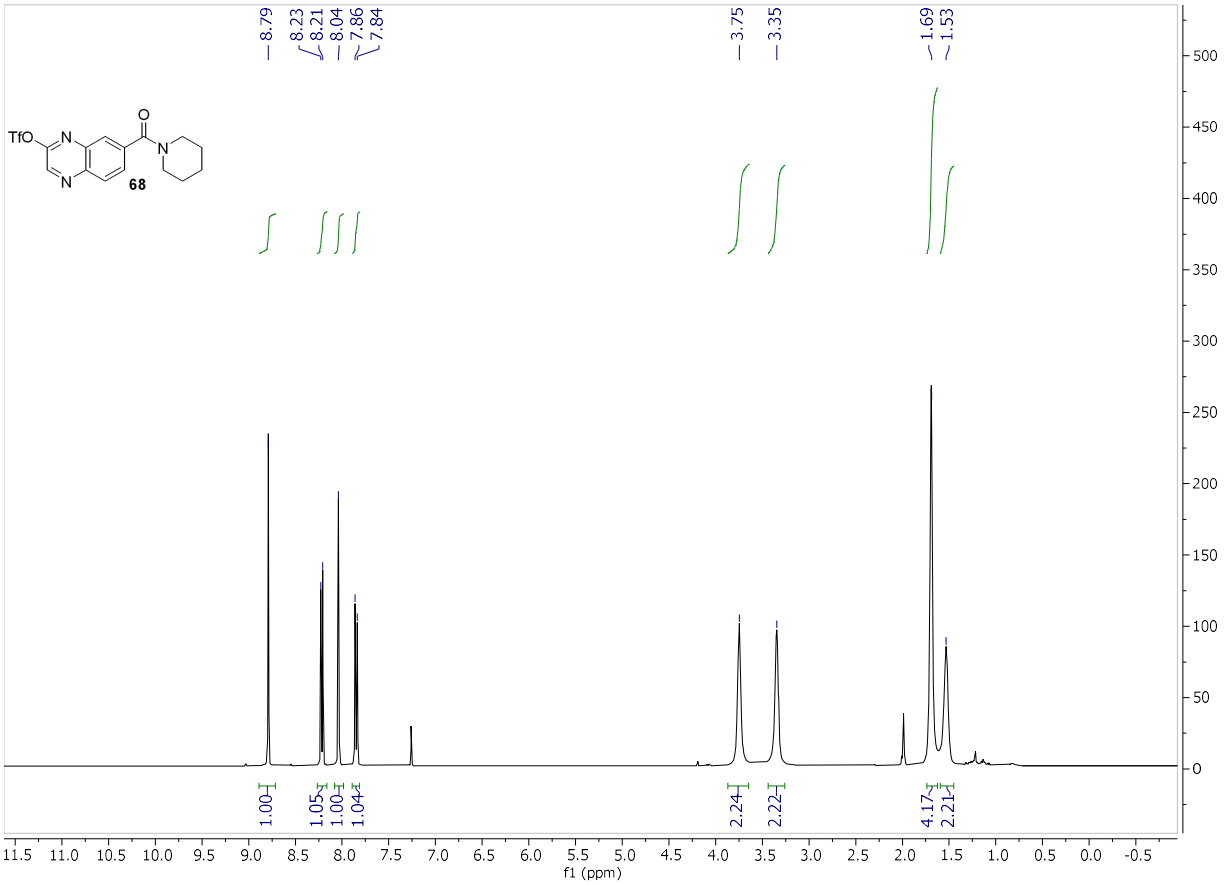

Ph
N
Ph
N
O
N
OMe
24
f1 (ppm)

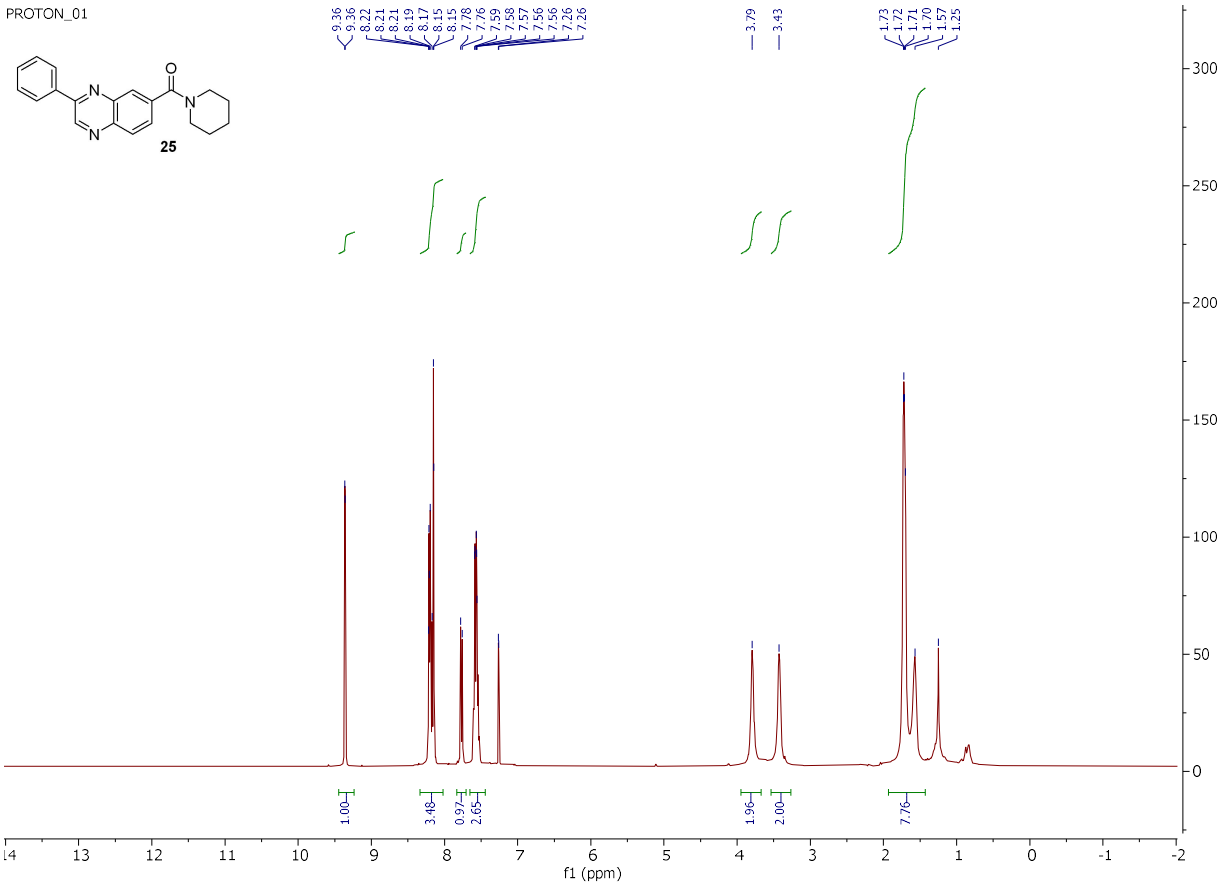

intermediate towards 65
f1 (ppm)

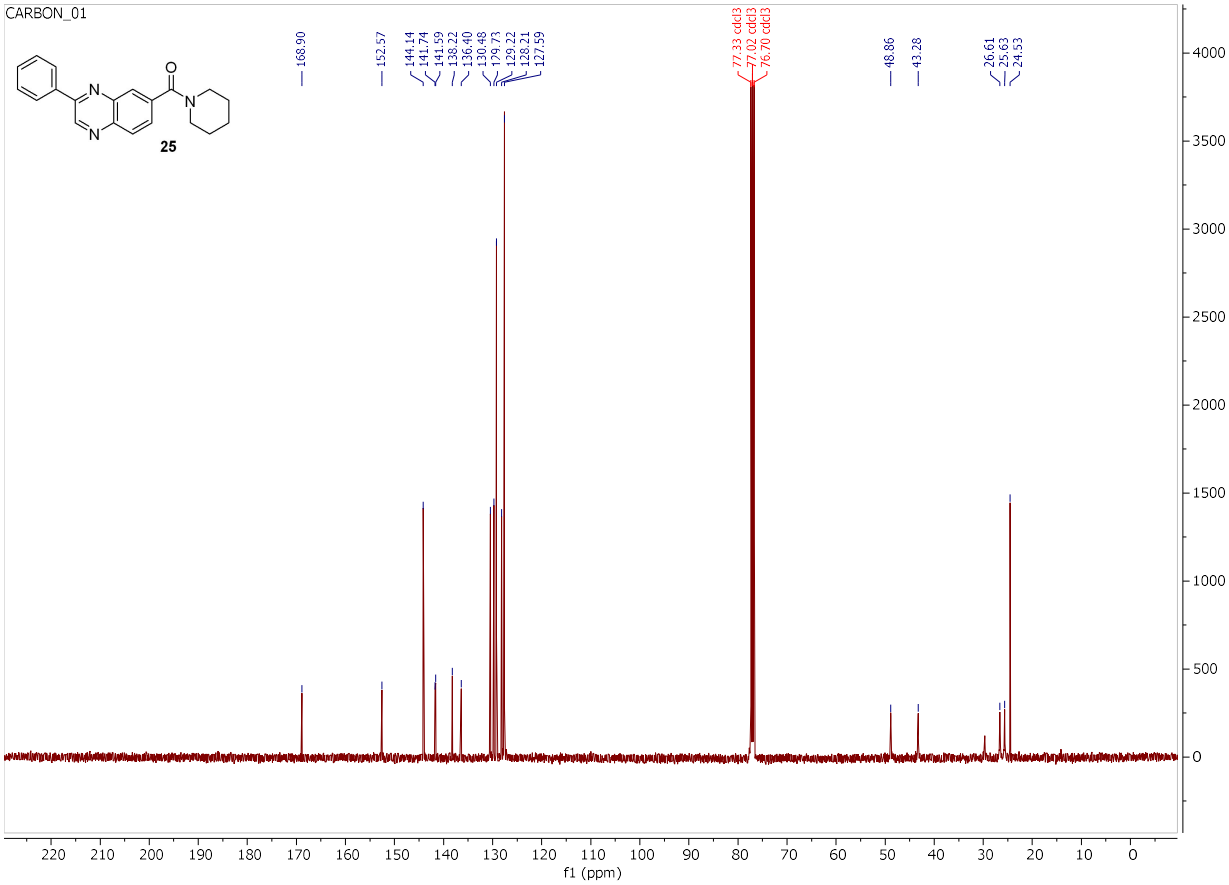

65
f1 (ppm)

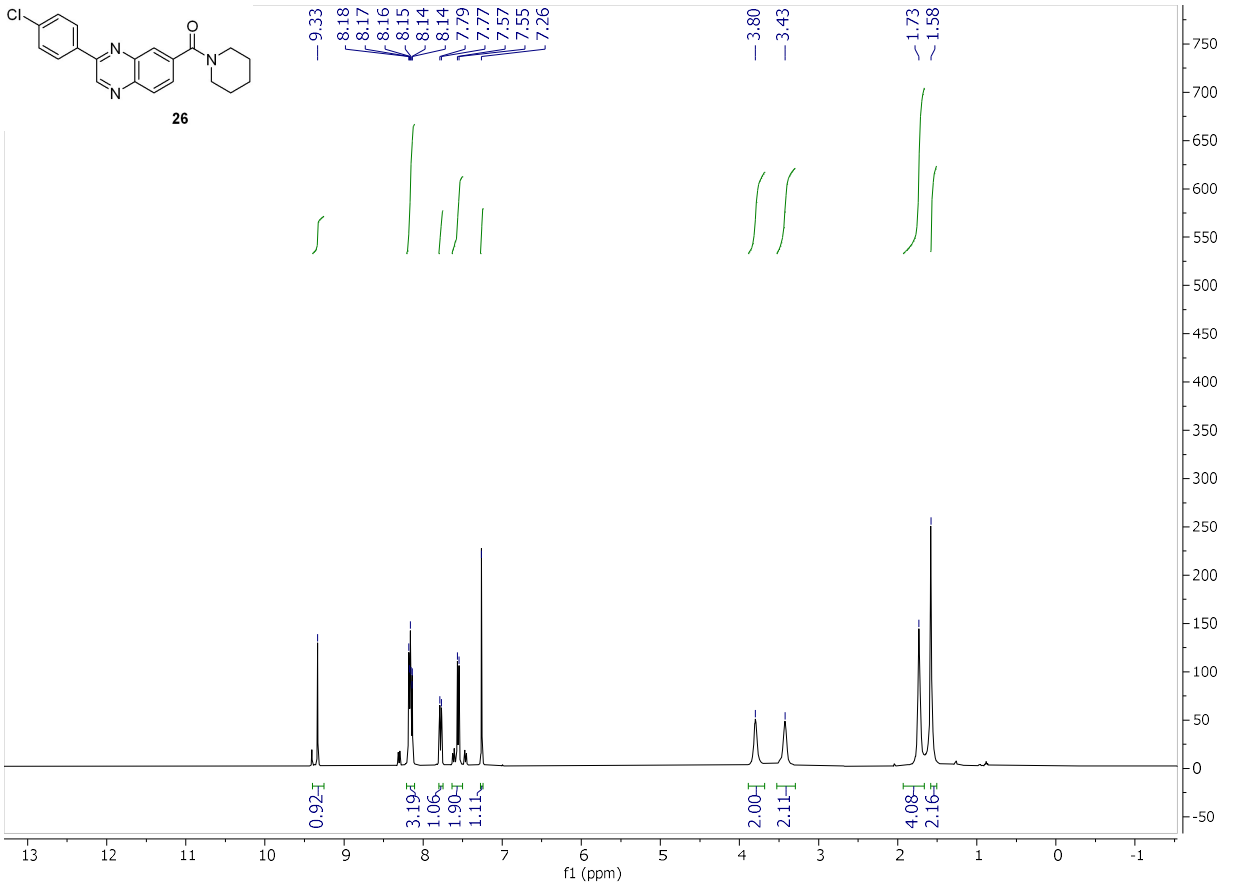

10.31
6.80
6.78
6.62
6.60
6.29
3.76
3.41
1.59
1.57
1.47
1.46
66
1.01
1.00
1.06
1.00
1.99
4.15
6.28
f1 (ppm)

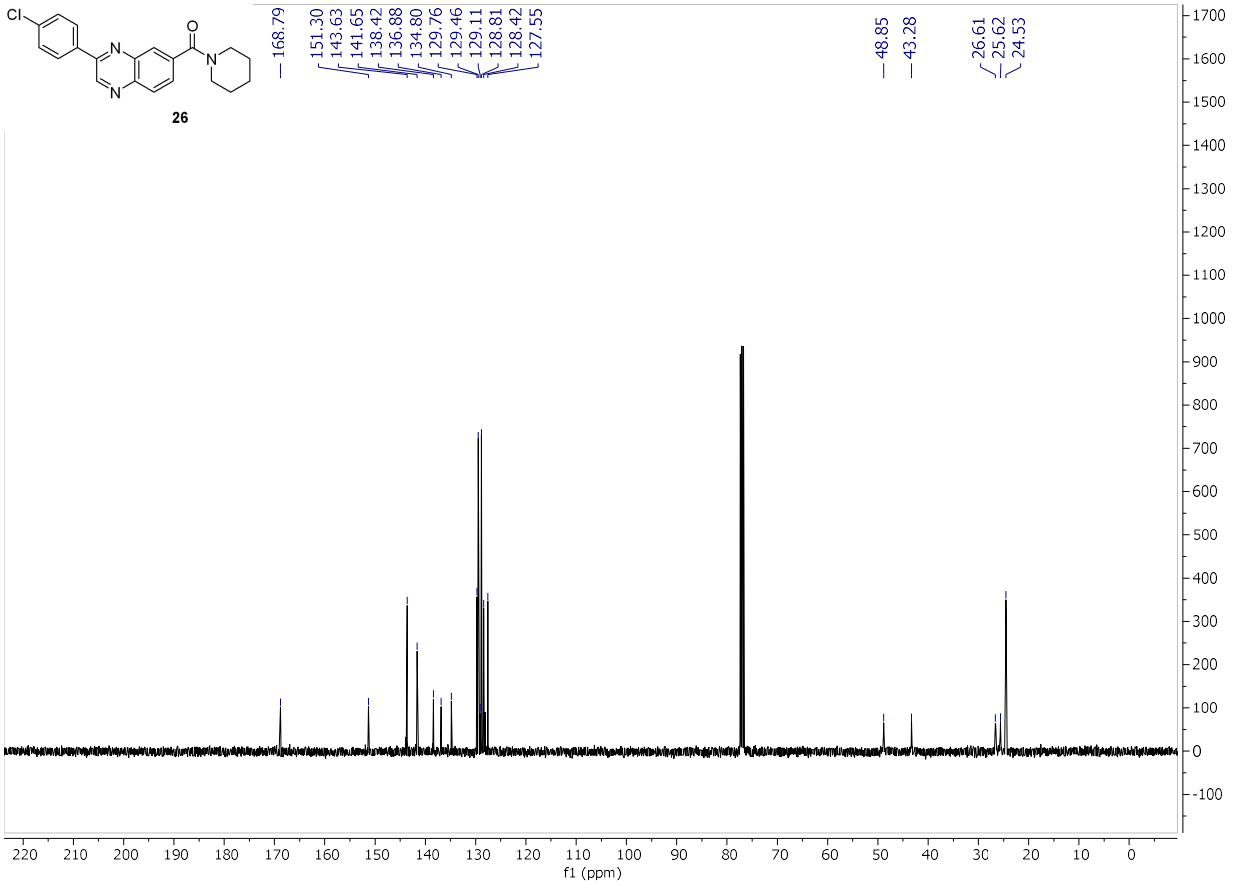

12.50
8.20
7.82
7.80
7.26
7.24
3.58
1.63
1.61
1.60
1.59
1.55
1.44
HO
67
1.15
1.00
1.12
2.03
4.09
6.40
f1 (ppm)

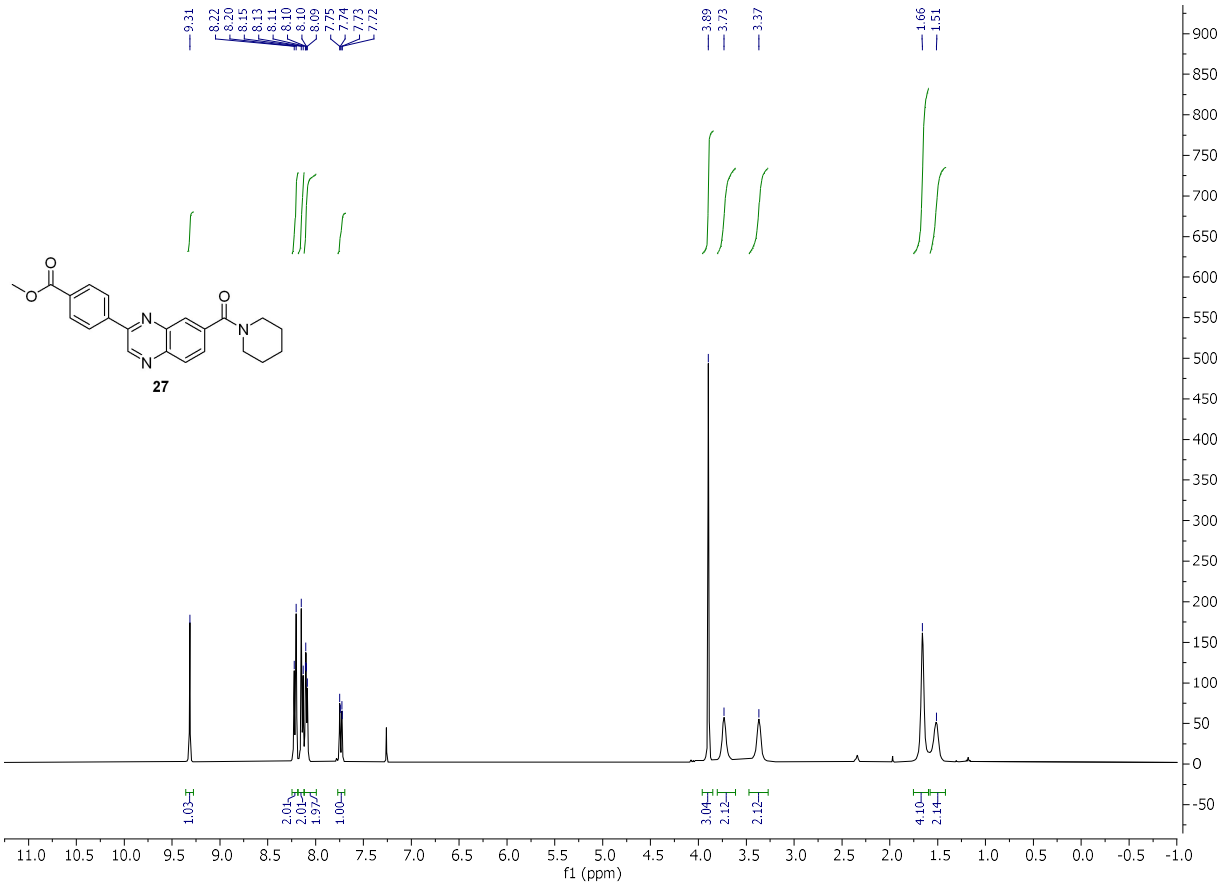

8.79
8.23
8.21
8.04
7.86
7.84
3.75
3.35
1.69
1.53
TfO
N
N
O
N
68
1.00
1.05
1.00
1.04
2.24
2.22
4.17
2.21
f1 (ppm)


PROTON_01
25
9.36
9.36
8.22
8.21
8.19
8.17
8.15
7.78
7.76
7.59
7.58
7.57
7.56
7.56
7.26
7.26
3.79
3.43
1.73
1.72
1.71
1.70
1.57
1.25
1.00
3.48
0.97
2.65
1.96
2.00
7.76
f1 (ppm)

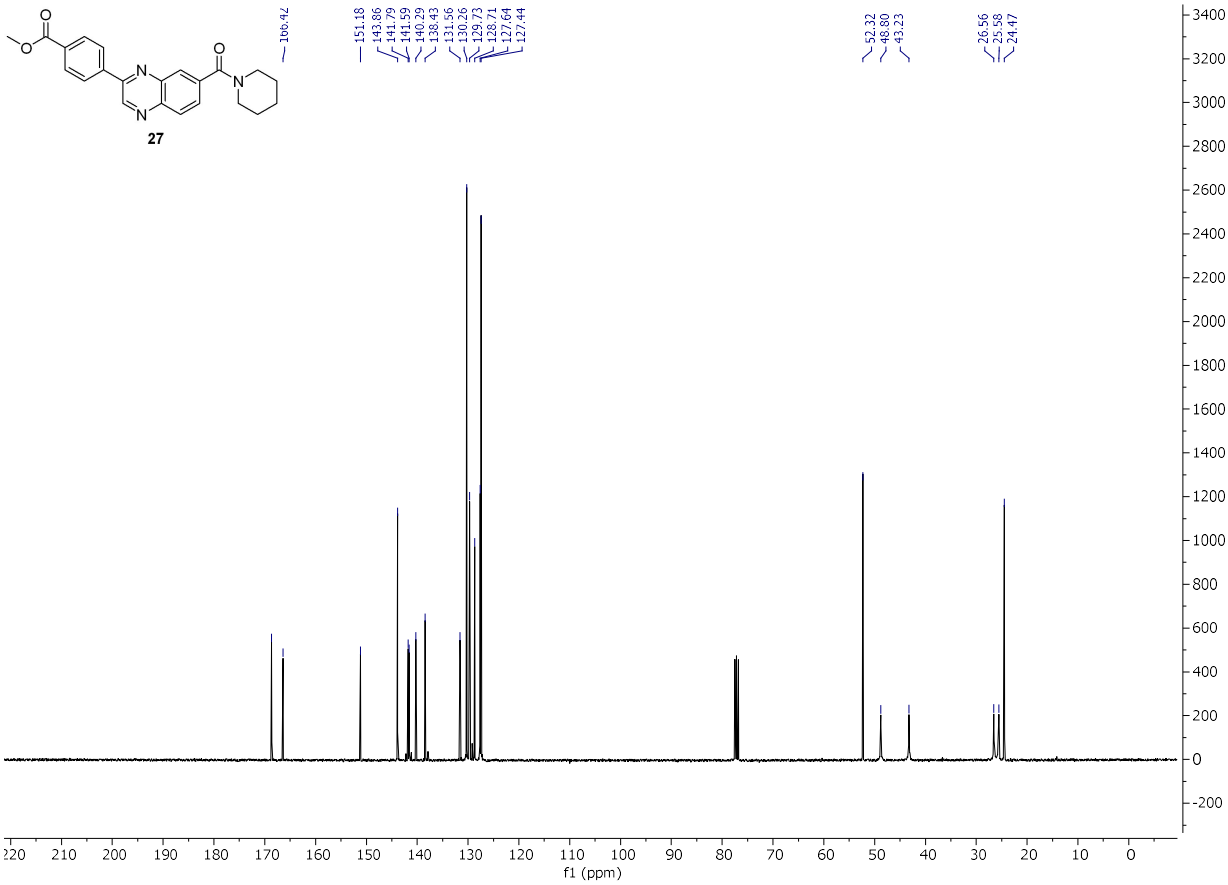

CARBON_01
25
168.90
152.57
144.14
141.74
141.59
138.22
136.40
130.48
129.73
129.22
128.21
127.59
77.33 cdcl3
77.02 cdcl3
76.70 cdcl3
48.86
43.28
26.61
25.63
24.53
f1 (ppm)


26
9.33
8.18
8.17
8.16
8.15
8.14
8.14
7.79
7.77
7.57
7.55
7.26
3.80
3.43
1.73
1.58
0.92
3.19
1.06
1.90
1.11
2.00
2.11
4.08
2.16
f1 (ppm)

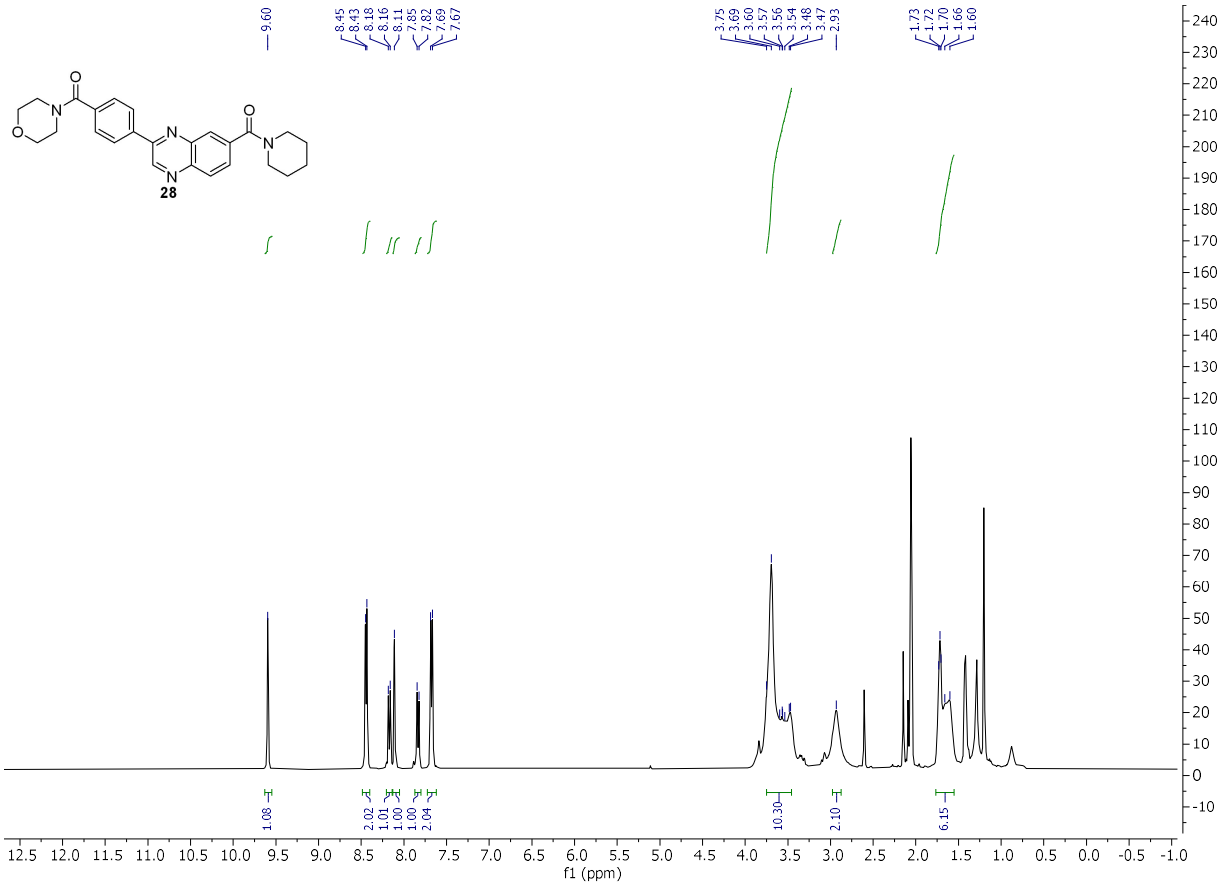

26
168.79
151.30
143.63
141.65
138.42
136.88
134.80
129.76
129.46
129.11
128.81
128.42
127.55
48.85
43.28
26.61
25.62
24.53
f1 (ppm)

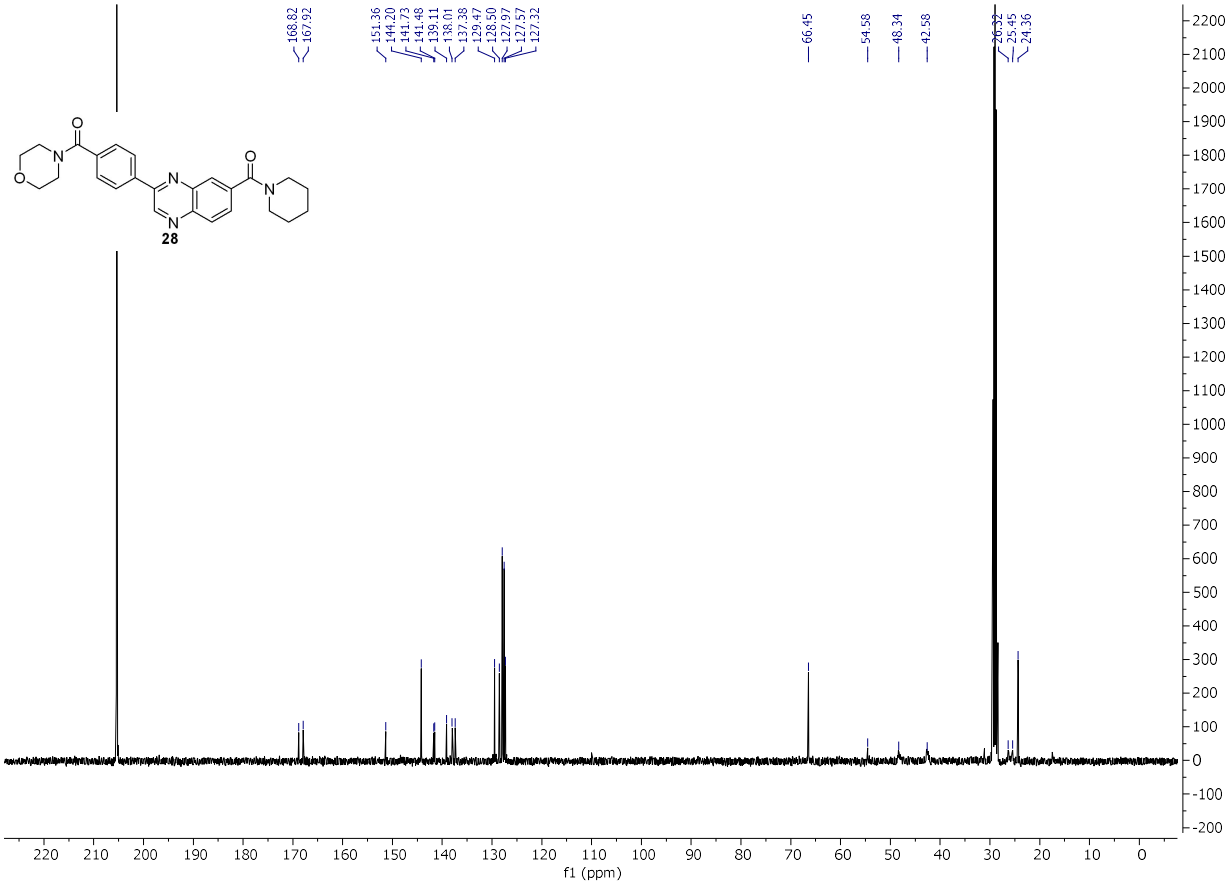

9.31
8.22
8.20
8.15
8.13
8.11
8.10
8.10
8.09
7.75
7.74
7.73
7.72
3.89
3.73
3.37
1.66
1.51
1.03
2.01
2.01
1.97
1.00
3.04
2.12
2.12
4.10
2.14
f1 (ppm)

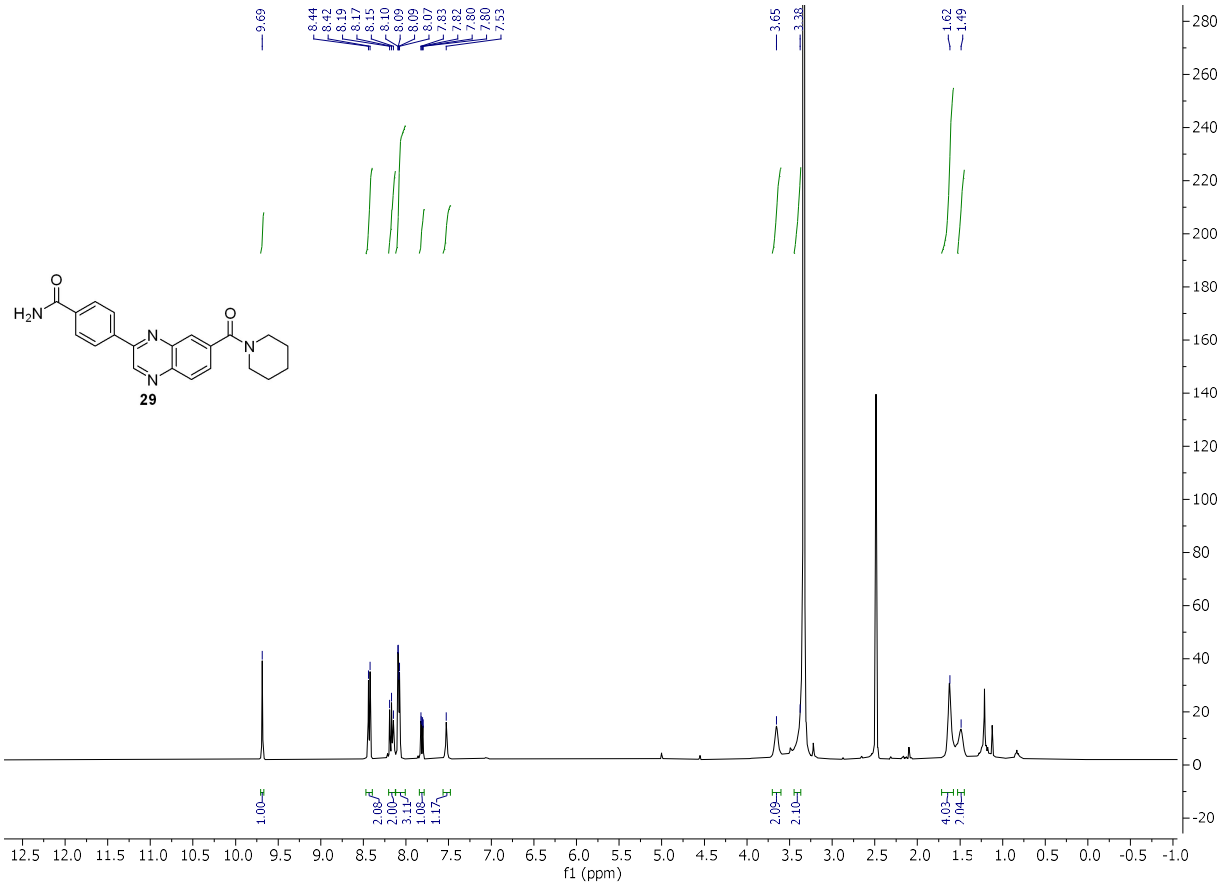
27

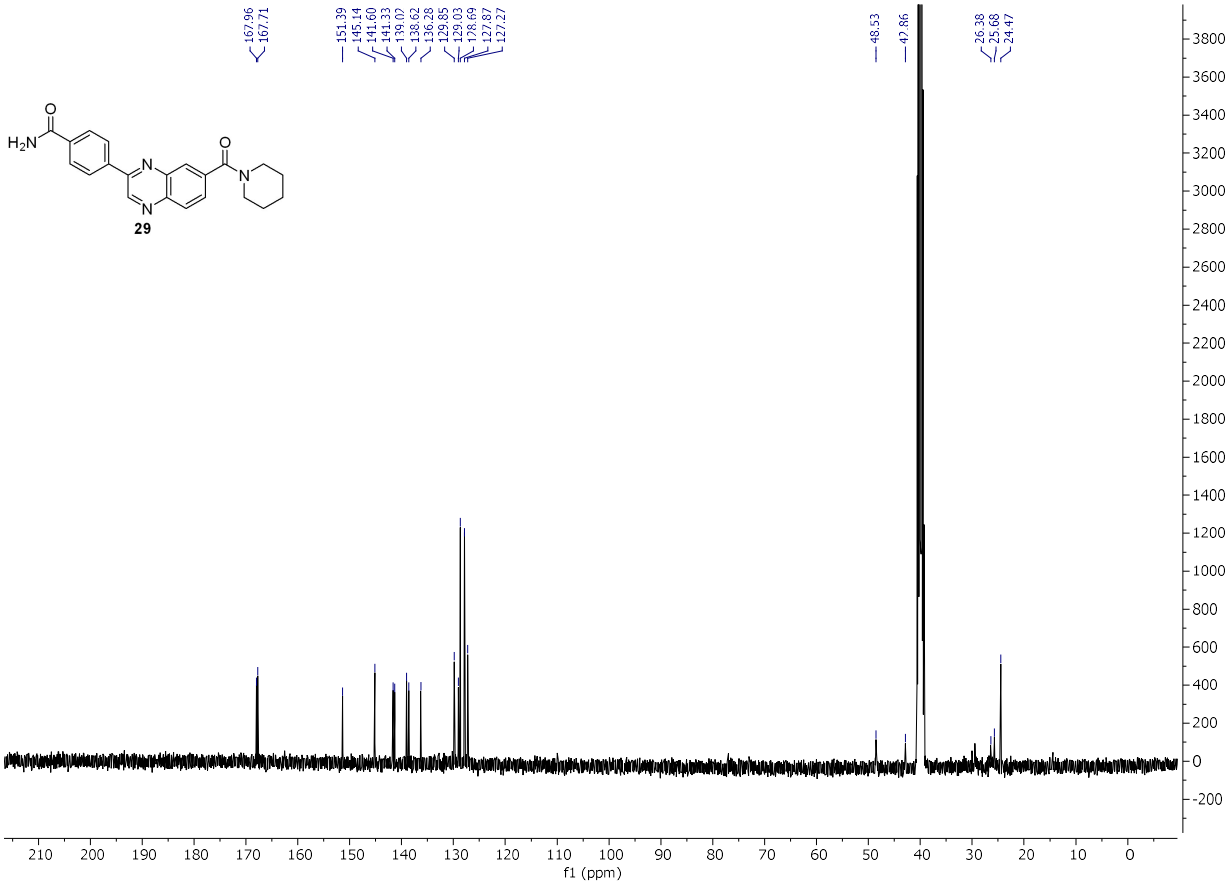

166.42
151.18
143.86
141.79
141.59
140.39
140.43
138.43
131.56
130.26
129.73
128.71
127.64
127.44
52.32
48.80
43.23
26.56
25.58
24.47
f1 (ppm)

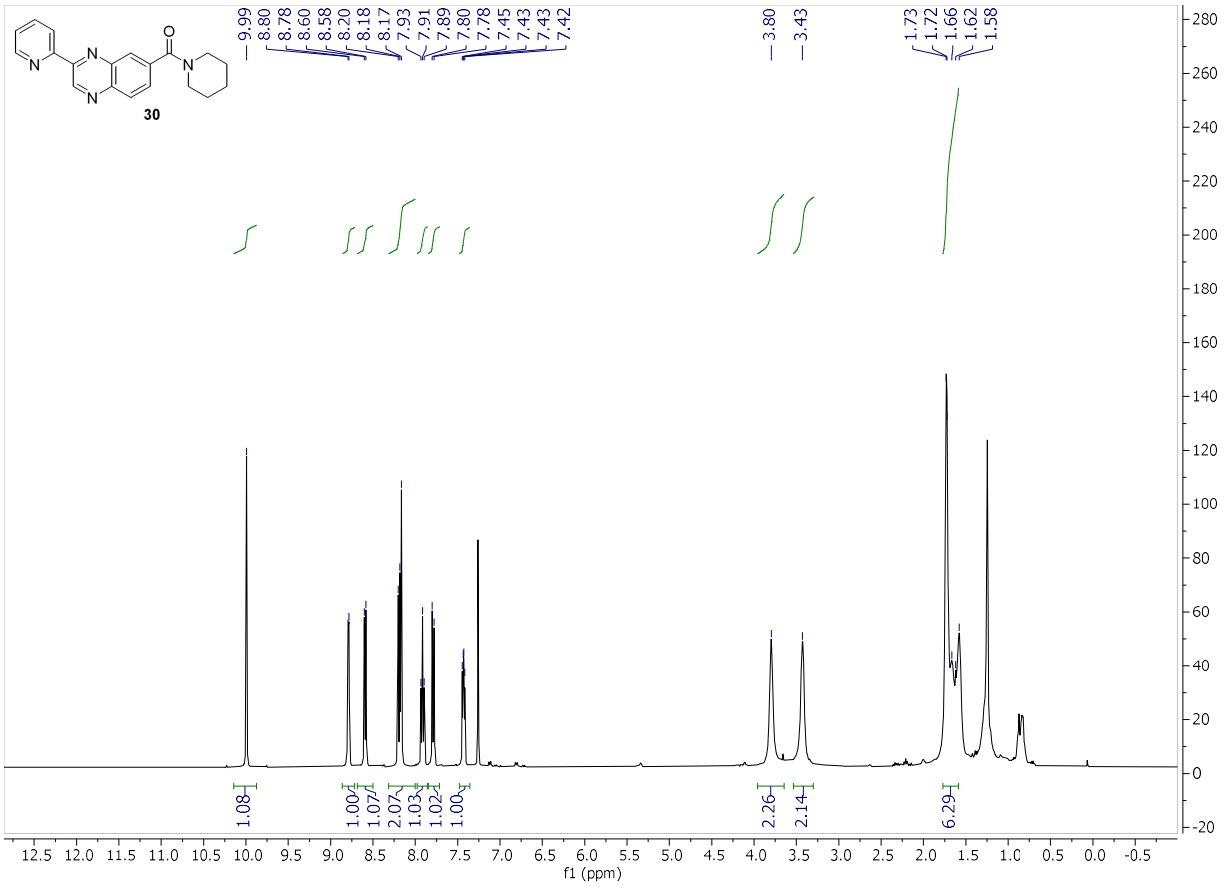
27

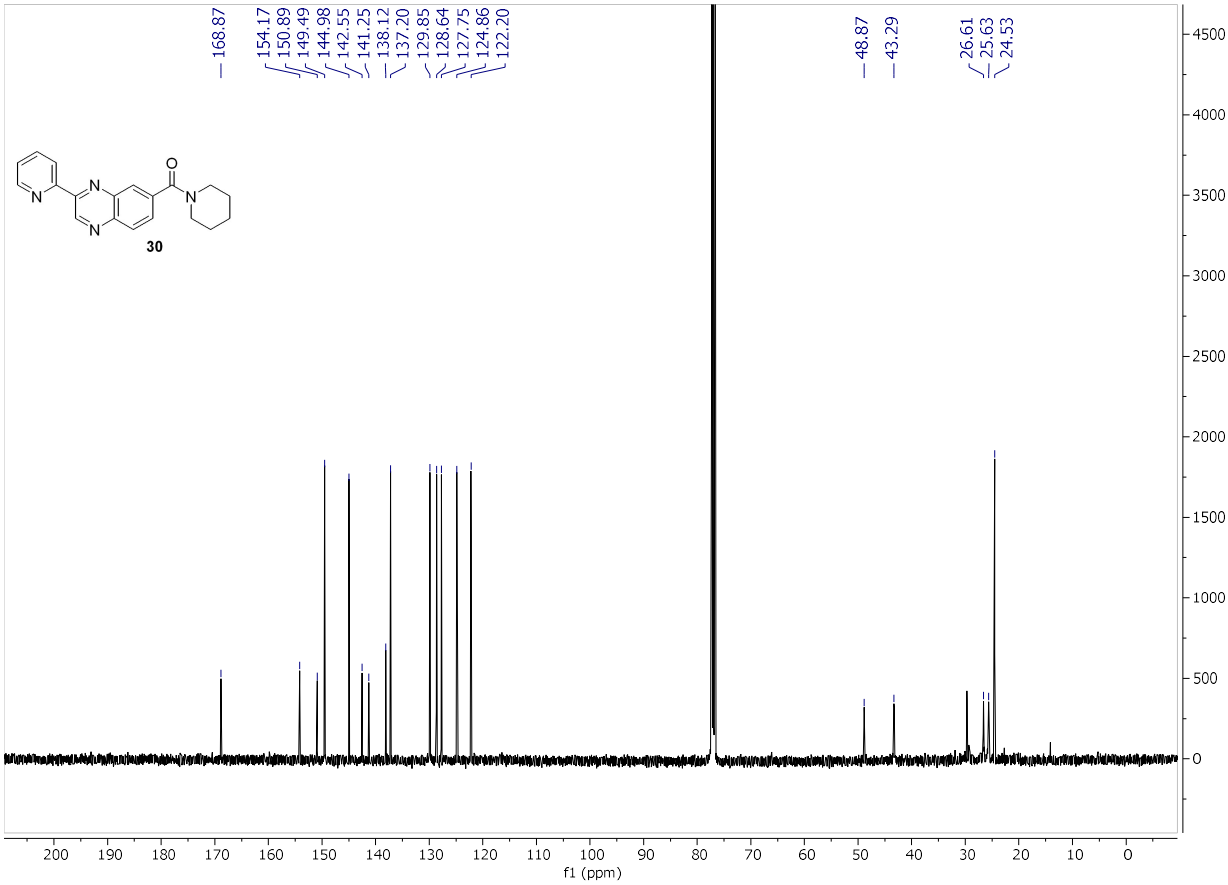

9.60
8.45
8.43
8.18
8.16
8.11
7.85
7.82
7.69
7.67
3.75
3.69
3.60
3.57
3.56
3.54
3.48
3.47
2.93
1.73
1.72
1.70
1.66
1.60
1.08
2.02
1.01
1.00
1.00
2.04
10.30
2.10
6.15
f1 (ppm)

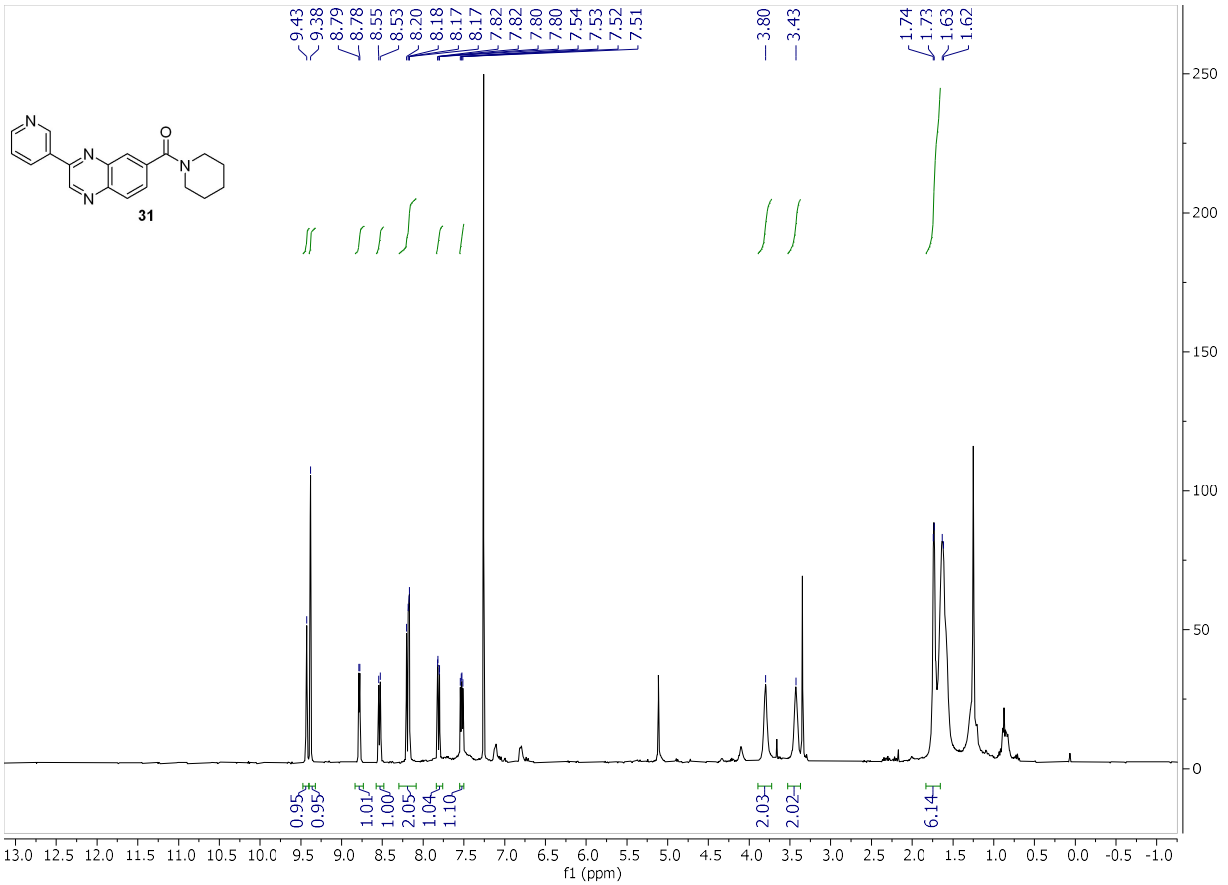

168.82
167.92
151.36
144.20
141.73
141.48
139.11
138.01
137.38
129.47
128.50
127.97
127.57
127.32
66.45
54.58
48.34
42.58
26.32
25.45
24.36
f1 (ppm)

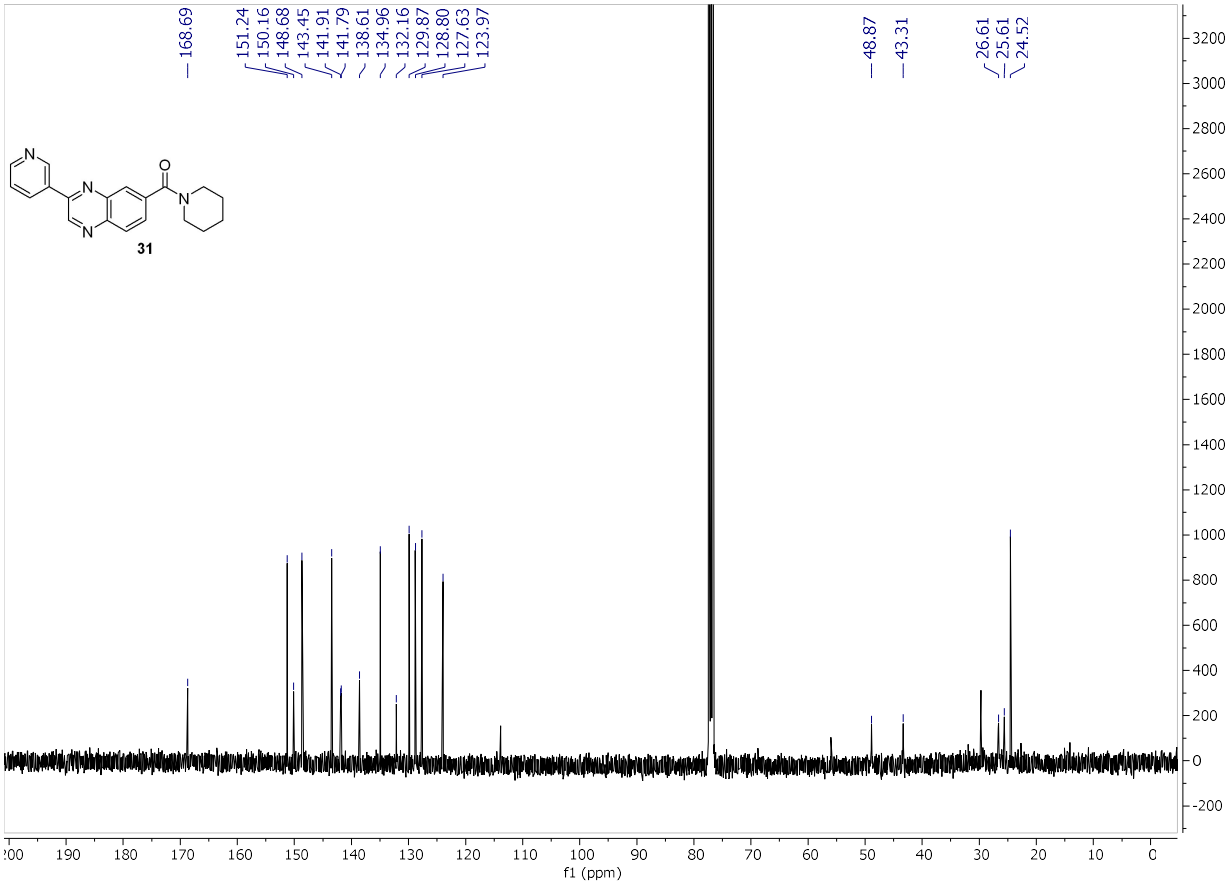

9.69
8.44
8.42
8.19
8.17
8.15
8.10
8.09
8.09
8.07
7.83
7.82
7.80
7.80
7.53
3.65
3.38
1.62
1.49
1.00
2.08
2.00
3.14
1.08
1.17
2.09
2.10
4.03
2.04
29
f1 (ppm)

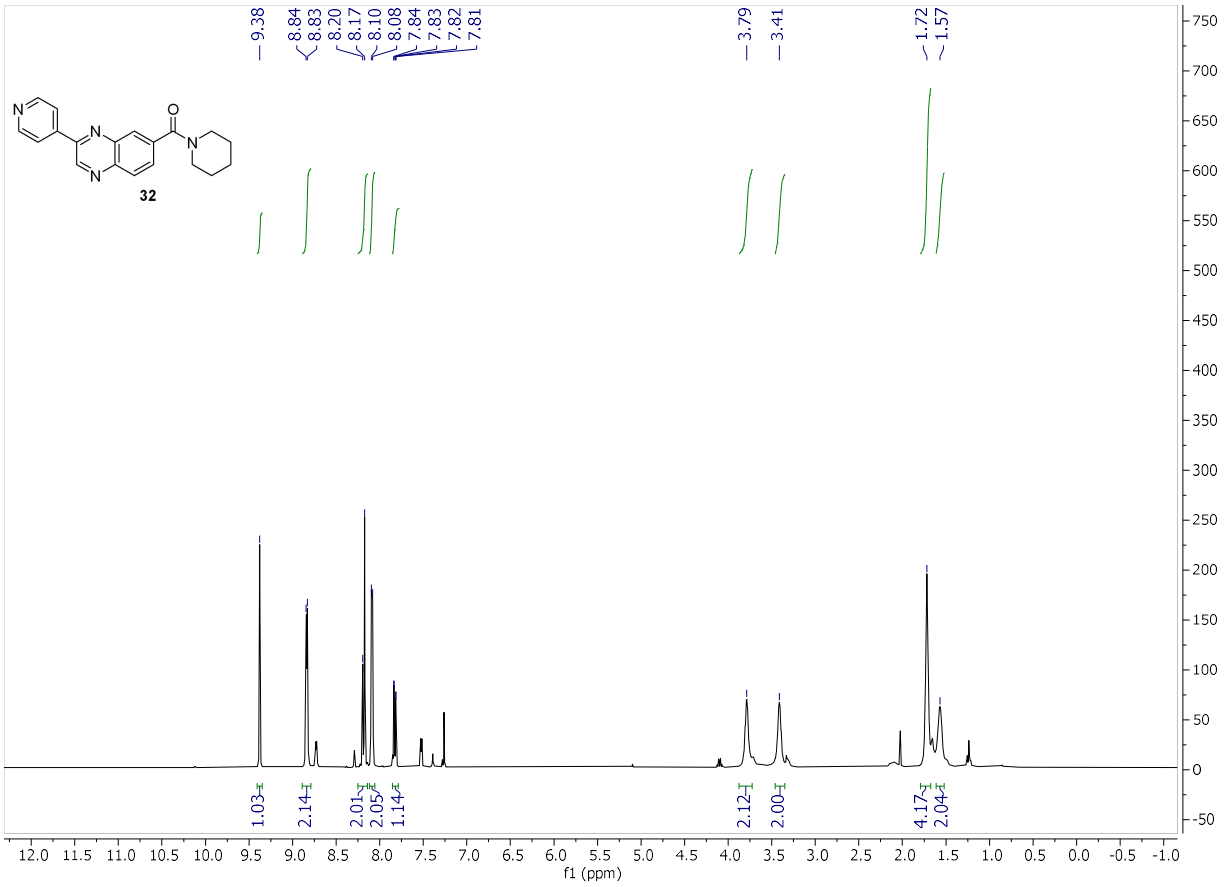

167.96
167.71
151.39
145.14
141.60
141.33
139.07
138.62
136.28
129.85
129.03
128.69
127.87
127.27
48.53
47.86
26.38
25.68
24.47
29
f1 (ppm)


30
9.99
8.80
8.78
8.60
8.58
8.20
8.18
8.17
7.93
7.91
7.89
7.80
7.78
7.45
7.43
7.43
7.42
3.80
3.43
1.73
1.72
1.66
1.62
1.58
1.08
1.00
1.07
2.07
1.03
1.02
1.00
2.26
2.14
6.29
f1 (ppm)

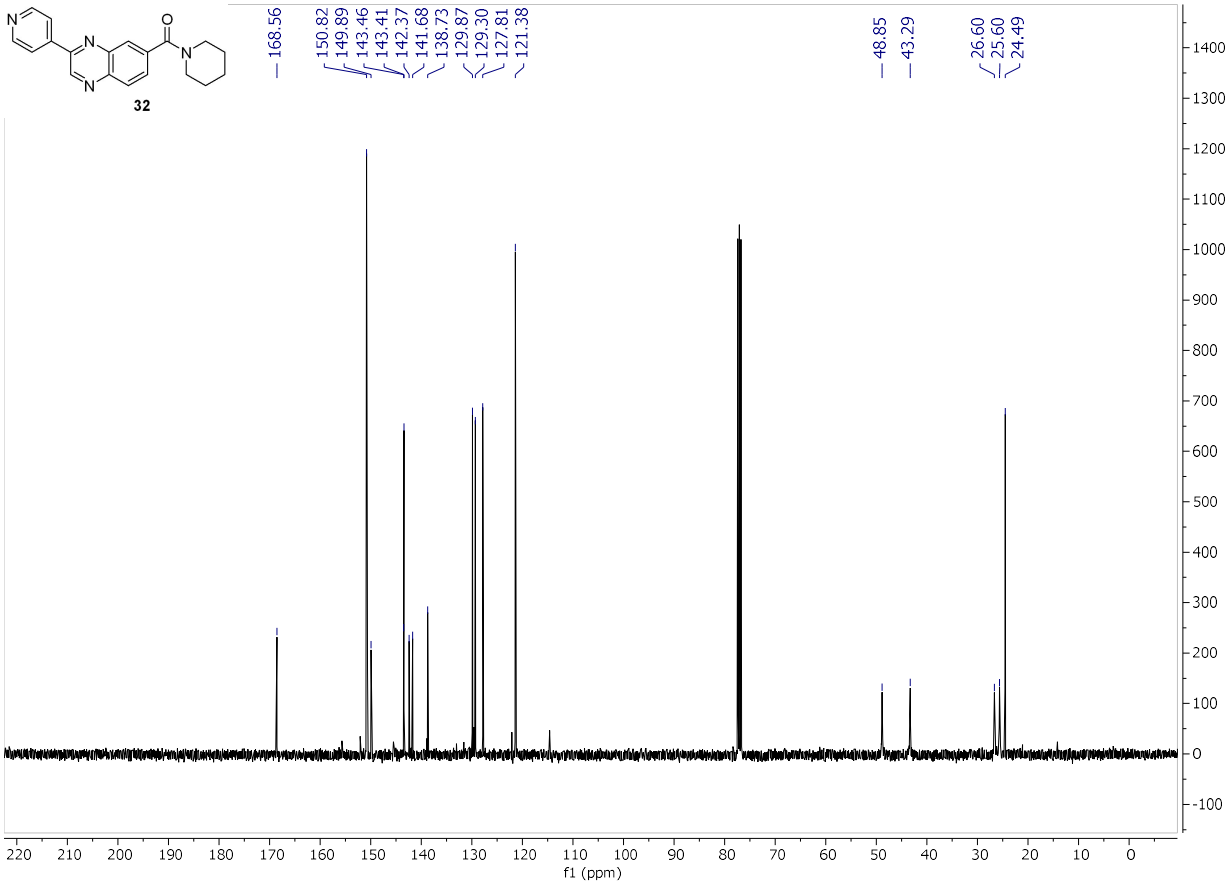

30
168.87
154.17
150.89
149.49
144.98
142.55
141.25
138.12
137.20
129.85
128.64
127.75
124.86
122.20
48.87
43.29
26.61
25.63
24.53
f1 (ppm)


9.43
9.38
8.79
8.78
8.55
8.53
8.20
8.18
8.17
8.17
7.82
7.82
7.80
7.80
7.54
7.53
7.52
7.51
3.80
3.43
1.74
1.73
1.63
1.62
31
0.95
0.95
1.01
1.00
2.05
1.04
1.10
2.03
2.02
6.14
f1 (ppm)


168.69
151.24
150.16
148.68
143.45
141.91
141.79
138.61
134.96
132.16
129.87
128.80
127.63
123.97
48.87
43.31
26.61
25.61
24.52
31
f1 (ppm)


9.38
8.84
8.83
8.20
8.17
8.10
8.08
7.84
7.83
7.82
7.81
3.79
3.41
1.72
1.57
1.03
2.14
2.01
2.05
1.14
2.12
2.00
4.17
2.04
f1 (ppm)

32


168.56
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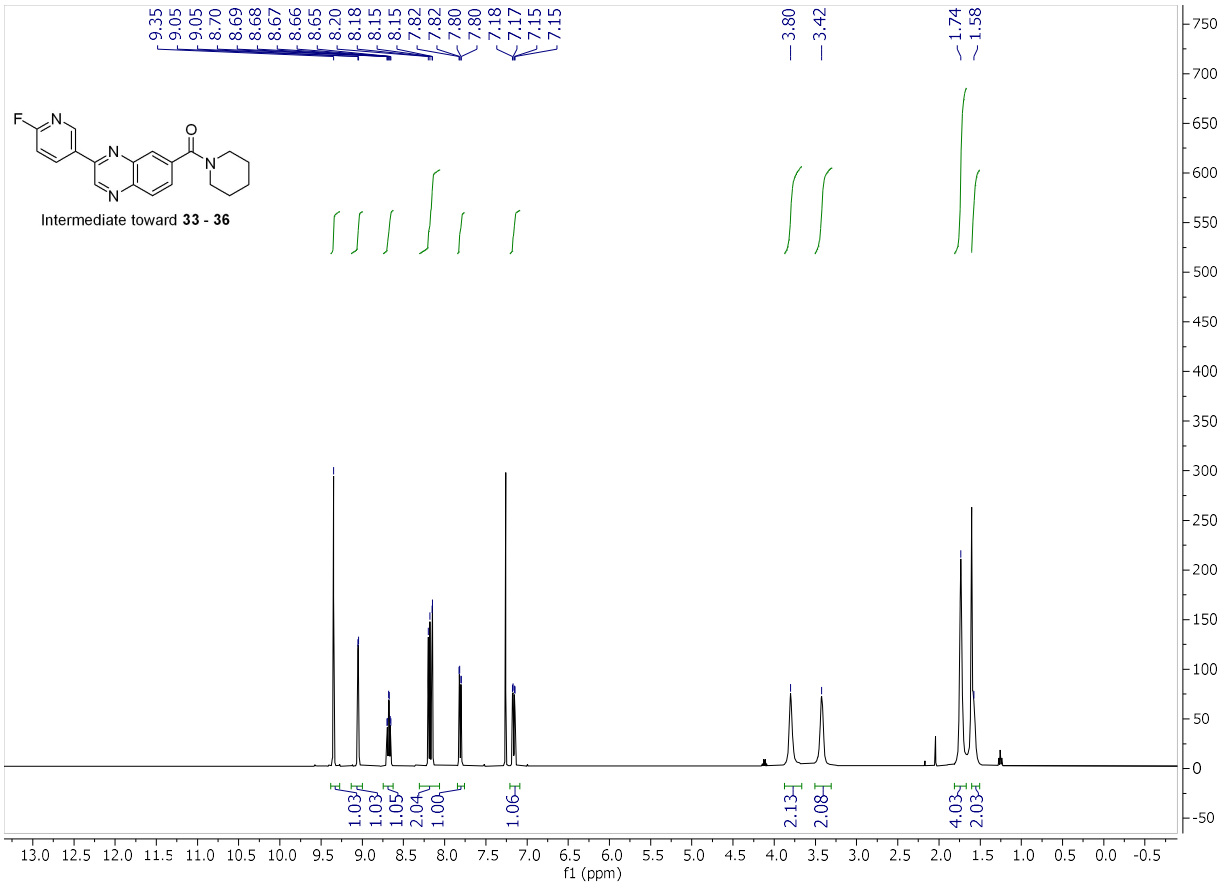
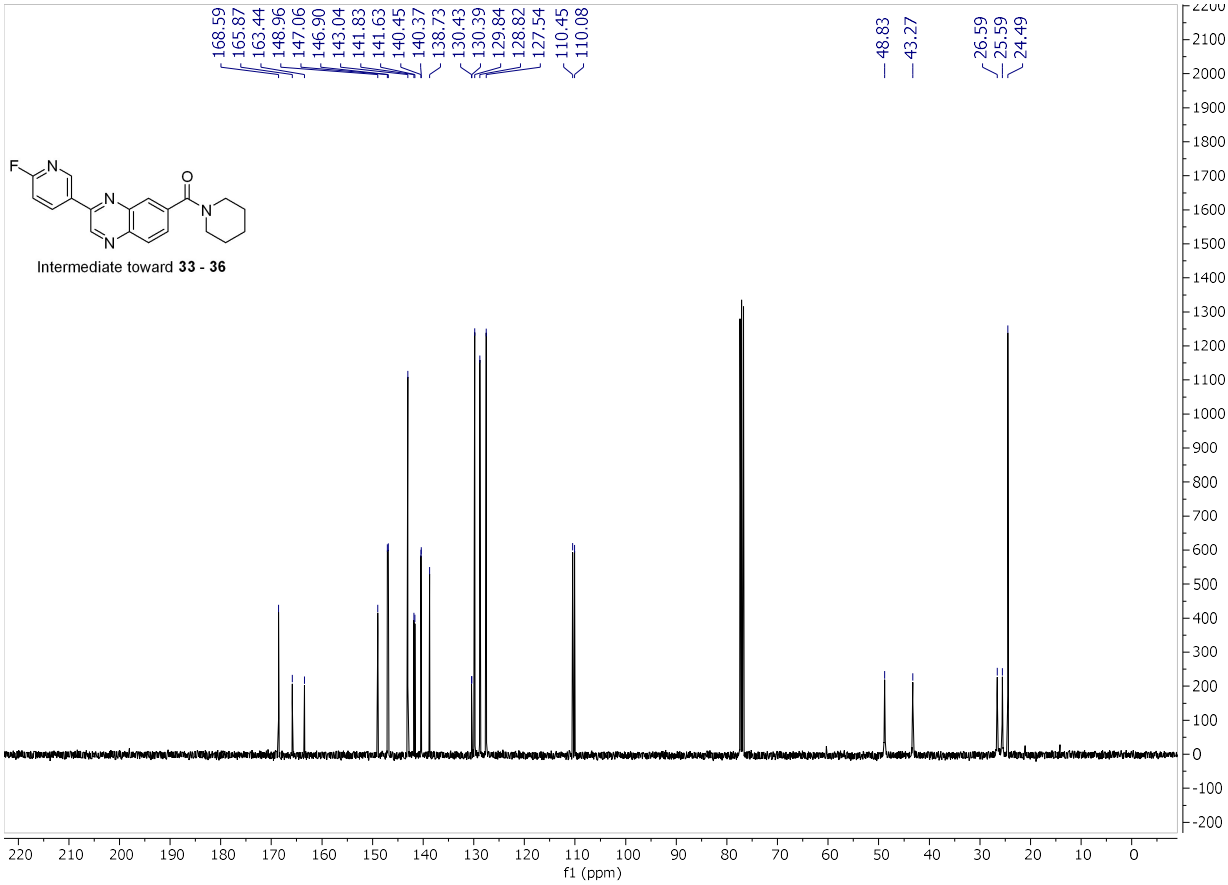
149.89
143.46
143.41
142.37
141.68
138.73
129.87
129.30
127.81
121.38
48.85
43.29
26.60
25.60
24.49
f1 (ppm)

32


9.35
9.05
9.05
8.70
8.69
8.68
8.67
8.66
8.65
8.20
8.18
8.15
8.15
7.82
7.82
7.80
7.80
7.18
7.17
7.15
7.15
3.80
3.42
1.74
1.58
Intermediate toward 33 - 36
1.03
1.03
1.05
2.04
1.00
1.06
2.13
2.08
4.03
2.03
f1 (ppm)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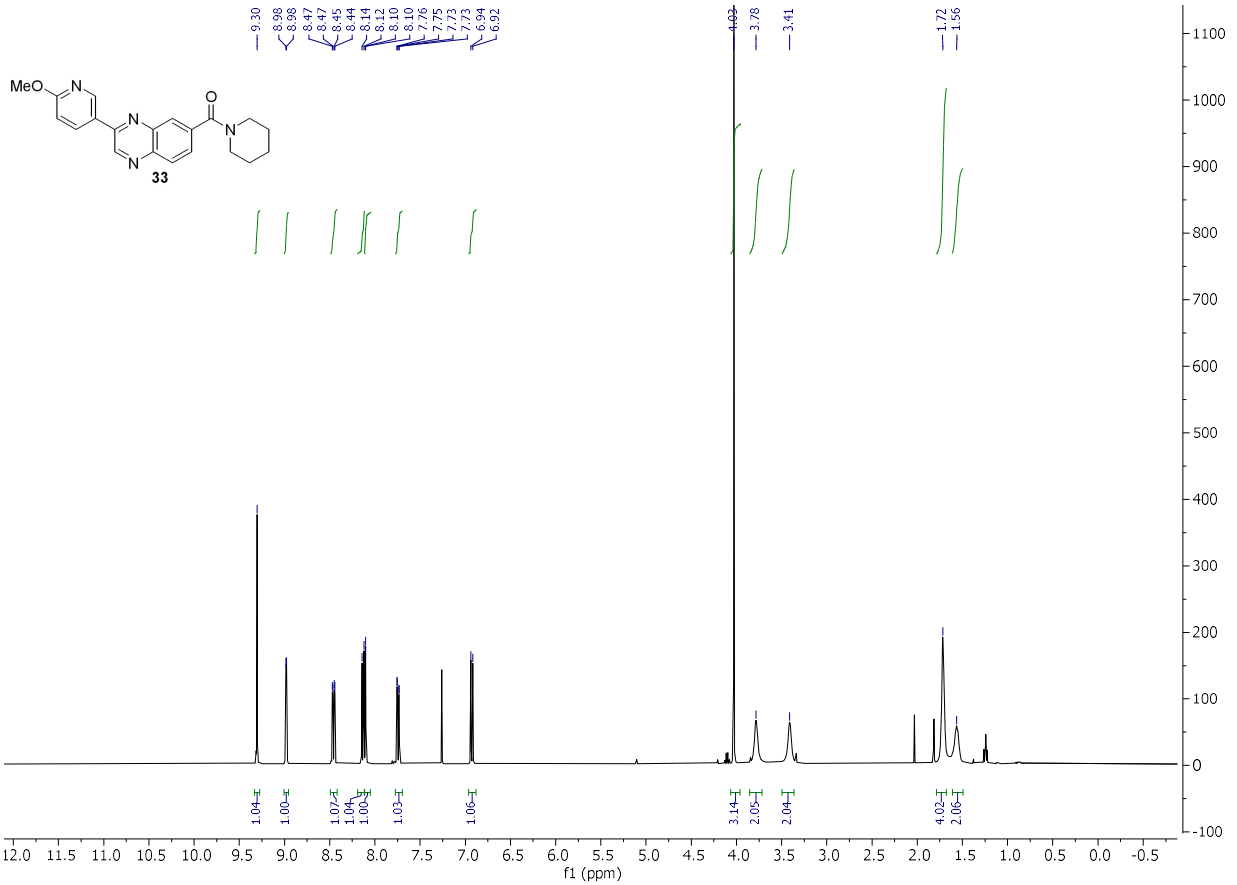
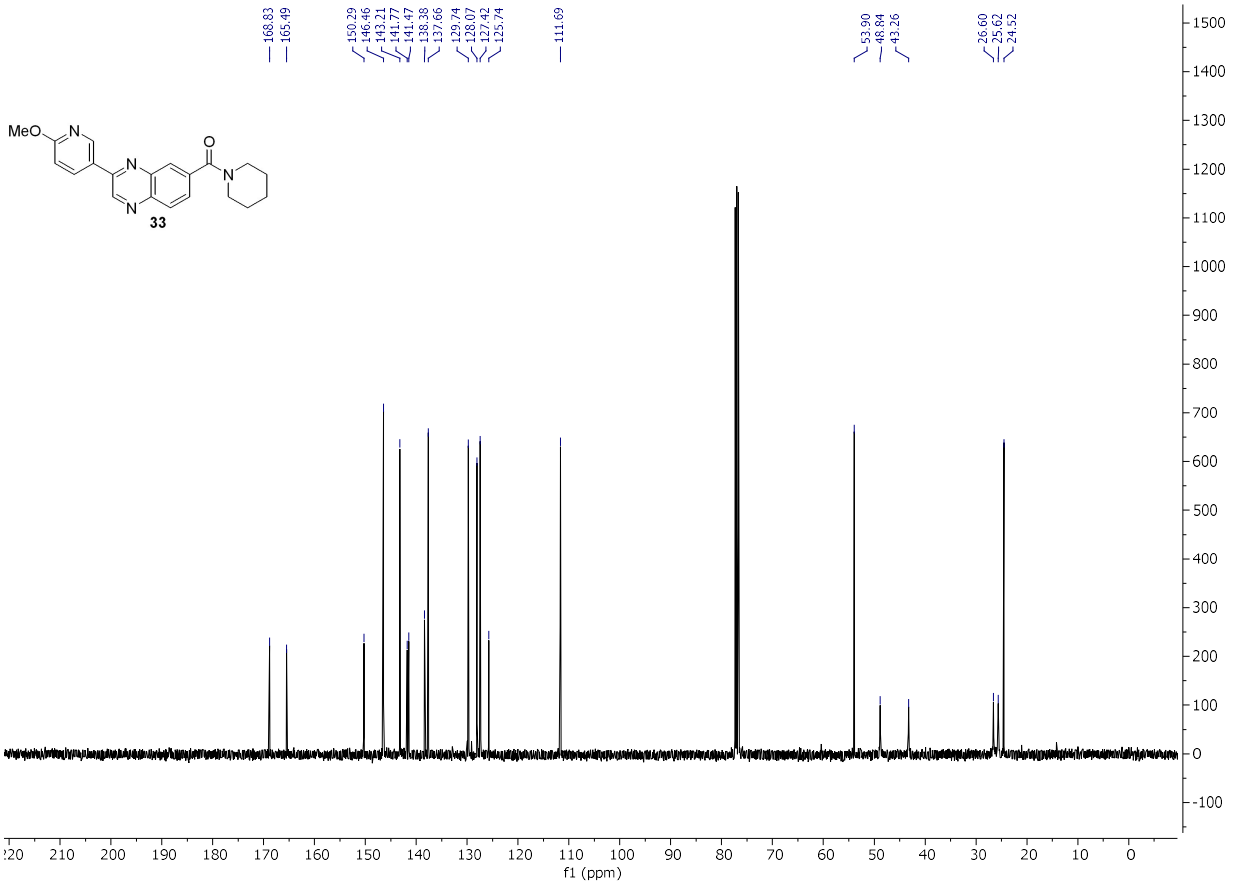
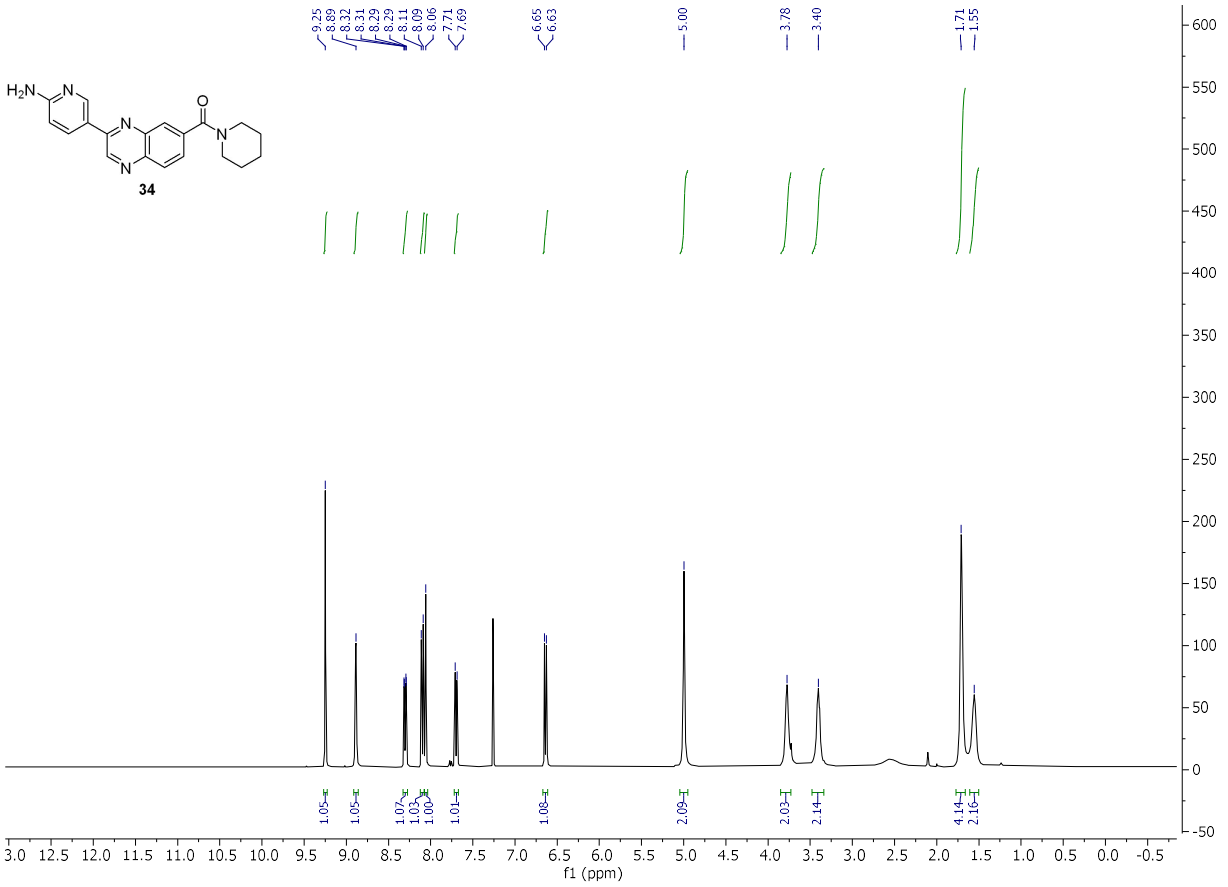
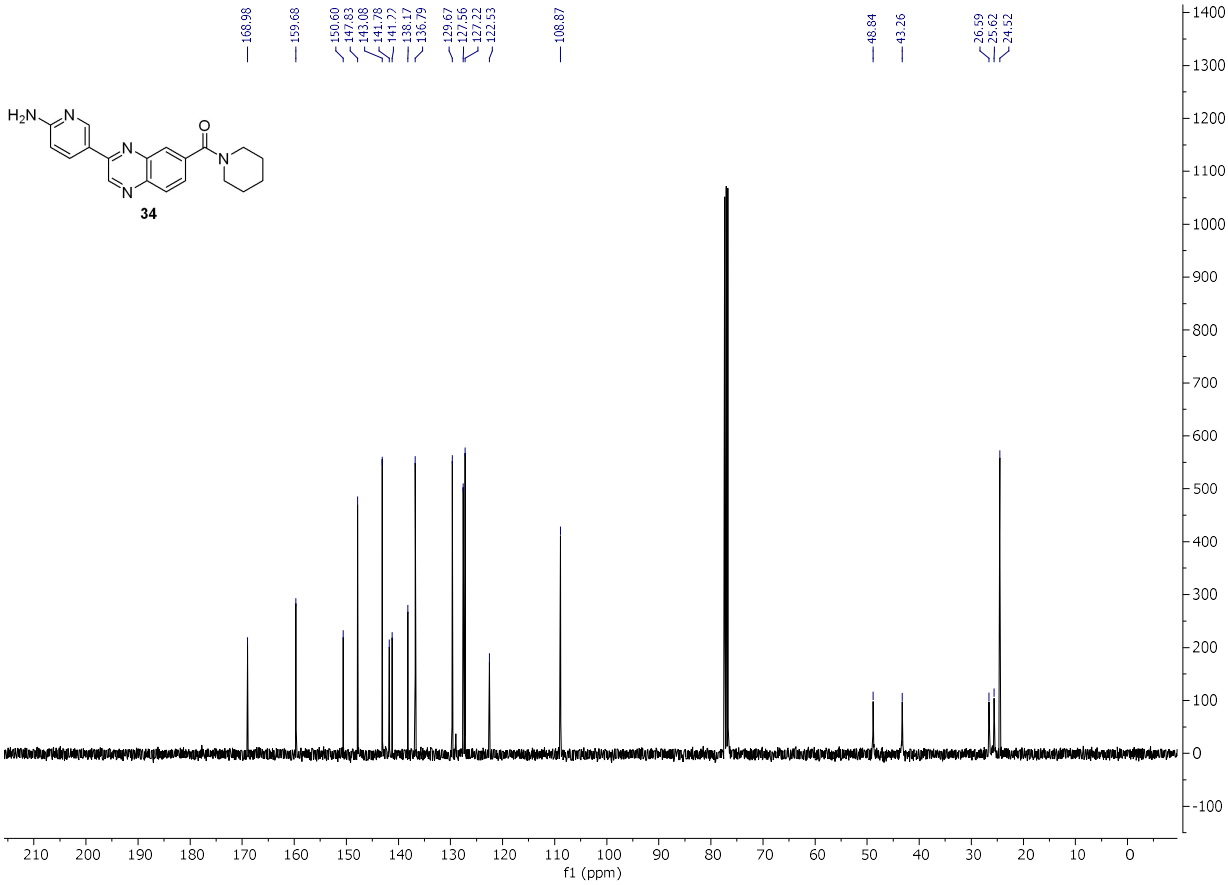
165.87
163.44
148.96
147.06
146.90
143.04
141.83
141.63
140.45
140.37
138.73
130.43
130.39
129.84
128.82
127.54
110.45
110.08
48.83
43.27
26.59
25.59
24.49
Intermediate toward 33 - 36
f1 (ppm)


9.30
8.98
8.98
8.47
8.47
8.45
8.44
8.14
8.12
8.10
8.10
7.76
7.75
7.73
7.73
6.94
6.92
4.03
3.78
3.41
1.72
1.56
MeO
N
O
N
N
N
33
1.04
1.00
1.07
1.04
1.00
1.03
1.06
3.14
2.05
2.04
4.02
2.06
f1 (ppm)


168.83
165.49
150.29
146.46
143.21
141.77
141.47
138.38
137.66
129.74
128.07
127.42
125.74
111.69
53.90
48.84
43.26
26.60
25.62
24.52
MeO
N
O
N
N
N
33
f1 (ppm)


9.25
8.89
8.32
8.31
8.29
8.29
8.11
8.09
8.06
7.71
7.69
6.65
6.63
5.00
3.78
3.40
1.71
1.55
34
f1 (ppm)


168.98
159.68
150.60
147.83
143.08
141.78
141.77
138.17
136.79
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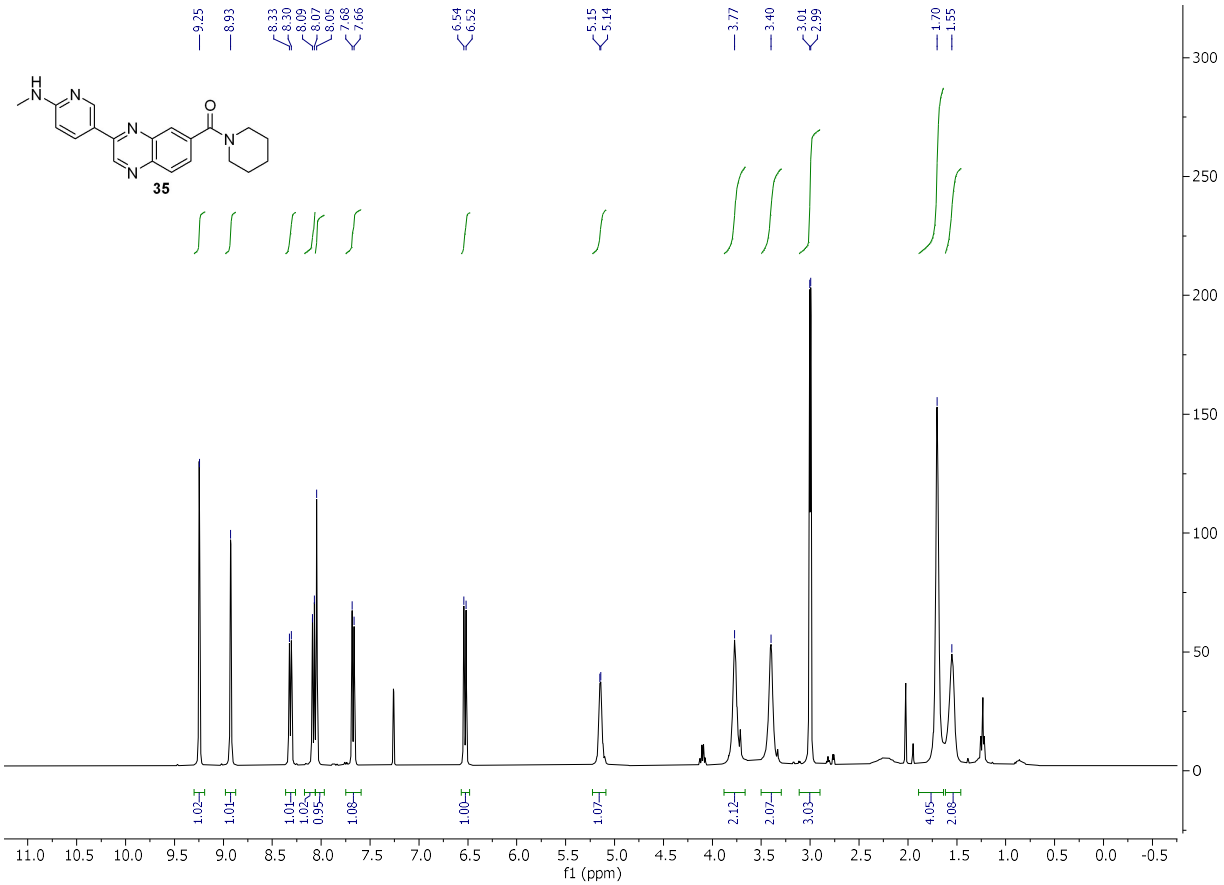
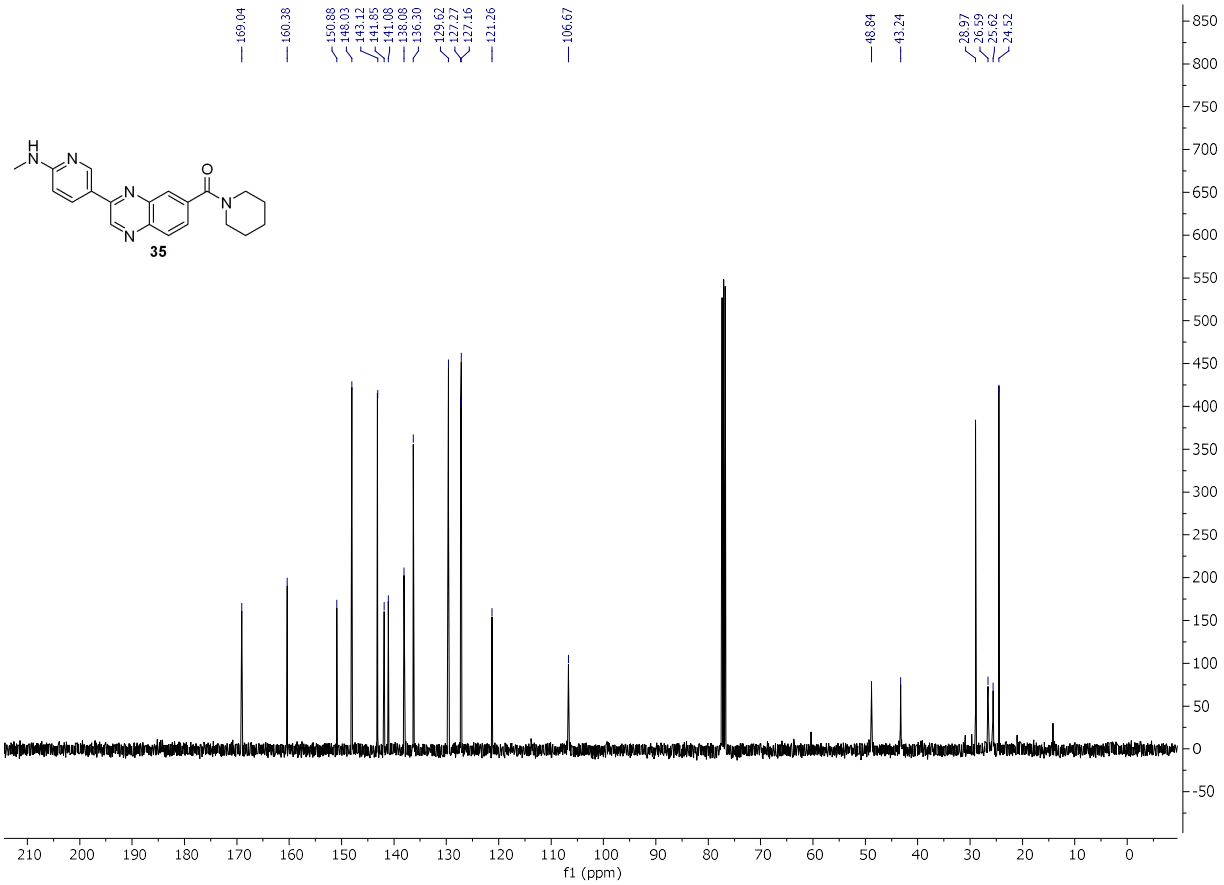
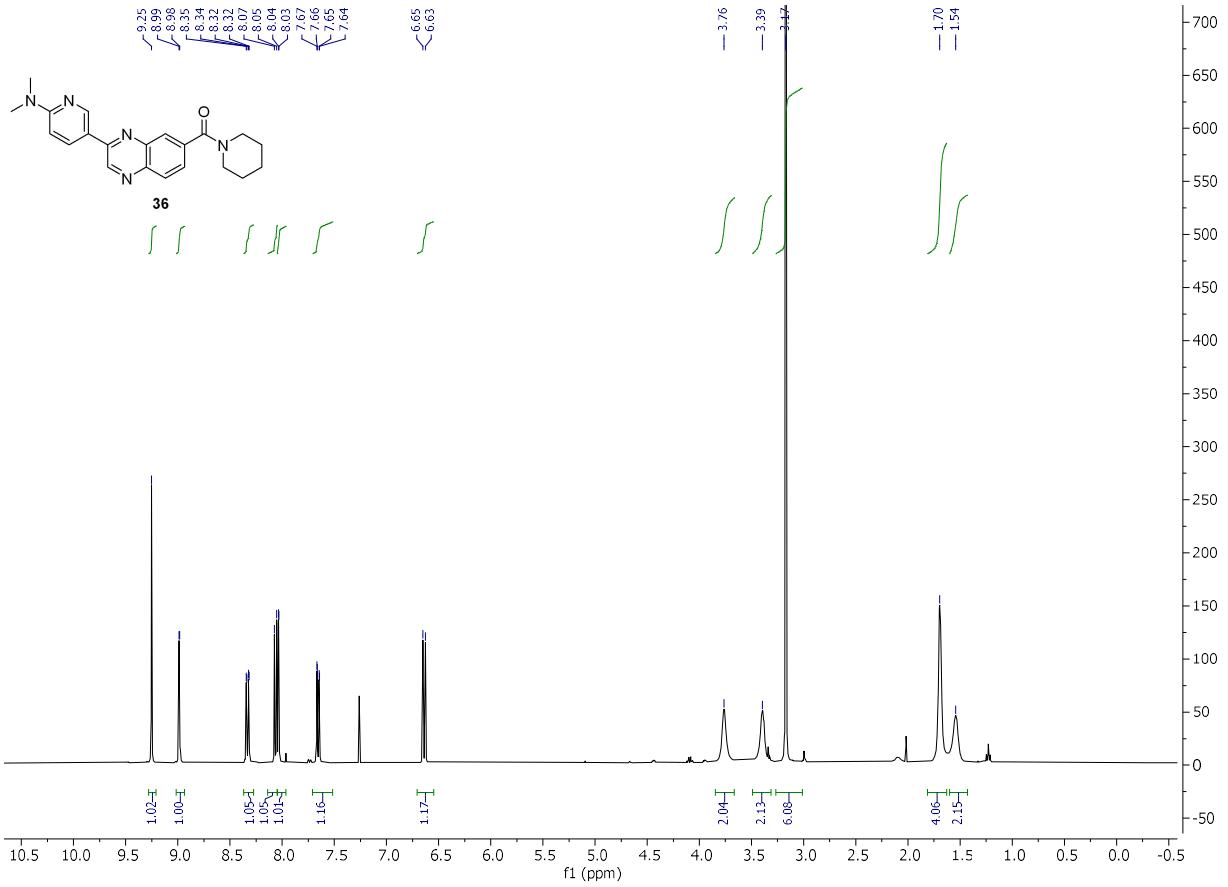
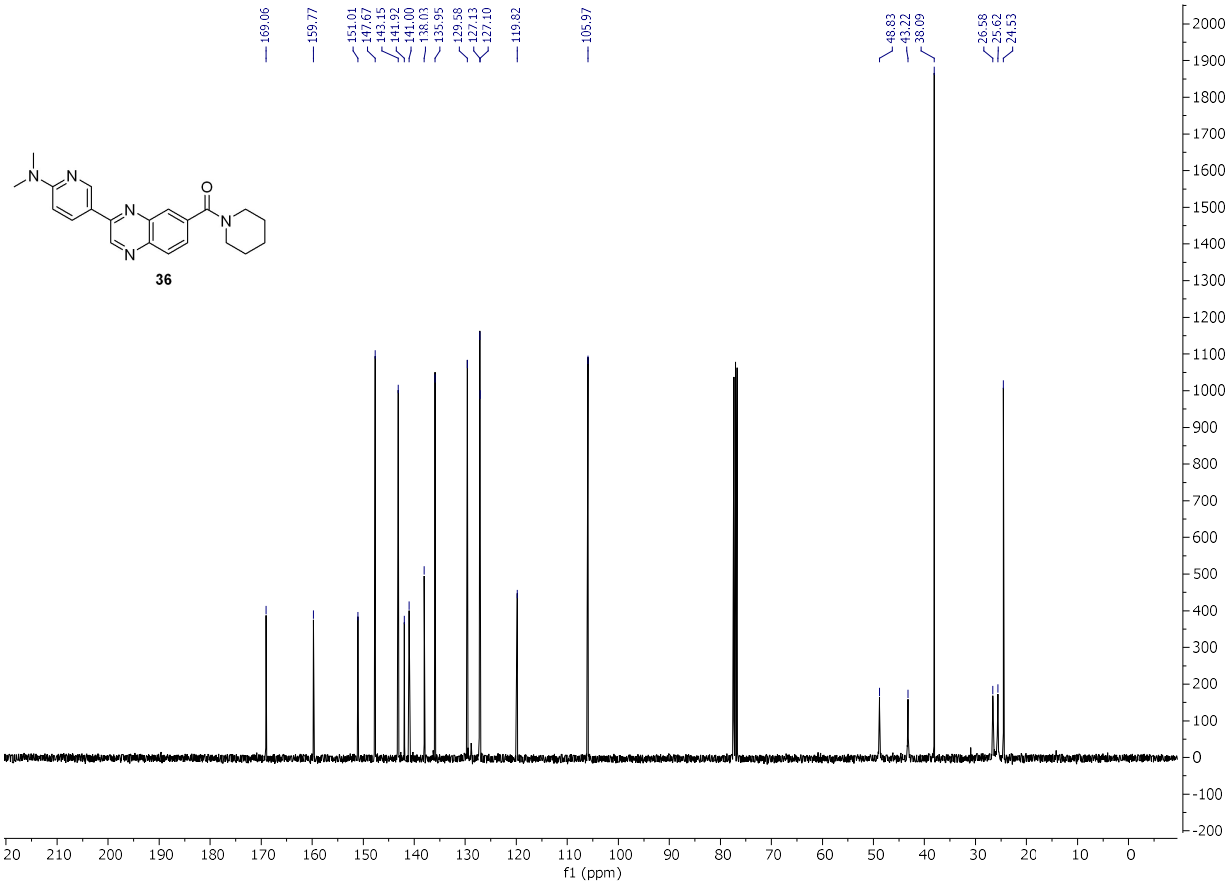
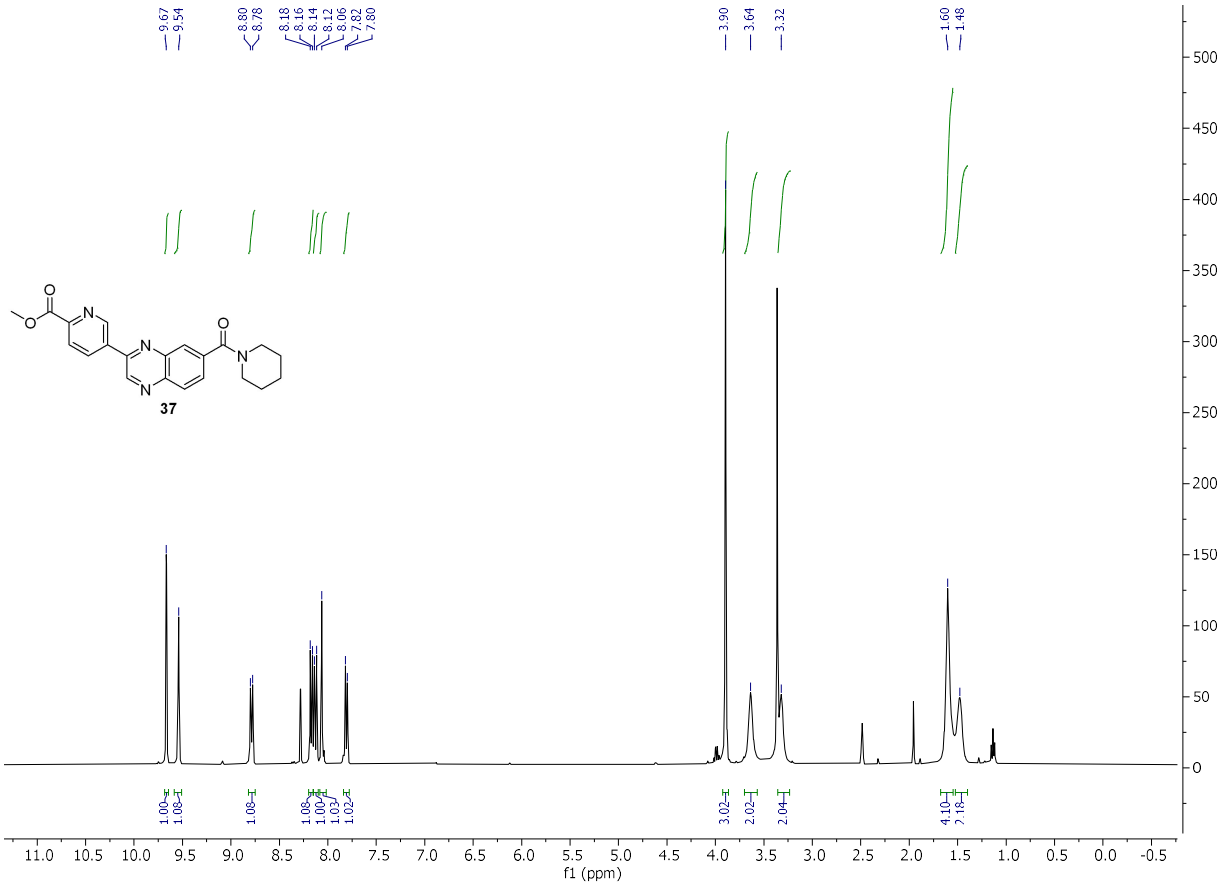
127.22
122.53
108.87
48.84
43.26
26.59
25.62
24.52
34
f1 (ppm)


9.25
8.93
8.33
8.30
8.09
8.07
8.05
7.68
7.66
6.54
6.52
5.15
5.14
3.77
3.40
3.01
2.99
1.70
1.55
35
1.02
1.01
1.01
1.02
0.95
1.08
1.00
1.07
2.12
2.07
3.03
4.05
2.08
f1 (ppm)


169.04
160.38
150.88
148.03
143.12
141.85
141.08
138.08
136.30
129.62
127.27
127.16
121.26
106.67
48.84
43.24
28.97
26.59
25.62
24.52
35
f1 (ppm)


9.25
8.99
8.98
8.35
8.34
8.32
8.32
8.07
8.05
8.04
8.03
7.67
7.66
7.65
7.64
6.65
6.63
3.76
3.39
1.70
1.54
36
1.02
1.00
1.05
1.05
1.01
1.16
1.17
2.04
2.13
6.08
4.06
2.15
f1 (ppm)


169.06
159.77
151.01
147.67
143.15
141.92
141.00
138.03
135.95
129.58
127.13
127.10
119.82
105.97
48.83
43.22
38.09
26.58
25.62
24.53
36
f1 (ppm)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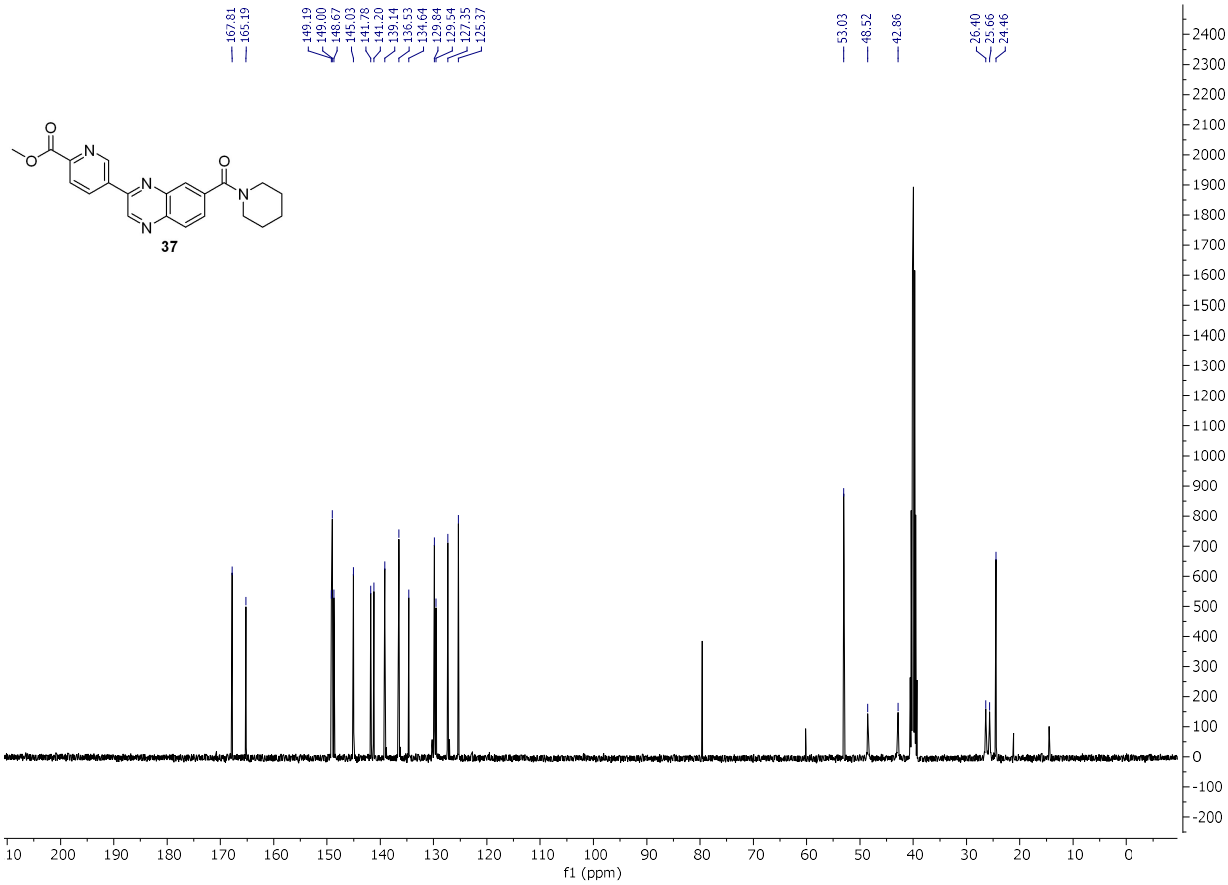
9.54
8.80
8.78
8.18
8.16
8.14
8.12
8.06
7.82
7.80
3.90
3.64
3.32
1.60
1.48
37
f1 (ppm)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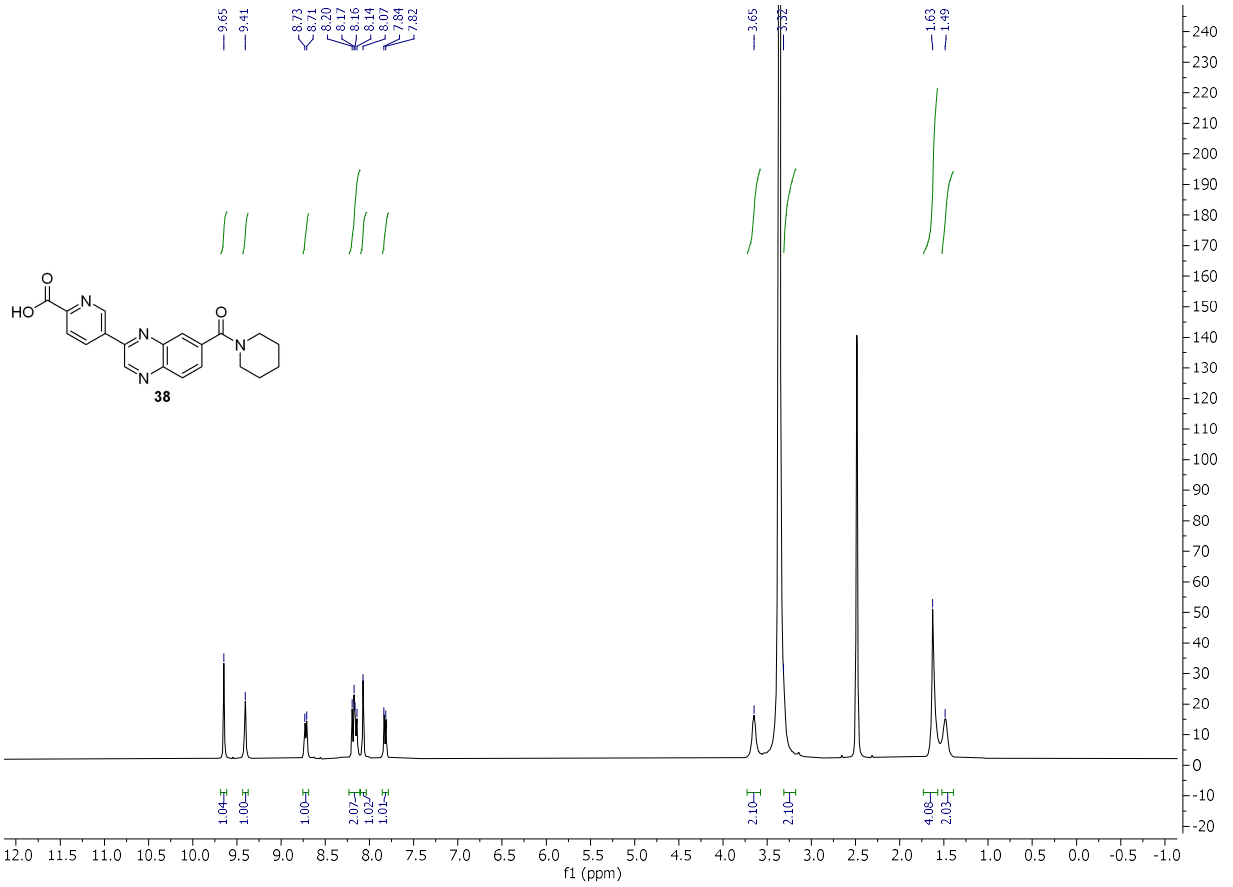
165.19
149.19
149.00
148.67
145.03
141.78
141.20
139.14
136.53
134.64
129.84
129.54
127.35
125.37
53.03
48.52
42.86
26.40
25.66
24.46
37
f1 (ppm)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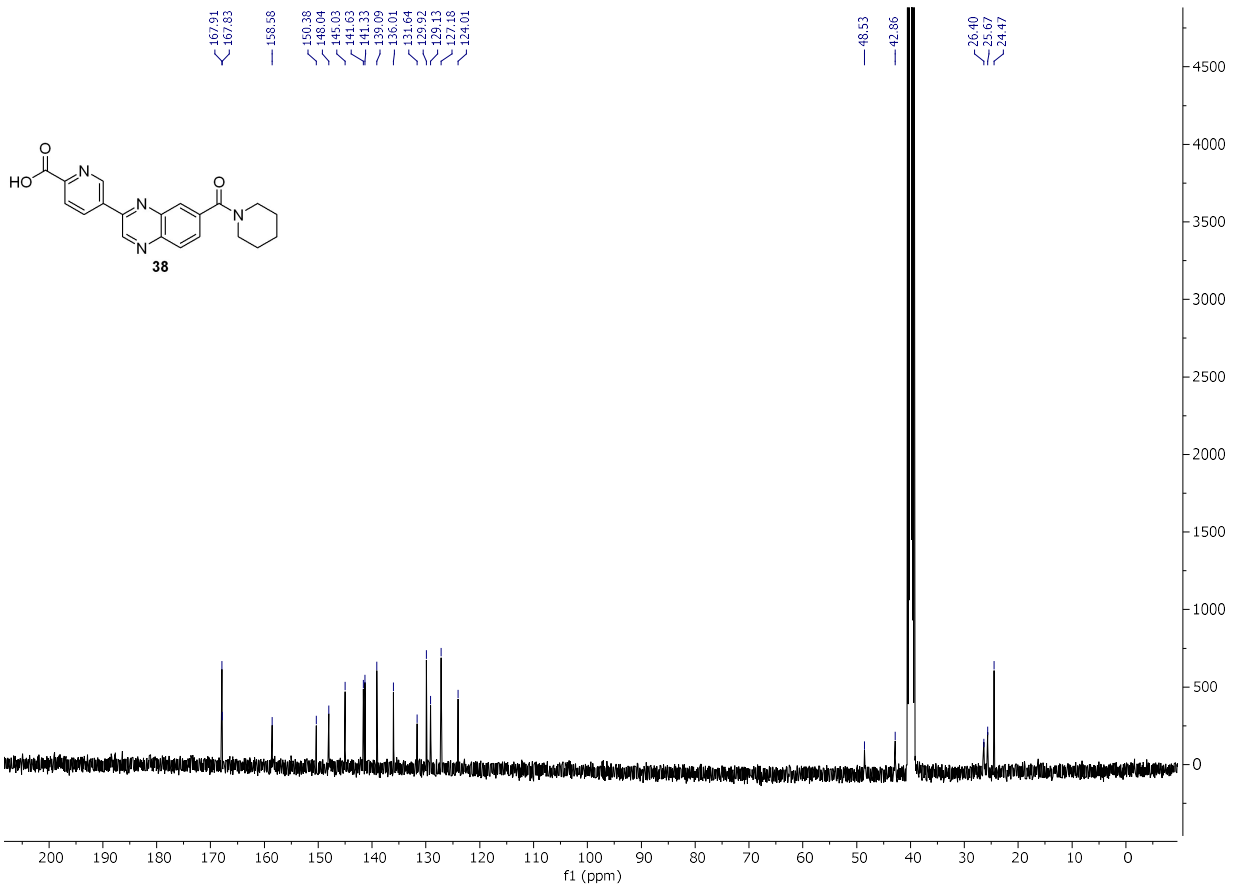
9.41
8.73
8.71
8.20
8.17
8.16
8.14
8.07
7.84
7.82
3.65
3.32
1.63
1.49
38
1.04
1.00
1.00
2.07
1.02
1.01
2.10
2.10
4.08
2.03
f1 (ppm)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167.83
158.58
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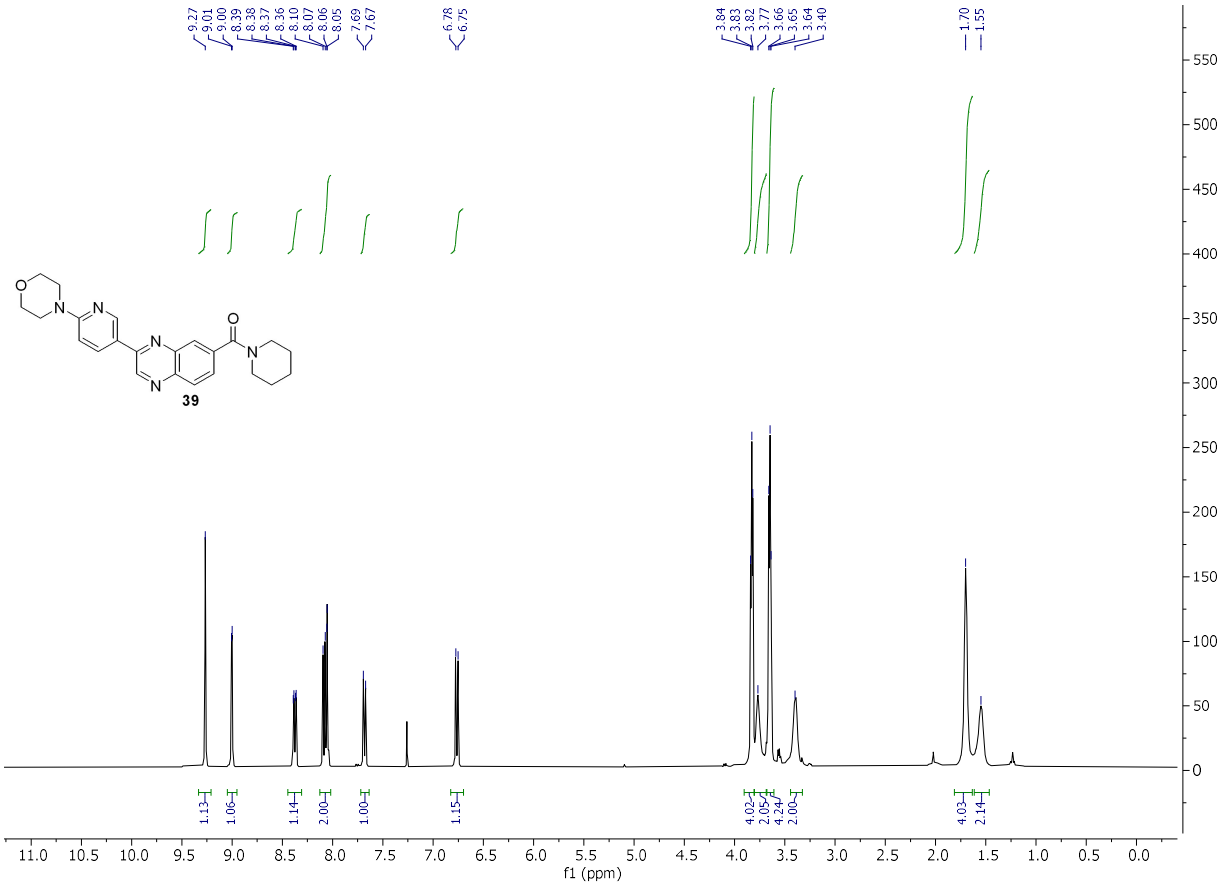
148.04
145.03
141.63
141.33
139.09
136.01
131.64
129.92
129.13
127.18
124.01
48.53
42.86
26.40
25.67
24.47
38
f1 (ppm)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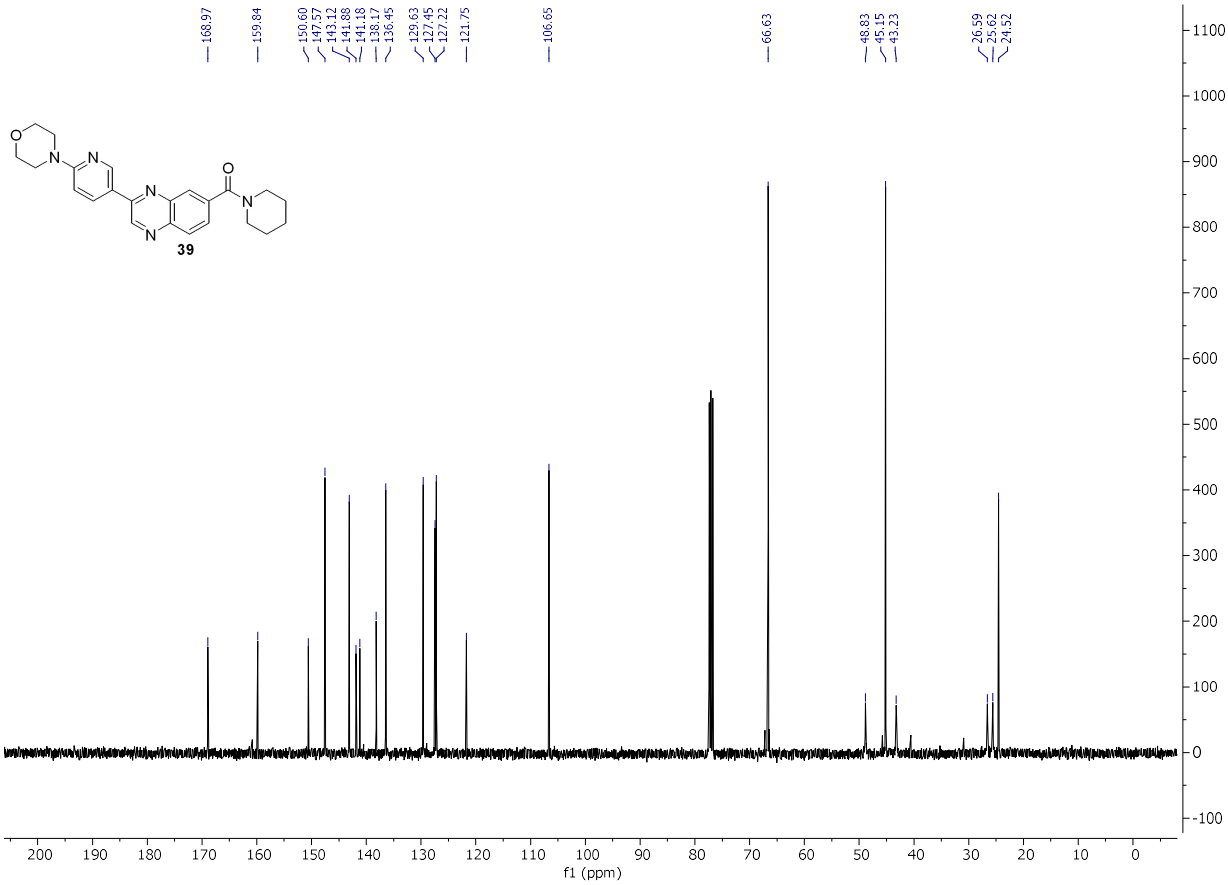
9.00
8.39
8.38
8.37
8.36
8.10
8.07
8.06
8.05
7.69
7.67
6.78
6.75
3.84
3.83
3.82
3.77
3.66
3.65
3.64
3.40
1.70
1.55
1.13
1.06
1.14
2.00
1.00
1.15
4.02
2.05
4.24
2.00
4.03
2.14
39
f1 (ppm)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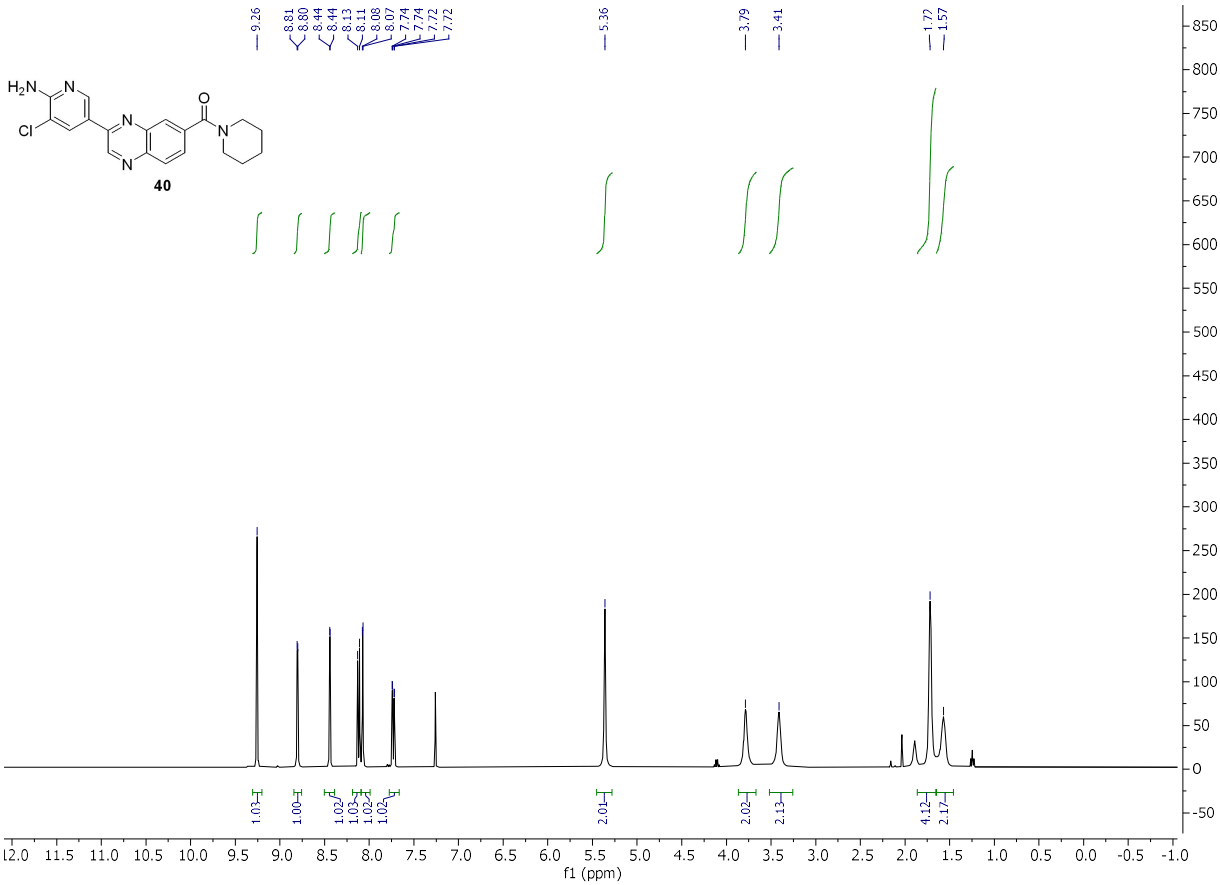
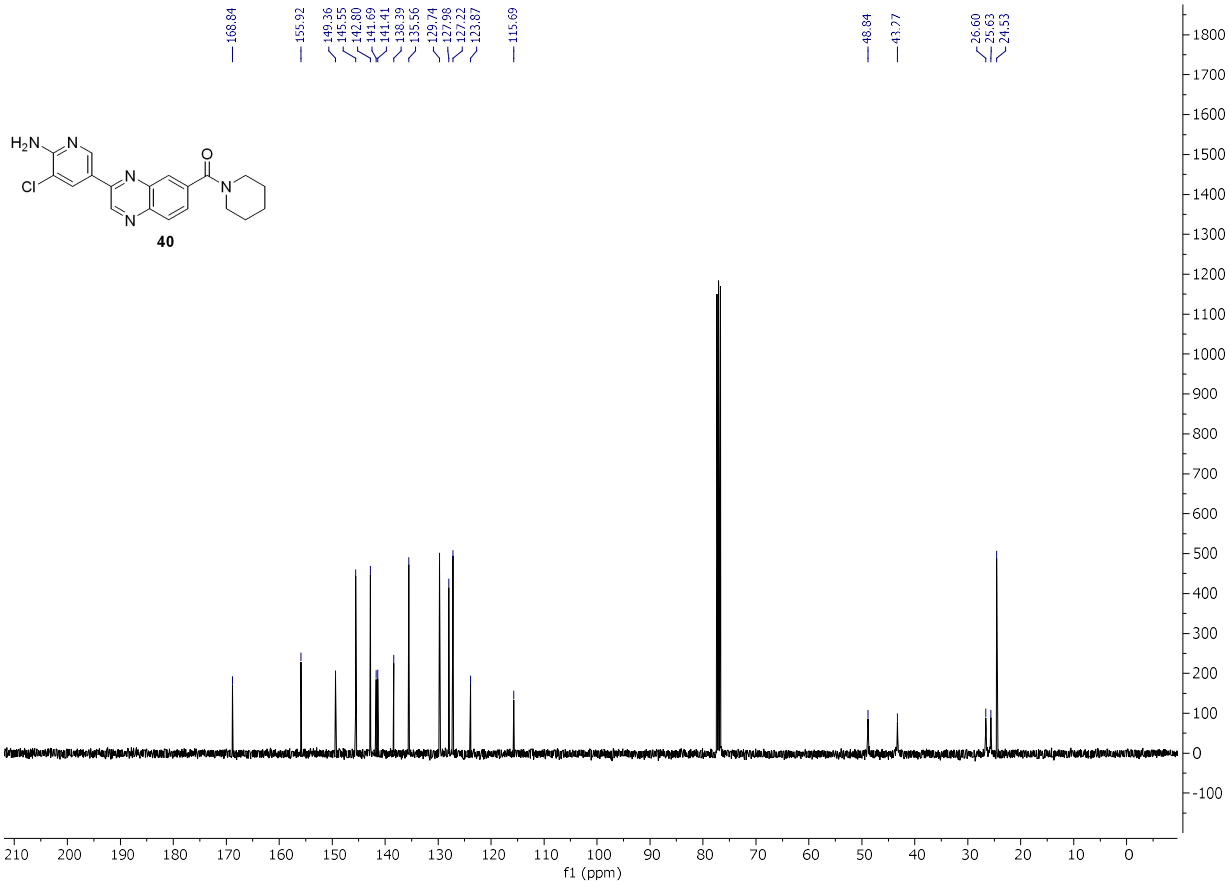
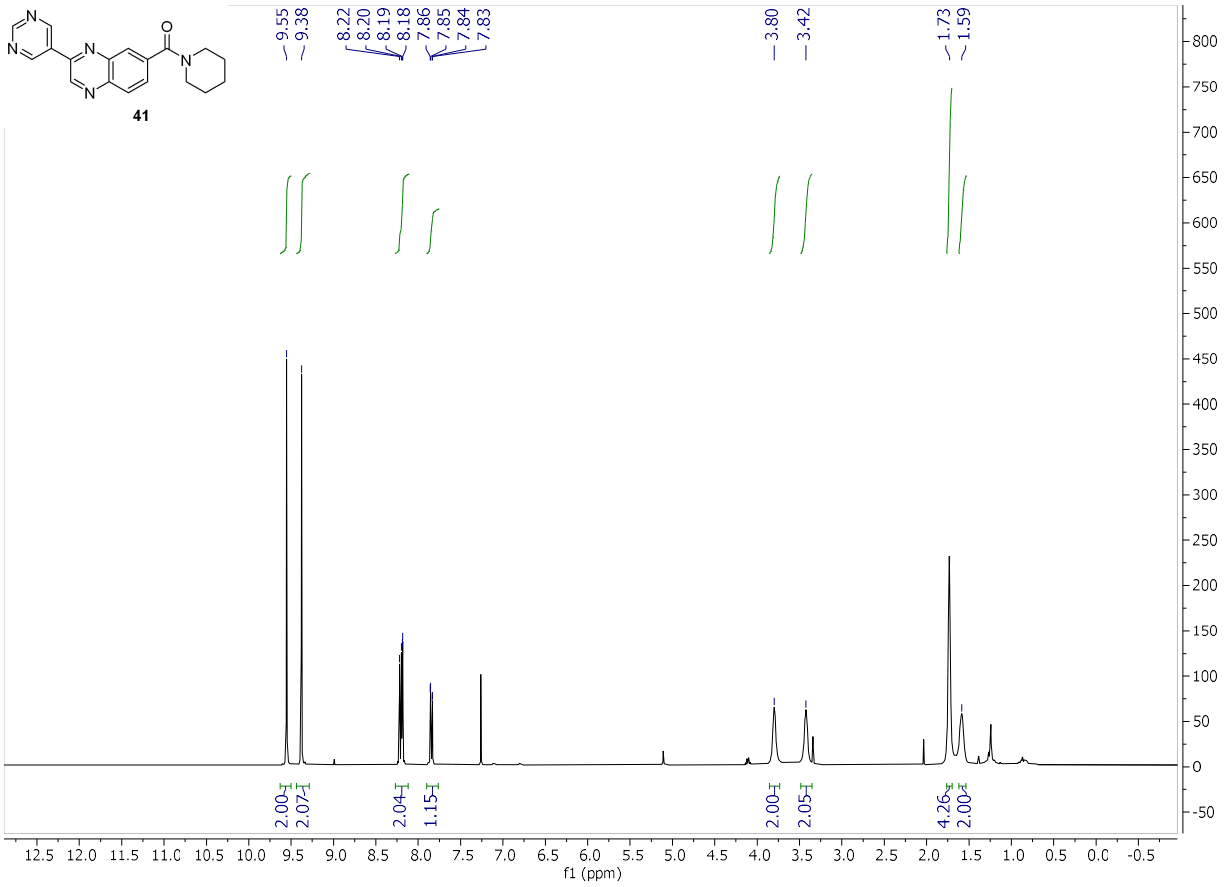
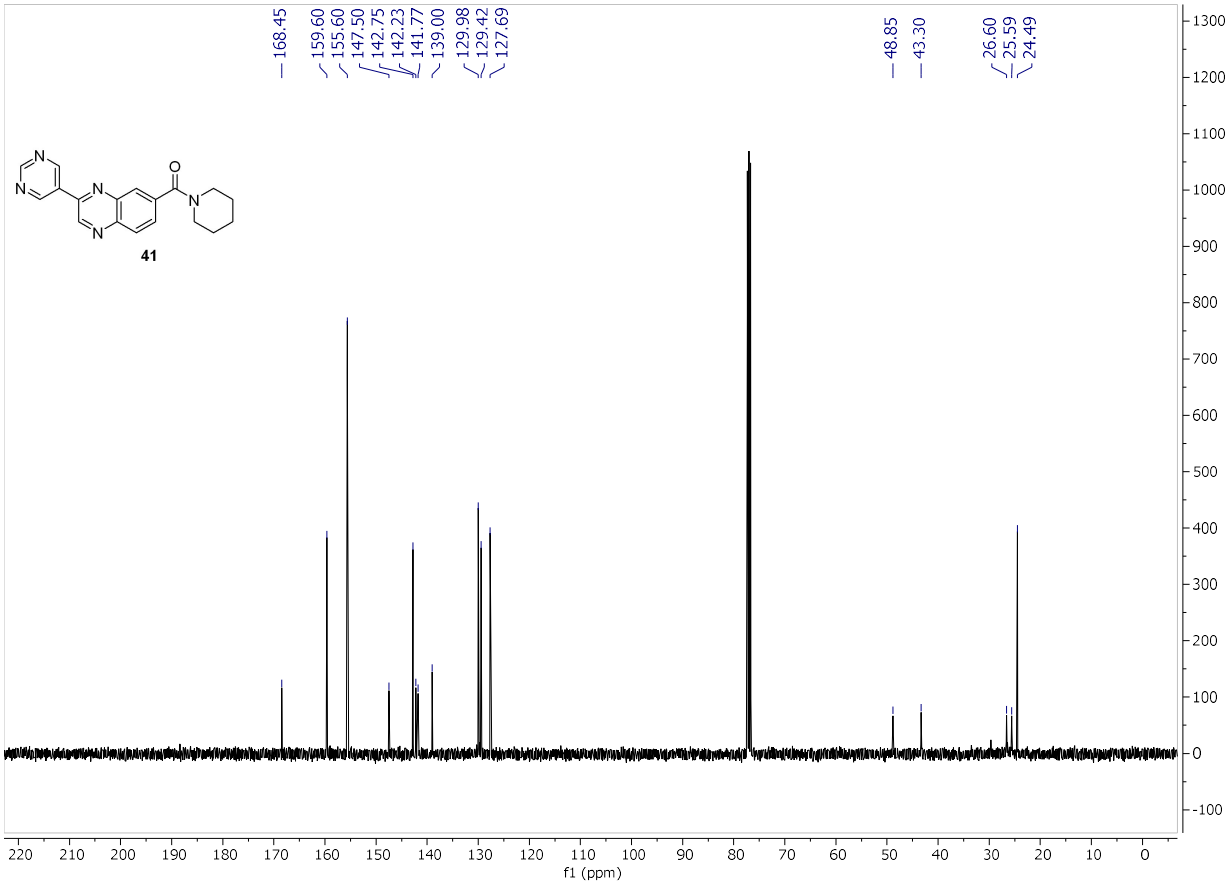
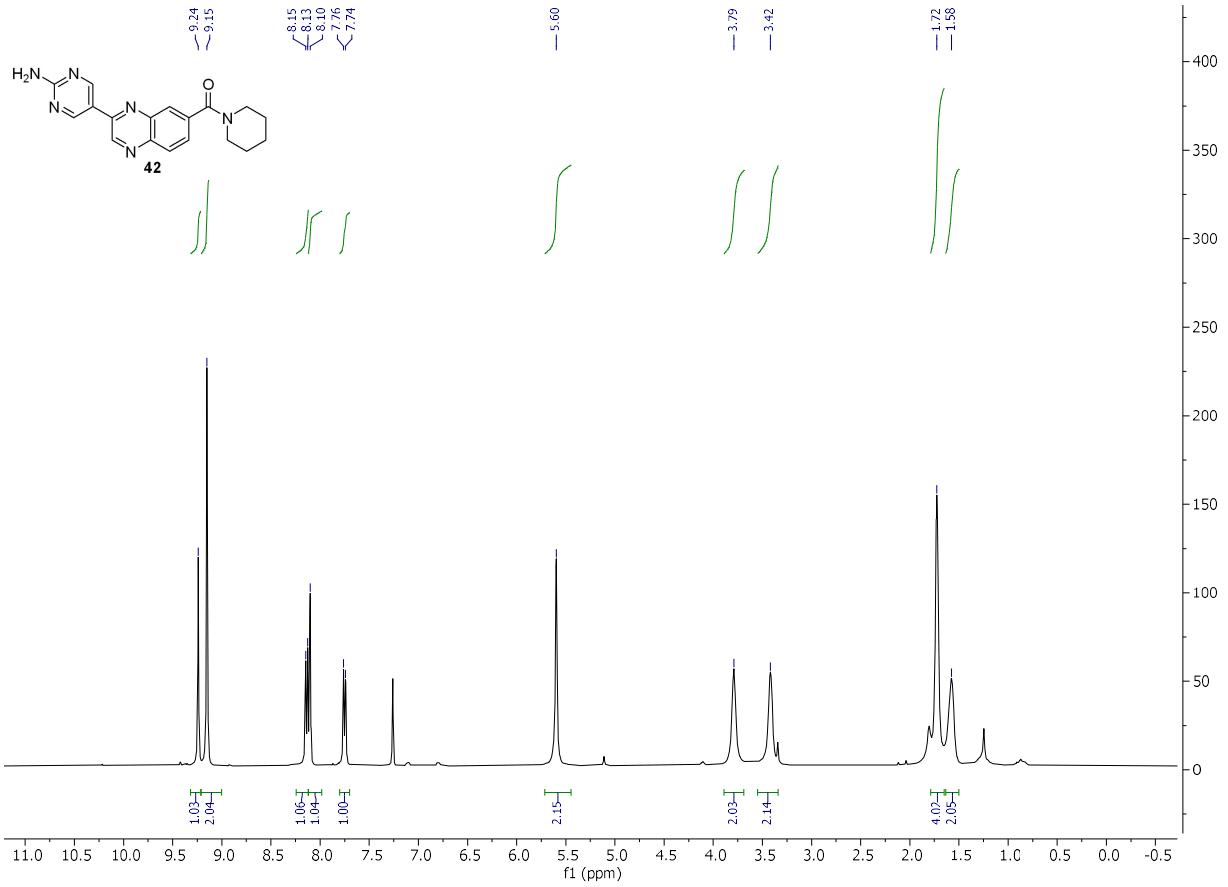
159.84
150.60
147.57
143.12
141.88
141.18
138.17
136.45
129.63
127.45
127.22
121.75
106.65
66.63
48.83
45.15
43.23
26.59
25.62
24.52
39
f1 (ppm)

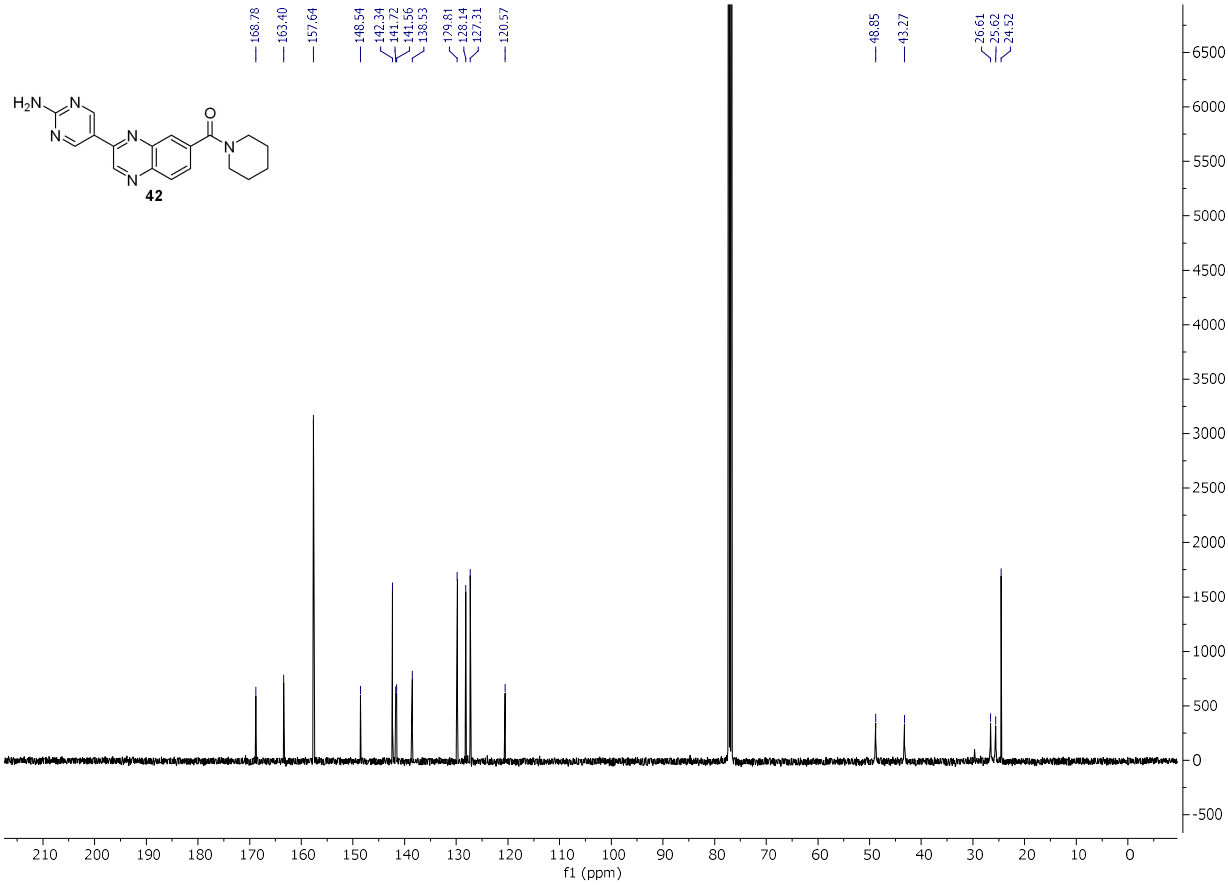

9.26
8.81
8.80
8.44
8.44
8.13
8.11
8.08
8.07
7.74
7.74
7.72
7.72
5.36
3.79
3.41
1.77
1.57
1.03
1.00
1.02
1.03
1.02
1.02
2.01
2.02
2.13
4.12
2.17
f1 (ppm)

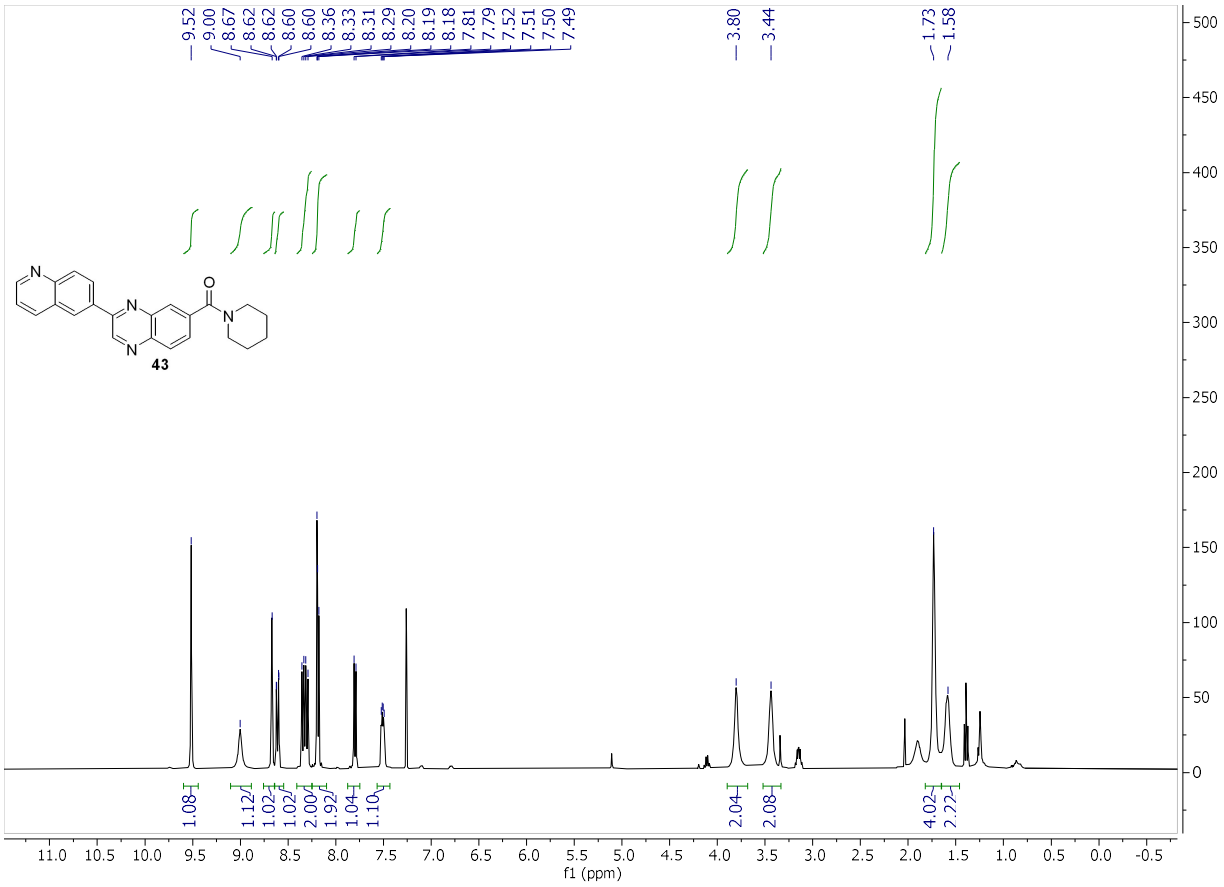

168.84
155.92
149.36
145.55
142.80
141.69
141.41
138.39
135.56
129.74
127.98
127.22
123.87
115.69
48.84
43.77
26.60
25.63
24.53
f1 (ppm)

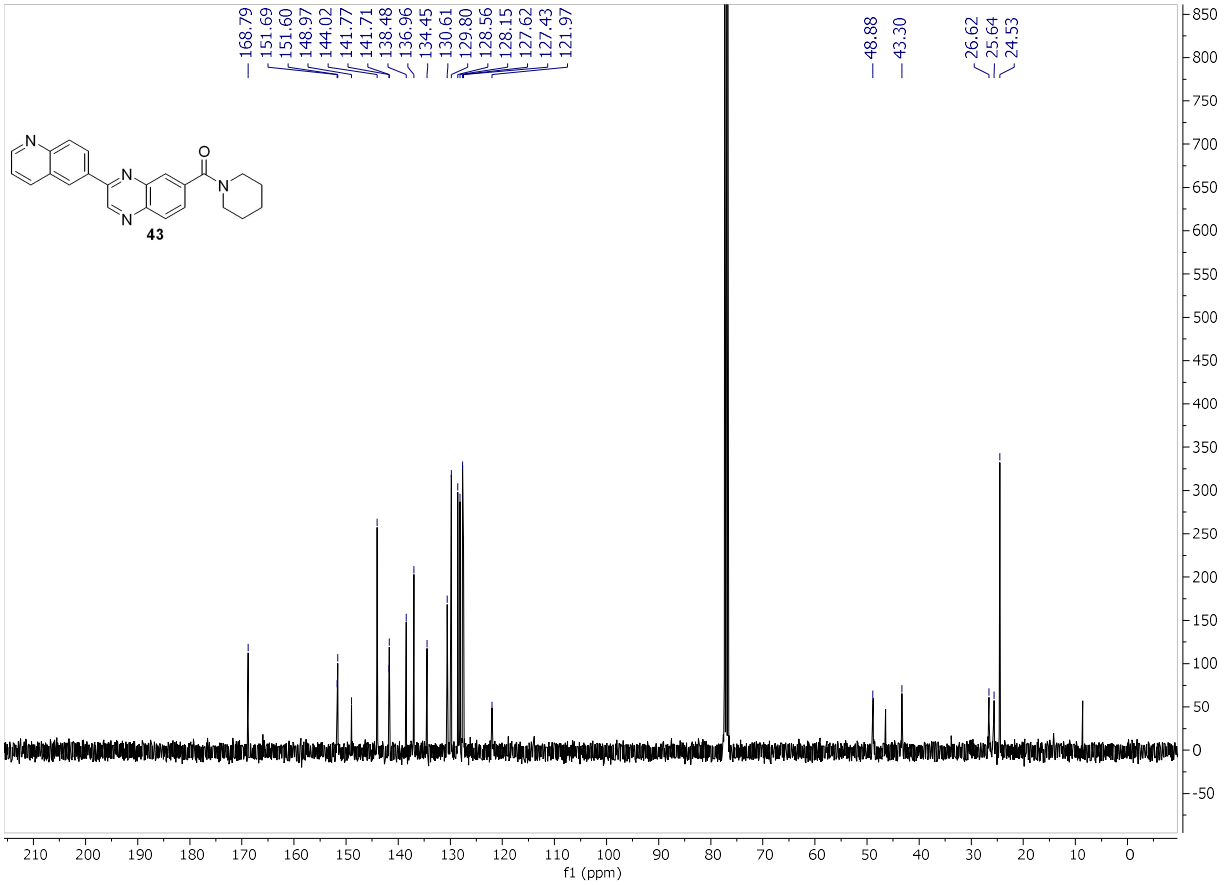

41
9.55
9.38
8.22
8.20
8.19
8.18
7.86
7.85
7.84
7.83
3.80
3.42
1.73
1.59
2.00
2.07
2.04
1.15
2.00
2.05
4.26
2.00
f1 (ppm)


41
168.45
159.60
155.60
147.50
142.75
142.23
141.77
139.00
129.98
129.42
127.69
48.85
43.30
26.60
25.59
24.49
f1 (ppm)


9.24
9.15
8.15
8.13
8.10
7.76
7.74
5.60
3.79
3.42
1.72
1.58
42
1.03
2.04
1.06
1.04
1.00
2.15
2.03
2.14
4.02
2.05
f1 (ppm)


168.78
163.40
157.64
148.54
142.34
141.72
141.56
138.53
129.81
128.14
127.31
120.57
48.85
43.27
26.61
25.62
24.52
42
f1 (ppm)


9.52
9.00
8.67
8.62
8.62
8.60
8.60
8.36
8.33
8.31
8.29
8.20
8.19
8.18
7.81
7.79
7.52
7.51
7.50
7.49
3.80
3.44
1.73
1.58
1.08
1.12
1.02
1.02
2.00
1.92
1.04
1.10
2.04
2.08
4.02
2.22
f1 (ppm)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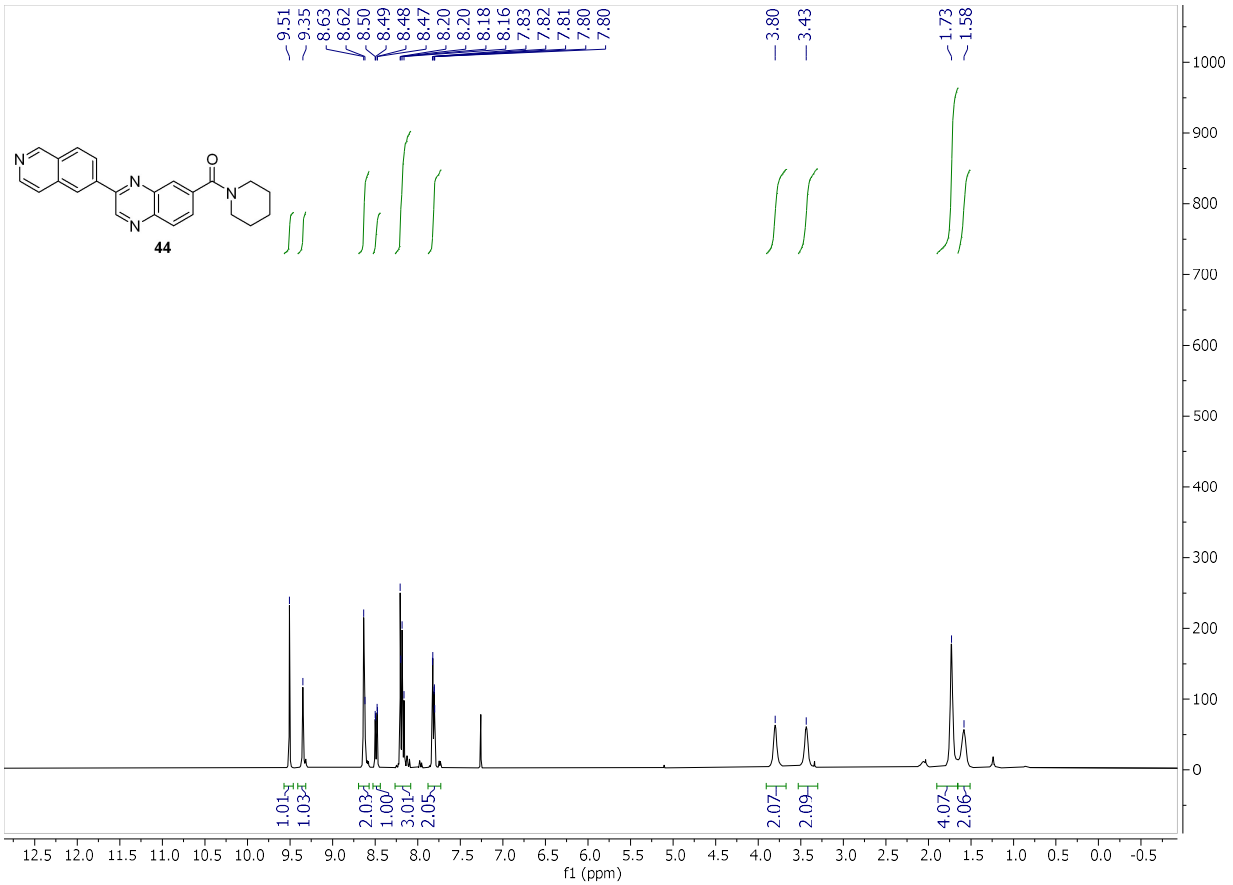
151.69
151.60
148.97
144.02
141.77
141.71
138.48
136.96
134.45
130.61
129.80
128.56
128.15
127.62
127.43
121.97
48.88
43.30
26.62
25.64
24.53
f1 (ppm)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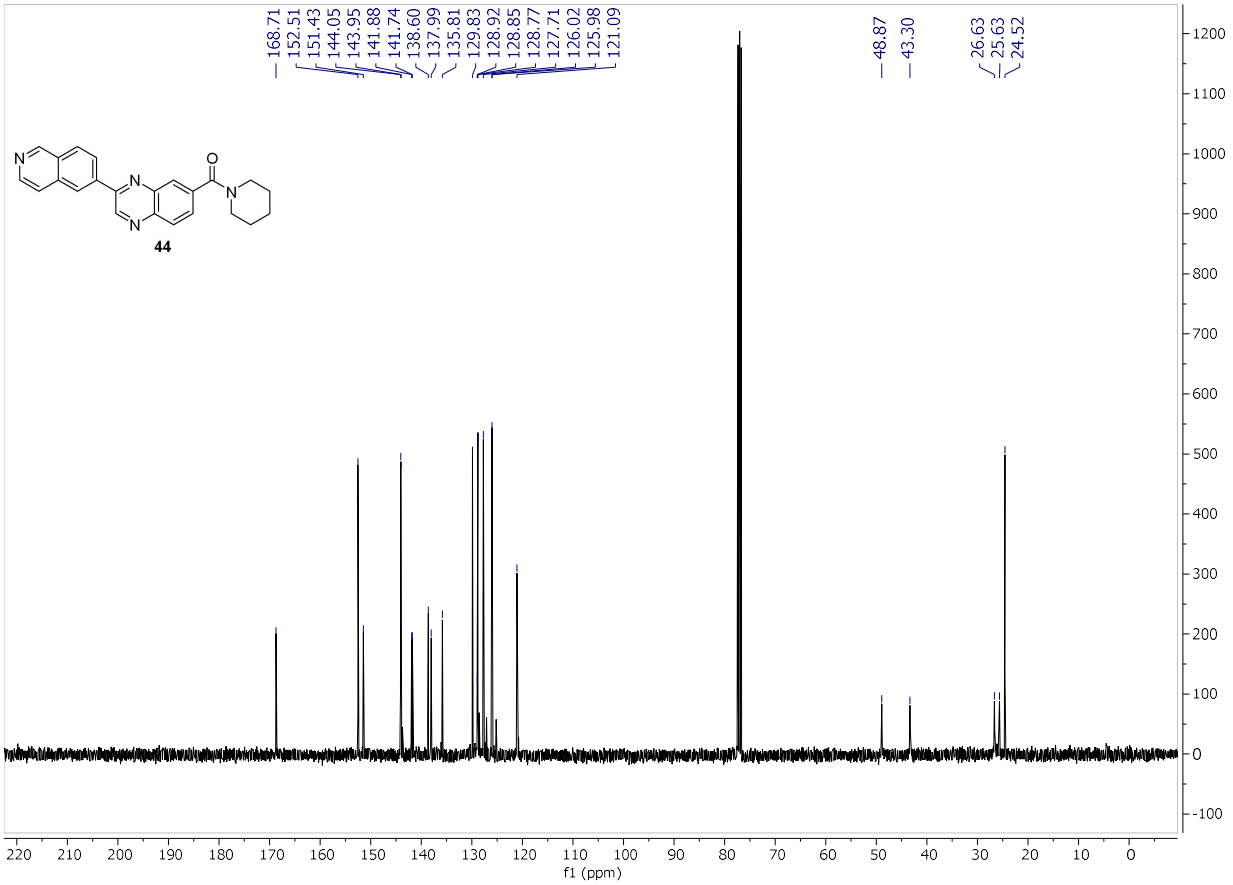
9.35
8.63
8.62
8.50
8.49
8.48
8.47
8.20
8.20
8.18
8.16
7.83
7.82
7.81
7.80
7.80
3.80
3.43
1.73
1.58
44
1.01
1.03
2.03
1.00
3.01
2.05
2.07
2.09
4.07
2.06
f1 (ppm)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151.43
144.05
143.95
141.88
141.74
138.60
137.99
135.81
129.83
128.92
128.85
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125.98
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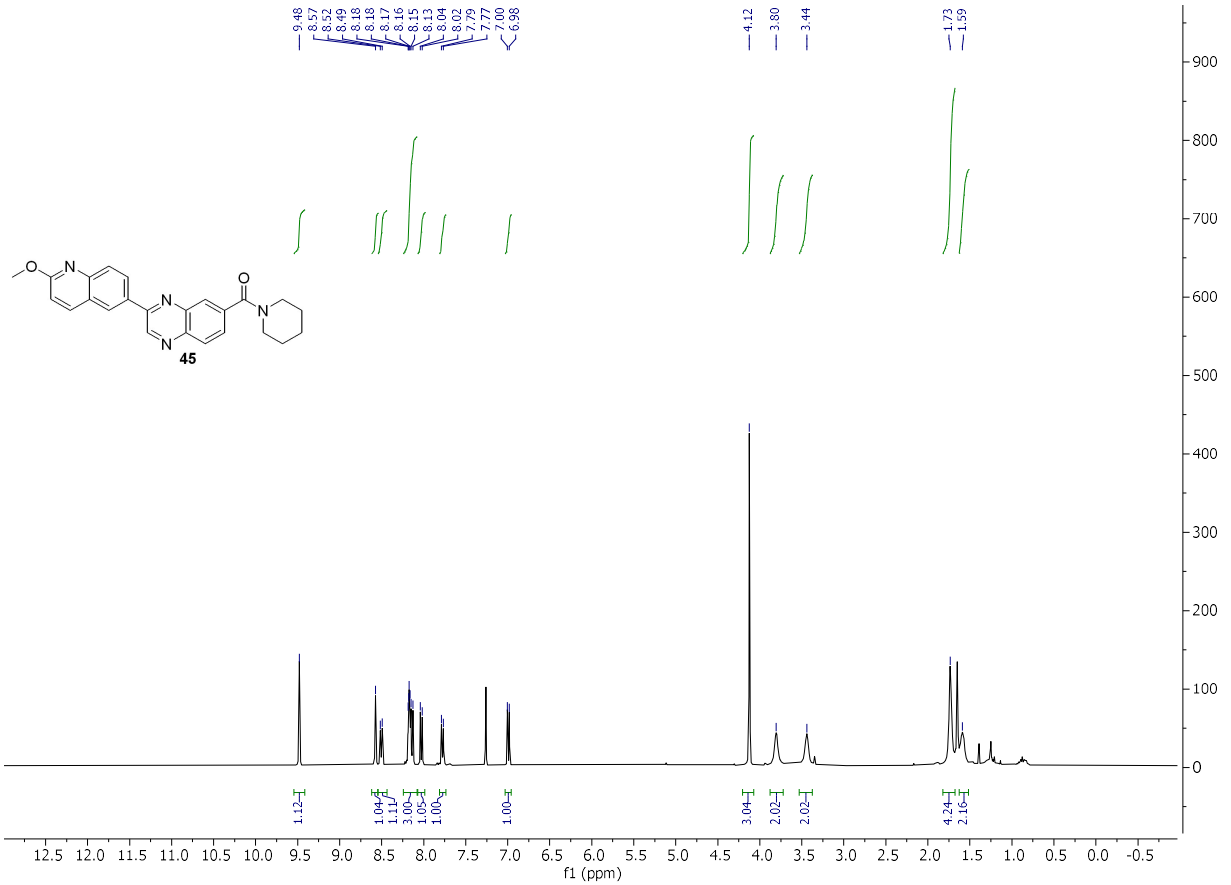
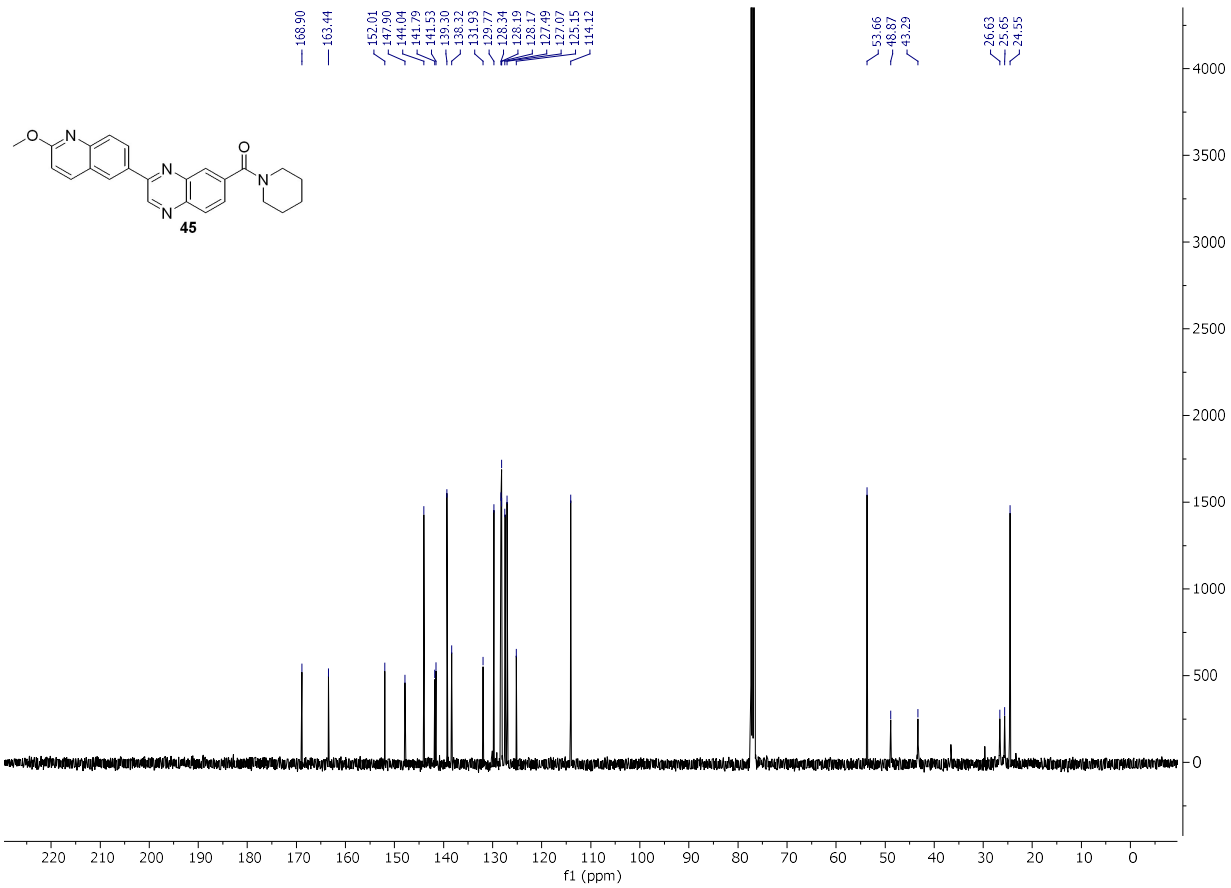
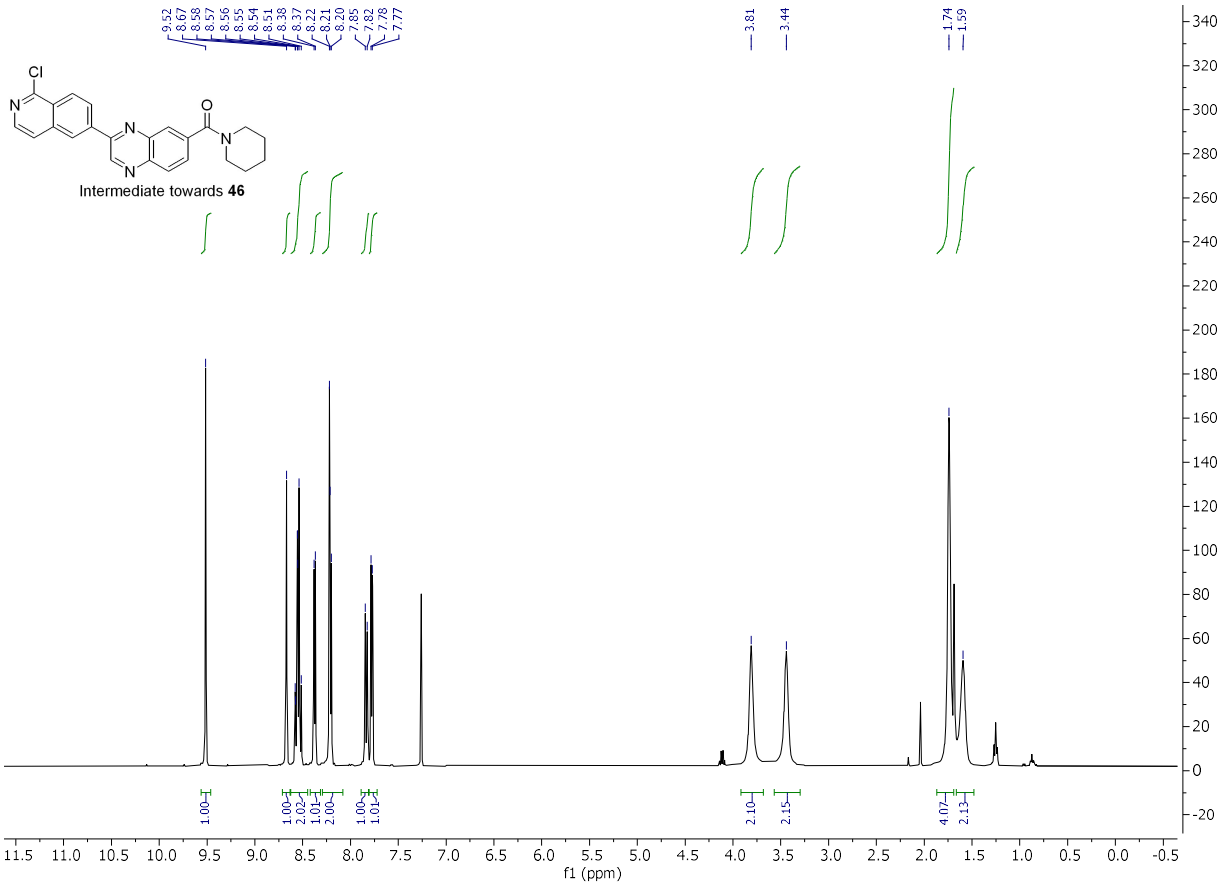
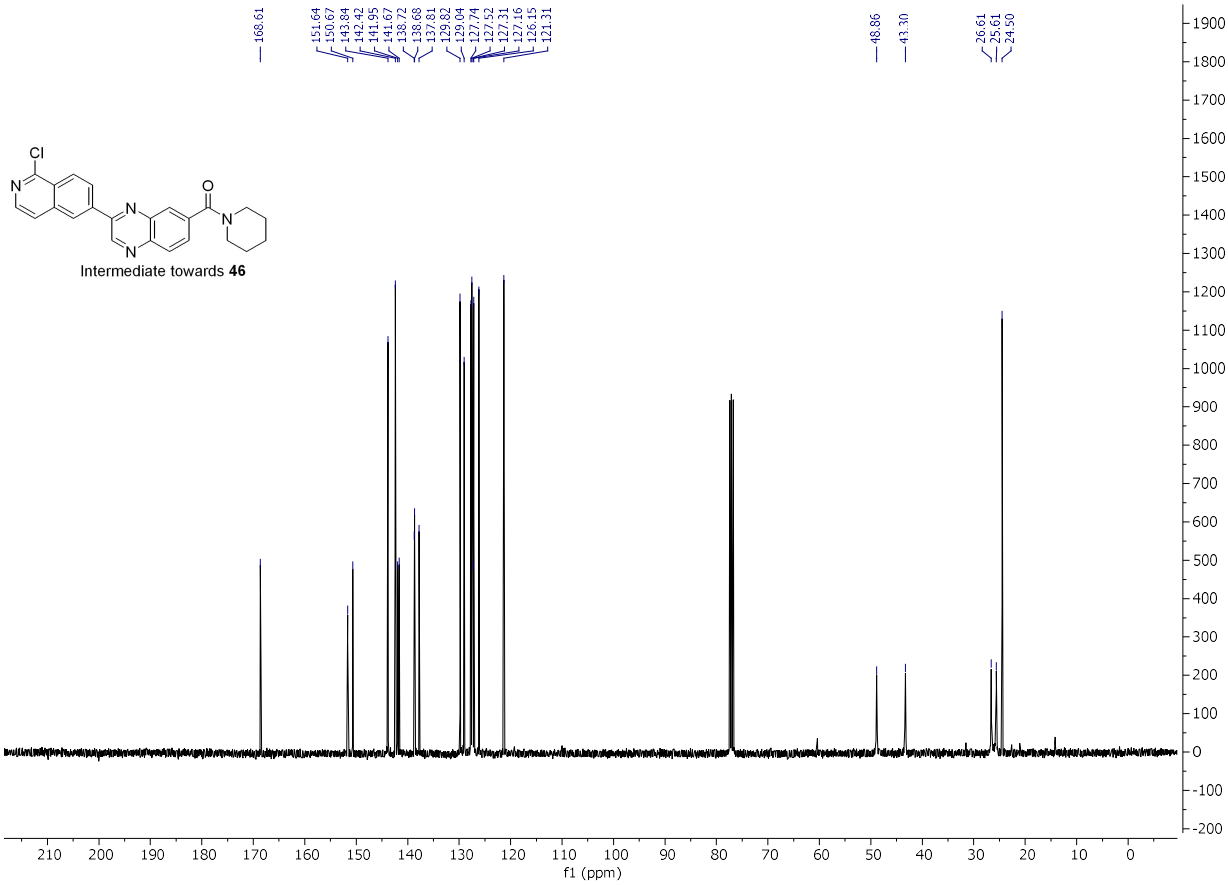
43.30
26.63
25.63
24.52
44
f1 (ppm)


9.48
8.57
8.52
8.49
8.18
8.18
8.17
8.16
8.15
8.13
8.04
8.02
7.79
7.77
7.00
6.98
4.12
3.80
3.44
1.73
1.59
45
1.12
1.04
1.14
3.00
1.05
1.00
1.00
3.04
2.02
2.02
4.24
2.16
f1 (ppm)


168.90
163.44
152.01
147.90
144.04
141.79
141.53
139.30
138.32
131.93
129.77
128.34
128.19
128.17
127.49
127.07
125.15
114.12
53.66
48.87
43.29
26.63
25.65
24.55
45
f1 (ppm)


9.52
8.67
8.58
8.57
8.56
8.55
8.54
8.51
8.38
8.37
8.22
8.21
8.20
7.85
7.82
7.78
7.77
3.81
3.44
1.74
1.59
Cl
N
O
N
N
N
Intermediate towards 46
1.00
1.00
2.02
1.01
2.00
1.00
1.01
2.10
2.15
4.07
2.13
f1 (ppm)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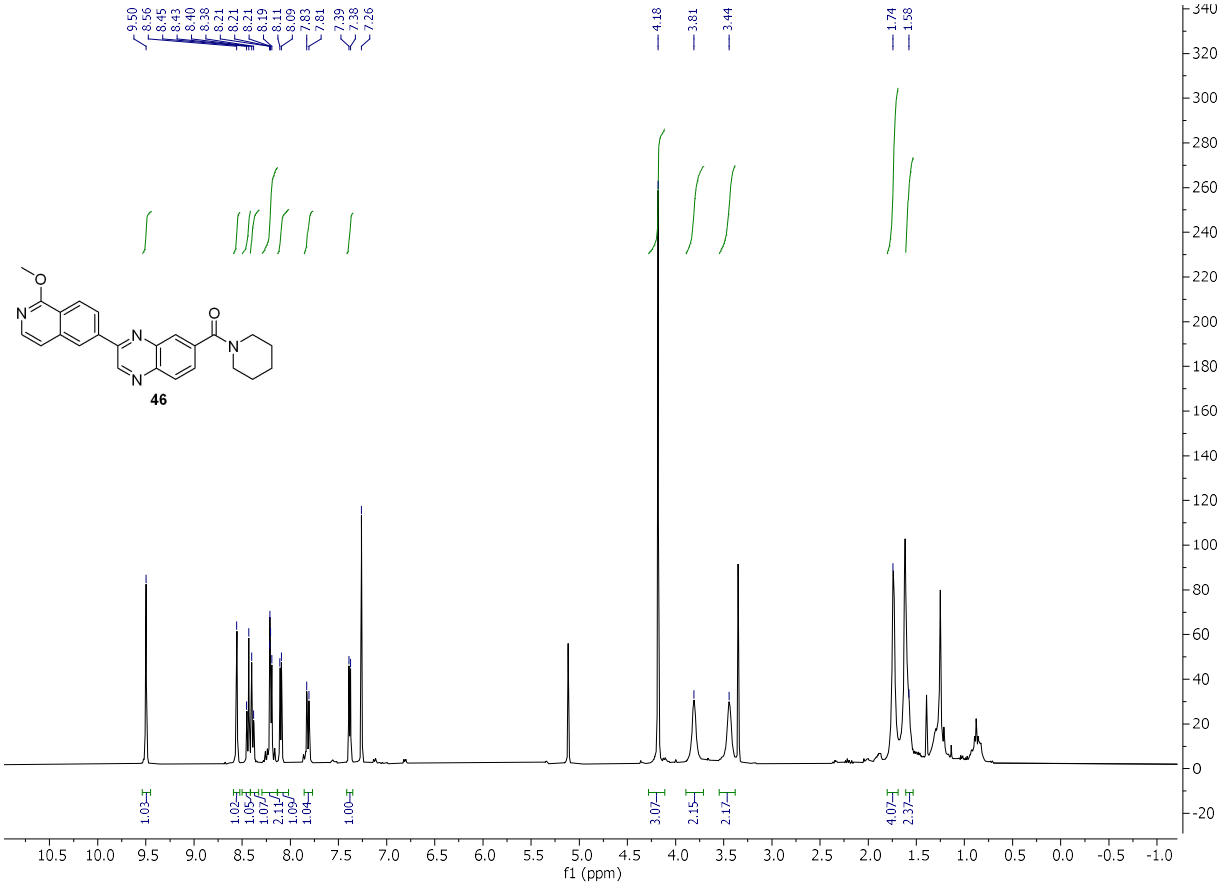
143.84
142.42
141.95
141.67
138.72
138.68
137.81
129.82
129.04
127.74
127.52
127.31
127.16
126.15
121.31
48.86
43.30
26.61
25.61
24.50
Cl
N
O
N
N
N
Intermediate towards 46
f1 (ppm)


9.50
8.56
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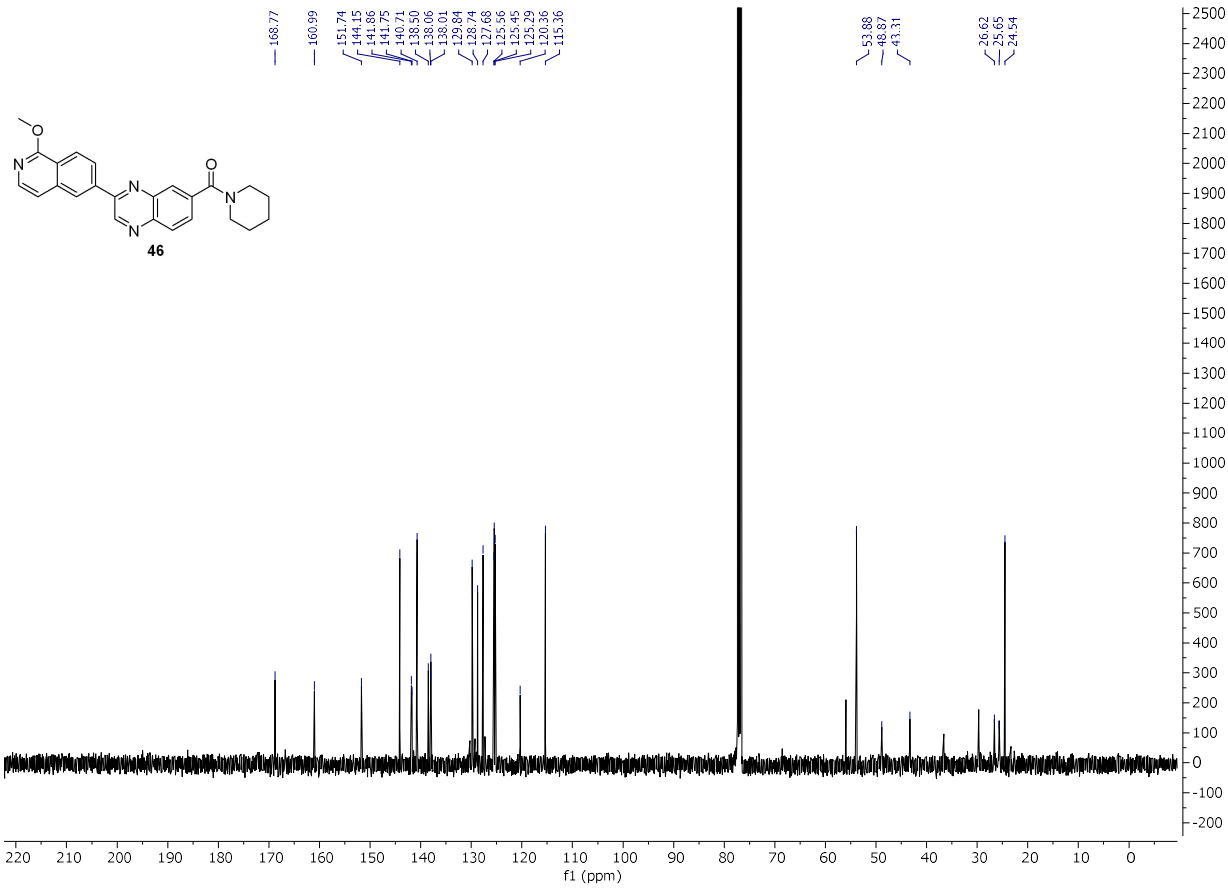
8.40
8.38
8.21
8.21
8.21
8.19
8.11
8.09
7.83
7.81
7.39
7.38
7.26
4.18
3.81
3.44
1.74
1.58
1.03
1.02
1.05
1.07
2.11
1.09
1.04
1.00
3.07
2.15
2.17
4.07
2.37
f1 (ppm)

46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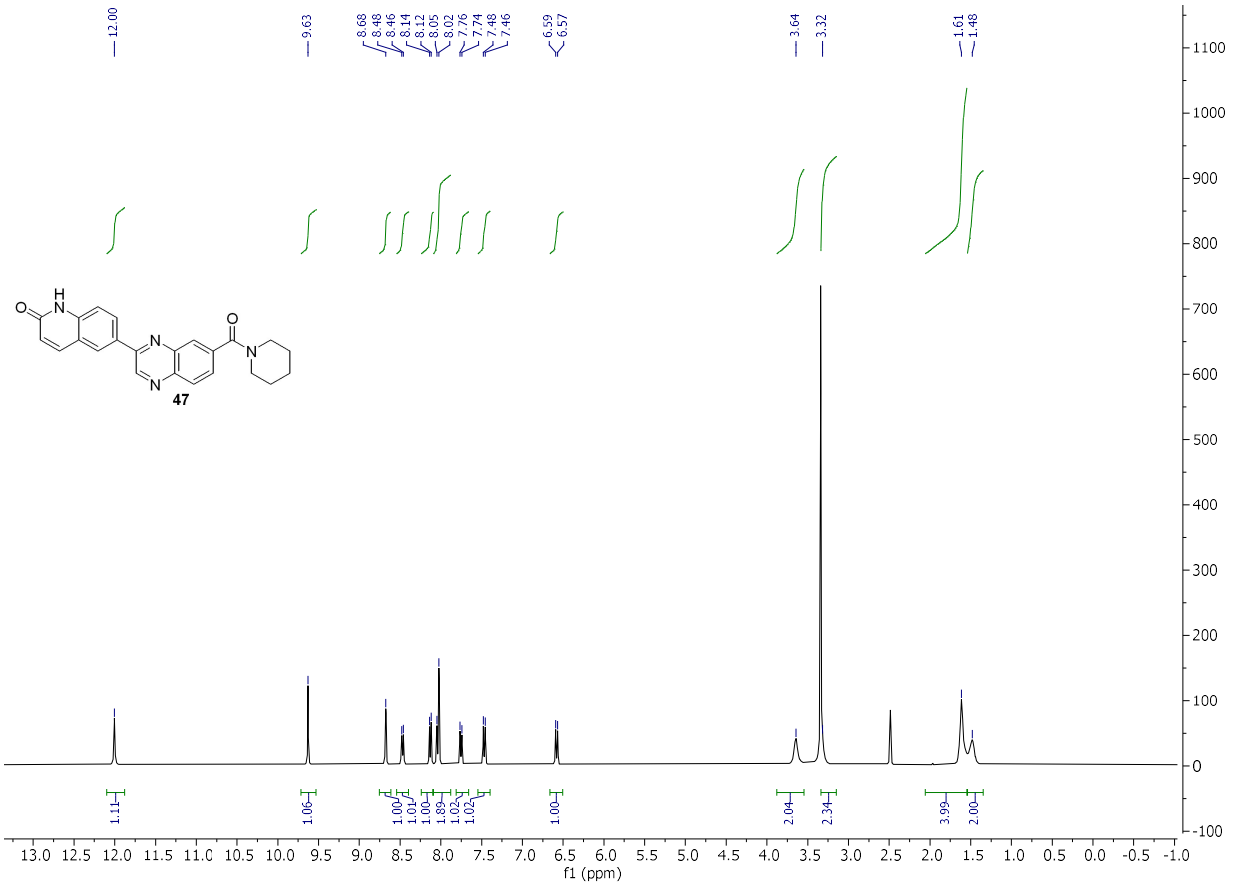
144.15
141.86
141.75
140.71
138.50
138.06
138.01
129.84
128.74
127.68
125.56
125.45
125.29
120.36
115.36
53.88
48.87
43.31
26.62
25.65
24.54
f1 (ppm)

46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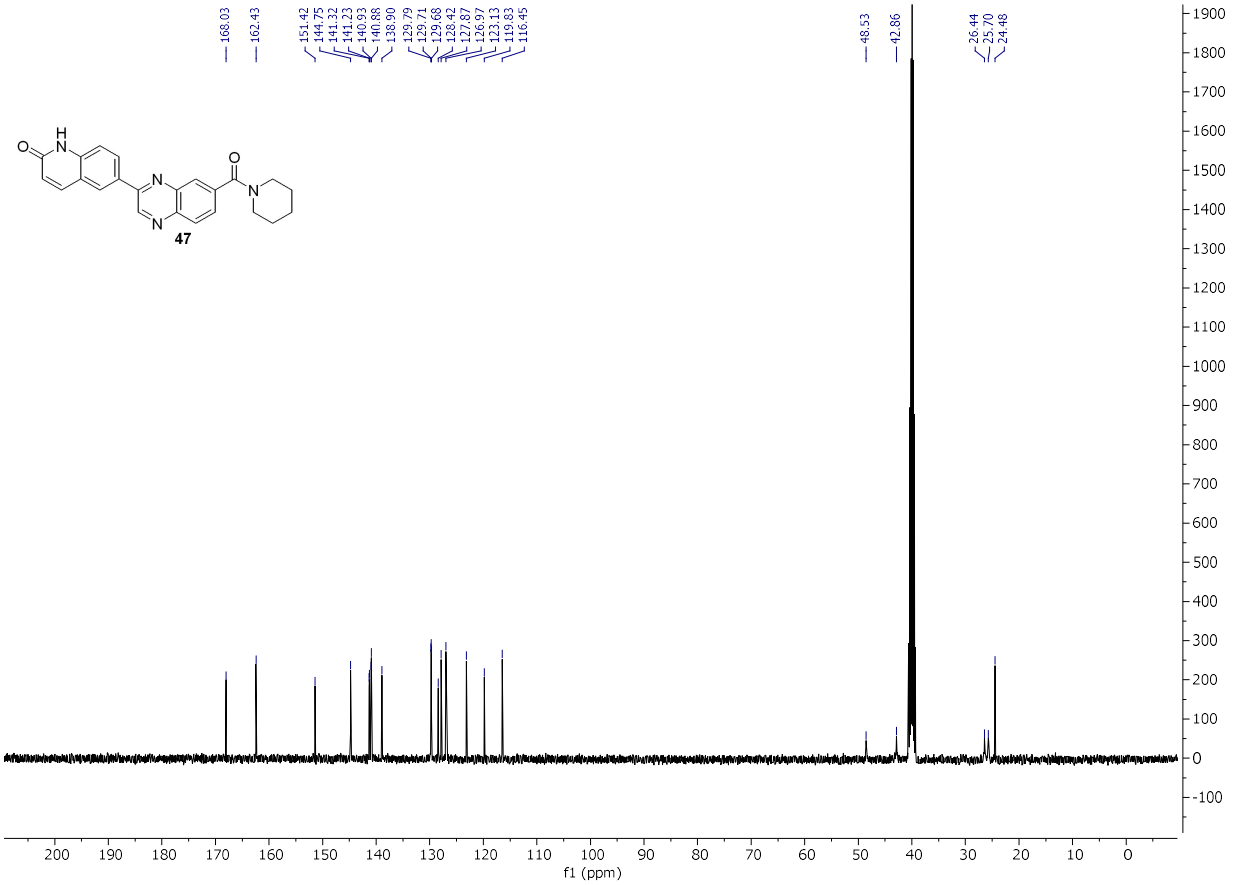
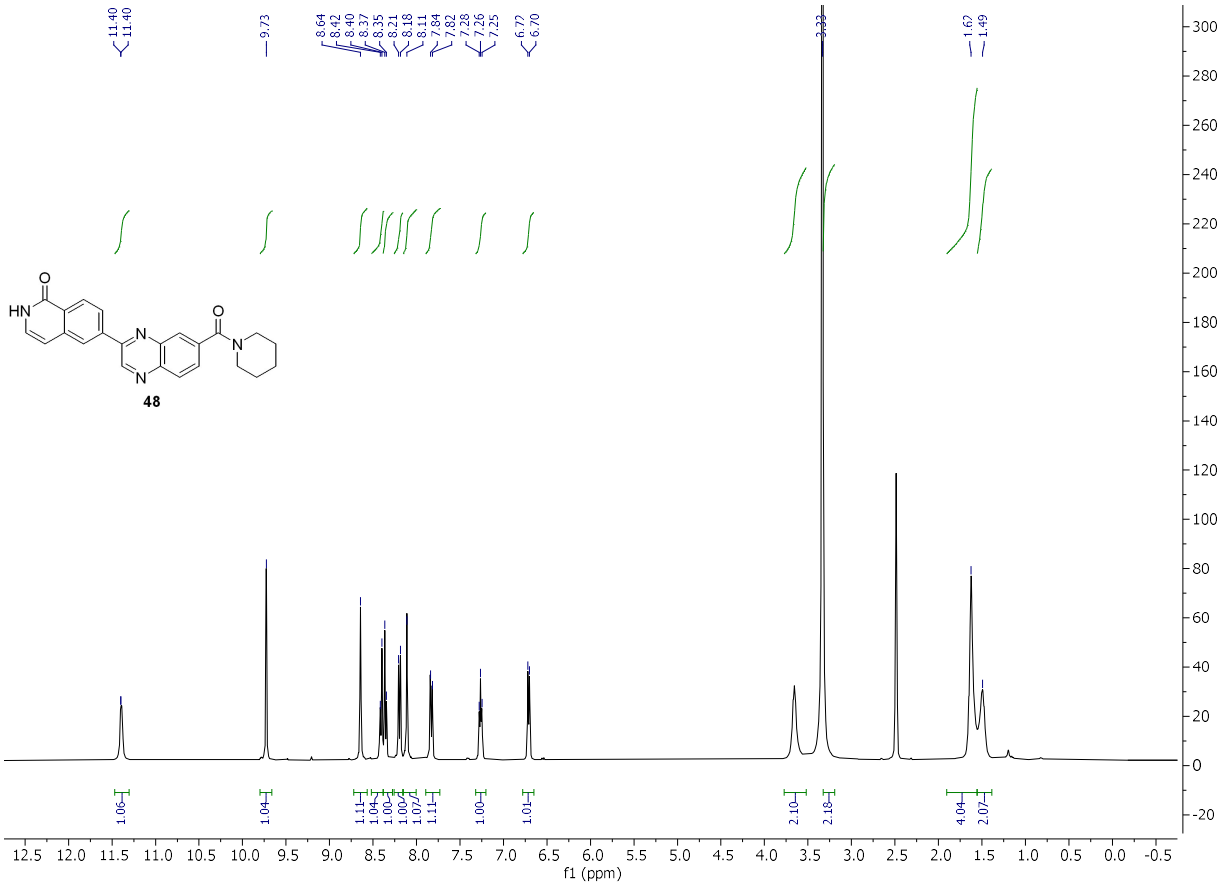
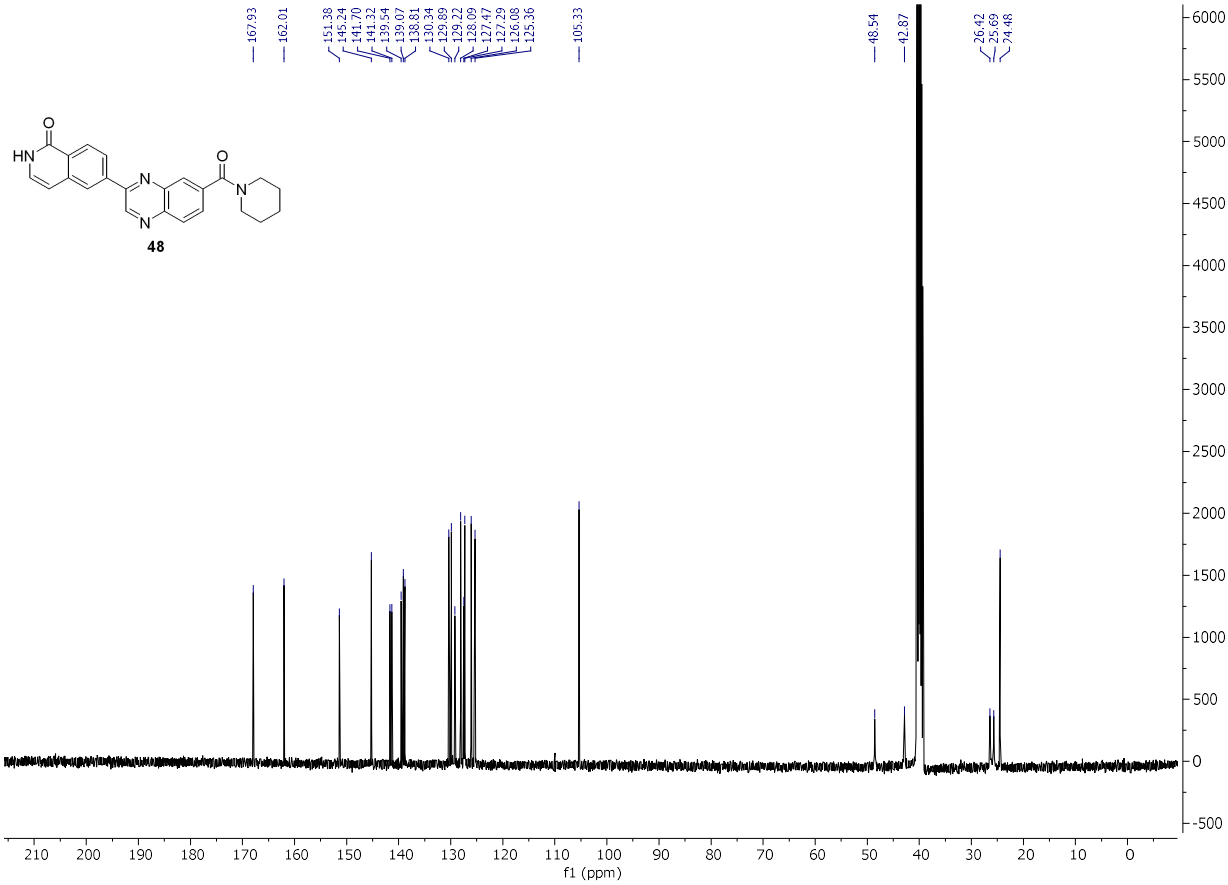
9.63
8.68
8.48
8.46
8.14
8.12
8.05
8.02
7.76
7.74
7.48
7.46
6.59
6.57
3.64
3.32
1.61
1.48
47
f1 (ppm)

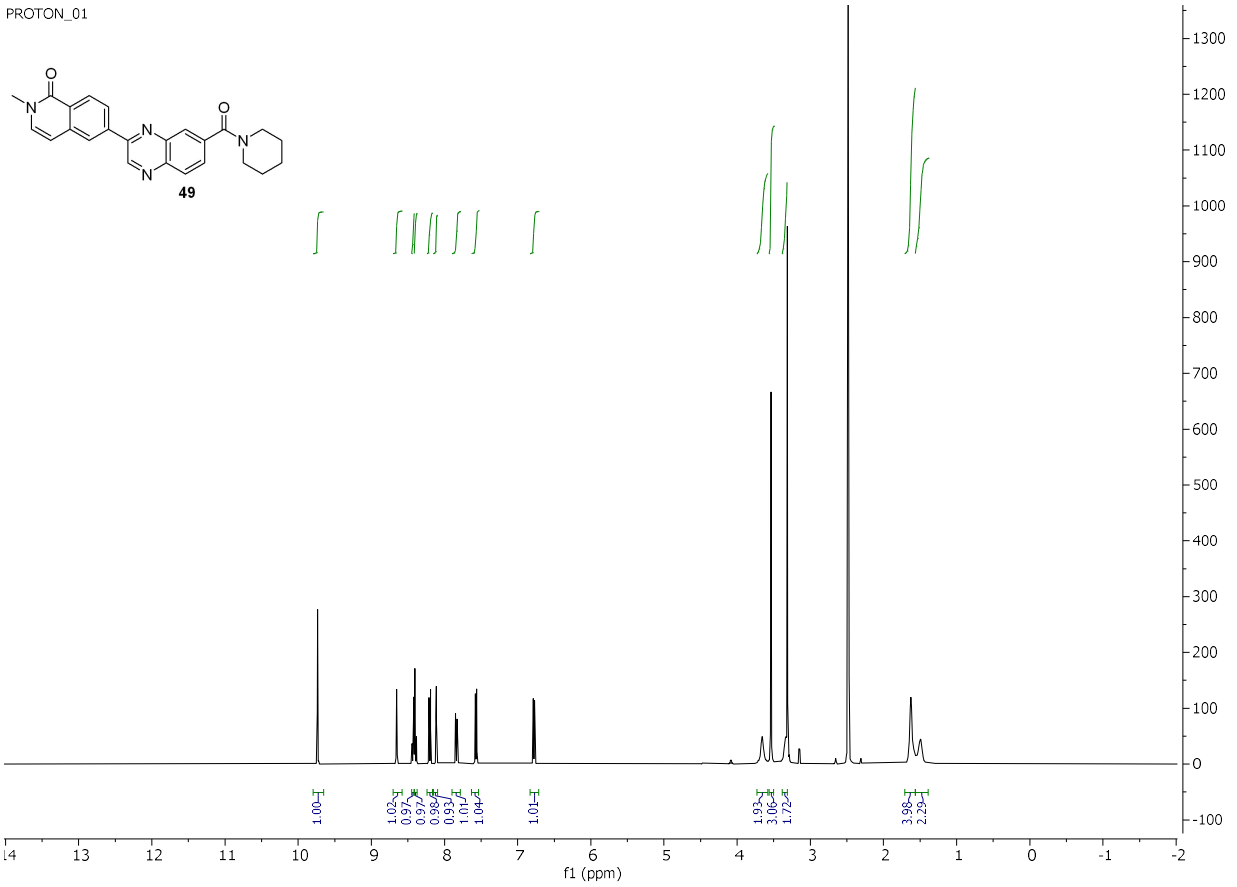

168.03
162.43
151.42
144.75
141.32
141.23
140.93
140.88
138.90
129.79
129.71
129.68
128.42
127.87
126.97
123.13
119.83
116.45
48.53
42.86
26.44
25.70
24.48
47
f1 (ppm)

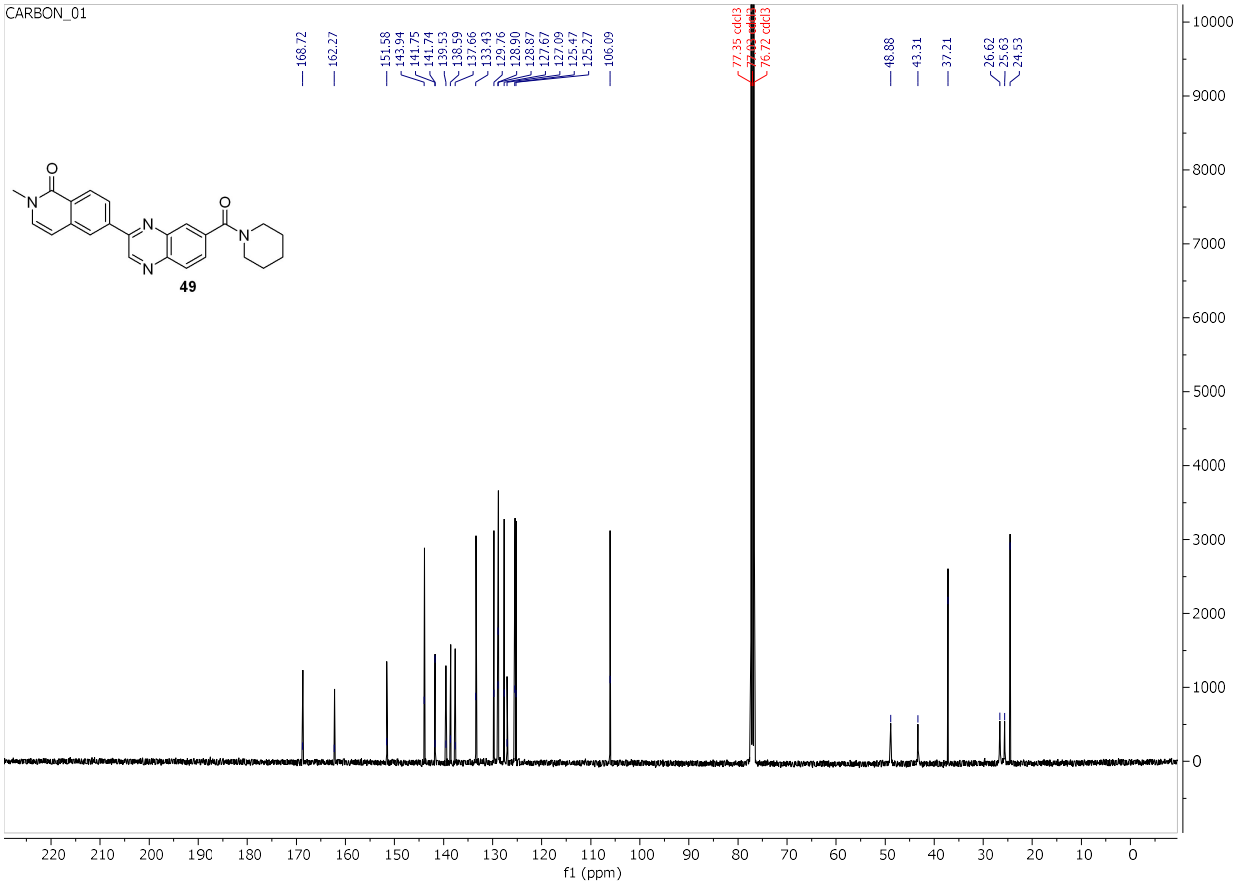

11.40
11.40
9.73
8.64
8.42
8.40
8.37
8.35
8.21
8.18
8.11
7.84
7.82
7.28
7.26
7.25
6.77
6.70
3.33
1.67
1.49
1.06
1.04
1.11
1.04
1.00
1.00
1.07
1.11
1.00
1.01
2.10
2.18
4.04
2.07
f1 (ppm)

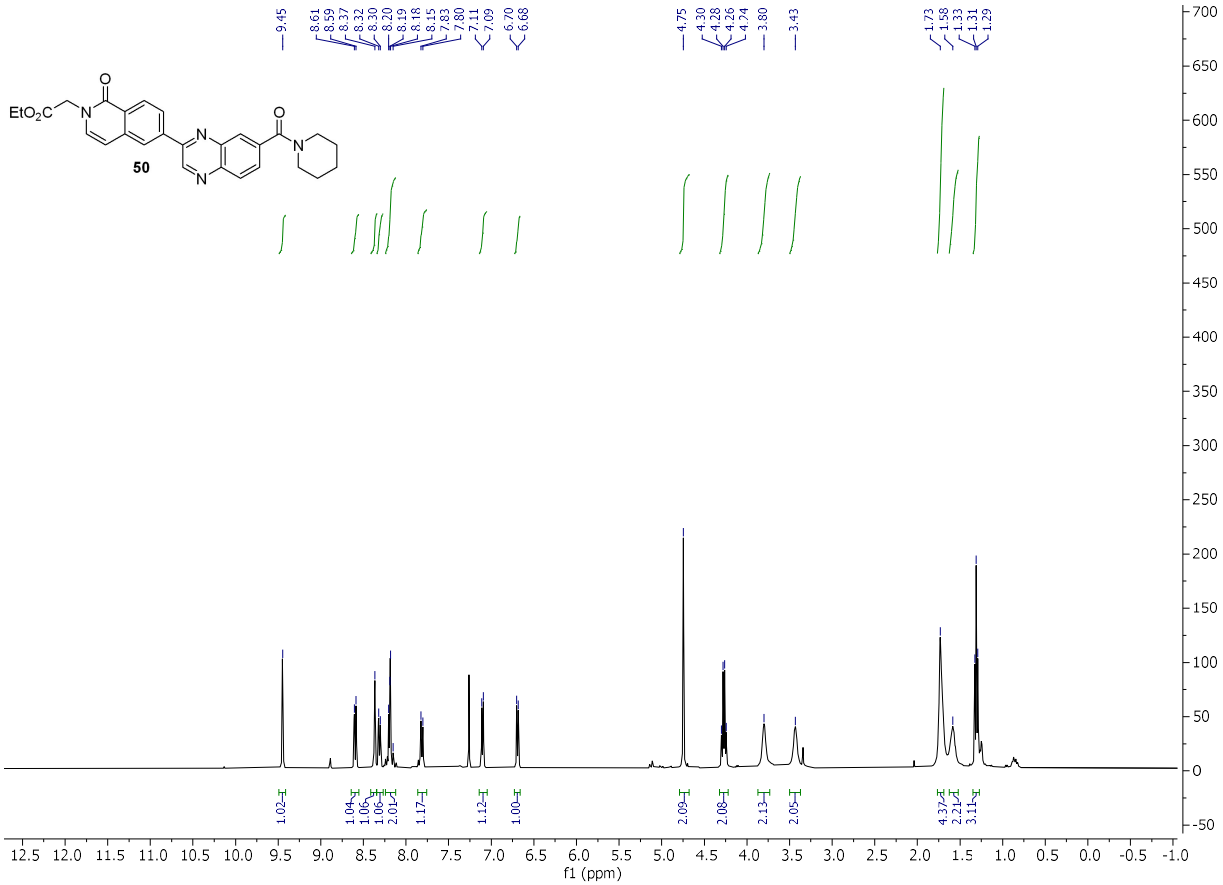
48


167.93
162.01
151.38
145.24
141.70
141.32
139.54
139.07
138.81
130.34
129.89
129.22
128.09
127.47
127.29
126.08
125.36
105.33
48.54
42.87
26.42
25.69
24.48
f1 (ppm)

48


PROTON_01
49
1.00
1.02
0.97
0.97
0.98
0.95
1.01
1.04
1.01
1.93
3.06
1.72
3.98
2.29
f1 (ppm)


CARBON_01
49
168.72
162.27
151.58
143.94
141.75
141.74
139.53
138.59
137.66
133.43
129.76
128.90
128.87
127.67
127.09
125.47
125.27
106.09
77.35 cdcl3
76.72 cdcl3
48.88
43.31
37.21
26.62
25.63
24.53
f1 (ppm)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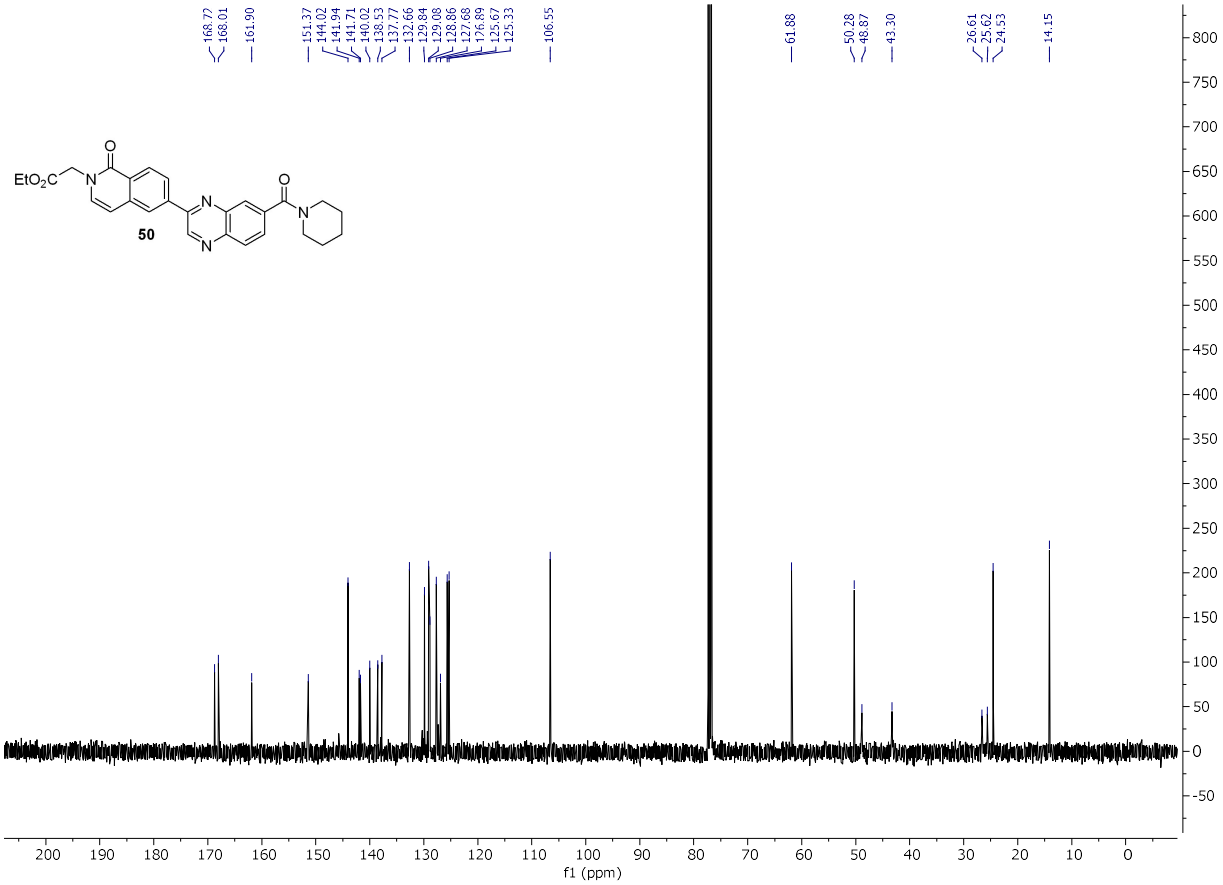
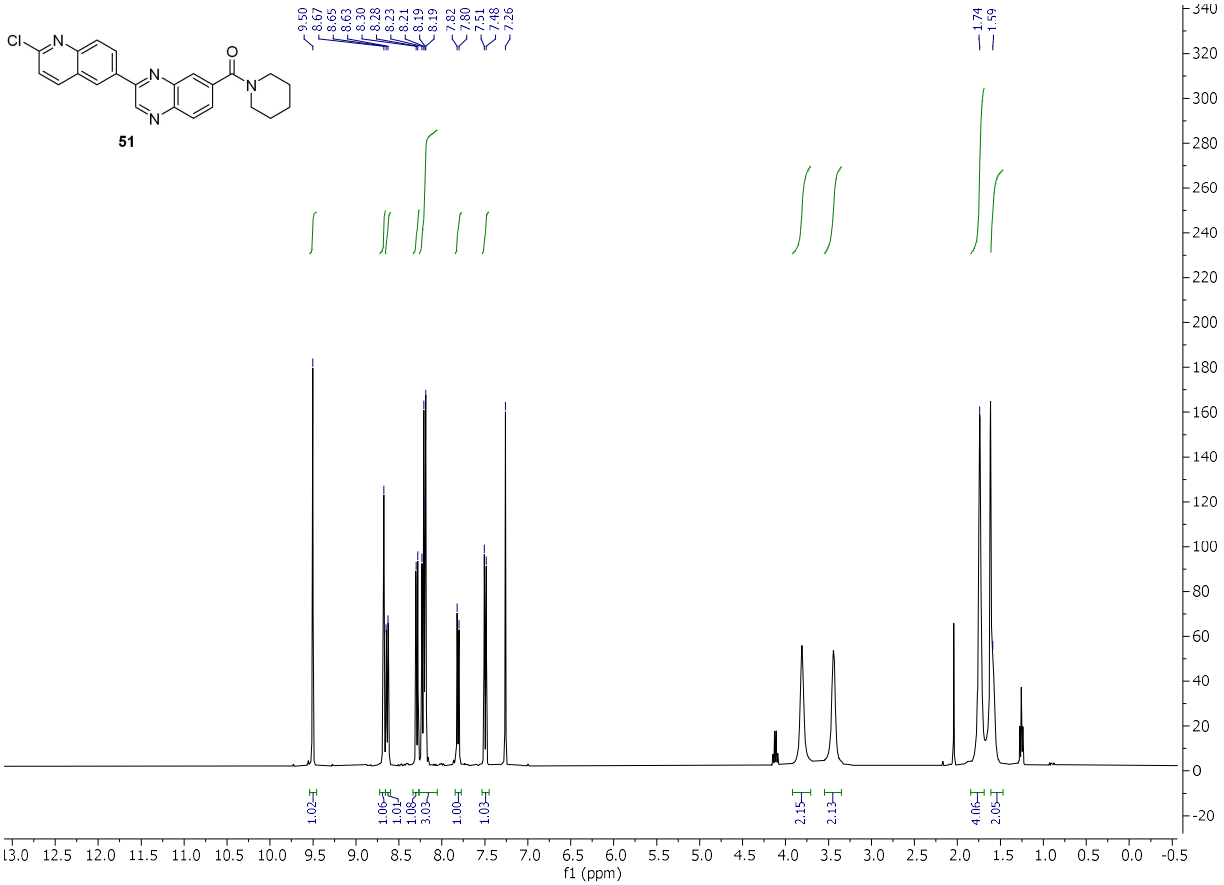
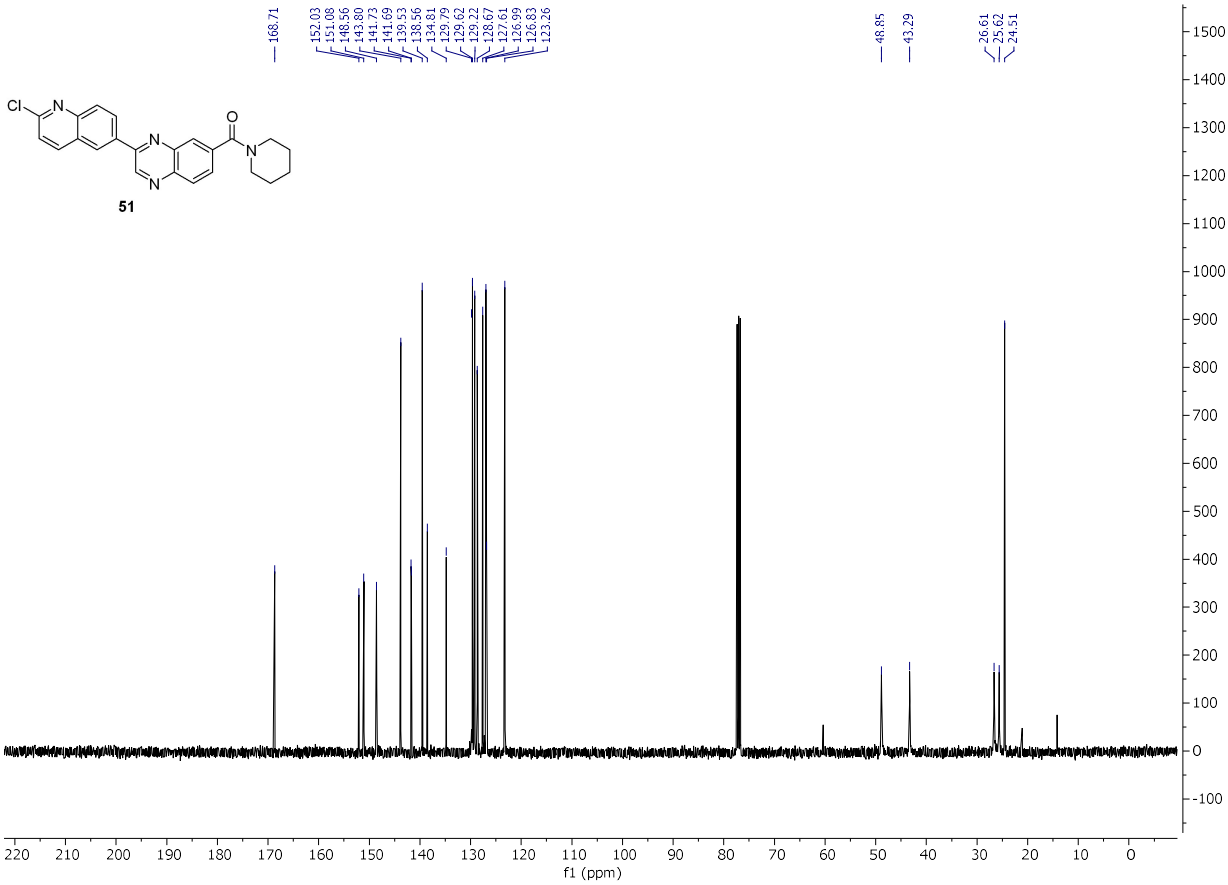
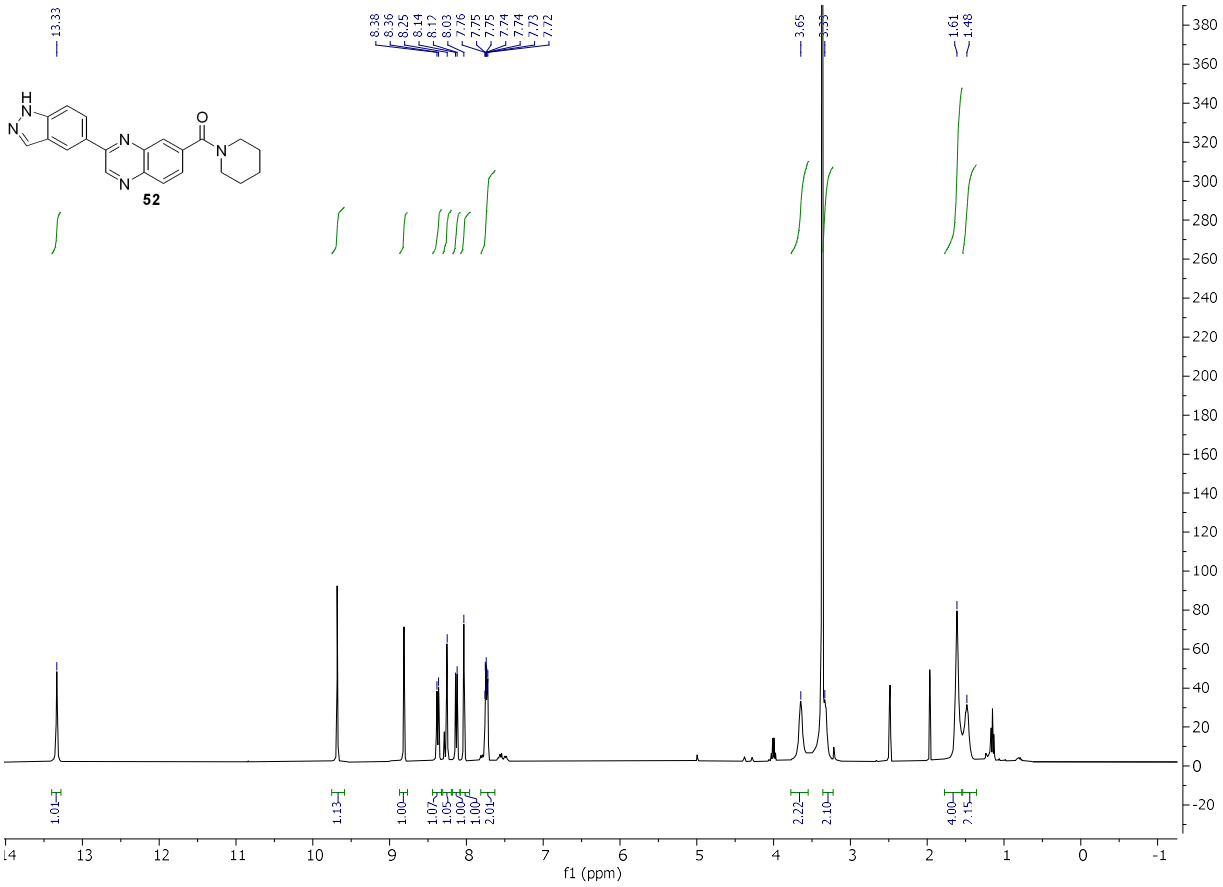
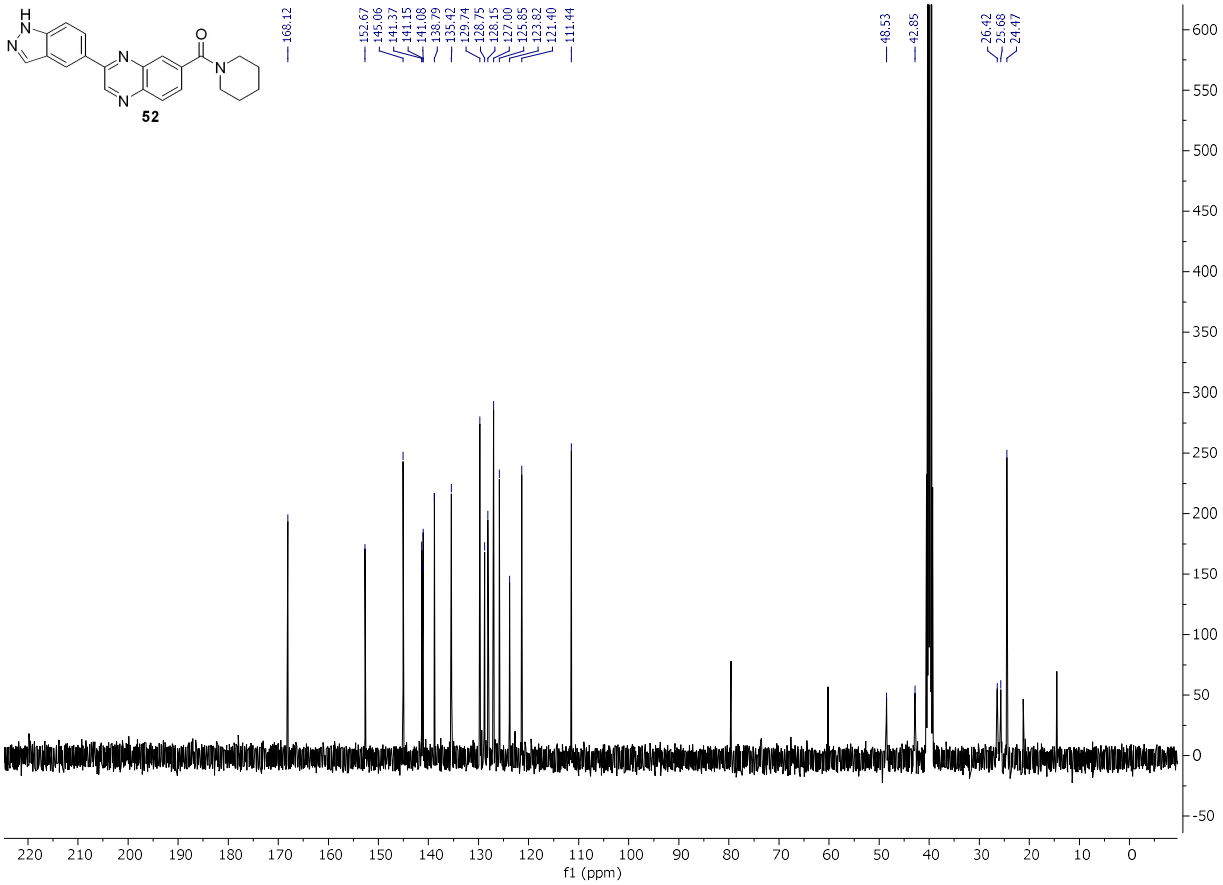
8.61
8.59
8.37
8.32
8.30
8.20
8.19
8.18
8.15
7.83
7.80
7.11
7.09
6.70
6.68
4.75
4.30
4.28
4.26
4.24
3.80
3.43
1.73
1.58
1.33
1.31
1.29
1.02
1.04
1.06
1.06
2.01
1.17
1.12
1.00
2.09
2.08
2.13
2.05
4.37
2.21
3.11
f1 (ppm)


168.77
168.01
161.90
151.37
144.02
141.94
141.71
140.02
138.53
137.77
132.66
129.84
129.08
128.86
127.68
126.89
125.67
125.33
106.55
61.88
50.28
48.87
43.30
26.61
25.62
24.53
14.15
f1 (ppm)


51
9.50
8.67
8.65
8.63
8.30
8.28
8.23
8.21
8.19
8.19
7.82
7.80
7.51
7.48
7.26
1.74
1.59
1.02
1.06
1.01
1.08
3.03
1.00
1.03
2.15
2.13
4.06
2.05
f1 (ppm)


51
168.71
152.03
151.08
148.56
143.80
141.73
141.69
139.53
138.56
134.81
129.79
129.62
129.22
128.67
127.61
126.99
126.83
123.26
48.85
43.29
26.61
25.62
24.51
f1 (ppm)


13.33
8.38
8.36
8.25
8.14
8.17
8.03
7.76
7.75
7.75
7.74
7.74
7.73
7.72
3.65
3.33
1.61
1.48
52
1.01
1.13
1.00
1.07
1.05
1.00
1.00
2.01
2.22
2.10
4.00
3.15
f1 (ppm)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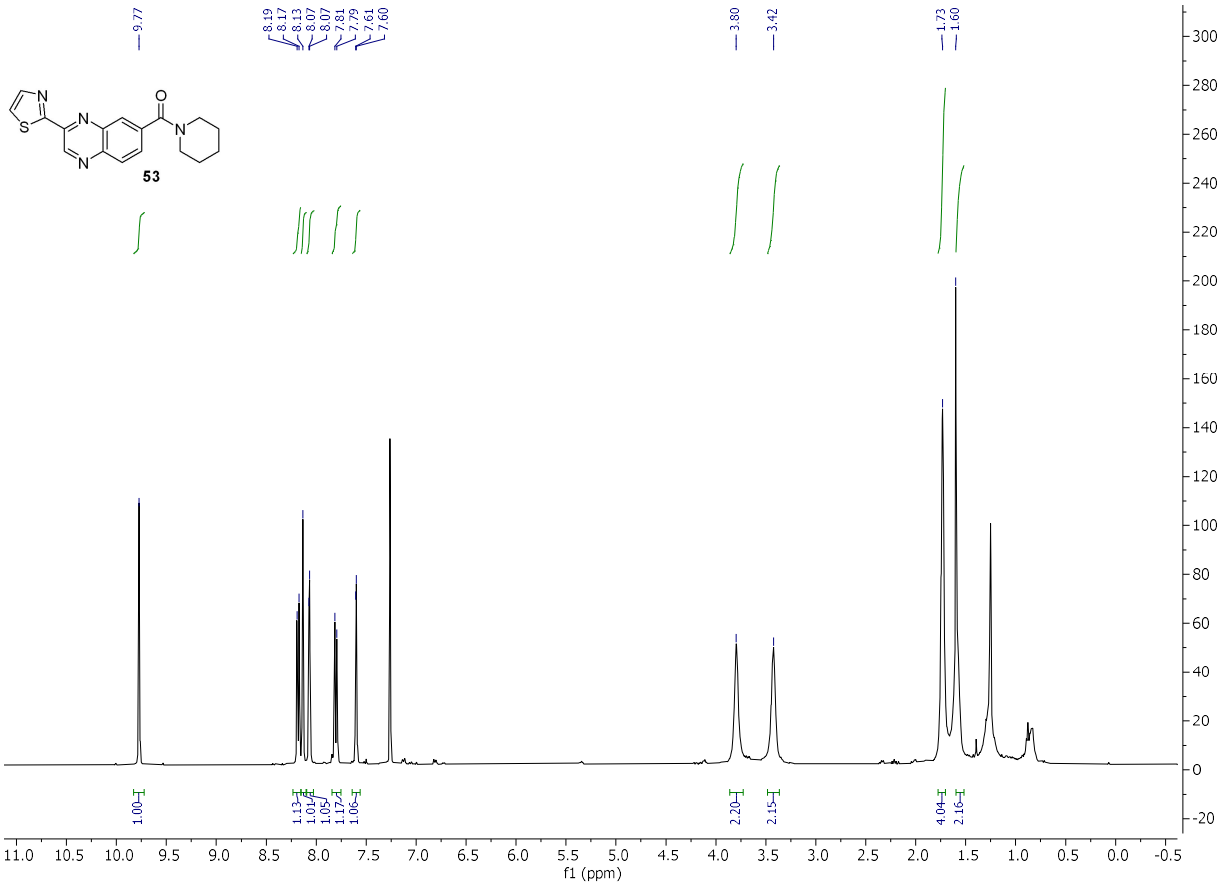
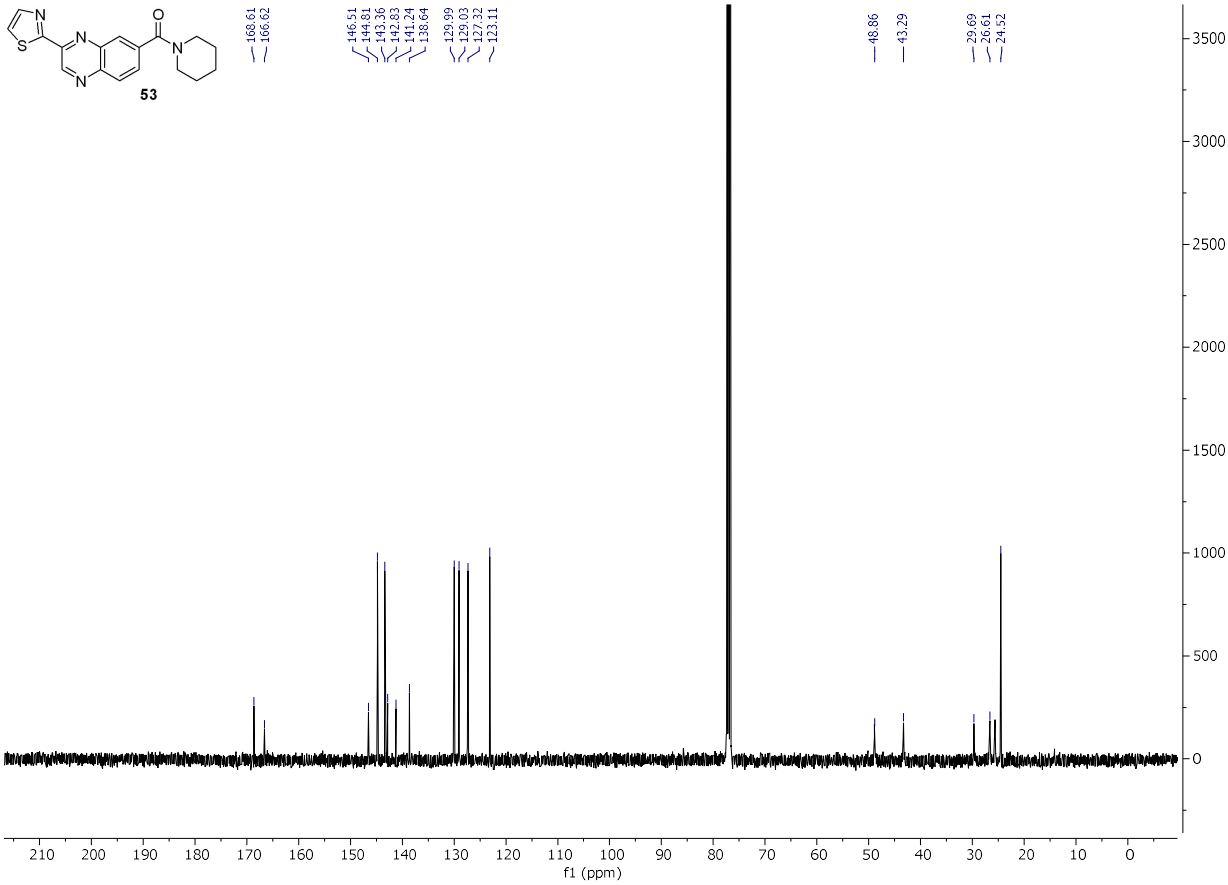
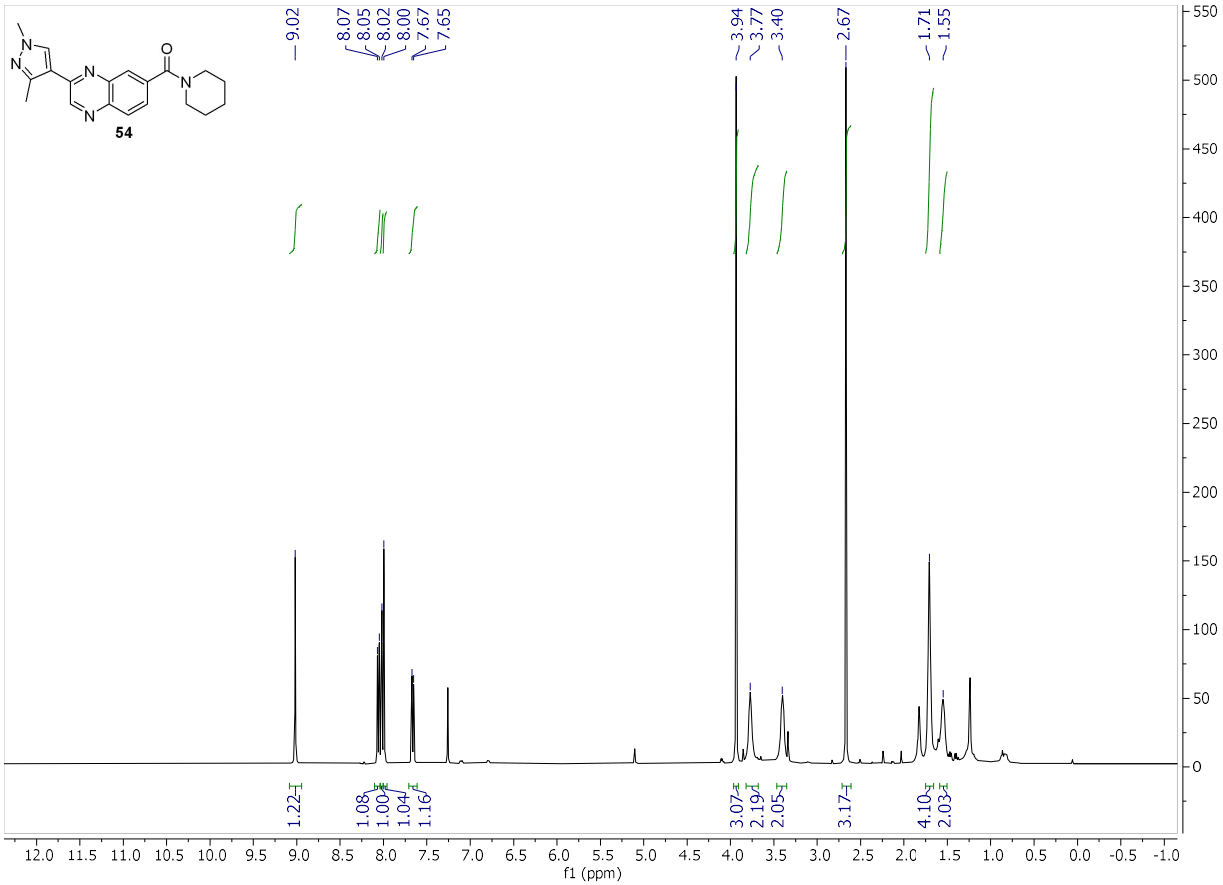
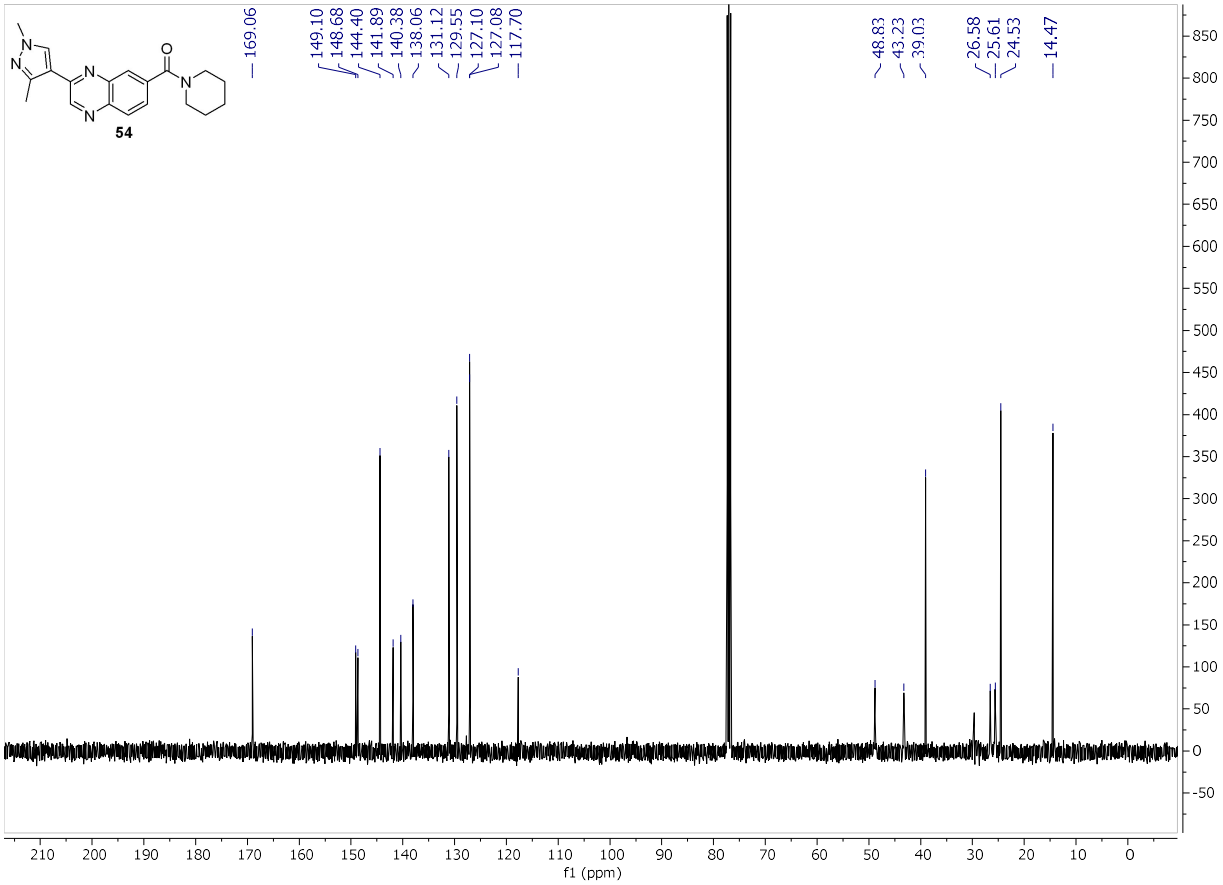
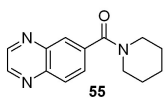
152.67
145.06
141.37
141.15
141.08
138.79
135.42
129.74
128.75
128.15
127.00
125.85
123.82
121.40
111.44
48.53
42.85
26.42
25.68
24.47
52
f1 (ppm)


9.77
8.19
8.17
8.13
8.07
8.07
7.81
7.79
7.61
7.60
3.80
3.42
1.73
1.60
53
1.00
1.13
1.01
1.05
1.17
1.06
2.20
2.15
4.04
2.16
f1 (ppm)

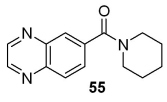

168.61
166.62
146.51
144.81
143.36
142.83
141.24
138.64
129.99
129.03
127.32
123.11
48.86
43.29
29.69
26.61
24.52
53
f1 (ppm)


54
9.02
8.07
8.05
8.02
8.00
7.67
7.65
3.94
3.77
3.40
2.67
1.71
1.55
1.22
1.08
1.00
1.04
1.16
3.07
2.19
2.05
3.17
4.10
2.03
f1 (ppm)

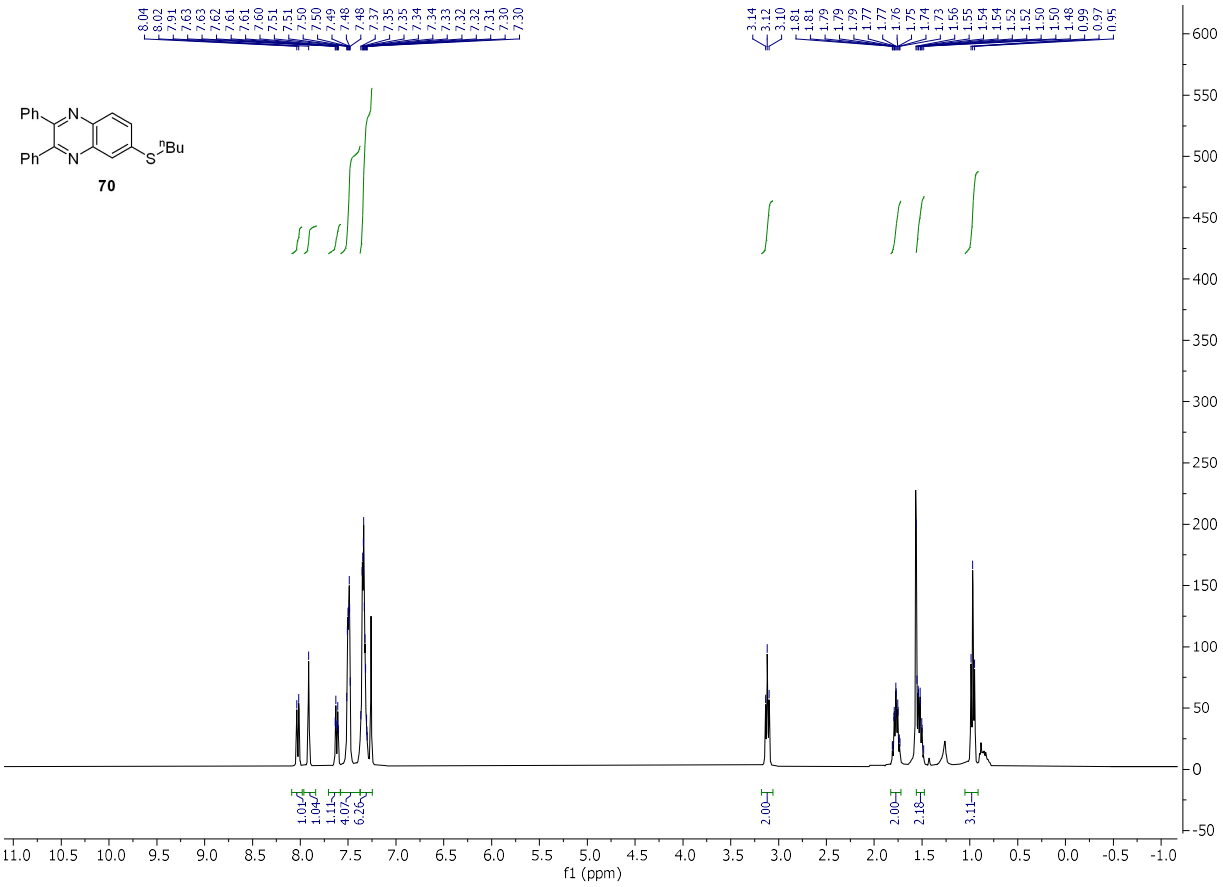

54
169.06
149.10
148.68
144.40
141.89
140.38
138.06
131.12
129.55
127.10
127.08
117.70
48.83
43.23
39.03
26.58
25.61
24.53
14.47
f1 (ppm)

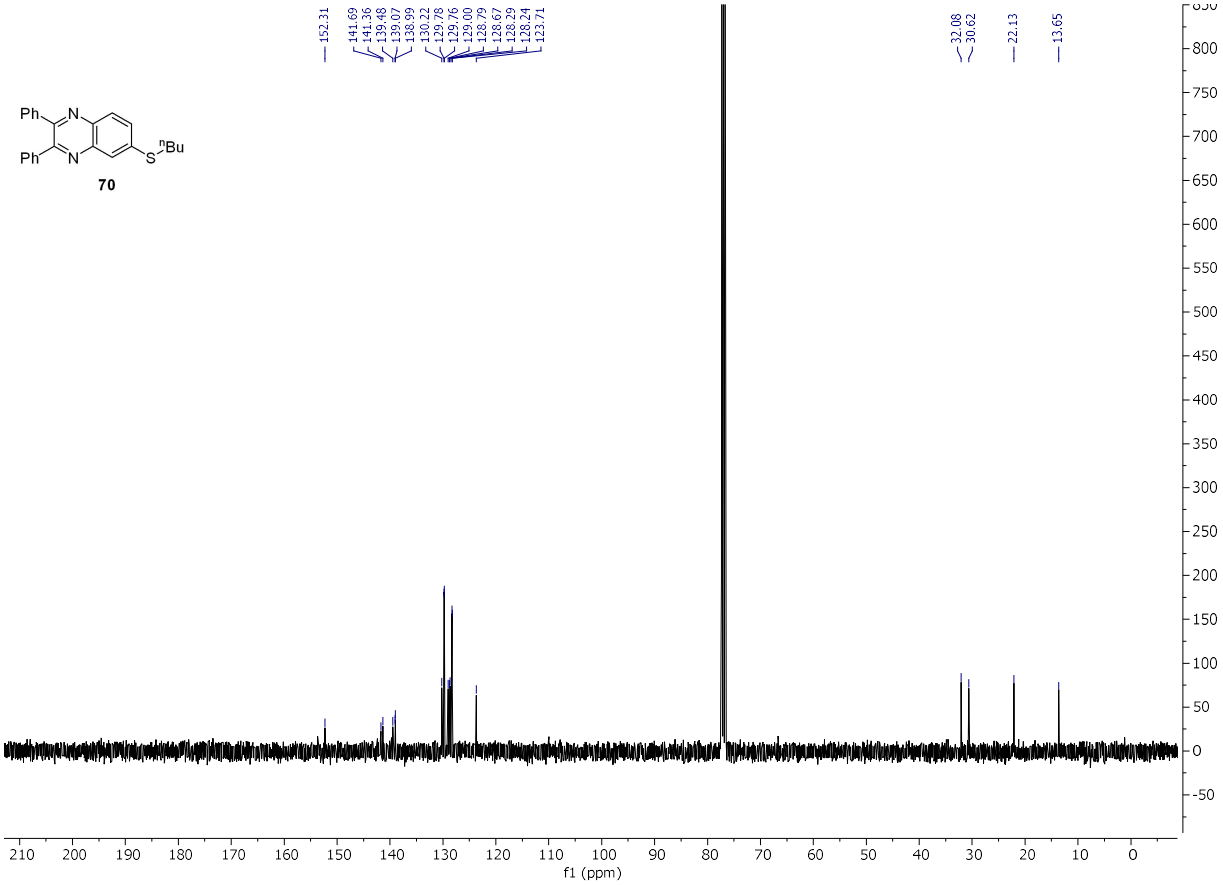

55

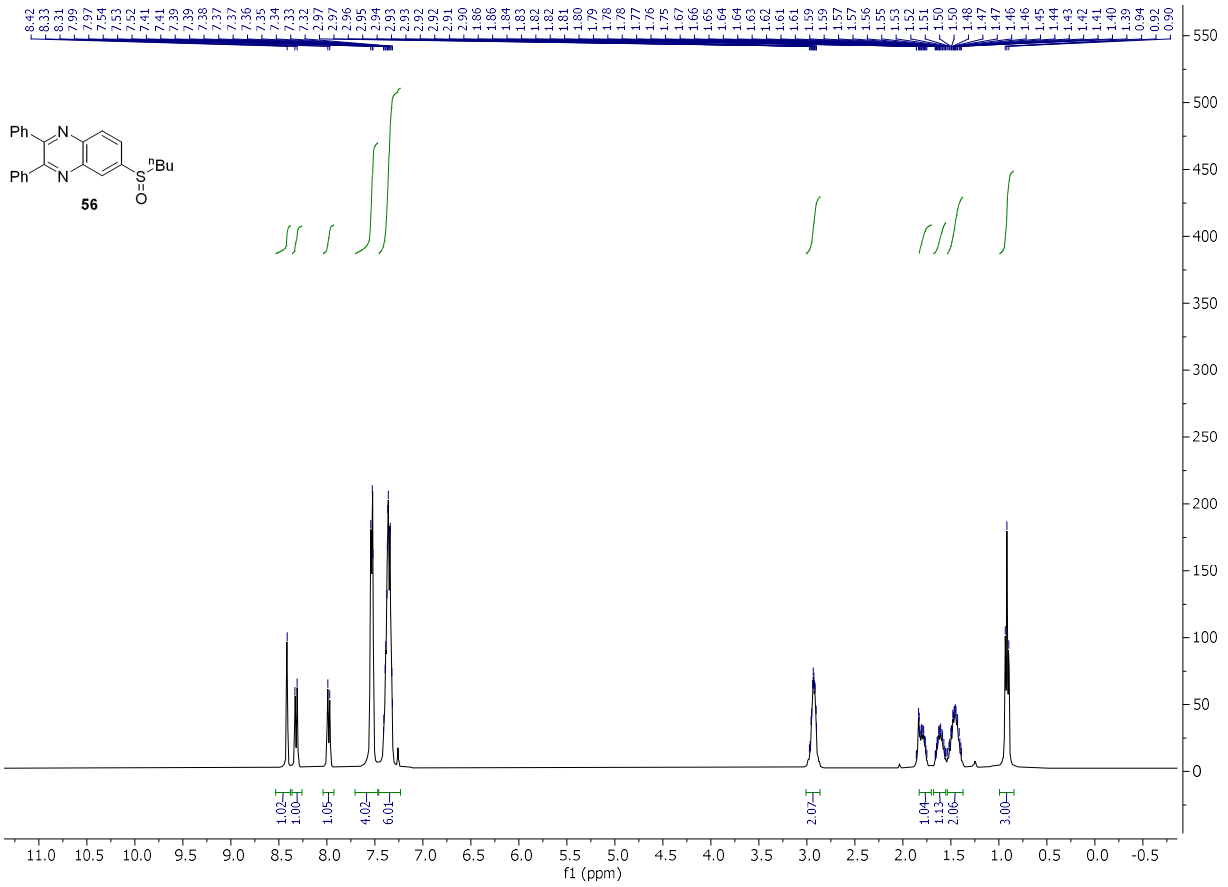
8.89
8.89
8.17
8.15
8.12
8.11
7.82
7.82
7.80
7.79
3.79
3.40
1.72
1.56
2.01
1.04
1.00
1.13
2.03
2.05
4.33
2.15
f1 (ppm)

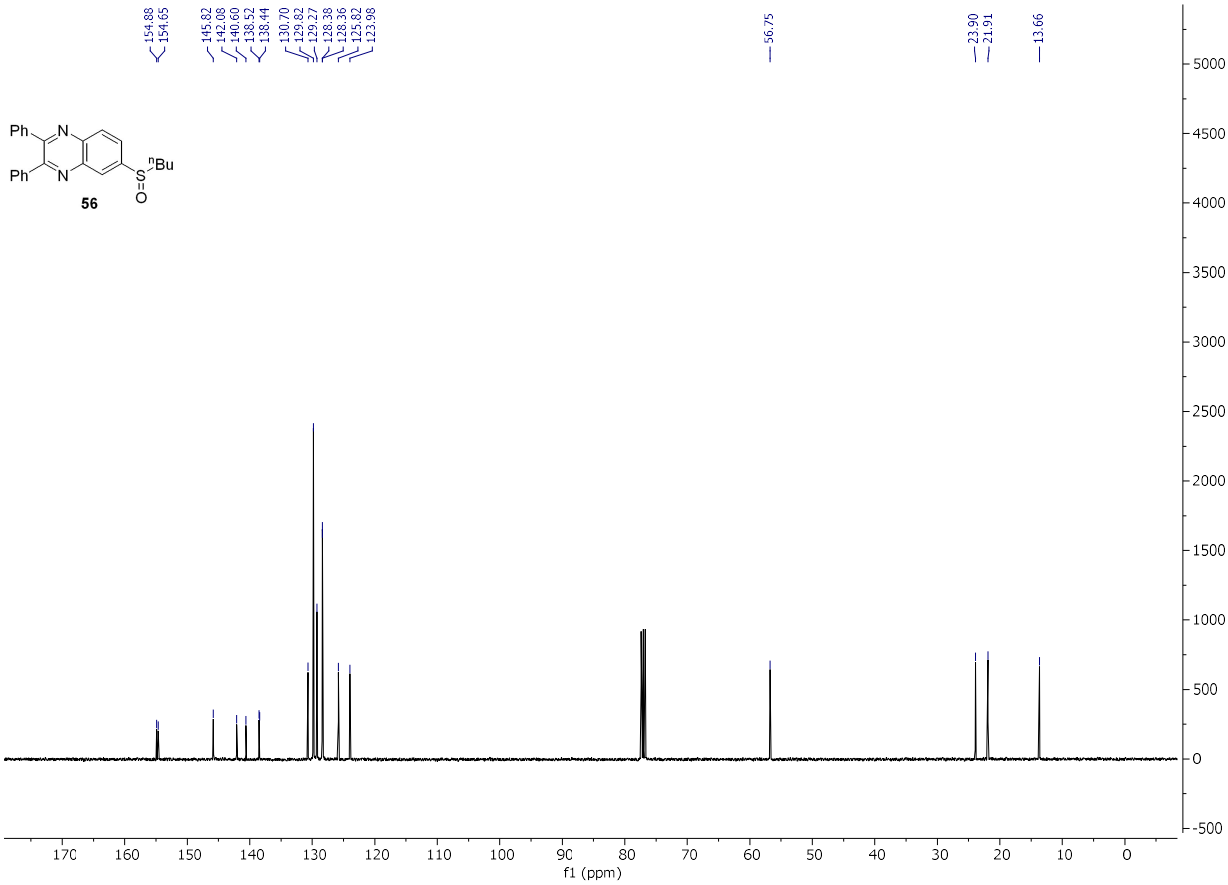

55

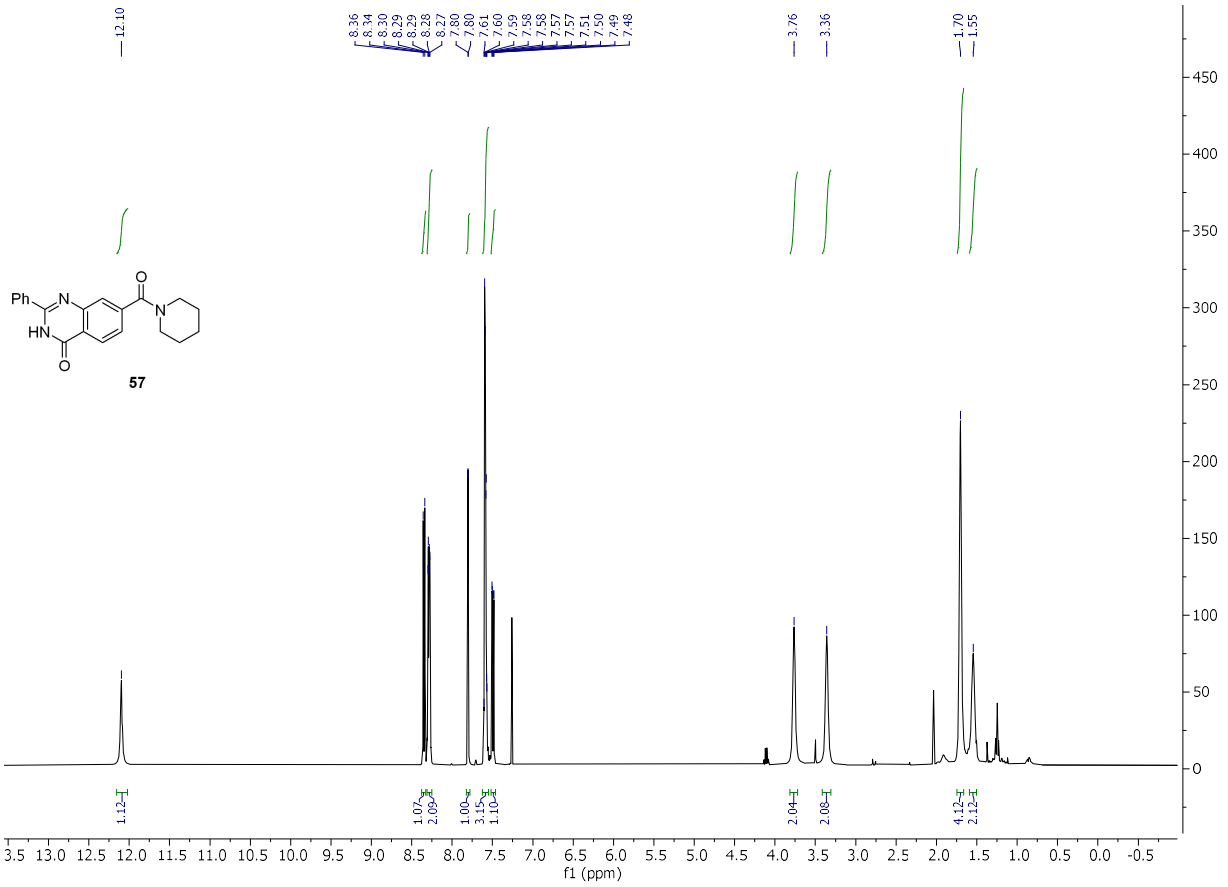
168.68
145.73
143.06
142.46
138.05
130.13
128.77
127.55
48.82
43.27
26.57
25.60
24.51
f1 (ppm)

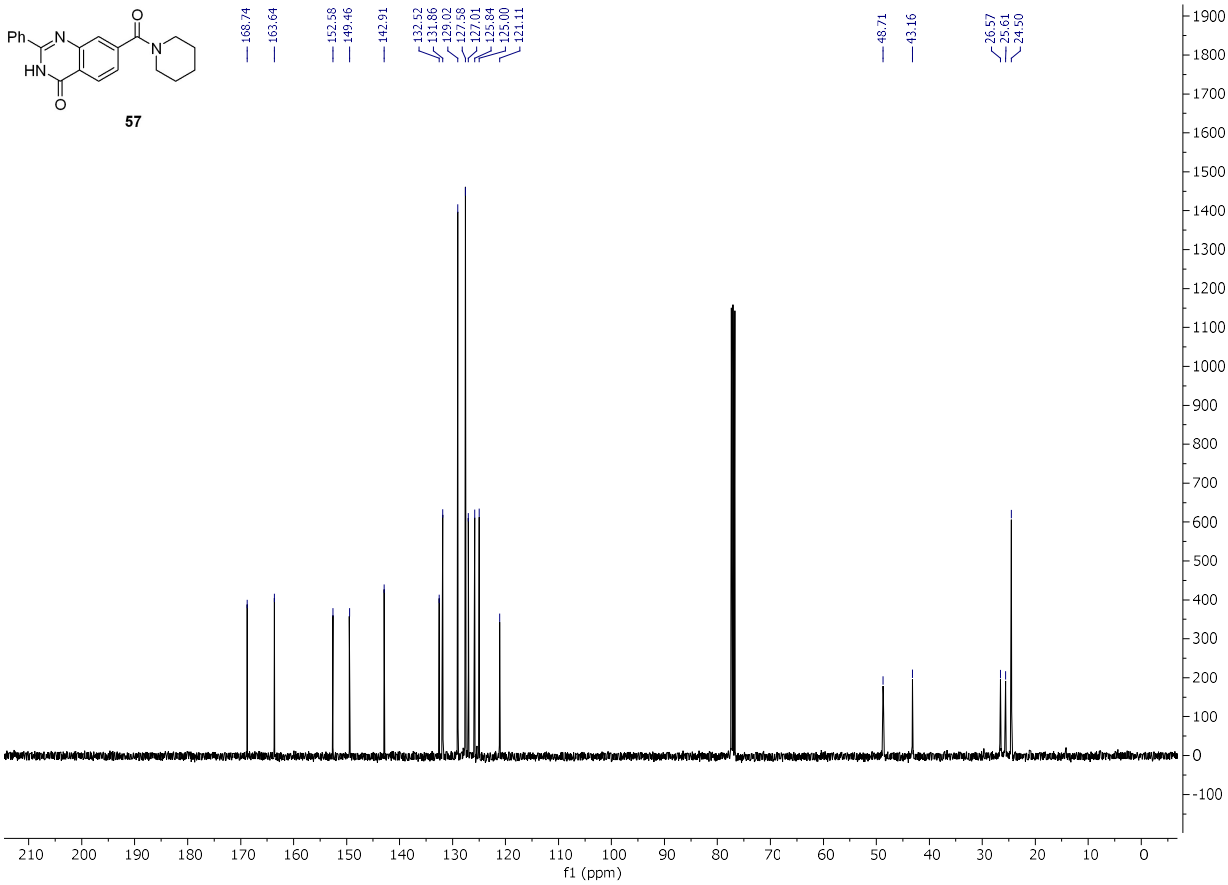

70
f1 (ppm)

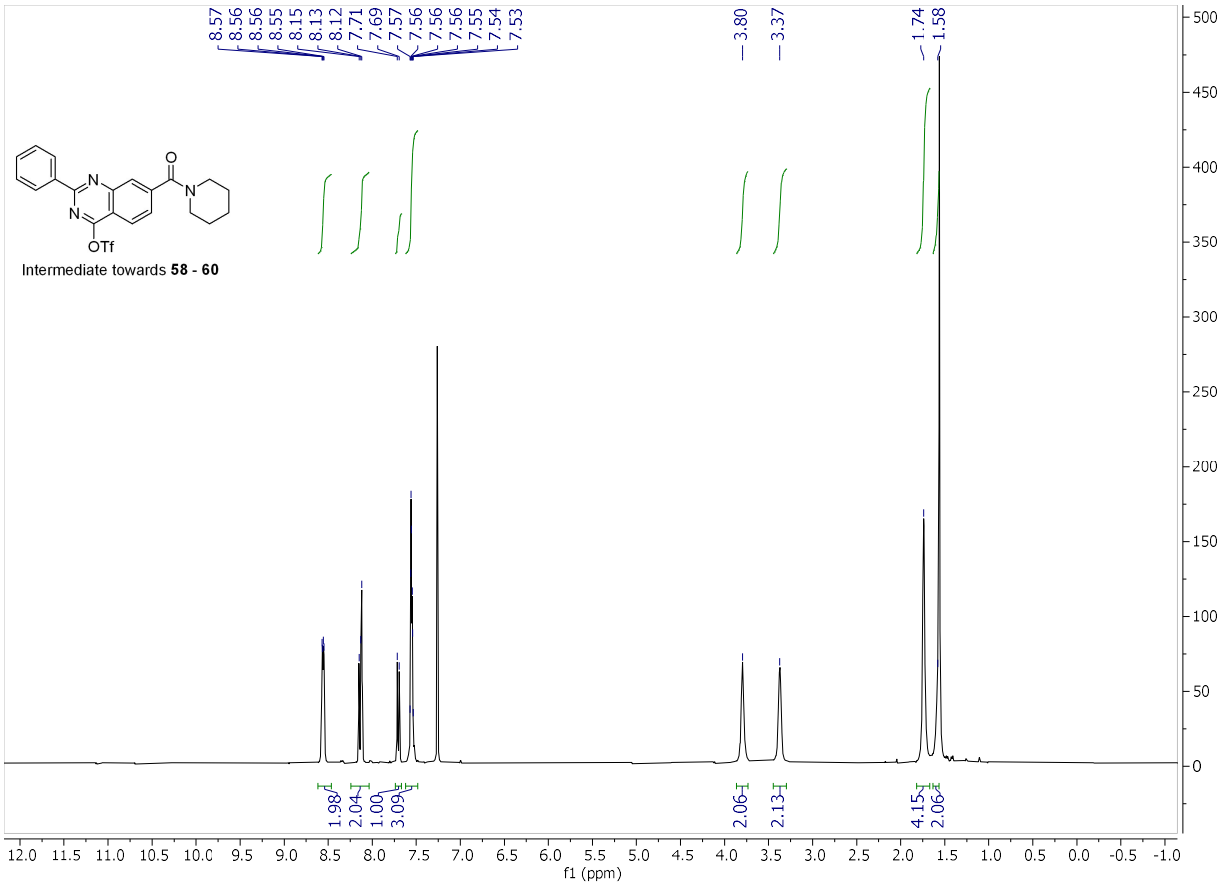

70
f1 (ppm)


Ph
N
Ph
N
nBu
S
O
56
1.02
1.00
1.05
4.02
6.01
2.07
1.04
1.13
2.06
3.00
f1 (ppm)


154.88
154.65
145.82
142.08
140.60
138.52
138.44
130.70
129.82
129.27
128.38
128.36
125.82
123.98
56.75
23.90
21.91
13.66
Ph
N
Ph
N
nBu
S
O
56
f1 (ppm)


12.10
8.36
8.34
8.30
8.29
8.29
8.28
8.27
7.80
7.80
7.61
7.60
7.59
7.58
7.58
7.57
7.57
7.51
7.50
7.49
7.48
3.76
3.36
1.70
1.55
Ph
N
HN
O
O
N
57
1.12
1.07
2.09
1.00
3.15
1.10
2.04
2.08
4.12
2.12
f1 (ppm)


Ph
N
HN
O
O
N
57
168.74
163.64
152.58
149.46
142.91
132.52
131.86
129.02
127.58
127.01
125.84
125.00
121.11
48.71
43.16
26.57
25.61
24.50
f1 (ppm)


8.57
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8.55
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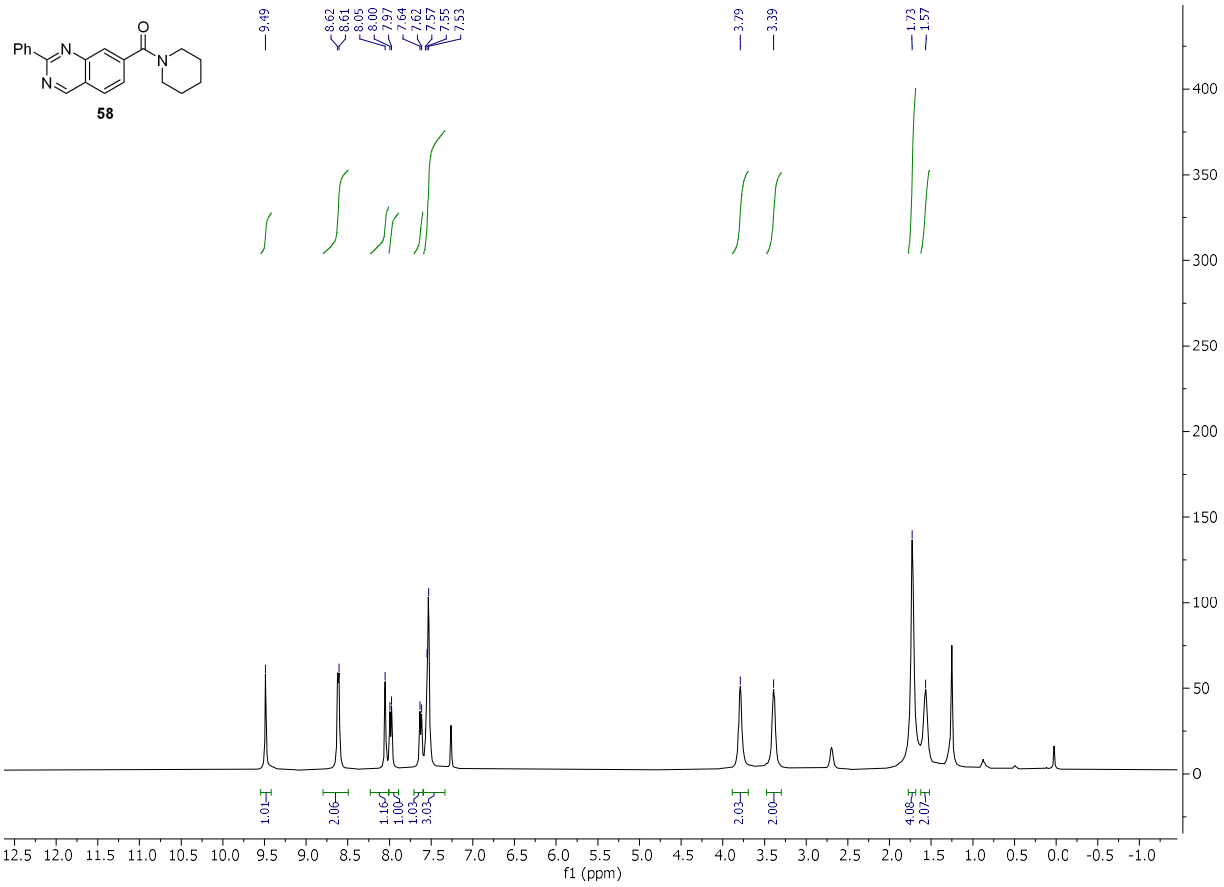
8.13
8.12
7.71
7.69
7.57
7.56
7.56
7.56
7.55
7.54
7.53
3.80
3.37
1.74
1.58
OTf
Intermediate towards 58 - 60
1.98
2.04
1.00
3.09
2.06
2.13
4.15
2.06
f1 (ppm)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9.49
8.62
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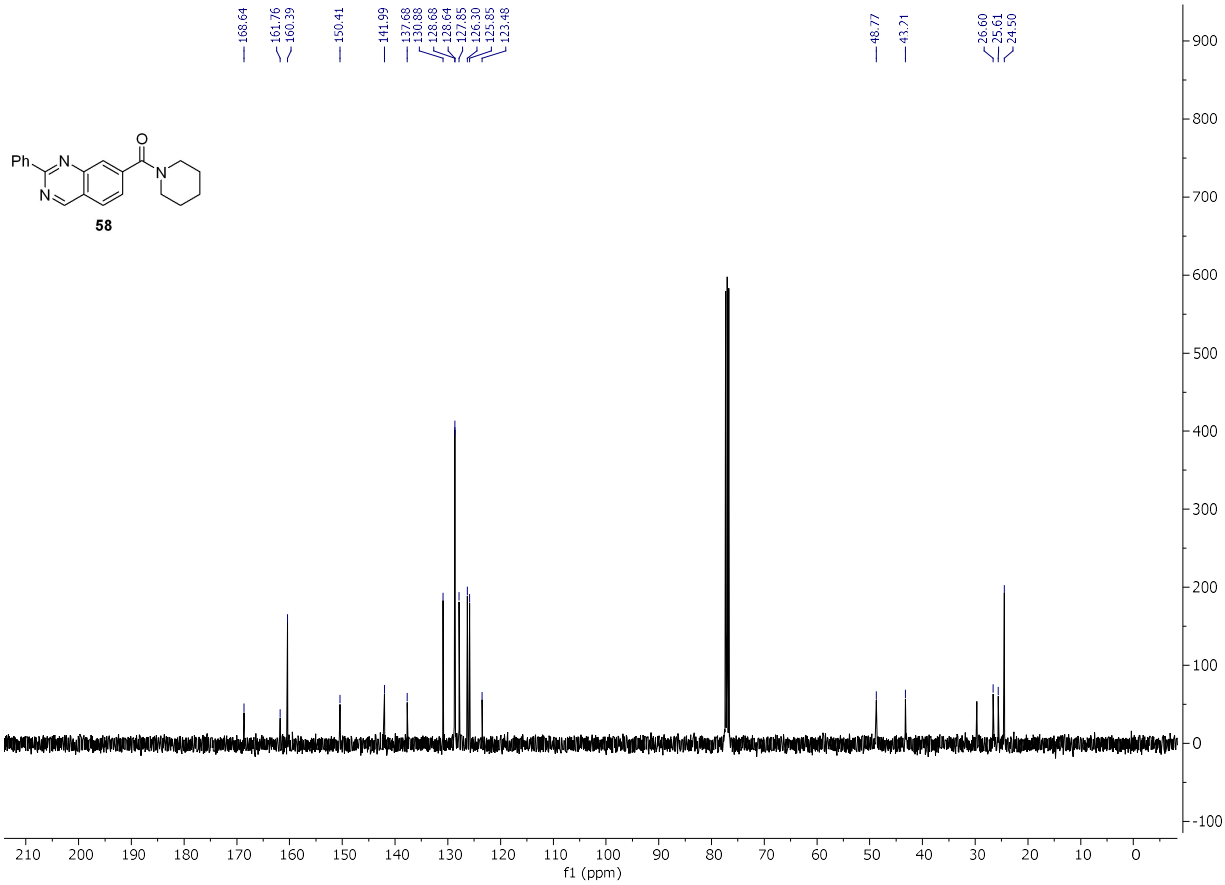
8.00
7.97
7.64
7.62
7.57
7.55
7.53
3.79
3.39
1.73
1.57
1.01
2.06
1.16
1.00
1.03
3.03
2.03
2.00
4.08
2.07
f1 (ppm)


58
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137.68
130.88
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128.64
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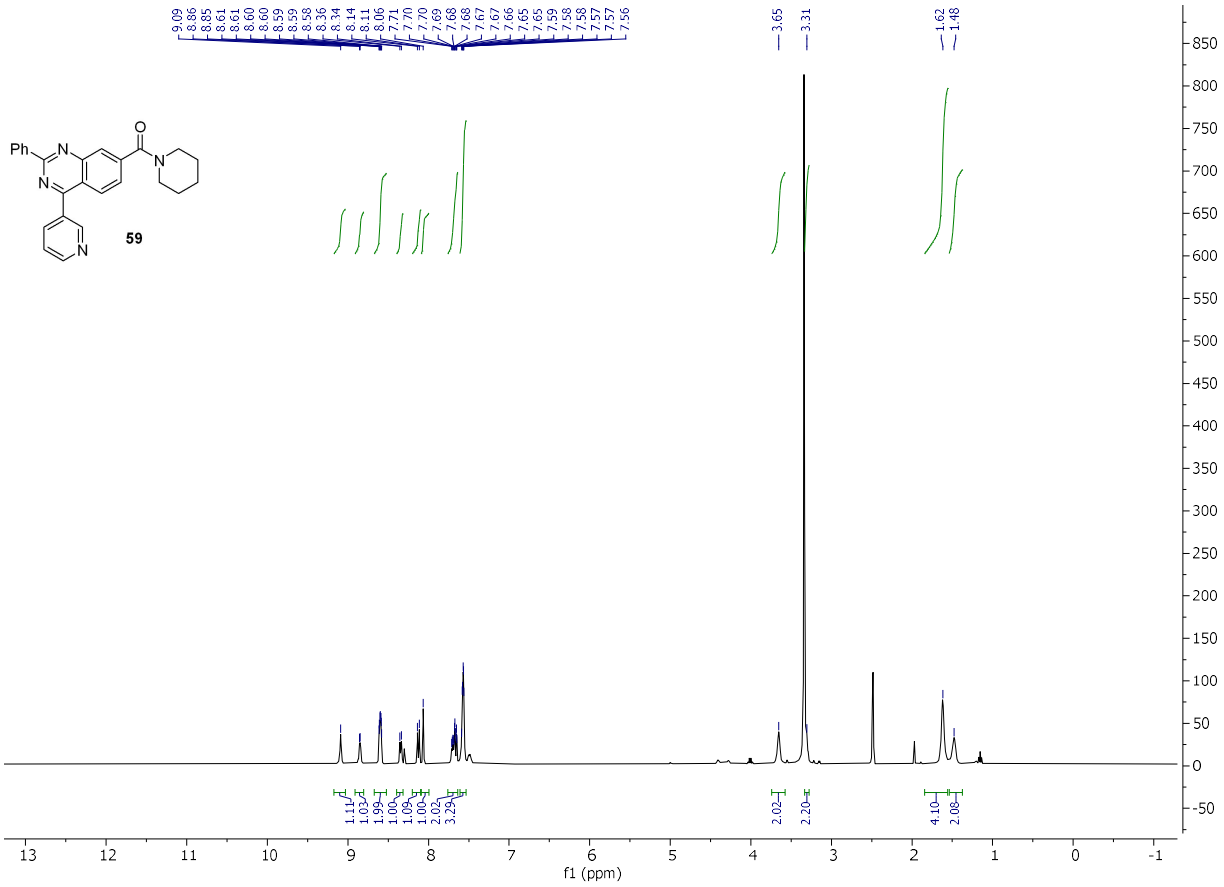
126.30
125.85
123.48
48.77
43.21
26.60
25.61
24.50
f1 (ppm)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8.60
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8.59
8.59
8.58
8.58
8.36
8.34
8.14
8.11
8.06
7.71
7.70
7.70
7.69
7.68
7.68
7.67
7.67
7.66
7.65
7.65
7.59
7.58
7.58
7.57
7.57
7.56
3.65
3.31
1.62
1.48
Ph
N
N
O
N
N
59
1.11
1.02
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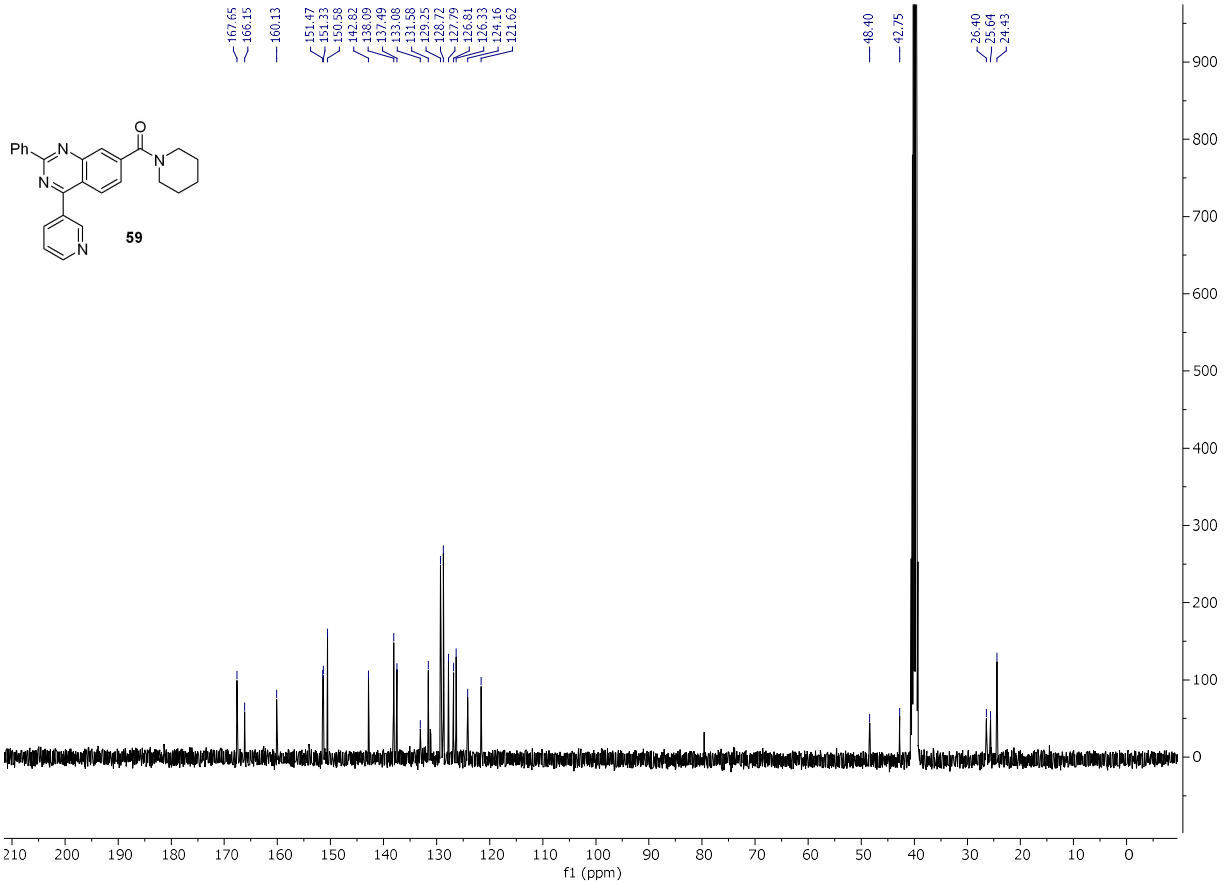
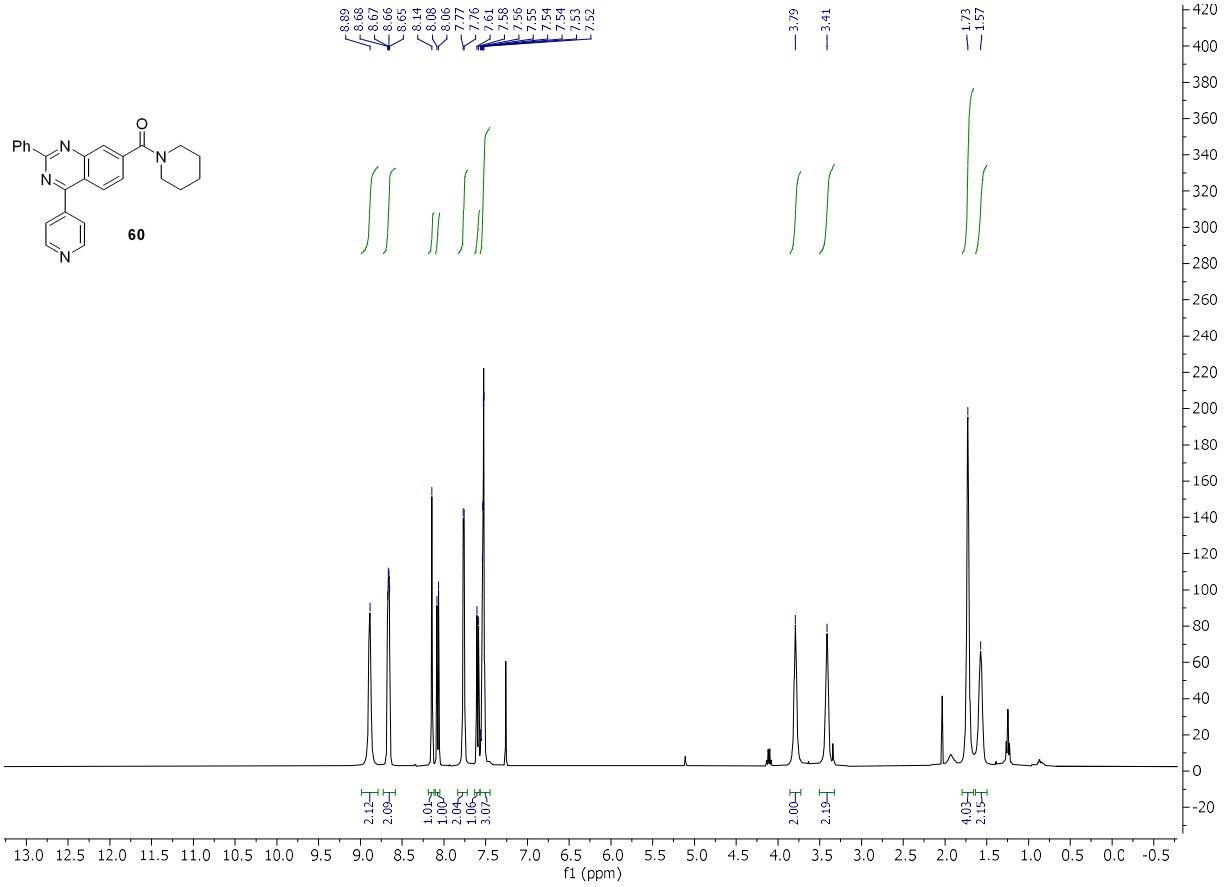
1.08
1.00
2.02
3.29
2.02
2.20
4.10
2.08
f1 (ppm)


167.65
166.15
160.13
151.47
151.33
150.58
142.82
138.09
137.49
133.08
131.58
129.25
128.72
127.79
126.81
126.33
124.16
121.62
48.40
42.75
26.40
25.64
24.43
Ph
N
N
O
N
N
59
f1 (ppm)


8.89
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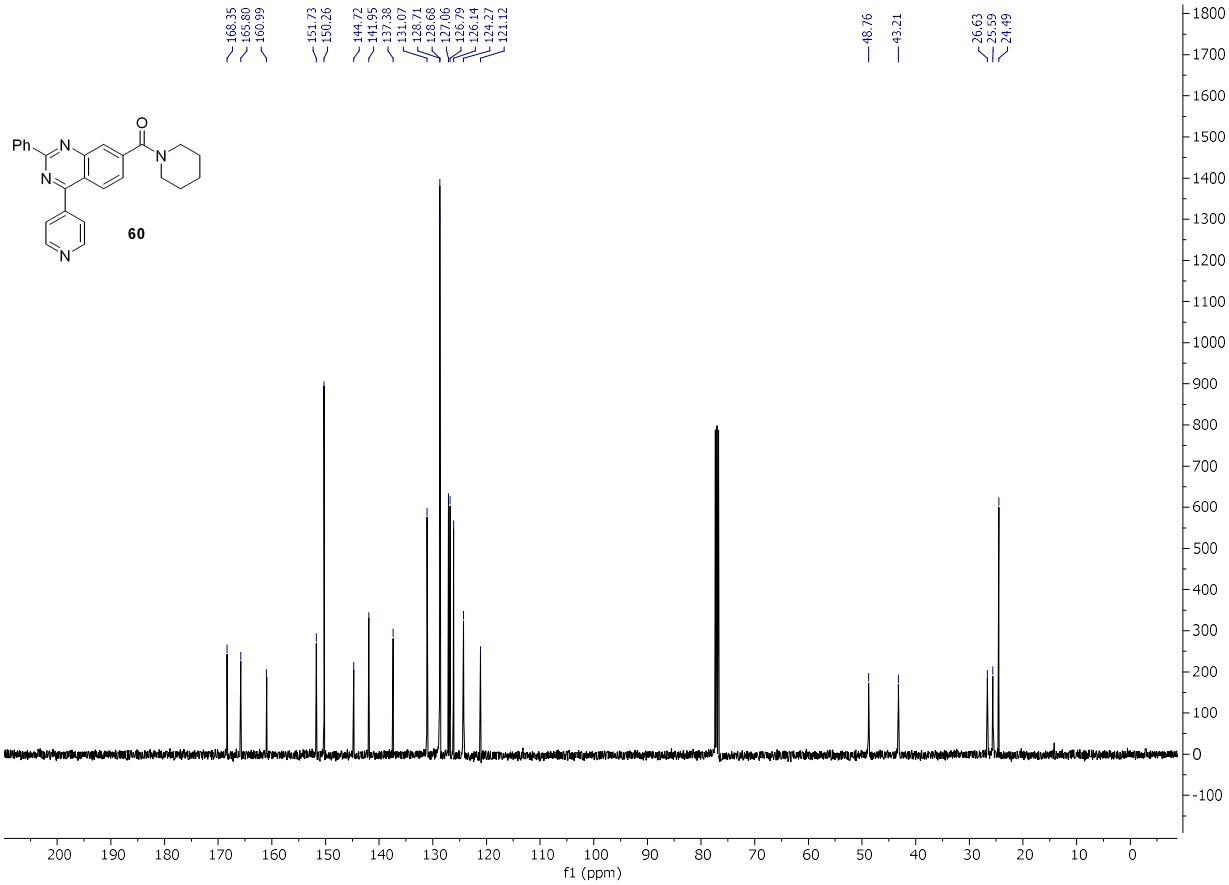
8.67
8.66
8.65
8.14
8.08
8.06
7.77
7.76
7.61
7.58
7.56
7.55
7.54
7.54
7.53
7.52
3.79
3.41
1.73
1.57
Ph
N
N
O
N
N
60
2.12
2.09
1.01
1.00
2.04
1.06
3.07
2.00
2.19
4.03
2.15
f1 (ppm)


168.35
165.80
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151.73
150.26
144.72
141.95
137.38
131.07
128.71
128.68
127.06
126.79
126.14
124.27
121.12
48.76
43.21
26.63
25.59
24.49
Ph
N
N
O
N
N
60
f1 (ppm)