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Synthetic Methods

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Pd-Catalyzed Vicinal Amino Alcohols Synthesis from Allyl Amines via *in Situ* Tether Formation and Carboetherification**

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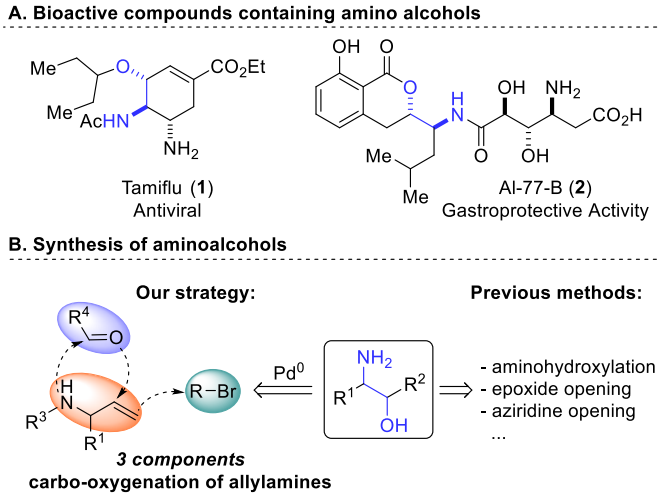
((optional))

***Abstract**: Vicinal amino alcohols are important structural motifs of bioactive compounds. Herein, we report an efficient method for their synthesis based on the palladium-catalyzed oxy- alkynylation, arylation or vinylation of allylic amines. High regio- and stereoselectivity were ensured through the in situ formation of a hemiaminal tether using the cheap commercially available trifluoroacetaldehyde in its hemiacetal form. The obtained compounds are important building blocks, which can be orthogonally deprotected to give either free alcohols, amines or terminal alkynes.*

Vicinal amino alcohols are highly important structural motifs found in bioactive compounds such as the drug Tamiflu (**1**) or the natural product AI-77-B (**2**)[1] (Scheme 1, **A**). They have also been broadly applied as chiral ligands and auxiliaries. Therefore, there is a strong interest in the development of new methods to access them. Two of the most common synthetic approaches are the ring-opening of epoxides or aziridines and the metal-catalyzed aminohydroxylation of alkenes (Scheme 1, **B**).[2] Although straightforward, these methods are often plagued by regioselectivity issues.[2b] The use of tethers has emerged as a viable strategy to achieve better selectivity and reactivity in organic synthesis.[3] However, this method often lacks efficiency as extra steps are required for tether introduction and removal. Regarding the synthesis of vicinal amino alcohols, allyl amines are particularly attractive starting materials: numerous methods are available for their synthesis and the high nucleophilicity of nitrogen should allow the *in situ* formation of a hemiaminal tether by reaction with an aldehyde. Amino alcohol synthesis could be accompanied by the introduction of a second functional group onto the alkene allowing a maximal increase in molecular complexity (Scheme 1, **B**). The formation of a valuable C-C bond would be especially interesting, yet more challenging than the introduction of a second heteroatom.[4] Concerning the multi-functionalization of unactivated olefins, palladium catalysis has been highly successful in the last decades,[5] but has not yet been applied to the outlined strategy.[6]

Precedence for the projected *in situ* formation of a hemiaminal tether using allyl amines and aldehydes can be found in the elegant metal-free approach developed by Beauchemin and co-workers for the cope-type hydroamination of allylic amines (Scheme 2, **A**).[7] However, the use of an aldehyde as tether has never been reported for the Pd-catalyzed *multi*-functionalization of olefins. Even in the broader field of palladium catalysis, the potential of this approach has been only scarcely explored. Menche and co-workers developed an elegant synthesis of 1,3-diols via a domino acetal-formation/Tsuji-Trost reaction starting from homo-allylic alcohols.[8] Hiemstra and co-workers, and more recently Stahl and co-workers, reported the use of hemiaminals for the Wacker cyclization reaction starting from allyl amines and alcohols, but the diastereoselectivity was low for the former and an additional step was needed to install the tether for both methods.[9]



Scheme 1. Importance and synthesis of vicinal amino alcohols.

Based on this precedence and our interest in olefin oxy- and aminoalkynylation,[10] we demonstrate herein that trifluoroacetaldehyde used as its cheap hemiacetal form **3** enables the Pd-catalyzed carbo-oxygenation of allyl amines through a one-pot tethered process. In this transformation, amino alcohols are successfully formed with the concomitant introduction of alkynyl, aryl or vinyl groups (Scheme 2, **B**). This versatile strategy combines key advantages of both intramolecular and intermolecular reactions: high reactivity, stereo-, regio- and diastereoselectivity, as well as the use of simple starting materials.

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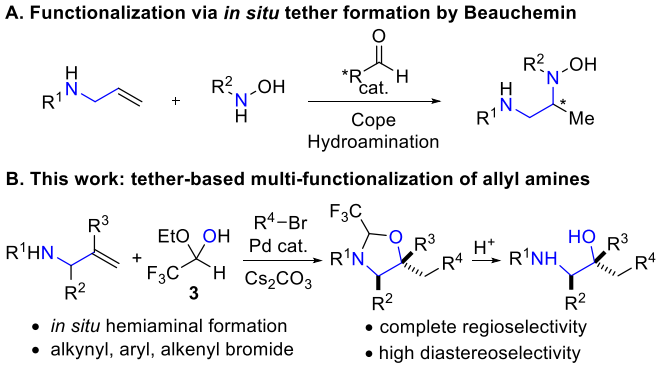
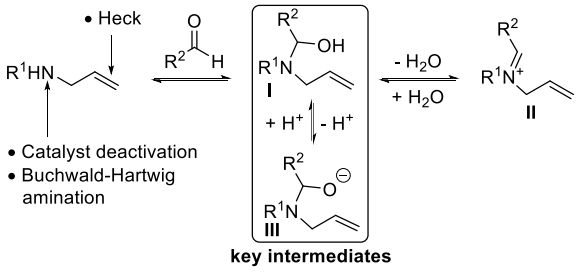


Scheme 2. The tether strategy for allyl amine functionalization.

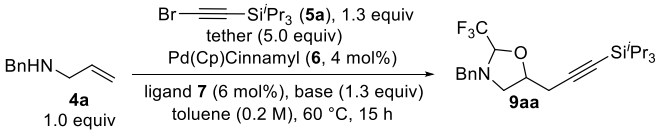
In order to develop a one-pot tethered synthesis of amino alcohols starting from allyl amines, it is first important to analyze the key parameters for success of this challenging process (Scheme 3). First, the allyl amine starting materials could react directly with palladium, leading to catalyst deactivation or side reactions such as Heck coupling and Buchwald-Hartwig type C-N bond formation. To avoid these pitfalls, formation of the hemiaminal intermediate **I** should be both fast and thermodynamically favored. Second, formation of a reactive iminium intermediate **II** should be avoided, as it can lead to unproductive aminal formation with the allyl amine. Basic conditions should be better suited in this respect, as formation of the iminium is usually acid-catalyzed. This would furthermore facilitate olefin functionalization via a faster *syn* oxypalladation on intermediate **III**. Indeed, we had shown in our previous work that basic conditions were necessary for the oxyalkynylation of olefins using a Pd^0 catalyst.[10c,d] However, hemiaminal formation is usually performed under slightly acidic conditions.



Scheme 3. Speculative analysis for the tether formation step.

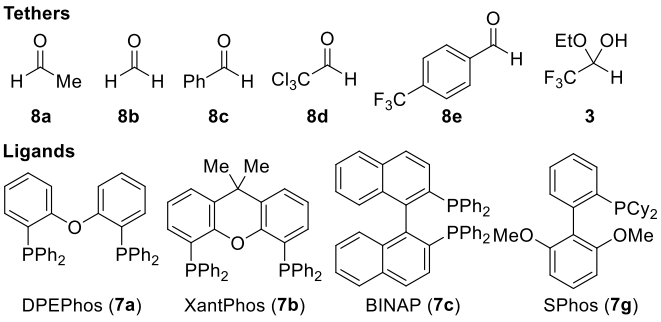
With these challenges in mind, we started our studies by examining the reaction of benzyl allyl amine (**4a**) with triisopropylsilylethynyl bromide (**5a**) in the presence of different bases and aldehydes **8** using the conditions optimized for the intramolecular oxyalkynylation reaction (Pd^0 catalyst,[11] DPE-Phos (**7a**) as ligand, toluene, 60 °C) (Table 1).[10c] No product could be observed when using reported tether precursors such as acetaldehyde (**8a**) or formaldehyde (**8b**) (entries 1 and 2).[8,9] A small amount (about 5% yield) of desired product **9aa** could be obtained only with benzaldehyde (**8c**) (entry 3). We speculated that this failure was due to the inefficient formation of the half aminal under the basic reaction conditions. To accelerate the formation of this key intermediate, more electron-deficient aldehydes were then examined (entries 4-6). With chloral (**8d**) and *para*-trifluoromethylbenzaldehyde (**8e**), **9aa** could indeed be obtained in 5 and 25% yield respectively (entries 4 and 5). Finally, the best result was obtained with the commercial hemiacetal form **3** of trifluoroacetaldehyde,[12] and the oxyalkynylation product **9aa** could be isolated in 92% yield after optimization of the reaction conditions (entry 6).[13] The best results were obtained using five equivalents of **3**. Nevertheless, **9aa** could still be isolated in 71% yield when only 1.1 equivalents of **3** were used (entry 7). The base played also a critical role in the success of the reaction, as both potassium carbonate (entry 8) or sodium *tert*-butoxide (entry 9) gave inferior results. Product **9aa** was obtained with low diastereoselectivity (< 2:1 dr) under all the reaction conditions tested, but this is inconsequential when considering that the trifluoromethyl stereocenter is not present in the final amino alcohol product.[14]

Table 1. Optimization of the tethered oxyalkynylation.[a]



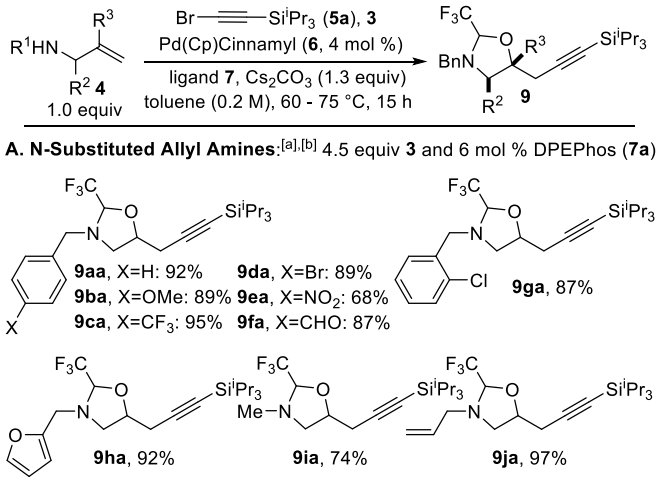
entry	tether	ligand	base	Yield[b]
1	**8a** (5.0 equiv)	DPEPhos (**7a**)	Cs_2CO_3	< 1%
2	**8b** (5.0 equiv)	DPEPhos (**7a**)	Cs_2CO_3	< 1%
3	**8c** (5.0 equiv)	DPEPhos (**7a**)	Cs_2CO_3	5%
4	**8d** (5.0 equiv)	DPEPhos (**7a**)	Cs_2CO_3	5%
5	**8e** (5.0 equiv)	DPEPhos (**7a**)	Cs_2CO_3	25%
6	**3** (5.0 equiv)	DPEPhos (**7a**)	Cs_2CO_3	92%[e]
7	**3** (1.0 equiv)	DPEPhos (**7a**)	Cs_2CO_3	71%
8	**3** (5.0 equiv)	DPEPhos (**7a**)	K_2CO_3	76%
9	**3** (5.0 equiv)	DPEPhos (**7a**)	NaO^{t}Bu	8%
10	**3** (5.0 equiv)	XantPhos (**7b**)	Cs_2CO_3	8%
11	**3** (1.5 equiv)	XantPhos (**7b**)	Cs_2CO_3	59%
12	**3** (5.0 equiv)	BINAP (**7c**)	Cs_2CO_3	6%
13[c]	**3** (5.0 equiv)	PPh_3 (**7d**)	Cs_2CO_3	<5%
14[c]	**3** (1.5 equiv)	(2-Furyl)$_3$P (**7e**)	Cs_2CO_3	93%
15[c]	**3** (1.5 equiv)	(4-$CF_3C_6H_4$)$_3$P (**7f**)	Cs_2CO_3	82%
16[d]	**3** (1.5 equiv)	SPhos (**7g**)	Cs_2CO_3	40%

[a]Reactions were carried out on a 0.10 mmol scale. [b]Yields were calculated from ^{1}H NMR spectra by using trimethoxybenzene as internal standard. [c]12 mol% of ligand was used. [d]8 mol% of ligand was used. [e]Yield of isolated product on 0.30 mmol scale.



The phosphine ligand had also a strong effect on the outcome of the reaction. Other biphosphine ligands gave **9aa** in lower yields (entries 10-12). Interestingly, with XantPhos (**7b**) a better yield was obtained when only 1.5 equivalents of **3** were used (entry 11). Finally, the results obtained with monophosphine ligands were highly dependent of their structure. Whereas nearly no product formation was observed with triphenylphosphine (**7d**) (entry 13), good results were obtained with less electron-rich aryl phosphines

(entries 14 and 15). In particular tris(2-furyl)phosphine (**7e**) gave **9aa** in 93% yield (entry 14). The more sterically hindered electron-rich SPhos ligand (**7g**) led to the formation of **9aa** in only 40% yield (entry 16). From the screening of ligands, two optimum conditions emerged with either DPEPhos (**7a**) or tris(2-furyl)phosphine (**7e**) as ligands (entries 6 and 14). As more reproducible results were obtained on preparative scale using DPEPhos (**7a**) as ligand, it was used to examine the scope of the reaction (Scheme 4).[15]



Scheme 4. Scope of allylamines in the tethered-oxyalkynylation reaction. [a] Reactions were carried out on a 0.30 mmol scale. Yield of isolated products. [b] The dr was was lower than 2:1 [c]The dr was enriched from 4:1 to 12:1 during column chromatography.

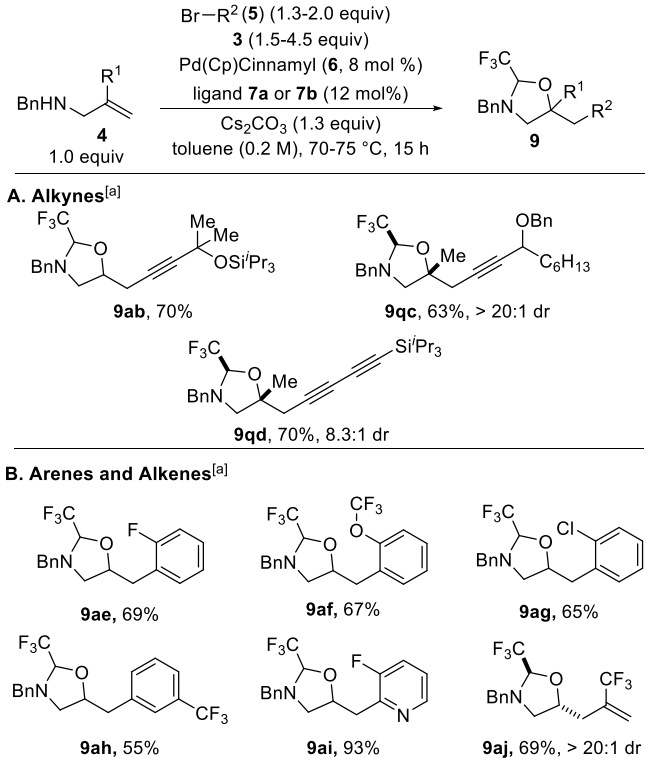
We started by investigating the functional group tolerance of the oxyalkynylation by modifying the benzyl group on the allyl amine (Scheme 4, **A**). The reaction was successful in the presence of an ether, a trifluoromethyl, a bromo and a nitro groups, as well as an aldehyde (product **9ba-fa**). It is particularly interesting to see that an aryl bromide group can be tolerated. This clearly indicated a higher reactivity of the alkynyl bromide towards oxidative addition. Oxazolines bearing an *ortho*-chlorobenzyl group or a furan heterocycle were obtained in 87% and 92% yield respectively (products **9ga** and **9ha**). Finally, the reaction was also successful for a simple methyl (product **9ia**) or allyl (product **9ja**) substituent. In contrast, only traces of product were observed when anilines or amides/carbamates were used as starting materials.[13]

We then turned to the use of amines bearing a substituent at the allylic position (Scheme 4, **B**). This class of starting materials is especially interesting, as the existing stereocenter could be expected to control the formation of the C-O bond and more functionalized products are obtained. Unfortunately, only very low yields were observed when using diphosphines as ligands. In this case, tris(2-furyl)phosphine (**7e**) was the ligand of choice, and oxazoline **9ka** derived from methyl-substituted allyl amine **9k**, was obtained in 81% yield as a major diastereoisomer. With larger alkyl substituents, a nearly perfect diastereoselectivity was observed (products **9la** and **9ma**). Aryl substituents could also be used: Phenyl-substituted oxazoline **9na** was obtained in 90% and more than 12:1 dr, whereas heterocycle-substituted products **9oa** and **9pa** were formed in good yields but lower diastereoselectivity.

Substitution of the olefin of the allyl amine was examined next (Scheme 4, **C**). 1,2-disubstituted olefins could not be used in the reaction. In contrast, the formation of tertiary ethers was possible when using XanthPhos (**7b**) as ligand. The reaction was successful in the case of a simple methyl group (product **9qa**) and also for more functionalized alkyl chains (products **9ra** and **9sa**).

Up to now, only triisopropylsilylethynylbromide (**5a**) had been used as partner for the multi-functionalization reaction. This was based on the excellent properties of this substrate in oxyalkynylation reactions[10c] and also its synthetic versatility as a precursor of terminal alkynes. Nevertheless, the use of functionalized alkynes would give a more convergent access into molecular complexity. Good yields could also be obtained with alkynes derived from tertiary or secondary propargylic alcohols (products **9ab** and **9qc**) and diynes (product **9qd**) (Scheme 5, **A**).

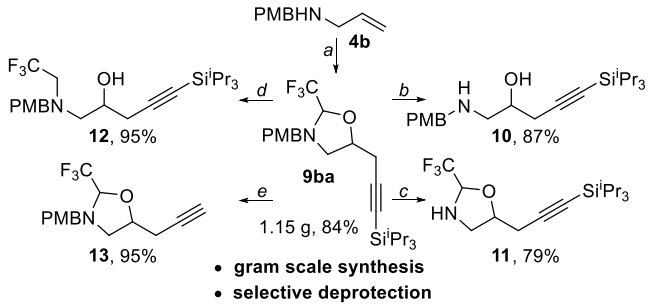
We finally extended the developed tether-strategy to oxyarylation (Scheme 5, **B**).[16] The reaction was successful



Scheme 5. Scope of electrophiles in the tethered-oxyfunctionalization reaction. [a] Reactions were carried out on a 0.30 mmol scale. Yield of isolated products. The dr was lower than 3:1, unless otherwise noted.

provided aryl bromides slightly activated by an electron-withdrawing group were used. Benzene bromides bearing a trifluoromethyl, a fluoro, a trifluoromethoxy or a chlorine group gave the oxyarylation products **9ae-h** in 55-69% yield. Oxazoline **9ai** bearing a pyridine heterocycle could be obtained in 93% yield. Finally, oxyalkenylation was also successful and gave trifluormethyl-substituted alkene **9aj** in 69% yield.

The obtained building blocks are highly useful, as they contain three orthogonally protected functional groups (an alcohol, an amine and an alkyne). To demonstrate this synthetic potential, **9ba** was synthesized on the gram scale (2.51 mmol, 1.15 g, 84%) and subjected to selective deprotection (Scheme 6). The hemiaminal tether could be readily removed, affording the aminoalcohol **10** in 87% yield. Access to amine **11** was possible via DDQ-promoted PMB cleavage. Reductive opening of the hemiaminal yielded trifluoroethylamine **12** in excellent yield, while TIPS removal afforded the further functionalizable terminal alkyne **13**.



Scheme 6. Scale-up and orthogonal deprotections. Reaction conditions: a) 4.5 equiv **3**, 1.3 equiv **5a**, 4 mol% **6**, 6 mol% **7a**, 1.3 equiv Cs_2CO_3 in toluene at 60 °C; b) *p*-Toluenesulfonic acid, THF/MeOH, 60 °C; c) DDQ, CH_2Cl_2/H_2O; d) DIBAL-H, toluene, -78 to -25 °C; e) TBAF, THF.

In conclusion, we have developed the first Pd-catalyzed tethered carbo-etherification of allylamines for the synthesis of vicinal amino alcohols. The use of the hemiacetal of trifluoroacetaldehyde for *in situ* tether formation was key to enable high yield, regio- and diastereoselectivity under mild conditions. The reaction proceeded with broad scope and high functional group tolerance. The versatility of our method was highlighted by the possibility to introduce alkynyl, aryl and vinyl groups onto the alkene. Free alcohols, amines or terminal alkynes could be obtained orthogonally in one single step from the synthesized products. Future work will focus on the development of an asymmetric version of the transformation and the extension to other classes of tethers.

Keywords: 1,2 amino alcohols • tether • hemiaminal • Pd-catalysis • alkenes

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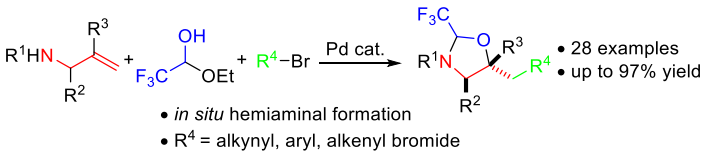
Pd-Catalyzed Vicinal Amino Alcohols Synthesis from Allyl Amines via *in Situ* Tether Formation and Carboetherification



Vicinal amino alcohols are important structural motifs of bioactive compounds. Herein, we report an efficient method for their synthesis based on the palladium-catalyzed oxy- alkynylation, arylation or vinylation of allyl amines. High regio- and stereoselectivity were ensured through the *in situ* formation of a hemiaminal tether using the cheap commercially available trifluoroacetaldehyde in its hemiacetal form.

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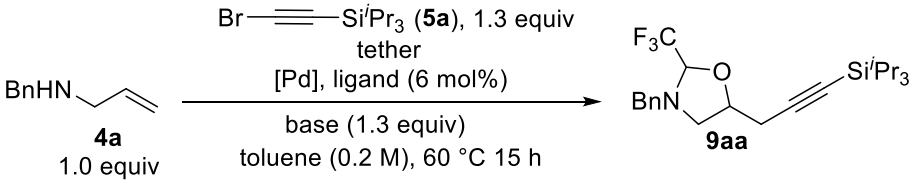
1. General Methods

All reactions were carried out in oven dried glassware under an atmosphere of nitrogen, unless stated otherwise. For quantitative flash chromatography technical grade solvents were used. For flash chromatography for analysis, HPLC grade solvents from Sigma-Aldrich were used. THF, Et_2O, CH_3CN, toluene, hexane and CH_2Cl_2 were dried by passage over activated alumina under nitrogen atmosphere (H_2O content < 10 ppm, *Karl-Fischer* titration). In some cases solvents were degassed using freeze-thaw cycle. All chemicals were purchased from Acros, Aldrich, Fluka, VWR, Fluorochem, Aplichem or Merck and used without further purification, unless stated otherwise. Chromatographic purification was performed as flash chromatography using Macherey-Nagel silica 40-63, 60 Å, using the solvents indicated as eluent with 0.1-0.5 bar pressure. TLC was performed on Merck silica gel 60 F_{254} TLC aluminium plates and visualized with UV light and potassium permanganate stain. Melting points were measured on a calibrated Büchi B-540 melting point apparatus using open glass capillaries. ^{1}H-NMR spectra were recorded on a Bruker DPX-400 400 MHz spectrometer in chloroform-d unless otherwise stated. All signals are reported in ppm with the internal chloroform signal at 7.26 ppm as standard unless otherwise stated. The data is being reported as (s = singlet, d = doublet, t = triplet, q = quadruplet, qi = quintet, m = multiplet or unresolved, br = broad signal, app = apparent, coupling constant(s) in Hz, integration, interpretation).^{13}C-NMR spectra were recorded with ^{1}H-decoupling on a Bruker DPX-400 100 MHz spectrometer in chloroform-d unless otherwise stated. All signals are reported in ppm with the internal chloroform signal at 77.0 ppm as standard unless otherwise stated. Infrared spectra were recorded on a JASCO FT-IR B4100 spectrophotometer with an ATR PRO410-S and a ZnSe prisma and are reported as cm^{-1} (w = weak, m = medium, s = strong, br = broad). Gas chromatographic and low resolution mass spectrometric measurements were performed on a Perkin-Elmer Clarus 600 gas chromatographer and mass spectrometer using a Perkin-Elmer Elite fused silica column (length: 30 m, diameter: 0.32 mm) and Helium as carrier gas. High resolution mass spectrometric measurements were performed by the mass spectrometry service of ISIC at the EPFL on a MICROMASS (ESI) Q-TOF Ultima API. Caesium carbonate was purchased from Aldrich and used without further purification. The bulk of this material is stored under nitrogen in a Vacuum Atmospheres Glovebox. Small portions (3-5 g) were removed from the glovebox in glass vials and weighed in the air. DPEPhos and XANTPhos were purchased from Acros and tri(2-furyl)phosphine was purchased from Aldrich. Allyamines **4a**, **4b**, **4d**, **4f**, **4g**, **4h**, **4i**, **4j**, **4q** are commercially available from Fluorochem, Aldrich and Acros. Diastereomeric mixtures have been assigned by 2D NMR experiments including COSY/ROESY/HSQC/HMBC.

2. Optimization.

General method for the optimization:
A sealed oven-dry microwave vial under nitrogen was charged with dry degassed toluene (0.3 mL), the tether , the allylamine (0.100 mmol, 1.0 eq) and (bromoethynyl)triisopropylsilane (34 mg, 0.13 mmol, 1.3 eq). The resulting solution was stirred 10-60 min at 50 °C and subsequently transferred *via* canula to a sealed oven-dry 2 mL microwave vial under nitrogen containing the palladium source, the ligand and the base (0.130 mmol, 1.3 eq) and dry degassed toluene (0.20 mL) that have been previously premixed at 50 °C for 3 min. The resulting mixture was stirred at 60 °C for 15 h. The reaction mixture was cooled to 23 °C, concentrated under reduced pressure and analyzed by NMR spectroscopy.

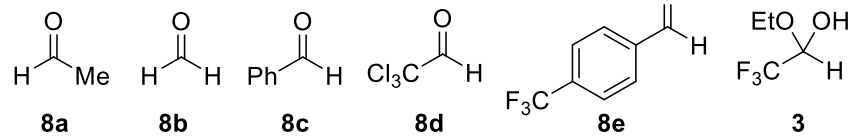


Entry[a]	Tether	Pd source	Ligand	Base	Yield[b]
1	**8a** (5.0 equiv)	**6** (4 mol%)	DPEPhos (**7a**)	Cs_2CO_3	< 1%
2	**8b** (5.0 equiv)	**6** (4 mol%)	DPEPhos (**7a**)	Cs_2CO_3	< 1%
3	**8c** (5.0 equiv)	**6** (4 mol%)	DPEPhos (**7a**)	Cs_2CO_3	5%
4	**8d** (5.0 equiv)	**6** (4 mol%)	DPEPhos (**7a**)	Cs_2CO_3	5%
5	**8e** (5.0 equiv)	**6** (4 mol%)	DPEPhos (**7a**)	Cs_2CO_3	25%
6	**3** (5.0 equiv)	**6** (4 mol%)	DPEPhos (**7a**)	Cs_2CO_3	92%[c]
7	**3** (1.0 equiv)	**6** (4 mol%)	DPEPhos (**7a**)	Cs_2CO_3	71%
8	**3** (5.0 equiv)	**6** (4 mol%)	DPEPhos (**7a**)	K_2CO_3	76%
9	**3** (5.0 equiv)	**6** (4 mol%)	DPEPhos (**7a**)	NaO^{t}Bu	8%
10	**3** (1.2 equiv)	$Pd(dba)_2$ (8 mol%)	DPEPhos (**7a**) (16 mol %)	CsOH	<5%
11	**3** (1.2 equiv)	$Pd(dba)_2$ (8 mol%)	DPEPhos (**7a**) (16 mol %)	K_3PO_4	<5%
12	**3** (1.2 equiv)	$Pd(dba)_2$ (8 mol%)	DPEPhos (**7a**) (16 mol %)	EtN(^{i}Pr)$_2$	<5%
13	**3** (5.0 equiv)	**6** (4 mol%)	XantPhos (**7b**)	Cs_2CO_3	8%
14	**3** (1.5 equiv)	**6** (4 mol%)	XantPhos (**7b**)	Cs_2CO_3	59%
15	**3** (5.0 equiv)	**6** (4 mol%)	BINAP (**7c**)	Cs_2CO_3	6%
16	**3** (5.0 equiv)	**6** (4 mol%)	PPh_3 (**7d**) (12 mol %)	Cs_2CO_3	<5%
17	**3** (1.5 equiv)	**6** (4 mol%)	(2-Furyl)$_3$P **7e** (12 mol %)	Cs_2CO_3	93%
18	**3** (1.5 equiv)	**6** (4 mol%)	(4-$CF_3C_6H_4$)$_3$P **7f** (12 mol %)	Cs_2CO_3	82%
19	**3** (1.5 equiv)	**6** (4 mol%)	SPhos **(7g)** (8 mol %)	Cs_2CO_3	40%
20	**3** (1.5 equiv)	**6** (4 mol%)	(2-Furyl)$_3$P **7e** (12 mol %)	Cs_2CO_3	93%
21	**3** (1.5 equiv)	**6** (4 mol%)	(4-$CF_3C_6H_4$)$_3$P **7f** (12 mol %)	Cs_2CO_3	82%
22	**3** (1.5 equiv)	**6** (4 mol%)	JohnPhos (8 mol %)	Cs_2CO_3	<5%
23	**3** (1.5 equiv)	**6** (4 mol%)	XPhos (8 mol %)	Cs_2CO_3	<5%
24	**3** (1.5 equiv)	**6** (4 mol%)	PCy_3 (12 mol %)	Cs_2CO_3	<5%
25	**3** (1.5 equiv)	**6** (4 mol%)	P^{n}Bu$_3$ (12 mol %)	Cs_2CO_3	<5%

26	**3** (1.5 equiv)	**6** (4 mol%)	$P(O^iPr)_3$ (12 mol %)	Cs_2CO_3	<5%
27	**3** (5.0 equiv)	none	DPEPhos (**7a**)	Cs_2CO_3	< 1%
28	**3** (1.2 equiv)	$Pd(dba)_2$ (8 mol%)	DPEPhos (**7a**) (16 mol %)	Cs_2CO_3	55%
29	**3** (1.2 equiv)	$[Pd(allyl)(COD)]BF_4$ (8mol%)	DPEPhos (**7a**) (12 mol %)	Cs_2CO_3	47%
30	**3** (1.2 equiv)	Pd_2dba_3 (8 mol %)	DPEPhos (**7a**) (24 mol %)	Cs_2CO_3	69%
31	**3** (1.2 equiv)	Pd_2dba_3 (4 mol %)	DPEPhos (**7a**) (12 mol %)	Cs_2CO_3	44%
32	**3** (5.0 equiv)	**6** (2 mol%)	DPEPhos (**7a**) (3 mol %)	Cs_2CO_3	84%
33[d]	**3** (5.0 equiv)	**6** (4 mol%)	DPEPhos (**7a**)	Cs_2CO_3	87%
34	**3** (5.0 equiv)	**6** (4 mol%)	DPEPhos (**7a**) (4 mol%)	Cs_2CO_3	87%
35	**3** (5.0 equiv)	**6** (4 mol%)	DPEPhos (**7a**) (8 mol%)	Cs_2CO_3	83%
36[e]	**3** (1.2 equiv)	$Pd(dba)_2$ (8 mol%)	DPEPhos (**7a**) (16 mol%)	Cs_2CO_3	< 5%
37[f]	**3** (1.2 equiv)	$Pd(dba)_2$ (8 mol%)	DPEPhos (**7a**) (16 mol%)	Cs_2CO_3	13%

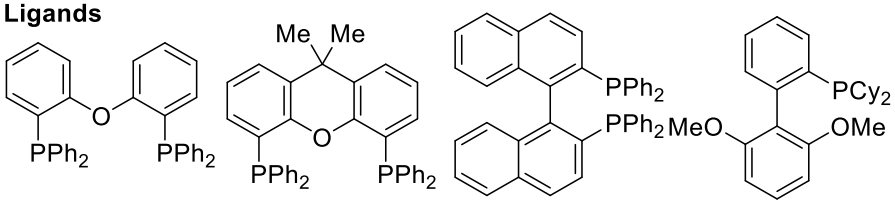
[a] Reactions were carried out on a 0.10 mmol scale in a sealed tube. [b] Yields were calculated from 1H NMR spectra by using trimethoxybenzene as internal standard. [c] Yield of isolated product on 0.30 mmol scale. [d] Reaction performed at 75 °C. [e] *tert*-butyl allylcarbamate was used instead of 4a. [f] *N*-allyl-4-methoxyaniline was used instead of 4a.

Tethers



8a **8b** **8c** **8d** **8e** **3**

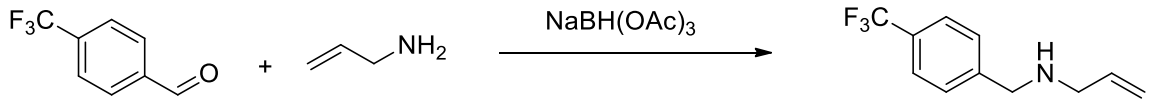
Ligands



DPEPhos (**7a**) XantPhos (**7b**) BINAP (**7c**) SPhos (**7g**)

3. Synthesis of starting materials.

N-(4-(Trifluoromethyl)benzyl)prop-2-en-1-amine (4c)

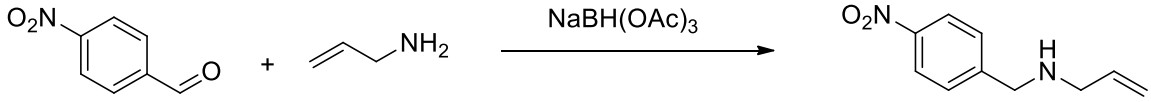


15 **16** **4c**

4-(Trifluoromethyl)benzaldehyde (**15**) (1.37 mL, 10.0 mmol, 1.0 eq) and prop-2-en-1-amine (**16**) (0.571 g, 10.0 mmol, 1.0 eq) were mixed in 1,2-dichloroethane (35 mL) and then treated with sodium triacetoxyborohydride (3.0 g, 14 mmol, , 1.4 eq). The mixture was stirred at rt under a N_2 atmosphere for 2.5 h. The reaction mixture was quenched by adding aqueous saturated $NaHCO_3$ (15 mL), and the product was extracted with EtOAc (3x30 mL). The EtOAc extract was dried ($MgSO_4$), and the solvent was evaporated under reduced pressure. The crude product was purified by column chromatography (SiO_2, 10:1:0.1 Pentane:EtOAc:Et_3N) to afford the title compound **4c** as a pale yellow oil (1.83 g, 8.50 mmol, 85% yield).

R_f 0.20 (Pentane:EtOAc 4:1).
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.58 (d, *J* = 8.0 Hz, 2H, Ar*H*), 7.45 (d, *J* = 8.0 Hz, 2H, Ar*H*), 5.92 (ddt, *J* = 17.2, 10.3, 6.0 Hz, 1H, C*H*CH_2), 5.21 (m, 1H, CHCH_2), 5.14 (m, 1H, CHCH_2), 3.86 (s, 2H, ArCH_2), 3.28 (m, 2H, NCH_2), 1.65 (bs, 1H, N*H*).
^{13}C NMR (101 MHz, Chloroform-*d*) δ 144.4, 136.5, 129.4 (q, *J* = 32.2 Hz), 128.5, 125.5 (m), 124.5 (q, *J* = 272.2 Hz), 116.5, 52.7, 51.8.
IR ν_{max} 3394 (w), 2831 (w), 2830 (w), 1646 (w), 1620 (w), 1458 (w), 1420 (w), 1329 (s), 1167 (m), 1127 (s), 1069 (w), 1021 (w), 925 (w), 844 (w), 823 (w), 796 (w), 784 (w), 763 (w), 728 (w).
HRMS (ESI) calcd. for $C_{11}H_{13}F_3N^+$ $[M+H]^+$ 216.0995; found 216.0994.

N-(4-Nitrobenzyl)prop-2-en-1-amine (4e)



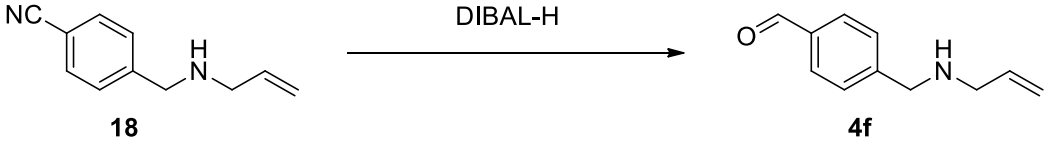
17 **16** **4e**

4-Nitrobenzaldehyde (**17**) (1.21 g, 8.00 mmol) and allylamine (**16**) (0.46 g, 8.0 mmol) were dissolved in 25 mL dichloroethane. Sodium triacetoborohydride (5.1 g, 24 mmol, 3.0 eq) was then added to the solution and the resulting mixture was stirred at RT for 1.5h. The reaction was then quenched with saturated $NaHCO_3$ (15 mL), the product was extracted with EtOAc (3x25 mL), then poured into 1 M aq. HCl (50 mL). The aqueous layer was washed with EtOAc (3x25 mL), and basified (pH 14) with KOH. The resulting aqueous layer was extracted with CH_2Cl_2 (3x25 mL). The combined organic layers were washed with saturated aqueous NaCl and dried ($MgSO_4$). The solvent was evaporated to give the crude product that was purified by column chromatography (SiO_2 2:1:0.1 Pentane:EtOAc:Et_3N) to afford the title compound **4e** as an orange oil (1.32 g, 8.50 mmol, 86% yield, 95 % purity).

R_f 0.10 (Pentane:EtOAc 4:1).
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.19 (d, *J* = 8.6 Hz, 2H, Ar*H*), 7.51 (d, *J* = 8.6 Hz, 2H, Ar*H*), 5.91 (ddt, *J* = 16.4, 10.3, 5.9 Hz, 1H, C*H*=CH_2), 5.27 – 5.08 (m, 2H, CH=CH_2), 3.90 (s, 2H, ArCH_2), 3.28 (m, 2H, NCH_2), 1.51 (bs, 1H, N*H*).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 148.0, 147.2, 136.2, 128.8, 123.7, 116.8, 52.3, 51.8.
IR ν_{max} 3668 (w), 3080 (w), 2975 (s), 2906 (s), 1729 (w), 1674 (w), 1651 (w), 1603 (w), 1522 (s), 1454 (w), 1409 (m), 1402 (m), 1388 (m), 1348 (s), 1253 (w), 1204 (w), 1177 (w), 1136 (w), 1071 (s), 1062 (s), 915 (w), 860 (w), 803 (w), 739 (w).
Spectra data was consistent with the values reported in literature.[1]

4-((Allylamino)methyl)benzaldehyde (4f)

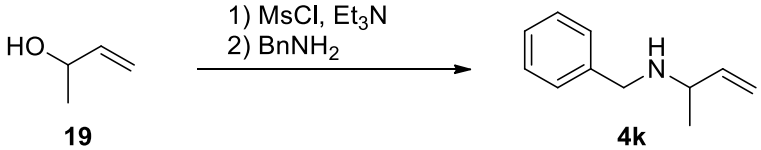


18 **4f**

To a solution of 4-((allylamino)methyl)benzonitrile (**18**) (0.861 g, 5.00 mmol, 1.0 eq) in anhydrous toluene (12.5 mL) was added DIBAL-H (1 M in hexane, 6.50 mL, 6.50 mmol, 1.3 eq), keeping the internal temperature between -10 and -5 °C. After stirring at 0 °C for 2 h, ice cold HCl (10% aq. sol., 50 mL) was added carefully. The layers were separated and the aqueous phase washed with CH_2Cl_2 (3x15 mL). The resulting aqueous layer was basified (pH 14) with KOH and extracted with CH_2Cl_2 (3x50 mL). The combined organic layers were washed with saturated aqueous NaCl and dried ($MgSO_4$). The solvent was evaporated to give the crude product that was purified by passing through a short pad of silica, eluting with EtOAc to afford the pure title compound **4fa** as a pale yellow oil (0.797 g, 4.55 mmol, 91% yield).
N. B.: this compound readily polymerized, preventing us from obtaining a clean ^{13}C NMR spectrum .

^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.00 (s, 1H, C*H*O), 7.89 – 7.78 (m, 2H, Ar*H*), 7.57 – 7.45 (m, 2H, Ar*H*), 5.93 (ddt, *J* = 17.1, 10.2, 6.0 Hz, 1H, C*H*CH_2), 5.25 – 5.17 (m, 1H, CHCH_2), 5.16 – 5.10 (m, 1H, CHCH_2), 3.89 (s, 2H, ArCH_2), 3.29 (m, 2H, NCH_2), 1.52 (bs, 1H, N*H*).
IR ν_{max} 3664 (w), 3074 (w), 2995 (w), 2916 (w), 2827 (m), 2735 (w), 1698 (s), 1643 (w), 1607 (m), 1578 (w), 1449 (w), 1420 (w), 1389 (w), 1363 (w), 1341 (w), 1304 (w), 1254 (w), 1210 (m), 1166 (m), 1108 (w), 1072 (w), 997 (m), 922 (m), 848 (m), 823 (m), 783 (m).
HRMS (ESI) calcd. for $C_{11}H_{14}NO^+$ $[M+H]^+$ 176.1070; found 176.1068.

N-Benzylbut-3-en-2-amine (4k)



19 **4k**

Following a reported procedure, [2]

1) $MeSO_2Cl$ (2.86 g, 25.0 mmol, 1.25 eq) was added dropwise at 0 °C to a CH_2Cl_2 (60 mL) solution of but-3-en-2-ol (**19**) (1.44 g, 20.0 mmol, 1.0 eq) and Et_3N (3.04 g, 30.0 mmol, 1.5 eq). The mixture was stirred at the same temperature for 2 h, resulting in a large amount of white precipitate. Saturated Na_2CO_3 (30 mL) was then added to quench the reaction. After the separation of the organic layer, extraction of the aqueous layer with CH_2Cl_2 (20 mL x 2) and washing with brine, the combined organic layer was dried with $MgSO_4$. The solvent was

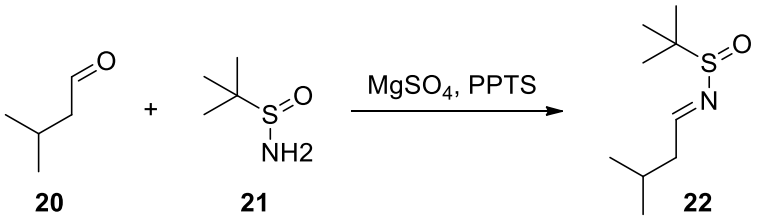
[1] Benedetti, E.; Lomazzi, M.; Tibiletti, F.; Goddard, J.-P.; Fensterbank, L.; Malacria, M.; Palmisano, G.; Penoni, A. *Synthesis,* **2012**, *44*, 3523.
[2] Zhao, S.-B.; Bilodeau, E.; Lemieux, V.; Beauchemin , A. M. *Org. Lett.* **2012,** *14*, 5082.

removed under reduced pressure, and the residue was dried under vacuum to afford but-3- en-2-yl methanesulfonate (3.15 g, 21.0 mmol, <= 100%), which was used directly in next step.

2) But-3-en-2-yl methanesulfonate (2.13 g, 14.0 mmol, 1.0 eq) was added dropwise to a rapidly stirring neat benzyl amine solution (4.50 g, 42.0 mmol, 3.0 eq) at room temperature. After stirring overnight, NaOH (10%, 10 mL) was added. After extraction with CH_2Cl_2 (20 mL), separation of organic layer, drying with Na_2SO_4, and removal of the solvent under reduced pressure, the residue was purified by column chromatography (EtOAc:Hexanes 3:1) to afford the title compound **4k** as a colorless oil (2.48 g, 15.4 mmol, 77% yield for 2 steps).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.30-7.22 (m, 5H, Ar*H*), 5.72 (ddd, *J* = 17.6, 10.1, 7.6 Hz 1H, C*H*CH_2), 5.14 (m, 1H, CHCH_2), 5.09 (m, 1H, CHCH_2), 3.80 (d, *J* = 13.1 Hz 1H, PhCH_2), 3.67 (d, *J* = 13.1 Hz 1H, PhCH_2), 3.20 (m, 1H, NC*H*), 1.26 (br, NH, 1H, N*H*) 1.16 (d, *J* = 6.5 Hz, 3H, Me).
^{13}C NMR (100 MHz, Chloroform-*d*) δ 142.7, 140.8, 128.5, 128.3, 126.9, 114.8, 56.2, 51.5, 21.9.
Spectra data was consistent with the values reported in literature.[3]

2-Methyl-N-(3-methylbutylidene)propane-2- sulfinamide (22)



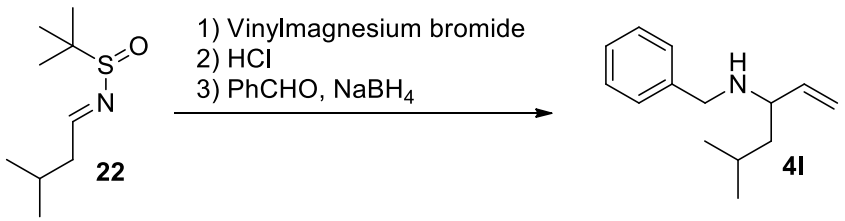
20 **21** **22**

To a solution of 3-methylbutanal (**20**) (1.24 g, 14.4 mmol, 1.2 eq) in CH_2Cl_2 (74 mL) were added successively 2-methylpropane-2-sulfinamide (**21**) (1.45 g, 12.0 mmol, 1.0 eq), $MgSO_4$ (7.22 g, 60.0 mmol, 5.0 eq) and PPTS (0.302 g, 1.20 mmol, 0.10 eq). The resulting white suspension was stirred at rt for 20 h, then filtered through a pad of Celite and concentrated in vacuo. Column chromatography of the residue on (SiO_2, Pentane:EtOAc 8:2) afforded the title compound **22** as a colourless oil (1.99 g, 10.6 mmol, 88 % yield).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.06 (t, 1 H, *J* = 5.2 Hz, N*H*), 2.45-2.37 (m, 2 H, CH_2), 2.12-1.99 (m, 1 H, C*H*), 1.20 (s, 9 H, *t*Bu), 0.99 (d, 6 H, *J* = 6.6 Hz, CH(CH_3)$_2$).
Spectra data was consistent with the values reported in literature.[4]

N-Benzyl-5-methylhex-1-en-3-amine (4l)

[3] Dubovyk, I.; Watson, I. D. G.; Yudin, A. K. *J. Am. Chem. Soc.* **2007**, *129*, 14172.
[4] Frantz, M.-C.; Pierce, J. G.; Pierce, J. M.; Kangying, L.; Qingwai, W.; Johnson, M.; Wipf, P. *Org. Lett.* **2011,** *13*, 2318.



1) Following a slightly modified procedure,[5] a solution of vinyl magnesium bromide in THF (1.0 M, 15.9 mL, 15.9 mmol, 3.0 eq) was added via cannula to a cooled (-48 °C) solution of 2-methyl-N-(3-methylbutylidene)propane-2-sulfinamide (**22**) (1.00 g, 5.28 mmol, 1.0 eq) in CH_2Cl_2 (26.4 mL). The reaction mixture was stirred at -48 °C for 8 h and then allowed to slowly warm to rt overnight (12 h). The reaction was quenched with a 1:2:1 brine/water/NH_4Cl solution (30 mL) while stirring in water bath. Stirring was continued for 30 min until all solid particles were dissolved. Upon separation of the layers, the aqueous layer was extracted once with CH_2Cl_2, and the combined CH_2Cl_2 layers were dried. After filtration through a Celite pad followed by concentration under reduced pressure, the resultant 2-methyl-N-(5-methylhex-1-en-3-yl)propane-2-sulfinamide was collected as a yellow oil (1.02 g, <4.69 mmol, <89% yield). The crude product was directly used for the next step.

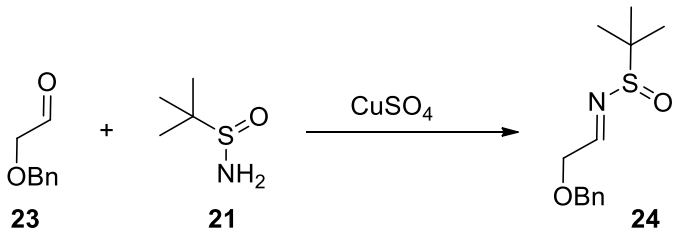
2) Following a slightly modified procedure,[5] (2-methyl-N-(5-methylhex-1-en-3-yl)propane-2-sulfinamide (1.02 g, 4.69 mmol) was cleaved by addition of a 2 N HCl solution in Et_2O (4.69 mL, 9.38 mmol, 2.0 eq) and methanol (5 mL). After 30 min, the reagents/solvents were removed by passing N_2 over the solution. The resultant amine salts were re-dissolved in CH_2Cl_2 (30 mL) and washed with 1 M KOH (3x15 mL) in order to obtain the free amine. Upon drying, filtration, and solvent removal under reduced pressure, the crude free amine was obtained as a yellow solution in CH_2Cl_2 that was directly used in the next step without further purification.

3) 5-Methylhex-1-en-3-amine (398 mg, 3.52 mmol, 1.0 eq) and benzaldehyde (0.356 mL, 3.52 mmol, 1.0 eq) were mixed in methanol (11 mL) at rt under a N_2 atmosphere. The mixture was stirred at rt until the aldimine formation was completed (TLC). The reaction mixture was carefully treated with solid sodium borohydride (266 mg, 7.03 mmol, 2 eq). The reaction mixture was stirred for 2 hour and quenched with 1 M KOH (10 mL). The product was extracted with CH_2Cl_2 (3x20 mL). The combined organic phases were concentrated under reduced pressure and dissolved in 15 mL Et_2O. The organic phase was extracted with HCl 1M (3x20 mL). The resulting aqueous phase was basified with KOH (pH 14) and extracted with CH_2Cl_2 (3x20 mL). The combined organic extract was washed with saturated aqueous NaCl and dried ($MgSO_4$). The solvent was evaporated under reduced pressure to give the crude product that was purified by passing through a short pad of silica, eluting with CH_2Cl_2 and then EtOAc:Et_3N (100:1) to afford the pure title compound **4l** as a colourless oil (679 mg, 3.34 mmol, 63% yield over 3 steps).

^{1}H NMR (400 MHz, Chloroform-*d*) 7.34 – 7.29 (m, 4H, Ar*H*), 7.27 – 7.20 (m, 1H, Ar*H*), 5.60 (ddd, *J* = 17.0, 10.3, 8.3 Hz, 1H, C*H*=CH_2), 5.16 – 5.08 (m, 2H, CH=C*H*$_2$), 3.83 (d, *J* = 13.1 Hz, 1H, PhC*H*$_2$), 3.63 (d, *J* = 13.1 Hz, 1H, PhC*H*$_2$), 3.12 – 3.05 (m, 1H, NC*H*), 1.66 (m, 1H, $(CH_3)_2$C*H*), 1.56 – 1.42 (bs, 1H, N*H*), 1.42 – 1.25 (m, 2H, $(CH_3)_2$CHC*H*$_2$), 0.87 (d, *J* = 3.4 Hz, 3H, (C*H*$_3$)$_2$CH), 0.85 (d, *J* = 3.4 Hz, 3H, (C*H*$_3$)$_2$CH).
^{13}C NMR (101 MHz, Chloroform-*d*) δ 141.6, 140.8, 128.5, 128.3, 126.9, 116.0, 59.5, 51.4, 45.2, 24.8, 23.2, 22.6.
^{1}H NMR Spectra data was consistent with the values reported in literature.[6]

[5] Lee, A.; Ellman, J. A. *Org. Lett.* **2001**, *3*, 3707.
[6] Brettle, R.; Jafri, I. A. *J. Chem. Soc., Perkin Trans. 1* **1983,** 387.

N-(2-(benzyloxy)ethylidene)-2-methylpropane-2-sulfinamide (24)

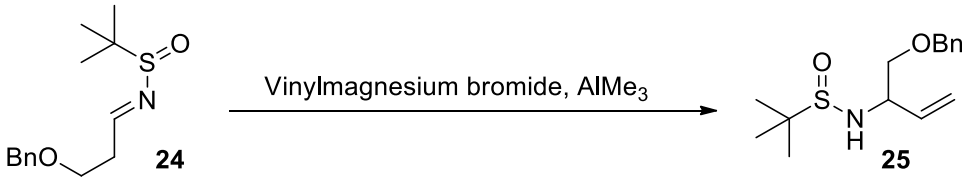


23 **21** **24**

To a 0.5 M solution of 2-methylpropane-2-sulfinamide (**21**) (533 mg, 4.40 mmol, 1.1 eq) in CH_2Cl_2 (8 mL) was added $CuSO_4$ (1.60 g, 10.0 mmol, 2.5 eq) and the 2-(benzyloxy)acetaldehyde (**23**) (601 mg, 4.00 mmol, 1.0 eq). The reaction mixture was stirred for 72 h at rt. The reaction mixture was filtered through a pad of Celite, and the filter cake was washed with CH_2Cl_2 and the filtrate concentrated under reduced pressure. Purification by column chromatography (SiO_2, Pentane:EtOAc 4:1 to 1:1) afforded the title compound **24** as a clear colourless oil (973 mg, 3.84 mmol, 96% yield).

^{1}H NMR (400 MHz, CDCl3) δ 8.14-8.12 (t, 1H, *J* = 3.2 Hz, NC*H*), 7.38-7.31 (m, 5H, Ar*H*), 4.64 (s, 2H, PhCH_2), 4.45-4.41 (m, 1H, OCH_2), 4.41-4.36 (m, 1H, OCH_2), 1.22 (s, 9H, tBu).
Spectra data was consistent with the values reported in literature.[7]

N-(1-(Benzyloxy)but-3-en-2-yl)-2-methylpropane-2-sulfinamide (25)



24 **25**

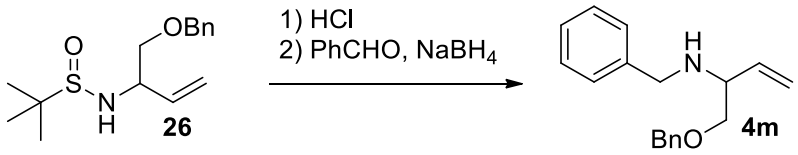
Following a reported procedure,[8] a solution of trimethylaluminum (2.0 M, 1.30 mL, 2.60 mmol, 1.1 eq) in toluene was slowly added to a solution of N-(2-(benzyloxy)ethylidene)-2-methylpropane-2-sulfinamide (**24**) (600 mg, 2.37 mmol, 1.0 eq) in toluene (11.2 mL) at -78 °C. The solution was stirred for 30 min at this temperature and a solution of vinylmagnesium bromide (1.0 M, 3.43 mL, 3.43 mmol, 1.45 eq) in THF was slowly added keeping the internal temperature below -70 °C. The reaction mixture was stirred at -78 °C until complete conversion of the imine was observed by TLC. The reaction was then quenched with a saturated solution of Na_2SO_4 and let warm up to rt. The phases were then separated. The organic phase was dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by column chromatography (Pentane:EtOAc 4:1) to afford the title compound **25** a pale yellow oil (548 mg, 1.95 mmol, 82% yield).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.39 – 7.27 (m, 5H, Ar*H*), 5.66 (ddd, *J* = 17.2, 10.3, 7.0 Hz, 1H, C*H*=CH$_2$), 5.35 (m, 1H, CH=CH_2), 5.24 (m, 1H, CH=CH_2), 4.61 (d, *J* = 12.0 Hz, 1H, O CH_2Ph), 4.49 (d, *J* = 12.0 Hz, 1H, OCH_2Ph), 4.11 (m, 1H, NC*H*), 3.86 (bs, 1H, N*H*), 3.58 (dd, *J* = 9.6, 4.2 Hz, 1H, BnOCH_2), 3.48 (dd, *J* = 9.6, 7.9 Hz, 1H, BnOCH_2), 1.22 (s, 9H, *t*Bu).

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

[7] Tang, T. P.; Volkman, S. K.; Ellman, J. A. *J. Org. Chem.* **2001**, *66*, 8772.
[8] Van den Nieuwendijk, A. M. C. H.; Ruben, M.; Engelsma, S. E.; Risseeuw, M. D. P.; van den Berg, R. J. B. H. N.; Boot, R. G.; Aerts, J. M.; Brussee, J.; van der Marel, G. A.; Overkleeft, H. S. *Org. Lett.*, **2010,** *12*, 3957.

N-Benzyl-1-(benzyloxy)but-3-en-2-amine (4m)



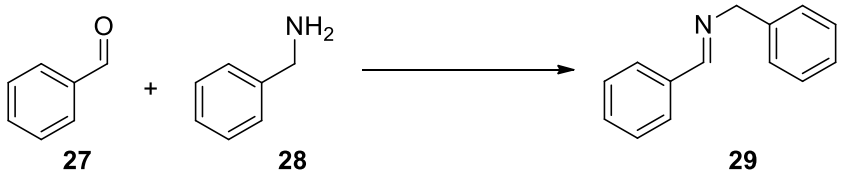
Multistep procedure:

1) Following a slightly modified procedure,[5] N-1-(benzyloxy)but-3-en-2-yl)-2-methylpropane-2-sulfinamide (**26**) (550 mg, 1.95 mmol, 1.0 eq) was cleaved by addition of a HCl solution (2 N in Et_2O, 1.95 mL, 3.90 mmol, 2.0 eq) and methanol (4 mL). After 30 min, the reagents/solvents were removed by passing N_2 over the solution. The resultant amine salts were re-dissolved in CH_2Cl_2 (20 mL) and washed with 1 M KOH (15 mL) in order to obtain the free amine. Upon drying ($MgSO_4$), filtration, and solvent removal under reduced pressure, the crude free amine was obtained as a yellow solution in CH_2Cl_2 that was directly used in the next step without further purification.

2) 1-(Benzyloxy)but-3-en-2-amine (340 mg, 1.92 mmol, 1.0 eq) and benzaldehyde (0.194 mL, 1.92 mmol, 1.0 eq) were mixed in methanol (5 mL) with 4Å MS at rt under a N_2 atmosphere. The mixture was stirred at rt until the aldimine formation was completed (TLC monitoring). The aldimine in MeOH was carefully treated with solid $NaBH_4$ (116 mg, 3.07 mmol, 1.6 eq). The reaction mixture was stirred for 1 hour and quenched with 1 M KOH (5 mL). The product was extracted with CH_2Cl_2 (3x20 mL). The combined organic phases were dried over $MgSO_4$ and concentrated under reduced pressure. The crude product was purified by passing through a short pad of silica, eluting with Pentane:EtOAc:Et_3N 9:1:0.1 to afford the pure title compound **4m** as a colourless oil (430 mg, 1.61 mmol, 83% yield over 2 steps).

R_f 0.55 (Pentane:EtOAc 3:1).
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.38 – 7.21 (m, 10H, Ar*H*), 5.70 (ddd, *J* = 17.5, 10.2, 7.5 Hz, 1H, C*H*=CH$_2$), 5.31 – 5.18 (m, 2H, CH=C*H*$_2$), 4.54 – 4.46 (m, 2H, OC*H*$_2$Ph), 3.86 (d, *J* = 13.3 Hz, 1H, PhC*H*$_2$N), 3.65 (d, *J* = 13.4 Hz, 1H, PhC*H*$_2$N), 3.53 – 3.36 (overlapping signals, 3 m, 3H, BnOC*H*$_2$ and NC*H*), 1.99 (bs, 1H, N*H*).
^{13}C NMR (101 MHz, Chloroform-*d*) δ 140.7, 138.3, 137.9, 128.6, 128.5, 128.3, 127.8, 127.7, 126.9, 117.9, 73.6, 73.3, 60.7, 51.3.
IR ν_{max} 3371 (w), 3033 (w), 2857 (w), 1701 (w), 1609 (w), 1496 (w), 1459 (w), 1362 (w), 1209 (w), 1164 (w), 1098 (s), 1028 (w), 1000 (w), 928 (w), 844 (w), 810 (w), 798 (w), 784 (w), 740 (s).
HRMS (ESI) calcd for $C_{18}H_{22}NO^+$ $[M+H]^+$ 268.1696; found 268.1702.

N-benzyl-1-phenylmethanimine (29)

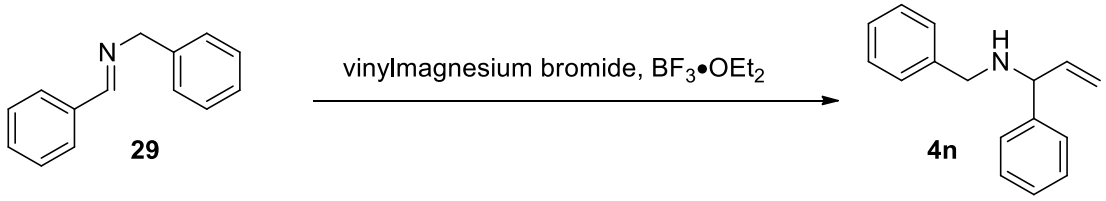


Following a reported procedure,[9] a 250 mL flask was charged with 3Å MS (30 g), flame-dried and cooled under a positive pressure of nitrogen. CH_2Cl_2 (50 mL) and benzaldehyde (**27**) (4.05 mL, 40.0 mmol, 1.02 eq) were added. Benzylamine (**28**) (4.29 mL, 39.2 mmol, 1.00 eq) was then added dropwise and the reaction was followed by TLC. After completion of the reaction, the

molecular sieves were removed by filtration, and the product was concentrated under reduced pressure. Vacuum distillation was directly made to purify the product (118 °C under reduced pressure) to give a colorless liquid. The residue was purified by vacuum distillation under reduced pressure (118 °C, 0.05 mmHg) to afford the title compound **29** as a colorless oil (4.62 g, 24.4 mmol, 62% yield).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.40 (s, 1H, NC*H*), 7.80-7.78 (m, 2H, Ar*H*), 7.44-7.41 (m, 3H, Ar*H*), 7.37-7.33 (m, 4H, Ar*H*), 7.29-7.25 (m, 1H, Ar*H*), 4.84 (d, 2 H, PhCH_2).
Spectra data was consistent with the values reported in literature.[9]

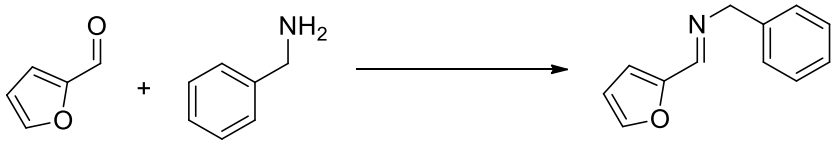
N-benzyl-1-phenylprop-2-en-1-amine (4n)



Following a slightly modified procedure,[10] N-benzylidene-1-phenylmethanamine (**29**) (1.17 g, 6.00 mmol, 1.0 eq) was dissolved in toluene (15 mL), cooled to -78 ºC, and $BF_3{\cdot}Et_2O$ (48 %Wt, 7.92 mL, 30.0 mmol, 5.0 eq) was added under N_2. After 10 min at -78 ºC, a solution of vinyl magnesium bromide in THF (0.7 M, 34.3 mL, 24.0 mmol, 4.0 eq) was added dropwise. The resulting mixture was allowed to slowly warm up to rt and stirred for further 2 h. Then, the reaction mixture was poured into 2 N aqueous NaOH (30 mL), and extracted with Et_2O (3x30 mL). The organic layer was dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by column chromatography (SiO_2, Pentane:EtOAc:Et_3N 10:1:0.1) to afford the title compound **4n** as a colorless oil (0.992 g, 4.44 mmol, 74% yield).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.40 – 7.30 (m, 8H, Ar*H*), 7.26 (m, 2H, Ar*H*), 5.95 (ddd, *J* = 17.2, 10.2, 7.1 Hz, 1H, C*H*=CH_2), 5.28 – 5.18 (m, 1H, CH=CH_2), 5.16 – 5.10 (m, 1H, CH=CH_2), 4.23 (d, *J* = 7.2 Hz, 1H, PhC*H*), 3.78 – 3.69 (m, 2H, PhCH_2), 1.61 (bs, 1H, N*H*).
^{13}C NMR (101 MHz, Chloroform-*d*) δ 142.9, 141.1, 140.5, 128.7, 128.5, 128.3, 127.5, 127.3, 127.0, 115.3, 65.2, 51.4.
Spectra data was consistent with the values reported in literature.[11]

N-benzyl-1-(furan-2-yl)methanimine (31)



30 28 31

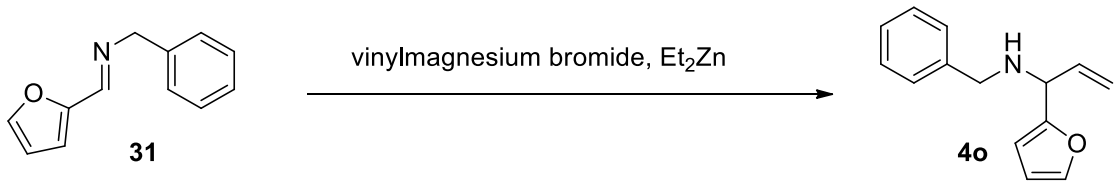
Following a reported procedure,[9] a 250 mL flask was charged with 3Å MS (30 g), flame-dried and cooled under a positive pressure of nitrogen. CH_2Cl_2 (50 mL) and 2-furaldehyde (**30**) (3.30 mL, 40.0 mmol, 1.02 eq) were added. Benzylamine (**28**) (4.29 mL, 39.2 mmol, 1.00 eq) was then added dropwise and the reaction was followed by TLC. After completion of the reaction, the molecular sieves were removed by filtration, and the product was concentrated under reduced

[9] Joly, G. D.; Jacobsen, E. N. *J. Am. Chem. Soc.* **2004,** *126*, 4102.
[10] Solé, D.; Serrano, O. *J. Org. Chem.* **2010,** *75*, 6267.
[11] Takeuchi, R.; Ue, N.; Tanabe, K.; Yamashita, K.; Shiga, N. *J. Am. Chem. Soc.* **2001**, *123*, 9525.

pressure. Vacuum distillation was directly made to purify the product (118 °C under reduced pressure) to give a colorless liquid. The residue was purified by vacuum distillation under reduced pressure (127 °C, 0.05 mmHg) to afford the title compound **31** as a colorless oil (5.89 g, 31.8 mmol, 81% yield).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.16 (s, 1H, NC*H*), 7.52-7.47 (m, 1H, HetAr*H*), 7.35-7.29 (m, 4H, Ar*H*), 7.27-7.23 (m, 1H, Ar*H*), 6.77 (d, *J* = 3.3 Hz, 1H, HetAr*H*), 6.47 (dd, *J* = 1.8, 3.4 Hz, 1H, HetAr*H*), 4.78 (s, 2 H, PhCH_2).
Spectra data was consistent with the values reported in literature.[9]

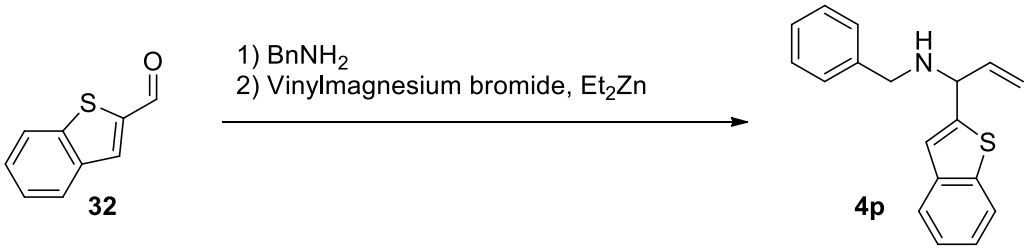
N-benzyl-1-(furan-2-yl)prop-2-en-1-amine (4o)



Following a slightly modified procedure,[12] a solution of distilled N-(furan-2-ylmethylene)-1-phenylmethanamine (**31**) (1.11 g, 6.00 mmol, 1.0 eq) in anhydrous THF (20 mL) was prepared under nitrogen. After cooling to -78 °C, a diethyl zinc solution in hexanes (1 M, 9.00 mL, 9.00 mmol, 1.5 eq) and, 10 min later, a solution vinylmagnesium bromide in THF (0.7 M, 12.9 mL, 9.00 mmol, 1.5 eq) were added. The stirred solution was kept for 1 h at -78 °C, afterwards the cooling bath was removed. When the reaction mixture reached room temperature, dilution with 5% w/v aq. NaOH (10 mL) and extraction with ethyl ether (3x15 mL) followed. The organic phases were collected, dried ($MgSO_4$) and concentrated under vacuum. The crude amine was purified by column chromatography (SiO_2, Pentane:EtOAc:Et_3N 10/1/0.1 to 4:1:0.1) to afford the title compound **4o** as a colourless oil (1.05 g, 4.92 mmol, 82 % yield).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.38 (m, 1H, HetAr*H*), 7.35 – 7.29 (m, 4H, Ar*H*), 7.29 – 7.22 (m, 1H, Ar*H*), 6.33 (dd, *J* = 3.1, 1.8 Hz, 1H, HetAr*H*), 6.21 (d, *J* = 3.1 Hz, 1H, HetAr*H*), 5.98 (ddd, *J* = 17.2, 10.2, 7.1 Hz, 1H, C*H*=CH_2), 5.31 – 5.20 (m, 2H, CH=CH_2), 4.32 (d, *J* = 7.1 Hz, 1H, NC*H*), 3.77 (s, 2H, PhCH_2), 1.82 (bs, 1H, N*H*).
^{13}C NMR (101 MHz, Chloroform-*d*) δ 155.4, 142.0, 140.1, 137.6, 128.6, 128.4, 127.1, 117.1, 110.2, 106.6, 58.4, 51.1.
Spectra data was consistent with the values reported in literature.[13]

1-(Benzo[b]thiophen-2-yl)-N-benzylprop-2-en-1-amine (4p)



Multistep procedure:

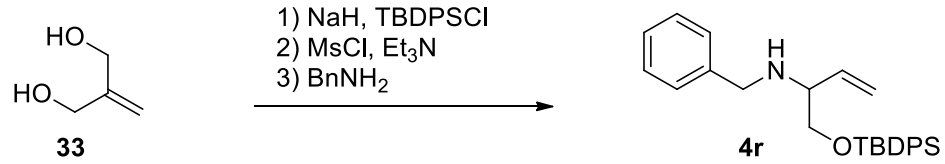
[12] Ghelfi, F.; Parsons, A. F.; Tommasini, D.; Mucci, A. *Eur. J. Org. Chem.* **2001**, 1845.
[13] Leitner, A.; Shu, C.; Hartwig, J. F. *Org. Lett.* **2005**, *7*, 1093.

1) Following a slightly modified procedure,[10] a 25 mL flask was charged with 3Å MS (4 g), flame-dried and cooled under a positive pressure of nitrogen. CH_2Cl_2 (17 mL) and benzothiophene-2-carbaldehyde (**32**) (0.827 g, 5.10 mmol, 1.02 eq) were added. Benzylamine (0.546 mL, 5.00 mmol, 1.00 eq) was then added dropwise and the reaction was followed by TLC. After completion of the reaction, The crude mixture was filtered over celite, dried under reduced pressure, and directly used in the next step.

2) Following a slightly modified procedure,[13] a solution of N-(benzo[b]thiophen-2-ylmethylene)-1-phenylmethanamine (1.26 g, 5.00 mmol, 1.0 eq) in anhydrous THF (16 mL) was prepared under nitrogen. After cooling to -78 °C, a diethyl zinc solution in hexanes (1.0 M, 12.5 mL, 12.5 mmol, 2.5 eq) and a solution of vinylmagnesium bromide in THF (1.0 M, 12.5 mL, 12.5 mmol, 2.5 eq) were added. The stirred solution was kept for 1 h at -78 °C, afterwards the cooling bath was removed. When the reaction mixture reached room temperature, dilution with 5% w/v aq. NaOH (10 mL) and extraction with diethyl ether (3x15 mL) followed. The organic layers were collected, dried ($MgSO_4$) and concentrated under vacuum. The crude amine was purified by column chromatography (SiO_2, Pentane:EtOAc:Et_3N 15:1:0.1) to afford the title compound **4p** as a colourless oil (0.992 g, 3.55 mmol, 71 % yield).

R_f 0.20 (Pentane:EtOAc:Et_3N 14:1:0.1).
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.86 – 7.82 (m, 1H, HetAr*H*), 7.75 – 7.69 (m, 1H, HetAr*H*), 7.43 – 7.27 (m, 7H, HetAr*H and* Ar*H*), 7.23 – 7.19 (m, 1H, HetAr*H*), 6.04 (ddd, *J* = 17.1, 10.1, 7.3 Hz, 1H, C*H*=CH_2), 5.35 (dt, *J* = 17.1, 1.2 Hz, 1H, CH=CH_2), 5.27 (dt, *J* = 10.1, 1.1 Hz, 1H, CH=CH_2), 4.61 – 4.55 (m, 1H, NC*H*), 3.87 (s, 2H, PhCH_2), 1.85 (bs, 1H, N*H*).
^{13}C NMR (101 MHz, Chloroform-*d*) δ 148.8, 140.1, 139.9, 139.7, 139.6, 128.6, 128.3, 127.2, 124.2, 124.0, 123.3, 122.6, 120.9, 116.7, 61.1, 51.1.
IR ν_{max} 3321 (w), 3060 (w), 3028 (w), 2978 (w), 2921 (w), 2839 (w), 1640 (w), 1603 (w), 1495 (w), 1456 (m), 1414 (w), 1359 (w), 1338 (w), 1310 (w), 1276 (w), 1253 (w), 1189 (w), 1149 (w), 1127 (w), 1074 (w), 1023 (w), 990 (w), 927 (m), 859 (w), 830 (m), 744 (s).
HRMS (ESI) calcd for $C_{18}H_{18}NS^+$ $[M+H]^+$ 280.1154; found 280.1146.

N-Benzyl-2-(((tert-butyldiphenylsilyl)oxy)methyl)prop-2-en-1-amine (4r)



33 **4r**

Multisptep procedure:
1) Following a reported procedure,[14] 2-methylenepropane-1,3-diol (**33**) (0.50 mL, 6.1 mmol) was dissolved in THF (15 mL), the solution was cooled at 0 °C before the addition of NaH (0.25 g 60% dispersed in mineral oil, 6.1 mmol, 1.0 eq). After 1 h, TBDPSCl (1.6 mL, 6.1 mmol, 1.0 eq) was added and the reaction was stirred at room temperature for 18-20 h. The solution was then cooled to 0 °C and quenched with iced water and then extracted with diethyl ether (3 x 50 mL). The organic layers are recombined and washed with a saturated solution of K_2CO_3 (50 mL), brine (50 mL) and dried over Na_2SO_4. Evaporation of the solvent afforded compound 21 (2.0 g, 6.1 mmol, 99% yield) as a colorless oil which was directly used in the next step.

2) Methanesulfonyl chloride (0.296 mL, 3.83 mmol, 1.25 eq) was added dropwise to a solution of 2-(((tert-butyldiphenylsilyl)oxy) methyl)prop-2-en-1-ol (1.00 g, 3.06 mmol, 1.0 eq) and Et_3N

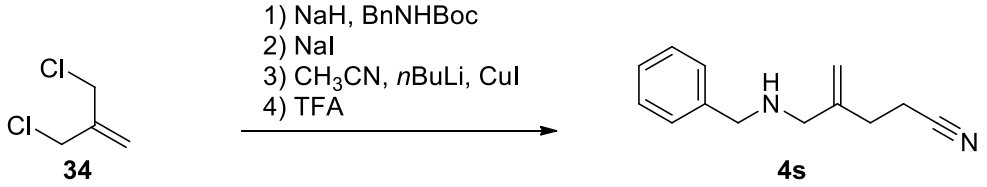
[14] Russo, F.; Wangsell,F.; Saevmarker, J.; Jacobsson, M.; Larhed, M. *Tetrahedron* **2009,** *65,* 10047.

(0.640 mL, 4.59 mmol, 1.5 eq) in CH_2Cl_2 (60 mL) at 0 °C. The mixture was stirred at the same temperature for 2 h. Saturated Na_2CO_3 (30 mL) was then added to quench the reaction. After the separation of the organic layer, extraction of the aqueous layer with CH_2Cl_2 (2x20 mL), the combined organic layers were washed with brine, dried with $MgSO_4$, concentrated under reduced pressure to afford the crude 2-(((tert-butyldiphenylsilyl)oxy)methyl)allyl methanesulfonate, which was used directly in the next step.

3) 2-(((Tert-butyldiphenylsilyl)oxy)methyl)allyl methanesulfonate was added dropwise to a rapidly stirring neat benzyl amine solution (4.50 g, 42.0 mmol) at 0 °C. The reaction mixture was stirred for 15 h at rt. The crude product was purified by column chromatography (SiO_2 10:1:0.1 Pentane:EtOAc:Et_3N) to afford the title compound **4r** as a pale yellow oil (861 mg, 2.07 mmol, 68% yield).

R_f 0.75 (Pentane:EtOAc 4:1).
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.71 – 7.65 (m, 4H, Ar*H*), 7.45 – 7.34 (m, 6H, Ar*H*), 7.33 – 7.22 (m, 5H, Ar*H*), 5.25 (d, *J* = 1.7 Hz, 1H, C=CH_2), 5.07 (d, *J* = 1.7 Hz, 1H, C=CH_2), 4.22 (s, 2H, TBDPSOCH_2), 3.72 (s, 2H, PhCH_2), 3.27 (s, 2H, BnNCH_2), 1.55 (bs, 1H, N*H*), 1.06 (s, 9H, *t*Bu).
^{13}C NMR (101 MHz, Chloroform-*d*) δ 146.4, 140.4, 135.7, 133.7, 129.8, 128.5, 128.3, 127.8, 127.0, 110.8, 65.8, 53.2, 51.4, 27.0, 19.4.
IR ν_{max} 3069 (w), 3052 (w), 3029 (w), 2956 (m), 2933 (m), 2890 (w), 2858 (m), 1594 (w), 1458 (w), 1432 (w), 1390 (w), 1110 (s), 910 (w), 826 (m), 741 (s).
HRMS (ESI) calcd. for $C_{27}H_{34}NOSi^+$ $[M+H]^+$ 416.2404; found 416.2412.

4-((Benzylamino)methyl)pent-4-enenitrile (4s)



34 **4s**

Multistep procedure:
1) Following a slightly modified procedure,[15] *tert*-butyl benzylcarbamate (5.00 g, 24.1 mmol, 1.0 eq) and 3-chloro-2-(chloromethyl)prop-1-ene (**34**) (3.35 mL, 28.9 mmol, 1.2 eq) were dissolved in DMF (25 mL). NaH (1.45 g, 36.2 mmol, 1.5 eq) was added to the clear colorless solution which immediately turned to a cloudy mixture. After 6 h, the reaction was quenched by dropwise addition of water (100 mL), and then diluted with diethyl ether (ca. 120 mL). The layers were separated, and the organic layer was washed successively with water (3x30 mL), then brine (50 mL), dried ($MgSO_4$), and the solvent was removed under reduced pressure. The residue was purified by passing through a short pad of silica, eluting with Pentane:CH_2Cl_2 1:1 and the crude product was directly engaged in the next step.

2) Tert-butyl benzyl(2-(chloromethyl)allyl)carbamate (1.77 g, 6.00 mmol, 1.0 eq) and NaI (2.53 g, 16.9 mmol, 2.8 eq) were refluxed in 20 mL acetone for 15 h. The reaction mixture was cooled down, filtered over Celite and concentrated under reduced pressure. The crude was directly used in the next step.

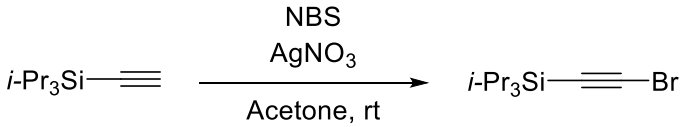
[15] Aponick, A.; Dietz, A. L.; Pearson, W. H. *Eur. J. Org. Chem.* **2008**, 4264.

3) A cooled 2.5 M solution of *n*BuLi in hexanes (2.74 mL, 6.84 mmol, 2.65 eq) was added to a solution of acetonitrile (0.460 mL, 8.81 mmol, 3.41 eq) in THF (12 mL) at -78 °C under nitrogen. After 40 min at this temperature, the mixture was warmed to -25 °C and copper(I) iodide (1.69 g, 8.88 mmol, 3.44 eq) was added. After stirring for 15 min. at -25 °C the brick-colored solution of cyanomethylcopper was treated with tert-butyl benzyl(2-(iodomethyl)allyl)carbamate (1.00 g, 2.58 mmol, 1.0 eq) in THF (8 mL). After 1.5 h at -25 °C, aqueous ammonium chloride (30 mL) was added and the product was extracted with ether (2x30 mL). The combined organic phase were washed with brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude was directly used in the next step.

4) TFA (1.5 mL) was added to a solution of *tert*-butyl benzyl(4-cyano-2-methylenebutyl)carbamate (640 mg, 2.13 mmol) in CH_2Cl_2 (2.2 mL) at 0 °C. The reaction mixture was warmed up to rt and stirred for 3 h. Then 1 N NaOH was added (5 mL) and the reaction mixture was stirred for 10 min. Then the layers were separated and the aqueous extracted once with CH_2Cl_2 (20 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated. The crude product was purified by column chromatography (SiO_2, Pentane:EtOAc:Et_3N 3:1:0.1) to afford the title compound **4s** as a pale yellow oil (303 mg, 1.51 mmol, 31 % overall yield).

R_f 0.20 (Pentane:EtOAc 3:1).
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.36 – 7.31 (m, 4H, Ar*H*), 7.30 – 7.24 (m, 1H, Ar*H*), 5.14 (s, 1H, C=CH_2), 5.01 (s, 1H, C=CH_2), 3.77 (s, 2H, PhCH_2), 3.25 (s, 2H, BnNCH_2), 2.58 – 2.43 (overlapping signals, 2 m, 4H, CH_2CN and CH_2CH_2CN), 1.77 (s, 1H, NH).
^{13}C NMR (101 MHz, Chloroform-*d*) δ 144.3, 140.3, 128.5, 128.2, 127.1, 119.6, 113.4, 53.8, 53.3, 30.0, 16.3.
IR ν_{max} 3336 (w), 3078 (w), 3029 (m), 2985 (w), 2922 (m), 2835 (m), 2834 (m), 2247 (w), 2105 (w), 1737 (m), 1648 (m), 1492 (w), 1450 (m), 1204 (w), 1114 (w), 909 (m), 741 (s).
HRMS (ESI) calcd. for $C_{13}H_{17}N_2^+$ $[M+H]^+$ 201.1386; found 201.1390.

2-Bromo-1-tri*iso*propylsilyl acetylene (5a)



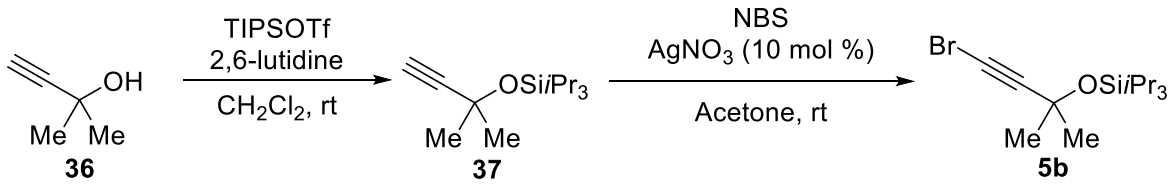
35 **5a**

Following a reported procedure,[16] tri*iso*propylsilylacetylene (**35**) (813 mg, 4.45 mmol, 1.00 equiv) was dissolved in acetone (30 mL). *N*-bromosuccinimide (925 mg, 5.19 mmol, 1.16 equiv) was added, followed by $AgNO_3$ (76 mg, 0.44 mmol, 0.1 equiv). The resulting mixture was stirred at room temperature for 3 h and it was then poured onto ice. After ice being allowed to melt, the aqueous layer was extracted with pentane (3 x 30 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated *in vacuo* to afford pure 2-bromo-1-tri*iso*propylsilyl acetylene (**5a**) (1.16 g, 4.43 mmol, 99%) as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.20-0.97 (m, 21 H, TIPS).
^{13}C NMR (100 MHz, $CDCl_3$) δ 83.5, 61.7, 18.5, 11.3.
Spectra data was consistent with the values reported in literature.[16]

[16] Jiang, M. X.; Rawat, M.; Wulff, W. D. *J. Am. Chem. Soc.*, **2004**, *126*, 5970.

((4-Bromo-2-methylbut-3-yn-2-yl)oxy)triisopropylsilane (5b)

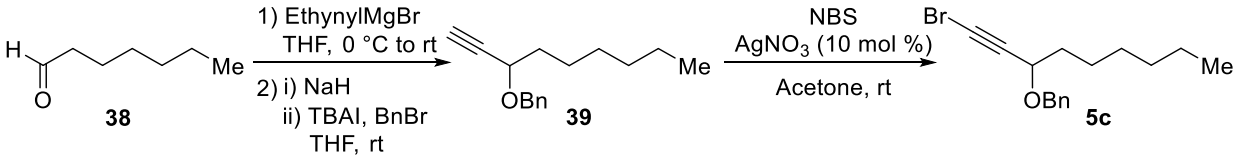


Following a reported procedure,[17] 2-methylbut-3-yn-2-ol (**36**) (0.34 mL, 3.5 mmol, 1.0 equiv.) and 2,6-lutidine (freshly distilled on CaH_2, 0.41 mL, 3.5 mmol, 1.0 equiv.) were dissolved in CH_2Cl_2 (12 mL). TIPSOTf (0.94 mL, 3.5 mmol, 1.0 equiv.) was added dropwise to the solution at 0 °C. The solution was allowed to warm to rt overnight and then quenched with a saturated aqueous $NaHCO_3$ solution and the aqueous layer was extracted with CH_2Cl_2 (3 x 10 mL). The combined organic layers were washed with H_2O, dried over $MgSO_4$, filtered and the solvent was removed *in vacuo*. Purification by column chromatography (SiO_2, pentane) afforded TIPS-protected propargyl alcohol **37** as a colorless oil (622 mg, 2.59 mmol, 74% yield), which was used directly for the next step.

Following a reported procedure,[18] propargyl alcohol **37** (603 mg, 2.51 mmol, 1.0 equiv.) was dissolved in acetone (17 mL). N-bromosuccinimide (535 mg, 3.01 mmol,1.2 eq) and $AgNO_3$ (42 mg, 0.25 mmol, 0.1 eq) are added to the resulting solution in this order and the mixture is stirred at rt for 6 hours, until complete consumption of the starting material according to TLC. It was then poured onto iced water. The aqueous layer was extracted with pentane (3 times) and the combined organic extracts were dried over $MgSO_4$, filtered and the solvent removed by evaporation under reduced pressure. After purification by column chromatography (SiO_2, pentane), bromoalkyne **5b** was obtained as a colorless oil (733 mg, 2.30 mmol, 91% yield).in 95% purity as judged by ^{1}H NMR.

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.51 (s, 6 H, Me), 1.18-1.03 (m, 21 H, TIPS).
^{13}C NMR (100 MHz, $CDCl_3$) δ 85.4, 67.2, 42.7, 32.9, 18.3, 13.0.
Spectra data was consistent with the values reported in literature.[18]

(((1-Bromonon-1-yn-3-yl)oxy)methyl)benzene (5c)



Following a slightly modified reported procedure,[19] heptaldehyde (**38**) (1.22 mL, 8.76 mmol, 1.0 equiv.) was added dropwise to a solution of ethynyl magnesium bromide (0.5 M in THF, 22.8 mL, 11.4 mmol, 1.3 equiv.) at 0 °C. After 30 min, the cooling bath was removed to reach rt and the solution was stirred for further 2 h. The reaction was then quenched by addition of aqueous HCl (1.0 M, 15 mL) and the mixture was extracted with Et_2O (3 x 20 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered and the solvent was removed under

[17] Nishimura, T.; Nagaosa, M.; Hayashi, T. *Tetrahedron Lett.* **2011**, *52*, 2185.
[18] S. Nicolai, R. Sedigh-Zadeh, J. Waser, *J. Org. Chem* **2013**, *78*, 3783.
[19] Buzas, A.; Gagosz, F. *J. Am. Chem. Soc.* **2006**, *128*, 12614.

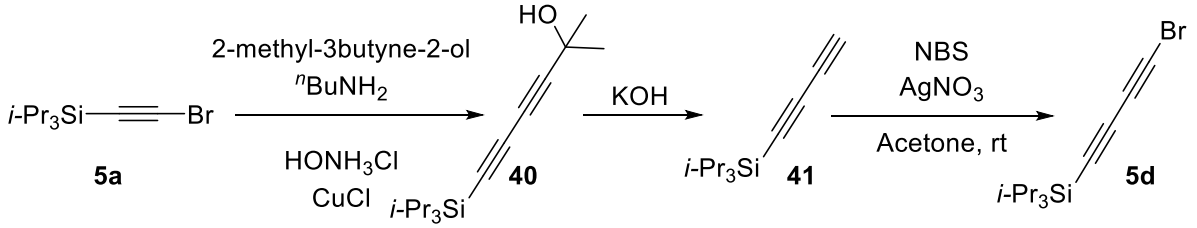
reduced pressure. Purification by column chromatography (SiO_2, pentane/EtOAc 20/1) afforded the corresponding propargyl alcohol as a yellow oil (943 mg, 6.73 mmol, 77% yield).

Following a reported procedure,[20] the propargyl alcohol (701 mg, 5.00 mmol, 1.0 equiv.) was added dropwise to a suspension of NaH (168 mg, 7.00 mmol, 1.4 equiv.) in THF (24 mL). The solution was stirred for 2 h and then TBAI (92.3 mg, 0.250 mmol, 0.05 equiv.) and benzyl bromide (0.84 mL, 7.0 mmol, 1.4 equiv.) were added sequentially. The resulting mixture was stirred overnight and then quenched by slow addition of H_2O. The aqueous layer was extracted with Et_2O (3 x 40 mL) and the combined organic layers were washed with brine, dried over $MgSO_4$, filtered and the solvent was removed *in vacuo*. Purification by column chromatography (SiO_2, pentane/EtOAc 20/1) afforded the *O*-benzylated propargyl alcohol **39** as a yellow oil (1.12 mg, 4.86 mmol, 97% yield).

Following a reported procedure,[18] propargyl alcohol **39** (1.12 g, 4.86 mmol, 1.0 equiv.) was dissolved in acetone (33 mL). N-bromosuccinimide (1.04 g, 5.83 mmol,1.2 eq) and $AgNO_3$ (83 mg, 0.49 mmol, 0.1 eq) are added to the resulting solution in this order and the mixture is stirred at rt for 6 hours, until complete consumption of the starting material according to TLC. It was then poured onto iced water. The aqueous layer was extracted with pentane (3 times) and the combined organic extracts were dried over $MgSO_4$, filtered and the solvent removed by evaporation under reduced pressure. After purification by chromatography column (SiO_2, Pentane/EtOAc 98/2), bromoalkyne **5c** was obtained as a pale yellow oil (1.06 g, 3.43 mmol, 71% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37-7.27 (m, 5 H, Ar H), 4.78 (d, 1 H, *J* = 11.7 Hz, benzyl CH_2), 4.49 (d, 1 H, *J* = 11.7 Hz, benzyl CH_2), 4.09 (t, 1 H, *J* = 6.6 Hz, CHO), 1.74 (ddd, 2 H, *J* = 13.2, 6.6, 2.0 Hz, CH_2), 1.44 (m, 2 H, CH_2), 1.35-1.25 (m, 6 H, CH_2), 0.88 (t, 3 H, *J* = 6.7 Hz, Me).
^{13}C NMR (100 MHz, $CDCl_3$) δ 137.8, 128.4, 128.0, 127.7, 79.5, 70.7, 69.6, 45.1, 35.6, 31.7, 28.9, 25.2, 22.6, 14.1.
Spectra data was consistent with the values reported in literature.[18]

(Bromobuta-1,3-diyn-1-yl)triisopropylsilane (5d)



Following a reported procedure,[16] to a mixture of MeOH (1 mL) and H_2O (0.5 mL) were added *n*-butylamine (0.88 g, 12 mmol, 3 equiv), 2-methyl-3-butyne-2-ol (0.67 g, 8.0 mmol, 2 equiv), copper (I) chloride (59 mg, 0.60 mmol, 0.15 equiv) and hydroxyaminehydrochloride (82 mg, 1.2 mmol, 0.3 equiv) in this order. The alkynyl bromide **5a** (4.0 mmol, 0.15 eq) was diluted with MeOH (5 mL) and was added dropwise to the mixture. Then the reaction mixture was stirred at room temperature for 36 hours. The reaction was quenched with H_2O and extracted with ether. The organic layer was washed with H_2O, brine and dried with $MgSO_4$.and the solvents removed under reduced pressure. The crude product was purified by column chromatography (SiO_2, Pentane:EtOAc 10:1) affording **40** (0.61 g, 2.3 mmol, 58%) as a white solid, which was used directly for the next step.

Following a reported procedure,[16] powdered KOH (0.28 g, 5.0 mmol, 2.2 eq) was added in one portion to a solution of the diyne alcohol **40** (2.3 mmol) in benzene (110 mL). The

[20] Trost, B. M.; Fandrick, D. R.; Dinh, D. C. *J. Am. Chem. Soc.* **2005**, *127*, 14186.

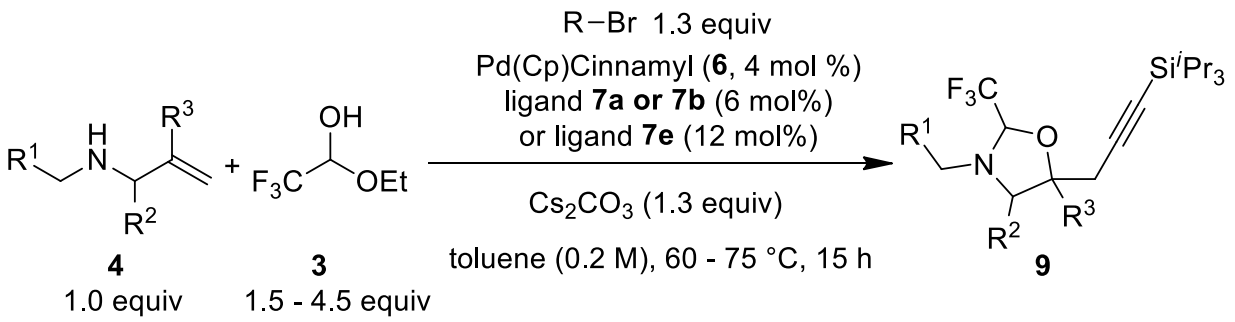
resulting mixture was heated and refluxed under N_2 until the reaction was complete as monitored by TLC. The reaction mixture was cooled to room temperature. Solids were removed by filtration through Celite. After concentration, the product was purified by column chromatography (SiO_2, pentane), affording **41** (0.407 g, 1.97 mmol, 85%) as a clear colorless liquid, which was immediately used in the next step.

Following a slightly modified procedure,[16] diyne **41** was dissolved in acetone (13 mL). N-bromosuccinimide (421 mg, 2.36 mmol,1.2 eq) and $AgNO_3$ (33 mg, 0.20 mmol, 0.1 eq) were added to the resulting solution in this order and the mixture was stirred at rt for 6 hours, until complete consumption of the starting material according to TLC. It was then poured onto iced water. The aqueous layer was extracted with pentane (3 times) and the combined organic extracts were dried over $MgSO_4$, filtered and the solvent removed by evaporation under reduced pressure. After purification by column chromatography (SiO_2, pentane), bromoalkyne **5d** was obtained as a pale yellow oil (422 mg, 1.47 mmol, 75% yield, 90% purity as judge by ^{1}H NMR) that turned orange upon exposure to air. This bromoalkyne was immediately used for catalysis.[21]

R_f 0.80 (Pentane).
^{1}H NMR (400 MHz, $CDCl_3$) δ 1.26-0.97 (m, 21 H, TIPS).
^{13}C NMR (100 MHz, $CDCl_3$) δ 89.9, 80.9, 66.3, 39.3, 18.7, 11.4.
IR ν_{max} 2943 (w), 2864 (m), 2238 (m), 2173 (m), 2120 (m), 2091 (m), 1461 (m), 1107 (s), 995 (s), 881 (s), 662 (w).

[21] No high resolution molecular mass could be obtained for this unstable compound.

4. Pd-catalyzed tandem hemiaminalization carbo-oxygenation of allylamines.



General procedure A

A sealed oven-dry 2 mL microwave vial under nitrogen was charged with dry degassed toluene (0.80 mL), 1-ethoxy-2,2,2-trifluoroethanol (**3**) (0.185 mL, 1.35 mmol, 4.5 eq), the allylamine **4** (0.300 mmol) and the appropriate alkynyl or alkenyl or aryl bromide (1.3 or 2.0 eq). The resulting solution was stirred 10-15 min at 50 °C and subsequently transferred *via* canula to a sealed oven-dry 5 mL microwave vial under nitrogen containing cinnamyl(cyclopenta-2,4-dien-1-yl)palladium (**6**) (3.5 mg, 0.012 mmol, 4 mol%), DPEPHOS (**7a**) (9.7 mg, 0.018 mmol, 6 mol%), cesium carbonate (127 mg, 0.390 mmol, 1.3 eq) and dry degassed toluene (0.70 mL) that have been previously premixed at 50 °C for 3 min. The resulting mixture was stirred at 60 °C for 15 h. The reaction mixture was cooled to 23 °C, concentrated to half its volume and directly purified by column chromatography using the indicated solvents.
NB: the dr was determined by integration of OC*H*CH_2 peaks in the ^{1}H NMR spectra, unless otherwise noted.

General procedure B for α-branched allylamines

A sealed oven-dry 2 mL microwave vial under nitrogen was charged with dry degassed toluene (0.80 mL), 1-ethoxy-2,2,2-trifluoroethanol (**3**) (0.123 mL, 0.900 mmol, 3.0 eq), the allylamine **4** (0.300 mmol) and (bromoethynyl)triisopropylsilane (**5a**) (102 mg, 0.390 mmol, 1.3 eq). The resulting solution was stirred 10-15 min at 50 °C and subsequently transferred *via* canula to a sealed oven-dry 5 mL microwave vial under nitrogen containing cinnamyl(cyclopenta-2,4-dien-1-yl)palladium (**6**) (3.5 mg, 0.012 mmol, 4 mol%), tri(2-furyl)phosphine (**7e**) (8.4 mg, 0.036 mmol, 12 mol %), cesium carbonate (127 mg, 0.390 mmol, 1.3 eq) and dry degassed toluene (0.70 mL) that have been previously premixed at 50 °C for 3 min. The resulting mixture was stirred at 75 °C for 15 h. The reaction mixture was cooled to 23 °C, concentrated to half its volume and directly purified by column chromatography using the indicated solvents.

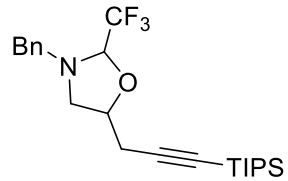
General procedure C for 1,1-disubstituted olefins

A sealed oven-dry 2 mL microwave vial under nitrogen was charged with dry degassed toluene (0.80 mL), 1-ethoxy-2,2,2-trifluoroethanol (**3**) (0.062 mL, 0.45 mmol, 1.5 eq), the allylamine (0.300 mmol) and the appropriate alkynyl bromide (0.390 mmol, 1.3 eq). The resulting solution was stirred 10-15 min at 50 °C and subsequently transferred *via* canula to a sealed oven-dry 5 mL microwave vial under nitrogen containing cinnamyl(cyclopenta-2,4-dien-1-yl)palladium (**6**) (3.5 mg, 0.012 mmol, 4 mol %), XANTPhos (**7b**) (10.4 mg, 0.018 mmol, 6 mol%), cesium carbonate (127 mg, 0.390 mmol, 1.3 eq) and dry degassed toluene (0.70 mL) that have been previously

premixed at 50 °C for 3 min. The resulting mixture was stirred at 75 °C for 15 h. The reaction mixture was cooled to 23 °C, concentrated to half its volume and directly purified by column chromatography using the indicated solvents.

N. B.: the signals corresponding to the TIPS in the ^{13}C NMR spectra are often not differentiated for the diastereisomers.

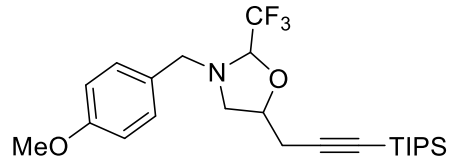
3-Benzyl-2-(trifluoromethyl)-5-(3-(triisopropylsilyl)prop-2-yn-1-yl)oxazolidine (9aa)



Following General Procedure **A**, the title compound was prepared from N-benzylprop-2-en-1-amine (**4a**) (44.2 mg, 0.300 mmol) and (bromoethynyl)triisopropylsilane (**5a**) (102 mg, 0.390 mmol). The crude oil was purified by column chromatography (SiO_2 15:1 to 7:1 Pentane: CH_2Cl_2) affording the title compound **9aa** (117 mg, 0.275 mmol, 92% yield, 1:1 dr in the crude ^1H NMR) as a yellow oil.

R_f 0.50 (Pentane/CH_2Cl_2 4/1).
^1H NMR (400 MHz, $CDCl_3$) mixture of diastereoisomers 1(*A*):1(*B*) δ 7.38 – 7.26 (m, 10H, Ar*H A* + *B*), 4.68 (m, 2H, C*H*CF_3, *A* + *B*), 4.41 (m, 1H, OC*H A*), 4.26 (m, 1H, OC*H B*), 4.17 (d, *J* = 12.9 Hz, 1H, CH_2Ph *A*), 3.99 (d, *J* = 13.1 Hz, 1H, CH_2Ph *B*), 3.84 (d, *J* = 13.1 Hz, 1H, CH_2Ph *B*), 3.72 (d, *J* = 12.9 Hz, 1H, CH_2Ph *A*), 3.29 (dd, *J* = 9.3, 5.6 Hz, 1H, CH_2N *A*), 3.14 – 3.06 (m, 2H, CH_2N *B*), 2.81 – 2.69 (overlapping signals, 2 m, 2H, CH_2CC *B*, CH_2N *A*), 2.66 (dd, *J* = 17.0, 4.5 Hz, 1H, CH_2CC *A*), 2.57 (dd, *J* = 17.0, 7.2 Hz, 1H, CH_2CC *A*), 2.45 (dd, *J* = 16.6, 9.1 Hz, 1H, CH_2CC *B*), 1.03 (m, 42H, TIPS *A* and *B*).
^{13}C NMR (101 MHz, $CDCl_3$) δ 137.8, 137.6, 128.9, 128.7, 128.7, 128.6, 127.9, 127.7, 123.7 (q, *J* = 285 Hz), 123.3 (q, *J* = 283 Hz), 103.4, 103.1, 92.9 (q, *J* = 33.8 Hz), 91.7 (q, *J* = 33.3 Hz), 83.6, 83.2, 77.2, 75.8, 59.7, 59.4, 56.7, 56.6, 25.0, 24.9, 18.7, 11.3.[22]
IR ν_{max} 3035 (w), 2943 (m), 2893 (w), 2867 (m), 2177 (w), 1678 (w), 1464 (w), 1385 (w), 1384 (w), 1293 (w), 1170 (s), 1104 (w), 1025 (w), 1002 (w), 885 (w), 734 (w).
HRMS calcd for $C_{23}F_3H_{35}NOSi^+$ $[M+H]^+$ 426.2435; found 426.2437.

3-(4-Methoxybenzyl)-2-(trifluoromethyl)-5-(3-(triisopropylsilyl)prop-2-yn-1-yl)oxazolidine (9ba)



Following General Procedure **A**, the title compound was prepared from N-(4-methoxybenzyl)prop-2-en-1-amine (**4b**) (53.2 mg, 0.300 mmol) and (bromoethynyl)triisopropylsilane (**5a**) (102 mg, 0.390 mmol). The crude oil was purified by column chromatography (SiO_2 15:1 to 3:1 Pentane:CH_2Cl_2) affording the title compound **9ba** (121 mg, 0.266 mmol, 89% yield, 1.1:1 dr determined by integration in the crude ^1H NMR) as a yellow oil.

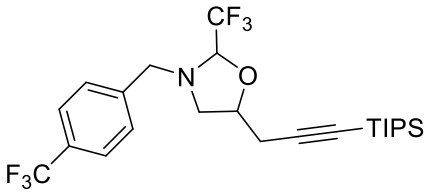
On larger scale, a slightly different procedure was used:
An oven-dried 50 mL schlenk equipped with a magnetic stirring bar was cooled under a stream of nitrogen and charged with cinnamyl(cyclopenta-2,4-dien-1-yl)palladium (**6**) (35 mg, 0.12 mmol, 4 mol%), DPEPHOS (**7a**) (97 mg, 0.18 mmol, 6 mol%) and cesium carbonate (1.27 g, 3.90 mmol, 1.3 eq) and sealed with a rubber septum. The schlenk was evacuated and backfilled with

[22] The peaks of the TIPS signaled could not be resolved for the diastereoisomers.

nitrogen, and this procedure was repeated three times. Then, dry degassed toluene (7.0 mL) was added and the resulting mixture was stirred at 50 °C for 10 min.
A sealed oven-dry 20 mL microwave vial under nitrogen was charged with dry degassed toluene (0.80 mL), 1-ethoxy-2,2,2-trifluoroethanol (**3**) (1.85 mL, 13.5 mmol, 4.5 eq), N-(4-methoxybenzyl)prop-2-en-1-amine (**4b**) (532 mg, 3.00 mmol, 1.0 eq) and (bromoethynyl)triisopropylsilane (**5a**) (1.02 g, 3.90 mmol, 1.3 eq). The resulting solution was stirred 15 min at 50 °C and subsequently transferred *via* canula into the schlenk. The resulting mixture was stirred at 60 °C for 15 h. The reaction mixture was cooled to 23 °C, filtered over a pad of silica, eluting with diethyl ether. The volatiles were removed and the residue was purified by column chromatography (SiO_2 15:1 to 3:1 Pentane:CH_2Cl_2) affording the title compound **9ba** (1.15 g, 2.51 mmol, 84 % yield, 1.1:1 dr determined by integration in the crude ^{1}H NMR) as a yellow oil.

R$_f$ 0.20 (Pentane/CH_2Cl_2 4/1).
^{1}H NMR (400 MHz, $CDCl_3$) mixture of diastereoisomers 1.1(*A*):1(*B*) δ 7.29 – 7.21 (m, 4H, Ar*H A + B*), 6.91 – 6.84 (m, 4H, Ar*H A + B*), 4.66 (m, 2H, C*H*CF_3, *A + B*), 4.40 (m, 1H, OC*H B*), 4.23 (m, 1H, OC*H A*), 4.09 (d, *J* = 12.7 Hz, 1H, C*H$_2$*Ph *B*), 3.91 (d, *J* = 13.0 Hz, 1H, C*H$_2$*Ph *A*), 3.81 (overlapping signals, 2s, 6H, ArOC*H$_3$*), 3.78 (d, *J* = 13.0 Hz, 1H, C*H$_2$*Ph *A*), 3.67 (d, *J* = 12.7 Hz, 1H, C*H$_2$*Ph *B*), 3.27 (dd, *J* = 9.4, 5.6 Hz, 1H, C*H$_2$*N *B*), 3.19 – 3.11 (m, 1H, C*H$_2$*N *A*), 3.09 – 3.02 (m, 1H, C*H$_2$*N *A*), 2.80 – 2.69 (overlapping signals, 2 m, 2H, C*H$_2$*CC *A*, C*H$_2$*N *B*), 2.65 (dd, *J* = 16.9, 4.5 Hz, 1H, C*H$_2$*CC *B*), 2.56 (dd, *J* = 16.9, 7.3 Hz, 1H, C*H$_2$*CC *B*), 2.43 (dd, *J* = 16.5, 9.1 Hz, 1H, C*H$_2$*CC *A*), 1.08 – 0.99 (m, 42H, TIPS *A* and *B*).
^{13}C NMR (101 MHz, Chloroform-*d*) δ 159.3, 159.2, 130.1, 130.0, 129.9, 129.63, 123.8 (q, *J* = 284.6 Hz), 123.4 (q, *J* = 283.2 Hz), 114.1, 114.0, 103.4, 103.2, 92.7 (q, *J* = 33.6 Hz), 91.6 (q, *J* = 33.3 Hz), 83.6, 83.1, 77.3, 75.8, 59.1, 58.7, 56.6, 56.5, 55.4 (2C), 25.1, 24.9, 18.7, 11.3.[22]
IR ν_{max} 2944 (m), 2898 (w), 2866 (m), 2177 (w), 1615 (w), 1516 (m), 1465 (w), 1381 (w), 1295 (m), 1251 (m), 1168 (s), 1106 (w), 1036 (m), 999 (w), 913 (w), 885 (w), 837 (w), 738 (m).
HRMS calcd for $C_{24}F_3H_{37}NO_2Si^+$ $[M+H]^+$ 456.2540; found 456.2530.

2-(Trifluoromethyl)-3-(4-(trifluoromethyl)benzyl)-5-(3-(triisopropylsilyl)prop-2-yn-1-yl)oxazolidine (9ca)

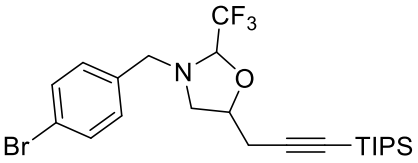


Following General Procedure **A**, the title compound was prepared from N-(4-(trifluoromethyl)benzyl)prop-2-en-1-amine (**4c**) (64.6 mg, 0.300 mmol) and (bromoethynyl)triisopropylsilane (**5a**) (102 mg, 0.390 mmol). The crude oil was purified by column chromatography (SiO_2 15:1 to 9:1 Pentane:CH_2Cl_2) affording the title compound **9ca** (141 mg, 0.286 mmol, 95% yield, 1:1 dr determined by integration in the crude ^{1}H NMR) as a yellow oil.

R$_f$ 0.60 (Pentane/CH_2Cl_2 4/1).
^{1}H NMR (400 MHz, $CDCl_3$) mixture of diastereoisomers 1(*A*):1(*B*) δ 7.65 – 7.56 (m, 4H, Ar*H A + B*), 7.55 – 7.41 (m, 4H, Ar*H A + B*), 4.75 – 4.60 (m, 2H, C*H*CF_3, *A + B*), 4.48 – 4.39 (m, 1H, OC*H B*), 4.36 – 4.26 (m, 1H, OC*H A*), 4.22 (d, *J* = 13.4 Hz, 1H, C*H$_2$*Ph *B*), 4.07 (d, *J* = 13.7 Hz, 1H, C*H$_2$*Ph *A*), 3.88 (d, *J* = 13.7 Hz, 1H, C*H$_2$*Ph *A*), 3.79 (d, *J* = 13.4 Hz, 1H, C*H$_2$*Ph *B*), 3.28 (dd, *J* = 9.2, 5.6 Hz, 1H, C*H$_2$*N *B*), 3.16 – 3.01 (m, 2H, C*H$_2$*N *A*), 2.77 (dd, *J* = 16.6, 4.9 Hz, 1H, C*H$_2$*CC *A*), 2.73 – 2.63 (overlapping signals, 2 m, 2H, C*H$_2$*N *B* + C*H$_2$*CC *B*), 2.59 (dd, *J* = 17.0, 7.1 Hz, 1H, C*H$_2$*CC *B*), 2.48 (dd, *J* = 16.6, 9.1 Hz, 1H, C*H$_2$*CC *A*), 1.11 – 0.92 (m, 42H, TIPS *A* and *B*).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 142.0, 141.9, 130.2 (q, *J* = 32.3 Hz), 130.0 (q, *J* = 32.3 Hz), 128.9, 128.8, 125.6 (2C), 124.3 (q, *J* = 272.1 Hz), 124.2 (q, *J* = 272.1 Hz), 123.7 (q, *J* = 283.9 Hz), 123.4 (q, *J* = 283.2 Hz), 103.2, 102.9, 93.0 (q, *J* = 33.6 Hz), 91.8 (q, *J* = 33.4 Hz), 83.9, 83.4, 77.4, 76.0, 59.2, 58.9, 56.8, 56.7, 25.0, 24.8, 18.7, 18.6, 11.3, 11.2.
IR ν_{max} 3668 (w), 2975 (m), 2904 (m), 2256 (w), 1701 (w), 1457 (w), 1400 (w), 1388 (w), 1327 (w), 1291 (w), 1250 (w), 1236 (w), 1172 (w), 1071 (m), 1062 (m), 1054 (m), 907 (s), 732 (s).
HRMS calcd. for $C_{24}H_{34}F_6NOSi^+$ $[M+H]^+$ 494.2308; found 494.2312.

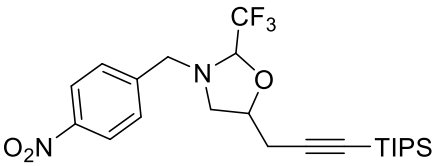
3-(4-Bromobenzyl)-2-(trifluoromethyl)-5-(3-(triisopropylsilyl)prop-2-yn-1-yl)oxazolidine (9da)



Following General Procedure **A**, the title compound was prepared from N-(4-methoxybenzyl)prop-2-en-1-amine (**4d**) (53.2 mg, 0.300 mmol) and (bromoethynyl)triisopropylsilane (**5a**) (102 mg, 0.390 mmol). The crude oil was purified by column chromatography (SiO_2 15:1 to 7:1 Pentane:CH_2Cl_2) affording the title compound **9da** (148 mg, 0.293 mmol, 89% yield, 1:1 dr determined by integration in the crude ^{1}H NMR) as a yellow oil.

R$_f$ 0.50 (Pentane/CH_2Cl_2 4/1).
^{1}H NMR (400 MHz, $CDCl_3$) mixture of diastereoisomers 1(*A*):1(*B*) δ 7.50 – 7.43 (m, 4H, Ar*H A + B*), 7.25 – 7.20 (m, 4H, Ar*H A + B*), 4.69 – 4.60 (m, 2H, C*H*CF_3, *A + B*), 4.46 – 4.37 (m, 1H, OC*H B*), 4.33 – 4.24 (m, 1H, OC*H A*), 4.11 (d, *J* = 13.1 Hz, 1H, C*H*$_2$Ph *B*), 3.95 (d, *J* = 13.4 Hz, 1H, C*H*$_2$Ph *A*), 3.77 (d, *J* = 13.4 Hz, 1H, C*H*$_2$Ph *A*), 3.68 (d, *J* = 13.1 Hz, 1H, C*H*$_2$Ph *B*), 3.27 (dd, *J* = 9.3, 5.6 Hz, 1H, C*H*$_2$N *B*), 3.08 (d, *J* = 6.8 Hz, 2H, C*H*$_2$N *A*), 2.76 (dd, *J* = 16.6, 4.9 Hz, 1H, C*H*$_2$CC *A*), 2.72 – 2.62 (overlapping signals, 2 m, 2H, C*H*$_2$CC *B*, C*H*$_2$N *B*), 2.58 (dd, *J* = 17.0, 7.1 Hz, 1H, C*H*$_2$CC *B*), 2.46 (dd, *J* = 16.6, 9.0 Hz, 1H, C*H*$_2$CC *A*), 1.12 – 0.93 (m, 42H, TIPS *A* and *B*).
^{13}C NMR (101 MHz, Chloroform-*d*) δ 136.9, 136.7, 131.8, 131.7, 130.4, 130.3, 123.7 (q, *J* = 284.5 Hz), 123.3 (d, *J* = 283.3 Hz), 121.7, 121.6, 103.2, 103.0, 92.9 (q, *J* = 33.9 Hz), 91.7 (q, *J* = 33.3 Hz), 83.8, 83.3, 77.3, 75.9, 59.0, 58.7, 56.7, 56.5, 25.0, 24.8, 18.7, 18.6, 11.32, 11.30.
IR ν_{max} 2942 (m), 2894 (w), 2865 (m), 2176 (w), 1487 (w), 1465 (w), 1407 (w), 1381 (w), 1339 (w), 1324 (w), 1292 (m), 1239 (w), 1156 (s), 1154 (s), 1103 (m), 1072 (m), 1015 (m), 924 (w), 883 (m), 859 (w), 835 (w), 806 (w), 741 (w).
HRMS calcd. for $C_{23}H_{34}BrF_3NOSi^+$ $[M+H]^+$ 504.1540; found 504.1544.

3-(4-Nitrobenzyl)-2-(trifluoromethyl)-5-(3-(triisopropylsilyl)prop-2-yn-1-yl)oxazolidine (9ea)



Following General Procedure **A**, the title compound was prepared from N-(4-nitrobenzyl)prop-2-en-1-amine (**4e**) (0.058 g, 0.30 mmol)and (bromoethynyl)triisopropylsilane (**5a**) (102 mg, 0.390 mmol). The crude oil was purified by column chromatography (SiO_2 10:1 to 3:1 Pentane:CH_2Cl_2) affording the title compound **9ea** (96 mg, 0.20 mmol, 68% yield, 1.2:1 dr determined by integration in the crude ^{1}H NMR) as a yellow oil.

R$_f$ 0.35 (Pentane/CH_2Cl_2 3/1).
^{1}H NMR (400 MHz, $CDCl_3$) mixture of diastereoisomers 1.2(*A*):1(*B*) δ 8.24 – 8.16 (m, 4H, Ar*H A + B*), 7.54 (t, *J* = 8.5 Hz, 4H, Ar*H A + B*), 4.73 – 4.62 (m, 2H, C*H*CF_3, *A + B*), 4.50 – 4.41 (m,

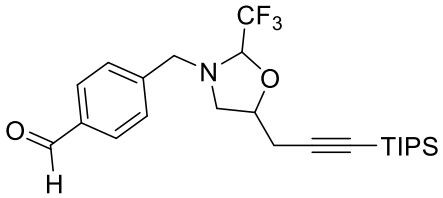
1H, OC*H A*), 4.38 – 4.29 (m, 1H, OC*H B*), 4.25 (d, *J* = 14.0 Hz, 1H, C*H*$_2$Ph *A*), 4.11 (d, *J* = 14.2 Hz, 1H, C*H*$_2$Ph *B*), 3.94 (d, *J* = 14.2 Hz, 1H, C*H*$_2$Ph *B*), 3.87 (d, *J* = 14.0 Hz, 1H, C*H*$_2$Ph *A*), 3.31 (dd, *J* = 9.2, 5.7 Hz, 1H, C*H*$_2$N *A*), 3.13 (m, 1H, C*H*$_2$N *B*), 3.05 (m, 1H, C*H*$_2$N *B*), 2.77 (dd, *J* = 16.6, 4.9 Hz, 1H, C*H*$_2$CC *B*), 2.74 – 2.64 (m, 2H, C*H*$_2$CC *A* and C*H*$_2$N *A*), 2.61 (dd, *J* = 17.0, 7.0 Hz, 1H, C*H*$_2$CC *A*), 2.49 (dd, *J* = 16.6, 9.0 Hz, 1H, C*H*$_2$CC *B*), 1.03 (m, 42H, TIPS *A*), 1.00 (m, 21H, TIPS *B*).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 147.7, 147.6, 145.6, 145.6, 129.2, 129.1, 123.9 (2C), 123.6 (q, *J* = 284.7 Hz), 123.2 (q, *J* = 283.2 Hz), 103.0, 102.8, 93.1 (q, *J* = 34.0 Hz), 91.9 (q, *J* = 33.5 Hz), 83.9, 83.4, 77.5, 76.0, 59.0, 58.8, 56.9, 56.7, 24.9, 24.8, 18.7, 11.3.[22]

IR ν_{max} 2944 (m), 2894 (w), 2865 (m), 2177 (w), 1606 (w), 1525 (s), 1465 (w), 1347 (s), 1292 (m), 1151 (s), 1108 (m), 1058 (w), 1020 (w), 997 (w), 924 (w), 883 (m), 854 (m), 736 (w), 735 (w).

HRMS calcd. for $C_{23}H_{34}F_3N_2O_3Si^+$ $[M+H]^+$ 471.2285; found 471.2281.

4-((2-(Trifluoromethyl)-5-(3-(triisopropylsilyl)prop-2-yn-1-yl)oxazolidin-3-yl)methyl)benzaldehyde (9fa)



Following General Procedure **A**, the title compound was prepared from freshly purified 4-((allylamino)methyl)benzaldehyde (**4f**) (52.6 mg, 0.300 mmol) and (bromoethynyl)triisopropylsilane (**5a**) (102 mg, 0.390 mmol). The crude oil was purified by column chromatography (SiO_2 6:1 to 3:1 Pentane:CH_2Cl_2) affording the title compound **9fa** (118 mg, 0.260 mmol, 87% yield, 1:1 dr determined by integration in the crude ^{1}H NMR) as a yellow oil.

R$_f$ 0.40 (Pentane/CH_2Cl_2 4/1).

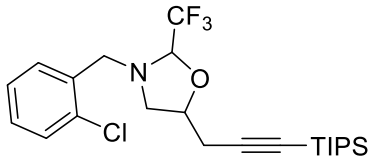
^{1}H NMR (400 MHz, $CDCl_3$) mixture of diastereoisomers 1 (*A*):1(*B*) δ 10.00 (s, 2H, *CHO A* + *B*), 7.93 – 7.76 (m, 4H, Ar*H A* + *B*), 7.53 (dd, *J* = 8.1, 6.6 Hz, 4H, Ar*H A* + *B*), 4.72 – 4.63 (m, 2H, C*H*CF_3, *A* + *B*), 4.48 – 4.39 (m, 1H, OC*H B*), 4.35 – 4.26 (m, 1H, OC*H A*), 4.24 (d, *J* = 13.6 Hz, 1H, C*H*$_2$Ph *B*), 4.08 (d, *J* = 13.9 Hz, 1H, C*H*$_2$Ph *A*), 3.91 (d, *J* = 13.9 Hz, 1H, C*H*$_2$Ph *A*), 3.82 (d, *J* = 13.6 Hz, 1H, C*H*$_2$Ph *B*), 3.30 (dd, *J* = 9.2, 5.6 Hz, 1H, C*H*$_2$N *B*), 3.15 – 3.03 (m, 2H, C*H*$_2$N *A*), 2.81 – 2.63 (overlapping signals, 3 m, 3H, C*H*$_2$CC *A*, C*H*$_2$N *B* and C*H*$_2$CC *B*), 2.59 (dd, *J* = 17.0, 7.0 Hz, 1H, C*H*$_2$CC *B*), 2.47 (dd, *J* = 16.6, 9.0 Hz, 1H, C*H*$_2$CC *A*), 1.10 – 0.91 (m, 42H, TIPS *A* and *B*).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 192.0, 191.9, 145.0, 144.8, 136.0, 135.9, 130.1 (2C), 129.1, 129.0, 123.8 (q, *J* = 284.6 Hz), 123.4 (q, *J* = 283.2 Hz), 103.1, 102.8, 93.0 (q, *J* = 33.8 Hz), 91.8 (q, *J* = 33.4 Hz), 83.8, 83.3, 77.4, 75.9, 59.4, 59.1, 56.8, 56.7, 24.9, 24.8, 18.7, 18.6, 11.3, 11.2.

IR ν_{max} 2944 (m), 2893 (w), 2865 (m), 2734 (w), 2256 (w), 2176 (w), 1703 (m), 1609 (w), 1581 (w), 1465 (w), 1428 (w), 1384 (w), 1293 (m), 1239 (w), 1207 (m), 1166 (s), 1057 (w), 1020 (w), 997 (w), 912 (m), 884 (m), 851 (w), 828 (w), 783 (w), 735 (s).

HRMS calcd. for $C_{24}H_{35}F_3NO_2Si^+$ $[M+H]^+$ 454.2384; found 454.2384.

3-(2-chlorobenzyl)-2-(trifluoromethyl)-5-(3-(triisopropylsilyl)prop-2-yn-1-yl)oxazolidine (9ga)

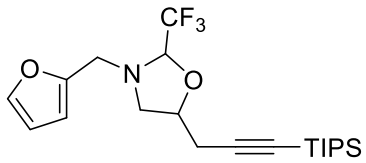


Following General Procedure **A**, the title compound was prepared from N-(2-chlorobenzyl)prop-2-en-1-amine (**4g**) (54.5 mg, 0.300 mmol) and (bromoethynyl)triisopropylsilane (**5a**) (102 mg, 0.390 mmol). The crude oil was purified by column

chromatography (SiO_2 15:1 to 10:1 Pentane:CH_2Cl_2) affording the title compound **9ga** (120 mg, 0.261 mmol, 87% yield, 1.3:1 dr determined by integration in the crude ^{1}H NMR) as a yellow oil.

R_f 0.60 (Pentane/CH_2Cl_2 4/1).
^{1}H NMR (400 MHz, $CDCl_3$) mixture of diastereoisomers 1.3(*A*):1(*B*) δ 7.59 – 7.50 (m, 2H, Ar*H A* + *B*), 7.40 – 7.34 (m, 2H, Ar*H A* + *B*), 7.32 – 7.19 (m, 4H, Ar*H A* + *B*), 4.78 – 4.70 (m, 2H, C*H*CF_3, *A* + *B*), 4.49 – 4.41 (m, 1H, OC*H B*), 4.38 – 4.28 (m, 1H, OC*H A*), 4.17 (d, *J* = 14.1 Hz, 1H, C*H*$_2$Ph *B*), 4.08 – 4.02 (overlapping signals, m, 3H, C*H*$_2$Ph *A* + C*H*$_2$Ph*B*), 3.37 (dd, *J* = 9.2, 5.6 Hz, 1H, C*H*$_2$N *B*), 3.19 – 3.06 (m, 2H, C*H*$_2$N *A*), 2.85 – 2.75 (overlapping signals, 2 m, 2H, C*H*$_2$CC *A*, C*H*$_2$N *B*), 2.69 (dd, *J* = 16.9, 4.5 Hz, 1H, C*H*$_2$CC *B*), 2.60 (dd, *J* = 16.9, 7.3 Hz, 1H, C*H*$_2$CC *B*), 2.49 (dd, *J* = 16.6, 9.0 Hz, 1H, C*H*$_2$CC *A*), 1.13 – 0.94 (m, 42H, TIPS *A* and *B*).
^{13}C NMR (101 MHz, Chloroform-*d*) δ 135.5, 135.4, 133.9, 133.8, 130.6, 130.5, 129.7, 129.6, 128.9, 128.8, 127.1, 127.0, 123.8 (q, *J* = 284.6 Hz), 123.5 (q, *J* = 283.2 Hz), 103.3, 103.0, 93.4 (q, *J* = 33.8 Hz), 92.0 (q, *J* = 33.4 Hz), 83.7, 83.2, 77.4, 75.9, 56.8 (2C), 56.6, 56.1, 25.0, 24.9, 18.7, 11.3.[22]
IR ν_{max} 3069 (w), 2944 (m), 2894 (w), 2866 (m), 2177 (w), 1466 (m), 1382 (w), 1336 (w), 1324 (w), 1292 (m), 1240 (w), 1151 (s), 1035 (m), 997 (w), 924 (w), 883 (m), 858 (w), 752 (m).
HRMS calcd for $C_{23}H_{34}ClF_3NOSi^+$ $[M+H]^+$ 460.2045; found 460.2048.

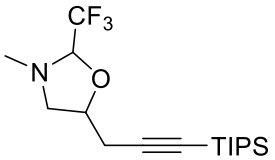
3-(Furan-2-ylmethyl)-2-(trifluoromethyl)-5-(3-(triisopropylsilyl)prop-2-yn-1-yl)oxazolidine (9ha)



Following General Procedure **A**, the title compound was prepared from N-(furan-2-ylmethyl)prop-2-en-1-amine (**4h**) (41 mg, 0.30 mmol) and (bromoethynyl)triisopropylsilane (**5a**) (102 mg, 0.390 mmol). The crude oil was purified by column chromatography (SiO_2 20:1 to 7:1 Pentane:CH_2Cl_2) affording the title compound **9ha** (115 mg, 0.282 mmol, 92% yield, 1:1 dr determined by integration of the CF_3C*H* protons in the crude ^{1}H NMR) as a yellow oil.

R_f 0.45 (Pentane/ CH_2Cl_2 5/1).
^{1}H NMR (400 MHz, $CDCl_3$) mixture of diastereoisomers 1(*A*):1(*B*) δ 7.40 (dd, *J* = 2.0, 0.8 Hz, 2H, HetAr*H A* + *B*), 6.36 – 6.32 (m, 2H, HetAr*H A* + *B*), 6.28 – 6.24 (m, 2H, HetAr*H A* + *B*), 4.80 (q, *J* = 5.2 Hz, 1H, C*H*CF_3 *A*), 4.73 (q, *J* = 5.0 Hz, 1H, C*H*CF_3 *B*), 4.45 – 4.37 (m, 1H, OC*H B*), 4.02 (d, *J* = 14.6 Hz, 1H, C*H*$_2$Ph*B*), 3.96 (d, *J* = 14.9 Hz, 1H, C*H*$_2$Ph *A*), 3.92 – 3.82 (overlapping signals, 3m, 3H, C*H*$_2$Ph *A* + C*H*$_2$Ph*B* and OC*H A*), 3.43 (dd, *J* = 9.3, 5.7 Hz, 1H, C*H*$_2$N *B*), 3.31 (ddd, *J* = 11.8, 5.8, 1.2 Hz, 1H, C*H*$_2$N *A*), 3.12 (ddd, *J* = 11.8, 8.4, 1.3 Hz, 1H, C*H*$_2$N *A*), 2.87 (m, 1H, C*H*$_2$N *B*), 2.71 (dd, *J* = 16.6, 4.7 Hz, 1H, C*H*$_2$CC *A* + *B*), 2.65 (overlapping signals, 2 m, 2H, C*H*$_2$CC *A* + *B*), 2.43 – 2.34 (overlapping signals, 2 m, 2H, C*H*$_2$CC *A* + *B*), 1.10 – 0.97 (m, 42H, TIPS *A* + *B*).
^{13}C NMR (101 MHz, Chloroform-*d*) δ 151.0, 150.9, 143.0, 142.9, 123.8 (q, *J* = 284.4 Hz), 123.4 (q, *J* = 282.9 Hz), 110.6, 110.4, 109.5, 109.3, 103.3, 103.1, 92.3 (q, *J* = 33.9 Hz), 90.7 (q, *J* = 33.5 Hz), 83.5, 83.1, 77.4, 76.3, 56.5, 56.3, 51.2, 50.1, 25.0, 24.8, 18.7, 11.3.[22]
IR ν_{max} 2944 (m), 2895 (w), 2866 (m), 2177 (w), 1504 (w), 1465 (w), 1386 (w), 1324 (w), 1293 (m), 1150 (s), 1077 (w), 1016 (m), 916 (w), 884 (m), 857 (w), 737 (s).
HRMS calcd for $C_{21}H_{33}F_3NO_2Si^+$ $[M+H]^+$ 416.2227; found 416.2229.

3-Methyl-2-(trifluoromethyl)-5-(3-(triisopropylsilyl)prop-2-yn-1-yl)oxazolidine (9ia)



Following General Procedure **A**, the title compound was prepared from N-methylprop-2-en-1-amine (**4i**) (21.3 mg, 0.300 mmol) and (bromoethynyl)triisopropylsilane (**5a**) (102 mg, 0.390 mmol). The crude oil (2:1 dr determined by integration of the NC*H*$_2$ protons in the crude ^{1}H NMR) was purified by column chromatography (SiO_2 10:1 to 3:1 Pentane:CH_2Cl_2) affording the title compound **9ia** (78 mg, 0.22 mmol, 74% yield, 1.9:1 dr determined by integration of the NC*H*$_2$ protons in the ^{1}H NMR) as a yellow oil.

R$_f$ 0.20 (Pentane/CH_2Cl_2 4/1).

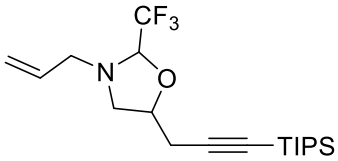
^{1}H NMR (400 MHz, Chloroform-*d*) mixture of diastereoisomers 1.9(*A*):1(*B*) δ 4.48 – 4.24 (m, 4H, C*H*CF$_3$ and OC*H A* + *B*), 3.46 (dd, *J* = 8.8, 5.1 Hz, 2H, C*H*$_2$N *A*), 3.20 (dd, *J* = 11.1, 6.1 Hz, 1H, C*H*$_2$N *B*), 2.97 (dd, *J* = 11.1, 6.0 Hz, 1H, C*H*$_2$N *B*), 2.76 – 2.63 (overlapping signals, 3 m, 3H, C*H*$_2$N *A* and C*H*$_2$CC *A* + *B*), 2.61 – 2.47 (overlapping signals, 4 m, 8H, C*H*$_2$CC *A* + *B* and C*H*$_3$ *A* + *B*), 1.15 – 0.93 (m, 42H, TIPS *A* and *B*).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 123.8 (d, *J* = 283.9 Hz), 123.3 (d, *J* = 282.9 Hz), 103.5, 102.9, 94.3 (q, *J* = 33.6 Hz), 93.0 (q, *J* = 33.2 Hz), 83.7, 83.0, 77.4, 76.1, 59.5, 58.9, 42.4, 41.3, 25.3, 24.5, 18.7, 18.7, 11.3.[22]

IR ν_{max} 2944 (w), 2894 (w), 2893 (w), 2866 (w), 2815 (w), 2814 (w), 2177 (w), 1464 (w), 1295 (w), 1249 (w), 1224 (w), 1154 (s), 1097 (w), 1070 (w), 1028 (w), 1000 (w), 911 (m), 884 (w), 855 (w), 735 (s).

HRMS calcd. for $C_{17}H_{31}F_3NOSi^+$ $[M+H]^+$ 350.2122; found 350.2115.

3-Allyl-2-(trifluoromethyl)-5-(3-(triisopropylsilyl)prop-2-yn-1-yl)oxazolidine (9ja)



Following General Procedure **A**, the title compound was prepared from diallylamine (**4j**) (37.3 µl, 0.300 mmol) and (bromoethynyl)triisopropylsilane (**5a**) (102 mg, 0.390 mmol). The crude oil was purified by column chromatography (SiO_2 15:1 to 8:1 Pentane:CH_2Cl_2) affording the title compound **9ja** (109 mg, 0.290 mmol, 97 % yield, 1:1 dr determined by integration in the crude ^{1}H NMR) as a yellow oil.

R$_f$ 0.40 (Pentane/ CH_2Cl_2 4/1).

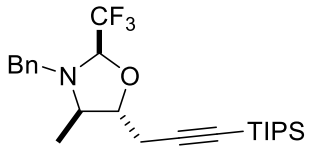
^{1}H NMR (400 MHz, $CDCl_3$) mixture of diastereoisomers 1(*A*):1(*B*) δ 5.95 – 5.79 (m, 2H, CH_2=C*H A* + *B*), 5.28 – 5.14 (m, 4H, C*H*$_2$=CH *A* + *B*), 4.64 (q, *J* = 5.5 Hz, 1H, C*H*CF$_3$ *A*), 4.58 (q, *J* = 5.1 Hz, 1H, C*H*CF$_3$ *B*), 4.46 – 4.36 (m, 1H, OC*H A*), 4.29 – 4.18 (m, 1H, OC*H B*), 3.59 – 3.51 (m, 1H, C*H*$_2$CH=CH$_2$ *B*), 3.48 – 3.24 (m, 4H, C*H*$_2$N *B* and C*H*$_2$CH=CH$_2$ *A* + *B*), 3.22 – 3.14 (m, 1H, C*H*$_2$N *A*), 3.14 – 3.05 (m, 1H, C*H*$_2$N *A*), 2.81 – 2.72 (m, 2H, C*H*$_2$N *B* and C*H*$_2$CC *A*), 2.69 (dd, *J* = 16.9, 4.4 Hz, 1H, C*H*$_2$CC *B*), 2.56 (dd, *J* = 16.9, 7.6 Hz, 1H, C*H*$_2$CC *B*), 2.43 (dd, *J* = 16.5, 9.1 Hz, 1H, C*H*$_2$CC *A*), 1.13 – 0.93 (m, 42H, TIPS *A* and *B*).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 134.5, 134.4, 123.8 (q, *J* = 284.5 Hz), 123.4 (q, *J* = 282.9 Hz), 119.0, 118.5, 103.3, 103.1, 92.7 (q, *J* = 33.7 Hz), 91.3 (q, *J* = 33.2 Hz), 83.6, 83.2, 77.4, 75.9, 58.9, 58.2, 56.8, 56.6, 25.0 (2C), 18.7, 18.7, 11.3.[22]

IR ν_{max} 2944 (m), 2896 (w), 2866 (m), 2177 (w), 1604 (w), 1526 (w), 1465 (w), 1346 (m), 1292 (m), 1167 (s), 1150 (s), 1108 (m), 1058 (w), 1022 (m), 996 (m), 926 (w), 883 (m), 853 (m), 737 (w).

HRMS calcd. for $C_{19}H_{33}F_3NOSi^+$ $[M+H]^+$ 376.2278; found 376.2270.

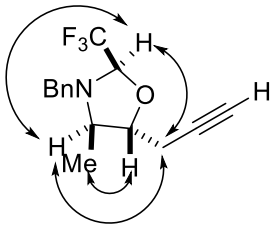
3-Benzyl-4-methyl-2-(trifluoromethyl)-5-(3-(triisopropylsilyl)prop-2-yn-1-yl)oxazolidine (9ka)



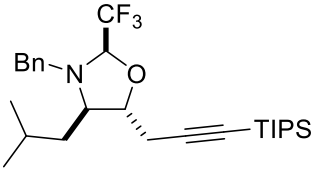
Following General Procedure **B**, the title compound was prepared from N-benzylbut-3-en-2-amine (**4ka**) (48.4 mg, 0.300 mmol) and (bromoethynyl)triisopropylsilane (**5a**) (102 mg, 0.390 mmol, 1.3 eq). The crude oil (18.9:1.3:1 dr determined by integration in the crude ^{19}F NMR) was purified by column chromatography (SiO_2 15:1 to 7:1 Pentane:CH_2Cl_2) affording the title compound **9ka** (107 mg, 0.243 mmol, 81 % yield, 21.8:1.1:1 dr determined by integration in the ^{19}F NMR) as a yellow oil.

R$_f$ 0.50 (Pentane/ CH_2Cl_2 4/1).
^{1}H NMR (400 MHz, $CDCl_3$) major diastereoisomer δ 7.42 – 7.26 (m, 5H, Ar*H*), 4.69 (q, *J* = 5.0 Hz, 1H, C*H*CF$_3$), 4.08 (d, *J* = 13.9 Hz, 1H, C*H*$_2$Ph), 3.97 – 3.87 (m, 2H, OC*H* and C*H*$_2$Ph), 3.13 – 3.02 (m, 1H, NC*H*), 2.62 (d, *J* = 5.3 Hz, 2H, C*H*$_2$CC), 1.14 – 0.96 (m, 24H, TIPS and Me).
^{13}C NMR (101 MHz, $CDCl_3$) major diastereoisomer δ 137.9, 129.0, 128.5, 127.6, 123.8 (d, *J* = 284.7 Hz), 103.1, 91.5 (q, *J* = 33.3 Hz), 83.7, 83.4, 64.3, 58.4, 23.8, 18.8, 18.1, 11.4.
IR ν_{max} 3032 (w), 2942 (m), 2897 (w), 2866 (m), 2177 (w), 1462 (w), 1383 (w), 1320 (w), 1292 (m), 1149 (s), 1085 (w), 1020 (w), 994 (w), 883 (w), 858 (w), 732 (w).
HRMS calcd for $C_{24}H_{37}F_3NOSi^+$ $[M+H]^+$ 440.2591; found 440.2599.

Stereochemistry assigned by ROESY on compound **13**.



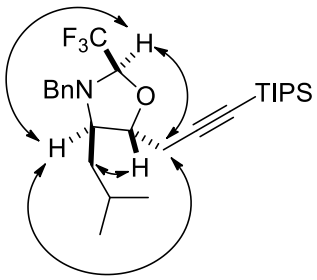
3-Benzyl-4-isobutyl-2-(trifluoromethyl)-5-(3-(triisopropylsilyl)prop-2-yn-1-yl)oxazolidine (9la)



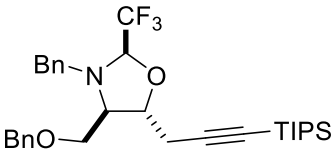
Following General Procedure **B**, the title compound was prepared from N-benzyl-5-methylhex-1-en-3-amine (**4l**) (61.0 mg, 0.300 mmol) and (bromoethynyl)triisopropylsilane (**5a**) (102 mg, 0.390 mmol, 1.3 eq). The crude oil (>20:1 dr determined by integration in ^{19}F NMR) was purified by column chromatography (SiO_2 15:1 to 7:1 Pentane:CH_2Cl_2) affording the title compound **9la** (103 mg, 0.214 mmol, 71% yield, >20:1 dr determined by integration in ^{19}F NMR) as a yellow oil.

R$_f$ 0.60 (Pentane/CH_2Cl_2 6/1).
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.37 – 7.27 (m, 5H, Ar*H*), 4.72 (q, *J* = 5.5 Hz, 1H, C*H*CF$_3$), 4.08 – 3.96 (overlapping signals, 3H, C*H*$_2$Ph and OC*H*), 3.30 (app q, *J* = 6.6 Hz, 1H, NC*H*), 2.65 (dd, *J* = 17.2, 6.2 Hz, 1H, CCC*H*$_2$), 2.59 (dd, *J* = 17.2, 4.3 Hz, 1H, CCC*H*$_2$), 1.69 – 1.57 (m, 1H, (CH$_3$)$_2$C*H*), 1.45 – 1.29 (m, 2H, (CH$_3$)$_2$CHC*H*$_2$), 1.16 – 1.04 (m, 21H, TIPS), 0.83 (app t, *J* = 6.1 Hz, 6H, C*H*$_3$).
^{13}C NMR (101 MHz, $CDCl_3$) δ 138.2, 129.3, 128.5, 127.8, 123.5 (q, *J* = 284.9 Hz), 103.5, 92.5 (q, *J* = 33.6 Hz), 83.6, 83.0, 66.3, 60.8, 44.1, 25.3, 25.1, 23.0, 22.9, 18.8, 11.4.
IR ν_{max} 3032 (w), 2952 (m), 2900 (w), 2867 (w), 2176 (w), 1464 (w), 1386 (w), 1370 (w), 1291 (w), 1170 (s), 1149 (s), 1082 (w), 1020 (w), 992 (w), 910 (m), 884 (w), 859 (w), 735 (s).
HRMS calcd for $C_{27}H_{43}F_3NOSi^+$ $[M+H]^+$ 482.3061; found 482.3061.

Stereochemistry assigned by ROESY.



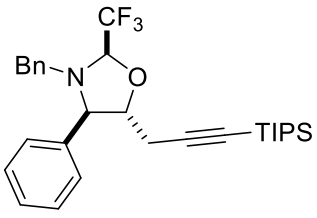
3-Benzyl-4-((benzyloxy)methyl)-2-(trifluoromethyl)-5-(3-(triisopropylsilyl)prop-2-yn-1-yl)oxazolidine (9ma)



Following General Procedure **B** with cinnamyl(cyclopenta-2,4-dien-1-yl)palladium (**6**) (6.9 mg, 0.024 mmol, 8 mol %), tri(2-furyl)phosphine (**7e**) (17 mg, 0.072 mmol, 24 mol%), the title compound was prepared from N-benzyl-1-(benzyloxy)but-3-en-2-amine (**4m**) (80.0 mg, 0.300 mmol). and (bromoethynyl)triisopropylsilane (**5a**) (102 mg, 0.390 mmol, 1.3 eq). The crude oil (29.4:1.5:1 dr determined by integration in the crude ^{19}F NMR) was purified by column chromatography (SiO_2 10:1 Pentane:CH_2Cl_2) affording the title compound **9ma** (102 mg, 0.187 mmol, 62% yield, 35.6:1.3:1 dr determined by integration in ^{19}F NMR) as a yellow oil.

R$_f$ 0.35 (Pentane/CH_2Cl_2 4/1).
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.34 – 7.24 (m, 8H, Ar*H*), 7.23 – 7.19 (m, 2H, Ar*H*), 4.78 (q, *J* = 5.1 Hz, 1H, C*H*CF$_3$), 4.35 (s, 2H, OC*H*$_2$Ph), 4.26 – 4.20 (m, 1H, OC*H*), 4.09 (d, *J* = 13.4 Hz, 1H, NC*H*$_2$Ph), 4.01 (d, *J* = 13.4 Hz, 1H, NC*H*$_2$Ph), 3.42 – 3.32 (overlapping signals, 2 m, 2H, NC*H* and BnOC*H*$_2$), 3.27 – 3.19 (m, 1H, BnOC*H*$_2$), 2.77 (dd, *J* = 17.3, 5.1 Hz, 1H, CCC*H*$_2$), 2.63 (dd, *J* = 17.3, 4.3 Hz, 1H, CCC*H*$_2$), 1.18 – 1.03 (m, 21H, TIPS).
^{13}C NMR (101 MHz, $CDCl_3$) major diastereoisomer only δ 138.2, 138.1, 129.1, 128.6, 128.5, 127.8, 127.7, 127.5, 123.6 (q, *J* = 284.8 Hz), 103.9, 92.5 (q, *J* = 33.4 Hz), 83.4, 81.8, 73.3, 72.4, 66.8, 60.0, 25.2, 18.8, 11.5.
IR ν_{max} 3033 (w), 2943 (m), 2899 (w), 2865 (m), 2817 (w), 2175 (w), 1730 (w), 1669 (w), 1496 (w), 1460 (w1374 (w), 1290 (m), 1261 (w), 1253 (w), 1170 (s), 1145 (s), 1082 (m), 1020 (w), 913 (w), 885 (w), 861 (w), 853 (w), 843 (w), 736 (m).
HRMS calcd for $C_{31}H_{43}F_3NO_2Si^+$ $[M+H]^+$ 546.3010; found 546.3031.
Stereochemistry assigned by analogy.

3-Benzyl-4-phenyl-2-(trifluoromethyl)-5-(3-(triisopropylsilyl)prop-2-yn-1-yl)oxazolidine (9na)



Following General Procedure **B** with cinnamyl(cyclopenta-2,4-dien-1-yl)palladium (**6**) (6.9 mg, 0.024 mmol, 8 mol %), tri(2-furyl)phosphine (7**e**) (17 mg, 0.072 mmol, 24 mol%), the title compound was prepared from N-benzyl-1-phenylprop-2-en-1-amine (**4n**) (67.0 mg, 0.300 mmol) and (bromoethynyl)triisopropylsilane (**5a**) (102 mg, 0.390 mmol, 1.3 eq). The crude oil (11.4:1.2:1 dr determined by integration in the crude ^{1}H NMR) was purified by column chromatography (SiO_2 15:1 to 10:1 Pentane:CH_2Cl_2) affording the title compound **9na** (136 mg, 0.271 mmol, 90% yield, 12.5:1.3:1 dr determined by integration in the ^{1}H NMR) as a yellow oil.

R_f 0.50 (Pentane/CH_2Cl_2 5/1).

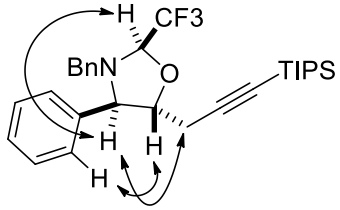
^{1}H NMR (400 MHz, $CDCl_3$) major diastereoisomer δ 7.42 – 7.37 (m, 2H, Ar*H*), 7.36 – 7.15 (m, 6H, Ar*H*), 7.13 – 7.07 (m, 2H, Ar*H*), 4.85 (q, *J* = 4.8 Hz, 1H, C*H*CF_3), 4.15 – 4.05 (overlapping signals, 2 m, 2H, OC*H* and NC*H*), 3.95 (d, *J* = 13.9 Hz, 1H, CH_2Ph), 3.90 (d, *J* = 13.9 Hz, 1H, CH_2Ph), 2.69 (dd, *J* = 17.7, 3.7 Hz, 1H, CH_2CC), 2.40 (dd, *J* = 17.7, 3.9 Hz, 1H, CH_2CC), 1.12 – 0.95 (m, 21H, TIPS).

^{13}C NMR (101 MHz, $CDCl_3$) δ 137.3, 135.7, 129.8, 128.8, 128.3, 128.3, 128.0, 127.6, 124.1 (d, *J* = 285.3 Hz), 103.0, 89.8 (q, *J* = 33.4 Hz), 83.9, 83.7, 70.7, 56.1, 21.9, 18.8, 11.4.

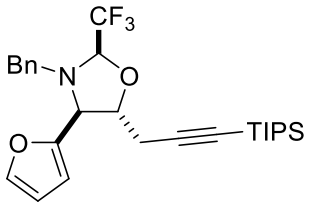
IR ν_{max} 2936 (m), 2863 (m), 2175 (w), 1462 (w), 1291 (w), 1152 (s), 915 (m), 821 (w), 746 (s).

HRMS calcd for $C_{29}H_{39}F_3NOSi^+$ $[M+H]^+$ 502.2748; found 502.2750.

Stereochemistry assigned by ROESY.



3-Benzyl-4-(furan-2-yl)-2-(trifluoromethyl)-5-(3-(triisopropylsilyl)prop-2-yn-1-yl)oxazolidine (9oa)



Following General Procedure **B** with cinnamyl(cyclopenta-2,4-dien-1-yl)palladium (**6**) (6.9 mg, 0.024 mmol, 8 mol %), tri(2-furyl)phosphine (**7e**) (17 mg, 0.072 mmol, 24 mol%), the title compound was prepared from N-benzyl-1-(furan-2-yl)prop-2-en-1-amine (**4o**) (0.064 g, 0.30 mmol) and (bromoethynyl)triisopropylsilane (**5a**) (102 mg, 0.390 mmol, 1.3 eq). The crude oil (9.0:4:1:1 dr determined by integration in the crude ^{1}H NMR) was purified by column chromatography (SiO_2 :1 Pentane:CH_2Cl_2) affording the title compound **9oa** (0.119 g, 0.242 mmol, 81% yield, 8.4:4:2:1 dr determined by integration in the ^{1}H NMR) as a yellow oil.

R_f 0.55 (Pentane/CH_2Cl_2 4/1).

^{1}H NMR (400 MHz, $CDCl_3$) for the two main diastereoisomers 2(*A*):1(*B*) δ 7.48 (d, *J* = 1.8 Hz, 1H, HetAr*H B*), 7.36 – 7.13 (m, 11H, Ar*H A* + *B*), 6.38 – 6.35 (m, 1H, HetAr*H B*), 6.21 (m, 1H, HetAr*H*, *A*), 6.17 (m, 1H, HetAr*H*, *A*), 6.12 – 6.10 (m, 1H, HetAr*H B*), 4.99 (q, *J* = 4.3 Hz, 1H, C*H*CF_3 *B*), 4.79 (q, *J* = 4.9 Hz, 1H, C*H*CF_3 *A*), 4.64 (m, 1H, OC*H B*), 4.45 – 4.37 (m, 1H, OC*H A*), 4.29 (d, *J* = 4.5 Hz, 1H, NC*H B*), 4.20 (d, *J* = 8.6 Hz, 1H, NC*H A*), 4.03 (d, *J* = 13.9 Hz, 1H, CH_2Ph *A*), 4.02 (d, *J* = 13.7 Hz, 1H, CH_2Ph *B*), 3.97 (d, *J* = 13.9 Hz, 1H, CH_2Ph *A*), 3.39 (d, *J* = 13.7 Hz, 1H, CH_2Ph *B*), 2.73 (dd, *J* = 17.5, 4.5 Hz, 1H, CH_2CC *A*), 2.50 (overlapping signals, 2 m, 2H, CH_2CC *A* + *B*), 2.00 (dd, *J* = 16.6, 9.0 Hz, 1H, CH_2CC *B*), 1.13 – 1.02 (m, 21H, TIPS *A*), 1.02 – 0.92 (m, 21H, TIPS *B*).

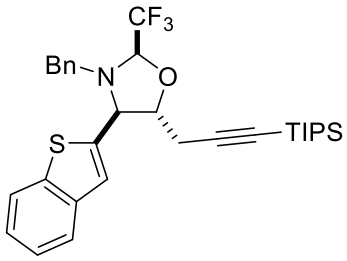
^{13}C NMR (101 MHz, $CDCl_3$) for the two main diastereoisomers δ 150.8, 150.4, 143.2, 142.7, 137.9, 136.4, 129.2 (2C), 128.4, 128.4, 127.6, 127.4, 124.1 (q, *J* = 285.0 Hz), 123.8 (q, *J* = 284.8 Hz), 112.2, 110.4, 110.2, 108.8, 103.0, 102.7, 90.5 (q, *J* = 33.9 Hz), 89.9 (q, *J* = 33.3 Hz), 83.9, 83.1, 80.8, 80.5, 65.0, 59.9, 57.3, 52.0, 23.0, 21.8, 18.6, 11.3.

IR ν_{max} 2943 (w), 2890 (w), 2865 (m), 2178 (w), 1713 (w), 1463 (w), 1291 (m), 1151 (s), 1013 (w), 911 (m), 884 (w), 854 (w), 735 (s).

HRMS calcd for $C_{27}H_{37}F_3NO_2Si^+$ $[M+H]^+$ 492.2540; found 492.2531.

Stereochemistry assigned by analogy.

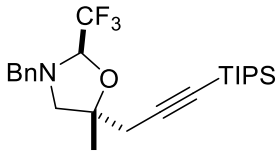
4-(Benzo[b]thiophen-2-yl)-3-benzyl-2-(trifluoromethyl)-5-(3-(triisopropylsilyl)prop-2-yn-1-yl)oxazolidine (9pa)



Following General Procedure **B** with cinnamyl(cyclopenta-2,4-dien-1-yl)palladium (**6**) (6.9 mg, 0.024 mmol, 8 mol %) and tri(2-furyl)phosphine (7e) (17.0 mg, 0.072 mmol, 24 mol%), the title compound was prepared from 1-(benzo[b]thiophen-2-yl)-N-benzylprop-2-en-1-amine (**4p**) (84 mg, 0.30 mmol) and (bromoethynyl)triisopropylsilane (102 mg, 0.390 mmol, 1.3 eq). The crude oil (4:1 dr determined by integration in the crude ^{19}F NMR) was purified by column chromatography (SiO_2 14:1 Pentane:CH_2Cl_2) affording the title compound **9pa** (121 mg, 0.217 mmol, 72% yield, 12:1 dr determined by integration in the ^{19}F NMR) as a yellow oil.

R$_f$ 0.55 (Pentane/CH_2Cl_2 6/1).
^{1}H NMR (400 MHz, $CDCl_3$) major diastereoisomer δ 7.85 – 7.79 (m, 1H, HetAr*H*), 7.73 – 7.68 (m, 1H, HetAr*H*), 7.38 – 7.20 (m, 8H, Ar*H*), 4.85 (q, *J* = 4.7 Hz, 1H, C*H*CF_3), 4.50 (d, *J* = 8.6 Hz, 1H, C*H*N), 4.34 – 4.28 (m, 1H, OC*H*), 4.10 (d, *J* = 14.1 Hz, 1H, C*H*$_2$Ph), 3.98 (d, *J* = 14.1 Hz, 1H, C*H*$_2$Ph), 2.76 (dd, *J* = 17.7, 4.4 Hz, 1H, C*H*$_2$CC), 2.56 (dd, *J* = 17.7, 4.2 Hz, 1H, C*H*$_2$CC), 1.11 – 0.97 (m, 21H, TIPS).
^{13}C NMR (101 MHz, $CDCl_3$) major diastereoisomer δ 143.1, 140.0, 139.7, 135.3, 129.9, 128.5, 127.9, 124.5, 124.4, 123.8 (q, *J* = 285.3 Hz), 123.4, 123.1, 122.7, 102.3, 89.4 (q, *J* = 33.9 Hz), 84.2, 82.8, 66.7, 55.7, 22.3, 18.8, 11.3.
IR ν_{max} 3064 (w), 3033 (w), 2944 (m), 2894 (w), 2866 (m), 2178 (w), 1727 (w), 1658 (w), 1601 (w), 1497 (w), 1463 (w), 1380 (w), 1350 (w), 1293 (m), 1247 (w), 1153 (s), 1078 (w), 1025 (w), 1004 (w), 974 (w), 913 (w), 885 (w), 854 (w), 746 (m).
HRMS calcd for $C_{31}F_3H_{39}NOSSi^+$ $[M+H]^+$ 558.2468; found 558.2460.
Stereochemistry assigned by analogy.

3-Benzyl-5-methyl-2-(trifluoromethyl)-5-(3-(triisopropylsilyl)prop-2-yn-1-yl)oxazolidine (9qa)

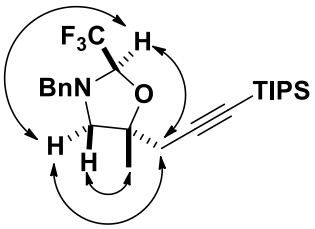


Following General Procedure **C**, the title compound was prepared from N-benzyl-2-methylprop-2-en-1-amine (**4q**) (48.4 mg, 0.300 mmol) and (bromoethynyl)triisopropylsilane (**5a**) (102 mg, 0.390 mmol). The crude oil (>20:1 dr determined by integration in the crude ^{1}H NMR) was purified by column chromatography (SiO_2 15:1 to 7:1 Pentane:CH_2Cl_2) affording the title compound **9qa** (116 mg, 0.264 mmol, 88 % yield, > 20:1 dr determined by ^{1}H NMR) as a pale yellow oil.

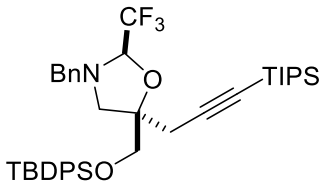
R$_f$ 0.60 (Pentane/CH_2Cl_2 4/1).
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.37 – 7.26 (m, 5H, Ar*H*), 4.71 (q, *J* = 4.7 Hz, 1H, C*H*CF_3), 4.15 (d, *J* = 13.1 Hz, 1H, C*H*$_2$Ph), 3.78 (d, *J* = 13.2 Hz, 1H, C*H*$_2$Ph), 3.08 (d, *J* = 10.2 Hz, 1H, C*H*$_2$N), 2.97 (d, *J* = 10.2 Hz, 1H, C*H*$_2$N), 2.60 (d, *J* = 16.8 Hz, 1H, C*H*$_2$CC), 2.53 (d, *J* = 16.8 Hz, 1H, C*H*$_2$CC), 1.44 (s, 3H, C*H*$_3$), 1.04 (m, 21H, TIPS).
^{13}C NMR (101 MHz, Chloroform-*d*) δ 138.1, 128.62, 128.58, 127.6, 123.6 (q, *J* = 284), 104.5, 92.3 (q, *J* = 33.4 Hz), 83.9, 83.3, 60.6, 58.7, 32.3, 25.1, 18.7, 11.4.

IR ν_{max} 3086 (w), 3066 (w), 3032 (w), 2943 (m), 2895 (w), 2866 (m), 2176 (w), 2175 (w), 1493 (w), 1462 (w), 1381 (w), 1294 (m), 1239 (w), 1209 (w), 1157 (s), 1100 (m), 1077 (w), 1036 (w), 994 (w), 915 (w), 884 (w), 857 (w), 722 (w).
HRMS (ESI) calcd for $C_{24}F_3H_{37}NOSi^+$ $[M+H]^+$ 440.2591; found 440.2599.

Stereochemistry was assigned by 2D ROESY NMR experiment.



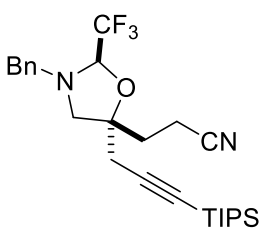
3-Benzyl-5-methyl-2-(trifluoromethyl)-5-(3-(triisopropylsilyl)prop-2-yn-1-yl)oxazolidine (9ra)



Following General Procedure **C**, the title compound was prepared from N-benzyl-2-(((tert-butyldiphenylsilyl)oxy)methyl)prop-2-en-1-amine (**4r**) (125 mg, 0.300 mmol) and (bromoethynyl)triisopropylsilane (**5a**) (102 mg, 0.390 mmol, 1.3 eq). The crude oil (> 20:1 dr determined by integration in the crude ^{1}H NMR) was purified by column chromatography (SiO_2 15:1 to 7:1 Pentane:CH_2Cl_2) affording the title compound **9ra** (106 mg, 0.153 mmol, 51% yield, >20:1 dr determined by ^{1}H NMR) as a pale yellow oil.

R$_f$ 0.55 (Pentane/CH_2Cl_2 4/1).
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.71 – 7.61 (m, 4H, Ar*H*), 7.49 – 7.27 (m, 11H, Ar*H*), 4.80 (q, *J* = 4.4 Hz, 1H, C*H*CF$_3$), 4.19 (d, *J* = 13.1 Hz, 1H, C*H$_2$*Ph), 3.84 (d, *J* = 10.3 Hz, 1H, C*H$_2$*OSi), 3.78 (d, *J* = 13.1 Hz, 1H, C*H$_2$*Ph), 3.64 (d, *J* = 10.3 Hz, 1H, C*H$_2$*OSi), 3.14 (d, *J* = 10.3 Hz, 1H, C*H$_2$*N), 3.09 (d, *J* = 10.3 Hz, 1H, C*H$_2$*N), 3.00 (d, *J* = 16.9 Hz, 1H, C*H$_2$*CC), 2.67 (d, *J* = 17.0 Hz, 1H, C*H$_2$*CC), 1.09 (m, 21H, TIPS), 1.05 (s, 9H, *t*-Bu).
^{13}C NMR (101 MHz, Chloroform-*d*) δ 138.0, 135.7, 135.7, 133.3, 133.2, 129.83, 129.82, 128.6, 128.5, 127.8 (2C), 127.6, 123.3 (q, *J* = 283.5 Hz), 104.5, 92.5 (q, *J* = 33.4 Hz), 86.0, 83.4, 66.6, 58.6, 56.6, 27.2, 26.9, 19.4, 18.8, 11.5.
IR ν_{max} 3070 (w), 2939 (m), 2892 (w), 2863 (m), 2175 (w), 1465 (w), 1428 (w), 1384 (w), 1369 (w), 1293 (m), 1158 (s), 1110 (s), 1036 (w), 997 (w), 912 (w), 884 (w), 858 (w), 821 (m), 738 (m).
HRMS (ESI) calcd for $C_{40}F_3H_{55}NO_2Si_2^+$ $[M+H]^+$ 694.3718; found 694.3719.
Stereochemistry was assigned by analogy.

3-(3-Benzyl-2-(trifluoromethyl)-5-(3-(triisopropylsilyl)prop-2-yn-1-yl)oxazolidin-5-yl)propanenitrile (9sa)

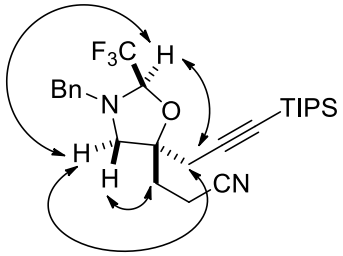


Following General Procedure **C**, the title compound was prepared from 4-((benzylamino)methyl)pent-4-enenitrile (**4s**) (60.1 mg, 0.300 mmol) and (bromoethynyl)triisopropylsilane (**5a**) (102 mg, 0.390 mmol, 1.3 eq).
The crude oil (>20:1 dr determined by integration in the crude ^{1}H NMR) was purified by column chromatography (SiO_2 3:1 Pentane:CH_2Cl_2)

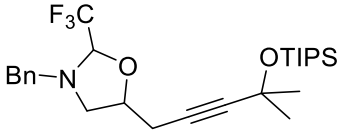
affording the title compound **9sa** (91 mg, 0.19 mmol, 63 % yield, >20:1 dr determined by ^{1}H NMR) as a pale yellow oil.

R$_f$ 0.25 (Pentane/CH_2Cl_2 2/1).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.27 (m, 5H, Ar*H*), 4.70 (q, *J* = 4.4 Hz, 1H, C*H*CF_3), 4.18 (d, *J* = 13.0 Hz, 1H, C*H*$_2$Ph), 3.68 (d, *J* = 13.0 Hz, 1H, C*H*$_2$Ph), 3.04 (d, *J* = 10.4 Hz, 1H, C*H*$_2$N), 3.00 (d, *J* = 10.4 Hz, 1H, C*H*$_2$N), 2.60 (d, *J* = 17.1 Hz, 1H, C*H*$_2$CC), 2.54 (d, *J* = 17.1 Hz, 1H, C*H*$_2$CC), 2.51 – 2.44 (m, 2H, C*H*$_2$CN), 2.18 – 2.10 (m, 2H, C*H*$_2$CH$_2$CN), 1.04 (m, 21H, TIPS).
^{13}C NMR (101 MHz, $CDCl_3$) δ 137.3, 128.8, 128.6, 127.9, 123.3 (q, *J* = 283.5 Hz), 119.6, 102.6, 91.9 (q, *J* = 33.5 Hz), 84.9, 83.8, 60.0, 57.9, 33.2, 29.5, 18.7, 11.8, 11.3.
IR ν_{max} 3033 (w), 2945 (m), 2894 (w), 2866 (m), 2253 (w), 2176 (w), 1462 (w), 1380 (w), 1291 (m), 1163 (s), 1082 (w), 1031 (w), 993 (w), 910 (s), 888 (w), 857 (w), 733 (s).
HRMS (ESI) calcd for $C_{26}F_3H_{38}N_2OSi^+$ $[M+H]^+$ 479.2700; found 479.2696.

Stereochemistry was assigned by 2D ROESY NMR experiment.



3-Benzyl-5-(4-methyl-4-((triisopropylsilyl)oxy)pent-2-yn-1-yl)-2-(trifluoromethyl)oxazolidine (9ab)

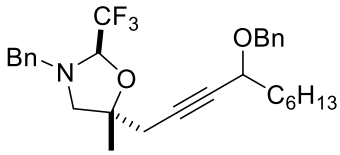


Following General Procedure **A** with cinnamyl(cyclopenta-2,4-dien-1-yl)palladium (**6**) (6.9 mg, 0.024 mmol, 8 mol %), DPEPhos (**7a**) (19.4 mg, 0.036 mmol, 12 mol%), the title compound was prepared from N-benzylprop-2-en-1-amine (**4a**) (44.2 mg, 0.300 mmol) and ((4-bromo-2-methylbut-3-yn-2-yl)oxy)triisopropylsilane (**5b**) (125 mg, 0.390 mmol, 1.3 eq). The crude oil (1:1 dr determined by integration in the crude ^{1}H NMR) was purified by column chromatography (SiO_2 14:1 Pentane:CH_2Cl_2) affording the title compound **9ab** (101 mg, 0.209 mmol, 70 % yield, 1:1 dr determined by integration in the ^{1}H NMR).

R$_f$ 0.60 (Pentane/CH_2Cl_2 6/1).
^{1}H NMR (400 MHz, $CDCl_3$) mixture of diastereoisomers 1(*A*):1(*B*) δ 7.40 – 7.27 (m, 10H, Ar*H A* + *B*), 4.72 – 4.62 (m, 2H, C*H*CF_3, *A* + *B*), 4.37 (m, 1H, OC*H A*), 4.24 (m, 1H, OC*H B*), 4.18 (d, *J* = 13.2 Hz, 1H, C*H*$_2$Ph *A*), 3.99 (d, *J* = 13.3 Hz, 1H, C*H*$_2$Ph *B*), 3.84 (d, *J* = 13.3 Hz, 1H, C*H*$_2$Ph *B*), 3.74 (d, *J* = 13.1 Hz, 1H, C*H*$_2$Ph *A*), 3.31 (dd, *J* = 9.4, 5.6 Hz, 1H, C*H*$_2$N *A*), 3.14 – 3.06 (m, 1H, C*H*$_2$N *B*), 3.00 (m, 1H, C*H*$_2$N *B*), 2.72 – 2.54 (overlapping signals, 3 m, 3H, C*H*$_2$CC *B*, C*H*$_2$N *A* and C*H*$_2$CC *A*), 2.49 – 2.32 (overlapping signals, m, 2H, C*H*$_2$CC *B*, C*H*$_2$CC *A*), 1.46-1.45 (overlapping signals, 2 s, 12H, C*H*$_3$ *A* and *B*), 1.15 – 1.01 (m, 42H, TIPS *A* and *B*).
^{13}C NMR (101 MHz, $CDCl_3$) δ 137.8, 137.7, 128.70 (2C), 128.67, 128.6, 127.9 , 127.7, 123.8 (q, *J* = 285 Hz), 123.4 (q, *J* = 283 Hz), 92.8 (q, *J* = 33.7 Hz), 91.6 (q, *J* = 33.2 Hz), 88.3, 88.0, 75.8, 66.3 (overlapping signals, 2 s), 59.7, 59.3, 56.8, 56.7, 33.5 (overlapping signals), 24.03, 23.97, 18.4, 13.1.

IR ν_{max} 2942 (w), 2895 (w), 2867 (w), 1464 (w), 1379 (w), 1294 (w), 1245 (w), 1166 (s), 1054 (m), 885 (w), 699 (w).
HRMS calcd for $C_{26}H_{41}F_3NO_2Si^+$ $[M+H]^+$ 484.2853; found 484.2852.

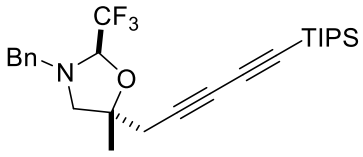
3-Benzyl-5-(4-(benzyloxy)dec-2-yn-1-yl)-5-methyl-2-(trifluoromethyl)oxazolidine (9qc)



Following General Procedure **C** with cinnamyl(cyclopenta-2,4-dien-1-yl)palladium (**6**) (6.9 mg, 0.024 mmol, 8 mol %), XANTPhos (**7b**) (20.8 mg, 0.036 mmol, 12 mol%), the title compound was prepared from N-benzyl-2-methylprop-2-en-1-amine (**4q**) (48.4 mg, 0.300 mmol) and (((1-bromonon-1-yn-3-yl)oxy)methyl)benzene (**5c**) (121 mg, 0.390 mmol, 1.3 eq). The crude oil was purified by column chromatography (SiO_2 8:1 Pentane:CH_2Cl_2) affording the title compound **9qc** (92 mg, 0.19 mmol, 63% yield**,** single diastereoisomer by crude ^{19}F NMR) as a yellow oil.

R$_f$ 0.20 (Pentane:CH_2Cl_2 4:1).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 – 7.27 (m, 10H), 4.80 – 4.72 (overlapping signals, 2 m, 2H, C*H*CF_3 and OC*H*$_2$Ph), 4.49 (m, 1H, OC*H*$_2$Ph), 4.18 (d, *J* = 13.3 Hz, 1H, NC*H*$_2$Ph), 4.09 (t, *J* = 6.4 Hz, 1H, OC*H*CC), 3.80 (d, *J* = 13.3 Hz, 1H, NC*H*$_2$Ph), 3.05 (d, *J* = 10.1 Hz, 1H, NC*H*$_2$), 2.99 (d, *J* = 10.1 Hz, 1H, NC*H*$_2$), 2.60 (d, *J* = 17.0 Hz, 1H, C*H*$_2$CC), 2.58 (d, *J* = 17.0 Hz, 1H, C*H*$_2$CC), 1.83 – 1.66 (m, 2H, CCCHC*H*$_2$), 1.53 – 1.40 (overlapping signals, s and m, 5H, NCH$_2$CC*H*$_3$ and CCCHCHC*H*$_2$), 1.37 – 1.24 (m, 6H, MeC*H*$_2$C*H*$_2$C*H*$_2$), 0.96 – 0.86 (m, 3H, Me).
^{13}C NMR (101 MHz, $CDCl_3$) δ 138.2, 138.0, 128.63, 128.5, 128.4, 128.0, 127.7, 127.6, 123.6 (q, *J* = 284.1 Hz), 92.2 (q, *J* = 33.3 Hz), 83.8, 82.2, 81.9, 70.5, 69.0, 60.9, 58.5, 36.1, 31.9, 31.2, 29.1, 25.5, 25.1, 22.7, 14.2.
IR ν_{max} 3064 (w), 3032 (w), 2930 (m), 2858 (m), 2250 (w), 1496 (w), 1456 (w), 1379 (w), 1332 (w), 1293 (m), 1208 (w), 1153 (s), 1094 (s), 1074 (m), 1035 (w), 985 (w), 911 (m), 855 (w), 734 (s).
HRMS (ESI) calcd for $C_{29}H_{37}F_3NO_2^+$ $[M+H]^+$ 488.2771; found 488.2777.
Stereochemistry was assigned by analogy.

3-Benzyl-5-methyl-2-(trifluoromethyl)-5-(5-(triisopropylsilyl)penta-2,4-diyn-1-yl)oxazolidine (9qd)

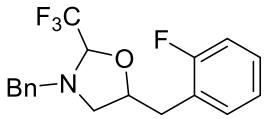


Following General Procedure **C** with cinnamyl(cyclopenta-2,4-dien-1-yl)palladium (**6**) (6.9 mg, 0.024 mmol, 8 mol %), XANTPhos (**7b**) (20.8 mg, 0.036 mmol, 12 mol%), the title compound was prepared from N-benzyl-2-methylprop-2-en-1-amine (**4q**) (48.4 mg, 0.300 mmol) and (bromobuta-1,3-diyn-1-yl)triisopropylsilane (**5d**) (111 mg, 0.390 mmol, 1.3 eq). The crude oil (7.2:1 dr determined by integration in the crude ^{19}F NMR) was purified by column chromatography (SiO_2 12:1 Pentane:CH_2Cl_2) affording the title compound **9qd** (97 mg, 0.21 mmol, 70% yield, 8.3:1 dr determined by integration in the ^{19}F NMR) as a pale yellow oil.

R$_f$ 0.60 (Pentane:CH_2Cl_2 4:1).
^{1}H NMR (400 MHz, $CDCl_3$) mixture of diastereoisomers 8.3(*A)*:1(*B)* δ 7.40 – 7.27 (m, 10H, Ar*H A + B),* 4.75 (q, *J* = 4.7 Hz, 2H, C*H*CF_3 *A + B),* 4.17 (d, *J* = 13.5 Hz, 2H, C*H*$_2$Ph *A + B),* 3.86 (d, *J* = 13.5 Hz, 1H, C*H*$_2$Ph *A),* 3.79 (d, *J* = 13.2 Hz, 1H, C*H*$_2$Ph *B),* 3.08 (d, *J* = 10.3 Hz,

2H, C*H*$_2$N *A + B)*, 2.96 (d, *J* = 10.3, 2H, C*H*$_2$N *A + B)*, 2.66 (d, *J* = 17.3, 1H, C*H*$_2$CC *A)*, 2.62 (d, *J* = 17.3, 1H, C*H*$_2$CC *A)*, 2.61 (d, *J* = 16.8, 1H, C*H*$_2$CC *B)*, 2.58 (d, *J* = 16.8, 1H, C*H*$_2$CC *B)*, 1.46 (s, 6H, C*H*$_3$ *A + B)*, 1.10 (s, 42H, TIPS *A + B)*.
^{13}C NMR (101 MHz, $CDCl_3$) major diastereomer δ 138.1, 128.7, 128.4, 127.6, 123.5 (q, *J* = 285 Hz), 92.2 (q, *J* = 33 Hz), 89.7, 83.7, 81.6, 74.3, 68.2, 61.1, 58.5, 32.0, 25.4, 18.7, 11.4.
IR ν_{max} 2944 (m), 2894 (w), 2867 (m), 2226 (w), 2106 (w), 1461 (w), 1381 (w), 1293 (m), 1262 (w), 1240 (w), 1155 (s), 1100 (m), 1076 (w), 1036 (w), 1025 (w), 995 (w), 917 (w), 883 (w), 855 (w), 822 (w), 728 (w).
HRMS (ESI) calcd for $C_{26}F_3H_{37}NOSi^+$ $[M+H]^+$ 464.2591; found 464.2600.
Stereochemistry was assigned by analogy.

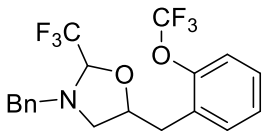
3-Benzyl-5-(2-fluorobenzyl)-2-(trifluoromethyl)oxazolidine (9ae)



Following General Procedure **A** with cinnamyl(cyclopenta-2,4-dien-1-yl)palladium (**6**) (6.9 mg, 0.024 mmol, 8 mol %), DPEPhos (**7a**) (19 mg, 0.036 mmol, 12 mol%), the title compound was prepared from N-benzylprop-2-en-1-amine (**4a**) (44.2 mg, 0.300 mmol), 1-ethoxy-2,2,2-trifluoroethanol (**3**) (0.123 mL, 0.900 mmol, 3.0 eq) and 1-bromo-2-fluorobenzene (**5e**) (0.066 ml, 0.60 mmol, 2 eq) at 70 °C. The crude oil (2:1 dr determined by integration in the crude ^{1}H NMR) was purified by column chromatography (SiO_2 10:1 Pentane:CH_2Cl_2) affording the title compound **9ae** (70 mg, 0.21 mmol, 69 % yield, 2:1 dr determined by integration in the ^{1}H NMR) as a pale yellow oil.

R$_f$ 0.35 (Pentane:CH_2Cl_2 4:1).
^{1}H NMR (400 MHz, $CDCl_3$) mixture of diastereoisomers 2(*A)*:1(*B)* δ 7.39 – 7.17 (m, 14H, Ar*H A + B)*, 7.10 – 6.96 (m, 4H, Ar*H A + B)*, 4.72 – 4.63 (m, 2H, C*H*CF$_3$ *A + B)*, 4.59 – 4.50 (m, 1H, OC*H A)*, 4.44 – 4.34 (m, 1H, OC*H B)*, 4.09 (d, *J* = 13.2 Hz, 1H, C*H*$_2$Ph *A)*, 3.95 (d, *J* = 13.3 Hz, 1H, C*H*$_2$Ph *B)*, 3.83 (d, *J* = 13.3 Hz, 1H, C*H*$_2$Ph *B)*, 3.64 (d, *J* = 13.2 Hz, 1H, C*H*$_2$Ph *A)*, 3.18 (dd, *J* = 9.3, 5.5 Hz, 1H, C*H*$_2$N *A)*, 3.09 – 2.87 (overlapping signals, m, 6H, C*H*$_2$N *B* and C*H*$_2$Ar *A + B)*, 2.53 – 2.43 (m, 1H, C*H*$_2$N *A)*.
^{13}C NMR (101 MHz, $CDCl_3$) δ 161.2 (d, *J* = 245.2 Hz), 161.1 (d, *J* = 245.4 Hz), 138.0, 137.9, 131.8 (d, *J* = 4.7 Hz), 131.6 (d, *J* = 4.5 Hz), 128.8 – 128.4 (overlapping signals, m), 127.8, 127.6, 124.6 (d, *J* = 15.8 Hz), 124.39 – 124.21 (overlapping signals, m), 124.2 (q, *J* = 284.9 Hz), 124.0 (d, *J* = 15.9 Hz), 123.7 (q, *J* = 283.3 Hz), 115.5 (d, *J* = 22.3 Hz), 115.4 (d, *J* = 22.2 Hz), 92.7 (q, *J* = 33.5 Hz), 91.4 (q, *J* = 33.1 Hz), 79.0, 76.8, 59.9, 59.2, 56.8, 56.6, 33.4, 32.9.
IR ν_{max} 3085 (w), 3066 (w), 3034 (w), 2935 (w), 2842 (w), 1587 (w), 1494 (m), 1456 (w), 1293 (m), 1292 (m), 1233 (m), 1163 (s), 1036 (w), 989 (w), 928 (w), 859 (w), 827 (w), 761 (m), 760 (m), 734 (w).
HRMS (ESI) calcd for $C_{18}H_{18}F_4NO^+$ $[M+H]^+$ 340.1319; found 340.1315.

3-Benzyl-5-(2-(trifluoromethoxy)benzyl)-2-(trifluoromethyl)oxazolidine (9af)

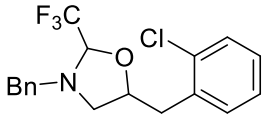


Following General Procedure **A** with cinnamyl(cyclopenta-2,4-dien-1-yl)palladium (**6**) (6.9 mg, 0.024 mmol, 8 mol %), DPEPhos (**7a**) (19 mg, 0.036 mmol, 12 mol%), the title compound was prepared from N-benzylprop-2-en-1-amine (**4a**) (44.2 mg, 0.300 mmol), 1-ethoxy-2,2,2-trifluoroethanol (**3**) (0.123 mL, 0.900 mmol, 3.0 eq) and 1-bromo-2-(trifluoromethoxy)benzene (**5f**) (0.089 ml, 0.60 mmol, 2 eq) at 70 °C. The crude oil (1.9:1 dr determined by integration in the crude ^{1}H NMR) was purified by column chromatography (SiO_2

10:1 Pentane:CH_2Cl_2) affording the title compound **9af** (81 mg, 0.20 mmol, 67% yield, 1.6:1 dr determined by integration in the ^{1}H NMR) as a yellow oil.

R_f 0.40 (Pentane:CH_2Cl_2 4:1).
^{1}H NMR (400 MHz, $CDCl_3$) mixture of diastereoisomers 1.6(*A)*:1(*B)* δ 7.38 – 7.21 (m, 18H, Ar*H A + B)*, 4.73 – 4.65 (m, 2H, C*H*CF_3 *A + B)*, 4.60 – 4.51 (m, 1H, OC*H A)*, 4.43 – 4.34 (m, 1H, OC*H B)*, 4.13 (d, *J* = 13.1 Hz, 1H, C*H*$_2$Ph *A)*, 3.97 (d, *J* = 13.3 Hz, 1H, C*H*$_2$Ph *B)*, 3.85 (d, *J* = 13.3 Hz, 1H, C*H*$_2$Ph *B)*, 3.68 (d, *J* = 13.1 Hz, 1H, C*H*$_2$Ph *A)*, 3.20 (dd, *J* = 9.3, 5.4 Hz, 1H, C*H*$_2$N *A)*, 3.11 – 2.91 (m, 6H, C*H*$_2$Ar *A + B* and C*H*$_2$N *B)*, 2.49 (app t, *J* = 8.8 Hz, 1H, C*H*$_2$N *A)*.
^{13}C NMR (101 MHz, $CDCl_3$) δ 147.9 – 147.7 (m, 2C), 137.9, 137.8, 132.1, 131.6, 130.3, 129.8, 128.8, 128.7, 128.6, 128.5, 128.3 (2C), 127.8, 127.7, 127.0, 126.9, 124.0 (q, *J* = 284.8 Hz), 123.5 (q, *J* = 283.3 Hz), 120.9 (q, *J* = 257.5 Hz, 2C), 120.5 (q, *J* = 1.7 Hz), 120.4 (d, *J* = 1.6 Hz), 92.8 (q, *J* = 33.5 Hz), 91.3 (q, *J* = 33.2 Hz), 78.9, 76.7, 59.9, 59.2, 56.9, 56.7, 34.3, 33.7.
IR ν_{max} 3068 (w), 3034 (w), 2932 (w), 2848 (w), 1495 (w), 1455 (w), 1377 (w), 1255 (s), 1221 (s), 1150 (s), 1047 (w), 1026 (w), 989 (w), 927 (w), 858 (w), 761 (w), 728 (w).
HRMS (ESI) calcd for $C_{19}H_{18}F_6NO_2^+$ $[M+H]^+$ 406.1236; found 406.1230.

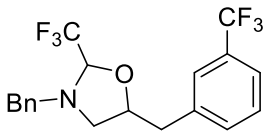
3-Benzyl-5-(2-chlorobenzyl)-2-(trifluoromethyl)oxazolidine (9ag)



Following General Procedure **A** with cinnamyl(cyclopenta-2,4-dien-1-yl)palladium (**6**) (6.9 mg, 0.024 mmol, 8 mol %), DPEPhos (**7a**) (19 mg, 0.036 mmol, 12 mol%), the title compound was prepared from N-benzylprop-2-en-1-amine (**4a**) (44.2 mg, 0.300 mmol), 1-ethoxy-2,2,2-trifluoroethanol (**3**) (0.123 mL, 0.900 mmol, 3.0 eq) and 1-bromo-2-chlorobenzene (**5g**) (0.070 mL, 0.60 mmol, 2 eq) at 70 °C. The crude oil (2:1 dr determined by integration in the crude ^{1}H NMR) was purified by column chromatography (SiO_2 10:1 Pentane:CH_2Cl_2) affording the title compound **9ag** (69 mg, 0.19 mmol, 65% yield, 1.9:1 dr determined by integration in the ^{1}H NMR) as a pale yellow oil.

R_f 0.40 (Pentane:CH_2Cl_2 4:1).
^{1}H NMR (400 MHz, $CDCl_3$) mixture of diastereoisomers 1.9(*A)*:1(*B)* δ 7.40 – 7.32 (m, 10H, Ar*H A + B)*, 7.32 – 7.27 (m, 4H, Ar*H A + B)*, 7.24 – 7.16 (m, 4H, Ar*H A + B)*, 4.73 – 4.67 (m, 2H, C*H*CF_3 *A + B)*, 4.66 – 4.58 (m, 1H, OC*H A)*, 4.52 – 4.43 (m, 1H, OC*H B)*, 4.13 (d, *J* = 13.2 Hz, 1H, C*H*$_2$Ph *A)*, 3.97 (d, *J* = 13.4 Hz, 1H, C*H*$_2$Ph *B)*, 3.86 (d, *J* = 13.4 Hz, 1H, C*H*$_2$Ph *B)*, 3.69 (d, *J* = 13.2 Hz, 1H, C*H*$_2$Ph *A)*, 3.25 – 3.14 (m, 2H, C*H*$_2$N *A* and C*H*$_2$Ar *A*), 3.14 – 2.99 (m, 5H, C*H*$_2$N *B* and C*H*$_2$Ar *A + B)*, 2.54 (app t, *J* = 8.8 Hz, 1H, C*H*$_2$N *A)*.
^{13}C NMR (101 MHz, $CDCl_3$) δ 137.9, 137.8, 135.5, 135.0, 134.3, 134.1, 131.8, 131.4, 129.7, 129.6, 128.7, 128.6, 128.6, 128.5, 128.3 (2C), 127.8, 127.6, 127.1 (2C), 124.0 (q, *J* = 284.9 Hz), 123.5 (q, *J* = 283.3 Hz), 92.7 (q, *J* = 33.6 Hz), 91.3 (q, *J* = 33.1 Hz), 78.7, 76.4, 59.9, 59.2, 56.7, 56.6, 37.7, 37.2.
IR ν_{max} 3066 (w), 3031 (w), 2934 (w), 2899 (w), 2841 (w), 1476 (w), 1449 (w), 1379 (w), 1342 (w), 1291 (m), 1145 (s), 1098 (m), 1050 (m), 986 (w), 928 (w), 857 (w), 754 (m), 736 (m).
HRMS (ESI) calcd for $C_{18}H_{18}ClF_3NO^+$ $[M+H]^+$ 356.1024; found 356.1019.

3-benzyl-2-(trifluoromethyl)-5-(3-(trifluoromethyl)benzyl)oxazolidine (9ah)

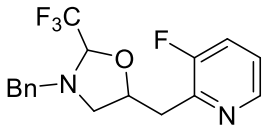


Following General Procedure **A** with cinnamyl(cyclopenta-2,4-dien-1-yl)palladium (**6**) (6.9 mg, 0.024 mmol, 8 mol %), DPEPhos (**7a**) (19 mg,

0.036 mmol, 12 mol%), the title compound was prepared from N-benzylprop-2-en-1-amine (**4a**) (44.2 mg, 0.300 mmol), 1-ethoxy-2,2,2-trifluoroethanol (**3**) (0.123 mL, 0.900 mmol, 3.0 eq) and 1-bromo-3-(trifluoromethyl)benzene (**5h**) (0.084 mL, 0.60 mmol, 2 eq) at 70 °C. The crude oil (2.5:1 dr determined by integration in the crude ^{1}H NMR) was purified by column chromatography (SiO_2 10:1 Pentane:CH_2Cl_2) affording the title compound **9ah** (64 mg, 0.16 mmol, 55% yield, 2.6:1 dr determined by integration in the ^{1}H NMR) as a pale yellow oil.

R$_f$ 0.40 (Pentane:CH_2Cl_2 4:1).
^{1}H NMR (400 MHz, $CDCl_3$) mixture of diastereoisomers 2.6(*A)*:1(*B)* δ 7.54 – 7.24 (m, 18H, Ar*H A + B)*, 4.75 – 4.63 (m, 2H, C*H*CF_3 *A + B)*, 4.59 – 4.50 (m, 1H, OC*H A)*, 4.39 – 4.29 (m, 1H, OC*H B)*, 4.08 (d, *J* = 13.2 Hz, 1H, C*H$_2$*Ph *A)*, 3.97 (d, *J* = 13.3 Hz, 1H, C*H$_2$*Ph *B)*, 3.84 (d, *J* = 13.3 Hz, 1H, C*H$_2$*Ph *B)*, 3.60 (d, *J* = 13.2 Hz, 1H, C*H$_2$*Ph *A)*, 3.18 (dd, *J* = 9.2, 5.5 Hz, 1H, C*H$_2$*N *A)*, 3.09 – 2.97 (m, 4H, C*H$_2$*Ar *A + B* and C*H$_2$*N *B*), 2.92 (dd, *J* = 14.2, 6.1 Hz, 1H, C*H$_2$*Ar *A)*, 2.85 (dd, *J* = 13.9, 5.4 Hz, 1H, C*H$_2$*Ar *B)*, 2.43 (app t, *J* = 8.9 Hz, 1H, C*H$_2$*N *A)*.
^{13}C NMR (101 MHz, $CDCl_3$) δ 138.7, 138.1, 137.8, 137.7, 132.8, 132.7, 131.0 (q, *J* = 32.2 Hz, 2C), 129.1, 129.0, 128.7 (2C), 128.6, 128.6, 127.9, 127.7, 126.1 (q, *J* = 3.7 Hz), 126.0 (q, *J* = 3.9 Hz), 124.3 (q, *J* = 272.2 Hz), 124.2 (q, *J* = 272.2 Hz), 124.0 (q, *J* = 284.6 Hz), 123.9 – 123.6 (2 overlapping q), 123.5 (q, *J* = 283.1 Hz), 92.8 (q, *J* = 33.5 Hz), 91.3 (q, *J* = 33.2 Hz), 79.5, 77.7, 60.0, 59.0, 56.6, 56.5, 40.0, 39.6.[23]
IR ν_{max} 3068 (w), 3034 (w), 2948 (w), 2829 (w), 1695 (w), 1496 (w), 1452 (w), 1332 (s), 1293 (m), 1164 (s), 1131 (s), 1079 (m), 1026 (w), 918 (w), 859 (w), 803 (w), 733 (w).
HRMS (ESI) calcd for $C_{19}H_{18}F_6NO^+$ $[M+H]^+$ 390.1287; found 390.1287.

3-Benzyl-5-((3-fluoropyridin-2-yl)methyl)-2-(trifluoromethyl)oxazolidine (9ai)



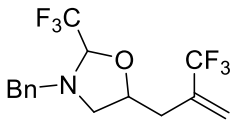
Following General Procedure **A** with cinnamyl(cyclopenta-2,4-dien-1-yl)palladium (**6**) (6.9 mg, 0.024 mmol, 8 mol %), DPEPhos (**7a**) (19 mg, 0.036 mmol, 12 mol%), the title compound was prepared from N-benzylprop-2-en-1-amine (**4a**) (44.2 mg, 0.300 mmol), 1-ethoxy-2,2,2-trifluoroethanol (**3**) (0.123 mL, 0.900 mmol, 3.0 eq) and 2-bromo-3-fluoropyridine (**5i**) (106 mg, 0.600 mmol, 2 eq) at 70 °C. The crude oil (1.4:1 dr determined by integration of PhC*H$_2$*N peaks in the ^{1}H NMR) was purified by column chromatography (SiO_2 10:1:0.1 Pentane:EtOAc:Et_3N) affording the title compound **9ai** (95 mg, 0.28 mmol, 93 % yield, 1.4:1 dr determined by integration of PhC*H$_2$*N peaks in the ^{1}H NMR) as a pale yellow oil.

R$_f$ 0.35 (Pentane:EtOAc 4:1).
^{1}H NMR (400 MHz, $CDCl_3$) mixture of diastereoisomers 1.4(*A)*:1(*B)* 8.34 (m, 2H, Ar*H A + B)*, 7.38 – 7.24 (m, 12H, Ar*H A + B)*, 7.17 (m, 2H, Ar*H A + B)*, 4.79 – 4.65 (m, 2H, C*H*CF_3 *A + B* and OC*H A + B)*, 4.16 (d, *J* = 13.2 Hz, 1H, C*H$_2$*Ph *A)*, 3.97 (d, *J* = 13.4 Hz, 1H, C*H$_2$*Ph *B)*, 3.89 (d, *J* = 13.4 Hz, 1H, C*H$_2$*Ph *B)*, 3.75 (d, *J* = 13.2 Hz, 1H, C*H$_2$*Ph *A)*, 3.37 (dd, *J* = 6.4, 2.3 Hz, 1H, C*H$_2$*Ar *B)*, 3.33 (dd, *J* = 6.2, 2.3 Hz, 1H, C*H$_2$*Ar *A)*, 3.29 (dd, *J* = 9.5, 5.5 Hz, 1H, C*H$_2$*N *A)*, 3.18 – 2.98 (m, 4H, C*H$_2$*N *B* and C*H$_2$*Ar *A + B)*, 2.61 (app t, *J* = 8.8 Hz, 1H, C*H$_2$*N *A)*.
^{13}C NMR (101 MHz, $CDCl_3$) δ 158.1 (d, *J* = 256.8 Hz), 158.0 (d, *J* = 256.8 Hz), 146.3 (d, *J* = 15.5 Hz), 145.9 (d, *J* = 15.3 Hz), 145.2 (d, *J* = 5.5 Hz), 145.1 (d, *J* = 5.5 Hz), 138.0, 137.9, 128.7, 128.6, 128.5, 128.5, 127.7, 127.6, 124.0 (q, *J* = 284.6 Hz), 123.7 (q, *J* = 283.2 Hz), 123.3 (d, *J* = 3.7 Hz), 123.1 (d, *J* = 3.7 Hz), 122.9 (d, *J* = 19.8 Hz), 122.8 (d, *J* = 19.8 Hz), 92.8 (q, *J* = 33.7 Hz), 91.3 (q, *J* = 33.2 Hz), 78.1, 75.8, 60.0, 59.4, 57.2, 56.7, 36.1, 35.3.

[23] Not all signals in ^{13}C NMR could be resolved.

IR ν_{max} 3069 (w), 3031 (w), 2936 (w), 2846 (w), 1739 (w), 1603 (w), 1452 (m), 1375 (w), 1340 (w), 1291 (m), 1250 (m), 1161 (s), 1055 (w), 1036 (w), 985 (w), 914 (w), 857 (w), 804 (w), 732 (m).
HRMS (ESI) calcd for $C_{17}H_{17}F_4N_2O^+$ $[M+H]^+$ 341.1272; found 341.1276.

3-Benzyl-5-(2-fluorobenzyl)-2-(trifluoromethyl)oxazolidine (9aj)

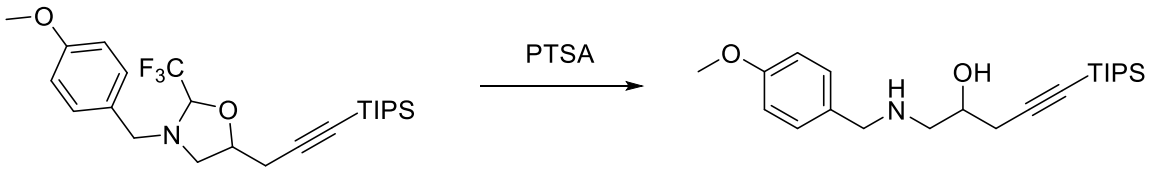


Following General Procedure **A** with cinnamyl(cyclopenta-2,4-dien-1-yl)palladium (**6**) (6.9 mg, 0.024 mmol, 8 mol %), DPEPhos (**7a**) (19 mg, 0.036 mmol, 12 mol%), the title compound was prepared from N-benzylprop-2-en-1-amine (**4a**) (44.2 mg, 0.300 mmol), 1-ethoxy-2,2,2-trifluoroethanol (**3**) (0.123 mL, 0.900 mmol, 3.0 eq) and 2-bromo-3,3,3-trifluoroprop-1-ene (**5j**) (0.085 ml, 0.66 mmol, 2 eq) at 70 °C. The crude oil (>20:1 dr determined by integration in the crude ^{1}H NMR) was purified by column chromatography (SiO_2 10:1 Pentane:CH_2Cl_2) affording the title compound **9aj** (70 mg, 0.21 mmol, 69 % yield, >20:1 dr determined by integration in the ^{1}H NMR) as a pale yellow oil.

R$_f$ 0.35 (Pentane:CH_2Cl_2 4:1).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.27 (m, 5H, Ar*H*), 4.68 (q, *J* = 4.9 Hz, 1H, C*H*CF_3), 4.54 – 4.44 (m, 1H, OC*H*), 4.19 (d, *J* = 13.1 Hz, 1H, C*H*$_2$Ph), 3.72 (d, *J* = 13.1 Hz, 1H, C*H*$_2$Ph), 3.27 (dd, *J* = 9.1, 5.4 Hz, 1H, C*H*$_2$N), 2.58 (dd, *J* = 15.7, 7.6 Hz, 1H, C*H*$_2$CC), 2.46 – 2.37 (overlapping signals, 2 m, 2H, C*H*$_2$N and C*H*$_2$CC).
^{13}C NMR (101 MHz, $CDCl_3$) δ 137.7, 134.4 (q, *J* = 30.3 Hz), 128.7, 128.6, 127.8, 123.9 (d, *J* = 284.7 Hz), 123.5 (q, *J* = 273.3 Hz), 120.6 (q, *J* = 5.7 Hz), 91.2 (q, *J* = 33.4 Hz), 77.1, 59.2, 57.1, 33.6.
IR ν_{max} 2924 (w), 2853 (w), 1452 (w), 1419 (w), 1372 (w), 1342 (w), 1294 (m), 1170 (s), 1131 (s), 1036 (w), 951 (w), 857 (w), 731 (w).
HRMS (ESI) calcd for $C_{15}H_{16}F_6NO^+$ $[M+H]^+$ 340.1131; found 340.1132.

5. Products transformations

1-((4-Methoxybenzyl)amino)-5-(triisopropylsilyl)pent-4-yn-2-ol oxazolidine (10)



9ba **10**

To a solution of 3-(4-methoxybenzyl)-2-(trifluoromethyl)-5-(3-(triisopropylsilyl)prop-2-yn-1-yl)oxazolidine (**9ba**) (91 mg, 0.20 mmol, 1.0 eq, 1.1:1 dr) in wet THF (9.0 mL) and Methanol (1.0 mL) was added 4-methylbenzenesulfonic acid (241 mg, 1.40 mmol, 7.0 eq). The reaction mixture was stirred at 60 °C for 20h, and then cooled down to rt and diluted with CH_2Cl_2 (20 mL). The organic layer was washed with aqueous 2 M NaOH solution (2x10 mL), dried over MgSO4, filtered and concentrated under reduced pressure. The residue was purified by column chromatography (SiO2, CH_2Cl_2:Methanol:Et_3N 100:3:0 to 85:14:1) affording the title compound **10** as a pale yellow oil (65 mg, 0.17 mmol, 87 % yield).

R$_f$ 0.10 (EtOAc:Et_3N 99:1).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24 – 7.19 (m, 2H, Ar*H*), 6.85 – 6.80 (m, 2H, Ar*H*), 3.86 – 3.79 (m, 1H, OC*H*), 3.78 – 3.71 (m, 2H, ArC*H*$_2$), 3.76 (s, 3H, OC*H*$_3$), 3.02 (br s, 2H, O*H* and N*H*), 2.87 (dd, *J* = 12.2, 3.4 Hz, 1H, NC*H*$_2$), 2.65 (dd, *J* = 12.2, 8.4 Hz, 1H, NC*H*$_2$), 2.50 (dd, *J* = 16.8, 5.4 Hz, 1H, C*H*$_2$CC), 2.38 (dd, *J* = 16.8, 7.0 Hz, 1H, C*H*$_2$CC), 1.05 – 0.94 (m, 21H, TIPS).
^{13}C NMR (101 MHz, $CDCl_3$) δ 159.1, 131.2, 129.6, 114.1, 104.4, 83.4, 68.1, 55.4, 53.2, 53.1, 26.6, 18.8, 11.4.
IR ν_{max} 3374 (w), 3287 (w), 2942 (s), 2898 (m), 2864 (s), 2172 (w), 1613 (w), 1514 (m), 1464 (m), 1302 (w), 1249 (s), 1178 (w), 1110 (w), 1077 (w), 1036 (m), 913 (w), 884 (m), 823 (w), 735 (m).
HRMS (ESI) calcd for $C_{22}H_{38}NO_2Si^+$ $[M+H]^+$ 376.2666; found 376.2666.

2-(trifluoromethyl)-5-(3-(triisopropylsilyl)prop-2-yn-1-yl)oxazolidine (11)

9ba **11**

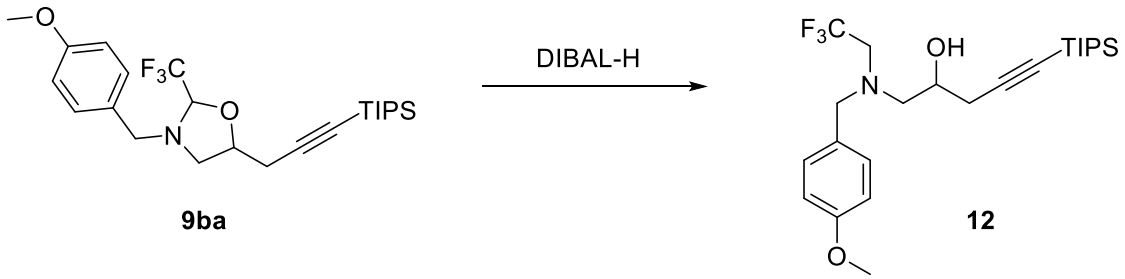
Following a slightly modified procedure,[24] to a solution of DDQ (54.5 mg, 0.240 mmol, 1.2 eq) in CH_2Cl_2 (0.80 mL) and water (0.050 mL) at 0 °C was slowly added a solution of 3-(4-methoxybenzyl)-2-(trifluoromethyl)-5-(3-(triisopropylsilyl)prop-2-yn-1-yl)oxazolidine (**9ba**) (91 mg, 0.20 mmol, 1.0 eq, 1.1:1 dr) in CH_2Cl_2 (0.40 ml). The mixture was stirred at rt for 10 h and then poured in ice cold water (10 mL) and extracted with CH_2Cl_2 (2x10 mL). The combined organic phase was dried over $MgSO_4$, filtered and concentrated under reduced pressure. The

[24] Lehmann, L.; Friebe M.; Brumby T.; Suelzle D.; Platzek J. (Schering Aktiengesellschaft) WO2004/87656 A1, **2004**.

crude residue was purified by preparative TLC (SiO_2, Toluene:CH_2Cl_2 3:2) affording the title compound **11** (53 mg, 0.16 mmol, 79% yield, 1.1:1 dr by integration of the OC*H* peak in the ^{1}H NMR) as a colourless oil.

R$_f$ 0.35 (Toluene:CH_2Cl_2 4:1).
^{1}H NMR (400 MHz, $CDCl_3$) mixture of diastereoisomers 1.1(*A*):1(*B*) δ 5.04 (q, *J* = 5.8 Hz, 1H, C*H*CF_3 *A*), 4.93 (q, *J* = 5.4 Hz, 1H, C*H*CF_3 *B*), 4.42 – 4.34 (m, 1H, OC*H A*), 4.13 – 4.03 (m, 1H, OC*H B*), 3.46 (ddd, *J* = 12.0, 5.7, 1.4 Hz, 1H, C*H*$_2$N *B*), 3.36 – 3.20 (m, 2H, C*H*$_2$N *A*), 3.00 – 2.85 (m, 2H, C*H*$_2$N *B* and N*H*), 2.81 (dd, *J* = 16.7, 4.7 Hz, 1H, C*H*$_2$CC *B*), 2.69 (bs, 1H, N*H*), 2.58 (dd, *J* = 17.1, 5.6 Hz, 1H, C*H*$_2$CC *A*), 2.53 – 2.41 (m, 2H, C*H*$_2$CC *A* + *B*), 1.10 – 0.97 (m, 42H, TIPS).
^{13}C NMR (101 MHz, $CDCl_3$) δ 123.5 (d, *J* = 283.6 Hz), 123.3 (d, *J* = 282.5 Hz), 104.0, 103.1, 88.7 (d, *J* = 33.8 Hz), 88.5 (d, *J* = 34.0 Hz), 83.4, 83.3, 77.7, 76.1, 51.0, 49.7, 26.3, 24.8, 18.7, 18.7, 11.3.[25]
IR ν_{max} 2946 (w), 2896 (w), 2866 (w), 2254 (w), 2171 (w), 1513 (w), 1464 (w), 1383 (w), 1290 (w), 1251 (w), 1174 (w), 1150 (w), 1119 (w), 1092 (w), 1034 (w), 994 (w), 993 (w), 908 (s), 732 (s).
HRMS (ESI) calcd for $C_{16}H_{29}F_3NOSi^+$ $[M+H]^+$ 336.1965; found 336.1967.

1-((4-Methoxybenzyl)(2,2,2-trifluoroethyl)amino)-5-(triisopropylsilyl)pent-4-yn-2-ol (12)



9ba **12**

Following a slightly modified procedure,[26] a 1.0 M solution of DIBAL-H in hexanes (0.59 ml, 0.59 mmol, 3.0 eq) was added over 20 min into a solution of 3-(4-methoxybenzyl)-2-(trifluoromethyl)-5-(3-(triisopropylsilyl)prop-2-yn-1-yl)oxazolidine (**9ba**) (91 mg, 0.20 mmol, 1.0 eq, 1.1:1 dr) in dry toluene (1.5 ml) at -78 °C under nitrogen. The reaction mixture was allowed to slowly warm up to -25 °C and stirred at this temperature for 12 h. The reaction was quenched by slow addition of EtOAc (2 mL) at -25 °C and then an aqueous solution of Roch salt sat. (1.5 mL) at 0 °C and stirred for further 45 min. The mixture was extracted with EtOAc (2x10 mL). The combined organic phase was dried over $MgSO_4$, filtered and concentrated under reduced pressure, affording the pure title compound **12** (86 mg, 0.19 mmol, 95 % yield) as a colourless oil, without any further purification.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24 – 7.18 (m, 2H, Ar*H*), 6.90 – 6.84 (m, 2H, Ar*H*), 3.86 (d, *J* = 13.6 Hz, 1H, C*H*$_2$Ph), 3.82 – 3.75 (m, 1H, OC*H*), 3.80 (s, 3H, OC*H*$_3$), 3.72 (d, *J* = 13.6 Hz, 1H, C*H*$_2$Ph), 3.16 (qd, *J* = 9.4, 3.7 Hz, 2H, C*H*$_2$$CF_3$), 2.98 (dd, *J* = 13.3, 3.7 Hz, 1H, NC*H*$_2$), 2.77 – 2.65 (m, 2H, O*H* and NC*H*$_2$), 2.53 (dd, *J* = 16.8, 5.2 Hz, 1H, C*H*$_2$CC), 2.38 (dd, *J* = 16.8, 7.1 Hz, 1H, C*H*$_2$CC), 1.12 – 0.92 (m, 21H, TIPS).

[25] One TIPS signal did not split.
[26] Kielland, N., Vicente-García, E., Revés, M., Isambert, N., Arévalo, M. J. and Lavilla, R. *Adv. Synth. Catal*, **2013,** *355*, 3273.

^{13}C NMR (101 MHz, $CDCl_3$) δ 159.3, 130.3, 129.6, 125.9 (q, *J* = 281.6 Hz), 114.1, 104.1, 83.6, 67.2, 60.0, 58.8, 55.3, 54.6 (q, *J* = 30.2 Hz), 25.9, 18.7, 11.3.
IR ν_{max} 3525 (w), 3465 (w), 2943 (m), 2898 (w), 2865 (m), 2173 (w), 1613 (w), 1588 (w), 1514 (m), 1464 (m), 1419 (w), 1377 (w), 1304 (m), 1250 (s), 1176 (m), 1143 (s), 1085 (s), 1036 (s), 930 (w), 884 (m), 818 (m), 741 (m).
HRMS (ESI) calcd for $C_{24}H_{39}F_3NO_2Si^+$ $[M+H]^+$ 458.2697; found 458.2694.

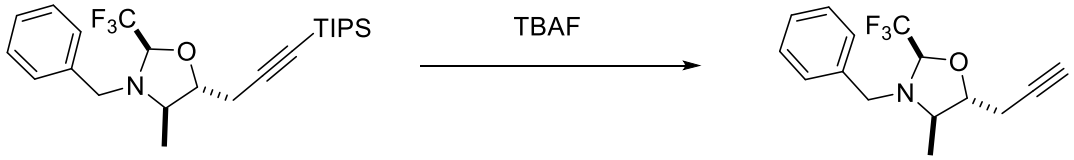
3-(4-Methoxybenzyl)-5-(prop-2-yn-1-yl)-2-(trifluoromethyl)oxazolidine (13)

9ba **13**

To a solution of 3-(4-methoxybenzyl)-2-(trifluoromethyl)-5-(3-(triisopropylsilyl)prop-2-yn-1-yl)oxazolidine (**9ba**) (0.091 g, 0.20 mmol, 1.0 eq, 1.1:1 dr) in THF (2.2 ml) at rt was added a 1.0 M solution of TBAF in THF (0.40 ml, 0.40 mmol, 2.0 eq). The reaction mixture was stirred for 30 min (TLC monitoring). The reaction was quenched by addition of an aqueous solution of NH_4Cl sat, diluted with diethyl ether (30 mL). The organic phase was washed with brine (2x5 mL), dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude residue was purified by preparative TLC (SiO_2, Heptane:CH_2Cl_2 1:1) affording the title compound **13** (0.057 g, 0.19 mmol, 95 % yield, 1.15: 1 dr by integration of the OC*H* peak in the ^{1}H NMR) as a colourless oil.

R_f 0.45 (Pentane:CH_2Cl_2 1:1).
^{1}H NMR (400 MHz, $CDCl_3$) mixture of diastereoisomers 1.15(*A*):1(*B*) δ 7.30 – 7.23 (m, 4H, Ar*H A* + *B*), 6.91 – 6.85 (m, 4H, Ar*H A* + *B*), 4.74 – 4.63 (m, 2H, C*H*CF_3 *A* + *B*), 4.46 – 4.36 (m, 1H, OC*H B*), 4.32 – 4.22 (m, 1H, OC*H A*), 4.10 (d, *J* = 12.9 Hz, 1H, CH_2Ph *B*), 3.91 (d, *J* = 13.0 Hz, 1H, CH_2Ph *A*), 3.84 – 3.77 (overlapping signals, 7H, CH_2Ph *A* and OCH_3 *A* + *B*), 3.71 (d, *J* = 12.9 Hz, 1H, CH_2Ph *B*), 3.32 (dd, *J* = 9.5, 5.8 Hz, 1H, CH_2N *B*), 3.15 (ddd, *J* = 12.0, 5.8, 1.4 Hz, 1H, CH_2N *A*), 3.01 (ddd, *J* = 11.8, 8.1, 1.4 Hz, 1H, CH_2N *A*), 2.68 – 2.55 (m, 3H, CH_2N *B* and CH_2CC *A* + *B*), 2.49 (ddd, *J* = 16.8, 7.0, 2.7 Hz, 1H, CH_2CC *B*), 2.40 (ddd, *J* = 16.6, 7.9, 2.7 Hz, 1H, CH_2CC *A*), 2.01 (t, *J* = 2.7 Hz, 1H, CC*H B*), 1.99 (t, *J* = 2.7 Hz, 1H, CC*H B*).
^{13}C NMR (101 MHz, $CDCl_3$) δ 159.3, 159.2, 130.0, 129.9, 129.8, 129.6, 123.8 (d, *J* = 284.8 Hz), 123.4 (d, *J* = 283.3 Hz), 114.1, 114.0, 92.7 (q, *J* = 33.6 Hz), 91.6 (q, *J* = 33.3 Hz), 79.7, 79.4, 77.1, 75.5, 70.9, 70.4, 59.1, 58.6, 56.4 (2C), 55.4 (2C), 23.7, 23.7.
IR ν_{max} 3381 (w), 2943 (m), 2867 (m), 2173 (w), 1613 (w), 1514 (m), 1464 (w), 1250 (s), 1143 (s), 1087 (m), 1031 (s), 884 (w), 824 (w), 738 (w).
HRMS (APPI) calcd for $C_{15}H_{16}F_3NO_2$ [M+] 299.1133; found 299.1140.

3-Benzyl-4-methyl-5-(prop-2-yn-1-yl)-2-(trifluoromethyl)oxazolidine (14)

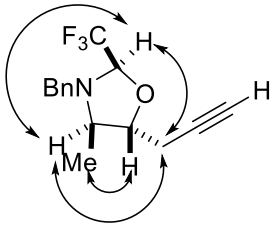


9ka **14**

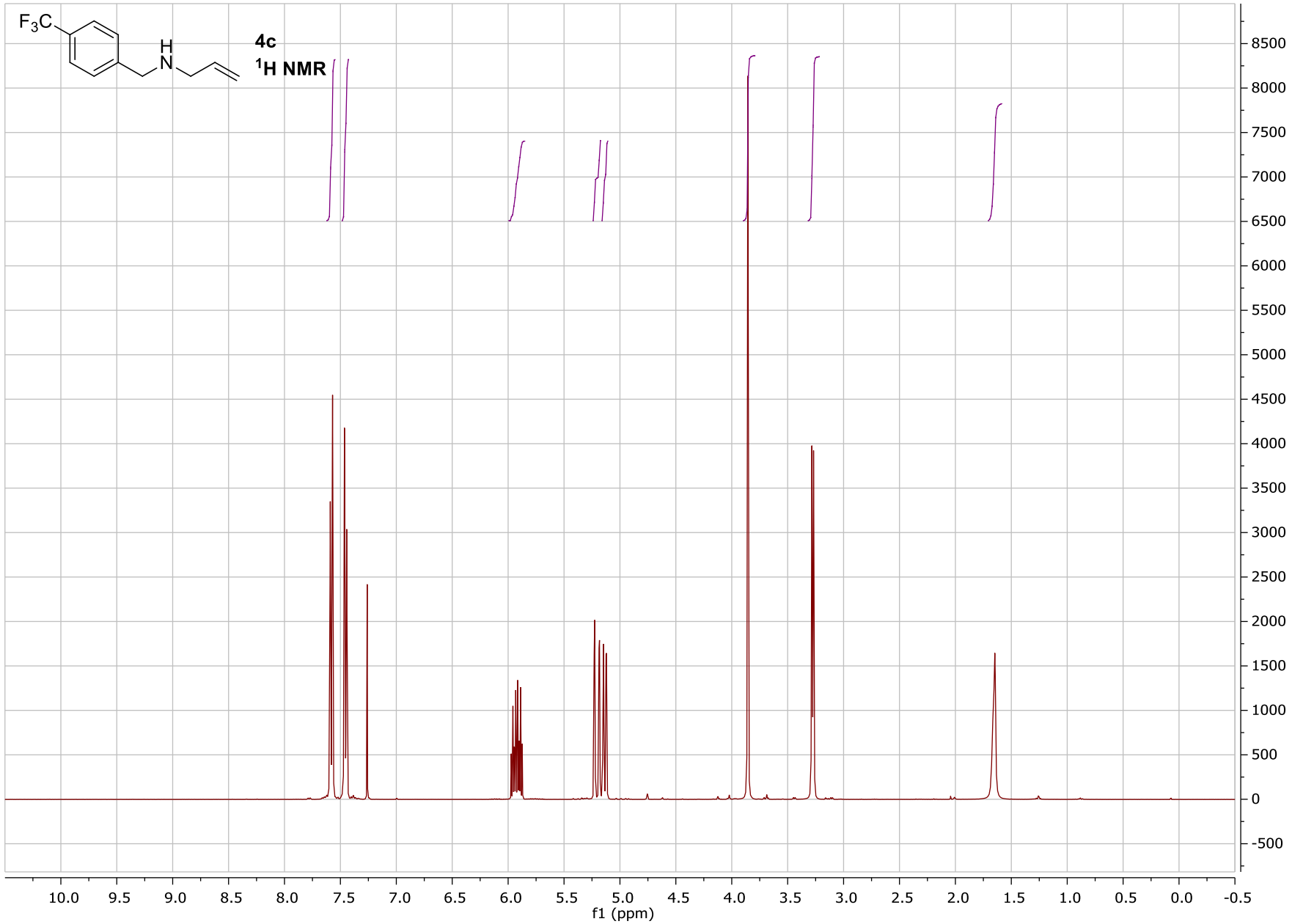
To a solution of 3-benzyl-4-methyl-2-(trifluoromethyl)-5-(3-(triisopropylsilyl)prop-2-yn-1-yl)oxazolidine (**9ba**) (33 mg, 0.075 mmol, 1.0 eq, 21.8:1.1:1) in THF (0.80 mL) at rt was added was added a 1.0 M solution of TBAF in THF (0.15 mL, 0.15 mmol, 2.0 eq). The reaction mixture was stirred for 30 min (TLC monitoring). The reaction was quenched by addition of a solution of sat. NH_4Cl and diluted with diethyl ether (5 mL). The organic layer was washed with brine (2x2 mL), dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude residue was purified by column chromatography (SiO_2, Pentane:CH_2Cl_2 8:1 to 4:1) affording the title compound **14** (19 mg, 0.067 mmol, 89 % yield, 15.6:1 dr by integration of the C*H*CF_3 peak in the ^{1}H NMR) as a colourless oil.

R$_f$ 0.25 (Pentane:CH_2Cl_2 4:1).
^{1}H NMR (400 MHz, $CDCl_3$) main diastereoisomer δ 7.36 – 7.27 (m, 5H, Ar*H*), 4.73 (q, *J* = 5.0 Hz, 1H, C*H*CF_3), 4.08 (d, *J* = 14.0 Hz, 1H, C*H$_2$*Ph), 3.98 – 3.89 (m, 2H, OC*H* and C*H$_2$*Ph), 3.08 – 2.99 (m, 1H, NC*H*), 2.58 (ddd, *J* = 17.1, 5.7, 2.7 Hz, 1H, C*H$_2$*CC), 2.51 (ddd, *J* = 17.2, 4.8, 2.7 Hz, 1H, C*H$_2$*CC), 2.03 (t, *J* = 2.7 Hz, 1H, CC*H*), 1.01 (d, *J* = 6.1 Hz, 3H, Me).
^{13}C NMR (101 MHz, $CDCl_3$) δ ^{13}C NMR (101 MHz, $CDCl_3$) δ 137.7, 129.1, 128.5, 127.7, 123.8 (q, *J* = 284.7 Hz), 91.4 (q, *J* = 33.4 Hz), 83.1, 79.3, 71.0, 63.8, 58.0, 22.4, 18.0.
IR ν_{max} 2944 (m), 2895 (w), 2867 (m), 2180 (w), 1677 (w), 1462 (w), 1384 (w), 1292 (m), 1149 (s), 1082 (w), 1018 (w), 994 (w), 883 (w), 859 (w), 730 (w).
HRMS (ESI) calcd for $C_{15}F_3H_{17}NO^+$ $[M+H]^+$ 284.1257; found 284.1267.

Stereochemistry assigned by ROESY



6. Spectra of new compounds (^{1}HNMR, ^{13}CNMR, IR)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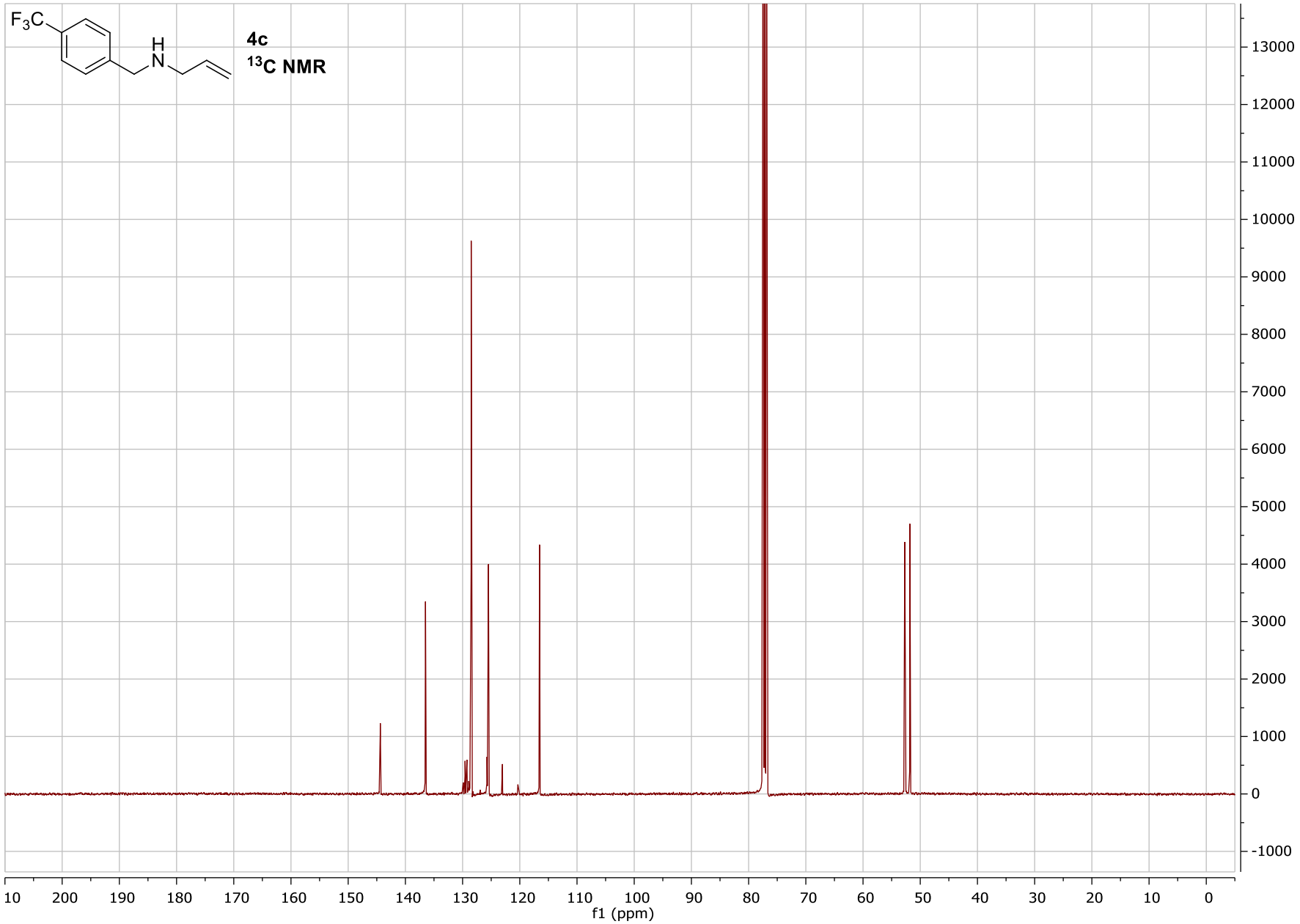
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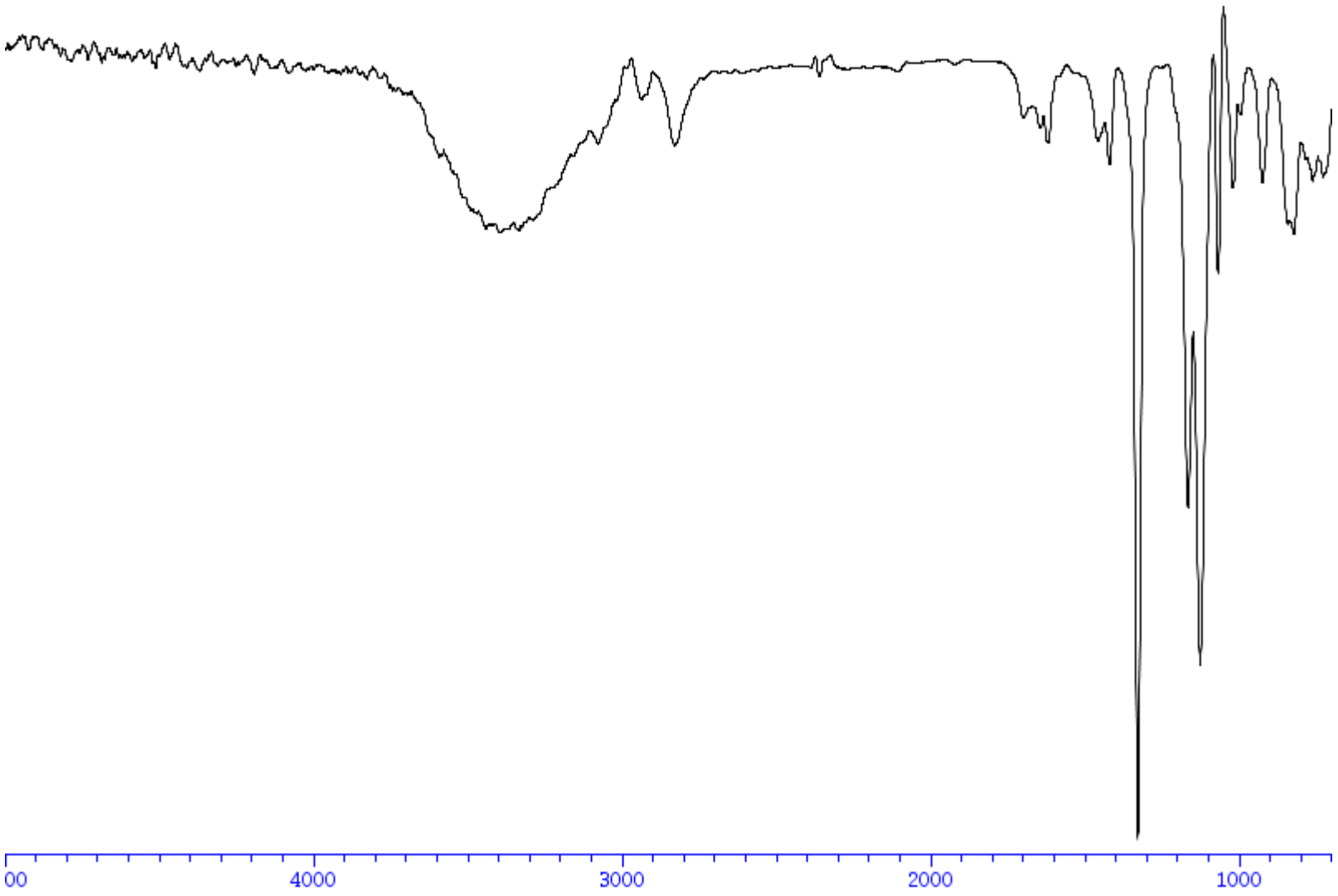
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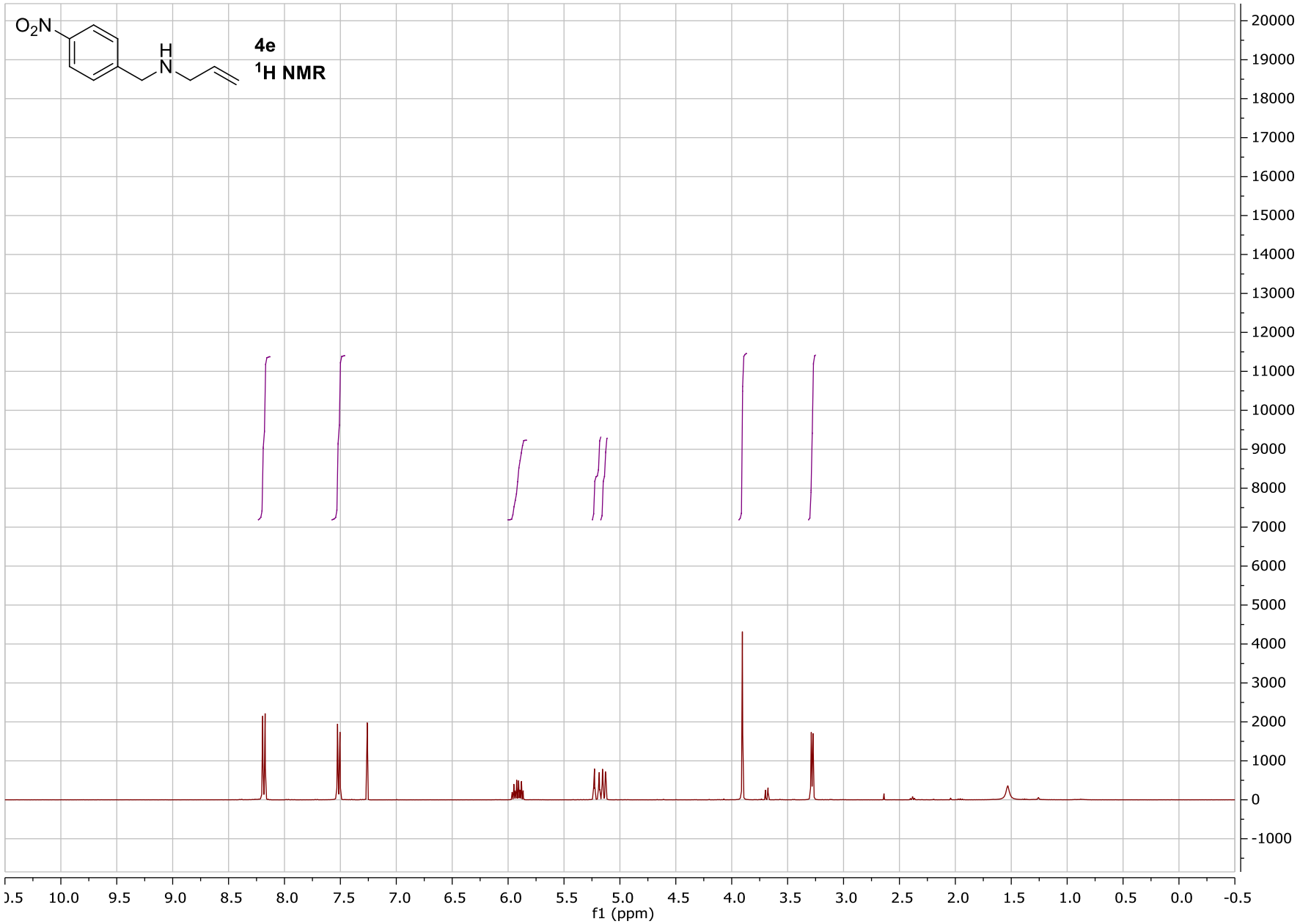
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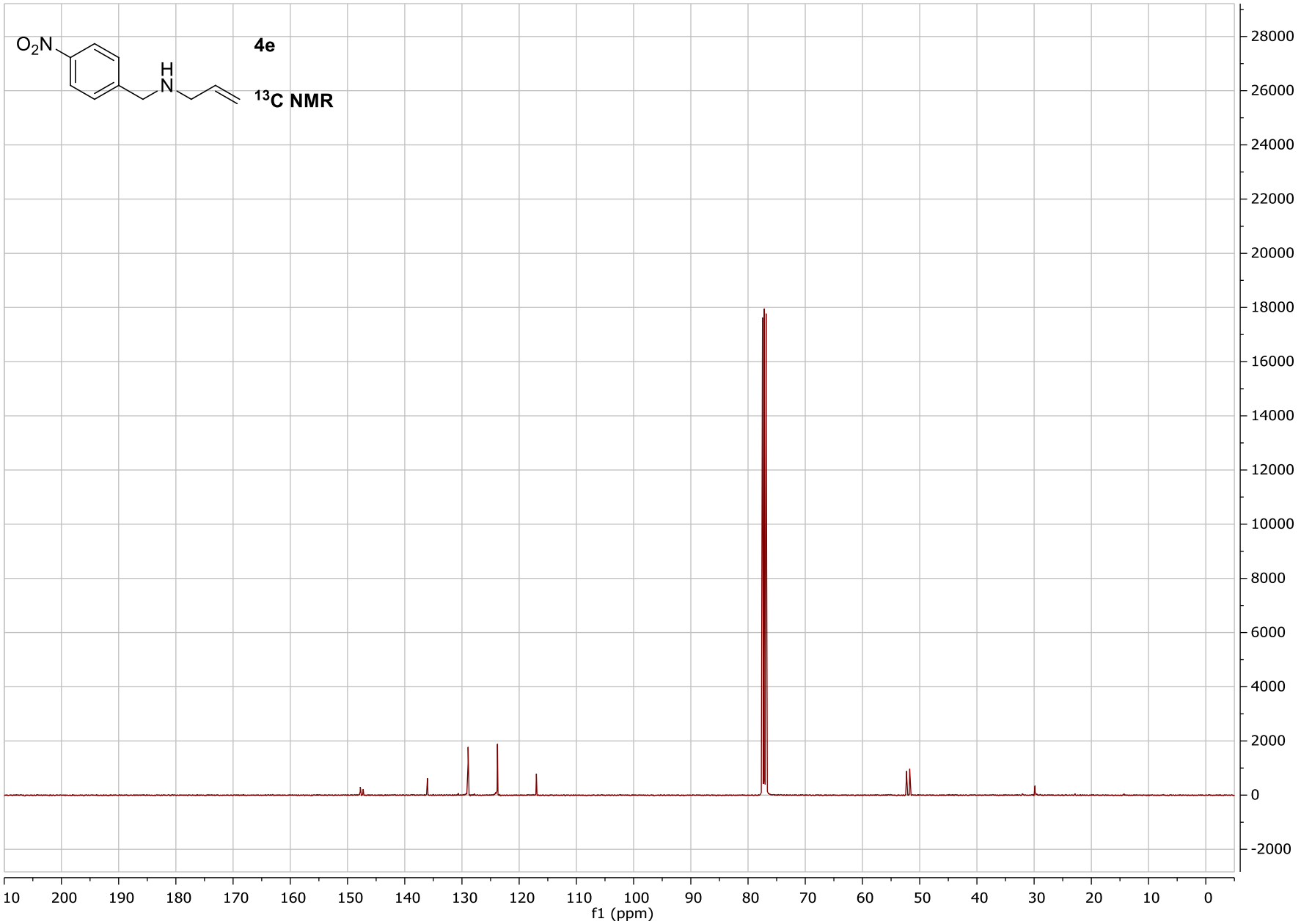
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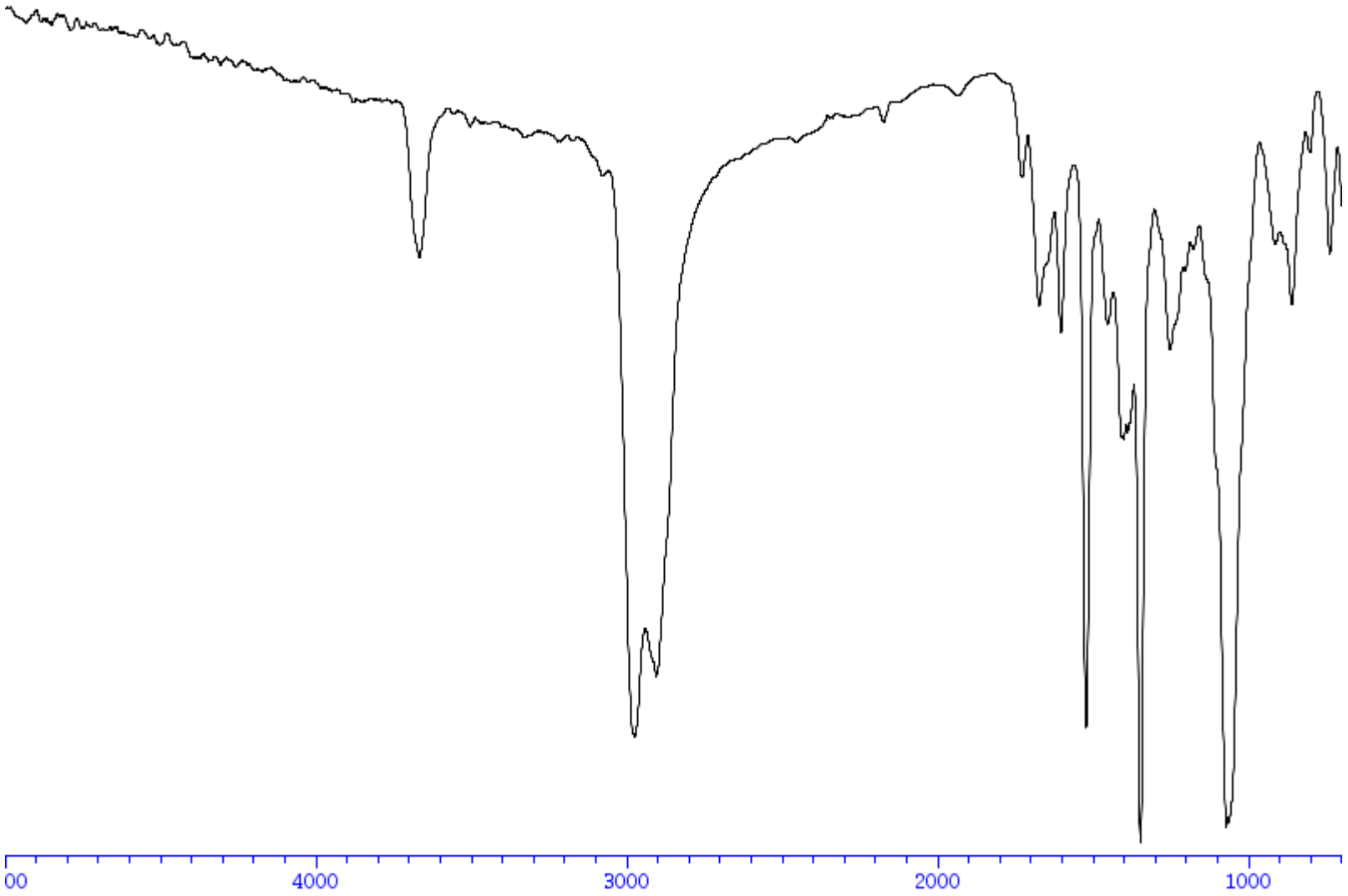
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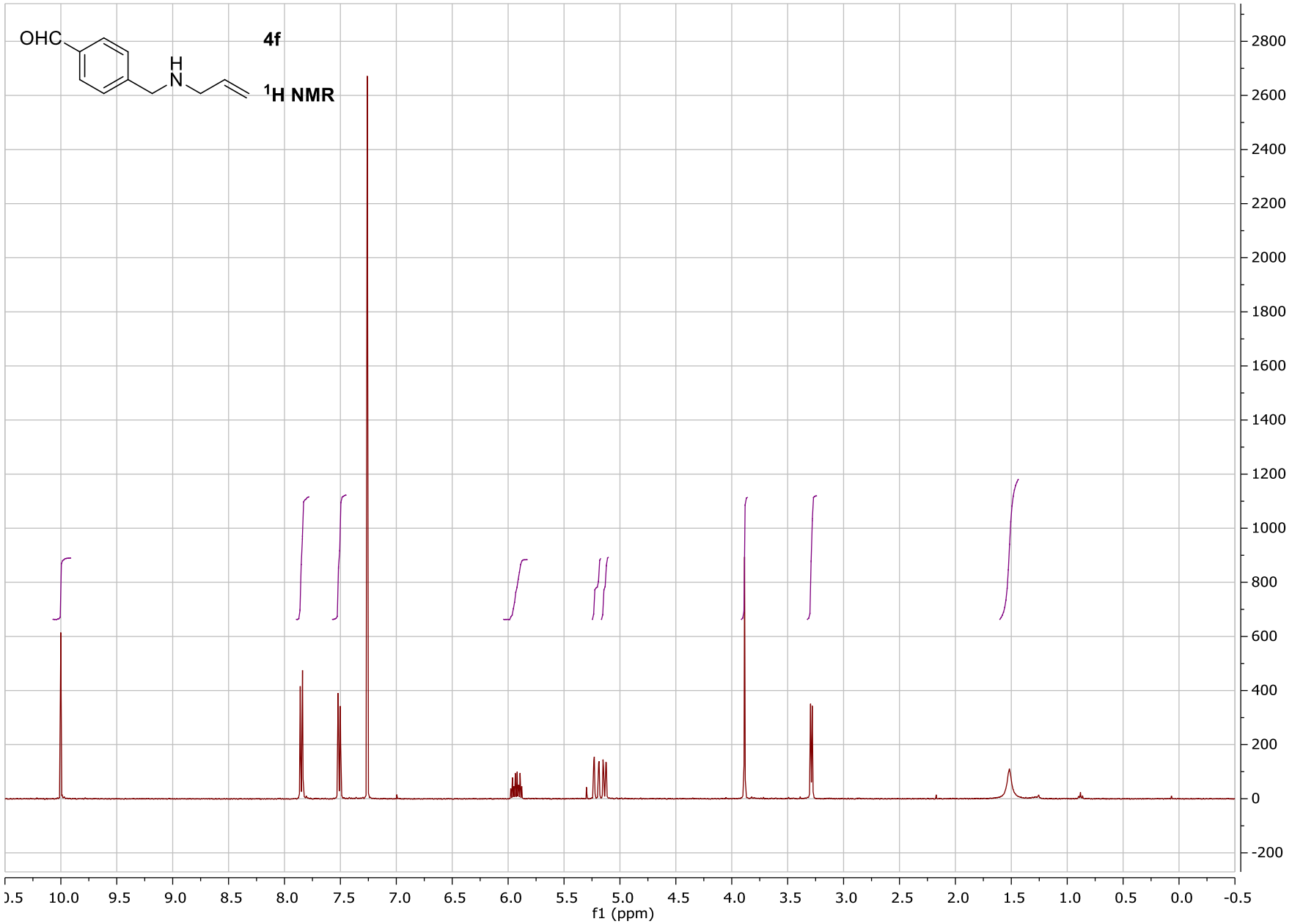
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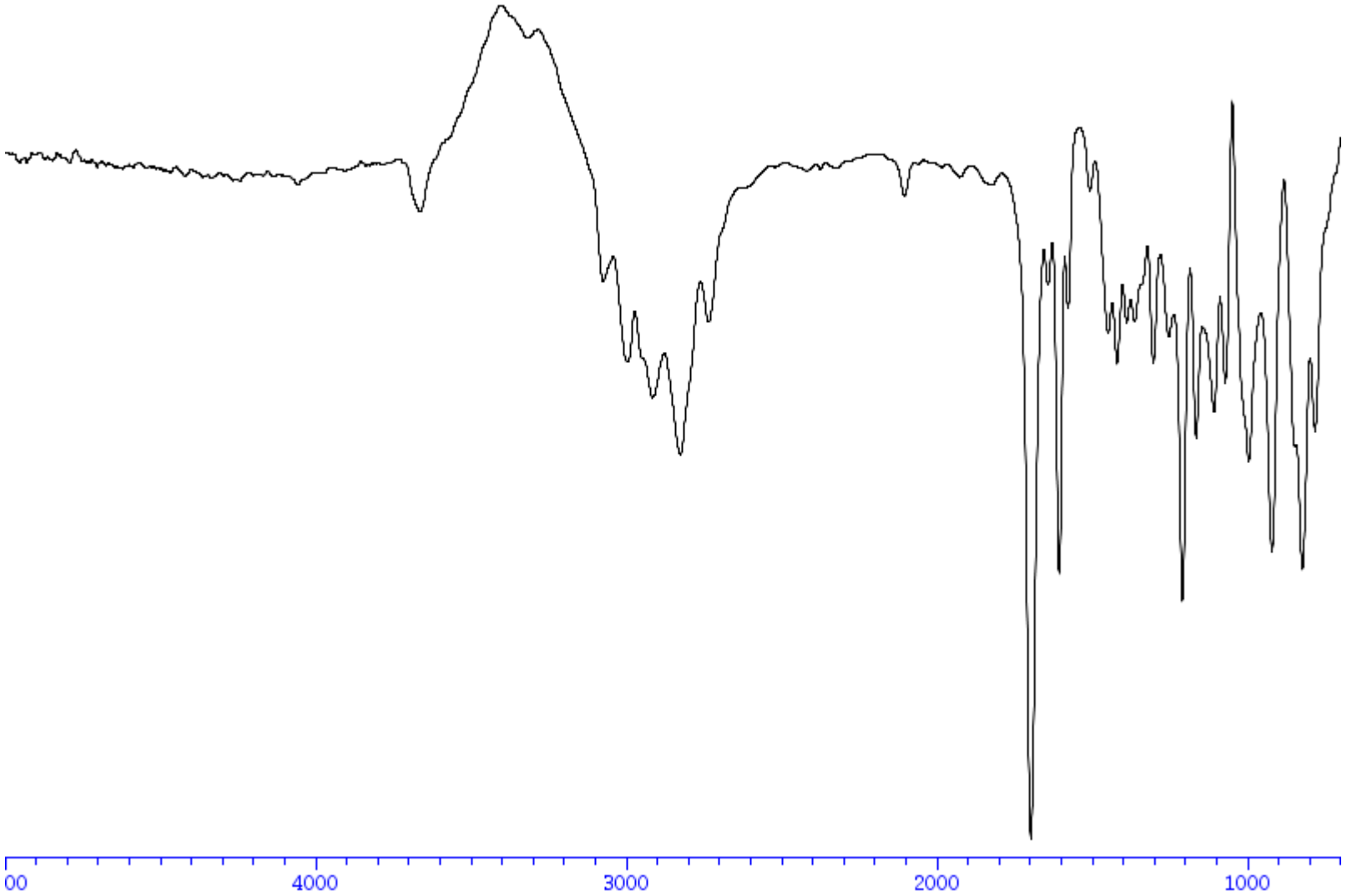
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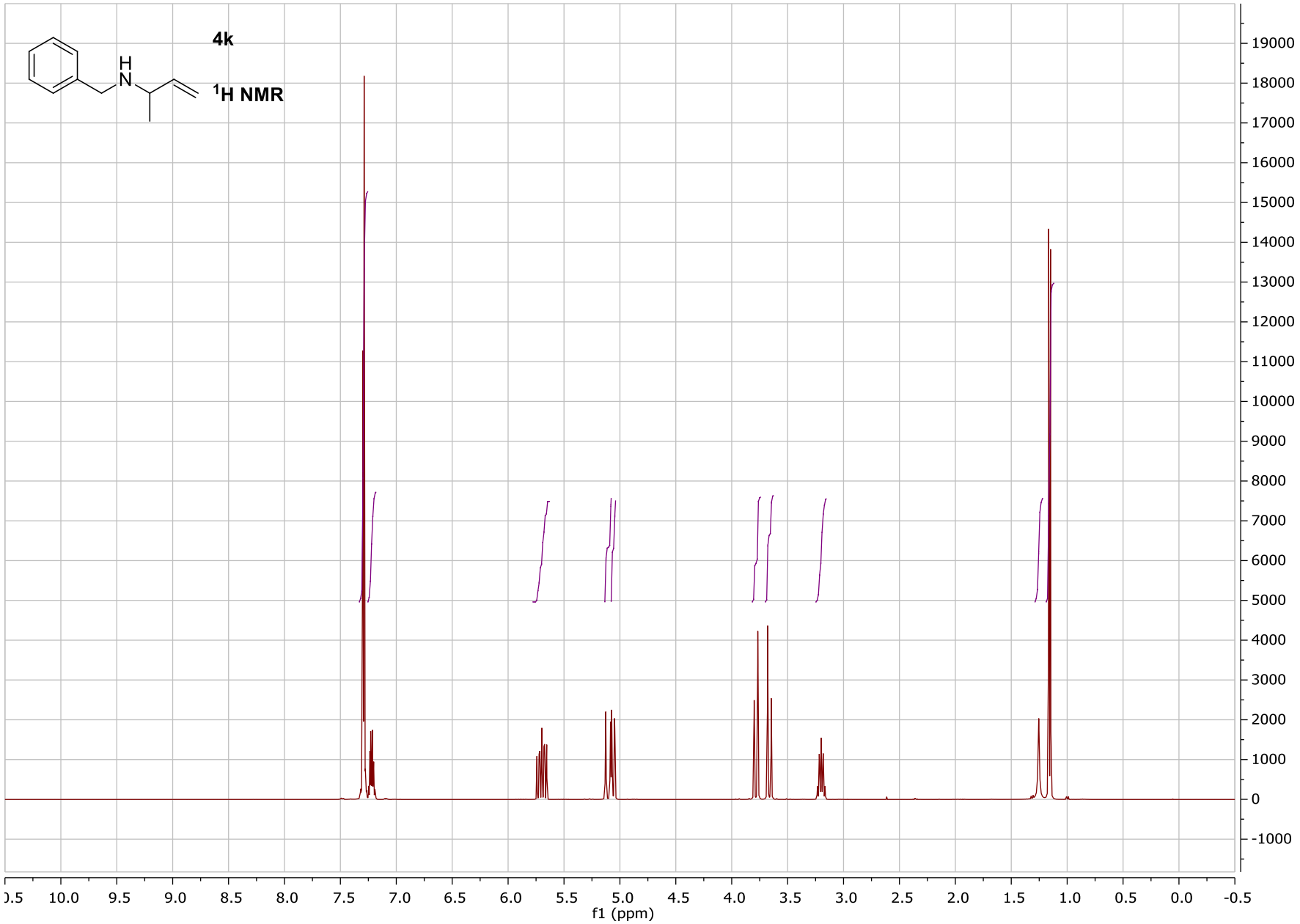
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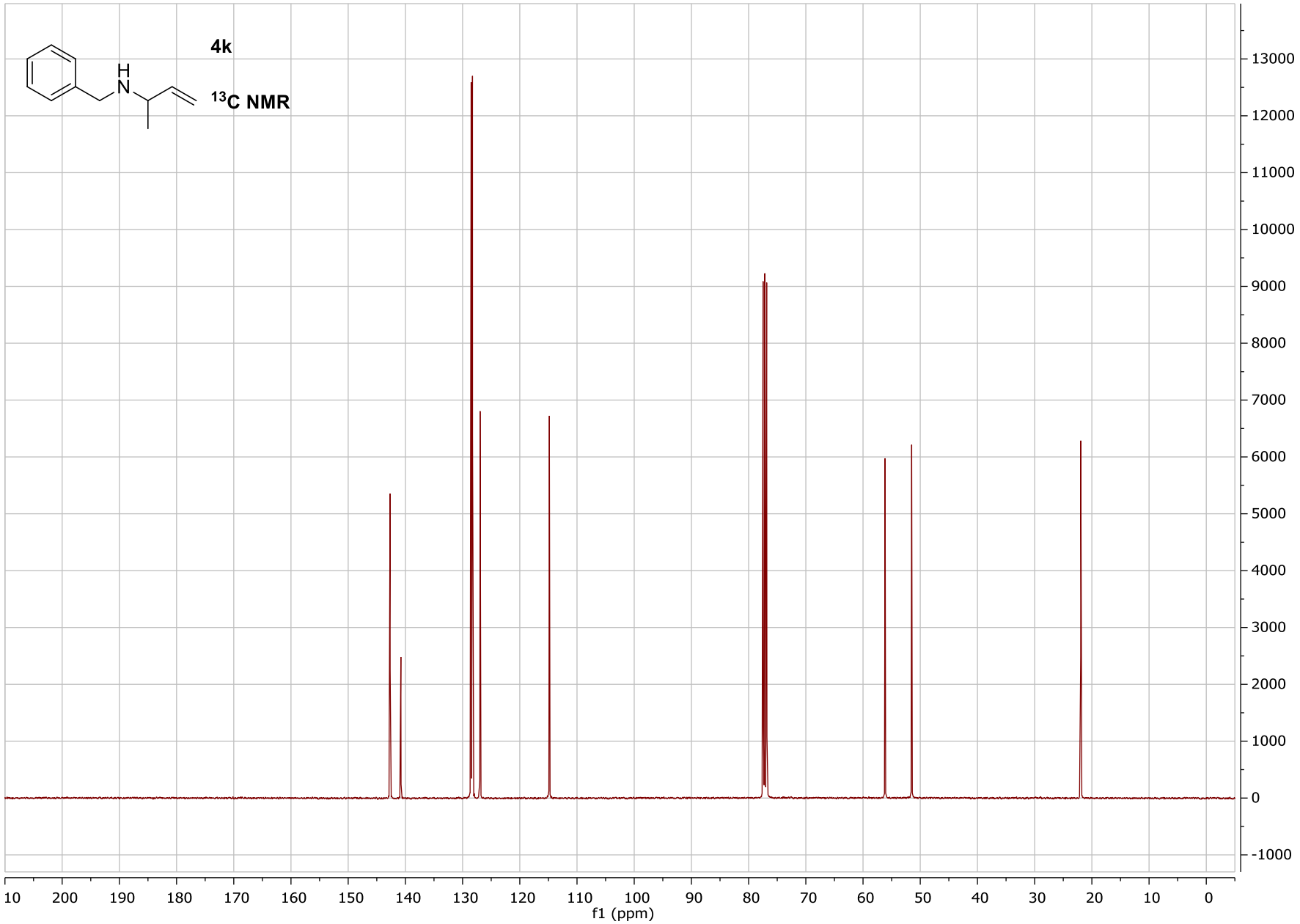
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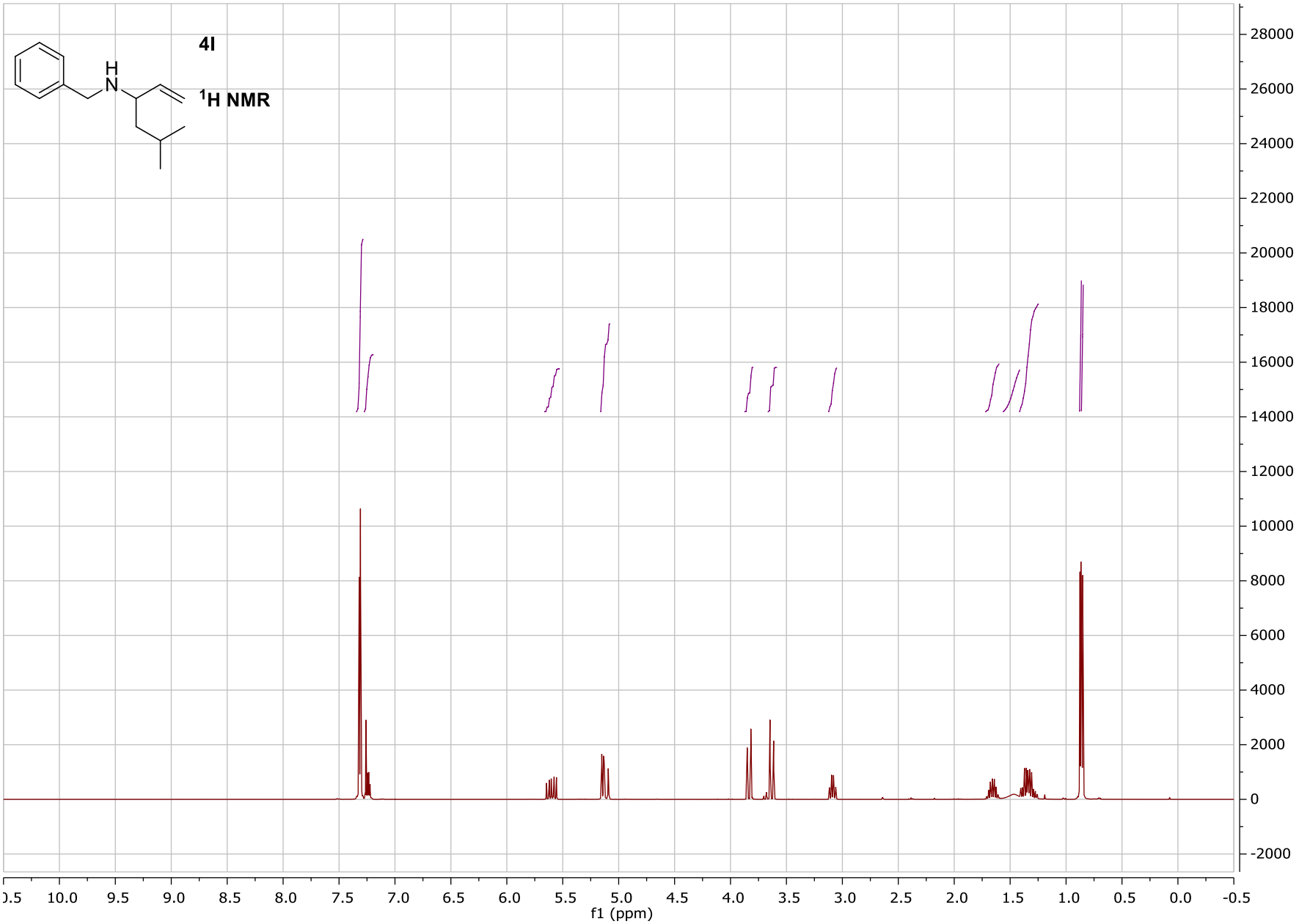
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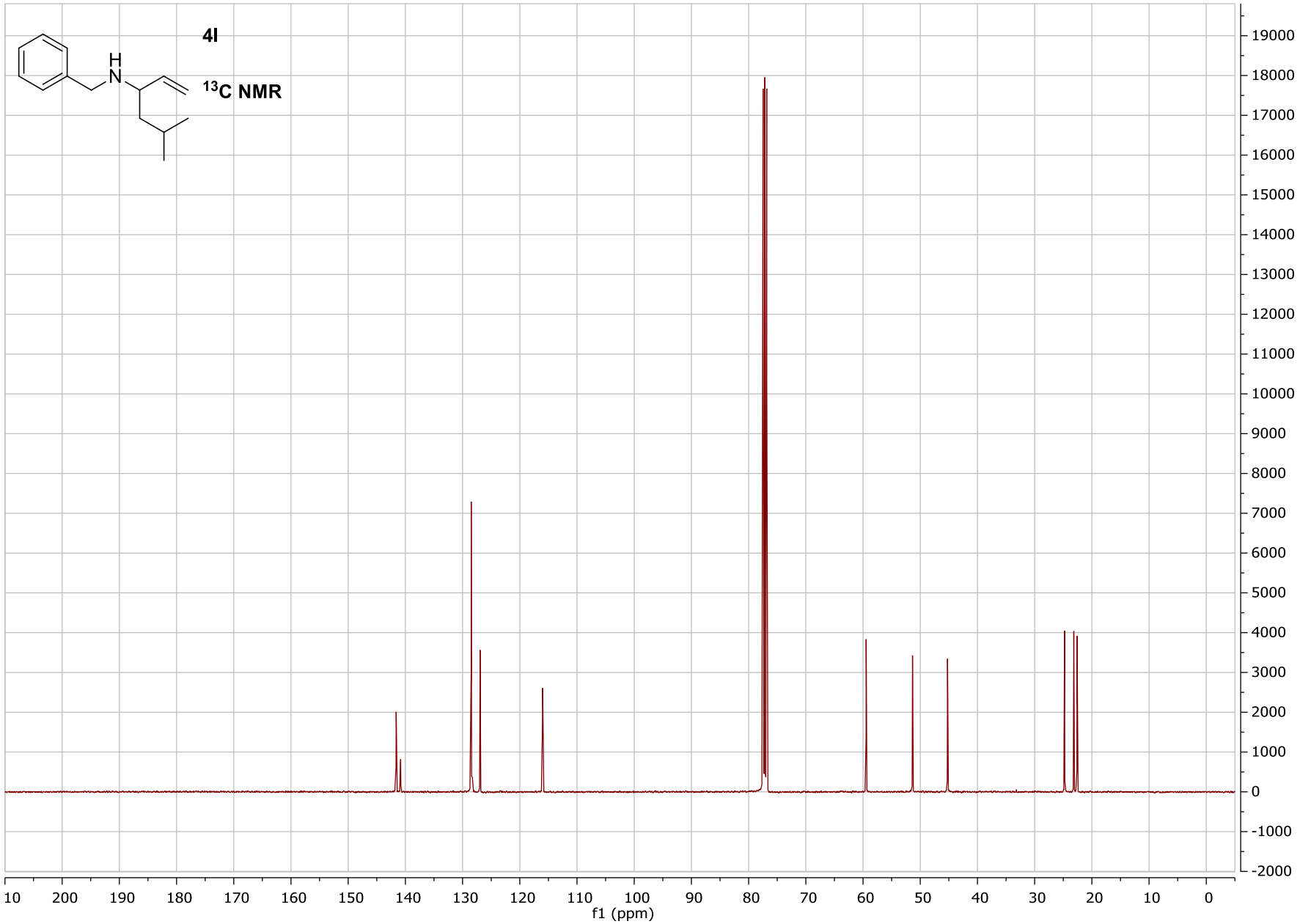
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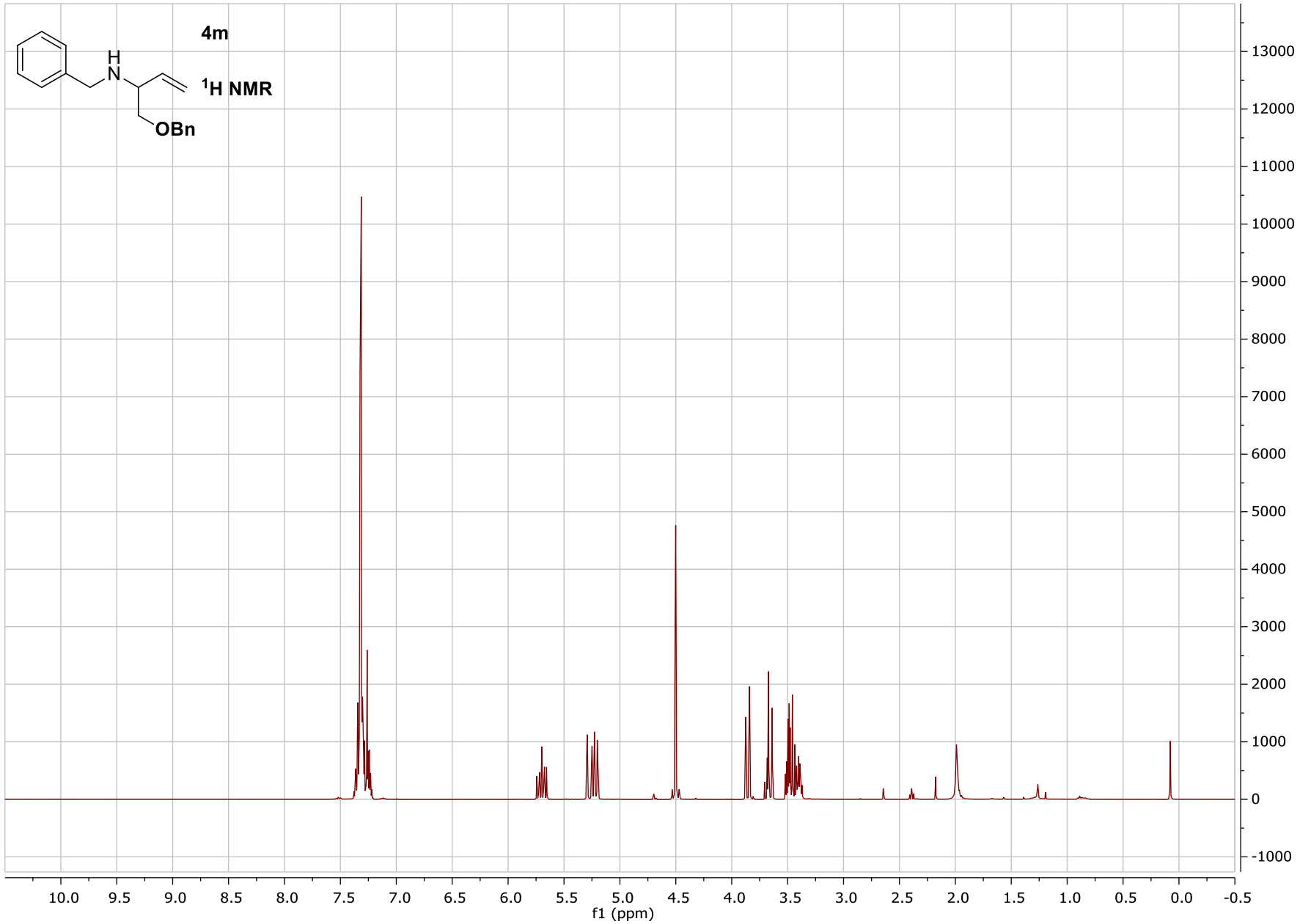
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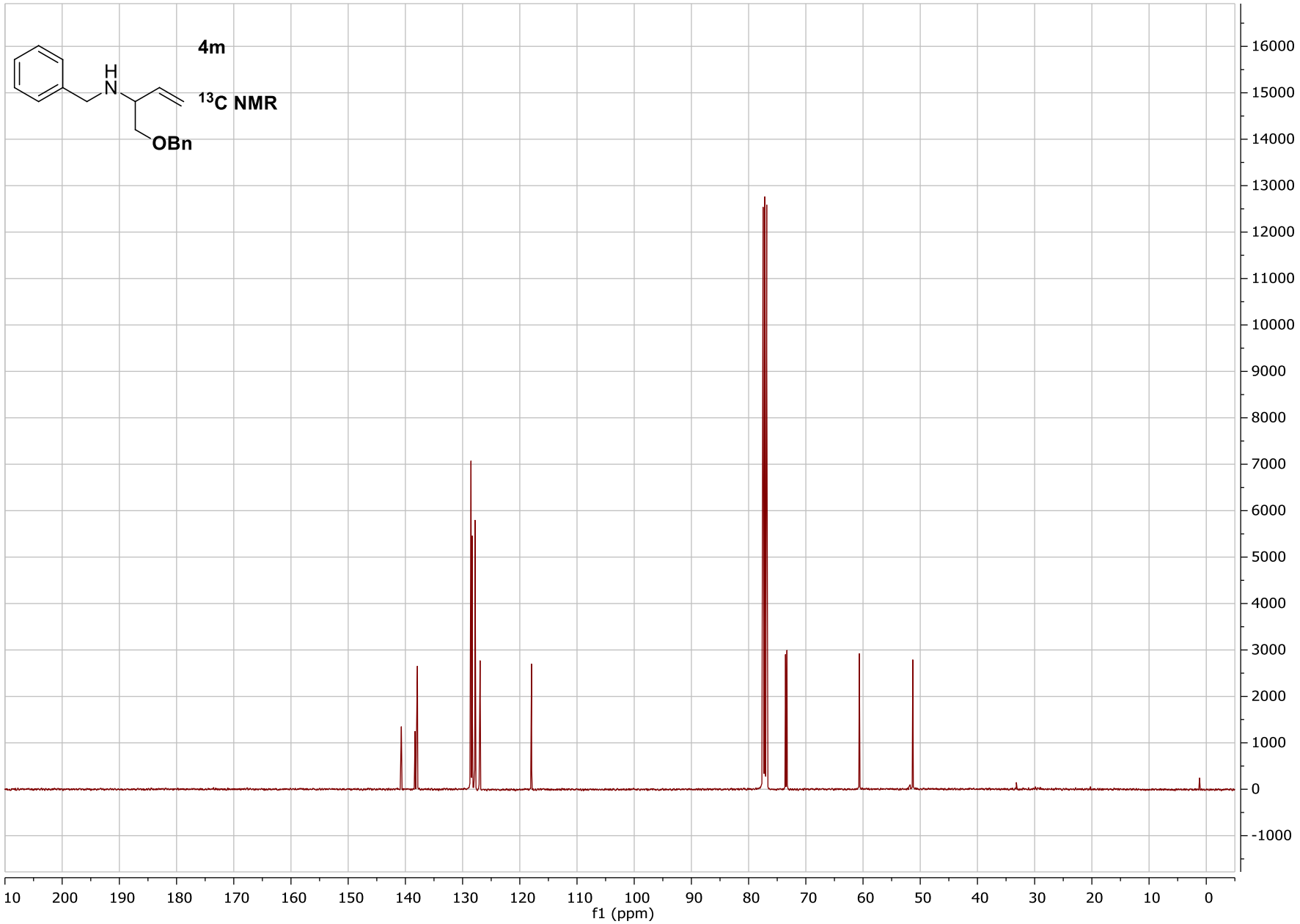
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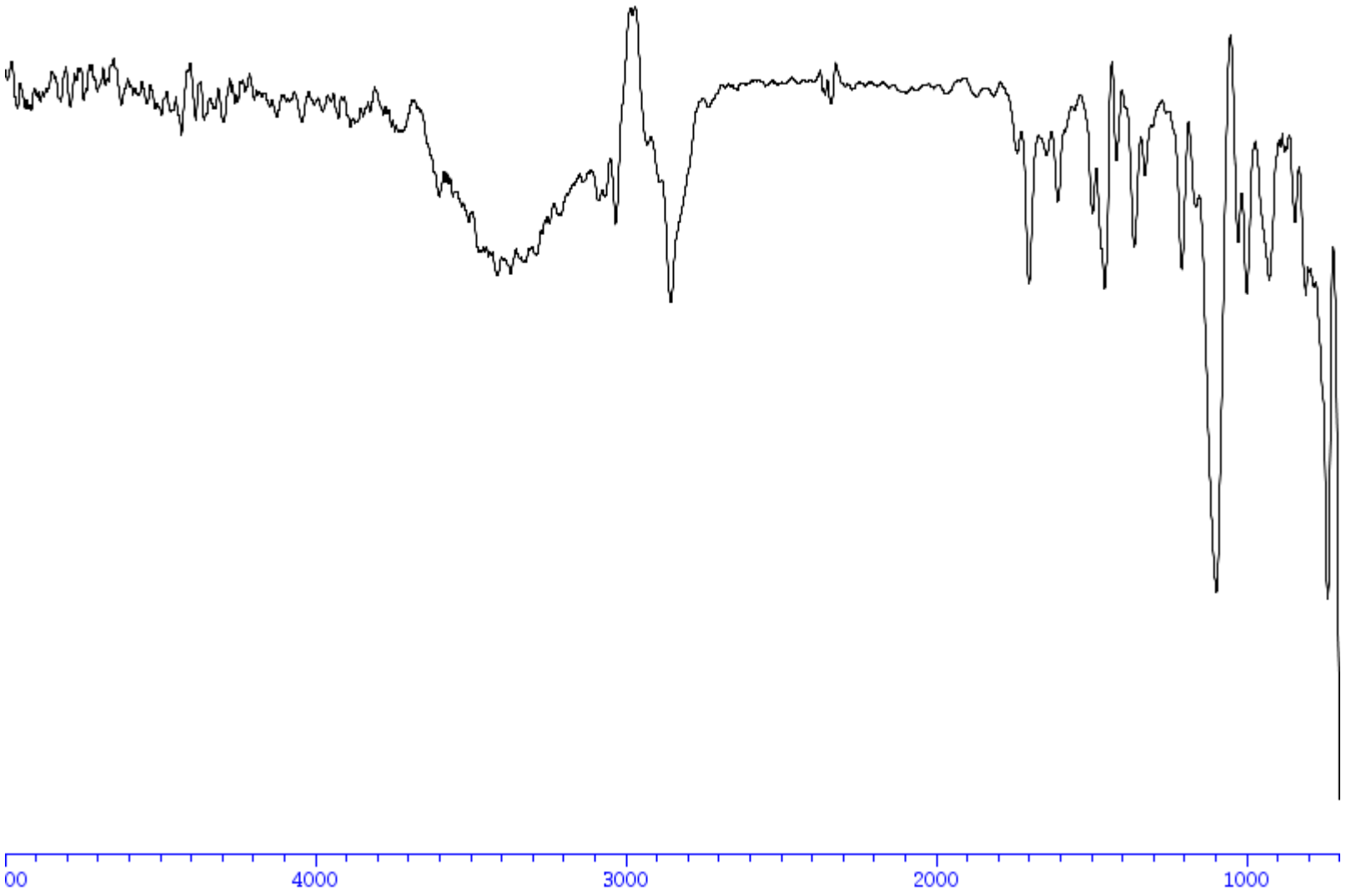
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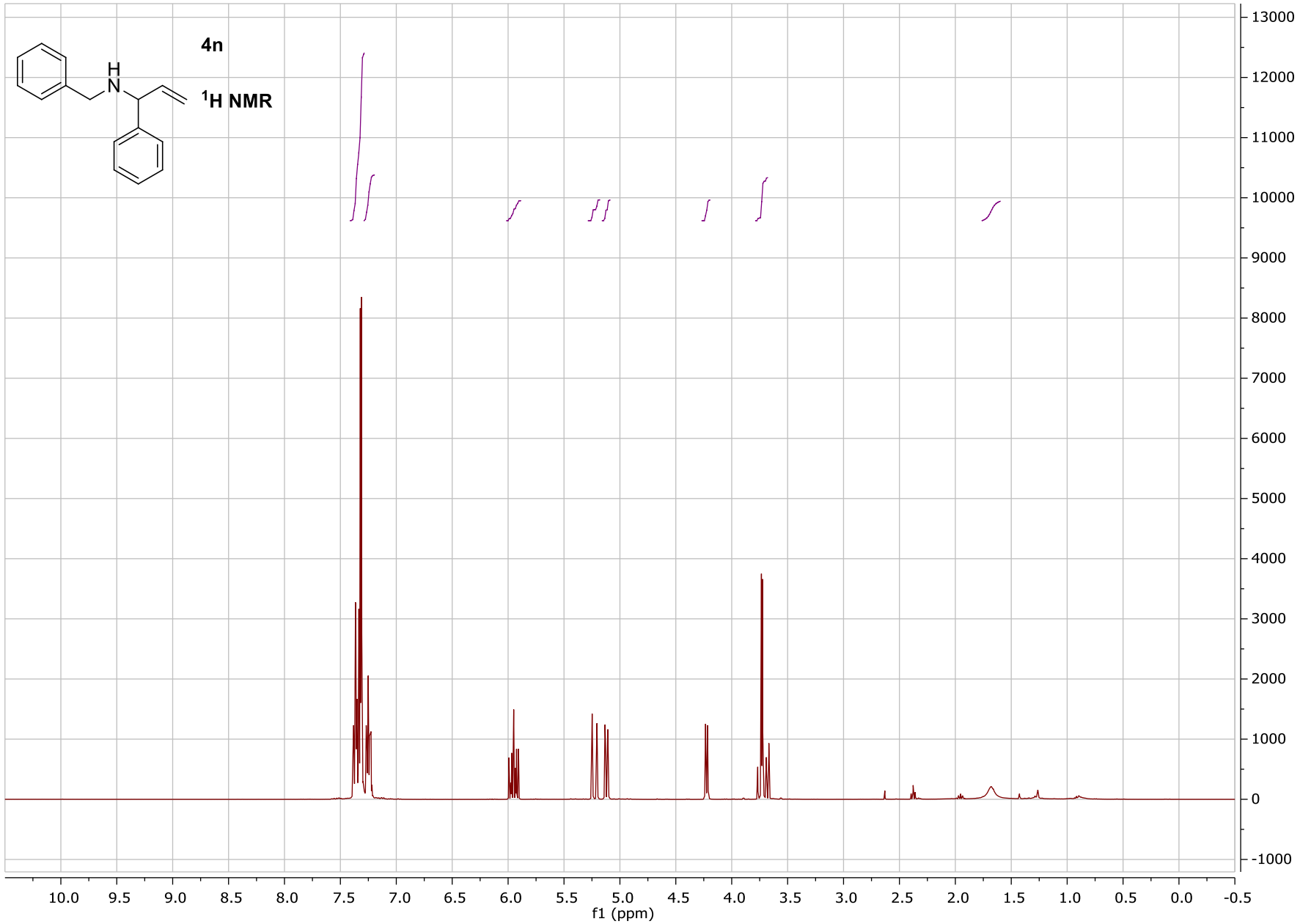
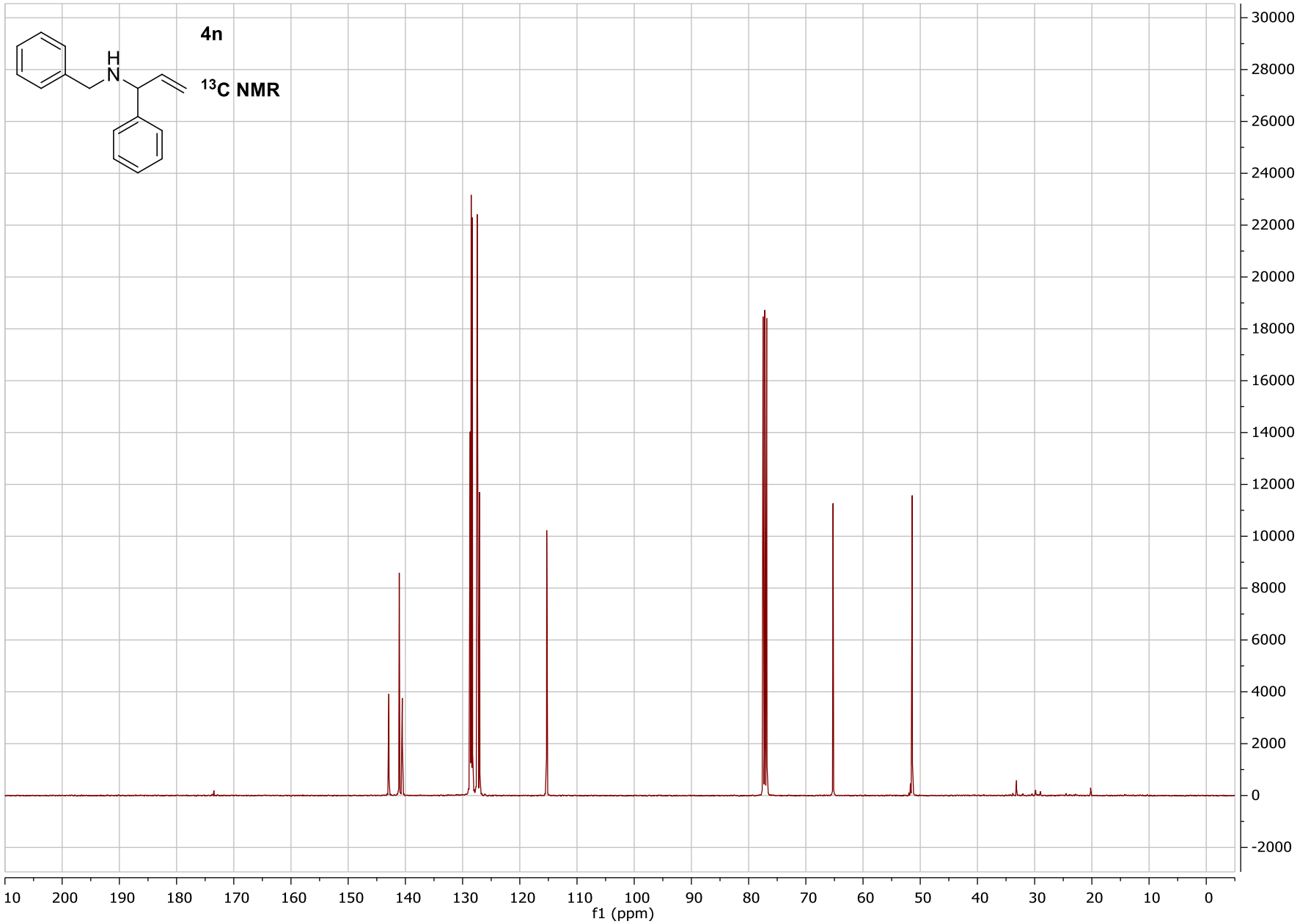
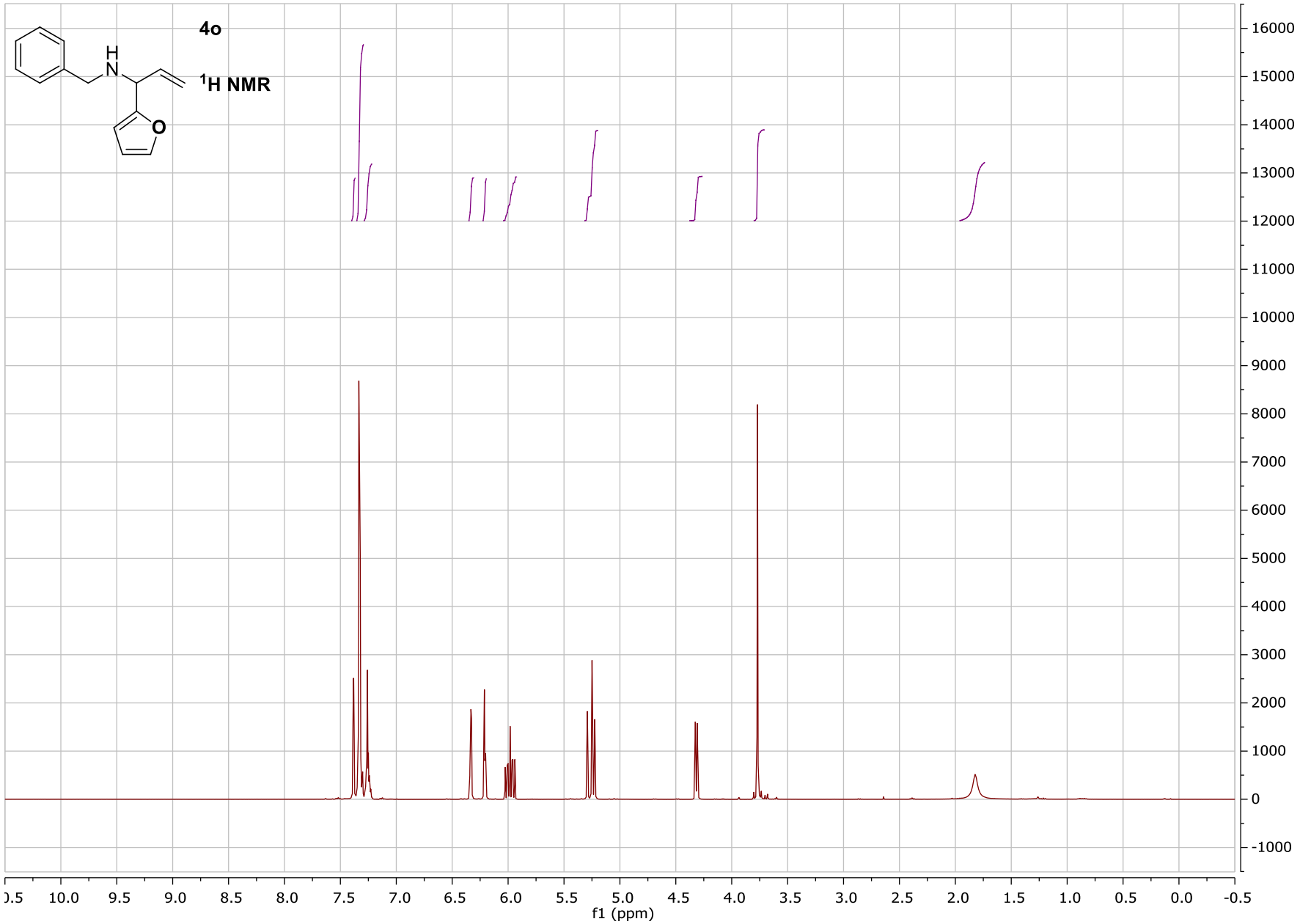
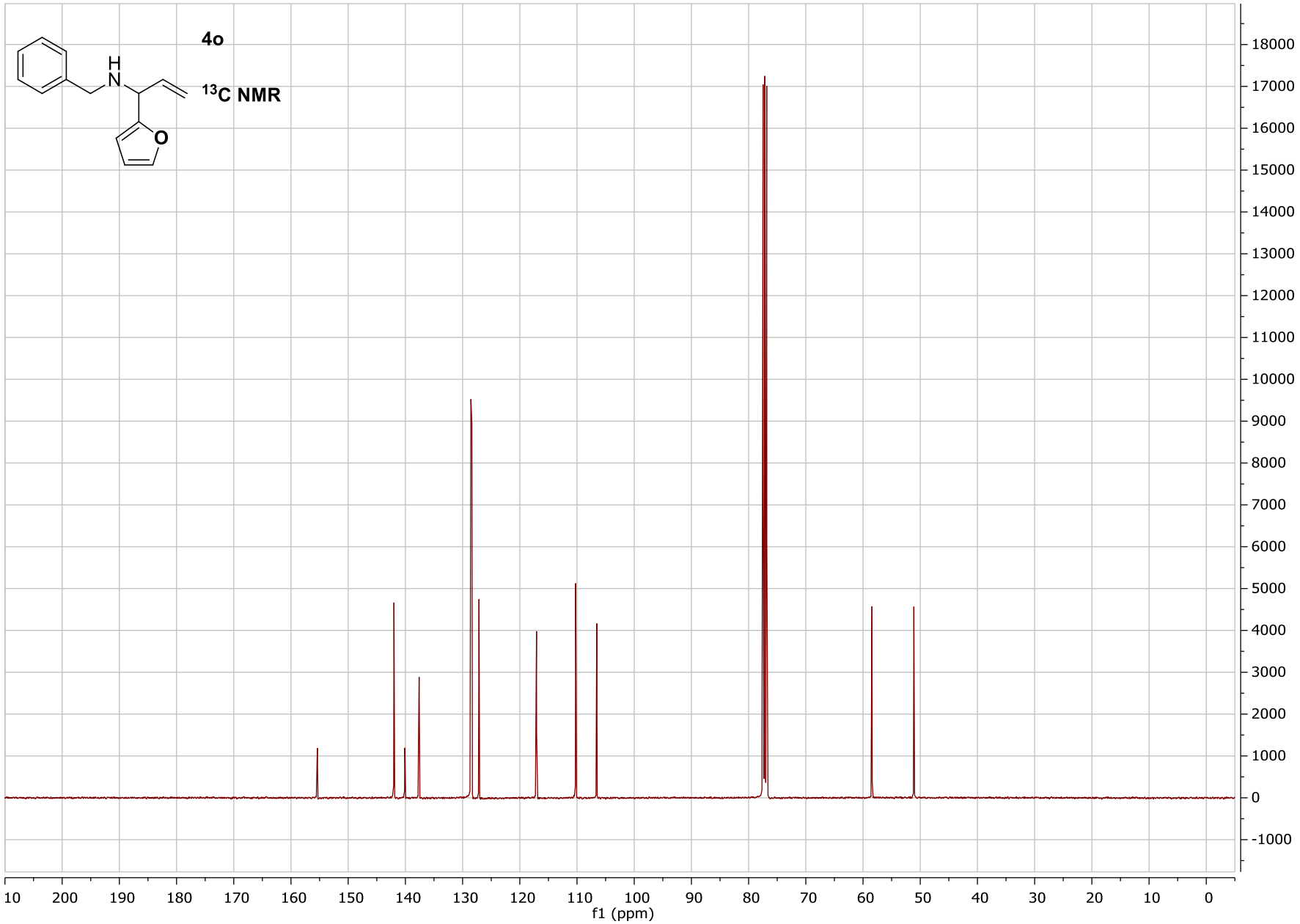
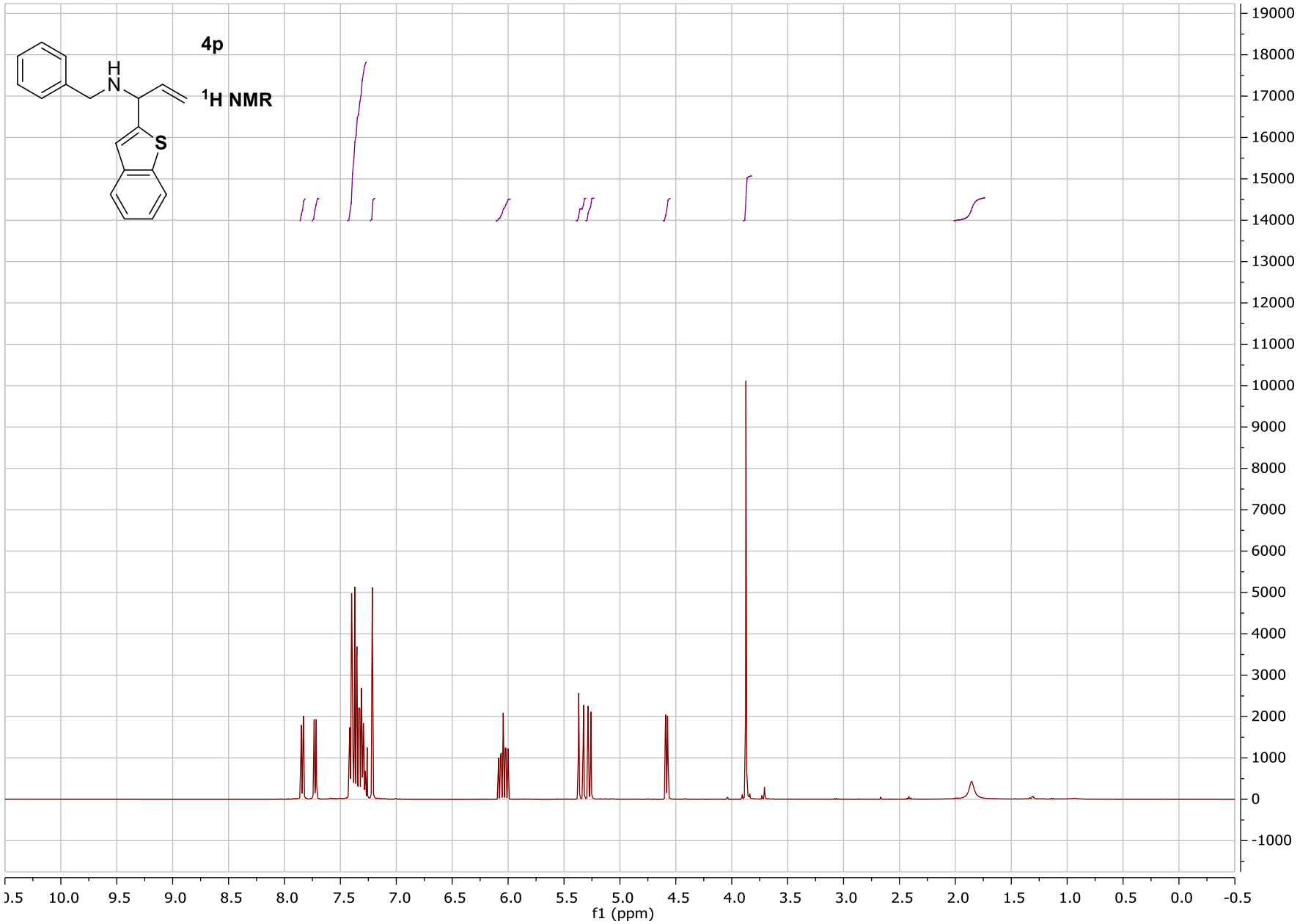
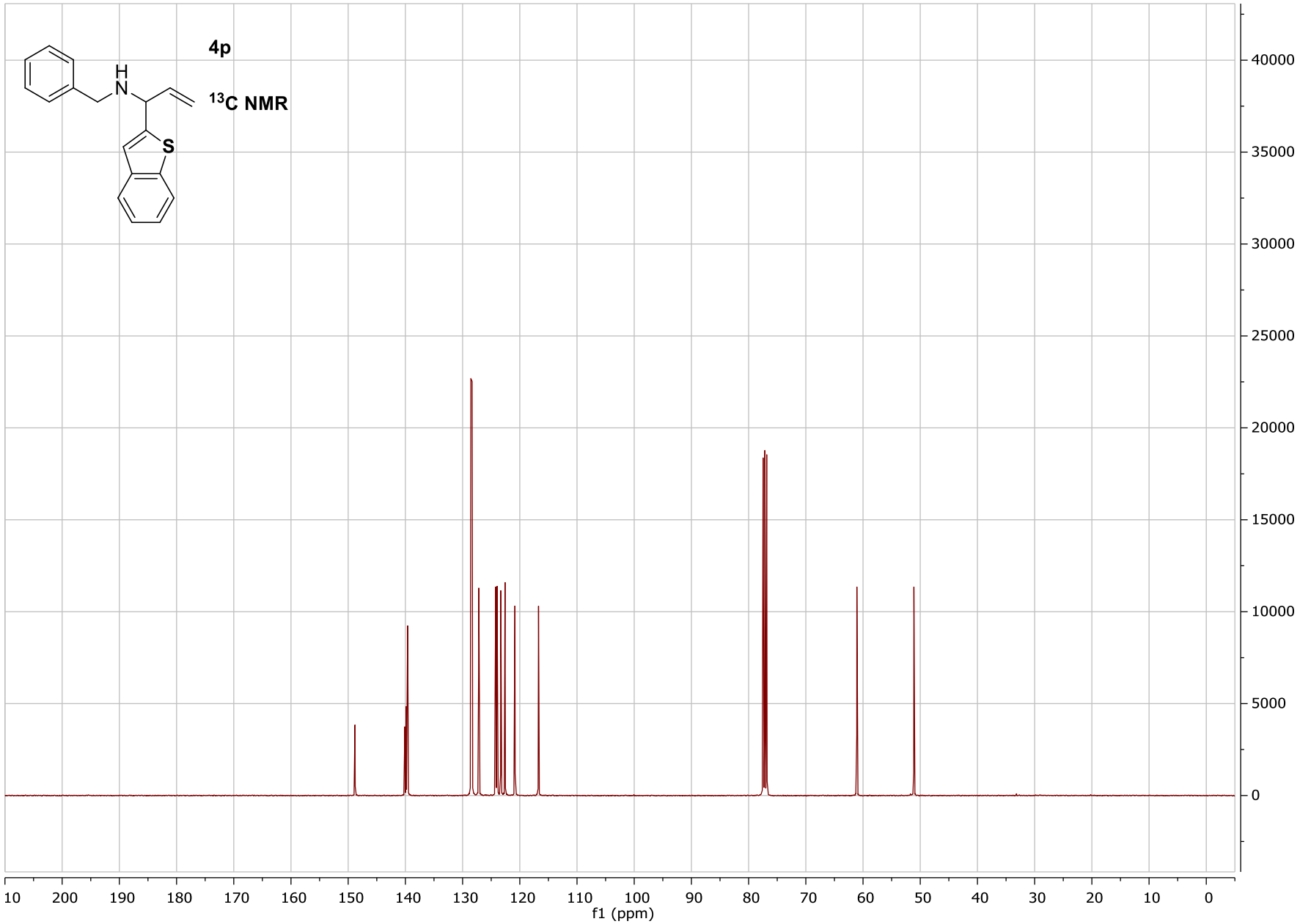

4n
^{1}H NMR
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

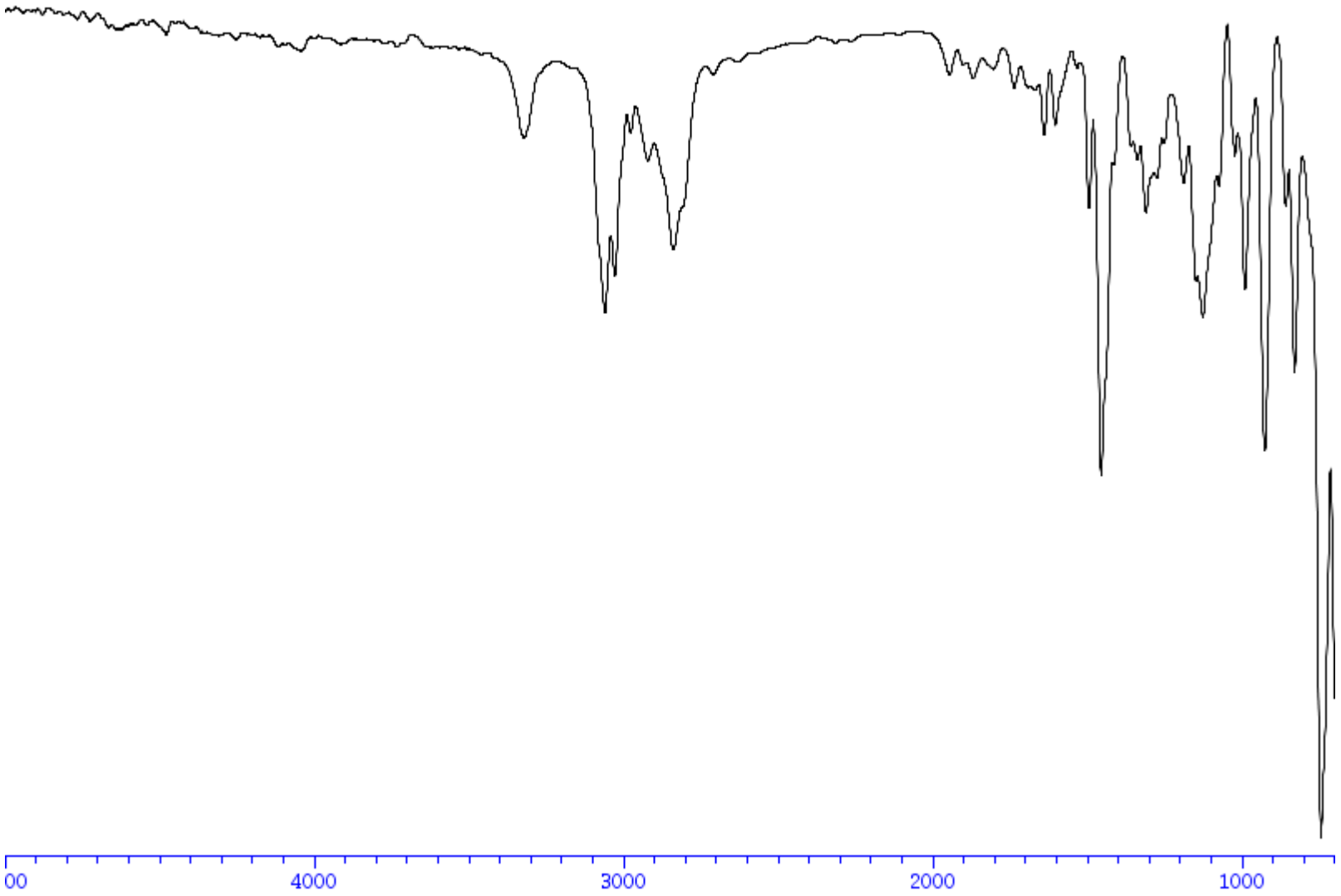

4n
^{13}C NMR
H
N
30000
28000
26000
24000
22000
20000
18000
16000
14000
12000
10000
8000
6000
4000
2000
0
-2000
10
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

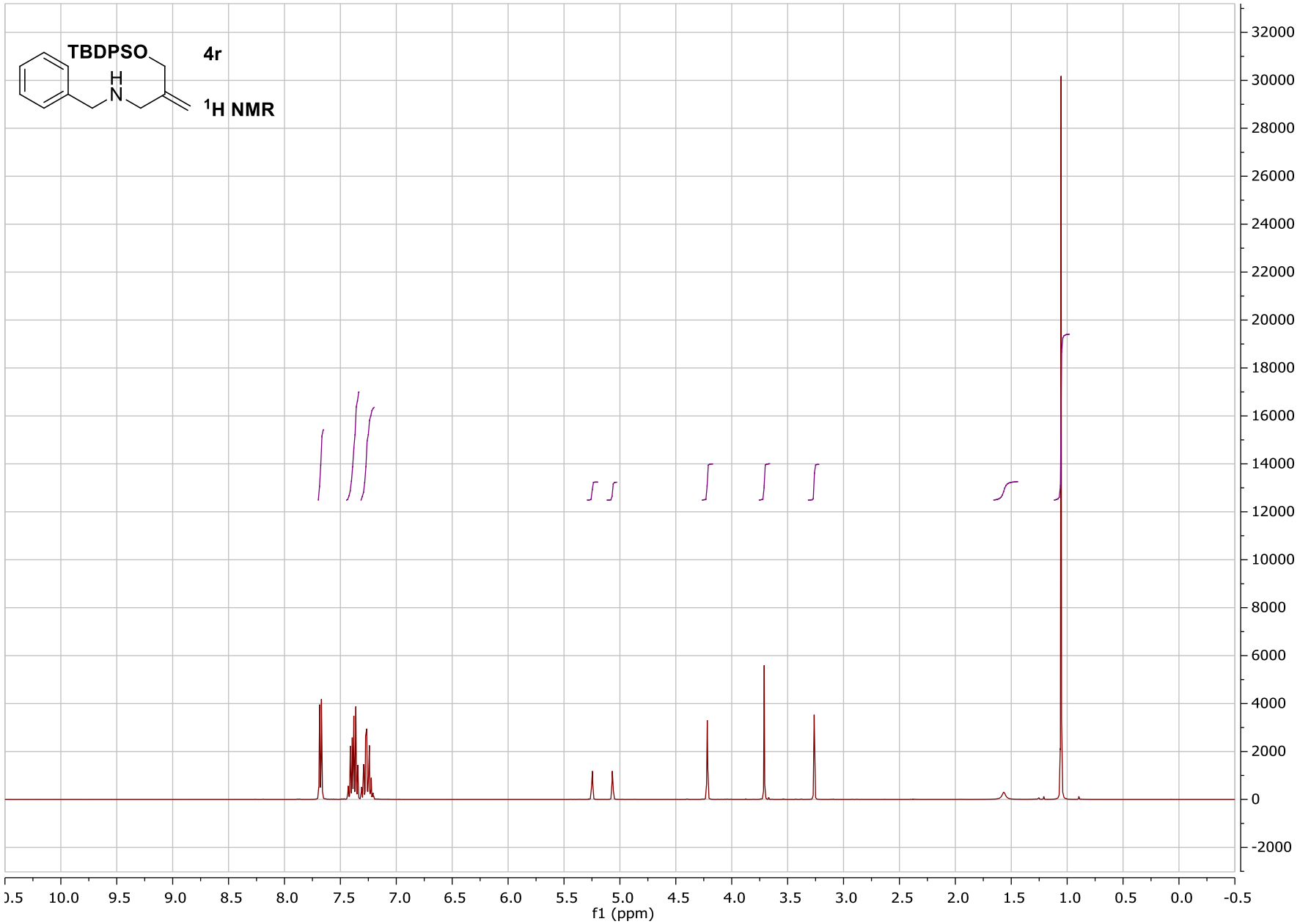

4o
1H NMR
H
N
O
16000
15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

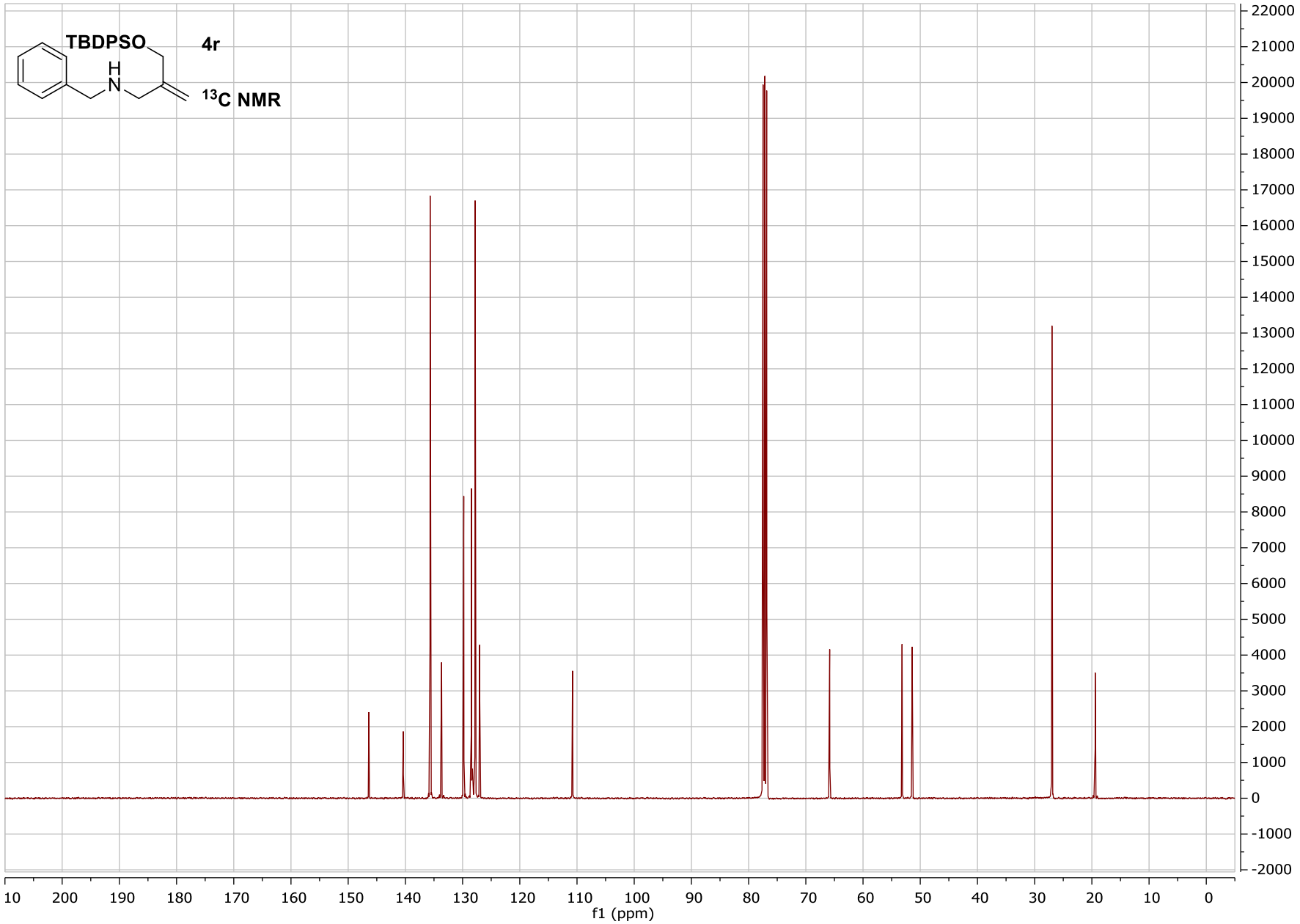

4o
13C NMR
H
N
O
18000
17000
16000
15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
10
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

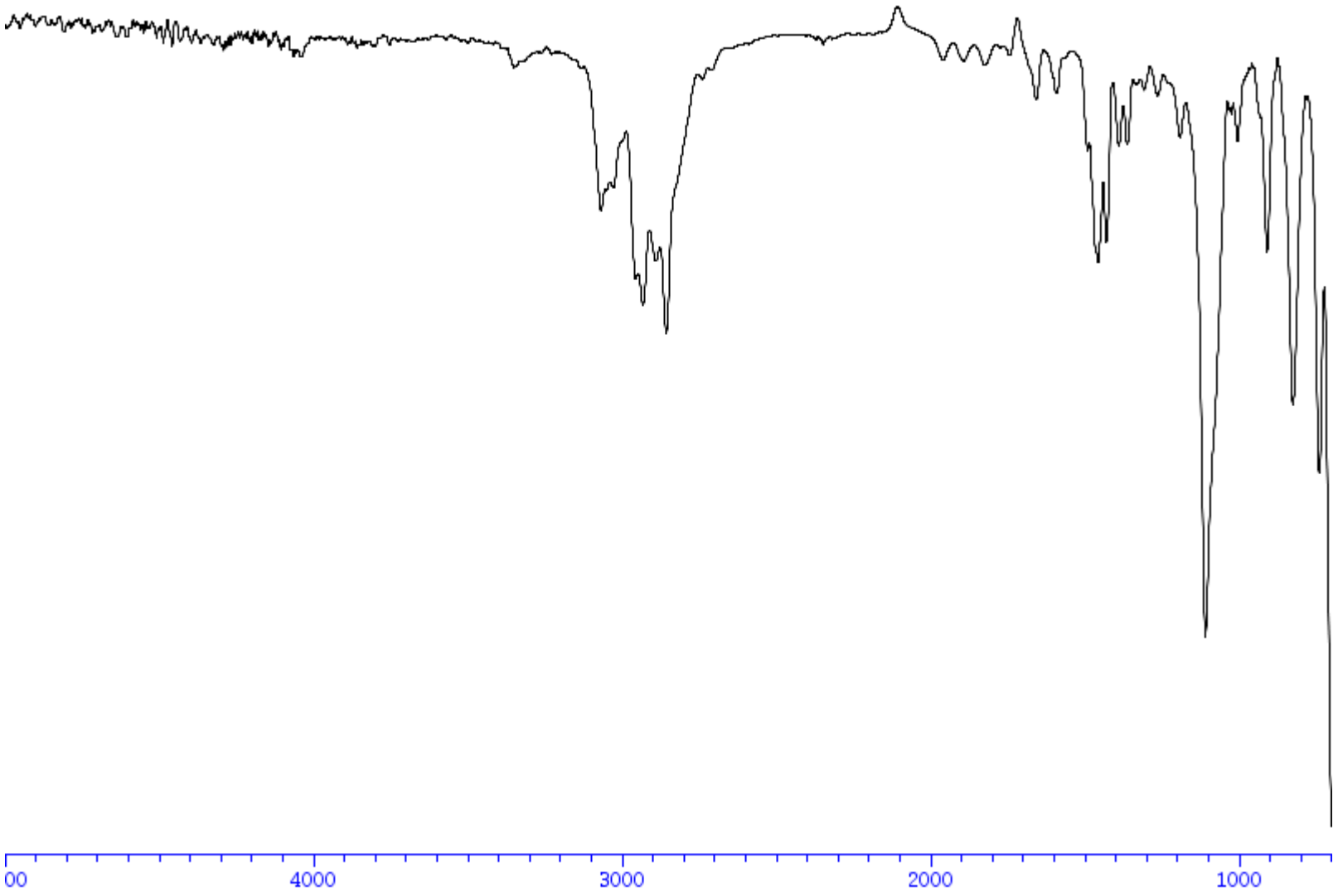

4p
^{1}H NMR
H
N
S
19000
18000
17000
16000
15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

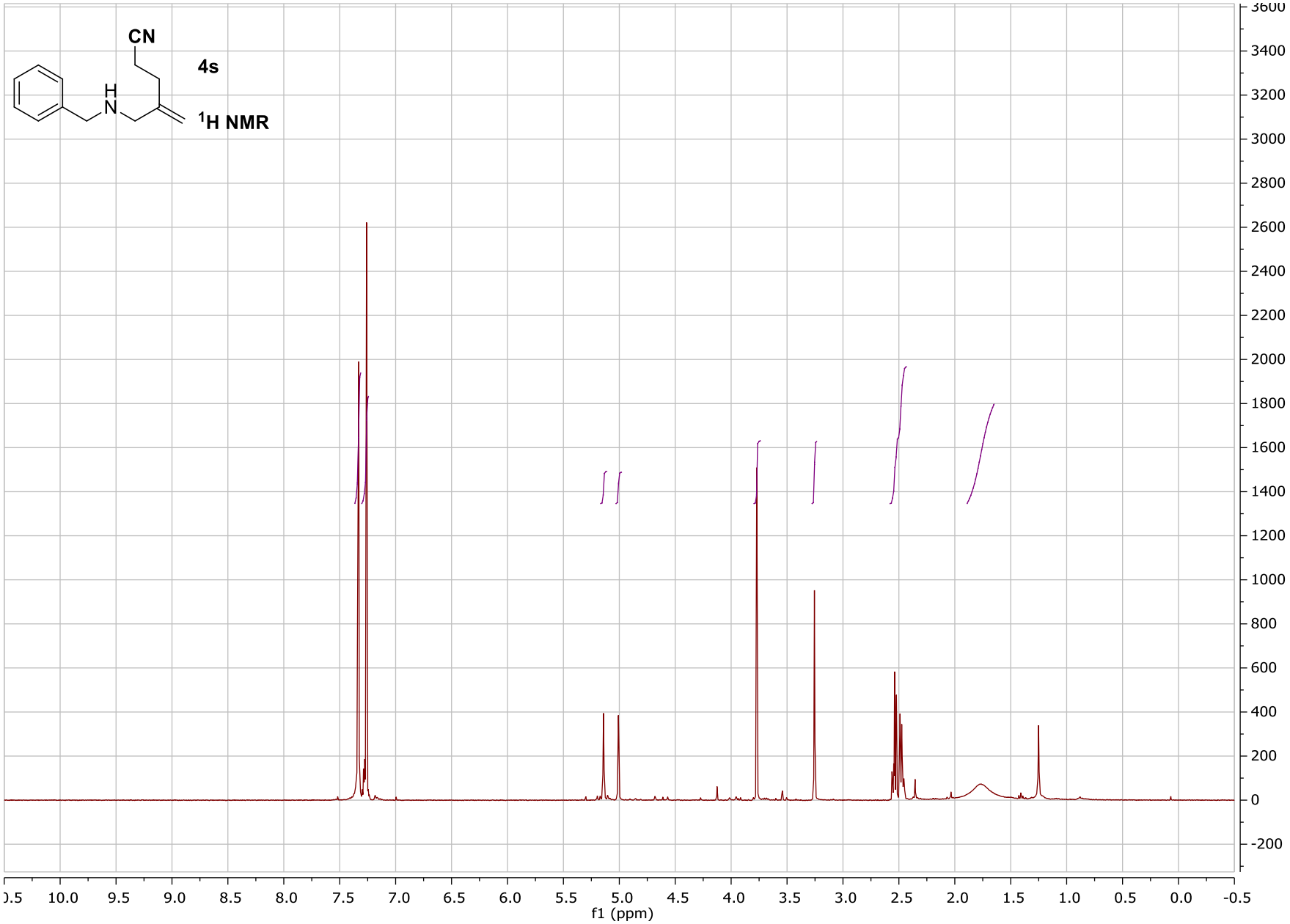

4p
^{13}C NMR
H
N
S
40000
35000
30000
25000
20000
15000
10000
5000
0
10
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

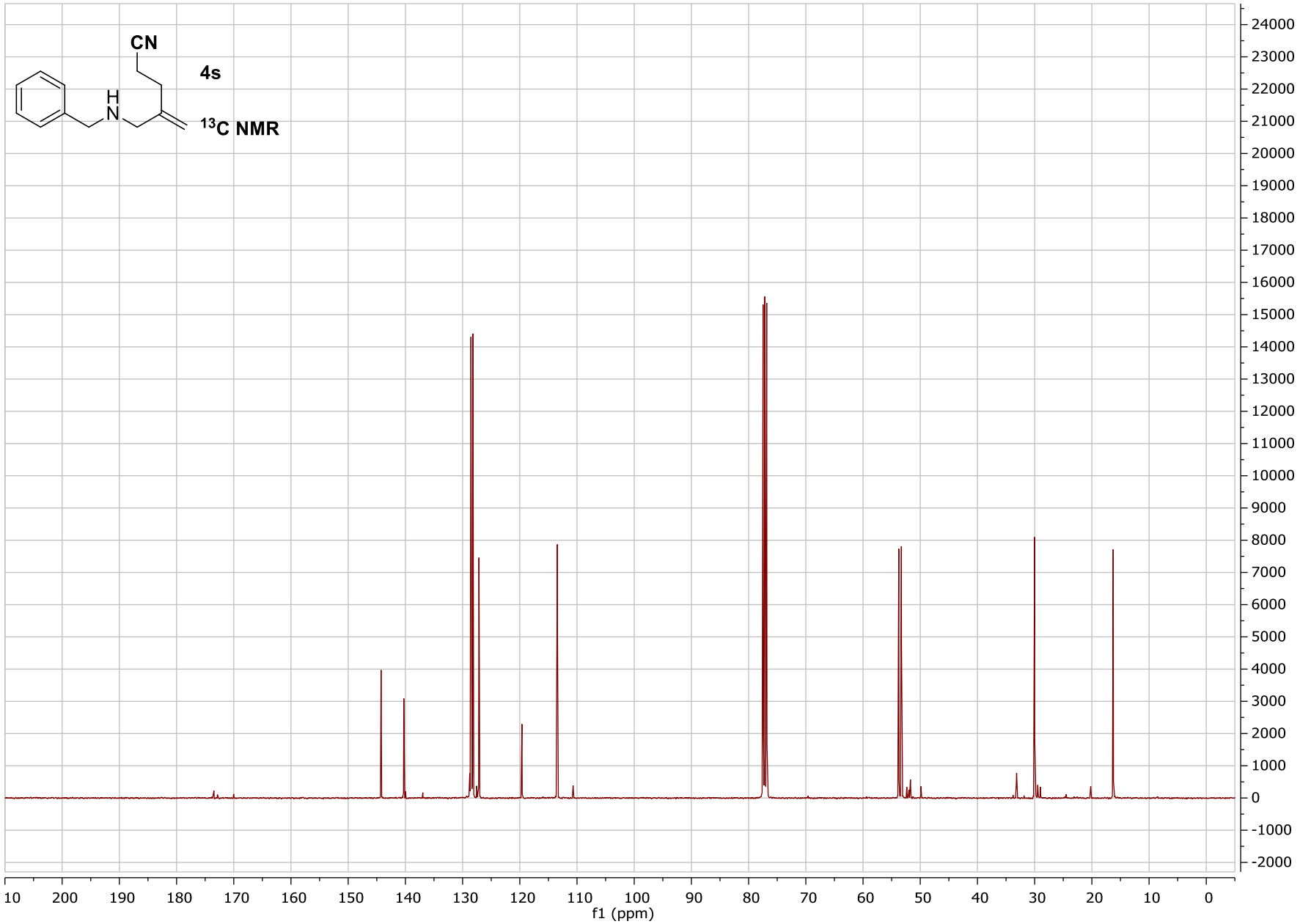

00
4000
3000
2000
1000

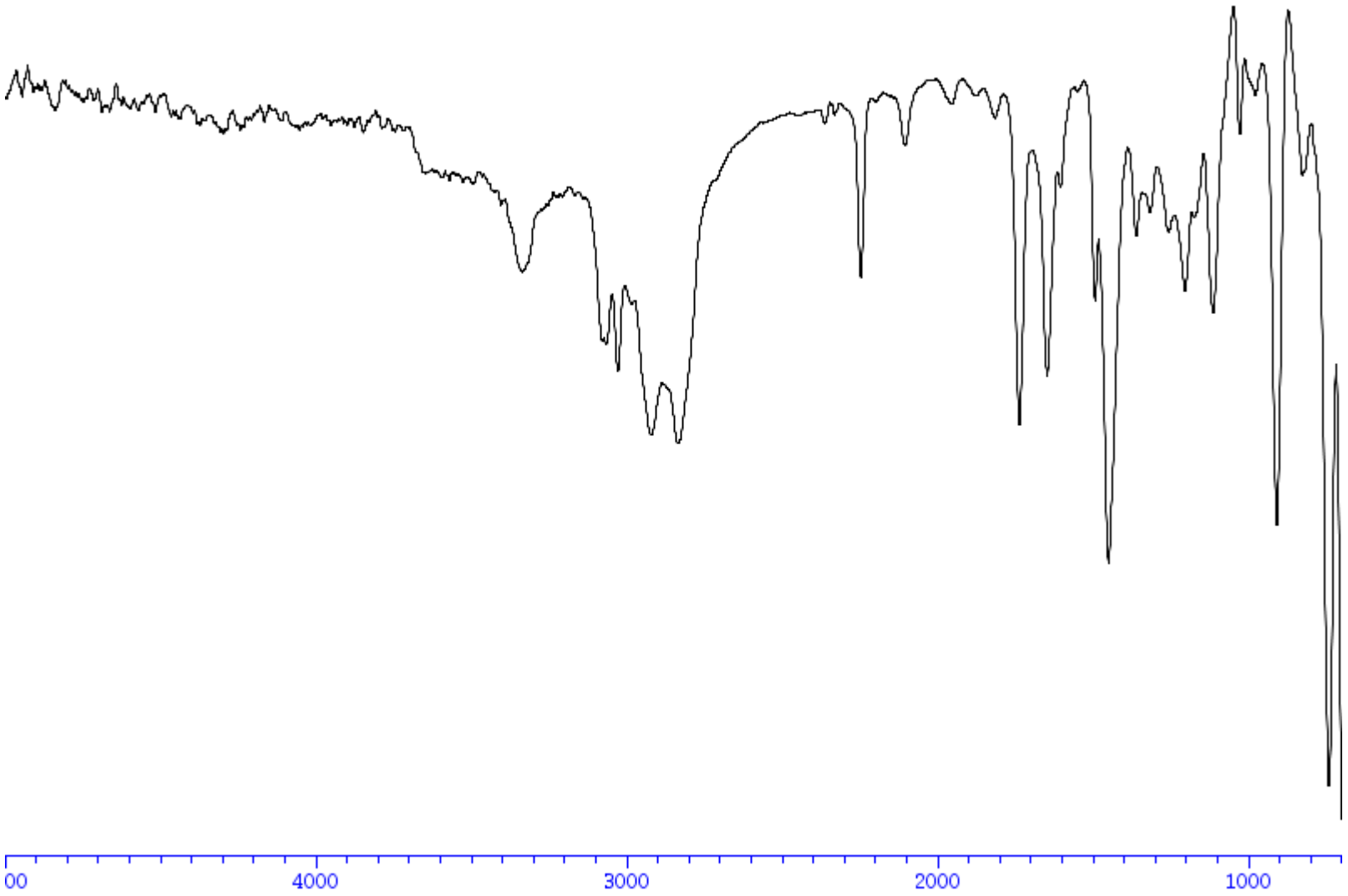

TBDPSO
4r
H
N
1H NMR
32000
30000
28000
26000
24000
22000
20000
18000
16000
14000
12000
10000
8000
6000
4000
2000
0
-2000
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

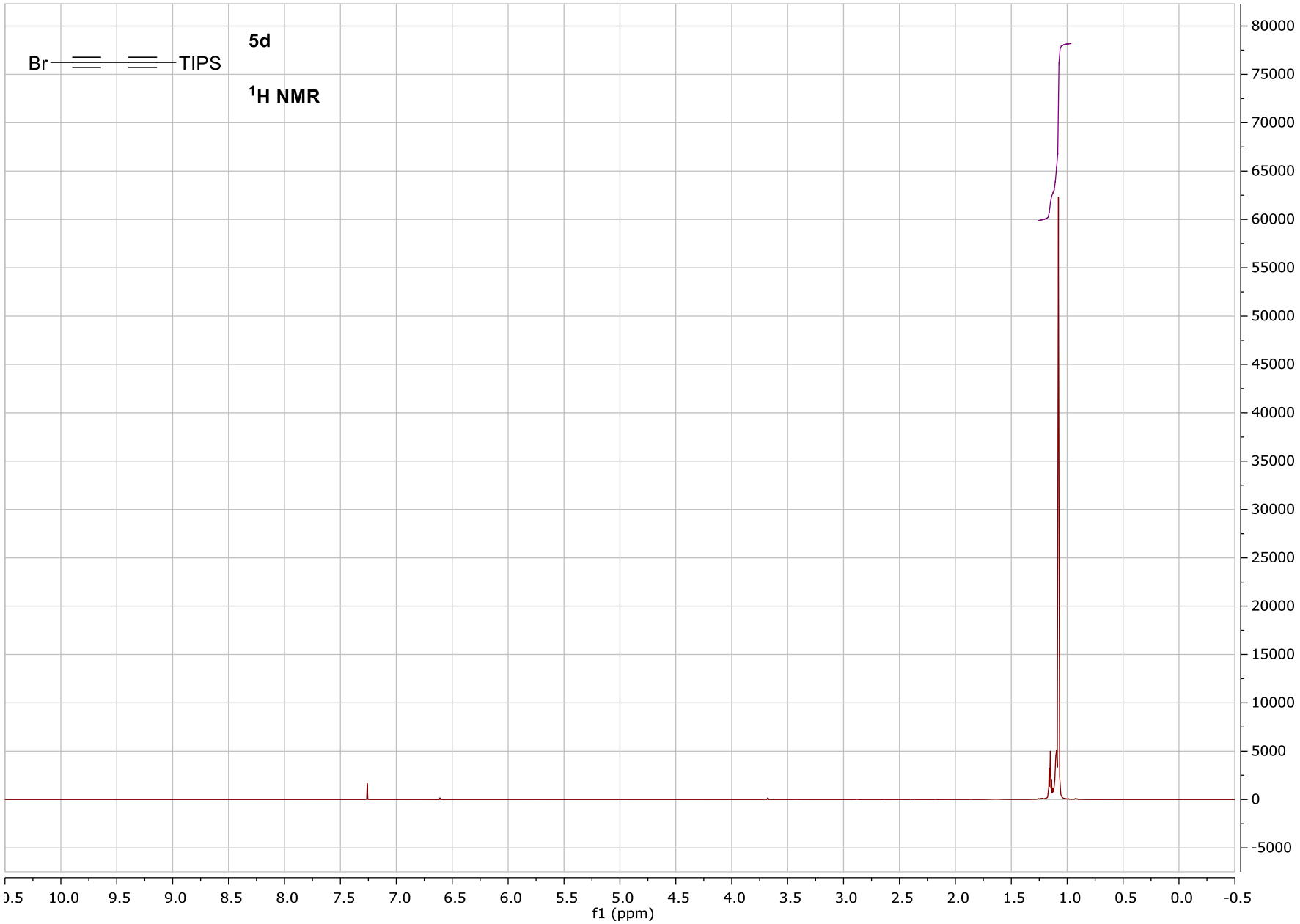

TBDPSO
H
N
4r
13C NMR
22000
21000
20000
19000
18000
17000
16000
15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
-2000
10
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

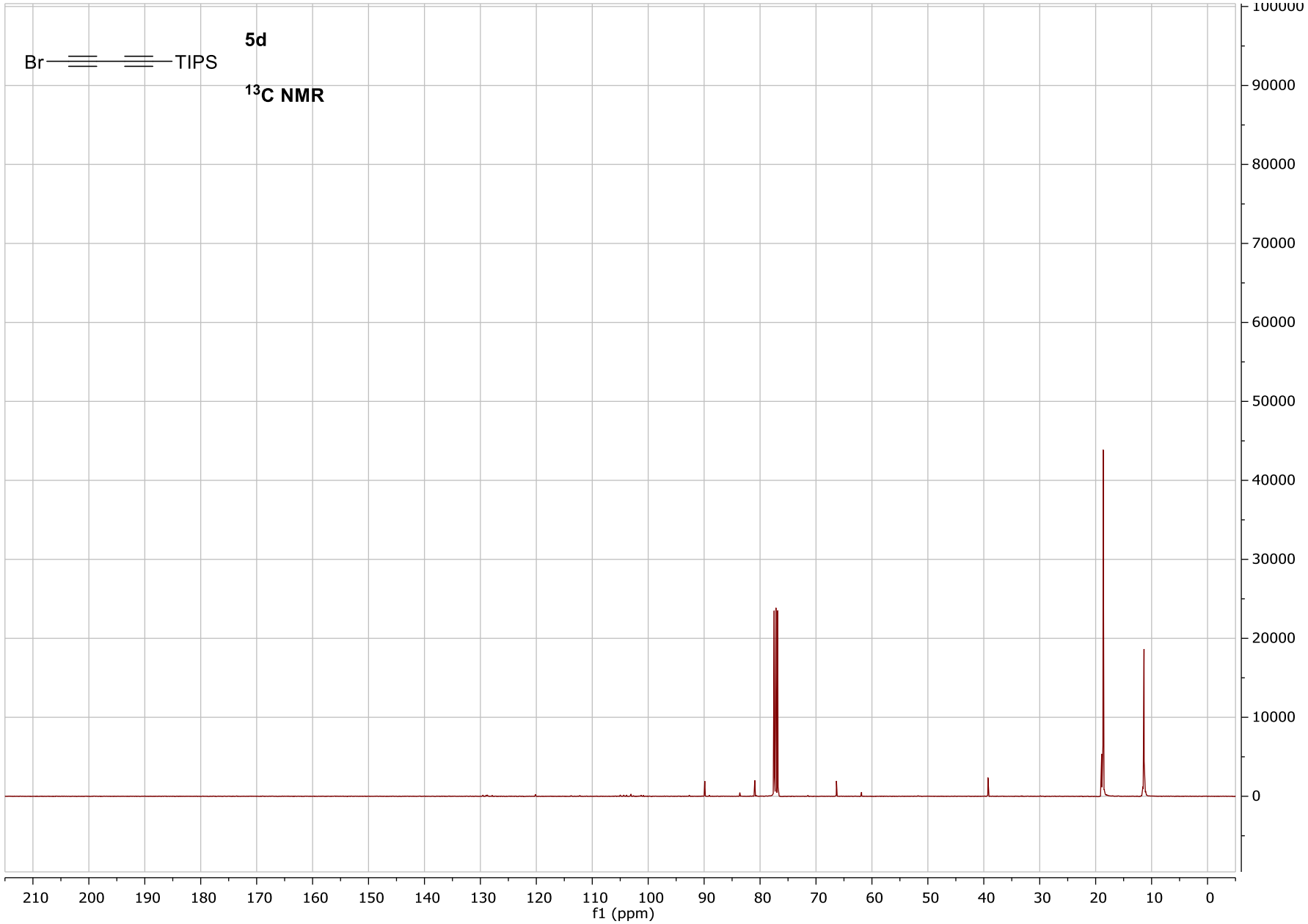

00
4000
3000
2000
1000

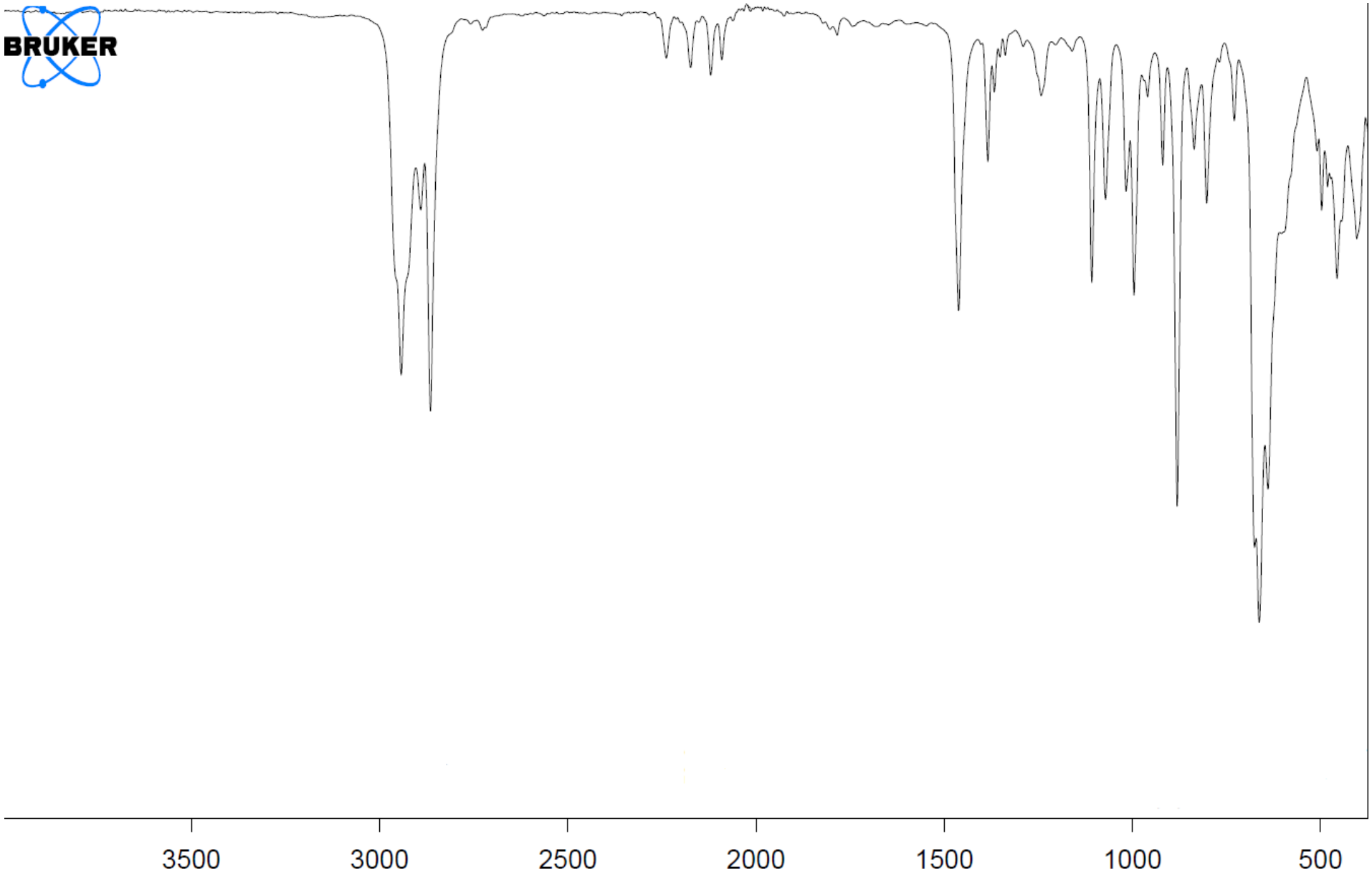

CN
4s
H
N
^{1}H NMR
f1 (ppm)

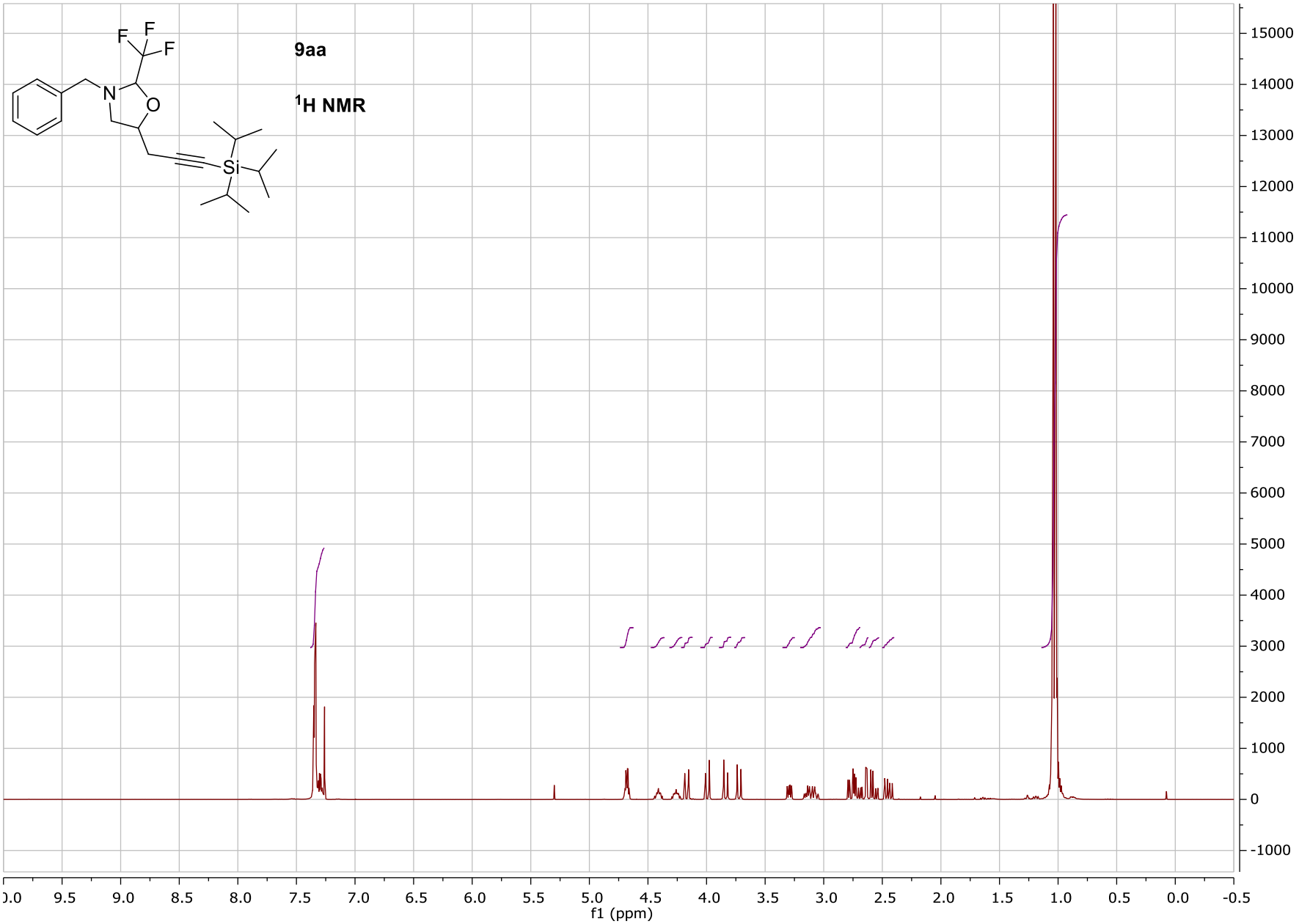

CN
4s
H
N
13C NMR
24000
23000
22000
21000
20000
19000
18000
17000
16000
15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
-2000
10
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

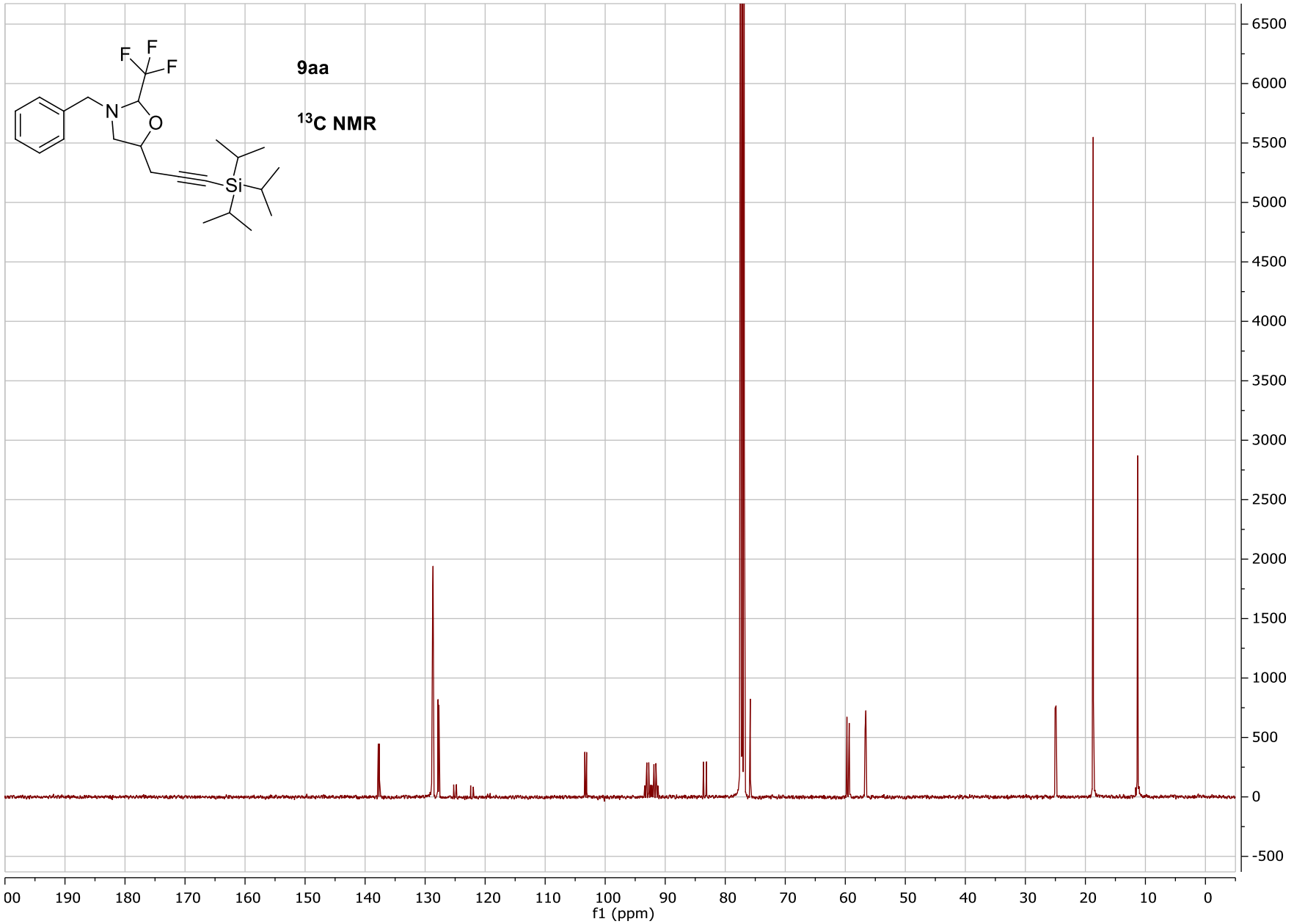

00
4000
3000
2000
1000

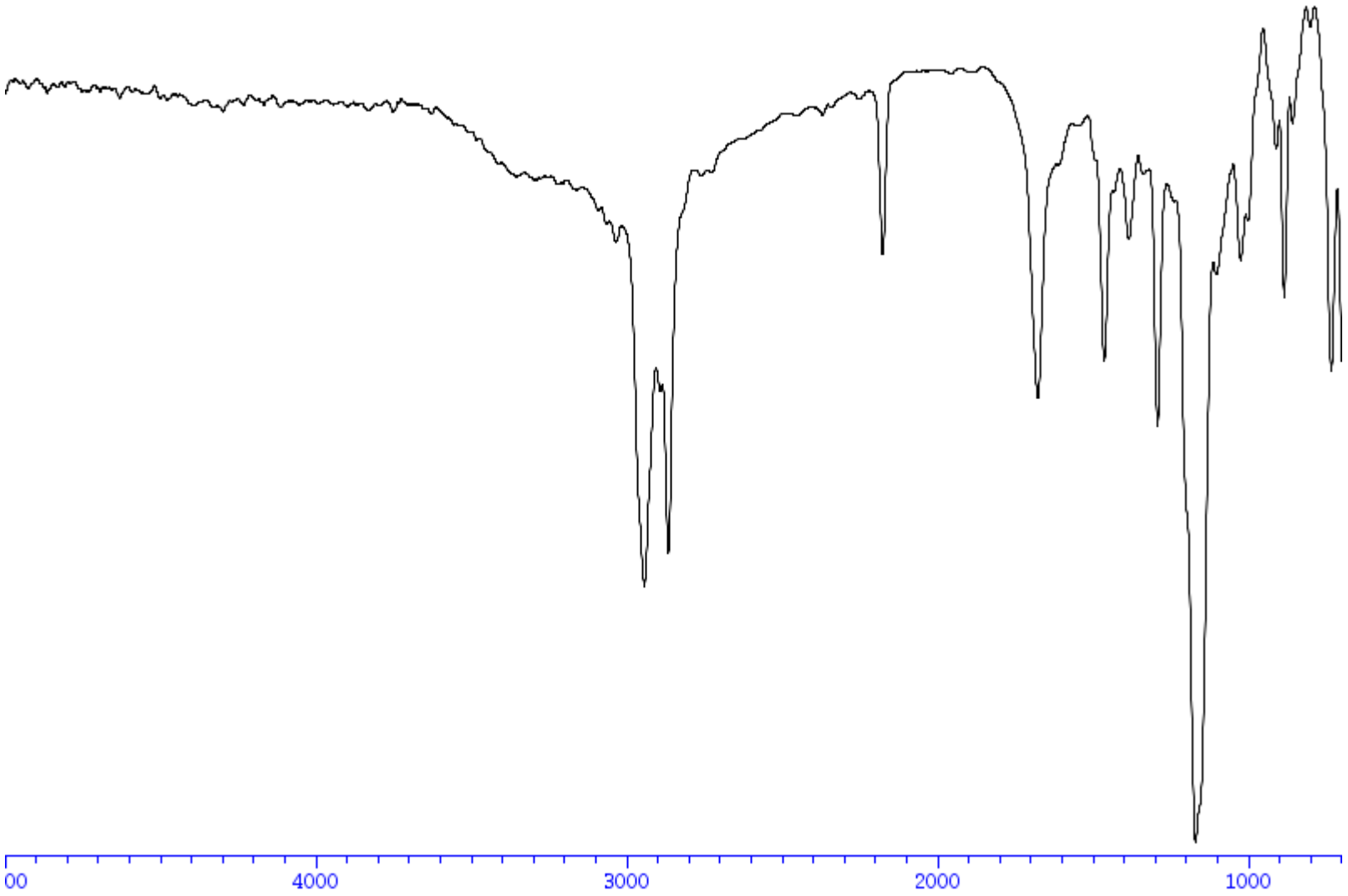

5d
Br
TIPS
1H NMR
80000
75000
70000
65000
60000
55000
50000
45000
40000
35000
30000
25000
20000
15000
10000
5000
0
-5000
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

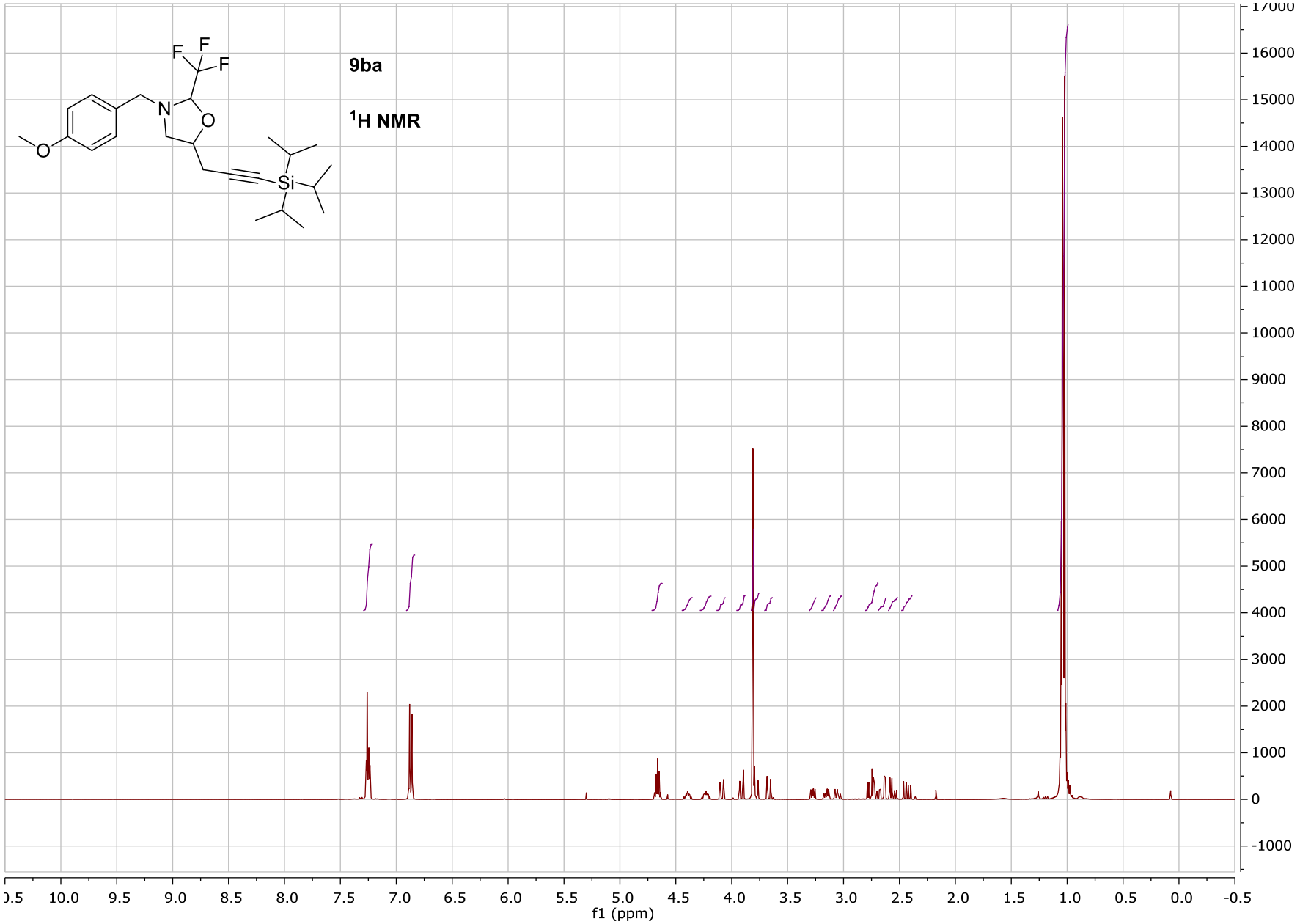

5d
Br
TIPS
13C NMR
100000
90000
80000
70000
60000
50000
40000
30000
20000
10000
0
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

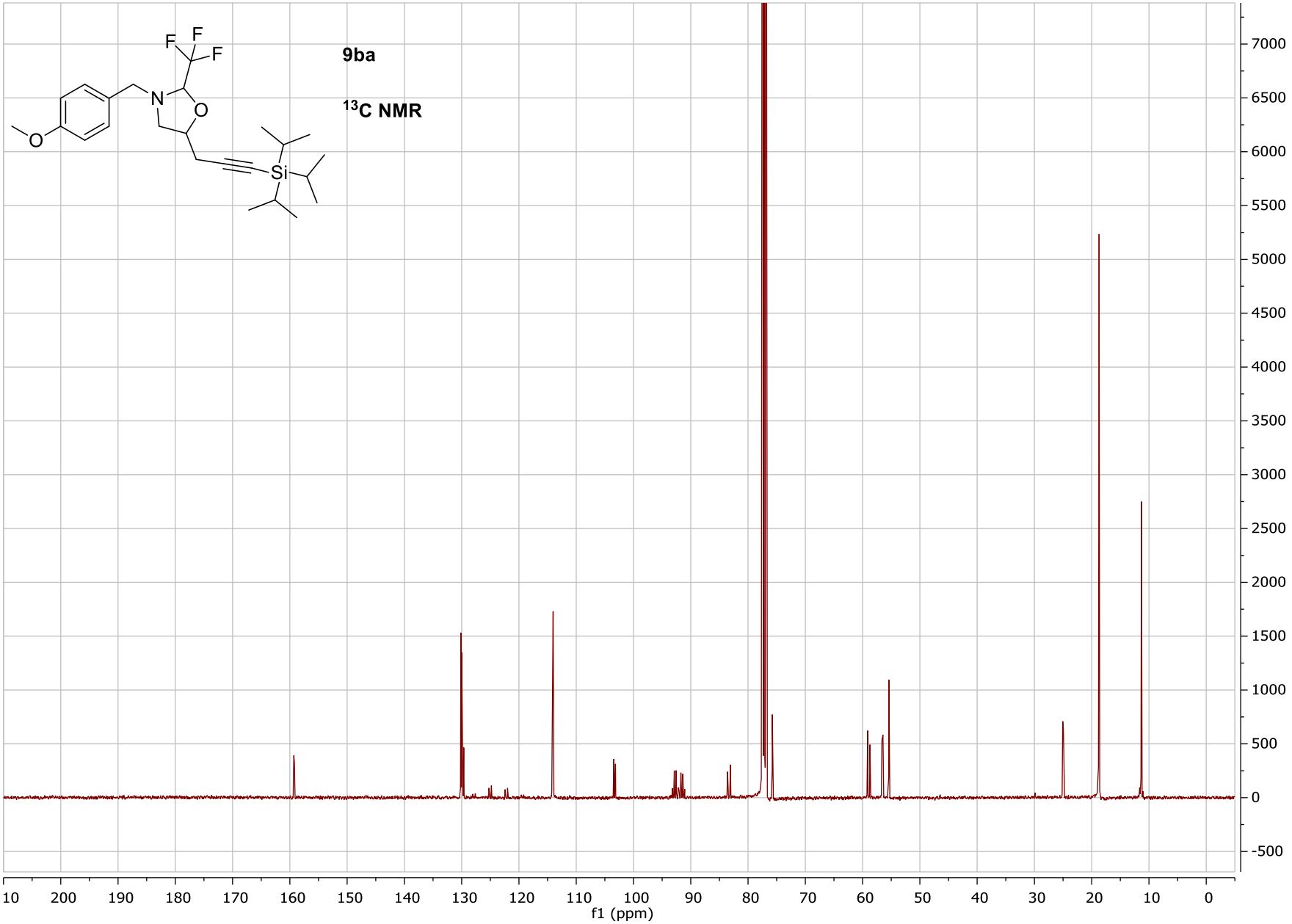

BRUKER
3500
3000
2500
2000
1500
1000
500

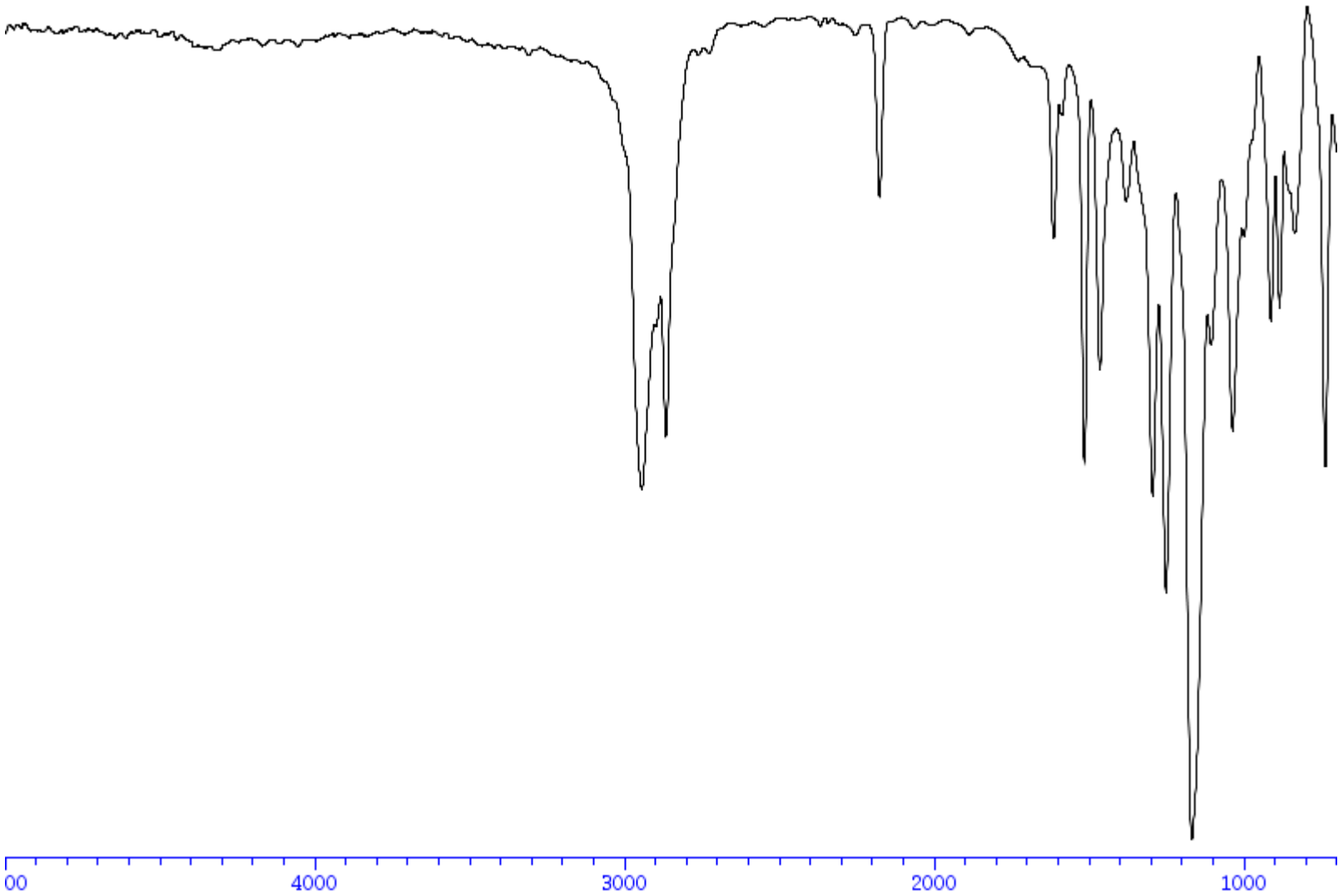

F
F
F
N
O
Si
9aa
^{1}H NMR
15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

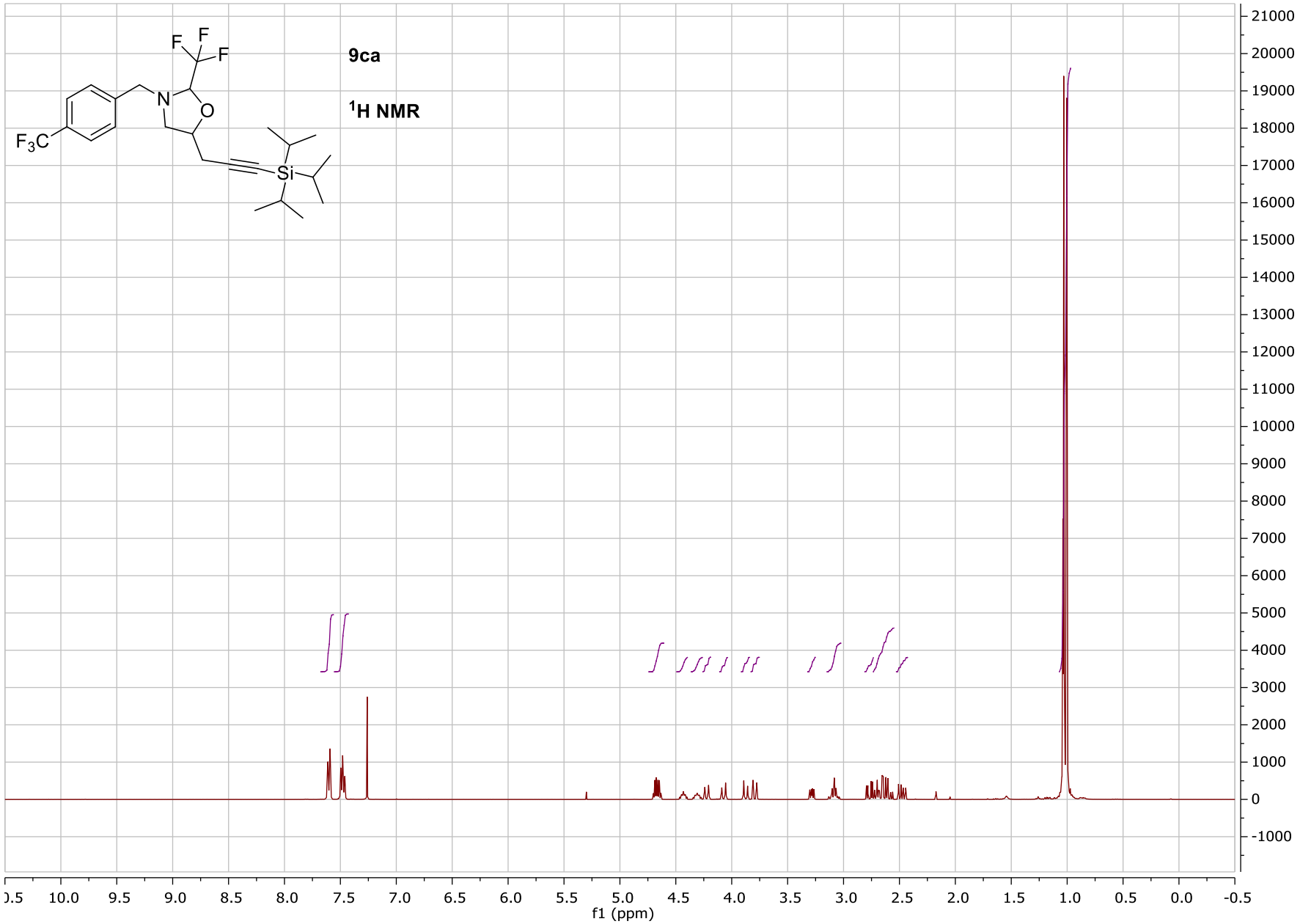

9aa
13C NMR
F
F
F
N
O
Si
6500
6000
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
-500
00
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

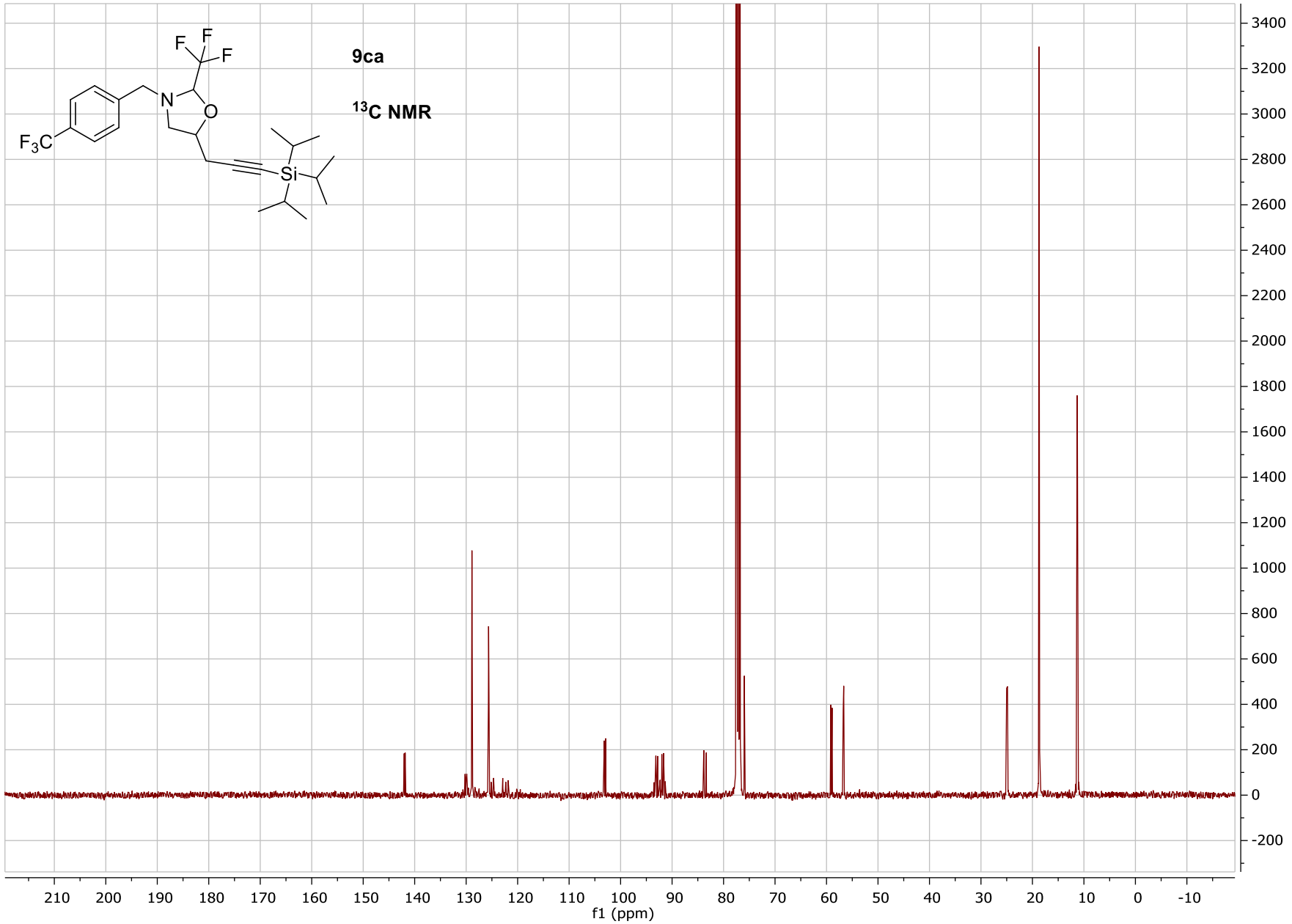

00
4000
3000
2000
1000

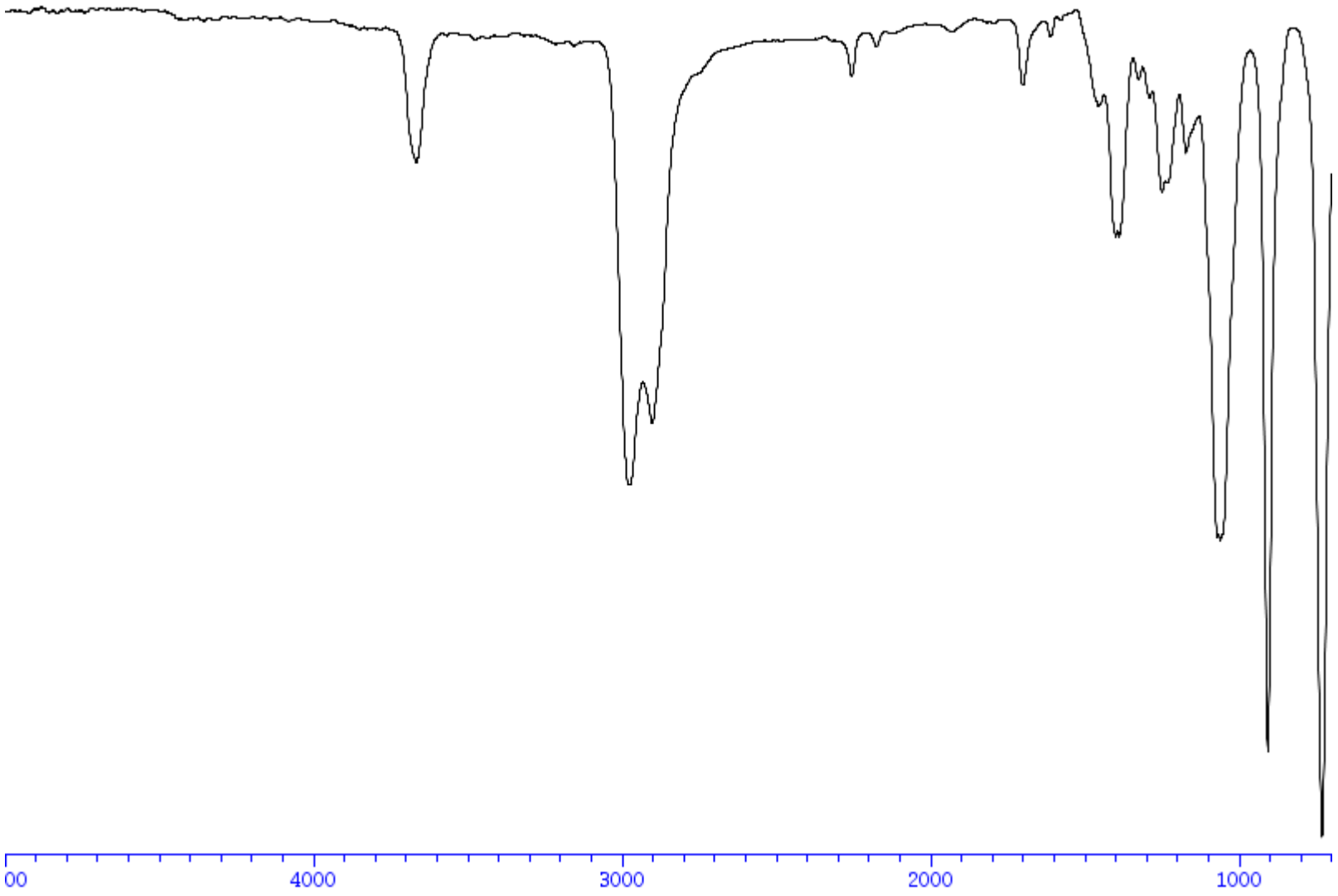

9ba
^{1}H NMR
F
F
F
N
O
O
Si
f1 (ppm)

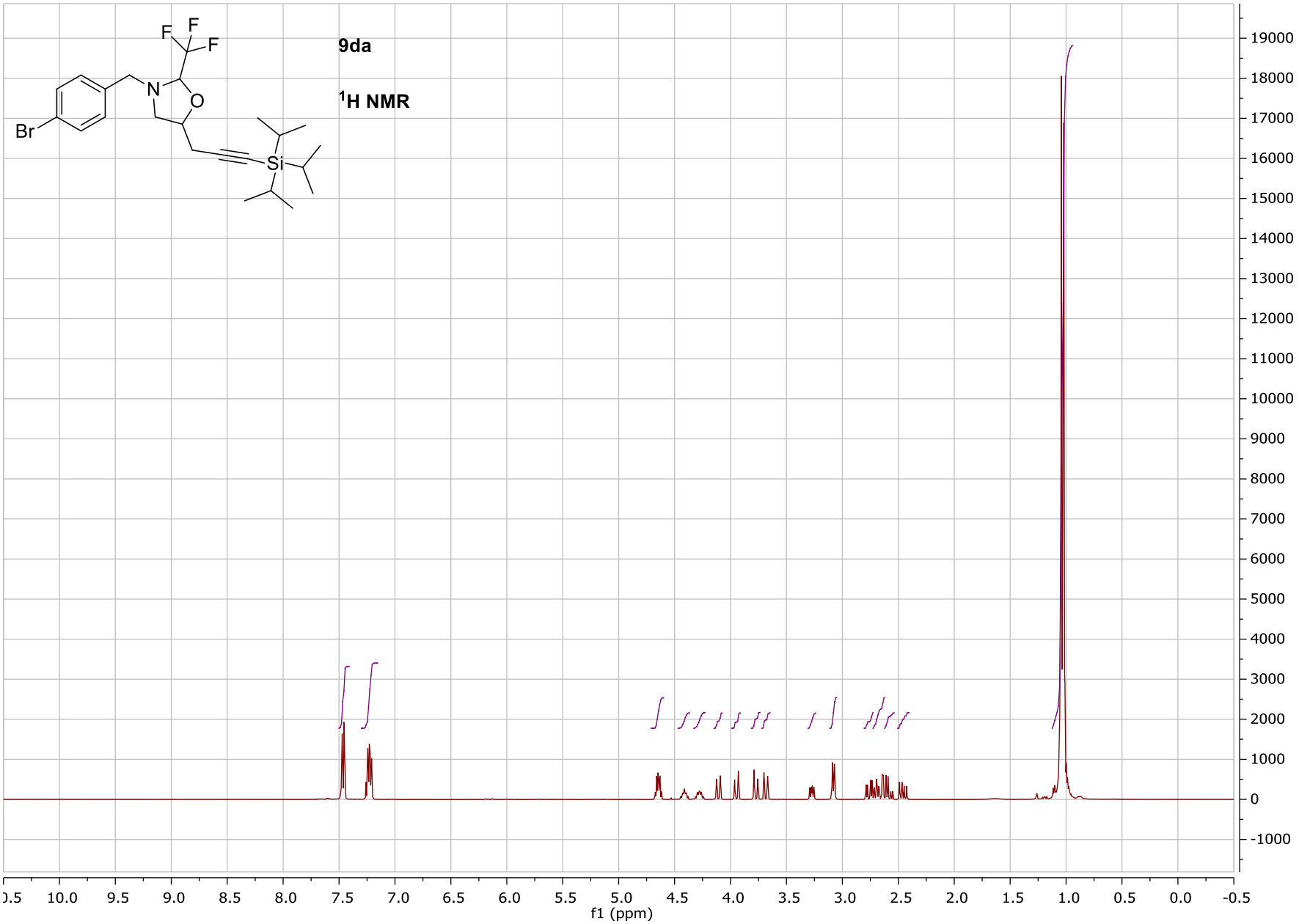

9ba
13C NMR
F
F
F
N
O
O
Si
7000
6500
6000
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
-500
10
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

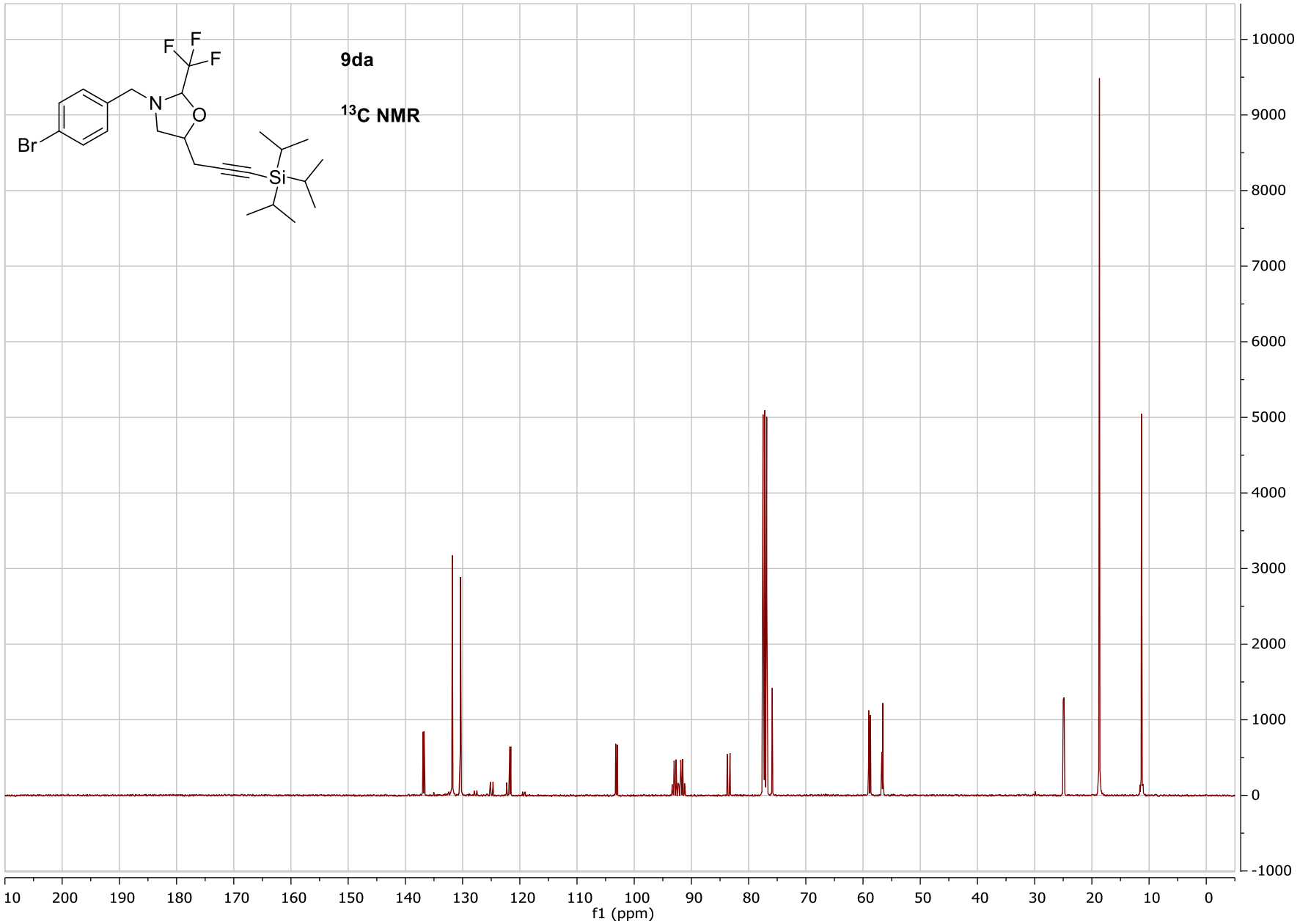

00
4000
3000
2000
1000

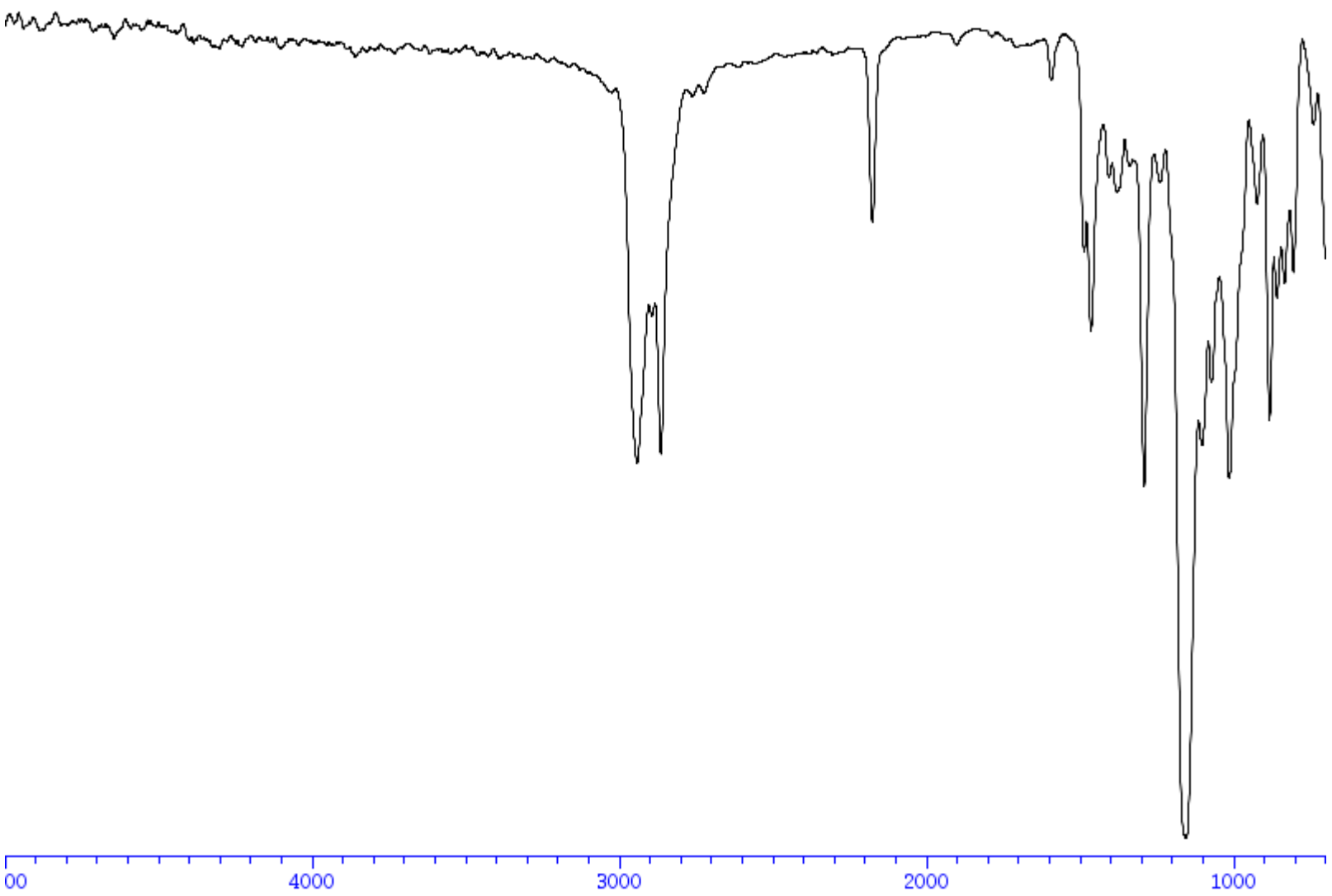

9ca
^{1}H NMR
F
F
F
N
O
F_3C
Si
21000
20000
19000
18000
17000
16000
15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

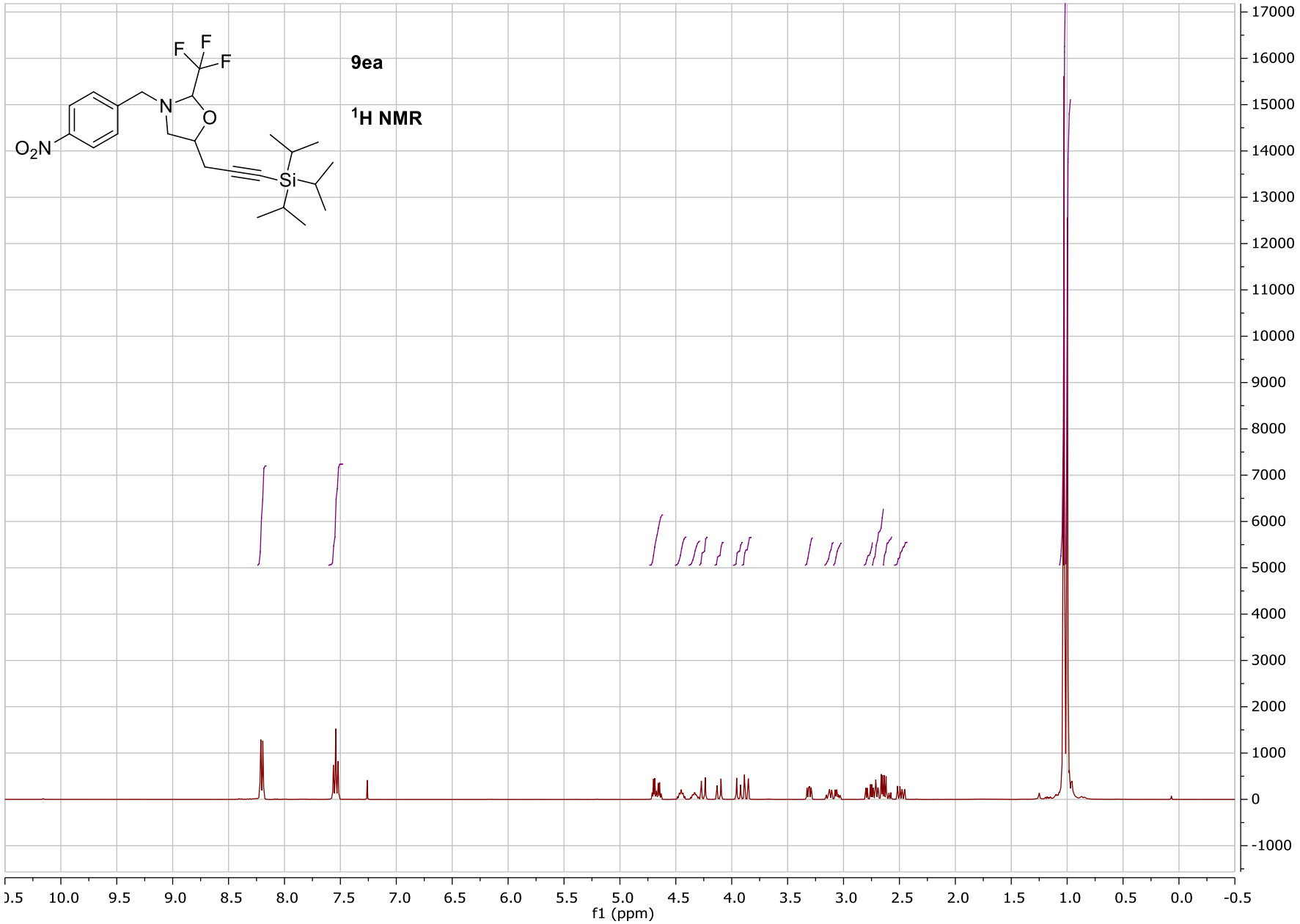

9ca
13C NMR
F
F
F
N
O
F3C
Si
3400
3200
3000
2800
2600
2400
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0
-200
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

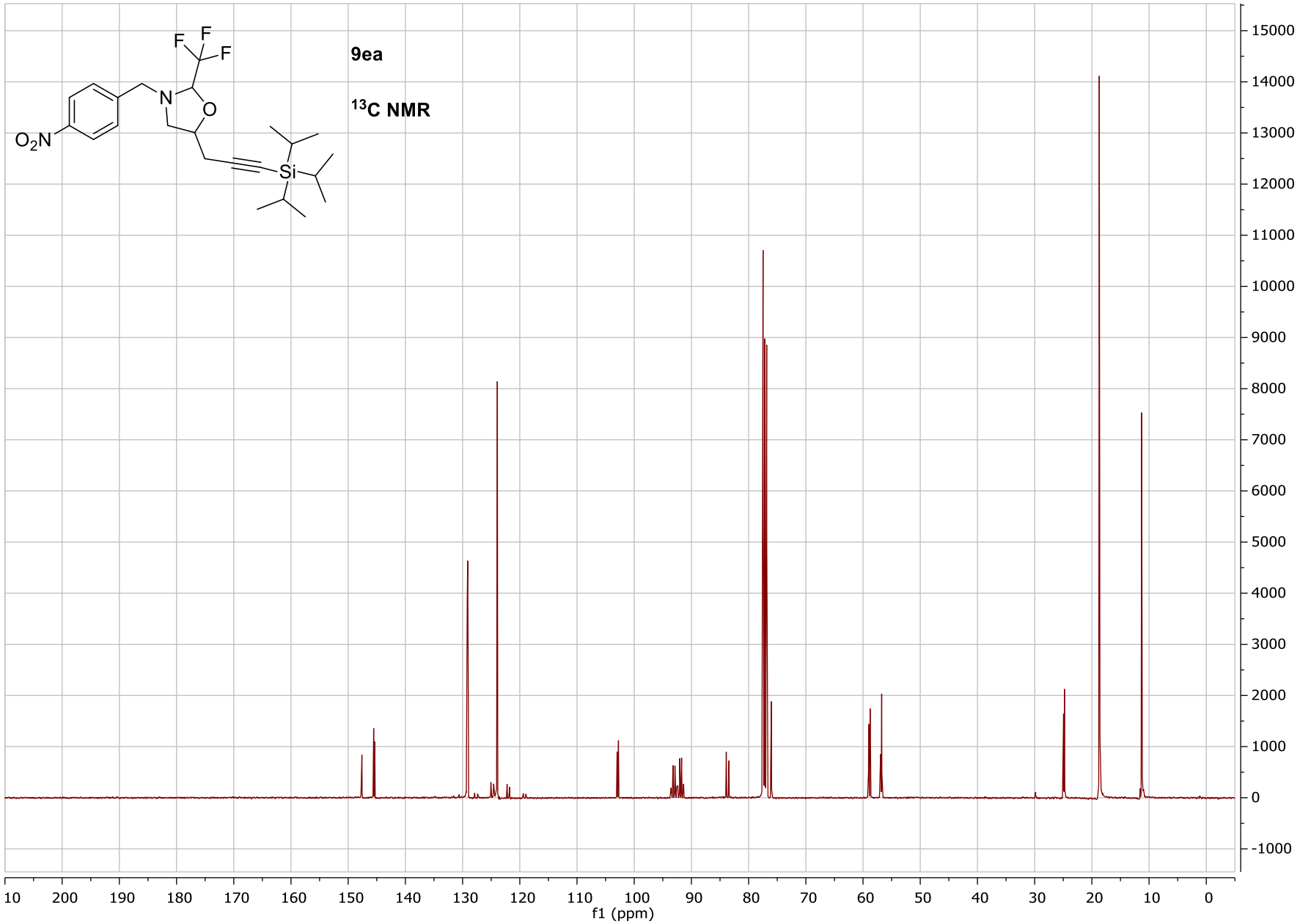

00
4000
3000
2000
1000

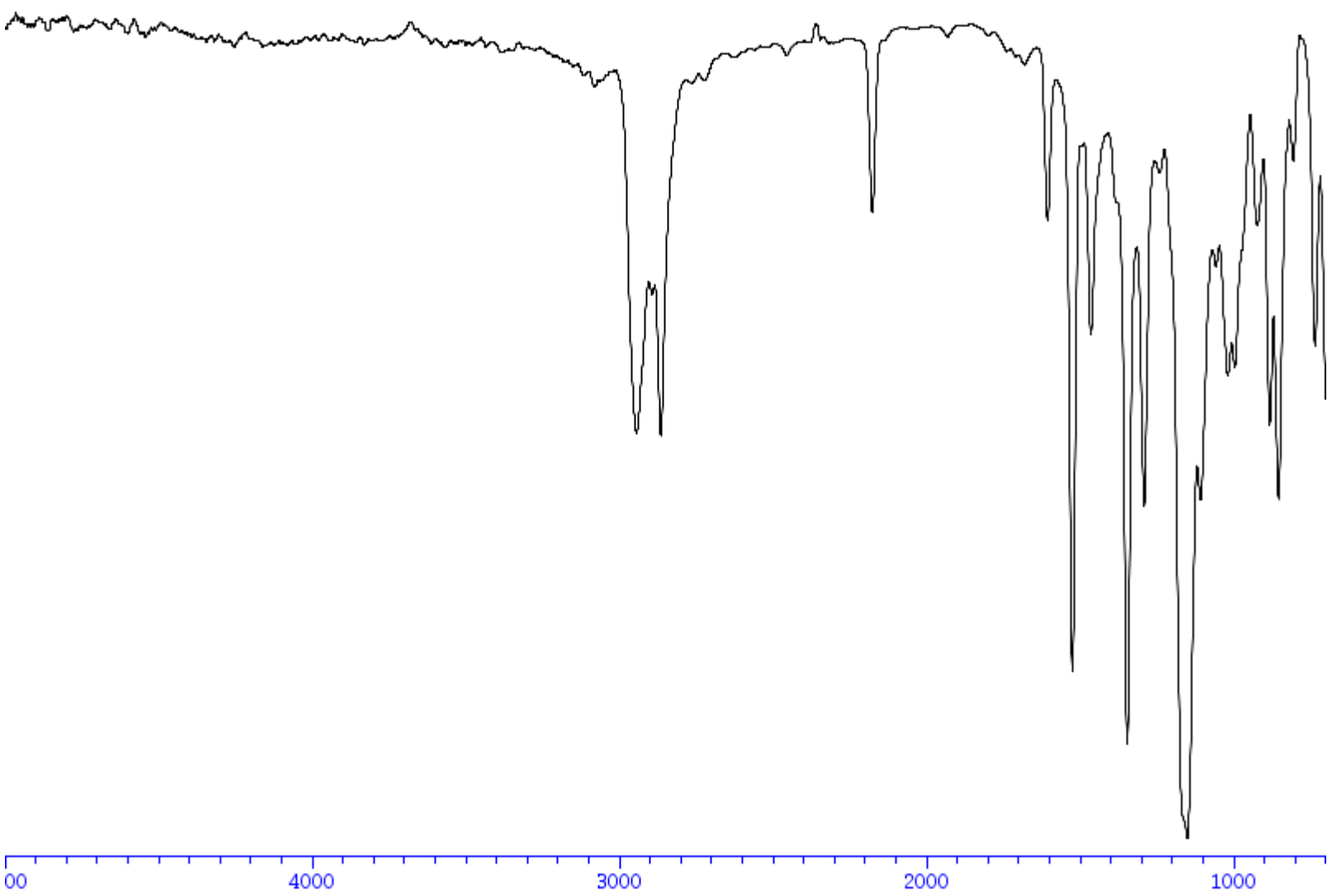

9da
^{1}H NMR
F
F
F
N
O
Br
Si
19000
18000
17000
16000
15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

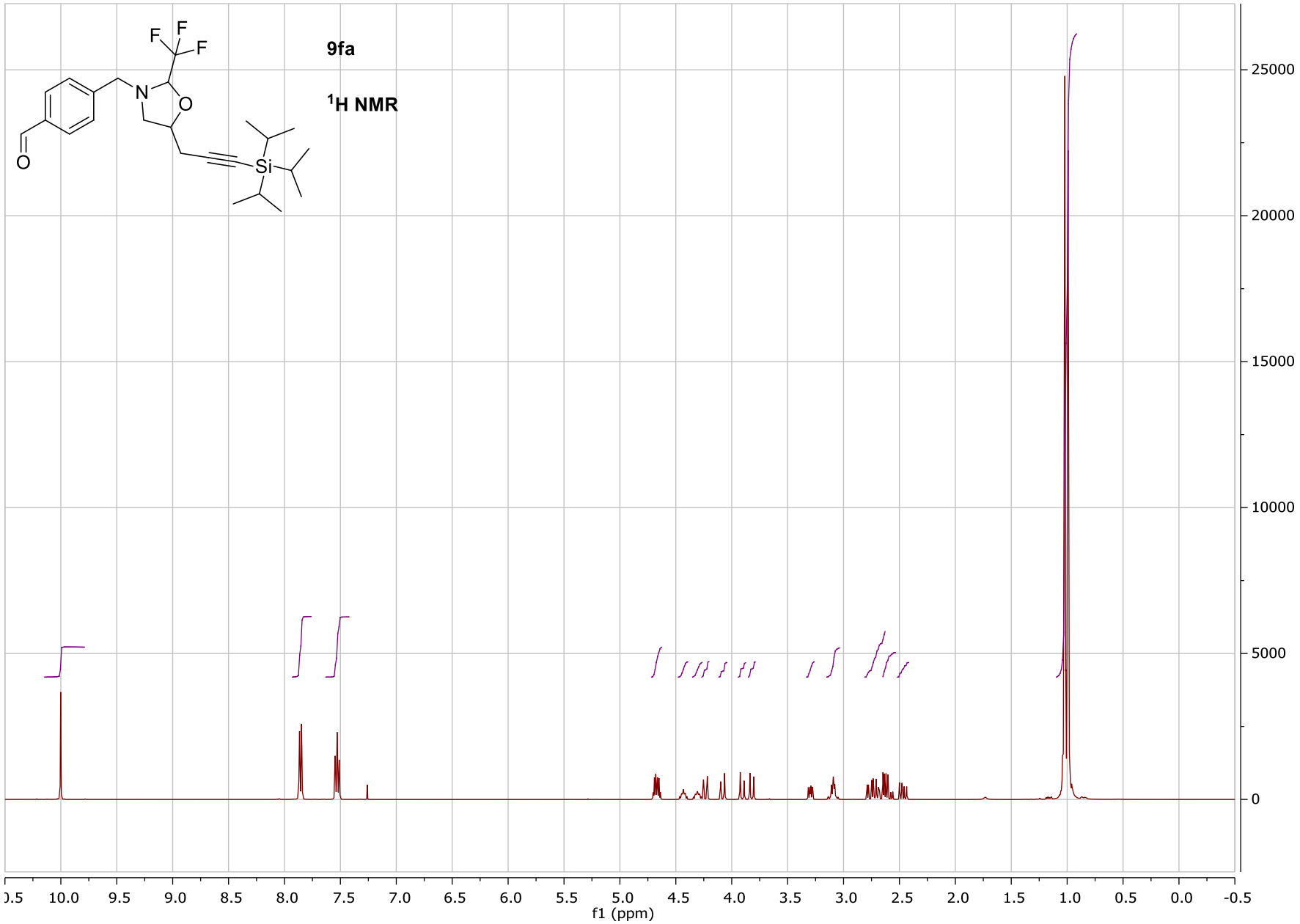

9da
13C NMR
F
F
F
N
O
Br
Si
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
10
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


00
4000
3000
2000
1000


9ea
^{1}H NMR
F
F
F
N
O
O_2N
Si
17000
16000
15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)


9ea
13C NMR
F
F
F
N
O
O2N
Si
15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
10
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


00
4000
3000
2000
1000


9fa
^{1}H NMR
F
F
F
N
O
O
Si
25000
20000
15000
10000
5000
0
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
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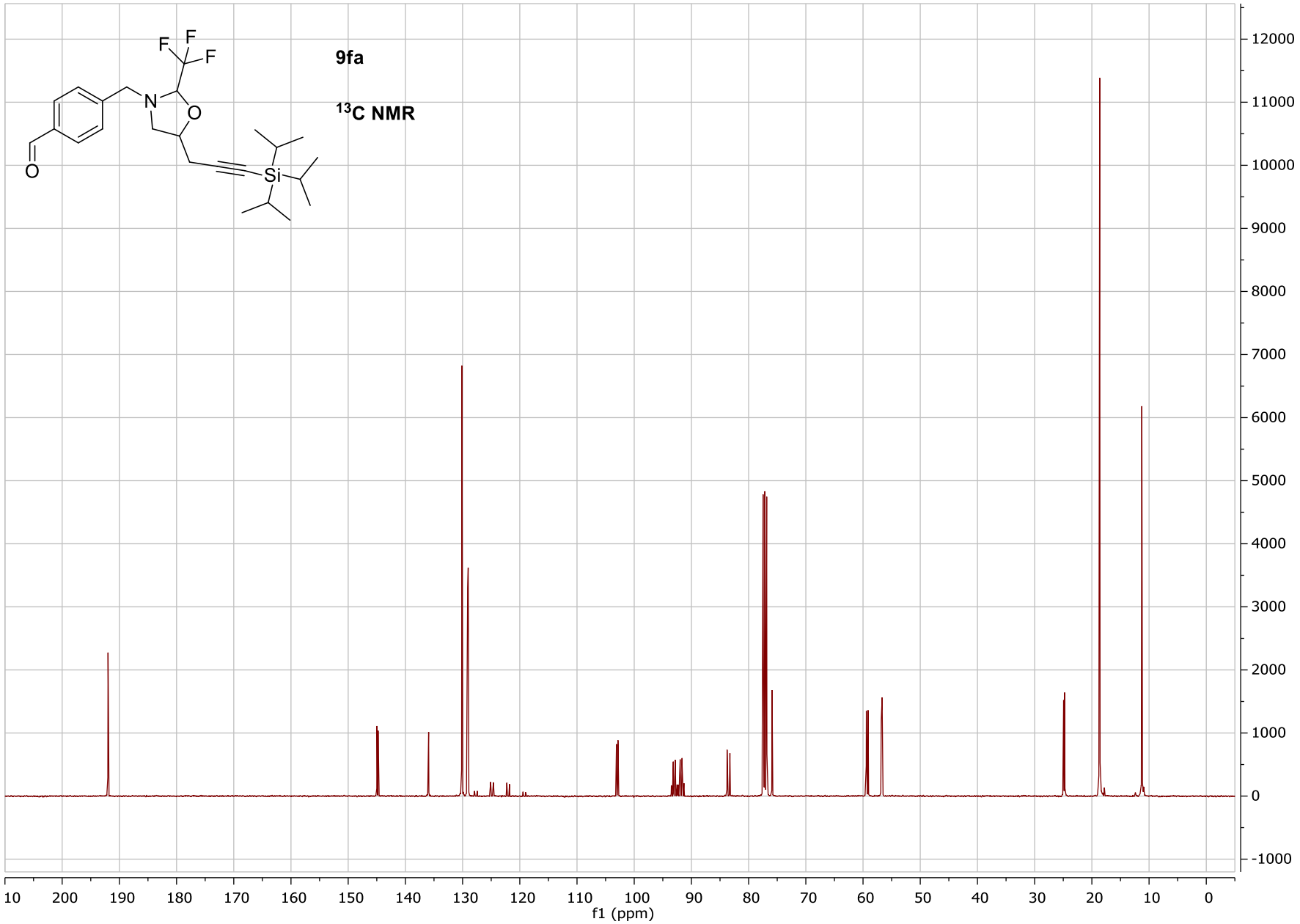
-0.5
f1 (ppm)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13C NMR
F
F
F
N
O
O
Si
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
10
200
190
180
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100
90
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50
40
30
20
10
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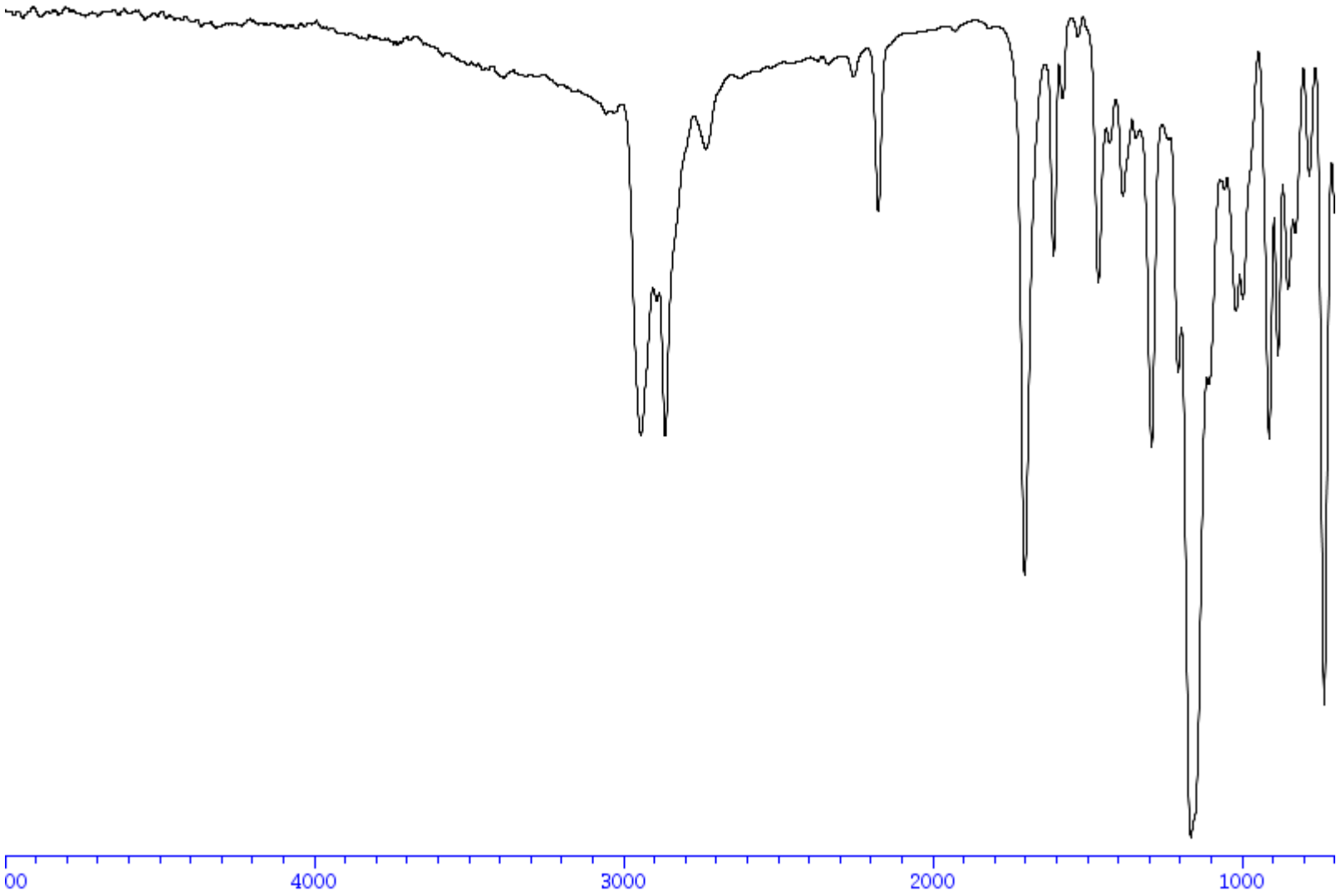
f1 (ppm)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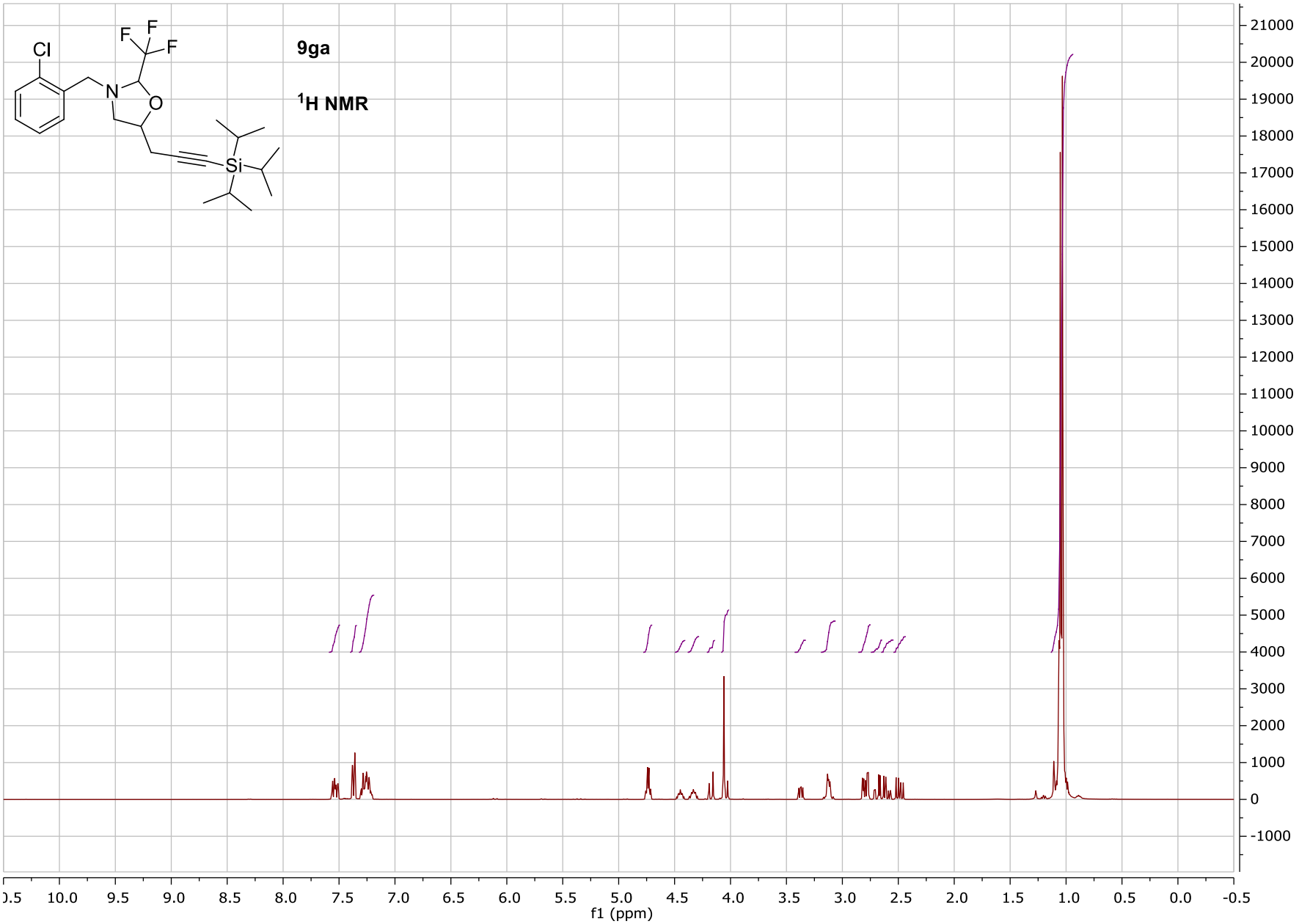
Cl
F
F
F
N
O
Si
9ga
^{1}H NMR
21000
20000
19000
18000
17000
16000
15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
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3.0
2.5
2.0
1.5
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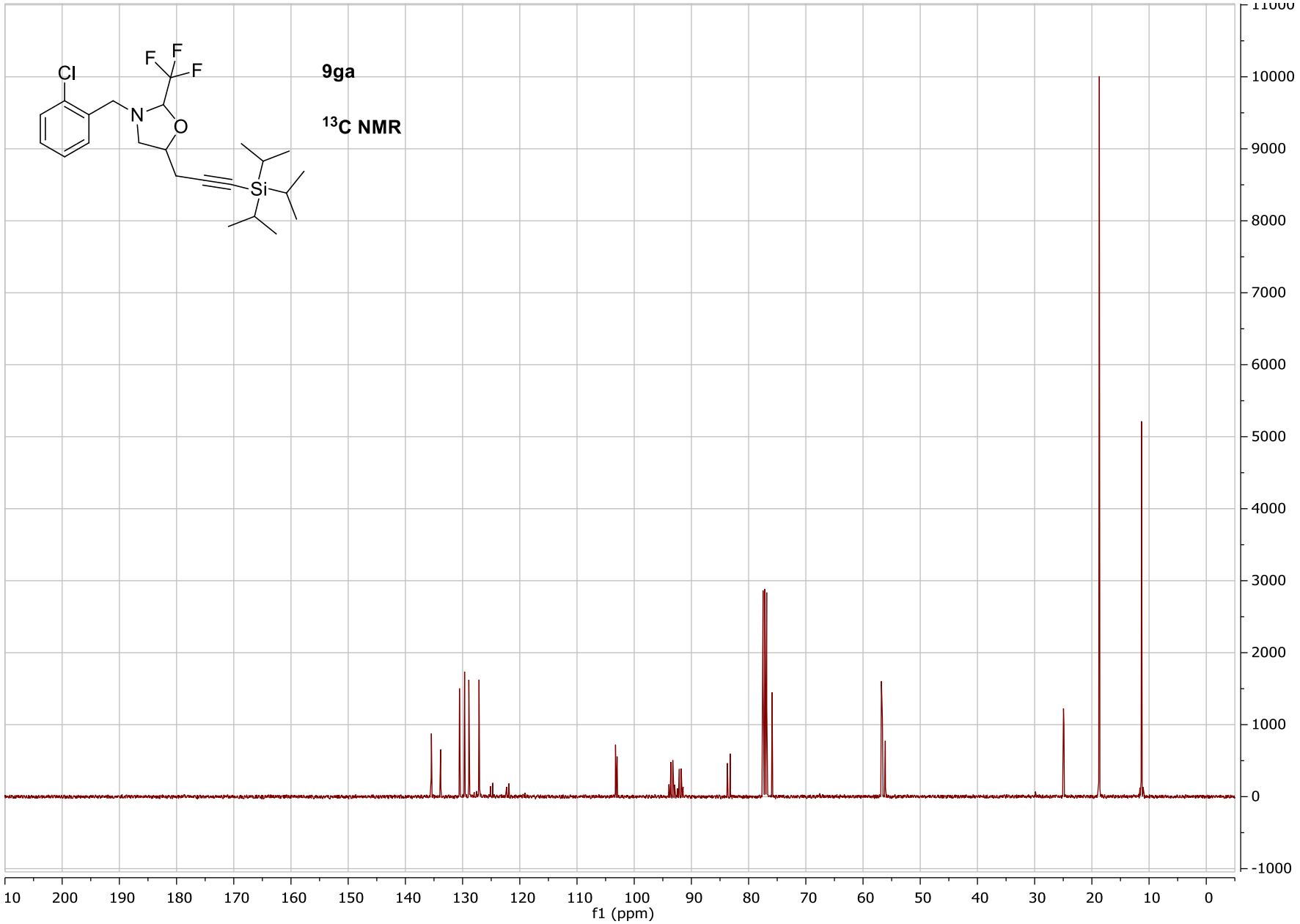
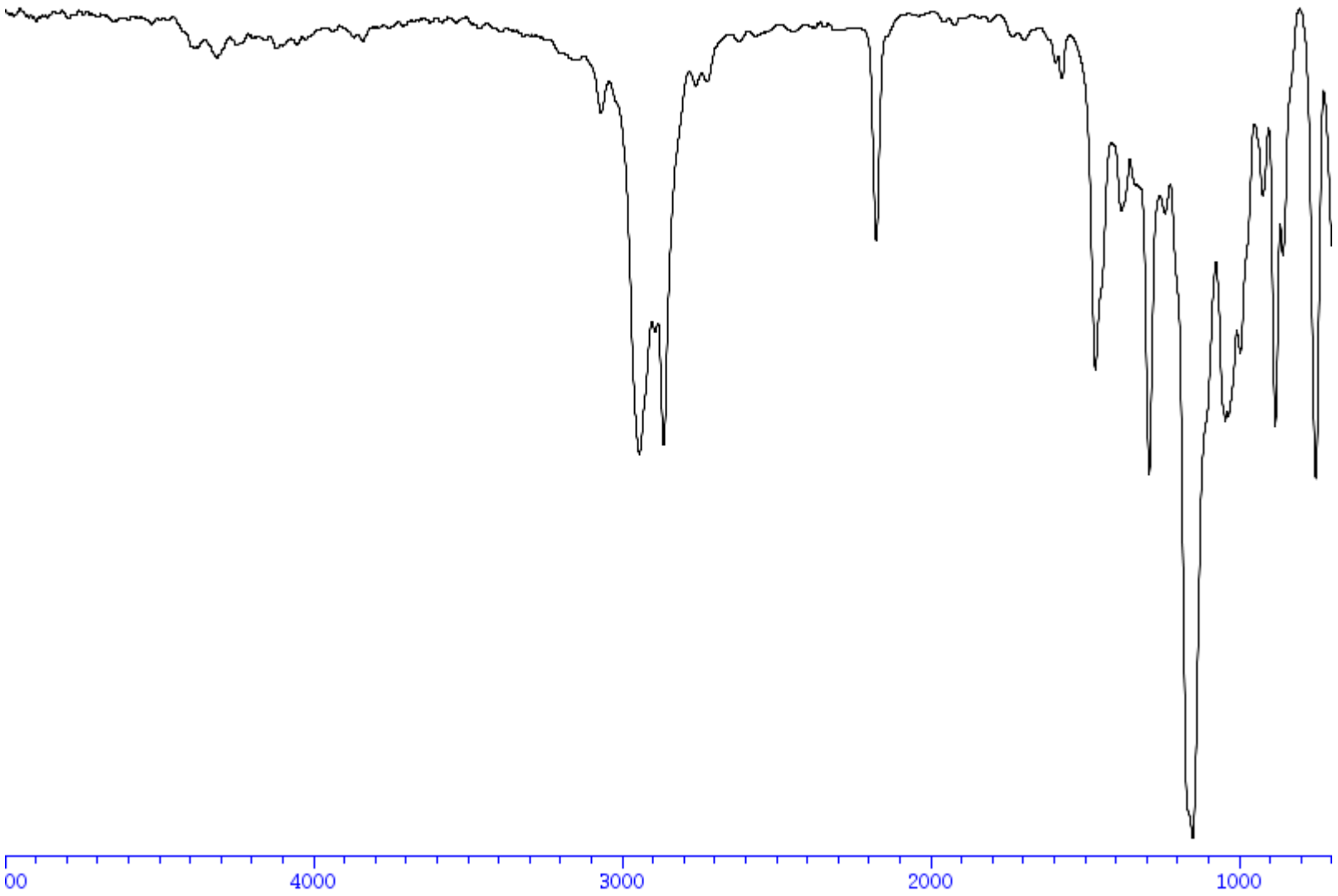
0.5
0.0
-0.5
f1 (ppm)


Cl
F
F
F
N
O
Si
9ga
13C NMR
f1 (ppm)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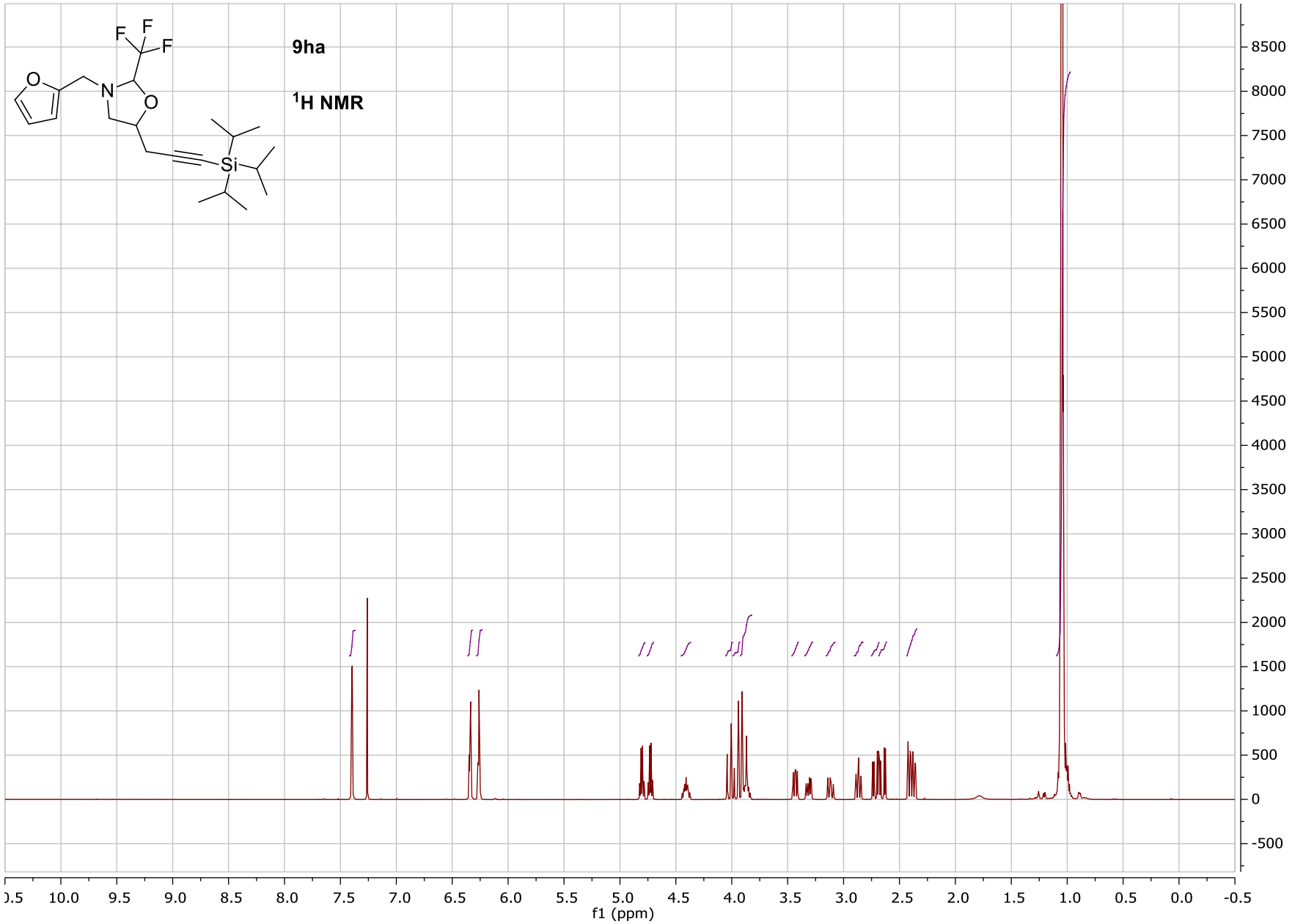
9ha
1H NMR
F
F
F
O
N
O
Si
8500
8000
7500
7000
6500
6000
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
-500
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
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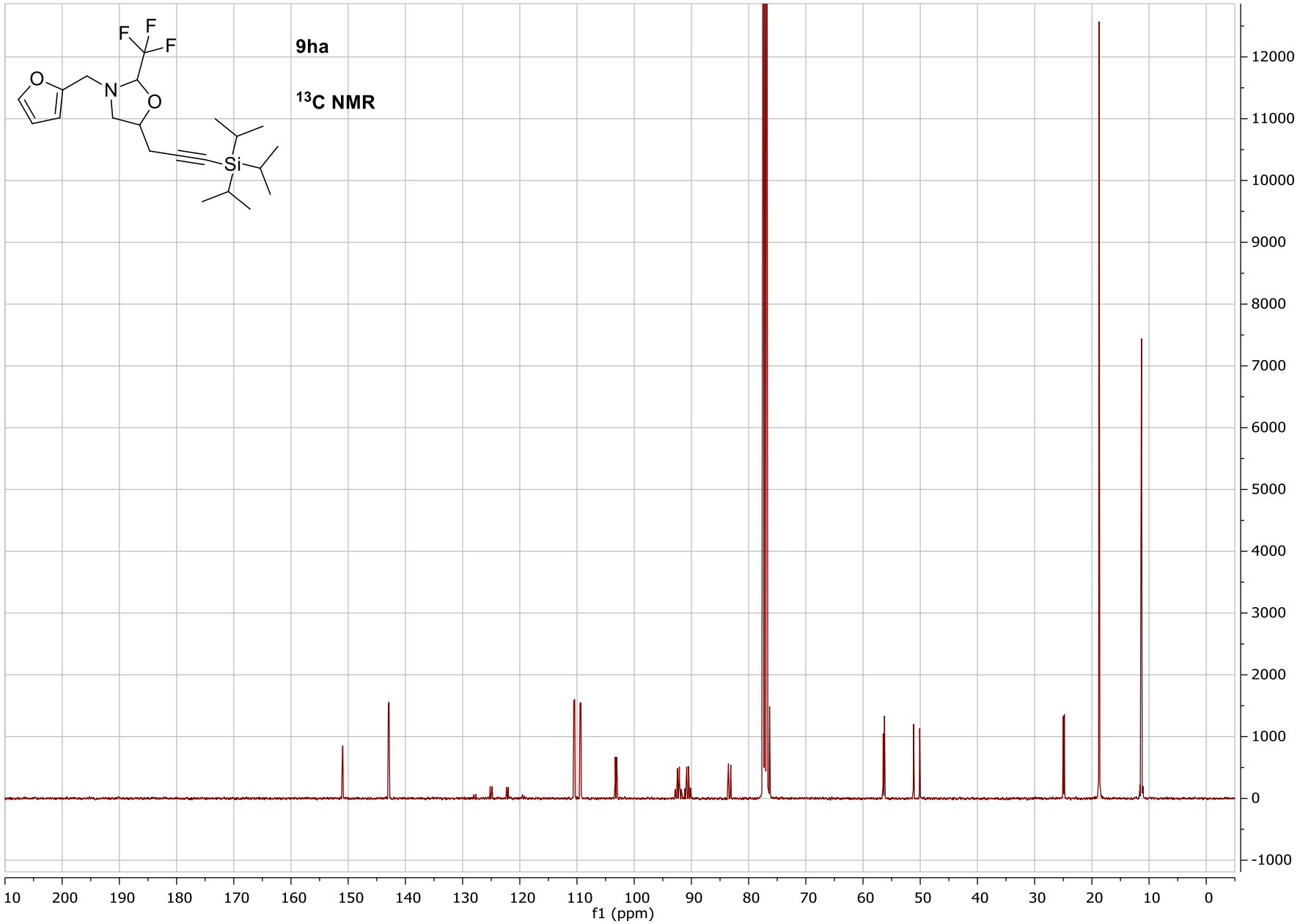
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)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13C NMR
F
F
F
O
N
O
Si
12000
11000
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8000
7000
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4000
3000
2000
1000
0
-1000
10
200
190
180
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90
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50
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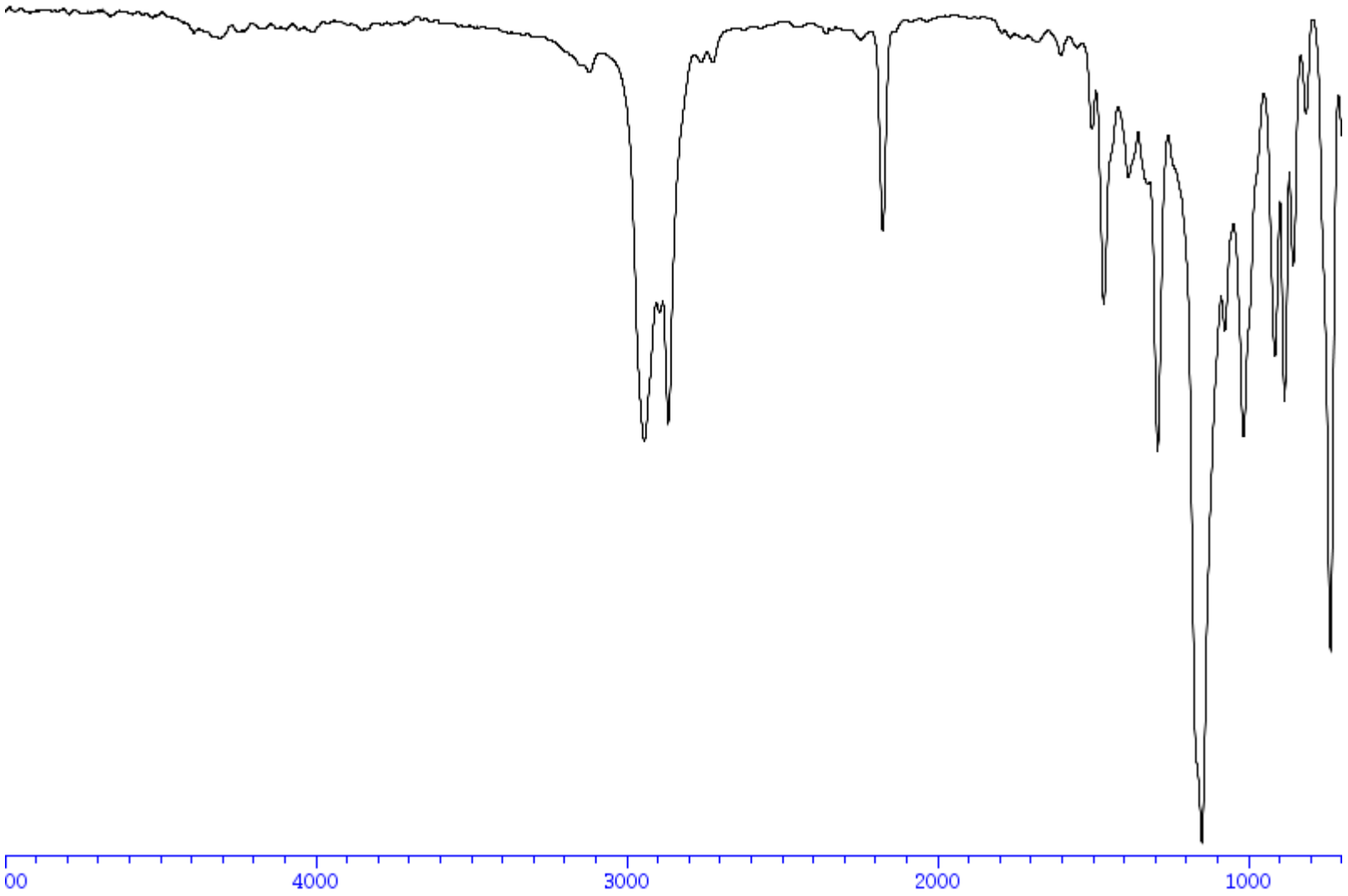
f1 (ppm)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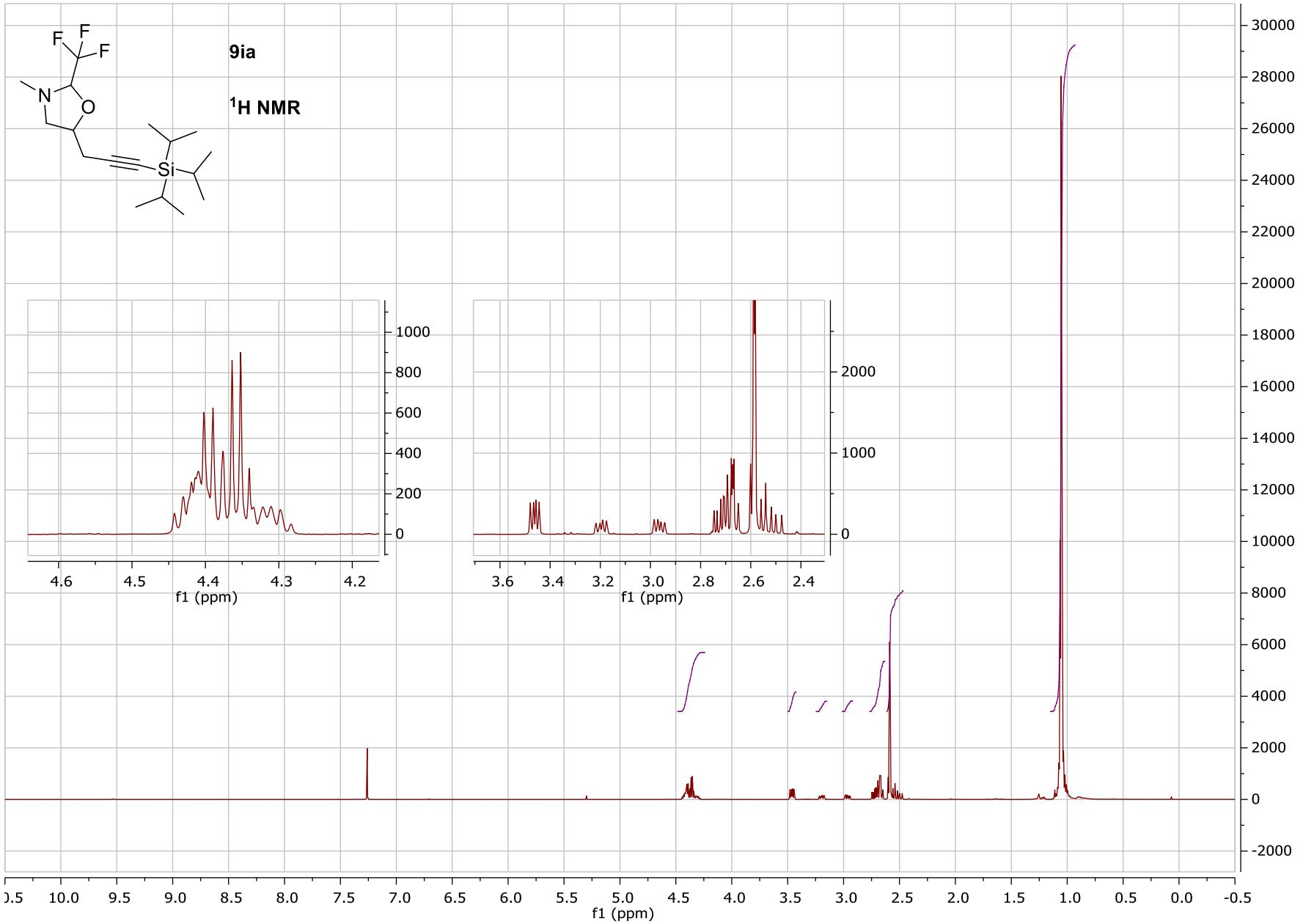
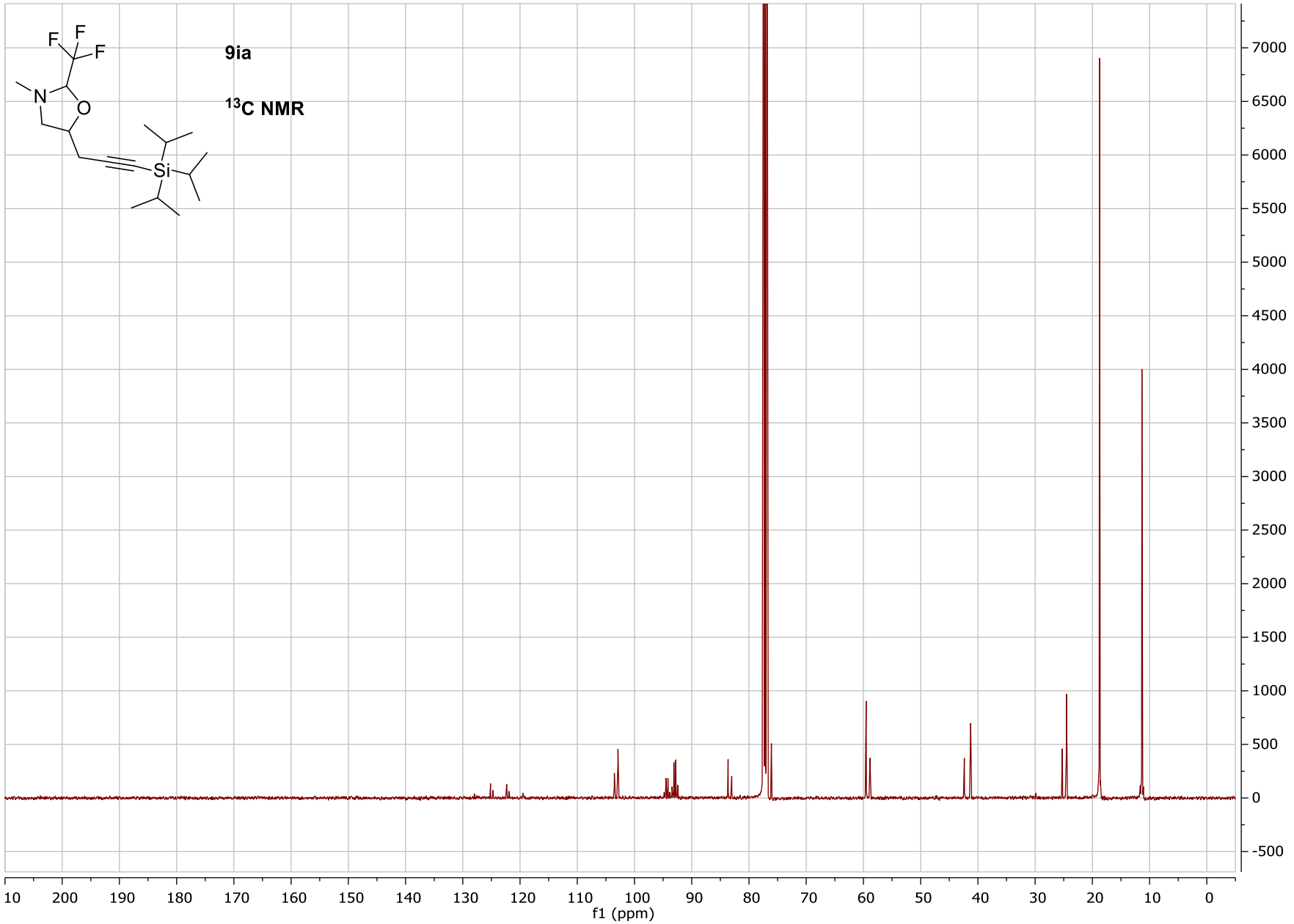

9ia
1H NMR
F
F
F
N
O
Si
f1 (ppm)
f1 (ppm)
f1 (ppm)


9ia
13C NMR
F
F
F
N
O
Si
7000
6500
6000
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
-500
10
200
190
180
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130
120
110
100
90
80
70
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50
40
30
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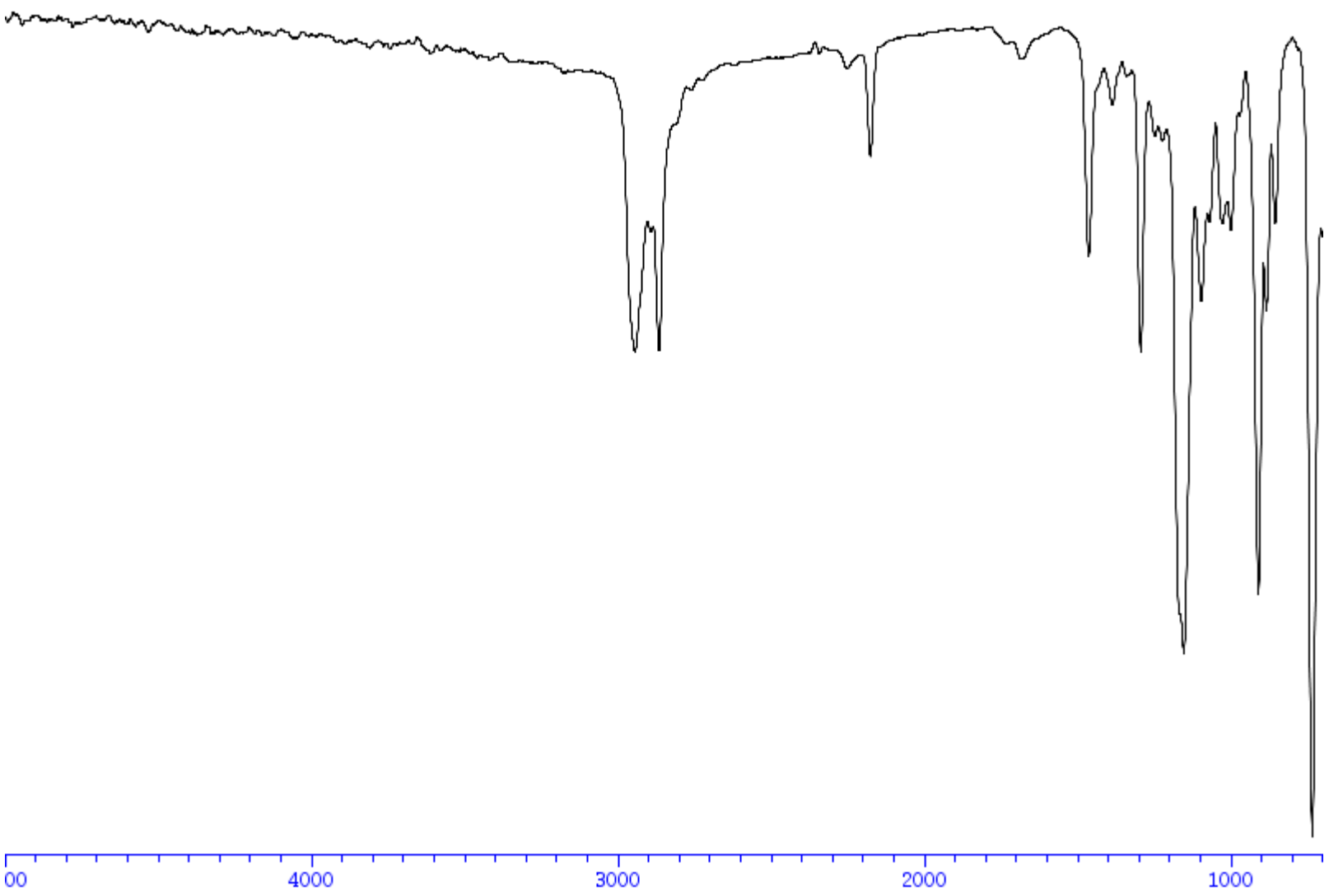
10
0
f1 (ppm)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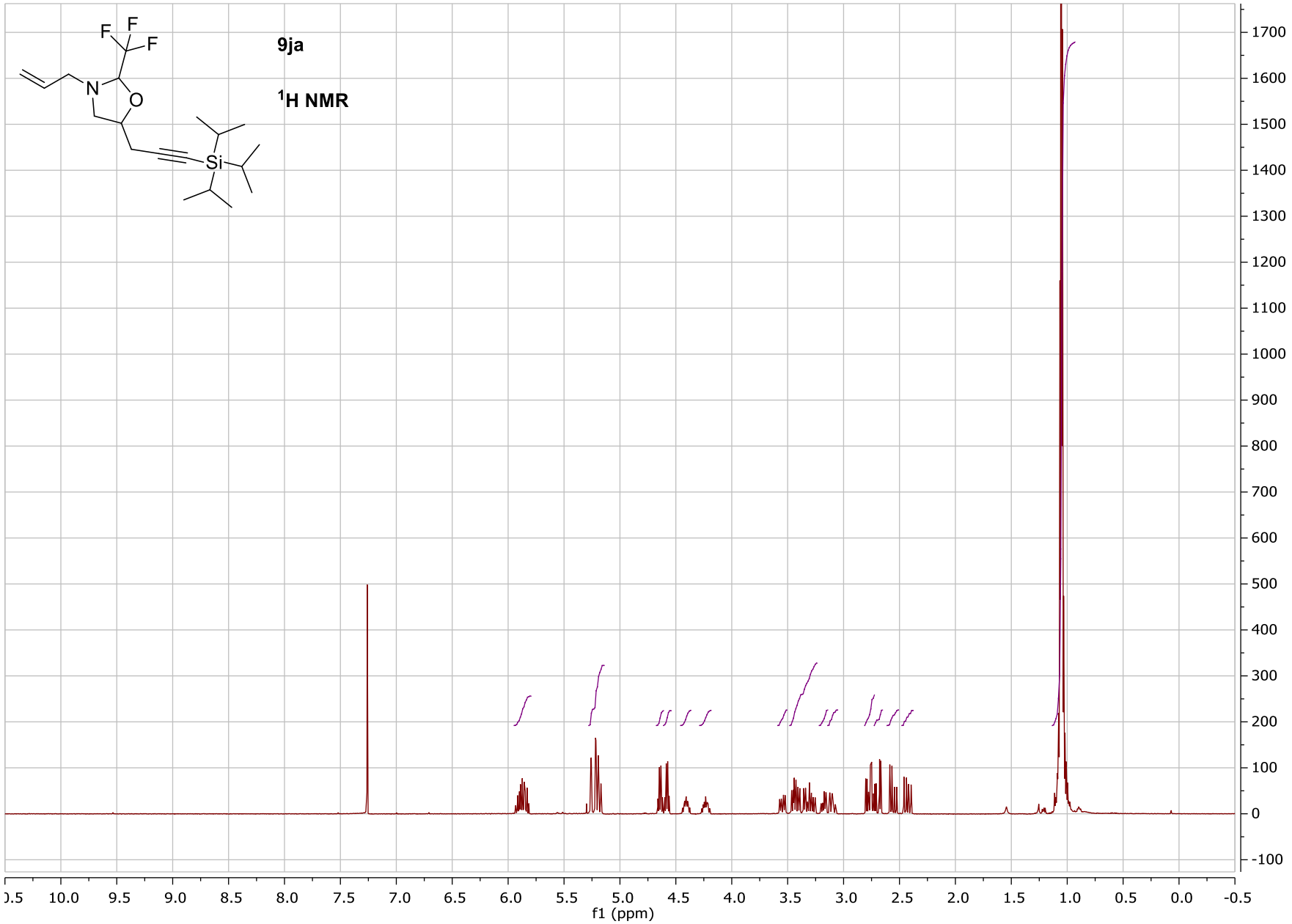
1000


F
F
F
N
O
Si
9ja
1H NMR
1700
1600
1500
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
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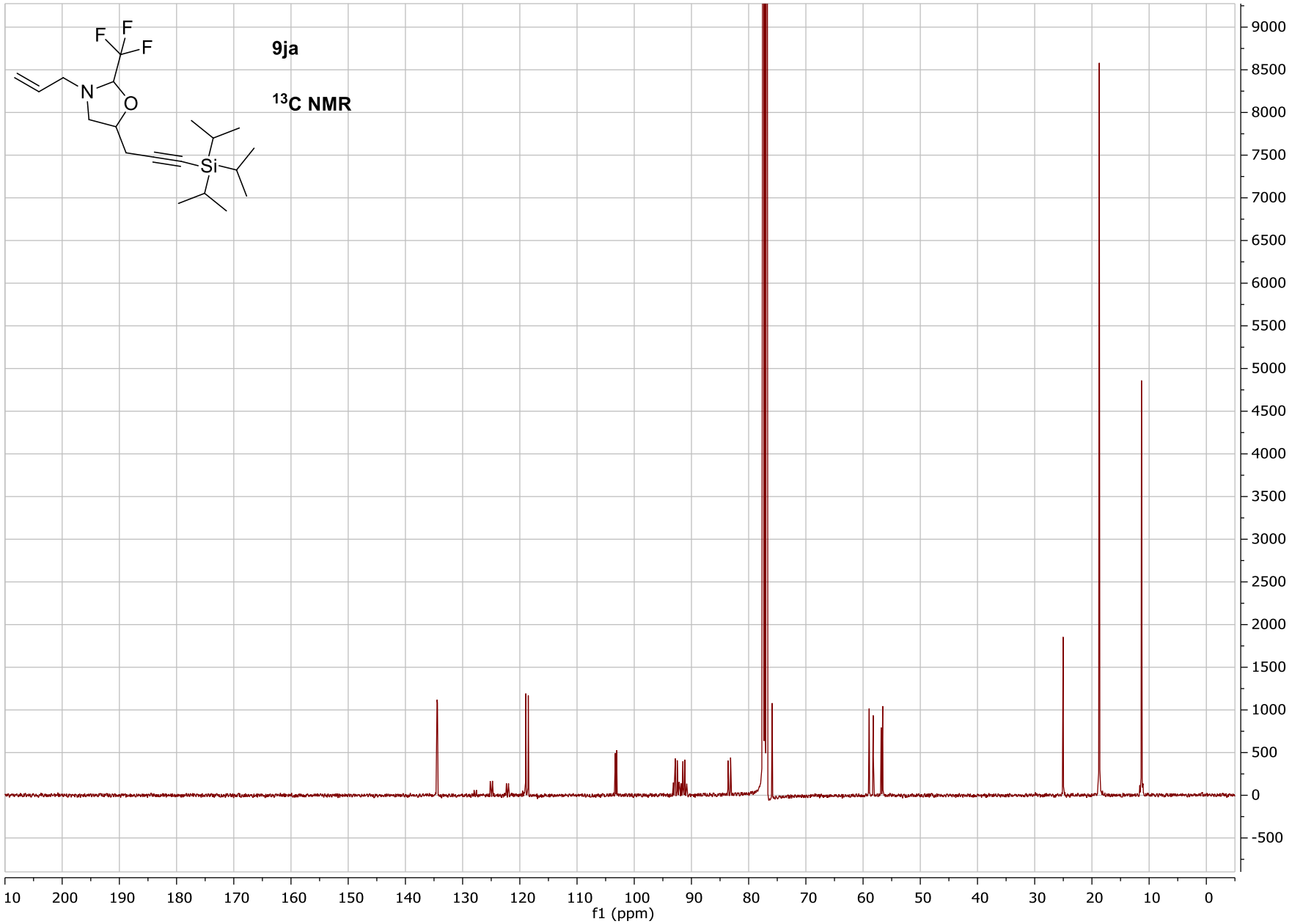
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)


9ja
13C NMR
F
F
F
N
O
Si
9000
8500
8000
7500
7000
6500
6000
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
-500
10
200
190
180
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160
150
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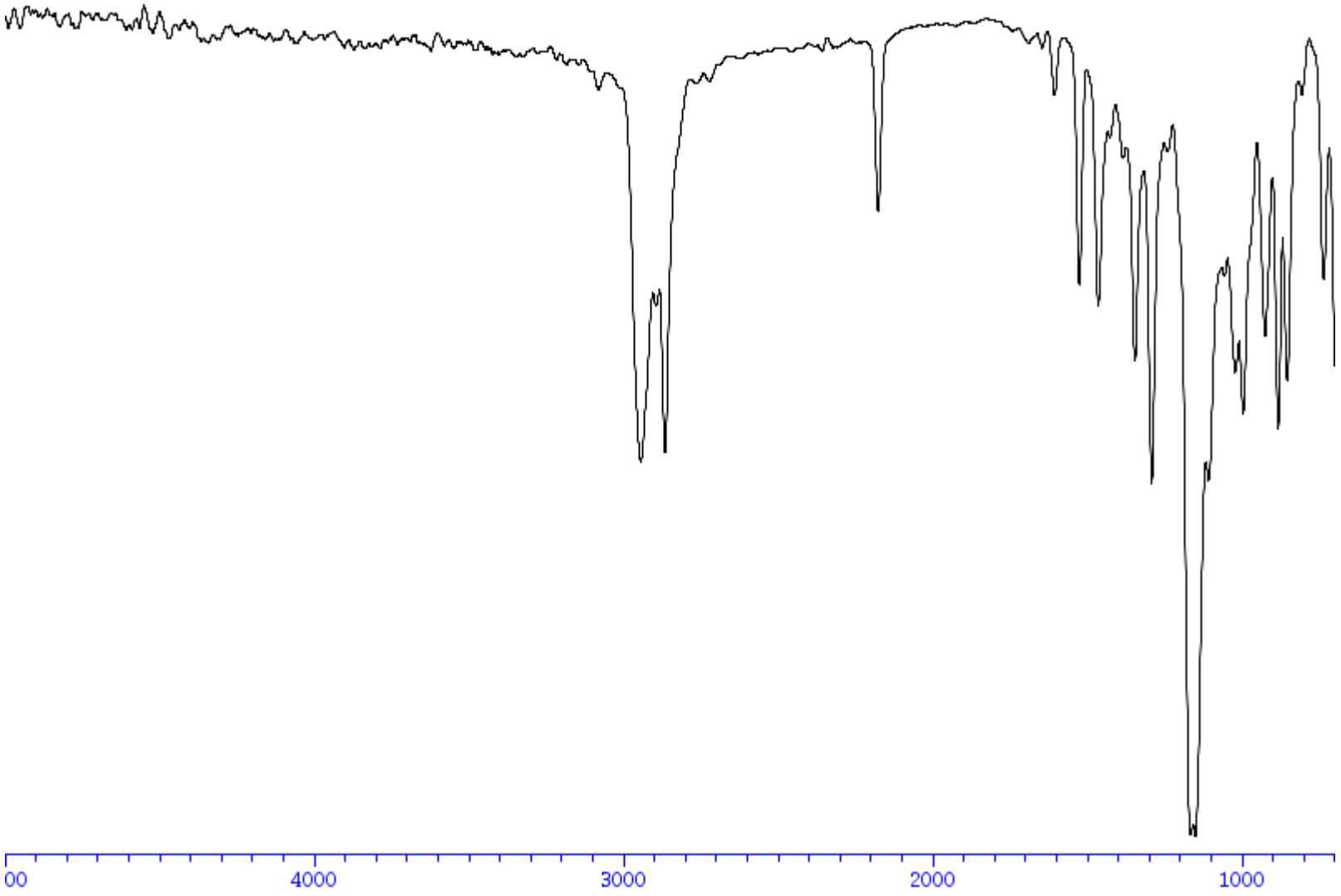
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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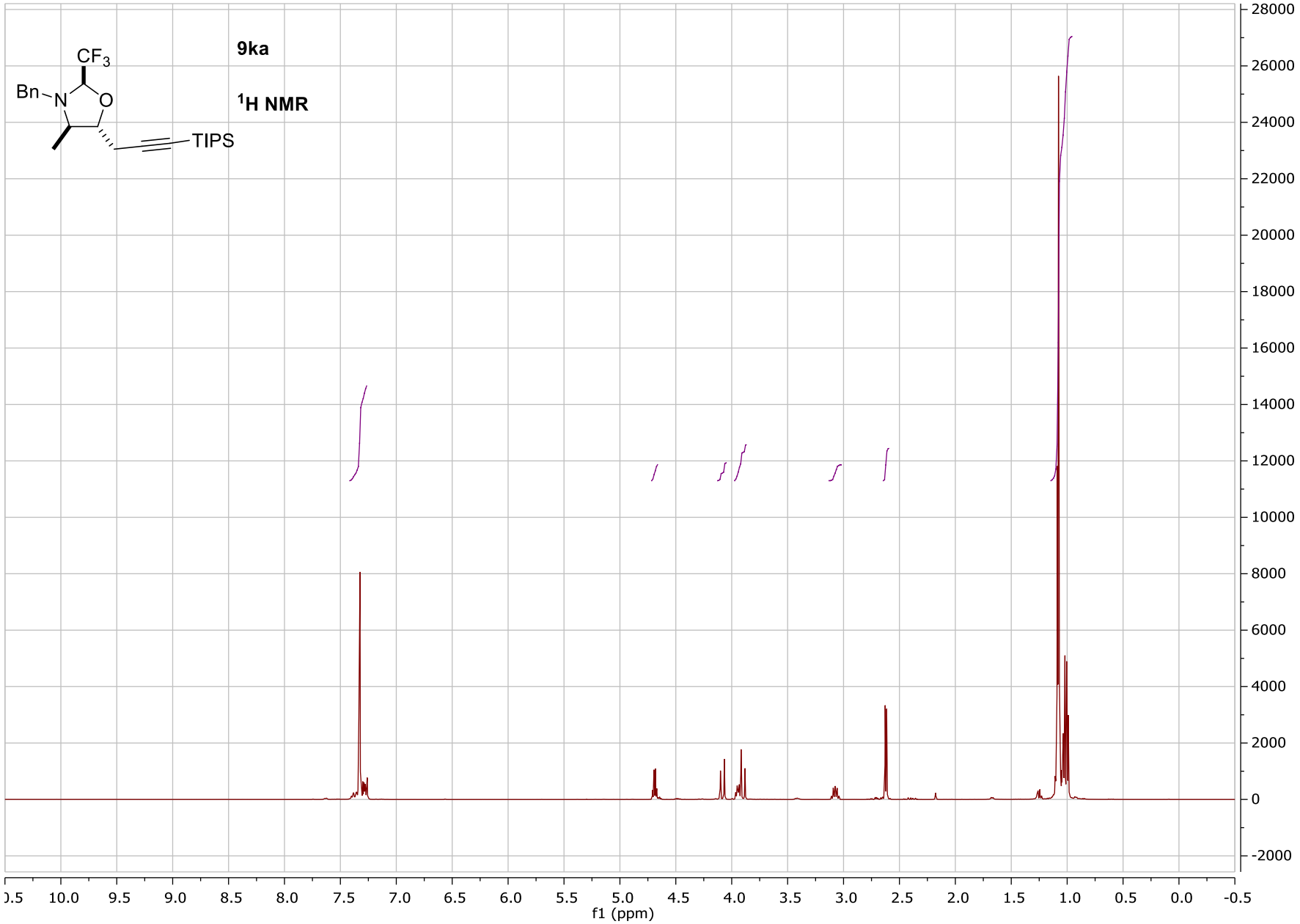
9ka
^{1}H NMR
CF3
Bn
N
O
TIPS
28000
26000
24000
22000
20000
18000
16000
14000
12000
10000
8000
6000
4000
2000
0
-2000
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
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3.0
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2.0
1.5
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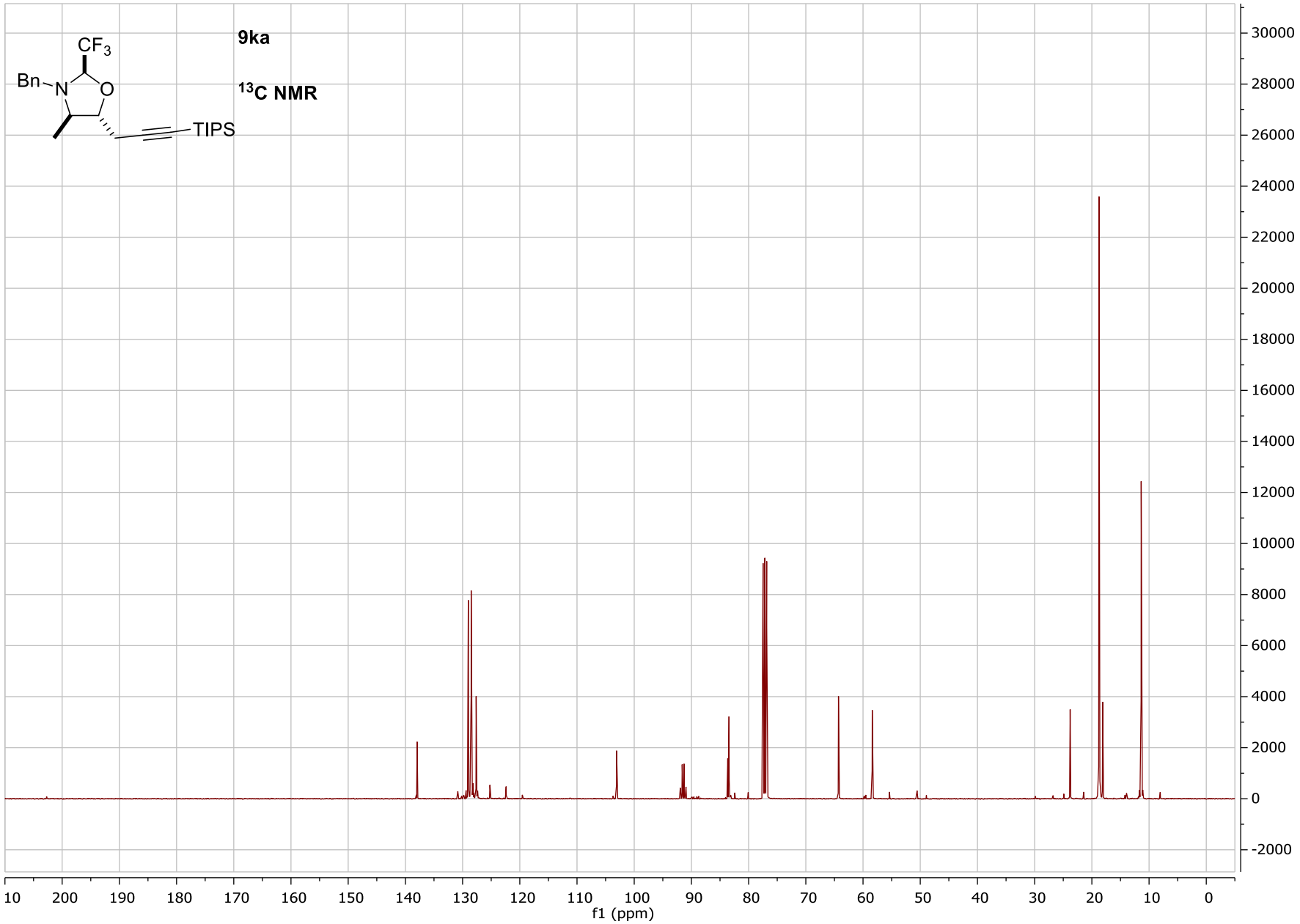
0.5
0.0
-0.5
f1 (ppm)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13C NMR
CF3
Bn
N
O
TIPS
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26000
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20000
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14000
12000
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8000
6000
4000
2000
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190
180
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90
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50
40
30
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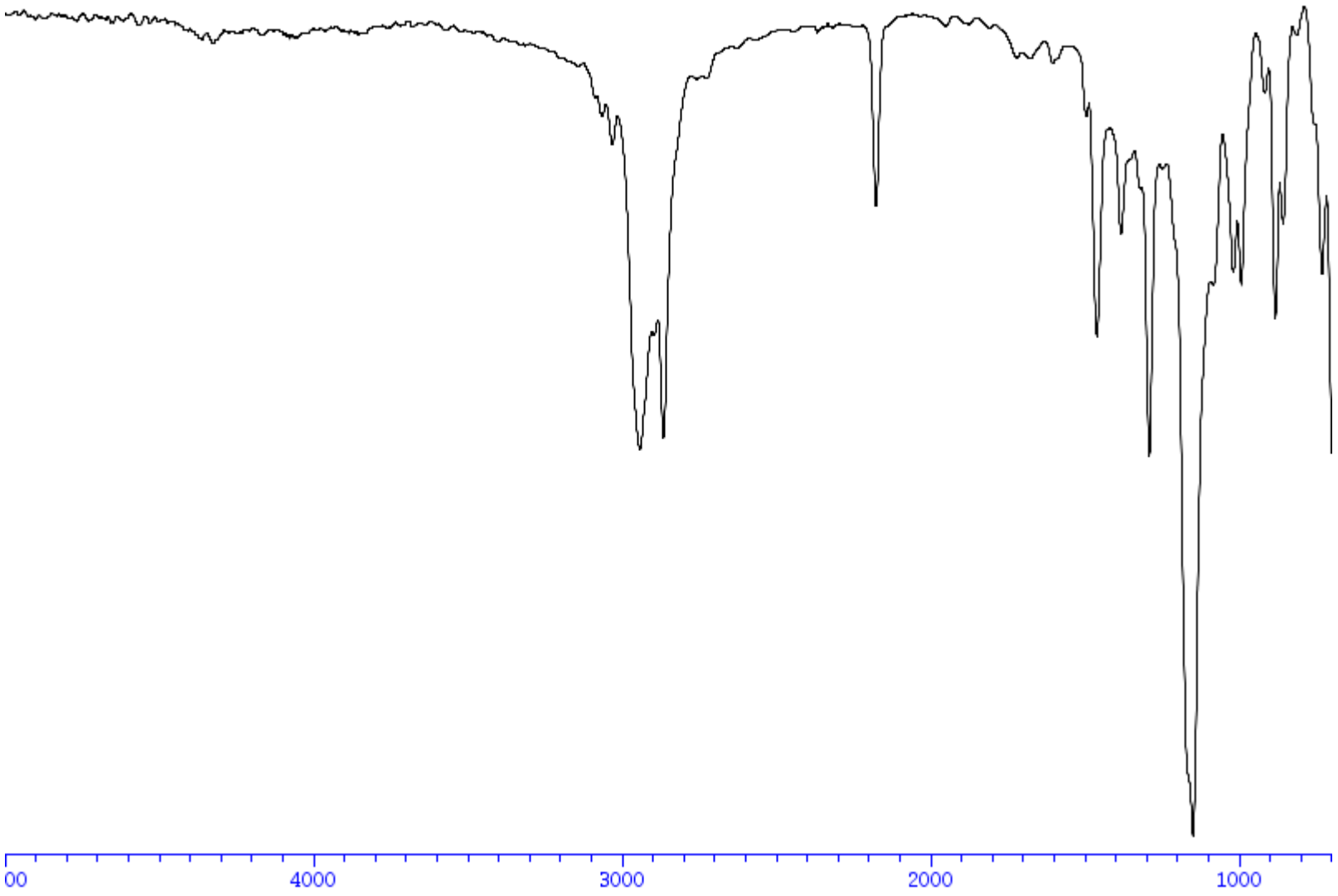
f1 (ppm)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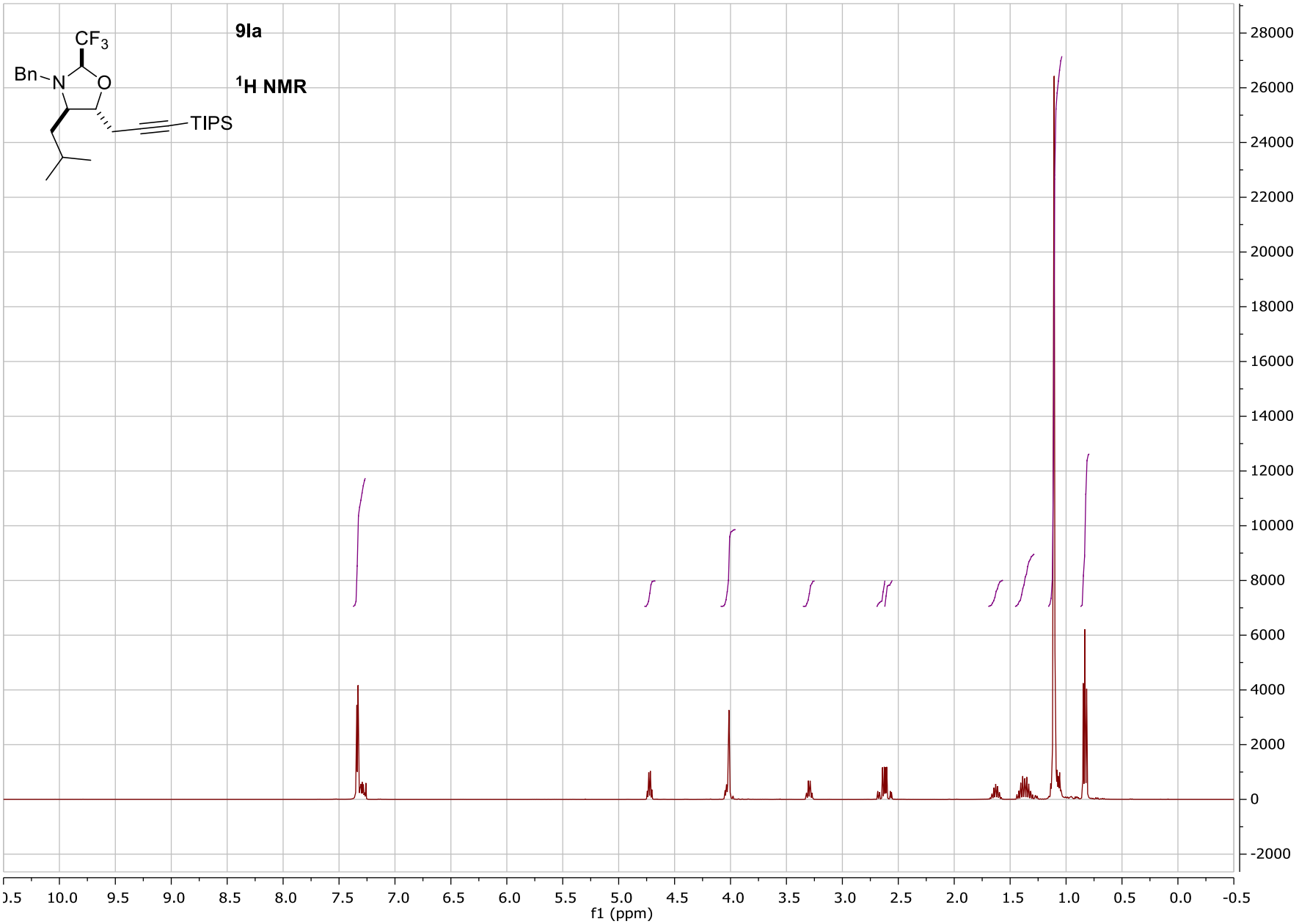
9Ia
^{1}H NMR
CF3
Bn
N
O
TIPS
28000
26000
24000
22000
20000
18000
16000
14000
12000
10000
8000
6000
4000
2000
0
-2000
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
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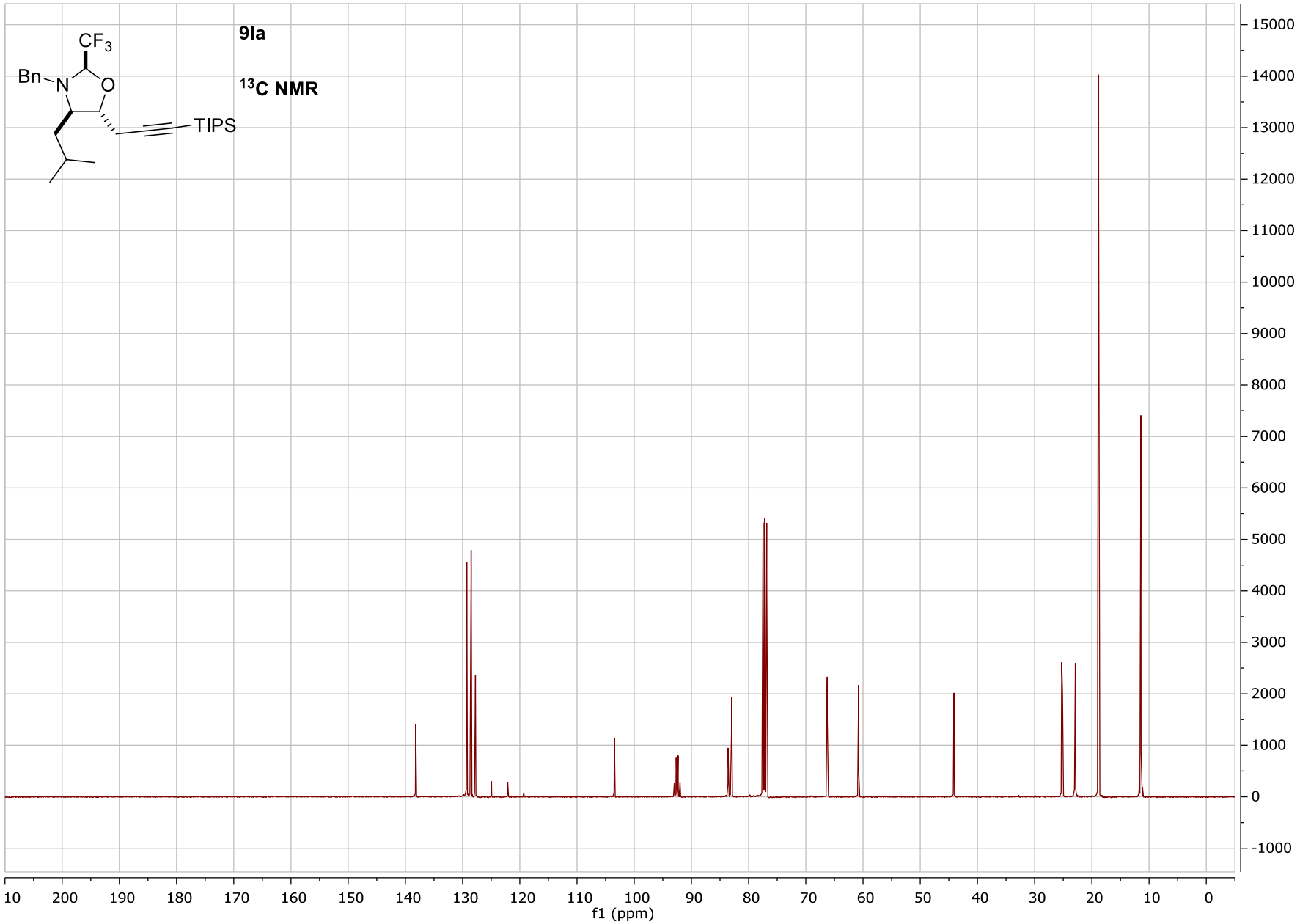
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)


9la
13C NMR
CF3
Bn
N
O
TIPS
15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
10
200
190
180
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130
120
110
100
90
80
70
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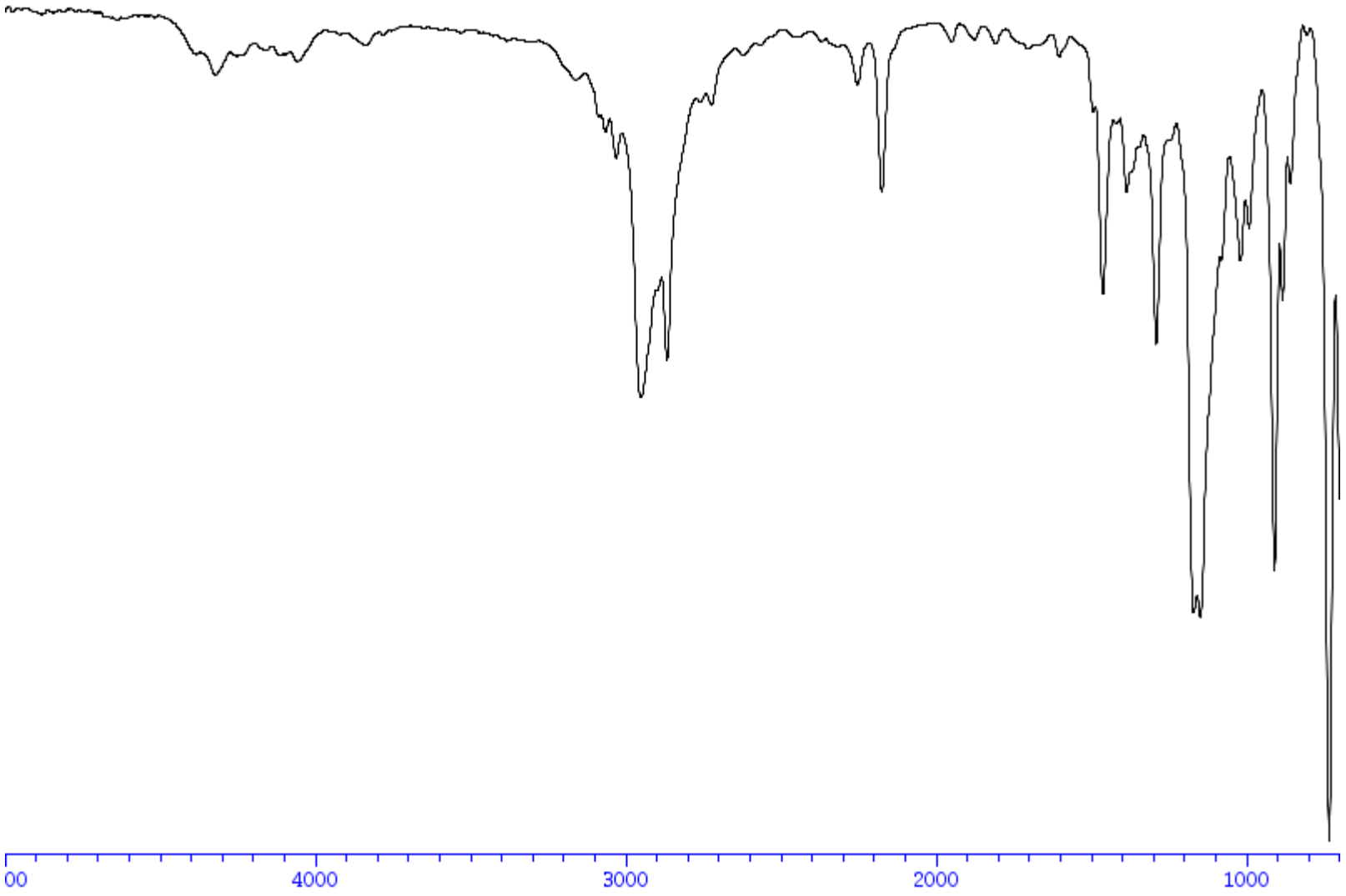
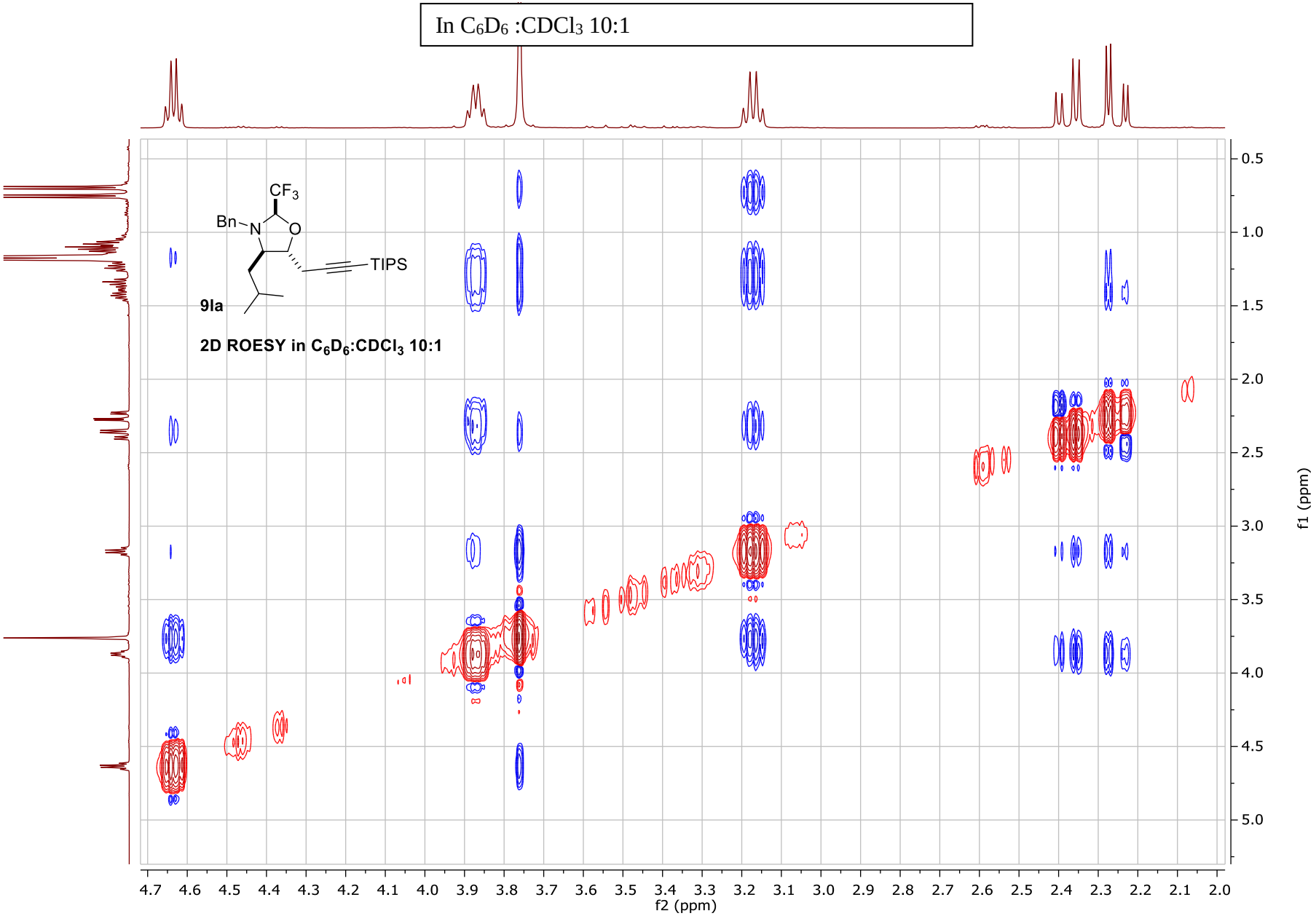
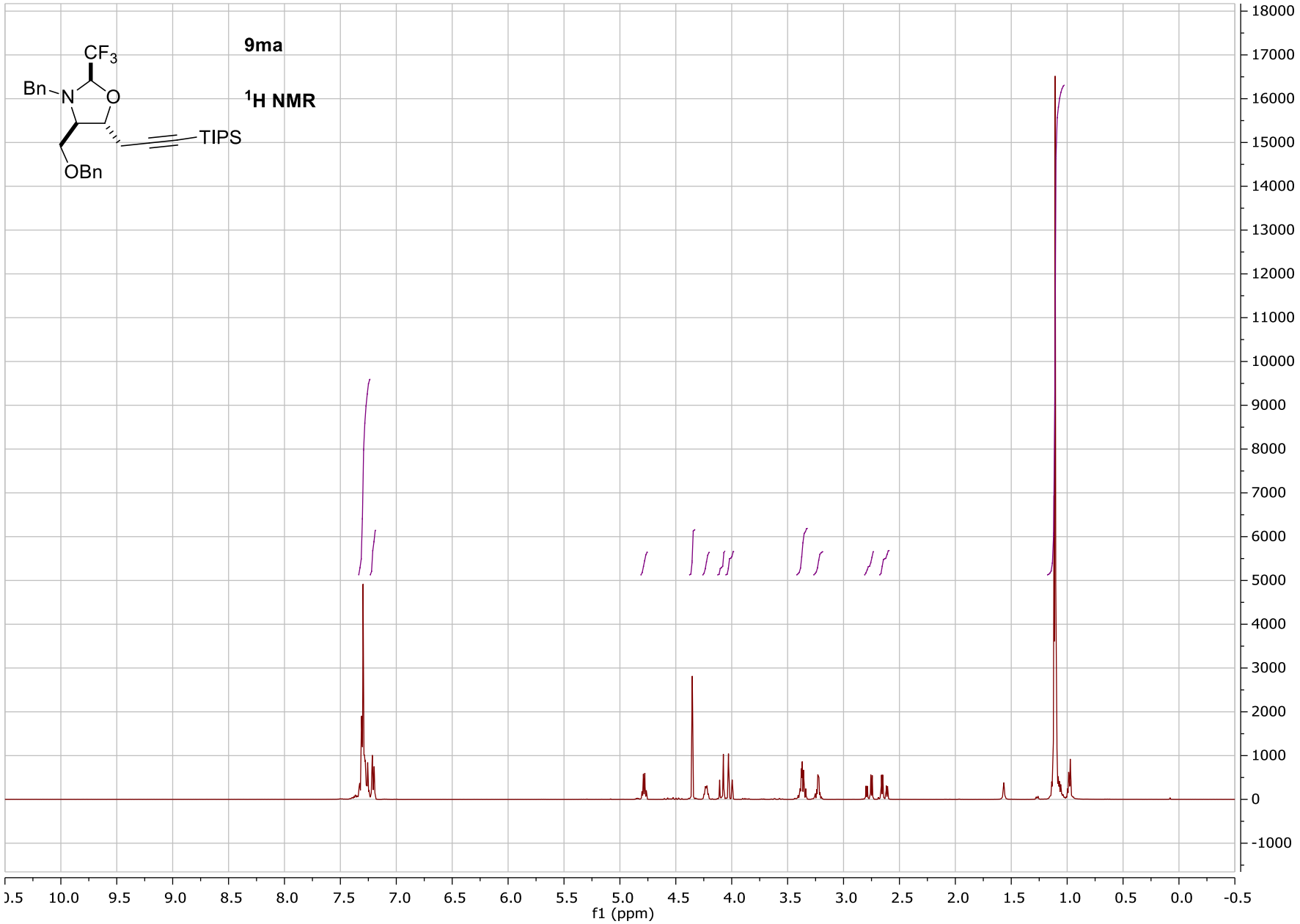
50
40
30
20
10
0
f1 (ppm)


00
4000
3000
2000
1000


In C6D6 :CDCl3 10:1
CF3
Bn
N
O
TIPS
9Ia
2D ROESY in C6D6:CDCl3 10:1
f2 (ppm)
f1 (ppm)


9ma
^{1}H NMR
CF3
Bn
N
O
TIPS
OBn
18000
17000
16000
15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
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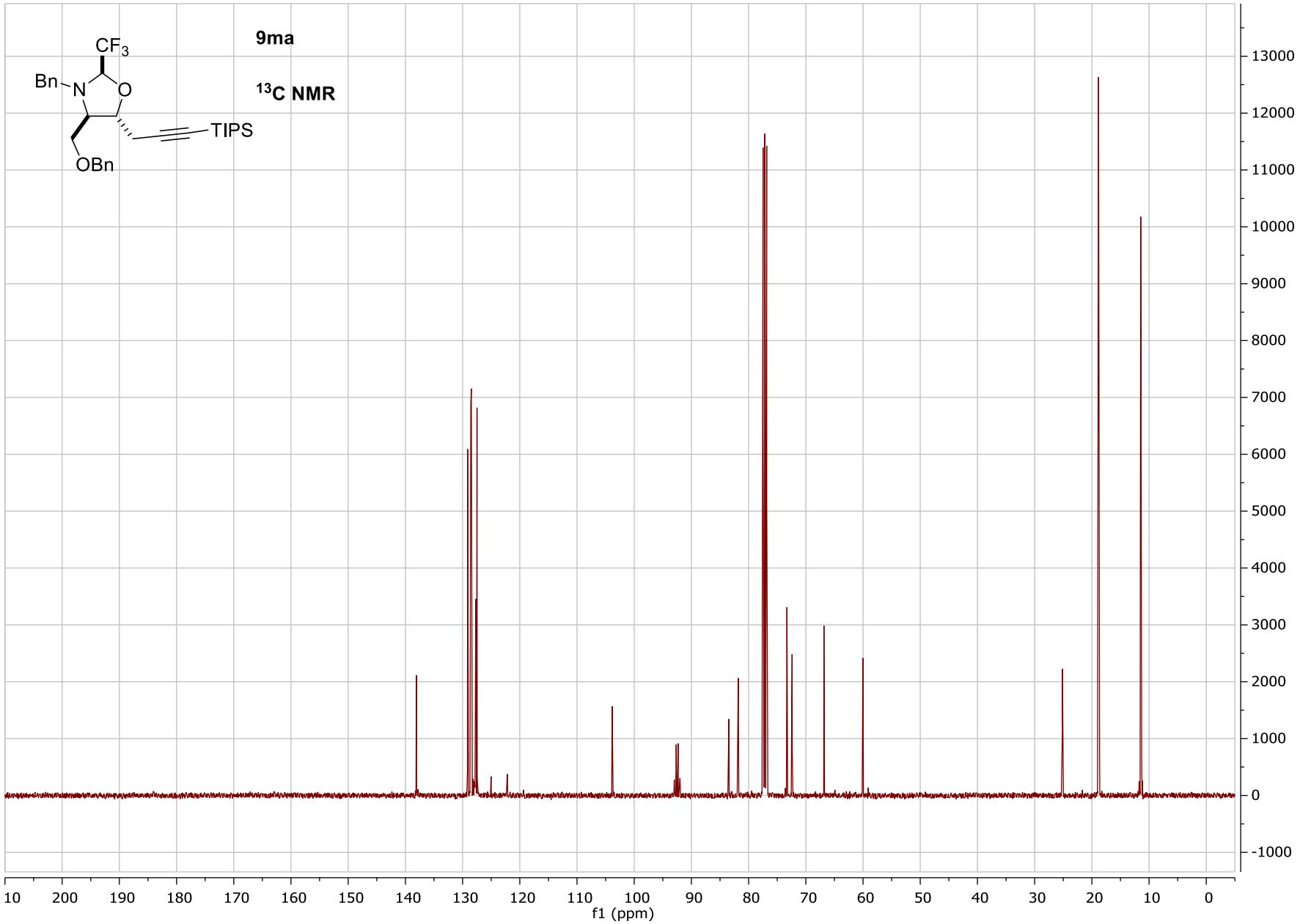
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)


9ma
13C NMR
CF3
Bn
N
O
TIPS
OBn
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
10
200
190
180
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150
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130
120
110
100
90
80
70
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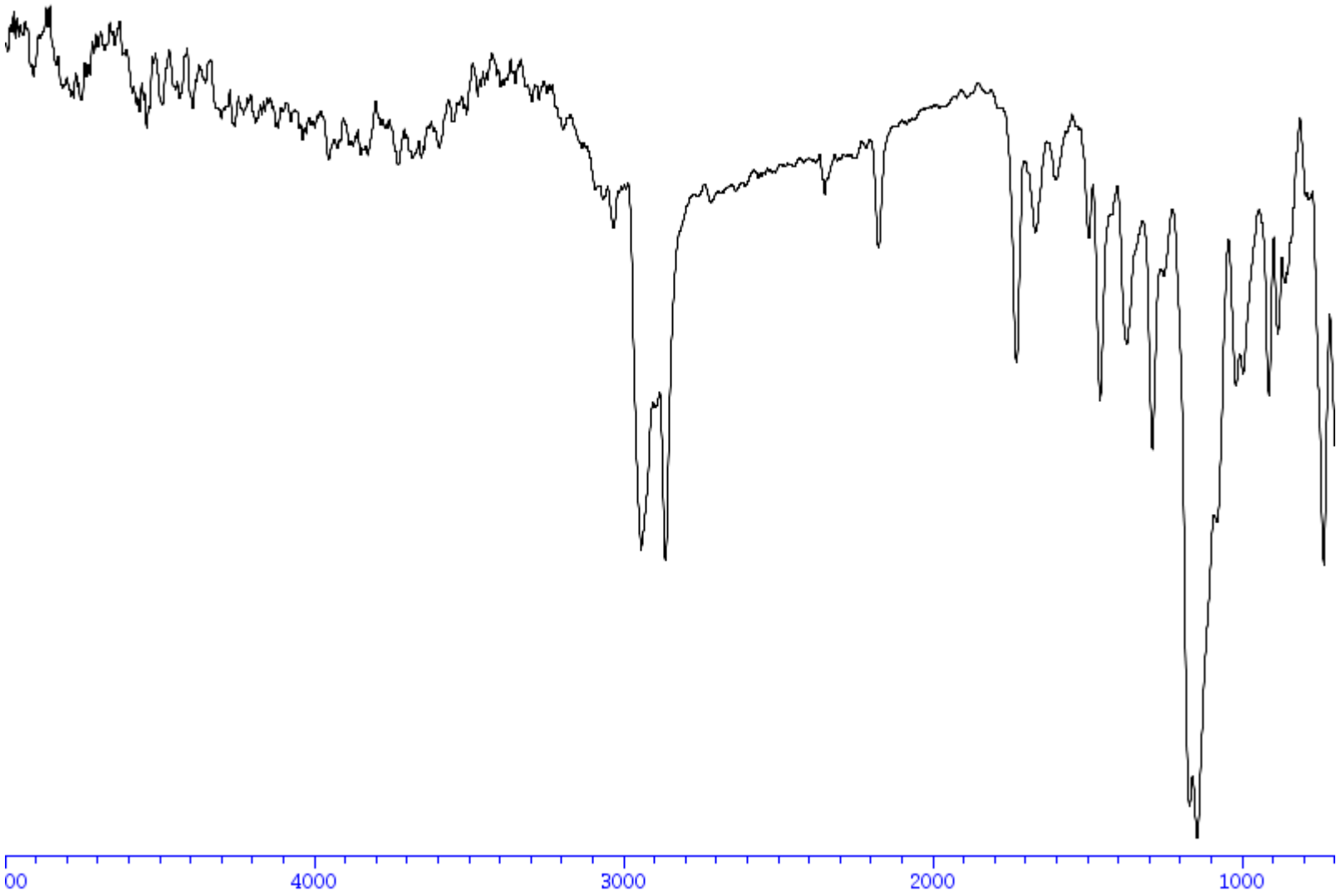
50
40
30
20
10
0
f1 (ppm)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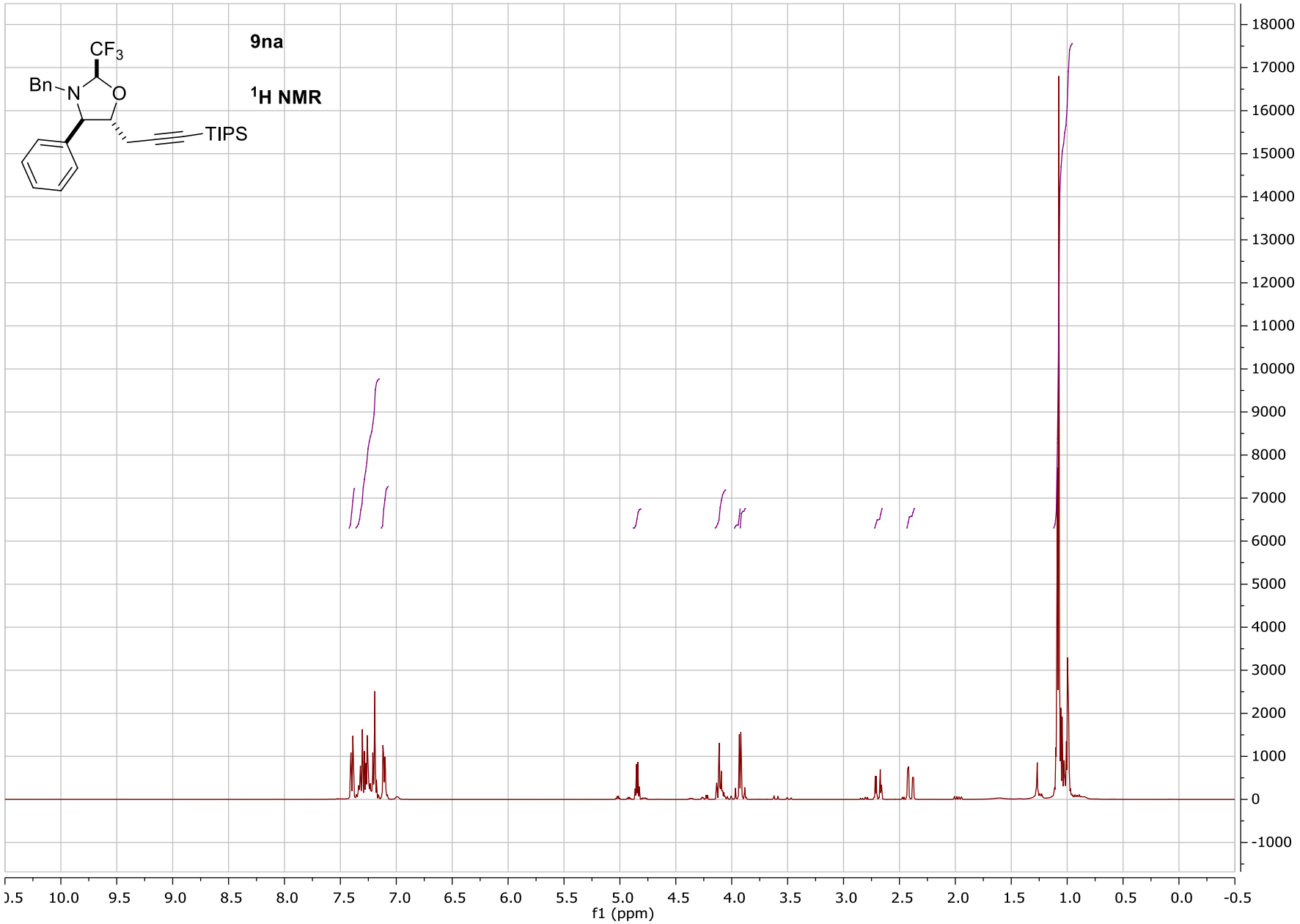
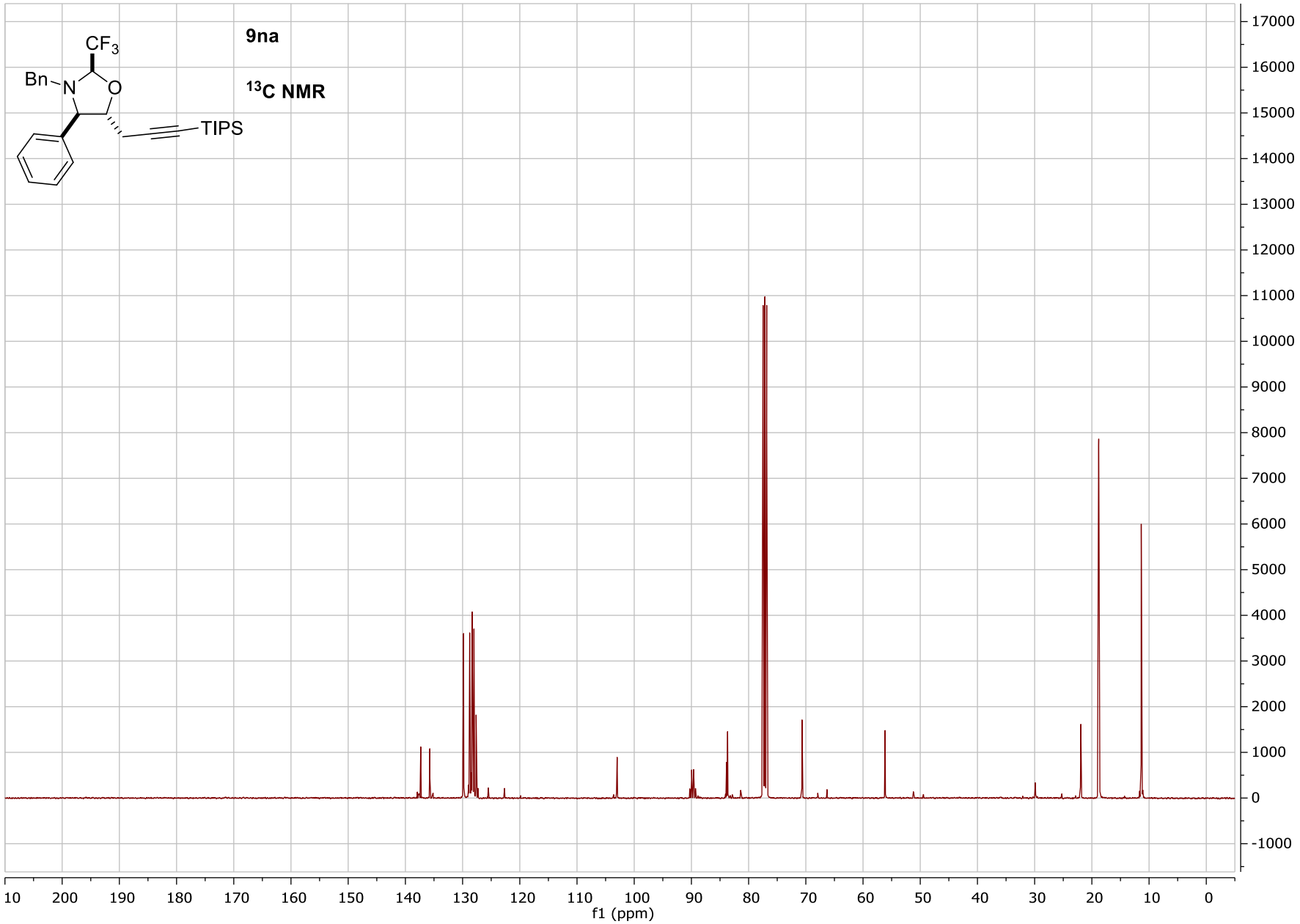

9na
^{1}H NMR
CF3
Bn
N
O
TIPS
f1 (ppm)


9na
13C NMR
CF3
Bn
N
O
TIPS
17000
16000
15000
14000
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12000
11000
10000
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8000
7000
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5000
4000
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2000
1000
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180
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10
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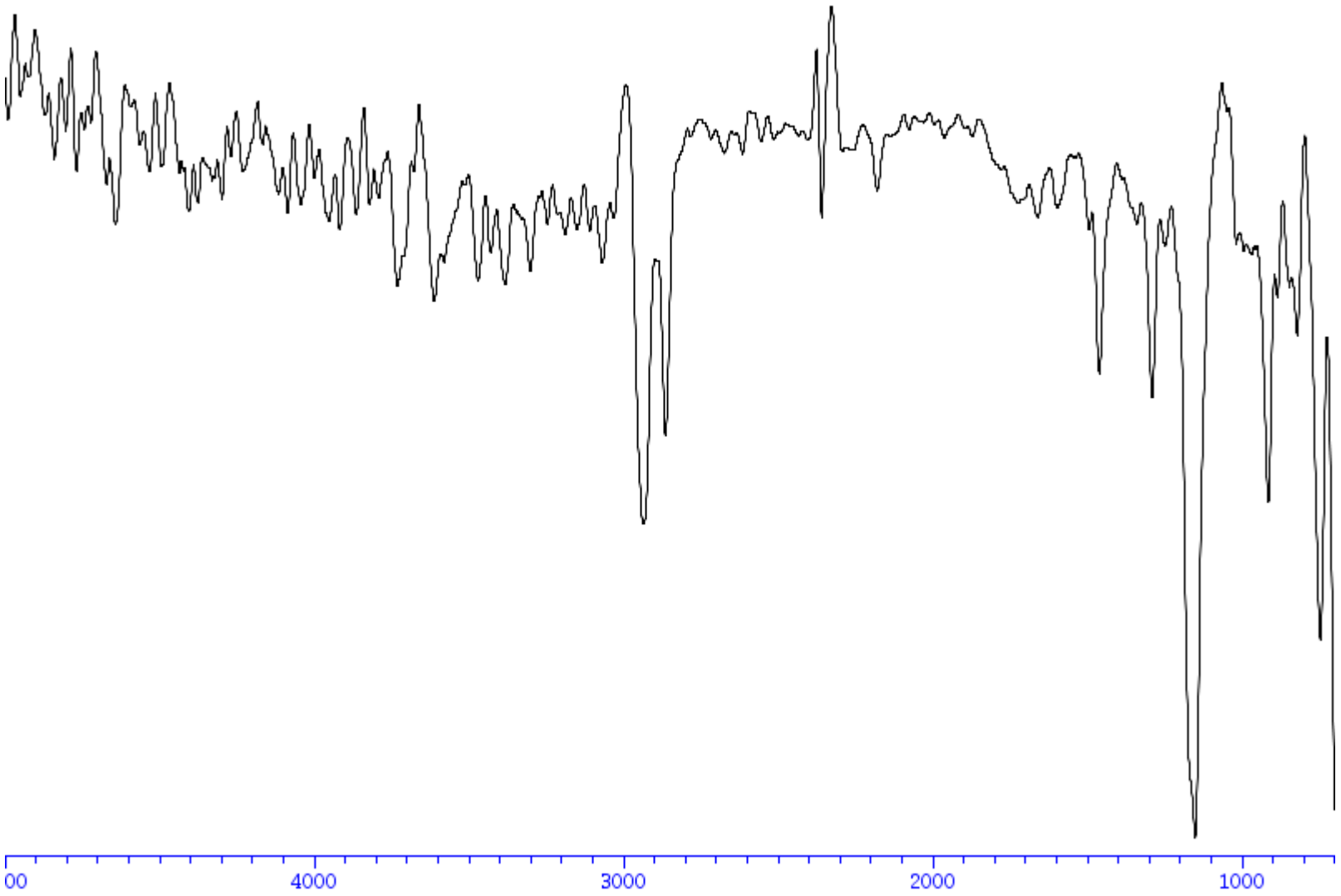
f1 (ppm)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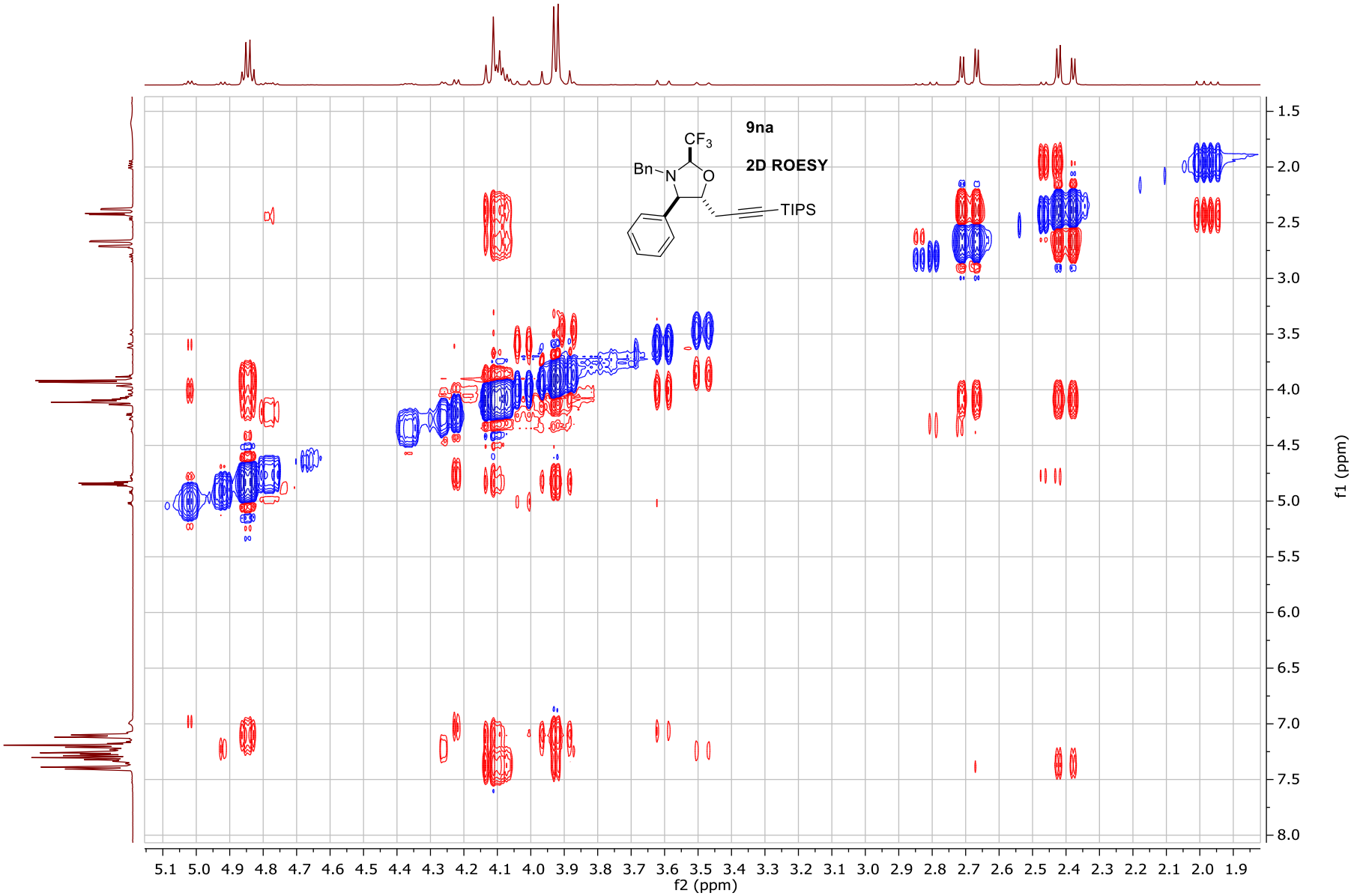
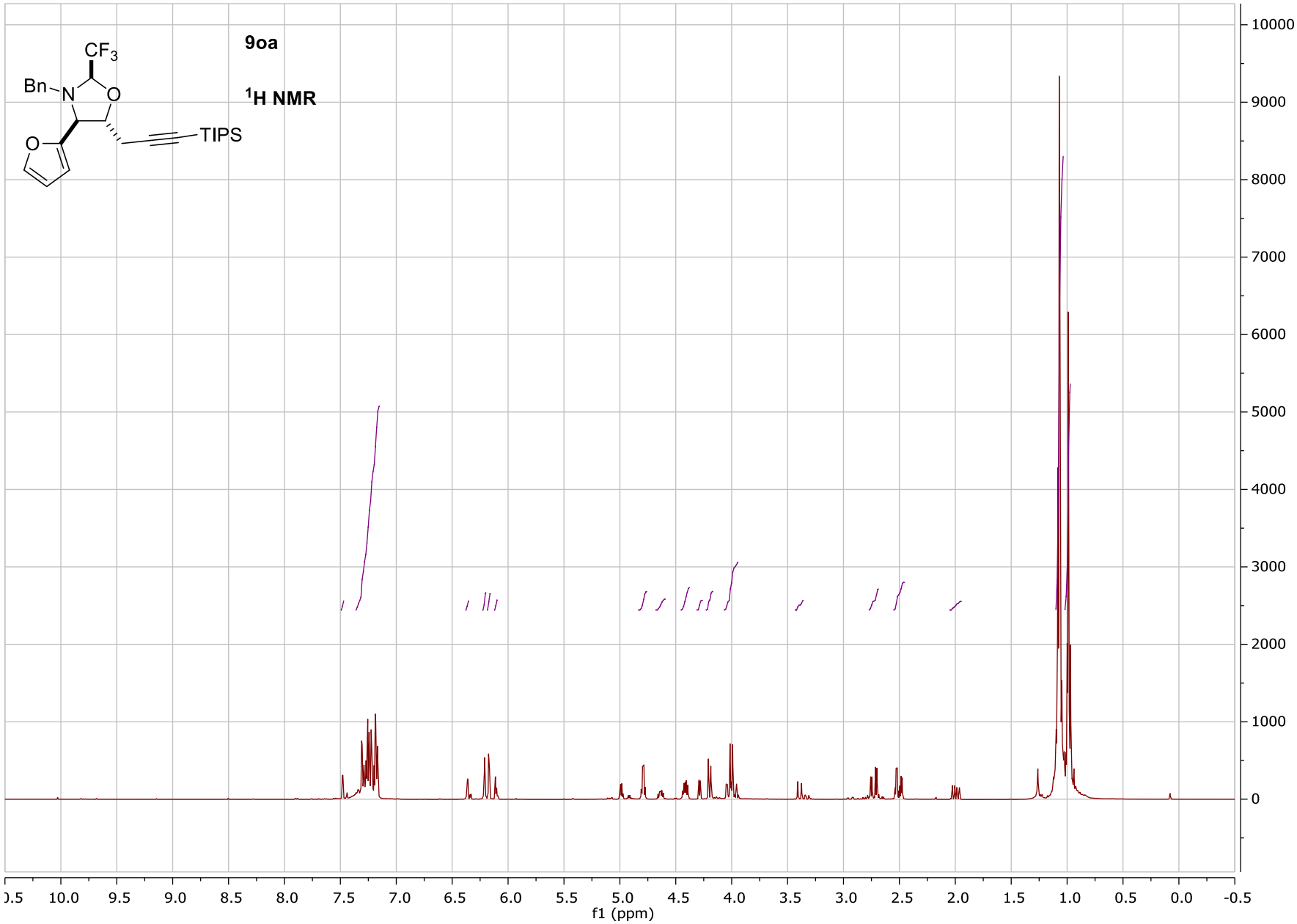
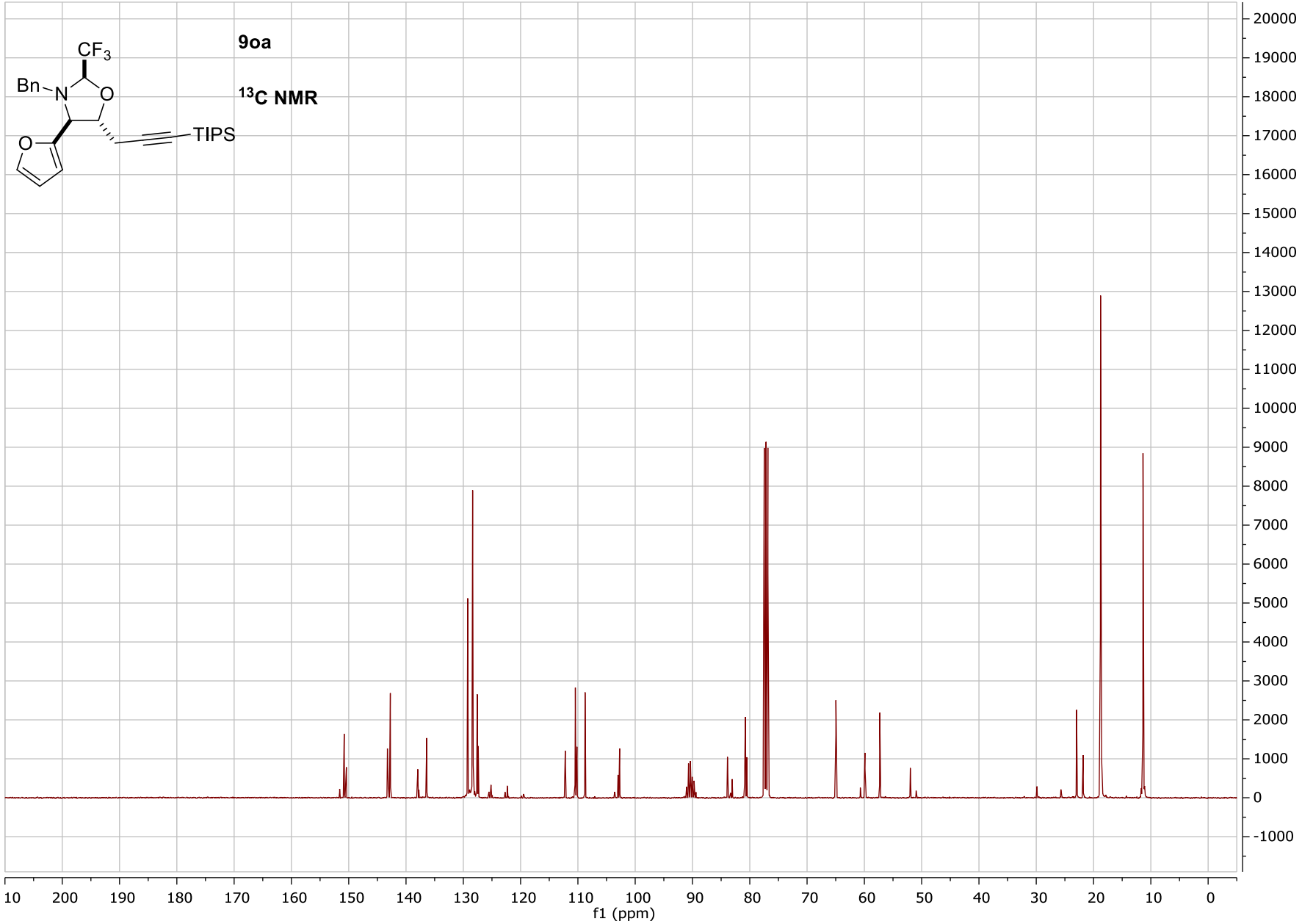

9na
2D ROESY
CF3
Bn
N
O
TIPS
f2 (ppm)
f1 (ppm)


9oa
^{1}H NMR
CF3
Bn
N
O
O
TIPS
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)


9oa
13C NMR
CF3
Bn
N
O
O
TIPS
20000
19000
18000
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16000
15000
14000
13000
12000
11000
10000
9000
8000
7000
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5000
4000
3000
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0
-1000
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190
180
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90
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70
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50
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30
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10
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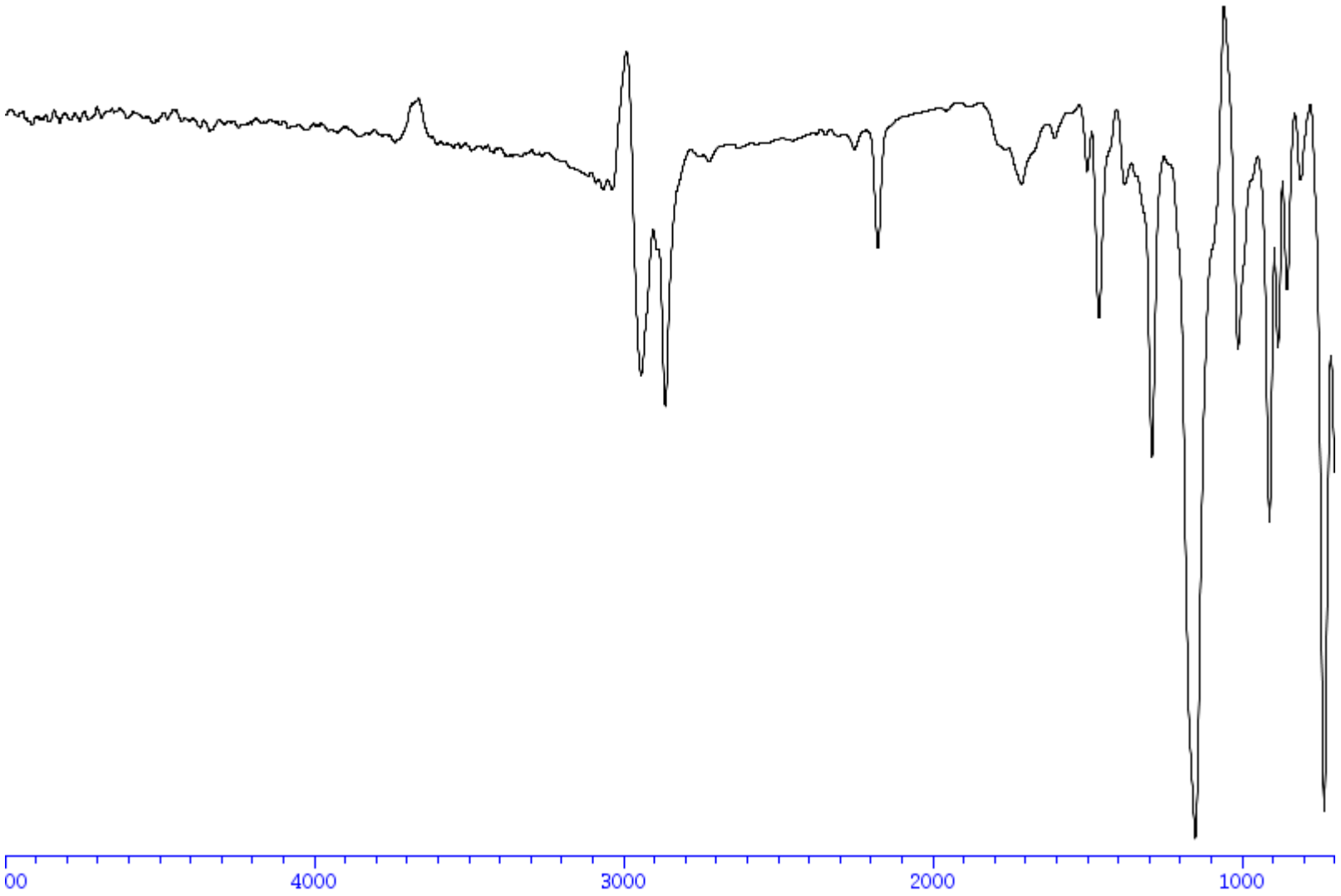
f1 (ppm)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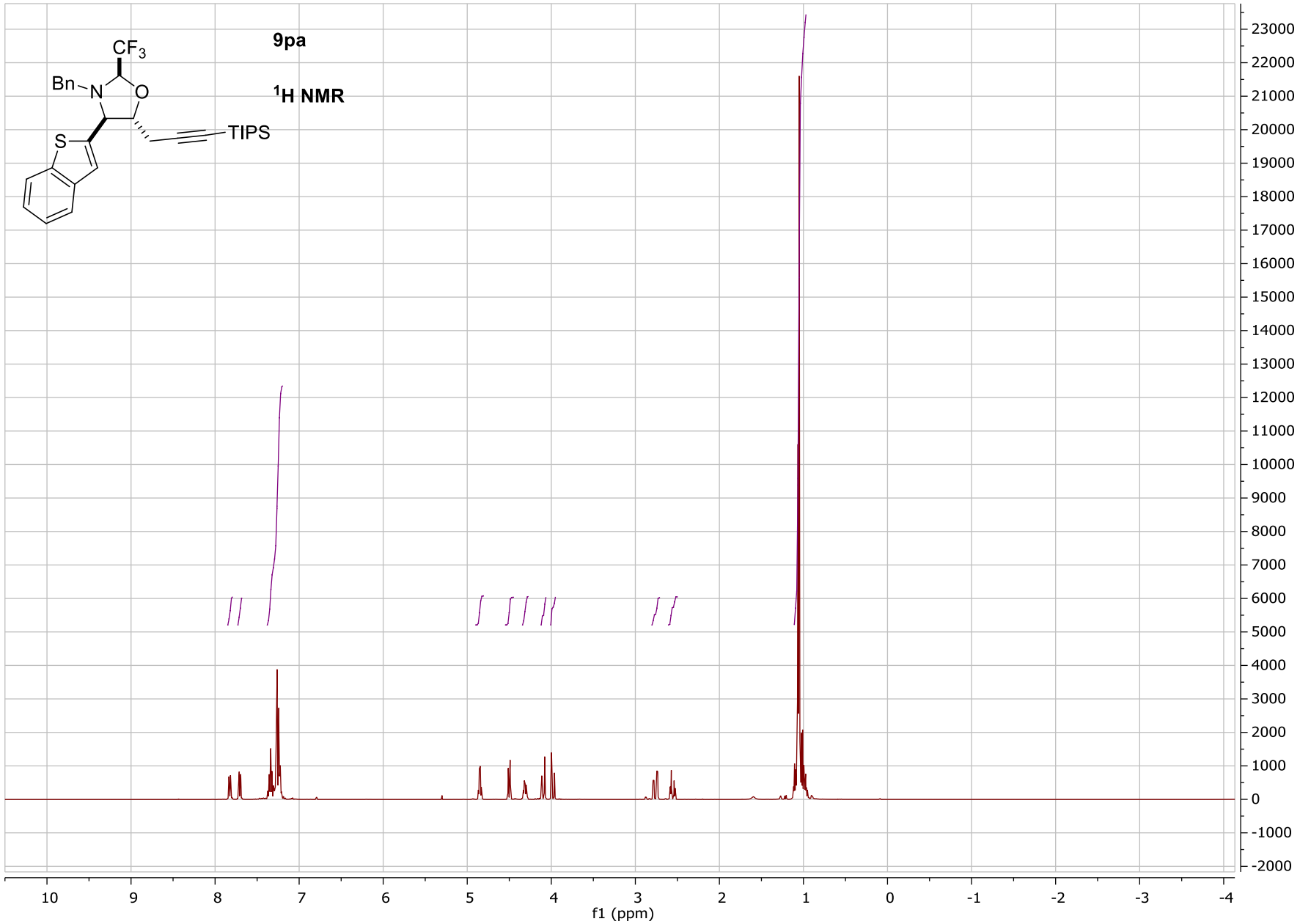
1000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CF3
Bn
N
O
S
TIPS
23000
22000
21000
20000
19000
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16000
15000
14000
13000
12000
11000
10000
9000
8000
7000
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5000
4000
3000
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1000
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-1000
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10
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6
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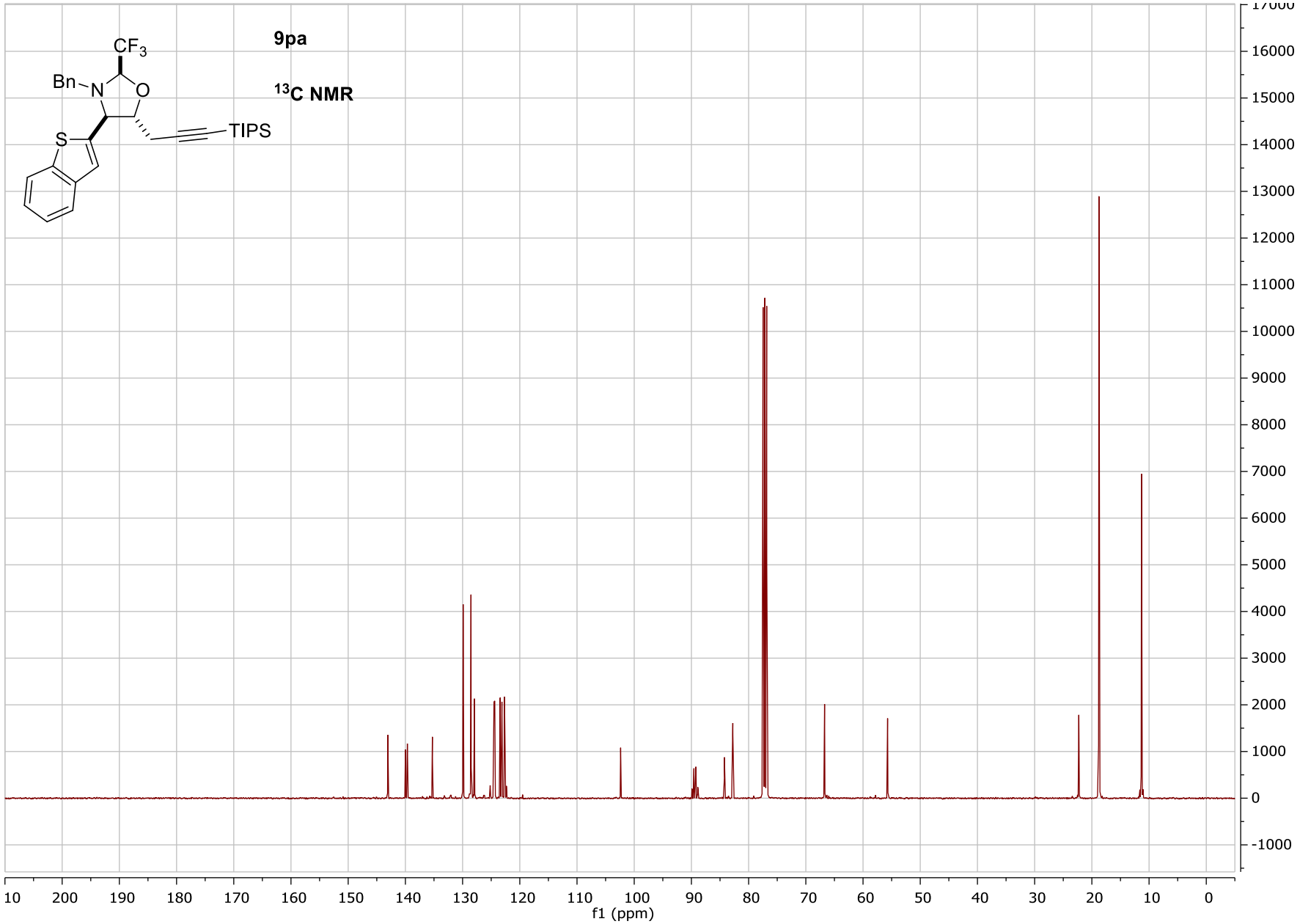
4
3
2
1
0
-1
-2
-3
-4
f1 (ppm)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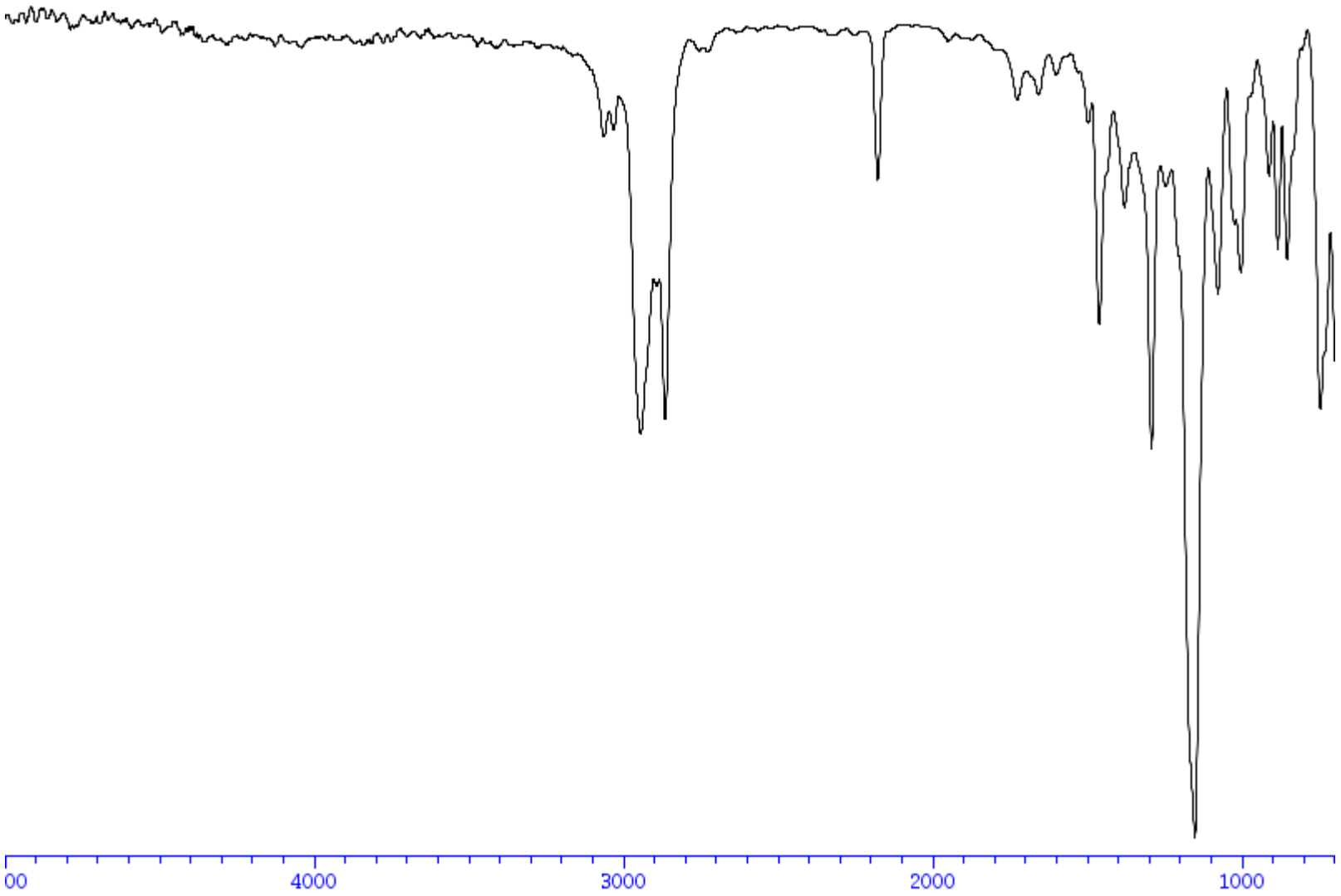
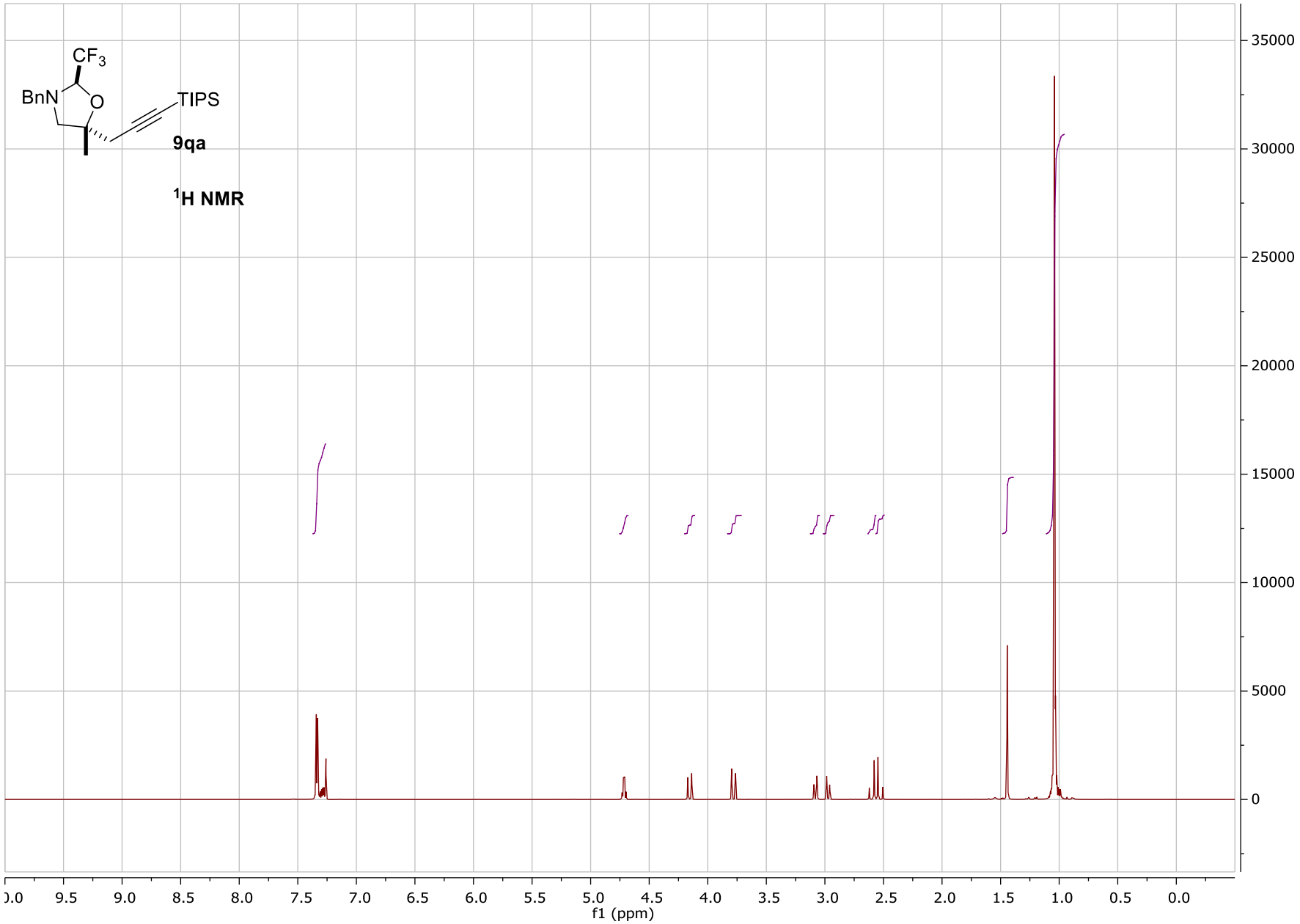
13C NMR
CF3
Bn
N
O
S
TIPS
f1 (ppm)


00
4000
3000
2000
1000


CF3
BnN
O
TIPS
9qa
1H NMR
35000
30000
25000
20000
15000
10000
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9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
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1.5
1.0
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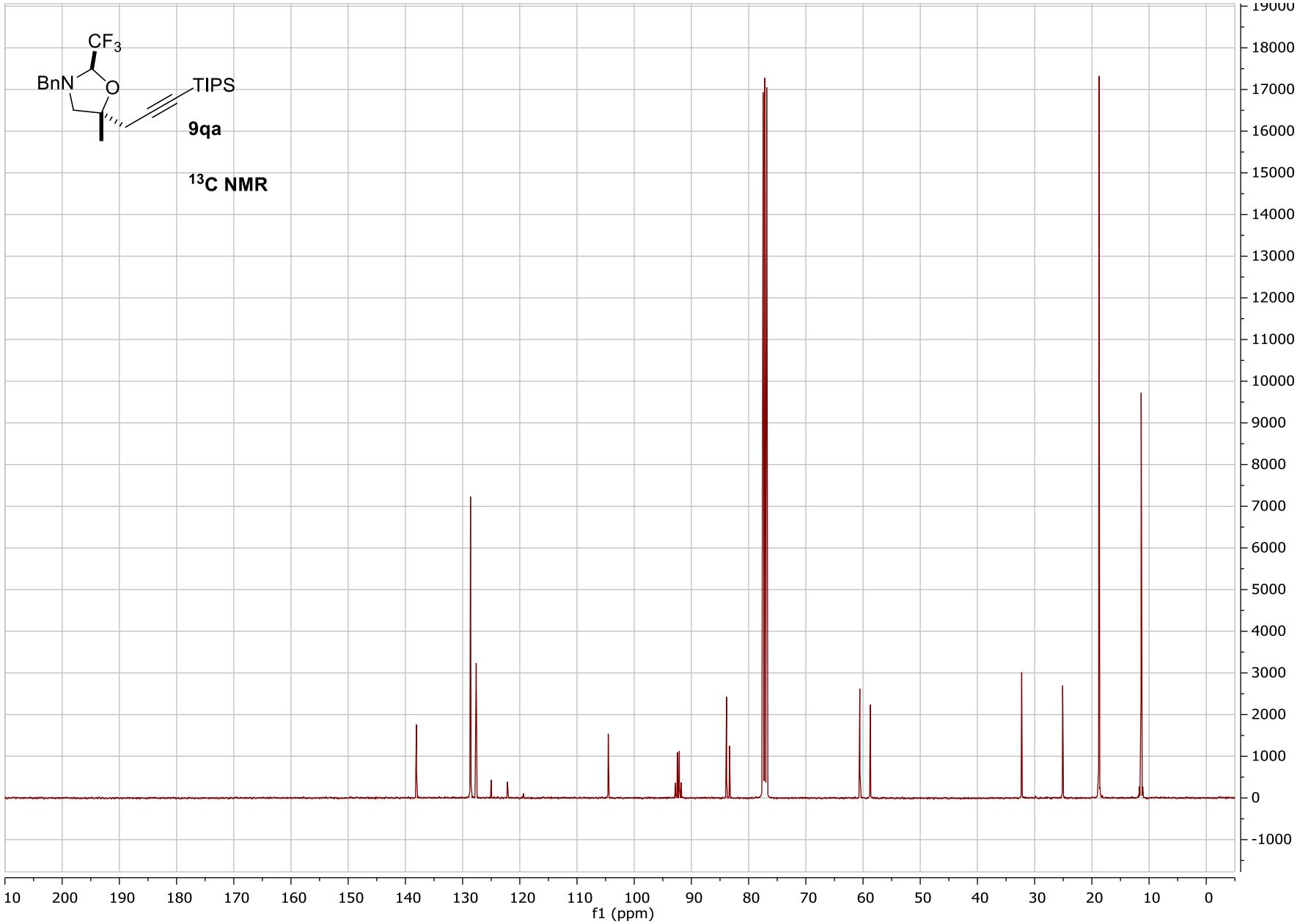
0.0
f1 (ppm)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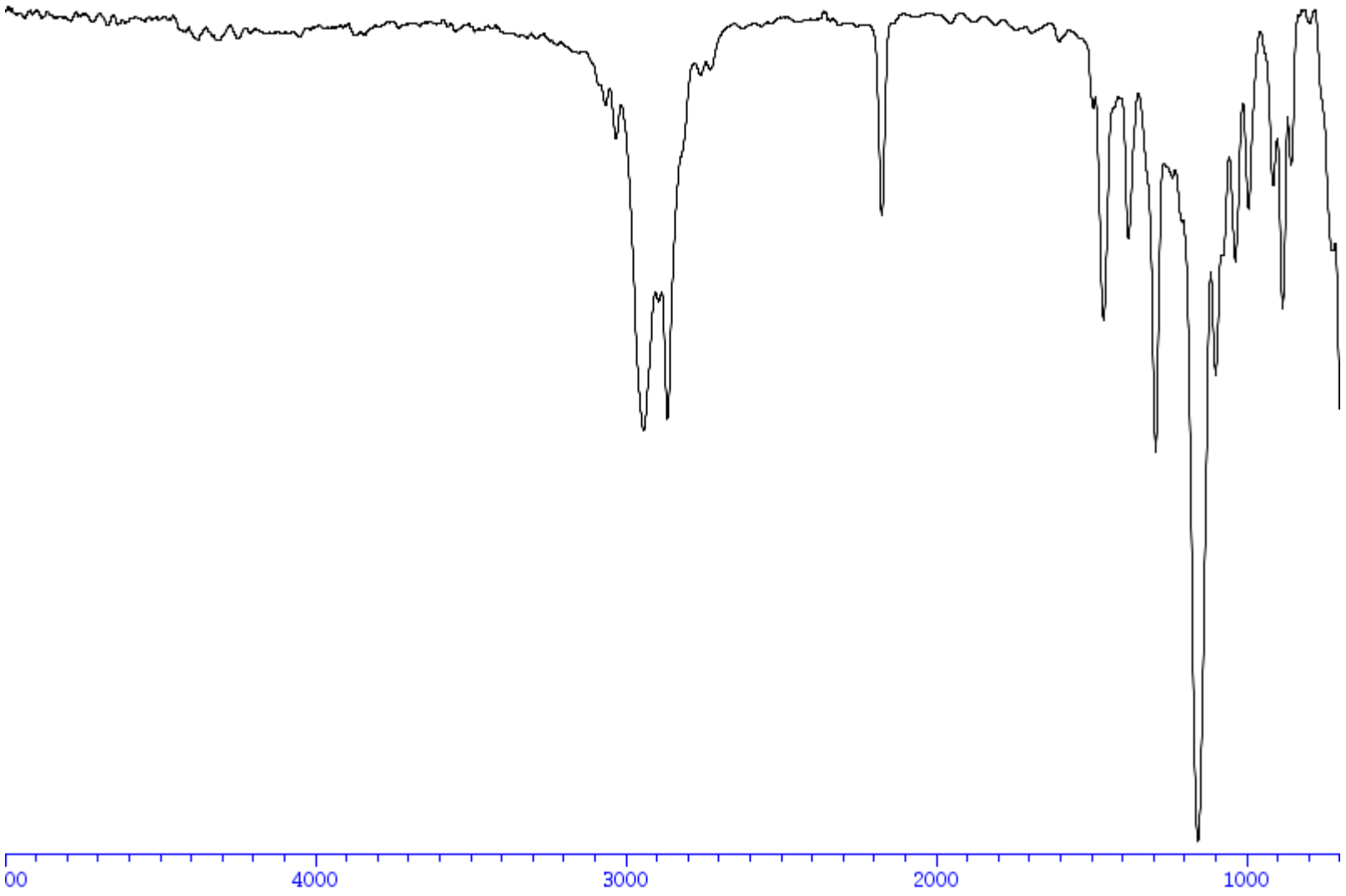
O
TIPS
9qa
13C NMR
f1 (ppm)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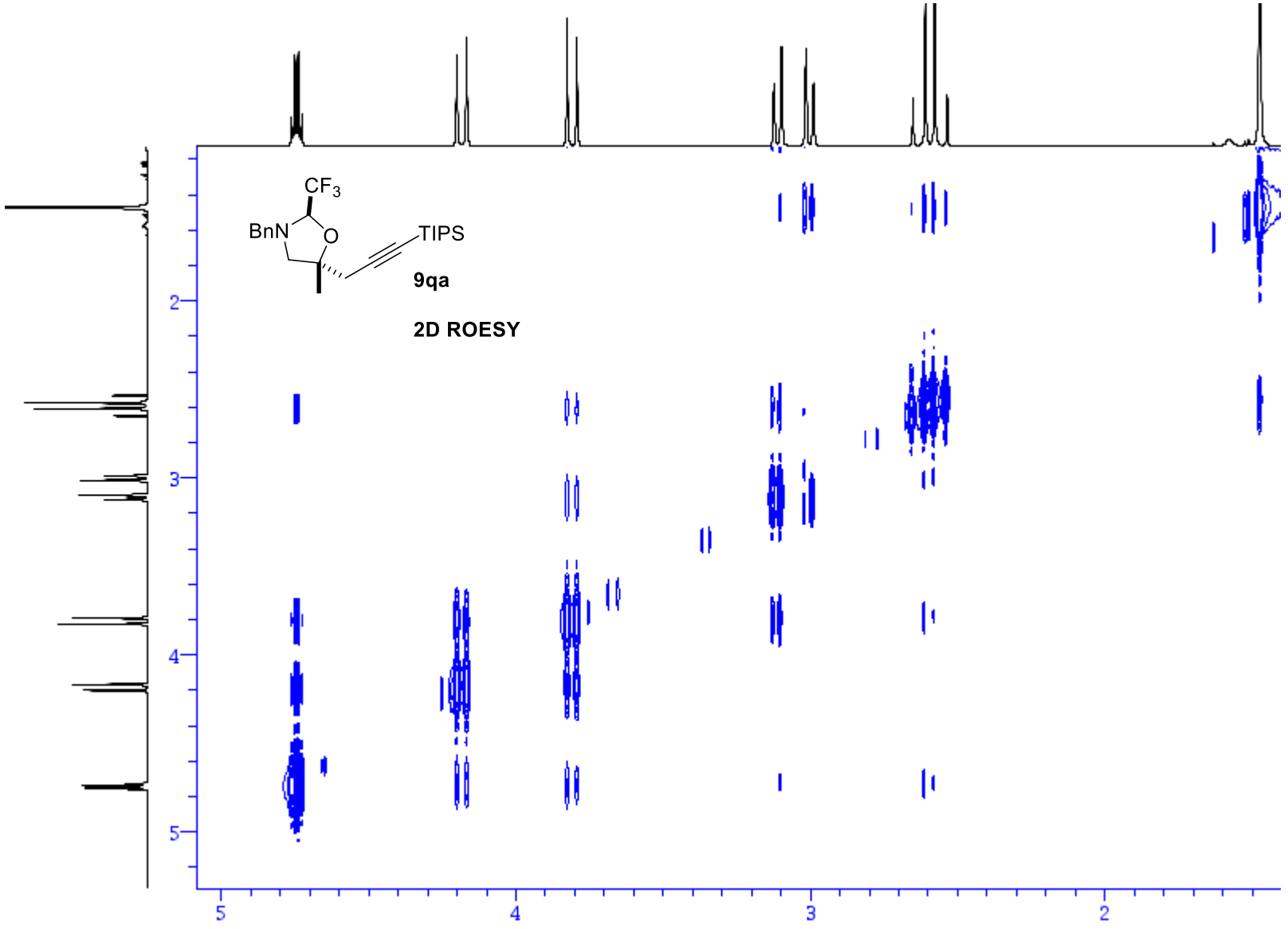
1000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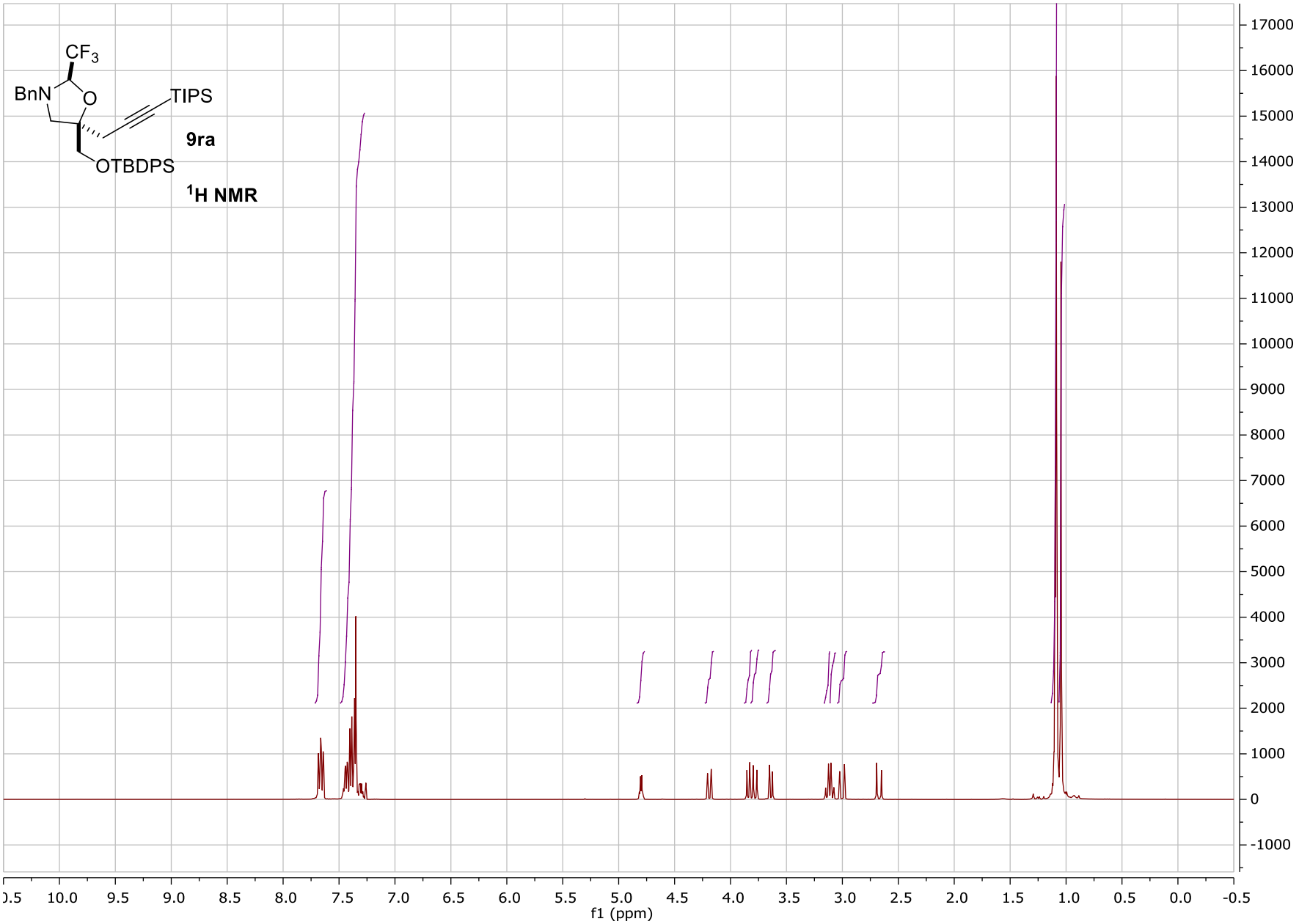
O
TIPS
9qa
2D ROESY
2
3
4
5
5
4
3
2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BnN
O
TIPS
OTBDPS
9ra
1H NMR
17000
16000
15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
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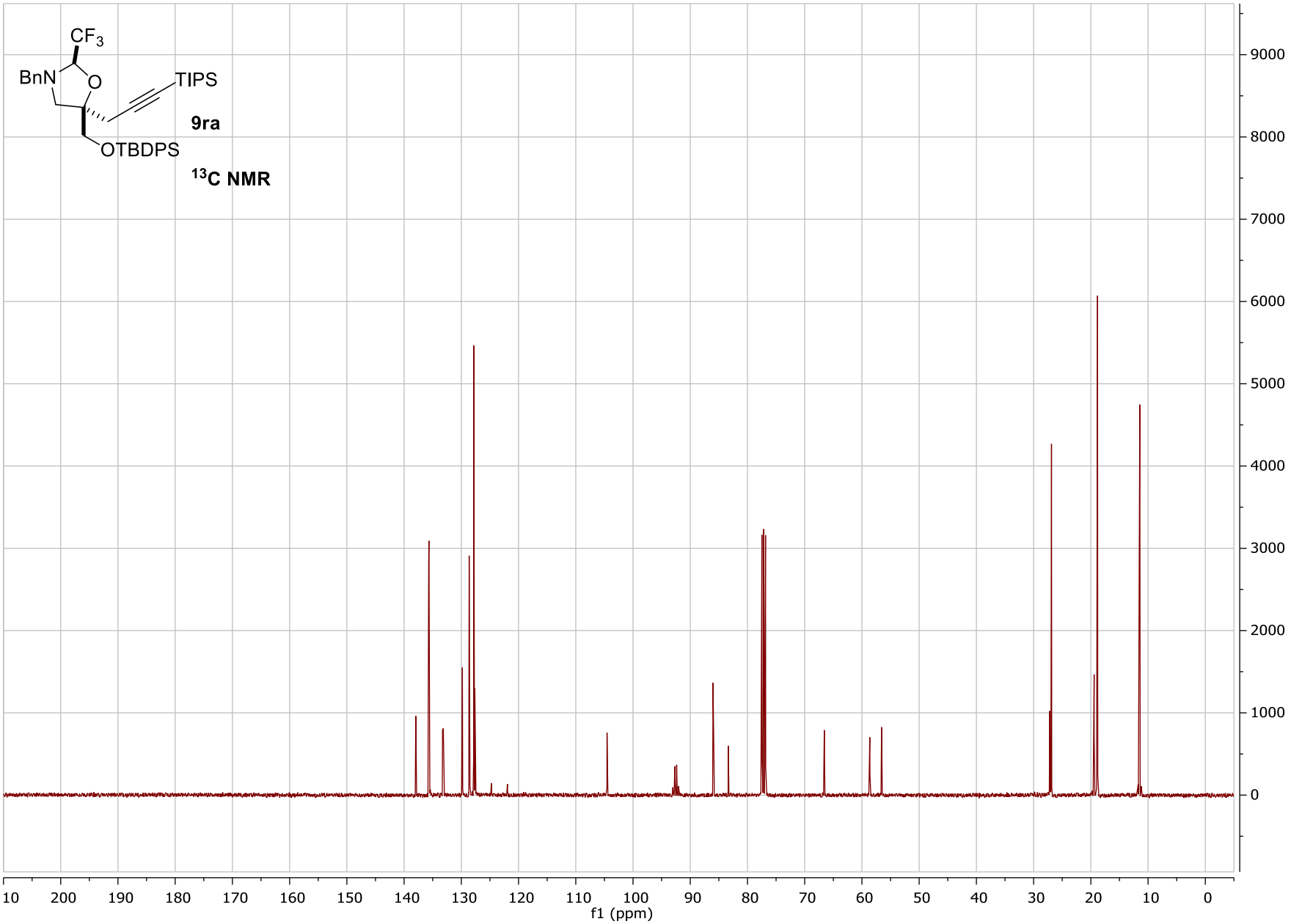
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)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BnN
O
TIPS
OTBDPS
9ra
13C NMR
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
10
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
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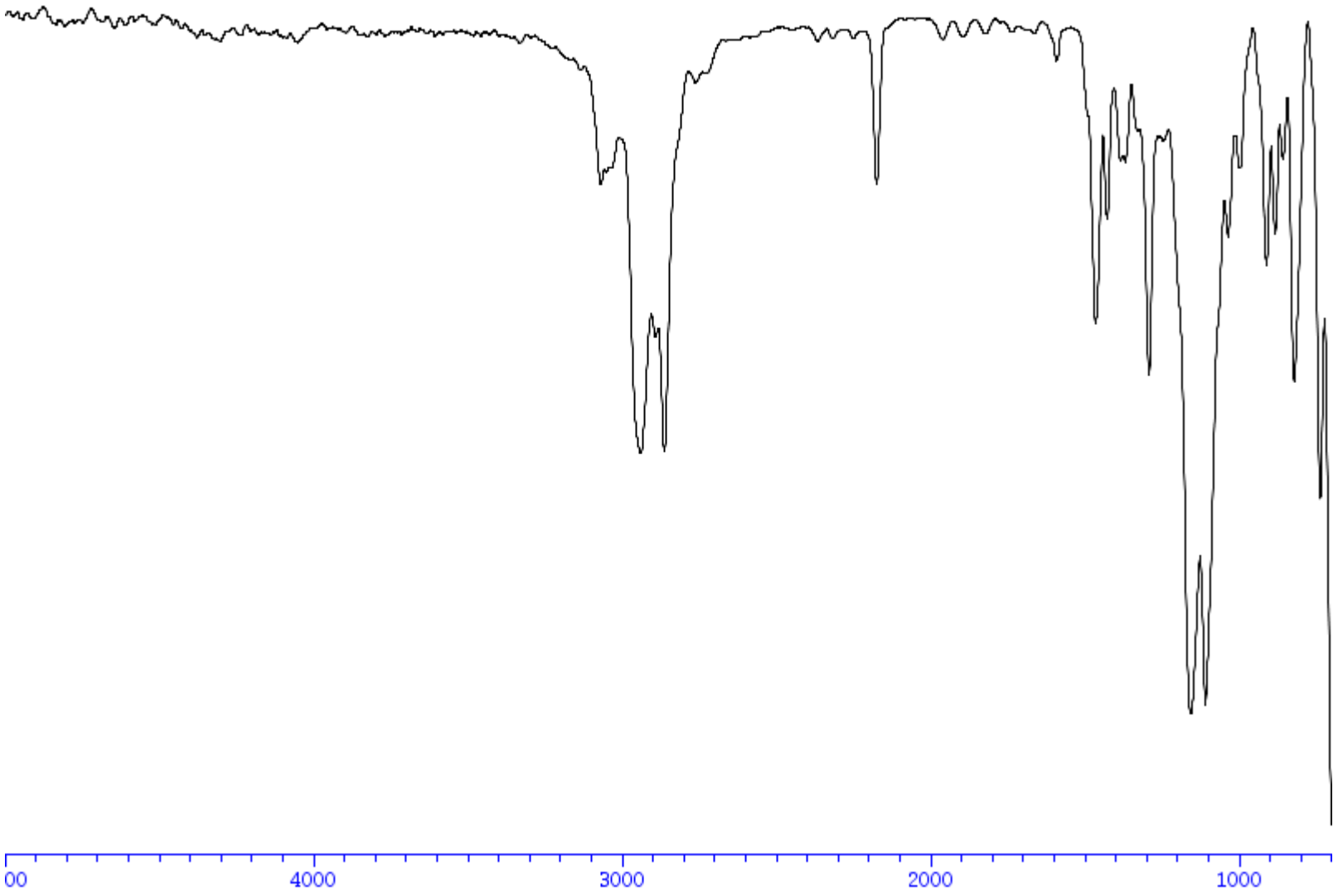
20
10
0
f1 (ppm)


00
4000
3000
2000
1000


CF3
BnN
O
TIPS
CN
9sa
1H NMR
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9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
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4.0
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3.0
2.5
2.0
1.5
1.0
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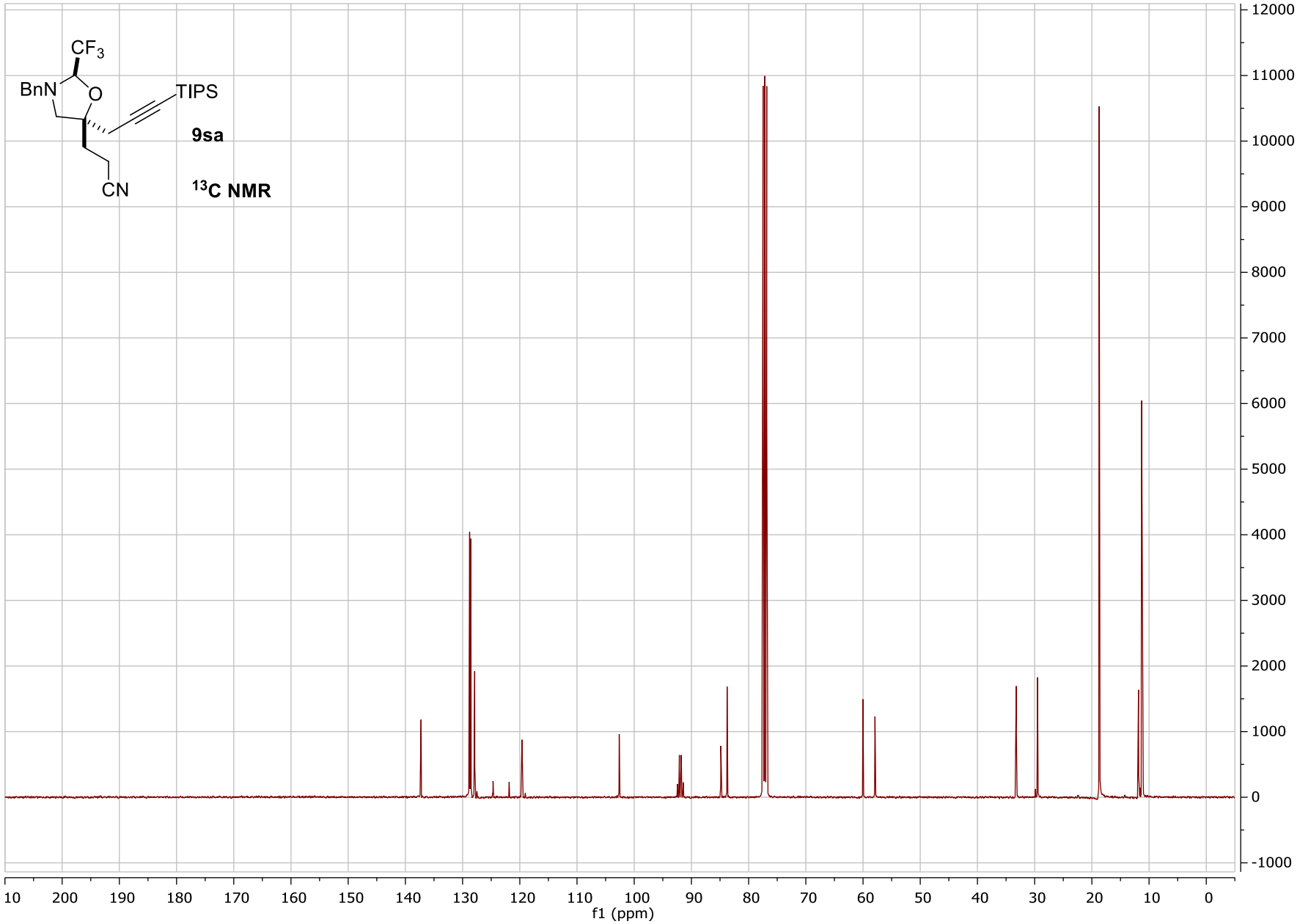
0.0


CF3
BnN
O
TIPS
CN
9sa
13C NMR
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
10
200
190
180
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110
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90
80
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50
40
30
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10
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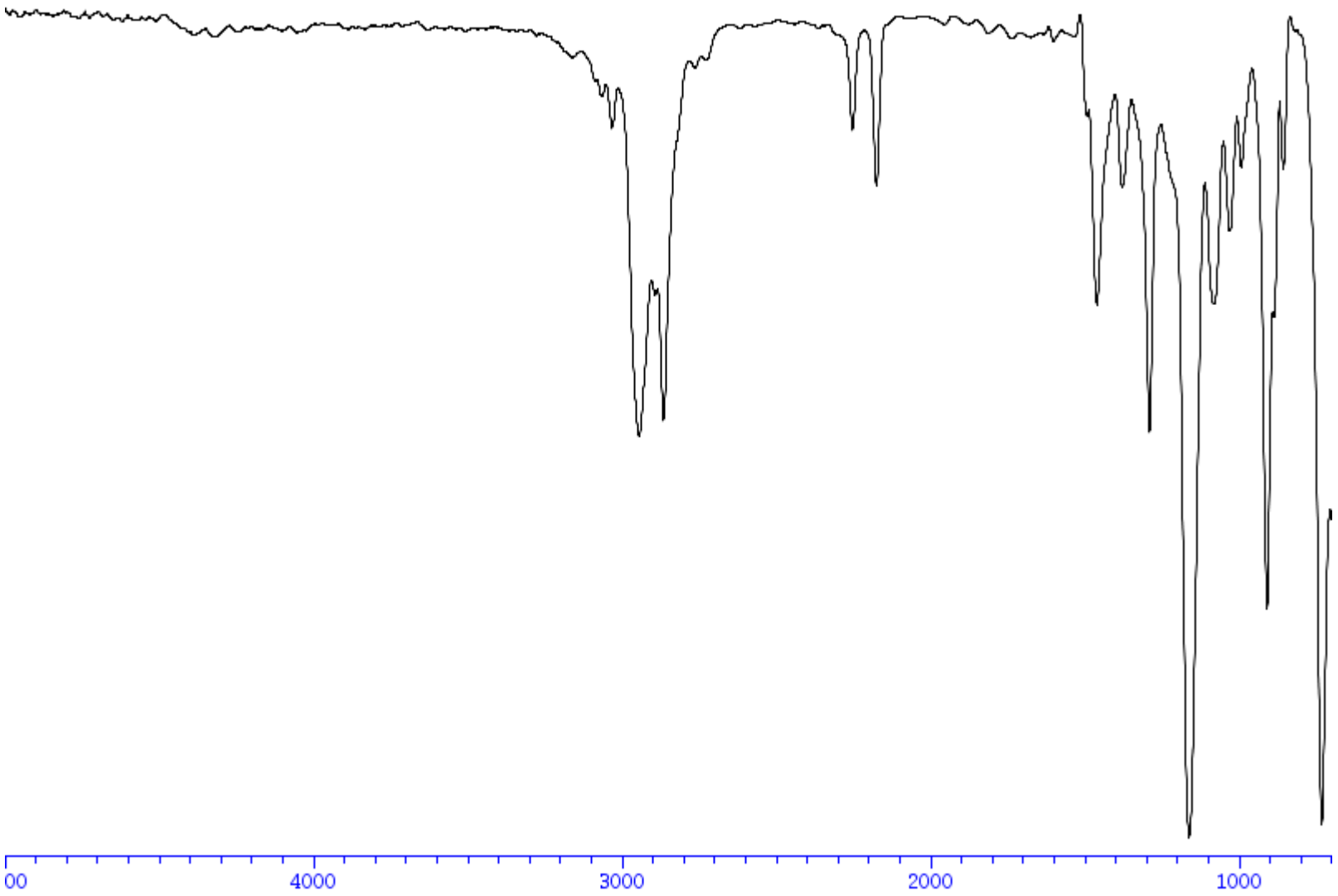
f1 (ppm)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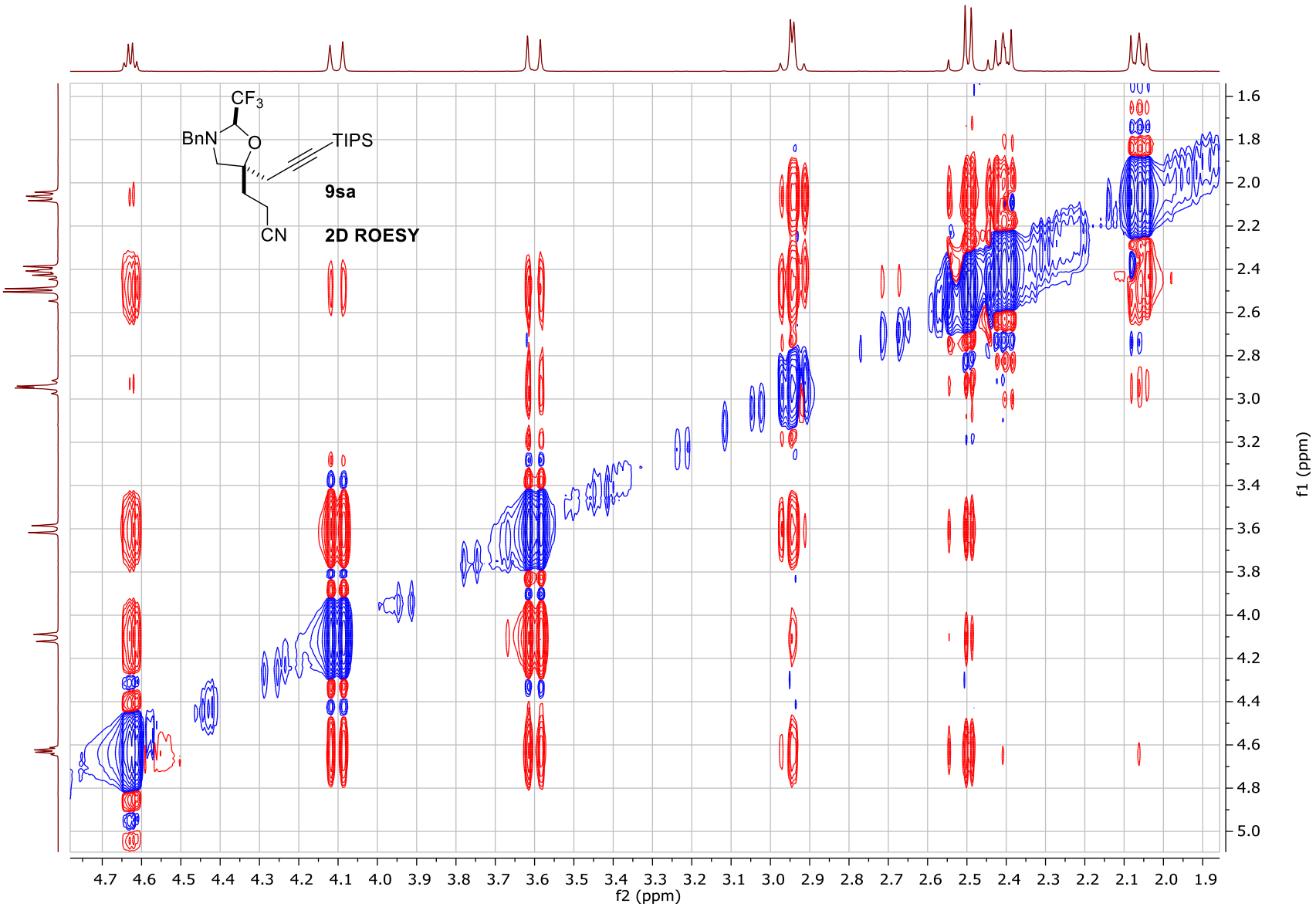
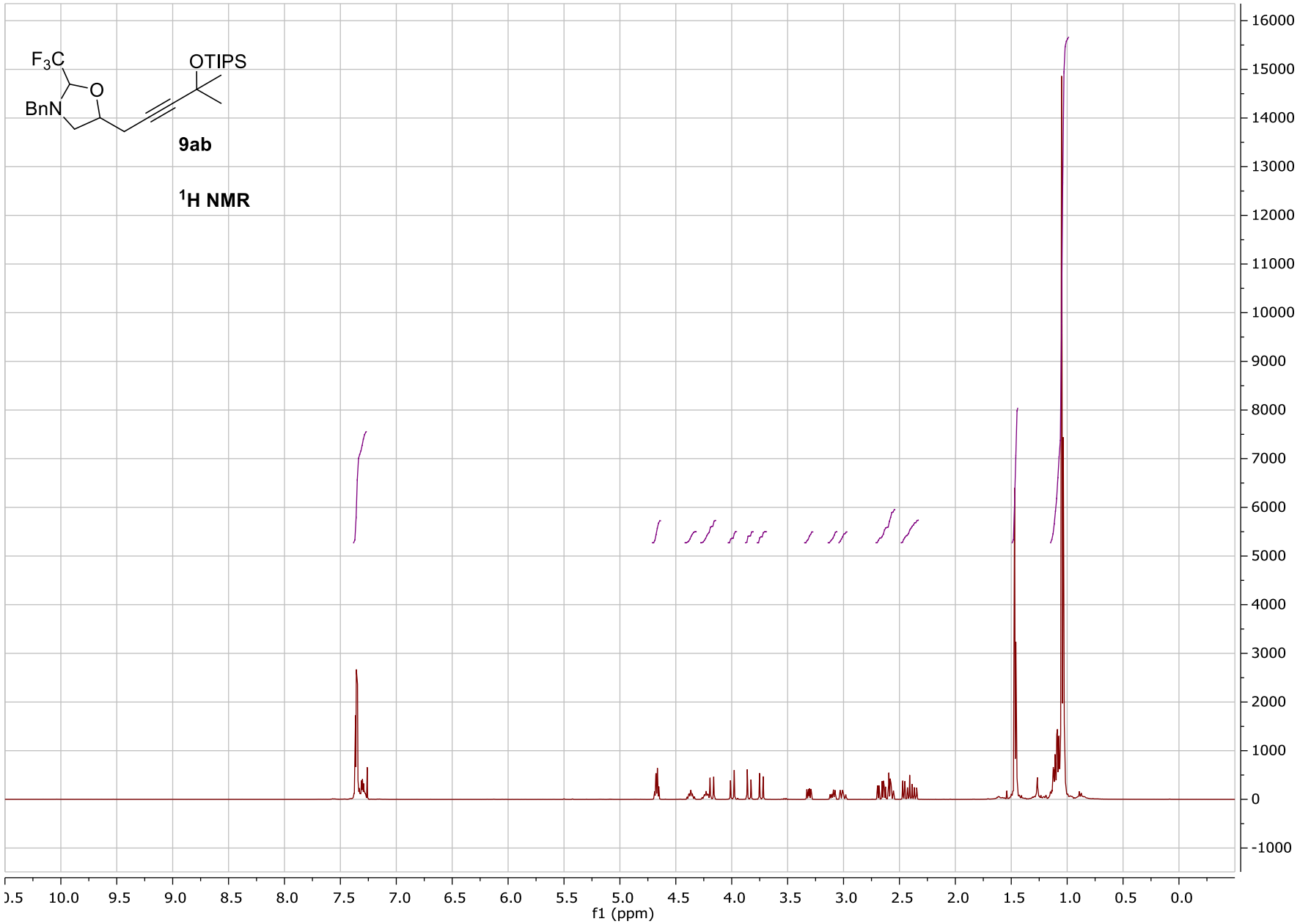
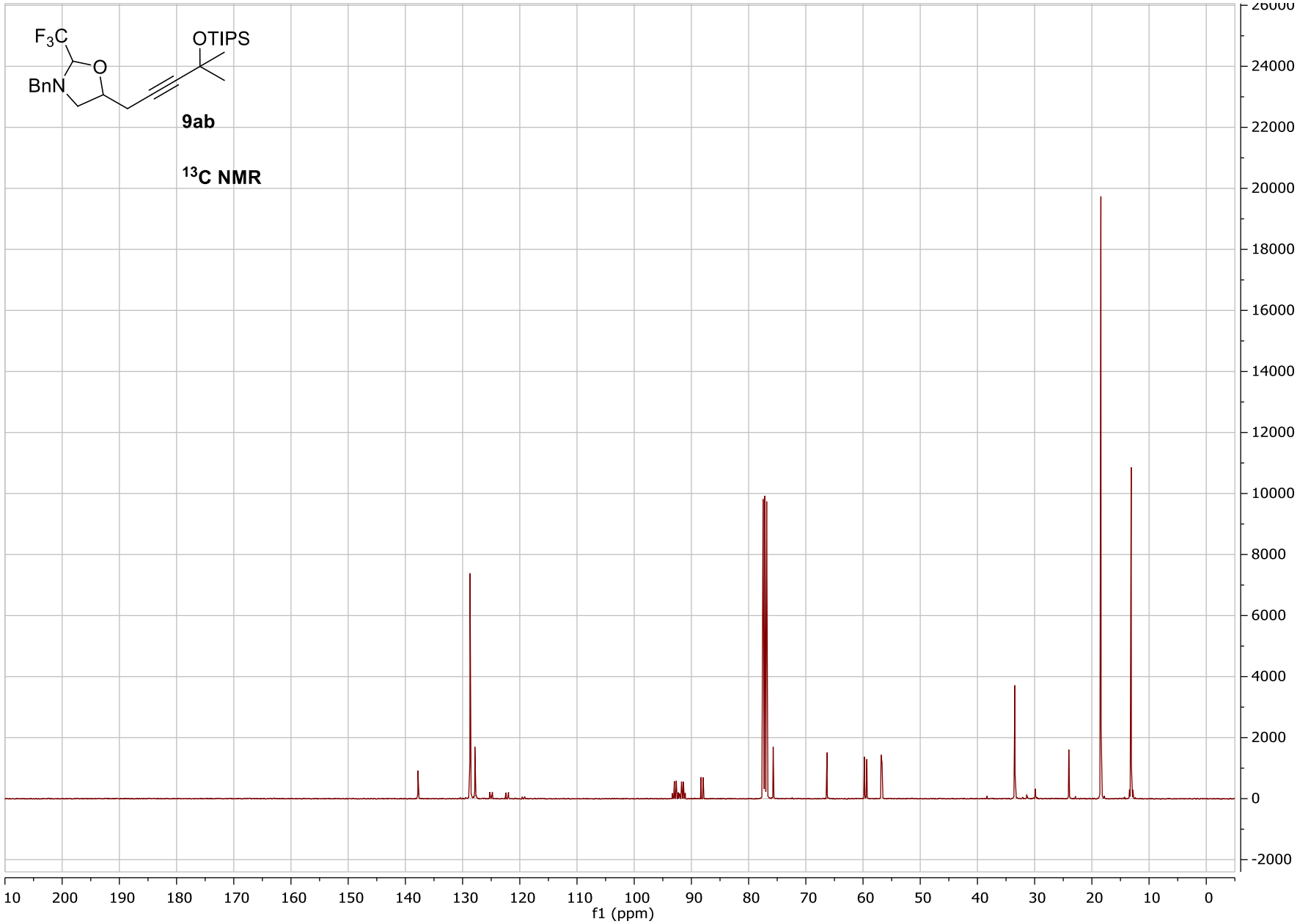
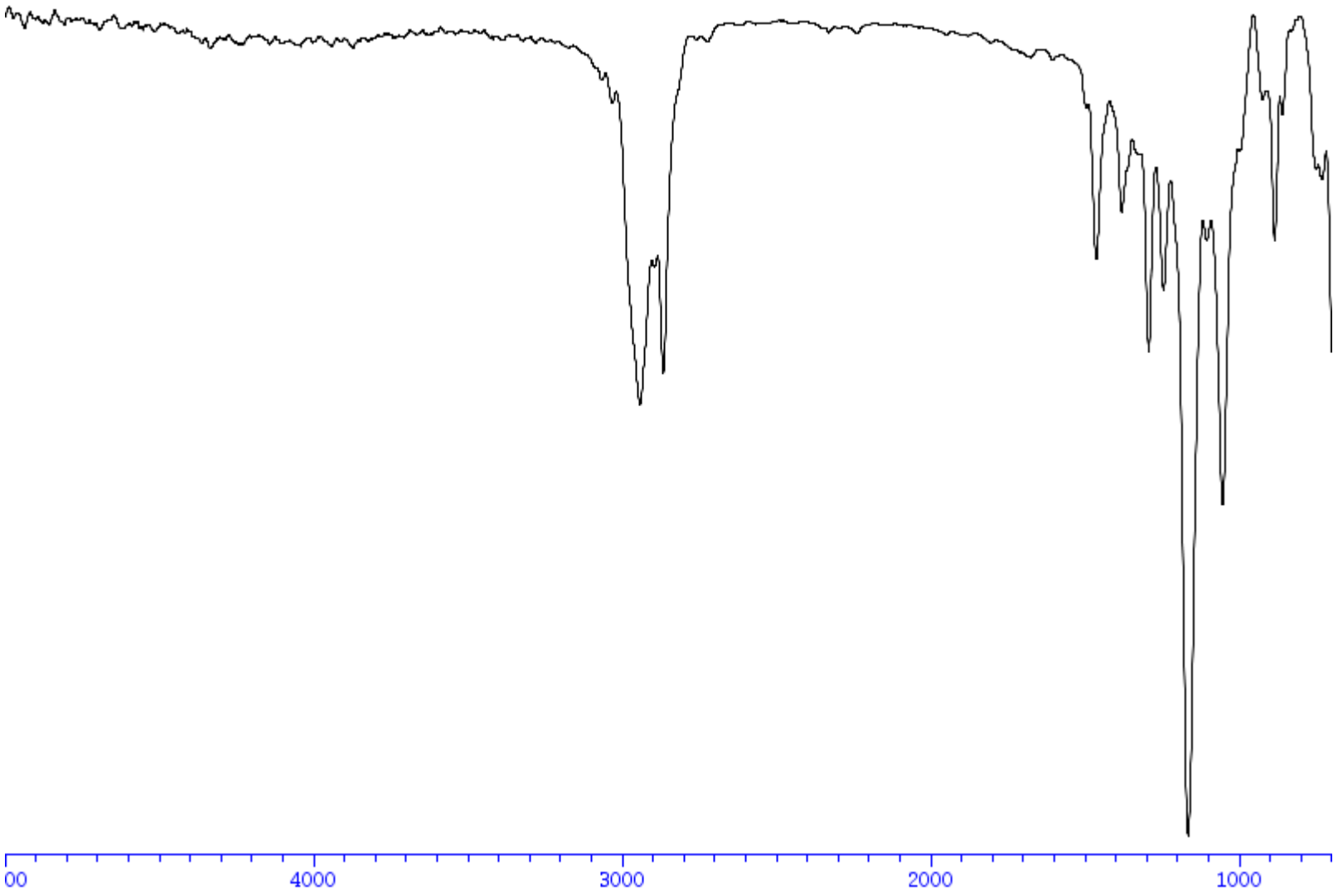
2000
1000


CF3
BnN
O
TIPS
CN
9sa
2D ROESY
f2 (ppm)
f1 (ppm)


F3C
OTIPS
BnN
O
9ab
1H NMR
16000
15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


F3C
O
BnN
OTIPS
9ab
13C NMR
f1 (ppm)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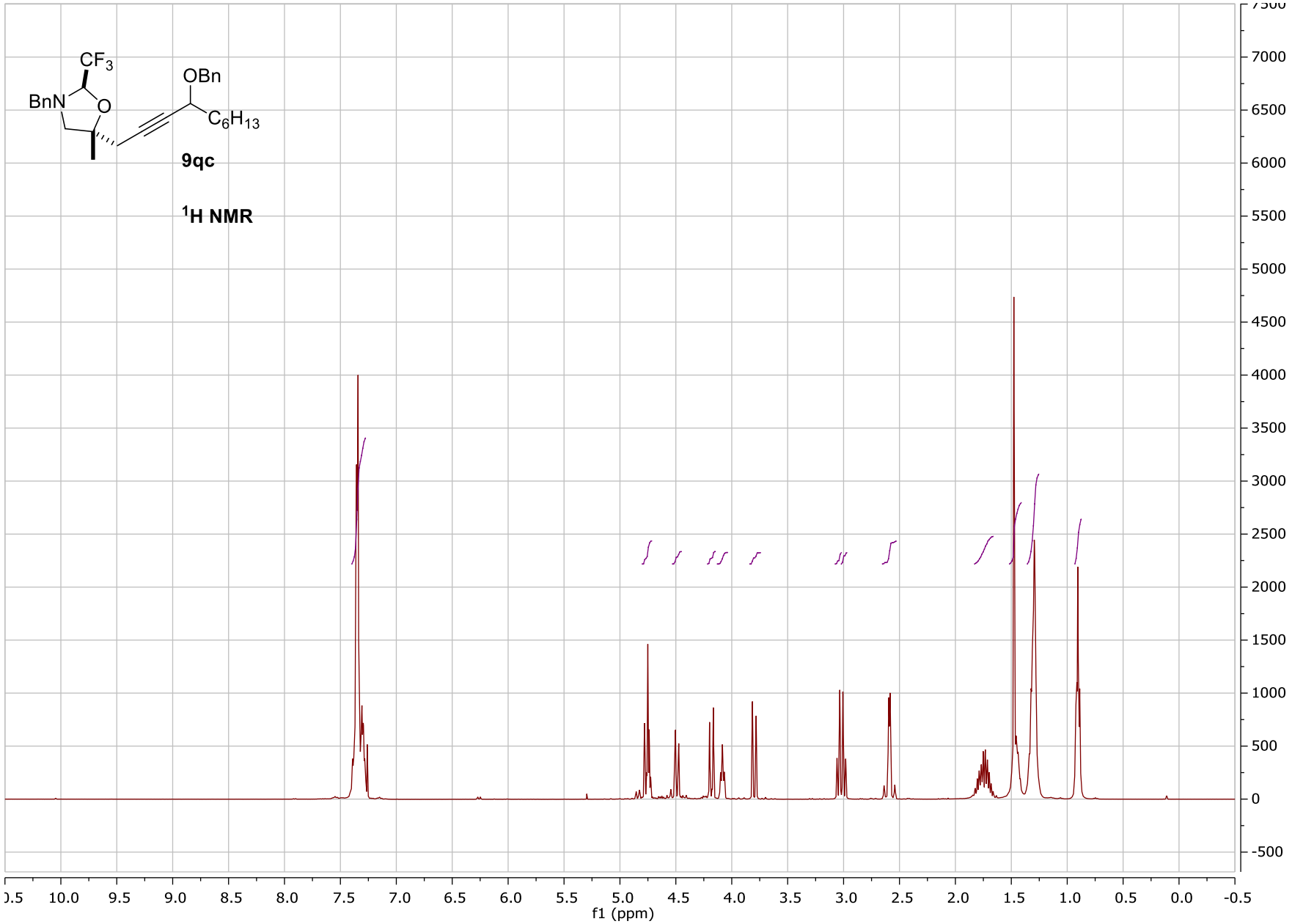
3000
2000
1000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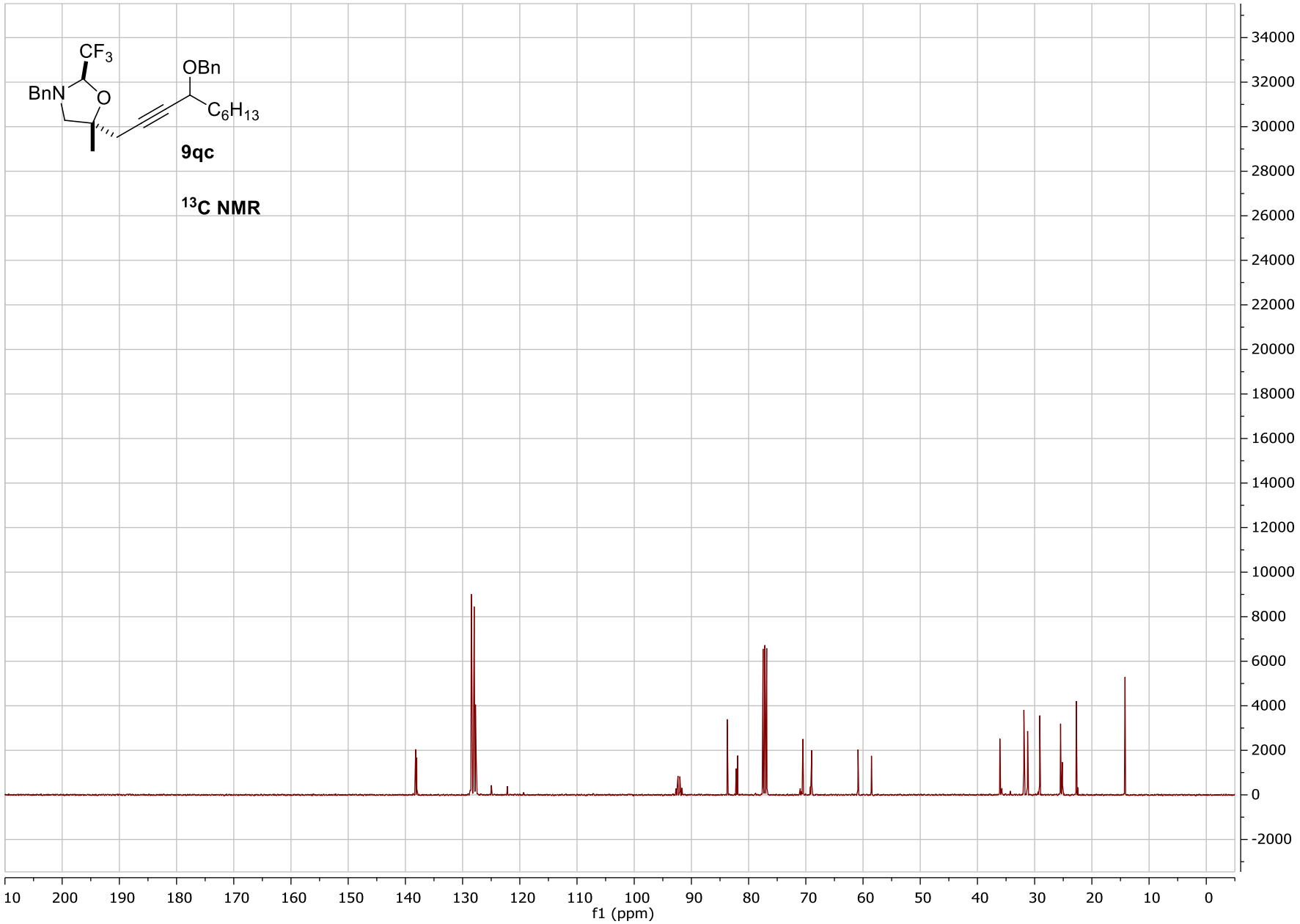
OBn
BnN
O
C6H13
9qc
1H NMR
f1 (ppm)


CF3
OBn
BnN
O
C6H13
9qc
13C NMR
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32000
30000
28000
26000
24000
22000
20000
18000
16000
14000
12000
10000
8000
6000
4000
2000
0
-2000
10
200
190
180
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120
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80
70
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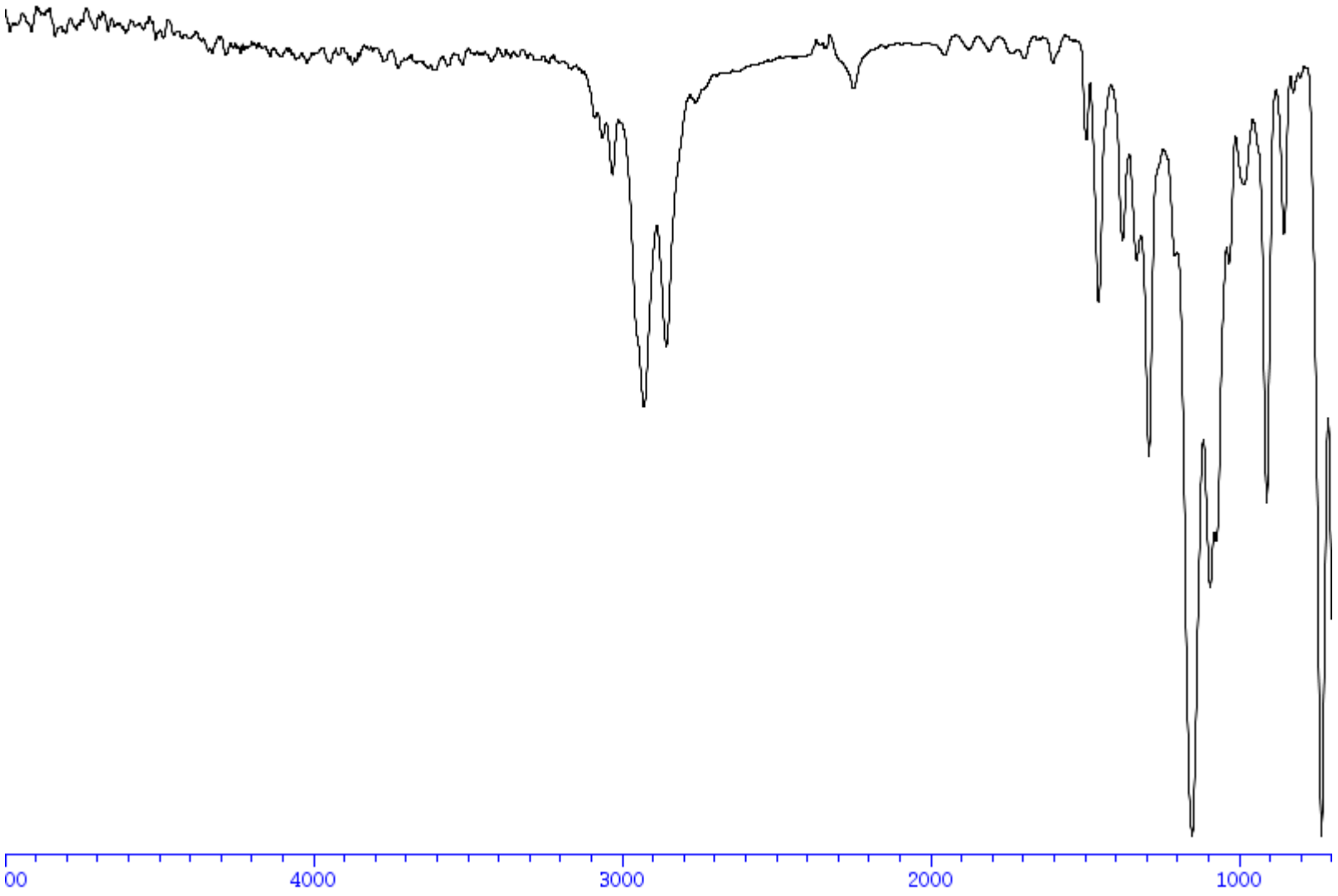
10
0
f1 (ppm)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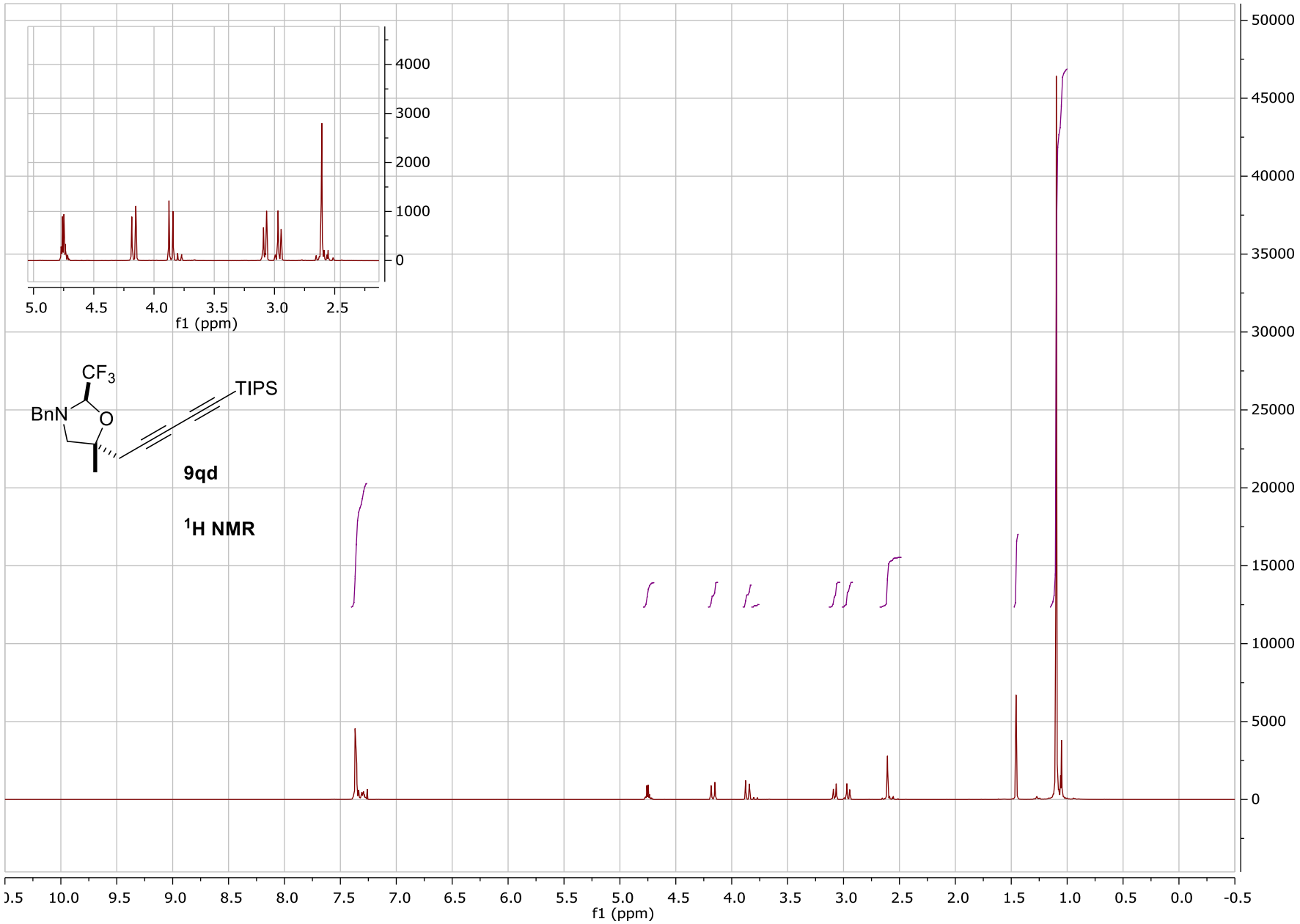
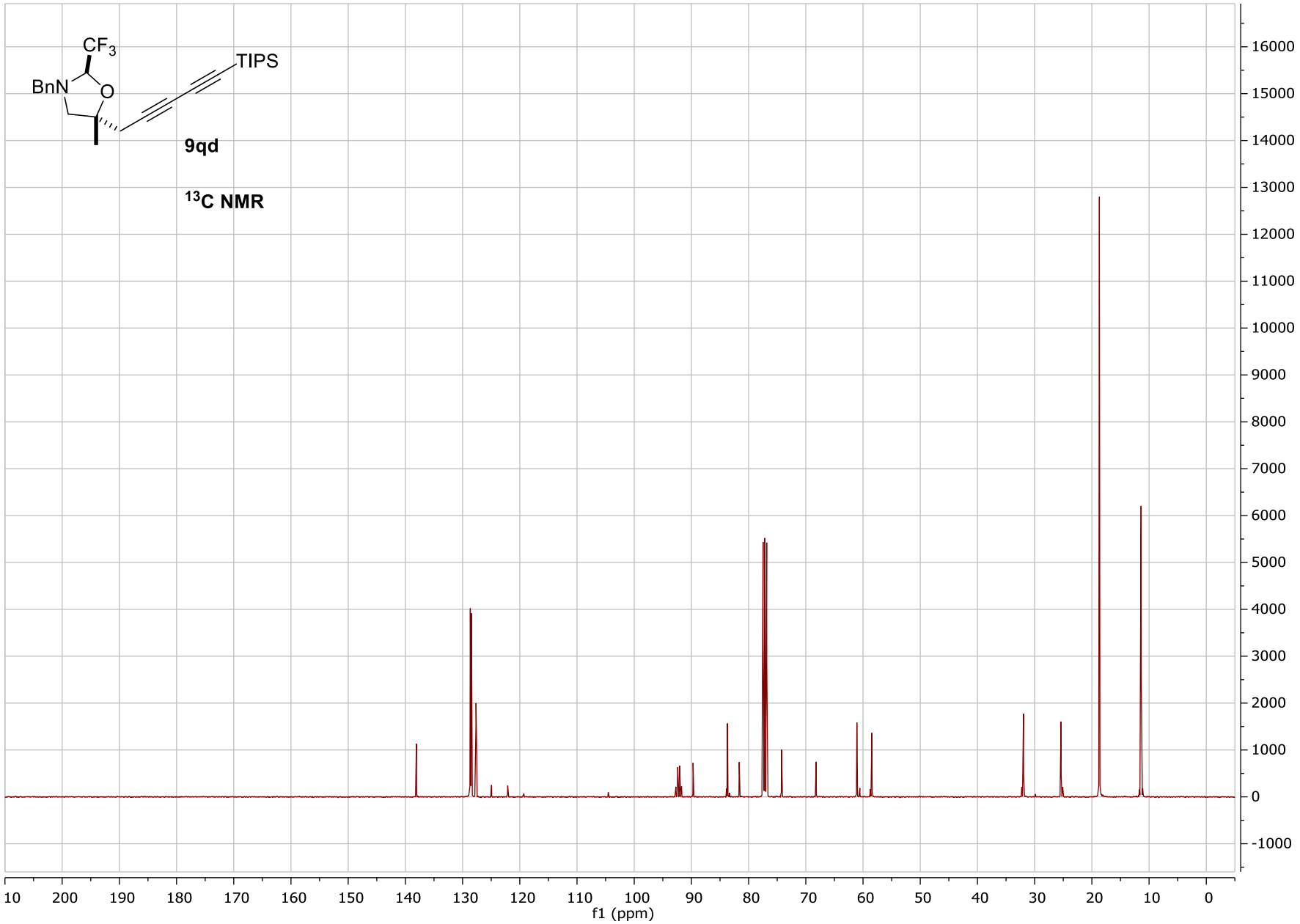

CF3
BnN
O
TIPS
9qd
1H NMR
f1 (ppm)
f1 (ppm)


CF3
BnN
O
TIPS
9qd
13C NMR
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15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
10
200
190
180
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130
120
110
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90
80
70
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50
40
30
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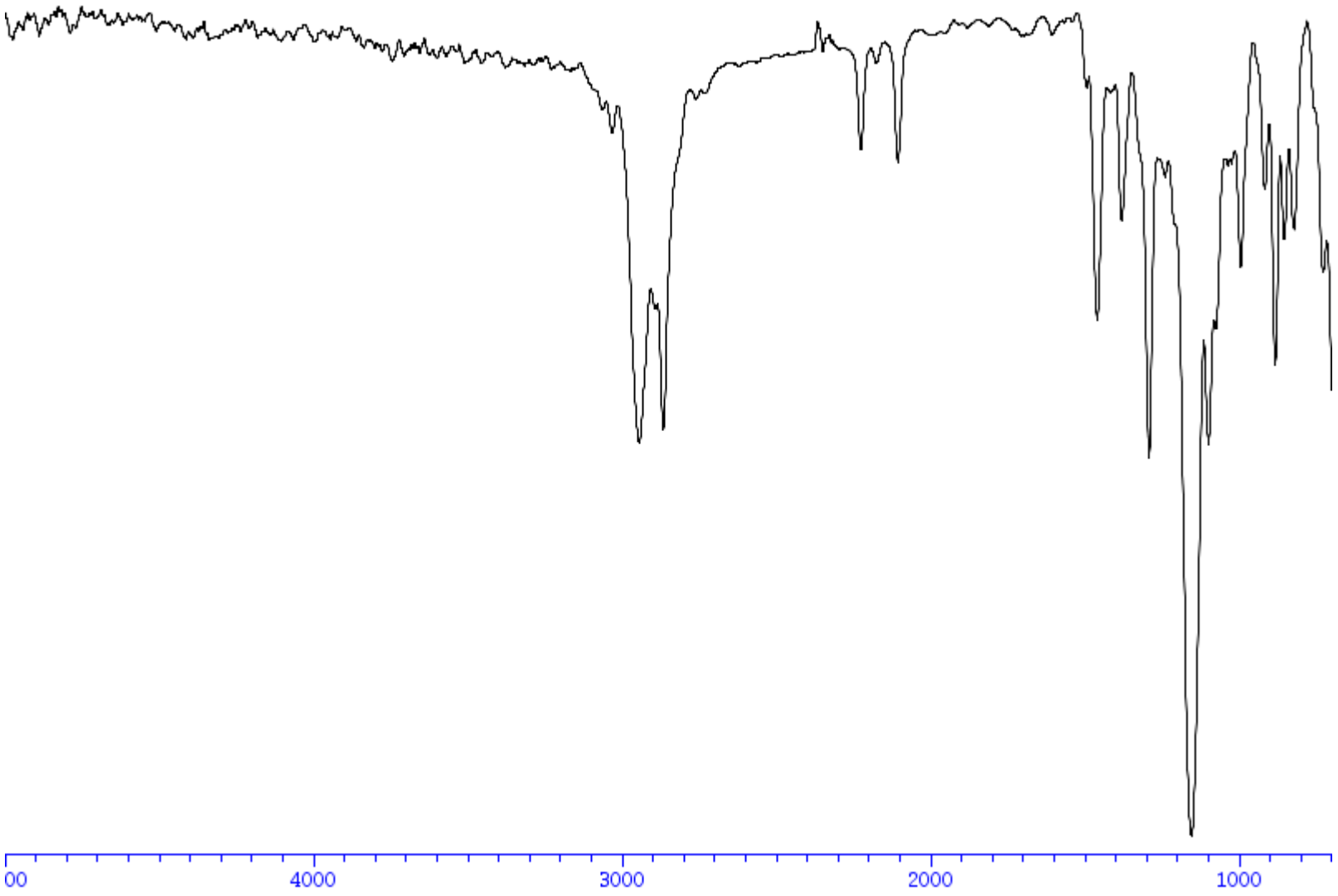
10
0
f1 (ppm)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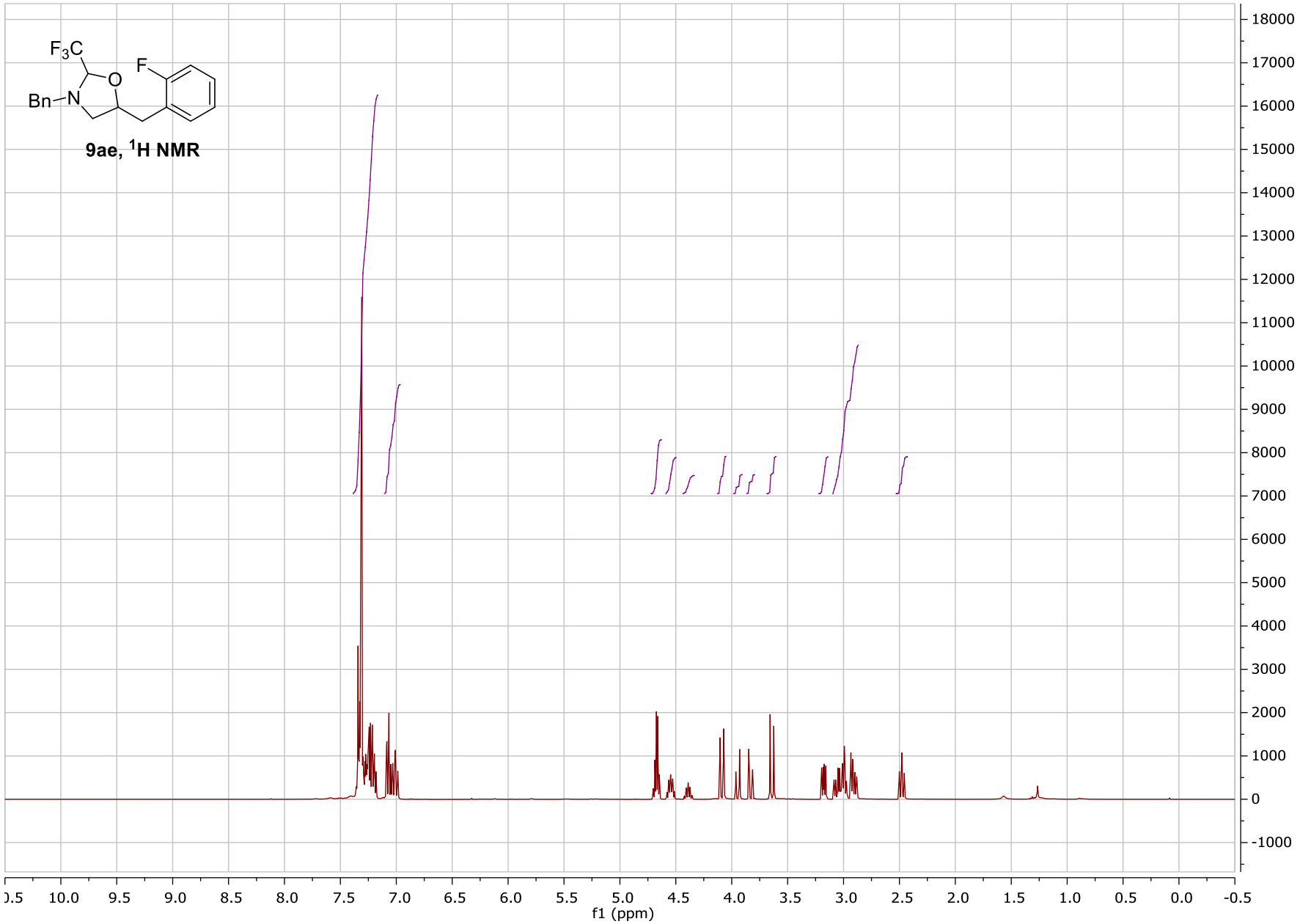
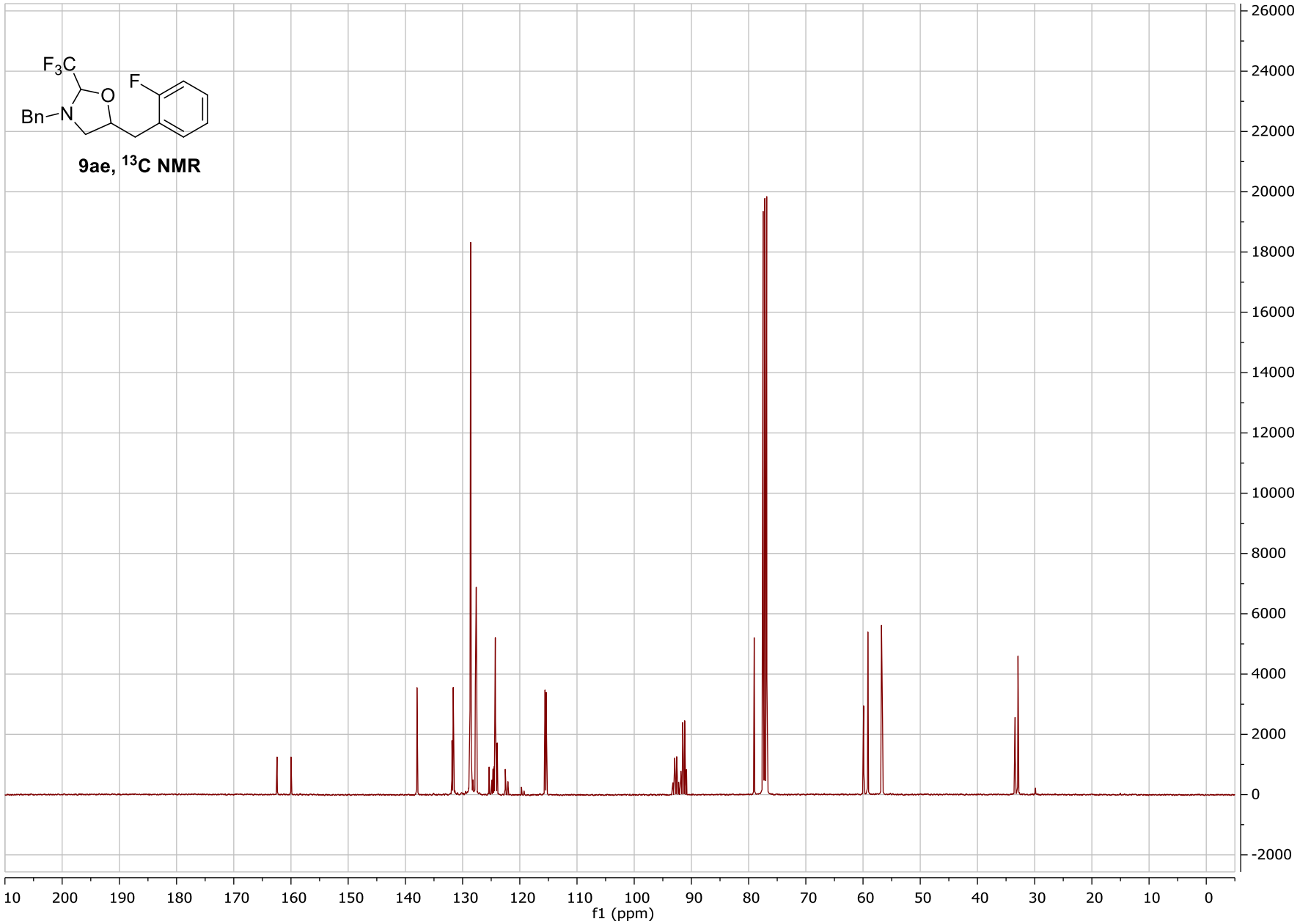
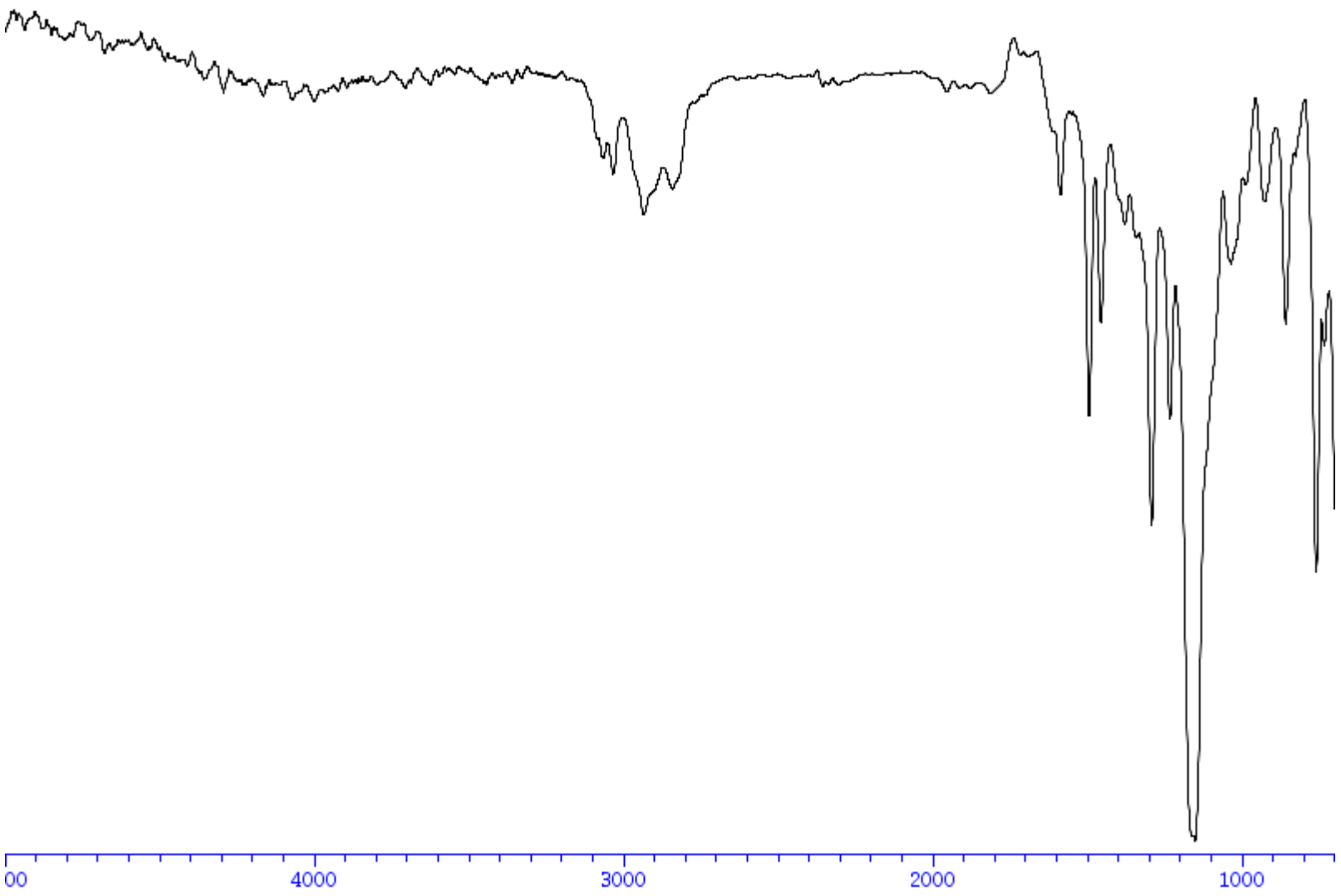
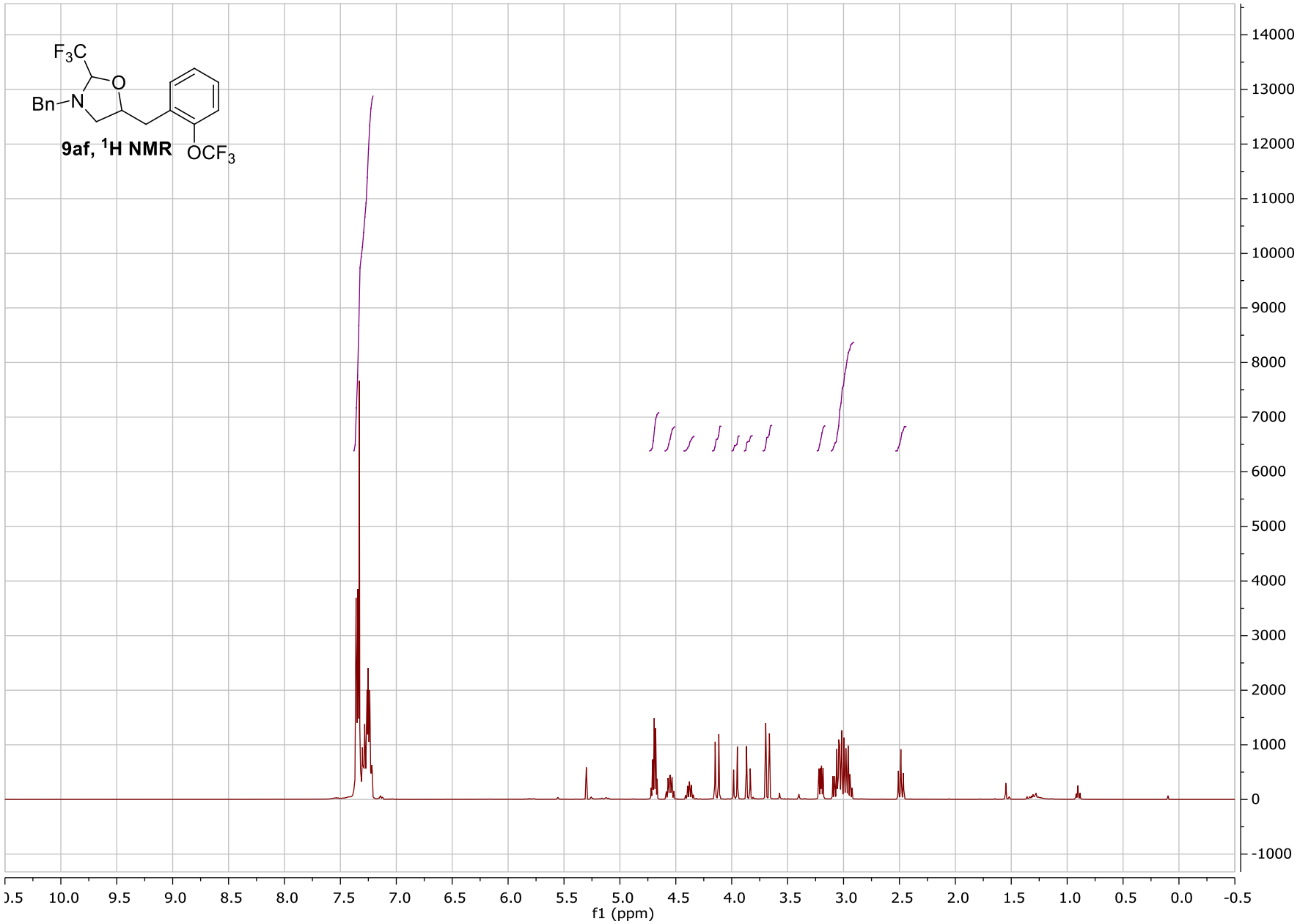
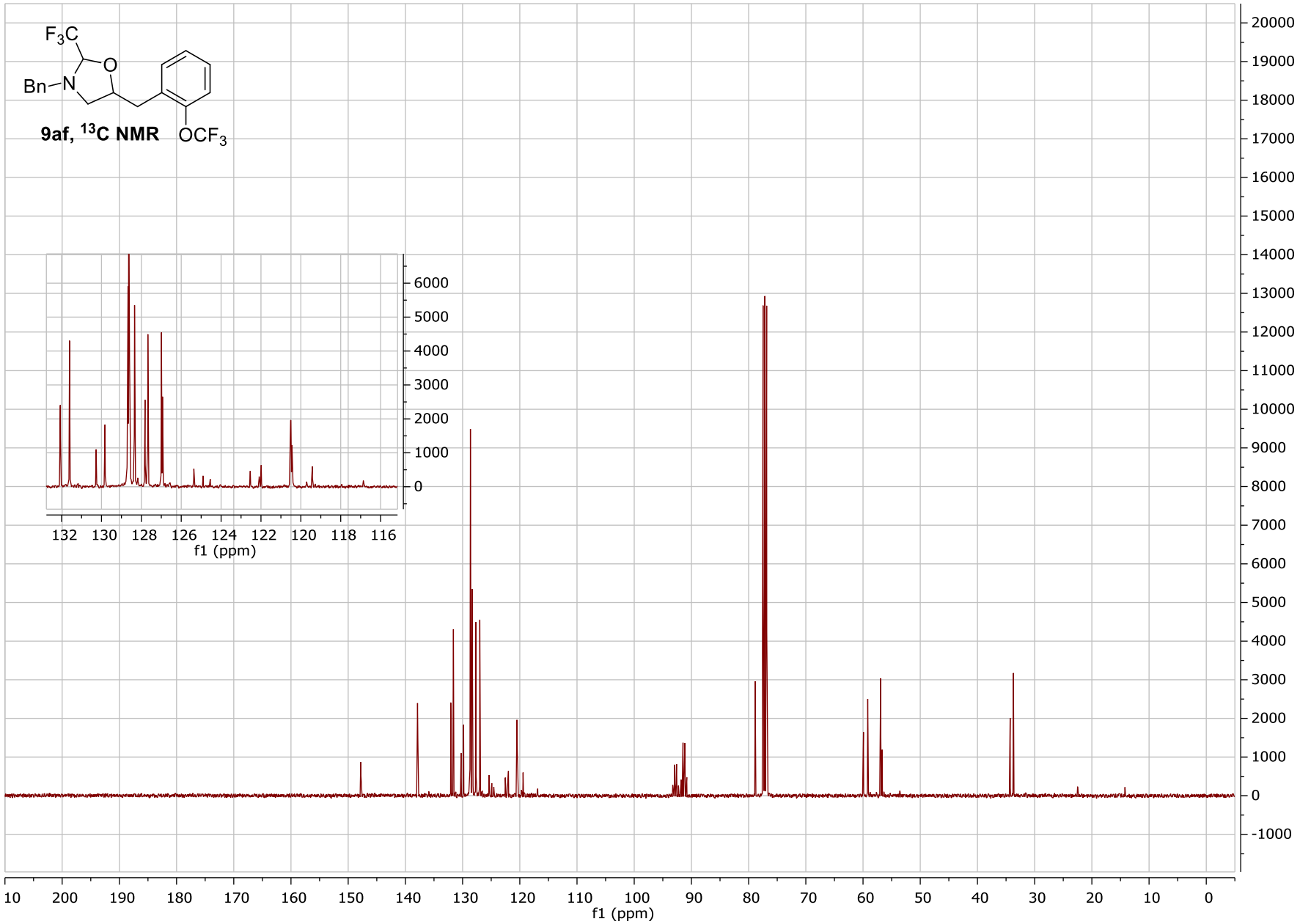
1000

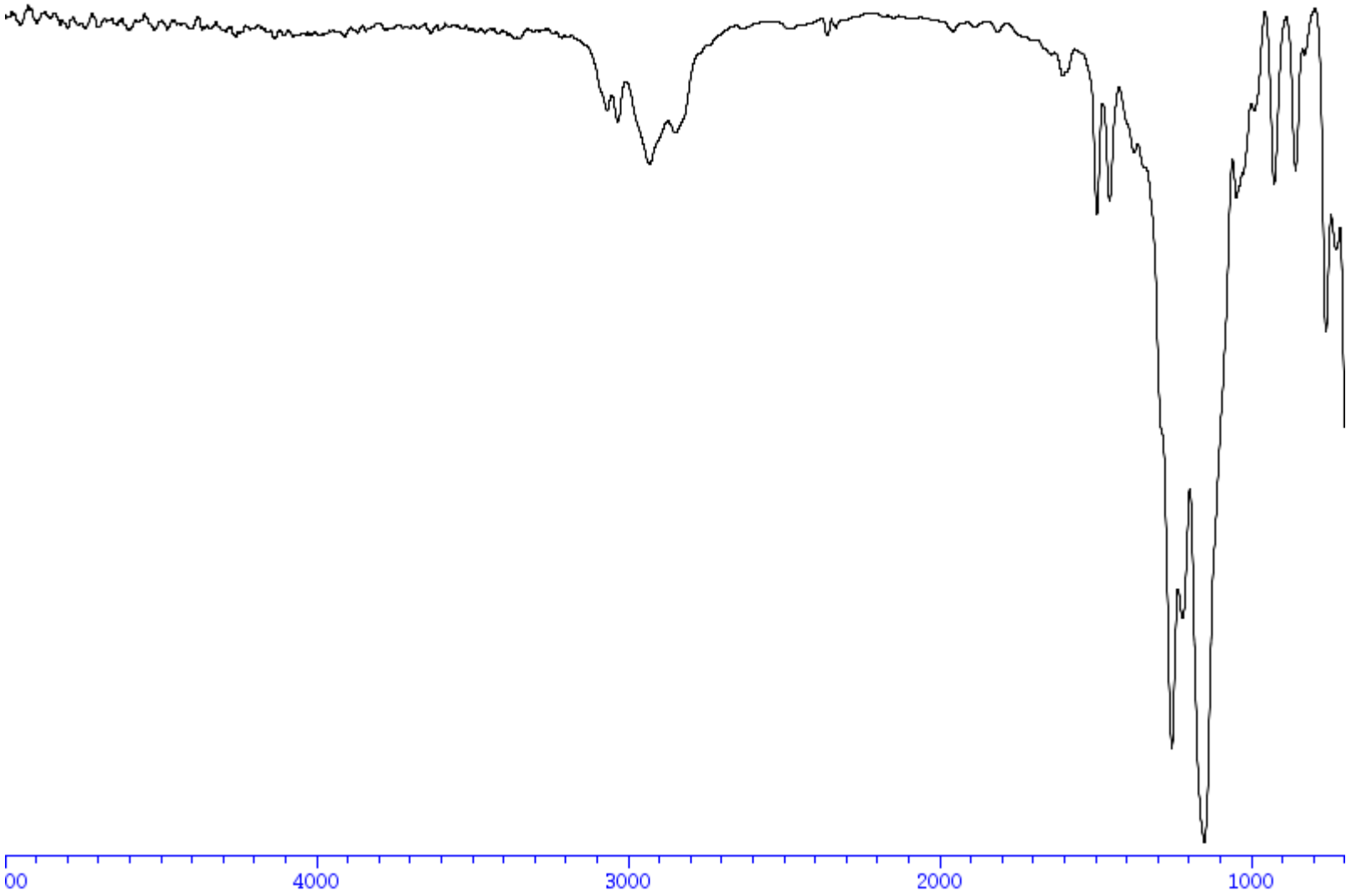

F3C
O
F
Bn
N
9ae, 1H NMR
18000
17000
16000
15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)


F3C
F
Bn–N
O
9ae, 13C NMR
26000
24000
22000
20000
18000
16000
14000
12000
10000
8000
6000
4000
2000
0
-2000
10 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


00
4000
3000
2000
1000


F3C
O
Bn–N
OCF3
9af, 1H NMR
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)


F3C
O
Bn
N
9af, 13C NMR
OCF3
f1 (ppm)
f1 (ppm)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2000
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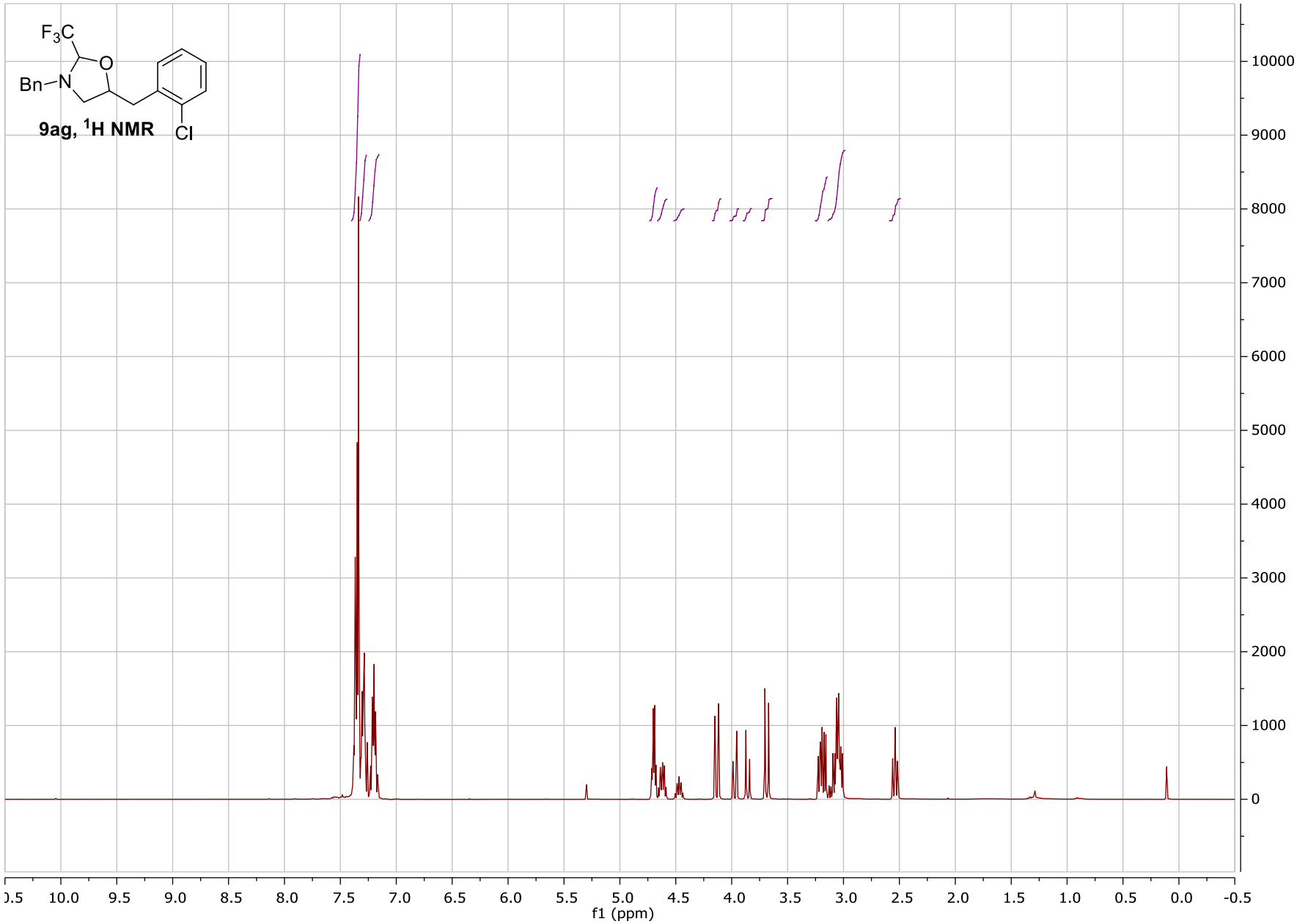
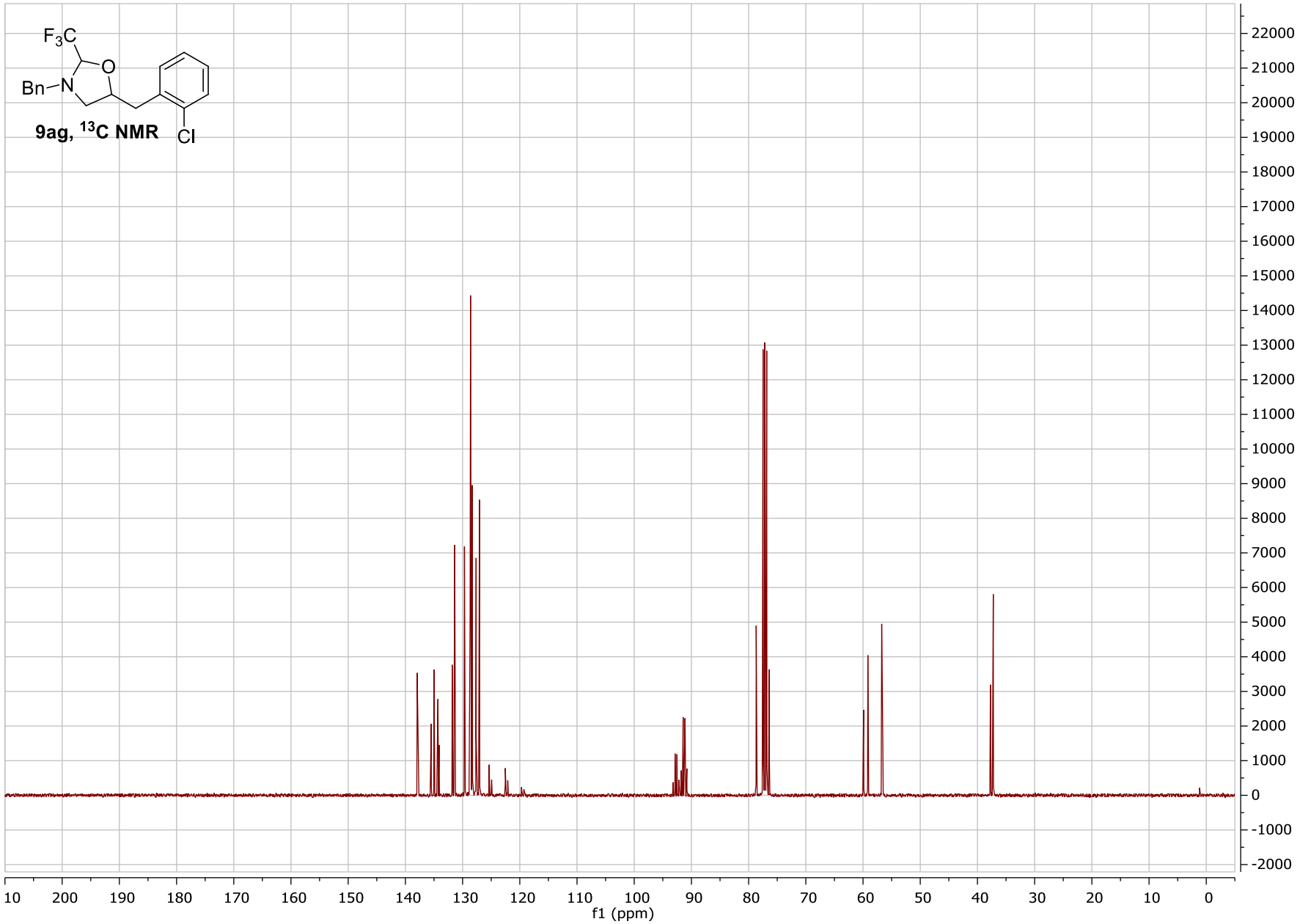

F3C
O
Bn
N
Cl
9ag, 1H NMR
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)


F3C
O
Bn
N
Cl
9ag, 13C NMR
22000
21000
20000
19000
18000
17000
16000
15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
-2000
10
200
190
180
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130
120
110
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90
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70
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50
40
30
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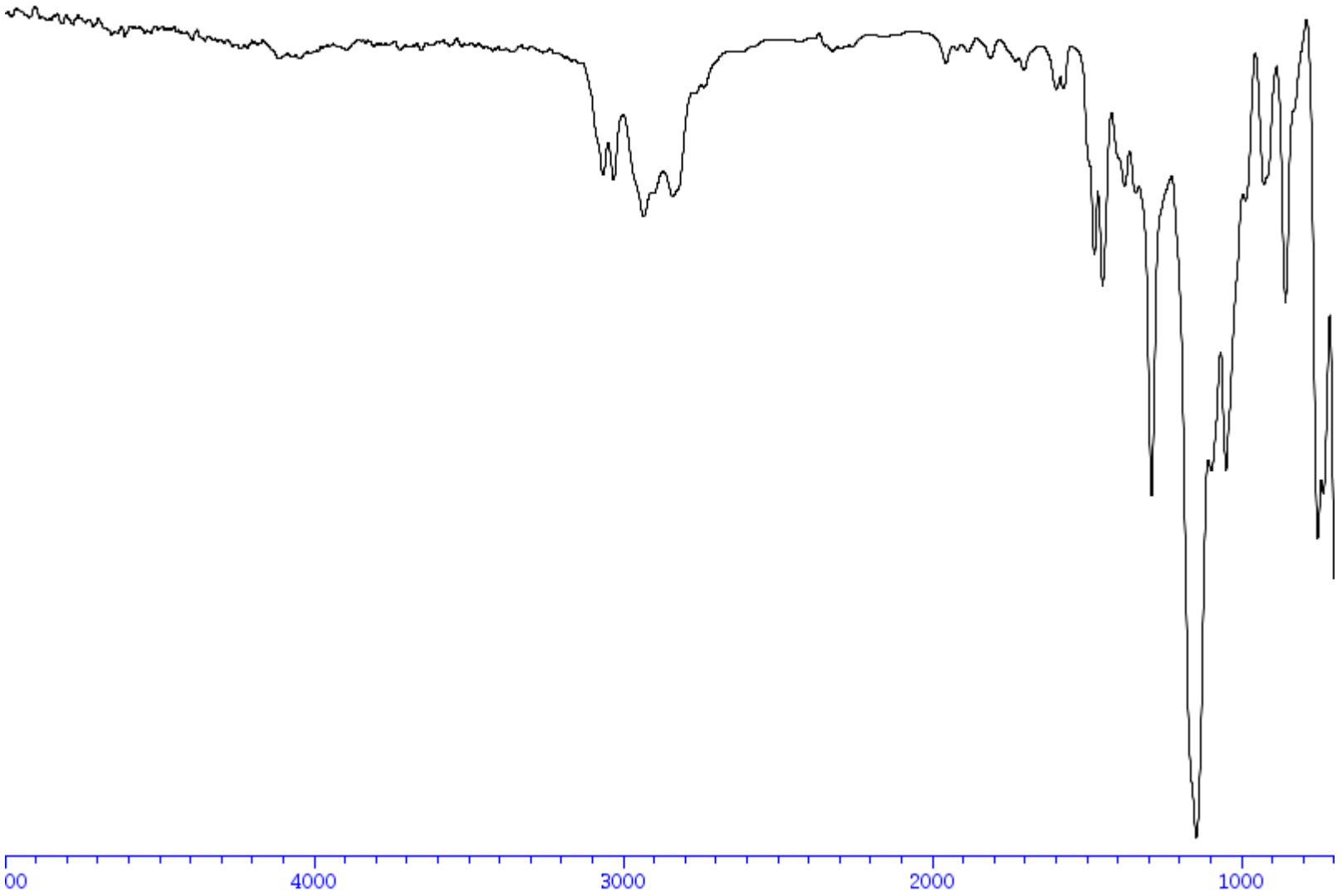
10
0
f1 (ppm)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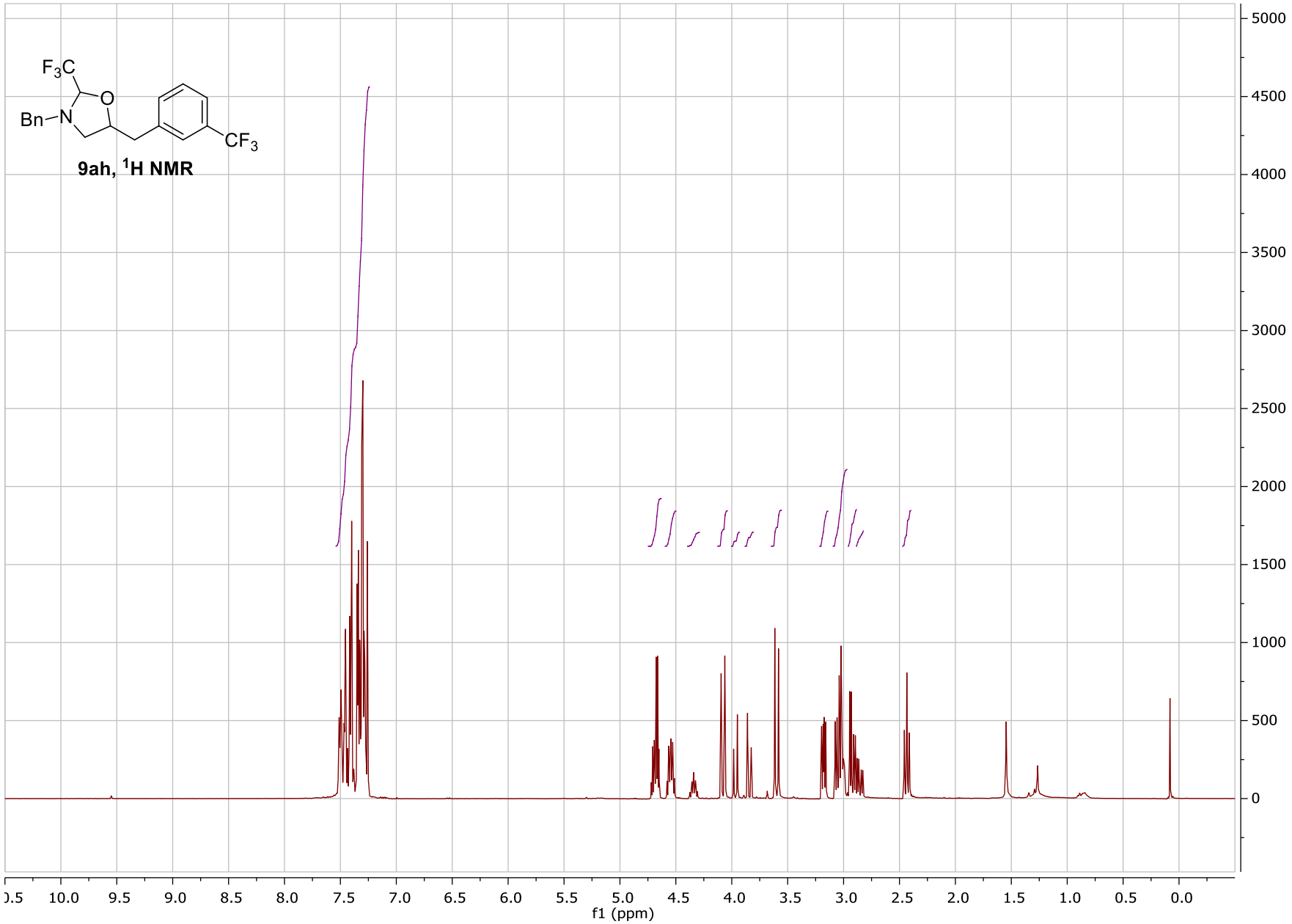
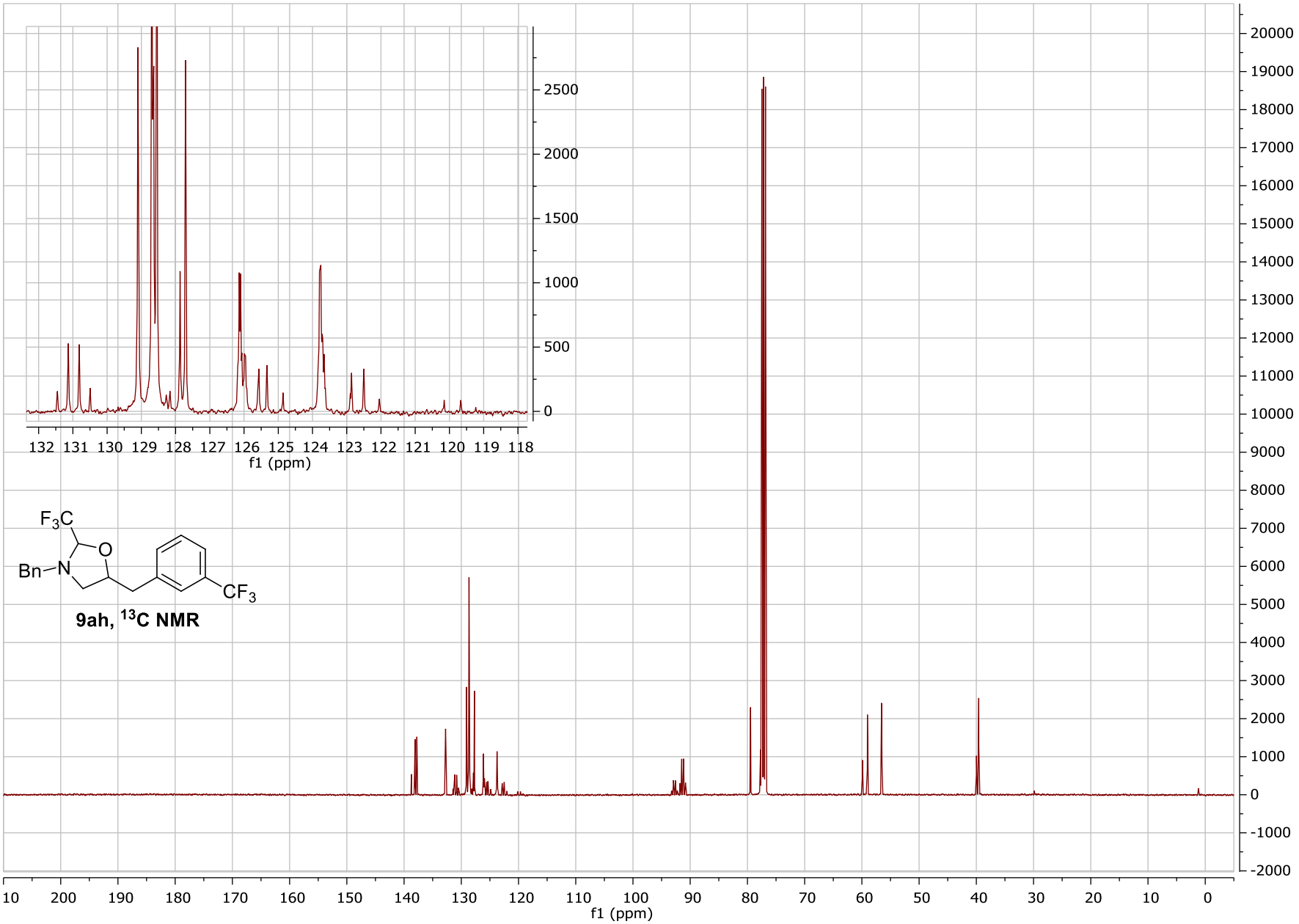
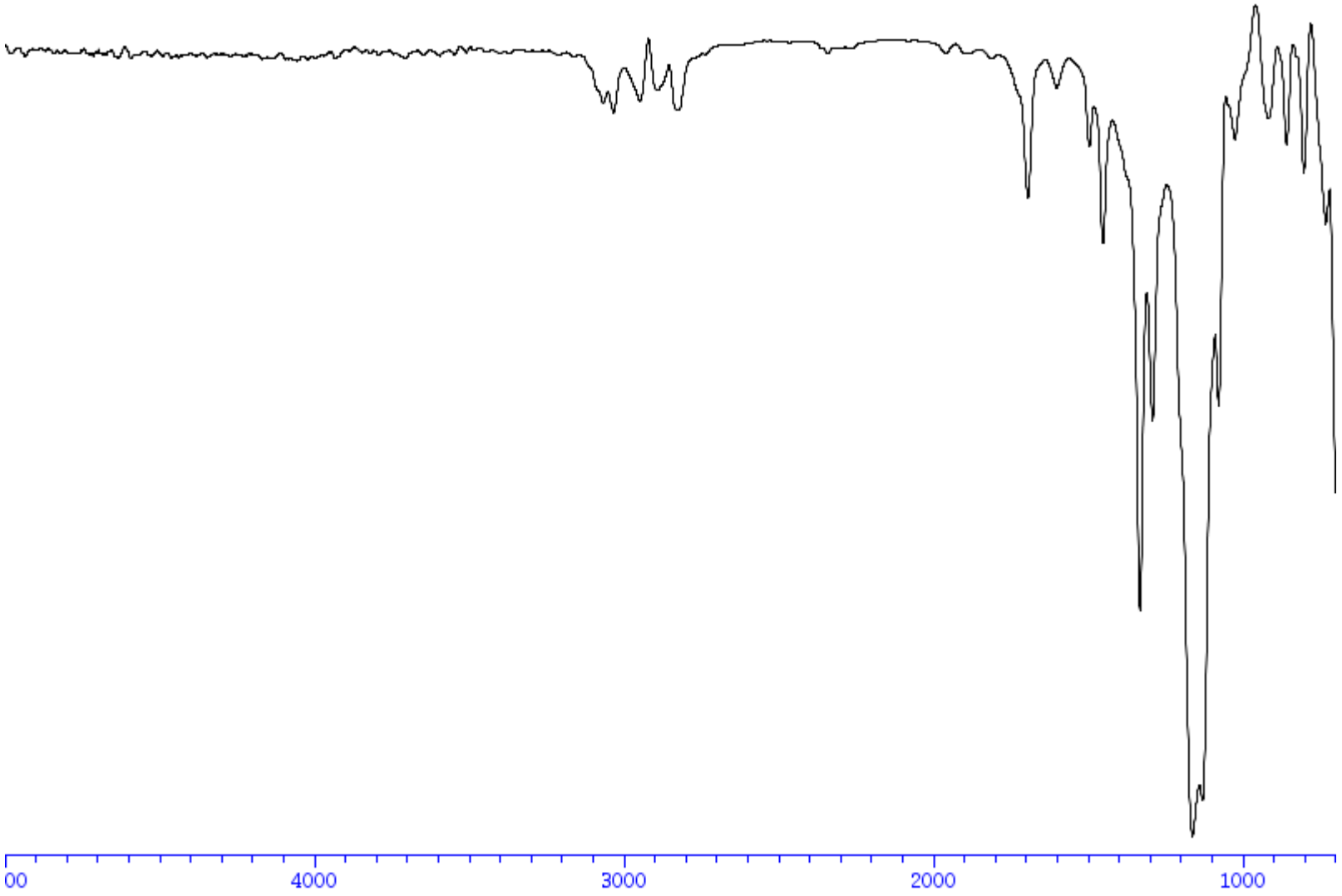
1000


F3C
O
Bn
N
CF3
9ah, 1H NMR
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


F3C
O
Bn
N
CF3
9ah, 13C NMR
f1 (ppm)
f1 (ppm)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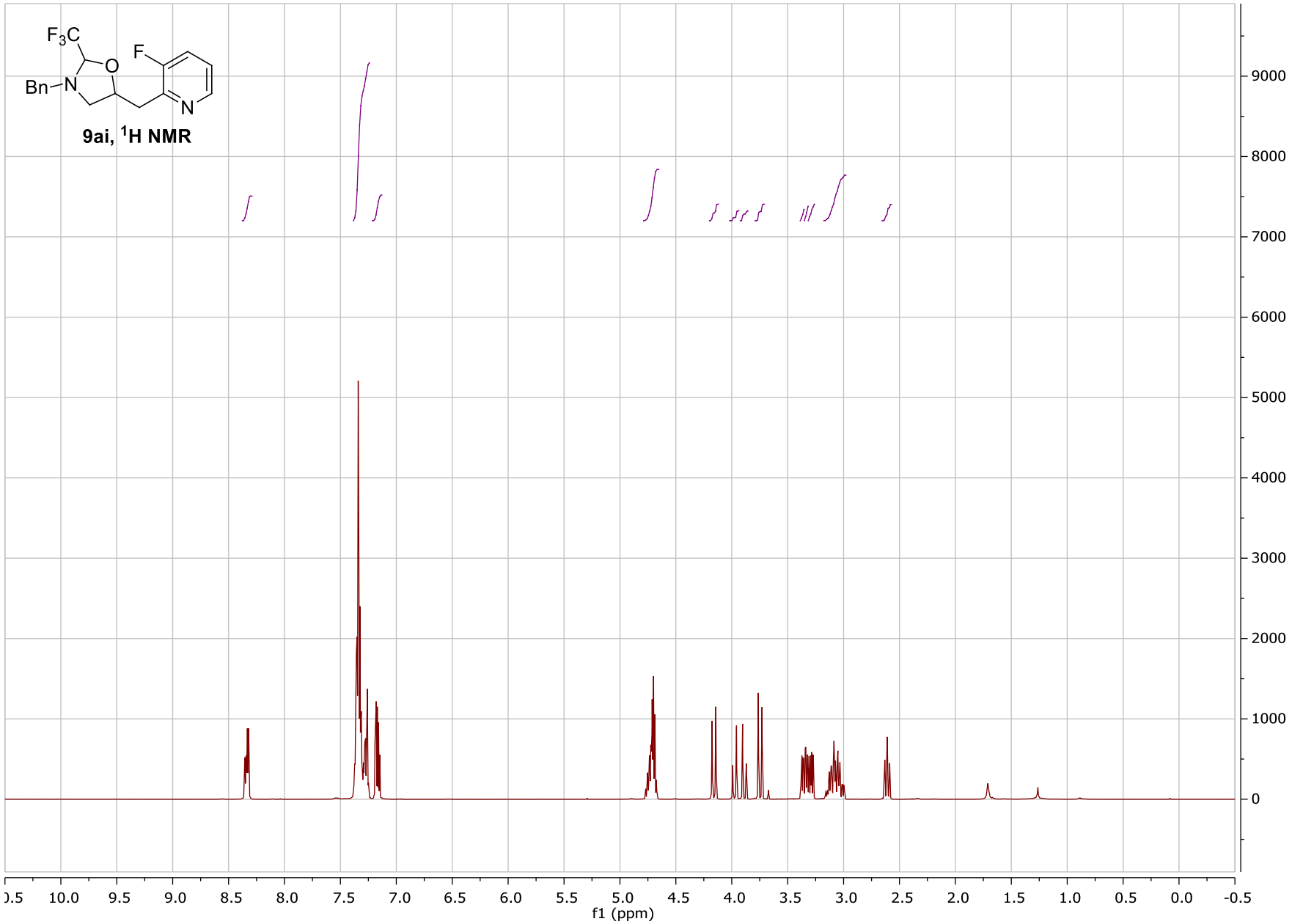
1000


F3C
O
F
Bn
N
N
9ai, 1H NMR
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
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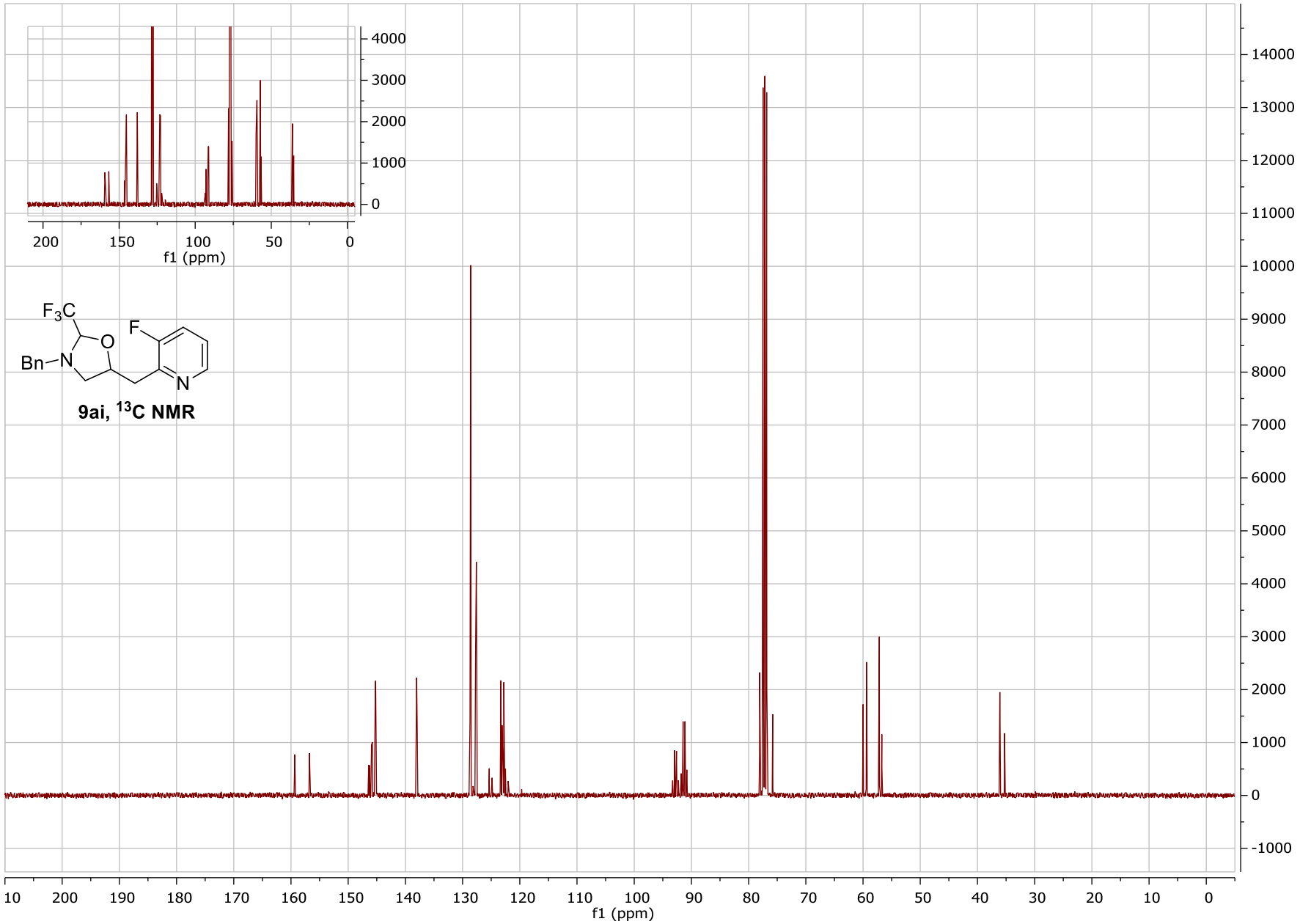
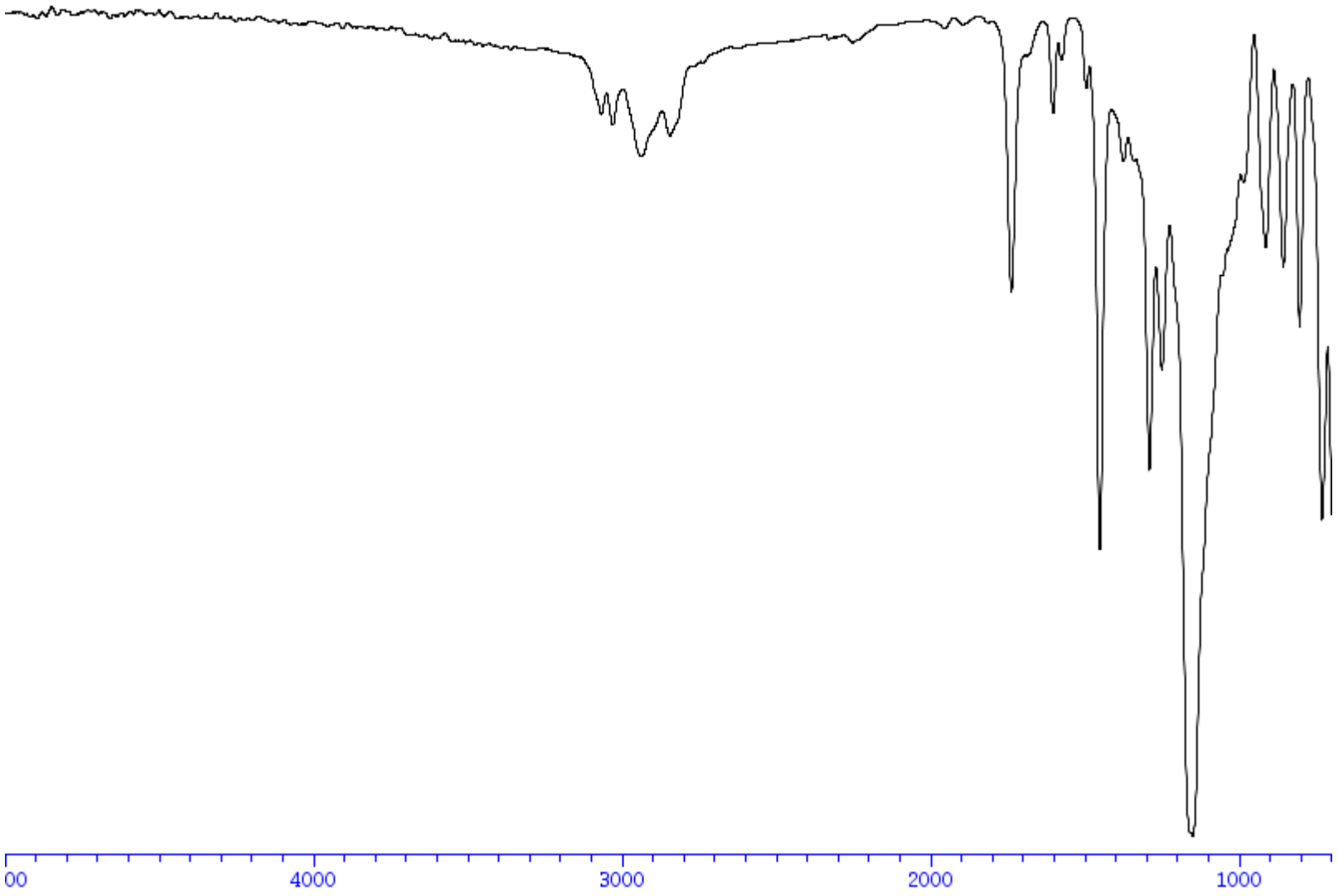
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)


F3C
O
F
Bn
N
N
9ai, 13C NMR
f1 (ppm)
f1 (ppm)


00
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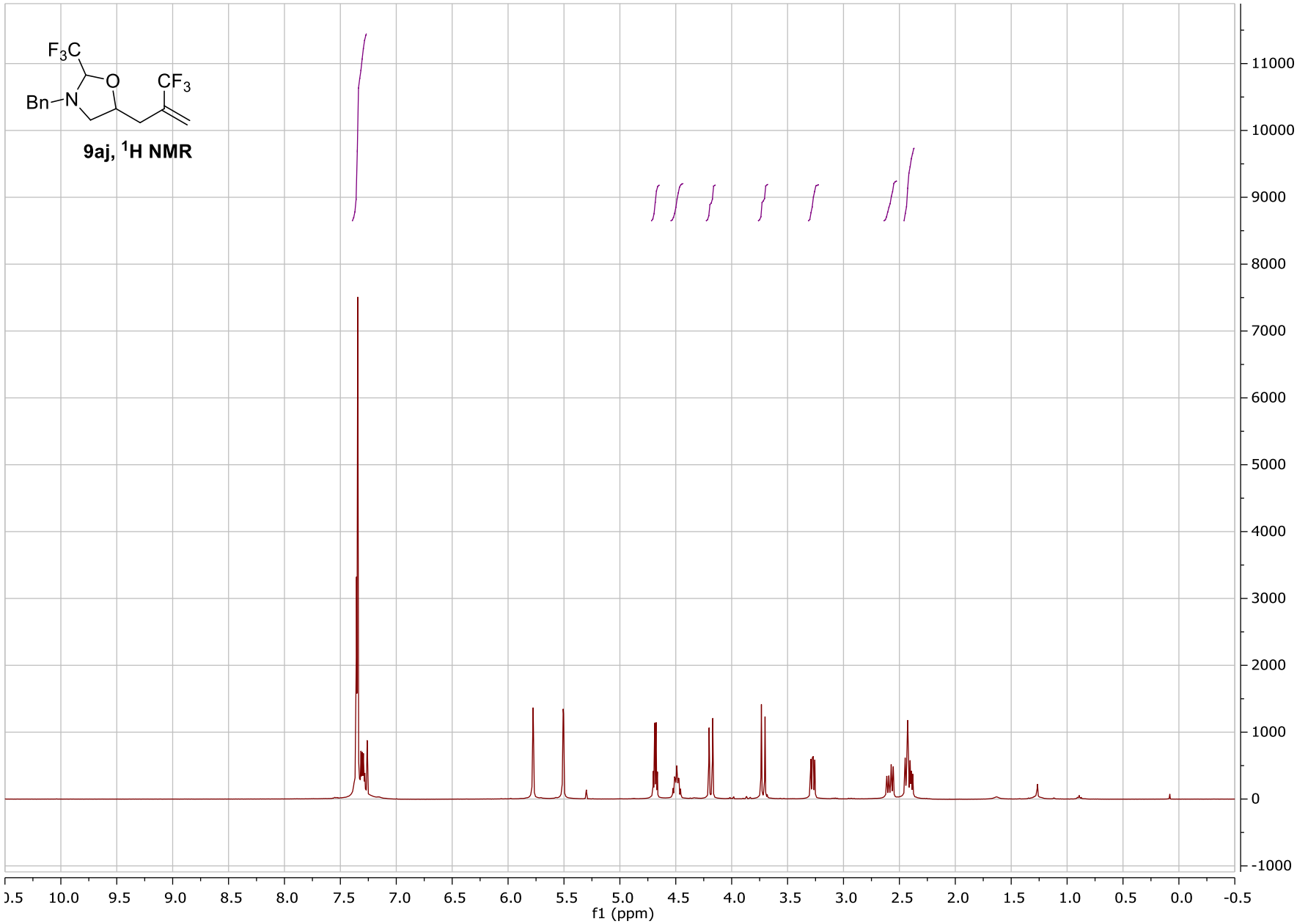
F3C
O
CF3
Bn
N
9aj, 1H NMR
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
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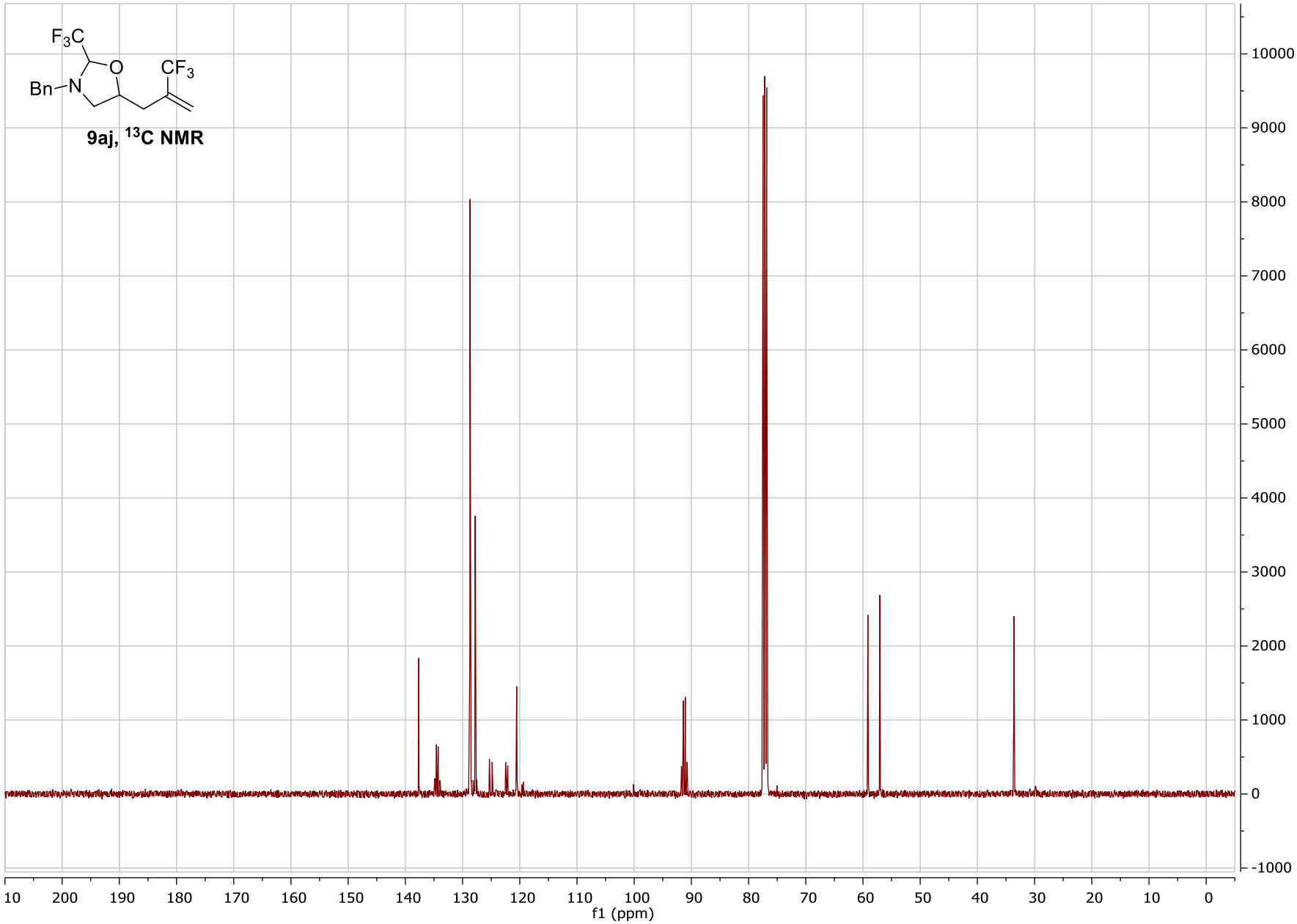
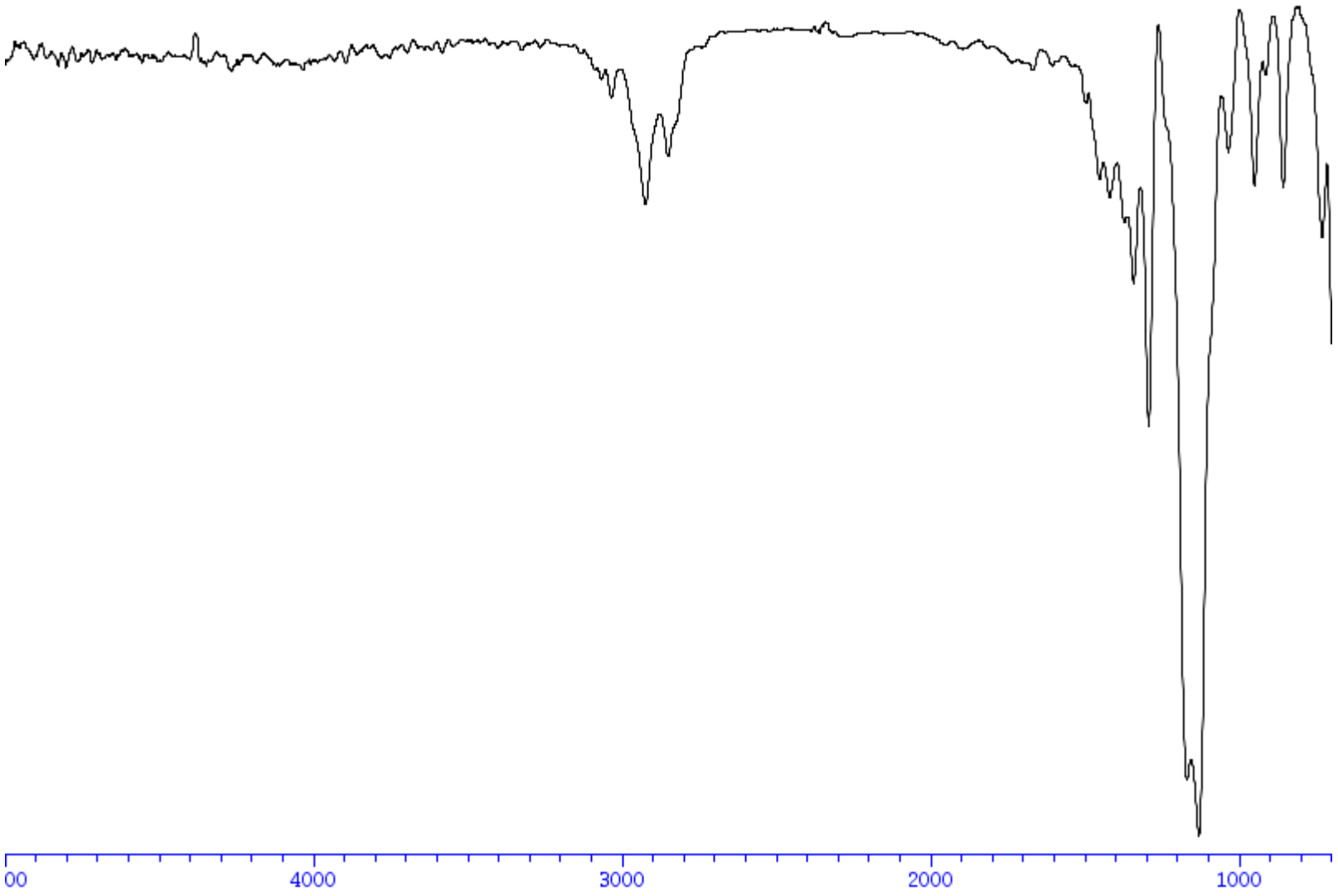
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)


F3C
O
CF3
Bn
N
9aj, 13C NMR
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
10
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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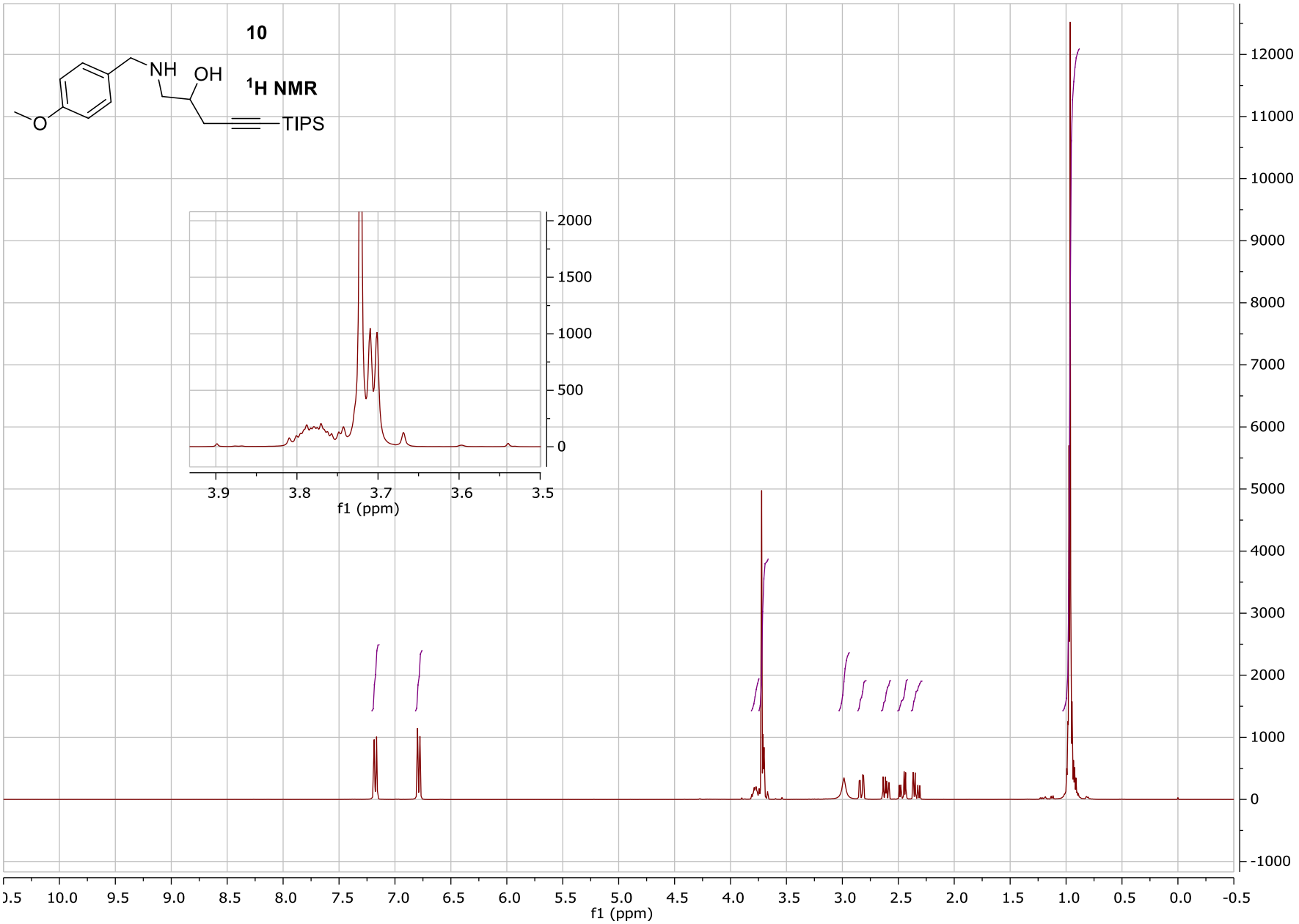
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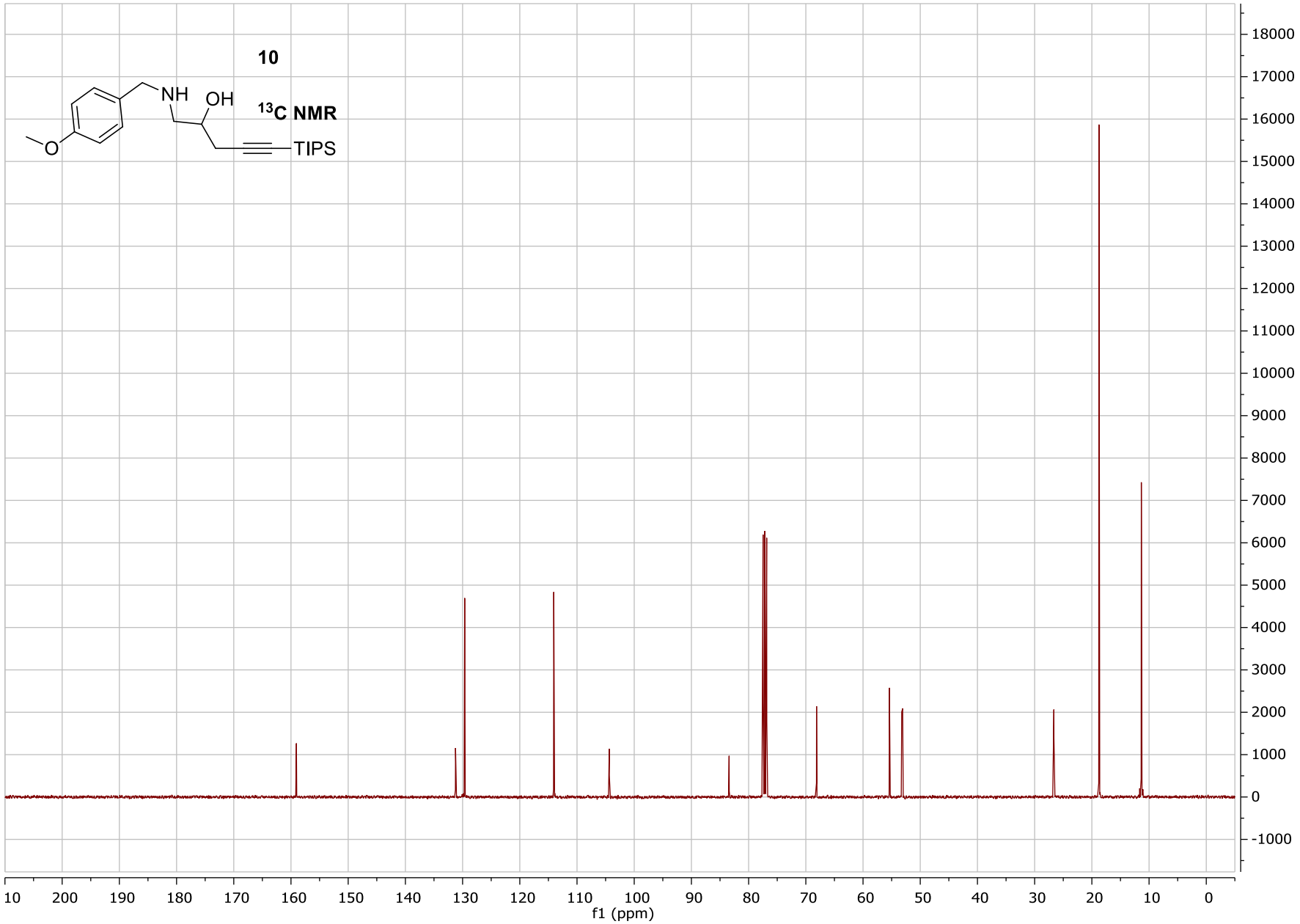
OH
O
TIPS
1H NMR
f1 (ppm)
f1 (ppm)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OH
O
TIPS
13C NMR
18000
17000
16000
15000
14000
13000
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11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
10
200
190
180
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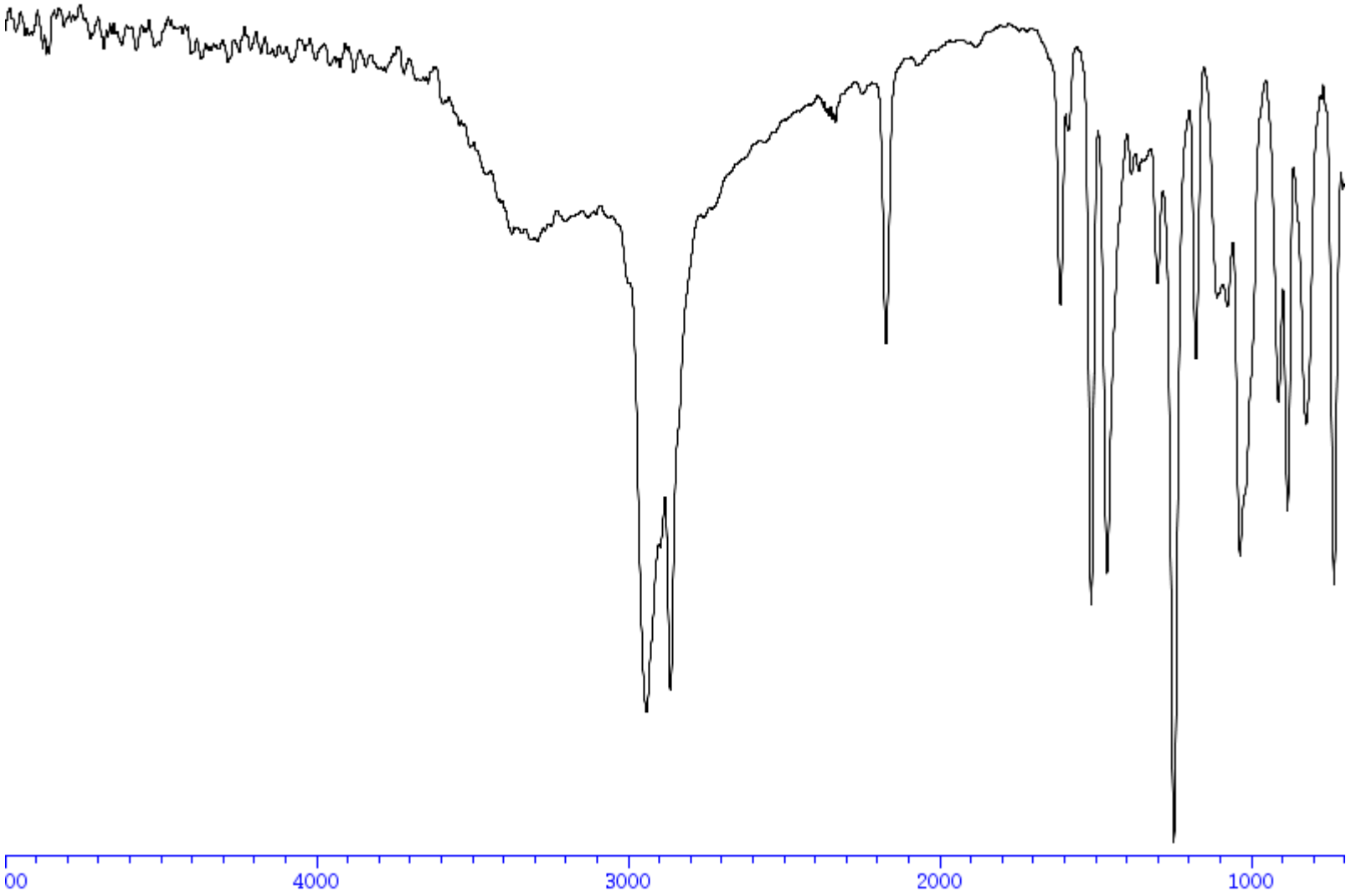
f1 (ppm)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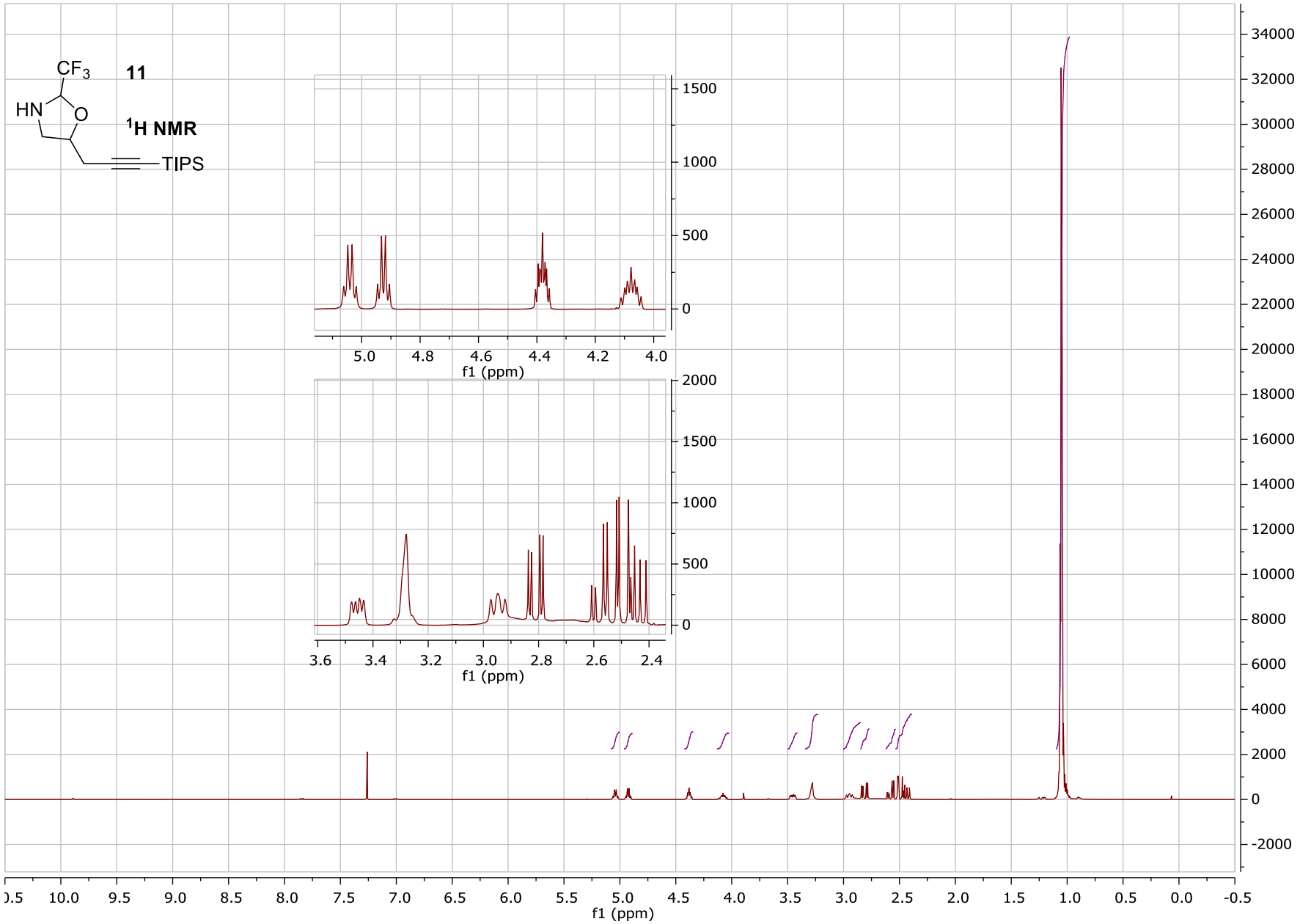
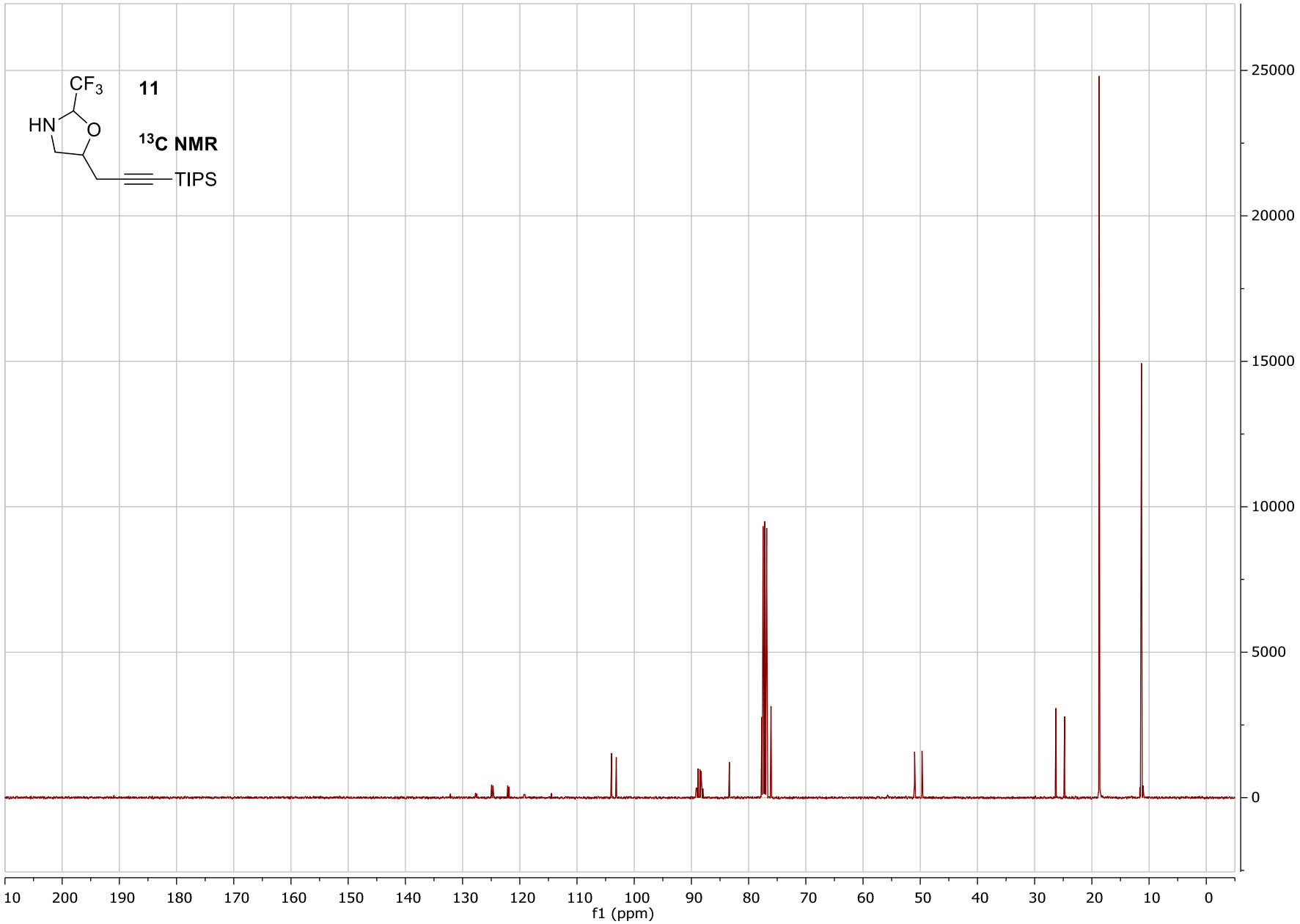

CF3
HN
O
TIPS
11
1H NMR
f1 (ppm)
f1 (ppm)
f1 (ppm)


CF3
HN
O
TIPS
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13C NMR
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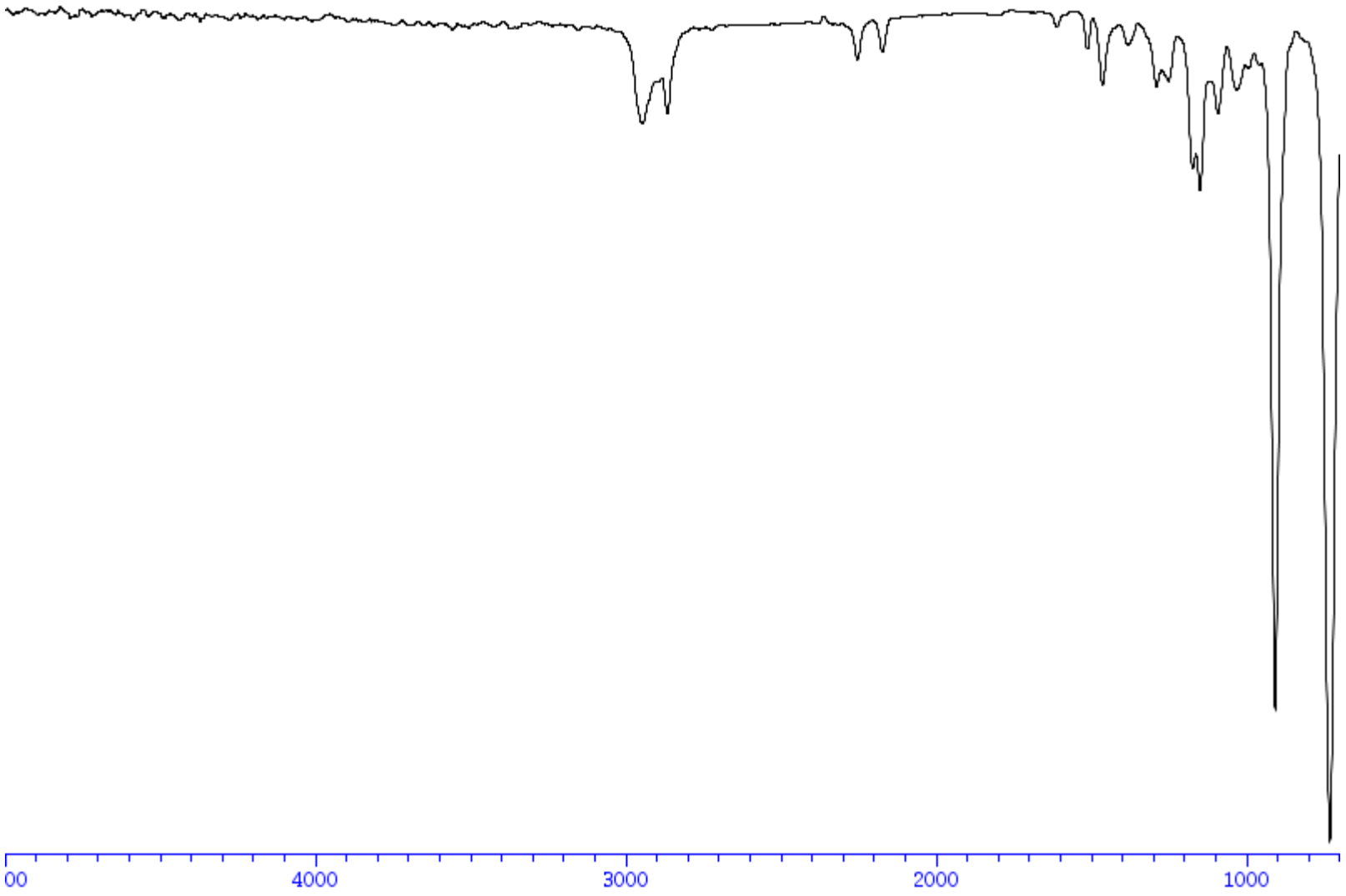
f1 (ppm)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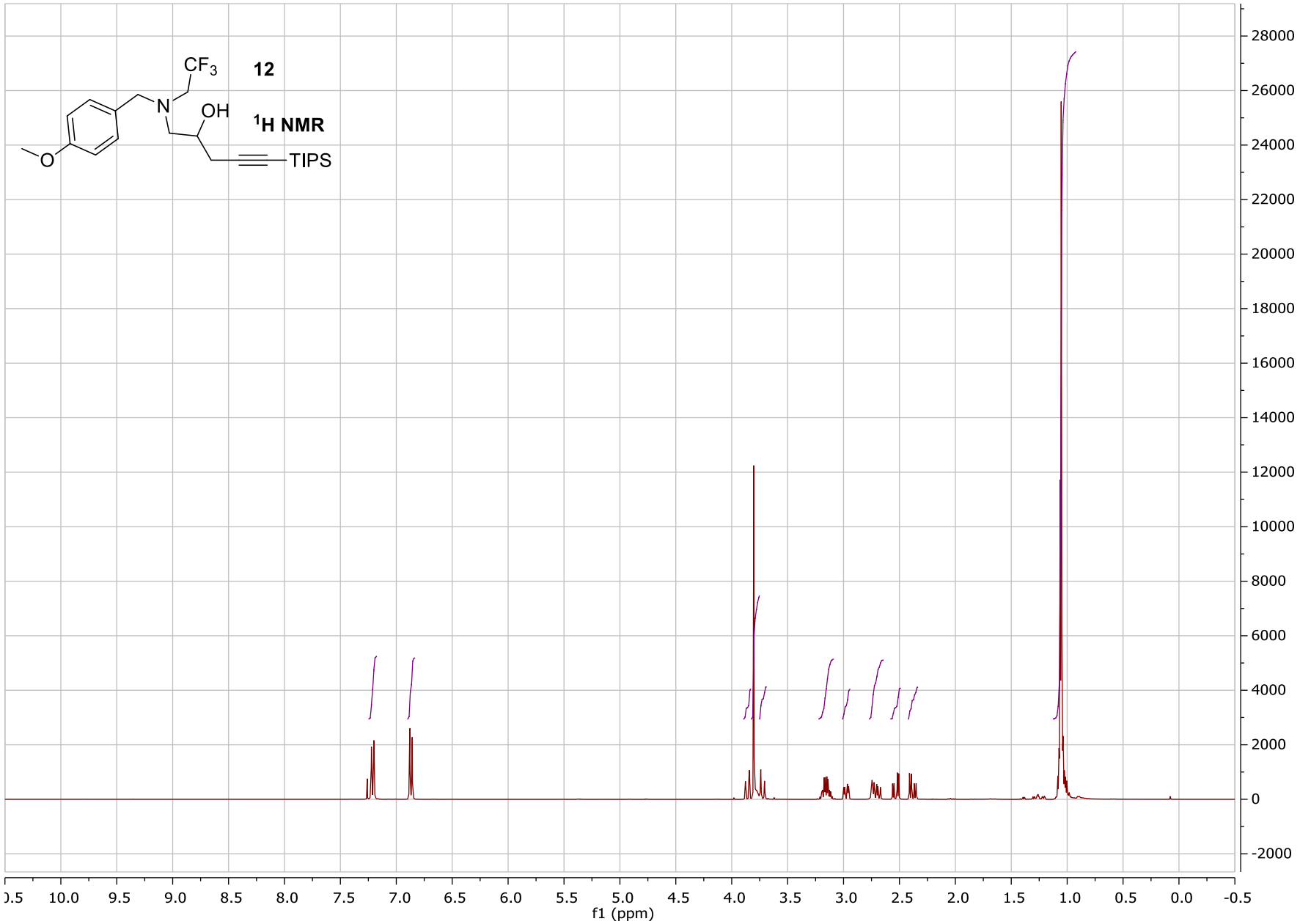
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12
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OH
1H NMR
O
TIPS
28000
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24000
22000
20000
18000
16000
14000
12000
10000
8000
6000
4000
2000
0
-2000
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
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3.0
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0.5
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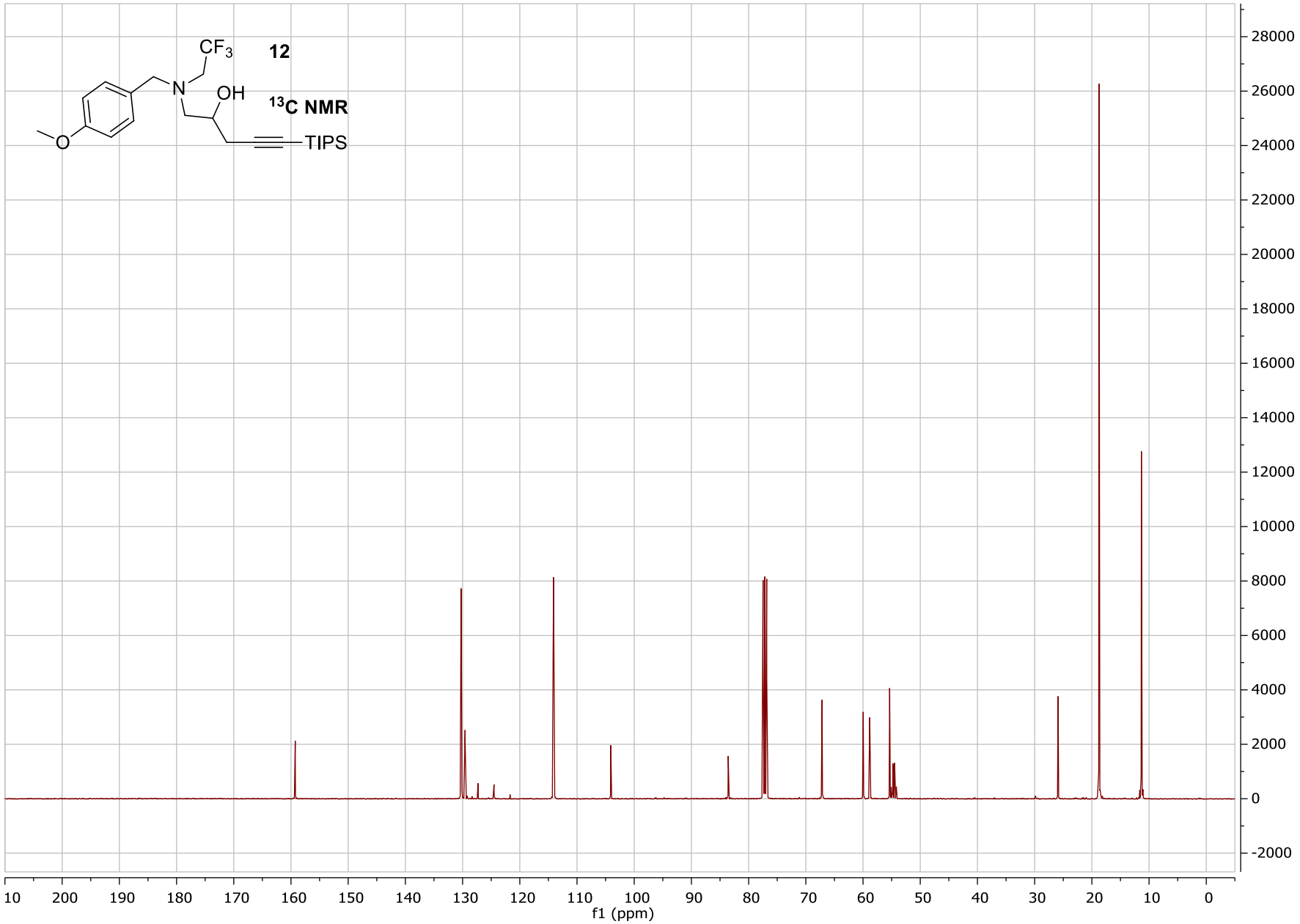
-0.5
f1 (ppm)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13C NMR
O
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10000
8000
6000
4000
2000
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200
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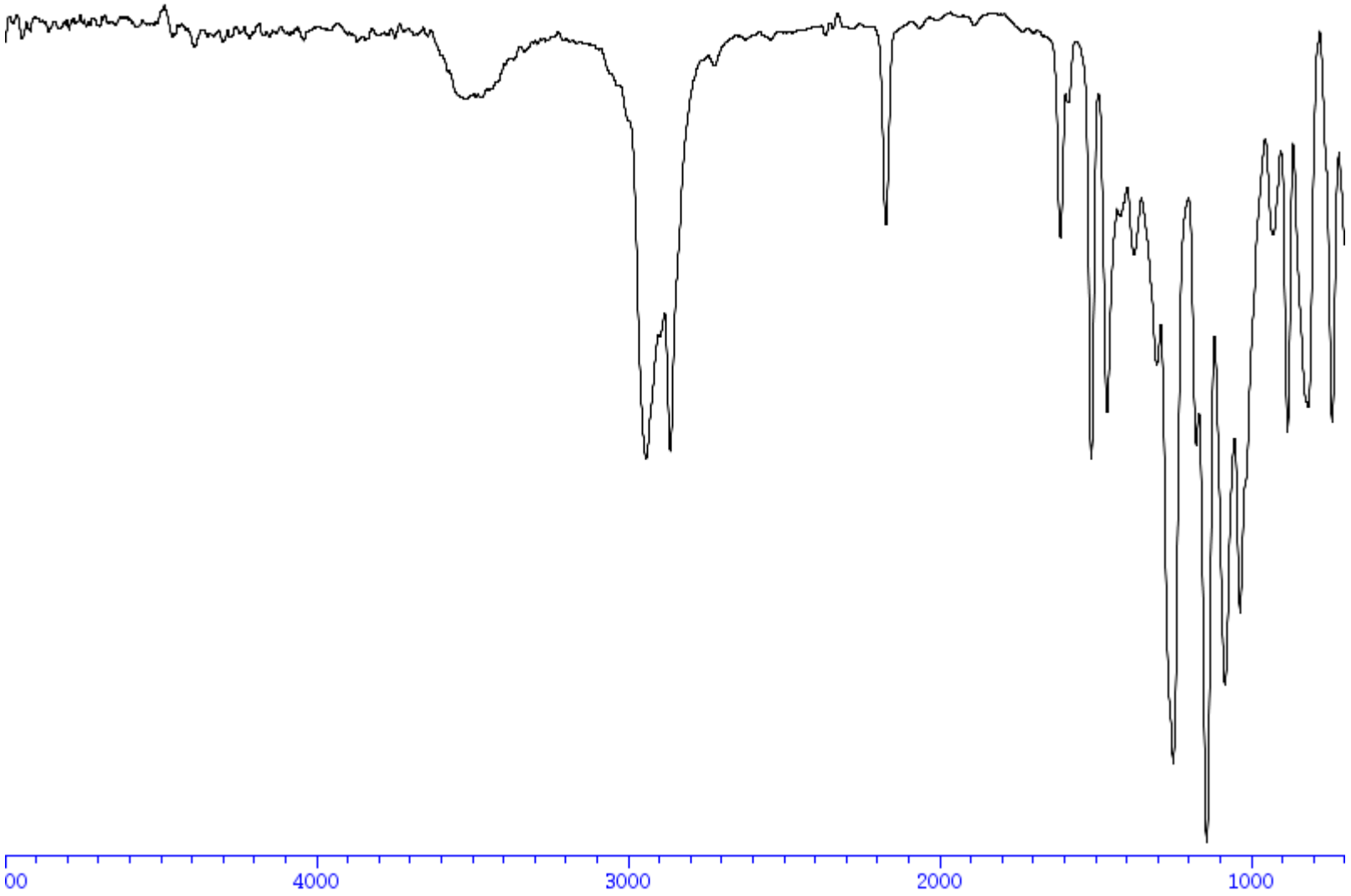
f1 (ppm)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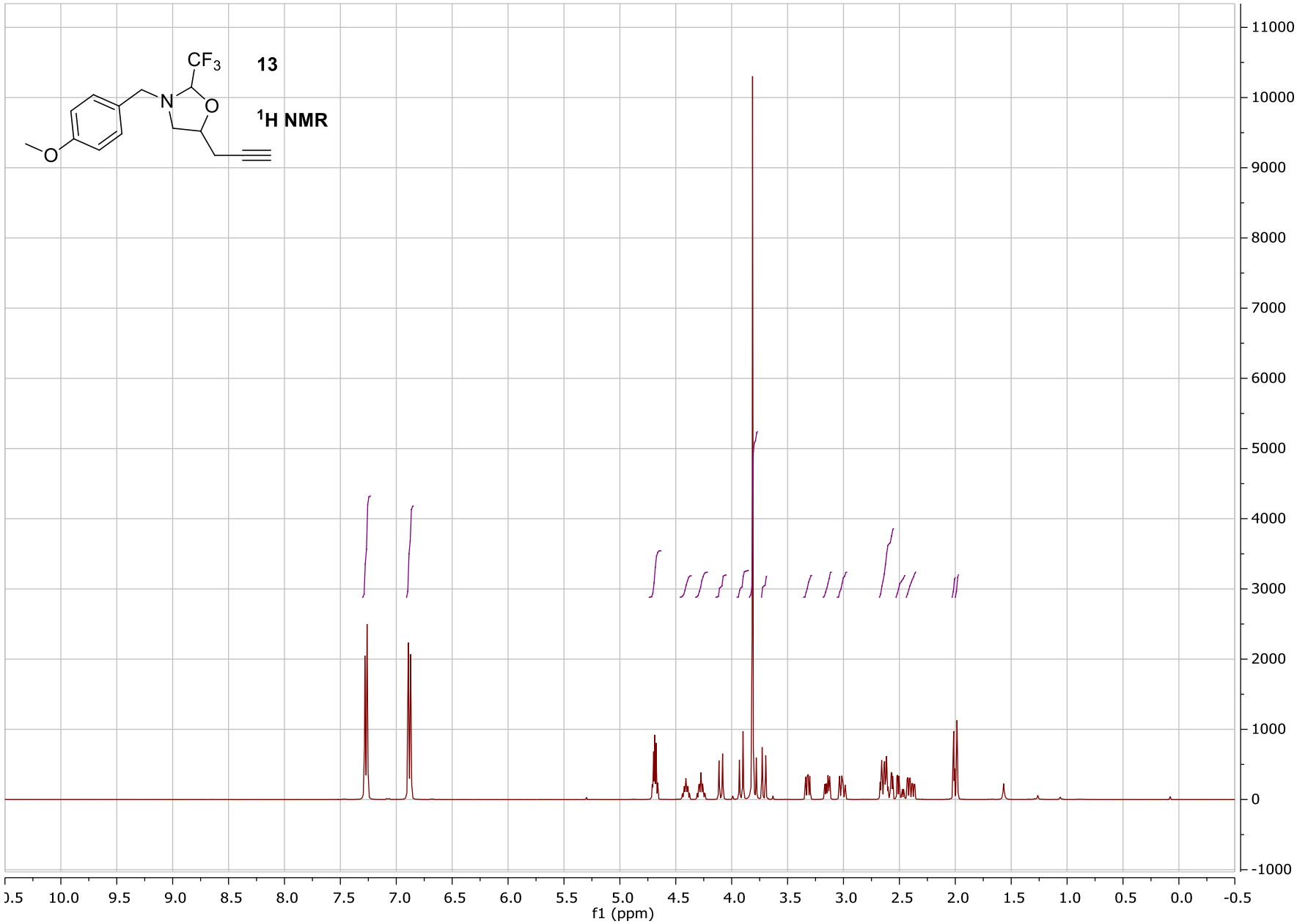
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O
O
13
1H NMR
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10000
9000
8000
7000
6000
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4000
3000
2000
1000
0
-1000
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
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2.0
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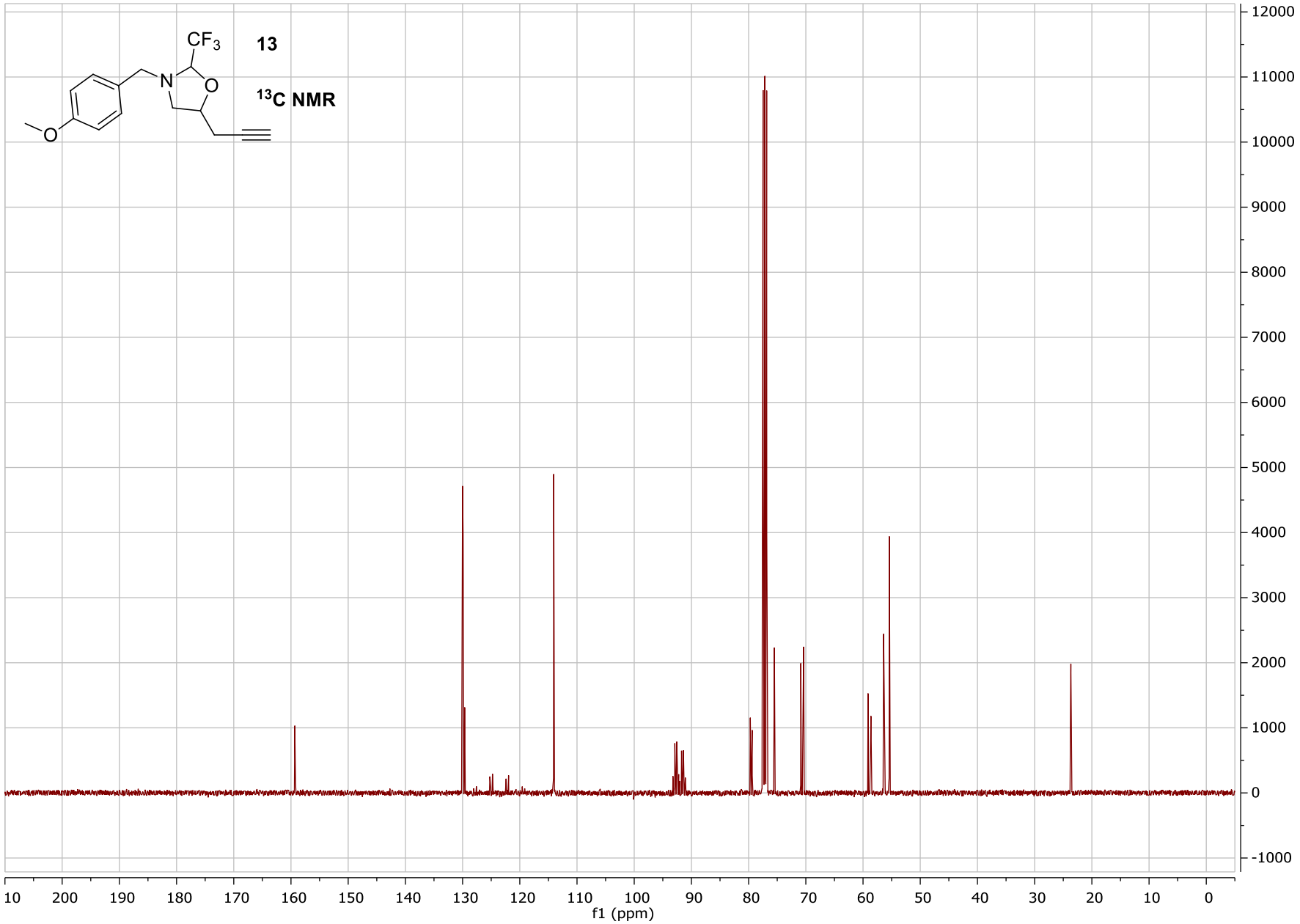
0.0
-0.5
f1 (ppm)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O
O
13
13C NMR
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11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
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200
190
180
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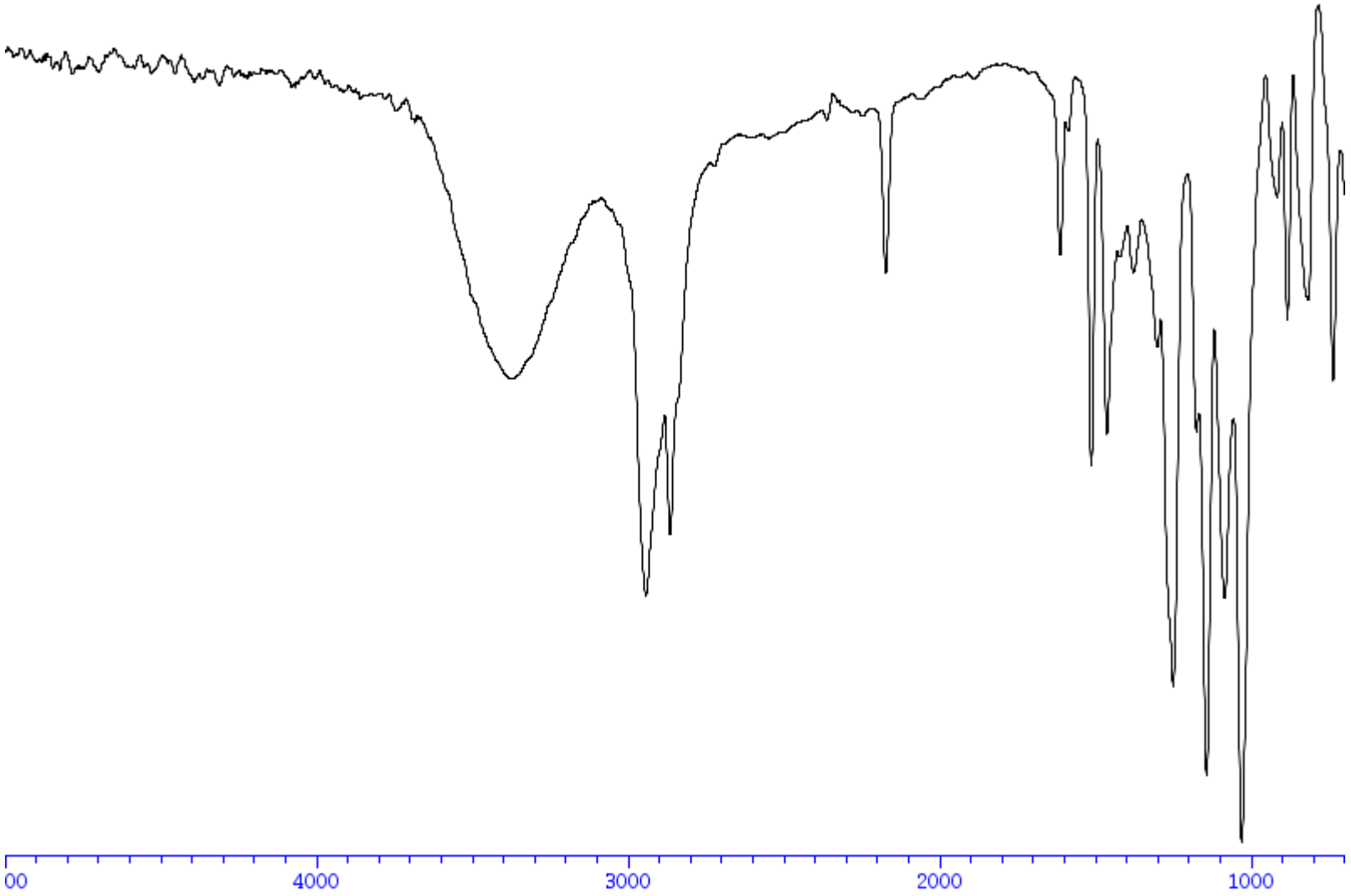
f1 (ppm)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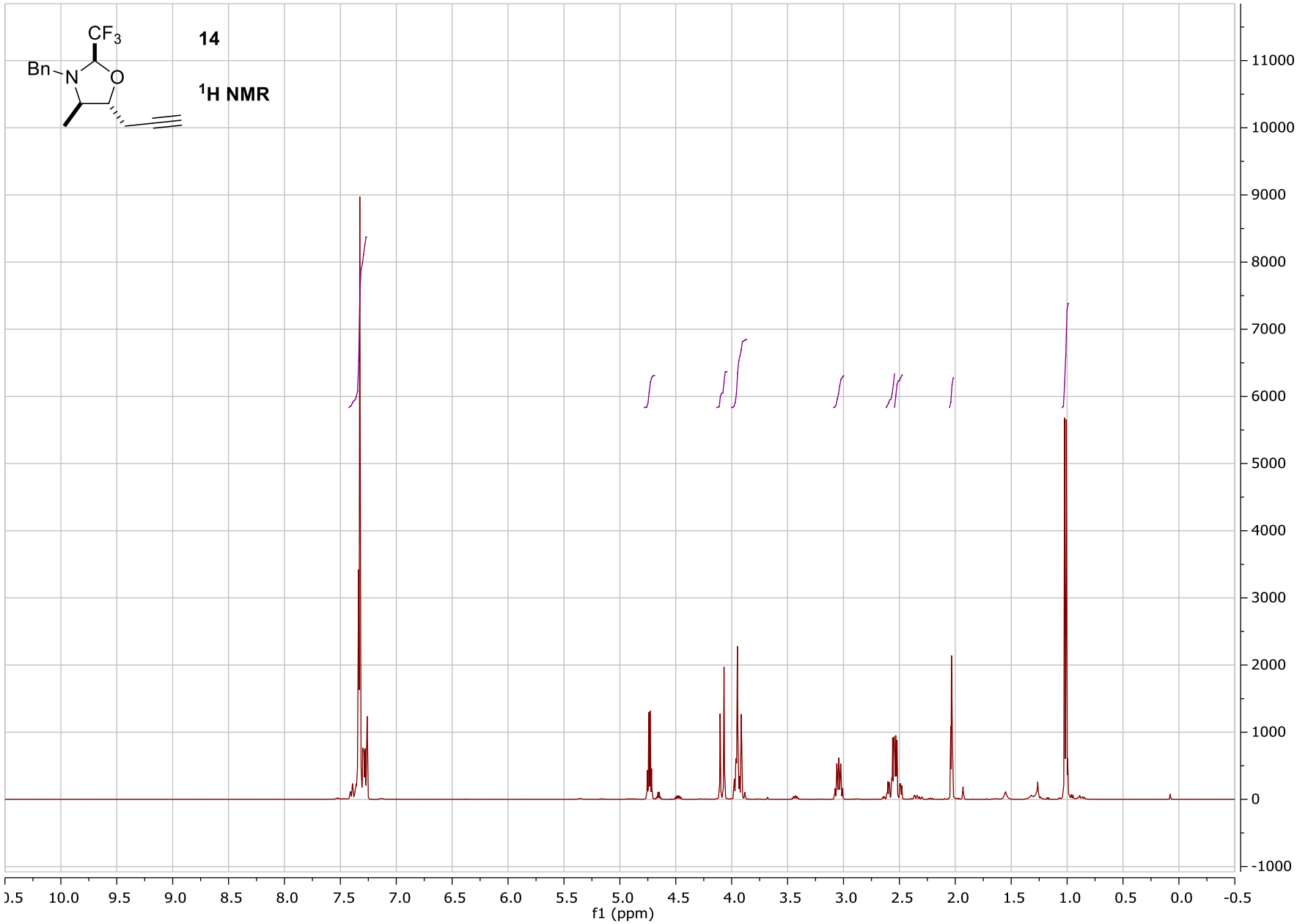
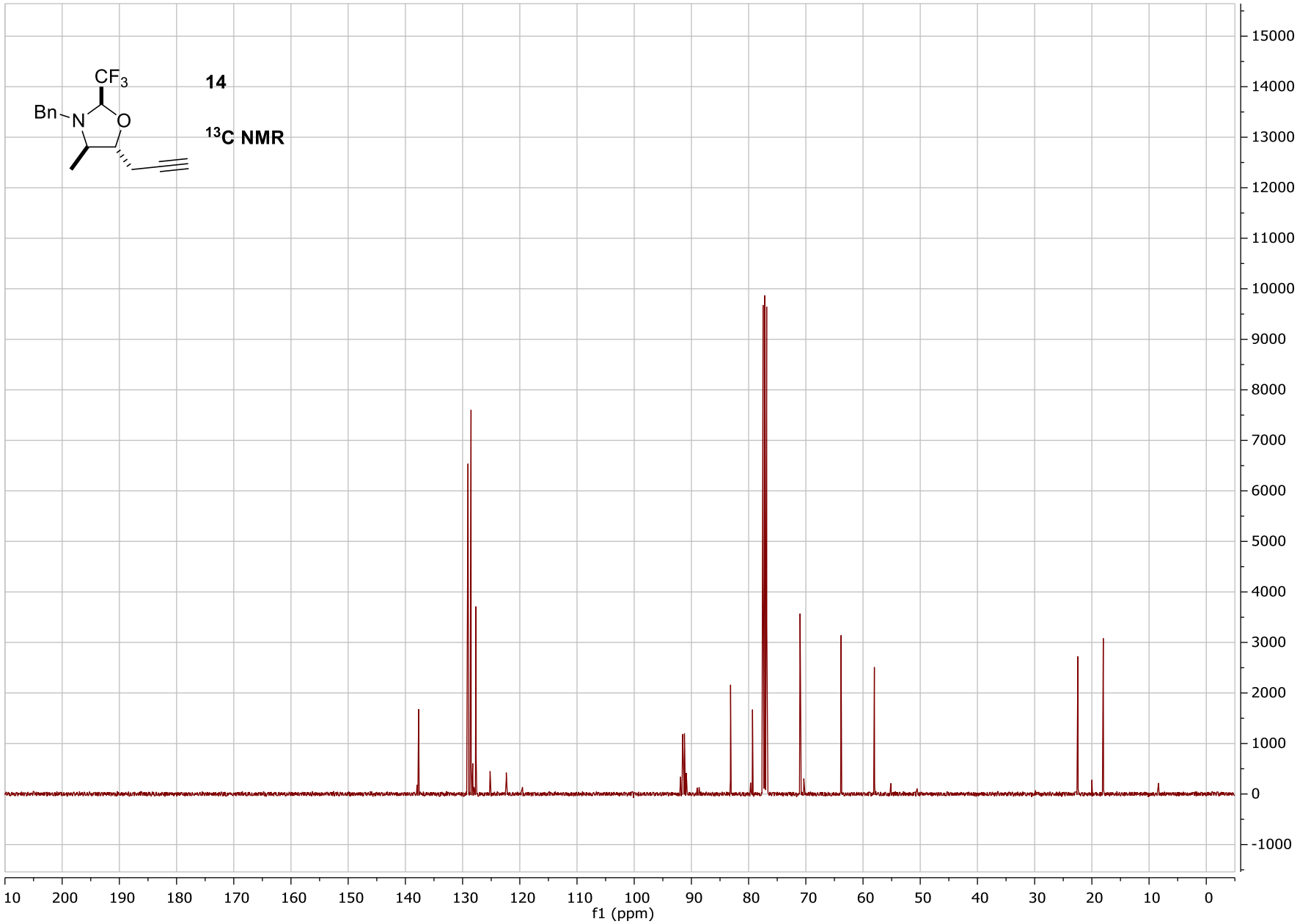

CF3
Bn
N
O
14
1H NMR
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)


CF3
Bn
N
O
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13C NMR
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14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
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10
200
190
180
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120
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100
90
80
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50
40
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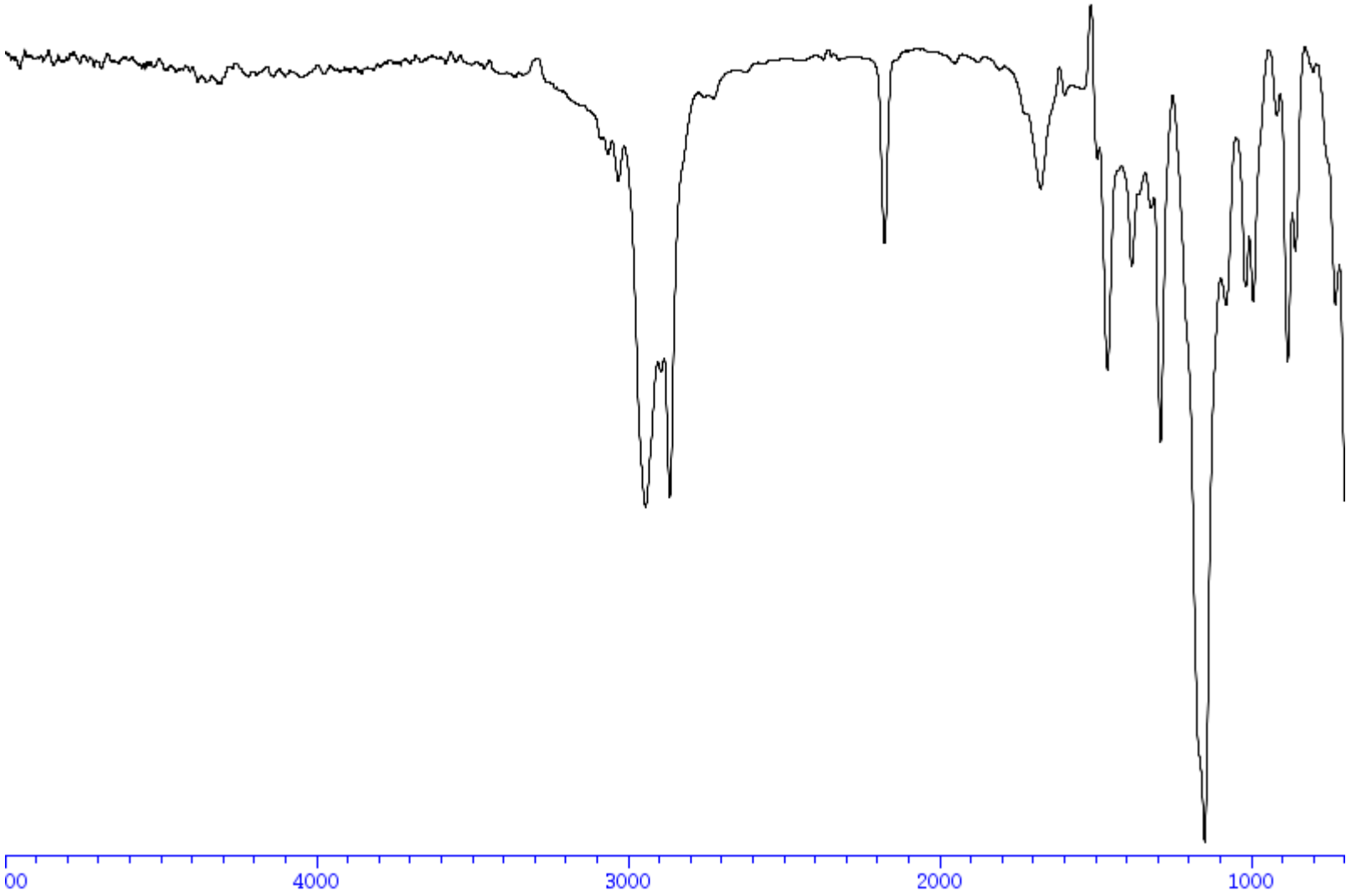
10
0
f1 (ppm)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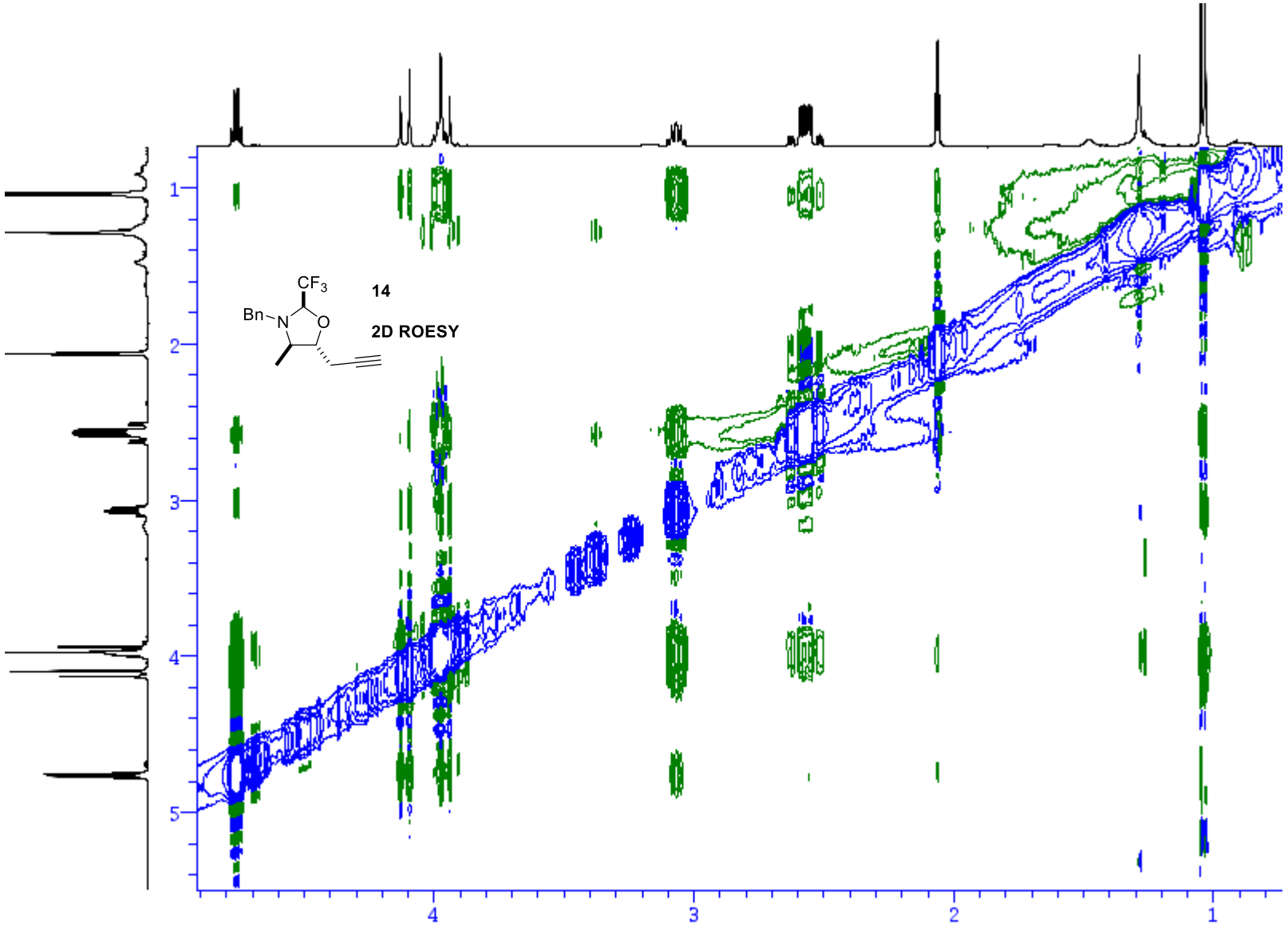
CF3
Bn
N
O
14
2D ROESY
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3
4
5
4
3
2
1