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RESEARCH ARTICLE

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Benzylic C(sp^3)–H Azidation: Copper *vs* Iron Catalysis

Angel Rentería-Gómez[+],[a] Rubén O. Torres-Ochoa[+],[b] Pierre Palamini[+],[c] Raphaël Simonet-Davin,[c] Qian Wang,[a] Jérôme Waser,*[c] and Jieping Zhu*[a]

[a] Laboratory of Synthesis and Natural Products, Institute of Chemical Sciences and Engineering, École Polytechnique Fédérale de Lausanne, EPFL-SB-ISIC-LSPN, BCH 5304, 1015 Lausanne, Switzerland, e-mail: jieping.zhu@epfl.ch

[b] Instituto de Química, Universidad Nacional Autónoma de México, Circuito Exterior, Ciudad Universitaria, 04510, Ciudad de México, México

[c] Laboratory of Catalysis and Organic Synthesis, Institute of Chemical Sciences and Engineering, École Polytechnique Fédérale de Lausanne, EPFL-SB-ISIC-LCSO, BCH 4306, 1015 Lausanne, Switzerland, e-mail: jerome.waser@epfl.ch

Dedicated to Prof. Dr. *Alois Fürstner*, President of the 56th Bürgenstock-Conference 2023

The generation of benzylic radicals through hydrogen atom abstraction (HAT) has been a recent research focus and various C(sp^3)–H bond functionalization protocols have been developed relying on this elementary step. We report herein copper- and iron-catalyzed C(sp^3)–H benzylic azidation reactions using *m*CPBA and NFSI as oxidant, respectively, and $TMSN_3$ as azide source. The reaction is thought to be initiated *via* intermolecular abstraction of benzylic hydrogen by the *in situ* generated heteroatom-centered radicals. The $Fe(OTf)_3$-catalyzed azidation protocol displays good chemoselectivity as it takes place preferentially at the secondary and tertiary benzylic C(sp^3)–H bonds over the primary benzylic and tertiary aliphatic carbons. Efforts on the development of catalytic enantioselective processes are also documented.

Keywords: C–H functionalization, azidation, catalysis, radical, hydrogen atom transfer (HAT).

Introduction

Taking advantage of the easy generation of heteroatom-centered radicals (X$^\bullet$) and the much higher bond dissociation energy (BDE) of the X–H bonds (about 105 kcal/mol for amide N–H and aliphatic alcohol O–H bonds) relative to the C(sp^3)–H bonds (90–100 kcal/mol), hydrogen atom abstraction (HAT) has been developed into an effective way for the generation of reactive carbon radicals from non-activated C(sp^3)–H bonds.[1] The classic Hofmann-Löffler-Freytag (HLF) reaction,[2,3] Kharash-Sosnovsky allylic oxidation[4] and Barton nitrite ester reaction[5] involve in fact this key elementary reaction. Among various C–C and C–X bond forming processes, the azidation of C(sp^3)–H bond is of particularly interest due to the synthetic versatility of the resulting azido compounds.[6] The relatively low bond dissociation energy of the benzylic C–H bonds (~90 kcal/mol)[7] renders it particularly susceptible for the generation of benzylic radicals *via* HAT process and indeed, a number of elegant methodologies have been developed exploring this reaction manifold.[8–12] While stoichiometric amounts of hypervalent iodine reagents alone were initially used to reach this goal,[13–18] catalytic processes using electrochemical oxidation,[19] photoredox catalysis[20,21] and transition metal catalysts, such as manganese,[22–25] iron,[26–29] copper,[30–32] have been developed recently. Alternatively, the oxidation of electron-rich alkylarenes and heteroarenes

[+] These authors contributed equally to this work.

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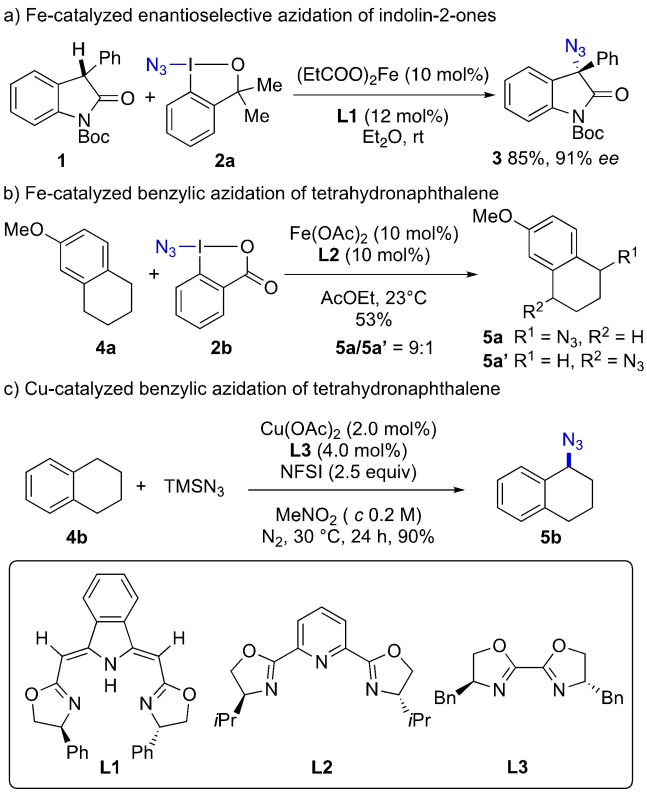
to radical cations followed by deprotonation has also been developed for the generation of benzylic radicals that can further evolve to the benzyl azides.[33,34]

Importantly, the Fe-catalyzed enantioselective azidation of indolin-2-ones **1** using 1-azido-3,3-dimethyl-3-(1*H*)-1,2-benziodoxole (**2a**) in the presence of chiral tridentate ligand **L1** afforded product **3** in 85% yield with 91% *ee* (*Scheme 1a*).[26] Recently, the Mn-catalyzed asymmetric azidation of indolines using an *in situ* generated hypervalent iodine reagent (PhIO, NaN_3) has been developed.[25] However, a general method allowing asymmetric azidation of simple benzylic C(sp^3)–H bond involving HAT as an initiation step is still highly demanding. As a matter of fact, the iron-catalyzed azidation of 6-methoxy-1,2,3,4-tetrahydronaphthalene (**4a**) with azidobenziodoxolone (**2b**, Zhdankin's reagent) in the presence of chiral ligand **L2** provided the regioisomeric azido compounds in a racemic form (*Scheme 1b*).[28] Similarly, copper-catalyzed reaction of tetralin (**4b**) with $TMSN_3$ in the presence of *N*-fluorobenzenesulfonimide (NFSI) and chiral ligand **L3** furnished **5b** without enantioselectivity (*Scheme 1c*).[32]



Scheme 1. Transition metal-catalyzed C(sp^3)–H azidation: Literature precedents.

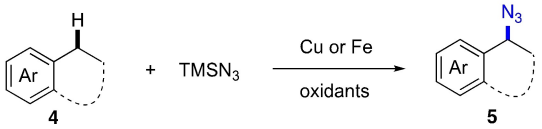
Our groups have been interested in developing C(sp^3)–H azidation methodologies using hypervalent iodine reagent[35–37] and transition metal catalysis.[38–41] As a continuation of this research program, we report herein our studies on the copper- and iron-catalyzed C(sp^3)–H azidation reaction including attempts on the development of catalytic enantioselective process (*Scheme 2*).

Results and Discussion

Copper Catalysis

At the outset of our research, hypervalent iodine reagents were used as an azide source in most of the metal-catalyzed azidation processes.[22–32] Considering the safety issues associated with especially Zhdankin reagent (**2b**),[37] its *in situ* generation was firstly examined. Gratifyingly, reaction of 6-methoxy-1,2,3,4-tetrahydronaphthalene (**4a**) with 1-acetoxy-1,2-benziodoxol-3-(1*H*)-one (AcOBX **6**) (*Figure 1*) and $TMSN_3$[14] in the presence of CuI (20 mol%) afforded indeed the azidation product **5a** in 42% yield (*Table 1*, entry 1). The use of iodine (III) reagent (AcOBX **6**) can be avoided as azide **5a** was obtained in a similar yield by replacing AcOBX with 2-iodobenzoic acid and *m*CPBA (entry 2). It was subsequently found that formation of a hypervalent iodine reagent was not required for this transformation as a better yield of **5a** was obtained in the absence of 2-iodobenzoic acid (entry 3). A slightly higher yield of **5a** was obtained using NFSI as oxidant and $Cu(OTf)_2$ (5.0 mol%) as catalyst (entry 4).

The catalytic enantioselective version of this azidation process was briefly investigated. Whereas the reaction of **4a** with $TMSN_3$ was shut down with chiral



Scheme 2. This work: Cu- and Fe-catalyzed benzylic C(sp^3)–H azidation.

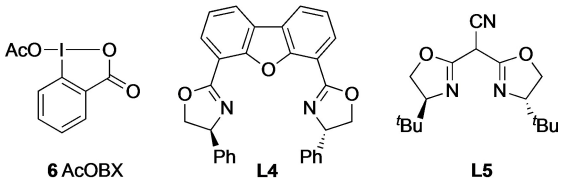
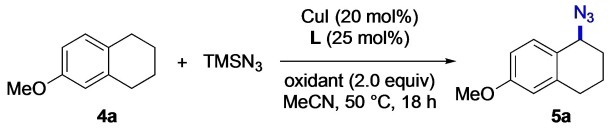


Figure 1. Structures of hypervalent iodine reagent and ligands.

Table 1. Preliminary studies on the copper-catalyzed azidation of **4a**.[a]



4a 5a

Entry	Oxidant	Ligand	Yield (%)[b]	ee (%)
1	AcOBX (**6**)	/	42	n.d.
2	2-iodobenzoic acid/ *m*CPBA	/	37	n.d.
3	*m*CPBA	/	49 (47)[c]	n.d.
4	NFSI[d]	/	51 (52)[c]	n.d.
5[e]	*m*CPBA	**L4**	<5	n.d.
6[e]	*m*CPBA	**L5**	38[c]	0

[a] Reaction conditions: **4a** (0.4 mmol), $TMSN_3$ (2.0 equiv), oxidant (2.0 equiv), CuI (20 mol%), ligand (25 mol%), MeCN (*c* 0.1 M). [b] Determined by ^{1}H-NMR using mesitylene as internal standard. [c] Isolated yield. [d] $Cu(OTf)_2$ (5 mol%) was used as catalyst. [e] The reaction was performed at 0.1 mmol scale. Enantiomeric excess was determined by HPLC on chiral stationary phase. AcOBX = 1-acetoxy-1,2-benziodoxo-3-[1*H*]-one; *m*CPBA = *meta*-chloroperbenzoic acid; NFSI = *N*-fluorobenzenesulfonimide.

Table 2. Survey of reaction conditions for iron-catalyzed azidation of **4b**.[a]

4b 5b

Entry	$Fe(OTf)_3$	Oxidant (equiv)	%Yield[b]
1	0.2 equiv	$(tBuO)_2$ (3.0)	18[b]
2	0.1 equiv	$(tBuO)_2$ (3.0)	20[b]
3	0.1 equiv	BzO*t*Bu (3.0)	27[b]
4	0.1 equiv	*t*BuOOH in decane (3.0)	28[b]
5	0.1 equiv	Cumene hydroperoxide (3.0)	27[b]
6	0.1 equiv	Dicumyl peroxide (3.0)	37[b]
7	0.1 equiv	$(BzO)_2$ (3.0)	44[c]
8	0.05 equiv	$(BzO)_2$ (3.0)	55[c]
9	0.025 equiv	$(BzO)_2$ (3.0)	45
10	0.05 equiv	Selectfluor (3.0)	36[c,d]
11	0.05 equiv	$C_5H_5N^+F\cdot BF_4$ (3.0)	0
12	**0.05 equiv**	**NFSI (2.0)**	**79**[c]

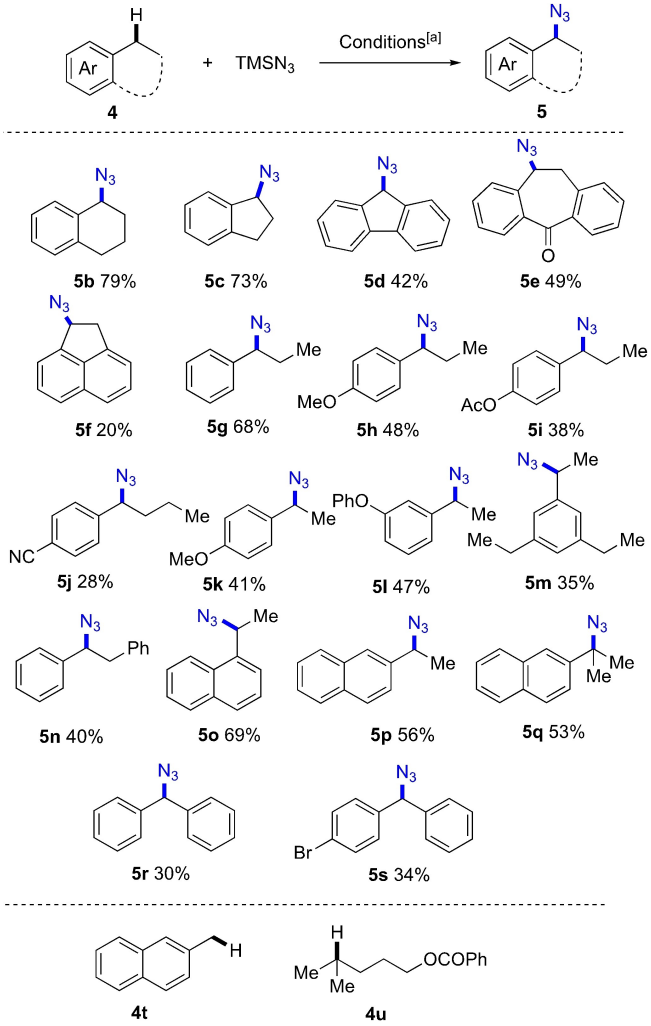
[a] Reaction conditions: **4b** (0.08 mmol), $Fe(OTf)_3$ (0.025–0.2 equiv), $TMSN_3$ (3.0 equiv), oxidant (2.0–3.0 equiv) in MeCN (*c* 0.1 M) at 50 °C for 24 h under nitrogen atmosphere. [b] Determined by ^{1}H-NMR using 1,3,5-trimethoxybenzene as internal standard. [c] Isolated yield. [d] Reaction was completed in 7 h. Selectfluor = 1-(chloromethyl)-4-fluoro-1,4-diazabicyclo[2.2.2]octane bis(tetrafluoroborate); $C_5H_5N^+F\cdot BF_4$ = *N*-fluoropyridinium tetrafluoroborate.

tridentate dibenzofuran-4,6-bis(oxazoline) (DBFOX) ligand **L4** (entry 5), the same reaction performed in the presence of bisoxazoline **L5** afforded **5a** in 38% yield. However, the obtained product in both cases was racemic. While the work was in progress, the Stahl group reported a highly efficient C–H benzylic azidation protocol using NFSI as an oxidant.[32] They also observed that only racemic products were formed in the presence of a diverse set of chiral ligands and provided detailed mechanistic studies that could account for these results. Consequently, we stopped our efforts in this direction.

Iron Catalysis

The reaction of tetralin **4b** with $TMSN_3$ was chosen as a test reaction. Initial screening of the iron salts and the solvents[42] using *tert*-butyl peroxide (3.0 equiv) as oxidant indicated that $Fe(OTf)_3$ (0.2 equiv) in MeCN at 50 °C can indeed catalyze the conversion of **4b** to **5b**, albeit with a low yield (*Table 2*, entry 1, for details, see *Supporting Information*). Conditions were therefore further fine-tuned varying the loading of the catalyst and the oxidants. A similar yield of **5b** was obtained when the loading of $Fe(OTf)_3$ was reduced to 0.1 equiv. (entry 2). Among other peroxides examined (entries 3–7), benzoyl peroxide afforded the best yield of **5b** (entry 7) and a loading of 0.05 equiv. of $Fe(OTf)_3$ was found to be optimum (entries 7–9). Subsequent survey of oxidants showed that Selectfluor was also a competent oxidant (entry 10), while *N*-fluoropyridinium tetrafluoroborate failed to promote the reaction (entry 11). Finally, NFSI was found to be the most effective oxidant for the desired transformation (entry 12). Overall, the optimum conditions consisted of performing the reaction of **4b** with $TMSN_3$ in the presence of $Fe(OTf)_3$ (0.05 equiv) and NFSI in MeCN at 50 °C. Under these conditions **4b** was converted to **5b** in 79% isolated yield. The formation of 1,4-diazidotetralin was merely detectable under these conditions.

With optimum conditions in hand, the scope of this benzylic C(sp^3)–H azidation was explored (*Scheme 3*). Like tetralin, indane was efficiently transformed to azide **5c** in 73% yield. 9*H*-Fluorene and dibenzosuberone were converted to the corresponding azido derivatives **5d** and **5e** in yields of 42% and 49%, respectively. However, azidation of acenaphthene furnished **5f** in only 20% yield at 75% conversion. We noted that the azidation of dibenzosuberone proceeded cleanly and the moderate yield was due to the

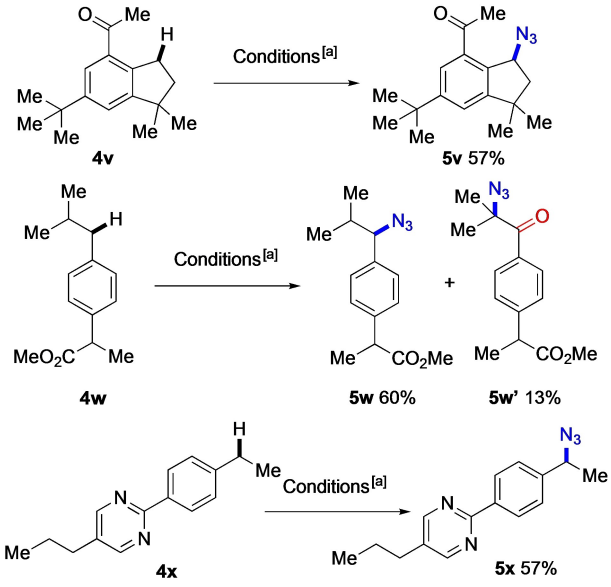


Scheme 3. Reaction scope. [a] Standard conditions: **4** (0.1 mmol), $Fe(OTf)_3$ (0.05 equiv), $TMSN_3$ (3.0–5.0 equiv), NFSI (2.0 equiv) in MeCN (*c* 0.1 M) at 50 °C.

low conversion under standard conditions (50% conversion for 49% of **5e**). Different alkylarenes were next examined. Propylbenzene was transformed to (1-azidopropyl)benzene (**5g**) in 68% yield. The reaction was found to be sensitive to the electronic nature of the arene as the presence of both electron-donating and electron-withdrawing groups in the aromatic ring reduced the reaction efficiency (**5h**–**5l**). While the low conversion accounted for the low yield of **5j** (30% conversion for 28% yield of **5j**), decomposition of starting materials was observed in the case of electron-rich aromatic compounds. Monoazidation took place with 1,3,5-triethylbenzene and 1,2-diphenylethane furnishing azides **5m** and **5n**, respectively, in moderate yields. Both 1-ethylnaphthalene and 2-ethylnaphthalene participated in the reaction with the former providing noticeable higher yield of the azidation product than the latter (**5o** *vs* **5p**). A tertiary benzylic C(sp^3)–H bond took part in the reaction giving the azide **5q** in 53%. Finally, diphenylmethanes with lower BDE of benzylic C(sp^3)–H bond (82 kcal/mol) afforded the products in only moderate yields (**5r**, **5s**). Interestingly, 2-methylnaphthalene (**4t**) and 4-methylpentyl benzoate (**4u**) were unreactive under the optimized conditions indicating the possibility of selective functionalization of secondary/tertiary C-(sp^3)–H benzylic bond in the presence of the primary benzylic C–H and aliphatic tertiary C–H bonds.

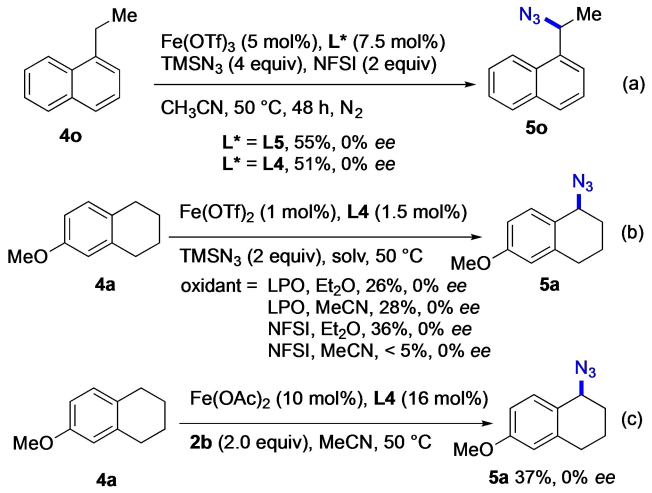
Examples of chemo- and regio-selective azidation are depicted in *Scheme 4*. Celestolide (**4v**), a polysubstituted indane used as a musk in the fragrance industry, underwent selective azidation at benzylic position to produce azido derivative **5v** in 57% yield. The methyl ketone motif remained untouched. Ibuprofen methyl ester (**4w**) was preferably azidated on the most electron-rich benzylic position, at the expense of the other one α to the ester function, to afford **5w** in 60% yield. Interestingly, a minor product **5w'** resulting from the azidation of the tertiary C(sp^3)–H bond followed by oxidation of the benzylic position was isolated along with the expected azide **5w**. Finally, selective azidation of 2-(4-ethylphenyl)-5-propylpyrimidine (**4x**) furnished the product **5x** in 57% yield.

Catalytic enantioselective azidation was next examined using 1-ethylnaphthalene (**4o**) as a test substrate.



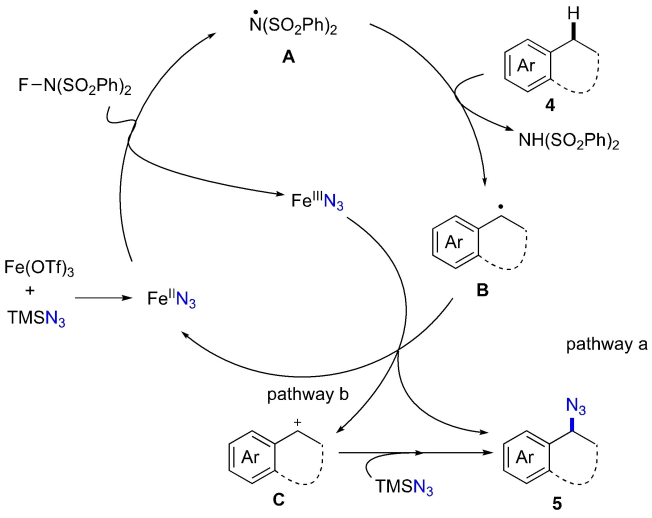
Scheme 4. Chemo- and regio-selective benzylic C(sp^3)–H azidation. [a] Standard conditions: **4v-x** (0.1 mmol), $Fe(OTf)_3$ (0.05 equiv), $TMSN_3$ (4.0 equiv), NFSI (2.0 equiv) in MeCN (*c* 0.1 M) at 50 °C.

While the reaction occurred in the presence of ligand **L5** or **L4** to afford product **5o** in the yields of 55% and 51%, respectively, the product obtained in both cases was unfortunately racemic (*Scheme 5a*). It is interesting to note that Bao and co-workers have successfully developed efficient decarboxylative C(sp^3)–H azidation of benzylic peresters[43] and amidoazidation of styrene derivatives[44,45] employing this family of ligands. We therefore briefly examined the conditions reported in their work using **4a** as a test substrate in the presence of $Fe(OTf)_2$ (1.0 mol%) and ligand **L4** (1.5 mol%). With lauroyl peroxide (LPO) as oxidant in Et_2O or MeCN, racemic **5a** was formed in yields of 26% and 28%, respectively (*Scheme 5b*). Using NFSI as oxidant, the same reaction took place in Et_2O affording **5a** in 36% yield, but again in a racemic form. However, only a trace amount of **5a** was formed when the reaction was performed in MeCN. Finally, slightly modified conditions of Hartwig and co-workers[28] were applied to **4a** by replacing the PyBOX ligand **L2** with DBFOX ligand **L4** (*Scheme 5c*). Compound **5a** was formed in 37% yield, but again in a racemic form.



Scheme 5. Attempts on catalytic enantioselective azidation of **4a** and **4o**.

Control experiments were conducted to gain insight on the reaction mechanism. No reaction occurred between **4b** and $TMSN_3$ in the absence of NFSI under otherwise standard conditions. However, the reaction did take place without $Fe(OTf)_3$, albeit in a much reduced yield (39% vs 79% under standard conditions). On the basis of our experimental observation and literature precedents, a possible reaction pathway similar to the one proposed by Hartwig and co-workers[29] is shown in *Scheme 6*. *In situ* generation of Fe^{II} species followed by single electron transfer (SET) with NFSI would afford bis-sulfonylamidyl radical **A** with concurrent generation of Fe^{III} species. Intermolecular HAT between **A** and substrate **4** would provide the benzylic radical **B** which could react with $Fe^{III}N_3$ *via* out-sphere transfer of the azido group to afford the observed product **5** with concurrent generation of Fe^{II} species completing therefore the catalytic cycle (pathway a). Alternatively, radical **B** could be further oxidized by Fe^{III} to generate the benzylic cation **C** and the Fe^{II} species. An off-cycle trapping of carbocation **C** by azide would then furnish the product **5**.



Scheme 6. Possible reaction pathways.

Conclusions

In summary, we developed copper- and iron-catalyzed C(sp^3)–H benzylic azidation reactions using *m*CPBA and NFSI as oxidant, respectively, and $TMSN_3$ as azide source. The difficulties encountered in rendering this reaction enantioselective is in sharp contrast to the metal-catalyzed asymmetric cyanation of radical intermediates.[46,47] The latter transformation is known to readily undergo inner-sphere cyanide transfer, facilitating therefore chirality transfer from the ligand (catalyst) to the substrate.

Experimental Section

General Procedure for the Cu-Catalyzed Azidation

In an oven-dried vial, CuI (20 mol%) and the ligand (25 mol%) were dissolved in CH_3CN (0.1 M) under a nitrogen atmosphere, and the mixture was stirred at 21 °C for 30 minutes. Then, the benzylic substrates **4**

(0.4 mmol, 1 equiv), oxidant (2 equiv) and $TMSN_3$ (2 equiv) were sequentially added. The reaction mixture was stirred at 50 °C for 18 h. The reaction mixture was filtered through silica and celite and evaporated under reduced pressure. The residue was purified by column chromatography (SiO_2, pentane:EtOAc = 99:1 to 95:5) to afford the benzylic azide **5**.

General Procedure for the Fe-Catalyzed Azidation

In a nitrogen-filled glovebox, $Fe(OTf)_3$ (0.05 equiv), NFSI (2 equiv), and the corresponding substrate **4** (0.1 mmol) were combined in an oven-dried vial. The vial was sealed with a Teflon cap and brought out of the glovebox without solvent. Dry acetonitrile (0.1 M) was added to the reaction mixture under N_2, followed by $TMSN_3$ (3.0–5.0 equiv). The reaction mixture was stirred at 50 °C for 24–96 h, followed by filtration through a small amount of silica with ethyl acetate. The solvent was then evaporated, leaving a residue that was purified using hexane/ethyl acetate on a silica gel column chromatography to obtain the corresponding benzylic azide **5**.

Author Contribution Statement

A.R.-G., R.O.T.-O., P.P., R.S.-D., Q.W., J.W. and J.Z. conceived and designed the experiments. A.R.-G., R.O.T.-O., P.P. and R.S.-D. carried out the experiments. A.R.-G., R.O.T.-O., P.P., Q.W., J.W. and J.Z. interpreted the results and co-wrote the paper. All authors have given approval to the final version of the manuscript.

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Data Availability Statement

The data that support the findings of this study are available in the supplementary material of this article. The original word file of the *Supporting Information* is available on zenodo (DOI: https://doi.org/10.5281/zenodo.10620282). The authors have cited additional references within the *Supporting Information* (Ref [48–64]).

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Supporting information

1. General information

All reagents were purchased from commercial sources (Aldrich, Acros, Merck, Combi-blocks, TCI, Fluorochem, Fluka, and VWR International) and were used as received unless otherwise noted. Sensitive compounds were stored in a desiccator or glove box if required. The glassware used for the preparation and handling of air-sensitive materials was dried overnight in an oven (T > 150 °C) or under vacuum with a heat gun (T > 200 °C). When solvents are indicated as dry, they were either purchased as such, distilled prior to use, or were dried by a passage through a column of anhydrous alumina or copper using a Puresolv MD 5 from Innovative Technology Inc., based on Grubb's design.[1] Flash column chromatography was carried out with Silicycle P60 silica: 230–400 mesh (40-63 µm) silica.

NMR spectra were recorded at room temperature on Bruker AvanceIII-400, Bruker Avance-400, or Bruker DPX-400 spectrometer. ^{1}H frequency was at 400.13 MHz, and ^{13}C frequency was at 100.62 MHz. Chemical shifts (δ) were reported in parts per million (ppm) relative to residual solvent peaks rounded to the nearest 0.01 MHz for proton and 0.1 MHz for carbon (ref: $CHCl_3$ [^{1}H: 7.26 ppm, ^{13}C: 77.16 ppm]; DMSO-d_6: [^{1}H: 2.50 ppm, ^{13}C: 39.52 ppm]). Coupling constants (*J*) were reported in Hz to the nearest 0.1 Hz. Peak multiplicity was indicated as follows: s (singlet), d (doublet), t (triplet), q (quartet), quint (quintet), sext (sextet), sept (septet), m (multiplet), and br (broad). The attribution of peaks was done using the multiplicities and integrals of the peaks. High-resolution mass spectrometric measurements were performed by the mass spectrometry service of ISIC at the EPFL. IR spectra were recorded on an Alpha-P Bruker FT-IR Spectrometer, and absorbance frequencies are reported in reciprocal centimeters (cm^{-1}).

Reactions were monitored by TLC and visualized by a dual short wave/long wave UV lamp and stained with an ethanolic solution of vanillin, *p*-anisaldehyde, phosphomolybdic acid, or with a basic solution of potassium permanganate.

NMR yields were determined using 1,3,5-trimethoxybenzene, and mesitylene as external standards.

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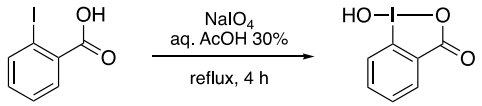
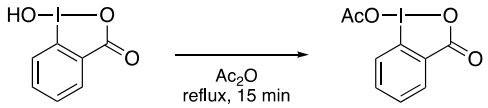
2. Exploration of the copper-catalyzed azidation

2.1 Synthesis of starting materials and ligands



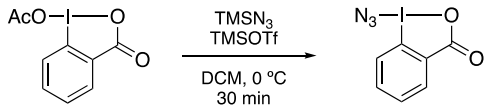
S2 **S2**

1-Hydroxy-1,2-benziodoxol-3(1*H*)-one (S2). Following a reported procedure,[2] $NaIO_4$ (18.1 g, 84.7 mmol, 1.05 equiv) and 2-iodobenzoic acid **S1** (20.0 g, 80.6 mmol, 1 equiv) were suspended in a mixture of AcOH (36 mL) and water (84 mL). The mixture was vigorously stirred and refluxed for 4 h. The reaction mixture was then diluted with cold water (100 mL) and allowed to cool to 21 °C protected from light. The crude product was collected by filtration, washed on the filter with ice water (3 x 50 mL) and acetone (3 x 50 mL), and air-dried in the dark to give the pure product **S2** (19.4 g, 73.6 mmol, 91%) as a white solid. **^{1}H NMR** (DMSO-d_6, 400 MHz) δ 8.02 (d, *J* = 1.5 Hz, 1H), 8.01-7.93 (m, 1H), 7.84 (dd, *J* = 8.2, 1.1 Hz, 1H), 7.70 (td, *J* = 7.4, 1.1 Hz, 1H). **^{13}C NMR** (DMSO-d_6, 100 MHz): δ 167.7, 134.5, 131.5, 131.1, 130.4, 126.3, 120.4. Spectroscopic data was consistent with the values reported in the literature.



S2 **6**

1-Acetoxy-1,2-benziodoxol-3-(1*H*)-one (AcOBX, 6). Following a reported procedure,[3] a suspension of **S2** (5.0 g, 19 mmol, 1 equiv) in acetic anhydride (19 mL) was refluxed until total dissolution (≈ 15 min). The resulting clear solution was allowed to cool to room temperature and then cooled to 5 °C in the fridge. The white crystals were filtered, washed with pentane (3 x 30 mL), and dried under reduced pressure to afford 1-acetoxy-1,2-benziodoxol-3-(1*H*)-one **6** (5.0 g, 16 mmol, 86%) as a white solid. **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 8.26 (dd, *J* = 7.6, 1.6 Hz, 1H), 8.01 (dd, *J* = 8.1, 0.9 Hz, 1H), 7.96-7.90 (m, 1H), 7.72 (td, *J* = 7.4, 1.0 Hz, 1H), 2.26 (s, 3H). **^{13}C NMR** ($CDCl_3$, 100 MHz): δ 176.5, 168.2, 136.2, 133.3, 131.4, 129.4, 129.1, 118.4, 20.4. Spectroscopic data was consistent with the values reported in the literature.[4]

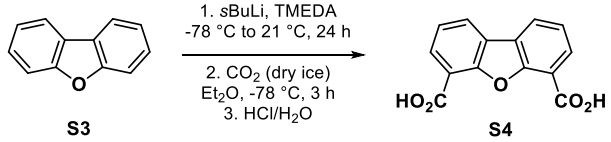


6 **2b**

Caution: For safety reasons, the reaction and work-up were carried out behind an anti-blast shield with explosion-proof gloves!

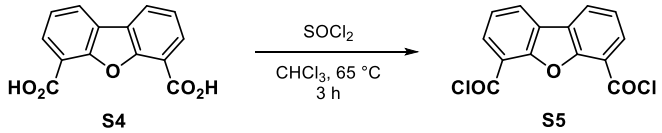
[2] Kraszkiewicz, L.; Skulski, L. *Arkivoc* **2003**, *2003*, 120.
[3] Grenet, E.; Waser, J. *Org. Lett.* **2018**, *20*, 1473.
[4] Bertho, S.; Rey-Rodriguez, R.; Colas, C.; Retailleau, P.; Gillaizeau, I. *Chem. Eur. J.* **2017**, *23*, 17674.

Azidobenziodoxolone (ABX, 2b). Following a reported procedure,[5] acetatebenziodoxolone **6** (AcOBX) (0.31 g, 1.0 mmol, 1 equiv) was dissolved in dry dichloromethane (2 mL). To the solution cooled down to 0 °C using an ice bath, $TMSN_3$ (0.20 mL, 1.5 mmol, 1.5 equiv) was added dropwise followed by one drop of trimethylsilyl trifluoromethanesulfonate (ca. 0.9 µL, 5.0 µmol, 5 mol%) and the resulting mixture was stirred for 30 minutes at 0 °C under a nitrogen atmosphere. Pentane (12 mL) was added, and the suspension was vigorously stirred for 10 minutes. The solid was then filtered, washed with pentane, and dried for 15 minutes on the frit under air. Azidobenziodoxolone (ABX, **2b**) (0.30 g, 0.99 mmol, 99%) was obtained as a pale-yellow solid. **^{1}H NMR** (DMSO-d_6, 400 MHz) δ 8.02 (dd, *J* = 7.7, 1.4 Hz, 1H), 7.97 (m, 1H), 7.85 (dd, *J*= 8.2, 0.7 Hz, 1H), 7.71 (td, *J* = 7.6, 1.2 Hz, 1H). **^{13}C NMR** (DMSO-d_6, 101 MHz) δ 167.7, 134.5, 131.5, 131.1, 130.4, 126.3,120.4. Spectroscopic data was consistent with the values reported in the literature.



S3 S4

Dibenzofuran-4,6-dicarboxylic acid (S4). Following the reported procedure,[6] *N,N,N′,N′*-tetramethylethane-1,2-diamine (5.30 mL, 35.3 mmol, 3 equiv) was added to a solution of dibenzofuran **S3** (2.00 g, 11.8 mmol, 1 equiv) in anhydrous ether (80.0 mL) under nitrogen and the mixture was cooled at -78 °C. *s*BuLi (25.2 mL, 35.3 mmol, 1.40 M, 3 equiv) was added to this cooled mixture dropwise. The reaction mixture was then stirred at 21 °C for 18 h under nitrogen. The reaction mixture was cooled down to -78 °C. CO_2 was bubbled for 4 h at -78 °C using dry ice passing through a drying reagent tube. Then, the reaction mixture was filtrated, and the slight brown precipitate was washed with diethyl ether (3 x 50 mL). The solid was then suspended in distilled water (60 mL) and strongly stirred. 4 N HCl was added dropwise until pH <2. The mixture was stirred for 1 h at room temperature. The mixture was then filtered and washed with water (3 x 20 mL) and diethyl ether (3 x 20 mL). The resulting slightly beige solid was dried under vacuum to afford dibenzofuran-4,6-dicarboxylic acid **S4** (2.69 g, 10.5 mmol, 89% yield) as a white powder. **^{1}H NMR** (DMSO-d_6, 400 MHz) δ 13.28 (s, 2H), 8.47 (dd, *J* = 7.7, 1.4 Hz, 2H), 8.07 (dd, *J* = 7.7, 1.4 Hz, 2H), 7.55 (t, *J* = 7.7 Hz, 2H). **^{13}C NMR** (DMSO-d_6, 101 MHz) δ 165.3, 154.2, 129.9, 125.8, 124.5, 123.3, 116.5. Spectroscopic data was consistent with the values reported in the literature.

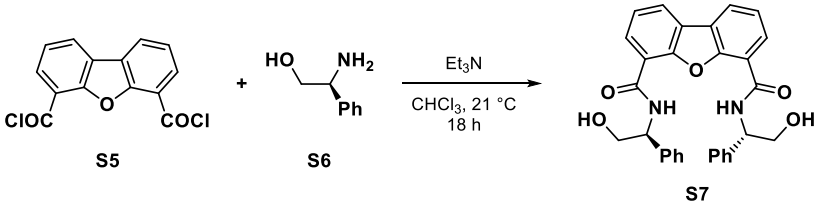


S4 S5

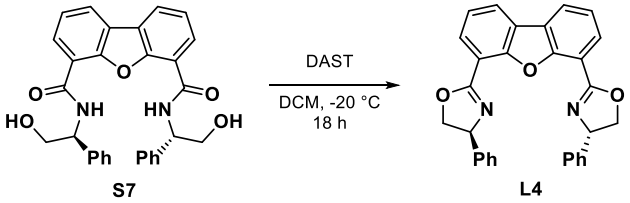
Dibenzofuran-4,6-dicarbonyl dichloride (S5). Following the reported procedure,[6] in an oven-dried vial under nitrogen, dibenzofuran-4,6-dicarboxylic acid **S4** (500 mg, 1.95 mmol, 1 equiv) was dissolved in chloroform (13 mL). Thionyl chloride (4.27 mL, 58.5 mmol, 30 equiv) and one drop of DMF were added. The tube was sealed under nitrogen and the reaction mixture was heated at 65 °C for 7 h. The reaction mixture was cooled down to 25 °C. A white precipitate formed. The mixture was cooled down to 0 °C then rapidly filtered and washed with a small amount of cold chloroform. The white powder was then dried under vacuum to afford dibenzofuran-4,6-dicarbonyl chloride **S5** (478 mg, 1.63 mmol, 84% yield). **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 8.37-8.28 (m, 4H), 7.59 (t, *J* = 7.8 Hz, 2H). **^{13}C NMR** ($CDCl_3$, 101 MHz) δ 163.6, 154.8,

[5] Alazet, S.; Preindl, J.; Simonet-Davin, R.; Nicolai, S.; Nanchen, A.; Meyer, T.; Waser, J. **2018**, *J. Org. Chem.* **2018**, *83*, 12334.
[6] Iserloh, U.; Oderaotoshi, Y.; Kanemasa, S.; Curran, D. P. *Org. Synth.* **2003**, *80*, 46.

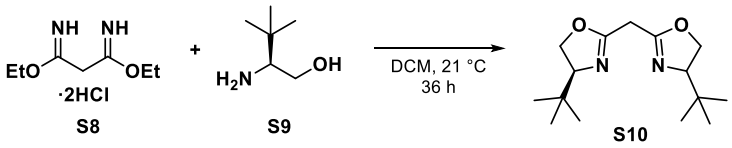
132.8, 127.9, 124.9, 124.1, 119.4. Spectroscopic data was consistent with the values reported in the literature.



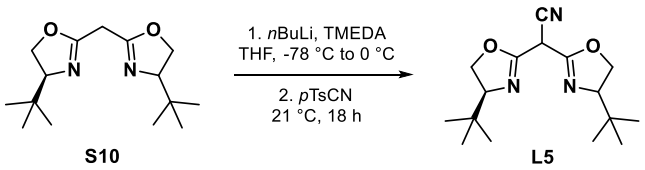
(*S*,*S*)-Dibenzofuran-4,6-dicarboxylic acid bis(2-hydroxy-1-phenylethyl) amide (S7). Following the reported procedure,[6] in an oven-dried vial, dibenzofuran-4,6-dicarbonyl chloride **S5** (500 mg, 1.71 mmol, 1 equiv) was dissolved in chloroform (12 mL) under a nitrogen atmosphere. The suspension was cooled down to 0 °C and a solution of *(2S)*-2-phenylglycinol (531 mg, 3.75 mmol, 2.2 equiv) and triethylamine (0.523 mL, 3.75 mmol, 2.2 equiv) of chloroform (8 mL) was slowly added over 5 minutes. The reaction mixture was then allowed to warm up at 21 °C and stirred for 18 h. Then, 10 mL chloroform and 500 mg of NH_4Cl were added. The suspension was stirred for 1 h and filtered. The residue was washed with chloroform and filtered. The solid residue was triturated in THF for 1 h and then filtered. The filtrate was combined, and solvents were removed under reduced pressure. The crude mixture was purified using column chromatography (SiO_2, DCM:MeOH = 99:1 to 98:2) to afford *(S,S)*-dibenzofuran-4,6-dicarboxylic acid bis(2-hydroxy-1-phenylethyl) amide **S7** (637 mg, 1.29 mmol, 75% yield) as a white solid. **^{1}H NMR** (DMSO-d_6, 400 MHz) δ 8.82 (d, *J* = 8.2 Hz, 2H), 8.39 (dd, *J* = 7.7, 1.3 Hz, 2H), 8.01 (dd, *J* = 7.6, 1.3 Hz, 2H), 7.57 (t, *J* = 7.7 Hz, 2H), 7.52-7.45 (m, 4H), 7.30-7.19 (m, 6H), 5.20 (td, *J* = 7.7, 5.6 Hz, 2H), 4.99 (t, *J* = 5.9 Hz, 2H), 3.81-3.66 (m, 4H). **^{13}C NMR** (DMSO-d_6, 101 MHz) δ 163.3, 152.6, 140.8, 128.2, 127.7, 127.1, 126.9, 124.3, 123.9, 123.5, 119.7, 64.8, 56.0. Spectroscopic data was consistent with the values reported in the literature.



(*S*,*S*)-4,6-Dibenzofurandiyl-2,2'-bis(4-phenyloxazoline) (DBFOX-Ph) L4. Following the reported procedure,[6] in an oven-dried microwave vial, (*S,S*)-dibenzofuran-4,6-dicarboxylic acid bis(2-hydroxy-1-phenylethyl) amide **S7** (500 mg, 1.01 mmol, 1 equiv) was dissolved in DCM (15 mL). The solution was cooled at -20 °C. Then, DAST (0.323 mL, 2.33 mmol, 2.3 equiv) was added slowly and the reaction was stirred for 18 h at -20 °C. 5 mL of 25% aq. NH_3 was added, and the mixture was extracted with DCM (3 x 20 mL). The organic layers were gathered and washed with brine, dried over $MgSO_4$, filtered off and solvents were removed under reduced pressure. The crude was purified using column chromatography (SiO_2, DCM:MeOH = 98:2) to afford (*S*,*S*)-4,6-dibenzofurandiyl-2,2'-bis(4-phenyloxazoline) (DBFOX-Ph) **L4** (410 mg, 0.895 mmol, 89% yield) as a whitish powder. **^{1}H NMR** (DMSO-d_6, 400 MHz) δ 8.46 (dd, *J* = 7.7, 1.3 Hz, 2H), 8.09 (dd, *J* = 7.7, 1.3 Hz, 2H), 7.58 (t, *J* = 7.7 Hz, 2H), 7.46-7.41 (m, 4H), 7.38-7.32 (m, 4H), 7.29-7.24 (m, 2H), 5.55 (dd, *J* = 10.1, 8.3 Hz, 2H), 4.94 (dd, *J* = 10.2, 8.4 Hz, 2H), 4.26 (t, *J* = 8.3 Hz, 2H). **^{13}C NMR** (DMSO-d_6, 101 MHz) δ 160.7, 153.4, 142.8, 128.6, 128.5, 127.21, 126.6, 124.7, 124.5, 123.5, 112.8, 74.3, 69.0. Spectroscopic data was consistent with the values reported in the literature.



Bis((*S*)-4-(*tert*-butyl)-4,5-dihydrooxazol-2-yl)methane (S10). Following the reported procedure,[7] to a solution of diethyl malonimidate dihydrochloride **S8** (500 mg, 2.16 mmol, 1 equiv) in DCM (40 mL) was added (2*S*)-2-amino-3,3-dimethylbutan-1-ol (503 mg, 4.29 mmol, 2 equiv). The resulting cloudy solution was stirred at 21 °C for 36 h. The reaction mixture was diluted with water (50 mL) and extracted with DCM (3 x 30 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, and solvents were removed under reduced pressure. The resulting oily residue was distilled (Kugelrohr distillation, 170 °C at 0.4 mbar) to afford bis((*S*)-4-(*tert*-butyl)-4,5-dihydrooxazol-2-yl)methane **S10** (231 mg, 0.866 mmol, 40% yield) as a white solid. **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 4.20 (dd, *J* = 10.1, 8.7 Hz, 2H), 4.08 (dd, *J* = 8.7, 7.8 Hz, 2H), 3.92-3.83 (m, 2H), 3.34 (t, *J* = 1.2 Hz, 2H), 0.89 (s, 18H). **^{13}C NMR** ($CDCl_3$, 101 MHz) δ 161.6, 76.0, 69.3, 33.8, 28.5, 25.9. Spectroscopic data was consistent with the values reported in the literature.

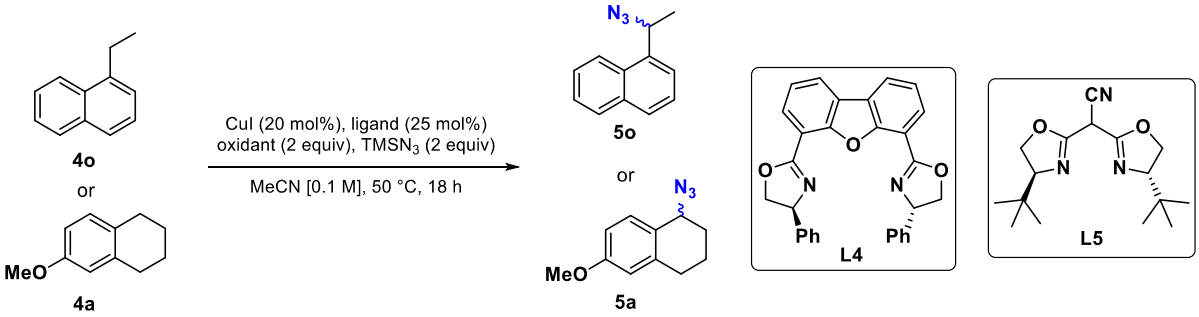


2-((*S*)-4-(*tert*-Butyl)-4,5-dihydrooxazol-2-yl)-2-((*S*)-4-(*tert*-butyl)oxazolidin-2- ylidene)acetonitrile (L5). Following the reported procedure,[8] in an oven-dried microwave tube, bis((*S*)-4-(*tert*-butyl)-4,5-dihydrooxazol-2- yl)methane **S10** (200 mg, 0.751 mmol, 1 equiv) was dissolved in THF (6 mL). The solution was cooled to -78 °C and *n*BuLi (2.50 M in hexanes, 0.450 mL, 1.13 mmol, 1.5 equiv) was slowly added, followed by *N,N,N′,N′*-tetramethylethane-1,2-diamine (0.169 mL, 1.13 mmol, 1.5 equiv). The mixture was stirred at -78 °C for 1 h, then 0 °C for 30 min, then cooled to -78 °C. *p*-Toluenesulfonyl cyanide (204 mg, 1.13 mmol, 1.5 equiv) was then added, and the mixture was allowed to warm at 21 °C and stirred for 15 h. A saturated aqueous NH_4Cl solution was added and stirred for 5 min, then extracted with EtOAc (3 x 20 mL). The organic layers were gathered, washed with brine, dried with $MgSO_4$, and solvents were removed under reduced pressure. The crude was purified by column chromatography (SiO_2, pentane:EtOAc = 8:2 to 6:4) to afford 2-((*S*)-4-(*tert*-butyl)-4,5-dihydrooxazol-2-yl)-2-((*S*)-4-(*tert*-butyl)oxazolidin-2-ylidene)acetonitrile **L5** (152 mg, 0.523 mmol, 70% yield) as a white solid. **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 4.42 (t, *J* = 9.2 Hz, 2H), 4.27 (dd, *J* = 9.0, 6.8 Hz, 2H), 3.87 (dd, *J* = 9.3, 6.9 Hz, 2H), 0.89 (s, 18H). **^{13}C NMR** ($CDCl_3$, 101 MHz) δ 167.3, 117.2, 70.3, 70.2, 33.8, 25.5. Spectroscopic data was consistent with the values reported in the literature.

[7] Pisella, G.; Gagnebin, A.; Waser, J. *Org. Lett.* **2020**, *22*, 3884.
[8] Pezzetta, C.; Bonifazi, D.; Davidson, R. W. M. *Org. Lett.* **2019**, *21*, 8957.

2.2 Study of copper-catalyzed enantioselective benzylic C(sp^3)-H azidation

Table S1 Screening of the conditions



Entry	Substrate	Oxidant	Ligand	Yield (%)[a]	*ee* (%)[b]
1	**4o**	*m*CPBA	/	17[c]	No determined
2	**4o**	*m*CPBA	**L4**	9[c]	No determined
3	**4o**	*m*CPBA	**L5**	1[c]	No determined
4	**4a**	*m*CPBA	/	47	0
5	**4a**	*m*CPBA	**L4**	<5%	No determined
6	**4a**	*m*CPBA	**L5**	38	0
7	**4a**	AcOBX (**6**)	/	42[c]	No determined
8	**4a**	2-Iodobenzoic acid/ *m*CPBA	/	37[c]	No determined
9[d]	**4a**	NFSI	/	52%	No determined

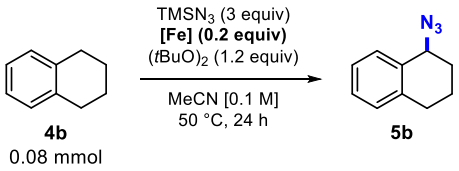
[a]Isolated yield
[b]Enantiomeric excess was determined by HPLC on a chiral stationary phase
[c]Determined by ^{1}H NMR using mesitylene as an internal standard
[d]$Cu(OTf)_2$ (5 mol%) was used as catalyst

General procedure: In an oven-dried vial, CuI (20 mol%) and ligand (25 mol%) were dissolved in CH_3CN (0.1 M) under a nitrogen atmosphere, and the mixture was stirred at 21 °C for 30 minutes. Then, the benzylic substrate **4o** or **4a** (0.4 mmol, 1 equiv), oxidant (2 equiv), $TMSN_3$ (2 equiv) were sequentially added. The reaction mixture was stirred at 50 °C for 18 h. The reaction mixture was filtered through silica and celite and evaporated under reduced pressure. The residue was purified by column chromatography (SiO_2, pentane:EtOAc = 99:1 to 95:5) to afford the benzylic azide.

3. Exploration of the iron-catalyzed azidation

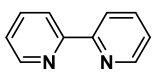
3.1 Optimization of the reaction conditions

Table S2 Selection of the catalyst

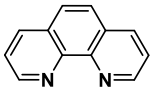


Entry	Ligand	[Fe]	Result
1	-	$Fe(acac)_3$	No reaction
2	**L1S**	$Fe(acac)_3$	No reaction
3	**L2S**	$Fe(acac)_3$	No reaction
4	**L3S**	$Fe(acac)_3$	No reaction
5	-	$Fe(acac)_2$	No reaction
6	**L1S**	$Fe(acac)_2$	No reaction
7	**L2S**	$Fe(acac)_2$	Traces of DP
8	**L3S**	$Fe(acac)_2$	No reaction
9	-	$FeBr_2$	Traces of DP
10	**L1S**	$FeBr_2$	No reaction
11	**L2S**	$FeBr_2$	Traces of DP
12	**L3S**	$FeBr_2$	No reaction
13	-	FeF_3	Traces of DP
14	**L1S**	FeF_3	Traces of DP
15	**L2S**	FeF_3	Traces of DP
16	**L3S**	FeF_3	No reaction
17	-	$Fe(OAc)_2$	No reaction
18	**L1S**	$Fe(OAc)_2$	No reaction
19	**L2S**	$Fe(OAc)_2$	No reaction
20	**L3S**	$Fe(OAc)_2$	No reaction
21	-	$Fe(OTf)_3$	<10% NMR yield Complex mixture, incomplete transformation
22	**L1S**	$Fe(OTf)_3$	Traces of DP
23	**L2S**	$Fe(OTf)_3$	Traces of DP
24	**L3S**	$Fe(OTf)_3$	Traces of DP
25	-	$Fe(OTf)_2$	Traces of DP
26[a]	**-**	**$Fe(OTf)_3$**	**18% NMR yield** Incomplete transformation

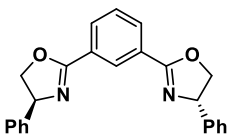
[a]3 equiv of $(tBuO)_2$ were used



L1S

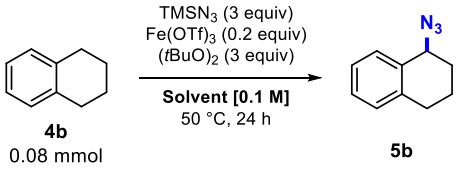


L2S



L3S

Table S3 Selection of the solvent

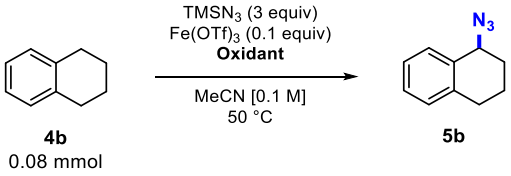


4b
0.08 mmol

5b

Entry	Solvent	Result
1	**MeCN**	**18% NMR yield**
2	DCE	No reaction
3	AcOEt	Traces of DP
4	THF	No reaction
5	1,2-DME	No reaction
6	*t*BuOH	No reaction
7	1,4-Dioxane	No reaction
8	TFE	Traces of DP
9	$MeNO_2$	No reaction
10	PhMe	Traces of DP
11	Acetone	No reaction
12	Et_2O	No reaction

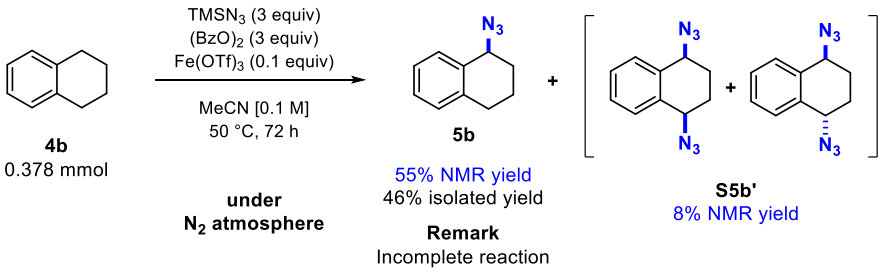
Table S4 Selection of the oxidant



Entry	Variation	NMR yield
1[a]	(tBuO)$_2$ (3 equiv), 24 h	18%
2	(tBuO)$_2$ (3 equiv), 24 h	20%
3	TBHP solution in decane (3 equiv), 24 h	28%
4	BzO-OtBu (3 equiv), 24 h	27%
5	Cumene hydroperoxide (3 equiv), 24 h	27%
6	Dicumyl peroxide (3 equiv), 24 h	37%
7	2,5-Bis(*tert*-butylperoxy)-2,5-dimethylhexane (3 equiv), 24 h (Luperox® 101)	20%
8	**(BzO)$_2$ (3 equiv), 24 h**	**48% (44%[b])**
9	(BzO)$_2$ (1.5 equiv), 24 h	21%
10	(BzO)$_2$ (3 equiv portionwise; 1 equiv/2 h) then 19 h	28%
11	(BzO)$_2$ (3 equiv), 12 h	36%
12	(BzO)$_2$ (5 equiv), 12 h	34%
13	(BzO)$_2$ (3 equiv portionwise; 1 equiv/ 12 h then 36 h	20%
14	(BzO)$_2$ (3 equiv), 12 h, CH_3CN [0.25 M]	44%
15	(BzO)$_2$ (6 equiv), 24 h	22%
16	**(BzO)$_2$ (3 equiv), 72 h**	**55% (46%[c])**

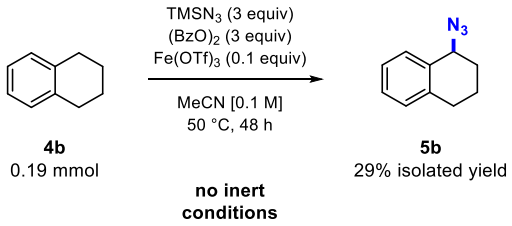
[a]0.2 equiv of Fe(OTf)$_3$ were used
[b]Isolated yield, 0.19 mmol scale, incomplete transformation
[c]Isolated yield, 0.378 mmol scale, incomplete transformation

Under the found conditions at this point, **5b** was synthesized in a **46%** isolated yield. As a remark, the **formation of diazide by-product S5b' was observed** (Scheme S1).

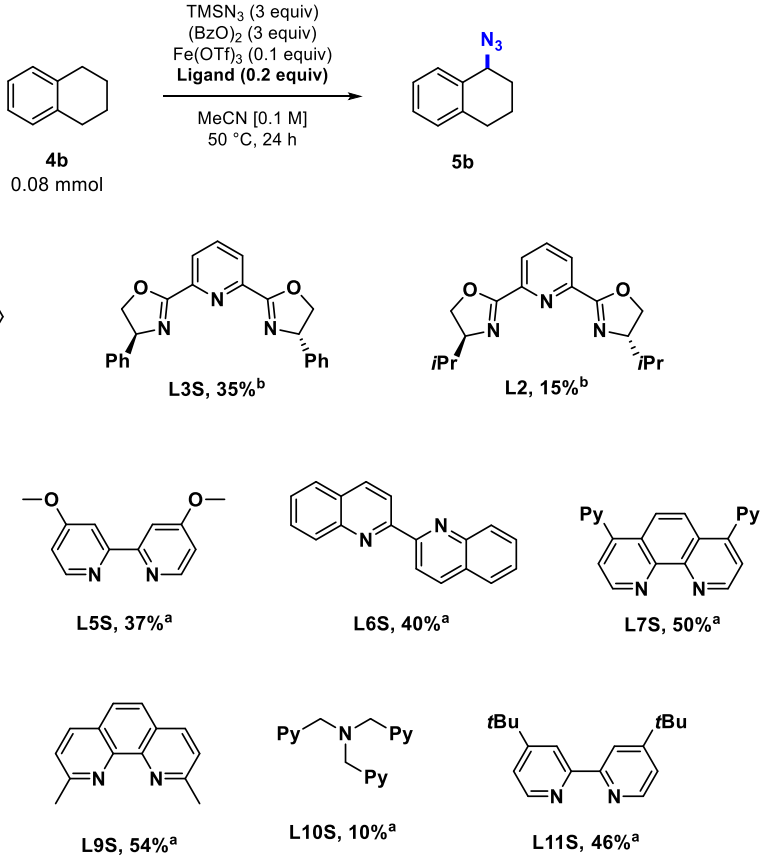


Scheme S1 Reaction performed using 0.378 mmol of **4b** (Table 3, entry 15).

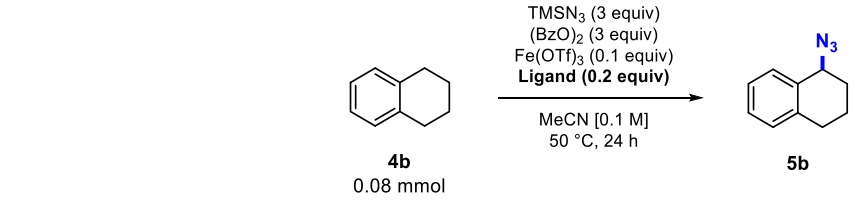
It is important to note that if the reaction is not done under inert conditions, the yield decreases considerably (Scheme S2).



Scheme S2 Reaction performed under air.

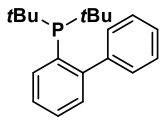


Scheme S3 Evaluation of ligands in the reaction.
([a]NMR yield; [b]Isolated yield)

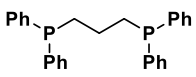


4b
0.08 mmol

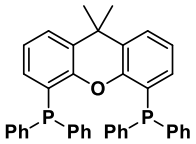
5b



L12S, JohnPhos
34%[a]

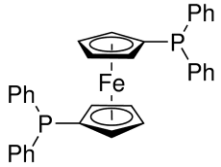


L13S, dppp
49%[a]

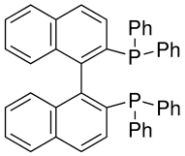


L14S, XantPhos
54%[a]

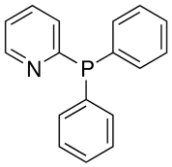
L15S, 57%[a]
48%[b] from
0.19 mmol of SM



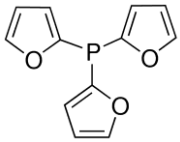
L16S, dppf
47%[a]



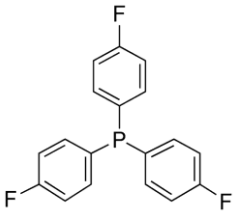
L17S, BINAP
52%[a]



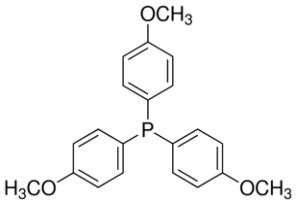
L18S, 56%[a]



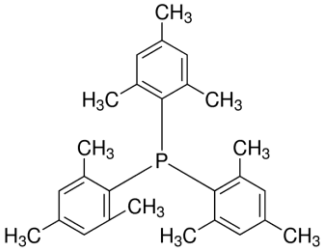
L19S, 49%[a]



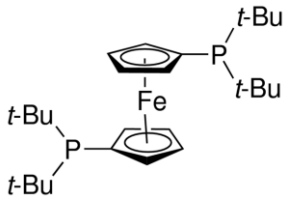
L20S, 47%[a]



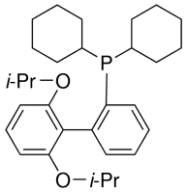
L21S, 56%[a]



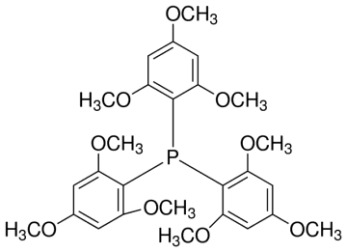
L22S, 48%[a]



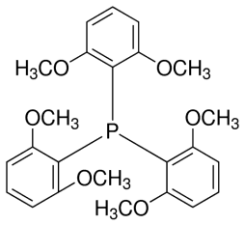
L23S, 40%[a]



L24S, 65%[a]
56%[b] from
0.19 mmol SM



L25S, 63%[a]

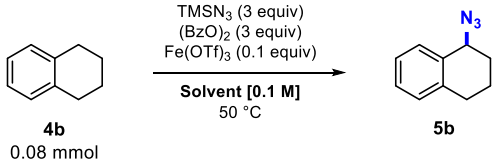


L26S, 50%[a]

Scheme S4 Evaluation of ligands in the reaction (continuation).
([a] NMR yield; [b] Isolated yield)

Even though a higher yield was observed in the presence of phosphine ligands, in a control experiment we observed the complete oxidation of PPh_3 to $O=PPh_3$ under the reaction conditions. So, the next entries were performed without the addition of such a component.

Table S5 Additional modified parameters in the reaction.

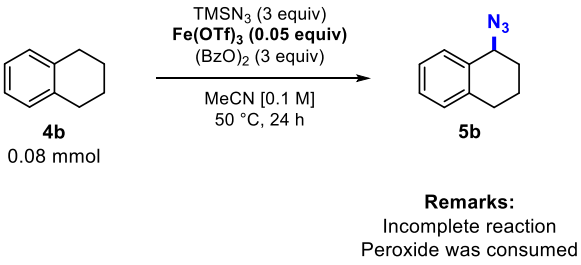


Entry	Variation	NMR yield
1	**MeCN, 72 h**	**55%**
2	Trifluorotoluene, 24 h	54%
3	MeOH:CH_3CN, 24 h	25%
4	Isobutyronitrile, 24 h	50%
5	Benzene, 24 h	39%
6[a]	$Cu(OTf)_2$ (0.1 equiv), MeCN [0.1 M], 24 h	36%

[a]$Fe(OTf)_3$ was not used

A better yield was obtained using only 0.05 equiv of $Fe(OTf)_3$ (Table S6). **Note:** Full conversion was not reached in any of those experiments.

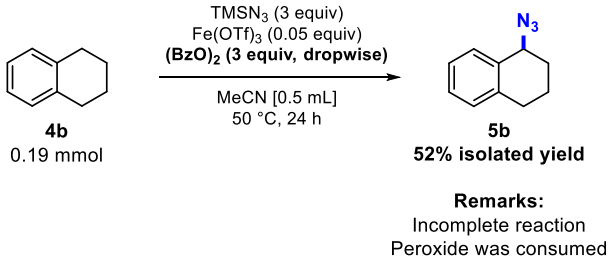
Table S6 Catalyst loading exploration.



Entry	Catalyst loading / time	Result
1	0.1 equiv, 72 h	55% (46%[a])
2	0.1 equiv, 24 h	48% (44%[b])
3	**0.05 equiv, 24 h**	**59% (55%[b])**
4	0.025 equiv, 24 h	45%[c]

[a]Isolated yield, 0.378 mmol scale
[b]Isolated yield, 0.19 mmol scale
[c]Determined by ^1H NMR using 1,3,5-trimethoxybenzene as an internal standard

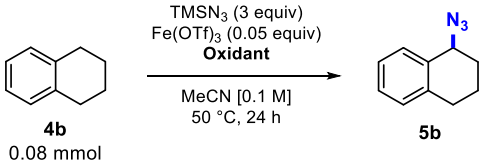
A solution of 3 equiv of $(BzO)_2$ in 2.0 mL of MeCN was added dropwise during 9 h at 50 °C, then the reaction was stirred overnight at the same temperature (24h in total). The slow addition of the peroxide did not improve the yield (Scheme S5).

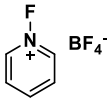


Scheme S5 Reaction performed adding the oxidant dropwise.

In the previous experiment, it was noticed that $(BzO)_2$ degraded quickly, a factor which might affect not reaching the full conversion. To avoid such an issue, additional oxidants were evaluated (Table S7).

Table S7 Evaluation of other oxidants.

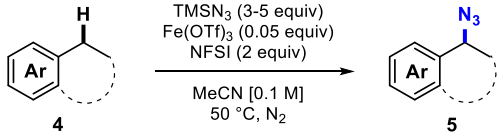


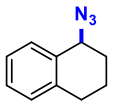
Entry	Oxidant/Variation	Result
1[a]	**NFSI (2 equiv)**	**79% isolated yield, full conversion**
2	NFSI (2 equiv) without $Fe(OTf)_3$	39% NMR yield, not full conversion
3	NFSI (1 equiv)	26% NMR yield, not full conversion
4	NFSI (1.5 equiv)	58% NMR yield, not full conversion
5	Selectfluor™ (2 equiv), 7 h	36% NMR yield, full conversion
6	Selectfluor™ (1 equiv) without $Fe(OTf)_3$, 24 h	58% NMR yield, full conversion
7	**Selectfluor™ (2 equiv), without $Fe(OTf)_3$, 1 h**	**55% isolated yield, full conversion**
8	$K_2S_2O_8$ (2 equiv)	Traces of DP
9	 (2 equiv)	No reaction
10	**NFSI (2 equiv), rt, 48 h**	Traces of DP

[a]0.19 mmol scale

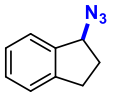
With the optimized conditions in hand, the scope was explored (**Scheme S6**). In most cases, the reaction was clean. The main observed issue in several experiments was the incomplete conversion despite either extending the reaction time or adding more equivalents of $TMSN_3$.

3.2 Reaction scope



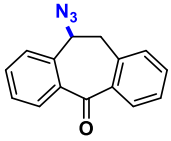


5b, 79%
24 h, 3 equiv $TMSN_3$
full conversion



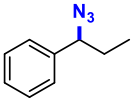
5c, 73%
48 h, 5 equiv $TMSN_3$
full conversion

5d, 42%
48 h, 3 equiv $TMSN_3$
62% conversion

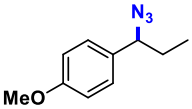


5e, 49%
48 h, 4 equiv $TMSN_3$
50% conversion

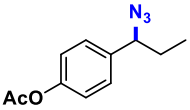
5f, 20%
72 h, 3 equiv $TMSN_3$
75% conversion



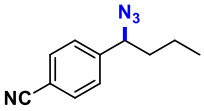
5g, 68%
48 h, 3 equiv $TMSN_3$
full conversion



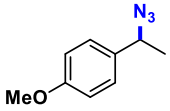
5h, 48%
72 h, 4 equiv $TMSN_3$
88% conversion



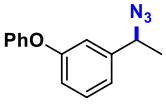
5i, 38%
72 h, 4 equiv $TMSN_3$
62% conversion



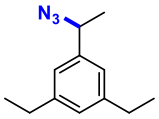
5j, 28%
48 h, 5 equiv $TMSN_3$
30% conversion



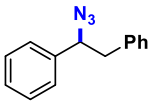
5k, 41%
96 h, 3 equiv $TMSN_3$
85% conversion



5l, 47%
72 h, 4 equiv $TMSN_3$
46% conversion

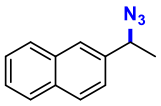


5m, 35%
24 h, 3 equiv $TMSN_3$
full conversion

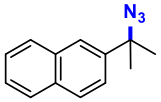


5n, 40%
48 h, 3 equiv $TMSN_3$
64% conversion

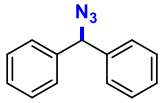
5o, 69%
48 h, 5 equiv $TMSN_3$
70% conversion



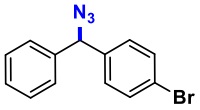
5p, 56%
48 h, 5 equiv $TMSN_3$
55% conversion



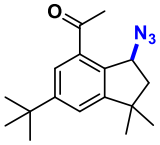
5q, 53%
48 h, 3 equiv $TMSN_3$
92% conversion



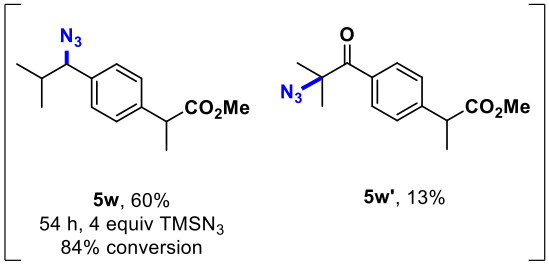
5r, 30%
72 h, 3 equiv $TMSN_3$
52% conversion



5s, 34%,
48 h, 4 equiv $TMSN_3$
72% conversion

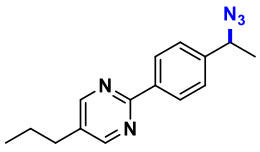


5v, 57%
48 h, 4 equiv $TMSN_3$
full conversion



5w, 60%
54 h, 4 equiv $TMSN_3$
84% conversion

5w', 13%

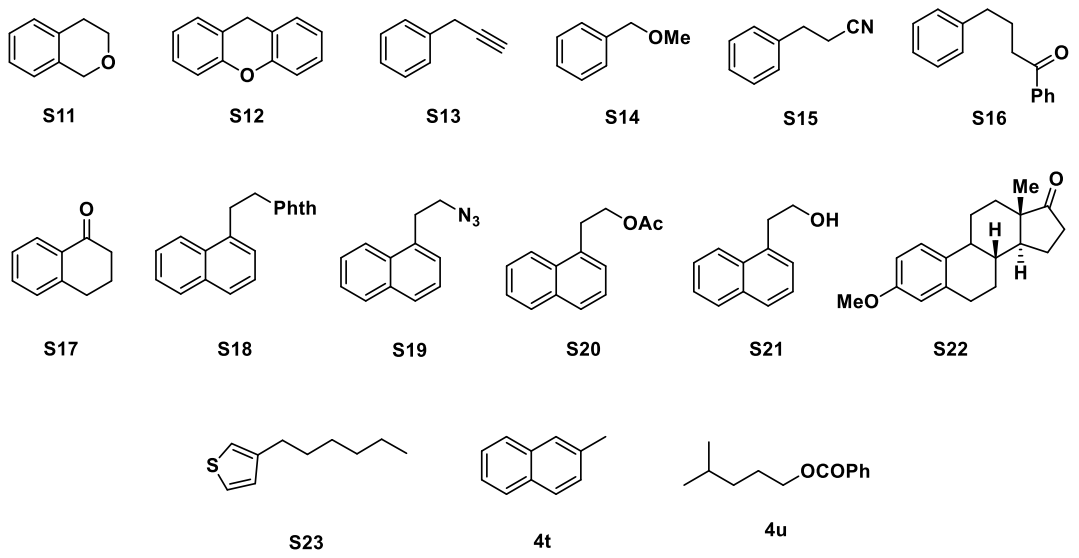


5x, 57%
48 h, 4 equiv $TMSN_3$
full conversion

Scheme **S6** Reaction scope of the iron-catalyzed azidation.

3.3 Failed substrates

List of substrates failed to undergo the azidation reaction (Scheme S7).

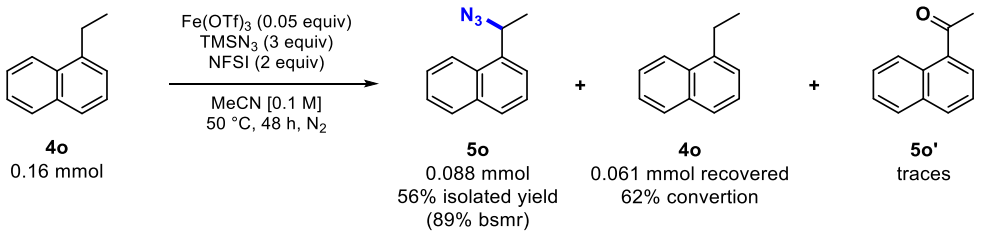


Scheme **S7** Failed substrates.

3.4 Reaction re-optimization using substrate 4o

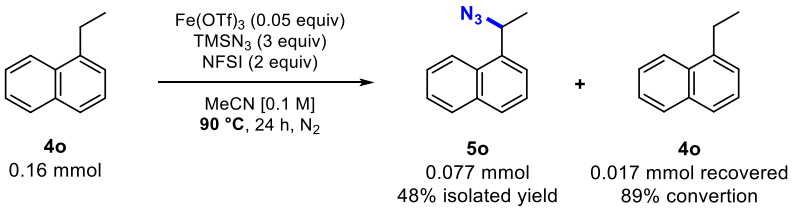
Since the main observed issue in the reaction corresponded to not reaching the full conversion, additional efforts were made to induce the complete consumption of the substrate.

Since azidation of 1-ethylnaphthalene **4o** under aforementioned conditions afforded the desired product cleanly but with moderate conversion (Scheme S8), it was chosen as substrate for further optimization.



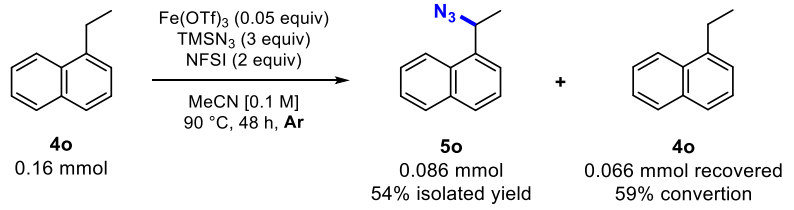
Scheme S8 Reaction products using the optimized conditions.

An increase in the temperature of the reaction did not improve the yield despite observing a higher conversion (Scheme S9).



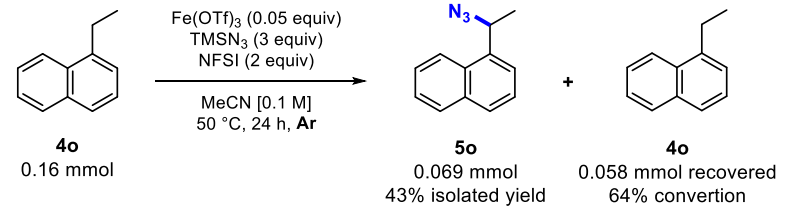
Scheme S9 Reaction performed at 90 °C.

The use of argon instead of nitrogen as inert atmosphere did not improve both the yield and the conversion (Scheme S10).



Scheme S10 Reaction performed under argon atmosphere.

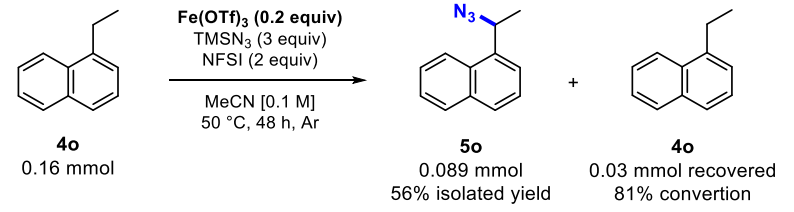
The dropwise addition of the oxidant in a period of 9 h did not enhance the yield and afforded a complex mixture (Scheme S11).



Remark: NFSI was dissolved in 1 mL of MeCN, then added dropwise in 9 h at 50 °C. The reaction was stirred at same temperature overnight.

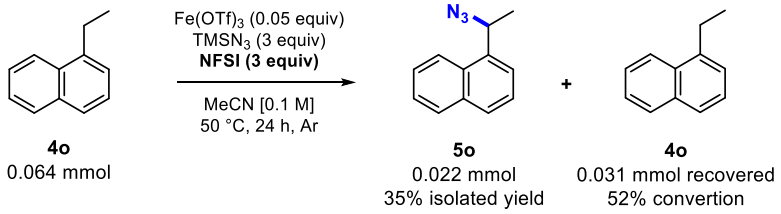
Scheme S11 Reaction performed with the addition of the oxidant portionwise.

An increment in the amount of the catalyst had an insignificant impact in the yield (Scheme **S12**).



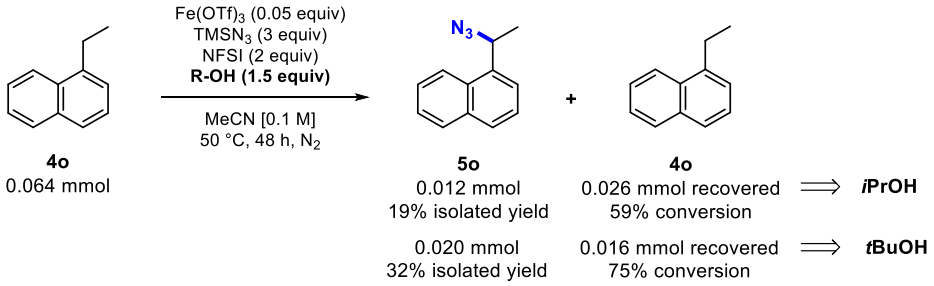
Scheme S12 Reaction performed with 0.2 equiv of the catalyst.

When the equivalents of NFSI were increased, the yield diminished considerably (Scheme S13).



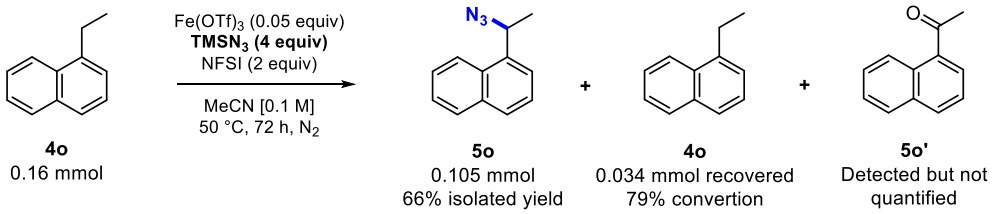
Scheme S13 Reaction performed increasing the amount of NFSI.

Since it has been reported that mild proton donors can promote this type of reactions, a couple of experiments were conducted using *i*PrOH and *t*BuOH as additives.[9] In both reactions the yields significantly decreased, and a more complex mixture was observed (Scheme S14).



Scheme S14 Reaction performed in the presence of alcohols as additives.

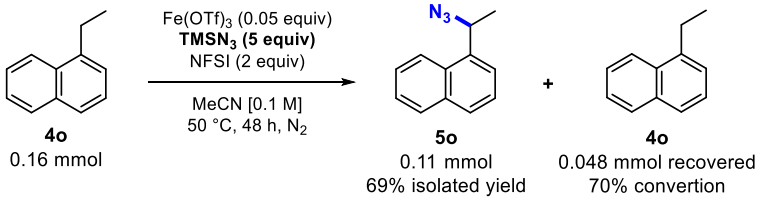
Although the use of 4 equiv of $TMSN_3$ and extending the reaction time up to 72 h slightly improved the yield, full conversion was not reached (Scheme S15). In this experiment, 1-acetylnaphthalene was observed.



Scheme S15 Reaction performed using 4 equiv of $TMSN_3$.

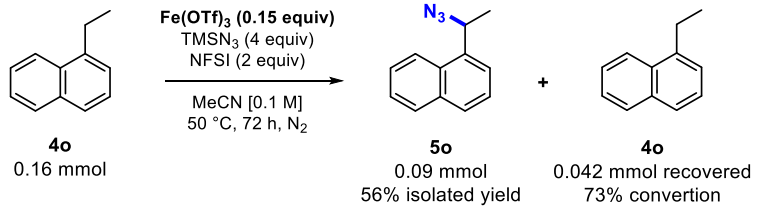
Performing the reaction in a nitrogen-filled glovebox using 5 equivalents of $TMSN_3$ afforded a slight increase in yield (Scheme S16).

[9] Shen, S.-J.; Zhu, C.-L.; Lu, D.-F.; Xu, H. *ACS Catalysis*, **2018**, *8*, 4473.



Scheme S16 Reaction performed in a glovebox.

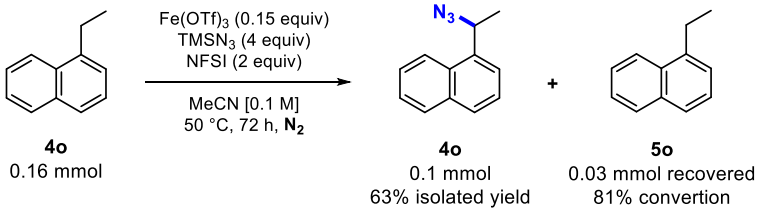
Portionwise addition of the catalyst (0.05 mol%/24 h) until completing 0.15 equiv failed in providing a higher yield and the reaction gave a more complex mixture (Scheme S17).



Remark: The reaction was run inside of a glovebox, and $Fe(OTf)_3$ was added portionwise every 24 h

Scheme S17 Reaction performed by adding the catalyst portionwise.

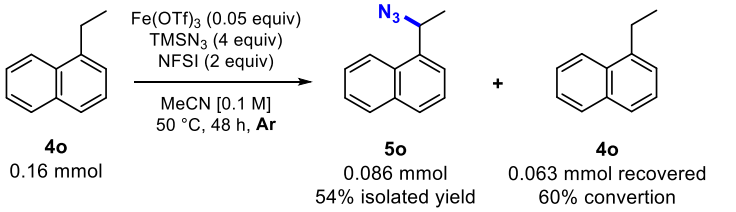
Portionwise addition of both catalyst and $TMSN_3$ led to an increase in conversion but a similar yield as before (Scheme S18).



Remark: The reaction was run inside of a glovebox, 0.05 equiv of $Fe(OTf)_3$ and 1.3 equiv of $TMSN_3$ were added portionwise every 24 h

Scheme S18 Reaction performed by adding the catalyst and $TMSN_3$ portionwise.

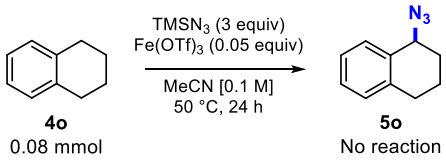
Finally, a portionwise addition of NFSI and $TMSN_3$ was carried out but the yield and conversion did not improve (Scheme S19).



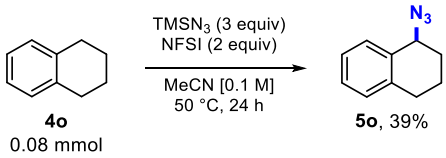
Remark: The reaction was run inside of a glovebox, 0.5 equiv NFSI and 1 equiv of $TMSN_3$ were added portionwise every 12 h

Scheme S19 Reaction performed by adding the catalyst and $TMSN_3$ portionwise.

3.5 Control experiments



Scheme **S20** Experiment carried out in the absence of oxidant.



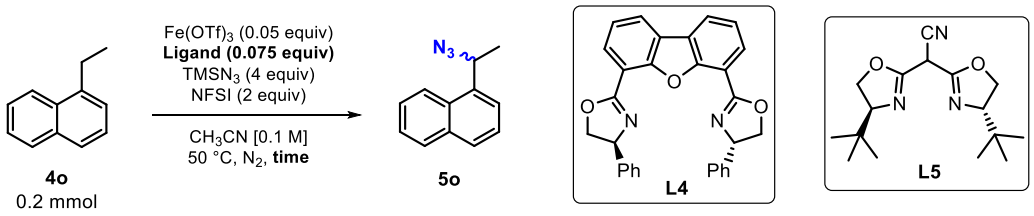
Scheme **S21** Experiment carried out in absence of a catalyst.

3.6 Study of an iron-catalyzed enantioselective benzylic C(sp^3)-H azidation

To evaluate a possible chiral induction in the reaction, additional experiments were carried out using 1-ethylnaphthalene as a model substrate in the presence of **L4**[10] and **L5**.[11] Unfortunately, no asymmetric induction was observed (Table S8).

General procedure: In an oven-dried vial, $Fe(OTf)_3$ (5 mol%) and ligand (7.5 mol%) were dissolved in DCM (0.5 mL) under a nitrogen atmosphere, and the mixture was stirred at 21 °C for 30 minutes. DCM was removed with a nitrogen flow (this pre-stirring was performed only in entries 5 and 6). Then, substrate (0.1 mmol, 1 equiv), oxidant (2 equiv), acetonitrile (0.1 M), $TMSN_3$ (4 equiv) were sequentially added. The reaction mixture was stirred at 50 °C for 48 h. The reaction mixture was filtered through silica and celite and evaporated under reduced pressure. The residue was purified by column chromatography chromatography (SiO_2, pentane:EtOAc = 99:1) to afford azide **5o**.

Table S8 Enantioselective investigation of the rection.



Entry	Ligand	Time	Yield (%)[a]	*ee* (%)[b]
1	-	24 h	34	-
2	-	48 h	60	-
3	**L4**	48 h	51	0
4	**L5**	48 h	55	0

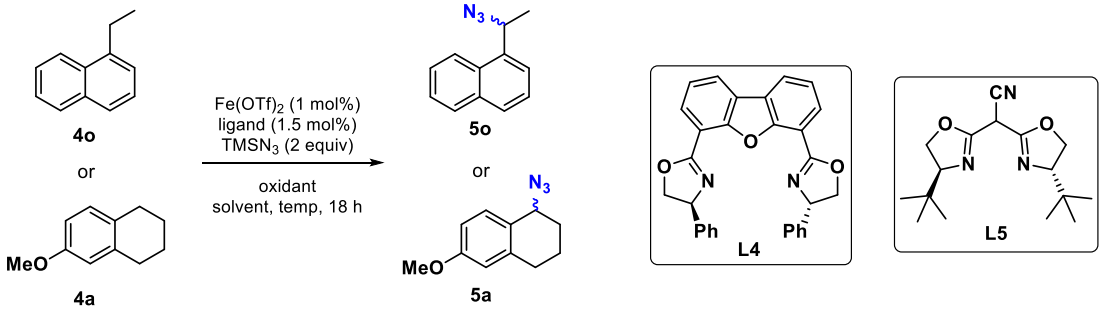
[10] Wang, K.; Li, Y.; Li, X.; Li, D.; Bao, H. *Org. Lett.* **2021**, *23*, 8847.
[11] Wu, L.; Zhang, Z.; Wu, D.; Wang, F.; Chen, P.; Lin, Z.; Liu, G. *Angew. Chem. Int. Ed.* **2021**, *60*, 6997.

5[c]	**L4**	48 h	32	0
6[c]	**L5**	48 h	41	0

[a]Isolated yield
[b]Enantiomeric excess was determined by HPLC on chiral stationary phase
[c]Pre-stirring of iron and ligand for 30 min in DCM

General procedure for $Fe(OTf)_2$-catalyzed azidation: In an oven-dried vial, $Fe(OTf)_2$ (1 mol%) and ligand (1.5 mol%) were dissolved in DCM (0.5 mL) under a nitrogen atmosphere, and the mixture was stirred at 21 °C for 30 minutes. DCM was removed with a nitrogen flow. Then, solvent (0.1 M), substrate **4o** (0.1 mmol, 1 equiv), oxidant (2 equiv), $TMSN_3$ (2 equiv) were sequentially added. The reaction mixture was stirred at 50 °C for 18 h. The reaction mixture was filtered through silica and celite and evaporated under reduced pressure. The residue was purified by column chromatography of silica gel to afford azide **5o**.

Table S9 Optimization for the benzylic C-H azidation.

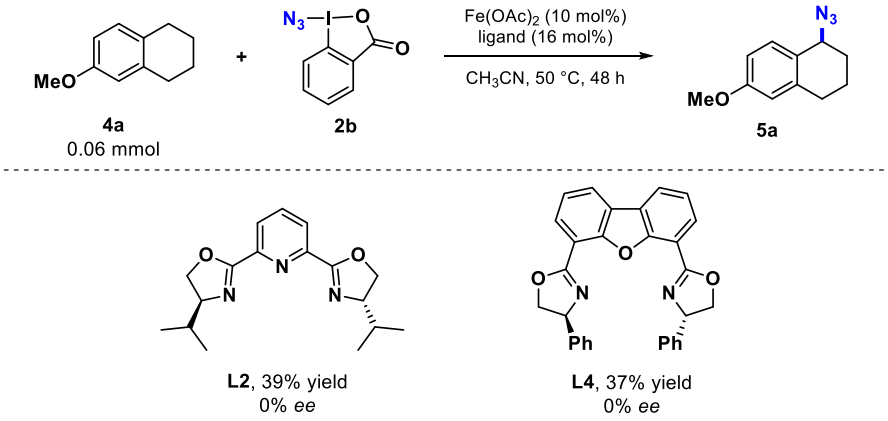


Entry	Substrate	Ligand	Oxidant	Solvent	Temp (°C)	Yield (%)[a]	*ee* (%)[b]
1	**4o**	**L4**	LPO	Et_2O	rt	0	/
2	**4o**	**L4**	*m*CPBA	Et_2O	rt	0	/
3	**4o**	**L5**	*m*CPBA	Et_2O	rt	0	/
4	**4a**	**L4**	NFSI	Et_2O	50	36	0
5	**4a**	**L4**	NHPI	Et_2O	50	5	0
6	**4a**	**L4**	NHPI/LPO	Et_2O	50	25	0
7	**4a**	**L4**	LPO	Et_2O	50	26	0
8	**4a**	**L4**	NFSI	CH_3CN	50	3[c]	n.d.
9	**4a**	**L4**	NHPI	CH_3CN	50	8	0
10	**4a**	**L4**	NHPI/LPO	CH_3CN	50	35	0
11	**4a**	**L4**	LPO	CH_3CN	50	28	0
12	**4o**	**L4**	NHPI	CH_3CN	50	0	n.d.
13	**4a**	**L4**	LPO	Et_2O	rt	1[c]	n.d.
14	**4a**	**L4**	NFSI	Et_2O	rt	4[c]	n.d.
15[d]	**4a**	**L4**	LPO	Et_2O	rt	4[c]	n.d.
16[d]	**4a**	**L4**	NFSI	Et_2O	rt	7[c]	n.d.

[a]Isolated yield
[b]Enantiomeric excess was determined by HPLC on chiral stationary phase
[c]Determined by ^1H NMR using mesitylene as internal standard
[d]Reaction time: 4 days

General procedure for $Fe(OAc)_2$-catalyzed azidation using **4a** as a model substrate: In an oven-dried vial, $Fe(OAc)_2$ (10 mol%) and ligand (16 mol%) were dissolved in MeCN (0.2 M) under a nitrogen atmosphere,

and the mixture was stirred at room temperature for 40 minutes. Then, 6-methoxy-1,2,3,4-tetrahydronaphthalene **4a** (0.1 mmol, 1 equiv) was added followed by ABX **2b** (2 equiv). The reaction mixture was stirred at 50 °C for 48 h. The crude reaction mixture was then treated with 1 mL of Et_2O and filtered through basic alumina. The basic alumina was washed with Et_2O. The solvent was evaporated from the combined resulting solutions. The residue was purified by prep TLC (pentane:EtOAc : 98:2) to afford azide **5a**.



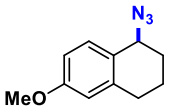
Scheme S22 Additional experiments following Hartwig's conditions.

3.7 General procedure for the iron-catalyzed azidation

In a nitrogen-filled glovebox, $Fe(OTf)_3$ (0.05 equiv), NFSI (2 equiv), and the corresponding substrate (0.1 mmol) were combined in an oven-dried vial. The vial was sealed with a Teflon cap and brought out of the glovebox without solvent. Dry acetonitrile (0.1 M) was added to the reaction mixture under N_2, followed by $TMSN_3$ (3.0-5.0 equiv). The reaction mixture was stirred at 50°C for 24-96 hours, followed by filtration through a small amount of silica with ethyl acetate. The solvent was then evaporated, leaving a residue that was purified using hexane/ethyl acetate on a silica gel column chromatography to obtain the corresponding benzylic azide.

Note: In the case of products **5c**, **5j**, and **5p**, the reaction was completely performed inside the glovebox.

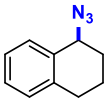
3.8 Synthesized products



5a

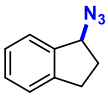
1-Azido-6-methoxy-1,2,3,4-tetrahydronaphthalene (5a).[12] This compound was obtained following the general procedure 2.2 (Table S1, entry 4) using 0.4 mmol of compound **4a** in 47% yield (38.1 mg) as a light-yellow oil (SiO_2, eluent: pentane/EtOAc = 99:1 to 95:5). **^{1}H NMR** ($CDCl_3$, 400 MHz) δ δ 7.22 (d, *J* = 8.5 Hz, 1H), 6.78 (dd, *J* = 8.5, 2.7 Hz, 1H), 6.66 (d, *J* = 2.7 Hz, 1H), 4.58-4.49 (m, 1H), 3.80 (s, 3H), 2.87-2.66 (m, 2H), 2.07-1.89 (m, 3H), 1.81 (qd, *J* = 5.3, 2.8 Hz, 1H). **^{13}C NMR** ($CDCl_3$, 101 MHz) δ 159.4, 139.0, 130.6, 126.2, 114.0, 112.5, 59.3, 55.4, 29.5, 29.3, 18.9.

[12] Lanzi, M.; Merad, J.; Boyarskaya, D. V.; Maestri, G.; Allain, C.; Masson, G. *Org. Lett.* **2018**, *20*, 5247.



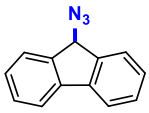
5b

1-Azido-1,2,3,4-tetrahydronaphthalene (5b).[13] This compound was obtained following the general procedure 3.7 in 79% yield (13.7 mg) using 3 equivalents of $TMSN_3$ (24 h) as a colorless oil (SiO_2, eluent: petroleum ethers). **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.34-7.32 (m, 1H), 7.28-7.24 (m, 2H), 7.18-7.16 (m, 1H), 4.60 (t, J = 4.3 Hz, 1H), 2.92-2.85 (m, 1H), 2.82-2.74 (m, 1H), 2.08-1.95 (m, 3H), 1.90-1.81 (m, 1H).



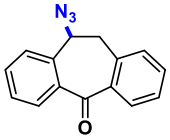
5c

1-Azido-2,3-dihydro-1*H*-indene (5c).[14] This compound was obtained following the general procedure 3.7 in 73% yield (11.6 mg) using 5 equivalents of $TMSN_3$ (48 h) as a colorless oil (SiO_2, eluent: petroleum ethers). **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.37 (d, *J* = 7.1 Hz, 1H), 7.29-7.22 (m, 3H), 4.84 (t, *J* = 5.9 Hz, 1H), 3.06 (dt, *J* = 15.1, 7.2 Hz, 1H), 2.85 (dt, *J* = 15.4, 6.8 Hz, 1H), 2.41 (dq, *J* = 14.6, 7.6 Hz, 1H), 2.10 (ddt, *J* = 13.1, 8.9, 5.1 Hz, 1H).



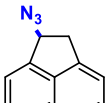
5d

9-Azido-9*H*-fluorene (5d).[15] This compound was obtained following the general procedure 3.7 in 42% yield (8.7 mg) using 3 equivalents of $TMSN_3$ (48 h) as a white solid (SiO_2, eluent: petroleum ethers). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.71 (d, *J* = 7.5 Hz, 2H), 7.63 (d, *J* = 7.5 Hz, 2H), 7.46 – 7.43 (m, 2H), 7.37 (td, *J* = 7.4, 1.1 Hz, 2H), 5.21 (s, 1H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 141.8, 140.9, 129.6, 128.1, 125.4, 120.4, 64.4.



5e

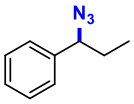
10-Azido-10,11-dihydro-5*H*-dibenzo[a,d][7]annulen-5-one (5e).[16] This compound was obtained following the general procedure 3.7 in 49% yield (12.2 mg) using 4 equivalents of $TMSN_3$ (48 h) as a yellow oil (SiO_2, eluent: petroleum ethers/EtOAc = 97:3). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.03 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.99 (dd, *J* = 7.9, 1.6 Hz, 1H), 7.57 (td, *J* = 7.5, 1.5 Hz, 1H), 7.51 – 7.46 (m, 2H), 7.44 – 7.42 (m, 1H), 7.39 (td, *J* = 7.3, 1.2 Hz, 1H), 7.28 – 7.26 (m, 1H), 4.99 (dd, *J* = 7.5, 2.0 Hz, 1H), 3.60 (dd, *J* = 16.2, 1.2 Hz, 1H), 3.46 (dd, *J* = 16.0, 7.5 Hz, 1H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 194.6, 138.6, 138.2 (2C), 135.5, 132.9, 132.8, 131.2, 130.8, 130.3, 129.1, 128.6, 127.6, 63.5, 39.9.



5f

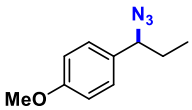
1-Azido-1,2-dihydroacenaphthylene (5f).[17] This compound was obtained in 20% yield (4.0 mg) following the general procedure 3.7 using 3 equivalents of $TMSN_3$ (72 h) as a colorless oil (SiO_2, eluent: petroleum ethers). **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.79 (d, *J* = 7.7 Hz, 1H), 7.68 (d, *J* = 8.3 Hz, 1H), 7.59-7.49 (m, 3H), 7.33 (d, *J* = 6.5 Hz, 1H), 5.37 (d, *J* = 6.5 Hz, 1H), 3.80 (dd, *J* = 17.5, 7.4 Hz, 1H), 3.39 (d, *J* = 17.5 Hz, 1H).

[13] Suh, S.-E.; Chen, S.-J.; Mandal, M.; Guzei, I. A.; Cramer, C. J.; Stahl, S. S. *J. Am. Chem. Soc.* **2020**, *142*, 11388.
[14] Niu, L.; Jiang, C.; Liang, Y.; Liu. D.; Bu, F.; Shi, R.; Chen. H.; Chowdhury, A. D.; Lei, A. *J. Am. Chem. Soc.* **2020**, *142*, 1769.
[15] Myers, E. L.; Raines, R. T. *Angew. Chem. Int. Ed.* **2009**, *48*, 2359.
[16] Huang, X.; Bergsten, T. M.; Groves, J. T. *J. Am. Chem. Soc.* **2015**, *137*, 5300.
[17] Li, X.; Song, J.-N.; Karmakar, S.; Lu, Y.; Lv, Y.; Liao, P.; Liu, Z. *Chem. Commun.* **2022**, *58*, 13783.



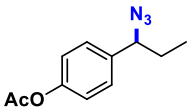
5g

(1-Azidopropyl)benzene (5g).[18] This compound was obtained following the general procedure 3.7 in 68% yield (11.0 mg) using 3 equivalents of $TMSN_3$ (48 h) as a pale yellow oil (SiO_2, eluent: petroleum ethers). **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.41-7.29 (m, 5H), 4.35 (t, *J* = 7.1 Hz, 1H), 1.93-1.74 (m, 2H), 0.94 (t, *J* = 7.4 Hz, 3H).



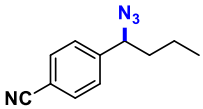
5h

(1-Azidopropyl)-4-methoxybenzene (5h).[19] This compound was obtained following the general procedure 3.7 in 48% yield (9.2 mg) using 4 equivalents of $TMSN_3$ (72 h) as a yellow oil (SiO_2, eluent: petroleum ethers/EtOAc = 98:2). **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.22 (d, *J* = 8.1 Hz, 2H), 6.91 (d, *J* = 8.1 Hz, 2H), 4.29 (t, *J* = 7.1 Hz, 1H), 3.82 (s, 3H), 1.91-1.70 (m, 2H), 0.92 (t, *J* = 7.3 Hz, 3H).



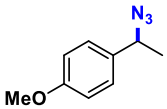
5i

4-(1-Azidopropyl)phenyl acetate (5i).[20] This compound was obtained following the general procedure 3.7 in 38% yield (8.4 mg) using 4 equivalents of $TMSN_3$ (72 h) as a pale yellow oil (SiO_2, eluent: petroleum ethers/EtOAc = 97:3). **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.30 (d, *J* = 8.5 Hz, 2H), 7.10 (d, *J* = 8.6 Hz, 2H), 4.35 (t, *J* = 7.1 Hz, 1H), 2.30 (s, 3H), 1.89-1.74 (m, 2H), 0.94 (t, *J* = 7.4 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 169.5, 150.5, 137.5, 128.1 (2C), 121.9 (2C), 67.4, 29.6, 21.3, 10.9. **IR** (ν_{max}, cm^{-1}) 2091, 1771, 1763, 1752, 1508, 1215, 1204, 1189, 1165, 909. **HRMS** (APPI/LTQ-Orbitrap) m/z: $[M]^+$ Calcd for $C_{11}H_{13}N_3O_2^+$ 219.1002; Found 219.1008.



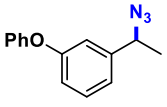
5j

4-(1-Azidobutyl)benzonitrile (5j). This compound was obtained following the general procedure 3.7 in 30% yield (6.0 mg) using 5 equivalents of $TMSN_3$ (48 h) as a light-yellow oil (SiO_2, eluent: petroleum ethers/EtOAc = 98:2). **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.68 (d, *J* = 8.4 Hz, 2H), 7.41 (d, *J* = 8.4 Hz, 2H), 4.49 (dd, *J* = 7.9, 6.3 Hz, 1H), 1.86-1.77 (m, 1H), 1.74-1.65 (m, 1H), 1.46-1.25 (m, 2H), 0.94 (t, *J* = 7.4 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 145.5, 132.8 (2C), 127.7 (2C), 118.6, 112.2, 65.6, 38.5, 19.4, 13.8. **IR** (ν_{max}, cm^{-1}) 2117, 2109, 2092, 1261, 1245, 835. **HRMS** (ESI/QTOF) m/z: $[M + Na]^+$ Calcd for $C_{11}H_{12}N_4Na^+$ 223.0955; Found 223.0963.



5k

(1-Azidoethyl)-4-methoxybenzene (5k).[21] This compound was obtained following the general procedure 3.7 in 41% yield (7.3 mg) using 3 equivalents of $TMSN_3$ (96 h) as a colorless oil (SiO_2, eluent: petroleum ethers/EtOAc = 98:2). **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.26 (d, *J* = 8.6 Hz, 2H), 6.91 (d, *J* = 8.7 Hz, 2H), 4.57 (q, *J* = 6.8 Hz, 1H), 3.82 (s, 3H), 1.51 (d, *J* = 6.8 Hz, 3H).

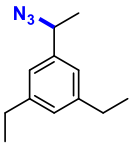


5l

1-(1-Azidoethyl)-3-phenoxybenzene (5l). This compound was obtained following the general procedure 3.7 in 47% yield (11.3 mg) using 4 equivalents of $TMSN_3$ (72 h) as a light-yellow oil (SiO_2, eluent: petroleum ethers/EtOAc = 98:2). **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.37-7.31 (m, 3H), 7.13 (td, *J* = 7.3, 1.1 Hz, 1H), 7.08-6.99 (m, 4H), 6.95 (ddd, *J* = 8.2, 2.5, 1.0 Hz, 1H), 4.59 (q, *J* = 6.8 Hz, 1H), 1.51 (d, *J* = 6.9 Hz, 3H). **^{13}C NMR** ($CDCl_3$, 101 MHz) δ

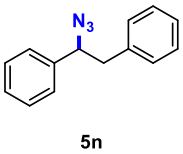
[18] Lenstra, D. C.; Lentingand, P. E.; Mecinović, J. *Green Chem.* **2018**, *20*, 4418.
[19]. Barluenga, J.; Toma-Gamasa, M.; Valdés, C. *Angew. Chem. Int. Ed.* **2012**, *51*, 5950.
[20] Gupta, S.; Han, J.; Kim, Y.; Lee, S. W.; Rhee, Y. H.; Park, J. *J. Org. Chem.* **2014**, *79*, 9094.
[21] Sawama, Y.; Nagata, S.; Yabe, Y.; Morita, K.; Monguchi, Y.; Sajiki, H. *Chem. Eur. J.* **2012**, *18*, 16608.

157.8, 157.0, 143.1, 130.2, 130.0 (2C), 123.6, 121.2, 119.2 (2C), 118.4, 116.9, 60.9, 21.7. **IR** (ν_{max}, cm^{-1}) 2110, 2099, 2089, 1485, 1249, 1233, 1212, 692; **HRMS** (APPI/LTQ-Orbitrap) m/z: $[M]^+$ Calcd for $C_{14}H_{13}N_3O^+$ 239.1053; Found 239.1052.



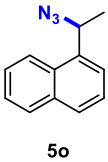
5m

1-(1-Azidoethyl)-3,5-diethylbenzene (5m).[14] This compound was obtained following the general procedure 3.7 in 35% yield (7.2 mg) using 3 equivalents of $TMSN_3$ (24 h) as a colorless oil (SiO_2, eluent: petroleum ethers). **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.00 (s, 1H), 6.97 (s, 2H), 4.57 (q, *J* = 6.7 Hz, 1H), 2.65 (q, *J* = 7.6 Hz, 4H), 1.53 (d, *J* = 6.8 Hz, 3H), 1.25 (t, *J* = 7.3 Hz, 6H).



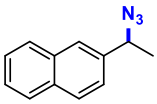
5n

(1-Azidoethane-1,2-diyl)dibenzene (5n).[14] This compound was obtained following the general procedure 3.7 in 40% yield (8.9 mg) using 3 equivalents of $TMSN_3$ (48 h) as a colorless oil (SiO_2, eluent: petroleum ethers). **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.32-7.14 (m, 8H), 7.08-7.06 (m, 2H), 4.59 (dd, *J* = 8.2, 6.2 Hz, 1H), 3.01 (dd, *J* = 13.8, 8.3 Hz, 1H), 2.95 (dd, *J* = 13.8, 6.2 Hz, 2H).



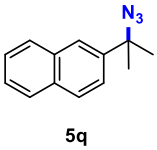
5o

1-(1-Azidoethyl)naphthalene (5o).[13] This compound was obtained following the general procedure 3.7 in 69% yield (21.8 mg) using 0.16 mmol of compound **4o** and 4 equivalents of $TMSN_3$ (48 h) as a colorless oil (SiO_2, eluent: pentane/EtOAc = 99:1). **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 8.10 (d, *J* = 8.4 Hz, 1H), 7.90 (m, 1H), 7.84 (d, *J* = 8.2 Hz, 1H), 7.60-7.48 (m, 4H), 5.36 (q, *J* = 6.8 Hz, 1H), 1.73 (d, *J* = 6.9 Hz, 3H). **^{13}C NMR** ($CDCl_3$, 101 MHz) δ 136.3, 134.1, 130.7, 129.2, 128.9, 126.6, 126.0, 125.5, 123.7, 123.1, 57.7, 20.8.



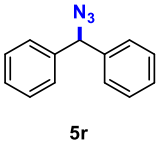
5p

2-(1-Azidoethyl)naphthalene (5p).[22] This compound was obtained following the general procedure 3.7 in 56% yield (11.0 mg) using 5 equivalents of $TMSN_3$ (48 h) as a colorless oil (SiO_2, eluent: petroleum ethers). **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.89-7.85 (m, 3H), 7.78 (s, 1H), 7.53-7.45 (m, 3H), 4.79 (q, *J* = 6.7 Hz, 1H), 1.63 (d, *J* = 6.8 Hz, 3H).



5q

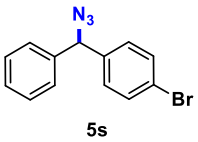
2-(2-Azidopropan-2-yl)naphthalene (5q). This compound was obtained following the general procedure 3.7 in 53% yield (11.2 mg) using 3 equivalents of $TMSN_3$ (48 h) as a light yellow oil (SiO_2, eluent: petroleum ethers). **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.88-7.83 (m, 4H), 7.58 (dd, *J* = 8.6, 2.1 Hz, 1H), 7.52-7.47 (m, 2H), 1.74 (s, 6H). **^{13}C NMR** ($CDCl_3$, 101 MHz,) δ 142.1, 133.2, 132.7, 128.6, 128.4, 127.6, 126.5, 126.3, 123.9, 123.8, 64.1, 28.4. **IR** (ν_{max}, cm^{-1}) 2095, 1275, 1263, 1244, 1233, 1140, 1130, 855, 815, 745. **HRMS** (APPI/LTQ-Orbitrap) m/z: $[M]^+$ Calcd for $C_{13}H_{13}N_3^+$ 211.1104; Found 211.1099.



5r

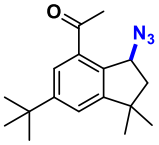
(Azidomethylene)dibenzene (5r).[13] This compound was obtained following the general procedure 3.7 in 30% yield (6.3 mg) using 3 equivalents of $TMSN_3$ (72 h) as a colorless oil (SiO_2, eluent: petroleum ethers). **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.39-7.29 (m, 10H), 5.72 (s, 1H).

[22] Tummatorn, J.; Thongsornkleeb, C.; Ruchirawat, S.; Thongaram, P.; Kaewmee, B. *Synthesis* **2015**, *47*, 323.



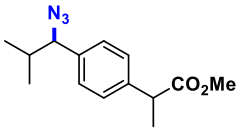
5s

1-(Azido(phenyl)methyl)-4-bromobenzene (5s).[13] This compound was obtained following the general procedure 3.7 in 34% yield (9.8 mg) using 4 equivalents of $TMSN_3$ (48 h) as a colorless oil (SiO_2, eluent: petroleum ethers). **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.48 (d, J = 8.2 Hz, 2H), 7.39-7.32 (m, 3H), 7.28 (d, J = 7.4 Hz, 2H), 7.19 (d, J = 8.3 Hz, 2H), 5.67 (s, 1H).



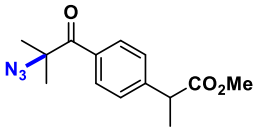
5v

1-(3-Azido-6-(*tert*-butyl)-1,1-dimethyl-2,3-dihydro-1H-inden-4-yl)ethan-1-one (5v).[13] This compound was obtained following the general procedure 3.7 in 47% yield (13.5 mg) using 4 equivalents of $TMSN_3$ (48 h) as a yellow oil (SiO_2, eluent: petroleum ethers/EtOAc = 98:2). **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.75 (s, 1H), 7.40 (s, 1H), 5.59 (d, *J* = 7.3 Hz, 1H), 2.65 (s, 3H), 2.19 (dd, *J* = 13.7, 7.3 Hz, 1H), 2.07 (d, *J* = 13.7 Hz, 1H), 1.37 (s, 9H), 1.34 (s, 3H), 1.32 (s, 3H).



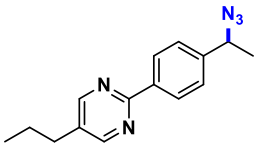
5w

Methyl 2-(4-(1-azido-2-methylpropyl)phenyl)propanoate (5w).[14] This compound was obtained following the general procedure 3.7 in 60% yield (15.7 mg) using 4 equivalents of $TMSN_3$ (54 h) as a colorless oil (SiO_2, eluent: petroleum ethers/EtOAc = 97:3). **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.29 (d, *J* = 7.8 Hz, 2H), 7.21 (d, *J* = 7.9 Hz, 2H), 4.12 (d, *J* = 7.8 Hz, 1H), 3.73 (q, *J* = 7.2 Hz, 1H), 3.67 (s, 3H), 2.01-1.93 (m, 1H), 1.50 (d, *J* = 7.1 Hz, 3H), 1.01 (d, *J* = 6.6 Hz, 3H), 0.79 (d, *J* = 6.7 Hz, 3H).



5w'

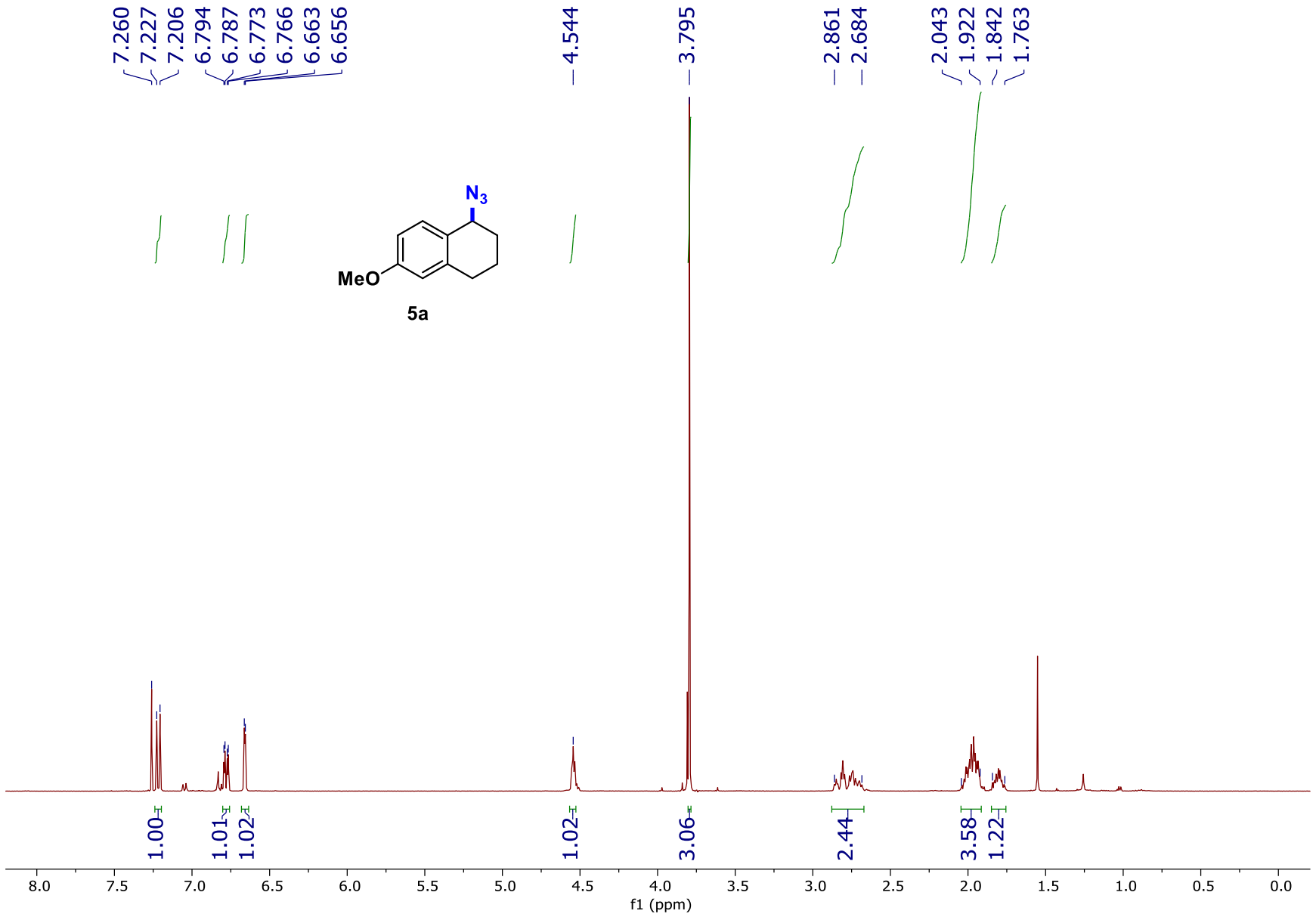
Methyl 2-(4-(2-azido-2-methylpropanoyl)phenyl)propanoate (5w'). This compound was obtained following the general procedure 3.7 as a side-product in 13% yield (3.7 mg) using 4 equivalents of $TMSN_3$ (54 h) as a light-yellow oil (SiO_2, eluent: petroleum ethers/EtOAc = 97:3). **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 8.08 (d, *J* = 8.3 Hz, 2H), 7.38 (d, *J* = 8.3 Hz, 2H), 3.79 (q, *J* = 7.1 Hz, 1H), 3.68 (s, 3H), 1.60 (s, 6H), 1.53 (d, *J* = 7.2 Hz, 3H). **^{13}C NMR** ($CDCl_3$, 101 MHz) δ 198.87, 174.37, 145.78, 133.37, 130.47, 127.71, 67.69, 52.39, 45.57, 25.10, 18.51.



5x

2-(4-(1-Azidoethyl)phenyl)-5-propylpyrimidine (5x).[16] This compound was obtained following the general procedure 3.7 in 57% yield (15.3 mg) using 4 equivalents of $TMSN_3$ (24 h) as a yellow oil (SiO_2, eluent: petroleum ethers/EtOAc = 98:2). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.63 (s, 2H), 8.42 (d, *J* = 8.5 Hz, 2H), 7.44 (d, *J* = 8.2 Hz, 2H), 4.69 (q, *J* = 6.9 Hz, 1H), 2.61 (t, *J* = 7.7 Hz, 2H), 1.70 (h, *J* = 7.3 Hz, 2H), 1.57 (d, *J* = 6.9 Hz, 3H), 1.00 (t, *J* = 7.3 Hz, 3H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 162.3, 157.2, 143.2, 137.7, 133.0, 128.5, 126.7, 61.0, 32.3, 24.1, 21.7, 13.7.

4. NMR spectra of the synthesized azide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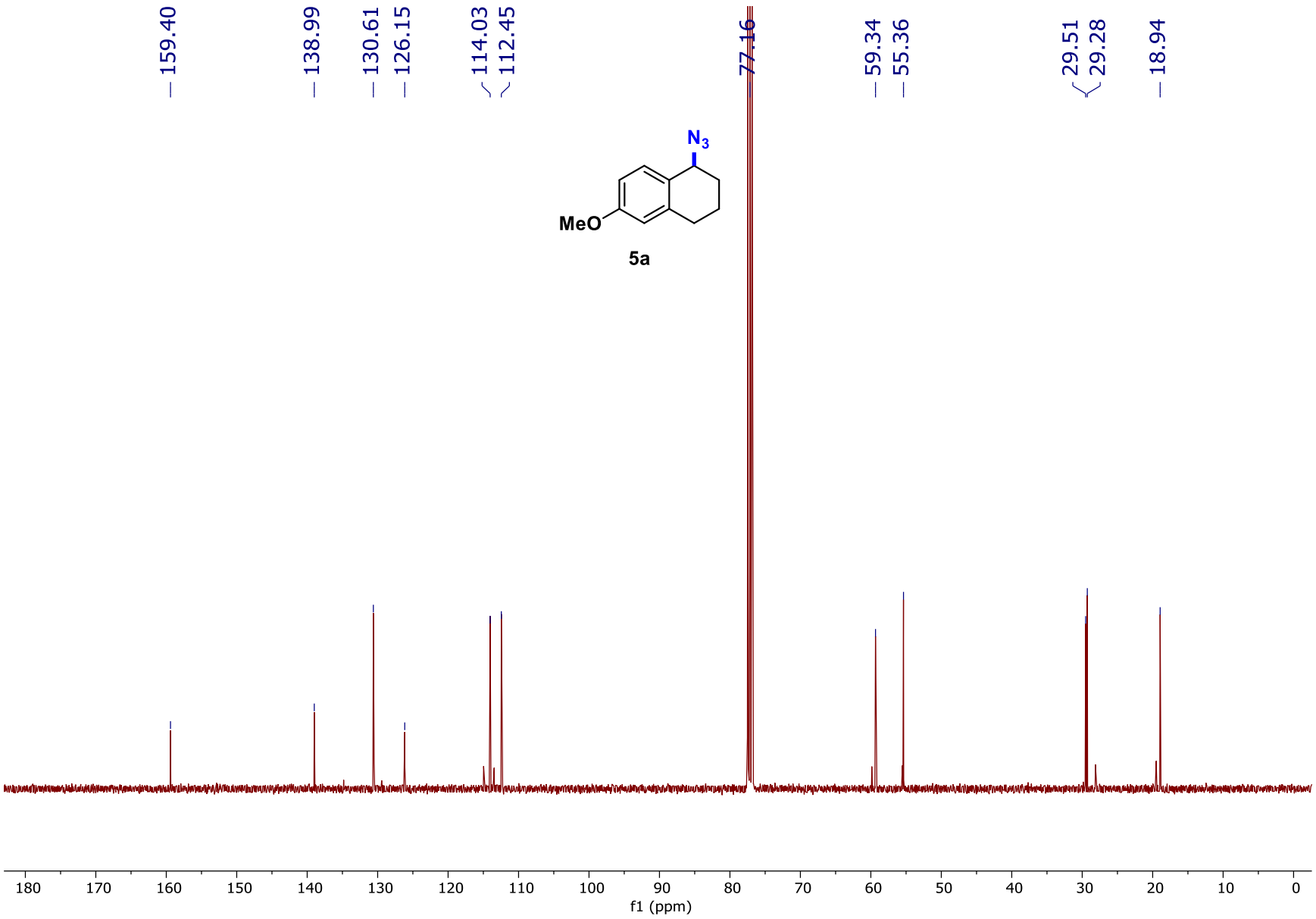
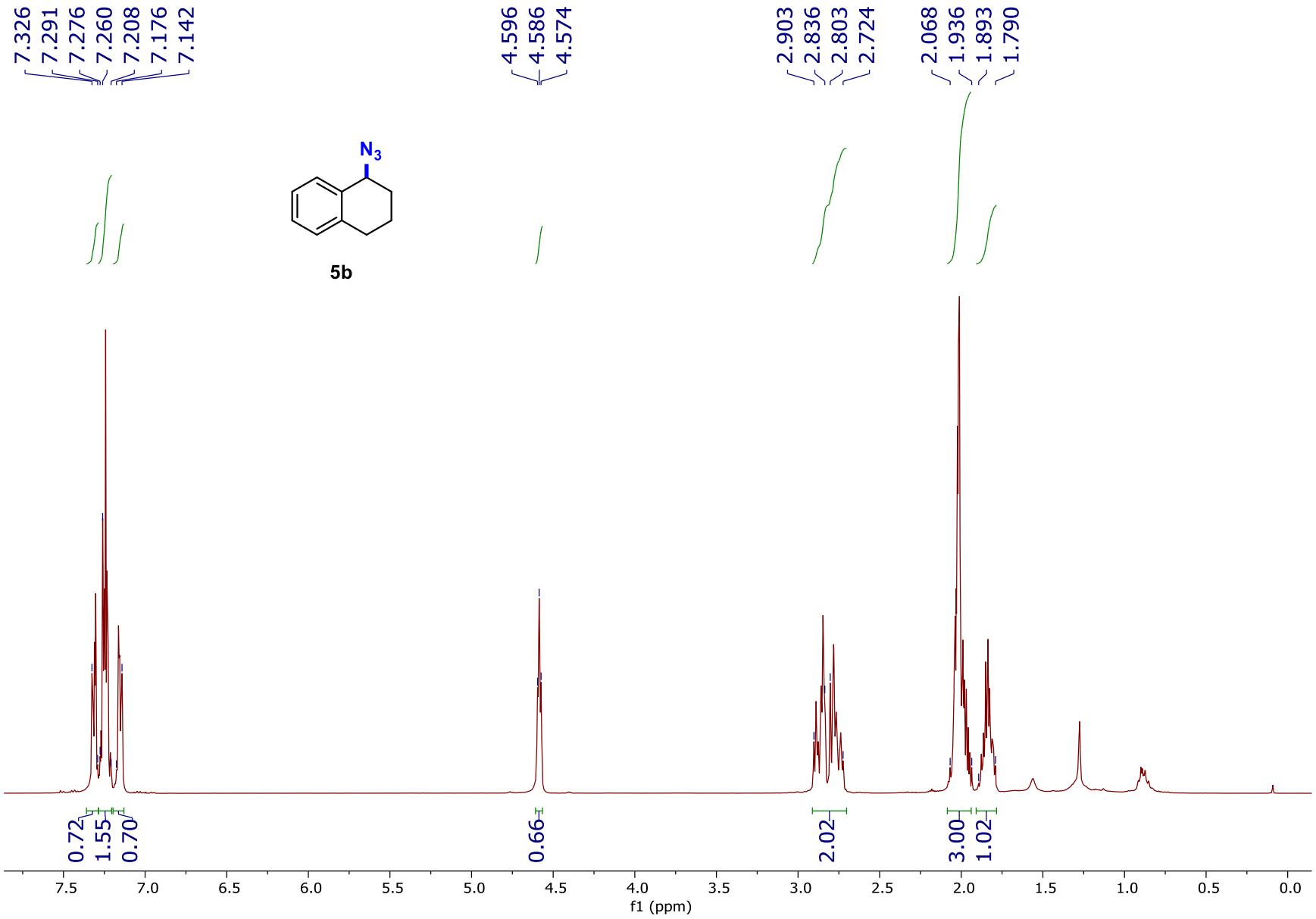
6.794
6.787
6.773
6.766
6.663
6.656
4.544
3.795
2.861
2.684
2.043
1.922
1.842
1.763
N3
MeO
5a
1.00
1.01
1.02
1.02
3.06
2.44
3.58
1.22
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


159.40
138.99
130.61
126.15
114.03
112.45
77.16
59.34
55.36
29.51
29.28
18.94
N3
MeO
5a
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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7.276
7.260
7.208
7.176
7.142
4.596
4.586
4.574
2.903
2.836
2.803
2.724
2.068
1.936
1.893
1.790
N3
5b
0.72
1.55
0.70
0.66
2.02
3.00
1.02
7.5
7.0
6.5
6.0
5.5
5.0
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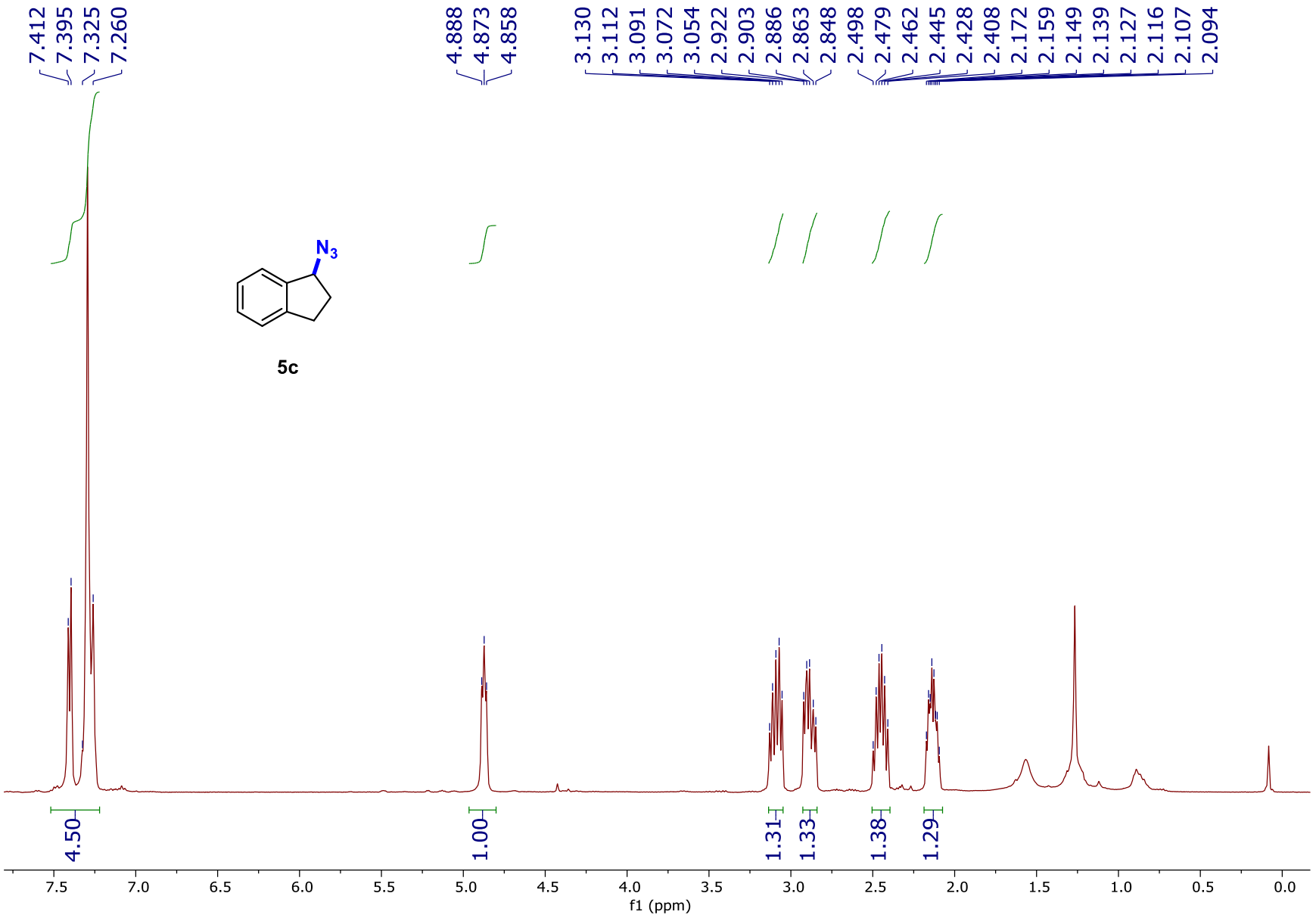
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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7.325
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4.873
4.858
3.130
3.112
3.091
3.072
3.054
2.922
2.903
2.886
2.863
2.848
2.498
2.479
2.462
2.445
2.428
2.408
2.172
2.159
2.149
2.139
2.127
2.116
2.107
2.094
N3
5c
4.50
1.00
1.31
1.33
1.38
1.29
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
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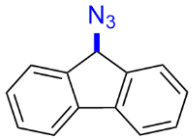
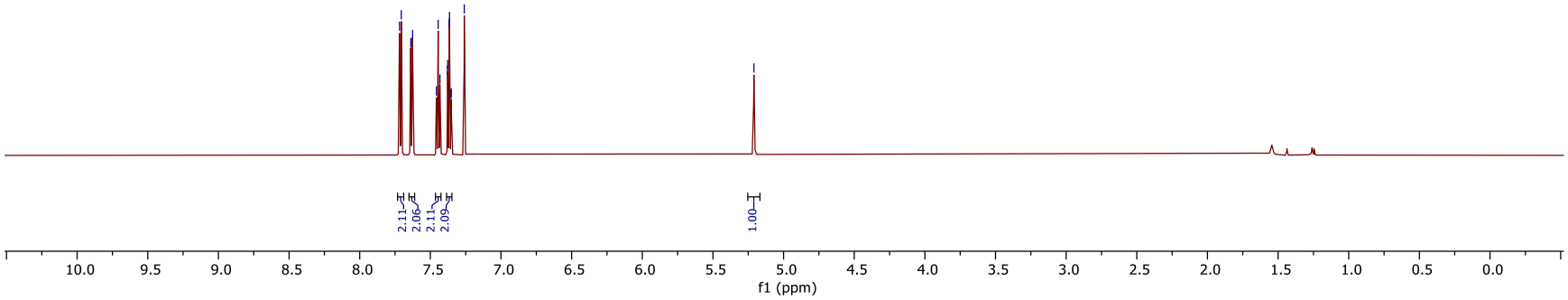
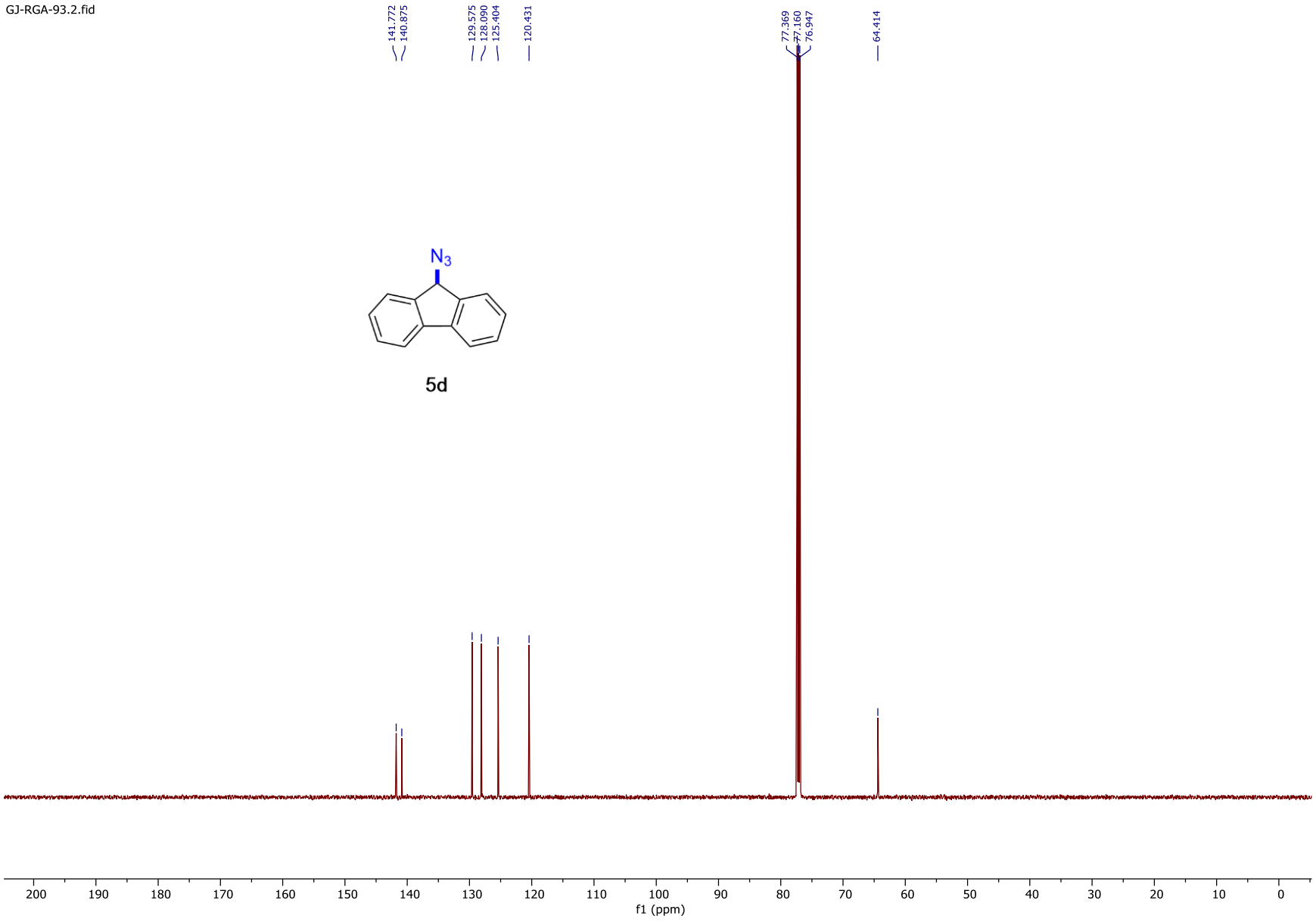
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

GJ-RGA-93.1.fid



5d




GJ-RGA-93.2.fid
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129.575
128.090
125.404
120.431
77.369
77.160
76.947
64.414
N3
5d
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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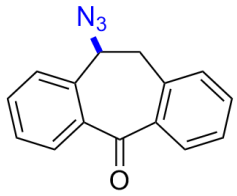
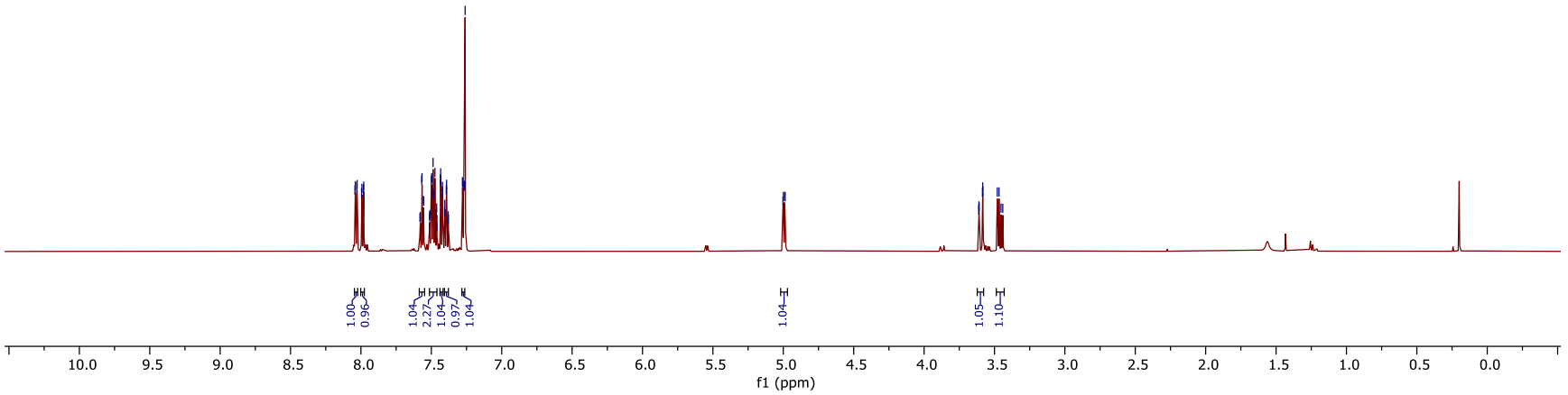
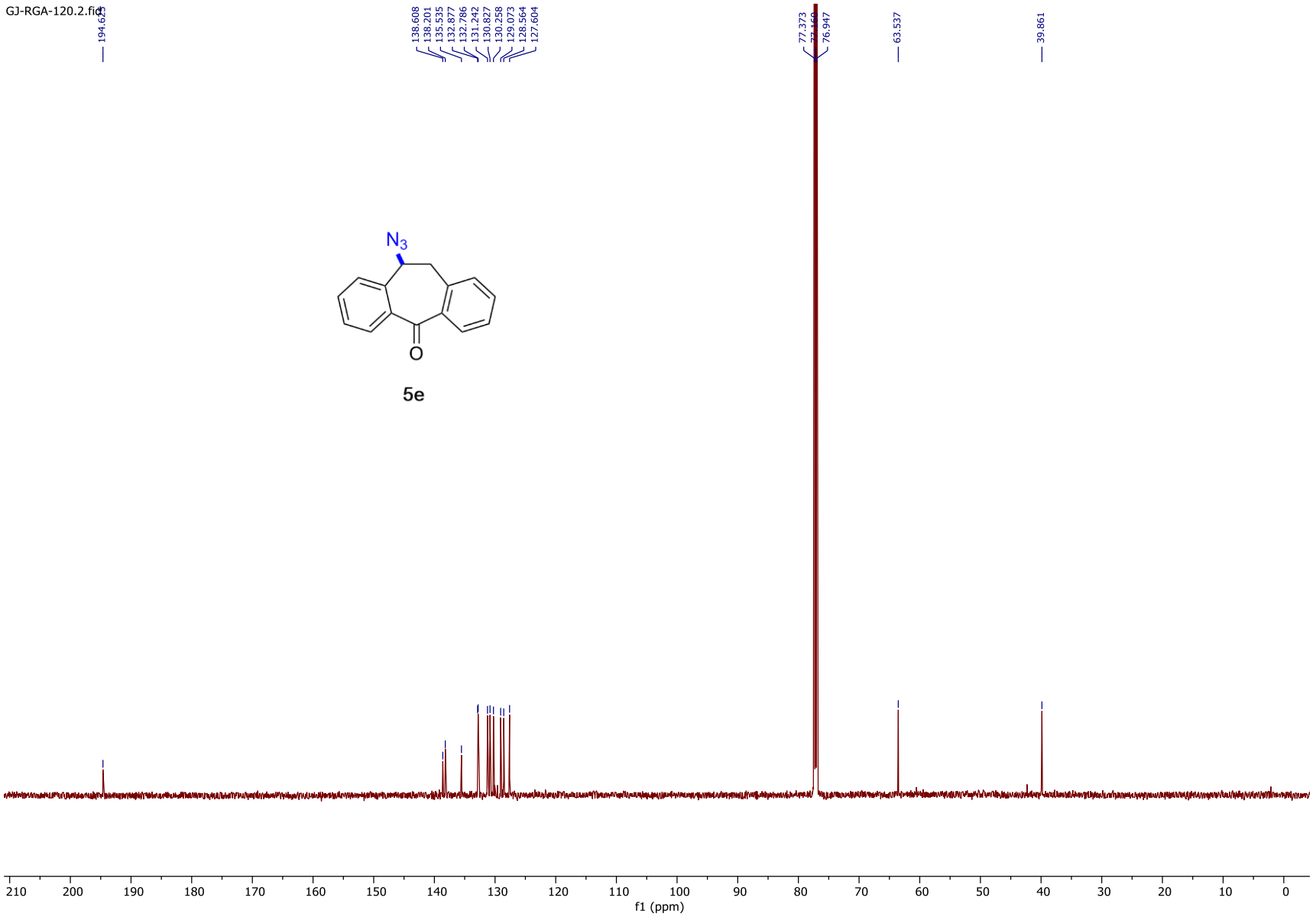


5e




GJ-RGA-120.2.fid
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138.201
135.535
132.877
132.786
131.242
130.827
130.258
129.073
128.564
127.604
77.373
77.160
76.947
63.537
39.861
N3
O
5e
210
200
190
180
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150
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130
120
110
100
90
80
70
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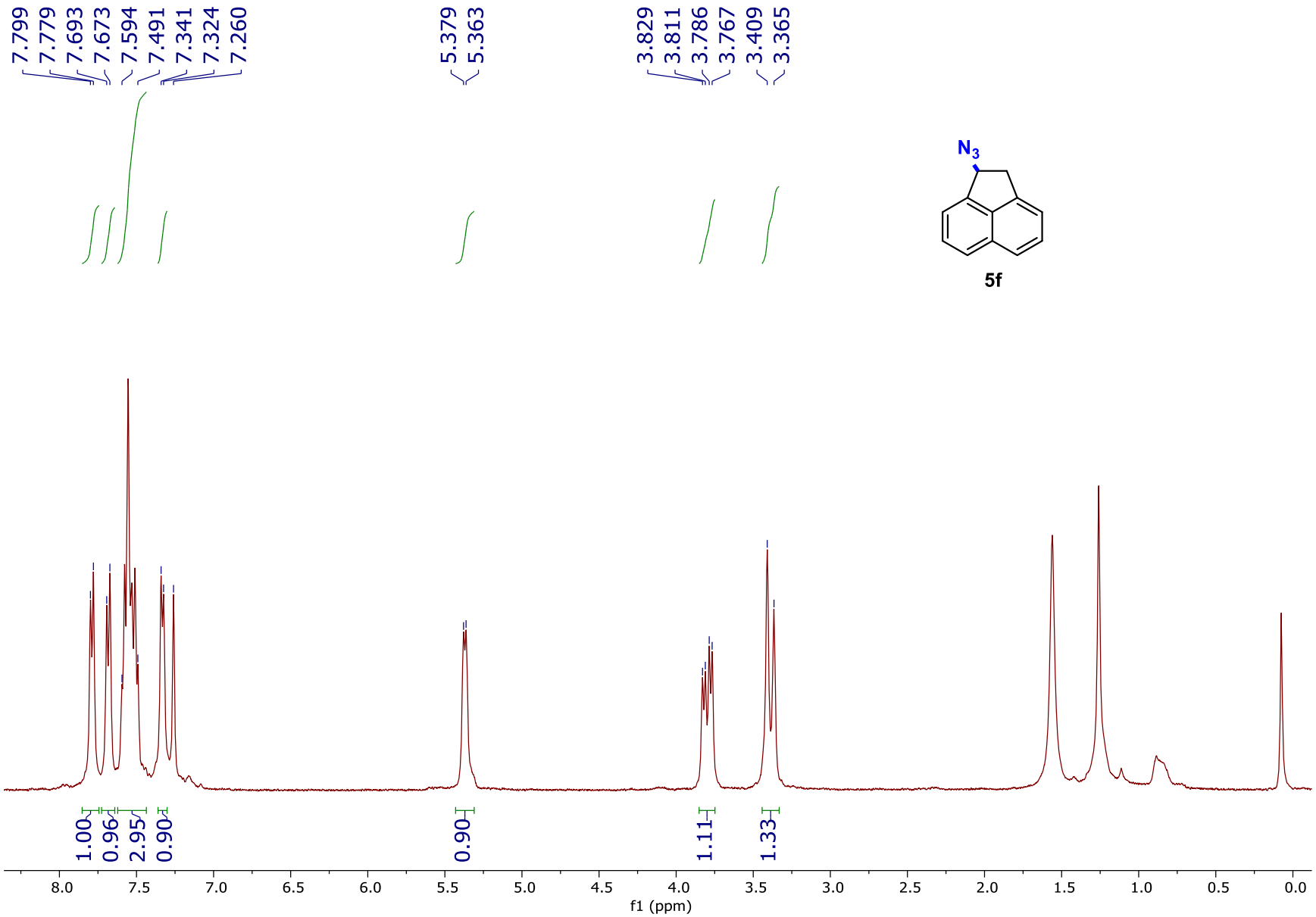
50
40
30
20
10
0
f1 (ppm)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3.811
3.786
3.767
3.409
3.365
N3
5f
1.00
0.96
2.95
0.90
0.90
1.11
1.33
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
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3.0
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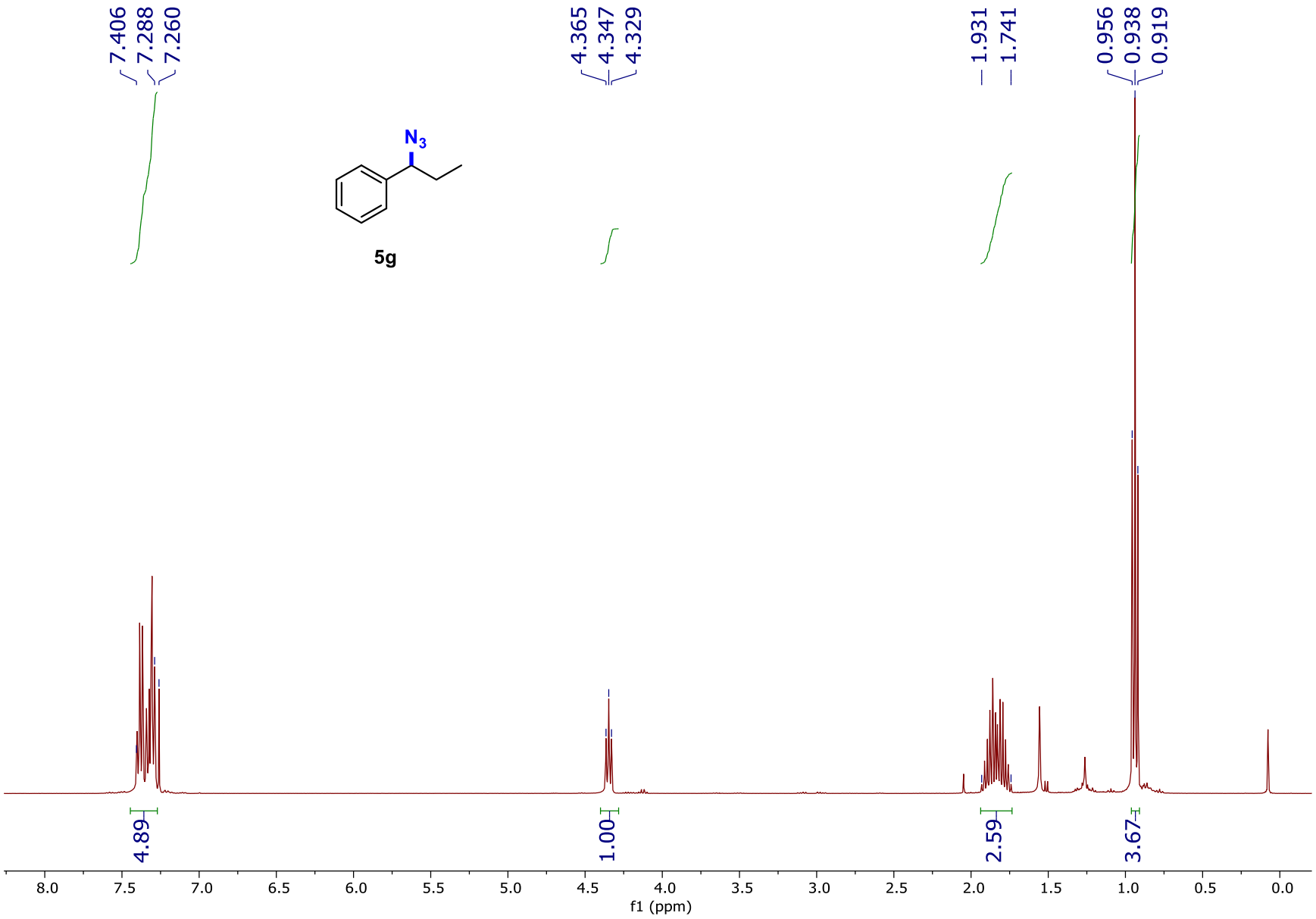
0.0
f1 (ppm)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1.741
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0.938
0.919
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5g
4.89
1.00
2.59
3.67
8.0
7.5
7.0
6.5
6.0
5.5
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3.5
3.0
2.5
2.0
1.5
1.0
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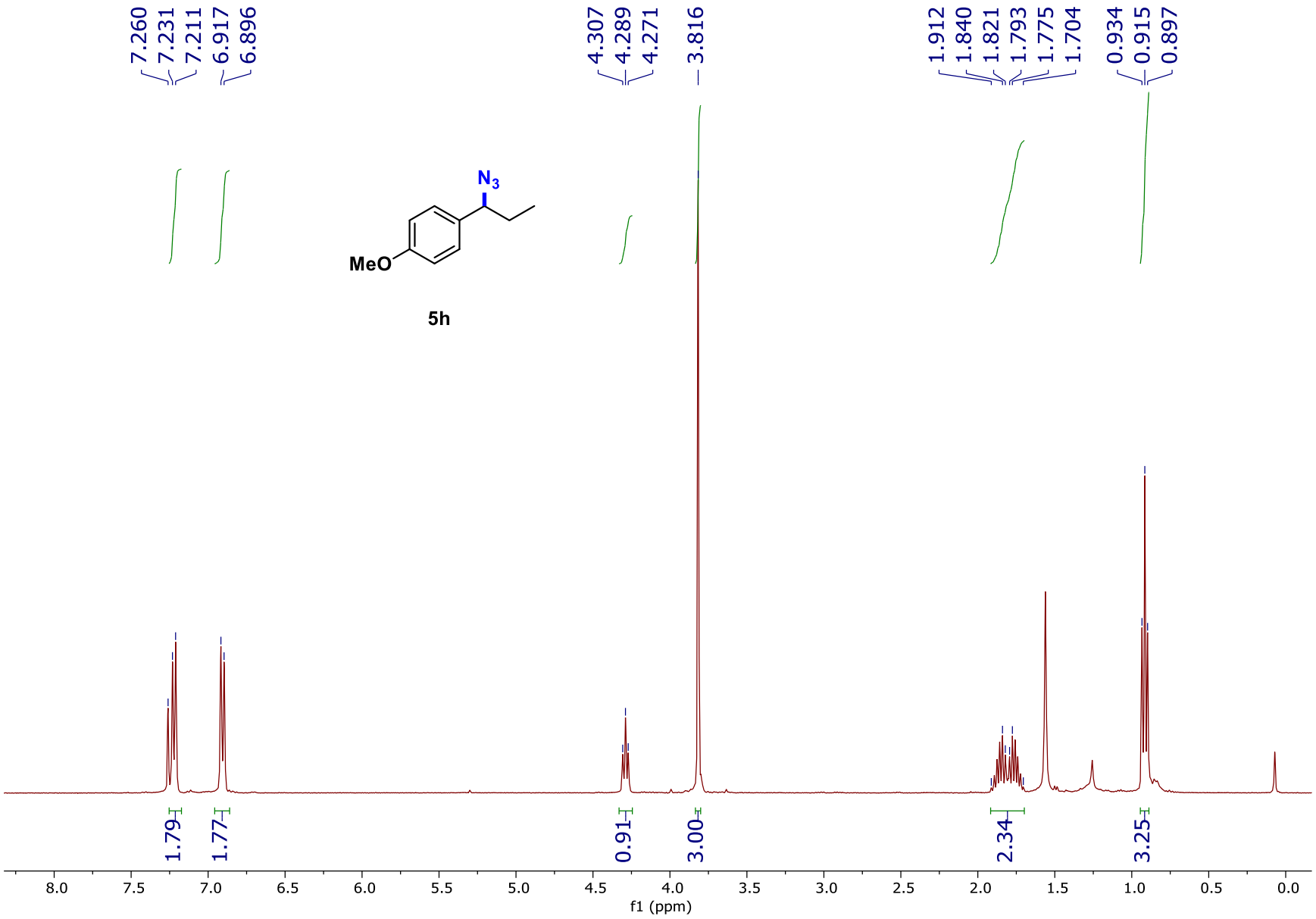
0.0
f1 (ppm)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7.211
6.917
6.896
4.307
4.289
4.271
3.816
1.912
1.840
1.821
1.793
1.775
1.704
0.934
0.915
0.897
N3
MeO
5h
1.79
1.77
0.91
3.00
2.34
3.25
8.0
7.5
7.0
6.5
6.0
5.5
5.0
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4.0
3.5
3.0
2.5
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1.0
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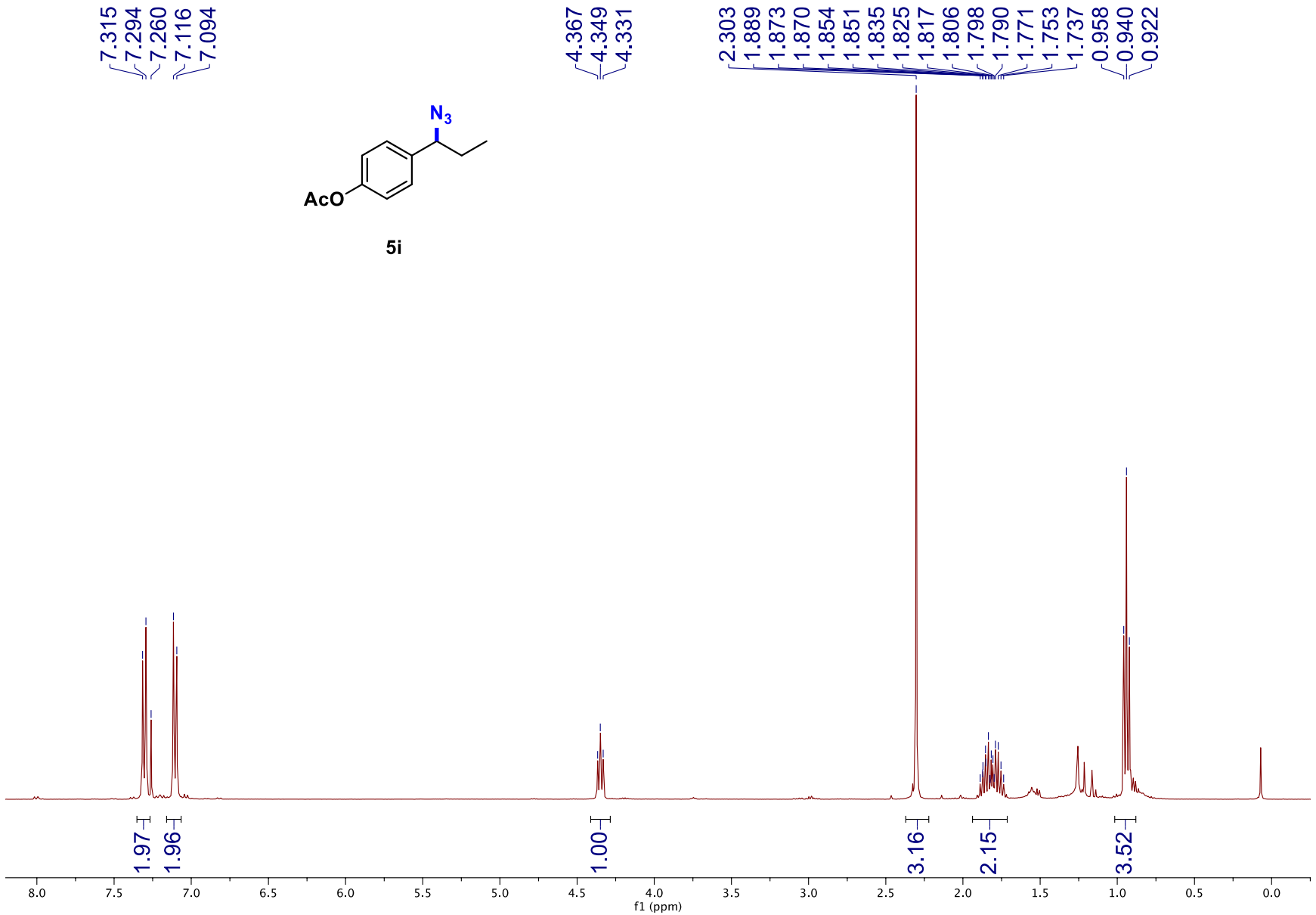
0.0
f1 (ppm)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1.854
1.851
1.835
1.825
1.817
1.806
1.798
1.790
1.771
1.753
1.737
0.958
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AcO
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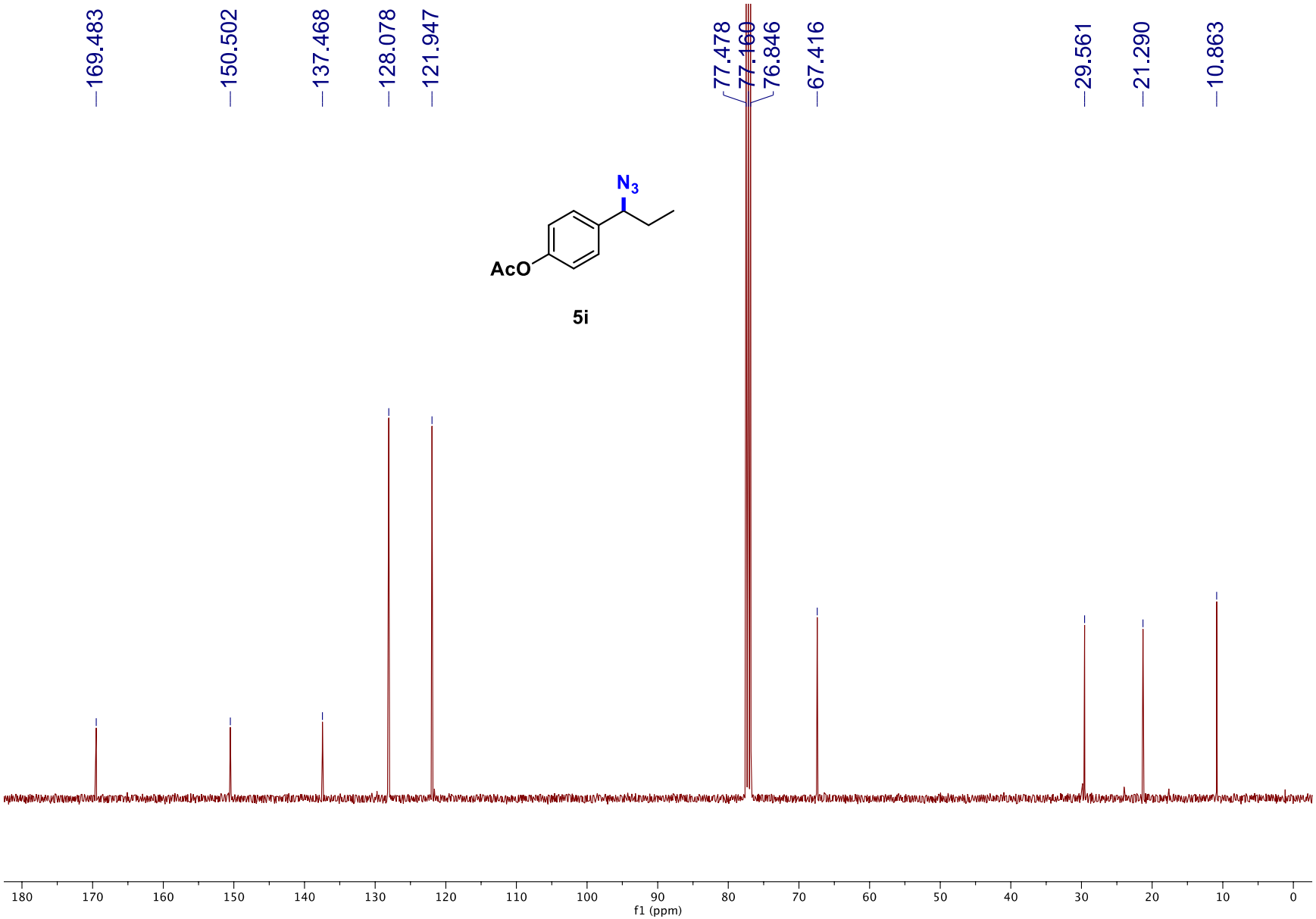
2.15
3.52
f1 (ppm)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128.078
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77.478
77.160
76.846
67.416
29.561
21.290
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AcO
5i
180
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160
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130
120
110
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90
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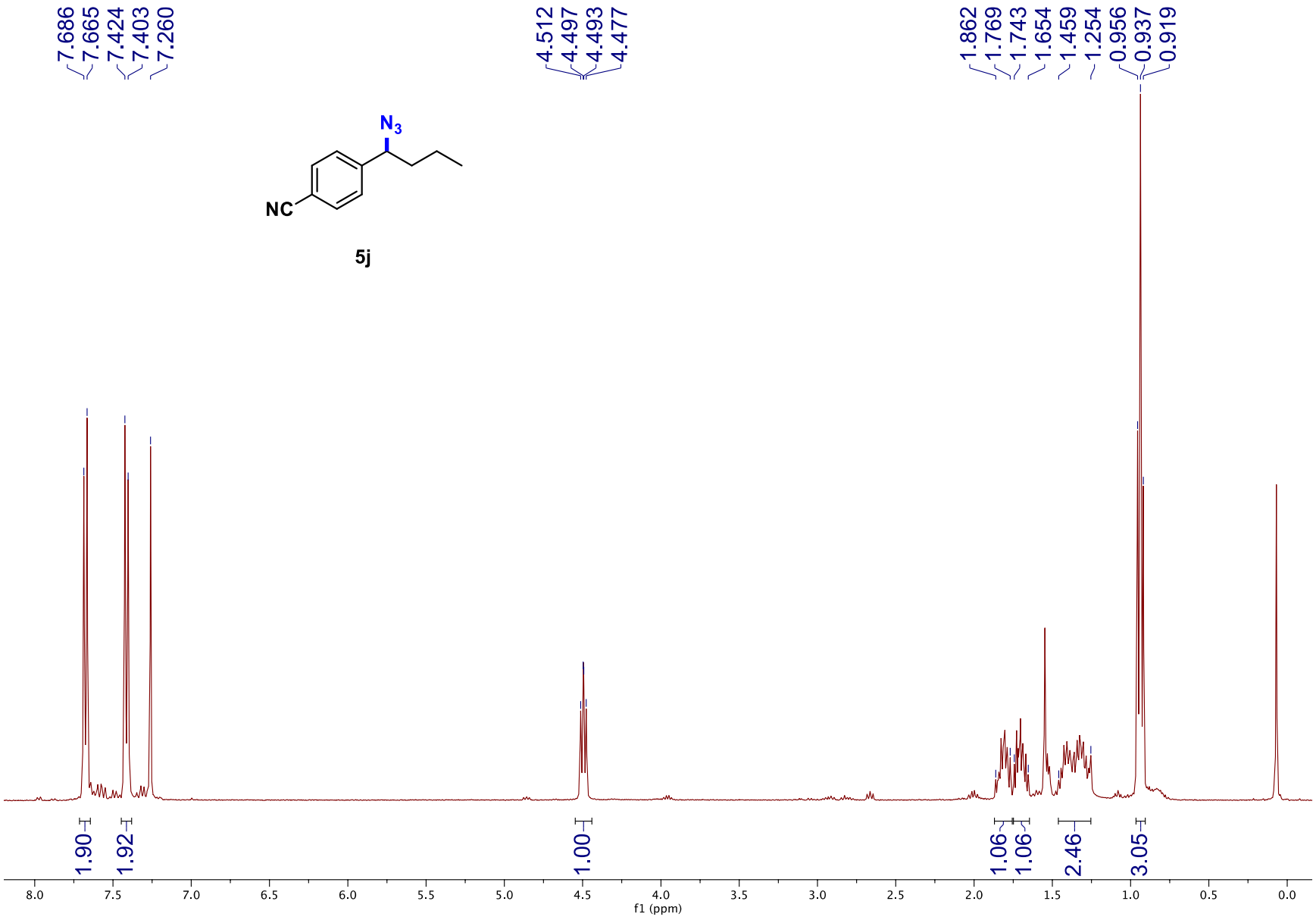
70
60
50
40
30
20
10
0
f1 (ppm)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7.260
4.512
4.497
4.493
4.477
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1.769
1.743
1.654
1.459
1.254
0.956
0.937
0.919
N3
NC
5j
1.90
1.92
1.00
1.06
1.06
2.46
3.05
8.0
7.5
7.0
6.5
6.0
5.5
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3.0
2.5
2.0
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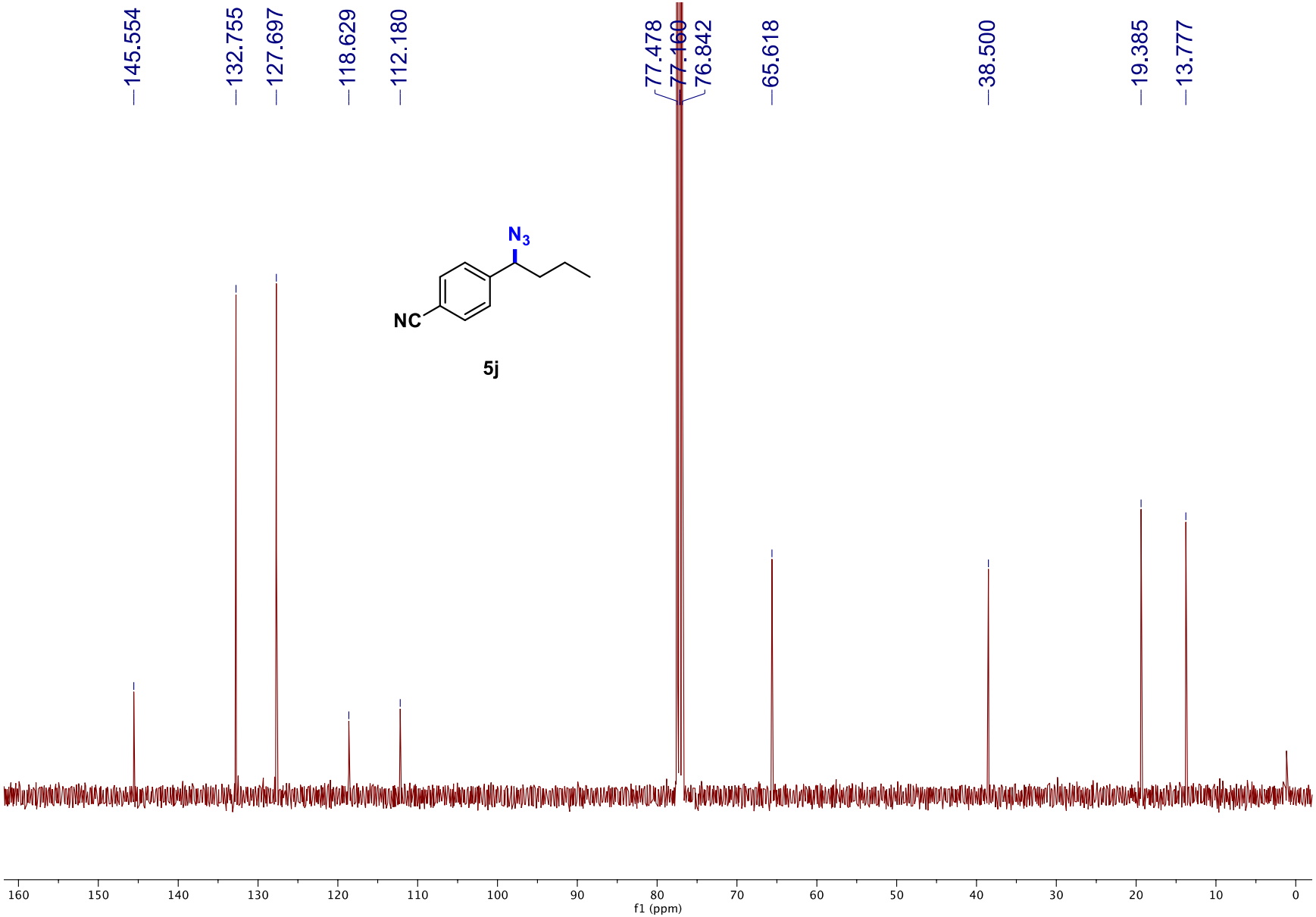
1.0
0.5
0.0
f1 (ppm)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118.629
112.180
77.478
77.160
76.842
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38.500
19.385
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N3
NC
5j
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130
120
110
100
90
80
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60
50
40
30
20
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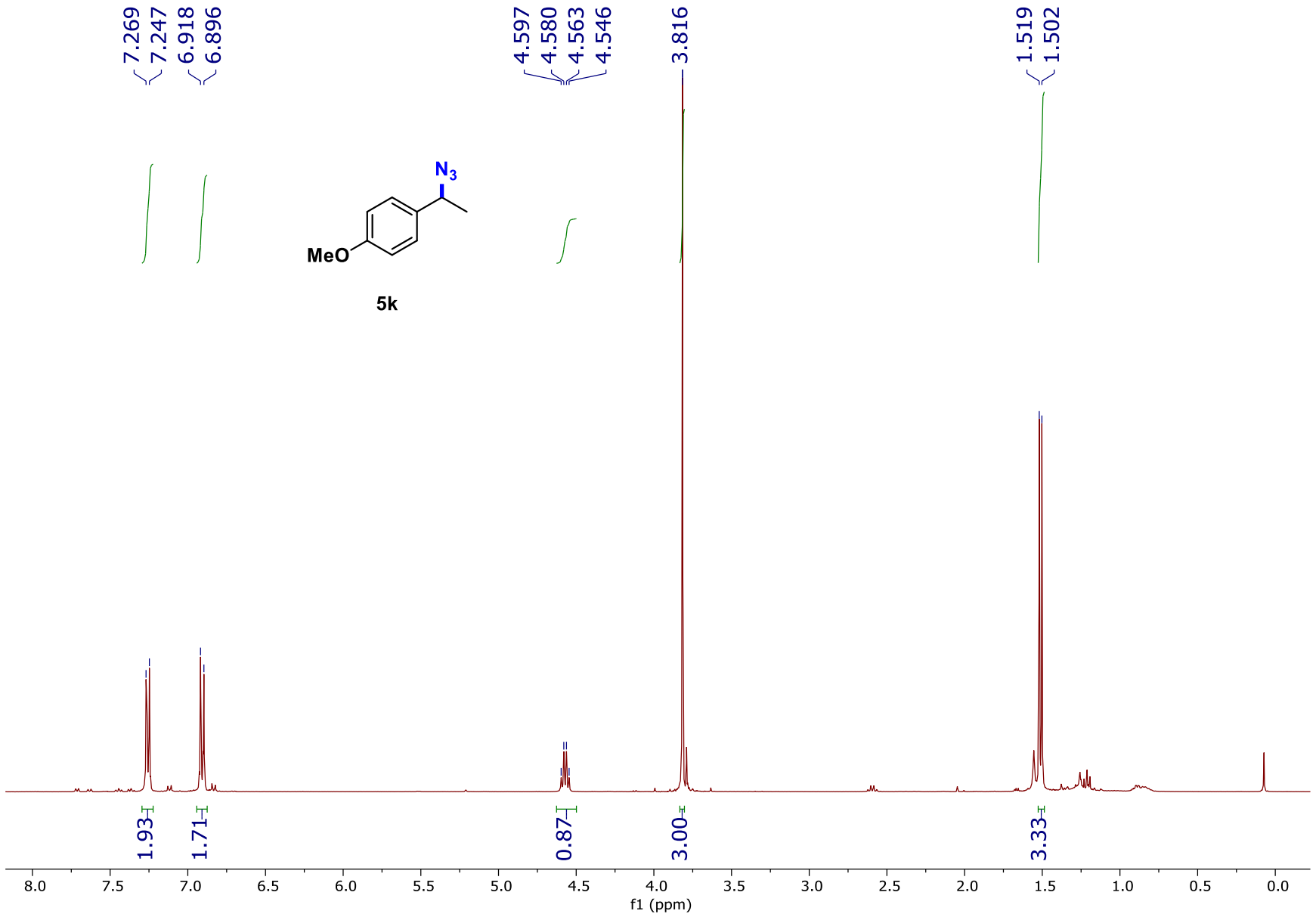
0
f1 (ppm)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4.546
3.816
1.519
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MeO
5k
1.93
1.71
0.87
3.00
3.33
8.0
7.5
7.0
6.5
6.0
5.5
5.0
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3.5
3.0
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1.0
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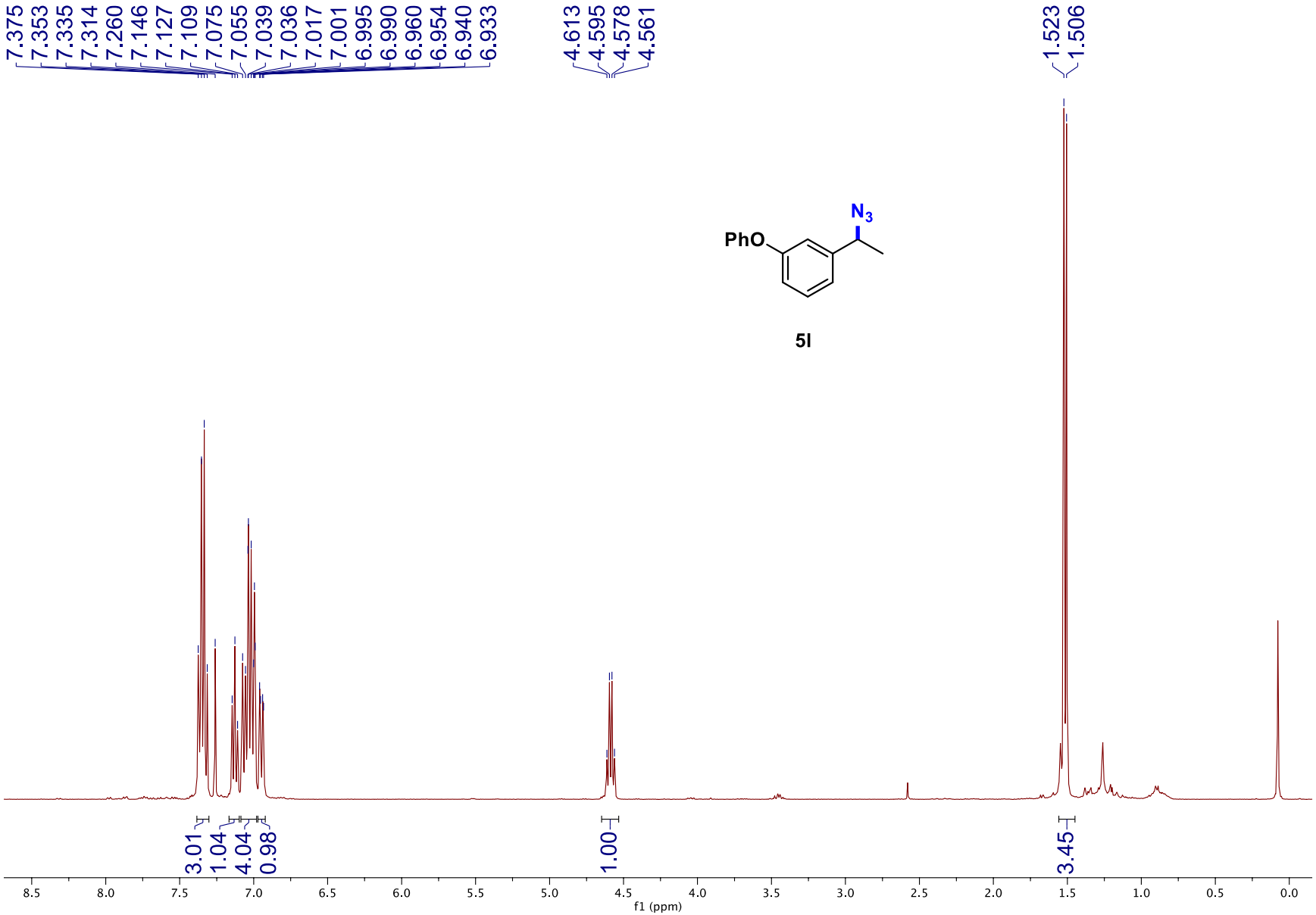
f1 (ppm)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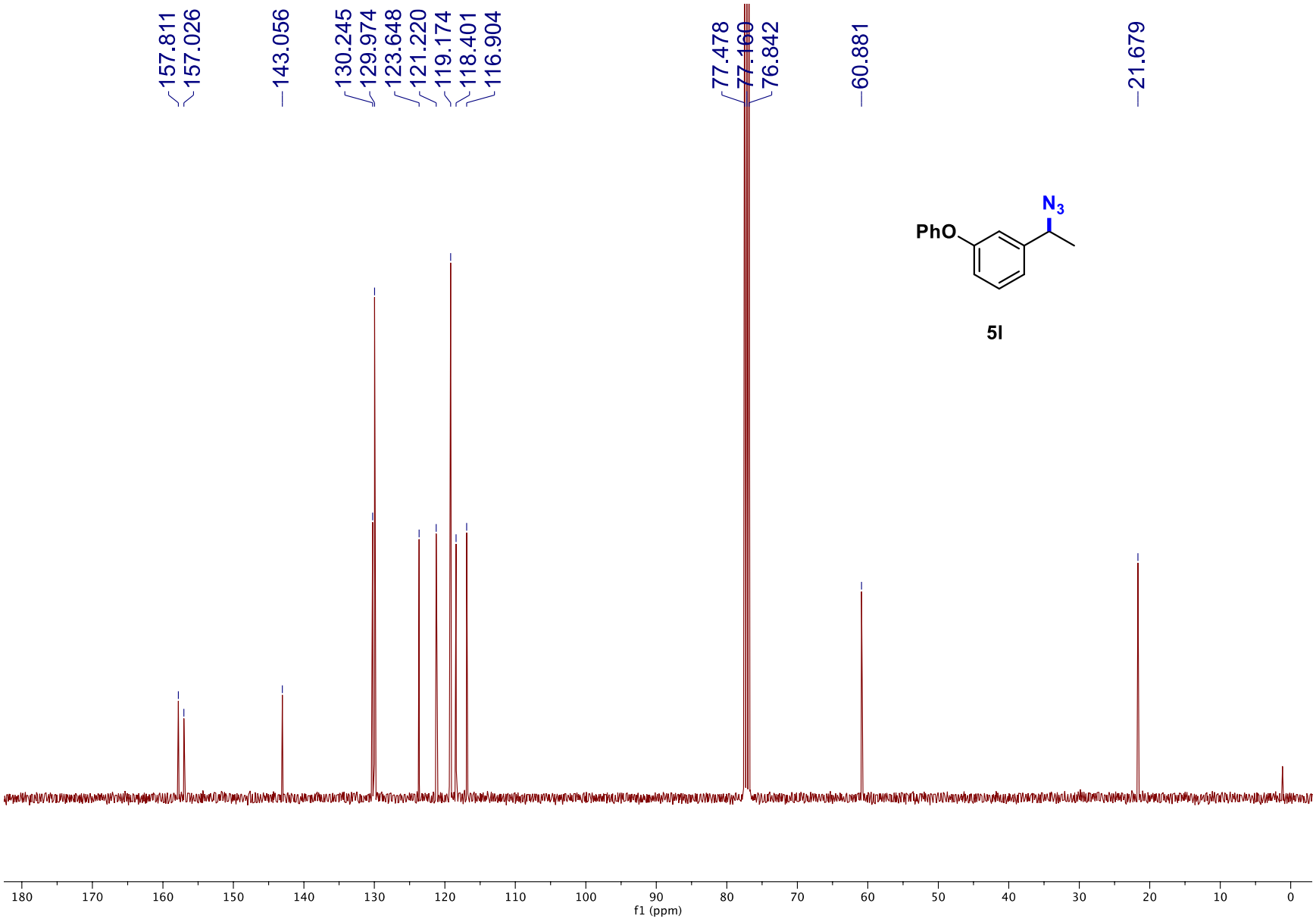
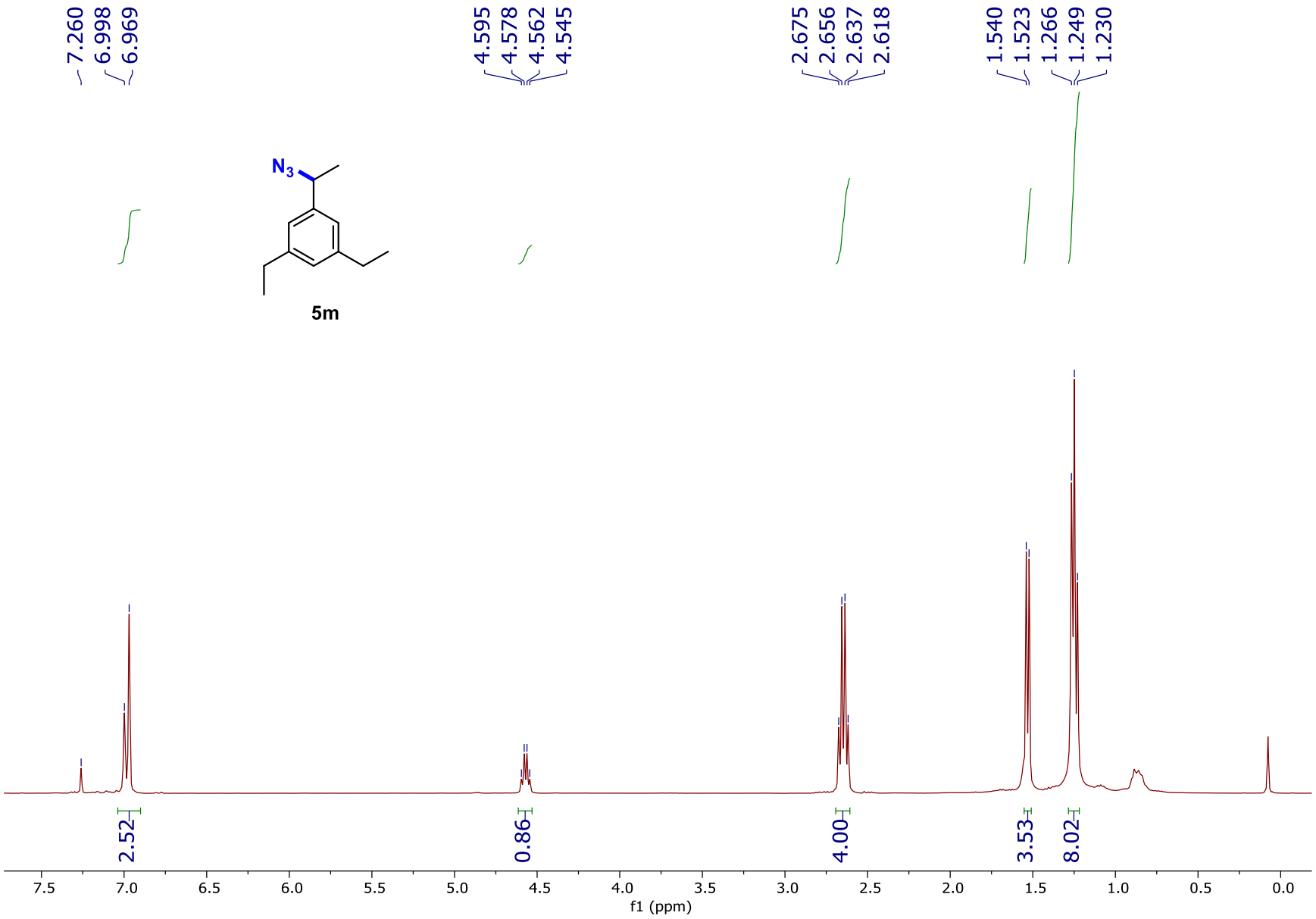
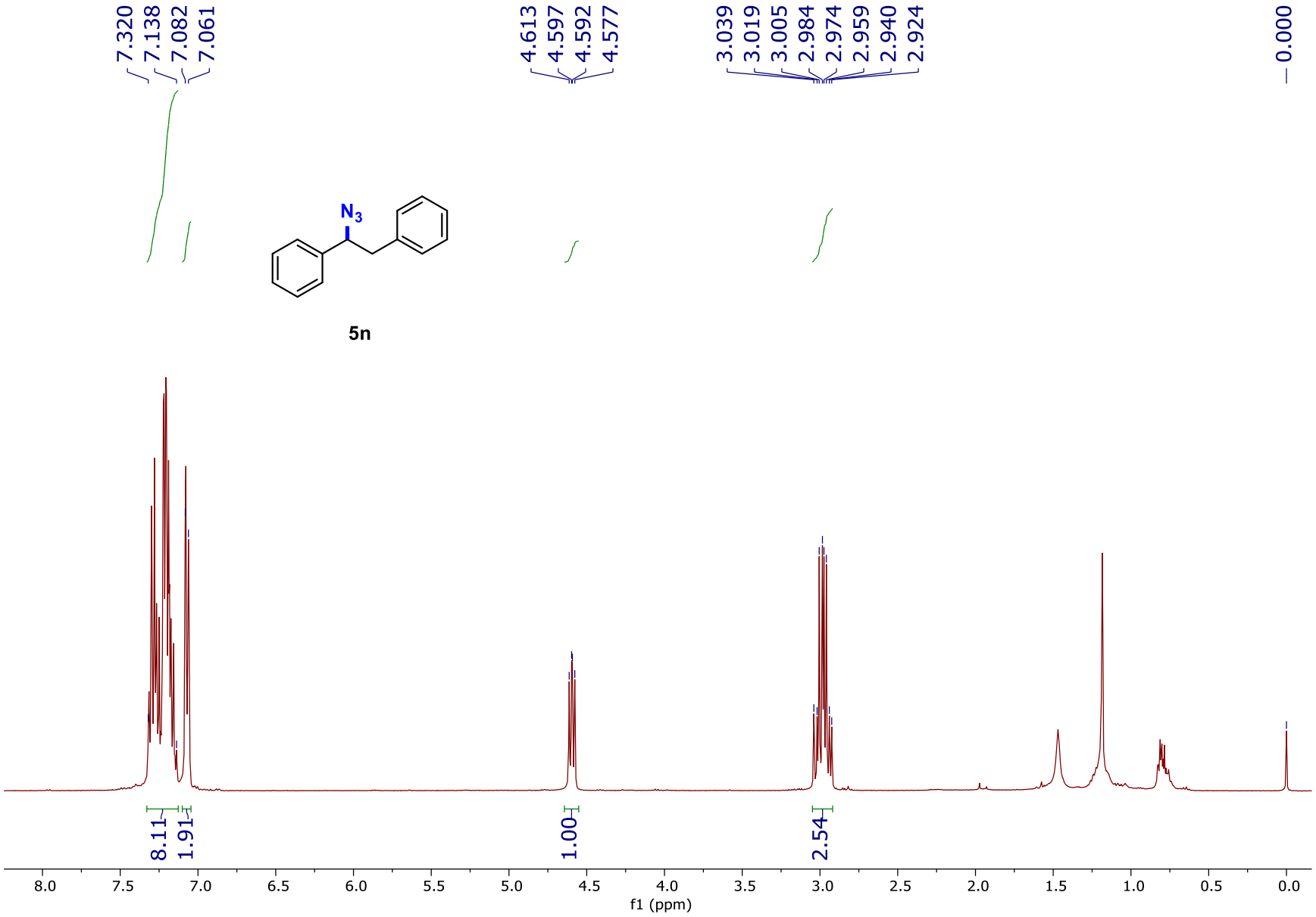
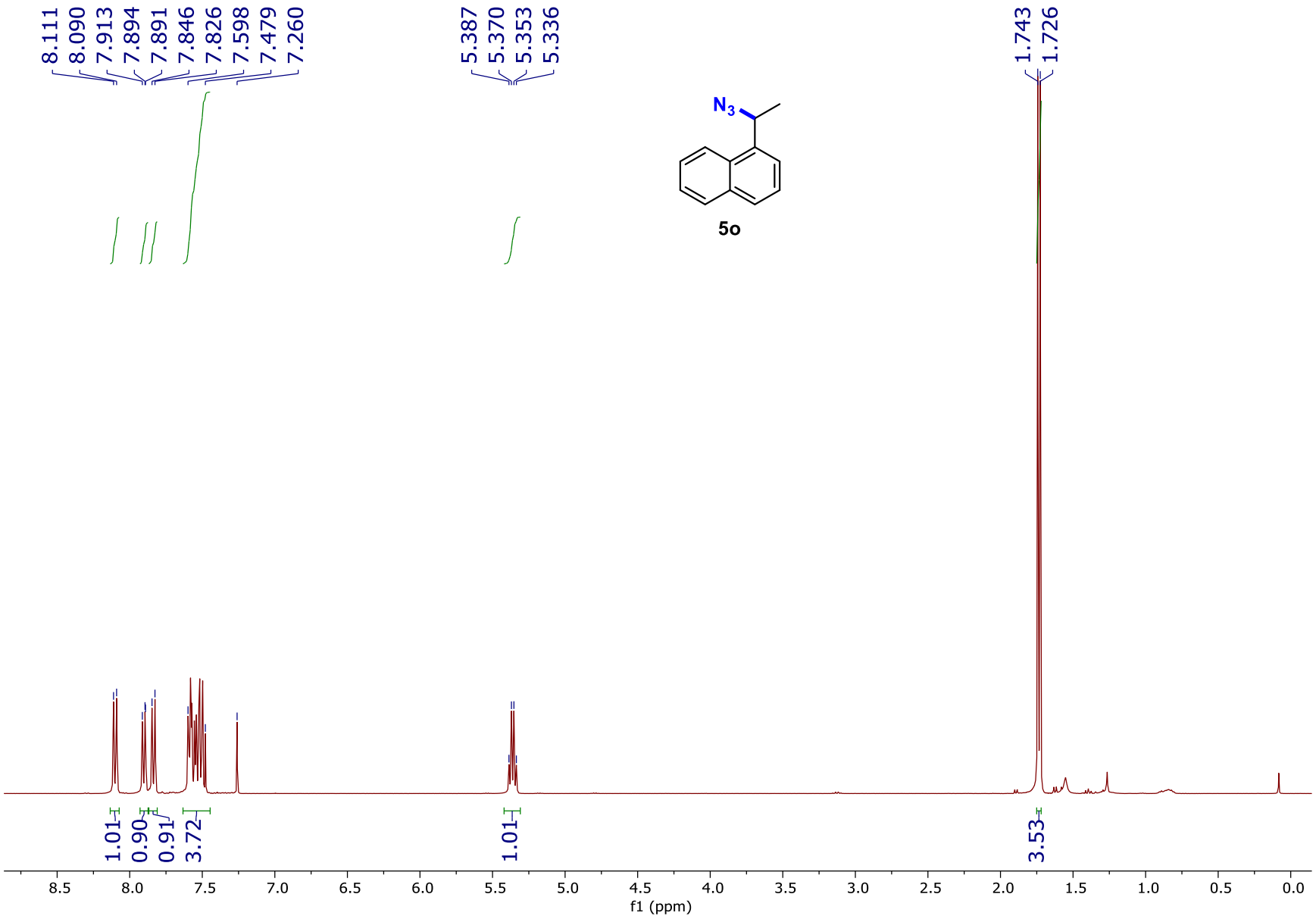
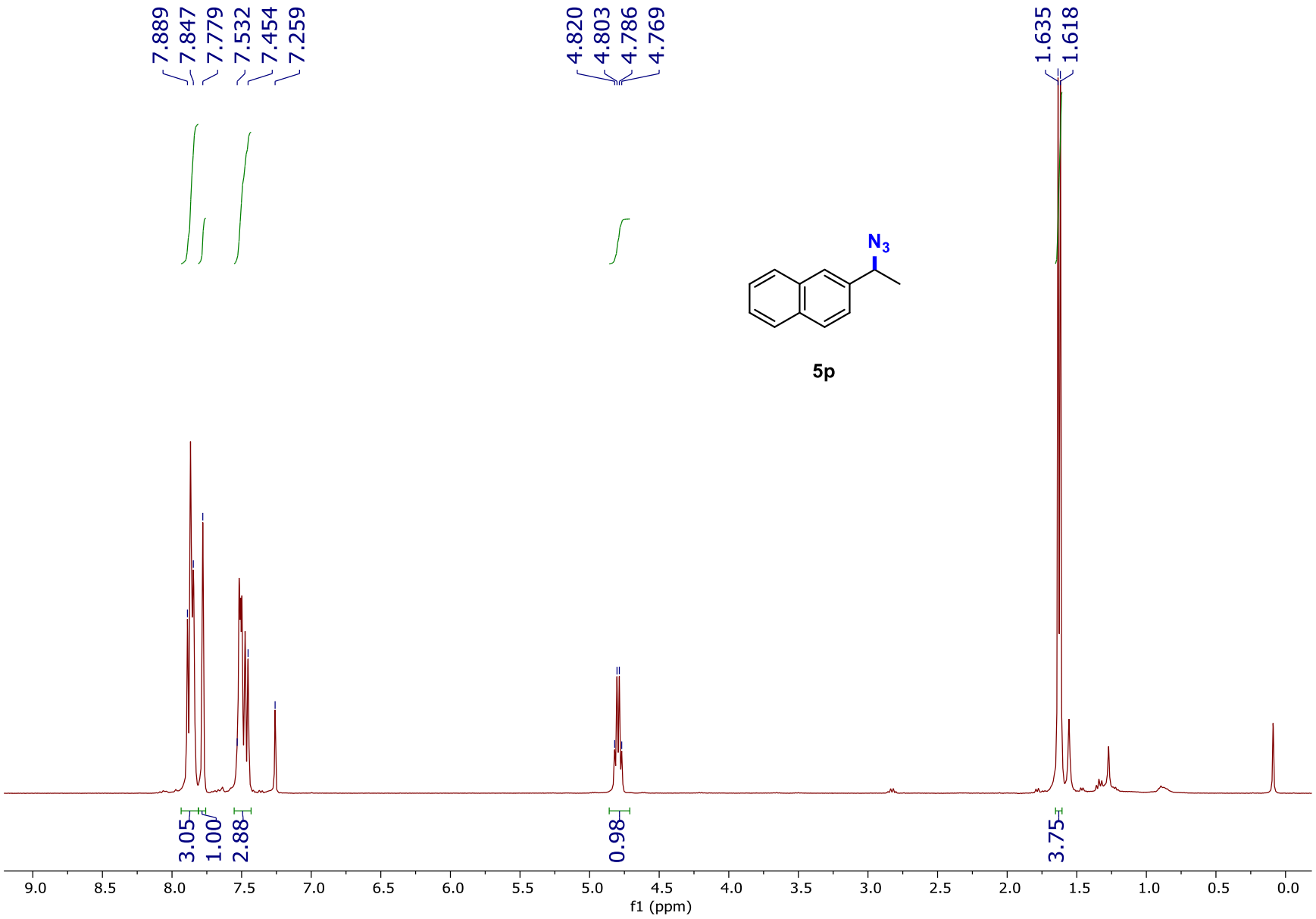
6.990
6.960
6.954
6.940
6.933
4.613
4.595
4.578
4.561
1.523
1.506
PhO
N3
5l
3.01
1.04
4.04
0.98
1.00
3.45
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

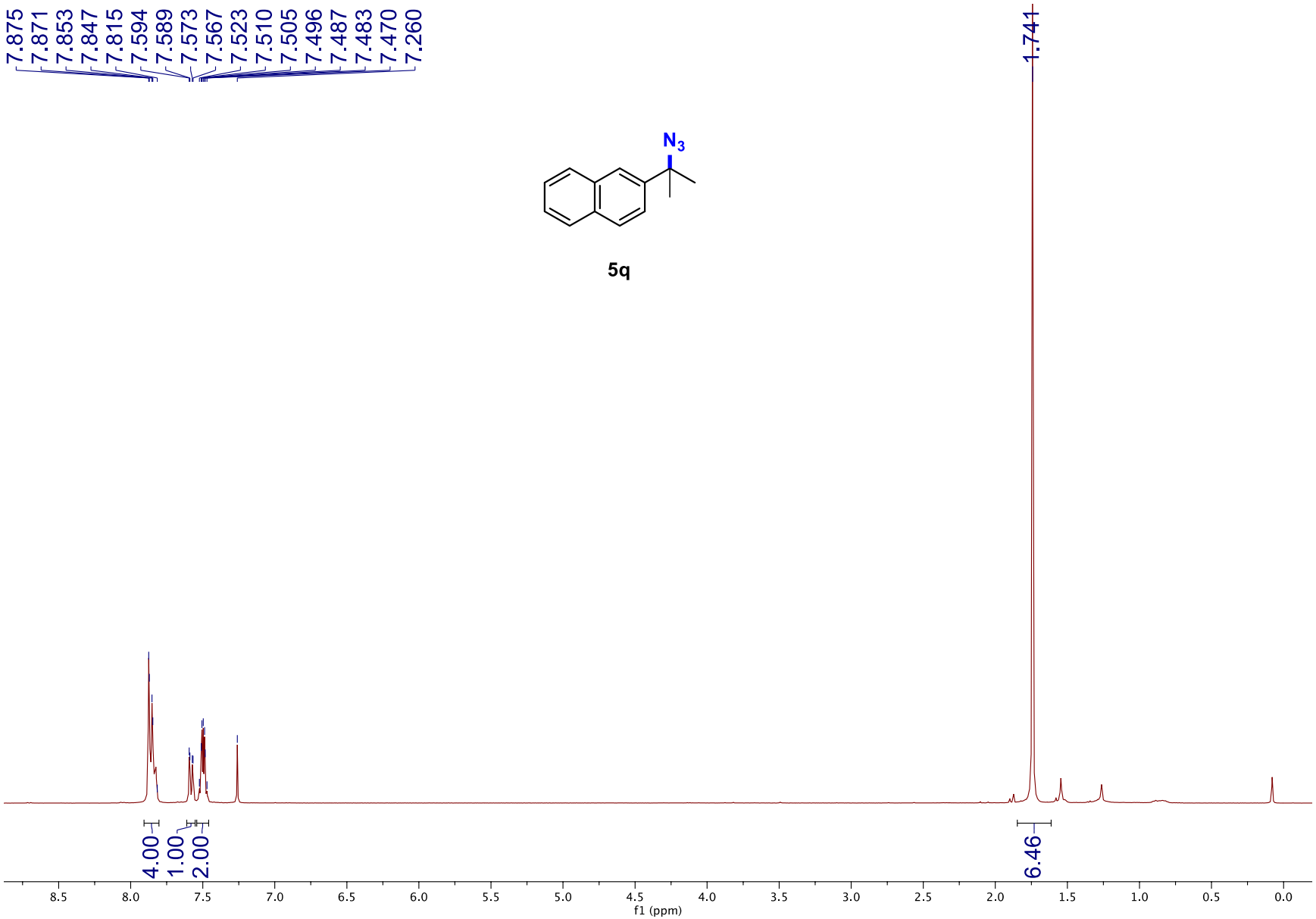

157.811
157.026
143.056
130.245
129.974
123.648
121.220
119.174
118.401
116.904
77.478
77.160
76.842
60.881
21.679
PhO
N3
5l
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


7.260
6.998
6.969
4.595
4.578
4.562
4.545
2.675
2.656
2.637
2.618
1.540
1.523
1.266
1.249
1.230
N3
5m
2.52
0.86
4.00
3.53
8.02
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)

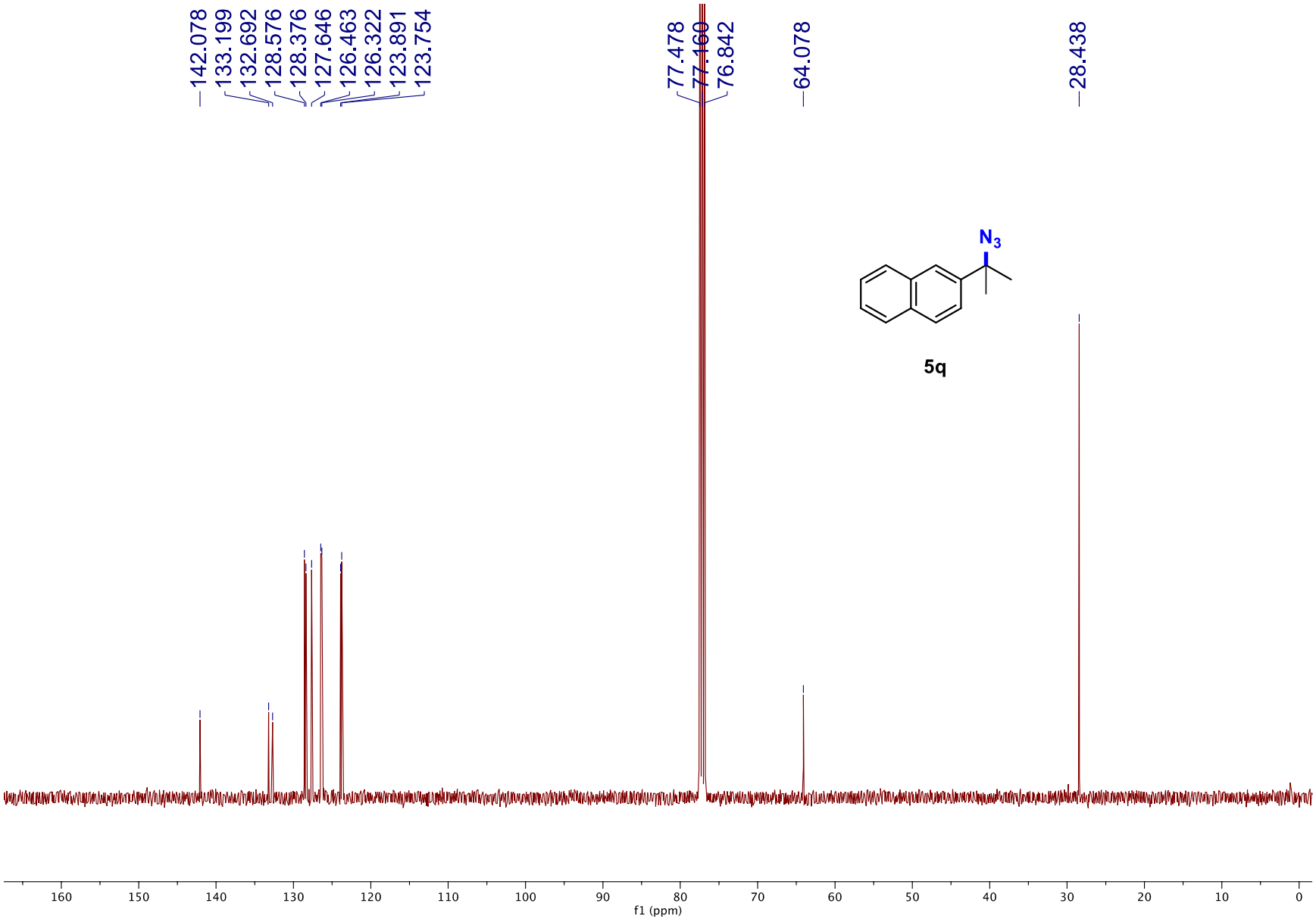

7.320
7.138
7.082
7.061
4.613
4.597
4.592
4.577
3.039
3.019
3.005
2.984
2.974
2.959
2.940
2.924
0.000
N3
5n
8.11
1.91
1.00
2.54
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

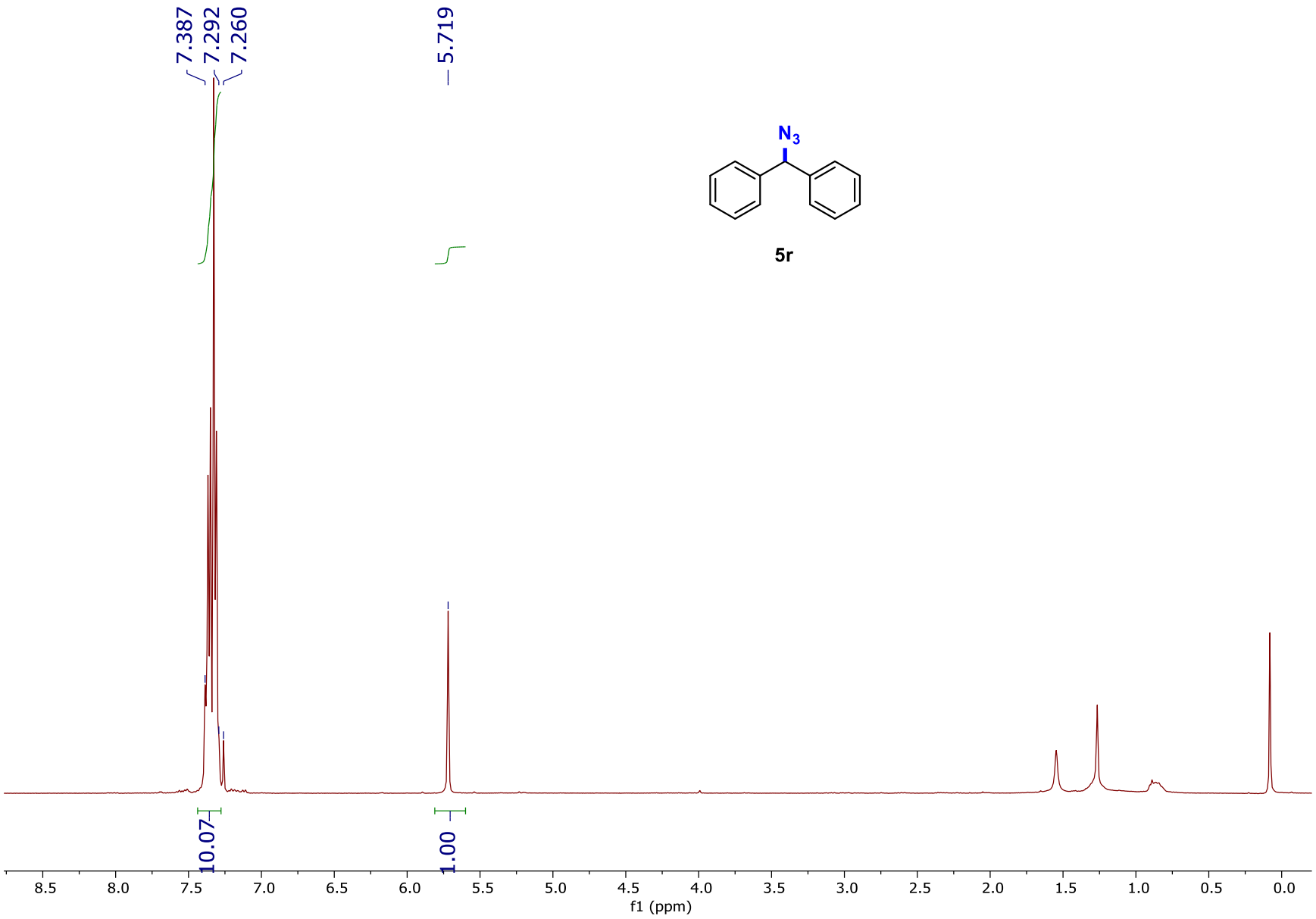

8.111
8.090
7.913
7.894
7.891
7.846
7.826
7.598
7.479
7.260
5.387
5.370
5.353
5.336
1.743
1.726
N3
5o
1.01
0.90
0.91
3.72
1.01
3.53
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

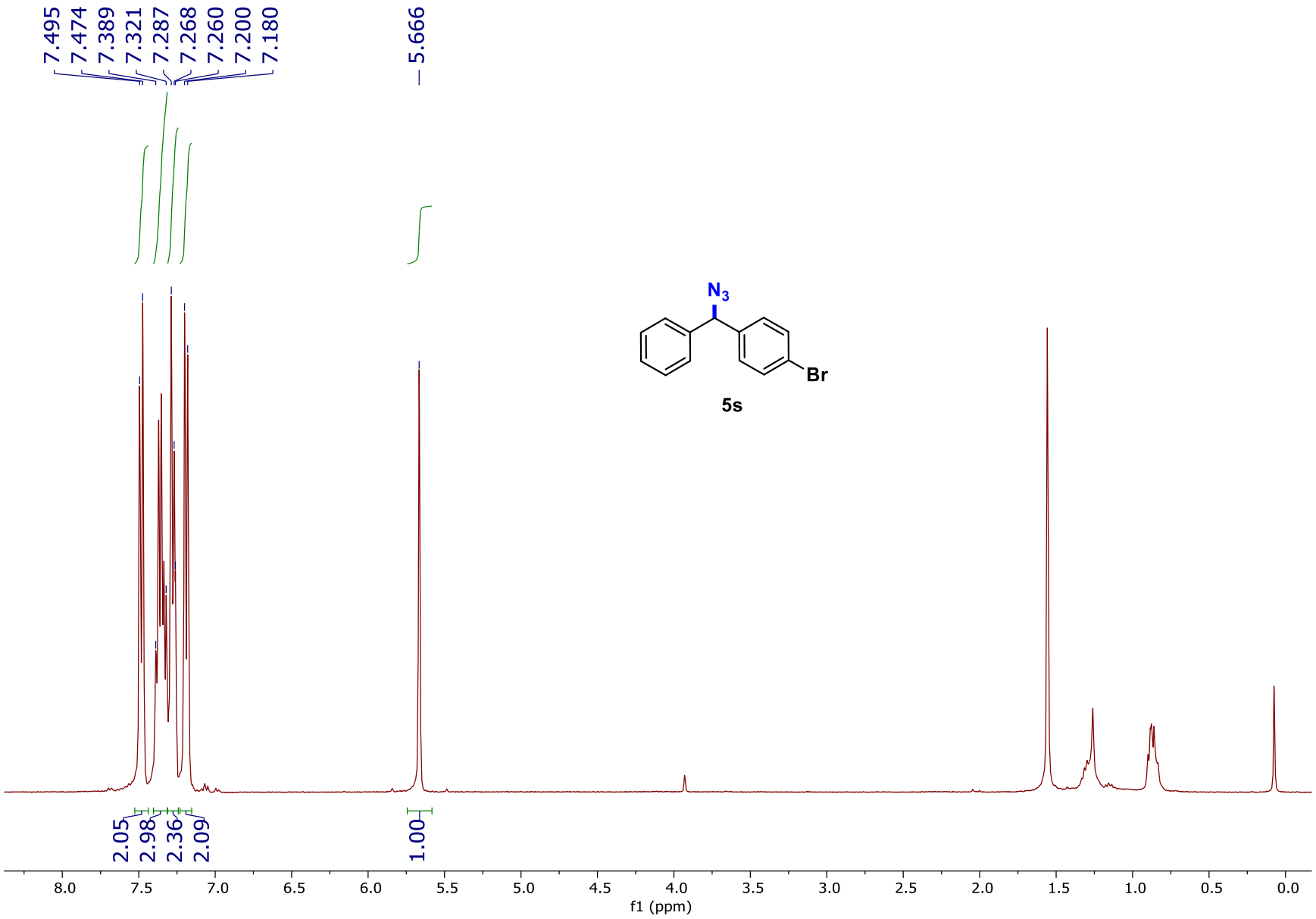

7.889
7.847
7.779
7.532
7.454
7.259
4.820
4.803
4.786
4.769
1.635
1.618
N3
5p
3.05
1.00
2.88
0.98
3.75
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

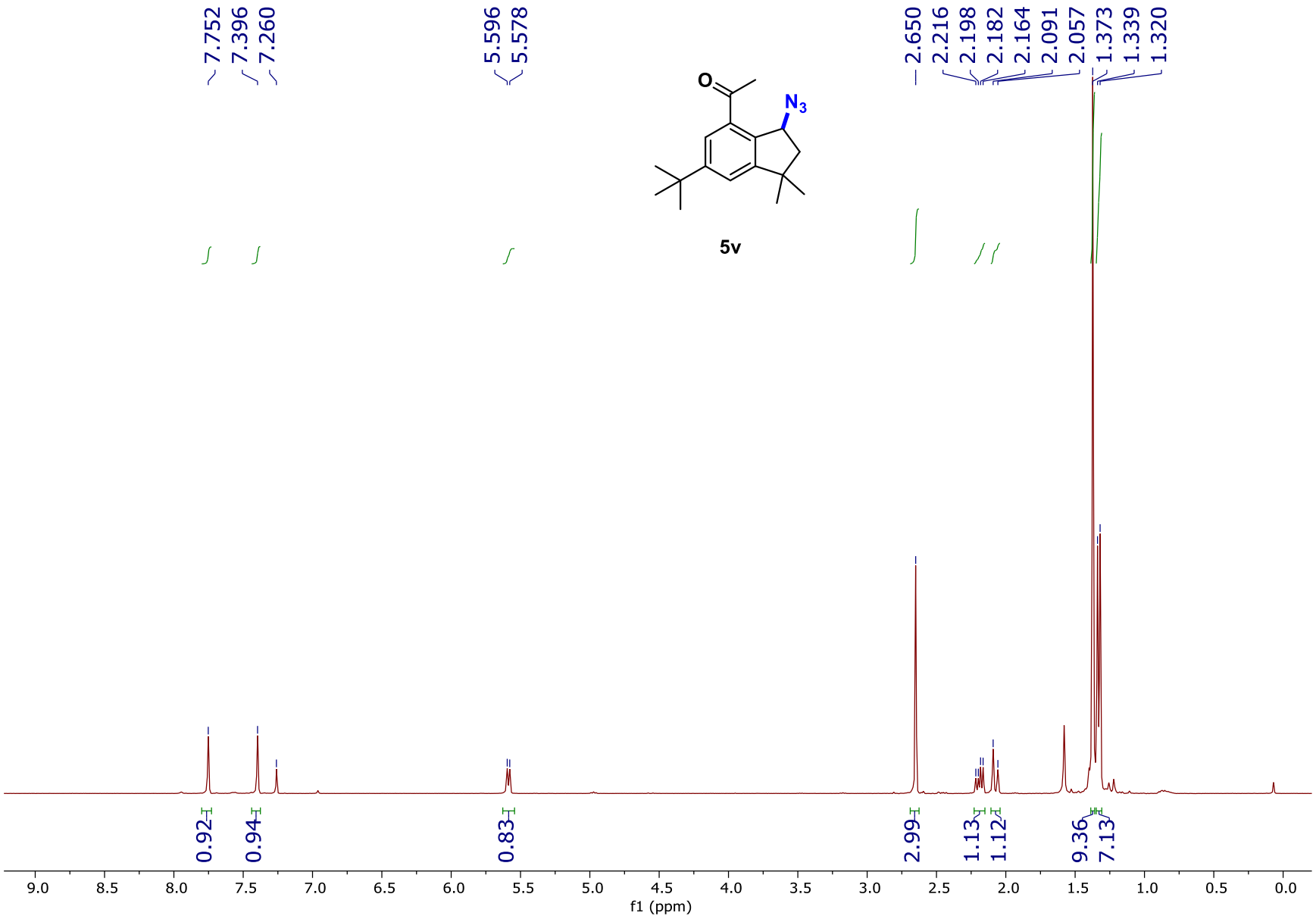

7.875
7.871
7.853
7.847
7.815
7.594
7.589
7.573
7.567
7.523
7.510
7.505
7.496
7.487
7.483
7.470
7.260
1.741
N3
4.00
1.00
2.00
6.46
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

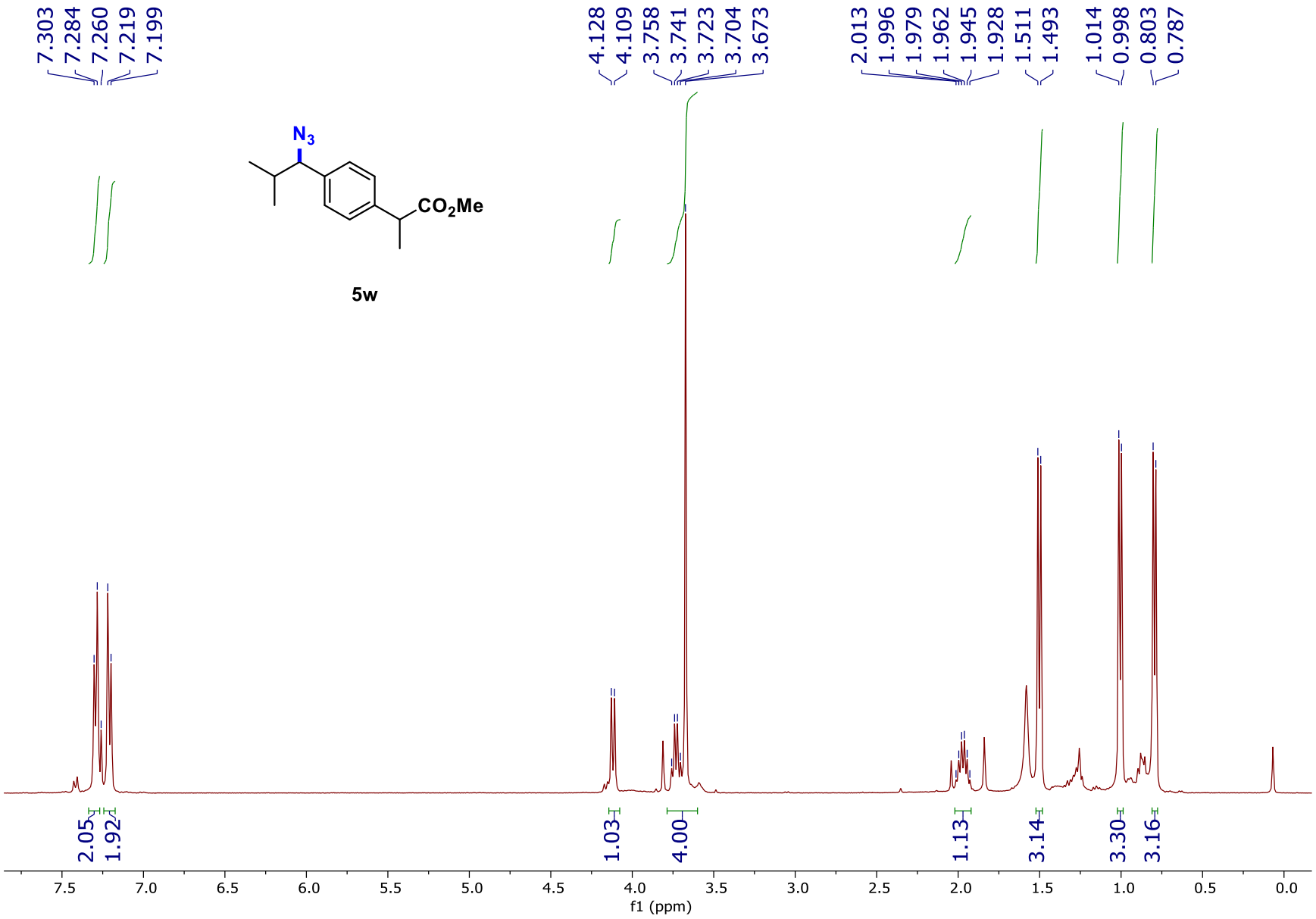
5q

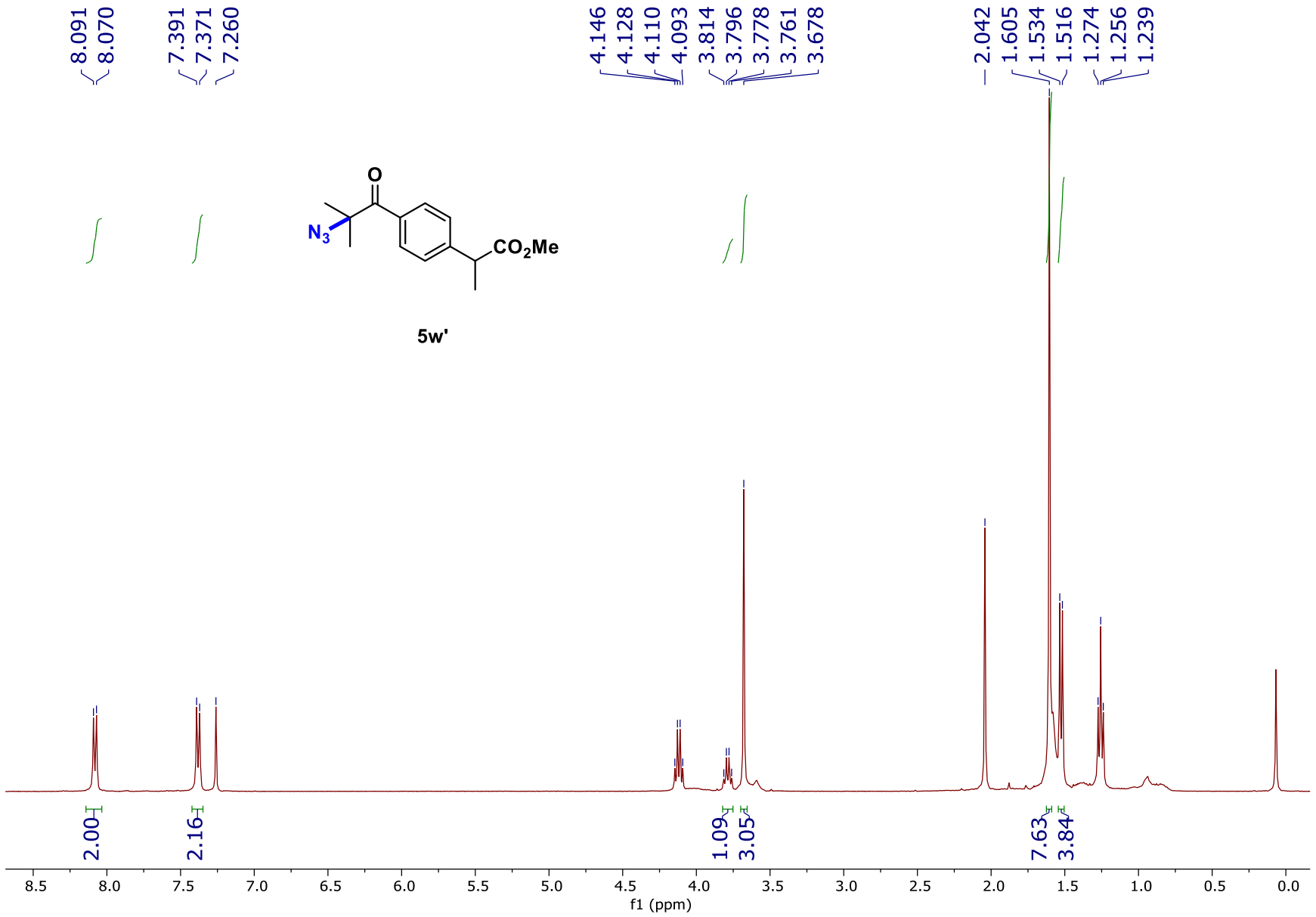

142.078
133.199
132.692
128.576
128.376
127.646
126.463
126.322
123.891
123.754
77.478
77.160
76.842
64.078
28.438
N3
5q
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

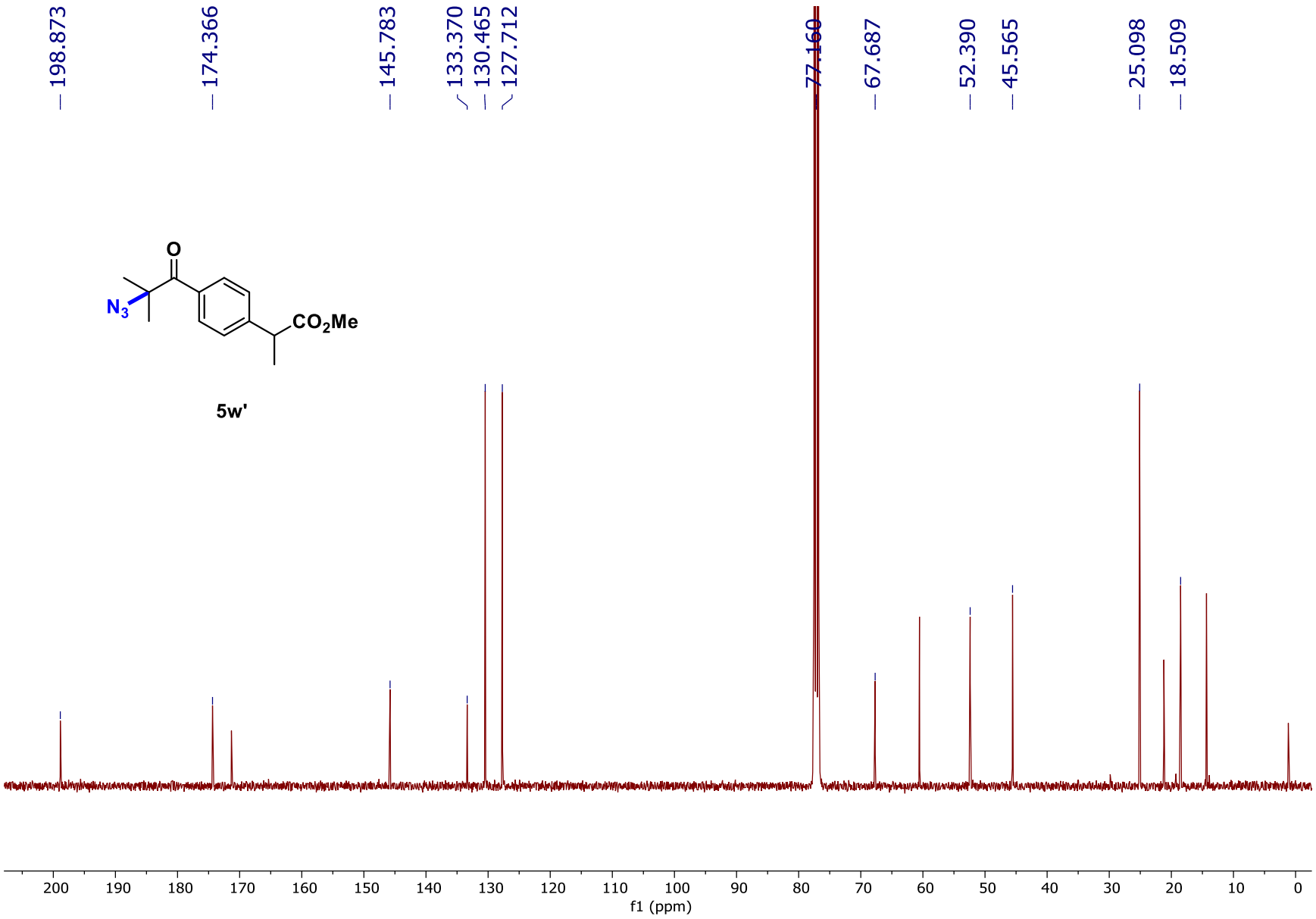

7.387
7.292
7.260
5.719
N3
5r
10.07
1.00
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


7.495
7.474
7.389
7.321
7.287
7.268
7.260
7.200
7.180
5.666
N3
Br
5s
2.05
2.98
2.36
2.09
1.00
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)


7.752
7.396
7.260
5.596
5.578
2.650
2.216
2.198
2.182
2.164
2.091
2.057
1.373
1.339
1.320
O
N3
5v
0.92
0.94
0.83
2.99
1.13
1.12
9.36
7.13
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)

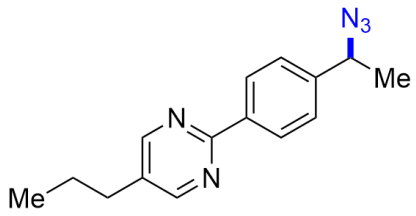

7.303
7.284
7.260
7.219
7.199
4.128
4.109
3.758
3.741
3.723
3.704
3.673
2.013
1.996
1.979
1.962
1.945
1.928
1.511
1.493
1.014
0.998
0.803
0.787
N3
CO2Me
5w
2.05
1.92
1.03
4.00
1.13
3.14
3.30
3.16
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


8.091
8.070
7.391
7.371
7.260
4.146
4.128
4.110
4.093
3.814
3.796
3.778
3.761
3.678
2.042
1.605
1.534
1.516
1.274
1.256
1.239
O
N3
CO2Me
5w'
2.00
2.16
1.09
3.05
7.63
3.84
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)

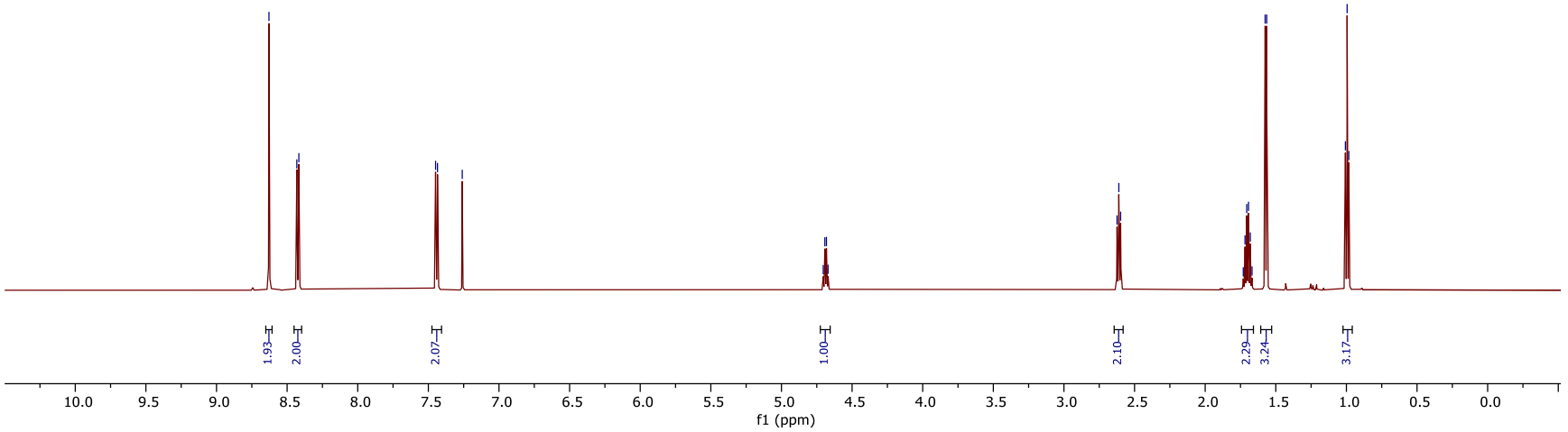

198.873
174.366
145.783
133.370
130.465
127.712
77.160
67.687
52.390
45.565
25.098
18.509
O
N3
CO2Me
5w'
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

GJ-RGA-140.1.fid

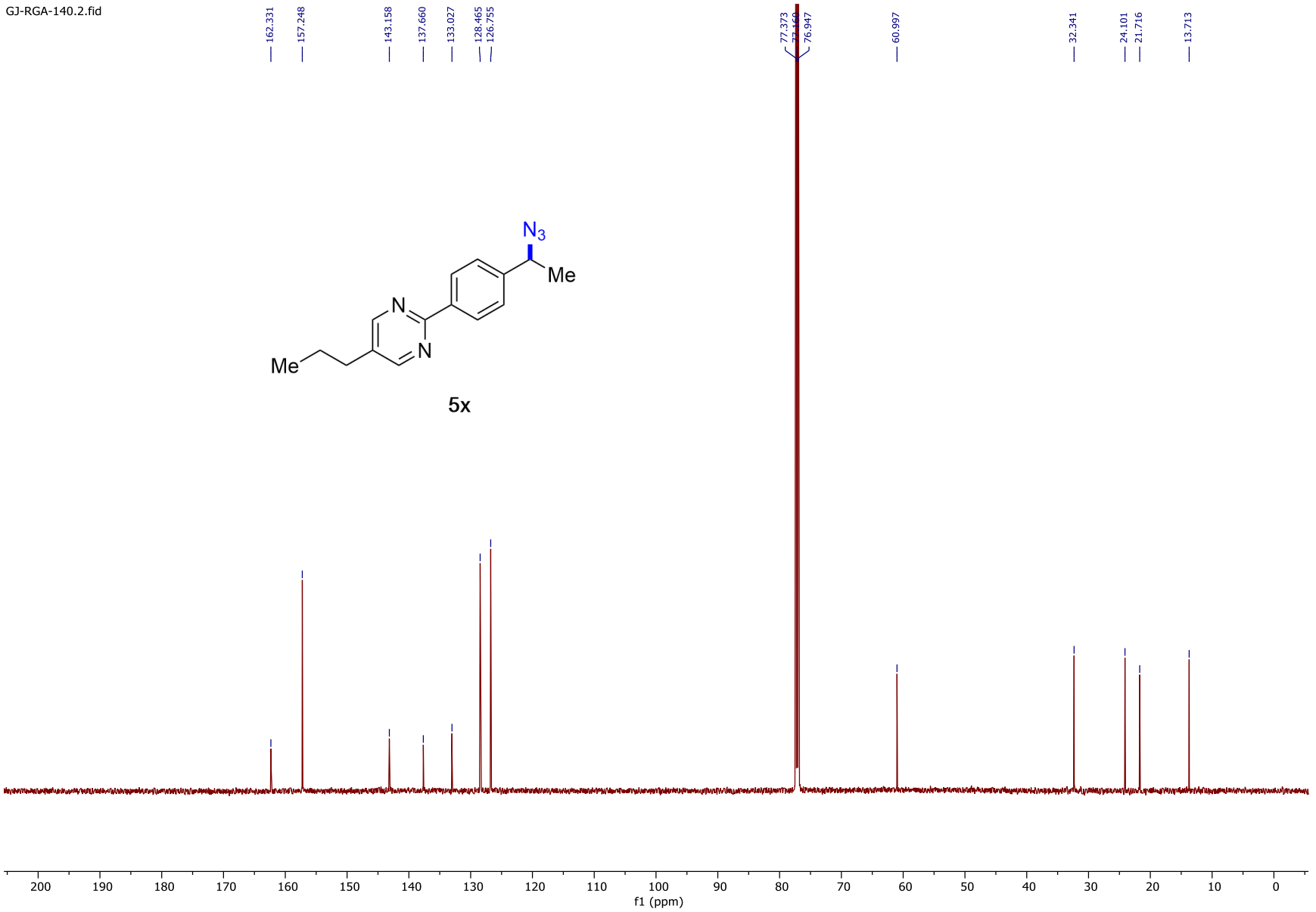
8.628
8.431
8.417
7.449
7.435
7.260
4.704
4.693
4.682
4.670
2.624
2.611
2.599
1.730
1.718
1.706
1.693
1.681
1.668
1.576
1.564
1.007
0.995
0.983



5x



GJ-RGA-140.2.fid



5x