Supplementary Material (ESI) for Organic & Biomolecular Chemistry

Electronic Supplementary Information

Synthesis of trifluoromethyl cyclohexyl, cyclohexenyl and aryl compounds via stepwise Robinson annulation

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Contents:

1. General experimental methods:

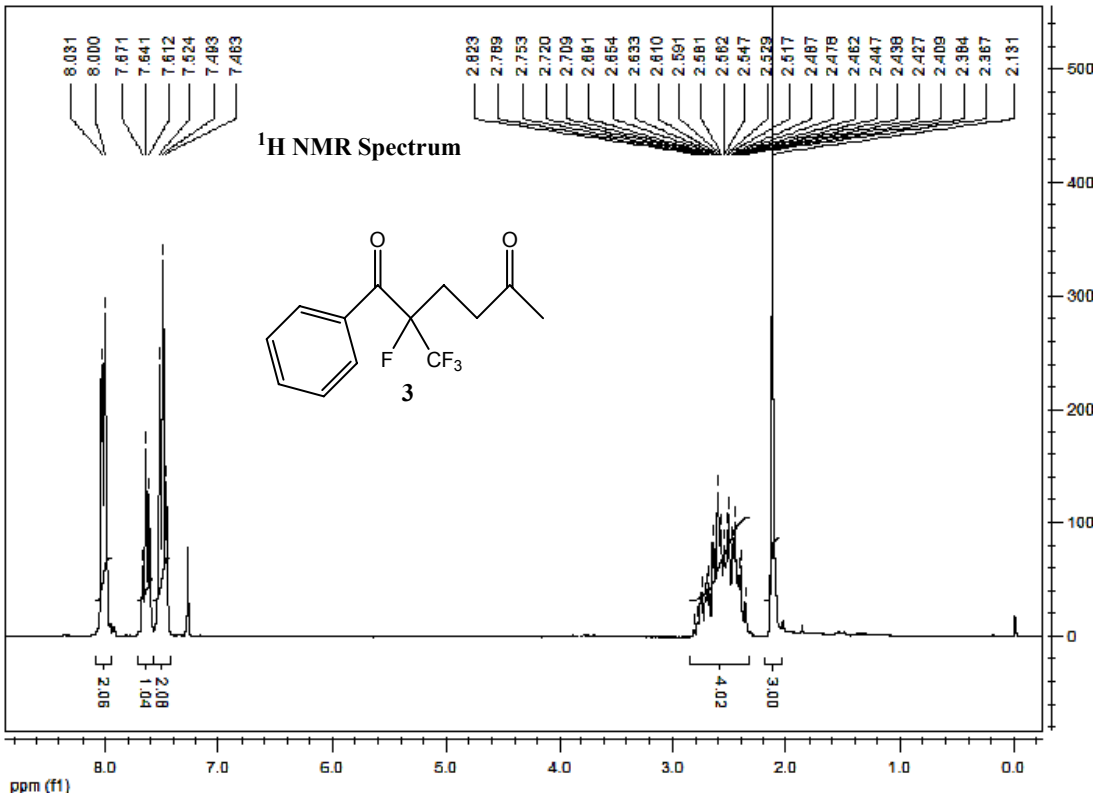
Except noted otherwise, reagents and starting materials were obtained from common commercial sources and used as received. Pentafluoroethyltrimethylsilane was distilled (b.p. 60-70 °C) before used. Cesium fluorine was activated before use by heating under reduce pressure during overnight. THF was distilled from sodium-benzophenone. CH_2Cl_2 was distilled from CaH_2. Methanol (HPLC grade) was used without further purification.

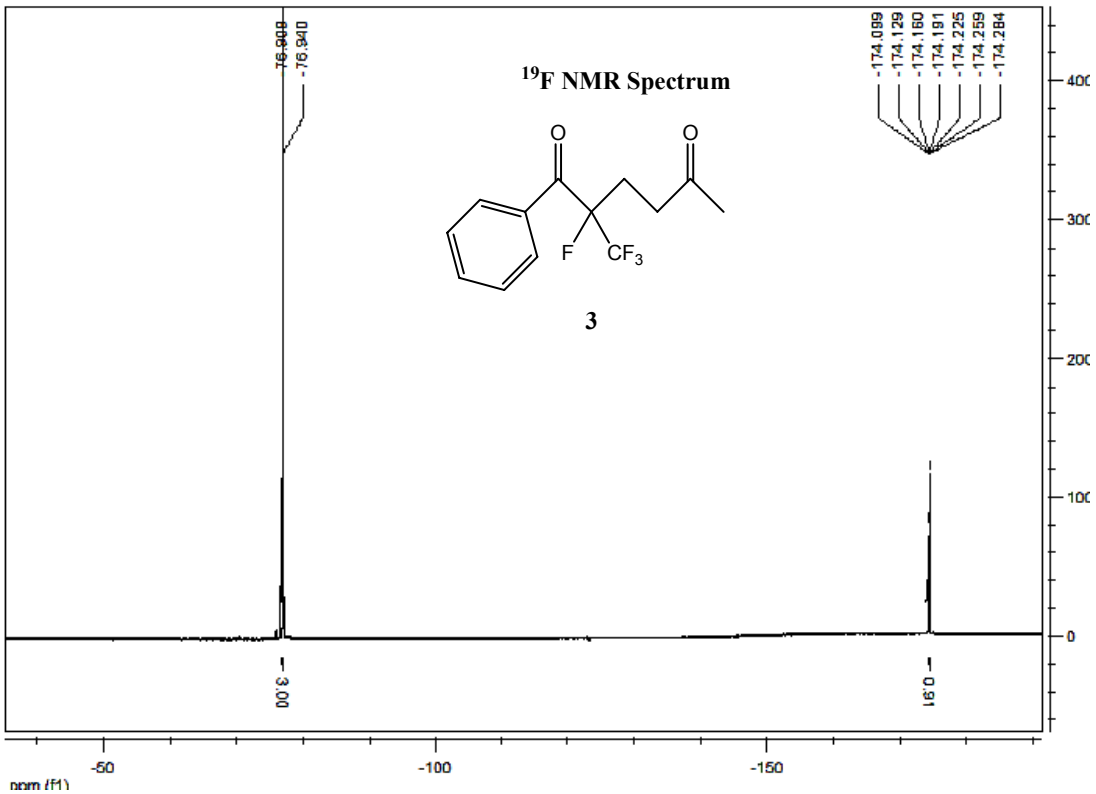
Thin–layer chromatography using precoated aluminium backed plates (Merck Kieselgel 60F254) were visualized by UV light and by an alcoholic solution of phosphomolybdic acid or an aqueous solution of potassium permanganate. Preparative centrifugal thin–layer chromatography were carried out on a Chromatotron, Model 7924T (Harrison Research, Palo Alto, CA, U.S.A.). The rotors were coated with silica gel 60 PF_{254} containing gypsum, the layer thickness was 1, 2 or 4 mm, depending on the amount of product to purify. Melting points (mp) were determined on a Stuart SMP3 Melting Point Model and were uncorrected. NMR spectra were recorded on a AC 250 Bruker spectrometer in $CDCl_3$, at frequencies of 250 MHz for ^1H, 235.3 MHz for ^{19}F and 62.9 MHz for ^{13}C NMR. Chemicals shifts (δ) are reported in ppm relative to TMS for ^1H and ^{13}C NMR spectra and to $CFCl_3$ for ^{19}F NMR spectra. Coupling constant (J) are reported in Hertz (Hz). In the ^{13}C NMR data, reported signal multiplicities are related to C-F coupling. Except noted otherwise, ^{19}F NMR spectra are not decoupled ^1H. The following abbreviations are used to indicate the multiplicities: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), br s (broad singlet). HRMS were recorded on a Micromass ESI-Q–TOF mass spectrometer using an electrospray source in negative mode (ESI^-) or on a Micromass EI-GCT mass spectrometer using an electronic impact source (EI+). Elemental analysis were performed on a Thermo-Electron Flash EA 1112 Series apparatus and analyses fell within ± 0.4 % of the calculated values.

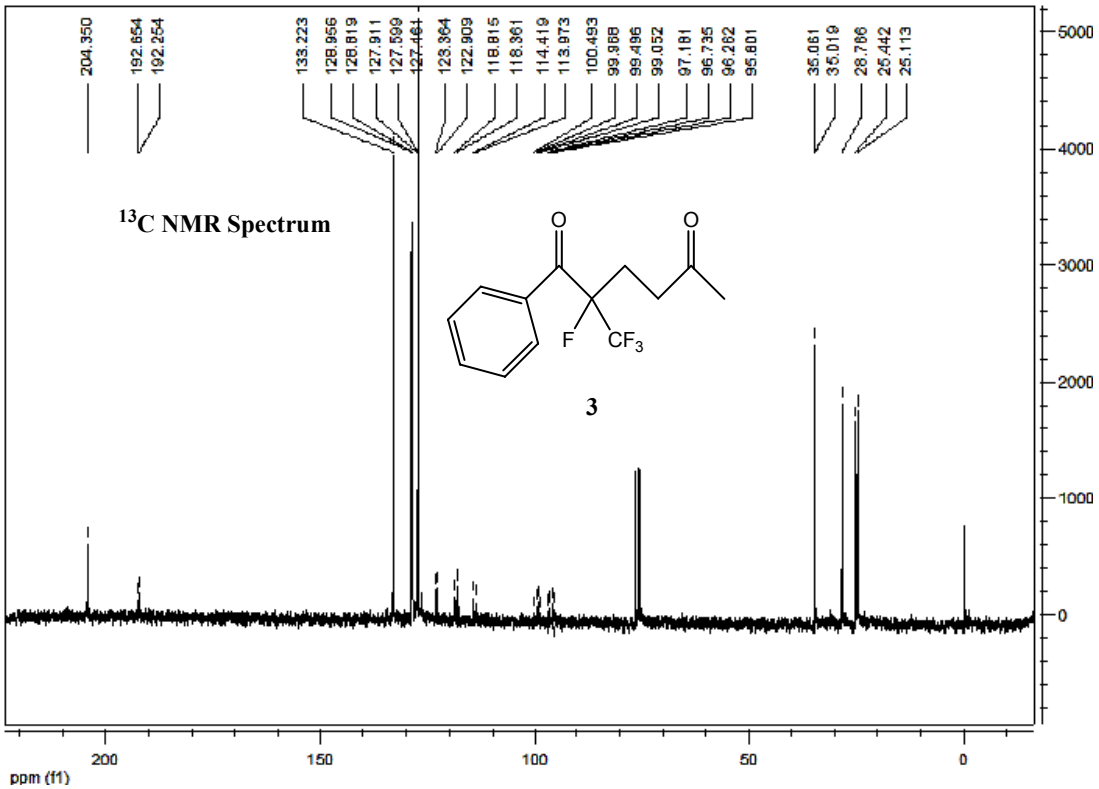
1-Phenyl-2,3,3,3-tetrafluoro-1-trimethylsiloxypropene **2** was prepared according to the method described by Uneyama and al.[1] Others reagents and solvents were obtained from common commercial sources and used as received.

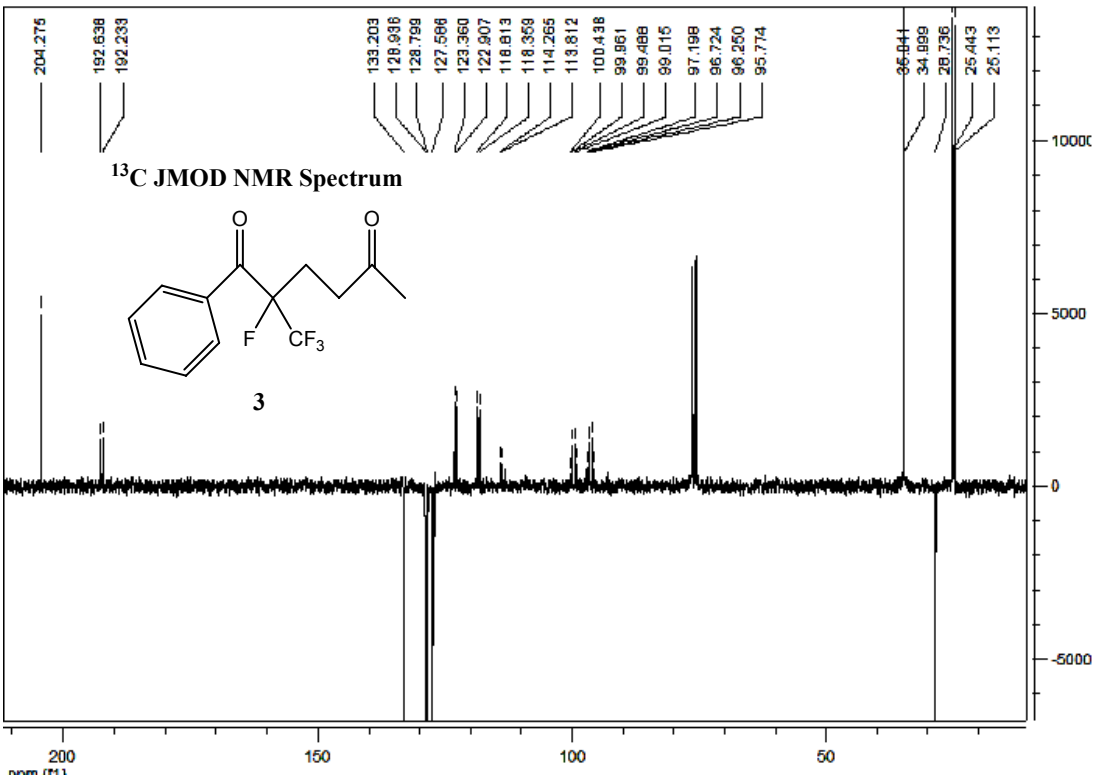
[1] Nakamura, Y.; Ozeki, Y.; Uneyama, K. *J. Fluor. Chem*. **2008**, *129*, 274-279.

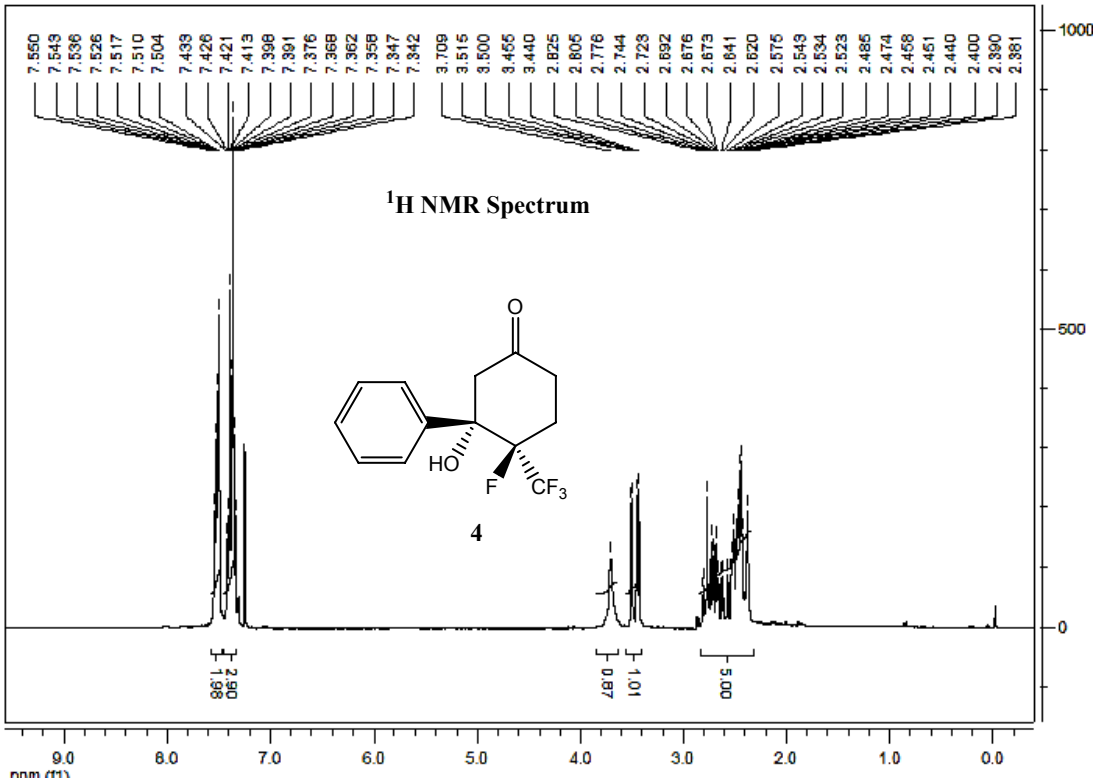
2. ^{1}H, ^{19}F and ^{13}C NMR spectra


^{1}H NMR Spectrum
8.031
8.000
7.671
7.641
7.612
7.524
7.493
7.463
2.823
2.789
2.753
2.720
2.709
2.691
2.654
2.633
2.610
2.591
2.581
2.562
2.547
2.529
2.517
2.487
2.478
2.462
2.447
2.436
2.427
2.409
2.384
2.367
2.131
O
O
F
CF$_3$
3
2.06
1.04
2.08
4.02
3.00
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (f1)


^{19}F NMR Spectrum
-76.908
-76.940
-174.099
-174.129
-174.160
-174.191
-174.225
-174.259
-174.284
O
O
F
CF$_3$
3
3.00
0.91
-50
-100
-150
ppm (f1)

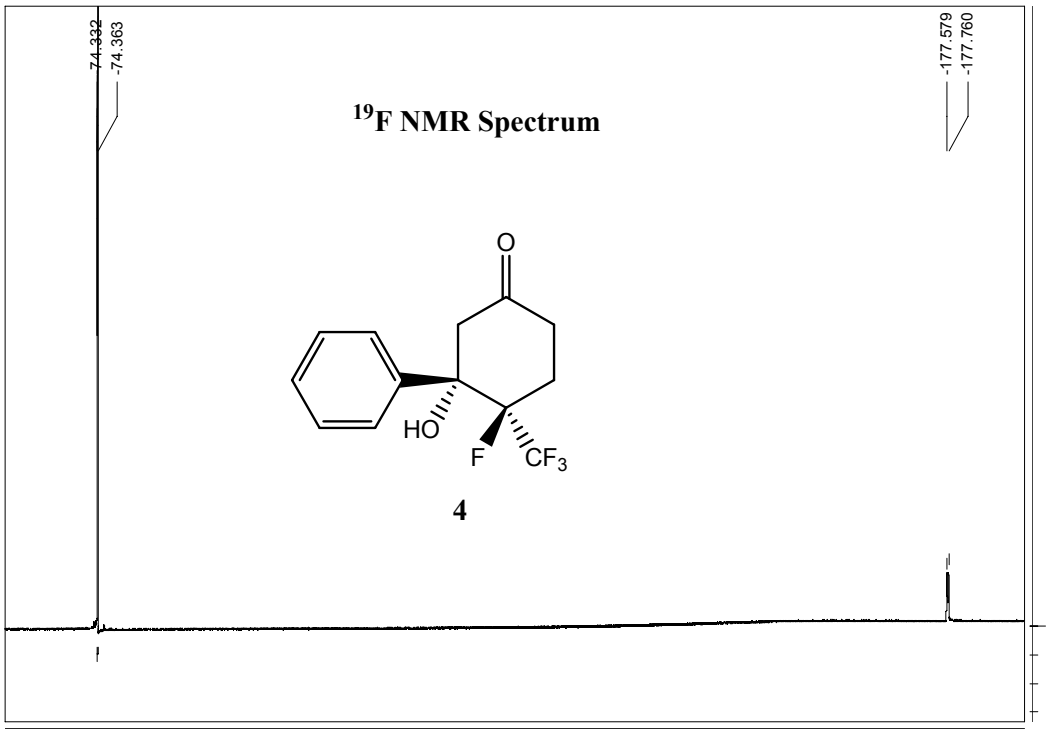

204.350
192.654
192.254
133.223
128.956
128.819
127.911
127.599
127.461
123.364
122.909
118.815
118.361
114.419
113.973
100.493
99.988
99.496
99.052
97.181
96.735
96.262
95.801
35.061
35.019
28.786
25.442
25.113
13C NMR Spectrum
O
O
F
CF3
3
5000
4000
3000
2000
1000
0
200
150
100
50
0
ppm (f1)


204.275
192.638
192.233
133.203
128.936
128.799
127.586
123.360
122.907
118.813
118.359
114.265
113.812
100.438
99.961
99.488
99.015
97.198
96.724
96.250
95.774
35.041
34.999
28.736
25.443
25.113
13C JMOD NMR Spectrum
O
O
F
CF3
3
10000
5000
0
-5000
200
150
100
50



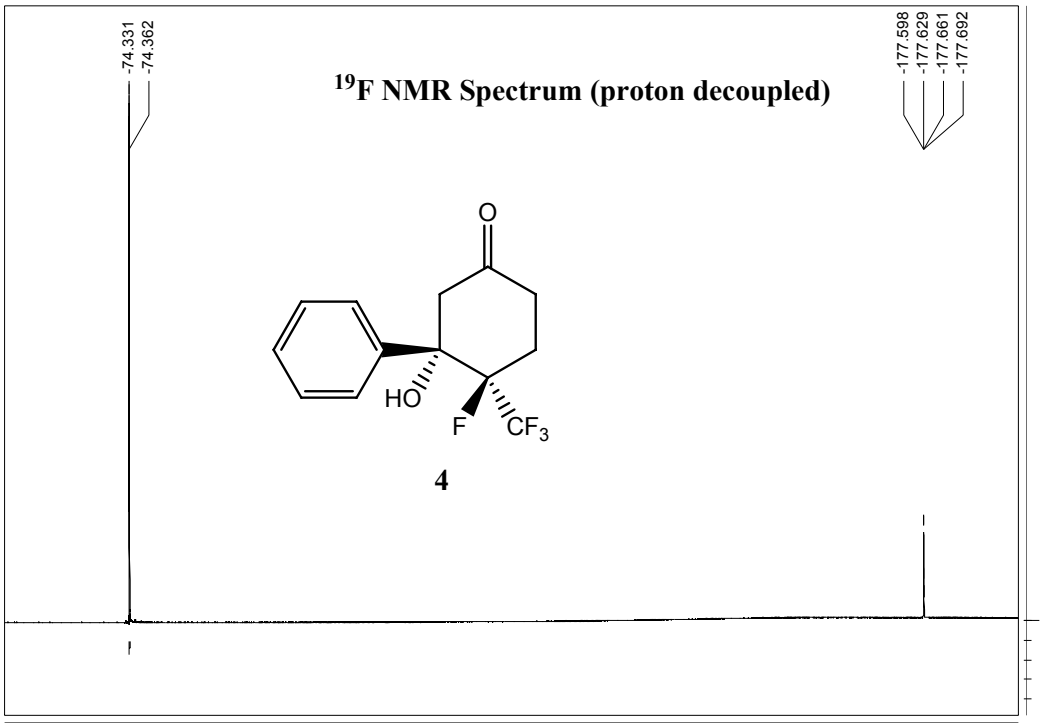
^{1}H NMR Spectrum

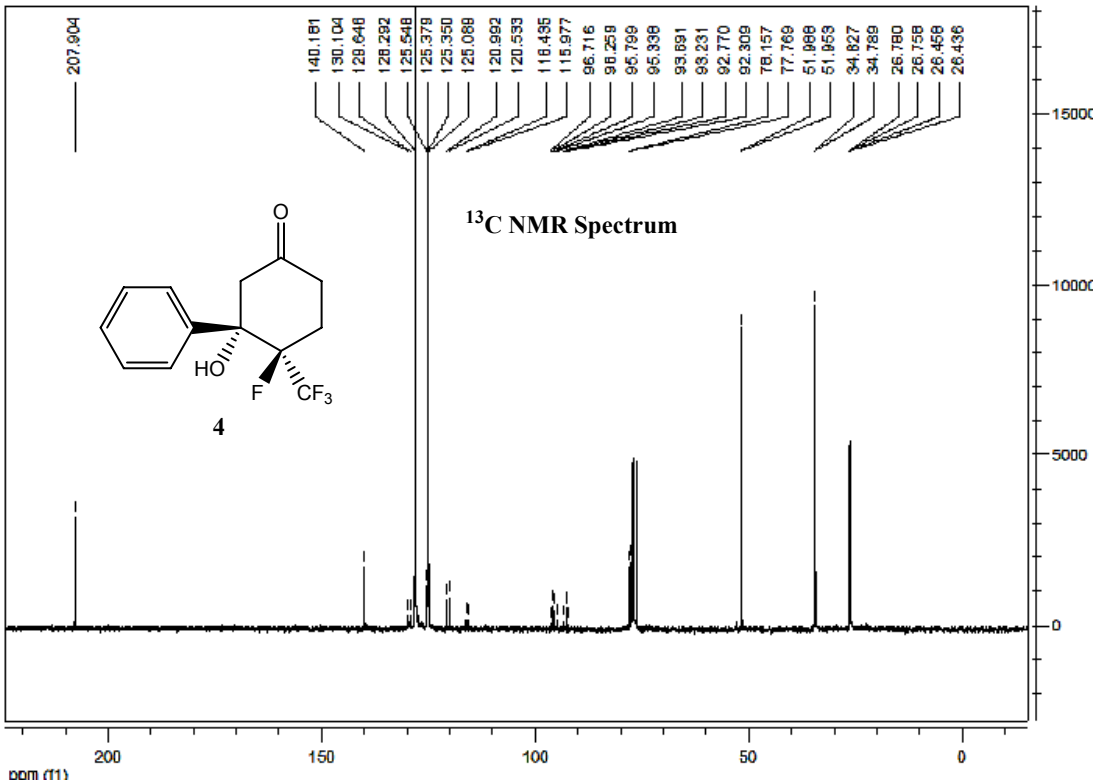
4

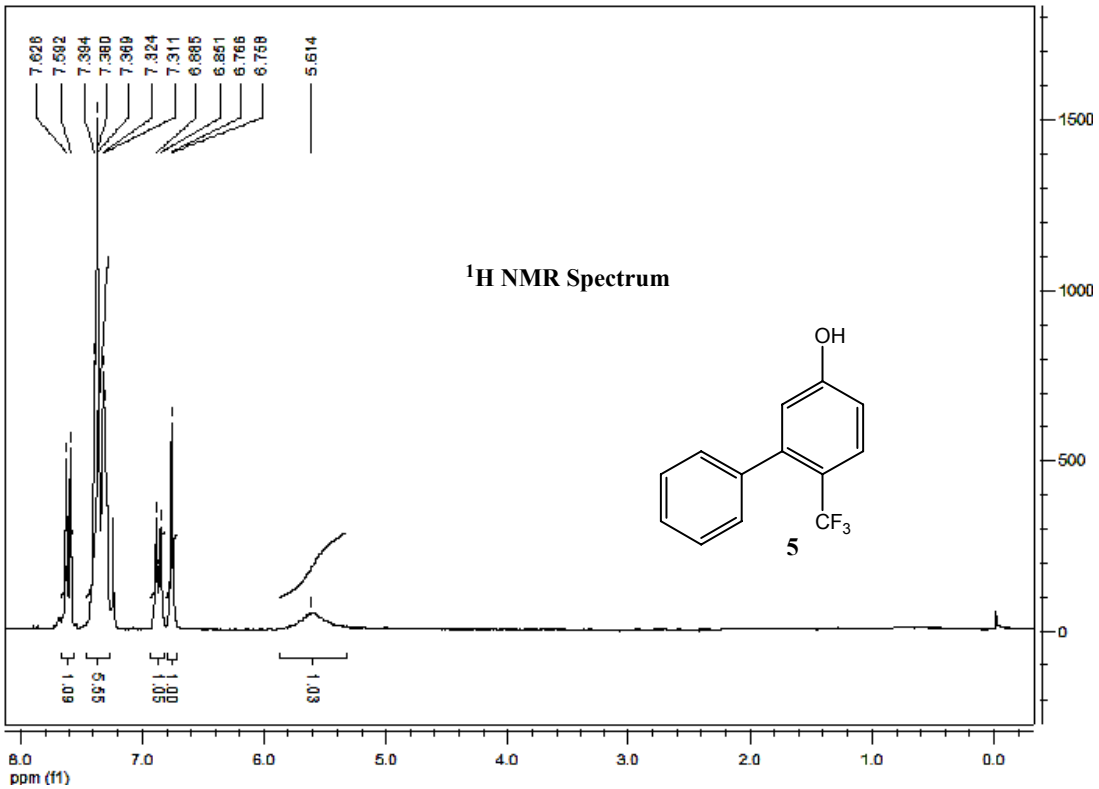


^{19}F NMR Spectrum

4

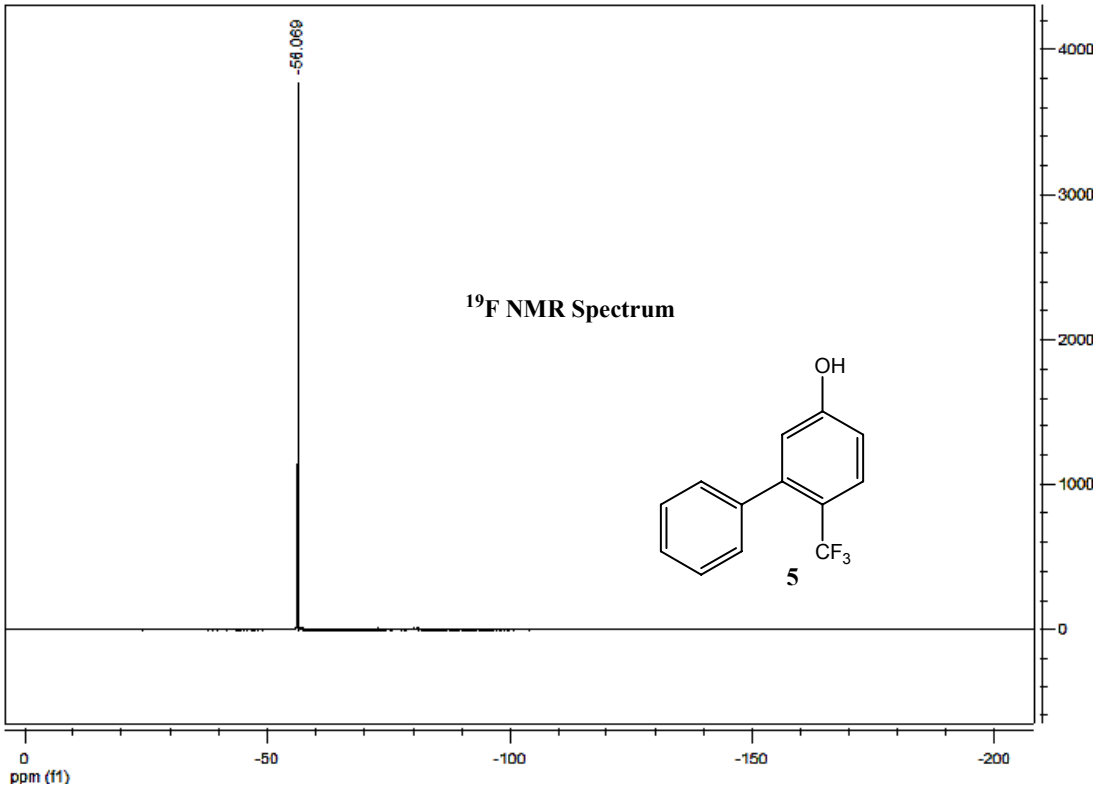

-74.331
-74.362
-177.598
-177.629
-177.661
-177.692
19F NMR Spectrum (proton decoupled)
O
HO
F
CF3
4


207.904
140.181
130.104
128.648
128.292
125.548
125.379
125.350
125.088
120.992
120.533
118.435
115.977
96.716
96.259
95.799
95.338
93.691
93.231
92.770
92.309
78.157
77.769
51.998
51.953
34.827
34.789
26.780
26.758
26.458
26.436
13C NMR Spectrum
O
HO
F
CF3
4
15000
10000
5000
0
200
150
100
50
0
ppm (f1)



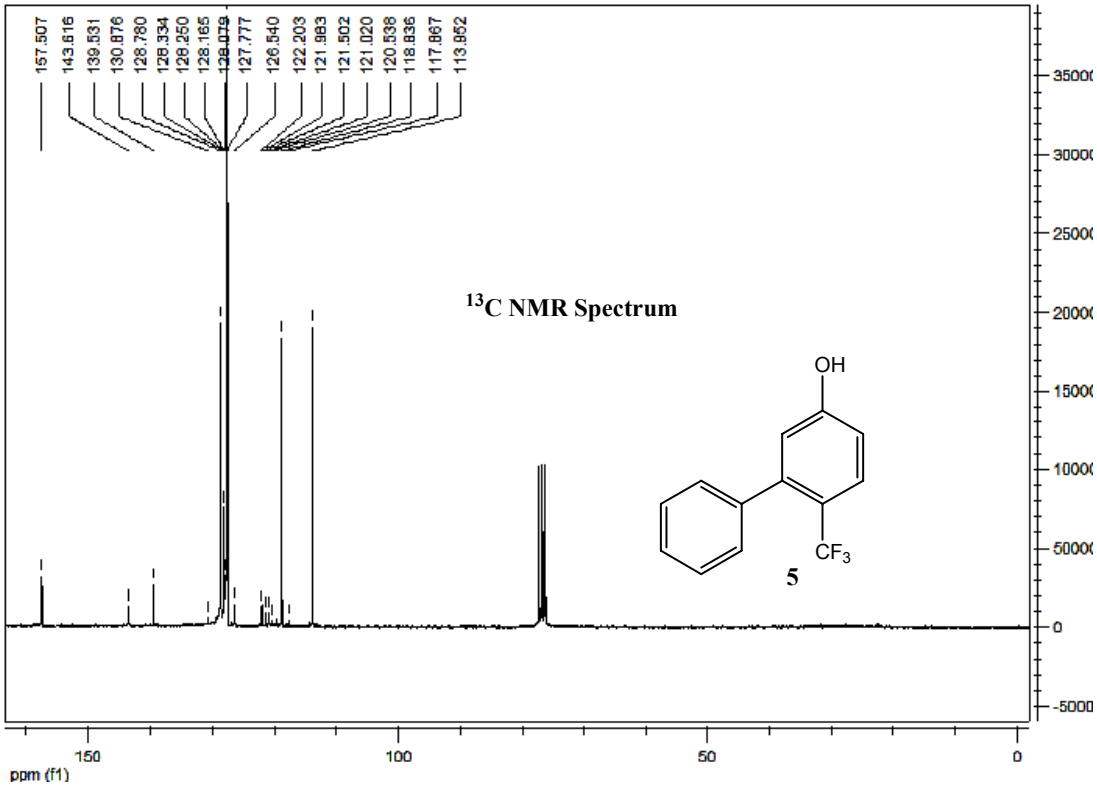
^{1}H NMR Spectrum

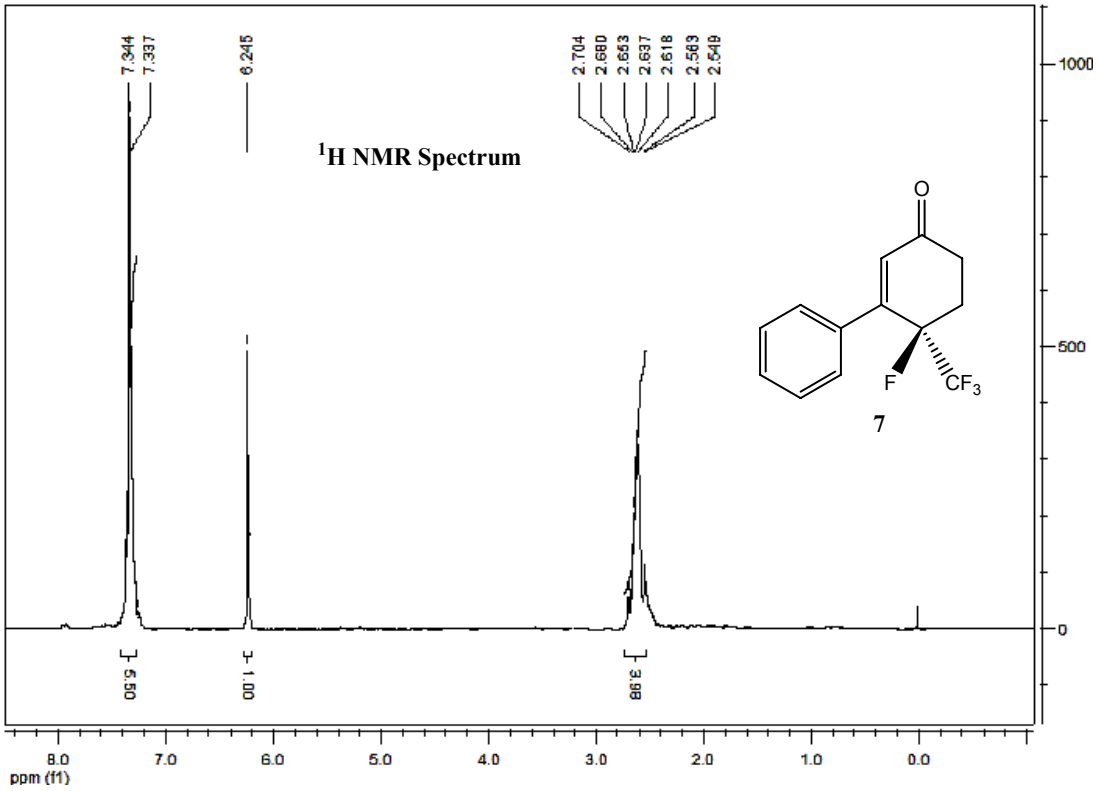
5



^{19}F NMR Spectrum

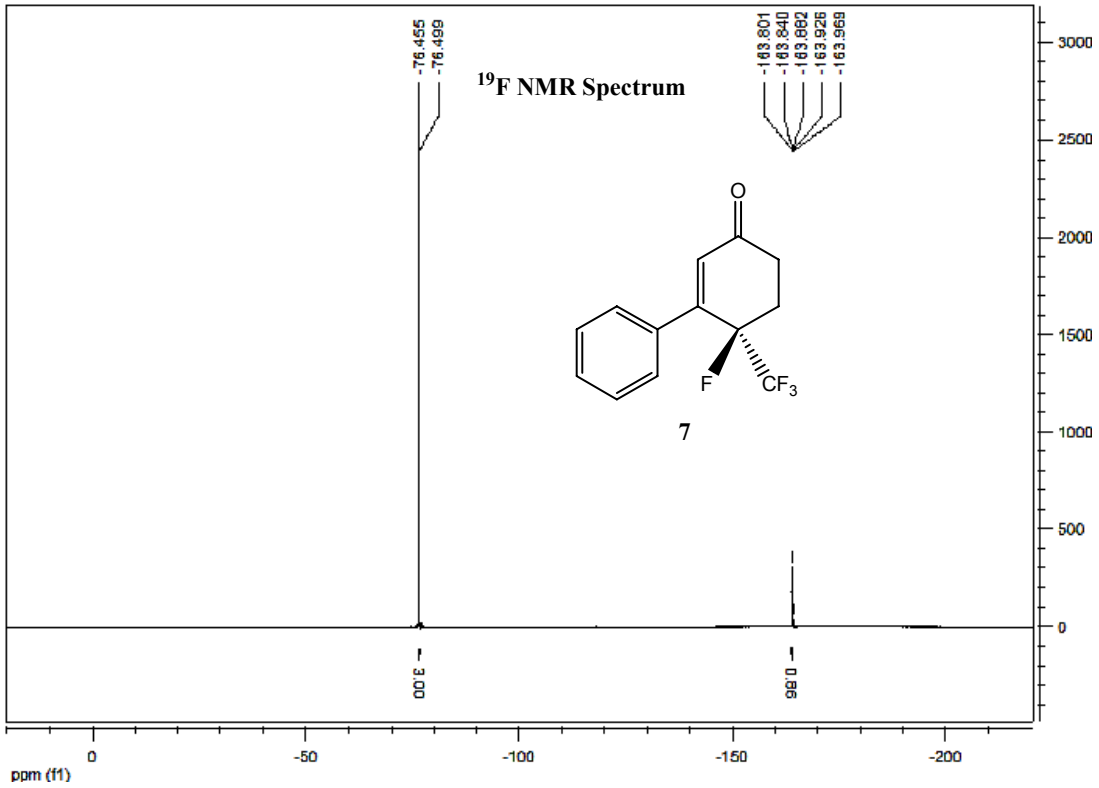
5


157.507
143.616
139.531
130.876
128.780
128.334
128.250
128.165
128.079
127.777
126.540
122.203
121.983
121.502
121.020
120.538
118.836
117.867
113.852
^{13}C NMR Spectrum
OH
CF3
5
35000
30000
25000
20000
15000
10000
5000
0
-5000
150
100
50
0
ppm (f1)



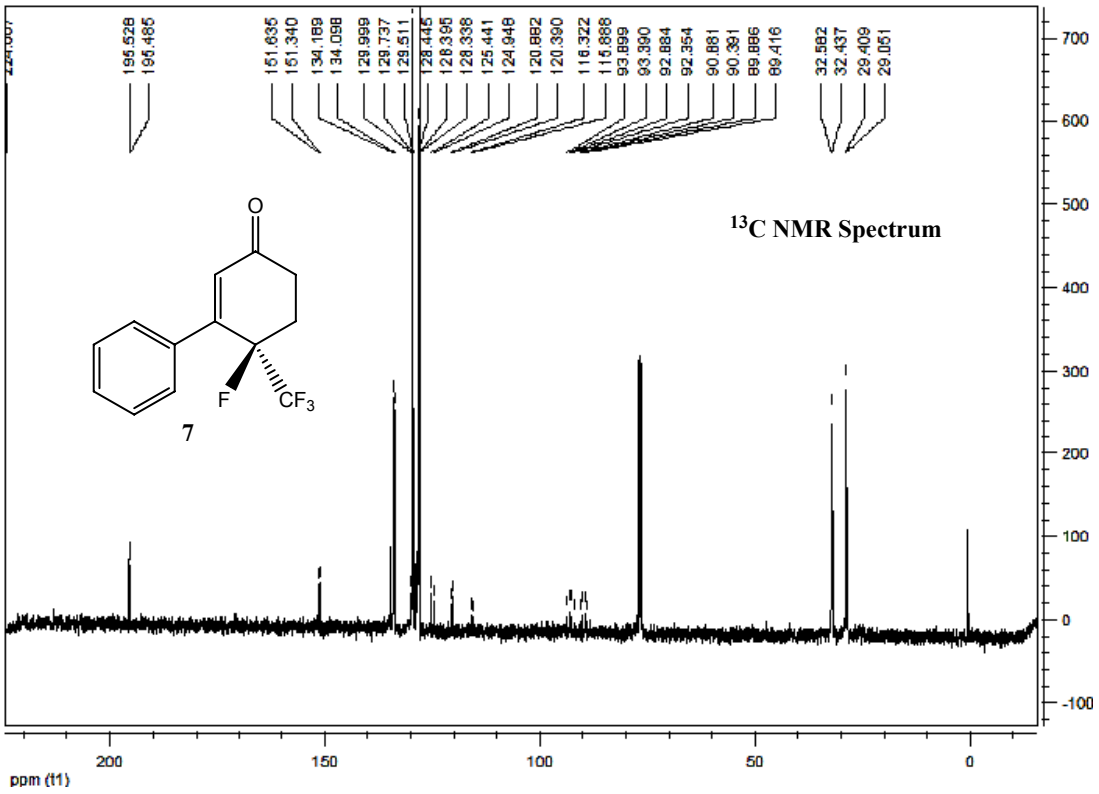
^{1}H NMR Spectrum

7

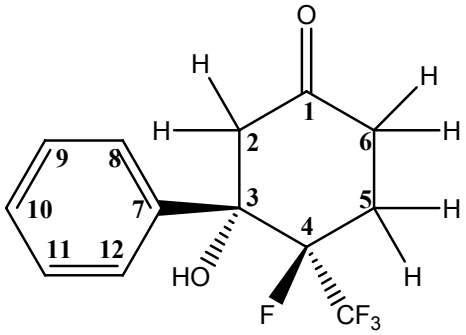


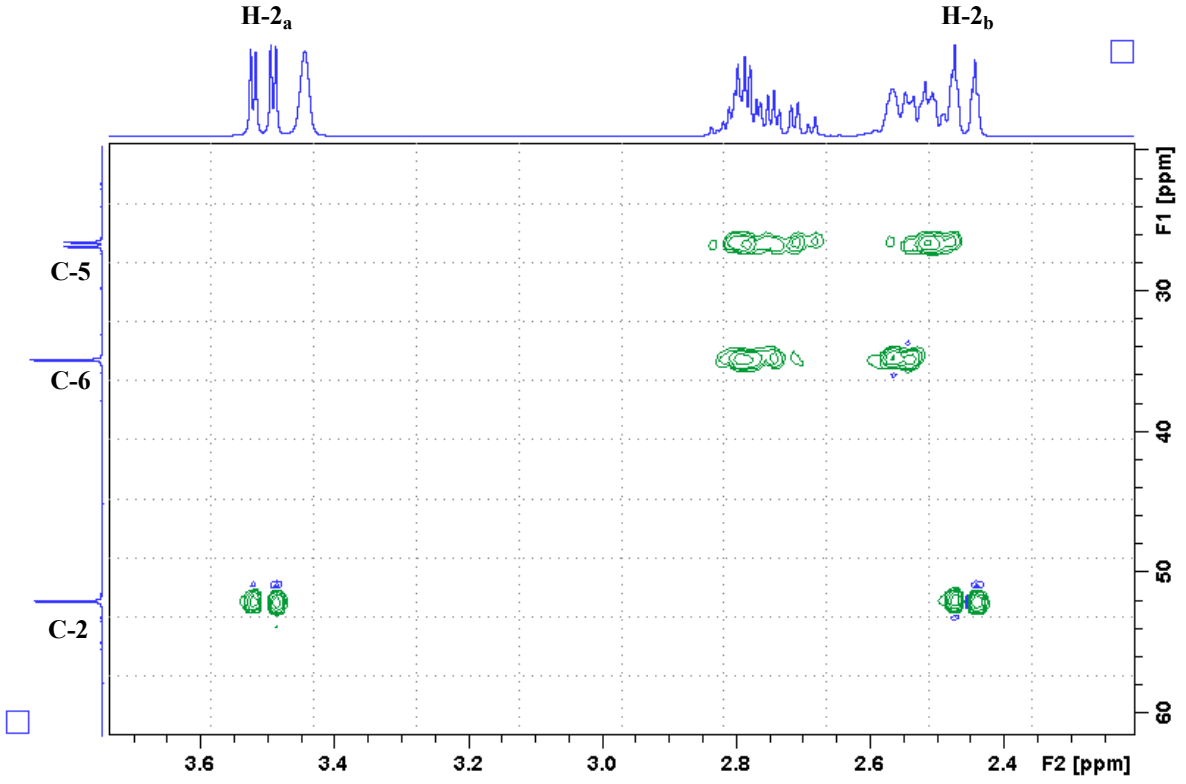
^{19}F NMR Spectrum

7

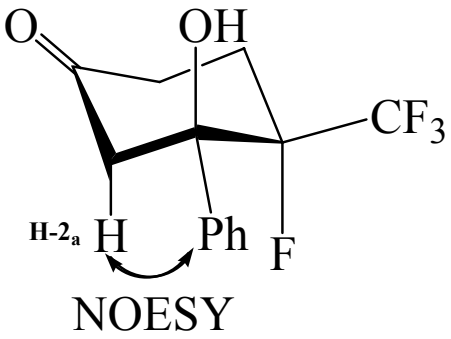

195.528
195.485
151.635
151.340
134.189
134.098
129.999
129.737
129.511
128.445
128.395
128.338
125.441
124.948
120.882
120.390
116.322
115.888
93.899
93.390
92.884
92.354
90.881
90.391
89.886
89.416
32.582
32.437
29.409
29.051
O
F
CF3
7
13C NMR Spectrum
700
600
500
400
300
200
100
0
-100
200
150
100
50
0
ppm (t1)

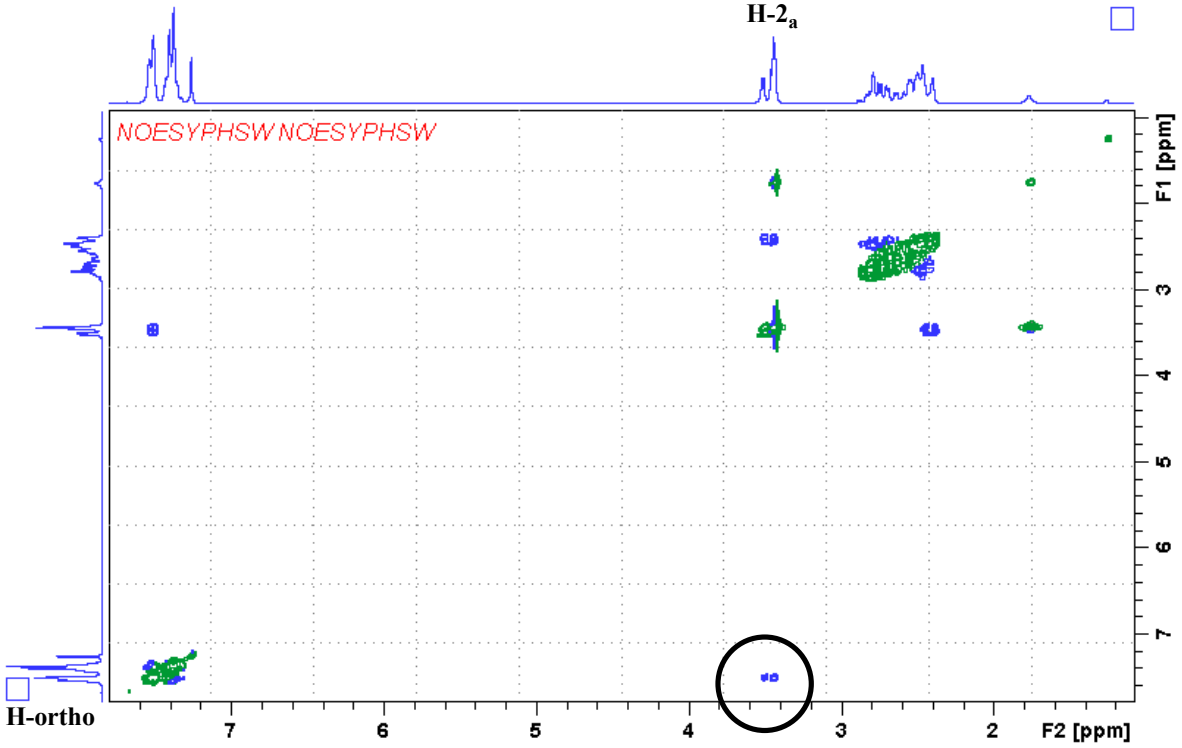
3. HSQC (Heteronuclear Single Quantum Correlation) ^{13}C-^{1}H spectrum of compound 4





4. NOESY (Nuclear Overhauser Effect SpectropscopY) ^{1}H-^{1}H spectrum of compound 4





5. HOESY (Heteronuclear Overhauser Effect SpectropscopY) ^{19}F-^{1}H spectrum of compound 4