

Palladium-Catalyzed Carboamination of Allylic Alcohols Using a Trifluoroacetaldehyde-Derived Tether

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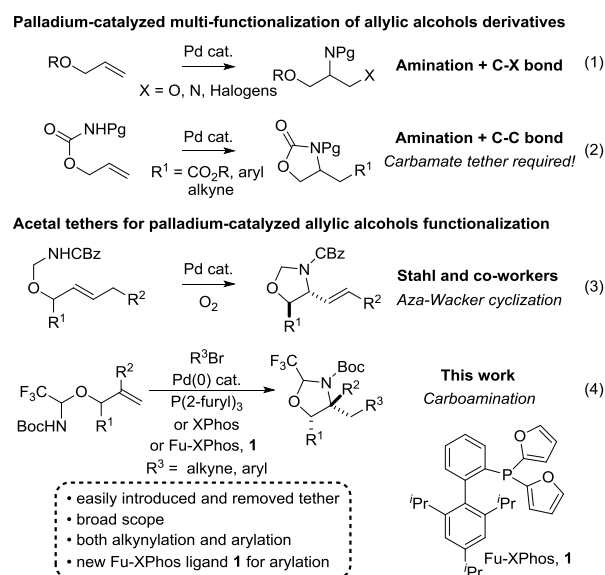
ABSTRACT: The selective palladium-catalyzed carboamination of allylic alcohols is reported based on the use of an easily introduced trifluoroacetaldehyde-derived tether. Aminoalkynylation reactions were realized using alkynyl bromides and commercially available phosphine ligands. For aminoarylations, a new biaryl phosphine ligand, “Fu-XPhos”, was introduced to overcome a competitive Heck pathway. The carboamination products were obtained in high yields and diastereoselectivity. The tether could be easily removed to give value-added amino alcohol building blocks.

Allylic alcohols are broadly available and versatile building blocks in organic synthesis.¹ The inductive or directing effect of the alcohol or its derivatives can be used to achieve selective functionalization of the alkene double bond. In particular, amination reactions have been intensively investigated as they give access to 1,2- and 1,3-aminoalcohols,² which are essential building blocks for the synthesis of bioactive natural and synthetic compounds.³ Palladium catalysis has been especially successful in this respect, leading to synthetically highly useful multi-functionalization reactions such as aminohydroxylation⁴ or diamination⁵ (Scheme 1, eq 1). Reactions allowing the simultaneous formation of a carbon-nitrogen and a carbon-carbon bond have been less investigated, despite their high potential for the synthesis of more complex building blocks. Important breakthroughs have been achieved by the use of carbamates or imidates based tethers on the alcohol (Scheme 1, eq 2).⁶ Nevertheless, the reported scope of these transformations remains narrow and the tethers require often harsh conditions for cleavage. In this respect, the use of hemi-aminal tethers would appear highly attractive for the functionalization of allylic alcohols, as they can be more easily removed. In fact, Hiemstra and co-workers and Stahl and co-workers have pioneered the use of such tethers for Wacker-type oxidative cyclization reactions (Scheme 1, eq 3).⁷ Nevertheless, several separated steps were still needed to install and remove such tethers, and they were never used for more complex transformation involving multiple bond forming events.

Recently, our group introduced (hemi)aminal tethers derived from trifluoroacetaldehyde for the carboamination of allylic amines to give aminoalcohols and diamines.⁸ We wondered if the same strategy could be applied to allylic alcohols. In this case, the lower nucleophilicity of alcohols compared to amines was expected to be a major challenge for the efficiency of tether installation.

Herein, we report the successful implementation of this strategy for the synthesis of aminoalcohols, which are structurally complementary to those obtained from allylic amines. Both amino-alkynylation and amino-arylation reactions were achieved in high yields starting from pre-formed hemiaminal ethers. In situ formation of the tether was also possible with a slightly lower yield. In the case of aminoarylation, a new phosphine ligand (“Fu-XPhos”, **1**) had to be designed to overcome a competitive Heck pathway. The introduced tether could be easily removed under mild acidic conditions to give the free amino alcohols.

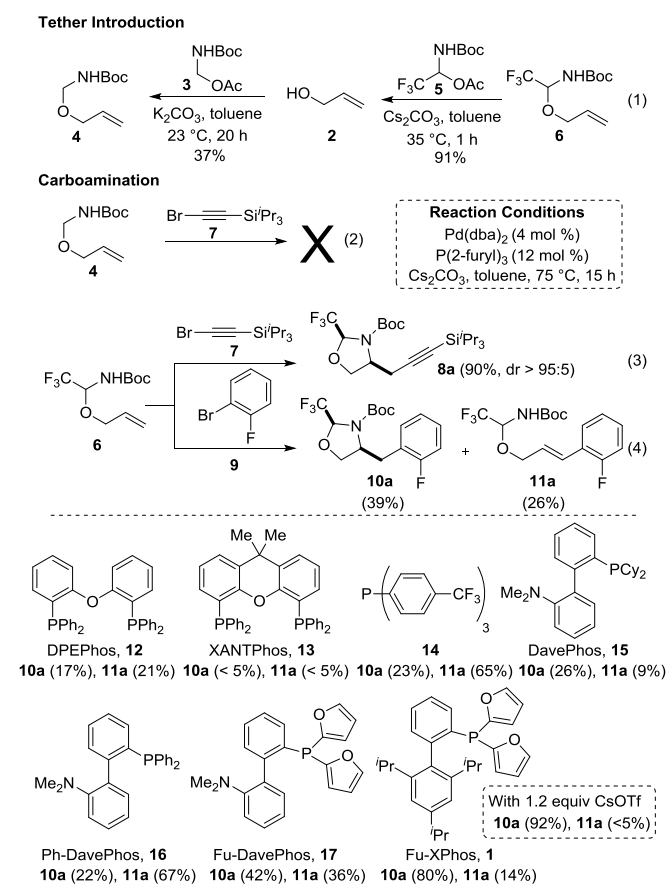
Scheme 1 Palladium-catalyzed functionalization of allylic alcohol derivatives.



To start our studies, we first synthesized hemiaminal ethers **4** and **6** from allylic alcohol **2** using either the reported tether precursor **3** derived from formaldehyde^{7b} or

the trifluoroacetaldehyde derivative **5** used in our previous studies (Scheme 2, eq 1).^{8b} Interestingly, the presence of the trifluoromethyl group allowed a more efficient formation of the hemiaminal ether (91% vs 37%). The conditions developed for allylic amines were then applied to the carboalkynylation of hemiaminal ether **4** with alkynyl bromide **7**, but no product formation could be observed (Scheme 2, eq 2). In contrast, carboamination product **8a** could be obtained in 90% yield as a single diastereoisomer after only minor optimization of the reaction conditions (Scheme 2, eq 3).⁹ However, only a moderate yield of arylation product **10a** could be obtained, due to the competitive formation of Heck product **11a** (Scheme 2, eq 4).

Scheme 2 Preliminary results on tether introduction, carboamination and ligand effect on aminoarylation.

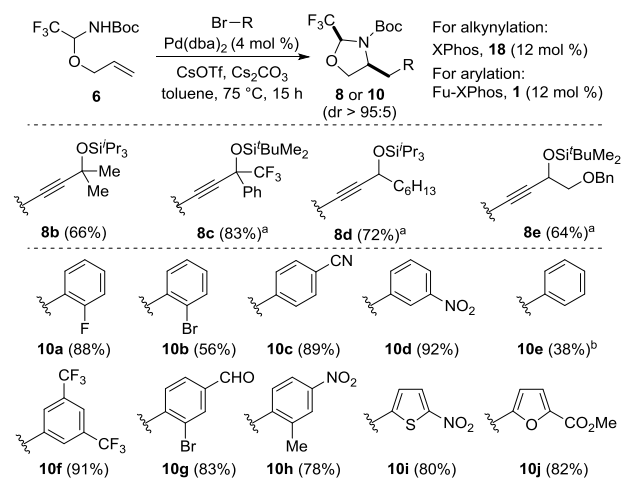


As the yield of arylation product **10a** could not be improved by changing the reaction product conditions, we decided to examine other phosphine ligands. Bidentate phosphine ligands **12** and **13**, which had been successful in our previous work with allyl amines,⁸ gave low yields and selectivity. A good yield was obtained with electron-deficient aryl phosphine **14**, but formation of the Heck product **11a** was favored. We then investigated the use of Buchwald-type biaryl monophosphine ligands.¹⁰ Interestingly, the use of DavePhos **15** led to an increased selectivity for aminoarylation, but with low overall yield. Replacing the cyclohexyl groups by benzene groups (Ph-DavePhos, **16**) restored the reactivity, but formation of the Heck product **11a** became again favored. At this point, we wondered if the

favorable effect of the furyl substituent on the phosphine could be also important for Buchwald-type phosphines. The new Fu-DavePhos ligand **17** could be easily accessed in two steps. The use of **17** indeed led to an increase in selectivity and **10a** could be isolated in 42% yield. The selectivity could be further increased by using the sterically more hindered Fu-XPhos ligand **1**. Finally, the desired product **10a** could be obtained in 92% with less than 5% formation of the Heck product **11a** using cesium triflate as additive.¹¹

The scope of the amino-alkynylation and arylation of hemiaminal ether **6** was then examined (Scheme 3). Propargylic silyl ethers **8b-e** could be obtained in good yields in this transformation with XPhos **18** as ligand. Fu-Xphos **1** was confirmed as the best ligand for arylation. Benzene derivatives **10a-d** bearing electron-withdrawing groups such as fluorine, bromine, cyano or nitro were isolated in high yields. The electron-withdrawing group was required to obtain good yields: Only 38% **10e** could be observed when using phenyl bromide as reagent. In this case, it was not possible to overcome completely the Heck pathway. Furthermore, both multi-substituted benzene rings **10f-h** and heterocycles **10i-j** could be accessed from hemiaminal **6**.

Scheme 3 Scope of the carboamination of hemiaminal ether **6**.



^aObtained as a 1:1 mixture of diastereoisomer at the propargylic center. ^bNMR yield.

Substituted allylic alcohols were then examined in the amino-alkynylation and -arylation reactions (Table 1). When branched hemiaminal ether **19** was used as a 50:50 mixture of diastereoisomers, aminoalcohol derivative **20** was obtained in 73% yield and 67:33 dr (Table 1, entry 1).¹² The synthesis of the corresponding aminoarylation product **21** was also successful (Table 1, entry 2). When symmetrical bisallylic hemiaminal ether **22** was used, amino-alkynylation product **23** was formed in 65% yield as a single diastereoisomer (Table 1, entry 3). The use of α,α -disubstituted olefins was also possible: Both amino-alkynylation and -arylation products **25** and **26** were obtained in good yield and diastereoselectivity (Table 1, entries 4 and 5). Finally, the more complex amino alcohol

derivative **28** could be also accessed in 57% yield, but with lower diastereoselectivity (Table 1, entry 6).

To further increase the efficiency of the carboamination process, we then investigated if the hemiaminal tether could be installed *in situ*. Both the amino-alkynylation and -arylation were indeed successful in the one-pot process and products **8a** and **10f** were obtained in 64% and 62% yield respectively (Scheme 4, eq 1 and 2). Nevertheless, a significant decrease in yield was observed when compared to the use of isolated hemiaminal **6**. Finally, the introduced tether could be removed easily by treatment with trifluoroacetic acid (TFA) followed by methanolysis to give the ammonium salt in quantitative yield (Scheme 4, eq 3).

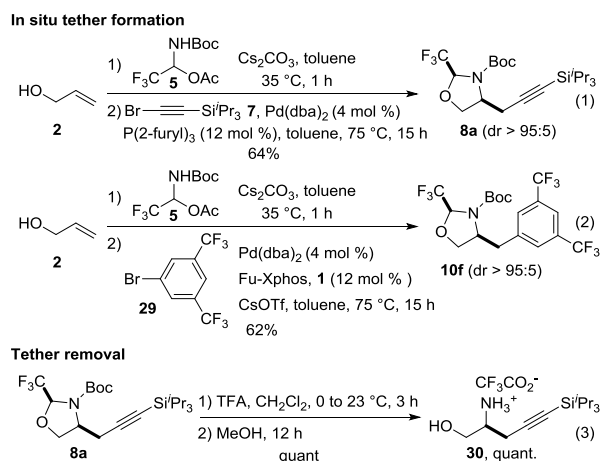
Table 1. Amino -Alkynylation and -Arylation of Substituted Allylic Alcohols.

entry	substrate	RBr	ligand additive	product (yield, dr)
1		7	P(2-furyl) ₃	 20 (73%, dr = 67:33)
2		9	1 CsOTf	 21 (77%, dr = 60:40)
3		7	P(2-furyl) ₃	 23 (65%, dr > 95:5)
4		7	18	 25 (60%, dr = 91:9)
5		9	1 CsOTf	 26 (61%, dr > 95:5)
6		7	18	 28 (57%, dr = 73:27)

In conclusion, we have reported the first carboamination of allylic alcohols based on the use of a trifluoroacetaldehyde tether. Both alkynylation and arylation products could be obtained in good yield and diastereoselectivity, giving amino alcohol derivatives with complementary substitution patterns compared to those obtained from allylic amines. The hemiaminal tethers were easily introduced and could be removed in a single step to give amino alcohols in quantitative yields. These results fur-

ther highlight the versatility of tethers derived from trifluoroacetaldehyde, and set the basis for the development of further highly selective transformations of olefins in future works.

Scheme 4 In situ tether formation and tether removal.



ASSOCIATED CONTENT

Supporting Information

Experimental procedures and analytical data for all new compounds. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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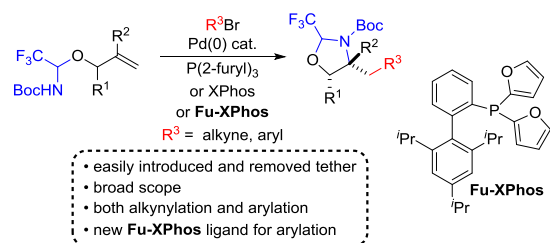
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(9) See the Supporting Information for a full list of tested reaction conditions.

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(12) The relative stereochemistry of the major diastereoisomers of compounds **21**, **23** and **25** could be established by 2D NMR experiments, the structure of the other major diastereoisomers was assigned by analogy. The relative stereochemistry of the minor diastereoisomer of **21** could be assigned as all-*cis*. Only two diastereoisomers were observed in entries 1-3.



Supporting Information

112 pages

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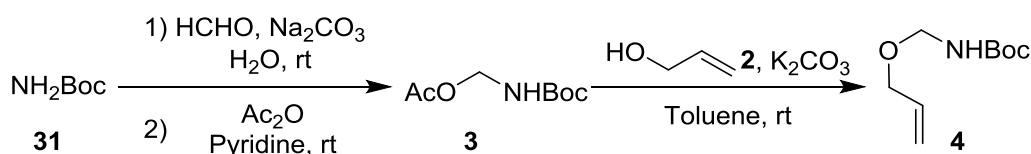
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1) General methods

All reactions were carried out in oven dried glassware under an atmosphere of nitrogen, unless stated otherwise. For quantitative flash chromatography technical grade solvents were used. For flash chromatography for analysis, HPLC grade solvents from Sigma-Aldrich were used. THF, Et₂O, CH₃CN, toluene, hexane and CH₂Cl₂ were dried by passage over activated alumina under nitrogen atmosphere (H₂O content < 10 ppm, Karl-Fischer titration). NEt₃ and pyridine were distilled under nitrogen from KOH. All chemicals were purchased from Acros, Aldrich, Fluka, VWR, Aplichem or Merck and used as such unless stated otherwise. Chromatographic purification was performed as flash chromatography using Macherey-Nagel silica 40-63, 60 Å. TLC was performed on Merck silica gel 60 F254 TLC glass plates and visualized with UV light, permanganate stain, CAN stain or Anisaldehyde stain. Melting points were measured on a calibrated Büchi B-540 melting point apparatus using open glass capillaries. ¹H-NMR spectra were recorded on a Bruker DPX-400 400 MHz spectrometer in chloroform-d, CD₂Cl₂, C₆D₆, DMSO-d₆, CD₃OD; all signals are reported in ppm with the internal chloroform signal at 7.26 ppm, the internal CD₂Cl₂ signal at 5.32 ppm, the internal C₆D₆-signal at 7.16 ppm, the internal DMSO signal at 2.50 ppm or the internal methanol signal at 3.30 ppm as standard. The data is being reported as (s = singlet, d = doublet, t = triplet, q = quadruplet, quint = quintet, m = multiplet or unresolved, bs = broad signal, coupling constant(s) in Hz, integration; interpretation). ¹³C-NMR spectra were recorded with ¹H-decoupling on a Bruker DPX-400 100 MHz spectrometer in chloroform-d, CD₂Cl₂, C₆D₆, DMSO-d₆, CD₃OD; all signals are reported in ppm with the internal chloroform signal at 77.0 ppm, the internal CD₂Cl₂ signal at 54.0 ppm, the internal C₆D₆-signal at 128.4 ppm, the internal DMSO signal at 39.5 ppm or the internal methanol signal at 49.0 ppm as standard.. Infrared spectra were recorded on a JASCO FT-IR B4100 spectrophotometer with an ATR PRO410-S and a ZnSe prisma and are reported as cm⁻¹ (w = weak, m = medium, s = strong, sh = shoulder, br = broad). Gas chromatographic and low resolution mass spectrometric measurements were performed on a Perkin-Elmer Clarus 600 gas chromatographer and mass spectrometer using a Perkin-Elmer Elite fused silica column (length: 30 m, diameter: 0.32 mm) and Helium as carrier gas. High resolution mass spectrometric measurements were performed by the mass spectrometry service of ISIC at the EPFL on a MICROMASS (ESI) Q-TOF Ultima API.

2) Synthesis of the Hemiaminals

Tert-butyl ((allyloxy)methyl)carbamate (**4**)



- 1) Compound **3** was prepared as previously described,¹ to a 100 mL round-bottom flask, *tert*-butyl carbamate (**31**) (2.34 g, 20.0 mmol, 1 equiv.) and formaldehyde (0.84 g, 28 mmol, 1.4 equiv.) were added to a solution of sodium carbonate (1.06 g, 10.0 mmol, 0.5 equiv.), in Water (30 mL). The mixture was heated until complete dissolution was reached (around 65 °C) and was then cooled to room temperature and stirred overnight. The mixture was then extracted with ethyl acetate. The organic extracts were rinsed with brine, dried over anhydrous Na₂SO₄ and concentrated under vacuum to dryness. Considering its potential instability the crude product obtained (1.780 g, 12.07 mmol) was directly engaged in the next step. Acetic anhydride (1.71 mL, 18.1 mmol, 1.5 equiv.) was added dropwise to a solution of *tert*-butyl (hydroxymethyl)carbamate (1.78 g, 12.07 mmol, 1 equiv.) in dry pyridine (23 mL) at 0 °C. The solution was allowed to reach room temperature and then stirred for 18 hours. The mixture was then diluted with ethyl acetate and washed with 1N HCl. The organic layer was rinse with brine, dried over anhydrous Na₂SO₄, concentrated to dryness under vacuum to give the crude product as a colorless oil. The crude residue was purified by column chromatography (Pentane:EtOAc 9:1) affording the acylated compound **3** (600 mg, 3.17 mmol, 32 % yield over two steps) that was also directly engaged in the next step.
- 2) Under nitrogen atmosphere, in a 25 mL round-bottom flask was added K₂CO₃ (877 mg, 6.34 mmol, 2 equiv.) to a stirred solution of allyl alcohol (**2**) (431 μL, 6.34 mmol, 2 equiv.) in Toluene (6.3 mL). Then ((*tert*-butoxycarbonyl)amino)methyl acetate (**3**) (600 mg, 3.17 mmol, 1 equiv.) was added and the resulting suspension was stirred for 20 h. The reaction mixture was then filtered through a plug of silica and eluted with ethyl acetate. The filtrate was then evaporated under reduced pressure to give the crude product as a colorless oil. The crude residue was purified by column chromatography (SiO₂, Pentane:EtOAc 4:1) affording the title compound **4** (217 mg, 1.16 mmol, 37 % yield) as a colorless oil.

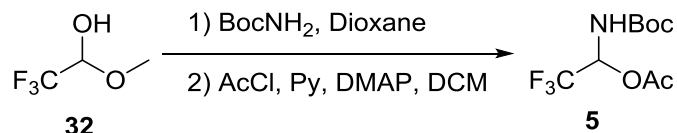
¹H NMR (400 MHz, Chloroform-*d*) δ 5.98 – 5.84 (m, 1H, CH=CH₂), 5.29 (dq, *J* = 17.3, 1.7 Hz, 1H, CH=CH₂), 5.26 (s, 1H, NH), 5.18 (dt, *J* = 10.4, 1.5 Hz, 1H, CH=CH₂), 4.65 (d, *J* = 7.0 Hz, 2H, OCH₂N), 4.03 (d, *J* = 5.3 Hz, 2H, OCH₂CH), 1.46 (s, 9H, Boc).

¹³C NMR (101 MHz, Chloroform-*d*) δ 155.7, 134.6, 117.2, 80.2, 71.6, 69.1, 28.4.

¹ S. Fustero, D. Jiménez, J. Moscardó, S. Catalán, C. Del Pozo, *Org. Lett.*, **2007**, *9* (25), 5283-5286.

The characterization data is corresponding to the reported values.¹

1-((*Tert*-butoxycarbonyl)amino)-2,2,2-trifluoroethyl acetate (**5**)



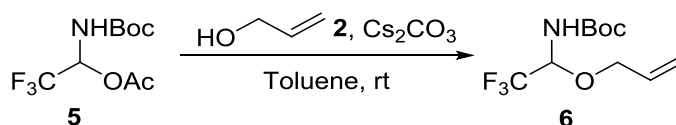
- 1) Following a slightly modified procedure,² a 100 mL pressure tube was charged with *tert*-butyl carbamate (7.03 g, 60.0 mmol), 2,2,2-trifluoro-1-methoxyethanol (**32**) (7.69 mL, 66.0 mmol, 1.1 equiv), 4Å MS (10 g) and dioxane (80 mL). The tube was sealed under nitrogen atmosphere. The resulting mixture was heated at 100 °C for 5 d and then cooled down to rt. The mixture was filtered over Celite and the cake was washed with ether (3x20 mL). The volatiles were removed under reduced pressure and the resulting solid was recrystallized in chloroform to afford white crystals (8.20 g, 38.1 mmol, 64% for 2 crops).
- 2) To a solution of pyridine (1.84 mL, 22.8 mmol, 1.4 equiv) and DMAP (50 mg, 0.41 mmol, 2.5 mol%) in dichloromethane (80 mL) at 0 °C was slowly added acetyl chloride (1.39 mL, 19.5 mmol, 1.2 equiv). To the resulting mixture was added *tert*-butyl (2,2,2-trifluoro-1-hydroxyethyl)carbamate (3.50 g, 16.3 mmol) portion-wise. Then the mixture was stirred at 0 °C for 20 min and quenched with water (10 mL). The pH was adjusted to 2 by addition of 0.1 N HCl and the layers were separated. The organic layer was washed with 0.1 N HCl (3x20 mL) and brine (30 mL), dried over MgSO₄, filtered and concentrated under reduced pressure. The crude residue was purified by column chromatography (Pentane:EtOAc 10:1) affording the title compound **5** (4.05 g, 15.8 mmol, 97 % yield) as a white solid.

¹H NMR (400 MHz, Chloroform-*d*) δ 6.66 (bs, 1H, *CHCF*₃), 5.25 (bs, 1H, *NH*), 2.08 (s, 3H, *COCH*₃), 1.41 (s, 9H, *C(CH*₃)₃).

¹³C NMR (101 MHz, Chloroform-*d*) δ 168.0, 152.9, 123.1 (q, *J* = 281.3), 82.2, 72.0 (q, *J* = 39.1 Hz), 28.1, 20.5.

The characterization data is corresponding to the reported values.²

Tert-butyl (1-(allyloxy)-2,2,2-trifluoroethyl)carbamate (**6**)



² U. Orcel, J. Waser, *Angew. Chem. Int. Ed.* **2016**, *55*, 12881.

To a stirred solution of prop-2-en-1-ol (**2**) (240 μ L, 3.54 mmol, 1.3 equiv.) in toluene (5.4 mL) at room temperature was added Cs₂CO₃ (1.33 g, 4.08 mmol, 1.5 equiv.). Then 1-((*tert*-butoxycarbonyl)amino)-2,2,2-trifluoroethyl acetate (**5**) (0.70 g, 2.7 mmol, 1 equiv.) was added and the resulting mixture was stirred for 3h. After completion of the reaction according to TLC (Pentane:DCM 2:3), the reaction mixture was filtered through a plug of silica and eluted with ethyl acetate. The filtrate was then evaporated under reduced pressure to give the title compound **6** (1.26 g, 4.95 mmol, 91% yield) as a yellow oil.

R_f = 0.4 (Pentane:DCM 2:3).

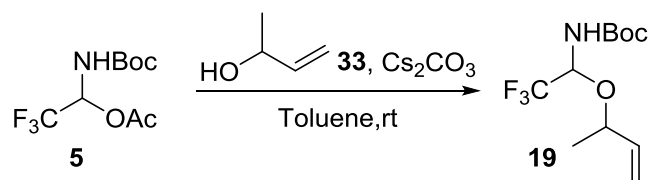
¹H NMR (400 MHz, Chloroform-*d*) δ 5.90 (dddd, J = 16.9, 10.4, 6.3, 5.3 Hz, 1H, CH=CH₂), 5.35 (m, CHCF₃ and CH=CH₂), 5.27 (d, J = 10.3 Hz, 1H, CH=CH₂), 5.14 (d, J = 10.7 Hz, 1H, NH), 4.22 (dd, J = 12.6, 5.0 Hz, 1H, OCH₂), 4.10 (dd, J = 12.7, 6.2 Hz, 1H, OCH₂), 1.47 (s, 9H, Boc).

¹³C NMR (101 MHz, Chloroform-*d*) δ 154.7, 132.8, 122.7 (q, J = 281.6 Hz), 119.0, 81.5, 78.5 – 77.4 (m), 69.9, 28.6.

IR ν_{\max} 3449 (w), 3448 (w), 3327 (w), 3326 (w), 3325 (w), 2983 (w), 2934 (w), 2890 (w), 2886 (w), 2885 (w), 2362 (w), 2361 (w), 2336 (w), 1711 (m), 1514 (m), 1465 (w), 1398 (w), 1368 (w), 1348 (w), 1276 (w), 1250 (m), 1184 (s), 1153 (s), 1087 (m), 1086 (m), 1054 (m), 1022 (w), 933 (w), 887 (w), 850 (w).

HRMS (ESI) calcd for C₁₀H₁₆F₃NNaO₃⁺ [M+Na]⁺ 278.0974; found 278.0970.

Tert-butyl (1-(but-3-en-2-yloxy)-2,2,2-trifluoroethyl)carbamate (**19**)



To a stirred solution of but-3-en-2-ol (**33**) (153 μ L, 1.76 mmol, 1.0 equiv.) in toluene (4.4 mL) at room temperature was added Cs₂CO₃ (691 mg, 2.12 mmol, 1.2 equiv.). Then 1-((*tert*-butoxycarbonyl)amino)-2,2,2-trifluoroethyl acetate (**5**) (500 mg, 1.94 mmol, 1.1 equiv.) was added and the resulting mixture was stirred overnight. The reaction mixture was then filtered through a plug of silica eluted with ethyl acetate, the volatiles were then removed under reduced pressure and the residue was purified by column chromatography (SiO₂, Pentane:DCM 2:3) to afford the title compound **19** (195 mg, 0.720 mmol, 41 % yield) as a colorless oil.

R_f 0.45 (Pentane:DCM 2:3).

¹H NMR (400 MHz, Acetonitrile-*d*₃), 1:1 mixture of diastereoisomers A and B : δ 6.20 (bs, 2H, CHCF₃ A and B), 5.82 (ddd, J = 17.2, 10.5, 6.5 Hz, 1H, CHCH₂ A), 5.72 (ddd, J = 17.0, 10.4, 7.7 Hz, 1H, CHCH₂ B), 5.41 (dq, J = 10.7, 5.4 Hz, 1H, CHCH₂ A), 5.36 – 5.30 (m, 1H, CHCH₂ B), 5.30 – 5.17 (m, 3H, CHCH₂ A, NH A and B), 5.09 (d, J = 10.5 Hz, 1H, CHCH₂

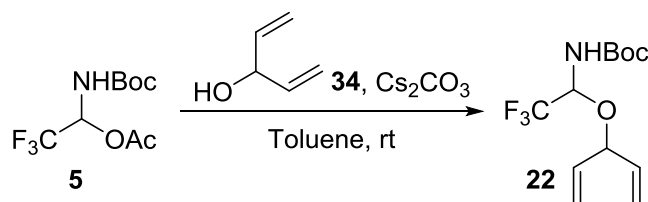
B), 4.21 (p, $J = 6.5$ Hz, 1H, CH₃CHO A), 4.12 (p, $J = 6.8$ Hz, 1H, CH₃CHO B), 1.44 (s, 9H, Boc A), 1.42 (s, 9H, Boc B), 1.25 (d, $J = 3.2$ Hz, 3H, Me A), 1.23 (d, $J = 3.2$ Hz, 3H, Me B).

¹³C NMR (101 MHz, Acetonitrile-*d*₃) δ 155.9, 155.6, 140.3, 138.7, 123.8 (q, $J = 281.9$, 281.5 Hz), 123.7 (q, $J = 280.5$ Hz), 118.9, 115.9, 81.2, 81.1, 78.5 (q, $J = 35.1$ Hz), 77.5, 77.4 – 76.4 (m), 75.6, 28.3, 28.3, 21.5, 20.7.

IR ν_{\max} 3452 (w), 3334 (w), 3085 (w), 2983 (w), 2937 (w), 1714 (s), 1504 (m), 1458 (w), 1397 (w), 1370 (m), 1346 (m), 1280 (m), 1249 (m), 1184 (s), 1152 (s), 1084 (m), 1051 (s), 1025 (m), 993 (w), 923 (m), 889 (m), 853 (w).

HRMS (ESI) calcd for C₁₁H₁₈F₃NNaO₃⁺ [M+Na]⁺ 292.1131; found 292.1133.

***Tert*-butyl (2,2,2-trifluoro-1-(penta-1,4-dien-3-yloxy)ethyl)carbamate (22)**



To a stirred solution of penta-1,4-dien-3-ol (**34**) (0.23 mL, 2.4 mmol, 1 equiv.) in toluene (6 mL) at rt was added Cs₂CO₃ (930 mg, 2.85 mmol, 1.2 equiv.). Then 1-((*tert*-butoxycarbonyl)amino)-2,2,2-trifluoroethyl acetate (**5**) (673 mg, 2.62 mmol, 1.1 equiv.) was added and the resulting mixture was stirred overnight. The reaction mixture was then filtered through a plug of silica eluted with ethyl acetate, the volatiles were then removed under reduced pressure and the residue was purified by column chromatography (SiO₂, Pentane:DCM 1:1) to afford the title compound **22** (340 mg, 1.21 mmol, 51 % yield) as a colorless oil.

R_f 0.45 (Pentane:DCM 1:1).

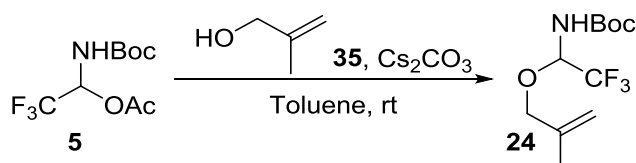
¹H NMR (400 MHz, Chloroform-*d*) δ 5.84 (ddd, $J = 17.3$, 10.5, 5.9 Hz, 1H, CH=CH₂), 5.73 (ddd, $J = 17.5$, 10.2, 7.4 Hz, 1H, CH=CH₂), 5.47 – 5.32 (m, 3H, CHCF₃ and CH=CH₂), 5.28 (dt, $J = 17.3$, 1.4 Hz, 1H, CH=CH₂), 5.20 (dt, $J = 10.5$, 1.3 Hz, 1H, CH=CH₂), 5.14 (d, $J = 10.7$ Hz, 1H, NH), 4.50 (dd, $J = 7.6$, 5.8 Hz, 1H, OCHC_{sp2}), 1.47 (s, 9H, Boc).

¹³C NMR (101 MHz, Chloroform-*d*) δ 154.5, 136.5, 135.2, 122.5 (q, $J = 281.4$ Hz), 119.9, 117.0, 81.4, 80.4, 76.4 (q, $J = 34.5$ Hz), 28.3.

IR ν_{\max} 3747 (w), 3733 (w), 3689 (w), 3673 (w), 3648 (w), 3628 (w), 3448 (w), 3419 (w), 3329 (w), 3088 (w), 2984 (w), 2933 (w), 2885 (w), 2884 (w), 2855 (w), 2361 (s), 2340 (m), 1771 (w), 1731 (m), 1717 (m), 1650 (w), 1555 (w), 1506 (m), 1460 (w), 1416 (w), 1396 (w), 1370 (m), 1351 (w), 1281 (m), 1250 (m), 1187 (s), 1152 (s), 1086 (m), 1051 (s), 1026 (m), 988 (w), 933 (m), 908 (w), 876 (w), 850 (w).

HRMS (ESI) calcd for C₁₂H₁₈F₃NNaO₃⁺ [M+Na]⁺ 304.1131; found 304.1133.

Tert-butyl (2,2,2-trifluoro-1-((2-methylallyl)oxy)ethyl)carbamate (**24**)



To a stirred solution of 2-methylprop-2-en-1-ol (**35**) (127 μL , 1.50 mmol, 1 equiv.) in toluene (3 mL) at rt was added Cs_2CO_3 (586 mg, 1.80 mmol, 1.2 equiv.). Then 1-((*tert*-butoxycarbonyl)amino)-2,2,2-trifluoroethyl acetate (**5**) (424 mg, 1.65 mmol, 1.1 equiv.) was added and the resulting mixture was stirred at the same temperature overnight. The reaction mixture was then filtered through a plug of silica eluted with ethyl acetate, the volatiles were then removed under reduced pressure and the residue was purified by column chromatography (SiO_2 , Pentane:DCM 2:3) to afford the title compound **24** (339 mg, 1.26 mmol, 84 % yield) as a colorless oil.

R_f 0.6 (Pentane:DCM 2:3).

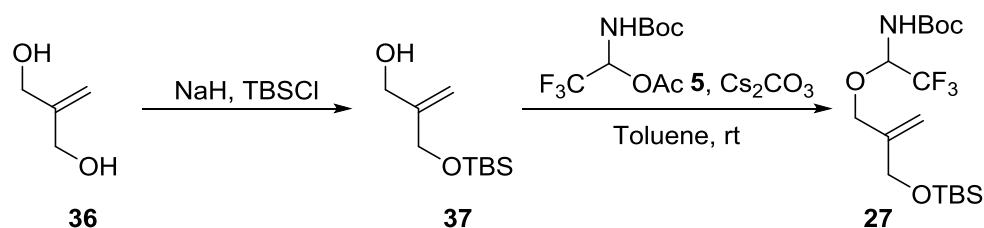
$^1\text{H NMR}$ (400 MHz, Chloroform-*d*) δ 5.33 (dq, $J = 9.6, 4.8$ Hz, 1H, CHCF_3), 5.12 (d, $J = 10.6$ Hz, 1H, NH), 5.02 (s, 1H, $\text{C}=\text{CH}_2$), 4.98 (s, 1H, $\text{C}=\text{CH}_2$), 4.10 (d, $J = 12.4$ Hz, 1H, OCH_2), 4.01 (d, $J = 12.4$ Hz, 1H, OCH_2), 1.75 (s, 3H, Me), 1.47 (s, 9H, Boc).

$^{13}\text{C NMR}$ (101 MHz, Chloroform-*d*) δ 154.7, 140.4, 122.4 (q, $J = 281.6$ Hz), 114.4, 81.5, 78.6 – 77.3 (m), 72.9, 28.3, 19.4.

$\text{IR } \nu_{\text{max}}$ 3453 (w), 3326 (w), 3217 (w), 2982 (w), 2939 (w), 2870 (w), 1712 (m), 1508 (m), 1458 (w), 1395 (w), 1370 (m), 1342 (w), 1282 (m), 1248 (m), 1186 (s), 1152 (s), 1093 (m), 1051 (m), 1025 (w), 993 (w), 895 (m), 852 (w).

HRMS (ESI) calcd for $\text{C}_{11}\text{H}_{18}\text{F}_3\text{NNaO}_3^+ [\text{M}+\text{Na}]^+$ 292.1131; found 292.1143.

Tert-butyl(1-((2-(((*tert*-butyldimethylsilyl)oxy)methyl)allyl)oxy)-2,2,2-trifluoroethyl)carbamate (**27**)



- 1) Following a reported procedure,³ to a flame-dried two-neck 50 mL round-bottom flask was added NaH (0.230 g, 5.68 mmol, 1 equiv.) in dry THF (18 mL). To the resulting

³ T. J. Senter, O. O. Fadeyi, C. W. Lindsley, *Org. Lett.*, **2012**, *14*,1869-1871.

mixture was added at 0 °C 2-methylenepropane-1,3-diol (**36**) (0.460 mL, 5.68 mmol, 1 equiv.) dropwise. The mixture was then brought to room temperature and stirred for 45 min. *Tert*-butylchlorodimethylsilane (0.860 g, 5.68 mmol, 1 equiv.) was then added in one batch and stirring was continued for an additional 1h. The reaction was quenched with H₂O, and extracted 3 times with ethyl acetate, washed with brine, dried with anhydrous MgSO₄, and concentrated in vacuo. the residue was purified by column chromatography (SiO₂, Pentane:EtOAc 9:1 to 4:1) to afford compound **37** (932 mg, 4.61 mmol, 81 % yield) as a colorless oil.

¹H NMR (400 MHz, Chloroform-*d*) δ 5.10 (q, *J* = 1.4 Hz, 1H, C=CH₂), 5.08 (q, *J* = 1.3 Hz, 1H, C=CH₂), 4.25 (s, 2H, CH₂OTBS), 4.17 (s, 2H, CH₂OH), 1.83 (d, *J* = 5.2 Hz, 1H, OH), 0.91 (s, 9H, TBS), 0.09 (s, 6H, TBS).

¹³C NMR (101 MHz, Chloroform-*d*) δ 147.6, 111.3, 65.3, 64.9, 26.0, 18.4, -5.3.

The characterization data is corresponding to the reported values.³

- 2) Under nitrogen atmosphere, to a stirred solution of 2-(((*tert*-butyldimethylsilyl)oxy)methyl)prop-2-en-1-ol (**37**) (400 mg, 1.98 mmol, 1 equiv.) in Toluene (5mL) at rt was added Cs₂CO₃ (773 mg, 2.37 mmol, 1.2 equiv.). Then 1-((*tert*-butoxycarbonyl)amino)-2,2,2-trifluoroethyl acetate (**5**) (559 mg, 2.17 mmol, 1.1 equiv.) was added and the resulting mixture was stirred at the same temperature overnight. The reaction mixture was then filtered through a plug of silica eluted with ethyl acetate, the volatiles were then removed under reduced pressure and the residue was purified by column chromatography (SiO₂, Pentane:DCM 2:3) to afford the title compound **27** (508 mg, 1.27 mmol, 64 % yield) as a colorless oil.

R_f 0.4 (Pentane:DCM 2:3).

¹H NMR (400 MHz, Chloroform-*d*) δ 5.33 (dq, *J* = 10.2, 5.0 Hz, 1H, CHCF₃), 5.27 (s, 1H, CCH₂), 5.16 (s, 1H, CCH₂), 5.13 (d, *J* = 10.5 Hz, 1H, NH), 4.22 (d, *J* = 12.3 Hz, 1H, CHOCH₂), 4.16 (s, 2H, SiOCH₂), 4.08 (d, *J* = 12.3 Hz, 1H, CHOCH₂), 1.47 (s, 9H, Boc), 0.91 (s, 9H, TBS), 0.07 (s, 6H, TBS).

¹³C NMR (101 MHz, Chloroform-*d*) δ 154.7, 143.5, 122.4 (q, *J* = 281.5 Hz), 114.1, 81.5, 78.6 – 77.2 (m), 69.4, 63.7, 28.3, 26.0, 18.5, -5.3.

IR ν_{max} 3449 (w), 3335 (w), 2957 (m), 2934 (m), 2890 (w), 2857 (w), 1730 (s), 1507 (m), 1466 (w), 1395 (w), 1367 (m), 1343 (w), 1284 (w), 1256 (m), 1190 (s), 1160 (s), 1087 (m), 1055 (m), 1027 (w), 1008 (w), 922 (w), 896 (w), 844 (s).

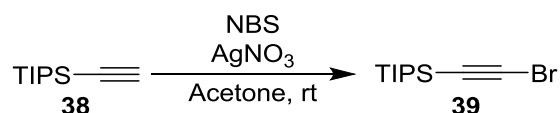
HRMS (ESI) calcd for C₁₇H₃₂F₃NNaO₄Si⁺ [M+Na]⁺ 422.1945; found 422.1952.

3) Synthesis of the Bromoalkynes

General procedure for the bromination of terminal alkynes:⁴

The terminal or silyl-protected alkyne (1.0 equiv) is dissolved in acetone (ca. 6.8 mL per mmol of alkyne). N-bromosuccinimide (1.2 equiv) and AgNO₃ (0.1 equiv) are added to the resulting solution in this order and the mixture is stirred at rt for 3-6 hours, until complete consumption of the starting material according to TLC. It was then poured onto iced water. The aqueous layer was extracted with pentane (3 times) and the combined organic extracts were dried over MgSO₄, filtered and the solvent removed by evaporation under reduced pressure. The bromo alkyne was isolated by column chromatography in 95-99% purity as judged by ¹H NMR.

2-Bromoethynyl-1-triisopropylsilane (39)



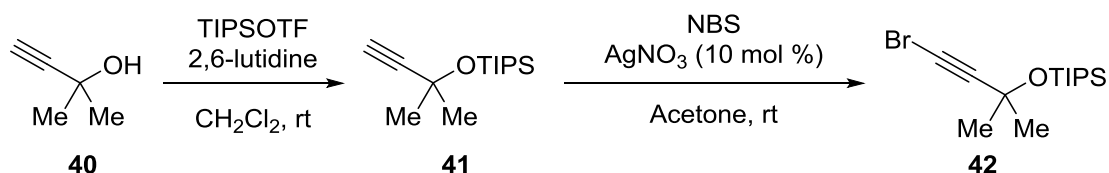
Triisopropylsilylacetylene (**38**) (813 mg, 4.45 mmol, 1.00 equiv) was brominated according to the general procedure. Bromoalkyne **39** was obtained as a colorless oil (1.16 g, 4.43 mmol, 99%) without further purification.

¹H NMR (400 MHz, CDCl₃) δ 1.20- 0.97 (m, 21 H, TIPS).

¹³C NMR (101 MHz, CDCl₃) δ 83.5, 61.7, 18.5, 11.3.

Spectra data was consistent with the values reported in literature.⁴

((4-Bromo-2-methylbut-3-yn-2-yl)oxy)triisopropylsilane (42)



- 1) Following a reported procedure,⁵ 2-methylbut-3-yn-2-ol (**40**) (0.34 mL, 3.5 mmol, 1.0 equiv) and 2,6-lutidine (freshly distilled on CaH₂, 0.41 mL, 3.5 mmol, 1.0 equiv) were dissolved in CH₂Cl₂ (12 mL). TIPSOTf (0.94 mL, 3.5 mmol, 1.0 equiv) was added dropwise to the solution at 0 °C. The solution was allowed to warm to rt overnight and

⁴ M. X. Jiang, M. Rawat, W. D. J. Wulff, *J. Am. Chem. Soc.*, **2004**, 126, 5970.

⁵ S. Nicolai, R. Sedigh-Zadeh, J. Waser, *J. Org. Chem.*, **2013**, 78 (8), 3783–3801.

then quenched with a saturated aqueous NaHCO₃ solution, and the aqueous layer was extracted with CH₂Cl₂ (3 × 10 mL). The combined organic layers were washed with H₂O, dried over MgSO₄, filtered, and the solvent was removed in vacuo. Purification by column chromatography (SiO₂, pentane) afforded TIPS-protected propargyl alcohol **41** as a colorless oil (622 mg, 2.59 mmol, 74% yield), which was used directly for the next step.

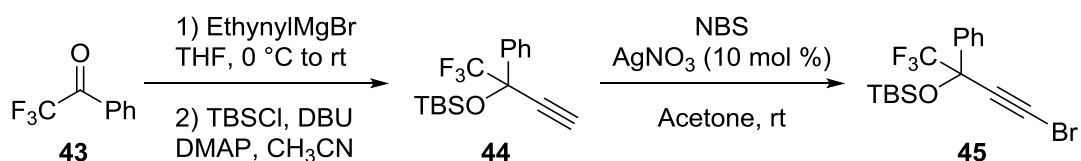
- Propargyl alcohol **41** (603 mg, 2.51 mmol, 1.0 equiv) was brominated according to the general procedure. After purification by column chromatography (SiO₂, pentane), bromoalkyne **42** was obtained as a colorless oil (733 mg, 2.30 mmol, 91% yield).

¹H NMR (400 MHz, Chloroform-*d*) δ 1.51 (s, 6H, Me), 1.18–1.03 (m, 21H, TIPS).

¹³C NMR (101 MHz, Chloroform-*d*) δ 85.4, 67.2, 42.7, 32.9, 18.3, 13.0.

The characterization data is corresponding to the reported values.⁵

((4-Bromo-1,1,1-trifluoro-2-phenylbut-3-yn-2-yl)oxy)(*tert*-butyl)dimethylsilane (45)



- Following a reported procedure,² to a 0.5 M solution of ethynylmagnesium bromide (7.0 mL, 3.5 mmol) in THF was slowly added 2,2,2-trifluoro-1-phenylethanone (**43**) (300 mg, 1.72 mmol) in THF (1 mL). After 3 h at rt the reaction mixture was quenched with water (1 mL) and then NH₄Cl sat solution was added (5 mL) and the mixture was diluted with DCM (10 mL). The layers were separated and the aqueous layer was extracted once with DCM (10 mL). The combined organic layers were dried over MgSO₄, filtered and concentrated under reduced pressure to afford a yellow oil that was engaged in the next step without further purification. TBS-Cl (0.422 g, 2.80 mmol, 1.4 equiv) was slowly added to a solution of the alcohol (0.400 g, 2.00 mmol), DBU (0.452 mL, 3.00 mmol, 1.5 equiv), DMAP (12 mg, 0.10 mmol, 0.05 equiv) in acetonitrile (6 mL) at 0 °C. The reaction mixture was stirred for 12 h at rt. The reaction mixture was quenched with water (5 mL) and extracted with DCM (3x5 mL). The combined organic layers were dried over MgSO₄, filtered and concentrated under reduced pressure. The crude residue was purified by column chromatography (SiO₂, Pentane) to afford compound **44** (0.460 g, 1.46 mmol, 73 % yield) as a clear oil that was directly engaged in the next step.
- O-Silylated propargyl alcohol **44** (450 mg, 1.43 mmol, 1.0 equiv.) was brominated according to the general procedure. After purification by column chromatography

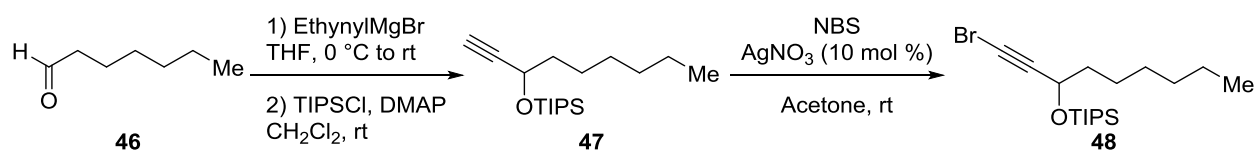
(SiO₂, pentane), bromo alkyne **45** was obtained as a colorless oil (531 mg, 1.35 mmol, 94% yield).

¹H NMR (400 MHz, Chloroform-*d*) δ 7.76 – 7.64 (m, 2H, ArH), 7.46 – 7.34 (m, 3H, ArH), 0.98 (s, 9H, t-Bu), 0.25 (s, 3H, Me), 0.03 (s, 3H, Me).

¹³C NMR (101 MHz, Chloroform-*d*) δ 136.9, 129.5, 128.1, 127.5, 123.1 (q, J = 286.3 Hz), 76.7, 75.4 (q, J = 32.5 Hz), 51.2, 25.9, 18.5, -3.4, -3.4.

Spectra data was consistent with the values reported in literature.²

((1-Bromonon-1-yn-3-yl)oxy)triisopropylsilane (**48**)



- 1) Following a slightly modified reported procedure,⁶ heptaldehyde (**46**) (1.22 mL, 8.76 mmol, 1.0 equiv.) was added dropwise to a solution of ethynyl magnesium bromide (0.5 M in THF, 22.8 mL, 11.4 mmol, 1.3 equiv.) at 0 °C. After 30 min, the cooling bath was removed to reach rt and the solution was stirred for further 2 h. The reaction was then quenched by addition of aqueous HCl (1.0 M, 15 mL) and the mixture was extracted with Et₂O (3 x 20 mL). The combined organic layers were washed with brine, dried over MgSO₄, filtered and the solvent was removed under reduced pressure. Purification by column chromatography (SiO₂, pentane/EtOAc 20/1) afforded the corresponding propargyl alcohol as a yellow oil (943 mg, 6.73 mmol, 77% yield). TIPSCl (1.36 mL, 6.36 mmol, 1.1 equiv.) and DMAP (777 mg, 6.36 mmol, 1.1 equiv.) were dissolved in CH₂Cl₂ (10 mL) at rt and a solution of propargyl alcohol (810 mg, 5.78 mmol, 1.0 equiv.) in CH₂Cl₂ (30 mL) was slowly added to the reaction mixture. The reaction was stirred overnight and then quenched by sequential addition of H₂O (36 mL) and aqueous HCl (2.0 M, 36 mL). The mixture was extracted with CH₂Cl₂ (3 x 20 mL) and the combined organic layers were washed with brine, dried over MgSO₄, filtered and the solvent was removed in vacuo. Purification by column chromatography (SiO₂, Pentane) afforded the O-silylated propargyl alcohol **47** as a colorless oil (1.04 g, 3.51 mmol, 61% yield).
- 2) O-Silylated propargyl alcohol **47** (890 mg, 3.00 mmol, 1.0 equiv.) was brominated according to the general procedure. After purification by column chromatography (SiO₂, pentane), bromo alkyne **48** was obtained as a colorless oil (1.04 g, 2.77 mmol, 92% yield).

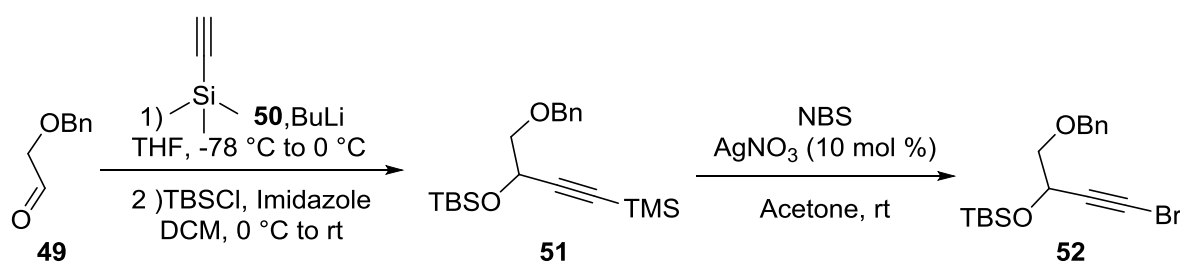
⁶ A. Buzas, F. Gagosz, *J. Am. Chem. Soc.*, **2006**, *128*, 12614.

¹H NMR (400 MHz, Chloroform-*d*) δ 4.48 (t, 1 H, $J = 6.3$ Hz, CHOTIPS), 1.69 (m, 2 H, OCHCH₂), 1.44 (m, 2 H, OCHCH₂CH₂), 1.36-1.26 (m, 6 H, (CH₂)₃), 1.17-1.04 (m, 21 H, TIPS), 0.89 (t, $J = 6.7$ Hz, 3H, Me).

¹³C NMR (101 MHz, Chloroform-*d*) δ 82.1, 64.0, 43.6, 38.7, 31.8, 29.0, 24.9, 22.6, 18.0, 18.0, 14.1, 12.3.

Spectra data was consistent with the values reported in literature.⁶

((1-(benzyloxy)-4-bromobut-3-yn-2-yl)oxy)(*tert*-butyl)dimethylsilane (52)



1) Following a reported procedure,⁷ ethynyltrimethylsilane (**50**) (0.460 mL, 3.33 mmol, 1 equiv.) was added to THF (3 mL) and stirred at -78 °C. To this solution was added *n*-butyllithium (2.5 M solution in hexanes, 1.99 mL, 4.99 mmol, 1.5 equiv.) slowly, and the resulting mixture was stirred at -78 °C for 30 min. To this solution was added 2-(benzyloxy)acetaldehyde (**49**) (0.470 mL, 3.33 mmol, 1 equiv.) in THF (1.8 mL) dropwise, and the resulting mixture was further stirred for 5 min at -78 °C and then at 0 °C for 1h30. Sat. NH₄Cl (5 mL) was added to the mixture at 0 °C, followed by extraction with EtOAc (3 × 10 mL). The combined organic layers were dried over MgSO₄, filtered and concentrated under reduced pressure to afford a yellow oil that was engaged in the next step without further purification. To a solution of 1-(benzyloxy)-4-(trimethylsilyl)but-3-yn-2-ol (567 mg, 2.28 mmol, 1.0 equiv.) in DCM (46 mL) at 0 °C were added imidazole (435 mg, 6.39 mmol, 2.8 equiv.) and after 10 min TBS-Cl (688 mg, 4.57 mmol, 2.0 equiv.). The reaction mixture was slowly allowed to warm up to rt and was left stirring overnight. The reaction mixture was quenched with water (15 mL) and the aqueous layer was extracted with DCM (3 × 20 mL). The combined organic layers were washed with brine, dried over MgSO₄, filtered and concentrated under reduced pressure. The crude residue was purified by column chromatography (SiO₂, Pentane:EtOAc 94:4) to afford compound **51** (0.724 g, 1.99 mmol, 62 % yield over two steps) as a clear oil that was directly engaged in the next step.

2) O-Silylated propargyl alcohol **51** (724 mg, 1.99 mmol, 1.0 equiv.) was brominated according to the general procedure. After purification by column chromatography

⁷ S. Singh, V. Gajulapati, M. Kim, J. Goo, J. Lee, K. Lee, C. Lee, L. Jeong, Y. Choi, *Synthesis*, **2016**, 48, 3050-3056.

(SiO₂, Pentane:EtOAc 96:4), bromo alkyne **52** was obtained as a pale yellow oil (580 mg, 1.57 mmol, 79% yield).

R_f 0.38 (Pentane:EtOAc 96:4).

¹H NMR (400 MHz, Chloroform-*d*) δ 7.28 – 7.16 (m, 5H, *ArH*), 4.53 (d, *J* = 2.2 Hz, 2H, *OCH₂C_{Ar}*), 4.49 (dd, *J* = 6.7, 5.2 Hz, 1H, *CHO*), 3.53 – 3.44 (m, 2H, *OCH₂CH*), 0.83 (s, 9H, TBS), 0.06 (s, 3H, TBS), 0.04 (s, 3H, TBS).

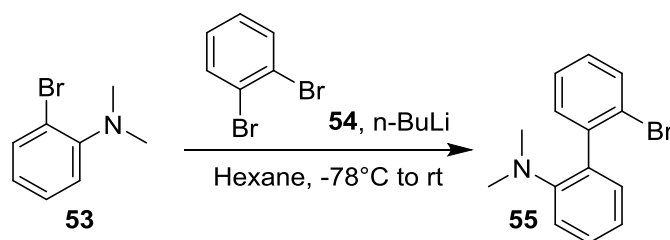
¹³C NMR (101 MHz, Chloroform-*d*) δ 138.2, 128.5, 127.8, 127.8, 79.6, 74.4, 73.6, 64.0, 45.3, 25.9, 18.4, -4.6, -4.8.

IR ν_{\max} 2980 (w), 2936 (w), 2910 (w), 1717 (s), 1643 (w), 1618 (w), 1585 (w), 1493 (m), 1458 (w), 1369 (s), 1329 (m), 1291 (w), 1234 (w), 1158 (s), 1134 (m), 1109 (m), 1072 (w), 1024 (w), 978 (w), 962 (w), 881 (w), 850 (m).

HRMS (ESI) calcd for C₁₇H₂₅BrNaO₂Si [M⁺] 391.0699; found 391.0701.

4) Synthesis of the New Phosphine Ligands : FuDavePhos (17) and FuXPhos (1)

2'-Bromo-N,N-dimethyl-[1,1'-biphenyl]-2-amine (55)



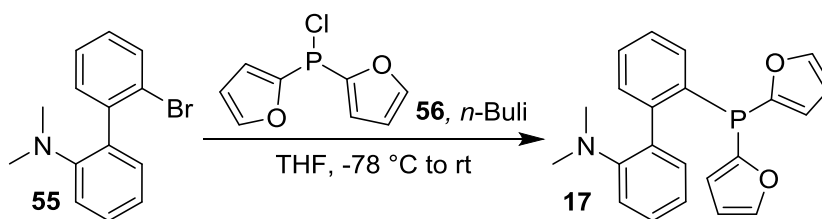
2-Bromo-N,N-dimethylaniline (**53**) (0.95 mL 6.6 mmol, 1.1 equiv.) was dissolved in dry hexane (13 mL) and *n*-BuLi (2.5 M solution in hexanes, 2.80 mL, 7.20 mmol, 1.2 equiv.) was added dropwise at -78 °C under nitrogen. The reaction was stirred 1 h at -78 °C and allowed to warm up to rt. Then 1,2-dibromobenzene (**54**) (0.72 mL, 6.0 mmol) was added dropwise. The resulting solution was then stirred for 2 h at reflux. The reaction was quenched by adding 15 mL of H₂O and the aqueous layer was extracted twice with Et₂O (2x15 mL), dried over MgSO₄, filtered and concentrated. The crude residue was purified by column chromatography (SiO₂, Pentane:DCM 98:2 to 82:18) affording the title compound **55** (0.573 g, 2.08 mmol, 35 % yield) as a white solid.

¹H NMR (400 MHz, Chloroform-*d*) δ 7.68 (dd, *J* = 8.0, 1.1 Hz, 1H, ArH), 7.41 – 7.31 (m, 3H, ArH), 7.21 – 7.17 (m, 1H, ArH), 7.15 (dd, *J* = 7.5, 1.8 Hz, 1H, ArH), 7.08 (d, *J* = 7.6 Hz, 1H, ArH), 7.02 (td, *J* = 7.5, 1.2 Hz, 1H, ArH), 2.56 (s, 6H, Me).

¹³C NMR (101 MHz, Chloroform-*d*) 151.2, 142.1, 133.5, 132.9, 131.6, 131.9, 128.3, 128.4, 127.2, 123.8, 121.0, 117.5, 43.1.

Spectra data was consistent with the values reported in literature.⁸

2'-(Di(furan-2-yl)phosphanyl)-N,N-dimethyl-[1,1'-biphenyl]-2-amine (17)



To a -78 °C solution of 2'-bromo-N,N-dimethyl-[1,1'-biphenyl]-2-amine (**55**) (200 mg, 0.724 mmol, 1.0 equiv.) in THF (2.5 mL) was added *n*-BuLi (2.5 M solution in hexanes, 0.319 mL, 0.797 mmol, 1.1 equiv.) dropwise. The reaction mixture was stirred at -78 °C for 40 min and chlorodi(furan-2-yl)phosphine (**56**) (153 mg, 0.760 mmol, 1.05 equiv.) diluted to reach 1 mL solution in toluene was added dropwise over 3 min. The reaction mixture was allowed to

⁸ I. Bonnaventure, A. B. Charrette, *J. Org. Chem.*, **2008**, *73* (16), 6330–6340.

warm up to rt slowly (with the acetone-dry ice bath) and was stirred at rt overnight. The reaction mixture was then quenched with 1 mL of H₂O, diluted with 10 mL of DCM and then washed with 5 mL of a saturated solution of NaHCO₃. The organic layer was dried over MgSO₄, filtered and concentrated under reduced pressure. The crude residue was purified by column chromatography (SiO₂, Pentane:DCM 95:5 to 50:50) affording the title compound **17** (254 mg, 0.703 mmol, 97 % yield) as an orange solid.

R_f 0.55 (Pentane:Et₂O 20:1).

m.p = 101-102 °C.

¹H NMR (400 MHz, Chloroform-*d*) δ 7.8 (ddd, *J* = 7.8, 4.1, 1.4 Hz, 1H, Ar*H*), 7.6 (d, *J* = 1.7 Hz, 1H, HetAr*H*), 7.5 (d, *J* = 1.7 Hz, 1H, HetAr*H*), 7.4 (td, *J* = 7.4, 1.4 Hz, 1H, Ar*H*), 7.4 – 7.3 (m, 3H, Ar*H*), 7.1 (dd, *J* = 7.5, 1.8 Hz, 1H, Ar*H*), 7.0 (q, *J* = 8.2, 7.4 Hz, 2H, Ar*H*), 6.5 (d, *J* = 3.2 Hz, 1H, HetAr*H*), 6.4 (dt, *J* = 3.2, 1.5 Hz, 1H, HetAr*H*), 6.4 (dq, *J* = 1.9, 1.0 Hz, 1H, HetAr*H*), 6.3 (dt, *J* = 3.3, 1.7 Hz, 1H, HetAr*H*), 2.3 (s, 6H, Me).

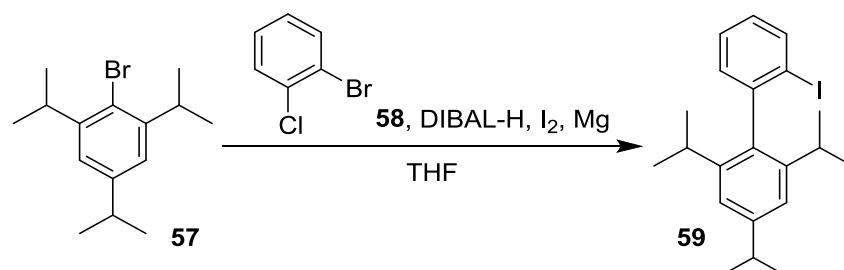
¹³C NMR (101 MHz, Chloroform-*d*) δ 153.0, 151.5, 146.8, 146.6, 135.2 (d, *J* = 2.0 Hz), 135.2, 134.5 (d, *J* = 5.2 Hz), 133.2, 131.9, 130.4 (d, *J* = 7.0 Hz), 129.9, 128.7, 126.9, 121.6, 120.0 (d, *J* = 23.3 Hz), 119.0 (d, *J* = 17.7 Hz), 117.7, 110.7, 110.6, 110.6 (d, *J* = 10.9 Hz), 42.9.

³¹P NMR (162 MHz, Chloroform-*d*) δ -56.6.

IR ν_{max} 3144 (w), 3116 (w), 3054 (w), 2982 (w), 2944 (w), 2862 (w), 2828 (m), 2781 (w), 1785 (w), 1681 (w), 1596 (w), 1551 (w), 1496 (m), 1455 (m), 1431 (w), 1367 (w), 1322 (w), 1286 (w), 1246 (w), 1211 (m), 1155 (m), 1113 (w), 1054 (w), 1008 (s), 948 (m), 906 (m), 883 (w), 820 (w).

HRMS (ESI) calcd for C₂₂H₂₁NO₂P⁺ [M+H]⁺ 362.1304; found 362.1306.

2'-Iodo-2,4,6-triisopropyl-1,1'-biphenyl (**59**)



Following a slightly modified procedure,⁹ a 25 mL two neck round bottom flask was charged with magnesium (0.583 g, 24.0 mmol, 2.4 equiv.), THF (5 mL) was then added followed by 2-bromo-1,3,5-triisopropylbenzene (**57**) (0.142 g, 0.500 mmol, 0.05 equiv.) and DIBAL-H (1 M solution in hexanes, 0.240 mL, 0.240 mmol). The reaction mixture was stirred at rt for 20 min and then 2-bromo-1,3,5-triisopropylbenzene (**57**) (2.46 mL, 9.70 mmol, 0.97 equiv.) was

⁹ J. D. Hicks, A. M. Hyde, A. M. Cuezva, S. L. Buchwald, *J. Am. Chem. Soc.*, **2009**, *131*(46), 16720-16734.

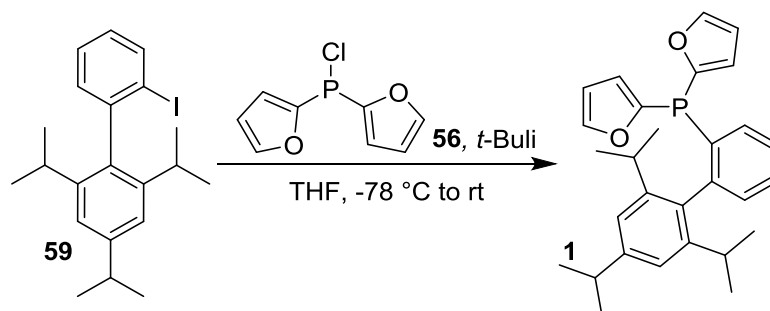
then added in THF (9 mL) and the reaction mixture was heated to reflux for 1h. Then 1-bromo-2-chlorobenzene (**58**) (1.28 mL, 11.0 mmol, 1.1 equiv.) was added over 30 min and the reaction mixture was further stirred 1h at reflux, then cooled to rt and a solution of iodine (2.79 g, 11.0 mmol, 1.1 equiv.) in THF (5 mL) was added until a deep purple color persisted. The reaction mixture was then quenched with MeOH and filtered. The filtrate was then washed with Na₂S₂O₃ and brine, then dried over Na₂SO₄, filtered and concentrated. The resulting solid (4.02 g) was crystallized from acetone (ca 15 mL) and further washed with pentane (3x5 mL) to yield the title compound **59** (1.95 g, 4.81 mmol, 48.1 % yield) as an off white crystalline solid.

¹H NMR (400 MHz, Chloroform-*d*) δ 7.95 (dd, *J* = 7.9, 1.2 Hz, 1H), 7.38 (td, *J* = 7.5, 1.3 Hz, 1H), 7.19 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.08 – 6.99 (m, 3H), 2.95 (p, *J* = 6.9 Hz, 1H), 2.39 (p, *J* = 6.8 Hz, 2H), 1.31 (d, *J* = 6.9 Hz, 6H), 1.22 (d, *J* = 6.9 Hz, 6H), 1.01 (d, *J* = 6.9 Hz, 6H).

¹³C NMR (101 MHz, Chloroform-*d*) δ 148.7, 146.0, 145.9, 139.3, 138.9, 130.7, 128.4, 127.9, 120.9, 102.6, 34.3, 30.8, 25.0, 24.2, 23.6.

Spectra data was consistent with the values reported in literature.⁹

Di(furan-2-yl)(2',4',6'-triisopropyl-[1,1'-biphenyl]-2-yl)phosphane (**1**)



To a -78 °C solution of 2'-iodo-2,4,6-triisopropyl-1,1'-biphenyl (**59**) (0.252 g, 0.700 mmol, 1 equiv.) in THF (2.41 mL) was added *tert*-butyllithium (2M (18%) solution in heptane, 0.81 mL, 1.4 mmol, 2 equiv.) dropwise. The reaction mixture was stirred at -78 °C for 70 min. Then chlorodi(furan-2-yl)phosphine (**56**) (0.136 g, 0.679 mmol, 0.97 equiv.) diluted to reach 1 mL solution in Toluene was added dropwise over 3 min. The reaction mixture was allowed to warm up to rt slowly (with the acetone-dry ice bath) and was stirred at rt overnight. The reaction mixture was then quenched with water (1 mL), diluted with DCM (10 mL) and then washed with a saturated solution of NaHCO₃ (5 mL). The organic layer was dried over MgSO₄, filtered and concentrated under reduced pressure. The crude residue was purified by column chromatography (SiO₂, Pentane:DCM 15:1) affording the title compound **1** (0.150 g, 0.337 mmol, 48 % yield) as a white solid.

R_f 0.65 (Pentane:Et₂O 20:1).

m.p = 138-139 °C.

¹H NMR (400 MHz, Chloroform-*d*) δ 7.84 – 7.79 (m, 1H, ArH), 7.60 (dd, $J = 1.8, 0.7$ Hz, 2H, HetArH), 7.40 – 7.35 (m, 2H, ArH), 7.19 – 7.14 (m, 1H), 7.01 (d, $J = 0.5$ Hz, 2H, ArH), 6.46 (dt, $J = 3.3, 0.9$ Hz, 2H, HetArH), 6.35 (dt, $J = 3.2, 1.6$ Hz, 2H, HetArH), 2.95 (p, $J = 6.9$ Hz, 1H, CH(CH₃)₂), 2.34 (p, $J = 6.8$ Hz, 2H, CH(CH₃)₂), 1.31 (d, $J = 6.9$ Hz, 6H, CH(CH₃)₂), 0.97 (dd, $J = 9.1, 6.8$ Hz, 12H, CH(CH₃)₂).

¹³C NMR (101 MHz, Chloroform-*d*) δ 151.5 (d, $J = 11.4$ Hz), 148.3, 147.2 (d, $J = 2.8$ Hz), 146.8, 146.6, 146.4, 135.9 (d, $J = 7.9$ Hz), 135.1 (d, $J = 3.1$ Hz), 133.7, 130.9 (d, $J = 7.1$ Hz), 129.3, 127.1, 120.6 (d, $J = 4.0$ Hz), 120.4, 110.8 (d, $J = 5.0$ Hz), 34.3, 30.8, 25.5, 24.2, 22.9.

³¹P NMR (162 MHz, Chloroform-*d*) δ -61.30.

IR ν_{\max} 2959 (s), 2927 (s), 2864 (m), 1723 (w), 1646 (w), 1607 (w), 1554 (w), 1500 (w), 1463 (m), 1380 (w), 1366 (w), 1319 (w), 1259 (w), 1217 (w), 1159 (w), 1135 (w), 1073 (w), 1009 (m), 965 (w), 907 (w), 880 (w), 845 (w).

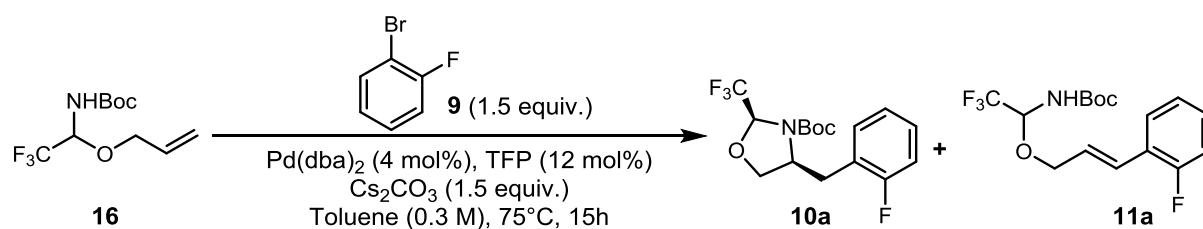
HRMS (ESI) calcd for C₂₉H₃₄O₂P⁺ [M+H]⁺ 445.2291; found 445.2294.

5) Optimization

General method for the optimization:

A sealed oven-dry microwave vial under nitrogen was charged with the hemiaminal (0.100 mmol, 1.0 equiv), the base, the palladium catalyst and the ligand. Then 1-bromo-2-fluorobenzene (16 μ l, 0.15 mmol) and dry degassed toluene (0.33 mL) were added *via* syringe to the vial. The resulting mixture was stirred at 75 °C for 15 h. The reaction mixture was cooled to 23 °C, filtered and concentrated under reduced pressure and analyzed by ¹H NMR spectroscopy. The yield was determined using 3,4,5-trichloropyridine (integration of propargylic protons) as internal standard.

Table 1 : Optimization with aryl bromides.

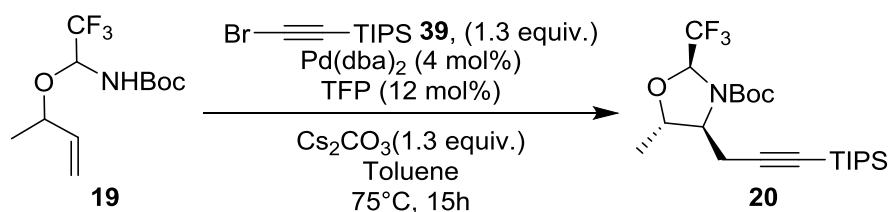


Entry	Changes from standard conditions	Yield of 10a (%) ^b	Yield of 11a (%) ^b
1	none	39	42
2	With LiOTf (1.2 equiv.) as additive	35	38
3	With NaOTf (1.2 equiv.) as additive	45	42
4	With KOTf (1.2 equiv.) as additive	48	45
5	With CsOTf (1.2 equiv.) as additive	51	42
6	dppf (6 mol%) instead of TFP	9	13
7	DPEPhos (6 mol%) instead of TFP	17	21
8	XANTPhos (6 mol%) instead of TFP	< 5	< 5
9	(<i>p</i> CF ₃ -C ₆ H ₄) ₃ P (12 mol%) instead of TFP	23	65
10	PhDavePhos (12 mol%) instead of TFP	22	67
11	Cy-JohnPhos (12 mol%) instead of TFP	14	14
12	XPhos (12 mol%) instead of TFP	34	5
13	RuPhos (6 mol%) instead of TFP	18	3
14	DavePhos (6 mol%) instead of TFP	26	9
15	Fu-DavePhos (12 mol%) instead of TFP	42	36
16	FuXPhos (12 mol%) instead of TFP	80	14
17	FuXPhos (12 mol%) instead of TFP and	92 (88) ^c	< 5

CsOTf (1.2 equiv.) as additive

^aReaction conditions: 0.10 mmol **16**, 0.15 mmol **9**, Additive (1.2 equiv), 0.3 M in Toluene, 15 h. ^bNMR yield using 3,4,5-trichloropyridine as internal standard. ^cIsolated yield on 0.30 mmol scale.

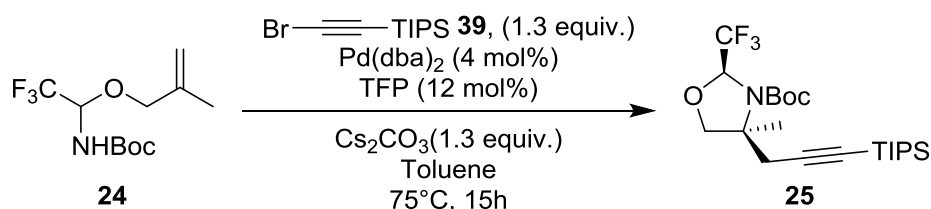
Table 2 : Optimization with branched hemiaminals



Entry	Changes from standard conditions	Yield of 20 (%) ^b	<i>d.r</i>
1	none	75 (73) ^c	67/33
2	With CsOTf (1.2 equiv.) as additive	54	67/33
3	XPhos (12 mol%) instead of TFP	25	67/33
4	Fu-DavePhos (12 mol%) instead of TFP	55	67/33
5	FuXPhos (12 mol%) instead of TFP	22	67/33

^aReaction conditions: 0.10 mmol **19**, Additive (1.2 equiv), 0.3 M in Toluene, 15 h. ^bNMR yield using 3,4,5-trichloropyridine as internal standard. ^cIsolated yield on 0.30 mmol scale.

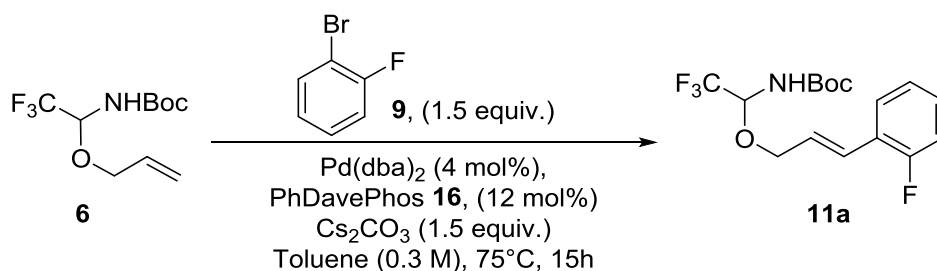
Table 3 : Optimization with 1,1-disubstituted Olefins



Entry	Changes from standard conditions	Yield of 20 (%) ^b	<i>d.r</i>
1	none	< 5	-
2	PhDavePhos (12 mol%) instead of TFP	< 5	-
3	DavePhos (12 mol%) instead of TFP	12%	-
4	Fu-DavePhos (12 mol%) instead of TFP	53%	10/1
5	FuXPhos (12 mol%) instead of TFP	16%	-
6	XPhos (12 mol%) instead of TFP	63 (60%) ^c	10/1

^aReaction conditions: 0.10 mmol **24**, 0.3 M in Toluene, 15 h. ^bNMR yield using 3,4,5-trichloropyridine as internal standard. ^cIsolated yield on 0.30 mmol scale.

6) Characterization of the Heck Side Product



To an oven-dried 5 mL microwave tube under nitrogen atmosphere were added *tert*-butyl(1-(allyloxy)-2,2,2-trifluoroethyl)carbamate (**6**) (77 mg, 0.30 mmol, 1 equiv.), Pd(dba)₂ (6.9 mg, 0.012 mmol, 0.04 equiv.), PhDavePhos (**16**) (9.2 mg, 0.024 mmol, 0.08 equiv.), and cesium carbonate (147 mg, 0.450 mmol, 1.5 equiv.). The tube was sealed, evacuated and backfilled with nitrogen (this process was repeated for a total of 3 times). Then 1 mL of degassed toluene (degassed using freeze-thaw cycles) and 1-bromo-2-fluorobenzene (**9**) (0.049 mL, 0.450 mmol, 1.5 equiv.) were added *via* syringe to the tube and the resulting mixture was heated to 75 °C. After 15 h stirring at 75 °C, the mixture was filtered over silica eluting with Et₂O and concentrated under reduced pressure. The crude oil was purified by column chromatography (SiO₂, Pentane:EtOAc 99:1 to 95:5) affording the title compound **11a** (0.070 g, 0.20 mmol, 67% yield) as a yellow oil.

R_f 0.35 (Pentane:DCM 1:1).

¹H NMR (400 MHz, Chloroform-*d*) δ 7.46 (td, *J* = 7.7, 1.7 Hz, 1H, Ar*H*), 7.22 (ddt, *J* = 7.3, 5.2, 2.1 Hz, 1H, Ar*H*), 7.12 – 7.01 (m, 2H, Ar*H*), 6.80 (dt, *J* = 15.9, 1.4 Hz, 1H, C_{Ar}CHCH), 6.35 (dt, *J* = 16.1, 6.2 Hz, 1H, C_{Ar}CHCH), 5.41 (dq, *J* = 10.0, 4.9 Hz, 1H, CHCF₃), 5.22 (d, *J* = 10.5 Hz, 1H, NH), 4.40 (dd, *J* = 12.2, 5.9 Hz, 1H, OCH₂), 4.31 (dd, *J* = 12.7, 6.8 Hz, 1H, OCH₂), 1.47 (s, 9H, Boc).

¹³C NMR (101 MHz, Chloroform-*d*) δ 160.5 (d, *J* = 249.8 Hz), 154.6, 129.4 (d, *J* = 8.7 Hz), 128.7, 127.9 (d, *J* = 3.8 Hz), 126.8, 126.6 (d, *J* = 6.2 Hz), 124.2 (d, *J* = 3.7 Hz), 122.8 (q, *J* = 284.1 Hz), 115.9 (d, *J* = 22.1 Hz), 81.6, 78.3 (q, *J* = 34.8 Hz), 70.0, 28.3.

IR ν_{max} 3668 (w), 3326 (w), 2984 (s), 2904 (m), 1758 (w), 1722 (w), 1697 (w), 1519 (w), 1494 (w), 1457 (w), 1398 (m), 1377 (m), 1255 (m), 1191 (m), 1157 (m), 1053 (s), 968 (w), 894 (m).

HRMS (ESI) calcd for C₁₆H₁₉F₄NNaO₃⁺ [M+Na]⁺ 372.1193; found 372.1190.

7) Pd-catalyzed Carboamination of Allylcohols

General procedure A

To an oven-dried 5 mL microwave tube under nitrogen atmosphere were added the hemiaminal (0.30 mmol, 1.0 equiv.), Pd(dba)₂ (6.9 mg, 0.012 mmol), Tri(2-furyl)phosphine (8.4 mg, 0.036 mmol), and cesium carbonate (127 mg, 0.390 mmol). The tube was sealed, evacuated and backfilled with nitrogen (this process was repeated for a total of 3 times). Then 1 mL of degassed toluene (degassed using freeze-thaw cycles) and (bromoethynyl) trisopropylsilane (**39**) (93 μ L, 0.39 mmol) were added *via* syringe to the tube and the resulting mixture was heated to 75 °C. After 15 h stirring at 75 °C, the mixture was filtered over silica eluting with Et₂O and concentrated under reduced pressure. The crude residue was then purified by column chromatography using the indicated solvents.

General procedure B for alkynylbromides and 1,1-disubstituted olefins

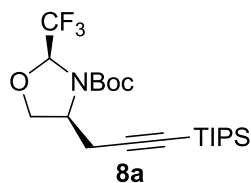
To an oven-dried 5 mL microwave tube under nitrogen atmosphere were added the hemiaminal (0.3 mmol, 1.0 equiv.), Pd(dba)₂ (6.9 mg, 0.012 mmol), XPhos (**18**) (17.2 mg, 0.0360 mmol), and cesium carbonate (127 mg, 0.390 mmol). The tube was sealed, evacuated and backfilled with nitrogen (this process was repeated for a total of 3 times). Then 1 mL of degassed toluene (degassed using freeze-thaw cycles) and the alkynylbromide (0.39 mmol, 1.1 equiv.) were added *via* syringe to the tube and the resulting mixture was heated to 75 °C. After 15h stirring at 75 °C, the mixture was filtered over silica eluting with Et₂O and concentrated under reduced pressure. The crude residue was then purified by column chromatography using the indicated solvents.

General procedure C for arylbromides

To an oven-dried 5 mL microwave tube under nitrogen atmosphere were added the hemiaminal (0.30 mmol, 1.0 equiv.), Pd(dba)₂ (6.9 mg, 0.012 mmol), FuXPhos (**1**) (16 mg, 0.036 mmol), cesium trifluoromethanesulfonate (102 mg, 0.360 mmol) and cesium carbonate (147 mg, 0.450 mmol). The tube was sealed, evacuated and backfilled with nitrogen (this process was repeated for a total of 3 times). Then 1 mL of degassed toluene (degassed using freeze-thaw cycles) and the arylbromide (0.45 mmol, 1.5 equiv.) were added *via* syringe to the tube and the resulting mixture was heated to 75 °C. After 15h stirring at 75 °C, the mixture was filtered over silica eluting with Et₂O and concentrated under reduced pressure. The crude residue was then purified by column chromatography using the indicated solvents.

The stereochemistry of the major diastereomer of the obtained oxazolidines was assigned by analogy with compounds **20**, **23** and **25** for which 2D ROESY experiments were performed.

***Tert*-butyl-2-(trifluoromethyl)-4-(3-(triisopropylsilyl)prop-2-yn-1-yl)oxazolidine-3-carboxylate (**8a**)**



Following General Procedure A, the title compound was prepared from *tert*-butyl(1-(allyloxy)-2,2,2-trifluoroethyl)carbamate (**6**) (77 mg, 0.30 mmol, 1 equiv.), and (bromoethynyl)triisopropylsilane (**39**) (93 μ L, 0.39 mmol, 1.3 equiv.). The crude oil was purified by column chromatography (SiO₂, Pentane:AcOEt 19:1) affording the title compound **8a** (0.118 g, 0.270 mmol, 90 % yield, dr > 20:1 in the crude ¹H NMR) as a yellow oil.

R_f 0.65 (Pentane:EtOAc 9:1).

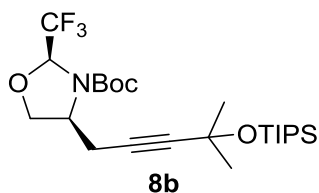
¹H NMR (400 MHz, Chloroform-*d*) δ 5.47 (bs, 1H, *CHCF*₃), 4.41 (t, *J* = 7.2 Hz, 1H, *OCH*₂), 4.28 – 4.06 (m, 2H, *OCH*₂ and *NCHCH*₂), 2.99 (d, *J* = 15.6 Hz, 1H, *CH*₂CC), 2.37 (dd, *J* = 16.4, 10.3 Hz, 1H, *CH*₂CC), 1.49 (s, 9H, Boc), 1.08-1.00 (m, 21H, TIPS).

¹³C NMR (101 MHz, Chloroform-*d*) δ 153.4, 123.1 (q, *J* = 286.2 Hz), 103.4, 85.7 (q, *J* = 35.4 Hz), 83.4, 82.5, 73.3, 56.5, 28.3, 24.6, 18.7, 11.3.

IR ν_{\max} 2944 (m), 2943 (m), 2868 (w), 2362 (w), 2337 (w), 2336 (w), 2176 (w), 1723 (s), 1722 (s), 1465 (w), 1367 (s), 1323 (w), 1288 (w), 1162 (s), 1135 (m), 1072 (w), 963 (m), 962 (m), 880 (w), 850 (w).

HRMS (ESI) calcd for C₂₁H₃₆F₃NNaO₃Si⁺ [*M*+Na]⁺ 458.2309; found 458.2309.

***Tert*-butyl-4-(4-methyl-4((triisopropylsilyl)oxy)pent-2-yn-1-yl)-2-(trifluoromethyl)oxazolidine-3-carboxylate (**8b**)**



Following General Procedure B, the title compound was prepared from *tert*-butyl(1-(allyloxy)-2,2,2-trifluoroethyl)carbamate (**6**) (77 mg, 0.30 mmol, 1 equiv.), and ((4-bromo-2-methylbut-3-yn-2-yl)oxy)triisopropylsilane (**42**) (125 mg, 0.390 mmol, 1.3 equiv.). The crude oil was purified by column chromatography (SiO₂, Pentane:Et₂O 99:1 to 95:5) affording the title compound **8b** (0.098 g, 0.19 mmol, 66 % yield, dr > 20:1 in the crude ¹H NMR) as a yellow oil.

R_f 0.3 (Pentane:DCM 7:3).

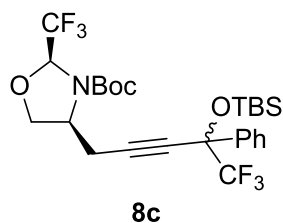
¹H NMR (400 MHz, Acetonitrile-*d*₃) δ 5.53 (q, *J* = 5.3 Hz, 1H, *CHCF*₃), 4.35 (ddd, *J* = 8.6, 7.2, 1.4 Hz, 1H, *OCH*₂), 4.11 (ddt, *J* = 9.8, 6.9, 3.5 Hz, 1H, *NCHCH*₂), 4.01 (ddd, *J* = 8.2, 6.8, 1.2 Hz, 1H, *OCH*₂), 2.76 (dd, *J* = 16.6, 4.2 Hz, 1H, *CH*₂-CC), 2.35 (dd, *J* = 16.6, 9.7 Hz, 1H, *CH*₂-CC), 1.46 (s, 6H, Me), 1.46 (s, 9H, Boc), 1.14 – 1.04 (m, 21H, TIPS).

¹³C NMR (101 MHz, Acetonitrile-*d*₃) δ 154.1, 123.8 (q, *J* = 285.4 Hz), 88.3, 86.0 (q, *J* = 34.9 Hz), 82.4, 78.4, 73.2, 66.7, 56.6, 33.3 (d, *J* = 2.8 Hz), 27.8, 23.3, 18.3, 13.4.

IR ν_{\max} 2941 (w), 2868 (w), 1723 (m), 1464 (w), 1366 (m), 1326 (w), 1287 (w), 1247 (w), 1160 (s), 1134 (m), 1054 (w), 961 (w), 909 (w), 882 (w), 849 (w).

HRMS (ESI) calcd for C₂₄H₄₂F₃NNaO₄Si⁺ [M+Na]⁺ 516.2727; found 516.2729.

***Tert*-butyl-4-(4-((*tert*-butyldimethylsilyl)oxy)-5,5,5-trifluoro-4-phenylpent-2-yn-1-yl)-2-(trifluoromethyl)oxazolidine-3-carboxylate (**8c**)**



Following General Procedure B, the title compound was prepared from *tert*-butyl(1-(allyloxy)-2,2,2-trifluoroethyl)carbamate (**6**) (77 mg, 0.30 mmol, 1 equiv.), and ((4-bromo-1,1,1-trifluoro-2-phenylbut-3-yn-2-yl)oxy)(*tert*-butyl)dimethylsilane (**45**) (153 mg, 0.390 mmol, 1.3 equiv.). The crude oil was purified by column chromatography (SiO₂, Pentane:Et₂O 99:1 to 95:5) affording the title compound **8c** (0.141 g, 0.248 mmol, 83 % yield, mixture of unresolved diastereoisomers at the propargylic center) as a yellow oil.

R_f 0.2 (Pentane:DCM 4:1).

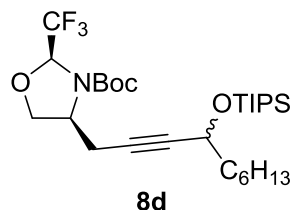
¹H NMR (400 MHz, Acetonitrile-*d*₃) δ 7.80 – 7.68 (m, 2H, *ArH*), 7.47 – 7.36 (m, 3H, *ArH*), 5.56 (q, *J* = 5.2 Hz, 1H, *CHCF*₃), 4.41 – 4.32 (m, 1H, *OCH*₂), 4.31 – 4.24 (m, 1H, *NCHCH*₂), 4.06 (td, *J* = 8.8, 6.2 Hz, 1H, *OCH*₂), 2.97 (dt, *J* = 16.9, 4.1 Hz, 1H, *CH*₂CC), 2.60 (ddd, *J* = 16.8, 9.2, 4.1 Hz, 1H, *CH*₂CC), 1.45 (s, 9H, Boc), 0.95 (s, 9H, TBS), 0.23 (app d, *J* = 1.2 Hz, 3H, TBS), 0.00 (app d, *J* = 3.8 Hz, 3H, TBS).

¹³C NMR (101 MHz, Acetonitrile-*d*₃) δ 154.4, 138.1, 130.4, 129.1 (d, *J* = 2.9 Hz), 128.4, 129.0 – 119.6 (m), 128.9 – 119.4 (m), 87.8, 86.4 (q, *J* = 35.0 Hz), 82.9, 78.9, 78.9 (diastereoisomer), 75.3 (q, *J* = 32.2 Hz), 73.5, 56.7, 28.2, 26.1, 23.8, 23.8 (diastereoisomer), 18.9, -3.0, -3.1 (diastereoisomer).

IR ν_{\max} 3067 (w), 3037 (w), 3010 (w), 2958 (w), 2934 (w), 2902 (w), 2859 (w), 1722 (m), 1468 (w), 1453 (w), 1367 (m), 1328 (w), 1287 (w), 1262 (w), 1175 (s), 1159 (s), 1135 (m), 1100 (m), 1077 (w), 1032 (w), 1007 (w), 961 (w), 914 (w), 865 (m), 842 (s).

HRMS (ESI) calcd for $C_{26}H_{35}F_6NNaO_4Si^+$ $[M+Na]^+$ 590.2132; found 590.2137

***Tert*-butyl-2-(trifluoromethyl)-4-(4-((*triisopropylsilyl*)oxy)dec-2-yn-1-yl)oxazolidine-3-carboxylate (**8d**)**



Following General Procedure B, the title compound was prepared from *tert*-butyl(1-(allyloxy)-2,2,2-trifluoroethyl)carbamate (**6**) (77 mg, 0.30 mmol, 1 equiv.), and ((1-bromonon-1-yn-3-yl)oxy)triisopropylsilane (**48**) (146 mg, 0.390 mmol, 1.3 equiv.). The crude oil was purified by column chromatography (SiO₂, Pentane:DCM 4:1) affording the title compound **8d** (0.118 g, 0.215 mmol, 72% yield, mixture of unresolved diastereoisomers at the propargylic center) as a yellow oil.

R_f 0.35 (Pentane:DCM 7:3).

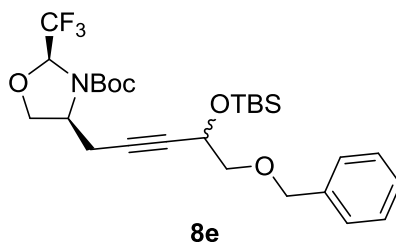
¹H NMR (400 MHz, Acetonitrile-*d*₃) δ 5.54 (q, *J* = 5.3 Hz, 1H, *CHCF*₃), 4.48 (tt, *J* = 6.2, 1.9 Hz, 1H, *NCHCH*₂), 4.34 (dddd, *J* = 8.5, 7.1, 3.3, 1.7 Hz, 1H, *CHOTIPS*), 4.13 (ddtd, *J* = 9.4, 7.3, 4.4, 1.9 Hz, 1H, *OCH*₂*CH*), 4.01 (ddd, *J* = 8.3, 7.0, 1.2 Hz, 1H, *OCH*₂*CH*), 2.78 (ddd, *J* = 16.7, 4.2, 1.9 Hz, 1H, *CH*₂*CC*), 2.38 (dddd, *J* = 16.6, 9.6, 3.0, 1.8 Hz, 1H, *CH*₂*CC*), 1.67 – 1.59 (m, 2H, *TIPSOCHCH*₂), 1.46 (s, 9H, *Boc*), 1.44 – 1.39 (m, 2H, *CHCH*₂*CH*₂), 1.34 – 1.27 (m, 6H, *CH*₂*CH*₂*CH*₂), 1.12 – 1.03 (m, 21H, *TIPS*), 0.91 – 0.86 (m, 3H, *CH*₂*CH*₃).

¹³C NMR (101 MHz, Acetonitrile-*d*₃) δ 154.4, 124.2 (q, *J* = 285.7 Hz), 86.4 (q, *J* = 35.0 Hz), 85.2, 82.7, 80.3, 80.3 (diastereoisomer), 73.6, 63.9, 57.2, 39.4, 32.1, 29.7, 28.2, 25.7, 23.6, 23.3, 18.4, 14.3, 13.0.

IR ν_{max} 2938 (m), 2866 (m), 1723 (s), 1463 (w), 1367 (s), 1326 (m), 1288 (w), 1256 (w), 1180 (s), 1160 (s), 1133 (m), 1103 (m), 1065 (m), 960 (w), 917 (w), 883 (m), 849 (w), 808 (w).

HRMS (ESI) calcd for $C_{28}H_{50}F_3NNaO_4Si^+$ $[M+Na]^+$ 572.3353; found 572.3354.

***Tert*-butyl-4-(5-(benzyloxy)-4-((*tert*-butyldimethylsilyl)oxy)pent-2-yn-1-yl)-2-(trifluoromethyl)oxazolidine-3-carboxylate (**8e**)**



Following General Procedure B, the title compound was prepared from *tert*-butyl(1-(allyloxy)-2,2,2-trifluoroethyl)carbamate (**6**) (77 mg, 0.30 mmol, 1 equiv.), and ((1-(benzyloxy)-4-bromobut-3-yn-2-yl)oxy)(*tert*-butyl)dimethylsilane (**52**) (144 mg, 0.390 mmol, 1.3 equiv.). The crude oil was purified by column chromatography (SiO₂, Pentane:Et₂O 99:1 to 95:5) affording the title compound **8e** (0.104 g, 0.191 mmol, 64 % yield, mixture of unresolved diastereoisomers at the propargylic center) as a yellow oil.

R_f 0.43 (Pentane:Et₂O 9:1).

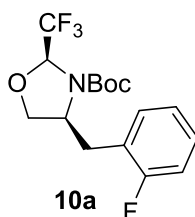
¹H NMR (400 MHz, Acetonitrile-*d*₃) δ 7.39 – 7.24 (m, 5H, ArH), 5.54 (q, *J* = 5.3 Hz, 1H, CHCF₃), 4.60 – 4.50 (m, 3H, CH₂C_{Ar} and CHOTBS), 4.33 (ddt, *J* = 8.5, 7.0, 1.5 Hz, 1H, OCH₂), 4.10 (ddt, *J* = 10.4, 6.6, 3.3 Hz, 1H, NCHCH₂), 4.00 (ddt, *J* = 8.3, 7.0, 1.3 Hz, 1H, OCH₂), 3.54 – 3.44 (m, 2H, CH₂OBn), 2.77 (ddt, *J* = 16.9, 3.6, 1.6 Hz, 1H, CH₂CC), 2.40 (dddd, *J* = 16.2, 9.4, 4.3, 1.9 Hz, 1H, CH₂CC), 1.45 (s, 9H, Boc), 0.90 (s, 9H, TBS), 0.11 (s, 3H, TBS), 0.10 (s, 3H, TBS).

¹³C NMR (101 MHz, Acetonitrile-*d*₃) δ 154.4, 139.6, 129.2, 128.5, 128.4, 129.1 – 119.6 (m), 86.4 (q, *J* = 34.9 Hz), 82.8, 82.6, 82.6 (diastereoisomer), 81.3, 81.3 (diastereoisomer), 75.5, 73.7, 73.5, 63.7, 57.0, 28.2, 26.1, 23.6, 23.5 (diastereoisomer), 18.8, -4.5, -4.7 (diastereoisomer).

IR ν_{max} 2956 (w), 2932 (m), 2858 (w), 1720 (s), 1470 (w), 1460 (w), 1366 (s), 1326 (w), 1288 (w), 1255 (w), 1178 (s), 1159 (s), 1131 (s), 1101 (s), 1028 (w), 1008 (w), 961 (m), 908 (w), 839 (s).

HRMS (ESI) calcd for C₂₇H₄₀F₃NNaO₅Si⁺ [M+Na]⁺ 566.2520; found 566.2526.

***Tert*-butyl-4-(2-fluorobenzyl)-2-(trifluoromethyl)oxazolidine-3-carboxylate (**10a**)**



Following General Procedure C, the title compound was prepared from *tert*-butyl(1-(allyloxy)-2,2,2-trifluoroethyl)carbamate (**6**) (77 mg, 0.30 mmol, 1 equiv.) and 1-bromo-2-fluorobenzene (**9**) (49 μ L, 0.45 mmol, 1.5 equiv.). The crude oil was purified by column chromatography (SiO₂, Pentane:EtOAc 99:1 to 95:5) affording the title compound **10a** (0.092 g, 0.26 mmol, 88% yield, dr > 20:1 in the crude ¹H NMR) as a yellow oil.

Rf 0.35 (Pentane:DCM 1:1).

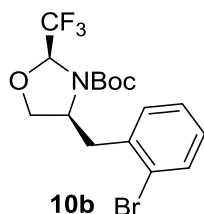
¹H NMR (400 MHz, Acetonitrile-*d*₃) δ 7.30 – 7.20 (m, 2H, ArH), 7.13 – 7.03 (m, 2H, ArH), 5.54 (q, *J* = 5.3 Hz, 1HCHCF₃), 4.35 (p, *J* = 6.8 Hz, 1H, NCHCH₂), 4.12 (ddq, *J* = 8.4, 7.2, 1.2 Hz, 1H, OCH₂), 3.96 (dd, *J* = 8.7, 5.8 Hz, 1H, OCH₂), 3.14 (dd, *J* = 13.5, 6.3 Hz, 1H, CH₂C_{Ar}), 2.84 (dd, *J* = 13.5, 8.0 Hz, 1H, CH₂C_{Ar}), 1.37 (s, 9H, Boc).

¹³C NMR (101 MHz, Acetonitrile-*d*₃) δ 162.3 (d, *J* = 243.7 Hz), 154.7, 132.8 (d, *J* = 5.0 Hz), 129.7 (d, *J* = 8.1 Hz), 125.6 (d, *J* = 11.4 Hz), 128. – 119.6 (m), 125.3 (d, *J* = 3.6 Hz), 116.1 (d, *J* = 22.2 Hz), 86.4 (q, *J* = 35.0 Hz), 82.4, 73.3, 58.2, 33.7, 28.1.

IR ν_{\max} 2981 (w), 2937 (w), 2910 (w), 1717 (s), 1585 (w), 1491 (m), 1458 (w), 1369 (s), 1329 (w), 1289 (w), 1234 (w), 1158 (s), 1134 (m), 1109 (m), 1073 (w), 1053 (w), 1029 (w), 979 (w), 962 (w), 910 (w), 881 (w), 850 (m).

HRMS (ESI) calcd for C₁₆H₁₈F₄NO₃ [M⁺] 348.1223; found 348.1209.

***Tert*-butyl-4-(2-bromobenzyl)-2-(trifluoromethyl)oxazolidine-3-carboxylate (**10b**)**



Following General Procedure C, the title compound was prepared from *tert*-butyl(1-(allyloxy)-2,2,2-trifluoroethyl)carbamate (**6**) (77 mg, 0.30 mmol, 1 equiv.) and 1,2-dibromobenzene (54 μ L, 0.45 mmol, 1.5 equiv.). The crude oil was purified by column chromatography (SiO₂, Pentane:EtOAc 98:2 to 95:5) affording the title compound **10b** (0.069 g, 0.17 mmol, 56% yield, dr > 20:1 in the crude ¹H NMR) as a yellow oil.

Rf 0.3 (Pentane:EtOAc 95:5).

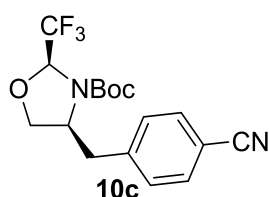
¹H NMR (400 MHz, Acetonitrile-*d*₃) δ 7.56 (dd, *J* = 8.1, 1.3 Hz, 1H, ArH), 7.30 – 7.20 (m, 2H, ArH), 7.18 – 7.11 (m, 1H, ArH), 5.55 (q, *J* = 5.2 Hz, 1H, CHCF₃), 4.48 (p, *J* = 7.1, 7.0, 6.5 Hz, 1H, NCHCH₂), 4.10 (ddd, *J* = 8.4, 7.2, 1.2 Hz, 1H, OCH₂), 3.99 (dd, *J* = 8.6, 5.1 Hz, 1H, OCH₂), 3.14 (dd, *J* = 13.7, 7.7 Hz, 1H, CH₂C_{Ar}), 2.98 (dd, *J* = 13.5, 7.0 Hz, 1H, CH₂C_{Ar}), 1.30 (s, 9H, Boc).

¹³C NMR (101 MHz, Acetonitrile-*d*₃) δ 154.7, 138.2, 133.7, 132.8, 129.6, 128.6, 125.5, 124.3 (q, *J* = 284.9 Hz), 86.5 (q, *J* = 35.0 Hz), 82.4, 73.0, 57.6, 40.2, 28.1.

IR ν_{\max} 2979 (w), 2934 (w), 2878 (w), 2362 (w), 2337 (w), 1715 (s), 1476 (w), 1441 (w), 1367 (s), 1329 (m), 1287 (m), 1258 (w), 1157 (s), 1135 (m), 1106 (w), 1071 (w), 1049 (w), 1023 (w), 978 (w), 962 (w), 878 (w), 849 (w).

HRMS (ESI) calcd for C₁₆H₁₉⁷⁹BrF₃NNaO₃⁺ [M+Na]⁺ 432.0393; found 432.0390.

***Tert*-butyl-4-(4-cyanobenzyl)-2-(trifluoromethyl)oxazolidine-3-carboxylate (10c)**



Following General Procedure C, the title compound was prepared from *tert*-butyl(1-(allyloxy)-2,2,2-trifluoroethyl)carbamate (**6**) (77 mg, 0.30 mmol, 1 equiv.) and 4-bromobenzonitrile (82 mg, 0.45 mmol, 1.5 equiv.). The crude oil was purified by column chromatography (SiO₂, Pentane:EtOAc 9:1 to 4:1) affording the title compound **10c** (0.095 g, 0.27 mmol, 89% yield, dr > 20:1 in the crude ¹H NMR) as a yellow oil.

R_f 0.25 (Pentane:EtOAc 9:1).

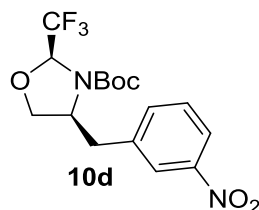
¹H NMR (400 MHz, Acetonitrile-*d*₃) δ 7.70 – 7.58 (m, 2H, ArH), 7.40 – 7.30 (m, 2H, ArH), 5.54 (q, *J* = 5.2 Hz, 1H, CHCF₃), 4.30 (p, *J* = 6.8 Hz, 1H, NCHCH₂), 4.11 (ddd, *J* = 8.4, 7.2, 1.2 Hz, 1H, OCH₂), 3.94 (dd, *J* = 8.8, 5.5 Hz, 1H, OCH₂), 3.14 (dd, *J* = 13.4, 6.6 Hz, 1H, CH₂C_{Ar}), 2.85 (dd, *J* = 13.3, 7.6 Hz, 1H, CH₂C_{Ar}), 1.34 (s, 9H, Boc).

¹³C NMR (101 MHz, Acetonitrile-*d*₃) δ 154.6, 144.6, 133.2, 131.3, 124.1 (q, *J* = 284.9 Hz), 119.7, 110.9, 86.3 (q, *J* = 35.0 Hz), 82.5, 73.2, 59.1, 40.1, 28.0.

IR ν_{\max} 2980 (w), 2935 (w), 2908 (w), 2229 (w), 1713 (s), 1609 (w), 1507 (w), 1481 (w), 1457 (w), 1366 (s), 1329 (m), 1288 (m), 1259 (w), 1155 (s), 1132 (s), 1109 (m), 1071 (w), 1022 (w), 981 (w), 960 (w), 912 (w), 879 (w), 847 (m), 820 (w).

HRMS (ESI) calcd for C₁₇H₂₀F₃N₂O₃⁺ [M+H]⁺ 357.1421; found 357.1428.

***Tert*-butyl-4-(3-nitrobenzyl)-2-(trifluoromethyl)oxazolidine-3-carboxylate (**10d**)**



Following General Procedure C, the title compound was prepared from *tert*-butyl(1-(allyloxy)-2,2,2-trifluoroethyl)carbamate (**6**) (77 mg, 0.30 mmol, 1 equiv.) and 1-bromo-3-nitrobenzene (91 mg, 0.45 mmol, 1.5 equiv.). The crude oil was purified by column chromatography (SiO₂, Pentane:EtOAc 98:2 to 95:5) affording the title compound **10d** (0.104 g, 0.276 mmol, 92% yield, dr > 20:1 in the crude ¹H NMR) as a yellow oil.

R_f 0.48 (Pentane:EtOAc 4:1).

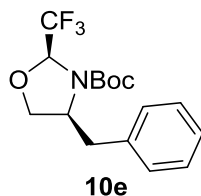
¹H NMR (400 MHz, Acetonitrile-*d*₃) δ 8.12 – 7.97 (m, 2H, ArH), 7.58 (dt, *J* = 7.8, 1.4 Hz, 1H, ArH), 7.51 (t, *J* = 7.8 Hz, 1H, ArH), 5.53 (q, *J* = 5.2 Hz, 1H, CHCF₃), 4.32 (p, *J* = 6.7 Hz, 1H, NCHCH₂), 4.13 (ddd, *J* = 8.3, 7.1, 1.3 Hz, 1H, OCH₂), 3.95 (dd, *J* = 8.6, 5.6 Hz, 1H, OCH₂), 3.13 (dd, *J* = 13.5, 6.8 Hz, 1H, CH₂C_{Ar}), 2.94 (dd, *J* = 13.5, 7.1 Hz, 1H, CH₂C_{Ar}), 1.31 (s, 9H, Boc).

¹³C NMR (101 MHz, Acetonitrile-*d*₃) δ 154.6, 149.3, 140.9, 136.9, 130.6, 125.1, 124.2 (q, *J* = 284.9 Hz), 122.5, 86.4 (q, *J* = 35.0 Hz), 82.5, 73.2, 59.2, 39.4, 28.1.

IR ν_{max} 2981 (w), 2936 (w), 2904 (w), 2369 (w), 2338 (w), 1713 (s), 1531 (s), 1354 (s), 1344 (m), 1289 (m), 1155 (s), 1132 (s), 1105 (m), 984 (w), 960 (w), 911 (w), 872 (w), 849 (w), 843 (w).

HRMS (ESI) calcd for C₁₆H₁₉F₃N₂NaO₅⁺ [M+Na]⁺ 399.1138; found 399.1142.

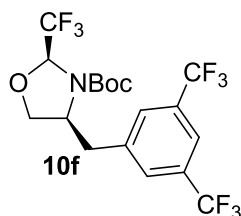
***Tert*-butyl (2*S*,4*S*)-4-benzyl-2-(trifluoromethyl)oxazolidine-3-carboxylate (**10e**)**



Following General Procedure C, the title compound was prepared from *tert*-butyl(1-(allyloxy)-2,2,2-trifluoroethyl)carbamate (**6**) (77 mg, 0.30 mmol, 1 equiv.) and bromobenzene (118 mg, 0.750 mmol, 1.5 equiv.). Title compound **10e** could not be obtained pure, the yield was of 38% (dr > 20:1 in the crude ¹H NMR) as estimated by ¹H NMR integration using 3,4,5-trichloropyridine as internal standard. Below are indicated ¹H NMR characteristic peaks.

¹H NMR (400 MHz, Chloroform-*d*) δ 7.33 – 7.27 (m, 5H, ArH), 5.51 (bs, 1H, CHCF₃), 4.25 (m, 1H, NCHCH₂), 4.04 (m, 2H, OCH₂), 3.44 – 3.34 (m, 1H, CH₂C_{Ar}), 2.67 (dd, *J* = 13.2, 10.0 Hz, 1H, CH₂C_{Ar}), 1.49 (s, 9H, Boc).

***Tert*-butyl-4-(3,5-bis(trifluoromethyl)benzyl)-2-(trifluoromethyl)oxazolidine-3-carboxylate (10f)**



Following General Procedure C, the title compound was prepared from *tert*-butyl(1-(allyloxy)-2,2,2-trifluoroethyl)carbamate (**6**) (77 mg, 0.30 mmol, 1 equiv.) and 1-bromo-3,5-bis(trifluoromethyl)benzene (**29**) (133 mg, 0.450 mmol, 1.5 equiv.). The crude oil was purified by column chromatography (SiO₂, Pentane:EtOAc 98:2 to 95:5) affording the title compound **10f** (0.128 g, 0.274 mmol, 91% yield, dr > 20:1 in the crude ¹H NMR) as a yellow oil.

R_f 0.55 (Pentane:EtOAc 4:1).

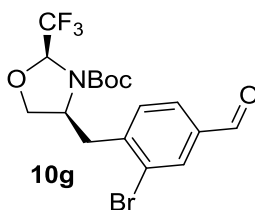
¹H NMR (400 MHz, Acetonitrile-*d*₃) δ 7.87 (s, 1H, ArH), 7.76 (s, 2H, ArH), 5.54 (q, *J* = 5.2 Hz, 1H, CHCF₃), 4.35 (p, *J* = 6.6 Hz, 1H, NCHCH₂), 4.18 (t, *J* = 7.8 Hz, 1H, OCH₂), 3.97 (dd, *J* = 8.6, 5.3 Hz, 1H, OCH₂), 3.08 (app dd, *J* = 7.0, 2.4 Hz, 2H, CH₂C_{Ar}), 1.29 (s, 9H, Boc).

¹³C NMR (101 MHz, Acetonitrile-*d*₃) δ 154.6, 141.9, 132.5 – 131.3 (m), 131.1 (d, *J* = 3.7 Hz), 124.6 (q, *J* = 271.8 Hz), 124.1 (q, *J* = 284.7 Hz), 121.4 (hept, *J* = 4.0 Hz), 86.5 (q, *J* = 35.1 Hz), 82.6, 72.9, 59.0, 39.0, 27.9.

IR ν_{\max} 2984 (w), 2937 (w), 2910 (w), 2362 (w), 2333 (w), 1717 (m), 1480 (w), 1464 (w), 1367 (m), 1330 (w), 1276 (s), 1160 (s), 1131 (s), 985 (w), 963 (w), 903 (w), 848 (w).

HRMS (ESI) calcd for C₁₈H₁₈F₉NNaO₃⁺ [M+Na]⁺ 490.1035; found 490.1040.

***Tert*-butyl-4-(2-bromo-4-formylbenzyl)-2-(trifluoromethyl)oxazolidine-3-carboxylate (10g)**



Following General Procedure C, the title compound was prepared from *tert*-butyl(1-(allyloxy)-2,2,2-trifluoroethyl)carbamate (**6**) (77 mg, 0.30 mmol, 1 equiv.) and 3,4-dibromobenzaldehyde (119 mg, 0.450 mmol, 1.5 equiv.). The crude oil was purified by column chromatography (SiO₂, Pentane:EtOAc 98:2 to 95:5) affording the title compound **10g** (0.109 g, 0.249 mmol, 83% yield > 20:1 in the crude ¹H NMR) as a yellow oil.

Rf 0.45 (Pentane:EtOAc 4:1).

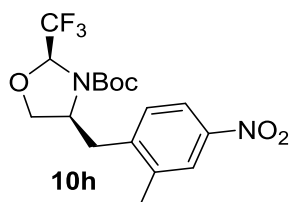
¹H NMR (400 MHz, Acetonitrile-*d*₃) δ 9.9 (s, 1H, CHO), 8.1 (d, *J* = 1.7 Hz, 1H, ArH), 7.8 (dd, *J* = 7.8, 1.7 Hz, 1H, ArH), 7.4 (d, *J* = 7.8 Hz, 1H, ArH), 5.6 (q, *J* = 5.1 Hz, 1H, CHCF₃), 4.5 (p, *J* = 6.9 Hz, 1H, NCHCH₂), 4.2 (ddt, *J* = 8.1, 7.1, 1.0 Hz, 1H, OCH₂), 4.0 (dd, *J* = 8.6, 4.7 Hz, 1H, OCH₂), 3.2 – 3.1 (m, 2H, CH₂C_{Ar}), 1.3 (s, 9H, Boc).

¹³C NMR (101 MHz, Acetonitrile-*d*₃) δ 192.0, 154.6, 145.1, 137.8, 134.3, 133.4, 129.3, 126.3, 124.2 (q, *J* = 284.6 Hz), 86.6 (q, *J* = 35.1 Hz), 82.5, 73.1, 57.3, 40.6, 28.0.

IR ν_{max} 3060 (w), 2983 (w), 2936 (w), 2838 (w), 2723 (w), 1706 (s), 1598 (w), 1557 (w), 1524 (w), 1481 (w), 1457 (w), 1366 (s), 1328 (m), 1287 (m), 1259 (w), 1157 (s), 1105 (w), 1072 (w), 1038 (w), 982 (w), 961 (w), 880 (w), 847 (w).

HRMS (ESI) calcd for C₁₇H₁₉⁷⁹BrF₃NNaO₄⁺ [M+Na]⁺ 460.0342; found 460.0343.

***Tert*-butyl-4-(2-methyl-4-nitrobenzyl)-2-(trifluoromethyl)oxazolidine-3-carboxylate (10h)**



Following General Procedure C, the title compound was prepared from *tert*-butyl(1-(allyloxy)-2,2,2-trifluoroethyl)carbamate (**6**) (77 mg, 0.30 mmol, 1 equiv.) and 1-bromo-2-methyl-4-nitrobenzene (97 mg, 0.45 mmol, 1.5 equiv.). The crude oil was purified by column chromatography (SiO₂, Pentane:EtOAc 95:5 to 90:10) affording the title compound **10h** (0.091 g, 0.23 mmol, 78% yield, dr > 20:1 in the crude ¹H NMR) as a yellow oil.

Rf 0.6 (Pentane:EtOAc 4:1).

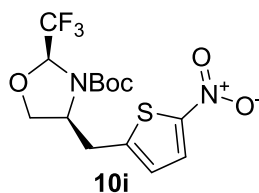
¹H NMR (400 MHz, Acetonitrile-*d*₃) δ 8.02 (d, *J* = 2.5 Hz, 1H, ArH), 7.93 (dd, *J* = 8.4, 2.5 Hz, 1H, ArH), 7.31 (d, *J* = 8.4 Hz, 1H, ArH), 5.57 (q, *J* = 5.2 Hz, 1H, CHCF₃), 4.37 (p, *J* = 7.1, 7.0, 6.3 Hz, 1H, NCHCH₂), 4.12 (ddd, *J* = 8.4, 7.2, 1.3 Hz, 1H, OCH₂), 3.97 (dd, *J* = 8.7, 5.3 Hz, 1H, OCH₂), 3.18 (dd, *J* = 13.6, 7.2 Hz, 1H, CH₂C_{Ar}), 2.89 (dd, *J* = 13.6, 7.5 Hz, 1H, CH₂C_{Ar}), 2.46 (s, 3H, Me), 1.31 (s, 9H, Boc).

¹³C NMR (101 MHz, Acetonitrile-*d*₃) δ 154.6, 147.8, 145.2, 140.1, 132.0, 125.6, 124.2 (q, *J* = 285.1 Hz), 121.7, 86.5 (q, *J* = 35.0 Hz), 82.6, 73.3, 57.4, 37.9, 28.1, 19.8.

IR ν_{\max} 3071 (w), 2981 (w), 2935 (w), 2910 (w), 1712 (s), 1613 (w), 1590 (w), 1522 (m), 1484 (w), 1459 (w), 1365 (s), 1350 (s), 1327 (m), 1288 (m), 1259 (w), 1156 (s), 1132 (m), 1101 (m), 1067 (w), 980 (w), 961 (w), 930 (w), 902 (w), 875 (w), 849 (m), 814 (w).

HRMS (ESI) calcd for C₁₇H₂₁F₃N₂O₅ [M⁺] 390.1403; found 390.1390.

***Tert*-butyl-4-((5-nitrothiophen-2-yl)methyl)-2-(trifluoromethyl)oxazolidine-3-carboxylate (**10i**)**



Following General Procedure C, the title compound was prepared from *tert*-butyl(1-(allyloxy)-2,2,2-trifluoroethyl)carbamate (**6**) (77 mg, 0.30 mmol, 1 equiv.) and 2-bromo-5-nitrothiophene (94 mg, 0.45 mmol, 1.5 equiv.). The crude oil was purified by column chromatography (SiO₂, Pentane:EtOAc 98:2 to 95:5) affording the title compound **10i** (0.092 g, 0.24 mmol, 80% yield, dr > 20:1 in the crude ¹H NMR) as a yellow oil.

R_f 0.35 (Pentane:EtOAc 4:1).

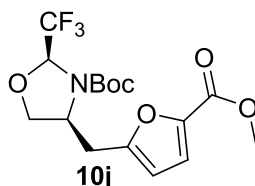
¹H NMR (400 MHz, Acetonitrile-*d*₃) δ 7.81 (d, *J* = 4.2 Hz, 1H, HetArH), 6.89 (dt, *J* = 4.2, 0.8 Hz, 1H, HetArH), 5.54 (q, *J* = 5.1 Hz, 1H, CHCF₃), 4.30 (dt, *J* = 12.5, 6.6 Hz, 1H, NCHCH₂), 4.18 (ddt, *J* = 8.8, 6.9, 1.0 Hz, 1H, OCH₂), 3.96 (ddd, *J* = 8.6, 5.0, 1.0 Hz, 1H, OCH₂), 3.18 (dd, *J* = 14.6, 7.0 Hz, 1H, CH₂HetAr), 3.09 (dd, *J* = 14.7, 6.8 Hz, 1H), 1.35 (s, 9H, Boc).

¹³C NMR (101 MHz, Acetonitrile-*d*₃) δ 154.5, 151.3, 150.2, 130.2, 127.9, 124.0 (q, *J* = 284.6 Hz), 86.4 (q, *J* = 35.0 Hz), 82.9, 73.0, 59.0, 34.8, 28.1.

IR ν_{\max} 3353 (w), 3111 (w), 2980 (w), 2897 (w), 2773 (w), 1715 (s), 1629 (w), 1542 (w), 1499 (m), 1437 (w), 1372 (m), 1338 (s), 1287 (m), 1253 (w), 1155 (s), 1070 (w), 1031 (w), 978 (w), 909 (w), 852 (w), 816 (m).

HRMS (ESI) calcd for C₁₄H₁₇F₃N₂NaO₅S⁺ [M+Na]⁺ 405.0702; found 405.0703.

***Tert*-butyl-4-((5-(methoxycarbonyl)furan-2-yl)methyl)-2-(trifluoromethyl)oxazolidine-3-carboxylate (**10j**)**



Following General Procedure C, the title compound was prepared from *tert*-butyl(1-(allyloxy)-2,2,2-trifluoroethyl)carbamate (**6**) (77 mg, 0.30 mmol, 1 equiv.) and methyl 5-bromofuran-2-carboxylate (92 mg, 0.45 mmol, 1.5 equiv.). The crude oil was purified by column chromatography (SiO₂, Pentane:EtOAc 98:2 to 95:5) affording the title compound **10j** (0.093 g, 0.25 mmol, 82% yield > 20:1 in the crude ¹H NMR) as a yellow oil.

R_f 0.4 (Pentane:EtOAc 4:1).

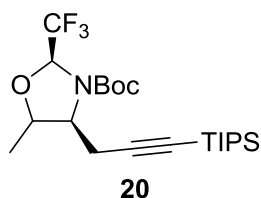
¹H NMR (400 MHz, Acetonitrile-*d*₃) δ 7.07 (d, *J* = 3.4 Hz, 1H, HetAr*H*), 6.25 (d, *J* = 3.4 Hz, 1H, HetAr*H*), 5.51 (q, *J* = 5.2 Hz, 1H, CHCF₃), 4.31 (p, *J* = 6.5 Hz, 1H, NCHCH₂), 4.21 (tq, *J* = 7.2, 1.2 Hz, 1H, OCH₂), 3.95 (ddd, *J* = 8.6, 5.8, 1.1 Hz, 1H, OCH₂), 3.76 (s, 3H, Me), 3.12 (dd, *J* = 14.9, 5.9 Hz, 1H, CH₂HetAr), 2.88 (dd, *J* = 14.9, 7.8 Hz, 1H, CH₂HetAr), 1.37 (s, 9H, Boc).

¹³C NMR (101 MHz, Acetonitrile-*d*₃) δ 159.7, 157.5, 154.4, 144.7, 124.5 (q, *J* = 283.8 Hz), 119.9, 110.8, 86.2 (q, *J* = 35.1 Hz), 82.6, 73.2, 57.0, 52.2, 32.7, 28.1.

IR ν_{max} 2981 (w), 2936 (w), 2907 (w), 1716 (s), 1598 (w), 1526 (w), 1481 (w), 1459 (w), 1439 (w), 1366 (s), 1307 (m), 1256 (w), 1156 (s), 1136 (s), 1075 (w), 1021 (w), 962 (m), 929 (w), 907 (w), 872 (w), 850 (w).

HRMS (ESI) calcd for C₁₆H₂₀F₃NNaO₆⁺ [M+Na]⁺ 402.1135; found 402.1132.

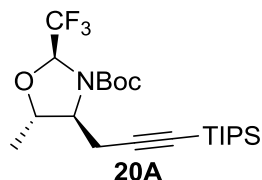
***Tert*-butyl-5-methyl-2-(trifluoromethyl)-4-(3-(triisopropylsilyl)prop-2-yn-1-yl)oxazolidine-3-carboxylate (**20**)**



Following General Procedure A, the title compound was prepared from *tert*-butyl (1-(but-3-en-2-yloxy)-2,2,2-trifluoroethyl)carbamate (**19**) (81 mg, 0.30 mmol, 1 equiv.) and (bromoethynyl)triisopropylsilane (**39**) (93 μL, 0.39 mmol, 1.3 equiv.). The crude oil was purified by column chromatography (SiO₂, Pentane:DCM 4:1 to 3:2) affording the two diastereoisomers of the title compound **20** in a 67/33 ratio (major diastereoisomer A : 0.067 g,

0.15 mmol; minor diastereoisomer B : 0.032 g, 0.071 mmol; 73% yield combined) as yellow oils.

Diastereoisomer A (Major):



R_f 0.33 (Pentane:DCM 4:1).

¹H NMR (400 MHz, Acetonitrile-*d*₃) δ 5.51 (q, *J* = 5.6 Hz, 1H, *CHCF*₃), 4.31 – 4.39 (m, 1H, *NCHCH*₂), 3.56 (ddd, *J* = 10.3, 7.2, 3.7 Hz, 1H, *OCHMe*), 2.89 (dd, *J* = 16.9, 3.7 Hz, 1H, *CH₂CC*), 2.44 (dd, *J* = 16.9, 9.6 Hz, 1H, *CH₂CC*), 1.43 (s, 9H, Boc), 1.40 (d, *J* = 6.1 Hz, 3H, Me), 1.01 – 1.05 (m, 21H, TIPS).

¹³C NMR (101 MHz, Acetonitrile-*d*₃) δ 154.4, 124.2 (q, *J* = 286.5 Hz), 104.7, 85.3 (q, *J* = 34.8 Hz), 84.0, 82.7, 82.4, 63.0, 28.2, 24.3, 20.3, 18.9, 11.9.

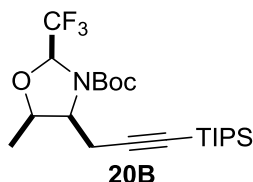
IR ν_{\max} 2941 (w), 2868 (w), 2175 (w), 1719 (s), 1464 (w), 1365 (s), 1316 (w), 1291 (w), 1167 (s), 1066 (w), 1022 (w), 945 (w), 878 (w), 854 (w).

HRMS (ESI) calcd for C₂₂H₃₈AgF₃NO₃Si⁺ [*M*+*Ag*]⁺ 556.1618; found 556.1625.

Stereochemistry assigned by ROESY.



Diastereoisomer B (Minor):



R_f 0.23 (Pentane:DCM 4:1).

¹H NMR (400 MHz, Acetonitrile-*d*₃) δ 5.40 (q, *J* = 4.2 Hz, 1H, *CHCF*₃), 4.33 – 4.18 (m, 2H, *NCHCH*₂ and *OCHMe*), 2.54 – 2.38 (m, 2H, *CH₂CC*), 1.44 (s, 9H, Boc), 1.32 (d, *J* = 6.2 Hz, 3H, Me), 1.07 – 1.01 (m, 21H, TIPS).

¹³C NMR (101 MHz, Acetonitrile-*d*₃) δ 154.0, 123.5 (q, *J* = 282.7 Hz), 106.2, 84.9 (q, *J* = 35.3 Hz), 82.9, 82.4, 77.9, 59.6, 28.3, 21.2, 18.9, 14.7, 12.0.

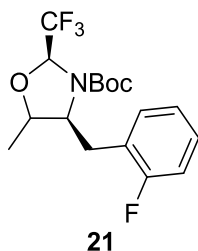
IR ν_{\max} 2944 (m), 2893 (w), 2867 (m), 2177 (w), 1721 (s), 1464 (w), 1372 (s), 1318 (m), 1284 (w), 1180 (s), 1160 (s), 1133 (w), 1085 (w), 988 (w), 941 (w), 886 (m), 848 (w).

HRMS (ESI) calcd for C₂₂H₃₈AgF₃NO₃Si⁺ [*M*+Ag]⁺ 556.1618; found 556.1626.

Stereochemistry assigned by ROESY.

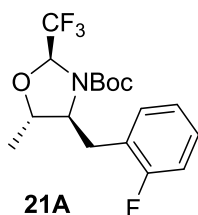


***Tert*-butyl 4-(2-fluorobenzyl)-5-methyl-2-(trifluoromethyl)oxazolidine-3-carboxylate (21)**



Following General Procedure C, the title compound was prepared from *tert*-butyl (1-(but-3-en-2-yloxy)-2,2,2-trifluoroethyl)carbamate (**19**) (81 mg, 0.30 mmol, 1 equiv.) and 1-bromo-2-fluorobenzene (**9**) (49 μ L, 0.45 mmol, 1.5 equiv.). The crude oil was purified by column chromatography (SiO₂, Pentane:Et₂O 99:1 to 95:5) affording the two diastereoisomers of the title compound **21** in a 60/40 ratio (major diastereoisomer A : 0.051 g, 0.140 mmol; minor diastereoisomer B : 0.033 g, 0.091 mmol; 77% yield combined) as yellow oils.

Diastereoisomer A (Major):



R_f 0.65 (Pentane:DCM 7:3).

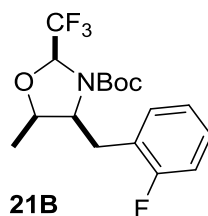
¹H NMR (400 MHz, Acetonitrile-*d*₃) δ 7.29 – 7.18 (m, 2H, ArH), 7.13 – 7.00 (m, 2H, ArH), 5.53 (q, *J* = 5.7 Hz, 1H, CHCF₃), 4.27 (p, *J* = 6.2 Hz, 1H, NCHCH₂), 3.77 (q, *J* = 6.9 Hz, 1H, OCHMe), 3.23 (dd, *J* = 13.4, 5.1 Hz, 1H, CH₂C_{Ar}), 2.82 (dd, *J* = 13.4, 8.4 Hz, 1H, CH₂C_{Ar}), 1.40 (s, 9H, Boc), 0.94 (d, *J* = 6.1 Hz, 3H, Me).

¹³C NMR (101 MHz, Acetonitrile-*d*₃) δ 162.2 (d, *J* = 243.5 Hz), 154.8, 132.9 (d, *J* = 5.1 Hz), 129.8 (d, *J* = 8.2 Hz), 125.2 (d, *J* = 3.6 Hz), 124.9 (d, *J* = 16.2 Hz), 128.9 – 119.9 (m), 116.0 (d, *J* = 22.2 Hz), 85.5 (q, *J* = 34.8 Hz), 82.4, 81.7, 64.3, 32.9, 28.1, 19.5.

IR ν_{max} 2984 (w), 2936 (w), 1719 (s), 1588 (w), 1522 (w), 1495 (w), 1458 (w), 1366 (s), 1327 (w), 1291 (w), 1257 (w), 1235 (w), 1181 (s), 1162 (s), 1137 (m), 1110 (w), 1072 (w), 1055 (w), 1025 (w), 954 (w), 876 (w), 852 (w).

HRMS (ESI) calcd for C₁₇H₂₁F₄NNaO₃⁺ [M+Na]⁺ 386.1350; found 386.1348.

Diastereoisomer B (Minor):



R_f 0.55 (Pentane:DCM 7:3).

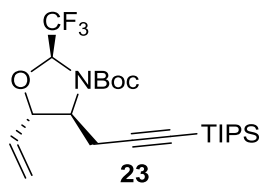
¹H NMR (400 MHz, Acetonitrile-*d*₃) δ 7.27 – 7.19 (m, 1H, ArH), 7.15 (td, *J* = 7.8, 2.0 Hz, 1H, ArH), 7.08 – 6.99 (m, 2H, ArH), 5.42 (q, *J* = 4.4 Hz, 1H, CHCF₃), 4.41 – 4.22 (m, 2H, NCHCH₂ and OCHMe), 2.93 (ddd, *J* = 13.6, 3.8, 1.2 Hz, 1H, CH₂C_{Ar}), 2.52 (ddd, *J* = 13.2, 11.6, 1.3 Hz, 1H, CH₂C_{Ar}), 1.32 (d, *J* = 6.1 Hz, 3H, Me), 1.10 (s, 9H, Boc).

¹³C NMR (101 MHz, Acetonitrile-*d*₃) δ 162.6 (d, *J* = 243.3 Hz), 154.5, 132.9 (d, *J* = 5.2 Hz), 129.1 (d, *J* = 8.3 Hz), 126.3 (d, *J* = 15.8 Hz), 124.8 (d, *J* = 3.6 Hz), 123.8 (q, *J* = 283.1 Hz), 115.8 (d, *J* = 22.1 Hz), 85.4 (q, *J* = 35.3 Hz), 81.8, 78.3, 60.4, 28.9, 27.8, 14.6.

IR ν_{max} 2984 (w), 2936 (w), 1714 (s), 1591 (w), 1495 (w), 1458 (w), 1368 (m), 1327 (w), 1302 (w), 1282 (w), 1258 (w), 1233 (w), 1176 (s), 1153 (s), 1129 (m), 1080 (m), 1059 (w), 1035 (w), 980 (w), 899 (m), 848 (w).

HRMS (ESI) calcd for C₁₇H₂₁F₄NNaO₃⁺ [M+Na]⁺ 386.1350; found 386.1346.

***Tert*-butyl-2-(trifluoromethyl)-4-(3-(triisopropylsilyl)prop-2-yn-1-yl)-5-vinyloxazolidine-3-carboxylate (**23**)**



Following General Procedure A, the title compound was prepared from *tert*-butyl(2,2,2-trifluoro-1-(penta-1,4-dien-3-yloxy)ethyl)carbamate (**22**) (84 mg, 0.30 mmol, 1 equiv.) and (bromoethynyl)triisopropylsilane (**39**) (93 μ L, 0.39 mmol, 1.3 equiv.). The crude oil was purified by column chromatography (SiO₂, Pentane:DCM 9:1 to 4:1)) affording the title compound **23** (0.090 g, 0.20 mmol, 65% yield, dr > 20:1 in the crude ¹H NMR) as a yellow oil.

Rf 0.4 (Pentane:DCM 4:1).

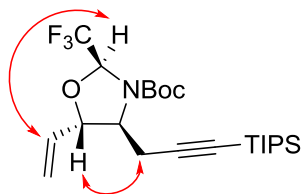
¹H NMR (400 MHz, Acetonitrile-*d*₃) δ 5.93 (ddd, $J = 16.9, 10.4, 6.3$ Hz, 1H, CH=C), 5.61 (q, $J = 5.3$ Hz, 1H, CHCF₃), 5.44 (dt, $J = 17.1, 1.3$ Hz, 1H, CH=CH₂), 5.29 (dt, $J = 10.4, 1.2$ Hz, 1H, CH=CH₂), 4.73 (tt, $J = 5.6, 1.2$ Hz, 1H, OCHCH), 3.82 (ddd, $J = 8.8, 6.5, 4.0$ Hz, 1H, NCHCH₂), 2.80 (dd, $J = 17.1, 4.0$ Hz, 1H, CH₂CC), 2.64 (dd, $J = 17.1, 8.8$ Hz, 1H, CH₂CC), 1.46 (s, 9H, Boc), 1.09 – 1.03 (m, 21H, TIPS).

¹³C NMR (101 MHz, Acetonitrile-*d*₃) δ 154.5, 135.6, 124.0 (q, $J = 285.5$ Hz), 119.6, 104.5, 85.9 (q, $J = 35.2$ Hz), 85.8, 84.3, 82.9, 61.8, 28.2, 24.1, 18.9, 11.9.

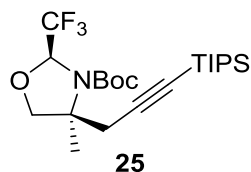
IR ν_{\max} 2944 (m), 2867 (m), 2176 (w), 1721 (s), 1464 (w), 1432 (w), 1370 (m), 1347 (m), 1318 (w), 1290 (m), 1257 (w), 1180 (s), 1161 (s), 1079 (w), 1018 (w), 991 (w), 937 (m), 884 (m), 848 (m).

HRMS (ESI) calcd for C₂₃H₃₈F₃NNaO₃Si⁺ [M+Na]⁺ 484.2465; found 484.2469.

Stereochemistry assigned by ROESY.



***Tert*-butyl-4-methyl-2-(trifluoromethyl)-4-(3-(triisopropylsilyl)prop-2-yn-1-yl)oxazolidine-3-carboxylate (**25**)**



Following General Procedure B, the title compound was prepared from *tert*-butyl (2,2,2-trifluoro-1-((2-methylallyl)oxy)ethyl)carbamate (**24**) (81 mg, 0.30 mmol, 1 equiv.), and (bromoethynyl)triisopropylsilane (**39**) (93 μ L, 0.39 mmol, 1.3 equiv.). The crude oil was purified by column chromatography (SiO₂, Pentane:DCM 4:1) affording the title compound **25** (0.081 g, 0.18 mmol, 60 % yield, dr of 80:20 in the crude and the pure ¹H NMR) as a yellow oil.

R_f 0.35 (Pentane:DCM 4:1).

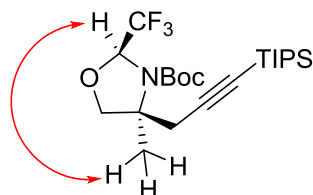
¹H NMR (400 MHz, Acetonitrile-*d*₃) major diastereoisomer δ 5.59 (q, *J* = 5.4 Hz, 1H, *CHCF*₃), 4.25 (d, *J* = 8.6 Hz, 1H, *OCH*₂), 4.04 (d, *J* = 8.8 Hz, 1H, *OCH*₂), 3.01 (bs, 1H, *CH*₂CC), 2.72 (d, *J* = 17.0 Hz, 1H, *CH*₂CC), 1.53 (s, 3H, Me), 1.46 (s, 9H, Boc), 1.07 (m, 21H, TIPS), minor diastereoisomer δ 5.59 (q, *J* = 5.4 Hz, 1H, *CHCF*₃), 4.34 (d, *J* = 8.4 Hz, 1H, *OCH*₂), 4.04 (d, *J* = 8.8 Hz, 1H, *OCH*₂), 3.01 (bs, 1H, *CH*₂CC), 2.65 (d, *J* = 17.0 Hz, 1H, *CH*₂CC), 1.53 (s, 3H, Me), 1.46 (s, 9H, Boc), 1.07 (m, 21H, TIPS).

¹³C NMR (101 MHz, Acetonitrile-*d*₃) major diastereoisomer δ 154.1, 124.5 (q, *J* = 288.0 Hz), 104.9, 86.8 (q, *J* = 34.6 Hz), 83.8, 82.6, 79.9, 63.2, 29.6, 28.3, 18.9, 12.1, 12.0.

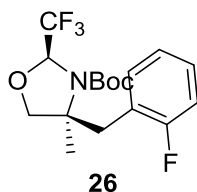
IR ν_{max} 2947 (m), 2868 (m), 2176 (w), 1718 (s), 1464 (w), 1361 (s), 1314 (w), 1285 (w), 1169 (s), 1156 (s), 1068 (m), 1031 (w), 964 (w), 915 (w), 877 (w), 851 (w).

HRMS (ESI) calcd for C₂₂H₃₈AgF₃NO₃Si⁺ [*M*+Ag]⁺ 556.1618; found 556.1625.

Stereochemistry assigned by ROESY.



***Tert*-butyl-4-(2-fluorobenzyl)-4-methyl-2-(trifluoromethyl)oxazolidine-3-carboxylate (**26**)**



Following General Procedure C, the title compound was prepared from *tert*-butyl (2,2,2-trifluoro-1-((2-methylallyl)oxy)ethyl)carbamate (**24**) (81 mg, 0.30 mmol, 1 equiv.), and 1-bromo-2-fluorobenzene (**9**) (49 μ L, 0.45 mmol, 1.5 equiv.). The crude oil was purified by column chromatography (SiO₂, Pentane:DCM 7:3) affording the title compound **26** (0.066 g, 0.18 mmol, 61 % yield, dr > 20:1 in the crude ¹H NMR) as a yellow oil.

R_f 0.34 (Pentane:DCM 7:3).

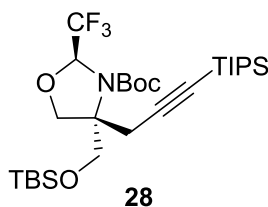
¹H NMR (400 MHz, Acetonitrile-*d*₃) δ 7.30 – 7.23 (m, 2H, ArH), 7.11 – 7.02 (m, 2H, ArH), 5.51 (bs, 1H, CHCF₃), 4.05 (s, 1H, OCH₂C_q), 3.85 (d, *J* = 8.8 Hz, 1H, OCH₂C_q), 3.24 (bs, 2H, CH₂C_{Ar}), 1.49 (s, 9H, Boc), 1.47 (s, 3H, Me).

¹³C NMR (101 MHz, Acetonitrile-*d*₃) δ 162.3 (d, *J* = 242.7 Hz), 152.8, 133.4 (d, *J* = 4.4 Hz), 129.4 (d, *J* = 8.3 Hz), 124.7 (d, *J* = 3.5 Hz), 124.2 (d, *J* = 15.7 Hz), 123.8 (q, *J* = 287.9 Hz), 115.6 (d, *J* = 23.1 Hz), 85.9 (q, *J* = 28.6 Hz), 82.2, 77.5, 64.5, 34.5, 27.9, 23.6.

IR ν_{max} 2980 (w), 2938 (w), 1713 (s), 1620 (w), 1587 (w), 1492 (m), 1458 (w), 1359 (s), 1326 (w), 1286 (m), 1232 (w), 1163 (s), 1146 (s), 1114 (w), 1036 (w), 956 (m), 871 (w), 846 (m), 812 (w).

HRMS (ESI) calcd for C₁₇H₂₁F₄NNaO₃⁺ [M+Na]⁺ 386.1350; found 386.1355.

***Tert*-butyl(2*S*,4*S*)-4-(((*tert*-butyldimethylsilyl)oxy)methyl)-2-(trifluoromethyl)-4-(3-(triisopropylsilyl)prop-2-yn-1-yl)oxazolidine-3-carboxylate (**28**)**



Following General Procedure B, the title compound was prepared from *tert*-butyl (1-((2-(((*tert*-butyldimethylsilyl)oxy)methyl)allyl)oxy)-2,2,2-trifluoroethyl)carbamate (**27**) (120 mg, 0.300 mmol, 1 equiv.), and (bromoethynyl)triisopropylsilane (**39**) (93 μ L, 0.39 mmol, 1.3 equiv.). The crude oil was purified by column chromatography (SiO₂, Pentane:DCM 4:1) affording the title compound **28** (0.099 g, 0.17 mmol, 57 % yield, dr of 73:27 in the crude and the pure ¹H NMR) as a yellow oil.

R_f 0.38 (Pentane:DCM 4:1).

¹H NMR (400 MHz, Acetonitrile-*d*₃) major diastereoisomer δ 5.52 (s, 1H, *CHCF*₃), 4.36 – 4.21 (m, 2H, *TBSOCH*₂), 3.86 (d, *J* = 10.1 Hz, 2H, *OCH*₂*C*_q), 2.68 (d, *J* = 17.2 Hz, 2H, *CH*₂*CC*), 1.44 (s, 9H, Boc), 1.05 (m, *J* = 3.6 Hz, 21H, TIPS), 0.88 (s, 9H, TBS), 0.05 (s, 6H, TBS); minor diastereoisomer δ 5.52 (s, 1H, *CHCF*₃), 4.37 – 4.17 (m, 3H, *OCH*₂*C*_q and *TBSOCH*₂), 4.02 (s, 1H, *OCH*₂*C*_q), 2.98 (d, *J* = 17.3 Hz, 1H, *CH*₂*CC*), 2.86 (d, *J* = 17.8 Hz, 1H, *CH*₂*CC*), 1.44 (s, 9H, Boc), 1.12 – 0.93 (m, 21H, TIPS), 0.88 (s, 9H, TBS), 0.05 (s, 6H, TBS).

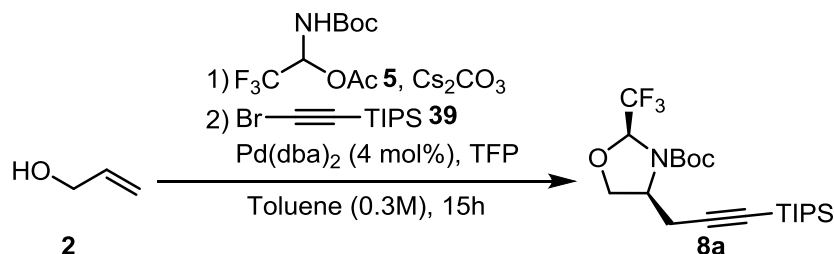
¹³C NMR (101 MHz, Acetonitrile-*d*₃) major diastereoisomer δ 152.5, 124.6 (q, *J* = 287.8 Hz), 104.3, 87.7 (t, *J* = 32.9 Hz), 84.2, 82.5, 77.3, 65.8, 63.7, 28.4, 26.1, 18.9, 18.7, 12.0, -5.3, -5.4; minor diastereoisomer **¹³C NMR (101 MHz, Acetonitrile-*d*₃)** δ 153.8, 130.0 – 119.7 (m), 104.3, 87.7 (t, *J* = 33.0 Hz), 84.2, 82.5, 78.3, 66.8, 63.7, 28.4, 26.1, 18.9, 18.7, 12.0, -5.3, -5.4.

IR ν_{max} 2942 (m), 2894 (w), 2865 (m), 2718 (w), 2175 (w), 1718 (s), 1468 (w), 1367 (m), 1326 (w), 1281 (w), 1257 (w), 1170 (s), 1115 (m), 1060 (w), 1020 (m), 975 (w), 936 (w), 885 (w), 838 (s).

HRMS (ESI) calcd for C₂₈H₅₂F₃NNaO₄Si₂⁺ [M+Na]⁺ 602.3279; found 602.3285.

8) In Situ Tether Formation and Pd-catalyzed and Carboamination of Allylalcohols

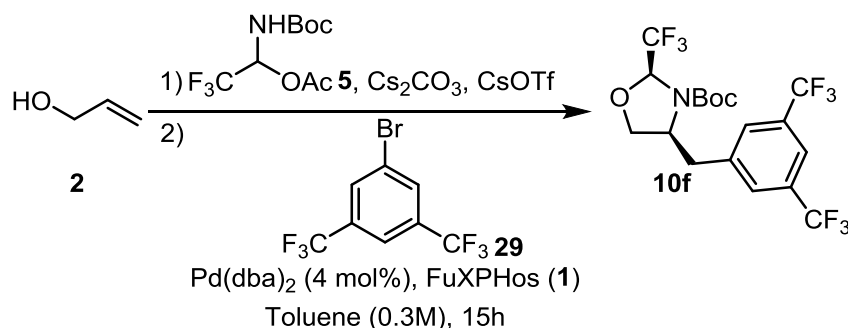
Tert-butyl-2-(trifluoromethyl)-4-(3-(triisopropylsilyl)prop-2-yn-1-yl)oxazolidine-3-carboxylate (**8a**)



To an oven-dried 5 mL microwave tube under nitrogen atmosphere were added 1-((*tert*-butoxycarbonyl)amino)-2,2,2-trifluoroethyl acetate (**5**) (0.085 g, 0.33 mmol, 1.1 equiv.) and cesium carbonate (225 mg, 0.690 mmol, 2.3 equiv.). The tube was sealed, evacuated and backfilled with nitrogen (this was repeated for a total of 3 times). Then dry degassed toluene was added (0.69 mL) followed by prop-2-en-1-ol (**2**) (0.020 mL, 0.3 mmol, 1 equiv.). The resulting mixture was stirred for 3h at 35 °C. Then (bromoethynyl)triisopropylsilane (**39**) (102 mg, 0.390 mmol, 1.3 equiv.) and a 0.3 mL stock solution containing $\text{Pd}(\text{dba})_2$ (6.90 mg, 12.0 μmol , 0.04 equiv.) and Tri(2-furyl)phosphine (8.36 mg, 0.036 mmol, 0.12 equiv.) in toluene were added via syringe. The resulting mixture was stirred for 15 h at 75 °C, then cooled down, filtered over silica eluting with Et_2O and concentrated under reduced pressure. The crude residue was then purified by column chromatography (SiO_2 , Pentane:DCM 7:3 to 3:2) affording the title compound **8a** (0.083 g, 0.19 mmol, 64% yield, dr > 20:1 in the crude ^1H NMR) as a yellow oil.

Characterisation as previously described.

Tert-butyl-4-(3,5-bis(trifluoromethyl)benzyl)-2-(trifluoromethyl)oxazolidine-3-carboxylate (**10f**)



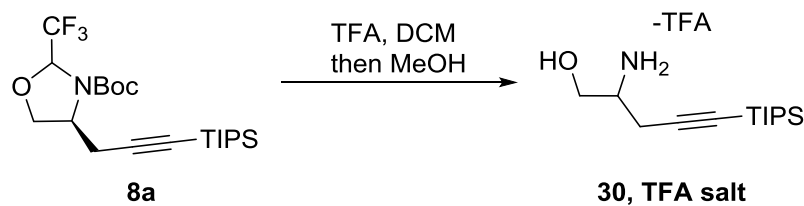
To an oven-dried microwave vial under nitrogen atmosphere were added 1-((*tert*-butoxycarbonyl)amino)-2,2,2-trifluoroethyl acetate (**5**) (0.089 g, 0.35 mmol, 1.15 equiv.), cesium trifluoromethanesulfonate (0.102 g, 0.360 mmol, 1.2 equiv.) and cesium carbonate

(0.244 g, 0.750 mmol, 2.5 equiv.). The tube was fitted with a rubber septum, sealed with electrical tape and evacuated and back-filled with nitrogen (this process was repeated a total of three times). Then prop-2-en-1-ol (**2**) (20 μ L, 0.3 mmol, 1 equiv.), 1-bromo-3,5-bis(trifluoromethyl)benzene (**29**) (78 μ L, 0.45 mmol, 1.5 equiv.) and Toluene (0.69 mL) were added. The resulting mixture was stirred for 3h at 35 °C. Then a 0.3 mL stock solution containing Pd(dba)₂ (6.90 mg, 12.0 μ mol, 0.04 equiv.) and Di(furan-2-yl)(2',4',6'-triisopropyl-[1,1'-biphenyl]-2-yl)phosphine (**1**) (0.016 g, 0.036 mmol, 0.12 equiv.) in toluene were added via syringe. The resulting mixture was stirred for 15 h at 75 °C, then cooled down, filtered over silica eluting with Et₂O and concentrated under reduced pressure. The crude residue was then purified by column chromatography (SiO₂, Pentane:EtOAc 98:2 to 95:5) affording the title compound **10f** (0.087 g, 0.19 mmol, 62% yield, dr > 20:1 in the crude ¹H NMR) as a yellow oil.

Characterisation as previously described.

9) Tether Removal

1-Hydroxy-5-(triisopropylsilyl)pent-4-yn-2-aminium 2,2,2-trifluoroacetate (**30**)



A solution of (2R,4R)-*tert*-butyl 2-(trifluoromethyl)-4-(3-(triisopropylsilyl)prop-2-yn-1-yl)oxazolidine-3-carboxylate (**8a**) (0.13 g, 0.30 mmol, 1 equiv.) in DCM (1.88 mL) was treated with TFA (0.69 mL) at 0 °C and then stirred at rt for 3 h. Then dry methanol (1 mL) was added to the reaction mixture and it was left stirring for 12 h. The volatiles were removed under reduced pressure. The residue was further dried by co-evaporation with toluene to afford the pure title compound **30** (111 mg, 0.300 mmol, quantitative yield) as a brown solid.

m.p = 107-108 °C.

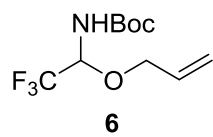
¹H NMR (400 MHz, Acetonitrile-*d*₃) δ 7.53 (bs, 3H, NH₃⁺), 4.04 (dd, *J* = 12.2, 3.5 Hz, 1H, HOCH₂), 3.91 (dd, *J* = 12.2, 6.3 Hz, 1H, HOCH₂), 3.60 (dtd, *J* = 7.7, 6.2, 3.5 Hz, 1H, NH₃CH), 2.83 (m, 2H, CH₂CC), 1.24 (m, 21H, TIPS).

¹³C NMR (101 MHz, Acetonitrile-*d*₃) δ 162.4 (q, *J* = 35.4 Hz), 117.5 (q, *J* = 291.5 Hz), 102.8, 85.4, 60.9, 53.4, 21.1, 18.9, 11.9.

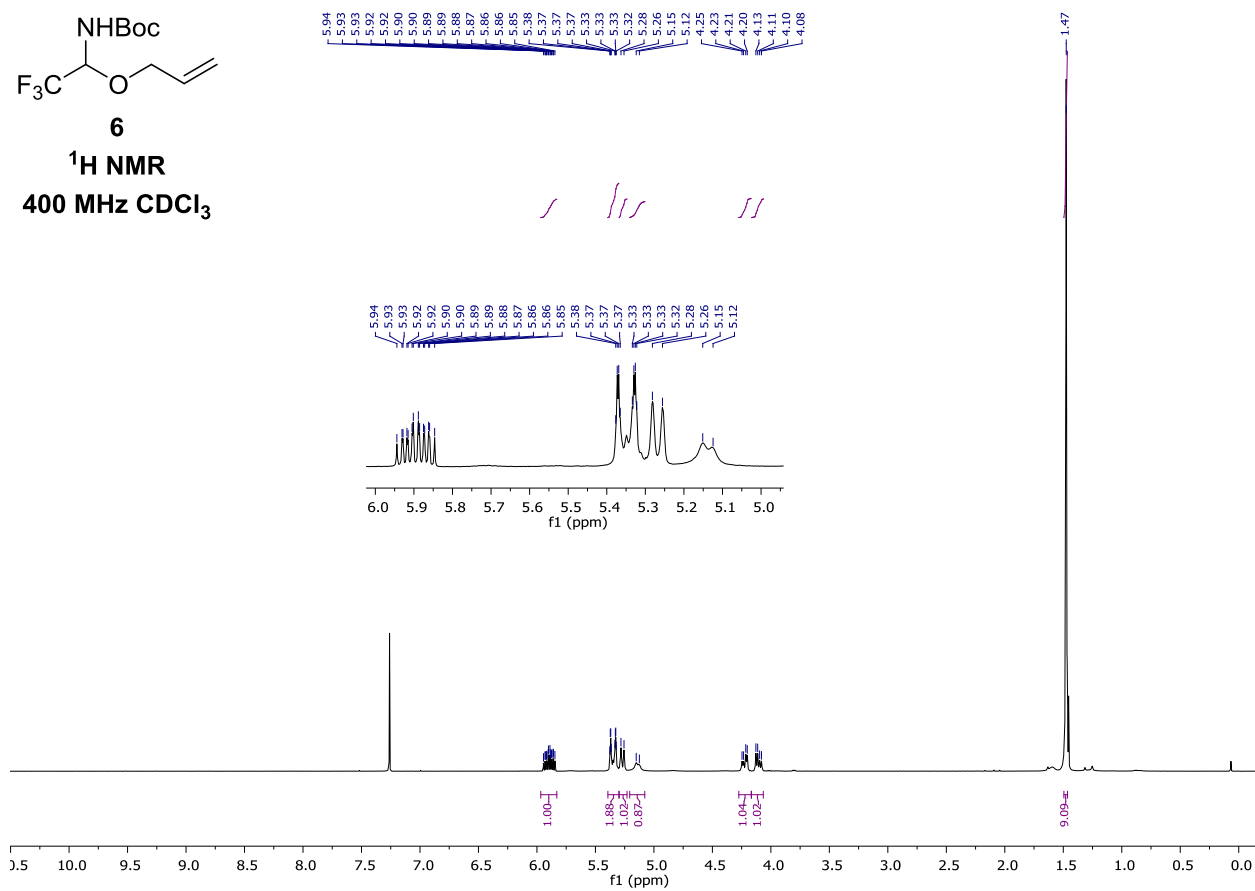
IR ν_{\max} 3237 (w), 3189 (w), 2956 (w), 2941 (w), 2865 (w), 2183 (w), 1677 (s), 1528 (w), 1462 (w), 1374 (w), 1183 (s), 1142 (s), 1030 (w), 995 (w), 884 (w), 844 (w).

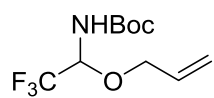
HRMS (ESI) calcd for C₁₄H₃₀NOSi [M⁺] 256.2091; found 256.2092.

10) Spectra of new compounds (¹H NMR, ¹³C NMR, IR)



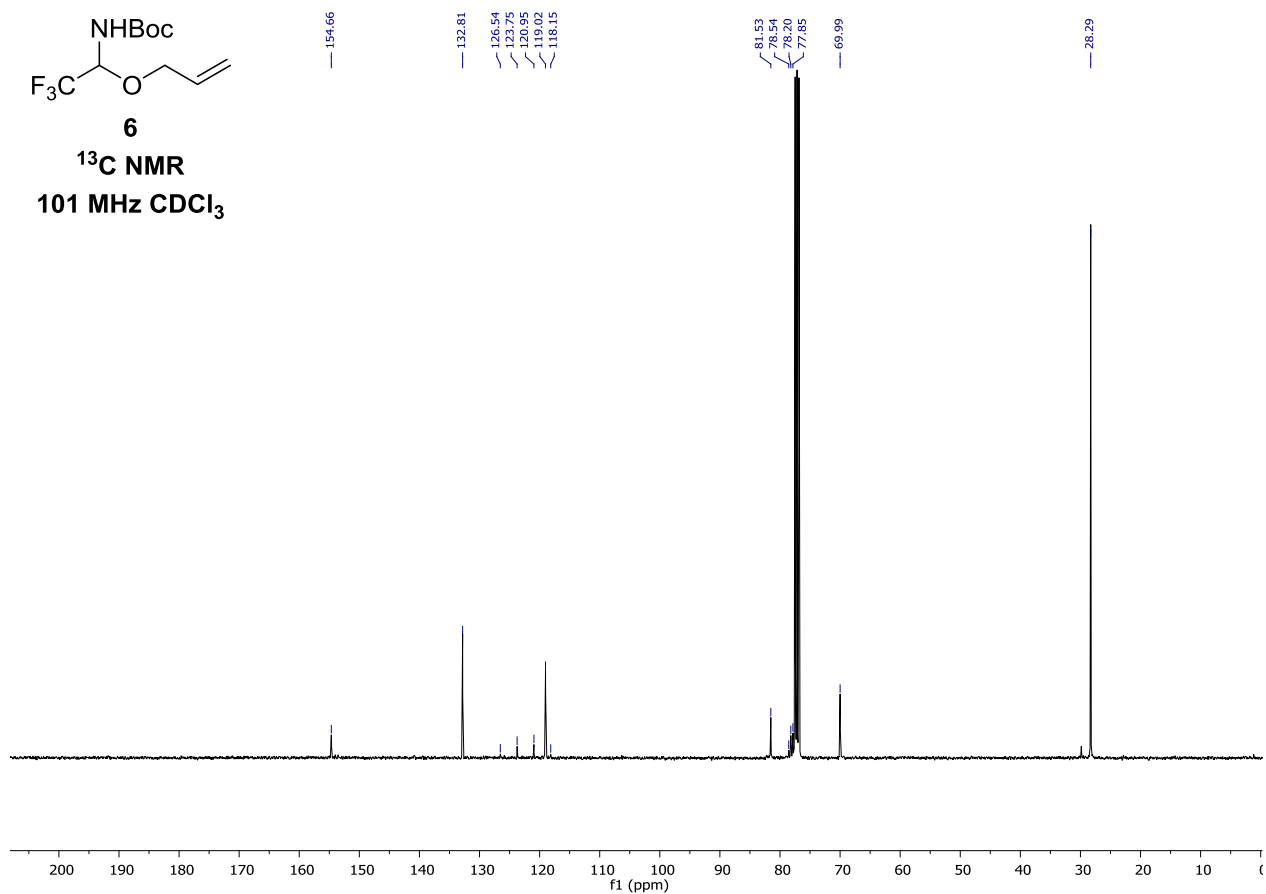
¹H NMR
400 MHz CDCl₃

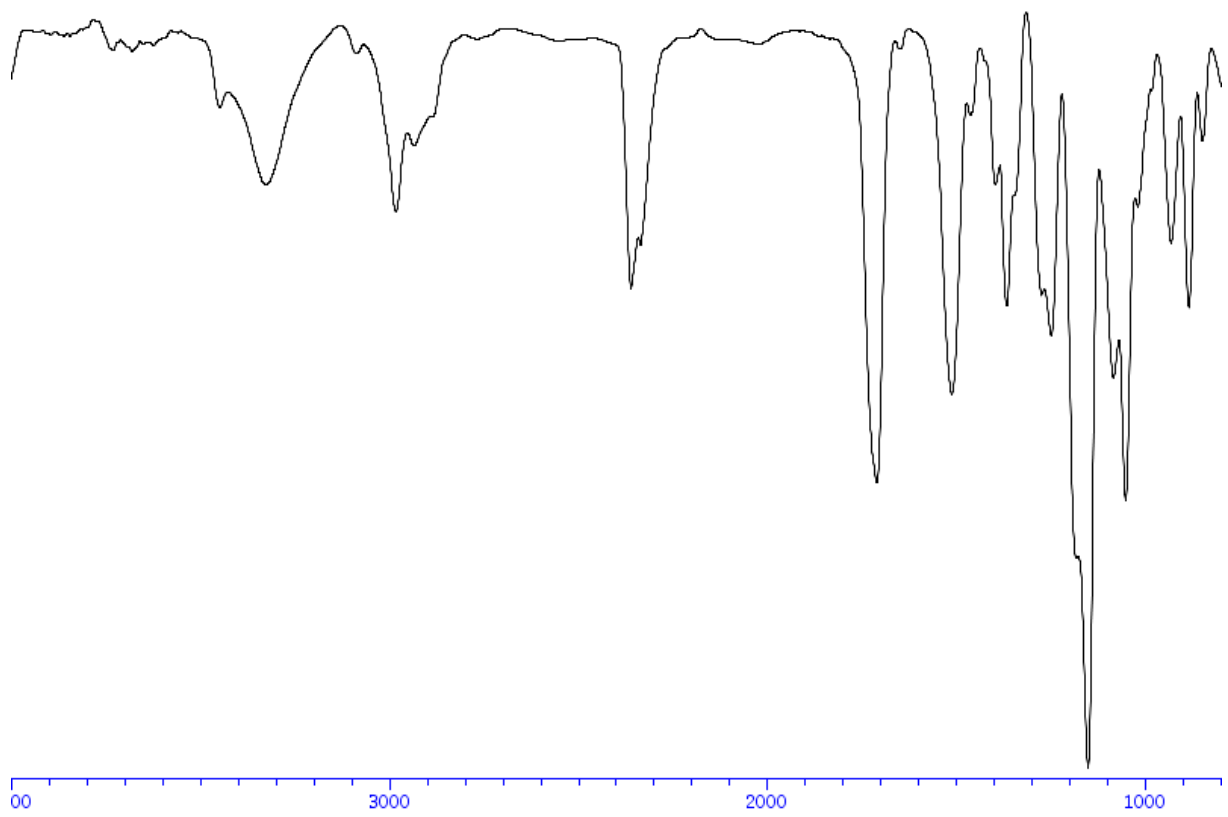


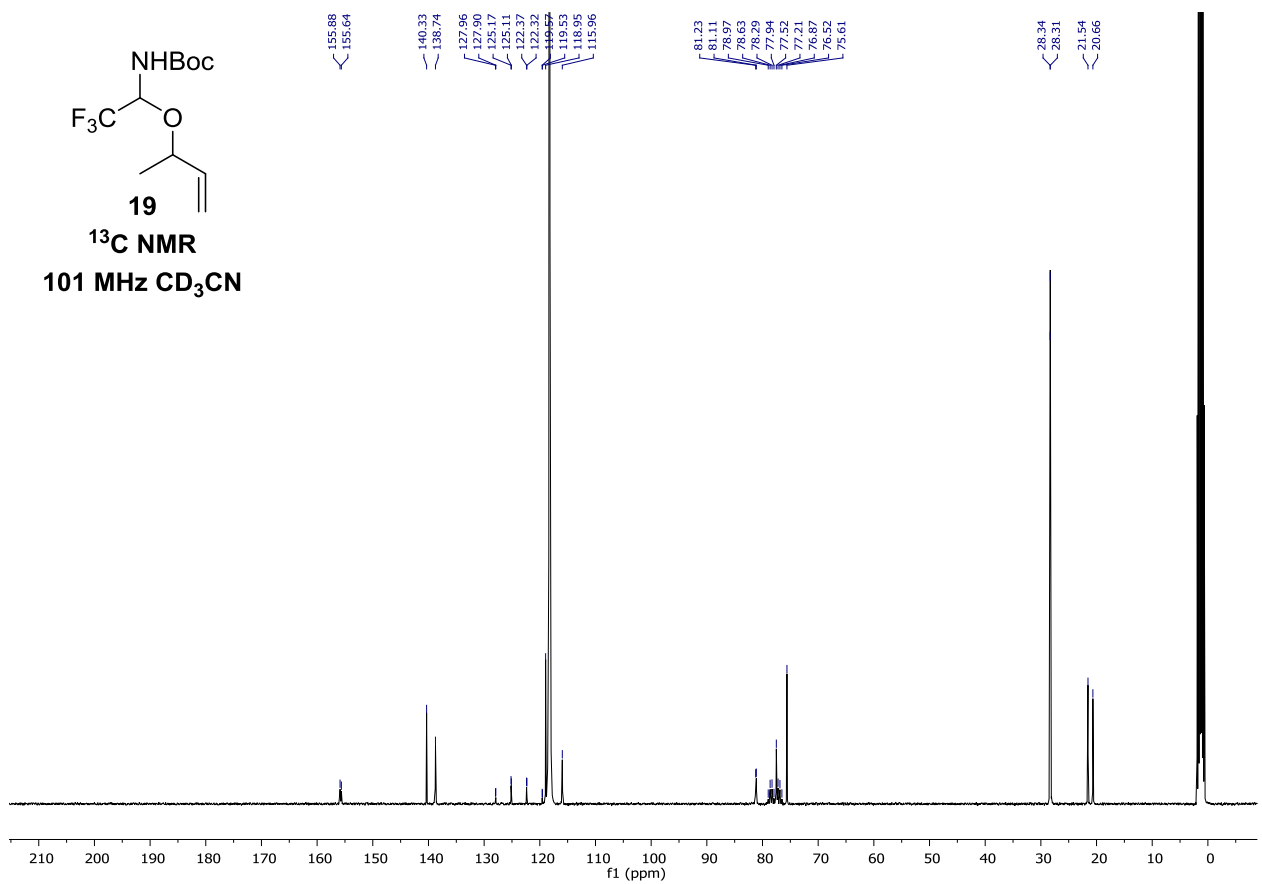
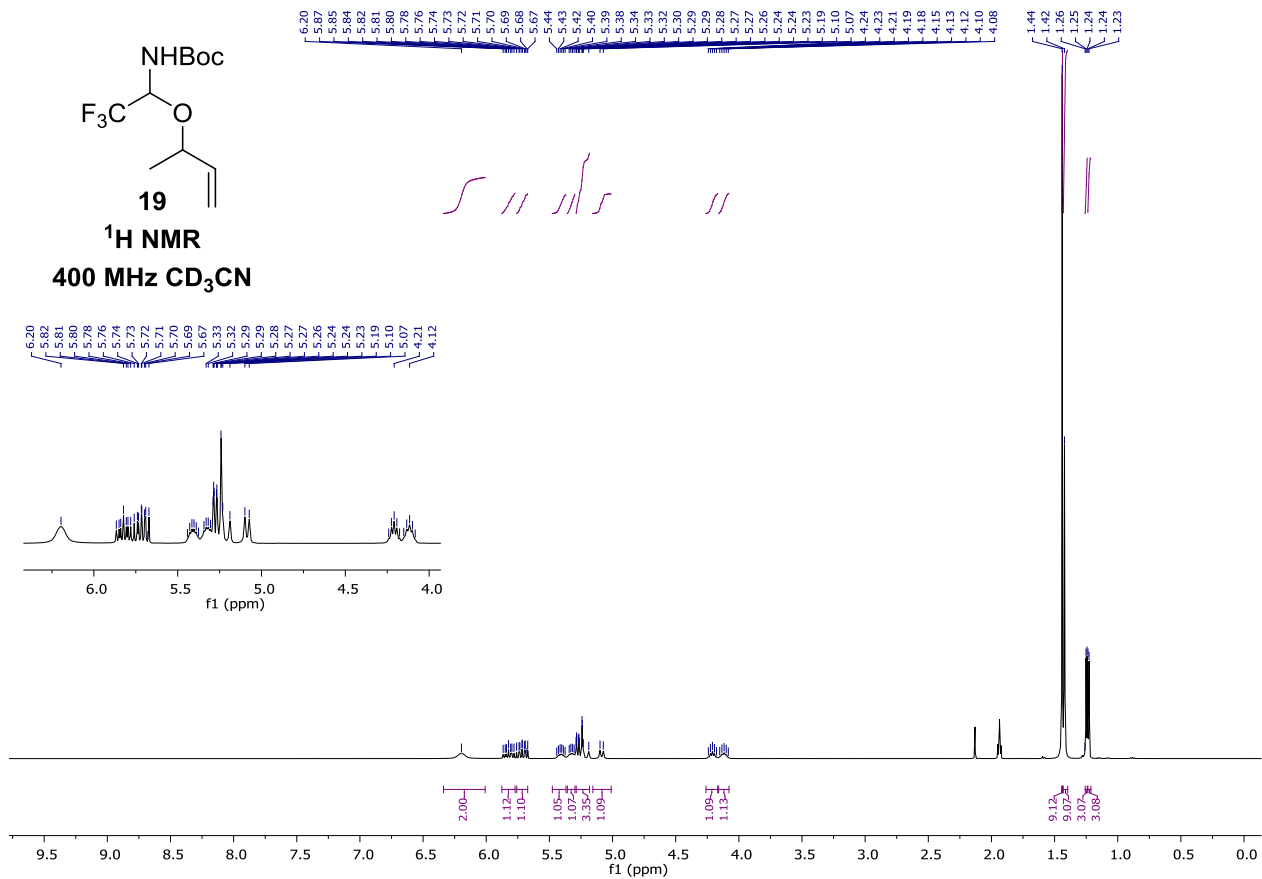


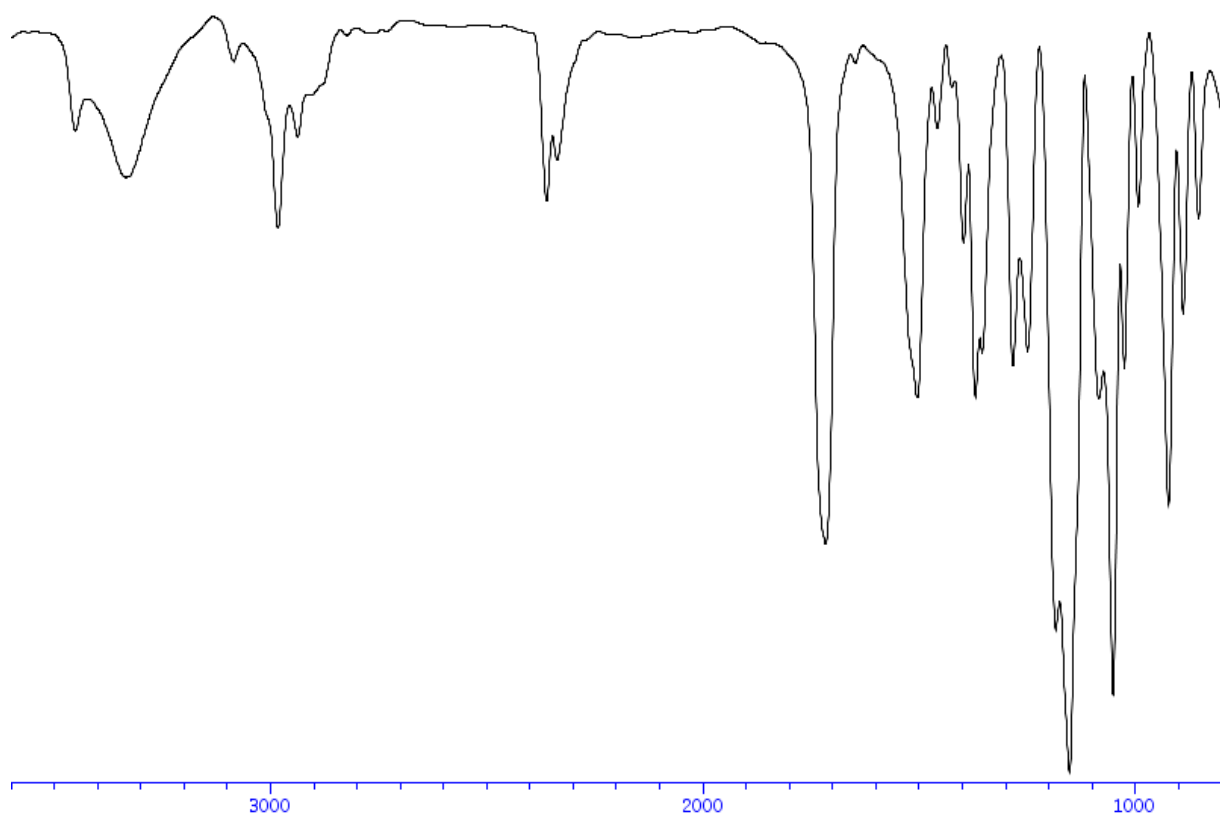
6

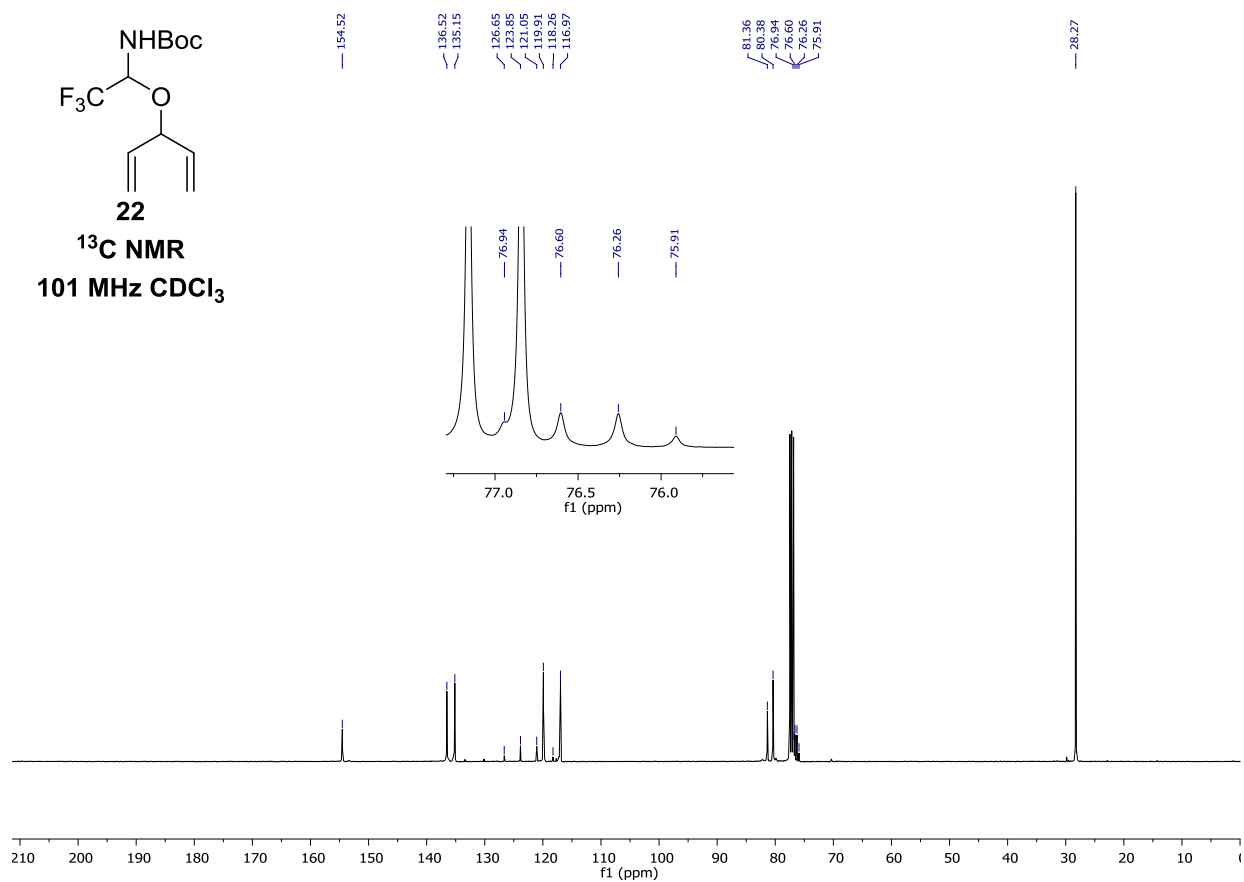
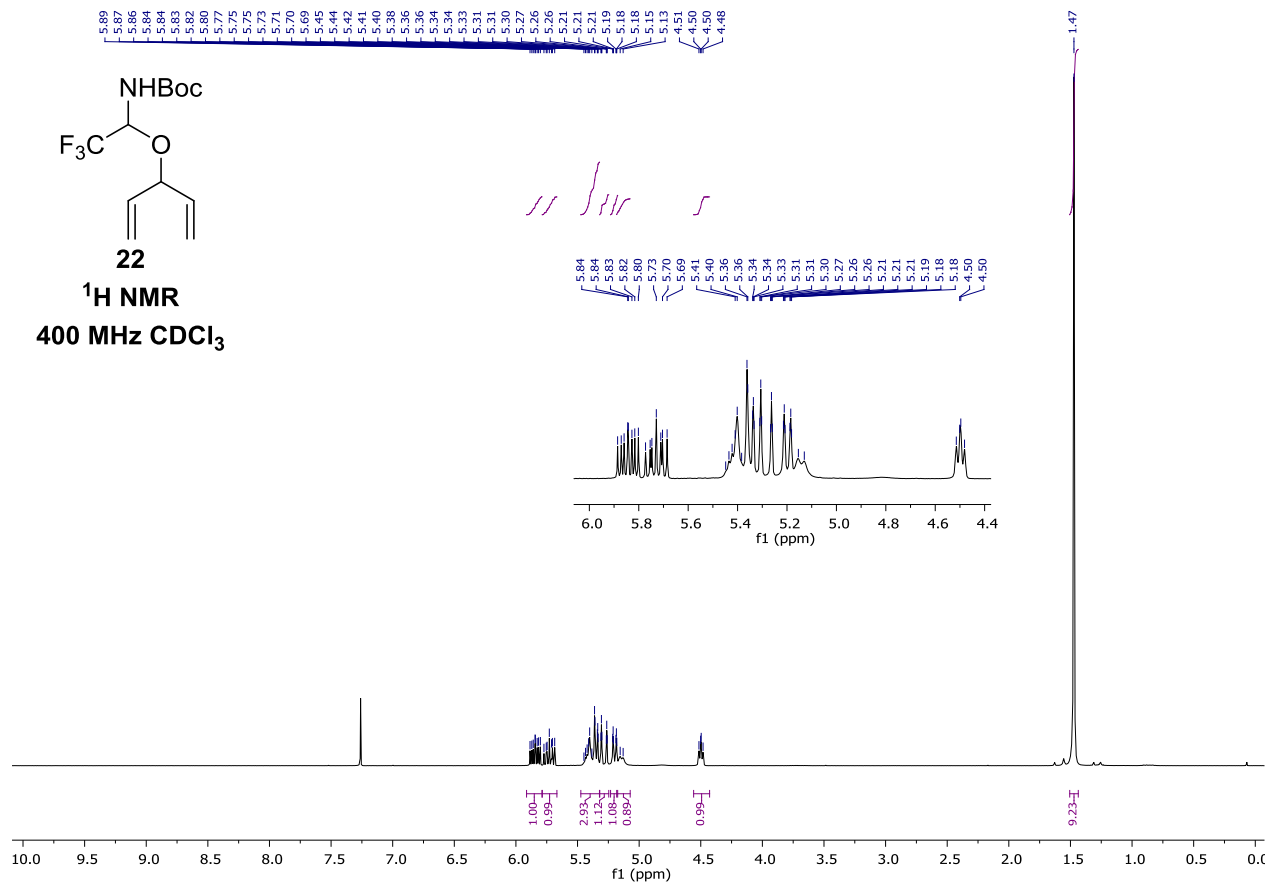
¹³C NMR
101 MHz CDCl₃

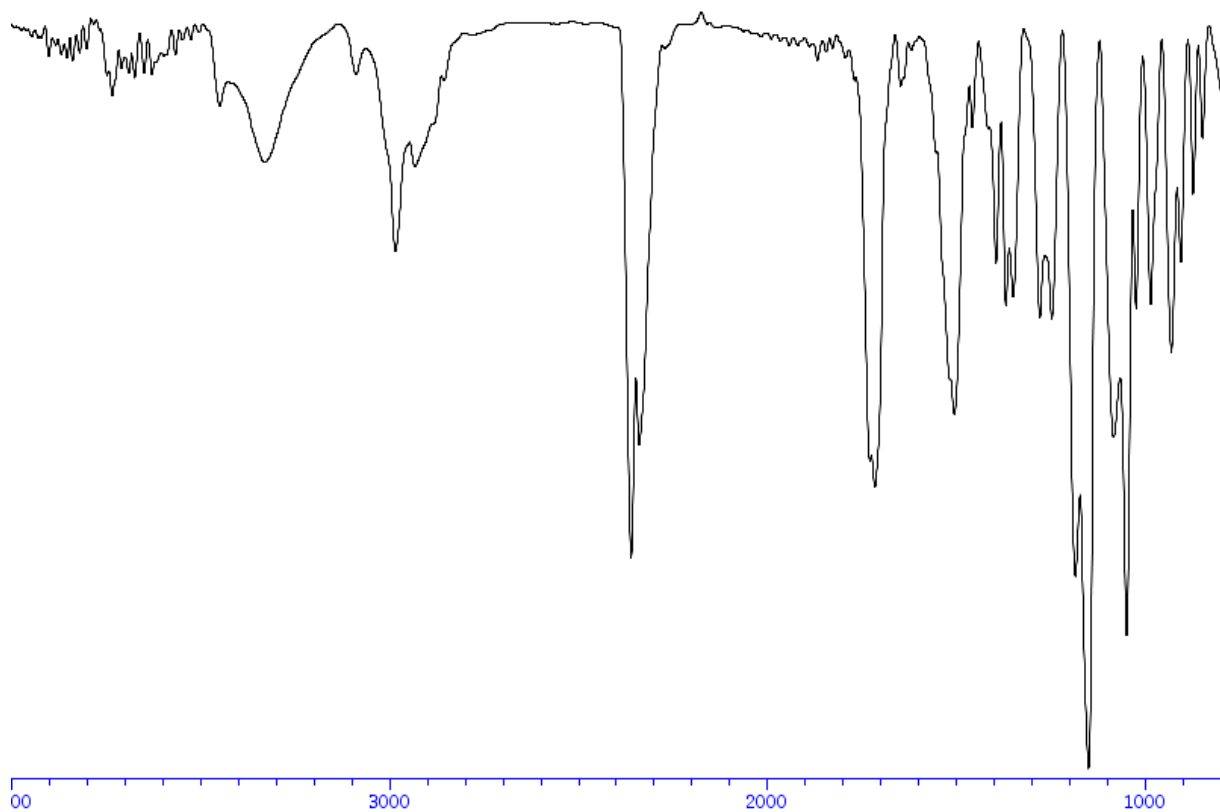


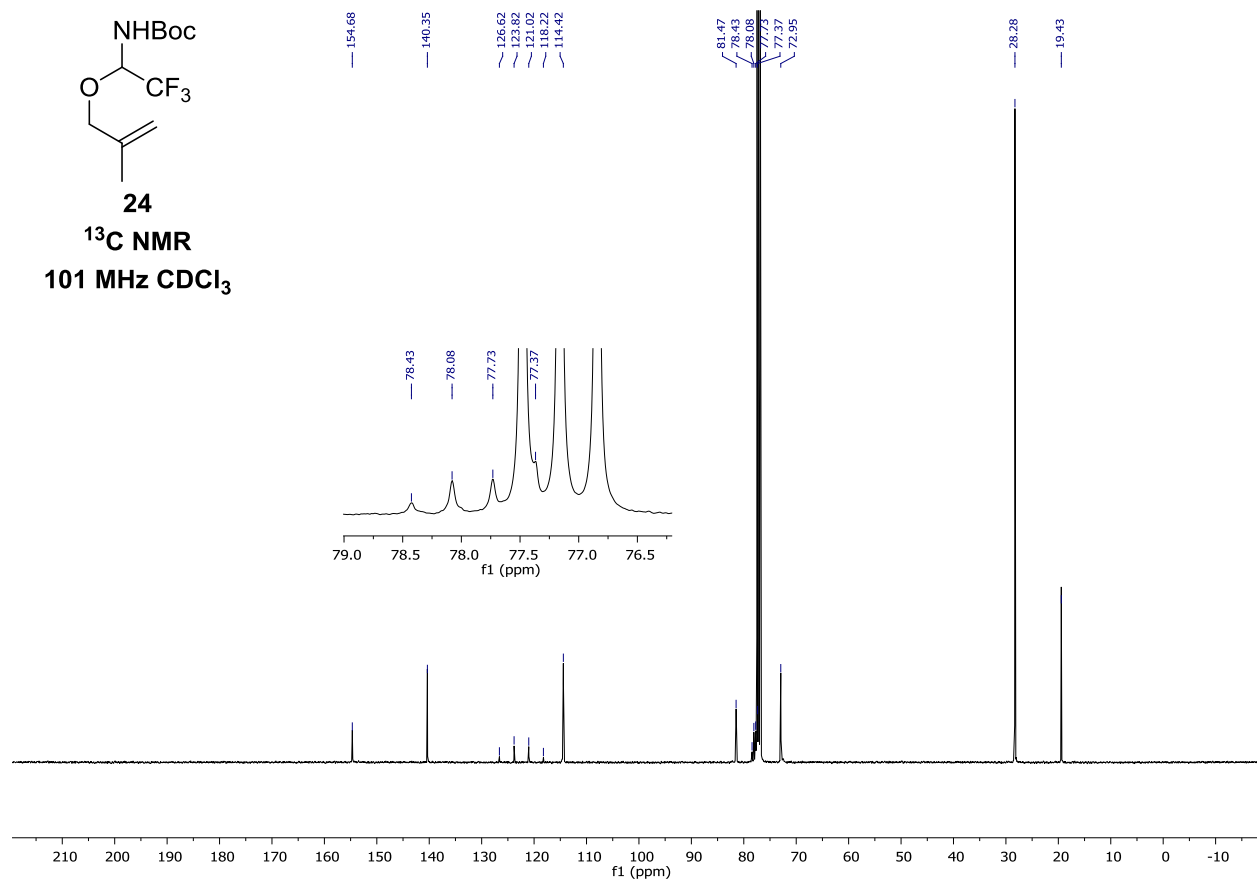
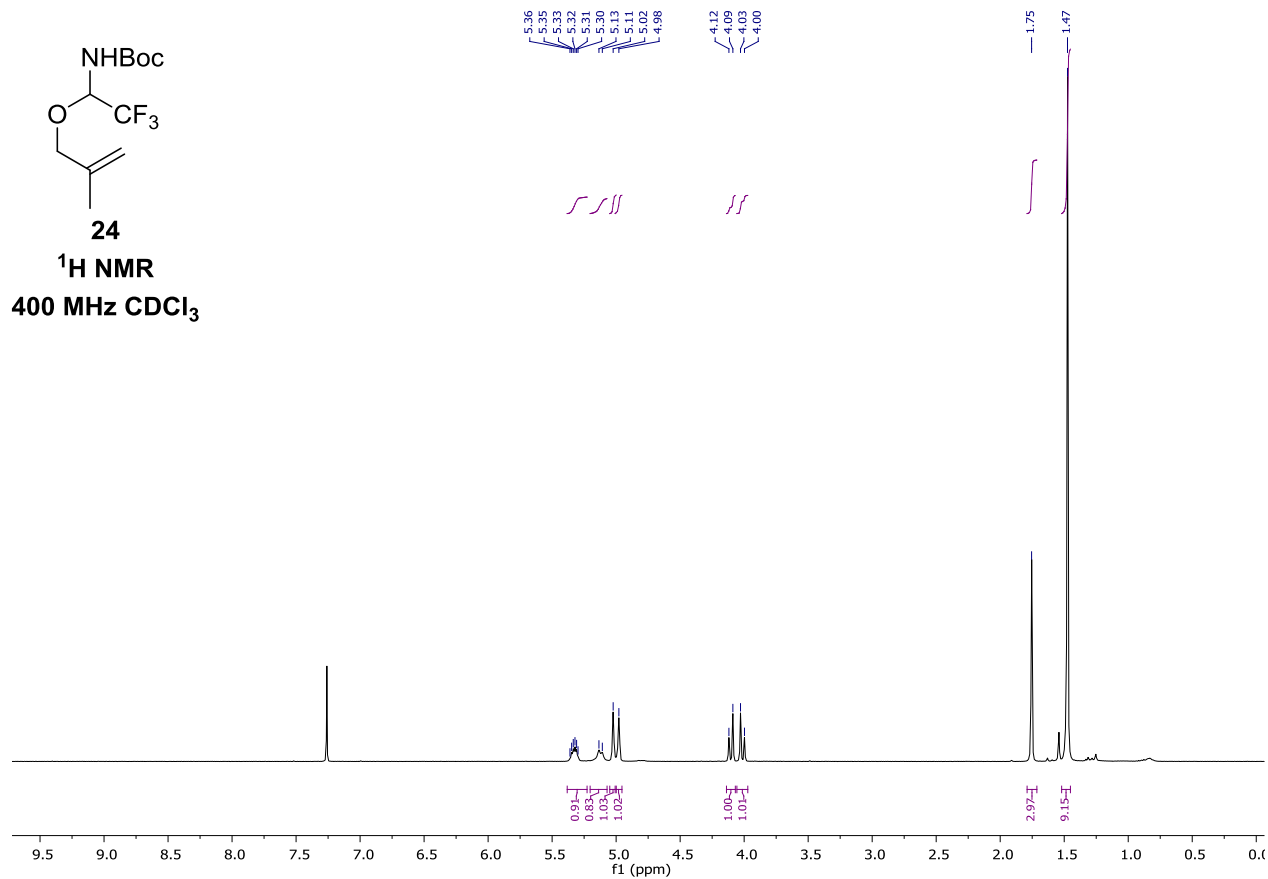


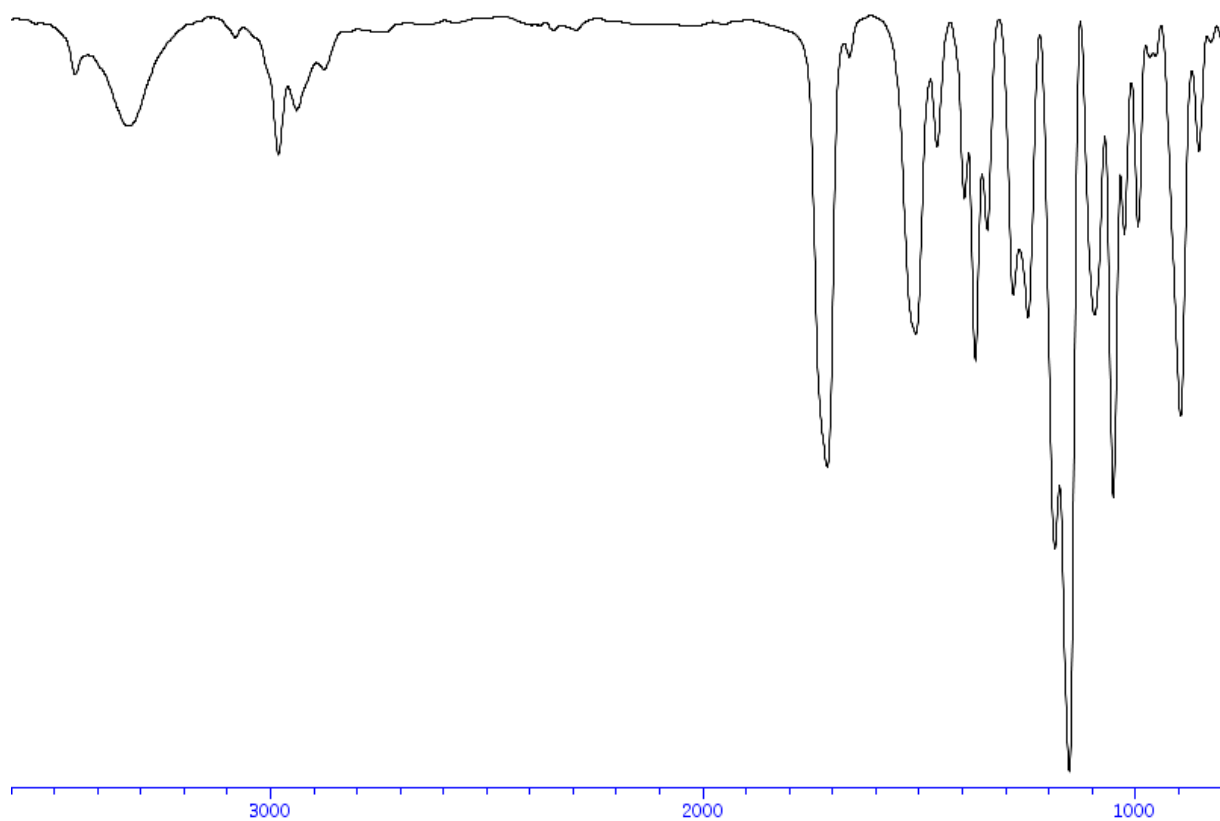


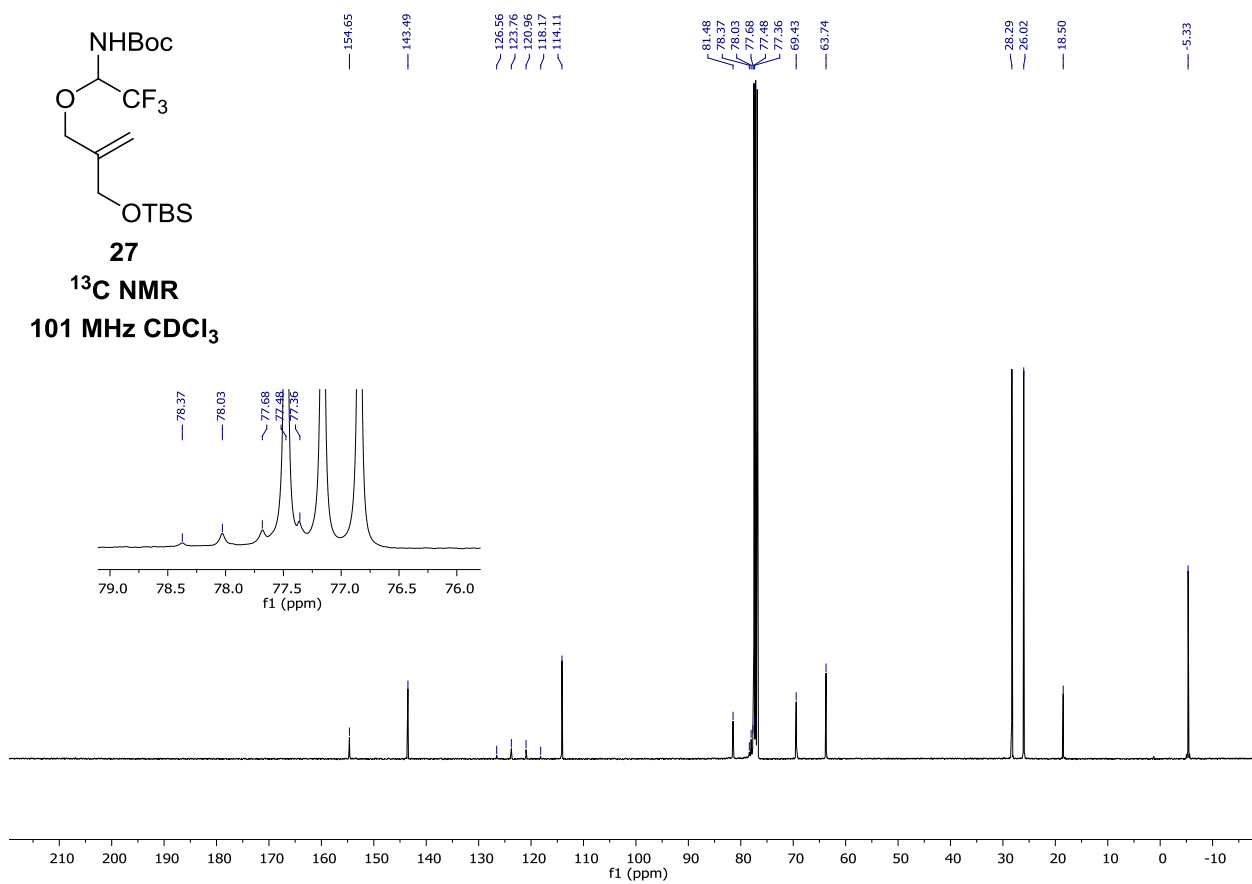
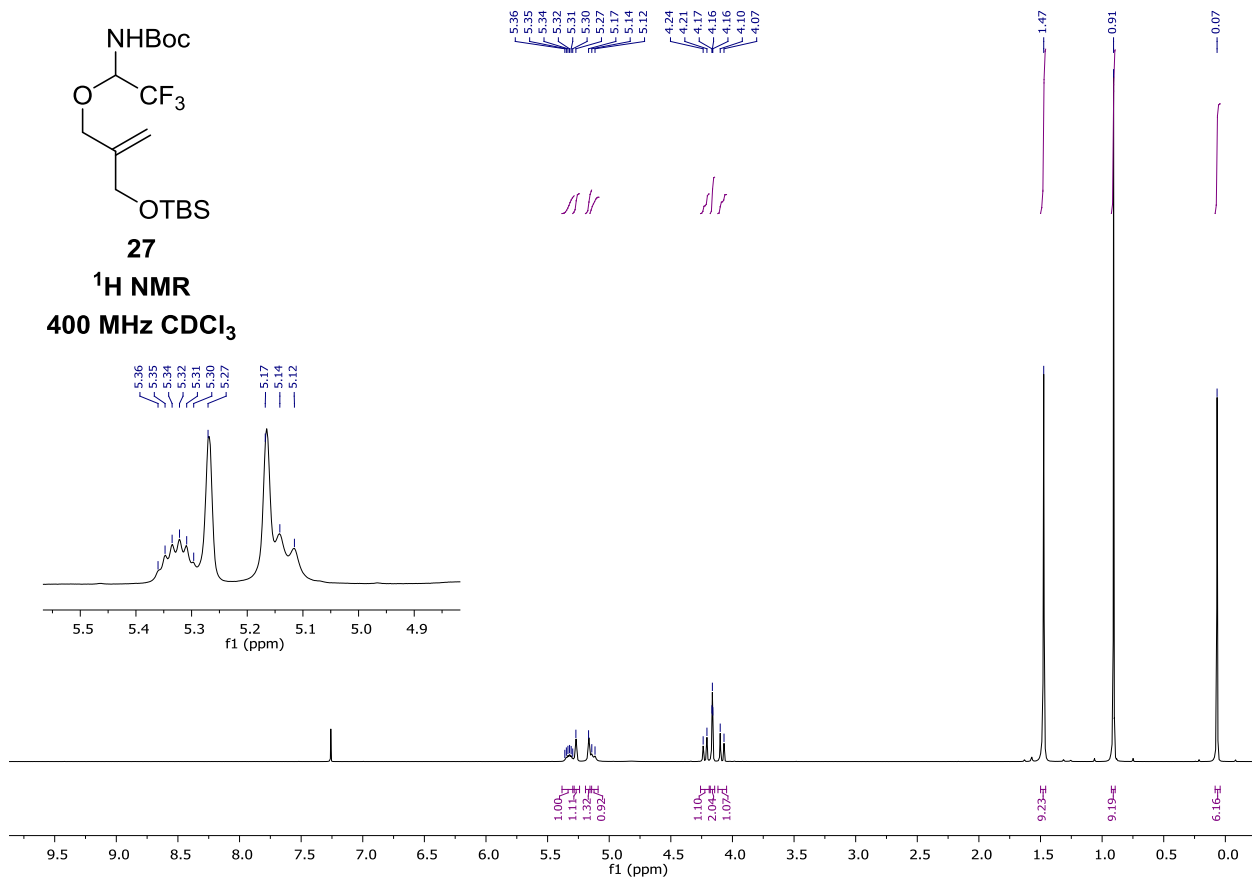


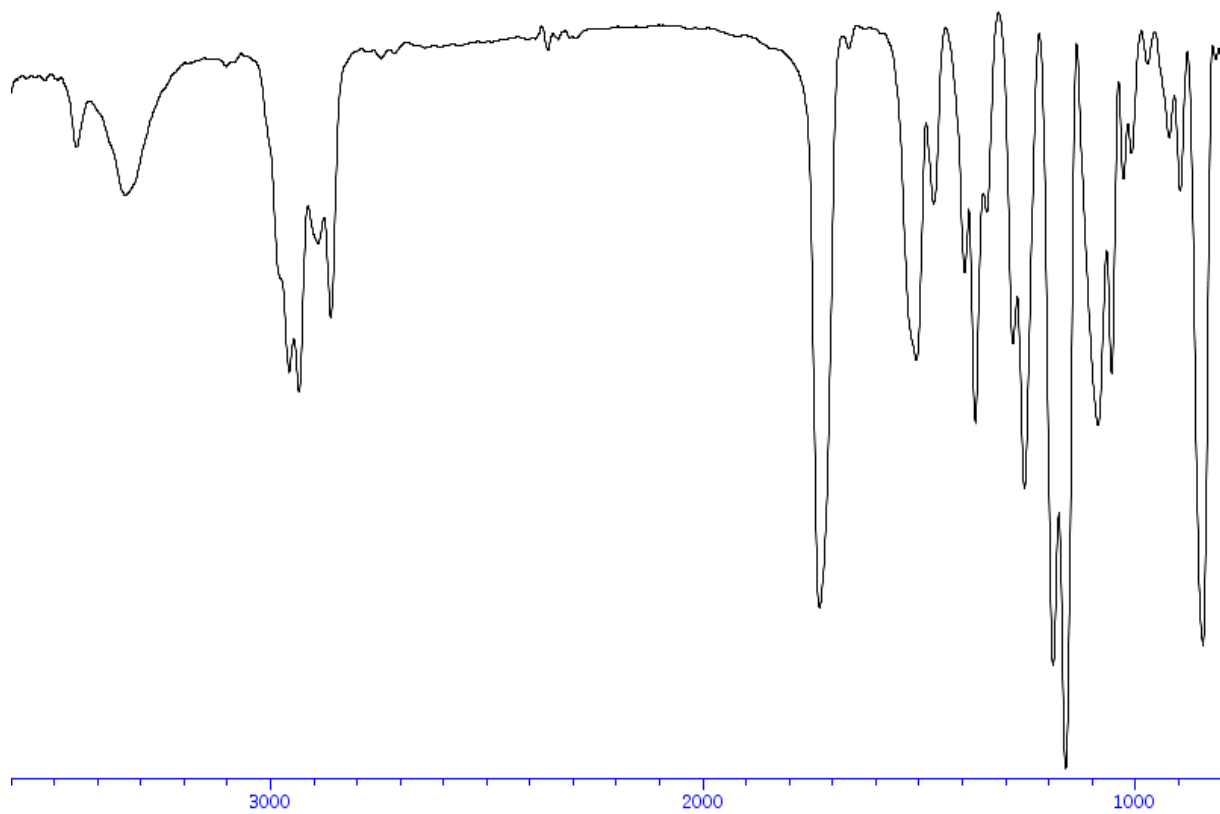


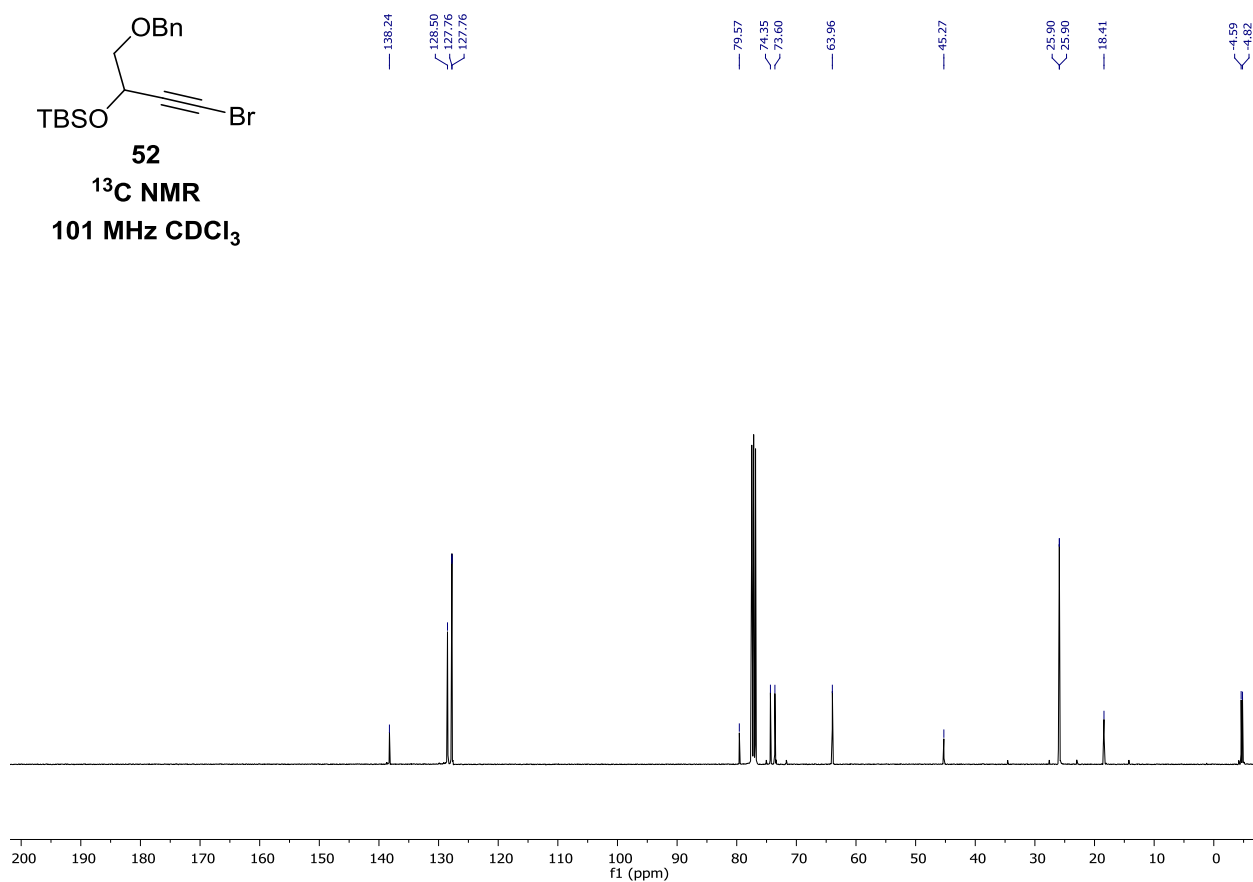
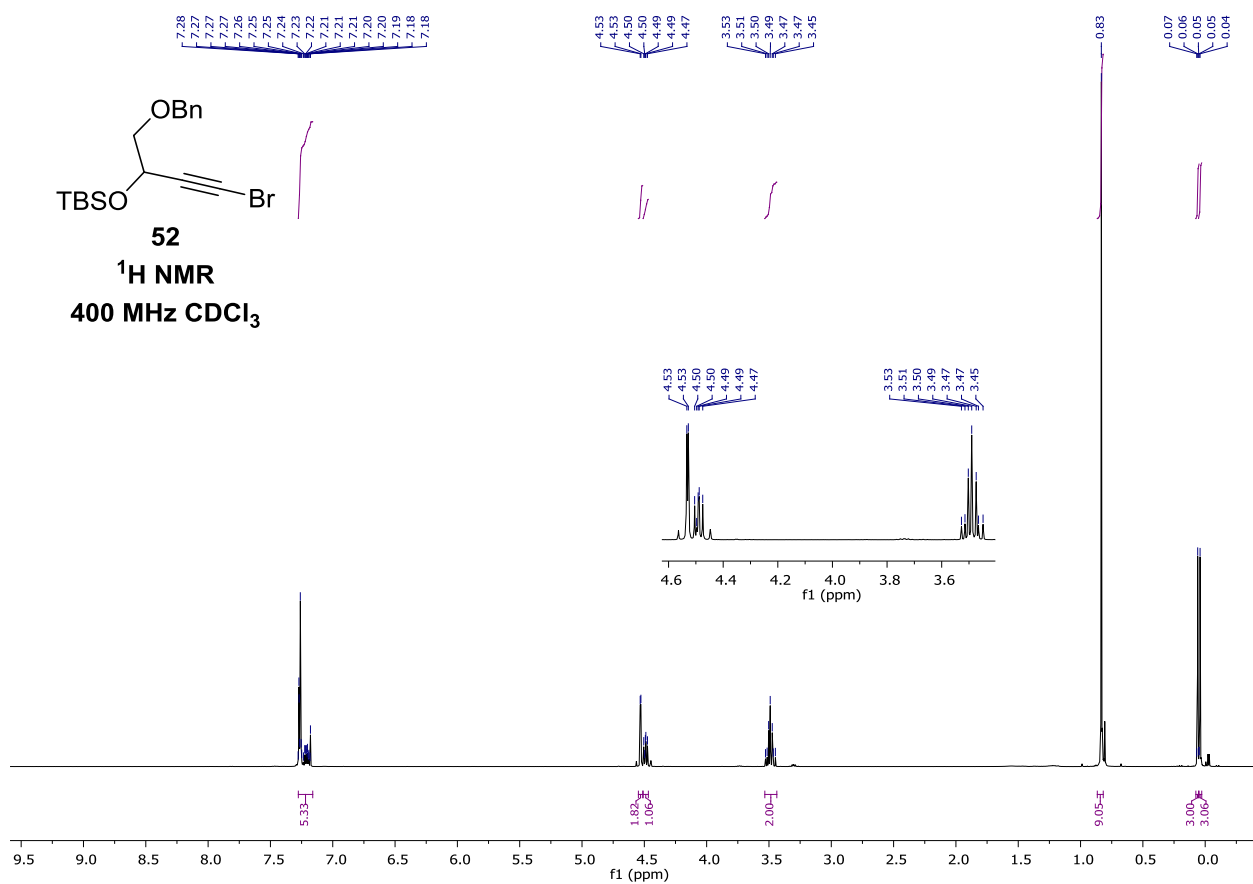


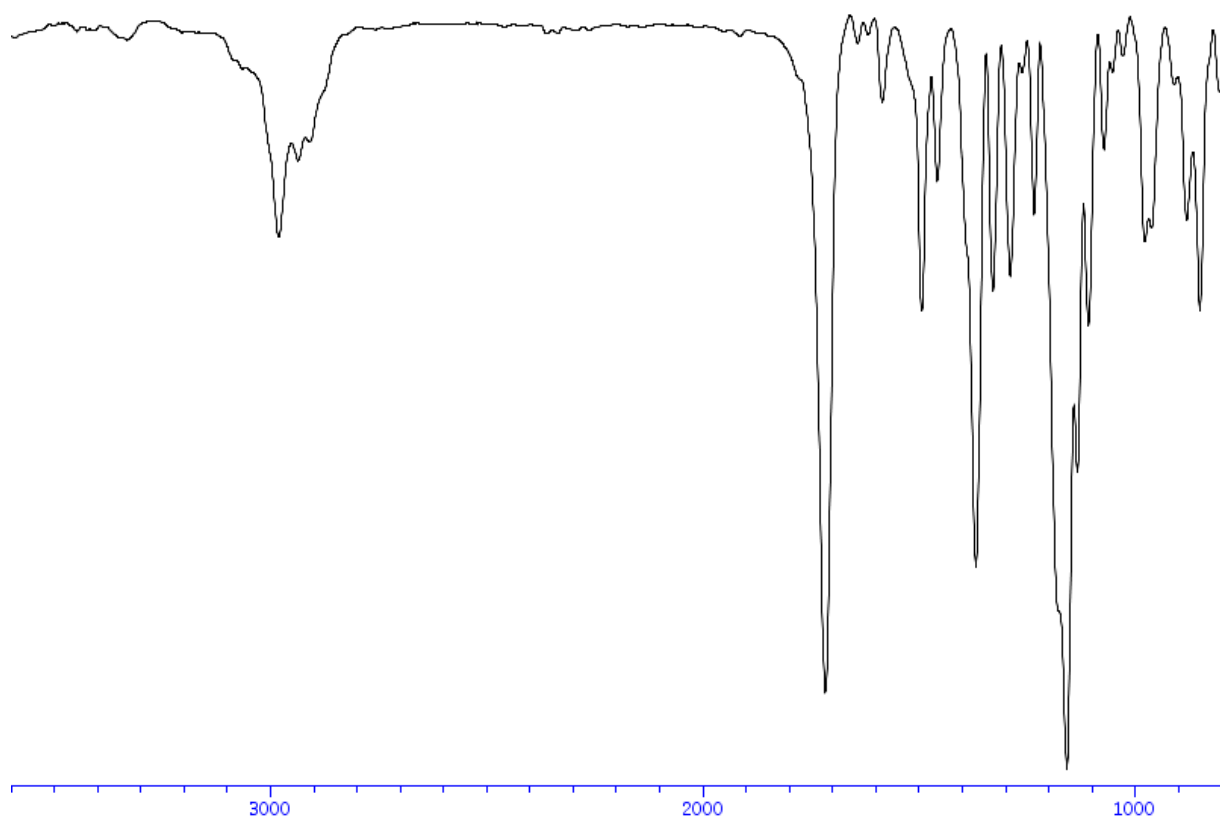


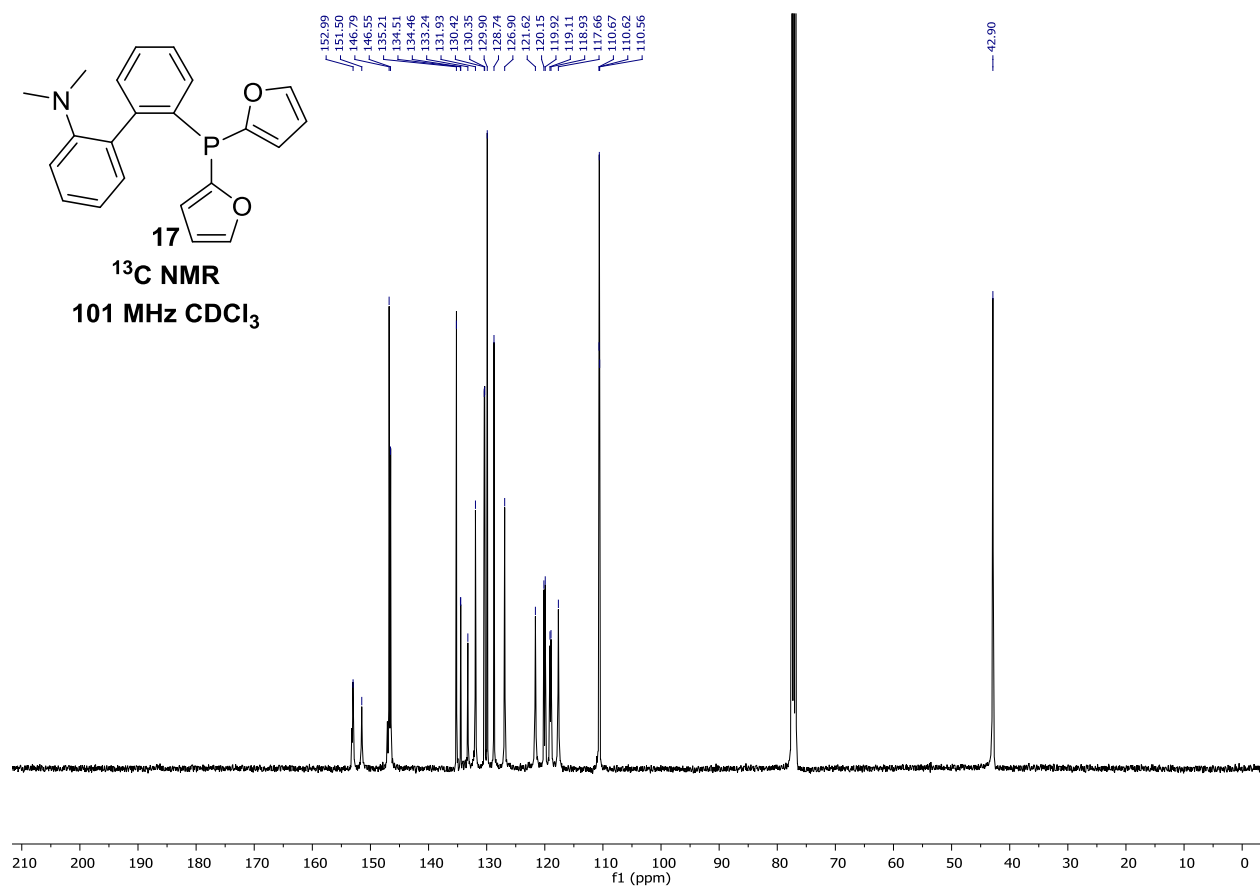
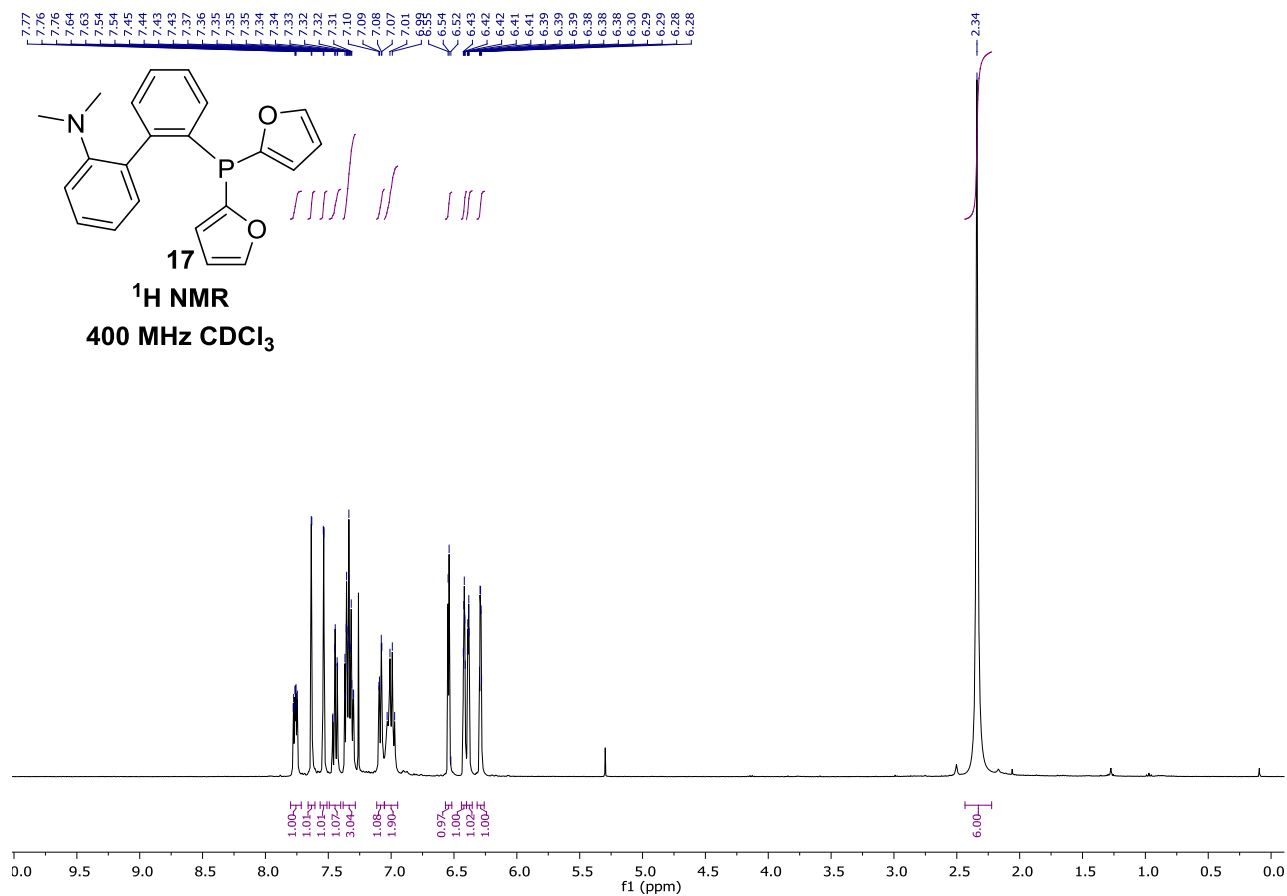


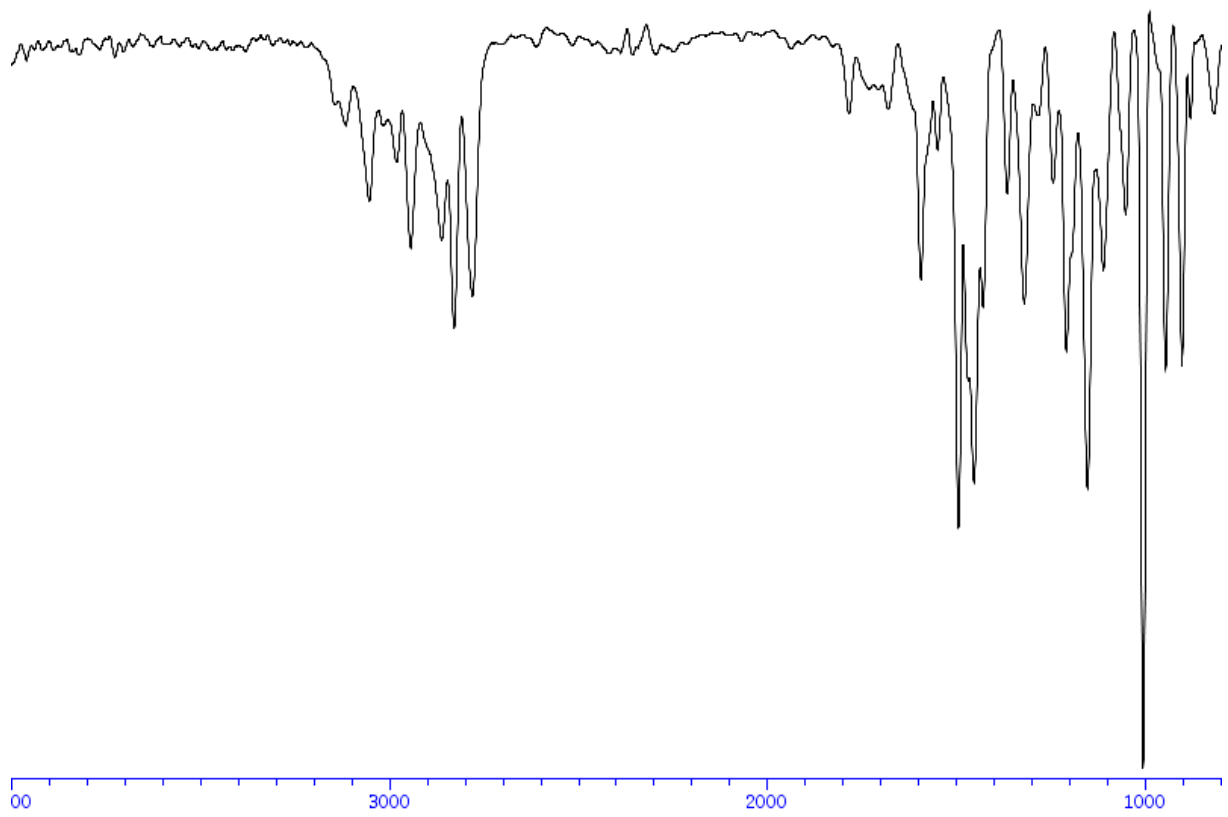


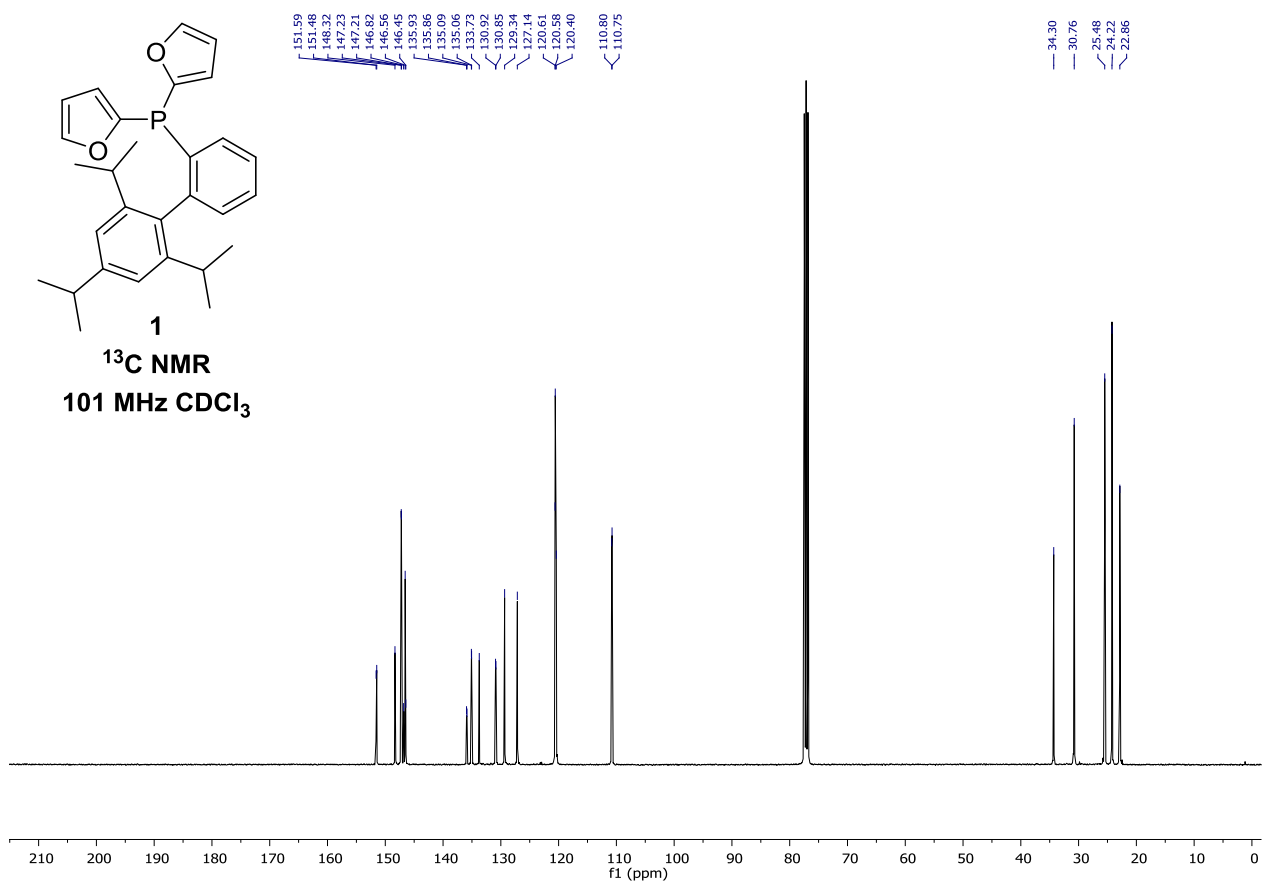
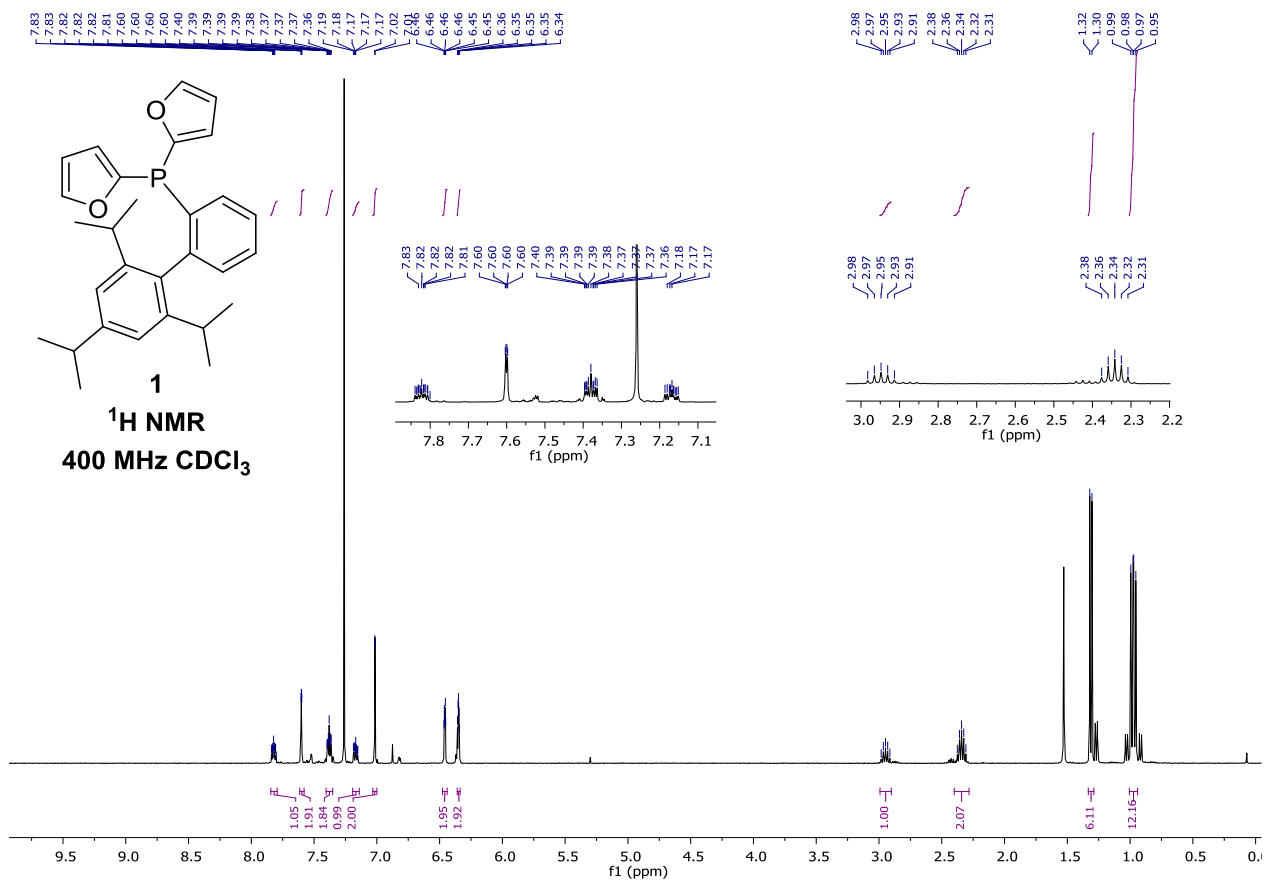


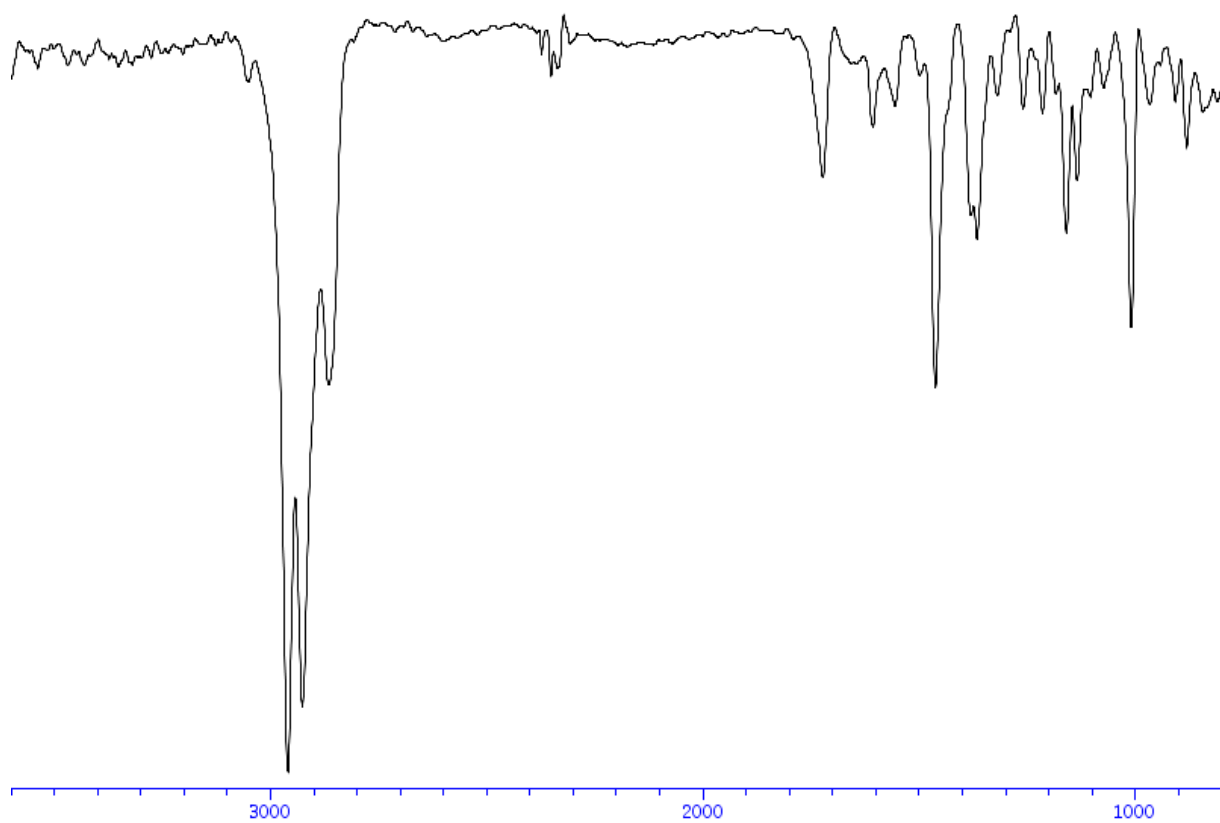


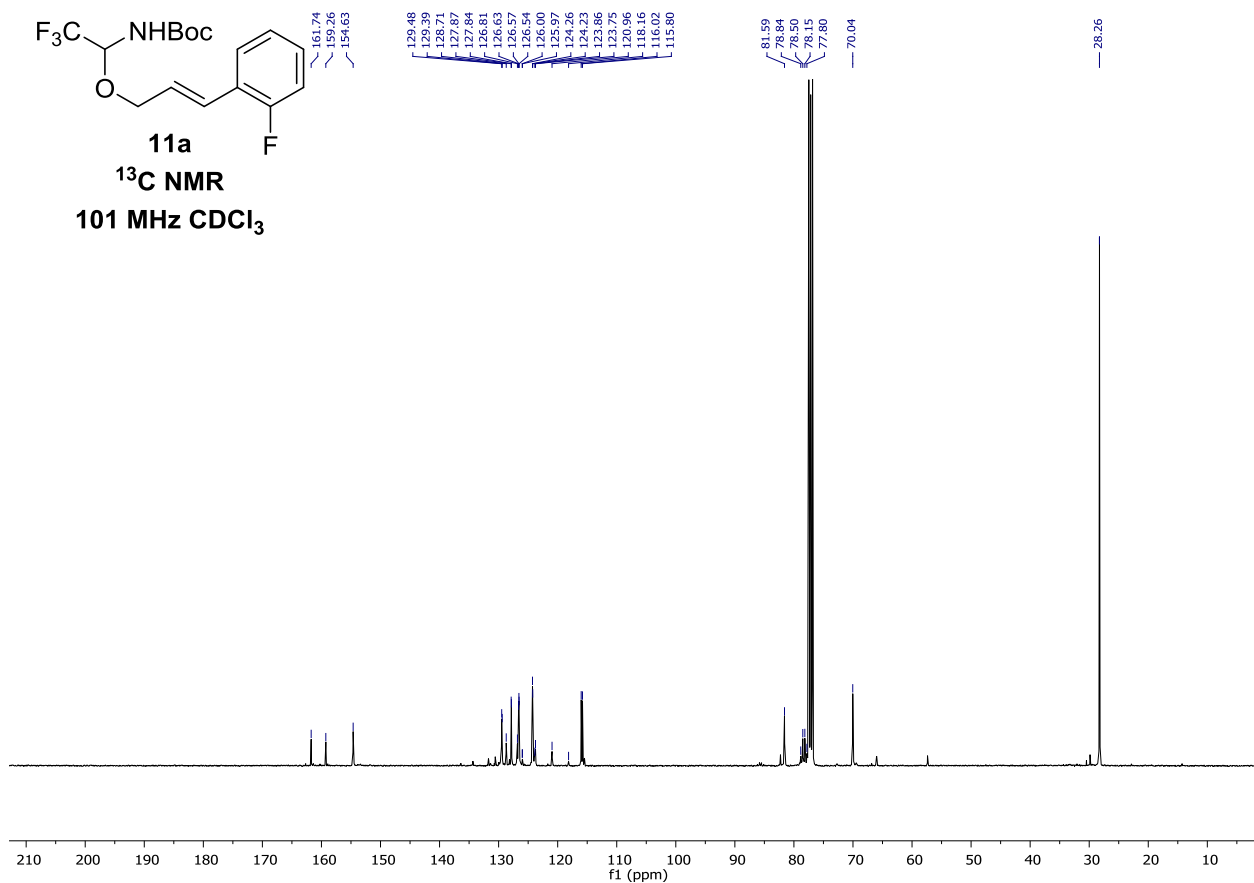
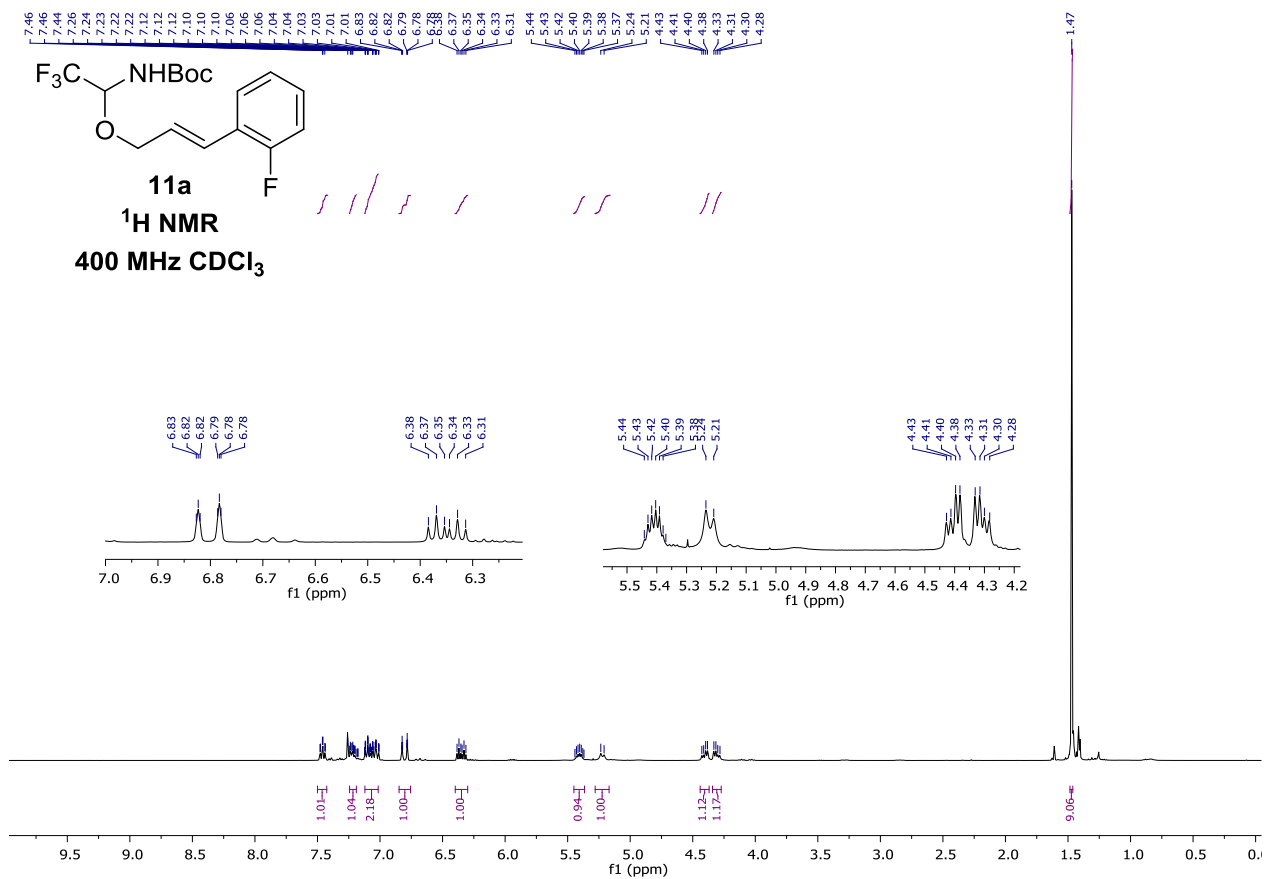


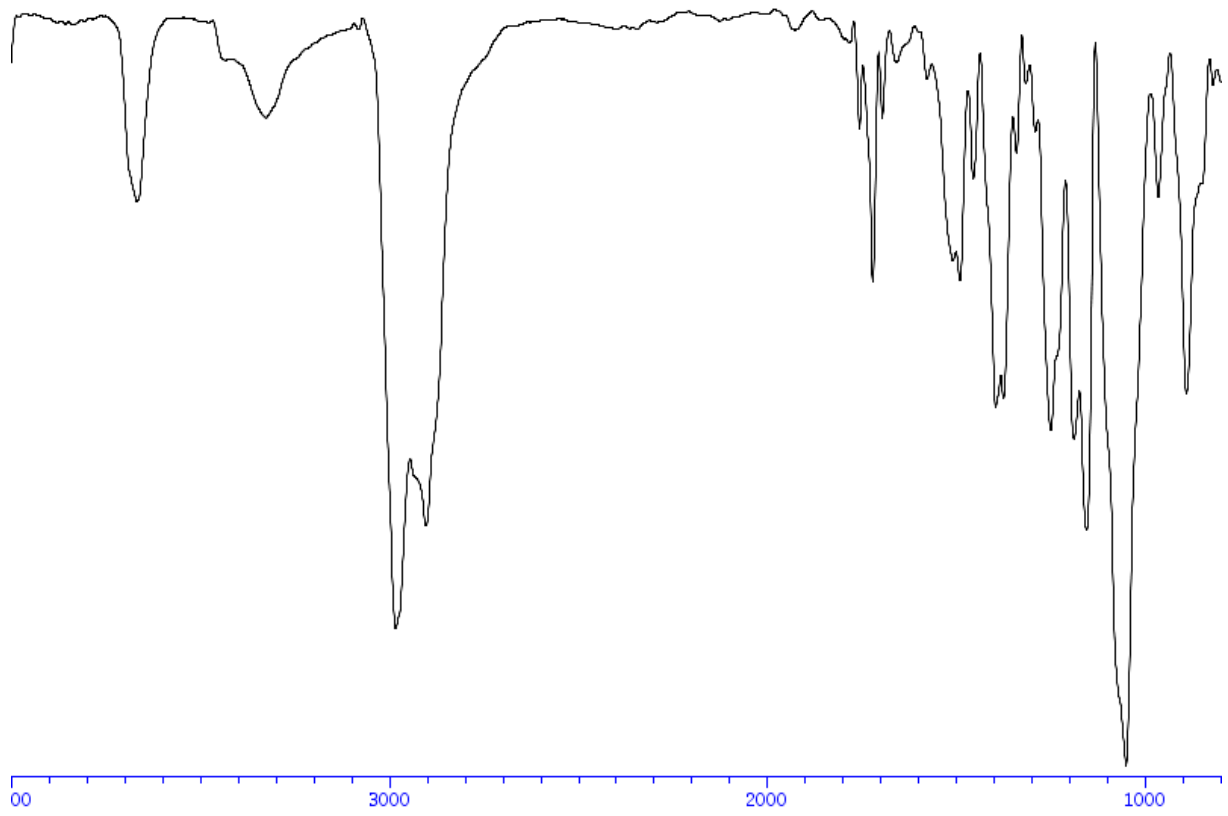


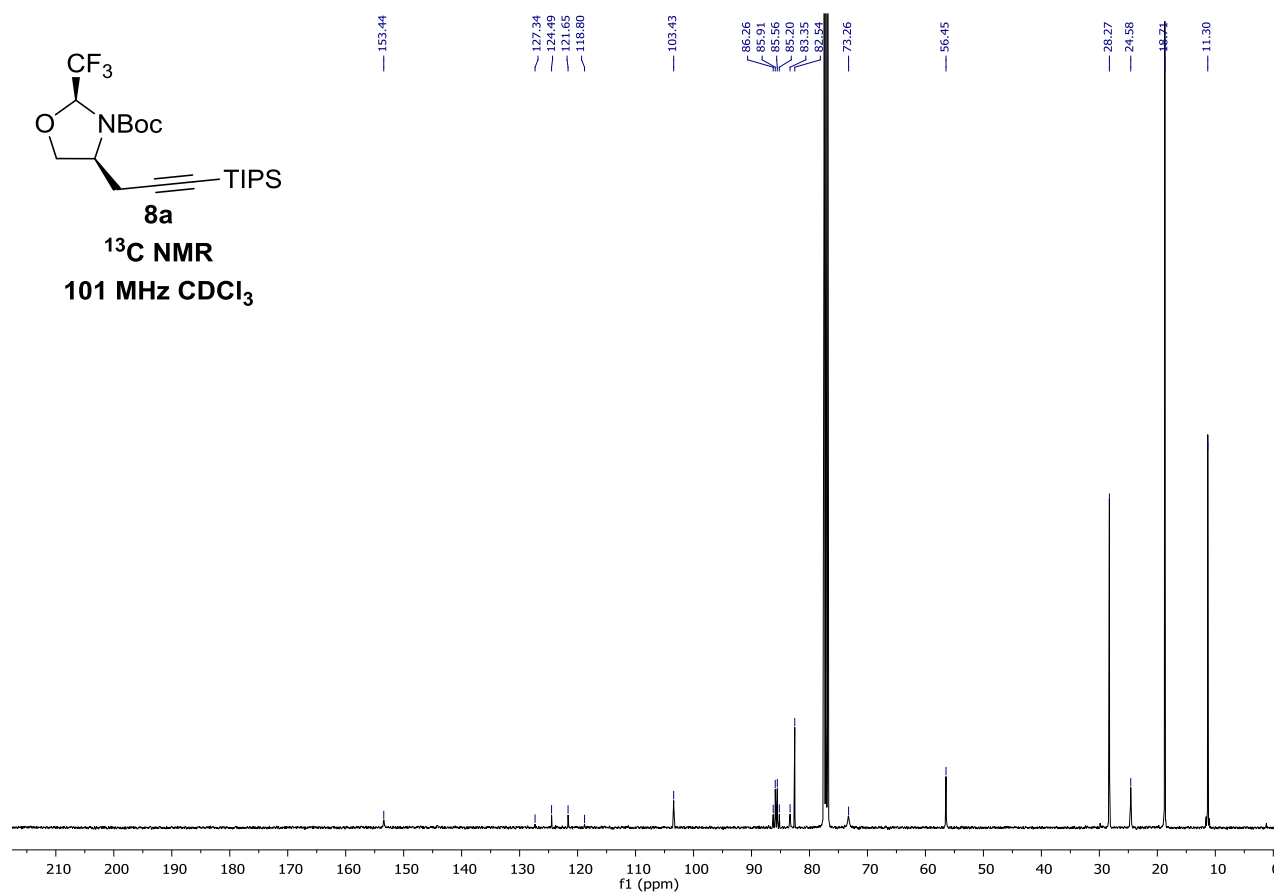
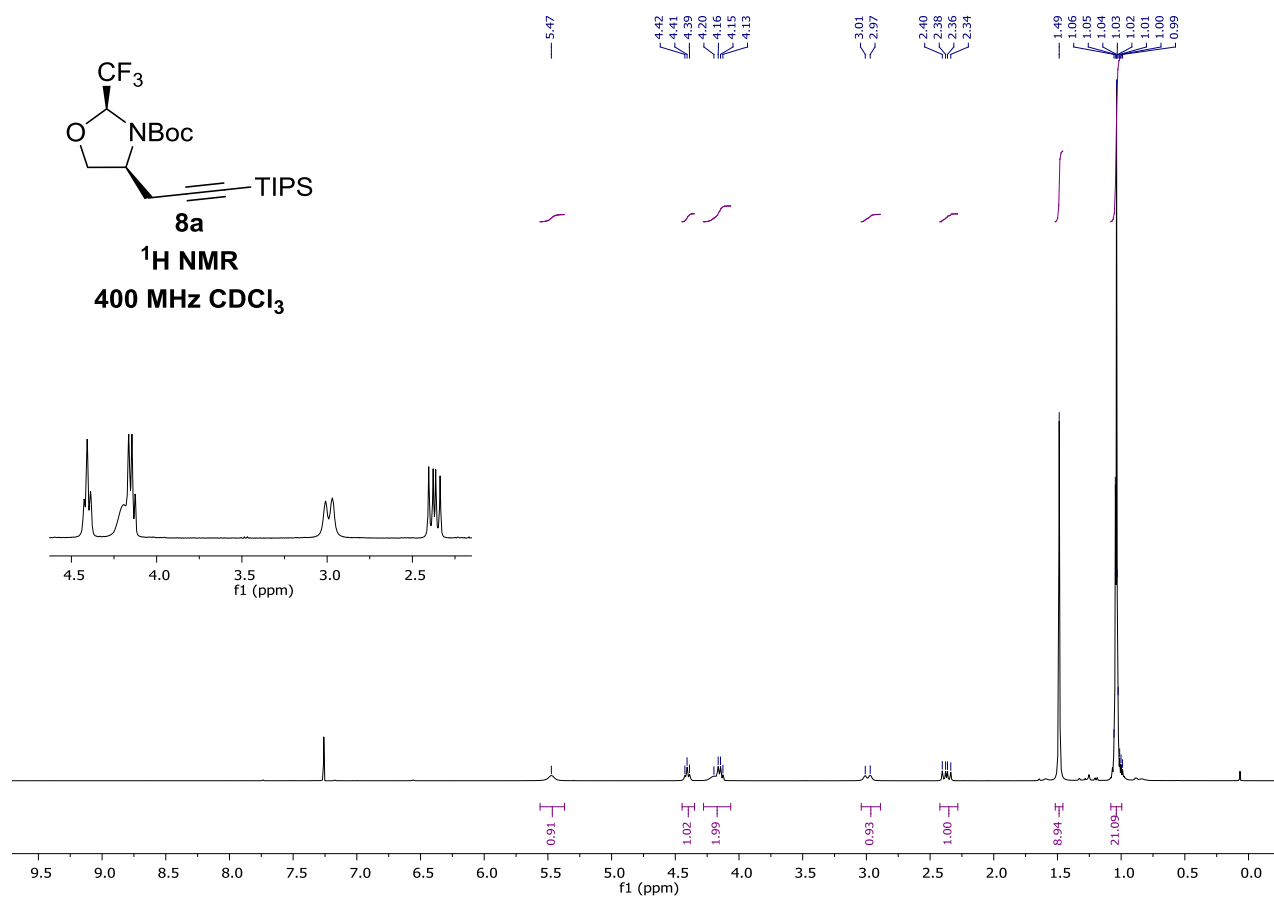


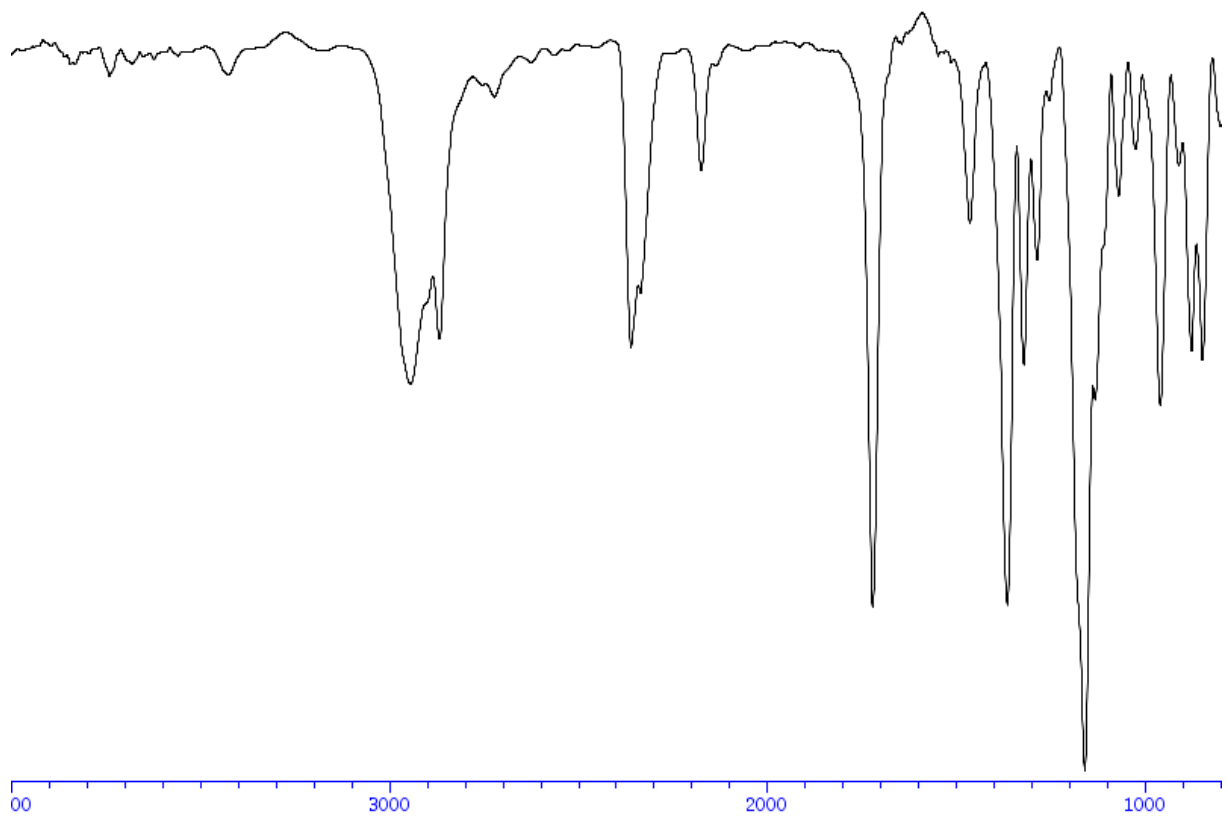


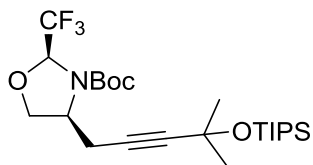




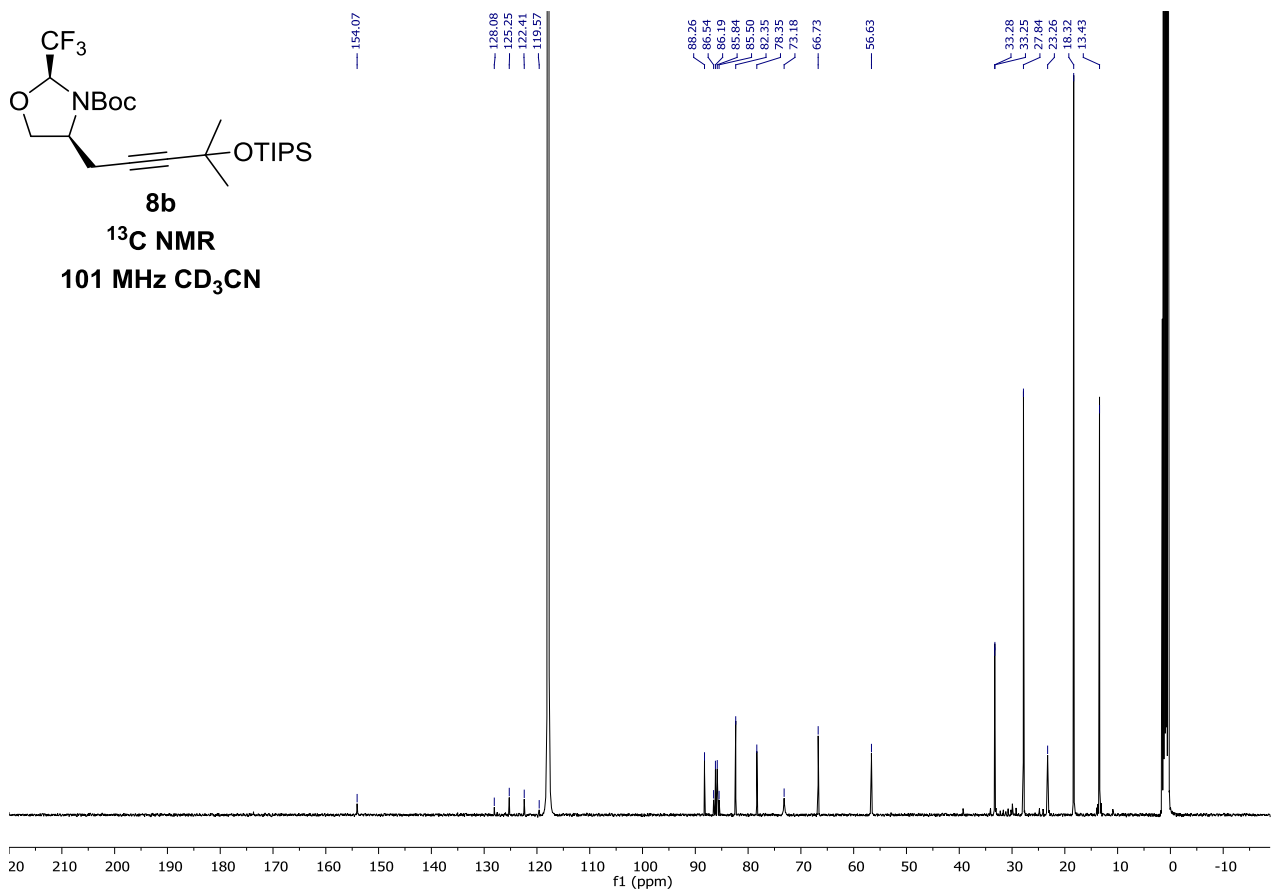
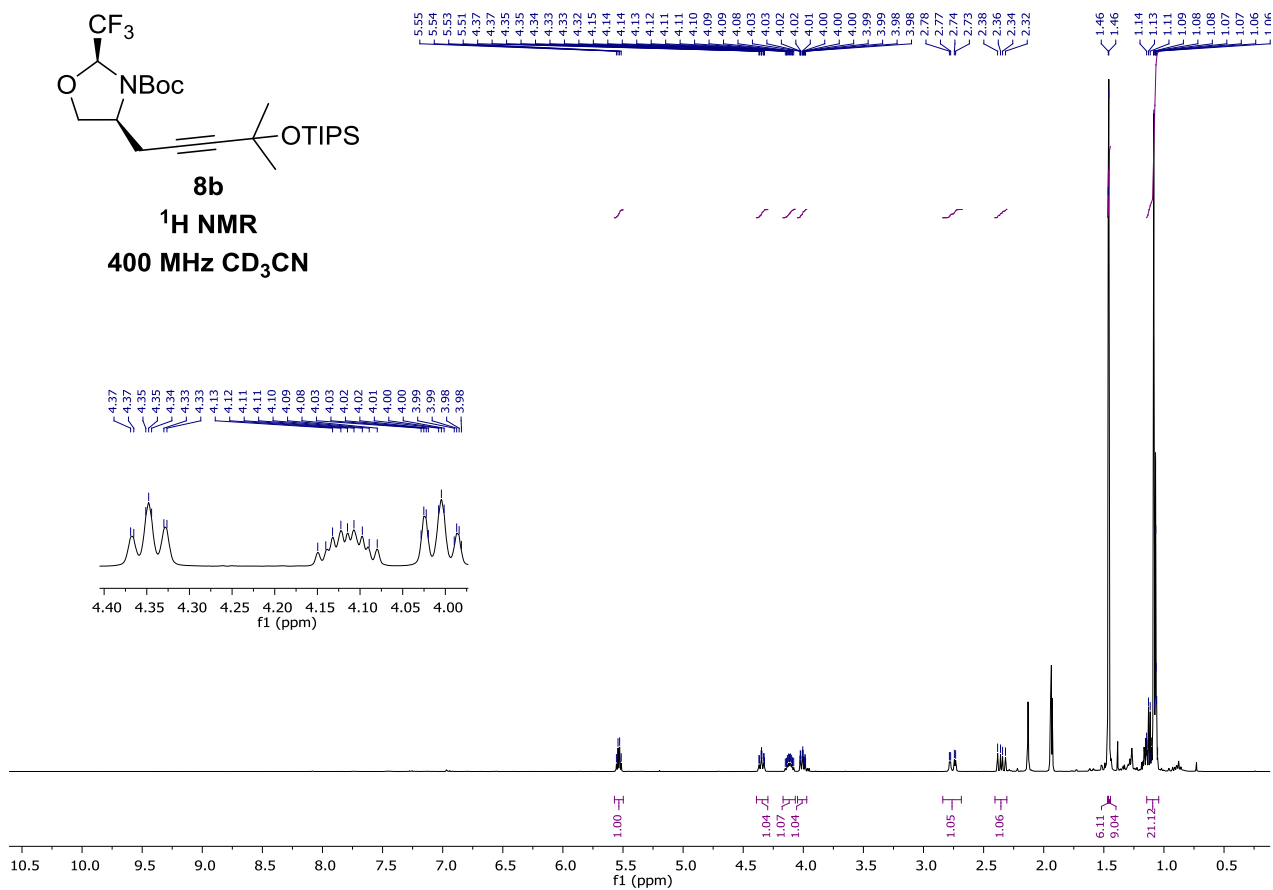


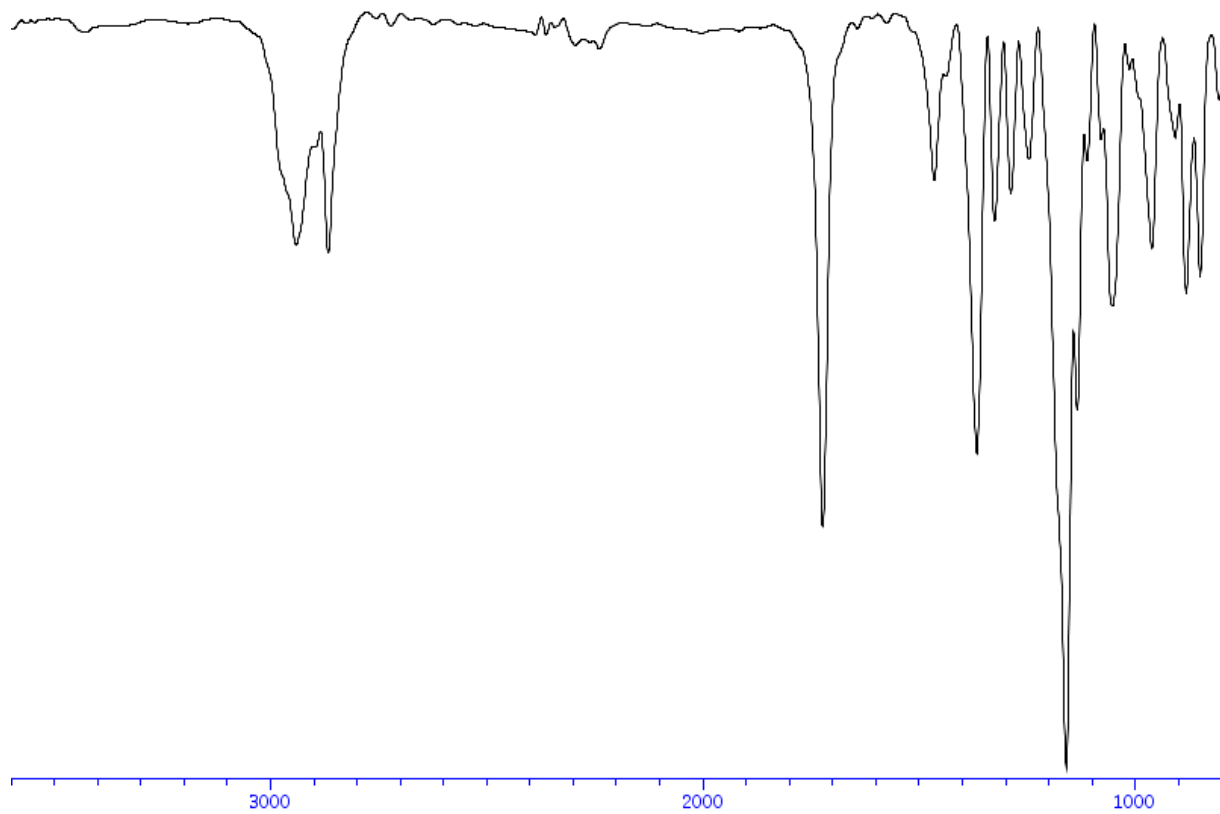


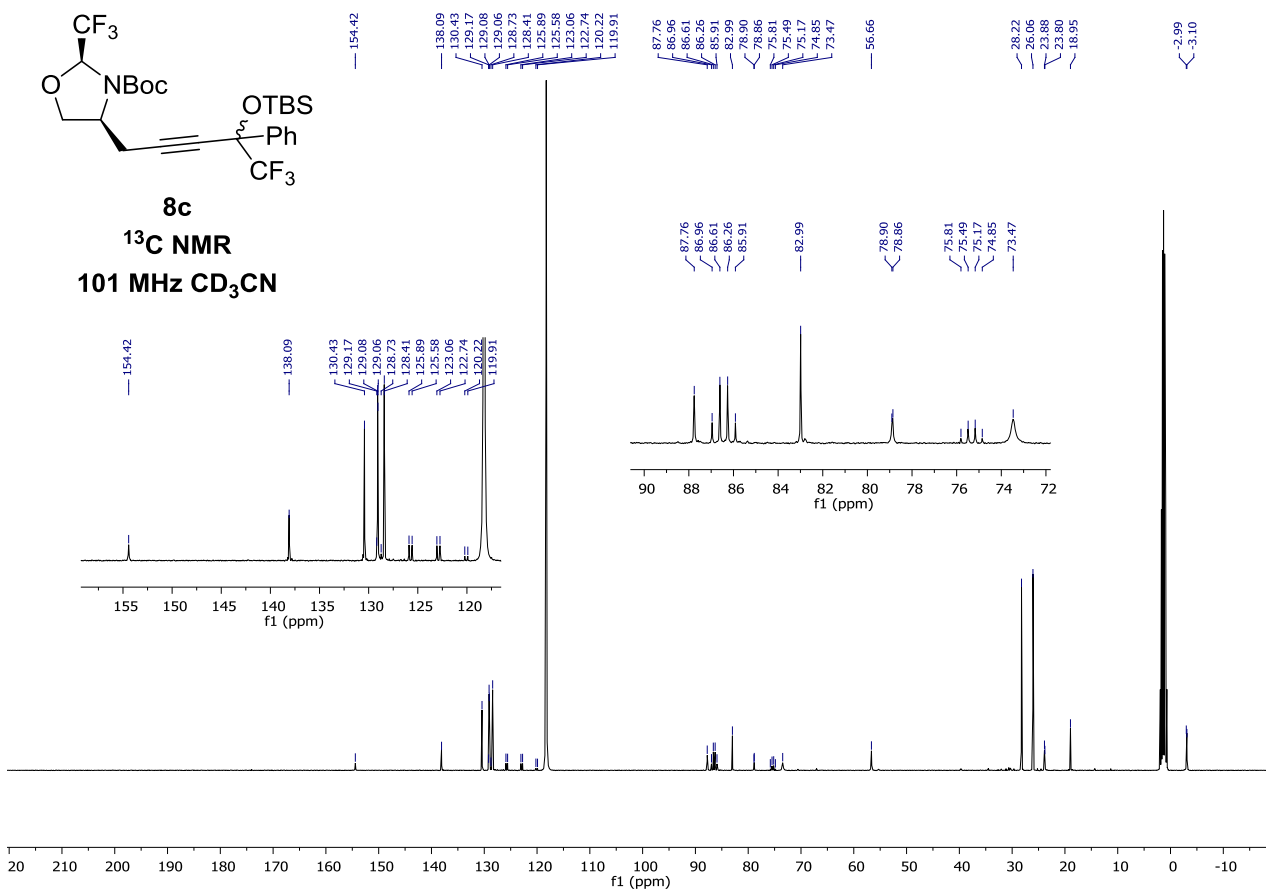
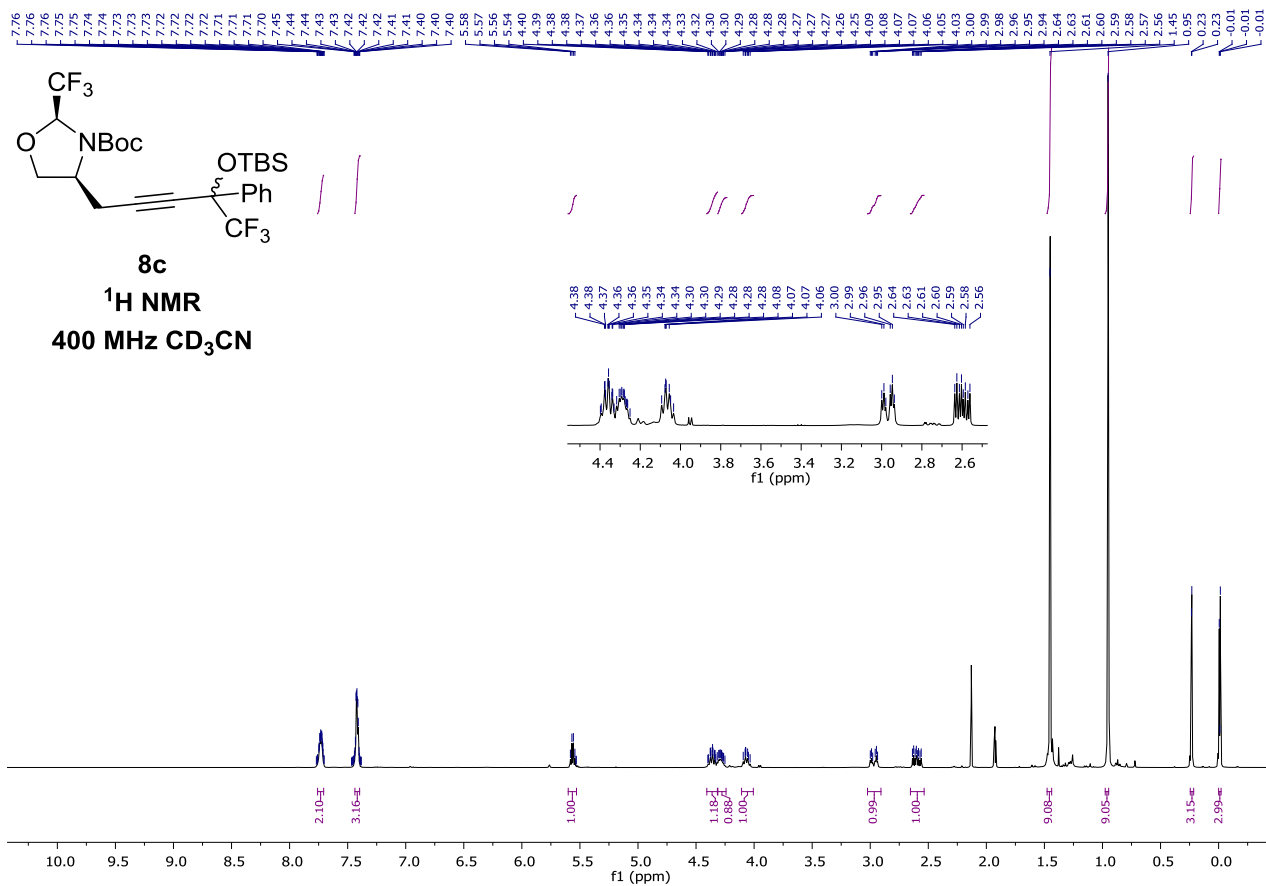


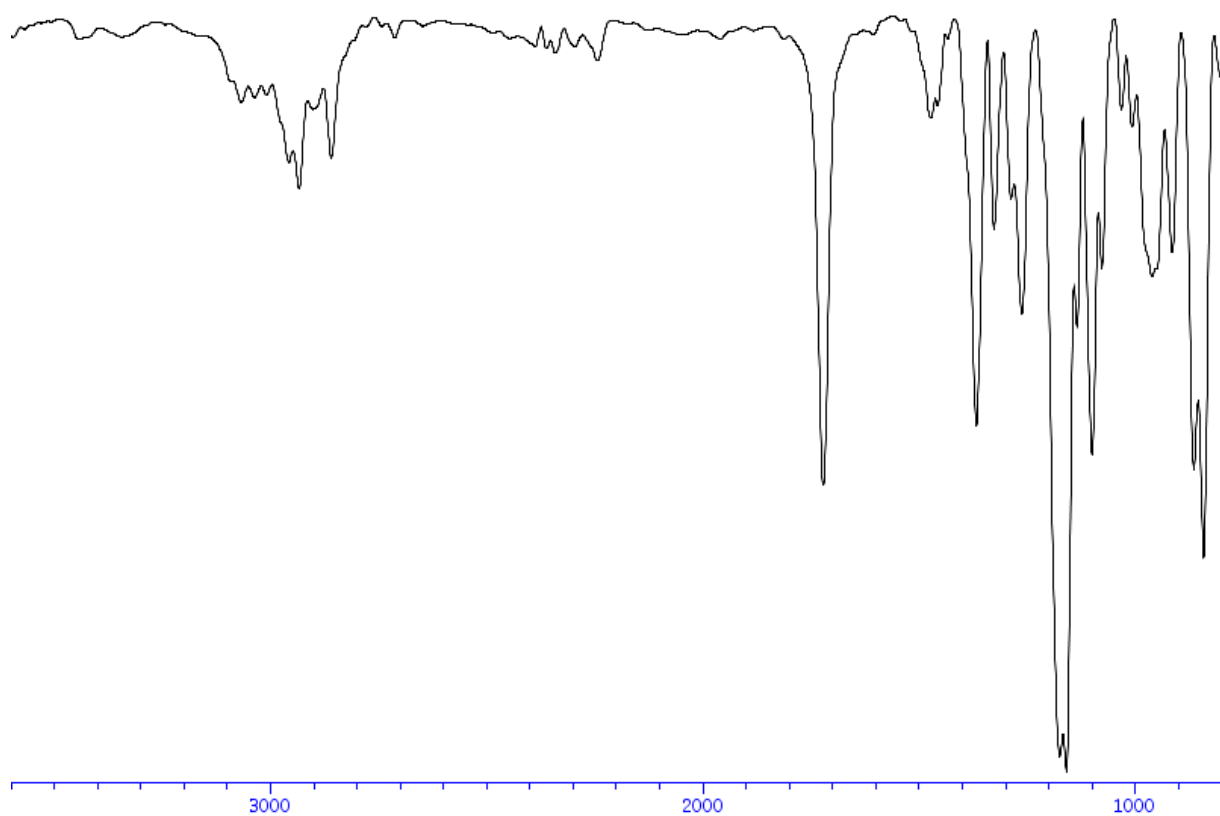


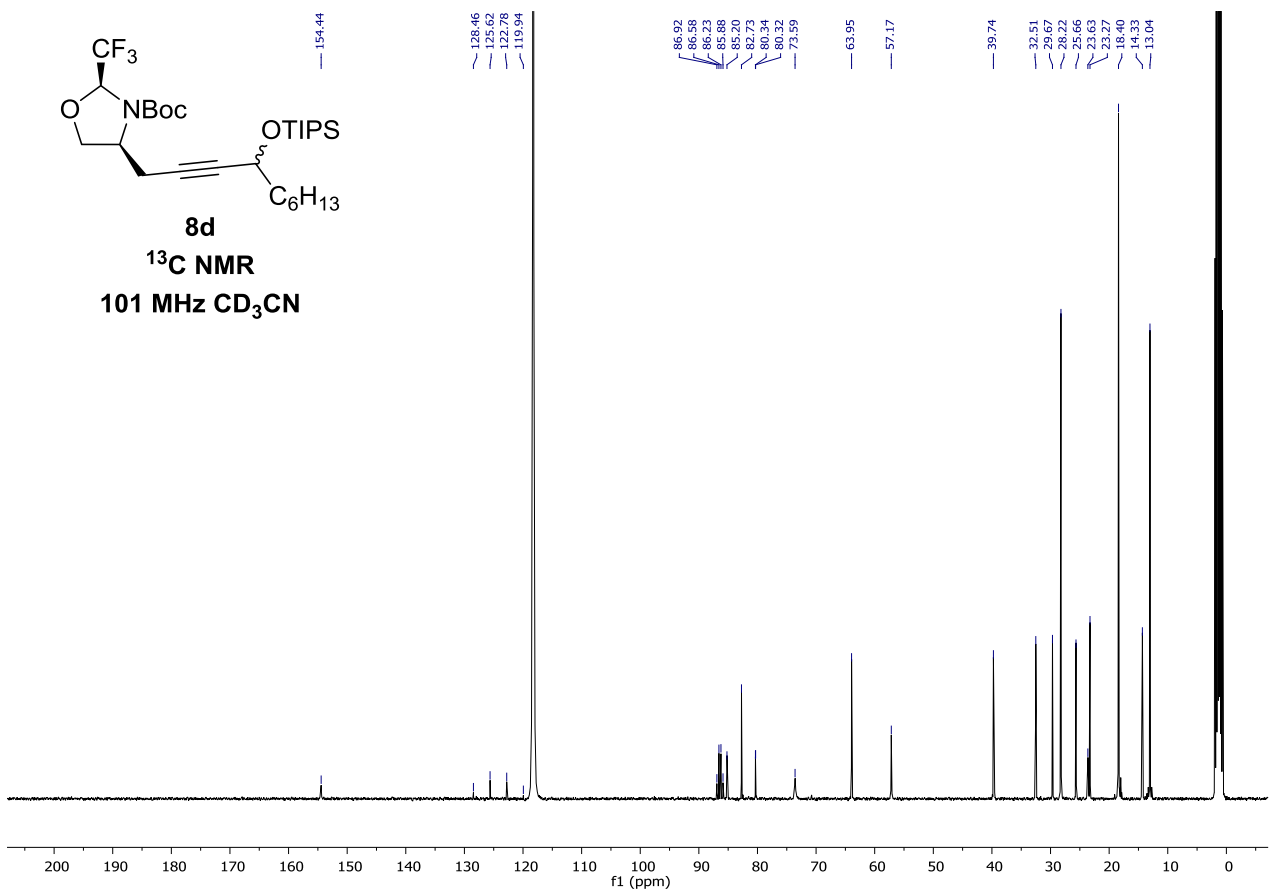
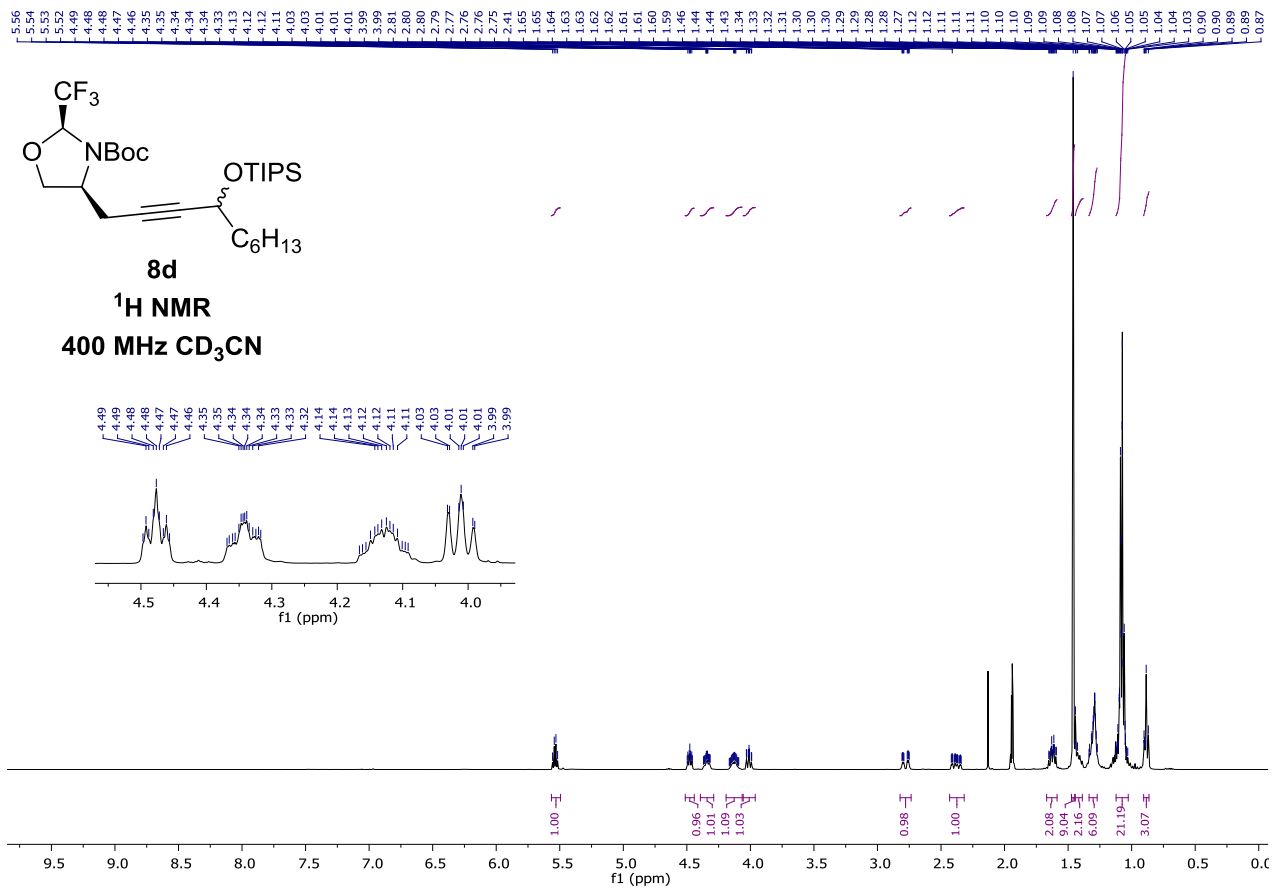
¹H NMR
400 MHz CD₃CN

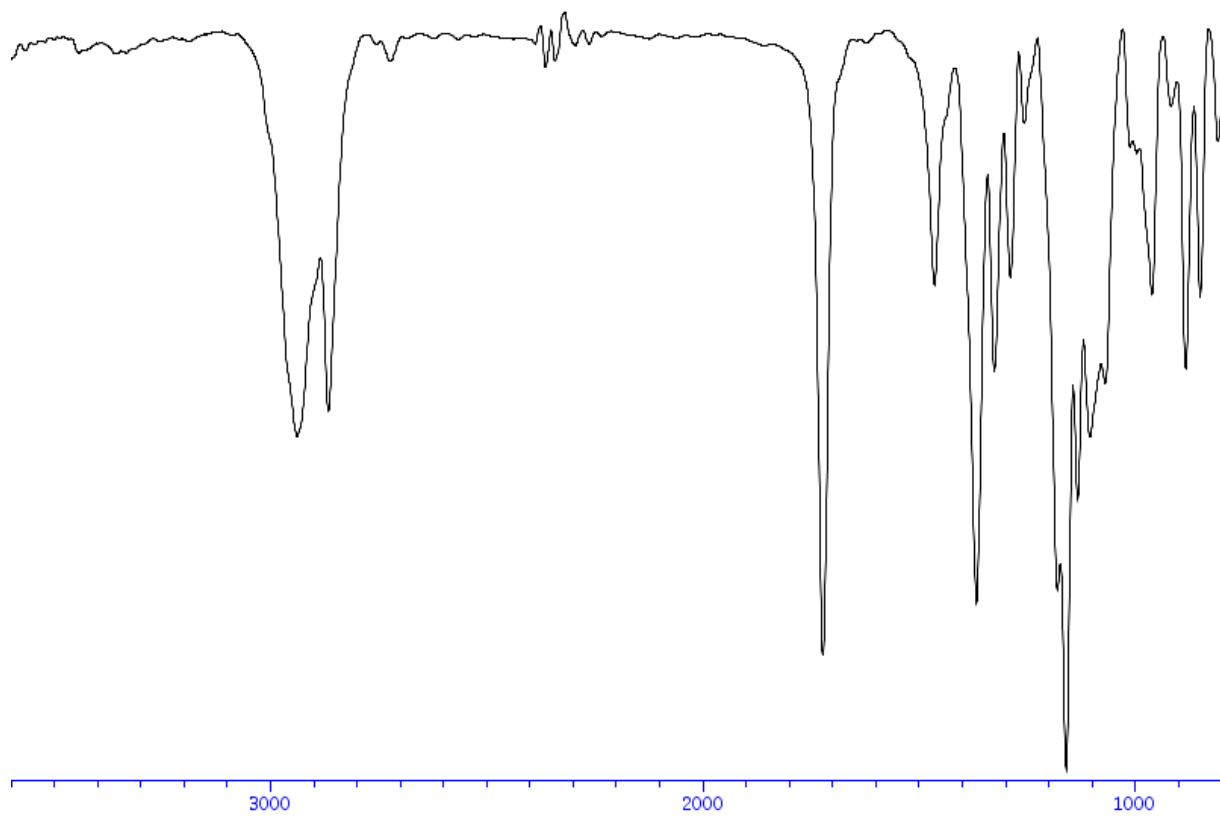


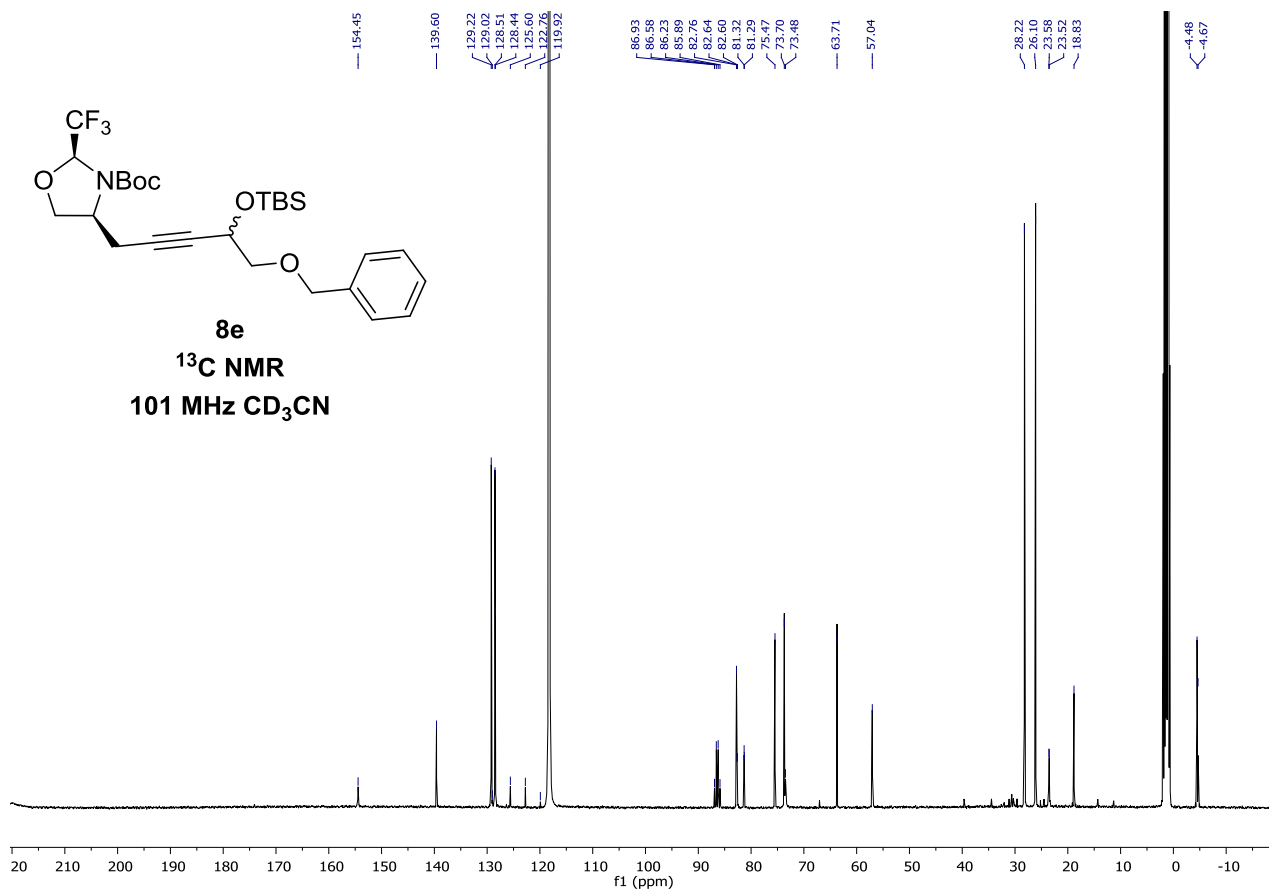
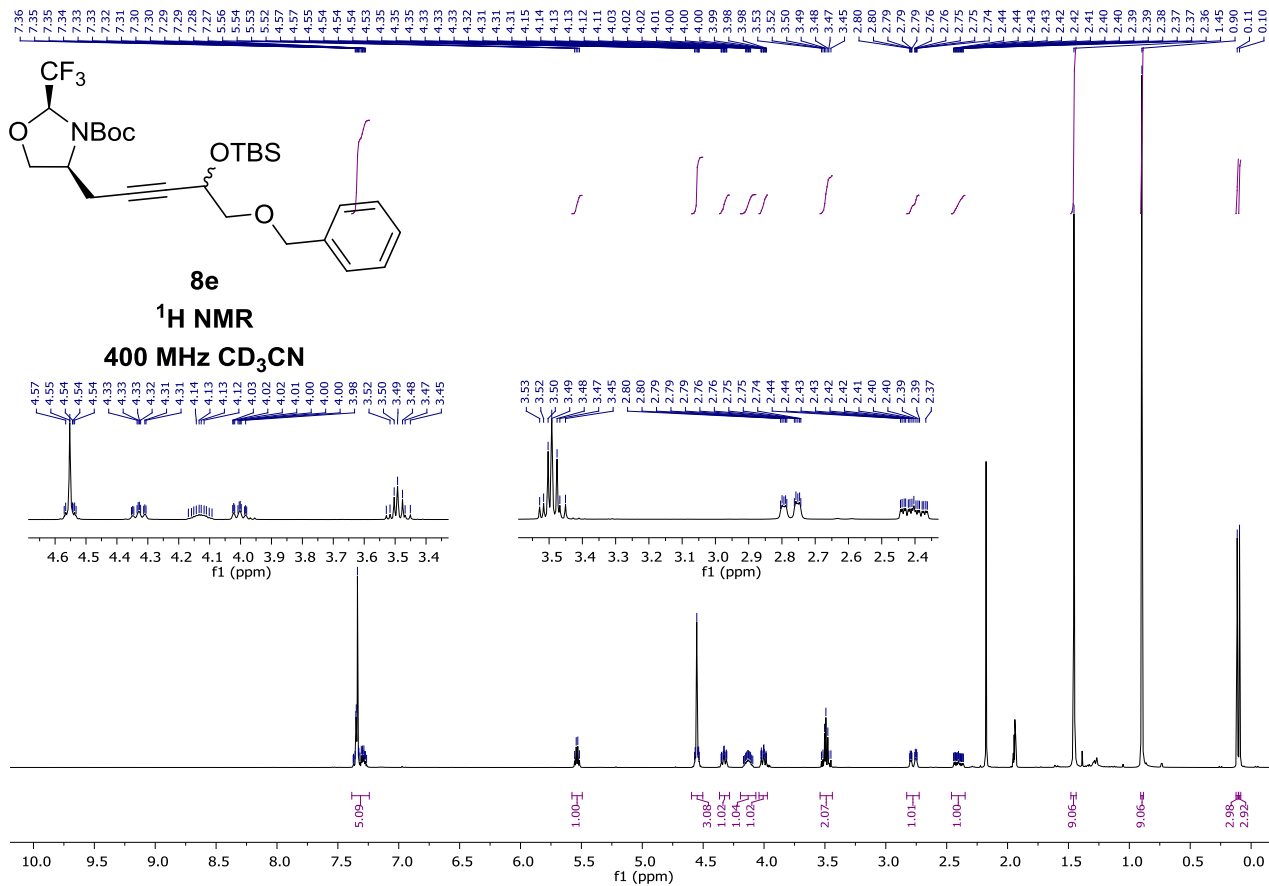


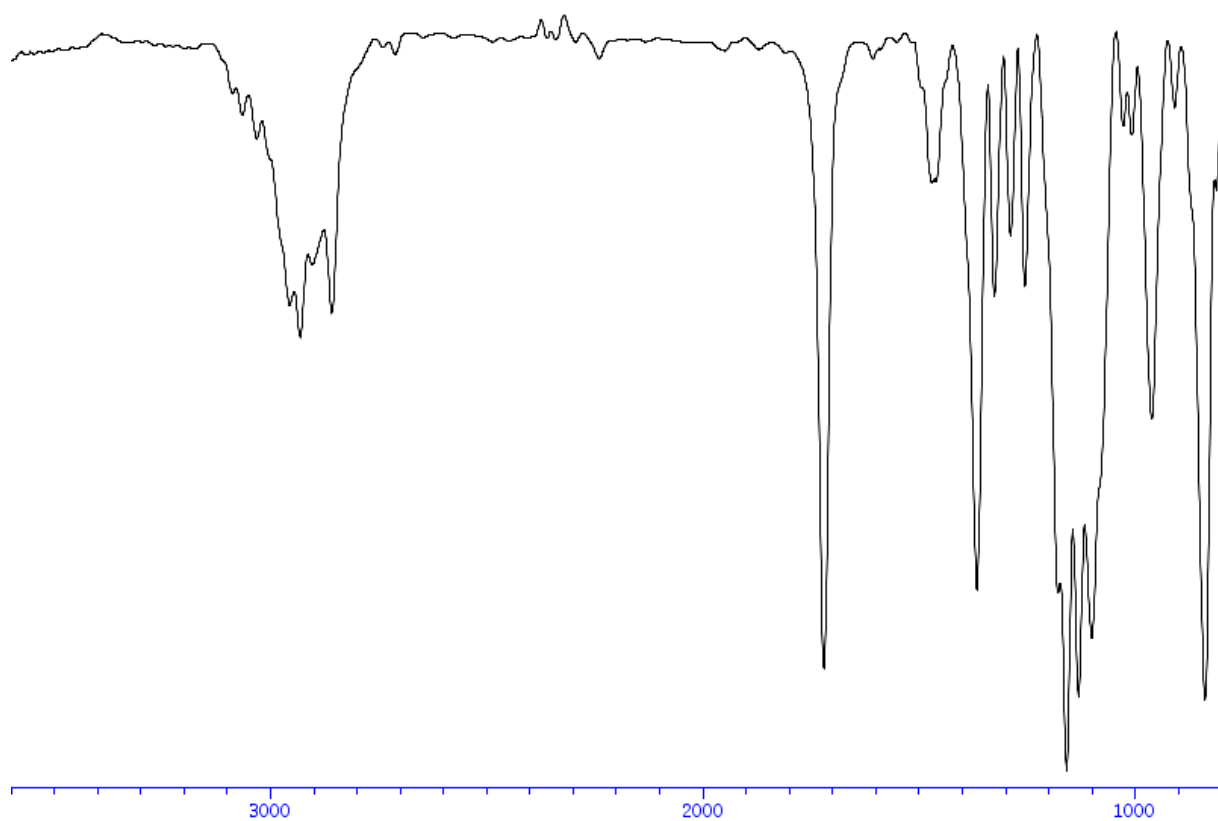


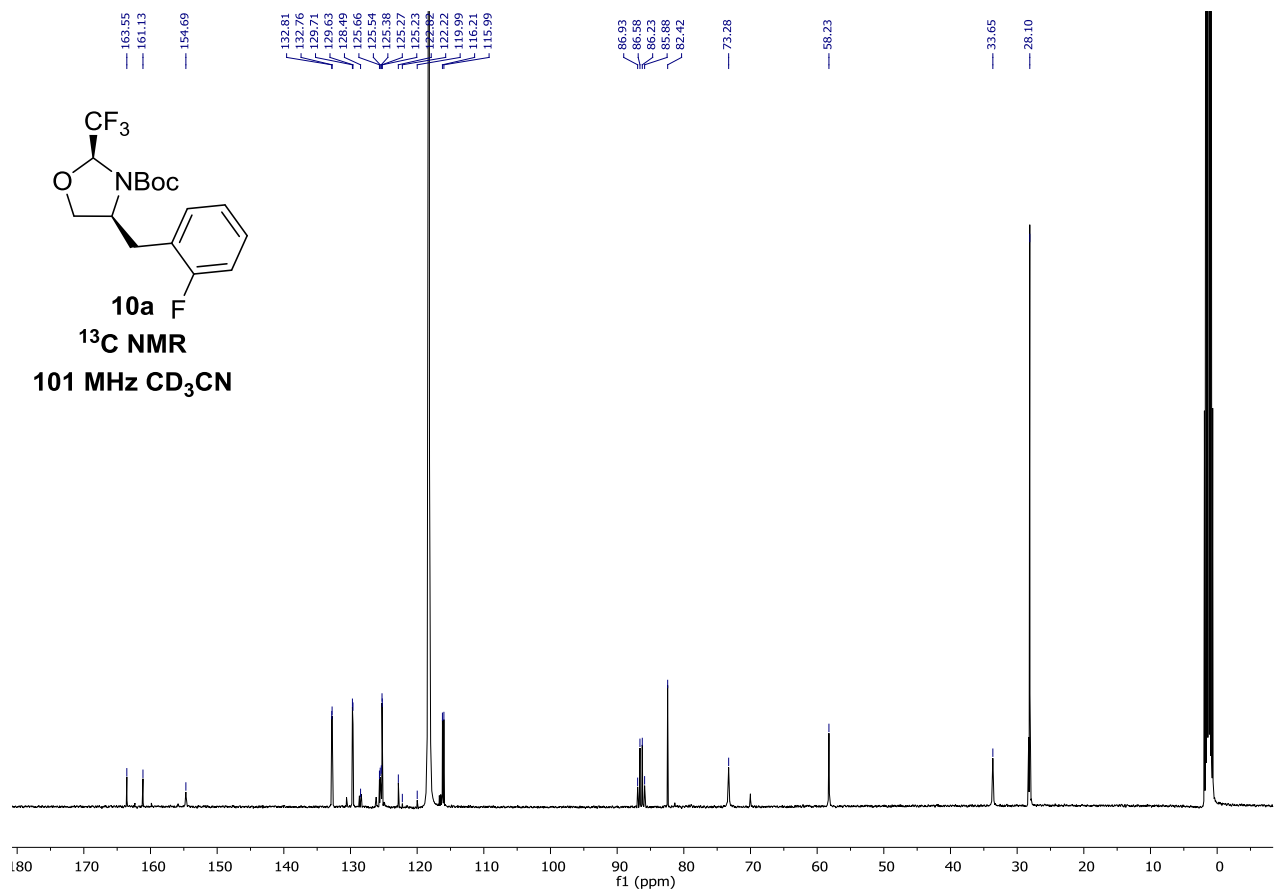
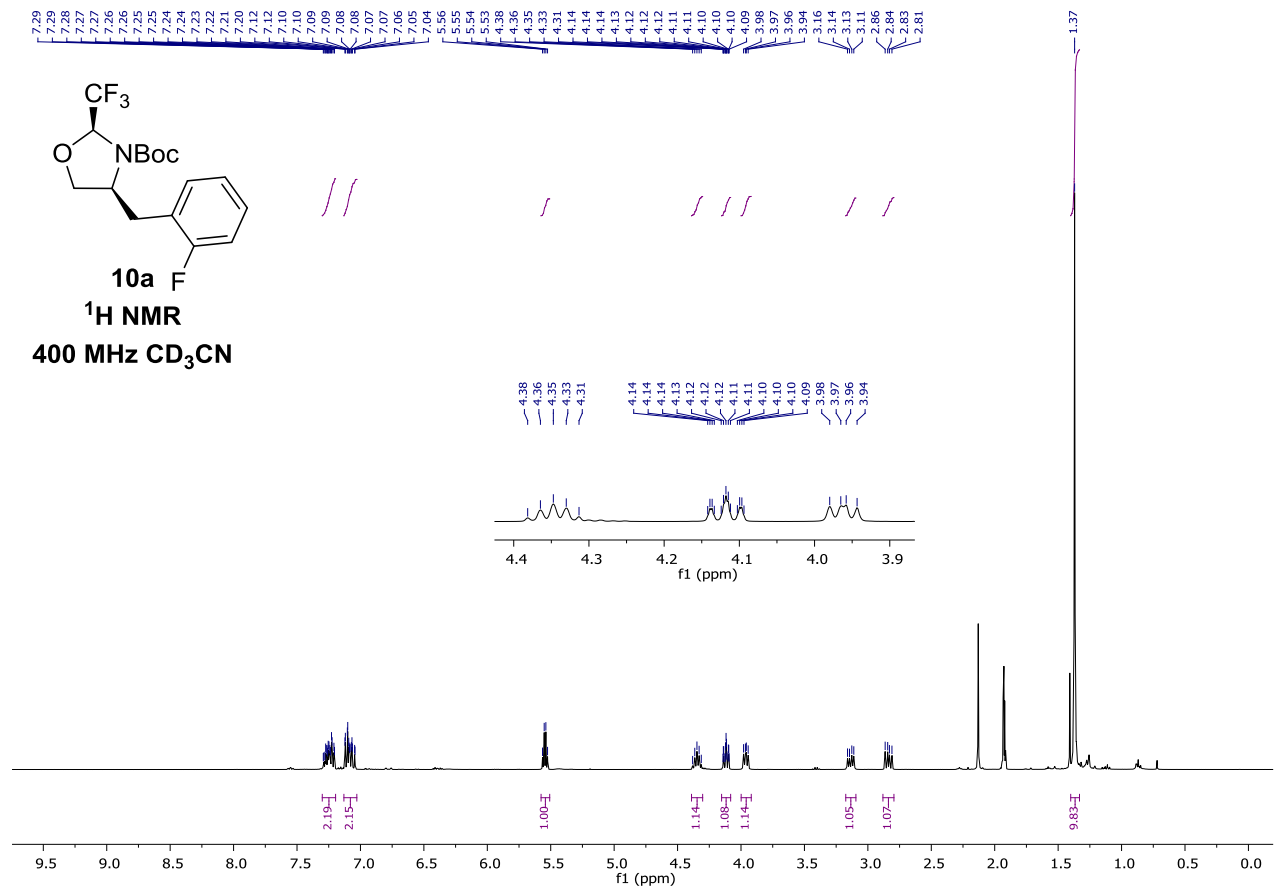


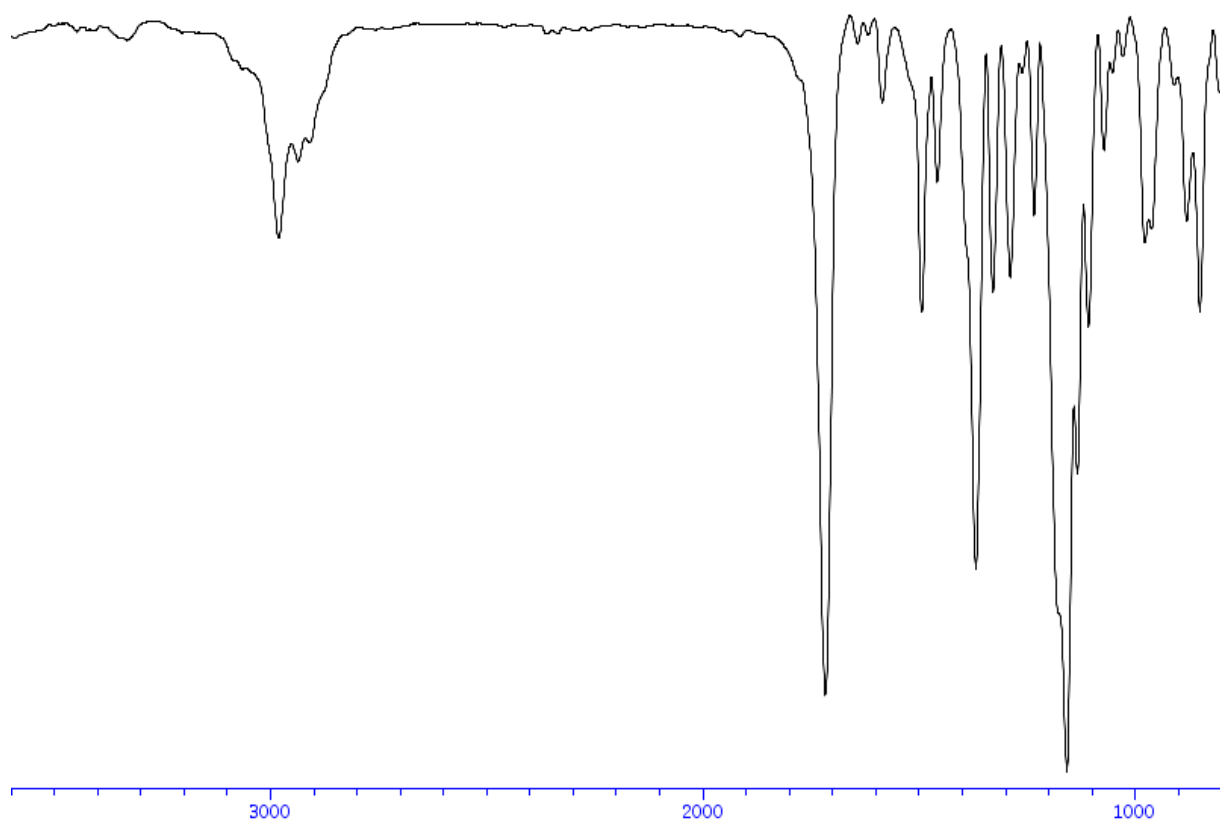


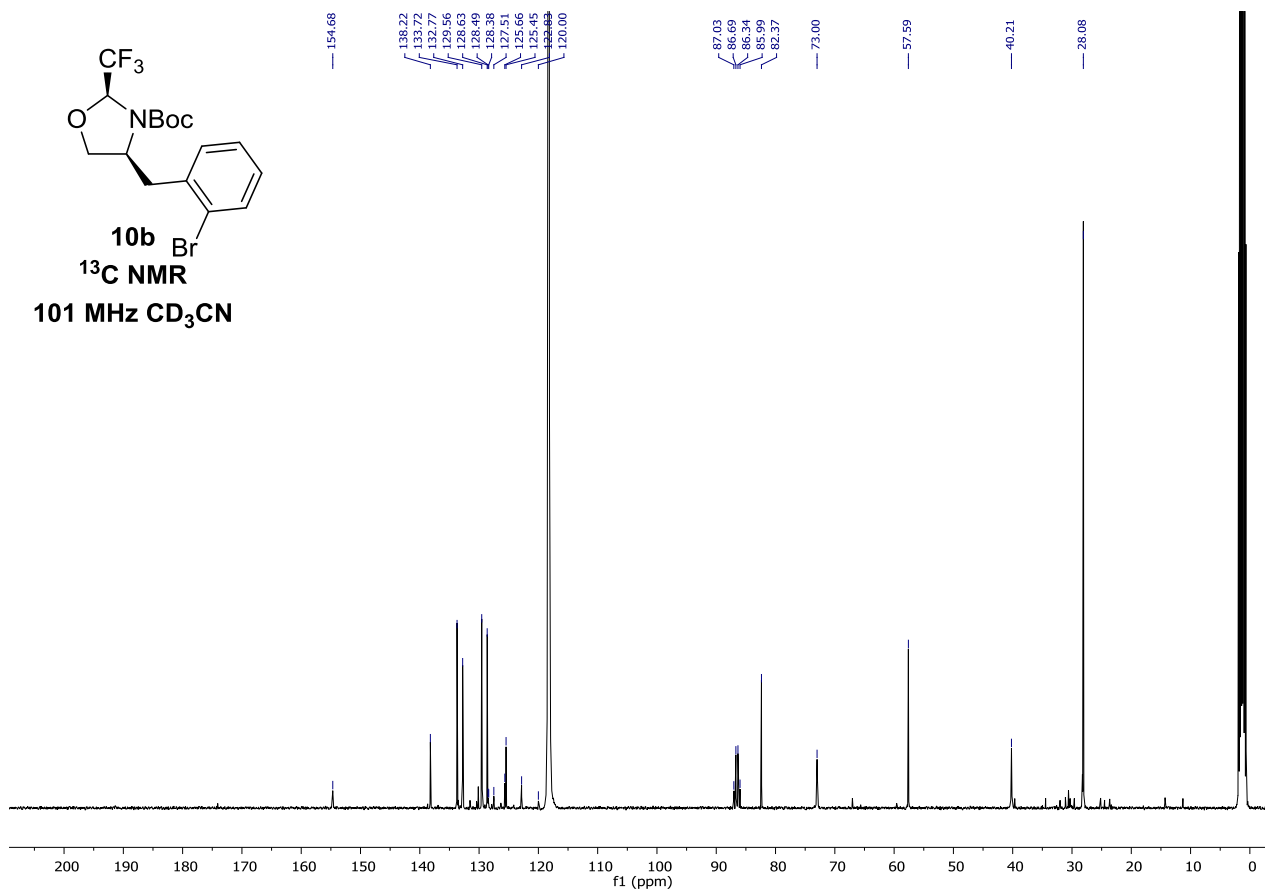
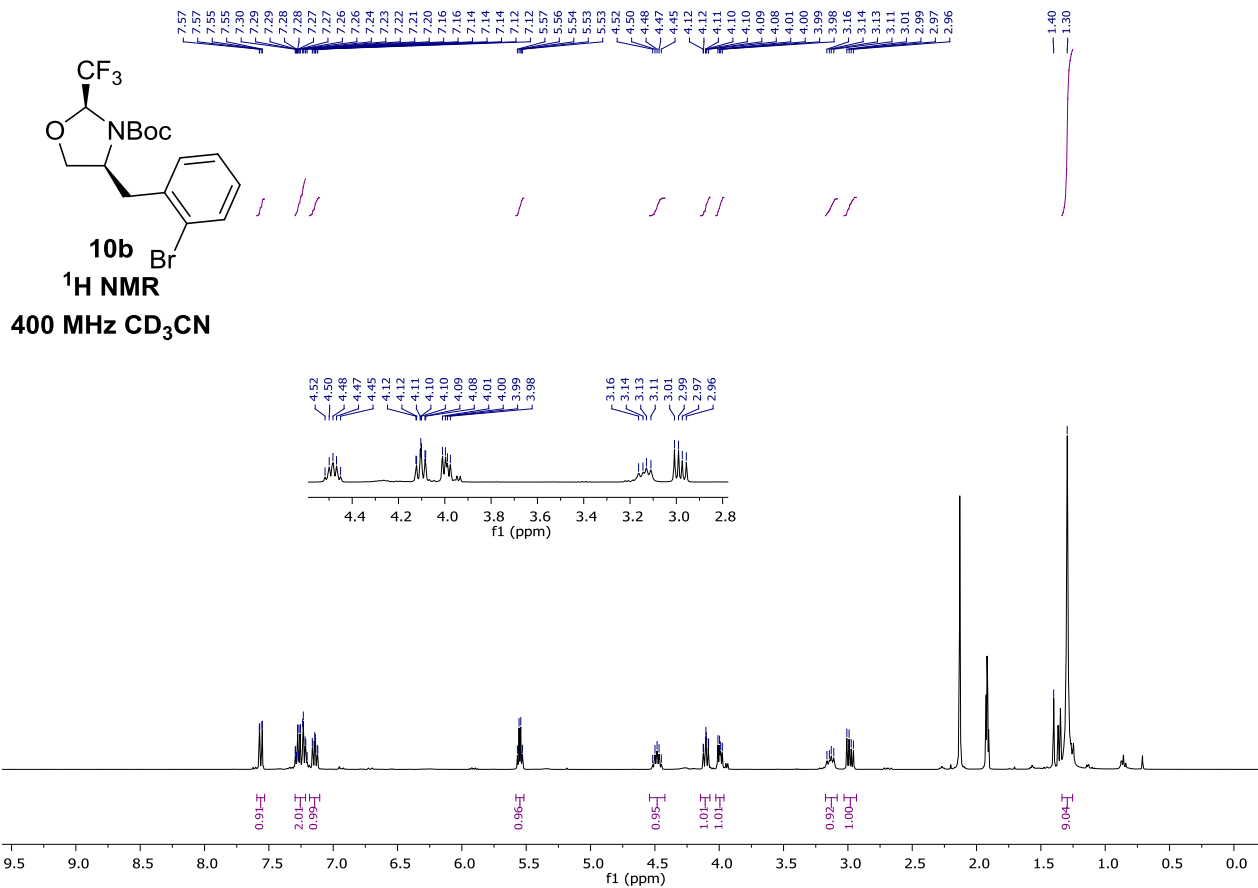


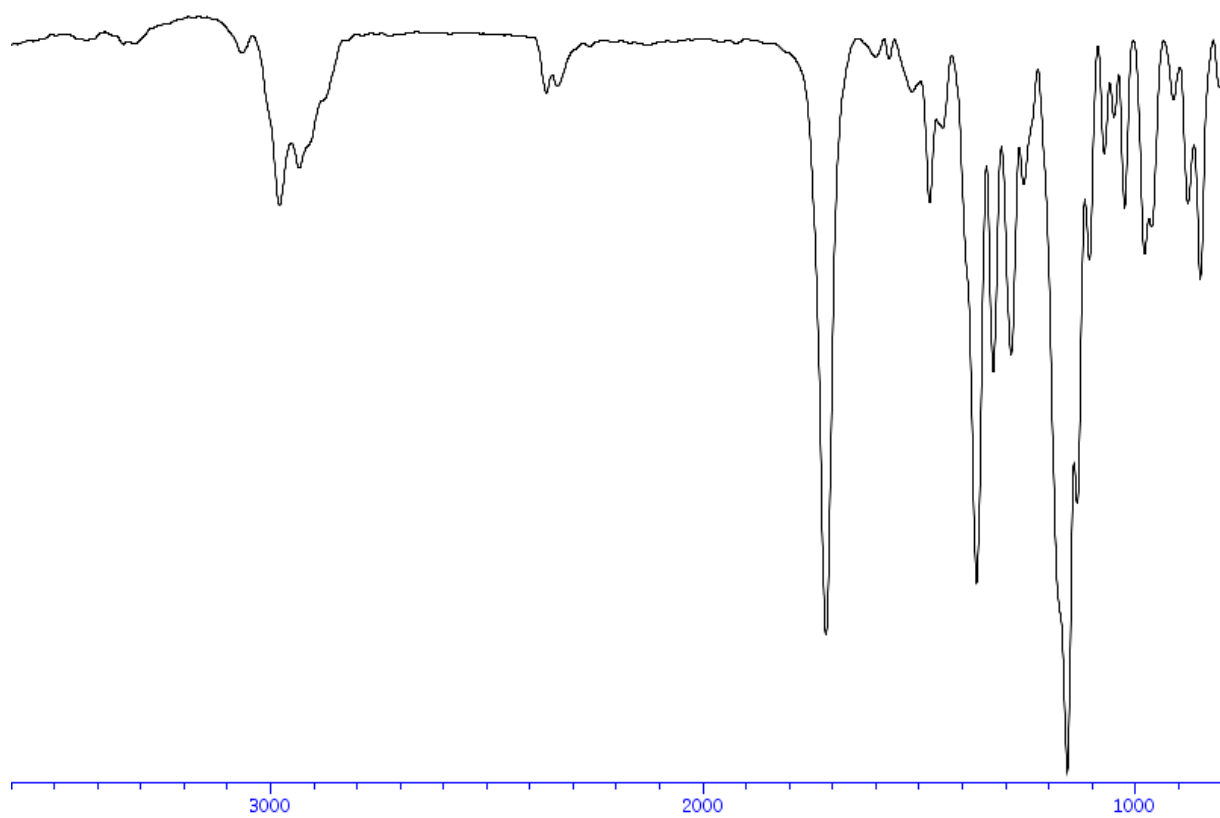


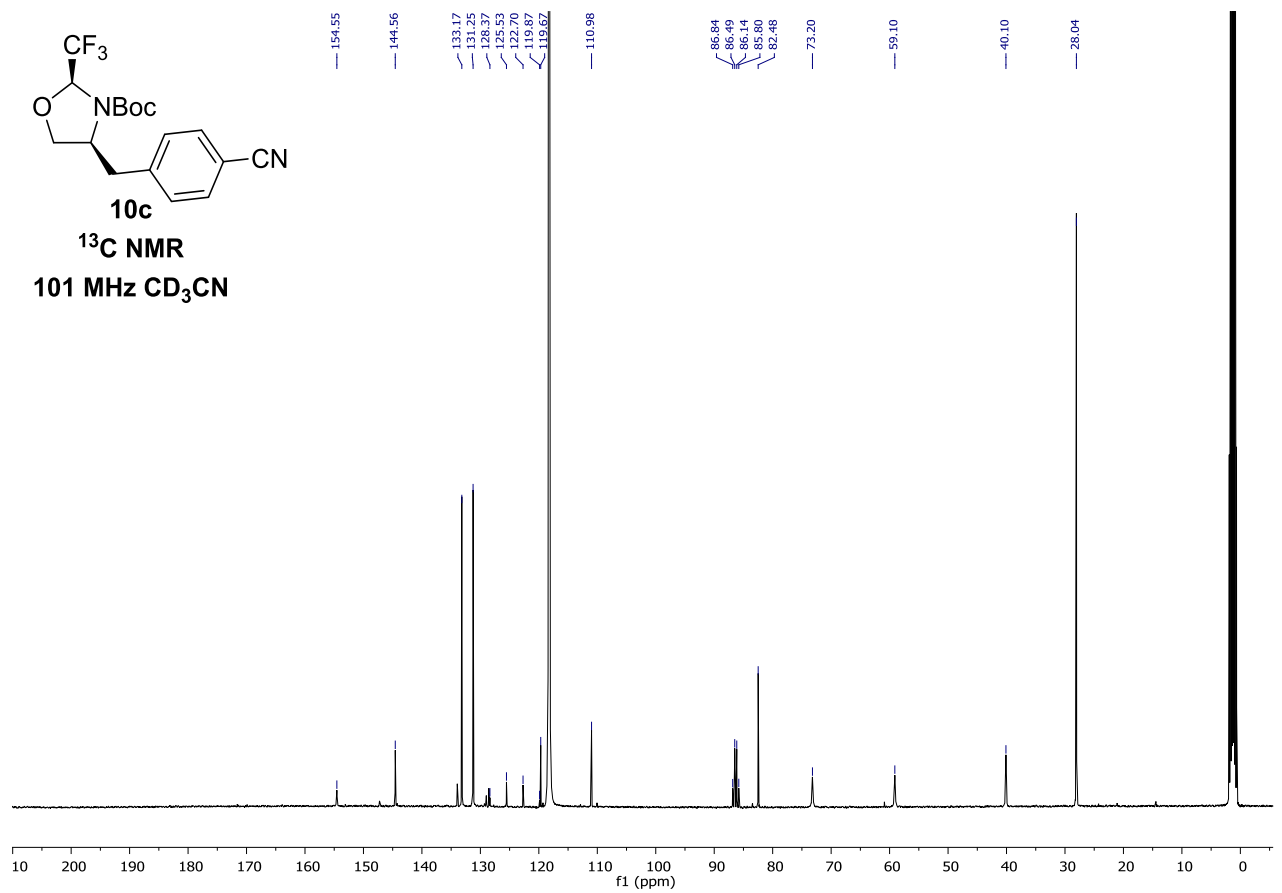
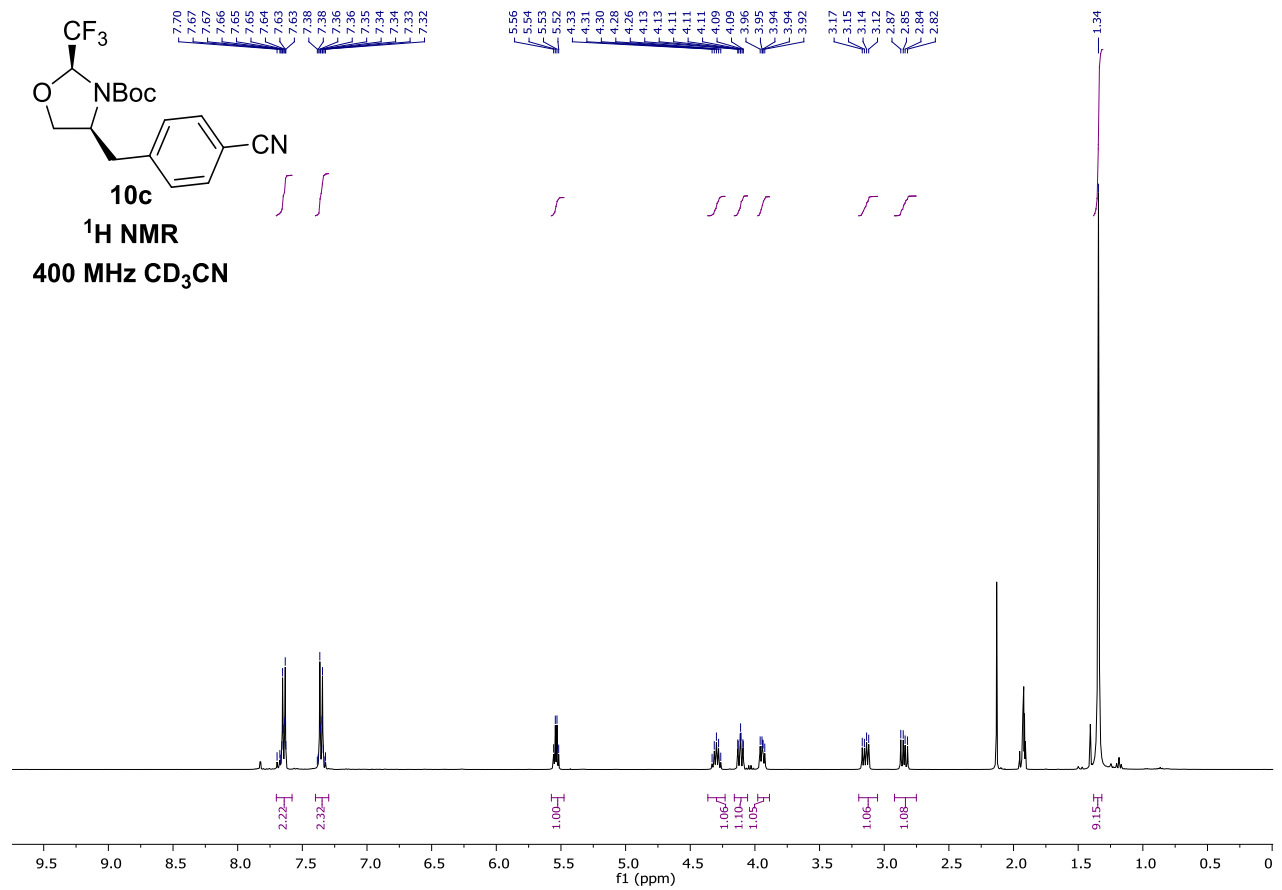


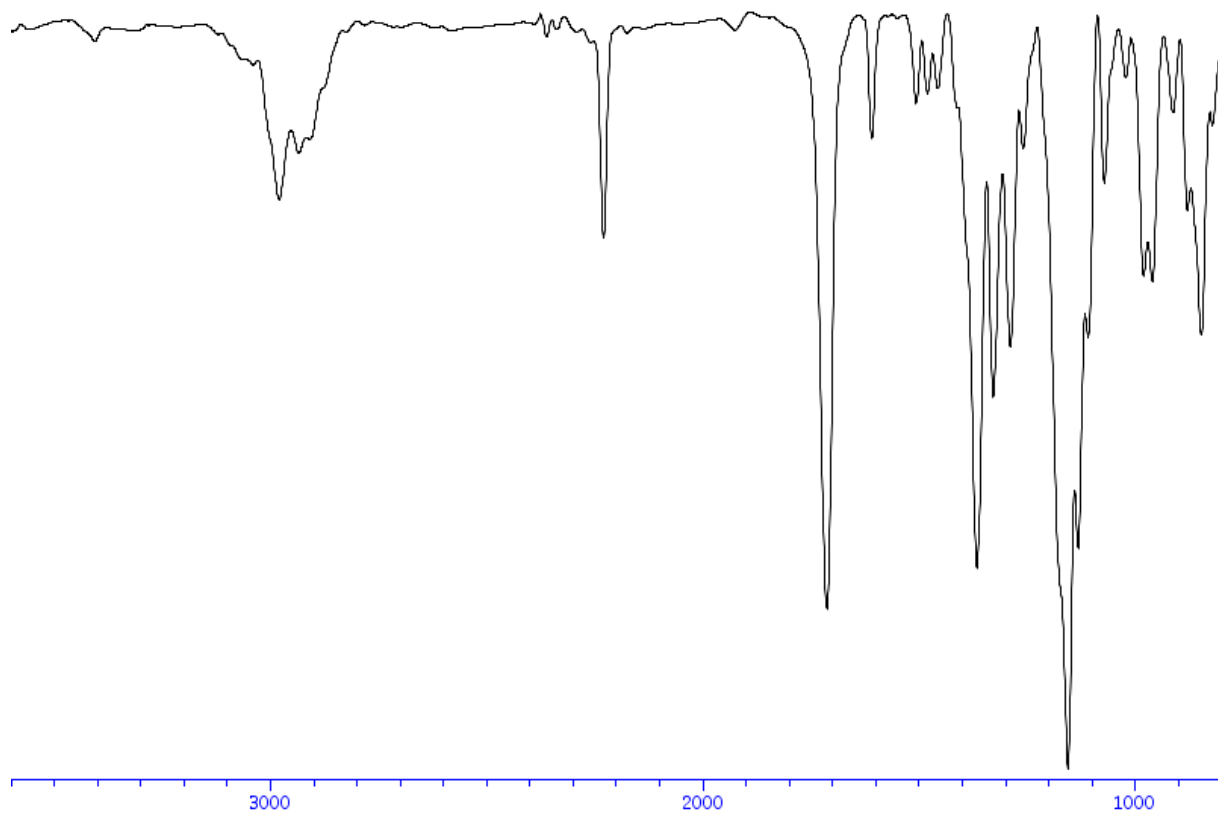


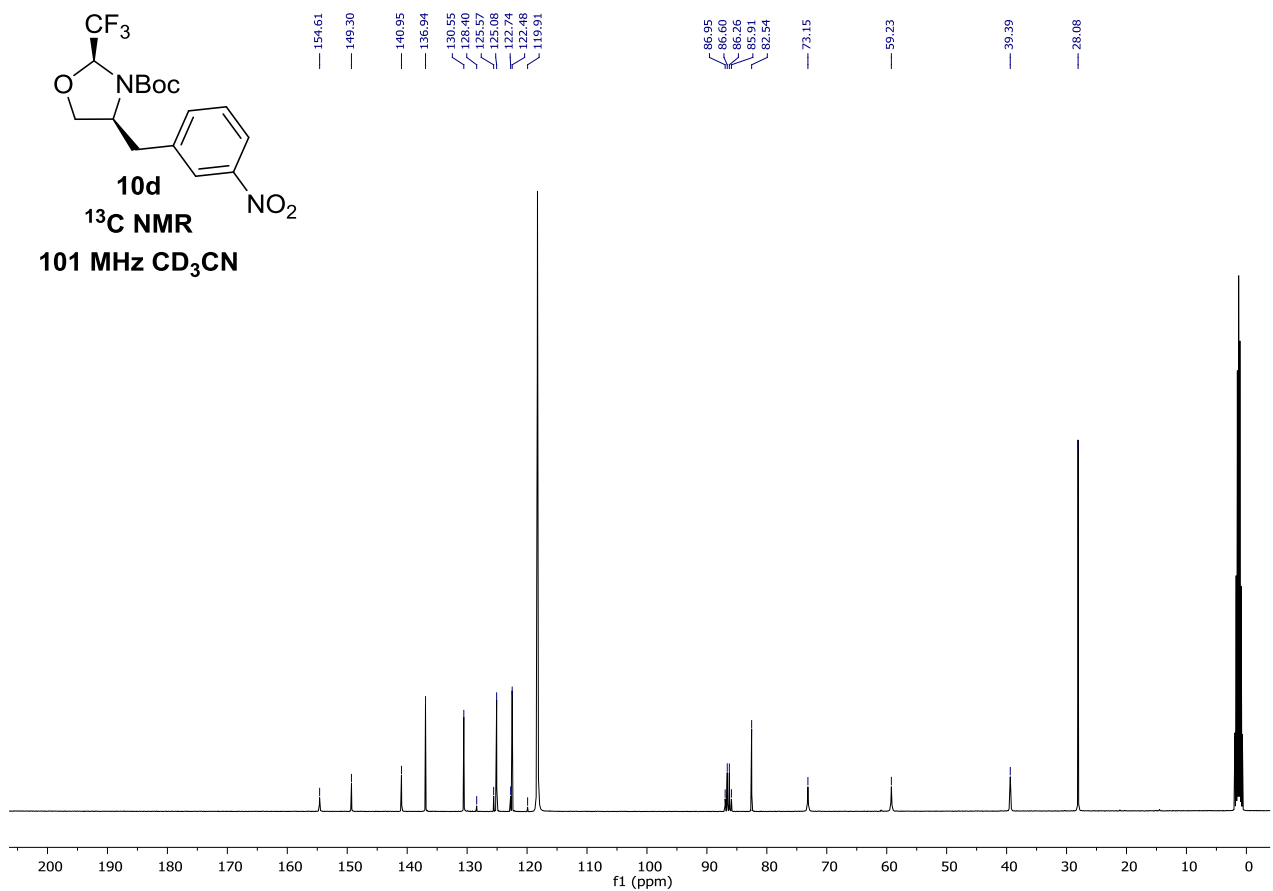
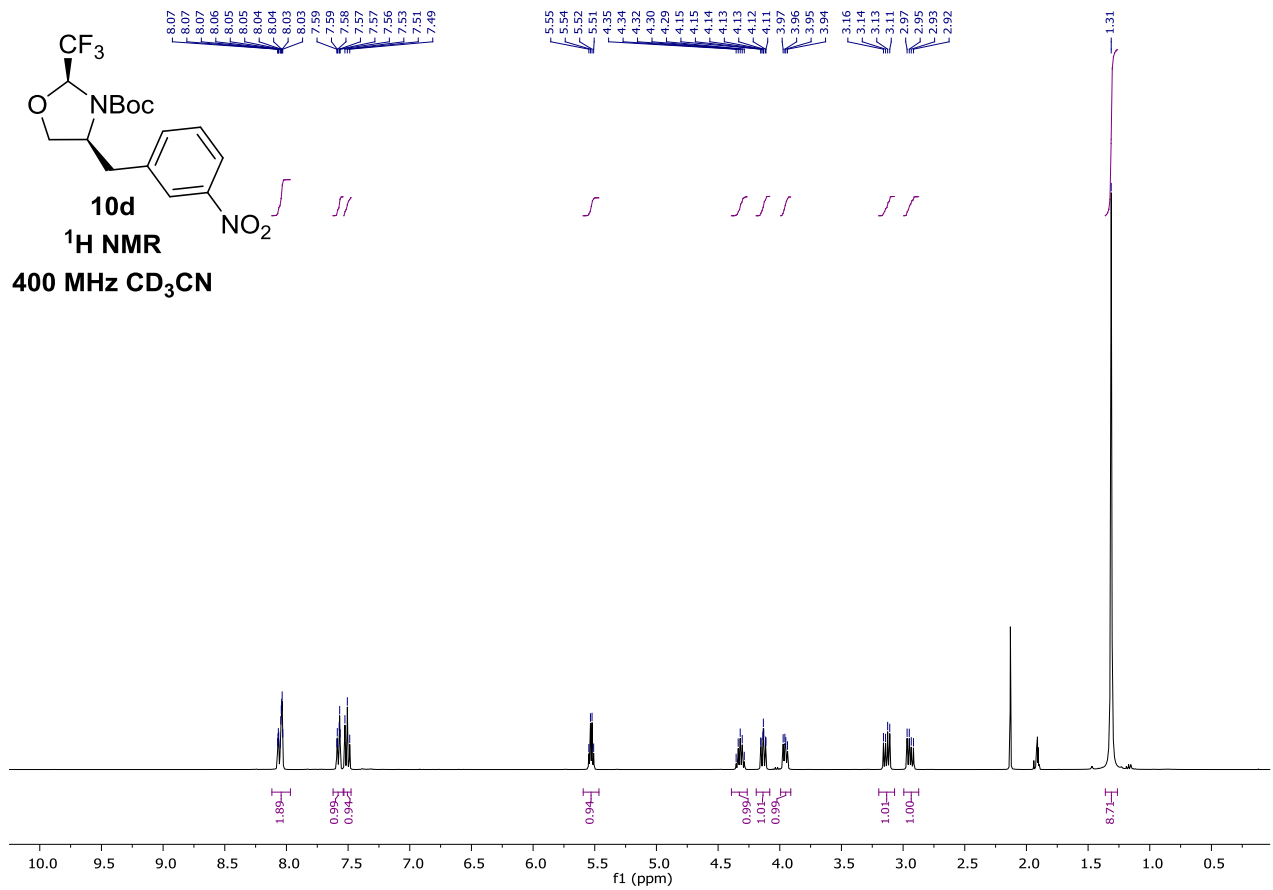


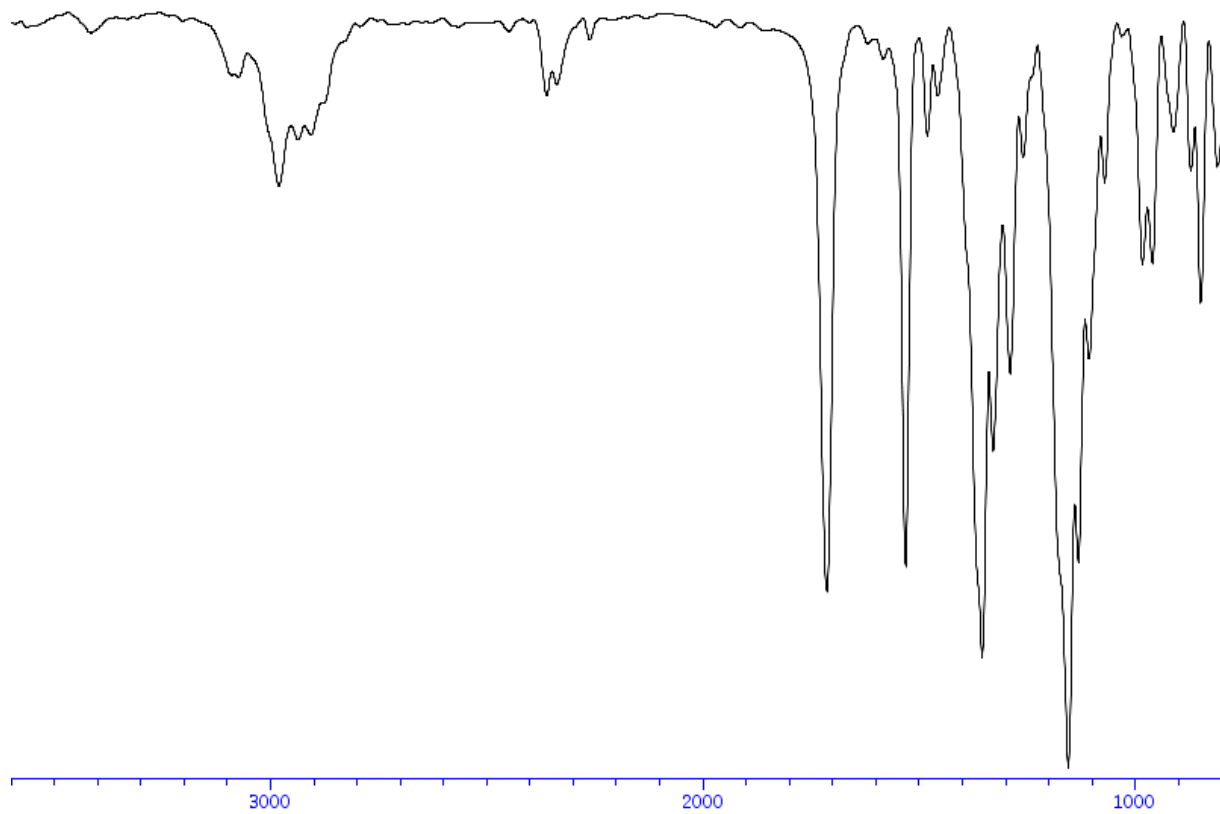


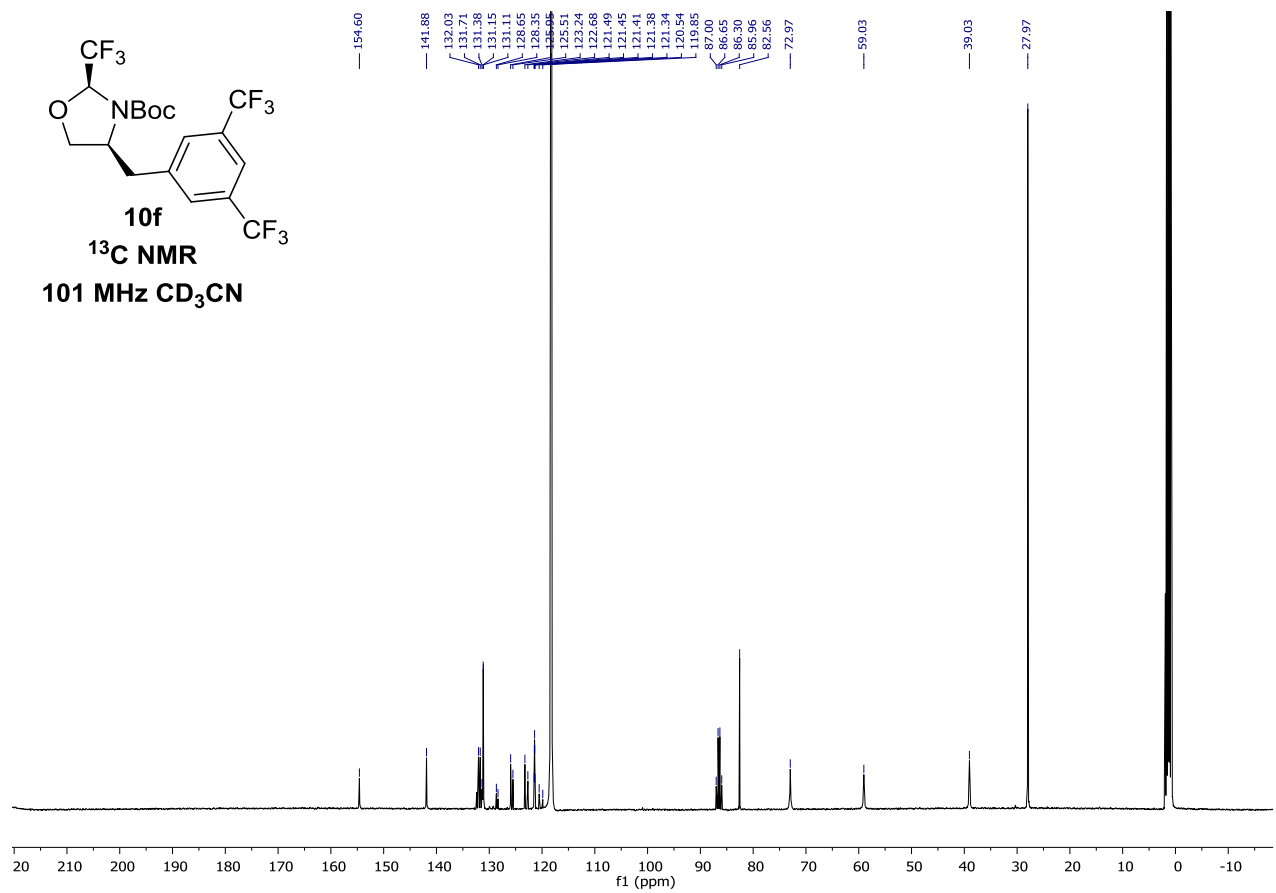
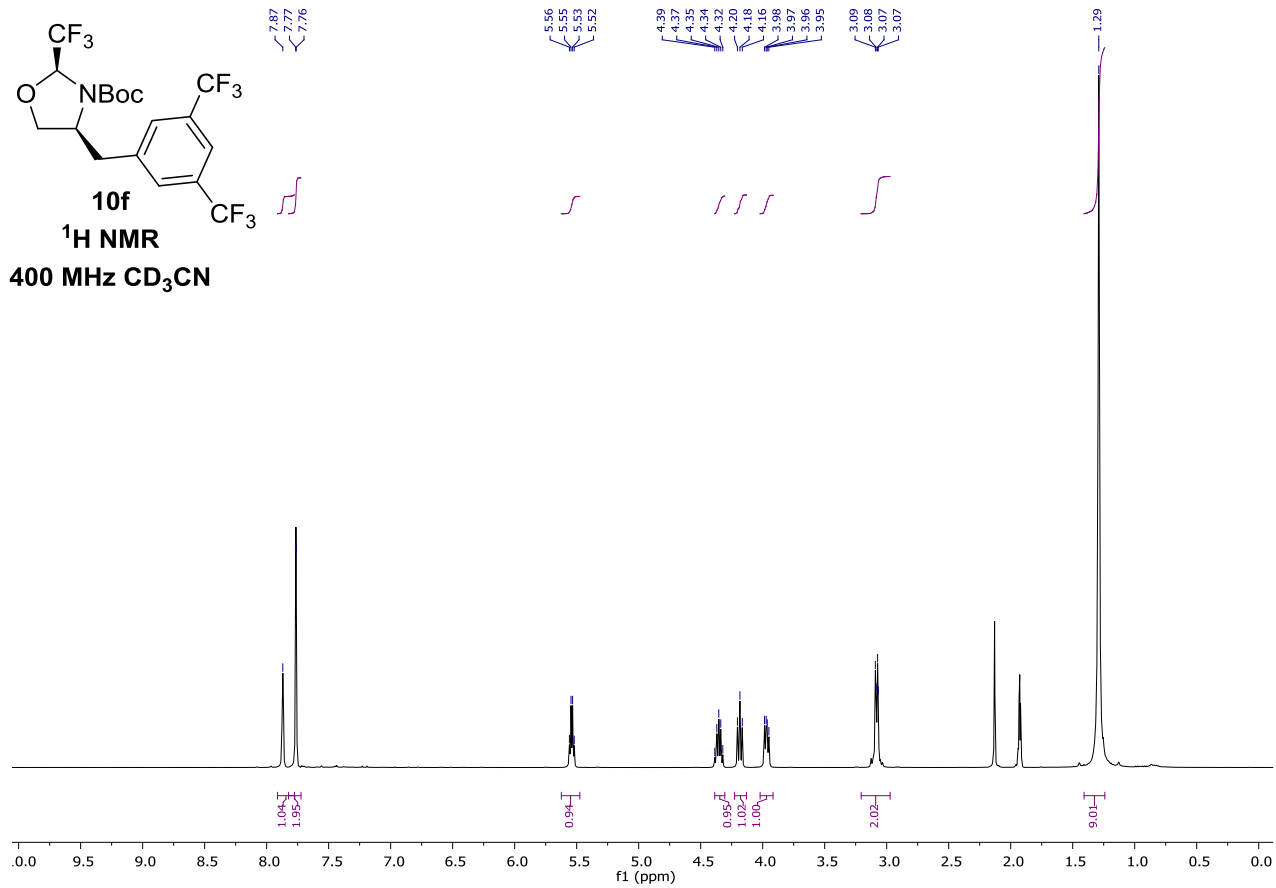


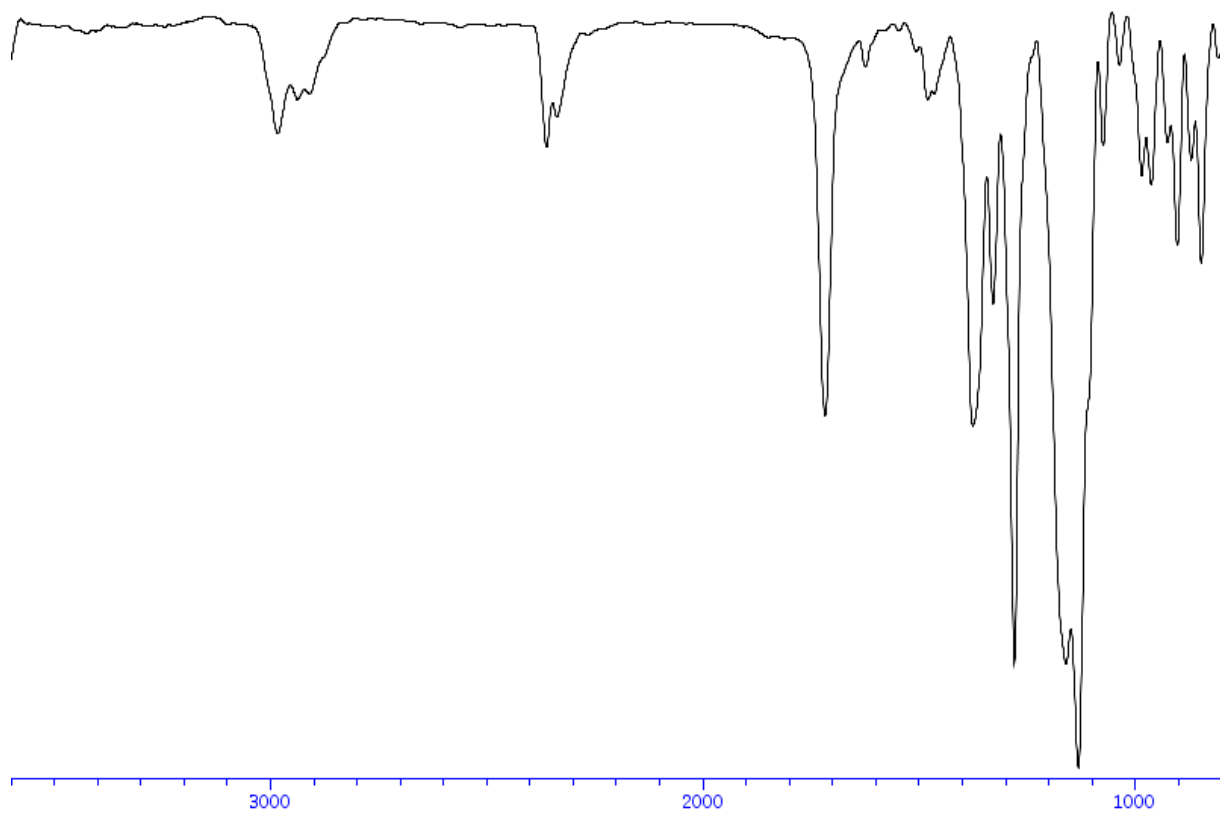


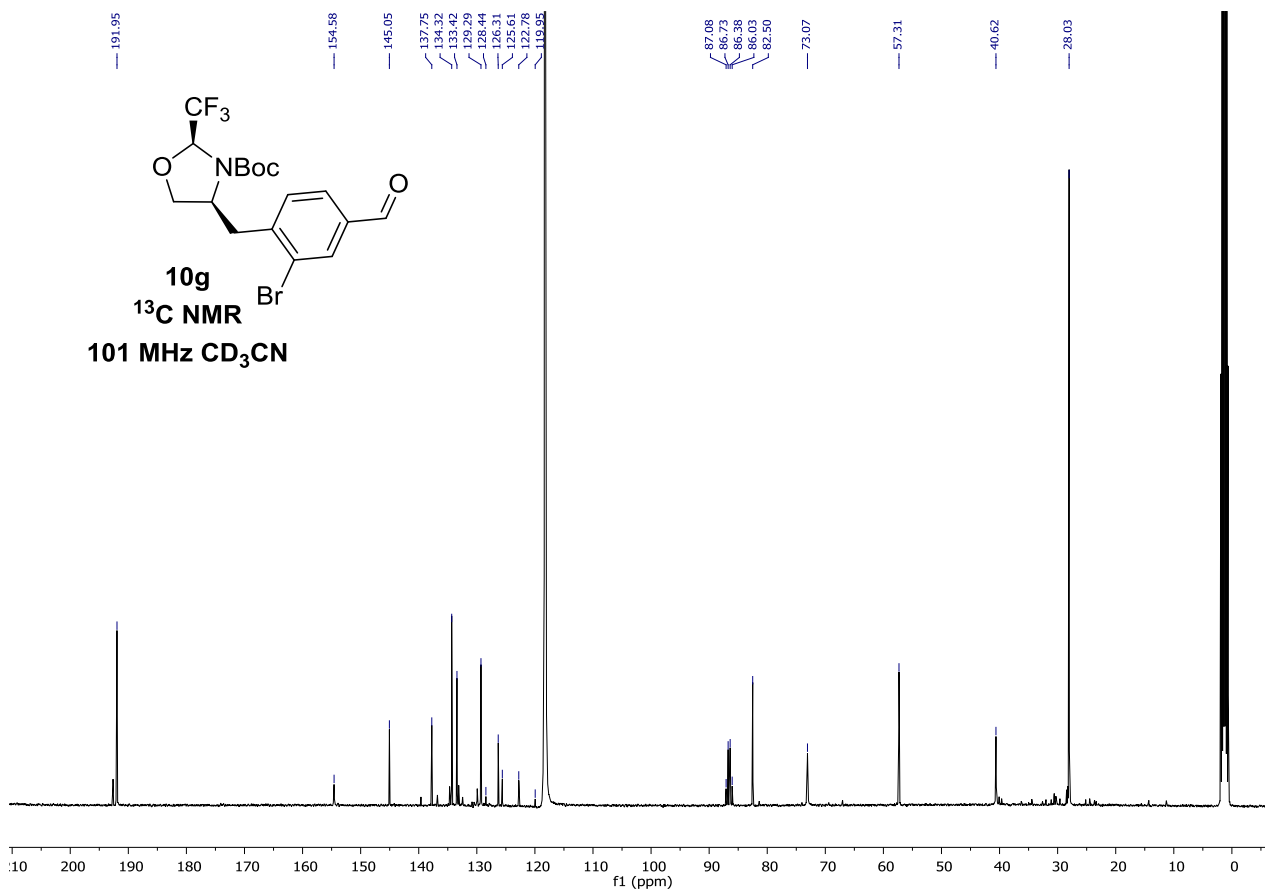
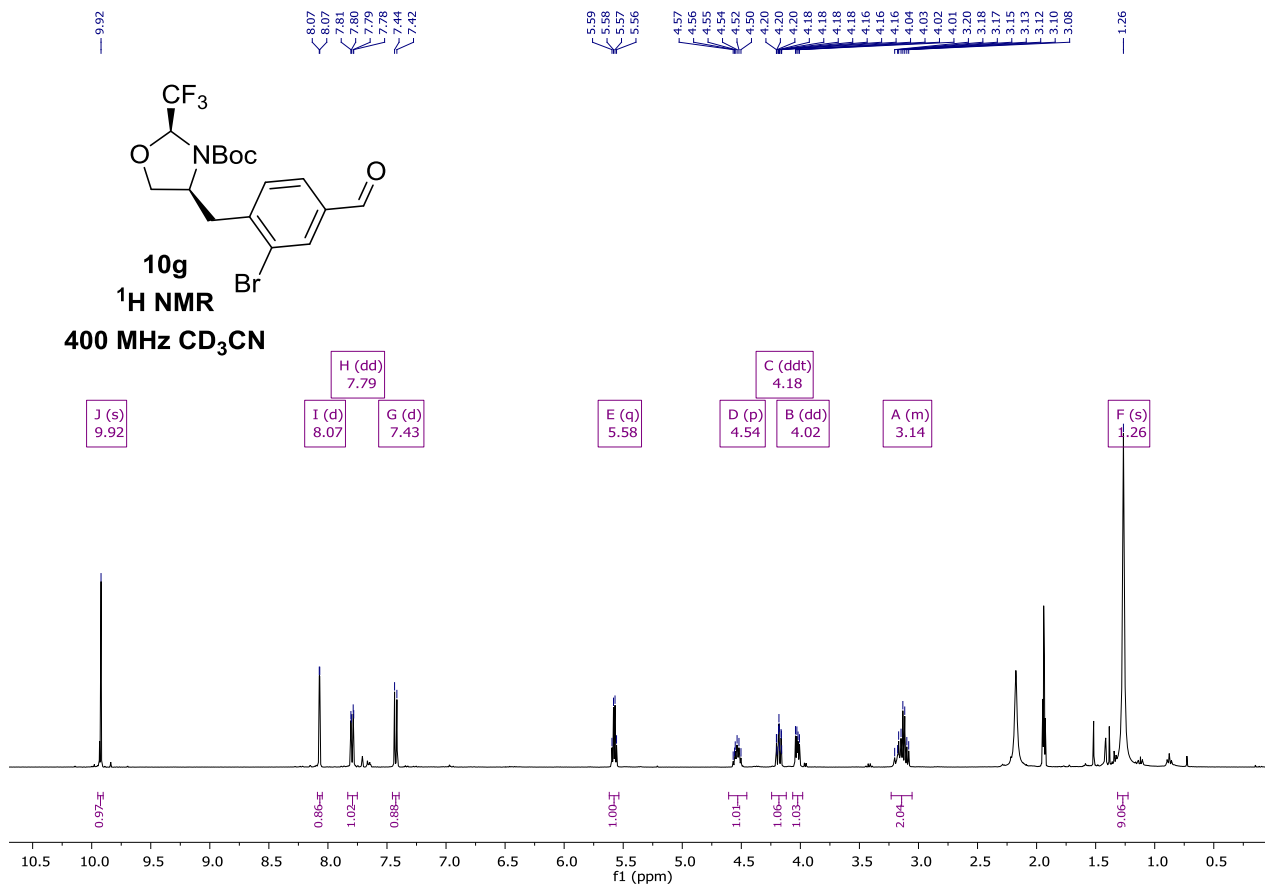


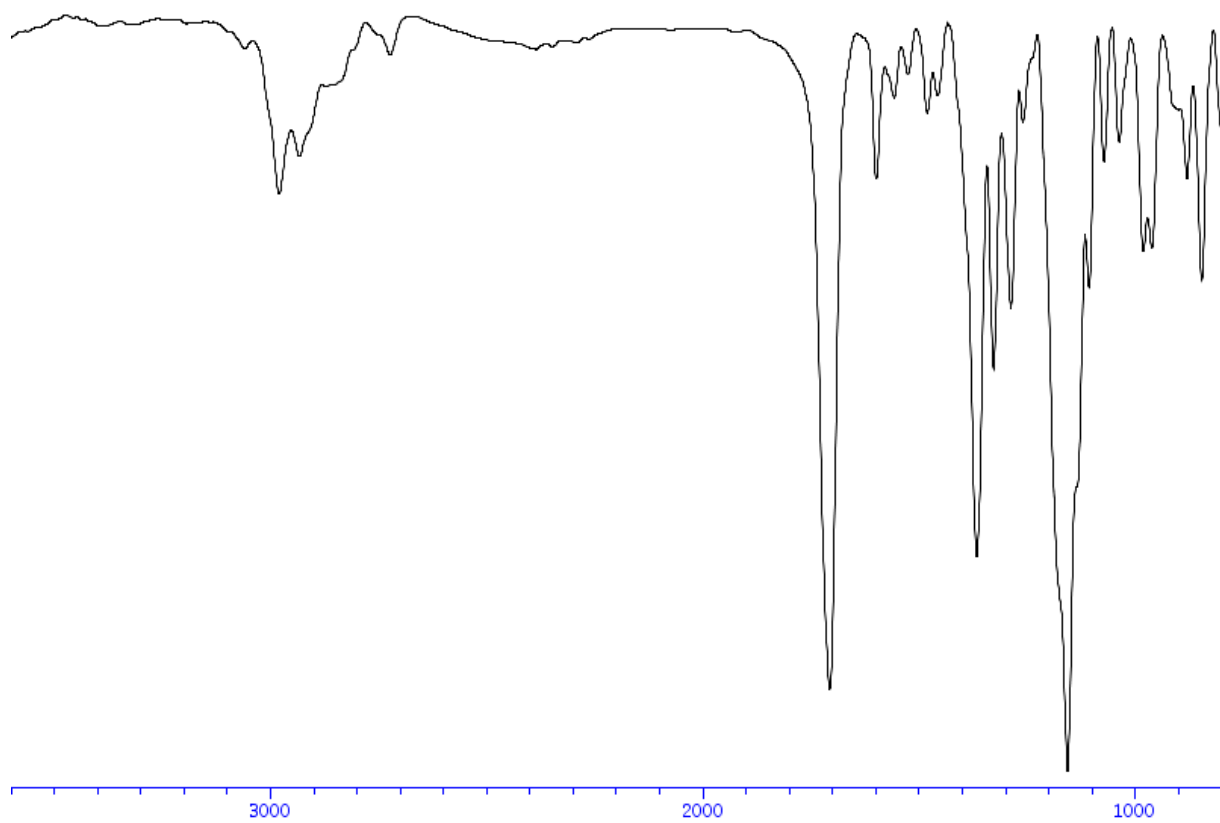


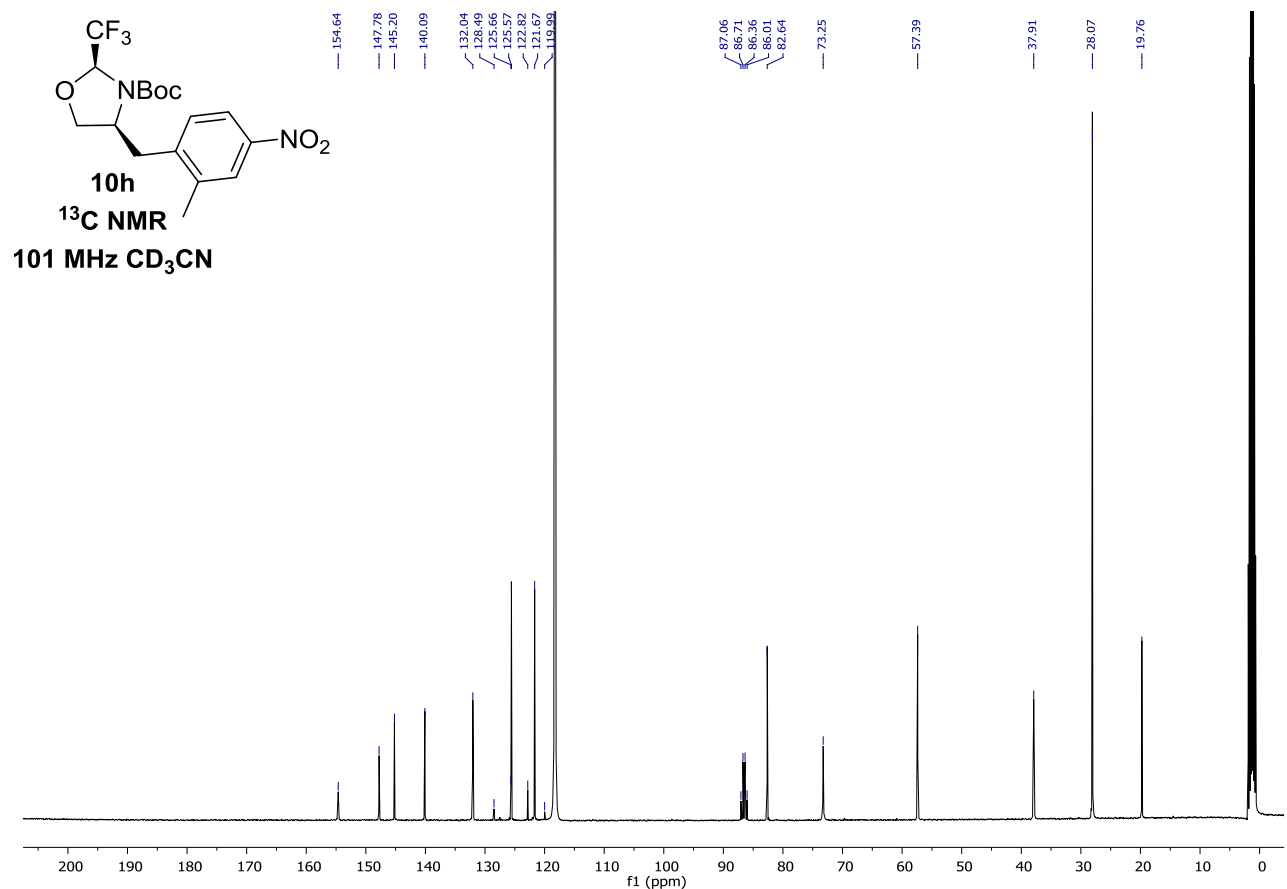
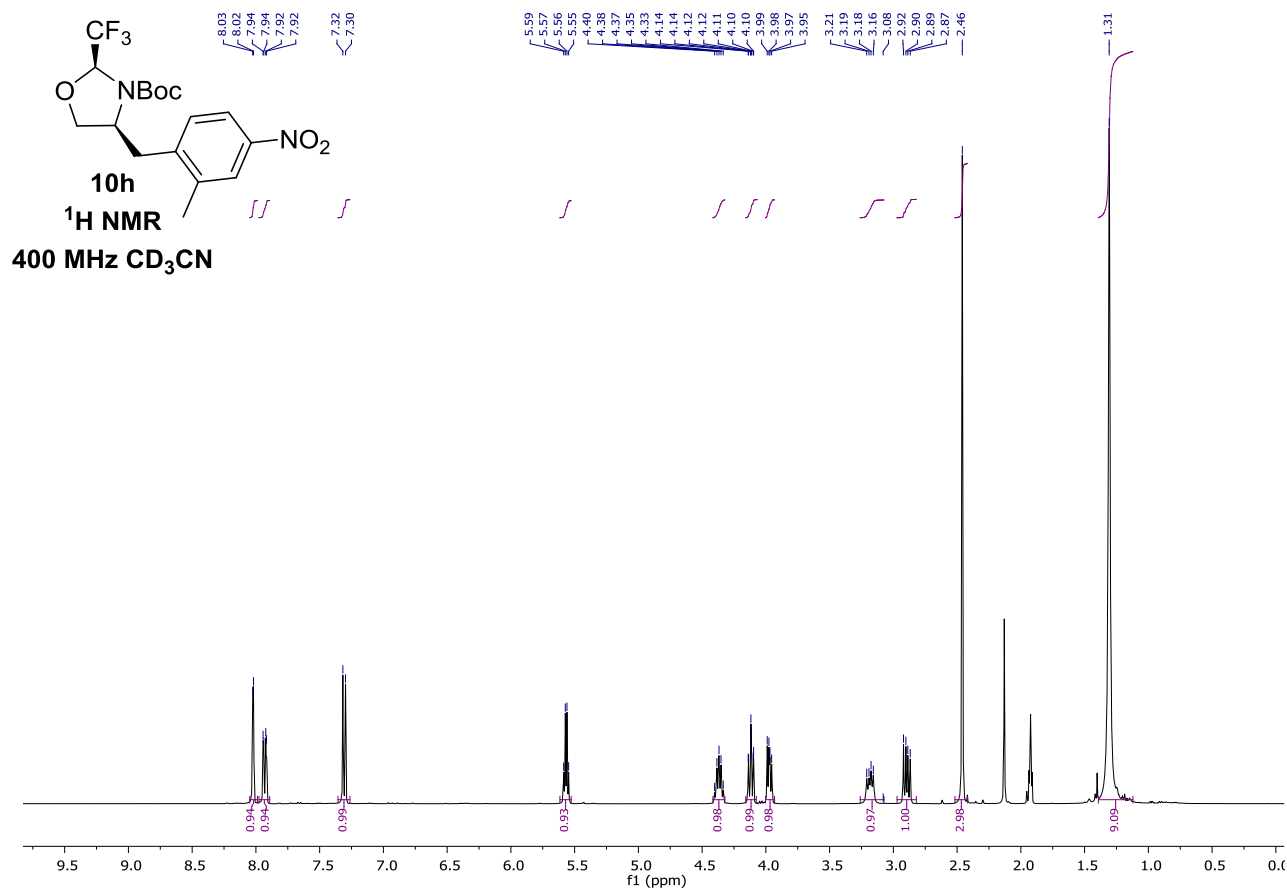


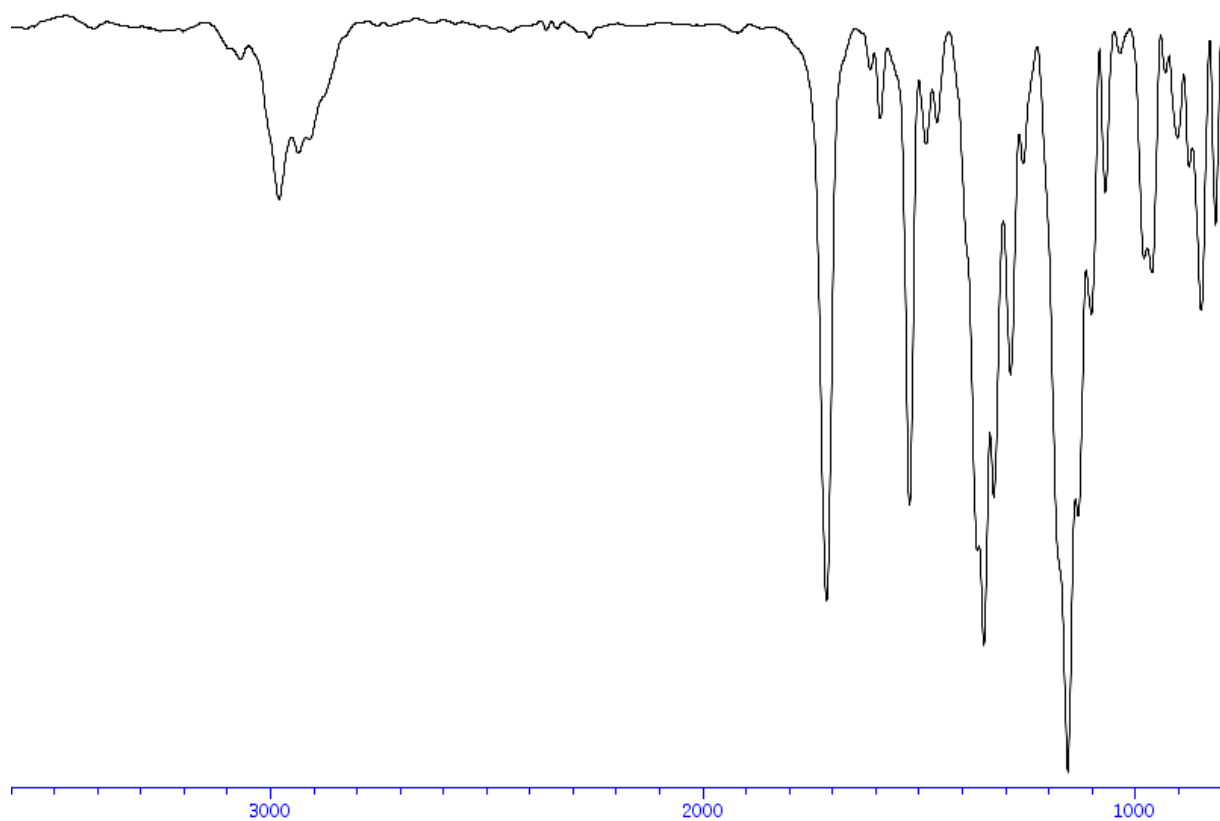


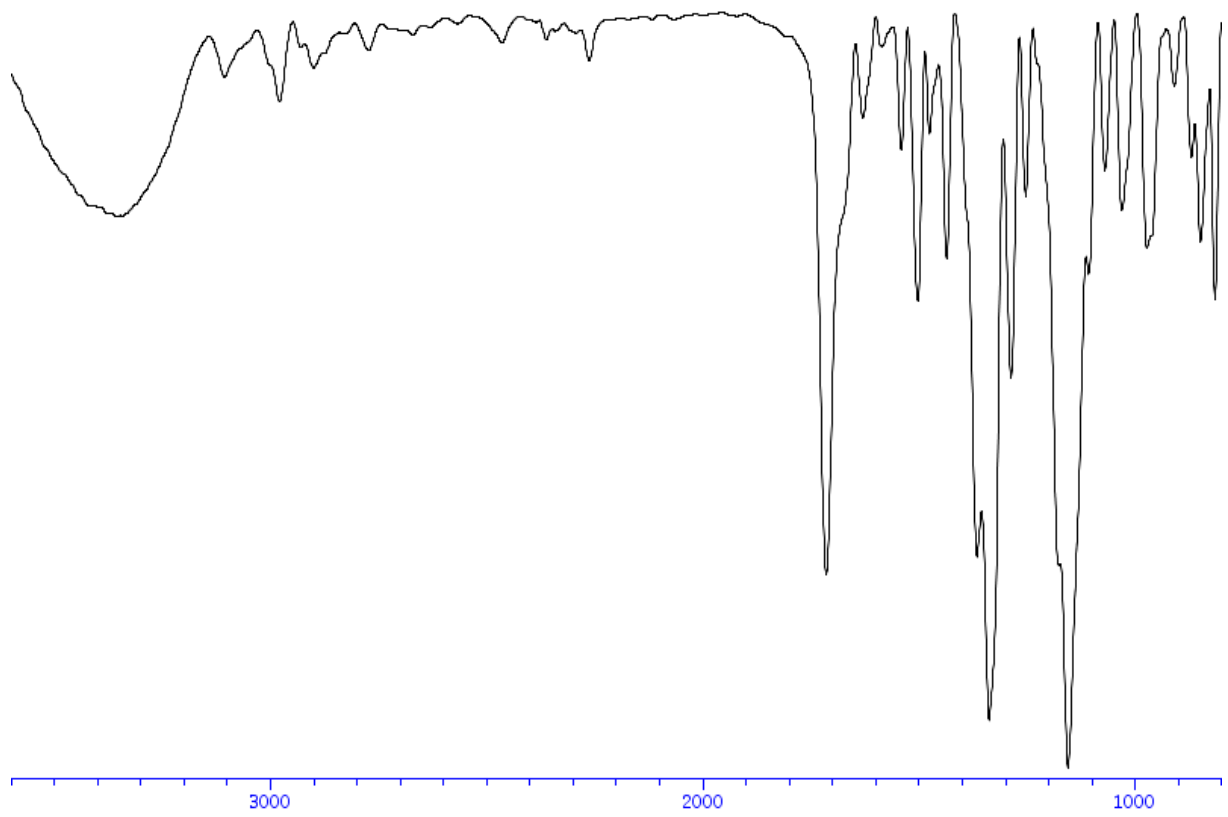


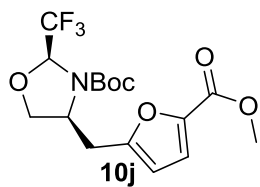




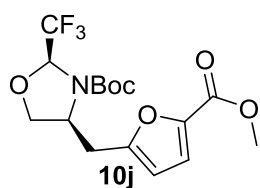
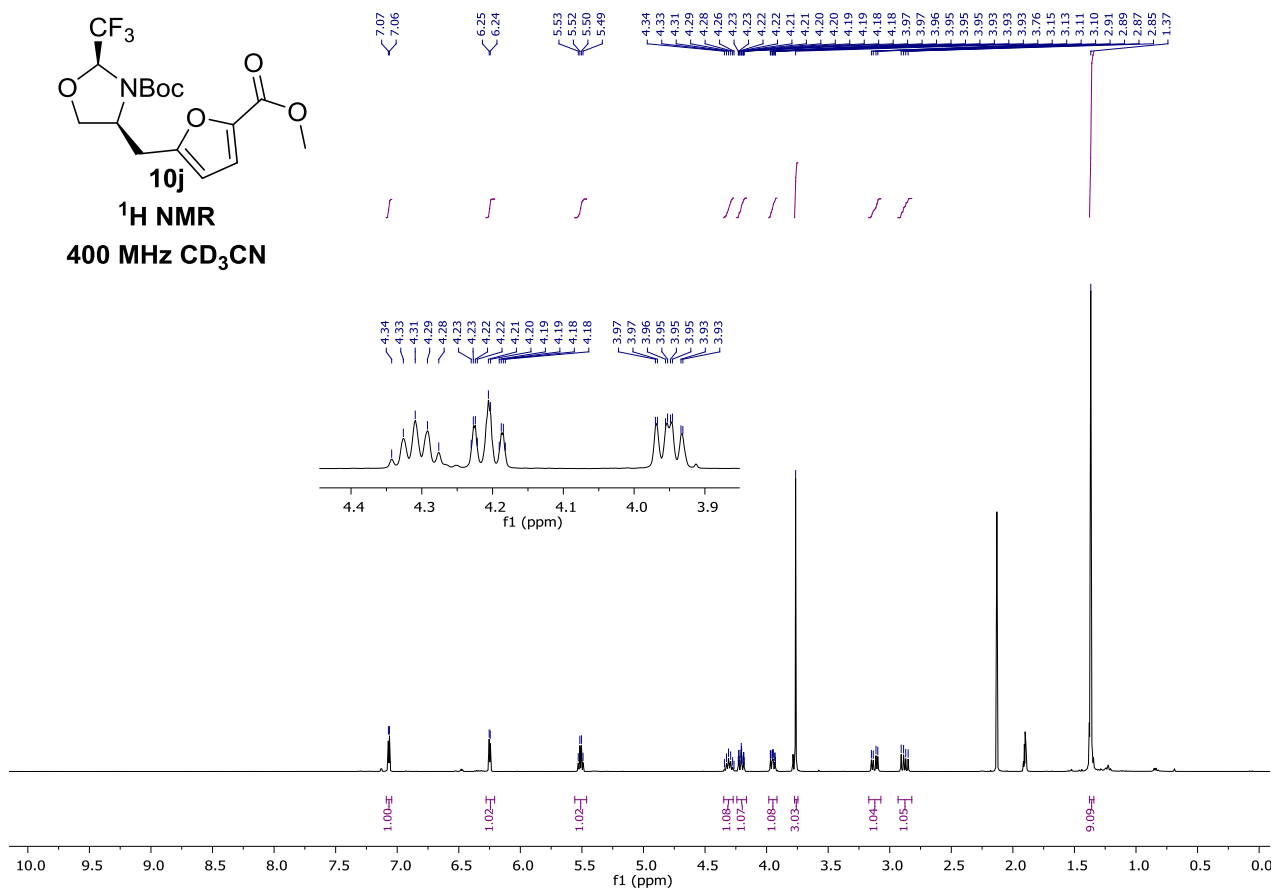




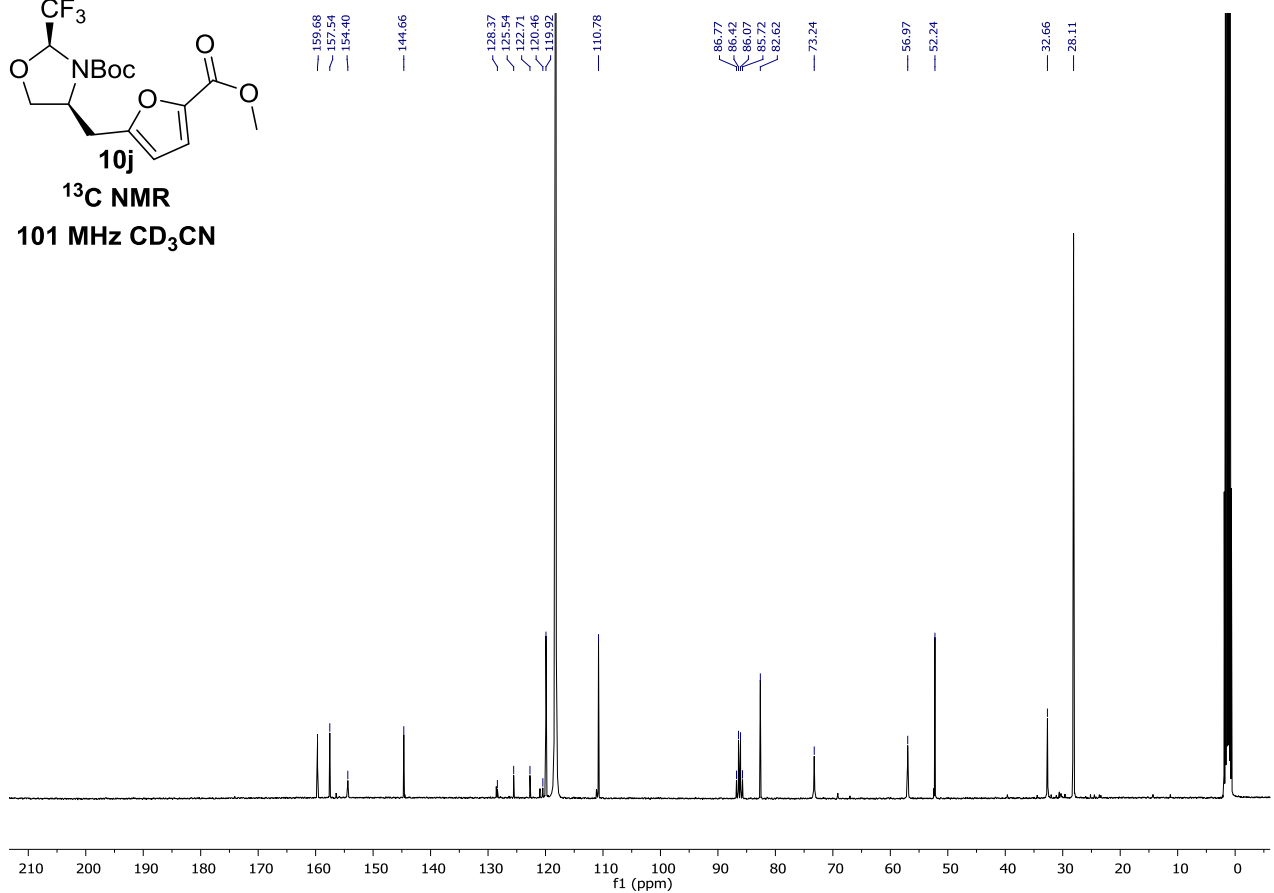


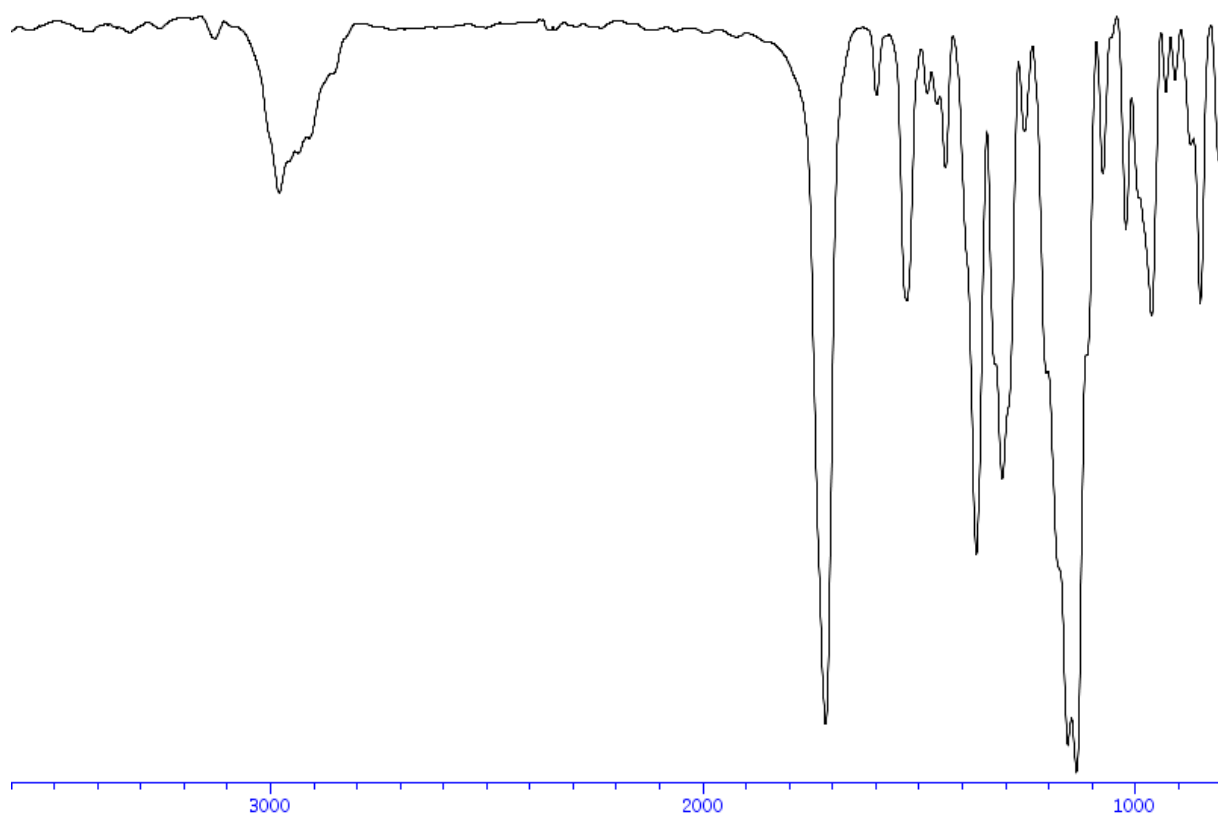


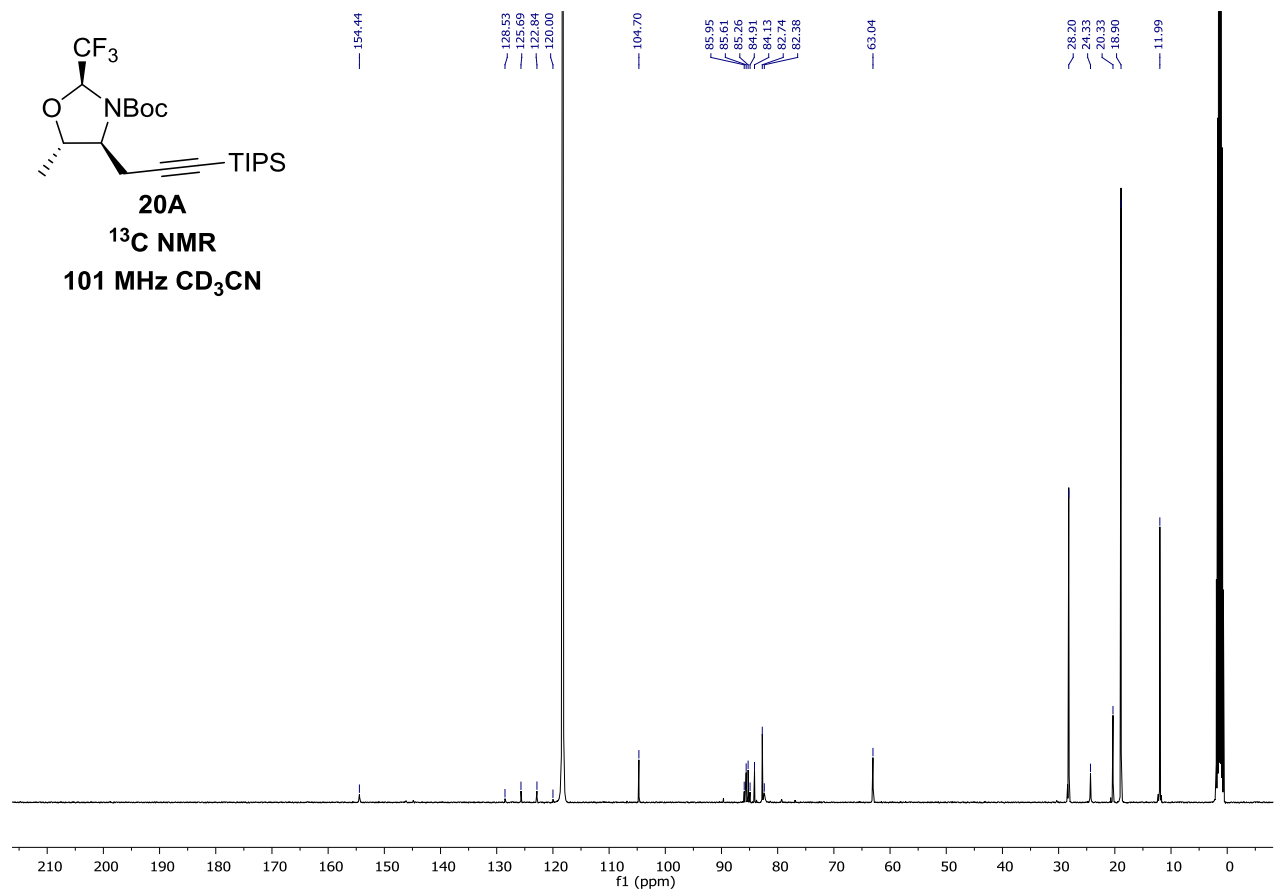
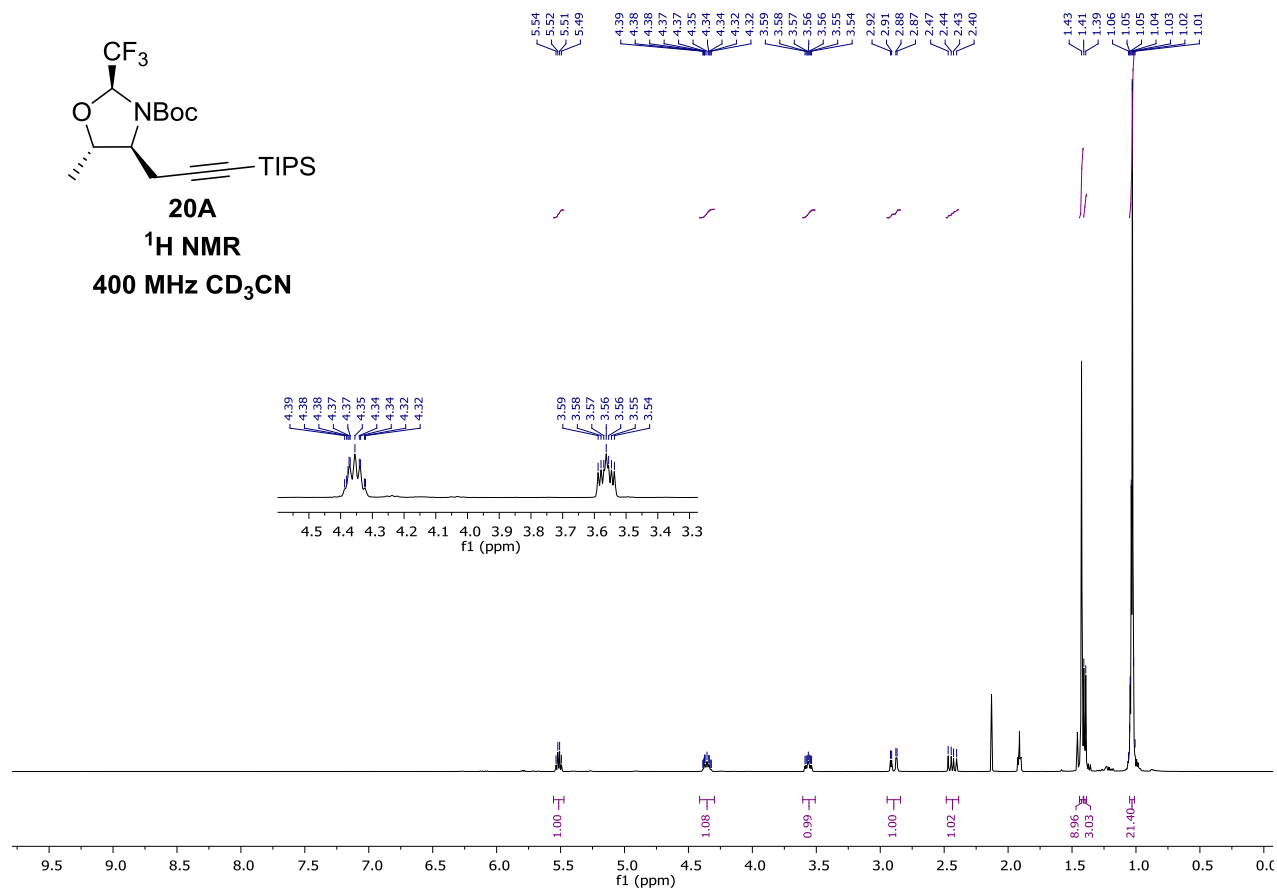
¹H NMR
400 MHz CD₃CN

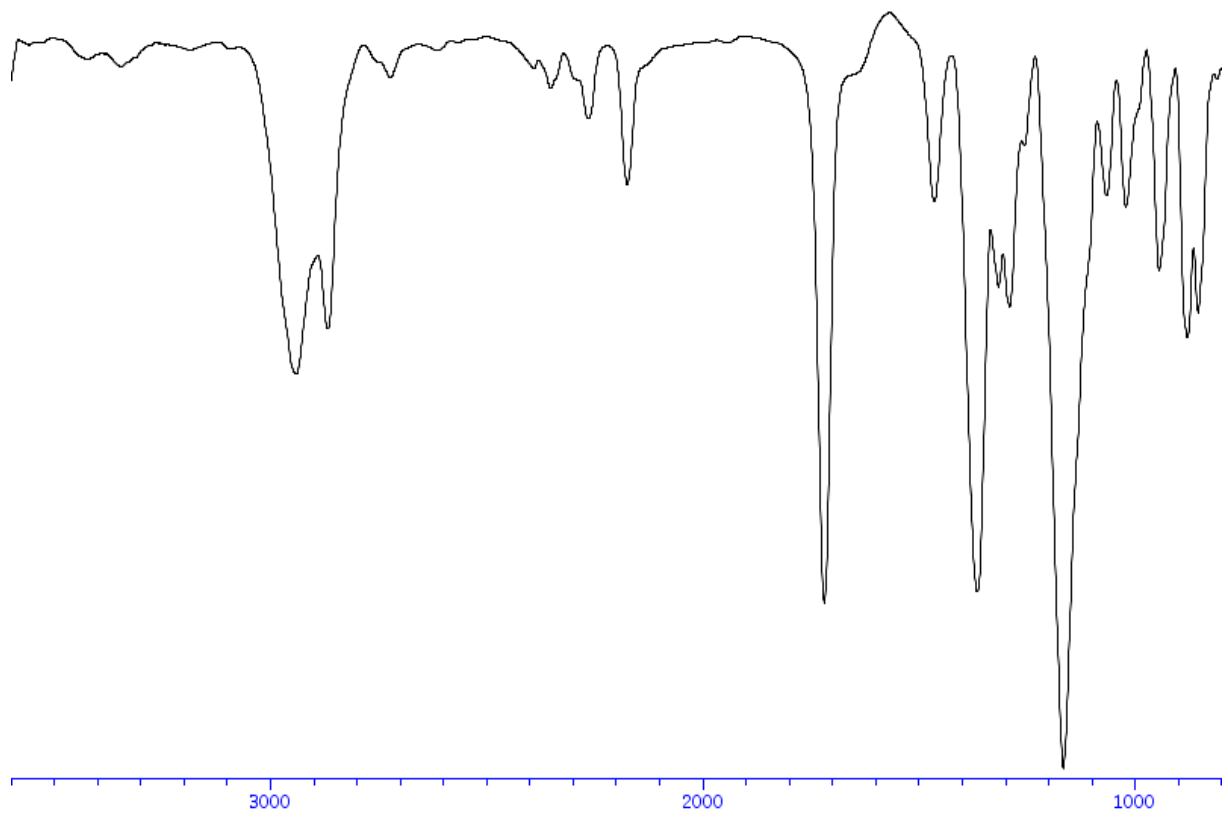


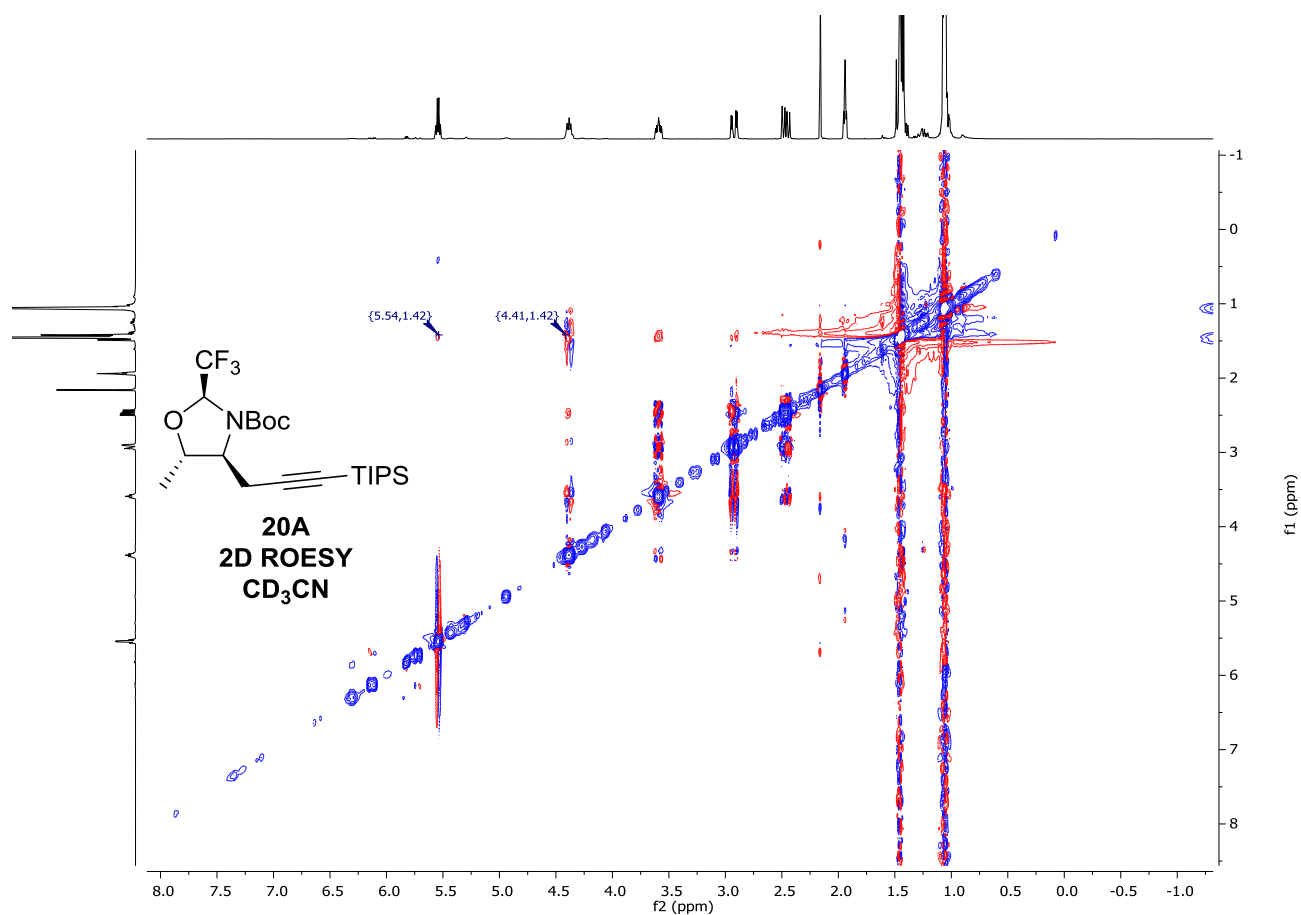
¹³C NMR
101 MHz CD₃CN

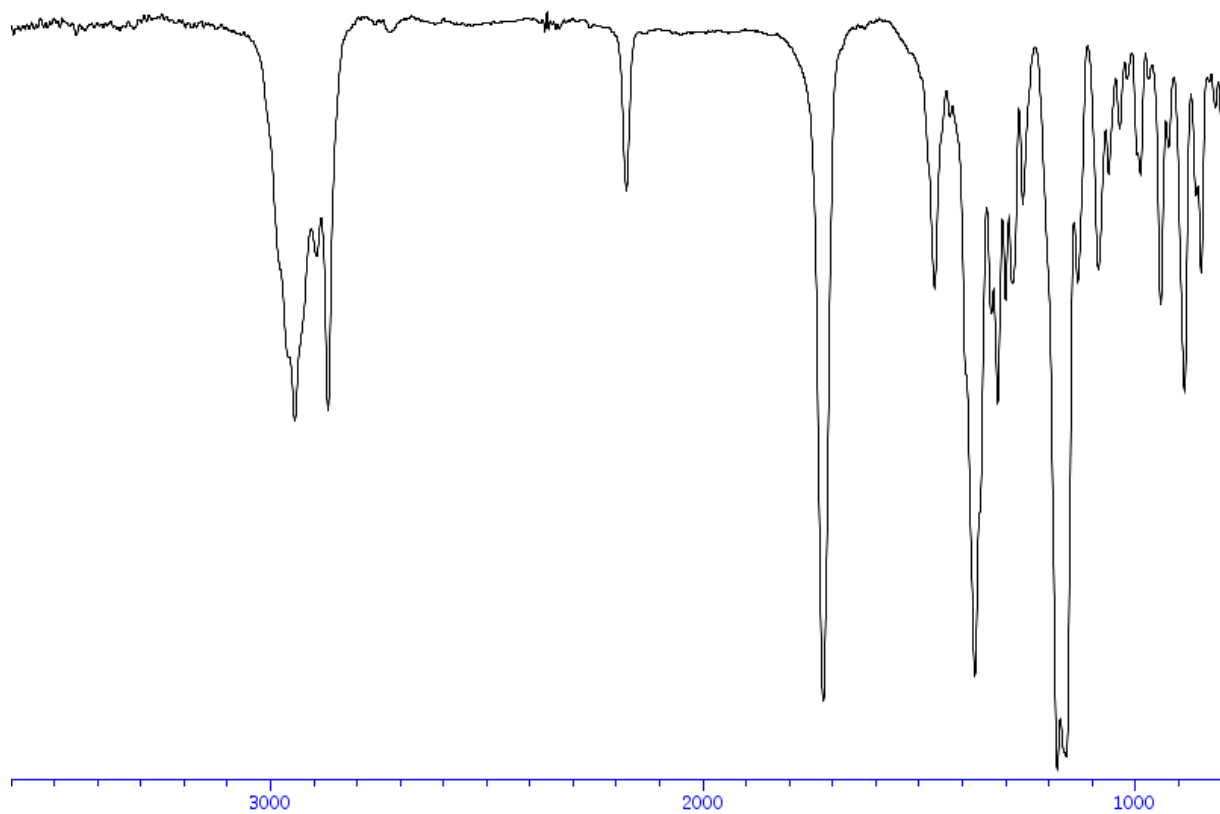


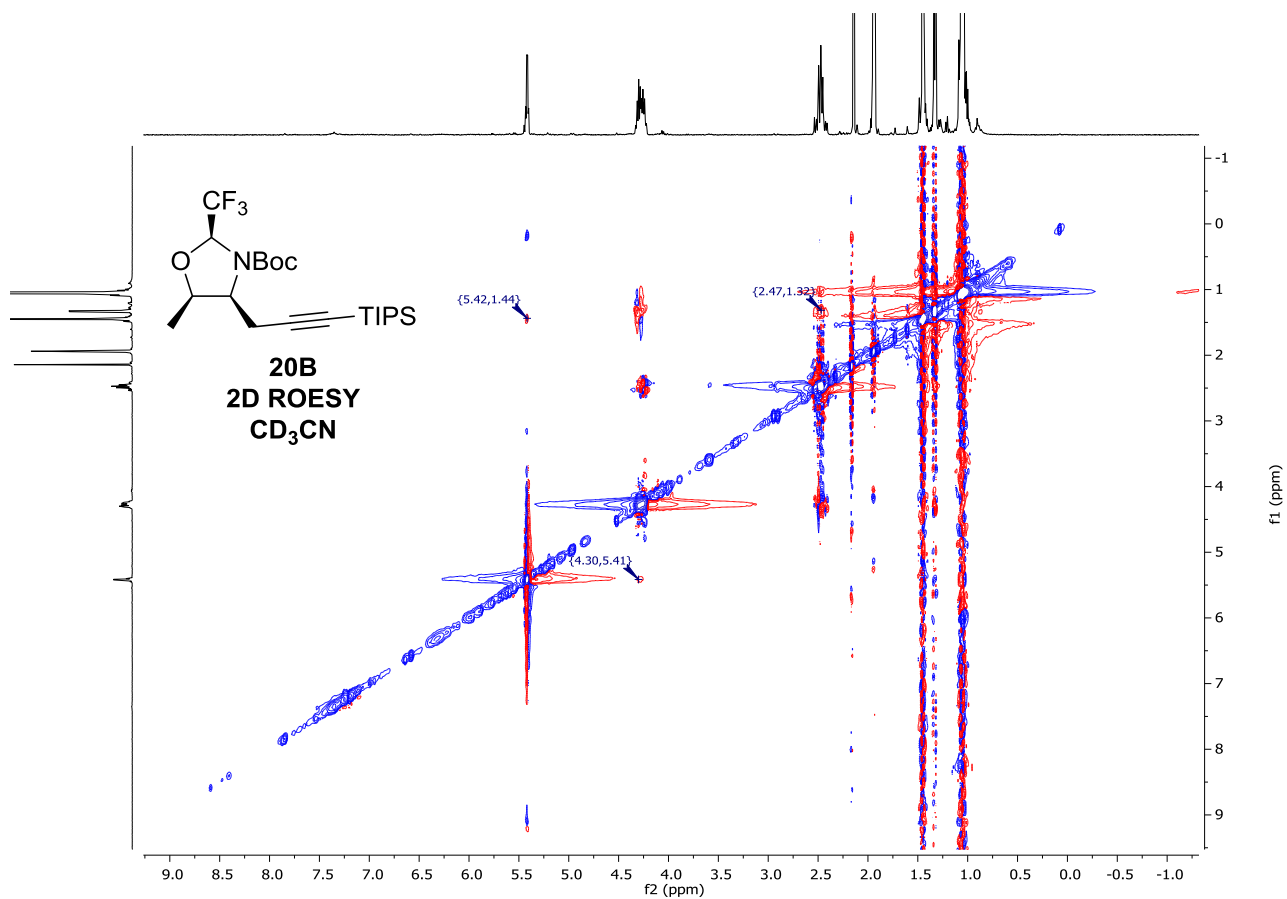


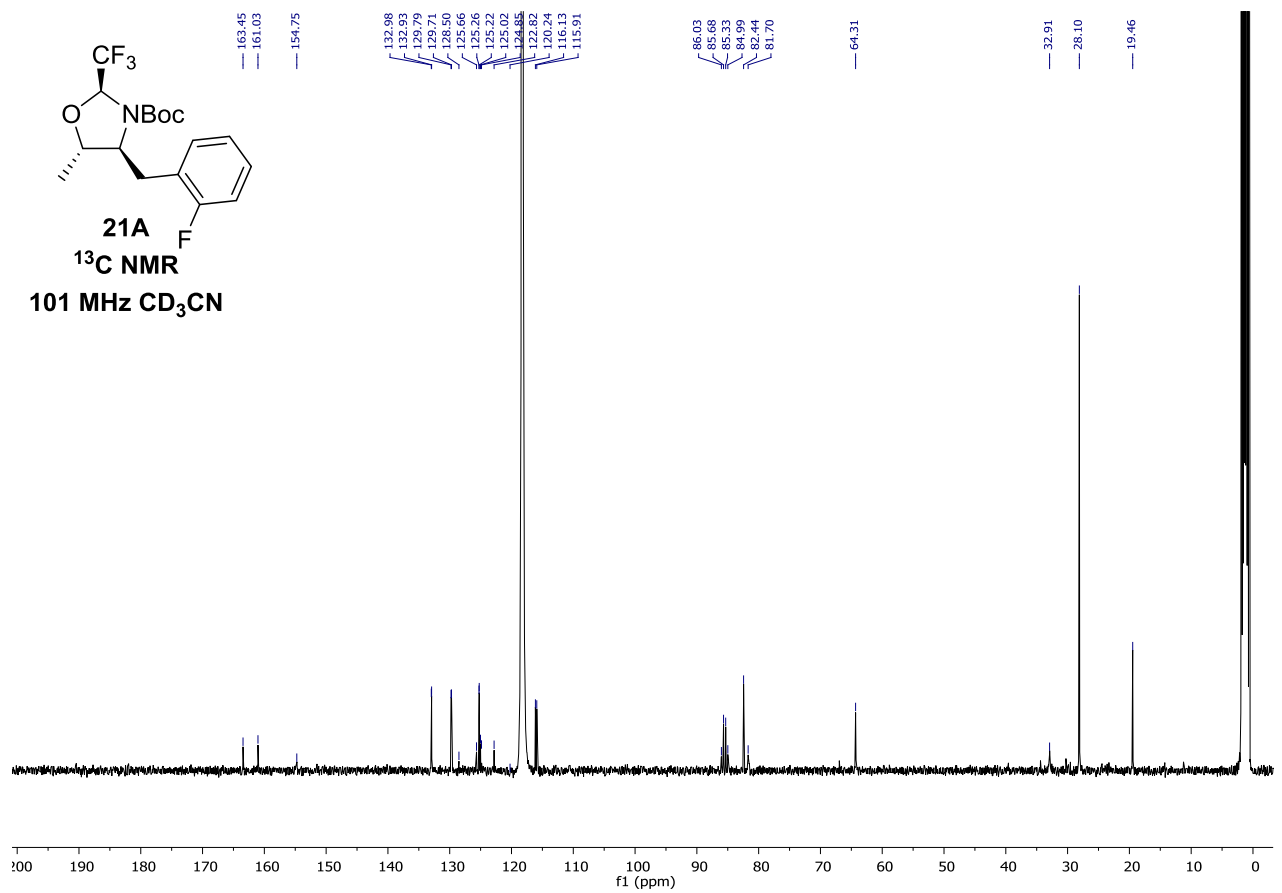
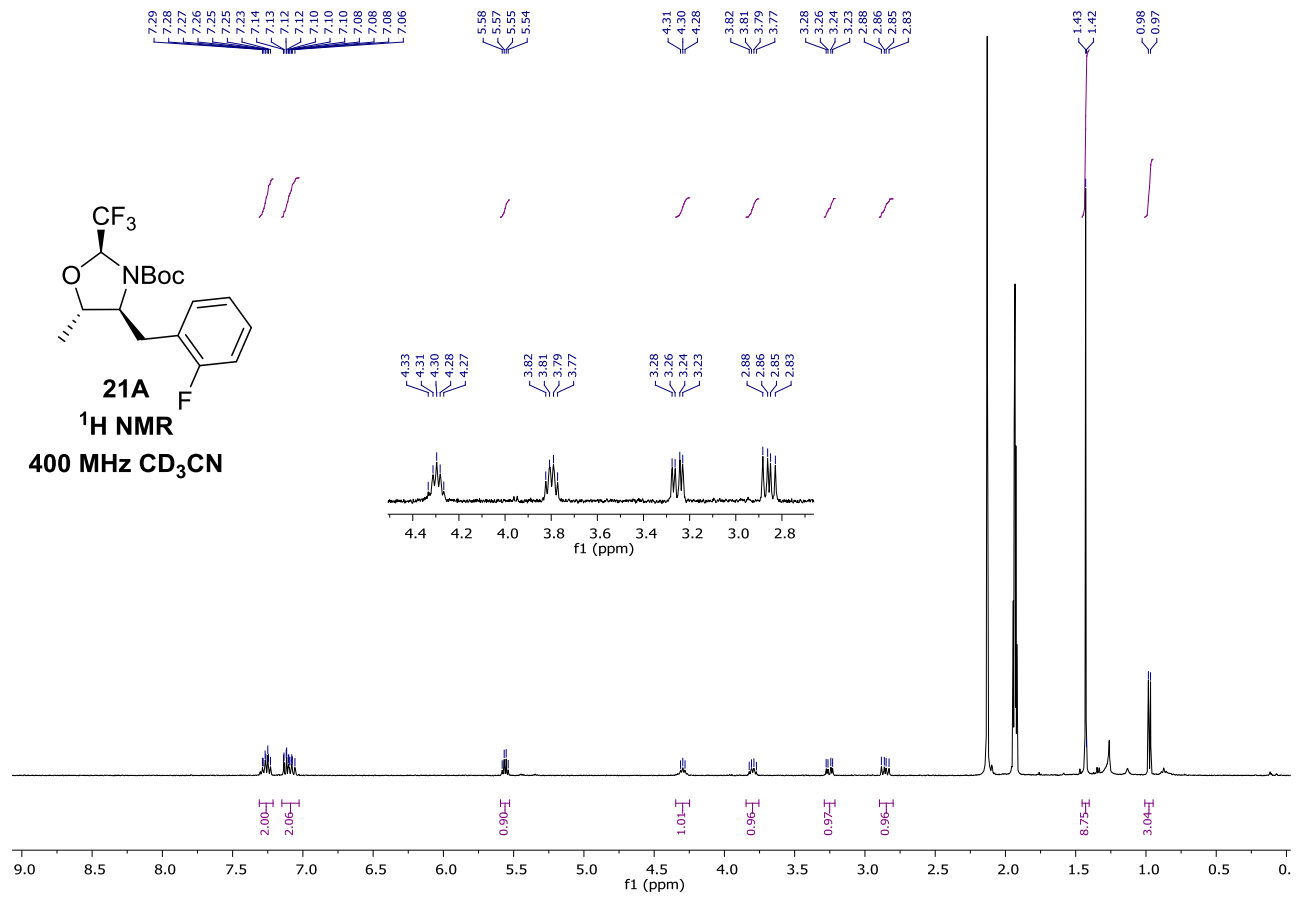


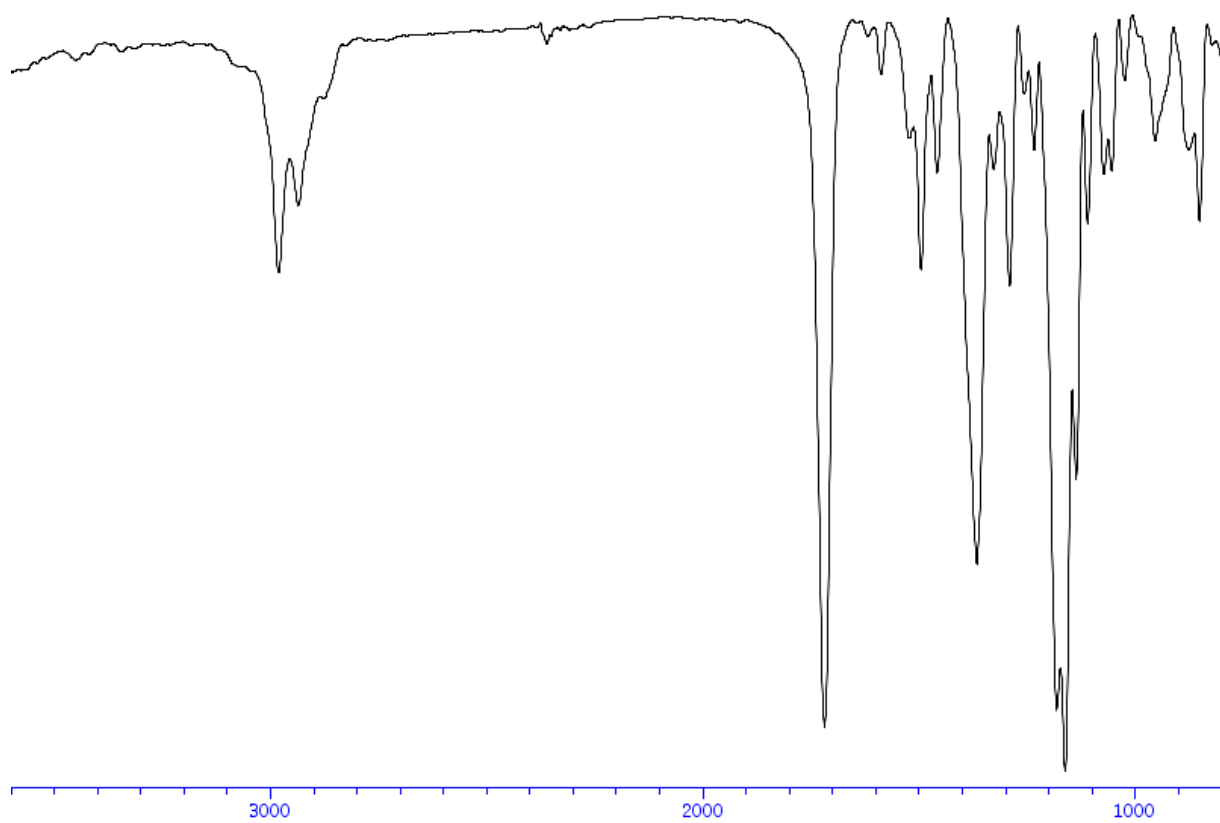


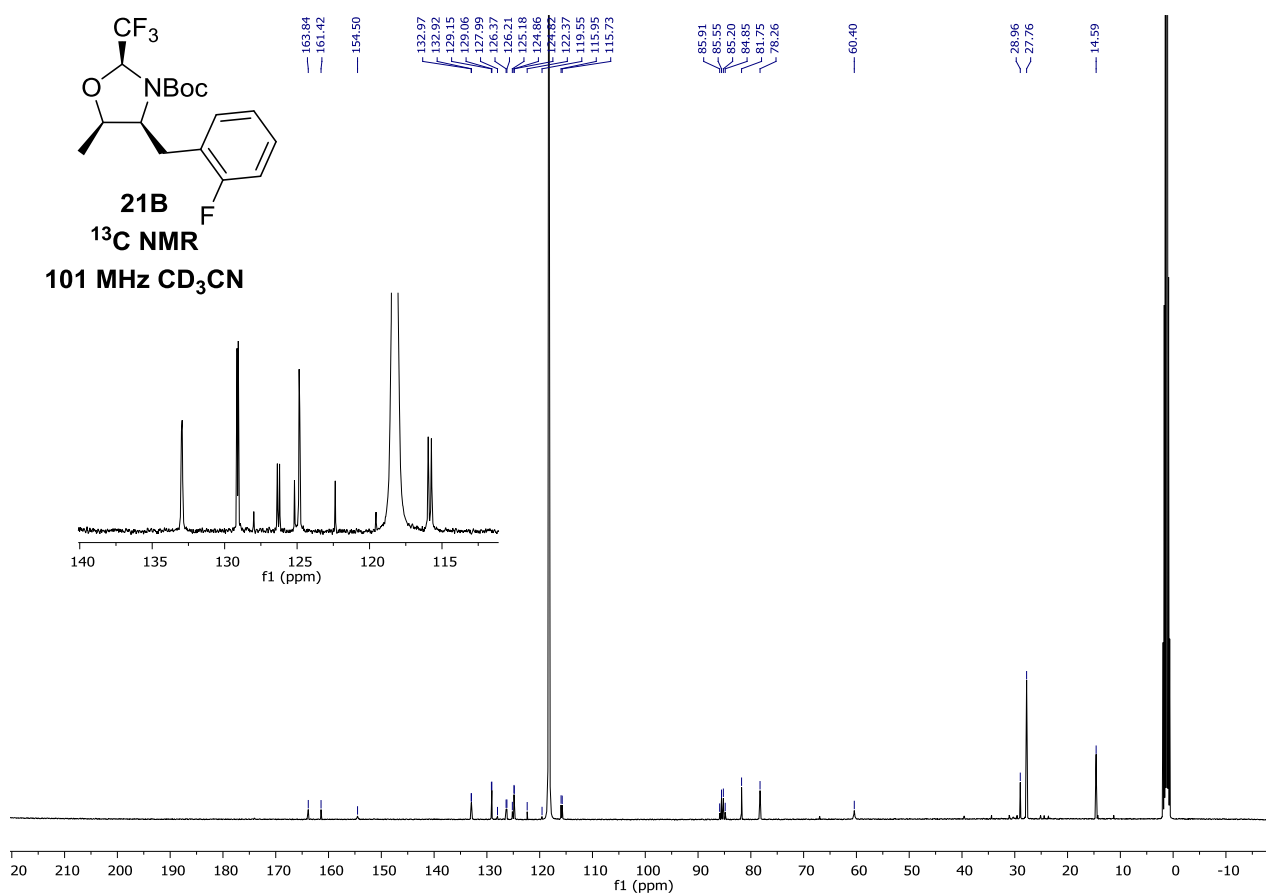
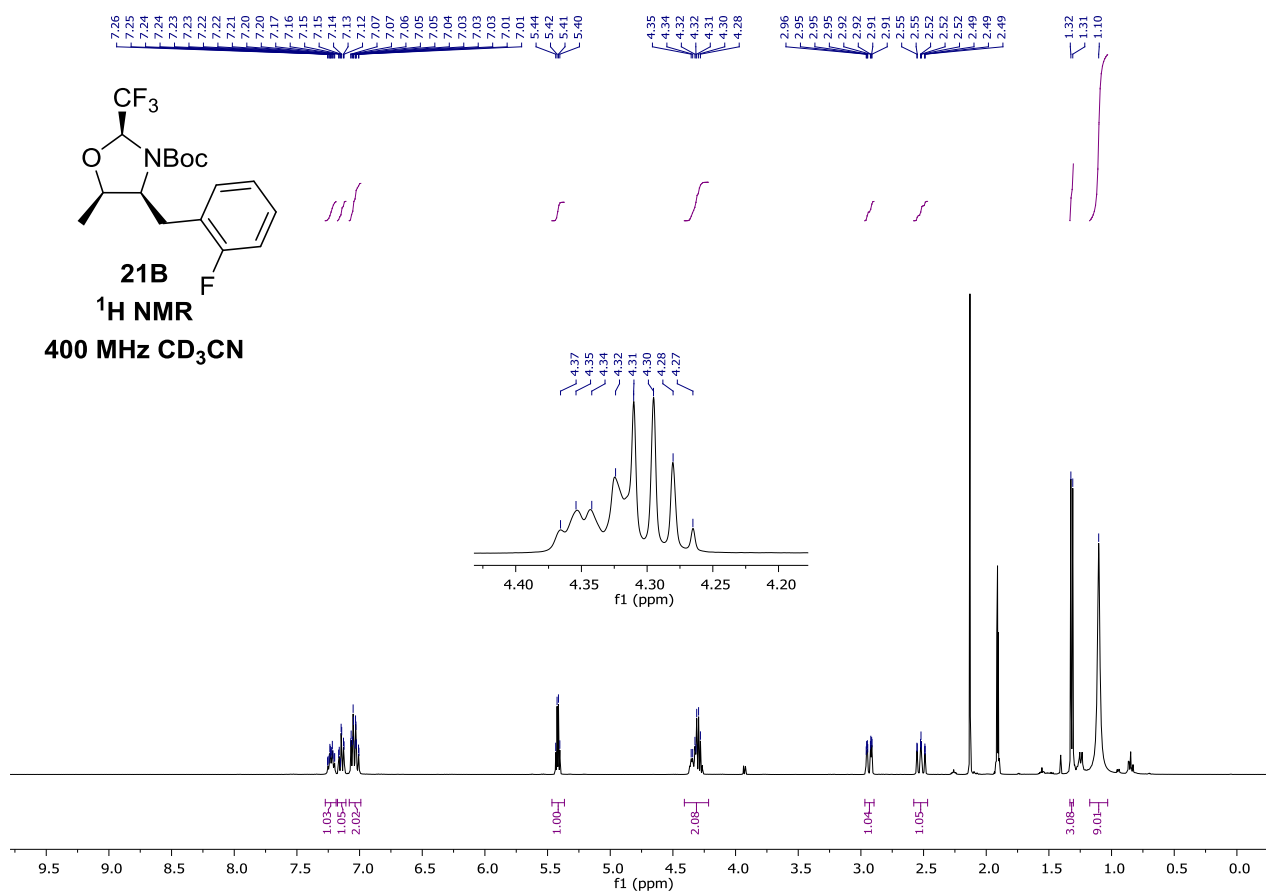


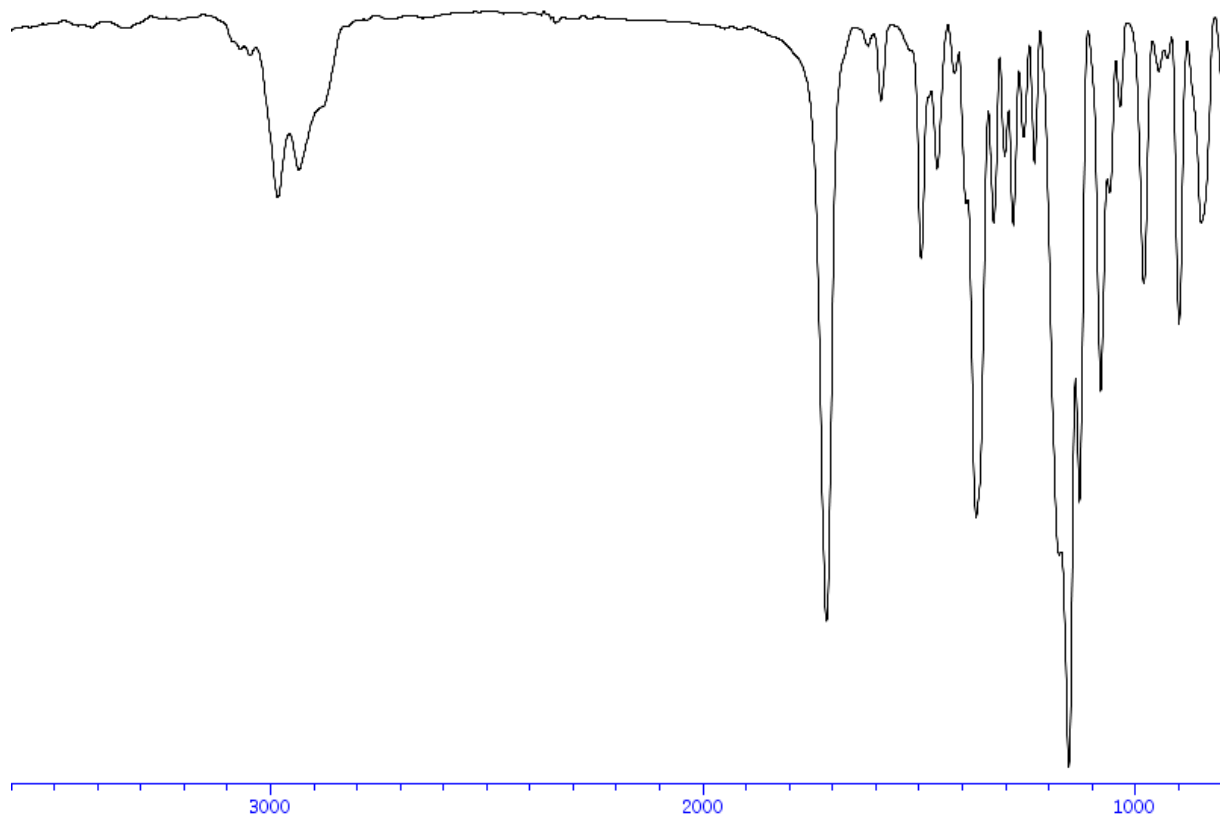


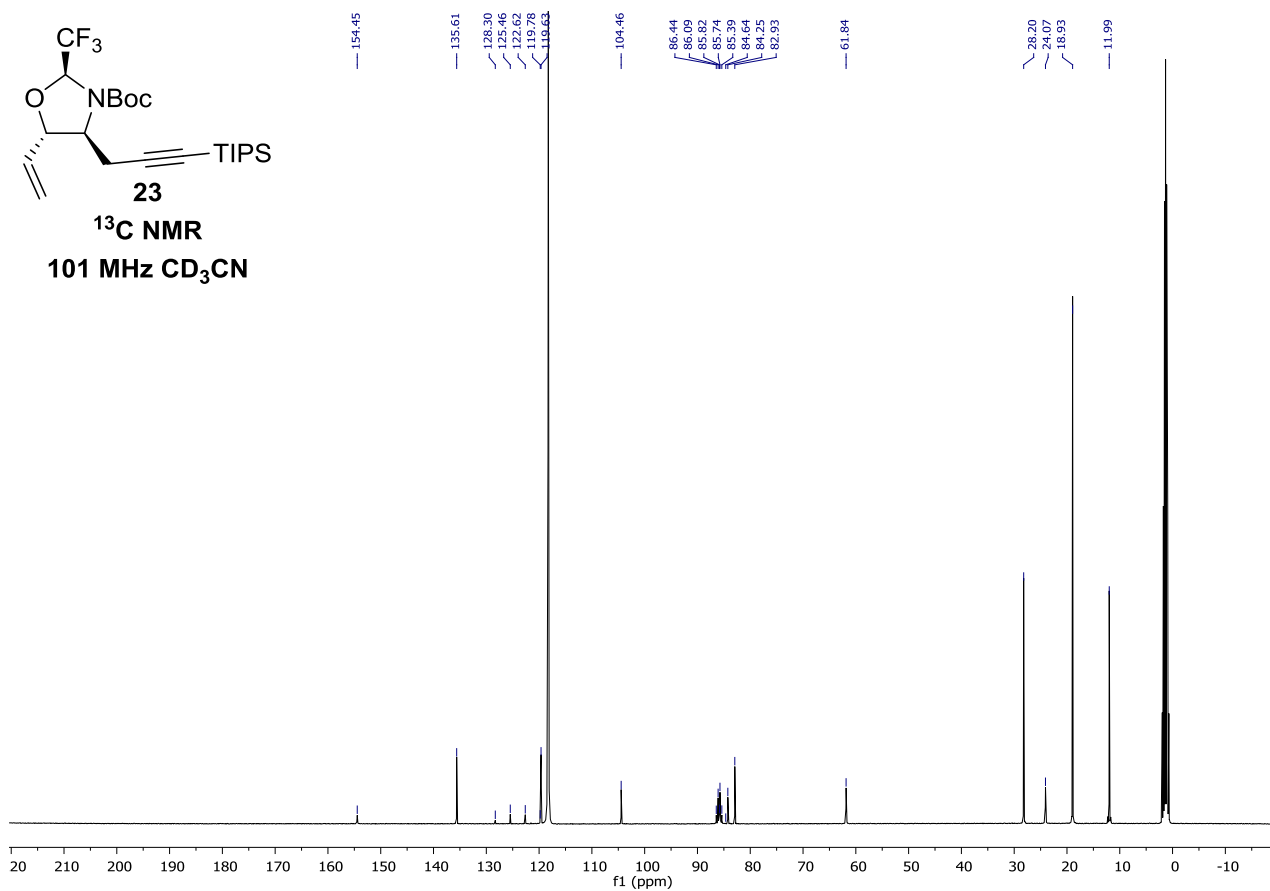
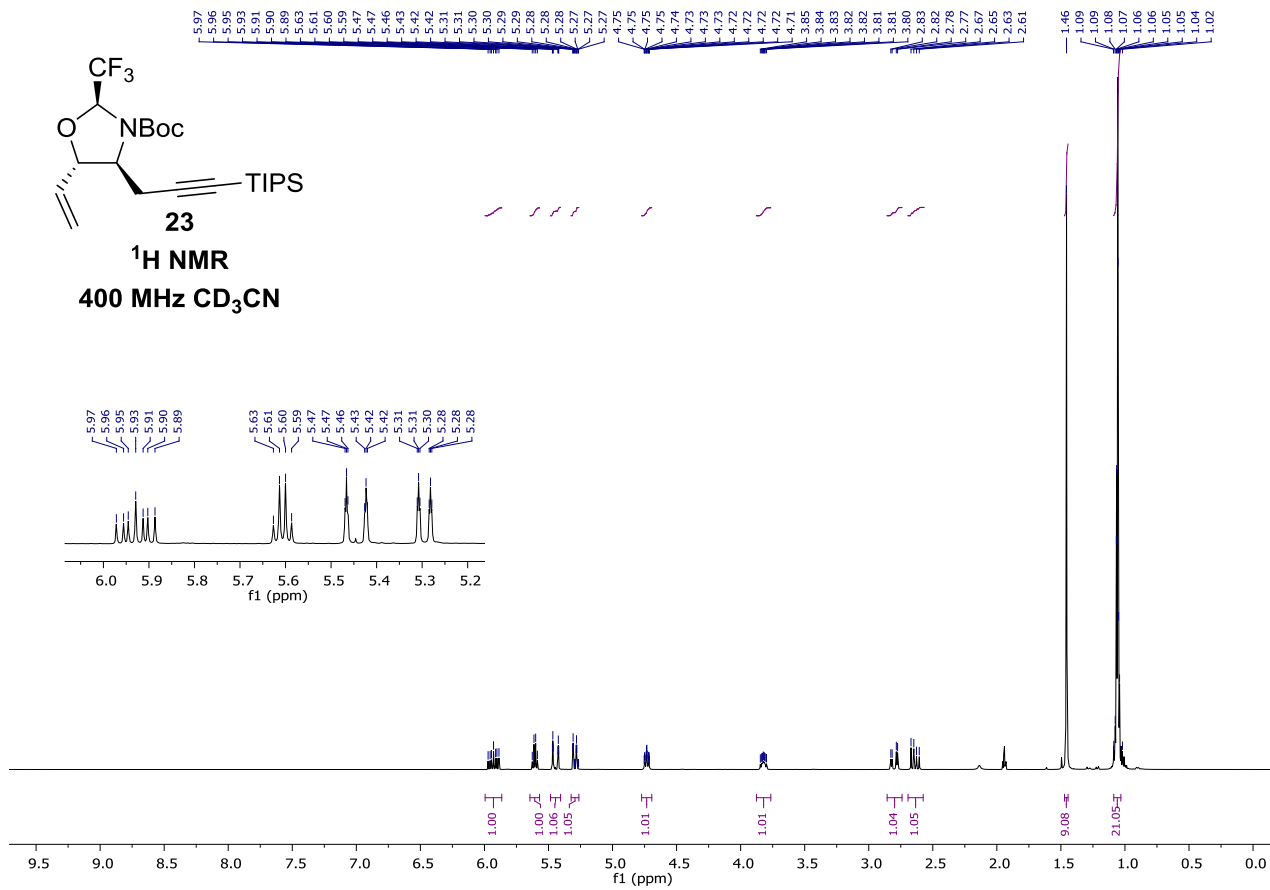


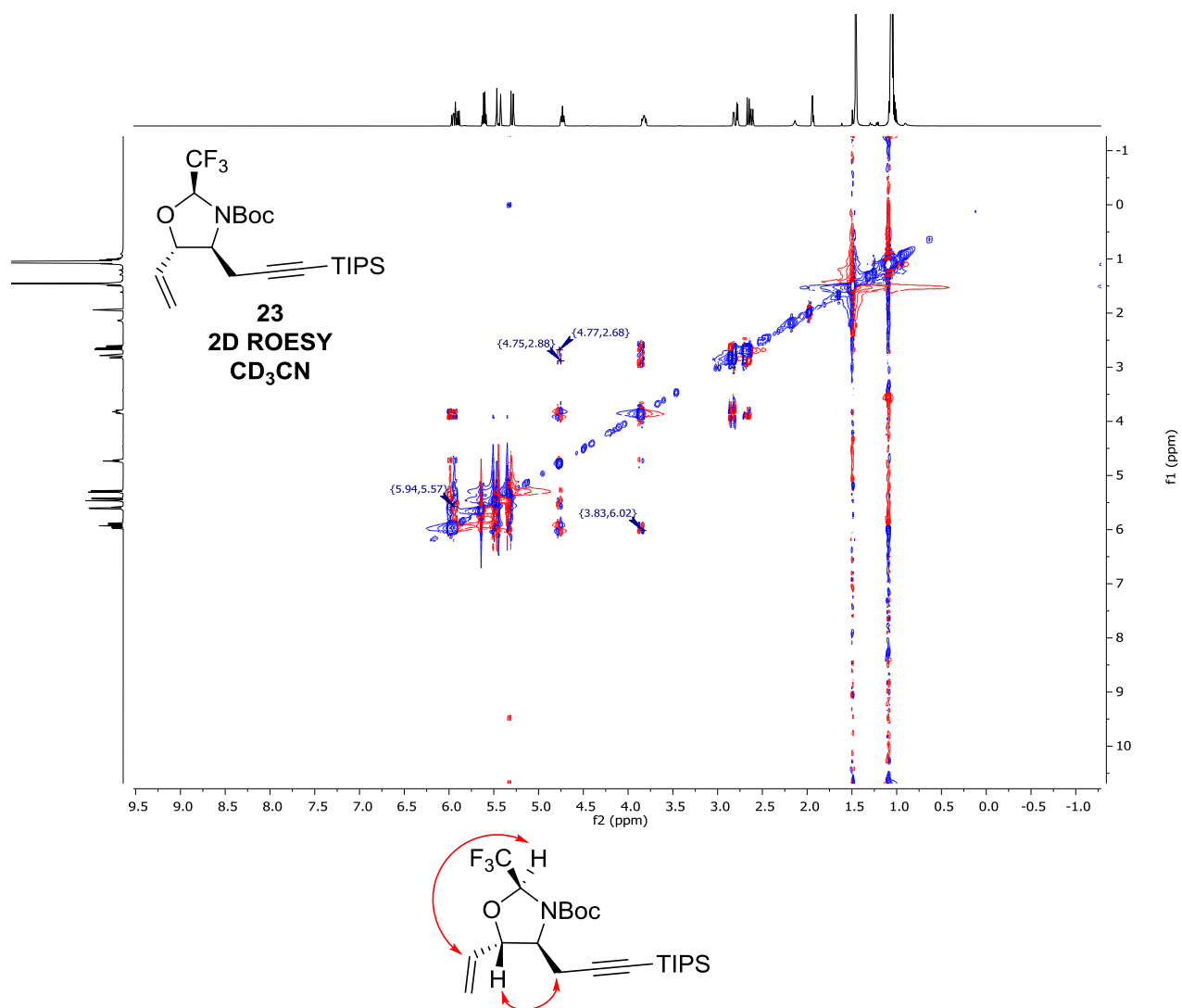


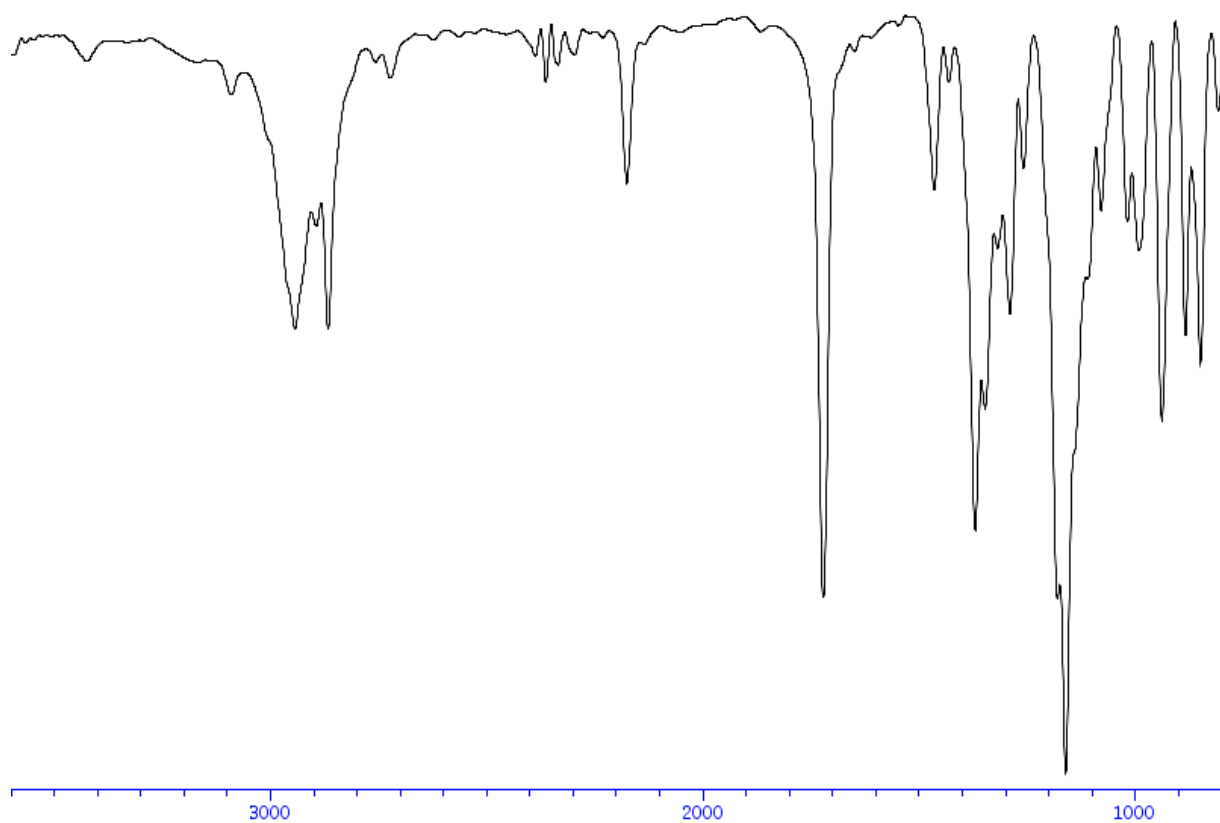


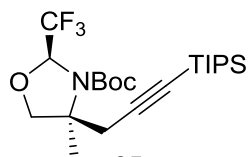








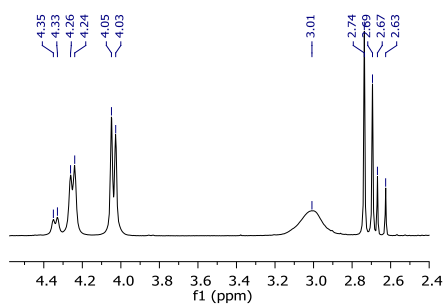




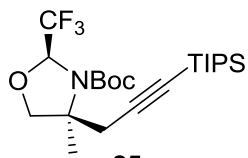
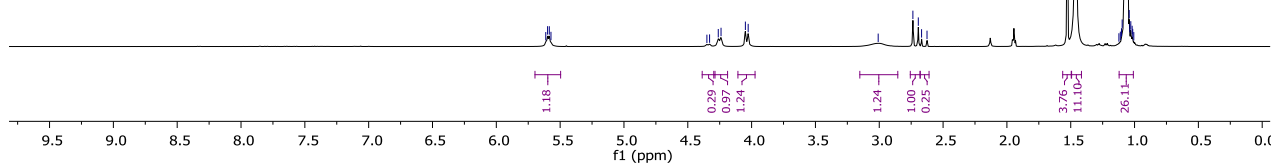
25

¹H NMR

400 MHz CD₃CN



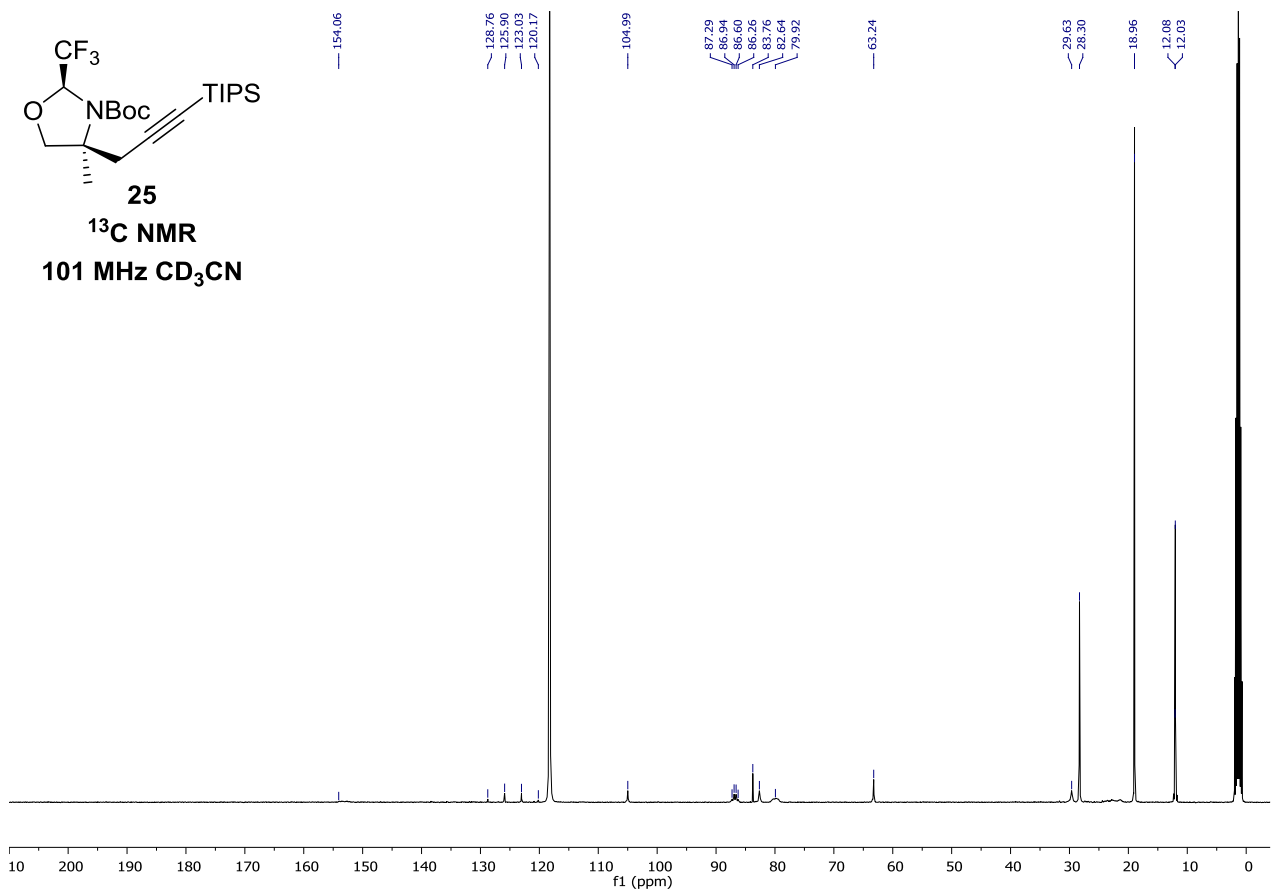
5.61
5.60
5.58
5.57
4.35
4.33
4.26
4.24
4.05
4.03
3.01
2.74
2.69
2.67
2.63
1.53
1.46
1.10
1.08
1.07
1.06
1.05
1.04
1.04
1.03
1.02
1.01

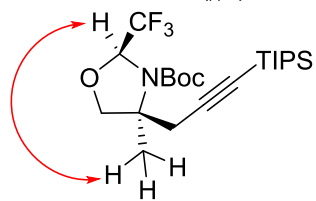
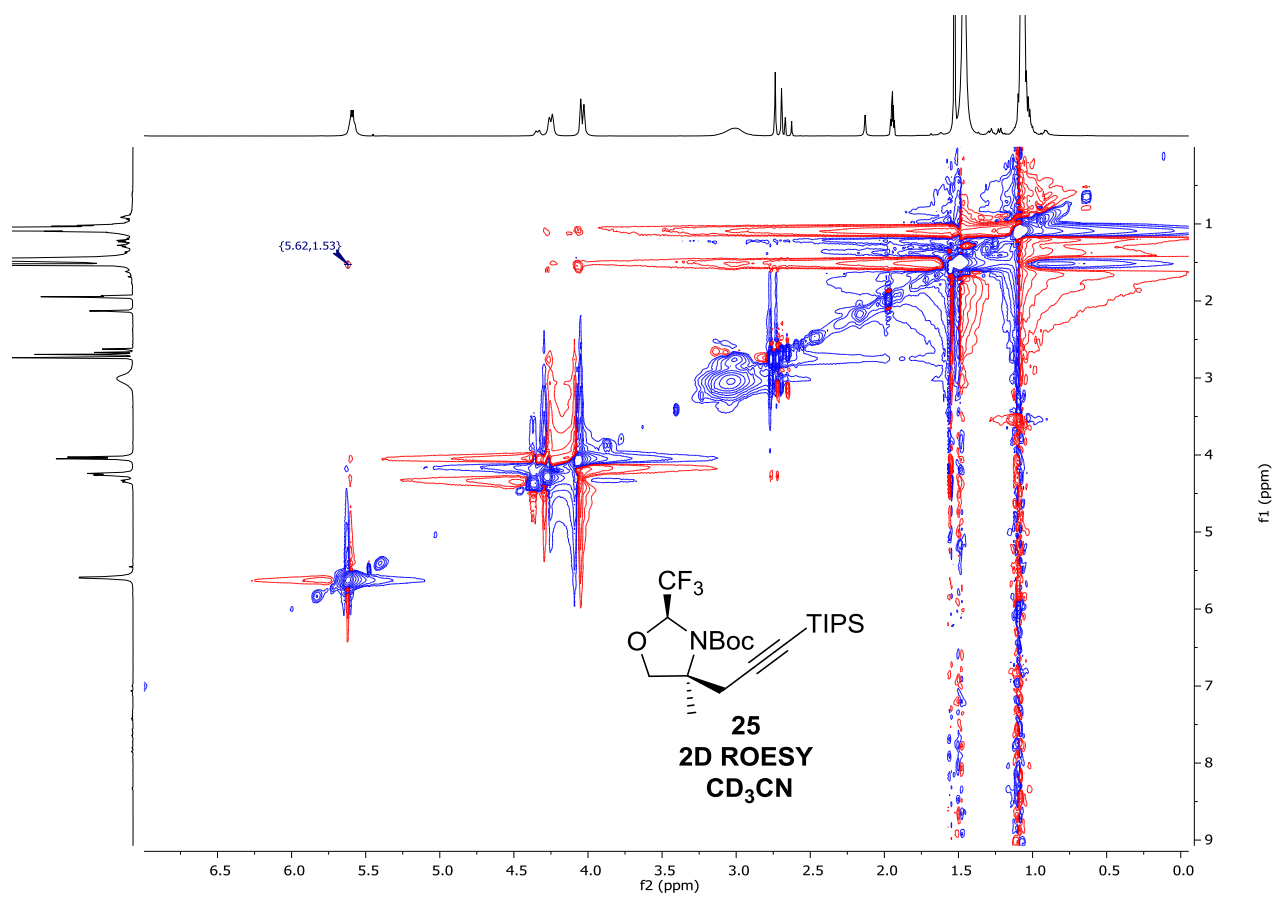


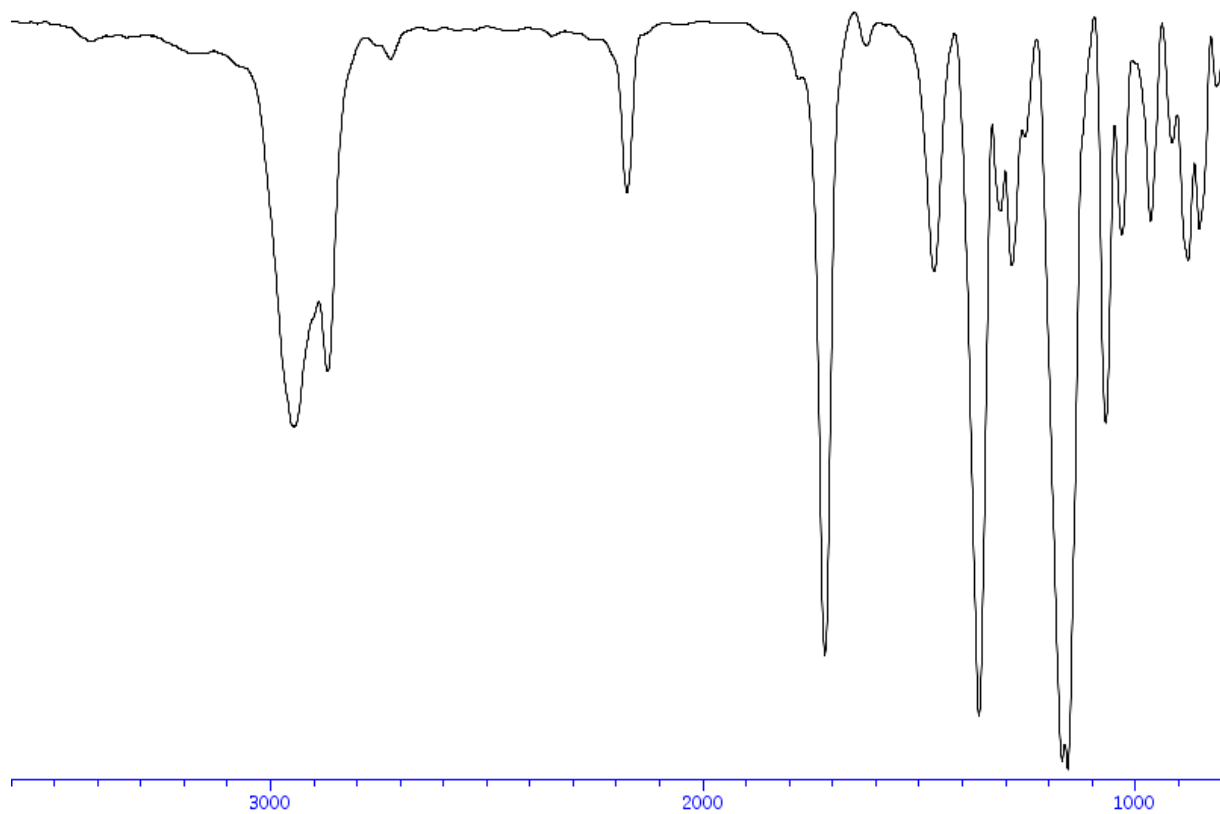
25

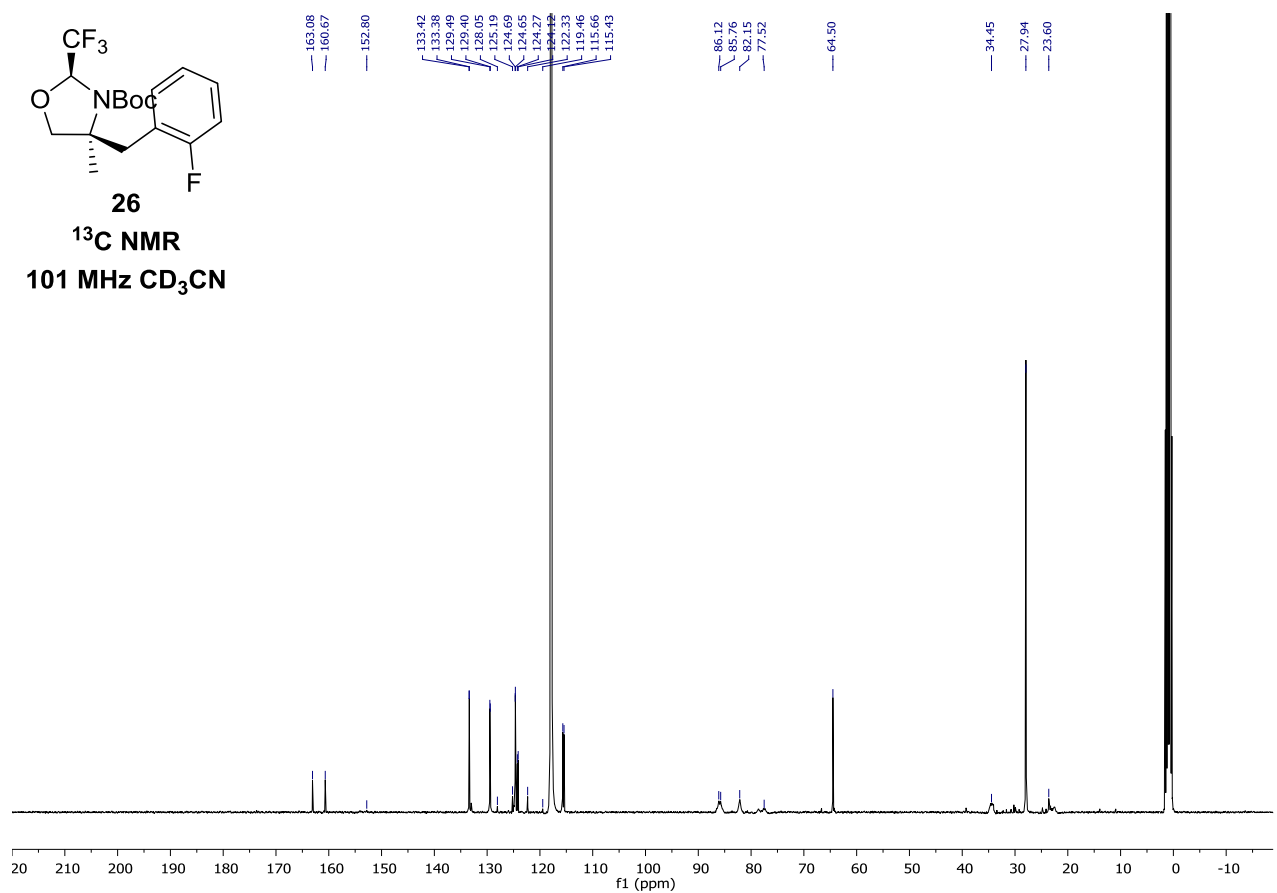
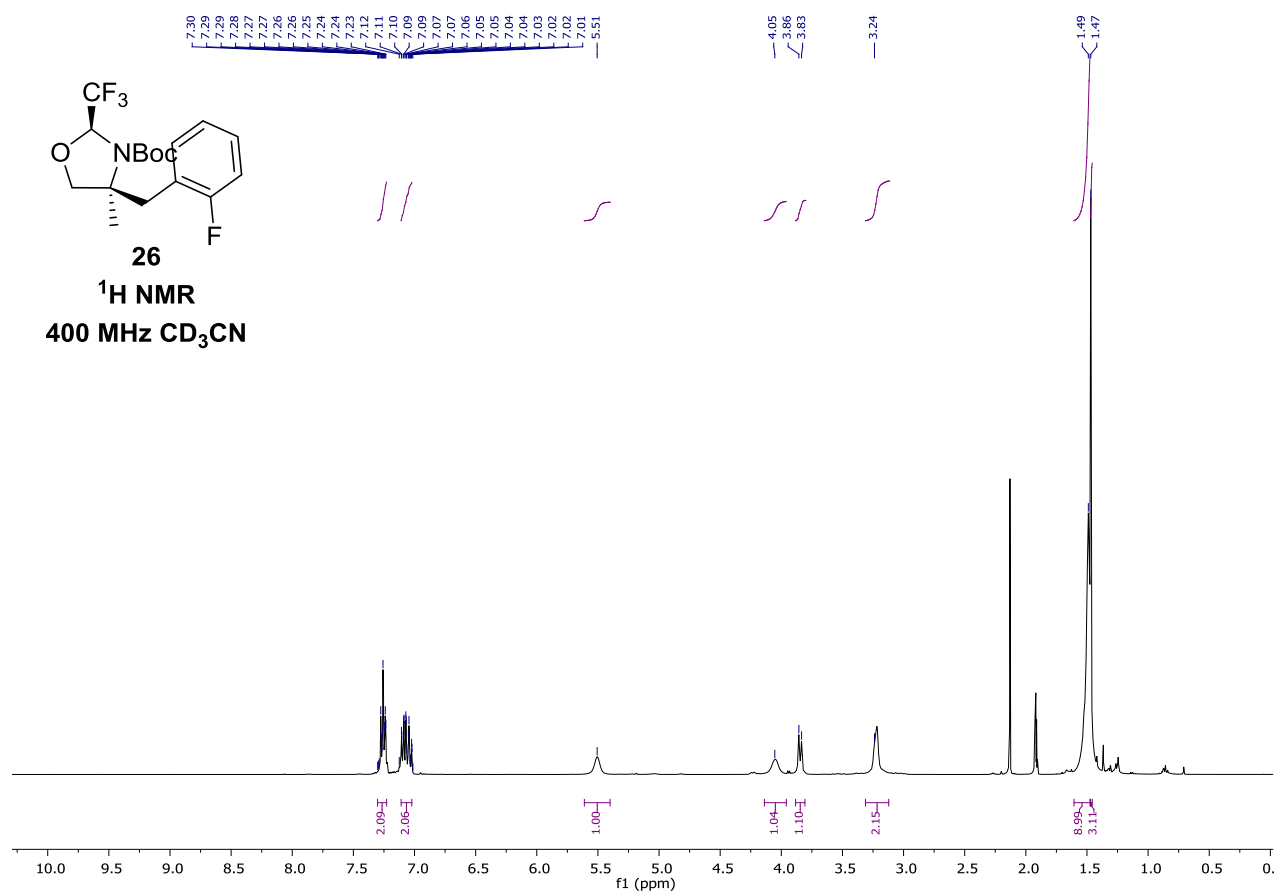
¹³C NMR

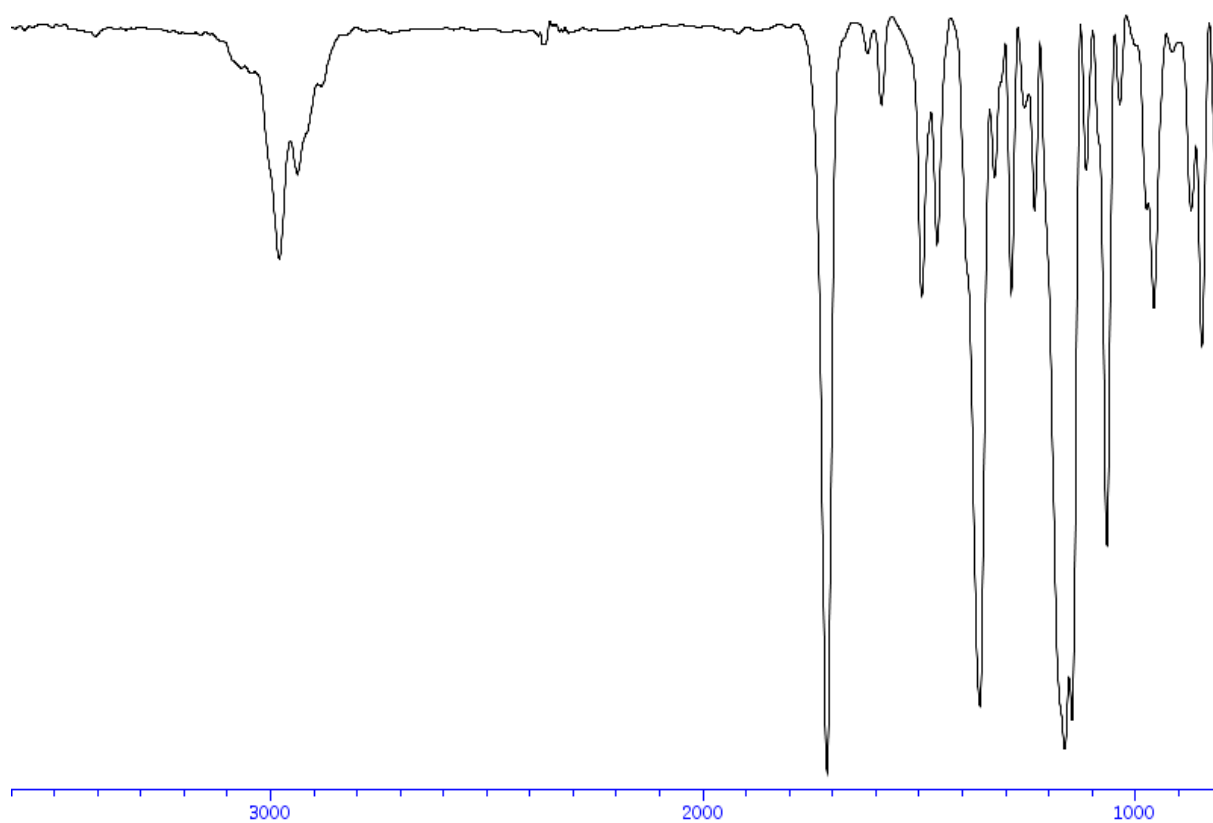
101 MHz CD₃CN

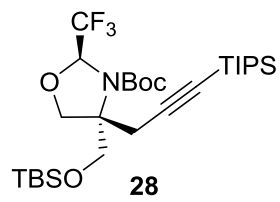




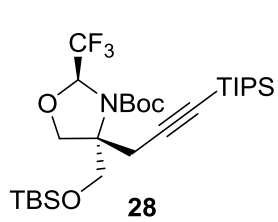
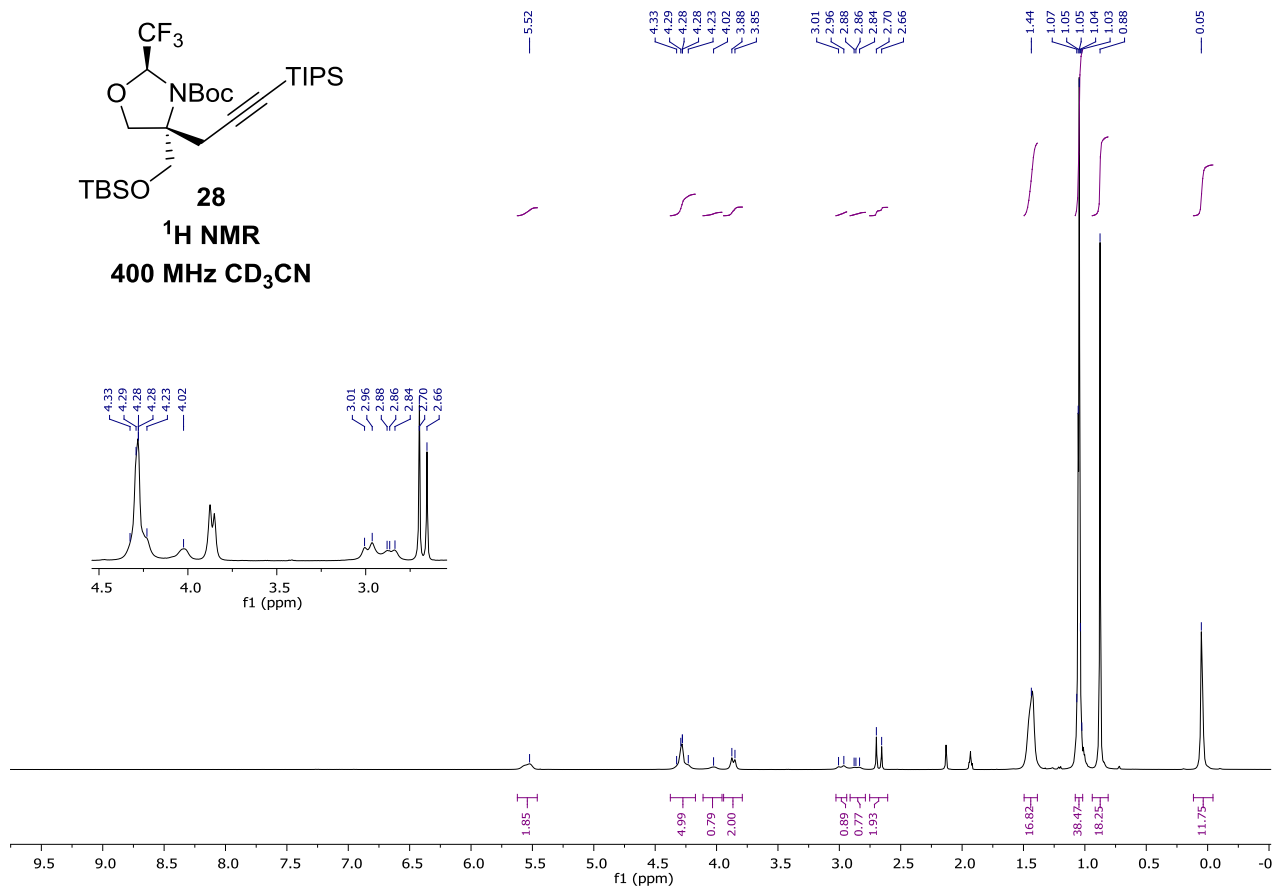








¹H NMR
 400 MHz CD₃CN



¹³C NMR
 101 MHz CD₃CN

