Supporting Information

Divergent Synthesis of Photoaffinity Probe Candidates by Click Reactions of Azido-Substituted Aryltrifuloromethyldiazirines

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Contents

Chemicals

Dichloromethane (deoxygenated), dichloromethane (normal grade used for extraction), *N*,*N*-dimethylformamide (DMF, deoxygenated), diethyl ether (super dehydrated), tetrahydrofuran (THF, deoxygenated), acetonitrile (MeCN, super dehydrated), methanol (MeOH, deoxygenated), dimethylsulfoxide (DMSO, super dehydrated), *n*-hexane, ultrapure water, and sodium azide were purchased from Wako Pure Chemical Industries.

Ethyl acetate (EtOAc), chloroform ($CHCl_3$), methanesulfonyl chloride, triethylamine, silver(I) oxide, Celite® (545RVS), copper(II) sulfate pentahydrate ($CuSO_4 \cdot 5H_2O$), L-ascorbic acid sodium salt, phenylacetylene, cesium fluoride, potassium carbonate, 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), acetylacetone, triphenylphosphine (PPh_3), ethanol, lithium chloride, *N*,*N*-diisopropylethylamine, trifluoroacetic acid (TFA), sodium hydrogen carbonate, sodium sulfate and dibromomethane were purchased from Nacalai Tesque, Inc.

(4-(3-(Trifluoromethyl)-3*H*-diazirin-3-yl)phenyl)methanol (**1**), 4-(3-(trifluoromethyl)-3*H*-diazirin-3-yl)benzoic acid (**4**), tetrabutylammonium iodide, 1-phenyl-1-propyne, diethyl acetylenedicarboxylate, tris((1-benzyl-1*H*-1,2,3-triazol-4-yl)methyl)amine (TBTA), 3-phenyl-1-propyne, 2-(trimethylsilyl)phenyl trifluoromethanesulfonate, lithium aluminum hydride (LAH), sodium borohydride, tributylphosphine (P^nBu_3), 1-(bis(dimethylamino)methylene)-1*H*-1,2,3-triazolo[4,5-*b*]pyridinium 3-oxide hexafluorophosphate (HATU), and methyl trifluoroacetate were purchased from Tokyo Chemical Industry.

N,*N*-Di(*p*-toluenesulfonyl)-4,8-diazacyclononyne was purchased from Kanto Chemical.

α,α,α-Trifluorotoluene, tributylphosphine tetrafluoroborate, 4-ethynyl-*N*,*N*-dimethylaniline (**21**), and dimethoxyethane (DME, anhydrous) were purchased from Sigma–Aldrich Japan.

Phenylacetaldehyde was purchased from Alfa Aesar.

(*R*)-2-((*tert*-Butoxycarbonyl)amino)pent-4-ynoic acid (**27**) was purchased from Acros Organics.

Palladium−charcoal (Pd/C, 10 wt %, wetted with water (51 wt %)) was purchased from N.E. CHEMCAT Corp.

NMR spectra for photoreactions of 11 and 13 (Figure 2A)

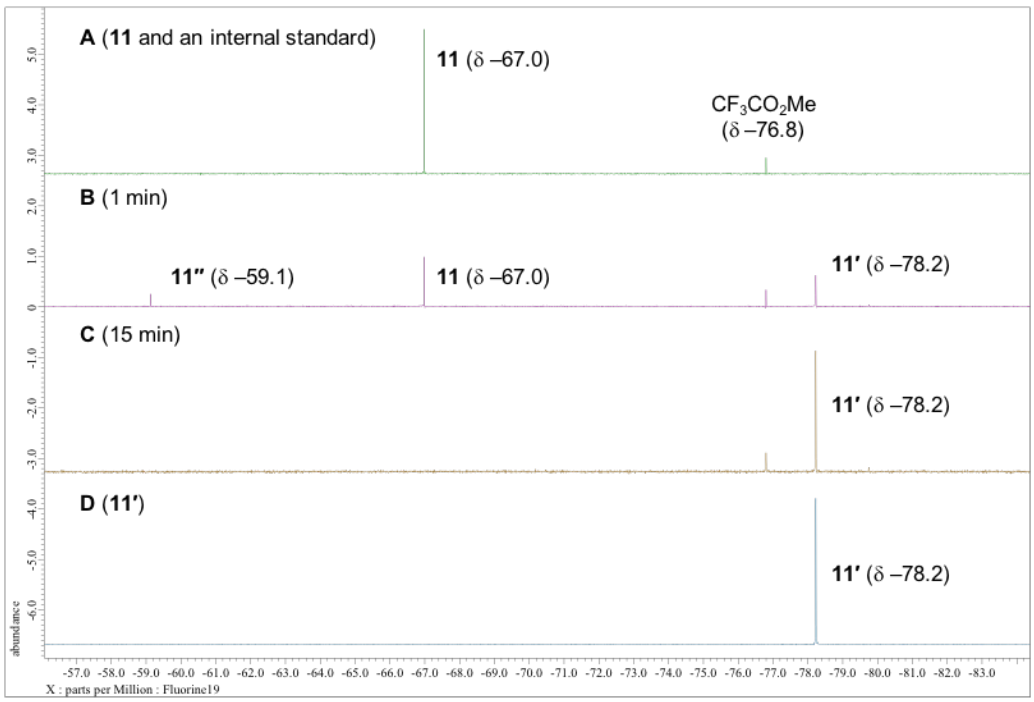


Figure S1. ^{19}F NMR spectra of **11** (1 mM) and CF_3CO_2Me in methanol-d_4 (**A**), photoreaction mixture after 1 min irradiation (**B**), photoreaction mixture after 15 min (**C**), and authentic **11′** in methanol-d_4 (**D**).

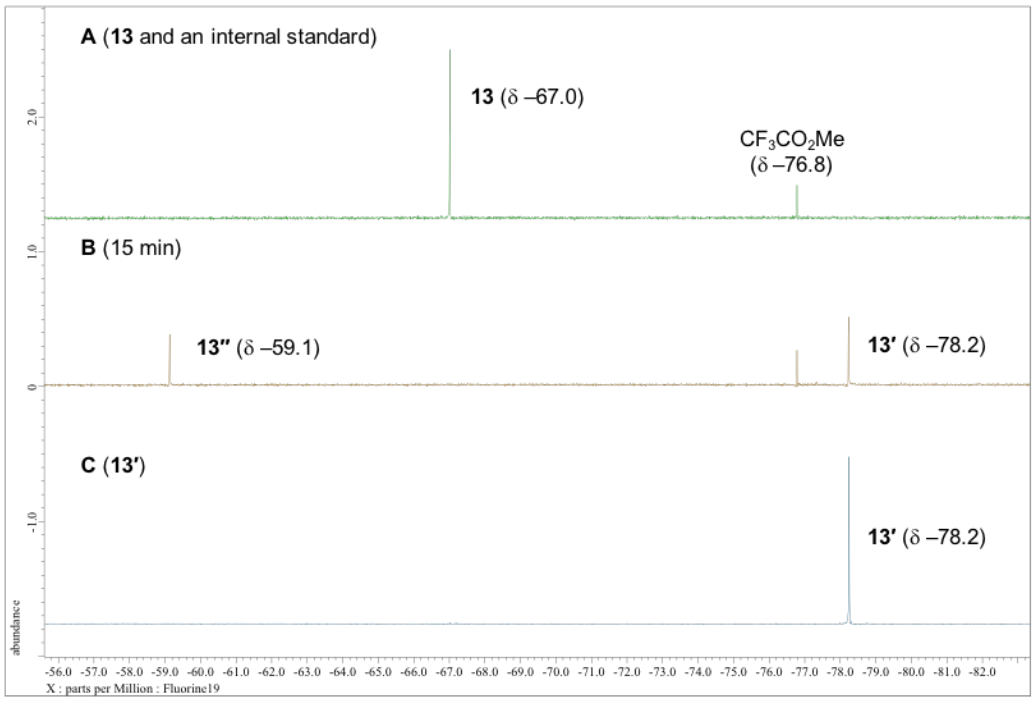
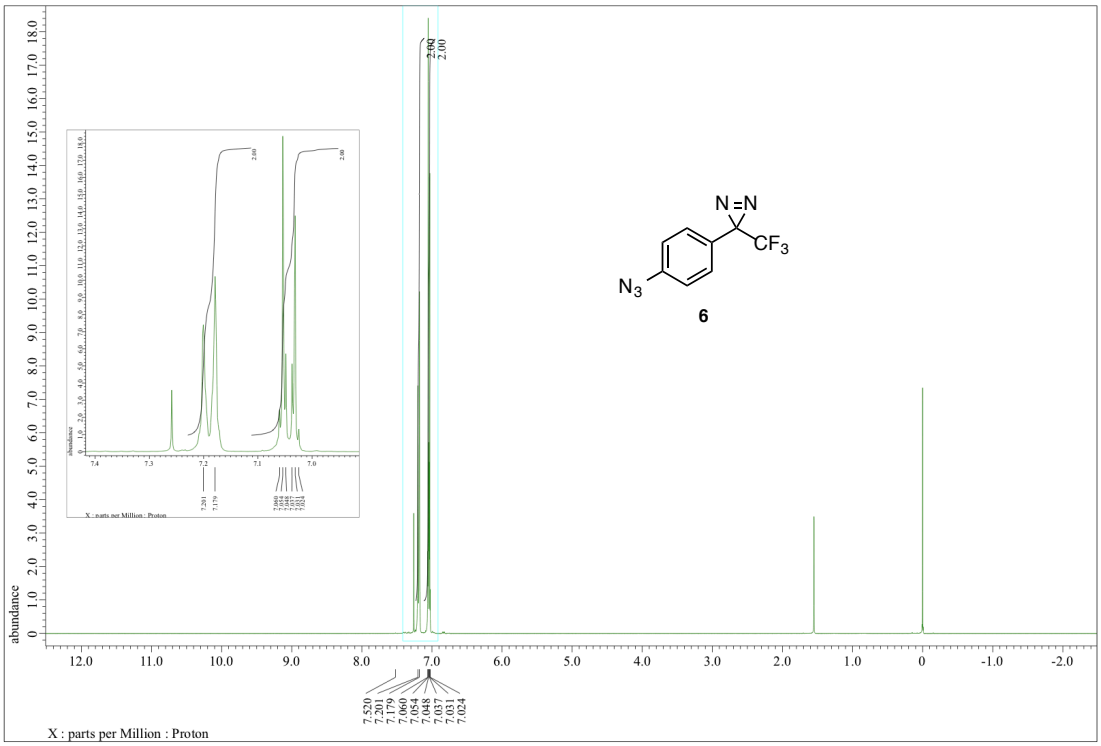
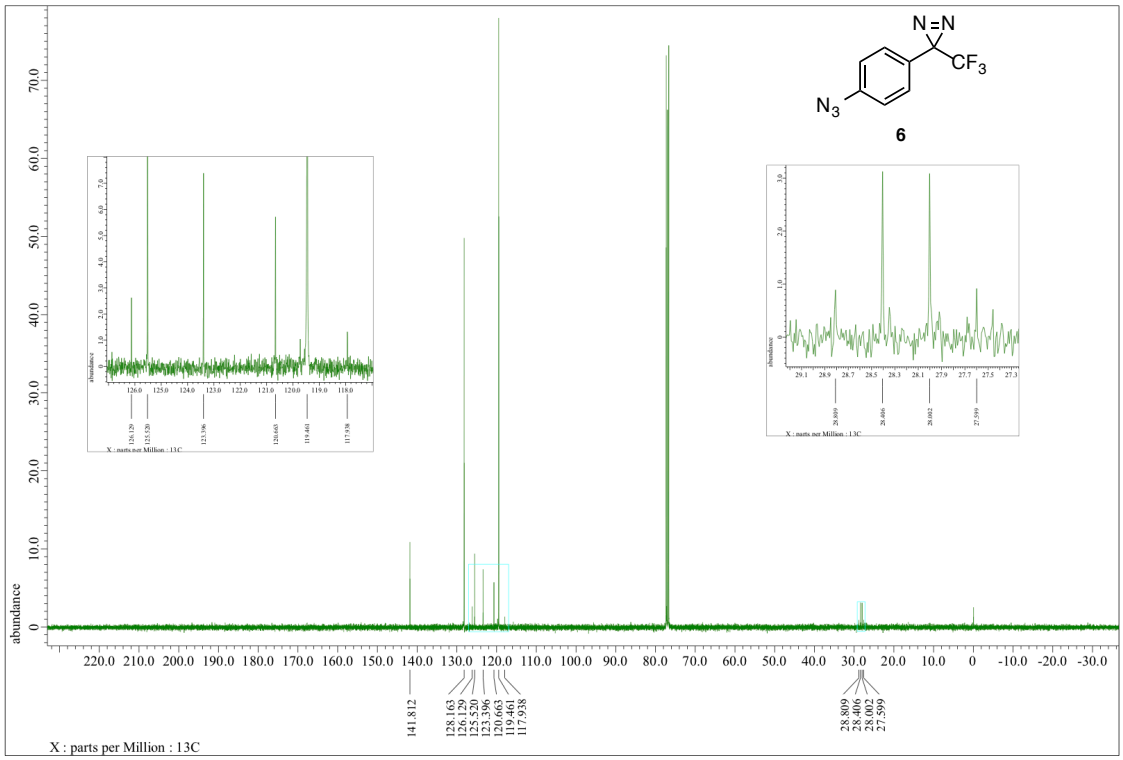


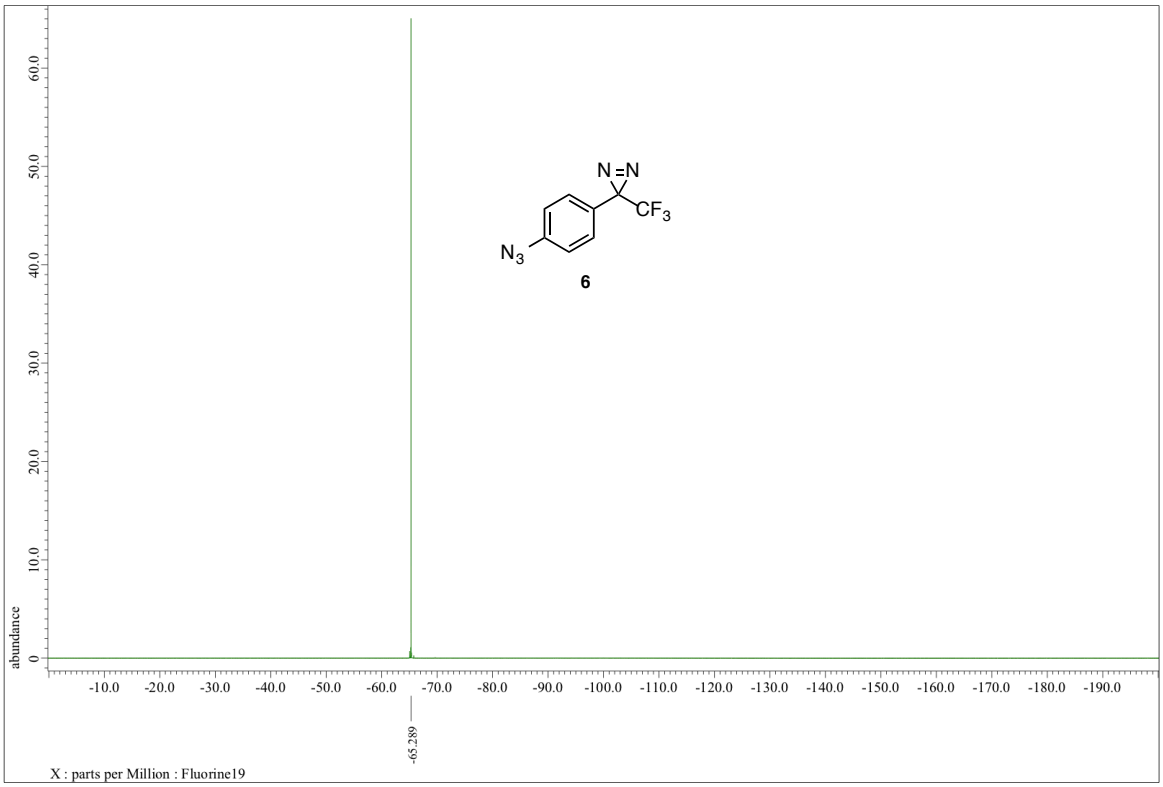
Figure S2. ^{19}F NMR spectra of **13** (1 mM) and CF_3CO_2Me in methanol-d_4 (**A**), photoreaction mixture after 15 min irradiation (**B**), and authentic **13′** in methanol-d_4 (**C**).

NMR spectra

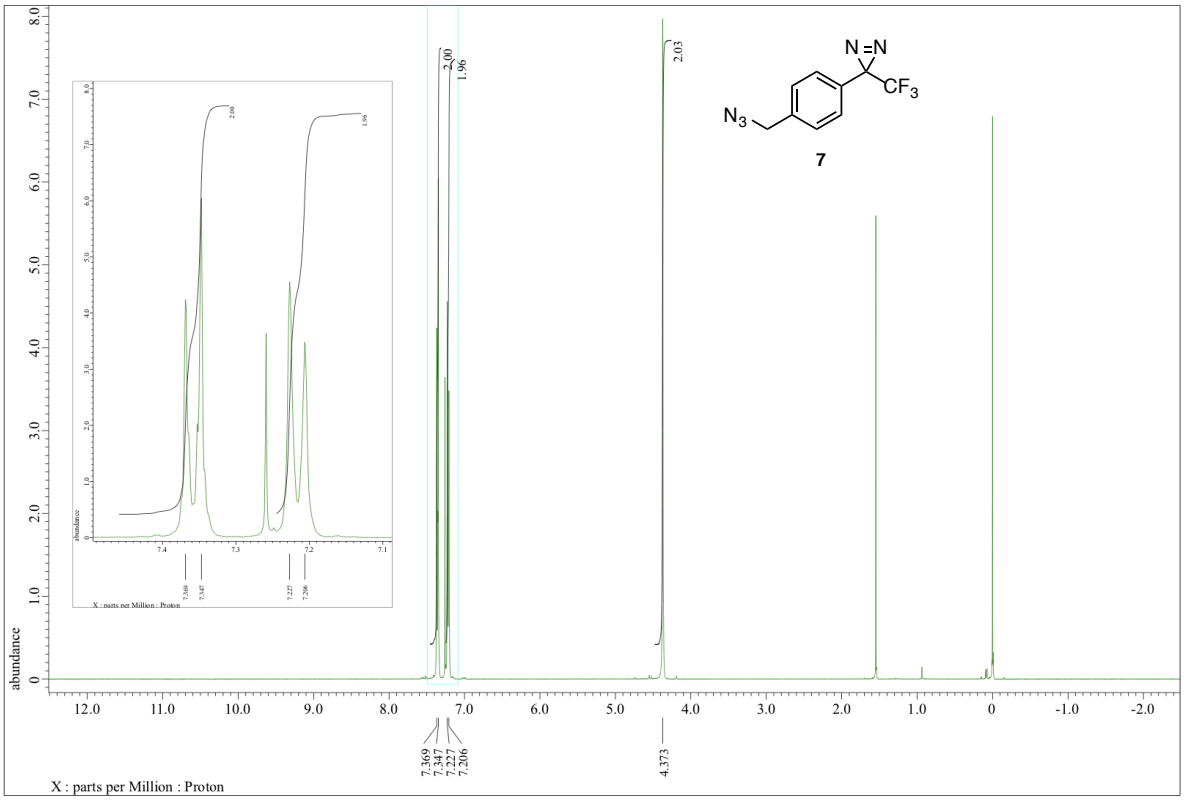
^{1}H, ^{13}C, and ^{19}F NMR spectra of **6** ($CDCl_3$)

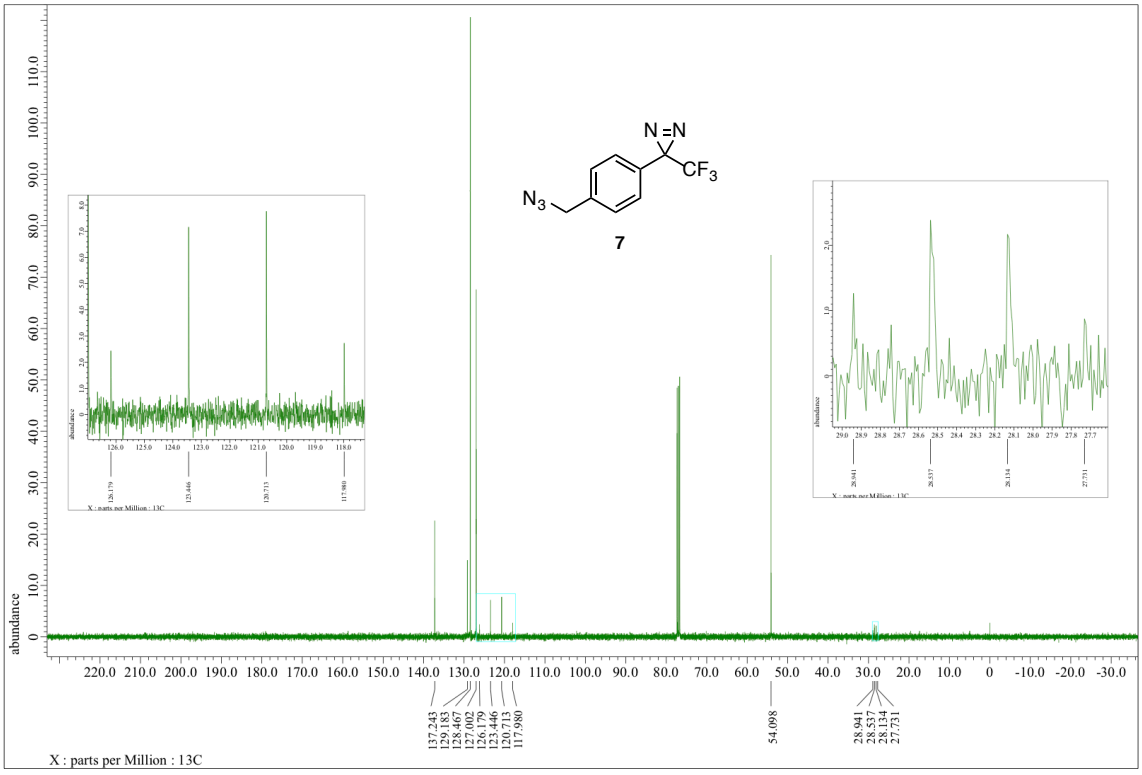


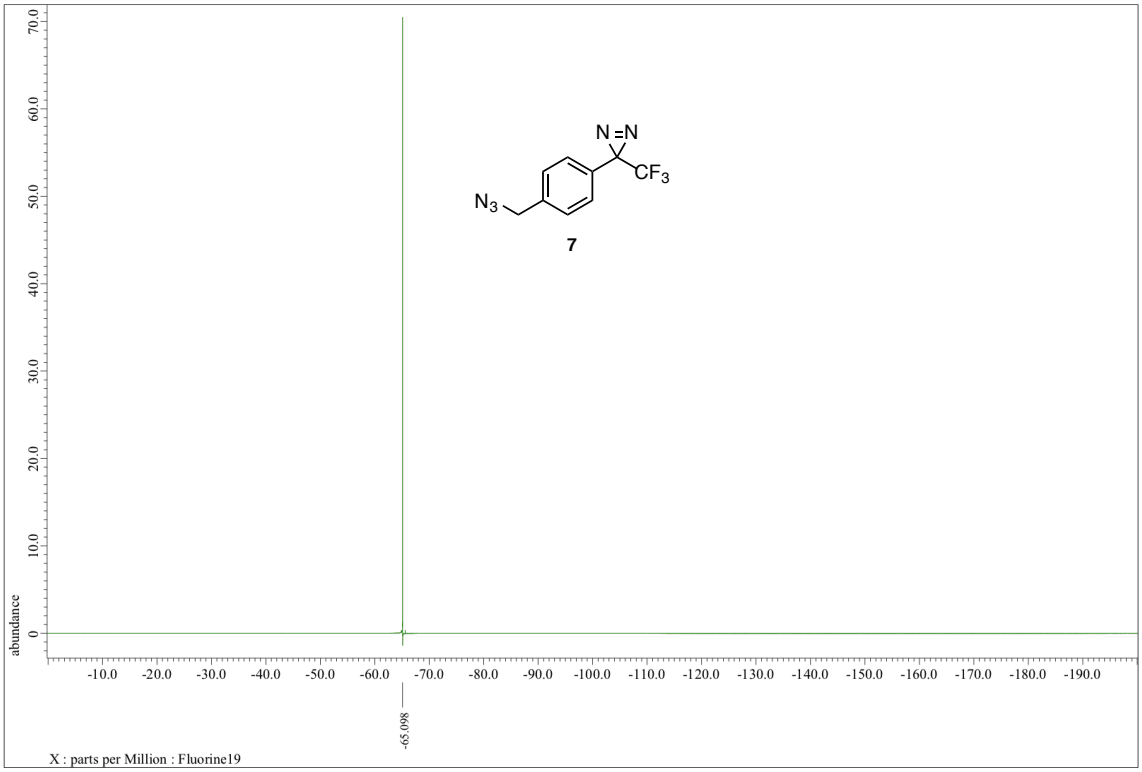



N=N
CF3
N3
6
abundance
60.0
50.0
40.0
30.0
20.0
10.0
0
-10.0 -20.0 -30.0 -40.0 -50.0 -60.0 -70.0 -80.0 -90.0 -100.0 -110.0 -120.0 -130.0 -140.0 -150.0 -160.0 -170.0 -180.0 -190.0
-65.289
X : parts per Million : Fluorine19

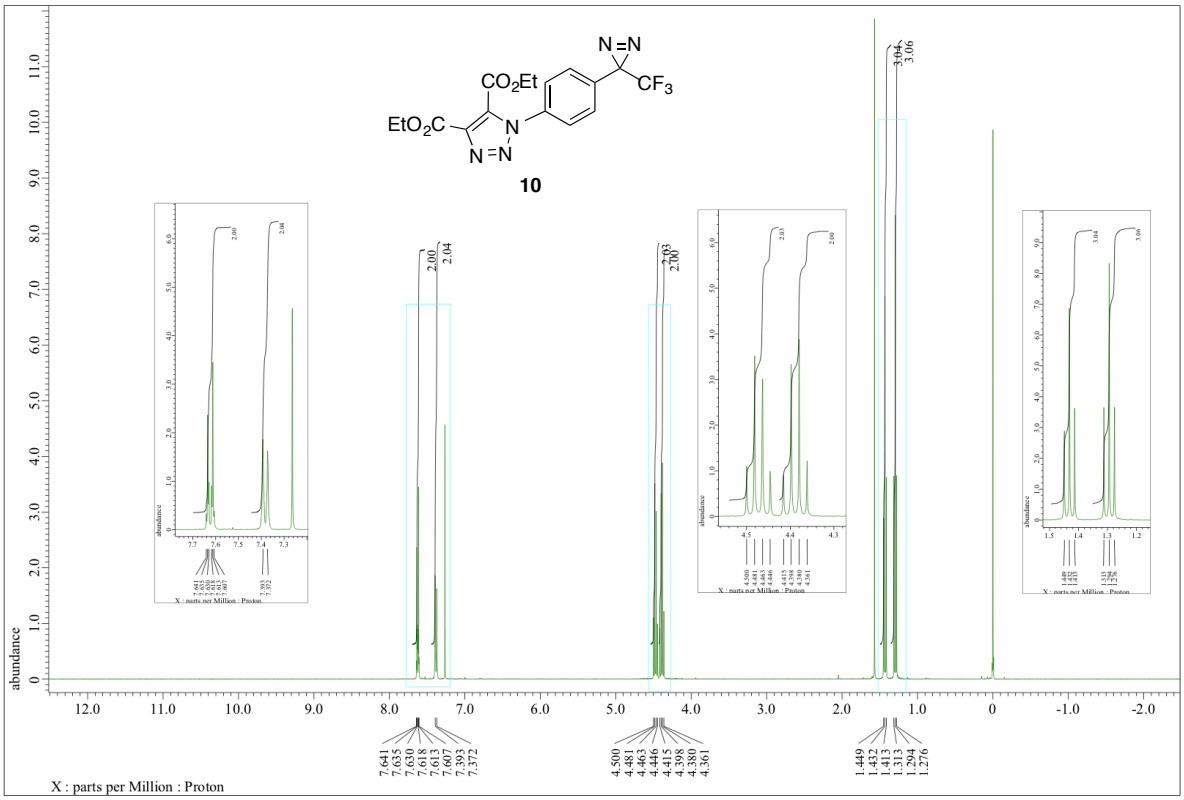
^{1}H, ^{13}C, and ^{19}F NMR spectra of **7** ($CDCl_3$)

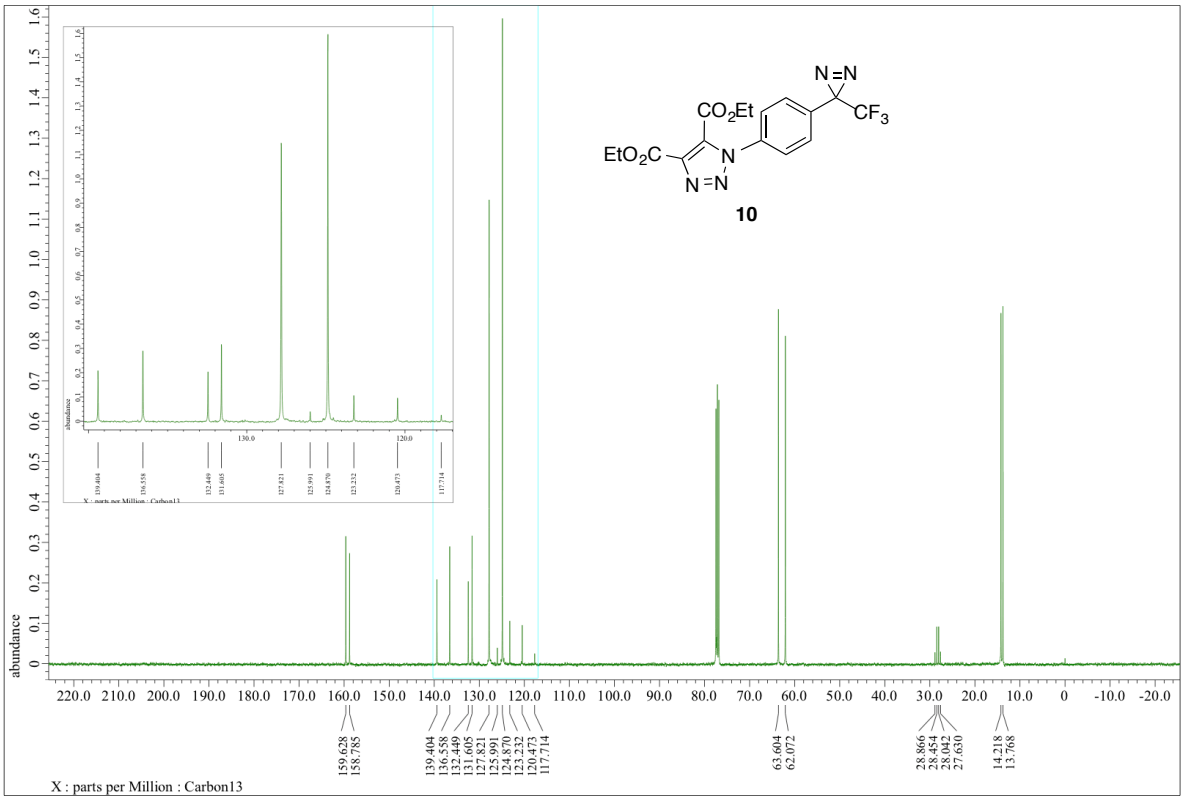


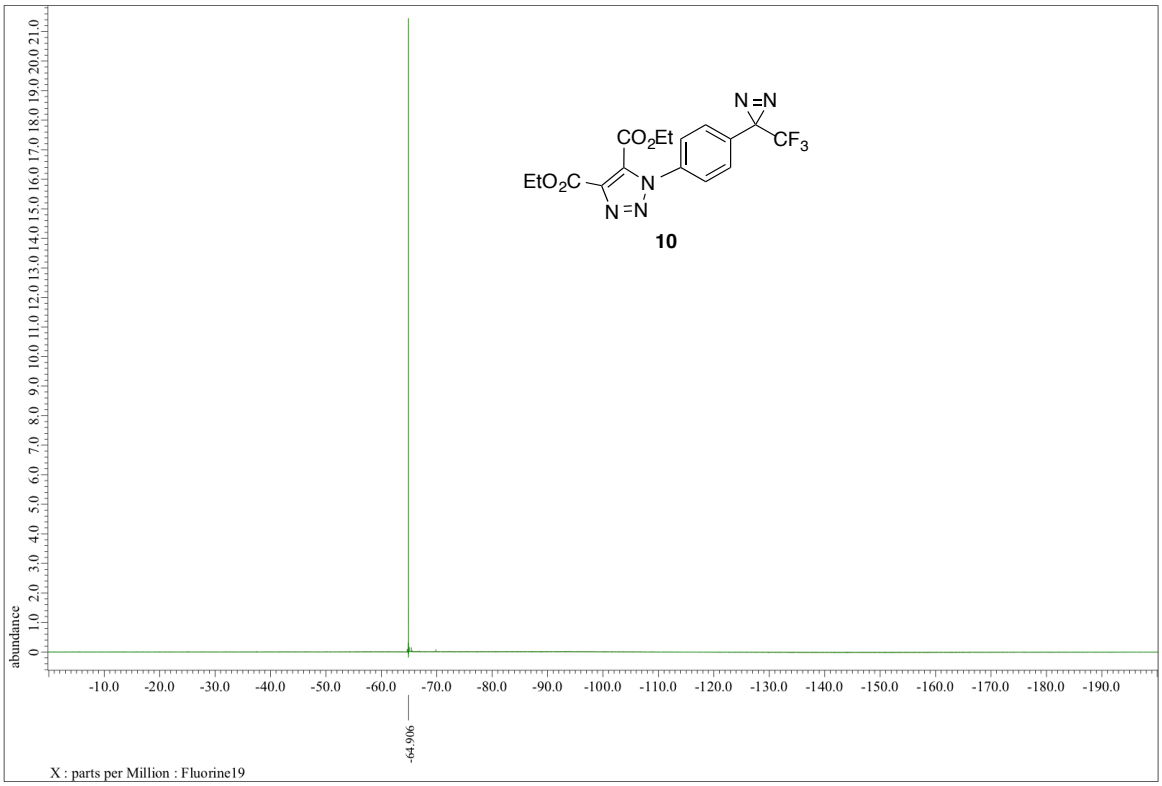



N=N
CF3
N3
7
abundance
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
-10.0 -20.0 -30.0 -40.0 -50.0 -60.0 -70.0 -80.0 -90.0 -100.0 -110.0 -120.0 -130.0 -140.0 -150.0 -160.0 -170.0 -180.0 -190.0
-65.098
X : parts per Million : Fluorine19

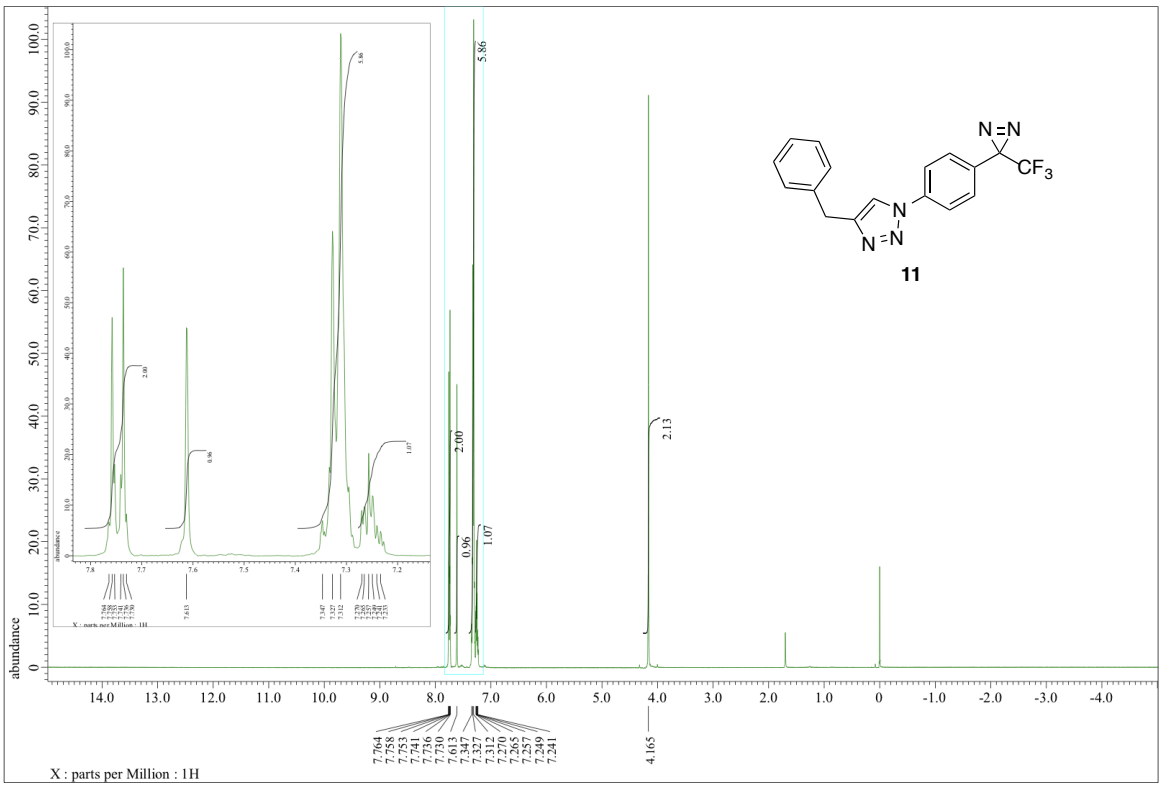
^{1}H, ^{13}C, and ^{19}F NMR spectra of **10** ($CDCl_3$)

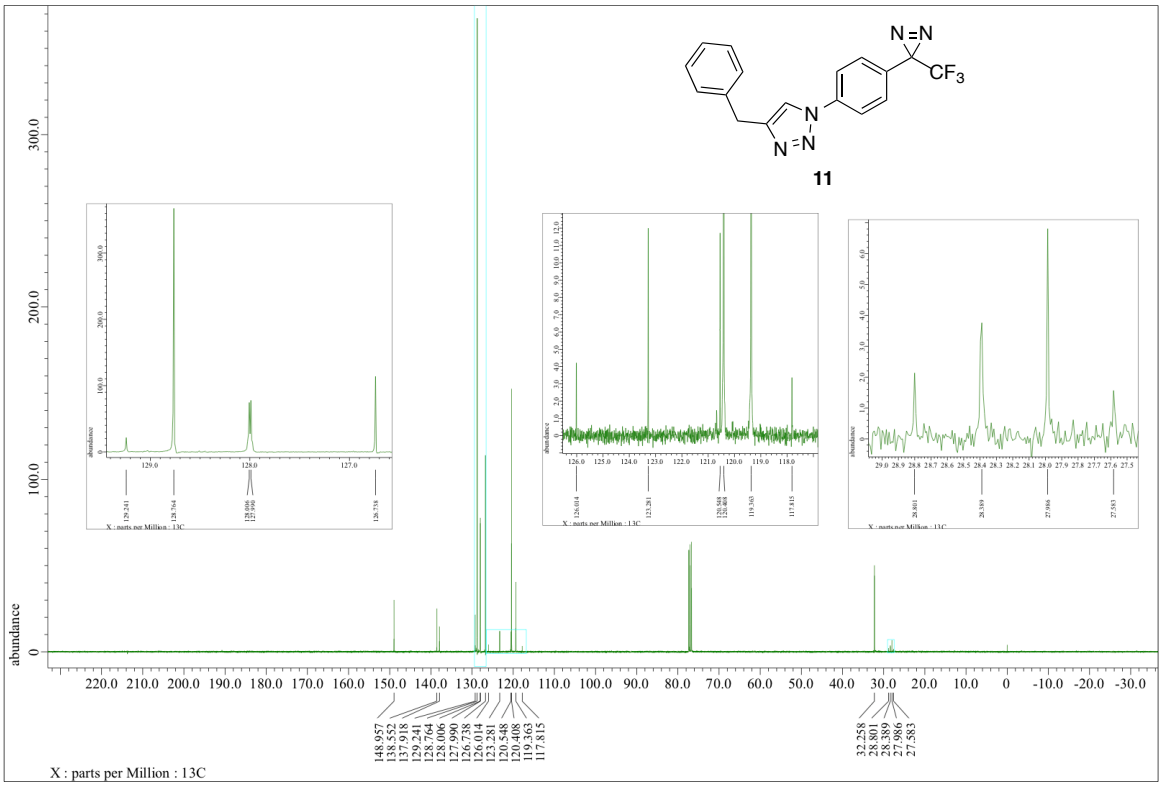


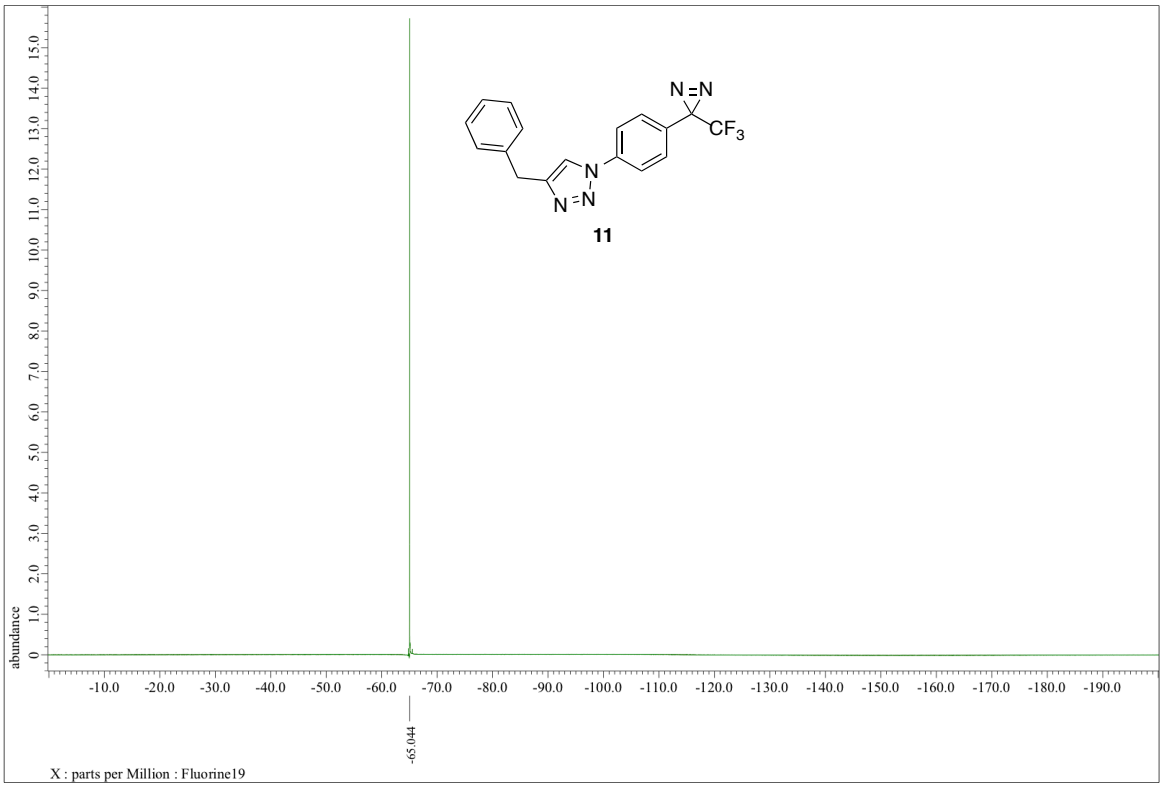



N=N
CO2Et
CF3
EtO2C
N
N=N
10
abundance
0 1.0 2.0 3.0 4.0 5.0 6.0 7.0 8.0 9.0 10.0 11.0 12.0 13.0 14.0 15.0 16.0 17.0 18.0 19.0 20.0 21.0
-10.0 -20.0 -30.0 -40.0 -50.0 -60.0 -70.0 -80.0 -90.0 -100.0 -110.0 -120.0 -130.0 -140.0 -150.0 -160.0 -170.0 -180.0 -190.0
-64.906
X : parts per Million : Fluorine19

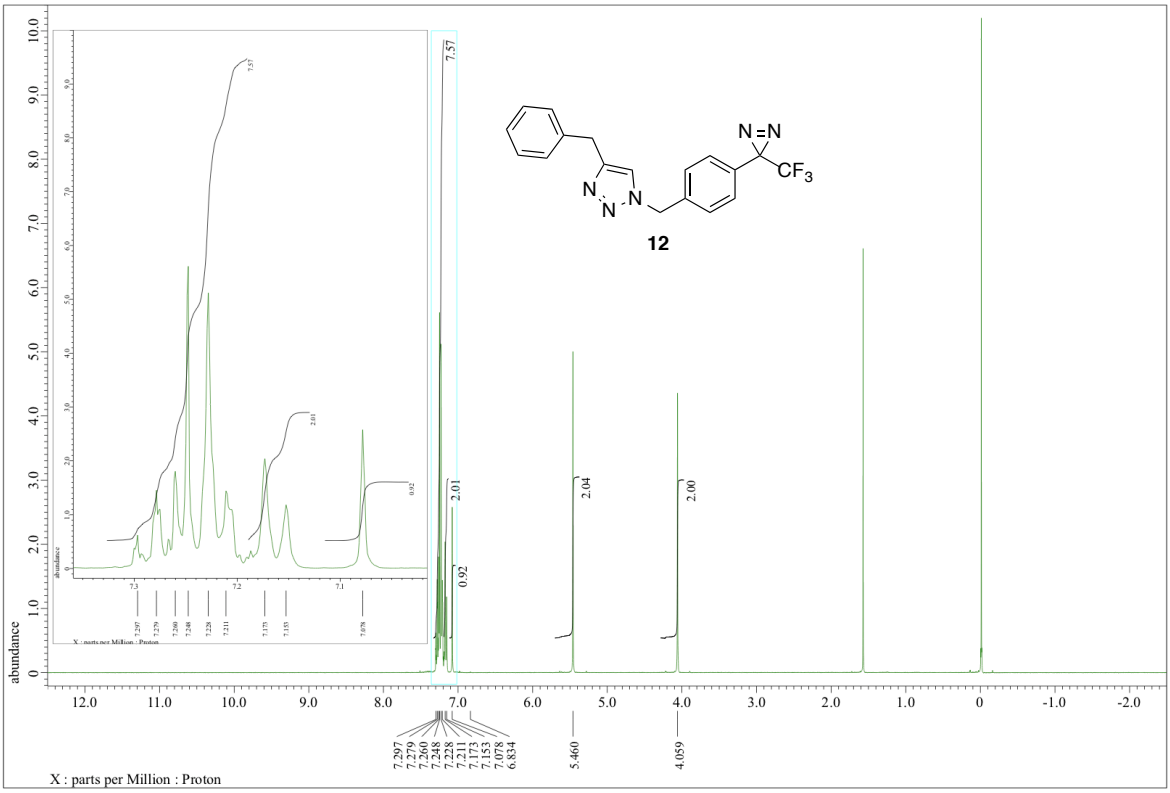
^{1}H, ^{13}C, and ^{19}F NMR spectra of **11** ($CDCl_3$)

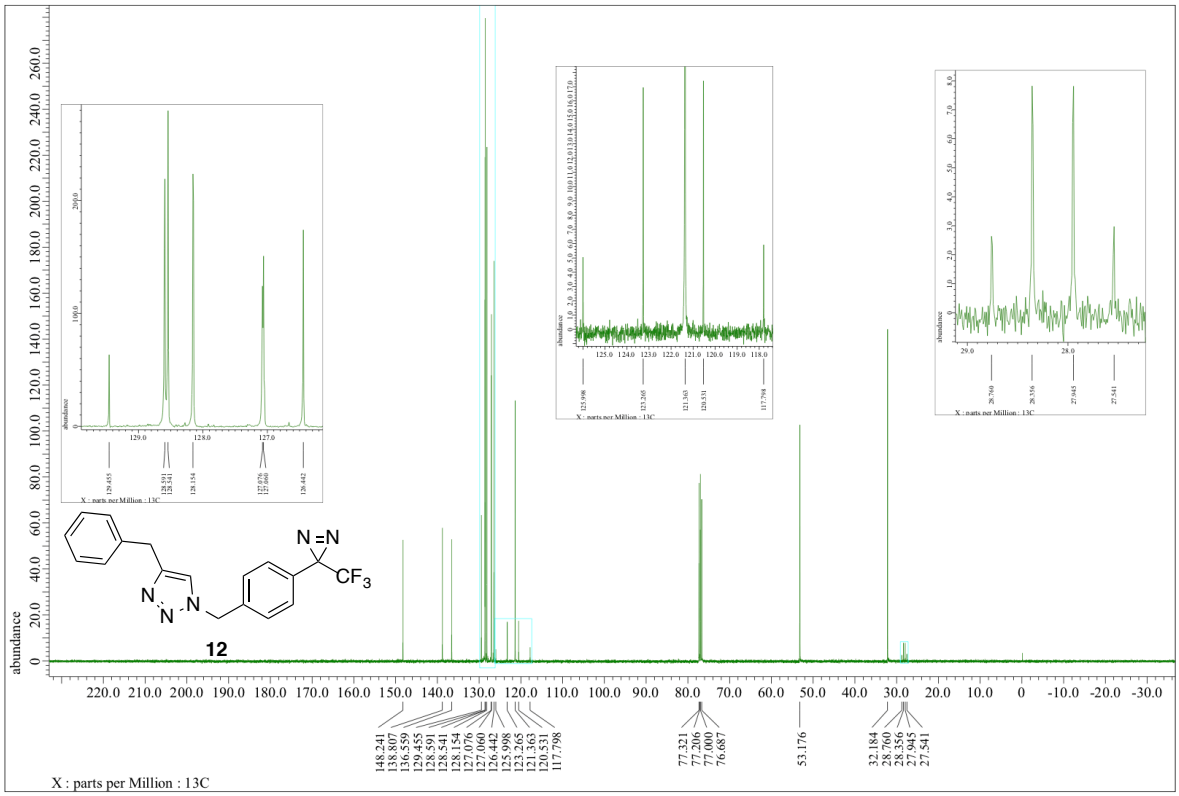


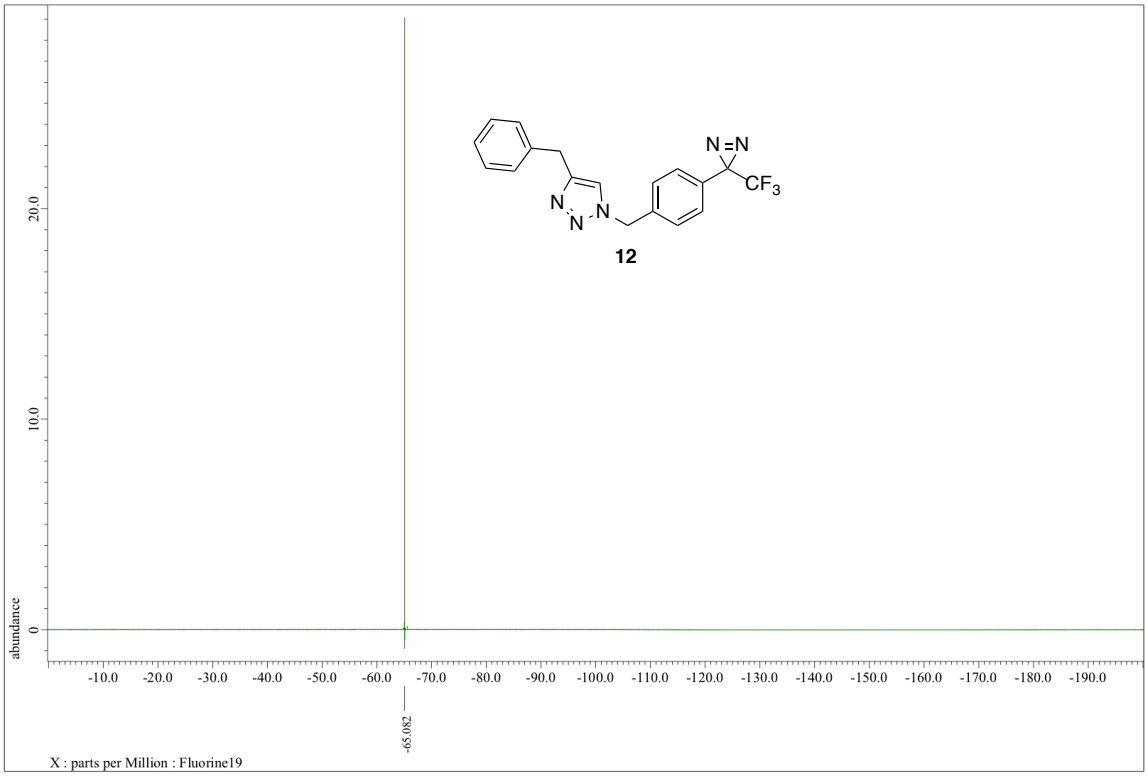



N=N
CF3
N
N=N
11
abundance
0
1.0
2.0
3.0
4.0
5.0
6.0
7.0
8.0
9.0
10.0
11.0
12.0
13.0
14.0
15.0
-10.0
-20.0
-30.0
-40.0
-50.0
-60.0
-70.0
-80.0
-90.0
-100.0
-110.0
-120.0
-130.0
-140.0
-150.0
-160.0
-170.0
-180.0
-190.0
-65.044
X : parts per Million : Fluorine19

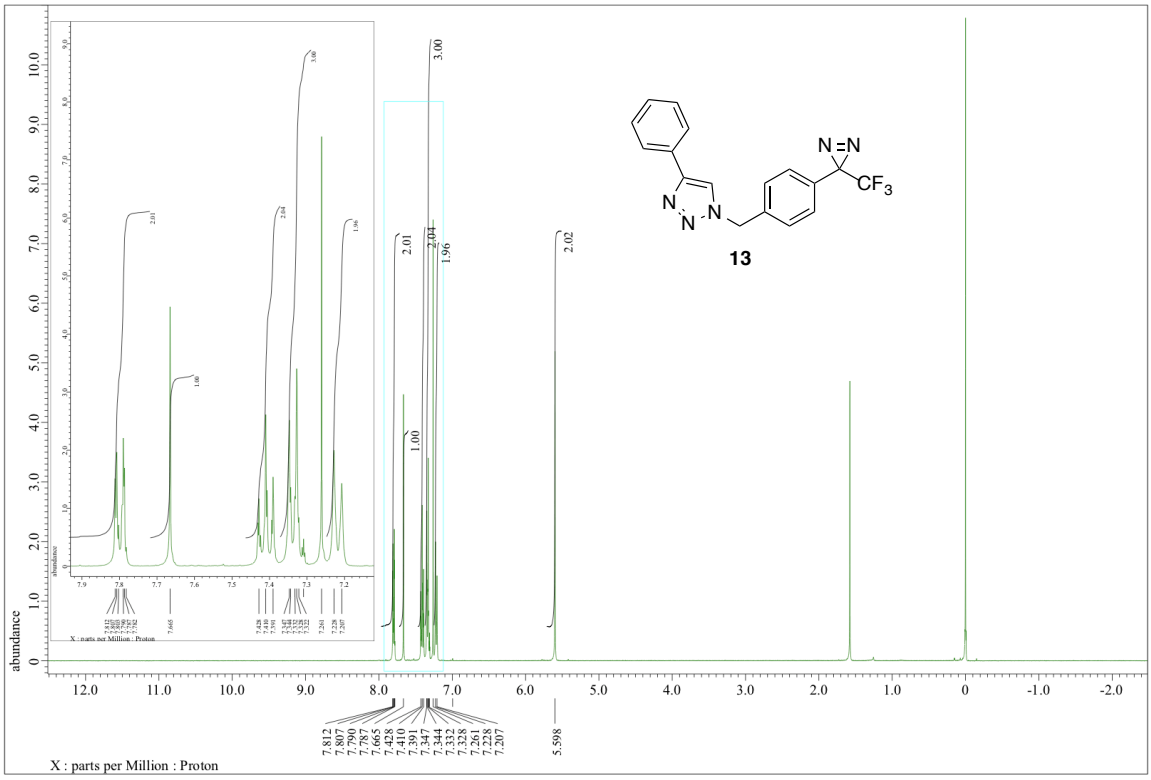
^{1}H, ^{13}C, and ^{19}F NMR spectra of **12** ($CDCl_3$)

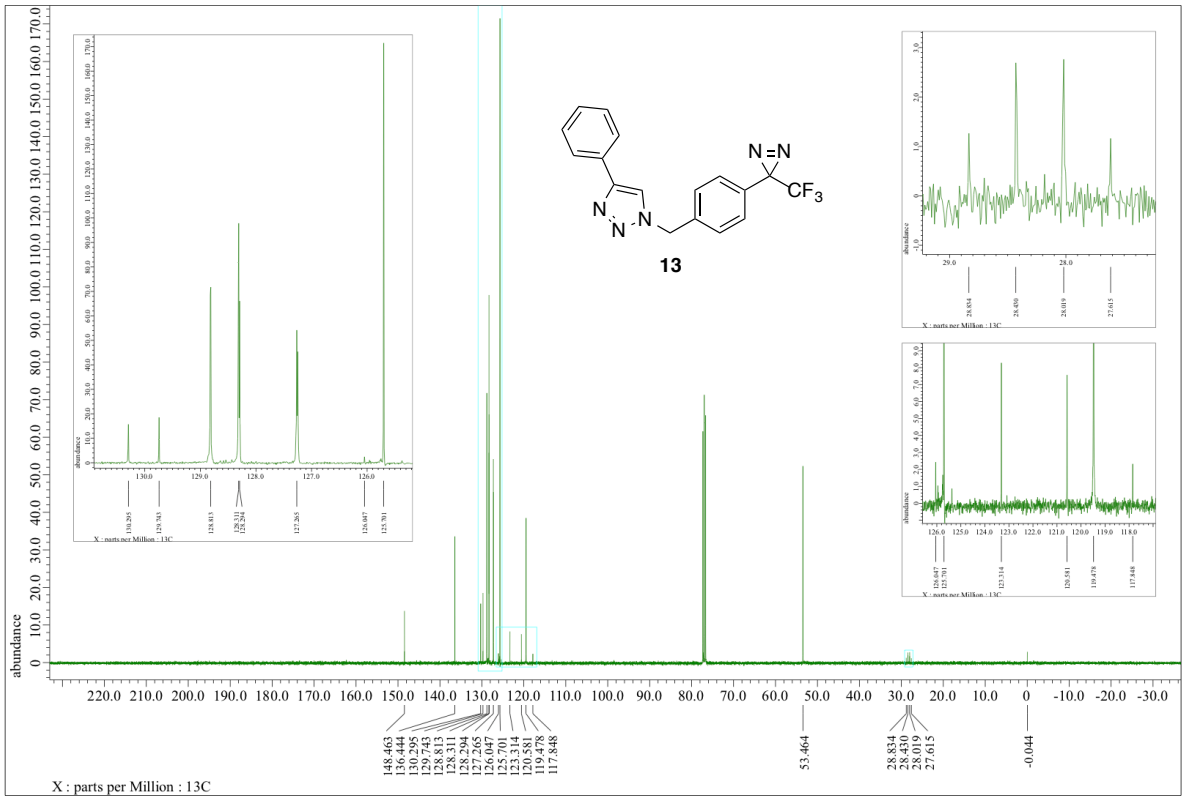


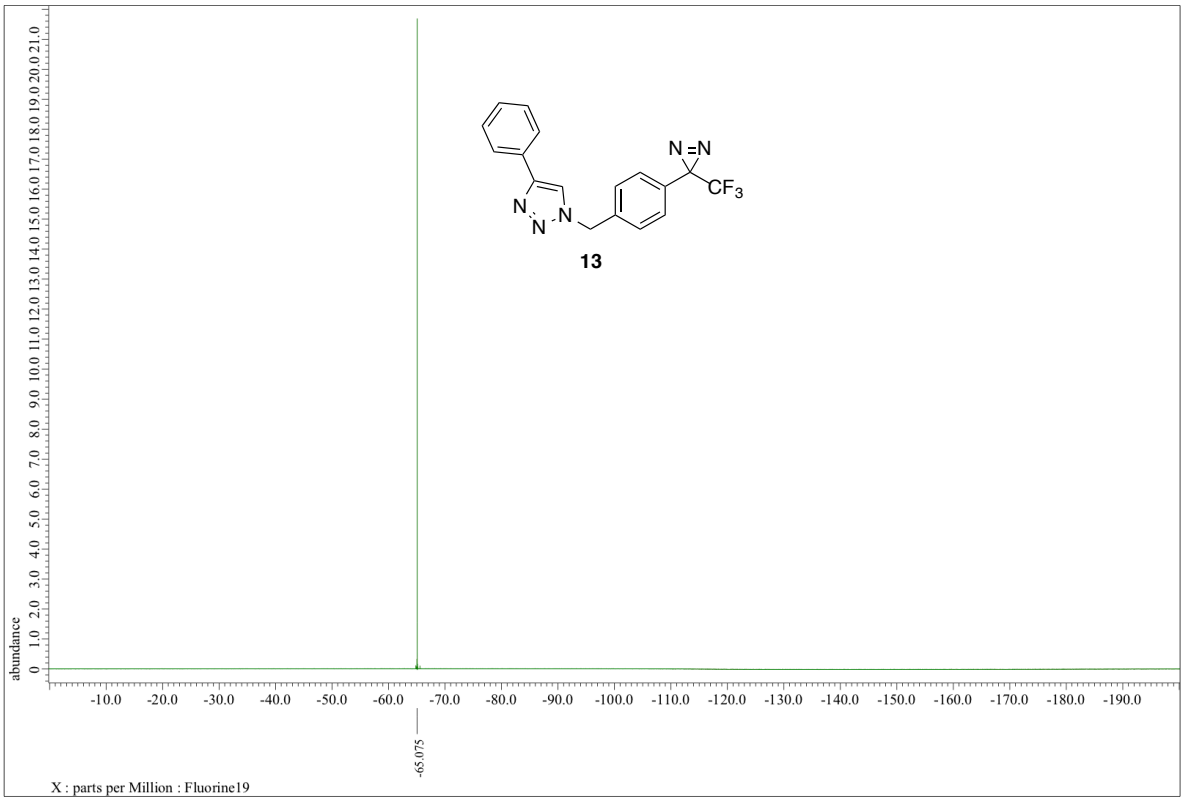



N=N
CF3
N
N
N
12
20.0
10.0
0
abundance
-10.0 -20.0 -30.0 -40.0 -50.0 -60.0 -70.0 -80.0 -90.0 -100.0 -110.0 -120.0 -130.0 -140.0 -150.0 -160.0 -170.0 -180.0 -190.0
-65.082
X : parts per Million : Fluorine19

^{1}H, ^{13}C, and ^{19}F NMR spectra of **13** ($CDCl_3$)

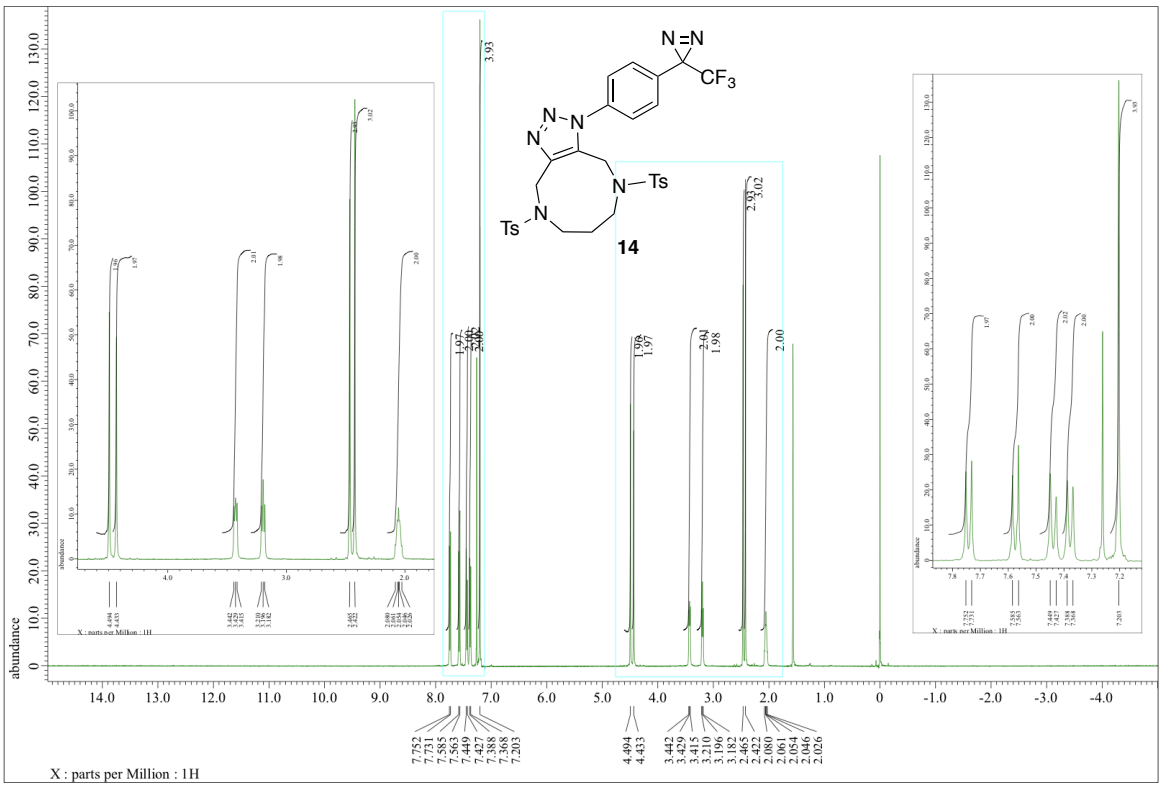


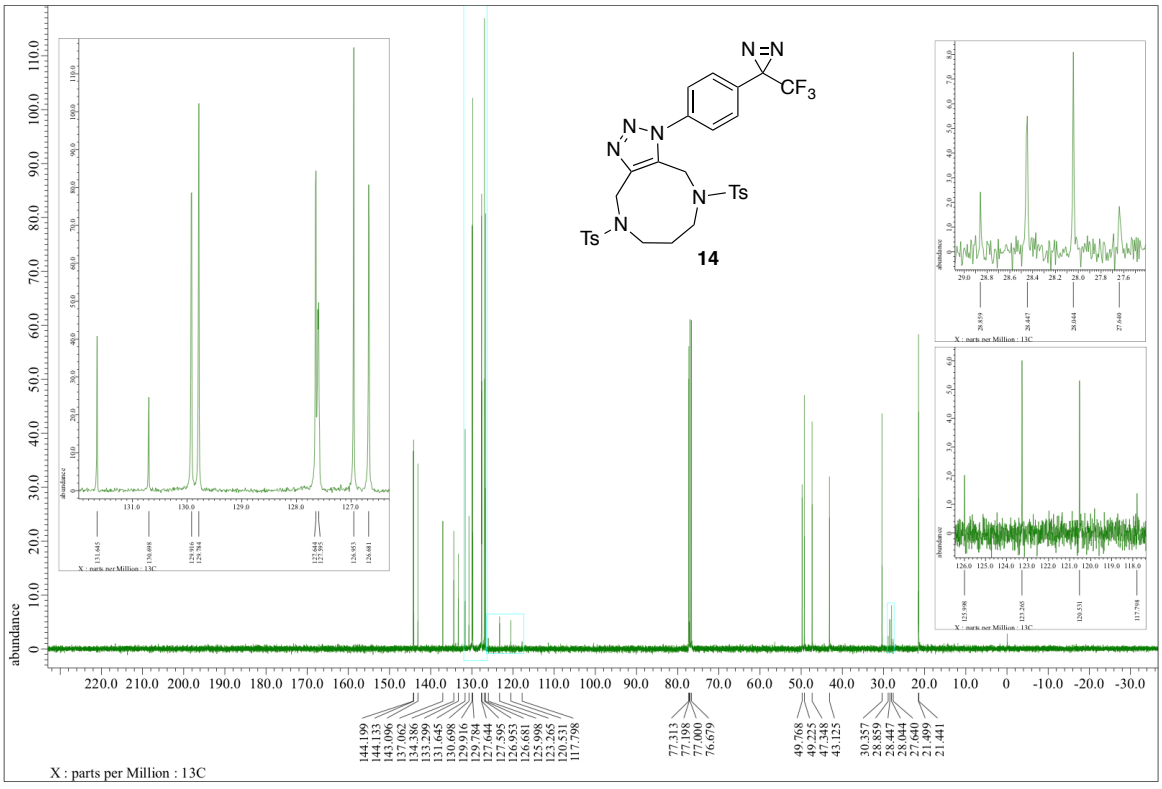


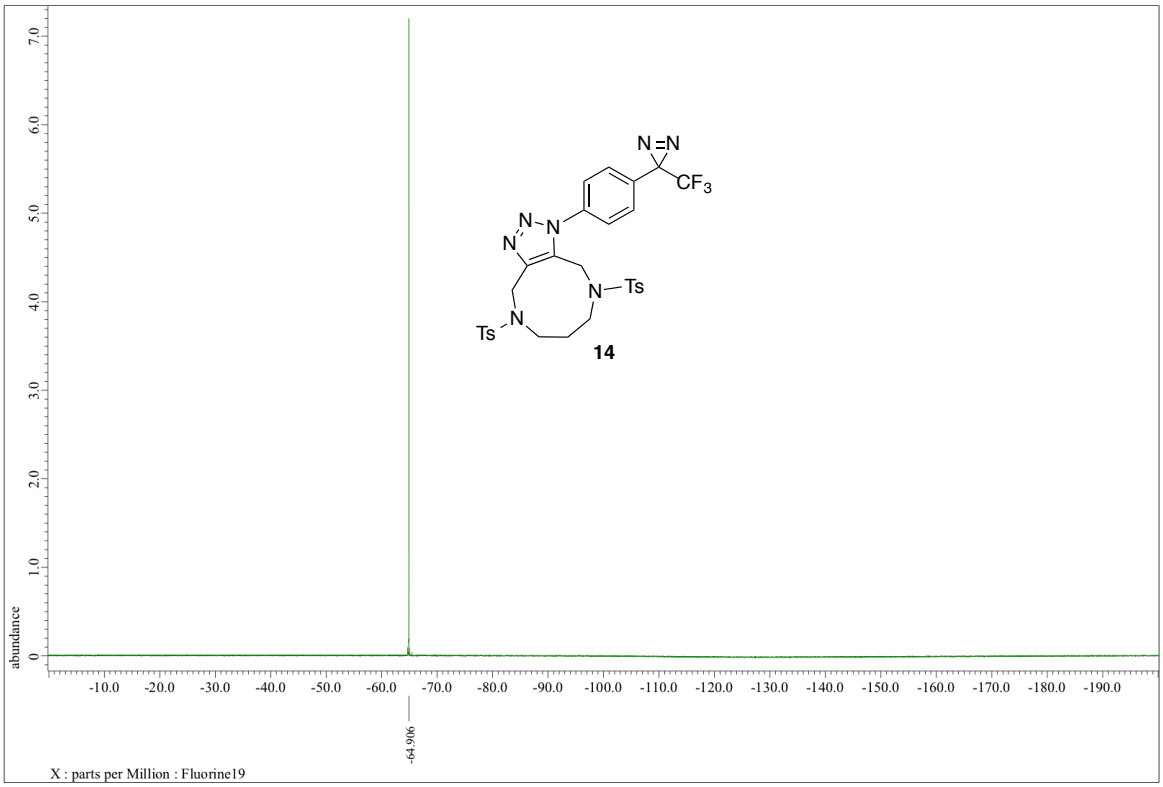

abundance
0 1.0 2.0 3.0 4.0 5.0 6.0 7.0 8.0 9.0 10.0 11.0 12.0 13.0 14.0 15.0 16.0 17.0 18.0 19.0 20.0 21.0
-10.0 -20.0 -30.0 -40.0 -50.0 -60.0 -70.0 -80.0 -90.0 -100.0 -110.0 -120.0 -130.0 -140.0 -150.0 -160.0 -170.0 -180.0 -190.0
-65.075
X : parts per Million : Fluorine19
N
N
N
N=N
CF3

13

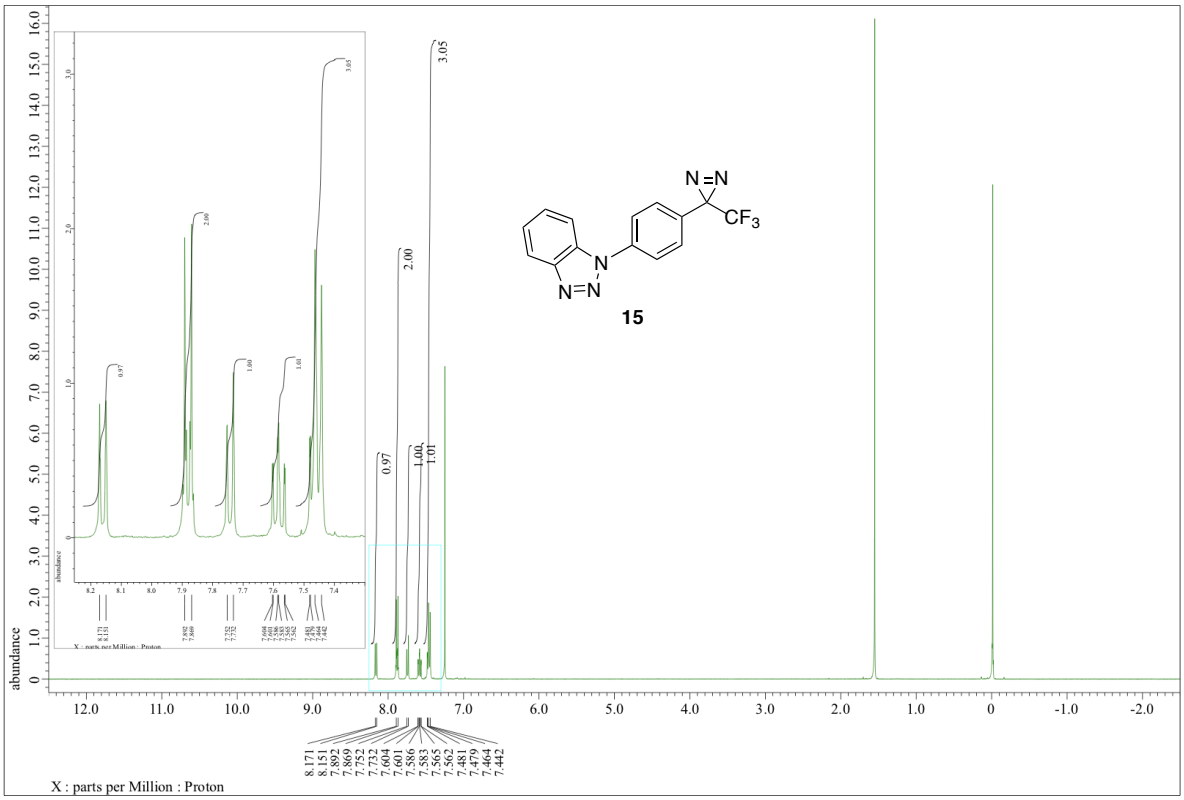
^{1}H, ^{13}C, and ^{19}F NMR spectra of **14** ($CDCl_3$)

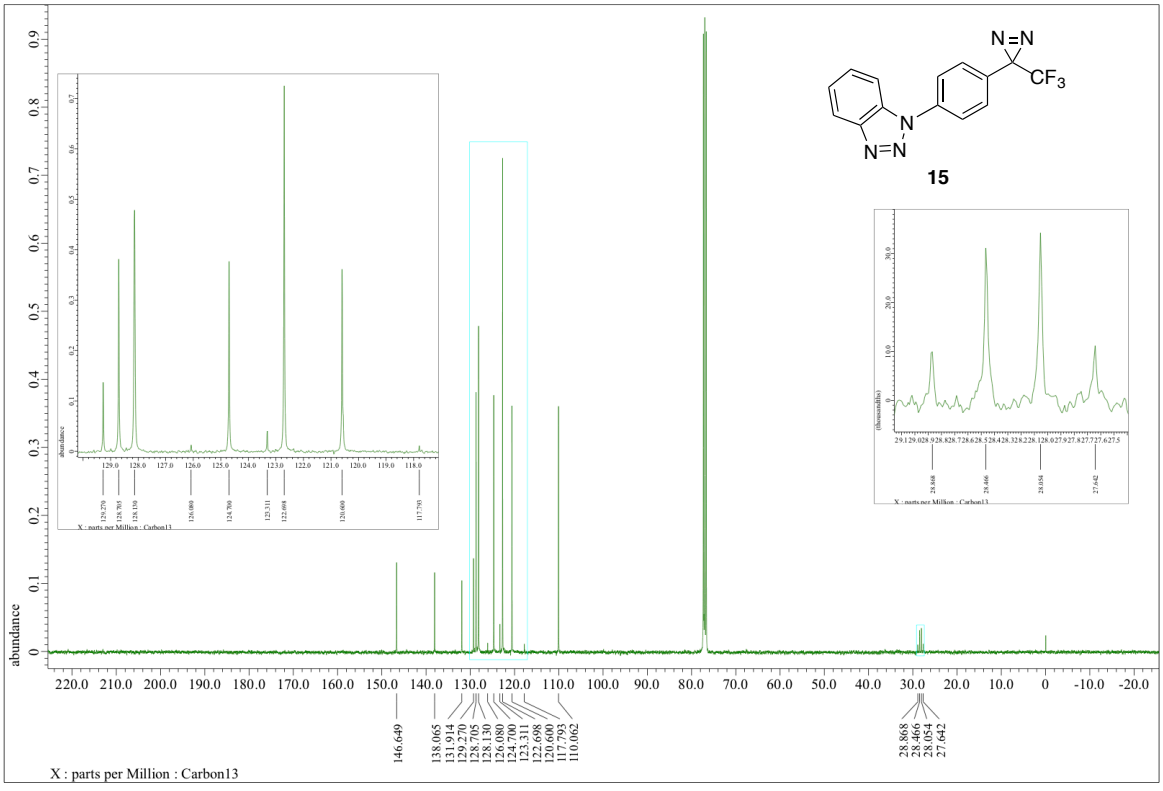


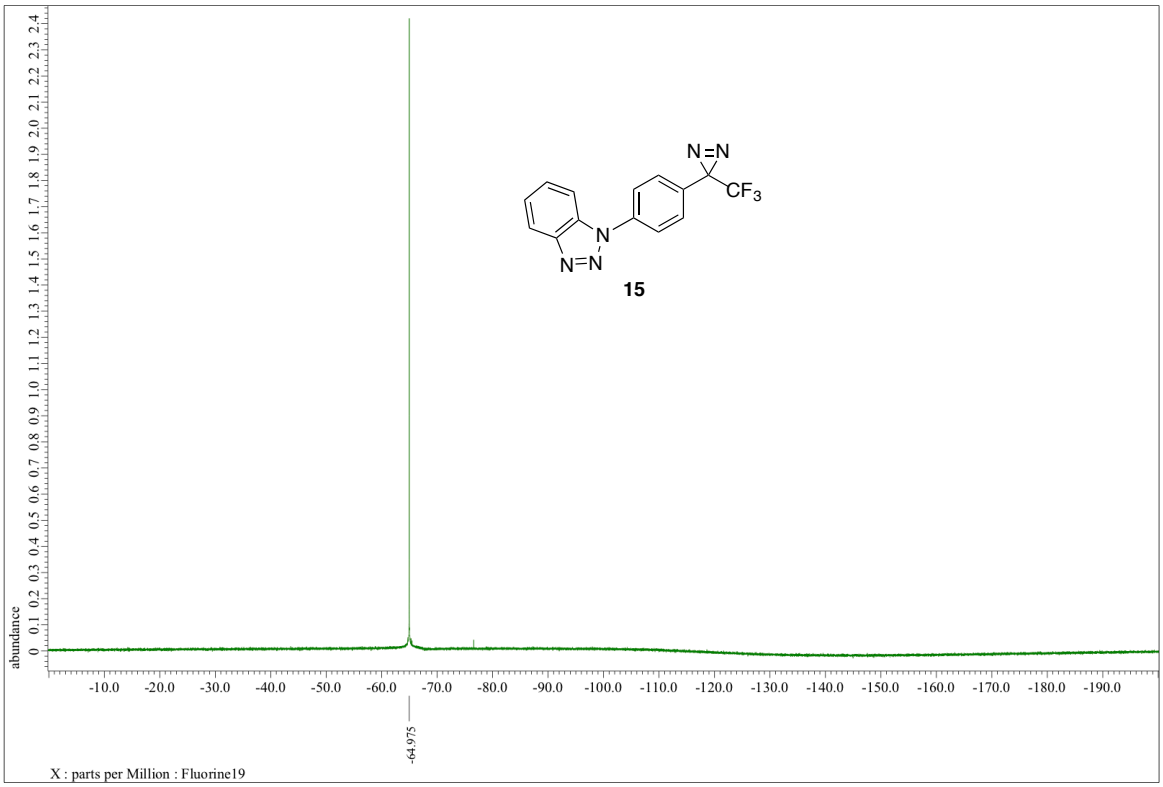



abundance
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
-10.0 -20.0 -30.0 -40.0 -50.0 -60.0 -70.0 -80.0 -90.0 -100.0 -110.0 -120.0 -130.0 -140.0 -150.0 -160.0 -170.0 -180.0 -190.0
-64.906
X : parts per Million : Fluorine19
N=N
CF3
N
N
N
N
Ts
Ts
N
14

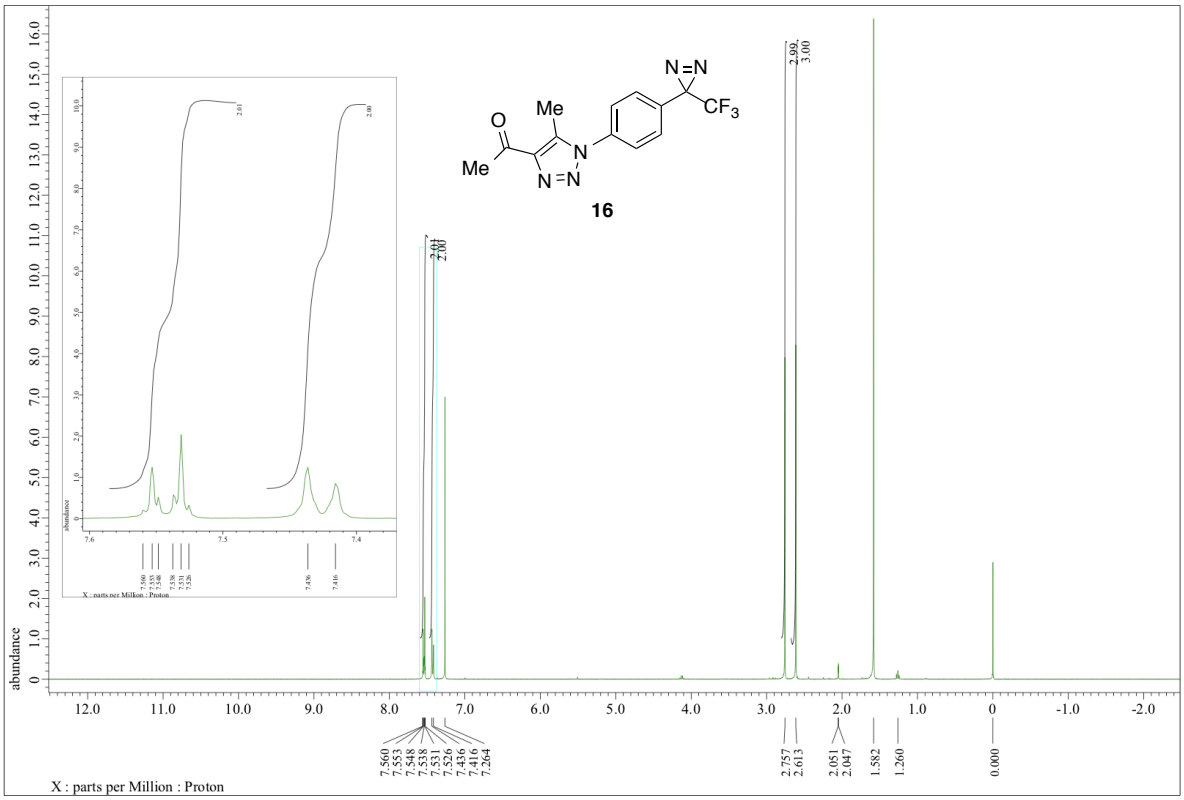
^{1}H, ^{13}C, and ^{19}F NMR spectra of **15** ($CDCl_3$)

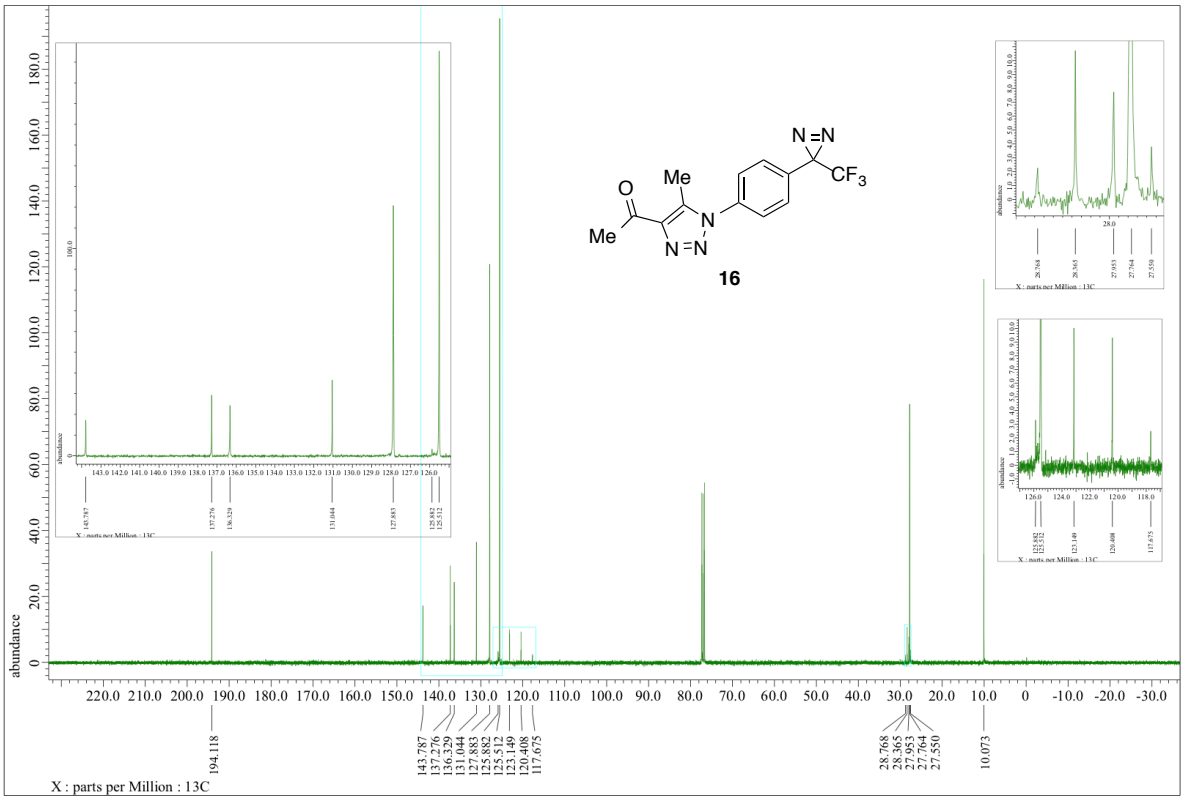


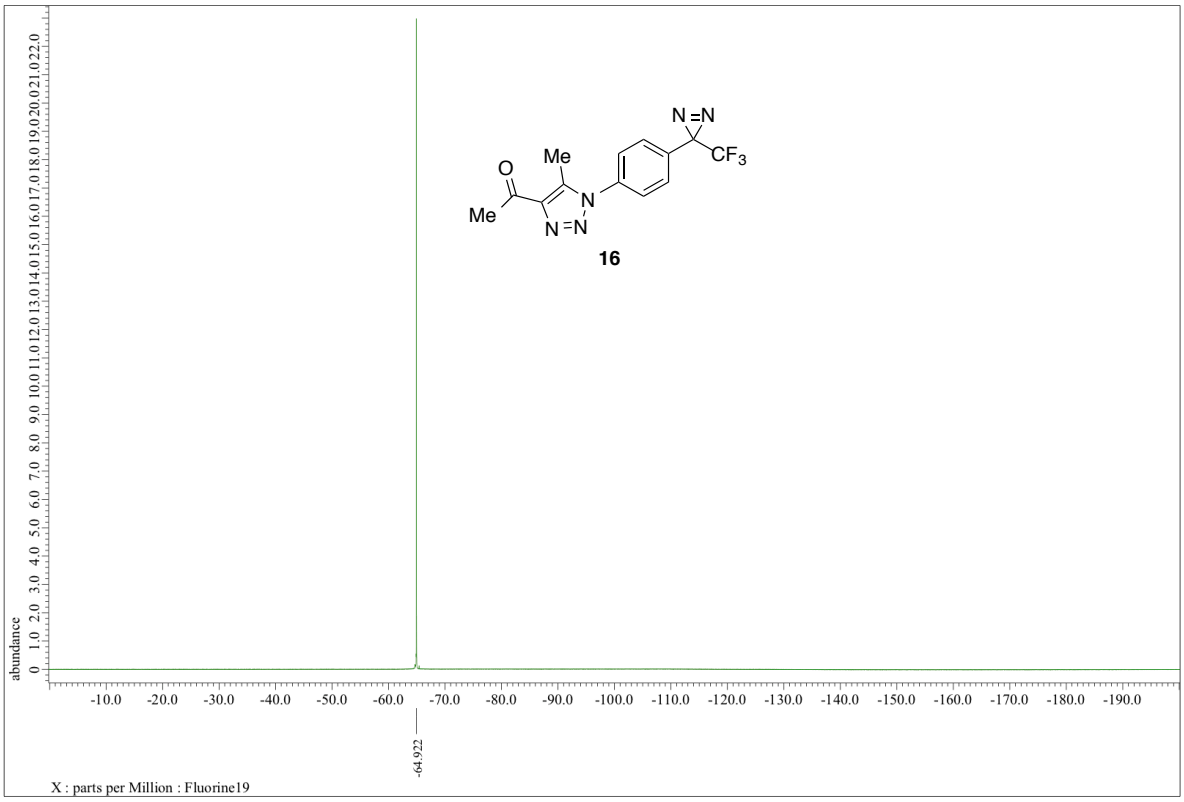



N=N
CF3
N
N=N
15
abundance
-64.975
X : parts per Million : Fluorine19

^{1}H, ^{13}C, and ^{19}F NMR spectra of **16** ($CDCl_3$)

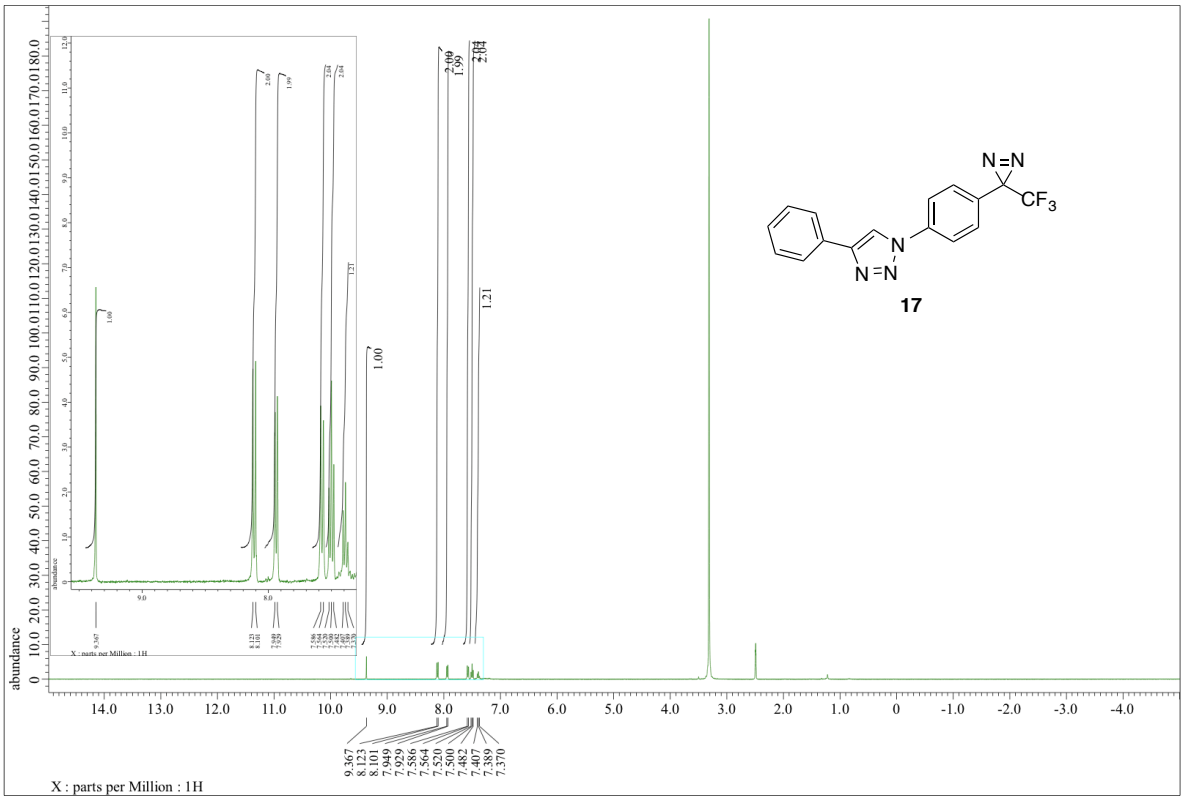


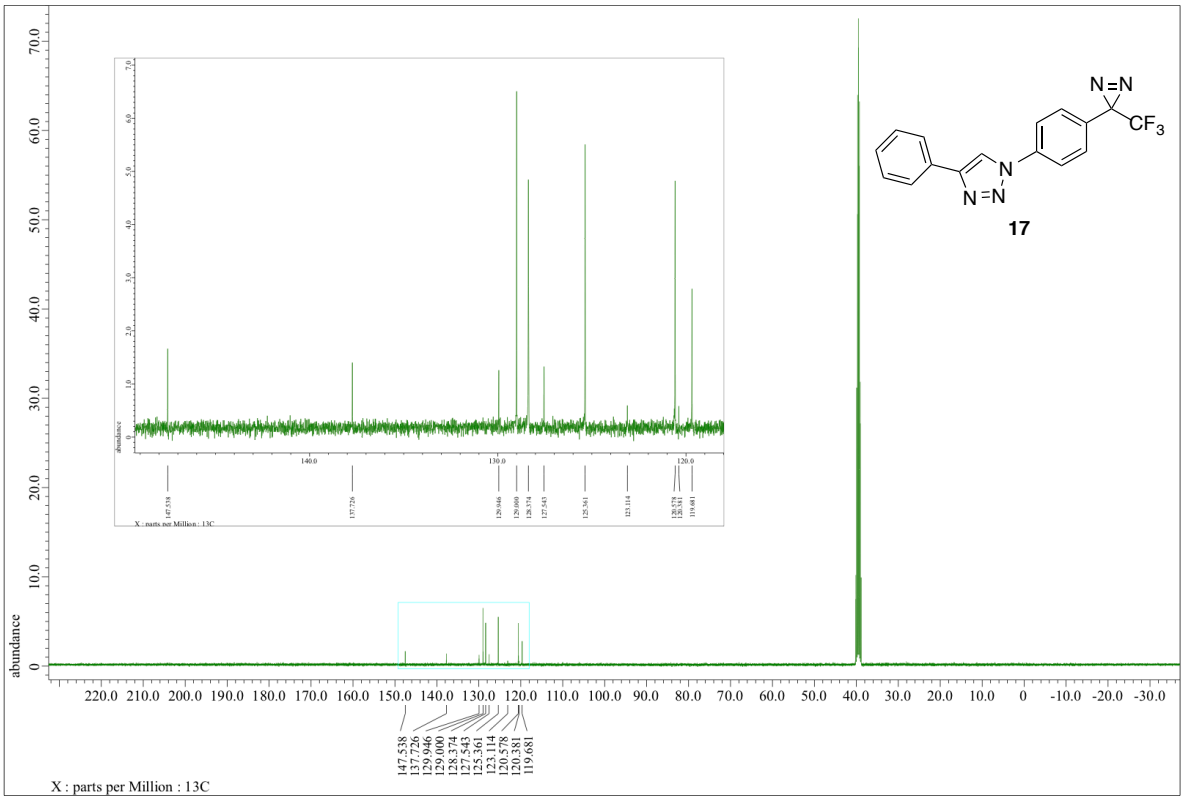


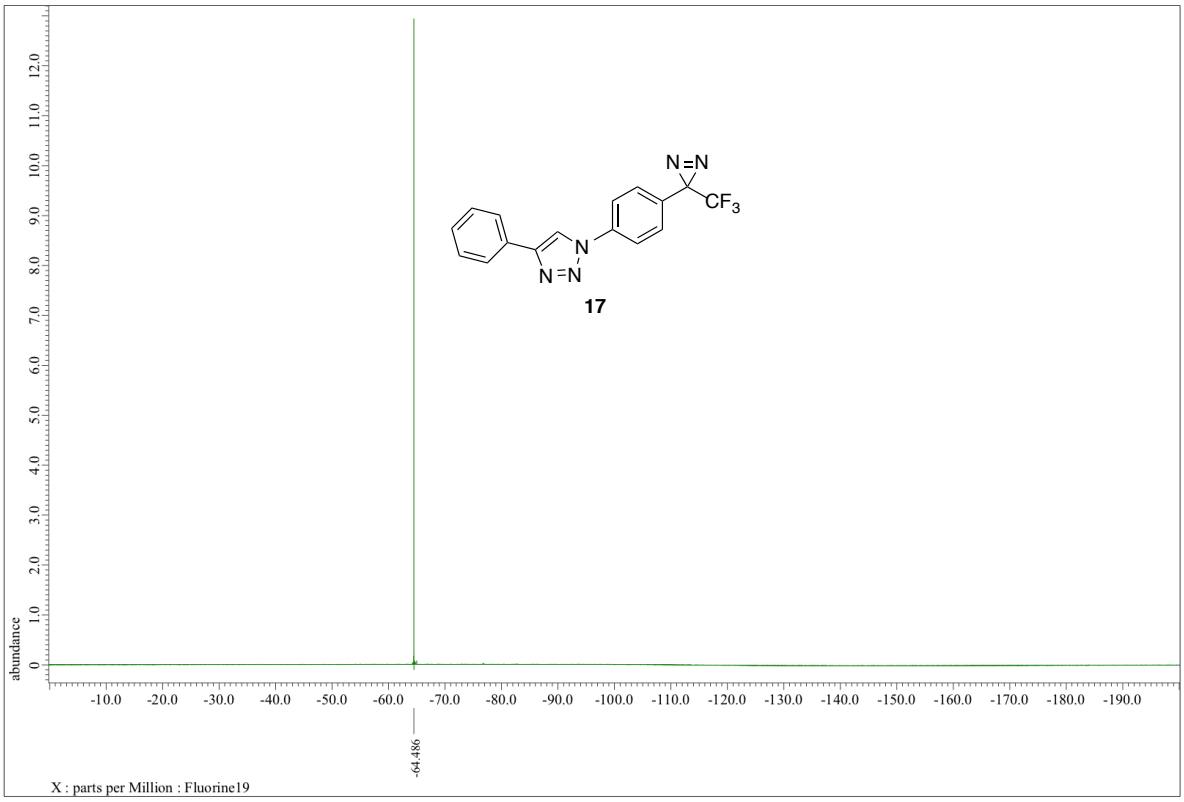

abundance
0 1.0 2.0 3.0 4.0 5.0 6.0 7.0 8.0 9.0 10.0 11.0 12.0 13.0 14.0 15.0 16.0 17.0 18.0 19.0 20.0 21.0 22.0
-10.0 -20.0 -30.0 -40.0 -50.0 -60.0 -70.0 -80.0 -90.0 -100.0 -110.0 -120.0 -130.0 -140.0 -150.0 -160.0 -170.0 -180.0 -190.0
-64.922
X : parts per Million : Fluorine19
N=N
CF3
Me
O
N
Me
N=N

16

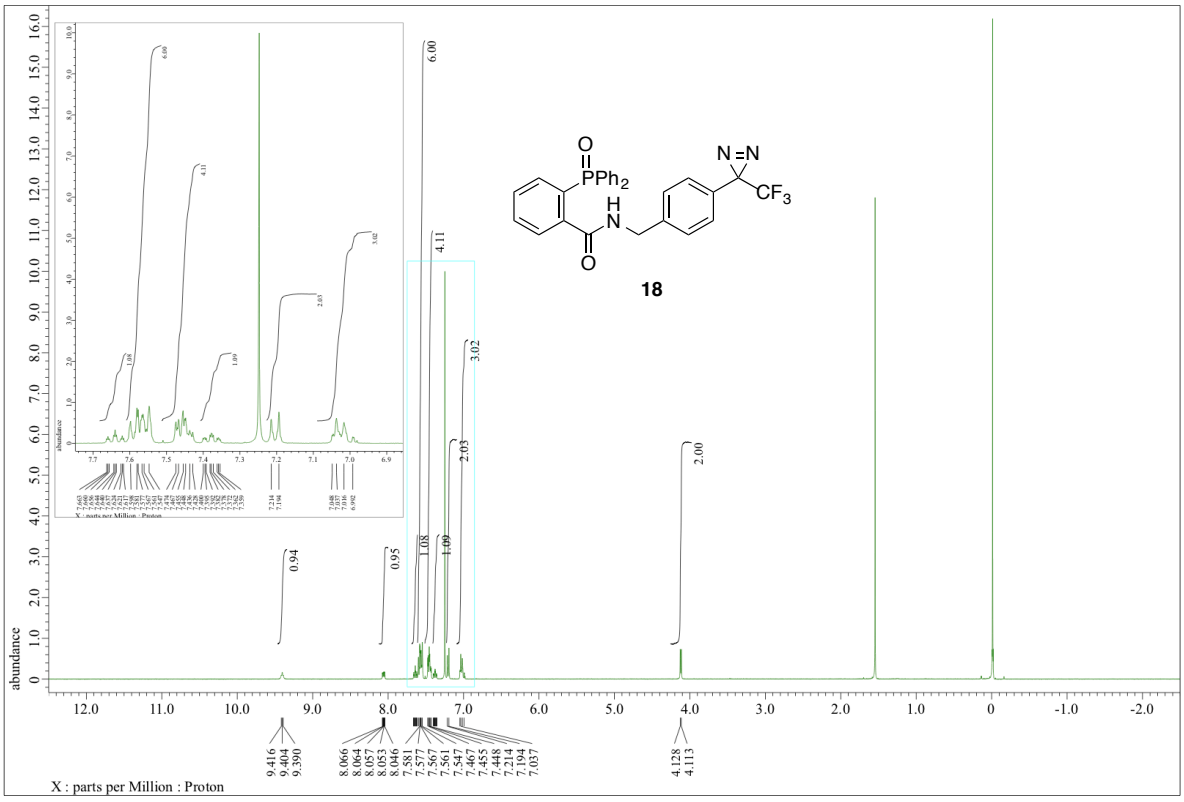
^{1}H, ^{13}C, and ^{19}F NMR spectra of **17** (DMSO-d_6)

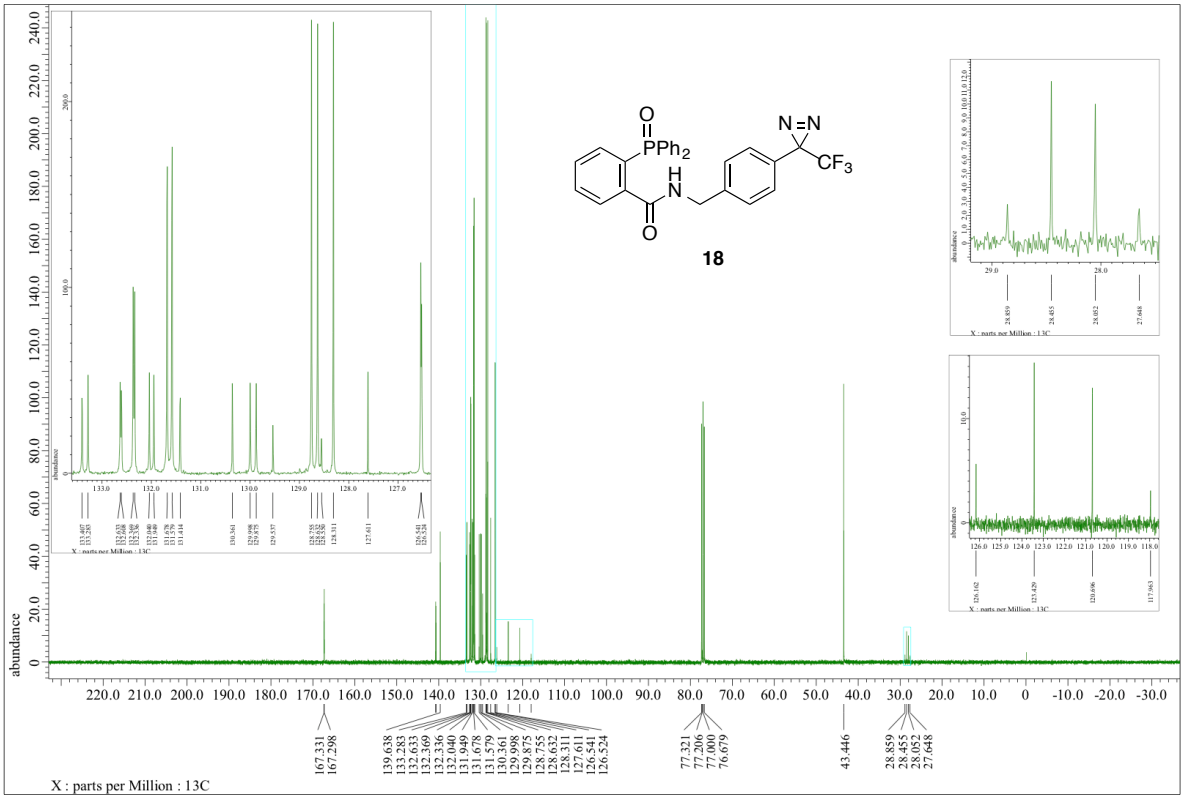


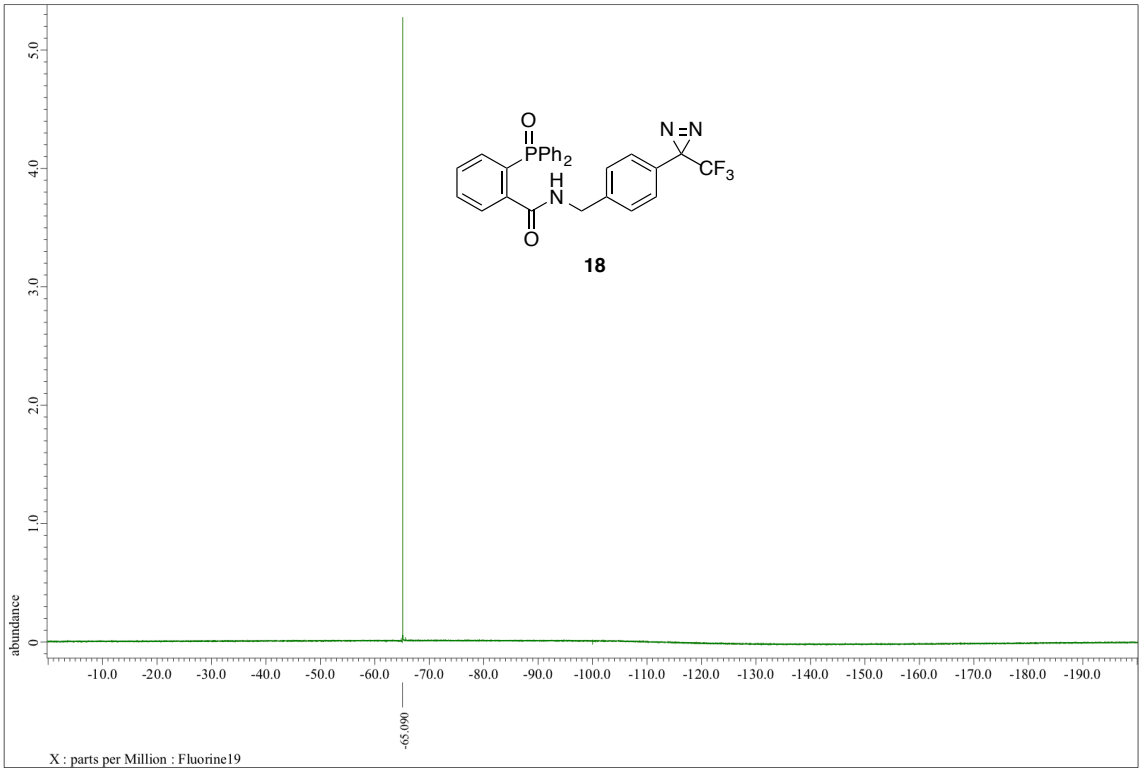


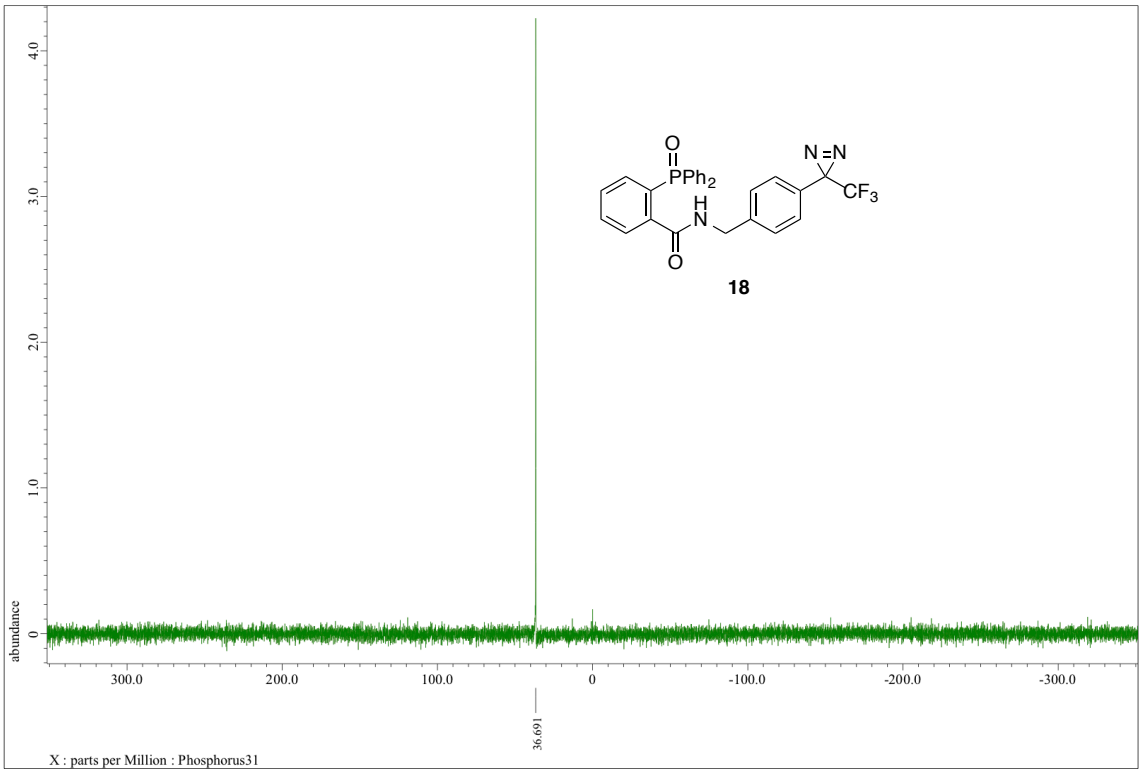

N=N
CF3
N
N=N
17
abundance
0
1.0
2.0
3.0
4.0
5.0
6.0
7.0
8.0
9.0
10.0
11.0
12.0
-10.0
-20.0
-30.0
-40.0
-50.0
-60.0
-70.0
-80.0
-90.0
-100.0
-110.0
-120.0
-130.0
-140.0
-150.0
-160.0
-170.0
-180.0
-190.0
-64.486
X : parts per Million : Fluorine19

^{1}H, ^{13}C, ^{19}F, and ^{31}P NMR spectra of **18** ($CDCl_3$)

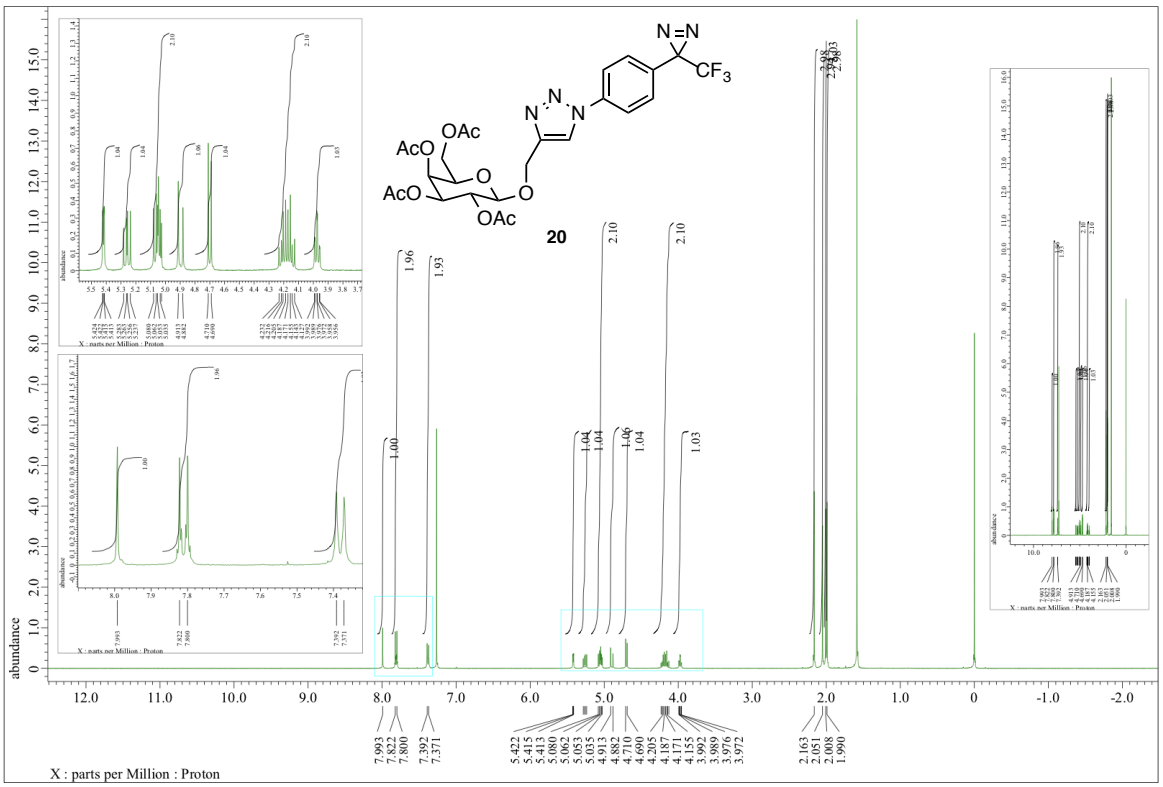


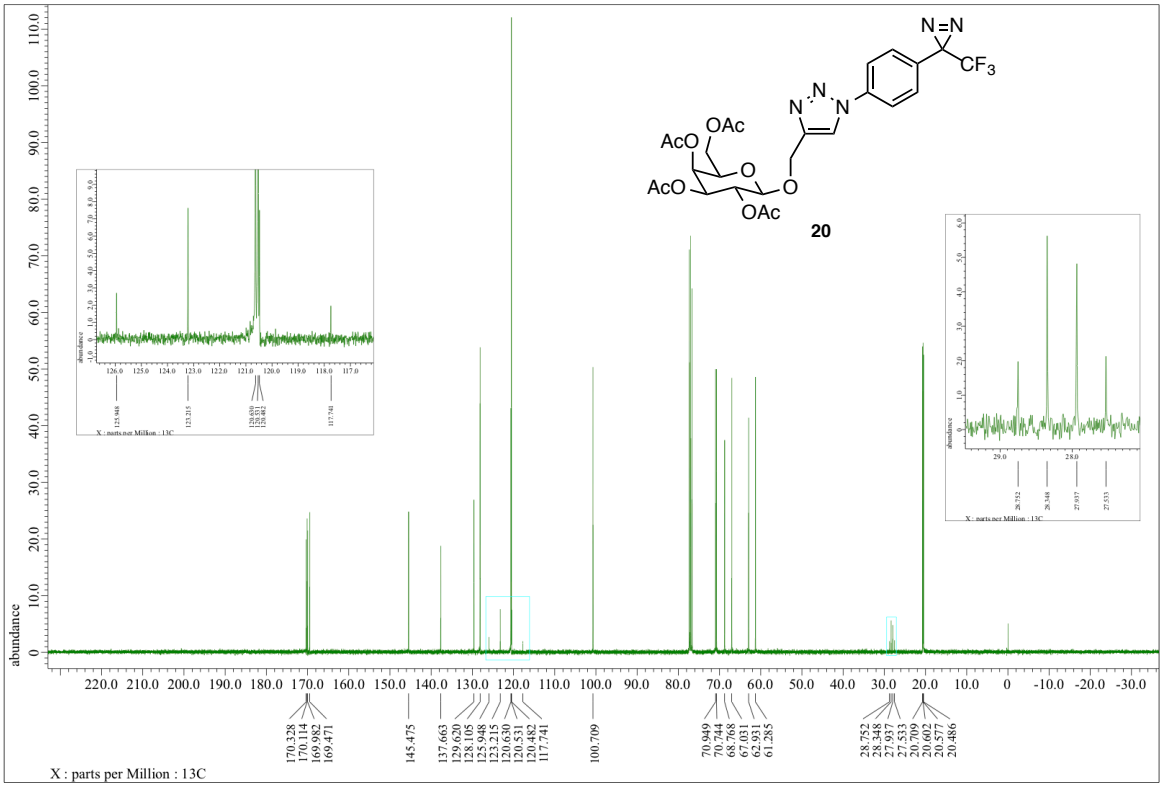


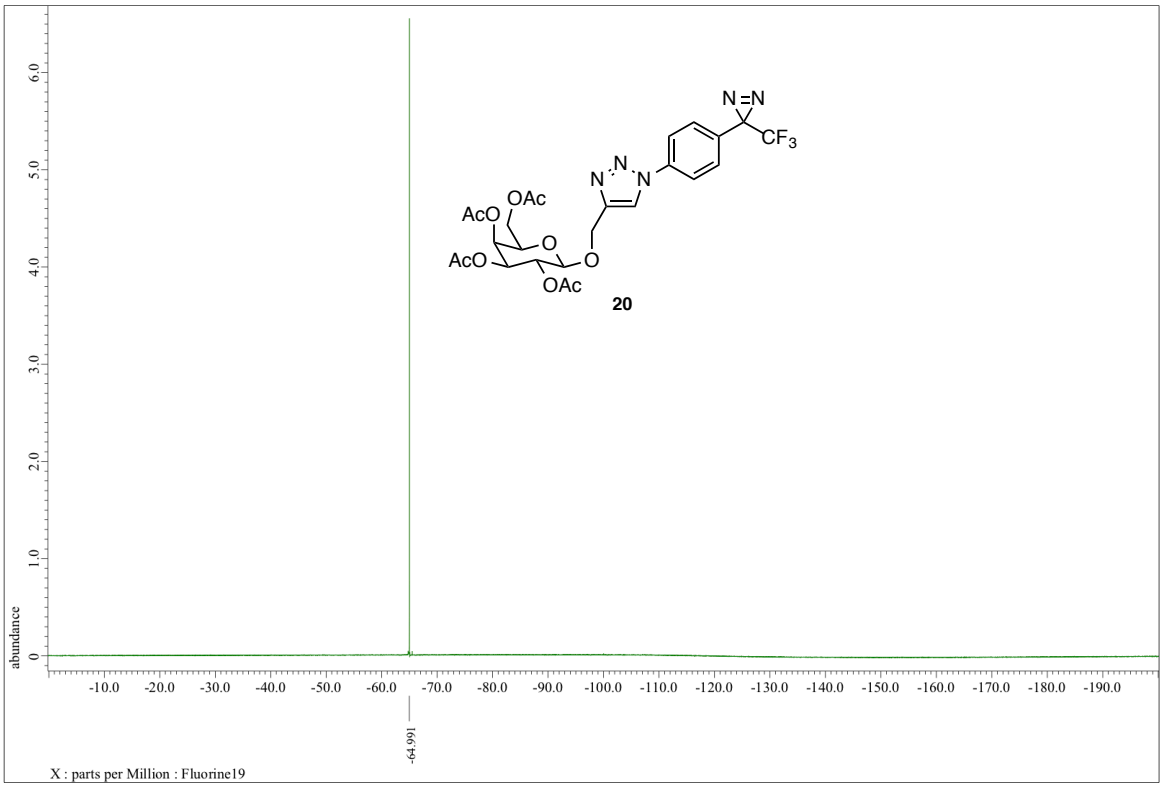

abundance
5.0
4.0
3.0
2.0
1.0
0
-10.0 -20.0 -30.0 -40.0 -50.0 -60.0 -70.0 -80.0 -90.0 -100.0 -110.0 -120.0 -130.0 -140.0 -150.0 -160.0 -170.0 -180.0 -190.0
-65.090
X : parts per Million : Fluorine19
O
PPh2
H
N
O
N=N
CF3
18


abundance
4.0
3.0
2.0
1.0
0
300.0 200.0 100.0 0 -100.0 -200.0 -300.0
36.691
X : parts per Million : Phosphorus31
O
PPh2
H
N
O
N=N
CF3
18

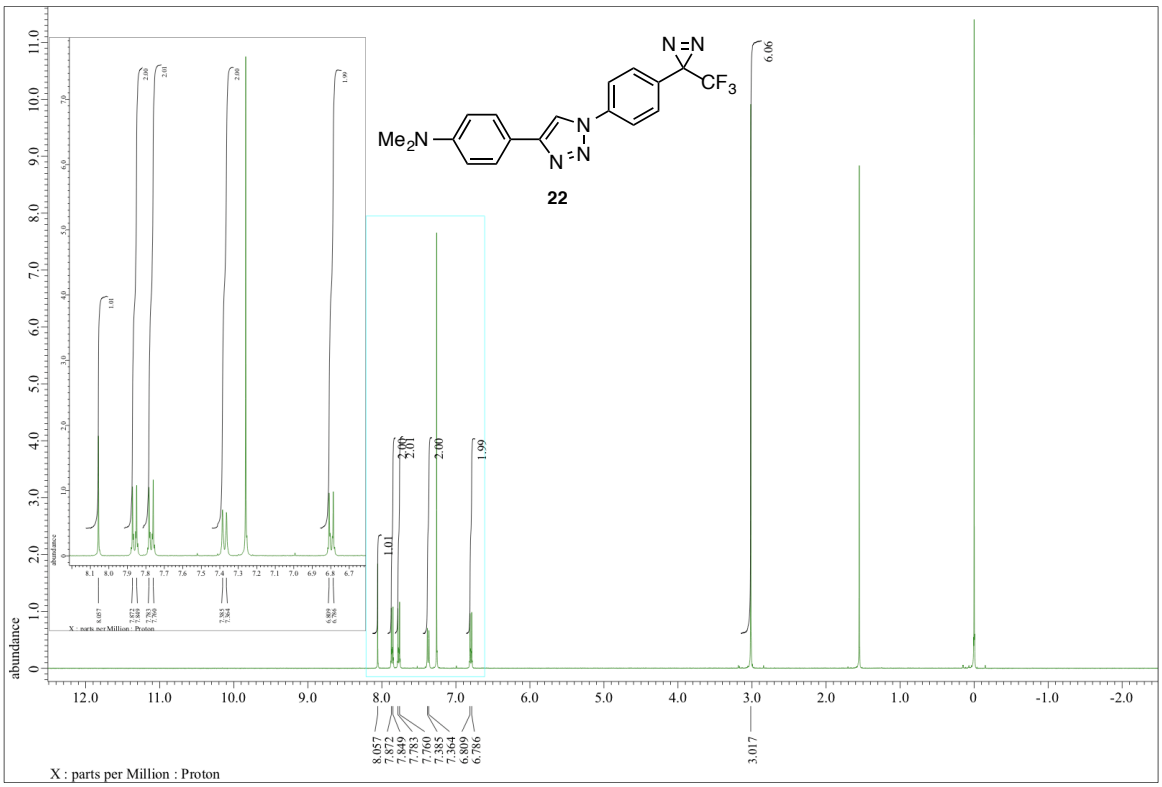
^{1}H, ^{13}C, and ^{19}F NMR spectra of **20** ($CDCl_3$)

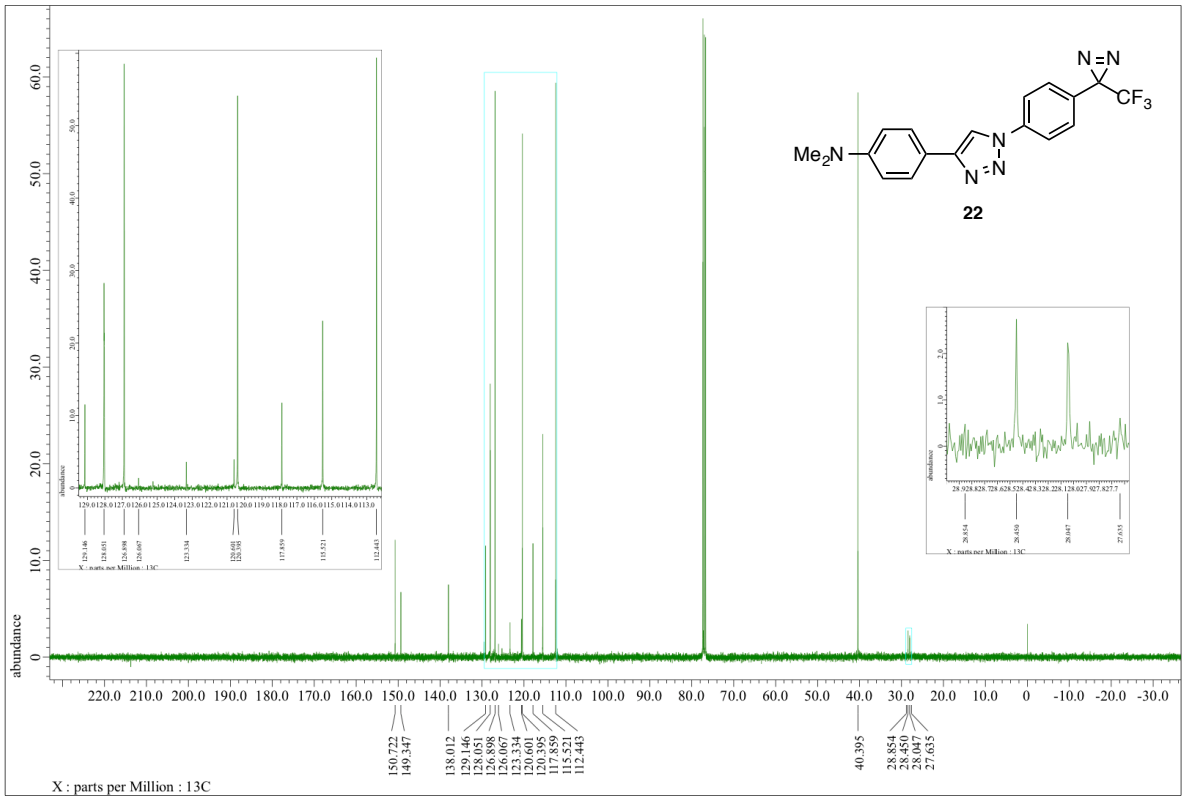


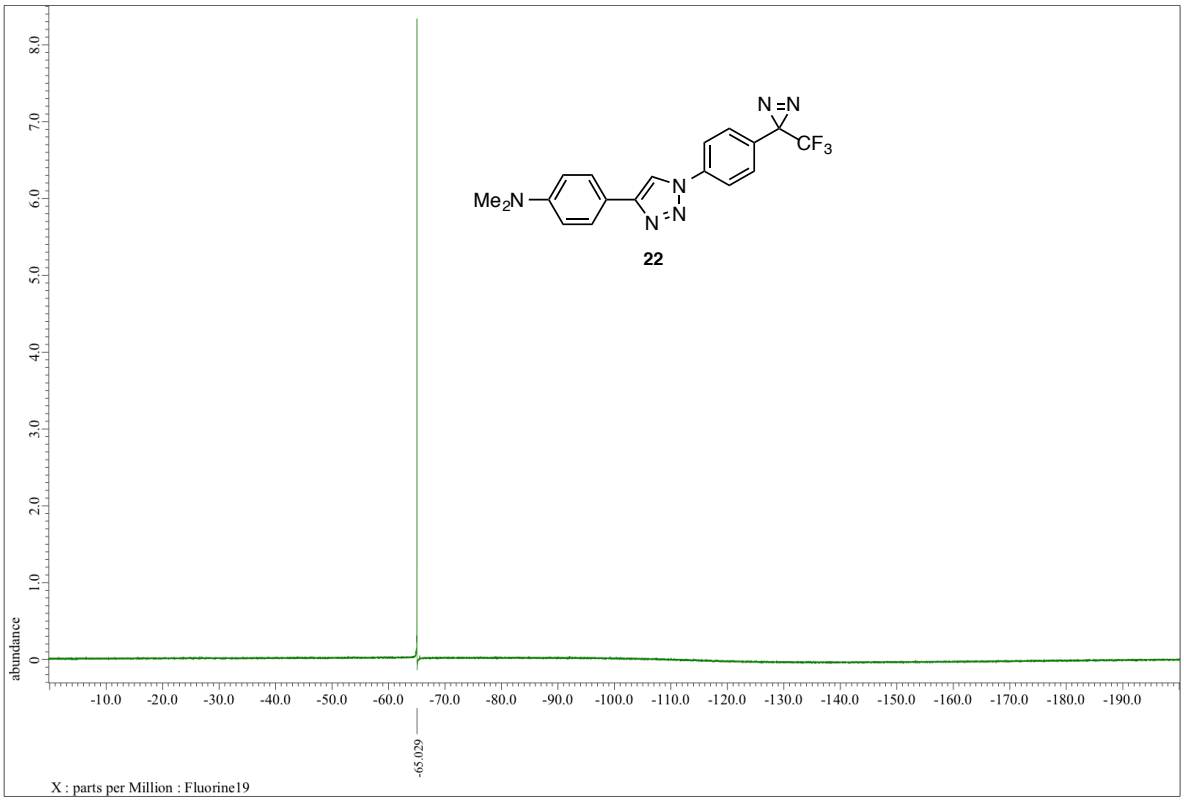



N=N
CF3
N
N
N
OAc
AcO
O
AcO
O
OAc
20
abundance
6.0
5.0
4.0
3.0
2.0
1.0
0
-10.0
-20.0
-30.0
-40.0
-50.0
-60.0
-70.0
-80.0
-90.0
-100.0
-110.0
-120.0
-130.0
-140.0
-150.0
-160.0
-170.0
-180.0
-190.0
-64.99
X : parts per Million : Fluorine19

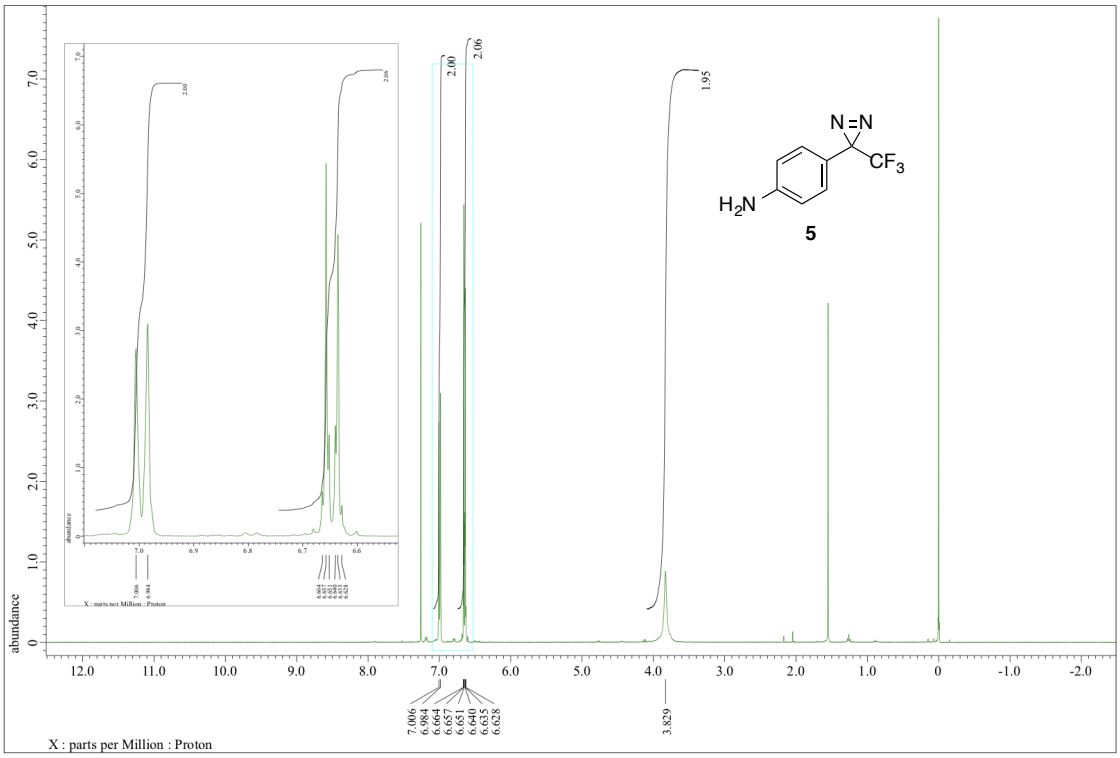
^{1}H, ^{13}C, and ^{19}F NMR spectra of **22** ($CDCl_3$)

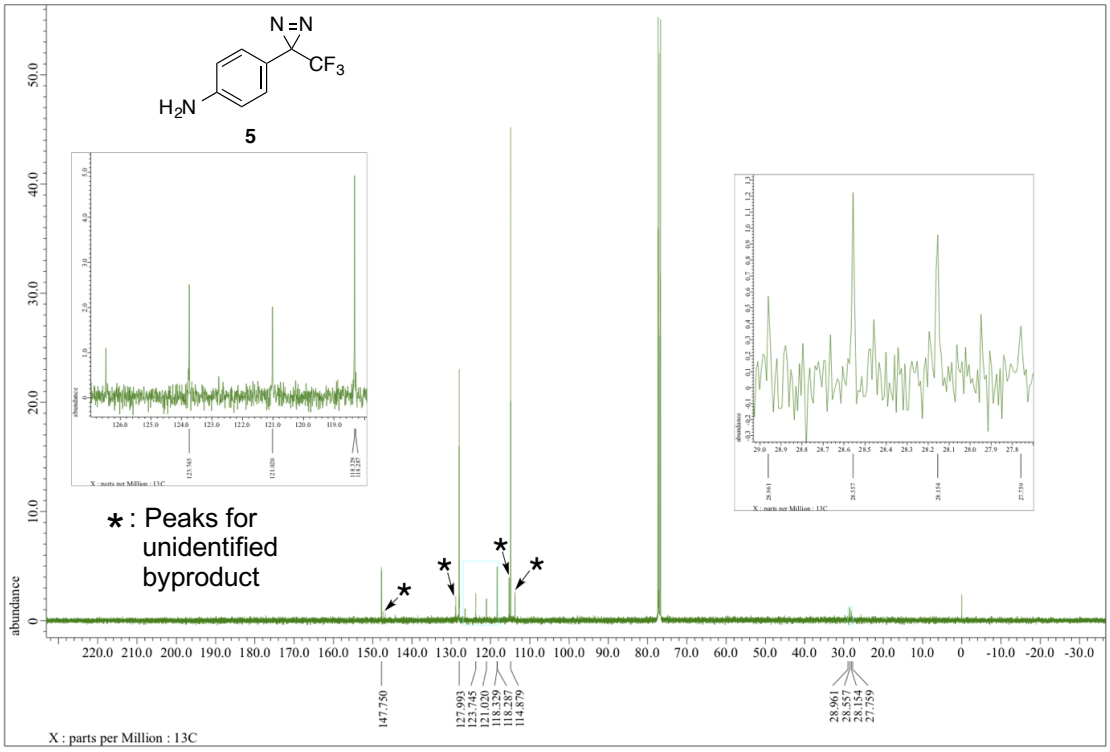


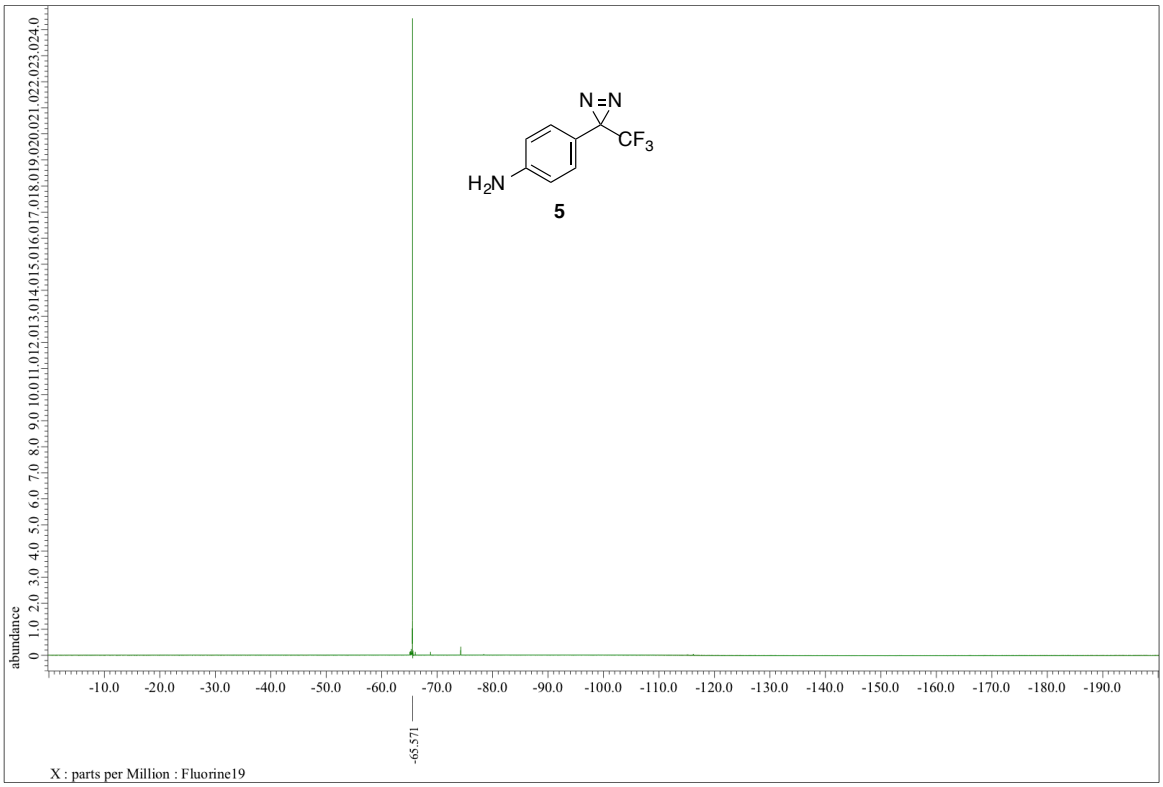



N=N
CF3
Me2N
N
N
22
abundance
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
-10.0
-20.0
-30.0
-40.0
-50.0
-60.0
-70.0
-80.0
-90.0
-100.0
-110.0
-120.0
-130.0
-140.0
-150.0
-160.0
-170.0
-180.0
-190.0
-65.029
X : parts per Million : Fluorine19

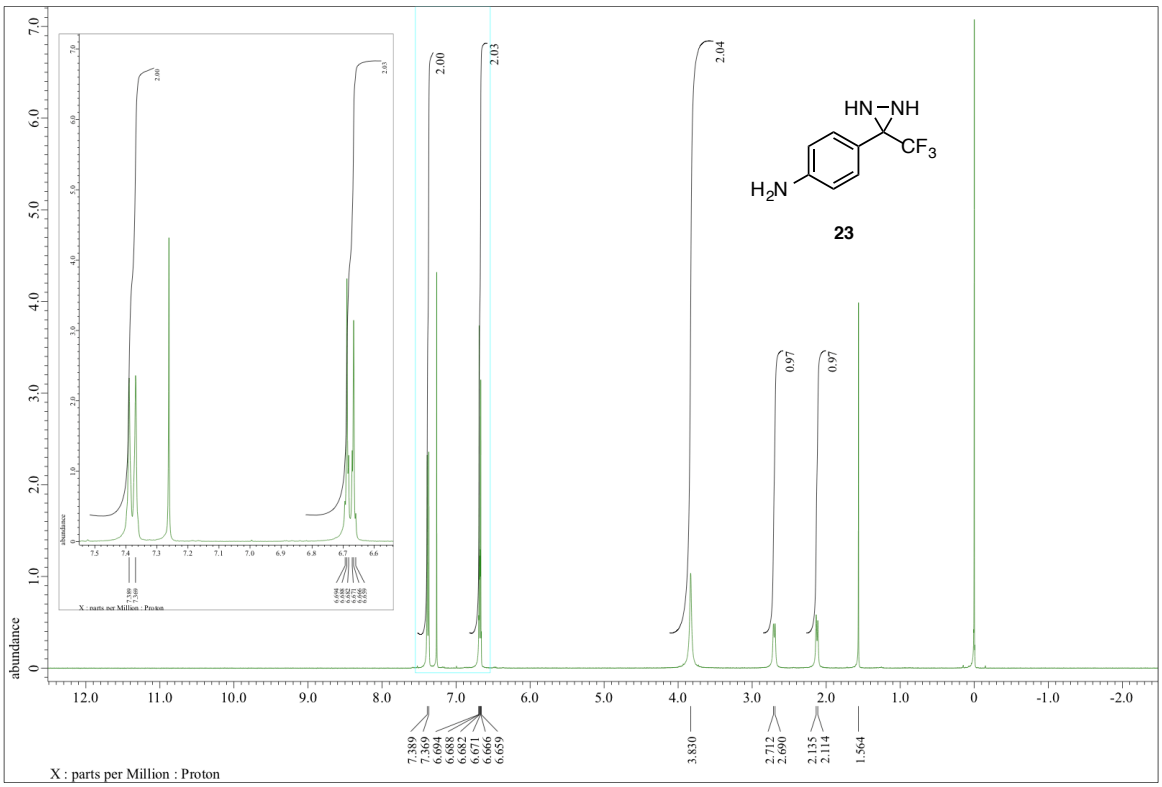
^{1}H, ^{13}C, and ^{19}F NMR spectra of **5** ($CDCl_3$)

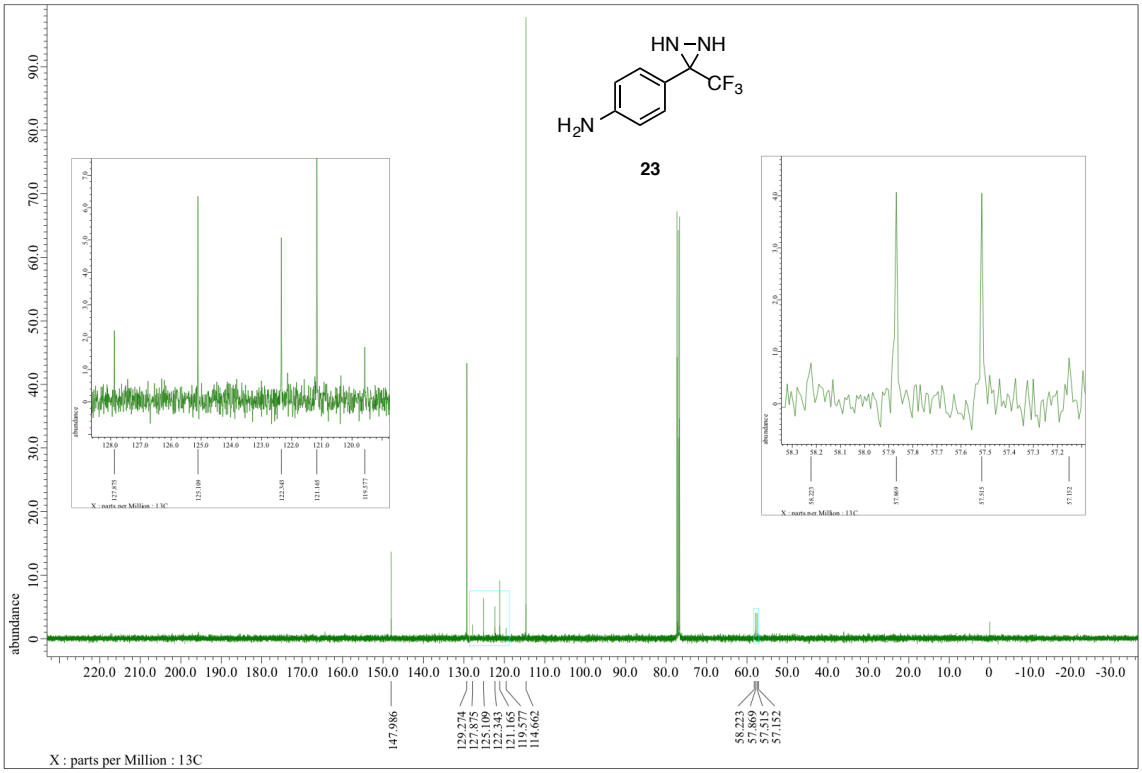


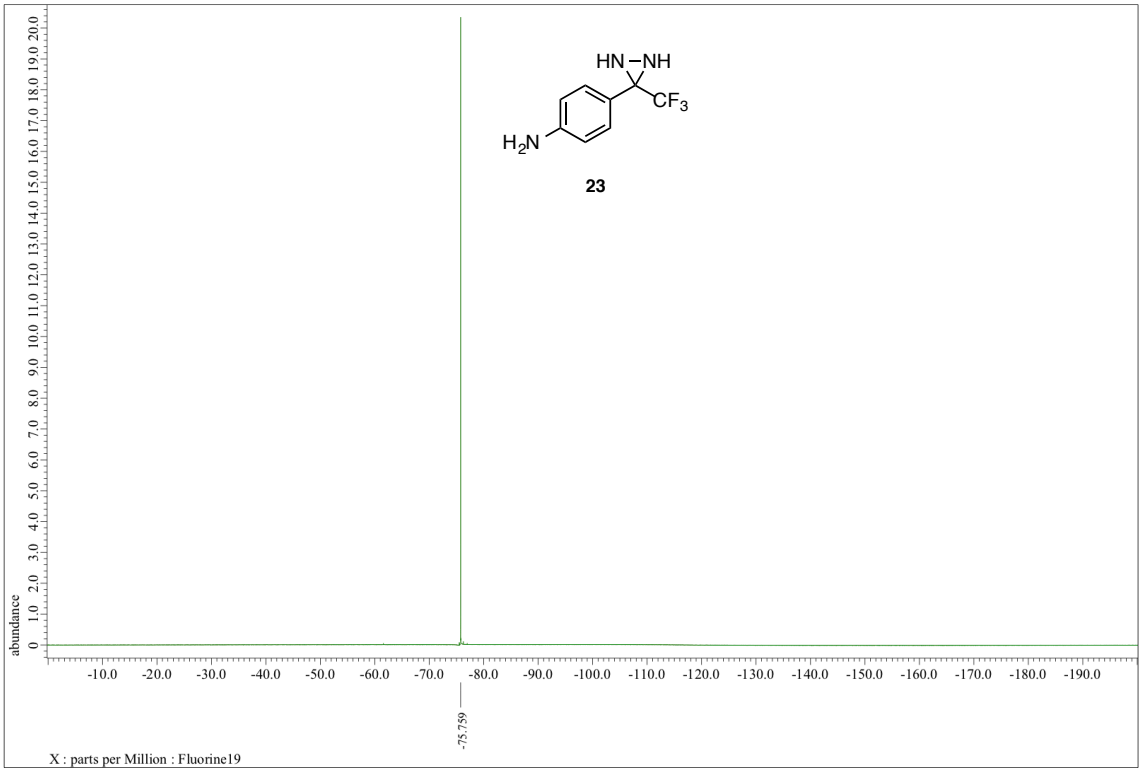



N=N
CF3
H2N
5
abundance
-65.571
X : parts per Million : Fluorine19

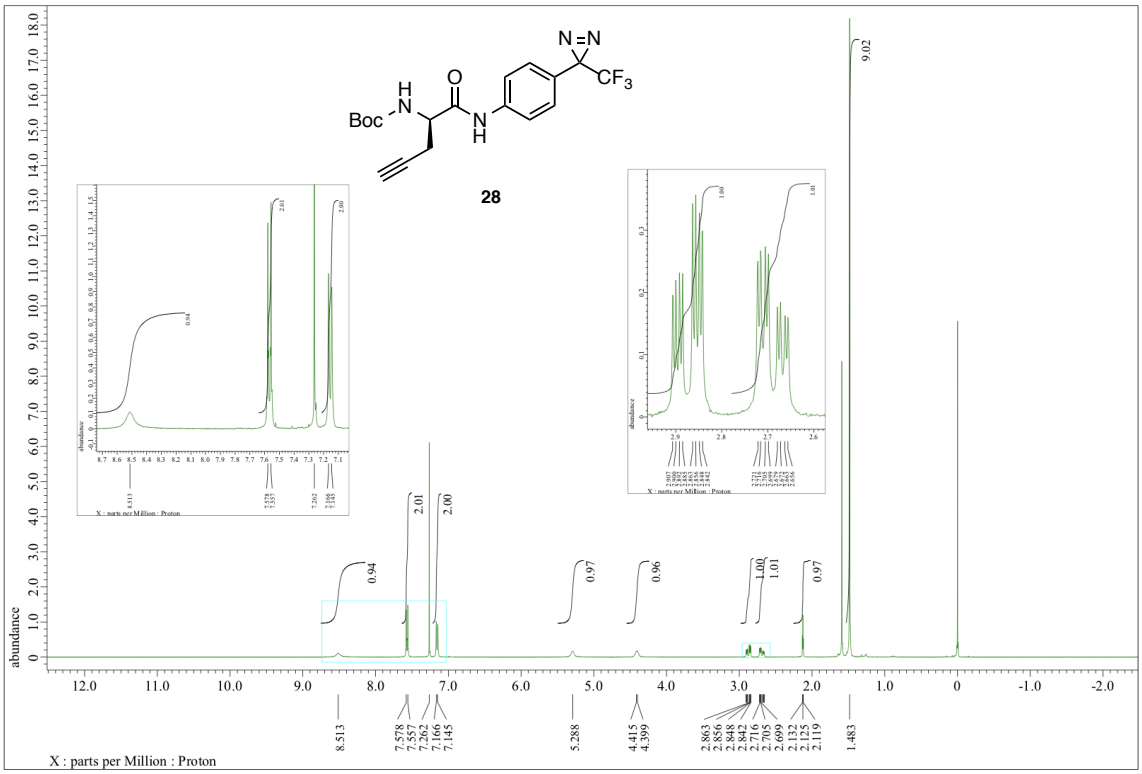
^{1}H, ^{13}C, and ^{19}F NMR spectra of **23** ($CDCl_3$)

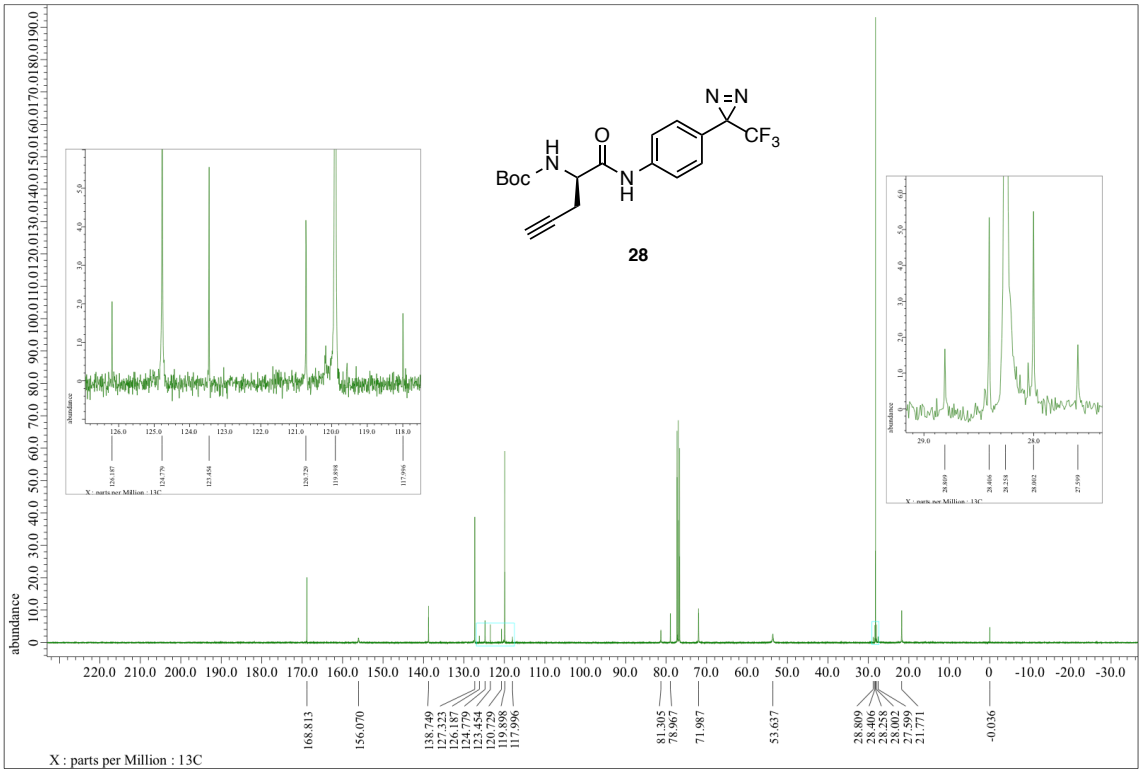


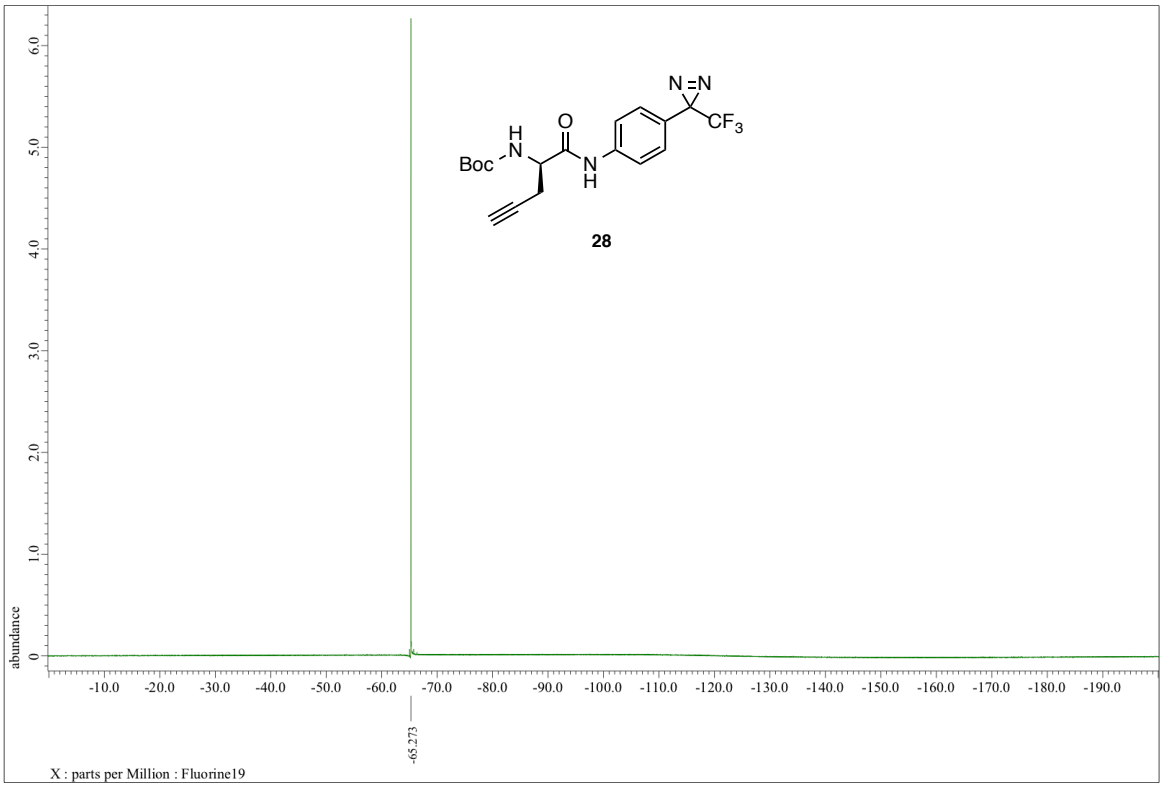



HN–NH
CF3
H2N
23
abundance
0 1.0 2.0 3.0 4.0 5.0 6.0 7.0 8.0 9.0 10.0 11.0 12.0 13.0 14.0 15.0 16.0 17.0 18.0 19.0 20.0
-10.0 -20.0 -30.0 -40.0 -50.0 -60.0 -70.0 -80.0 -90.0 -100.0 -110.0 -120.0 -130.0 -140.0 -150.0 -160.0 -170.0 -180.0 -190.0
-75.759
X : parts per Million : Fluorine19

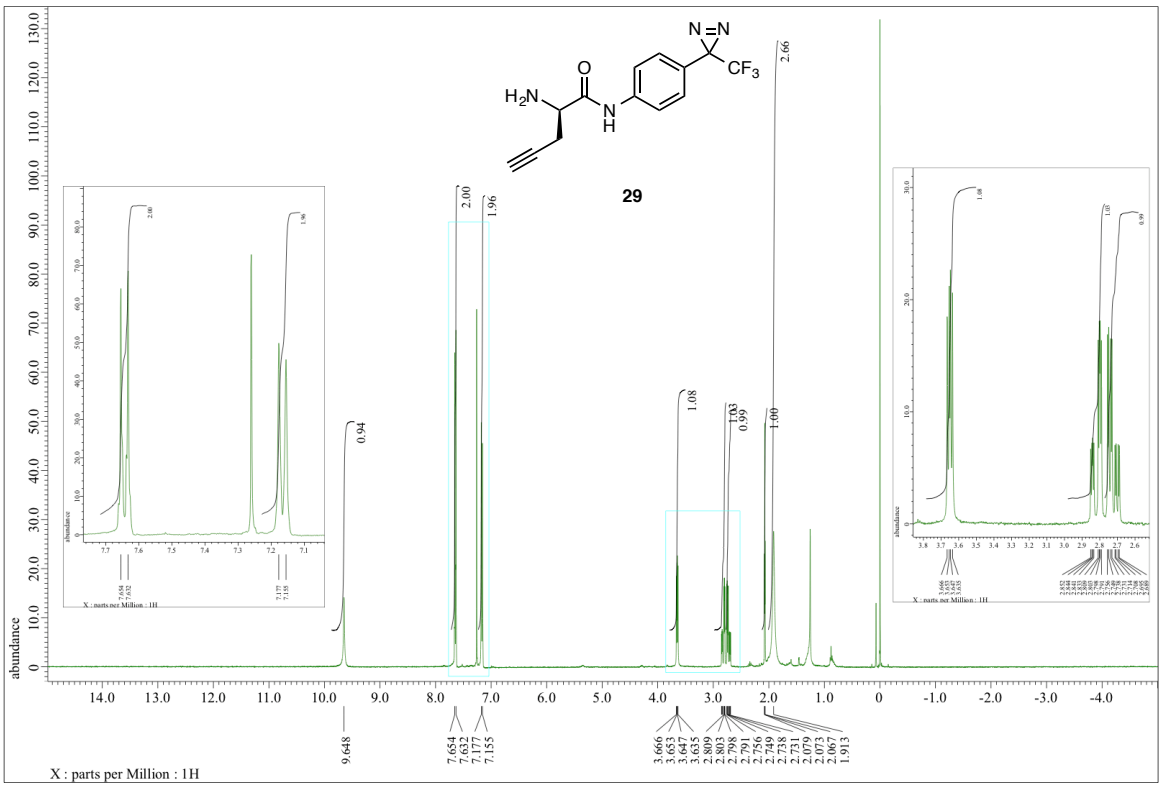
^{1}H, ^{13}C, and ^{19}F NMR spectra of **28** ($CDCl_3$)

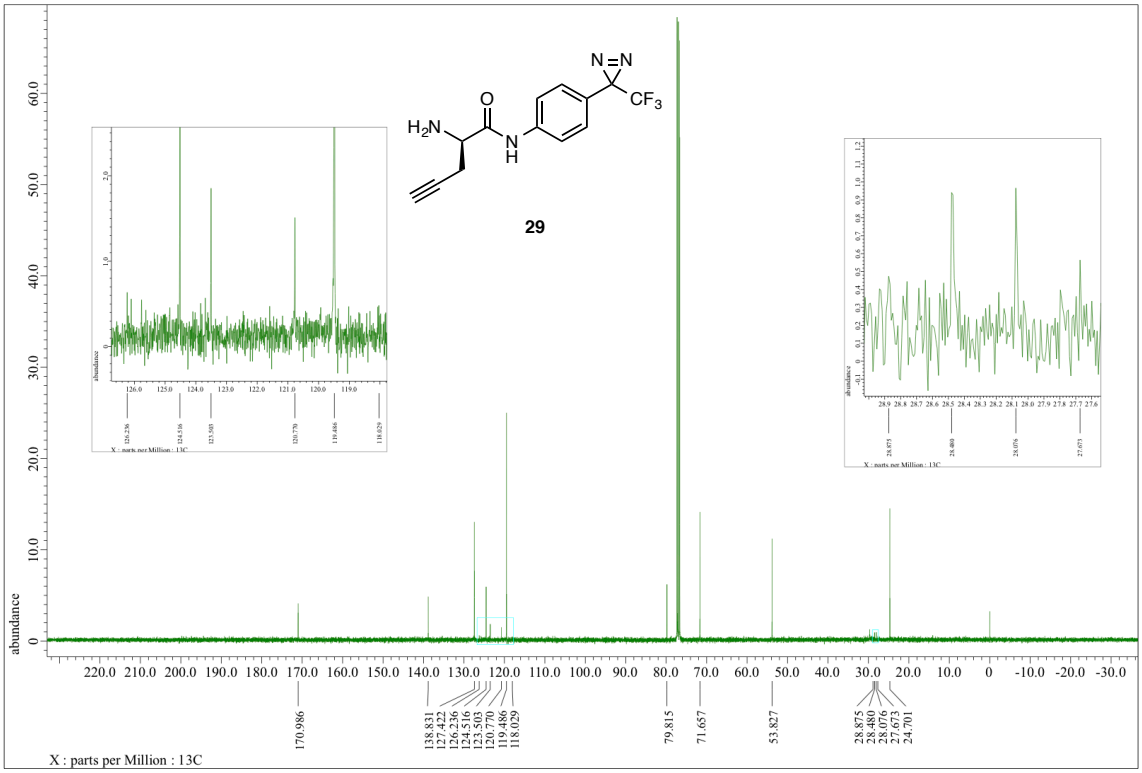


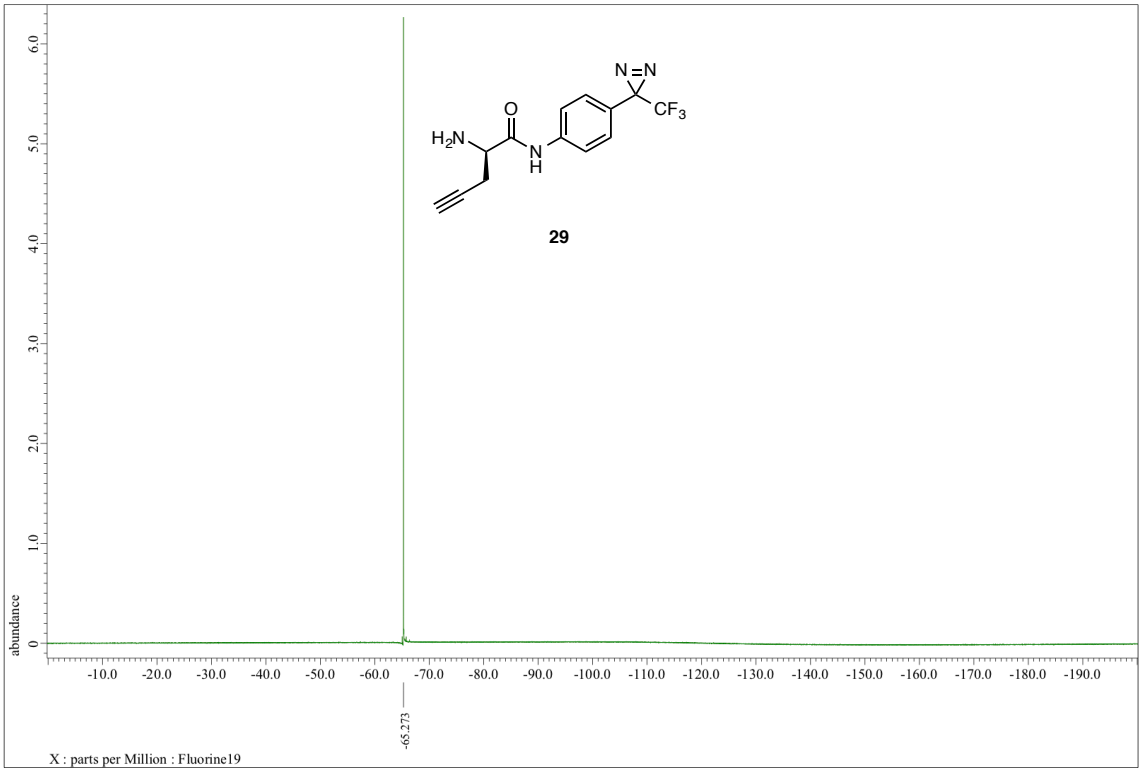



N=N
CF3
O
H
N
Boc
N
H
28
abundance
6.0
5.0
4.0
3.0
2.0
1.0
0
-10.0
-20.0
-30.0
-40.0
-50.0
-60.0
-70.0
-80.0
-90.0
-100.0
-110.0
-120.0
-130.0
-140.0
-150.0
-160.0
-170.0
-180.0
-190.0
-65.273
X : parts per Million : Fluorine19

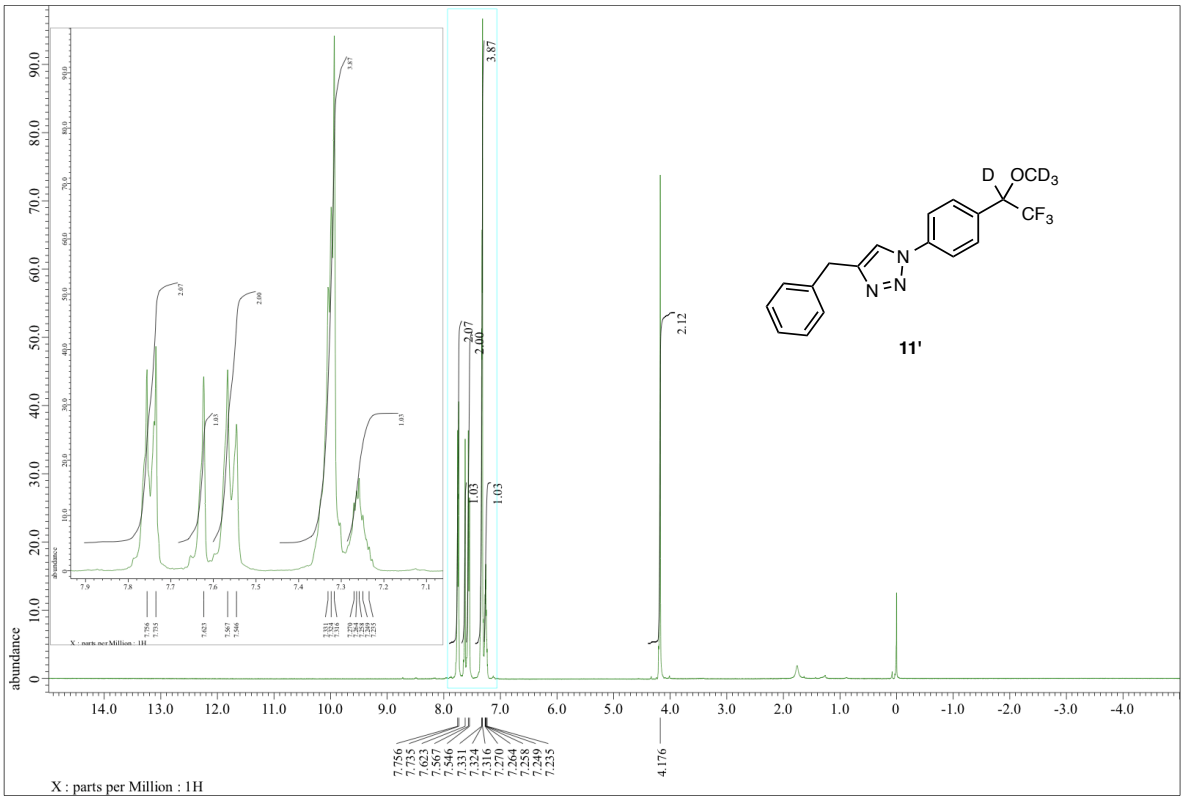
^{1}H, ^{13}C, and ^{19}F NMR spectra of **29** ($CDCl_3$)

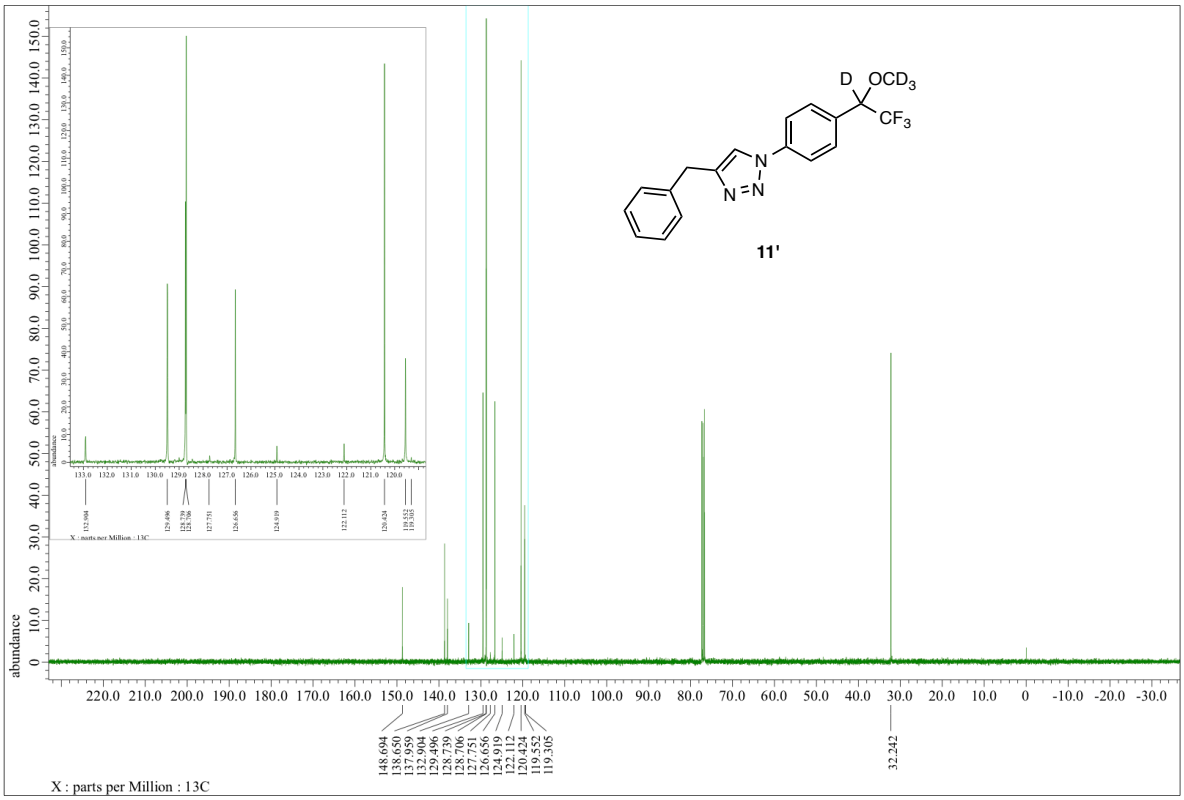


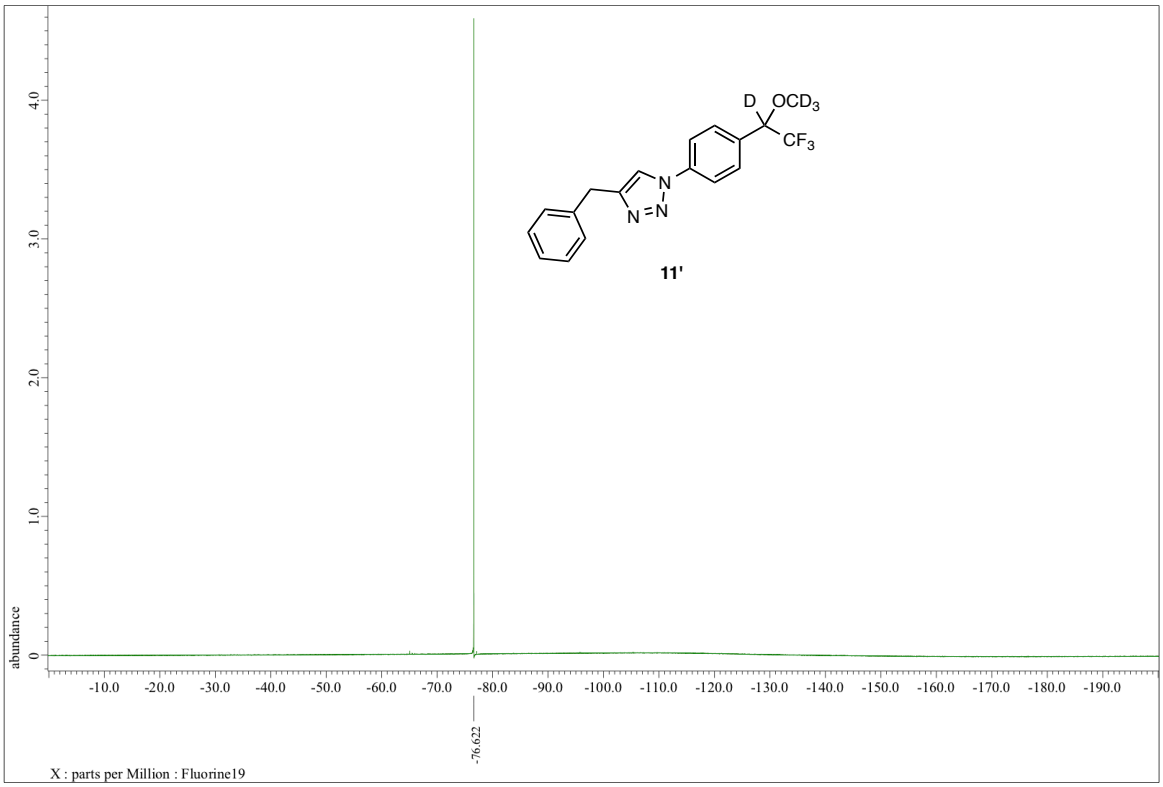



N=N
CF3
O
H2N
N
H
29
abundance
6.0
5.0
4.0
3.0
2.0
1.0
0
-10.0 -20.0 -30.0 -40.0 -50.0 -60.0 -70.0 -80.0 -90.0 -100.0 -110.0 -120.0 -130.0 -140.0 -150.0 -160.0 -170.0 -180.0 -190.0
-65.273
X : parts per Million : Fluorine19

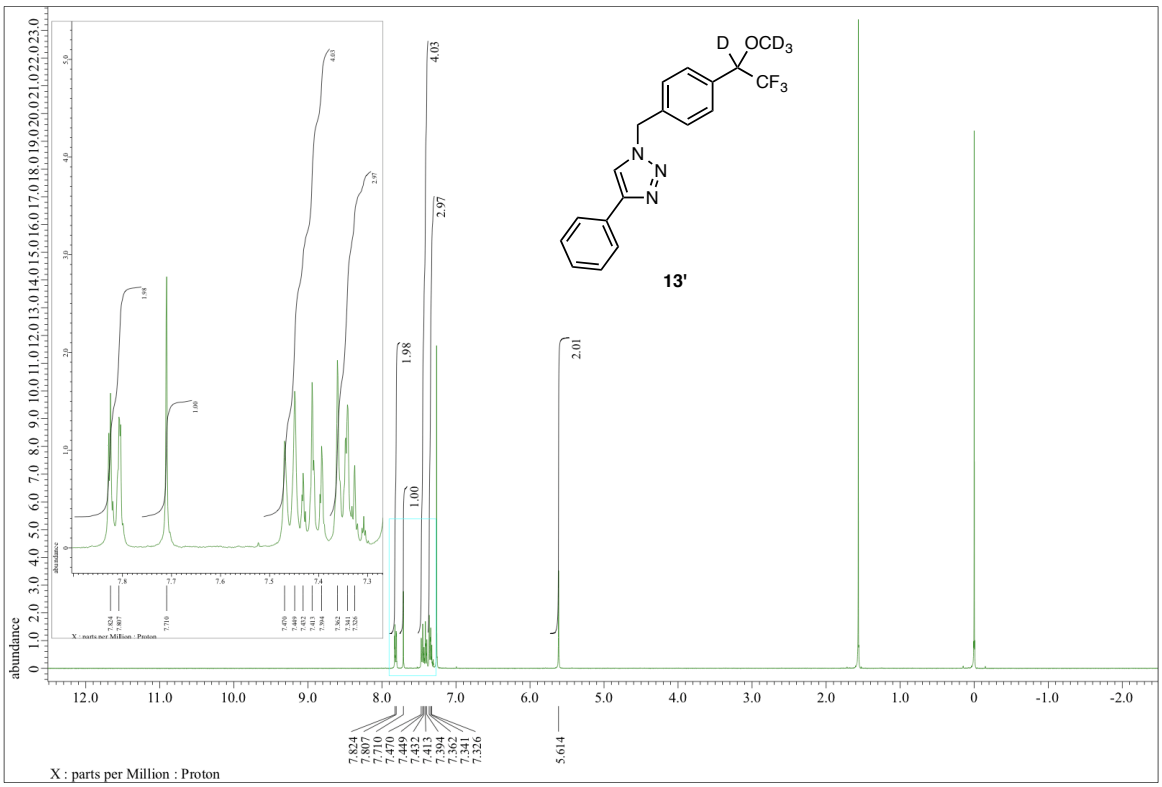
^{1}H, ^{13}C, and ^{19}F NMR spectra of **11′** ($CDCl_3$)

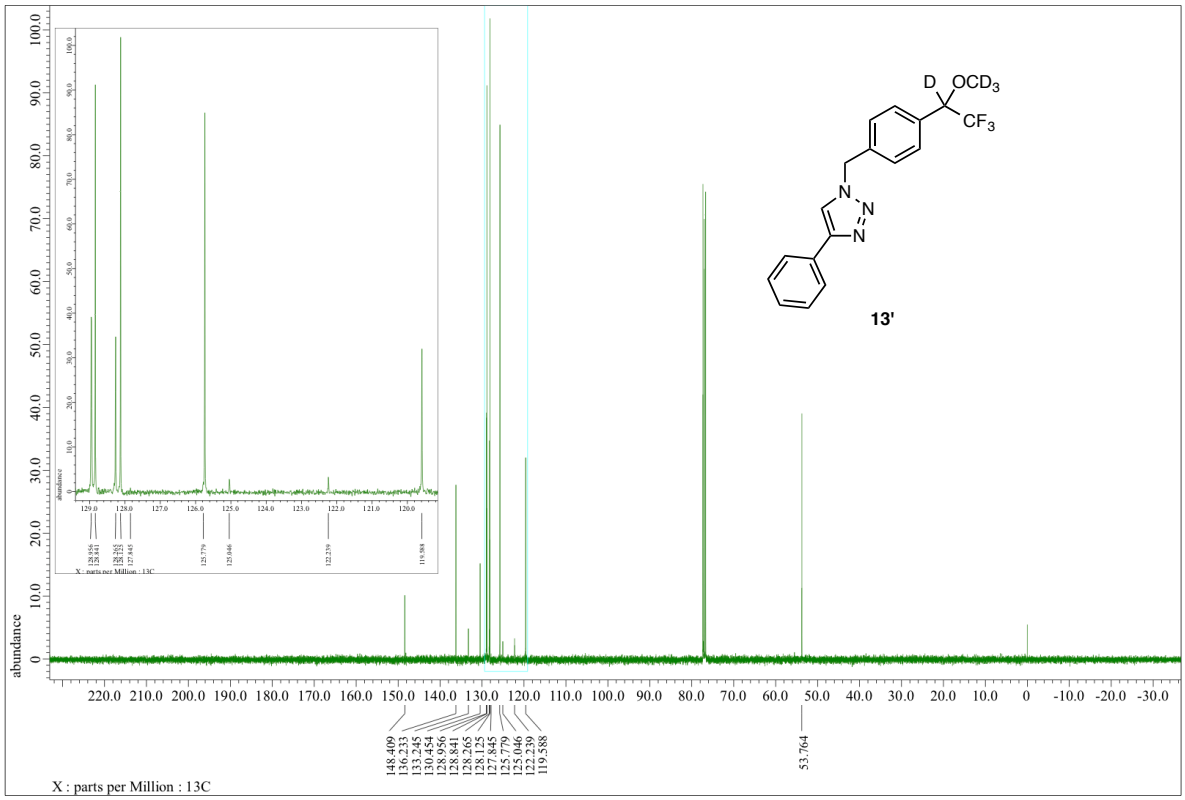


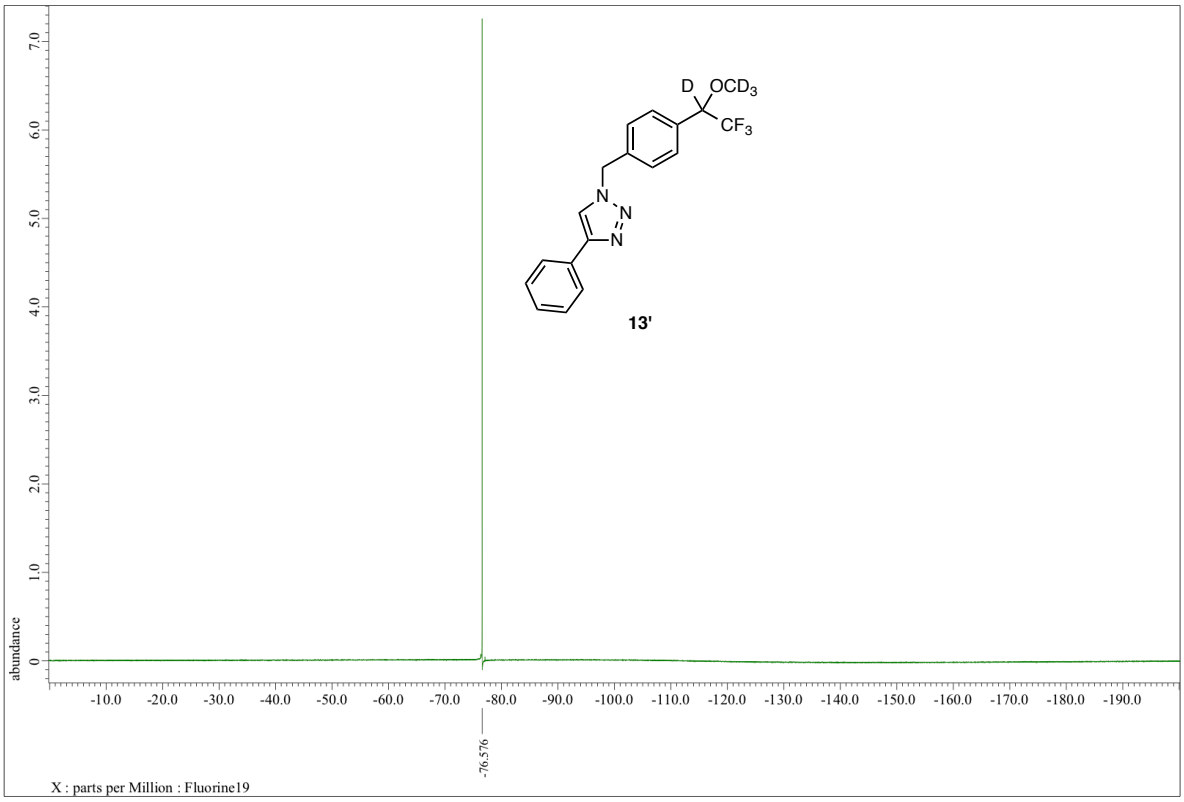



D
OCD3
CF3
N
N=N
11'
abundance
4.0
3.0
2.0
1.0
0
-10.0
-20.0
-30.0
-40.0
-50.0
-60.0
-70.0
-80.0
-90.0
-100.0
-110.0
-120.0
-130.0
-140.0
-150.0
-160.0
-170.0
-180.0
-190.0
-76.622
X : parts per Million : Fluorine19

^{1}H, ^{13}C, and ^{19}F NMR spectra of **13′** ($CDCl_3$)






D
OCD3
CF3
N
N
N
13'
abundance
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
-10.0
-20.0
-30.0
-40.0
-50.0
-60.0
-70.0
-80.0
-90.0
-100.0
-110.0
-120.0
-130.0
-140.0
-150.0
-160.0
-170.0
-180.0
-190.0
-76.576
X : parts per Million : Fluorine19