

Syntheses and Structure Activity Relationships of N-phenethyl-quinazolin-4-yl-amines as potent inhibitors of cytochrome *bd* oxidase in *Mycobacterium tuberculosis*

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SMH1-11.10.fid
3 (MeOD, 500 MHz)

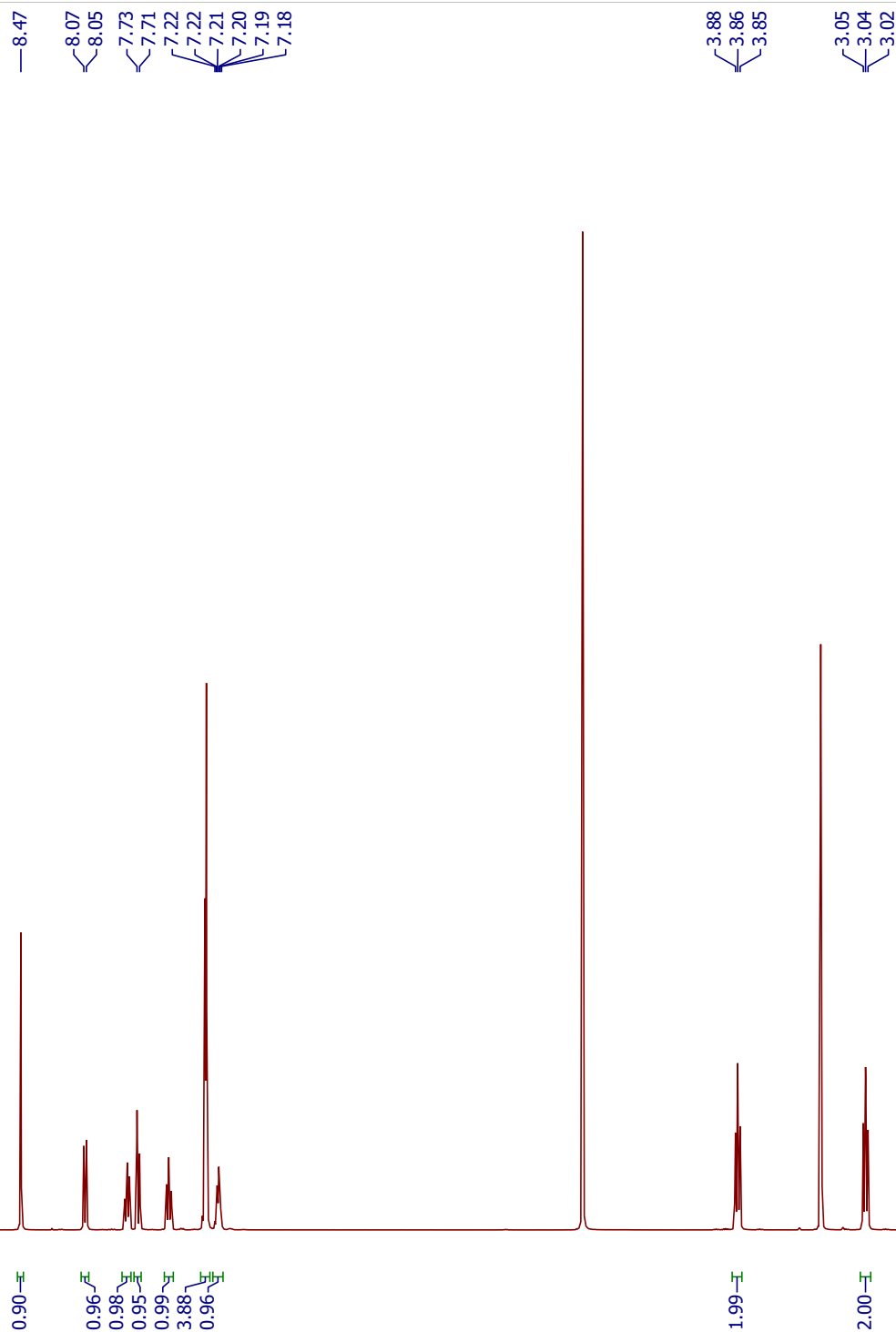
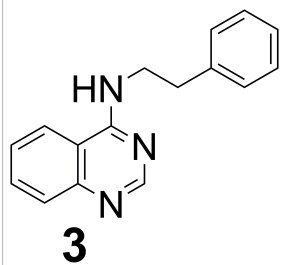
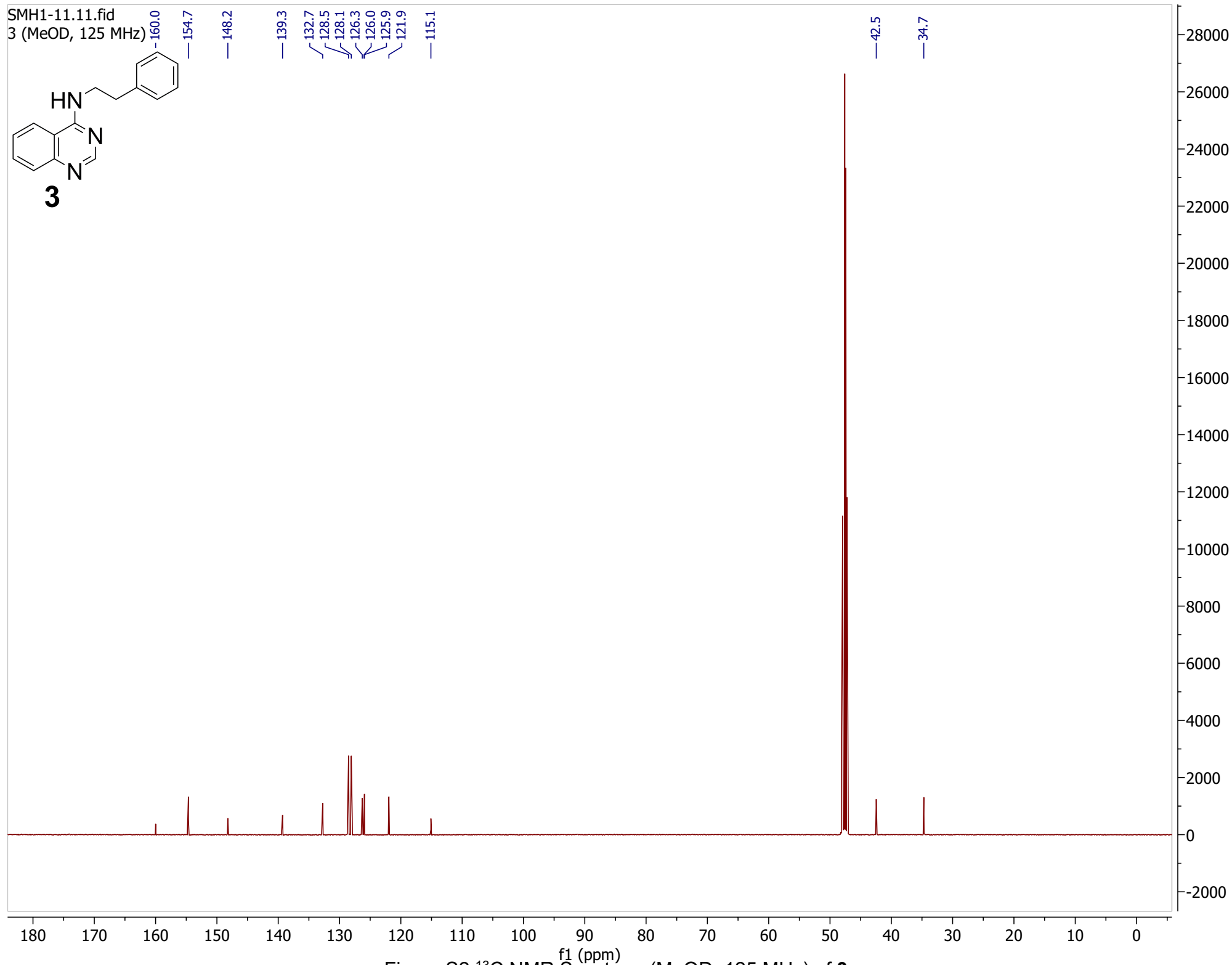
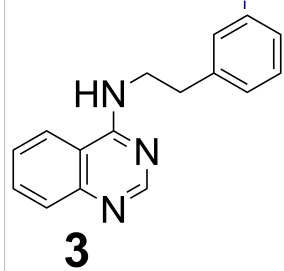


Figure S1 ¹H NMR Spectrum (MeOD, 500 MHz) of **3**

SMH1-11.11.fid
3 (MeOD, 125 MHz)



GM33-84-1.10.fid
6a (CDCl₃, 500 MHz)

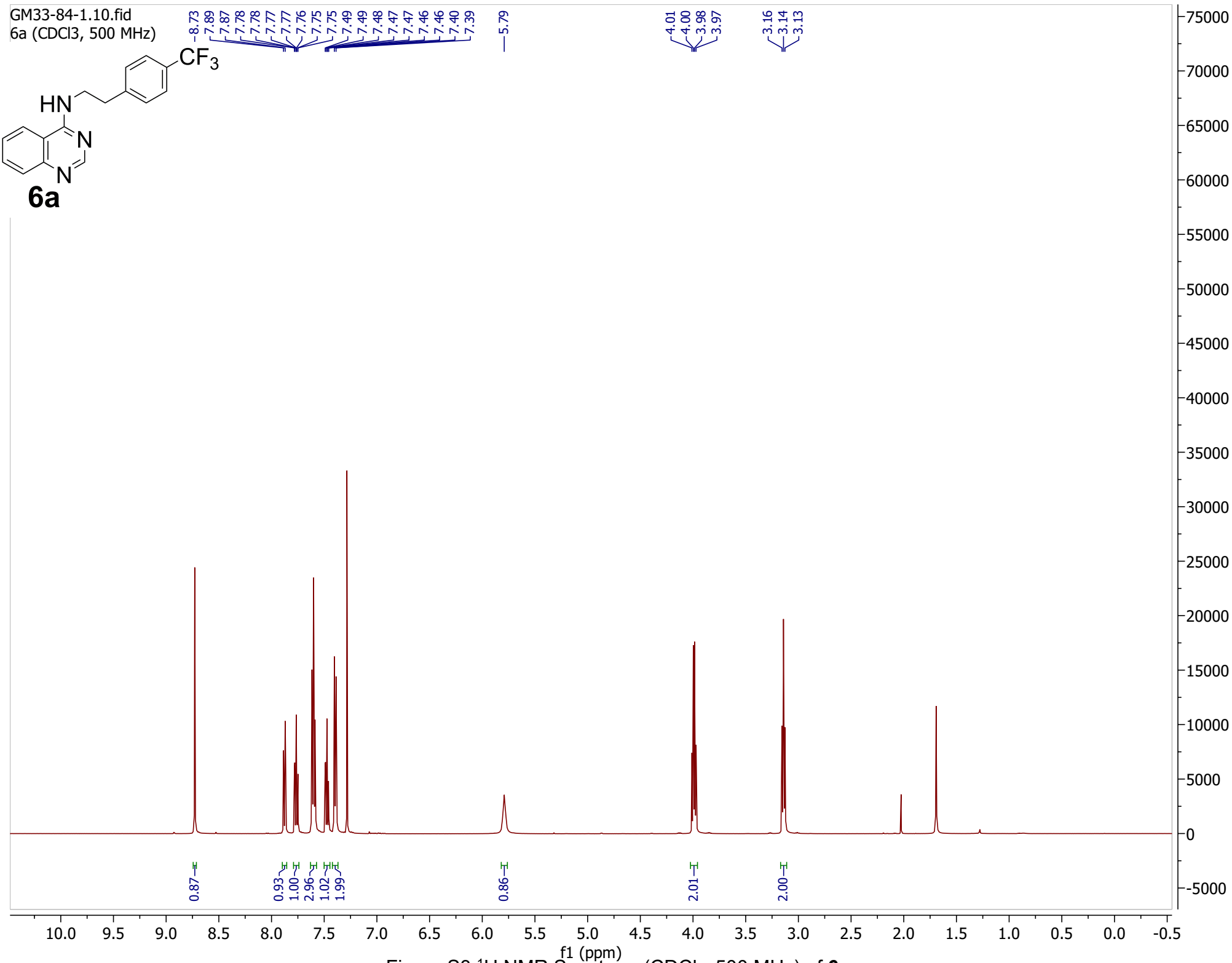
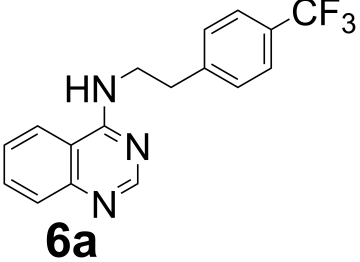


Figure S3 ¹H NMR Spectrum (CDCl₃, 500 MHz) of **6a**

GM33-84-1.11.fid
6a (CDCl₃, 125 MHz)

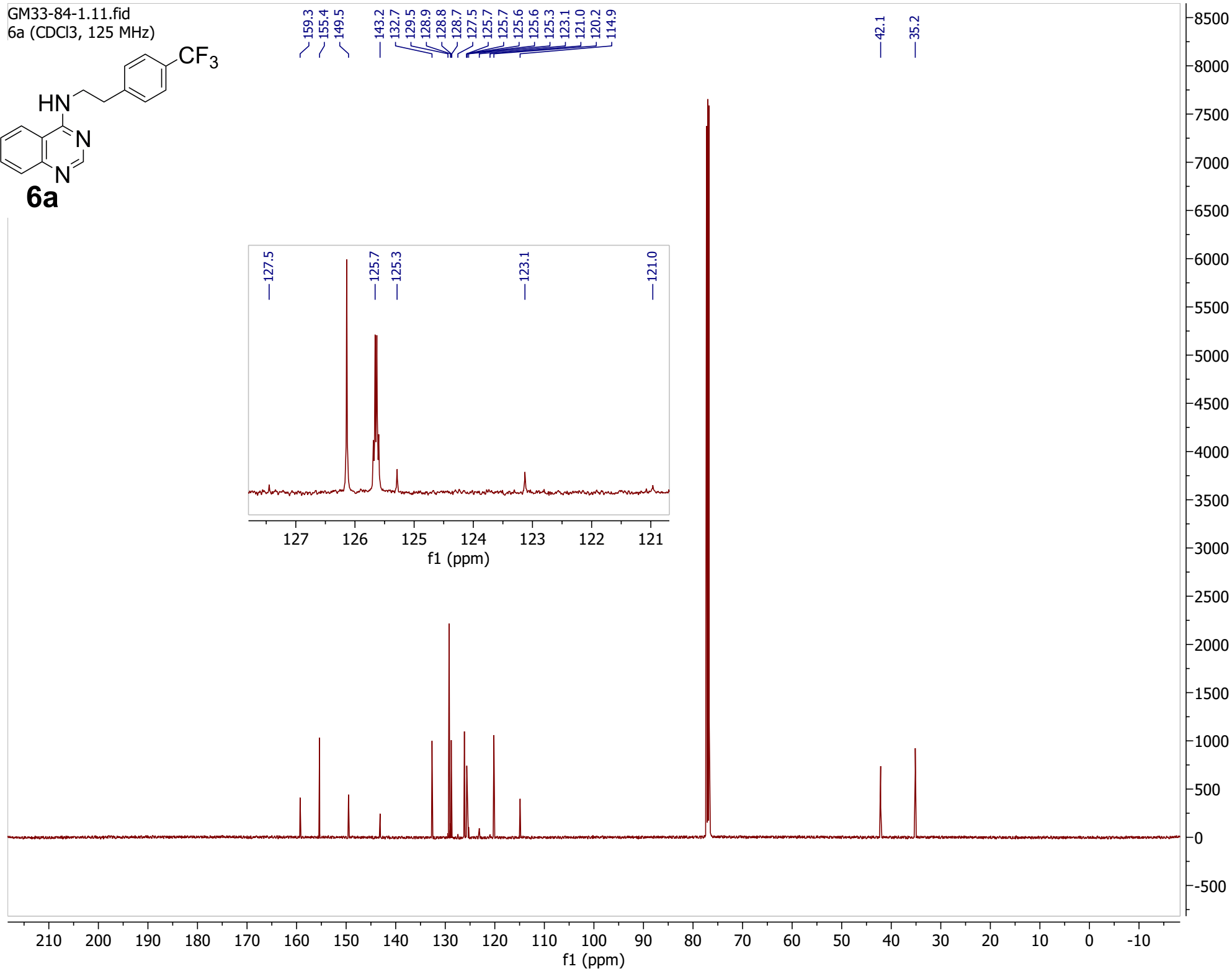
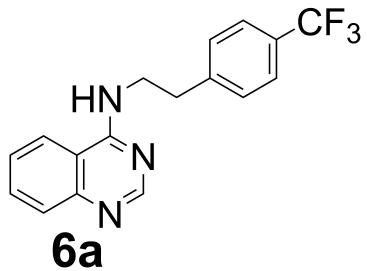


Figure S4 ¹³C NMR Spectrum (CDCl₃, 125 MHz) of **6a**

GM33-84-1.12.fid
6a (CDCl₃, 470 MHz)

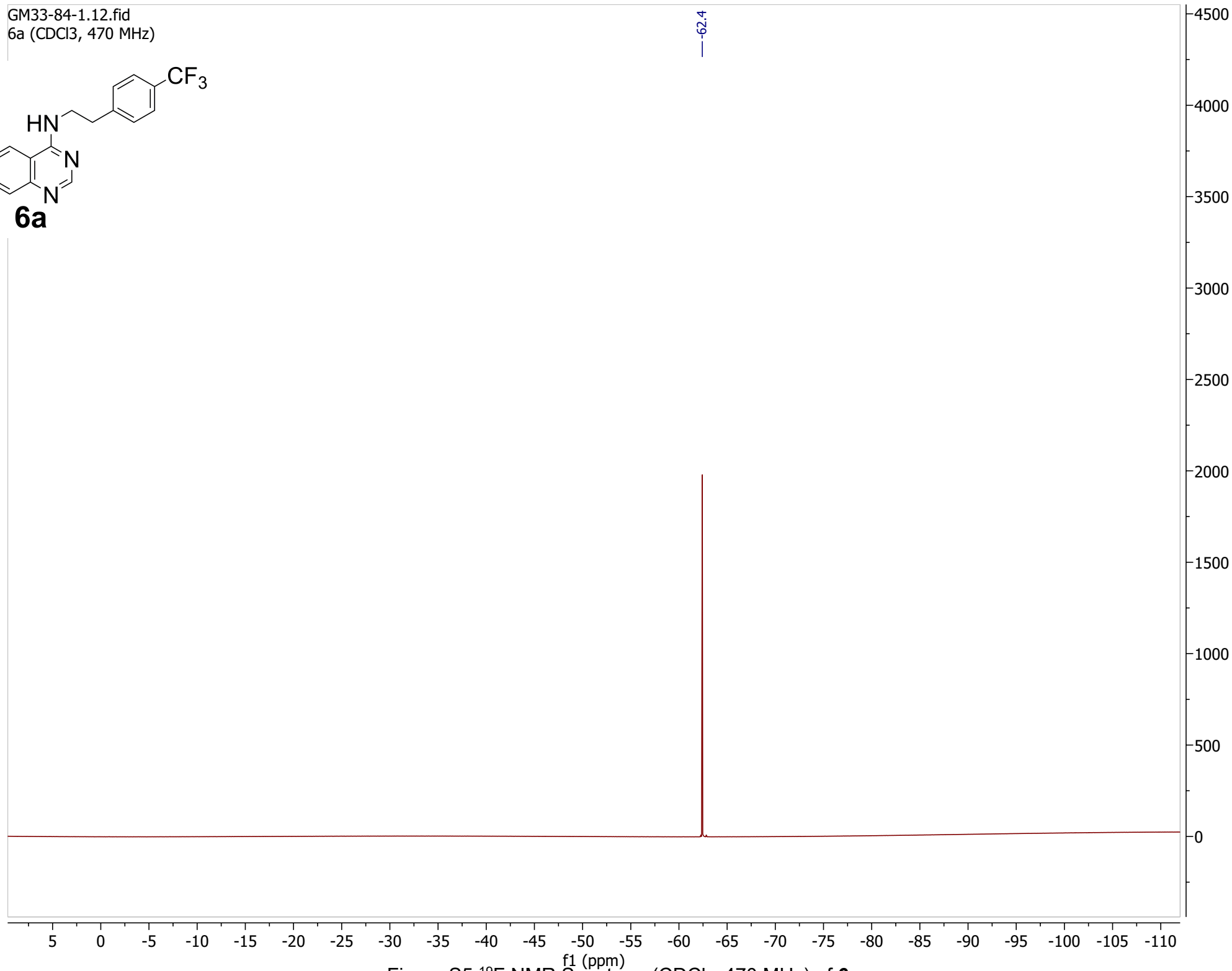
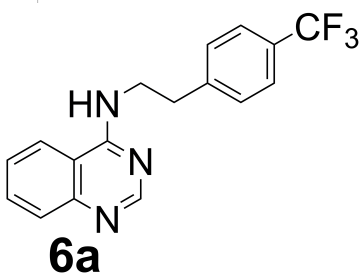


Figure S5 ¹⁹F NMR Spectrum (CDCl₃, 470 MHz) of **6a**

GM33-83-1-1.11.fid
7a (CDCl₃, 500 MHz)

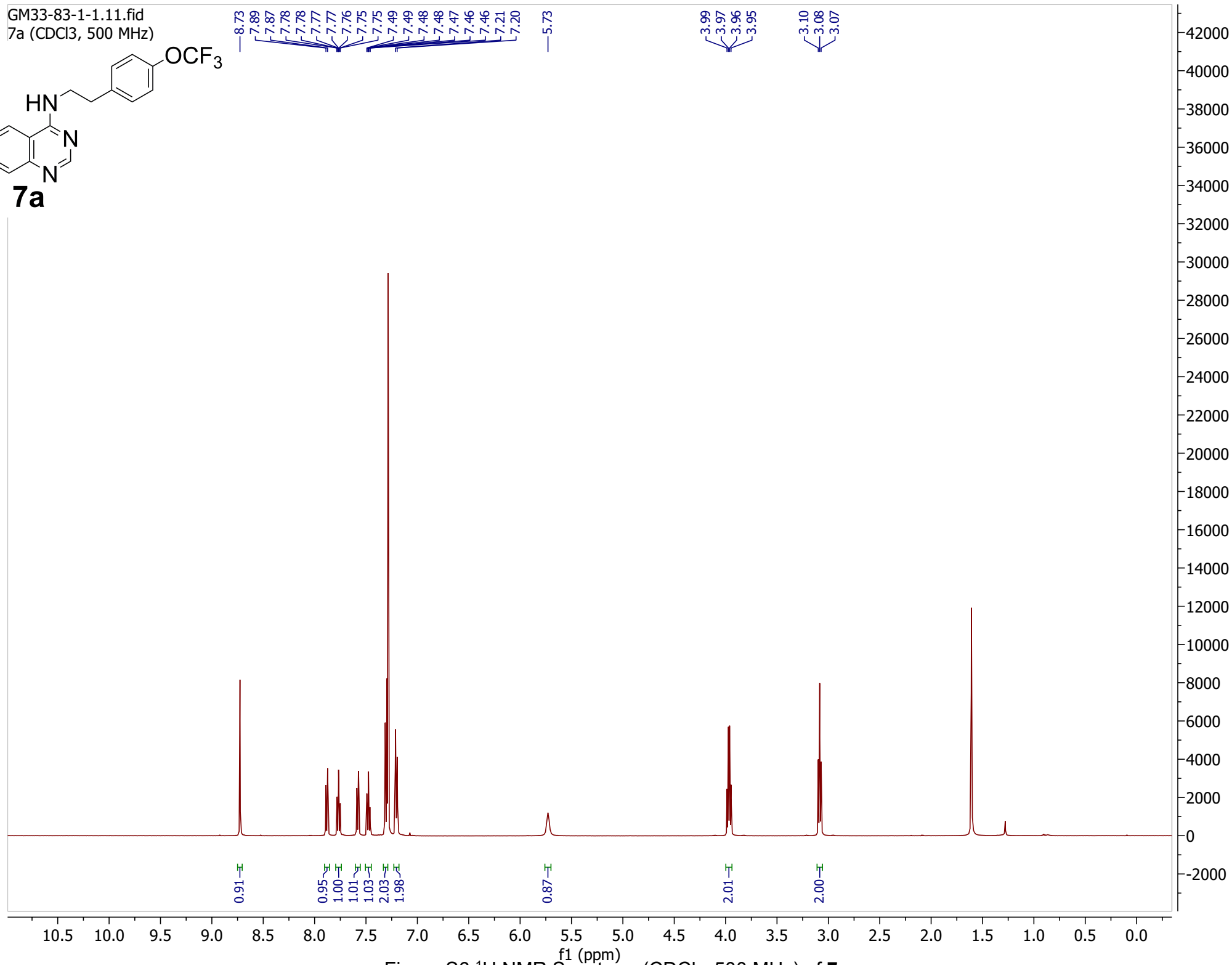
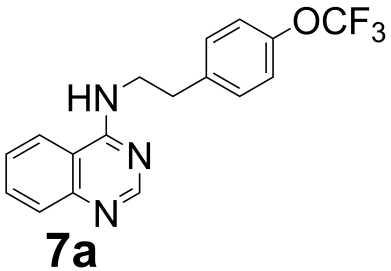
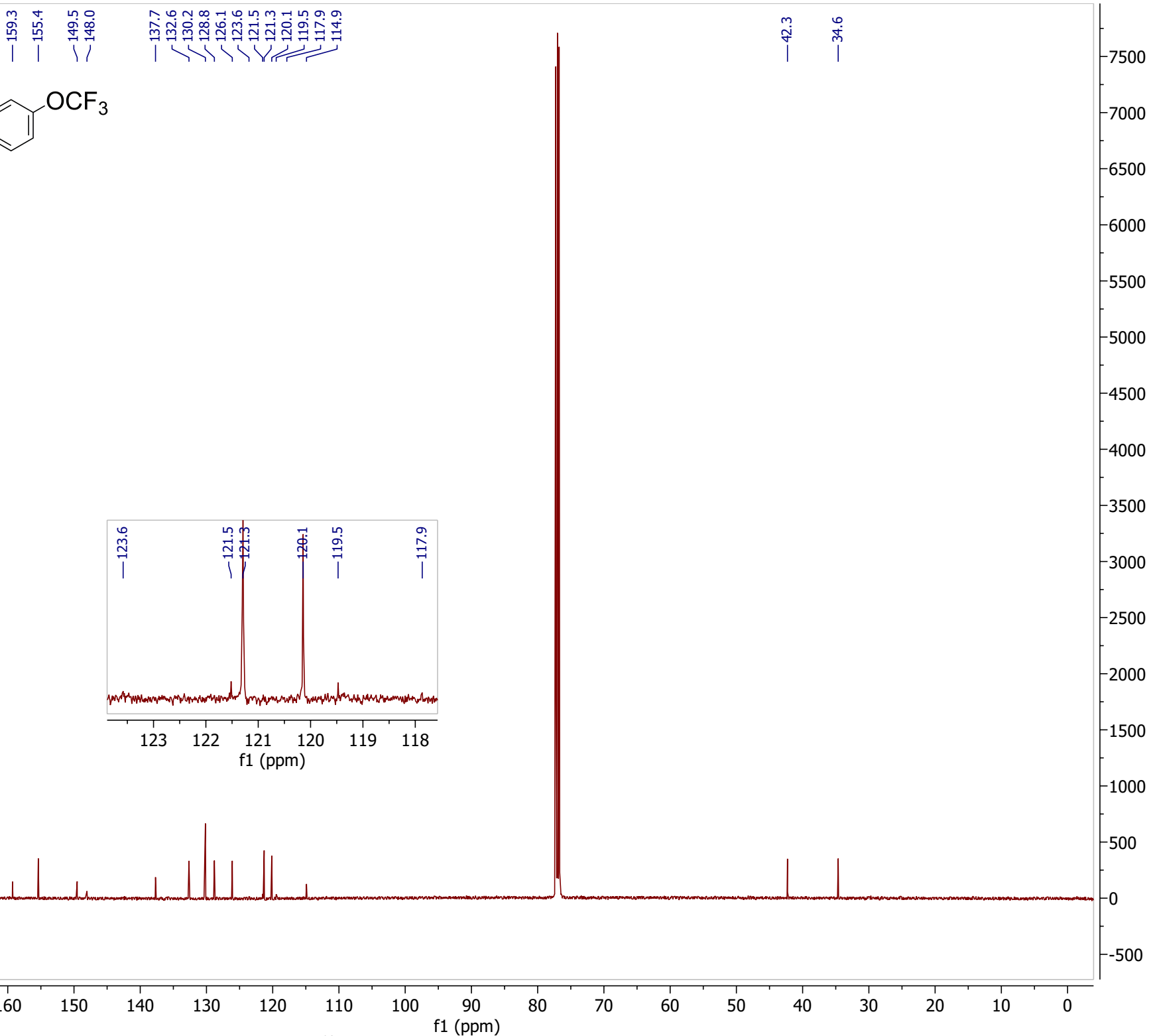
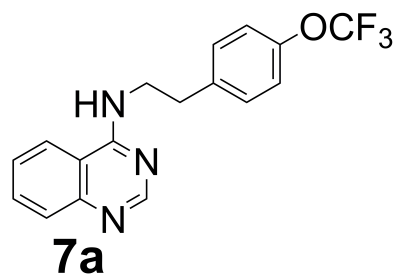


Figure S6 ¹H NMR Spectrum (CDCl₃, 500 MHz) of **7a**

GM33-83-1-1.12.fid
7a (CDCl₃, 125 MHz)



GM33-83-1-1.13.fid
7a (CDCl₃, 470 MHz)

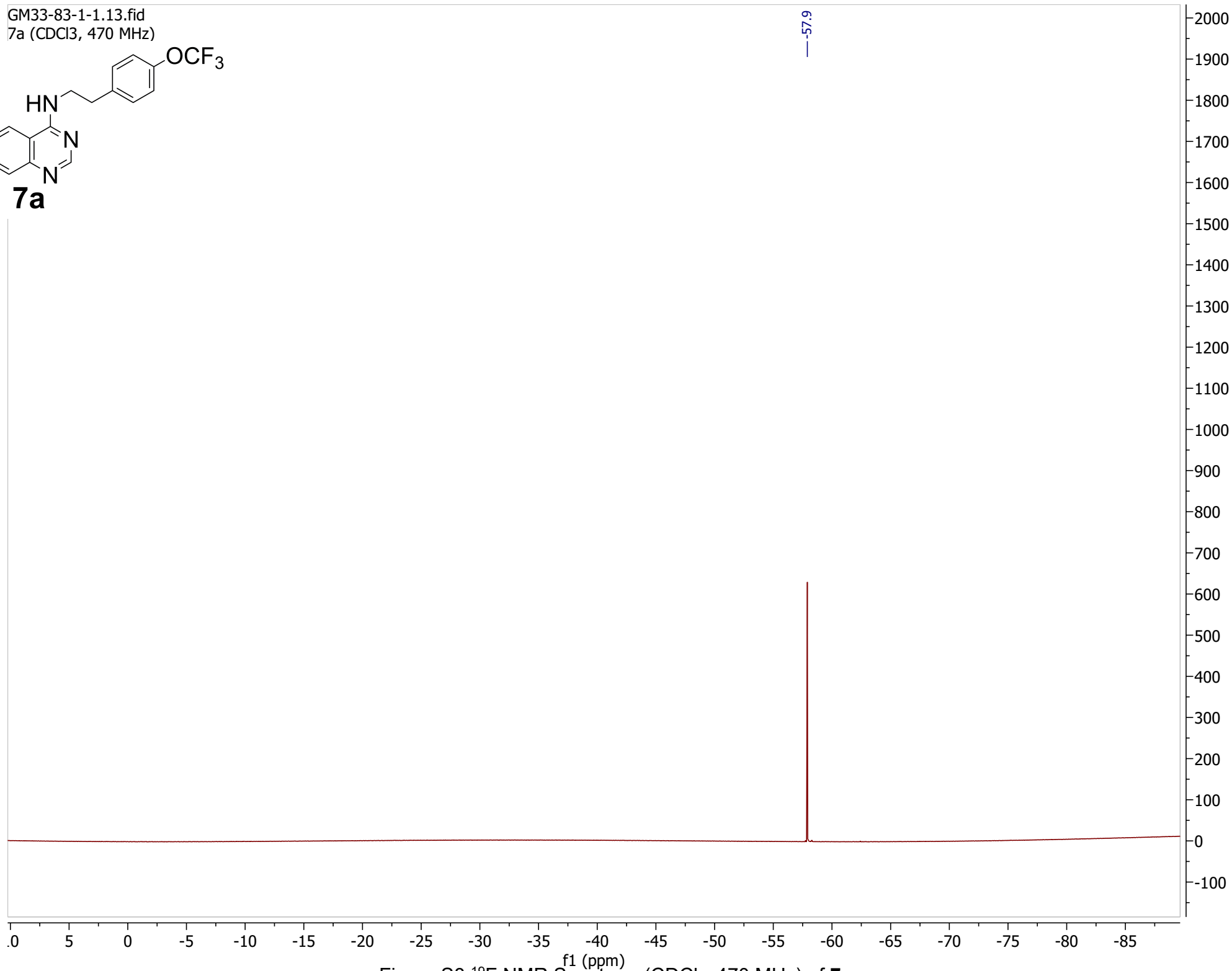
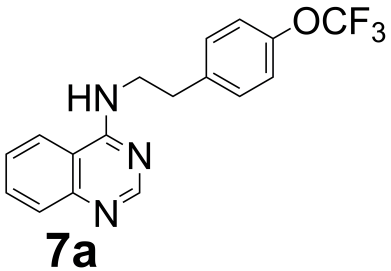


Figure S8 ¹⁹F NMR Spectrum (CDCl₃, 470 MHz) of **7a**

SMH1-26.10.fid
8a (d4-MeOD, 500 MHz)

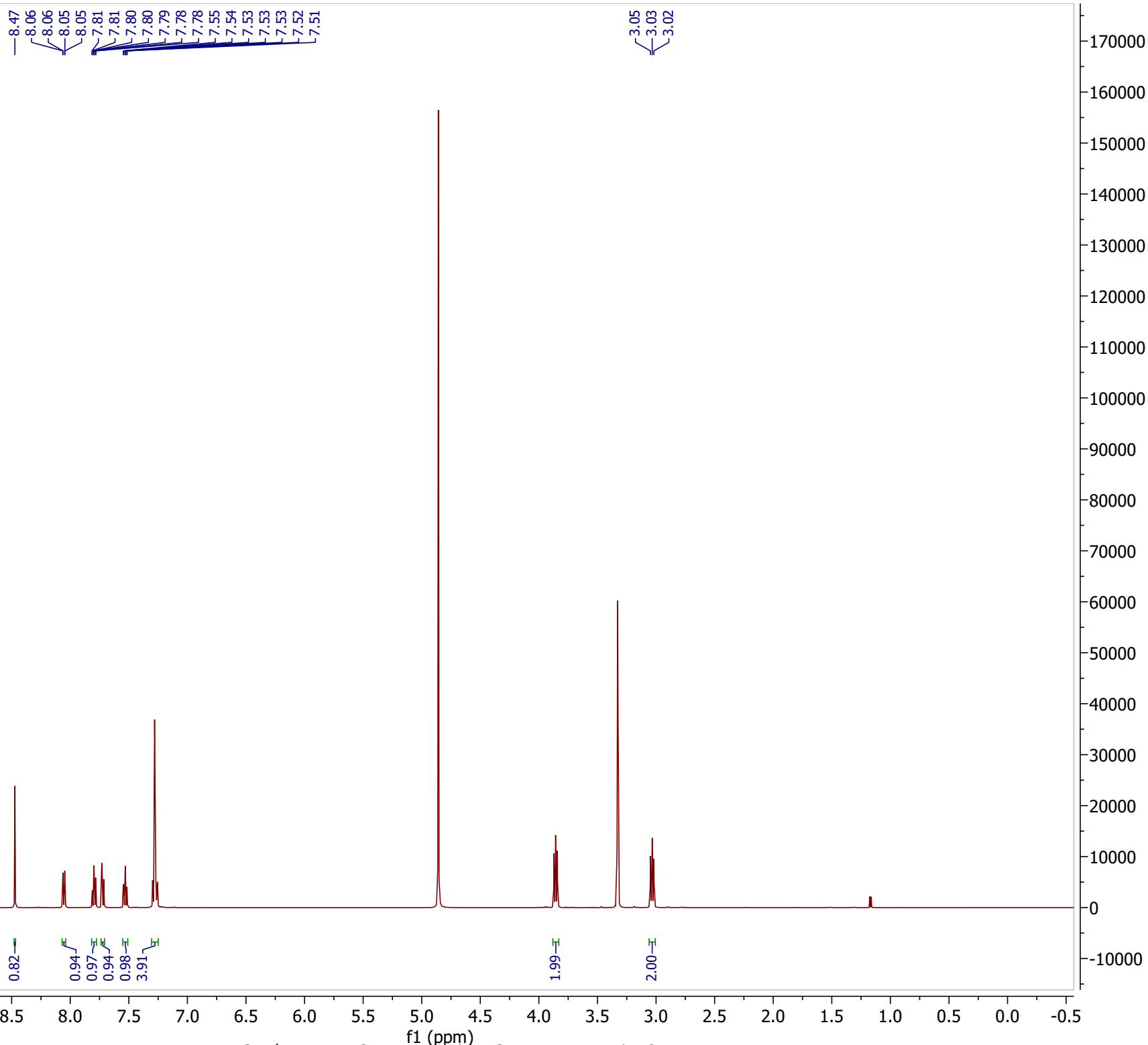
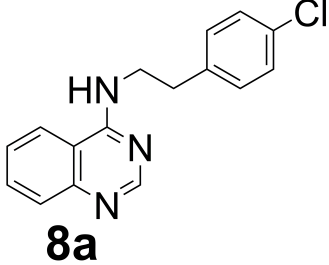
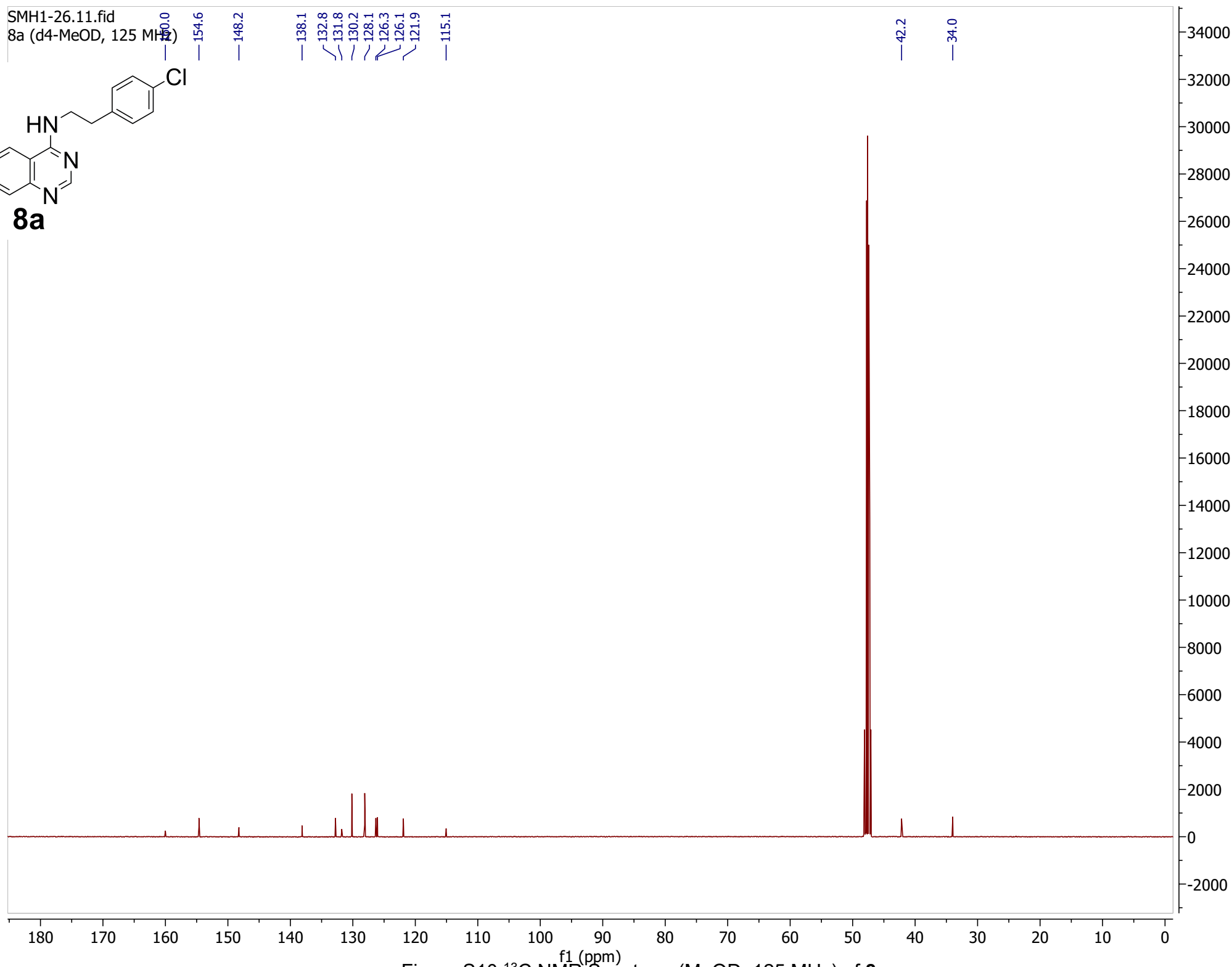
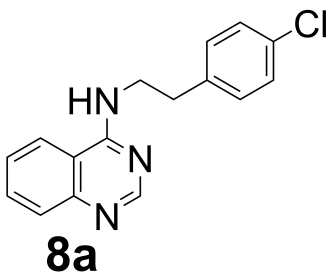


Figure S9 ^1H NMR Spectrum (MeOD, 500 MHz) of **8a**

SMH1-26.11.fid
8a (d4-MeOD, 125 MHz)



GM34-88-1.10.fid
9a (CDCl₃, 500 MHz)

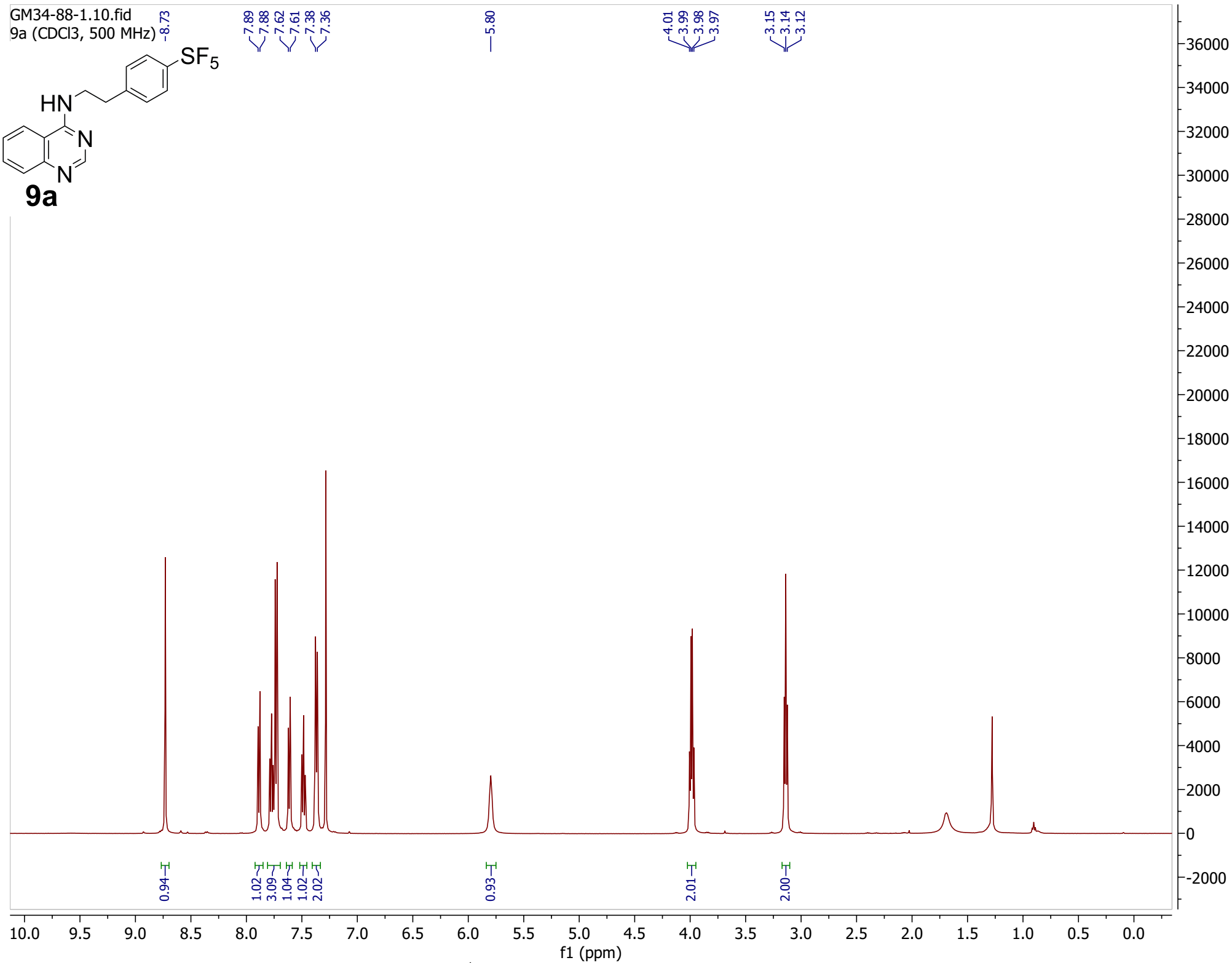
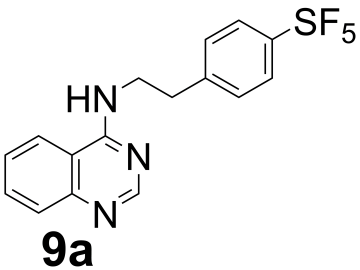


Figure S11 ¹H NMR Spectrum (CDCl₃, 500 MHz) of **9a**

GM34-88-1.6.fid
9a (CDCl₃, 125 MHz)

159.3
155.3
152.8
152.7
152.5
152.4
152.3

132.7
129.1
128.8
126.4
126.4
126.3
126.3
126.2
126.2
120.2
114.9

42.1

34.9

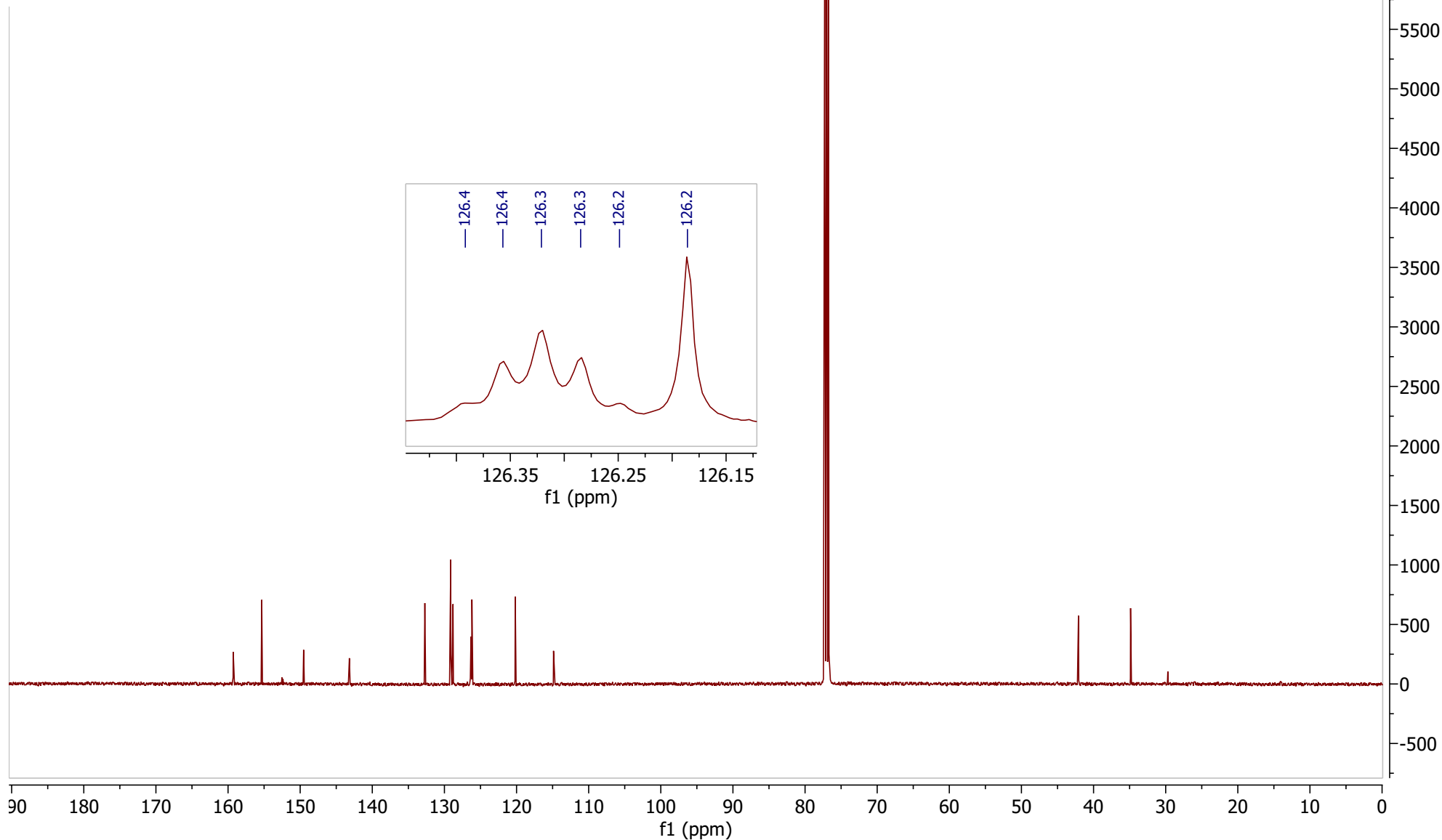
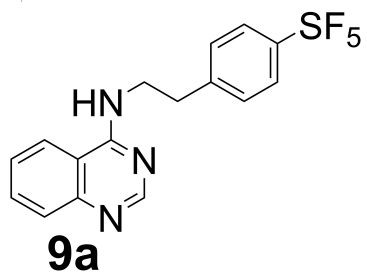


Figure S12 ¹³C NMR Spectrum (CDCl₃, 125 MHz) of **9a**

GM34-88-1-1.10.fid
9a (CDCl₃, 470 MHz)

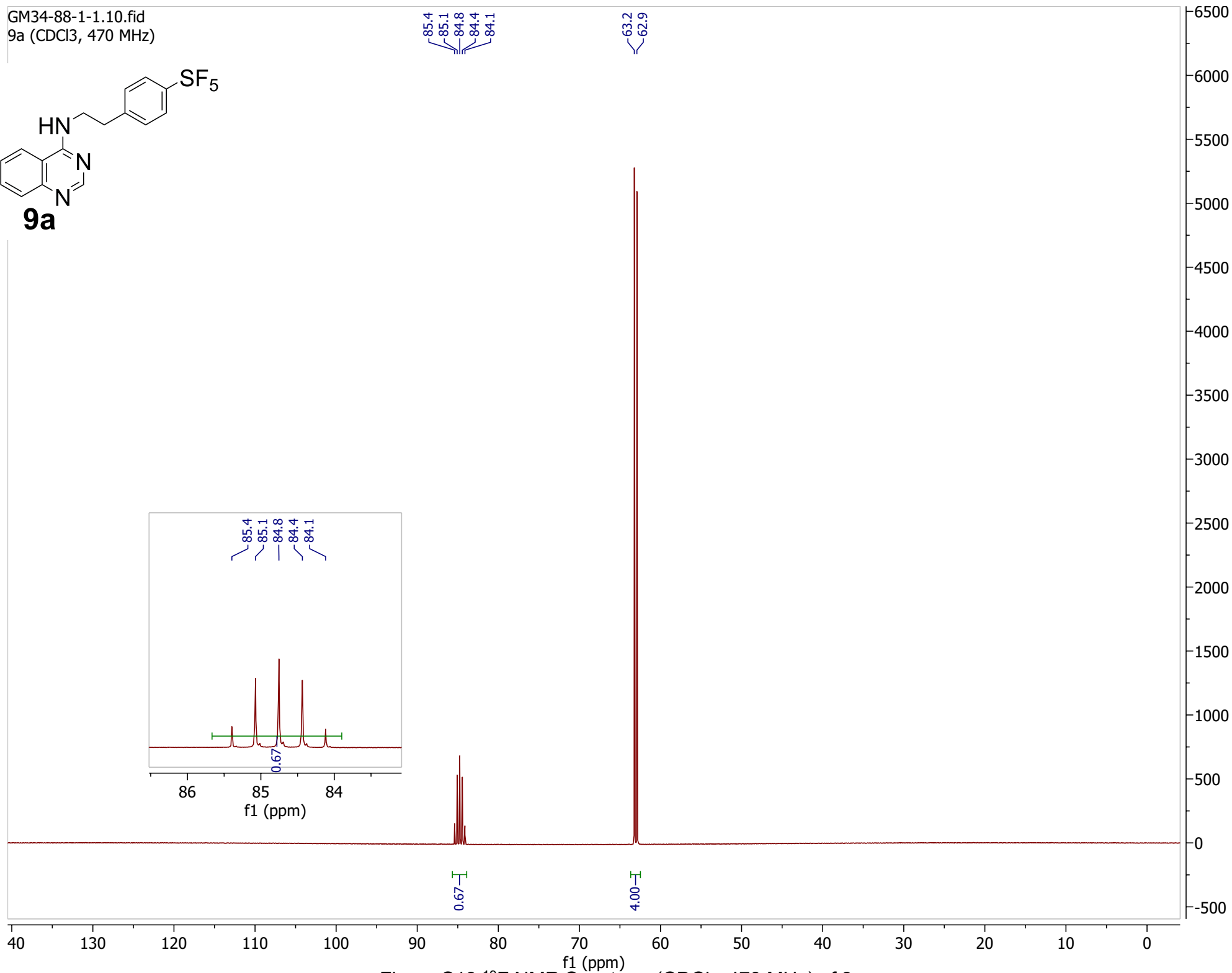
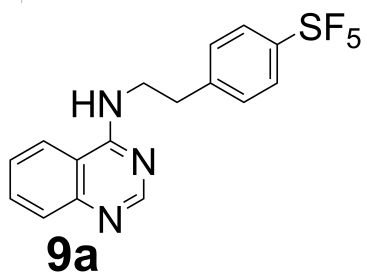


Figure S13 ¹⁹F NMR Spectrum (CDCl₃, 470 MHz) of **9a**

SMH1-28.10.fid
10a (CDCl₃, 500 MHz)

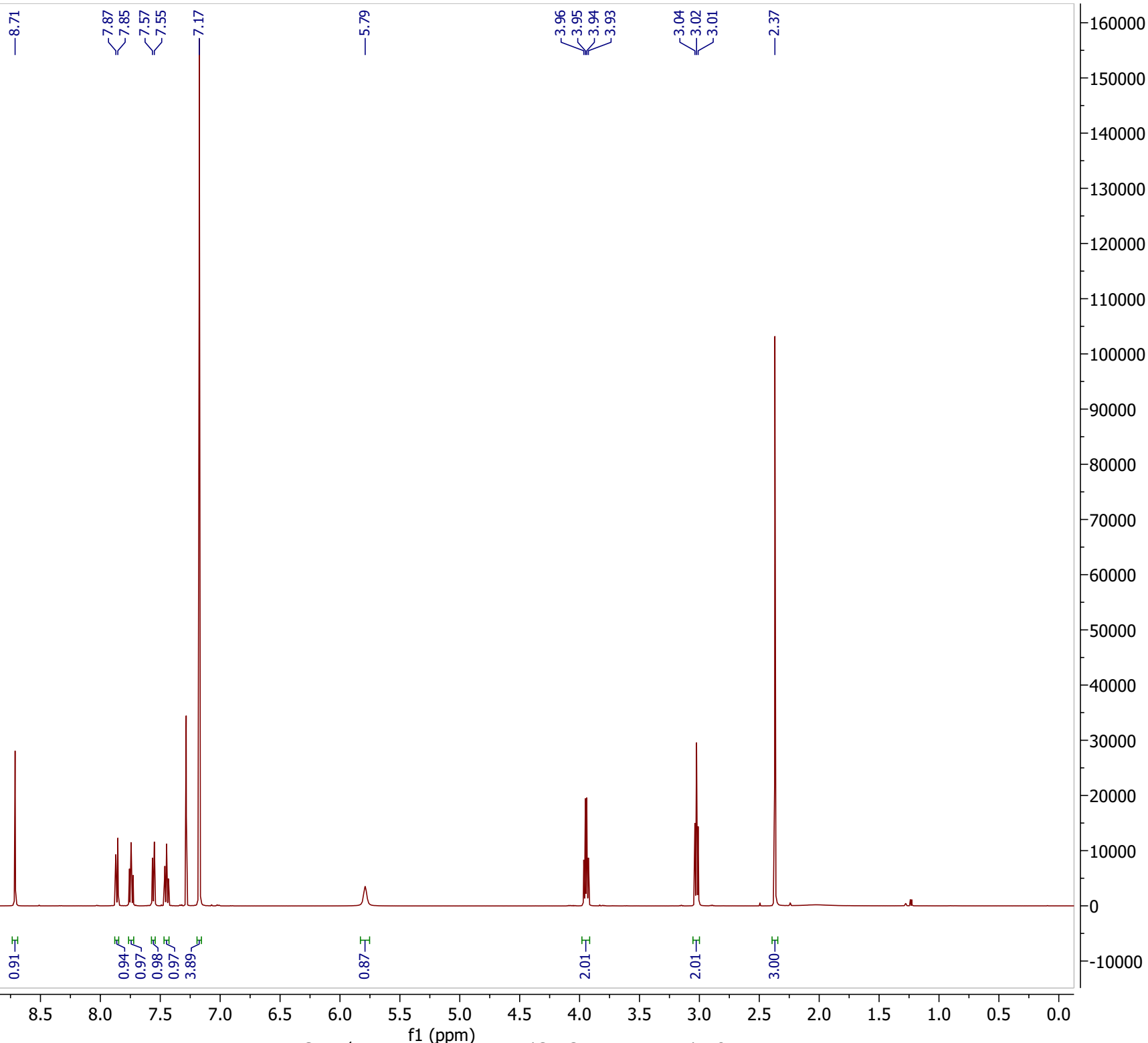
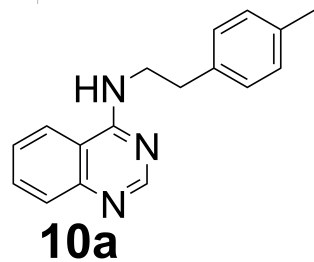


Figure S14 ¹H NMR Spectrum (CDCl₃, 500 MHz) of **10a**

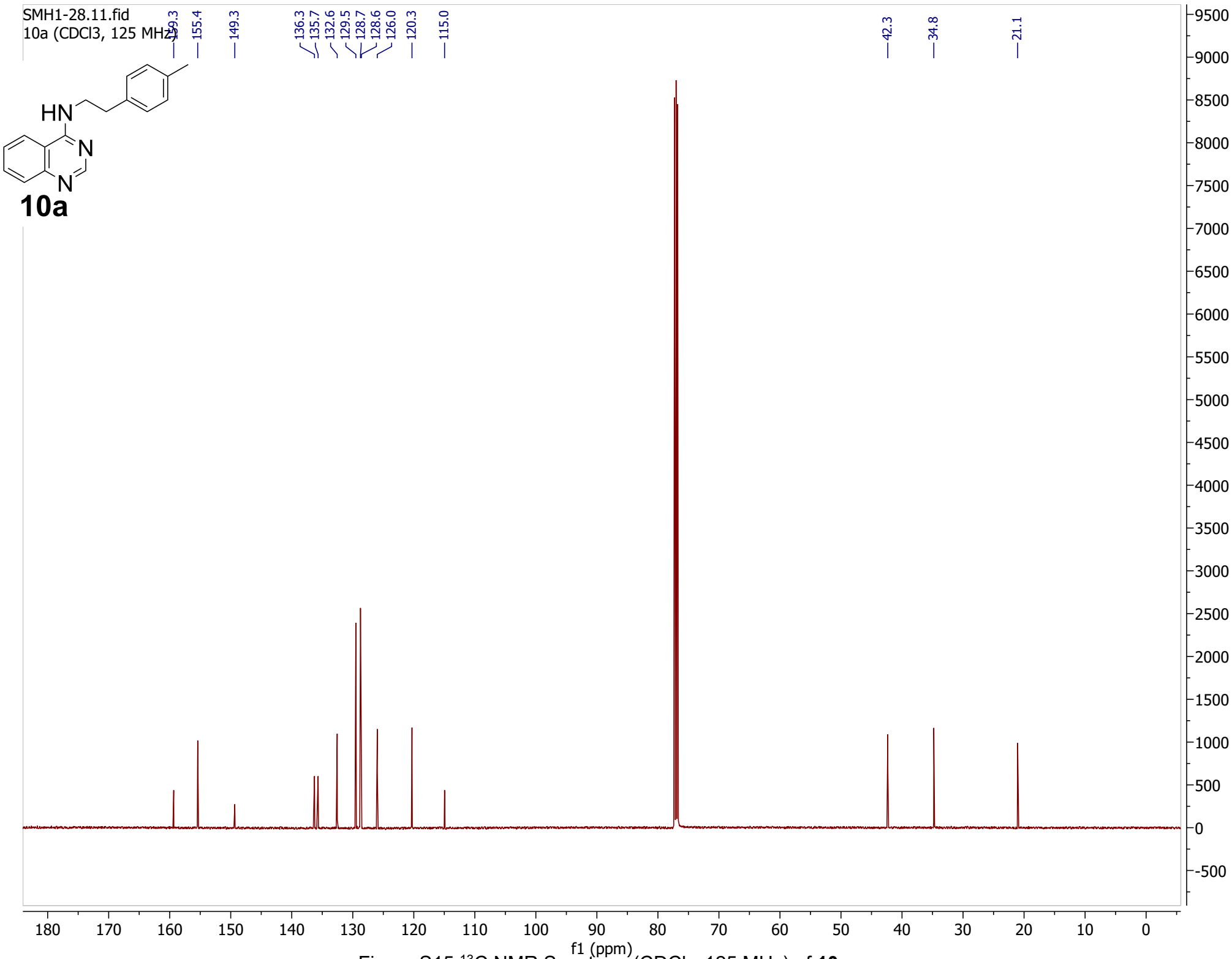
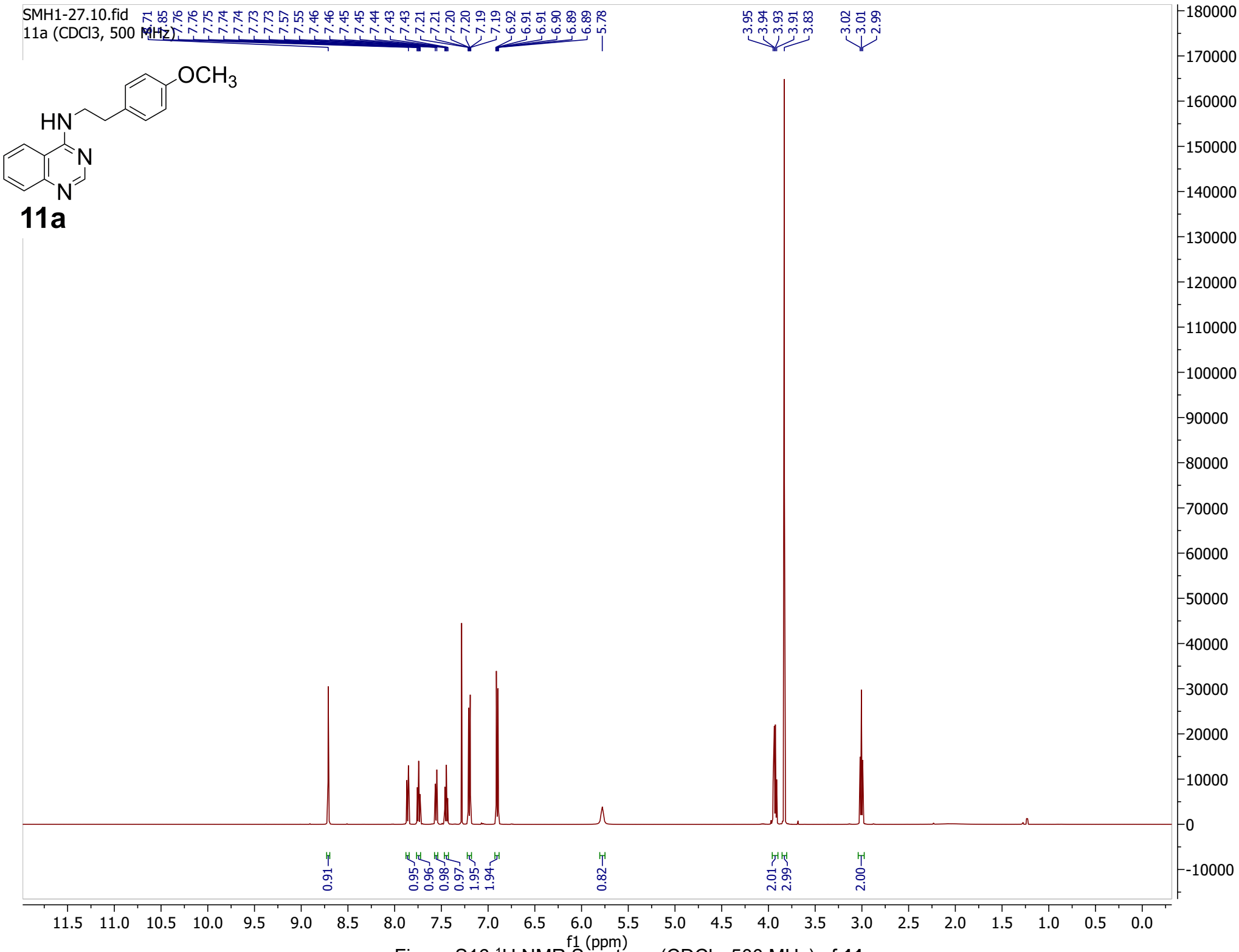


Figure S15 ¹³C NMR Spectrum (CDCl₃, 125 MHz) of **10a**



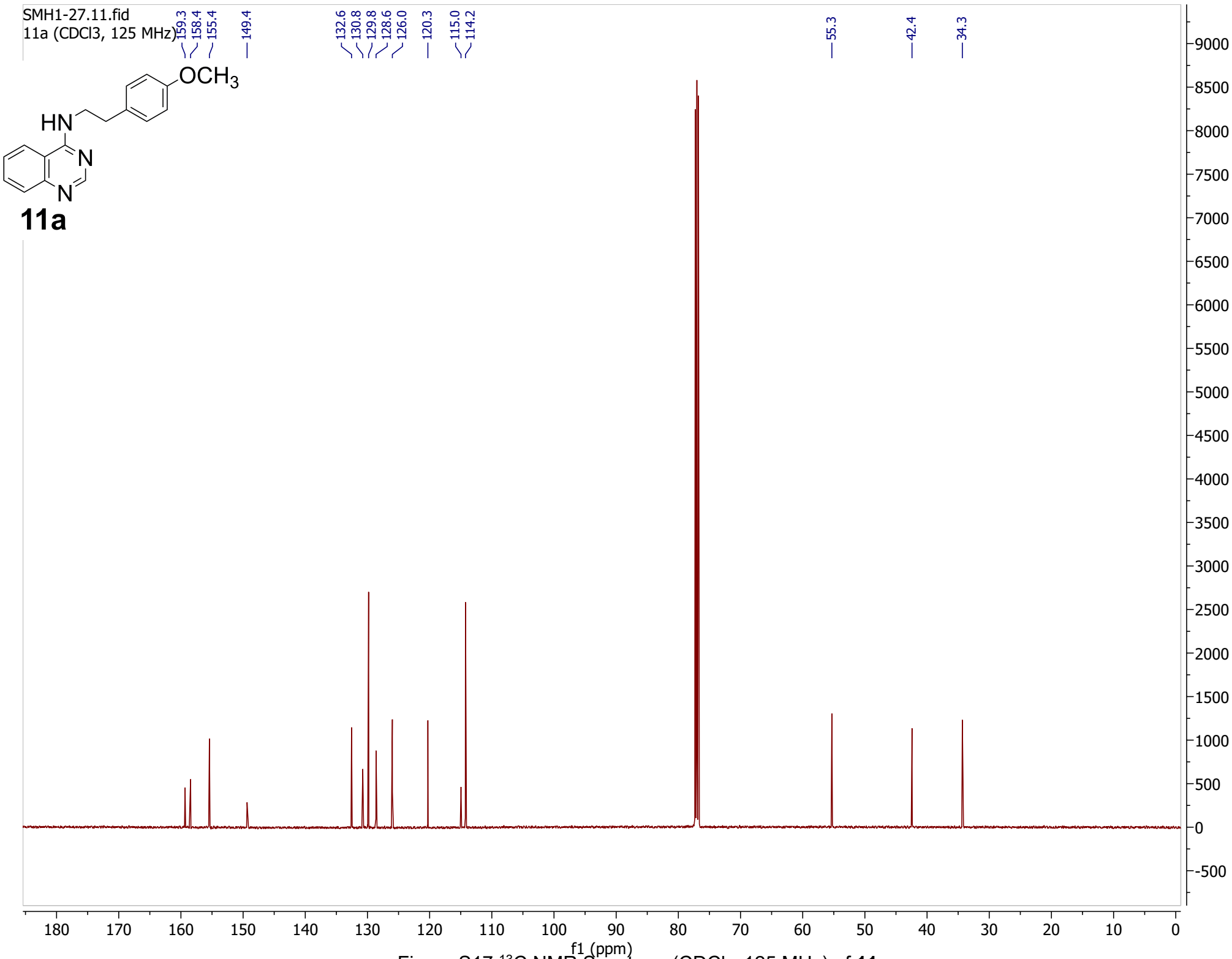


Figure S17 ¹³C NMR Spectrum (CDCl₃, 125 MHz) of **11a**

GM33-90-1.10.fid
12a (CDCl₃, 500 MHz)

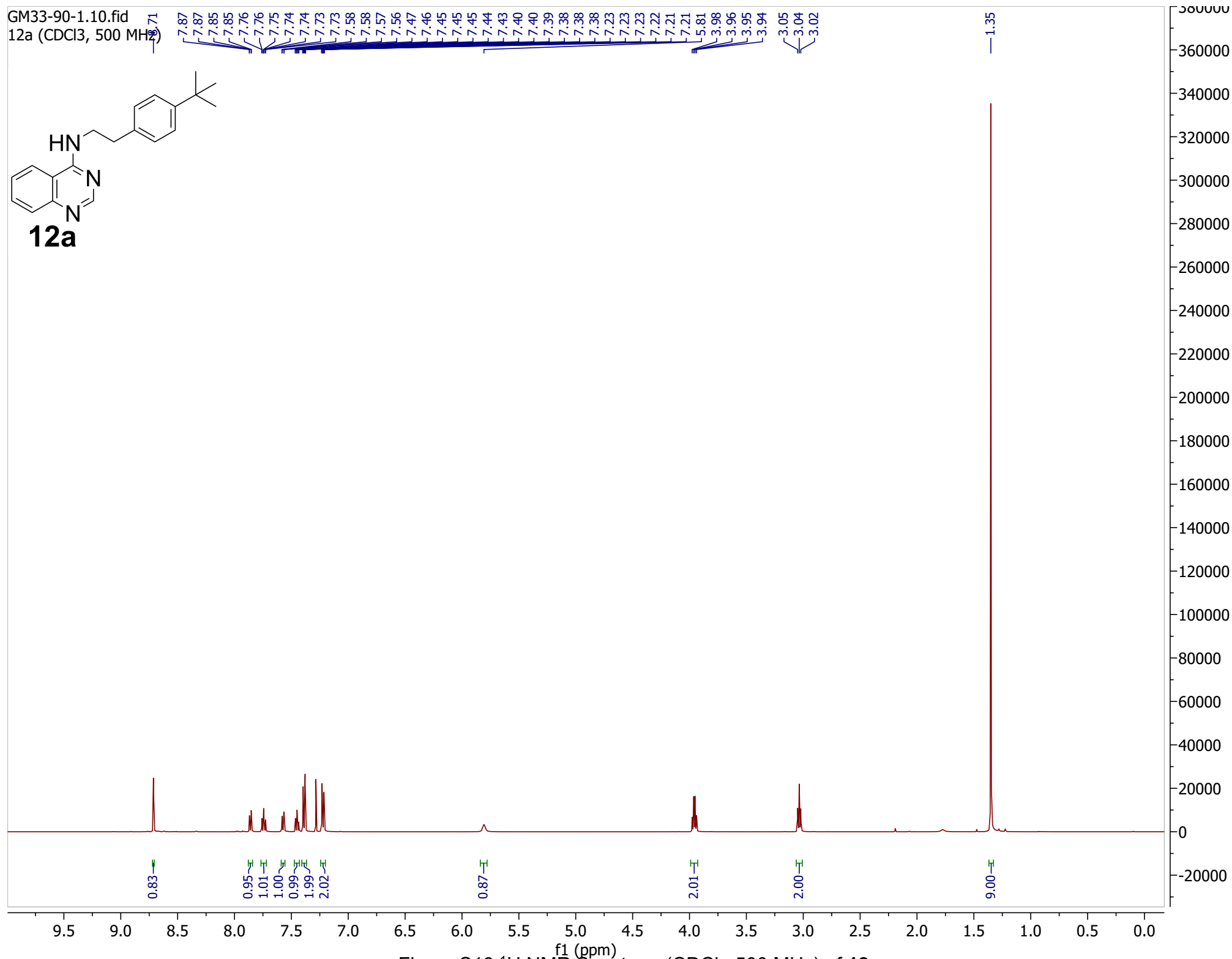
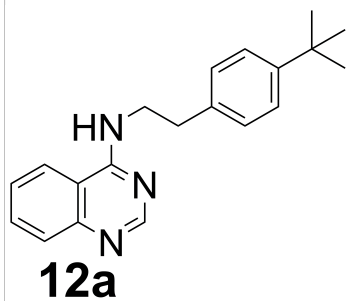
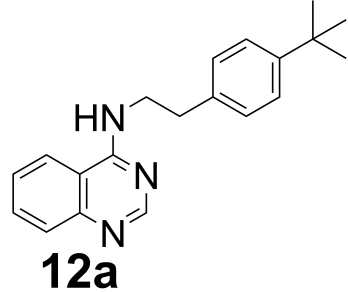


Figure S18 ¹H NMR Spectrum (CDCl₃, 500 MHz) of **12a**

GM33-90-1.11.fid
12a (CDCl₃, 125 MHz)



159.3
155.5
149.6
149.5

135.8
132.5
128.7
128.5
125.9
125.7
120.3
115.0

42.3
34.7
34.5
31.4

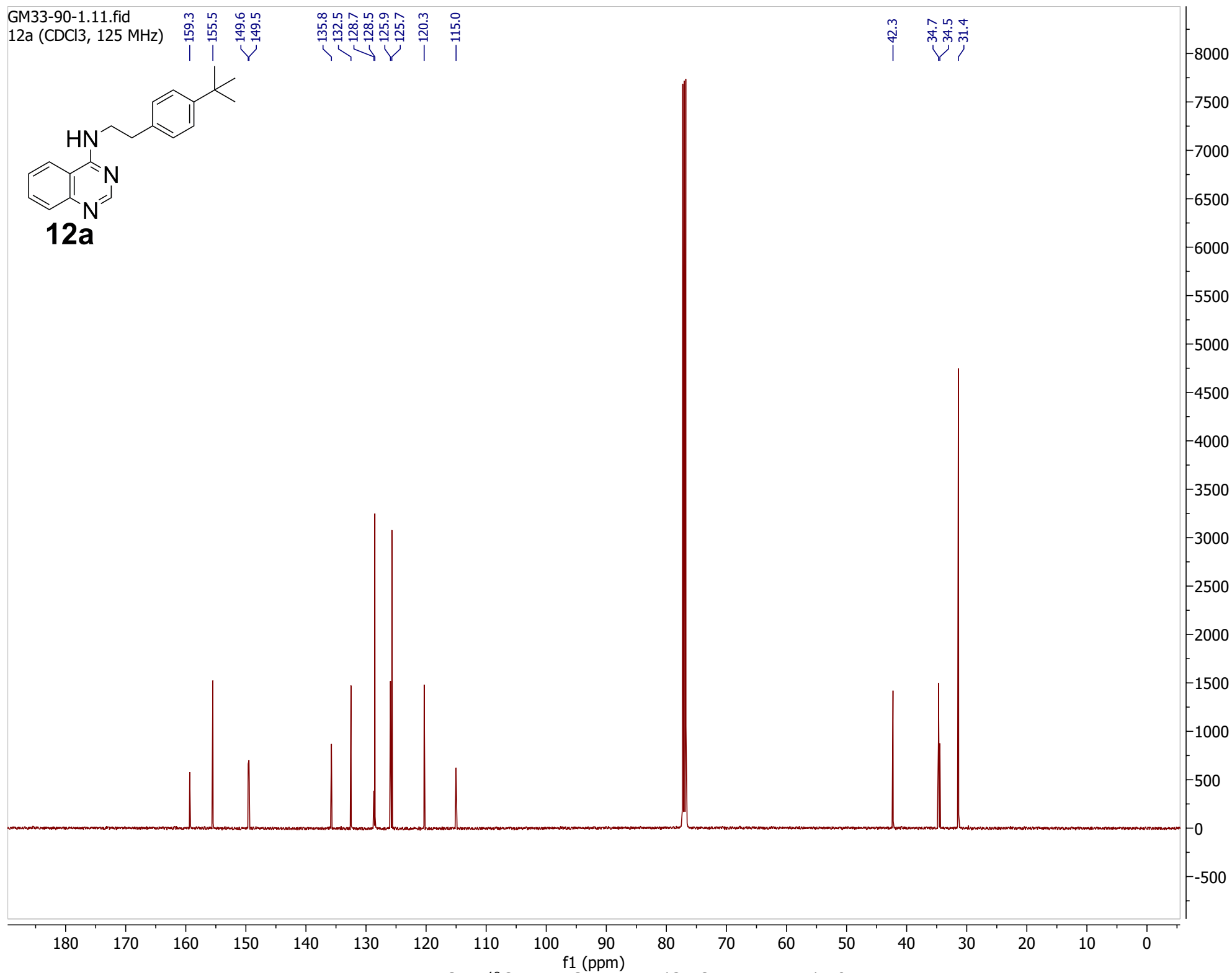
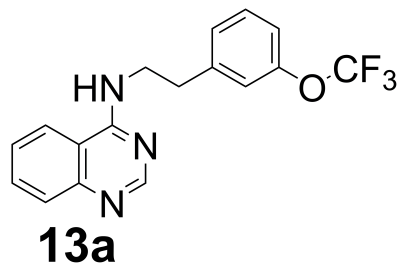


Figure S19 ¹³C NMR Spectrum (CDCl₃, 125 MHz) of **12a**

GM34-69-1.10.fid
13a (CDCl₃, 500 MHz)



8.72
7.86
7.77
7.77
7.76
7.75
7.74
7.74
7.60
7.59
7.48
7.48
7.46
7.46
7.45
7.45

5.83

3.99
3.98
3.97
3.95

3.11
3.09
3.08

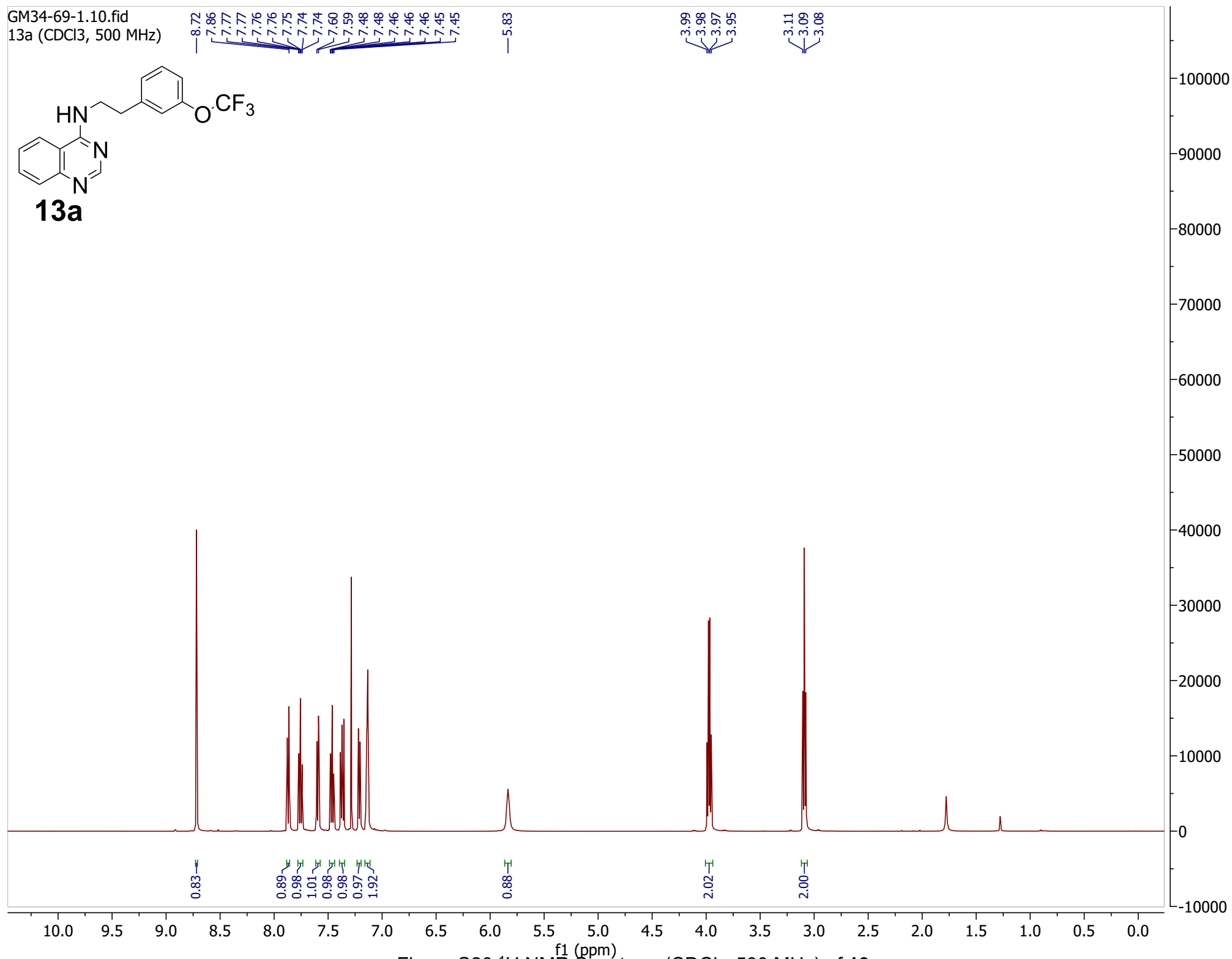


Figure S20 ¹H NMR Spectrum (CDCl₃, 500 MHz) of **13a**

GM34-69-1.11.fid
13a (CDCl₃, 125 MHz)

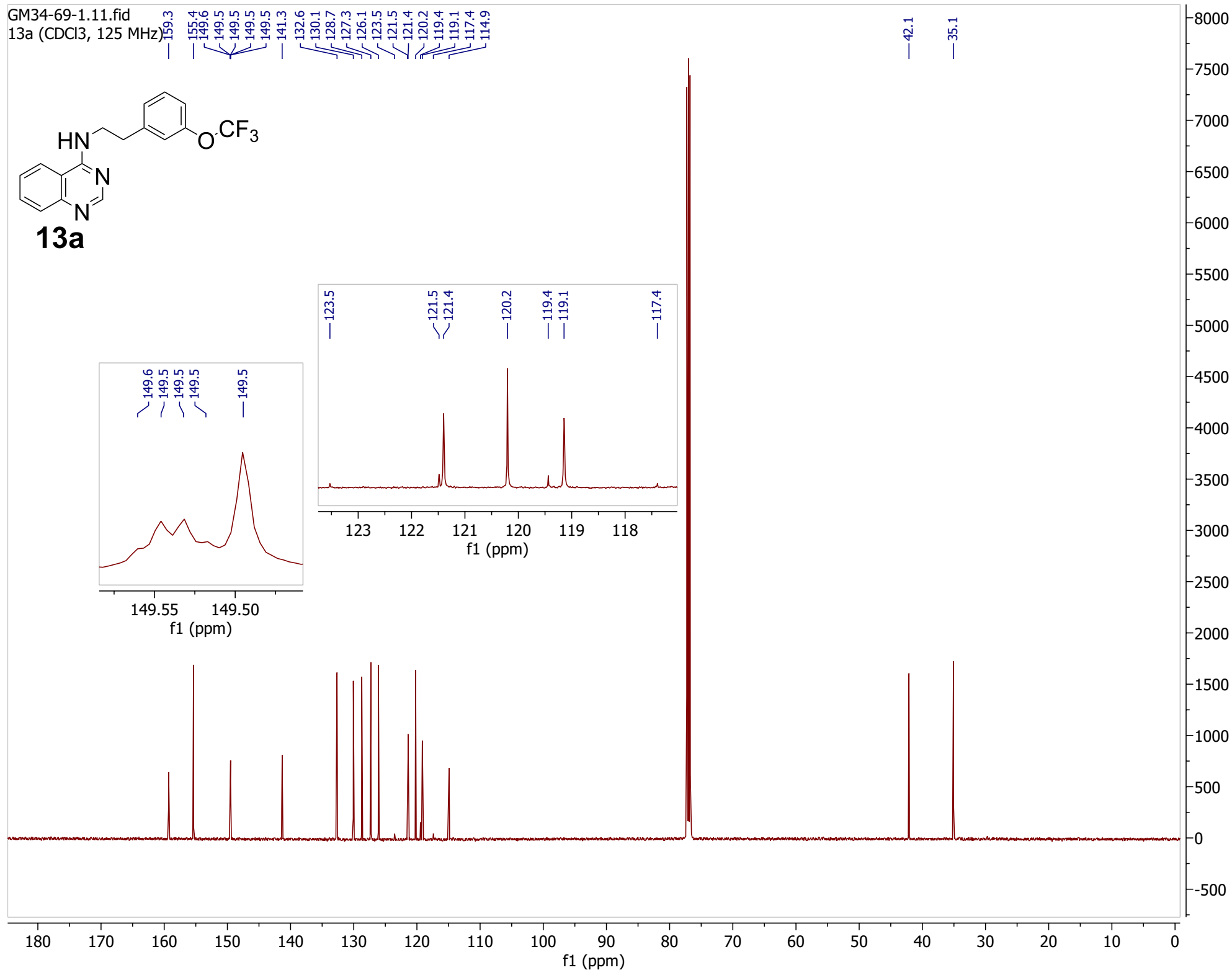
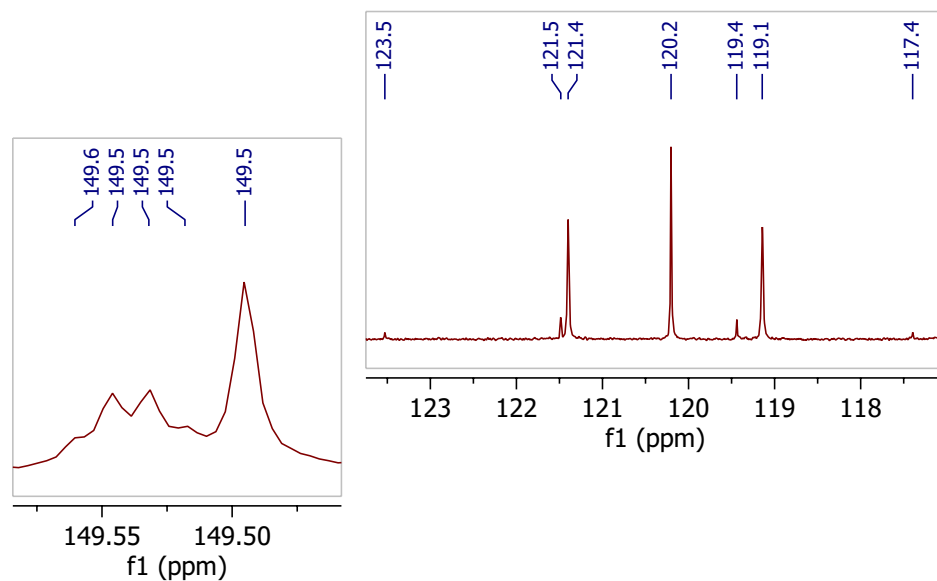
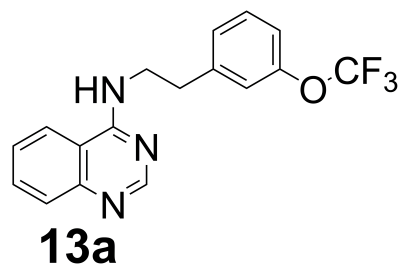


Figure S21 ¹³C NMR Spectrum (CDCl₃, 125 MHz) of **13a**

GM34-69-1.12.fid
13a (CDCl₃, 470 MHz)

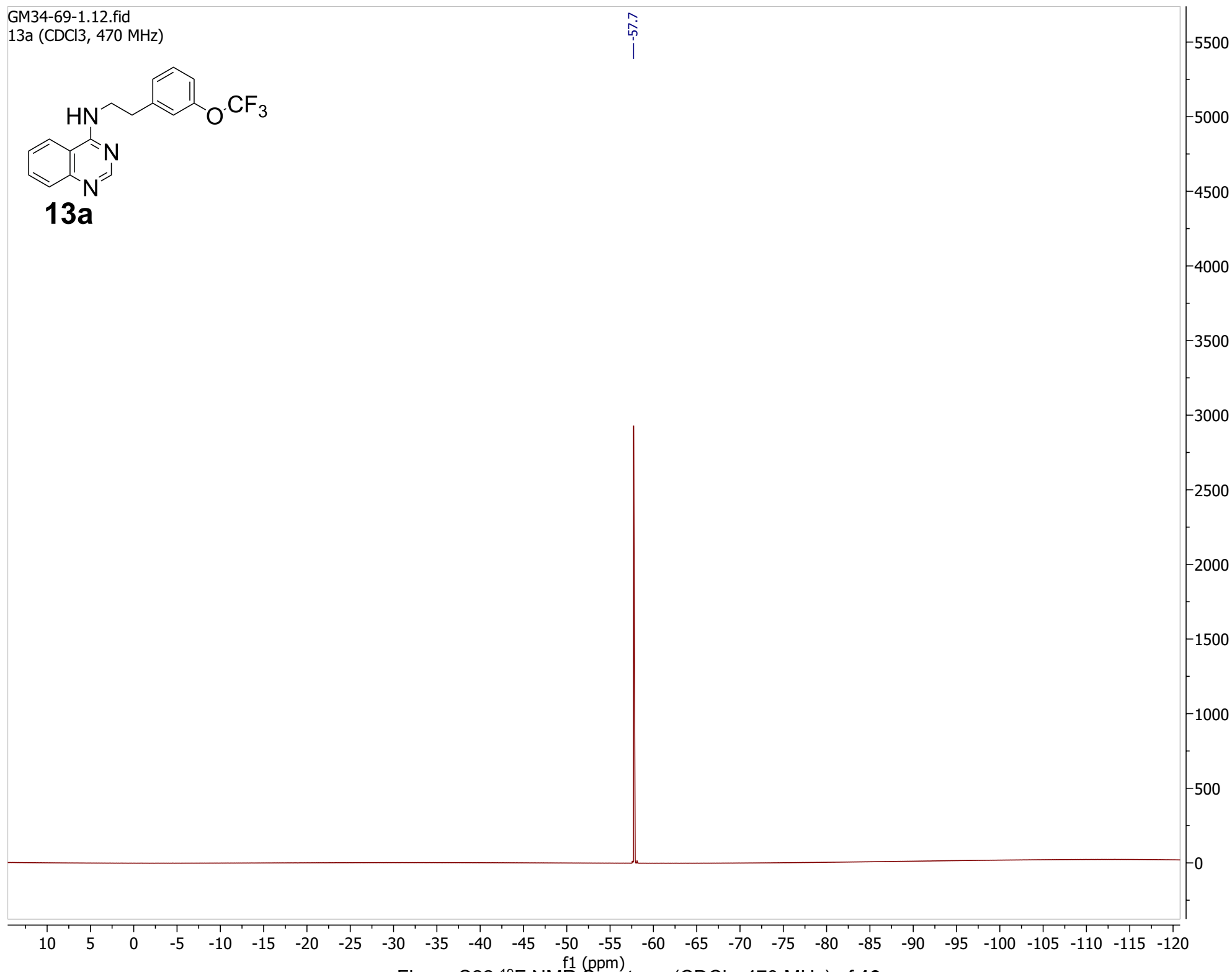
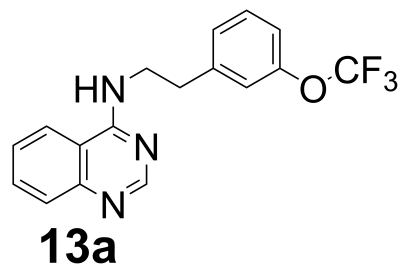


Figure S22 ¹⁹F NMR Spectrum (CDCl₃, 470 MHz) of **13a**

GM34-95-1.10.fid
14a (CDCl₃, 500 MHz)

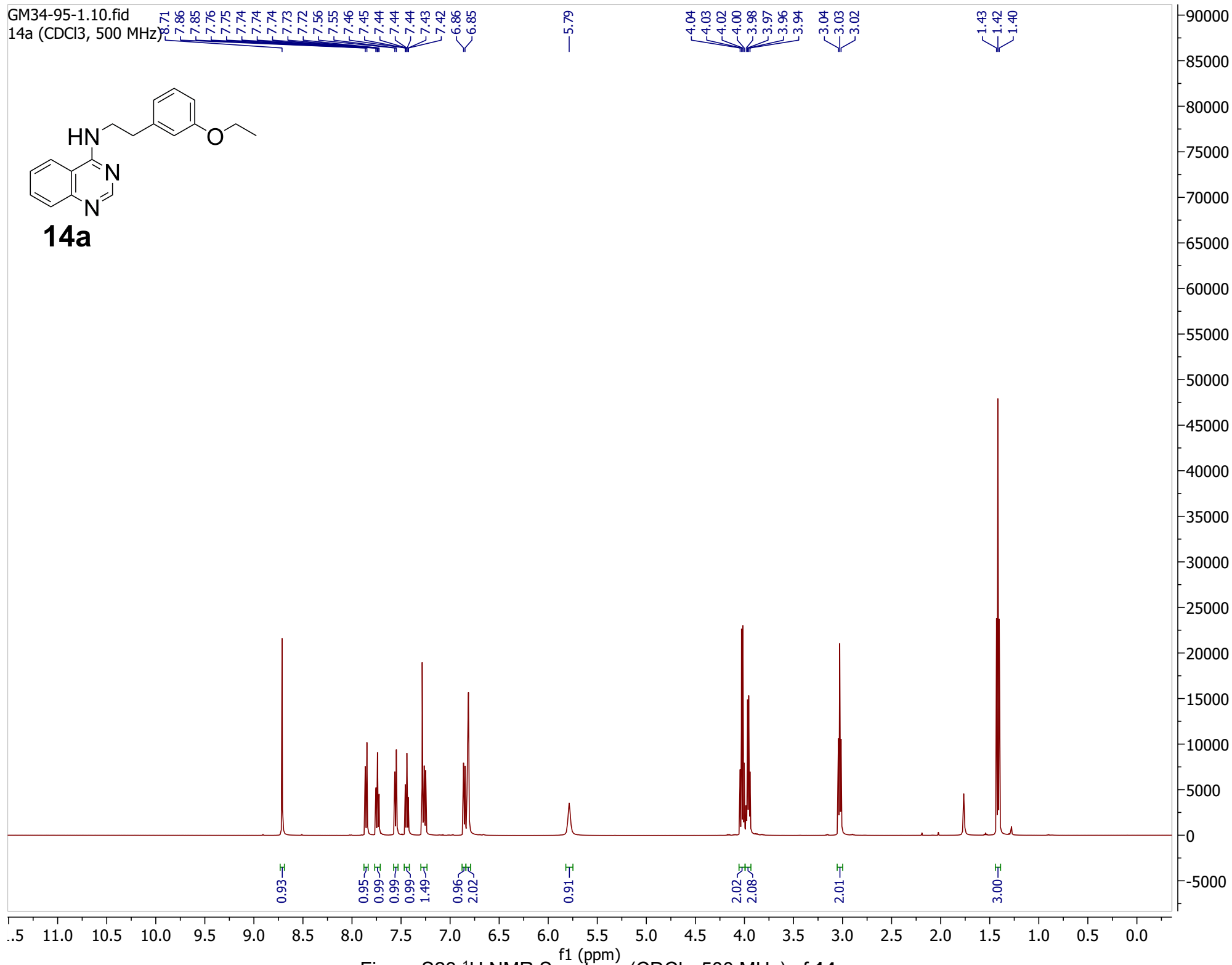
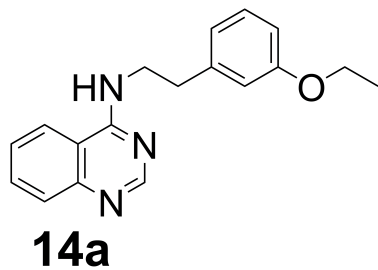
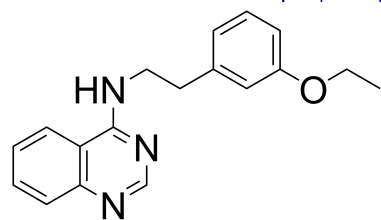


Figure S23 ¹H NMR Spectrum (CDCl₃, 500 MHz) of **14a**

GM34-95-1.11.fid
14a (CDCl₃, 125 MHz)



14a

159.4 159.3 155.5 149.5 140.4 132.5 129.8 128.7 126.0 121.0 120.3 115.1 115.0 112.6 63.4 42.1 35.3 14.8

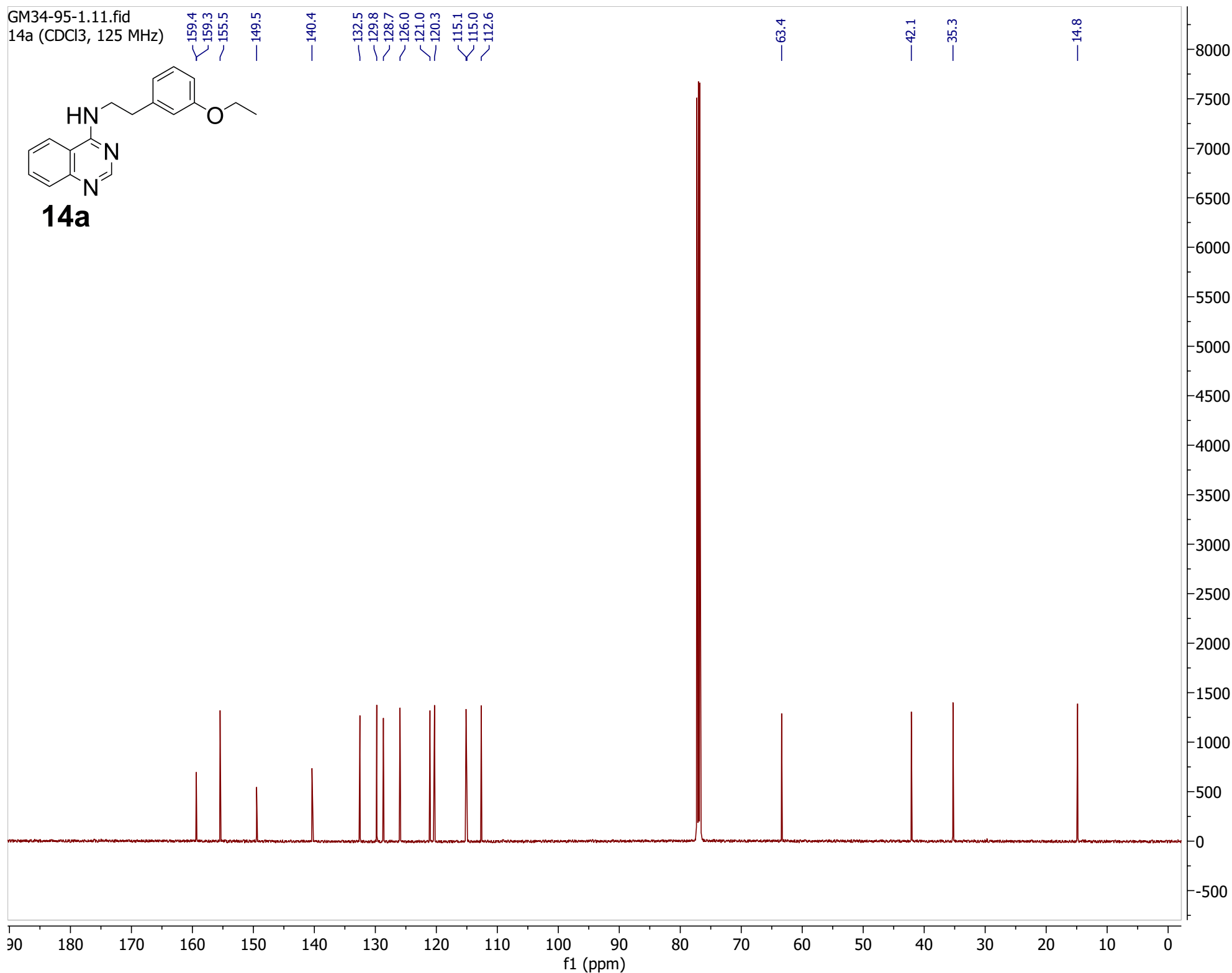


Figure S24 ¹³C NMR Spectrum (CDCl₃, 125 MHz) of **14a**

SMH1-38.10.fid
15a (CDCl₃, 500 MHz)

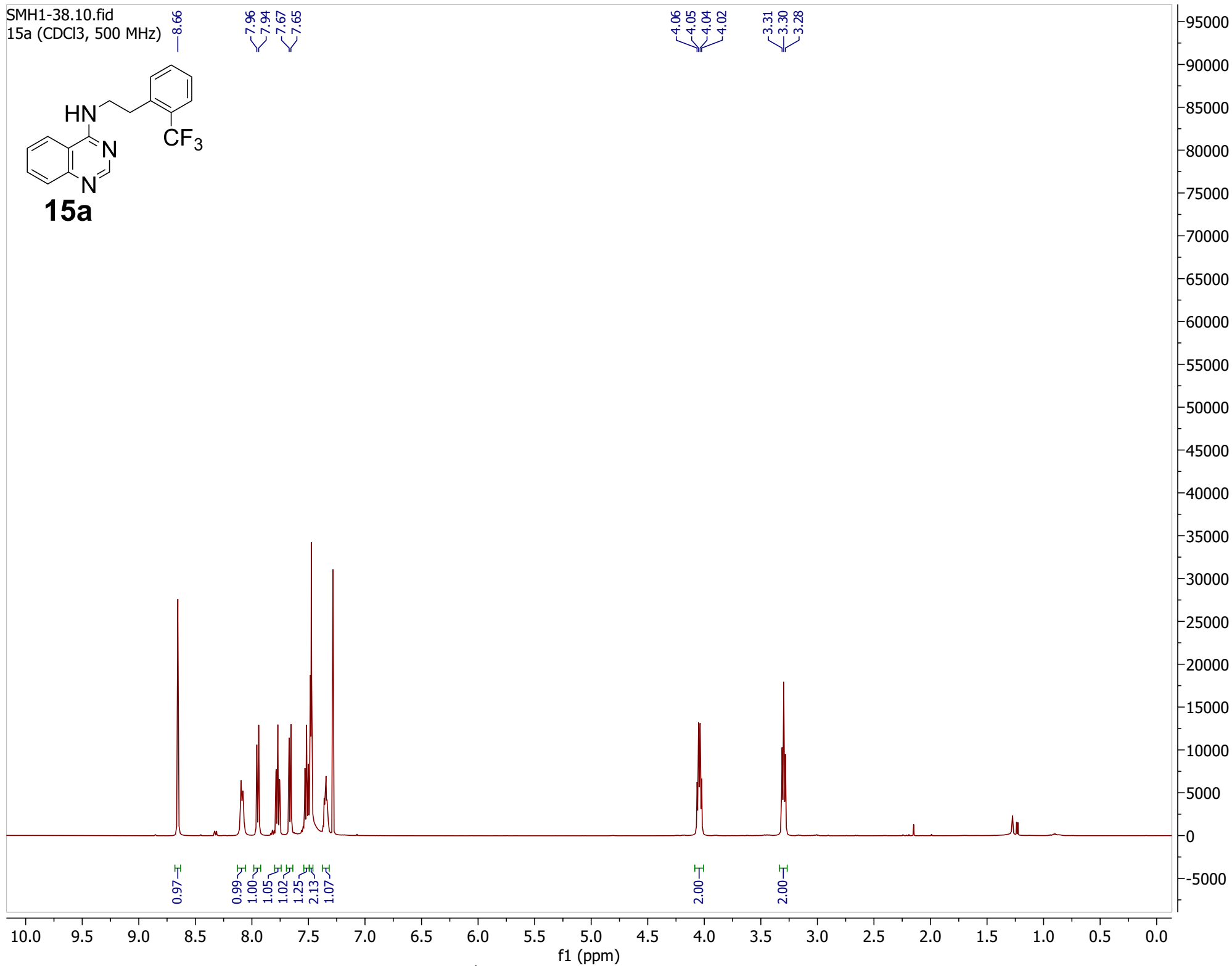
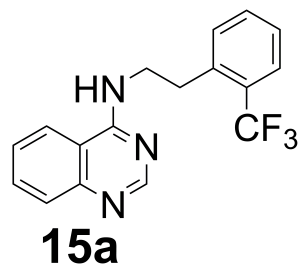


Figure S25 ¹H NMR Spectrum (CDCl₃, 500 MHz) of **15a**

SMH1-38.12.fid
15a (CDCl₃, 125 MHz)

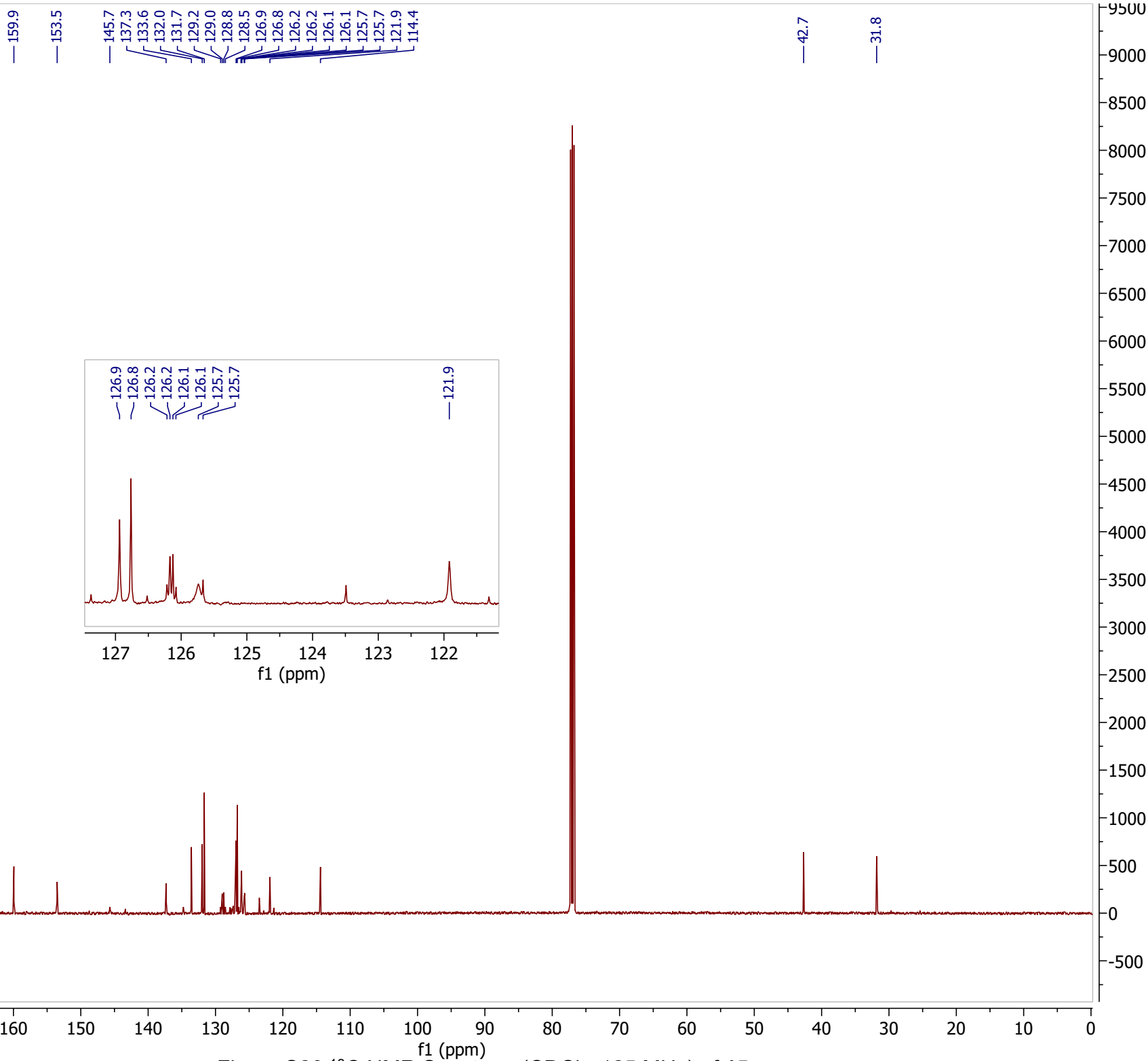
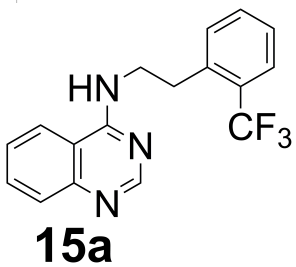


Figure S26 ¹³C NMR Spectrum (CDCl₃, 125 MHz) of **15a**

SMH1-38.11.fid
15a (CDCl₃, 470 MHz)

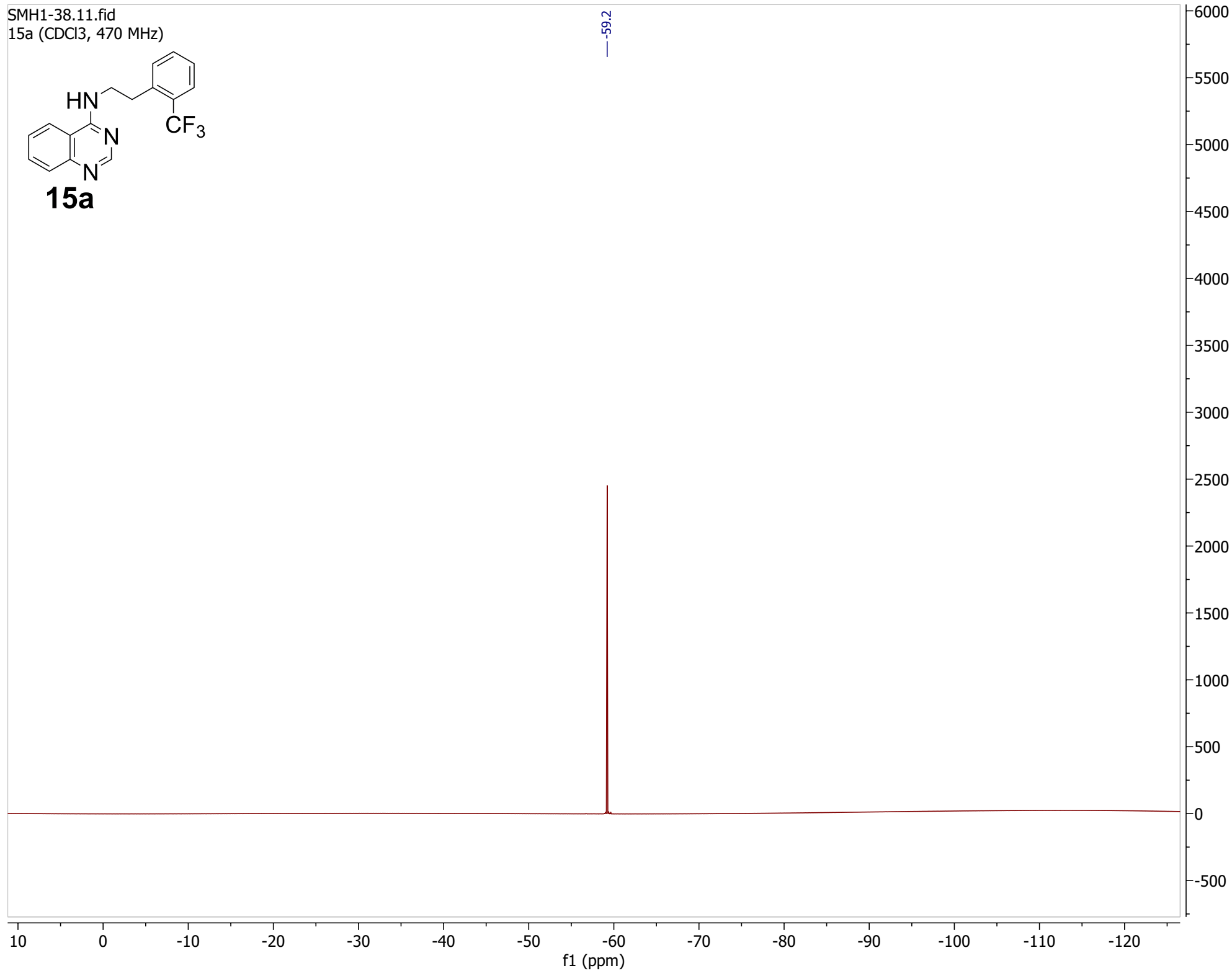
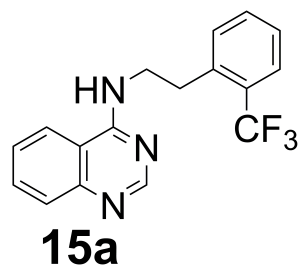


Figure S27 ¹⁹F NMR Spectrum (CDCl₃, 470 MHz) of **15a**

GM34-72-1.10.fid
16a (CDCl₃, 500 MHz)

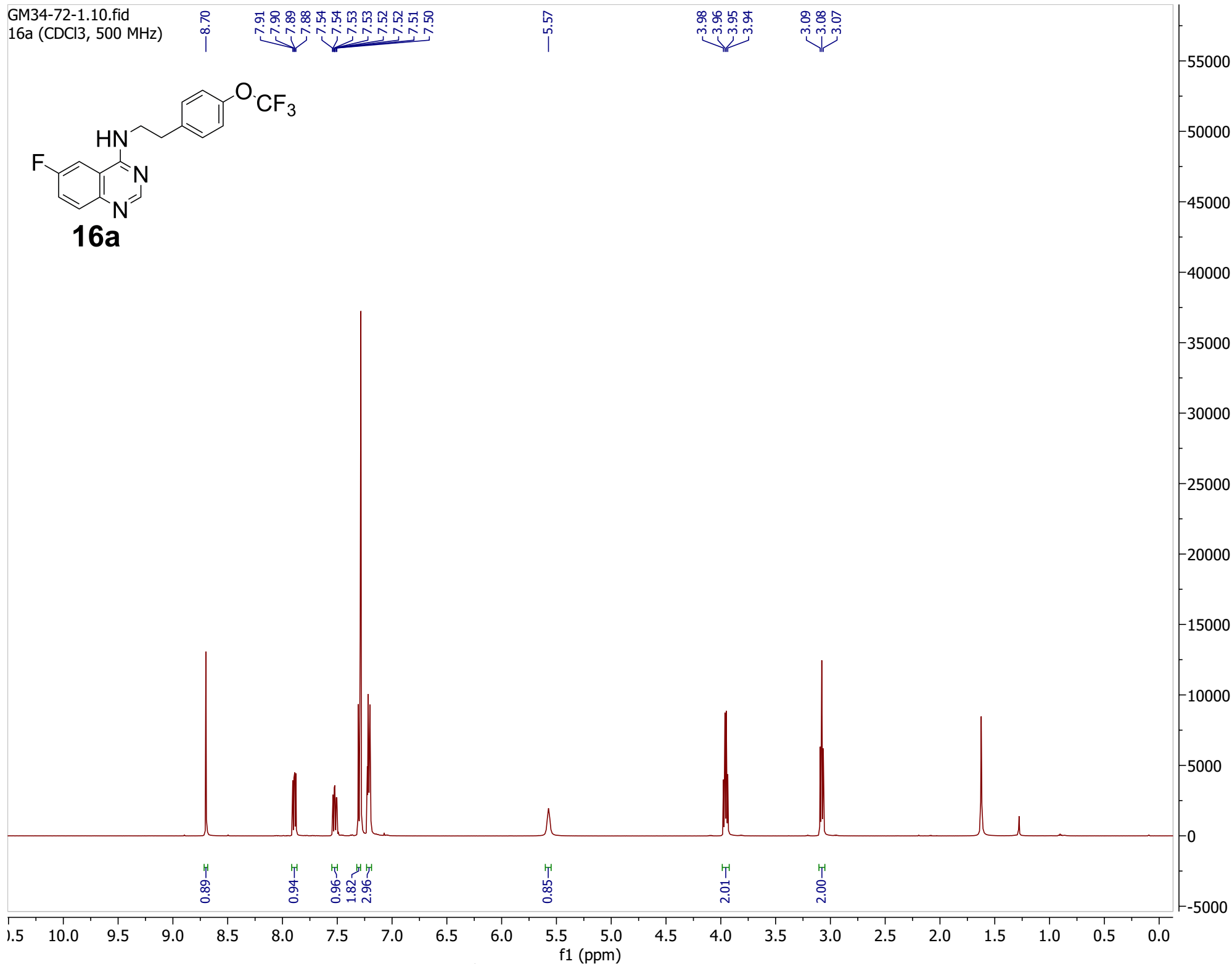
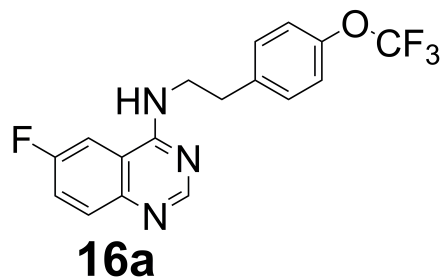


Figure S28 ¹H NMR Spectrum (CDCl₃, 500 MHz) of **16a**

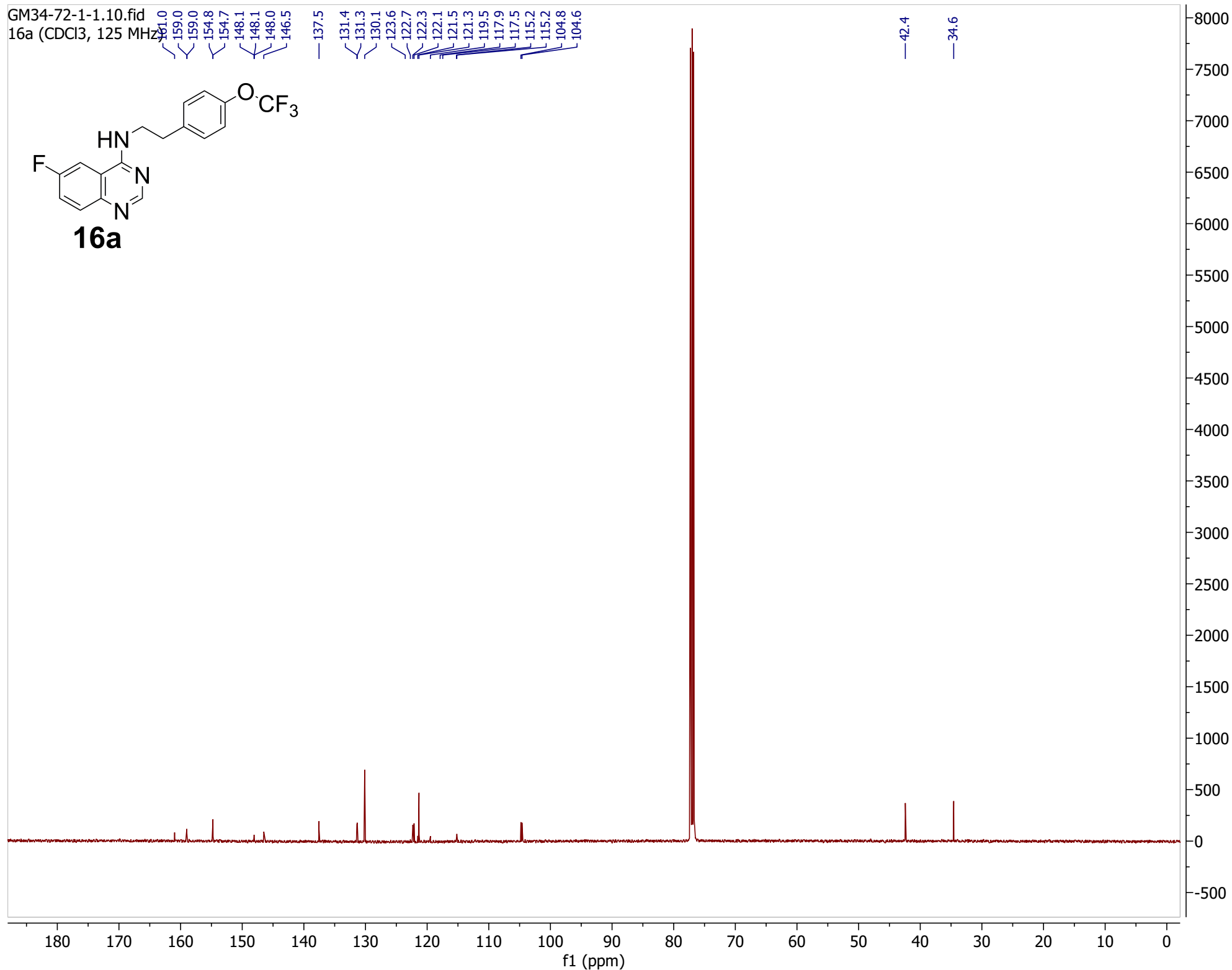


Figure S29 ¹³C NMR Spectrum (CDCl₃, 125 MHz) of **16a**

GM34-72-1.12.fid
16a (CDCl₃, 470 MHz)

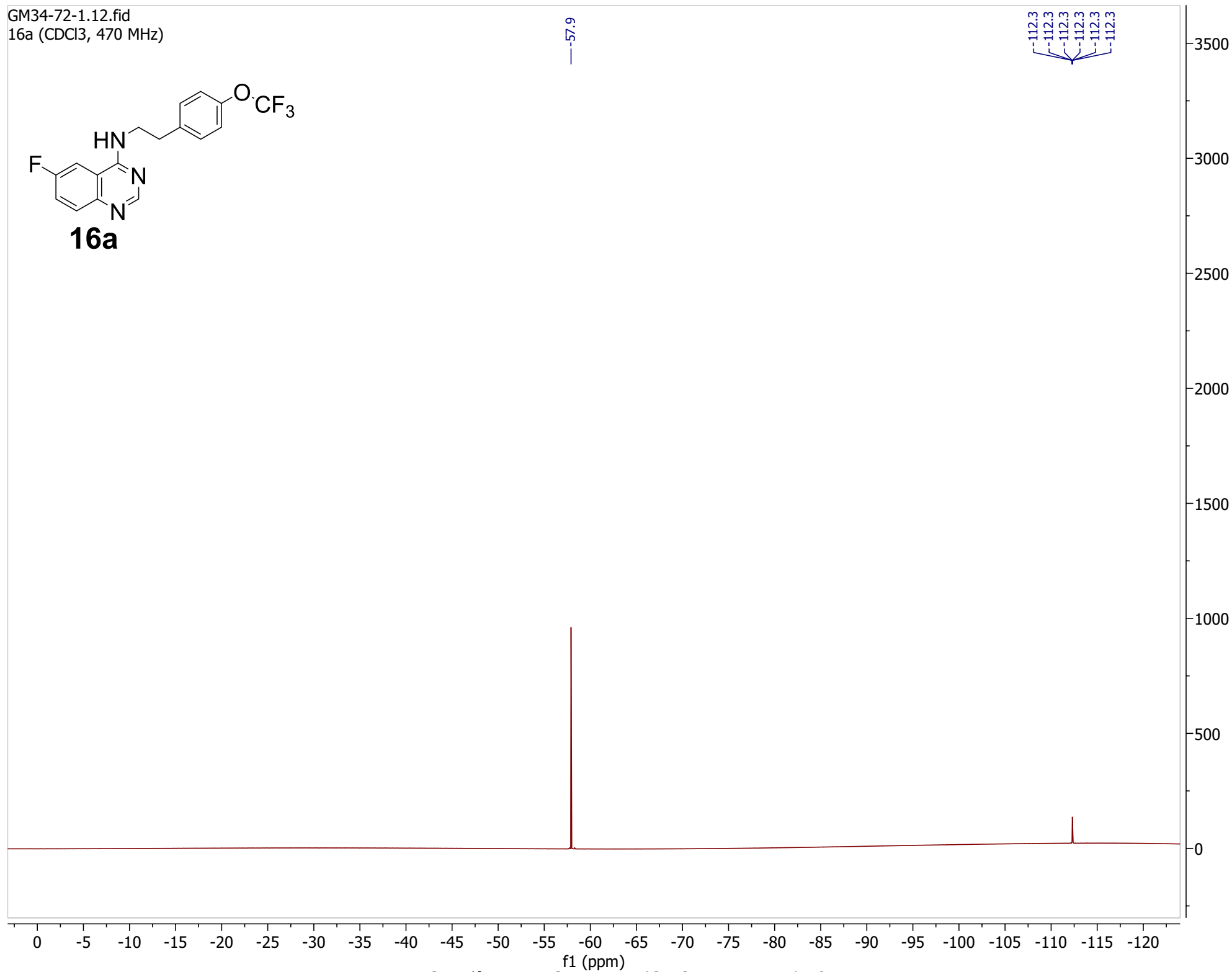
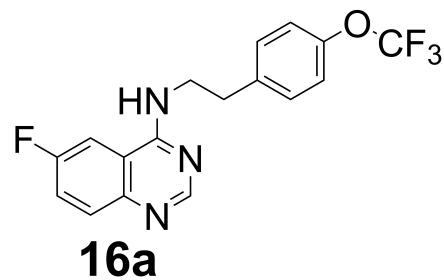


Figure S30 ¹⁹F NMR Spectrum (CDCl₃, 470 MHz) of **16a**

GM34-71-2.10.fid
17a (CDCl₃, 500 MHz)

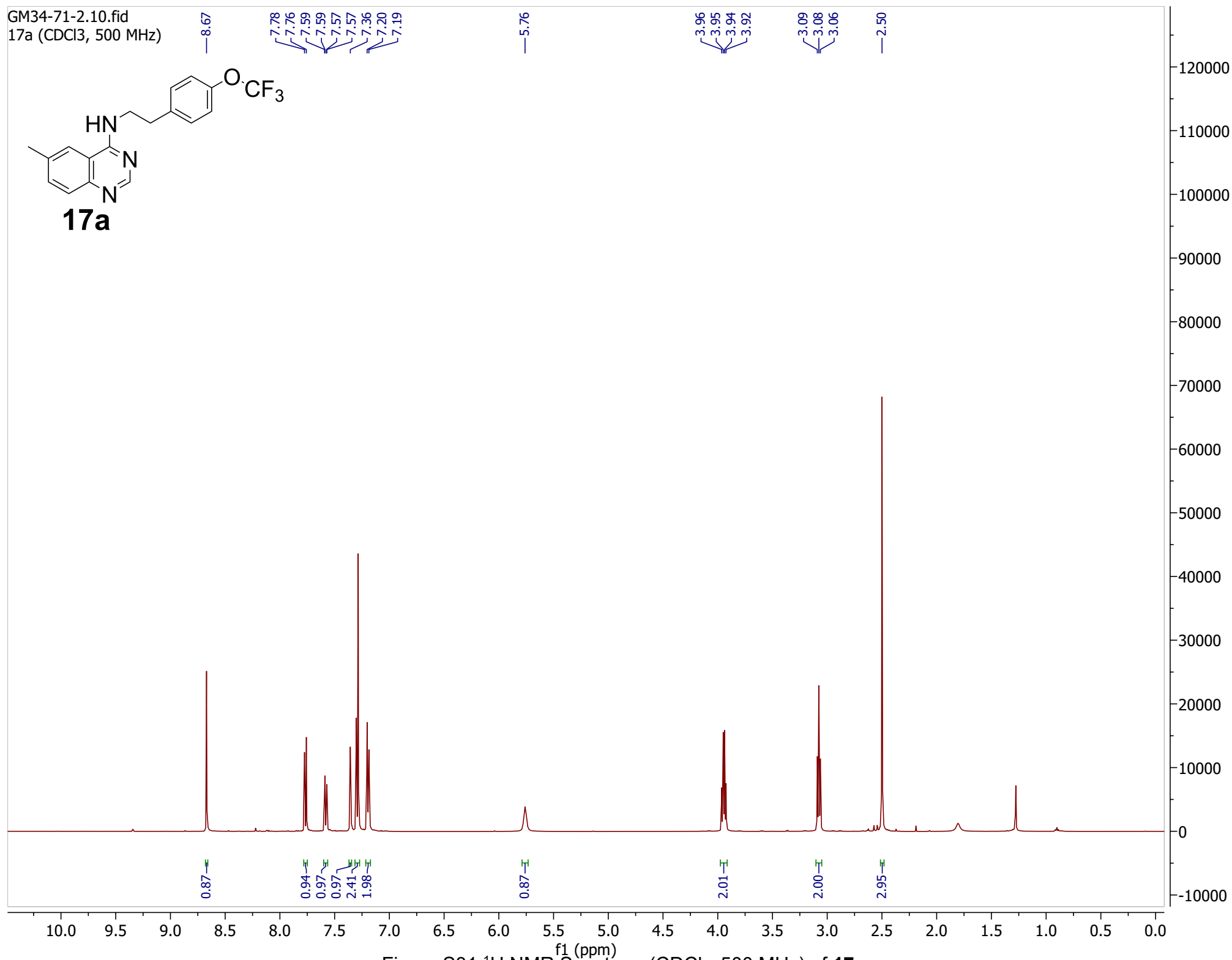
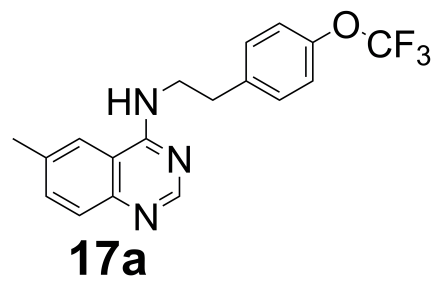


Figure S31 ¹H NMR Spectrum (CDCl₃, 500 MHz) of **17a**

GM34-71-2.11.fid
17a (CDCl₃, 125 MHz)

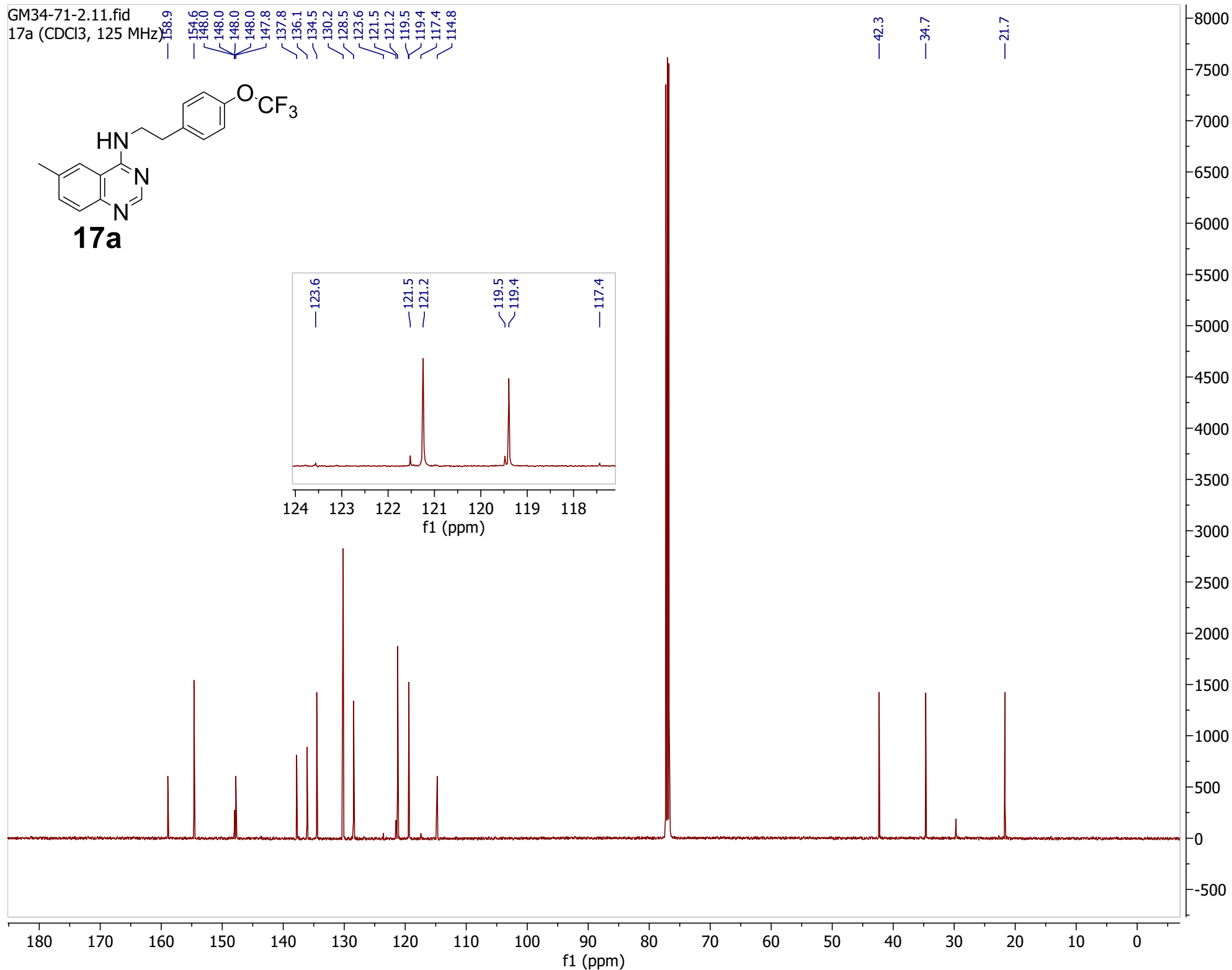
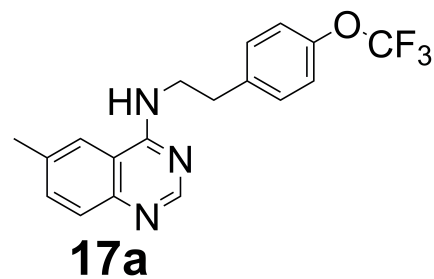


Figure S32 ¹³C NMR Spectrum (CDCl₃, 125 MHz) of **17a**

GM34-71-2.12.fid
17a (CDCl₃, 470 MHz)

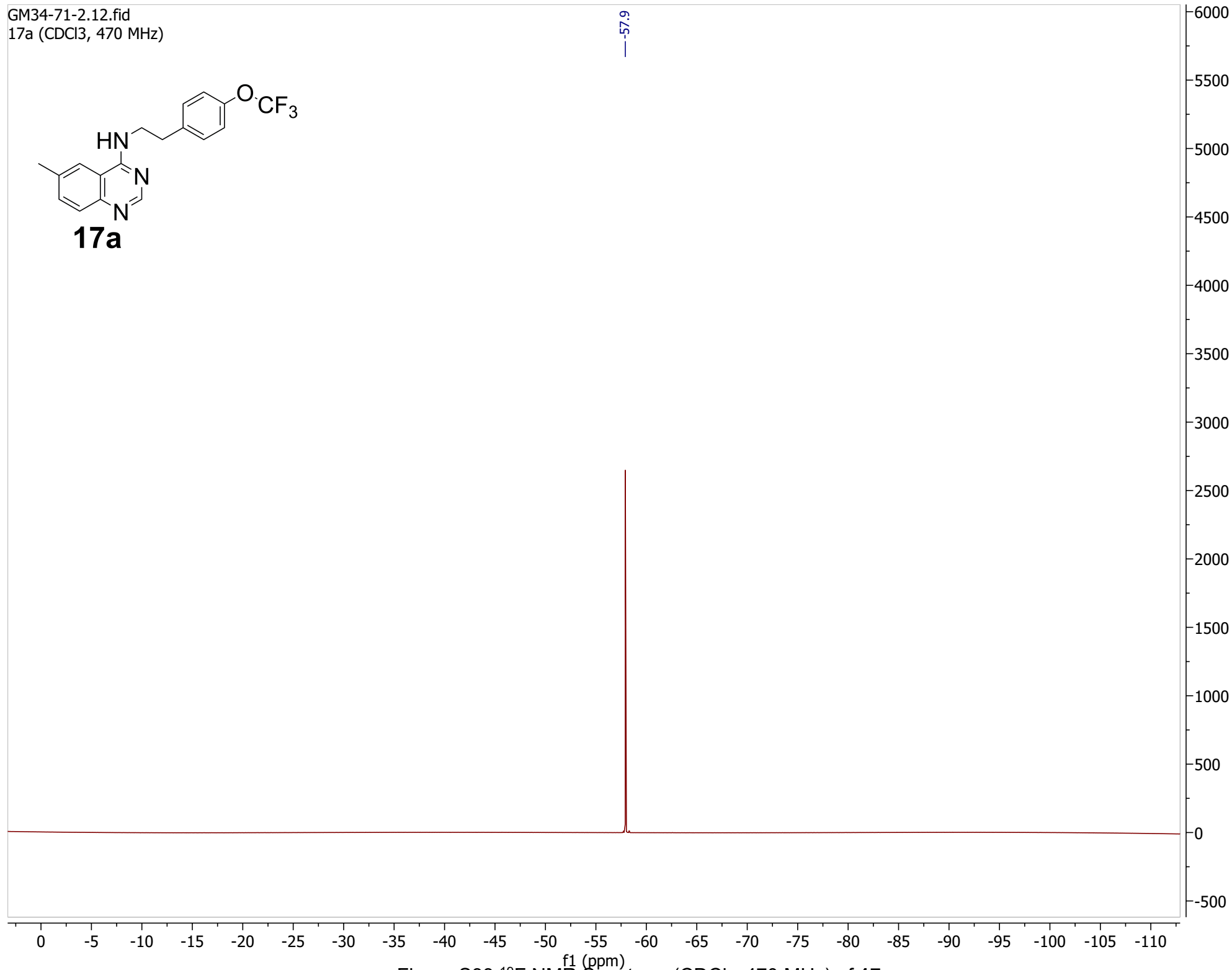
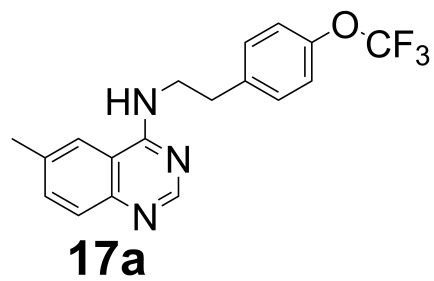


Figure S33 ¹⁹F NMR Spectrum (CDCl₃, 470 MHz) of **17a**

GM34-73-1.10.fid
18a (CDCl₃, 500 MHz)

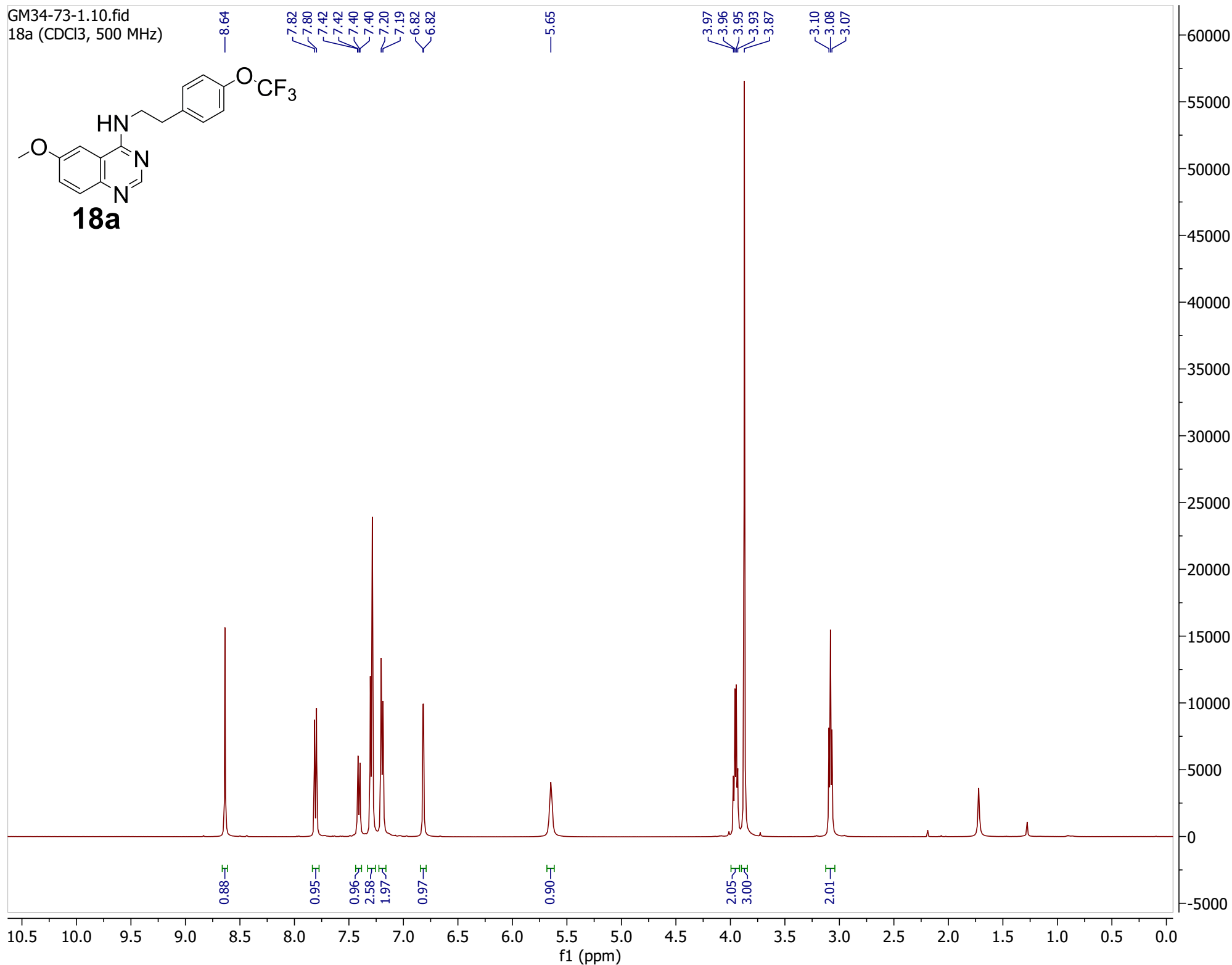
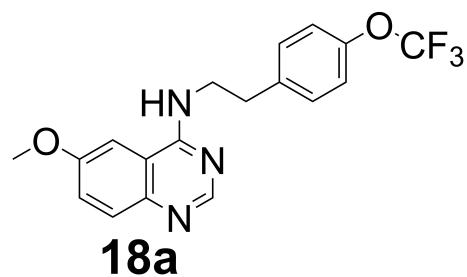


Figure S34 ¹H NMR Spectrum (CDCl₃, 500 MHz) of **18a**

GM34-73-1.11.fid
18a (CDCl₃, 125 MHz)

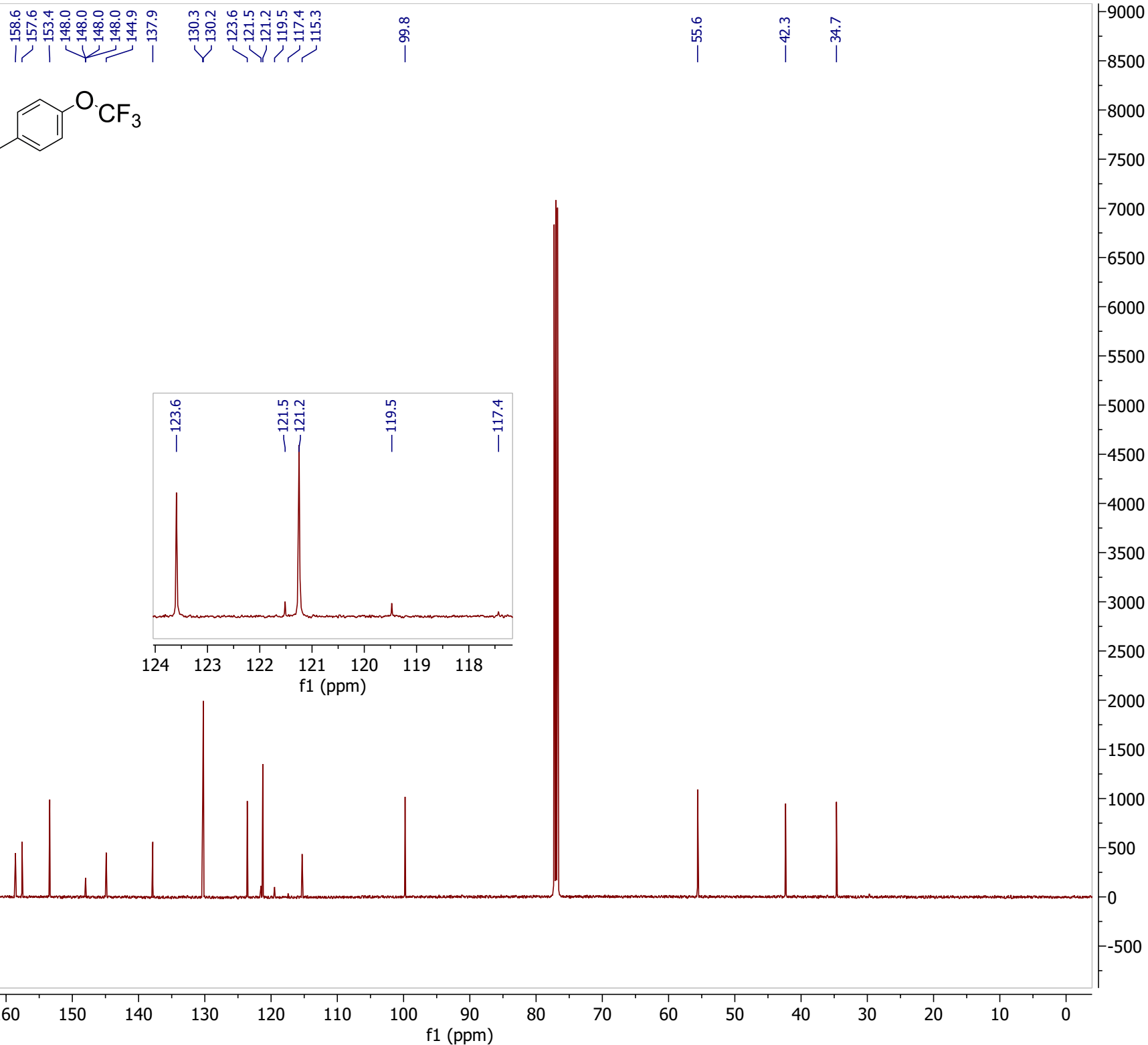
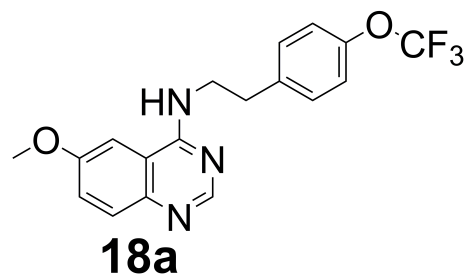


Figure S35 ¹³C NMR Spectrum (CDCl₃, 125 MHz) of **18a**

GM34-73-1.12.fid
18a (CDCl₃, 470 MHz)

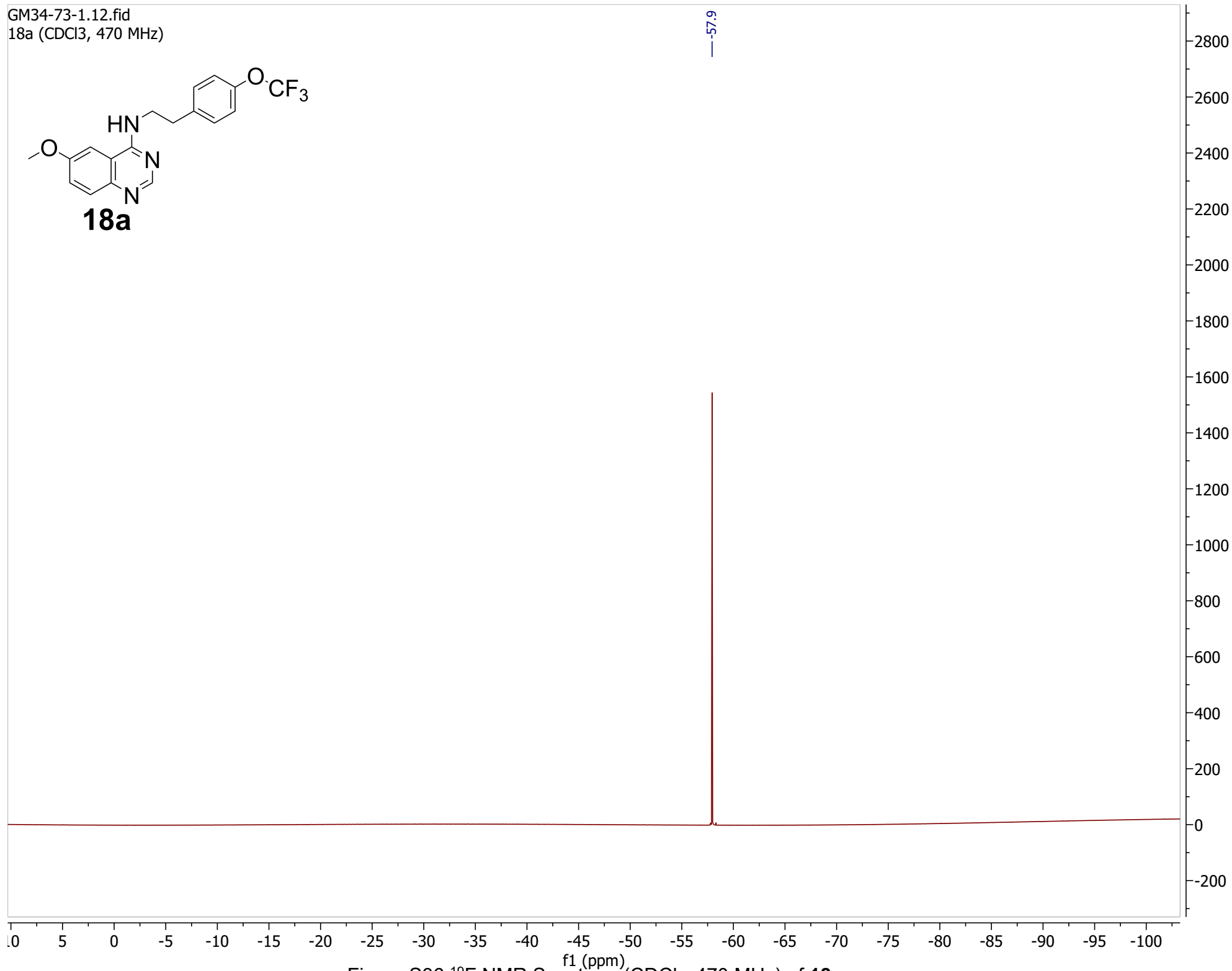
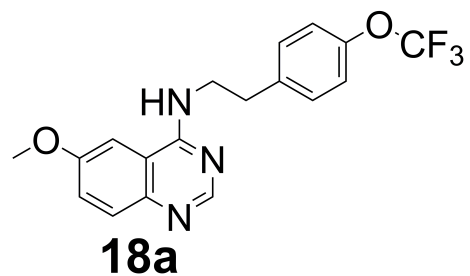


Figure S36 ¹⁹F NMR Spectrum (CDCl₃, 470 MHz) of **18a**

GM34-74-2.10.fid
19a (CDCl₃, 500 MHz)

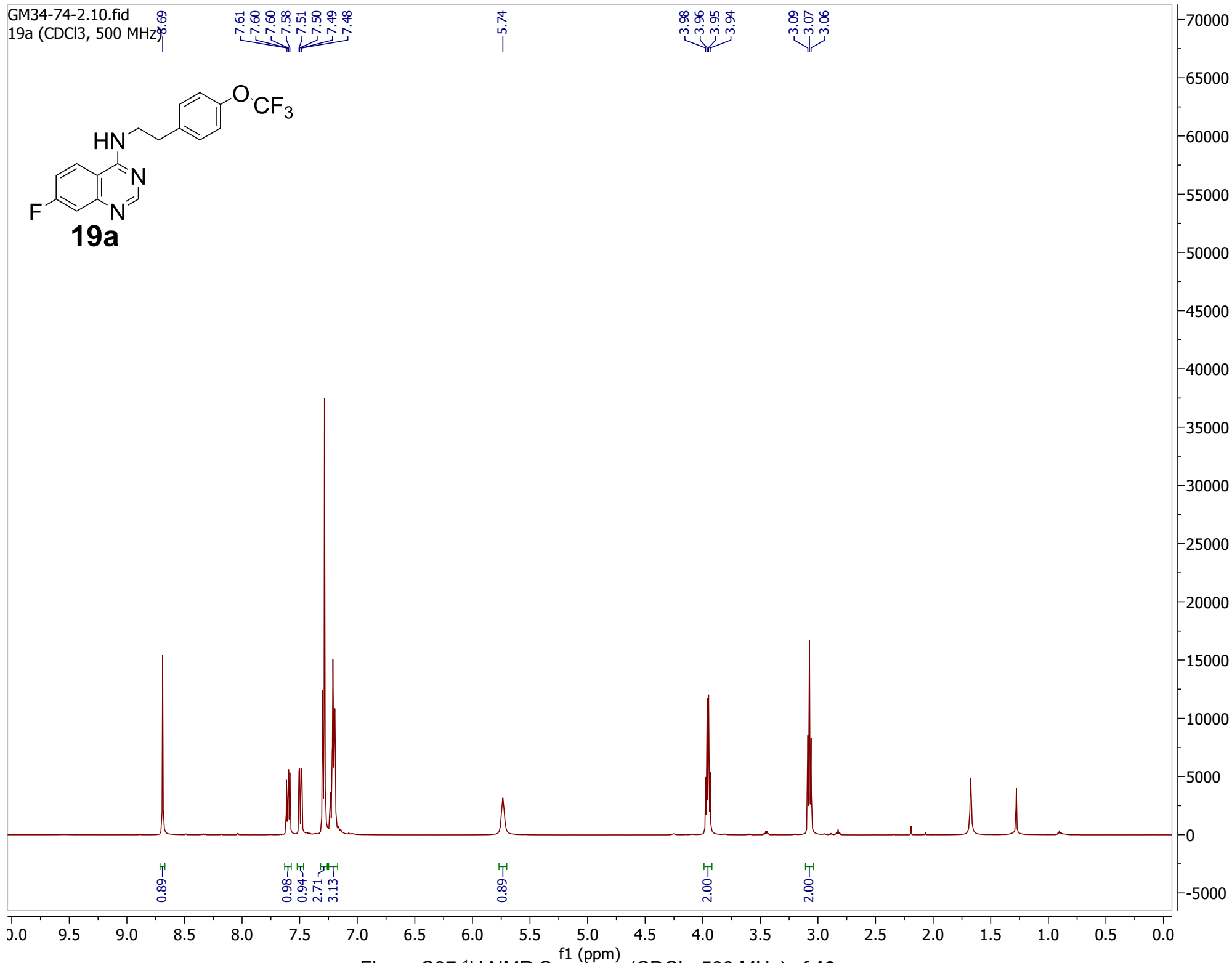
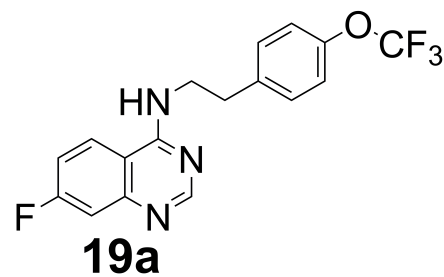
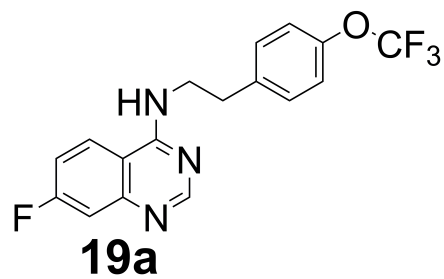


Figure S37 ¹H NMR Spectrum (CDCl₃, 500 MHz) of **19a**

GM34-74-2.11.fid
19a (CDCl₃, 125 MHz)



166.0
164.0
159.1
156.4
151.6
151.5
148.1
148.1
137.6
130.1
123.6
122.8
122.7
121.5
121.3
119.5
117.4
115.9
115.7
113.0
112.9
111.8

42.3

34.6

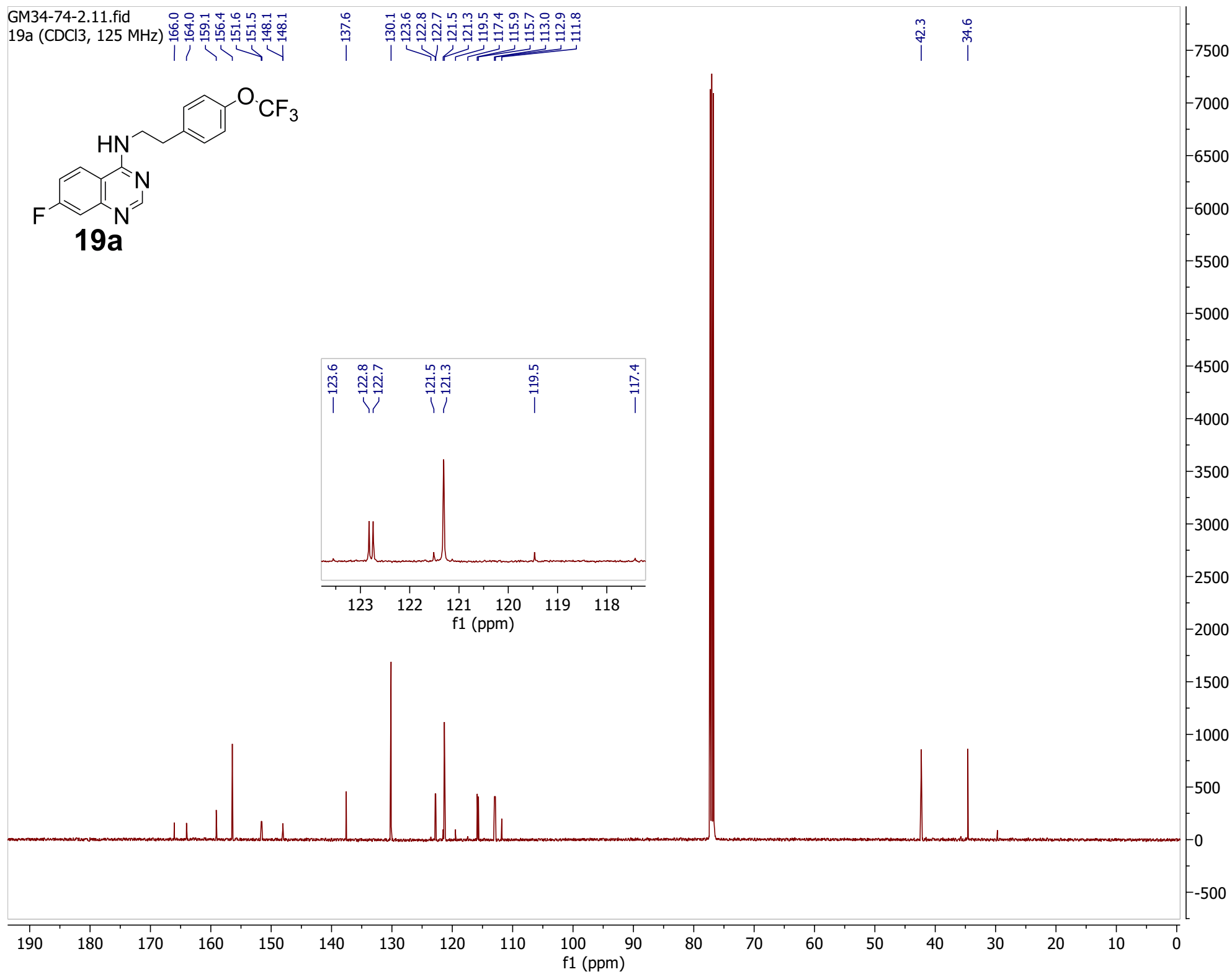
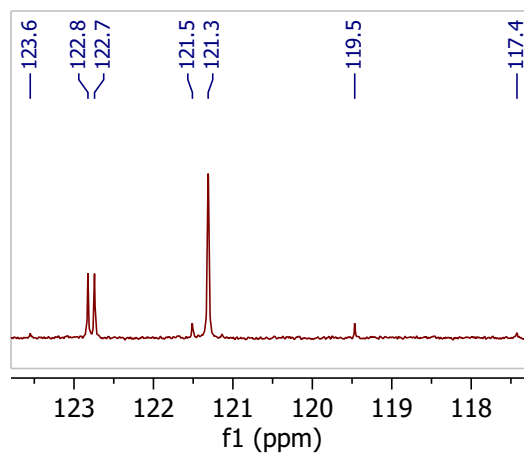


Figure S38 ¹³C NMR Spectrum (CDCl₃, 125 MHz) of **19a**

GM34-74-2.12.fid
19a (CDCl₃, 470 MHz)

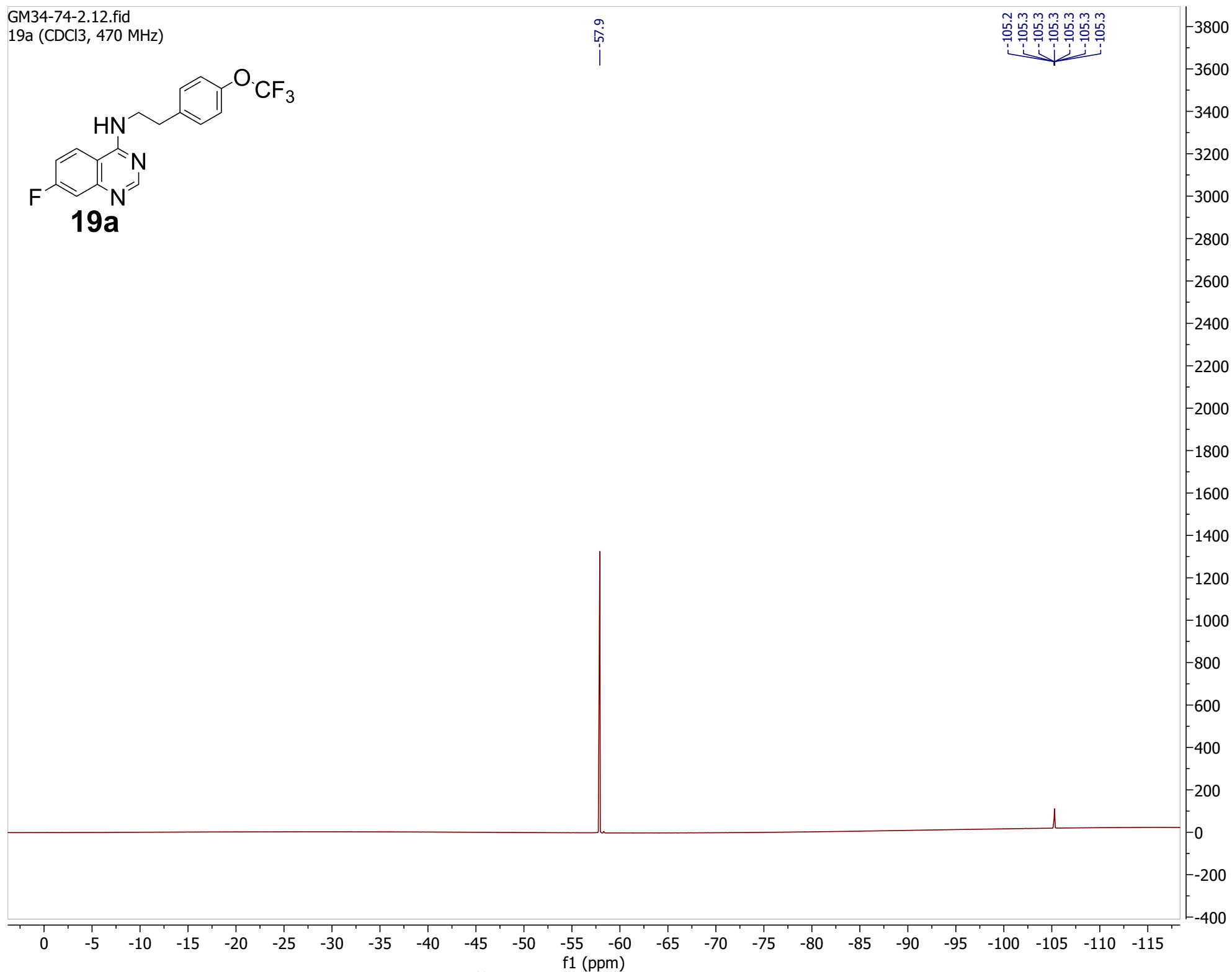
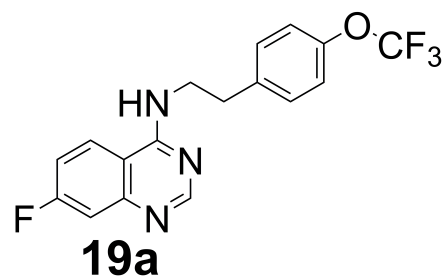


Figure S39 ¹⁹F NMR Spectrum (CDCl₃, 470 MHz) of **19a**

SMH12-49-1.10.fid
20a (MeOD, 500 MHz)

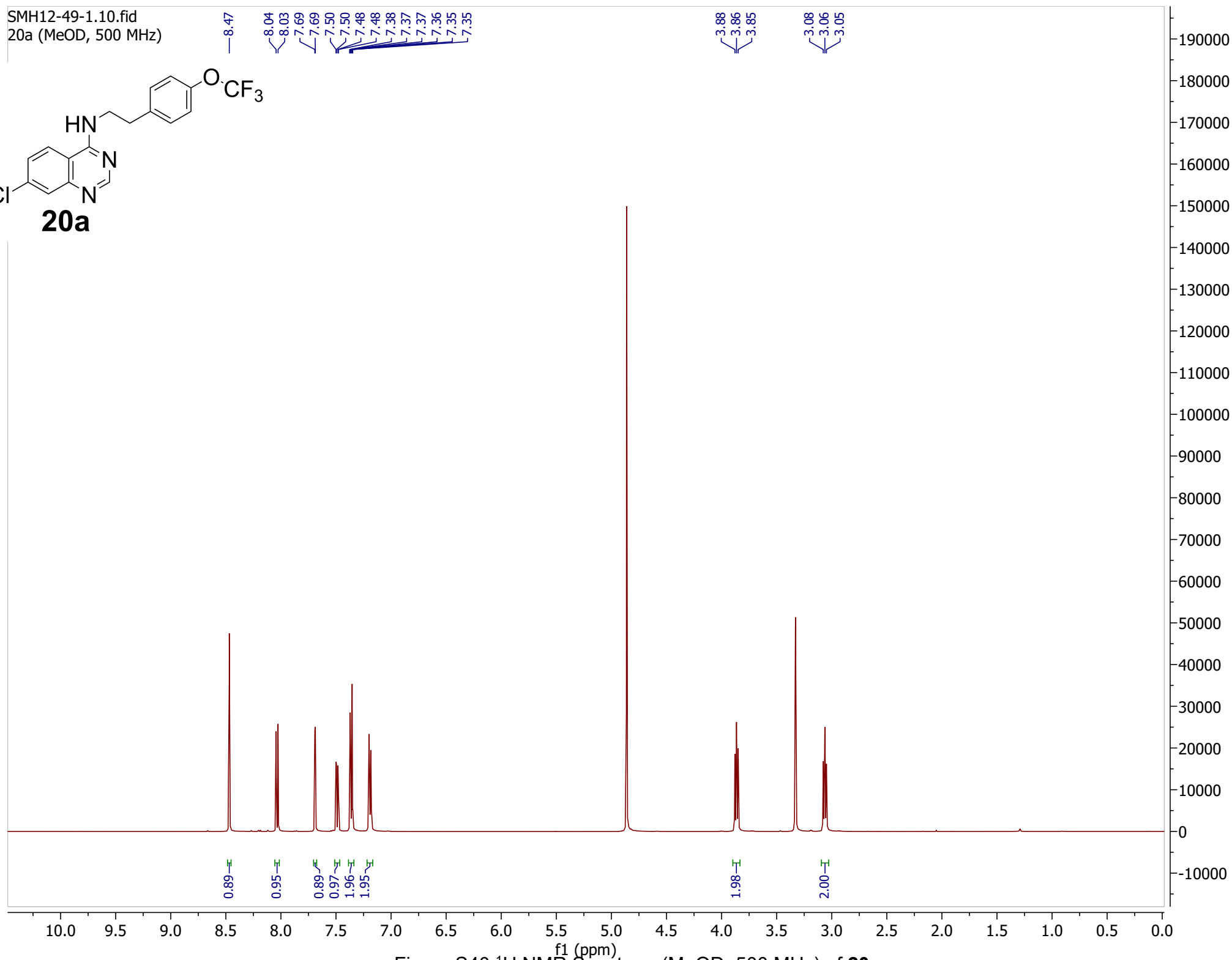
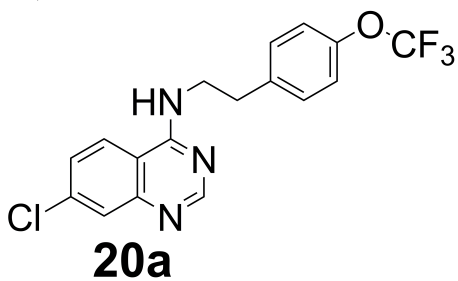


Figure S40 ^1H NMR Spectrum (MeOD, 500 MHz) of **20a**

SMH12-49-1.11.fid
20a (MeOD, 125 MHz)

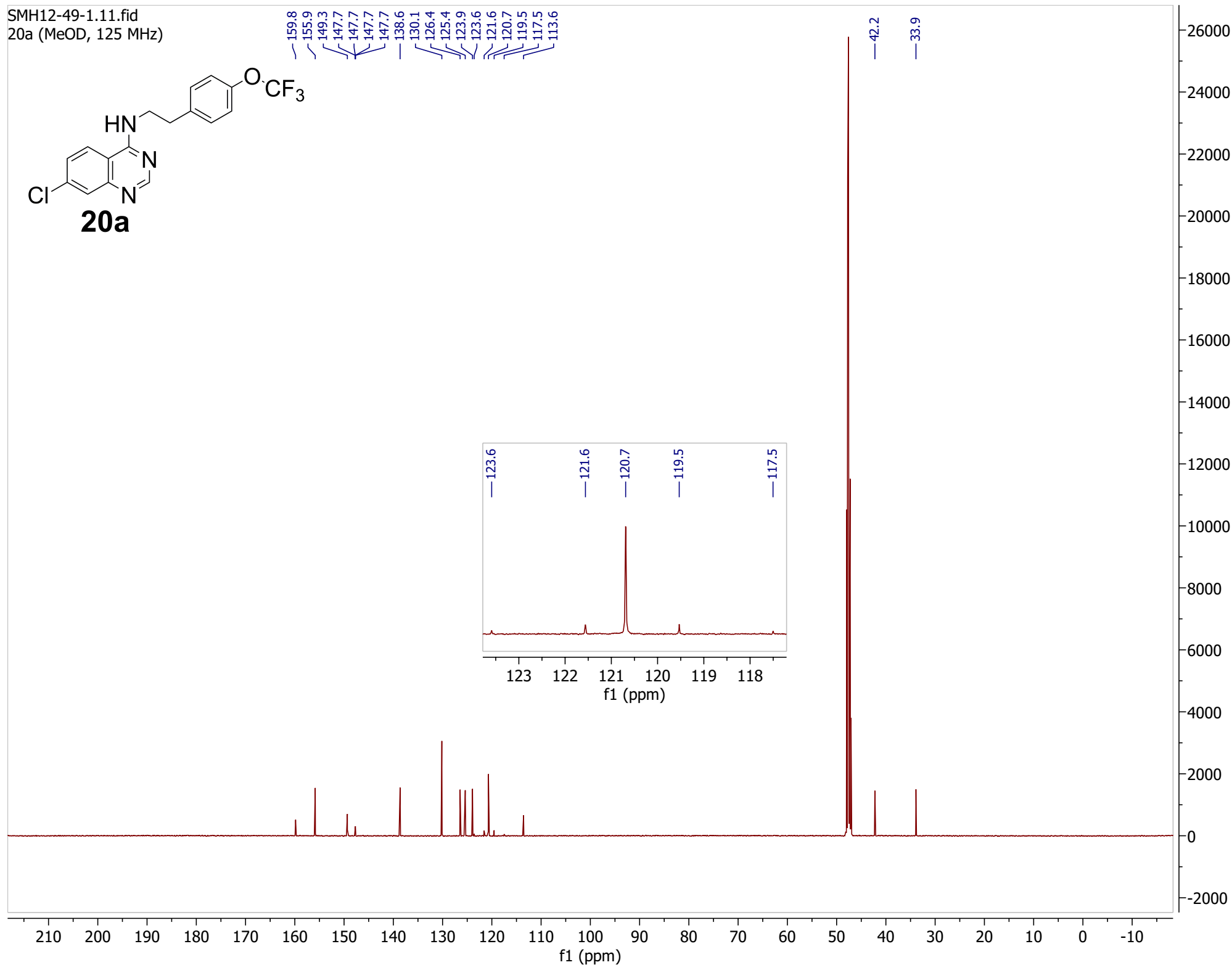
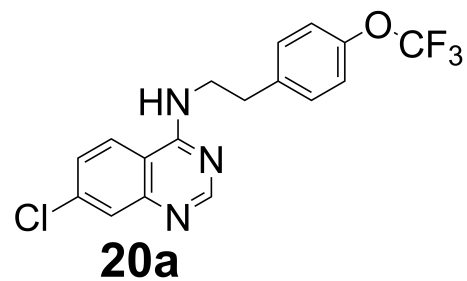


Figure S41 ¹³C NMR Spectrum (MeOD, 125 MHz) of **20a**

SMH12-49-1.12.fid
20a (MeOD, 470 MHz)

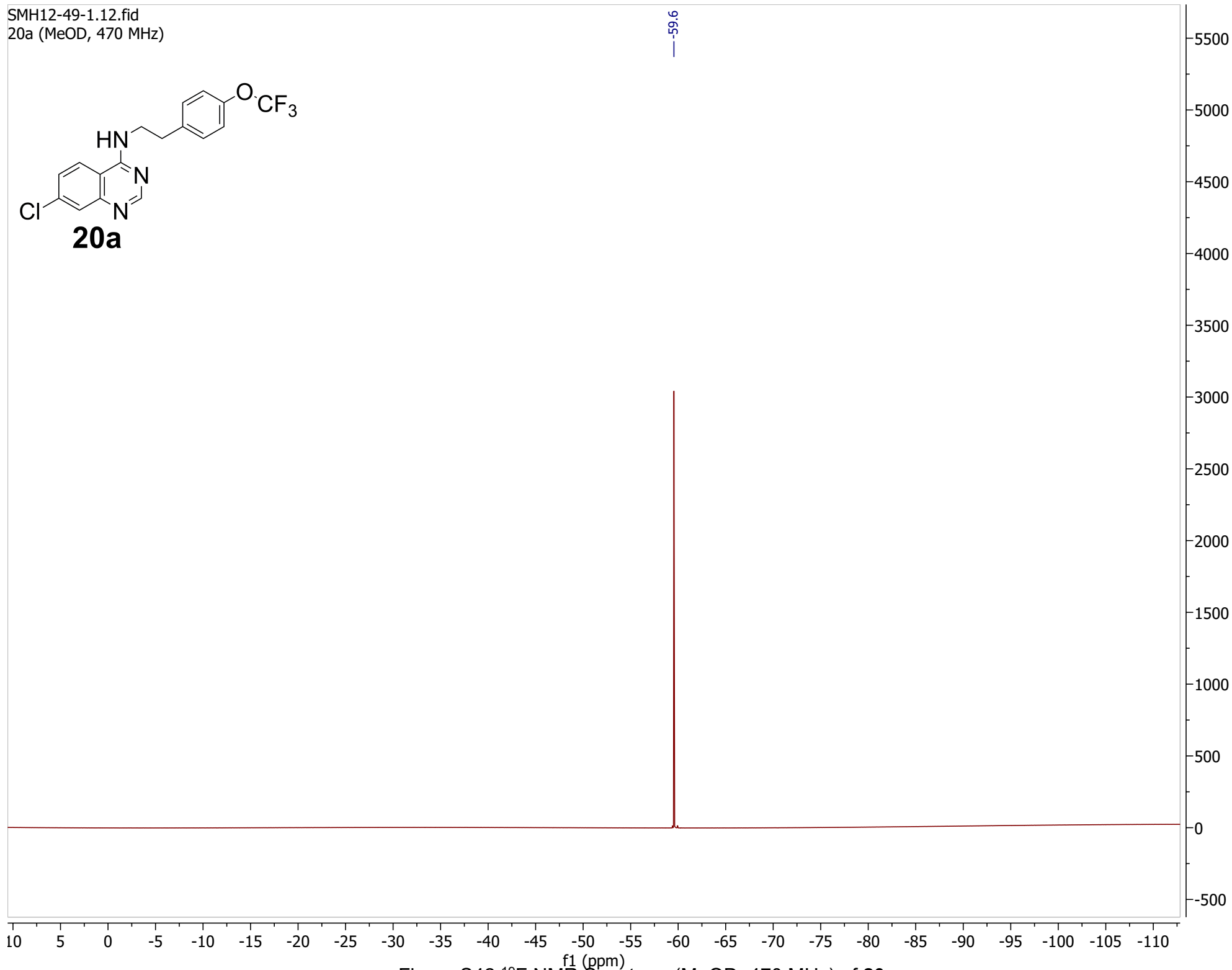
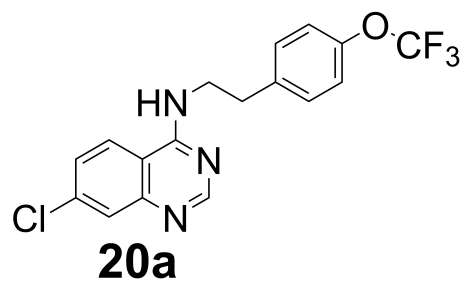


Figure S42 ¹⁹F NMR Spectrum (MeOD, 470 MHz) of **20a**

GM36-12-1.10.fid
21a (CDCl₃, 500 MHz)

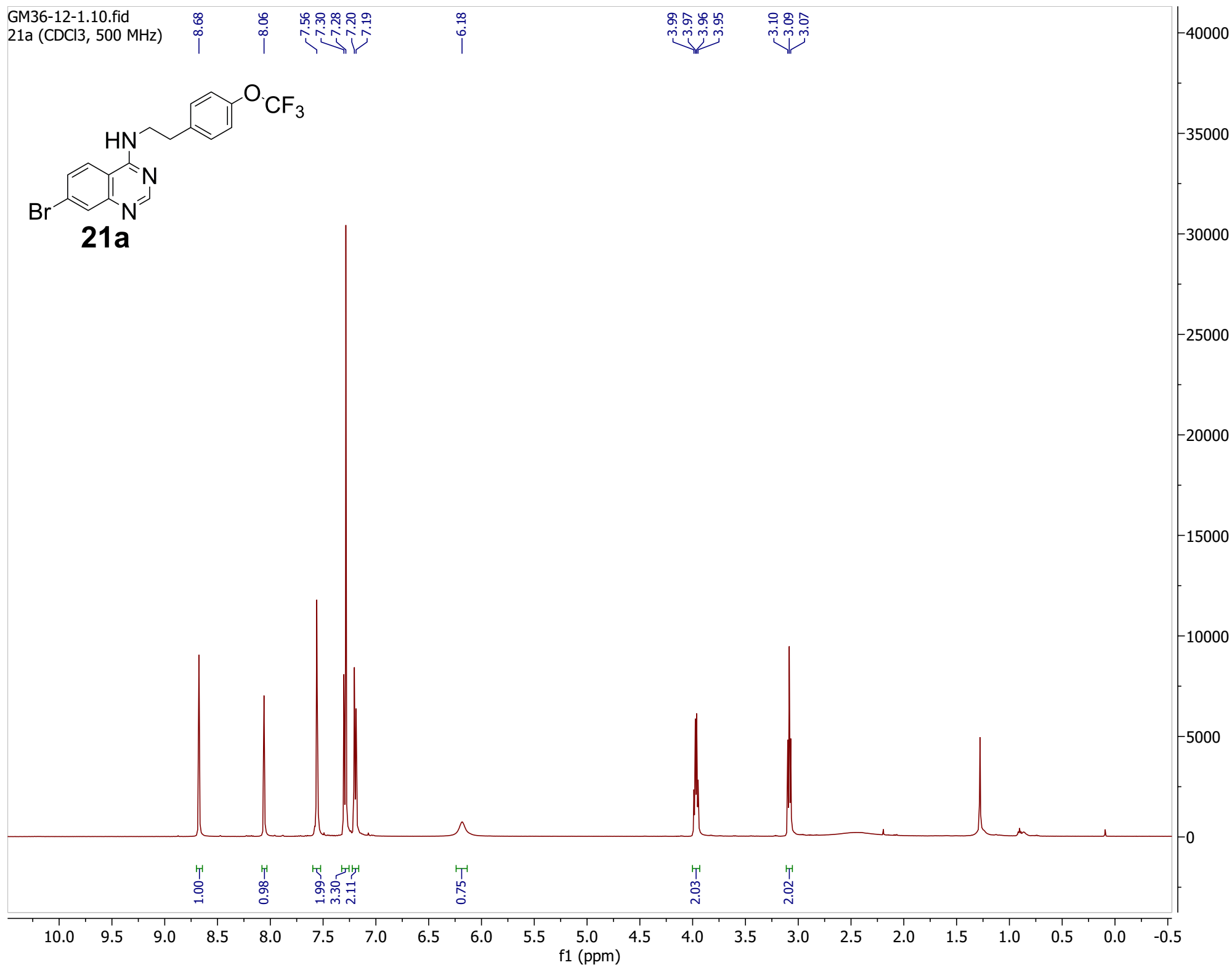
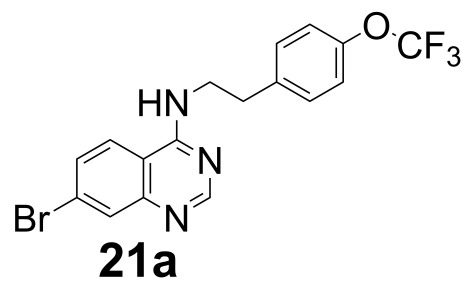
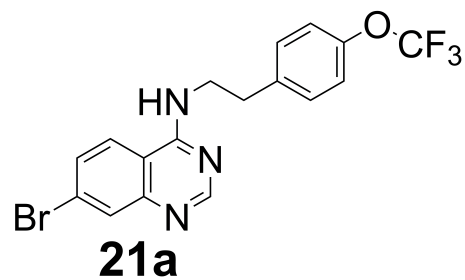


Figure S43 ¹H NMR Spectrum (CDCl₃, 500 MHz) of **21a**

GM36-12-1.11.fid
21a (CDCl₃, 125 MHz)



159.4
155.7
149.4
148.1
148.1
140.9
137.4
130.4
129.7
127.4
123.5
122.2
121.5
121.3
119.5
117.4
113.4

42.5
34.5

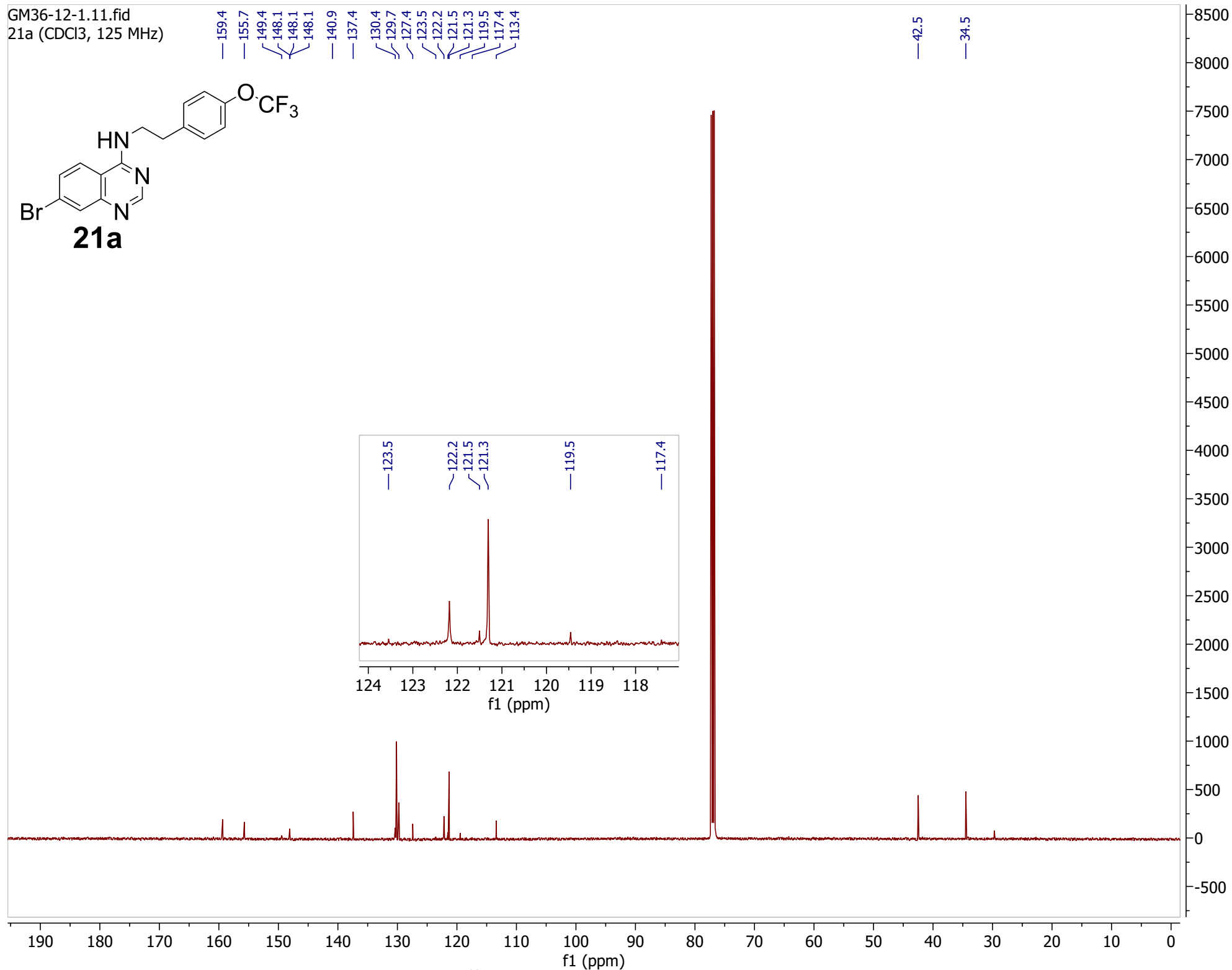
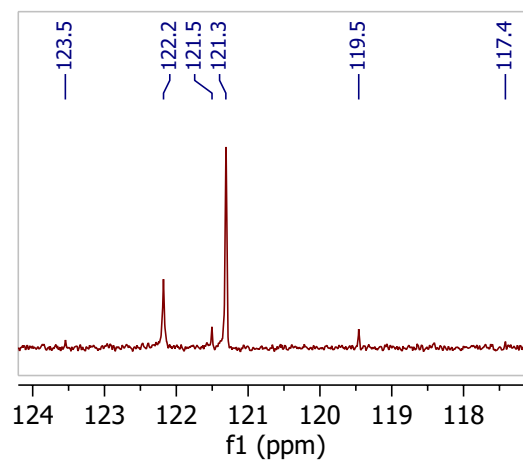


Figure S44 ¹³C NMR Spectrum (CDCl₃, 125 MHz) of **21a**

GM36-12-1.12.fid
21a (CDCl₃, 470 MHz)

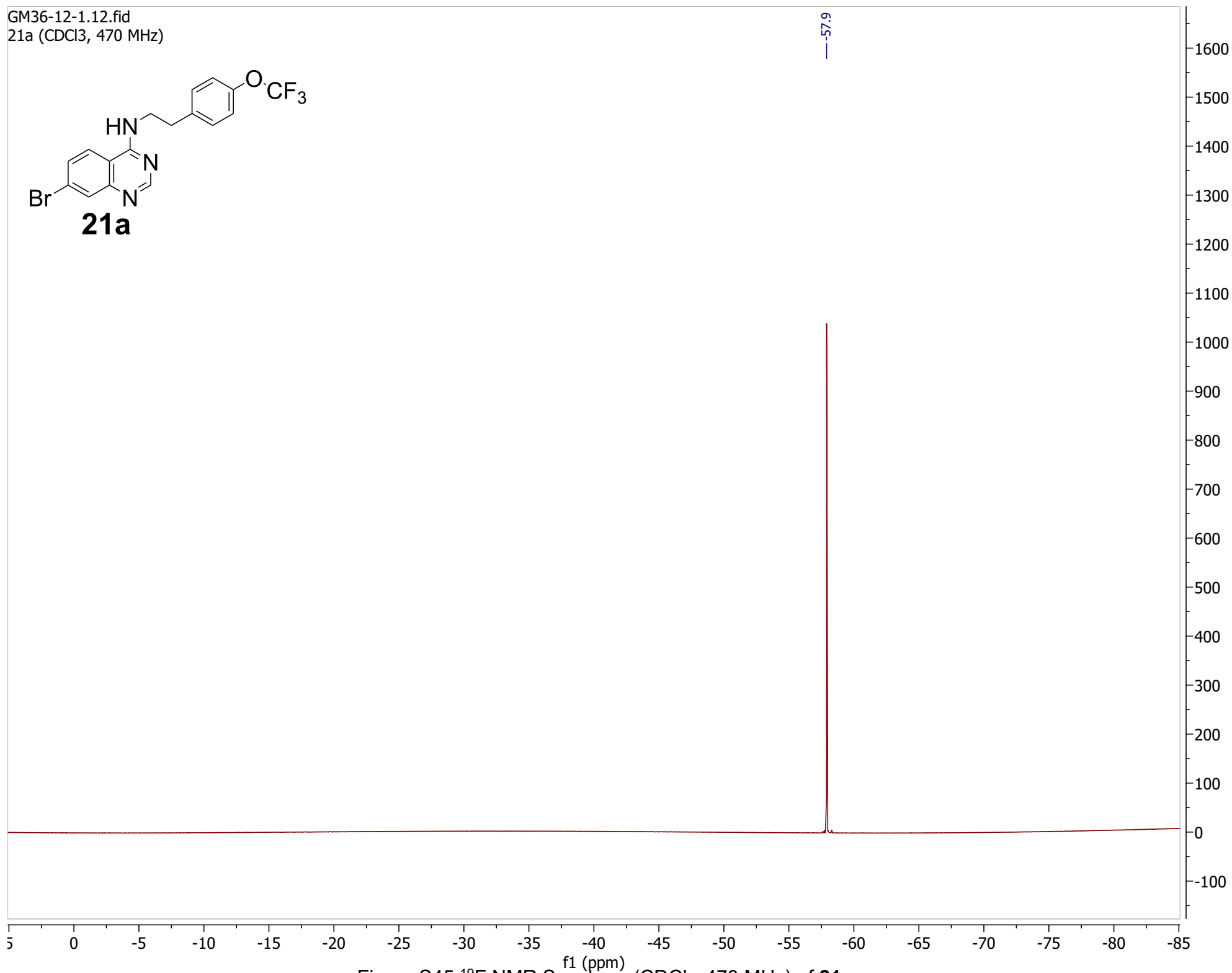
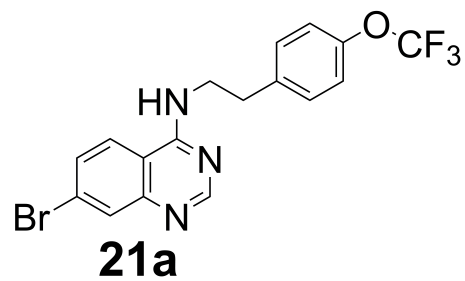
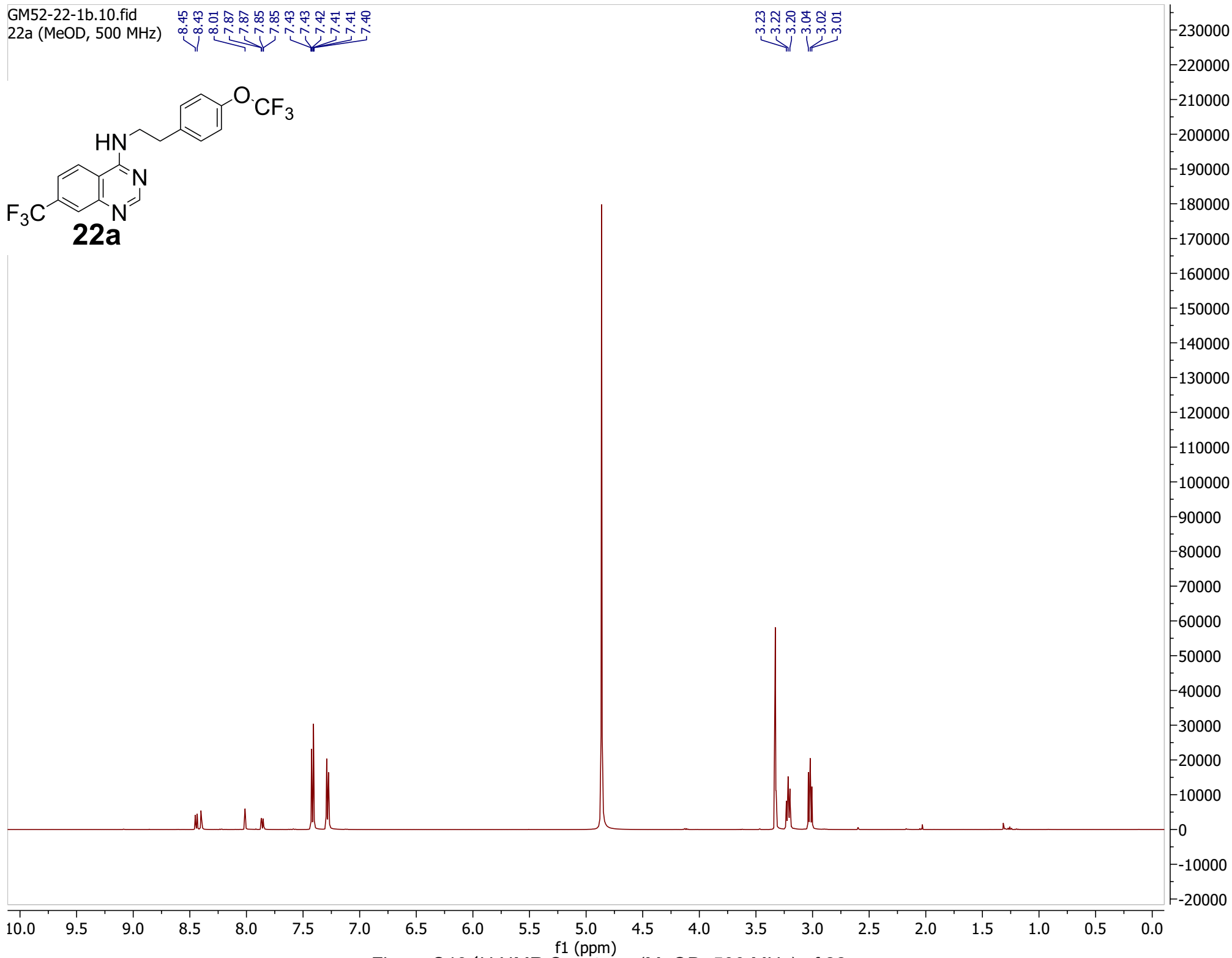
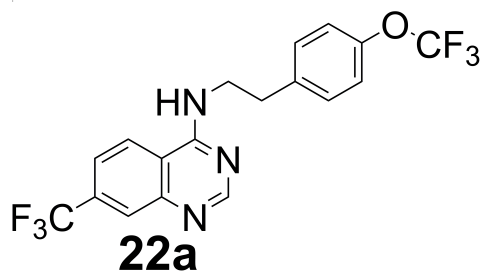


Figure S45 ¹⁹F NMR Spectrum (CDCl₃, 470 MHz) of **21a**

GM52-22-1b.10.fid
22a (MeOD, 500 MHz)

8.45
8.43
8.01
7.87
7.87
7.85
7.85
7.43
7.43
7.42
7.41
7.41
7.40

3.23
3.22
3.20
3.04
3.02
3.01



GM52-22-1b.11.fid
22a (MeOD, 125 MHz)

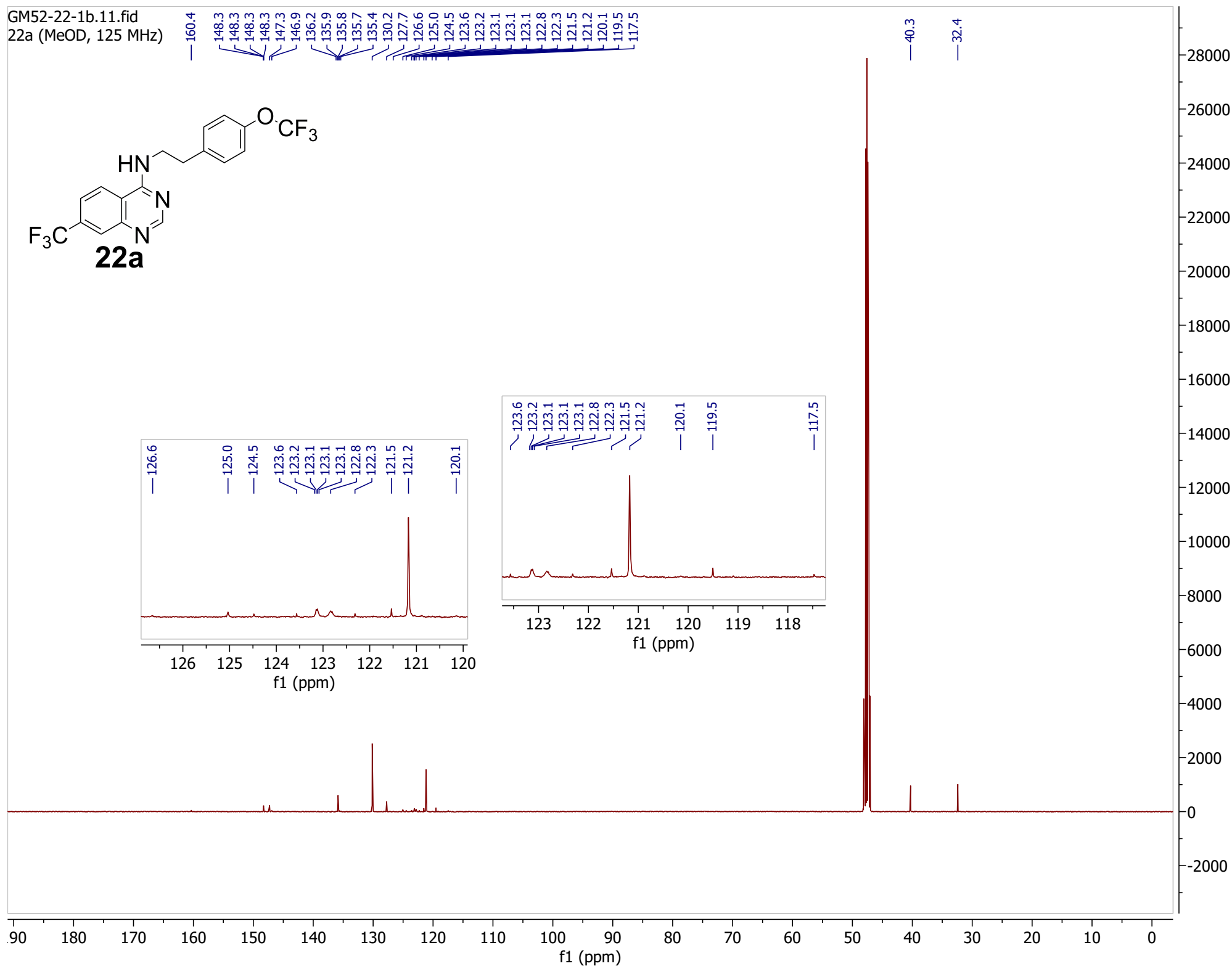
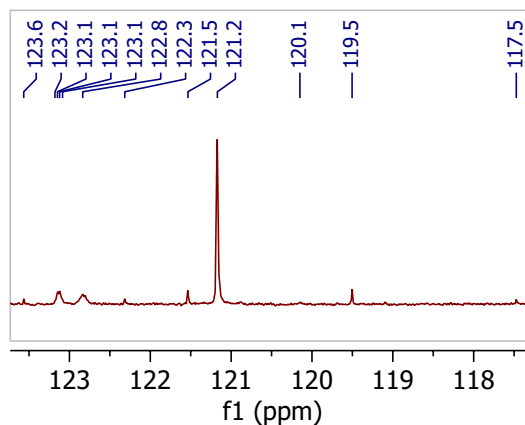
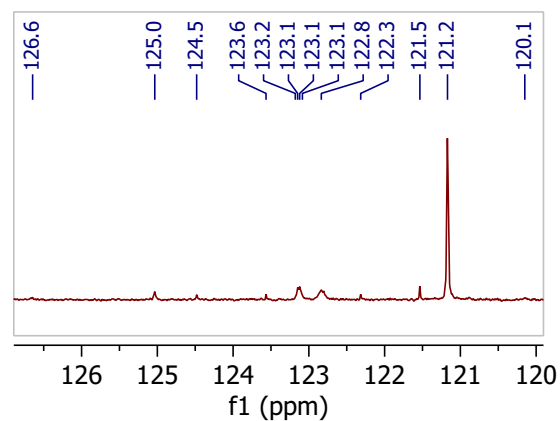
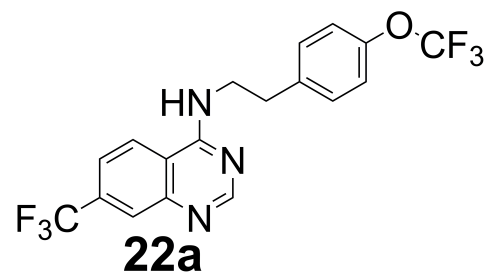


Figure S47 ^{13}C NMR Spectrum (MeOD, 125 MHz) of **22a**

GM52-22-1b.12.fid
22a (MeOD, 470 MHz)

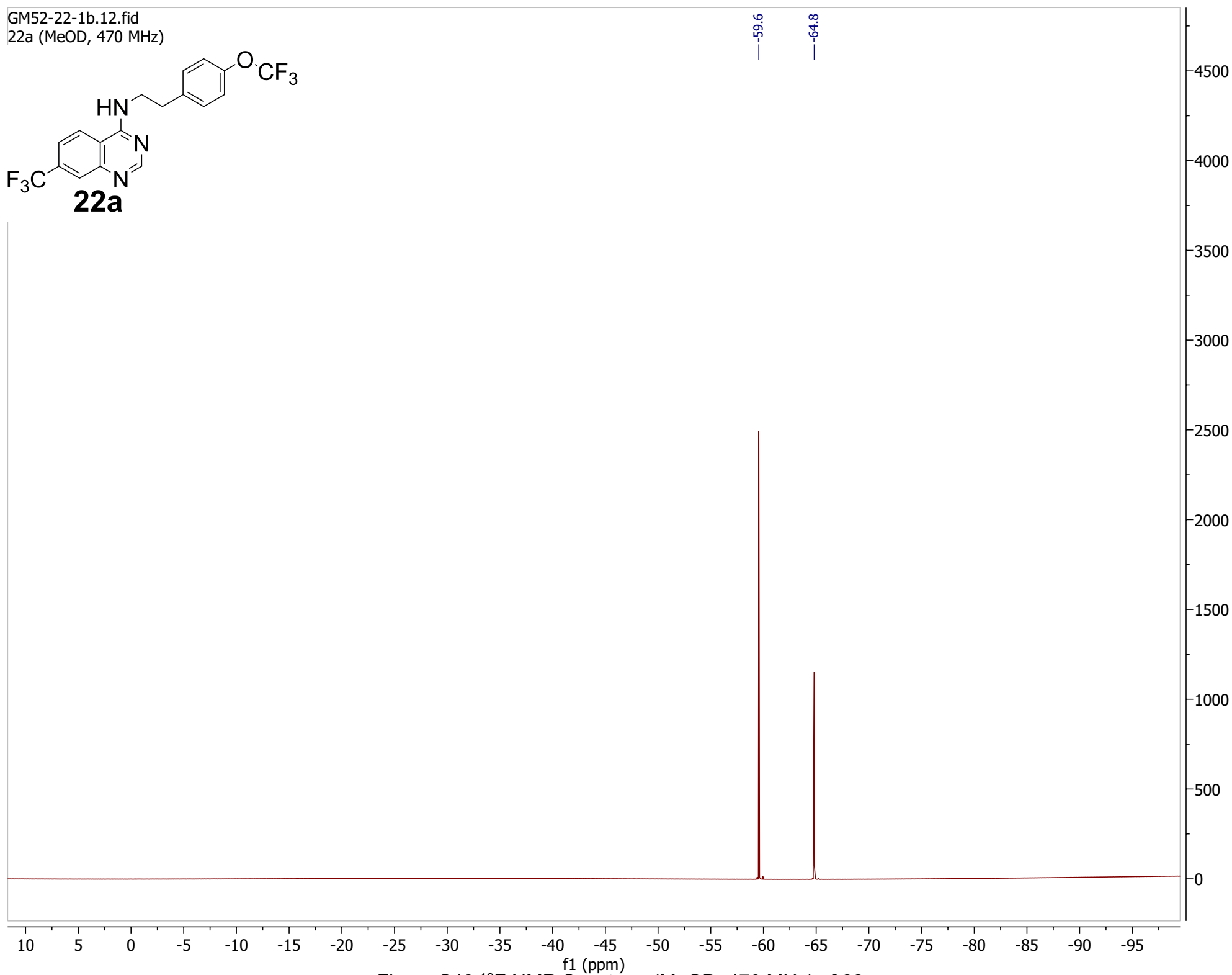
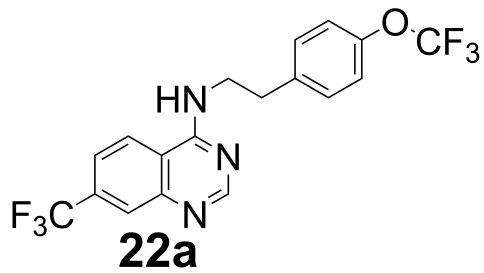


Figure S48 ^{19}F NMR Spectrum (MeOD, 470 MHz) of **22a**

SMH12-47-1.10.fid
23a (MeOD, 500 MHz)

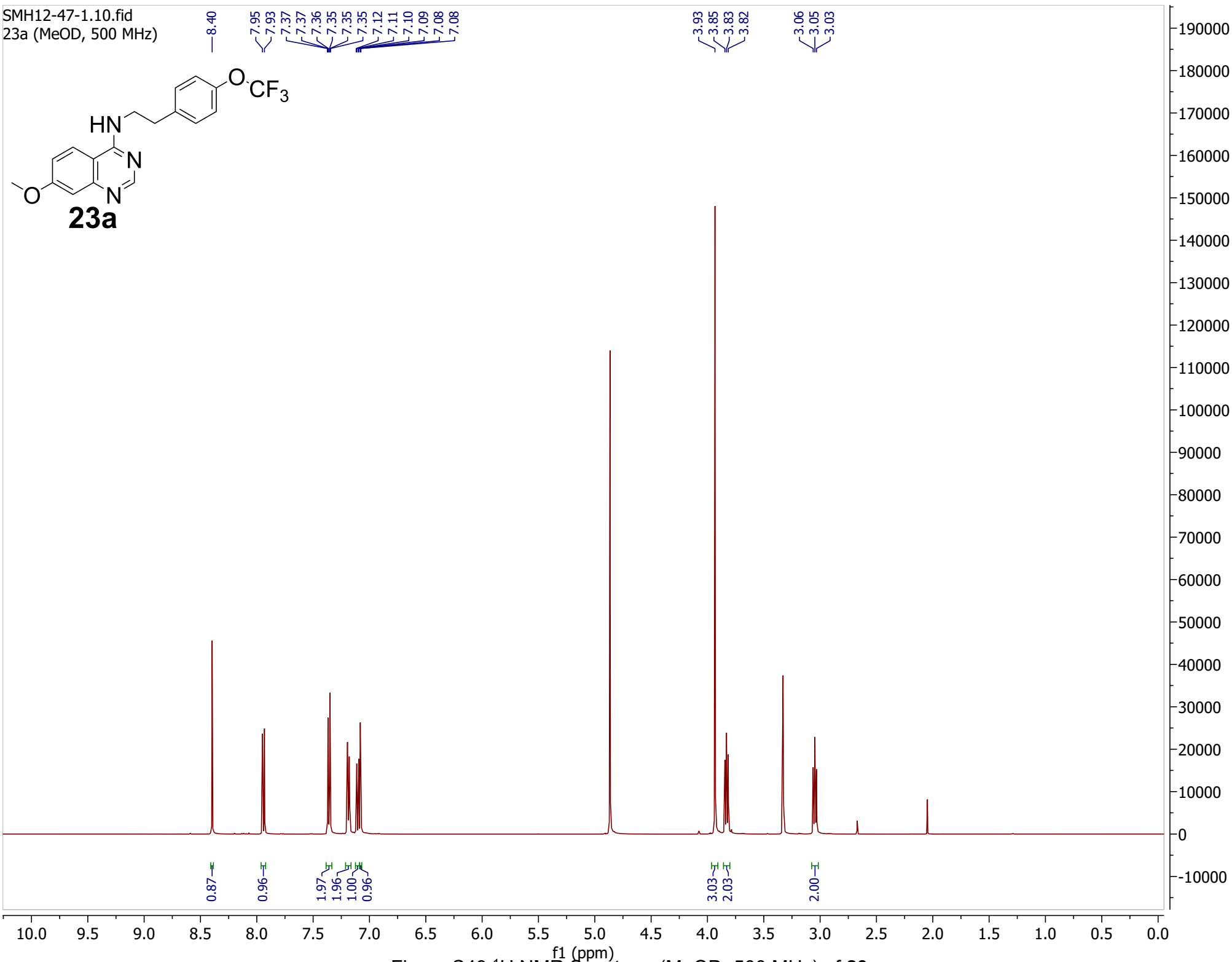


Figure S49 ^1H NMR Spectrum (MeOD, 500 MHz) of **23a**

SMH12-47-1.11.fid
23a (MeOD, 125 MHz)

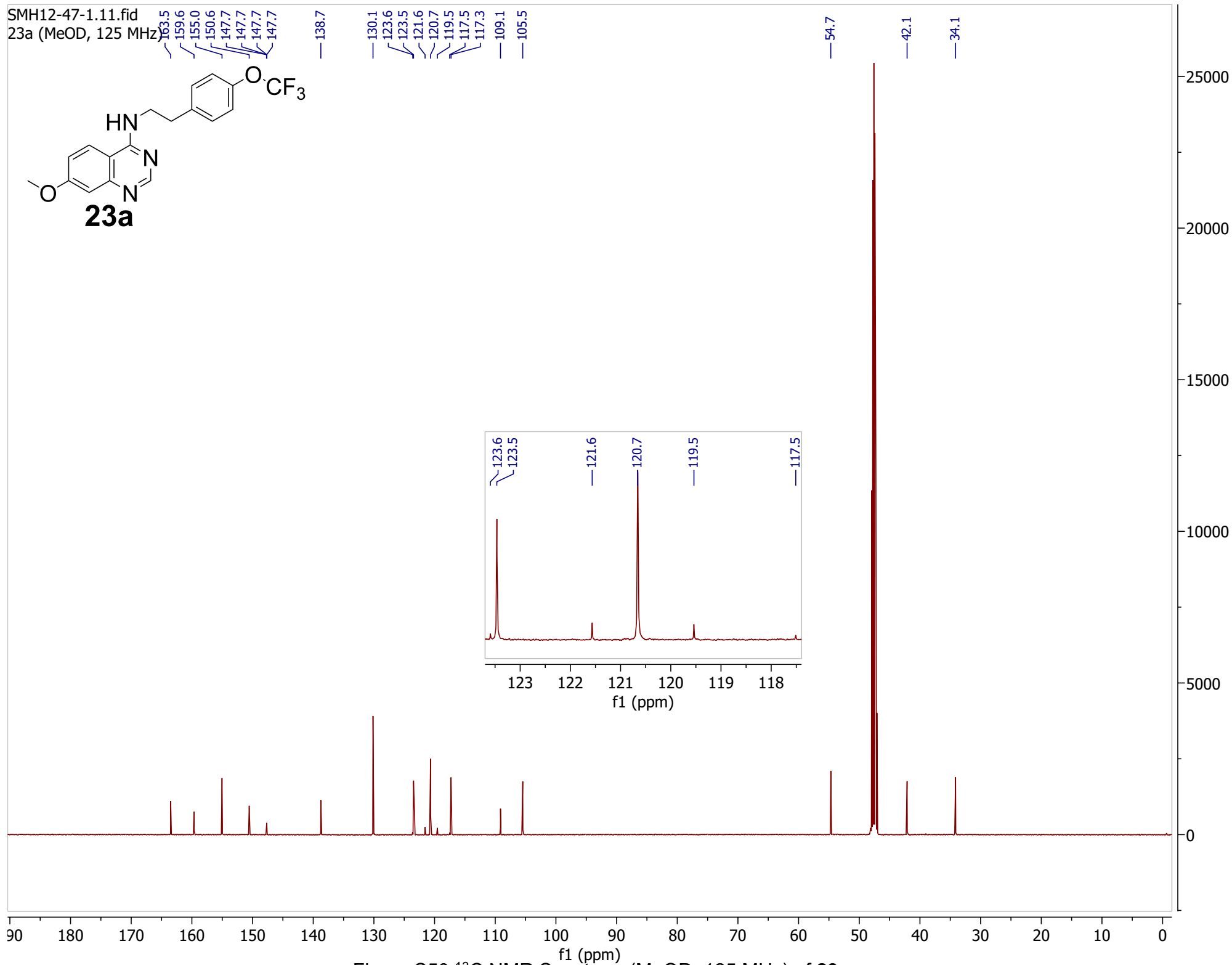
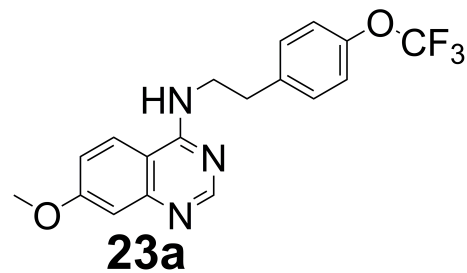


Figure S50 ¹³C NMR Spectrum (MeOD, 125 MHz) of **23a**

SMH12-47-1.12.fid
23a (MeOD, 470 MHz)

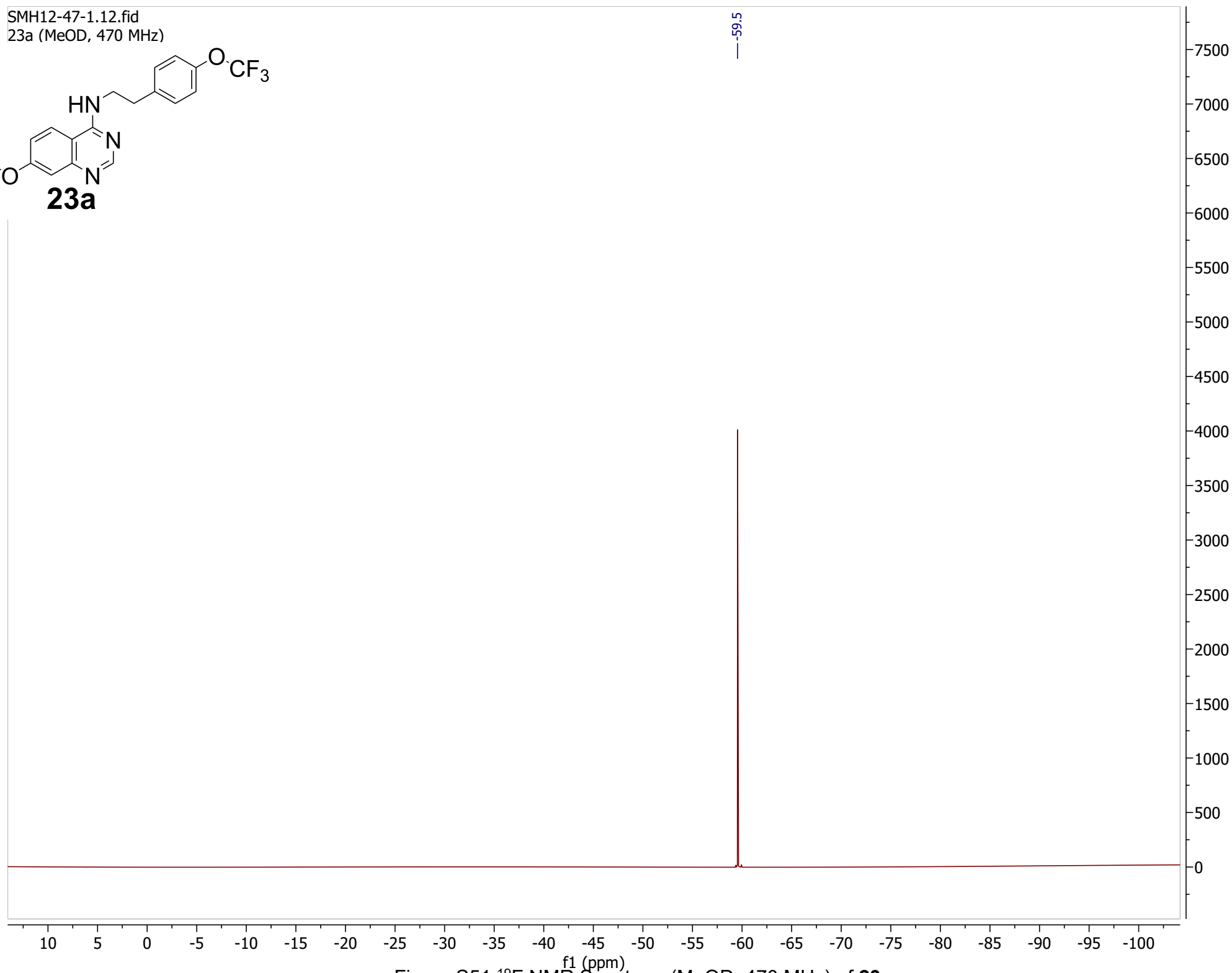
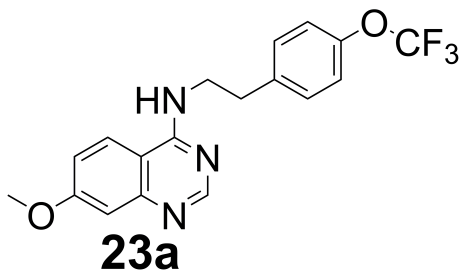


Figure S51 ^{19}F NMR Spectrum (MeOD, 470 MHz) of **23a**

GM34-75-2.10.fid
24a (CDCl₃, 500 MHz)

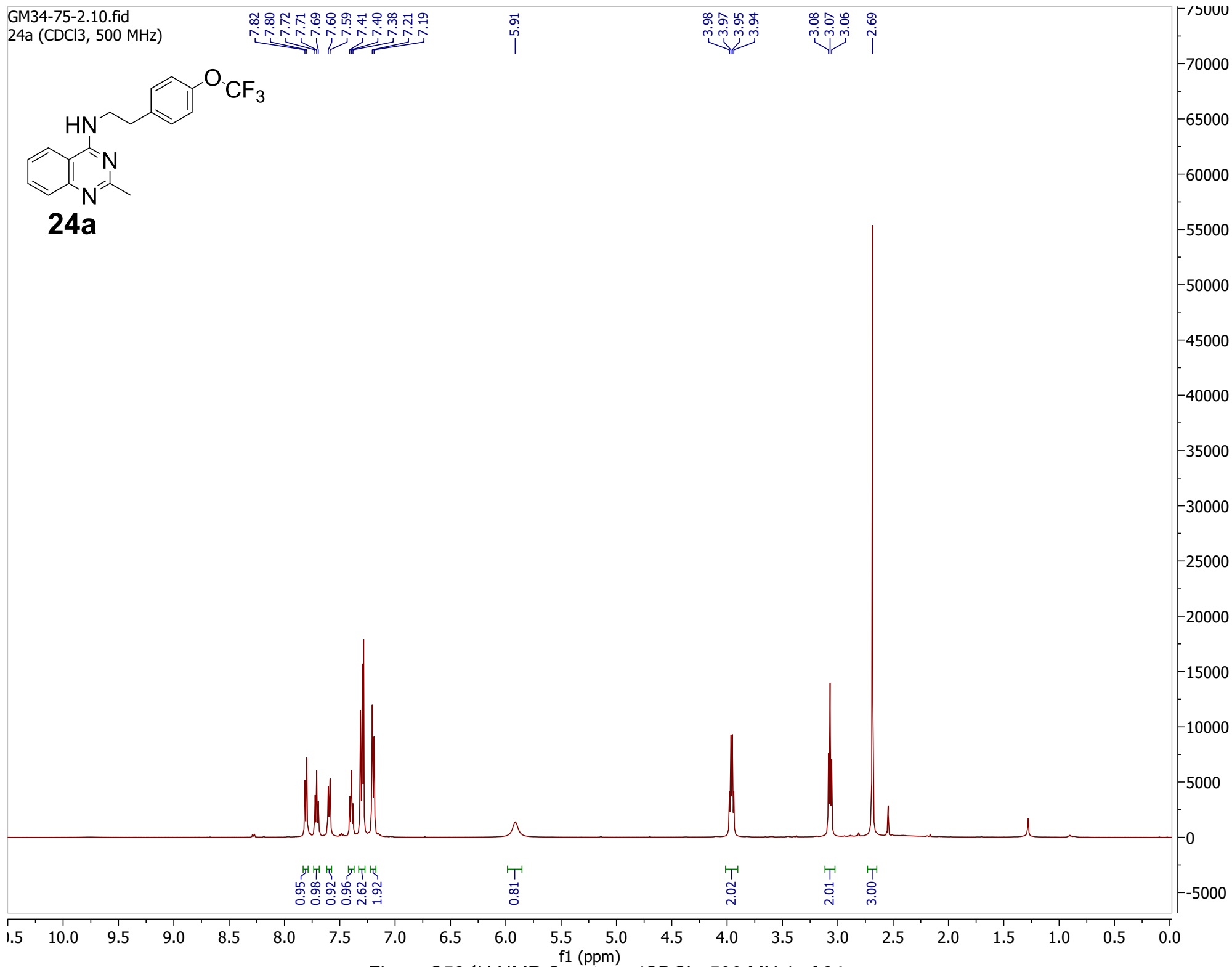
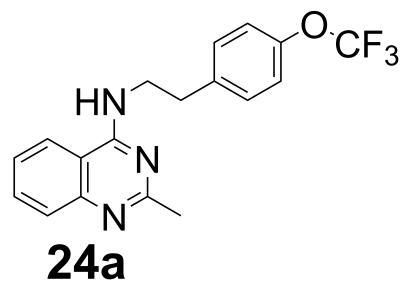
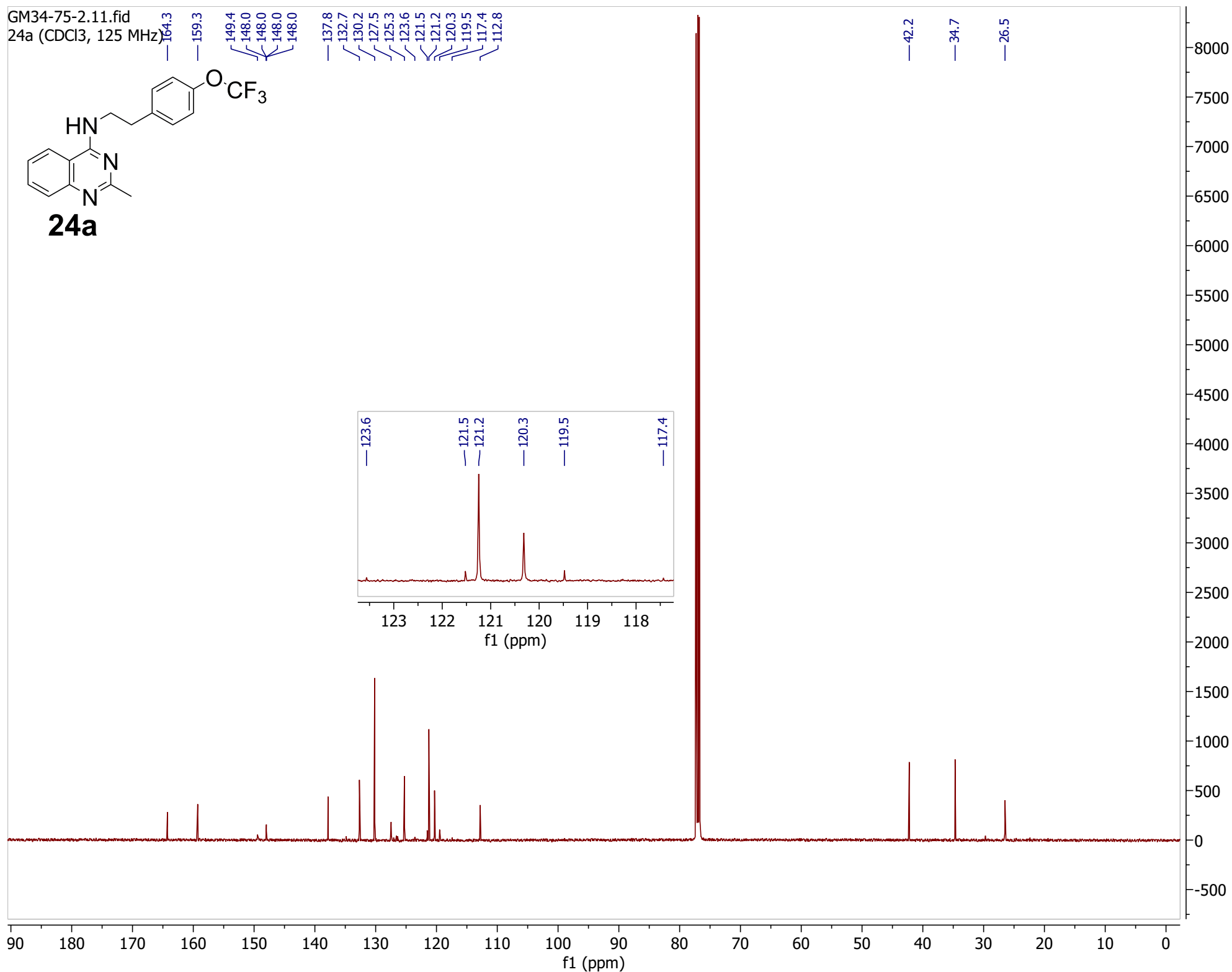
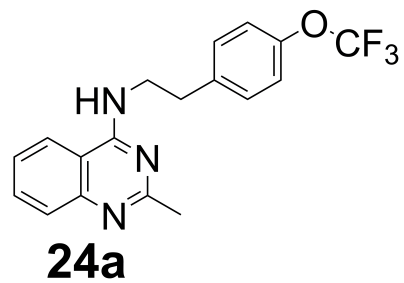


Figure S52 ¹H NMR Spectrum (CDCl₃, 500 MHz) of **24a**

GM34-75-2.11.fid

24a (CDCl₃, 125 MHz)Figure S53 ¹³C NMR Spectrum (CDCl₃, 125 MHz) of **24a**

GM34-75-2.12.fid
24a (CDCl₃, 470 MHz)

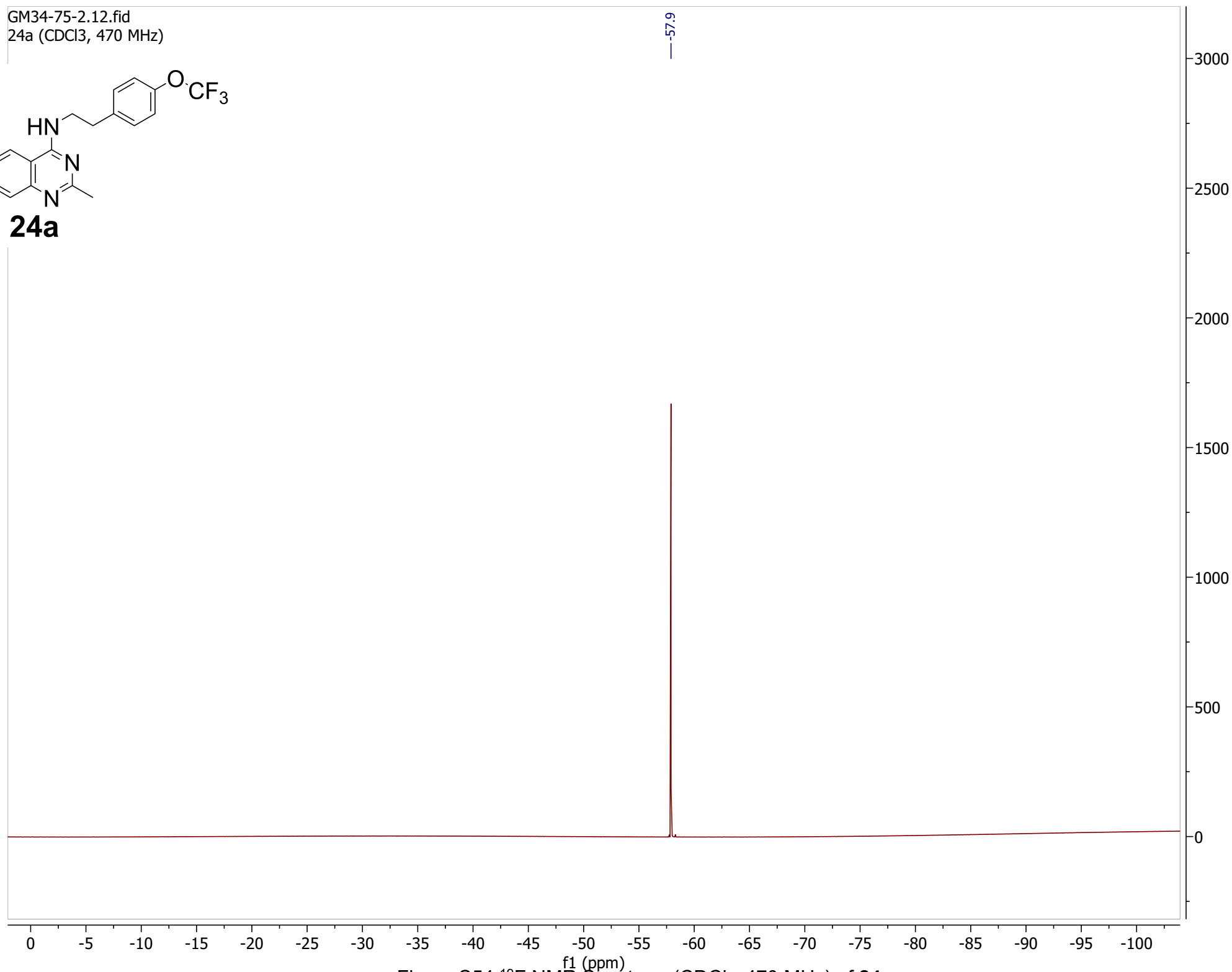
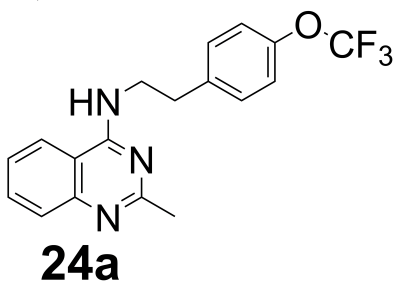


Figure S54 ¹⁹F NMR Spectrum (CDCl₃, 470 MHz) of **24a**

GM36-48-2.10.fid
25a (MeOD, 500 MHz)

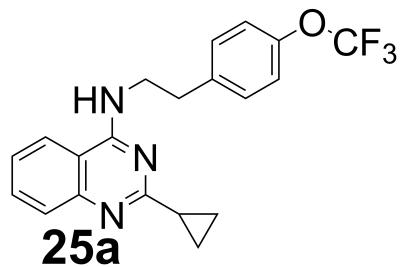


Figure S55 ^1H NMR Spectrum (MeOD, 500 MHz) of **25a**

GM36-48-2.11.fid
25a (MeOD, 125 MHz)

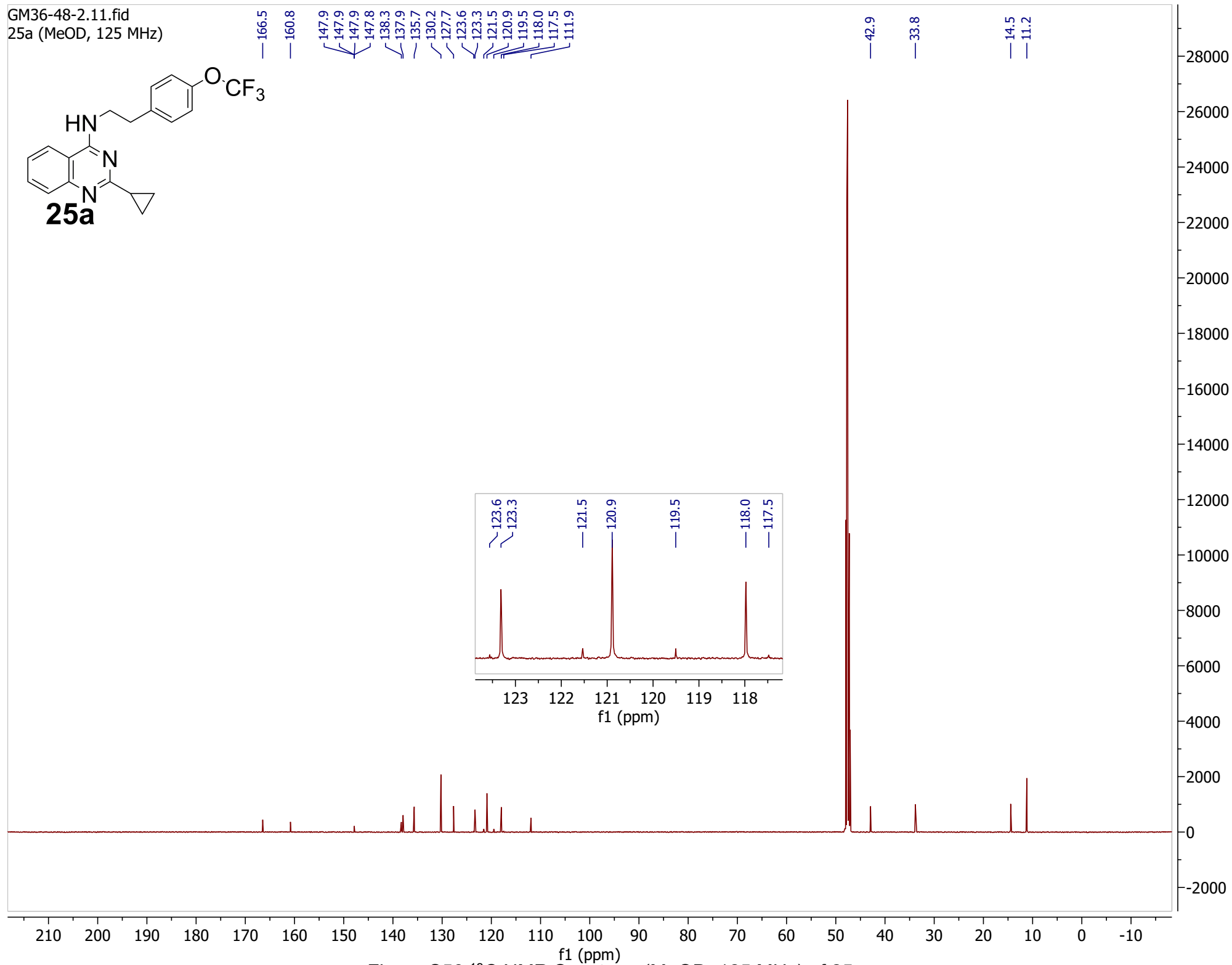
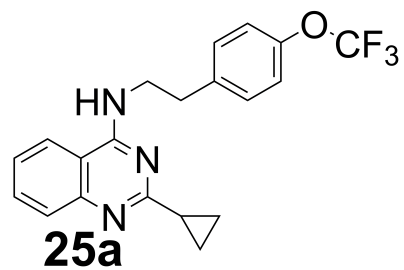


Figure S56 ^{13}C NMR Spectrum (MeOD, 125 MHz) of **25a**

GM36-48-2.12.fid
25a (MeOD, 470 MHz)

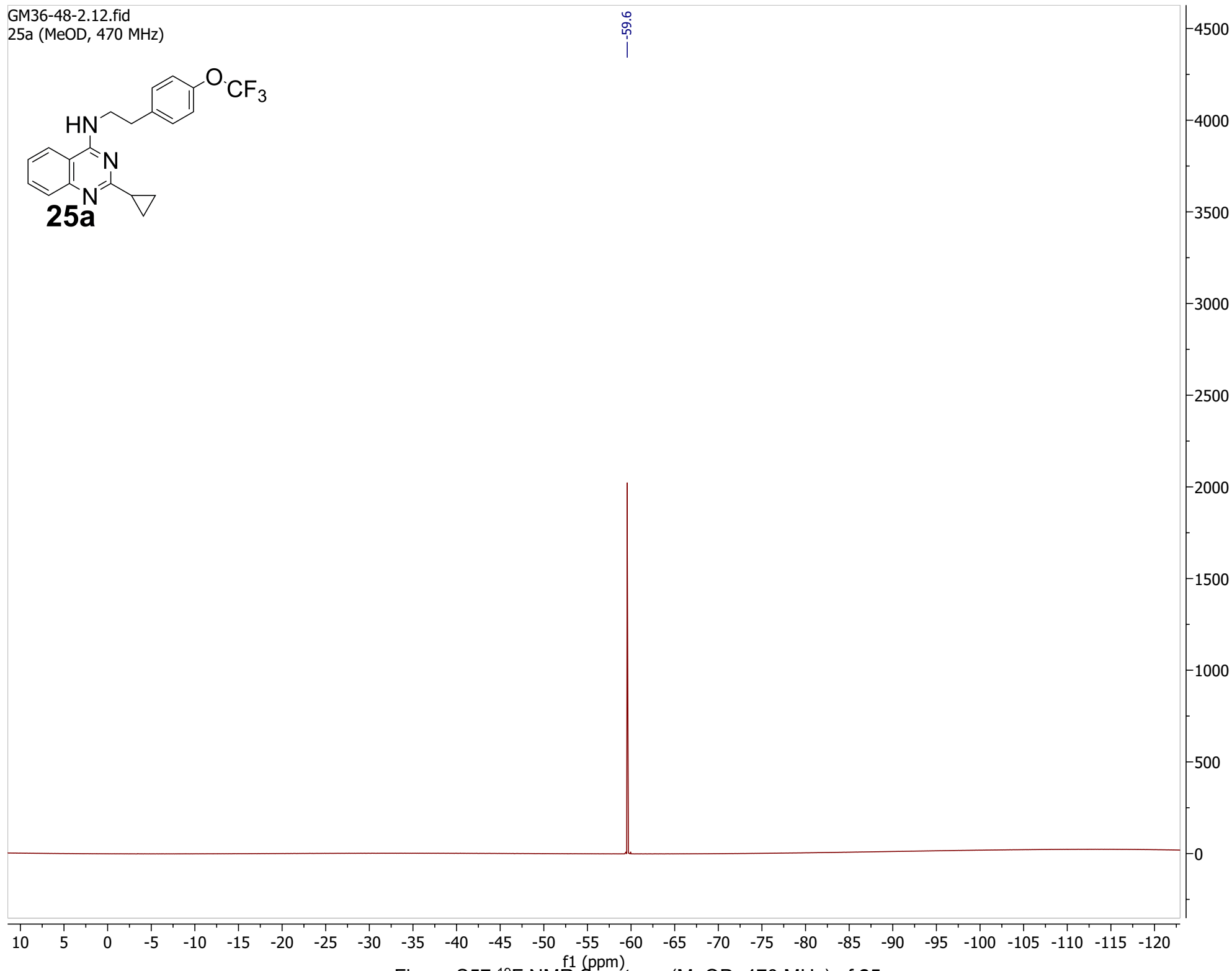
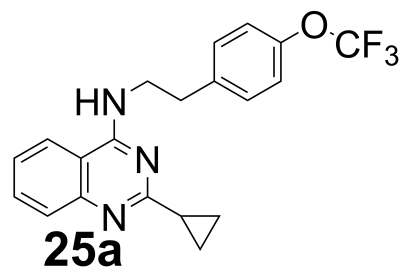
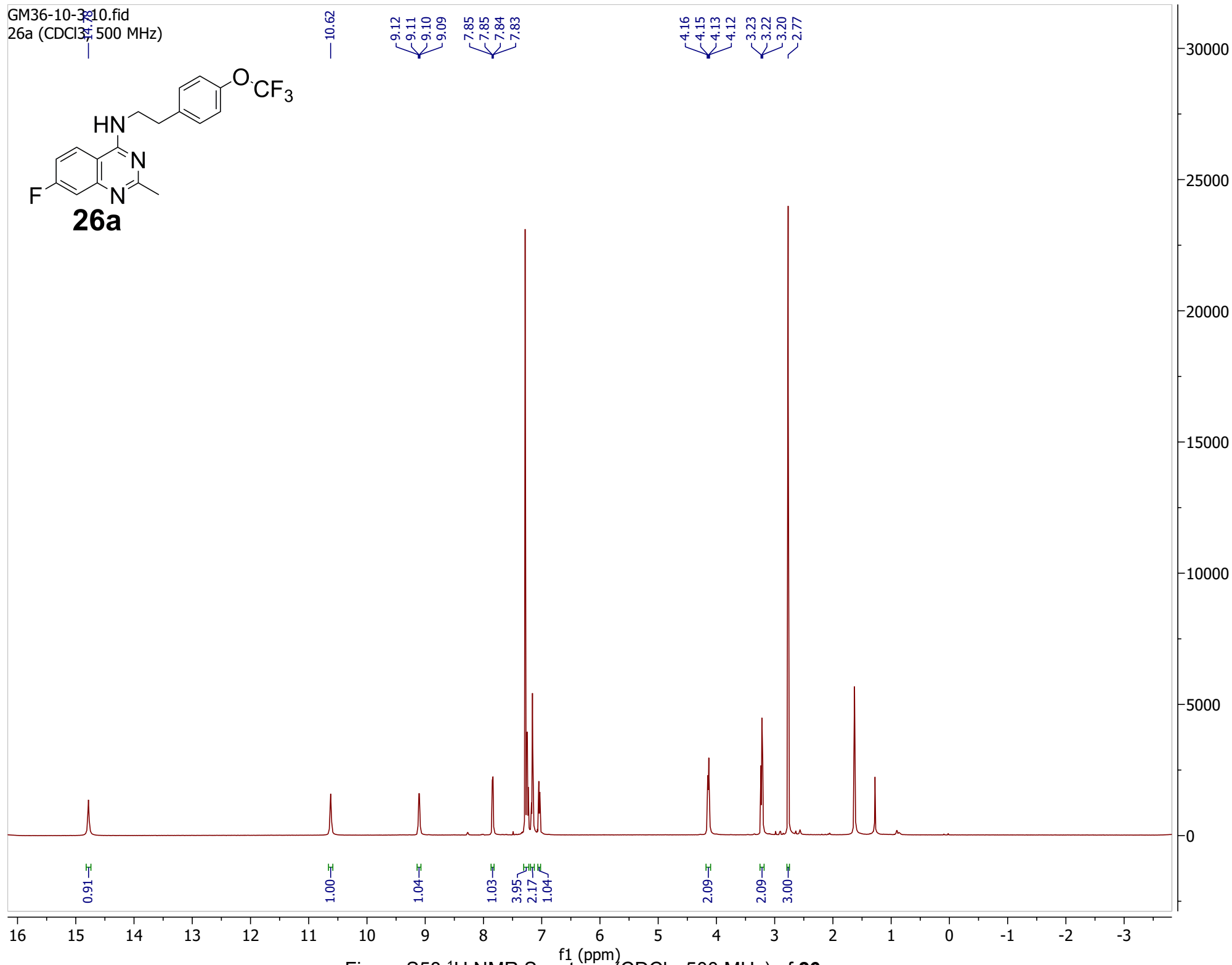
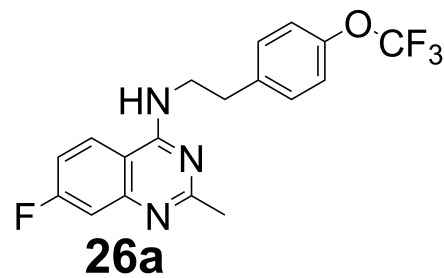
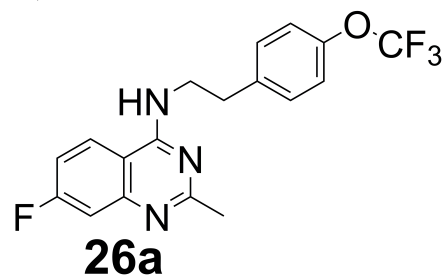


Figure S57 ^{19}F NMR Spectrum (MeOD, 470 MHz) of **25a**

GM36-10-310.fid
26a (CDCl₃, 500 MHz)



GM36-10-3.11.fid
26a (CDCl₃, 125 MHz)



167.2
165.1
162.0
160.0
149.3
149.3
140.7
140.5
140.4
129.8
128.8
128.7
127.4
123.4
121.4
119.4
119.1
117.3
117.0
116.8
108.6
104.8
104.6

43.1

34.6

22.4

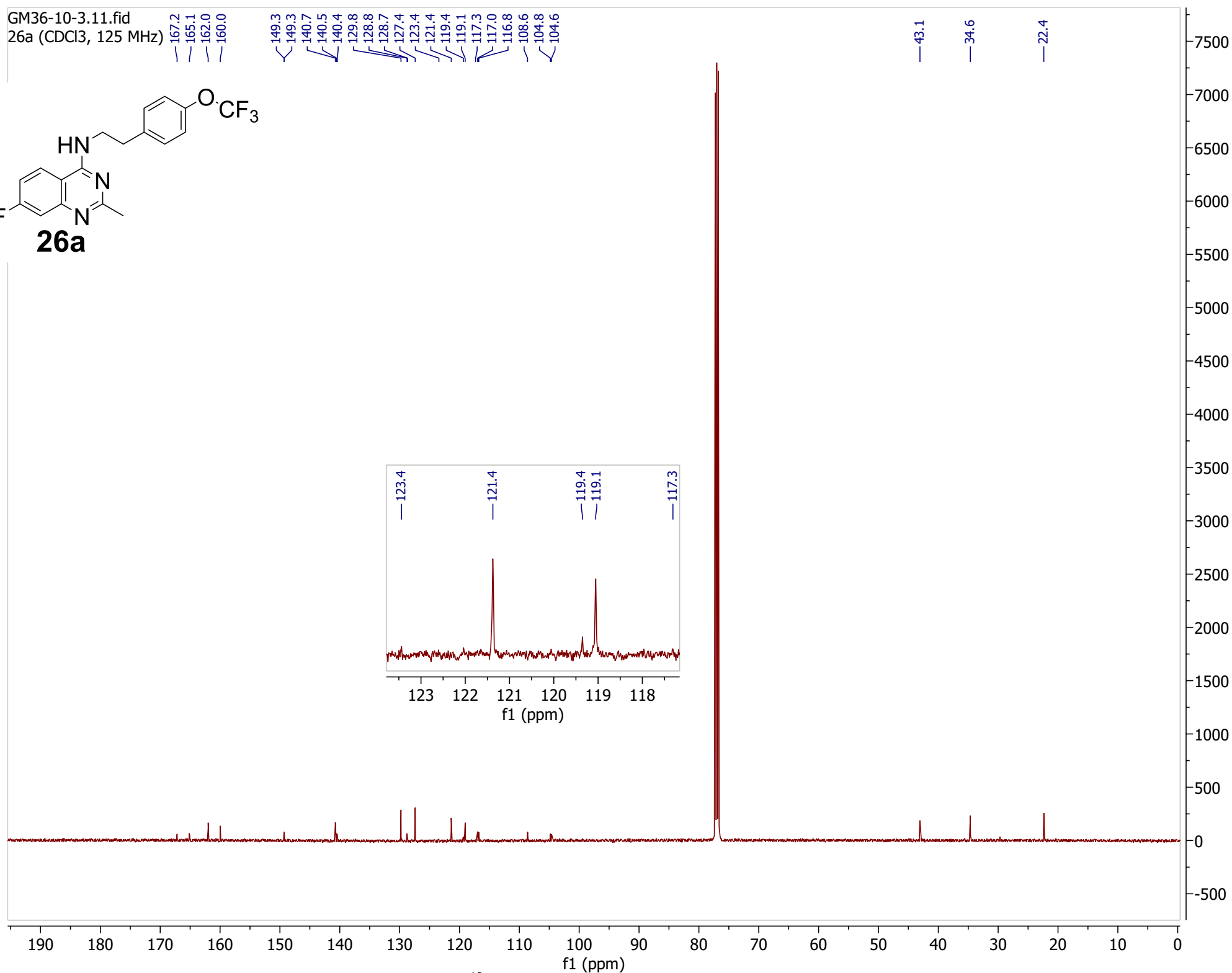
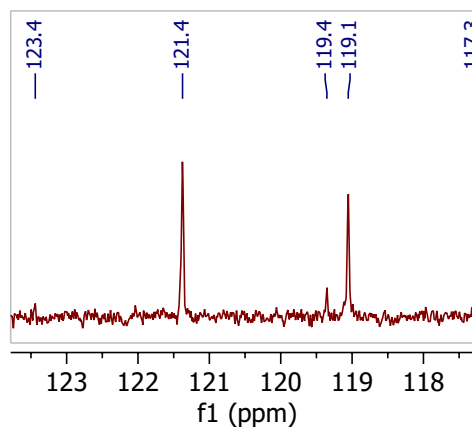


Figure S59 ¹³C NMR Spectrum (CDCl₃, 125 MHz) of **26a**

GM36-10-3.12.fid
26a (CDCl₃, 470 MHz)

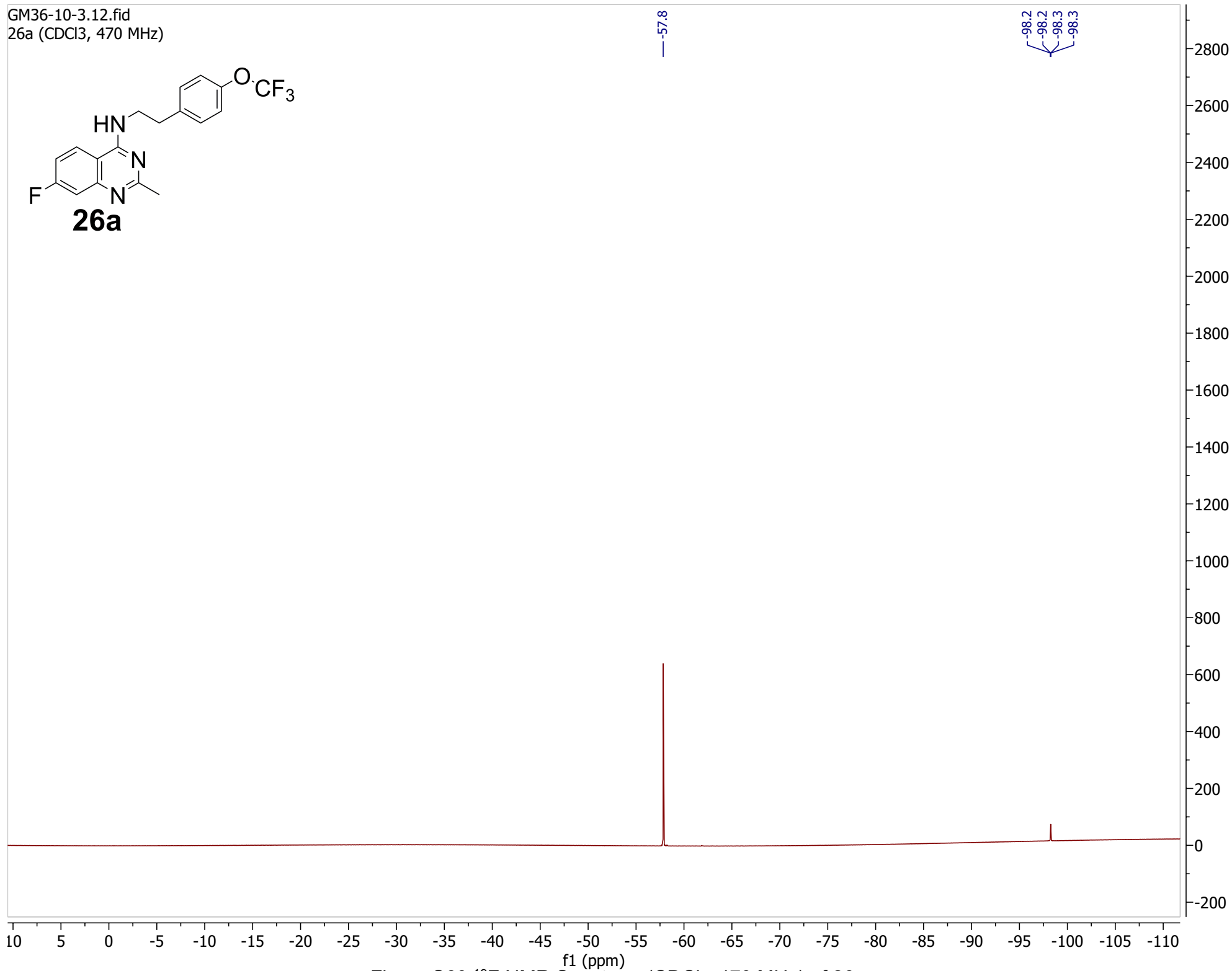
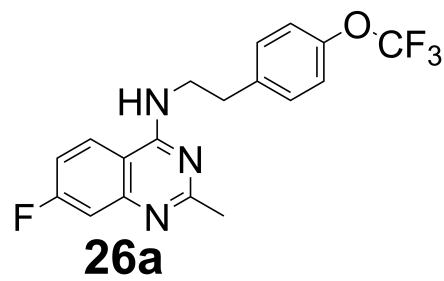
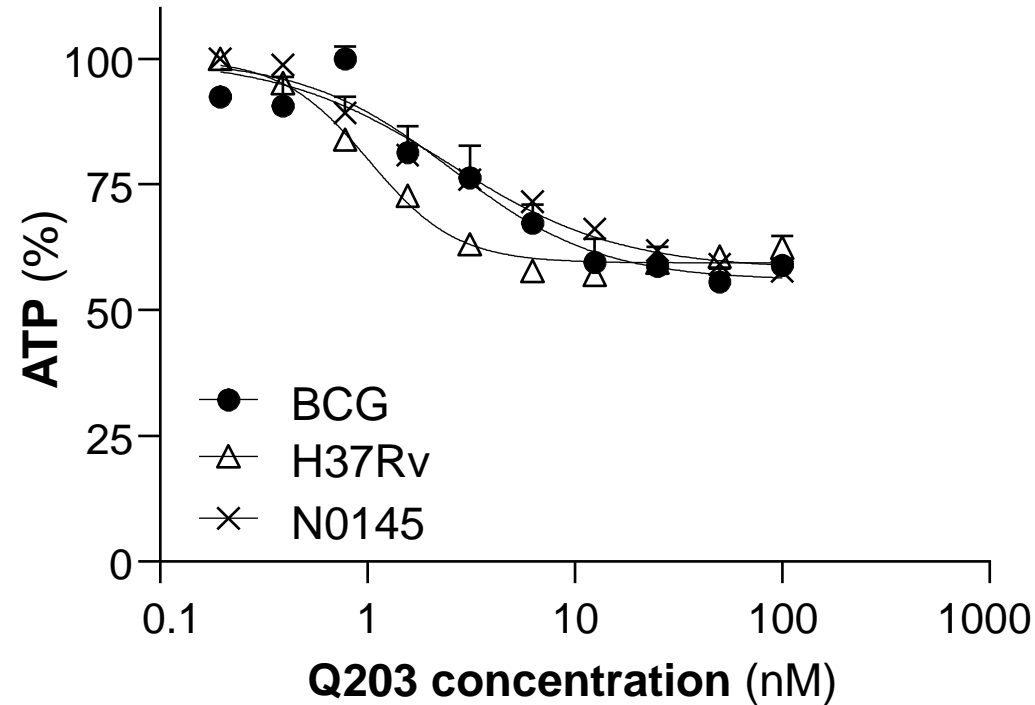


Figure S60 ¹⁹F NMR Spectrum (CDCl₃, 470 MHz) of **26a**



ATP dose response curves of Q203 in *M. bovis* BCG, *M. tuberculosis* H37Rv, and *M. tuberculosis* N0145. Q203 was tested in 10 points, two-fold serial dilution from a top concentration of 100 nM. ATP levels were measured after 15 hours of drug incubation. The ATP values were normalised to the untreated controls of each bacterial strain. Data are expressed as the mean \pm S.D. for each condition of a representative experiment. Q203 ATP IC₅₀ values were 2.6 nM for BCG, 1.0 nM for H37Rv, and 2.5 nM for N0145.

Figure S61 ATP dose response curves of Q203 in *M. bovis* BCG, *M. tuberculosis* H37Rv, and *M. tuberculosis* N0145