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Unprotected, primary 2-azidoamines are versatile precursors to vicinal diamines, which are among the most common motifs in biologically active compounds. Herein, we report their operationally simple synthesis through an iron-catalyzed difunctionalization of alkenes. A wide array of alkene substrates are tolerated, including complex drug-like molecules and a tripeptide. Facile derivatizations of the azidoamine group demonstrate the versatility of this masked diamine motif in chemoselective, orthogonal transformations. Applications of the methodology in the concise synthesis of RO 20-1724 and in a formal total synthesis of (±)-hamacanthin B further demonstrate the broad synthetic potential of this highly functional group tolerant reaction.

Direct Synthesis of Unprotected 2-Azidoamines from Alkenes via an Iron-Catalyzed Difunctionalization Reaction

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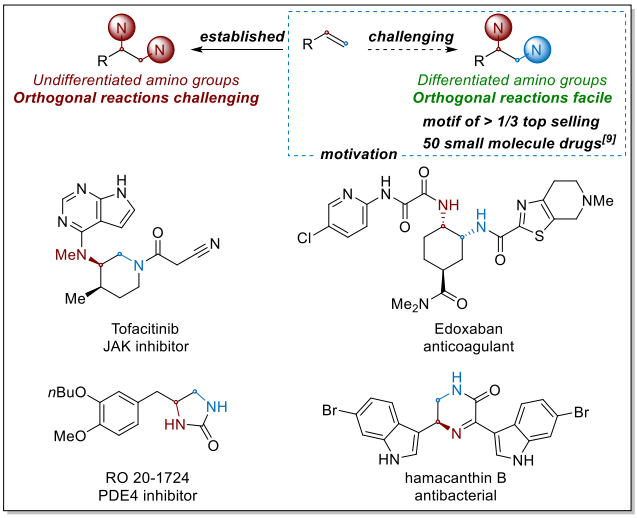
Supporting Information Placeholder

ABSTRACT: Unprotected, primary 2-azidoamines are versatile precursors to vicinal diamines, which are among the most common motifs in biologically active compounds. Herein, we report their operationally simple synthesis through an iron-catalyzed difunctionalization of alkenes. A wide array of alkene substrates are tolerated, including complex drug-like molecules and a tripeptide. Facile derivatizations of the azidoamine group demonstrate the versatility of this masked diamine motif in chemoselective, orthogonal transformations. Applications of the methodology in the concise synthesis of RO 20-1724 and in a formal total synthesis of (±)-hamacanthin B further demonstrate the broad synthetic potential of this highly functional group tolerant reaction.

Vicinal diamines are privileged structural motifs encountered across the molecular sciences, particularly in natural products, medicinal chemistry and catalysis.[1] Therefore, the rapid access to this ubiquitous functionality starting from simple hydrocarbon feedstocks, such as alkenes, can dramatically facilitate the synthesis and discovery of functional molecules. Several approaches have been explored to install two vicinal amino groups through the catalytic diamination of alkenes.[2] However, these reactions are still considerably limited when compared to well established methods for the synthesis of other important 1,2-difunctionalized alkanes, such as diols.[3] Besides the scope being often limited to activated alkenes, a more significant limitation is the lack of methods to access a diamine precursor which can be orthogonally transformed into synthetically relevant unsymmetrical diamine products (Scheme 1).

Scheme 1. Importance of unsymmetrical vicinal diamines



The azido group has recently emerged as a convenient amino group surrogate in formal catalytic diamination reactions (Scheme 2).[4] Most notably, Lin[5] and Xu[6] have described elegant electrochemical and iron-catalyzed processes, respectively, for the direct synthesis of diazides starting from a wide variety of alkenes (Scheme 2a). Whereas these reactions are powerful tools to access symmetrical vicinal diamines in two steps, they are less suitable in cases where two chemically distinct amino groups need to be orthogonally synthesized (e. g. through amide coupling), a scenario which is common in target-oriented synthesis.[7] Indeed, diazides suffer from poor regioselectivity upon monoreduction, making the direct synthesis of 2-azidoamines from alkenes highly challenging.[8]

Scheme 2. Synthesis of azido-containing, masked vicinal diamines from alkenes

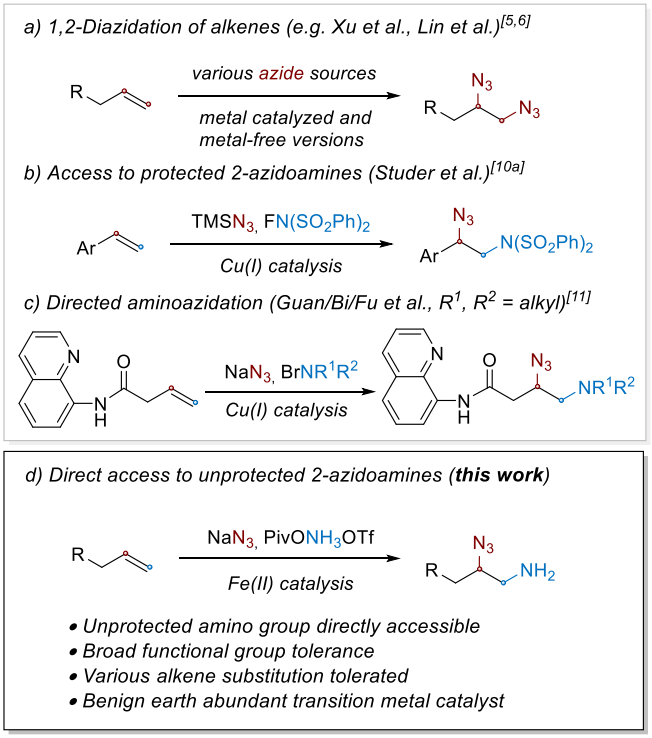
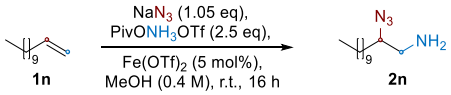


Table 1. Selected optimization results[a]



Entry	Deviation from standard conditions	Yield of 2[b]
1	None	68
2	Under inert atmosphere	65
3	$Fe(OAc)_2$	65
4	$Fe(OAc)_2$ trace metals basis (>99.99%)	66
5	No metal	<5
6	$AcONH_3OTf$ as reagent	43
7	1.5 eq $PivONH_3OTf$	43
8	Covalent azide source[c]	<5
9	MeCN as solvent	64
10	HFIP as solvent	<5

[a]See SI for detailed information. [b]H-NMR yields in % using trichloroethylene as an internal standard. [c]Such as trimethylsilyl azide, tosyl azide or diphenylphosphoryl azide.

Alternatively, some progress has been made to install both an azido group and a protected amino group. However, these reactions are synthetically limited because they either introduce a nearly unprotectable form of the amino group (e.g. $N(SO_2Ph)_2$, Scheme 2b)[10] or they rely on a suitably positioned directing group (Guan/Bi/Fu´s work, Scheme 2c).[11]

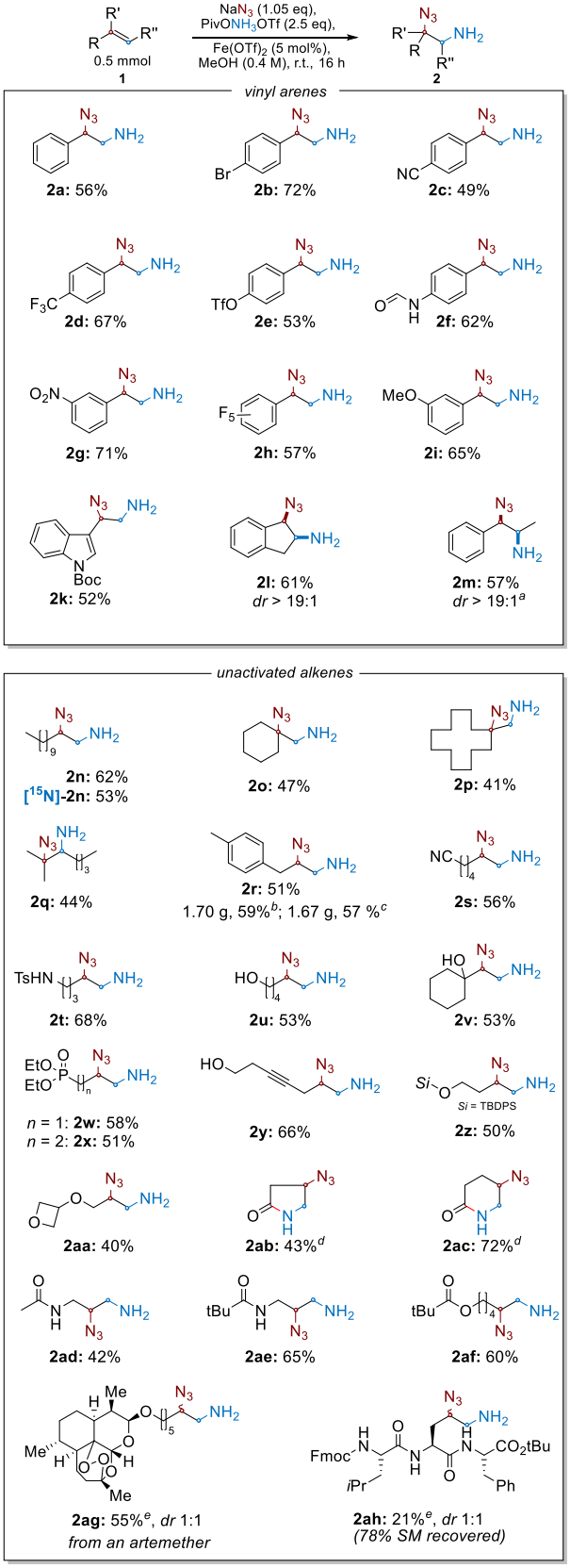
Thus, a simple, catalytic aminoazidation reaction exhibiting a broad substrate scope and allowing for the installation of, ideally, an unprotected amino group, would certainly allow for the step-economical and orthogonal synthesis of nearly any 1,2-diamine derivative, thereby accelerating the synthesis and discovery of bioactive molecules (Scheme 2d).[12–15]

Herein, we report an iron-catalyzed difunctionalization reaction of unactivated alkenes to directly access unprotected, primary 2-azidoamines. This process tolerates a broad substrate scope including unactivated mono-, di- and trisubstituted alkenes bearing unprotected polar functional groups commonly found in drug-like molecules.

Based on our recent research interest to access amino alcohols and 2-chloroamines under iron catalysis,[16] we set out to develop conditions for the aminoazidation of alkenes using a traditionally more challenging substrate, 1-dodecene (Table 1, for further details see SI). Evaluation of different azide salts in combination with different transition metal catalysts and hydroxylamine derivatives led us to identify suitable reaction conditions for the aminoazidation of 1-dodecene. Especially iron(II) acetate and triflate efficiently

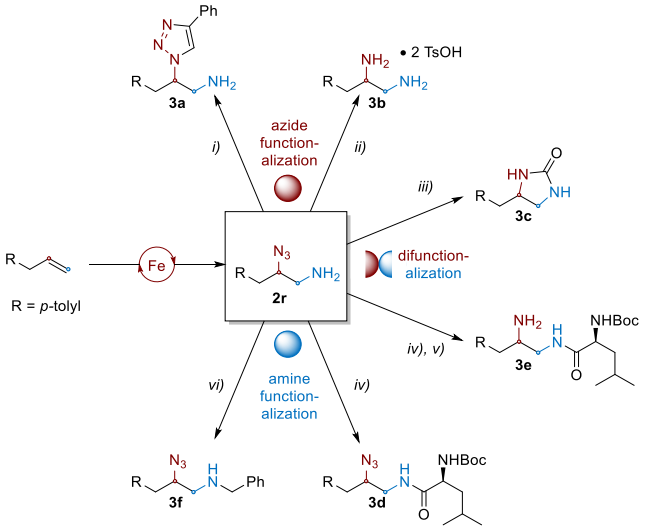
catalyzed the desired reaction in good yields using this usually unreactive substrate (Entries 1, 3, 4). The possible catalytic effect of impurities from the iron source was ruled out by a control experiment with a trace metals-based source which

Scheme 3. Scope of the aminoazidation reaction



Yields are of isolated products; *dr* determined by ^{1}H-NMR. [a](*E*)-alkene used. [b]Purified via column chromatography. [c]Purified via ammonium salt precipitation. [d]Starting from an ester bearing a terminal alkene. [e]See SI for detailed experimental information.

Scheme 4. Derivatization of azidoamine 2r



Conditions: i) Phenyl acetylene (1.2 eq), sodium ascorbate (0.4 eq), $CuSO_4$•5 H_2O (20%), tBuOH/H_2O, r.t., 62%; ii) PPh_3 (1.2 eq), THF/H_2O, 50 °C, then TsOH•H_2O (2.2 eq), Et_2O, r.t., 75%; iii) PMe_3 (1.1 eq), CO_2, MeCN, r.t., 67%; iv) *N*-Boc-Leu (1.2 eq), DIPEA (2.4 eq), HBTU (1.3 eq), THF, r.t., 70%; v) PMe_3 (3.4 eq), THF/H_2O, r.t., 79%; vi) benzaldehyde (1.2 eq), acetic acid (2.0 eq), $NaBH(OAc)_3$ (1.4 eq), DCE, r.t., 31%.

delivered the same outcome, confirming that the iron species plays a key role.[17] Covalent azide sources failed to afford any product while ionic azides were most suitable (Entry 8). Interestingly, this reaction can be performed open to air in technical grade methanol, a critical issue in the possible rapid adoption of this new reaction by synthetic practitioners.

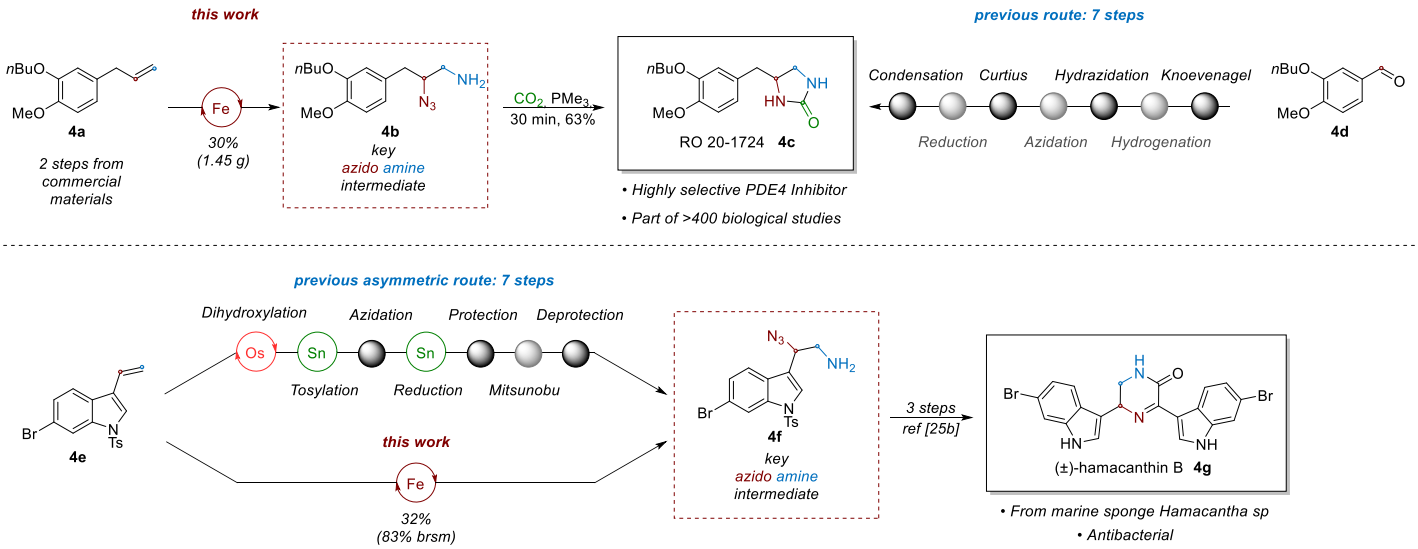
With the optimized conditions in hand, we then investigated the scope of the aminoazidation reaction (Scheme 3). Looking into aryl substituted alkenes, electron-poor (**2b**–**e, 2g**–**h**), as well as electron-rich (**2k**) systems were efficiently transformed into their corresponding azidoamines. Aryl substituted internal alkenes indene and *trans*-β-methyl styrene afforded *syn*-addition products **2l** and **2m** in excellent diastereoselectivity (*dr* > 19:1).

With regards to unactivated alkenes, mono-, 1,1-di- and trisubstituted alkenes performed well (**2n**–**q**). This is especially important, since the products bearing a tertiary azide offer the possibility to be transformed into an α-tertiary amine functionality, a common motif in natural products with only limited accessibility.[18]

Aside from various carbon scaffolds, several functional groups were found to be tolerated under the reaction conditions, such as aryl (pseudo)halides (**2b**, **2e**), multiple aryl substituents (**2b**–**l**), nitriles (**2c**, **2s**), protected amines (**2k**, **2t**, **2ah**), free alcohols (**2u**, **2v**, **2y**) and phosphonates (**2w**, **2x**). Remarkably, even alkynes in close proximity remained untouched (**2y**). Acid labile functionalities were also tolerated, e.g. free, tertiary alcohols (**2v**), silyl ethers (**2z**) and *N*-Boc protecting groups (**2k**, Boc = *tert*-butyloxycarbonyl). Furthermore, heterocycles (indole in **2k**, oxetane in **2aa**) further expanded the wide scope of this transformation. Synthetically relevant carboxylic acid derivatives, such as amides (**2ab**–**ae**), formamides (**2f**) and esters (**2af**), performed well under the reaction conditions. Interestingly, esters with a shorter alkenyl chain cyclized in the process to afford lactams **2ab** and **2ac** in a single step.

This excellent functional group tolerance encouraged us to tackle even more challenging substrates. An artemether derived substrate (**2ag**) was converted in moderate yield to the desired product, leaving the highly oxidized cage structure and the sensitive peroxo

Scheme 5. Synthetic applications of 2-azidoamines[23, 25]



group intact. Excitingly, an allyl glycine-based tripeptide reacted cleanly to form the corresponding azidoamine product **2ah** in an unoptimized 21% yield along with 78% of unreacted alkene starting material isolated, demonstrating the excellent chemoselectivity of this reaction. Another aspect worth mentioning here is the scalability of the presented methodology. On a gram scale, azidoamine **2r** was obtained in comparable yield and purity, regardless of the method of purification (see SI for further details). Collectively, these results clearly highlight the synthetic potential of this new methodology for early- and late-stage introduction of an azidoamine functionality.

Due to the high demand for the synthesis of isotopically labeled compounds, we synthesized a [^{15}N] labeled version of the reagent, starting from [^{15}N]-hydroxylamine.[19] This new reagent was used to generate the corresponding labeled product [^{15}N]-**2n** with excellent isotopic purity and in good yields, highlighting its potential for the rapid synthesis of [^{15}N]-compounds.

We next investigated the potential of azidoamines in subsequent synthetic transformations. Azides have found broad synthetic utility in copper-catalyzed azide-alkyne cycloaddition (CuAAC)[20] and Staudinger-bioconjugation.[21] Using the azidoamine as a starting material, a Click-type CuAAC reaction proceeded selectively at the azido group, leaving the unprotected amine untouched. The synthetic utility of the formed 2-azidoamines was further demonstrated through several orthogonal derivatization reactions (Scheme 4).

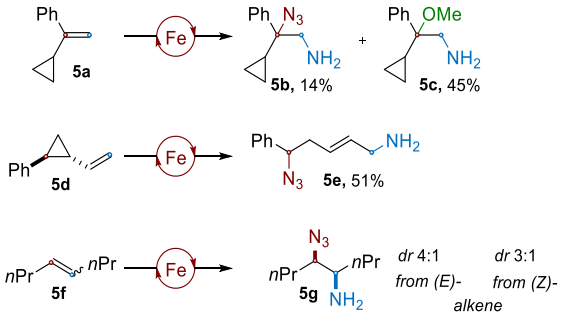
Subjecting **2r** to a phosphine mediated Staudinger reduction afforded diamine **3b** in good yield. Conventional reductive amination or amide coupling delivered secondary amine **3f** and amide 3**d**. The azide moiety of the latter could be further reduced in a subsequent step to obtain primary amine **3e**. This sequence clearly showcases the orthogonality of this simple masked diamine motif. Making combined use of both nitrogen moieties, a Staudinger/aza-Wittig (SAW) cyclization afforded directly imidazolidinone **3c** in one step.[22]

We next applied our methodology to the concise synthesis of biologically relevant molecules. RO 20-1724 (Scheme 5) is a highly specific inhibitor of cAMP-specific phosphodiesterase type IV (PDE 4, $IC_{50} = 2$ µM) commonly used in pharmaceutical research.[23] Starting from allyl aryl **4a**, we could access key intermediate **4b** on a 1.45 g scale through a direct iron-catalyzed aminoazidation reaction. Subjecting this intermediate to the adapted SAW conditions next afforded RO 20-1724 in 63% yield. This new route does not only decrease the step count significantly (previously reported: 7 steps), but, according to the report by the Audioso lab,[22] also bears the potential to introduce an isotopically labeled carbon atom through the use of labeled CO_2 in the last step.[24]

Furthermore, we utilized our methodology in the formal total synthesis of the antibacterial marine natural product hamacanthin B.[25] A previous enantioselective synthesis of (*S*)-**4g** relied on a 7-step sequence, which included several steps based on toxic compounds, such as an osmium catalyst and tin reagents, to access key intermediate **4f** which was next converted to the final natural product in three steps. Remarkably, our new aminoazidation reaction enabled us to completely bypass the 7-step sequence to access key intermediate **4f** in a single catalytic step, providing a new, shorter formal synthesis of the racemic form of this natural product.

Intrigued by the features of the presented methodology, we next conducted some control experiments to shed light on the reaction mechanism. Comparing the outcome of two different radical clocks, the cyclopropyl ring of the slower opening substrate **5a** was preserved, whereas the rapidly opening substrate **5d** readily underwent ring opening (Scheme 6).[26] Correlating it with rates reported in literature, the lifetime of the presumably formed radical could be tentatively stated as short-lived (**5a**$^{\bullet}$: $k_r = 4 \times 10^5$ s^{-1}, **5d**$^{\bullet}$: $k_r = 7 \times 10^{10}$ s^{-1}).[26] Furthermore, unactivated, internal alkenes (*E*)- and (*Z*)-oct-4-ene resulted in a very similar ratio of *cis*- and *trans*- product, supporting a stepwise mechanism involving a carbon-centered radical. At this stage it is not clear whether the amino group is introduced via an aminium radical[27] or an iron-based aminating species.[28]

Scheme 6. Control experiments



Yields are of isolated products; *dr* determined by GC-FID. See SI for detailed experimental information.

In conclusion, we have reported the direct synthesis of unprotected primary 2-azidoamines from a wide range of different alkenes. This mild and highly selective transformation provides an operationally simple and robust access to versatile 2-azidoamines using a benign and inexpensive iron catalyst. The products obtained can further engage in various derivatizations where the azidoamine motif functions as an ideal masked 1,2-diamine, enabling a fast and orthogonal transformation to many useful building blocks. In a broader context, these features emphasize the value of the presented methodology for the versatile synthesis of diamine derivatives which are ubiquitously found in bioactive molecules.

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Notes

The authors declare no competing financial interest.

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Supporting Information

Direct Synthesis of Unprotected 2-Azidoamines from Alkenes via an Iron-Catalyzed Difunctionalization Reaction

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General experimental details

Unless stated otherwise, reactions were performed under air in shelf-dry glassware or vials, with a Teflon-coated magnetic stirring bar. Chemicals were purchased from common suppliers and used without further purification, unless stated otherwise. Iron(II) trifluoromethanesulfonate was purchased from abcr GmbH in 98% purity. Reaction times stated as overnight were conducted for a non-specific time period between 12 and 16 h.

For purification *via* flash column chromatography, silica gel (Sigma Aldrich, 40 – 60 μm), solvents of technical grade and an air pressure of 0.3 – 0.5 bar was applied. For purification of primary amines mainly triethylamine-deactivated silica gel was used, prepared as followed:
A slurry of silica gel (50% v/v) in a solvent mixture (DCM:MeOH:NEt_3 10:1:0.5) was stirred for 2 h, poured into a chromatography column, flushed with 5x of the column volume with an amine-free solvent mixture (DCM:MeOH 10:1) and dried with pressurised air and under reduced pressure.[1] Analytical thin layer chromatography (TLC) was performed on Merck silica gel 60 F_{254} glass-backed plates and azidoamine products were mainly detected by ninhydrin stain alone or subsequently to a pre-treatment with a 10 wt.% solution of PPh_3 in DCM first.[2] Other products were visualized by potassium permanganate stain ($KMnO_4$) or under UV light.

^{1}H-, ^{13}C- and ^{19}F-NMR spectra were recorded at 25 °C on machines from Bruker (Bruker Avance III 400 MHz, Bruker Neo 400 MHz and Bruker Neo 500 MHz, all equipped with BBFO smart Probe) with the solvent resonance used as internal reference.[3] ^{19}F-spectra are referenced internally against hexafluorobenzene[4] (δ_F = - 164.9 ppm (s)). Spectral data are reported as followed: chemical shift δ/ppm, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, br = broad, m = multiplet; or combinations thereof; ^{13}C signals are singlets unless stated otherwise), coupling constants *J* in Hz, integration (^{1}H only), assignment. Spectra obtained with the presented methodology are assigned as fully as feasible, with the aid of ^{1}H-COSY, HSQC and HMBC experiments. High resolution mass spectrometry (HRMS) data was obtained using electron ionisation (EI) on a *Thermo scientific Q Exactive GC Orbitrap with direct Probe*, electrospray ionisation (ESI) on a *Bruker maXis – ESI-Qq-TOF-MS* or matrix-assisted laser desorption/ionisation (MALDI) on *Bruker solariX – MALDI-FTICR-MS* and are reported in *m/z*. All published data are within a range of *m/z* ± 3 ppm of theoretical values.

> **Caution (!) :** Both, inorganic[5] and organic azides[6] exhibit a potential explosion hazard, especially lithium azide (LiN_3) and organic azides with a low carbon/nitrogen ratio (<1.5). The latter rule of thumb was suggested from a process safety assessment conducted by Xu *et al*.[6] Further, under strongly acidic conditions, ionic azides can easily generate highly explosive, toxic and volatile hydrazoic acid HN_3. Considering these aspects, appropriate safety and disposal measurements should be undertaken when working with azides in general and azides with low C/N ratio should be handled in small quantities only.

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[1] Inspired by Volpin, G.; Vepřek, N. A.; Bellan, A. B.; Trauner, D. *Angew. Chem. Int. Ed.* **2017**, *56*, 897–901.
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[3] As in Gottlieb, H. E.; Kotlyar, V.; Nudelman, A. *J. Org. Chem.* **1997**, *62*, 7512-7515: $CDCl_3$: δ_H = 7.260 ppm (s), δ_C = 77.160 ppm (t); MeCN-d_3: δ = 1.940 ppm (p), δ_C = 1.320 ppm (hept); DMSO-d_6: δ_H = 2.500 ppm (p), δ_C = 39.520 ppm (hept).
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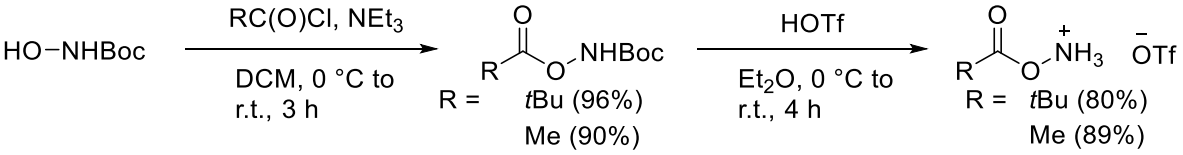
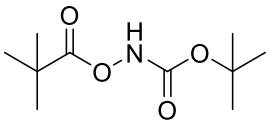
Experimental procedures and characterizations

Synthesis of aminating reagents



tert-Butyl pivaloyloxy carbamate (SI-1SM)

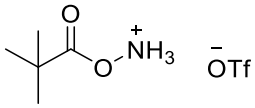


N-Boc hydroxylamine (30 g, 0.23 mol, 1.0 eq.) was dissolved in DCM (400 mL) and NEt_3 (31 mL, 23 g, 0.23 mol, 1.0 eq) was added.[7] At 0°C, pivaloyl chloride (28 mL, 28 g, 0.23 mol, 1.0 eq) was added dropwise over 30 min before the reaction was let to go to r.t.. After additional 2 h stirring, the reaction mixture was vacuum filtered and the filter cake was washed with DCM (40 mL). The filtrate was washed with water (200 mL), sat. aq. solution of $NaHCO_3$ (200 mL) and brine (200 mL). The organic layer was dried over Na_2SO_4, filtered and concentrated to yield *tert*-butyl pivaloyloxy carbamate **SI-1SM** (47 g, 216 mmol) as a colorless solid in 96% yield. Reported spectra match the ones published in literature.[8]

^{1}H-NMR (400 MHz, $CDCl_3$): δ_H = 7.76 (s, 1H), 1.49 (s, 9H), 1.30 (s, 9H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ_C = 178.0, 155.8, 83.2, 38.3, 28.2, 27.1.

_O_-Pivaloyl hydroxylamine triflic acid (SI-1)



tert-Butyl pivaloyloxy carbamate **SI-1SM** (45 g, 0.21 mol, 1.0 eq.) was dissolved in Et_2O (400 mL). At 0°C, triflic acid (18 mL, 31 g, 0.20 mol) was added dropwise over 30 min before the reaction was let to go to r.t.. After additional 3 h stirring, pentane (150 mL) was added to the reaction mixture. The resulting suspension was vacuum filtered, the reaction flask rinsed with more pentane (150 mL) and the filter cake washed with ice-cold DCM (150 mL). The filter cake was dried under reduced pressure and afforded *O*-pivaloyl hydroxylamine triflic acid SI-1 (45 g, 168 mmol, 80%) as a free-floating, colorless salt. Reported spectra resemble the ones published in literature.[8]

^{1}H-NMR (400 MHz, CD_3CN): δ_H = 9.89 (s, br, 3H), 1.29 (s, 9H).

^{13}C-NMR (101 MHz, CD_3CN): δ_C = 175.2, 121.6 (q, *J* = 319.3 Hz), 39.1, 26.8.

^{19}F-NMR (376 MHz, CD_3CN): δ_F = −79.4.

[7] In the course of this project, a detailed manuscript about the preparation of the aminating reagent was submitted to the journal *Organic Syntheses*.

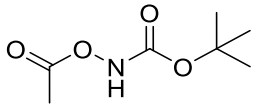
[8] Guimond, N.; Gorelsky, S. I.; Fagnou, K. *J. Am. Chem. Soc.* **2011**, *133*, 6449-6457.

A [^{15}N]-labeled reagent **[^{15}N]-SI-1** could be obtained by analog synthesis on 3 mmol scale, starting from [^{15}N]-hydroxylamine[9]. The final reagent was recrystallized from *n*BuOAc for purification.

^{1}H-NMR (400 MHz, CD_3CN): δ_H = 9.90 (s, br, 3H), 1.29 (s, 9H).

^{13}C-NMR (101 MHz, CD_3CN): δ_C = 175.2, 39.1, 26.8.

***tert*-Butyl acetoxycarbamate (SI-2SM)**

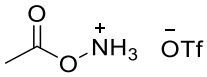


Analogous to the synthesis of *tert*-butyl pivaloyloxy carbamate**,** *N*-Boc hydroxylamine (3.33 g, 25 mmol, 1.0 eq.) was dissolved in DCM (40 mL) and NEt_3 (3.8 mL, 28 mol, 1.1 eq) was added. At 0°C, acetyl chloride (1.8 mL, 25 mol, 1.0 eq) was added dropwise and the reaction was let to go to r.t.. After additional 2 h of stirring, the reaction mixture was vacuum filtered and the filter cake was washed with DCM. The filtrate was washed with water (20 mL), sat. solution of $NaHCO_3$ (20 mL) and brine (20 mL). The organic layer was dried over Na_2SO_4, filtered and concentrated to yield the corresponding carbamate as colorless solid (3.95 g, 22.5 mmol, 90%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ_H = 7.90 (s, br, 1H), 2.20 (s, 3H), 1.49 (s, 9H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ_C = 170.2, 155.6, 83.4, 28.2, 18.5.

***O*-Acetyl hydroxylamine triflic acid (SI-2)**



Analogue to the synthesis of *O*-pivaloyl hydroxylamine triflic acid, *tert*-butyl acetoxycarbamate (3.95 g, 22.5 mmol, 1.0 eq) was dissolved in Et_2O (40 mL). At 0°C, triflic acid (2 mL, 22.7 mmol, 1.0 eq.) was added dropwise and the reaction was let to go to r.t.. After additional 3 h stirring, pentane (15 mL) was added to the reaction mixture. The resulting suspension was vacuum filtered and the filter cake washed with ice-cold DCM (3x5 mL). The filter cake was dried under reduced pressure and afforded *O*-acetoxy hydroxylamine triflic acid as a colorless solid (4.51 g, 20.0 mmol, 89%).

Spectroscopic data is in accordance to the one reported in literature.[10]

^{1}H-NMR (400 MHz, CD_3CN): δ_H = 10.01 (s, br, 3H), 2.23 (s, 3H).

^{13}C-NMR (101 MHz, CD_3CN): δ_C = 168.2, 121.4 (q, *J* = 318.8 Hz), 17.8.

^{19}F-NMR (376 MHz, CD_3CN): δ_F = −79.9.

[9]For *N*-Boc protection of [^{15}N]-hydroxylamine see N. Haga *et al.*, *J. Am. Chem. Soc.* **1992**, *114*, 9795–8906.
[10]N. Jiao *et al*., *Science* **2020**, *367*, 281–285.

Optimization of reaction conditions for the amino azidation reaction

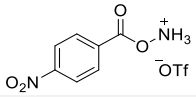
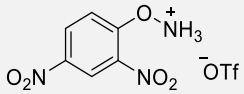
Under air, a 4 mL screw-cap vial was charged subsequently with a metal catalyst (0.01 mmol, 5 mol%), azide source (0.21 mmol, 1.05 eq), a stirring bar, solvent (0.5 mL, 0.4 M, technical grade), 1-dodecene (44 μL, 33 mg, 0.20 mmol, 1.0 eq) and aminating reagent (0.50 mmol, 2.5 eq). After stirring for 16 h at room temperature (ca. 25 °C), the reaction was diluted with an aqueous solution of NaOH (1 mL, 1 M), directly extracted with DCM (4 x 8 mL), dried over Na_2SO_4 and concentrated under reduced pressure. To the crude mixture, trichloroethylene (18 μL, 26 mg, 0.20 mmol) was added as internal analytical standard (δ_H = 6.45 (s, 1H)) and yields were calculated according to integration in ^{1}H-NMR (product signals at δ_H = 3.32 (m, 1H), 2.83 (dd, 1H) or 2.69 (dd, 1H) were used, depending on the cleanest signal). Selected results are summarized in table S1 below. Anhydrous lithium azide exhibits slightly higher activity, but was not chosen as final azide source due to its explosive character and lack of commercial source.

General procedure for amino azidation

A 0.02 M $Fe(OTf)_2$ stock solution was prepared by first weighing in $Fe(OTf)_2$ (107 mg, 0.302 mmol) into a 20 mL crimping vial and closing it with a septum cap in an argon operated glovebox. Subsequently, 15 mL of dry MeOH was added to complete the stock solution.

Under air, an 8 mL screw-cap vial was charged with alkene (0.5 mmol), a stirring bar and 1.3 mL of a 0.02 M $Fe(OTf)_2$ stock-solution in dry methanol. NaN_3 (34 mg, 0.52 mmol, 1.05 eq) and $PivONH_3OTf$ (334 mg, 1.25 mmol, 2.5 eq) were added subsequently to the reaction mixture and the reaction was stirred for 16 h at room temperature. Then, the reaction mixture was diluted with aqueous solution of NaOH (2.5 mL, 1 M), directly extracted with DCM (4 x 20 mL), dried over Na_2SO_4 and concentrated under reduced pressure. Purification by column chromatography using NEt_3-deactivated silica gel provided the 2-azidoamine product.

Table S1: Optimization for the aminoazidation reaction of alkenes.

Entry	*Catalyst (5 mol%)*	*Reagent (2.50 eq)*	*Azide (1.05 eq)*	*Solvent (0.4 M)*	*Additives*	*Yield/%*
1	$Fe(OTf)_2$	$PivONH_3OTf$	NaN_3	MeOH	-	68/66*
2	$Fe(OTf)_2$ (2 mol%)					53
3	$Fe(OAc)_2$, 97%					65/64*
4	$Fe(OAc)_2$, 97% (10 mol%)					60*
5	$Fe(OAc)_2$, ≥99.99%					66
6	$FeCp_2$, 99%					64
7	$Fe(acac)_2$, 95%					50
8	$Fe(NH_4)_2(SO_4)_2 \cdot 6\,H_2O$, ≥99.99%					40*
9	$Fe(acac)_3$, 99%					40*
10	$Fe(OEt)_3$, 99.6%					64
11		$PivONH_3OTf$ (1.5 eq)				43
12		$AcONH_3OTf$				43
13		Hydroxylamine-*O*-sulfonic acid				<5
14						<12
15						<5
16			NaN_3 1.5 eq			60
17			LiN_3[11,§]			72
18			KN_3[§]			57
19			$[Bu_4N]N_3$[§]			60
20			Covalent azides[12]			<5
21				MeOH (1 M)		50
22				MeOH (0.2 M)		44
23				HFIP		<5
24				MeCN		64
25				EtOH		19
26				LiOTf (1.1 eq)		69
27				NH_4OTf (1.1 eq)		41
28				5 °C		30
29				50 °C		37
30				inert atmosphere[§#]		65

* Entry based on 1-decene as substrate.

§ Anhydrous solvent was used.

Solids added in an argon operated glovebox, liquids added under nitrogen Schlenk conditions.

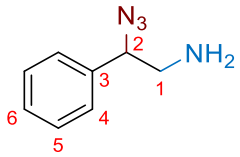
[11] Synthesised according G. Brauer *Handbuch der Präparativen Angorganischen Chemie*, 3rd Edition, Ferdinand Enke, Stuttgart 1975, ISBN 3-432-02328-6.

[12] Covalent azides such as $TMSN_3$, $P(O)(OPh)_2N_3$ or TsN_3.

Synthesis and characterization of 2-azidoamines

Azidoamines from vinyl arenes

2-Azido-2-phenylethan-1-amine (2a)



Following the general procedure for amino azidation using commercially available *styrene* (51.2 mg, 0.492 mmol) and purified by silica gel column chromatography (DCM:MeOH 100:0 to 98:2, NEt_3-deactivated SiO_2) provided the title compound as a yellow oil (44.5 mg, 0.274 mmol, 56%).

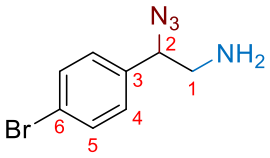
^{1}H-NMR (400 MHz, $CDCl_3$): δ_H = 7.44 – 7.28 (m, 5H, H4-6), 4.50 (t, *J* = 6.5 Hz, 1H, H2), 2.96 (d, *J* = 6.5 Hz, 2H, H1), 1.35 – 1.14 (m, 2H, NH_2).

^{13}C-NMR (101 MHz, $CDCl_3$): δ_C = 137.9 (C3), 129.0 (C5), 128.6 (C6), 127.2 (C4), 69.3 (C2), 48.0 (C1).

HRMS (MALDI): calc. for $C_8H_{11}N_4$ $[M+H]^+$ 163.0978, found 163.0975.

***R*$_f$:** 0.34 (DCM:MeOH 9:1)

2-Azido-2-(4-bromophenyl)ethan-1-amine (2b)



Following the general procedure for amino azidation using commercially available *4-bromostyrene* (91.5 mg, 0.500 mmol) and purified by silica gel column chromatography (DCM:MeOH 100:0 to 98:2, NEt_3-deactivated SiO_2) provided the title compound as a yellow oil (86.7 mg, 0.360 mmol, 72%).

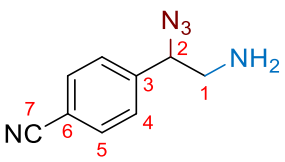
^{1}H-NMR (400 MHz, $CDCl_3$): δ_H = 7.57 – 7.47 (m, 2H, H5), 7.21 – 7.16 (m, 2H, H4), 4.46 (t, *J* = 6.4 Hz, 1H, H2), 2.91 (d, *J* = 6.4 Hz, 2H, H1), 1.31 (s, br, 2H, NH_2).

^{13}C-NMR (101 MHz, $CDCl_3$): δ_C = 137.0 (C3), 132.1 (C5), 128.8 (C4), 122.5 (C6), 68.5 (C2), 47.9 (C1).

HRMS (MALDI/ESI, CCA 1:10): calc. for $C_8H_{10}BrN_4$ $[M+H]^+$ 241.0083, found 241.0083.

***R*$_f$:** 0.37 (DCM:MeOH 9:1)

4-(2-Amino-1-azidoethyl)benzonitrile (2c)



Following the general procedure for amino azidation using commercially available *4-cyanostyrene* (65.6 mg, 0.508 mmol) and purified by silica gel column chromatography (DCM:MeOH 100:0 to 98:2, NEt_3-deactivated SiO_2) provided the title compound as a yellow oil (46.6 mg, 0.249 mmol, 49%).

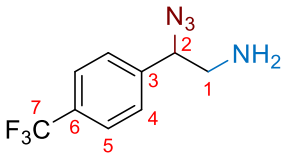
^{1}H-NMR (400 MHz, $CDCl_3$): δ_H = 7.71 – 7.66 (m, 2H, H5), 7.47 – 7.41 (m, 2H, H4), 4.57 (dd, *J* = 7.4, 5.1 Hz, 1H, H2), 3.02 – 2.89 (m, 2H, H1), 1.31 (s, br, 2H, NH_2).

^{13}C-NMR (101 MHz, $CDCl_3$): δ_C = 143.4 (C3), 132.8 (C5), 127.9 (C4), 118.5 (C6 or C7), 112.5 (C7 or C6), 68.5 (C2), 48.0 (C1).

HRMS (ESI+): calc. for $C_9H_{10}N_5$ $[M+H]^+$ 188.0931, found 188.0936.

***R*$_f$:** 0.52 (DCM:MeOH 9:1)

2-Azido-2-(4-(trifluoromethyl)phenyl)ethan-1-amine (2d)



Following the general procedure for amino azidation using commercially available *4-(trifluoromethyl) styrene* (88.6 mg, 0.515 mmol) and purified by silica gel column chromatography (DCM:MeOH 100:0 to 98:2, NEt_3-deactivated SiO_2) provided the title compound as a yellow oil (79.8 mg, 0.347 mmol, 67%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ_H = 7.65 (d, *J* = 8.1 Hz, 2H, H5), 7.44 (d, *J* = 8.0 Hz, 2H, H4), 4.57 (dd, *J* = 7.1, 5.6 Hz, 1H, H2), 3.01 – 2.90 (m, 2H, H1), 1.33 (s, br, 2H, NH_2).

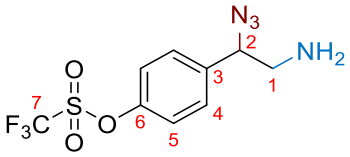
^{13}C-NMR (101 MHz, $CDCl_3$): δ_C = 142.0 (q, *J* = 1.3 Hz, C3), 130.8 (q, *J* = 32.6 Hz, C6), 127.5 (C4), 126.0 (q, *J* = 3.8 Hz, C5), 124.0 (q, *J* = 272.2 Hz, C7), 68.6 (C2), 48.0 (C1).

^{19}F-NMR (376 MHz, $CDCl_3$): δ_F = −65.8.

HRMS (ESI+): calc. for $C_9H_{10}F_3N_4$ $[M+H]^+$ 231.0852, found 231.0853.

***R*$_f$:** 0.43 (DCM:MeOH 9:1)

4-(2-Amino-1-azidoethyl)phenyl trifluoromethanesulfonate (2e)



Following the general procedure for amino azidation using *4-vinylphenyl trifluoromethanesulfonate* **1e** (127.4 mg, 0.505 mmol) and purified by silica gel column chromatography (DCM:MeOH 100:0 to 98:2, NEt_3-deactivated SiO_2) provided the title compound as a yellow oil (83.2 mg, 0.268 mmol, 53%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ_H = 7.44 – 7.39 (m, 2H, H5), 7.33 – 7.28 (m, 2H, H4), 4.55 (dd, *J* = 7.3, 5.4 Hz, 1H, H2), 2.99 – 2.89 (m, 2H, H1), 1.33 (s, br, 2H, NH_2).

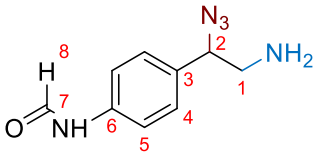
^{13}C-NMR (101 MHz, $CDCl_3$): δ_C = 149.4 (C6), 138.7 (C3), 129.0 (C5), 121.9 (C4), 118.8 (q, *J* = 320.8 Hz, C7)), 68.2 (C2), 48.1 (C1).

^{19}F-NMR (376 MHz, $CDCl_3$): δ_F = −76.0.

HRMS (ESI+): calc. for $C_9H_{10}F_3N_4O_3S$ $[M+H]^+$ 311.0420, found 311.0416.

***R*$_f$:** 0.39 (DCM:MeOH 9:1)

***N*-(4-(2-Amino-1-azidoethyl)phenyl)formamide (2f)**



Following the general procedure for amino azidation using *N-(4-vinylphenyl)formamide* **1f** (74.6 mg, 0.507 mmol) and purified by silica gel column chromatography (DCM:MeOH 100:0 to 98:2, NEt_3-deactivated SiO_2) provided the title compound as a yellow oil (64.1 mg, 0.312 mmol, 62%). The isolated compound contains in addition residual triethylamine originating from the pre-treated silica gel.

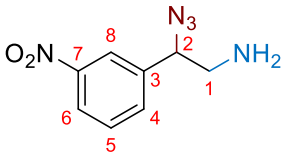
^{1}H-NMR (400 MHz, $CDCl_3$): δ_H = 8.71 (d, *J* = 10.0 Hz) and 8.38 (d, *J* = 1.8 Hz) rotameric to 1H (H8), 8.15 (s, br) and partially 7.63 – 7.53 (m) rotameric to 1H (NH), 7.63 – 7.53 (m, 1H, Ar), 7.34 – 7.27 (m, 2H, Ar), 7.16 – 7.04 (m, 1H, Ar), 4.49 (q, *J* = 6.4 Hz, 1H, H2), 2.94 (dd, *J* = 6.5, 4.6 Hz, 2H, H1), 1.41 (s, br, 2H, NH_2).

^{13}C-NMR (101 MHz, $CDCl_3$): δ_C = 162.3 and 159.1 rotameric (C7), 137.2 and 137.0 rotameric (C6), 135.0 and 134.3 rotameric (C3), 128.7 (C4/C5), 128.0 (C4/C5), 120.4 (C4/C5), 119.2 (C4/C5), 68.7 and 68.6 rotameric (C2), 47.9 (C1).

HRMS (ESI+): calc. for $C_9H_{11}N_5NaO$ $[M+Na]^+$ 228.0856, found 228.0859.

***R*$_f$:** 0.39 (DCM:MeOH 9:1)

2-Azido-2-(3-nitrophenyl)ethan-1-amine (2g)



Following the general procedure for amino azidation using commercially available *3-nitro styrene* (75.0 mg, 0.503 mmol) and purified by silica gel column chromatography (DCM:MeOH 100:0 to 98:2, NEt_3-deactivated SiO_2) provided the title compound as a yellow oil (73.7 mg, 0.356 mmol, 71%).

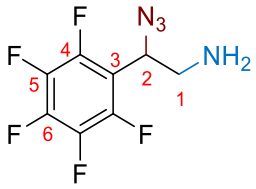
^{1}H-NMR (400 MHz, $CDCl_3$): δ_H = 8.23 – 8.16 (m, 2H, H6+H8), 7.70 – 7.64 (m, 1H, H4), 7.62 – 7.54 (m, 1H, H5), 4.64 (dd, *J* = 7.3, 5.2 Hz, 1H, H2), 3.06 – 2.94 (m, 2H, H1), 1.29 (s, br, 2H, NH_2).

^{13}C-NMR (101 MHz, $CDCl_3$): δ_C = 148.6 (C7), 140.4 (C3), 133.1 (C4), 130.0 (C5), 123.5 (C6), 122.1 (C8), 68.2 (C2), 48.0 (C1).

HRMS (ESI+): calc. for $C_8H_{10}N_5O_2$ $[M+H]^+$ 208.0829, found 208.0824.

***R*$_f$:** 0.40 (DCM:MeOH 9:1)

2-Azido-2-(perfluorophenyl)ethan-1-amine (2h)



Following the general procedure for amino azidation using commercially available *2,3,4,5,6-pentafluorostyrene* (70 µL, 97.4 mg, 0.502 mmol) and purified by silica gel column chromatography (DCM:MeOH 100:0 to 99:1, NEt_3-deactivated SiO_2) provided the title compound as a colorless oil (71.8 mg, 0.285 mmol, 57%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ_H = 4.85 (dd, *J* = 8.7, 5.6 Hz, 1H, H2), 3.30 – 2.92 (m, 2H, H1), 1.56 (s, br, 2H, NH_2).

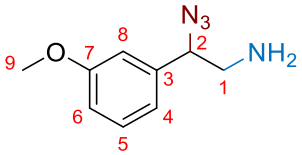
^{13}C-NMR (101 MHz, $CDCl_3$): δ_C = 146.8 – 143.6 (m), 143.0 – 139.7 (m), 139.4 – 135.9 (m), 111.5 (C3), 59.5 (C2), 45.0 (C1).

^{19}F NMR (376 MHz, $CDCl_3$): δ_F = −140.8 – −140.9 (m), −152.0 – −153.6 (m), −160.0 – −160.8 (m).

HRMS (ESI+): calc. for $C_8H_6F_5N_4$ $[M+H]^+$ 253.0507, found 253.0507.

***R*$_f$:** 0.30 (DCM:MeOH 19:1)

2-Azido-2-(3-methoxyphenyl)ethan-1-amine (2i)



Following the general procedure for amino azidation using commercially available *3-methoxy styrene* (67.4 mg, 0.502 mmol) and purified by silica gel column chromatography (DCM:MeOH 100:0 to 98:2, NEt_3-deactivated SiO_2) provided the title compound as a yellow oil (62.7 mg, 0.326 mmol, 65%).

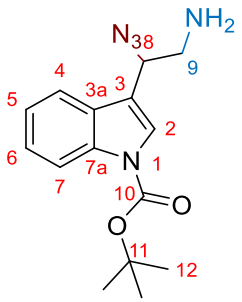
^{1}H-NMR (400 MHz, $CDCl_3$): δ_H = 7.34 – 7.28 (m, 1H, H5), 6.92 – 6.83 (m, 3H, H4+H6+H8), 4.47 (t, *J* = 6.4 Hz, 1H, H2), 3.82 (s, 3H, H9), 2.94 (d, *J* = 6.5 Hz, 2H, H1), 1.35 (s, br, 2H, NH_2).

^{13}C-NMR (101 MHz, $CDCl_3$): δ_C = 160.1 (C7), 139.4 (C3), 130.1 (C5), 119.4 (C4 or C8), 113.9 (C6), 112.9 (C8 or C4), 69.2 (C2), 55.4 (C9), 47.9 (C1).

HRMS (ESI+): calc. for $C_9H_{13}N_4O$ $[M+H]^+$ 193.1084, found 193.1085.

***R*$_f$:** 0.51 (DCM:MeOH 9:1)

***tert*-Butyl 3-(2-amino-1-azidoethyl)-1H-indole-1-carboxylate (2k)**



Following the general procedure for amino azidation using *tert-butyl 3-vinyl-1H-indole-1-carboxylate* **1k** (119.7 mg, 0.492 mmol) and purified by silica gel column chromatography (DCM:MeOH 100:0 to 97:3, NEt_3-deactivated SiO_2) provided the title compound as a yellow oil (77.3 mg, 0.257 mmol, 52%). In addition, the 1,2-aminomethoxylated product **2k-OMe** was observed and isolated (38.8 mg, 0.134 mmol, 27%; for characterization see below).

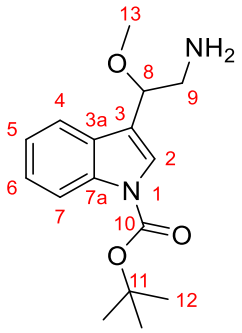
^{1}H-NMR (400 MHz, $CDCl_3$): δ_H = 8.17 (d, *J* = 8.4 Hz, 1H, H4), 7.65 – 7.59 (m, 2H, H2+H7), 7.36 (ddd, *J* = 8.4, 7.2, 1.3 Hz, 1H, H5), 7.30 – 7.23 (m, 1H, H6), 4.75 (t, *J* = 6.4 Hz, 1H, H8), 3.17 – 3.01 (m, 2H, H9), 1.68 (s, br, 11H, H12+NH_2).

^{13}C-NMR (101 MHz, $CDCl_3$): δ_C = 149.5 (C10), 135.9 (C7a), 128.3 (C3a), 125.1 (C5), 124.2 (C2), 123.0 (C6), 119.5 (C7), 117.1 (C3), 115.7 (C4), 84.3 (C11), 62.2 (C8), 46.1 (C9), 28.3 (C12).

HRMS (ESI+): calc. for $C_{15}H_{19}N_5NaO_2$ $[M+Na]^+$ 324.1431, found 324.1430.

***R*$_f$**: 0.40 (DCM:MeOH 9:1)

***tert*-Butyl 3-(2-amino-1-methoxyethyl)-1H-indole-1-carboxylate (2k-OMe)**



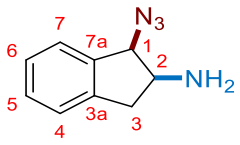
^{1}H-NMR (400 MHz, $CDCl_3$): δ_H = 8.15 (d, *J* = 8.4 Hz, 1H, H4), 7.69 – 7.64 (m, 1H, H7), 7.55 (s, 1H, H2), 7.33 (ddd, *J* = 8.4, 7.2, 1.3 Hz, 1H, H5), 7.23 (ddd, *J* = 8.2, 7.3, 1.1 Hz, 1H, H6), 4.44 (ddd, *J* = 7.4, 4.7, 0.7 Hz, 1H, H8), 3.34 (s, 3H, H13), 3.18 – 2.99 (m, 2H, H9), 1.68 (s, 11H, H12+NH_2).

^{13}C-NMR (101 MHz, $CDCl_3$): δ_C = 149.8 (C10), 136.0 (C7a), 129.0 (C3a), 124.7 (C5), 124.1 (C2), 122.8 (C6), 120.1 (C7), 119.3 (C3), 115.5 (C4), 84.0 (C11), 79.7 (C8), 57.0 (C13), 47.2 (C9), 28.3 (C12).

HRMS (ESI+): calc. for $C_{16}H_{22}N_2NaO_3$ $[M+Na]^+$ 313.1523, found 313.1522.

***R*$_f$**: 0.31 (DCM:MeOH 9:1)

***rac*-(1*R*,2*S*)-1-Azido-2,3-dihydro-1*H*-inden-2-amine (2l)**



Following the general procedure for amino azidation using commercially available *indene* (57.9 mg, 0.498 mmol) and purified by silica gel column chromatography (DCM:MeOH 100:0 to 98:2, NEt_3-deactivated SiO_2) provided the title compound as a red oil (52.6 mg, 0.302 mmol, 61%). Configuration and regiochemistry was proven by derivatization to literature known compound **2l-CO_2Et**.

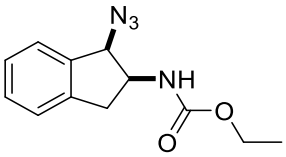
^{1}H-NMR (400 MHz, $CDCl_3$): δ_H = 7.41– 7.22 (m, 4H, H4+H5+H6+H7), 4.69 (d, *J* = 5.6 Hz, 1H, H1), 3.77 (ddd, *J* = 8.0, 6.9, 5.6 Hz, 1H, H2), 3.18 – 2.68 (m, 2H, H3), 1.61 (s, br, 2H, NH_2).

^{13}C-NMR (101 MHz, $CDCl_3$): δ_C = 142.1 (C3a or C7a), 139.1 (C7a or C3a), 129.4 (C4 or C5 or C6 or C7), 127.1 (C5 or C6 or C7 or C4), 125.4 (C6 or C7 or C4 or C5), 125.3 (C7 or C4 or C5 or C6), 69.2 (C1), 56.8 (C2), 39.6 (C3).

HRMS (ESI+): calc. for $C_9H_{10}N_4Na$ $[M+Na]^+$ 197.0798, found 197.0793.

***R*$_f$:** 0.48 (DCM:MeOH 9:1)

***rac*-Ethyl ((1*R*,2*S*)-1-azido-2,3-dihydro-1*H*-inden-2-yl)carbamate (2l-CO_2Et)**



To a solution of rac-(1*R*,2*S*)-1-azido-2,3-dihydro-1*H*-inden-2-amine **2l** (51 mg, 0.30 mmol, 1.0 eq) in DCM (1.5 mL) at 0 °C was added triethylamine (0.73 mL, 0.33 mmol, 1.1 eq) and dropwise ethyl chloroformate (32 µL, 0.33 mmol, 1.1 eq). The reaction mixture was allowed to go to r.t. and stirred overnight. The reaction mixture was diluted with DCM (10 mL) and washed with water (2 mL), 1M HCl (2 mL), water (2 mL) and brine before drying over Na_2SO_4. Purification via column chromatography (EtOAc:hex 5% to 15%, SiO_2) yielded ethyl carbamate **2l-CO_2Et** (23 mg, 0.092 mmol, 31%).

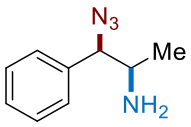
Spectroscopic data matches the one reported for the *cis*-isomer.[13]

^{1}H-NMR (400 MHz, $CDCl_3$): δ_H = 7.43 – 7.26 (m, 4H), 5.24 (d, *J* = 8.1 Hz, 1H), 4.90 (d, *J* = 5.9 Hz, 1H), 4.65 – 4.44 (m, 1H), 4.17 (q, *J* = 7.1 Hz, 2H), 3.22 (dd, *J* = 15.6, 7.4 Hz, 1H), 2.84 (dd, *J* = 15.5, 9.1 Hz, 1H), 1.28 (t, *J* = 7.1 Hz, 3H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ_C = 156.4, 141.1, 138.2, 129.9, 127.5, 125.5, 125.3, 66.5, 61.3, 54.4, 37.0, 14.7.

[13] Orlek, B. S.; Lightowler, D. *J. Chem. Soc., Perkin Trans. 1* **1993**, 1307-1312.

***rac*-(1*R*,2*R*)-1-Azido-1-phenylpropan-2-amine (2m)**



Following the general procedure for amino azidation using commercially available *(E)-prop-1-en-1-ylbenzene* (59.6 mg, 0.504 mmol) and purified by silica gel column chromatography (DCM:MeOH 100:0 to 98:2, NEt_3-deactivated SiO_2) provided the title compound as a yellow oil (51.0 mg, 0.289 mmol, 57%).

Spectroscopic data matches the one described in literature.[14]

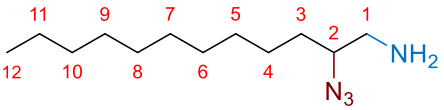
The use of (*E)-prop-1-en-1-ylbenzene* on 0.5 mmol scale yielded the same product in 47% yield and a *dr* of 5:1 (by GC-FID).[15]

^{1}H-NMR (400 MHz, $CDCl_3$): δ_H = 7.41 – 7.31 (m, 3H), 7.30 – 7.26 (m, 2H), 4.21 (d, *J* = 7.6 Hz, 1H), 3.08 (tt, *J* = 6.6, 5.6 Hz, 1H), 1.56 (s, br, 2H, NH_2), 0.95 (dd, *J* = 6.5, 0.9 Hz, 3H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ_C = 137.9, 128.9, 128.5, 127.6, 74.4, 51.9, 20.2.

Azidoamines from unactivated alkenes

2-Azidododecan-1-amine (2n)



Following the general procedure for amino azidation using commercially available *1-dodecene* (89.0 mg, 0.529 mmol) and purified by silica gel column chromatography (DCM:MeOH 100:0 to 99:1, NEt_3-deactivated SiO_2) provided the title compound as a colorless oil (74.5 mg, 0.329 mmol, 62%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ_H = 3.38 – 3.27 (m, 1H, H2), 2.88 – 2.61 (m, 2H, H1), 1.86 (s, br, 2H, NH_2), 1.55 – 1.50 (m, 2H, H3), 1.33 – 1.26 (m, 16H, H4 – H11), 0.90 – 0.85 (m, 3H, H12).

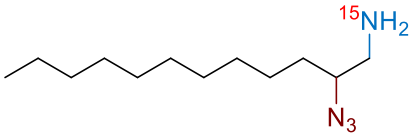
^{13}C-NMR (101 MHz, $CDCl_3$): δ_C = 65.7 (C2), 45.9 (C1), 32.1 (C3), 32.0, 29.71, 29.68, 29.60, 29.59, 29.5, 26.2, 22.8, 14.3 (C12).

HRMS (ESI+): calc. for $C_{12}H_{27}N_4$ $[M+H]^+$ 227.2230, found 227.2234.

***R*$_f$:** 0.40 (DCM:MeOH 9:1)

[14]G. Berger *et al. Bioorg. Med. Chem.* **2014**, *22*, 3527-3536.
[15]GC-FID 2025 from SHIMADZU with hydrogen as carrier gas and an OPTIMA® 5 Amine column from Macherey-Nagel was used for the analysis. An identical response factor was assumed for both isomers.

^{15}N-2-Azidododecan-1-amine (^{15}N-2n)



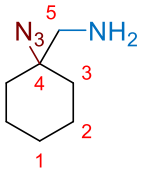
Following the general procedure for amino azidation on 0.1 mmol scale using commercially available *1-dodecene* (16.9 mg, 0.100 mmol) and ^{15}N-labelled aminating reagent, purification by silica gel column chromatography (DCM:MeOH 100:0 to 97:3, NEt_3-deactivated SiO_2) afforded the isotope labelled title compound as a colorless oil (12.0 mg, 0.0528 mmol, 53%). The ^{1}H- and ^{13}C-NMR data match with the data from the non-isotope labeled one (additional *J*(C,N) couplings are observed).

^{1}H-NMR (400 MHz, $CDCl_3$): δ_H = 3.36 – 3.24 (m, 1H), 2.87 – 2.64 (m, 2H), 1.52 (dt, *J* = 8.1, 6.6 Hz, 2H), 1.40 – 1.22 (m, 18H), 0.88 (t, J = 6.8 Hz, 3H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ_C = 66.02 (d, *J* = 1.4 Hz), 46.10 (d, *J* = 4.2 Hz), 32.11 (d, *J* = 1.1 Hz), 32.03, 29.71, 29.68, 29.61, 29.60, 29.45, 26.24, 22.82, 14.25.

HRMS (ESI+): calc. for $C_{12}H_{27}N_3{}^{15}N$ $[M+H]^+$ 228.2201, found 228.2201.

1-(Azidomethyl)cyclohexan-1-amine (2o)



Following the general procedure for amino azidation using commercially available *methylenecyclohexane* (47.9 mg, 0.498 mmol) and purified by silica gel column chromatography (DCM:MeOH 100:0 to 99:1, NEt_3-deactivated SiO_2) provided the title compound as a colorless oil (36.4 mg, 0.236 mmol, 47%).

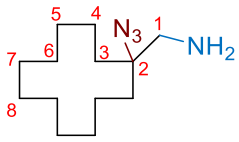
^{1}H-NMR (400 MHz, $CDCl_3$): δ_H = 2.73 (s, 2H, H5), 1.73 – 1.66 (m, 2H, H1/H2/H3), 1.60 – 1.51 (m, 4H, H2/H3/H1), 1.43 – 1.24 (m, 4H, H3/H1/H2), 1.19 (s, br, 2H, NH_2).

^{13}C-NMR (101 MHz, $CDCl_3$): δ_C = 65.2 (C4), 51.0 (C5), 32.3 (C3), 25.7 (C1), 22.1 (C2).

HRMS (ESI+): calc. for $C_7H_{15}N_4$ $[M+H]^+$ 155.1291, found 155.1292.

***R_f*:** 0.30 (DCM:MeOH 9:1)

(1-Azidocyclododecyl)methanamine (2p)



Following the general procedure for amino azidation using *methylenecyclododecane* (90.2 mg, 0.50 mmol) and purified by silica gel column chromatography (DCM:MeOH 100:0 to 99:1, NEt_3-deactivated SiO_2) provided the title compound as a colorless oil (48.9 mg, 0.205 mmol, 41%).

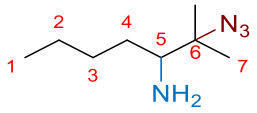
^{1}H-NMR (400 MHz, $CDCl_3$): δ_H = 2.62 (s, 2H, H1), 1.63 – 1.11 (m, 24H, H2-H8).

^{13}C-NMR (101 MHz, $CDCl_3$): δ_C = 68.4 (C2), 49.1 (C1), 29.7, 26.4, 26.0, 22.6, 22.0, 19.3.

HRMS (ESI+): calc. for $C_{13}H_{27}N_4$ $[M+H]^+$ 239.223, found 239.223.

***R*$_f$:** 0.15 (DCM:MeOH 19:1)

2-Azido-2-methylheptan-3-amine (2q)



Following the general procedure for amino azidation using *2-methyl-2-heptene* (55.6 mg, 0.495 mmol) and purified by silica gel column chromatography (DCM:MeOH 100:0 to 98:2, NEt_3-deactivated SiO_2) provided the title compound as a colorless oil (37.2 mg, 0.218 mmol, 44%).

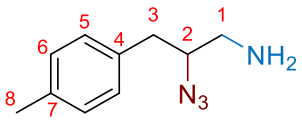
^{1}H-NMR (400 MHz, $CDCl_3$): δ_H = 2.54 (dd, *J* = 10.4, 1.8 Hz, 1H, H5), 1.58 – 1.46 (m, 2H, H2/H3/H4), 1.41 – 1.30 (m, 4H), 1.27 (s, 3H, H7/H7'), 1.24 (s, 3H, H7'/H7), 1.19 – 1.04 (m, 2H, NH_2), 0.94 – 0.88 (m, 3H, H1).

^{13}C-NMR (101 MHz, $CDCl_3$): δ_C = 65.7 (C6), 59.3 (C5), 31.7, 29.6, 23.1 (C7), 22.9 (C7'), 21.5, 14.2 (C1).

HRMS (ESI+): calc. for $C_8H_{19}N_4$ $[M+H]^+$ 171.1604, found 171.1603.

***R*$_f$:** 0.51 (DCM:MeOH 9:1)

2-Azido-3-(*p*-tolyl)propan-1-amine (2r)



Following the general procedure for amino azidation using commercially available *4-(allyl)toluene* (67.2 mg, 0.508 mmol) and purified by silica gel column chromatography (DCM:MeOH 100:0 to 98:2, NEt_3-deactivated SiO_2) provided the title compound as a yellow oil (49.3 mg, 0.259 mmol, 51%).

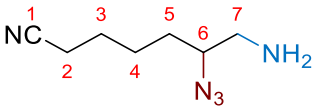
^{1}H-NMR (400 MHz, $CDCl_3$): δ_H = 7.16 – 7.08 (m, 4H, H5+H6), 3.60 – 3.52 (m, 1H, H2), 2.89 – 2.65 (m, 2H, H1), 2.81 (d, *J* = 7.0 Hz, 2H, H3), 2.33 (s, 3H, H8), 1.41 (s, br, 2H, NH_2).

^{13}C-NMR (101 MHz, $CDCl_3$): δ_C = 136.6 (C7), 134.3 (C4), 129.5 (C6), 129.2 (C5), 67.0 (C2), 45.5 (C1), 38.1 (C3), 21.2 (C8).

HRMS (ESI+): calc. for $C_{10}H_{15}N_4$ $[M+H]^+$ 191.1291, found 191.1296.

***R*$_f$:** 0.37 (DCM:MeOH 9:1)

7-Amino-6-azidoheptanenitrile (2s)



Following the general procedure for amino azidation using commercially available *6-heptenenitrile* (65 μL, 55 mg, 0.50 mmol) and purified by silica gel column chromatography (DCM: 98:2 to 96:4, NEt_3-deactivated SiO_2) provided the title compound as a yellow oil (46.7 mg, 0.28 mmol, 56%).

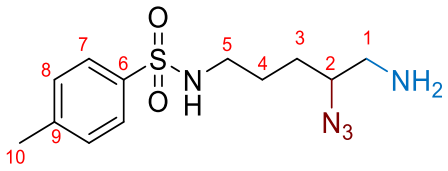
^{1}H-NMR (400 MHz, $CDCl_3$): δ_H = 3.32 (tq, *J* = 7.6, 4.2 Hz, 1H, H6), 2.89 – 2.67 (m, 2H, H7), 2.37 (t, *J* = 6.9 Hz, 2H, H2), 1.75 – 1.65 (m, 2H, H3), 1.65 – 1.45 (m, 6H, H4+H5+NH_2).

^{13}C-NMR (101 MHz, $CDCl_3$): δ_C = 119.5 (C1), 65.4 (C6), 46.0 (C7), 31.3 (C5), 25.4 (C3 or C4), 25.4 (C4 or C3), 17.2 (C2).

HRMS (ESI+): calc. for $C_7H_{14}N_5$ $[M+H]^+$ 168.1244, found 168.1246.

***R_f*:** 0.21 (DCM:MeOH 9:1)

2-Azido-5-tosylpentan-1-amine (2t)



Following the general procedure for amino azidation using starting material *1-methyl-4-(pent-4-en-1-ylsulfonyl)benzene* **1t** (118.0 mg, 0.493 mmol) and purified by silica gel column chromatography (DCM:MeOH 100:0 to 95:5, NEt_3-deactivated SiO_2) provided the title compound as a yellow oil (99.5 mg, 0.335 mmol, 68%).

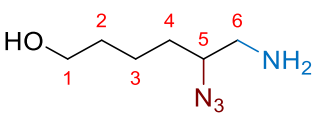
^{1}H-NMR (400 MHz, $CDCl_3$): δ_H = 7.76 – 7.72 (m, 2H, H7), 7.33 – 7.28 (m, 2H, H8), 5.03 (s, br, 1H, NH), 3.31 – 3.20 (m, 1H, H2), 3.00 – 2.92 (m, 2H, H5), 2.81 – 2.64 (m, 2H, H1), 2.42 (s, 3H, H10), 1.67 – 1.36 (m, 6H, H4+H3+NH_2).

^{13}C-NMR (101 MHz, $CDCl_3$): δ_C = 143.6 (C9), 137.0 (C6), 129.9 (C8), 127.2 (C6), 65.1 (C2), 45.9 (C1), 42.9 (C5), 28.9 (C3), 26.2 (C4), 21.6 (C10).

HRMS (ESI+): calc. for $C_{12}H_{20}N_5O_2S$ $[M+H]^+$ 298.1332, found 298.1333.

***R_f*:** 0.18 (DCM:MeOH 9:1)

6-Amino-5-azidohexan-1-ol (2u)



Following the general procedure for amino azidation using commercially available *hex-5-en-1-ol* (50.1 mg, 0.500 mmol) and purified by silica gel column chromatography (DCM:MeOH 98:2 to 95:5, NEt_3-deactivated SiO_2) provided the title compound as a yellow oil (41.9 mg, 0.265 mmol, 53%).

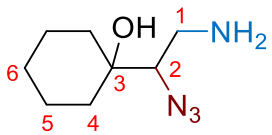
^{1}H-NMR (400 MHz, $CDCl_3$): δ_H = 3.65 (t, *J* = 6.2 Hz, 2H, H1), 3.37 – 3.28 (m, 1H, H5), 2.85 – 2.68 (m, 2H, H6), 1.64 – 1.46 (m, 6H, H2+H3+H4), 1.50 (s, br, 3H, OH+NH_2).

^{13}C-NMR (101 MHz, $CDCl_3$): δ_C = 65.8 (C5), 62.5 (C1), 45.9 (C6), 32.5 (C3 or C4), 31.8 (C4 or C3), 22.5 (C2).

HRMS (EI+): calc. for $C_6H_{15}N_4O$ $[M+H]^+$ 159.12404, found 159.12383.

***R_f*:** 0.13 (DCM:MeOH 4:1)

1-(2-Amino-1-azidoethyl)cyclohexan-1-ol (2v)



Following the general procedure for amino azidation using commercially available *1-vinyl cyclohexanol* (64.0 mg, 0.507 mmol) and purified by silica gel column chromatography (DCM:MeOH 100:0 to 96:4, NEt_3-deactivated SiO_2) provided the title compound as a yellow oil (49.4 mg, 0.268 mmol, 53%).

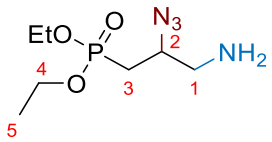
^{1}H-NMR (400 MHz, $CDCl_3$): δ_H = 3.23 (dd, *J* = 6.3, 4.3 Hz, 1H, H2), 3.18 – 3.00 (m, 2H, H1), 2.18 (s, br, 2H, NH_2), 1.76 – 1.69 (m, 1H, OH), 1.68 – 1.57 (m, 4H, H4/H5/H6), 1.57 – 1.47 (m, 2H, H4/H5/H6), 1.46 – 1.35 (m, 2H, H4/H5/H6), 1.28 – 1.12 (m, 2H, H4/H5/H6).

^{13}C-NMR (101 MHz, $CDCl_3$): δ_C = 74.2 (C3), 71.5 (C2), 41.7 (C1), 35.1 (C4), 34.7 (C4'), 25.8 (C6), 21.6 (C5), 21.5 (C5').

HRMS (ESI+): calc. for $C_8H_{17}N_4O$ $[M+H]^+$ 185.1397, found 185.1397.

***R_f*:** 0.06 (DCM:MeOH 9:1)

Diethyl (3-amino-2-azidopropyl)phosphonate (2w)



Following the general procedure for amino azidation using commercially available *diethyl allylphosphonate* (89.7 mg, 0.50 mmol) and purified by silica gel column chromatography (DCM:MeOH 100:0 to 95:5, NEt_3-deactivated SiO_2) provided the title compound as a yellow oil (68.6 mg, 0.290 mmol, 58%).

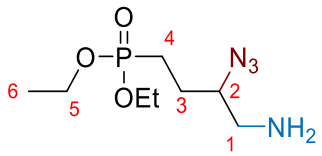
^{1}H-NMR (400 MHz, $CDCl_3$): δ_H = 4.19 – 4.00 (m, 4H, H4+H4'), 3.76 – 3.66 (m, 1H, H2), 2.97 – 2.74 (m, 2H, H1), 2.05 – 1.96 (m, 2H, H3), 1.74 (s, br, 2H, NH_2), 1.34 – 1.29 (m, 6H, H5+H5').

^{13}C-NMR (101 MHz, $CDCl_3$): δ_C = 62.1 (d, *J* = 3.1 Hz, C4 or C4'), 62.0 (d, *J* = 3.0 Hz, C4' or C4), 60.2 (d, *J* = 2.3 Hz, C2), 46.6 (d, *J* = 10.9 Hz, C1), 28.7 (d, *J* = 141.8 Hz, C3), 16.5 (d, *J* = 1.6 Hz, C5 or C5'), 16.5 (d, *J* = 1.6 Hz, C5' or C5).

HRMS (ESI+): calc. for $C_7H_{18}N_4O_3P$ $[M+H]^+$ 237.1111, found 237.1108.

***R*$_f$:** 0.24 (DCM:MeOH 9:1)

Diethyl (4-amino-3-azidobutyl)phosphonate (2x)



Following the general procedure for amino azidation using commercially available *diethyl 3-butenylphosphonate* (94.9 mg, 0.49 mmol) and purified by silica gel column chromatography (DCM:MeOH 100:0 to 95:5, NEt_3-deactivated SiO_2) provided the title compound as a yellow oil (62.9 mg, 0.25 mmol, 51%).

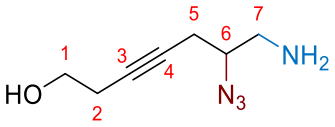
^{1}H-NMR (400 MHz, $CDCl_3$): δ_H = 4.13 – 3.99 (m, 4H, H5+H5'), 3.38 (tt, *J* = 7.8, 3.9 Hz, 1H, H2), 2.89 – 2.65 (m, 2H, H1), 1.94 – 1.63 (m, 4H, H3+H4), 1.58 (s, br, 2H, NH_2), 1.29 (dt, *J* = 9.4, 6.0 Hz, 6H, H6+H6').

^{13}C-NMR (101 MHz, $CDCl_3$): δ_C = 65.5 (d, *J* = 15.5 Hz, C2), 61.8 (d, *J* = 3.3 Hz, C5 or C5'), 61.7 (d, *J* = 3.3 Hz, C5' or C5), 45.8 (C1), 25.3 (d, *J* = 4.5 Hz, C3), 22.4 (d, *J* = 142.8 Hz, C4), 16.54 (C6 or C6'), 16.48 (C6' or C6).

HRMS (ESI+): calc. for $C_8H_{19}N_4NaO_3P$ $[M+Na]^+$ 273.1087, found 237.1087.

***R*$_f$:** 0.20 (DCM:MeOH 9:1)

7-Amino-6-azidohept-3-yn-1-ol (2y)



Following the general procedure for amino azidation using commercially available *hept-6-en-3-yn-1-ol* (56.9 mg, 0.52 mmol) and purified by silica gel column chromatography (DCM:MeOH 98:2 to 95:5, NEt_3-deactivated SiO_2) provided the title compound as a yellow oil (57.7 mg, 0.34 mmol, 66%).

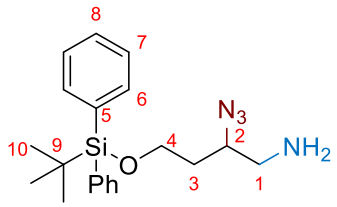
^{1}H-NMR (400 MHz, $CDCl_3$): δ_H = 3.68 (t, *J* = 6.2 Hz, 2H, H1), 3.56 – 3.47 (m, 1H, H6), 2.95 – 2.73 (m, 2H, H7), 2.47 (dtd, *J* = 6.3, 2.4, 1.3 Hz, 2H, H5), 2.42 (tt, *J* = 6.3, 2.3 Hz, 2H, H2), 2.01 – 1.90 (m, 3H, OH+NH_2).

^{13}C-NMR (101 MHz, $CDCl_3$): δ_C = 80.3 (C3), 77.2 (C4), 63.5 (C6), 61.1 (C1), 45.0 (C7), 23.3 (C2), 22.7 (C5).

HRMS (ESI+): calc. for $C_7H_{13}N_4O$ $[M+H]^+$ 169.1084, found 169.1084.

***R*$_f$:** 0.24 (DCM:MeOH 4:1)

2-Azido-4-((*tert*-butyldiphenylsilyl)oxy)butan-1-amine (2z)



Following the general procedure for amino azidation using *(but-3-en-1-yloxy)(tert-butyl)diphenylsilane* **1z** (153.8 mg, 0.50 mmol) and purified by silica gel column chromatography (DCM:MeOH 98:2, NEt_3-deactivated SiO_2) provided the title compound as a yellow oil (90.6 mg, 0.25 mmol, 50%).

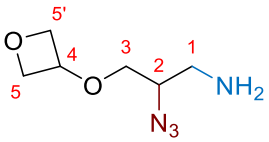
^{1}H-NMR (400 MHz, $CDCl_3$): δ_H = 7.69 – 7.64 (m, 4H, H6), 7.44 – 7.36 (m, 6H, H7+H8), 3.86 – 3.70 (m, 2H, H4), 3.68 – 3.59 (m, 1H, H2), 2.89 – 2.67 (m, 2H, H1), 1.94 (s, br, 2H, NH_2), 1.82 – 1.62 (m, 2H, H3), 1.07 – 1.04 (m, 9H, H10).

^{13}C-NMR (101 MHz, $CDCl_3$): δ_C = 135.70 (C6), 135.67 (C6'), 133.7 (C5), 133.6 (C5'), 129.90 (C8), 129.89 (C8'), 127.89 (C7), 127.88 (C7'), 62.8 (C2), 60.5 (C4), 46.2 (C1), 34.8 (C3), 27.0 (C10), 19.3 (C9).

HRMS (ESI+): calc. for $C_{20}H_{29}N_4OSi$ $[M+H]^+$ 369.2105, found 369.2109.

***R*$_f$:** 0.16 (DCM:MeOH 96:4)

2-Azido-3-(oxetan-3-yloxy)propan-1-amine (2aa)



Following the general procedure for amino azidation using commercially available *3-(allyloxy)oxetane* (57.1 mg, 0.50 mmol) and purified by silica gel column chromatography (DCM:MeOH 100:0 to 95:5, NEt_3-deactivated SiO_2) provided the title compound as a yellow oil (34.4 mg, 0.200 mmol, 40%).

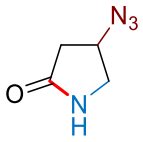
^{1}H-NMR (400 MHz, $CDCl_3$): δ_H = 4.80 – 4.70 (m, 2H, H5+H5'), 4.66 – 4.58 (m, 2H, H5+H5'), 4.58 – 4.52 (m, 1H, H4), 3.62 – 3.48 (m, 2H, H3), 3.45 (dd, *J* = 9.6, 6.8 Hz, 1H, H2), 2.91 – 2.70 (m, 2H, H1), 1.66 (s, br, 2H, NH_2).

^{13}C-NMR (101 MHz, $CDCl_3$): δ_C = 78.6 (C5), 78.5 (C5'), 73.0 (C4), 69.5 (C2), 63.8 (C3), 42.8 (C1).

HRMS (ESI+): calc. for $C_6H_{13}N_4O_2$ $[M+H]^+$ 173.1033, found 173.1034.

***R*$_f$:** 0.35 (DCM:MeOH 9:1)

4-Azidopyrrolidin-2-one (2ab)



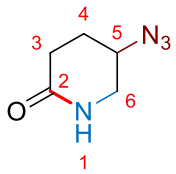
Following the general procedure and workup for amino azidation using commercially available *methyl 3-butenoate* (53.0 mg, 0.529 mmol) and purified by silica gel column chromatography (DCM:MeOH 100:0 to 98:2, NEt_3-deactivated SiO_2) provided the title compound as a yellow oil which solidifies upon standing at room temperature to an off-white amorphous solid (29.0 mg, 0.230 mmol, 43%).

The spectroscopic data matches the one reported in literature.[16]

^{1}H-NMR (400 MHz, $CDCl_3$): δ_H = 6.38 (s, br, 1H), 4.33 (tt, *J* = 7.1, 3.6 Hz, 1H), 3.71 – 3.66 (m, 1H), 3.39 – 3.32 (m, 1H), 2.66 (dd, *J* = 17.3, 7.5 Hz, 1H), 2.43 – 2.33 (m, 1H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ_C = 175.1, 56.6, 48.1, 36.6.

5-Azidopiperidin-2-one (2ac)



Following the general procedure and workup for amino azidation using commercially available *ethyl 4-pentenoate* (64.0 mg, 0.50 mmol) and purified by silica gel column chromatography (DCM:MeOH 100:0 to 95:5, NEt_3-deactivated SiO_2) provided the title compound as a yellow oil which solidifies upon standing at room temperature to an off-white amorphous solid (50.6 mg, 0.361 mmol, 72%).

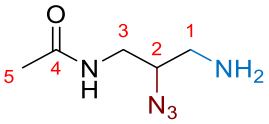
^{1}H-NMR (400 MHz, $CDCl_3$): δ_H = 6.96 (s, br, 1H, NH), 3.91 (ddt, *J* = 7.4, 5.5, 3.7 Hz, 1H, H5), 3.53 – 3.24 (m, 2H, H6), 2.60 – 2.32 (m, 2H, H3), 2.12 – 1.88 (m, 2H, H4).

^{13}C-NMR (101 MHz, $CDCl_3$): δ_C = 171.3 (C2), 54.0 (C5), 45.8 (C6), 27.9 (C3), 25.6 (C4).

HRMS (ESI+): calc. for $C_5H_9N_4O$ $[M+H]^+$ 141.0771, found 141.0772.

***R*$_f$:** 0.45 (DCM:MeOH 9:1)

***N*-(3-amino-2-azidopropyl)acetamide (2ad)**



Following the general procedure for amino azidation using *N-allylacetamide* **1ad** (50.0 mg, 0.504 mmol) and purified by silica gel column chromatography (DCM:MeOH 97:3 to 90:10, NEt_3-deactivated SiO_2) provided the title compound as a yellow oil (33.0 mg, 0.210 mmol, 42%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ_H = 6.12 (s, 1H, NH), 3.57 (tt, *J* = 6.6, 5.0 Hz, 1H, H2), 3.49 (ddd, *J* = 14.0, 6.1, 4.5 Hz, 1H, H3), 3.30 (dt, *J* = 14.0, 6.4 Hz, 1H, H3), 2.92 – 2.72 (m, 2H, H1), 2.00 (s, 3H, H5), 1.63 (s, br, 2H, NH_2).

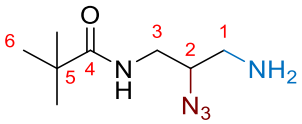
^{13}C-NMR (101 MHz, $CDCl_3$): δ_C = 170.7 (C4), 64.0 (C2), 43.5 (C1), 41.0 (C3), 23.3 (C5).

[16] K. E. Murphy-Benenato *et al., J. Med. Chem.* **2015**, *58*, 2195-2205.

HRMS (ESI+): calc. for $C_5H_{12}N_5O$ $[M+H]^+$ 158.1036, found 158.1039.

***R*$_f$:** 0.23 (DCM:MeOH 7:3)

_N_-(3-Amino-2-azidopropyl)pivalamide (2ae)



Following the general procedure for amino azidation using *N-allylpivalamide* **1ae**(72.5 mg, 0.51 mmol) and purified by silica gel column chromatography (DCM:MeOH 100:0 to 93:7, NEt_3-deactivated SiO_2) provided the title compound as a yellow oil (66.7 mg, 0.33 mmol, 65%).

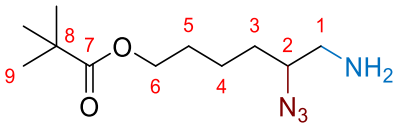
^{1}H-NMR (400 MHz, $CDCl_3$): δ_H = 6.28 (s, br, 1H, NH), 3.60 – 3.54 (m, 1H, H2), 3.49 (ddd, *J* = 14.0, 6.0, 4.5 Hz, 1H, H3), 3.36 – 3.28 (m, 1H, H3), 2.87 – 2.70 (m, 2H, H1), 1.60 (s, br, 2H, NH_2), 1.19 (s, 9H, H6).

^{13}C-NMR (101 MHz, $CDCl_3$): δ_C = 179.1 (C4), 63.9 (C2), 43.5 (C1), 41.2 (C3), 38.9 (C5), 27.6 (C6).

HRMS (ESI+): calc. for $C_8H_{18}N_5O$ $[M+H]^+$ 200.1506, found 200.1506.

***R*$_f$:** 0.17 (DCM:MeOH 9:1)

6-Amino-5-azidohexyl pivalate (2af)



Following the general procedure for amino azidation using *hex-5-en-1-yl pivalate* **1af** (92.5 mg, 0.50 mmol) and purified by silica gel column chromatography (DCM:MeOH 100:0 to 93:7, NEt_3-deactivated SiO_2) provided the title compound as a yellow oil (72.5 mg, 0.30 mmol, 60%).

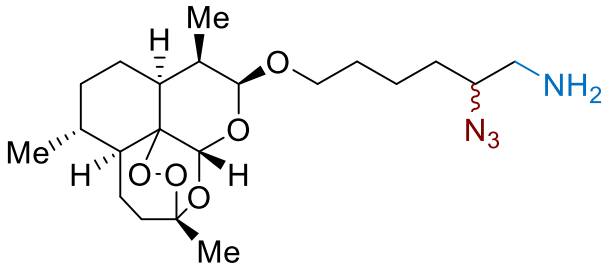
^{1}H-NMR (400 MHz, $CDCl_3$): δ_H = 4.05 (t, *J* = 6.4 Hz, 2H, H6), 3.33 – 3.24 (m, 1H, H2), 2.85 – 2.63 (m, 2H, H1), 1.70 – 1.60 (m, 2H, H5), 1.58 – 1.48 (m, 3H, H3+H4), 1.46 – 1.40 (m, 1H, H4), 1.31 (s, br, 2H, NH_2), 1.17 (s, 9H, H9).

^{13}C-NMR (101 MHz, $CDCl_3$): δ_C = 178.6 (C7), 65.7 (C2), 64.0 (C6), 46.0 (C1), 38.8 (C8), 31.7 (C3), 28.6 (C5), 27.3 (C9), 22.7 (C4).

HRMS (ESI+): calc. for $C_{11}H_{23}N_4O_2$ $[M+H]^+$ 243.1816, found 243.1814.

***R*$_f$:** 0.36 (DCM:MeOH 9:1)

2-azido-6-(((3*S*,5a*S*,6*R*,8a*S*,9*R*,10*S*,12*R*)-3,6,9-trimethyldecahydro-12*H*-3,12-epoxy[1,2]dioxepino[4,3-*i*]isochromen-10-yl)oxy)hexan-1-amine (2ag)



Hex-5-enyl artemether **1ag** (72.7 mg, 0.198 mmol, 1.0 eq) in 0.5 mL methanol was subjected to the general conditions for amino azidation (3.5 mg $Fe(OTf)_2$ from the stock solution, 13.7 mg NaN_3, 134 mg $PivONH_3OTf$). The resulting reaction mixture was worked up accordingly and purified by silica gel column chromatography (DCM:MeOH 100:0 to 97:3, NEt_3-deactivated SiO_2) to provide the title compound as a yellow oil which solidifies upon standing at room temperature to an off-white amorphous solid (46.2 mg, 0.109 mmol, 55%). The title compound was isolated as an inseparable mixture of α- and β-isomers in 1.0 : 2.5 ratio. Further, the product was isolated as a diastereoisomeric mixture resulting from the non-stereoselective installation of the azide; a 1:1 ratio is assumed.

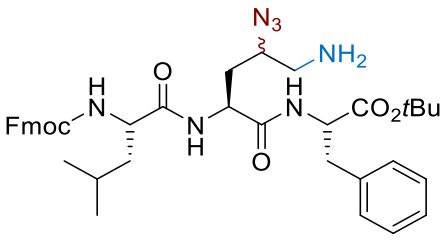
^{1}H-NMR (400 MHz, $CDCl_3$): δ_H = 5.38 (s, 0.7H), 5.32 (s, 0.3H), 4.77 (dd, *J* = 3.6, 1.0 Hz, 0.7H), 4.41 (d, *J* = 9.2 Hz, 0.3H), 3.98 (dt, *J* = 9.7, 5.9 Hz, 0.3H), 3.85 (dtd, *J* = 8.0, 6.0, 1.8 Hz, 0.7H), 3.43 – 3.34 (m, 1H), 3.33 – 3.26 (m, 1H), 2.85 – 2.68 (m, 2H), 2.65 – 2.29 (m, 2H), 2.08 – 1.97(m, 1H), 1.93 – 1.14 (m, 20H), 0.95 (d, *J* = 6.3 Hz, 3H), 0.89 (d, *J* = 7.6 Hz, 3H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ_C = 104.4, 104.2, 102.1, 100.2, 91.3, 88.1, 81.3, 80.5, 68.7, 68.6, 68.14, 68.05, 66.0, 65.9, 52.7, 51.8, 46.2, 46.1, 46.1, 46.0, 45.5, 44.6, 37.63, 37.62, 37.5, 36.6, 36.5, 34.8, 34.4, 32.8, 32.7, 31.94, 31.87, 31.82, 31.78, 31.1, 29.7, 29.6, 29.5, 26.3, 26.2, 24.8, 24.6, 23.12, 23.06, 22.82, 22.79, 20.5, 20.4, 13.2, 12.8.

HRMS (ESI+): calc. for $C_{21}H_{37}N_4O_5$ $[M+H]^+$ 425.2758, found 425.2752.

***R*$_f$:** 0.38 (DCM:MeOH 9:1)

(9*H*-fluoren-9-yl)methyl ((2*R*)-1-(((2*R*)-5-amino-4-azido-1-(((*R*)-1-(*tert*-butoxy)-1-oxo-3-phenylpropan-2-yl)amino)-1-oxopentan-2-yl)amino)-4-methyl-1-oxopentan-2-yl)-λ2-azanecarboxylate (2ah)



Fmoc-Leu-allyl-L-glycine-Phe-OtBu **1ah** (131.5 mg, 0.201 mmol, 1.0 eq) in 2 mL methanol was subjected to the general conditions for amino azidation (3.5 mg $Fe(OTf)_2$ from the stock solution, 13.7 mg NaN_3, 134 mg $PivONH_3OTf$). The resulting reaction mixture was worked up accordingly and purified by silica gel column chromatography (DCM:MeOH 100:0 to 97:3, NEt_3-deactivated SiO_2) to provide the title peptide as a yellow oil which solidifies upon standing at room temperature to an off-

white amorphous solid (29.5 mg, 0.041 mmol, 21%). The product was obtained as an inseparable mixture of diastereoisomers resulting from the non-stereoselective installation of the azide; a 1:1 ratio is assumed. The isolated compound contains in addition residual triethylamine originating from the pre-treated silica gel.

From the same run, spectroscopic clean starting material **1ah** (102.8 mg, 0.16 mmol, 78%) could be recovered during column chromatography.

^{1}H-NMR (400 MHz, $CDCl_3$): δ_H = 7.76 (d, *J* = 7.6 Hz, 2H), 7.57 (d, *J* = 7.2 Hz, 2H), 7.43 – 7.34 (m, 2H), 7.30 (t, *J* = 7.5 Hz, 2H), 7.27 – 7.09 (m, 5H), 5.40 (dd, *J* = 19.3, 8.0 Hz, 1H), 4.72 (d, *J* = 7.1 Hz, 1H), 4.64 – 4.49 (m, 1H), 4.50 – 4.39 (m, 1H), 4.39 – 4.28 (m, 1H), 4.20 (t, *J* = 7.0 Hz, 2H), 3.51 – 3.38 (m, 1H), 3.05 (d, *J* = 6.3 Hz, 2H), 2.86 – 2.65 (m, 2H), 1.97 – 1.76 (m, 2H), 1.72 – 1.47 (m, 3H), 1.39 (s, 9H), 1.26 (s, 2H), 0.99 – 0.77 (m, 8H).

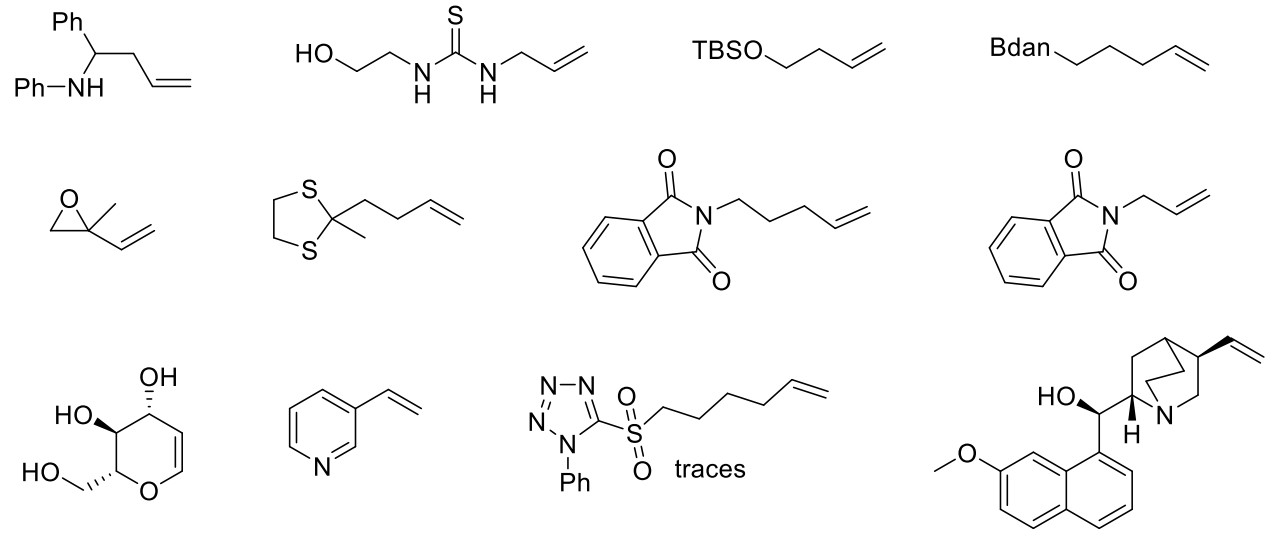
^{13}C-NMR (101 MHz, $CDCl_3$): δ_C = 172.53, 172.45, 170.41, 170.35, 170.33, 170.29, 156.4, 143.9, 141.4, 136.4, 136.3, 129.56, 129.52, 128.53, 128.51, 127.89, 127.87, 127.2, 127.1, 125.2, 125.1, 120.1, 82.5, 67.3, 67.2, 61.7, 61.1, 53.9, 51.0, 50.6, 47.3, 46.1, 45.2, 41.5, 41.4, 38.11, 38.05, 35.0, 29.8, 28.1, 24.85, 24.83, 23.10, 23.07, 22.0.

HRMS (ESI+): calc. for $C_{39}H_{49}N_7NaO_6$ $[M+Na]^+$ 734.3637, found 734.3626.

***R_f*:** 0.40 (DCM:MeOH 9:1)

Lower-yielding and not working substrates

failed substrates



lower yielding substrates

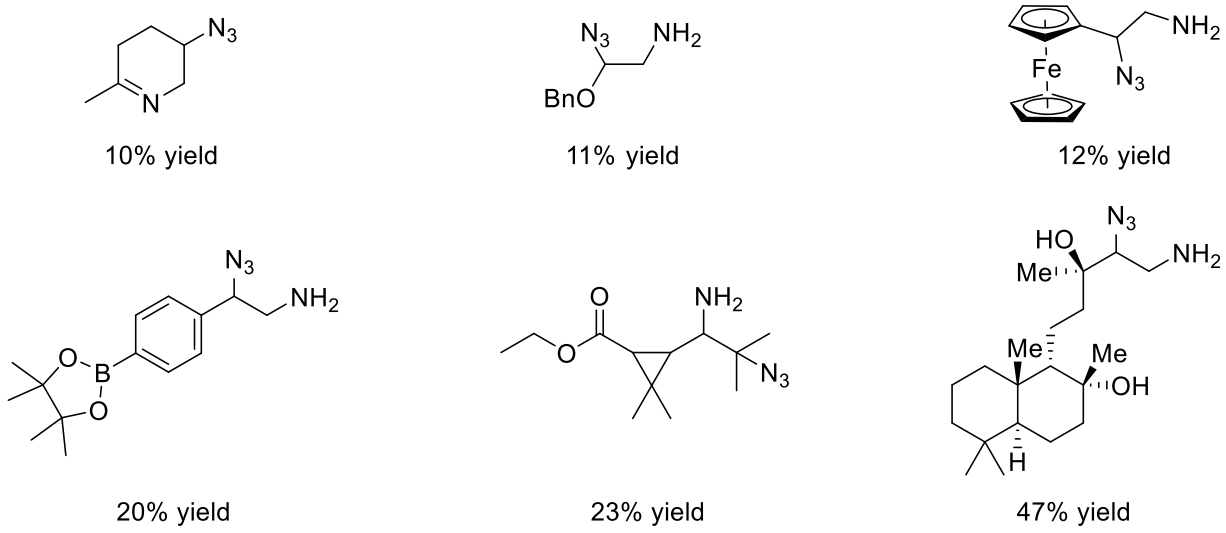
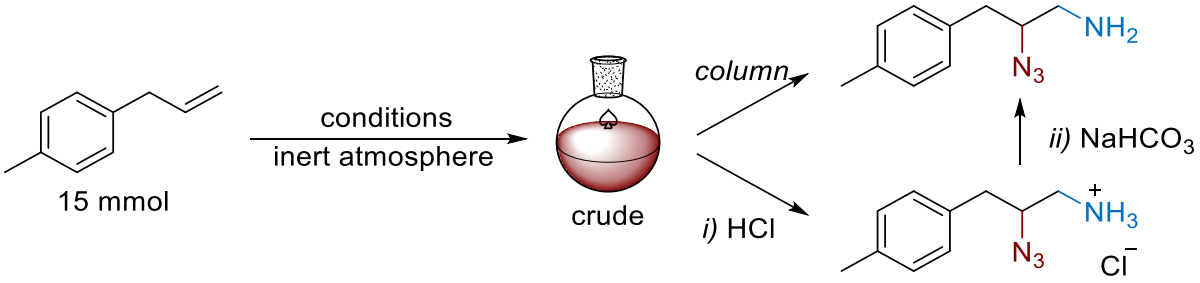


Figure 1: Selected examples outside the reaction scope or difficulties of isolation.

Scale-up experiments for 2-azido-3-(*p*-tolyl)propan-1-amine



To a 100 mL Schlenk-flask under an inert atmosphere, $Fe(OTf)_2$ (265 mg, 0.749 mmol, 5 mol%), dry MeOH (40 mL) and 4-(allyl)toluene (2.01 g, 15.2 mmol, 1.0 eq) were added subsequently. Aminating reagent $PivONH_3OTf$ (10.0 g, 37.4 mmol, 2.5 eq) was added and the reaction mixture stirred for 16 h at r.t. Then, 1 M aqueous NaOH (100 mL) was added to the reaction mixture, which was extracted with EtOAC (4x100 mL), washed with brine (50 mL), dried over Na_2SO_4 and concentrated under reduced pressure. Then, one of the two following purification method can be applied with the resulting NMR data shown below. For long-term storage, keep the obtained product cooled and in solution or as the ammonium chloride salt.

A) Purification *via* column chromatography (DCM:MeOH 100:0 to 98:2, NEt_3-deactivated SiO_2) yielded 1.70 g (59%) of product as a red oil.

B) The concentrated crude product was dissolved in 100 mL diethyl ether and treated with 10 mL of 2 M HCl in diethyl ether. The resulting precipitate was filtered off and combined with further precipitate resulting from cooling the filtrate overnight. After drying on air, 3.57 g of an off-white solid was obtained.[17] This solid was diluted with EtOAC (50 mL) and saturated aqueous $NaHCO_3$ (100 mL) was added. The aqueous phase was extracted with EtOAC (4x100 mL), the combined organic phases washed with brine (50 mL), dried over Na_2SO_4 and concentrated under reduced pressure to yield 1.67 g (57%) of product as a red oil.

[17] **^{1}H-NMR (400 MHz, DMSO-d_6):** δ_H = 8.22 (s, br, 3H), 7.29 – 7.06 (m, 4H), 4.00 (tdd, *J* = 9.0, 5.3, 3.6 Hz, 1H), 3.43 (s, br, 1H), 3.02 – 2.89 (m, 2H), 2.84 – 2.69 (m, 2H), 2.29 (s, 3H).

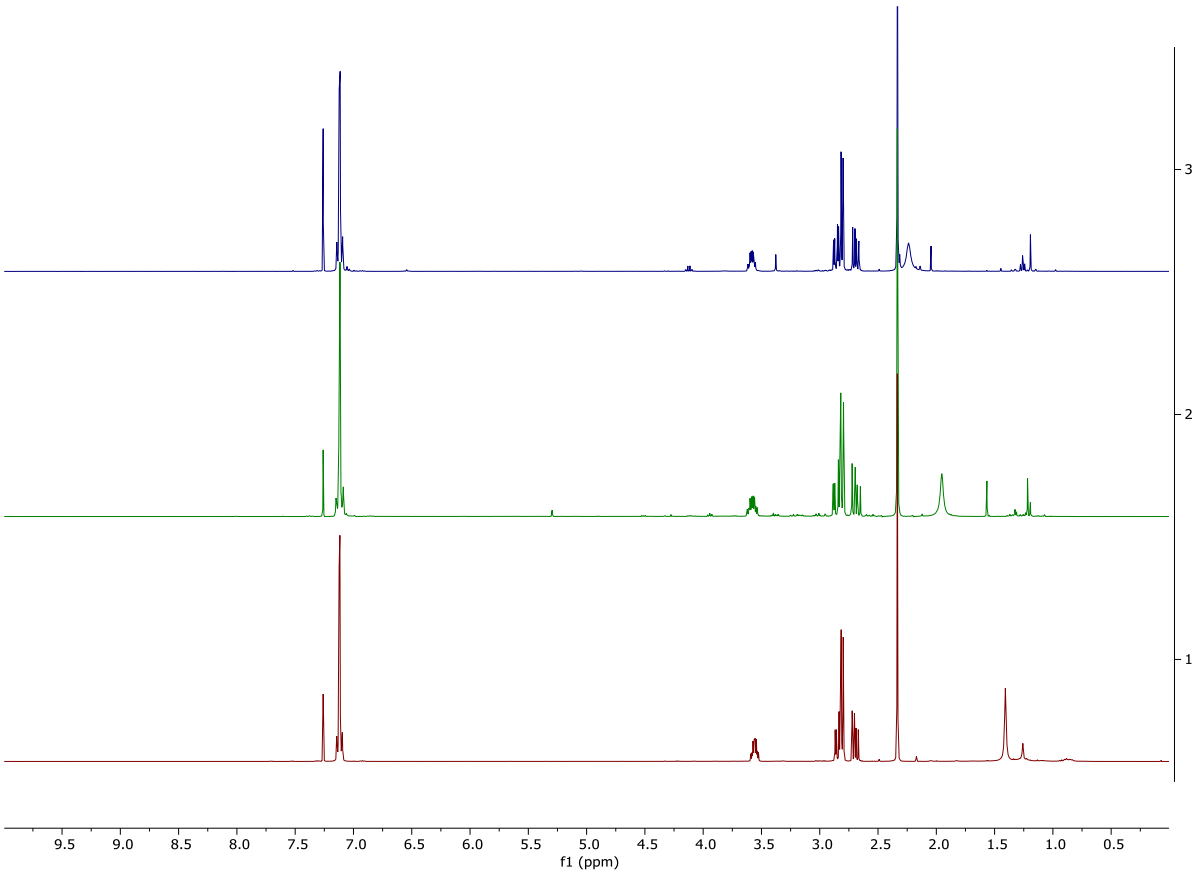
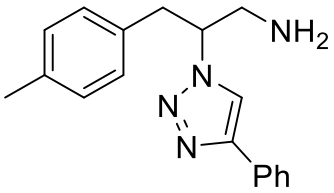


Figure 2: ^{1}H-NMR spectra of 2-azido-3-(p-tolyl)propan-1-amine after: purification B as HCl salt (above, blue), purification A via column chromatography (middle, green) and 0.5 mmol scale after column chromatography (below, red). The protons of the free amino group are interchangeable which causes its different chemical shifts in chloroform.

Derivatizations of 2-azido-3-(*p*-tolyl)propan-1-amine

2-(4-Phenyl-1*H*-1,2,3-triazol-1-yl)-3-(*p*-tolyl)propan-1-amine (3a)



2-Azido-3-(*p*-tolyl)propan-1-amine (104.1 mg, 0.547 mmol, 1.0 eq) was added to a 10 mL Schlenk-tube and evacuated and backfilled three times with a N_2-atmosphere. The azide was dissolved in a mixture of *tert*-butanol (1 mL) and water (0.5 mL). Phenylacetylene (66 µL, 0.60 mmol, 1.2 eq), $CuSO_4$ pentahydrate (25 mg, 0.10 mmol, 0.2 eq) and sodium ascorbate (40 mg, 0.20 mmol, 0.4 eq) were added subsequently. The reaction mixture was stirred at r.t. overnight. Then, 1 M NaOH (5 mL) was added, the reaction mixture was extracted with DCM (4x20 mL) and dried over Na_2SO_4. Purification via column chromatography (DCM:MeOH 100:0 to 97:3, NEt_3-deactivated SiO_2) yielded the title compound as an off-white solide (99.8 mg, 0.341 mmol, 62%).

^{1}H-NMR (500 MHz, CD_3CN): δ_H = 8.05 (s, 1H), 7.85 – 7.77 (m, 2H), 7.47 – 7.38 (m, 2H), 7.37 – 7.27 (m, 1H), 7.06 – 6.94 (m, 4H), 4.76 – 4.63 (m, 1H), 3.27 – 3.04 (m, 3H), 2.25 – 2.18 (m, 3H), 1.51 – 0.57 (m, br, 2H, NH2)

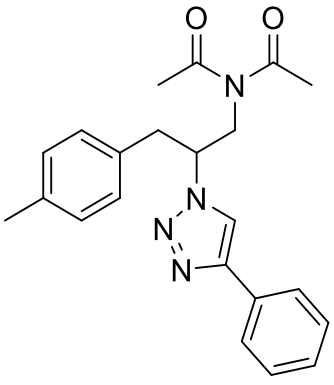
^{13}C-NMR (126 MHz, CD_3CN): δ_C = 147.6, 137.1, 135.5, 132.2, 130.0, 129.8, 129.8, 128.8, 126.2, 121.1, 39.0, 21.0.

HRMS (ESI+): calc. for $C_{18}H_{21}N_4$ $[M+H]^+$ 293.1761, found 293.1765.

***R*$_f$:** 0.24 (DCM:MeOH 9:1)

Due to discrepancy of the NMR spectra, amine **3a** was derivatized to its bis-acetal as followed:

***N*-Acetyl-*N*-(2-(4-phenyl-1*H*-1,2,3-triazol-1-yl)-3-(*p*-tolyl)propyl)acetamide(3a-Ac$_2$)**



2-(4-Phenyl-1*H*-1,2,3-triazol-1-yl)-3-(*p*-tolyl)propan-1-amine (19.2 mg, 0.0657 mmol, 1.0 eq) was dissolved in DCM (0.5 mL) and triethylamine (30 µL, 0.2150 mmol, 3.3 eq) and acetyl chloride (15 µL, 0.2100 mmol, 3.2 eq) were added subsequently. After stirring overnight, the reaction mixture was diluted with DCM (2 mL), washed with 1 M HCl, 1 M NaOH, brine (2 mL each), dried over Na_2SO_4 and

purified *via* column chromatography (EtOAc:hex 1:1, SiO_2). Bis-amide **3a**-Ac2 (15.4 mg, 0.0409 mmol, 62%) was obtained as a colorless solid.

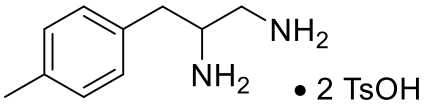
^{1}H-NMR (400 MHz, $CDCl_3$): δ_H = 7.75 – 7.67 (m, 2H), 7.43 – 7.28 (m, 4H), 7.04 – 6.97 (m, 2H), 6.96 – 6.89 (m, 2H), 5.01 – 4.87 (m, 1H), 4.36 – 4.13 (m, 2H), 3.40 (dd, *J* = 13.9, 10.0 Hz, 1H), 3.25 (dd, *J* = 13.9, 5.1 Hz, 1H), 2.26 (s, 6H), 2.25 (s, 3H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ_C = 173.6, 147.4, 136.9, 132.9, 130.4, 129.6, 128.9, 128.8, 128.4, 125.9, 121.5, 62.5, 49.8, 39.0, 26.1, 21.1.

HRMS (ESI+): calc. for $C_{22}H_{25}N_4O_2$ $[M+H]^+$ 377.1972, found 377.1970.

***R_f*:** 0.53 (EtOAc:hex 6:4)

3-(*p*-Tolyl)propane-1,2-diamine bis(4-methylbenzenesulfonate) (3b)



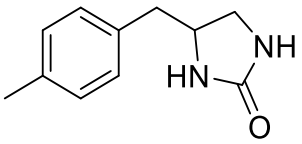
Analog to a procedure described by Xu and co-worker,[18] 2-azido-3-(*p*-tolyl)propan-1-amine (96.2 mg, 0.506 mmol, 1.0 eq) was dissolved in a mixture of THF/water (95:5; 3 mL). At 0 °C, PPh_3 (164 mg, 0.625 mmol, 1.2 eq) was added and the reaction mixture was allowed to warm to r.t. and stirred at 50 °C overnight. Then, the reaction mixture was quenched with 1 M NaOH (10 mL), extracted with DCM (4x20 mL), dried over Na_2SO_4 and concentrated. The resulting crude was suspended in a minimum amount of dry Et_2O, filtered over celite, diluted with dry Et_2O (total 5 mL) and added dropwise to a stirred solution of TsOH monohydrate (215 mg, 1.13 mmol, 2.2 eq) in dry Et_2O (10 mL). After 30 min, the precipitate was collected via vacuum filtration and air-dried. Bis *p*-toluenesulfonate diamine **3b** was obtained as off-white solid (193 mg, 0.379 mmol, 75%).

^{1}H-NMR (400 MHz, DMSO-d_6): δ_H = 7.95 (d, *J* = 25.8 Hz, 6H), 7.53 – 7.46 (m, 4H), 7.21 – 7.08 (m, 8H), 3.58 (s, 1H), 3.06 (dt, *J* = 12.8, 6.5 Hz, 1H), 2.98 – 2.80 (m, 3H), 2.29 (s, 9H).

^{13}C-NMR (101 MHz, DMSO-d_6): δ_C = 145.3, 137.9, 136.4, 132.1, 129.4, 129.3, 128.1, 125.5, 50.3, 35.5, 20.8, 20.7.

HRMS (ESI+): calc. for $C_{10}H_{17}N_2$ $[M+H]^+$ 400.2571, found 400.2569.

4-(4-Methylbenzyl)imidazolidin-2-one (3c)



Inspired by a protocol from Audisio *et* al.,[19] 2-azido-3-(*p*-tolyl)propan-1-amine (98.6 mg, 0.518 mmol, 1.0 eq) was added to a 10 mL Schlenk-tube, evacuated and backfilled three times with a CO_2-atmosphere and finally a CO_2-filled balloon was placed on top. Then, dry acetonitrile was freeze-pump-

[18] Yuan, Y.-A.; Lu, D.-F.; Chen, Y.-R.; Xu, H. *Angew. Chem. Int. Ed.* **2016**, *55*, 534-538.
[19] A. Del Vecchio *et al.*, *Angew. Chem. Int. Ed.* **2018**, *57*, 9744–9748.

thawed for three full cycles and eventually backfilled with a CO_2-atmosphere. 3.5 mL of this solvent was added to the amine. To the stirred reaction mixture, a solution of PMe_3 in 2-MeTHF (0.57 mL, 0.57 mmol, 1.1 eq) was added. After stirring for 30 min, the reaction mixture was concentrated and purified *via* column chromatography (EtOAc:hex 9:1 to DCM:MeOH 95:5, SiO_2) to yield the title compound (66.0 mg, 0.347 mmol, 67%) as an off-white solid.

Originally, the group of Audisio used terminal azides and PPh_2Me. Since they demonstrated, that the reaction is sensitive to sterically bulky phosphines, we opted for the less sterically congested PMe_3 for the transformation of secondary azides.

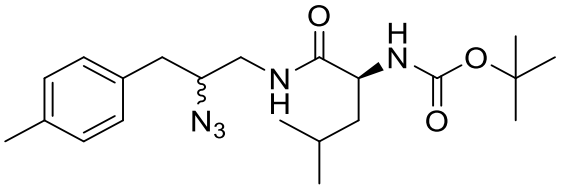
^{1}H-NMR (400 MHz, $CDCl_3$): δ_H = 7.16 – 7.01 (m, 4H), 5.27 (s, br, 1H), 4.99 (s, br, 1H), 4.02 – 3.89 (m, 1H), 3.54 (tt, *J* = 8.5, 1.1 Hz, 1H), 3.23 (ddd, *J* = 8.8, 6.0, 1.1 Hz, 1H), 2.80 (dd, *J* = 7.0, 2.4 Hz, 2H), 2.32 (s, 3H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ_C = 163.9, 136.5, 134.1, 129.5, 129.0, 54.4, 46.2, 41.5, 21.1.

HRMS (ESI+): calc. for $C_{11}H_{14}N_2NaO$ $[M+Na]^+$ 213.0998, found 213.0997.

***R*$_f$:** 0.59 (DCM:MeOH 9:1)

tert-Butyl ((2*S*)-1-((2-azido-3-(*p*-tolyl)propyl)amino)-4-methyl-1-oxopentan-2-yl)carbamate (3d)



Following a protocol from Zhang and Ye,[20] 2-azido-3-(*p*-tolyl)propan-1-amine (96.8 mg, 0.509 mmol, 1.0 eq) was dissolved under nitrogen in dry THF (3 mL). Subsequently, *N*-Boc protected Leucin (139 mg, 0.601 mmol, 1.2 eq), HBTU[21] (247 mg, 0.651 mmol, 1.3 eq) and DIPEA (221 mL, 1.24 mmol, 2.4 eq) were added and the reaction mixture was stirred overnight. Then, the reaction mixture was diluted with EtOAc (10 mL) and washed with a saturated solution of NH_4Cl (2 mL), 1M NaOH (2 mL), brine (2 mL) before being dried over Na_2SO_4. Purification via column chromatography (EtOAc:hex 2:8 to 3:7) yielded a 1:1 mixture of both diastereomers of the title compound as a yellow oil (138 mg, 0.356 mmol, 70%).

^{1}H-NMR (400 MHz, $CDCl_3$): δ_H = 7.17 – 7.05 (m, 4H), 6.42 (d, *J* = 21.0 Hz, 1H), 4.79 (s, 1H), 4.07 (s, 1H), 3.75 (ddt, *J* = 12.1, 10.2, 4.0 Hz, 1H), 3.59 – 3.48 (m, 1H), 3.13 (dddd, *J* = 13.8, 8.0, 5.7, 3.7 Hz, 1H), 2.89 – 2.70 (m, 2H), 2.33 (s, 3H), 1.74 – 1.63 (m, 2H), 1.48 (s, 1H), 1.44 (d, *J* = 1.9 Hz, 9H), 0.96 – 0.90 (m, 6H).

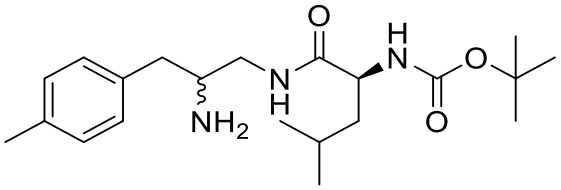
^{13}C-NMR (101 MHz, $CDCl_3$): δ_C = 172.9, 155.8, 136.8, 133.6, 129.6, 129.3, 80.4, 63.5, 63.4, 53.3, 42.8, 38.3, 38.3, 28.4, 24.9, 23.07, 23.01, 21.2.

HRMS (ESI+): calc. for $C_{21}H_{34}N_5O_3$ $[M+H]^+$ 404.2656, found 404.2655.

***R*$_f$:** 0.32 (EtOAc:hex 1:2)

[20] Zhang, L.; Ye, X.-S. *Chin. J. Chem.* **2017**, *35*, 1001-1008.
[21] 3-[Bis(dimethylamino)methyliumyl]-3*H*-benzotriazol-1-oxide hexafluorophosphate.

***tert*-butyl ((2*S*)-1-((2-amino-3-(*p*-tolyl)propyl)amino)-4-methyl-1-oxopentan-2-yl)carbamate (3e)**



Azide (b) (83.8 mg, 0.208 mmol, 1.0 eq) was dissolved in a mixture of THF/water (95:5; 2.5 mL). At 0 °C, PMe_3 (1 M in 2-MeTHF, 0.70 mL, 3.4 eq) was added and the reaction mixture was allowed to warm to r.t. and stirred overnight. Then, the reaction mixture was quenched with water (5 mL) and 1 M NaOH (5 mL) and was extracted with DCM (3x20 mL). Drying over Na_2SO_4 and purification *via* column chromatography (DCM:MeOH 100:0 to 96:4, NEt_3-deactivated SiO_2) yielded a 1:1 mixture of both diastereomers of amine **3e** (61.8 mg, 0.164 mmol, 79%) as a viscous yellow oil.

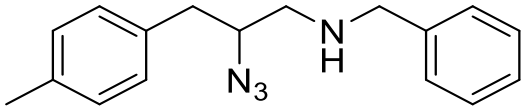
^{1}H-NMR (400 MHz, $CDCl_3$): δ_H = 7.15 – 7.02 (m, 4H), 6.61 – 6.52 (m, 1H), 4.91 (s, br, 1H), 4.06 (s, br, 1H), 3.47 – 3.36 (m, 1H), 3.07 (dddd, *J* = 18.1, 12.9, 9.0, 6.6 Hz, 2H), 2.75 (dd, *J* = 13.5, 4.6 Hz, 1H), 2.46 (ddd, *J* = 13.6, 8.1, 1.6 Hz, 1H), 2.32 (s, 3H), 1.72 – 1.61 (m, 2H), 1.52 – 1.46 (m, 1H), 1.43 (s, 9H), 1.29 – 1.20 (m, 2H), 0.93 (ddd, *J* = 6.1, 3.5, 2.5 Hz, 6H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ_C = 172.8, 136.2, 135.4, 135.4, 129.4, 129.3, 129.2, 80.2, 53.5, 52.4, 52.3, 45.4, 42.0, 41.5, 28.5, 24.9, 23.1, 22.2, 21.1.

HRMS (ESI+): calc. for $C_{21}H_{35}N_3NaO_3$ $[M+Na]^+$ 400.2571, found 400.2569.

***R*$_f$:** 0.33 (DCM:MeOH 9:1)

2-Azido-*N*-benzyl-3-(*p*-tolyl)propan-1-amine (3f)



2-Azido-3-(*p*-tolyl)propan-1-amine (96.8 mg, 0.509 mmol, 1.0 eq) was dissolved under nitrogen in dry 1,2-dichloroethane (3 mL). Benzaldehyde (61 μL, 0.598 mmol, 1.2 eq), acetic acid (57 μL, 1.00 mmol, 2.0 eq) and sodium tris(acetoxy)borohydride (148 mg, 0.698 mmol, 1.4 eq) were added subsequently and the reaction mixture was stirred overnight. Then, the reaction mixture was diluted with DCM (10 mL), washed with a saturated solution of $NaHCO_3$ (5 mL) which was extracted with DCM (3x5 mL). The combined organic layers were dried over Na_2SO_4, concentrated and purified via column chromatography (EtOAc:hex 2:8 to 3:7) to yield the title compound as a yellow oil (44.7 mg, 0.159 mmol, 31%).

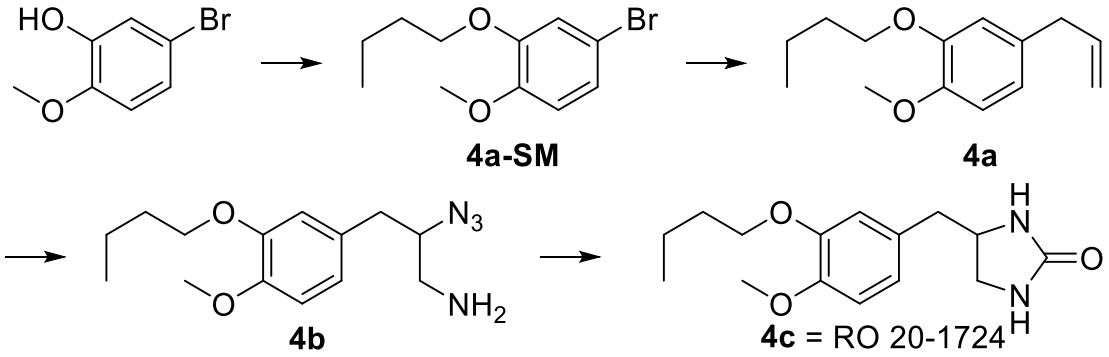
^{1}H-NMR (400 MHz, $CDCl_3$): δ_H = 7.39 – 7.26 (m, 5H), 7.15 – 7.06 (m, 4H), 3.85 – 3.74 (m, 2H), 3.74 – 3.67 (m, 1H), 2.82 (dd, *J* = 7.0, 5.2 Hz, 2H), 2.79 – 2.63 (m, 2H), 2.34 (s, 3H), 1.62 (s, 1H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ_C = 140.2, 136.5, 134.4, 129.4, 129.3, 128.6, 128.2, 127.2, 64.2, 53.9, 52.4, 38.6, 21.2.

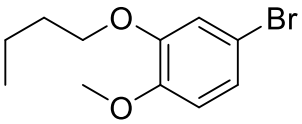
HRMS (ESI+): calc. for $C_{17}H_{21}N_4$ $[M+H]^+$ 281.1761, found 281.1766.

***R*$_f$:** 0.42 (EtOAC:hex 1:2)

Synthesis of RO 20-1724



4-Bromo-2-butoxy-1-methoxybenzene (4a-SM)



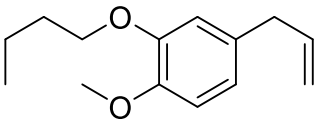
5-bromo-2-methoxyphenol (5.16 g, 25.4 mmol, 1.0 eq) was dissolved in DMF (100 mL). K_2CO_3 (10.4 g, 75.2 mmol, 3.0 eq) and *n*BuBr (3.2 mL, 29.9 mmol, 1.2 eq) were added subsequently. The reaction mixture was stirred at 80 °C for 24 h. Then, the reaction mixture was let to go to r.t. and the formed precipitate was filtered off. Water (400 mL) was added and the mixture was extracted with Et_2O (4x50 mL). The combined organic layers were washed with water (20 mL) and brine (2x30 mL) and dried over Na_2SO_4. Concentration under reduced pressure afforded spectroscopically pure title compound **4a-SM** as a yellow oil (6.42 g, 24.8 mmol, 97%) and was used in the next step without further purification.

^{1}H-NMR (400 MHz, $CDCl_3$): δ_H = 7.03 – 6.97 (m, 2H), 6.73 (d, *J* = 8.5 Hz, 1H), 3.99 (t, *J* = 6.8 Hz, 2H), 3.83 (s, 3H), 1.82 (ddt, *J* = 9.0, 7.9, 6.6 Hz, 2H), 1.56 – 1.43 (m, 2H), 0.98 (t, *J* = 7.4 Hz, 3H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ_C = 149.6, 148.9, 123.4, 116.4, 113.1, 112.8, 69.1, 56.3, 31.2, 19.3, 14.0.

HRMS (ESI+): calc. for $C_{11}H_{15}BrNaO_2$ $[M+Na]^+$ 281.0148, found 281.0145.

4-Allyl-2-butoxy-1-methoxybenzene (4a)



A three-necked flask with a dropping funnel, a reflux condenser and a connection to a Schlenk-line, was flame-dried for three times and flushed with nitrogen. Then, Magnesium turnings (678 mg, 27.9 mmol, 1.1 eq) and a pinch of iodine were added. Under static vacuum, the reaction was gently warmed with a heatgun, until purple vapors were visible. The flask was allowed to cool to r.t. and dry THF was added (50 mL). Aryl bromide a (6.39 g, 24.7 mmol, 1.0 eq) was dissolved in dry THF (40 mL) and about 1/10 was added to the reaction mixture. After the Grignard started, the remaining aryl bromide was added dropwise and the reaction mixture was stirred at 50 °C for 5 h. Then, the reaction was let to go to r.t. again and a solution of allyl bromide (4.3 mL, 49.8 mmol, 2.0 eq, freshly distilled over $CaCl_2$) in dry THF (20 mL) was added dropwise to the reaction mixture. The reaction mixture was again heated to 50 °C and stirred overnight. Then, the reaction was quenched at r.t. with an aqueous

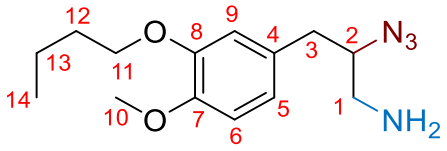
saturated solution of NH_4Cl (100 mL). The resulting solution was extracted with EtOAc (3x100 mL), the combined organic layers washed with brine (50 mL), dried over Na_2SO_4 and concentrated under reduced pressure. A dark-yellow liquid was obtained which proved to be a mixture between title compound **4a** (3.92 g, 17.7 mmol, 64%) and starting material **4a-SM** with the product in 77 wt.% (determined by ^{1}H-NMR). This mixture was subjected to the following reaction without further purification.

^{1}H-NMR (400 MHz, $CDCl_3$): δ_H = 6.94 – 6.66 (m, 3H), 6.04 – 5.84 (m, 1H), 5.14 – 4.94 (m, 2H), 4.01 (t, *J* = 6.8 Hz, 3H), 3.85 (d, *J* = 9.8 Hz, 3H), 3.32 (dtd, *J* = 6.7, 1.4, 0.7 Hz, 2H), 1.90 – 1.74 (m, 2H), 1.58 – 1.41 (m, 2H), 0.98 (t, *J* = 7.4 Hz, 3H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ_C = 148.7, 148.0, 137.9, 132.8, 120.5, 115.7, 113.8, 112.0, 68.8, 56.3, 39.9, 31.4, 19.4, 14.0.

HRMS (ESI+): calc. for $C_{14}H_{20}NaO_2$ $[M+Na]^+$ 243.1356, found 243.1353.

2-Azido-3-(3-butoxy-4-methoxyphenyl)propan-1-amine (4b)



To a 100 mL Schlenk-flask under an inert atmosphere, $Fe(OTf)_2$ (300 mg, 0.848 mmol, 5 mol%), dry MeOH (45 mL) and alkene (b) (4.89 g, 77 wt.% purity, 17.1 mmol, 1.0 eq) were added subsequently. Aminating reagent $PivONH_3OTf$ (11.3 g, 42.3 mmol, 2.5 eq) was added and the reaction mixture stirred for 16 h at r.t. Then, 1 M aqueous NaOH (100 mL) was added to the reaction mixture which was then extracted with EtOAC (4x100 mL), washed with brine (50 mL), dried over Na_2SO_4 and concentrated under reduced pressure. Purification by column chromatography (DCM:MeOH 100:0 to 95:5, NEt_3-deactivated SiO_2) afforded the title compound (1.45 g, 5.21 mmol, 30%) as a brown oil.

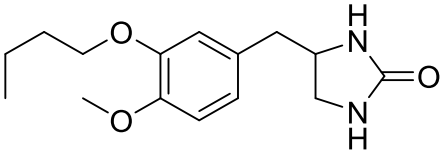
^{1}H-NMR (400 MHz, $CDCl_3$): δ_H = 6.87 – 6.63 (m, 3H, H5+H6+H9), 4.01 (t, *J* = 6.8, 2H, H11), 3.85 (s, 3H, H10), 3.60 – 3.48 (m, 1H, H2), 2.91 – 2.61 (m, 4H, H1+H3), 1.90 – 1.74 (m, 2H, H12), 1.59 – 1.40 (m, 2H, H13), 1.39 – 1.13 (m, 2H, NH_2), 0.98 (t, *J* = 7.4 Hz, 3H, H14).

^{13}C-NMR (101 MHz, $CDCl_3$): δ_C = 148.7 (C7/C8), 148.6 (C8/C7), 130.0 (C4), 121.4 (C5/C6/C9), 114.3 (C6/C9/C5), 112.0 (C9/C5/C6), 69.0 (C11), 67.2 (C2), 56.2 (C10), 45.6 (C1/C3), 38.2 (C3/C1), 31.4 (C12), 19.4 (C13), 14.0 (C14).

HRMS (ESI+): calc. for $C_{14}H_{23}N_4O_2$ $[M+H]^+$ 279.1816, found 279.1835.

***R_f*:** 0.26 (DCM:MeOH 9:1)

4-(3-Butoxy-4-methoxybenzyl)imidazolidin-2-one (4c)



Inspired by a protocol from Audisio *et* al.,[22] 2-azido-3-(3-butoxy-4-methoxyphenyl)propan-1-amine (c) (198.2 mg, 0.712 mmol, 1.0 eq) was added to a 10 mL Schlenk-tube, evacuated and backfilled three times with a CO_2-atmosphere and finally a CO_2-filled balloon was placed on top. Then, dry acetonitrile was freeze-pump-thawed for three full cycles and eventually backfilled with a CO_2-atmosphere. 3.5 mL of this solvent was added to the amine. To the stirred reaction mixture, a solution of PMe_3 in 2-MeTHF (0.78 mL, 0.78 mmol, 1.1 eq) was added. After stirring for 30 min, the reaction mixture was concentrated and purified via column chromatography (EtOAc:hex 9:1 to DCM:MeOH 95:5, SiO_2) to yield the title compound RO 20-1724 (125.3 mg, 0.450 mmol, 63%) as a brown solid.

Originally, the group of Audisio used terminal azides and PPh_2Me. Since they demonstrated, that the reaction is sensitive to sterically bulky phosphines, we opted for the less sterically congested PMe_3 for the transformation of secondary azides.

^{1}H-NMR (400 MHz, $CDCl_3$): δ_H = 6.83 – 6.79 (m, 1H), 6.73 – 6.68 (m, 2H), 4.61 (d, *J* = 17.3 Hz, 2H), 4.02 – 3.96 (m, 2H), 3.84 (s, 3H), 3.82 – 3.78 (m, 1H), 3.58 (td, *J* = 8.5, 0.9 Hz, 1H), 3.29 – 3.18 (m, 1H), 2.77 (dd, *J* = 7.0, 2.2 Hz, 2H), 1.86 – 1.76 (m, 2H), 1.56 – 1.45 (m, 2H), 0.98 (t, *J* = 7.4 Hz, 3H).

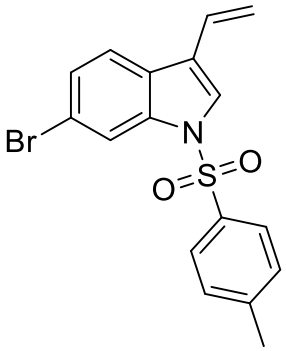
^{13}C-NMR (101 MHz, $CDCl_3$): δ_C = 163.4, 149.0, 148.6, 129.7, 121.2, 114.0, 112.2, 69.0, 56.2, 54.5, 46.2, 41.6, 31.4, 19.4, 14.0.

HRMS (ESI+): calc. for $C_{15}H_{22}N_2NaO_3$ $[M+Na]^+$ 301.1523, found 301.1524.

***R_f*:** 0.54 (DCM:MeOH 9:1)

Synthesis of an intermediate for the formal total synthesis of (±)-hamacanthin B

6-Bromo-1-tosyl-3-vinyl-1*H*-indole (4e)



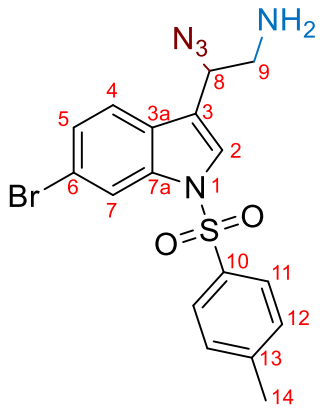
The title compound was prepared from *6-bromo-1H-indole-3-carbaldehyde* according to a literature procedure.[23] Its characterization data were matching the ones found in literature.

^{1}H-NMR (400 MHz, $CDCl_3$): δ_H = 8.18 (d, *J* = 1.7 Hz, 1H), 7.81 – 7.72 (m, 2H), 7.61 – 7.53 (m, 2H), 7.37 (dd, *J* = 8.5, 1.8 Hz, 1H), 7.28 – 7.20 (m, 2H), 6.71 (ddd, *J* = 17.8, 11.3, 0.7 Hz, 1H), 5.75 (dd, *J* = 17.8, 1.0 Hz, 1H), 5.35 (dd, *J* = 11.4, 1.0 Hz, 1H), 2.34 (s, 3H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ_C = 145.5, 136.2, 135.0, 130.2, 129.9, 127.9, 127.1, 127.0, 124.4, 121.6, 120.8, 118.7, 116.9, 116.0, 21.7.

[22] A. Del Vecchio *et al. Angew. Chem. Int. Ed.* **2018**, *57*, 9744–9748.
[23] Jiang, B.; Yang, C.-G.; Wang, J. *J. Org. Chem.* **2001**, *66*, 4865-4869.

2-Azido-2-(6-bromo-1-tosyl-1*H*-indol-3-yl)ethan-1-amine (4f)



Following the general procedure for amino azidation on a lower concentration (0.26 mmol scale, 0.2 M) using starting material *6-bromo-1H-indole-3-carbaldehyde* (96.0 mg, 0.255 mmol) and purified by silica gel column chromatography (DCM:MeOH 100:0 to 98:2, NEt_3-deactivated SiO_2) provided the title compound as an orange oil (35.1 mg, 0.0808 mmol, 32%).[24] Further, unreacted starting material could be recovered from the column chromatography (59.4 mg, 0.158 mmol, 62%). Similar to the run with *N*-Boc protected indole **2k**, an amino-methoxy ether could be observed as by-product.

^{1}H-NMR (400 MHz, $CDCl_3$): δ_H = 8.17 (dd, *J* = 1.7, 0.5 Hz, 1H, H7), 7.79 – 7.73 (m, 2H, H11), 7.57 (d, *J* = 0.8 Hz, 1H, H2), 7.46 – 7.43 (m, 1H, H4), 7.38 (dd, *J* = 8.5, 1.7 Hz, 1H, H5), 7.28 – 7.25 (m, 2H, H12), 4.70 – 4.65 (m, 1H, H8), 3.09 – 3.05 (m, 2H, H9), 2.36 (s, 3H, H14), 1.39 – 1.22 (m, 2H, NH_2).

^{13}C-NMR (101 MHz, $CDCl_3$): δ_C = 145.8 (C13), 136.2 (C7a), 134.7 (C10), 130.3 (C12), 127.6 (C3a), 127.1 (C5), 127.0 (C11), 124.8 (C2), 121.2 (C4), 119.3 (C6), 118.9 (C3), 117.1 (C7), 61.8 (C8), 46.2 (C9), 21.8 (C14).

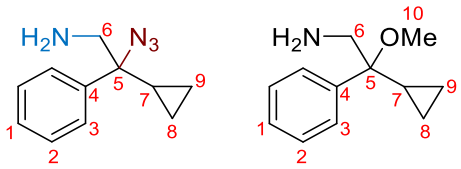
HRMS (ESI+): calc. for $C_{17}H_{16}BrN_5NaO_2S$ $[M+Na]^+$ 456.0100, found 456.0096.

[24] Compared to the *N*-Boc protected 3-vinyl indole, this *N*-Ts protected version showed way lower solubility in methanol which is probably accounting for the lower yield.

Experimental procedures for mechanistic experiments

Mechanistic experiments

2-Azido-2-cyclopropyl-2-phenylethan-1-amine (5b) and **2-cyclopropyl-2-methoxy-2-phenylethan-1-amine (5c)**



Following the general procedure for amino azidation using *(1-cyclopropylvinyl)benzene* **5a** (73.0 mg, 0.50 mmol) and purified by silica gel column chromatography (DCM:MeOH 100:0 to 99:1 to 98:2, NEt_3-deactivated SiO_2) provided the title compounds as colorless oils (14.2 mg, 0.070 mmol, 14%; 43.2 mg, 0.226 mmol, 45%).

Azide:

^{1}H-NMR (400 MHz, $CDCl_3$): δ_H = 7.47 – 7.27 (m, 5H, H1+2+3), 3.14 (d, *J* = 3.3 Hz, 2H, H6), 1.33 (tt, *J* = 8.4, 5.4 Hz, 1H, H7), 0.68 – 0.43 (m, 3H, H8+9), 0.37 (dtd, *J* = 9.6, 5.4, 4.0 Hz, 1H, H8/9).

^{13}C-NMR (101 MHz, $CDCl_3$): δ_C = 139.5 (C4), 128.7 (C3), 127.9 (C1), 127.1 (C2), 71.0 (C5), 50.5 (C6), 18.1 (C7), 1.4 (C8), 1.2 (C9).

HRMS (ESI+): calc. for $C_{11}H_{15}N_4$ $[M+H]^+$ 203.1291, found 203.1291.

***R_f*:** 0.24 (DCM:MeOH 19:1)

Methoxy:

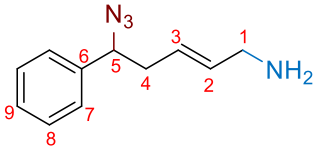
^{1}H-NMR (400 MHz, $CDCl_3$): δ_H = 7.42 – 7.30 (m, 4H, H2+3), 7.28 – 7.20 (m, 1H, H1), 3.26 (s, 3H, H10), 3.01 – 2.77 (m, 2H, H6), 1.31 (s, br, 2H, NH_2), 1.18 (tt, *J* = 8.5, 5.6 Hz, 1H, H7), 0.67 – 0.37 (m, 3H, H8+9), 0.31 (dtd, *J* = 9.4, 5.8, 4.4 Hz, 1H, H8).

^{13}C-NMR (101 MHz, $CDCl_3$): δ_C = 141.9 (C4), 128.1 (C3), 127.1 (C2), 127.1 (C1), 80.6 (C5), 50.4 (C10), 46.7 (C6), 17.5 (C7), 2.3 (C8), 1.0 (C9).

HRMS (ESI+): calc. for $C_{12}H_{18}NO$ $[M+H]^+$ 192.1383, found 192.1387.

***R_f*:** 0.08 (DCM:MeOH 19:1)

(*E*)-5-Azido-5-phenylpent-2-en-1-amine (5e)



Following the general procedure for amino azidation using *((1R*,2S*)-2-vinylcyclopropyl)benzene* **5d** (71.3 mg, 0.50 mmol) and purified by silica gel column chromatography (DCM:MeOH 100:0 to 98:2 to 95:5, NEt_3-deactivated SiO_2) provided the title compound as a colorless oil (51.1 mg, 0.253 mmol, 51%).

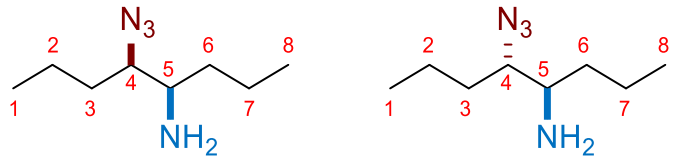
^{1}H-NMR (400 MHz, $CDCl_3$): δ_H = 7.39 – 7.23 (m, 5H, H7+8+9), 5.65 (dtt, *J* = 15.3, 5.7, 1.2 Hz, 1H, H2), 5.48 (dtt, *J* = 15.3, 6.9, 1.5 Hz, 1H, H3), 4.45 (dd, *J* = 8.1, 6.3 Hz, 1H, H5), 3.22 (dd, *J* = 5.7, 1.3 Hz, 2H, H1), 2.67 – 2.35 (m, 2H, H4), 1.39 (s, br, 2H, NH_2).

^{13}C-NMR (101 MHz, $CDCl_3$): δ_C = 139.3 (C6), 135.2 (C2), 128.8 (C8), 128.3 (C9), 126.9 (C7), 125.3 (C3), 66.1 (C5), 43.9 (C1), 39.3 (C4).

HRMS (ESI+): calc. for $C_{11}H_{15}N_4$ $[M+H]^+$ 203.1291, found 203.1293.

***R_f*:** 0.10 (DCM:MeOH 9:1)

5-Azidooctan-4-amine (5g)



major minor

Following the general procedure for amino azidation using *(Z)-oct-4-ene* (57.6 mg, 0.513 mmol) and purified by silica gel column chromatography (DCM:MeOH 100:0 to 97:3, NEt_3-deactivated SiO_2) provided the title compound as a colorless oil (34.2 mg, 0.201 mmol, 39%).

Analysis of a crude sample via GC-FID[25] revealed a diastereoisomeric ratio of 28:72 cis:trans-product. Analysis of a purified sample showed via ^{1}H-NMR and GC-FID the same ratio. To determine the stereoconfiguration, the mixture was derivatized to the known para-nitrobenzamide.

A comparable run using *(E)-oct-4-ene* resulted in a diastereoisomeric mixture with a product ratio of 21:79 cis:trans.

HRMS (ESI+): calc. for $C_{11}H_{15}N_4$ $[M+H]^+$ 203.1291, found 203.1293.

***R_f*:** 0.35 (DCM:MeOH 9:1)

For the major trans diastereoisomer:

^{1}H-NMR (400 MHz, $CDCl_3$): δ_H = 3.20 (dt, *J* = 8.9, 4.4 Hz, 1H, H4), 2.72 (dt, *J* = 7.9, 4.2 Hz, 1H, H5), 1.64 – 1.24 (m, 10H), 1.01 – 0.90 (m, 6H, H1+H8)

^{13}C-NMR (101 MHz, $CDCl_3$): δ_C = 67.9 (C4), 54.3 (C5), 37.3 (C3/C6), 33.6 (C6/C3), 19.8 (C2/C7), 19.6 (C7/C2), 14.2 (C1+C8).

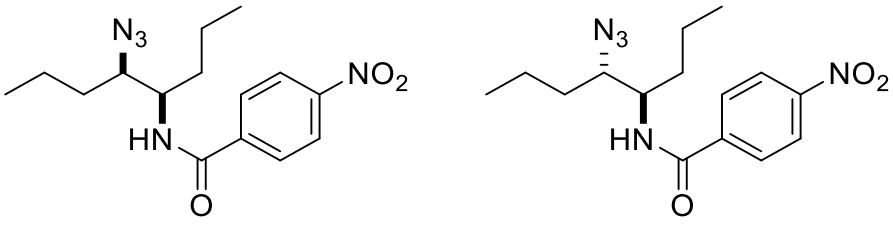
For the minor cis diastereoisomer:

^{1}H-NMR (400 MHz, $CDCl_3$): δ_H = 3.26 (dt, *J* = 8.9, 4.5 Hz, 1H, H4), 2.83 (dt, *J* = 8.1, 4.0 Hz, 1H, H5), 1.64 – 1.24 (m, 10H), 1.01 – 0.90 (m, 6H, H1+H8).

^{13}C-NMR (101 MHz, $CDCl_3$): δ_C = 68.7 (C4), 54.6 (C5), 35.4 (C3/C6), 32.1 (C6/C3), 20.0 (C2/C7), 19.7 (C7/C2), 14.1 (C1+C8).

[25] GC-FID 2025 from SHIMADZU with hydrogen as carrier gas and an OPTIMA® 5 Amine column from Macherey-Nagel was used for the analysis. An identical response factor was assumed for both isomers.

***N*-(5-Azidooctan-4-yl)-4-nitrobenzamide (5g-amide)**



5-Azidooctan-4-amine (16.6 mg, 0.10 mmol, 1.0 eq) was dissolved in DCM (0.5 mL) and triethylamine (42 μL, 0.30 mmol, 3.0 eq) and *p*-NO_2-benzoylchloride (47 mg, 0.25 mmol, 2.5 eq) were added subsequently. After stirring overnight, the reaction mixture was diluted with DCM (2 mL), washed with 1 M HCl, 1 M NaOH, brine (2 mL each), dried over Na_2SO_4 and purified *via* column chromatography (4:1 EtOAc:hex, SiO_2) to yield a mixture of diastereoisomers as a yellow oil (19.5 mg, 0.061 mmol, 60%). Comparing spectroscopic data with literature reveals the reported trans product as the major component in a 2.7:1 ratio compared to the other diastereoisomer.[26]

For the major trans product:

^{1}H-NMR (400 MHz, $CDCl_3$): δ_H = 8.29 (d, *J* = 8.7 Hz, 2H), 7.93 (d, *J* = 8.7 Hz, 2H), 6.12 (d, *J* = 9.6 Hz, 1H), 4.35 – 4.28 (m, 1H), 3.59 (ddd, *J* = 8.3, 6.4, 2.0 Hz, 1H), 1.67 – 1.38 (m, 8H), 1.02 – 0.92 (m, 6H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ_C = 165.4, 149.8, 140.1, 128.3, 124.0, 66.1, 52.0, 35.9, 34.5, 19.7, 19.5, 14.0, 14.0.

For the minor cis product:

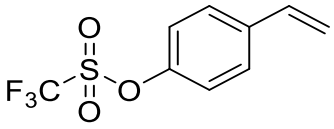
^{1}H-NMR (400 MHz, $CDCl_3$): δ_H = 8.32 – 8.27 (m, 2H), 7.95 – 7.91 (m, 2H), 6.22 (d, *J* = 8.9 Hz, 1H), 4.28 – 4.23 (m, 1H), 3.66 (ddd, *J* = 8.6, 4.9, 3.2 Hz, 1H), 1.67 – 1.38 (m, 8H), 1.02 – 0.92 (m, 6H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ_C = 165.3, 140.1, 132.4, 128.3, 124.0, 66.1, 52.9, 33.5, 30.5, 20.0, 19.5, 14.0, 14.0.

[26] Wu, B.; Gallucci, J. C.; Parquette, J. R.; RajanBabu, T.V. *Angew. Chem. Int. Ed.* **2009**, *48*, 1126–1129.

Synthesis of starting materials

4-Vinylphenyl trifluoromethanesulfonate (1e)

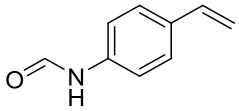


The title compound was prepared from *4-hydroxybenzaldehyde* according to a literature procedure.[27] Its characterization data were matching the ones found in literature.

^{1}H-NMR (400 MHz, $CDCl_3$): δ_H = 7.61 – 7.38 (m, 2H), 7.31 – 7.12 (m, 2H), 6.71 (dd, *J* = 17.6, 10.9 Hz, 1H), 5.77 (dd, *J* = 17.6, 0.6 Hz, 1H), 5.35 (dd, *J* = 10.9, 0.6 Hz, 1H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ_C = 149.0, 138.1, 135.2, 128.0, 121.6, 118.9 (q, *J* = 320.8 Hz), 116.2.

***N*-(4-Vinylphenyl)formamide (1f)**



According to a patent from Merck,[28] to 4-amino styrene (596 mg, 5.00 mmol, 1.00 eq) was added ethyl formate (1.2 mL, 15 mmol, 3.0 eq) and the reaction mixture stirred for 24 h at 50 °C. The reaction mixture was concentrated, before another portion of ethyl formate (1.2 mL, 15 mmol, 3.0 eq) was added and the reaction mixture stirred at 65 °C for 24 h. Then, the reaction mixture was concentrated again and the crude purified via column chromatography (EtOAc:hex 1:3, SiO_2) to yield *N*-(4-vinylphenyl)formamide **1f** as a colorless solid (612 mg, 4.16 mmol, 83%).

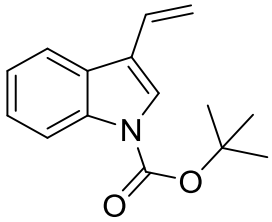
^{1}H-NMR (400 MHz, $CDCl_3$): δ_H = 8.70 (d, *J* = 11.4 Hz) and 8.38 (d, *J* = 1.8 Hz) rotameric to 1H, 7.81 (s, br) and 7.21 (s, br) rotameric to 1H, 7.53 – 7.48 (m, 1H), 7.44 – 7.33 (m, 2H), 7.08 – 7.00 (m, 1H), 6.68 (ddd, *J* = 17.6, 10.9, 2.2 Hz, 1H), 5.70 (ddd, *J* = 17.5, 5.3, 0.8 Hz, 1H), 5.28 – 5.17 (m, 1H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ_C = 162.2 and 158.8 rotameric, 136.4, 136.1 and 135.8 rotameric, 135.0 and 134.5 rotameric, 127.7, 127.1, 120.0, 119.0, 114.0 and 113.6 rotameric.

HRMS (ESI+): calc. for $C_9H_{10}NO$ $[M+H]^+$ 148.0757, found 148.0759.

***R*$_f$:** 0.42 (EtOAc:hex 1:1)

***tert*-Butyl 3-vinyl-1*H*-indole-1-carboxylate (1k)**



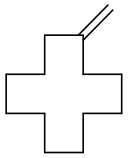
[27] R. Gilmour *et al.*, *Org. Lett.* **2018**, *20*, 8073-8076.
[28] WO2009/152027, 2009

The title compound was prepared from 1*H*-indole-3-carbaldehyde in a two-step procedure, starting with Boc-protection of the indole.[29,30] Spectroscopic data matches the literature.

^{1}H-NMR (400 MHz, $CDCl_3$): δ_H = 8.17 (d, *J* = 8.2 Hz, 1H), 7.80 (ddd, *J* = 7.7, 1.4, 0.7 Hz, 1H), 7.63 (s, 1H), 7.37 – 7.26 (m, 2H), 6.82 (ddd, *J* = 17.8, 11.3, 0.7 Hz, 1H), 5.82 (ddd, *J* = 17.8, 1.3, 0.5 Hz, 1H), 5.35 – 5.28 (m, 1H), 1.68 (s, 9H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ_C = 149.8, 136.1, 128.8, 128.3, 124.8, 124.1, 123.0, 120.1, 119.4, 115.5, 114.5, 84.0, 28.3.

Methylenecyclododecane (1p)



A 250 mL Schlenk-flask was flame-dried and flushed with N_2. Under N_2 it was charged with methyltriphenylphosphonium bromide (9.783 g, 27.386 mmol, 1.00 equiv.) and anhydrous THF (50 mL). The resulting suspension was cooled to −78 °C before *n*-BuLi (1.6 M in *n*-hexane; 18.00 mL, 28.800 mmol, 1.05 equiv.) was slowly added under stirring. The reaction mixture was allowed to warm to room temperature over 30 minutes before cyclododecanone (5.091 g, 27.596 mmol, 1.01 equiv.) was added. After stirring at room temperature for 12 hours, the reaction mixture was quenched by the addition of saturated aqueous NH_4Cl (50 mL). The aqueous reaction mixture was extracted with DCM (3x 50 mL). The combined organic layers were washed with brine, dried over $MgSO_4$ and concentrated under reduced pressure. The crude product was purified by flash column chromatography (SiO_2; Hex). The title compound was obtained as a colorless liquid (1.298 g, 7.198 mmol, 26%).

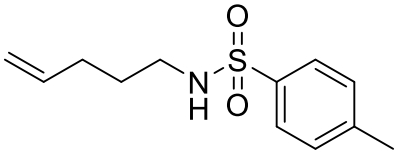
^{1}H-NMR (400 MHz, $CDCl_3$): δ_H = 4.80 – 4.78 (m, 2H), 2.08 – 2.02 (m, 4H), 1.54 – 1.47 (m, 4H), 1.34 – 1.25 (m, 14H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ_C = 147.7, 110.5, 33.2, 24.6, 24.3, 23.8, 23.4, 22.7.

HRMS (EI+): calc. for $C_{13}H_{24}$ $[M]^+$ 180.1873, found 180.1872.

***R_f*:** 0.90 (Hex)

4-Methyl-*N*-(pent-4-en-1-yl)benzenesulfonamide (1t)



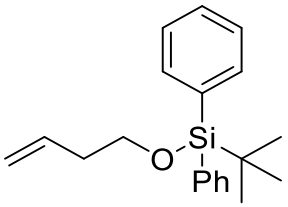
[29] J. Seok Lee, J. Shin, H.-S. Lee, H. Jae Shin, Y.-J. Lee, *Bull. Korean Chem. Soc.* **2013**, *34*, 357–357.
[30] J. Waser, B. Gaspar, H. Nambu, E. M. Carreira, *J. Am. Chem. Soc.* **2006**, *128*, 11693–11712.

The title compound was prepared from *5-bromopentene* according to a literature procedure.[31] Its characterization data were matching the ones found in literature.

^{1}H-NMR (400 MHz, $CDCl_3$): δ_H = 7.89 – 7.64 (m, 2H), 7.33 – 7.29 (m, 2H), 5.80 – 5.60 (m, 1H), 5.10 – 4.90 (m, 2H), 4.43 (s, 1H), 2.99 – 2.91 (m, 2H), 2.43 (s, 3H), 2.09 – 2.00 (m, 2H), 1.61 – 1.52 (m, 2H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ_C = 143.5, 137.4, 137.2, 129.8, 127.2, 115.8, 42.8, 30.8, 28.9, 21.7.

4-*tert*-Butyldiphenylsilyloxy-1-butene (1z)

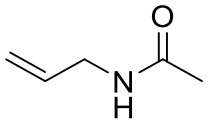


The title compound was prepared from *buten-3-ol* according to a literature procedure.[32] Its characterization data were matching the ones found in literature.

^{1}H-NMR (400 MHz, $CDCl_3$): δ_H = 7.83 – 7.61 (m, 4H), 7.49 – 7.33 (m, 6H), 5.98 – 5.67 (m, 1H), 5.19 – 4.76 (m, 2H), 3.73 (t, *J* = 6.7 Hz, 2H), 2.34 (qt, *J* = 6.8, 1.3 Hz, 2H), 1.07 (s, 9H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ_C = 135.7, 135.6, 134.1, 129.7, 127.7, 116.5, 63.7, 37.4, 27.0, 19.4.

***N*-Allylacetamide (1ad)**

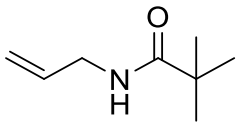


The title compound was prepared from *allylamine* according to a literature procedure.[33] Its characterization data were matching the ones found in literature.

^{1}H-NMR (400 MHz, $CDCl_3$): δ_H = 5.83 (ddt, *J* = 17.2, 10.2, 5.7 Hz, 1H), 5.62 (s, br, 1H), 5.22 – 5.11 (m, 2H), 3.87 (tt, *J* = 5.8, 1.6 Hz, 2H), 2.00 (s, 3H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ_C = 170.0, 134.3, 116.6, 42.2, 23.4.

***N*-Allylpivalamide (1ae)**



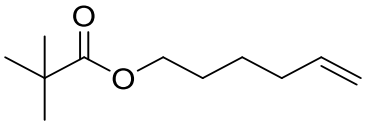
[31] M. Nickels *et al.*, *J. Mater. Chem.* **2010**, *20*, 4776-4780 and Y. Morino *et al. Tetrahedron* **2006**, *62*, 12247-12251.
[32] Brooks, J. L.; Xu, L.; Wiest, O.; Tan, D. S. *J. Org. Chem.* **2017**, *82*, 57-75.
[33] Lin, Y. A.; Chalker, J. M.; Davis, B. G. *J. Am. Chem. Soc.* **2010**, *132*, 16805-16811.

At 0 °C under a N_2 atmosphere, to a solution allyl amine (0.80 mL, 11 mmol, 1.0 eq) in DCM (25 mL) were added triethylamine (1.6 mL, 11 mmol, 1.0 eq) and pivaloyl chloride (1.3 mL, 11 mmol, 1.0 eq). The reaction mixture was let to go to r.t. and stirred overnight. Then, the reaction mixture was diluted with DCM (25 mL), washed with water (2x30 mL) and brine, before it was dried over Na_2SO_4. Concentration under reduced pressure resulted in spectroscopically pure *N*-allylpivalamide (1.4 g, 9.7 mmol, 90%) as a colorless oil. The spectroscopical data correspond to the ones found in literature.[34]

^{1}H-NMR (400 MHz, $CDCl_3$): δ_H = 5.89 – 5.78 (m, 1H), 5.69 (s, br, 1H), 5.24 – 5.06 (m, 2H), 3.87 (tt, *J* = 5.7, 1.6 Hz, 2H), 1.21 (s, 9H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ_C = 178.3, 134.7, 116.2, 42.0, 38.8, 27.8.

Hex-5-en-1-yl pivalate (1af)

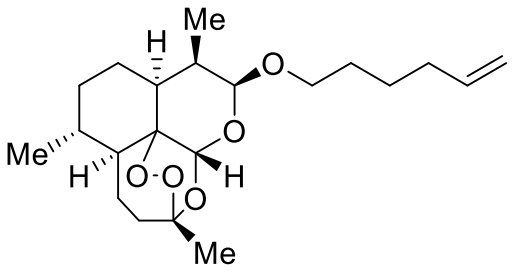


The title compound was prepared from 5-*hexen-1-ol* according to a literature procedure.[35] Its characterization data were matching the ones found in literature.

^{1}H-NMR (400 MHz, $CDCl_3$): δ_H = 5.86 – 5.70 (m, 1H), 5.06 – 4.91 (m, 2H), 4.06 (t, *J* = 6.5 Hz, 2H), 2.14 – 2.03 (m, 2H), 1.70 – 1.57 (m, 2H), 1.50 – 1.42 (m, 2H), 1.19 (s, 9H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ_C = 178.8, 138.6, 114.9, 64.4, 38.9, 33.4, 28.2, 27.4, 25.4.

Hex-5-enyl artemether (1ag)



According to a procedure published by Barua *et al.*,[36] to a stirred solution of dihydroartemisinin (250 mg, 0.879 mmol, 1.0 eq) in dry DCM (10 mL) was added phosphotungstic acid hydrate (126 mg, 0.044 mmol, 5 mol%). After 5 min, hex-5-enol (131 μL, 1.09 mmol, 1.24 eq) was added to the reaction mixture and stirring was continued further for 3 h. The reaction mixture was filtered, concentrated and purified via column chromatography (Hex:EtOAc 19:1 to 9:1, SiO_2) to yield hex-5-enyl artemether **1ag** (239.4 mg, 0.653 mmol, 74%) as a mixture of α- and β-isomers in 1.0 : 2.8 ratio.

[34] Gilbert, A.; Bertrand, X.; Paquin, J.-F. *Org. Lett.* **2018**, *20*, 7257-7260.
[35] Reid, W. B.; Spillane, J. J.; Krause, S. B.; Watson, D. A. *J. Am. Chem. Soc.* **2016**, *138*, 5539-5542.
[36] Bora, P. P.; Baruah, N.; Bez, G.; Barua, N. C. *Synthetic Communications* **2012**, *42*, 1218-1225.

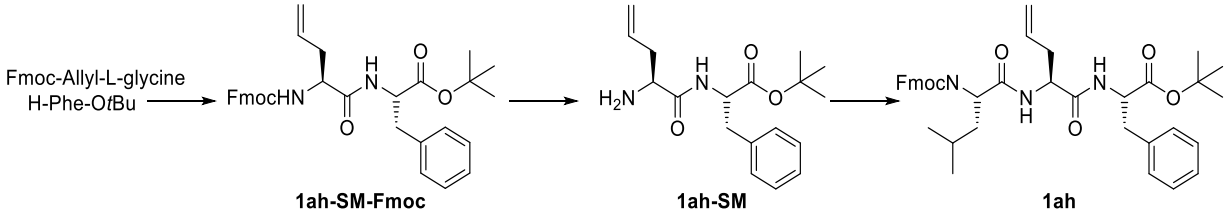
^{1}H-NMR (400 MHz, $CDCl_3$): δ_H = 5.80 (ddt, *J* = 16.9, 10.2, 6.6 Hz, 1H), 5.38 (s, 0.7H), 5.33 (s, 0.3H), 5.07 – 4.87 (m, 2H), 4.77 (dd, *J* = 3.5, 1.1 Hz, 0.7H), 4.41 (d, *J* = 9.2 Hz, 0.3H), 3.97 (dt, *J* = 9.6, 6.2 Hz, 0.3H), 3.84 (dt, *J* = 9.7, 6.4 Hz, 0.7H), 3.47 – 3.27 (ddt, *J* = 14.5, 9.7, 6.6 Hz, 1H), 2.68 – 2.30 (m, 2H), 2.12 – 1.99 (m, 3H), 1.91 – 1.46 (m, 10H), 1.44 (s, 3H), 1.37 – 1.20 (m, 3H), 0.95 (d, *J* = 6.3 Hz, 3H), 0.90 (d, *J* = 7.4 Hz, 3H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ_C = 139.0, 138.9, 114.62, 114.55, 104.4, 104.2, 102.1, 100.2, 91.4, 88.1, 81.3, 80.5, 69.0, 68.4, 52.8, 51.9, 45.5, 44.7, 37.6, 37.5, 36.6, 36.5, 34.8, 34.4, 33.7, 33.6, 32.8, 31.1, 29.3, 29.2, 26.4, 26.2, 25.7, 25.5, 24.9, 24.8, 24.6, 24.6, 20.5, 20.4, 13.2, 12.8.

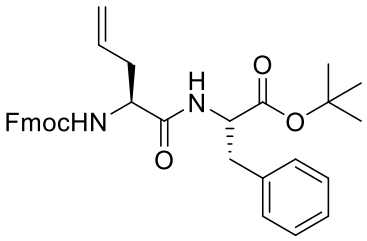
HRMS (ESI+): calc. for $C_{21}H_{34}NaO_5$ $[M+Na]^+$ 389.2298, found 389.2296.

***R_f*:** 0.56 (5:1 Hex:EtOAc)

Synthesis of tripeptide 1ah



Fmoc-allyl-L-glycine-Phe-OtBu (1ah-SM-Fmoc)



Fmoc-allyl-L-glycine (0.506 g, 1.500 mmol, 1.0 equiv.) and H-Phe-OtBu·HCl (0.386 g, 1.498 mmol, 1.0 equiv.) were dissolved in DMF (14 mL). To the resulting solution, DIPEA (0.63 mL, 3.704 mmol, 2.5 equiv.) and HATU (0.623 g, 1.638 mmol, 1.1 equiv.) were added. The reaction mixture was stirred at room temperature for 19 hours before Et_2O (25 mL) and water (50 mL) were added. The layers were separated and the aqueous layer was extracted with Et_2O (3x 25 mL). The combined organic layers were washed with brine, dried over $MgSO_4$ and concentrated under reduced pressure. The crude product was purified by flash column chromatography (SiO_2; Hex/EtOAc 3:1 to 2:1). The title compound was obtained as a yellow oil (0.808 g, 1.498 mmol, quant.). The NMR contains residual ethyl acetate.

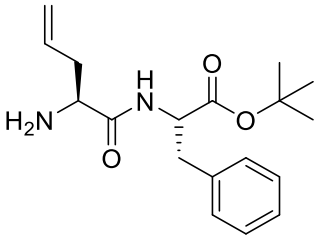
^{1}H-NMR (400 MHz, $CDCl_3$): δ_H = 7.79 – 7.74 (m, 2H), 7.58 (d, *J* = 7.5 Hz, 2H), 7.45 – 7.36 (m, 2H), 7.35 – 7.28 (m, 2H), 7.25 – 7.17 (m, 2H), 7.17 – 7.10 (m, 2H), 6.39 (d, *J* = 7.8 Hz, 1H), 6.39 (d, *J* = 7.8 Hz, 1H), 5.77 – 5.57 (m, 1H), 5.27 (d, br, *J* = 8.0 Hz, 1H), 5.21 – 5.03 (m, 2H), 4.73 (dt, *J* = 7.7, 6.1 Hz, 1H), 4.43 (dd, *J* = 10.5, 7.1 Hz, 1H), 4.38 – 4.30 (m, 1H), 4.22 (t, *J* = 7.0 Hz, 2H), 3.09 (t, *J* = 5.8 Hz, 2H), 2.49 (s, br, 2H), 1.40 (s, 9H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ_C = 170.4, 170.3, 156.1, 143.9, 141.4, 136.1, 132.8. 129.6, 128.5, 127.9, 127.2, 127.2, 125.2, 120.1, 119.5, 82.7, 67.3, 54.2, 53.8, 47.3, 38.2, 37.0, 28.1.

HRMS (ESI+): calc. for $C_{33}H_{37}N_2O_5$ $[M+H]^+$ 541.2697, found 541.2695.

***R_f*:** 0.23 (Hex:EtOAc 3:1)

H-allyl-L-glycine-Phe-OtBu (1ah-SM)



Fmoc-allyl-L-glycine-Phe-OtBu **1ah-SM-Fmoc** (0.808 g, 1.498 mmol, 1.0 equiv.) was dissolved in DMF (8.5 mL). Piperidine (0.750 mL, 7.575 mmol, 5.1 equiv.) was added under stirring and the reaction mixture was stirred at room temperature for 3 hours before DCM (20 mL) and water (80 mL) were added. The layers were separated and the aqueous layer was extracted with DCM (2x 20 mL). The combined organic layers were washed with brine, dried over $MgSO_4$ and concentrated under reduced pressure. The crude product was purified by flash column chromatography (SiO_2; DCM/MeOH 20:1). The title compound was obtained as a colorless oil (0.442 g, 1.388 mmol, 93%).

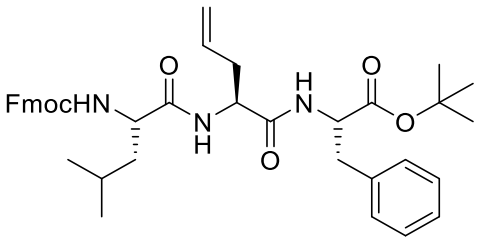
^{1}H-NMR (400 MHz, $CDCl_3$): δ_H = 7.78 (d, *J* = 8.4 Hz, 1H), 7.34 – 7.08 (m, 5H), 5.75 – 5.46 (m, 1H), 5.13 (s, 1H), 5.10 – 5.02 (m, 1H), 4.75 (dt, *J* = 8.4, 6.4 Hz, 1H), 3.39 (dd, *J* = 8.5, 3.9 Hz, 1H), 3.19 – 2.99 (m, 2H), 2.95 (d, *J* = 0.5 Hz, 1H), 2.88 (d, *J* = 0.6 Hz, 1H), 2.56 – 2.46 (m, 1H), 2.26 – 2.10 (m, 1H), 1.41 (s, 9H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ_C = 174.0, 170.9, 136.5, 134.5, 129.6, 128.4, 127.0, 118.9, 82.3, 54.0, 53.2, 39.5, 38.5, 28.1.

HRMS (ESI+): calc. for $C_{18}H_{26}N_2NaO_3$ $[M+Na]^+$ 341.1836, found 341.1839.

***R_f*:** 0.30 (DCM:MeOH 20:1)

Fmoc-Leu-allyl-L-glycine-Phe-OtBu (1ah)



Fmoc-Leu-OH (0.493 g, 1.395 mmol, 1.0 equiv.), H-allyl-L-glycine-Phe-OtBu **1ah-SM** (0.442 g, 1.388 mmol, 1.0 equiv.) and DIPEA (0.590 mL, 3.469 mmol, 2.5 equiv.) were dissolved in DMF (14 mL). HATU (0.581 mmol, 1.528 mmol, 1.1 equiv.) was added and the reaction mixture was stirred at room temperature for 11 hours. DCM (25 mL) and water (80 mL) were added and the layers were separated. The aqueous layer was extracted with DCM (2x 25 mL). The combined organic layers were washed with brine, dried over $MgSO_4$ and concentrated under reduced pressure. The crude product was purified by flash column chromatography (SiO_2; Hex/EtOAc 3:1 to 2:1 to 1:1). The title compound was obtained as a colorless solid (0.425 g, 0.651 mmol, 47%).

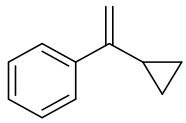
^{1}H-NMR (400 MHz, $CDCl_3$): δ_H = 7.76 (d, *J* = 7.6 Hz, 2H), 7.62 – 7.54 (m, 2H), 7.40 (tt, *J* = 7.6, 1.6 Hz, 2H), 7.35 – 7.28 (m, 2H), 2.27 – 7.18 (m, 3H), 7.13 (d, *J* = 7.1 Hz, 2H), 6.53 (t, *J* = 8.5 Hz, 1H), 5.64 (ddt, *J* = 17.2, 10.1, 7.1 Hz, 1H), 5.24 (d, *J* = 8.2 Hz, 1H), 5.13 – 4.94 (m, 2H), 4.71 (q, *J* = 6.5 Hz, 1H), 4.52 – 4.40 (m, 2H), 4.35 (t, *J* = 8.9 Hz, 1H), 4.21 (t, *J* = 7.0 Hz, 2H), 3.06 (d, *J* = 6.2 Hz, 2H), 2.80 (s, 1H), 2.53 – 2.40 (m, 2H), 1.68 – 1.57 (m, 2H), 1.56 – 1.46 (m, 1H), 1.39 (s, 9H), 0.93 (d, *J* = 5.8 Hz, 6H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ_C = 172.1, 170.3, 170.1, 156.3, 143.8, 141.4, 136.1, 132.7, 129.5, 128.5, 127.9, 127.2, 127.1, 125.1, 120.2, 119.4, 82.6, 67.2, 53.8, 53.6, 52.4, 47.3, 41.4, 38.1, 36.7, 28.0, 24.8, 23.1, 22.0.

HRMS (ESI+): calc. for $C_{39}H_{47}N_3NaO_6$ $[M+Na]^+$ 676.3357, found 676.3349.

***R_f*:** 0.13 (Hex:EtOAc 3:1)

(1-cyclopropylvinyl)benzene (5a)

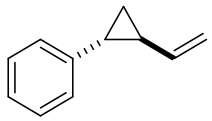


The title compound was prepared from *cyclopropyl(phenyl)methanone* according to a literature procedure.[37] Its characterization data were matching the ones found in literature.

^{1}H-NMR (400 MHz, $CDCl_3$): δ_H = 7.61 – 7.56 (m, 2H), 7.35 – 7.25 (m, 3H), 5.26 (d, *J* = 0.7 Hz, 1H), 4.92 (t, *J* = 1.2 Hz, 1H), 1.70 – 1.57 (m, 1H), 0.87 – 0.72 (m, 2H), 0.62 – 0.52 (m, 2H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ_C = 149.5, 141.8, 128.3, 127.6, 126.3, 109.2, 15.8, 6.8.

((1*R,2*S**)-2-vinylcyclopropyl)benzene (5d)**



The title compound was prepared from *trans-2-phenylcyclopropane-1-carboxylic acid* according to a literature procedure.[38] Its characterization data were matching the ones found in literature.

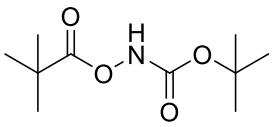
^{1}H-NMR (400 MHz, $CDCl_3$): δ_H = 7.31 – 7.24 (m, 2H), 7.19 – 7.13 (m, 1H), 7.08 (dt, *J* = 8.1, 1.3 Hz, 2H), 5.71 – 5.44 (m, 1H), 5.17 – 4.84 (m, 2H), 1.99 – 1.86 (m,1H), 1.77 – 1.61 (m, 1H), 1.24 – 1.17 (m, 1H), 1.15 – 1.08 (m, 1H).

^{13}C-NMR (101 MHz, $CDCl_3$): δ_C = 142.5, 140.8, 128.5, 125.8, 125.8, 112.7, 27.5, 25.4, 16.9.

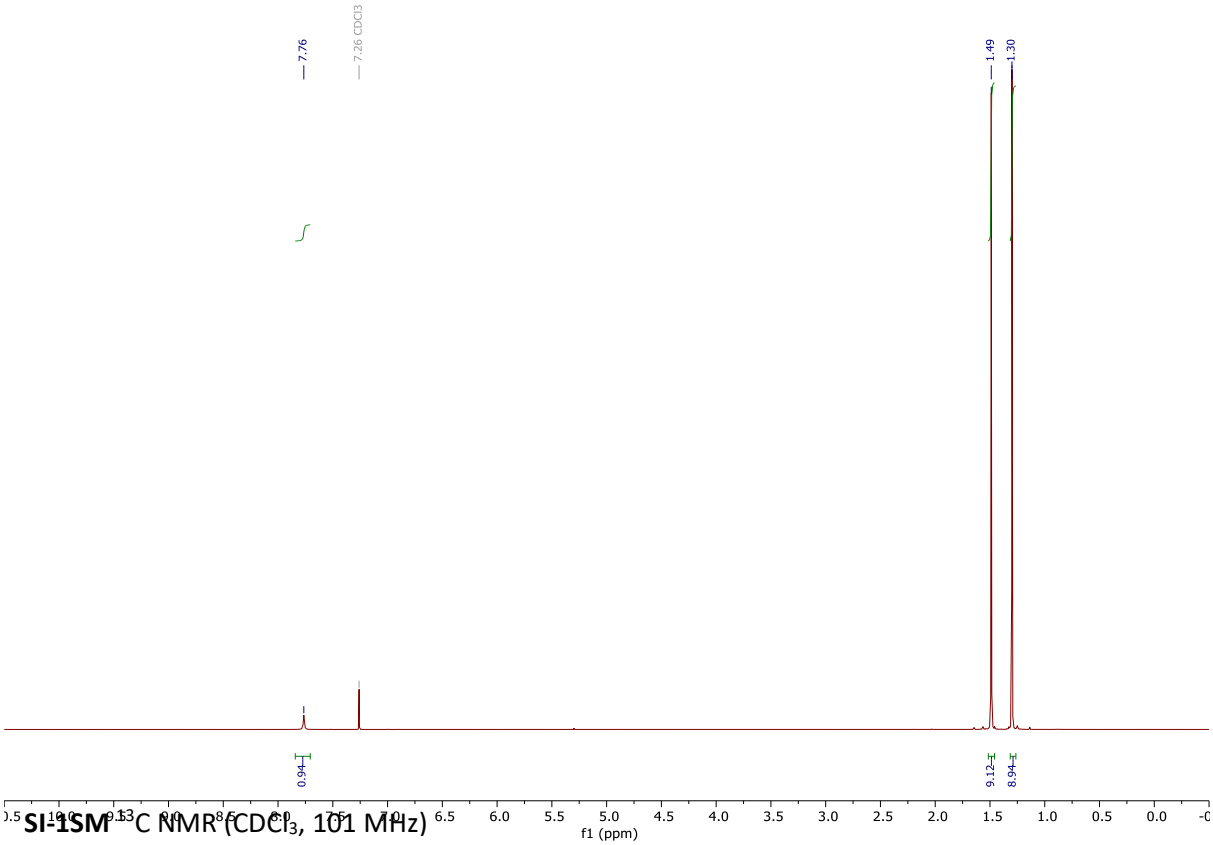
[37] N. Fu, G. S. Sauer, A. Saha, A. Loo, S. Lin, *Science* **2017**, *357*, 575–579.
[38] S. N. Gockel, T. L. Buchanan, K. L. Hull, *J. Am. Chem. Soc.* **2018**, *140*, 58–61.

Abbreviations

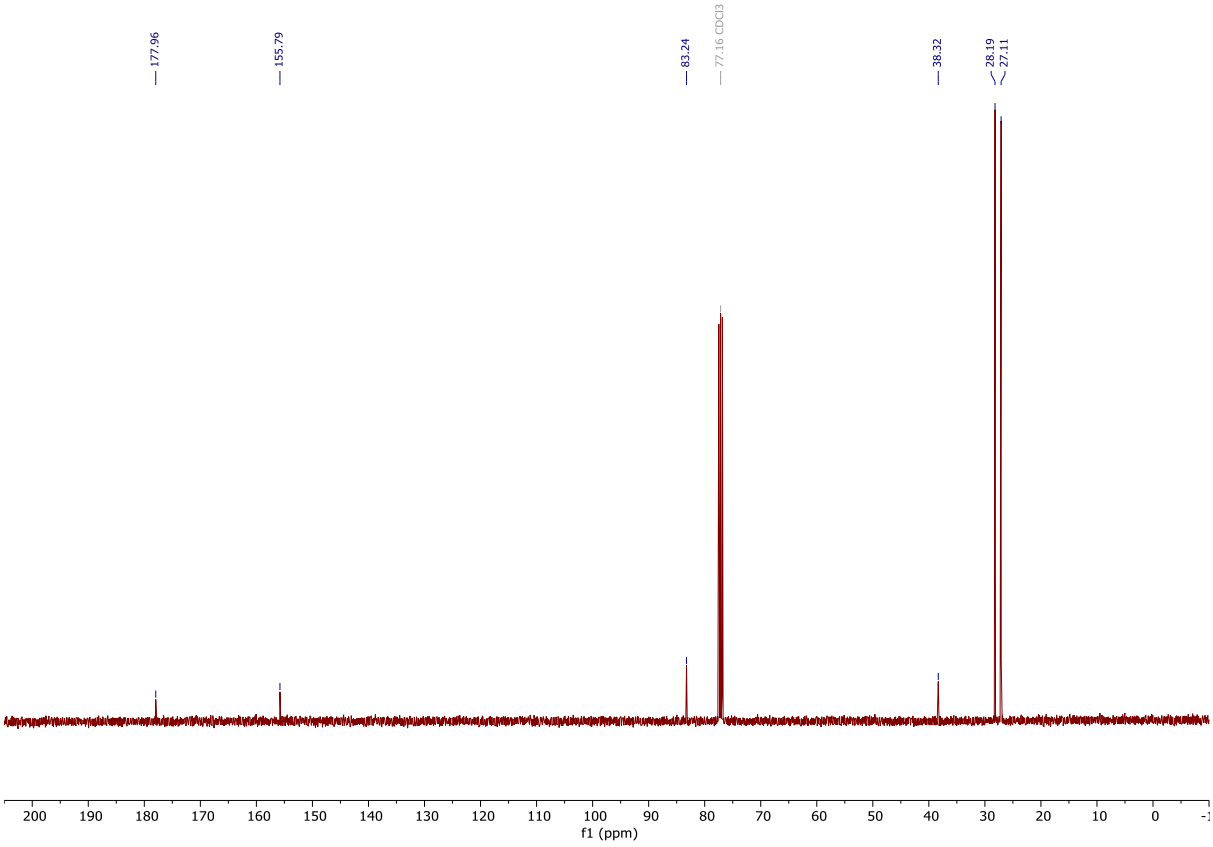
Ac	Acetyl
Boc	*tert*-Butyloxycarbonyl
*n*Bu	*n*-Butyl
*t*Bu	*tert*-Butyl
CCA	α-Cyano-4-hydroxycinnamic acid
DCM	Dichloromethane
DIPEA	*N*,*N*-Diisopropylethylamine
DMSO	Dimethylsulfoxide
ESI	Electrospray ionisation
Et	Ethyl
Fmoc	Fluorenylmethoxycarbonyl
HR-MS	High resolution mass spectrometry
Leu	L-Leucin
MALDI-TOF	Matrix-assisted laser desorption/ionization
Me	Methyl
NMR	Nuclear magnetic resonance spectroscopy
Piv	Pivaloyl / trimethylacetyl
Ph	Phenyl
Rf	Retention factor
Tf	Triflyl / trifluoromethanesulfonyl
THF	Tetrahydrofuran
Ts	Tosyl / toluenesulfonyl

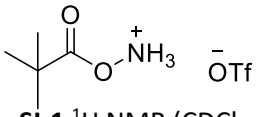


SI-1SM ^{1}H NMR ($CDCl_3$, 400 MHz)

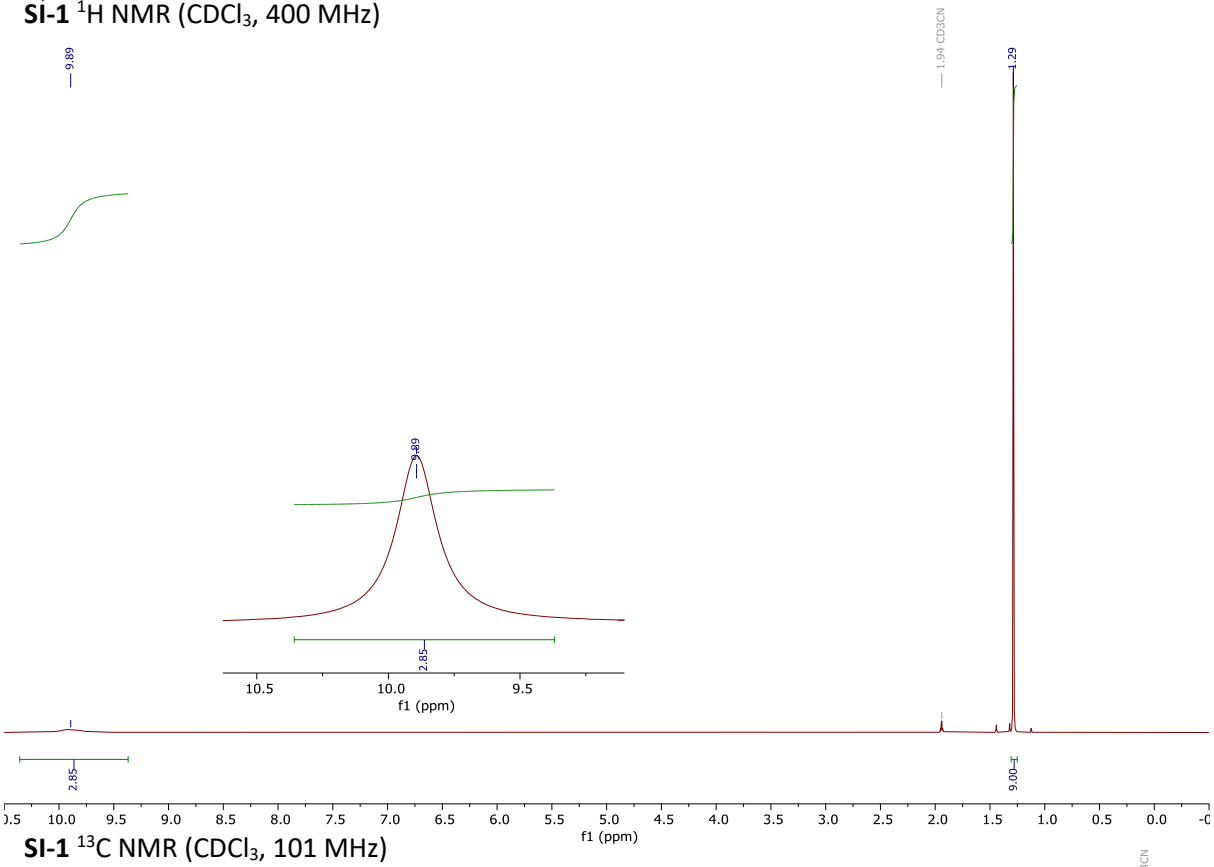


SI-1SM ^{13}C NMR ($CDCl_3$, 101 MHz)

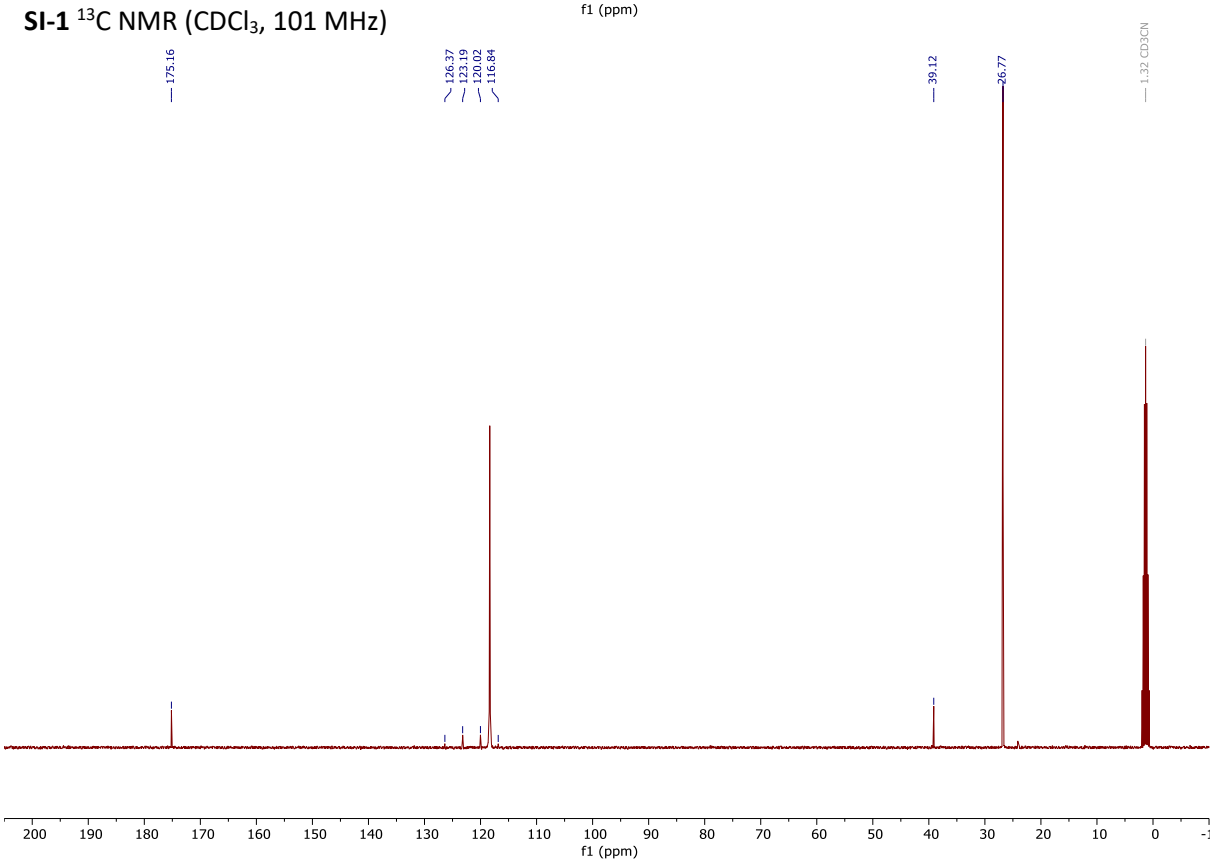


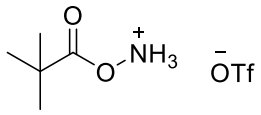


SI-1 ^{1}H NMR ($CDCl_3$, 400 MHz)

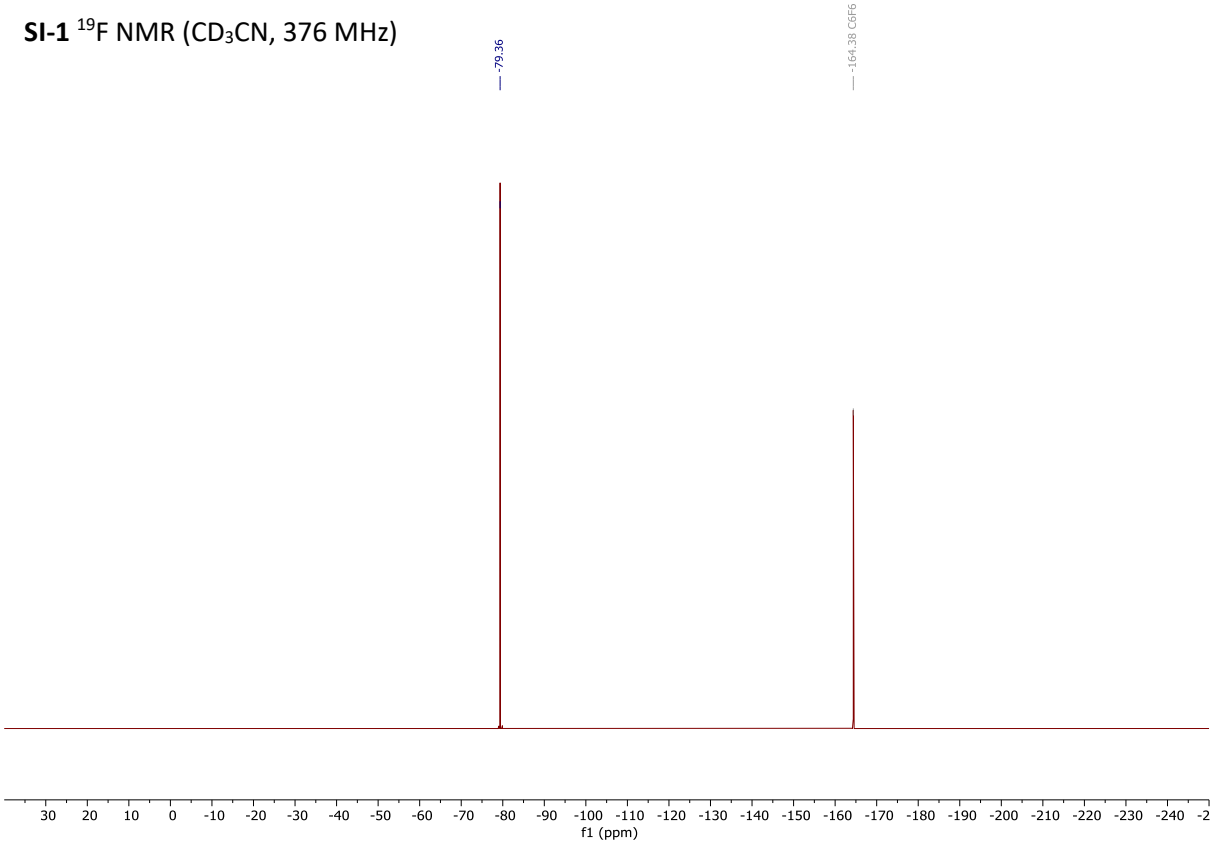


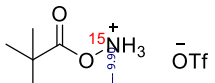
SI-1 ^{13}C NMR ($CDCl_3$, 101 MHz)



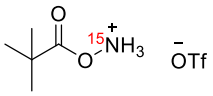


SI-1 ^{19}F NMR (CD_3CN, 376 MHz)

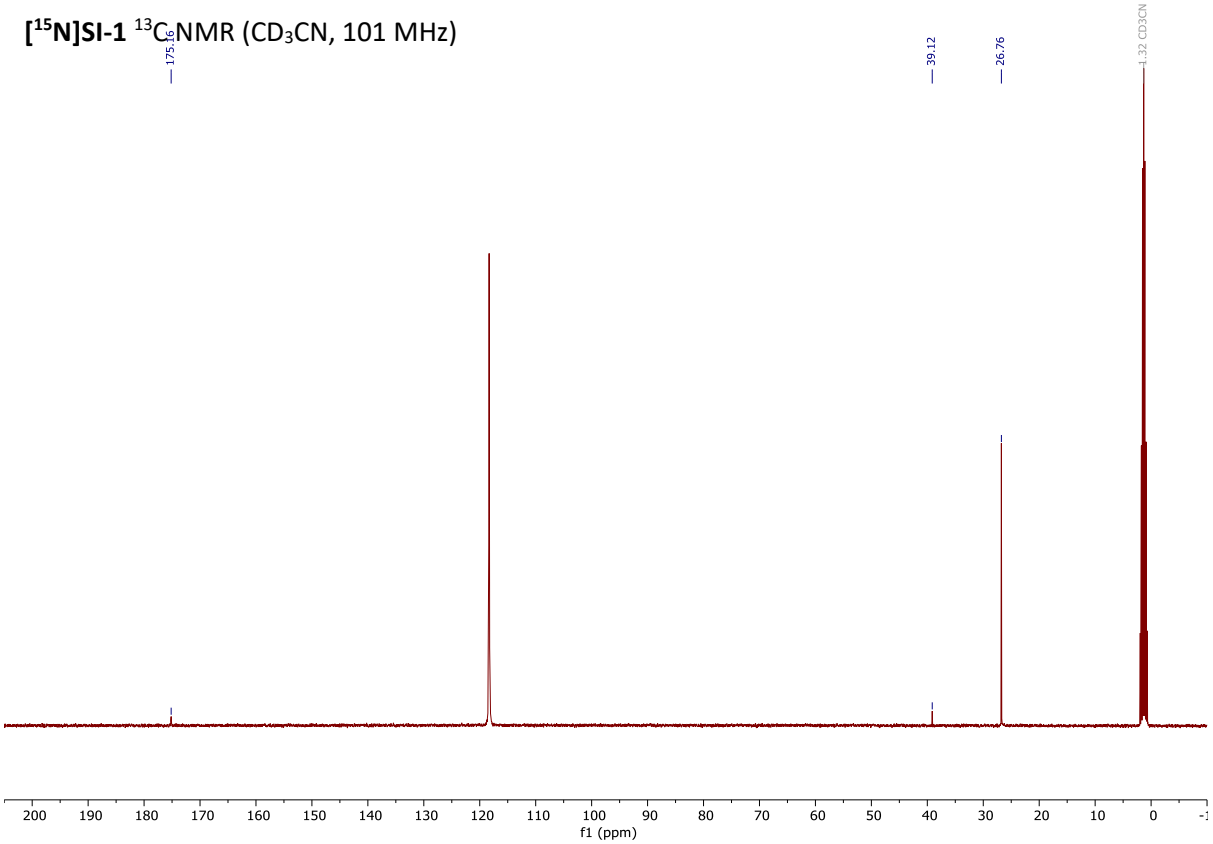


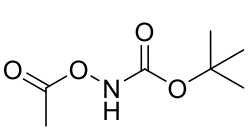


[^{15}N]SI-1 ^{1}H NMR (CD_3CN, 400 MHz)

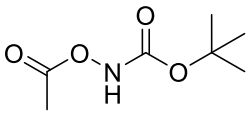


[^{15}N]SI-1 ^{13}C NMR (CD_3CN, 101 MHz)

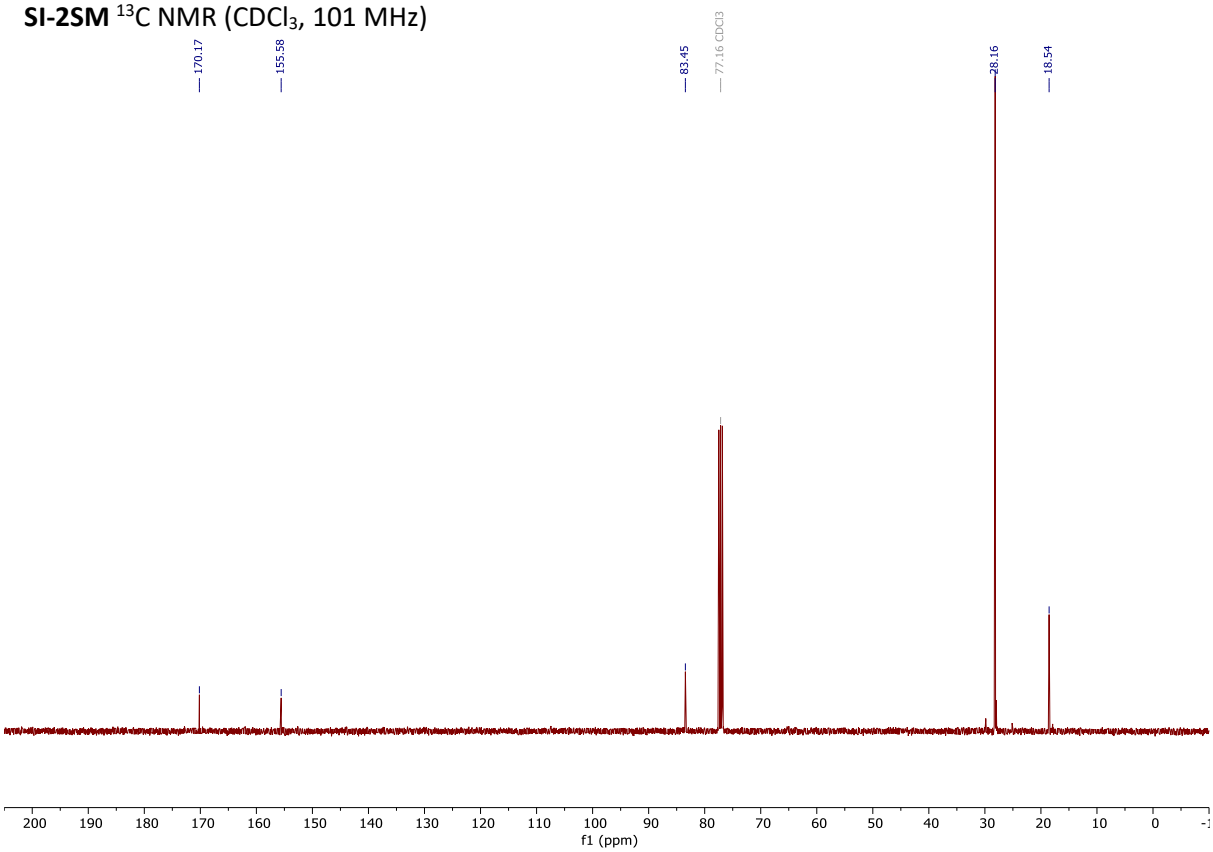


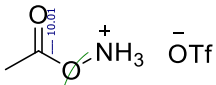


SI-2SM ^{1}H NMR ($CDCl_3$, 400 MHz)

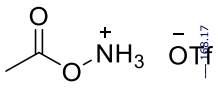


SI-2SM ^{13}C NMR ($CDCl_3$, 101 MHz)



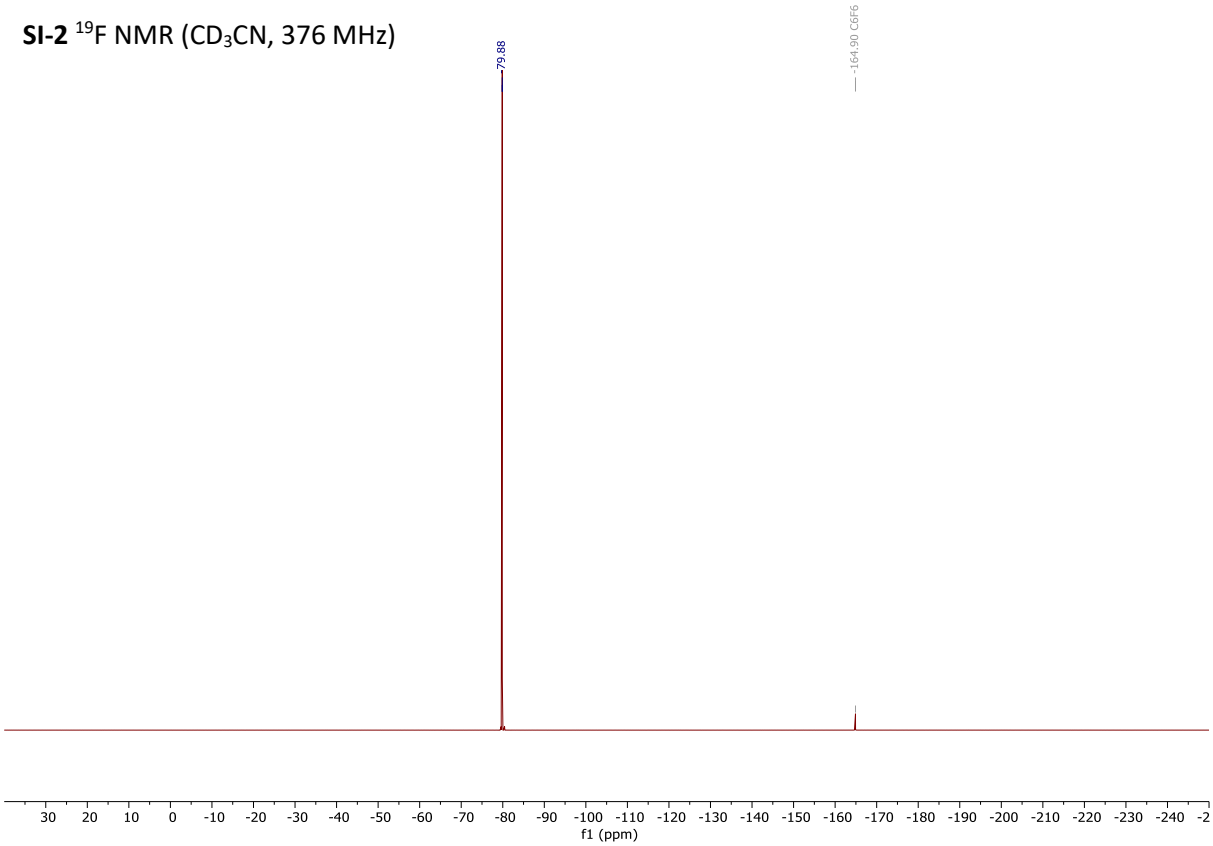


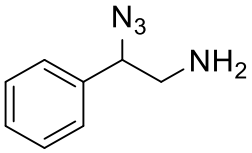
SI-2 ^{1}H NMR (CD_3CN, 400 MHz)



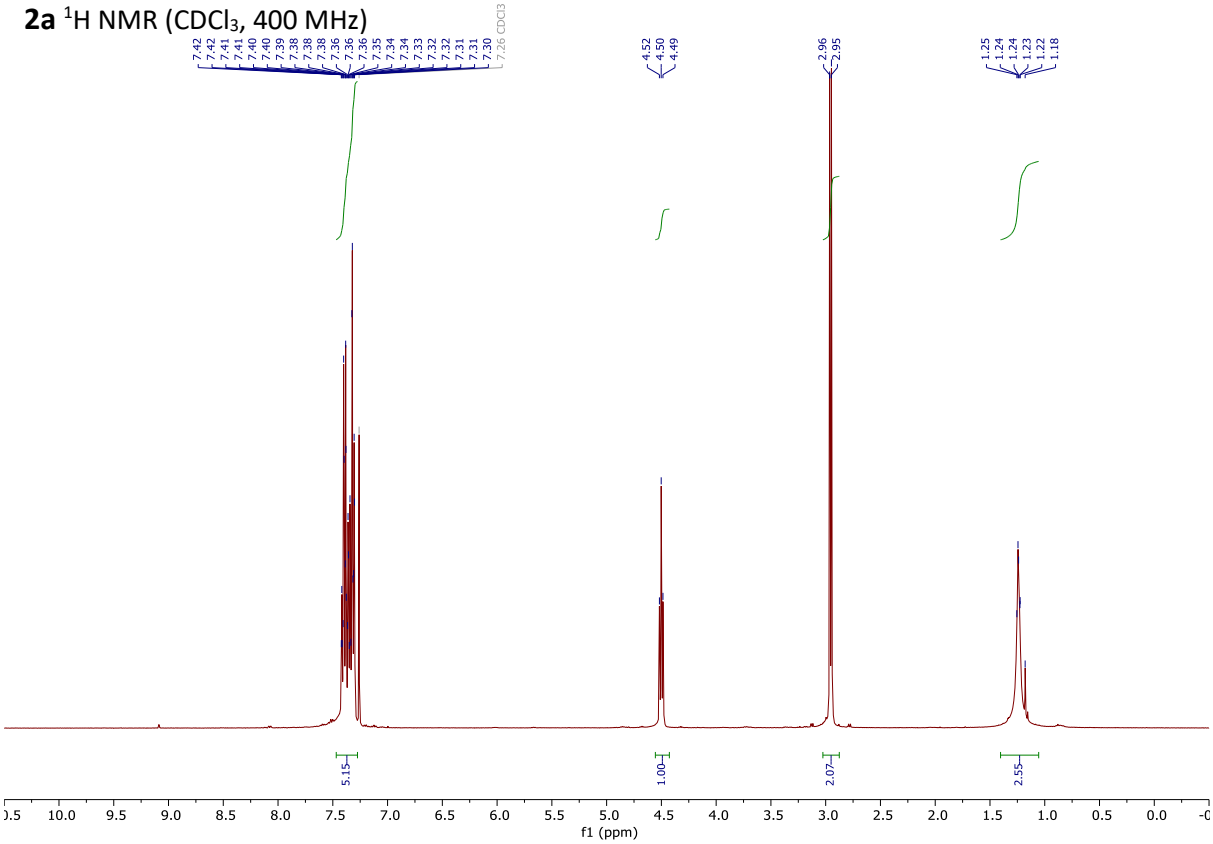
SI-2 ^{13}C NMR (CD_3CN, 400 MHz)

SI-2 ^{19}F NMR (CD_3CN, 376 MHz)

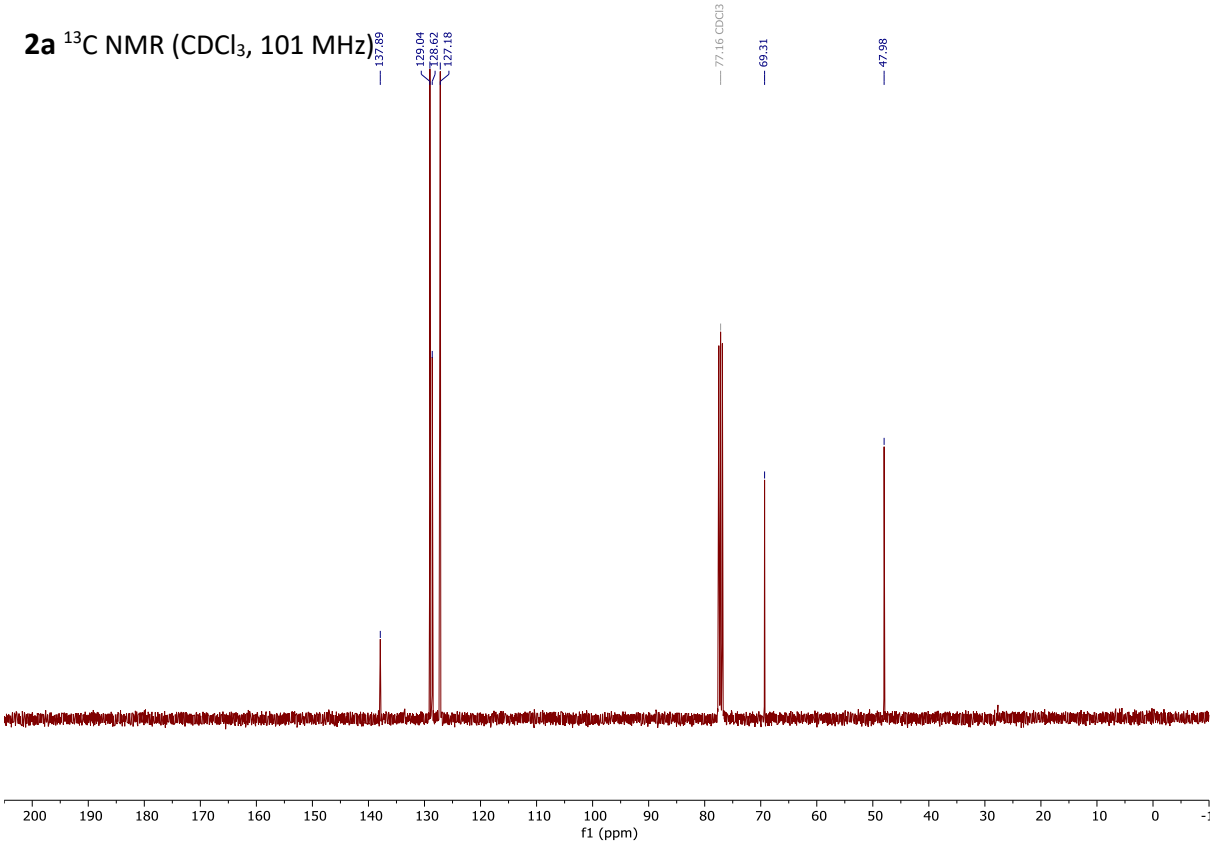


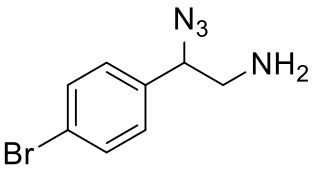


2a ^{1}H NMR ($CDCl_3$, 400 MHz)

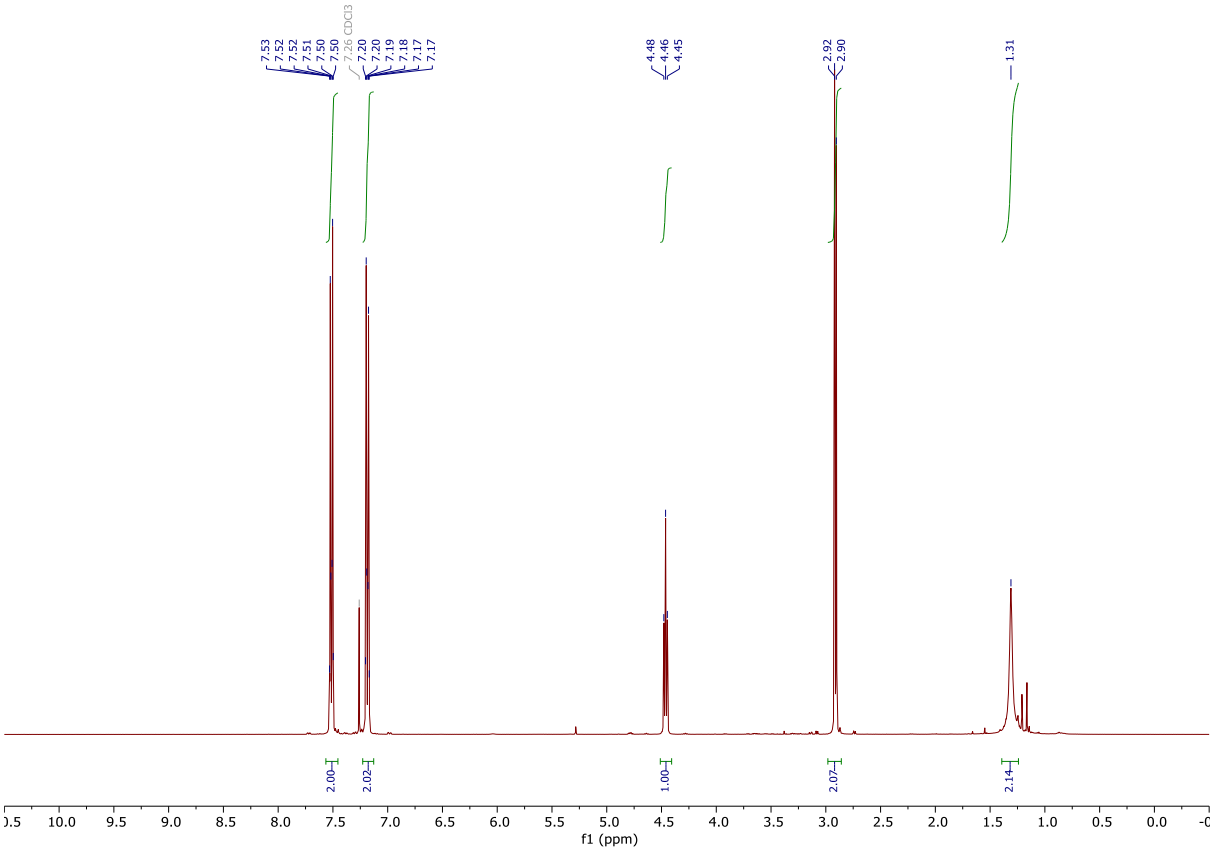


2a ^{13}C NMR ($CDCl_3$, 101 MHz)

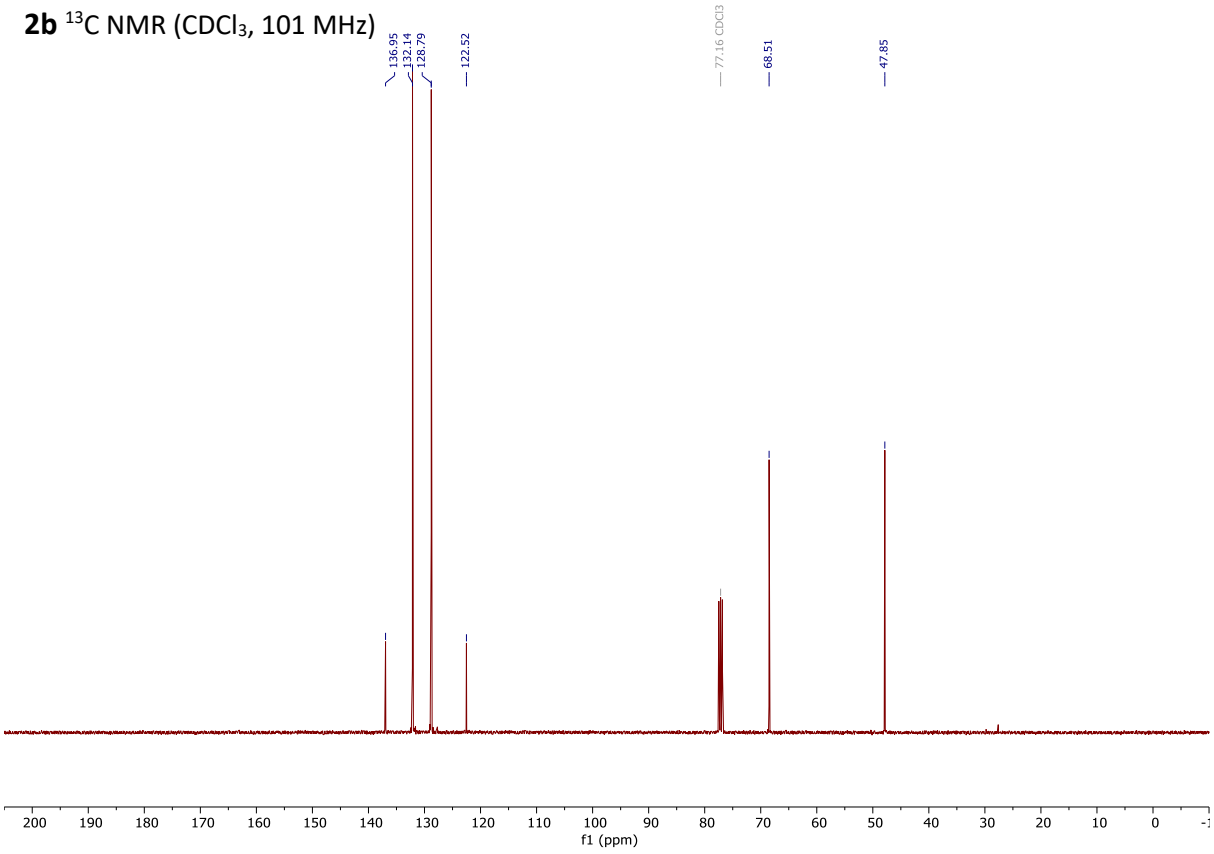


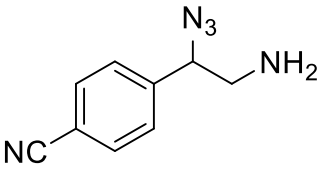


2b ^{1}H NMR ($CDCl_3$, 400 MHz)

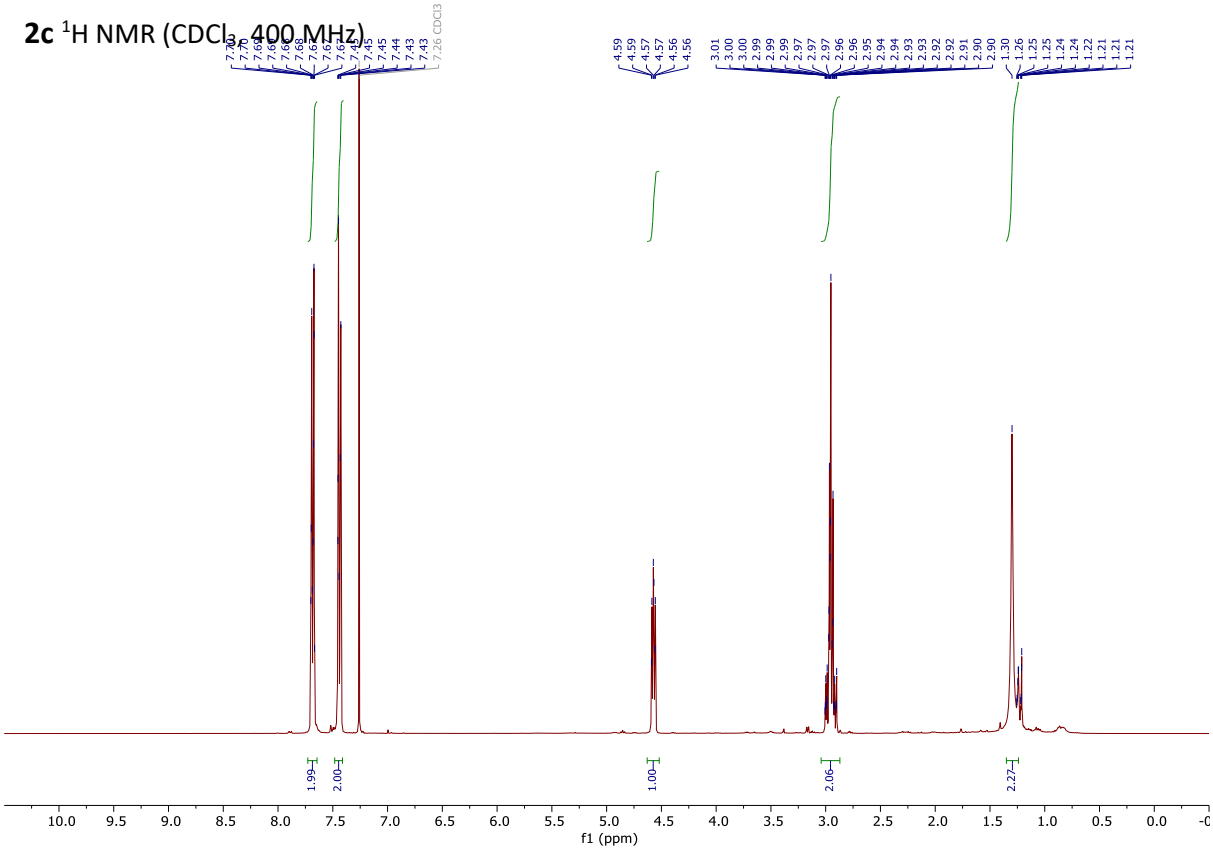


2b ^{13}C NMR ($CDCl_3$, 101 MHz)

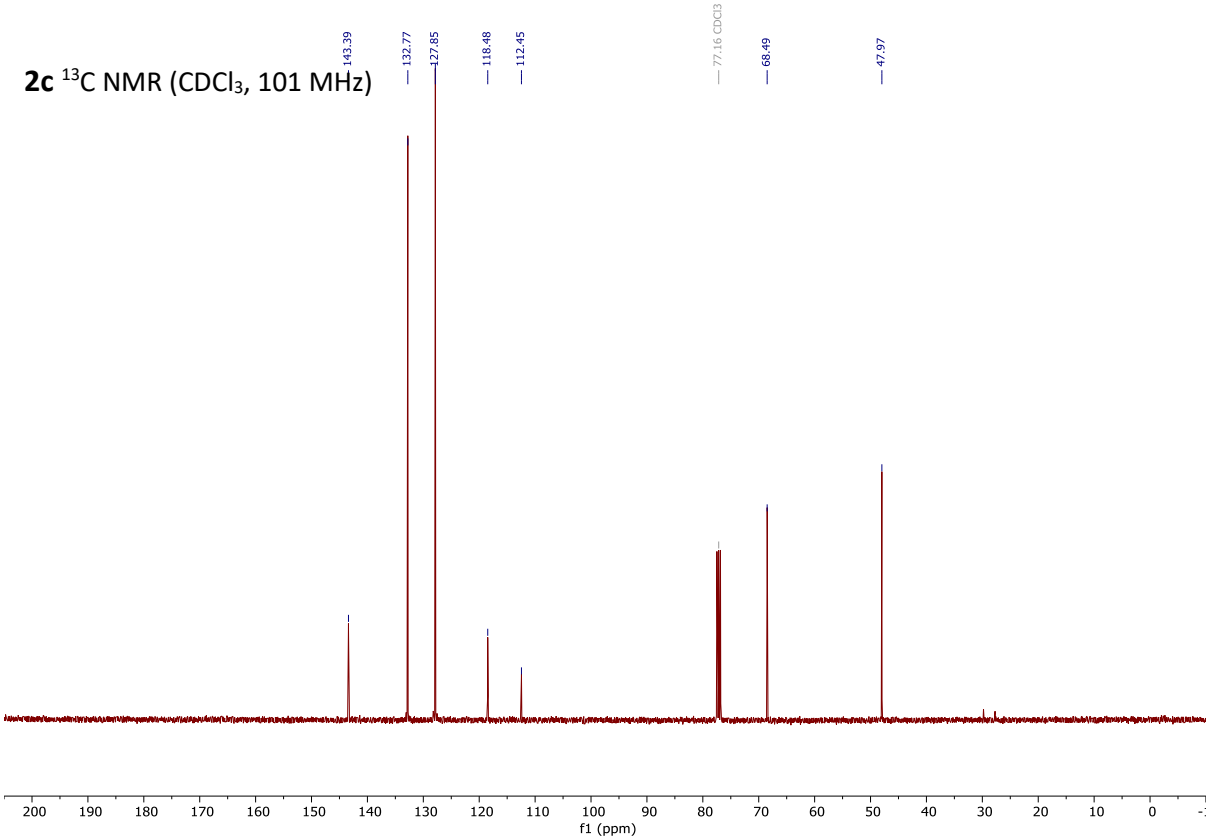


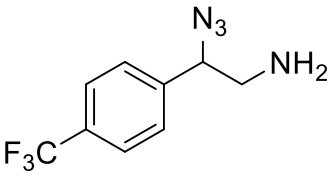


2c ^{1}H NMR ($CDCl_3$, 400 MHz)

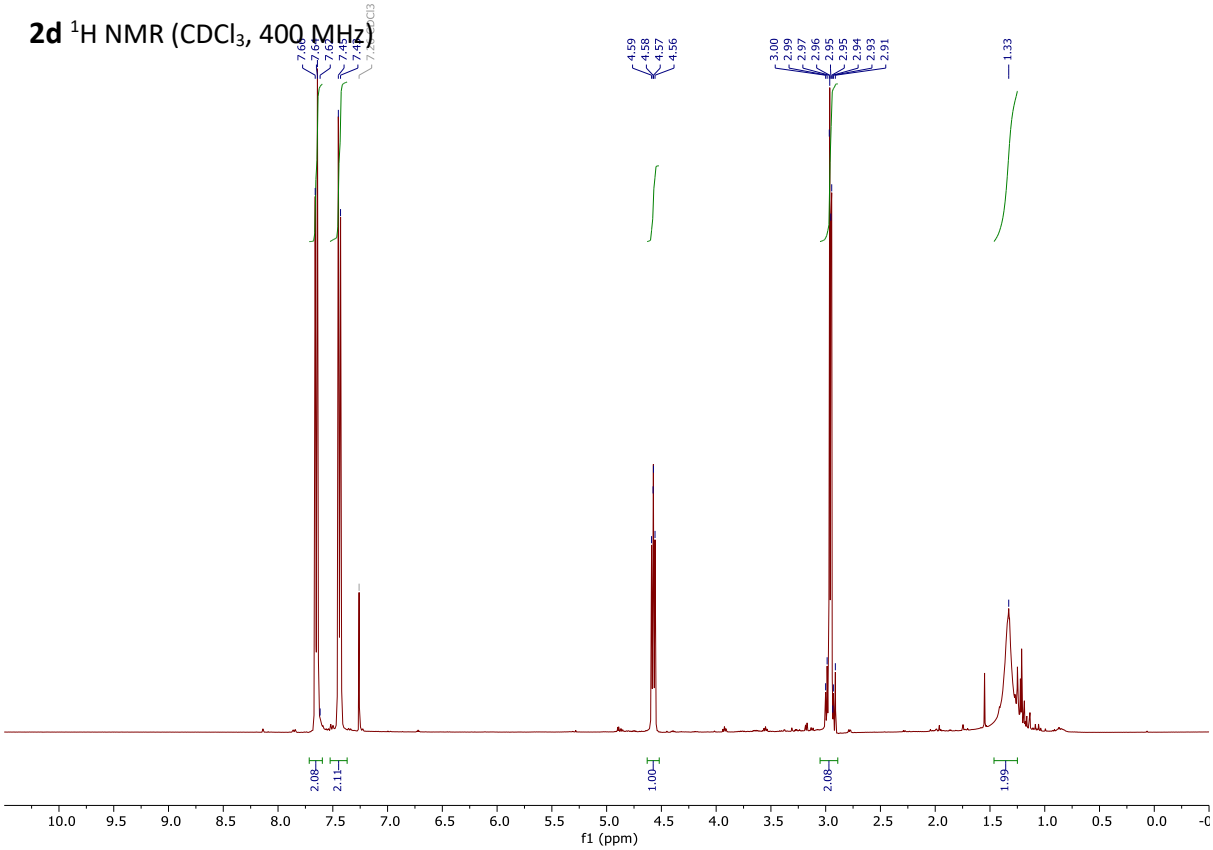


2c ^{13}C NMR ($CDCl_3$, 101 MHz)

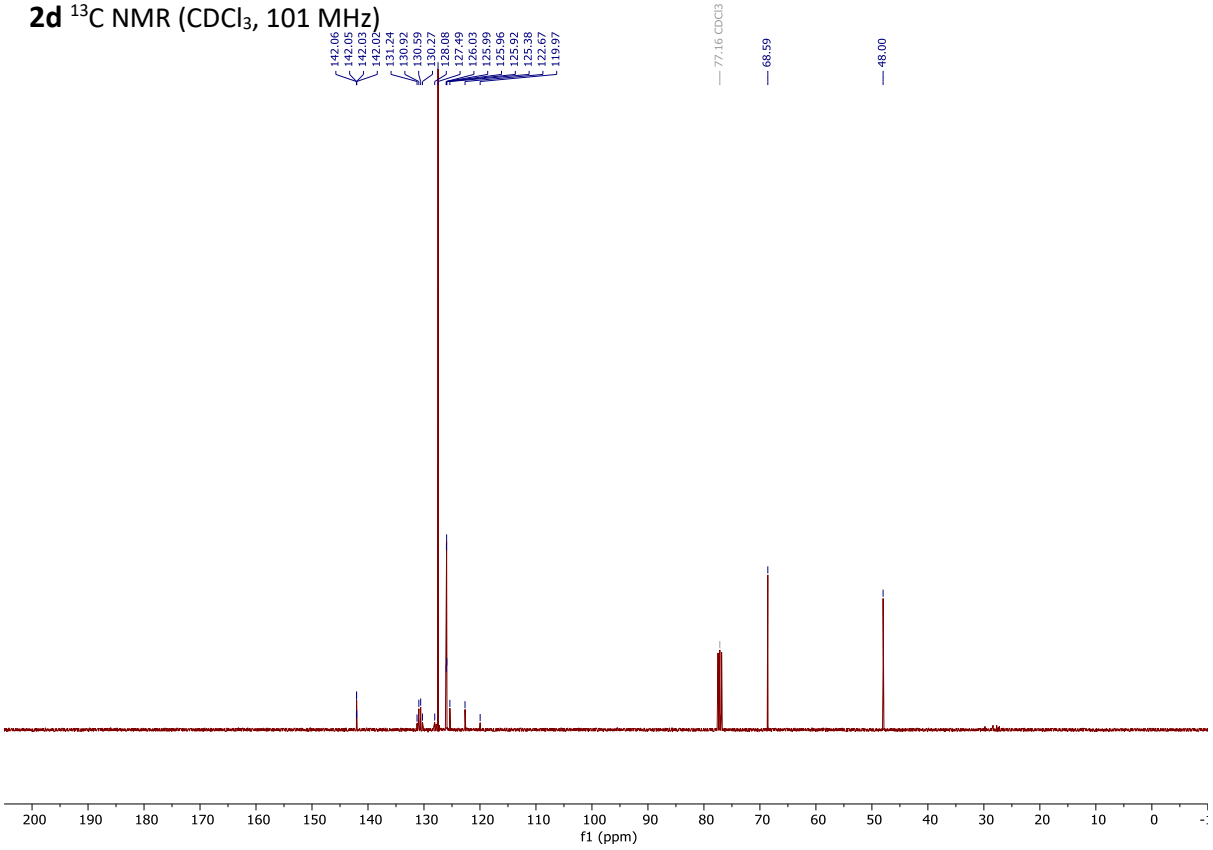


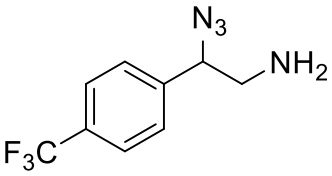


2d ^{1}H NMR ($CDCl_3$, 400 MHz)

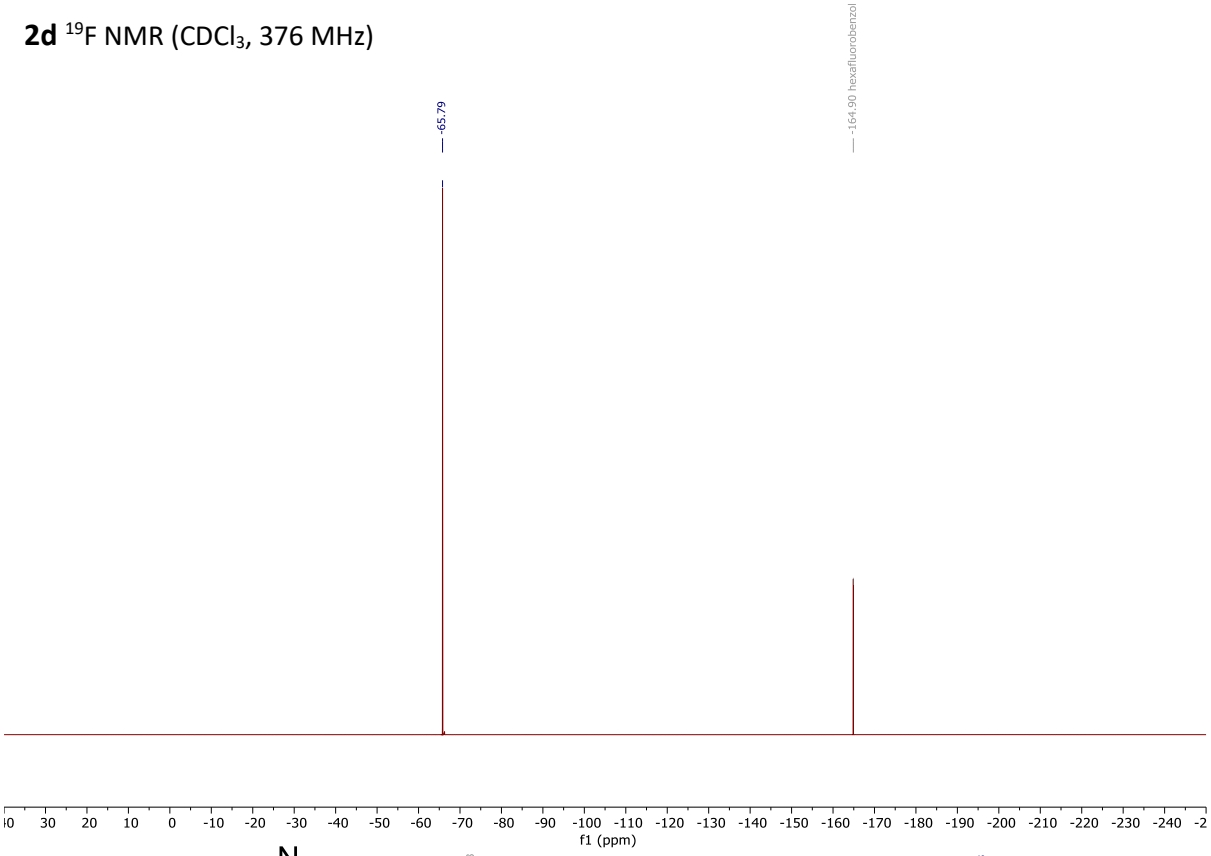


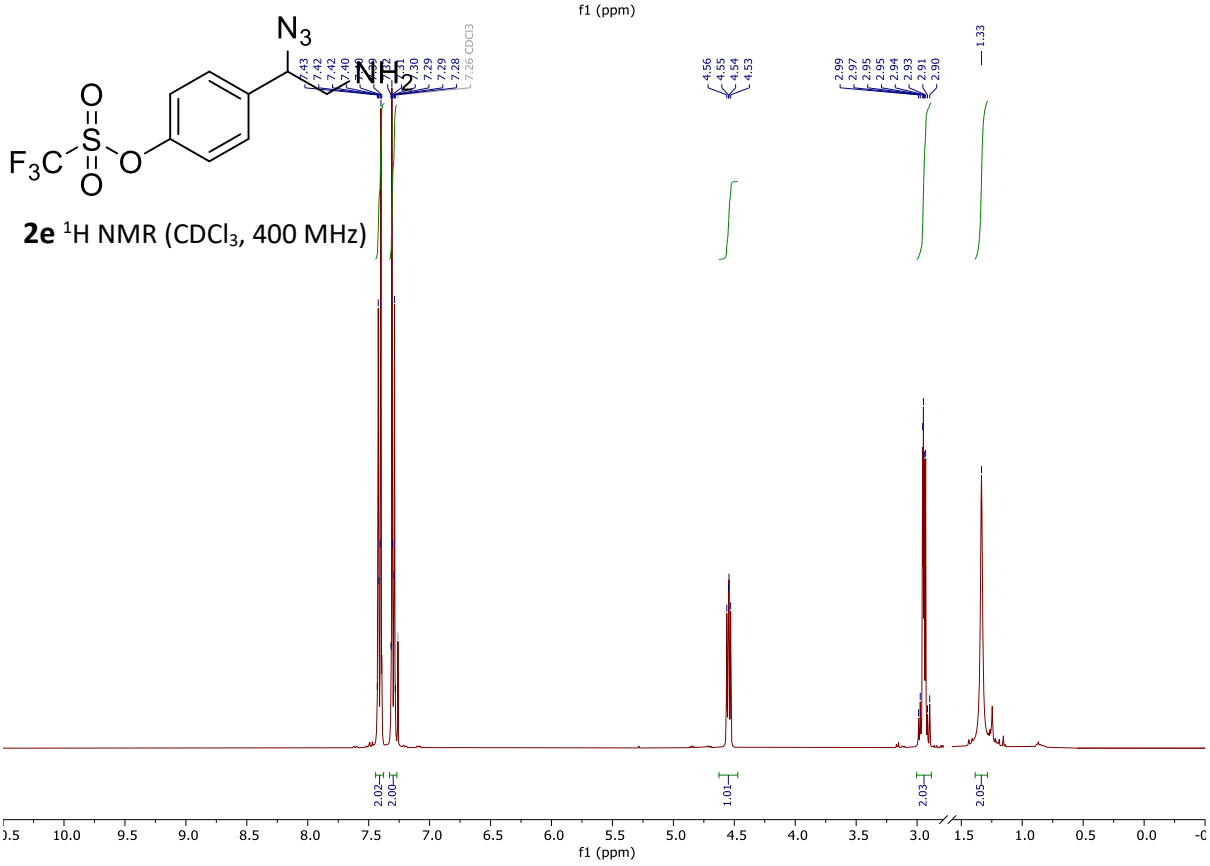
2d ^{13}C NMR ($CDCl_3$, 101 MHz)



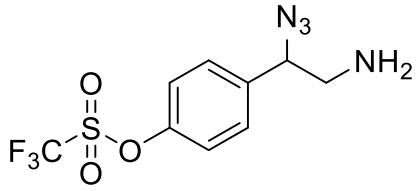


2d ^{19}F NMR ($CDCl_3$, 376 MHz)

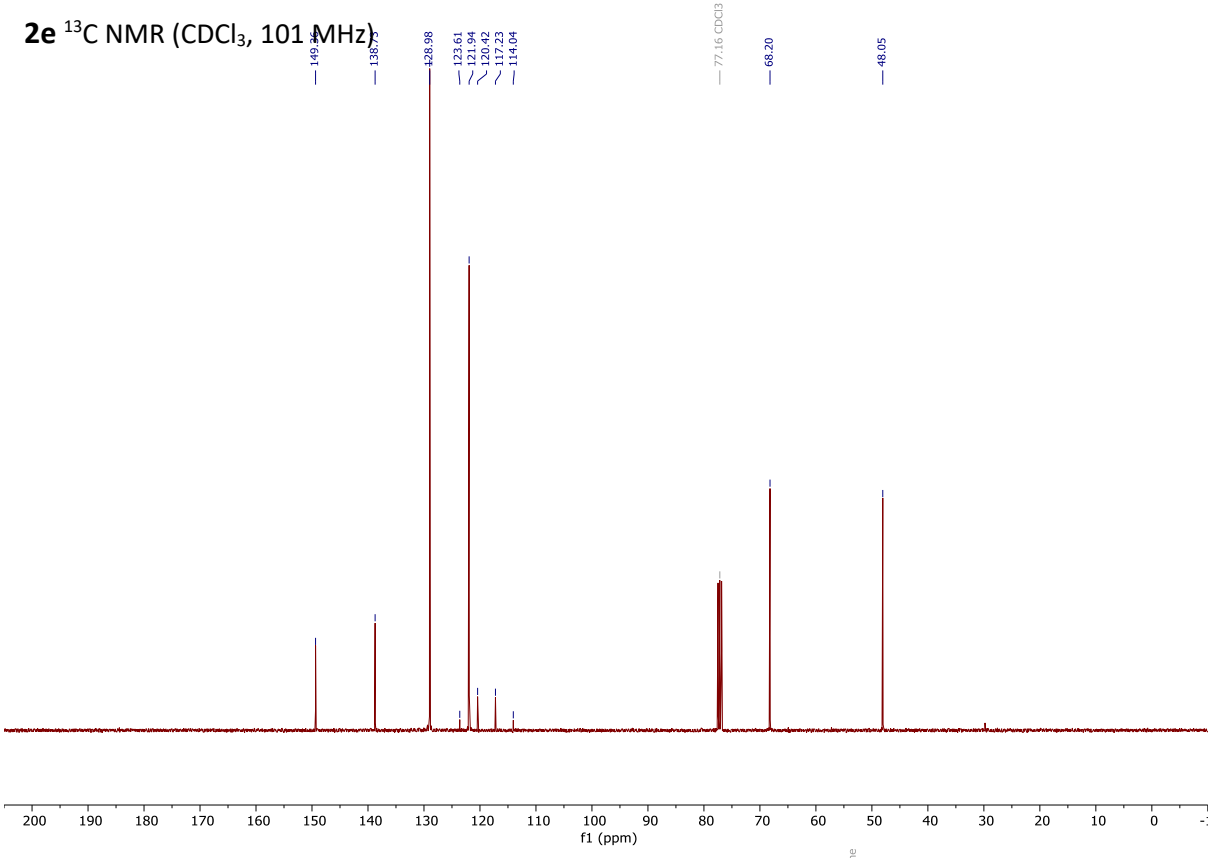




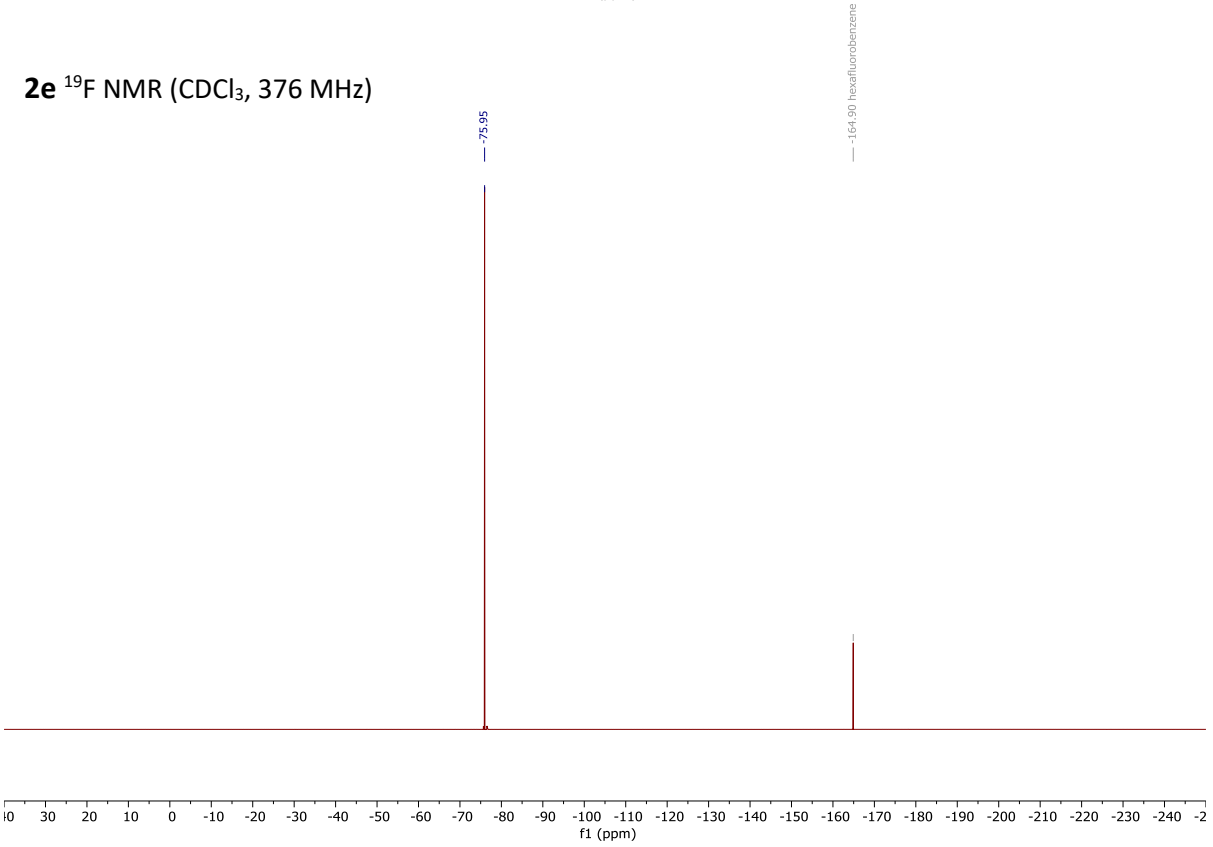
2e ^{1}H NMR ($CDCl_3$, 400 MHz)

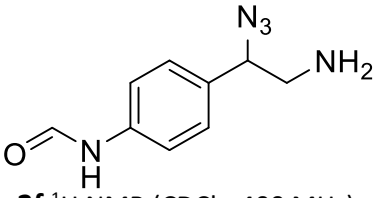


2e ^{13}C NMR ($CDCl_3$, 101 MHz)

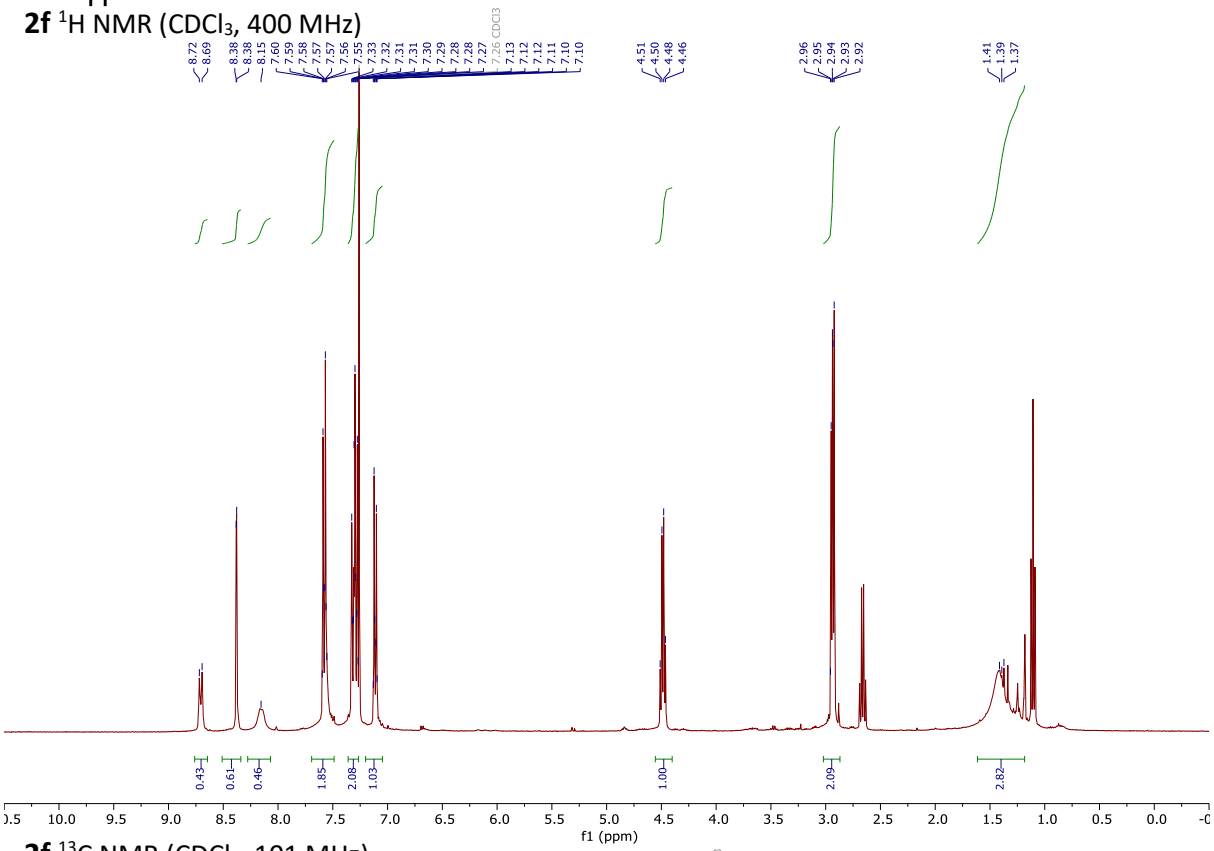


2e ^{19}F NMR ($CDCl_3$, 376 MHz)

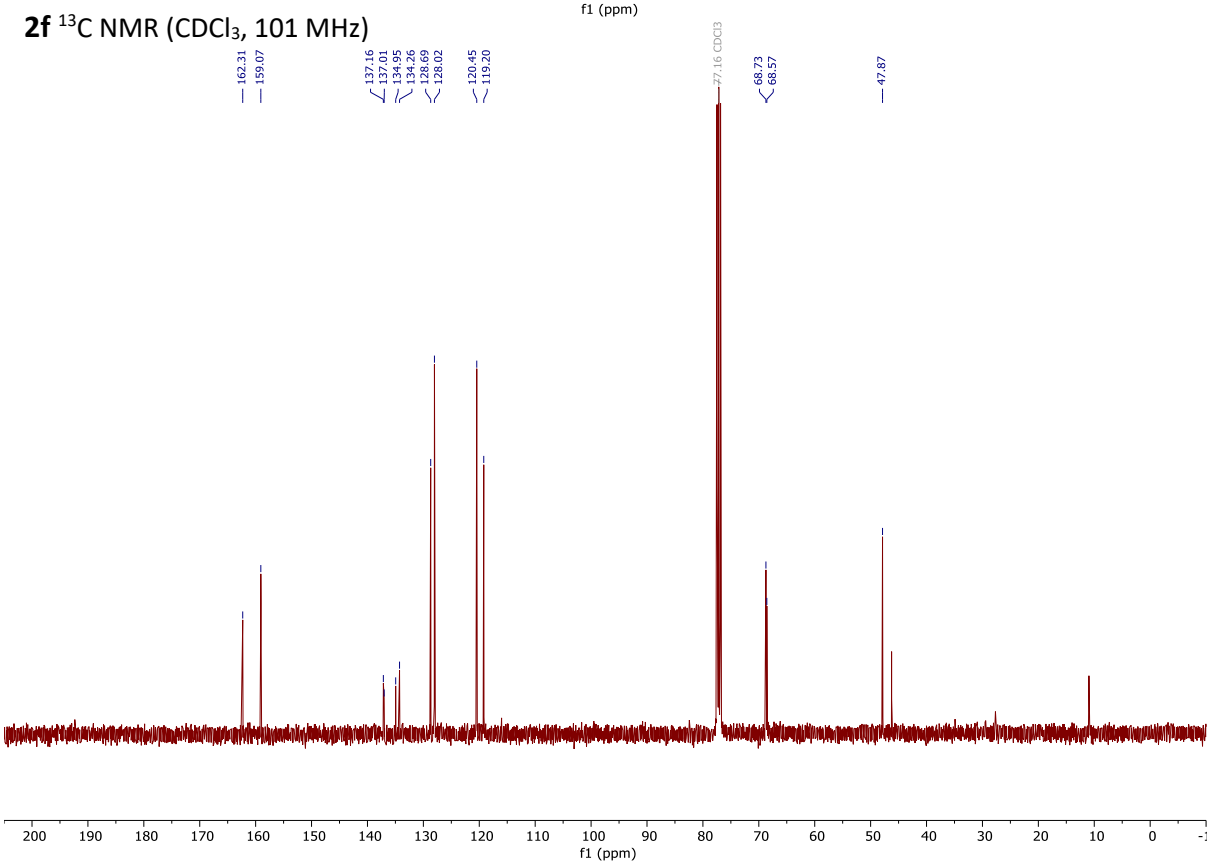


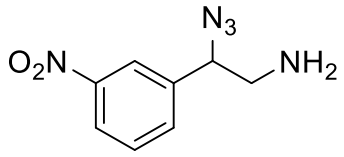


2f ^{1}H NMR ($CDCl_3$, 400 MHz)

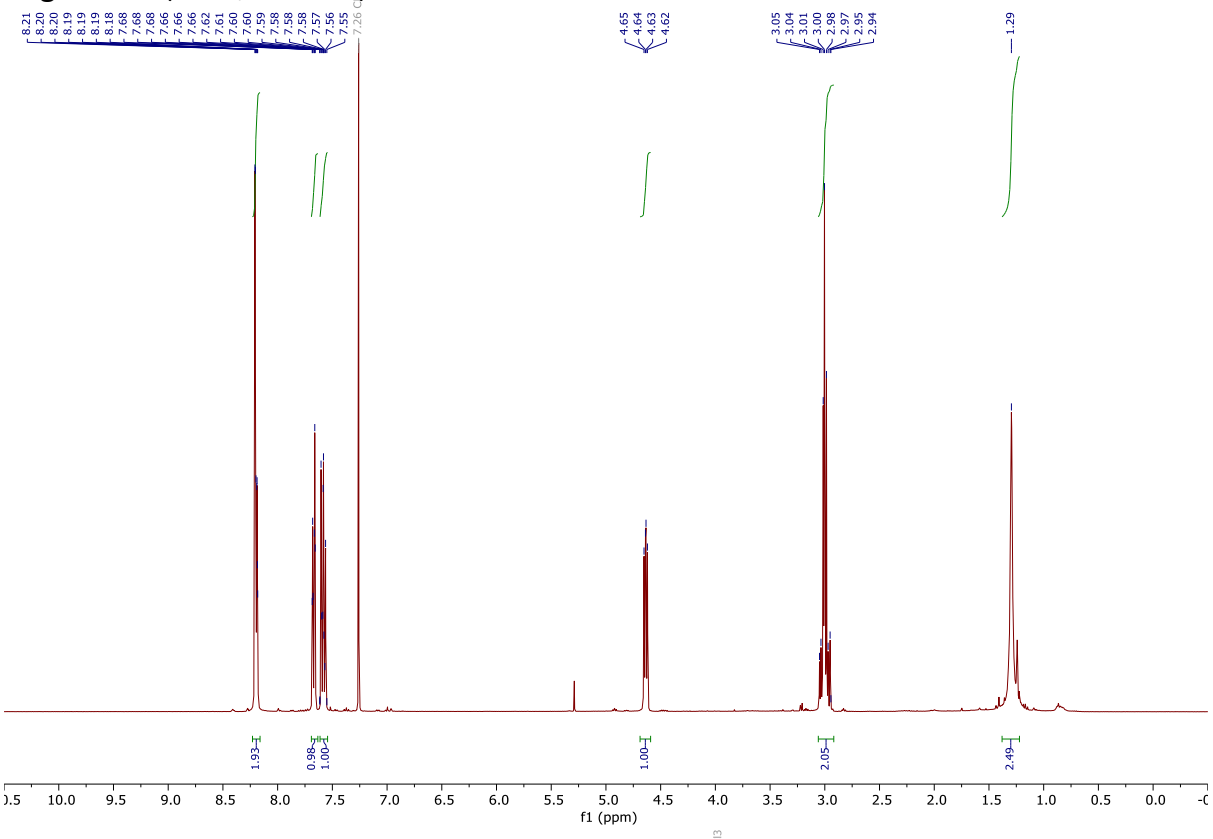


2f ^{13}C NMR ($CDCl_3$, 101 MHz)

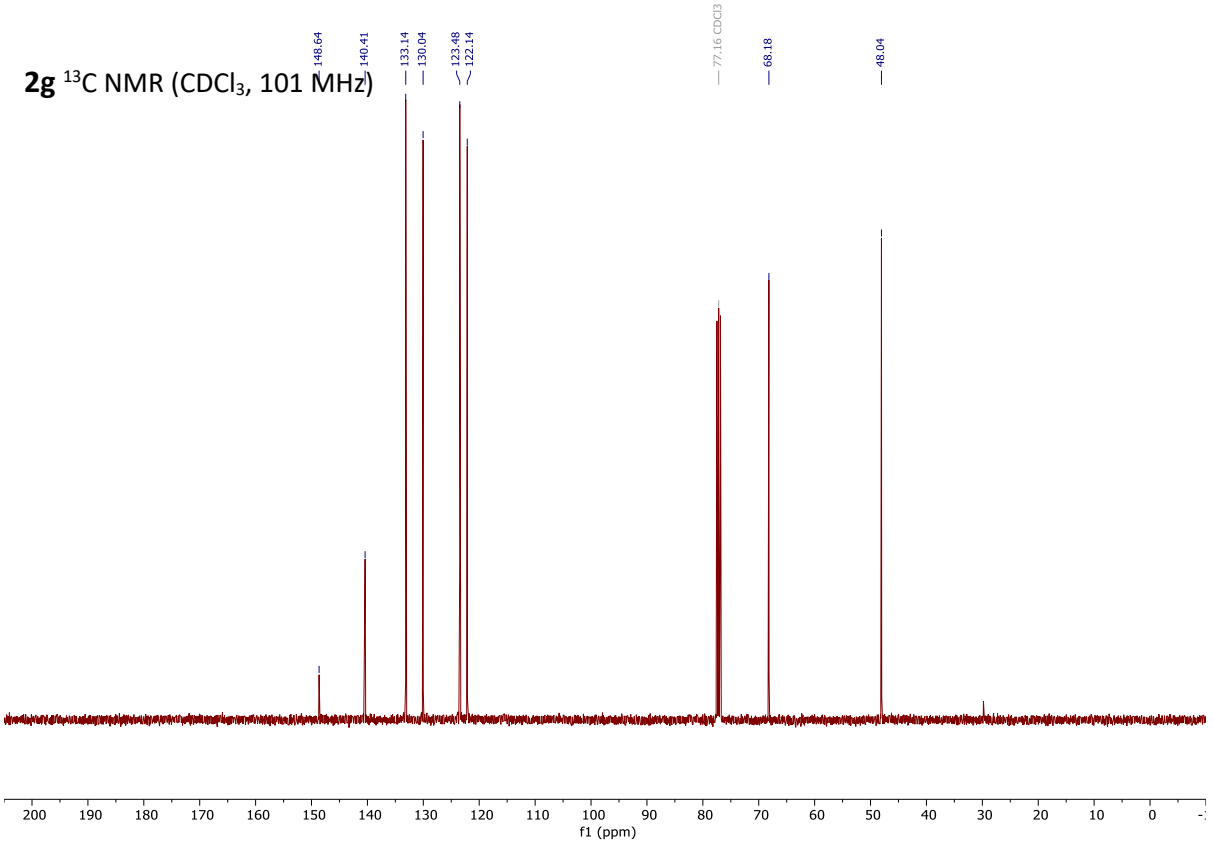


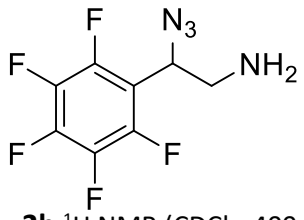


2g ^{1}H NMR ($CDCl_3$, 400 MHz)

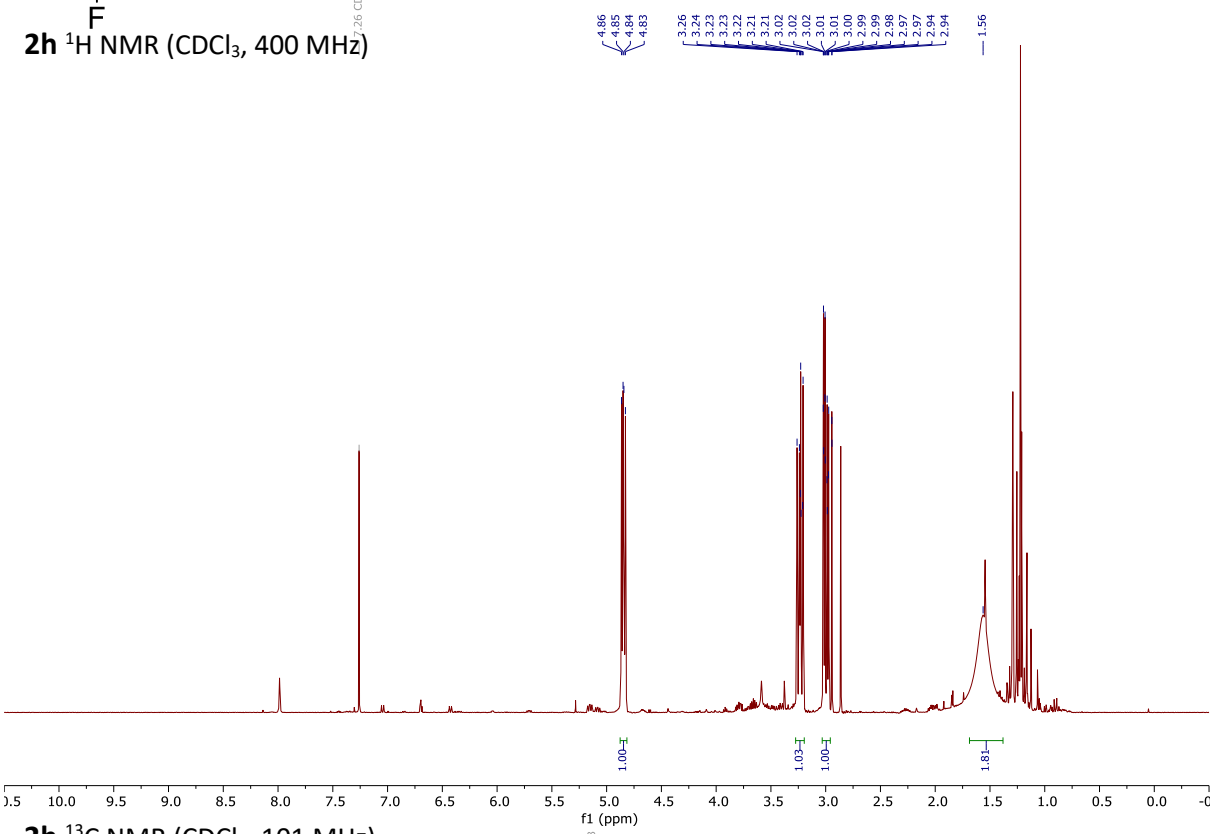


2g ^{13}C NMR ($CDCl_3$, 101 MHz)

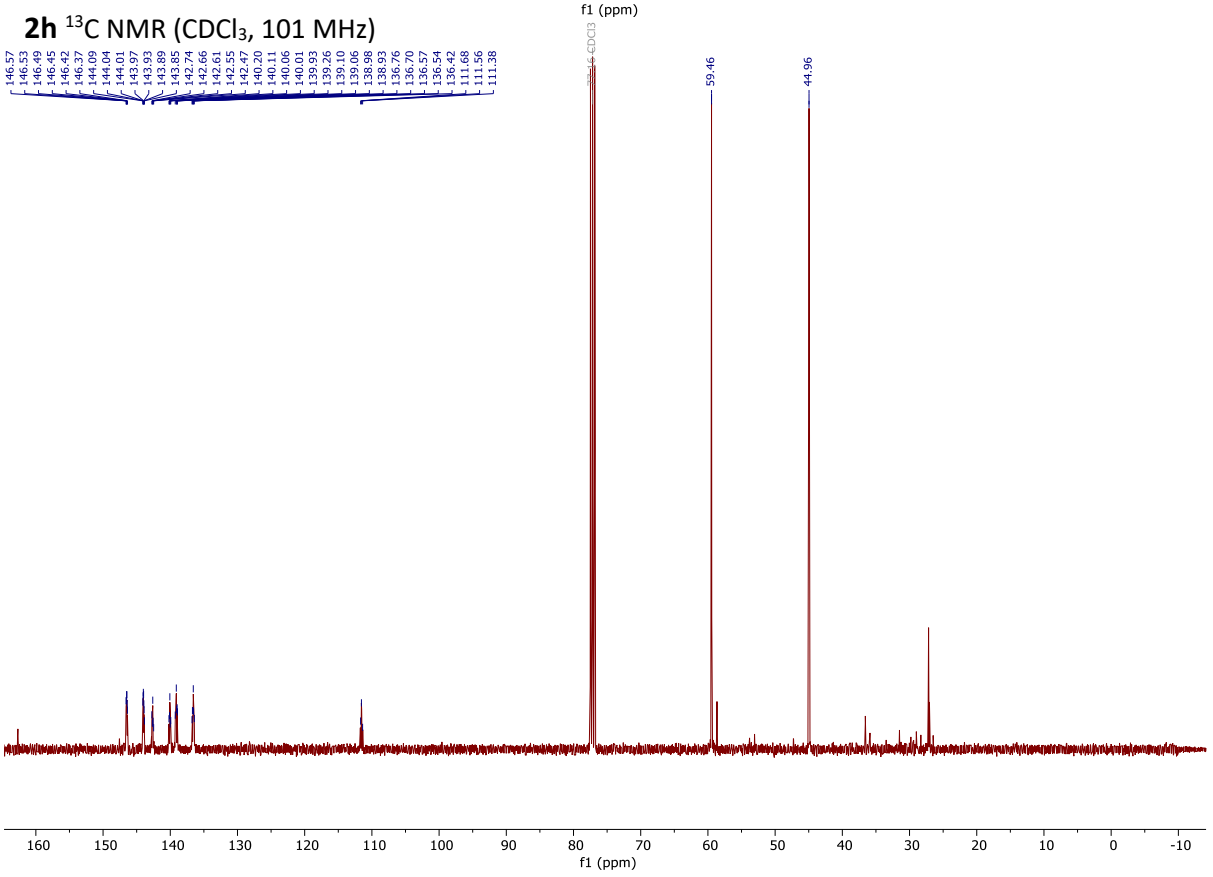


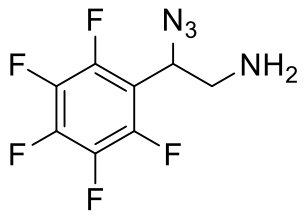


2h ^{1}H NMR ($CDCl_3$, 400 MHz)

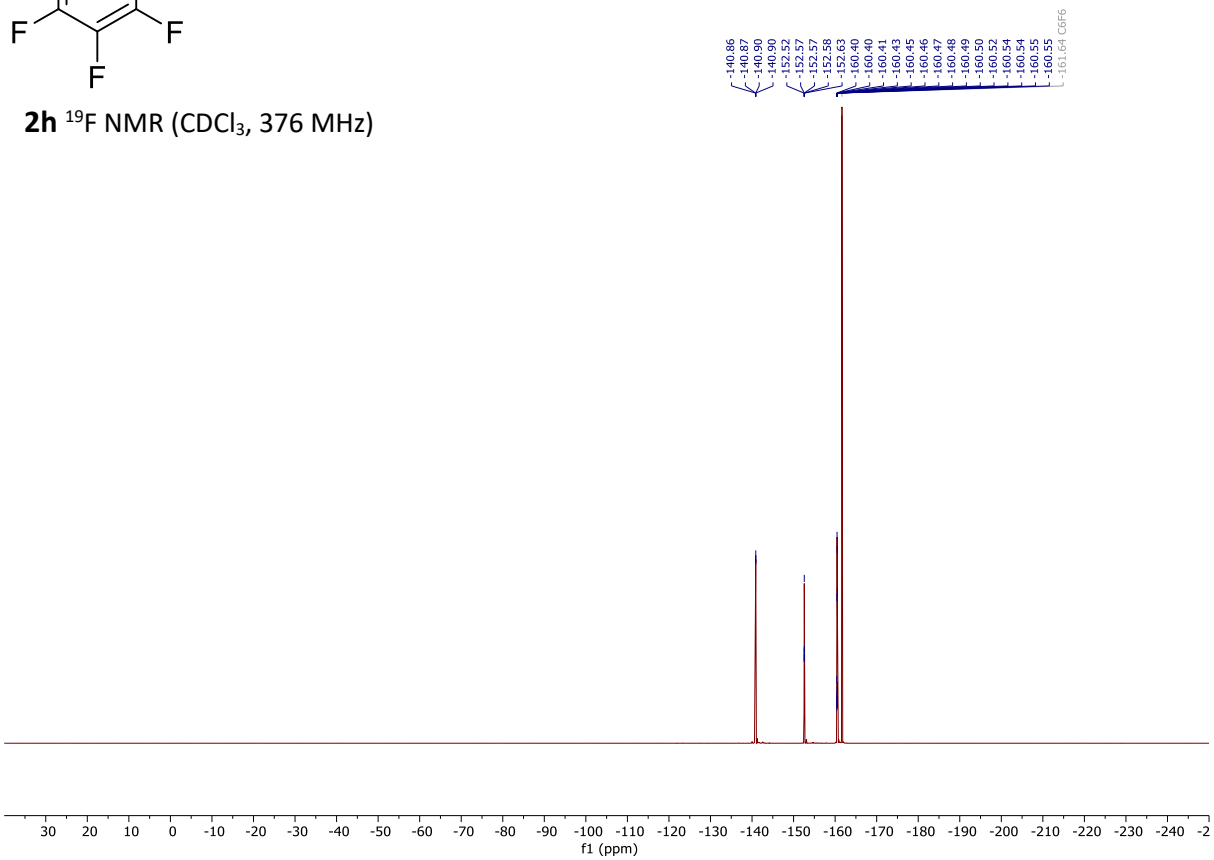


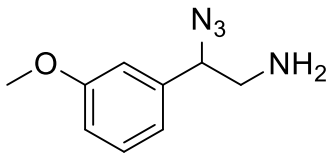
2h ^{13}C NMR ($CDCl_3$, 101 MHz)



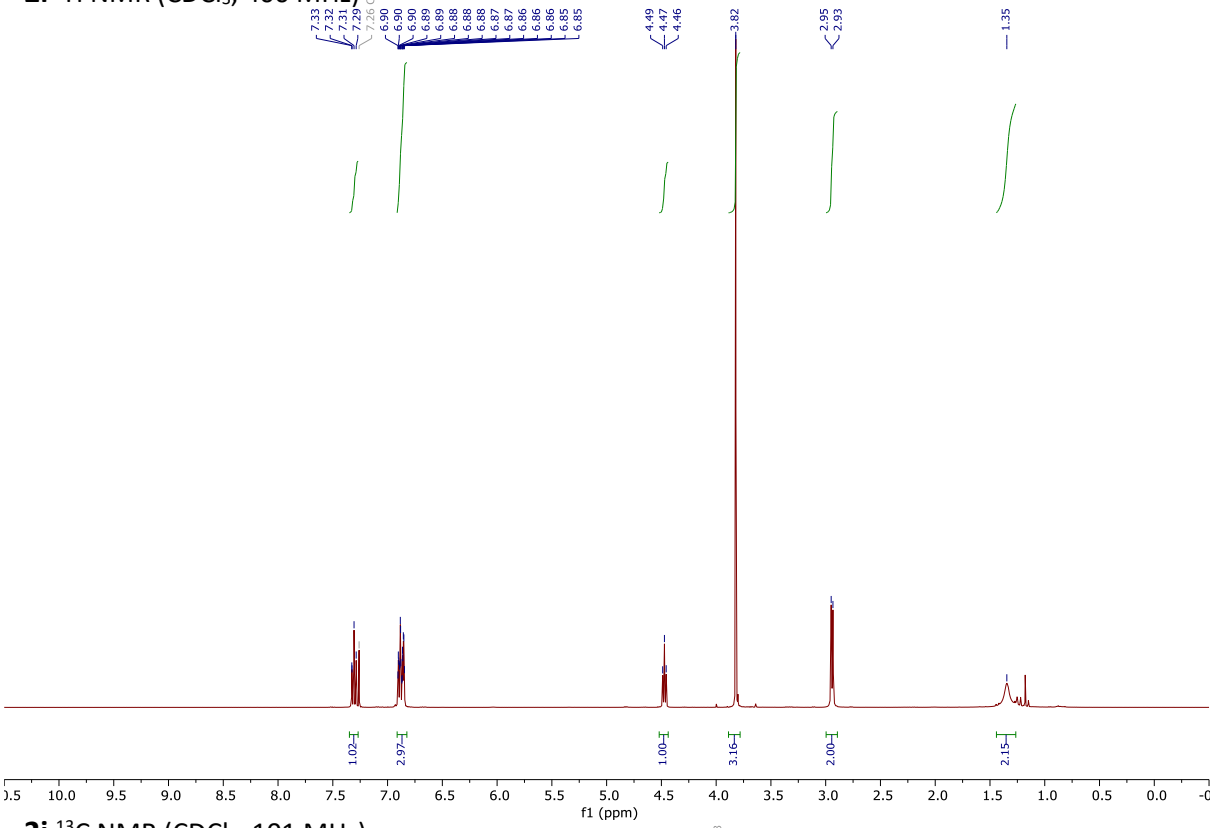


2h ^{19}F NMR ($CDCl_3$, 376 MHz)

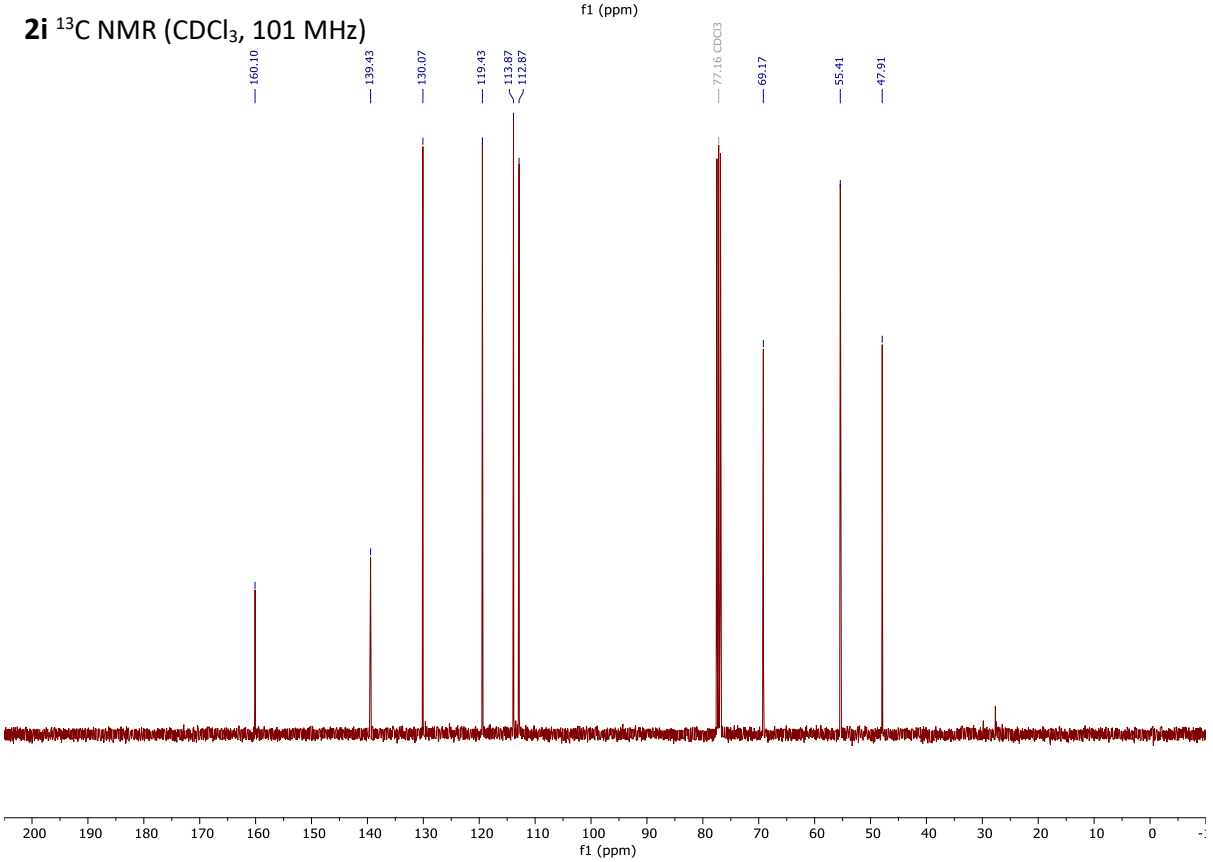


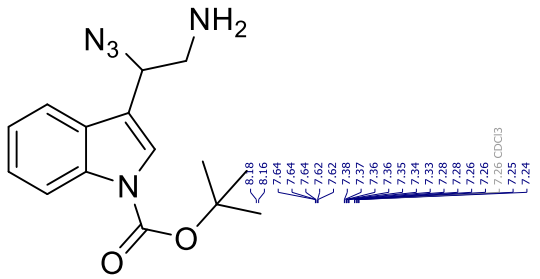


2i ^{1}H NMR ($CDCl_3$, 400 MHz)

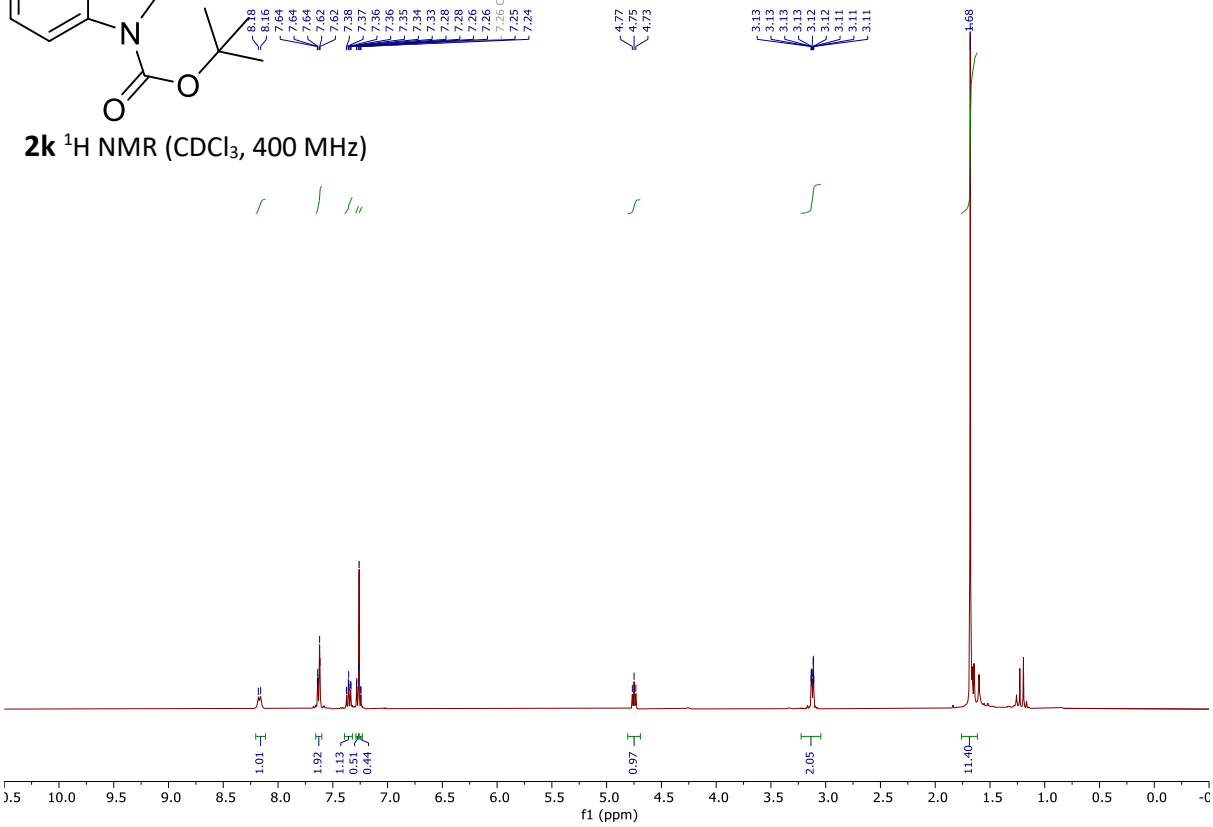


2i ^{13}C NMR ($CDCl_3$, 101 MHz)

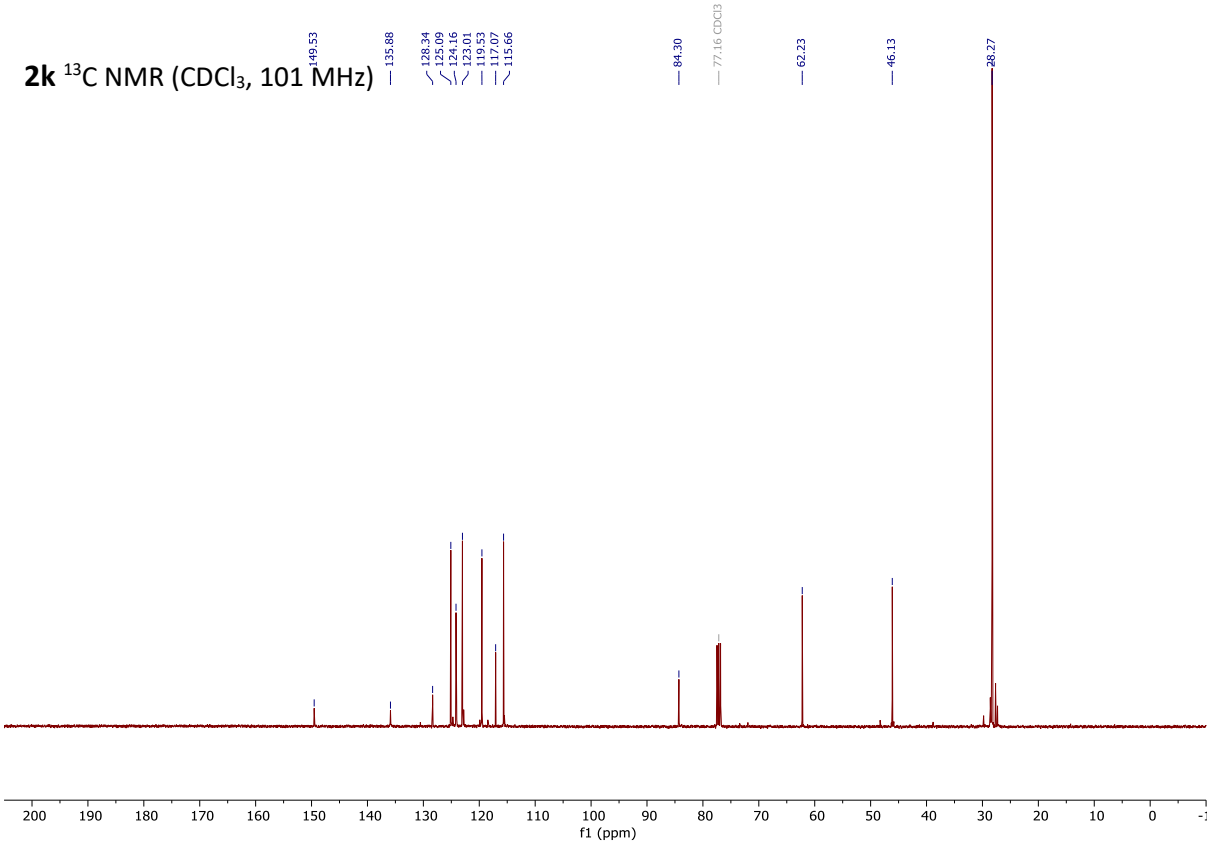


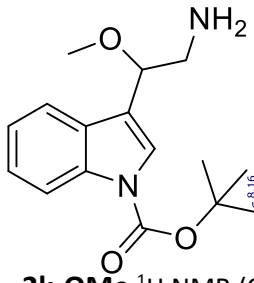


2k ^{1}H NMR ($CDCl_3$, 400 MHz)



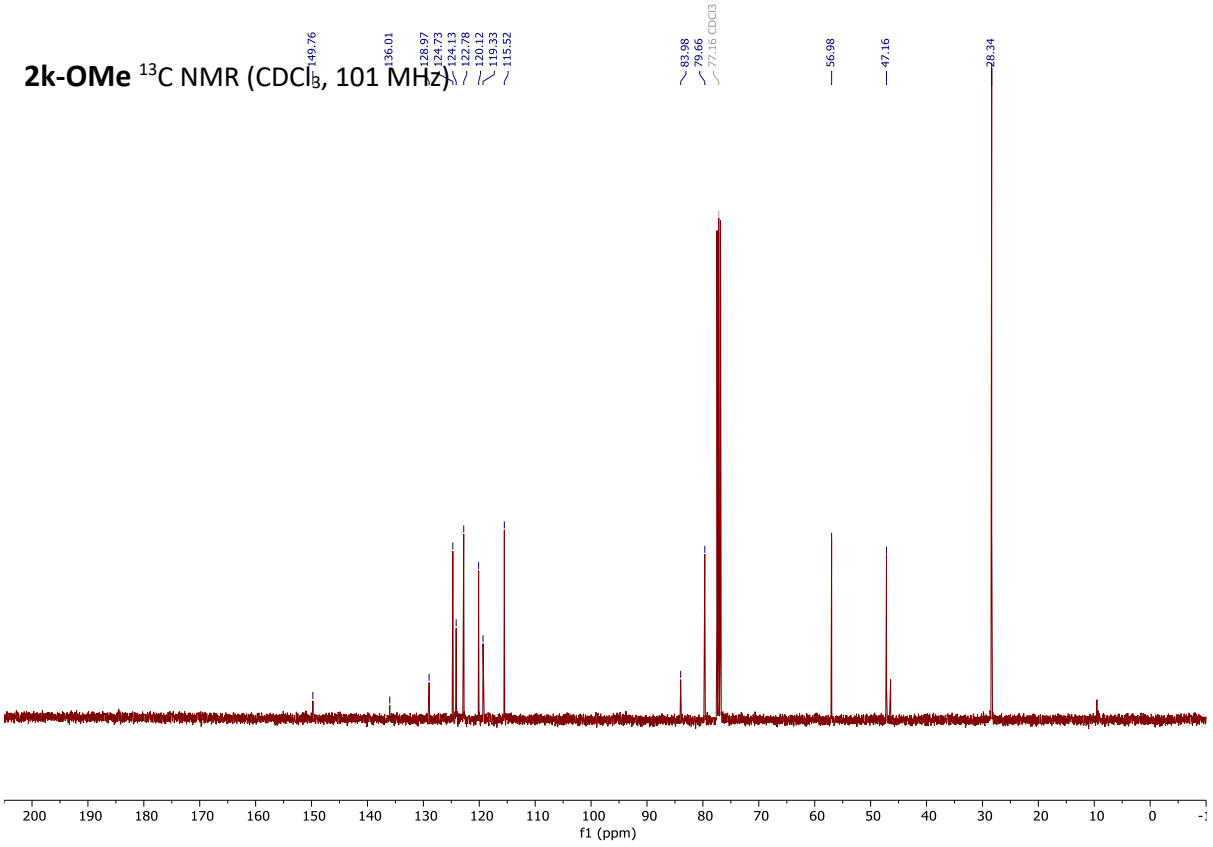
2k ^{13}C NMR ($CDCl_3$, 101 MHz)

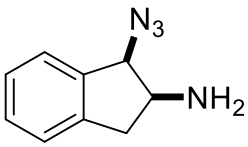




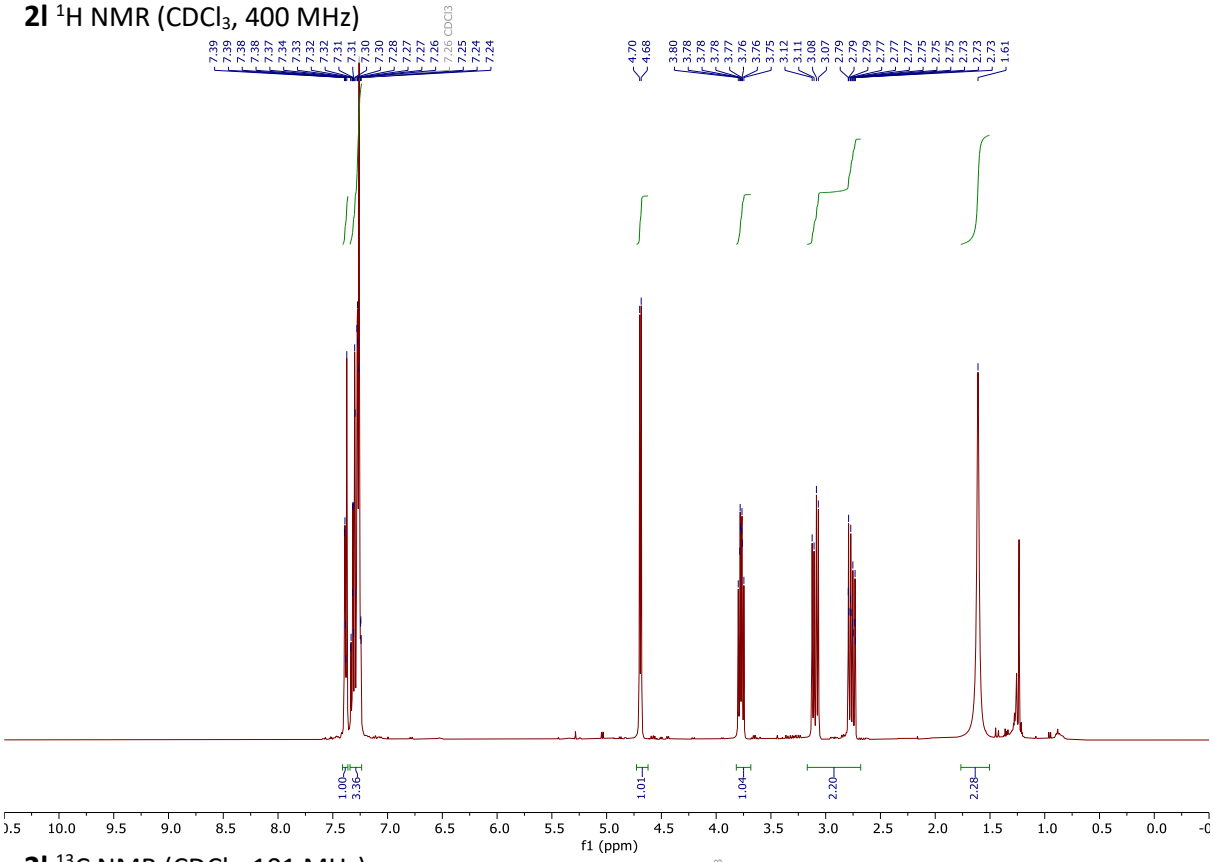
2k-OMe ^{1}H NMR ($CDCl_3$, 400 MHz)

2k-OMe ^{13}C NMR ($CDCl_3$, 101 MHz)

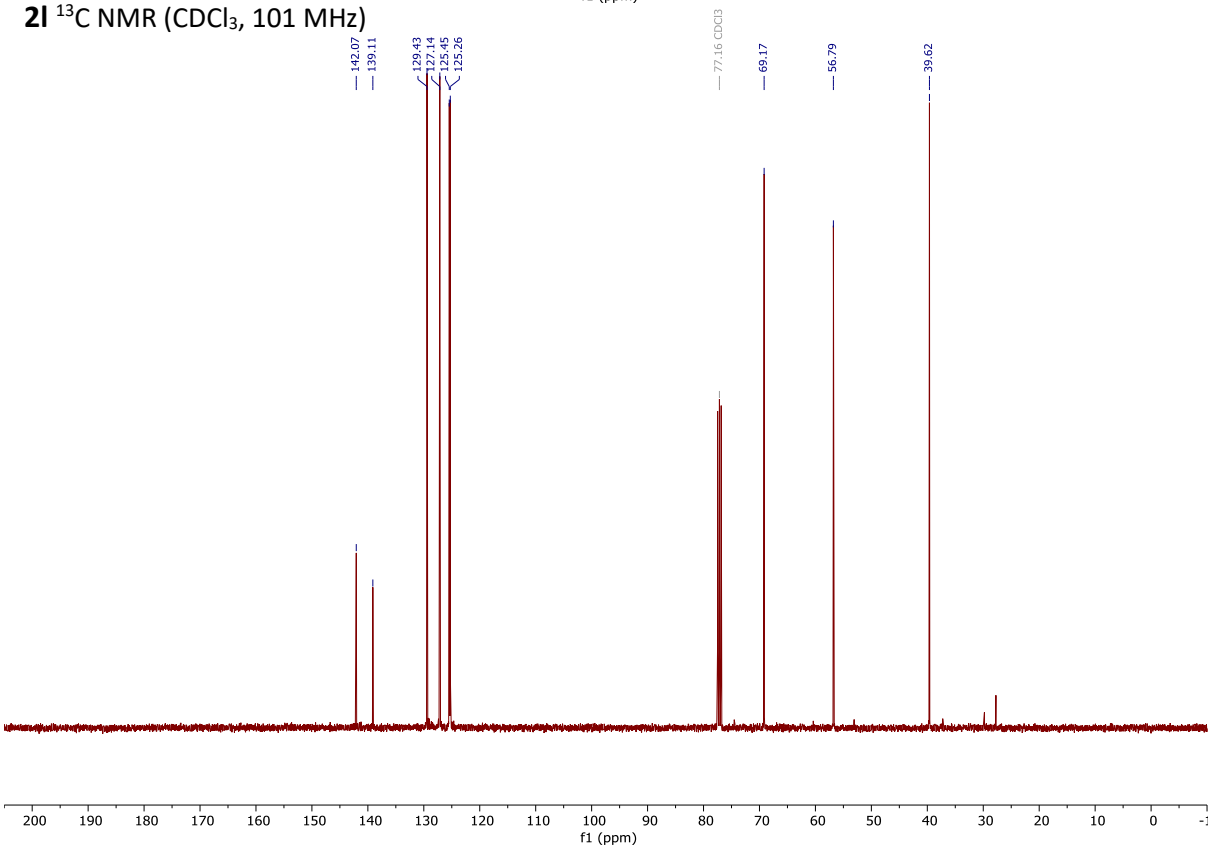


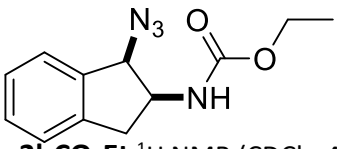


2l ^{1}H NMR ($CDCl_3$, 400 MHz)

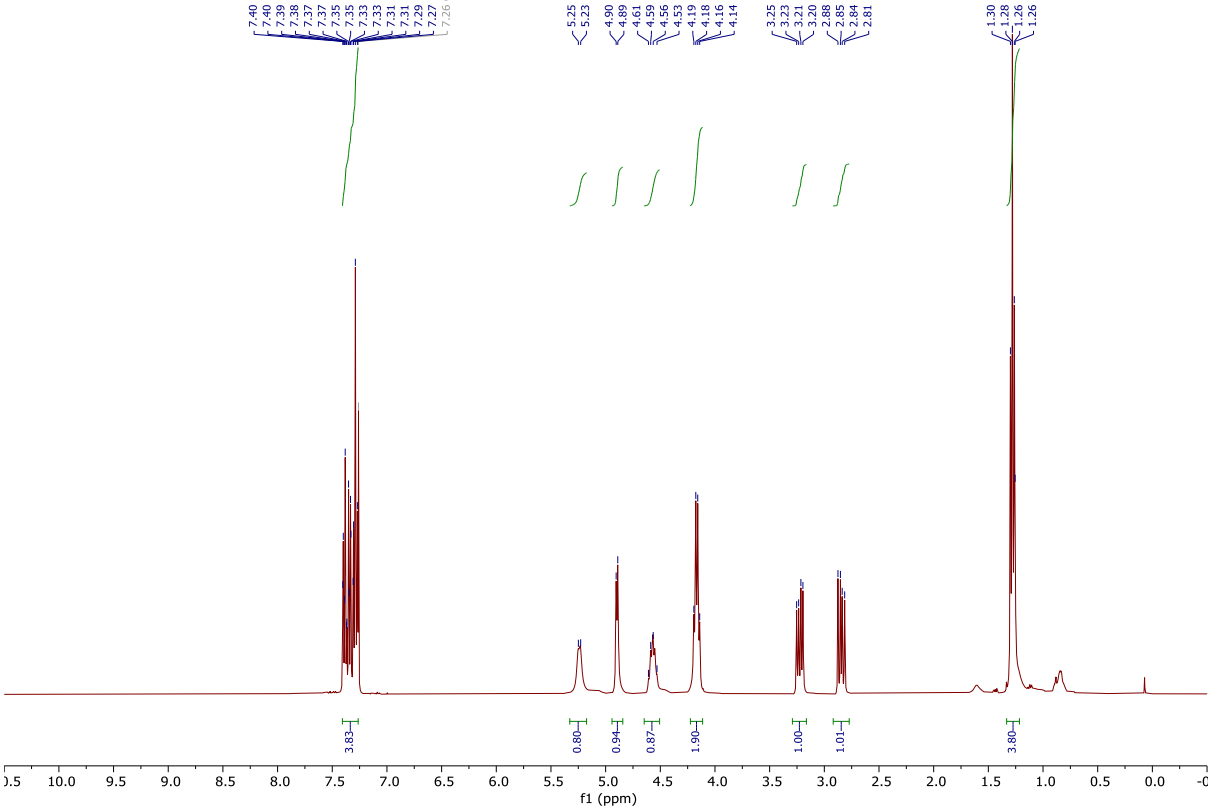


2l ^{13}C NMR ($CDCl_3$, 101 MHz)

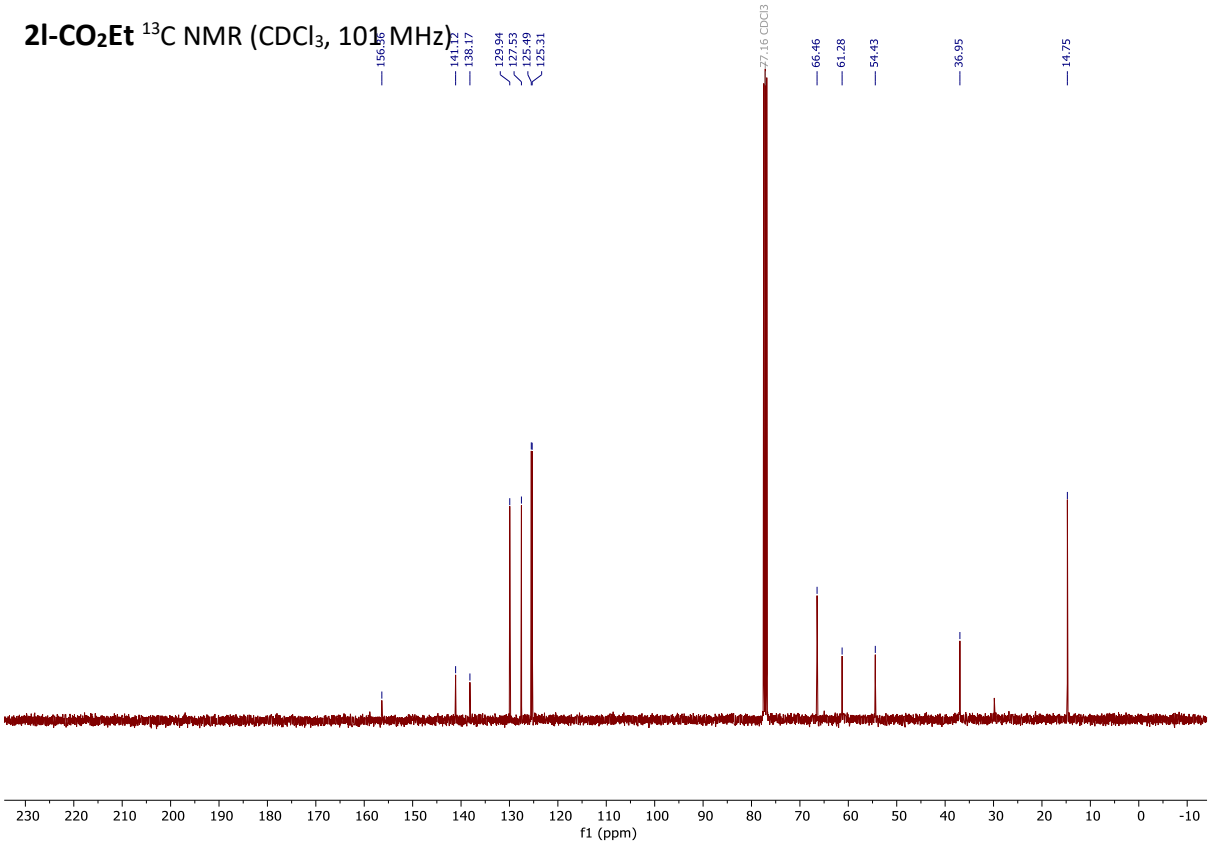


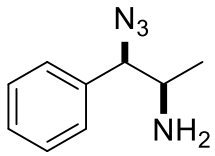


2l-CO_2Et ^{1}H NMR ($CDCl_3$, 400 MHz)

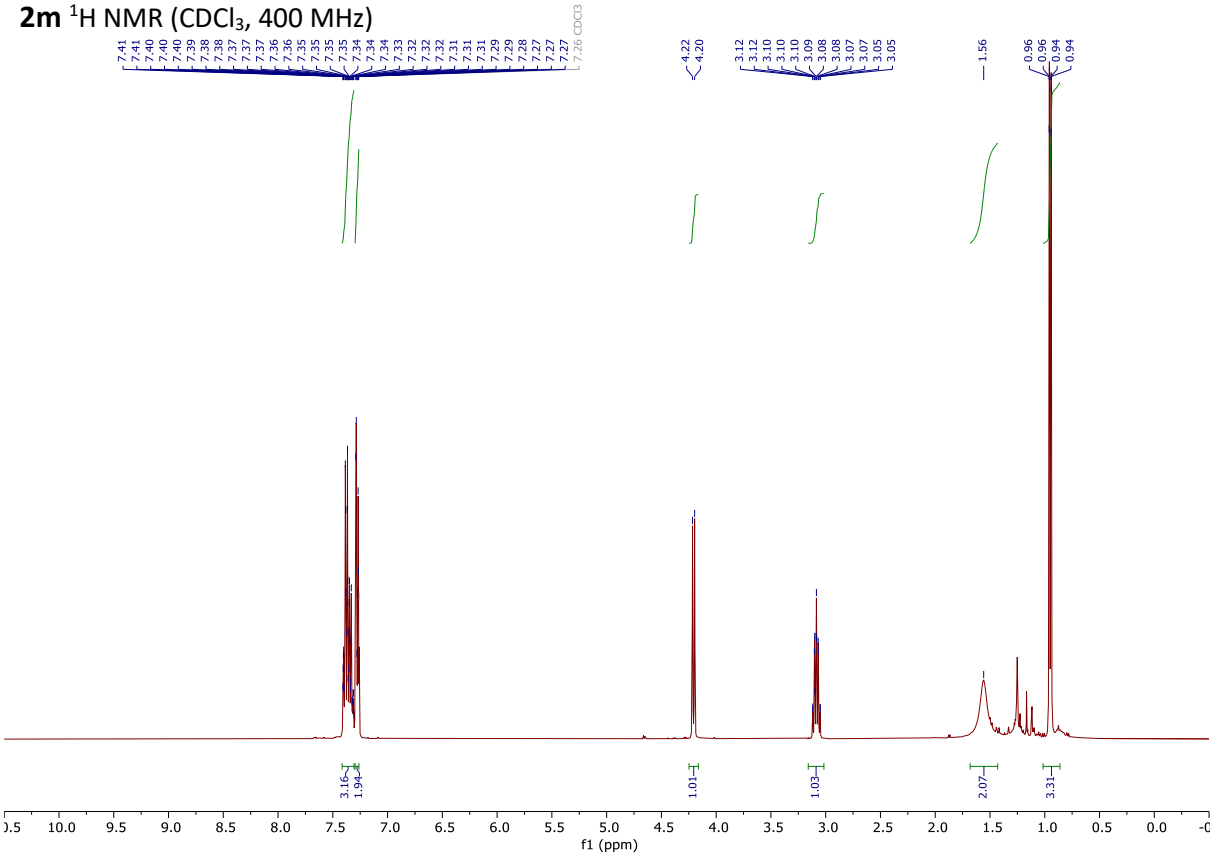


2l-CO_2Et ^{13}C NMR ($CDCl_3$, 101 MHz)

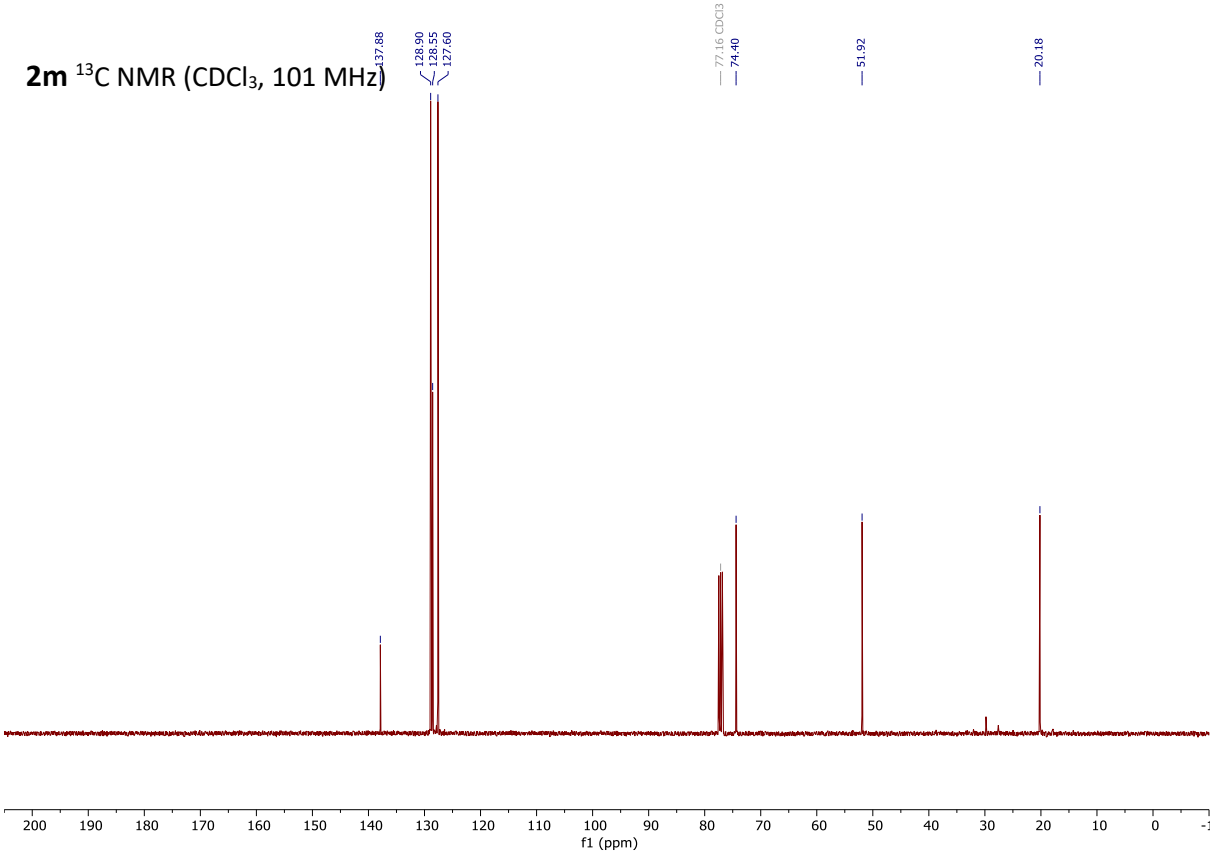


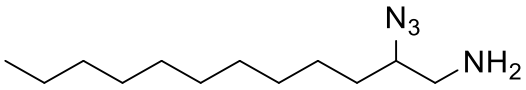


2m ^{1}H NMR ($CDCl_3$, 400 MHz)

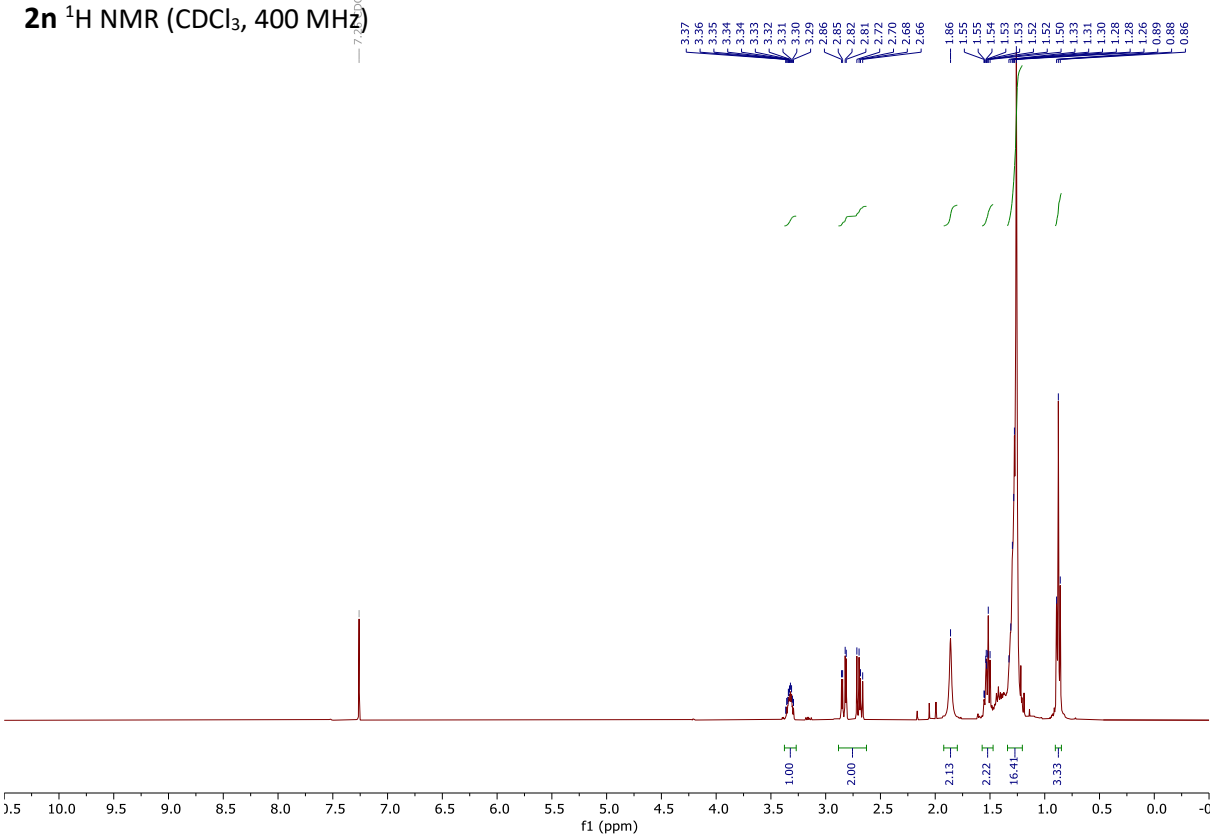


2m ^{13}C NMR ($CDCl_3$, 101 MHz)

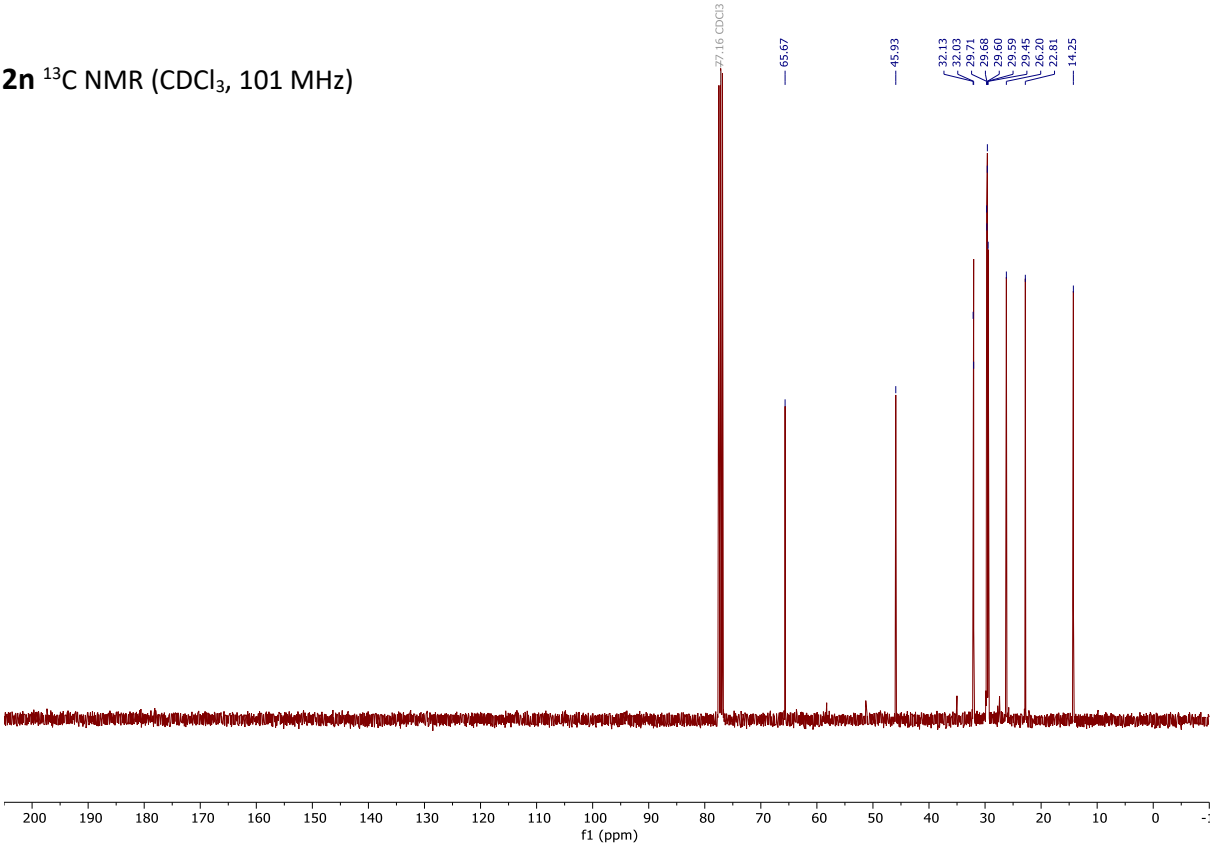


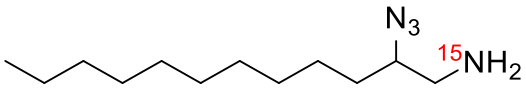


2n ^{1}H NMR ($CDCl_3$, 400 MHz)

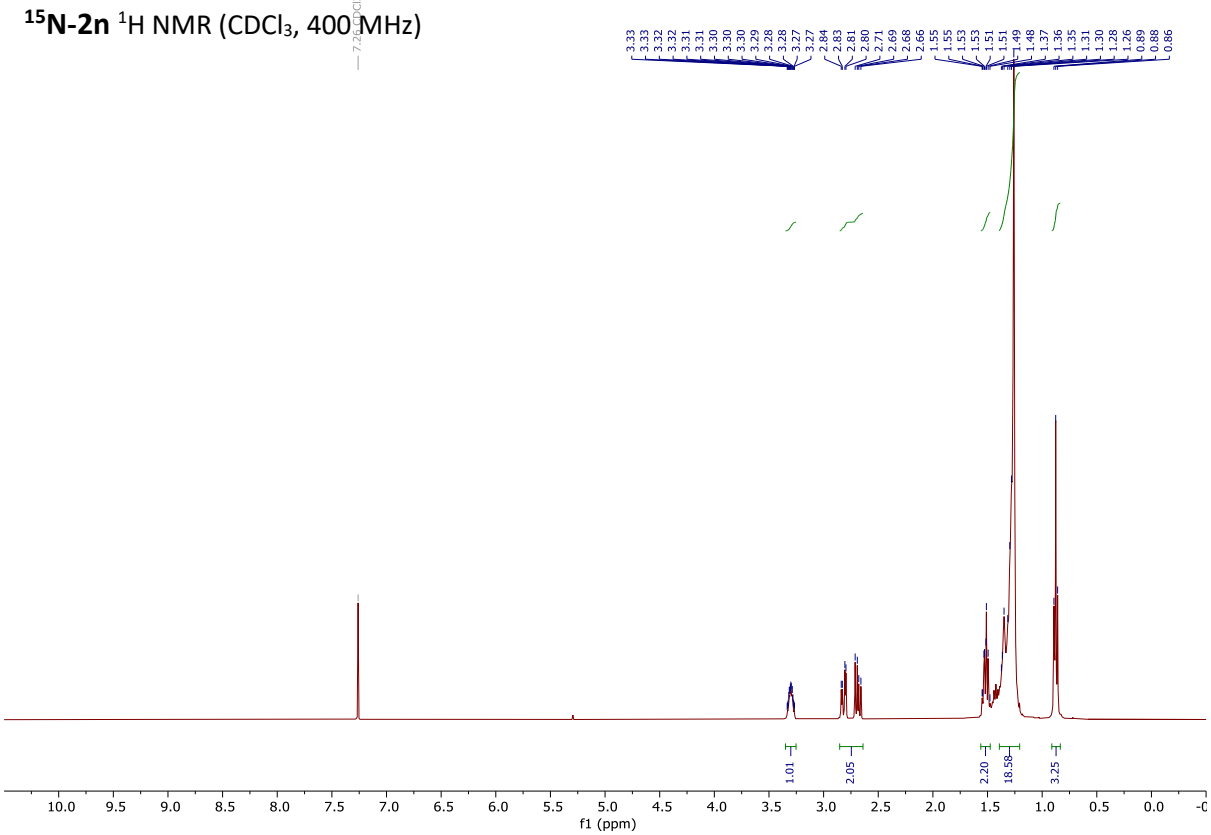


2n ^{13}C NMR ($CDCl_3$, 101 MHz)

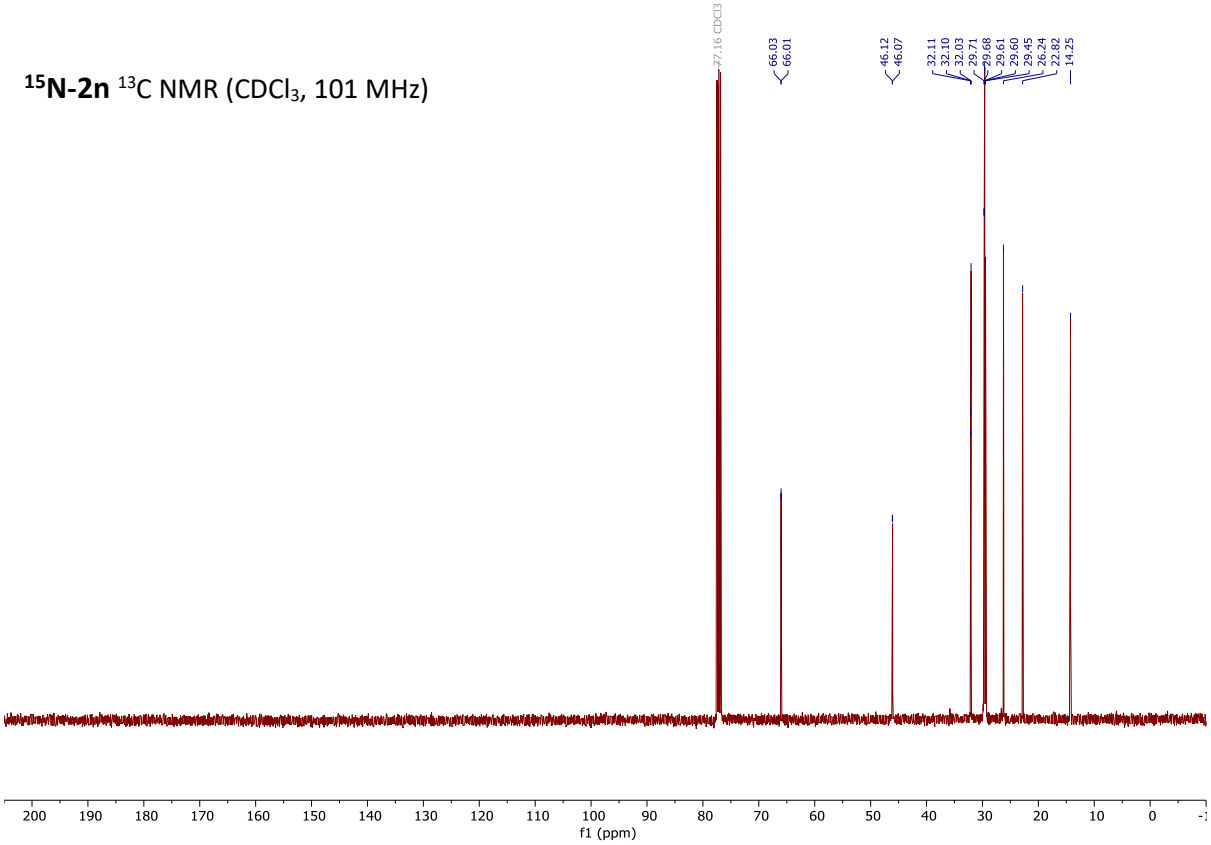


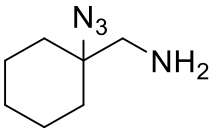


^{15}N-2n ^{1}H NMR ($CDCl_3$, 400 MHz)

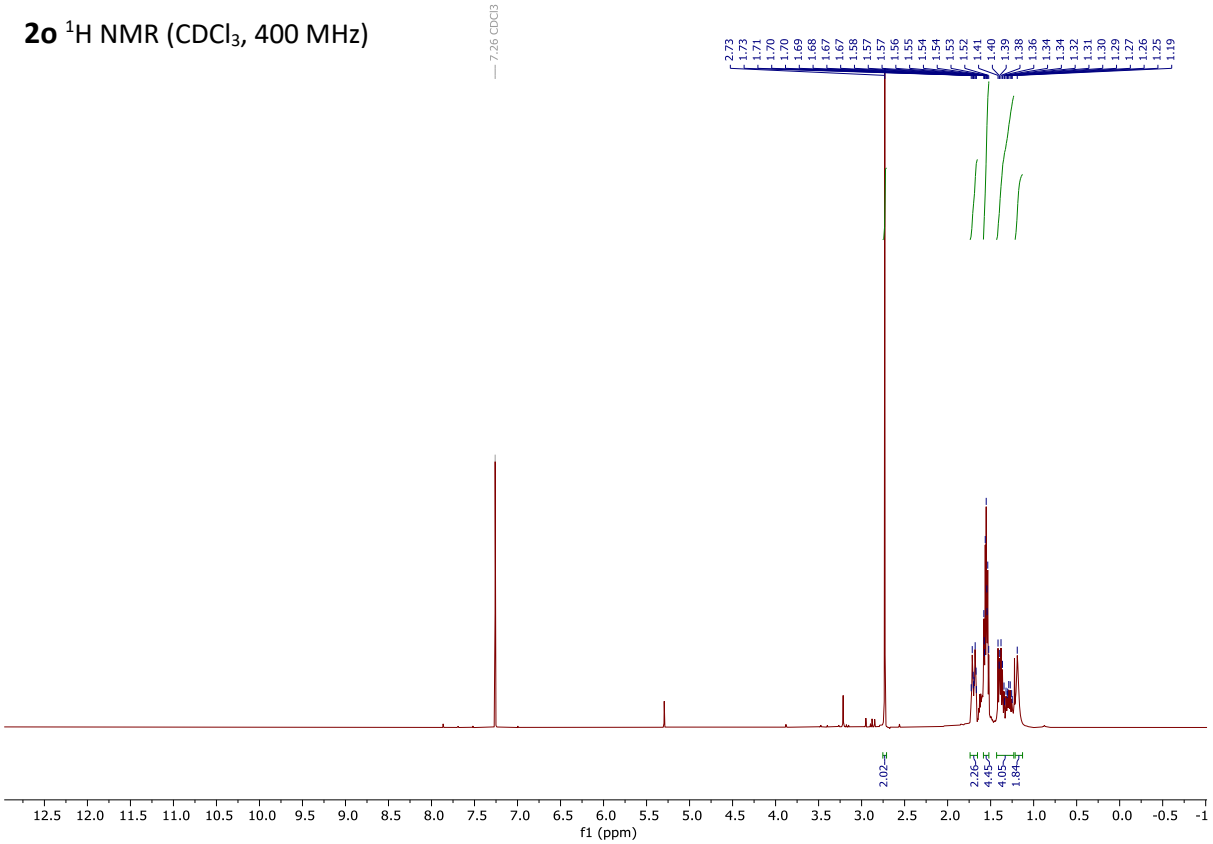


^{15}N-2n ^{13}C NMR ($CDCl_3$, 101 MHz)

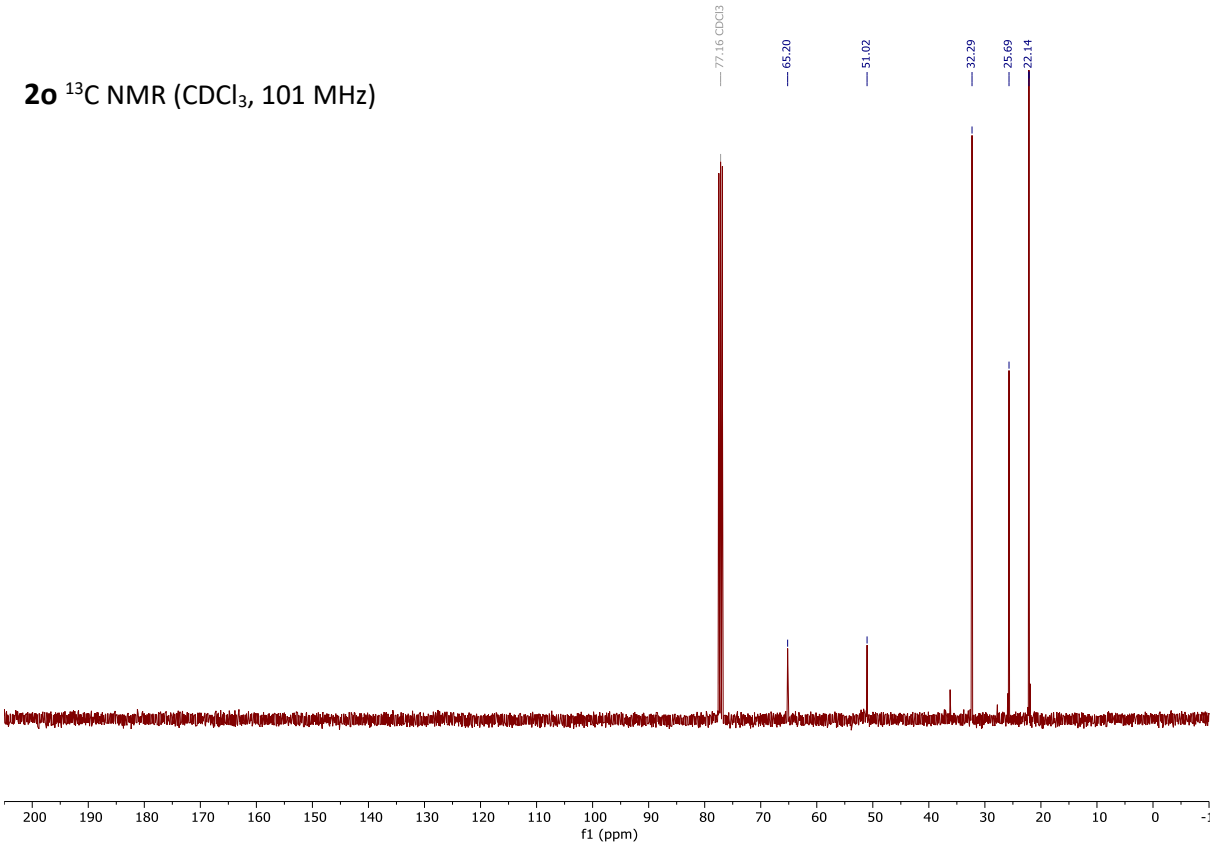


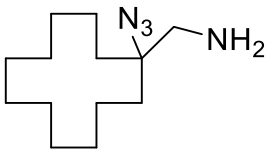


2o ^{1}H NMR ($CDCl_3$, 400 MHz)

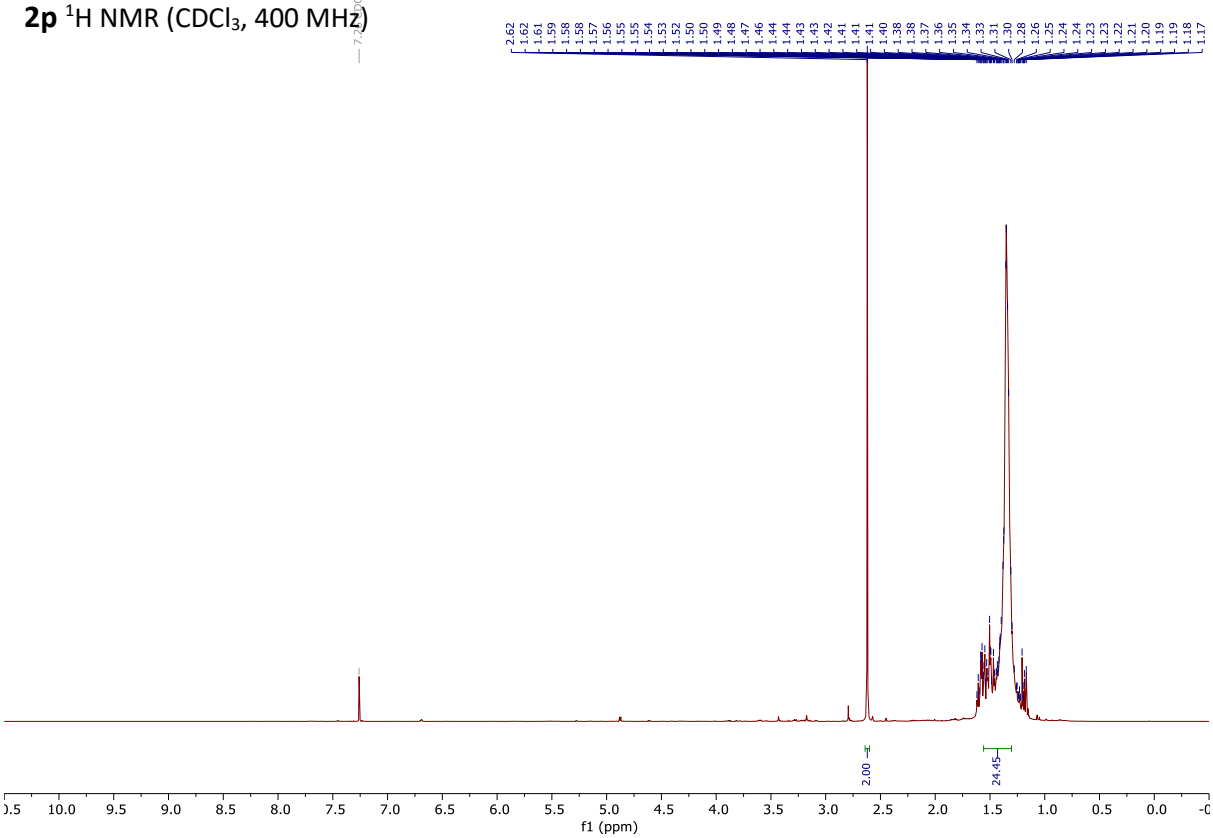


2o ^{13}C NMR ($CDCl_3$, 101 MHz)

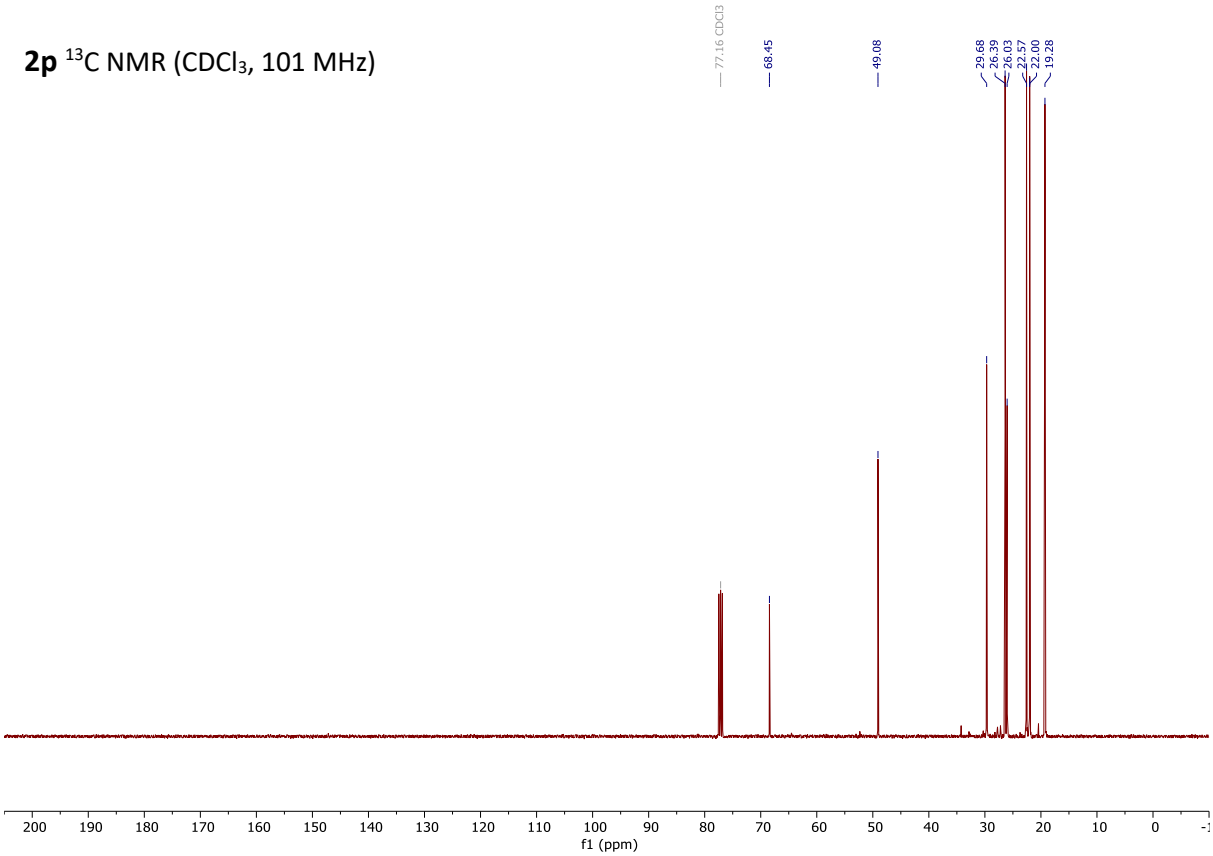


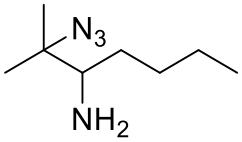


2p ^{1}H NMR ($CDCl_3$, 400 MHz)

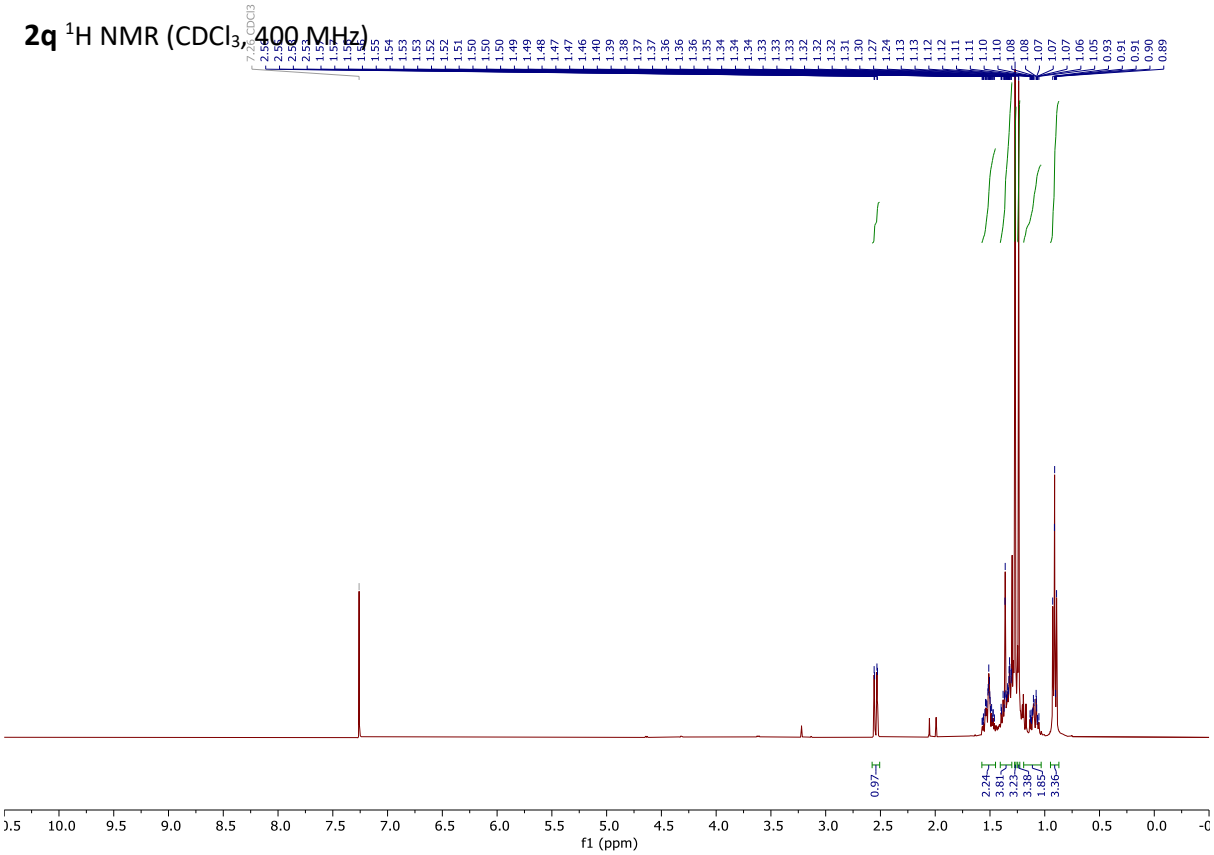


2p ^{13}C NMR ($CDCl_3$, 101 MHz)

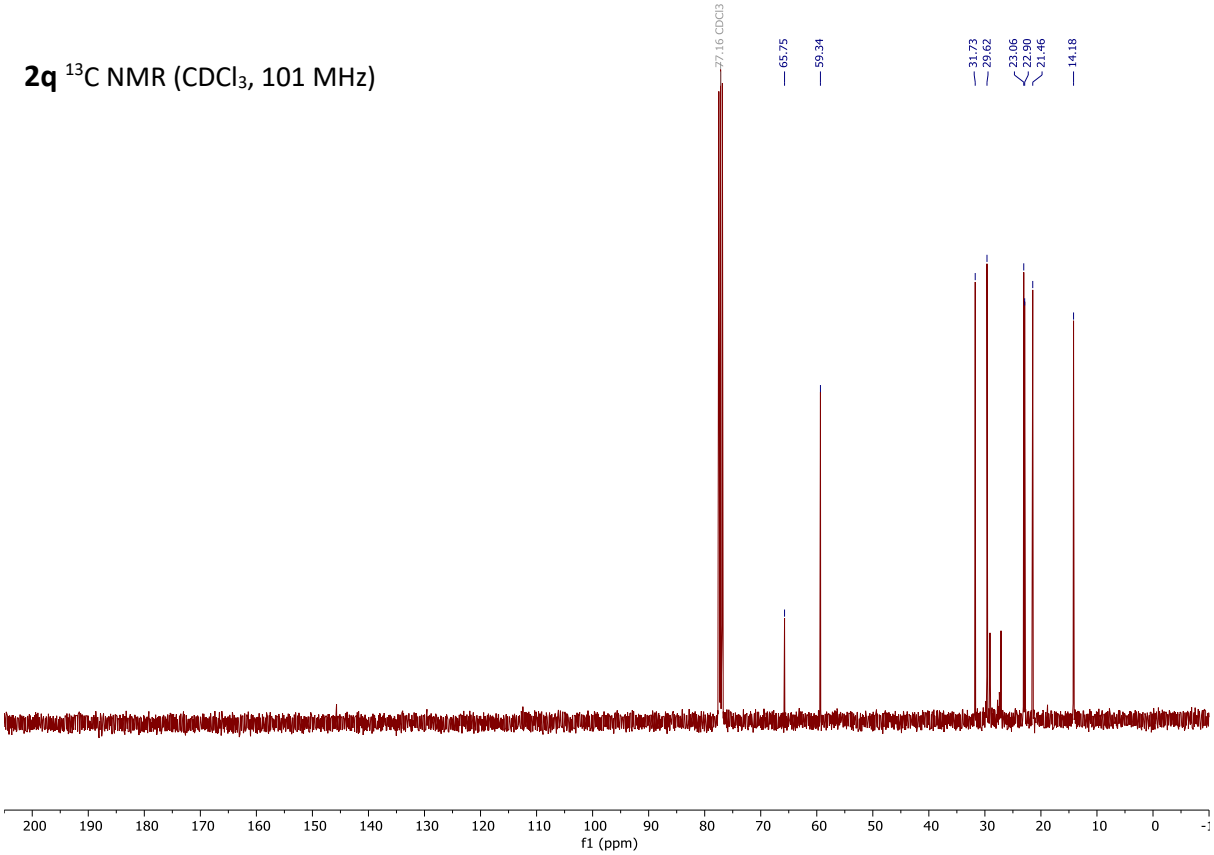


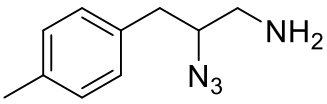


2q ^{1}H NMR ($CDCl_3$, 400 MHz)

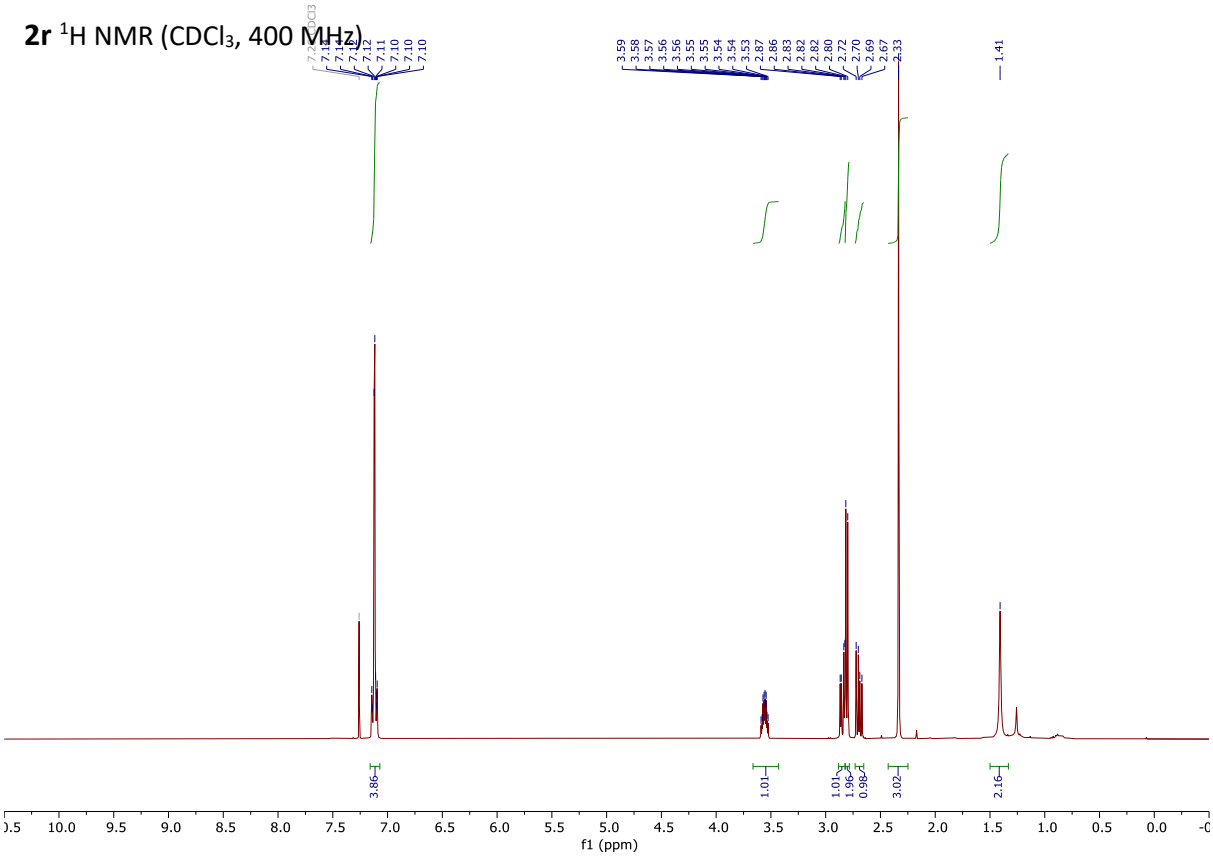


2q ^{13}C NMR ($CDCl_3$, 101 MHz)

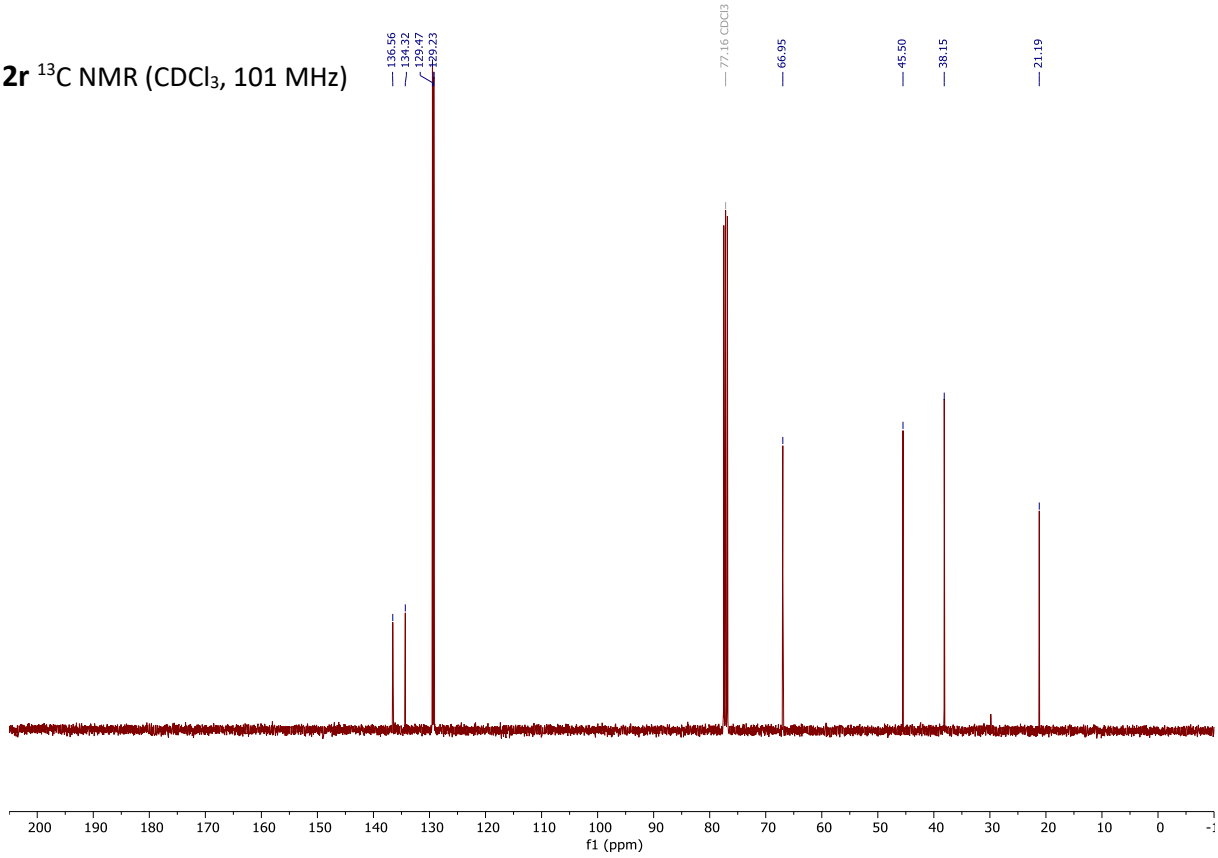


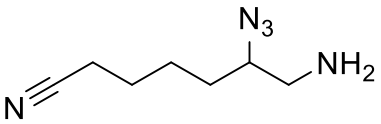


2r ^{1}H NMR ($CDCl_3$, 400 MHz)

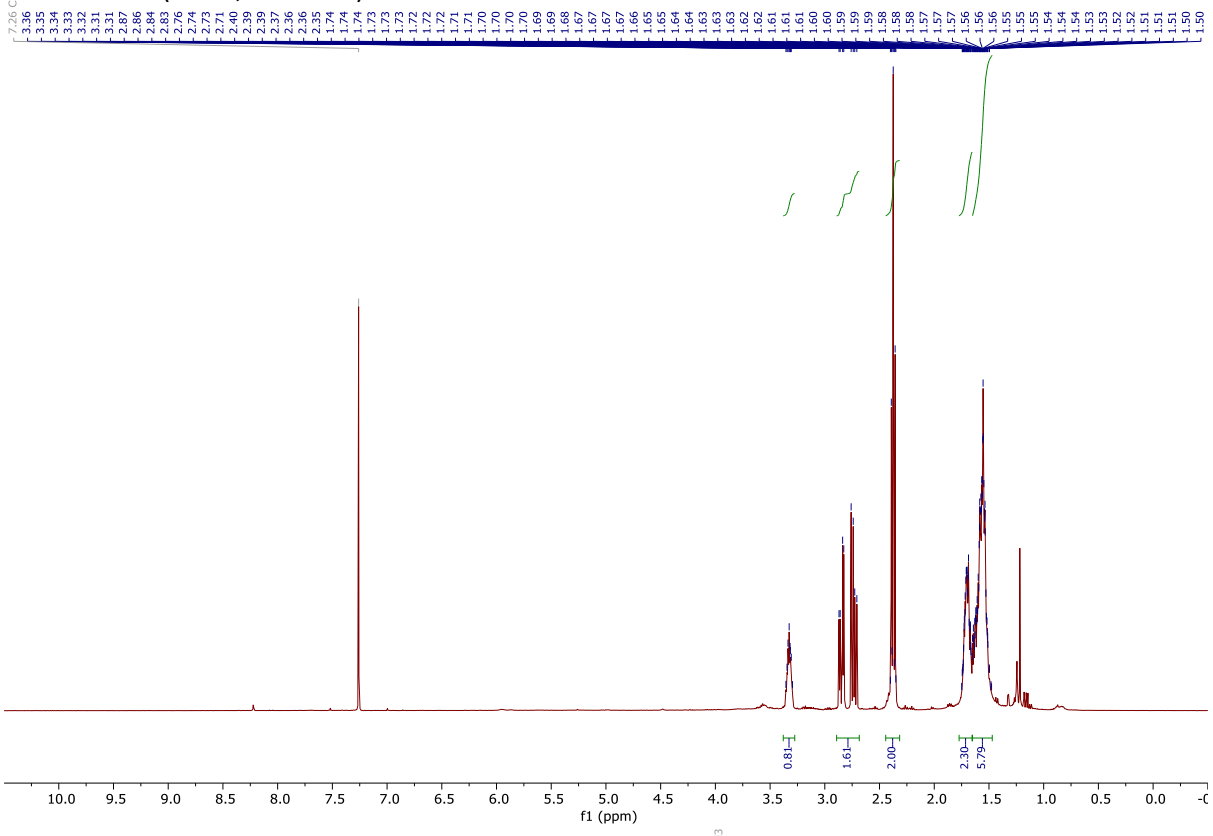


2r ^{13}C NMR ($CDCl_3$, 101 MHz)

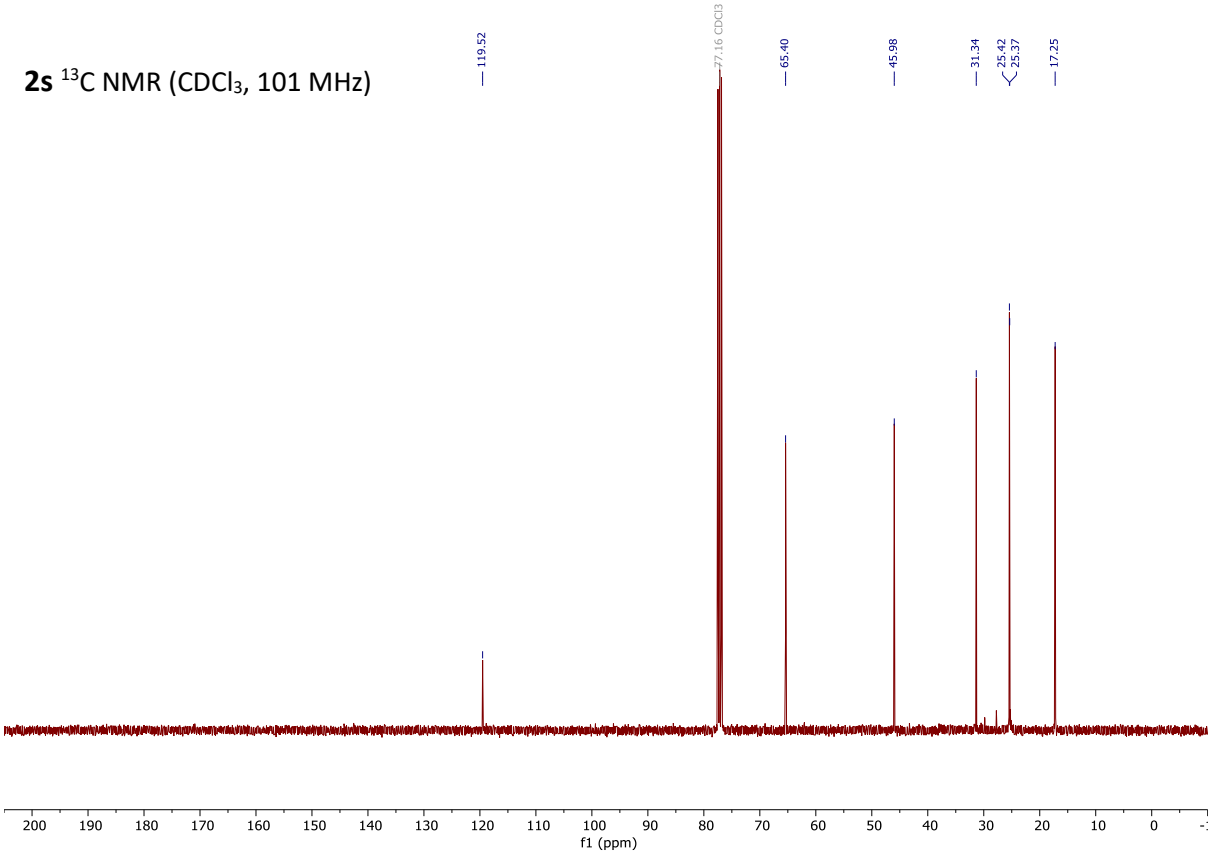


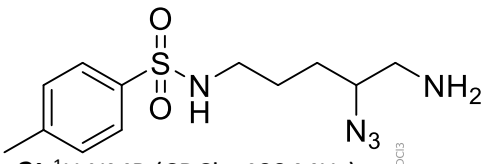


2s ^{1}H NMR ($CDCl_3$, 400 MHz)

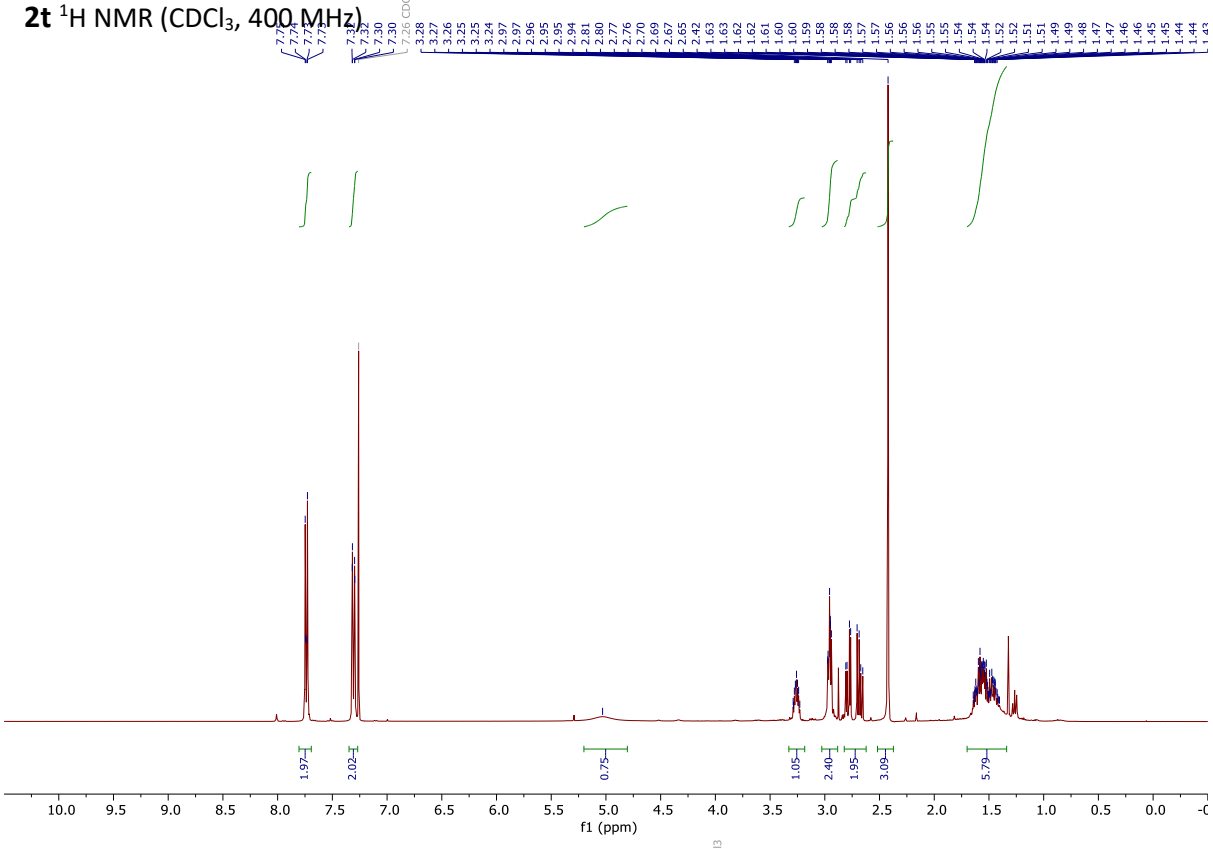


2s ^{13}C NMR ($CDCl_3$, 101 MHz)

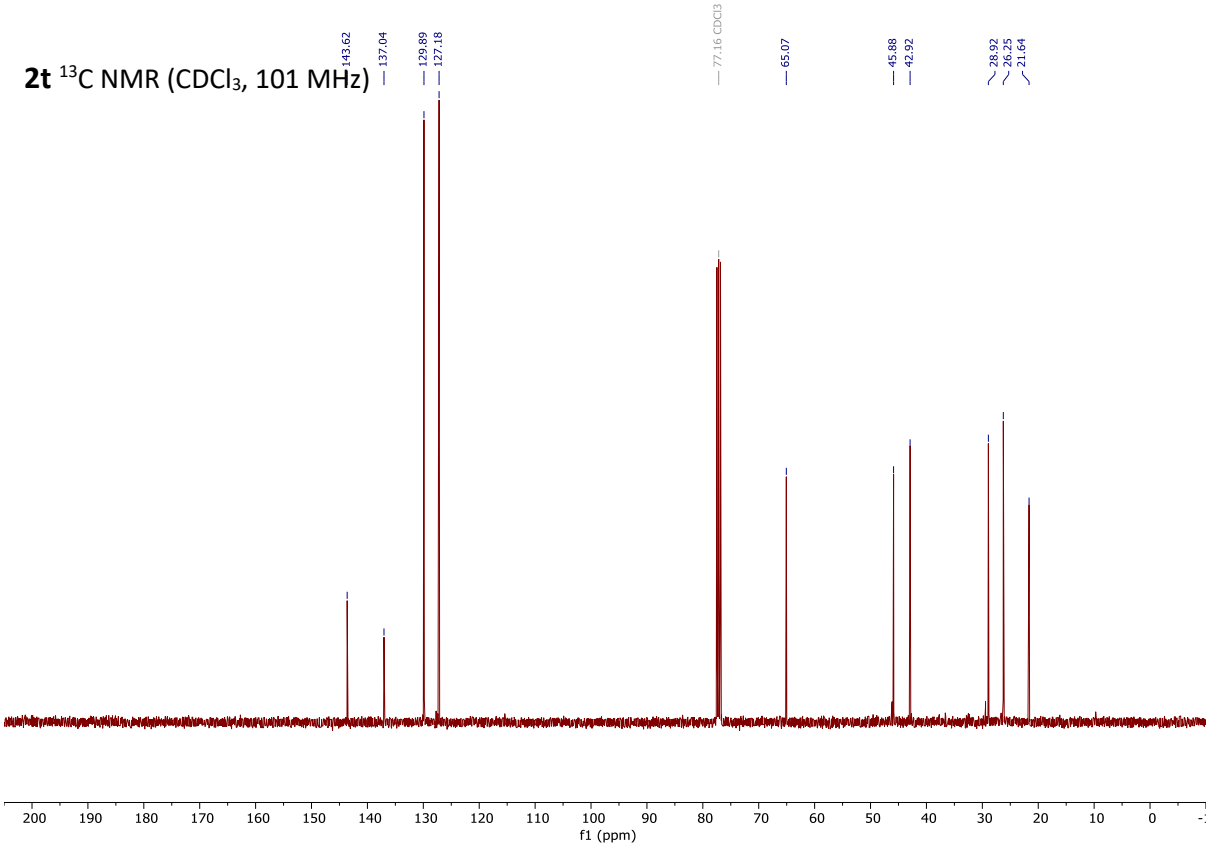


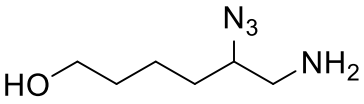


2t ^{1}H NMR ($CDCl_3$, 400 MHz)

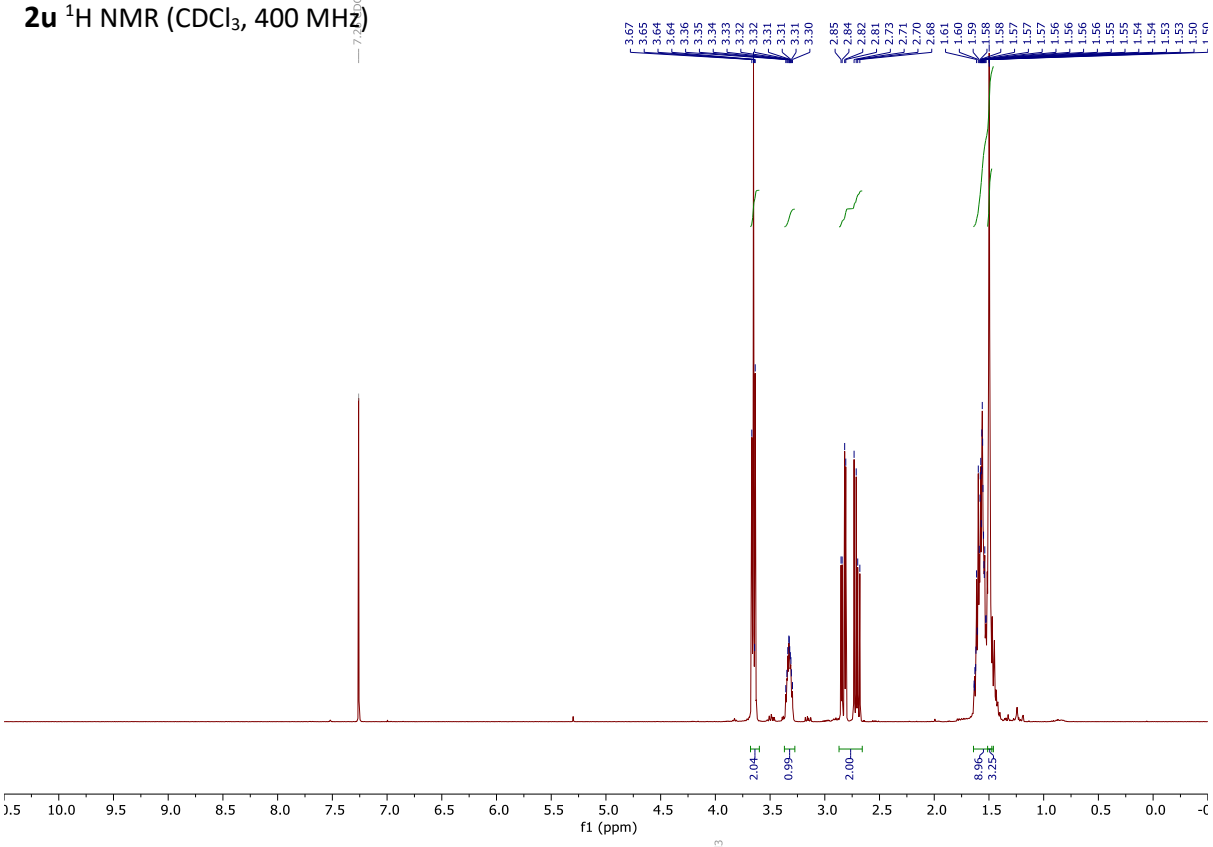


2t ^{13}C NMR ($CDCl_3$, 101 MHz)

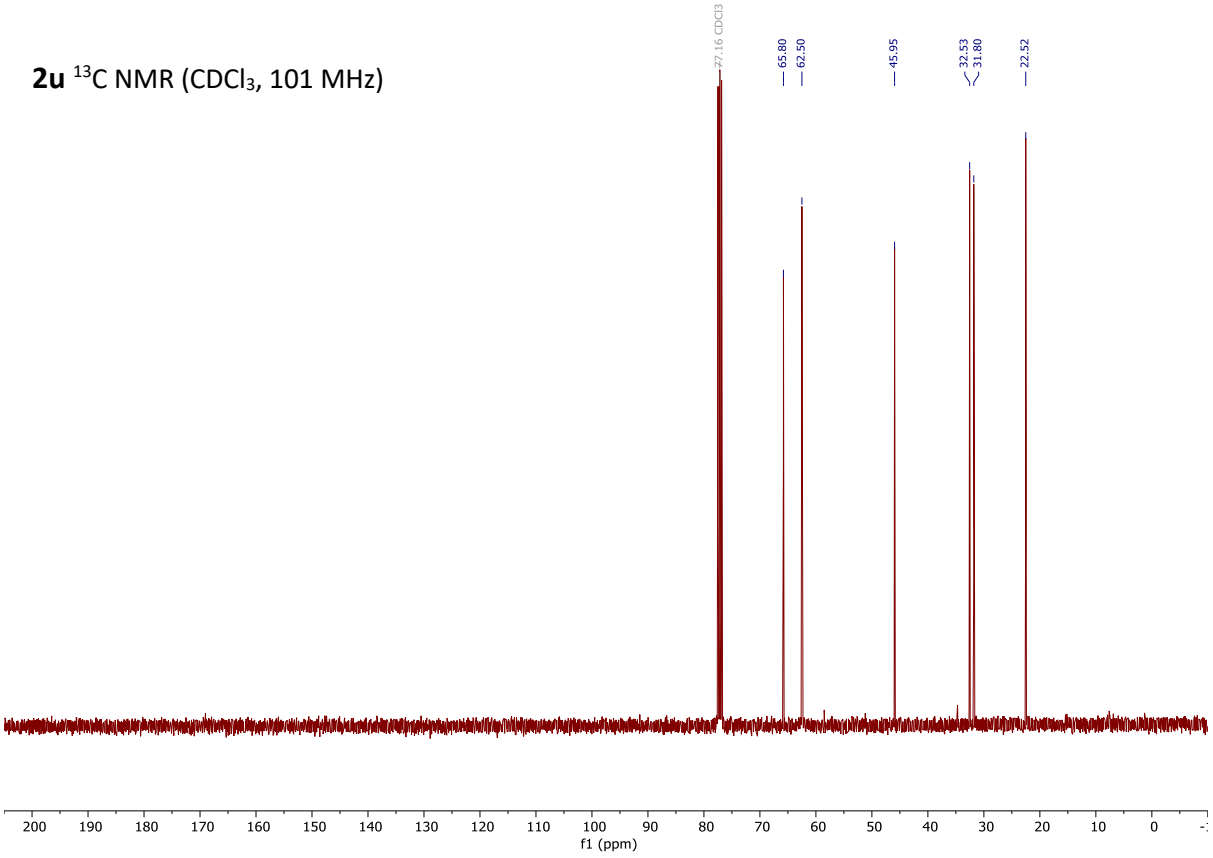


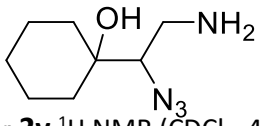


2u ^{1}H NMR ($CDCl_3$, 400 MHz)

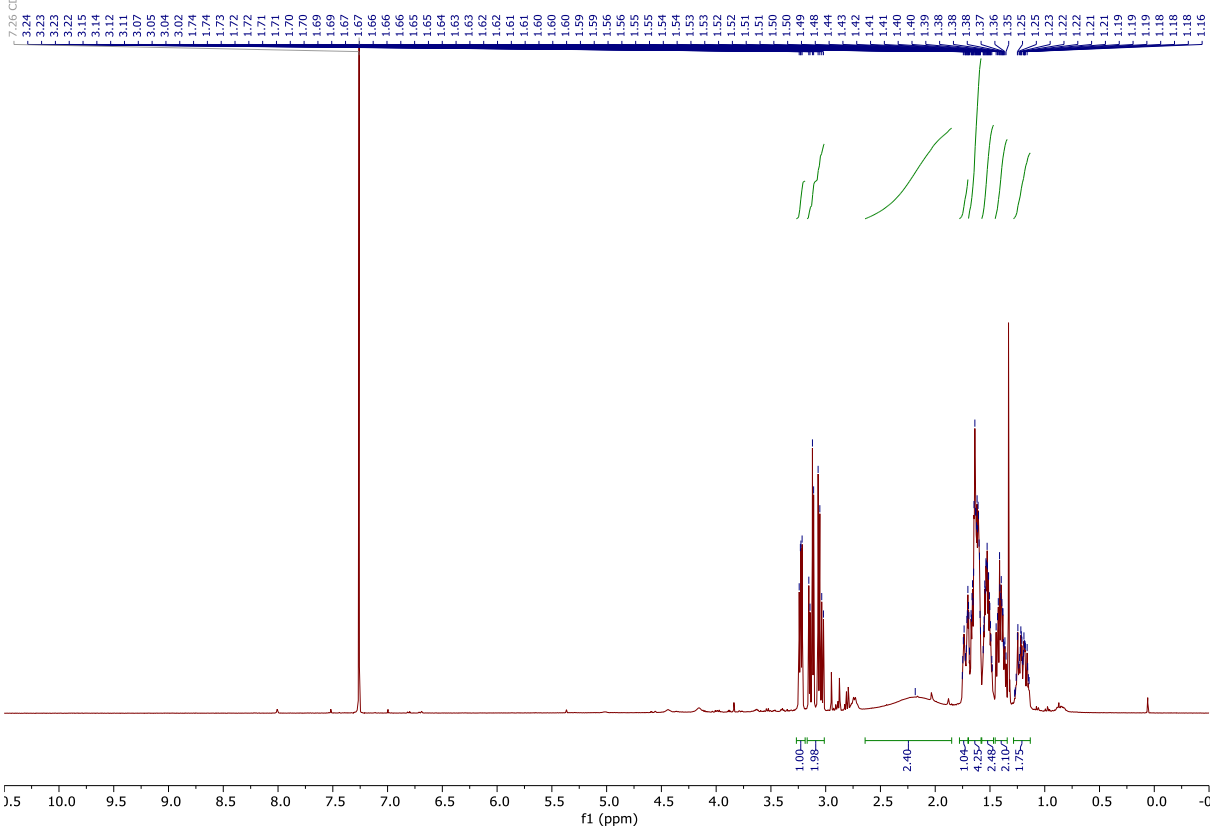


2u ^{13}C NMR ($CDCl_3$, 101 MHz)

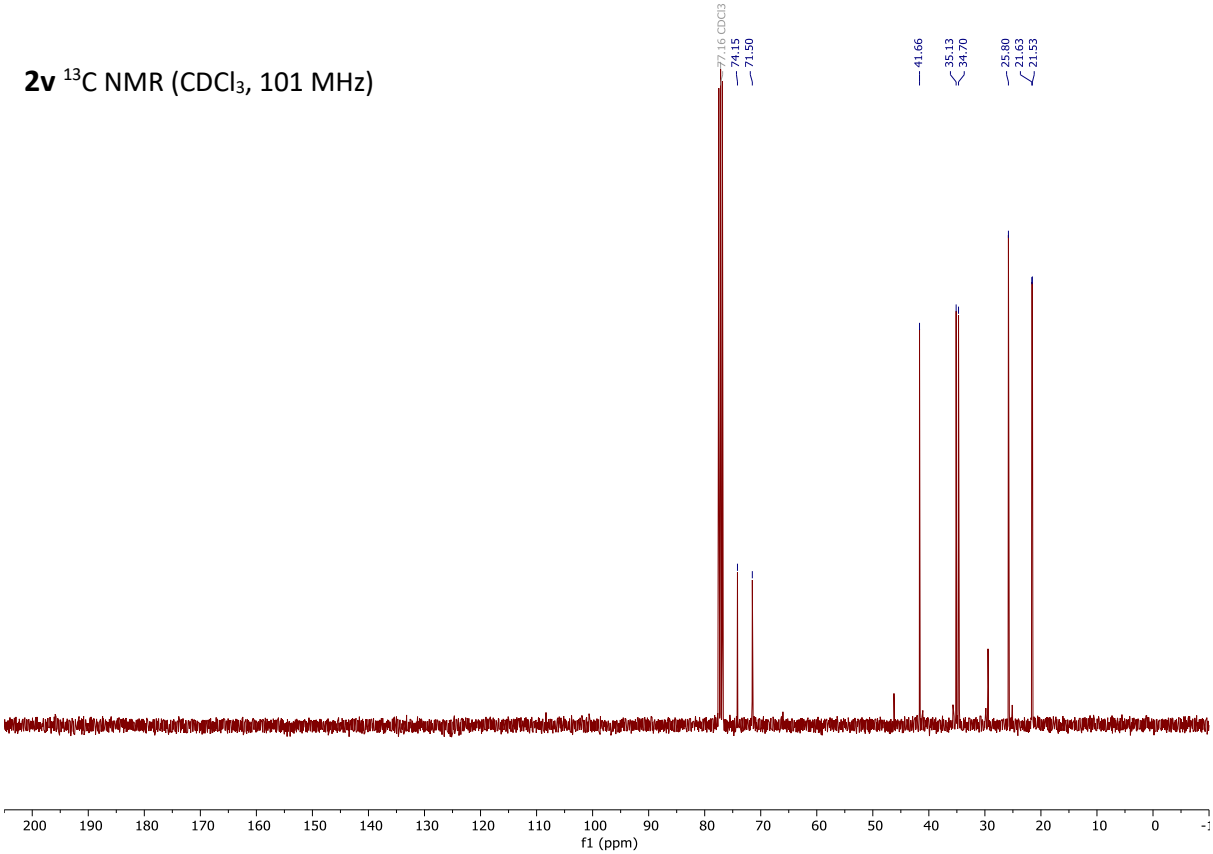


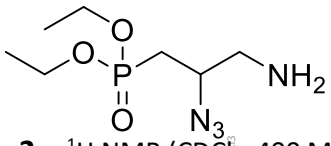


2v ^{1}H NMR ($CDCl_3$, 400 MHz)

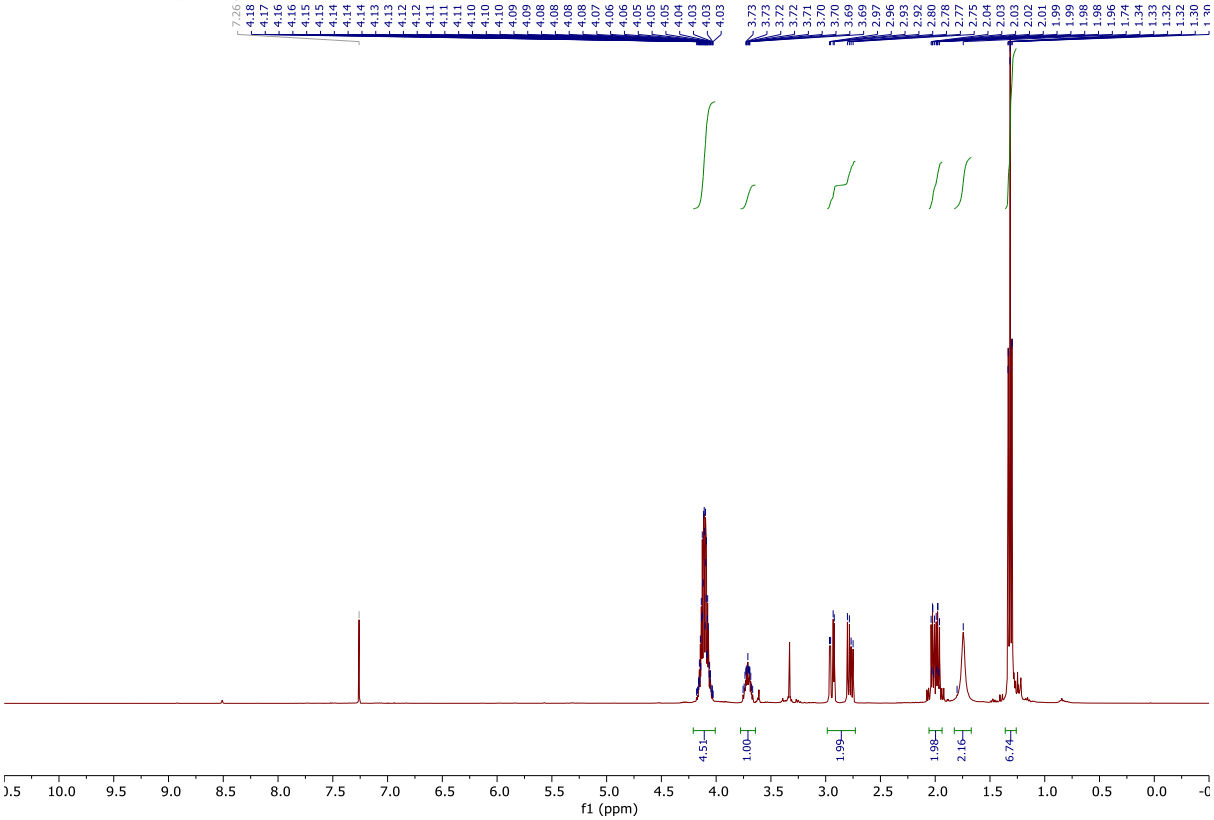


2v ^{13}C NMR ($CDCl_3$, 101 MHz)

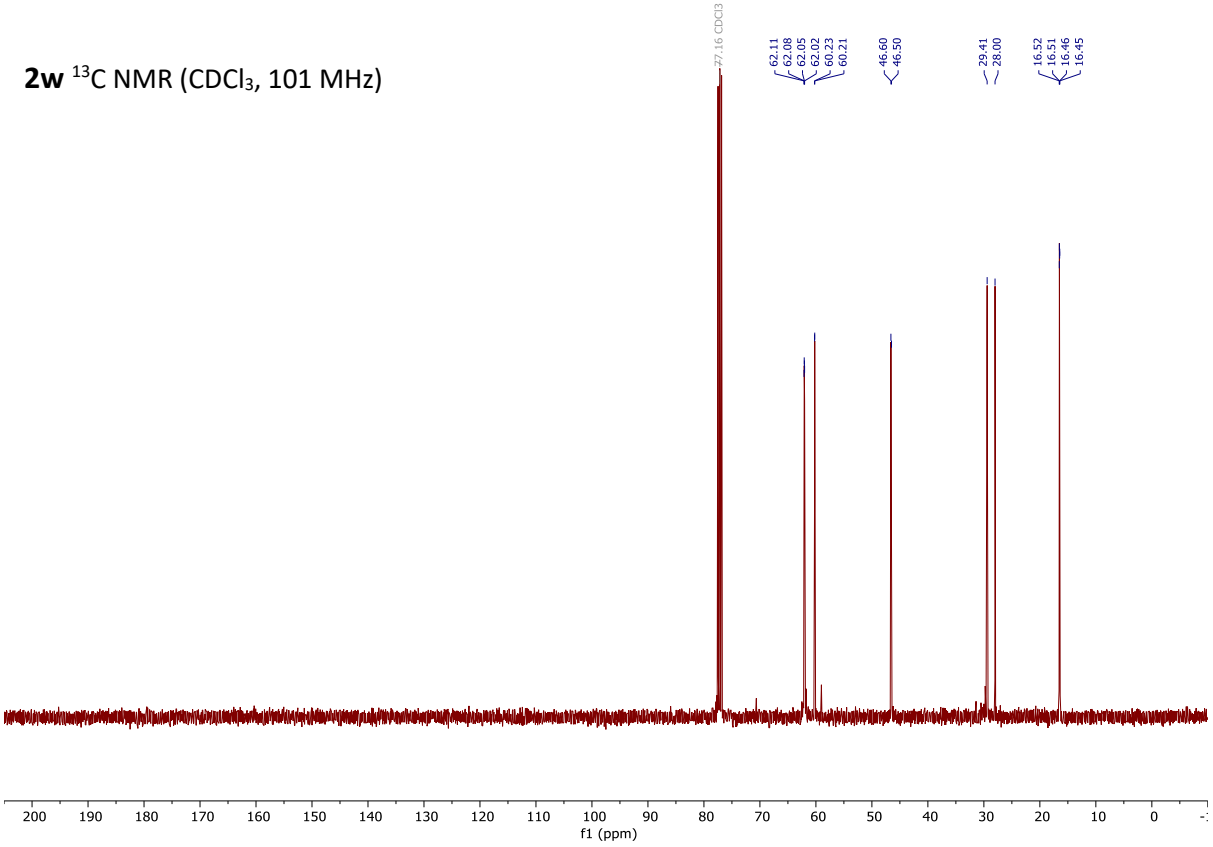


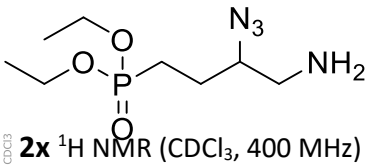


2w ^{1}H NMR ($CDCl_3$, 400 MHz)

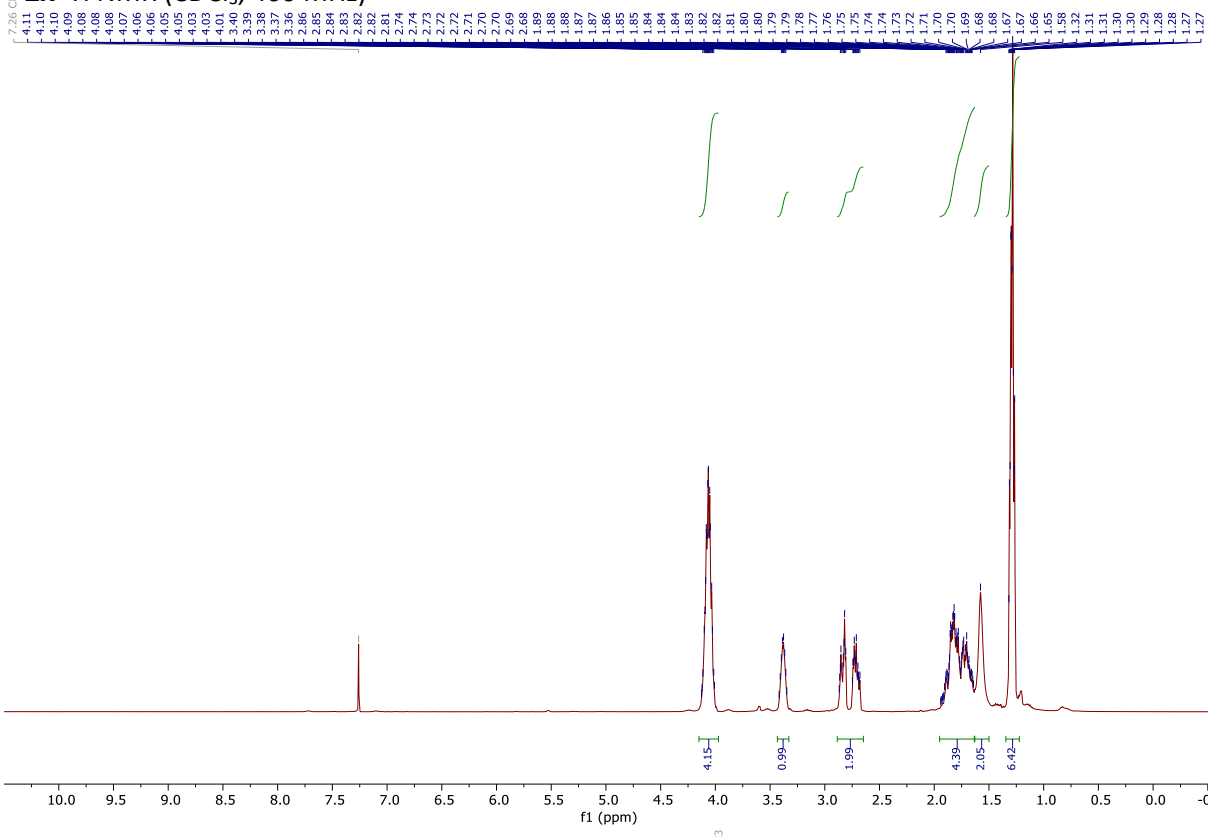


2w ^{13}C NMR ($CDCl_3$, 101 MHz)

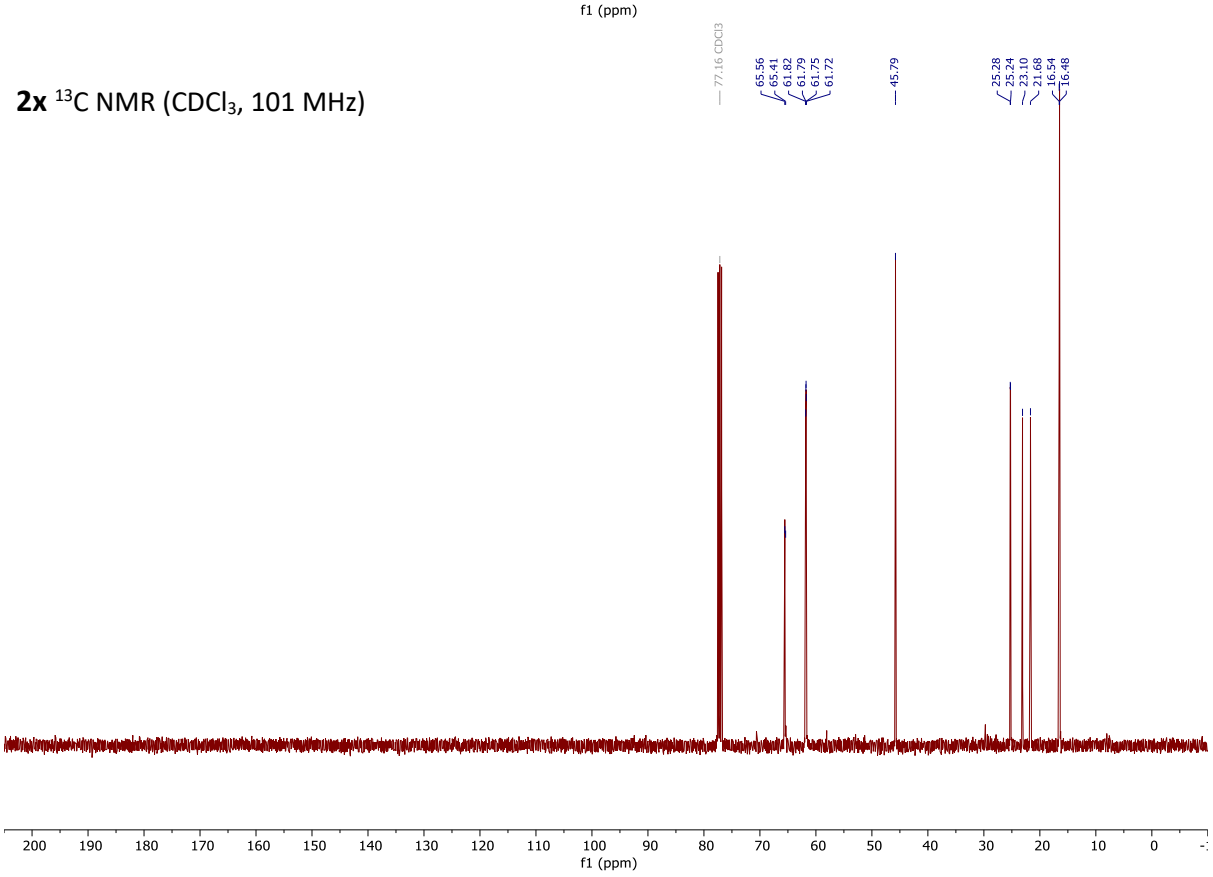


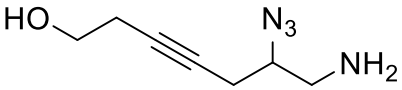


2x ^{1}H NMR ($CDCl_3$, 400 MHz)

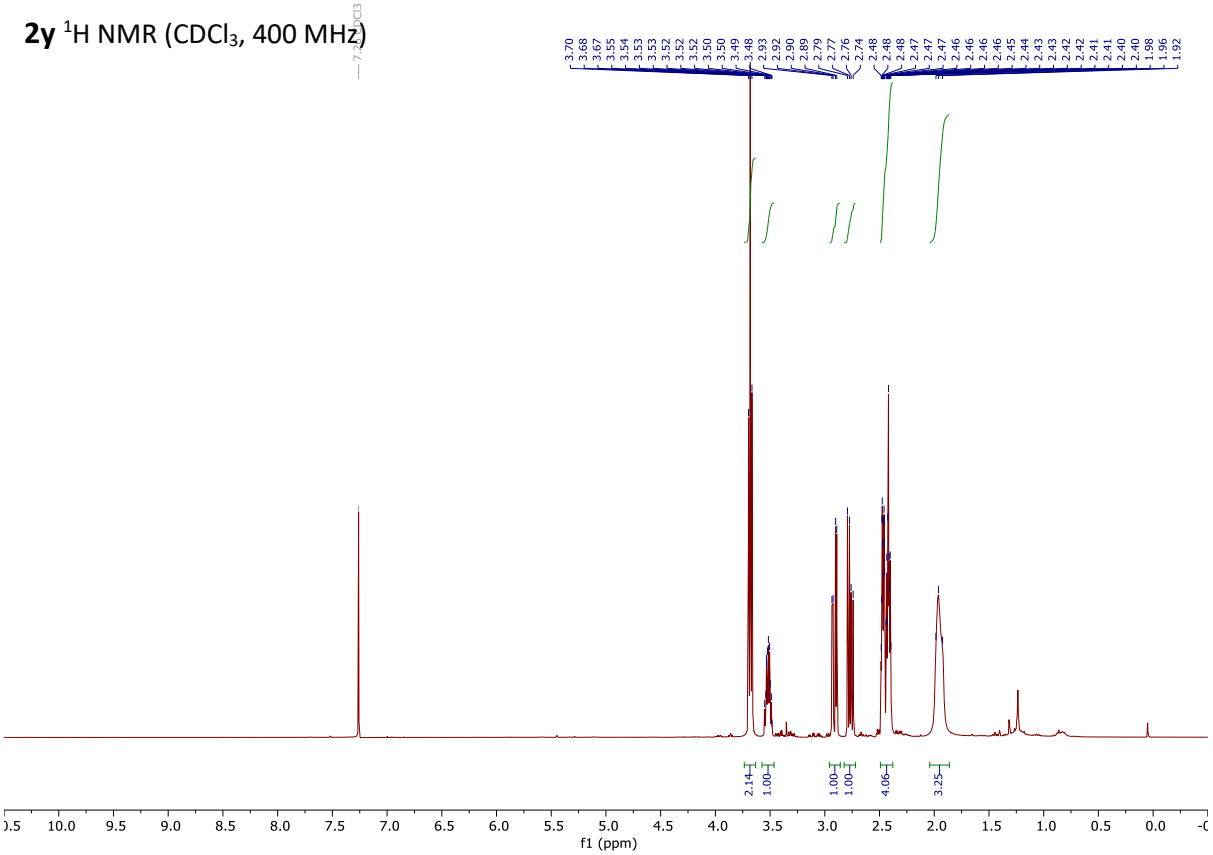


2x ^{13}C NMR ($CDCl_3$, 101 MHz)

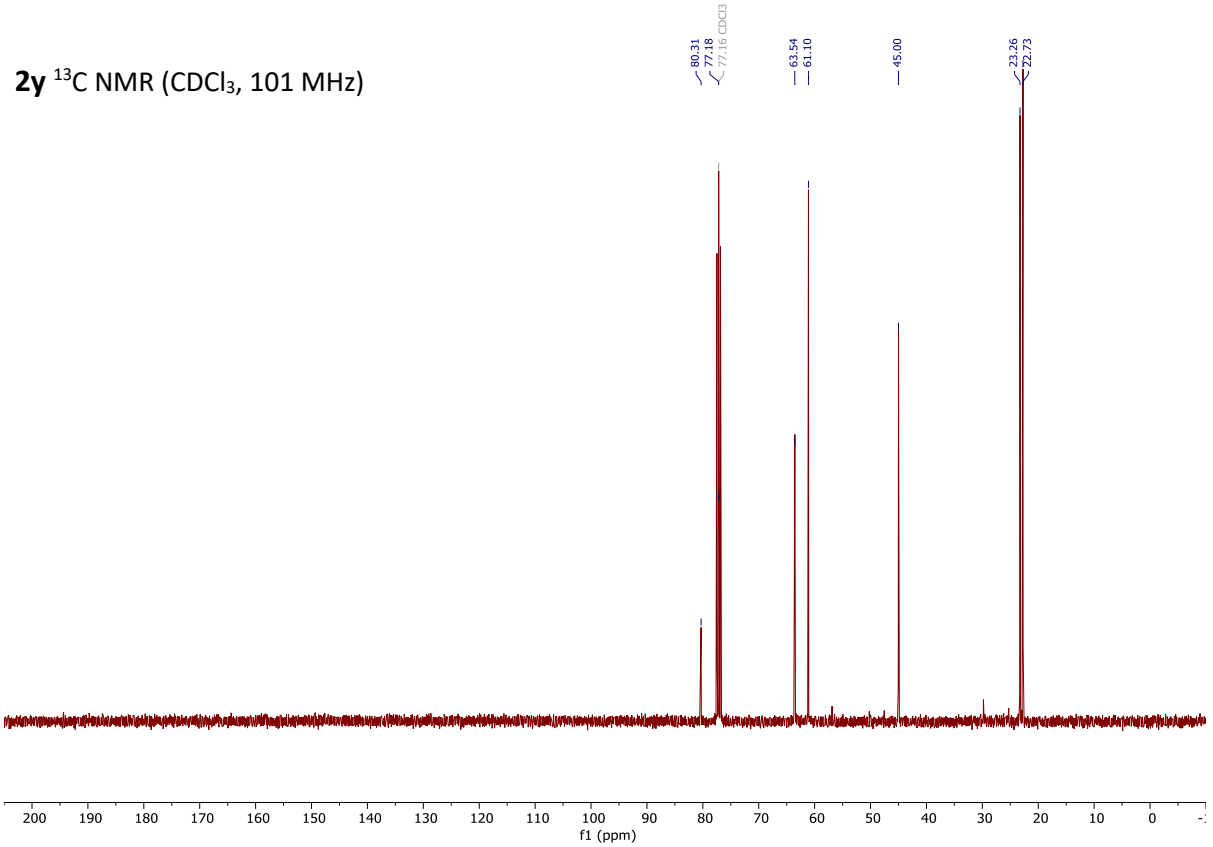


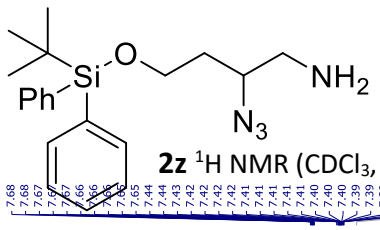


2y ^{1}H NMR ($CDCl_3$, 400 MHz)

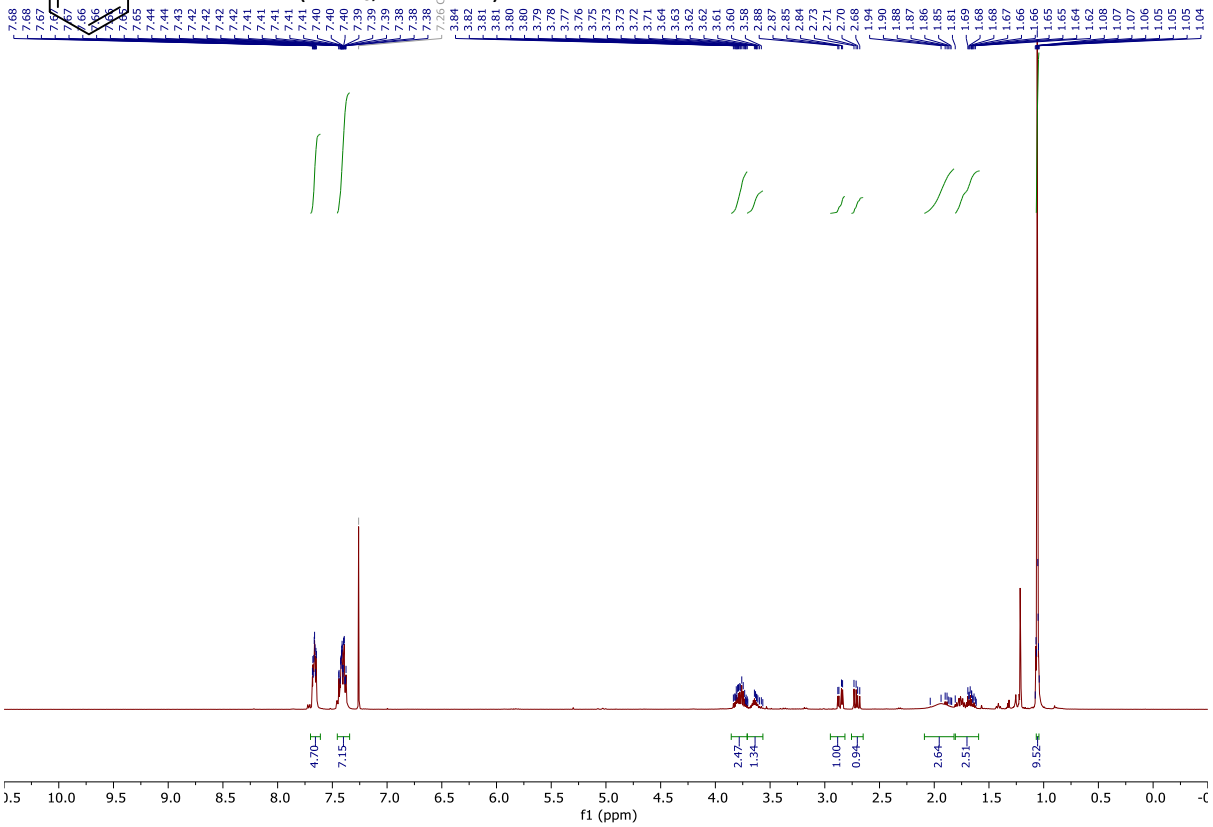


2y ^{13}C NMR ($CDCl_3$, 101 MHz)

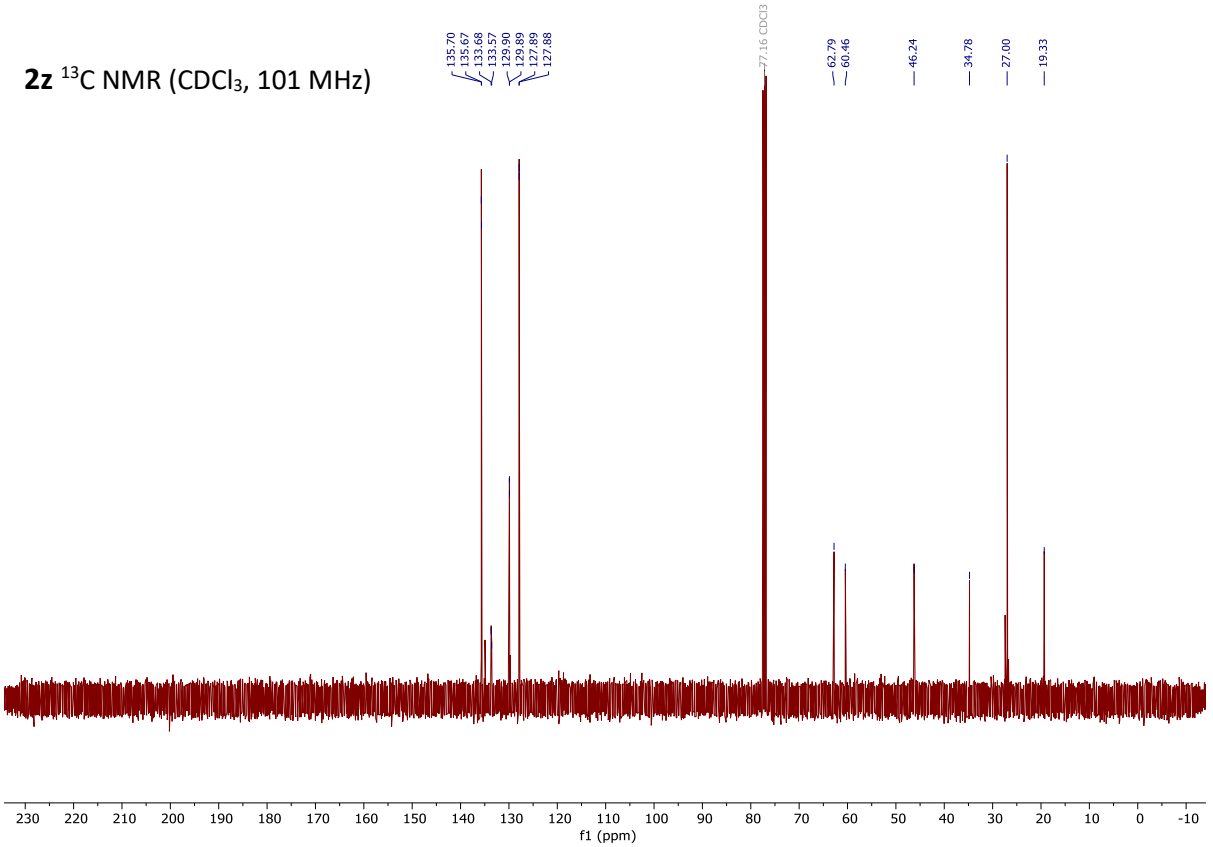


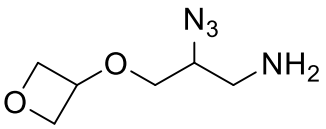


2z ^{1}H NMR ($CDCl_3$, 400 MHz)

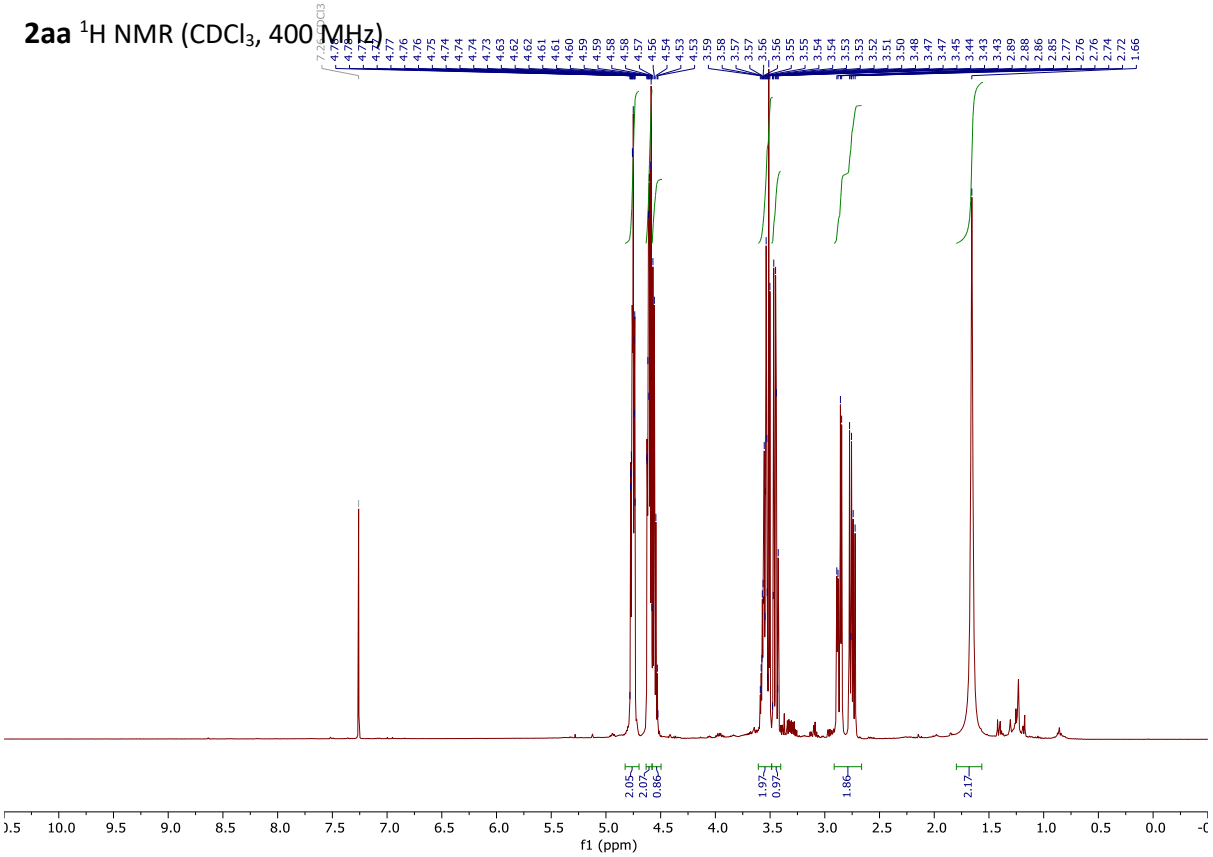


2z ^{13}C NMR ($CDCl_3$, 101 MHz)

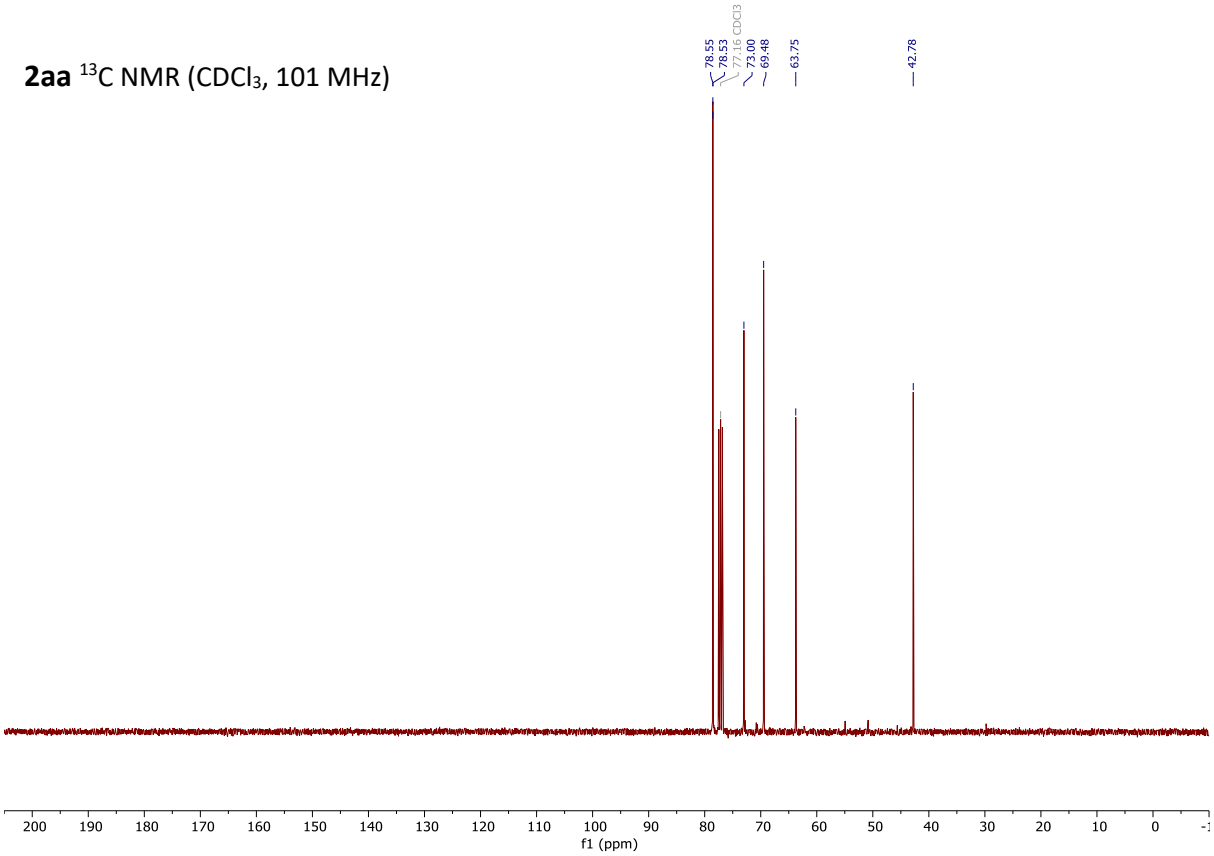


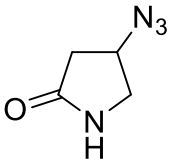


2aa ^{1}H NMR ($CDCl_3$, 400 MHz)

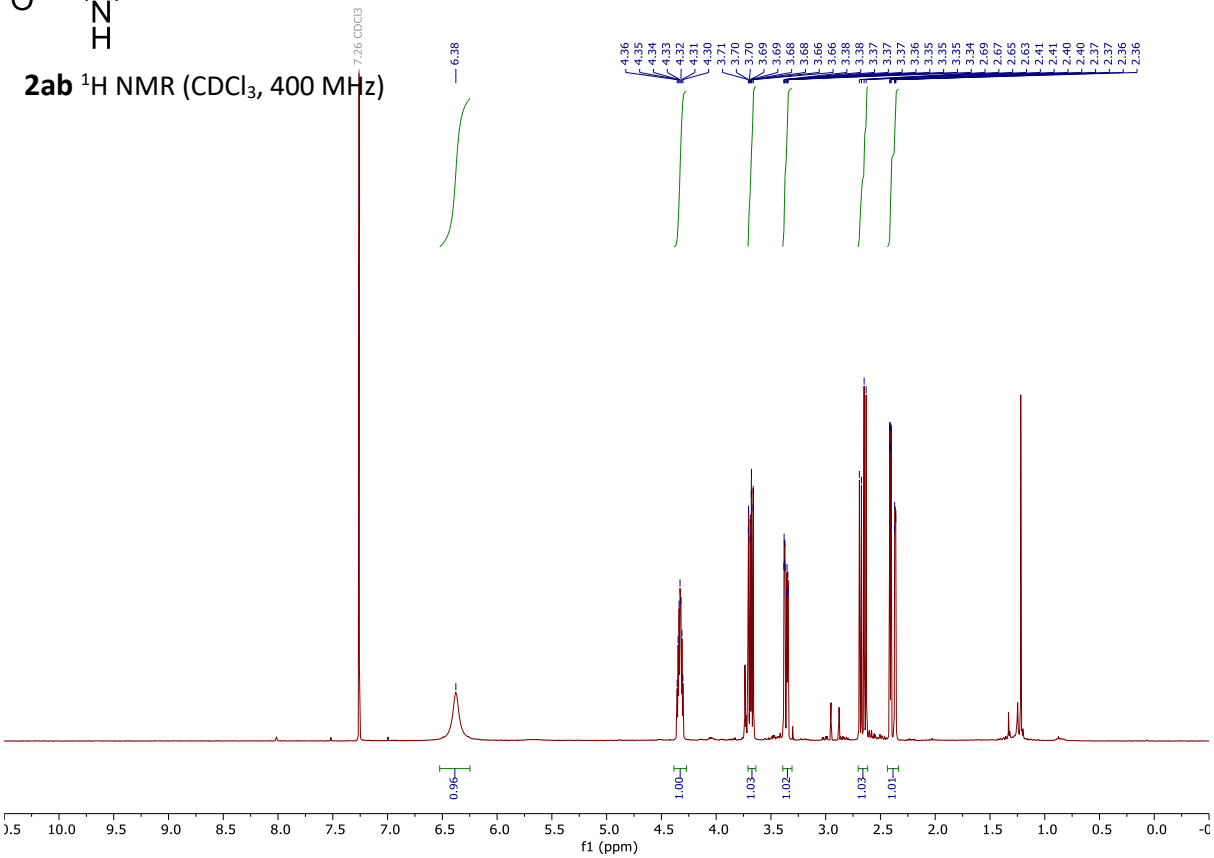


2aa ^{13}C NMR ($CDCl_3$, 101 MHz)

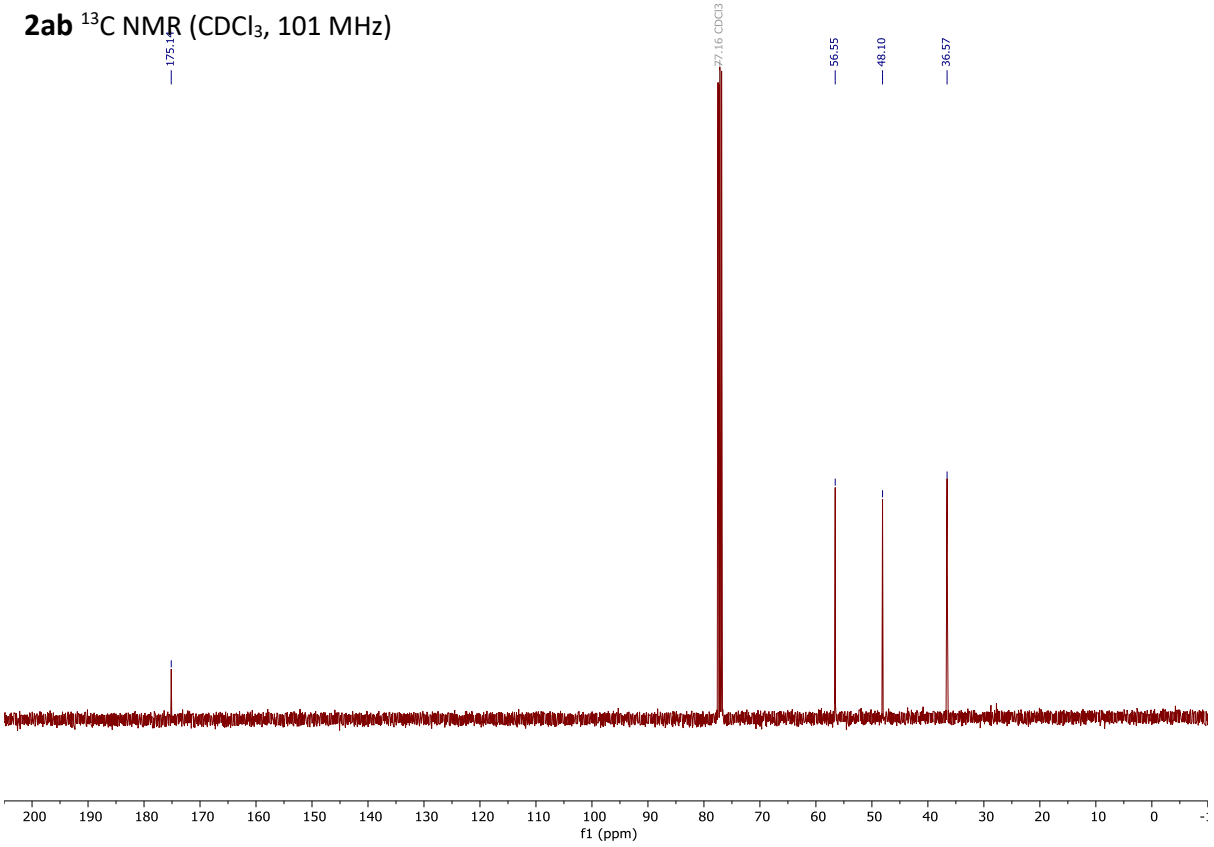


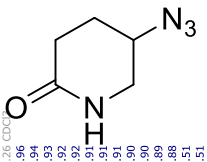


2ab ^{1}H NMR ($CDCl_3$, 400 MHz)

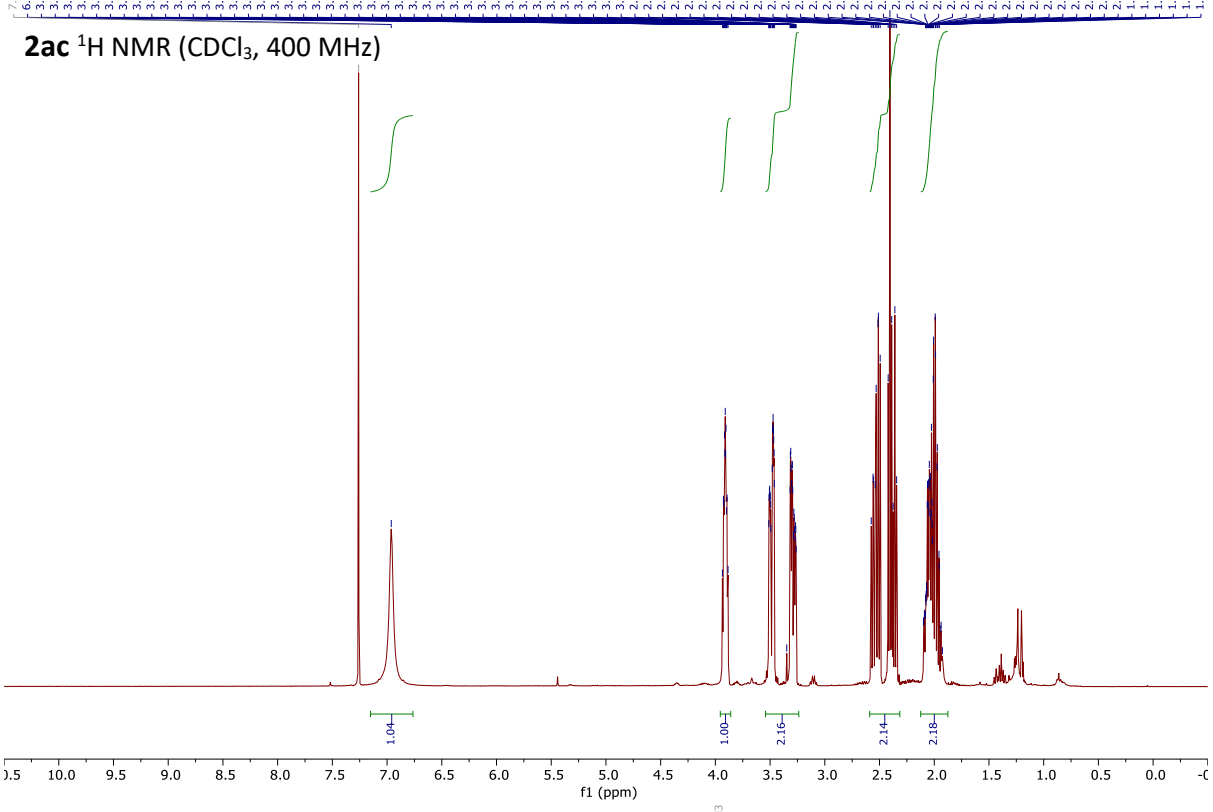


2ab ^{13}C NMR ($CDCl_3$, 101 MHz)

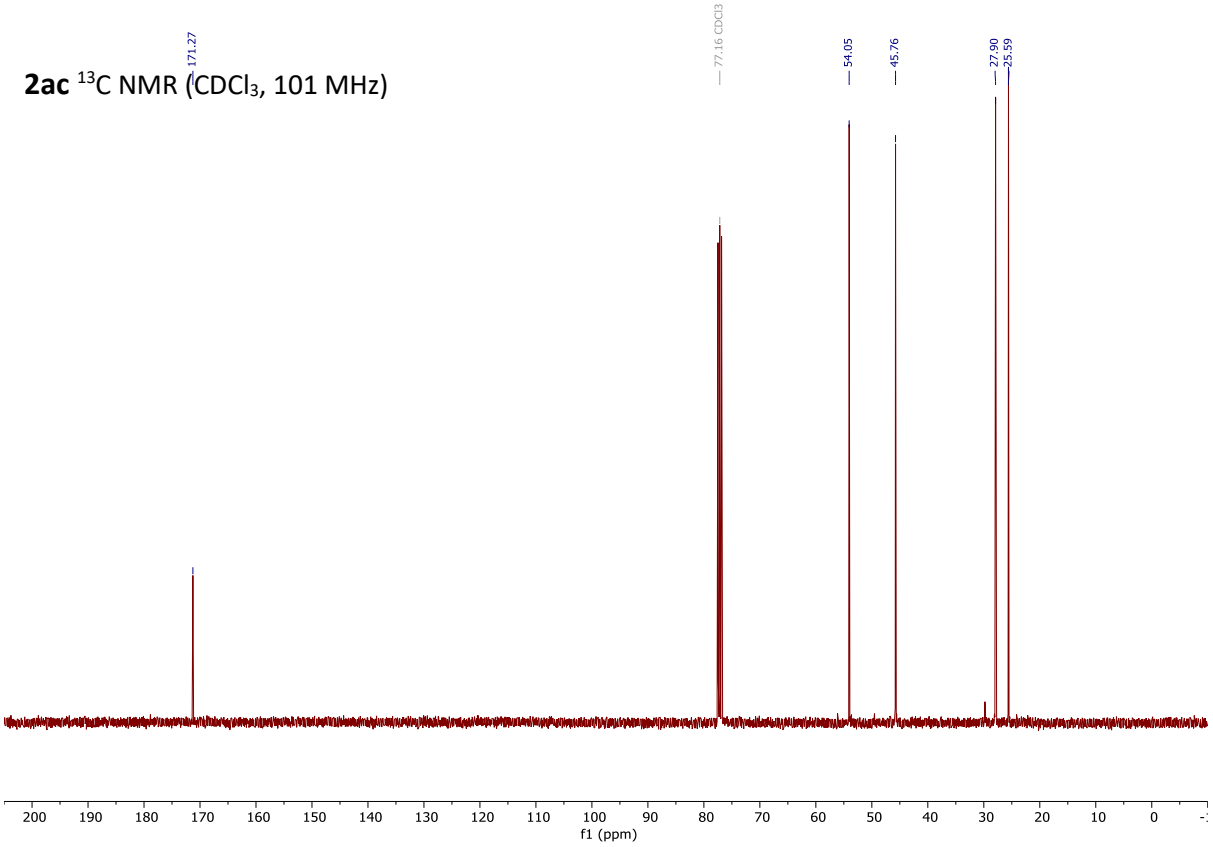


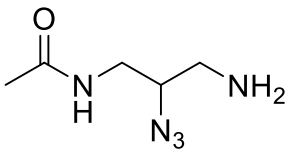


2ac ^{1}H NMR ($CDCl_3$, 400 MHz)

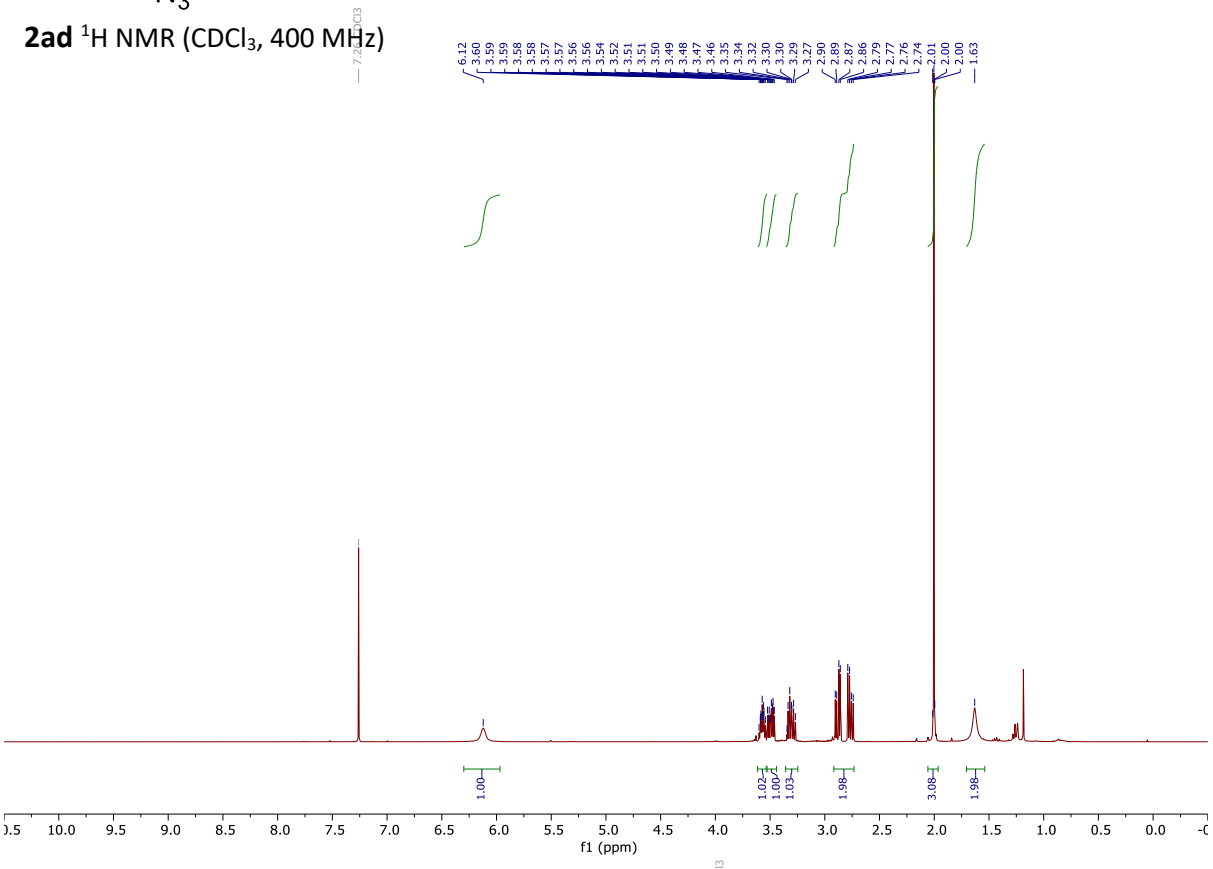


2ac ^{13}C NMR ($CDCl_3$, 101 MHz)

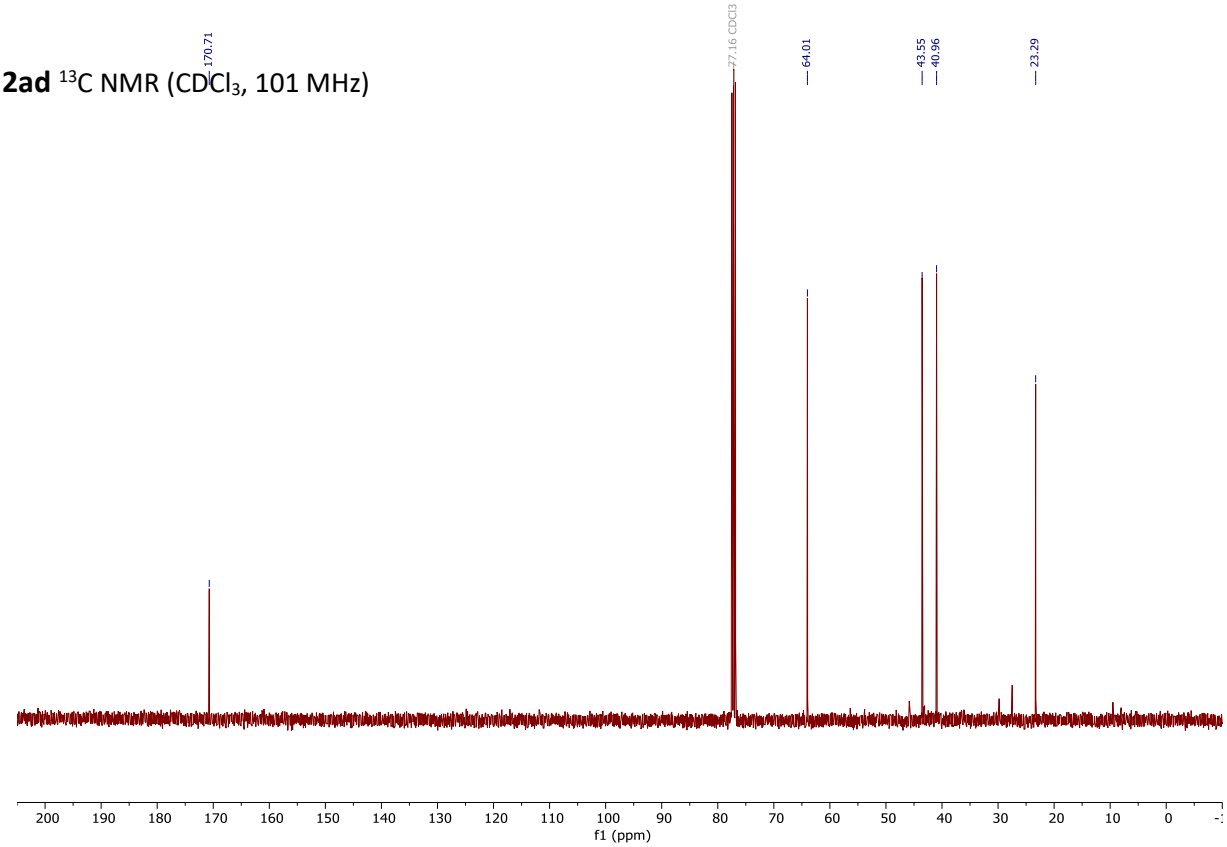


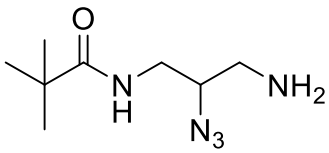


2ad ^{1}H NMR ($CDCl_3$, 400 MHz)

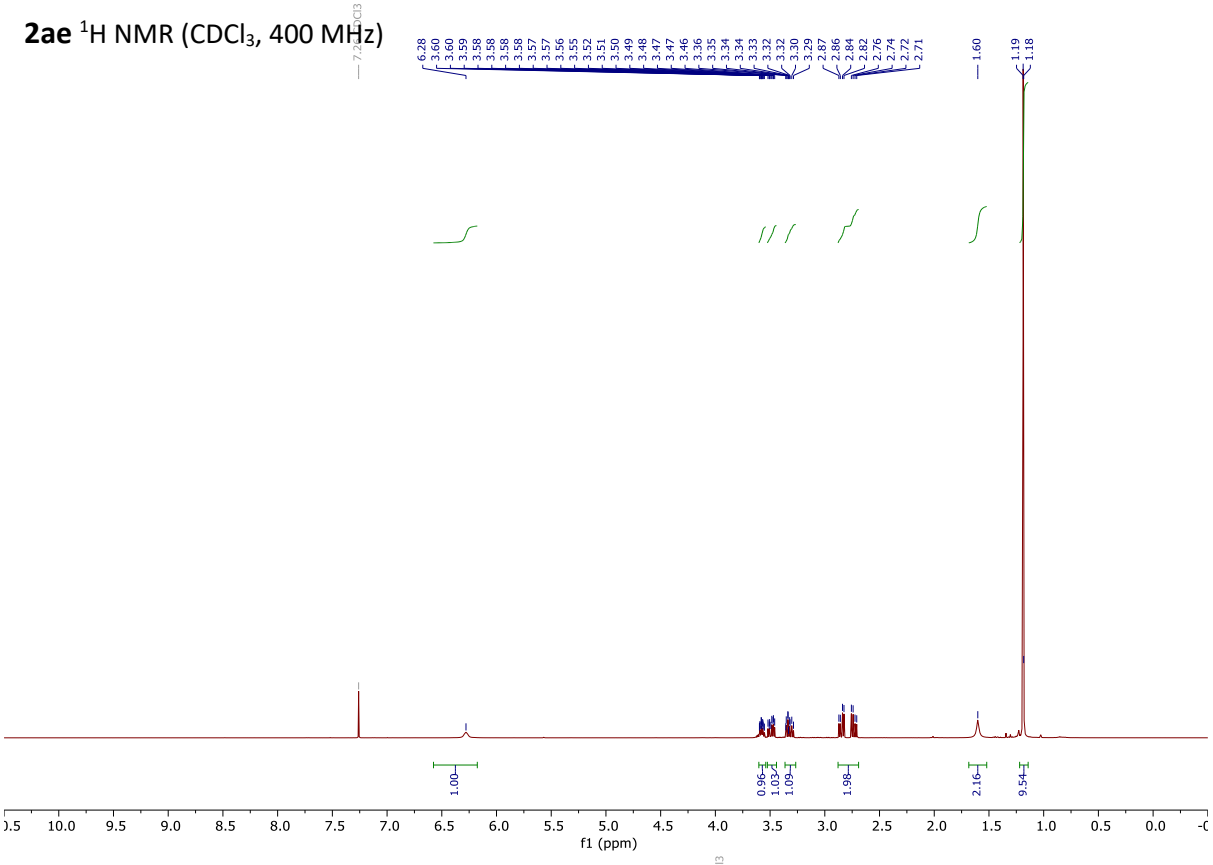


2ad ^{13}C NMR ($CDCl_3$, 101 MHz)

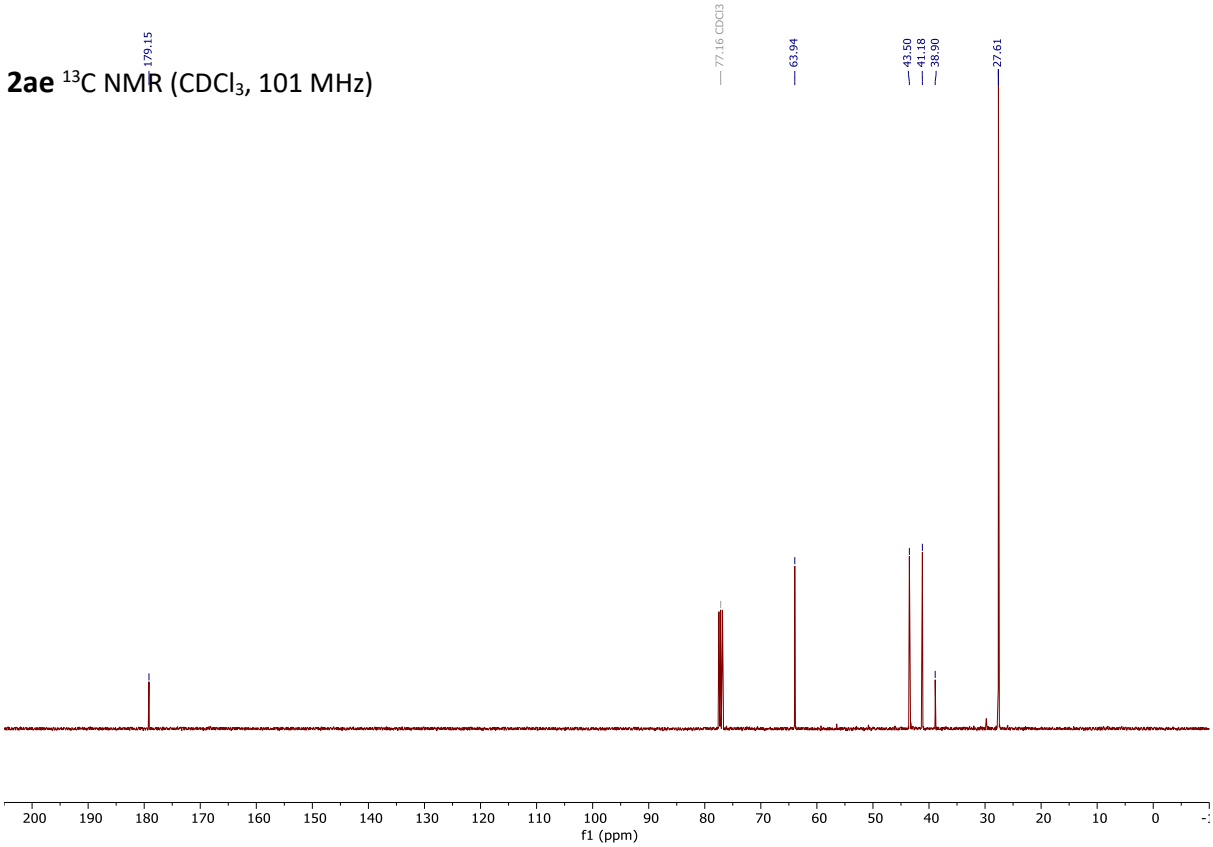


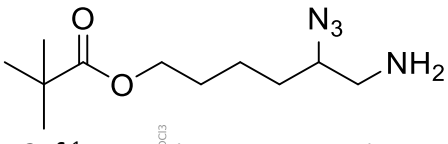


2ae ^{1}H NMR ($CDCl_3$, 400 MHz)

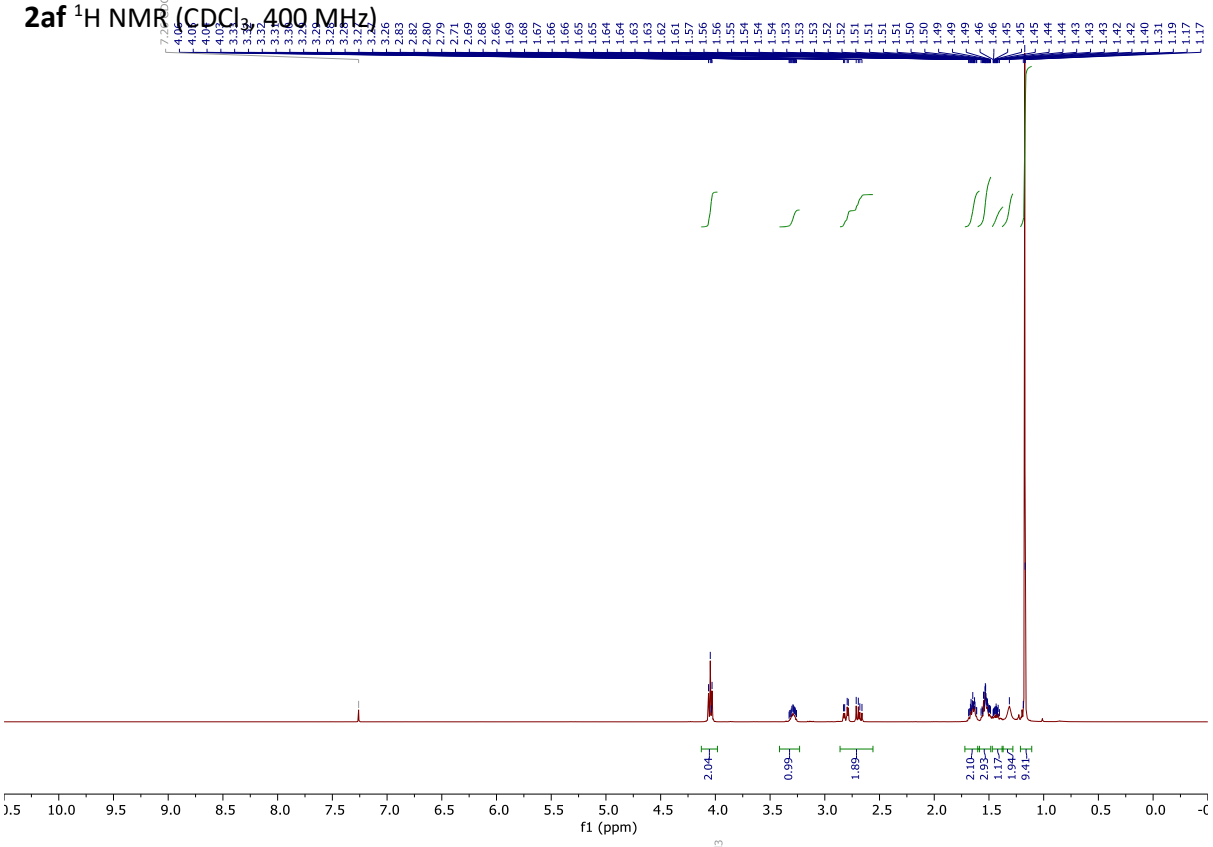


2ae ^{13}C NMR ($CDCl_3$, 101 MHz)

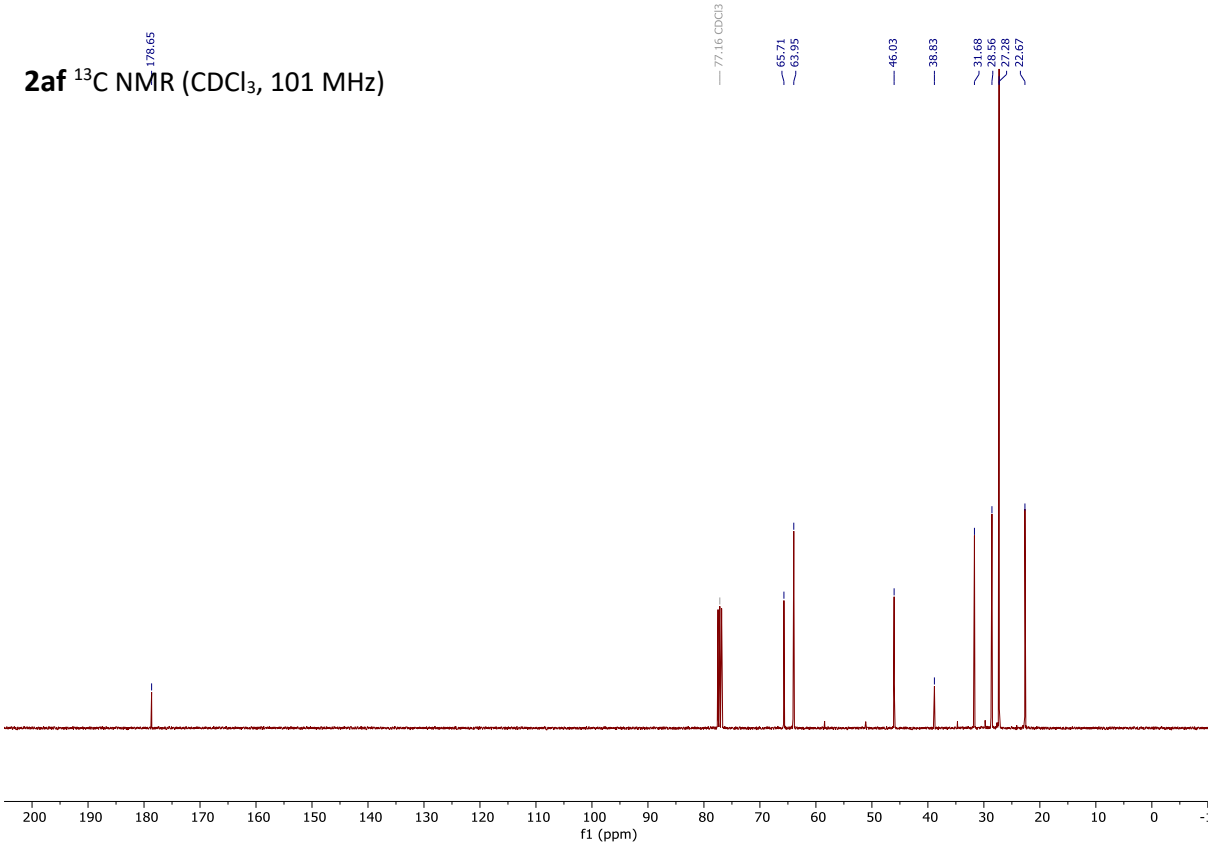


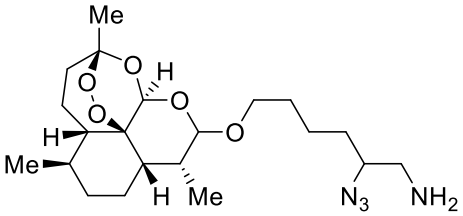


2af ^{1}H NMR ($CDCl_3$, 400 MHz)

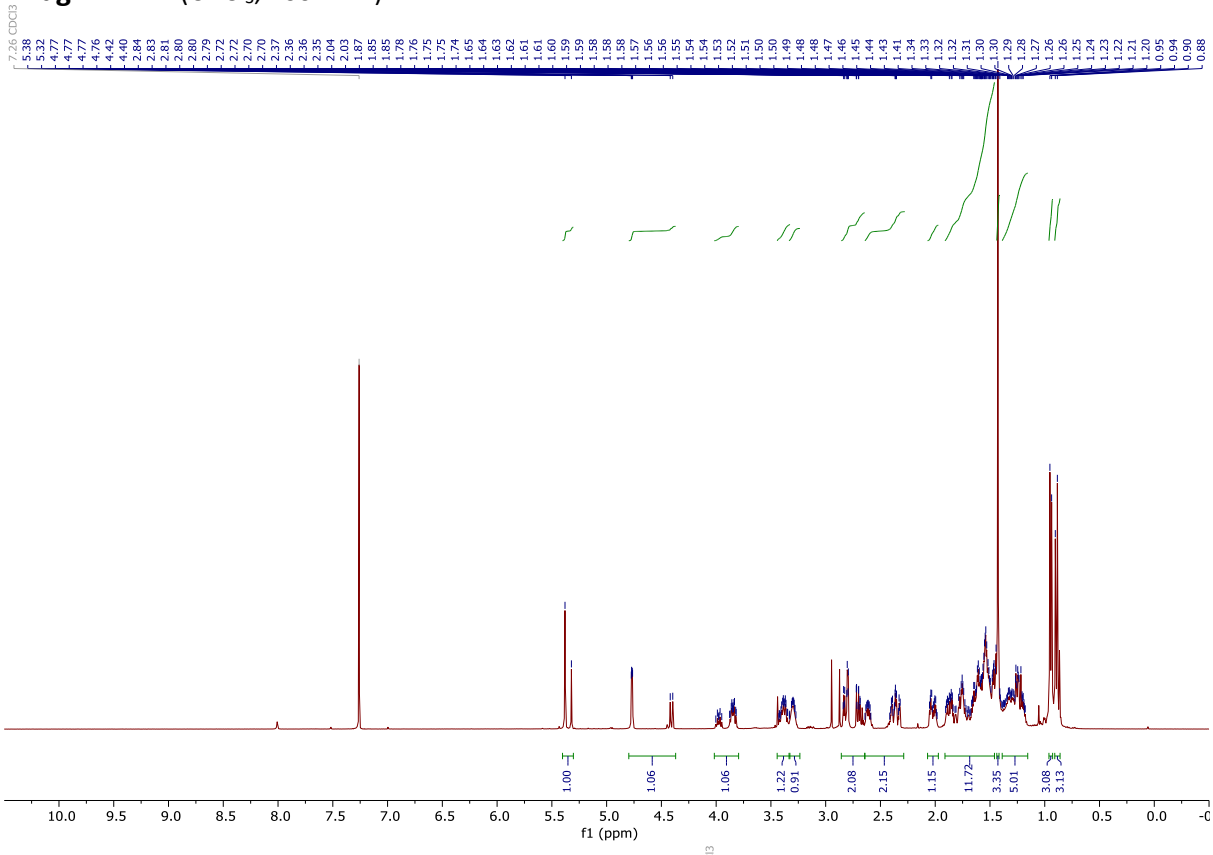


2af ^{13}C NMR ($CDCl_3$, 101 MHz)

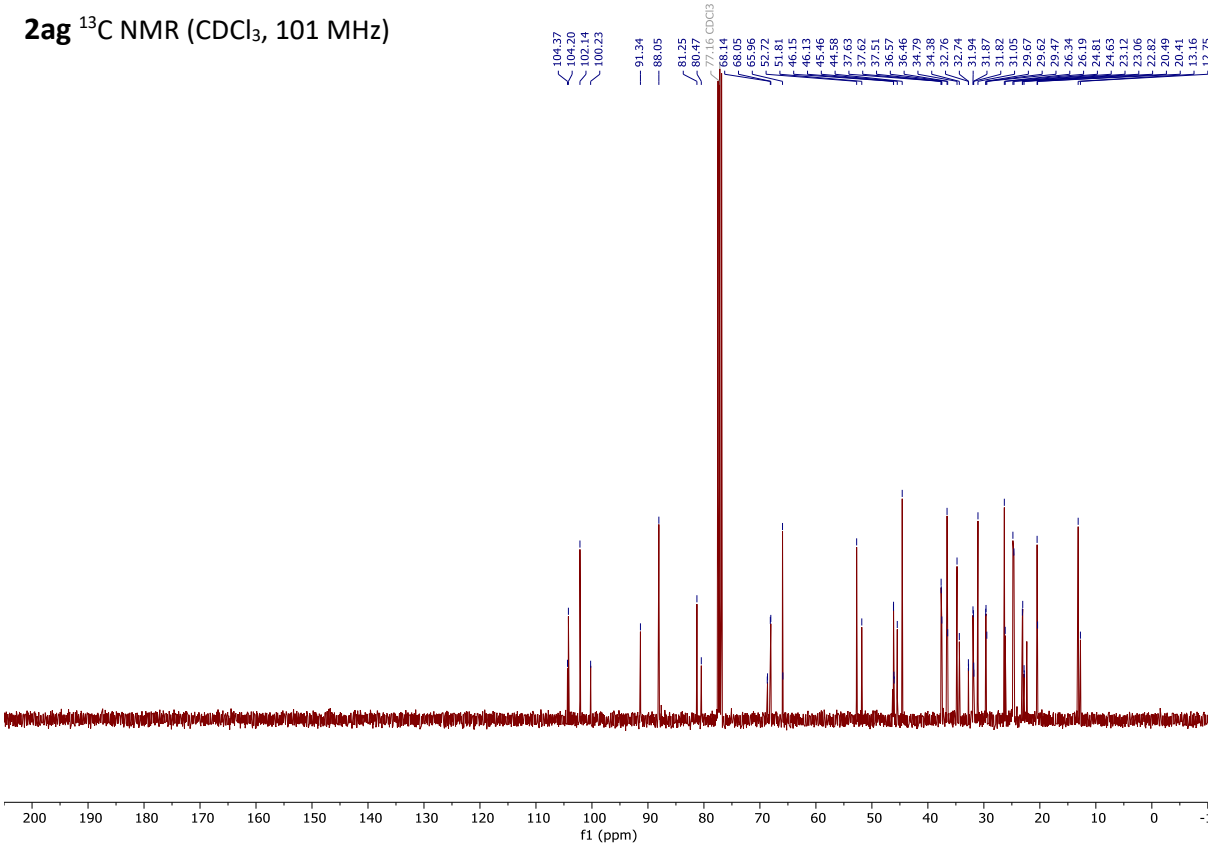




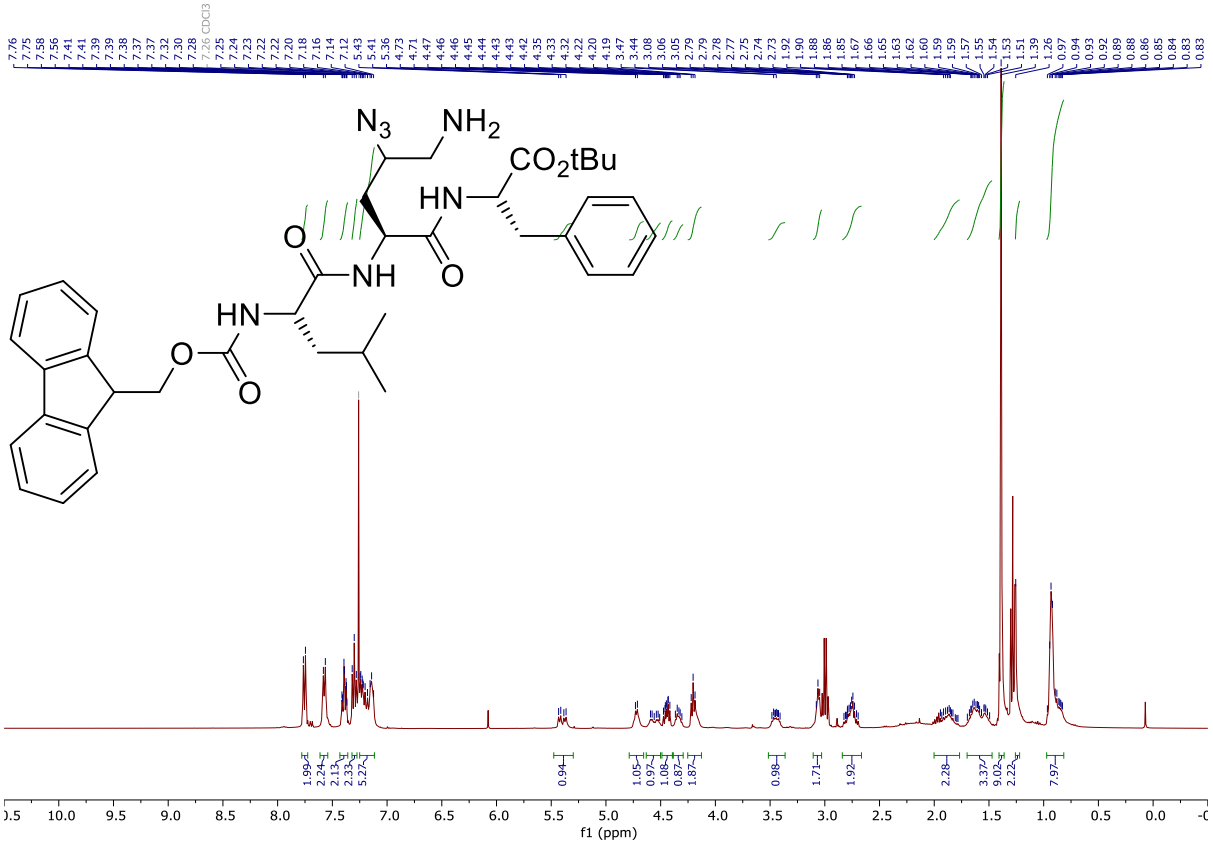
2ag ^{1}H NMR ($CDCl_3$, 400 MHz)



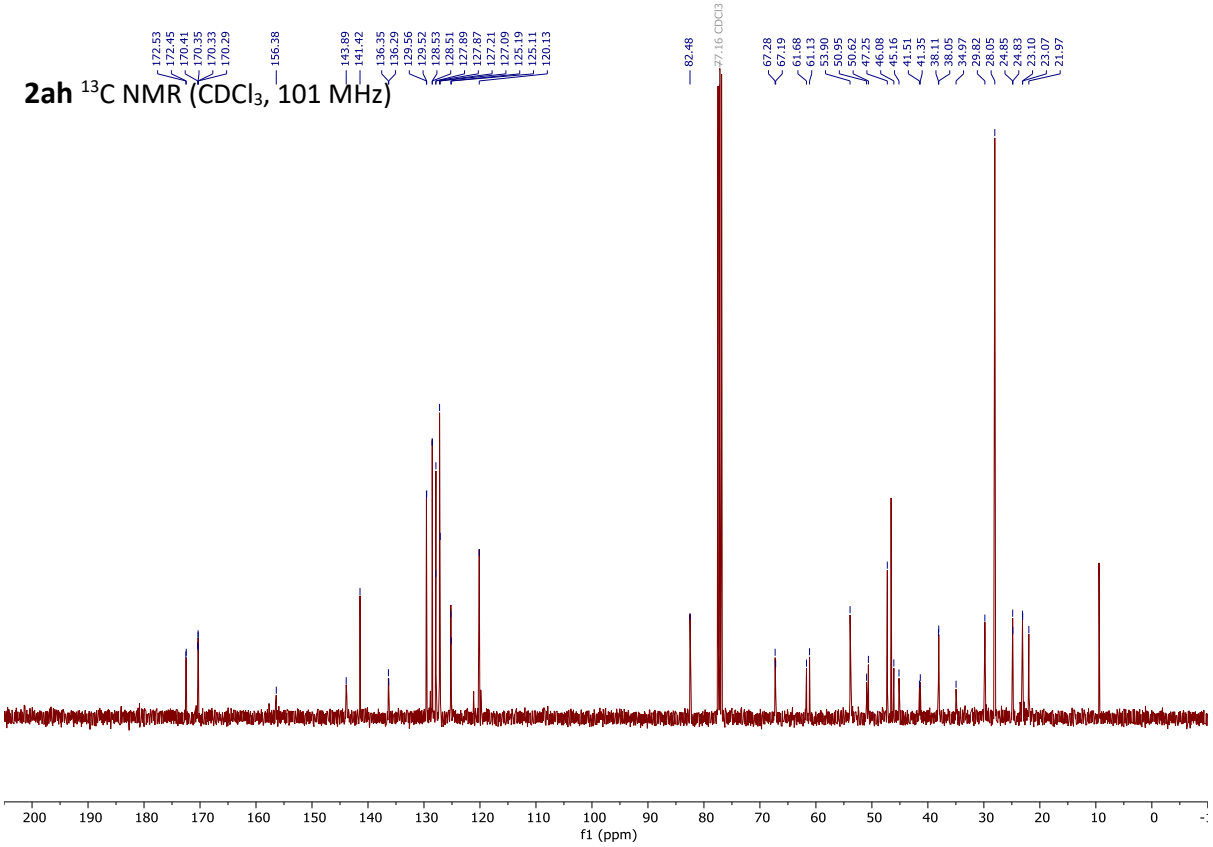
2ag ^{13}C NMR ($CDCl_3$, 101 MHz)

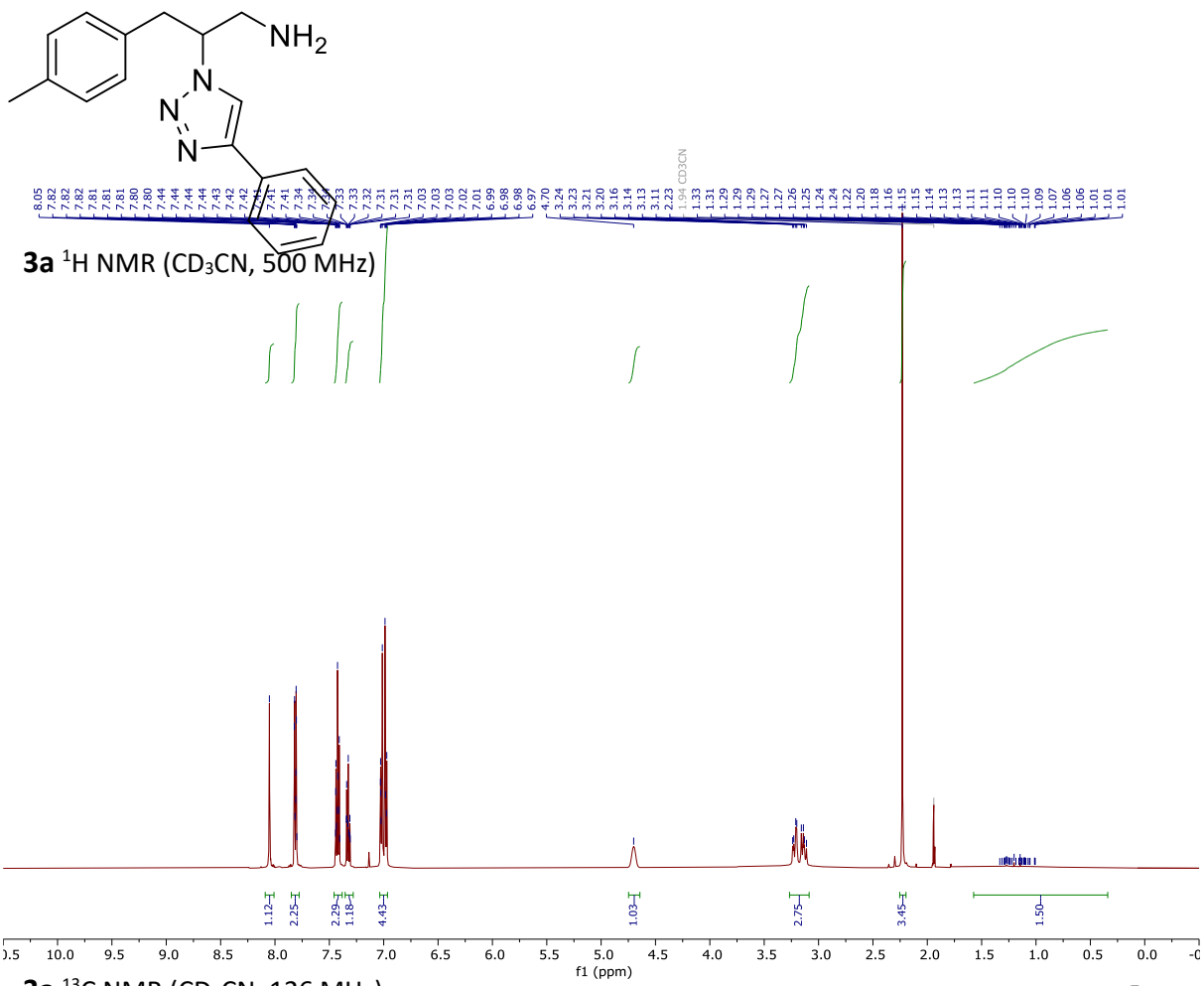


2ah ^{1}H NMR ($CDCl_3$, 400 MHz)

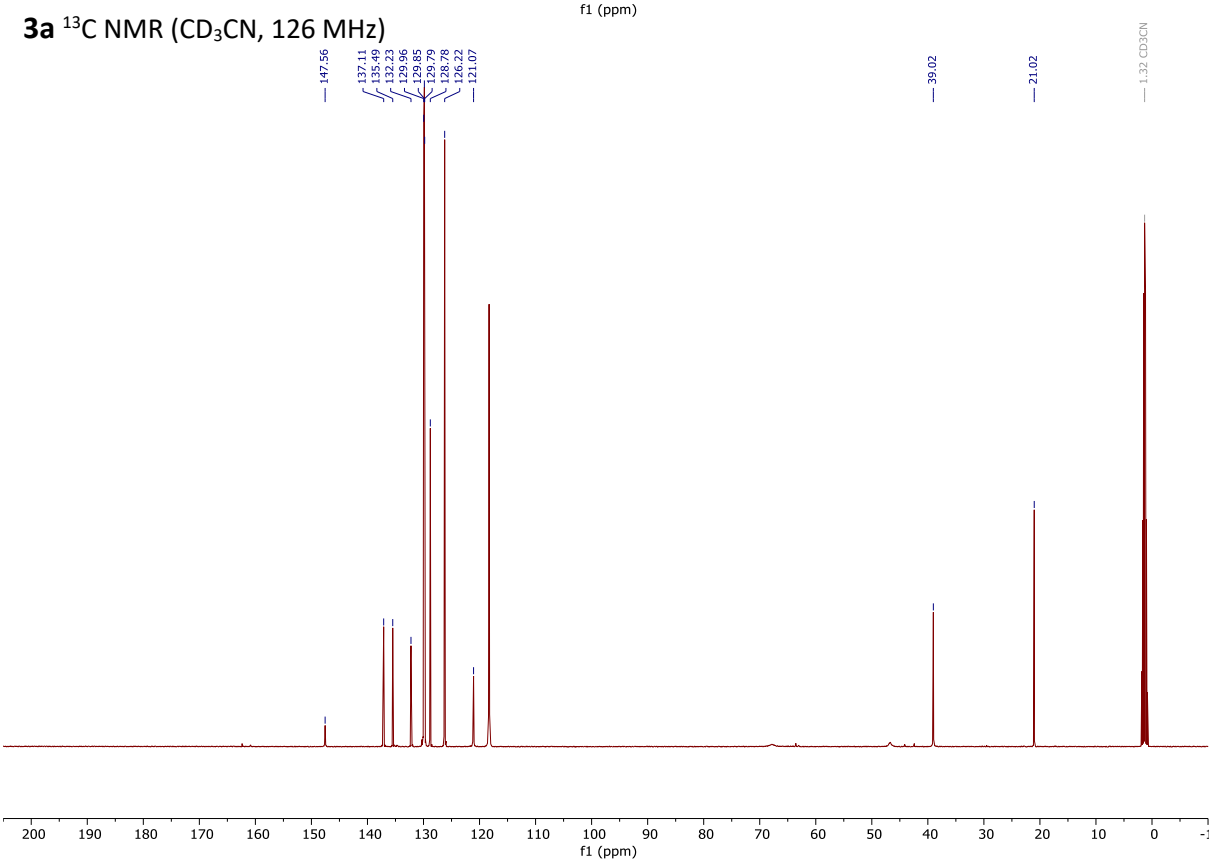


2ah ^{13}C NMR ($CDCl_3$, 101 MHz)

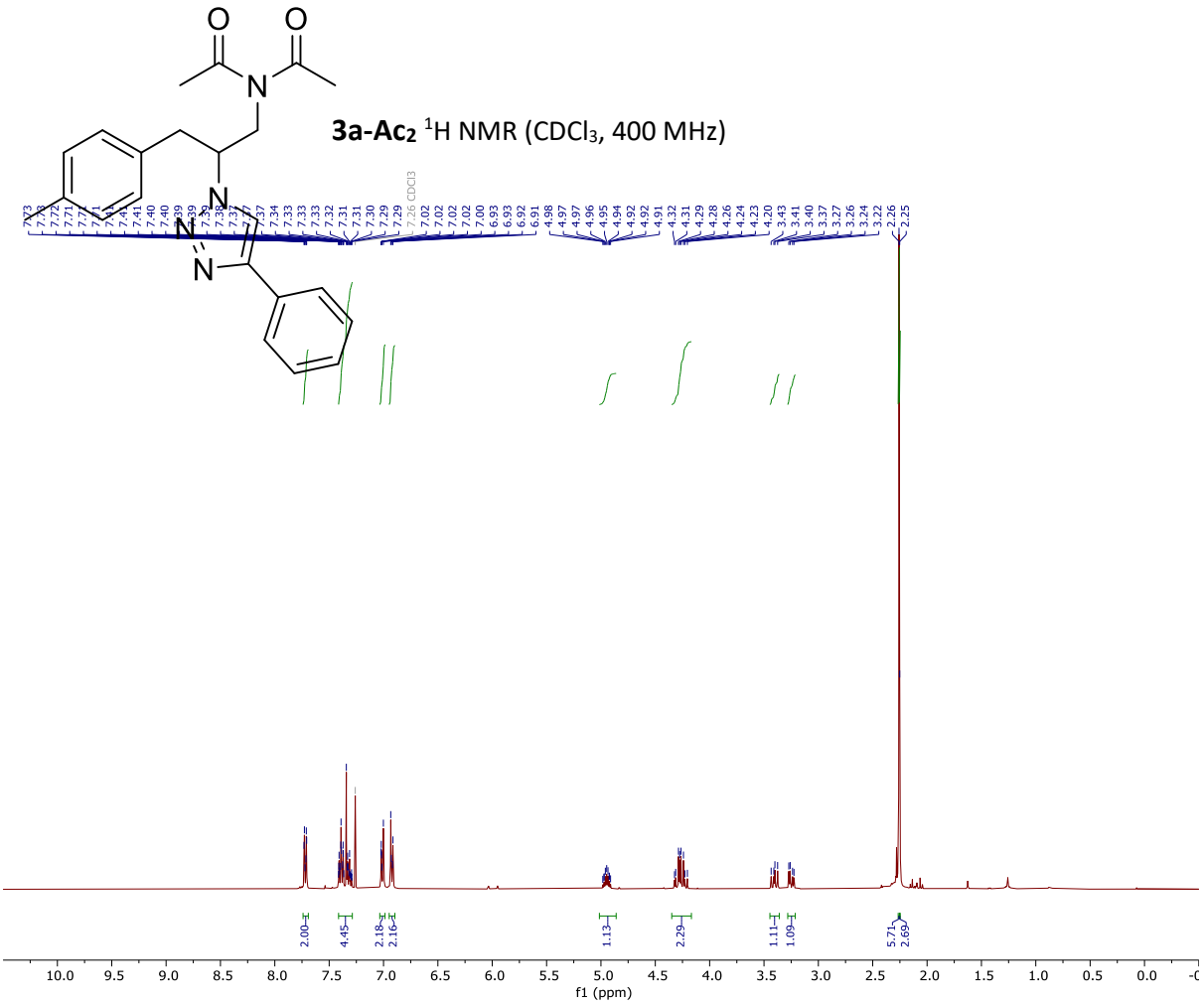




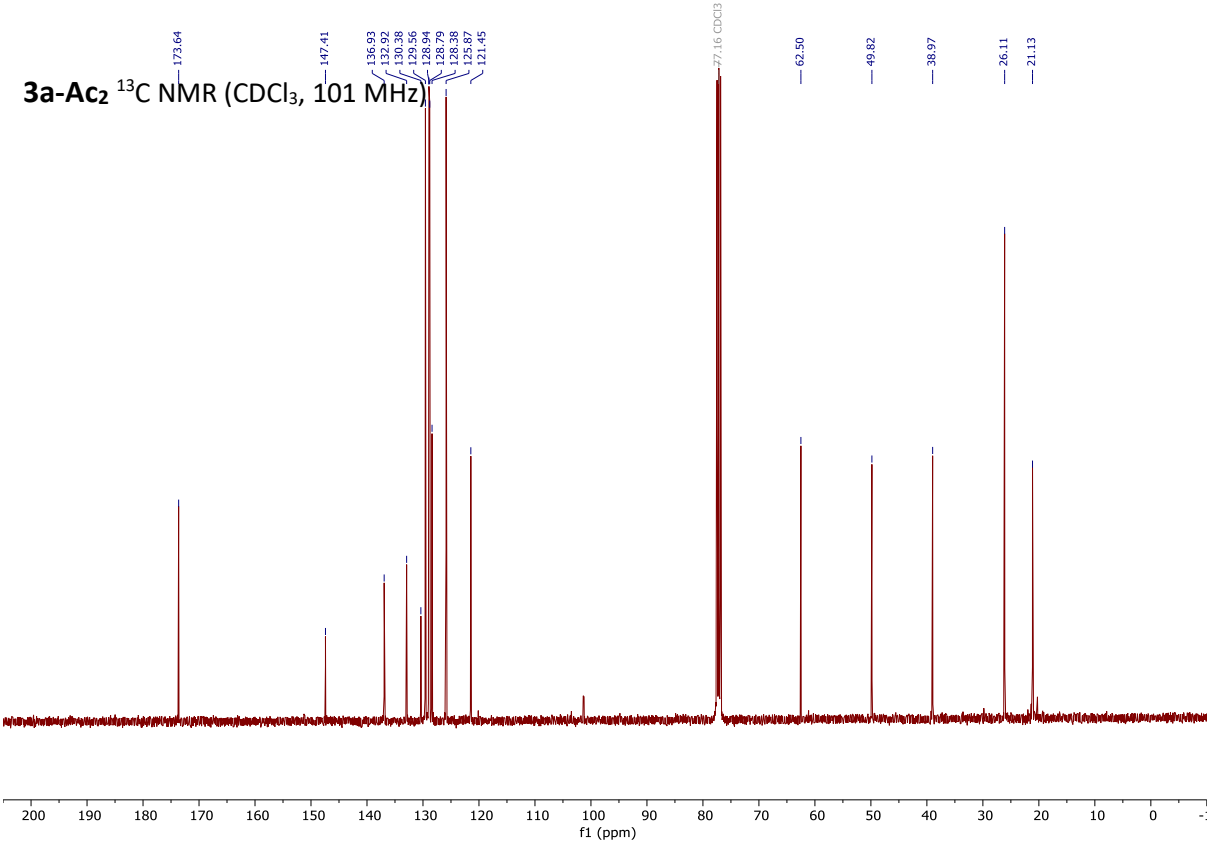
3a ^{1}H NMR (CD_3CN, 500 MHz)



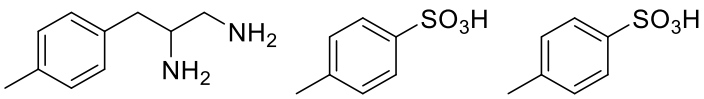
3a ^{13}C NMR (CD_3CN, 126 MHz)



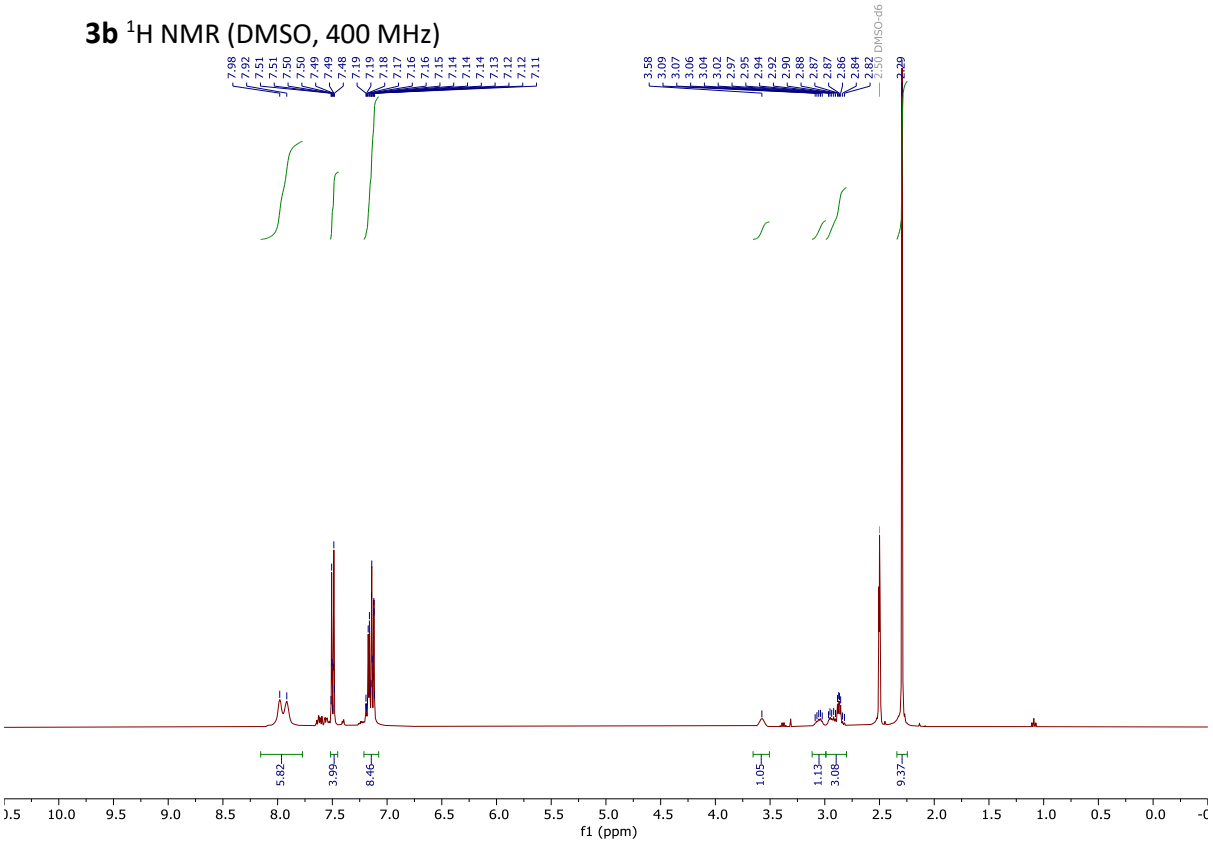
3a-Ac$_2$ ^{1}H NMR (CDCl$_3$, 400 MHz)



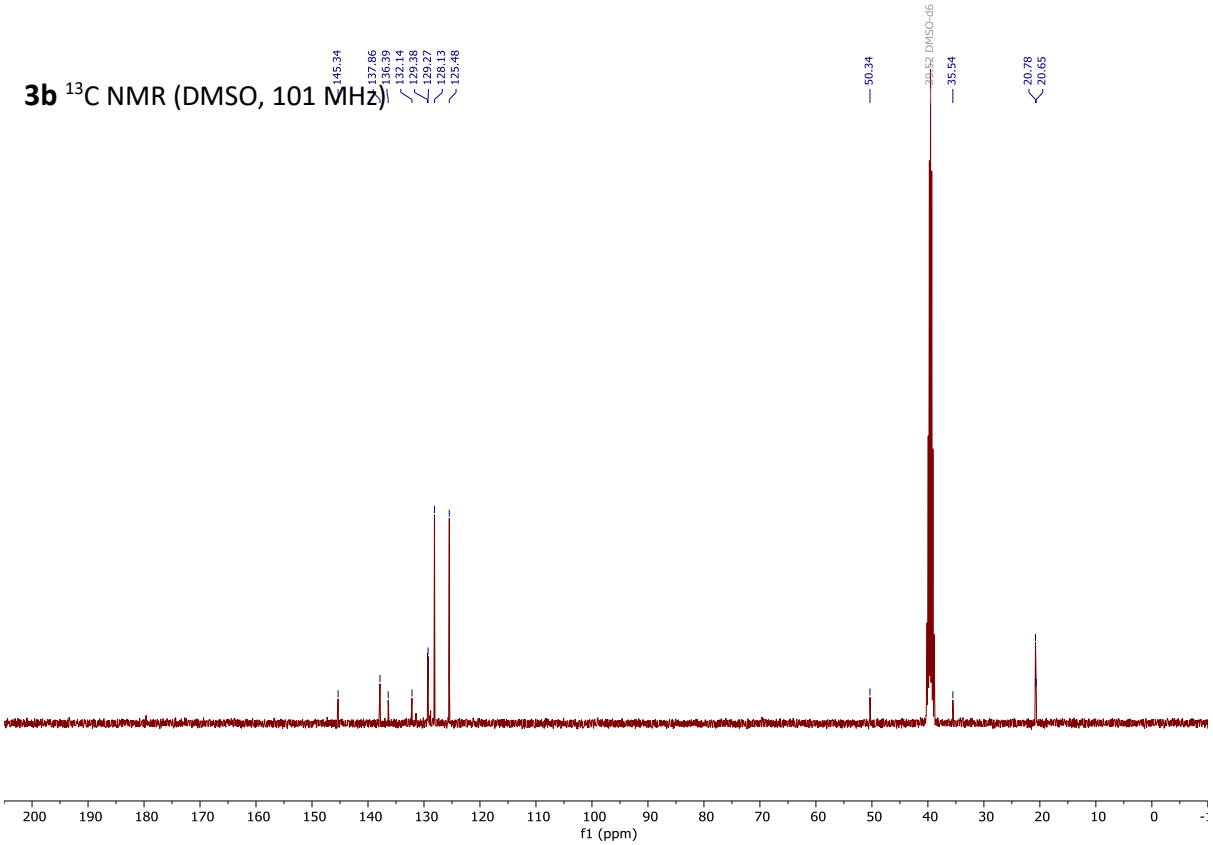
3a-Ac$_2$ ^{13}C NMR (CDCl$_3$, 101 MHz)

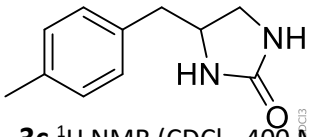


3b ^{1}H NMR (DMSO, 400 MHz)

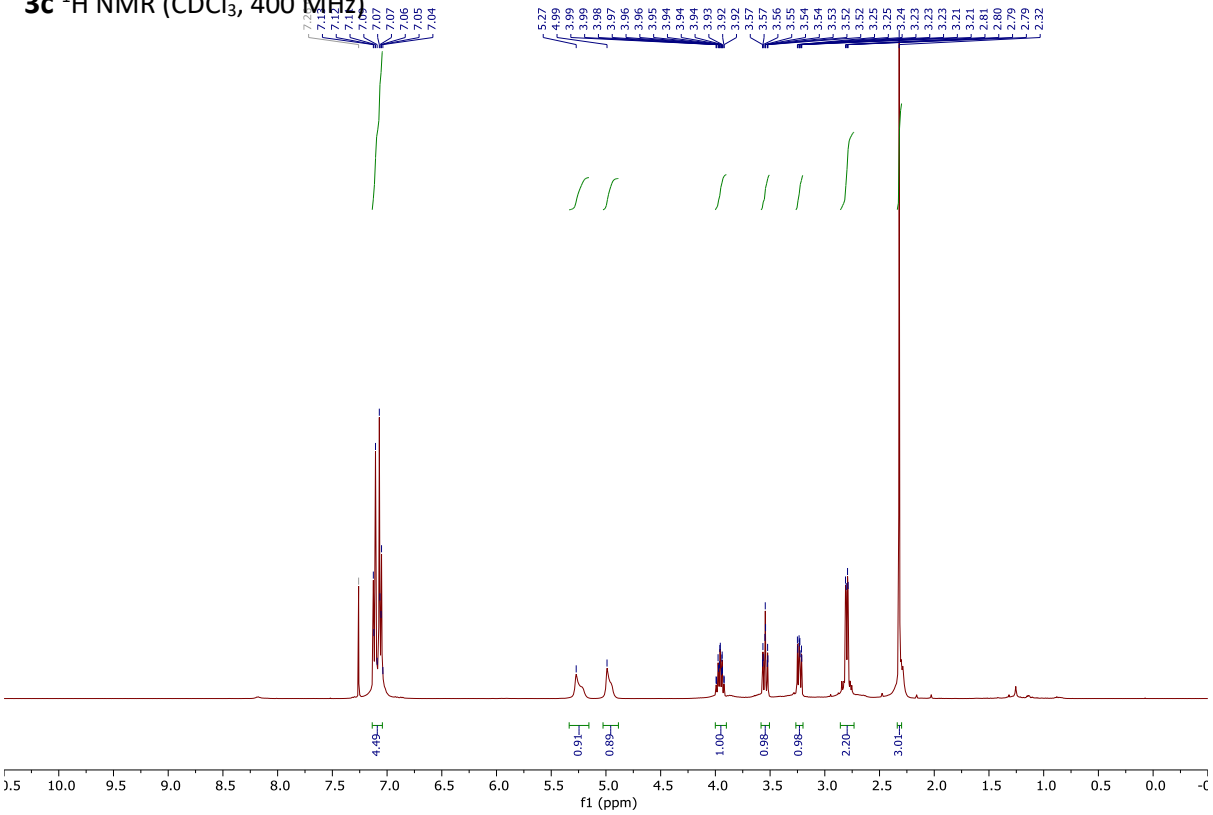


3b ^{13}C NMR (DMSO, 101 MHz)

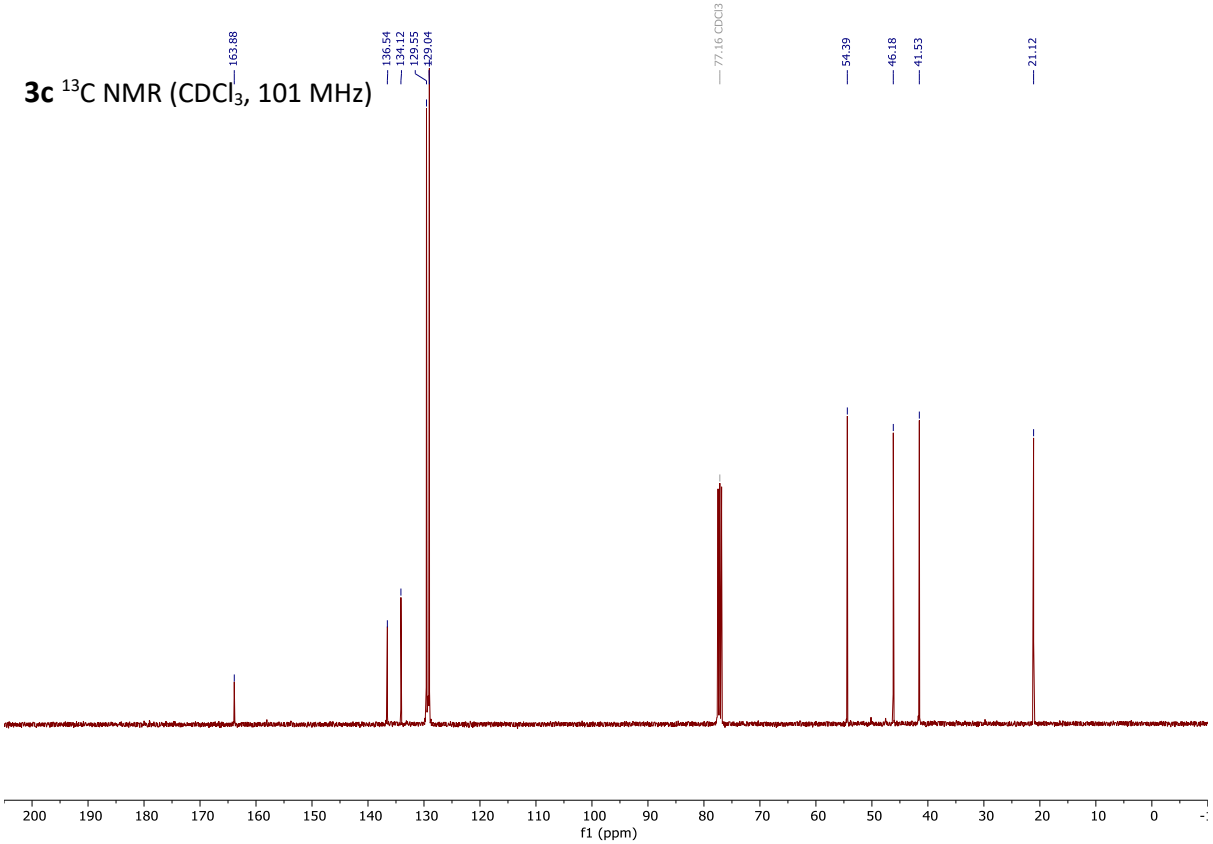


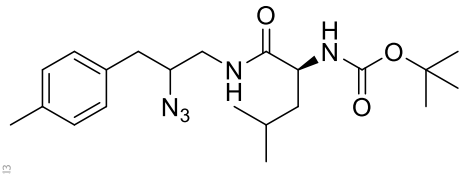


3c ^{1}H NMR ($CDCl_3$, 400 MHz)

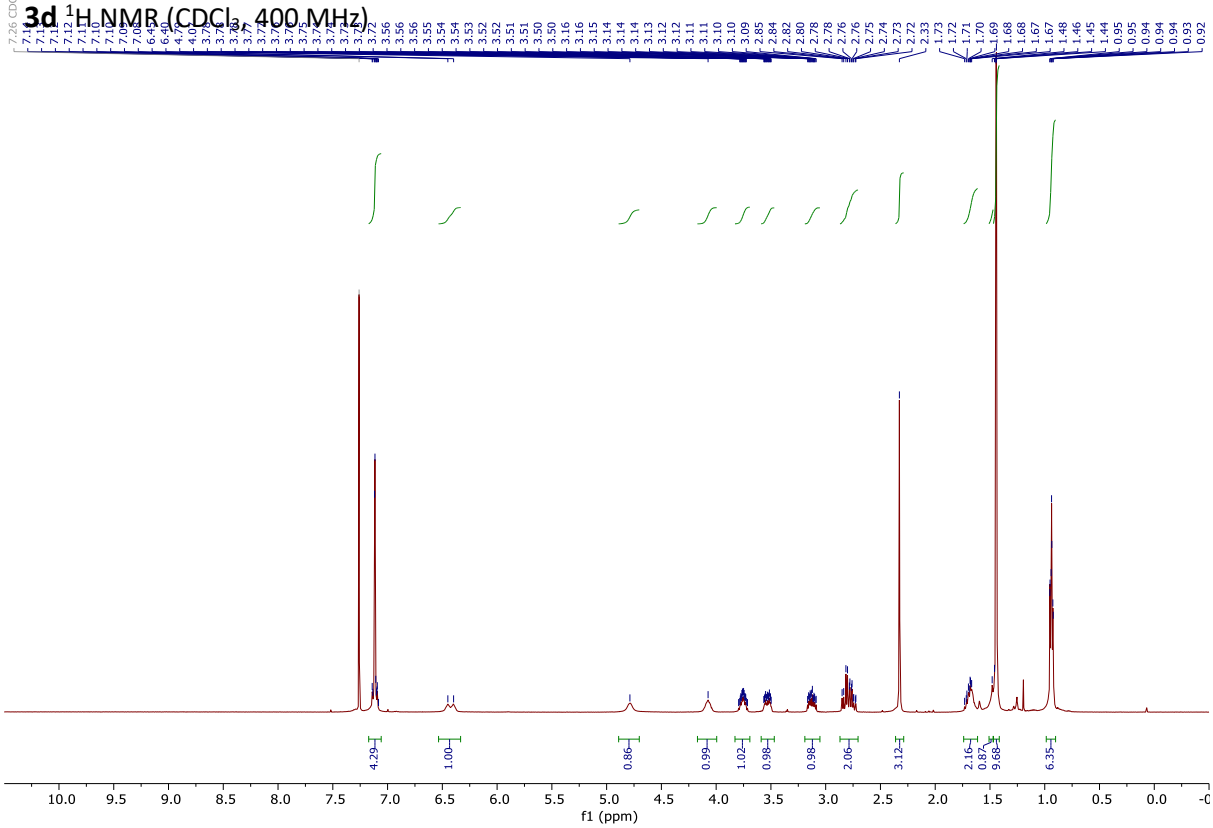


3c ^{13}C NMR ($CDCl_3$, 101 MHz)

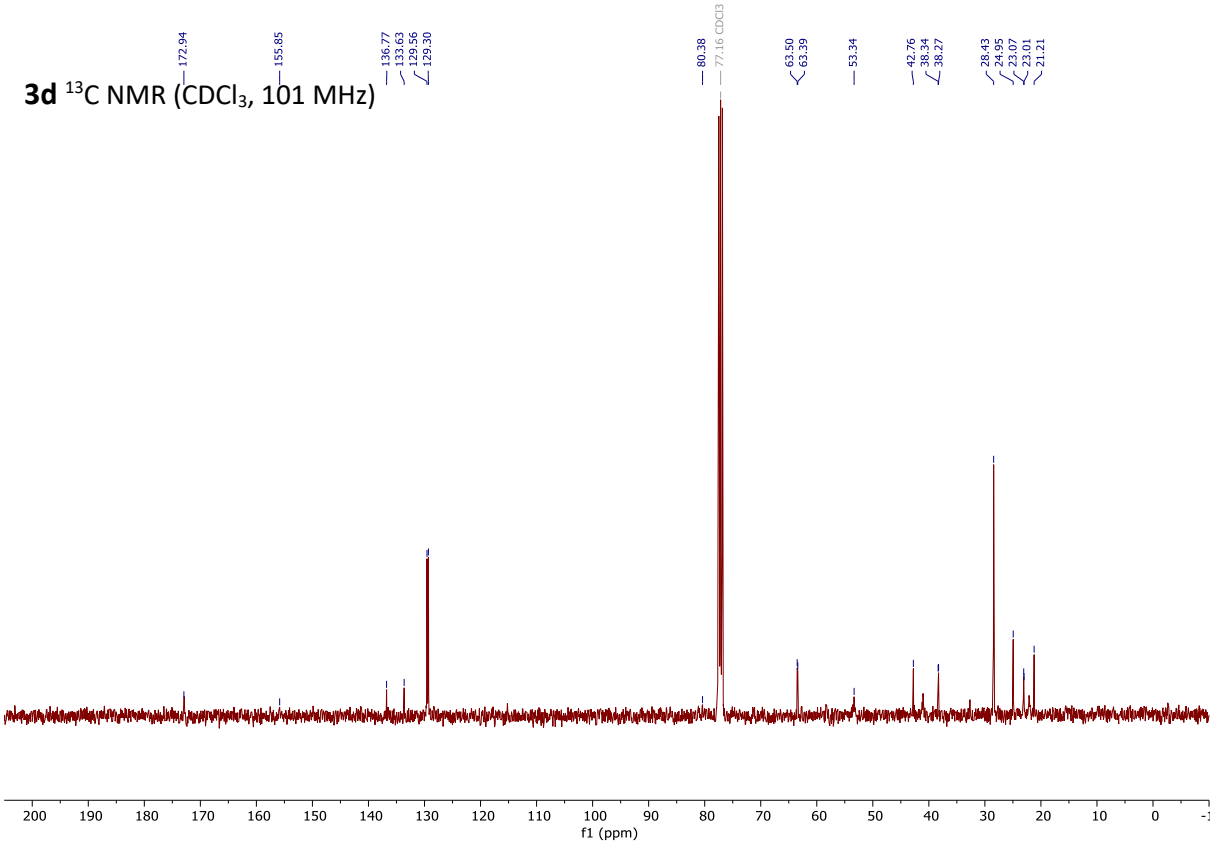


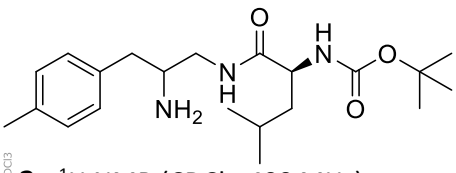


3d ^{1}H NMR ($CDCl_3$, 400 MHz)

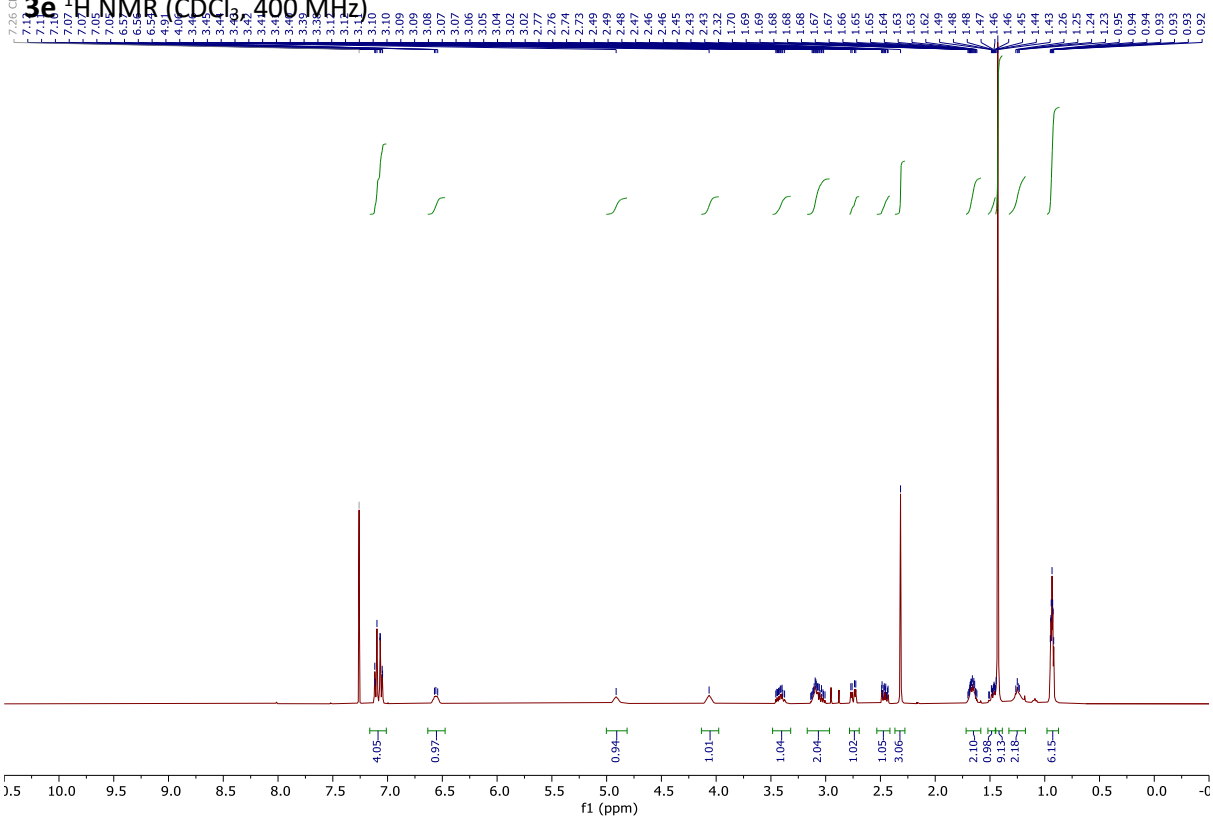


3d ^{13}C NMR ($CDCl_3$, 101 MHz)

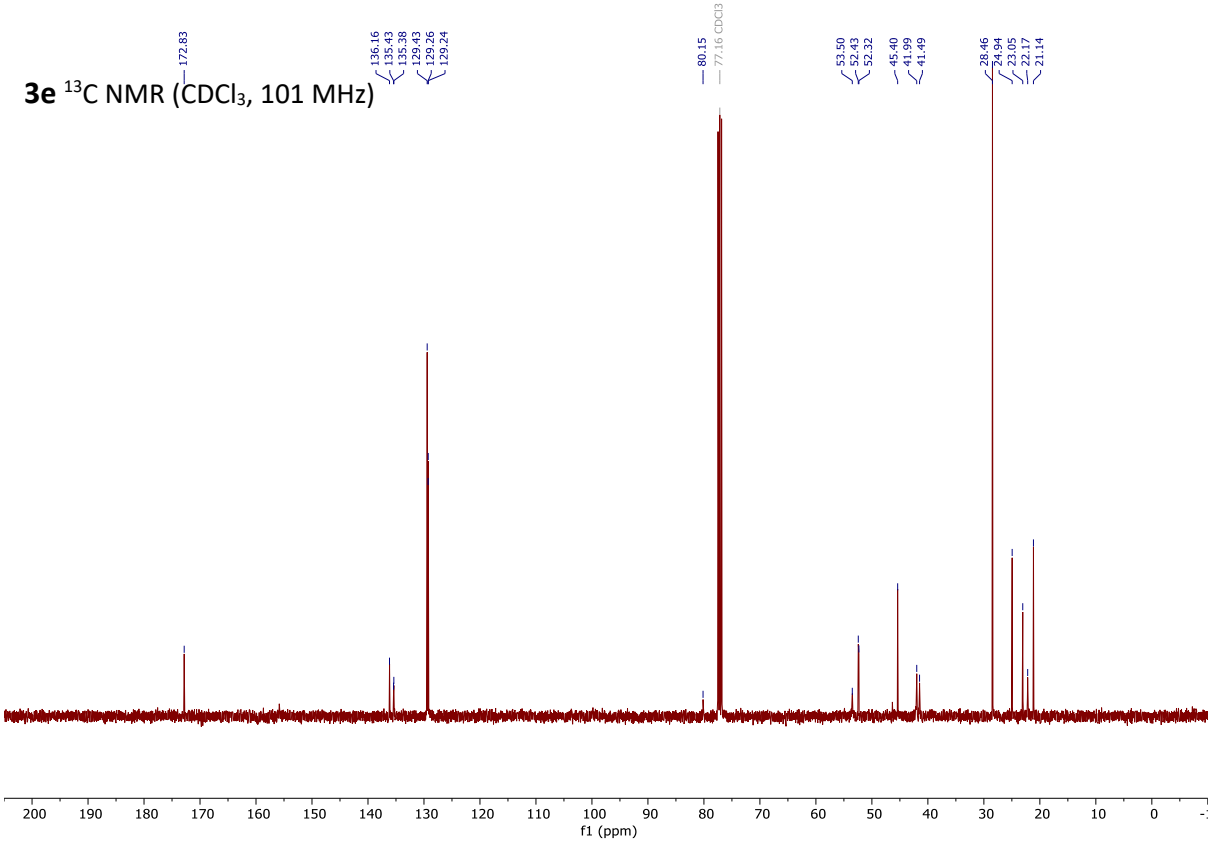


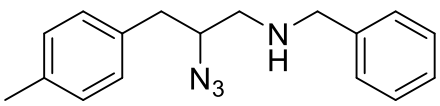


3e ^{1}H NMR ($CDCl_3$, 400 MHz)

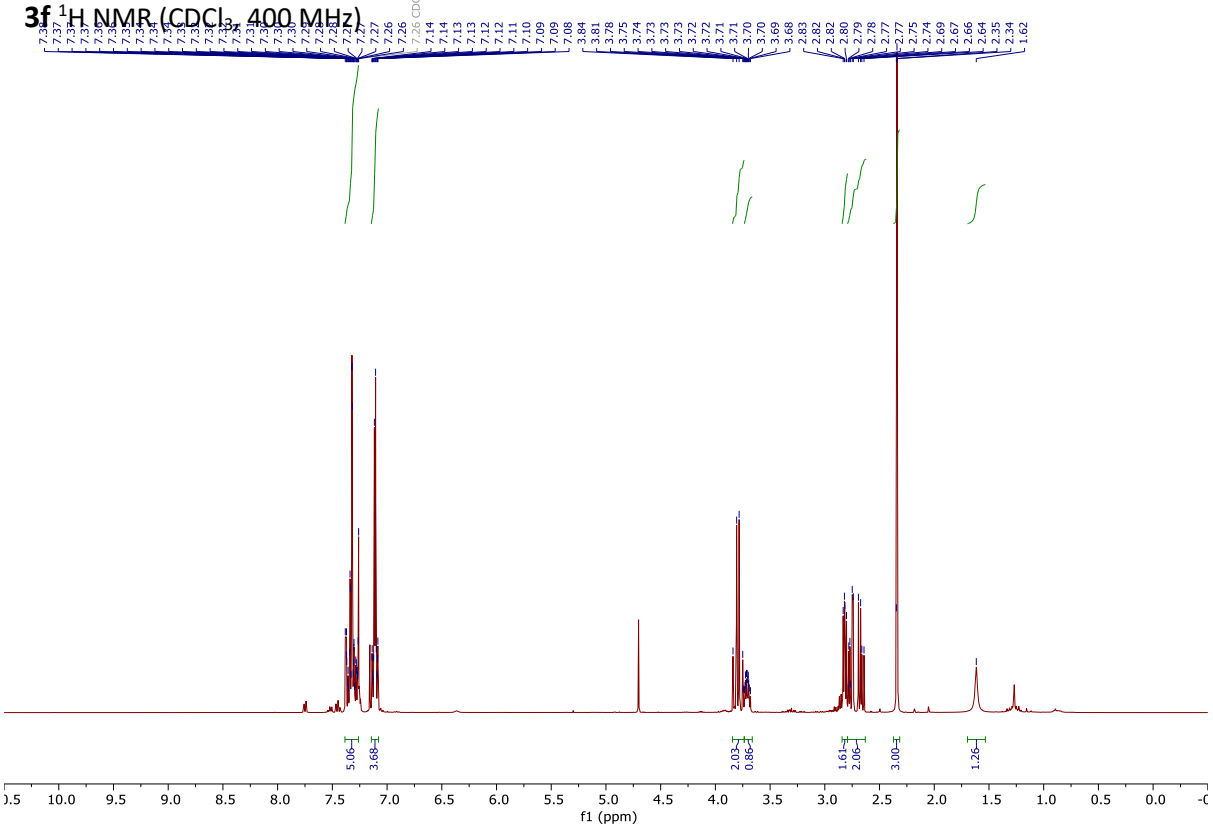


3e ^{13}C NMR ($CDCl_3$, 101 MHz)

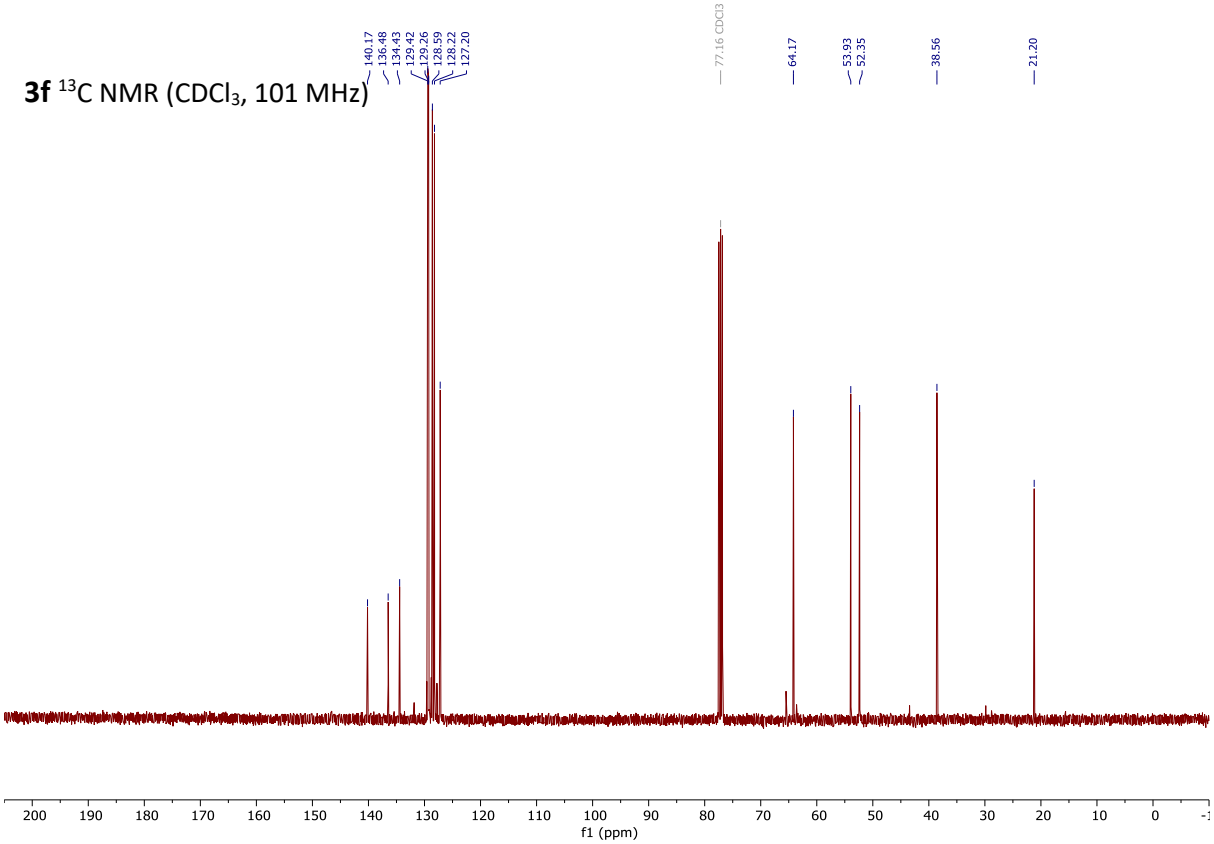


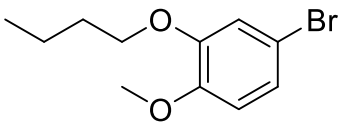


3f ^{1}H NMR ($CDCl_3$, 400 MHz)

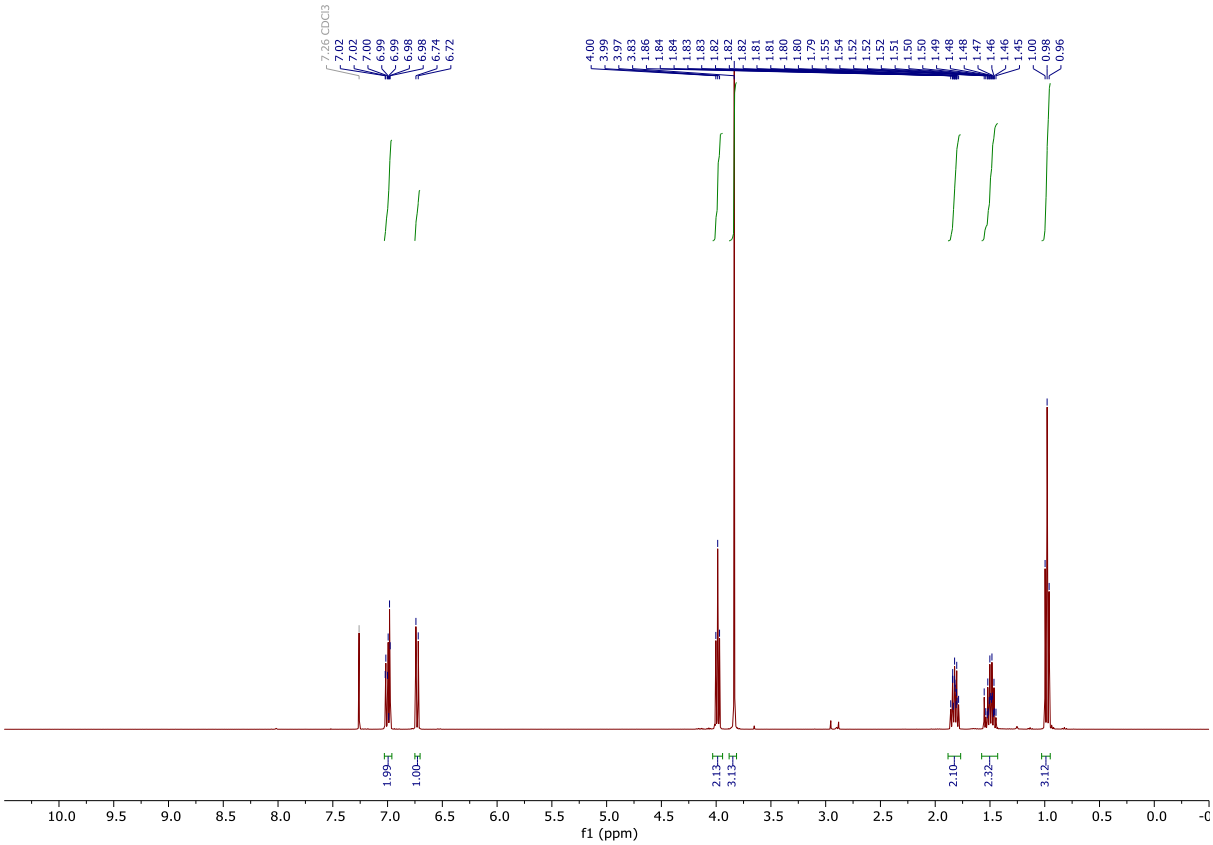


3f ^{13}C NMR ($CDCl_3$, 101 MHz)

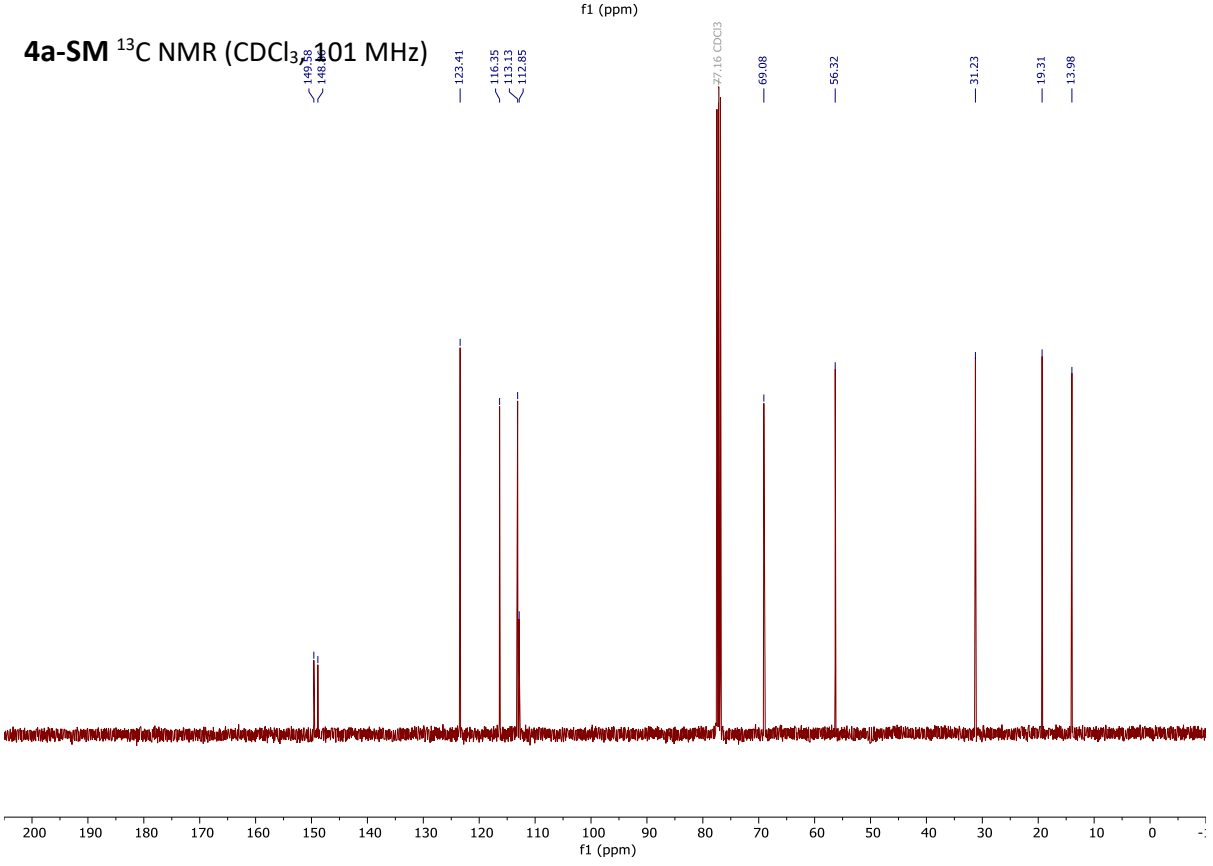


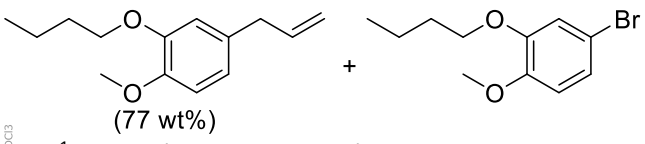


4a-SM ^{1}H NMR ($CDCl_3$, 400 MHz)



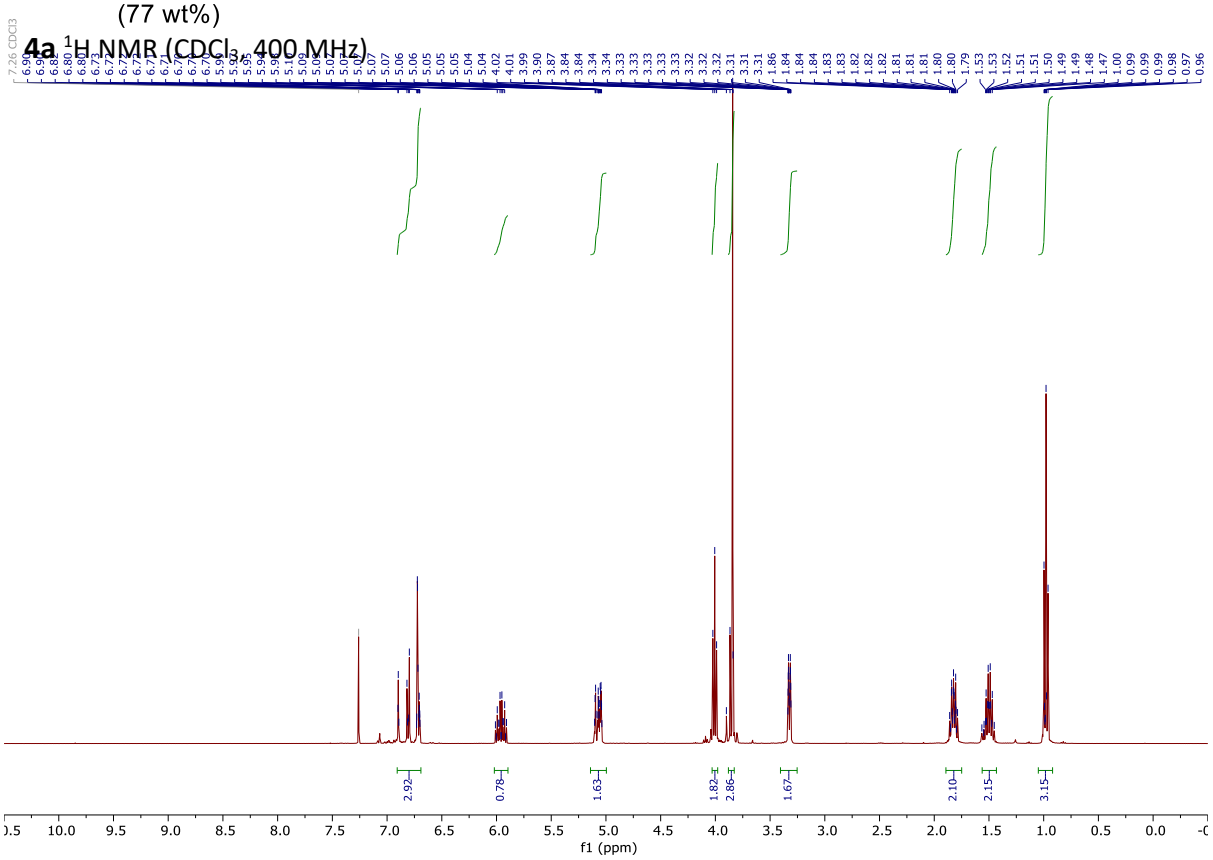
4a-SM ^{13}C NMR ($CDCl_3$, 101 MHz)



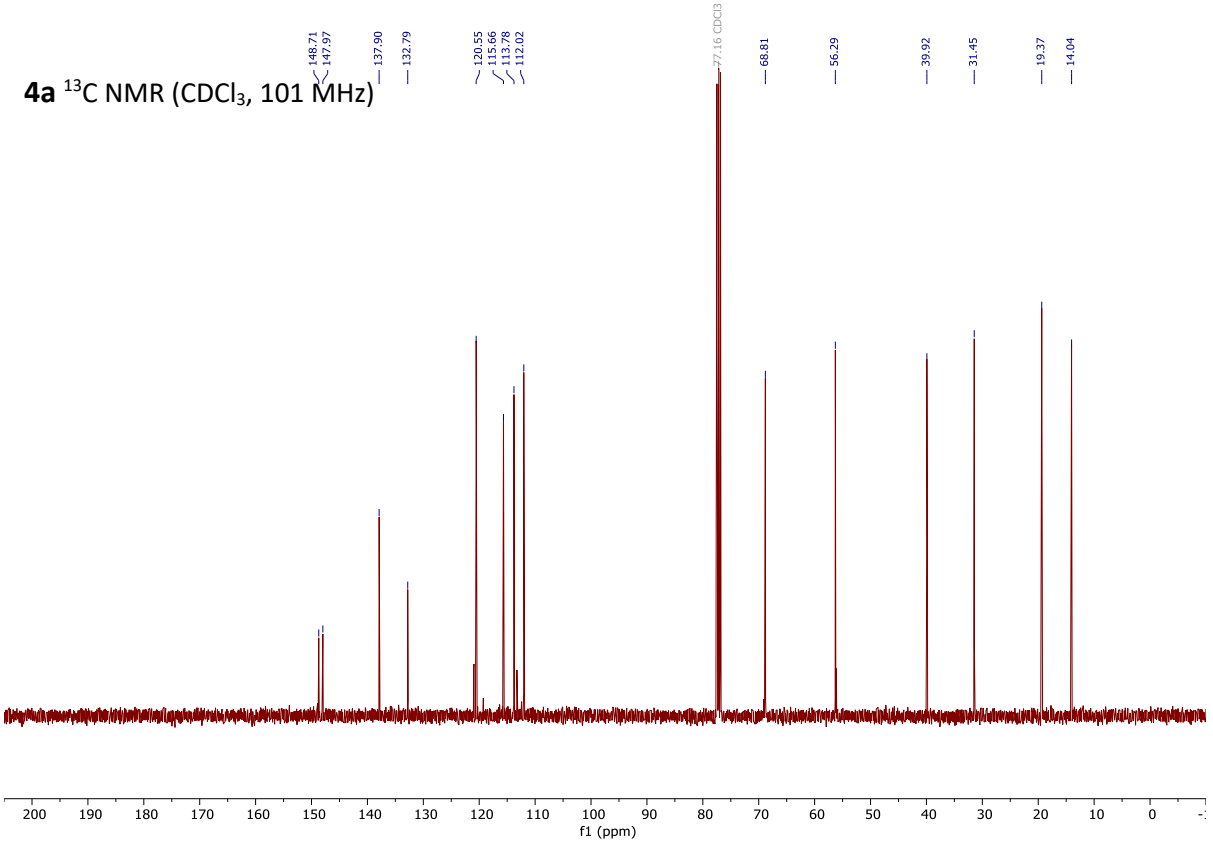


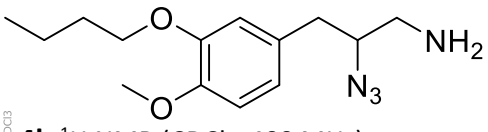
(77 wt%)

4a ^{1}H NMR ($CDCl_3$, 400 MHz)

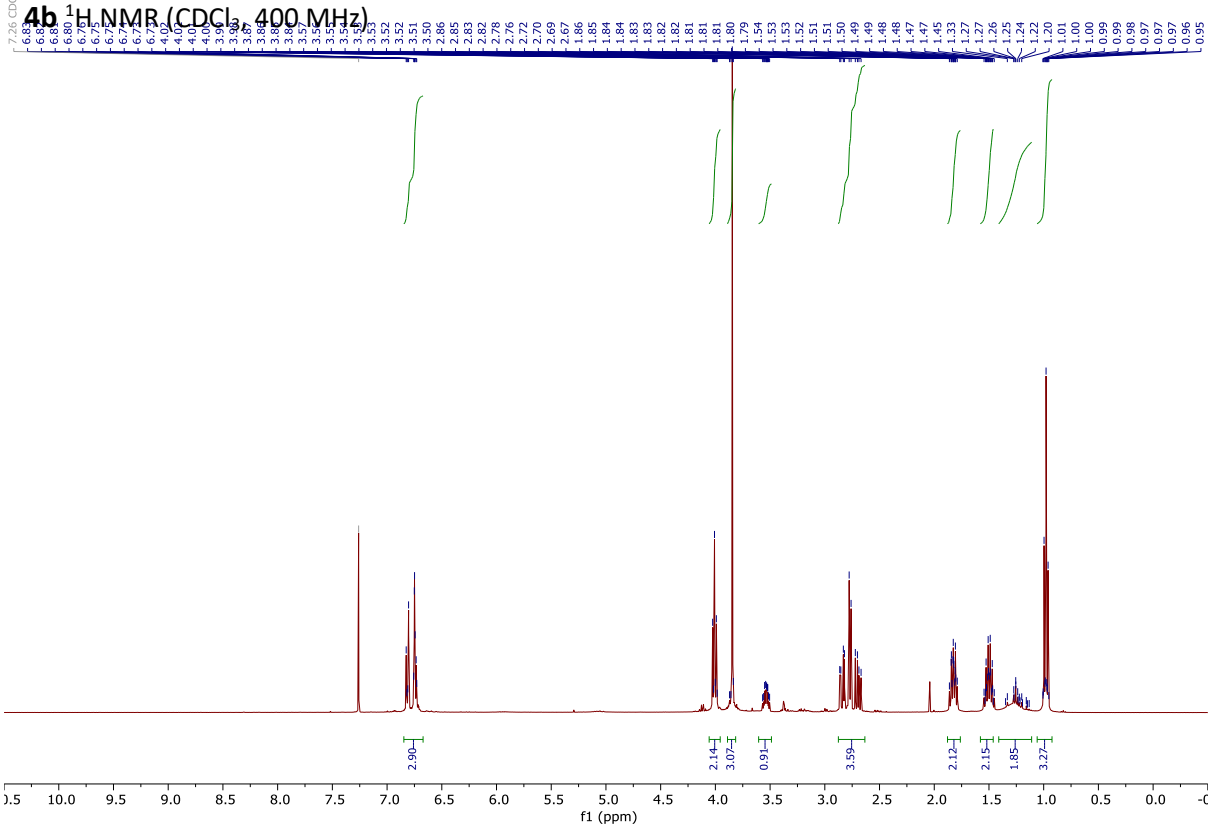


4a ^{13}C NMR ($CDCl_3$, 101 MHz)

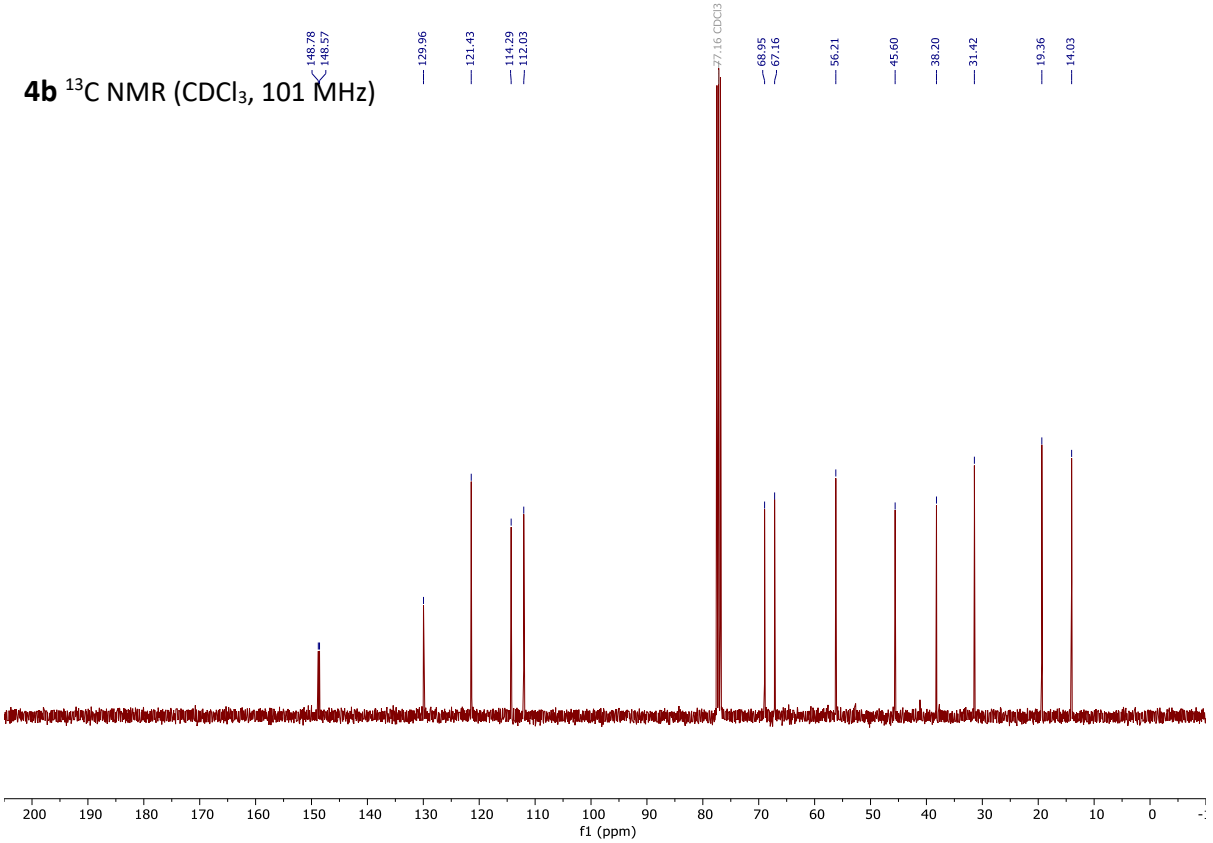


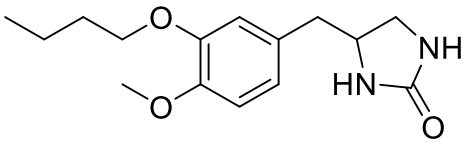


4b ^{1}H NMR ($CDCl_3$, 400 MHz)

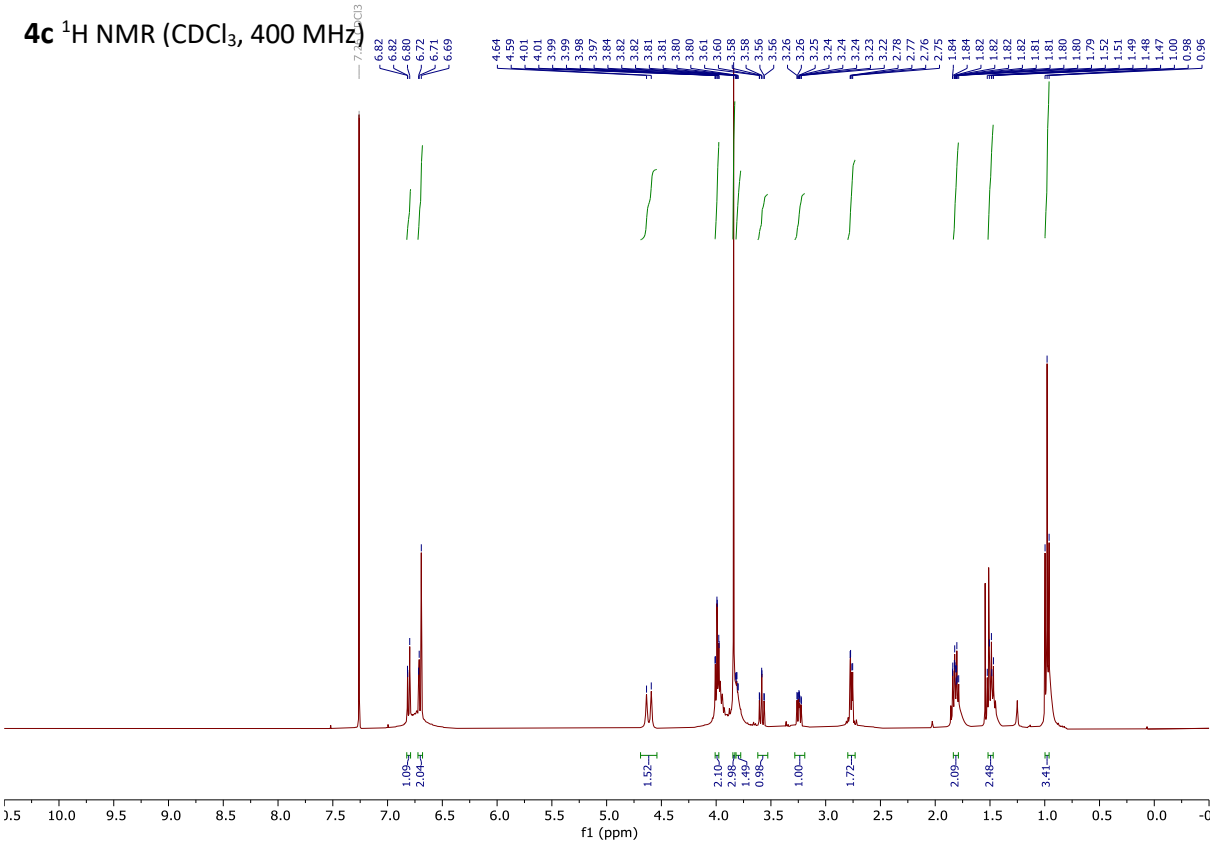


4b ^{13}C NMR ($CDCl_3$, 101 MHz)

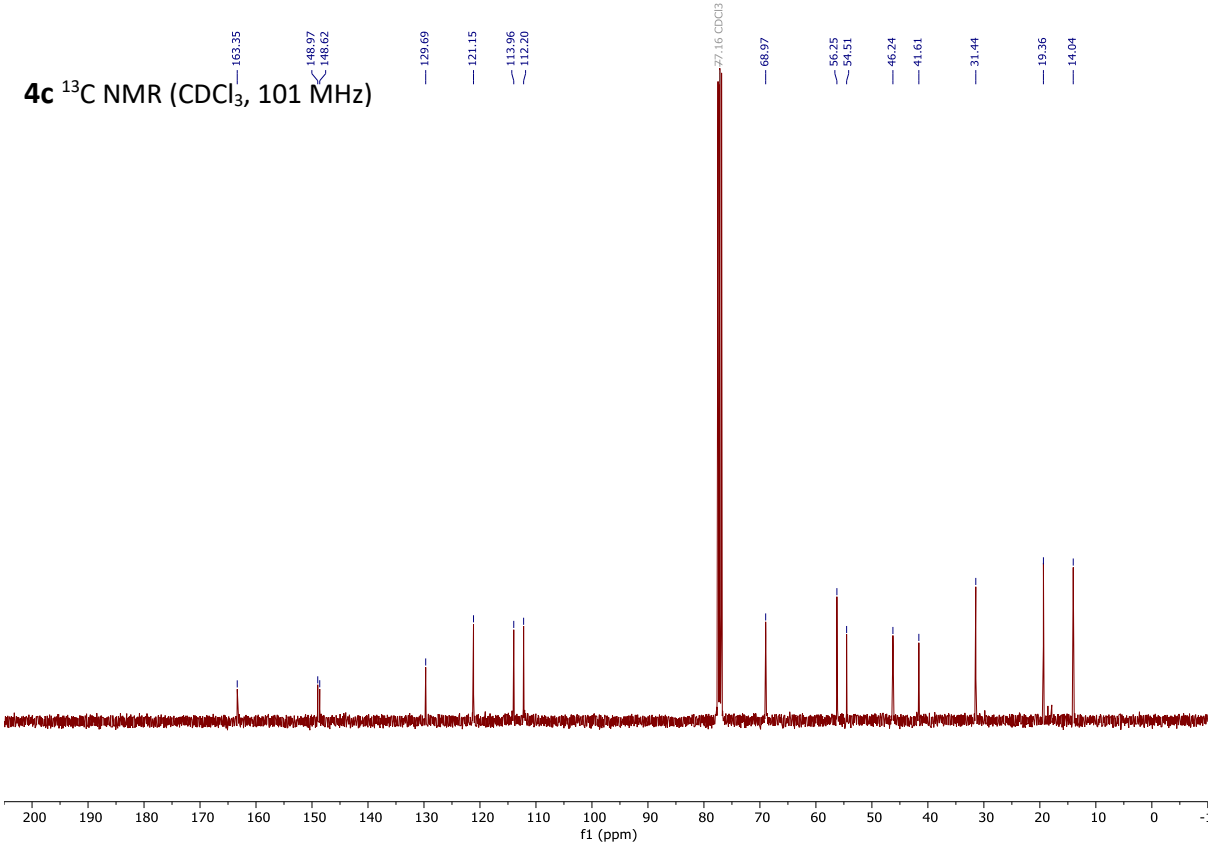


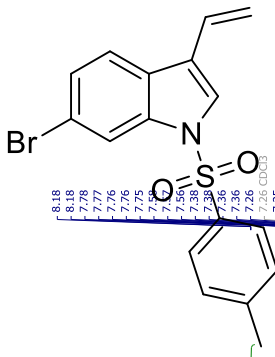


4c ^{1}H NMR ($CDCl_3$, 400 MHz)

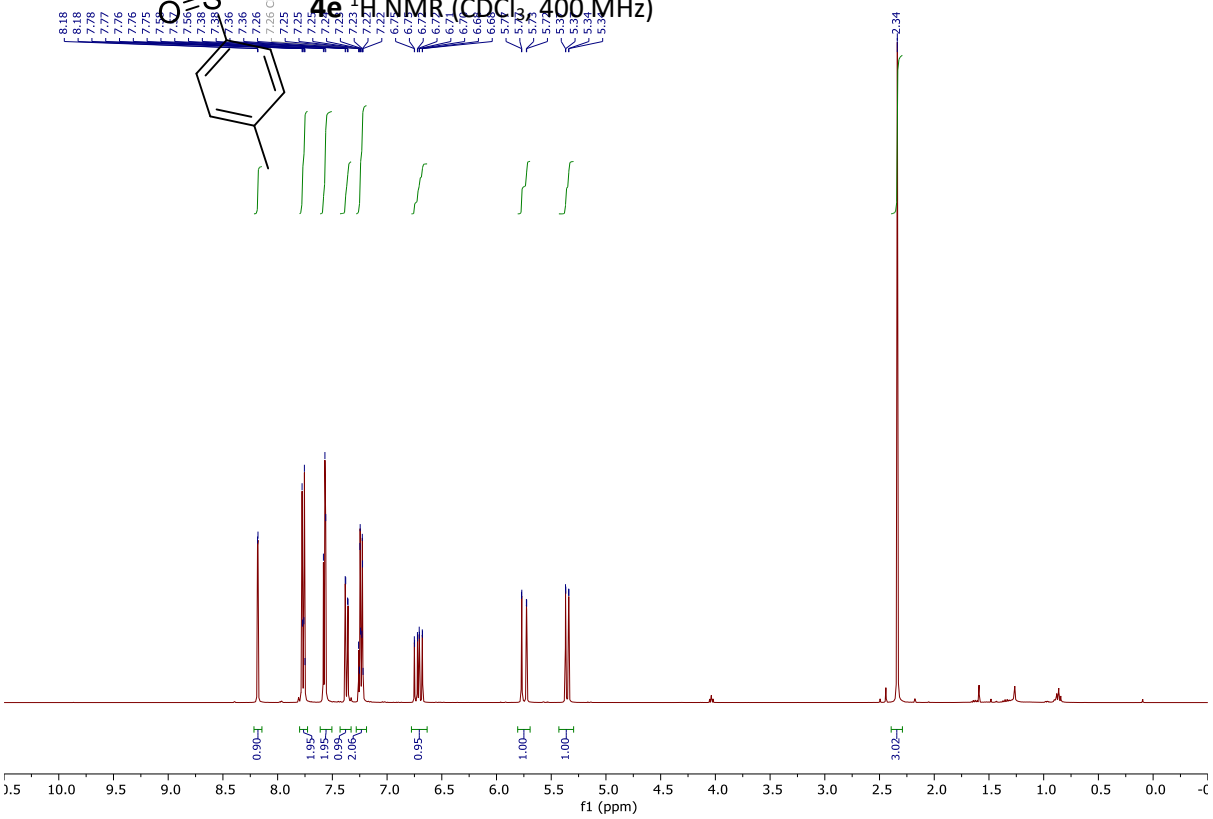


4c ^{13}C NMR ($CDCl_3$, 101 MHz)

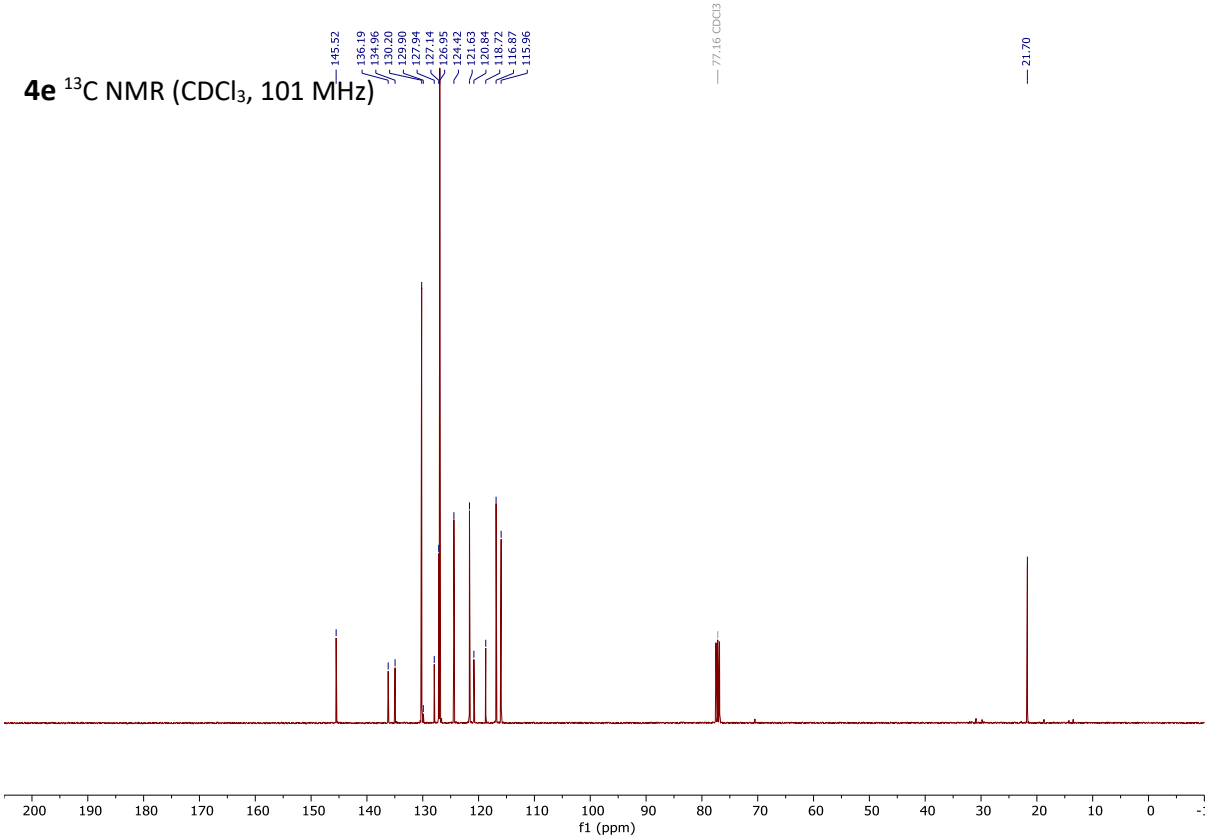


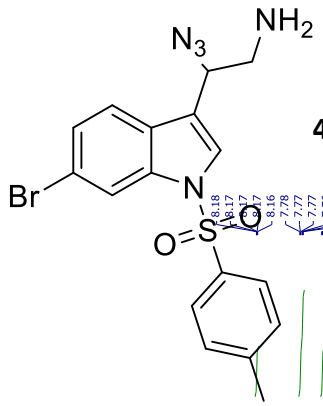


4e ^{1}H NMR ($CDCl_3$, 400 MHz)



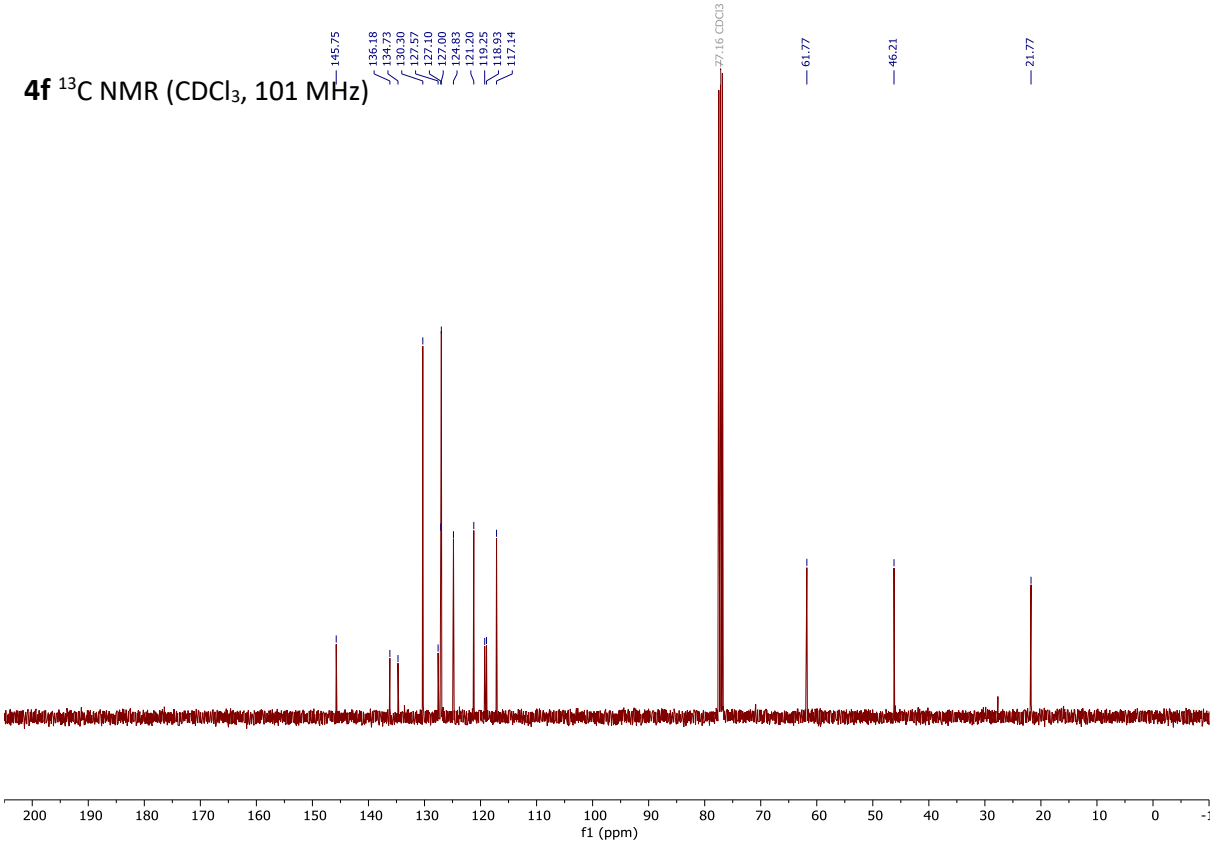
4e ^{13}C NMR ($CDCl_3$, 101 MHz)

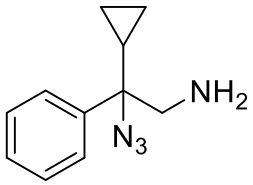




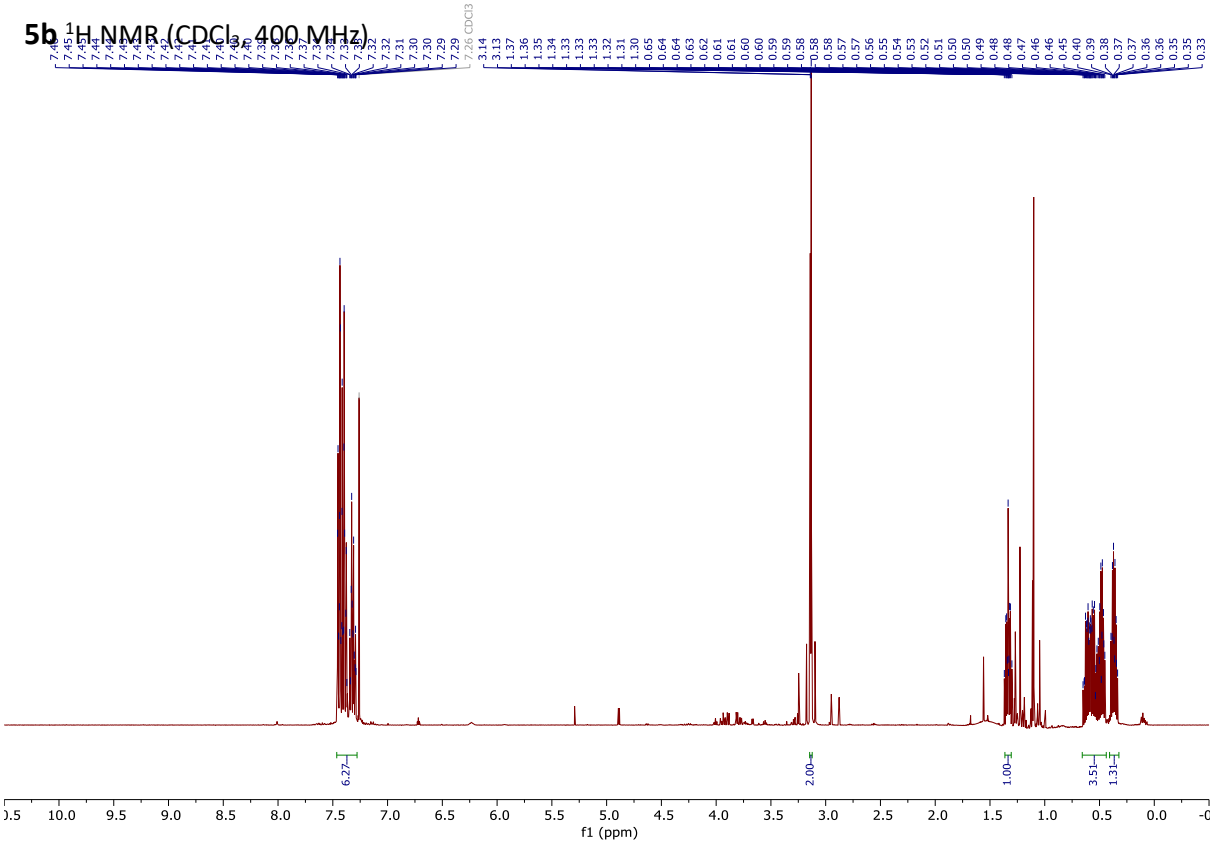
4f ^{1}H NMR ($CDCl_3$, 400 MHz)

4f ^{13}C NMR ($CDCl_3$, 101 MHz)

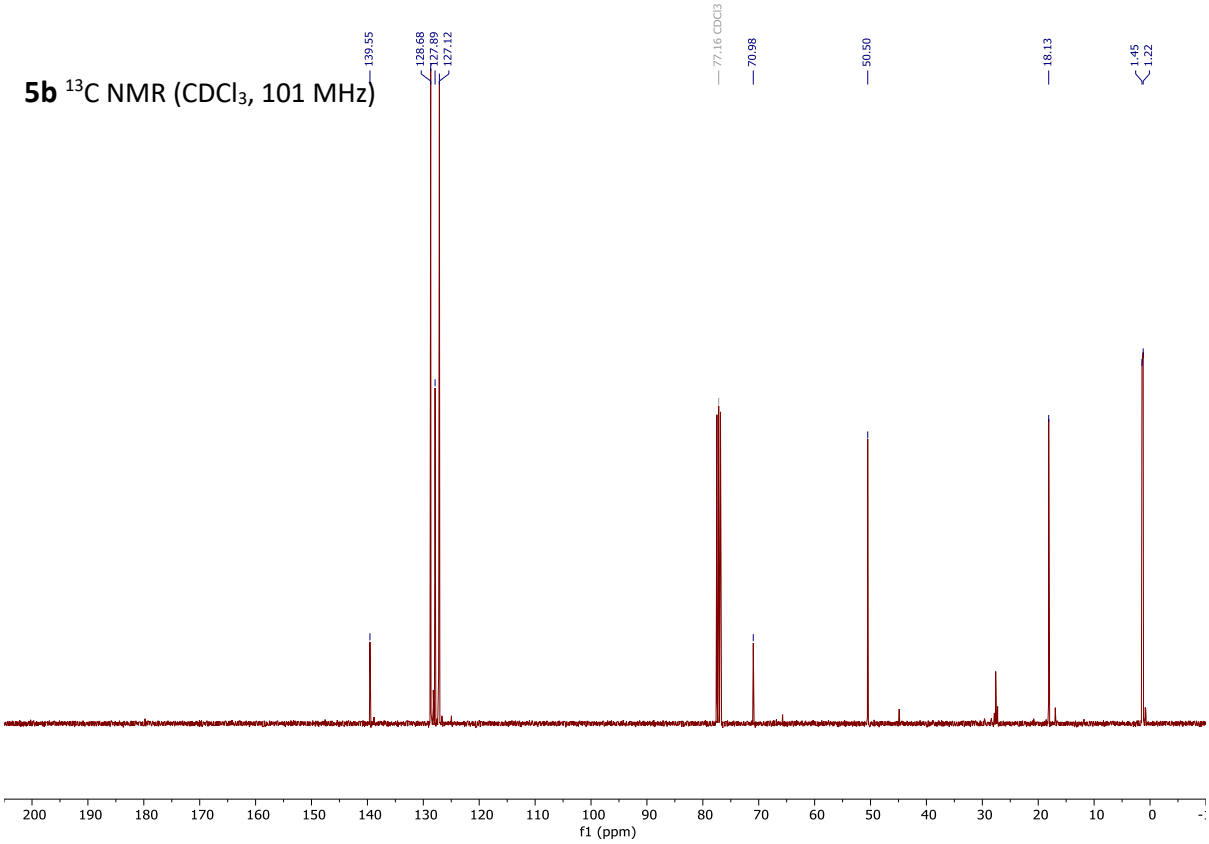


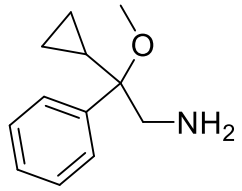


5b ^{1}H NMR ($CDCl_3$, 400 MHz)

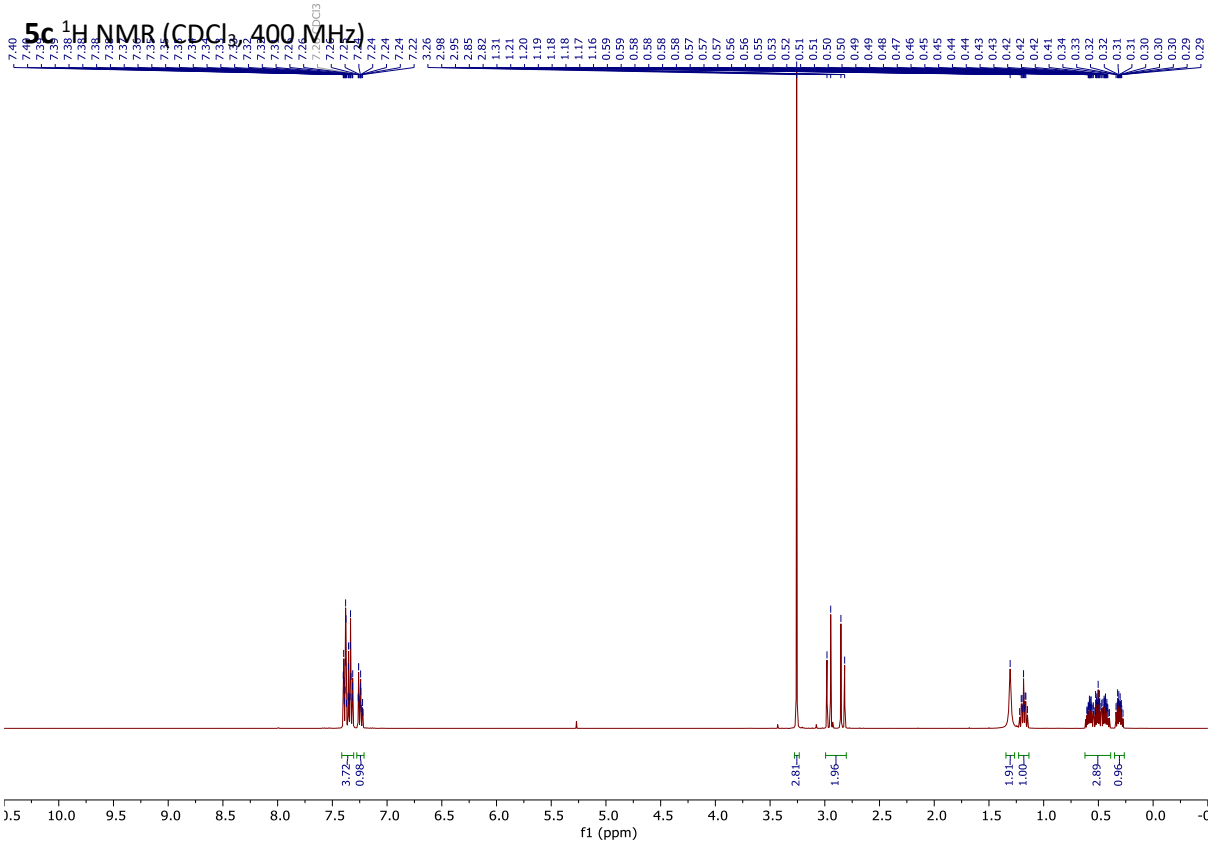


5b ^{13}C NMR ($CDCl_3$, 101 MHz)

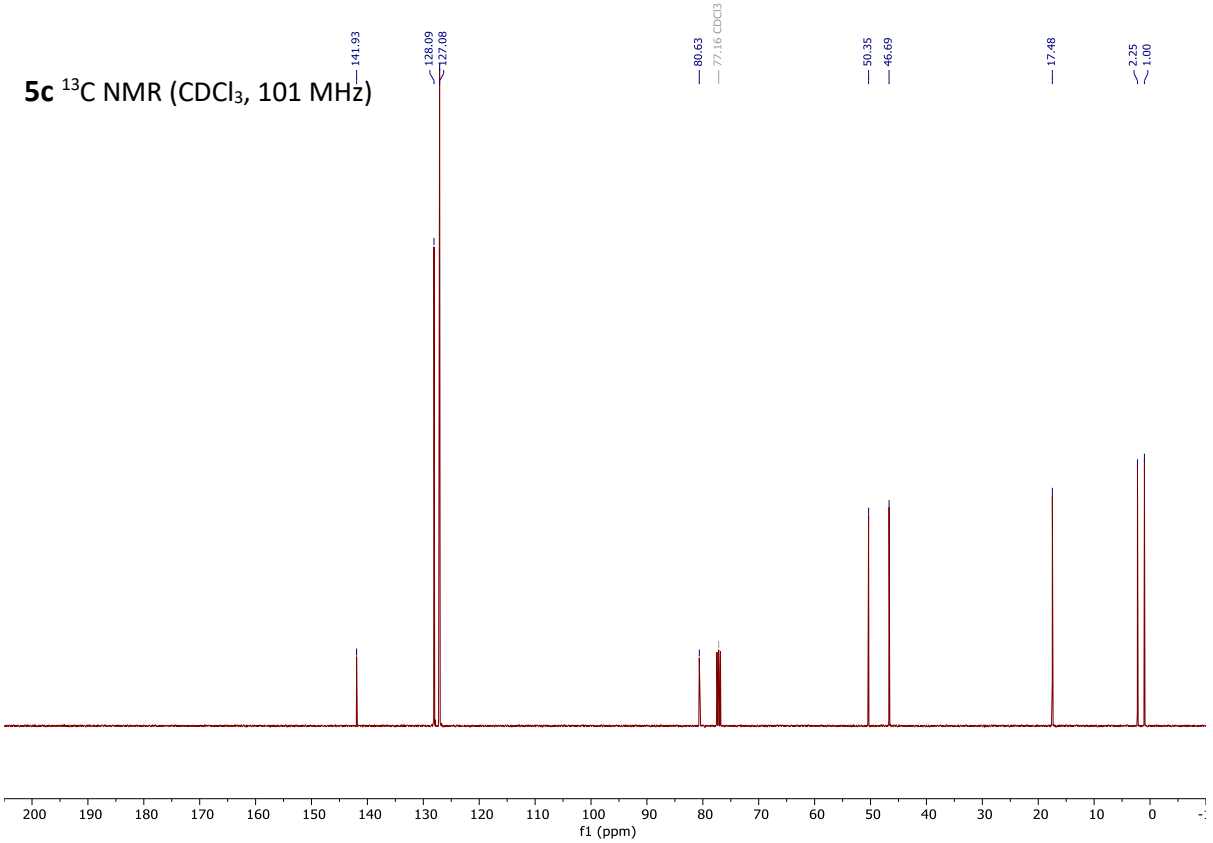


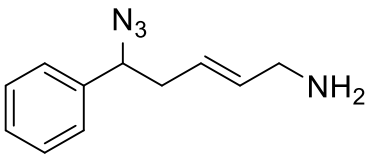


5c ^{1}H NMR ($CDCl_3$, 400 MHz)

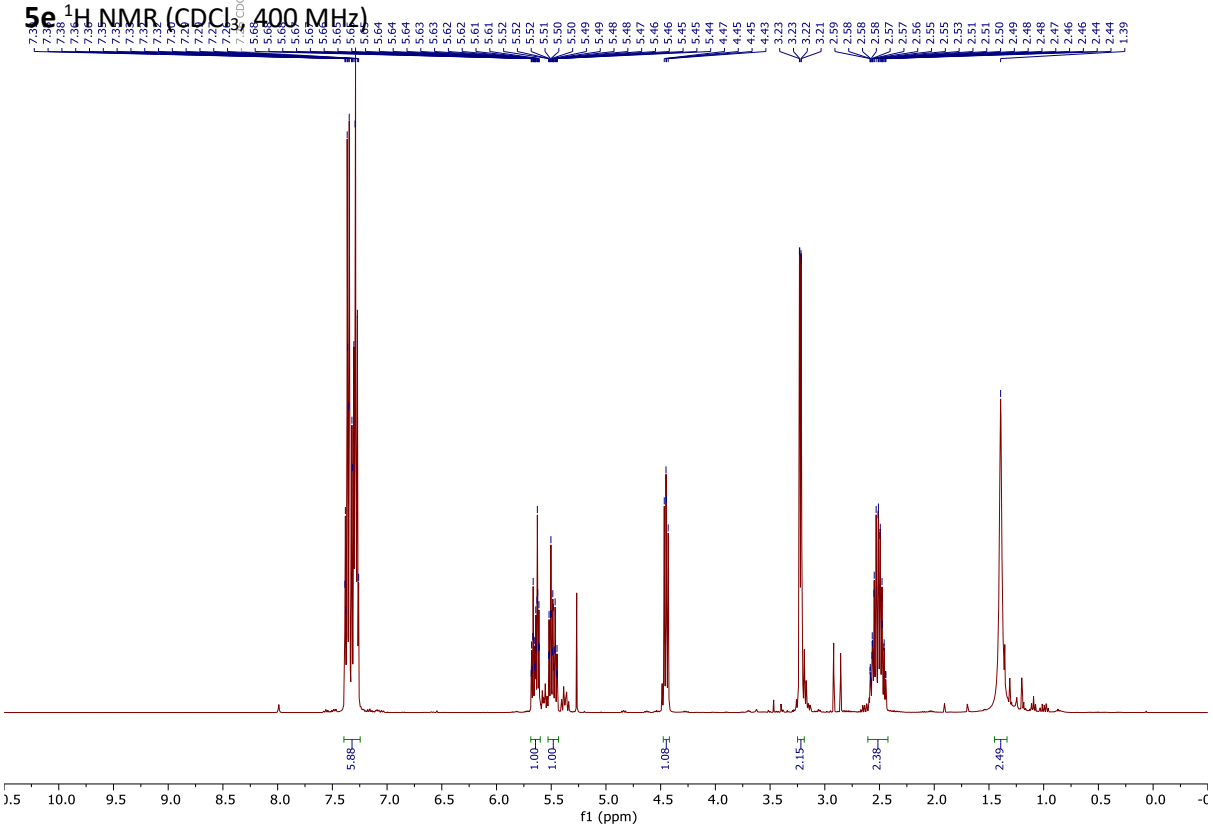


5c ^{13}C NMR ($CDCl_3$, 101 MHz)

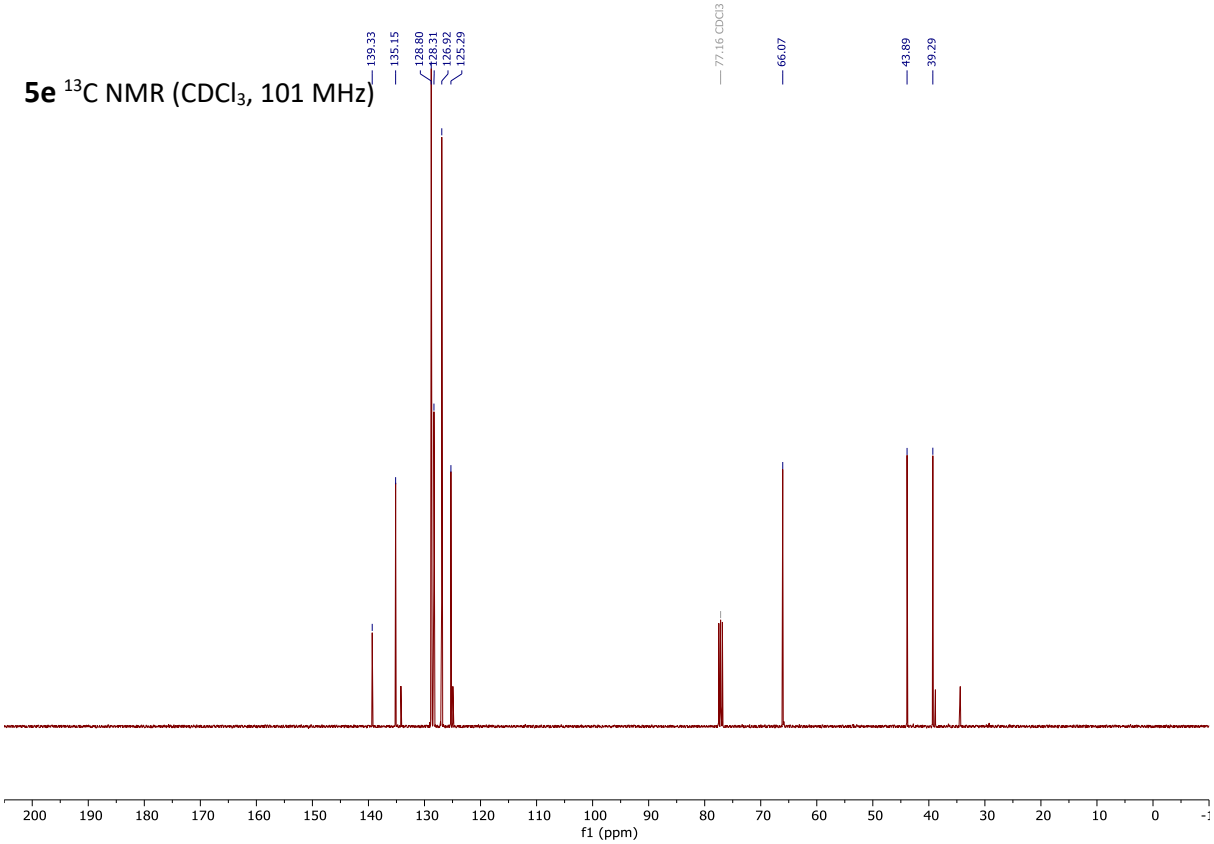


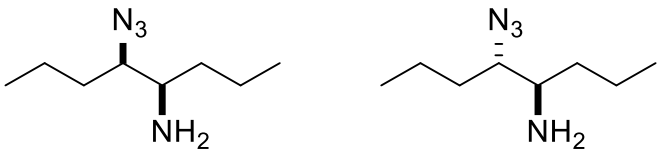


5e ^{1}H NMR ($CDCl_3$, 400 MHz)



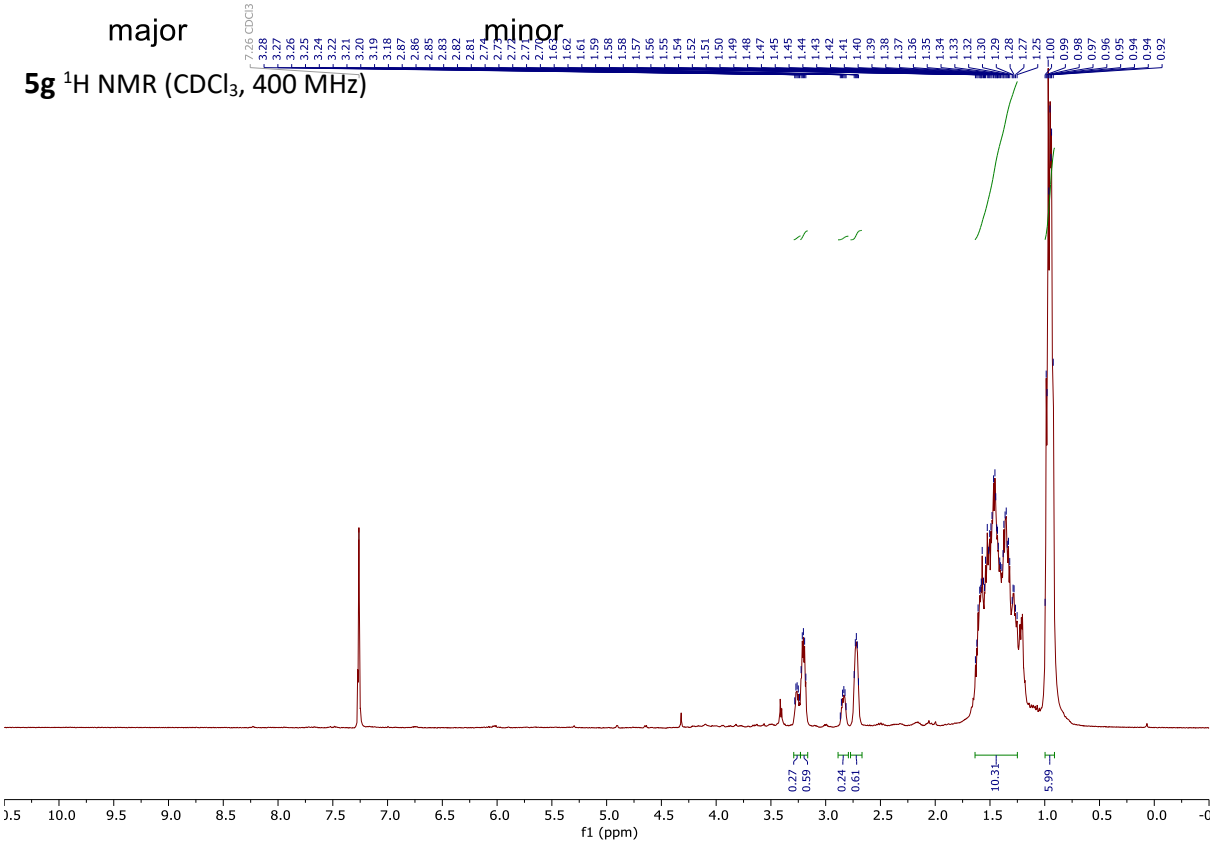
5e ^{13}C NMR ($CDCl_3$, 101 MHz)



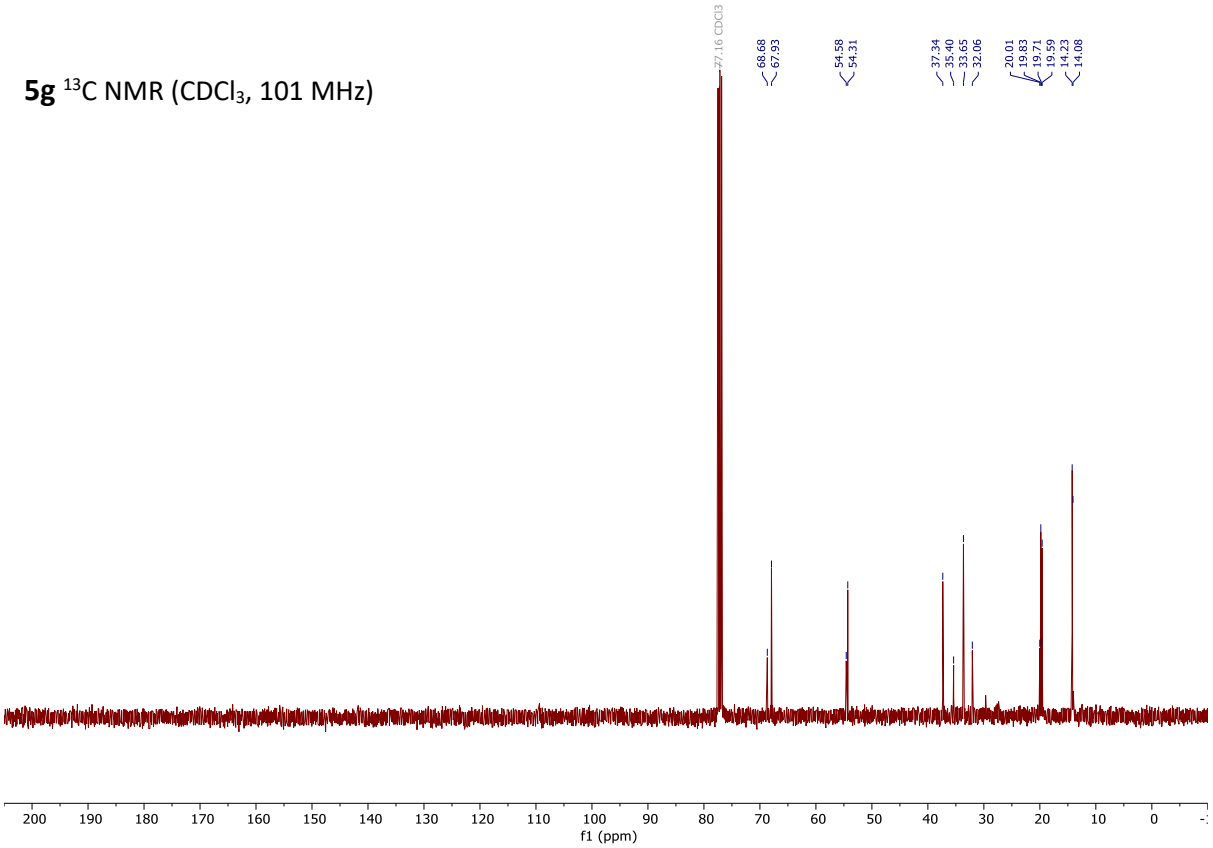


major minor

5g ^{1}H NMR ($CDCl_3$, 400 MHz)



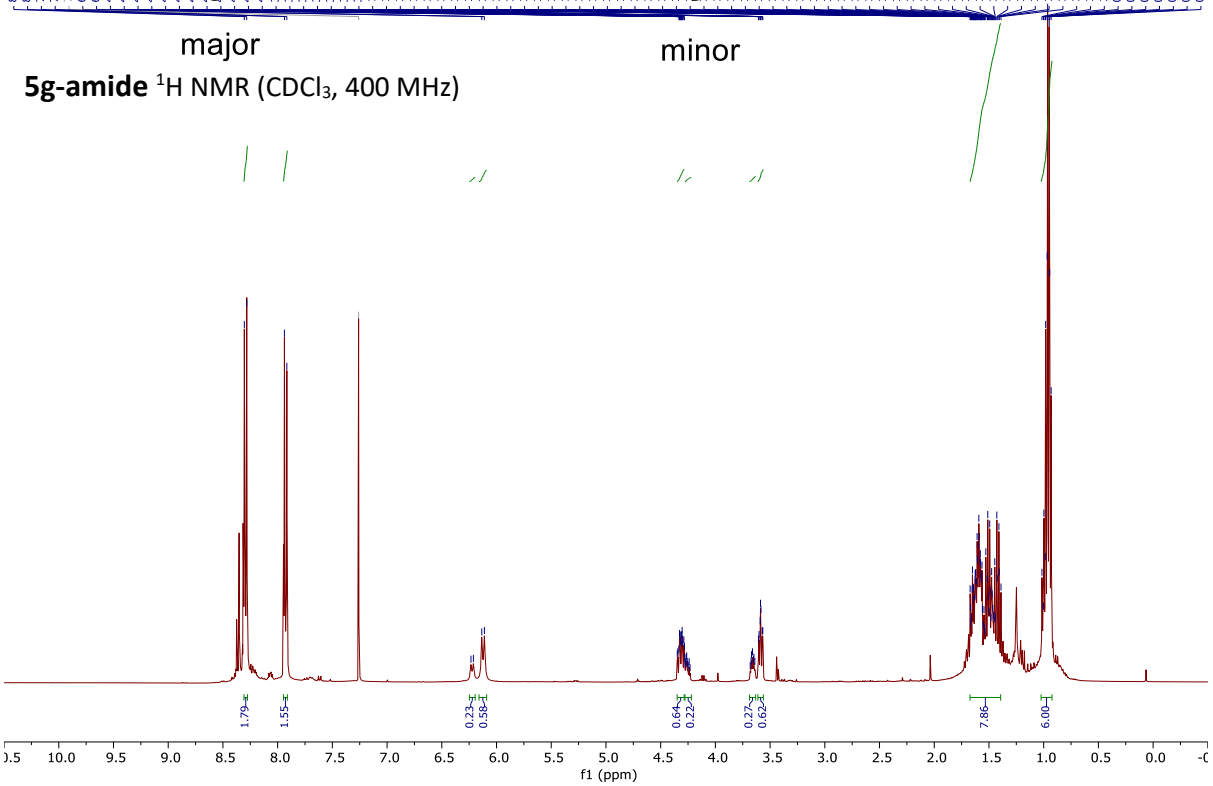
5g ^{13}C NMR ($CDCl_3$, 101 MHz)



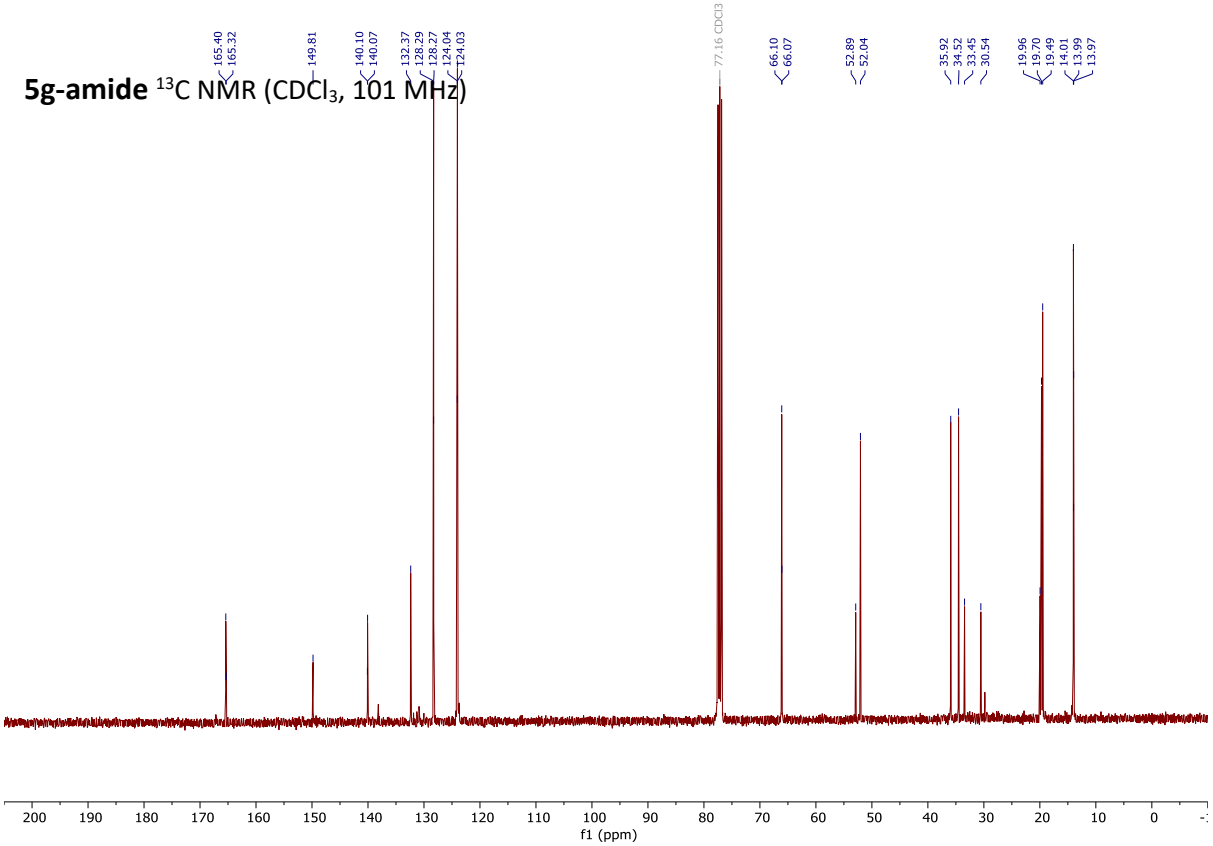
major

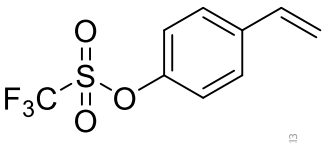
minor

5g-amide ^{1}H NMR ($CDCl_3$, 400 MHz)

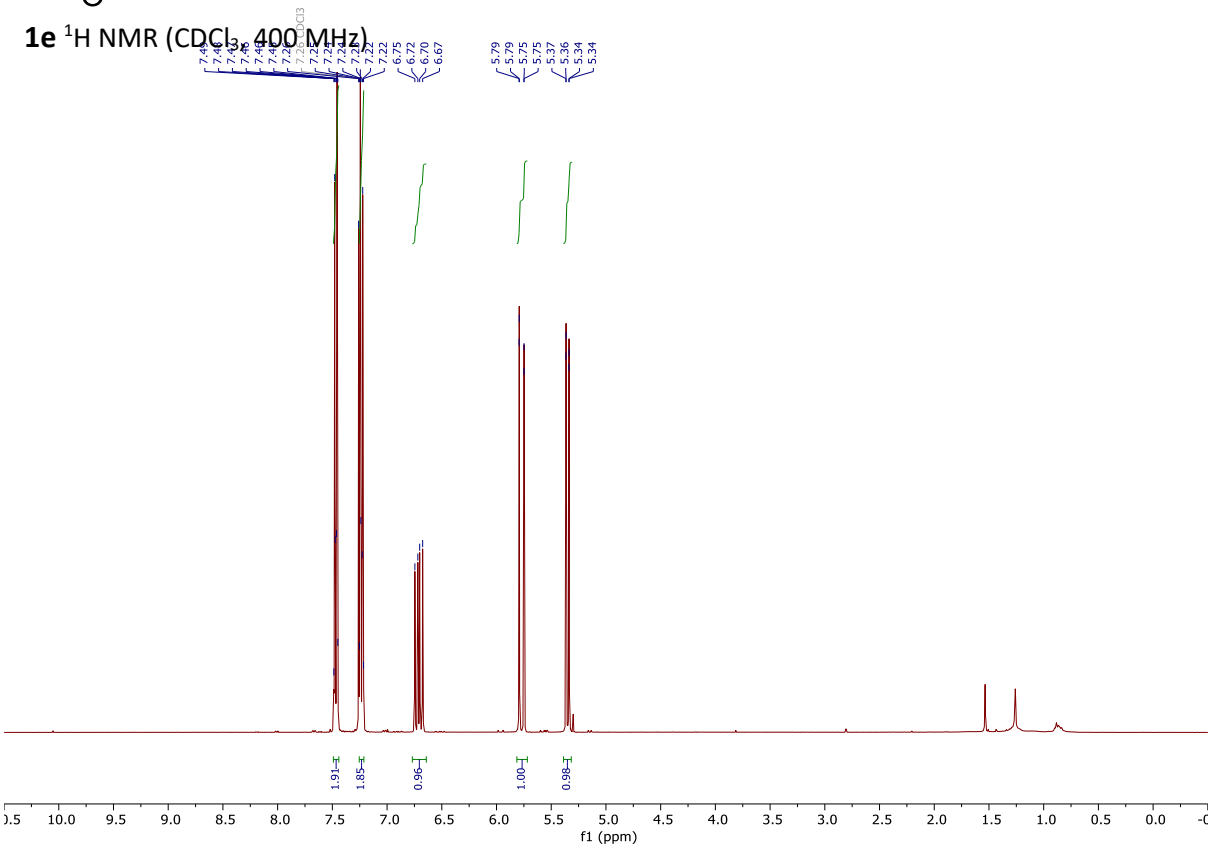


5g-amide ^{13}C NMR ($CDCl_3$, 101 MHz)

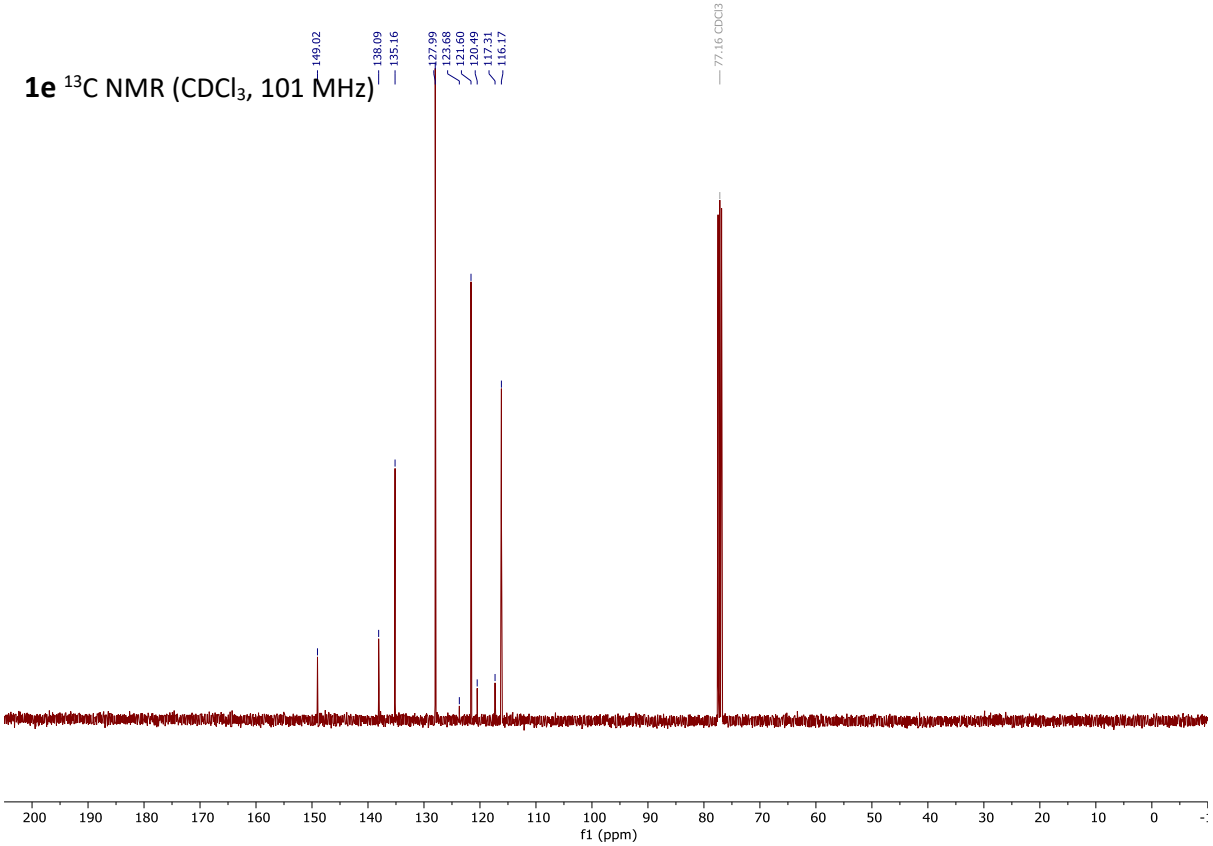


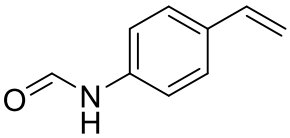


1e ^{1}H NMR ($CDCl_3$, 400 MHz)

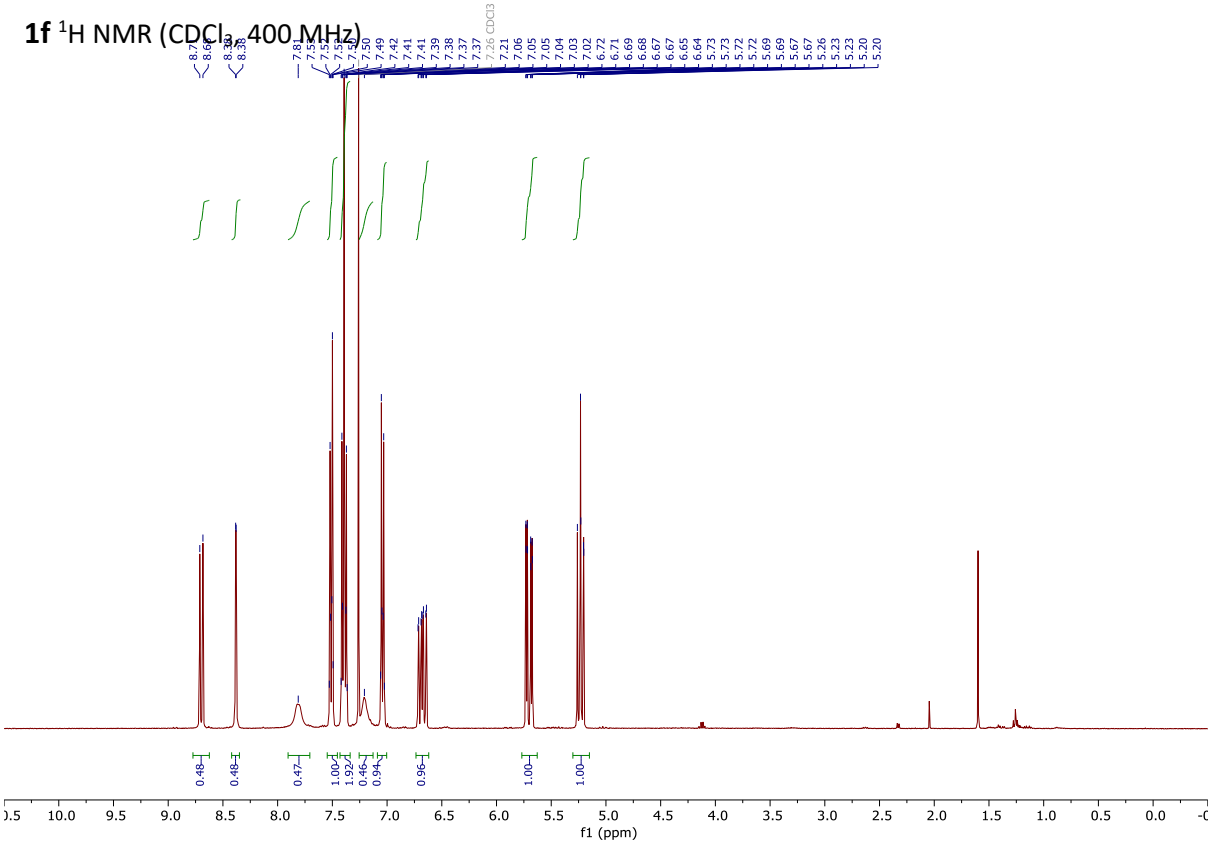


1e ^{13}C NMR ($CDCl_3$, 101 MHz)

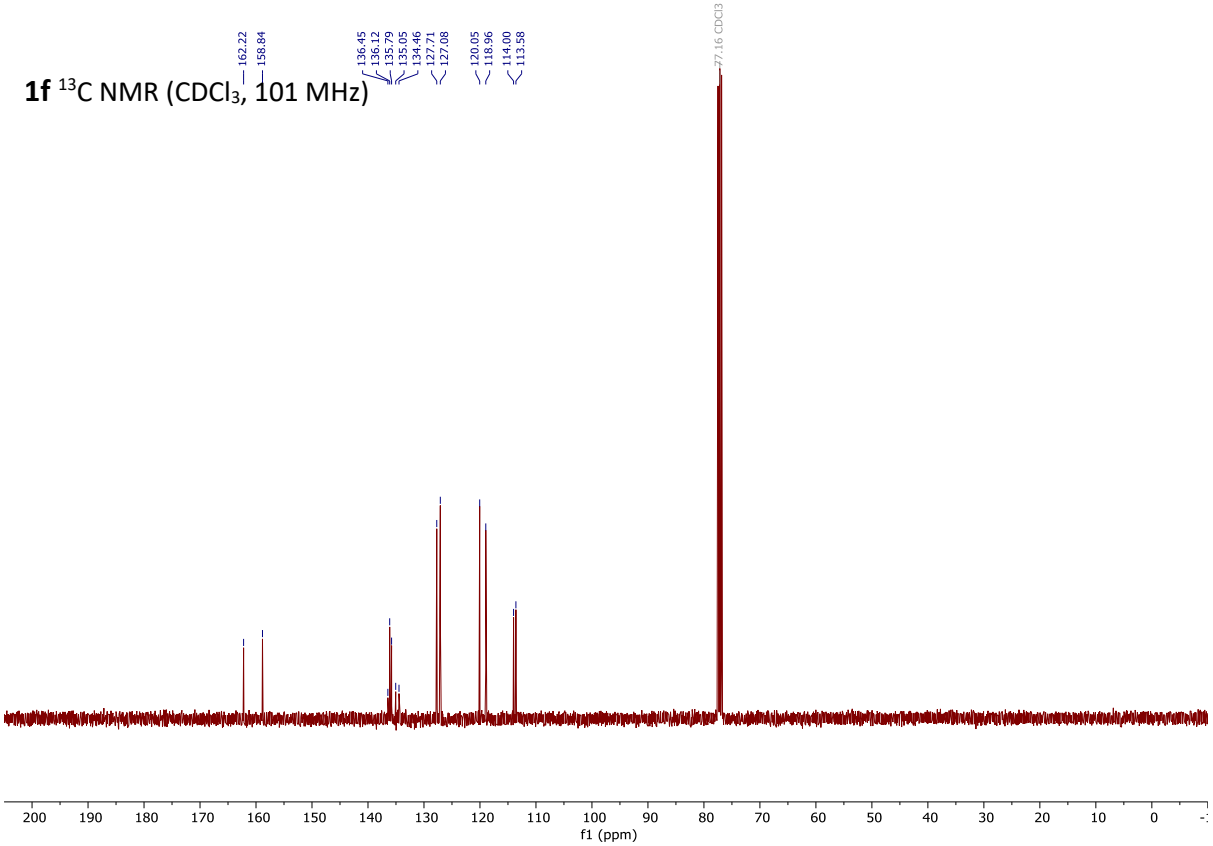


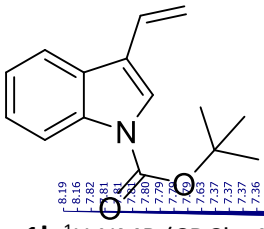


1f ^{1}H NMR ($CDCl_3$, 400 MHz)

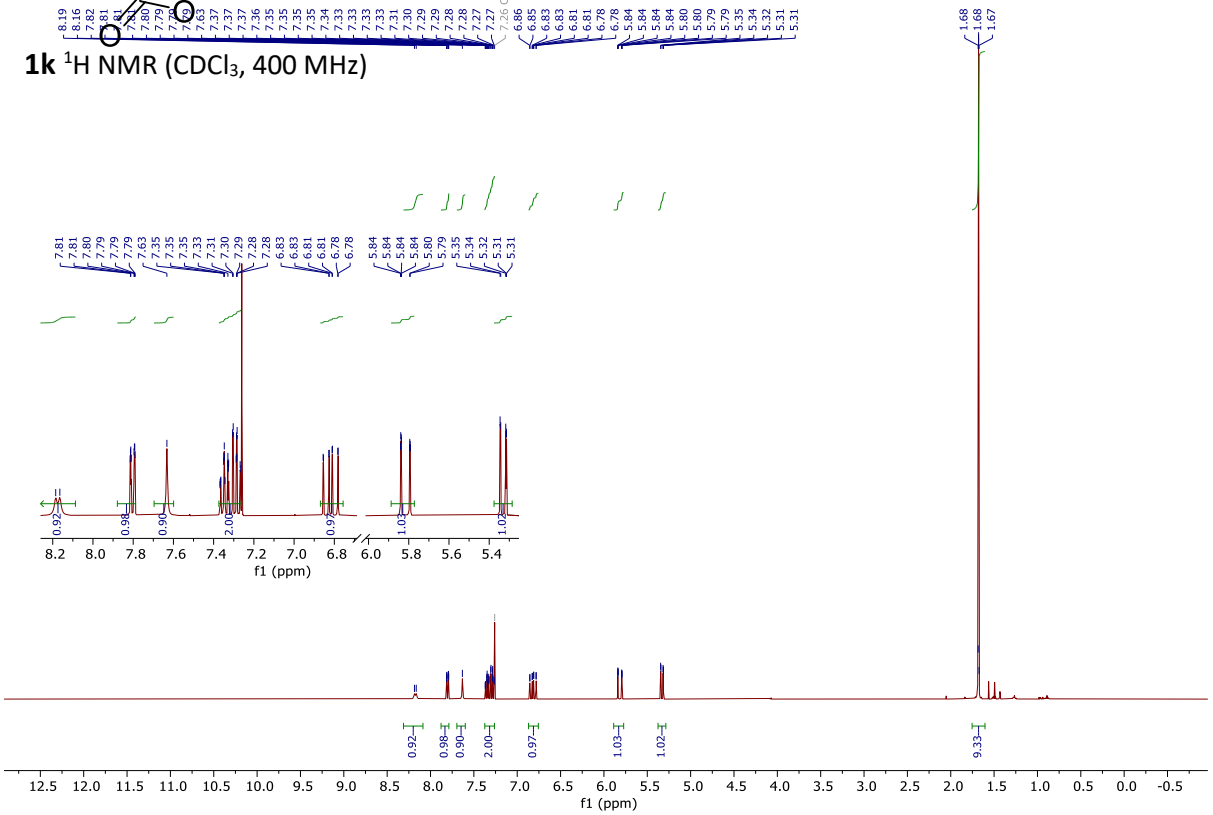


1f ^{13}C NMR ($CDCl_3$, 101 MHz)

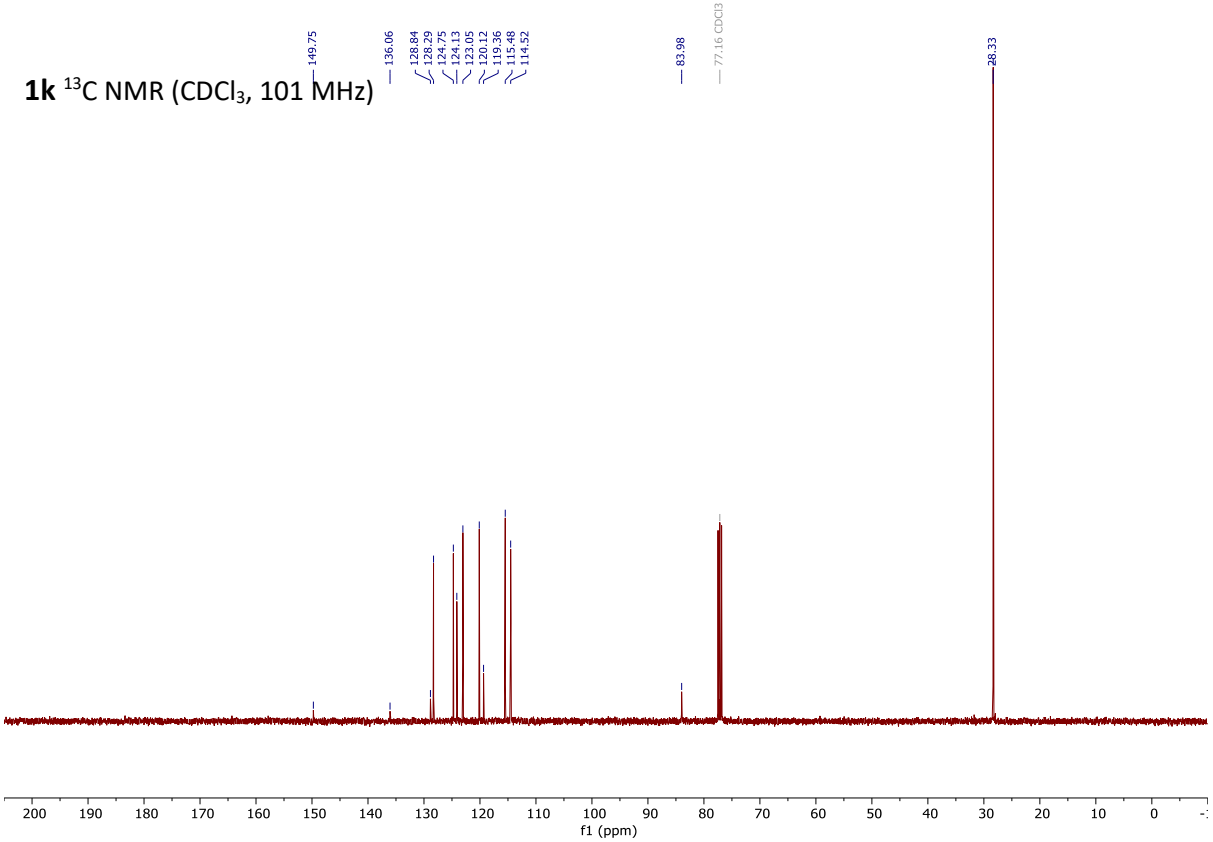


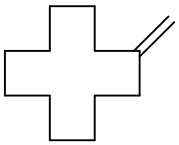


1k ^{1}H NMR ($CDCl_3$, 400 MHz)

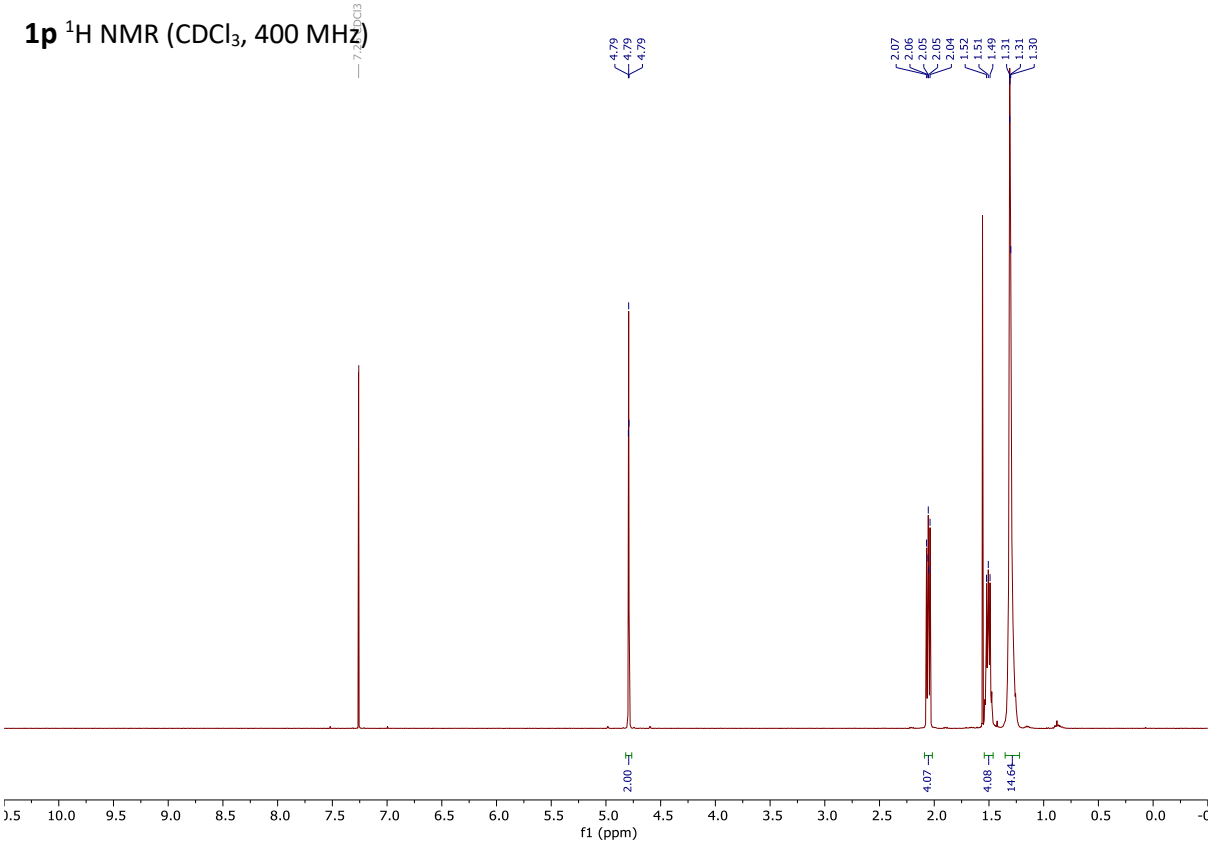


1k ^{13}C NMR ($CDCl_3$, 101 MHz)

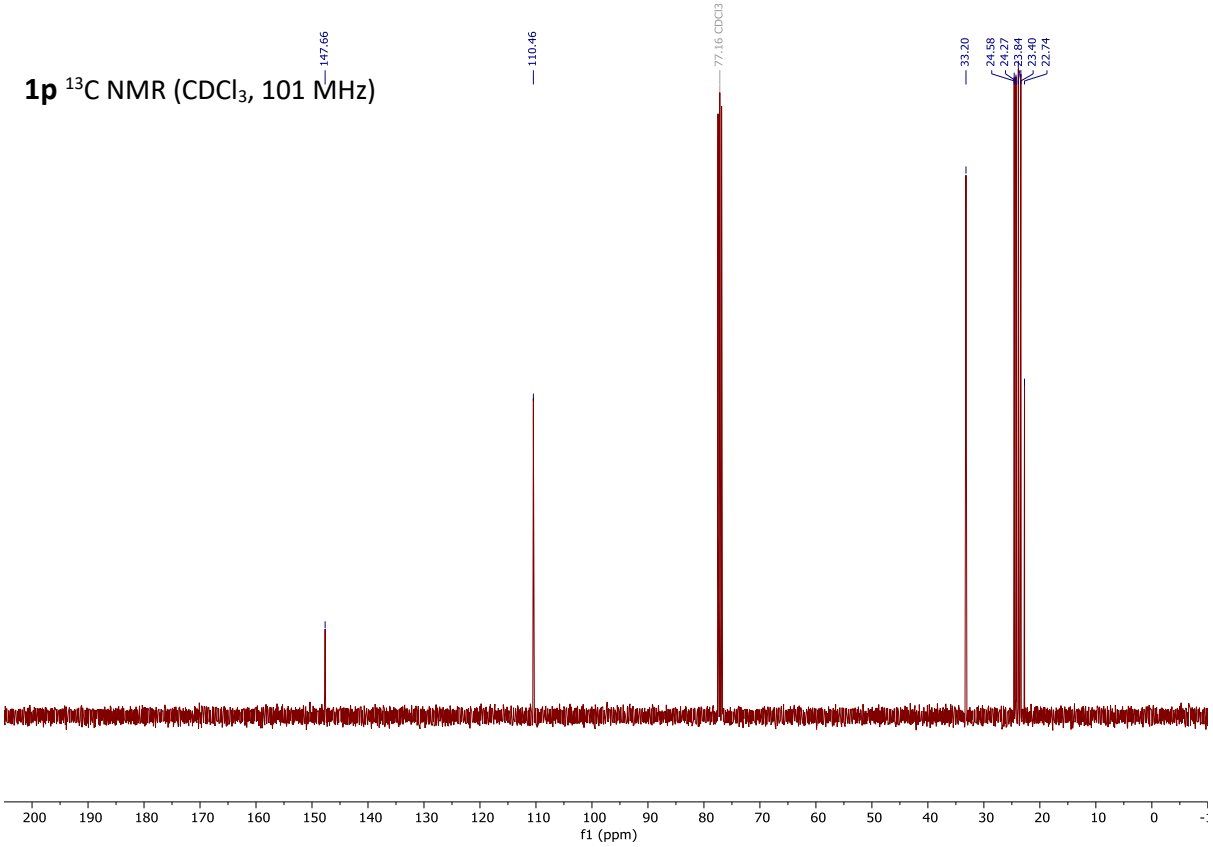


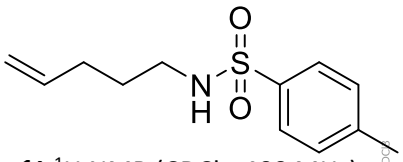


1p ^{1}H NMR ($CDCl_3$, 400 MHz)

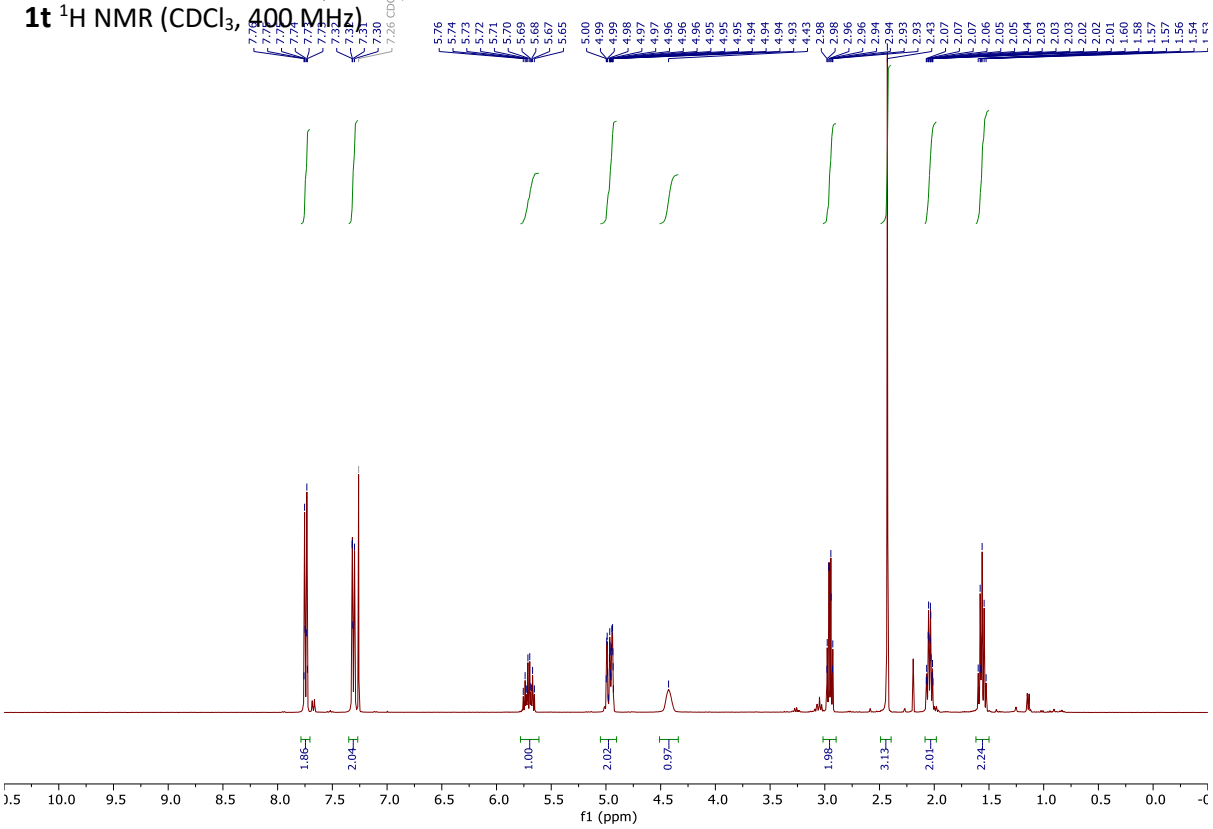


1p ^{13}C NMR ($CDCl_3$, 101 MHz)

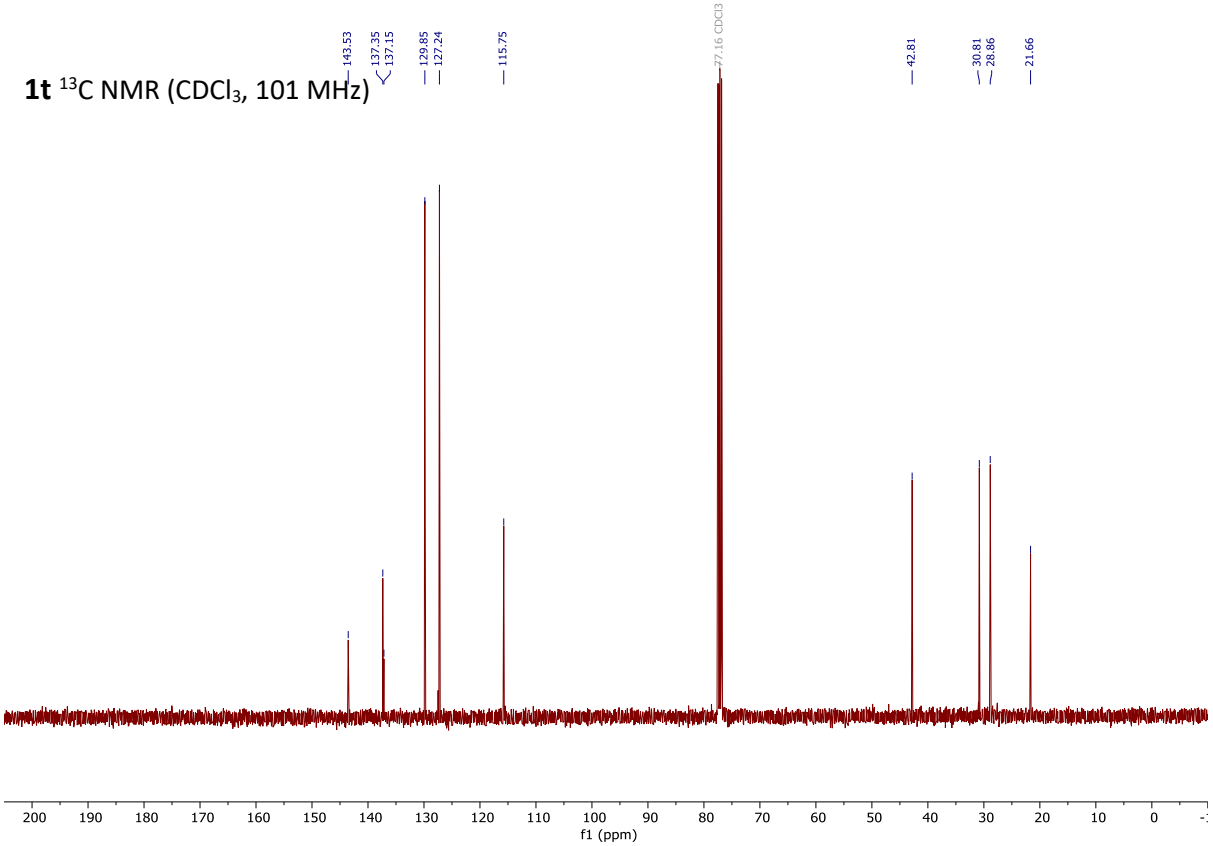


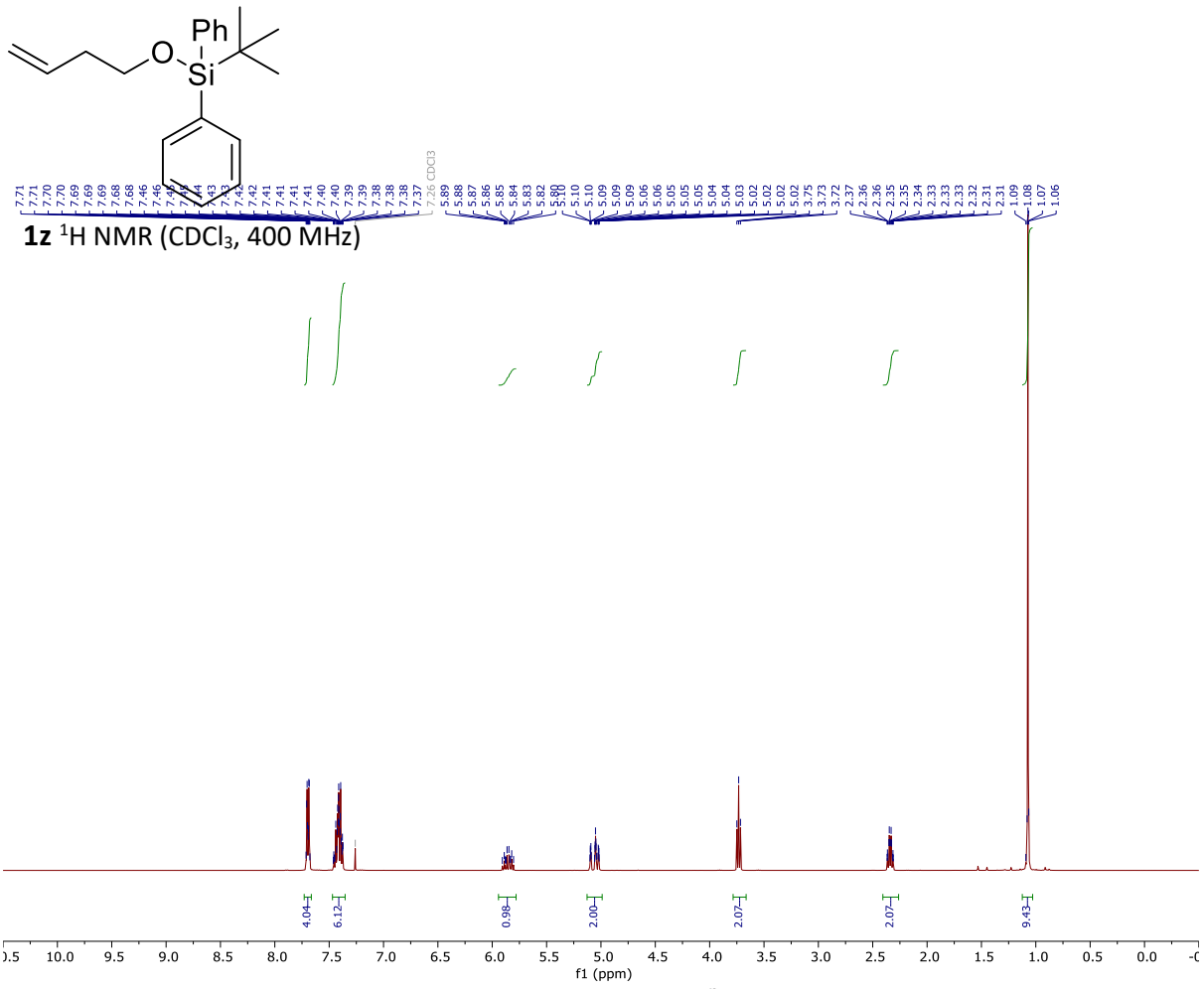


1t ^{1}H NMR ($CDCl_3$, 400 MHz)

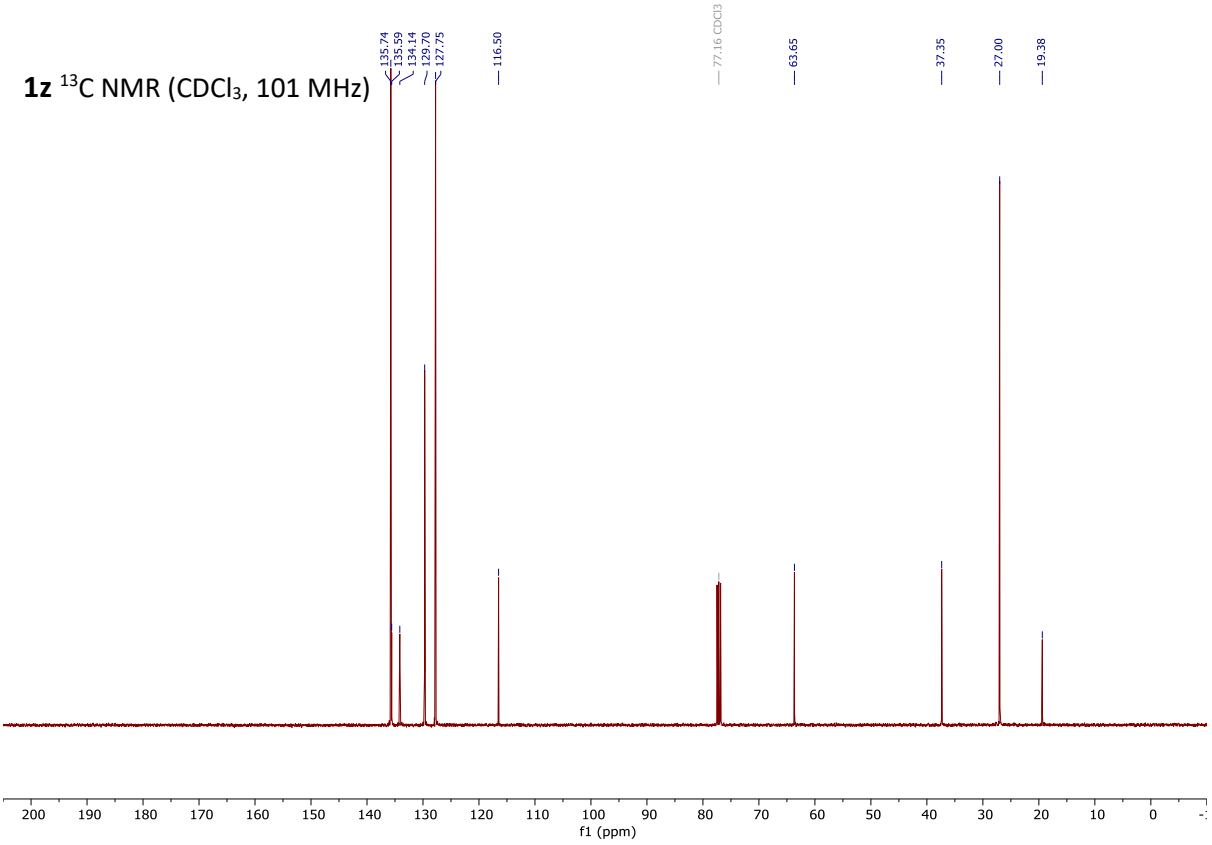


1t ^{13}C NMR ($CDCl_3$, 101 MHz)

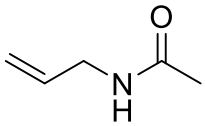




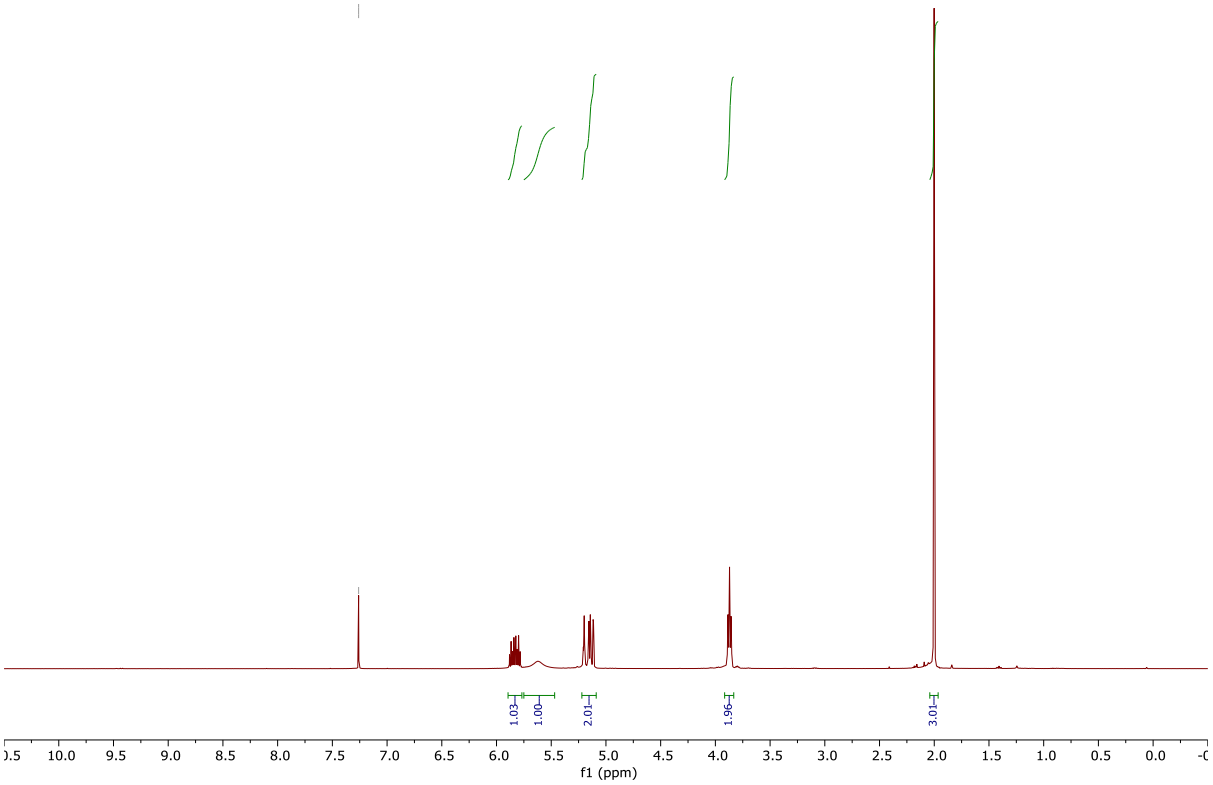
1z ^{1}H NMR ($CDCl_3$, 400 MHz)



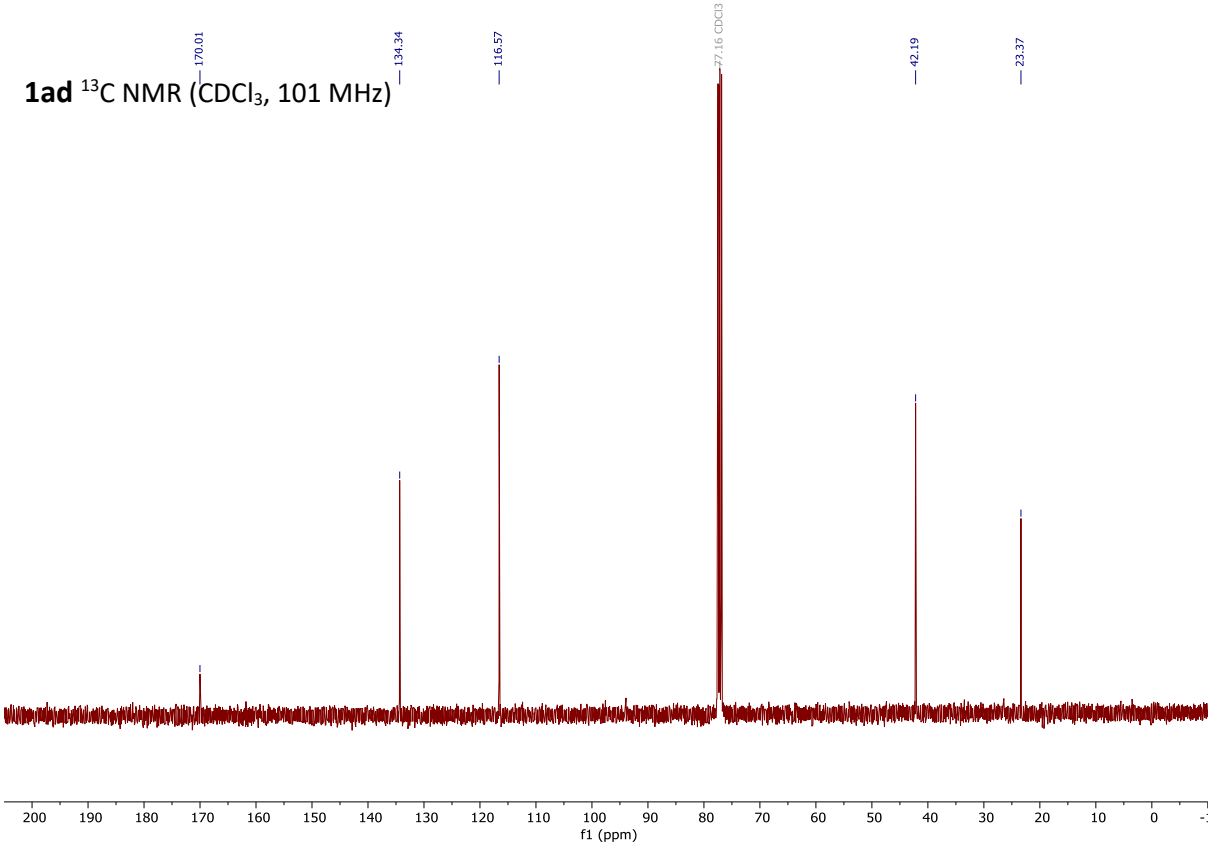
1z ^{13}C NMR ($CDCl_3$, 101 MHz)

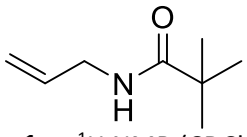


1ad ^{1}H NMR ($CDCl_3$, 400 MHz)

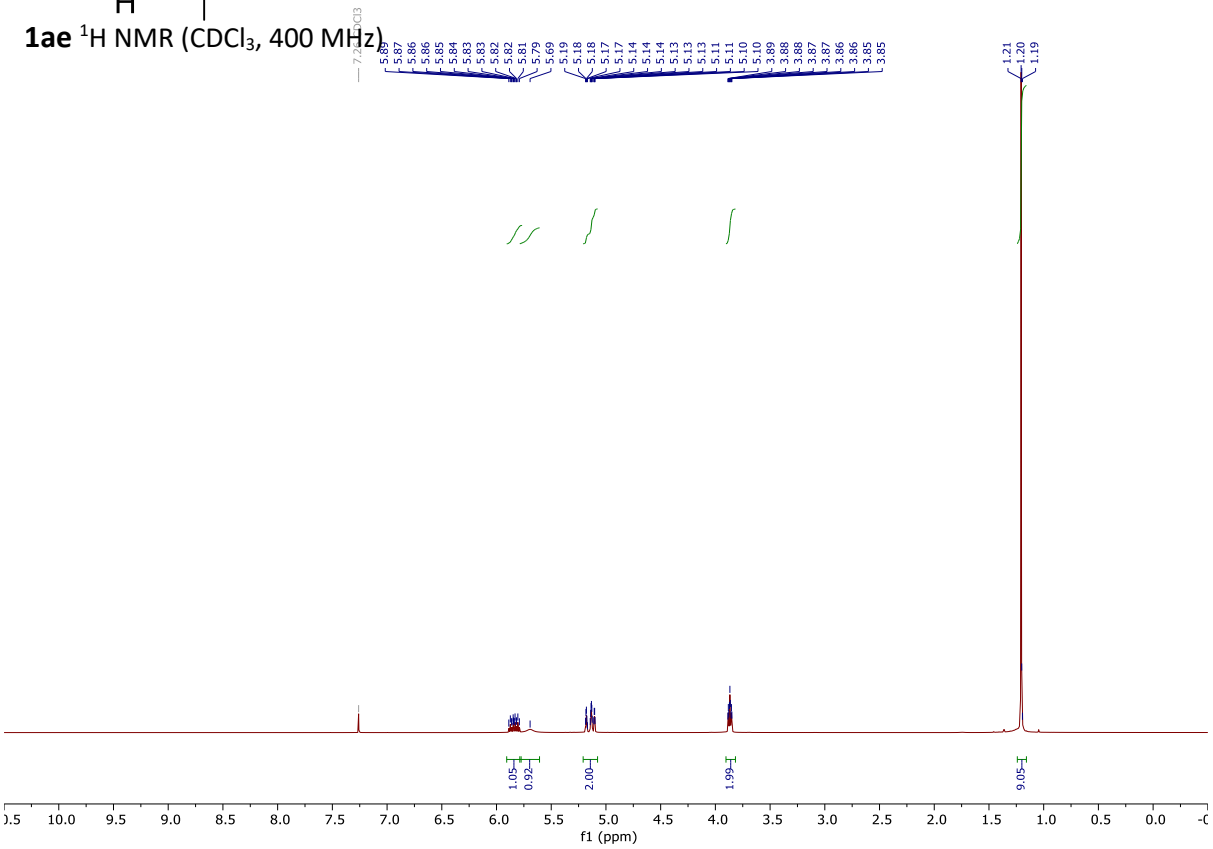


1ad ^{13}C NMR ($CDCl_3$, 101 MHz)

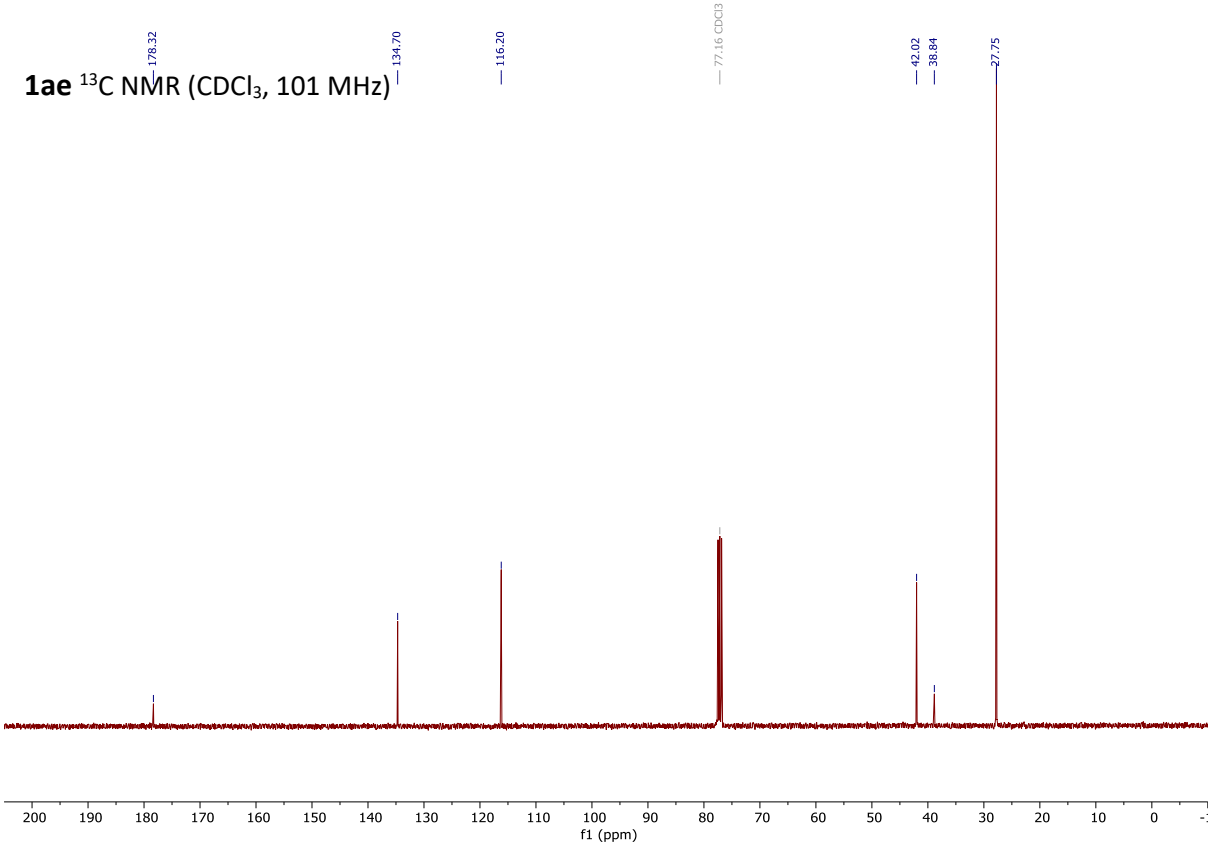


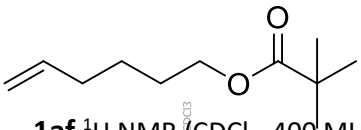


1ae ^{1}H NMR ($CDCl_3$, 400 MHz)

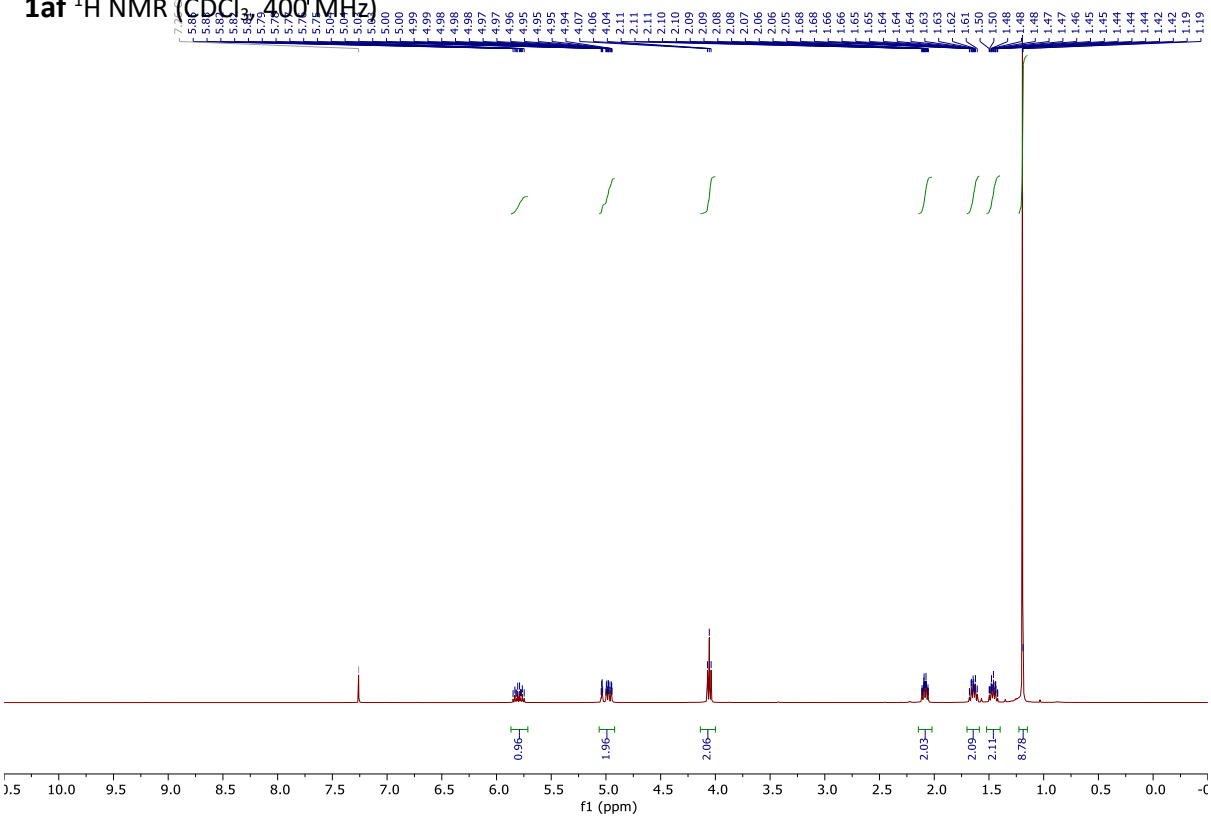


1ae ^{13}C NMR ($CDCl_3$, 101 MHz)

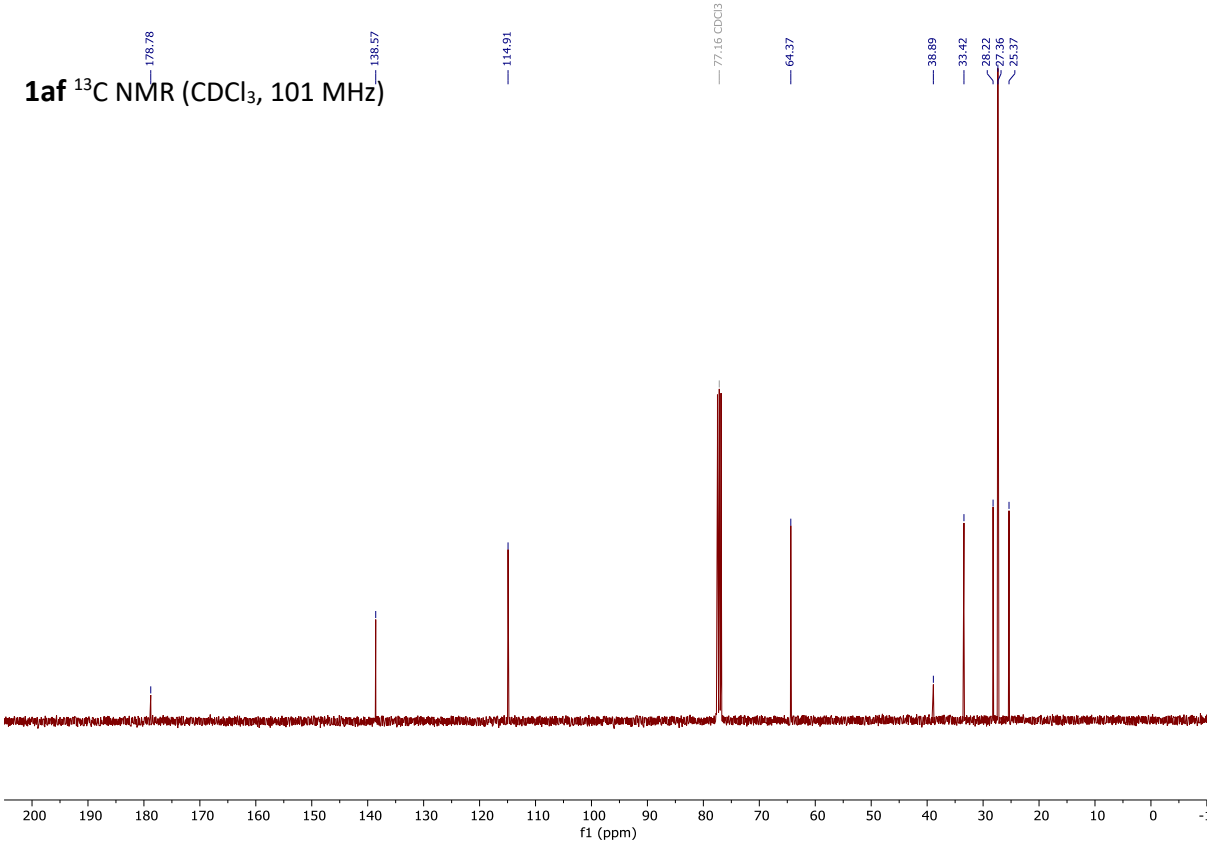


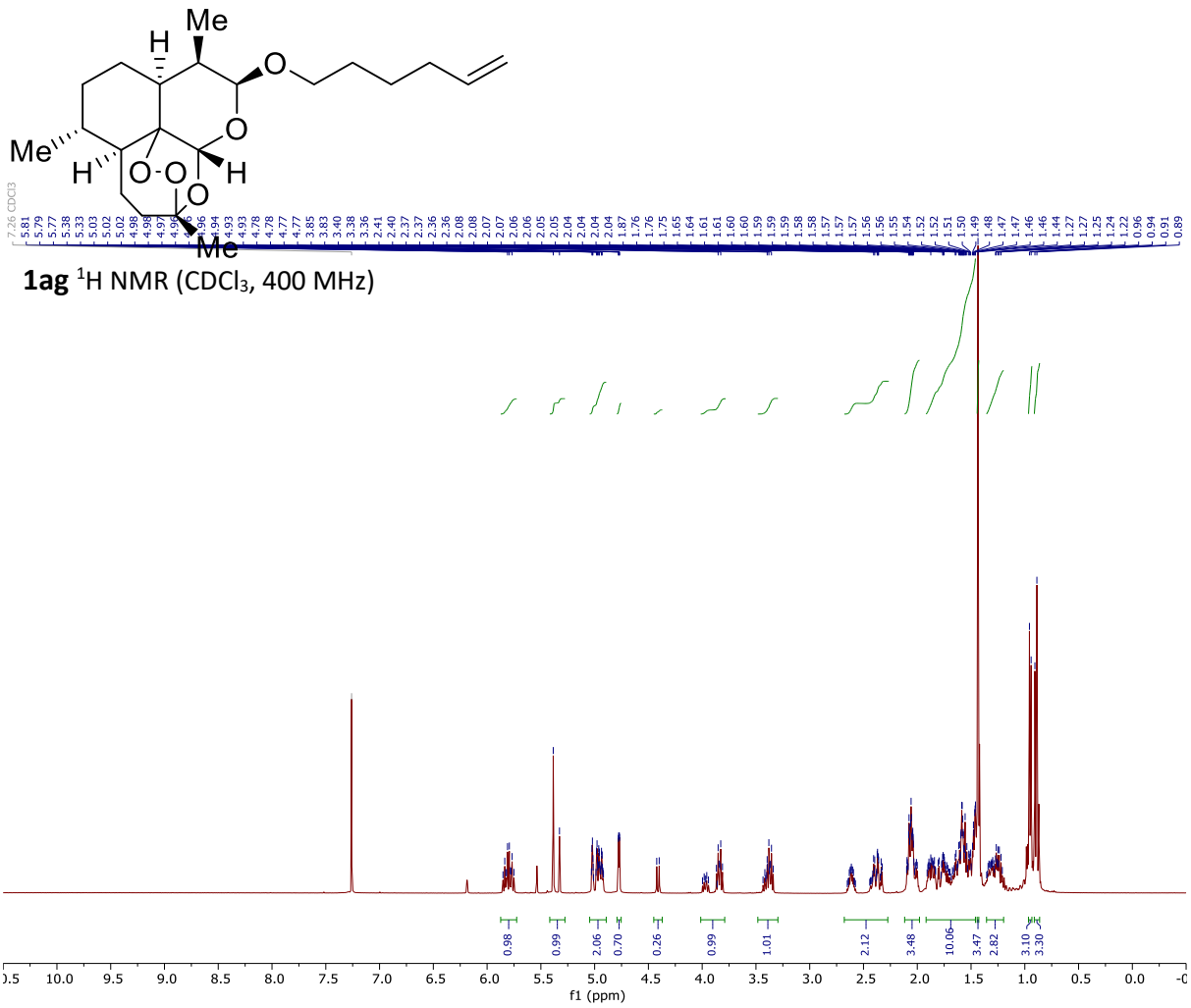


1af ^{1}H NMR ($CDCl_3$, 400 MHz)

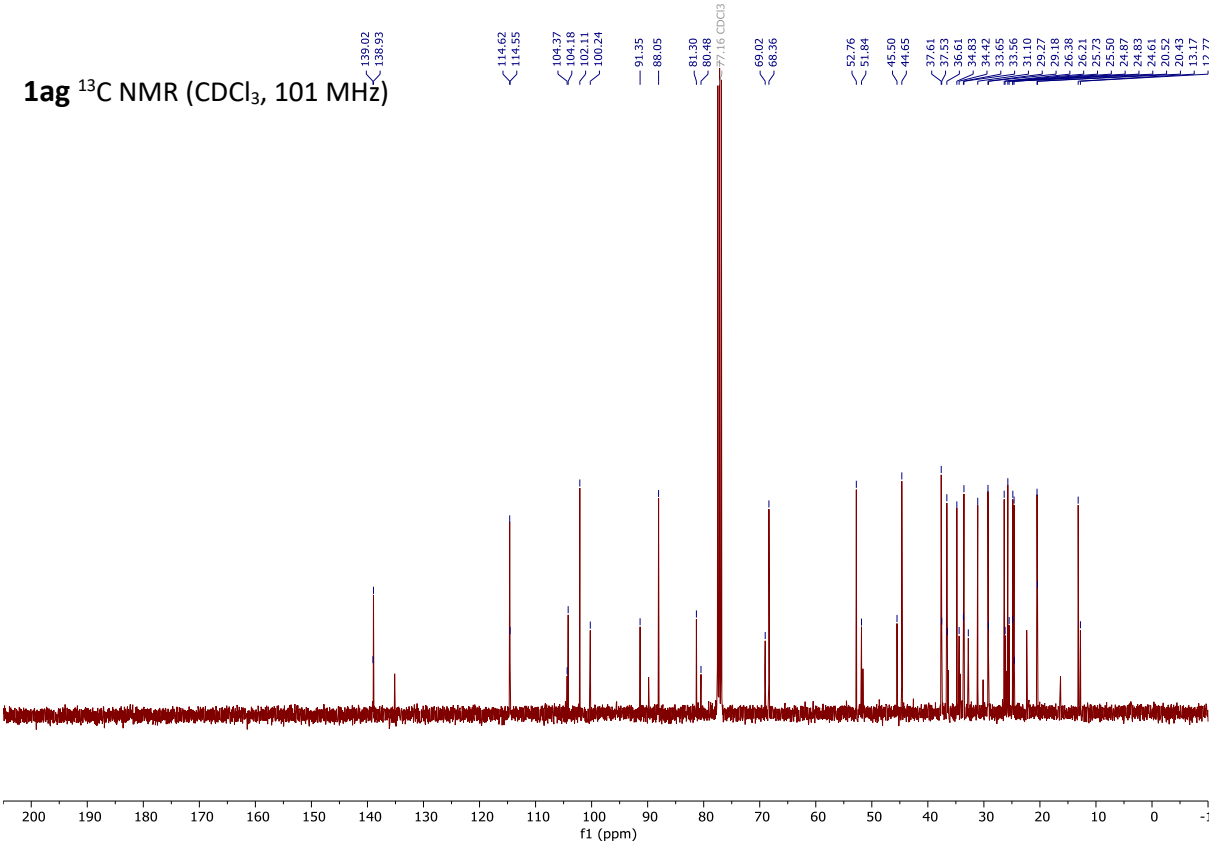


1af ^{13}C NMR ($CDCl_3$, 101 MHz)

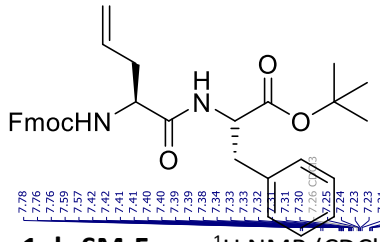




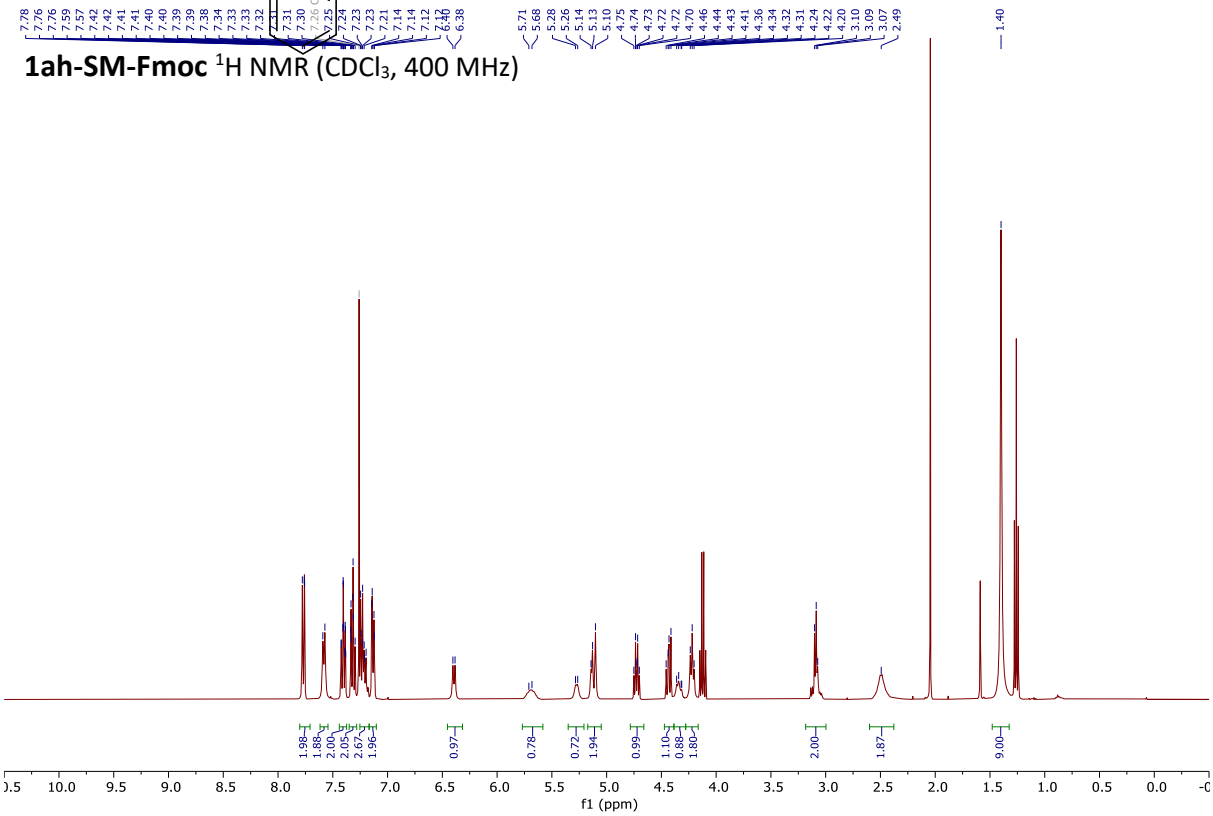
1ag ^{1}H NMR ($CDCl_3$, 400 MHz)



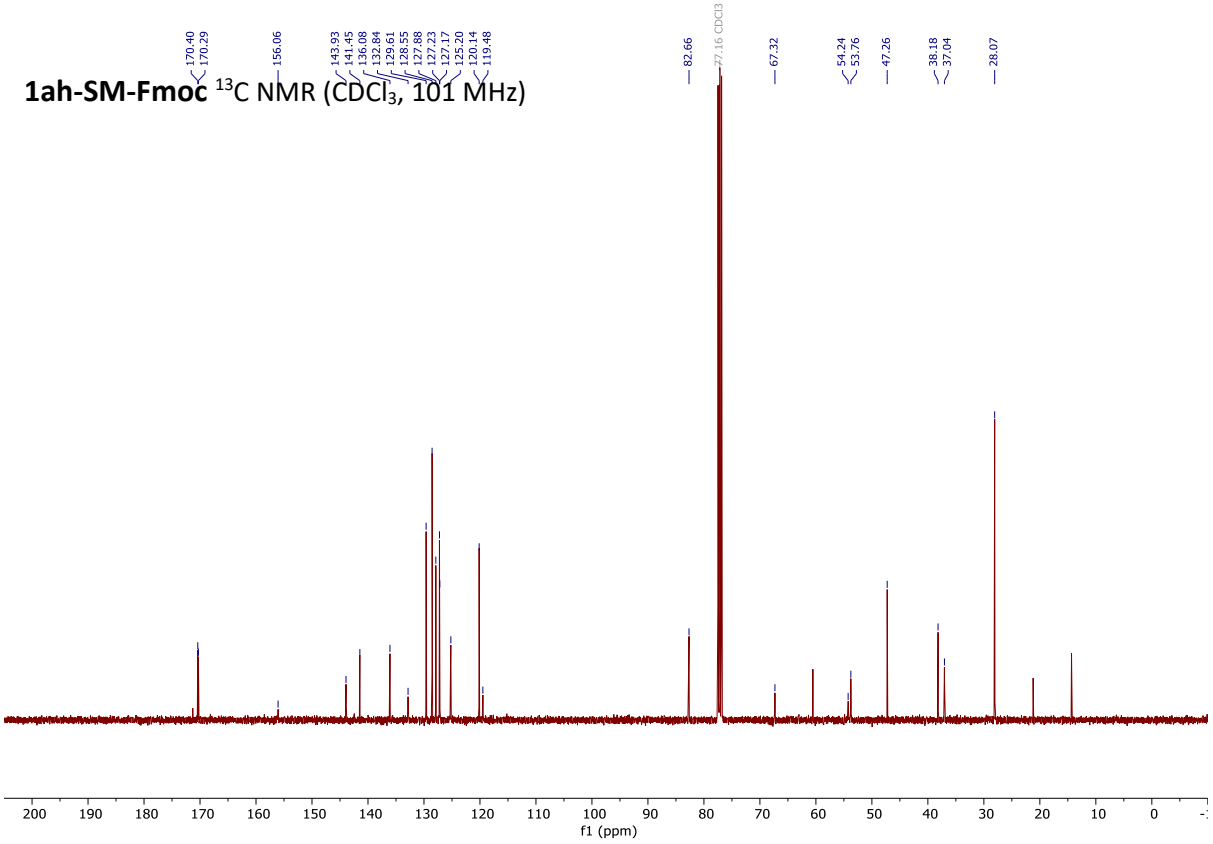
1ag ^{13}C NMR ($CDCl_3$, 101 MHz)

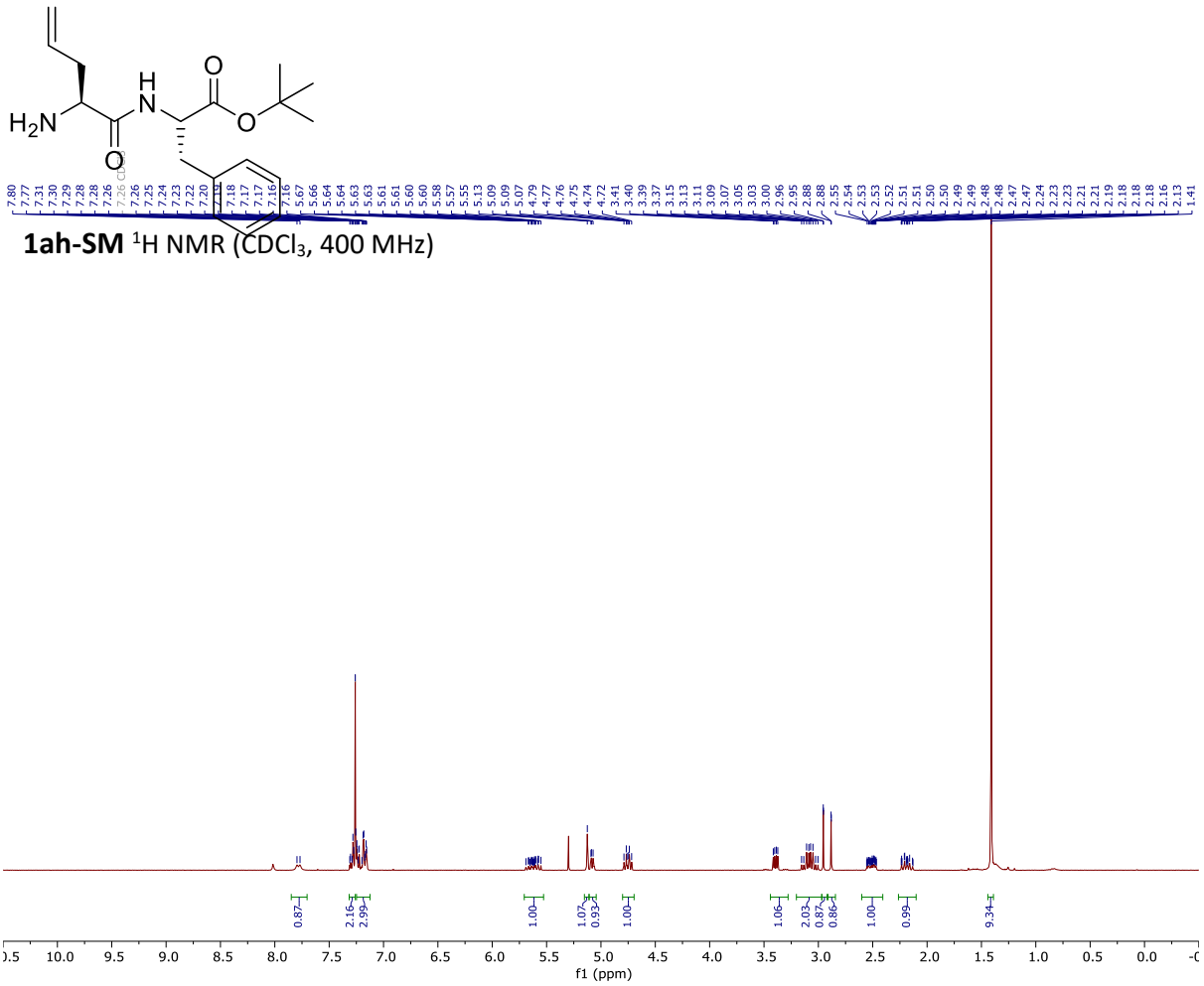


1ah-SM-Fmoc ^{1}H NMR ($CDCl_3$, 400 MHz)

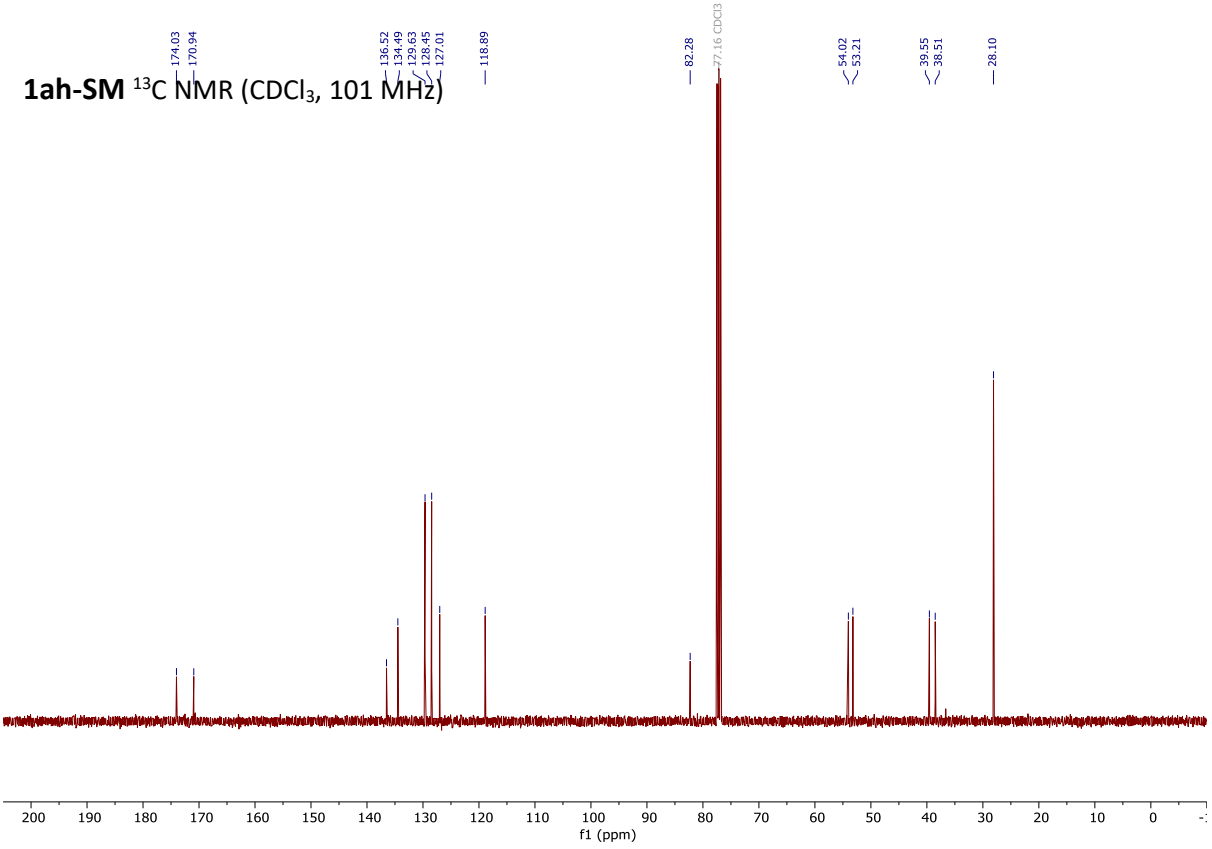


1ah-SM-Fmoc ^{13}C NMR ($CDCl_3$, 101 MHz)

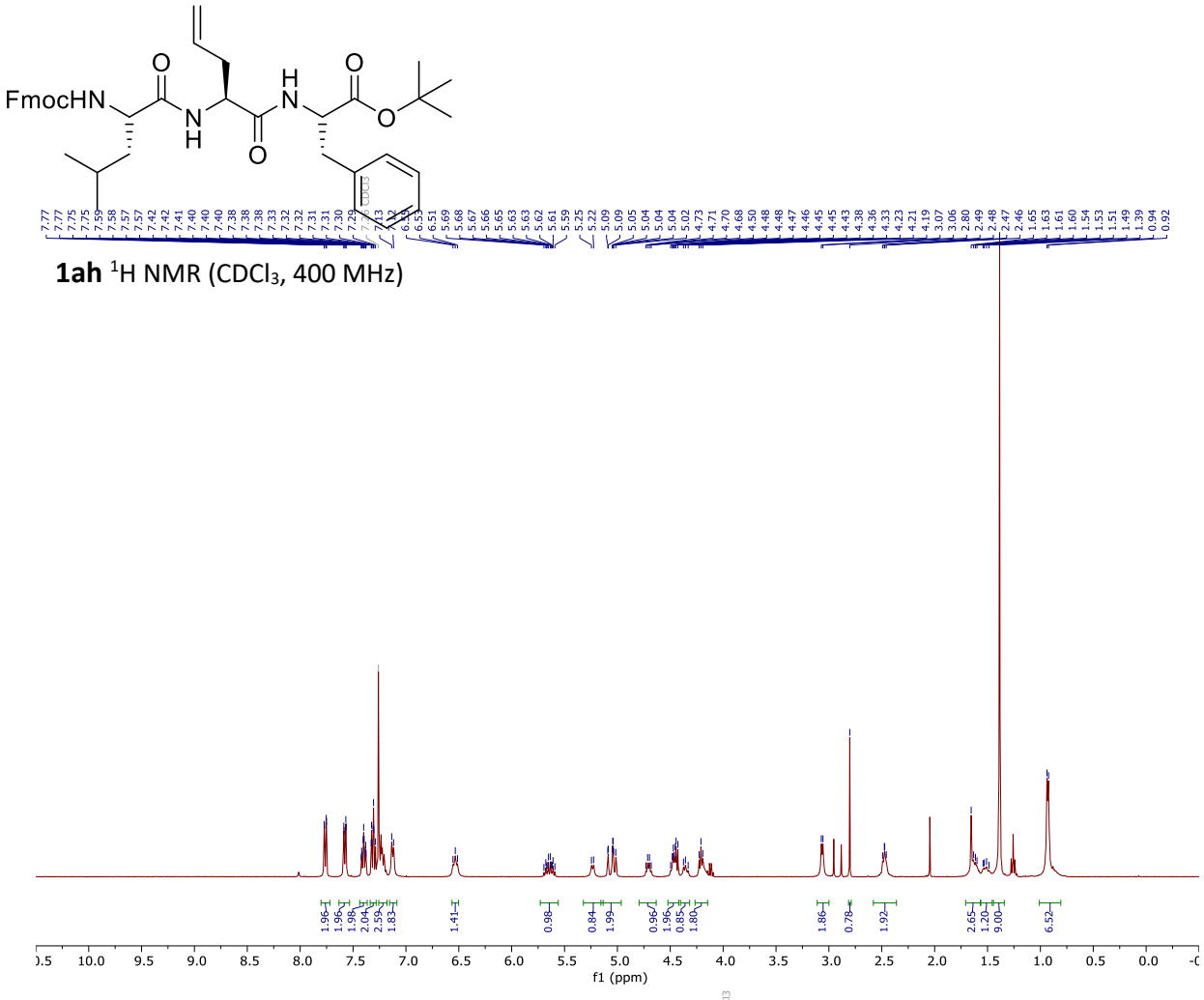




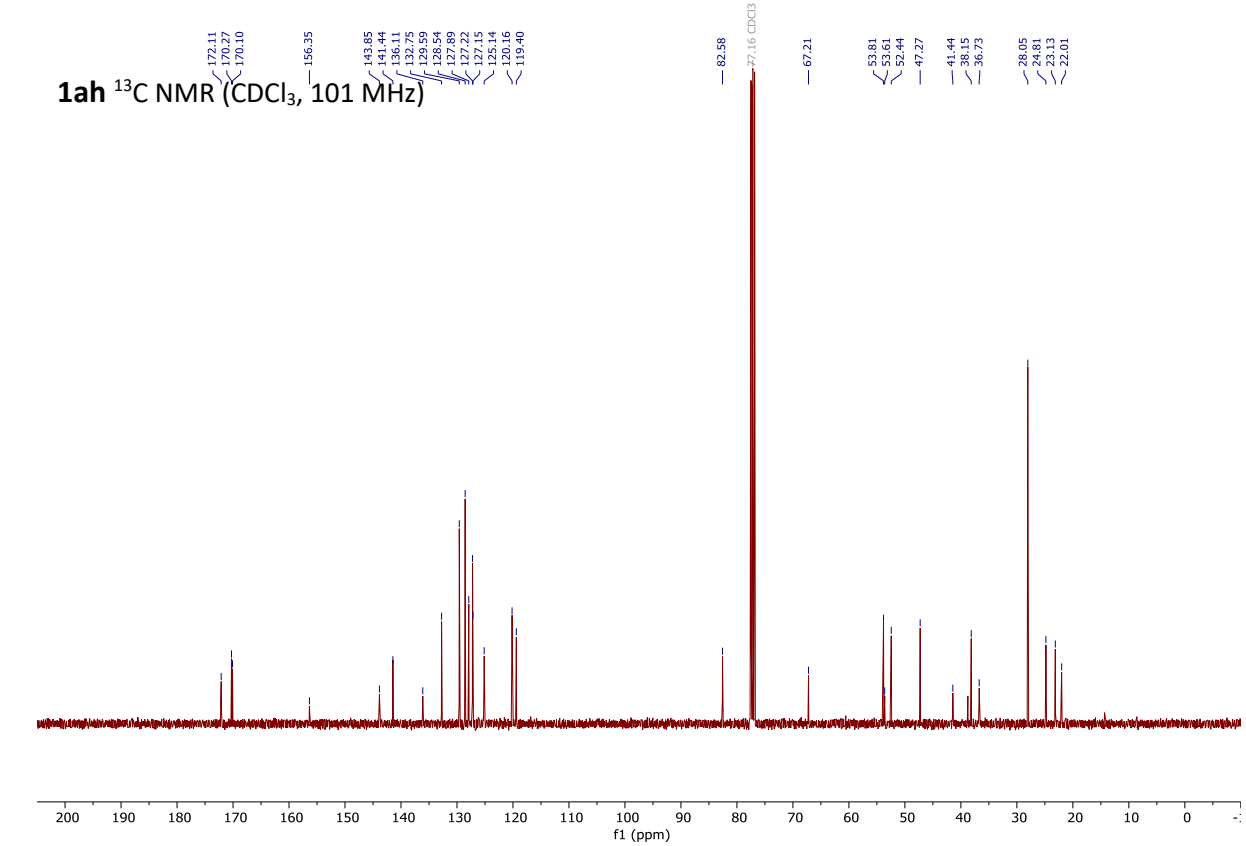
1ah-SM ^{1}H NMR ($CDCl_3$, 400 MHz)



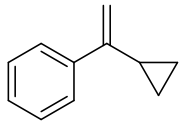
1ah-SM ^{13}C NMR ($CDCl_3$, 101 MHz)



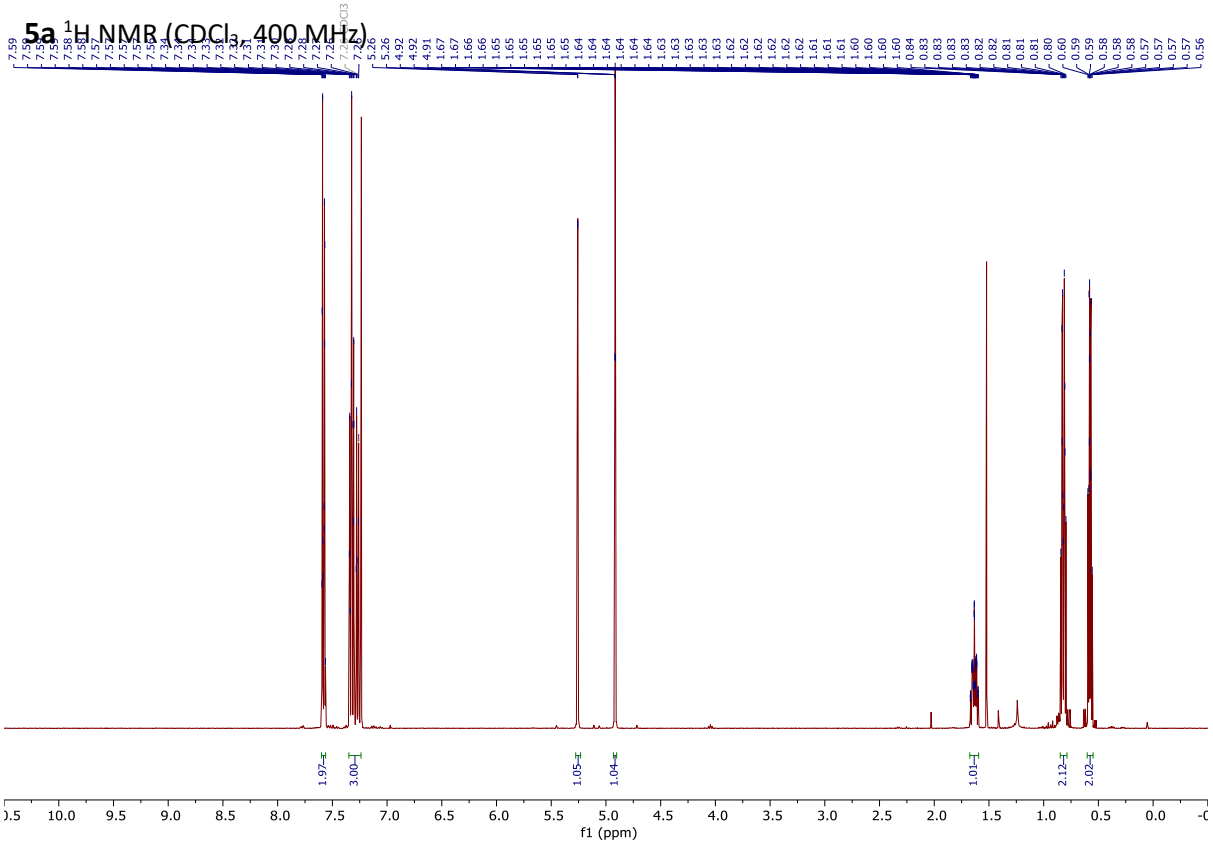
1ah ^{1}H NMR ($CDCl_3$, 400 MHz)



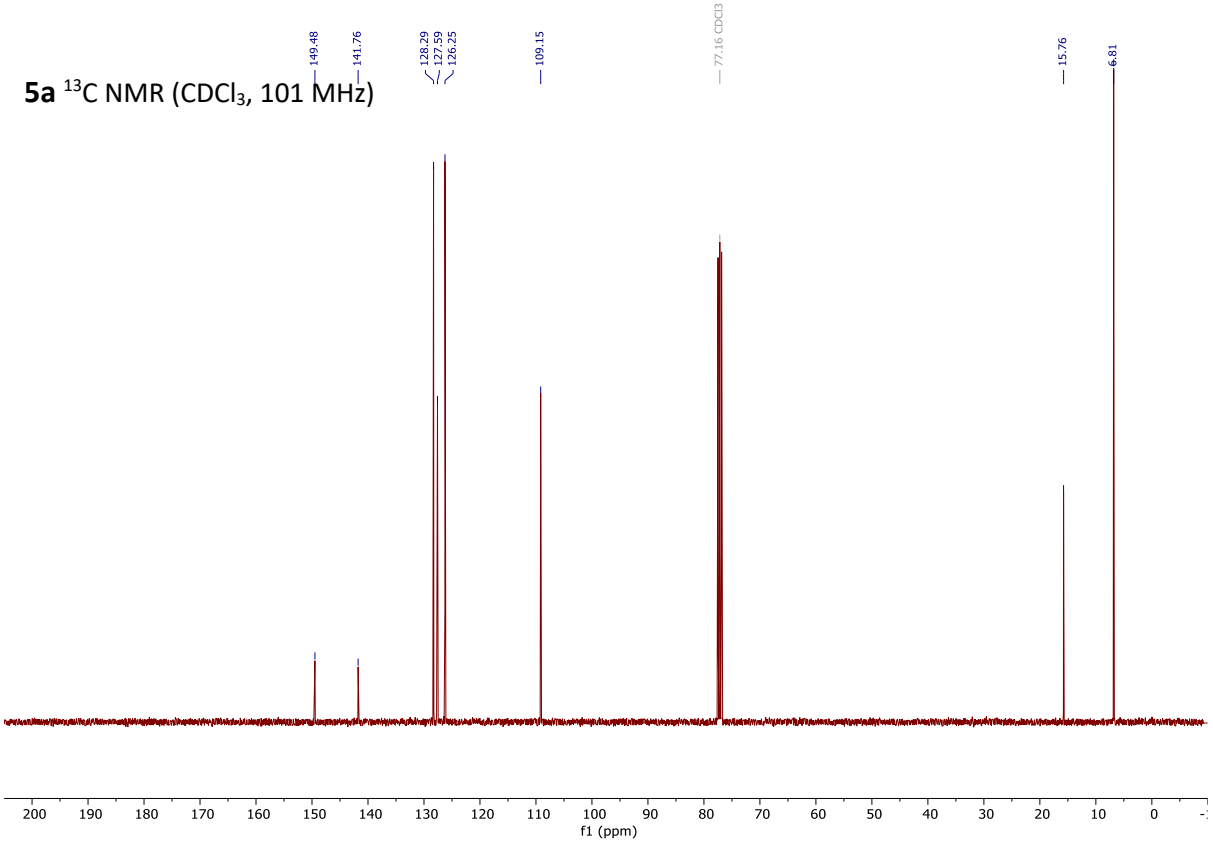
1ah ^{13}C NMR ($CDCl_3$, 101 MHz)

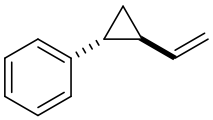


5a ^{1}H NMR ($CDCl_3$, 400 MHz)

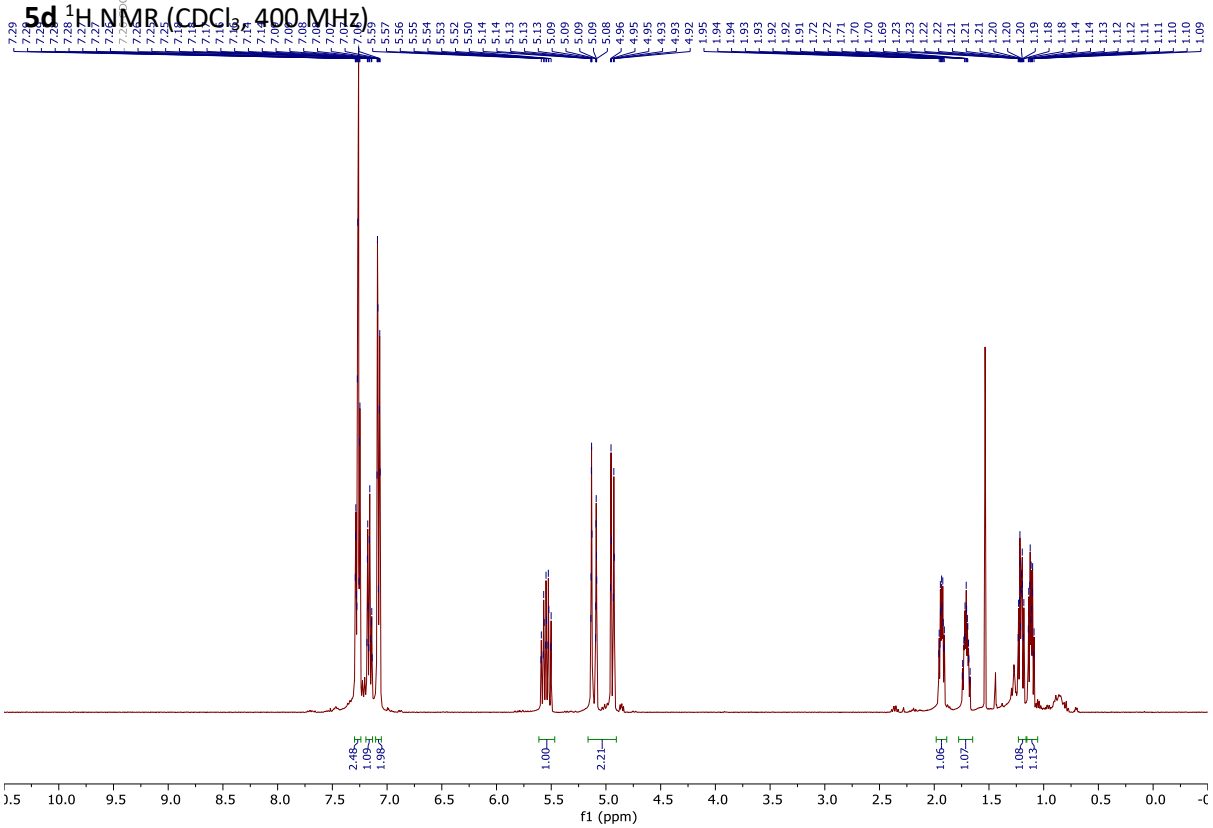


5a ^{13}C NMR ($CDCl_3$, 101 MHz)





5d ^{1}H NMR ($CDCl_3$, 400 MHz)



5d ^{13}C NMR ($CDCl_3$, 101 MHz)