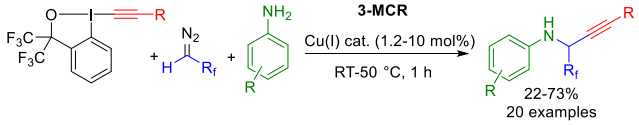
Cu(I)-Catalyzed *gem*-Aminoalkynylation of Diazo Compounds: Straightforward Synthesis of Fluorinated Propargylic Amines

Nieves P. Ramirez, Guillaume Pisella and Jerome Waser

Supporting Information Placeholder

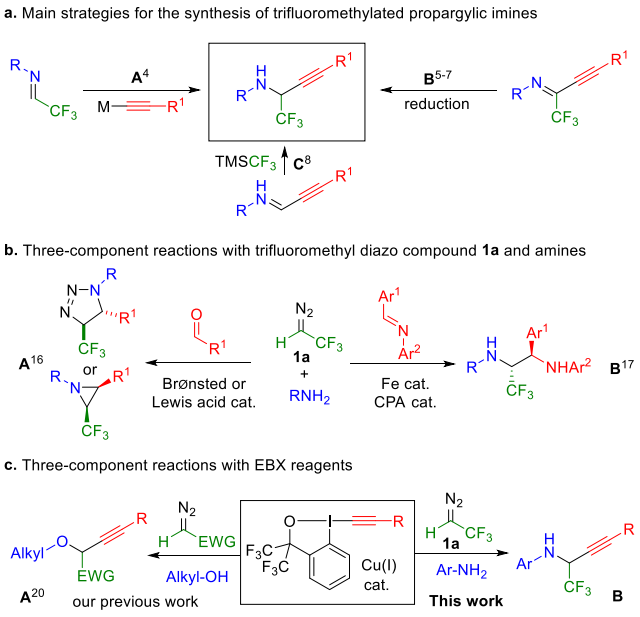


ABSTRACT: The *gem*-aminoalkynylation of fluorinated diazo compounds catalyzed by a simple Cu(I) salt is described. This 3-component reaction allows the straightforward synthesis of propargylic amines with broad functional group tolerance. Both electron-rich and electron-poor anilines can be used as nucleophiles and alkyl, aryl and silyl-substituted EthynylBenziodoXoles (EBX) as electrophiles.

Fluorine chemistry has become one of the most important areas of research in synthetic and medicinal chemistry. The introduction of fluorine atoms into organic molecules has a strong impact on their lipophilicity, acidity and hydrogen bonding affinity and increases as well their metabolic stability.[1,2] In particular, trifluoromethylated propargylic amines are an important subclass of building blocks, due to the synthetic versatility offered by the alkynyl and amine groups and the importance of α-trifluoromethylated amines in bioactive compounds.[3] The two most often used synthetic approaches to access them are the addition of metal acetylides on trifluoromethylated imines,[4] and the reduction/hydrogenation or addition of organometallic reagents to alkyne-substituted trifluoromethylated ketimines (Scheme 1a, **A** and **B**).[5-7] The addition of Ruppert-Prakash reagent to propargylic imines has also been reported (Scheme 1a, **C**).[8] However, the imines needed for these methods are often unstable and need to be prepared *in situ*. Alternative methods for accessing fluorinated propargylic amines avoiding the use of these intermediates would be therefore attractive.

In this context, diazo compounds are attractive starting materials in synthetic chemistry.[9] In the last decade, they have been especially successful in multi-component reactions involving ylide intermediates.[10] They give access to fluorinated building blocks either by using fluorine-containing partners in the multi-component reaction[11] or starting from fluorinated diazo compounds.[12] The latter approach has been exploited for the synthesis of nitrogen containing compounds using nitriles,[13] isocyanides,[14] NFSI[15] and amines[16,17] as partners. The use of broadly available nucleophilic amines is especially attractive and has been exploited both in the Brønsted or Lewis acid activation of diazo compounds for the addition to *in situ* formed imines to give aziridines[16a,b] or triazolines[16c] (Scheme 1b, **A**) and in the enantioselective synthesis of 1,2-diamines proceeding via an iron-carbene intermediates (Scheme 1b, **B**).[17] However, the synthesis of propargylic amines has never been reported starting from diazo compounds.

Scheme 1: Main strategies for the synthesis of trifluoromethylated propargylic imines and multi-component reactions with diazo compounds.

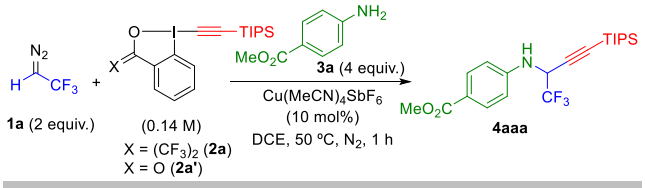


To access propargylic amines from a multi-component reaction with amines as nucleophiles, an electrophilic alkyne-transfer reagent would be required. Our group has popularized the use of ethynylbenziodoxol(on)es (EBX) cyclic hypervalent iodine reagents (HIR) for the Umpolung of the reactivity of alkynes.[18] We have in particular reported the two-component reaction between EBX and diazo compounds,[19] and a three-component reaction using alcohols as nucleophiles (Scheme 1c, **A**).[20] Herein, we report the exten-

sion of three-component reactions between diazo compounds and EBX reagents to anilines as nucleophiles, resulting in a Cu(I)-catalyzed *gem*-aminoalkynylation of diazo compounds for the straightforward synthesis of fluorinated propargylic amines (Scheme 1c, **B**).

During a preliminary screening of amine nucleophiles including aliphatic amines, anilines and carbamates, three-component products were observed only in the case of anilines with benziodoxole reagent **2a** and 2-diazo-1,1,1-trifluoroethane (**1a**). The reaction conditions were then optimized for methyl 4-aminobenzoate (**3a**) as nucleophile and the best results were obtained with 10 mol% $Cu(MeCN)_4SbF_6$ at 50 ºC during 1 h in DCE (Table 1). The desired product **4aaa** was obtained in 80% yield (entry 1).[21] Replacing the catalyst by the commercially available $Cu(MeCN)_4PF_6$ gave **4aaa** in slightly lower yield (73%) (entry 2). Other Cu(I) catalysts led to lower yields (entries 3 and 4). Cu(II) catalysts, such as $Cu(OTf)_2$ or $Cu(OAc)_2$, were also less efficient (entries 5 and 6). In presence of ligands, a lower yield was obtained, and no product was formed in absence of catalyst (see Supporting Information). In addition, the yield of **4aaa** decreased to 49% when the reaction was conducted under more diluted conditions 0.07 M and to 72% when more concentrated (entries 7 and 8). At room temperature, **4aaa** was obtained in 65% yield (entry 9).

Table 1. Optimization Studies



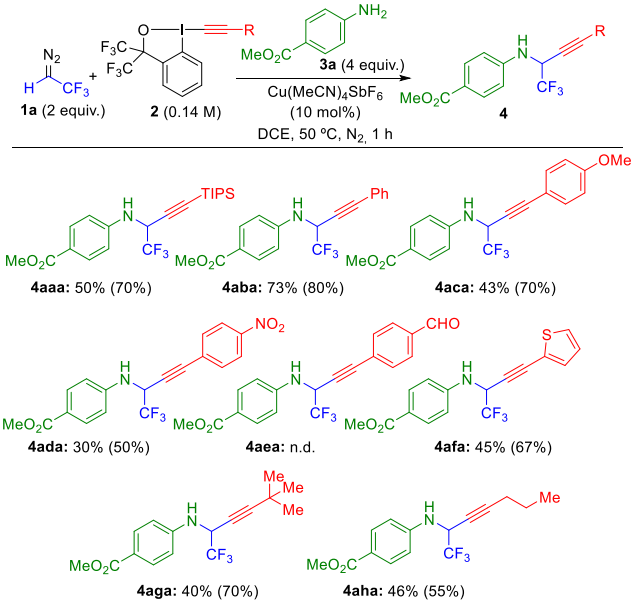
entry	deviation from standard conditions	yield of **4aaa**[%][a]
1	None	80
2	$Cu(MeCN)_4PF_6$	73
3	Cu(OTf)•PhMe	37
4	CuI	12
5	$Cu(OTf)_2$	50
6	$Cu(OAc)_2$	n.d.
7[b]	[**2a**] = 0.07 M	49
8[b]	[**2a**] = 0.2 M	72
9[b]	at 25 °C	65
10	PhCl	73
11	DCM, 40 ºC	77
12	PhMe	56
13	**1a** (1.5 equiv.)	66
14	**3a** (3 equiv.)	60
15	TIPS-EBX (**2a'**) instead of **2a**	n.d[c]
16	EDA instead of **1a**	n.d.

[a]Yield determined by ^{19}F NMR using $PhCF_3$ as internal standard at a 0.1 mmol scale; diazo compound **1a** was added in 30 min via a syringe pump (0.33 M in DCM, 0.6 mL). [b]Using 10 mol% $Cu(MeCN)_4PF_6$ as catalyst. [c]The two-component oxyalkynylation product was obtained as a major product.

The use of others chlorinated solvents (PhCl and DCM) led to the formation of **4aaa** in slightly lower yield (entries 10 and 11). The use of toluene afforded **4aaa** in only 56% yield (entry 12), and no product was obtained in acetonitrile (not shown, see Supporting Information). An excess of both **1a** and **3a** was needed as using a smaller amount led to lower yields (entries 13 and 14). This is mostly due to the formation of an aminal side-product **4aaa'** resulting from oxidative double addition of aniline **3a** on the diazo compound (See Supporting Information). The use of a benziodoxole hypervalent iodine regents was essential, as the corresponding benziodoxolone reagent TIPS-EBX (**2a'**) gave oxyalkynylation instead (entry 15). With ethyl diazoacetate (EDA) in place of **1a**, no product was observed (entry 16).

With optimized conditions in hand, we started the study of the scope and limitations for the *gem*-aminoalkynylation of diazo compounds.[22] Different EBX reagents were examined first (Scheme 2). On a 0.3 mmol scale, TIPS-alkyne product **4aaa** was obtained in 50% isolated yield.[23] Aryl alkynes could be also accessed, with phenyl-substituted alkyne **4aba** isolated in 73% yield. Both an electron-rich methoxy group and an electron-poor nitro group were tolerated on the benzene ring, giving products **4aca** and **4ada** in 43% and 30% isolated yield. Product **4aea** bearing an unprotected aldehyde could not be obtained. Thiophene-substituted alkyne **4afa** was isolated in 45% yield. Finally, aliphatic alkynes **4aga** and **4aha** could also be synthesized in 40% and 46% yield respectively.

Scheme 2. Scope and limitations of EBX reagents 2[a]



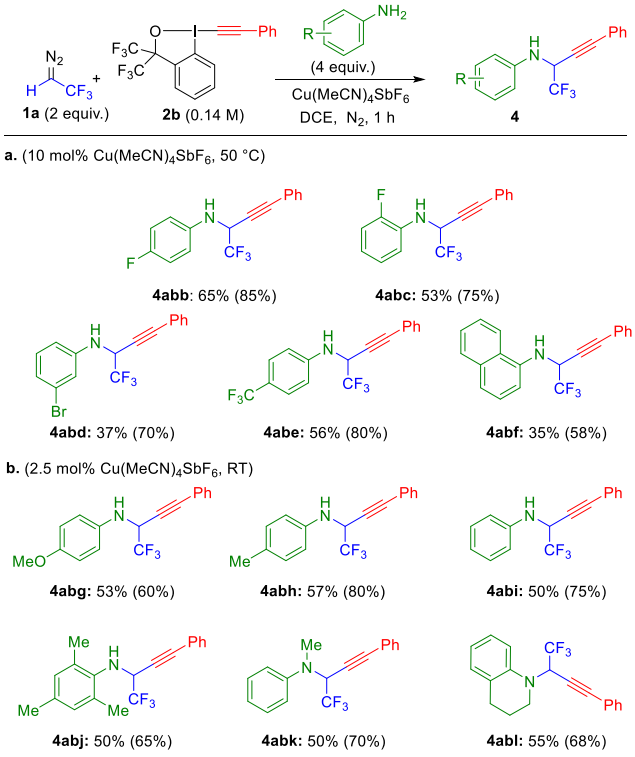
[a]Reactions were run with 0.3 mmol of **2**. Isolated yields of pure compounds. ^{19}F-NMR yields using $PhCF_3$ as internal standard are given in brackets. Diazo compound **1a** was added over 3 min as a 0.33-0.4 M solution in DCM.

We then studied the scope of anilines using benzenealkynyl benziodoxole **2b** and diazo **1a**, as the products were easier to purify (Scheme 3). In addition to **4aba**, *ortho*- and *para*-fluoro anilines afforded the corresponding propargylic amines **4abb** and **4abc** in 65% and 53% yield, respectively. *Meta*-bromo product **4abd** was obtained in 37% yield after purification. A more strongly electron-withdrawing *para*-CF_3 group was well tolerated leading to the formation of

4abe in 56% yield. The 1-naphthyl-substituted propargylic amine **4abf** was obtained in 35% yield. When *para*-nitroaniline was employed, the reaction did not take place.

However, when 4-methoxyaniline (**4g**) was submitted to the optimized reaction conditions, the desired product **4abg** was not obtained. Instead, direct coupling between EBX **2b** and aniline **4g** with loss of the iodine atom was observed by mass spectrometry. At this point, we re-optimized the reaction conditions (See Supporting Information) and we found that the use of 2.5 mol% of $Cu(MeCN)_4SbF_6$ and conducting the reaction at room temperature allowed the formation of **4abg** in 53% isolated yield. These new reaction conditions could be applied to other electron-rich anilines, such as *para*-toluidine, which afforded the desired product **4abh** in 57% yield. Aniline was also a good partner for this multicomponent reaction and the corresponding propargyl amine **4abi** was obtained in 50% isolated yield. The more bulky *ortho*-, *para*-methyl substituted aniline was also a good substrate leading to **4abj** in 50% yield. The use of *N*-alkylated anilines as nucleophiles was also possible. *N*-Methylaniline gave product **4abk** in 50% yield. The product derived from tetrahydroquinoline, **4abl**, was obtained in 55% yield. Interestingly, no alkynylation of the benzene ring of aniline was observed, whereas this transformation was occurring in the presence of a gold catalyst as reported by our group in 2012.[24]

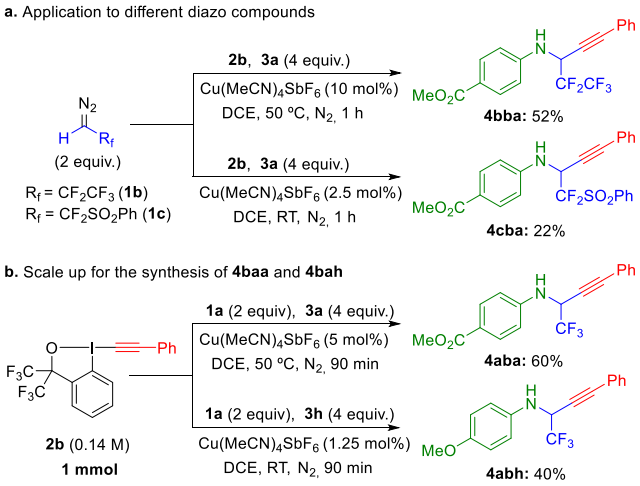
Scheme 3. Scope and limitations of anilines 3[a]



[a]Reactions were run with 0.3 mmol of **2**. Isolated yields of pure compounds. ^{19}F-NMR yields using $PhCF_3$ as internal standard are given in brackets. Diazo compound **1a** was added over 3 min as a 0.33-0.4 M solution in DCM.

Preliminary results were also obtained with different fluorinated diazo compounds (Scheme 4a). 3-Diazo-1,1,1,2,2-pentafluoropropane (**1b**) was well tolerated affording the desired product **4bba** in a 52% yield with 10 mol% catalyst at 50 °C. When diazo compound **1c** was used with 2.5 mol% catalyst at RT product **4cba** was obtained in 22% yield. The introduced CF_2SO_2Ph substituent is a well-established precursor of the CF_2H group.[25]

Scheme 4. Reaction with other diazo compounds (a) and scale up (b)



Finally, we scaled up the reaction to one mmol with anilines **3a** and **3h** (Scheme 4b). Products **4aba** and **4abh** were obtained in 60% and 40% yield. Remarkably, we observed full conversion of **2b** after 90 min with half the loading of Cu(I) catalyst in both cases. The further modification of propargylic amine **4abh** was previously reported by Zhou and co-wokers.[7b]Among other transformations, the removal of the PMP group, as well as the partial and/or complete reduction of the triple bond were described.

In summary, we have developed the *gem*-aminoalkynylation of diazo compounds using anilines as nucleophiles and EBX reagents as electrophiles for the synthesis of fluorinated propargylic amines. The key features of the protocol are: (a) the reaction takes place under mild conditions using a simple copper salt as catalyst; (b) the transformation tolerates a broad range of alkynes (silyl, aryl and alkyl-substituted) and anilines (electron-poor, neutral and electron-rich); (c) the obtained fluorinated propargylic building blocks are expected to be useful for synthetic and medicinal chemistry. Future works will focus on extending the scope of multi-component reactions involving diazo compounds and hypervalent iodine reagents, develop enantioselective variations and more in-depth investigations of the reaction mechanism.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website.

AUTHOR INFORMATION

Corresponding Author

Jerome Waser – *Laboratory of Catalysis and Organic Synthesis, Institut des Sciences et Ingenierie Chimique, Ecole Polytechnique Fédérale de Lausanne, CH-1015 Lausanne, Switzerland;* orcid.org/0000-0002-4570-914X; Email: jerome.waser@ epfl.

Authors

Nieves P. Ramirez – *Laboratory of Catalysis and Organic Synthesis, Institut des Sciences et Ingenierie Chimique, Ecole Polytechnique Fédérale de Lausanne, CH-1015 Lausanne, Switzerland.*

Guillaume Pisella – Laboratory of Catalysis and Organic Synthesis, Institut des Sciences et Ingenierie Chimique, Ecole Polytechnique Fédérale de Lausanne, CH-1015 Lausanne, Switzerland.

Notes

The authors declare no competing financial interest.

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(21) The structure of **4aaa** was confirmed by X-ray analysis. The data is available at the Cambridge Crystallography Data Center (ccdc number 2086310).
(22) We observed a slight improvement of the yield when the diazo compound was added dropwise manually over 3 min.
(23) ^{19}F NMR yield using $PhCF_3$ as internal standard are included in Scheme 2 and 3. The yields of isolated pure compounds are lower due to the difficult separation from hexafluoro-2-(2-iodophenyl)propan-2-ol formed from reagent **2** and other side products. See Supporting Information for details.
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Supporting Information for:

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Nieves P. Ramirez, Guillaume Pisella and Jerome Waser

Laboratory of Catalysis and Organic Synthesis, Ecole Polytechnique Fédérale de Lausanne,

EPFL SB ISIC LCSO, BCH 4306, 1015 Lausanne, Switzerland

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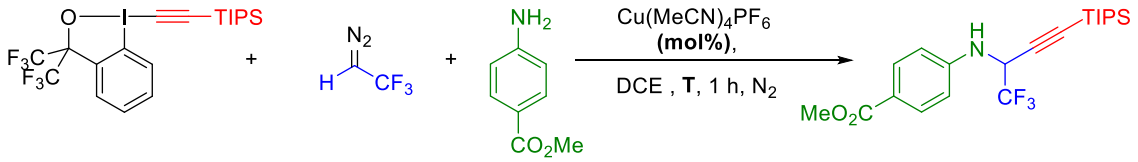
1. General Information

Reagents and solvents were purchased from different trading houses and were used without further purification, unless otherwise stated. TLCs were performed on silica gel 60 F254, using aluminium plates and visualized by exposure with UV. Flash chromatographies (FC) were carried out on handpacked columns of silica gel 60 (230 – 400 mesh). Infrared (IR) analysis was performed with a JASCO FT/IR b4100 spectrophotometer equipped with an ATR PRO410-S and a ZnSe prisma and are reported as cm^{-1} (w = weak, m = medium, s = strong, br = broad). High resolution mass spectra were performed by the mass spectrometry service of ISIC at EPFL on a MICROMASS (ESI) Ultima API (Waters Instrument). The NMR spectra were recorded on a Brucker DPX-400 spectrometer at 400 MHz for ^{1}H, 101 MHz for ^{13}C and 376 MHz for ^{19}F. The chemical shift (δ) for ^{1}H and ^{13}C are given in ppm and referenced to residual signals of the solvents (chloroform-d - 7.26 ppm ^{1}H NMR and 77.16 ppm ^{13}C NMR). ^{13}C NMR spectra were recorded with ^{1}H-decoupling and ^{19}FNMR as ^{19}F-non decoupling. Coupling constants are given in Hertz. The data is being reported using the following abbreviations.: s, singlet; d, doublet; q, quartet; m, multiplet; bs, broad signal; app, apparent. $Cu(MeCN)_4SbF_6$ was prepared according a reported procedure.[1]

2. Optimization studies

Reactions were performed on 0.1 scale in oven dried 6 mL microwave vials equipped with magnetic stirring bars. Unless otherwise stated, solids were weighed inside a glovebox and liquids were posteriorly added. Diazo compound **1a** (0.33 – 0.4 M in DCM was added dropwise via syringe pump addition over 30 min). Reactions were run during 1 h under the indicated conditions and then, monitored by TLC. Reaction mixtures were subsequently filtered through a short pad of celite and washed with EtOAc (15 mL). Finally, the solvent was removed under reduced pressure. Reaction yields were estimated by ^{19}F NMR using $PhCF_3$ (1 equiv) as internal standard (IS).

Table S1. Screening of % mol catalyst, temperature, and concentration of the reaction.

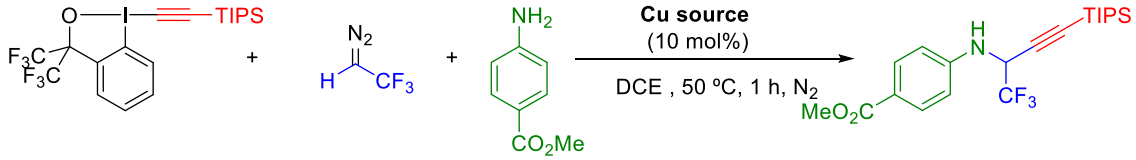


2a **[Concentration]** | **1a** (2 equiv.) | **3a** (4 equiv.) | **4aaa**

Entry	% mol of catalyst	T/ °C	[1a]/M	Yield/%[a]
1	5	50	0.07	15
2	10	rt	0.07	49
3	10	50	0.07	49
4	20	rt	0.07	52
5	10	50	0.03	13
6	**10**	**50**	**0.14**	**73**
7	10	rt	0.14	65
8	20	rt	0.14	58
8	10	50	0.2	72

[a] Determined by ^{19}FNMR using 1 equiv of $PhCF_3$

Table S2. Screening of Copper catalyst

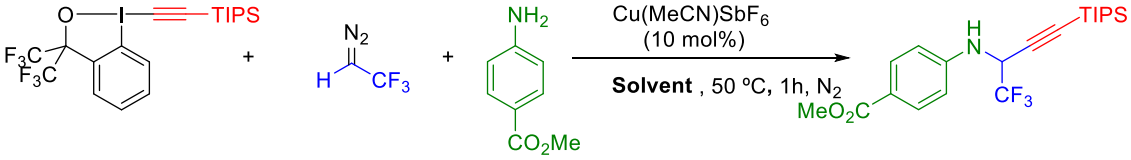


2a [0.14 M] + **1a** (2 equiv.) + **3a** (4 equiv.) → **4aaa**

Entry	Copper catalyst	Yield/%[a]
1	$Cu(MeCN)_4PF_6$	73
2	$Cu(MeCN)_4BF_4$	69
3	**$Cu(MeCN)_4SbF_6$**	**80**
4	Cu(OTf)xPhMe	50
5	$Cu(OTf_2)_2$	37
6	$Cu(OAc)_2$	Traces
7	CuI	Traces
8	CuCN	Traces

[a] Determined by ^{19}FNMR using 1 equiv of $PhCF_3$

Table S3. Screening of solvents

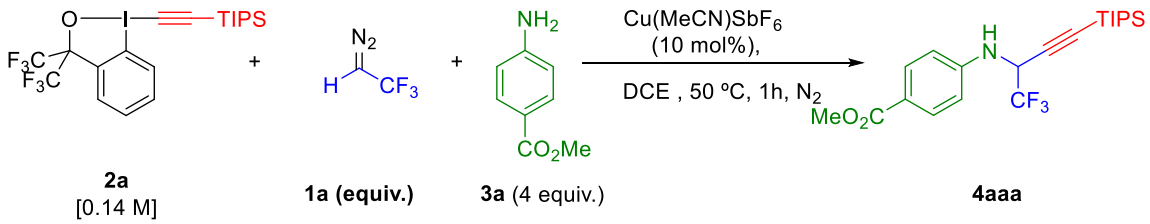


2a [0.14 M] + **1a** (2 equiv.) + **3a** (4 equiv.) → **4aaa**

Entry	Solvent	Yield/%[a]
1	**DCE**	**80**
2	DCE (RT)	64
3	DCE (70 °C)	28
4	DCM (40 °C)	77
5	DCM (RT)	65
2	PhCl	73
3	MeCN	-
4	PhMe	56

[a]Determined by ^{19}FNMR using 1 equiv of $PhCF_3$

Table S4. Screening of equivalents of 1a



2a
[0.14 M]

1a (equiv.)

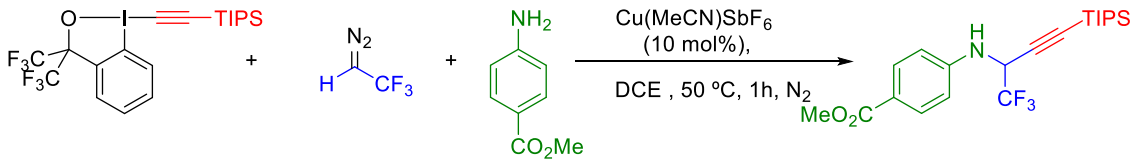
3a (4 equiv.)

4aaa

Entry	Equiv **1a**	Yield/%[a]
1	1.5	66
2	**2**	**80**
3	3	74

[a]Determined by ^{19}FNMR using 1 equiv of $PhCF_3$

Table S5. Screening of equivalents of 3a



2a
[0.14 M]

1a (2 equiv.)

3a (equiv.)

4aaa

Entry	Equiv **3a**	Yield/%[a]
1	1[b]	43
2	1[c]	22
3	2[d]	68
4	3[c]	73
5	3	60
6	**4**	**80**

[a]Determined by ^{19}FNMR using 1 equiv. of $PhCF_3$; [b]1 equiv. of **3a**; [c]1.5 equiv. **1a**; [d]3 equiv. **1a**; e

Table S7. Screening of ligands:

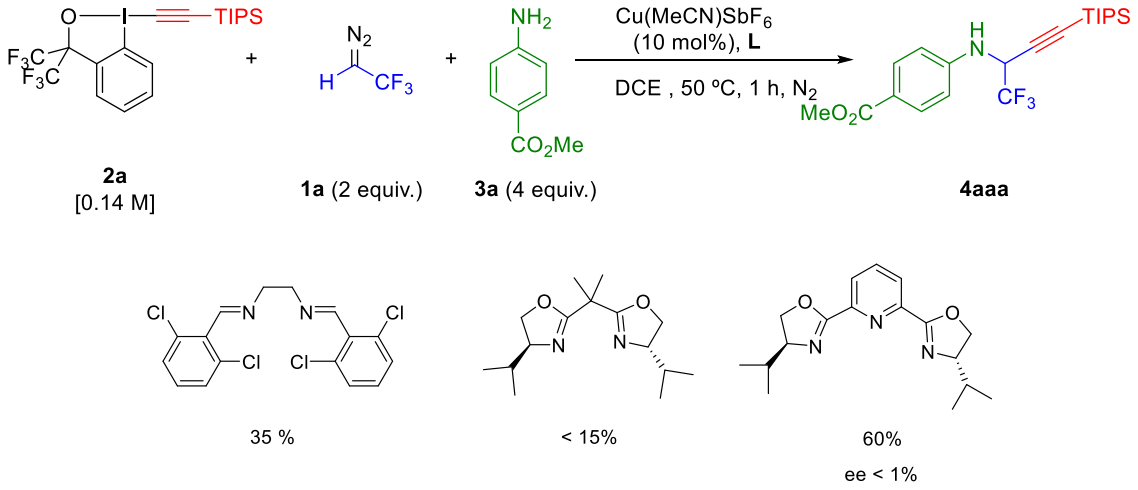
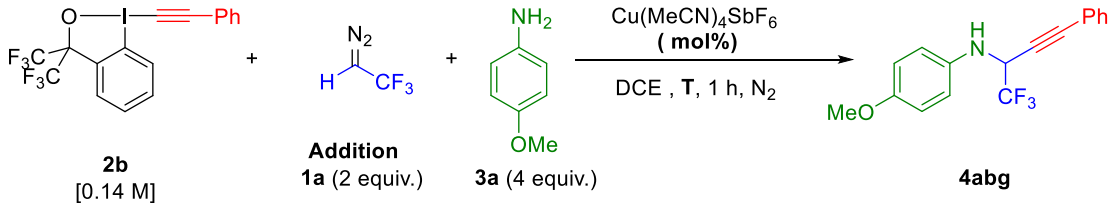


Table S8. Re-optimization of the reaction conditions for the synthesis of compound 4abg



Entry	Addition rate of **1a**	% mol Cu	T/ºC	Yield/%[a]
1	30	10	50	-
2	30	5	RT	43
3	30	2.5	RT	47
4	**Manually**	**2.5**	**RT**	**58**

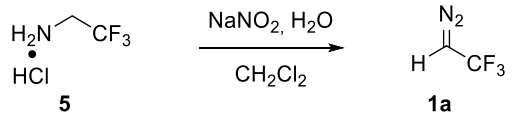
[a]Determined by ^{19}FNMR using 1 equiv of $PhCF_3$

3. Synthesis of Starting Materials

Compounds **1a**, **1b, 2a**, **2b**, **2e-2g**, were previously reported by our group. For this reason and to facilitate a better reproducibility, these procedures has been taken directly from the cited publication.[2]

3.1. Synthesis of diazo compounds (1a-1c)

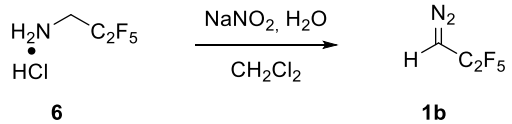
2,2,2-Trifluorodiazoethane (**1a**):[2]



5 **1a**

Following a reported procedure, under argon, 2,2,2-trifluoroethanamine hydrochloride (**5**) (0.678 g, 5.00 mmol, 1.00 equiv) and sodium nitrite (0.379 g, 5.50 mmol, 1.10 equiv) were dissolved in degassed CH_2Cl_2 (10 mL). Degassed water (1.00 mL, 55.5 mmol, 11.1 equiv) was added slowly at 0 °C. The solution was stirred for 2 h at 0 °C and 1 h at room temperature. The aqueous layer was frozen in the freezer overnight (-18 °C) and the organic layer was dried over a plug of potassium carbonate, transferred into a vial, sealed and stored at -18 °C. The concentration of the obtained solution was determined to be 0.37 M by ^{19}F NMR analysis (according to an internal reference, $PhCF_3$). **^{19}F NMR (377 MHz, CH_2Cl_2)** δ -55.6. The values of the NMR spectra are in accordance with reported literature data.[2]

3-Diazo-1,1,1,2,2-pentafluoropropane **(1b)**:[2]

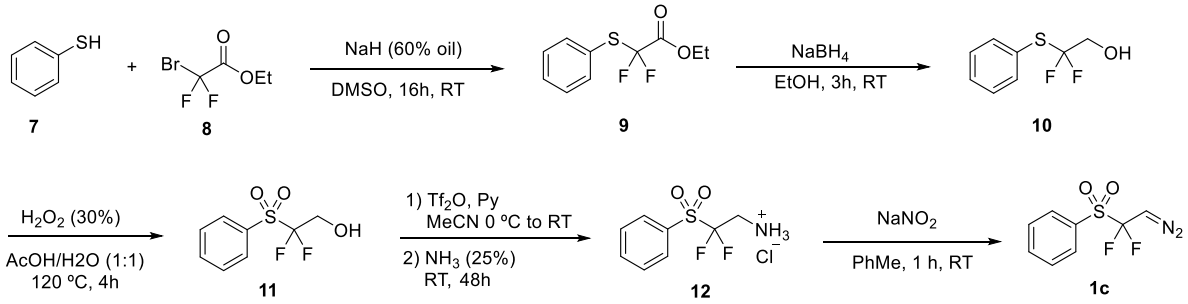


6 **1b**

Under argon, 2,2,2-trifluoroethanamine hydrochloride (**6**) (0.928 g, 5.00 mmol, 1.00 equiv) and sodium nitrite (0.379 g, 5.50 mmol, 1.10 equiv) were dissolved in degassed CH_2Cl_2 (10 mL). Degassed water (1.00 mL, 55.5 mmol, 11.1 equiv) was added slowly at 0 °C. The solution was stirred for 2 h at 0 °C and 1 h at room temperature. The organic layer was isolated, dried over $MgSO_4$, transferred into a vial, sealed and stored at -18 °C. The concentration of the obtained solution was determined to be 0.36 M by ^{19}F NMR analysis (according to an internal reference, $PhCF_3$). **^{19}F NMR (377 MHz, CH_2Cl_2)** δ -

88.96 – -89.01 (m), -110.98 – -111.03 (m). The values of the NMR spectra are in accordance with reported literature data.[2]

Synthesis of diazo **1c:**[7]



- Synthesis of ethyl 2,2-difluoro-2-(phenylthio)acetate (**9**):[8]

In an oven-dried one-necked round bottom flask, a solution of tiophenol (**7**)(5.50 mL, 50.0 mmol, 1.00 equiv.) in DMSO (50 mL) was prepared. Then, the suspension was heated at 40 ºC and stirred during 1 h under N_2 atmosphere. Then, ethyl bromodifluoroacetate (**8**) (7.10 mL, 55.0 mmol, 1.10 equiv) was added to the suspension and was stirred at the same conditions during 16 h. After this time, the reaction mixture was allowed to reach room temperature quenched with aqueous HCl (25 mL) and extracted with Et_2O (4 x 50 mL). Organic layers were combined and washed successively with H_2O (3 x 50 mL), brine (1 x 10 mL), dried over $MgSO_4$, filtered and evaporated under reduced pressure affording a yellow crude liquid. Compound **9** was obtained as a pale-yellow liquid after purification by flash column chromatography (6.5 g, 28.1 mmol, 75%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.65 - 7.59 (m, 2H, Ar*H*), 7.50 - 7.43 (m, 1H, Ar*H*), 7.43 - 7.35 (m, 2H, Ar*H*), 4.25 (q, *J* = 7.2 Hz, 2H, -C*H*$_2$CH$_3$), 1.25 (t, *J* = 7.2 Hz, 3H, CH_3). The values of the NMR spectra are in accordance with reported literature data.[8]

- 2,2-Difluoro-2-(phenylthio)ethan-1-ol (**10**):[9]

To a solution of compound **9** (5.00 g, 25.1 mmol, 1.00) in EtOH (50 mL) was added $NaBH_4$ (1.70 g, 43.0 mmol, 1.72 equiv.). The resulting suspension was stirred at room temperature during 3 h and carefully quenched with H_2O (20 mL). Then, the reaction mixture was extracted with Et_2O (3 x 30 mL). The organic layers were recombined, washed with brine (1 x 10 mL), and dried over $MgSO_4$. Finally, the solvent was removed under reduced pressure affording compound **10** as a pale-yellow liquid (2.9 g, 15 mmol, 70%). Compound **10** was used in the next step without further purification. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.65 - 7.59 (m, 2H, Ar*H*). 7.49 - 7.35 (m, 3H, Ar*H*), 3.87 (t, *J* = 11.9 Hz,

2H, -CF_2CH_2OH), 2.21 (br s,1H, -O*H*). The values of the NMR spectra are in accordance with reported literature data.[8]

- 2,2-Difluoro-2-(phenylsulfonyl)ethan-1-ol (**11**):[7]

To a solution of **10** (1.30 g, 7.10 mmol, 1.00 equiv.) in a 1:1 mixture of AcOH/H_2O (12 mL) was added dropwise aq. 30% H_2O_2 (1.70 mL, 15.6 mmol, 2.20 equiv.). The reaction mixture was heated at 120 ºC and stirred under N_2 atmosphere during 4 h. Then, the reaction mixture was allowed to reach room temperature, quenched with saturated $NaHCO_3$ (10 mL) and extracted with EtOAc (3 x 15 mL). The organic extracts were recombined, washed with brine (1 x 10 mL), dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure, affording compound **11** as a yellow solid (840 mg, 3.78 mmol, 53%). Compound **11** was used in the next step without further purification. **1H NMR (400 MHz, $CDCl_3$)** δ 7.95 - 7.93 (m, 2H, Ar*H*), 7.75 - 7.71 (m, 1H, Ar*H*), 7.61 - 7.53 (m, 1H, Ar*H*), 4.24 (t, *J* = 12.6 Hz, 2H, -CF_2CH_2-), 3.28 (br s, 1H, -O*H*). The values of the NMR spectra are in accordance with reported literature data.[7]

- 2,2-Difluoro-2-(phenylsulfonyl)ethan-1-aminium chloride (**12**):[7]

Pyridine (435 µL, 5.32 mmol, 1.40 equiv) was added to a solution of compound **11** (840 mg, 3.80 mmol, 1.00 equiv.) in MeCN (6.3 mL) and the reaction mixture was cooled to 0 ºC. Subsequently, Tf_2O (1.00 mL, 3.90 mmol, 1.03 equiv) was added dropwise and the reaction mixture was stirred at 0 ºC during 30 min under N_2 atmosphere. Then, the solution was allowed to reach room temperature and stirred 2 hours and NH_3 (25%) (2.5 mL) was added. The reaction mixture was stirred during 48 h at room temperature and then, quenched with H_2O (15 mL) and extracted with DCM (3 x 20 mL). The organic layers were recombined, washed with brine (1 x 10 mL), dried over $MgSO_4$, filtered and concentrated under reduced pressure affording a pale-yellow residue which was dissolved in DCM (3 mL). Then, a solution of HCl (2 N) in Et_2O (2.1 mL, 1 equiv.) was added and the resulting solution was stirred during 10 min. The formed red solid was filtered-off and washed with Et_2O (3 x 10 mL) affording compound **12** as a red solid (309 mg, 3.90 mmol, 32%). **^{1}H NMR (400 MHz, MeOD)** δ 8.07 (d, *J* = 7.3 Hz, 2H, Ar*H*), 7.98 - 7.93 (m, 1H, Ar*H*), 7.84 - 7.76 (m, 2H, Ar*H*), 4.02 (t, *J* = 15.5 Hz, 2H, -$CF_2CH_2NH_3$-). The values of the NMR spectra are in accordance with reported literature data.[7]

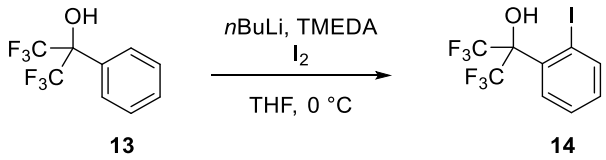
- ((2-Diazo-1,1-difluoroethyl)sulfonyl)benzene (**1c**):[7]

To a solution of **12** (174 mg, 0.750 mmol, 1.00 equiv.) in a mixture of PhMe (1.3 mL) and H_2O (130 µL) was added $NaNO_2$ (62 mg, 0.90 mmol, 1.20 equiv.). The resulting yellow solution was stirred at room temperature under N_2 atmosphere during 1 h. The reaction mixture was extracted with EtOAc (2x 5 mL) and the organic layer was washed with brine (1 x 2 mL), dried over $MgSO_4$ and the solvent was removed under reduced pressure affording a yellow residue. Compound **1c** was obtained as a yellow oil after purification by flash column chromatography (100 pentane to 80:20 pentane/EtOAc) (150 mg, 0.640 mmol, 85%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.95 - 7.92 (m, 2H, Ar*H*), 7.73 - 7.68 (m, 1H, Ar*H*), 7.60 - 7.54 (m, 2H, Ar*H*), 4.43 (t, *J* = 7.9 Hz, 1H-C*H*N_2); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 135.5, 132.5, 130.7, 129.5, 122.1 (t, *J* = 287.8 Hz), 37.8 (t, *J* = 39.2 Hz). The values of the NMR spectra are in accordance with reported literature data.[7]

3.1. Synthesis of Hypervalent Iodine Reagents

3..1.1. Synthesis of Precursors **13** and **14**

1,1,1,3,3,3-Hexafluoro-2-(2-iodophenyl)propan-2-ol **(13)**:[2]

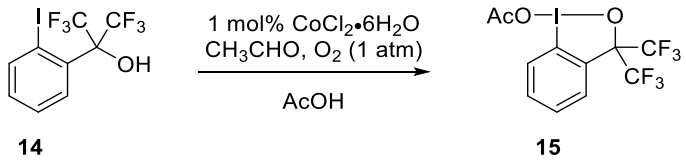


13 **14**

TMEDA (1.27 mL, 8.40 mmol, 0.20 equiv) was added to a solution of *n*-BuLi (37.0 mL, 92.0 mmol, 2.20 equiv, 2.5 M in hexanes). After 15 min, the cloudy solution was cooled to 0 °C and 1,1,1,3,3,3-hexafluoro-2-phenylpropan-2-ol (**13**) (7.07 mL, 42.0 mmol, 1.00 equiv) in THF (6.0 mL) was added dropwise. The reaction was stirred 30 min at 0 °C and then 18 h at room temperature. Then, THF (30.0 mL) was added, followed by the portionwise addition of I_2 (11.3 g, 44.5 mmol, 1.05 equiv) at 0 °C and the mixture was stirred at 0 °C for 30 min and 4 h at room temperature. The reaction was quenched with saturated aqueous NH_4Cl (50 mL) and extracted with diethyl ether (3 x 30 mL). The combined organic phases were washed with water, brine, dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. The crude product was purified by column chromatography using EtOAc/pentane 3:97 as eluent to afford 1,1,1,3,3,3-hexafluoro-2-(2-iodophenyl)propan-2-ol (**14**) as a colorless oil (13.9 g, 37.5 mmol, 89%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.13 (dd, *J* = 7.9, 1.4 Hz, 1H, Ar*H*), 7.63 (d, *J* = 8.2 Hz, 1H, Ar*H*), 7.43 (dt, *J* = 8.4, 1.4 Hz, 1H, Ar*H*), 7.11 (dt, *J* = 8.0, 1.5 Hz, 1H, Ar*H*), 4.23

(s, 1H, O*H*); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 144.7, 131.4, 130.0, 129.7, 128.0, 122.6 (q, J = 291.4 Hz), 90.6, 78.9 (q, J = 32.1 Hz); **^{19}F NMR (376 MHz, $CDCl_3$)** δ -73.4. The values of the NMR spectra are in accordance with reported literature data.[2]

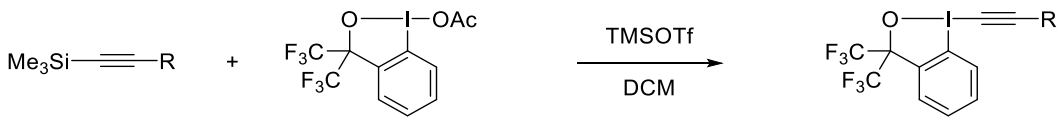
3,3-Bis(trifluoromethyl)-1λ^3-benzo[d][1,2]iodaoxol-1(3H)-yl acetate **(15)**:[2]



14 **15**

A 500 mL flsak was charged with glacial acetic acid (188 mL), 1,1,1,3,3,3-hexafluoro-2-(2-iodophenyl)propan-2-ol (**14**) (13.9 g, 37.5 mmol, 1.00 equiv) and cobalt(II) chloride hexahydrate (89.0 g, 0.375 mmol, 0.01 equiv). The reaction vessel was purged with O_2 for 5 min before acetaldehyde (21.4 mL, 379 mmol, 10.0 equiv) was added in one portion. The reaction mixture was stirred under 1 atm of O_2, delivered by inflated balloon, at room temperature for 12 h. Acetaldehyde (21.4 mL, 379 mmol, 10.00 equiv) was added and the reaction continue for 6 h. The solvent was removed under reduced pressure and the residue was dissolved in DCM. The organic layer was washed with distilled water (50 mL) and extracted with DCM (3 x 50 mL). The organic layer was dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. The obtained residue was triturated in pentane for 0.5 h, filtered and washed with pentane (operation repeated 2 times) to afford 3,3-bis(trifluoromethyl)-1λ^3-benzo[*d*][1,2]iodaoxol-1(3*H*)-yl acetate (**15**) as a white solid (9.91 g, 23.2 mmol, 62%). **^{1}H NMR (400 MHz, DMSO-d_6)** δ 7.93 (ddd, J = 8.4, 7.1, 1.6 Hz, 1H, Ar*H*), 7.85 – 7.69 (m, 3H, Ar*H*), 2.19 (s, 3H, (O)CC*H*$_3$); **^{13}C NMR (101 MHz, DMSO-d_6)** δ 174.4, 134.2, 131.4, 131.0, 130.8, 129.5 – 129.0 (m), 123.1 (q, J = 289.5 Hz), 116.1, 84.5 – 83.7 (m), 20.0; **^{19}F NMR (376 MHz, DMSO-d_6)** δ -75.1. The values of the NMR spectra are in accordance with reported literature data.[2]**Error! Bookmark not defined.**

3.1.2. Synthesis of Hypervalent Iodine Reagents (EBX') (**2a-2h**):[2]

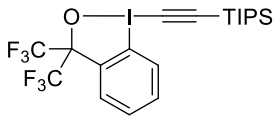


16a-17h **15** **2a-2h**

To a solution of 3,3-bis(trifluoromethyl)-1λ^3-benzo[*d*][1,2]iodaoxol-1(3*H*)-yl acetate (**15**) (1.00 equiv) in dry DCM (*c* = 0.2 M) was added trimethylsilyl

trifluoromethanesulfonate (1.10 equiv) dropwise at room temperature and the reaction mixture was stirred for 1 h. After this time, the corresponding trimethylethynylsilane (**16a-16h**) (1.10 equiv) was added and the mixture was stirred for 6 h at room temperature. The reaction mixture was then quenched with saturated aqueous $NaHCO_3$ solution and extracted with dichloromethane (3 times). The combined organic extracts were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by column chromatography using EtOAc/pentane as eluent to give the corresponding EBX' reagent (**2a-2h**).

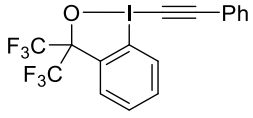
((3,3-Bis(trifluoromethyl)-1λ³-benzo[d][1,2]iodaoxol-1(3H) yl)ethynyl)triisopropylsilane **(2a)**:[2]



2a

Following the general procedure, starting from triisopropyl((trimethylsilyl)ethynyl)silane (**16a**) (2.80 g, 11.0 mmol) and 3,3-bis(trifluoromethyl)-1λ^3-benzo[*d*][1,2]iodaoxol-1(3*H*)-yl acetate (**15**) (4.28 g, 10.0 mmol), afforded ((3,3-bis(trifluoromethyl)-1λ^3-benzo[*d*][1,2]iodaoxol-1(3*H*)-yl)ethynyl)triisopropylsilane (**2a**) as a white solid (5.33 g, 9.68 mmol, 97%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.36 (dd, *J* = 7.9, 1.5 Hz, 1H, Ar*H*), 7.88 – 7.81 (m, 1H, Ar*H*), 7.74 – 7.62 (m, 2H, Ar*H*), 1.23 – 1.07 (m, 21H, TIPS); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 132.9, 131.3, 130.1, 130.2 – 130.0 (m), 128.3, 123.7 (q, *J* = 290.4 Hz), 112.3, 111.0, 81.6 (p, *J* = 29.5 Hz), 69.9, 18.7, 11.4; **^{19}F NMR (376 MHz, $CDCl_3$)** δ -76.2. The values of the NMR spectra are in accordance with reported literature data.[2]

1-(Phenylethynyl)-3,3-bis(trifluoromethyl)-1,3-dihydro-1λ³-benzo[d][1,2]iodaoxole **(2b)**:[2]

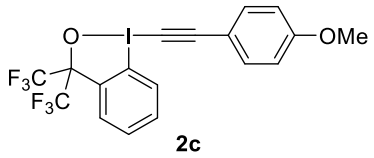


2b

Following the general procedure, starting from trimethyl(phenylethynyl)silane (**16b**) (192 mg, 1.10 mmol) and 3,3-bis(trifluoromethyl)-1λ^3-benzo[*d*][1,2]iodaoxol-1(3*H*)-yl acetate

(**15**) (428 mg, 1.00 mmol), afforded 1-(phenylethynyl)-3,3-bis(trifluoromethyl)-1,3-dihydro-1λ^3-benzo[*d*][1,2]iodaoxole (**2b**) as a white solid (395 mg, 0.840 mmol, 84%). **^{1}H NMR (400 MHz, CDCl$_3$)** δ 8.34 – 8.24 (m, 1H, Ar*H*), 7.86 (ddt, *J* = 7.4, 3.2, 1.4 Hz, 1H, Ar*H*), 7.75 – 7.66 (m, 2H, Ar*H*), 7.59 – 7.53 (m, 2H, Ar*H*), 7.48 – 7.37 (m, 3H, Ar*H*); **^{13}C NMR (101 MHz, CDCl$_3$)** δ 133.1, 132.8, 131.4, 130.3, 130.1, 130.0, 128.8, 128.5, 123.7 (q, *J* = 289.8 Hz), 121.4, 111.6, 105.4, 82.5 – 81.1 (m), 54.5; **^{19}F NMR (376 MHz, CDCl$_3$)** δ -76.2. The values of the NMR spectra are in accordance with reported literature data.[2]

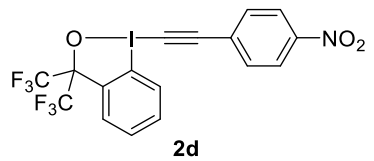
1-((4-methoxyphenyl)ethynyl)-3,3-bis(trifluoromethyl)-1,3-dihydro-λ^3 benzo[d][1,2]iodaoxole **(2c)**:[3]



2c

Following the general procedure, starting from ((4-methoxyphenyl)ethynyl)trimethylsilane (**16c**)[4] (225 mg, 1.10 mmol) and and 3,3-bis(trifluoromethyl)-1λ^3-benzo[*d*][1,2]iodaoxol-1(3*H*)-yl acetate (**15**) (428 mg, 1.00 mmol), afforded 1-((4-methoxyphenyl)ethynyl)-3,3-bis(trifluoromethyl)-1,3-dihydro-λ^3-benzo[*d*][1,2]iodaoxole (**2c**) as a yellow amorphous solid (260 mg, 0.520 mmol, 52%). **^{1}H NMR (400 MHz, CDCl$_3$)** δ 8.31 - 8.25 (m, 1H, Ar*H*), 7.88 - 7.79 (m, 1H, Ar*H*), 7.72 - 7.64 (m, 2H, Ar*H*), 7.55 - 7.48 (m, 2H, Ar*H*), 6.95 – 6.90 (m, 2H, Ar*H*), 3.85 (s, 1H, -OC*H$_3$*); **^{13}C NMR (101 MHz, CDCl$_3$)** δ 161.3, 134.6, 133.0, 131.3, 130.2, 130.0 (br s), 128.4, 123.8 (q, *J* = 290.3 Hz), 114.4, 113.3, 111.7, 106.0, 81.8 (q, *J* = 81.8 Hz), 55.6, 52.8; **^{19}F NMR (376 MHz, CDCl$_3$)** δ -76.2. The values of the NMR spectra are in accordance with reported literature data.[3]

1-((4-nitrophenyl)ethynyl)-3,3-bis(trifluoromethyl)-1,3-dihydro-λ^3-benzo[d][1,2]iodaoxole **(2d):**[5]

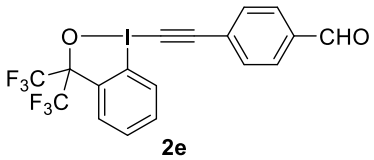


2d

Following the general procedure, starting from ((4-nitrophenyl)ethynyl)trimethylsilane (**16d**)[4] (241. mg, 1.10 mmol) and and 3,3-bis(trifluoromethyl)-1λ^3-

benzo[*d*][1,2]iodaoxol-1(3*H*)-yl acetate (**15**) (428 mg, 1.00 mmol), afforded 1-((4-nitrophenyl)ethynyl)-3,3-bis(trifluoromethyl)-1,3-dihydro-1l3-benzo[d][1,2]iodaoxole (**2d**) as a yellow amorphous solid (232 mg, 0.450 mmol, 45%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.30 - 8.25 (m, 2H Ar*H*), 8.24 - 8.21 (m, 1H, Ar*H*), 7.90 - 7.84 (m, 1H, Ar*H*), 7.78 - 7.68 (m, 4H, Ar*H*); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 148.2, 133.5, 133.3, 131.7, 130.2 (br s), 130.1, 128.5, 128.1, 127.9, 124.0, 123.6 (q, *J* = 289.8 Hz) 111.4, 102.3, 81.8 (m), 61.3; **^{19}F NMR (376 MHz, $CDCl_3$)** δ -76.1. The values of the NMR spectra are in accordance with reported literature data.[5]

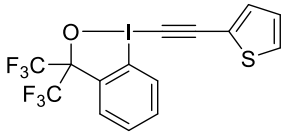
4-((3,3-bis(trifluoromethyl)-λ^3-benzo[d][1,2]iodaoxol-1(3H)-yl)ethynyl)benzaldehyde **(2e)**:[6]



2e

Following the general procedure, starting from 4-((trimethylsilyl)ethynyl)benzaldehyde (**16e**) (223 mg, 1.100 mmol) and 3,3-bis(trifluoromethyl)-1λ^3-benzo[*d*][1,2]iodaoxol-1(3*H*)-yl acetate (**15**) (428 mg, 1.00 mmol), afforded 4-((3,3-bis(trifluoromethyl)-λ^3-benzo[*d*][1,2]iodaoxol-1(3H)-yl)ethynyl)benzaldehyde (**2e**) (383 mg, 0.769 mmol, 77%) as a light yellow solid after 18 h of reaction. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 10.06 (s, 1H, -C*H*O), 8.29 - 8.21 (m, 1H, Ar*H*), 7.97 - 7.89 (m, 2H, Ar*H*), 7.87 (dtd, *J* = 7.0, 2.7, 1.4 Hz, 1H, Ar*H*), 7.78 - 7.66 (m, 4H, Ar*H*); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 191.2, 136.8, 133.3, 133.2, 131.6, 130.5 - 130.1 (m), 130.1, 129.8, 128.5, 127.4, 123.6 (q, *J* = 290.4 Hz), 111.4, 103.6, 82.8 - 80.7 (m), 59.5; **^{19}F NMR (376 MHz, $CDCl_3$)** δ -76.1. The values of the NMR spectra are in accordance with reported literature data.[6]

1-(Thiophen-2-ylethynyl)-3,3-bis(trifluoromethyl)-1,3-dihydro-1λ^3-benzo[d][1,2]iodaoxole **(2f)**:[2]

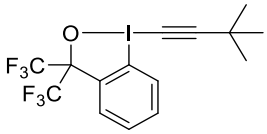


2f

Following general procedure, starting from trimethyl(thiophen-2-ylethynyl)silane (**16f**) (182 μL, 1.10 mmol) and 3,3-bis(trifluoromethyl)-1λ^3-benzo[*d*][1,2]iodaoxol-1(3*H*)-yl acetate (**15**) (428 mg, 1.00 mmol), afforded 1-(thiophen-2-ylethynyl)-3,3-

bis(trifluoromethyl)-1,3-dihydro-1λ^3-benzo[*d*][1,2]iodaoxole (**2f**) as an off-white solid (403 mg, 0.850 mmol, 85%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.30 – 8.19 (m, 1H, Ar*H*), 7.89 – 7.80 (m, 1H, Ar*H*), 7.76 – 7.66 (m, 2H, Ar*H*), 7.44 – 7.38 (m, 2H, Ar*H*), 7.07 (dd, J = 5.1, 3.7 Hz, 1H, Ar*H*); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 135.2, 133.2, 131.4, 130.2, 123.0, 129.9, 128.5, 127.5, 123.7 (q, *J* = 291.2 Hz), 121.3, 111.8, 98.4, 81.8 (p, *J* = 29.7 Hz), 59.7; **^{19}F NMR (376 MHz, $CDCl_3$)** δ -76.2. The values of the NMR spectra are in accordance with reported literature data.[2]

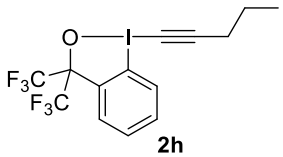
1-(3,3-Dimethylbut-1-yn-1-yl)-3,3-bis(trifluoromethyl)-1,3-dihydro-1λ^3-benzo[d][1,2]iodaoxole **(2g):**[2]



2g

Following the general procedure A, starting from (3,3-dimethylbut-1-yn-1-yl)trimethylsilane (**16g**) (229 μL, 1.10 mmol) and 3,3-bis(trifluoromethyl)-1λ^3-benzo[*d*][1,2]iodaoxol-1(3*H*)-yl acetate (**15**) (428 mg, 1.00 mmol), afforded 1-(3,3-dimethylbut-1-yn-1-yl)-3,3-bis(trifluoromethyl)-1,3-dihydro-1λ^3-benzo[*d*][1,2]iodaoxole (**2g**) as a white solid (350 mg, 0.780 mmol, 78%). **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.24 – 8.14 (m, 1H, Ar*H*), 7.89 – 7.78 (m, 1H, Ar*H*), 7.74 – 7.64 (m, 2H, Ar*H*), 1.34 (s, 9H, *tBu*); **^{13}C NMR (101 MHz, $CDCl_3$)** δ 132.7, 131.1, 130.3, 130.0, 128.0, 123.9 (q, *J* = 290.3 Hz), 116.1, 111.2, 81.9 (p, *J* = 29.6 Hz), 42.0, 30.8, 29.5; **^{19}F NMR (376 MHz, $CDCl_3$)** δ -76.2. The values of the NMR spectra are in accordance with reported literature data.[2]

1-(pent-1-yn-1-yl)-3,3-bis(trifluoromethyl)-1,3-dihydro-λ^3-benzo[d][1,2]iodaoxole (**2h**):



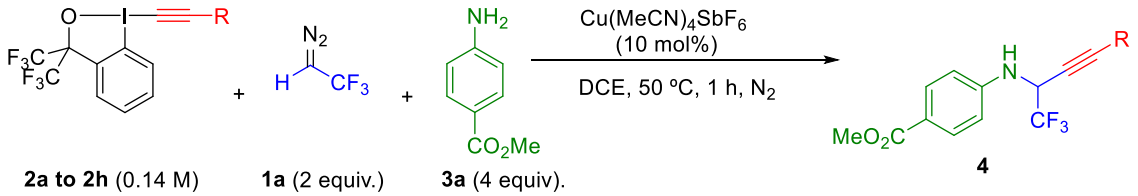
2h

Following the general procedure, starting from (3,3-dimethylbut-1-yn-1-yl)trimethylsilane (**16h**) (236 μL, 1.10 mmol) and 3,3-bis(trifluoromethyl)-1λ^3-benzo[*d*][1,2]iodaoxol-1(3*H*)-yl acetate (**15**) (500 mg, 1.17 mmol), afforded 1-(3,3-dimethylbut-1-yn-1-yl)-3,3-bis(trifluoromethyl)-1,3-dihydro-1λ^3-

benzo[*d*][1,2]iodaoxole (**2h**) as an off-white solid (340 mg, 0.780 mmol, 67% yield).· **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.28 – 8.17 (m, 1H, Ar*H*), 7.87 – 7.81 (m, 1H, Ar*H*), (tdd, *J* = 4.3, 2.5, 1.3 Hz, 1H, Ar*H*), 7.73 – 7.62 (m, 2H, Ar*H*), 2.51 (t, *J* = 7.0 Hz, 2H, -CC*H*$_2$CH$_2$-), 1.66 (h, *J* = 7.3 Hz, 2H, -CH$_2$C*H*$_2$CH$_3$), 1.06 (t, *J* = 7.4 Hz, 3H, -CH$_2$C*H*$_3$); **^{13}C NMR (101 MHz, CDCl3)** δ 132.9, 131.2, 130.2, 129.9 (m), 128.3, 123.7 (q, *J* = 290.7 Hz), 111.0, 108.1, 81.60 (m), 43.4, 22.4, 22.0, 13.7; **^{19}F NMR (376 MHz, $CDCl_3$)** δ -76.2; **IR** *(ν_{max}, cm^{-1})* 2966 (w), 2877 (w), 2252 (w), 2156 (w), 1458 (w), 1265 (m), 1188 (m), 1157 (m), 957 (m), 906 (s), 733 (s), 652 (w); **HRMS (ESI/QTOF)** *m/z*: $[M + H]^+$ *Calcd* for $C_{14}H_{12}F_6IO^+$ 436.9832; Found 436.9832.

4. General procedures for the preparation of compounds 4

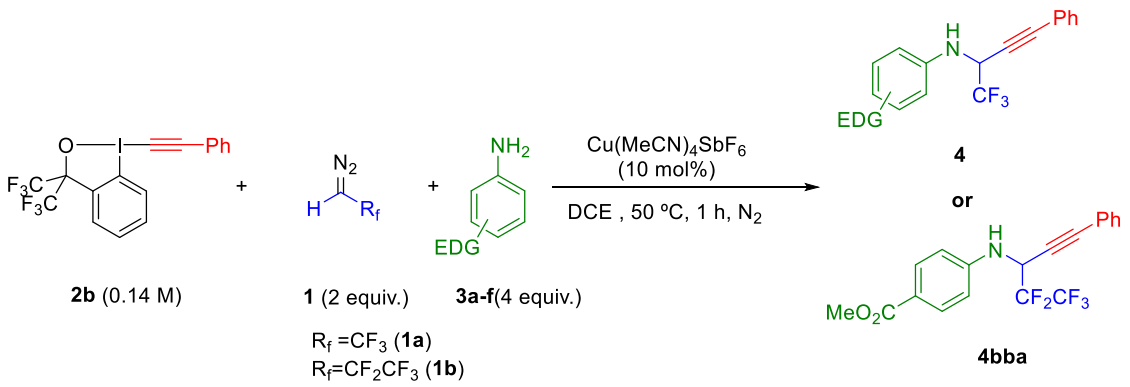
3.1. General Procedure A (compounds **4aaa** to **4aha**):



$Cu(MeCN)_4SbF_6$ (14.1 mg, 0.0300 mmol, 10 mol%) was added in an oven-dried MW vial followed by compound **2** (0.300 mmol, 1.00 equiv.). Then, the vial was capped, evacuated, and backfilled with N_2 (3 times). At this point, a solution of methyl 4-aminobenzoate (181 mg, 1.20 mmol, 4.00 equiv) in DCE (2.1 mL) was charged into the MW vial and the resulting solution was heated at 50 °C and equipped with a N_2 balloon. Once the temperature was reached, a solution of **1a** in DCM (0.33-0.36 M, 2.00 equiv.) was added dropwise over 3 min and the reaction mixture was stirred during 1 h under these conditions.

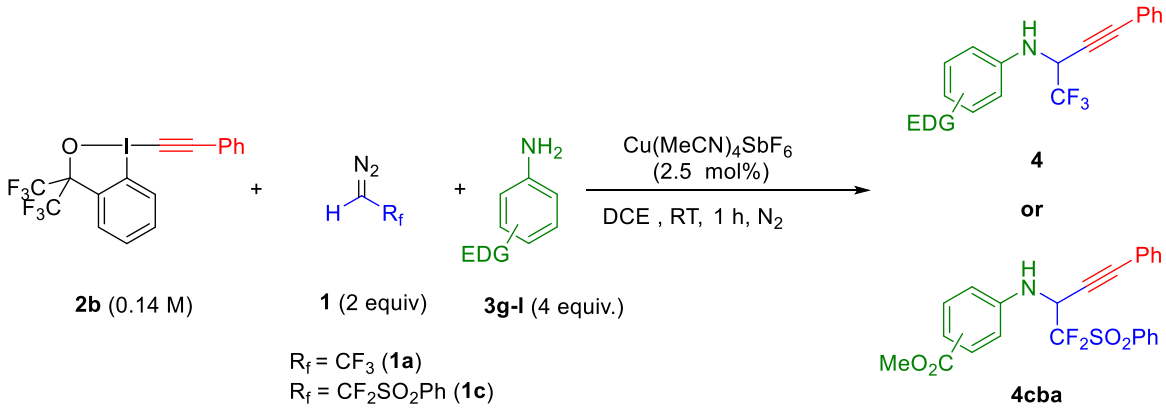
After this time, the reaction mixture was allowed to reach room temperature and monitored by TLC observing full conversion in most of the cases. The reaction mixture was filtered through a short pad of celite and washed with EtOAc (5 x 10 mL) and the solvent was removed under reduced pressure affording the corresponding product after flash column chromatography (For more details see the product characterization in 5).

4.1. *General Procedure B* (compounds **4aba** to **4abf** and **4bba**):



As described in General Procedure A, but using compound **2b** (141 mg, 0.300 mmol, 1.00 equiv), diazo compound **1a** (0.33-0.36 M, 2.00 equiv) and anilines (**3a** to **3f**) (4.00 equiv.); or diazo compound **1b** (0.4 M, 2.00 equiv) and aniline **3a** (180 mg, 1.20 mmol) for compound **4bba**

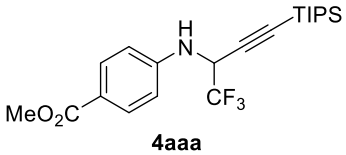
4.2. *General Procedure C* (compounds **4abg** to **4abl** and **4cba**):



As described in General Procedure A, but using $Cu(MeCN_4)SbF_6$ (3.5 mg, 7.5 µmol, 2.5 mol%), **2b** (141 mg, 0.300 mmol, 1.00 equiv), diazo compound **1a** (0.33-0.36 M, 2.00 equiv) and anilines **3g** to **3l** at room temperature.; or diazo **1c** (0.33 M in DCM, 106 mg, 0.460 mmol, 2.00 equiv.) and aniline **3a** (138 mg, 0.920, mmol, 4.00 equiv.) for compound **3cba**

5. Characterization of compounds 4

Methyl 4-((1,1,1-trifluoro-4-(triisopropylsilyl)but-3-yn-2-yl)amino)benzoate (**4aaa**):



Compound **4aaa** was prepared from ((3,3-bis(trifluoromethyl)-λ^3-benzo[*d*][1,2]iodaoxol-1(3*H*)-yl)ethynyl)triisopropylsilane (**1a**) (165 mg, 0.300 mmol, 1.00 equiv) following the GPC. It was purified by FC (100% Pentane to 94:6 Pentane/EtOAc) and obtained as a pale-yellow solid after trituration with pentane (62.1 mg, 0.150 mmol, 50%) [^{19}FNMR yield determined by $PhCF_3$ = 70%].

TLC R_f 0.14 (97:3 Pentane/EtOAc).

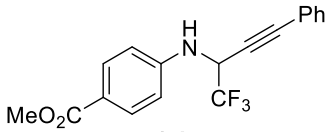
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, *J* = 8.8 Hz, 2H, Ar*H*), 6.73 (d, *J* = 8.9 Hz, 2H, Ar*H*), 4.82 (dt, *J* = 11.9, 5.8 Hz, 1H, -NHC*H*CF_3), 4.42 (d, *J* = 9.0 Hz, 1H, -N*H*$CHCF_3$), 3.87 (s, 3H, -OC*H*$_3$), 1.05 (s, 21H, TIPS).

^{13}C NMR (101 MHz, $CDCl_3$) δ 167.3, 148.9, 131.6, 123.6 (q, *J* = 282.4 Hz), 121.5, 113.2, 97.4, 89.7, 51.9, 49.7 (q, *J* = 34.7 Hz), 18.5, 11.1.

IR *(ν_{max}, cm^{-1})* 3352 (w), 2947 (m), 2870 (m), 1705 (s), 1608 (s), 1527 (m), 1442 (m), 1281 (s), 1184 (s), 1134 (s), 1018 (w), 883 (w), 771 (m), 845 (w).

HRMS (ESI/QTOF) *m/z:* $[M + H]^+$ *Calcd* for $C_{21}H_{31}F_3NO_2Si^+$ 414.2071; Found 414.2068.

Methyl 4-((1,1,1-trifluoro-4-phenylbut-3-yn-2-yl)amino)benzoate (**4aba**):



4aba

Compound **4aba** was prepared from 1-(phenylethynyl)-3,3-bis(trifluoromethyl)-1,3-dihydro-λ^3-benzo[*d*][1,2]iodaoxole (**2b**) (141 mg, 0.300 mmol, 1.00 equiv.) following the GPA. It was purified by FC (100% Pentane to 90:10 Pentane/EtOAc) and obtained as a pale-yellow amorphous solid (73.0 mg, 0.22 mmol, 73%). [^{19}FNMR yield determined by $PhCF_3$ = 80%].

<u>1 mmol experiment:</u> **2b** (470 mg, 1.00 mmol, 1.00 equiv.) and $Cu(MeCN)_4SbF_6$ (23.5 mg, 0.0500 mmol, 5 mol%) were added in an oven-dried MW tube. Then, the vial was capped, evacuated, and backfilled with N_2 (3 times). At this point, a solution of methyl 4-aminobenzoate (605 mg, 4.00 mmol, 4.00 equiv) in DCE (7.1 mL) was charged into the MW vial and the resulting solution was heated at 50 °C and equipped with a N_2 balloon. Once the temperature was reached, a solution of **1a** in DCM (0.34 M, 5.90 mL, 2.00 mmol, 2.00 equiv.) was added dropwise over 3 min and the reaction mixture was stirred during 90 min under these conditions.

After this time, the reaction mixture was allowed to reach room temperature and monitored by TLC observing full conversion in most of the cases. The reaction mixture was filtered through a short pad of celite and washed with EtOAc (5 x 10 mL) and the solvent was removed under reduced pressure affording the corresponding product after flash column chromatography (100% Pentane to 90:10 Pentane/EtOAc) (200 mg, 0.600 mmol, 60%).

TLC R_f 0.13 (95:5 Pentane/EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, *J* = 8.9 Hz, 2H, Ar*H*), 7.47 - 7.42 (m, 2H, Ar*H*), 7.40 - 7.29 (m, 3H, Ar*H*), 6.77 (d, *J* = 8.9 Hz, 2H, Ar*H*), 5.03 (dq, *J* = 9.2, 6.0 Hz, 1H, -NHC*H*CF_3), 4.58 (d, *J* = 9.2 Hz, 1H, -N*H*$CHCF_3$), 3.88 (s, 3H, -COOC*H*$_3$).

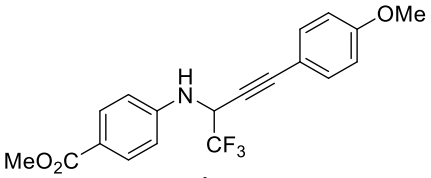
^{13}C NMR (101 MHz, $CDCl_3$) δ 167.0, 148.9, 132.1, 131.7, 129.5, 128.5, 123.6 (q, *J* = 282.4 Hz), 121.4, 121.1, 113.1, 86.7, 79.7 (d, *J* = 2.2 Hz), 51.9, 49.7 (q, *J* = 35.2 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -75.6 (d, *J* = 6.1 Hz).

IR *(ν_{max}, cm^{-1})* 3352 (w), 2947 (m), 2870 (m), 1705 (s), 1608 (s), 1527 (m), 1442 (m), 1281 (s), 1184 (s), 1134 (s), 1018 (w), 883 (w), 771 (m), 845 (w).

HRMS (ESI/QTOF) *m/z:* $[M + H]^+$ *Calcd*. for $C_{18}H_{15}F_3NO_2^+$ 334.1049; Found 334.1053.

Methyl 4-((1,1,1-trifluoro-4-(4-methoxyphenyl)but-3-yn-2-yl)amino)benzoate (**4aca**):



4aca

Compound **4aca** was prepared from 1-((4-methoxyphenyl)ethynyl)-3,3-bis(trifluoromethyl)-1,3-dihydro-λ^3-benzo[*d*][1,2]iodaoxole (**2c**) (150 mg, 0.300 mmol, 1.00 equiv) following the GPA. It was purified by FC (100% Pentane to 85:15 Pentane/EtOAc) and obtained as a pale-yellow solid after re-purification by PTLC (80:20 Pentane/EtOAc) (46.8 mg, 0.129 mmol, 43%). [^{19}FNMR yield determined by $PhCF_3$ = 70%].

TLC R_f 0.09 (95:5 Pentane/EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, *J* = 8.9 Hz, 2H, Ar*H*), 7.38 (d, *J* = 9.0 Hz, 2H, Ar*H*), 6.84 (d, *J* = 8.9 Hz, 2H, Ar*H*), 6.75 (d, *J* = 8.9 Hz, 2H, Ar*H*), 5.06 – 4.96 (m, 1H,

-NHC*H*CF_3), 4.45 (d, *J* = 9.0 Hz, 1H, -N*H*CHCF_3), 3.87 (s, 3H, COOC*H*$_3$), 3.81 (s, 3H, -OC*H*$_3$).

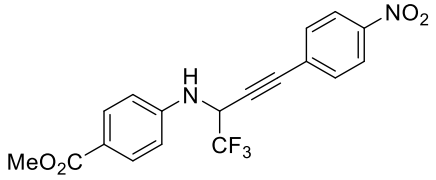
^{13}C NMR (101 MHz, $CDCl_3$) δ 167.0, 160.5, 148.9, 133.7, 131.7, 123.7 (q, *J* = 283.0 Hz), 119.5, 114.2, 113.1, 112.2, 86.8, 78.3, 55.5, 51.9, 49.8 (q, *J* = 34.8 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -75.7 (d, *J* = 6.1 Hz).

IR *(ν_{max}, cm^{-1})* 3359 (w), 2947 (w), 2245 (w), 1705 (w), 1608 (m), 1516 (w), 1439 (w), 1281 (m), 1257 (m), 1180 (m), 1130 (m), 1030 (w), 906 (s), 833 (w), 729 (s), 648 (w).

HRMS (ESI/QTOF) *m/z*: $[M + H]^+$ Calcd for $C_{19}H_{17}F_3NO_3^+$ 364.1155; Found 364.1153

Methyl 4-((2,2,2-trifluoro-1-(4-nitrophenyl)ethyl)amino)benzoate (**4ada**):



4ada

Compound **4ada** was prepared from 1-((4-nitrophenyl)ethynyl)-3,3-bis(trifluoromethyl)-1,3-dihydro-λ^3-benzo[*d*][1,2]iodaoxole (**2d**) (155 mg, 0.300 mmol, 1.00 equiv) following the GPA. It was purified by FC (100% Pentane to 75:25 Pentane/EtOAc) and obtained as a yellow amorphous solid after re-purification by PTLC (75:25 Pentane/EtOAc) (34.0 mg, 0.0900 mmol, 30%). [^{19}FNMR yield determined by $PhCF_3$ = 50%].

TLC R_f 0.08 (95:5 Pentane/EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20 (d, *J* = 9.0 Hz, 2H, Ar*H*), 7.96 (d, *J* = 8.9 Hz, 2H, Ar*H*), 7.60 (d, *J* = 9.0 Hz, 2H, Ar*H*), 6.77 (d, *J* = 8.9 Hz, 2H, Ar*H*), 5.07 (dq, *J* = 9.4, 5.9 Hz, 1H, -NHC*H*CF_3), 4.50 (d, *J* = 9.5 Hz, 1H, -N*H*CHCF_3), 3.88 (s, 3H, -COOC*H*$_3$).

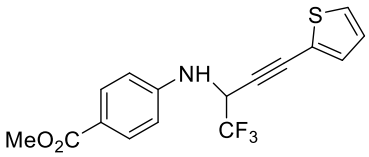
^{13}C NMR (101 MHz, $CDCl_3$) δ 166.9, 148.5, 148.0, 133.1, 131.8, 127.8, 123.8, 123.4 (q, *J* = 281.3 Hz), 122.0, 119.2, 113.2, 84.64-84.58 (m), 52.0, 49.7 (q, *J* = 35.2 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -75.3 (d, *J* = 6.1 Hz).

IR (ν_{max}, cm^{-1}) 3340 (w), 2951 (w), 1701 (s), 1604 (s), 1523 (s), 1439 (m), 1342 (s), 1281 (s), 1180 (s), 1130 (s), 910 (w), 849 (m), 737 (m), 764 (m), 698 (m)

HRMS (ESI/QTOF) *m/z*: $[M + H]^+$ Calcd for $C_{18}H_{14}F_3N_2O_4^+$ 379.0900; Found 379.0900.

Methyl 4-((1,1,1-trifluoro-4-(thiophen-2-yl)but-3-yn-2-yl)amino)benzoate (**4afa**):



4afa

Compound **4afa** was prepared from 1-(thiophen-2-ylethynyl)-3,3-bis(trifluoromethyl)-1,3-dihydro-λ^3-benzo[*d*][1,2]iodaoxole (**2f**) (143 mg, 0.300 mmol, 1.00 equiv) following the GPA. It was purified by FC (100% Pentane to 90:10 Pentane/EtOAc) and obtained as a pale-yellow solid after trituration with pentane (45.8 mg, 0.135 mmol, 45%). [^{19}FNMR yield determined by $PhCF_3$ = 67%].

TLC R_f 0.11 (95:5 Pentane/EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, *J* = 8.9 Hz, 2H, Ar*H*), 7.31 (dd, *J* = 5.1, 1.3 Hz, 1H, -SC*H*=CH-), 7.27 (dd, *J* = 3.7, 1.2 Hz, 1H, -SCH=C*H*-), 6.98 (dd, *J* = 5.1, 3.8 Hz, 1H, -SCH=CHC*H*-), 6.75 (d, *J* = 8.9 Hz, 2H, Ar*H*), 5.05 (dq, *J* = 9.2, 5.9 Hz, 1H, -NHC*H*CF_3), 4.54 (d, *J* = 9.2 Hz, 1H, -N*H*$CHCF_3$), 3.88 (s, 3H, -COOC*H*$_3$).

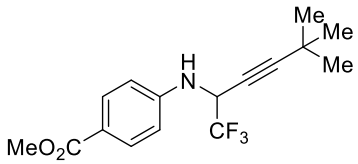
^{13}C NMR (101 MHz, $CDCl_3$) δ 167.0, 148.8, 133.8, 131.7, 128.6, 126.1 (q, *J* = 281.5 Hz), 127.2, 121.6, 120.8, 113.1, 83.5 (q, *J* = 2.6 Hz), 80.2, 51.9, 49.0 (q, *J* = 35.2 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -75.4 (d, *J* = 6.1 Hz).

IR *(ν_{max}, cm^{-1})* 3344 (w), 3105 (w), 3024 (w), 2951 (w), 2233 (w), 1701 (s), 1608 (s), 1527 (m), 1435 (m), 1281 (s), 1184 (s), 1130 (s), 964 (w), 845 (m), 768 (m), 706 (m).

HRMS (ESI/QTOF) *m/z*: $[M + H]^+$ *Calcd* for $C_{16}H_{13}F_3NO_2S^+$ 340.0614; Found 340.0611.

Methyl 4-((1,1,1-trifluoro-5,5-dimethylhex-3-yn-2-yl)amino)benzoate (**4aga**):



4aga

Compound **4aga** was prepared from 1-(3,3-dimethylbut-1-yn-1-yl)-3,3-bis(trifluoromethyl)-1,3-dihydro-λ^3-benzo[*d*][1,2]iodaoxole (**2g**) (135 mg, 0.300 mmol, 1.00 equiv) following the GPA. It was purified by FC (100% Pentane to 96:4 Pentane/EtOAc) and obtained as a pale-yellow solid after trituration with pentane (37.6 mg, 0.120 mmol, 40%). [^{19}FNMR yield determined by $PhCF_3$ = 70%].

TLC R_f 0.11 (97:3 Pentane/EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, *J* = 8.9 Hz, 2H, Ar*H*), 6.70 (d, *J* = 8.9 Hz, 2H, Ar*H*), 4.76 (dq, *J* = 8.9, 5.9 Hz, 1H, -NHC*H*CF_3), 4.34 (d, *J* = 8.9 Hz, 1H, -N*H*-), 3.87 (s, 3H, -COOC*H*$_3$), 1.21 (s, 9H, -C(C*H*$_3$)$_3$).

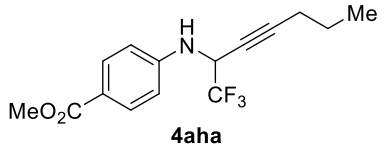
^{13}C NMR (101 MHz, $CDCl_3$) δ 167.1, 149.1, 131.6, 123.8 (q, *J* = 282.4 Hz), 121.2, 113.0, 96.0, 69.6 (q, *J* = 2.6 Hz), 51.9, 49.1 (q, *J* = 34.8 Hz), 30.6, 27.6.

^{19}F NMR (376 MHz, $CDCl_3$) δ -76.2 (d, *J* = 6.1 Hz).

IR (ν_{max}, cm^{-1}) 3352 (w), 2970 (w), 2249 (w), 1705 (s), 1608 (s), 1531 (m), 1439 (m), 1277 (s), 1180 (s), 1130 (s), 845 (w), 768 (m).

HRMS (ESI/QTOF) m/z: $[M + H]^+$ *Calcd* for $C_{16}H_{19}F_3NO_2^+$ 314.1362; Found 314.1366.

Methyl 4-((1,1,1-trifluorohept-3-yn-2-yl)amino)benzoate (**4aha**)



4aha

Compound **4aha** was prepared from 1-(pent-1-yn-1-yl)-3,3-bis(trifluoromethyl)-1,3-dihydro-λ^3-benzo[*d*][1,2]iodaoxole (**2h**) (80.0 mg, 0.180 mmol, 1.00 equiv) following the GPA. It was purified by FC (100% Pentane to 90:10 Pentane/EtOAc) and obtained as a pale-yellow solid after trituration with pentane (25.0 mg, 0.0800 mmol, 46%). [^{19}FNMR yield determined by $PhCF_3$ = 55%].

TLC R_f 0.22 (95:5 Pentane/EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, *J* = 8.8 Hz, 2H, Ar*H*), 6.70 (d, *J* = 8.9 Hz, 2H, Ar*H*), 4.83 – 4.70 (m, 1H, -NHC*H*CF_3), 4.32 (d, *J* = 9.0 Hz, 1H, -N*H*-), 3.87 (s, 3H, -COOC*H*$_3$), 2.19 (td, *J* = 7.0, 2.1 Hz, 2H, -CC*H*$_2$CH$_2$-), 1.53 (h, *J* = 7.3 Hz, 2H, -CH$_2$C*H*$_2$CH$_3$), 0.96 (t, *J* = 7.3 Hz, 3H, -C*H*$_2$C*H*$_3$).

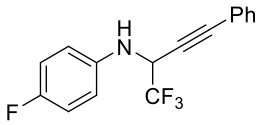
^{13}C NMR (101 MHz, $CDCl_3$) δ 167.0, 149.1, 131.6, 127.8 (q, *J* = 282.4 Hz), 121.3, 113.0, 88.0, 71.3 (d, *J* = 2.6 Hz), 51.9, 49.2 (q, *J* = 34.8 Hz), 21.7, 20.6, 13.4.

^{19}F NMR (376 MHz, $CDCl_3$) δ -76.1 (d, *J* = 6.1 Hz).

IR (ν_{max}, cm^{-1}) 3352 (w), 2962 (w), 1705 (s), 1608 (s), 1527 (m), 1439 (m), 1281 (s), 1180 (s), 1126 (s), 968 (w), 845 (w), 768 (m), 702 (w).

HRMS (ESI/QTOF) *m/z*: $[M + H]^+$ Calcd for $C_{15}H_{17}F_3NO_2^+$ 300.1206; Found 300.1198.

4-Fluoro-*N*-(1,1,1-trifluoro-4-phenylbut-3-yn-2-yl)aniline (**4abb**):



4abb

Compound **4abb** was prepared from 4-fluoroaniline (**3b**) (115 µL, 1.20 mmol, 4.00 equiv) following the GPB. It was purified by FC (100% Pentane to 97:3 Pentane/EtOAc) and obtained as a yellow oil after a re-purification by PTLC (95:5 Pentane/EtOAc) (57.2 mg, 0.195 mmol, 65%). [^{19}FNMR yield determined by $PhCF_3$ = 85%].

TLC R_f 0.2 (97:3 Pentane/EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 - 7.92 (m, 2H, Ar*H*), 7.38 - 7.30 (m, 3H, Ar*H*), 7.02 - 6.94 (m, 2H, Ar*H*), 6.81 - 6.71 (m, 2H, Ar*H*), 4.82 (dq, *J* = 9.5, 6.1 Hz, 1H, -NHC*H*CF_3), 3.93 (d, *J* = 9.5 Hz, 1H, -N*H*-).

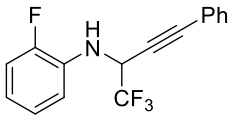
^{13}C NMR (101 MHz, $CDCl_3$) δ 157.6 (d, *J* = 238.4 Hz), 141.4 (d, *J* = 2.6 Hz), 141.4, 141.3, 132.1, 123.8 (q, *J* = 281.9 Hz), 121.4, 116.3 (d, *J* = 7.7 Hz), 116.1 (d, *J* = 22.7 Hz), 86.6, 80.5 (q, *J* = 2.6 Hz), 51.7 (q, *J* = 34.3 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -75.7 (d, *J* = 6.1 Hz), -124.2 (dq, *J* = 8.2, 4.1 Hz) ppm.

IR *(ν_{max}, cm^{-1})* 3421 (w), 3059 (w), 2927 (w), 2237 (w), 1512 (s), 1346 (m), 1257 (s), 1223 (s), 1184 (s), 1134 (s), 991 (w), 825 (m), 760 (m).

The values of the NMR spectra are in accordance with reported literature data [10]

2-Fluoro-*N*-(1,1,1-trifluoro-4-phenylbut-3-yn-2-yl)aniline (**4abc**)



4abc

Compound **4abc** was prepared from 2-fluoroaniline (**3c**) (116 µL, 1.20 mmol, 4.00 equiv) following the GPB. It was purified by FC (100% Pentane to 99:1 Pentane/EtOAc) and obtained as a yellow oil after a re-purification by PTLC (97:3 Pentane/EtOAc) (46.6 mg, 0.159 mmol, 53%). [^{19}FNMR yield determined by $PhCF_3$ = 75%].

TLC R_f 0.44 (97:3 Pentane/EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 - 7.44 (m, 2H, Ar*H*), 7.40 - 7.29 (m, 3H, Ar*H*), 7.11 - 7.02 (m, 2H, Ar*H*), 6.92 - 6.87 (m, 1H, Ar*H*), 6.85 – 6.80 (m, 1H, Ar*H*), 4.93 (dq, *J* = 9.4, 6.0 Hz, 1H, -NHC*H*CF_3), 4.37 (d, *J* = 12.8 Hz, 1H, -N*H*-).

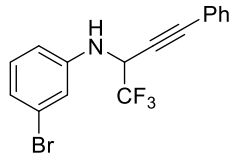
^{13}C NMR (101 MHz, $CDCl_3$) δ 152.3 (d, *J* = 240 Hz), 133.5 (d, *J* = 11.4 Hz), 132.2, 129.4, 128.5, 124.8 (d, *J* = 4.0 Hz), 123.8 (q, *J* = 280 Hz), 121.3, 120.1 (d, *J* = 7.3 Hz), 115.4 (d, *J* = 18.7 Hz), 114.2, 86.6, 80.1 (q, *J* = 2.6 Hz), 50.4 (q, *J* = 34.8 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -75.7 (d, *J* = 6.1 Hz), -134.5 (tq, *J* = 8.9, 4.1 Hz)

IR (ν_{max}, cm^{-1}) 3437 (w), 3062 (w), 2237 (w), 1620 (w), 1516 (m), 1454 (w), 1338 (m), 1257 (s), 1184 (s), 1134 (s), 752 (s), 849 (w), 1034 (w), 991 (w).

HRMS (ESI/QTOF) *m/z*: $[M + H]^+$ *Calcd* for $C_{16}H_{12}F_4N^+$294.0900; Found 294.0905.

3-Bromo-*N*-(1,1,1-trifluoro-4-phenylbut-3-yn-2-yl)aniline (**4abd**)



4abd

Compound **4abd** was prepared from 3-bromoaniline (**3d**) (133 µL, 1.20 mmol, 4.00 equiv) following the GPB. It was purified by FC (100% Pentane to 90:10 Pentane/EtOAc) and obtained as a yellow oil after a re-purification by PTLC (95:5 Pentane/EtOAc) (39.3 mg, 0.111 mmol, 37%). [^{19}FNMR yield determined by $PhCF_3$ = 70%].

TLC R_f 0.24 (97:3 Pentane/EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 - 7.44 (m, 2H, Ar*H*), 7.39 - 7.30 (m, 3H, Ar*H*), 7.14 - 7.08 (m, 1H, Ar*H*), 7.01 (ddd, *J* = 7.9, 1.8, 0.9 Hz, 1H, Ar*H*), 6.97 - 6.94 (m, 1H, Ar*H*), 6.70 (dd, *J* = 8.2, 1.4 Hz, 1H, Ar*H*), 4.89 (dq, *J* = 9.3, 6.0 Hz, 1H, -NHC*H*CF_3), 4.11 (d, *J* = 8.8 Hz, 1H, -N*H*$CHCF_3$).

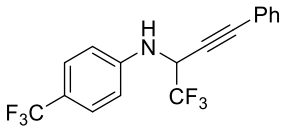
^{13}C NMR (101 MHz, $CDCl_3$) δ 146.4, 132.1, 130.9, 129.5, 128.6, 127.7 (q, *J* = 282.3 Hz), 123.4, 123.2, 121.2, 117.4, 113.1, 86.7, 80.0 (q, *J* = 2.6 Hz), 50.4 (q, *J* = 34.8 Hz) ppm.

^{19}F NMR (376 MHz, $CDCl_3$) δ -75.7 (d, *J* = 6.1 Hz)

IR (ν_{max}, cm^{-1}) 3417 (w), 3066 (w), 3024 (w), 2927 (w), 2237 (w), 1597 (m), 1500 (m), 1334 (w), 1257 (m), 1184 (m), 1134 (s), 1080 (w), 991 (w), 903 (w), 849 (w), 760 (s).

HRMS (ESI/QTOF) *m/z*: $[M + H]^+$ *Calcd* for $C_{16}H_{12}Br^{79}F_3N^+$ 354.0100; Found 354.0091.

N-(1,1,1-Trifluoro-4-phenylbut-3-yn-2-yl)-4-(trifluoromethyl)aniline (**4abe**):



4abe

Compound **4abe** was prepared from 4-trifluoromethylaniline (**3e**) (152 µL, 1.20 mmol, 4.00 equiv) following the GPB. It was purified by FC (100% Pentane to 90:10 Pentane/EtOAc) and obtained as a white amorphous solid after trituration with pentane (57.7 mg, 0.168 mmol, 56%). [^{19}FNMR yield determined by $PhCF_3$ = 80%].

TLC R_f 0.22 (97:3 Pentane/EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 – 7.50 (d, J = 8.2 Hz, 2H, Ar*H*), 7.48 – 7-44 (m, 2H), 7.42 – 7.30 (m, 3H), 6.82 (d, J = 8.5 Hz, 2H, Ar*H*), 4.99 (dq, J = 9.2, 5.9 Hz, 1H, -NHC*H*CF_3), 4.38 (d, J = 9.2 Hz, 1H, -N*H*CHCF_3).

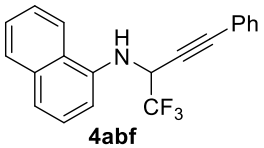
^{13}C NMR (101 MHz, $CDCl_3$) δ 147.7, 132.2, 129.6, 128.6, 127.0 (q, J = 3.7 Hz), 126.0, 124.7 (q, J = 271.1 Hz), 123.7 (q, J = 282.3 Hz). 122.0 (q, J = 32.6 Hz), 121.1, 113.6, 86.8, 79.7 (q, J = 2.6 Hz), 49.9 (q, J = 35.2 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -61.5 (s), -75.6 (d, J = 5.5 Hz).

IR *(ν_{max}, cm^{-1})* 3429 (w), 3066 (w), 2237 (w), 2114 (w), 1620 (m), 1531 (m), 1496 (w), 1327 (s), 1257 (m), 1184 (s), 1122 (s), 1068 (m), 1007 (w), 829 (m), 760 (m).

The values of the NMR spectra are in accordance with reported literature data.[11]

N-(1,1,1-trifluoro-4-phenylbut-3-yn-2-yl)naphthalen-1-amine (**4abf**)



4abf

Compound **4abf** was prepared from 1-naphtylamine (**3f**) (174 mg, 1.20 mmol, 4.00 equiv) following the GPB. It was purified by FC (100% Pentane) and obtained as a pale-yellow oil after a re-purification by PTLC 96:4 (Pentane/EtOAc) (34.2 mg, 0.105 mmol, 35%). [^{19}FNMR yield determined by $PhCF_3$ = 58%].

TLC R_f 0.20 (97:3 Pentane/EtOAc).

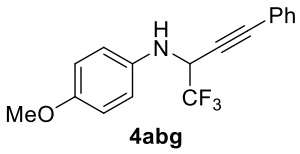
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 - 7.83 (m, 2H, Ar*H*), 7.56 - 7.50 (m, 2H, Ar*H*), 7.49 - 7.39 (m, 4H, Ar*H*), 7.38 - 7.29 (m, 3H, Ar*H*), 6.95 (d, J = 8.7 Hz, 1H, Ar*H*), 5.11 (dq, J = 9.8, 6.1 Hz, 1H, -NHC*H*CF_3), 4.59 (d, J = 9.8 Hz, 1H, -N*H*-).

^{13}C NMR (101 MHz, $CDCl_3$) δ 140.4, 134.5, 132.1, 129.3, 128.9, 128.5, 126.3, 126.2, 125.8, 124.9, 123.5 (q, J = 283.2 Hz), 121.5, 121.2, 120.4, 108.8, 86.4, 80.8 (d, J = 2.2 Hz), 51.0 (q, J = 34.3 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -75.3 (d, J = 6.1 Hz).

IR *(ν_{max}, cm^{-1})* 3444 (w), 3383 (w), 3062 (w), 2924 (w), 2854 (w), 2233 (w), 1585 (m), 1527 (m), 1485 (m), 1408 (m), 1346 (m), 1257 (s), 1188 (s), 1134 (s), 764 (s), 694 (m); The values of the NMR spectra are in accordance with reported literature data [10]

4-Methoxy-*N*-(1,1,1-trifluoro-4-phenylbut-3-yn-2-yl)aniline (**4abg**)



4abg

Compound **4abg** was prepared from 4-methoxyaniline (**3g**) (149 mg, 1.20 mmol, 4.00 equiv) following the GPC. It was purified by FC (100% Pentane to 95:5 Pentane/EtOAc) and obtained as a yellow oil after a re-purification by PTLC 95:5 (Pentane/EtOAc) (48.5 mg, 0.159 mmol, 53%). [^{19}FNMR yield determined by $PhCF_3$ = 58%].

1 mmol experiment: **2b** (470 mg, 1.00 mmol, 1.00 equiv.) and $Cu(MeCN)_4SbF_6$ (5.86 mg, 12.5 µmol, 1.25 mol%) were added in an oven-dried MW tube. Then, the vial was capped, evacuated, and backfilled with N_2 (3 times). At this point, a solution of *p*-anisidine (462 mg, 4.00 mmol, 4.00 equiv) in DCE (7.1 mL) was charged into the MW vial and the resulting solution was stirred at RT and equipped with a N_2 balloon. Finally, a solution of **1a** in DCM (0.34 M, 5.90 mL, 2.00 mmol, 2.00 equiv.) was added dropwise over 3 min and the reaction mixture was stirred during 90 min under these conditions.

After this time, the reaction mixture was allowed to reach room temperature and monitored by TLC observing full conversion in most of the cases. The reaction mixture was filtered through a short pad of celite and washed with EtOAc (5 x 10 mL) and the solvent was removed under reduced pressure affording the corresponding product after flash column chromatography (100% Pentane to 95:5 Pentane/EtOAc) (122 mg, 0.400 mmol, 40%).

TLC R_f 0.12 (97:3 Pentane/EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 - 7.40 (m, 2H, Ar*H*), 7.38 - 7.29 (m, 3H, Ar*H*), 6.88 - 6.78 (m, 4H, Ar*H*), 4.77 (d, *J* = 6.1 Hz, 1H, -N*H*-), 3.78 (s, 4H, -OCH_3 + -NHC*H*CF_3).

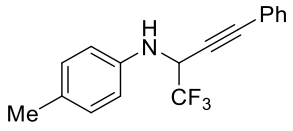
^{13}C NMR (101 MHz, $CDCl_3$) δ 154.3, 139.0, 132.1, 129.3, 128.5, 123.9 (q, *J* = 281.7 Hz), 121.6, 117.0, 115.0, 86.4, 81.0 (q, *J* = 2.6 Hz), 55.8, 52.3 (q, *J* = 33.7 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -75.7 (d, *J* = 6.1 Hz).

IR *(ν_{max}, cm^{-1})* 3356 (w), 3043 (w), 3005 (w), 2935 (w), 2843 (w), 2233 (w), 1516 (s), 1458 (w), 1346 (m), 1180 (s), 1242 (s), 1130 (s), 1034 (m), 825 (m), 760 (m).

The values of the NMR spectra are in accordance with reported literature data.[10]

4-Methyl-*N*-(1,1,1-trifluoro-4-phenylbut-3-yn-2-yl)aniline (**4abh**)



4abh

Compound **4abh** was prepared from 4-methylaniline (**3h**) (130 mg, 1.20 mmol, 4.00 equiv) following the GPC. It was purified by FC (100% Pentane to 95:5 Pentane/EtOAc) and obtained as a yellow oil after a re-purification by PTLC 95:5 (Pentane/EtOAc) (49.5 mg, 0.171 mmol, 57%).

TLC R_f 0.23 (97:3 Pentane/EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 - 7.42 (m, 2H, Ar*H*), 7.39 - 7.28 (m, 3H, Ar*H*), 7.08 (d, *J* = 8.7 Hz, 2H, Ar*H*), 6.73 (d, *J* = 8.5 Hz, 2H, Ar*H*), 4.87 (dq, *J* = 9.4, 6.1 Hz, 1H, -NHC*H*CF_3), 3.91 (d, *J* = 9.4 Hz, 1H, -N*H*-), 2.29 (s, 3H, -CH_3).

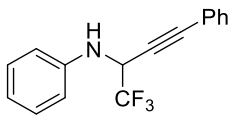
^{13}C NMR (101 MHz, $CDCl_3$) δ 142.8, 132.1, 130.1, 129.8, 129.3, 128.5, 123.9 (q, *J* = 281.7 Hz), 121.6, 115.0, 86.2, 80.9 (d, *J* = 2.6 Hz), 51.2 (q, *J* = 34.3 Hz), 20.6.

^{19}F NMR (376 MHz, $CDCl_3$) δ -75.7 (d, *J* = 6.1 Hz).

IR *(ν_{max}, cm^{-1})* 3410 (w), 3032 (w), 2927 (w), 2866 (w), 2233 (w), 1616 (w), 1520 (s), 1342 (m), 1257 (s), 1184 (s), 1134 (s), 991 (w), 810 (m), 760 (m).

The values of the NMR spectra are in accordance with reported literature data.[10]

N-(1,1,1-Trifluoro-4-phenylbut-3-yn-2-yl)aniline (**4abi**):



4abi

Compound **4abi** was prepared from aniline (**3i**) (111 µL, 1.20 mmol, 4.00 equiv) following the GPC. It was purified by FC (100% Pentane to 99:1 Pentane/EtOAc) and

obtained as a yellow oil after a re-purification by PTLC 95:5 (Pentane/EtOAc) (41.3 mg, 0.500 mmol, 50%). [^{19}FNMR yield determined by $PhCF_3$ = 75%].

TLC R_f 0.23 (97:3 Pentane/EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27 (d, J = 7.8 Hz, 2H, Ar*H*), 7.19 - 7.08 (m, 5H, Ar*H*), 6.74 - 6.70 (m, 1H, Ar*H*), 6.62 (d, J = 8.2 Hz, 2H, Ar*H*), 4.74 (dt, J = 12.3, 6.1 Hz, 1H, -NHC*H*CF_3), 3.87 (d, J = 9.3 Hz, 1H, -N*H*$CHCF_3$).

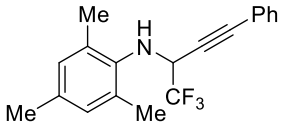
^{13}C NMR (101 MHz, $CDCl_3$) δ 145.1, 132.1, 129.6, 129.3, 128.5, 128.4 (q, J = 285.5 Hz), 121.5, 120.3, 114.6, 86.3, 80.6 (d, J = 2.6 Hz), 50.7 (q, J = 34.5 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -75.7 (d, J = 6.1 Hz).

IR *(ν_{max}, cm^{-1})* 3406 (w), 3032 (w), 2927 (w), 2862 (w), 2233 (w), 1624 (w), 1520 (m), 1346 (m), 1254 (s), 1184 (s), 1134 (s), 810 (m), 760 (m).

The values of the NMR spectra are in accordance with reported literature data.[10]

2,4,6-Trimethyl-*N*-(1,1,1-trifluoro-4-phenylbut-3-yn-2-yl)aniline (**4abj**):



4abj

Compound **4abj** was prepared from 2,4,6-trimethylaniline (**3j**) (172 µL, 1.20 mmol, 4.00 equiv) following the GPC. It was purified by FC (100% Pentane to 99.5/0.5 Pentane/EtOAc) and obtained as a yellow oil after a re-purification by PTLC 96:4 (Pentane/EtOAc) (47.6 mg, 0.150 mmol, 50%). [^{19}FNMR yield determined by $PhCF_3$ = 65%].

TLC R*f* 0.32 (97:3 Pentane/EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 - 7.40 (m, 2H, Ar*H*), 7.37 - 7.28 (m, 3H, Ar*H*), 6.89 (br s, 2H, Ar*H*), 4.49 (dq, J = 12.8, 6.4 Hz, 1H, -NHC*H*CF_3), 3.60 (d, J = 11.7 Hz, 1H, -N*H*$CHCF_3$), 2.39 (s, 6H, -CH_3), 2.27 (s, 3H, -CH_3).

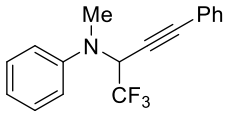
^{13}C NMR (101 MHz, $CDCl_3$) δ 139.4, 133.4, 131.9, 131.0, 129.9, 129.1, 128.5, 124.0 (q, J = 281.7 Hz), 121.8, 86.2, 82.3 (d, J = 2.6 Hz), 53.4 (q, J = 32.3 Hz), 20.8, 18.3 ppm.

^{19}F NMR (376 MHz, $CDCl_3$) δ -75.53 (d, J = 6.1 Hz).

IR *(ν_{max}, cm^{-1})* 3363 (w), 3012 (w), 2931 (w), 2862 (w), 2229 (w), 1485 (m), 1450 (m), 1346 (m), 1254 (s), 1184 (s), 1134 (s), 1092 (m), 1030 (w), 995 (w), 856 (w), 760 (s);

HRMS (ESI/QTOF) *m/z*: $[M + H]^+$ *Calcd* for $C_{19}H_{19}F_3N^+$318.1464; Found 318.1469.

N-Methyl-N-(1,1,1-trifluoro-4-phenylbut-3-yn-2-yl)aniline (**4abk**):



4abk

Compound **4abk** was prepared from N-methylaniline (**3k**) (133 µL, 1.20 mmol, 4.00 equiv) following the GPC. It was purified by FC (100% Pentane to 99:1 Pentane/EtOAc) and obtained as a yellow oil after a re-purification by PTLC 97:3 (Pentane/EtOAc) (43.4 mg, 0.150 mmol, 70%). [^{19}FNMR yield determined by $PhCF_3$ = 70%].

TLC R_f 0.32 (97:3 Pentane/EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 - 7.46 (m, 2H, Ar*H*), 7.41 - 7.28 (m, 5H, Ar*H*), 6.97 (d, *J* = 7.9 Hz, 1H, Ar*H*), 6.94 - 6.90 (m, 2H, Ar*H*), 5.25 (q, *J* = 6.8 Hz, 1H, -NCH_3CHCF_3), 3.10 (s, 3H, -CH_3).

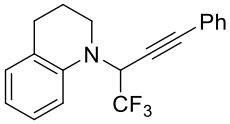
^{13}C NMR (101 MHz, $CDCl_3$) δ 149.5, 132.1, 129.5, 129.3, 128.5, 124.3 (q, *J* = 285.4 Hz), 120.1, 121.7, 115.2, 88.6, 78.5 (d, *J* = 2.2 Hz), 57.0 (q, *J* = 33.6 Hz), 34.8.

^{19}F NMR (376 MHz, $CDCl_3$) δ -73.2 (d, *J* = 7.5 Hz).

IR *(ν_{max}, cm^{-1})* 3059 (w), 2924 (w), 2823 (w), 2233 (w), 1593 (m), 1496 (s), 1369 (m), 1331 (m), 1261 (s), 1176 (s), 1138 (s), 1103 (s), 1034 (m).

HRMS (ESI/QTOF) *m/z*: $[M + H]^+$ *Calcd* for $C_{17}H_{15}F_3N^+$290.1151; Found 290.1160.

1-(1,1,1-Trifluoro-4-phenylbut-3-yn-2-yl)-1,2,3,4-tetrahydroquinoline (**4abl**)



4abl

Compound **4abl** was prepared from 1,2,3,4-tetrahydroquinoline (**3l**) (154 µL, 1.20 mmol, 4.00 equiv) following the GPC. It was purified by FC (100% Pentane to 98:2 Pentane/EtOAc) and obtained as a yellow oil after a re-purification by PTLC 97:3 (Pentane/EtOAc) (52.0 mg, 0.165 mmol, 55%). [^{19}FNMR yield determined by $PhCF_3$ = 68%].

TLC R_f 0.39 (97:3 Pentane/EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (dd, *J* = 7.8, 1.8 Hz, 2H, Ar*H*), 7.41 - 7.33 (m, 3H, Ar*H*), 7.17 - 7.10 (m, 1H, Ar*H*), 7.05 (d, *J* = 7.4 Hz, 1H, Ar*H*), 6.85 - 6.74 (m, 2H, Ar*H*), 5.35 (q, *J* = 6.8 Hz, 1H, -$NCHCF_3$), 3.76 (dt, *J* = 11.0, 5.0 Hz, 1H, -NCH_2CH_2-), 3.43 (dt,

J = 11.0, 5.0 Hz, 1H, -NCH$_2$C*H*$_2$-), 2.83 (t, *J* = 6.5 Hz, 2H, -NC*H*$_2$-), 2.06 - 1.96 (m, 2H, Ar-C*H*$_2$-CH$_2$-).

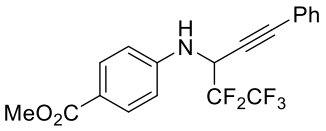
^{3}C NMR (101 MHz, CDCl$_3$) δ 144.3, 132.1, 130.0, 129.2, 128.5, 127.3, 124.5 (q, *J* = 285.4 Hz), 124.6, 121.7, 118.7, 112.8, 88.2, 78.8 (q, *J* = 2.6 Hz), 55.4 (q, *J* = 33.9 Hz), 45.7, 28.1, 21.9.

^{19}F NMR (376 MHz, CDCl$_3$) δ -73.2 (d, *J* = 6.8 Hz).

IR *(ν_{max}, cm^{-1})* 3062 (w), 3028 (w), 2935 (m), 2858 (w), 2233 (w), 1604 (m), 1496 (m), 1454 (m), 1354 (m), 1304 (m), 1254 (s), 1126 (s), 1176 (s), 1057 (w), 991 (w), 891 (w), 833 (w), 752 (s).

HRMS (ESI/QTOF) *m/z*: [M + H]$^+$ *Calcd* for $C_{19}H_{17}F_3N^+$316.1308; Found 316.1310.

Methyl 4-((4,4,5,5,5-pentafluoro-1-phenylpent-1-yn-3-yl)amino)benzoate (**4bba**)



4bba

Compound **4bba** was prepared following the GPB. It was purified by FC (100% Pentane to 97:3 Pentane/EtOAc) and obtained as a white solid after trituration with pentane (59.8 mg, 0.156 mmol, 52%).

TLC R_f 0.16 (95:5 Pentane/EtOAc).

^{1}H NMR (400 MHz, CDCl$_3$) δ 7.96 (d, *J* = 8.9 Hz, 2H, Ar*H*), 7.44 - 7.40 (m, 2H, Ar*H*), 7.39 - 7.29 (m, 3H, Ar*H*), 6.77 (d, *J* = 8.9 Hz, 2H, Ar*H*), 5.12 (q, *J* = 10.7 Hz, 1H, -C*H*CF$_2$CF$_3$), 4.44 (d, *J* = 9.7 Hz, 1H, -N*H*CHCF$_2$CF$_3$), 3.88 (s, 3H, -COOC*H*$_3$).

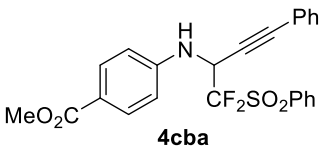
^{13}C NMR (101 MHz, CDCl$_3$) δ 167.0, 148.8, 132.1, 131.7, 129.5, 128.6, 121.7, 121.1, 120.4 (t, *J* = 35.2 Hz), 117.5 (t, *J* = 35.2 Hz), 113.3, 87.5, 79.2 (br s), 51.9, 48.2 (t, *J* = 26.0 Hz).

^{19}F NMR (376 MHz, CDCl$_3$) δ -80.9, -121.6 (dd, *J* = 138.3, 10.9 Hz).

IR (*ν_{max}, cm^{-1})* 3344 (w), 3043 (w), 2237 (w), 1705 (m), 1608 (s), 1527 (m), 1439 (m), 1281 (s), 1188 (s), 1119 (m), 1022 (w), 964 (w), 841 (w), 764 (m);

HRMS (ESI/QTOF) *m/z*: [M + H]$^+$ *Calcd* for $C_{19}H_{15}F_5NO_2^+$ 384.1017; Found 384.1026.

Methyl 4-((1,1-difluoro-4-phenyl-1-(phenylsulfonyl)but-3-yn-2-yl)amino)benzoate **(4cba)**:



4cba

Compound **4cba** was prepared following the GPC but using Cu(MeCN)4SbF$_6$ (2.7 mg, 2.5 mol%) and **2b** (108 mg, 0.230 mmol, 1.00 equiv.). It was purified by FC (100% Pentane to 70:30 Pentane/EtOAc) and obtained as a yellow oil after a re-purification by PTLC (65:35 Pentane/EtOAc) (22.8 mg, 0.0500 mmol, 22%).

TLC R_f 0.03 (95:5 Pentane/EtOAc).

^{1}H NMR (400 MHz, CDCl$_3$) δ 7.99 (d, J = 7.3 Hz, 2H, Ar*H*), 7.95 (d, J = 8.8 Hz, 2H, Ar*H*), 7.77 - 7.71 (m, 1H, Ar*H*), 7.62 - 7.55 (m, 2H, Ar*H*), 7.45 - 7.40 (m, 2H, Ar*H*), 7.37 - 7.27 (m, 3H, Ar*H*), 6.78 (d, J = 8.9 Hz, 2H, Ar*H*), 5.48 (ddd, J = 13.3, 9.9, 8.3 Hz, 1H, -NHC*H*CF$_2$-), 4.52 (d, J = 9.9 Hz, 1H, -N*H*CHCF$_2$-), 3.88 (s, 3H, -COOC*H*$_3$).

^{13}C NMR (101 MHz, CDCl$_3$) δ 167.1, 148.6, 135.7, 133.6, 132.2, 131.7, 130.8, 129.5, 129.4, 128.5, 121.6, 121.3, 118.6 (q, J = 297.7 Hz), 113.5, 87.8, 79.7 (br s), 51.9, 48.4 (dd, J = 26.2, 23.2 Hz).

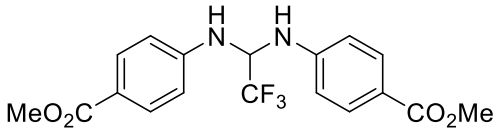
^{19}F NMR (376 MHz, CDCl$_3$) δ -104.7 (dd, J = 233.6, 8.2 Hz), -108.9 (dd, J = 233.7, 13.6 Hz).

IR *(ν_{max}, cm^{-1})* 3356 (w), 3024 (w), 2951 (w), 2237 (w), 1705 (s), 1608 (s), 1527 (m), 1442 (m), 1342 (m), 1284 (s), 1169 (s), 1115 (m), 841 (w), 760 (s), 690 (m).

HRMS (ESI/QTOF) *m/z*: $[M + H]^+$ *Calcd* for $C_{24}H_{20}F_2NO_4S^+$ 456.1076; Found 456.1087.

6. **Characterization of aminal side-product** 4aaa’

Dimethyl 4,4'-((2,2,2-trifluoroethane-1,1-diyl)bis(azanediyl))dibenzoate (**4aaa’**):



4aaa'

Yellow oil

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, *J* = 8.9 Hz, 4H, Ar*H*), 6.64 (d, *J* = 8.9 Hz, 4H, Ar*H*), 5.40 (td, *J* = 7.5, 4.8 Hz, 1H, -NHC*H*CF_3), 4.53 (d, *J* = 7.4 Hz, 2H, -N*H*-), 3.86 (s, 6H, -COOC*H*$_3$).

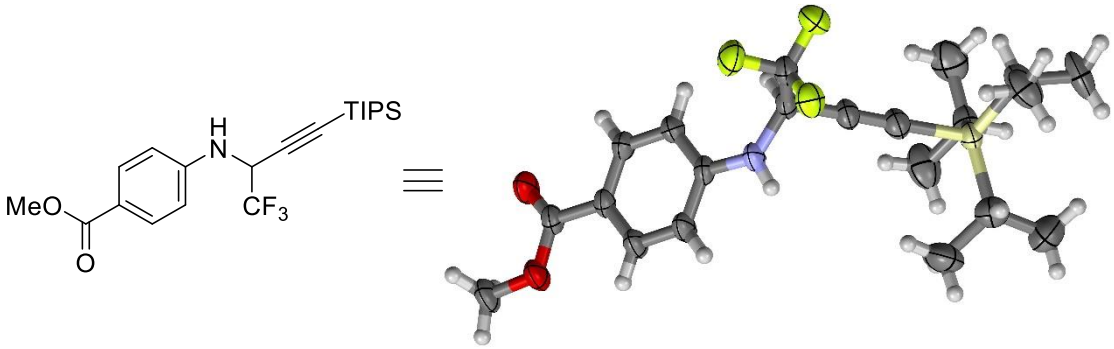
^{13}C NMR (101 MHz, $CDCl_3$) δ 166.9, 148.2, 131.9, 123.9 (q, *J* = 281.0 Hz), 121.9, 113.0, 64.9 (q, *J* = 33.4 Hz), 52.0.

^{19}F NMR (376 MHz, $CDCl_3$) δ -79.0.

IR *(ν_{max}, cm^{-1})* 3348 (w), 1608 (s), 1523 (m), 1439 (m), 1284 (s), 1184 (s), 1142 (m), 910 (w), 733 (m).

HRMS (nanochip-ESI/LTQ-Orbitrap) m/z: $[M + Na]^+$ Calcd for $C_{18}H_{17}F_3N_2NaO_4^+$ 405.1033; Found 405.1039

7. X-Ray structure for compound 4aaa



Compound **4aaa**. CCDC: 2086310

Empirical formula $C_{21}H_{30}F_3NO_2Si$

Formula weight 413.55

Temperature 130(1) K

Wavelength 1.54184 Å

Crystal system Triclinic

Space group *P*-1

Unit cell dimensions a = 7.9513(9) Å a= 89.560(10)°.

b = 9.7717(10) Å b= 75.444(11)°.

c = 15.144(2) Å g = 84.693(9)°.

Volume 1133.9(2) Å3

Z 2

Density (calculated) 1.211 Mg/m^3

Absorption coefficient 1.262 mm^{-1}

F(000) 440

Crystal size 0.621 x 0.137 x 0.078 mm^3

Q range for data collection 4.545 to 72.494°.

Index ranges $-9 \leq h \leq 5$, $-11 \leq k \leq 11$, $-18 \leq l \leq 18$

Reflections collected 7816

Independent reflections 4275 [R_{int} = 0.0525]

Completeness to q = 67.684° 98.6 %

Absorption correction Analytical

Max. and min. transmission 0.930 and 0.680

Refinement method Full-matrix least-squares on F2

Data / restraints / parameters 4275 / 0 / 264

Goodness-of-fit on F2 1.026

Final R indices [I > 2s(I)] R_1 = 0.0676, wR_2 = 0.1745

R indices (all data) R_1 = 0.0962, wR_2 = 0.2061

Largest diff. peak and hole 0.546 and -0.320 e.Å-3

8. References

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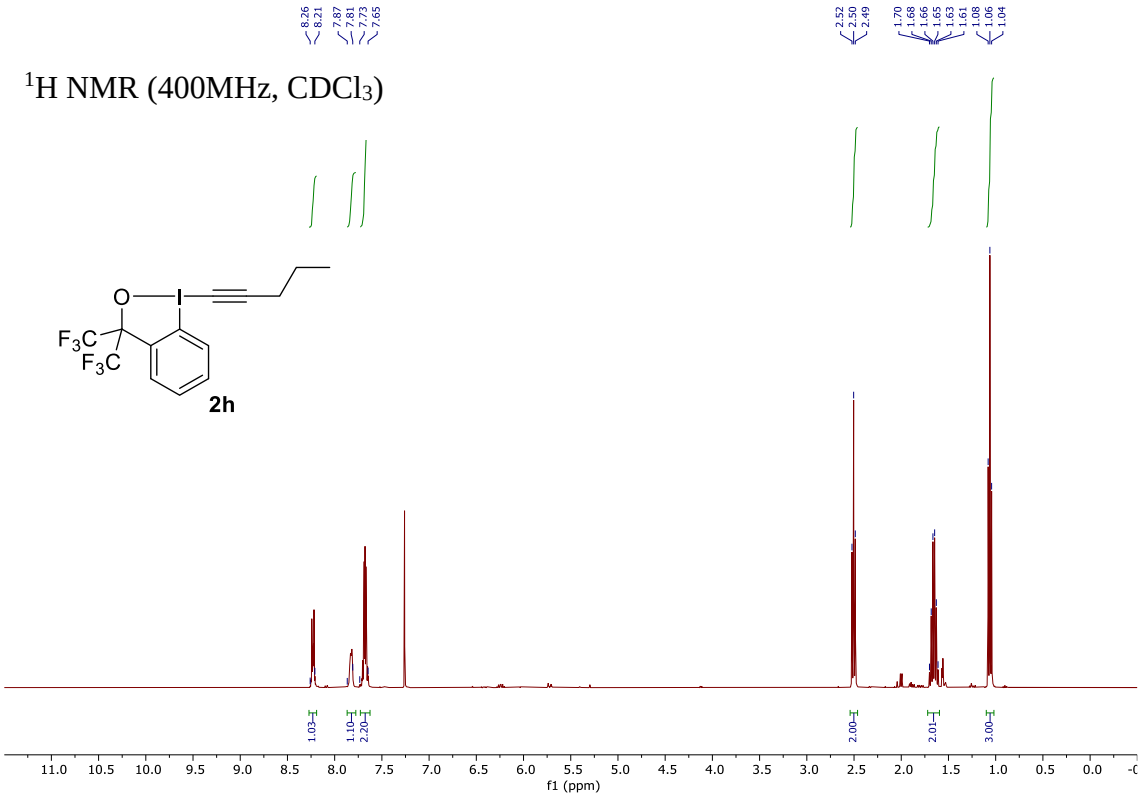
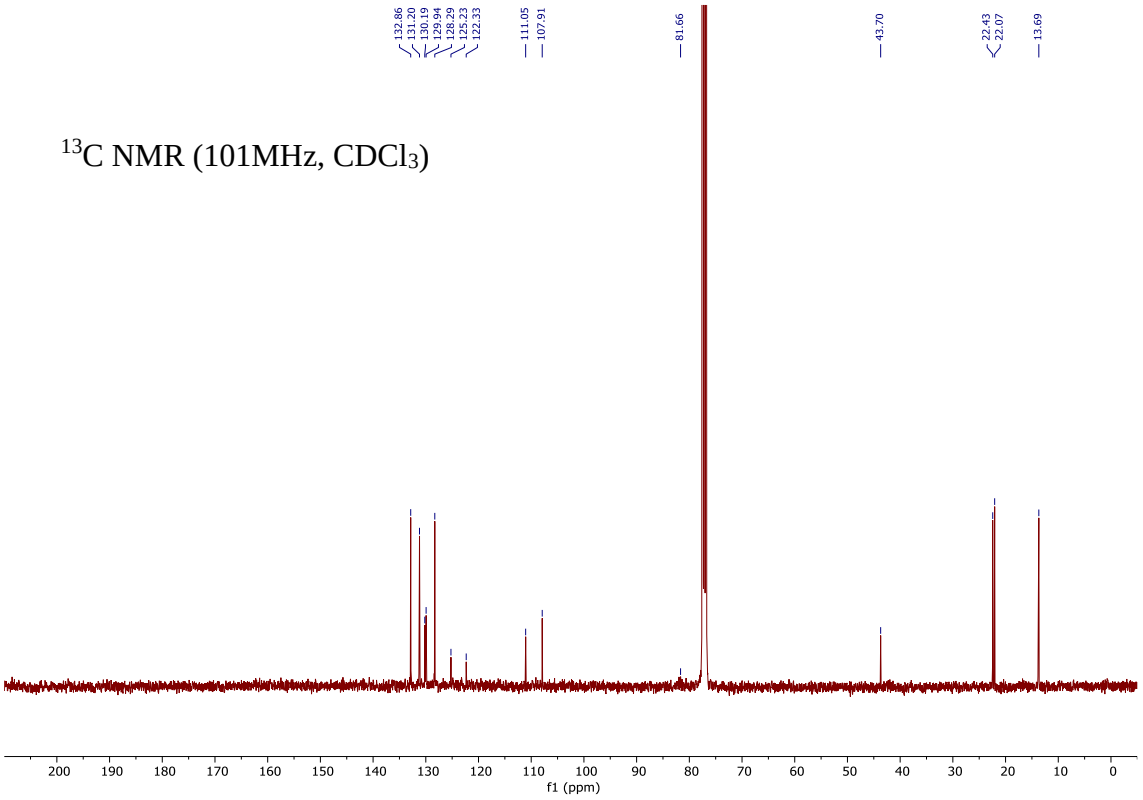
9. ^{1}H NMR, ^{13}C NMR and ^{19}F NMR spectra for new compounds

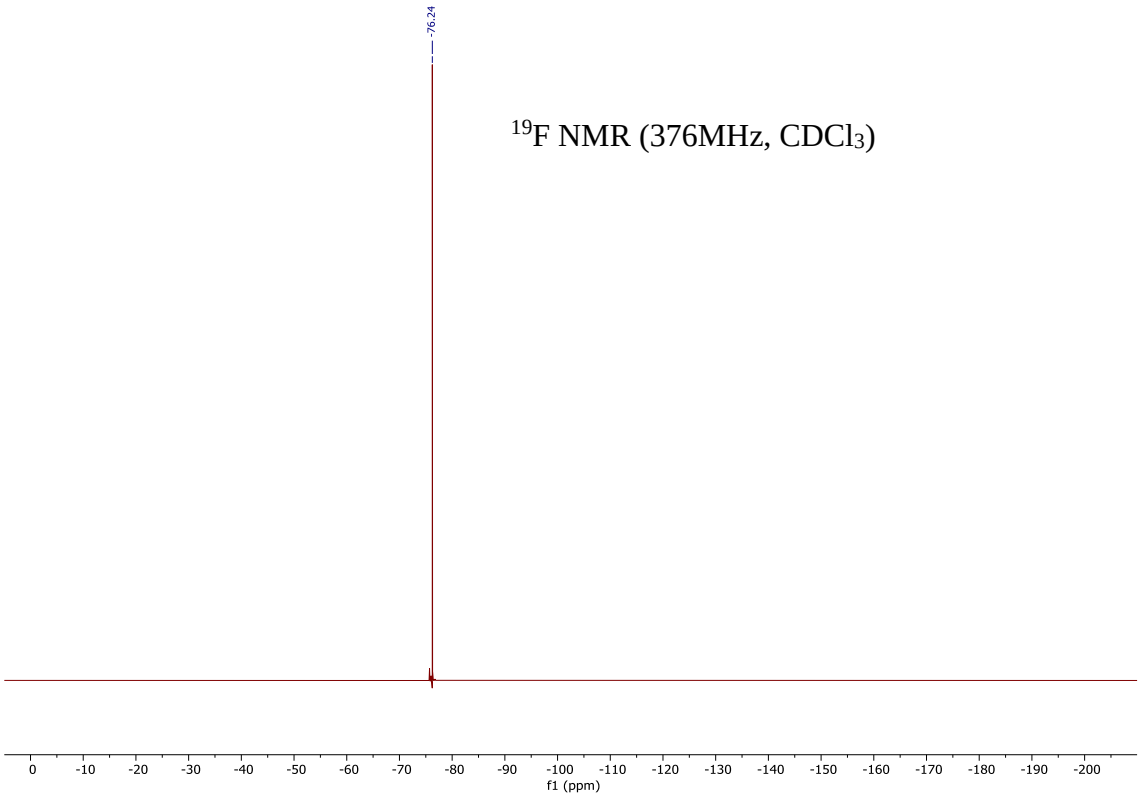
^{1}H NMR (400MHz, $CDCl_3$)



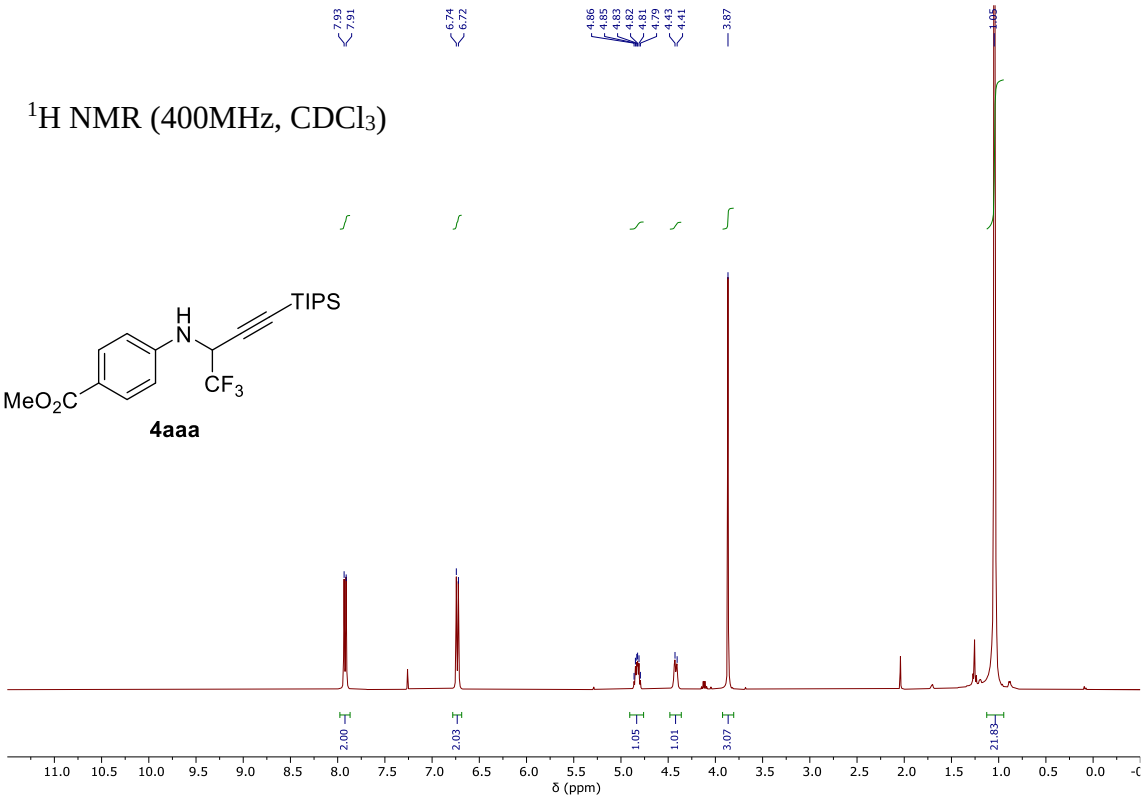
^{13}C NMR (101MHz, $CDCl_3$)



^{19}F NMR (376MHz, $CDCl_3$)

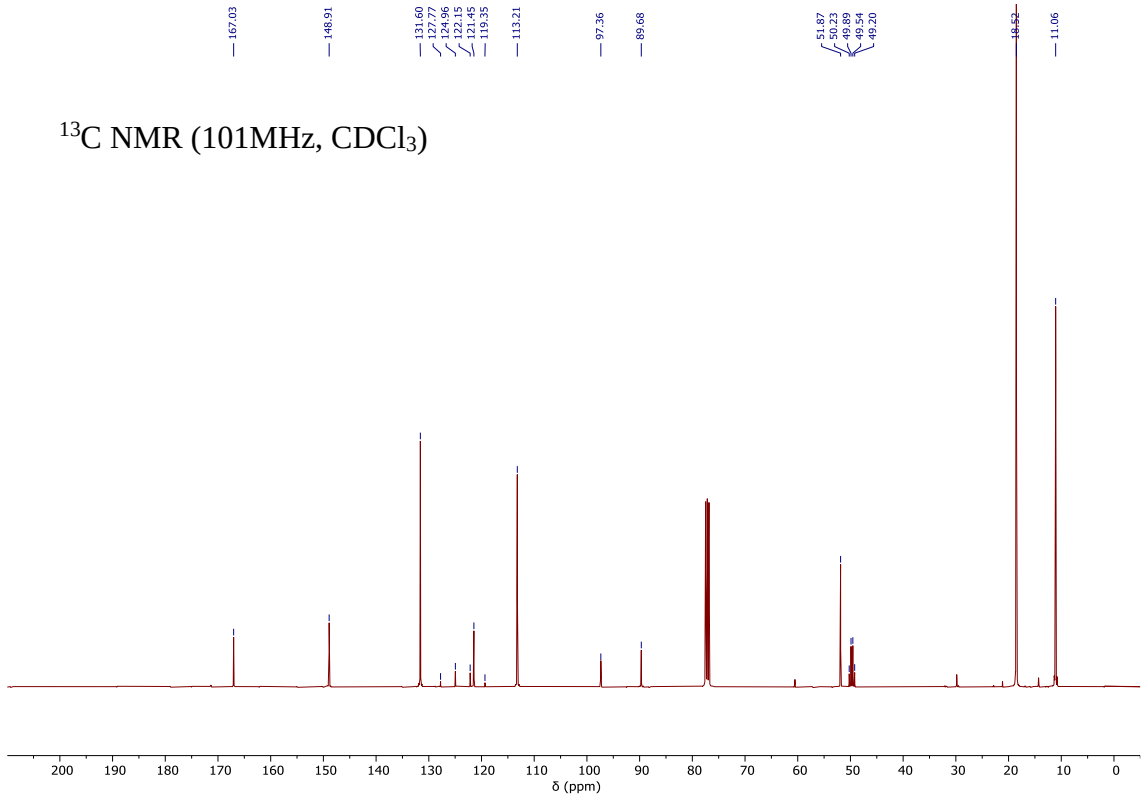


^{1}H NMR (400MHz, $CDCl_3$)

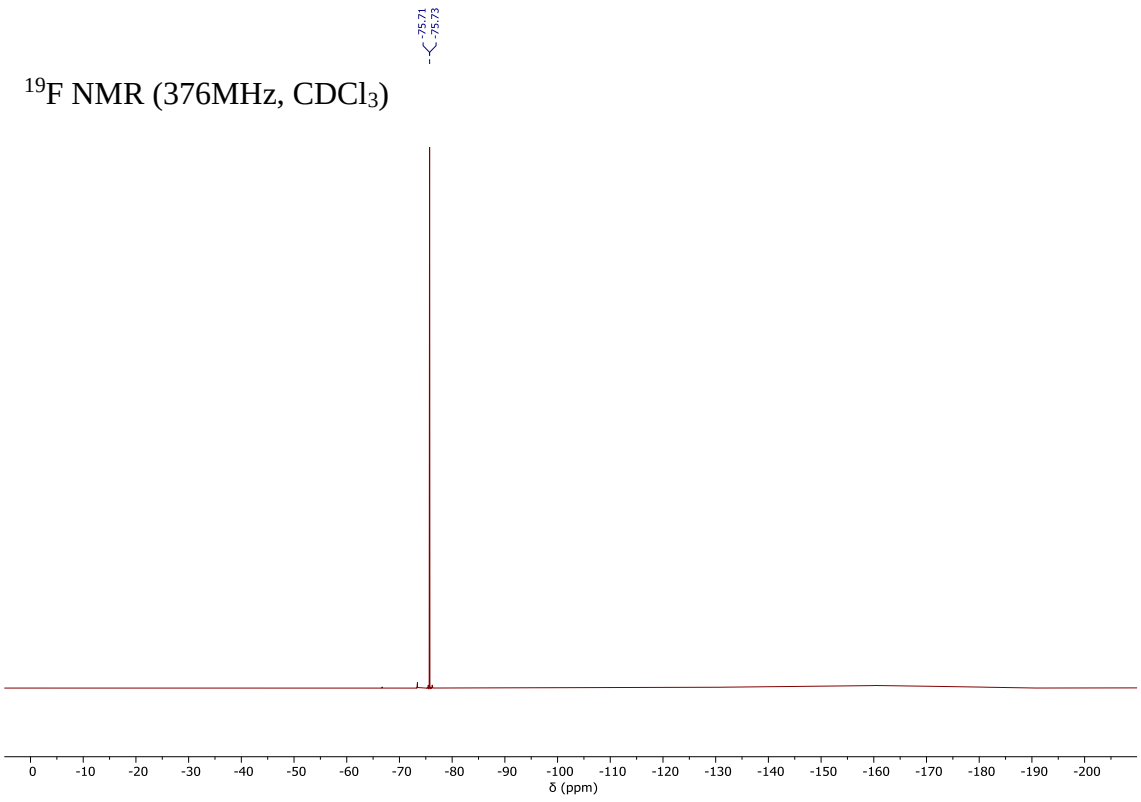


4aaa

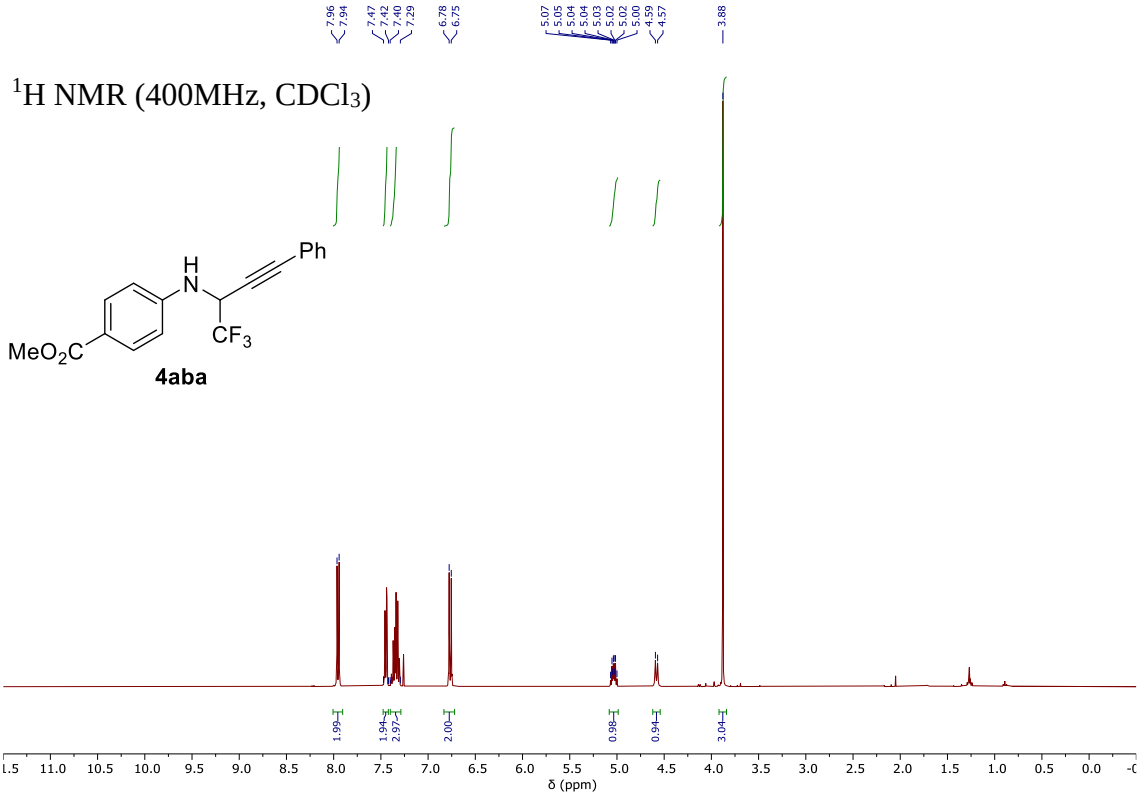
^{13}C NMR (101MHz, $CDCl_3$)



^{19}F NMR (376MHz, $CDCl_3$)

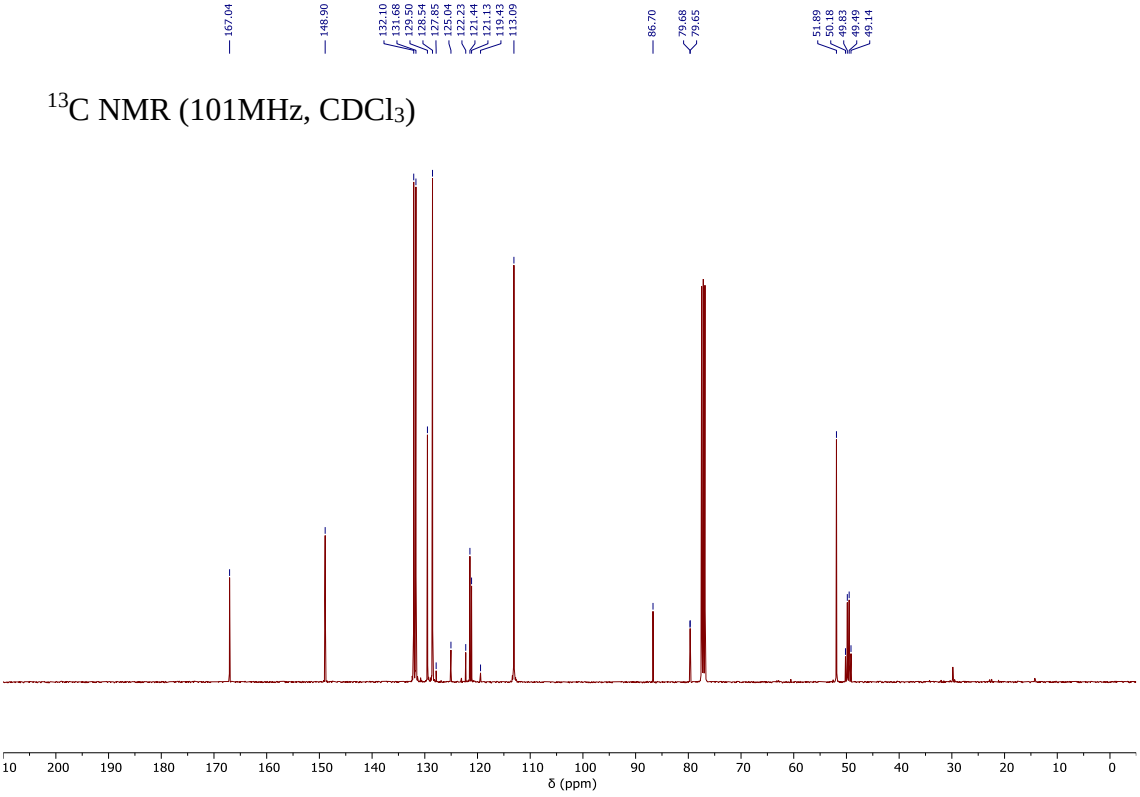


^{1}H NMR (400MHz, $CDCl_3$)

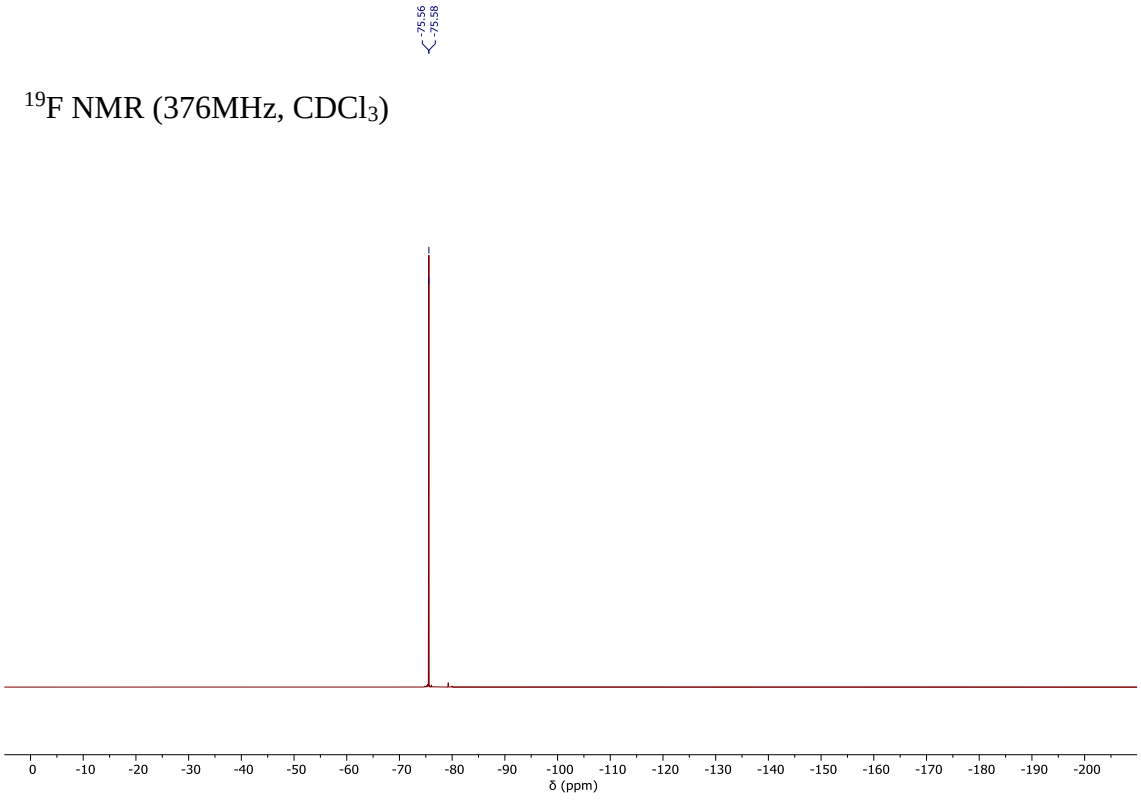


4aba

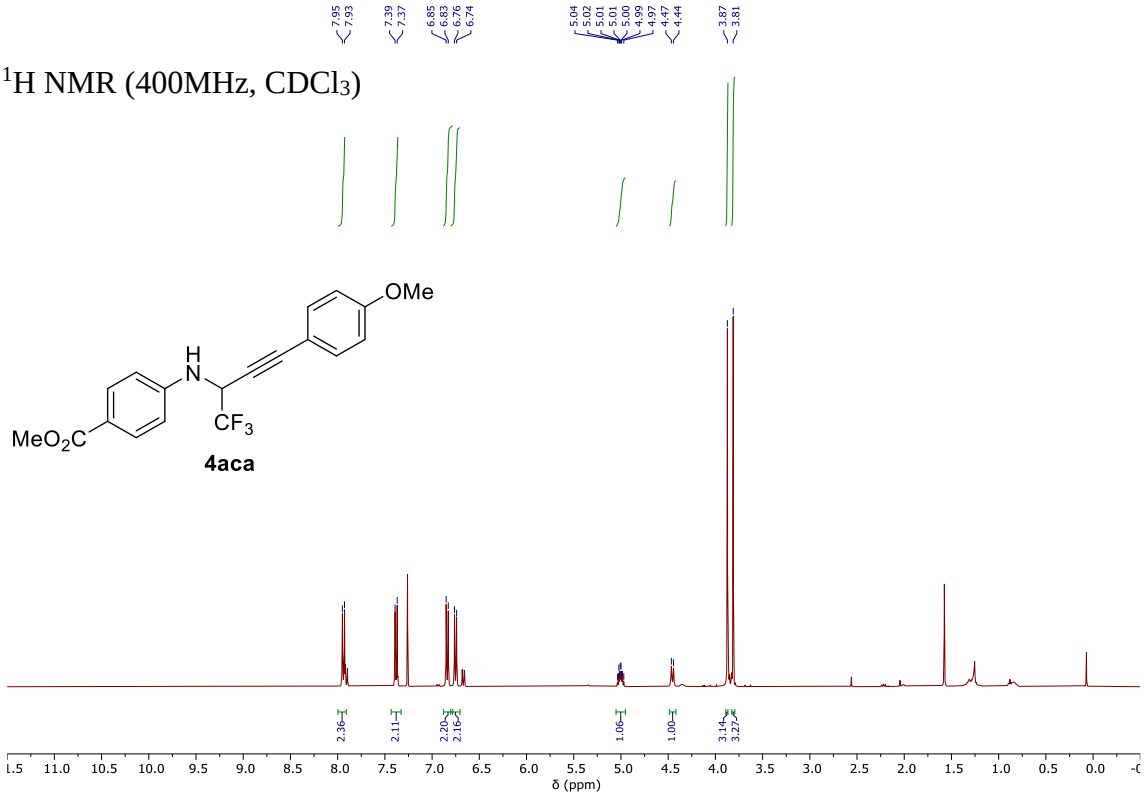
^{13}C NMR (101MHz, $CDCl_3$)



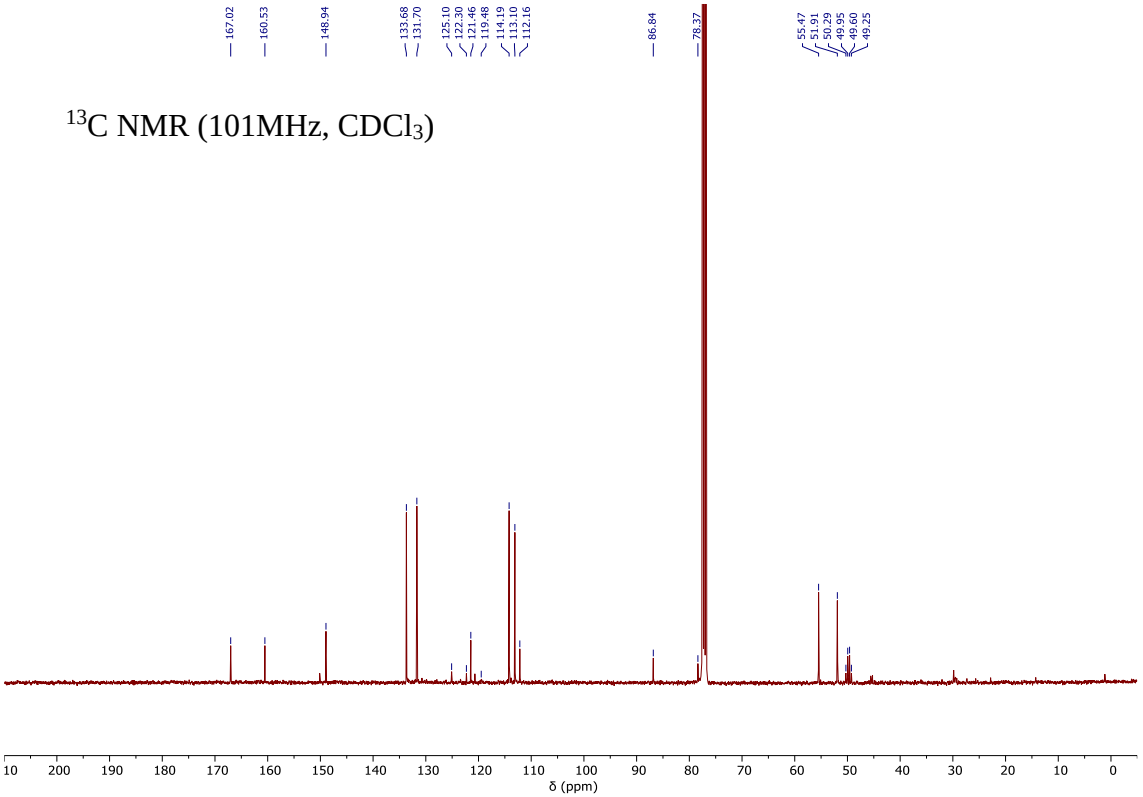
^{19}F NMR (376MHz, $CDCl_3$)



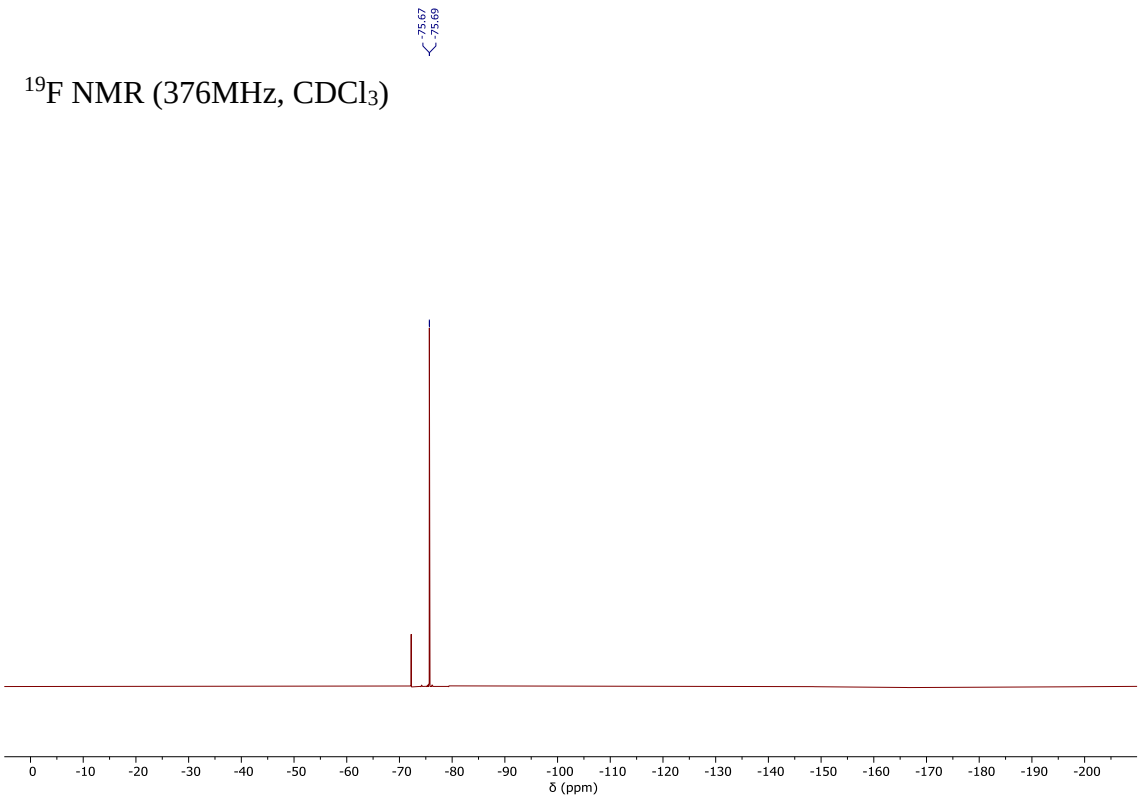
^{1}H NMR (400MHz, $CDCl_3$)



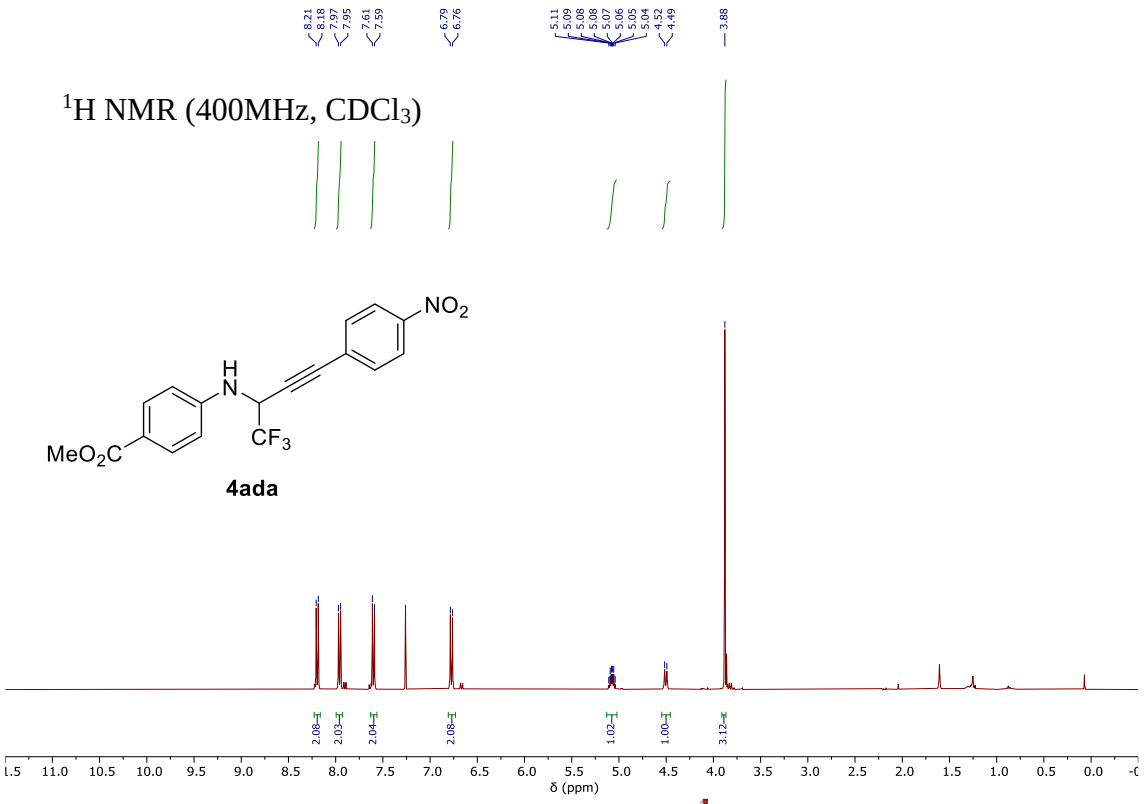
^{13}C NMR (101MHz, $CDCl_3$)



^{19}F NMR (376MHz, $CDCl_3$)



^{1}H NMR (400MHz, $CDCl_3$)



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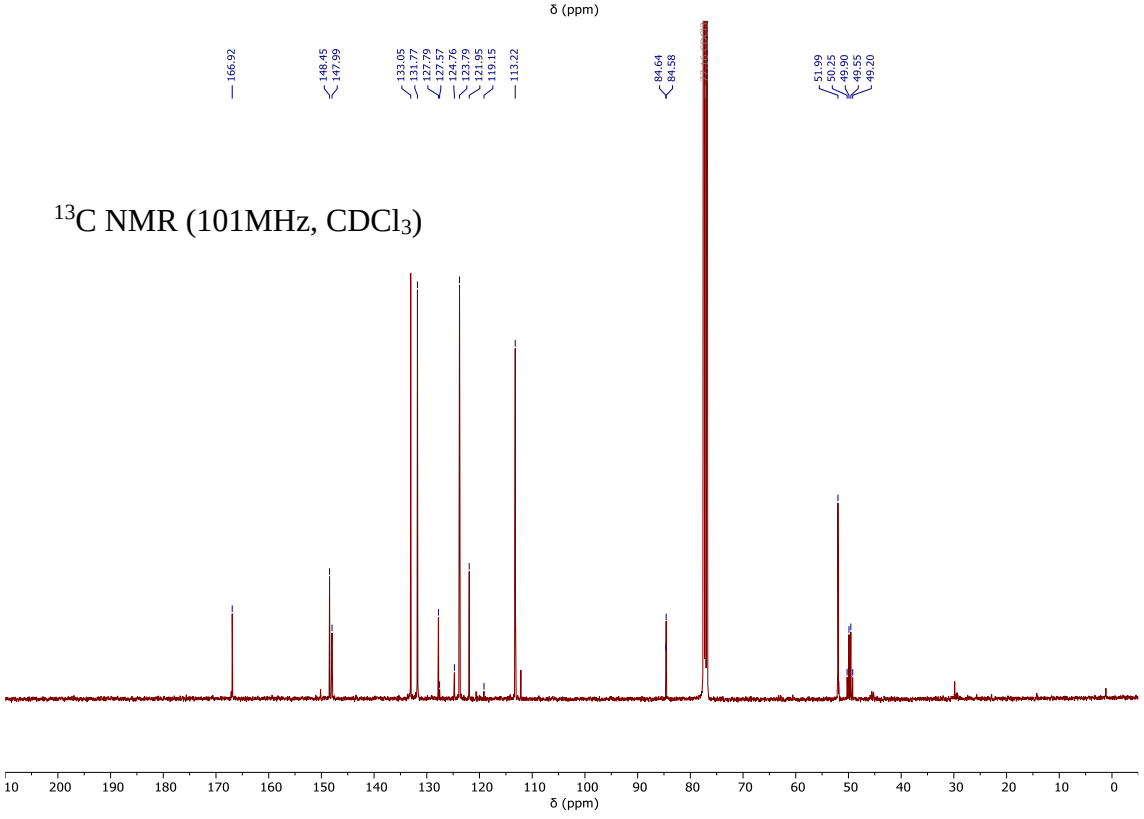
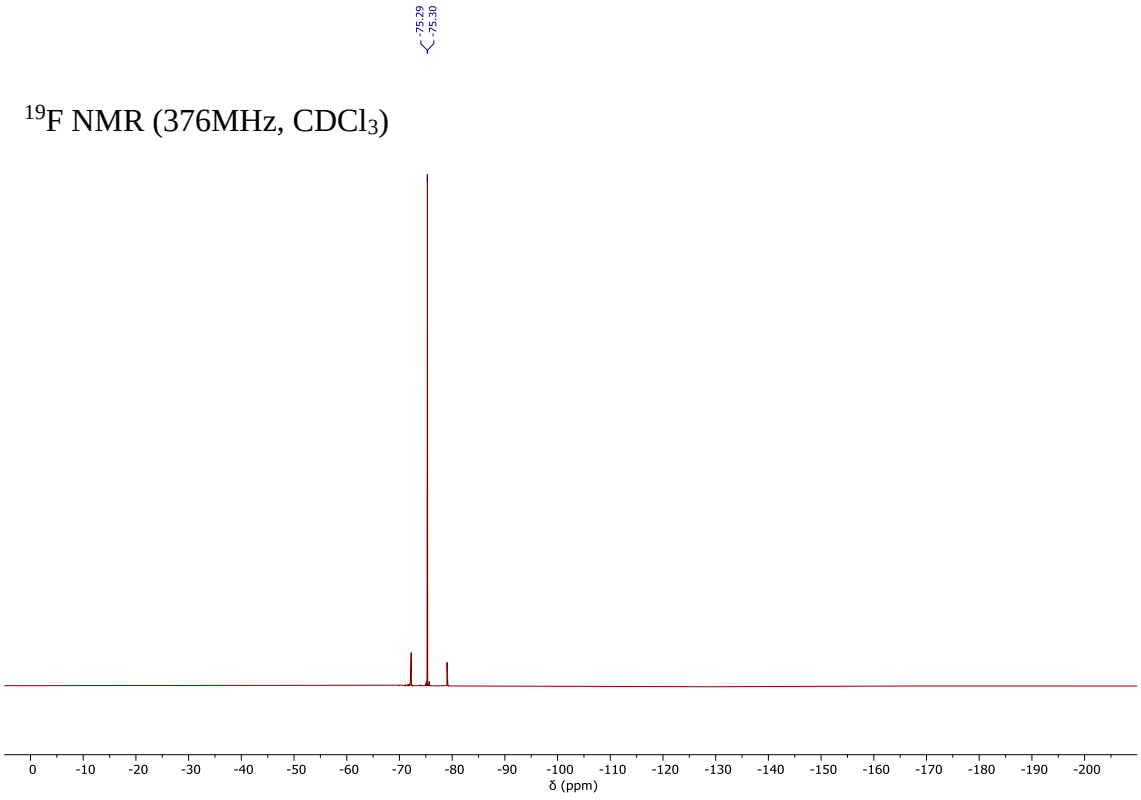
^{13}C NMR (101MHz, $CDCl_3$)



^{19}F NMR (376MHz, $CDCl_3$)



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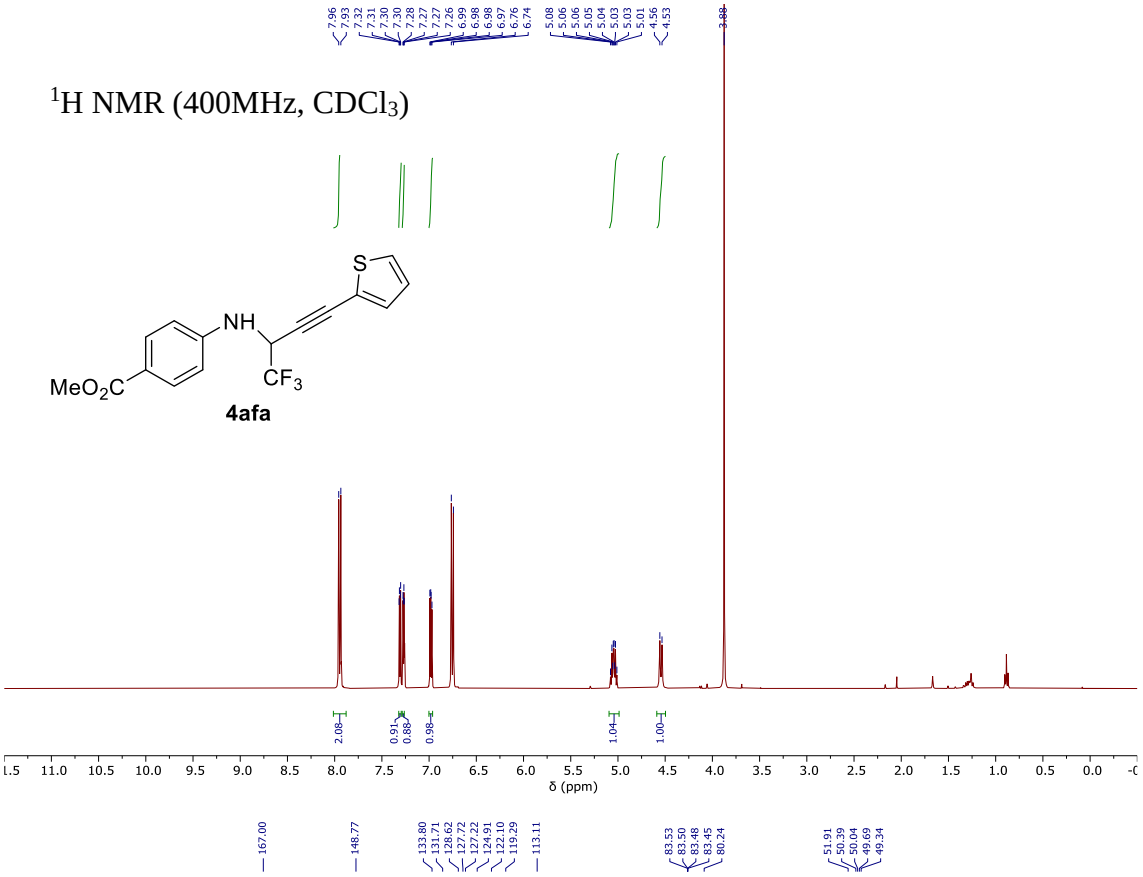
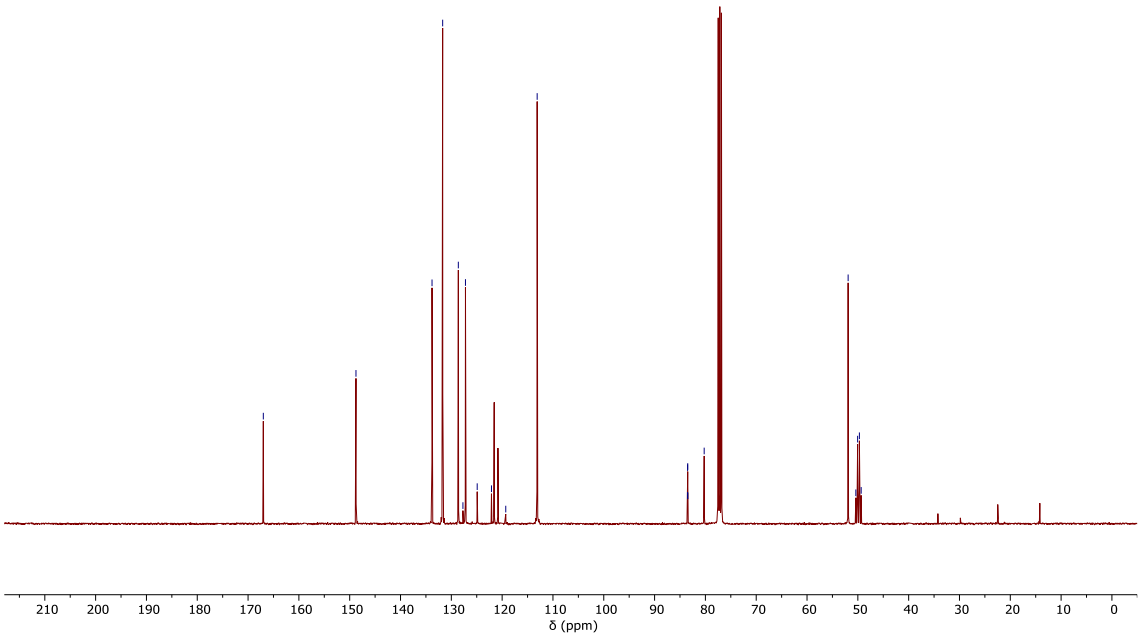


^{13}C NMR (101MHz, $CDCl_3$)



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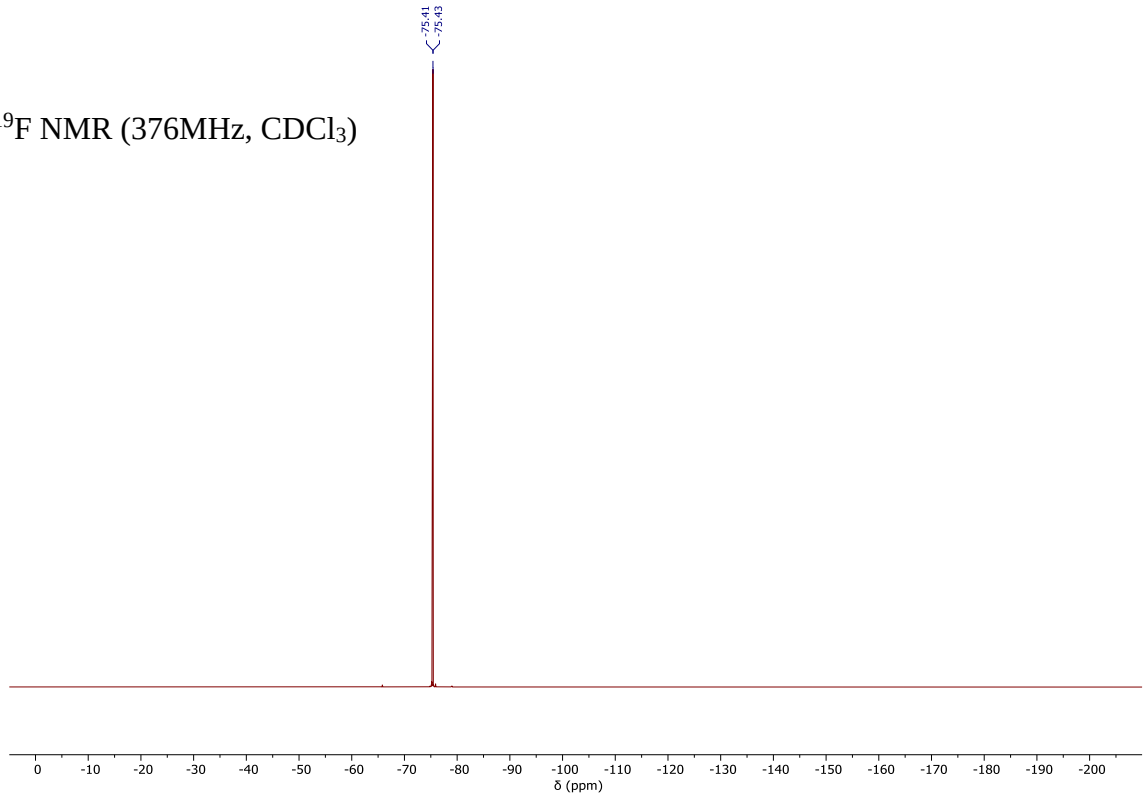

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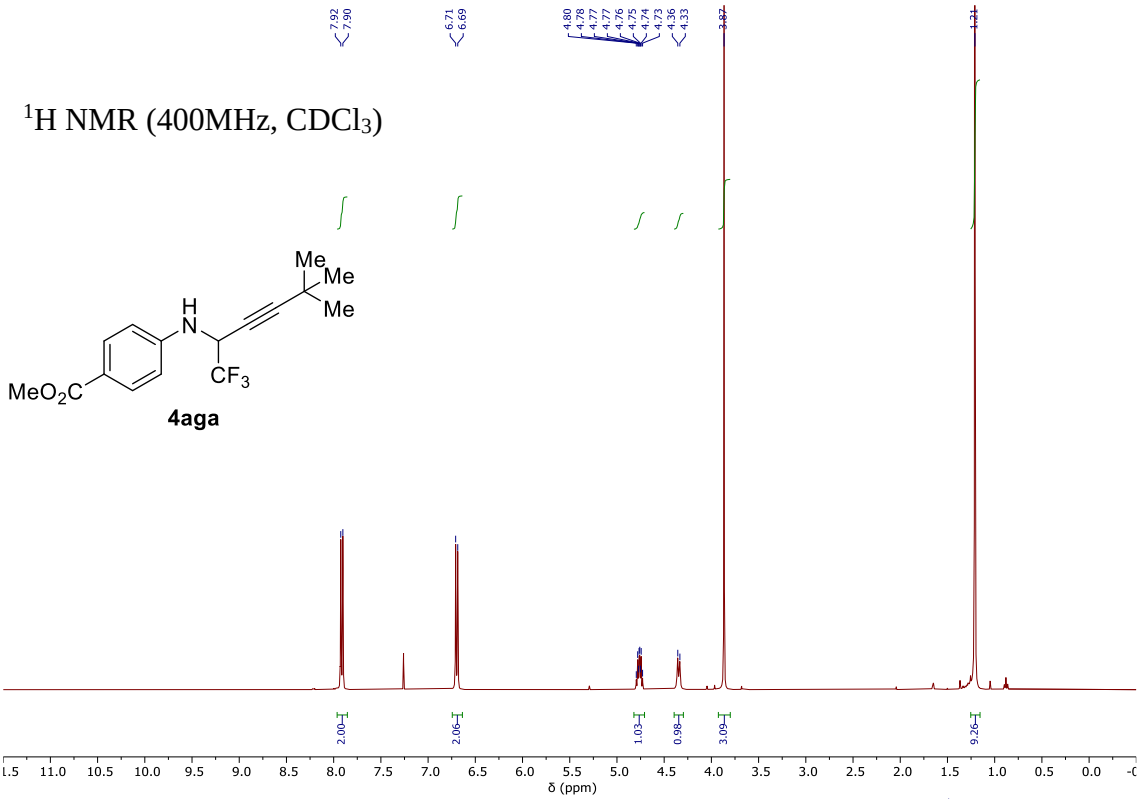
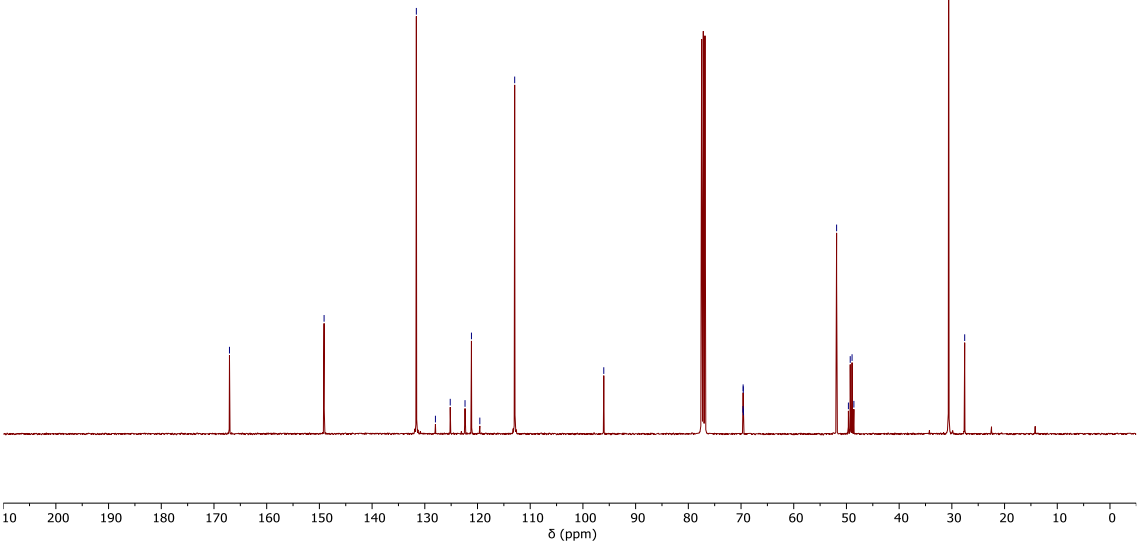
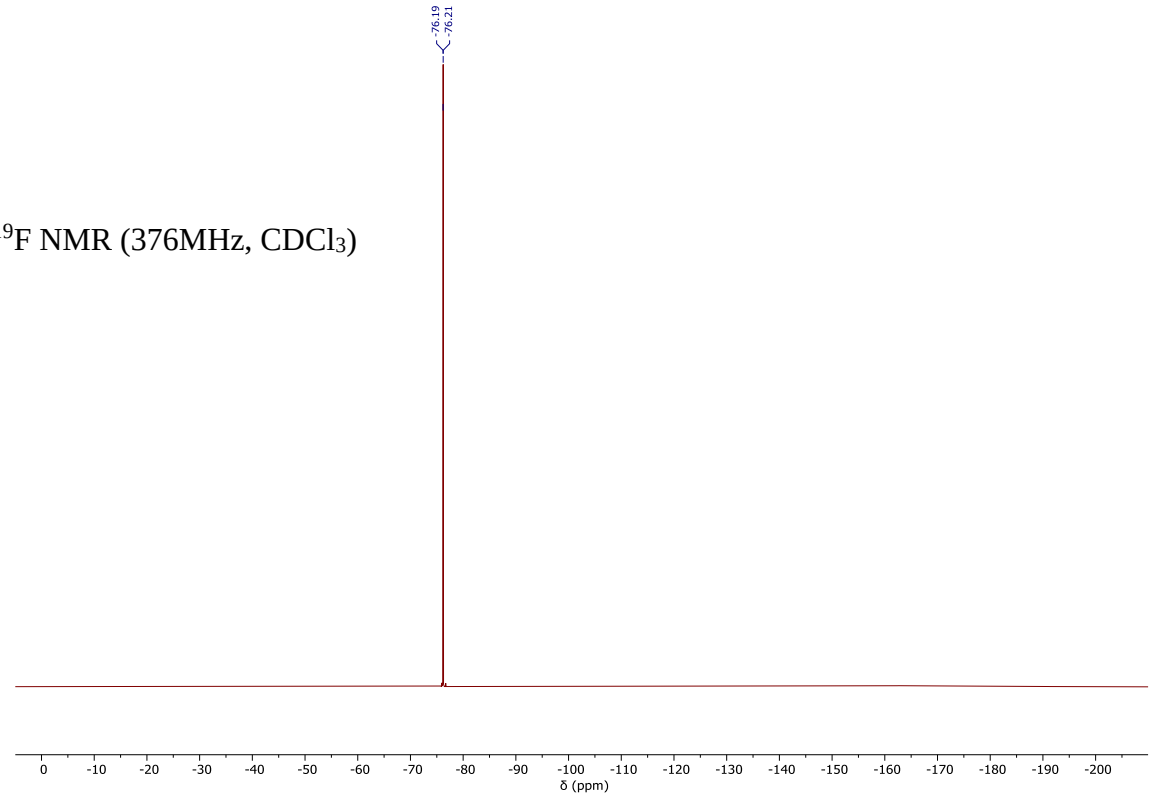


4aga

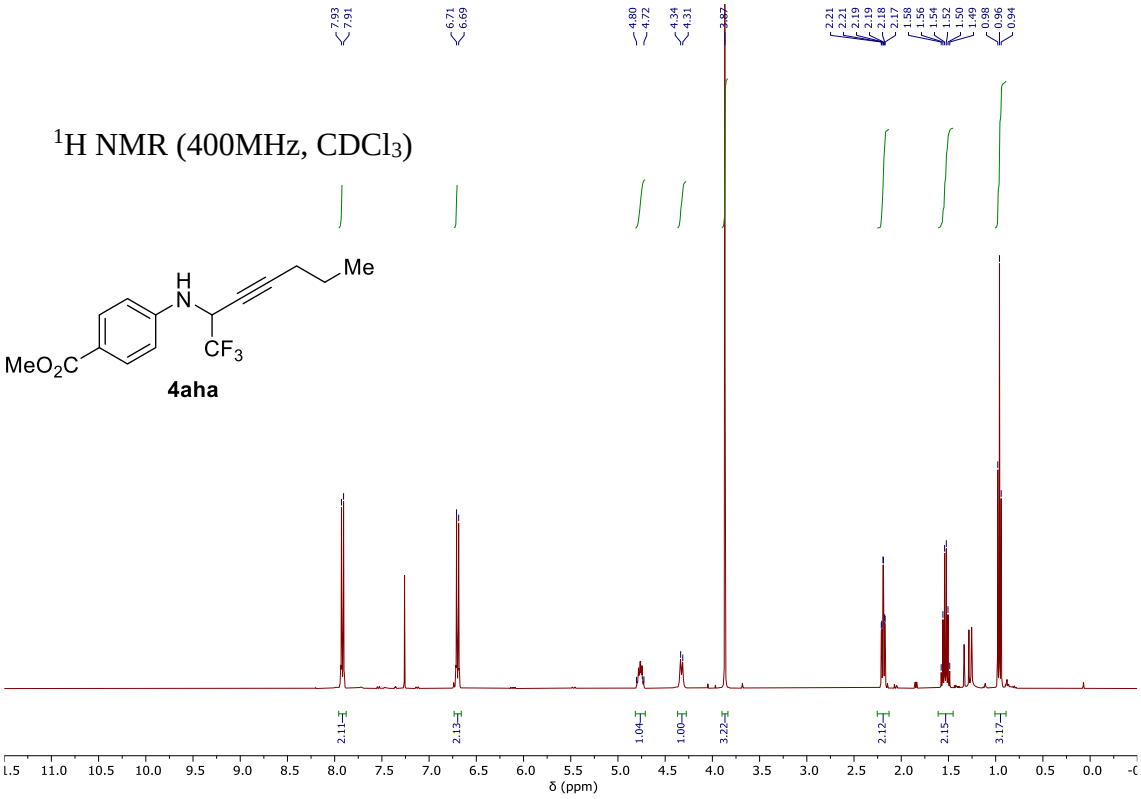
^{13}C NMR (101MHz, $CDCl_3$)



^{19}F NMR (376MHz, $CDCl_3$)

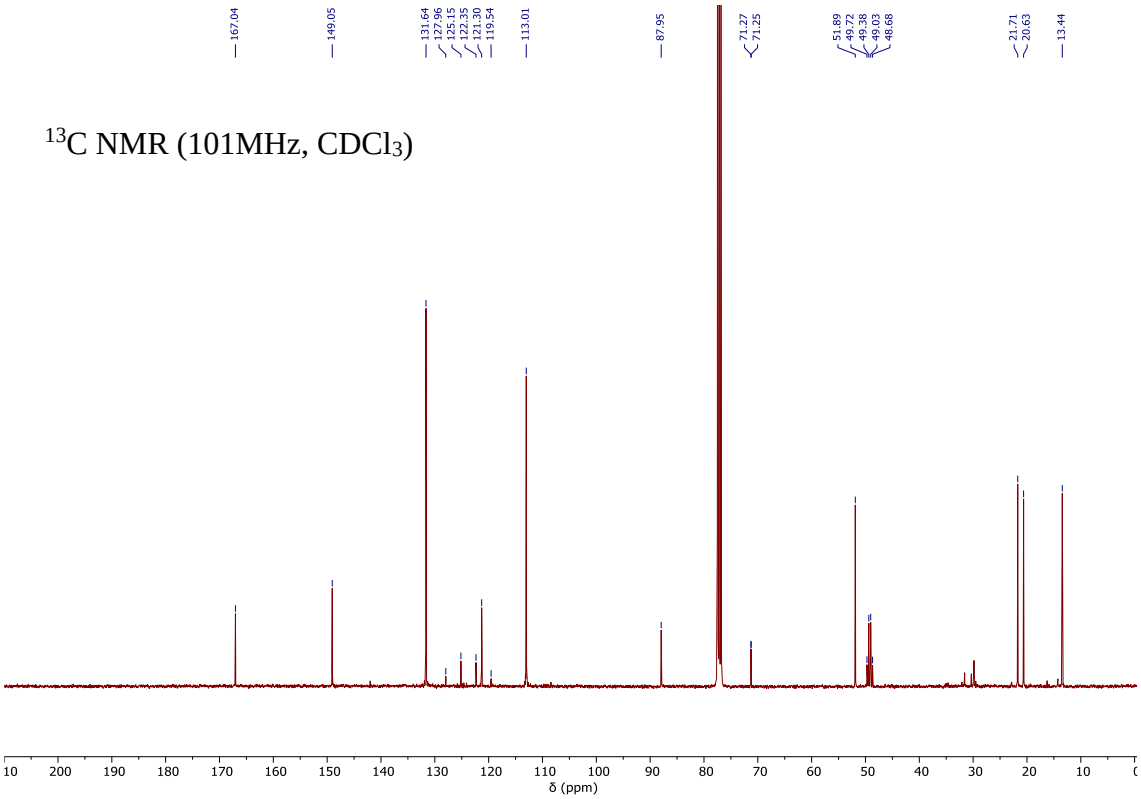


^{1}H NMR (400MHz, $CDCl_3$)

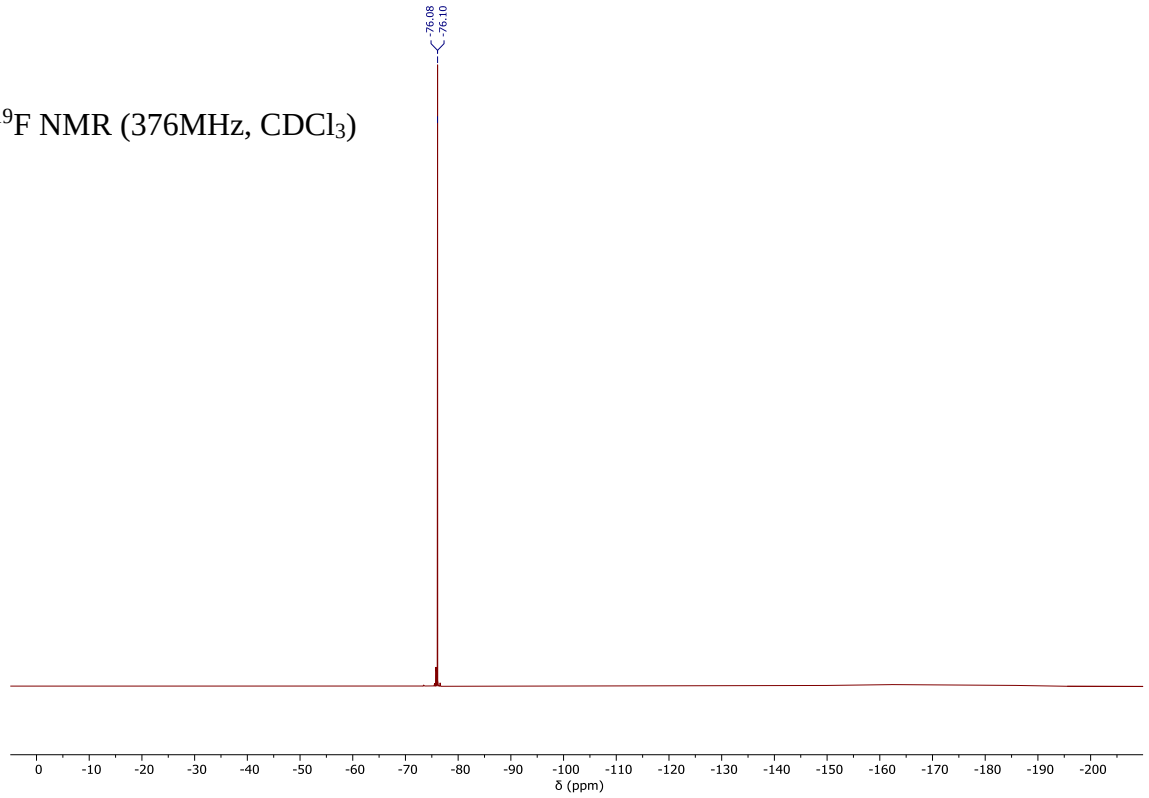


4aha

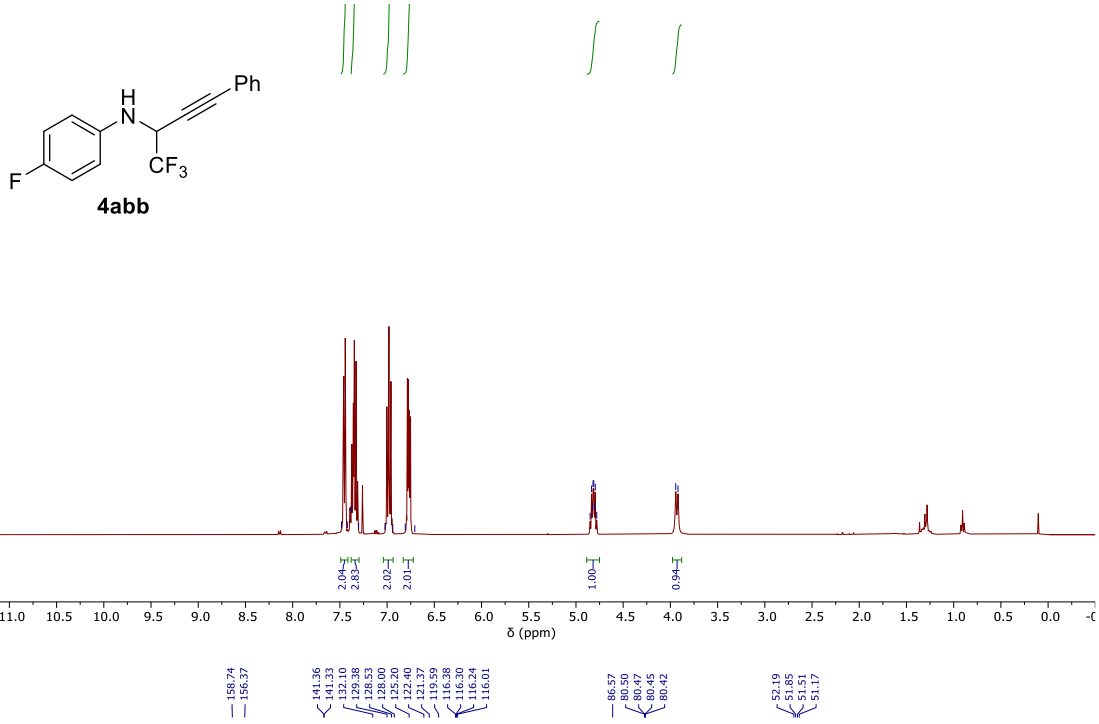
^{13}C NMR (101MHz, $CDCl_3$)



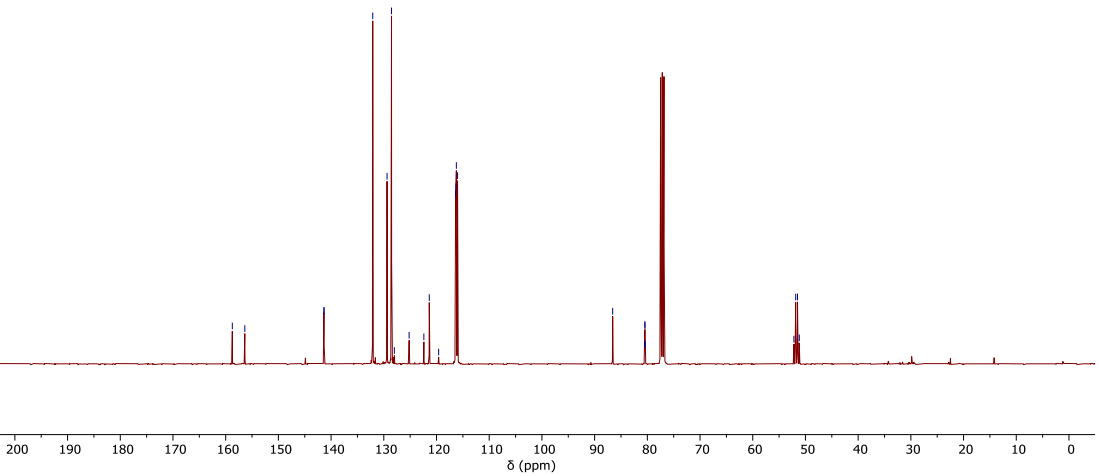
^{19}F NMR (376MHz, $CDCl_3$)



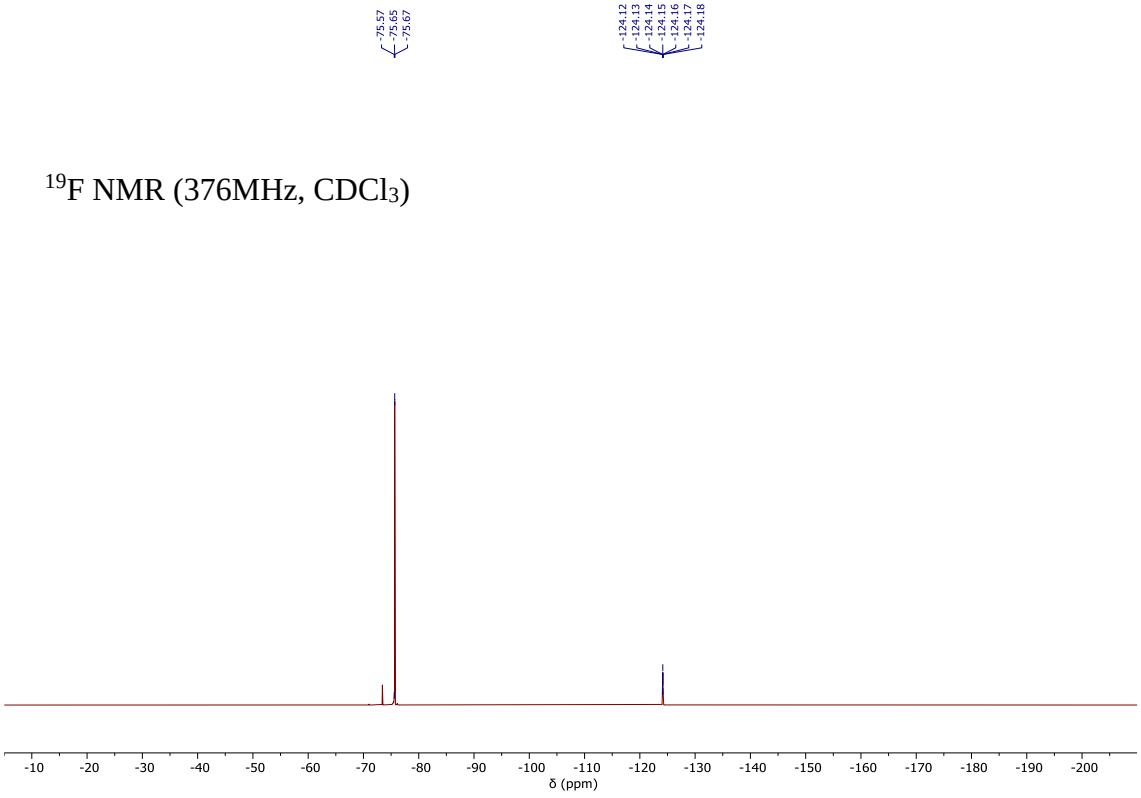
^{1}H NMR (400MHz, $CDCl_3$)



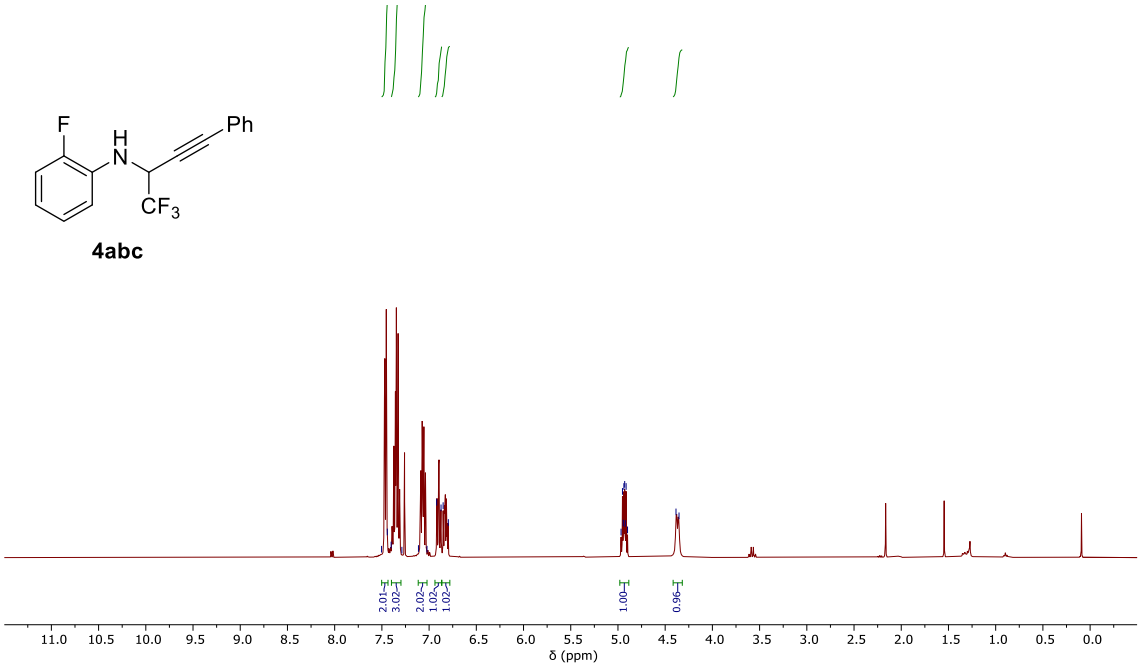
^{13}C NMR (101MHz, $CDCl_3$)



^{19}F NMR (376MHz, $CDCl_3$)



^{1}H NMR (400MHz, $CDCl_3$)



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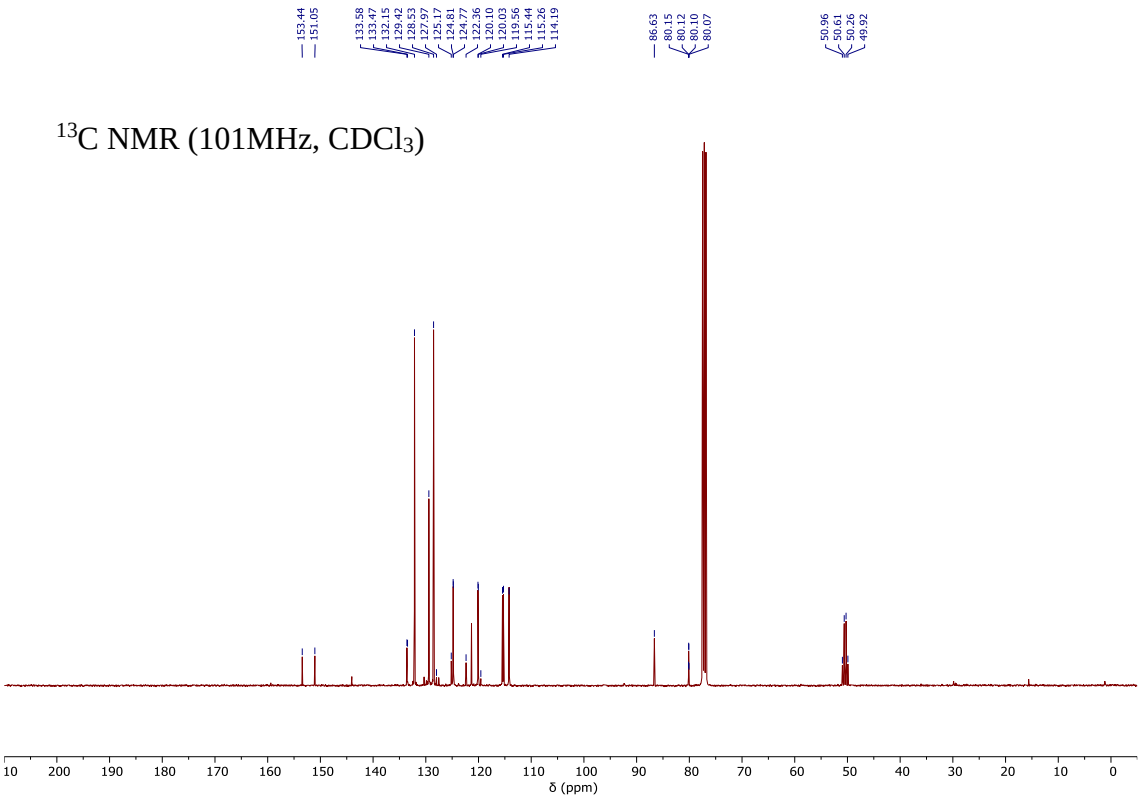
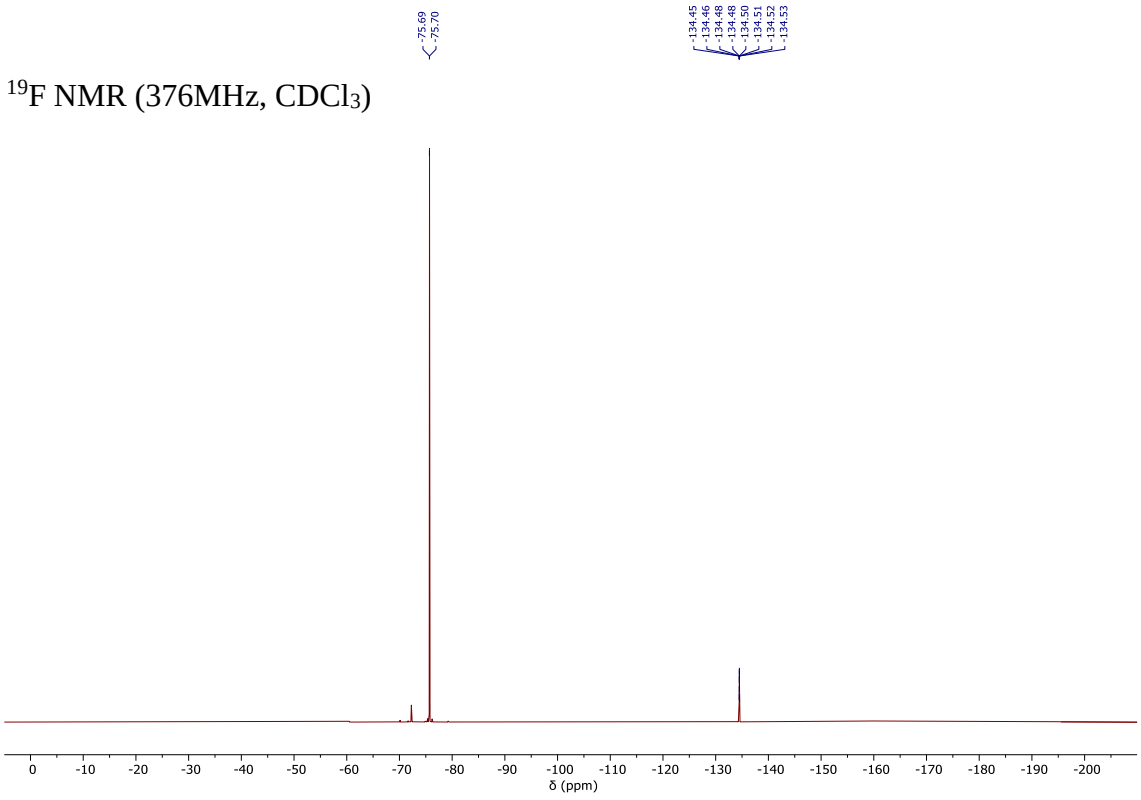
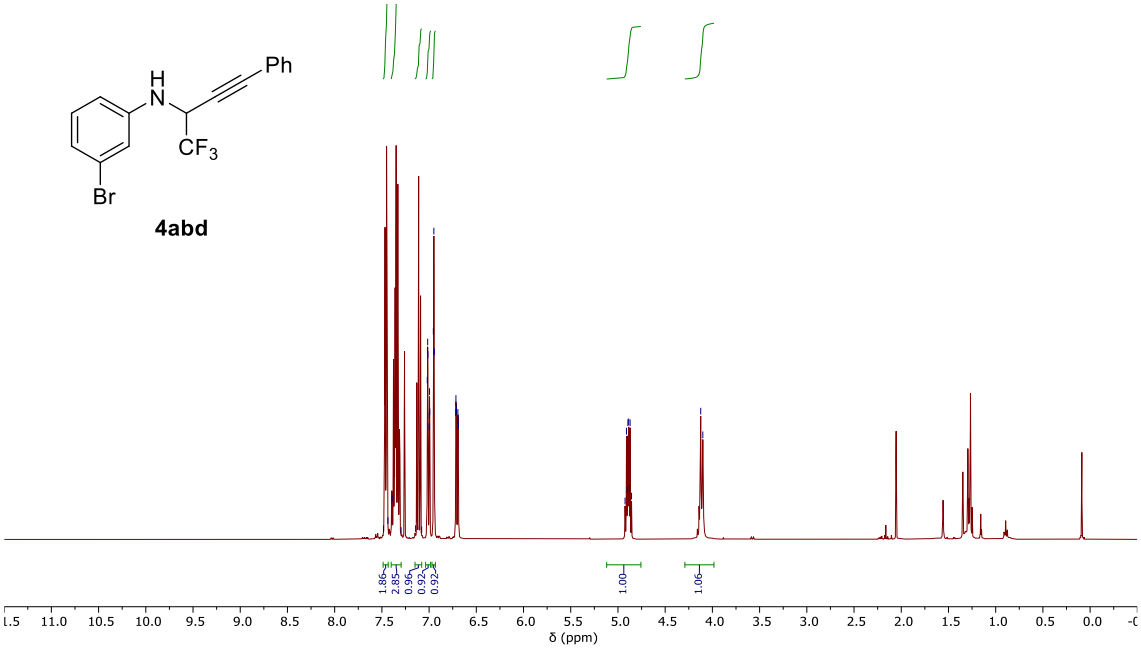


^{13}C NMR (101MHz, $CDCl_3$)

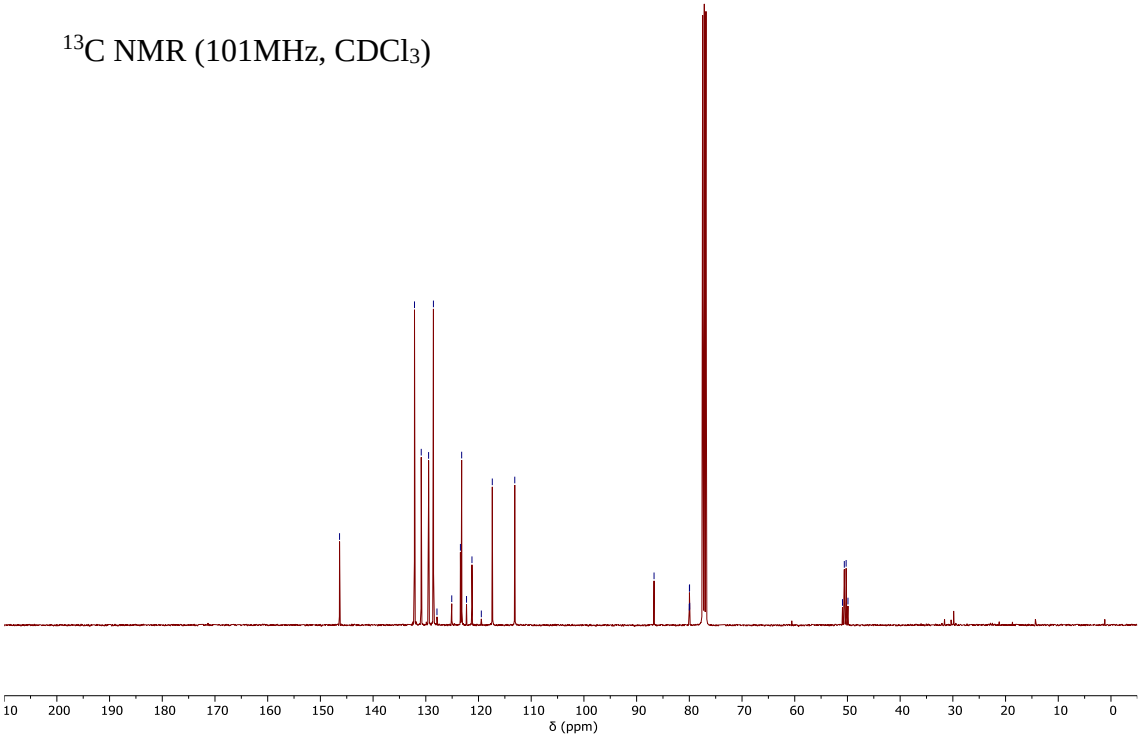
^{19}F NMR (376MHz, $CDCl_3$)



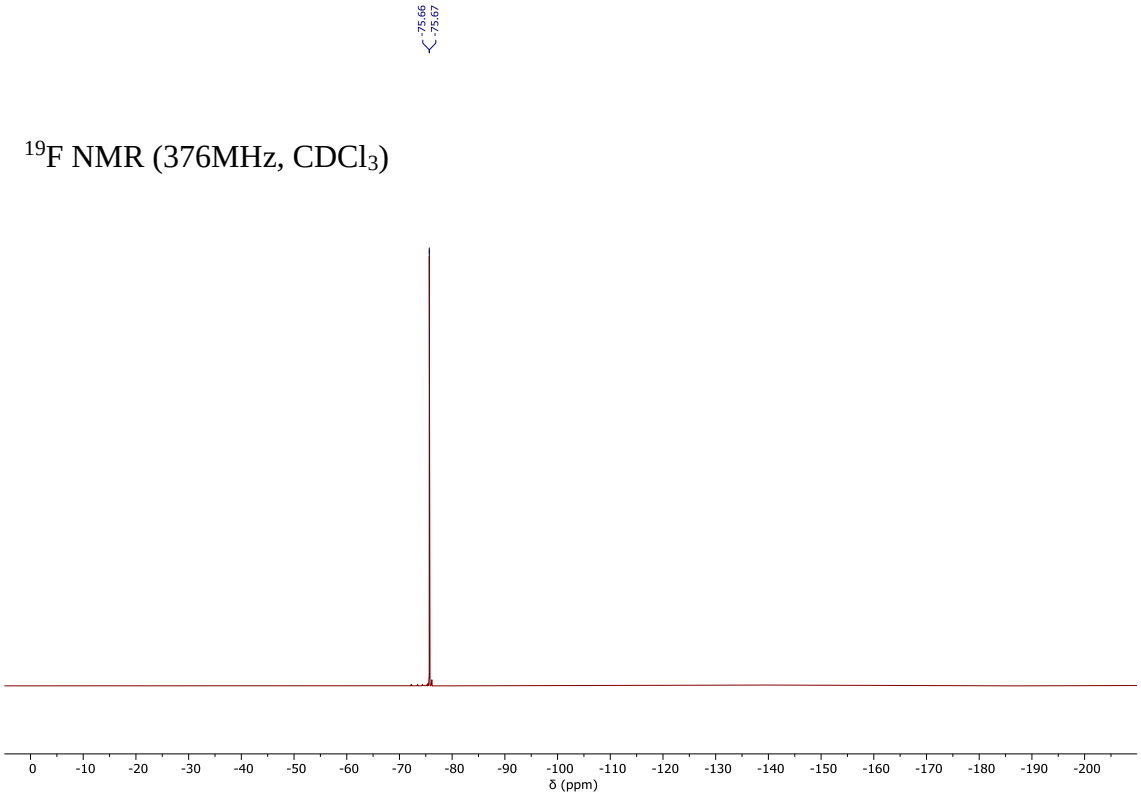
^{1}H NMR (400MHz, $CDCl_3$)



^{13}C NMR (101MHz, $CDCl_3$)



^{19}F NMR (376MHz, $CDCl_3$)



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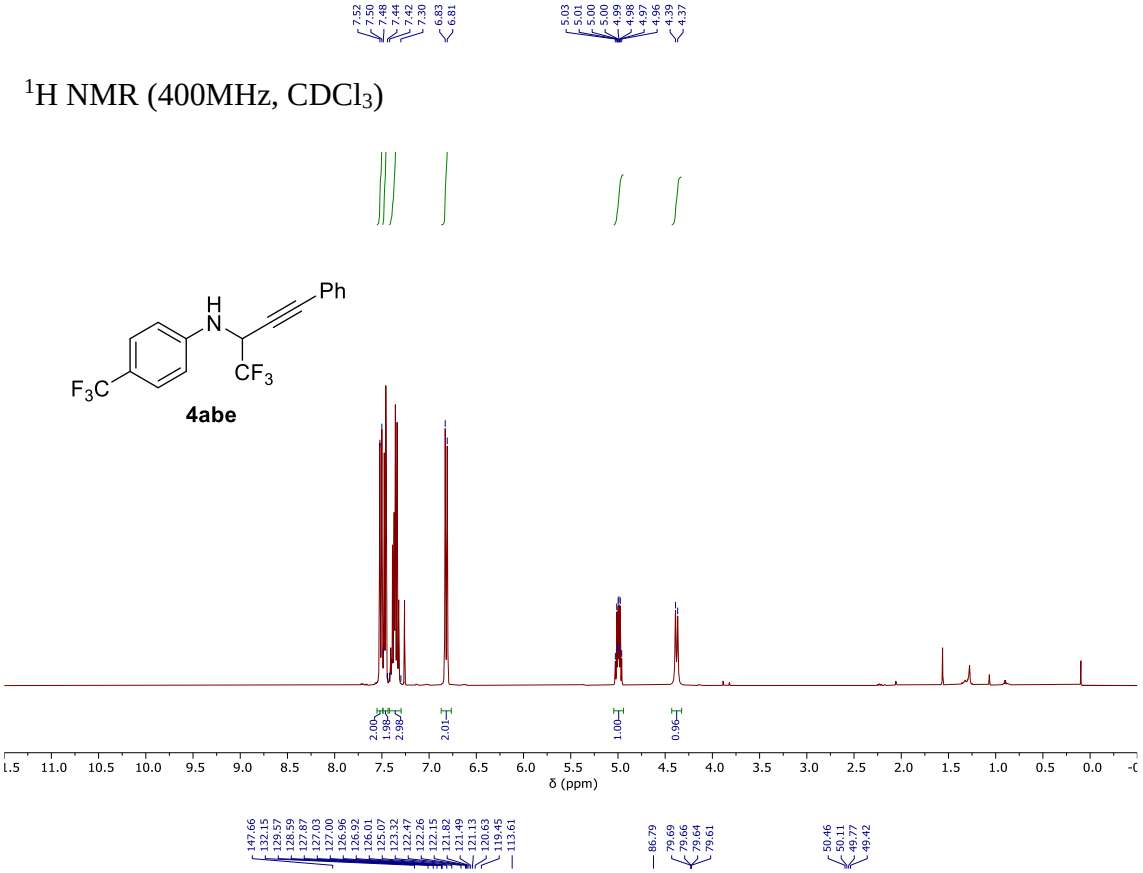
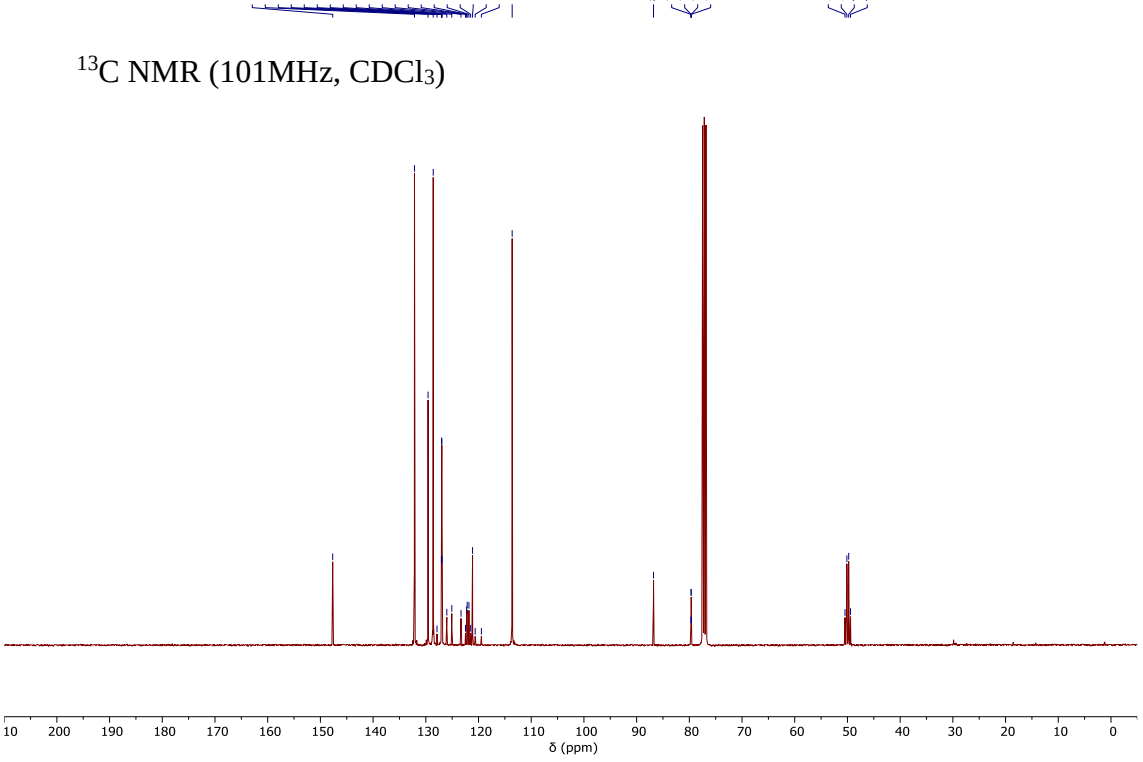


^{13}C NMR (101MHz, $CDCl_3$)



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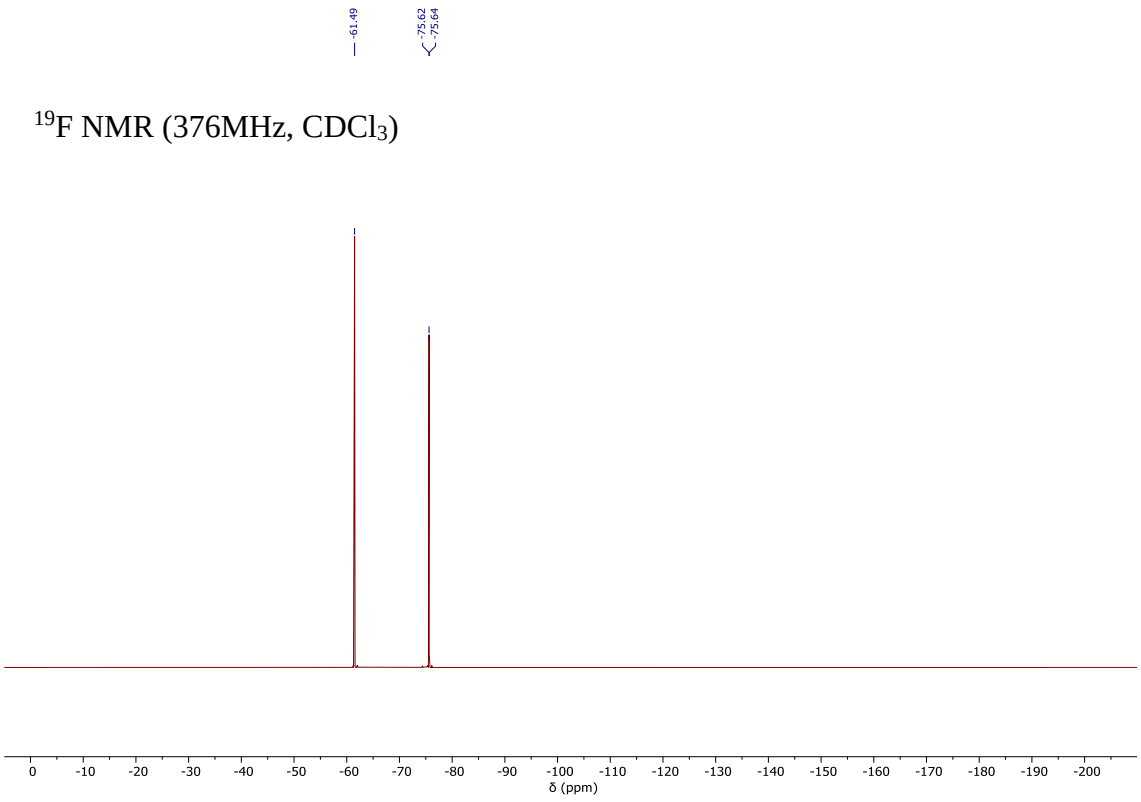
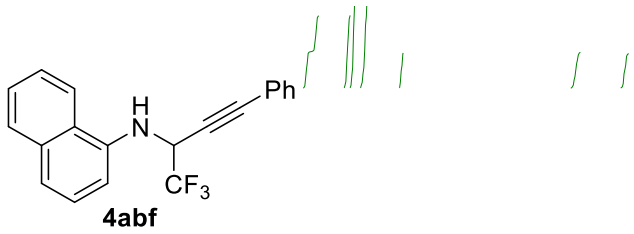
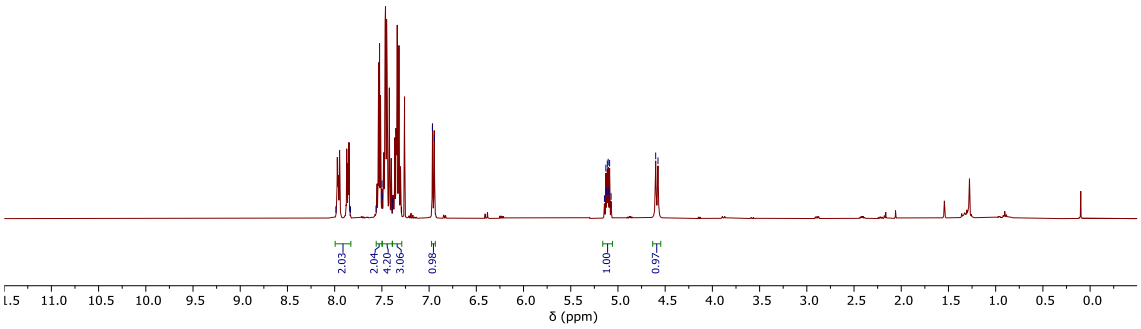


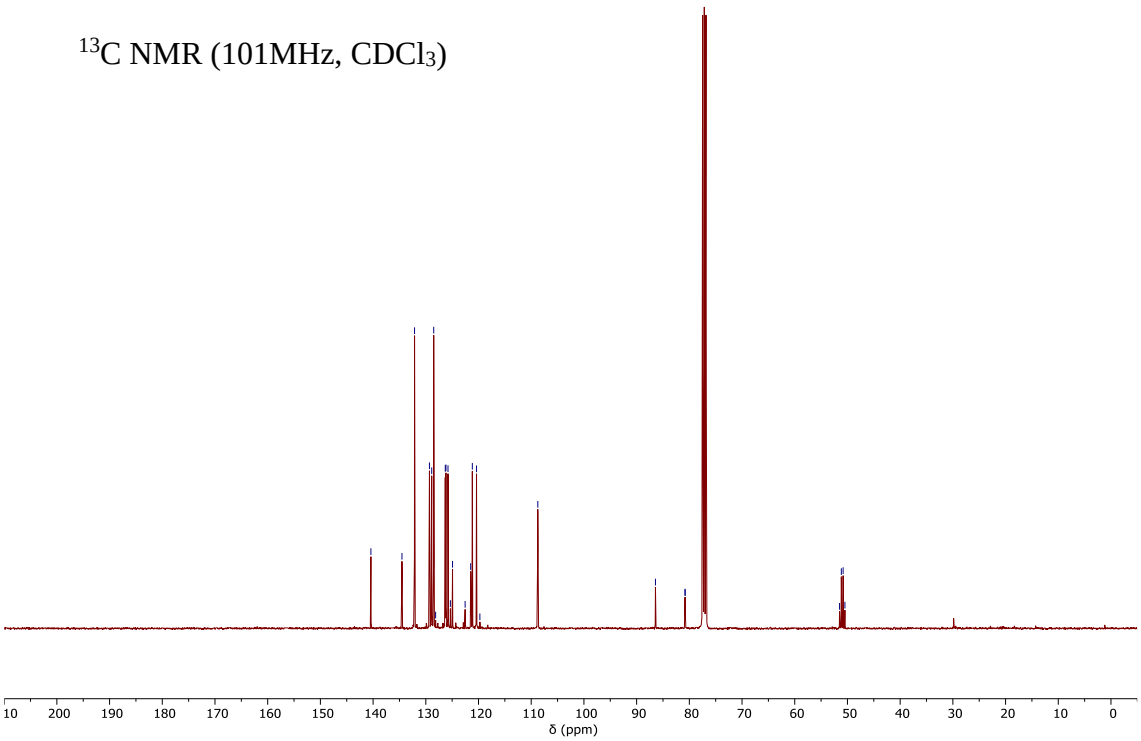
^{1}H NMR (400MHz, $CDCl_3$)



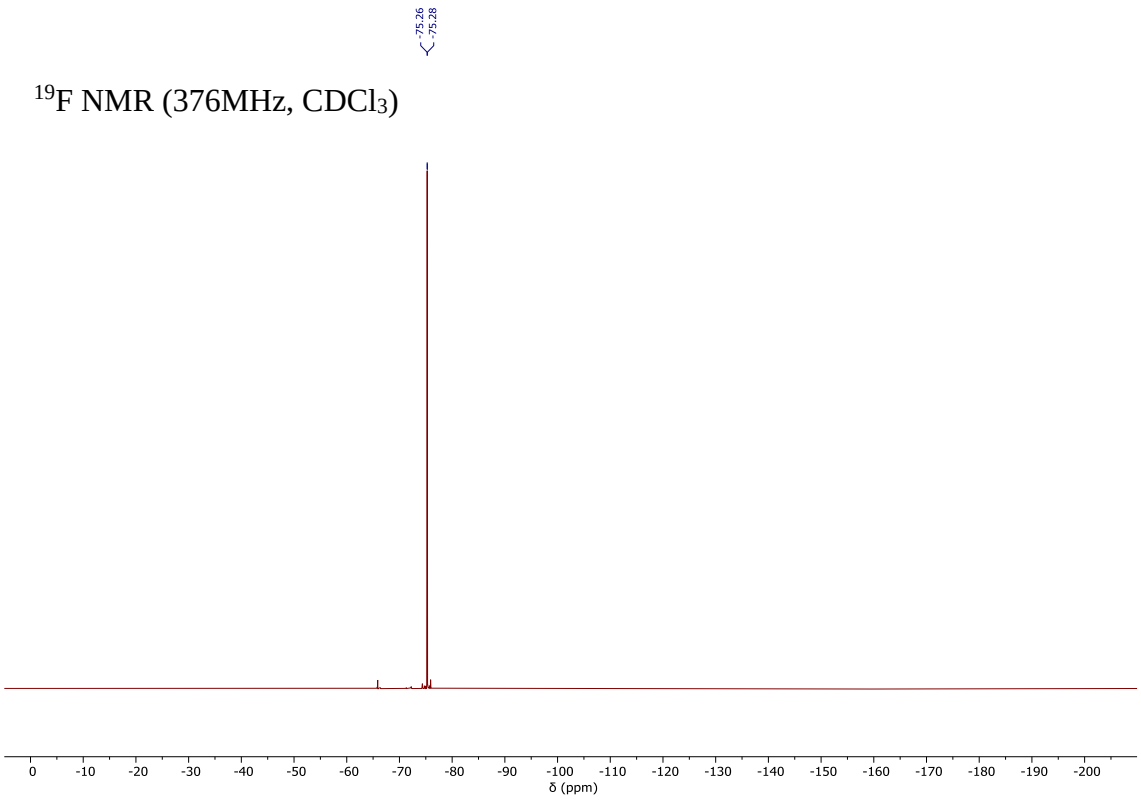
4abf



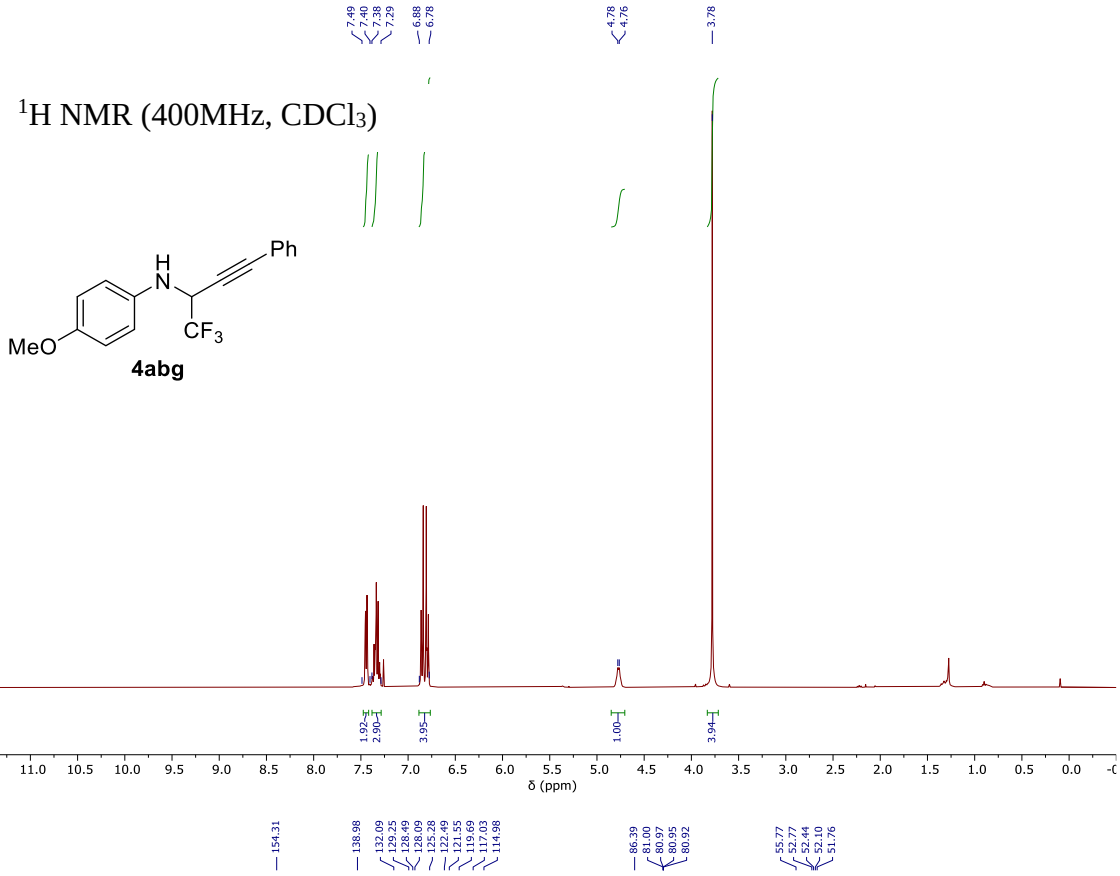
^{13}C NMR (101MHz, $CDCl_3$)



^{19}F NMR (376MHz, $CDCl_3$)

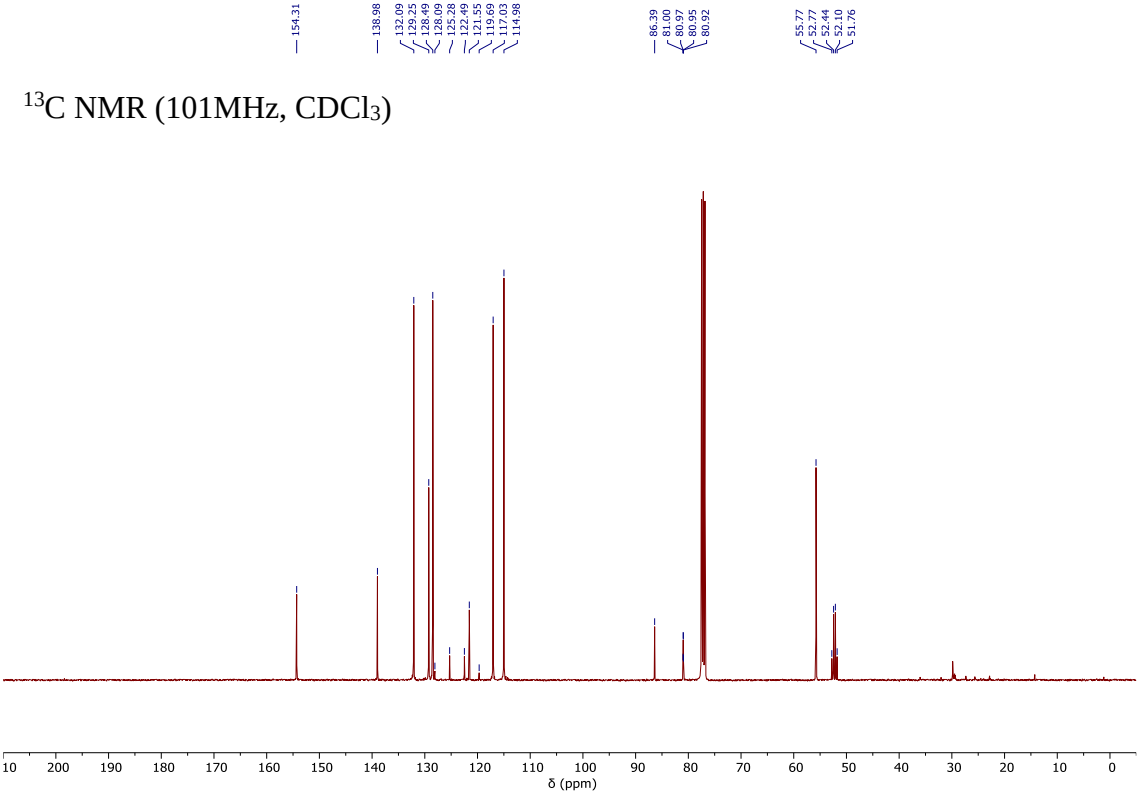


^{1}H NMR (400MHz, $CDCl_3$)

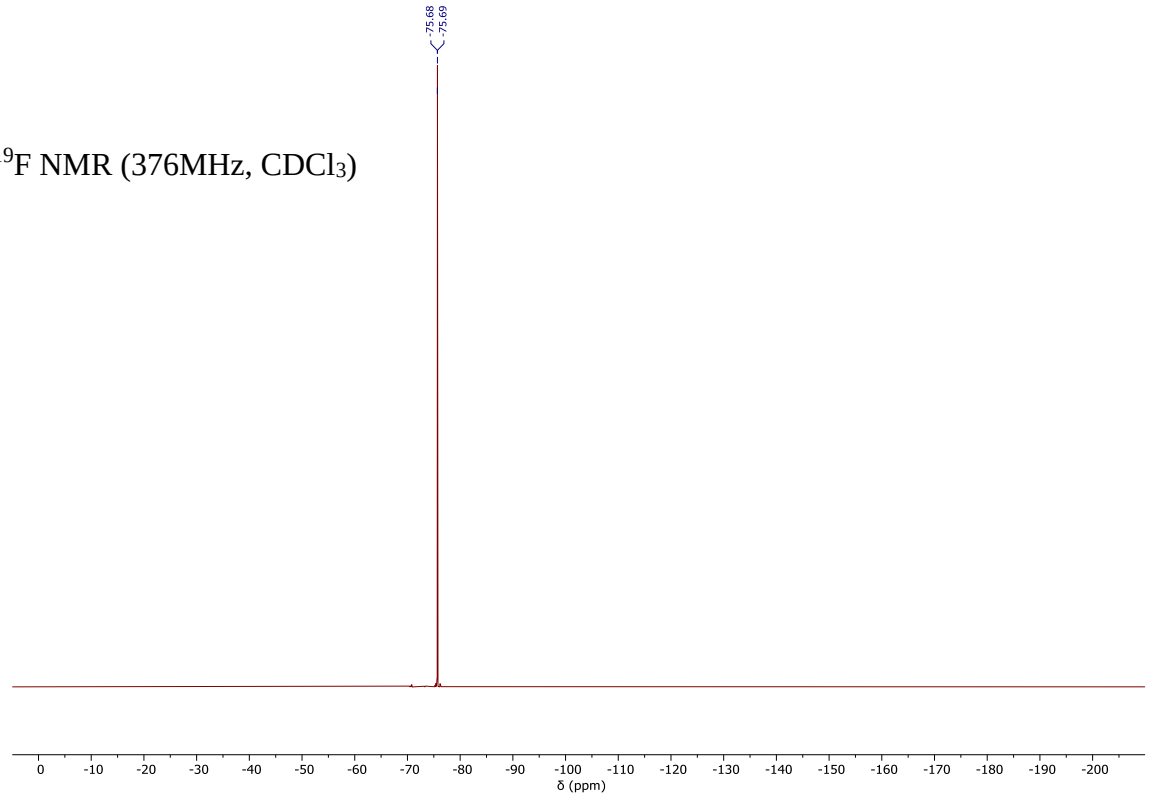


4abg

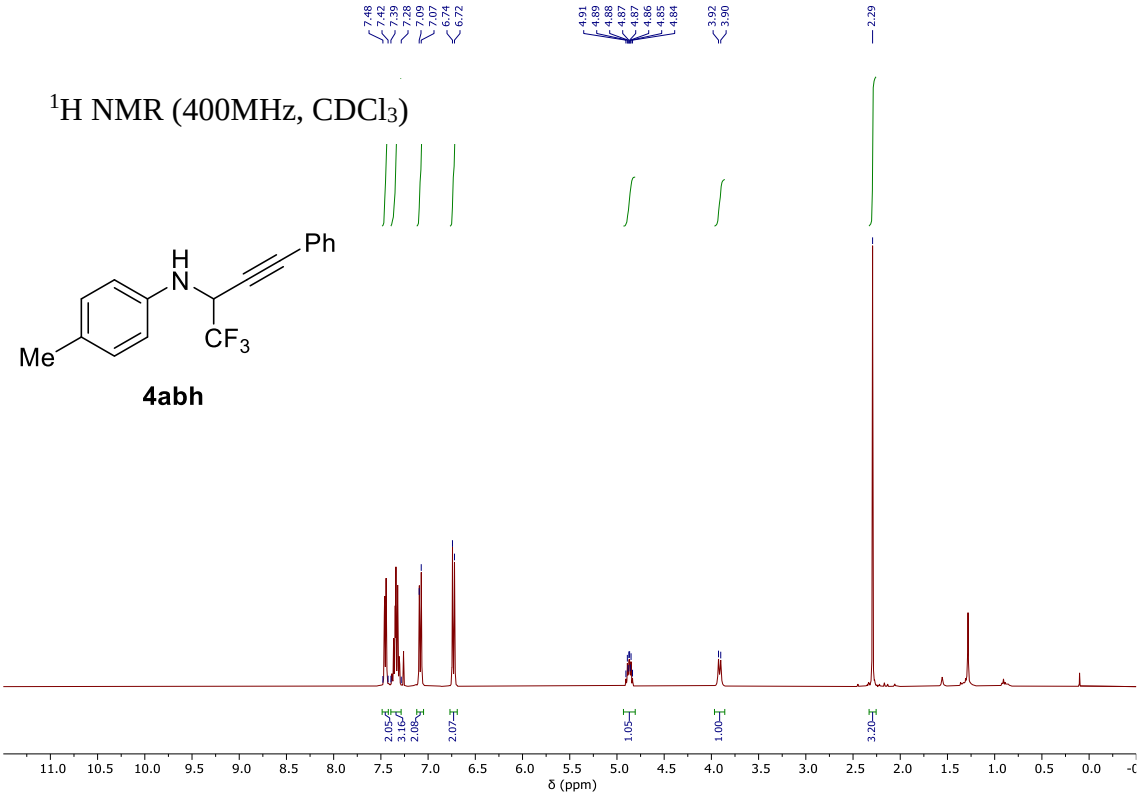
^{13}C NMR (101MHz, $CDCl_3$)



^{19}F NMR (376MHz, $CDCl_3$)

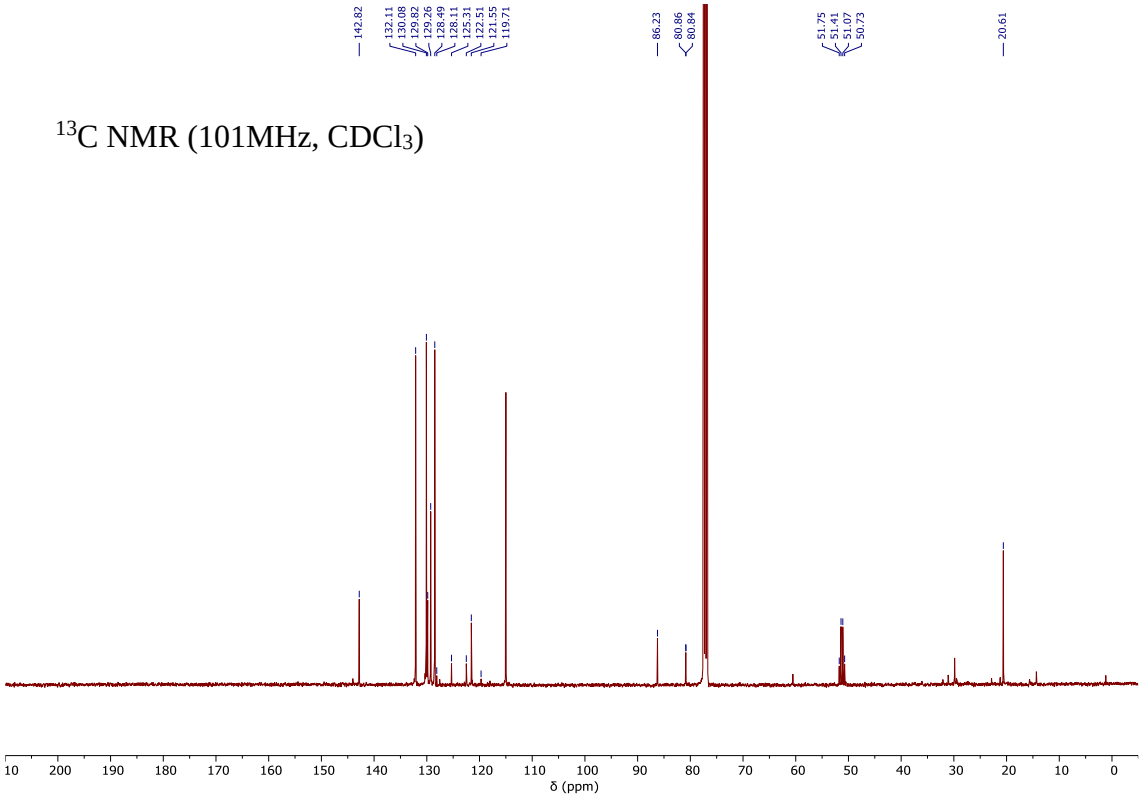


^{1}H NMR (400MHz, $CDCl_3$)

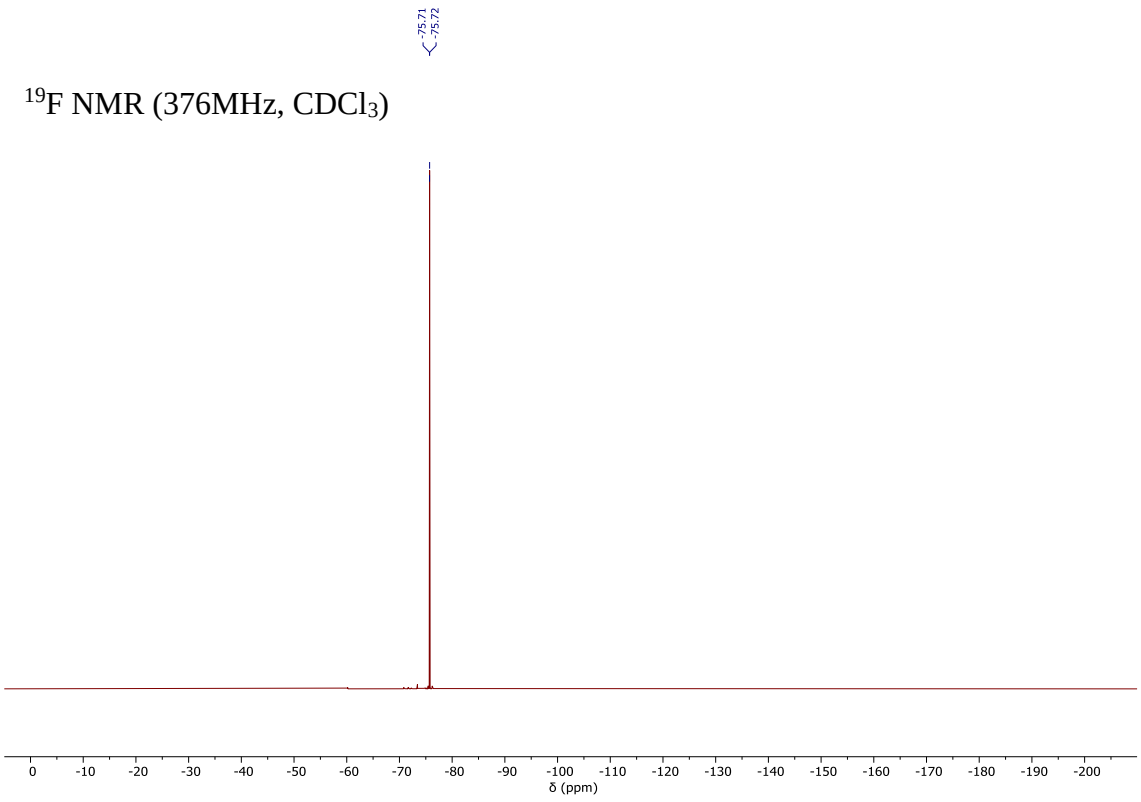


4abh

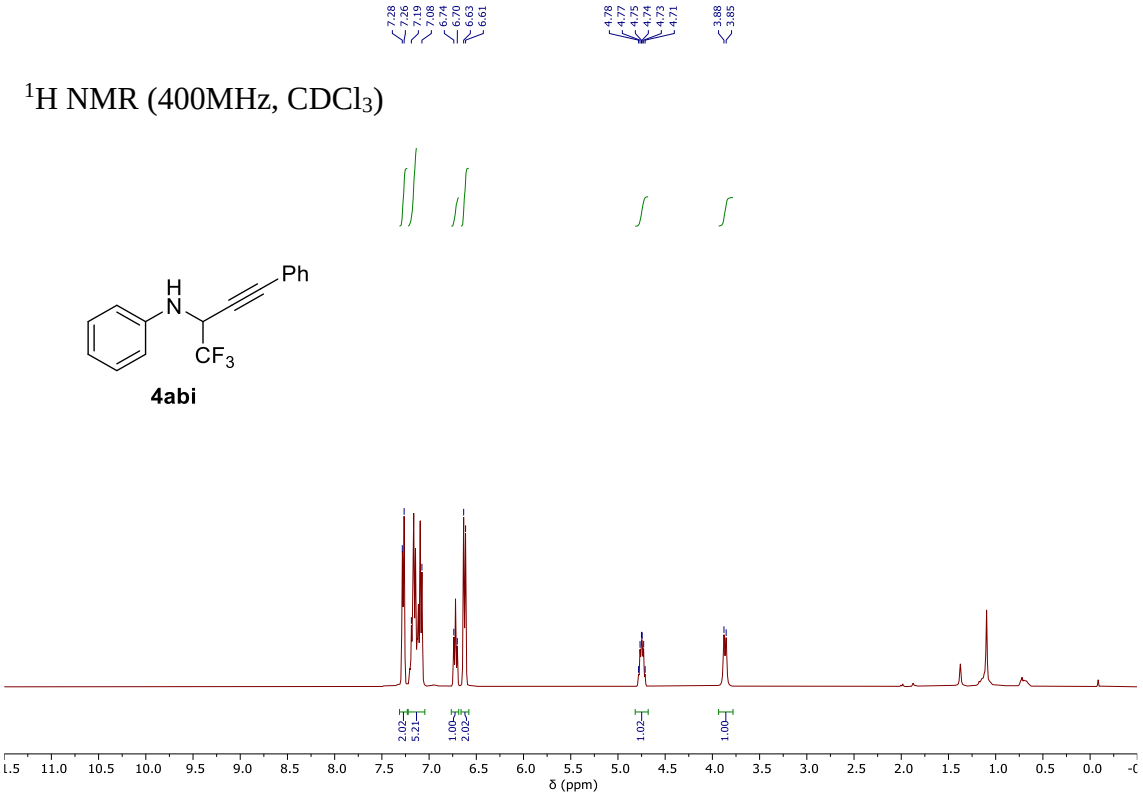
^{13}C NMR (101MHz, $CDCl_3$)



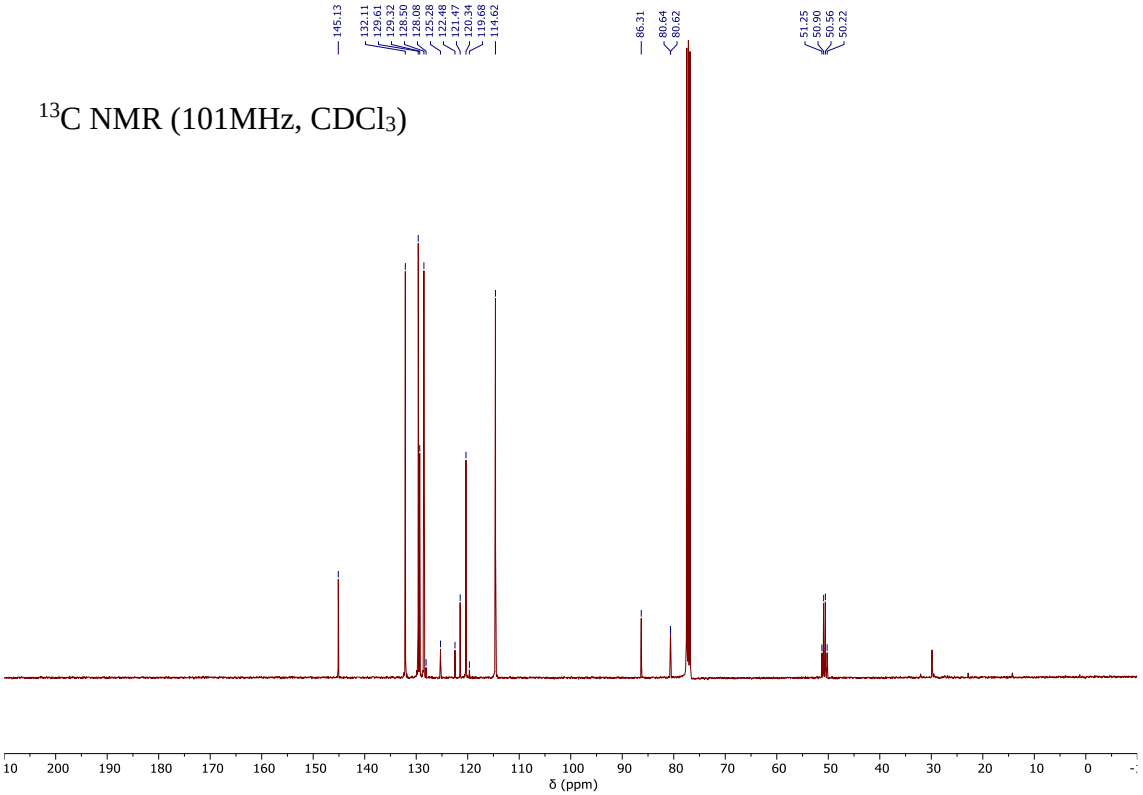
^{19}F NMR (376MHz, $CDCl_3$)



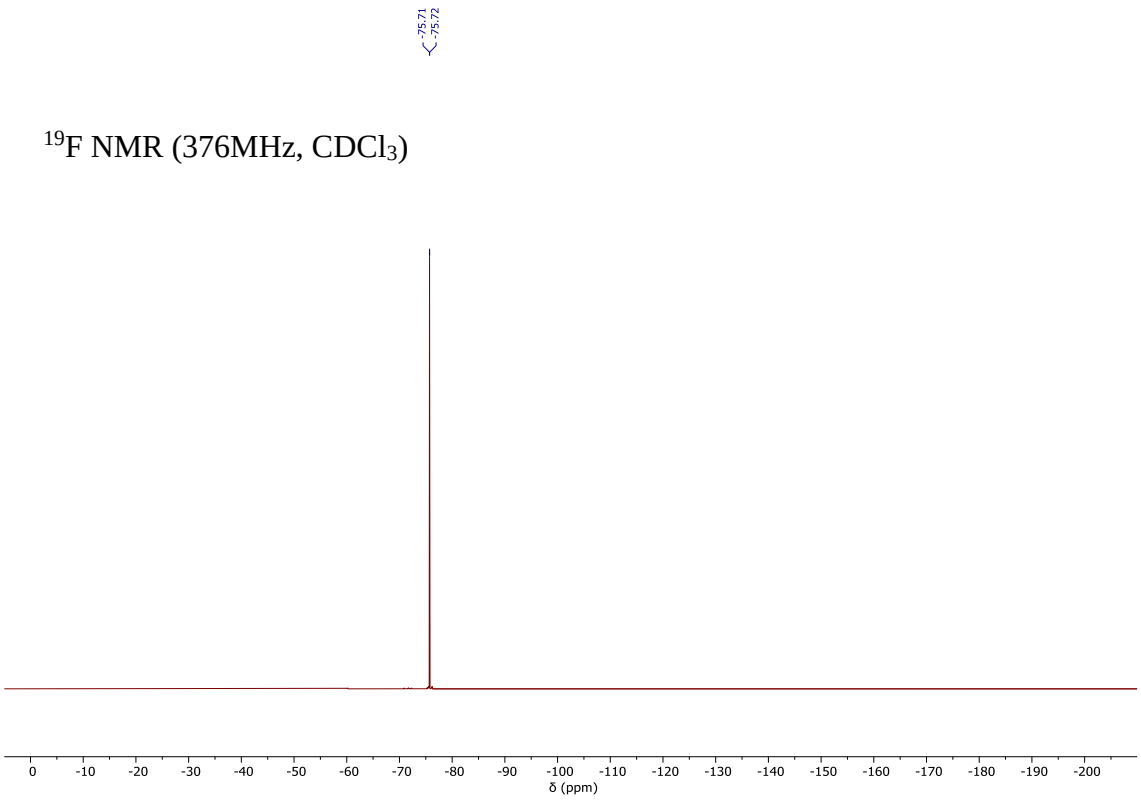
^{1}H NMR (400MHz, $CDCl_3$)



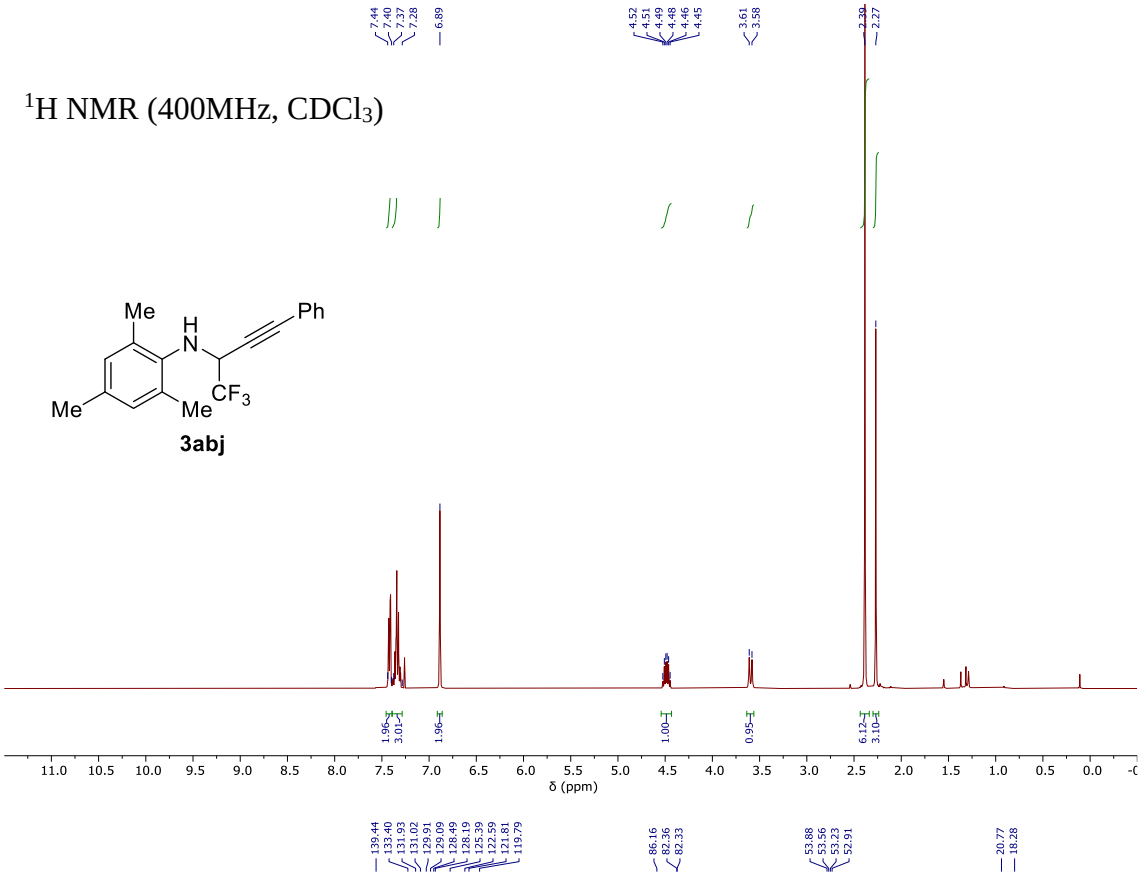
^{13}C NMR (101MHz, $CDCl_3$)



^{19}F NMR (376MHz, $CDCl_3$)

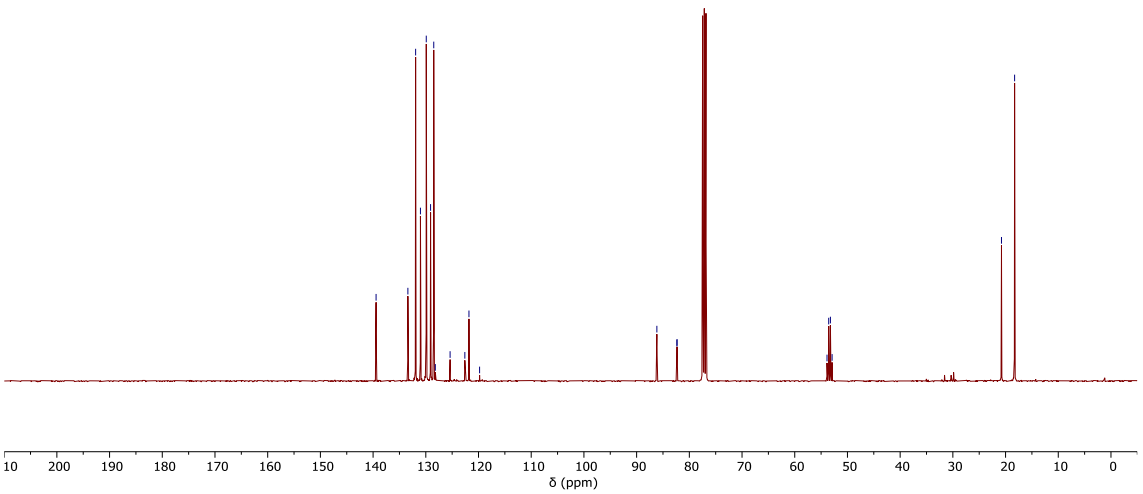


^{1}H NMR (400MHz, $CDCl_3$)

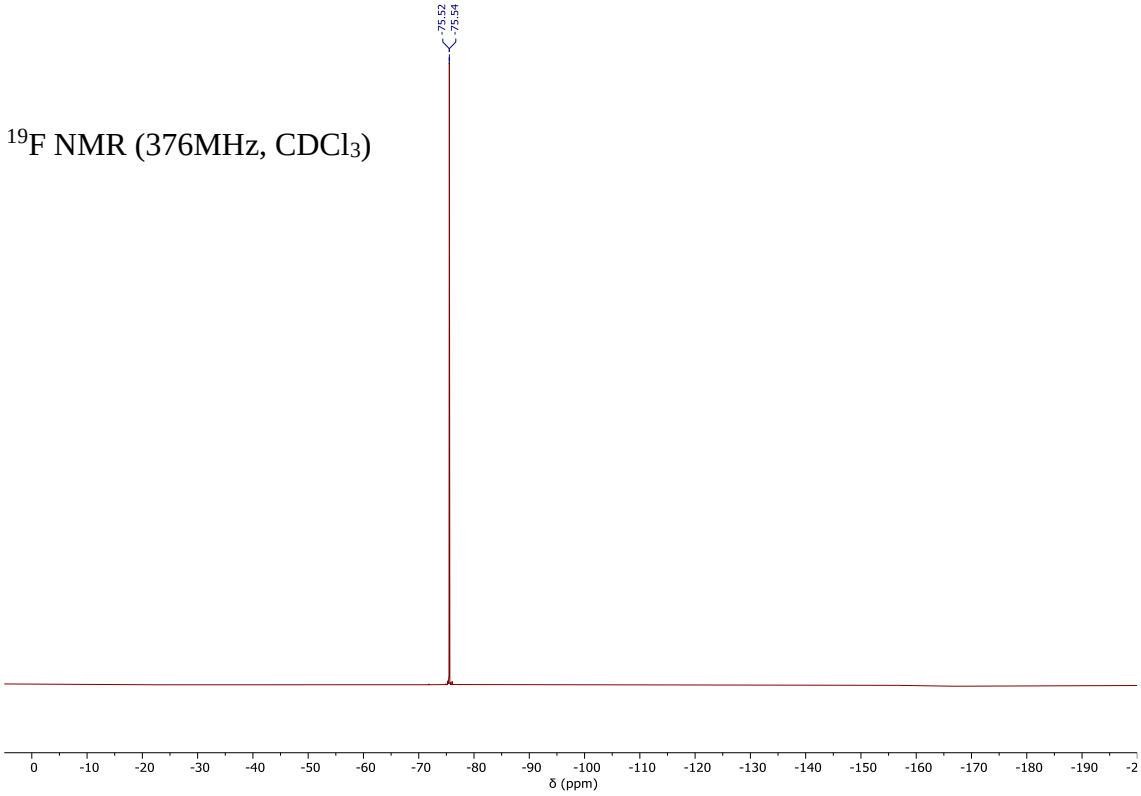


3abj

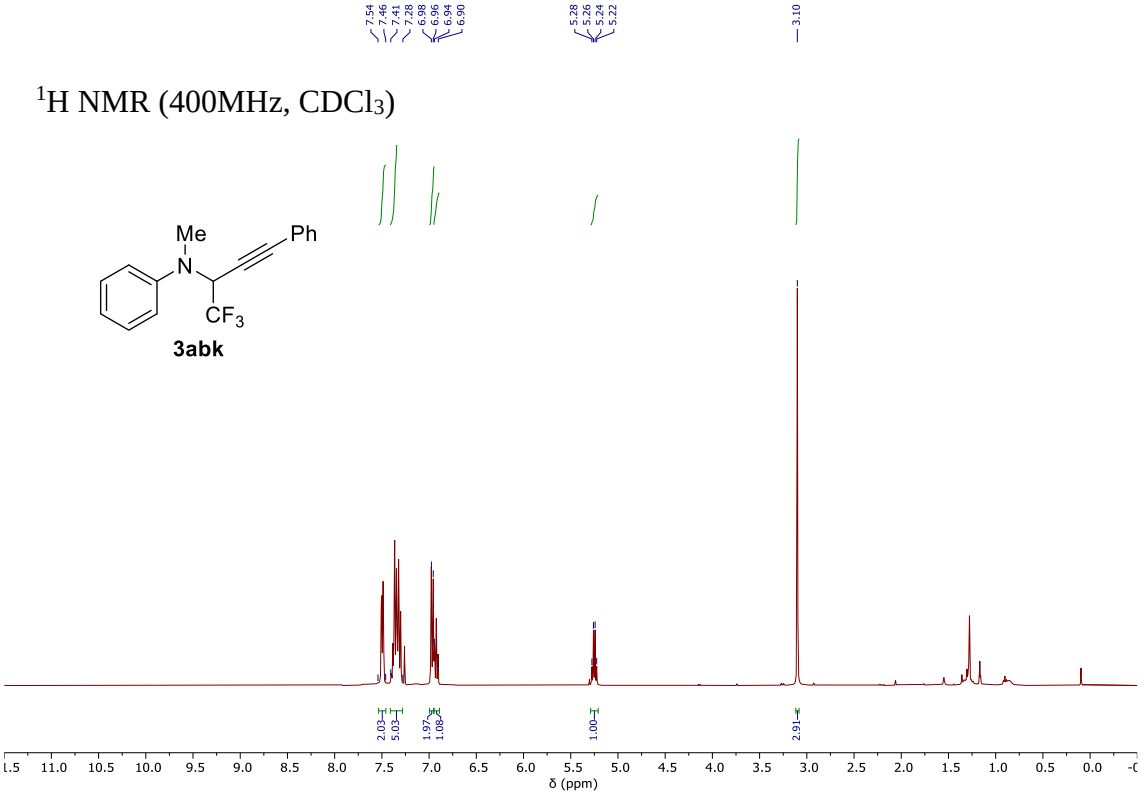
^{13}C NMR (101MHz, $CDCl_3$)



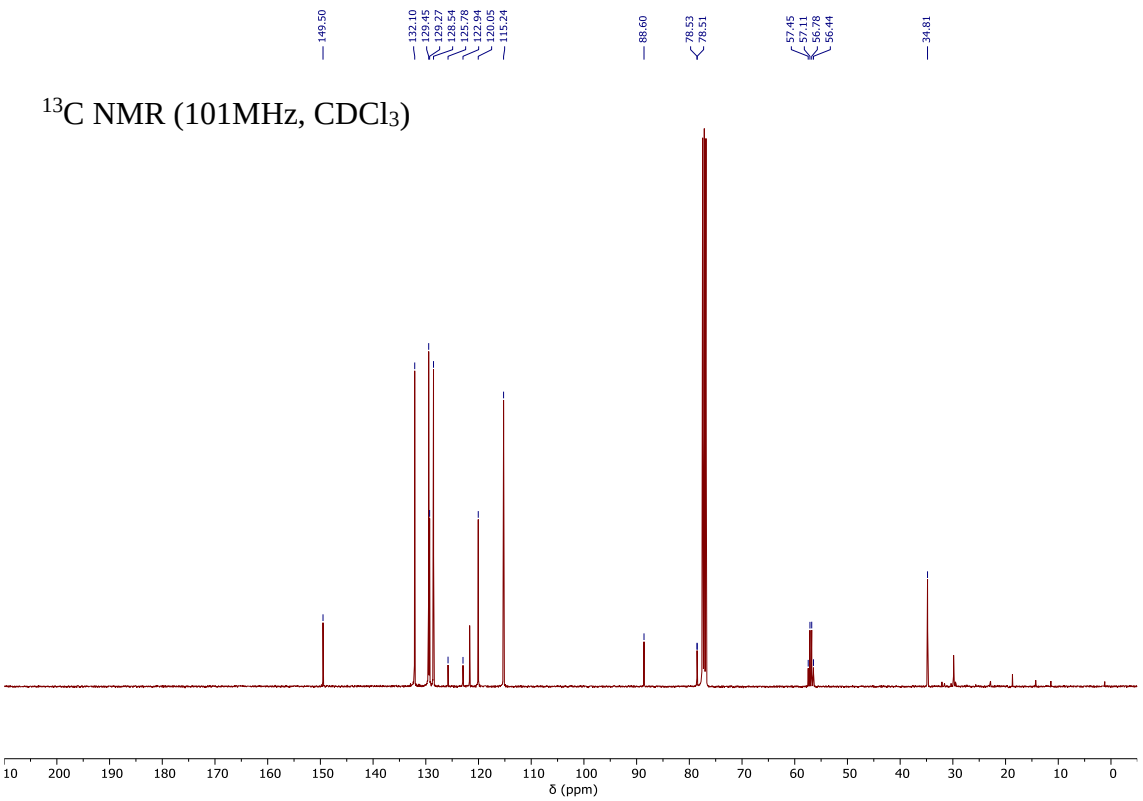
^{19}F NMR (376MHz, $CDCl_3$)



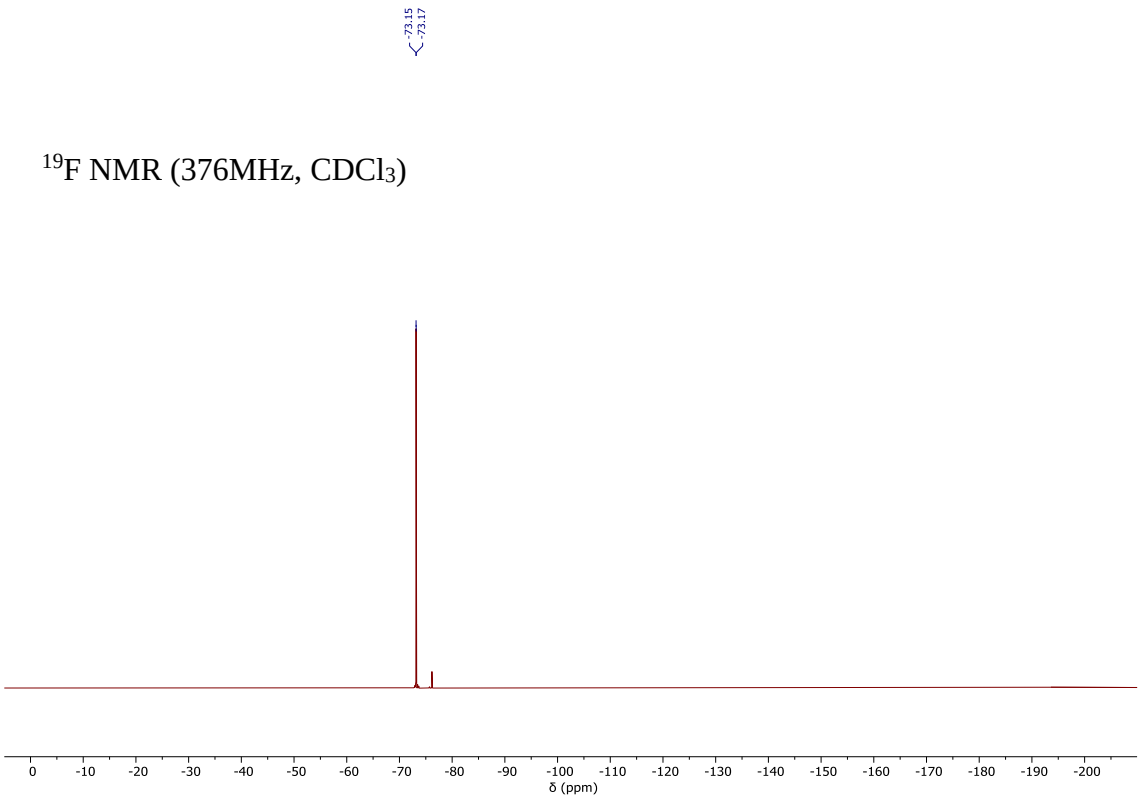
^{1}H NMR (400MHz, $CDCl_3$)



^{13}C NMR (101MHz, $CDCl_3$)

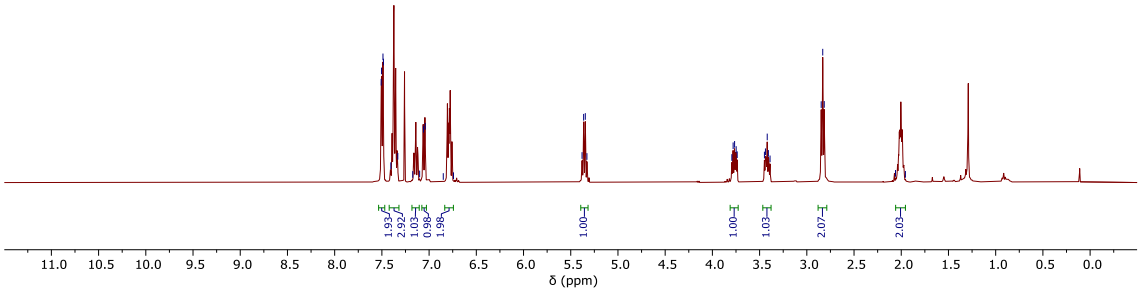


^{19}F NMR (376MHz, $CDCl_3$)

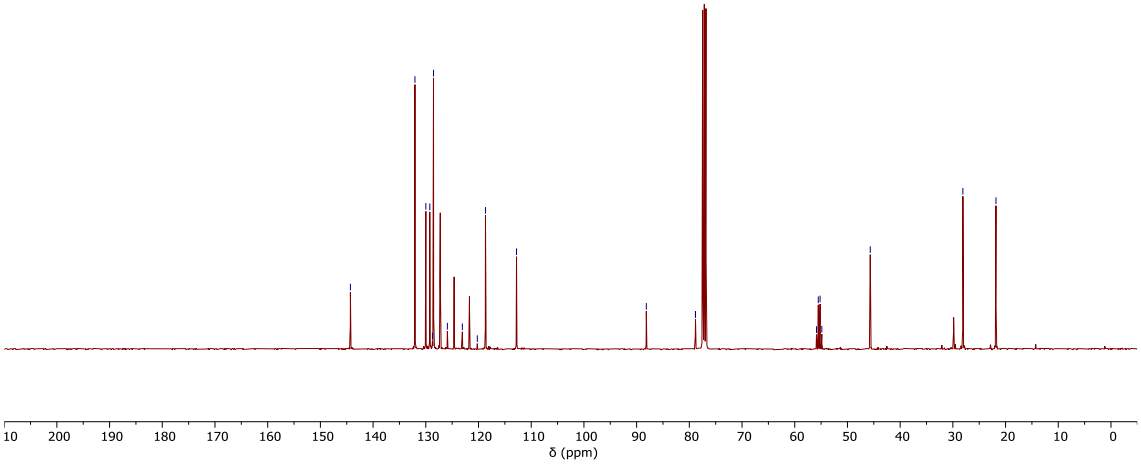


^{1}H NMR (400MHz, $CDCl_3$)

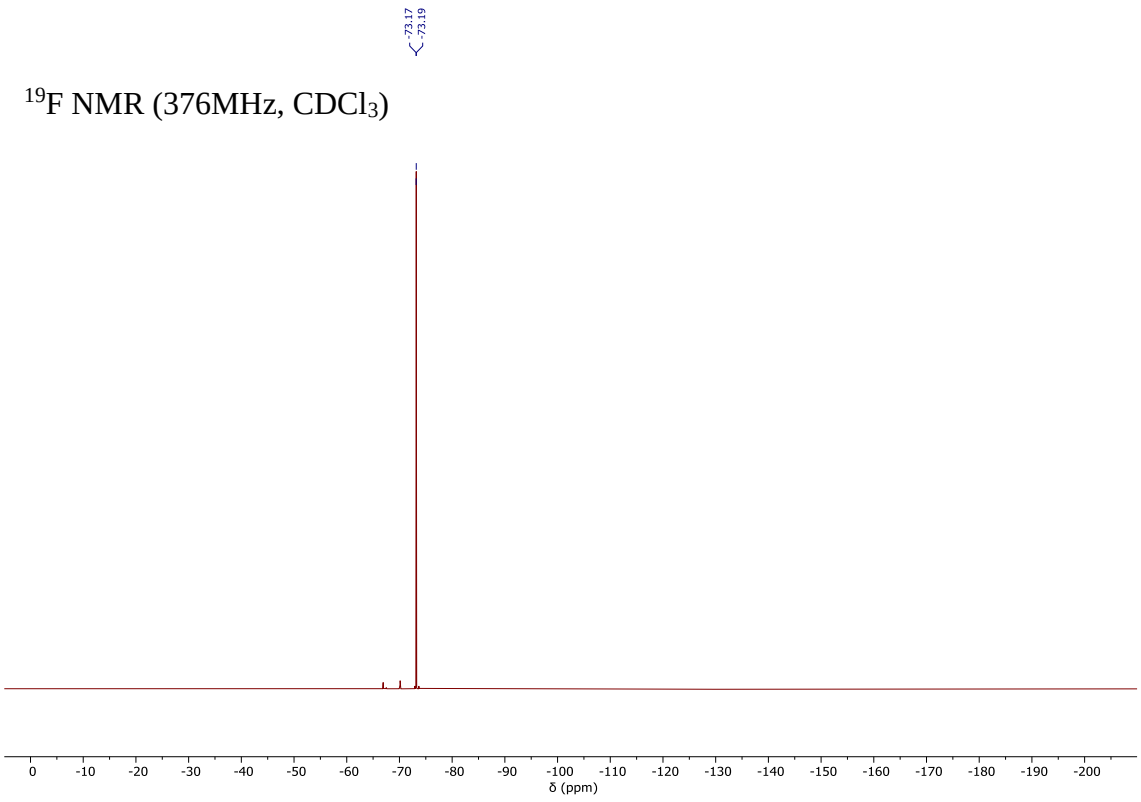
4abl



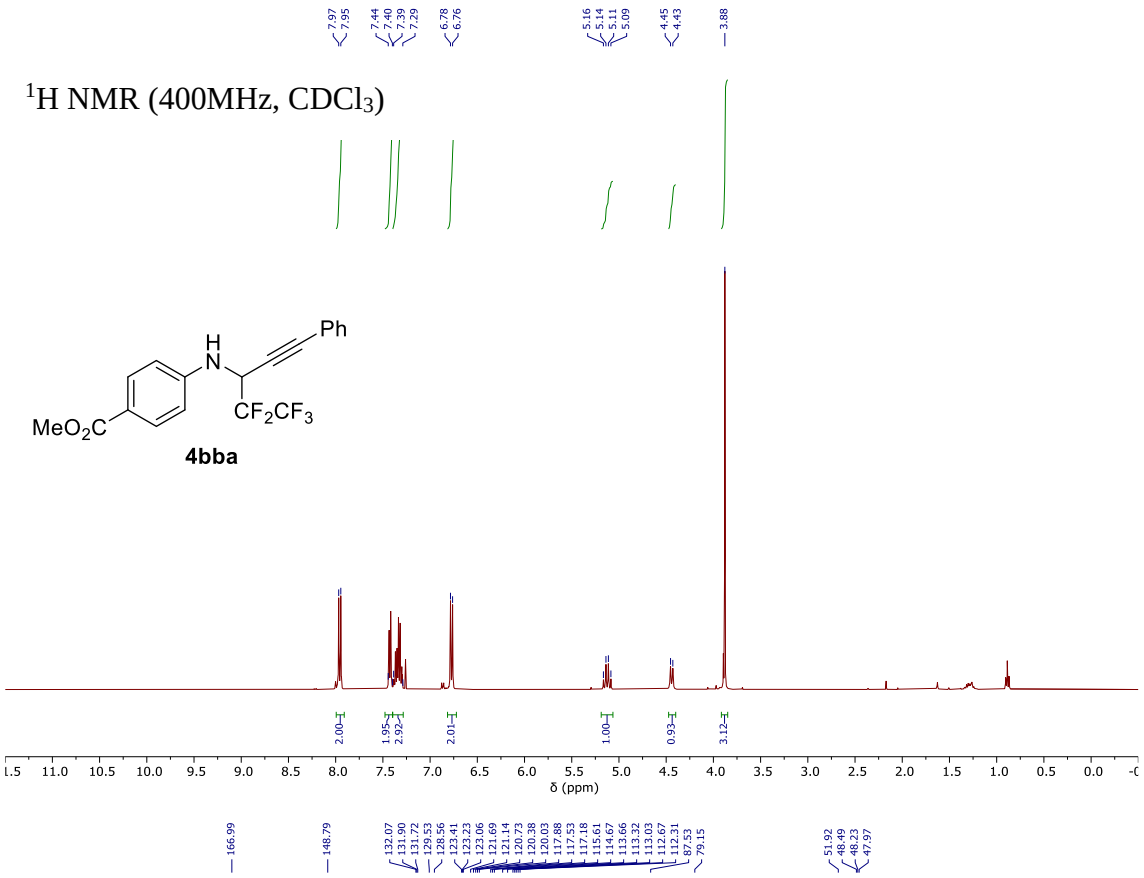
^{13}C NMR (101MHz, $CDCl_3$)



^{19}F NMR (376MHz, $CDCl_3$)

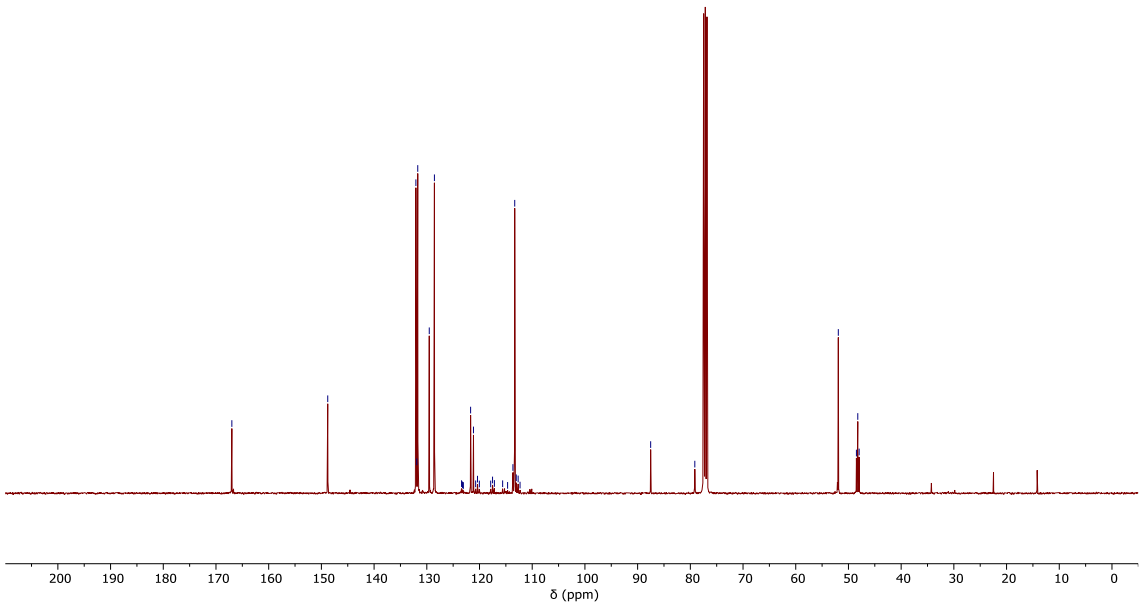


^{1}H NMR (400MHz, $CDCl_3$)

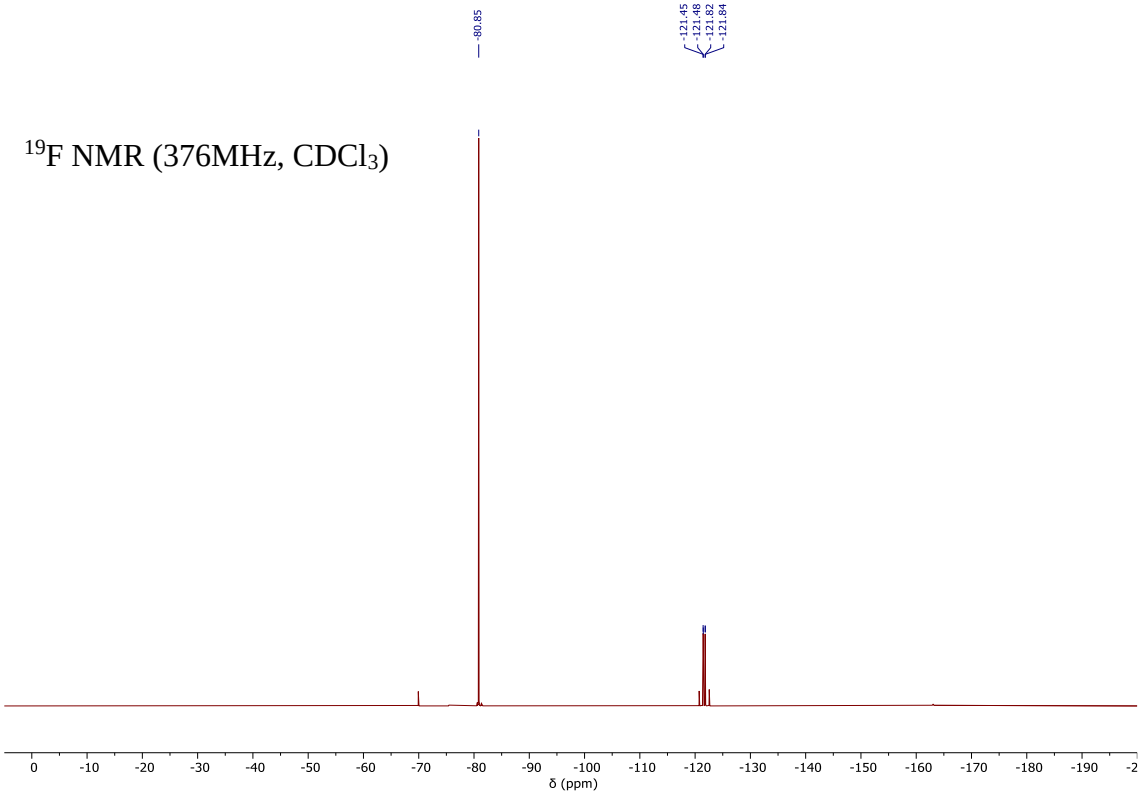


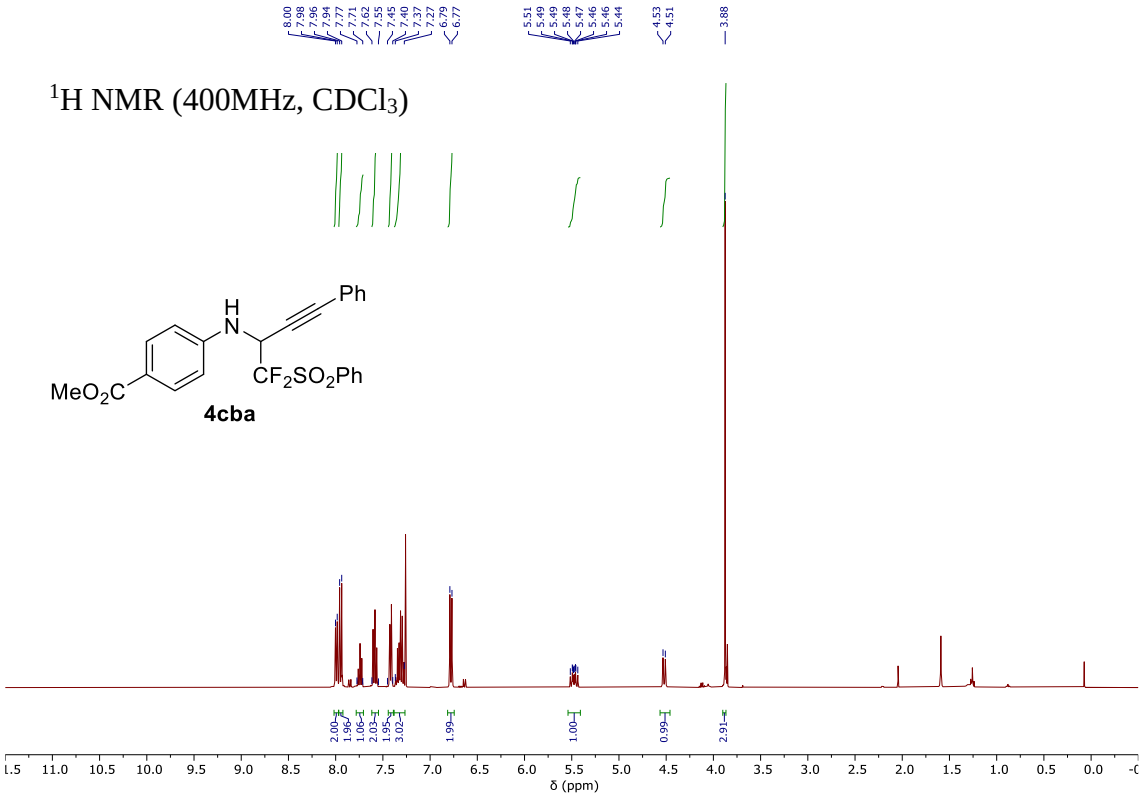
4bba

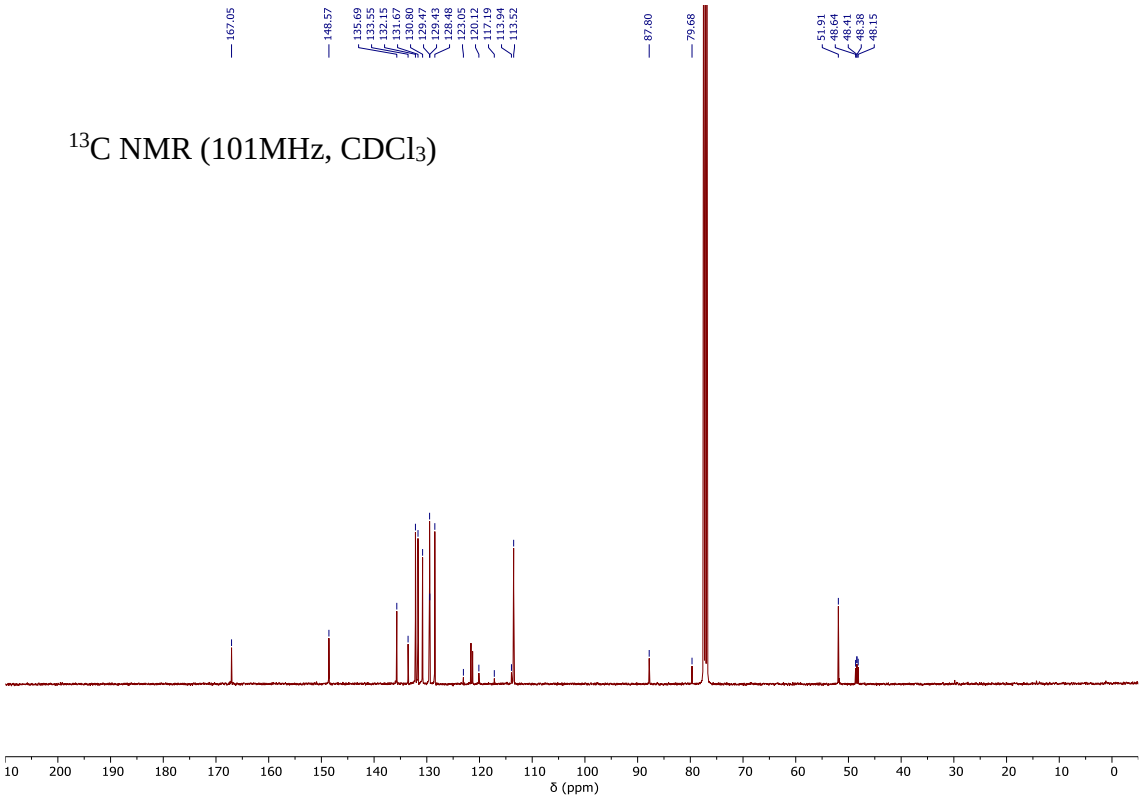
^{13}C NMR (101MHz, $CDCl_3$)

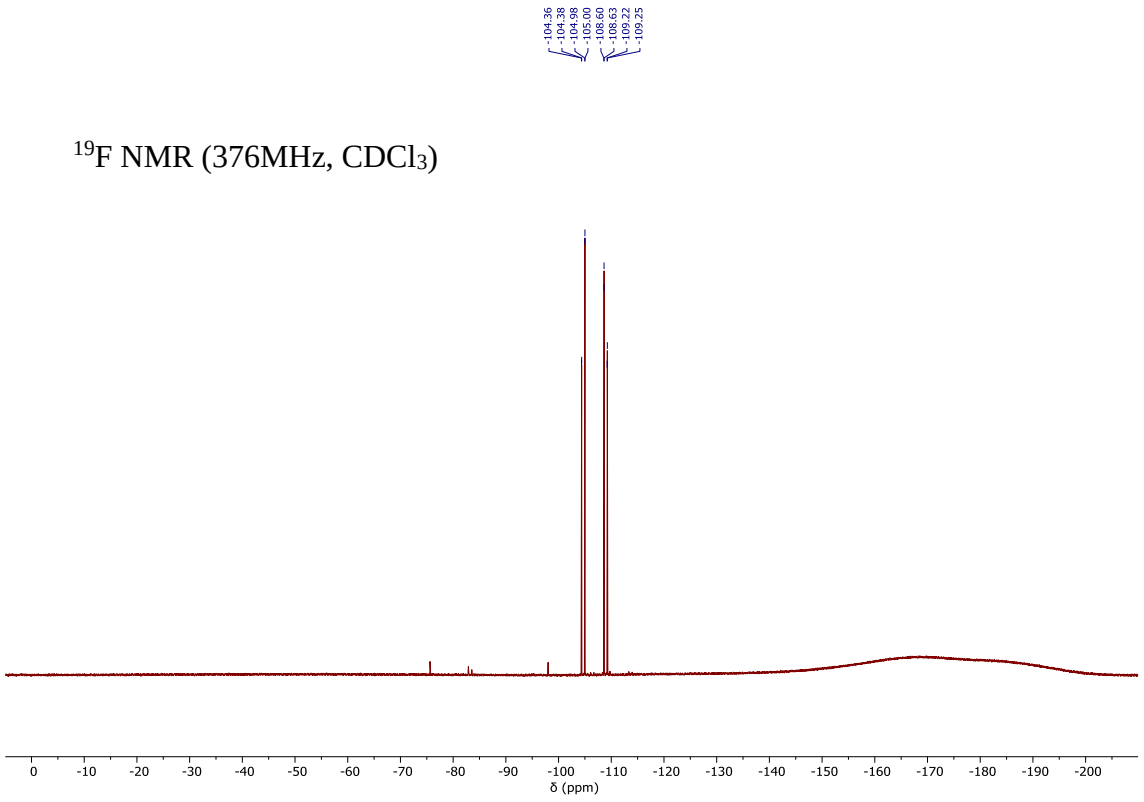


^{19}F NMR (376MHz, $CDCl_3$)

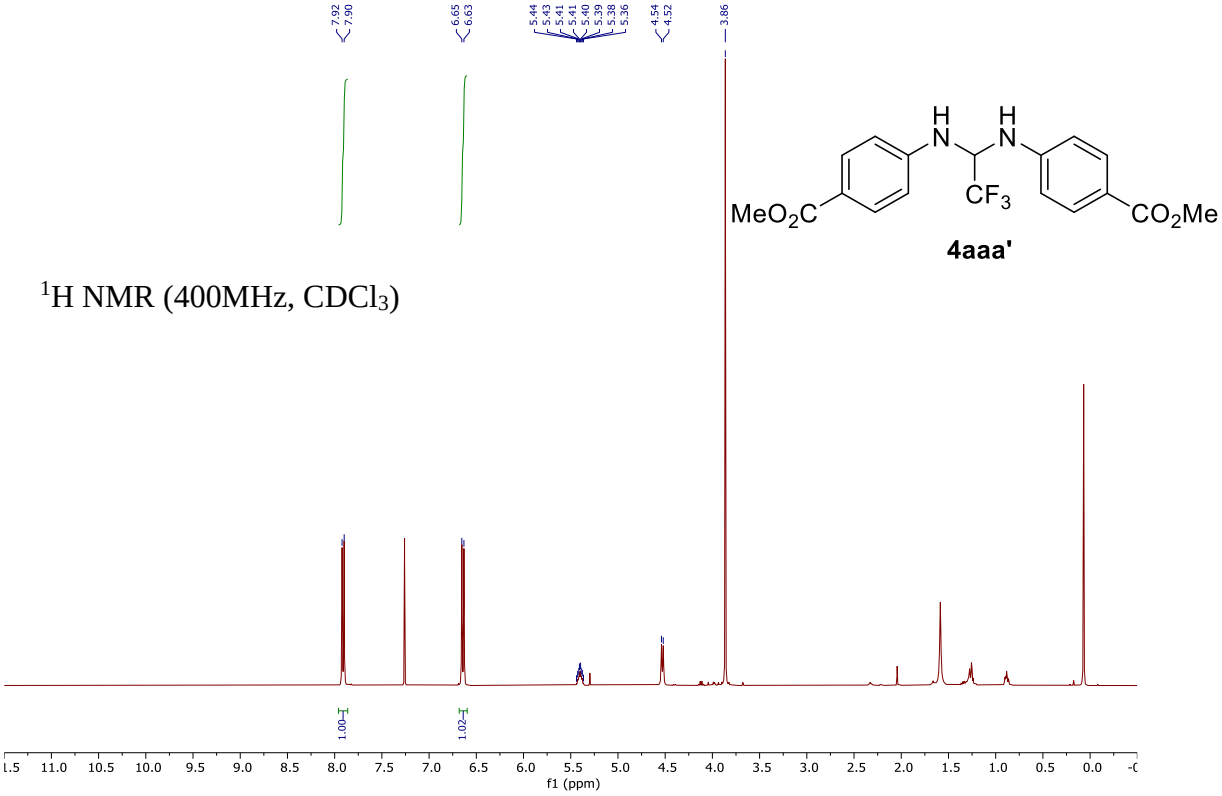



8.00
7.98
7.96
7.94
7.77
7.71
7.62
7.55
7.45
7.40
7.37
7.27
6.79
6.77
5.51
5.49
5.49
5.48
5.47
5.46
5.46
5.44
4.53
4.51
3.88
1H NMR (400MHz, CDCl3)
Ph
H
N
CF2SO2Ph
MeO2C
4cba
2.00
1.96
1.06
2.03
1.95
3.02
1.99
1.00
0.99
2.91
δ (ppm)


167.05
148.57
135.69
133.55
132.15
131.67
130.80
129.47
129.43
128.48
123.05
120.12
117.19
113.94
113.52
87.80
79.68
51.91
48.64
48.41
48.38
48.15
13C NMR (101MHz, CDCl3)
δ (ppm)

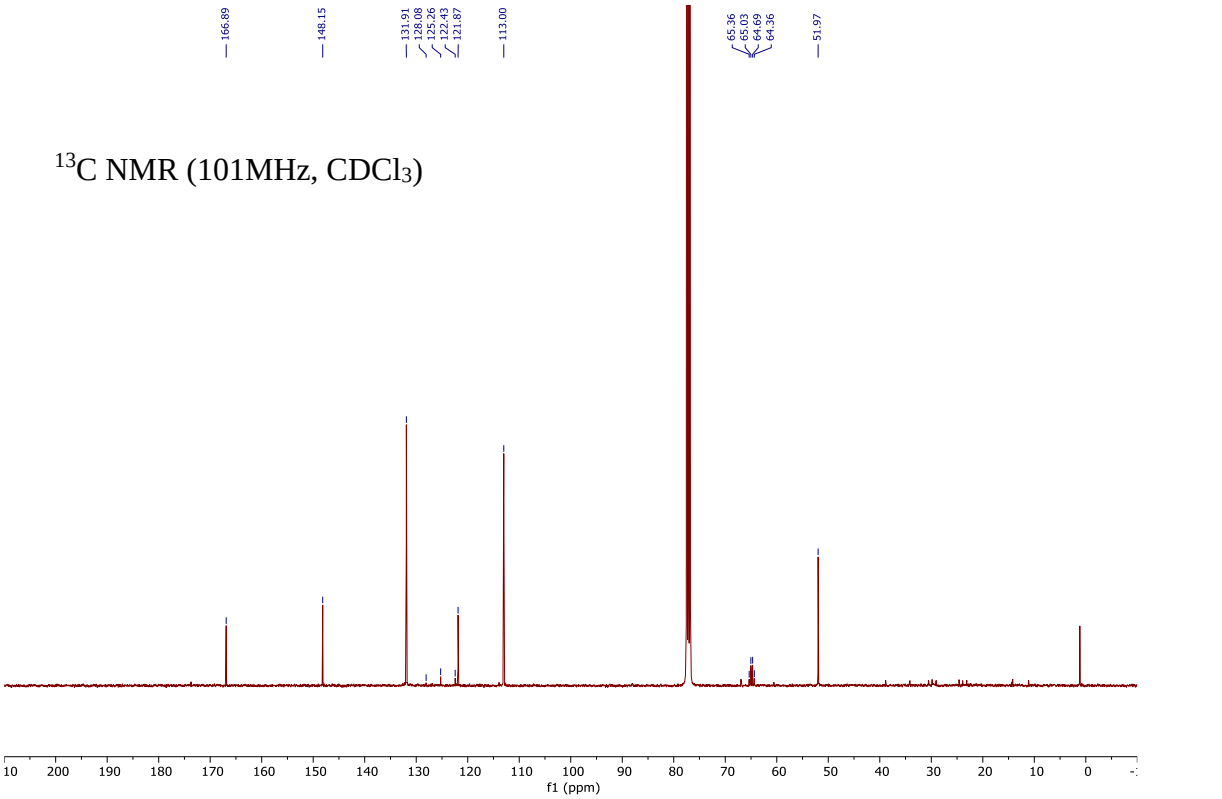


^{19}F NMR (376MHz, $CDCl_3$)



4aaa'

^{1}H NMR (400MHz, $CDCl_3$)



^{13}C NMR (101MHz, $CDCl_3$)

^{19}F NMR (376MHz, $CDCl_3$)