Supplementary Material

Design, synthesis, and biological evaluation of novel FAK scaffold inhibitors targeting the FAK-VEGFR3 protein-protein interaction.

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H
N
N
N
7
0.62
0.91
0.00
0.86
0.49
0.84
1.60
2.00
0.93
1.83
6.10
8
7
6
5
4
3
2
1
0

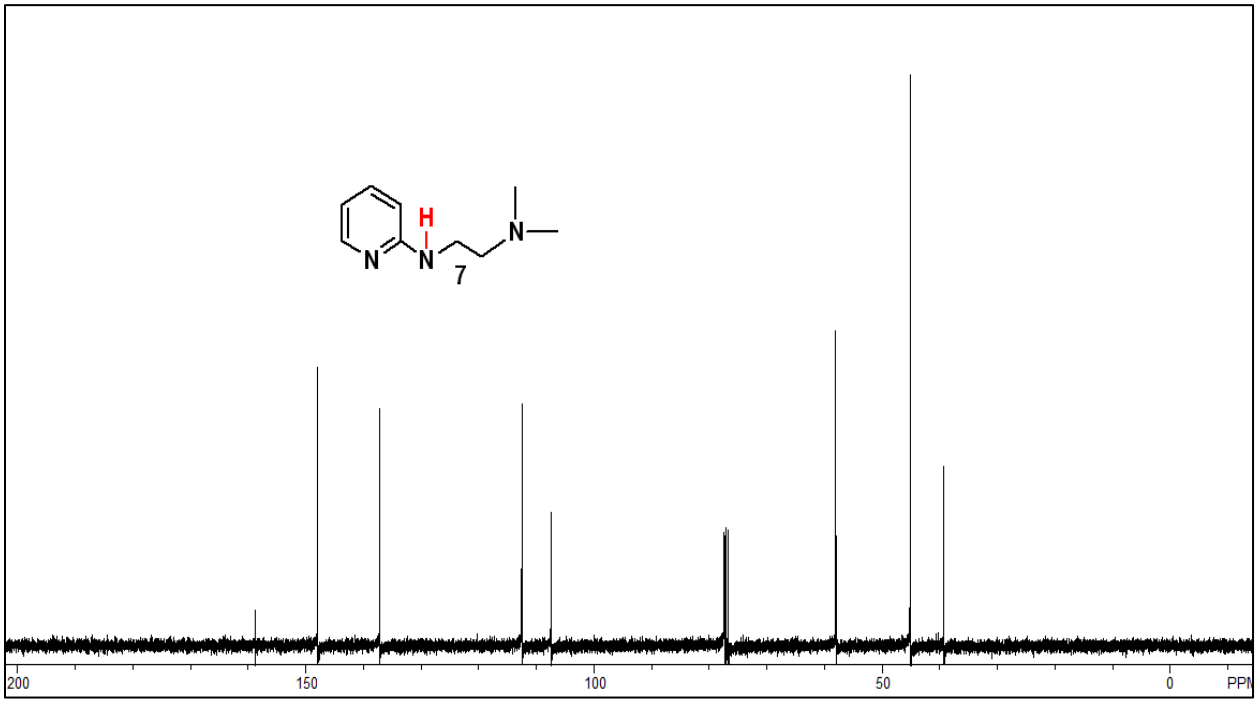
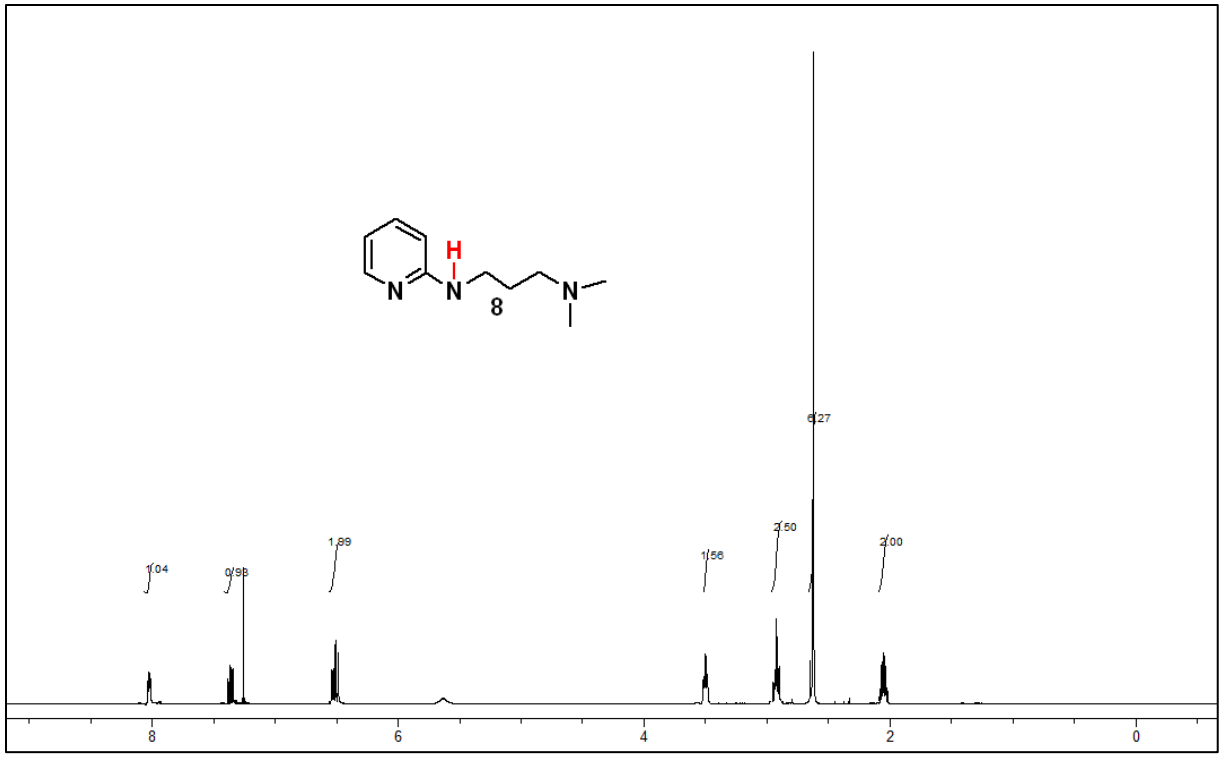

H
N
N
N
7
200
150
100
50
0
PPM

Figure S1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1.04
0.98
1.56
2.00
8
6
4
2
0

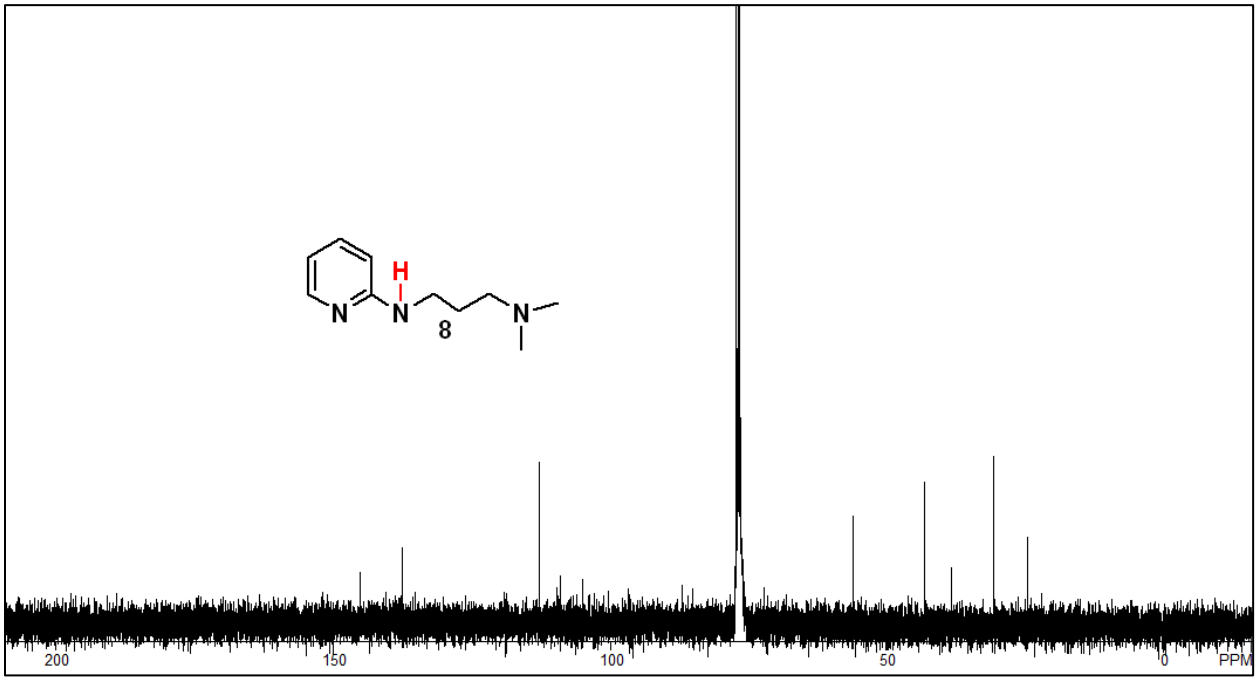

H
N
N
8
N
200
150
100
50
0
PPM

Figure S2

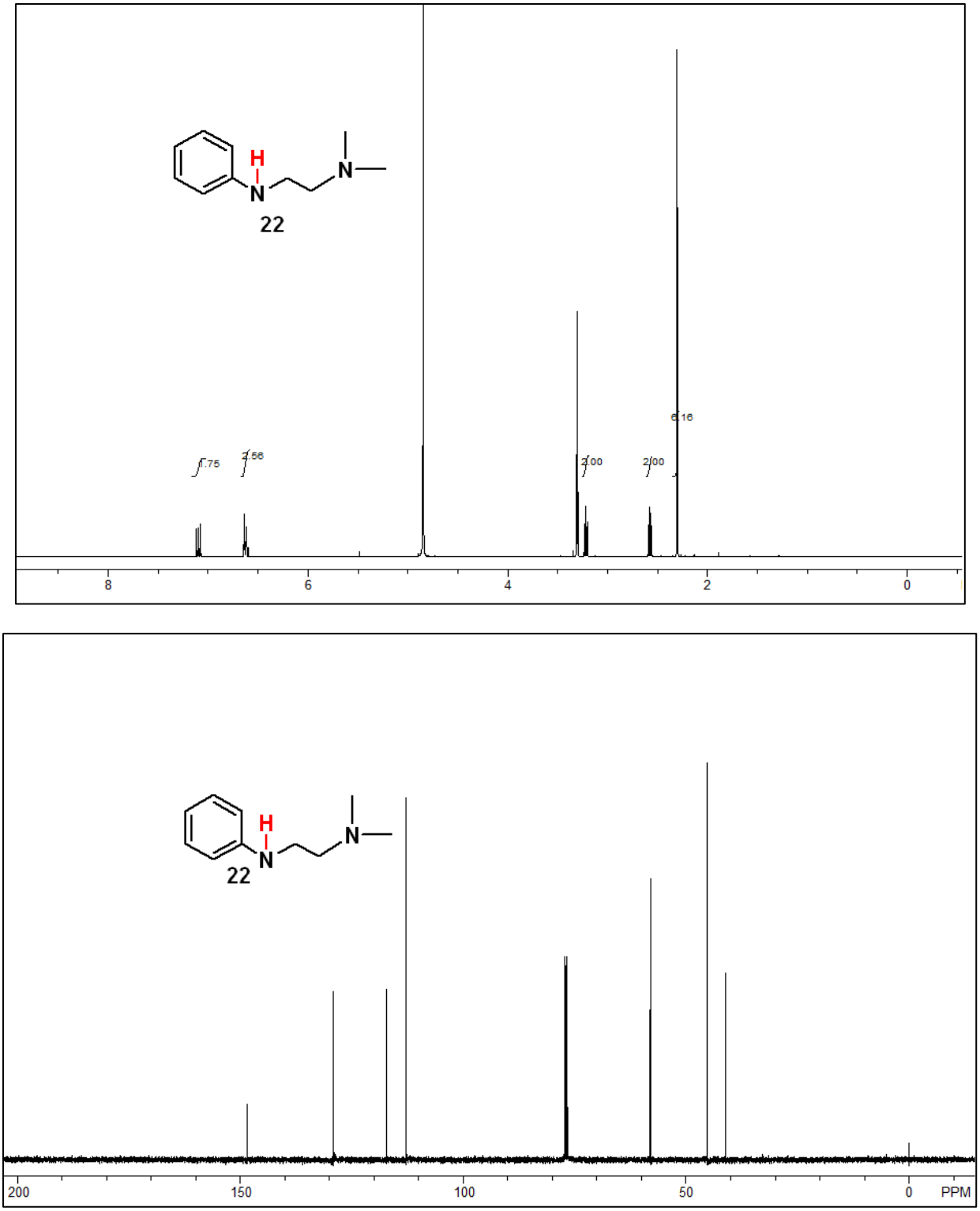
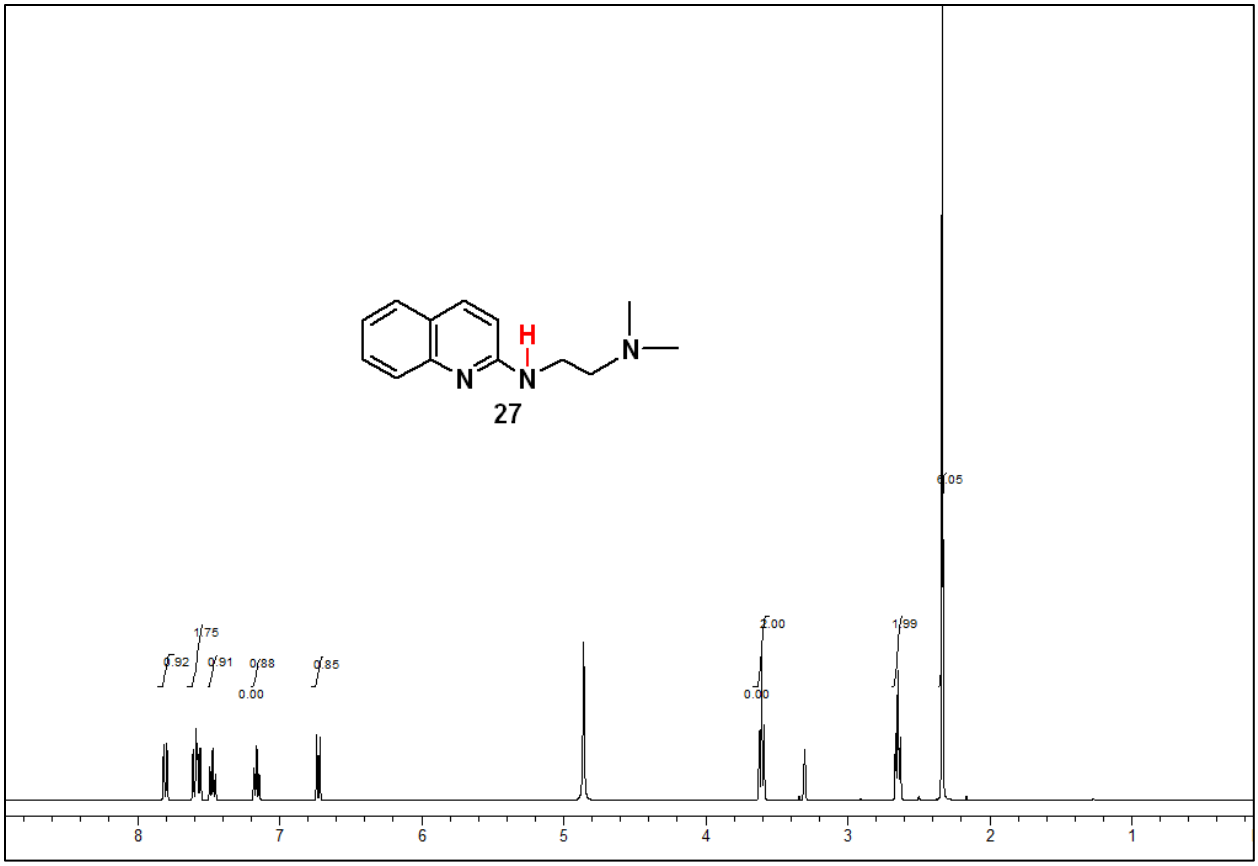


Figure S3


H
N
N
N
27
6.05
1.75
0.92
0.91
0.88
0.00
0.85
2.00
0.00
1.99
8
7
6
5
4
3
2
1

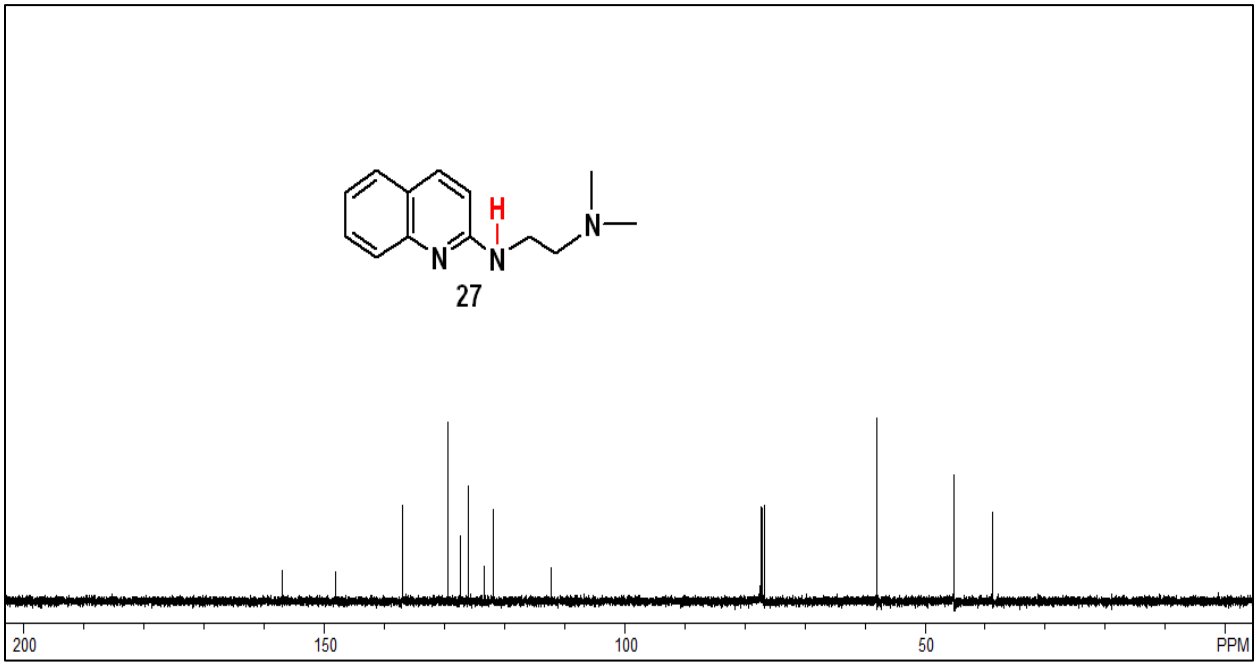

H
N
N
N
27
200
150
100
50
PPM

Figure S4

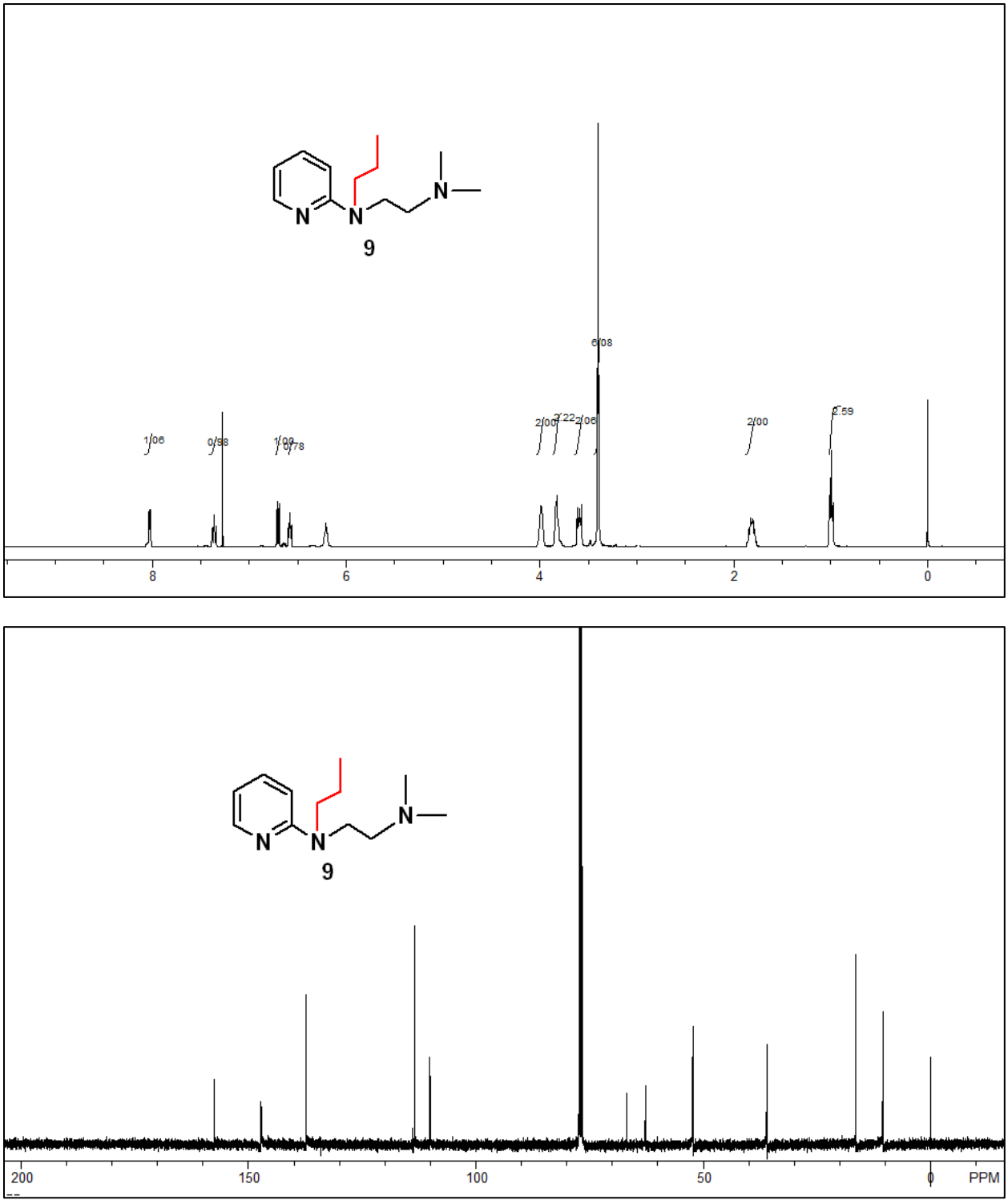
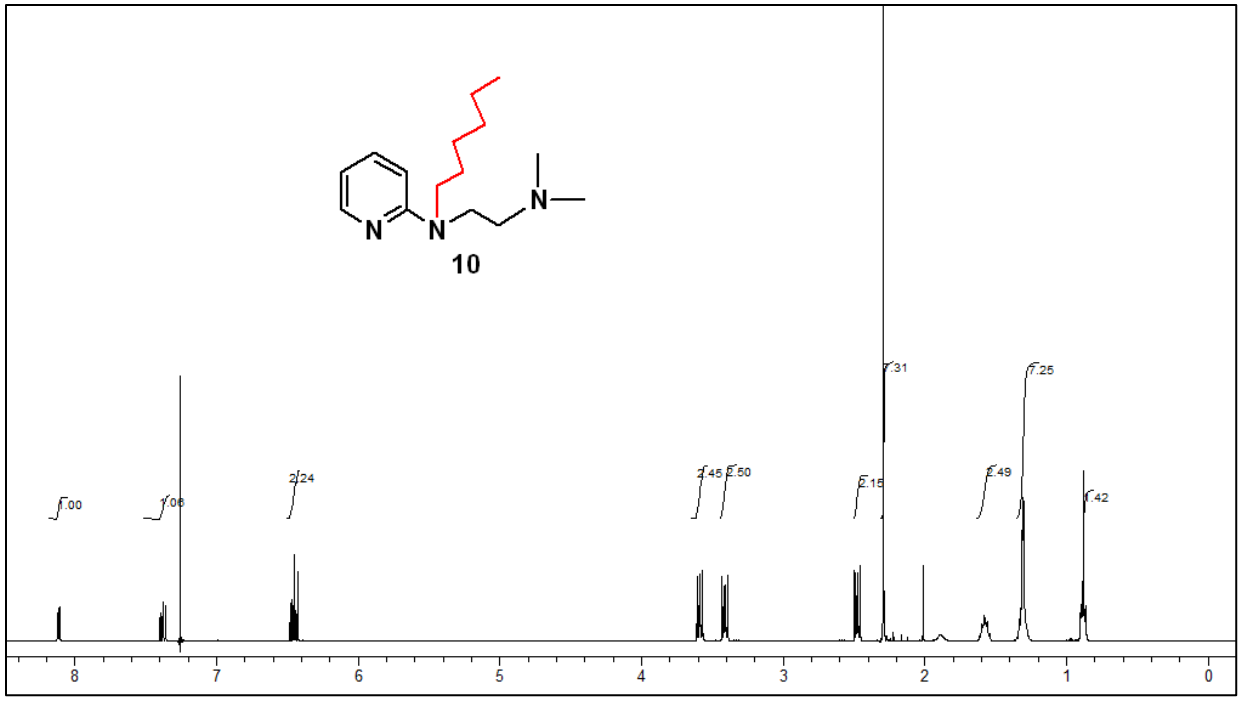

9
1.06
0.98
1.08
0.78
2.00
2.22
2.06
6.08
2.00
2.59
8
6
4
2
0
9
200
150
100
50
0
PPM

Figure S5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1.00
1.06
2.24
2.45
2.50
2.15
7.31
2.49
7.25
7.42
8
7
6
5
4
3
2
1
0

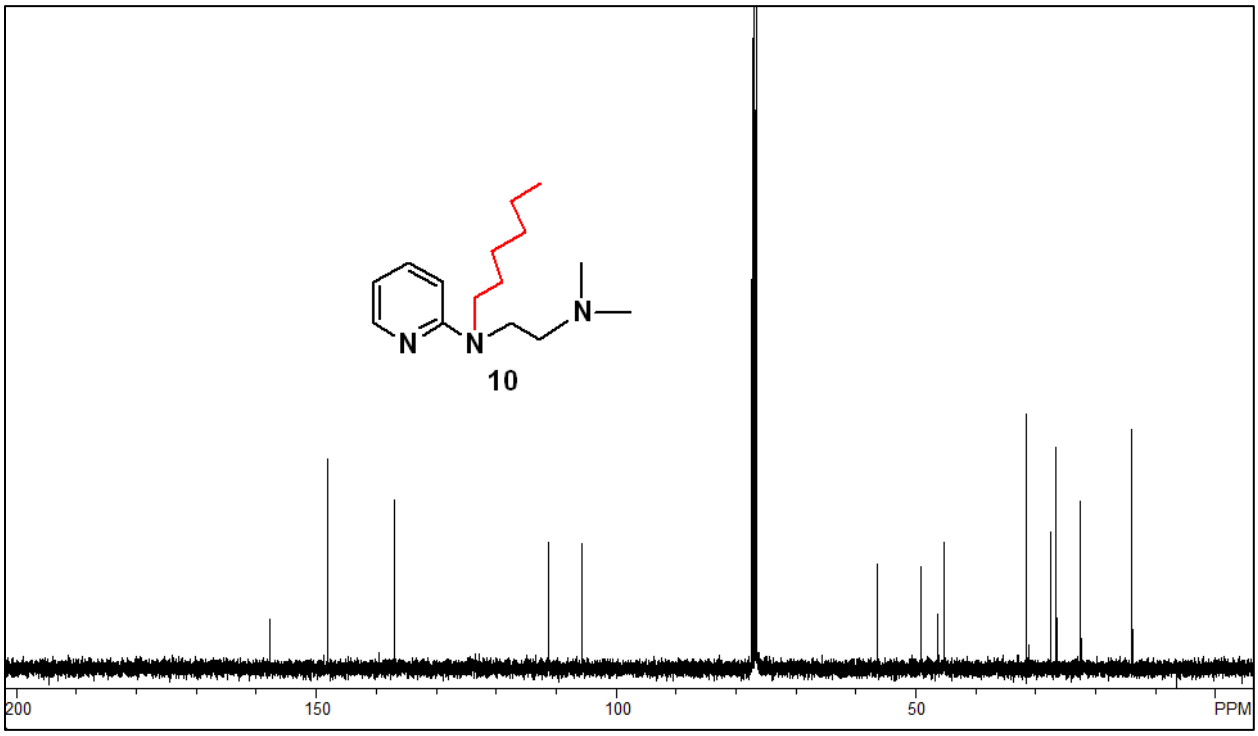
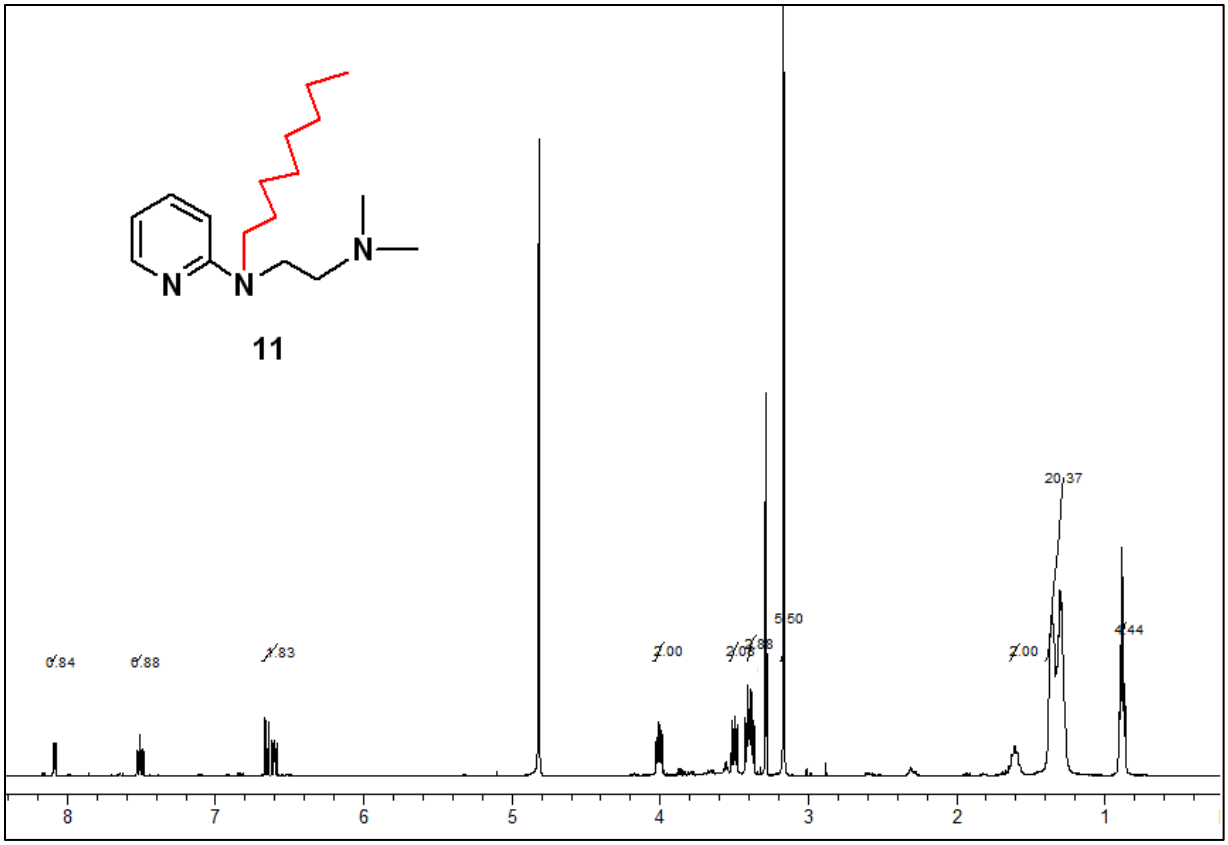

10
200
150
100
50
PPM

Figure S6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0.84
0.88
1.83
7.00
2.08
3.88
5.50
7.00
20.37
4.44
8
7
6
5
4
3
2
1

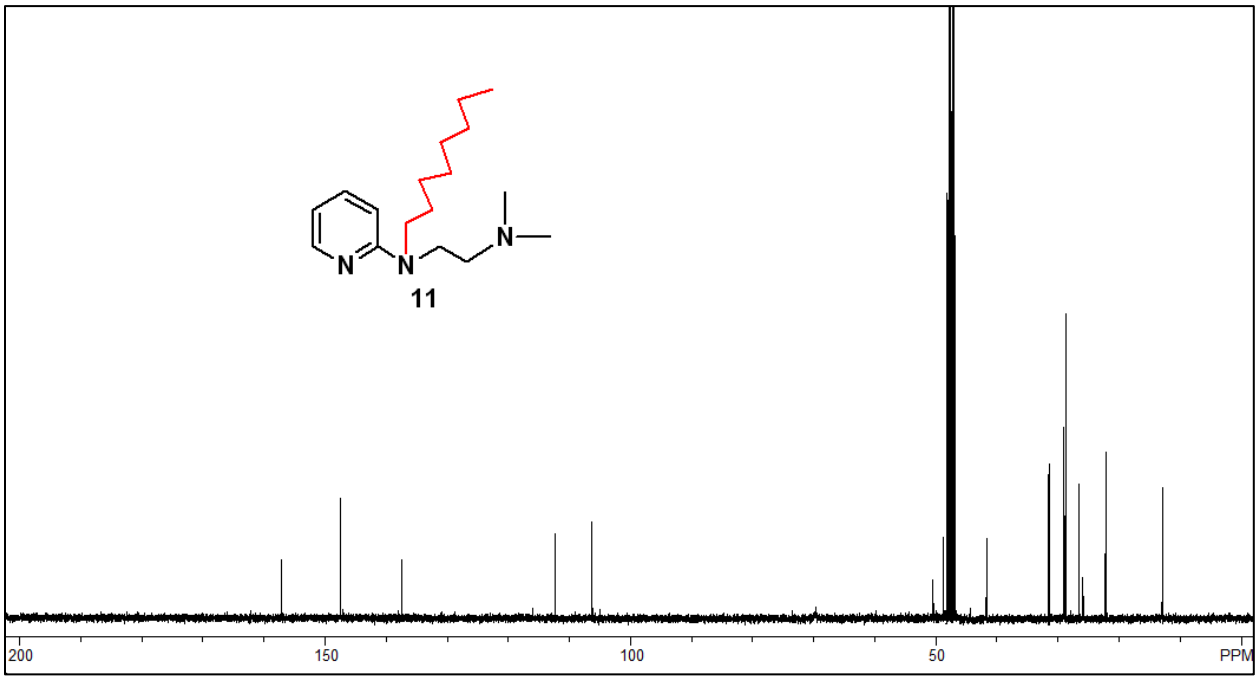
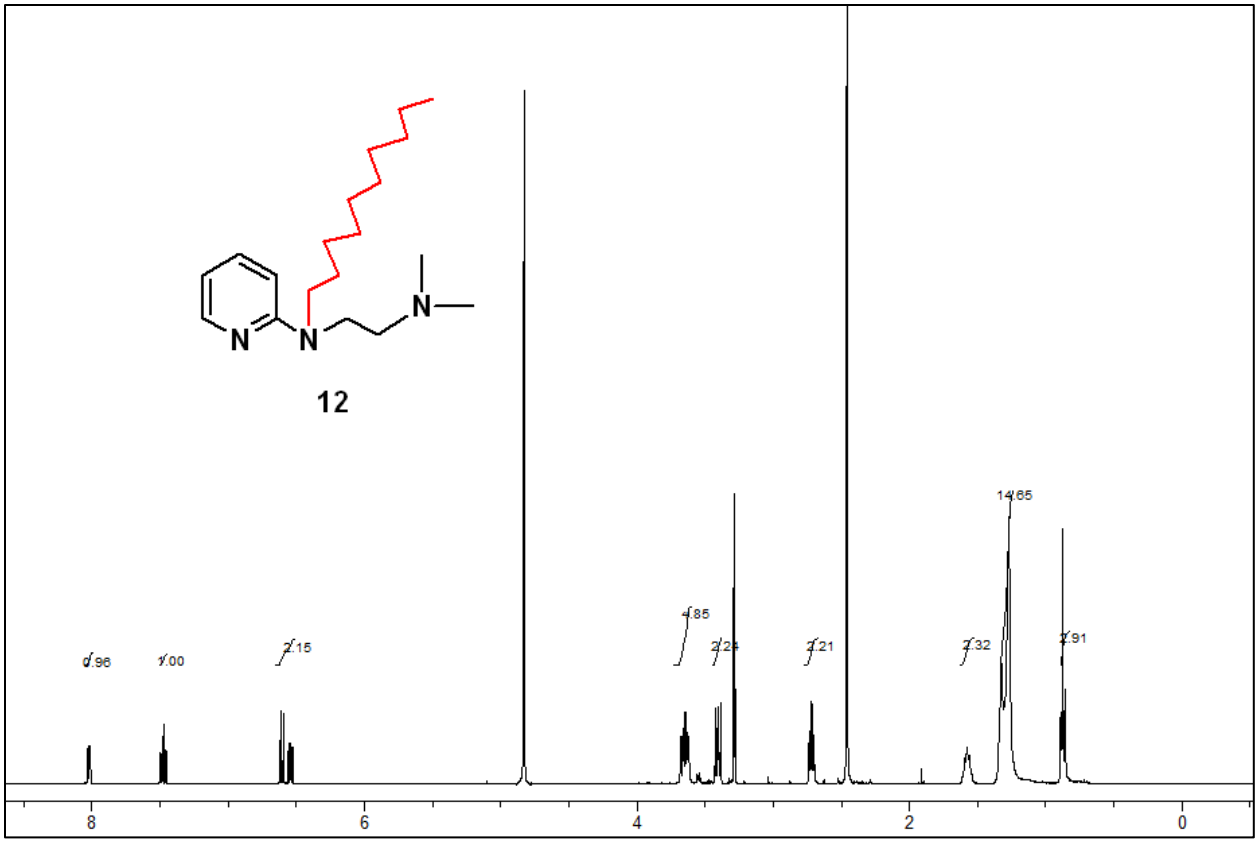

11
200
150
100
50
PPM

Figure S7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0.96
1.00
2.15
4.85
3.24
3.21
7.32
14.65
2.91
8
6
4
2
0

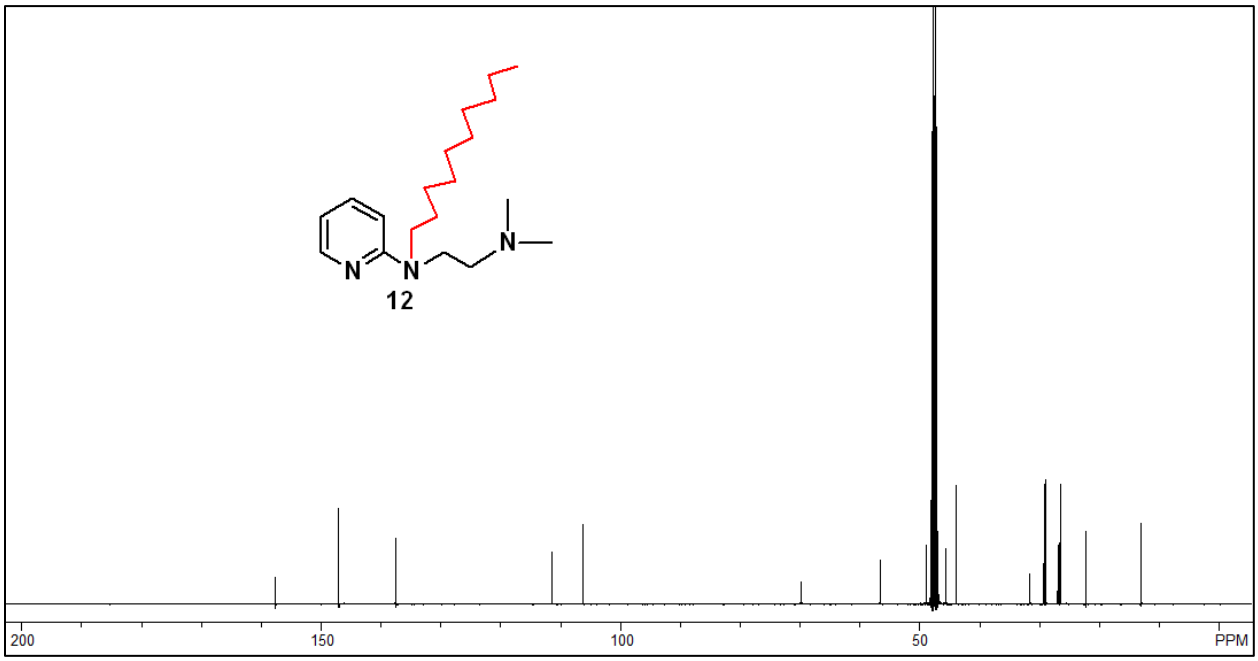
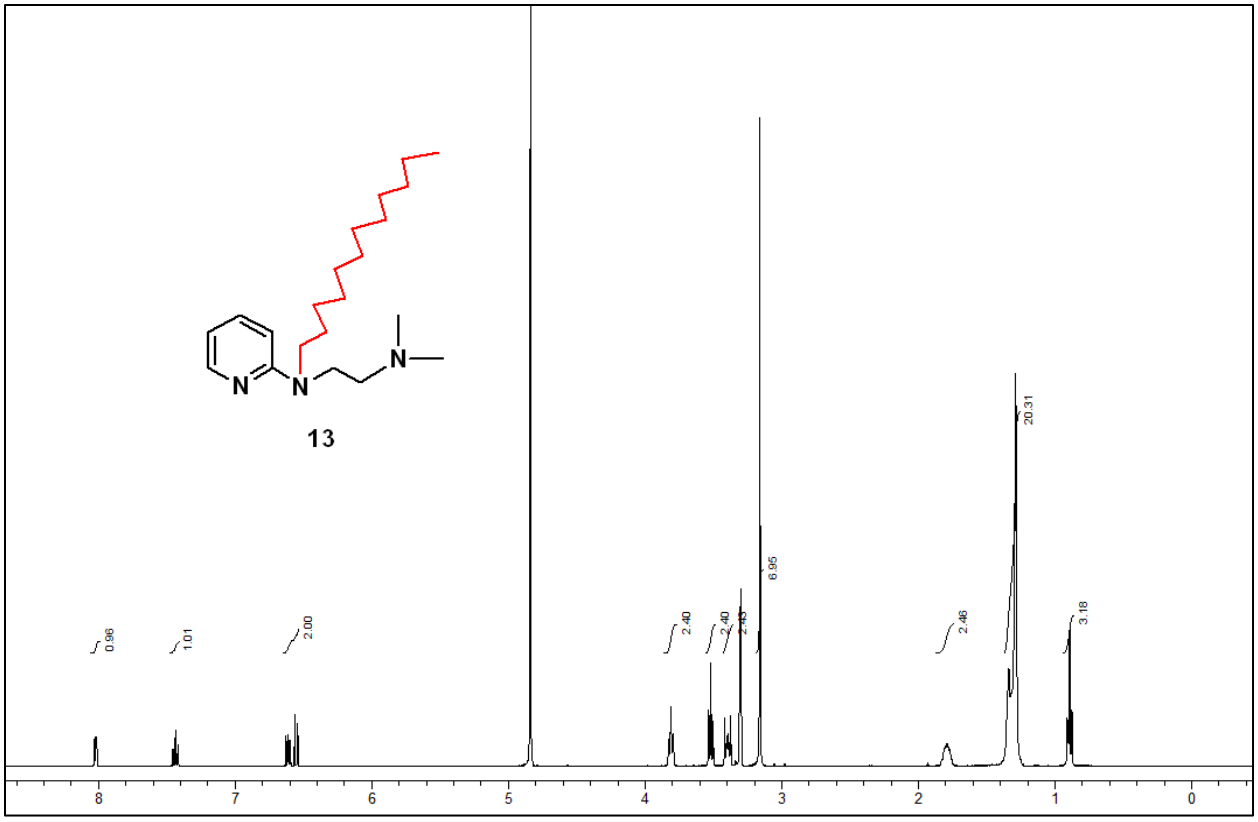

12
200
150
100
50
PPM

Figure S8


13
0.96
1.01
2.00
2.40
2.40
2.43
6.95
2.46
20.31
3.18
8
7
6
5
4
3
2
1
0

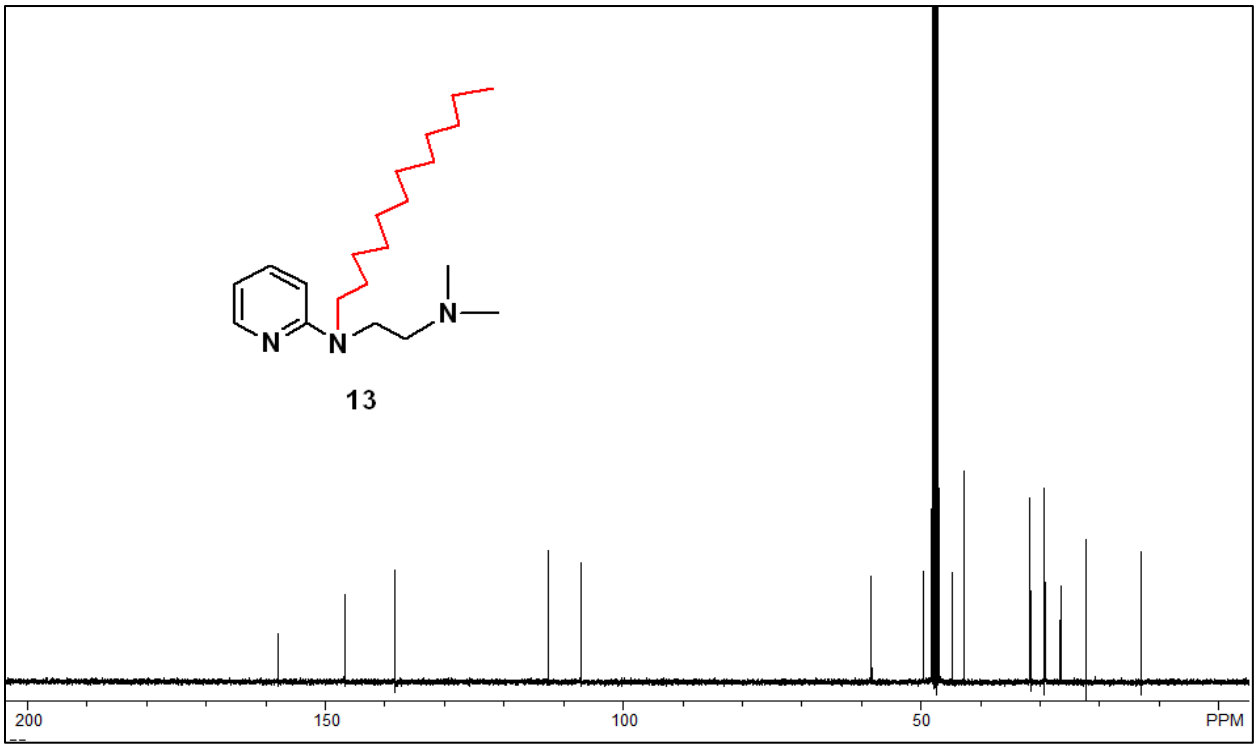
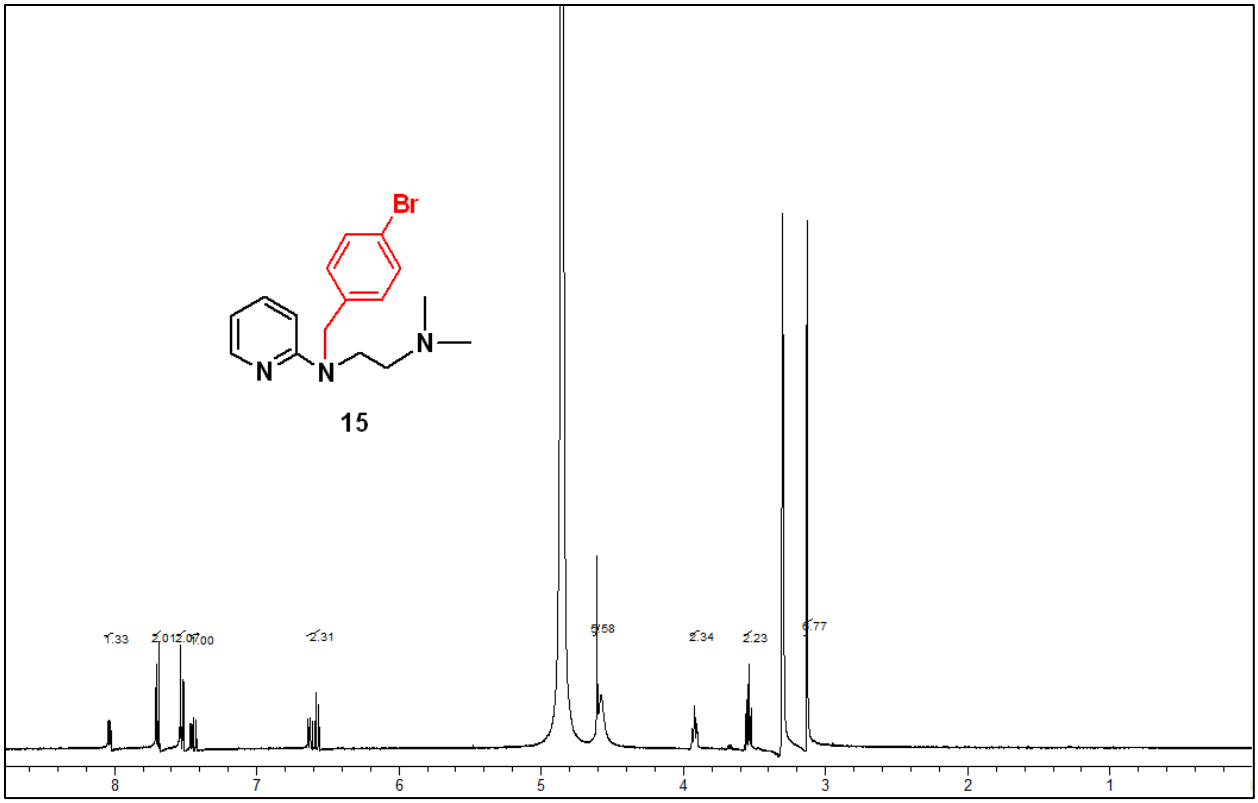

13
200
150
100
50
PPM

Figure S9


Br
N
N
N
15
1.33
2.01
2.07
2.00
2.31
5.58
2.34
2.23
9.77
8
7
6
5
4
3
2
1

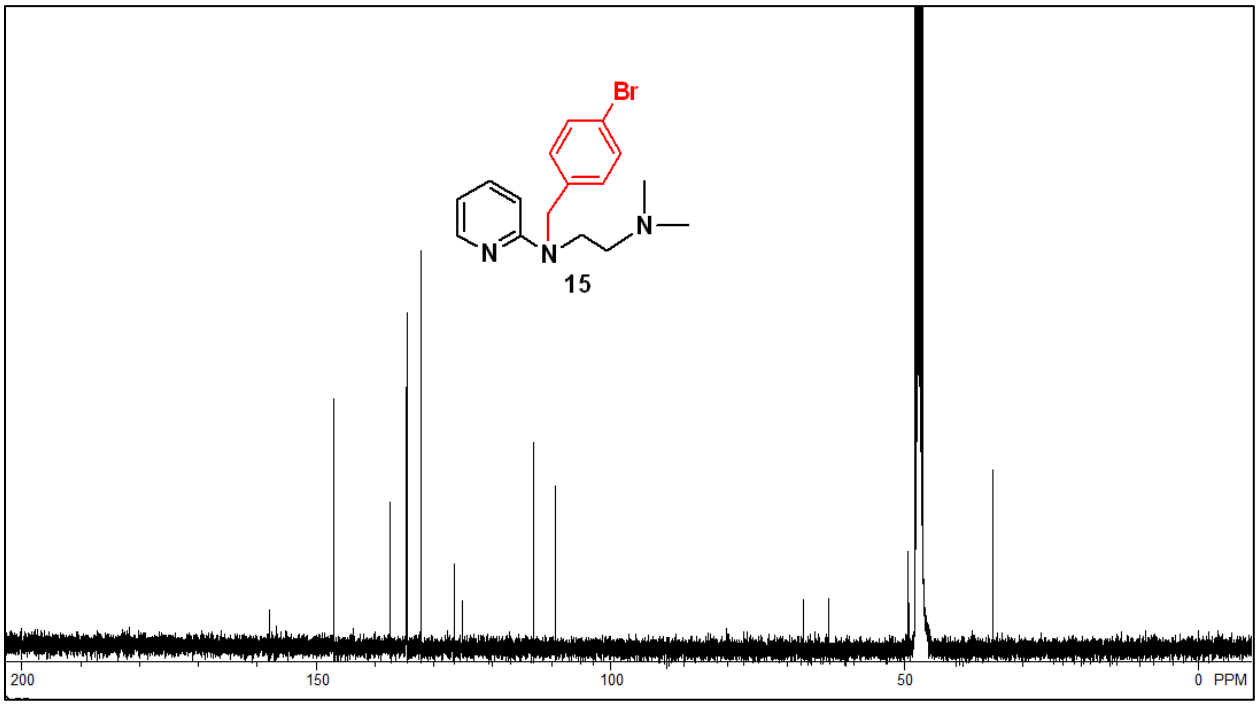
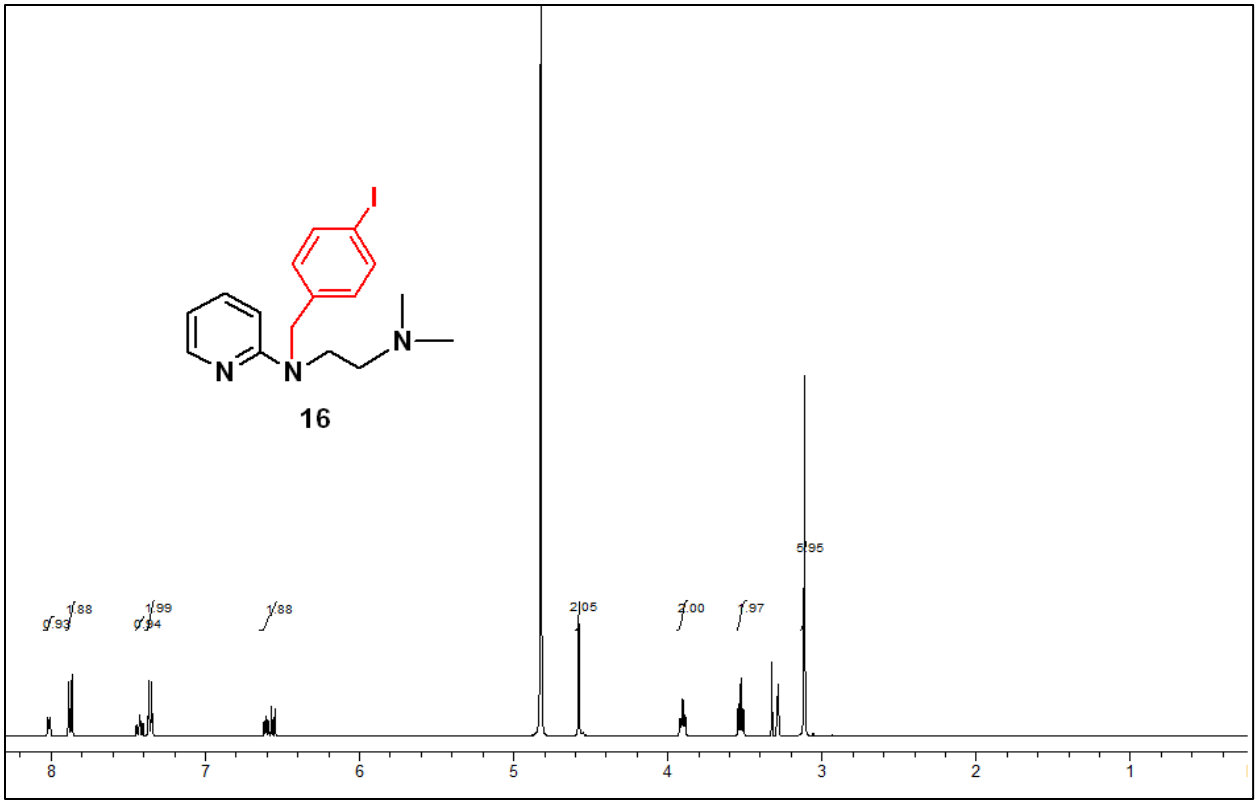

Br
N
N
N
15
200
150
100
50
0 PPM

Figure S10


I
N
N
N
16
1.88
1.99
1.88
2.05
2.00
1.97
5.95
8
7
6
5
4
3
2
1

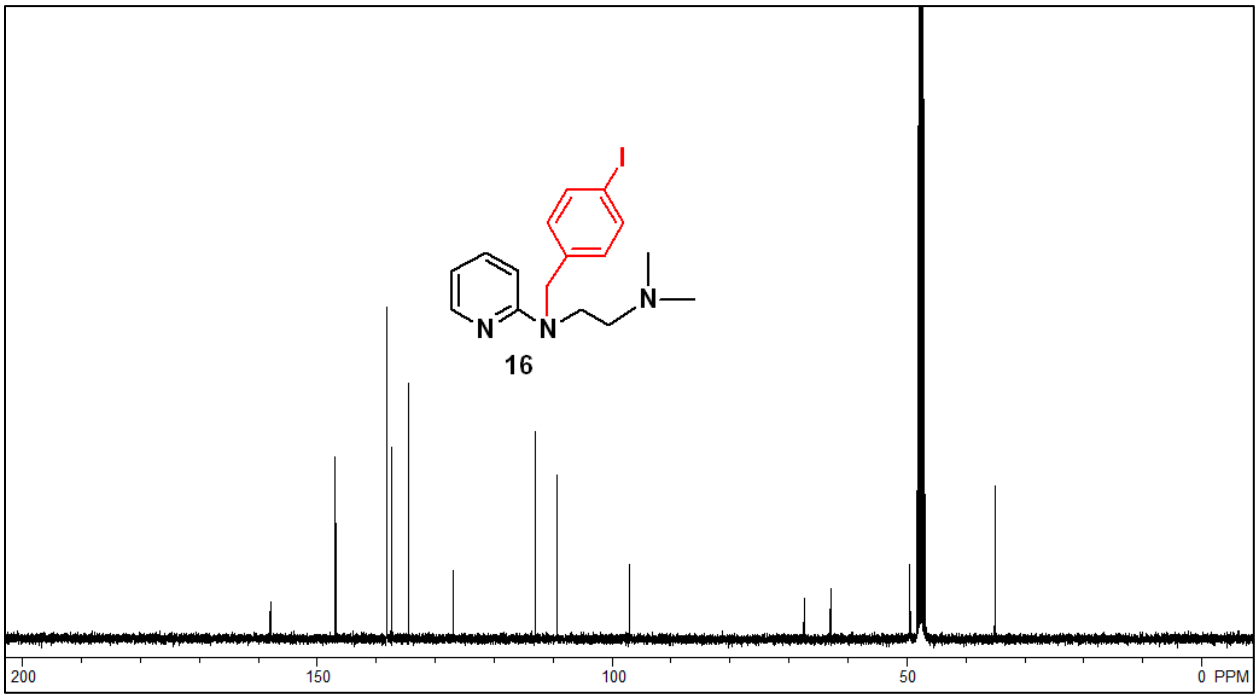

I
N
N
N
16
200
150
100
50
0 PPM

Figure S11

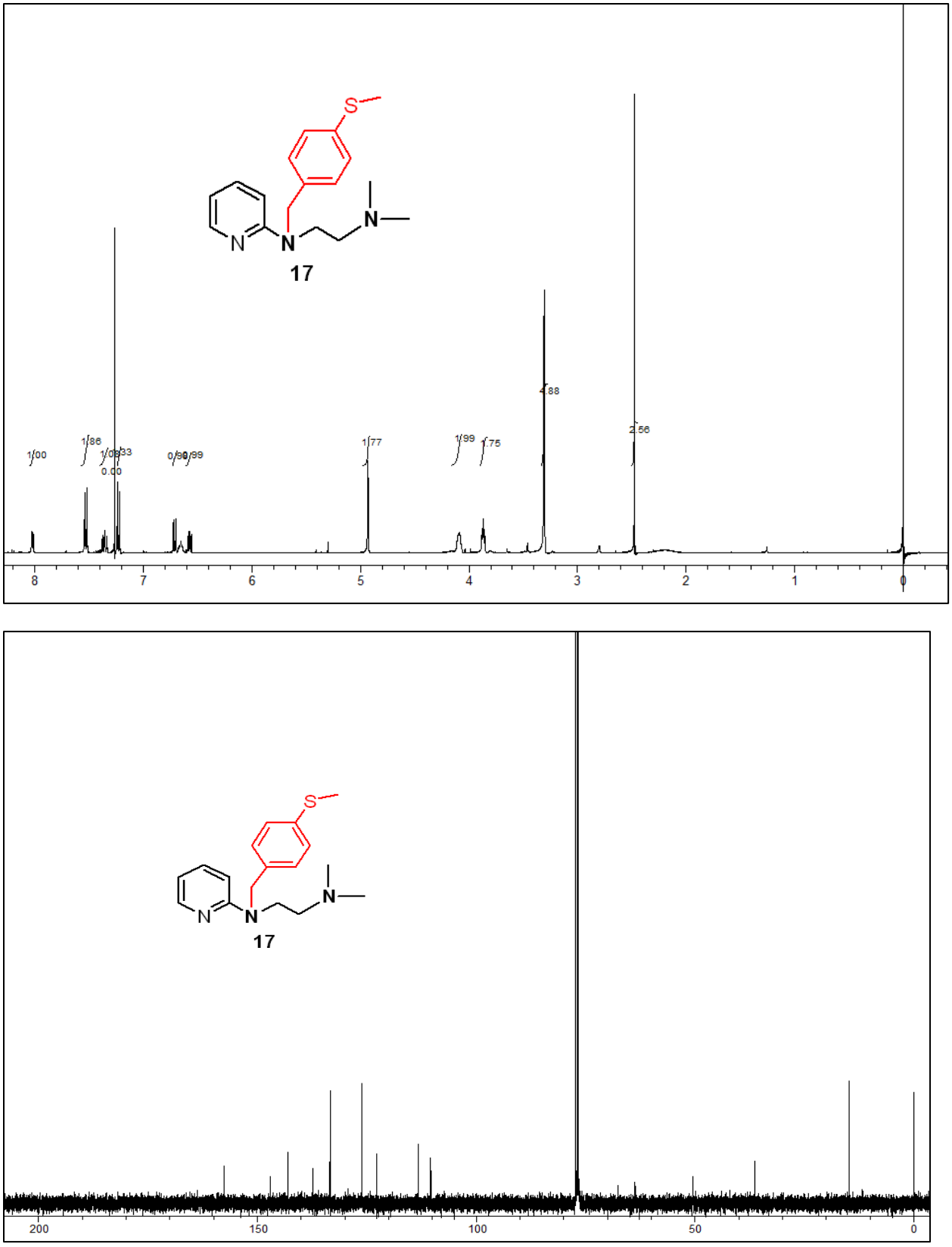
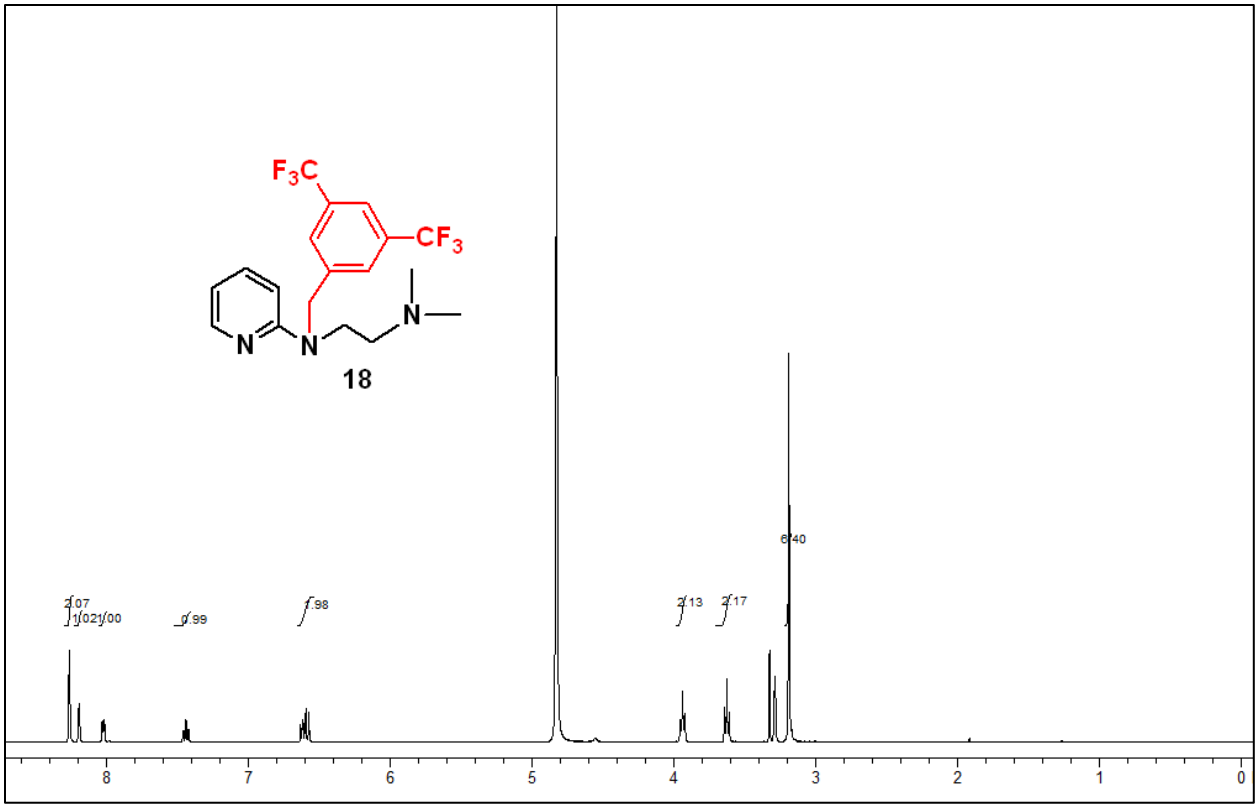

S
N
N
N
17
1.00
1.86
1.08
1.33
0.00
0.98
0.99
1.77
1.99
1.75
4.88
2.56
8
7
6
5
4
3
2
1
0
S
N
N
N
17
200
150
100
50
0

Figure S12



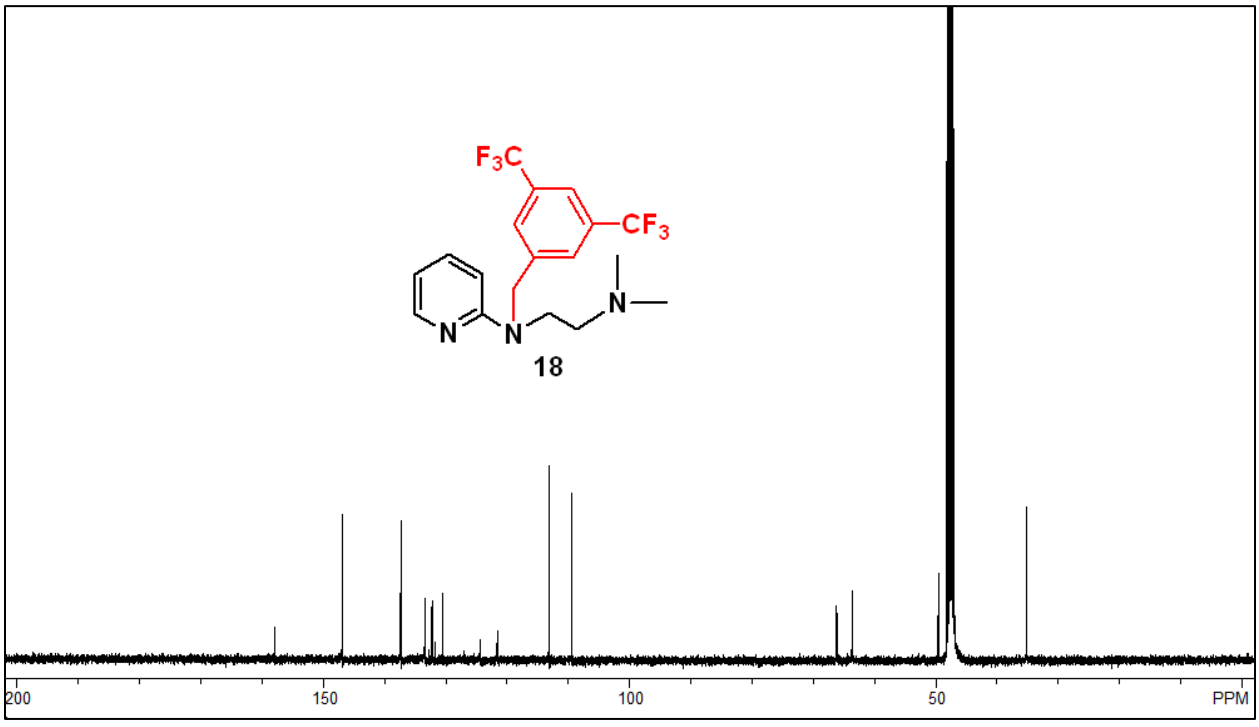


Figure S13

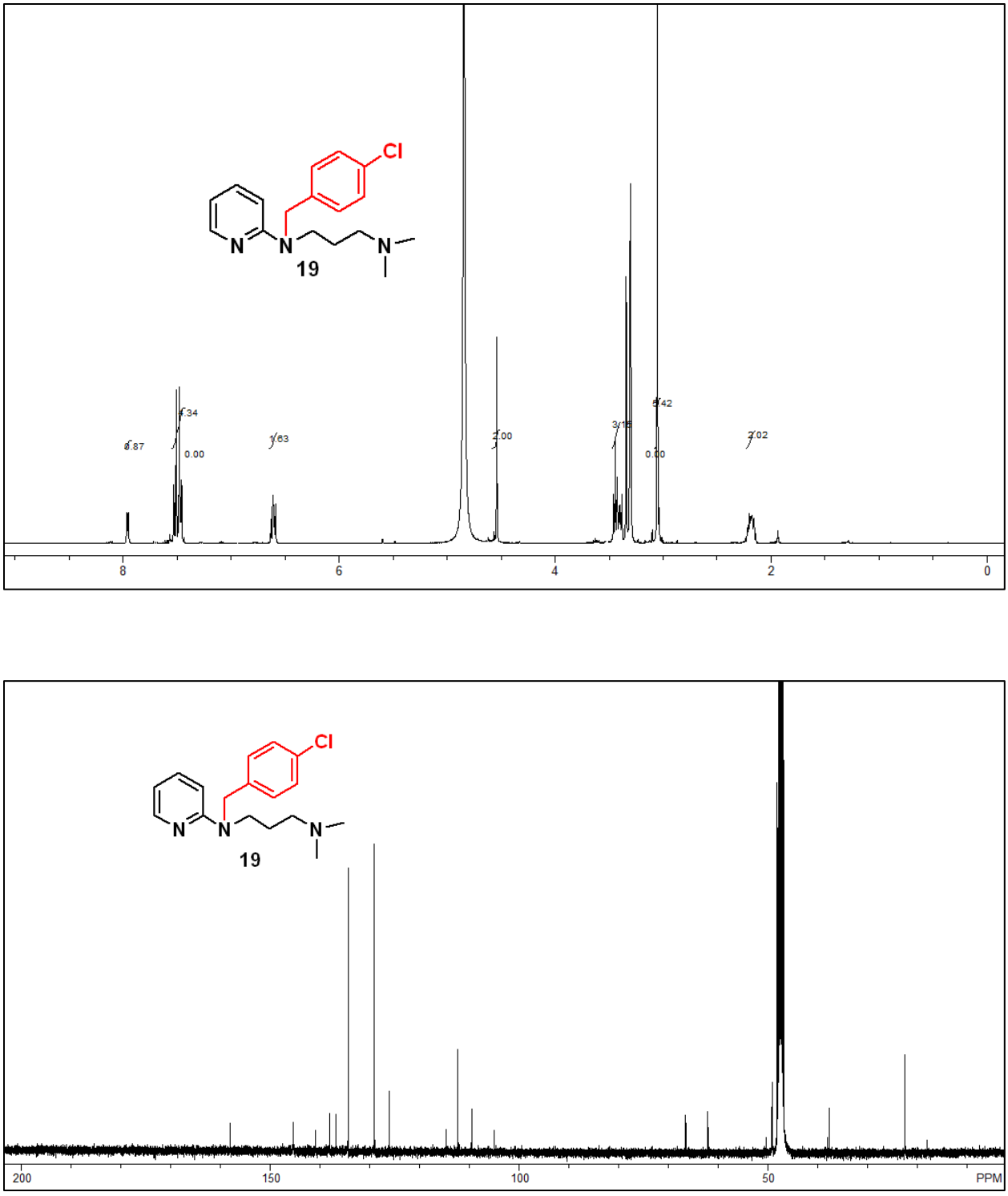

Cl
N
N
N
19
0.87
4.34
0.00
1.63
2.00
3.15
5.42
0.00
7.02
8
6
4
2
0
Cl
N
N
N
19
200
150
100
50
PPM

Figure S14

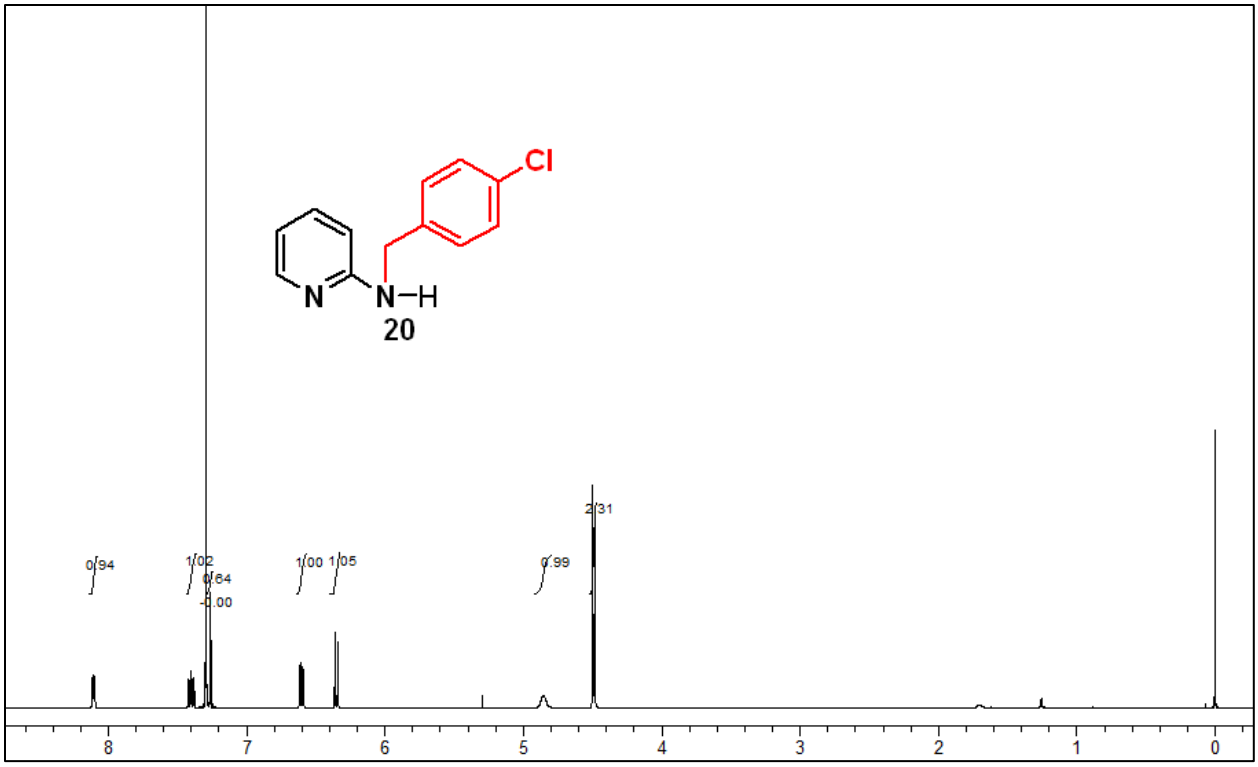


Figure S15

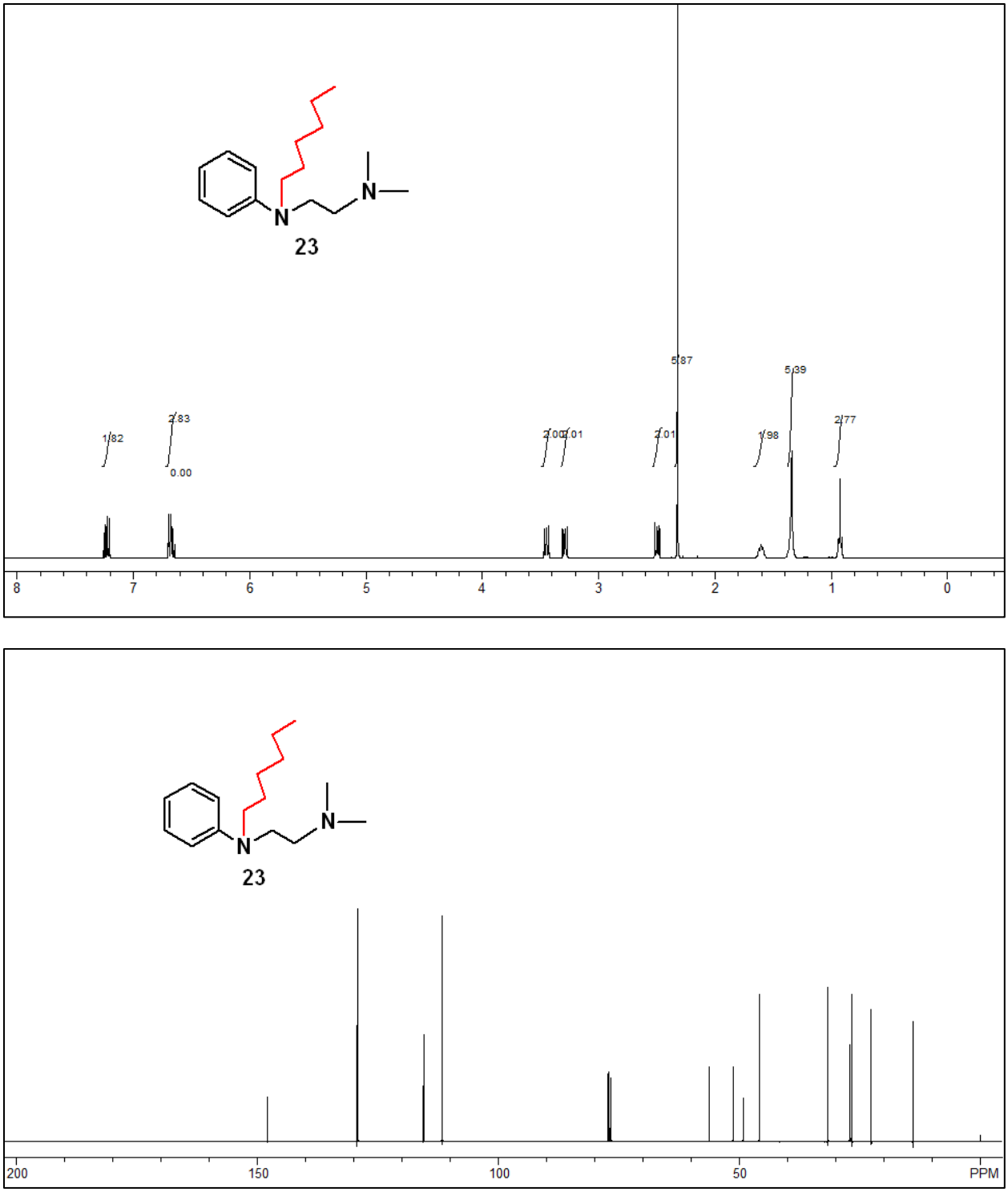

23
1.82
2.83
0.00
2.00
2.01
5.87
2.01
1.98
5.39
2.77
8
7
6
5
4
3
2
1
0
23
200
150
100
50
PPM

Figure S16

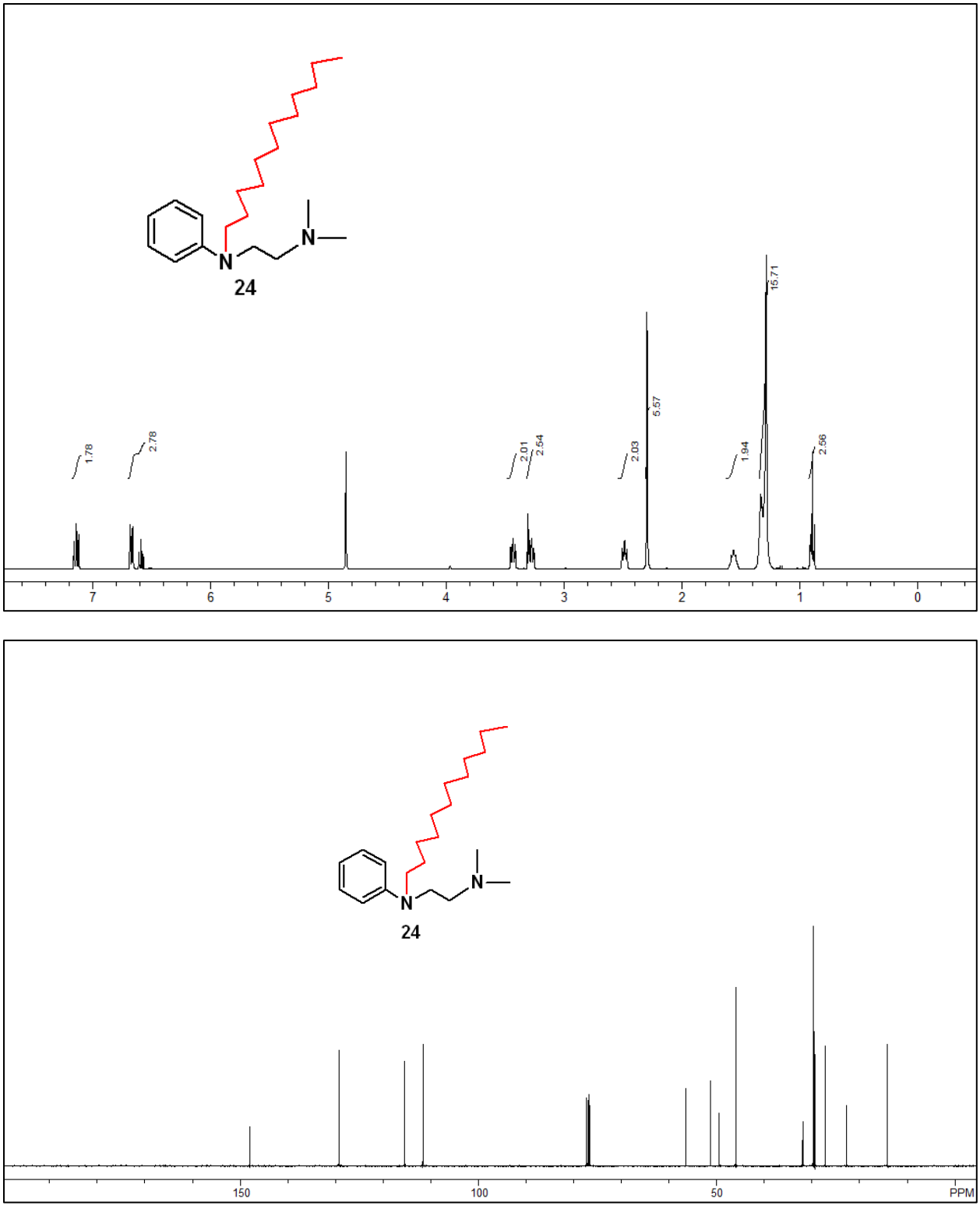

24
1.78
2.78
2.01
2.54
2.03
5.57
1.94
15.71
2.56
7
6
5
4
3
2
1
0
24
150
100
50
PPM

Figure S17

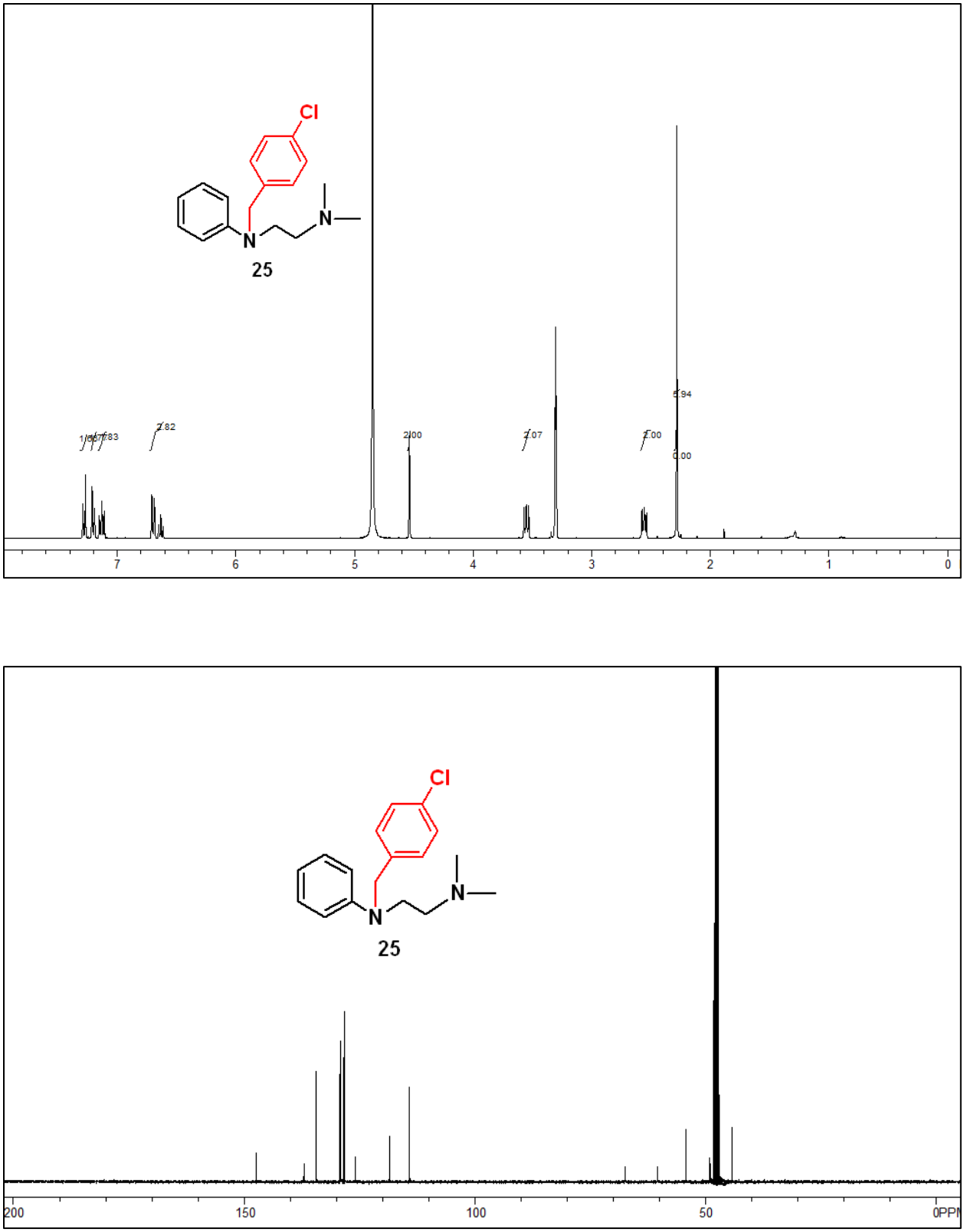

Cl
N
N
25
1.67
1.83
2.82
2.00
2.07
2.00
5.94
0.00
7
6
5
4
3
2
1
0
Cl
N
N
25
200
150
100
50
0PPM

Figure S18

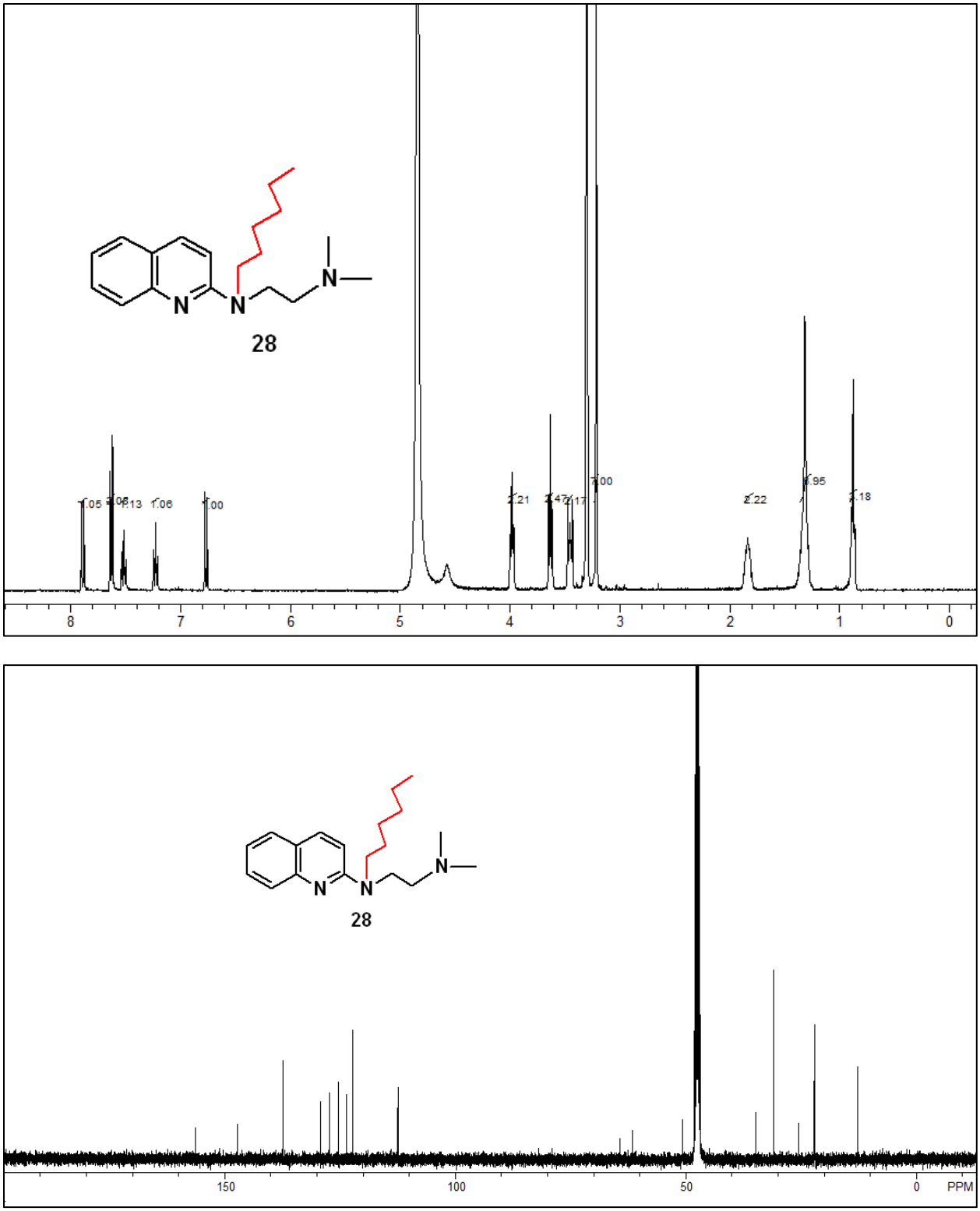

28
1.05
1.08
1.13
1.06
1.00
2.21
2.47
2.17
3.00
2.22
2.95
2.18
8
7
6
5
4
3
2
1
0
28
150
100
50
0
PPM

Figure S19

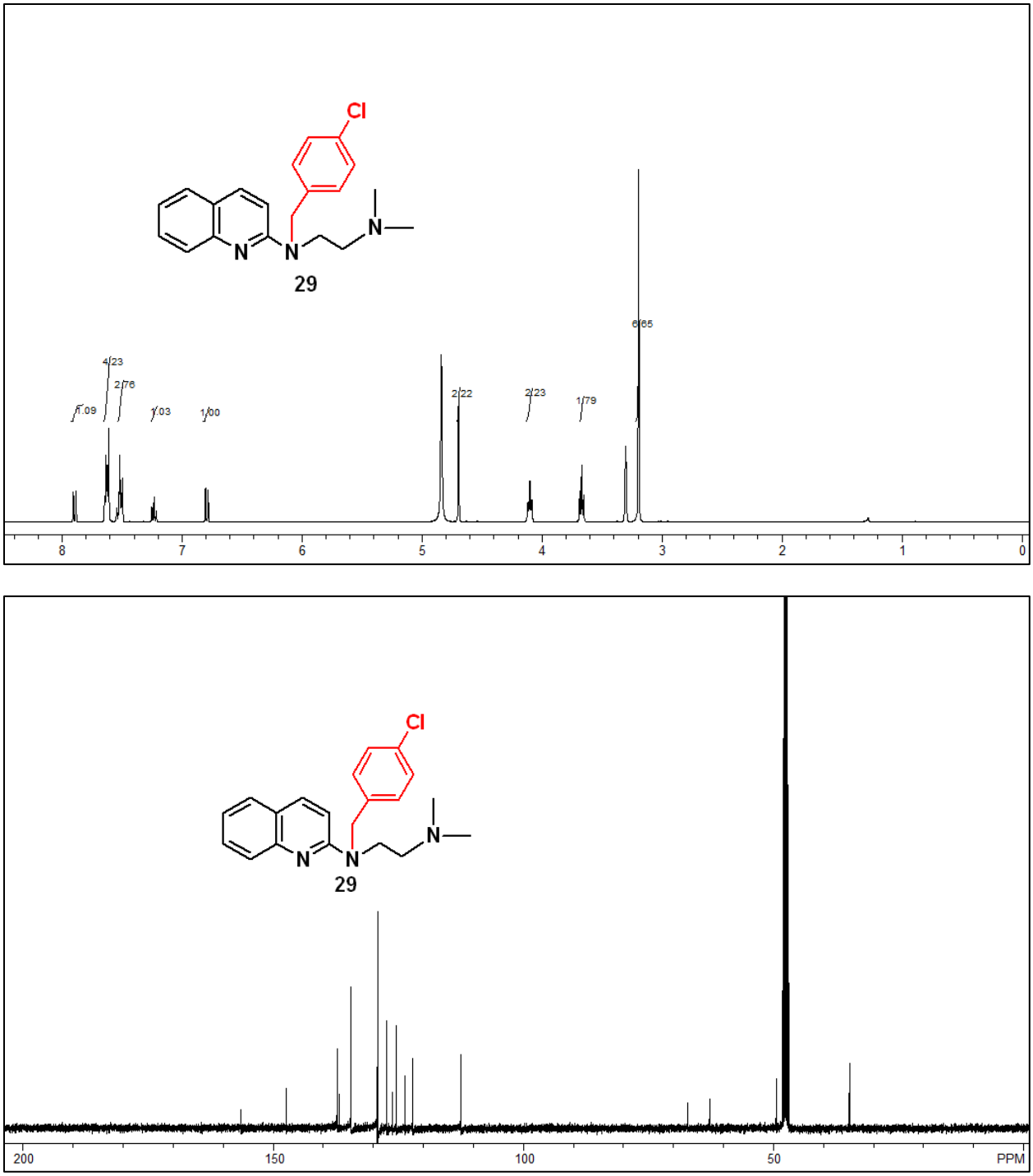

Cl
N
N
N
29
4.23
2.76
1.09
1.03
1.00
2.22
2.23
1.79
6.65
8
7
6
5
4
3
2
1
0
Cl
N
N
N
29
200
150
100
50
PPM

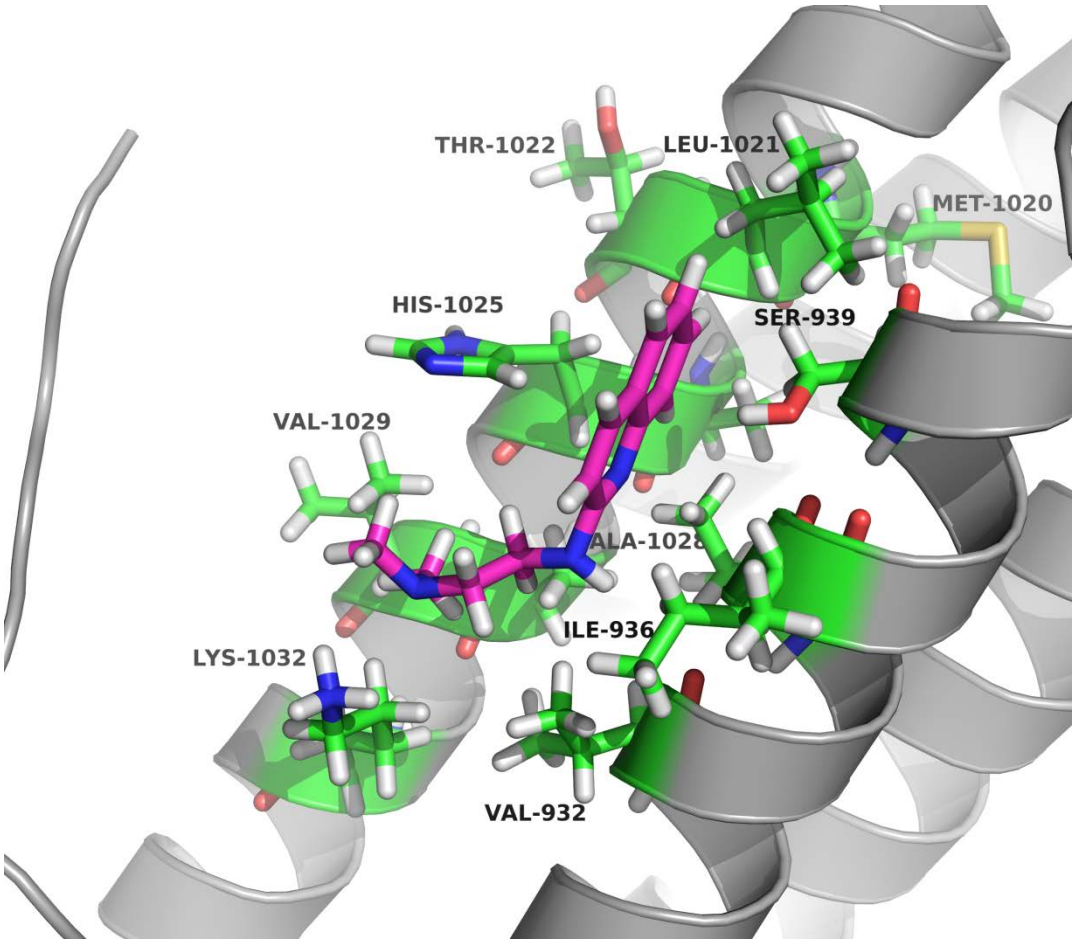
Figure S20

Table S1. Log P values of **1** analogs

Compound No.	Log P
1	1.721
7	-1.634
8	-2.053
9	0.364
10	1.295
11	1.962
12	2.723
13	3.712
15	1.771
16	2.030
17	1.792
18	2.847
19	1.650
20	3.086
23	1.563
24	4.883
25	2.087
27	0.277
28	2.653
29	2.704

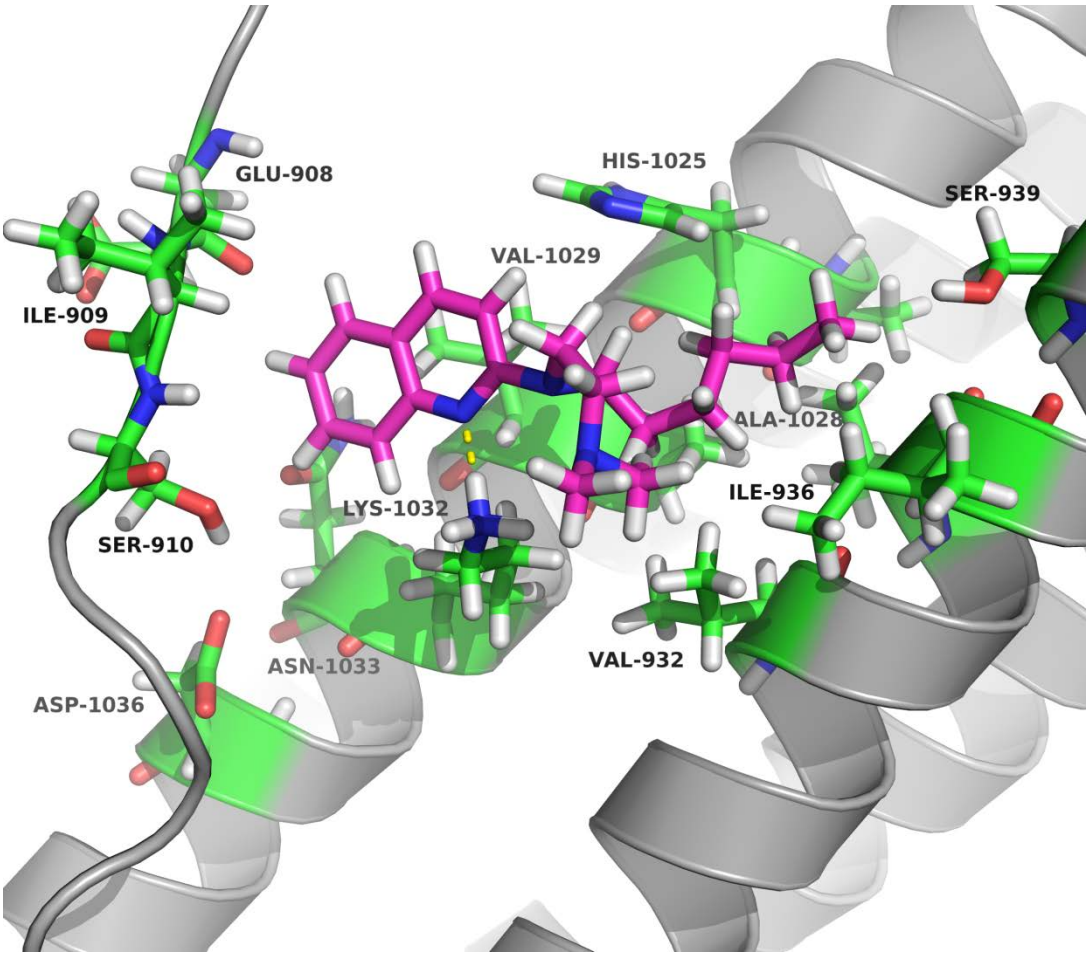
[a]Log P values were calculated using PALLUS software.

Figure S21. Predicted binding pose of compound **27** to the FAT domain of FAK.



Ribbon representation of the FAT domain (gray) showing the binding pose of analog **27** (magenta stick) and residues within 5 Angstroms of **27** (green stick).

Figure S22. Predicted binding pose of compound **28** to the FAT domain of FAK.



Ribbon representation of the FAT domain (gray) showing the binding pose of analog **28** (magenta stick) and residues within 5 Angstroms of **28** (green stick). A hydrogen bond (yellow dashed line) is formed between the quinoline ring of **28** and Lys 1032.