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SUPPORTING INFORMATION

Title: The First Proline-Catalyzed Friedlander Annulation: Regioselective Synthesis of 2-Substituted Quinoline Derivatives

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Ref. No.: O200800121

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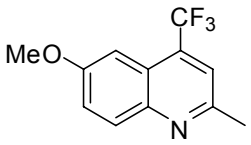
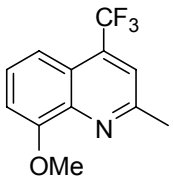
General information

All Commercially available reagents and solvents were used without further purification. Column chromatography was carried out on silica gel H (10 ± 40 mm). ^{1}H NMR spectra were recorded on 300 MHz and ^{13}C NMR spectra were recorded on 75 MHz. ^{19}F NMR spectra were recorded on 282 MHz using CF_3COOH (TFA) as an external standard. IR spectra were recorded on a FT-IR spectrometer and only major peaks are reported.

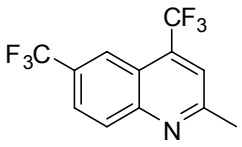
Characterization data of compounds 2b-2l and 3



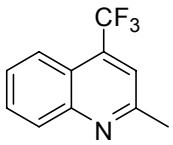
6-Methoxy-2-methyl-4-(trifluoromethyl)quinoline (2b): yellow solid, ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.00 (d, *J* = 9.3 Hz, 1H), 7.54 (s, 1H), 7.41 (dd, *J* = 9.0, 2.7 Hz, 1H), 7.32 (s, 1H), 3.95 (s, 3H), 2.76 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 158.0, 155.3, 144.6, 132.7, 130.7, 123.5, 122.5, 122.1, 118.9, 101.7, 55.3, 24.7; ^{19}F NMR (282 MHz, $CDCl_3$) δ = -62.8; MS (EI) m/e 241 (M^+, 100); IR (KBr) 3039, 1622, 1508, 1484, 1382, 1355, 1236; Anal. Calcd for $C_{12}H_{10}F_3NO$: C, 59.75; H, 4.18; N, 5.81. Found: C, 59.52; H, 4.28; N, 5.50.



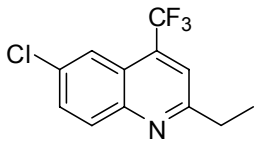
8-Methoxy-2-methyl-4-(trifluoromethyl)quinoline (2c): white solid, ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.63-7.67 (m, 2H), 7.53 (t, *J* =8.4 Hz, 1H), 7.12 (d, *J* = 7.5 Hz, 1H), 4.10 (s, 3H), 2.86 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 157.2, 154.9, 140.4, 134.1, 127.3, 123.3, 122.2, 119.4, 115.3, 108.2, 55.9, 25.5; ^{19}F NMR (282 MHz, $CDCl_3$) δ = -62.1; MS (EI) m/e (M^+, 100); IR (KBr) 3461, 1648, 1615, 1569, 1274, 1209; HRMS calcd. for $C_{12}H_{10}F_3NO^{+}$: 241.0714; found: 241.0708.



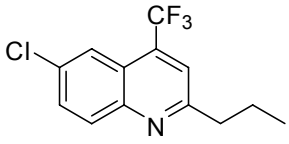
2-Methyl-4,6-bis(trifluoromethyl)quinoline (2d): white solid, ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.37 (s, 1H), 8.22 (d, *J* = 8.7 Hz, 1H), 7.95 (dd, *J* = 9.0, 1.8 Hz, 1H), 7.69 (s, 1H), 2.85 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 161.0, 149.5, 135.1, 130.7, 129.0, 125.8, 123.6, 122.9, 121.6, 120.5, 25.4; ^{19}F NMR (282 MHz, $CDCl_3$) δ = -61.8, -62.9; MS (EI) m/e 279 (M^+, 100); IR (KBr) 3072, 1622, 1479, 1319, 1284, 1264; HRMS calcd. for $C_{12}H_7F_6N^+$: 279.0483; found: 279.0492.



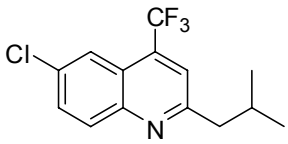
2-Methyl-4-(trifluoromethyl)quinoline (2e): white solid, ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.04-8.10 (m, 2H), 7.70-7.76 (m, 1H), 7.54-7.59 (m, 2H), 2.77 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 158.3, 148.6, 134.3, 130.1, 129.5, 127.2, 123.7, 123.4, 121.1, 118.9, 25.3; ^{19}F NMR (282 MHz, $CDCl_3$) δ = -62.0; MS (EI) m/e 211 (M^+, 67); IR (KBr) 1612, 1516, 1385, 1258.



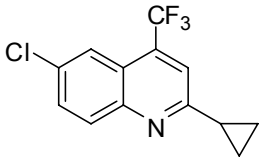
6-Chloro-2-ethyl-4-(trifluoromethyl)quinoline (2f): white solid, ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.06-8.09 (m, 2H), 7.71 (dd, *J* = 9.0, 2.4 Hz, 1H), 7.62 (s, 1H), 3.05 (q, *J* = 7.5 Hz, 2H), 1.42 (t, *J* =7.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 163.4, 146.9, 133.5, 133.2, 131.1, 130.8, 123.0, 122.7, 121.7, 118.6, 31.9, 13.2; ^{19}F NMR (282 MHz, $CDCl_3$) δ = -62.1; MS (EI) m/e 259 (M^+, 55.3); IR (KBr) 3074, 2982, 1950, 1797, 1748, 1618, 1560; Anal. Calcd for $C_{12}H_9ClF_3N$: C, 55.51; H, 3.49; N, 5.39. Found: C, 55.50; H, 3.62; N, 5.08.



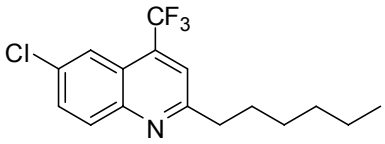
6-Chloro-2-propyl-4-(trifluoromethyl)quinoline (2g): white solid, ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.05-8.08 (m, 2H), 7.71 (dd, *J* = 9.3, 2.7 Hz, 1H), 7.60 (s, 1H), 3.00 (t, *J* = 7.5 Hz, 2H), 1.86 (m, 2H), 1.03 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 162.4, 146.9, 133.4, 133.2, 131.1, 130.9, 123.1, 122.7, 121.8, 119.0, 40.9, 22.6, 13.7; ^{19}F NMR (282 MHz, $CDCl_3$) δ = -62.2; MS (EI) m/e 271 (M^+, 62); IR (KBr) 2973, 1615, 1560, 1497; Anal. Calcd for $C_{13}H_{11}ClF_3N$: C, 57.05; H, 4.05; N, 5.12. Found: C, 57.29; H, 4.30; N, 4.92.



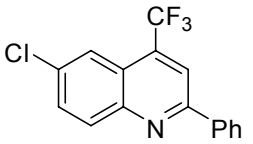
6-Chloro-2-isobutyl-4-(trifluoromethyl)quinoline (2h): white solid, ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.06-8.09 (m, 2H), 7.71 (dd, *J* = 9.0, 2.1 Hz, 1H), 7.56 (s, 1H), 2.89 (d, *J* = 7.2 Hz, 2H), 2.23 (m, 1H), 1.00 (s, 3H), 0.98 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 161.9, 146.9, 133.1, 133.0, 131.2, 130.9, 123.0, 122.7, 121.8, 119.5, 47.9, 29.1, 22.2;^{19}F NMR (282 MHz, $CDCl_3$) δ = -62.1; MS (EI) m/e 287 (M^+, 1.25); IR (KBr) 3072, 2959, 1609, 1559, 1494; Anal. Calcd for $C_{14}H_{13}ClF_3N$: C, 58.44; H, 4.55; N, 4.87. Found: C, 58.24; H, 4.59; N, 4.42.



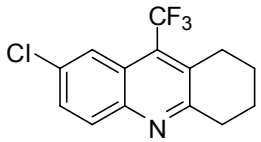
6-Chloro-2-cyclopropyl-4-(trifluoromethyl)quinoline (2i):[1] white solid, mp 62.1-63.9 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.02-7.99 (m, 1H), 7.97 (d, *J* = 9.0 Hz, 1H), 7.66 (dd, *J* = 9.0, 2.1 Hz, 1H), 7.54 (s, 1H), 2.25 (m, 1H), 1.20-1.26 (m, 2H), 1.12-1.18 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 163.1, 147.2, 132.9, 132.4, 130.8, 130.6, 123.0, 122.7, 121.3, 117.9, 17.9, 11.0; ^{19}F NMR (282 MHz, $CDCl_3$) δ = -62.2; IR (KBr) 3014, 1919, 1617, 1560, 1496.



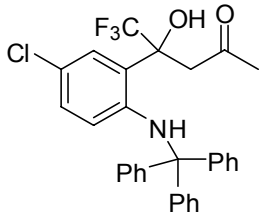
6-Chloro-2-hexyl-4-(trifluoromethyl)quinoline (2j): colorless oil, ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.05-8.08 (m, 2H), 7.71 (dd, *J* =9.0, 2.4 Hz, 1H), 7.60 (s, 1H), 3.00 (t, *J* = 7.5 Hz, 2H), 1.82 (m, 2H), 1.25-1.44 (m, 6H), 0.88 (t, *J* = 6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 162.6, 146.9, 133.4, 133.2, 131.1, 130.8, 123.0, 122.7, 121.8, 119.0, 39.0, 31.4, 29.5, 29.3, 28.9, 22.3, 13.8; ^{19}F NMR (282 MHz, $CDCl_3$) δ = -62.1; MS (EI) m/e 315 (M^+, 1.77); IR (KBr) 2959, 2930, 2860, 1614, 1561, 1496; HRMS calcd. for $C_{16}H_{18}ClF_3N^+$: 316.10743; found: 316.10735.



6-Chloro-2-phenyl-4-(trifluoromethyl)quinoline (2k)[1]: white solid, mp 116.6-118.4 °C ; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.17-8.22 (m, 4H), 8.11 (s, 1H), 7.76 (d, *J* = 8.7 Hz, 1H), 7.52-7.59 (m, 3H); ^{19}F NMR (282 MHz, $CDCl_3$) δ = -62.1; MS (EI) m/e 307 (M^+, 100); IR (KBr) 2923, 1611, 1550, 1492.

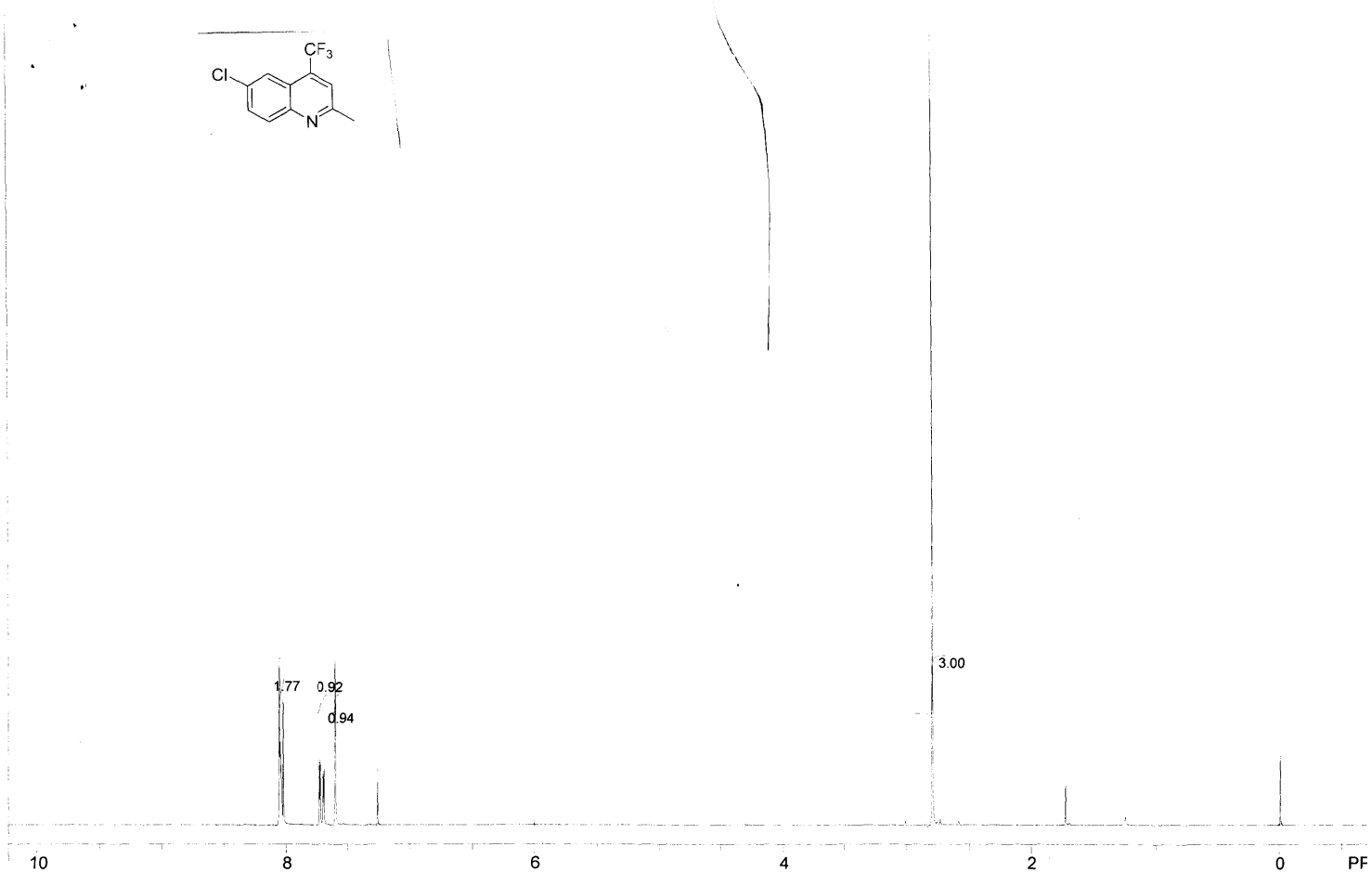


7-Chloro-9-(trifluoromethyl)-1,2,3,4-tetrahydroacridine (2l): yellow solid, ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.13 (m, 1H), 7.95 (d, *J* = 9.3 Hz, 1H), 7.62 (dd, *J* = 9.0, 2.1 Hz, 1H), 3.15-3.21 (m, 4H), 1.87-1.99 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 159.7, 144.8, 132.9, 131.5, 130.6, 130.2, 129.8, 126.6, 122.9, 122.9, 34.3, 27.07, 22.3, 21.6; ^{19}F NMR (282 MHz, $CDCl_3$) δ = -52.8; MS (EI) m/e 285 (M^+, 100); IR(KBr) 2938, 2866, 1606, 1568, 1487; Anal. Calcd for $C_{14}H_{11}ClF_3N$: C, 58.86; H, 3.88; N, 4.90. Found: C, 58.59; H, 4.09; N, 4.59.



4-(5-Chloro-2-(tritylamino)phenyl)-5,5,5-trifluoro-4-hydroxypentan-2-one (3): yellow solid, ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.12 (s, 1H), 7.34-7.17 (m, 15H), 6.87 (d, *J* = 2.1 Hz, 1H), 6.63 (dd, *J* = 8.7, 2.1 Hz, 1H), 6.49 (s, 1H), 6.08 (d, *J* = 8.7 Hz, 1H), 3.47 (d, *J* = 17.4 Hz, 1H), 3.18 (d, *J* = 17.4 Hz, 1H), 2.32 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 210.1, 145.5, 128.9, 128.3, 128.0, 127.89, 127.87, 127.0, 126.85, 126.83, 126.7, 120.0, 119.96, 118.8, 79.3, 71.2, 44.6, 32.4.

^{1}H NMR and ^{13}C NMR spectrum of compounds 2a-2l and 3



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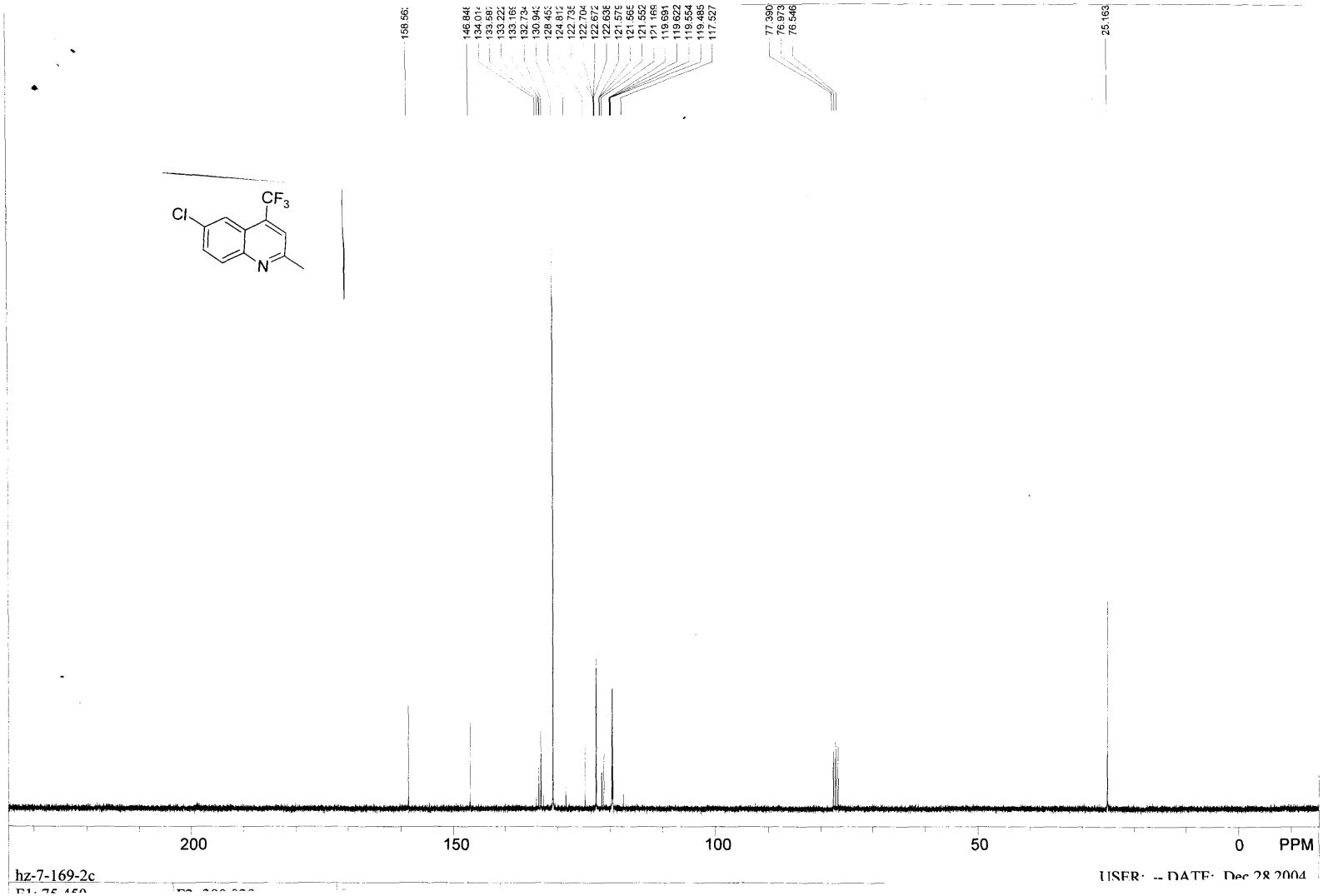
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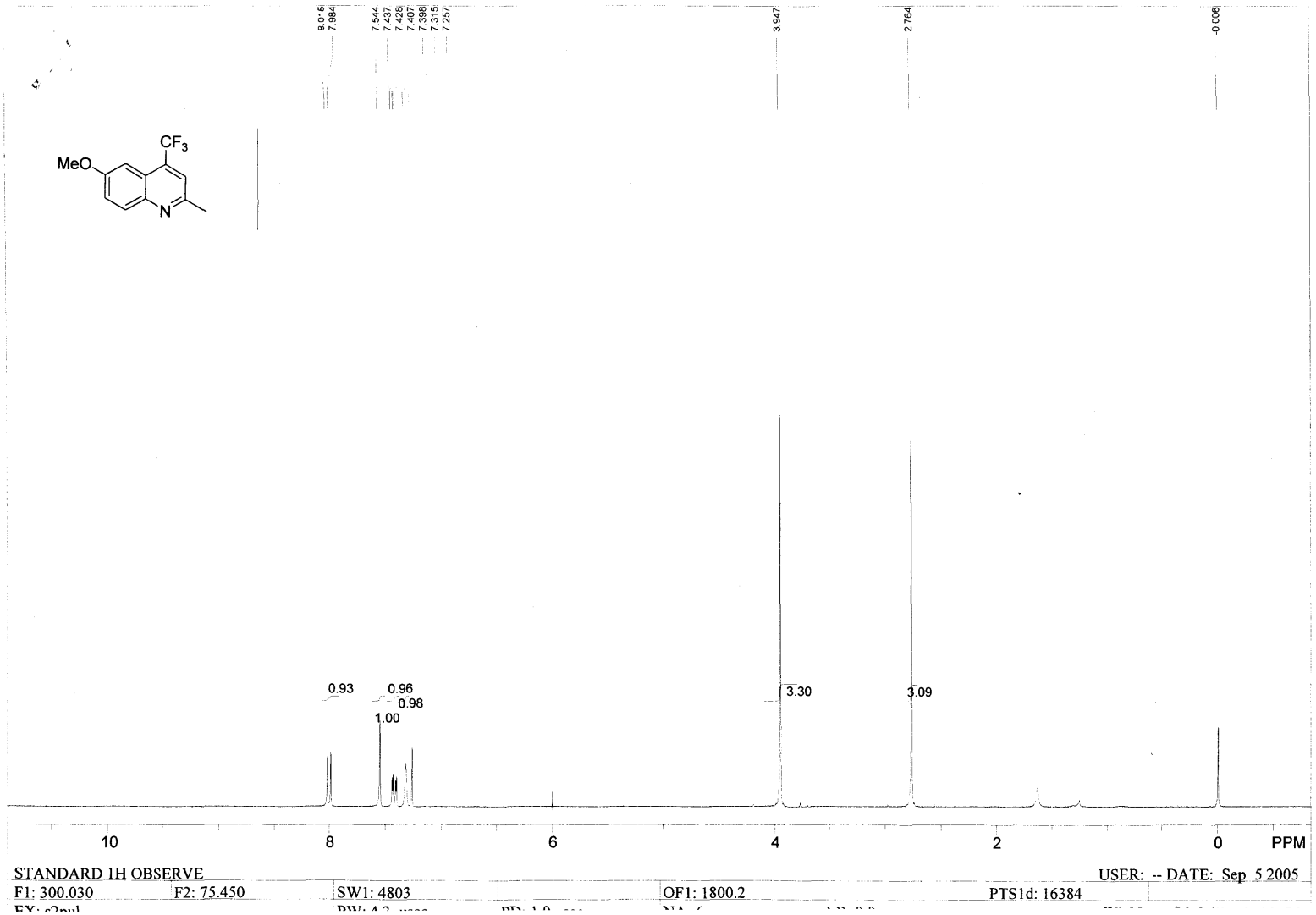
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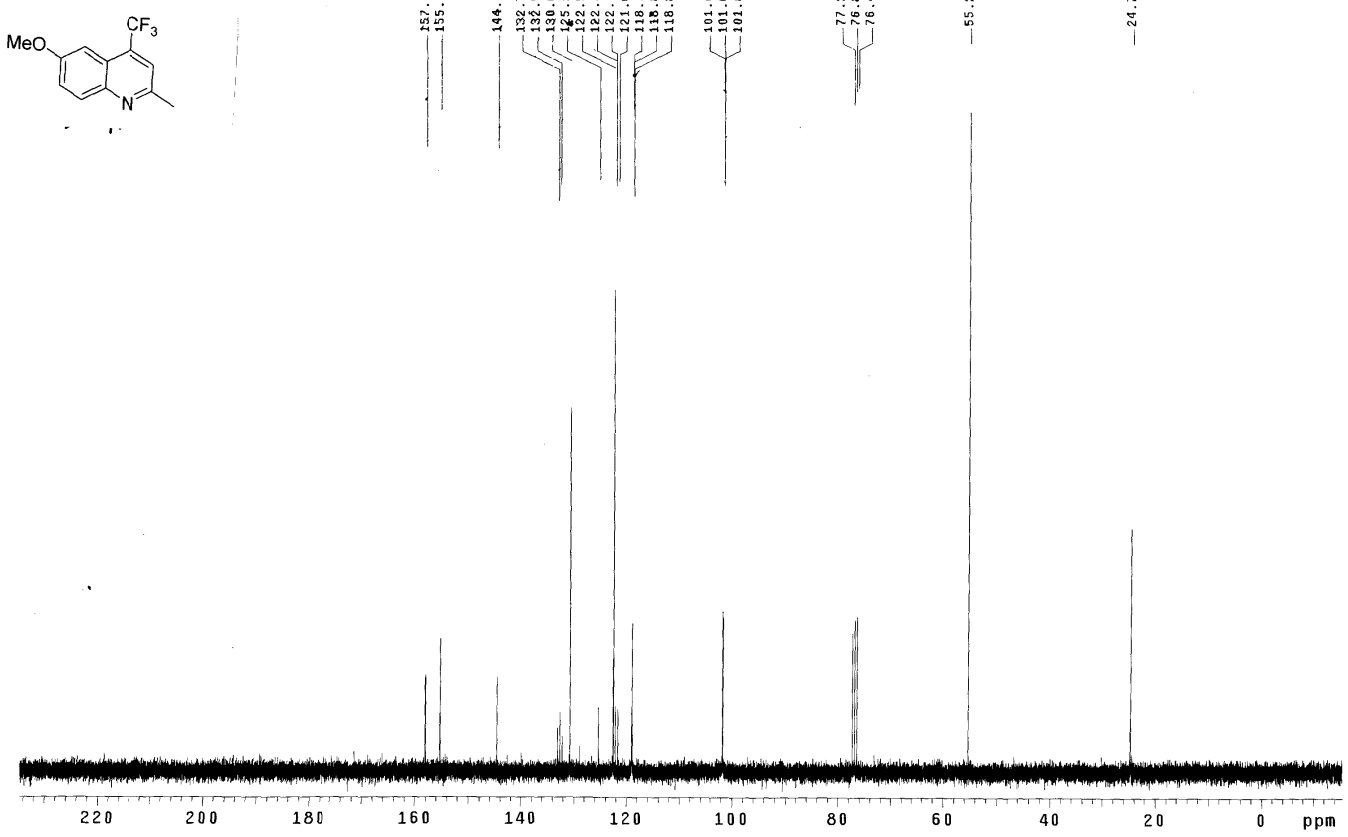

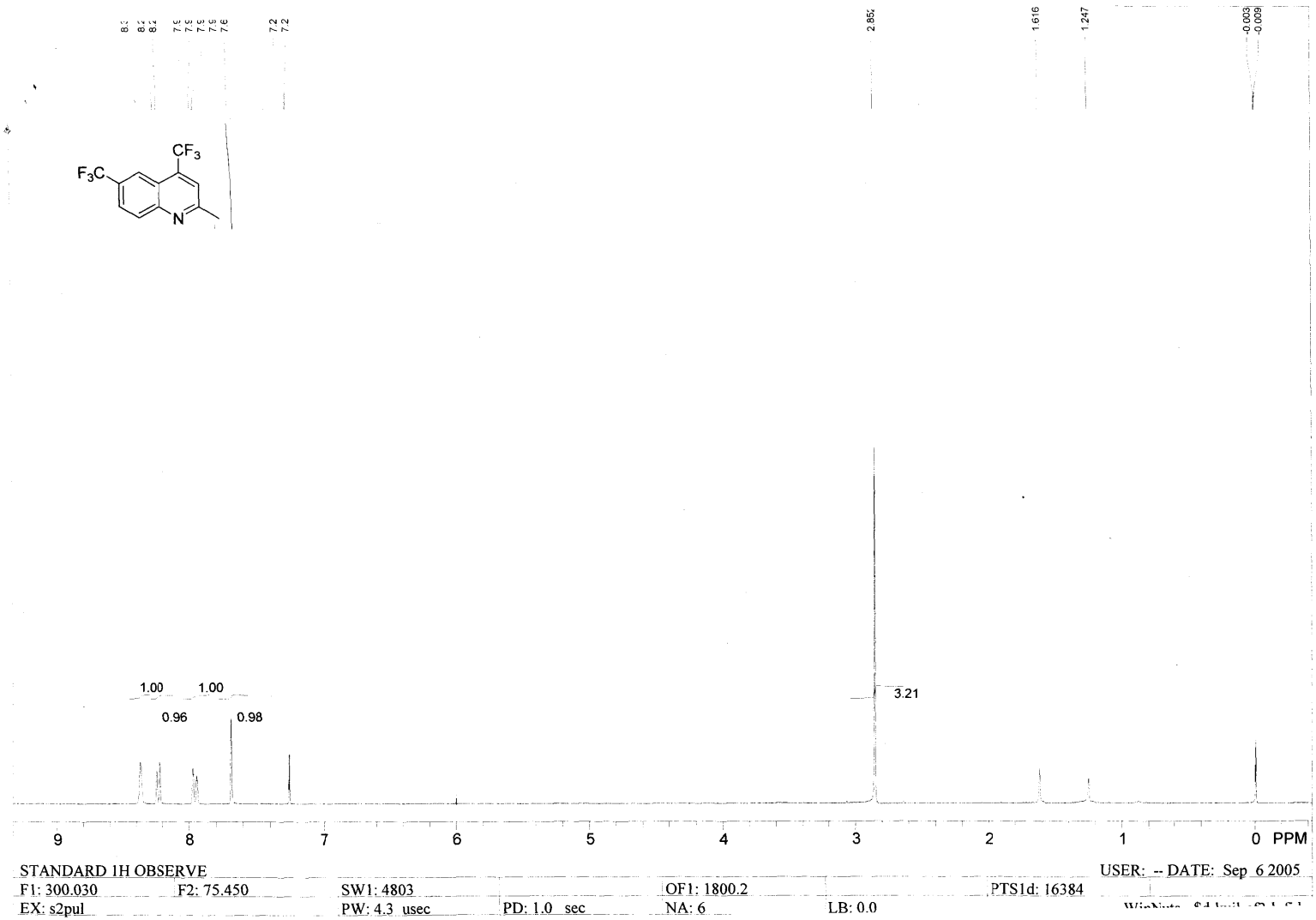
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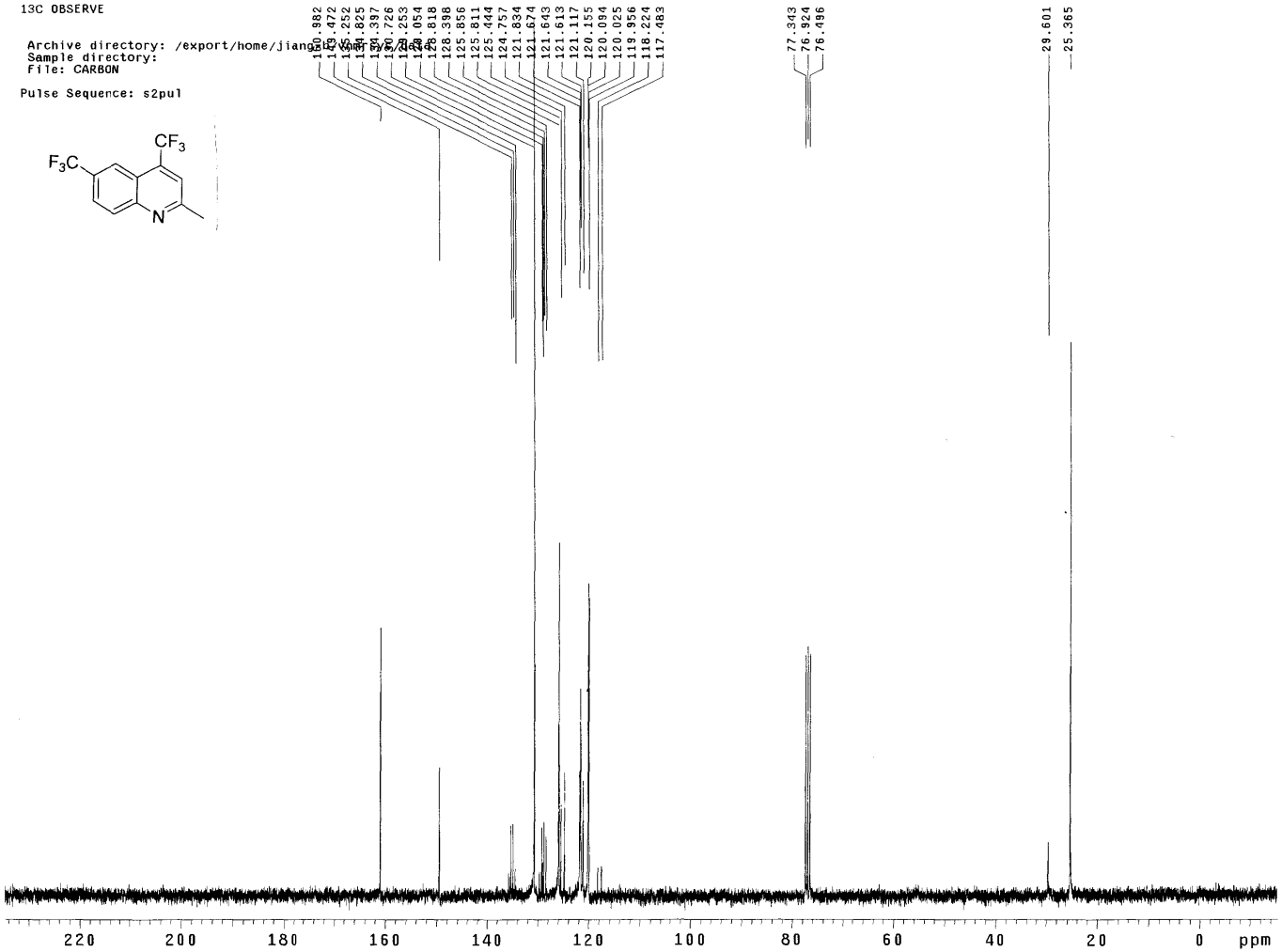
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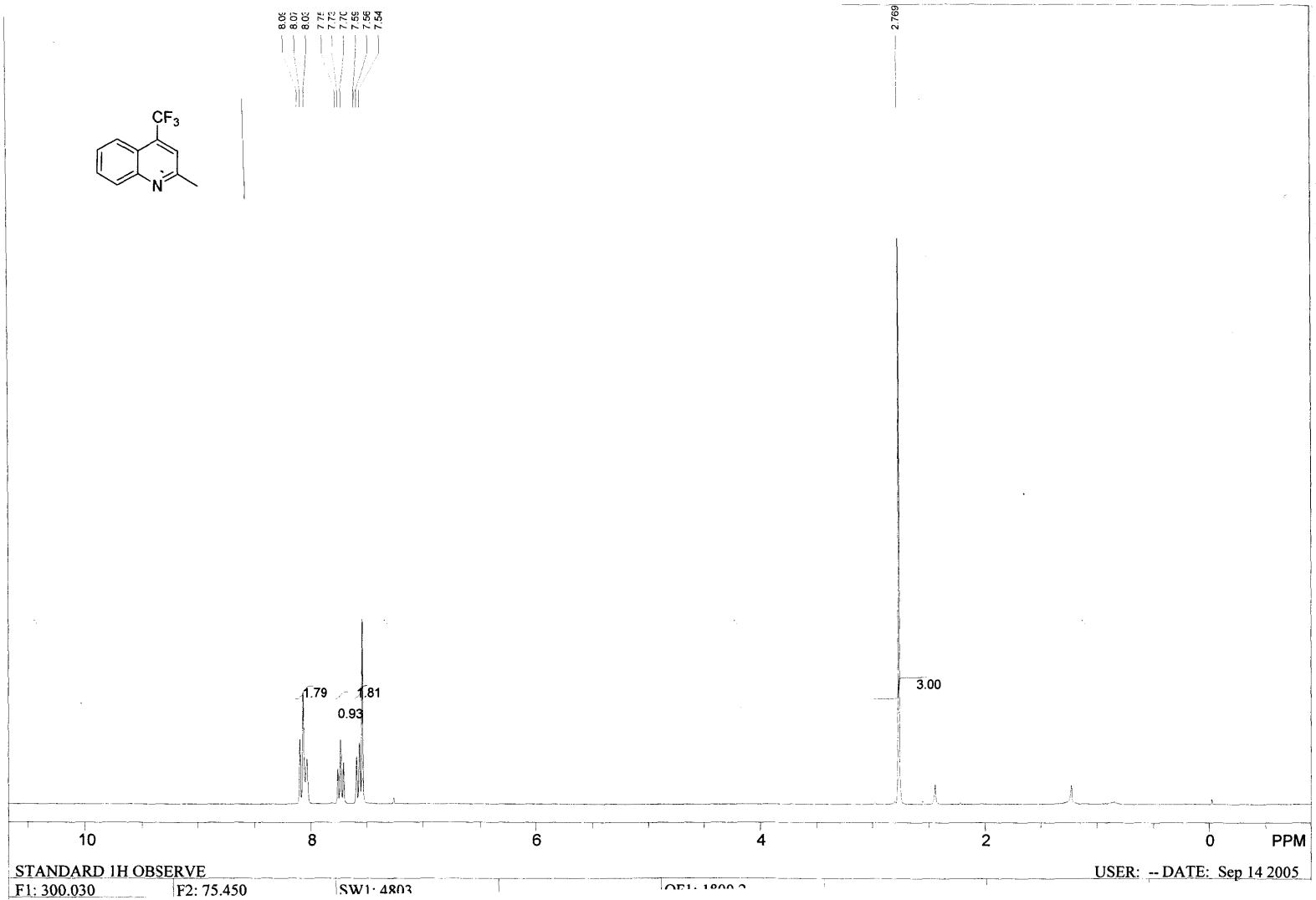
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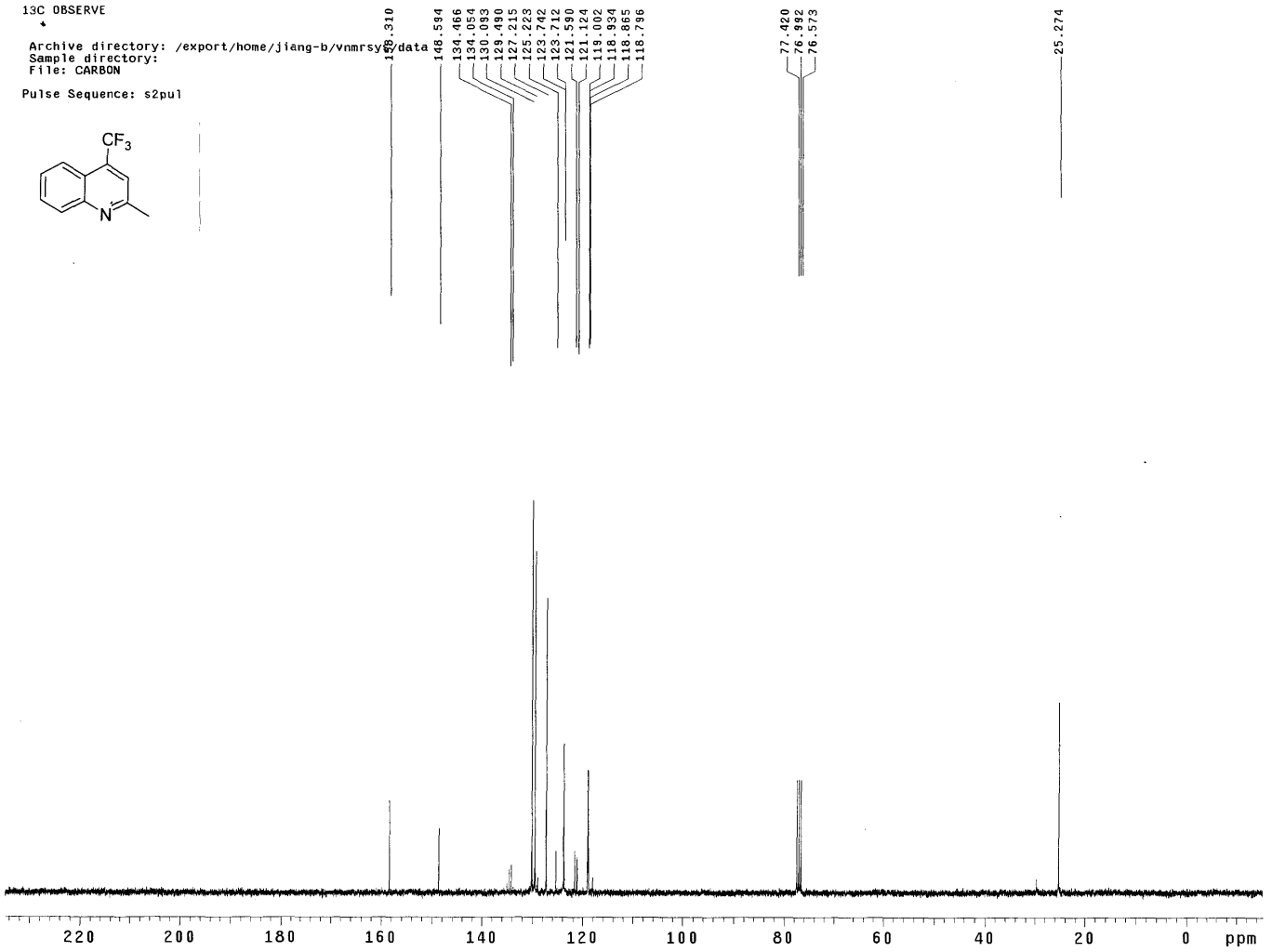
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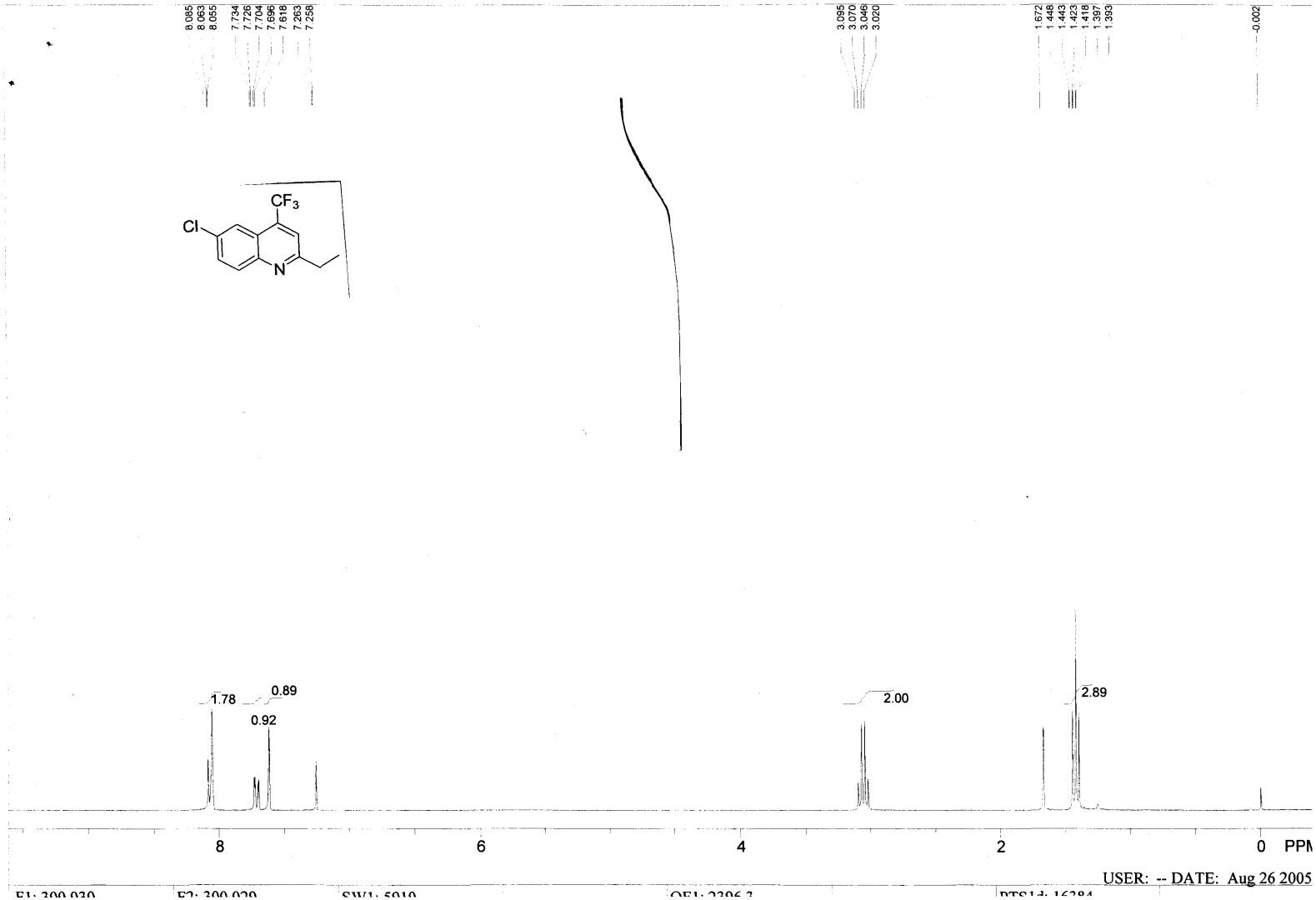
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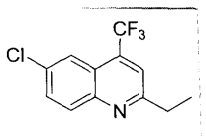
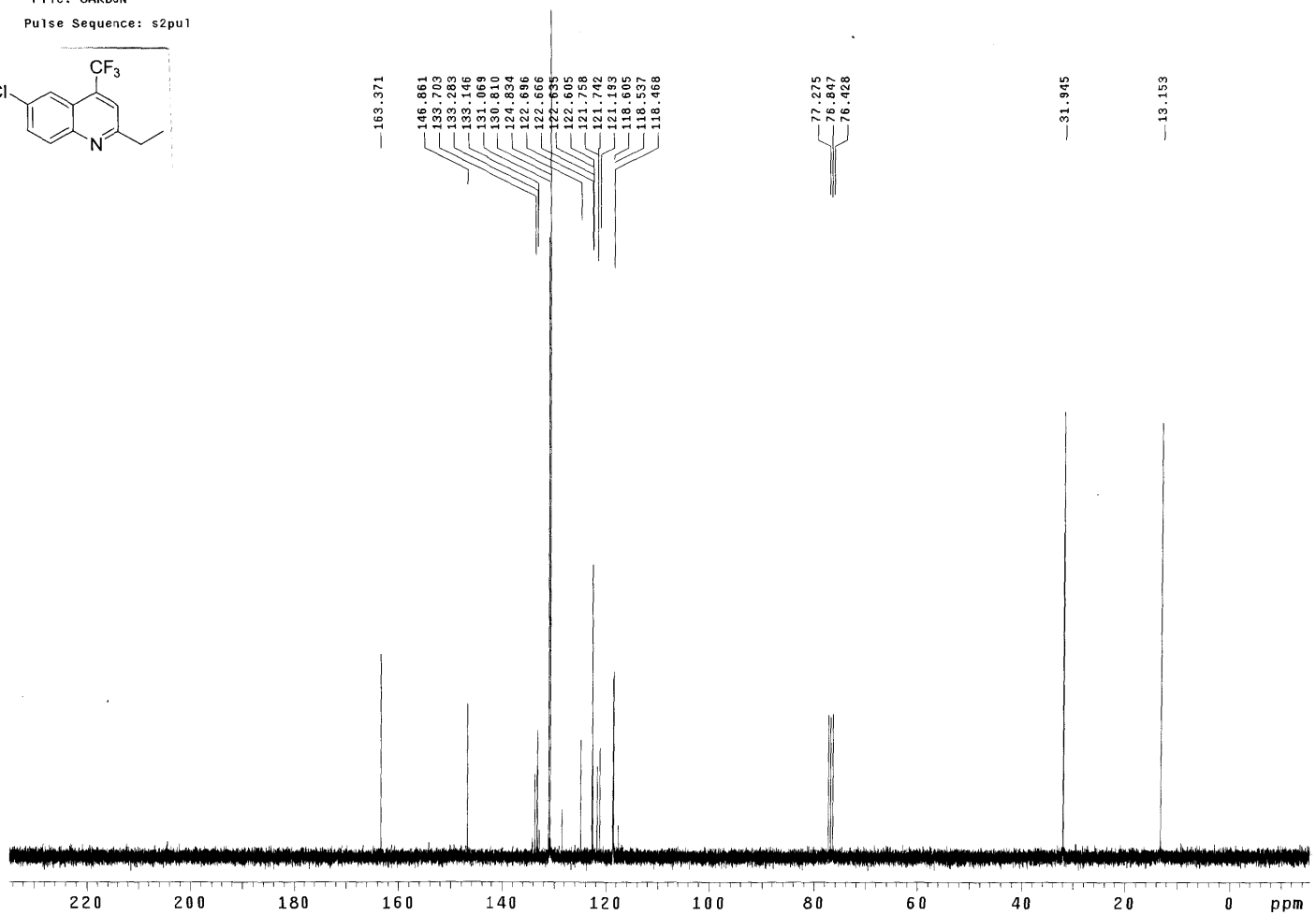
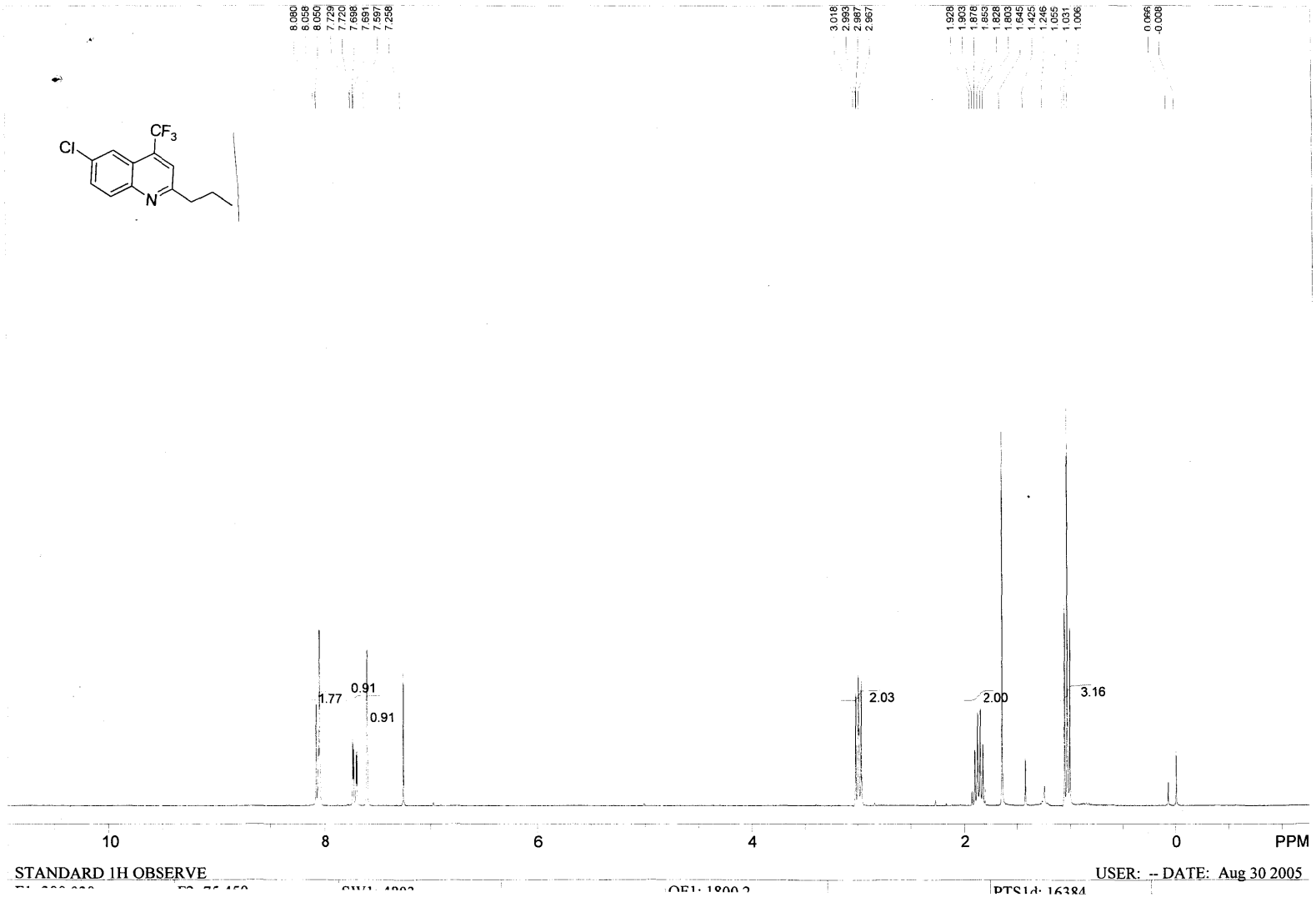
Pulse Sequence: s2pul



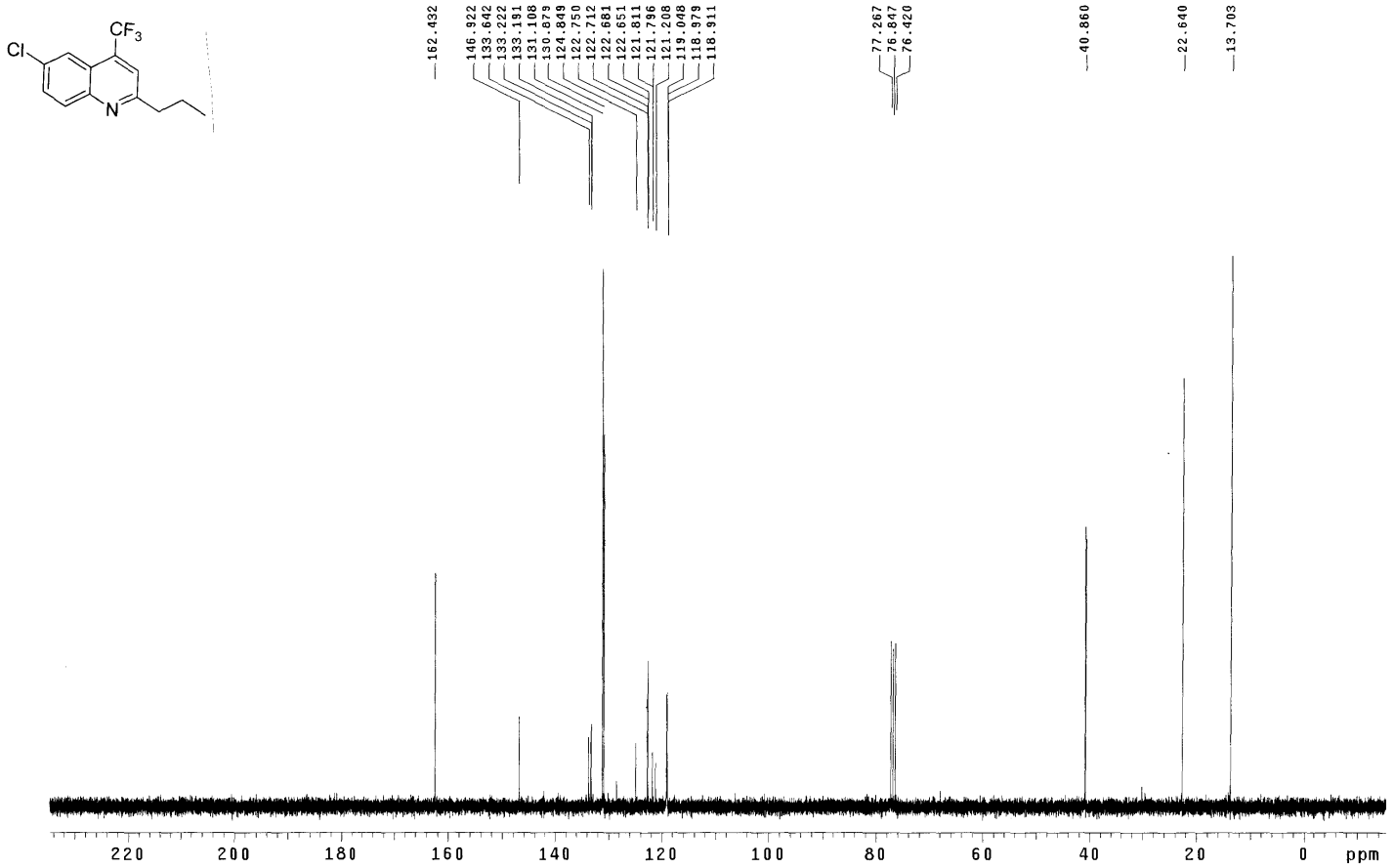


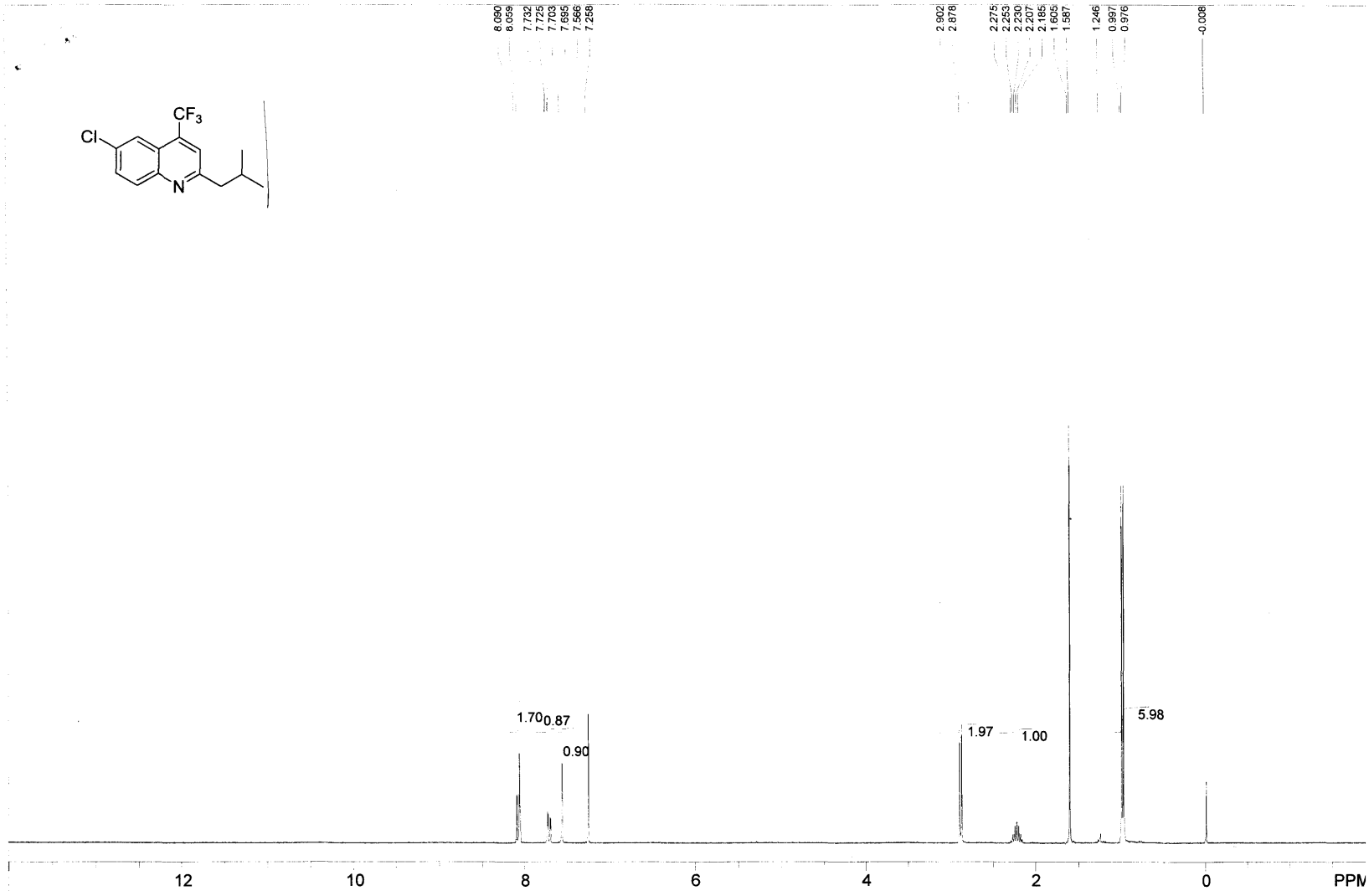

8.080
8.058
8.050
7.729
7.720
7.688
7.691
7.597
7.258
3.018
2.993
2.987
2.957
1.928
1.903
1.878
1.853
1.828
1.803
1.645
1.425
1.246
1.055
1.031
1.006
0.066
-0.008
Cl
CF3
N
1.77
0.91
0.91
2.03
2.00
3.16
10
8
6
4
2
0
PPM
STANDARD 1H OBSERVE
USER: -- DATE: Aug 30 2005

hz-8-182-c

Archive directory: /export/home/jiang-b/vnmrsys/data
Sample directory:
File: CARBON

Pulse Sequence: s2pul

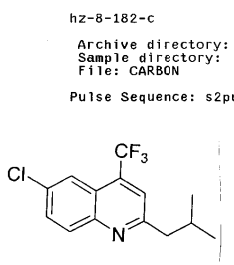


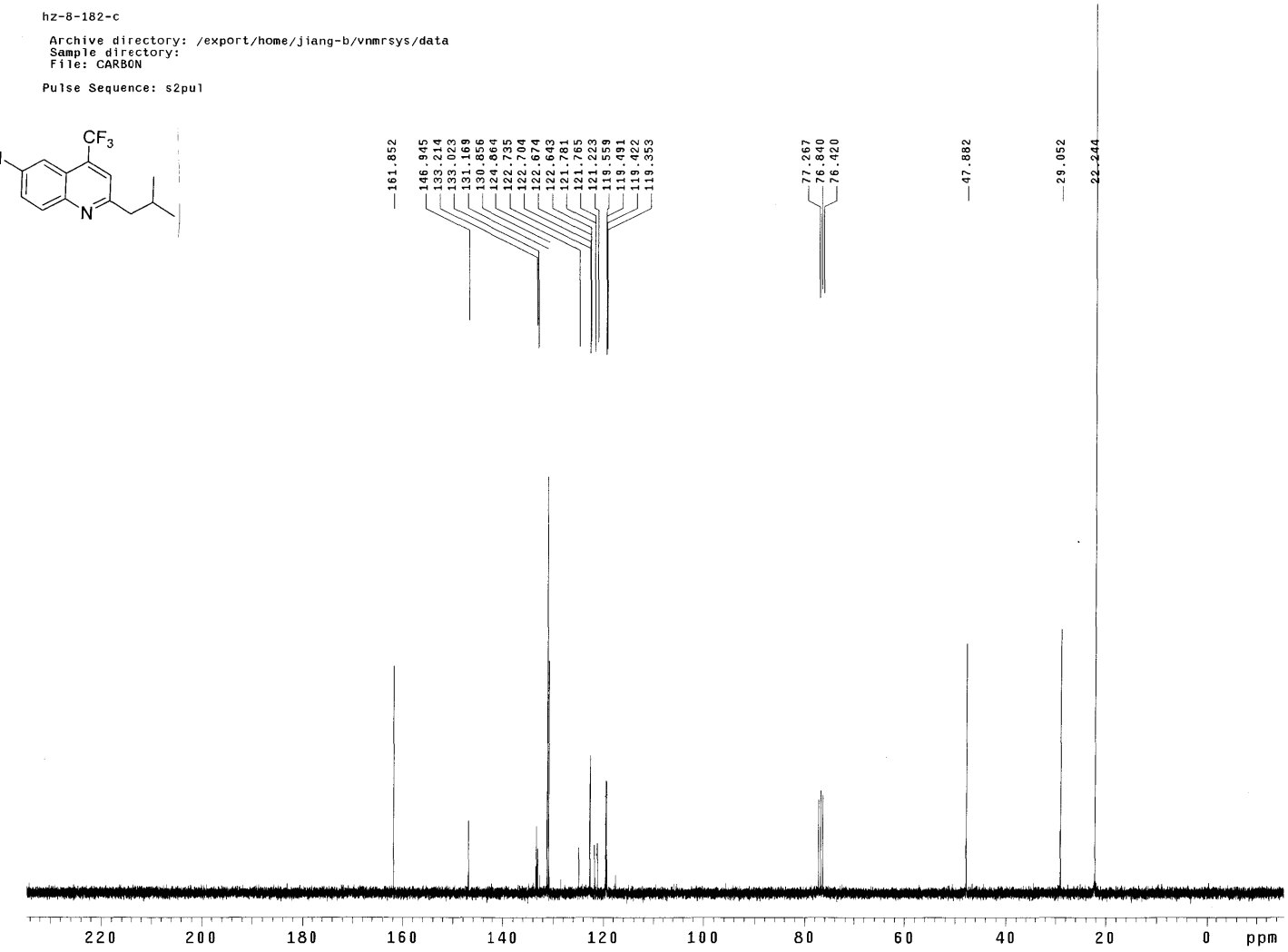

8.090
8.059
7.732
7.725
7.703
7.695
7.566
7.258
2.902
2.878
2.275
2.253
2.230
2.207
2.185
1.605
1.587
1.246
0.997
0.976
-0.008
Cl
CF3
N
1.70
0.87
0.90
1.97
1.00
5.98
12
10
8
6
4
2
0
PPM

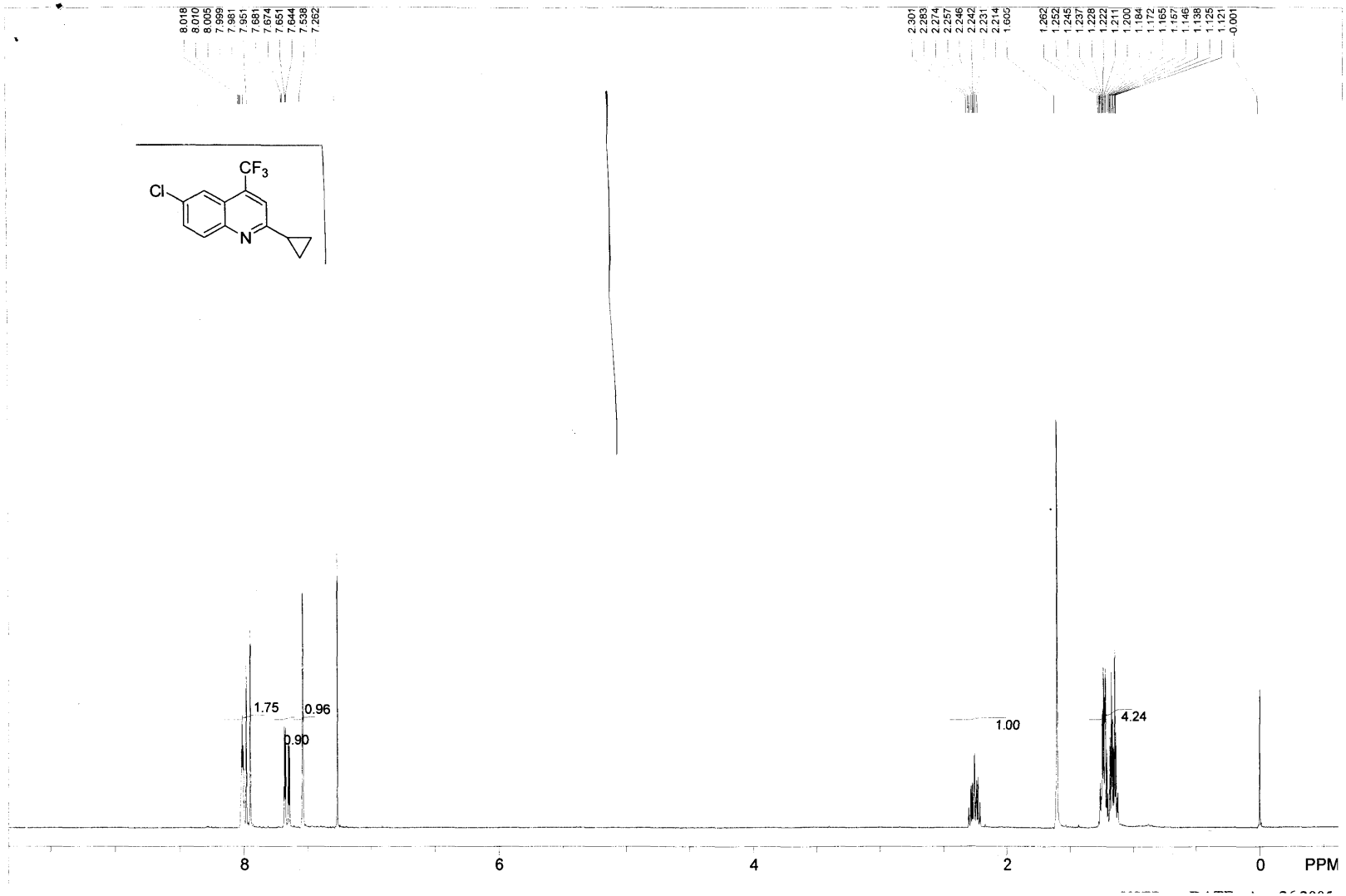
hz-8-182-c

Archive directory: /export/home/jiang-b/vnmrsys/data
Sample directory:
File: CARBON

Pulse Sequence: s2pul



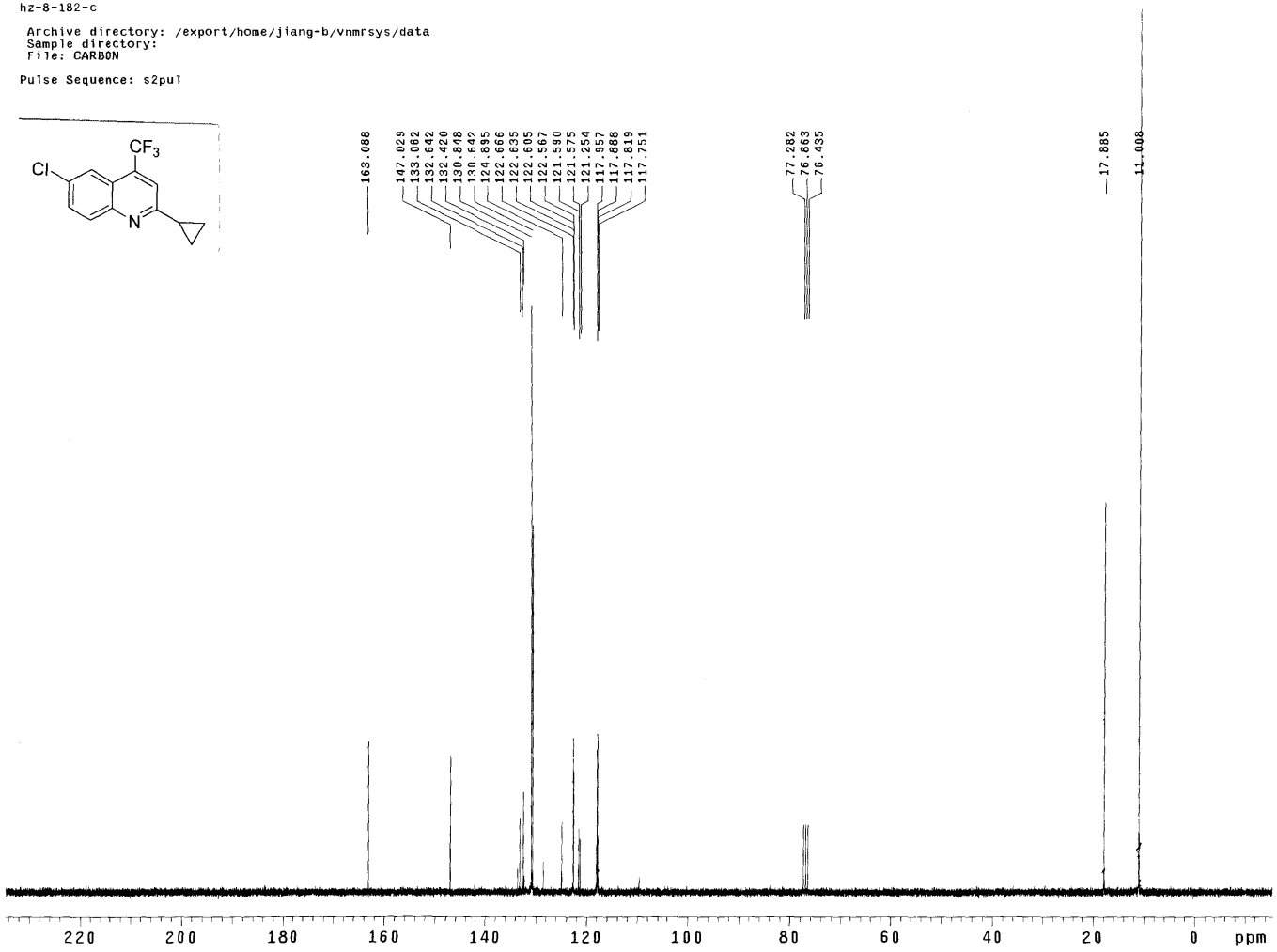


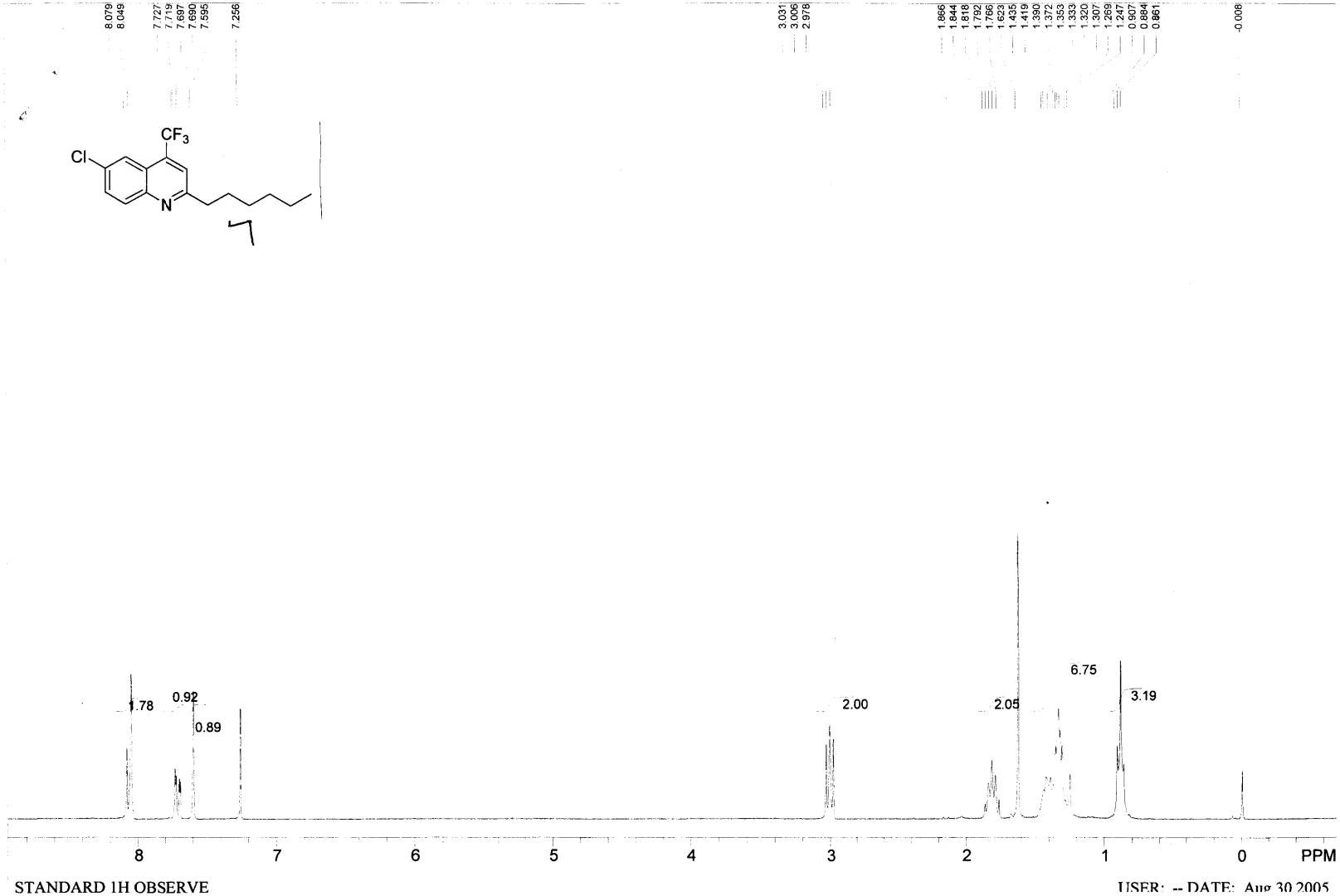

8.018
8.010
8.005
7.999
7.981
7.951
7.681
7.674
7.651
7.644
7.538
7.262
2.301
2.283
2.274
2.257
2.246
2.242
2.231
2.214
1.605
1.262
1.252
1.245
1.237
1.228
1.222
1.211
1.200
1.184
1.172
1.165
1.157
1.146
1.138
1.125
1.121
0.001
CF3
Cl
N
1.75
0.96
0.90
1.00
4.24
8
6
4
2
0
PPM

hz-8-182-c

Archive directory: /export/home/jiang-b/vnmrsys/data
Sample directory:
File: CARBON

Pulse Sequence: s2pul

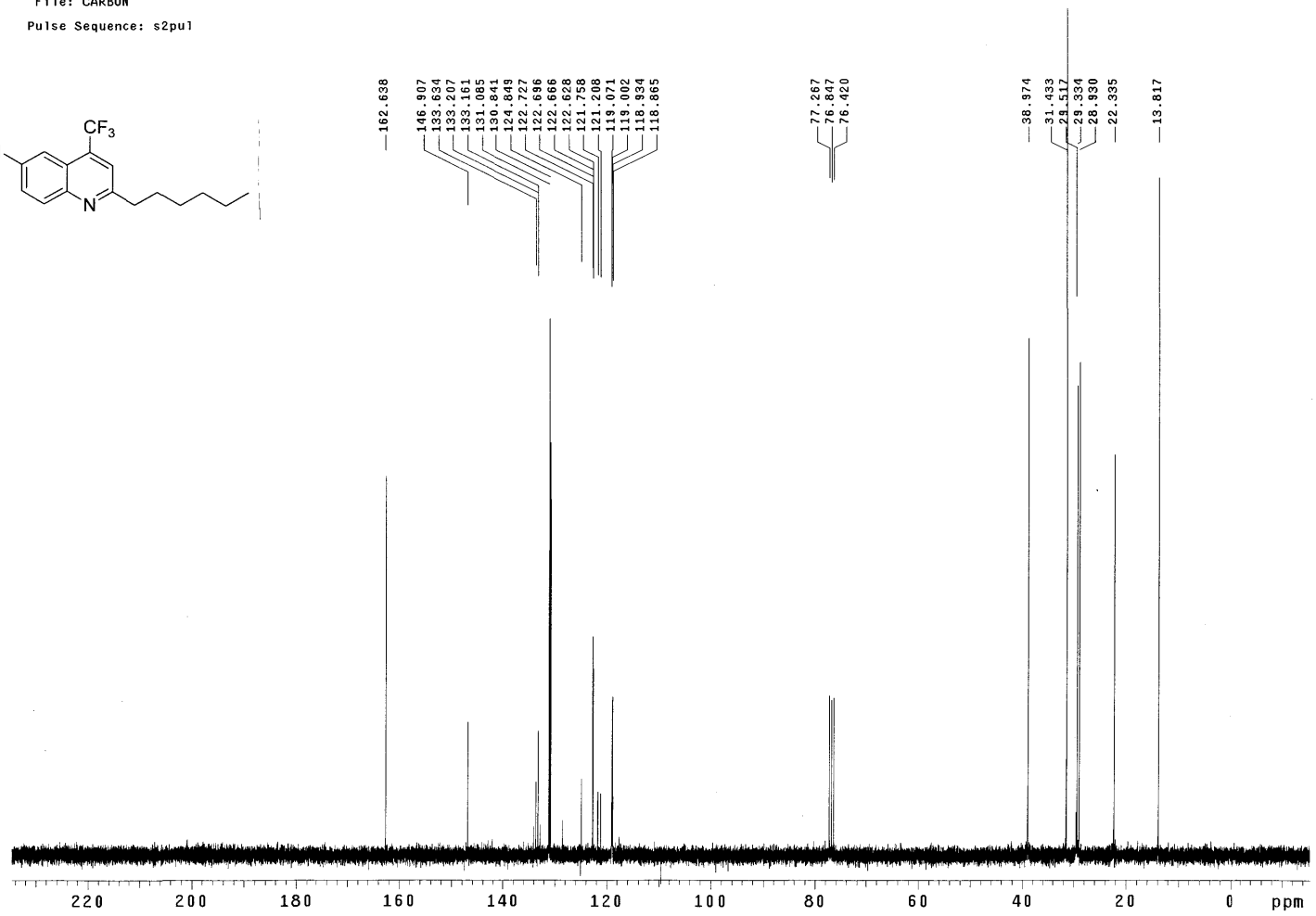


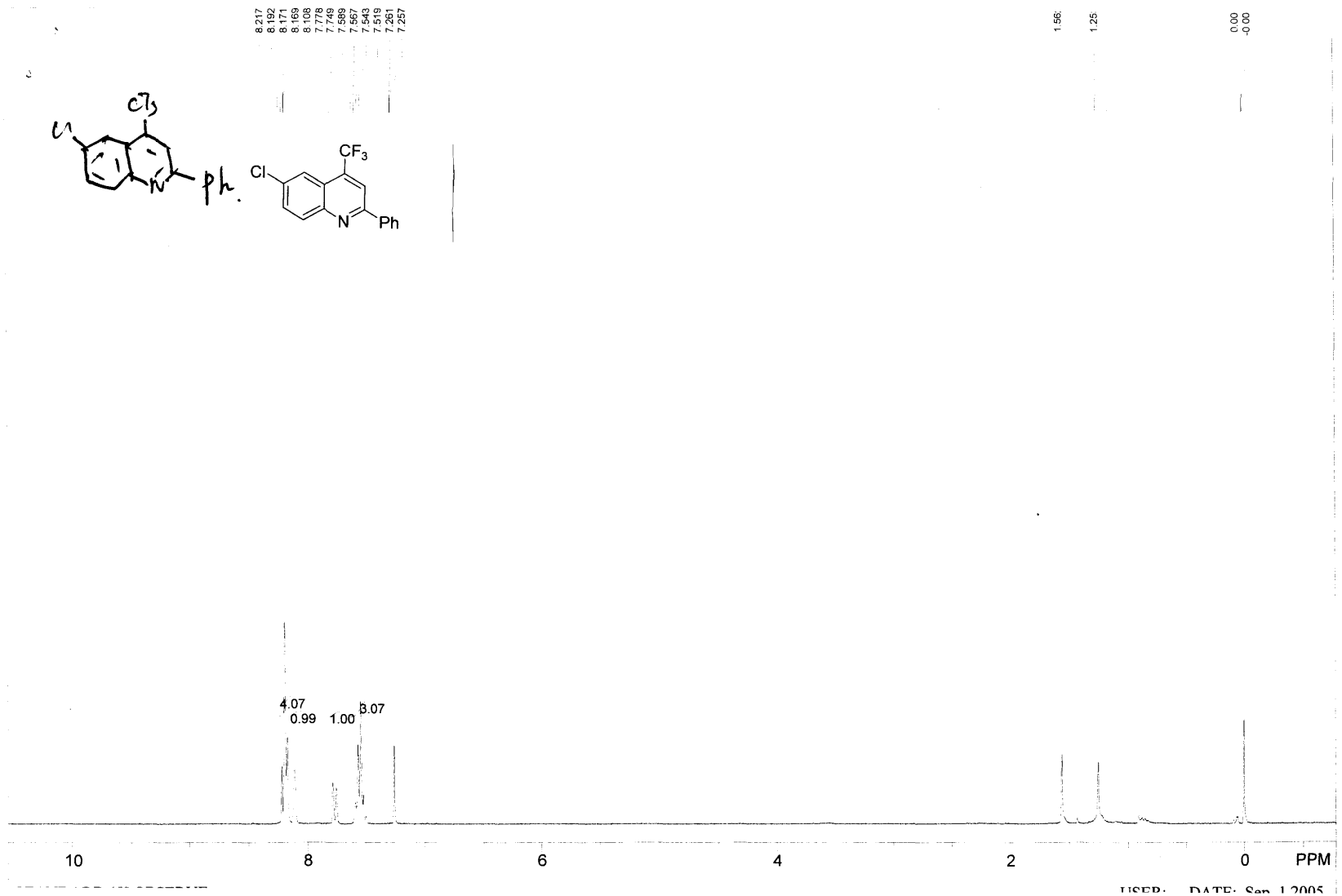

8.079
8.049
7.727
7.719
7.697
7.690
7.595
7.256
3.031
3.006
2.978
1.866
1.844
1.818
1.792
1.766
1.623
1.435
1.419
1.390
1.372
1.353
1.333
1.320
1.307
1.269
1.247
0.907
0.884
0.861
0.008
CF3
Cl
N
1.78
0.92
0.89
2.00
2.05
6.75
3.19
8
7
6
5
4
3
2
1
0
PPM
STANDARD 1H OBSERVE
USER: -- DATE: Aug 30 2005

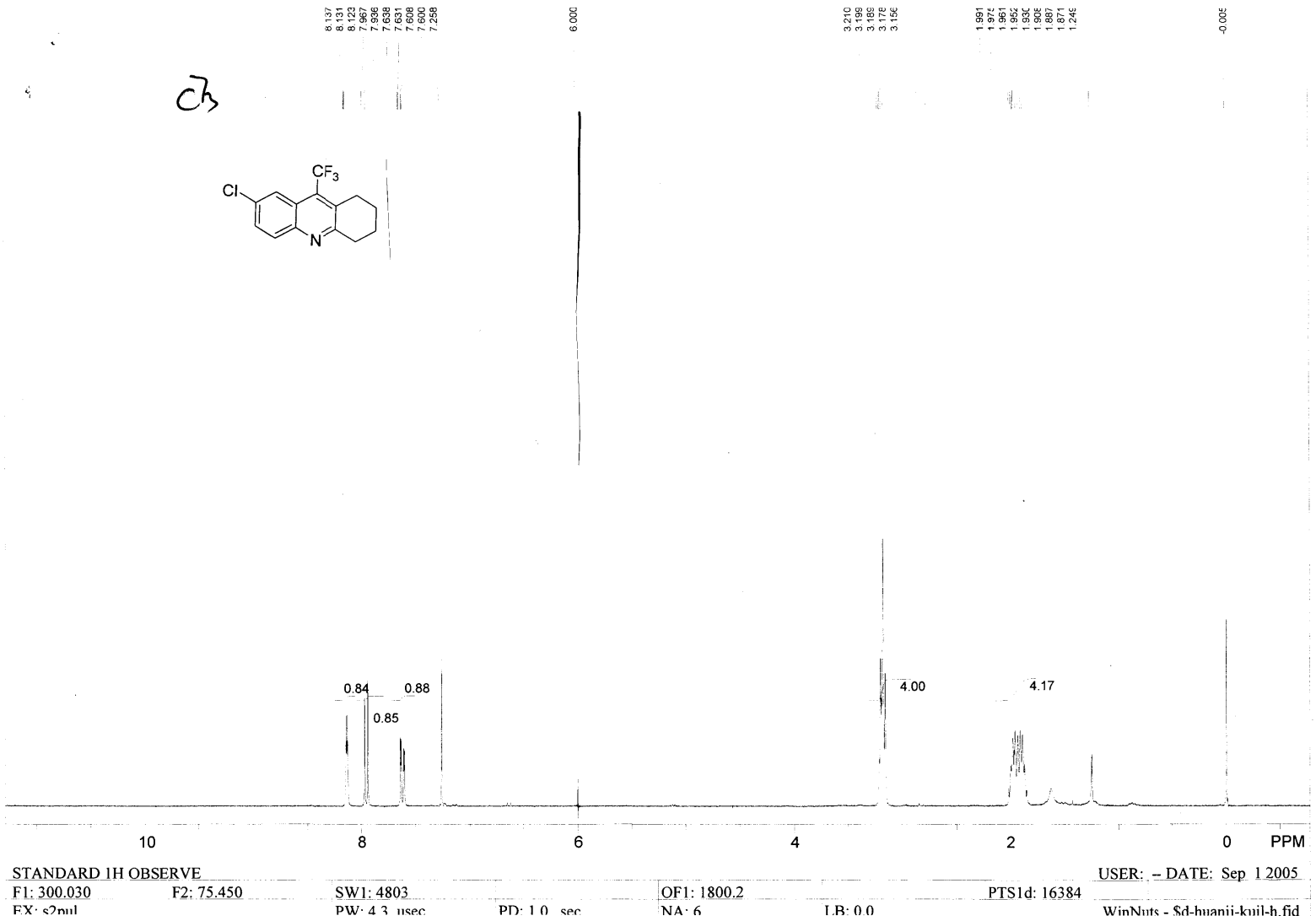
hz-8-182-c

Archive directory: /export/home/jiang-b/vnmrsys/data
Sample directory:
File: CARBON

Pulse Sequence: s2pul



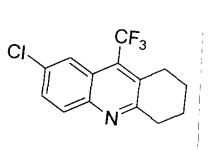

8.217
8.192
8.171
8.169
8.108
7.778
7.749
7.589
7.567
7.543
7.519
7.261
7.257
1.56
1.25
0.00
-0.00
CF3
Cl
N
Ph
4.07
0.99
1.00
3.07
10
8
6
4
2
0
PPM


8.137
8.131
8.123
7.967
7.936
7.638
7.631
7.608
7.600
7.258
6.000
3.210
3.199
3.188
3.172
3.156
1.991
1.972
1.961
1.952
1.930
1.908
1.887
1.871
1.245
-0.005
CF3
Cl
N
0.84
0.88
0.85
4.00
4.17
10
8
6
4
2
0
PPM
STANDARD 1H OBSERVE
USER: – DATE: Sep 1 2005
F1: 300.030
F2: 75.450
SW1: 4803
OF1: 1800.2
PTS1d: 16384
EX: s2pul
PW: 4.3 usec
PD: 1.0 sec
NA: 6
LB: 0.0
WinNuts - Sd-huanji-kuil-h.fid

hz-8-182-c

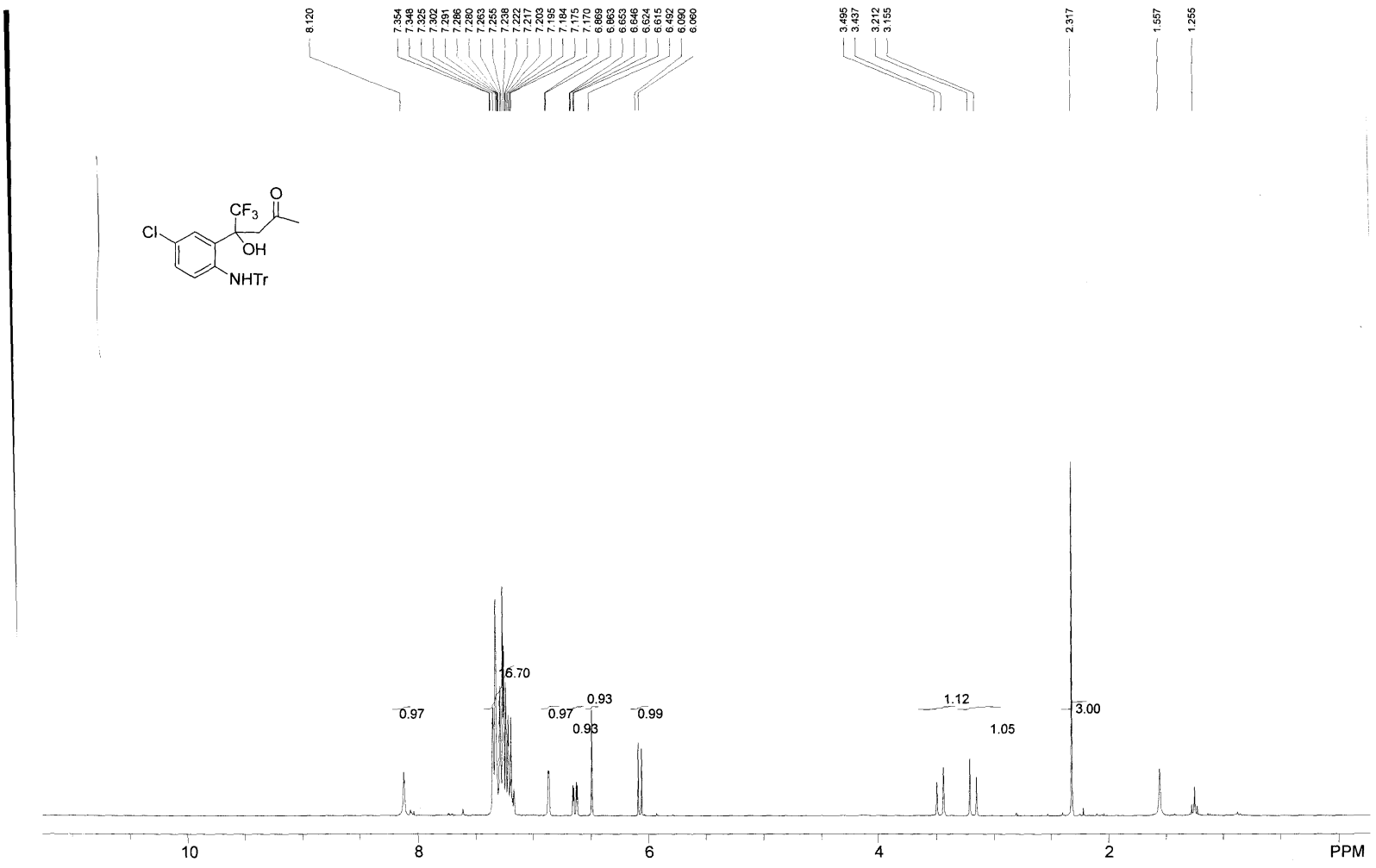
Archive directory: /export/home/jiang-b/vnmrsys/data
Sample directory:
File: CARBON

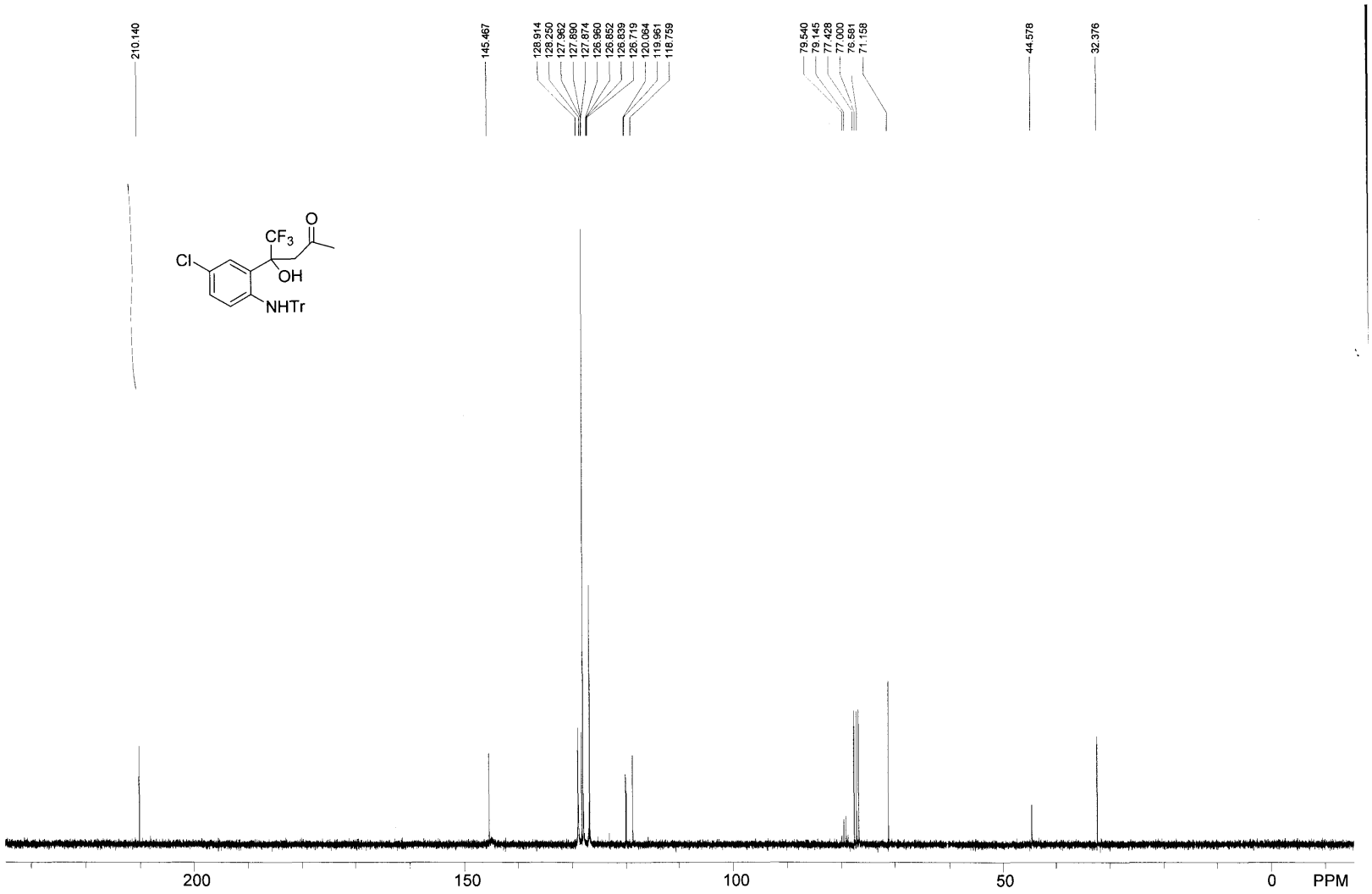
Pulse Sequence: s2pul



159.738
144.823
132.909
132.894
131.489
131.466
130.573
128.764
126.574
123.070
123.009
122.941
122.880
77.282
76.863
76.435
34.265
27.128
27.067
26.999
26.938
22.312
22.289
22.266
21.602

220 200 180 160 140 120 100 80 60 40 20 0 ppm


8.120
7.354
7.348
7.325
7.302
7.291
7.286
7.280
7.263
7.255
7.238
7.222
7.217
7.203
7.195
7.184
7.175
7.170
6.869
6.863
6.653
6.646
6.624
6.615
6.492
6.090
6.060
3.495
3.437
3.212
3.155
2.317
1.557
1.255
Cl
CF3
O
OH
NHTr
0.97
6.70
0.97
0.93
0.93
0.99
1.12
1.05
3.00
10
8
6
4
2
PPM


210.140
145.467
128.914
128.250
127.962
127.890
127.874
126.960
126.852
126.839
126.719
120.084
119.961
118.759
79.540
79.145
77.428
77.000
76.581
71.158
44.578
32.376
O
CF3
Cl
OH
NHTr
200
150
100
50
0
PPM

Reference

1. Jiang, B.; Si, Y. G. *J. Org. Chem.* 2002, *67*, 9449;