Supporting Information

Rhodium(III) Catalyzed Anti-Markovnikov Hydroamidation of Unactivated Alkenes Using Dioxazolones as Amidating Reagents

Noah Wagner-Carlberg, Tomislav Rovis*

Email: tr2504@columbia.edu

Department of Chemistry, Columbia University, New York, New York, 10027

Contents

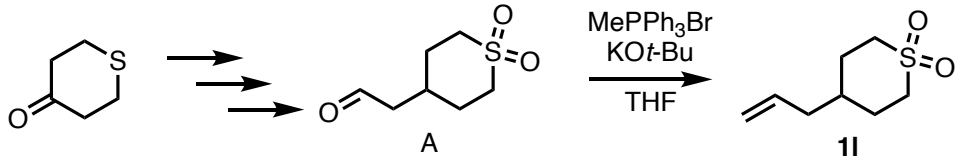
1. General Information

All glassware was used without oven or flame-drying unless otherwise stated. Anhydrous solvents and reagents were purchased from commercial sources and used without further purification. Flash chromatography was conducted either manually on SiliCycle® SilicaFlash® P60 (230- 400 mesh) silica gel, or automatically with Teledyne Isco Lumen CombiFlash, using RediSep Rf Disposable Flash columns. Thin layer chromatography (TLC) was performed on Silicycle 250μm silica gel 60 Å plates. Visualization was accomplished with UV light (254 nm) and KMnO4 or phosphomolybdic acid stains. The majority of products proved difficult to visualize on TLC, so were purified using the CombiFlash with evaporative light scattering detection. 1H, 19F NMR, and 13C NMR spectra were collected at ambient temperature on Bruker 400 MHz or Bruker Avance III 500 MHz spectrometers unless otherwise noted. Chemical shifts (δ) are reported in parts per million (ppm), coupling constants (J) are reported in Hz, and multiplicity is described using the following abbreviations: singlet (s), broad (b), multiplet (m), doublet (d), triplet (t), quartet (q), or combinations thereof. 1H NMR spectra were referenced to 7.26 ppm (CHCl3) or 0.0 ppm (TMS). 13C NMR spectra were referenced to 77.16 ppm (CDCl3) and all peaks given are singlet unless otherwise noted. High resolution mass spectra (HRMS) were obtained from Columbia University Mass Spectrometry Facility on a JOEL JMSHX110HF mass spectrometer using the ASAP ionization model.

2. Preparation of Starting Materials

$[Cp^{*CF3}RhCl_2]_2$ was prepared according to a literature procedure.[1] All dioxazolones were prepared according to literature procedures.[2,3] Alkenes **1a**, **1d**, **1i**, **1j**, **1o**, **1r**, **1s**, **1t**, **1u**, **1w**, **1x**, **1y**, **1z**, **1aa**, **1ab**, **1ac**, **1ad**, **1ae**, **1af**, **1ag**, **1ak**, and **1al** were purchased from commercial sources and used without purification. Alkenes **1e**, **1g**, **1h**, **1k**, **1l**, and **1q** were prepared according to procedures previously reported or referenced by our group.[4] Alkenes **1b**[5], **1c**[6], **1f**[7], **1m**[8], **1n**[9], **1p**[10], **1ai**, **3aj**[11], and **3ah**[12] were also prepared according to literature procedures.

Synthesis of 4-allyltetrahydro-2*H*-thiopyran 1,1-dioxide (1l)



The intermediate aldehyde A was prepared from commercially available tetrahydro-4*H*-thiopyran-4-one in five steps according to a literature procedure.[13]
Aldehyde A was converted to **1l** using a literature procedure for the synthesis of allyl cyclohexanes, and was isolated in 57% yield by column chromatography (20-33% EtOAc in Hexanes)[4].

^{1}H NMR: (500 MHz, $CDCl_3$) δ 5.75 (ddt, *J* = 17.3, 10.3, 7.1 Hz, 1H), 5.13 – 5.03 (m, 2H), 3.11 – 3.02 (m, 2H), 3.01 – 2.91 (m, 2H), 2.17 – 2.07 (m, 4H), 1.93 – 1.80 (m, 2H), 1.68 – 1.56 (m, 1H).

^{13}C NMR: (126 MHz, $CDCl_3$) δ 135.37, 117.48, 50.96, 39.48, 35.11, 29.62.

3. General Procedure for the Hydroamidation of Alkenes

To a 1.5-dram vial with magnetic stir bar were added 3.6 mg $[Cp^{*CF3}RhCl_2]_2$ (0.005 mmol, 5 mol%), and 15.2 mg K_2CO_3 (0.11 mmol, 1.1 equiv.) under air. To a second 1.5-dram vial were added alkene (0.1 mmol, 1 equiv.) and dioxazolone* (0.5 mmol, 5 equiv.) under air. In an argon atmosphere glovebox, the alkene and dioxazolone were dissolved in 200 μL of dry DCE, and the resulting solution was transferred to the vial containing $[Cp^{*CF3}RhCl_2]_2$ and K_2CO_3. 50 μL of dry *i*-PrOH were then added to this vial, and it was sealed by a screw cap with PTFE septum. Soon after the addition of *i*-PrOH, the reaction mixture darkened in color to a deep red. The vial was removed from the glovebox and heated to 70 ºC in a heating block for two hours, with stirring.

The reaction was then removed from heat and quenched by the addition of about 1 mL of EtOAc. Successful reactions generally exhibited pressure buildup due to the evolution of CO_2. This solution was filtered through a short celite plug, and the vial was rinsed with two further 1 mL portions of EtOAc that were also filtered through the plug. The plug was then flushed with one final portion of EtOAc. The filtrate was concentrated by rotary evaporator and a crude ^1H NMR spectrum was taken using $CDCl_3$ as solvent and 0.1 mmol mesitylene as internal standard.

Purification of the products was carried out using Teledyne Isco Lumen CombiFlash, and 4 g RediSep Rf Disposable Flash columns. Hexanes/EtOAc or hexanes/acetone was used as eluent, and linear gradients from pure hexanes to the desired solvent ratio were generally used.

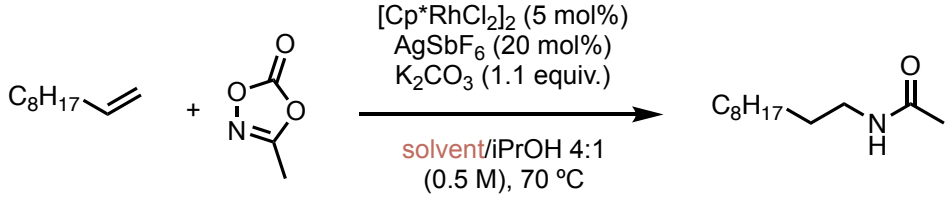
*Note: dioxazolones that are solid at room temperature were instead weighed into the vial containing $[Cp^{*CF3}RhCl_2]_2$ and K_2CO_3.

4. Detailed Optimization Information

Please note: these optimization studies reflect the chronological order of experimentation, and as such, the conditions for each screen may be different from the standard conditions, which impacts the yields as well. Also note that all reactions prior to the time screen were run for 20 h, and at this length there was sometimes inconsistency in the yield.

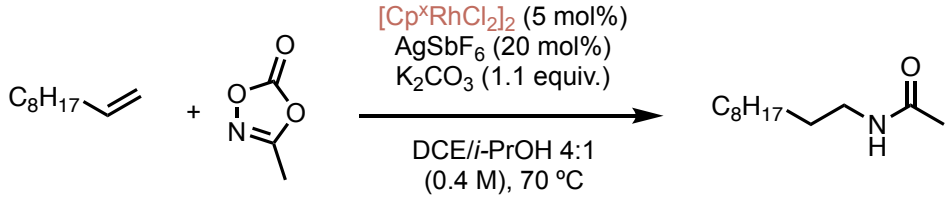
All optimization reactions do not deviate from the general procedure detailed in **Section 3**, other than in the identity of the catalyst, base, etc. The major exception to this is reactions with $AgSbF_6$. In those cases, after all other components were weighed into their respective vials, $AgSbF_6$ was weighed into the vial containing $[Cp^{*CF3}RhCl_2]_2$ and K_2CO_3 in an argon atmosphere glovebox. Then, the standard procedure for DCE transfer and *i*-PrOH addition was carried out as usual.

Table S1. Solvent screening



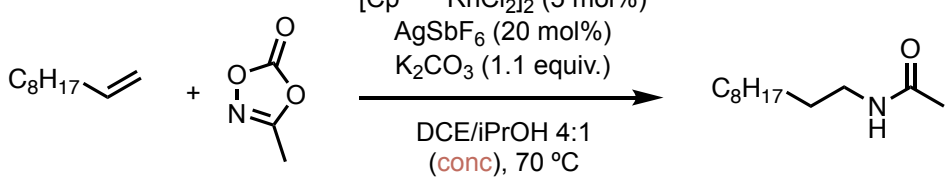
Solvent	Yield
DCE	25%
MeCN	6%
THF	15%
TFE	ND
$CHCl_3$	16%
toluene	14%

Table S2. Catalyst screening



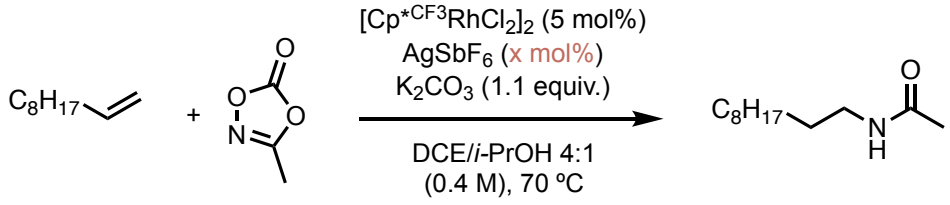
Rhodium catalyst	Yield
Cp^*	25%
Cp^t	3%
Cp^E	25%
Cp^{3M}	6%
Cp^{Ind*}	10%
Cp^{*CF3}	29%
Cp^{Me}	8%
Cp^{*tBu}	2%
$Cp^{PhbisCF3}$	ND
Cp^{TM}	7%

Table S3. Concentration screening



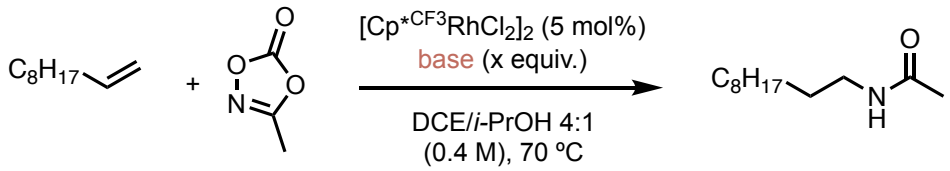
Concentration	Yield
0.5 M	29%
0.4 M	43%
0.3 M	14%
0.2 M	20%
0.1 M	14%

Table S4. Silver loading screening



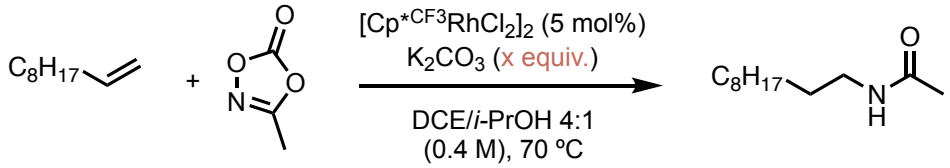
$AgSbF_6$ loading	Yield
20 mol%	25%
15 mol%	56%
10 mol%	62%
5 mol%	61%
—	72%

Table S4. Base screening



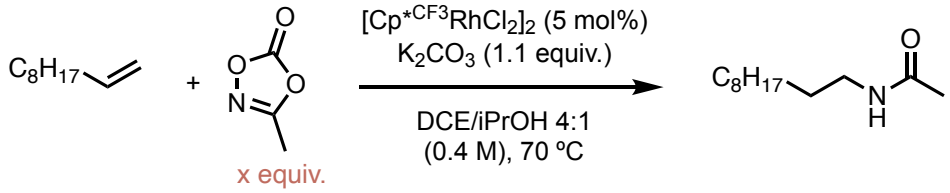
Base	Yield
Li_2CO_3	69%
Na_2CO_3	75%
K_2CO_3	78%
NaOAc	47%
KOAc	34%

Table S5. Base loading screening



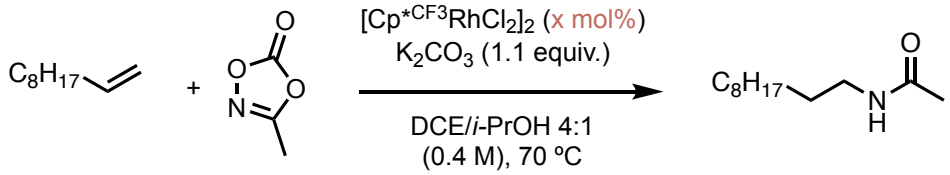
K_2CO_3 loading	Yield
0.7 equiv.	64%
0.9 equiv.	71%
1.1 equiv.	74%
1.3 equiv.	60%

Table S6. Dioxazolone loading screening



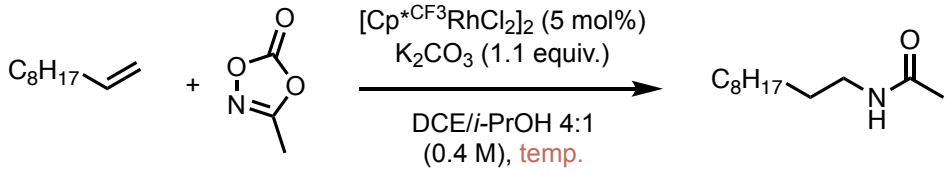
Dioxazolone loading	Yield
5 equiv.	78%
4 equiv.	69%
3 equiv.	61%
2 equiv.	55%

Table S7. Catalyst loading screening



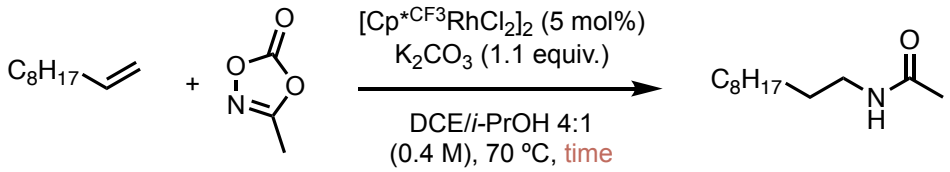
Rh loading	Yield
5 mol%	59%
4 mol%	43%
3 mol%	39%
2 mol%	25%
1 mol%	<5%

Table S8. Reaction temperature screening



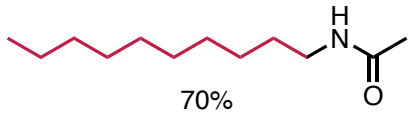
Temperature	Yield
rt (~20 °C)	55%
30 °C	53%
40 °C	55%
60 °C	67%
70 °C	78%
80 °C	75%

Table S9. Reaction time screening



Time	Yield
1 h	65%
2 h	79%
4 h	71%

5. Product Characterization



70%

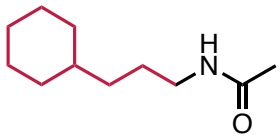
White solid

Spectral data match the literature.[14]

^{1}H NMR: (500 MHz, $CDCl_3$) δ 5.47 (br s, 1H), 3.25 (td, *J* = 7.3, 5.8 Hz, 2H), 1.99 (s, 3H), 1.51 (p, *J* = 7.3 Hz, 2H), 1.38 – 1.22 (m, 14H), 0.90 (t, *J* = 7.0 Hz, 3H).

^{13}C NMR: (126 MHz, $CDCl_3$) δ 169.93, 39.71, 31.88, 29.63, 29.54, 29.29, 26.93, 23.38, 22.67, 14.10.

Purification: elutes at 40% EtOAc



3a
71%

Pale yellow oil

^{1}H NMR: (500 MHz, $CDCl_3$) δ 5.46 (br s, 1H), 3.24 (td, *J* = 7.3, 5.7 Hz, 2H), 1.99 (s, 3H), 1.75 – 1.61 (m, 5H), 1.57 – 1.46 (m, 2H), 1.32 – 1.09 (m, 6H), 0.94 – 0.83 (m, 2H).

^{13}C NMR: (126 MHz, $CDCl_3$) δ 169.97, 40.03, 37.38, 34.60, 33.32, 26.98, 26.63, 26.33, 23.38.

HRMS-ESI (positive): M = $C_{11}H_{21}NO$, calculated (M+H) m/z: 184.1701, found: 184.1702

Purification: elutes at 35% EtOAc

3b
64%

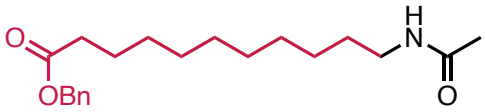
Colorless oil

^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.73 – 7.65 (m, 4H), 7.48 – 7.37 (m, 6H), 5.45 (br s, 1H), 3.68 (t, *J* = 6.4 Hz, 2H), 3.24 (td, *J* = 7.2, 5.7 Hz, 2H), 1.98 (s, 3H), 1.63 – 1.54 (m, 2H), 1.50 (m, 2H), 1.40 (m, 2H), 1.35 – 1.27 (m, 2H), 1.07 (s, 9H).

^{13}C NMR: ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.92, 135.58, 134.12, 129.53, 127.60, 63.81, 39.66, 32.42, 29.62, 26.90, 26.68, 25.53, 23.38, 19.23.

HRMS-ESI (positive): M = $C_{24}H_{35}NO_2Si$, calculated (M+Na) m/z: 420.2335, found: 420.2349

Purification: elutes at 40% EtOAc



3c
72%

White solid

^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.42 – 7.31 (m, 5H), 5.44 (br s, 1H), 5.14 (s, 2H), 3.25 (td, *J* = 7.3, 5.8 Hz, 2H), 2.37 (t, *J* = 7.5 Hz, 2H), 1.99 (s, 3H), 1.66 (p, *J* = 7.5 Hz, 2H), 1.50 (p, *J* = 7.2 Hz, 2H), 1.38 – 1.25 (m, 14H).

^{13}C NMR: (126 MHz, $CDCl_3$) δ 173.70, 169.93, 136.15, 128.55, 128.16, 66.07, 39.69, 34.33, 29.62, 29.41, 29.31, 29.23, 29.18, 29.08, 26.89, 24.93, 23.39.

HRMS-ESI (positive): M = $C_{20}H_{31}NO_3$, calculated (M+H) m/z: 334.2382, found: 334.1954

Purification: elutes at 45% EtOAc

3d
61%

White solid (76% NMR yield)

^{1}H NMR: (500 MHz, $CDCl_3$) δ 5.43 (br s, 1H), 3.66 (t, *J* = 6.7 Hz, 2H), 3.25 (td, *J* = 7.3, 5.8 Hz, 2H), 1.99 (s, 3H), 1.63 – 1.55 (p, 2H), 1.53 (p, *J* = 7.5 Hz, 2H), 1.42 – 1.26 (m, 14H).

^{13}C NMR: (126 MHz, $CDCl_3$) δ 169.95, 63.08, 39.70, 32.80, 29.62, 29.50, 29.45, 29.42, 29.36, 29.23, 26.87, 25.70, 23.39.

HRMS-ESI (positive): M = $C_{13}H_{27}NO_2$, calculated (M+H) m/z: 230.2120, found: 230.2136

Purification: elutes at 70% EtOAc

3e
89%

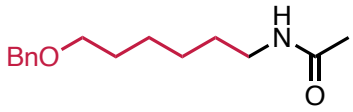
White solid

^{1}H NMR: (500 MHz, $CDCl_3$) δ 5.46 (br s, 1H), 3.27 (td, *J* = 6.9, 5.6 Hz, 2H), 2.00 (s, 3H), 1.95 – 1.78 (m, 6H), 1.76 – 1.63 (m, 7H), 1.57 – 1.41 (m, 6H).

^{13}C NMR: (126 MHz, $CDCl_3$) δ 169.91, 44.15, 40.03, 39.24, 38.39, 31.83, 31.61, 29.86, 28.29, 28.07, 27.77, 23.41.

HRMS-ESI (positive): M = $C_{15}H_{25}NO$, calculated (M+H) m/z: 236.2014, found: 236.2029

Purification: elutes at 35% EtOAc



3f
72%

Colorless oil

^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.40 – 7.29 (m, 5H), 5.42 (br s, 1H), 4.52 (s, 2H), 3.49 (t, *J* = 6.5 Hz, 2H), 3.25 (td, *J* = 7.2, 5.7 Hz, 2H), 1.98 (s, 3H), 1.69 – 1.59 (m, 2H), 1.58 – 1.48 (m, 2H), 1.47 – 1.31 (m, 4H).

^{13}C NMR: ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.93, 138.64, 128.37, 127.64, 127.52, 72.91, 70.28, 39.60, 29.64, 29.58, 26.74, 25.92, 23.38.

HRMS-ESI (positive): M = $C_{15}H_{23}NO_2$, calculated (M+H) m/z: 250.1807, found: 250.1817

Purification: elutes at 40% EtOAc

3g
70%

White solid

^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.89 – 7.82 (m, 2H), 7.72 (dd, *J* = 5.7, 3.1 Hz, 2H), 5.40 (br s, 1H), 3.70 (t, *J* = 7.3 Hz, 2H), 3.25 (q, *J* = 6.7 Hz, 2H), 1.98 (s, 3H), 1.71 (p, *J* = 7.2 Hz, 2H), 1.51 (p, *J* = 6.5 Hz, 2H), 1.44 – 1.10 (m, 14H).

^{13}C NMR: (126 MHz, $CDCl_3$) δ 169.73, 168.35, 133.72, 132.31, 123.07, 39.68, 38.07, 29.62, 29.46 – 29.24 (m), 29.17, 29.04, 28.50, 26.85, 26.78, 23.23.

HRMS-ESI (positive): M = $C_{21}H_{30}N_2O_3$, calculated (M+H) m/z: 359.2335, found: 359.2347

Purification: elutes at 60% EtOAc

3h
60%

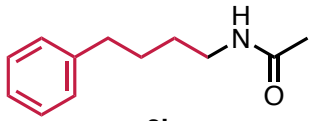
White solid

^{1}H NMR: (500 MHz, $CDCl_3$) δ 5.44 (br s, 1H), 4.07 (t, *J* = 6.8 Hz, 2H), 3.25 (td, *J* = 7.2, 5.7 Hz, 2H), 2.07 (s, 3H), 1.99 (s, 3H), 1.68 – 1.59 (m, 2H), 1.51 (t, *J* = 7.2 Hz, 2H), 1.41 – 1.25 (m, 14H).

^{13}C NMR: (126 MHz, $CDCl_3$) δ 171.26, 169.93, 64.64, 39.70, 29.63, 29.48, 29.44, 29.26, 29.21, 28.59, 26.90, 25.88, 23.39, 21.02.

HRMS-ESI (positive): M = $C_{15}H_{29}NO_3$, calculated (M+H) m/z: 272.2226, found: 272.2246

Purification: elutes at 50% EtOAc



3i
73%
Colorless oil

Spectral data match the literature.[15]

^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.35 – 7.27 (m, 2H), 7.25 – 7.16 (m, 3H), 5.41 (br s, 1H), 3.28 (td, *J* = 7.2, 5.8 Hz, 2H), 2.66 (t, *J* = 7.6 Hz, 2H), 1.98 (s, 3H), 1.73 – 1.63 (m, 2H), 1.60 – 1.51 (m, 2H).

^{13}C NMR: (126 MHz, $CDCl_3$) δ 169.95, 142.07, 128.40, 128.36, 125.85, 39.50, 35.48, 29.21, 28.66, 23.37.

Purification: elutes at 40% EtOAc

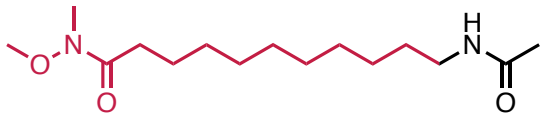
3j
78%
Colorless oil (88% NMR Yield)

^{1}H NMR: (500 MHz, $CDCl_3$) δ 5.48 (br s, 1H), 3.27 (td, *J* = 7.2, 5.9 Hz, 2H), 2.37 (t, *J* = 7.1 Hz, 2H), 2.00 (s, 3H), 1.69 (p, *J* = 7.2 Hz, 2H), 1.59 – 1.46 (m, 4H), 1.46 – 1.34 (m, 2H).

^{13}C NMR: ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.04, 119.72, 39.40, 29.43, 28.32, 26.05, 25.21, 23.39, 17.11.

HRMS-ESI (positive): M = $C_9H_{16}N_2O$, calculated (M+Na) m/z: 191.1160, found: 191.1185

Purification: elutes at 60% EtOAc



3k
49%
White solid

^{1}H NMR: (500 MHz, $CDCl_3$) δ 5.48 (br s, 1H), 3.70 (s, 3H), 3.25 (td, *J* = 7.2, 5.7 Hz, 2H), 3.20 (s, 3H), 2.43 (t, *J* = 7.6 Hz, 2H), 1.99 (s, 3H), 1.63 (m, 2H), 1.50 (m, 2H), 1.38 – 1.26 (m, 12H).

^{13}C NMR: (126 MHz, $CDCl_3$) δ 174.82, 169.95, 61.21, 39.70, 32.18, 31.91, 29.60, 29.41, 29.40, 29.28 (d, *J* = 13.5 Hz), 26.87, 24.62, 23.38.

HRMS-ESI (positive): M = $C_{15}H_{30}N_2O_3$, calculated (M+H) m/z: 287.2335, found: 287.2321

Purification: elutes at 100% EtOAc

3l
78%

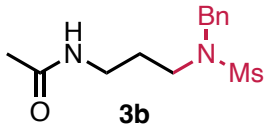
Pale yellow solid

^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.84 – 7.78 (m, 2H), 7.40 – 7.33 (m, 2H), 5.48 (br s, 1H), 4.04 (t, *J* = 6.5 Hz, 2H), 3.25 (td, *J* = 7.2, 5.7 Hz, 2H), 2.47 (s, 3H), 1.99 (s, 3H), 1.70 – 1.61 (m, 2H), 1.50 (p, *J* = 7.3 Hz, 2H), 1.36 – 1.19 (m, 14H).

^{13}C NMR: (126 MHz, $CDCl_3$) δ 169.97, 144.63, 133.27, 129.80, 127.88, 70.71, 39.69, 29.61, 29.40, 29.32, 29.30, 29.22, 28.85, 28.81, 26.87, 25.30, 23.38, 21.63.

HRMS-ESI (positive): M = $C_{20}H_{33}NO_4S$, calculated (M+H) m/z: 384.2209, found: 384.2220

Purification: elutes at 60% EtOAc



3b
88%

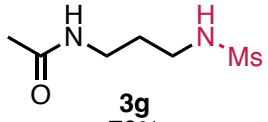
Viscous yellow oil

^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.44 – 7.32 (m, 5H), 6.02 (br s, 1H), 4.40 (s, 2H), 3.31 – 3.20 (m (td and t overlap), 4H), 2.82 (s, 3H), 1.95 (s, 3H), 1.68 – 1.59 (m, 2H).

^{13}C NMR: (126 MHz, $CDCl_3$) δ 170.24, 135.66, 128.91, 128.79, 128.38, 51.68, 44.86, 38.26, 35.57, 27.36, 23.33.

HRMS-ESI (positive): M = $C_{13}H_{20}N_2O_3S$, calculated (M+H) m/z: 285.1273, found: 285.1120

Purification: elutes at 90% EtOAc



3g
70%

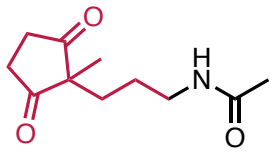
Pale red oil

^{1}H NMR: (500 MHz, $CDCl_3$) δ 5.89 (br s, 1H), 5.39 (br t, 1H), 3.41 (q, *J* = 6.4 Hz, 2H), 3.21 – 3.14 (td, 2H), 2.97 (s, 3H), 2.02 (s, 3H), 1.75 (tt, *J* = 7.5, 5.4 Hz, 2H).

^{13}C NMR: (126 MHz, $CDCl_3$) δ 171.21, 40.33, 39.90, 35.93, 30.51, 23.23.

HRMS-ESI (positive): M = $C_2H_{14}N_2O_3S$, calculated (M+Na) m/z: 217.0623, found: 217.0647

Purification: elutes at 50% acetone



3o
93%

Not isolated

^{1}H NMR: (400 MHz, $CDCl_3$) δ 6.07 (br s, 1H), 3.12 (td, *J* = 6.9, 5.8 Hz, 2H), 2.84 – 2.67 (m, 4H), 1.94 (s, 3H), 1.68 – 1.60 (m, 2H), 1.42 – 1.31 (m, 2H), 1.10 (s, 3H).

3p
82%

Pale yellow oil

^{1}H NMR: (500 MHz, $CDCl_3$) δ 5.46 (br s, 1H), 4.58 (dd, *J* = 4.6, 2.7 Hz, 1H), 3.89 (ddd, *J* = 11.0, 7.2, 3.5 Hz, 1H), 3.75 (dt, *J* = 9.6, 6.8 Hz, 1H), 3.52 (dddd, *J* = 11.0, 5.3, 3.7, 1.4 Hz, 1H), 3.40 (dt, *J* = 9.6, 6.5 Hz, 1H), 3.26 (td, *J* = 7.2, 5.8 Hz, 2H), 1.99 (s, 3H), 1.85 (qd, *J* = 7.5, 3.2 Hz, 1H), 1.77 – 1.69 (m, 1H), 1.69 – 1.49 (m, 8H), 1.49 – 1.32 (m, 4H).

^{13}C NMR: (126 MHz, $CDCl_3$) δ 169.96, 98.97, 67.48, 62.47, 39.62, 30.80, 29.63, 29.57, 26.74, 25.95, 25.49, 23.38, 19.76.

HRMS-ESI (positive): M = $C_{13}H_{25}NO_3$, calculated (M+Na) m/z: 266.1732, found: 266.1745

Purification: elutes at 60% EtOAc

3q
57%

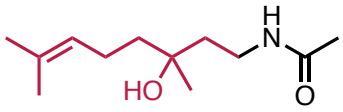
White solid

^{1}H NMR: (500 MHz, $CDCl_3$) δ 5.43 (br s, 1H), 3.43 (t, *J* = 6.8 Hz, 2H), 3.25 (td, *J* = 7.3, 5.8 Hz, 2H), 1.99 (s, 3H), 1.87 (p, *J* = 7.0 Hz, 2H), 1.51 (m, 2H), 1.43 (m, 2H), 1.31 (dd, *J* = 11.8, 6.5 Hz, 12H).

^{13}C NMR: (126 MHz, $CDCl_3$) δ 169.94, 39.70, 34.09, 32.83, 29.64, 29.47, 29.43, 29.39, 29.27, 28.74, 28.16, 26.91, 23.42.

HRMS-ESI (positive): M = $C_{13}H_{26}BrNO$, calculated (M+Na) m/z: 314.1096 and 316.1076, found: 314.1123 and 316.1104

Purification: elutes at 35% EtOAc



3r
52%
from linalool

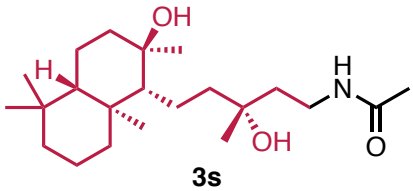
Colorless oil

^{1}H NMR: (500 MHz, $CDCl_3$) δ 6.30 (br s, 1H), 5.14 (dddd, *J* = 7.1, 5.7, 2.9, 1.5 Hz, 1H), 3.51 – 3.33 (m, 2H), 2.12 – 2.02 (m, 2H), 1.98 (s, 3H), 1.78 (s, 1H), 1.75-1.64 (m, 2h), 1.72 (d, *J* = 1.4 Hz, 3H), 1.65 (d, *J* = 1.2 Hz, 3H), 1.58 – 1.53 (m, 2H), 1.25 (s, 3H).

^{13}C NMR: (126 MHz, $CDCl_3$) δ 170.10, 132.28, 123.97, 73.32, 42.31, 39.72, 35.74, 26.75, 25.71, 23.42, 22.73, 17.70.

HRMS-ESI (positive): M = $C_{12}H_{23}NO_2$, calculated (M+Na) m/z: 236.1626, found: 236.1647

Purification: elutes at 40% acetone



3s
71%
from sclareol

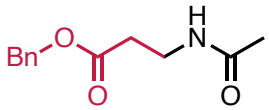
Colorless oil
Note: fresh sclareol from Thermo Fisher appeared to be diasteromerically impure by NMR, and as a result the NMR of the product also shows some peaks corresponding to a different diastereomer. The peaks for which this is most noticeable are the N–H proton at 6.50 ppm and the N–C α-protons at 3.41.

^{1}H NMR: (500 MHz, $CDCl_3$) δ 6.50 (br s, 1H), 3.47 (dq, *J* = 13.6, 6.2 Hz, 1H), 3.32 (dtd, *J* = 13.9, 7.0, 4.5 Hz, 1H), 1.97 (s, 3H), 1.86 (dt, *J* = 12.2, 3.3 Hz, 1H), 1.73 – 1.53 (m, 8H), 1.52-1.32 (m, 5H), 1.31 – 1.26 (m, 1H), 1.23 (s, 3H), 1.21 (s, *J* = 0.9 Hz, 3H), 1.20 – 1.12 (m, 1H), 1.04 – 0.92 (m, 2H), 0.89 (s, 3H), 0.81 (s, 3H), 0.81 (s, 3H).

^{13}C NMR: (126 MHz, $CDCl_3$) δ 170.13, 75.04, 73.47, 61.64, 56.03, 44.80, 44.26, 41.98, 40.67, 39.73, 39.22, 35.95, 33.37, 33.23, 26.07, 24.54, 23.45, 21.49, 20.53, 18.72, 18.40, 15.33.

HRMS-ESI (positive): M = $C_{22}H_{41}NO_3$, calculated (M+Na) m/z: 390.2984, found: 390.2988

Purification: elutes at 40% acetone



3t
63%

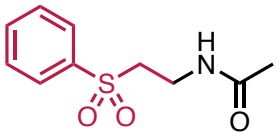
Pale yellow oil

^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.44 – 7.33 (m, 5H), 6.04 (br s, 1H), 5.17 (s, 2H), 3.55 (q, *J* = 6.1 Hz, 2H), 2.65 – 2.59 (m, 2H), 1.96 (s, 3H).

^{13}C NMR: (126 MHz, $CDCl_3$) δ 172.58, 170.03, 135.61, 128.66, 128.44, 128.25, 66.58, 34.91, 34.08, 23.29.

HRMS-ESI (positive): M = $C_{12}H_{15}NO_3$, calculated (M+H) m/z: 244.0950, found: 244.0962

Purification: elutes at 25% acetone



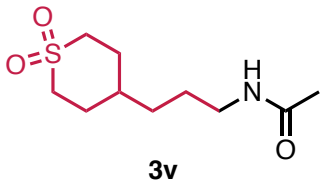
3u
53%
White solid

^{1}H NMR: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.97 – 7.91 (m, 2H), 7.75 – 7.68 (m, 1H), 7.66 – 7.59 (m, 2H), 6.29 (br s, 1H), 3.75 – 3.67 (m, 2H), 3.35 – 3.29 (m, 2H), 1.98 (s, 3H).

^{13}C NMR: ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.28, 138.97, 134.16, 129.58, 127.89, 55.48, 33.34, 23.16.

HRMS-ESI (positive): M = $C_{10}H_{13}NO_3S$, calculated (M+Na) m/z: 250.0514, found: 250.0537

Purification: elutes at 40% acetone



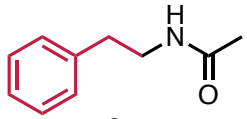
3v
86%
Pale orange solid

^{1}H NMR: (500 MHz, $CDCl_3$) δ 5.54 (br s, 1H), 3.26 (td, *J* = 7.2, 6.0 Hz, 2H), 3.10 – 3.02 (m, 2H), 3.02 – 2.92 (m, 2H), 2.15 – 2.02 (m, 2H), 2.00 (s, 3H), 1.86 (dddd, *J* = 16.3, 11.3, 9.6, 3.3 Hz, 2H), 1.62 – 1.50 (m, 3H), 1.43 – 1.33 (m, 2H).

^{13}C NMR: (126 MHz, $CDCl_3$) δ 170.12, 50.92, 39.43, 34.98, 32.25, 29.90, 27.21, 23.34.

HRMS-ESI (positive): M = $C_{10}H_{19}NO_3S$, calculated (M+H) m/z: 234.1164, found: 234.1157

Purification: elutes at 55% acetone



3w
86%

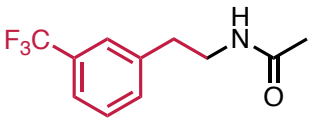
Pale yellow solid

Spectral data match the literature.[6]

^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.39 – 7.30 (m, 2H), 7.28 – 7.24 (m, 1H), 7.23 – 7.18 (m, 2H), 5.46 (br s, 1H), 3.55 (td, *J* = 6.9, 5.8 Hz, 2H), 2.84 (t, *J* = 6.9 Hz, 2H), 1.96 (s, 3H).

^{13}C NMR: ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.01, 138.88, 128.76, 128.67, 126.55, 40.64, 35.64, 23.34.

Purification: elutes at 40% EtOAc



3x
78%

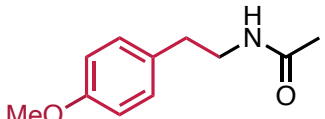
Colorless oil (93% NMR yield)

^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.52 (d, *J* = 7.7 Hz, 1H), 7.49 – 7.39 (m, 4H), 5.50 (s, 1H), 3.59 – 3.49 (m, 2H), 2.91 (t, *J* = 7.1 Hz, 2H), 1.98 (s, 3H).

^{13}C NMR: (126 MHz, $CDCl_3$) δ 170.12, 139.85, 132.16, 130.97 (q), 129.09, 125.49, 123.45, 40.54, 35.53, 23.28.

HRMS-ESI (positive): M = $C_{11}H_{12}F_3NO$, calculated (M+H) m/z: 232.0949, found: 232.0967

Purification: elutes at 45% EtOAc



3y
52%

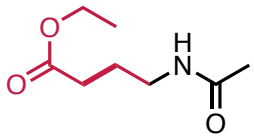
Yellow solid

Spectral data match the literature.[16]

^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.17 – 7.10 (m, 2H), 6.91 – 6.85 (m, 2H), 5.43 (s, 1H), 3.82 (s, 3H), 3.54 – 3.47 (m, 2H), 2.78 (t, *J* = 6.9 Hz, 2H), 1.96 (s, 3H).

^{13}C NMR: ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.00, 158.33, 130.83, 129.69, 114.10, 55.29, 40.82, 34.71, 23.36.

Purification: elutes at 50% EtOAc



3z
40%

Colorless oil (from ethyl crotonate)

^{1}H NMR: (500 MHz, $CDCl_3$) δ 5.72 (s, 1H), 4.16 (q, *J* = 7.1 Hz, 2H), 3.32 (td, *J* = 6.9, 5.7 Hz, 2H), 2.38 (t, *J* = 7.1 Hz, 2H), 1.99 (s, 3H), 1.86 (p, *J* = 7.0 Hz, 2H), 1.28 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR: (126 MHz, $CDCl_3$) δ 173.52, 170.13, 60.59, 39.15, 31.83, 24.59, 23.31, 14.21.

HRMS-ESI (positive): M = $C_8H_{15}NO_3$, calculated (M+Na) m/z: 196.0950, found: 196.0974

Purification: elutes at 25% EtOAc

3aa
35%

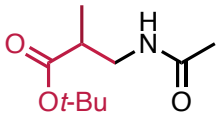
Yellow solid (from trans 3-penten-1-ol)

Spectral data match the literature.[17]

^{1}H NMR: (500 MHz, $CDCl_3$) δ 5.46 (br s, 1H), 3.67 (t, *J* = 6.5 Hz, 2H), 3.27 (td, *J* = 7.2, 5.9 Hz, 2H), 2.00 (s, 3H), 1.65 – 1.56 (m, 2H), 1.53 (m, 2H), 1.47 – 1.32 (m, 4H).

^{13}C NMR: (126 MHz, $CDCl_3$) δ 170.03, 62.74, 39.48, 32.55, 29.63, 26.52, 25.30, 23.38.

Purification: elutes at 80% EtOAc



3ab
95%

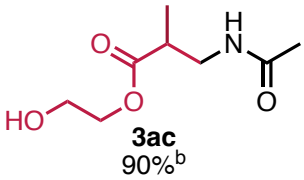
Pale yellow oil

^{1}H NMR: (500 MHz, $CDCl_3$) δ 6.01 (br s, 1H), 3.49 (ddd, *J* = 13.6, 6.6, 4.3 Hz, 1H), 3.27 (ddd, *J* = 13.8, 8.3, 5.6 Hz, 1H), 2.60 (dqd, *J* = 8.4, 7.3, 4.4 Hz, 1H), 1.99 (s, 3H), 1.47 (s, 9H), 1.16 (d, *J* = 7.2 Hz, 3H).

^{13}C NMR: (126 MHz, $CDCl_3$) δ 175.08, 170.06, 80.93, 41.67, 40.24, 28.07, 23.33, 14.96.

HRMS-ESI (positive): M = $C_{10}H_{19}NO_3$, calculated (M+Na) m/z: 224.14, found: 224.1284

Purification: elutes at 20% acetone



3ac
90%[b]

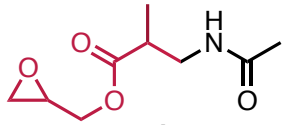
Pale yellow oil

^{1}H NMR: (500 MHz, $CDCl_3$) δ 6.18 (br s, 1H), 5.50 (br s, 2H), 4.31 (ddd, *J* = 11.8, 5.6, 3.8 Hz, 1H), 4.23 (ddd, *J* = 11.8, 5.2, 3.7 Hz, 1H), 3.87 – 3.82 (m, 2H), 3.60 (ddd, *J* = 13.8, 6.8, 4.2 Hz, 1H), 3.36 (ddd, *J* = 14.0, 8.4, 5.9 Hz, 1H), 2.74 (dddd, *J* = 10.1, 7.2, 4.2, 3.0 Hz, 1H), 1.99 (s, 3H), 1.22 (d, *J* = 7.2 Hz, 3H).

^{13}C NMR: (126 MHz, $CDCl_3$) δ 175.33, 170.58, 66.23, 60.88, 41.94, 40.01, 23.25, 14.70.

HRMS-ESI (positive): M = $C_8H_{15}NO_4$, calculated (M+Na) m/z: 212.0899, found: 212.0915

Purification: elutes at 40% acetone



3ad
70%, 1:1 dr

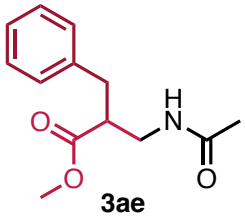
Orange oil

^{1}H NMR: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.03 (br s, 1H), 4.52 (ddd, *J* = 16.4, 12.3, 2.9 Hz, 1H), 3.99 (dd, *J* = 12.3, 6.0 Hz, 1H), 3.57 (dddd, *J* = 11.2, 10.1, 4.3, 3.2 Hz, 1H), 3.30 (dtd, *J* = 13.9, 8.2, 5.8 Hz, 1H), 3.26 – 3.22 (m, 1H), 2.88 (dt, *J* = 4.9, 4.1 Hz, 1H), 2.78 (dddd, *J* = 11.5, 7.2, 5.8, 2.8 Hz, 1H), 2.69 (dd, *J* = 4.9, 2.6 Hz, 1H), 1.99 (d, *J* = 1.9 Hz, 3H), 1.22 (dd, *J* = 7.2, 1.4 Hz, 3H).

^{13}C NMR: ^{13}C NMR (126 MHz, $CDCl_3$) δ 175.17, 170.22, 64.53 (d, *J* = 36.6 Hz), 49.27, 44.59 (d, *J* = 16.5 Hz), 41.68 (d, *J* = 3.3 Hz), 39.61 (d, *J* = 6.4 Hz), 23.27, 14.79 (d, *J* = 4.3 Hz).

HRMS-ESI (positive): M = $C_9H_{15}NO_4$, calculated (M+Na) m/z: 224.0899, found: 224.0921

Purification: elutes at 30% acetone



3ae
43%

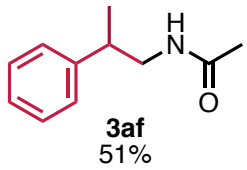
Pale yellow oil

Spectral data match the literature.[18]

^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.31 (dd, *J* = 8.1, 6.7 Hz, 2H), 7.27 – 7.21 (m, 1H), 7.20 – 7.14 (m, 2H), 5.84 (br s, 1H), 3.68 (s, 3H), 3.55 (ddd, *J* = 13.6, 6.2, 4.0 Hz, 1H), 3.38 (ddd, *J* = 13.8, 8.1, 5.8 Hz, 1H), 3.03 – 2.93 (m, 2H), 2.91 – 2.80 (m, 1H), 1.96 (s, 3H).

^{13}C NMR: ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.86, 170.10, 138.04, 128.84, 128.57, 126.70, 51.86, 46.67, 40.22, 36.06, 23.29.

Purification: elutes at 25% acetone



3af
51%

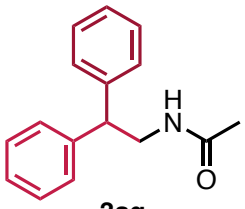
Colorless oil

Spectral data match the literature.[19]

^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.40 – 7.32 (m, 2H), 7.30 – 7.22 (m, 3H), 5.29 (br s, 1H), 3.68 (ddd, *J* = 13.2, 7.1, 5.8 Hz, 1H), 3.24 (ddd, *J* = 13.6, 9.0, 4.8 Hz, 1H), 3.01 – 2.88 (m, 1H), 1.92 (s, 2H), 1.30 (d, *J* = 7.0 Hz, 3H).

^{13}C NMR: (126 MHz, $CDCl_3$) δ 169.97, 144.09, 128.76, 127.20, 126.76, 46.12, 39.73, 23.31, 19.46.

Purification: elutes at 15% acetone



3ag
67%

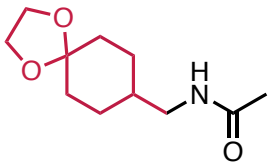
Pale yellow solid

Spectral data match the literature.[20]

^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.40 – 7.31 (m, 4H), 7.28 – 7.18 (m, 6H), 5.39 (br s, 1H), 4.20 (t, *J* = 8.0 Hz, 1H), 3.92 (dd, *J* = 7.9, 5.8 Hz, 2H), 1.91 (s, 3H).

^{13}C NMR: ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.00, 141.84, 128.76, 128.04, 126.87, 50.57, 43.85, 23.34.

Purification: elutes at 15% acetone



3ah
81%

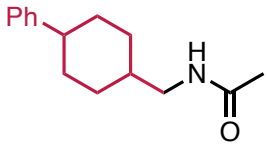
Colorless oil

^{1}H NMR: (500 MHz, $CDCl_3$) δ 5.52 (br s, 1H), 4.00 – 3.91 (m, 4H), 3.16 (t, *J* = 6.4 Hz, 2H), 2.01 (s, 3H), 1.77 (dddd, *J* = 17.9, 12.6, 4.7, 2.8 Hz, 4H), 1.59 – 1.48 (m, 3H), 1.36 – 1.24 (m, 2H).

^{13}C NMR: (126 MHz, $CDCl_3$) δ 170.06, 108.78, 64.26, 44.97, 36.51, 34.12, 27.83, 23.40.

HRMS-ESI (positive): M = $C_{11}H_{19}NO_3$, calculated (M+H) m/z: 214.1443, found: 214.1461

Purification: elutes at 65% EtOAc



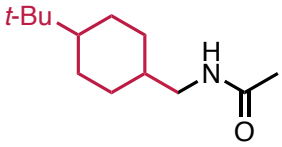
3ai
60%, 2.0:1 dr
Pale yellow solid

^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.31 (m , 3H), 7.22 (m, 4.5H), 5.60 (br s, 1H), 5.52 (br s, 0.5H), 3.38 (dd, *J* = 7.8, 5.9 Hz, 1H), 3.18 (t, *J* = 6.4 Hz, 2H), 2.61 (ddd, *J* = 14.1, 8.4, 5.7 Hz, 0.5H), 2.50 (tt, *J* = 12.2, 3.4 Hz, 1H), 2.02 (d, *J* = 1.0 Hz, 4.5H), 2.00 – 1.85 (m, 5H), 1.80 – 1.63 (m, 4H), 1.57 (ddt, *J* = 15.4, 8.6, 3.5 Hz, 1H), 1.49 (qd, *J* = 12.8, 3.1 Hz, 2H), 1.14 (qd, *J* = 12.8, 3.3 Hz, 2H).

^{13}C NMR: (126 MHz, $CDCl_3$) δ 170.12, 147.23, 146.88, 128.33 (d, *J* = 3.9 Hz), 126.85 (d, *J* = 17.0 Hz), 125.93 (d, *J* = 14.2 Hz), 45.82, 44.32, 43.28, 41.52, 37.63, 33.64, 33.46 (d, *J* = 14.9 Hz), 31.05, 28.80, 27.92, 23.41.

HRMS-ESI (positive): M = $C_{15}H_{21}NO$, calculated (M+H) m/z: 232.1701, found: 232.1725

Purification: elutes at 50% EtOAc



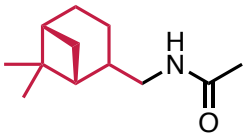
3aj
47%, 2.5:1 dr
White solid

^{1}H NMR: (500 MHz, $CDCl_3$) δ 5.53 (br s, 1H), 5.44 (br s, 0.5H), 3.29 (dd, *J* = 7.8, 5.8 Hz, 1H), 3.10 (dd, *J* = 6.8, 6.0 Hz, 2H), 2.00 (d, *J* = 2.8 Hz, 4H), 1.81 (dt, *J* = 12.9, 3.9 Hz, 4H), 1.69 (s, 1H), 1.59 – 1.53 (m, 1H), 1.45 – 1.34 (m, 1H), 1.20 – 1.08 (m, 1H), 1.06 – 0.88 (m, 5H), 0.85 (s, 13.5H).

^{13}C NMR: ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.04, 48.42, 48.07, 45.89, 40.86, 38.00, 32.80, 32.55, 32.41, 31.26, 28.55, 27.54, 27.48, 26.77, 23.39, 21.83.

HRMS-ESI (positive): M = $C_{13}H_{25}NO$, calculated (M+H) m/z: 212.20, found: 212.2036

Purification: elutes at 40% EtOAc



3ak
31%, 4.0:1 dr
from β-pinene

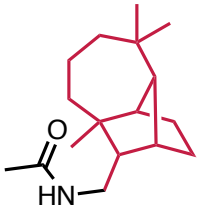
Colorless oil

^{1}H NMR: (500 MHz, $CDCl_3$) δ 5.43 (s, 1H), 3.20 – 2.98 (m, 2H), 2.18 – 2.00 (m, 2H), 1.99 (s, 3H), 1.93 – 1.87 (m, 1H), 1.82 – 1.73 (m, 2H), 1.68 (dtd, *J* = 14.6, 8.4, 1.6 Hz, 1H), 1.36 (d, *J* = 10.1 Hz, 1H), 1.23 (s, 2H), 0.85 (s, 2H).

^{13}C NMR: (126 MHz, $CDCl_3$) δ 170.00, 44.34, 43.26, 40.88, 35.09, 26.68, 24.08, 23.44, 23.36, 20.13, 19.74.

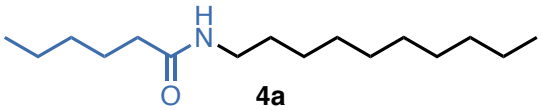
HRMS-ESI (positive): M = $C_{12}H_{21}NO$, calculated (M+H) m/z: 196.1701, found: 196.1719

Purification: elutes at 40% EtOAc



3al
14%, >20:1 dr
from (+)-longifolene

Not isolated



4a
78%

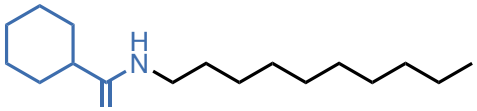
Pale yellow solid

^{1}H NMR: ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.41 (br s, 1H), 3.26 (td, *J* = 7.2, 5.8 Hz, 2H), 2.21 – 2.14 (m, 2H), 1.71 – 1.60 (m, 2H), 1.51 (p, *J* = 7.1 Hz, 2H), 1.41 – 1.24 (m, 18H), 0.91 (q, *J* = 7.1 Hz, 6H).

^{13}C NMR: (126 MHz, $CDCl_3$) δ 173.02, 39.50, 36.94, 31.89, 31.50, 29.70, 29.56, 29.54, 29.31, 26.93, 25.54, 22.68, 22.43, 14.12, 13.96.

HRMS-ESI (positive): M = $C_{16}H_{33}NO$, calculated (M+H) m/z: 256.2640, found: 256.2654

Purification: elutes at 15% EtOAc



4b
69%

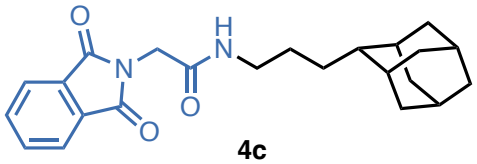
White solid

Spectral data match the literature.[1]

^{1}H NMR: (500 MHz, $CDCl_3$) δ 5.40 (br s, 1H), 3.25 (td, *J* = 7.3, 5.7 Hz, 2H), 2.07 (tt, *J* = 11.8, 3.5 Hz, 1H), 1.92 – 1.77 (m, 4H), 1.72 – 1.65 (m, 1H), 1.55 – 1.39 (m, 4H), 1.33 – 1.26 (m, 17H), 0.90 (t, *J* = 6.9 Hz, 3H).

^{13}C NMR: (126 MHz, $CDCl_3$) δ 175.92, 45.69, 39.32, 31.89, 29.78, 29.71, 29.54, 29.30, 26.90, 25.79, 22.68, 14.11.

Purification: elutes at 10% EtOAc



4c
57%

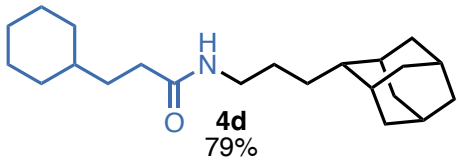
White solid

^{1}H NMR: (500 MHz, $CDCl_3$) δ 7.91 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.77 (dd, *J* = 5.5, 3.0 Hz, 2H), 5.78 (br s, 1H), 4.35 (s, 2H), 3.30 (td, *J* = 7.1, 5.7 Hz, 2H), 1.91 – 1.75 (m, 6H), 1.75 – 1.62 (m, 7H), 1.56 – 1.39 (m, 6H).

^{13}C NMR: (126 MHz, $CDCl_3$) δ 167.80, 165.88, 134.26, 132.02, 123.65, 44.06, 41.04, 40.23, 39.21, 38.39, 31.78, 31.56, 29.76, 28.28, 28.06, 27.58.

HRMS-ESI (positive): M = $C_{23}H_{28}N_2O_3$, calculated (M+H) m/z: 381.2178, found: 381.2188

Purification: elutes at 25% EtOAc



4d
79%

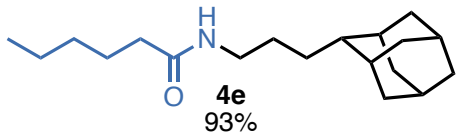
Colorless oil, some impurity remains (91% NMR yield)

^{1}H NMR: (500 MHz, $CDCl_3$) δ 5.41 (br s, 1H), 3.28 (m, 2H), 2.22 – 2.15 (m, 2H), 1.92 – 1.77 (m, 6H), 1.78 – 1.62 (m, 12H), 1.58 – 1.37 (m, 7H), 1.34 – 1.10 (m, 6H), 0.92 (qd, *J* = 12.8, 3.7 Hz, 3H).

^{13}C NMR: ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.29, 44.14, 39.83, 39.24, 38.40, 37.37, 34.43, 33.10, 31.83, 31.61, 29.86, 28.30, 28.08, 27.82, 26.56, 26.24.

HRMS-ESI (positive): M = $C_{22}H_{27}NO$, calculated (M+H) m/z: 332.2953, found: 332.2964

Purification: elutes at 10% EtOAc



4e
93%

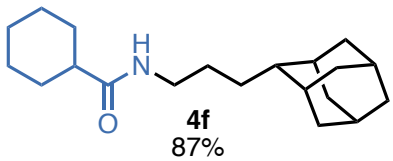
White solid

^{1}H NMR: (500 MHz, $CDCl_3$) δ 5.42 (br s, 1H), 3.27 (q, *J* = 6.5 Hz, 2H), 2.17 (t, *J* = 7.6 Hz, 2H), 1.92 – 1.77 (m, 6H), 1.75 – 1.59 (m, 9H), 1.55 – 1.41 (m, 6H), 1.33 (hd, *J* = 8.8, 4.7 Hz, 4H), 0.92 (t, *J* = 6.8 Hz, 3H).

^{13}C NMR: (126 MHz, $CDCl_3$) δ 173.01, 44.14, 39.81, 39.24, 38.39, 36.96, 31.83, 31.61, 31.50, 29.87, 28.30, 28.07, 27.84, 25.56, 22.44, 13.95.

HRMS-ESI (positive): M = $C_{19}H_{33}NO$, calculated (M+H) m/z: 292.2640, found: 292.2655

Purification: elutes at 10% EtOAc



4f
87%

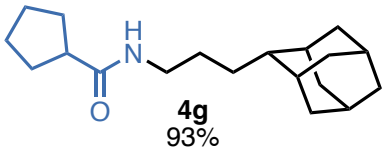
White solid

^{1}H NMR: (500 MHz, $CDCl_3$) δ 5.43 (br s, 1H), 3.26 (td, *J* = 6.9, 5.6 Hz, 2H), 2.07 (tt, *J* = 11.8, 3.5 Hz, 1H), 1.94 – 1.77 (m, 10H), 1.76 – 1.61 (m, 8H), 1.56 – 1.37 (m, 8H), 1.35 – 1.17 (m, 3H).

^{13}C NMR: (126 MHz, $CDCl_3$) δ 175.95, 45.70, 44.12, 39.64, 39.24, 38.40, 31.82, 31.61, 29.85, 29.79, 28.30, 28.07, 27.84, 25.79.

HRMS-ESI (positive): M = $C_{17}H_{33}NO$, calculated (M+H) m/z: 268.2640, found: 268.2620

Purification: elutes at 10% EtOAc



4g
93%

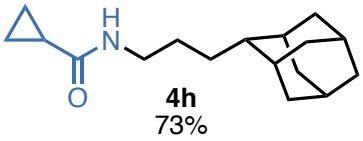
White solid

^{1}H NMR: (500 MHz, $CDCl_3$) δ 5.45 (br s, 1H), 3.31 – 3.23 (m, 2H), 2.51 (p, *J* = 7.9 Hz, 1H), 1.86 (m, 6H), 1.82 – 1.67 (m, 11H), 1.64 (m, 2H), 1.59 (m , 2H), 1.55 – 1.40 (m, 6H).

^{13}C NMR: (126 MHz, $CDCl_3$) δ 176.07, 46.05, 44.12, 39.83, 39.24, 38.40, 31.82, 31.61, 30.49, 29.86, 28.30, 28.07, 27.86, 25.92.

HRMS-ESI (positive): M = $C_{19}H_{31}NO$, calculated (M+H) m/z: 290.2484, found: 290.1592

Purification: elutes at 10% EtOAc



4h
73%

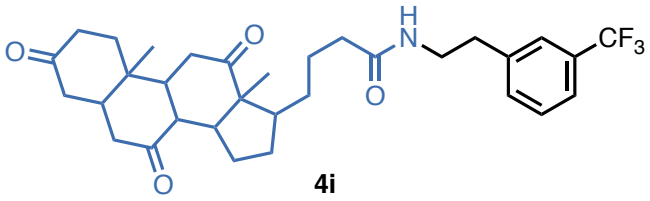
White solid

^{1}H NMR: (500 MHz, $CDCl_3$) δ 5.60 (br s, 1H), 3.29 (td, *J* = 6.9, 5.7 Hz, 2H), 1.92 – 1.78 (m, 6H), 1.76 – 1.62 (m, 7H), 1.58 – 1.42 (m, 6H), 1.33 (tt, *J* = 7.9, 4.6 Hz, 1H), 1.02 – 0.95 (m, 2H), 0.79 – 0.69 (m, 2H).

^{13}C NMR: (126 MHz, $CDCl_3$) δ 173.34, 44.15, 40.12, 39.25, 38.40, 31.83, 31.61, 29.88, 28.31, 28.08, 27.89, 14.82, 6.97.

HRMS-ESI (positive): M = $C_{17}H_{27}NO$, calculated (M+H) m/z: 262.2171, found: 262.9264

Purification: elutes at 10% EtOAc



4i
50%
from dehydrocholic acid

Colorless oil

^{1}H NMR: (500 MHz, $CDCl_3$) δ 5.45 (br t, 1H), 3.55 (td, *J* = 7.0, 5.9 Hz, 2H), 3.04 – 2.77 (m, 5H), 2.44 – 2.20 (m, 7H), 2.19 – 1.94 (m, 8H), 1.91 – 1.82 (m, 2H), 1.69 – 1.60 (m, 1H), 1.42 (s, 3H), 1.41 – 1.23 (m, 4H), 1.09 (s, 3H), 0.86 (d, *J* = 6.5 Hz, 3H).

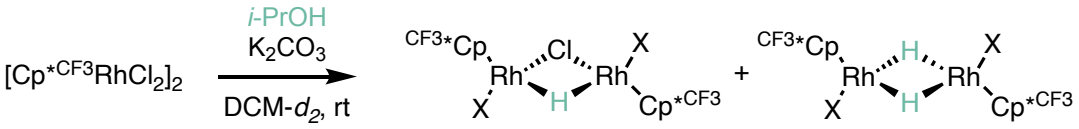
^{13}C NMR: (126 MHz, $CDCl_3$) δ 212.02, 209.01, 208.67, 173.33, 139.91, 132.18, 130.87 (q), 129.07, 125.51, 123.44, 56.92, 51.77, 49.00, 46.86, 45.58, 44.99, 42.80, 40.41, 38.64, 36.49, 36.03, 35.60, 35.48, 35.30, 33.61, 31.08, 27.56, 25.14, 21.92, 18.74, 11.88.

HRMS-ESI (positive): M = $C_{33}H_{42}F_3NO_4$, calculated (M+H) m/z: 574.3144, found: 574.3136

Purification: elutes at 10% EtOAc

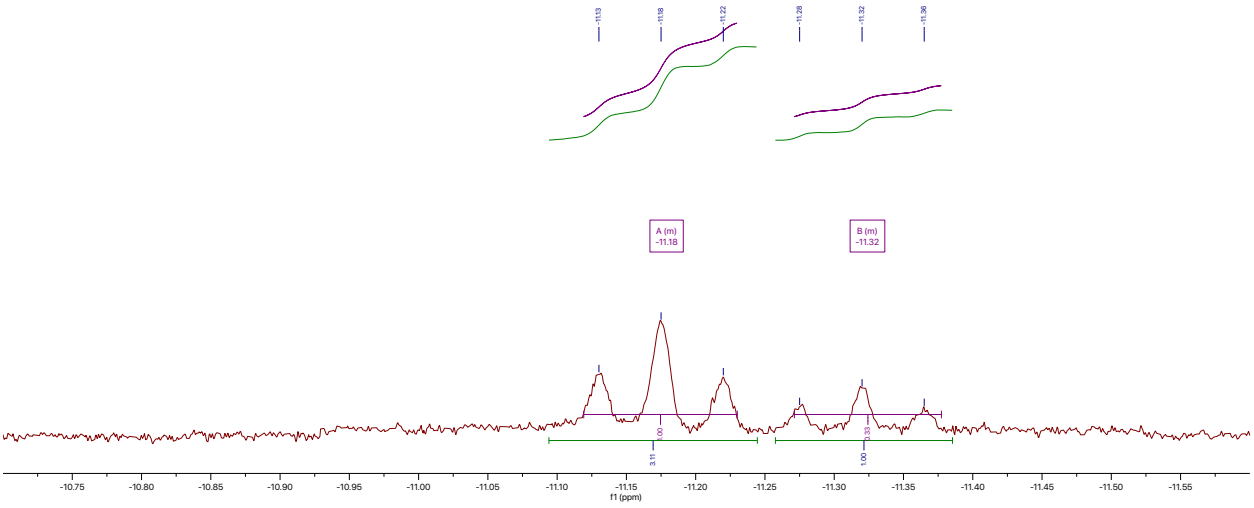
6. Mechanistic Studies

Observation of the Rhodium Hydride



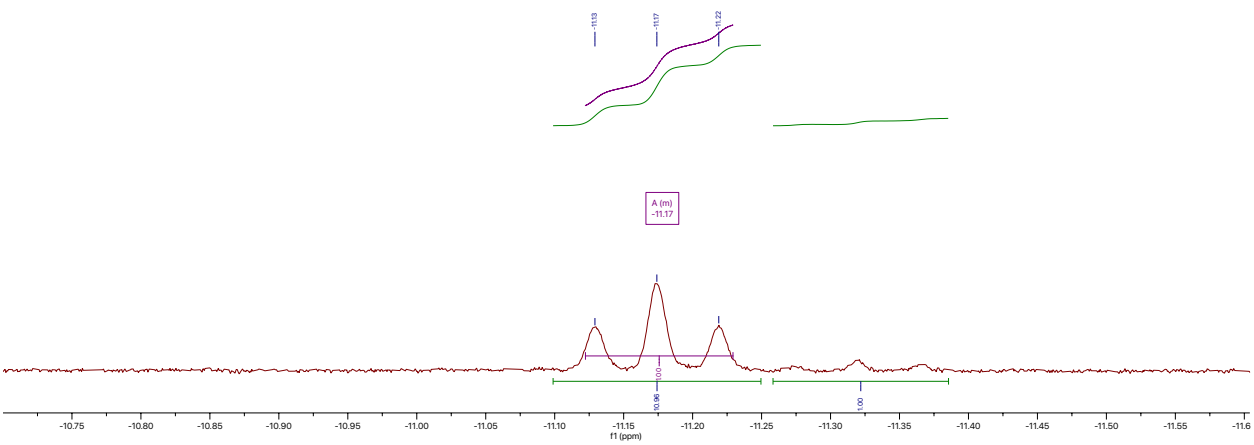
proposed structures

$[Cp^{*CF3}RhCl_2]_2$ (14.4 mg, 0.02 mmol) and K_2CO_3 (60.8 mg, 0.44 mmol) were weighed into a 1.5-dram vial with magnetic stir bar. Into another 1.5-dram vial were pipetted isopropanol (100 µL) and DCM-d_2 (400 µL). The solvents were transferred to the vial containing the solvents, and the solution was stirred for one minute, before being pipetted into an NMR tube. A standard ^{1}H NMR spectrum was then taken, revealing two distinct triplets in a 3:1 ratio at -11.18 -11.32 ppm respectively (J = 20 Hz). This ppm range is characteristic of Cp* rhodium hydride species.[21]



Given that rhodium is spin ½, we believe that the triplet signal observed may correspond to a rhodium dimer complex with a bridging hydride ligand.[22] Further, we believe that both the mono- and dihydride complexes can be formed, explaining the presence of two triplet signals with the same coupling constant in an unequal ratio.

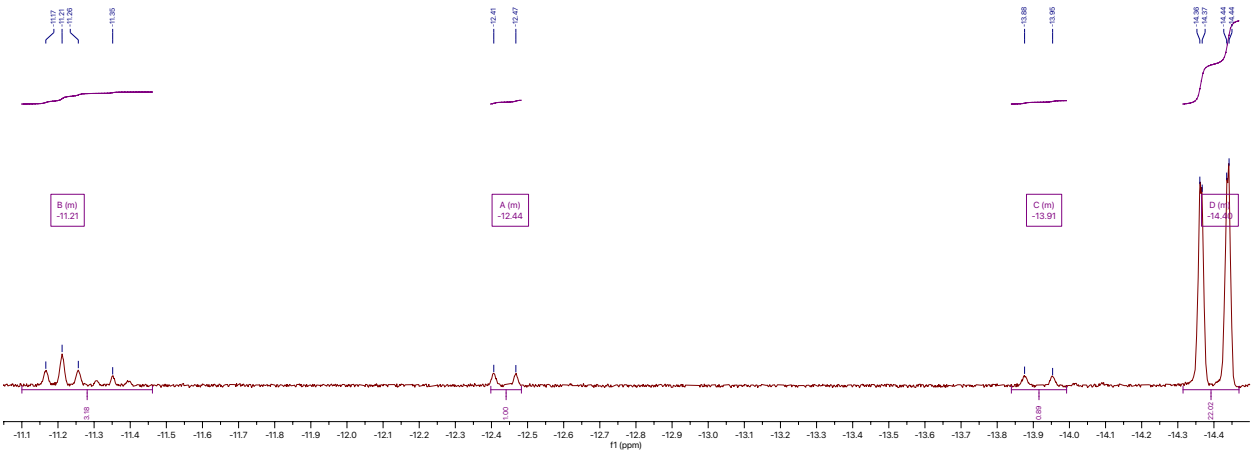
After 20 hours, a second ^{1}H NMR spectrum was taken of the same sample, and the rhodium hydride signal was still observed. The ratio of the two triplets had increased from 3:1 to 11:1, indicating equilibration of some kind. If we are correct that these signals belong to the mono- and dihydrides, it is likely that over time, one is converted to the other due to a difference in thermodynamic stability.



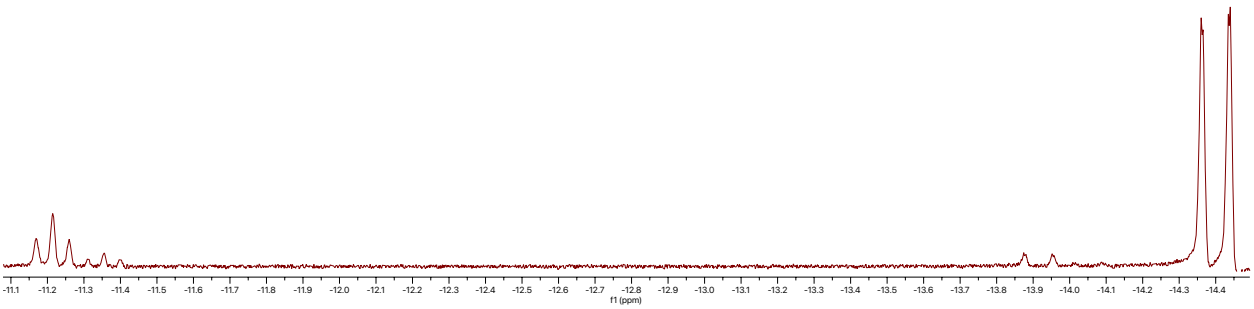
Additional experiments on solutions containing this rhodium hydride species were performed to see if it is the active catalyst in the hydroamidation reaction. Although adding alkene and dioxazolone to the solution and stirring for one hour resulted in 28% yield of the hydroamidation product, this just demonstrates that the solution is catalytically active, and does not necessarily point to the observed complex being active. In fact, further experiments suggest that this species is not catalytically active.

First, we formed the rhodium deuteride in the same way that we formed the hydride, using isopropanol-d_8, then adding1-decene to the solution, but no rhodium hydride signal was observed, indicating that proton-deuteron exchange does not occur. Additionally, when treating the rhodium hydride with alkene, dioxazolone, or both, consumption or change of the rhodium hydride signal was not observed. Finally, when we attempted to form the rhodium hydride species in the presence of alkene (adding 1-decene alongside isopropanol and DCM-d_2), we did not observe the rhodium hydride signal. Based on these experiments, we conclude that the observed rhodium hydride species is not an active species under the reaction conditions, however its observation is evidence that a rhodium hydride can be formed with isopropanol and K_2CO_3.

In search of further evidence that a rhodium hydride is active under our conditions, we formed a rhodium hydride complex stoichiometrically by adding 0.9 equivalents of Et_3SiH to $[Cp^{*CF3}RhCl_2]_2$ in DCM-d_2. By ^1H NMR, we observe multiple different rhodium hydride resonances. First, we observe the same pair of triplet signals discussed above. Farther upfield, a small doublet at -12.45 ppm (J = 30 Hz), which we believe to be a rhodium monohydride species,[21] then a similar doublet at -13.92 ppm (J = 35 Hz) that might be a dihydride based on the shift further upfield[23] and coupling constant that are similar to those of the large doublet at -14.39 ppm (J = 35 Hz). When we performed the same experiment with 9 equivalents of silane, this large doublet was the only hydride species observed, and in that experiment, we were able to get relative integrations of the hydride to Cp^{*CF3} methyl peaks in a 2:6 ratio, indicative of a dihydride.

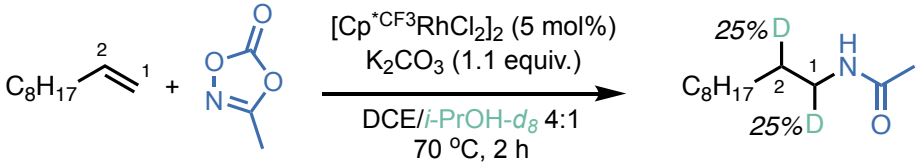


Adding alkene and dioxazolone to this solution and stirring for 15 minutes, we see consumption of the signal tentatively assigned as the monohydride, while the other rhodium hydride signals remain intact. The hydroamidation product is concurrently formed in trace yield. Based on this, we suggest that only the rhodium monohydride is catalytically active, while the predominant dihydride species are not.



To test the capability of Et_3SiH as a hydride donor under catalytic conditions, we subjected 1-decene to the standard conditions with Et_3SiH in lieu of isopropanol, and obtained the hydroamidated product in 6% yield. This supports the proposed mechanism of rhodium hydride formation as the first catalytic step. The low yield may be due to catalyst deactivation by formation of inactive dihydride species, as was observed in the stoichiometric experiments. If this is the case, slower hydride generation from isopropanol may be optimal to form active rhodium monohydride species that can react with the substrate before forming an inactive dihydride.

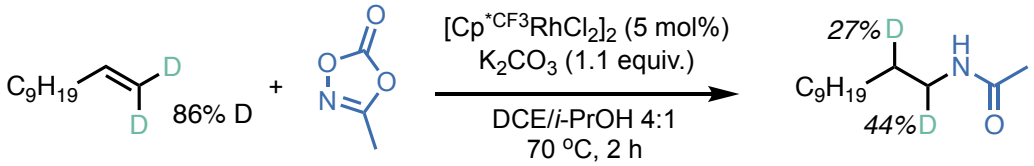
Formation of Rhodium Hydride from Isopropanol



Using the standard reaction conditions but substituting isopropanol-d_8 for regular isopropanol resulted in full deuterium incorporation in the product, supporting the notion that isopropanol acts as the hydride donor in this reaction.

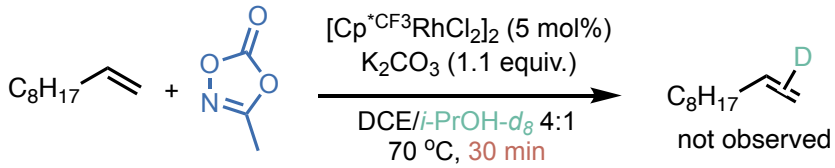
The fact that the deuterium incorporation is evenly distributed between C_1 and C_2 yields additional mechanistic information, suggesting that rhodium hydride migratory insertion into the alkene is both reversible and non-regioselective.

Reversibility of Migratory Insertion



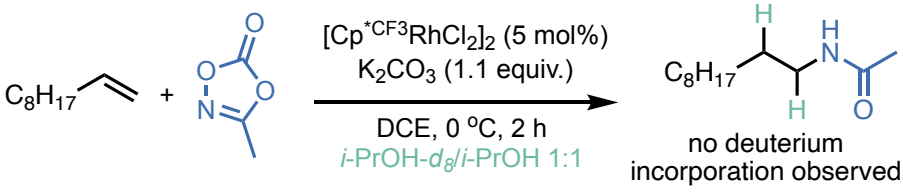
To further test the reversibility of the migratory insertion step we subjected 1-undecene deuterated at the 1 position to the standard conditions and observed that a significant amount of deuterium had moved from carbon 1 to carbon 2. This is consistent with a reversible migratory insertion step, in which a rhodium hydride may insert to yield a secondary alkylrhodium species. This can then undergo β-deuteride elimination and reinsertion to yield the terminal alkylrhodium species which can then be amidated, resulting in the formation of a product in which deuterium has shifted from the 1-carbon to the 2-carbon.

Reversibility of Alkene Coordination



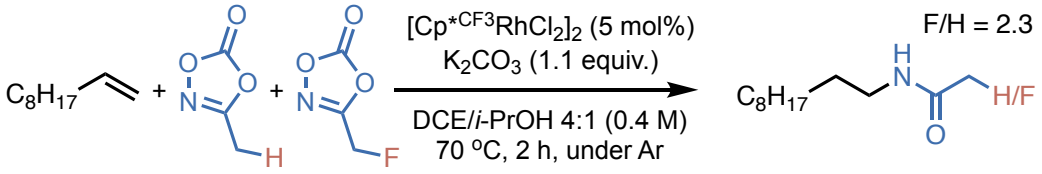
To test the reversibility of alkene coordination, we subjected 1-decene to the standard conditions using deuterated isopropanol. We stopped the reaction after just 30 minutes and reisolated remaining starting material. We were unable to detect any deuterium incorporation in the reisolated alkene, suggesting that the alkene coordination step is irreversible.

Kinetic Isotope Effect on Rhodium Hydride Formation



When employing a 1:1 mixture of isopropanol and isopropanol-d_8, we were surprised to observe no detectable deuterium incorporation in the product. This suggests a very strong primary KIE on the initial formation of the rhodium hydride species.

Turnover-Limiting Amidation Step

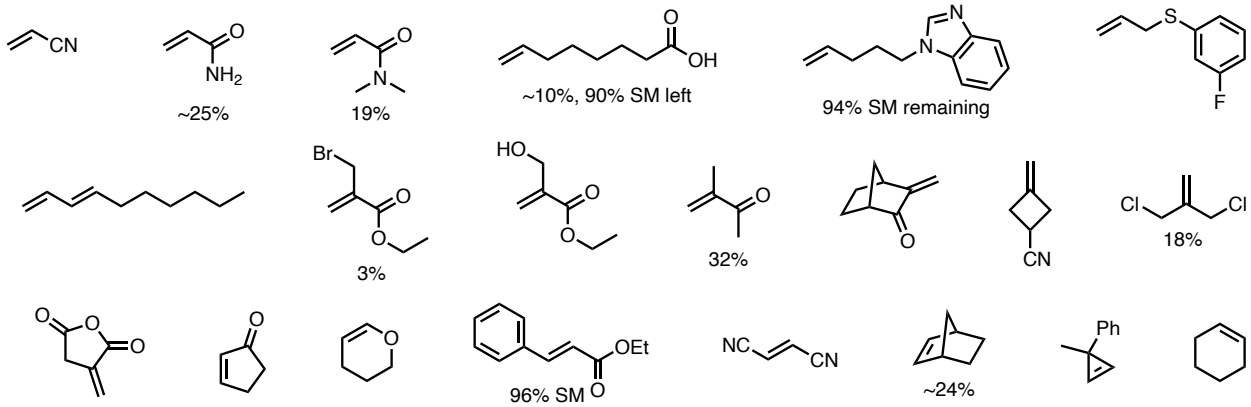


To determine which step of the amidation is likely to be turnover limiting, we conducted a competition experiment between the standard methyl dioxazolone and the fluoromethyl dioxazolone. Due to inductive effects of the added fluorine atom, the fluoromethyl dioxazolone is both less coordinating and more oxidizing than the methyl dioxazolone. Subjecting 1-decene to the standard conditions with 2.5 equiv. of methyl dioxazolone and 2.5 equiv. of fluoromethyl dioxazolone yielded a mixture of hydroamidated products with a 2.3:1 ratio of fluorinated to nonfluorinated products, meaning that the fluoromethyl dioxazolone outcompetes the methyl dioxazolone. We conclude that dioxazolone coordination is not turnover-limiting, since if that were the case, we would see the more coordinating methyl dioxazolone outcompete the fluoromethyl one. Additionally, this result suggests that dioxazolone activation to form the rhodium nitrenoid species is turnover-limiting, as the more easily activated fluoromethyl dioxazolone outcompetes the methyl one.

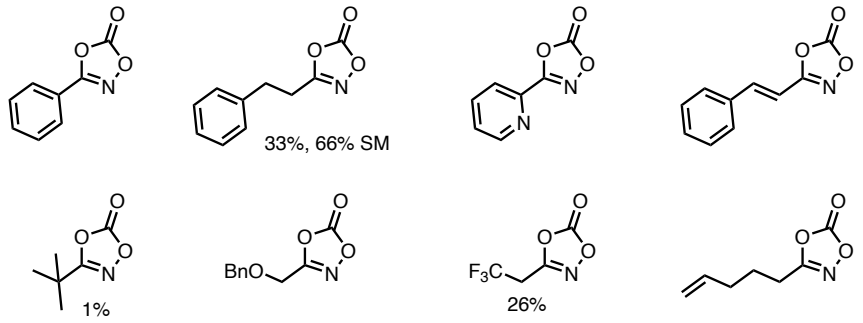
7. Unsuccessful Substrates

This section discloses substrates that were incompatible with the method, giving either no or low yield.

Incompatible Alkenes



Incompatible Dioxazolones



8. References

(1) Phipps, E. J. T.; Rovis, T. Rh(III)-Catalyzed C–H Activation-Initiated Directed Cyclopropanation of Allylic Alcohols. *J. Am. Chem. Soc.* **2019**, *141* (17), 6807–6811. https://doi.org/10.1021/jacs.9b02156.

(2) Lee, S.; Rovis, T. Rh(III)-Catalyzed Three-Component Syn-Carboamination of Alkenes Using Arylboronic Acids and Dioxazolones. **2021**. https://doi.org/10.26434/chemrxiv.14347277.v1.

(3) Burg, F.; Rovis, T. Diastereoselective Three-Component 3,4-Amino Oxygenation of 1,3-Dienes Catalyzed by a Cationic Heptamethylindenyl Rhodium(III) Complex. *J. Am. Chem. Soc.* **2021**, *143* (43), 17964–17969. https://doi.org/10.1021/jacs.1c09276.

(4) Lee, S.; Lei, H.; Rovis, T. A Rh(III)-Catalyzed Formal [4+1] Approach to Pyrrolidines from Unactivated Terminal Alkenes and Nitrene Sources. *J. Am. Chem. Soc.* **2019**, *141* (32), 12536–12540. https://doi.org/10.1021/jacs.9b07012.

(5) Brooks, J. L.; Xu, L.; Wiest, O.; Tan, D. S. Diastereoselective Synthesis of Highly Substituted Tetrahydrofurans by Pd-Catalyzed Tandem Oxidative Cyclization–Redox Relay Reactions Controlled by Intramolecular Hydrogen Bonding. *J. Org. Chem.* **2017**, *82* (1), 57–75. https://doi.org/10.1021/acs.joc.6b02053.

(6) Shigehisa, H.; Aoki, T.; Yamaguchi, S.; Shimizu, N.; Hiroya, K. Hydroalkoxylation of Unactivated Olefins with Carbon Radicals and Carbocation Species as Key Intermediates. *J. Am. Chem. Soc.* **2013**, *135* (28), 10306–10309. https://doi.org/10.1021/ja405219f.

(7) Rawat, V.; Chouthaiwale, P. V.; Suryavanshi, G.; Sudalai, A. A Concise Enantioselective Synthesis of (+)-Decarestrictine L via Proline-Catalyzed Sequential α-Aminooxylation and Horner–Wadsworth–Emmons Olefination. *Tetrahedron Asymmetry* **2009**, *20* (18), 2173–2177. https://doi.org/10.1016/j.tetasy.2009.08.026.

(8) Venning, A. R. O.; Bohan, P. T.; Alexanian, E. J. Palladium-Catalyzed, Ring-Forming Aromatic C–H Alkylations with Unactivated Alkyl Halides. *J. Am. Chem. Soc.* **2015**, *137* (11), 3731–3734. https://doi.org/10.1021/jacs.5b01365.

(9) Sánchez-Cantalejo, F.; Priest, J. D.; Davies, P. W. A Gold Carbene Manifold to Prepare Fused γ-Lactams by Oxidative Cyclisation of Ynamides. *Chem. – Eur. J.* **2018**, *24* (65), 17215–17219. https://doi.org/10.1002/chem.201804378.

(10) Yadav, J. S.; Murthy, P. V. A Concise Total Synthesis of (S)-Zearalenone and Zeranol. *Synthesis* **2011**, *2011* (13), 2117–2124. https://doi.org/10.1055/s-0030-1260058.

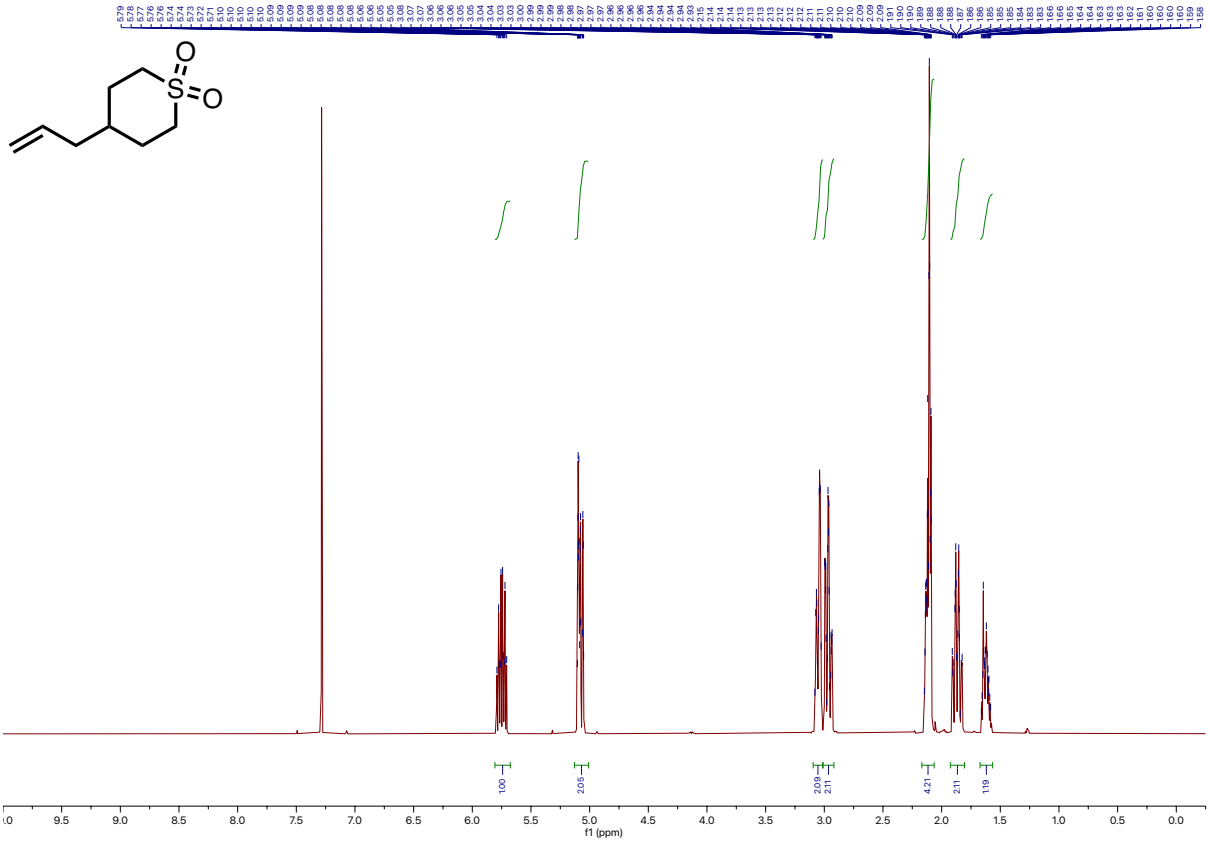
(11) Liu, X.; Rong, X.; Liu, S.; Lan, Y.; Liu, Q. Cobalt-Catalyzed Desymmetric Isomerization of Exocyclic Olefins. *J. Am. Chem. Soc.* **2021**, *143* (49), 20633–20639. https://doi.org/10.1021/jacs.1c11343.

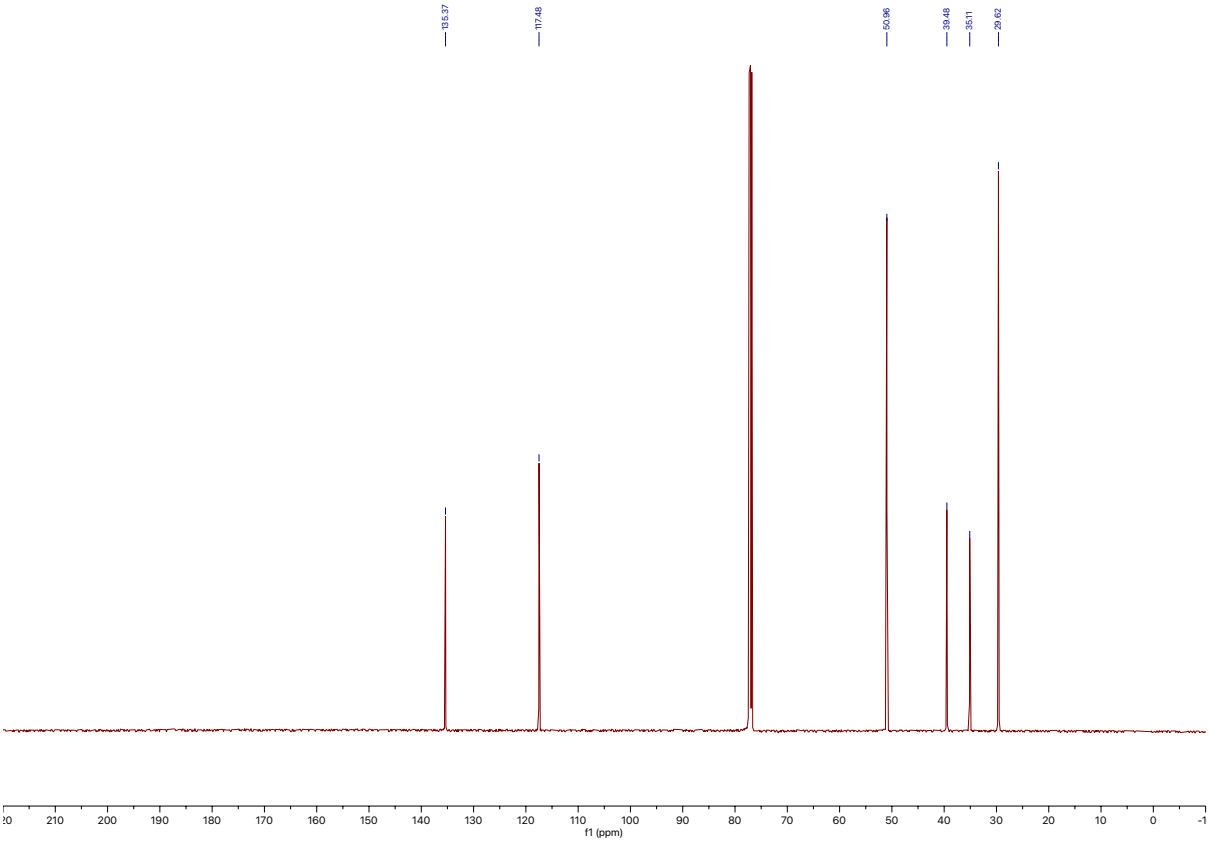
(12) Leonardi, A.; Motta, G.; Riva, C.; Guarneri, L.; Graziani, D.; De, T. C.; Karamfilova, K. D. Novel Spiroheterocyclic Compounds as Mglu5 Antagonists. WO2012004400A1, January 12, 2012.

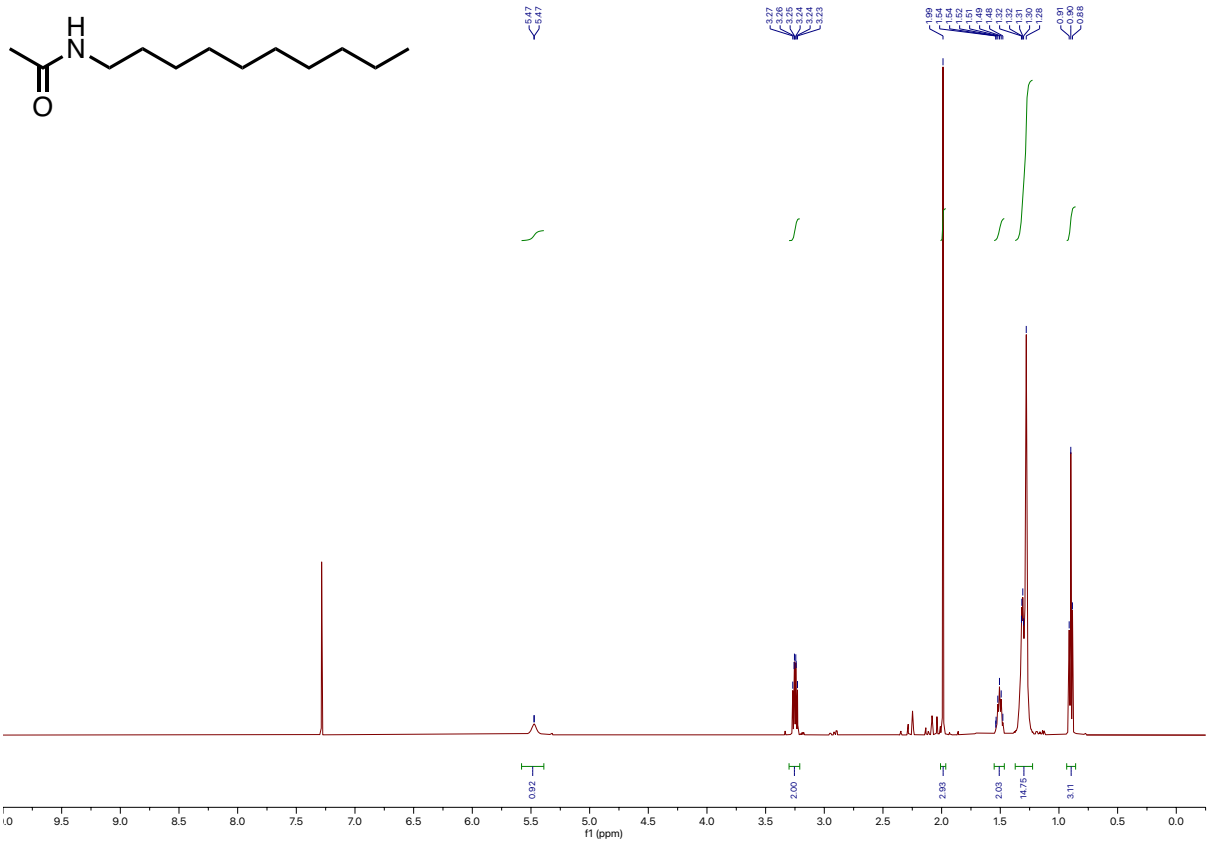
(13) Bamborough, P.; Chung, C.; Furze, R. C.; Grandi, P.; Michon, A.-M.; Watson, R. J.; Mitchell, D. J.; Barnett, H.; Prinjha, R. K.; Rau, C.; Sheppard, R. J.; Werner, T.; Demont, E. H. Aiming to Miss a Moving Target: Bromo and Extra Terminal Domain (BET) Selectivity in Constrained ATAD2 Inhibitors. *J. Med. Chem.* **2018**, *61* (18), 8321–8336. https://doi.org/10.1021/acs.jmedchem.8b00862.

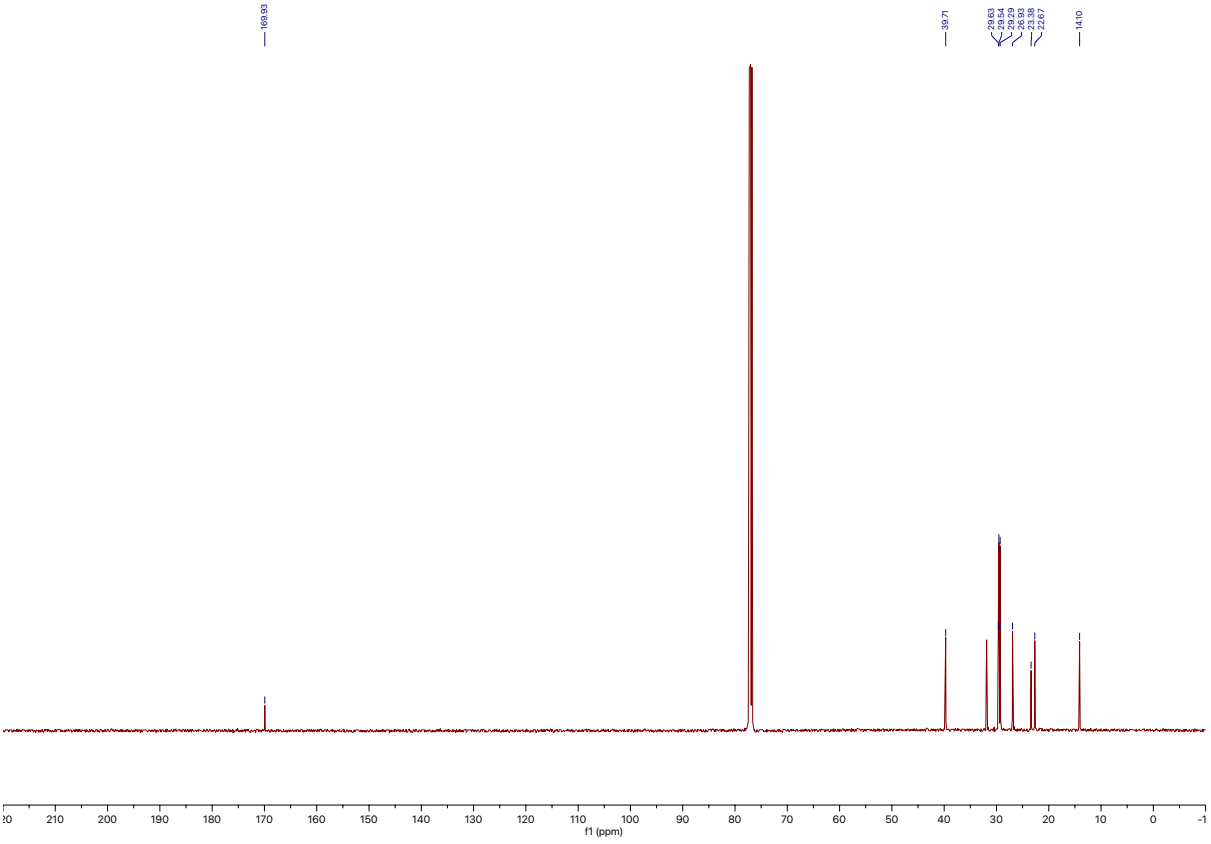
(14) Yashin, N. V.; Markov, P. O.; Sedenkova, K. N.; Vasilenko, D. A.; Grishin, Yu. K.; Kuznetsova, T. S.; Averina, E. B. Alkyl Perchlorates in the Ritter-Type Reaction. Synthesis of N-Alkylamides. *Russ. Chem. Bull.* **2020**, *69* (5), 980–985. https://doi.org/10.1007/s11172-020-2858-8.
(15) Rao, S. N.; Mohan, D. C.; Adimurthy, S. L-Proline: An Efficient Catalyst for Transamidation of Carboxamides with Amines. *Org. Lett.* **2013**, *15* (7), 1496–1499. https://doi.org/10.1021/ol4002625.
(16) Langlois, M.; Bremont, B.; Shen, S.; Poncet, A.; Andrieux, J.; Sicsic, S.; Serraz, I.; Mathe-Allainmat, M.; Renard, P.; Delagrange, P. Design and Synthesis of New Naphthalenic Derivatives as Ligands for 2-[125I]Iodomelatonin Binding Sites. *J. Med. Chem.* **1995**, *38* (12), 2050–2060. https://doi.org/10.1021/jm00012a004.
(17) Fernández, S.; Menéndez, E.; Gotor, V. Oxime Esters as Acylating Agents in the Aminolysis Reaction. A Simple and Chemoselective Method for the Preparation of Amides from Amino Alcohols. *Synthesis* **1991**, *1991* (09), 713–716. https://doi.org/10.1055/s-1991-26553.
(18) Guo, Y.; Shao, G.; Li, L.; Wu, W.; Li, R.; Li, J.; Song, J.; Qiu, L.; Prashad, M.; Kwong, F. Y. A General Approach to the Synthesis of B2-Amino Acid Derivatives via Highly Efficient Catalytic Asymmetric Hydrogenation of α-Aminomethylacrylates. *Adv. Synth. Catal.* **2010**, *352* (9), 1539–1553. https://doi.org/10.1002/adsc.201000122.
(19) Contente, M. L.; Pinto, A.; Molinari, F.; Paradisi, F. Biocatalytic N-Acylation of Amines in Water Using an Acyltransferase from Mycobacterium Smegmatis. *Adv. Synth. Catal.* **2018**, *360* (24), 4814–4819. https://doi.org/10.1002/adsc.201801061.
(20) Manolov, S.; Nikolova, S.; Ivanov, I. Silica-Supported Polyphosphoric Acid in the Synthesis of 4-Substituted Tetrahydroisoquinoline Derivatives. *Molecules* **2013**, *18* (2), 1869–1880. https://doi.org/10.3390/molecules18021869.
(21) Boyd, E. A.; Lionetti, D.; Henke, W. C.; Day, V. W.; Blakemore, J. D. Preparation, Characterization, and Electrochemical Activation of a Model [Cp*Rh] Hydride. *Inorg. Chem.* **2019**, *58* (6), 3606–3615. https://doi.org/10.1021/acs.inorgchem.8b02160.
(22) Colebrooke, S. A.; Duckett, S. B.; Lohman, J. A. B.; Eisenberg, R. Hydrogenation Studies Involving Halobis(Phosphine)–Rhodium(i) Dimers: Use of Parahydrogen Induced Polarisation To Detect Species Present at Low Concentration. *Chem. – Eur. J.* **2004**, *10* (10), 2459–2474. https://doi.org/10.1002/chem.200305466.
(23) Isobe, K.; Bailey, P. M.; Maitlis, P. M. Pentamethylcyclopentadienyl-Rhodium and -Iridium Complexes. Part 30. Trimethylphosphine-Chloro-, -Acetato-, and -Hydrido-Complexes and Related Compounds of (Hexamethylbenzene)Ruthenium. *J. Chem. Soc. Dalton Trans.* **1981**, No. 9, 2003–2008. https://doi.org/10.1039/DT9810002003.

10. NMR Spectra

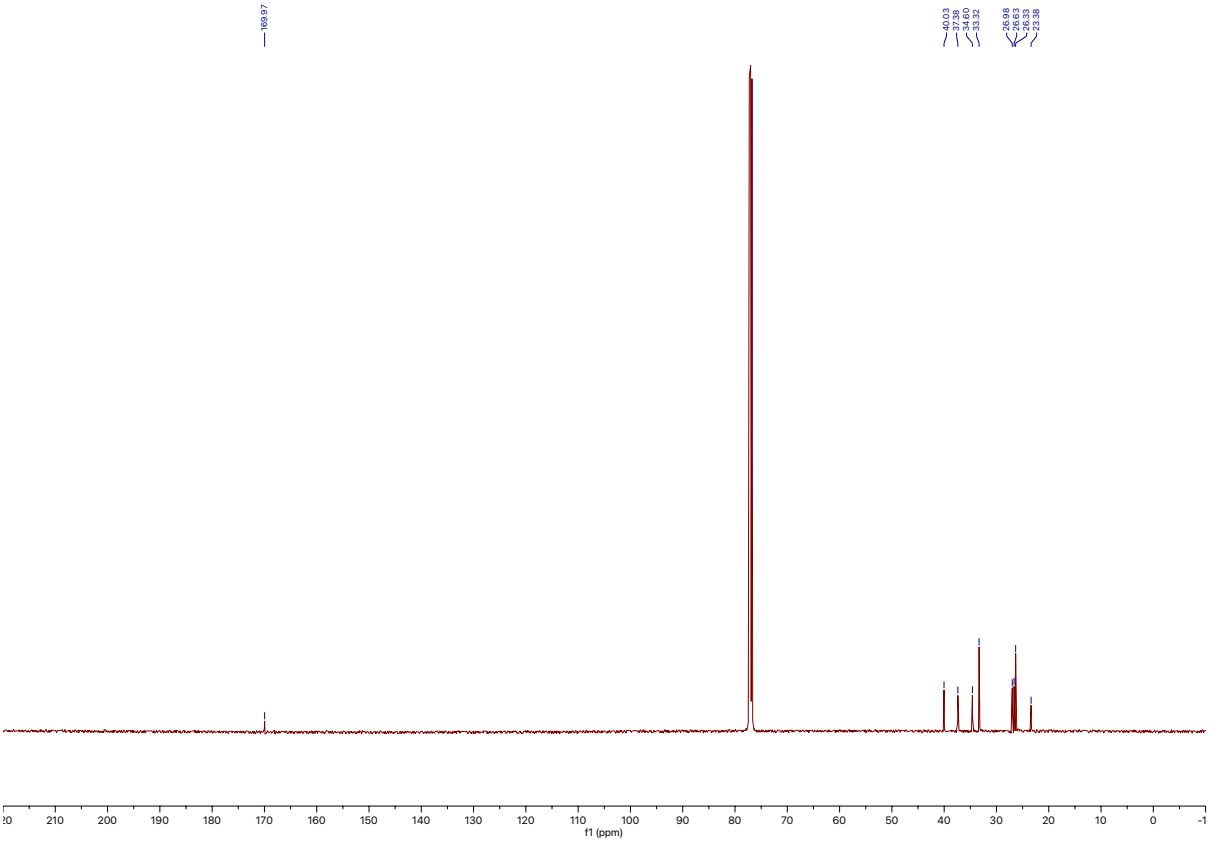


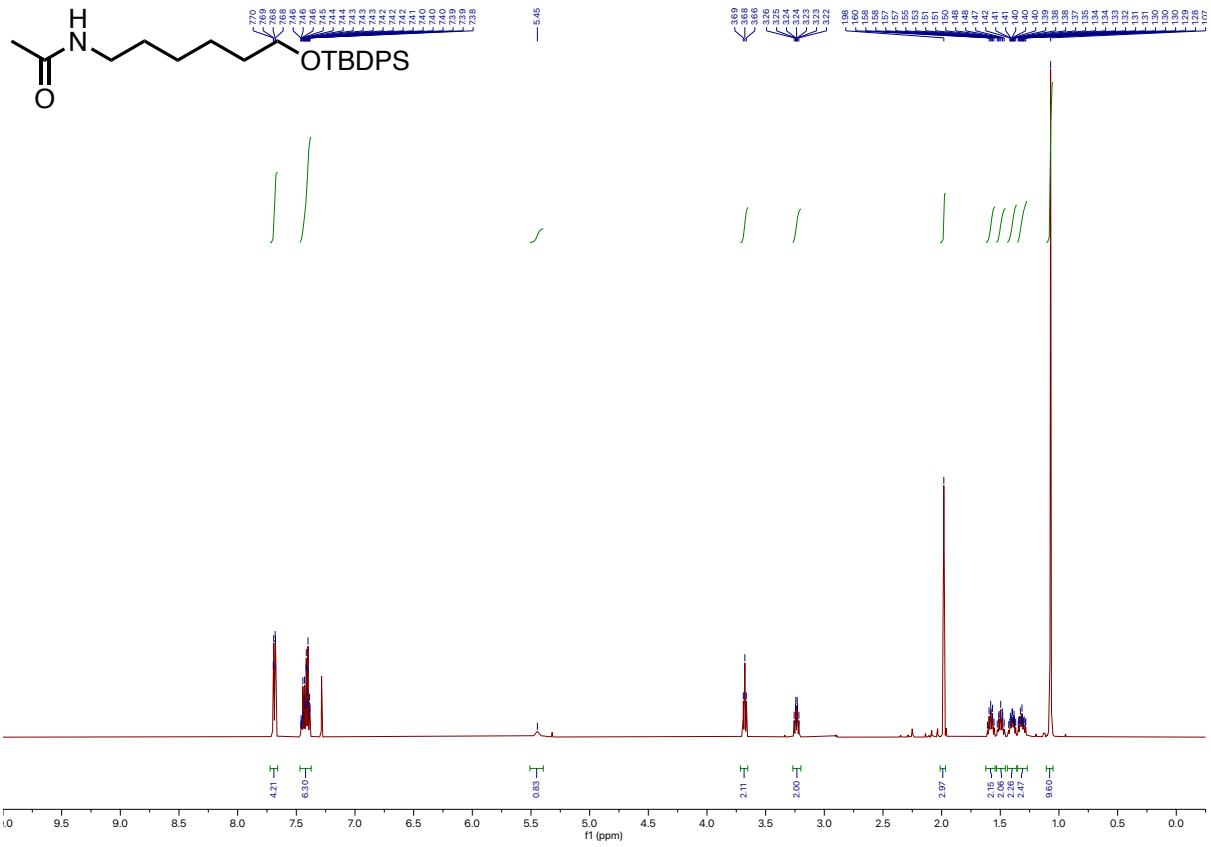


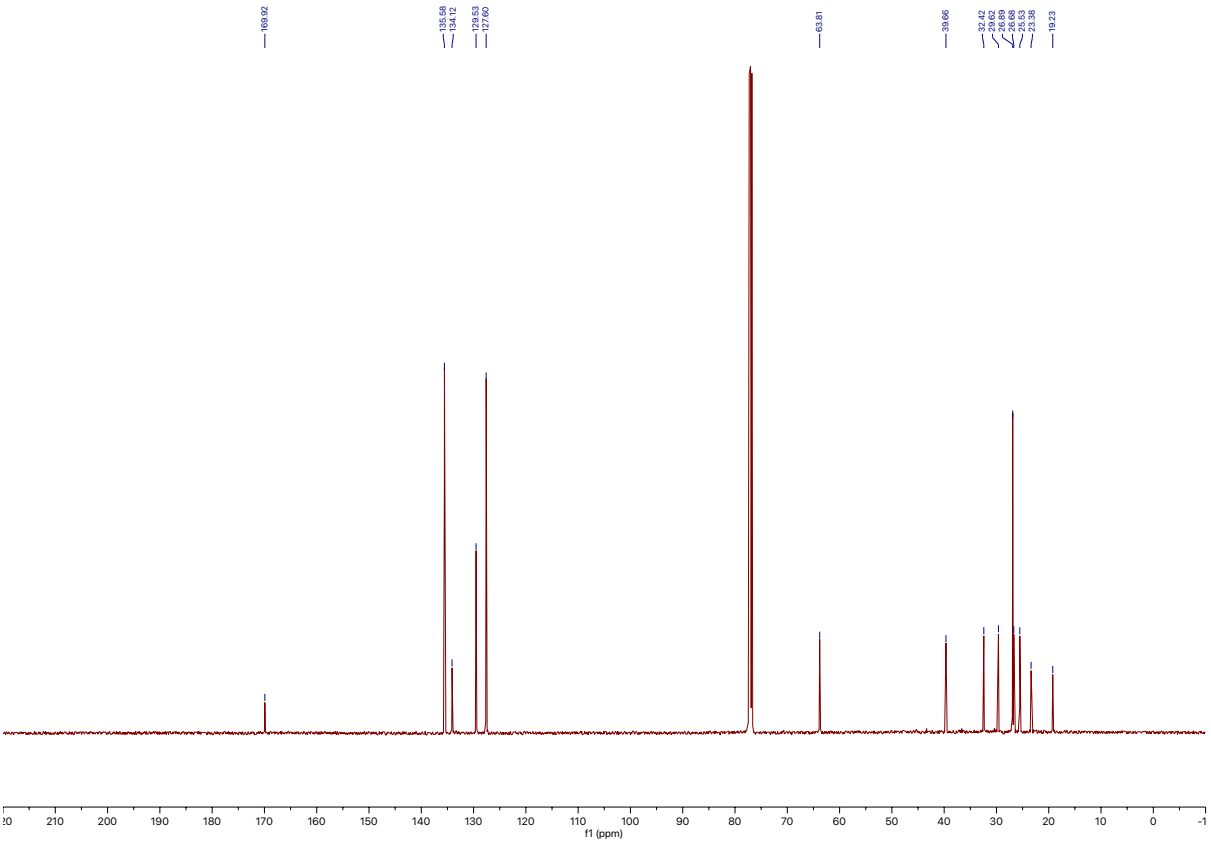

H
N
O
5.47
5.47
3.27
3.26
3.25
3.24
3.24
3.23
1.99
1.54
1.53
1.51
1.49
1.48
1.32
1.32
1.31
1.30
1.28
0.91
0.90
0.88
0.92
2.00
2.93
2.03
14.75
3.11
f1 (ppm)

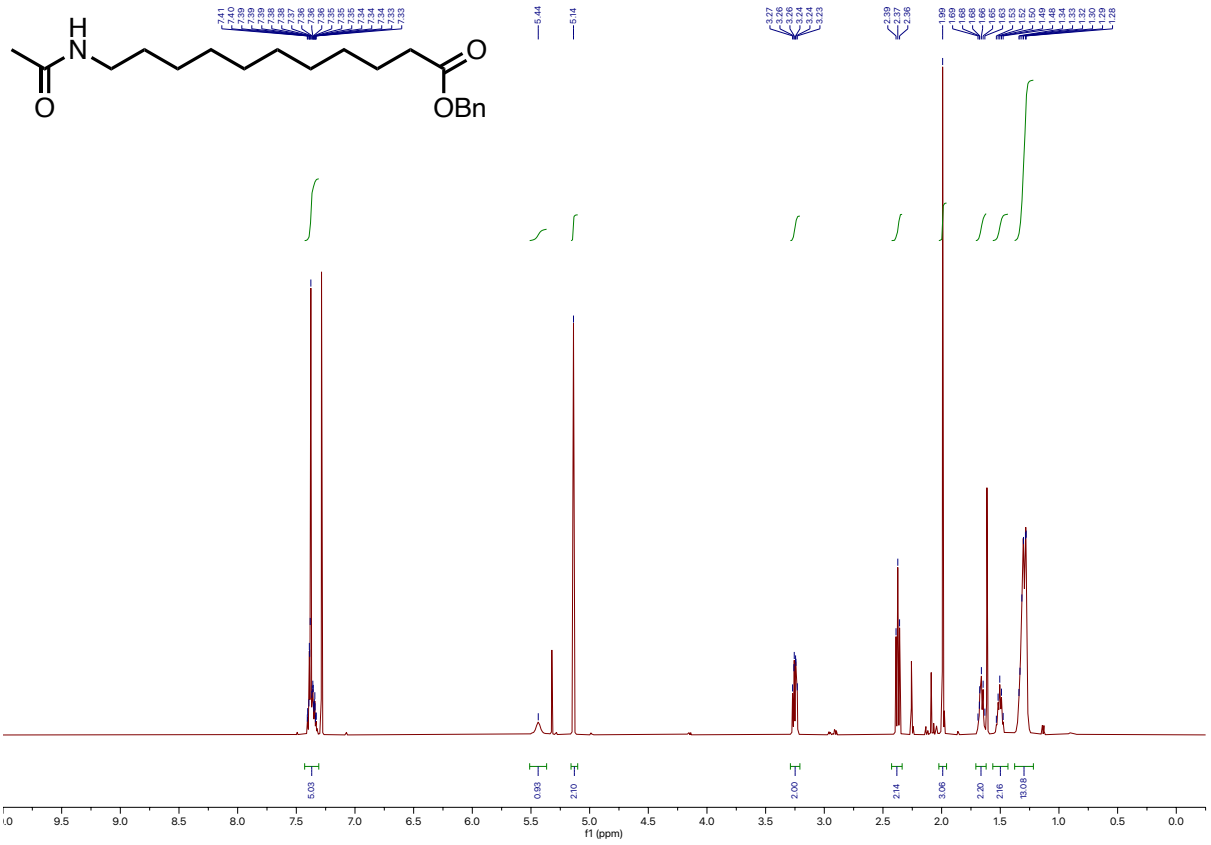

169.93
39.71
29.63
29.54
29.29
26.93
23.38
22.67
14.10
f1 (ppm)

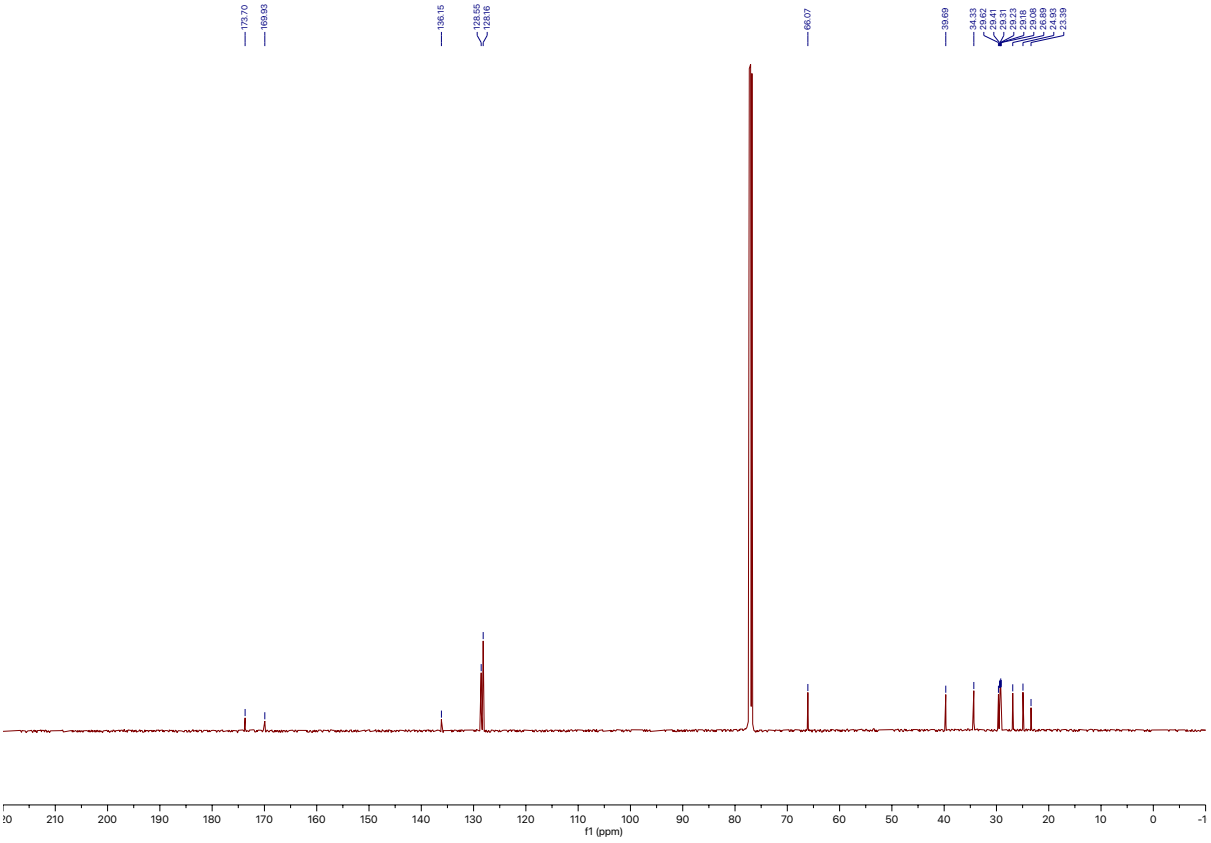

H
N
O
1.01
2.00
2.97
7.17
2.05
6.35
2.14
f1 (ppm)

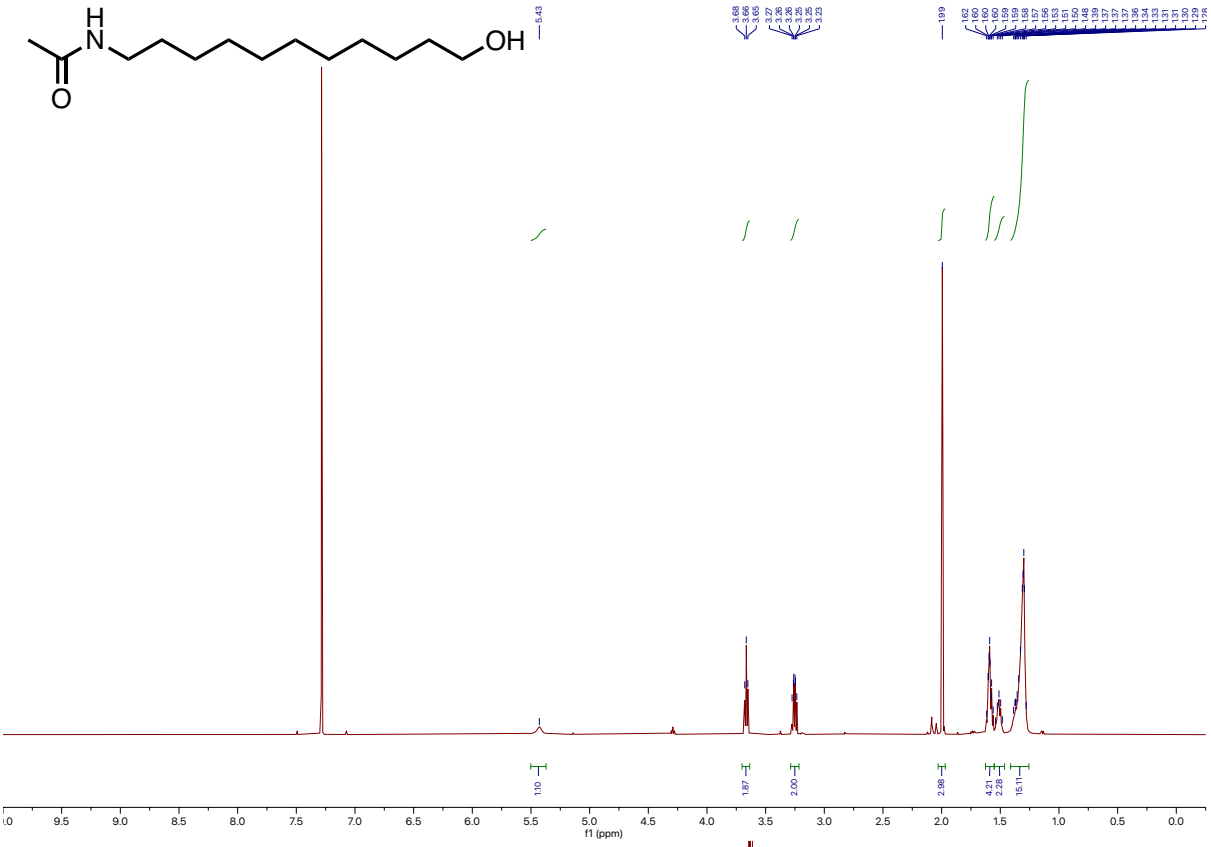

169.97
40.03
37.38
34.60
33.32
26.98
26.53
26.33
23.38
f1 (ppm)

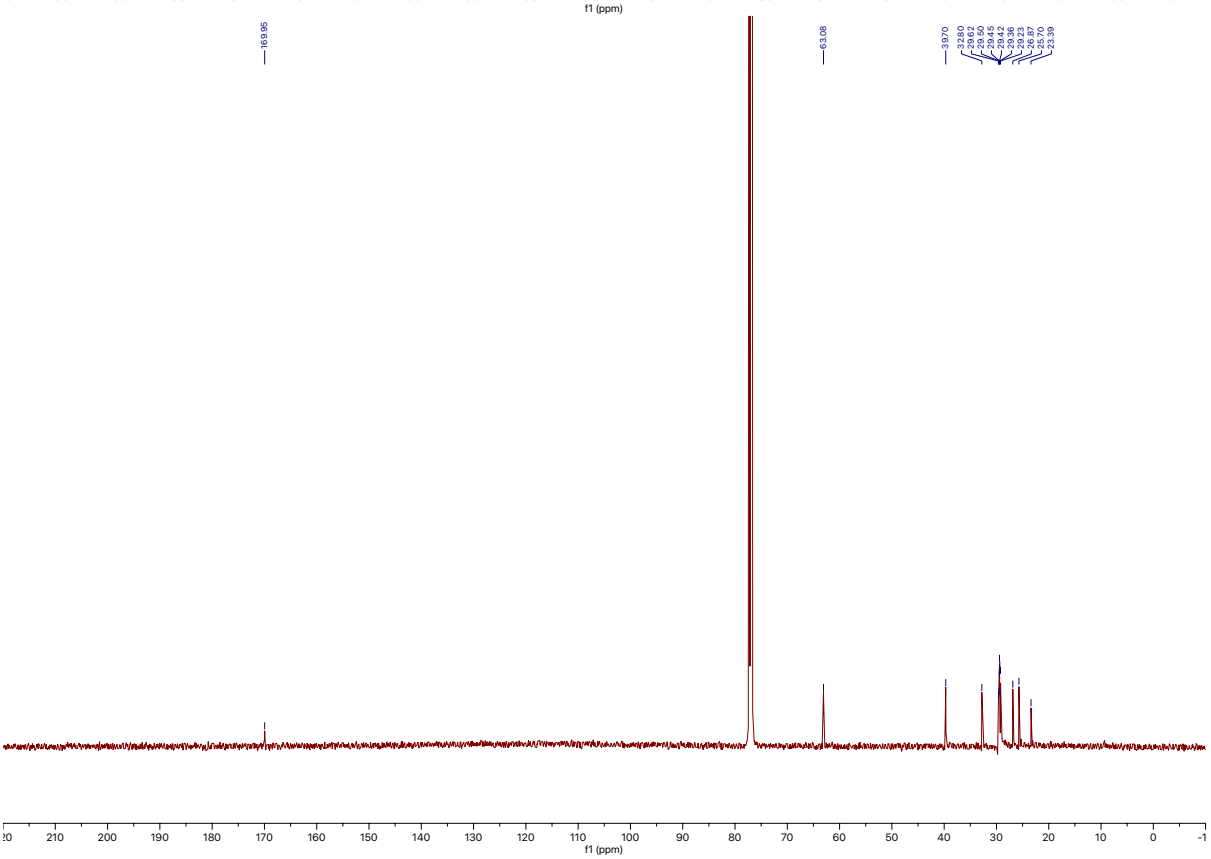

H
N
O
OTBDPS
f1 (ppm)

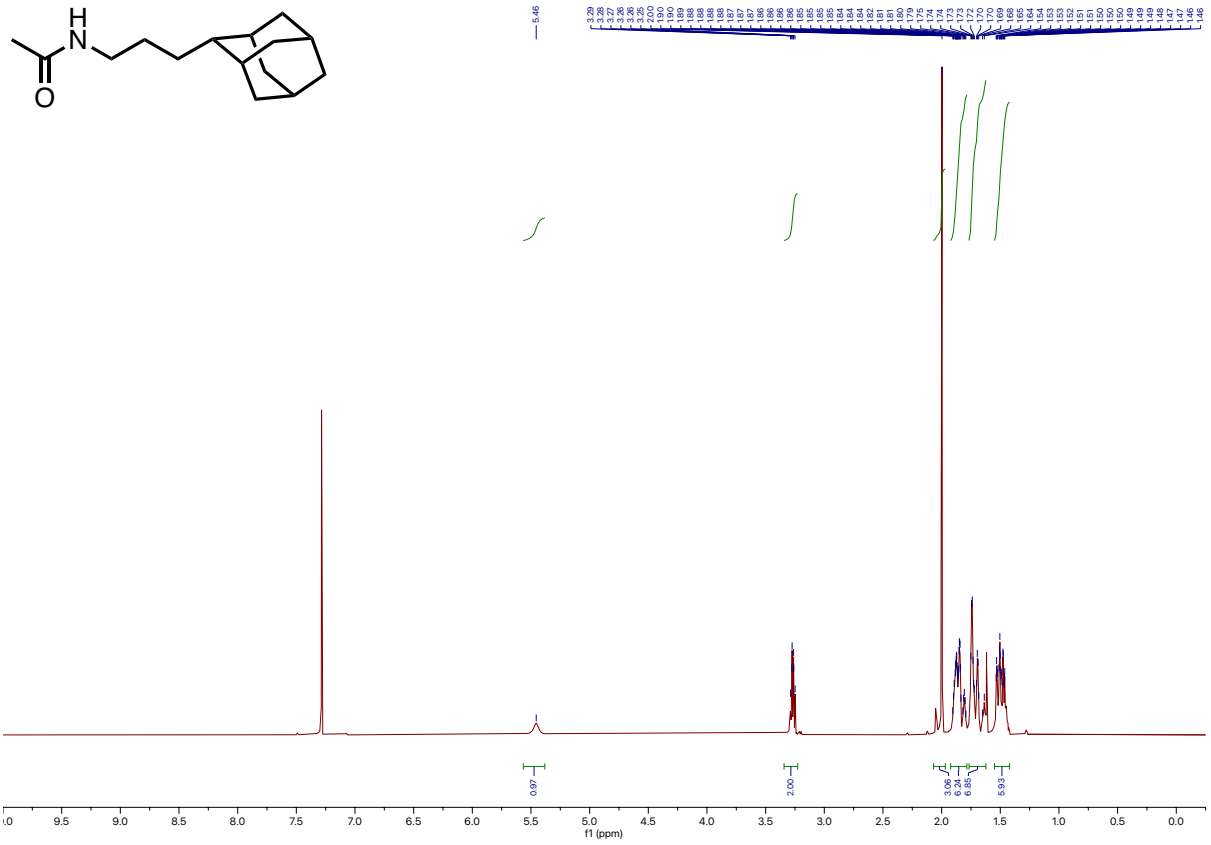

169.92
135.58
134.12
129.53
127.60
63.81
39.66
32.42
29.62
26.89
26.68
25.53
23.38
19.23
f1 (ppm)

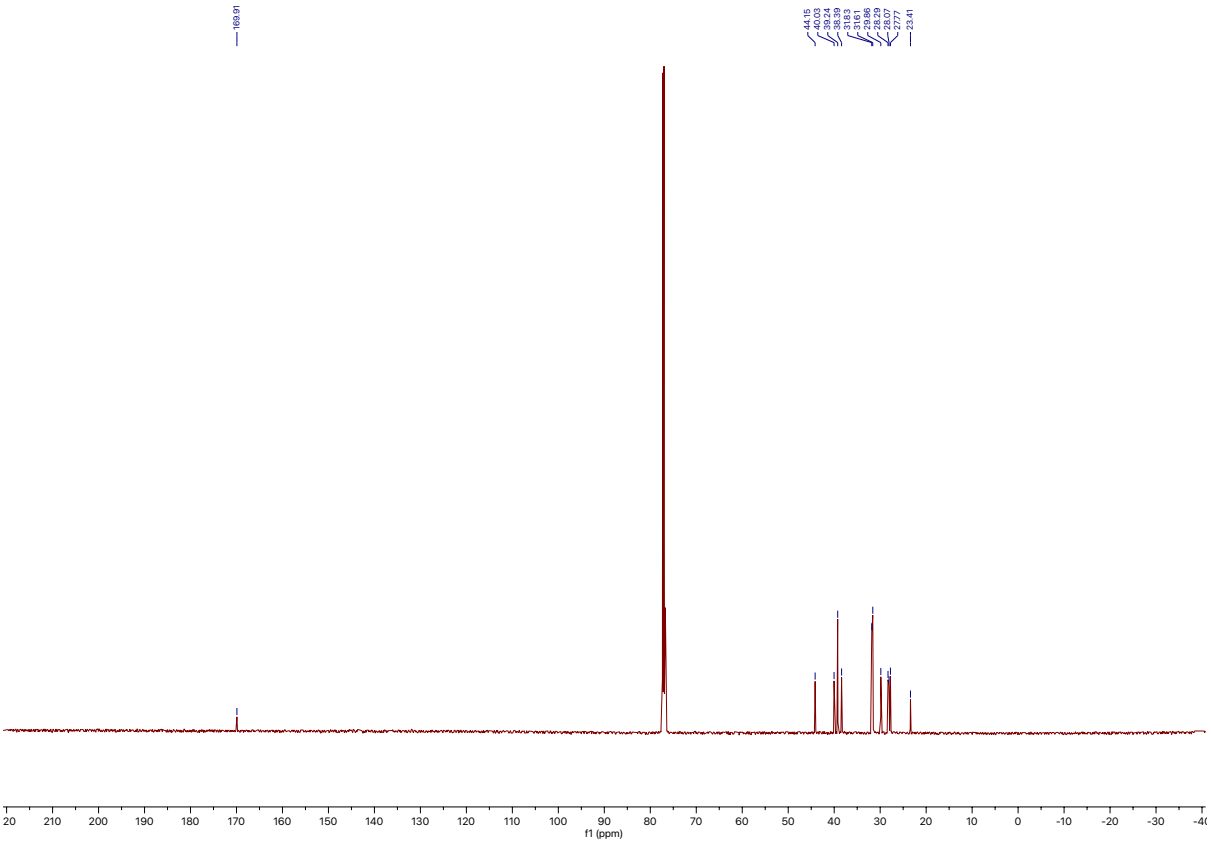

H
N
O
O
OBn
f1 (ppm)

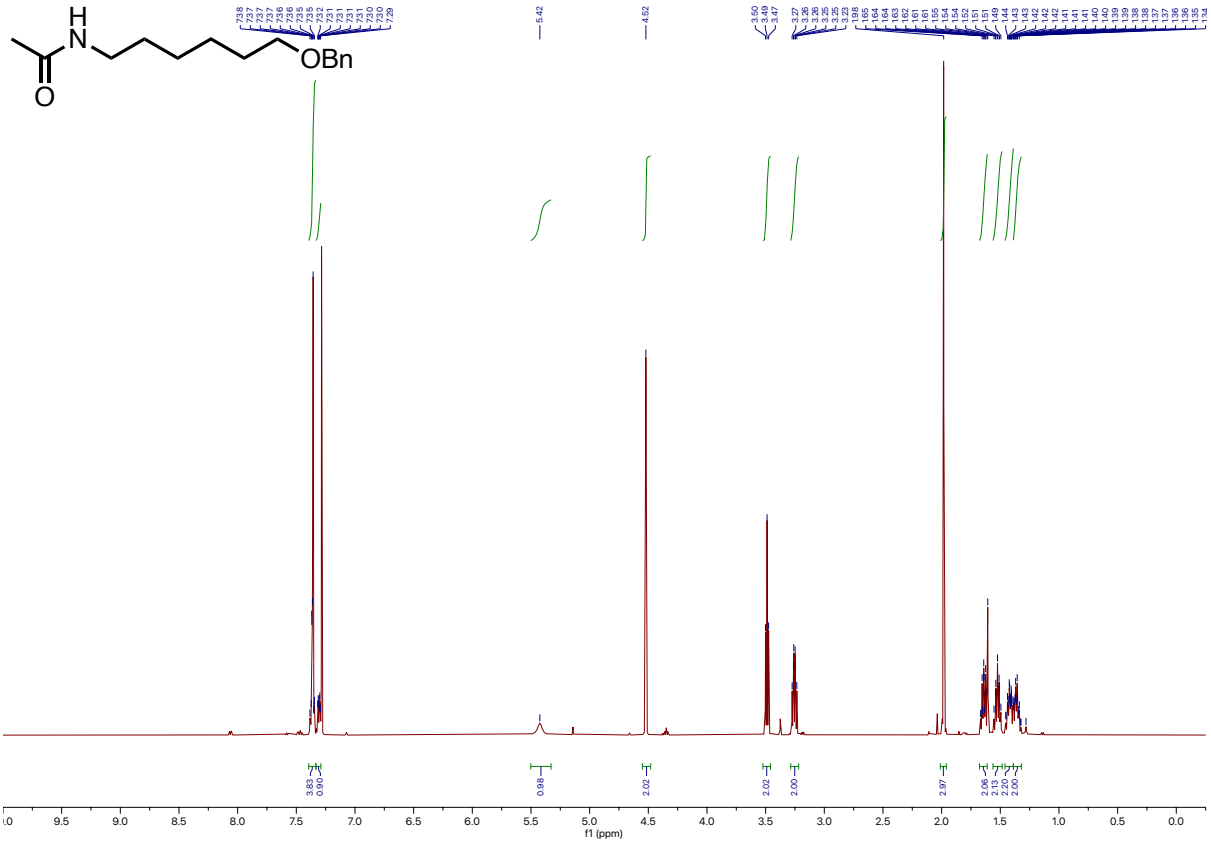

f1 (ppm)

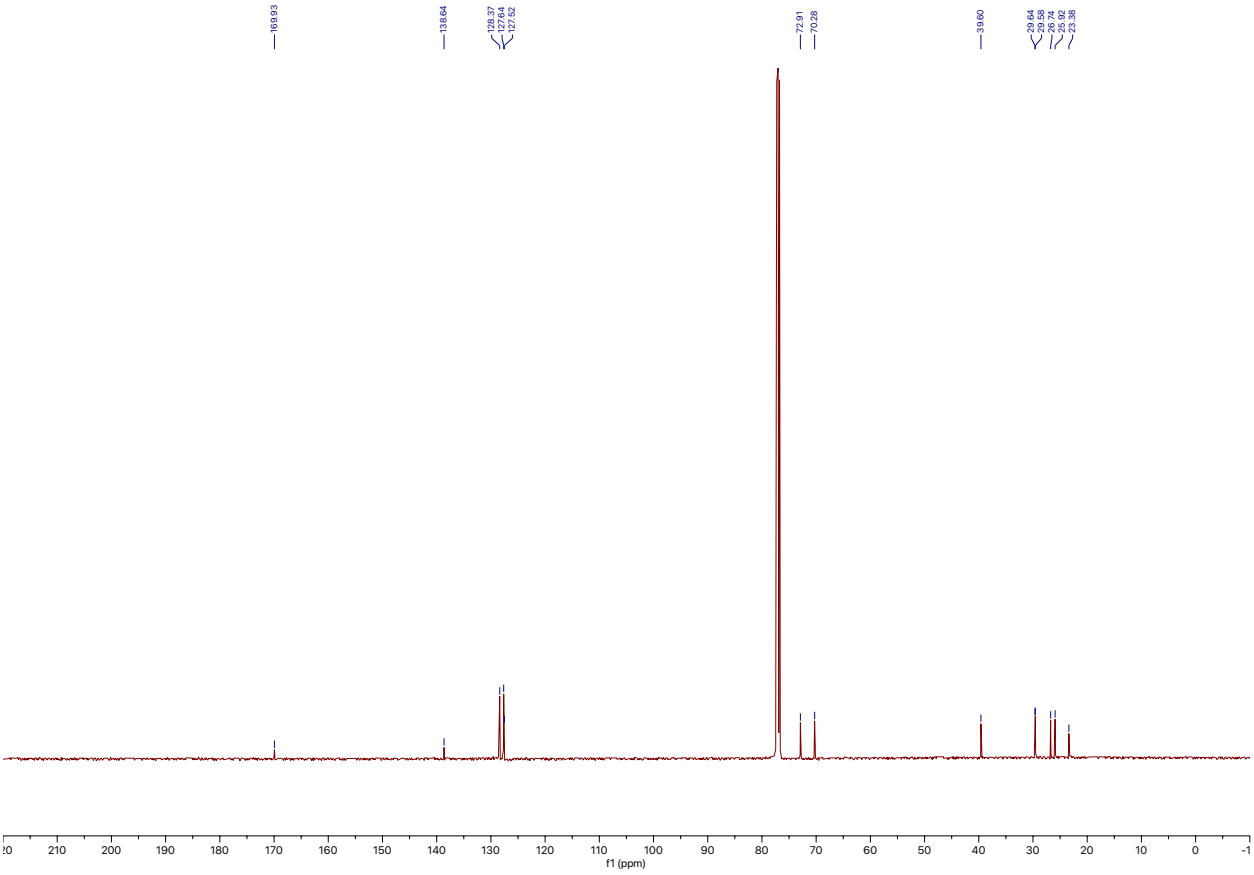

H
N
O
OH
f1 (ppm)

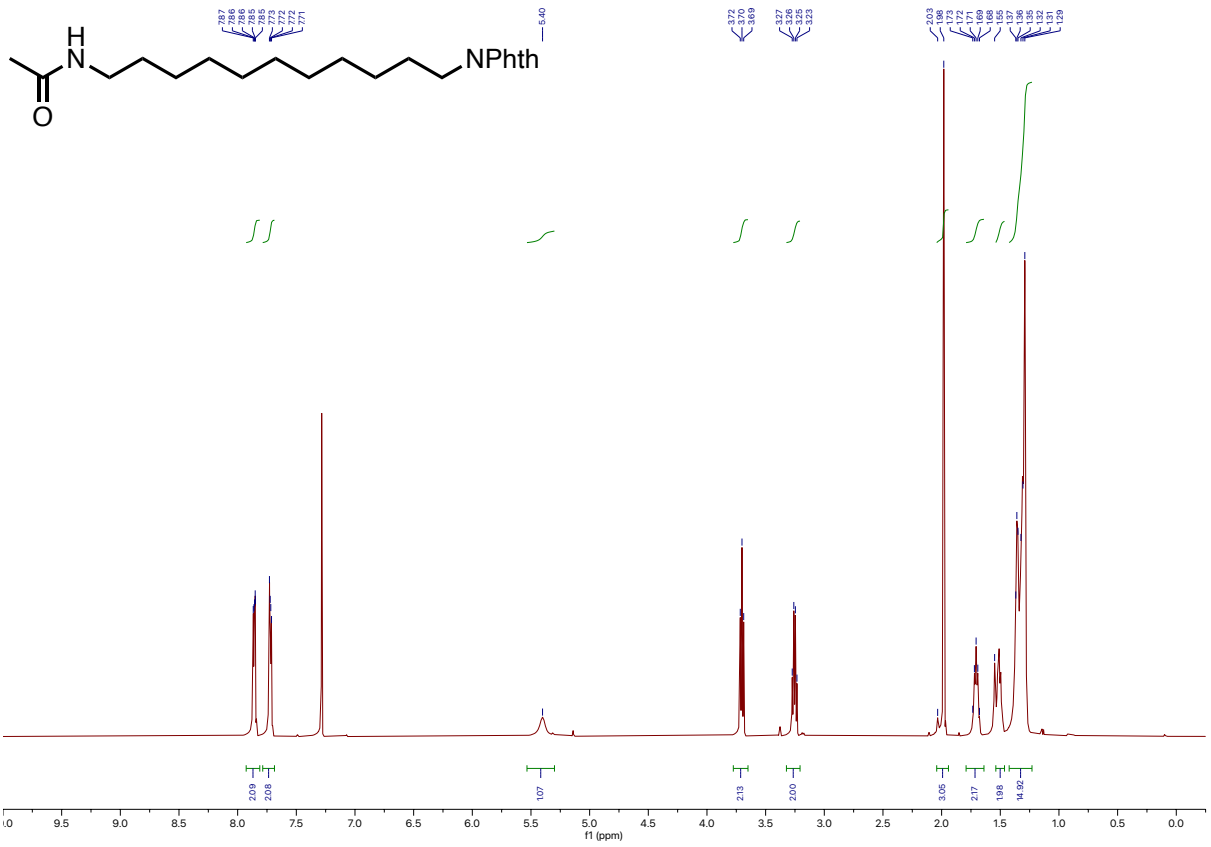

f1 (ppm)

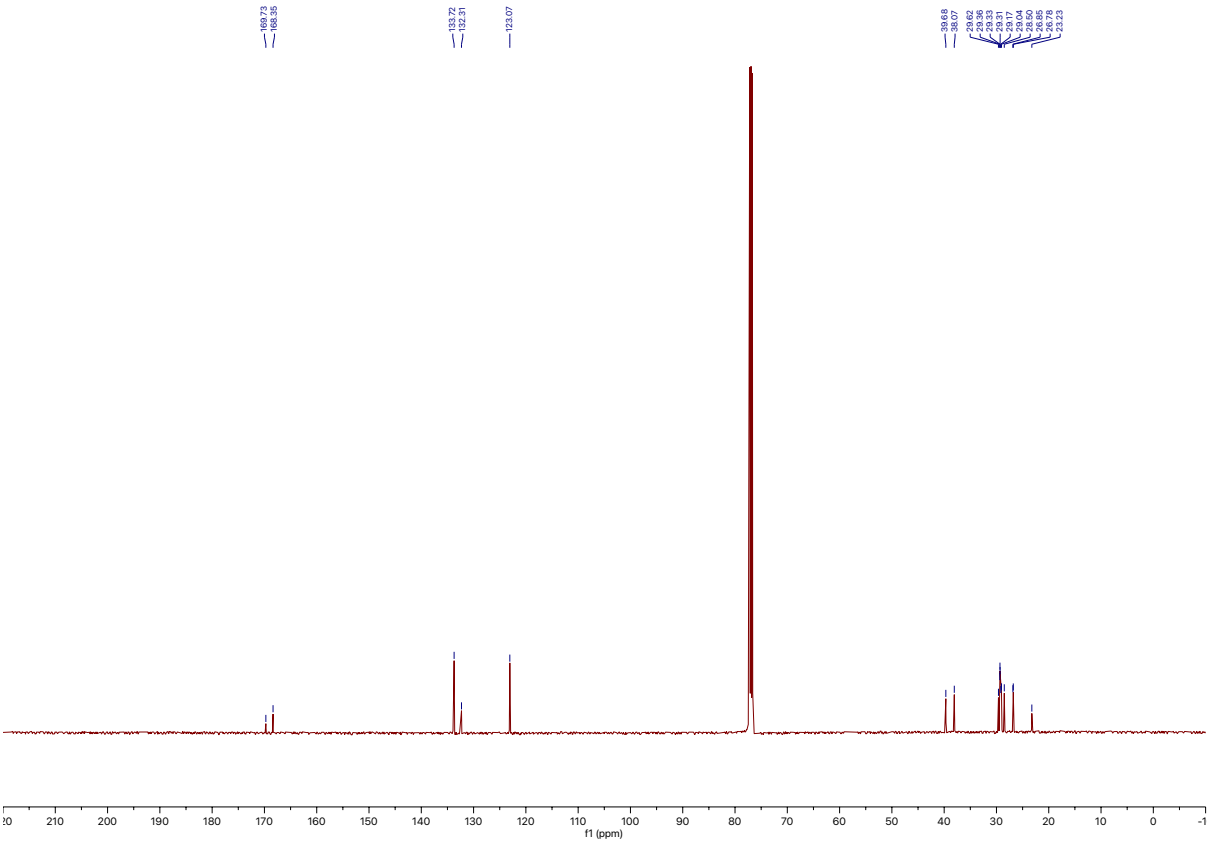

H
N
O
5.46
0.97
2.00
3.06
6.24
6.85
5.93
f1 (ppm)

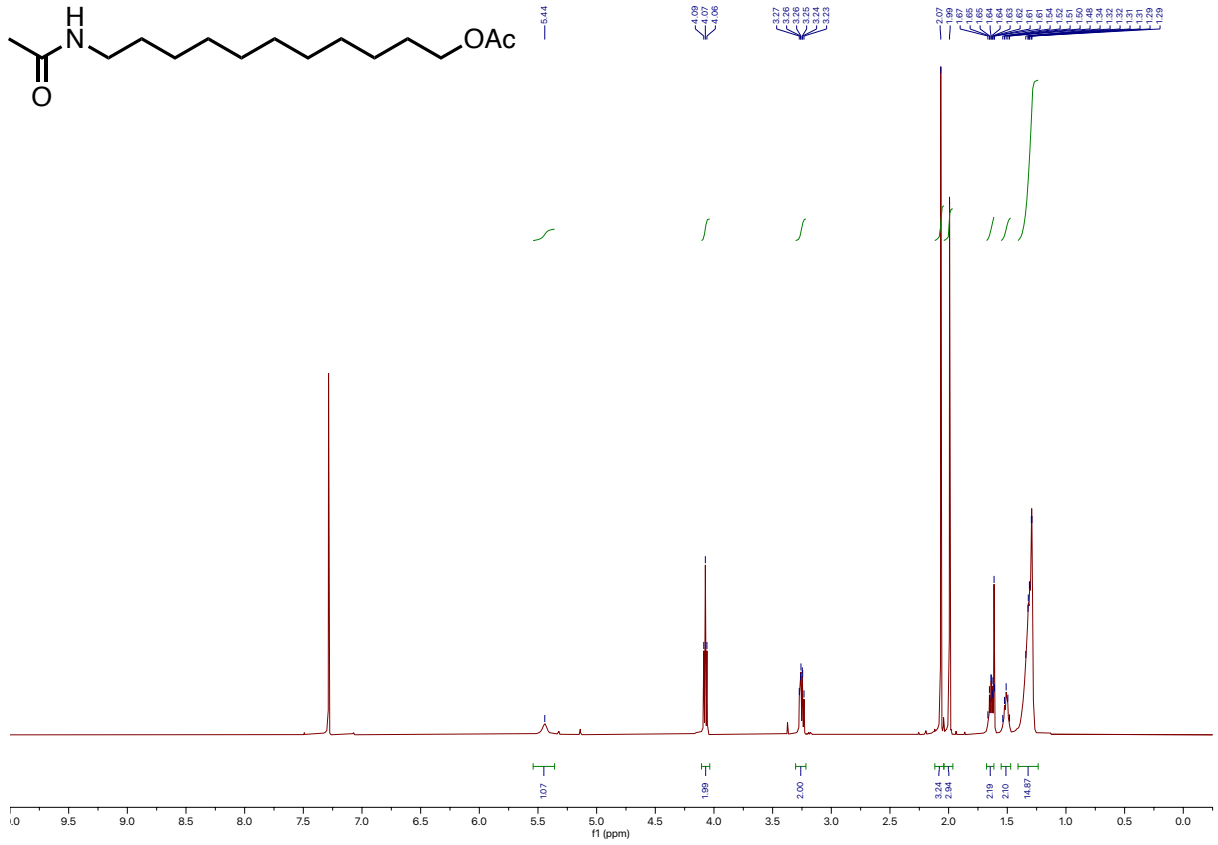

169.91
44.15
40.63
39.24
38.39
31.13
31.61
29.86
28.29
28.07
27.77
23.41
f1 (ppm)

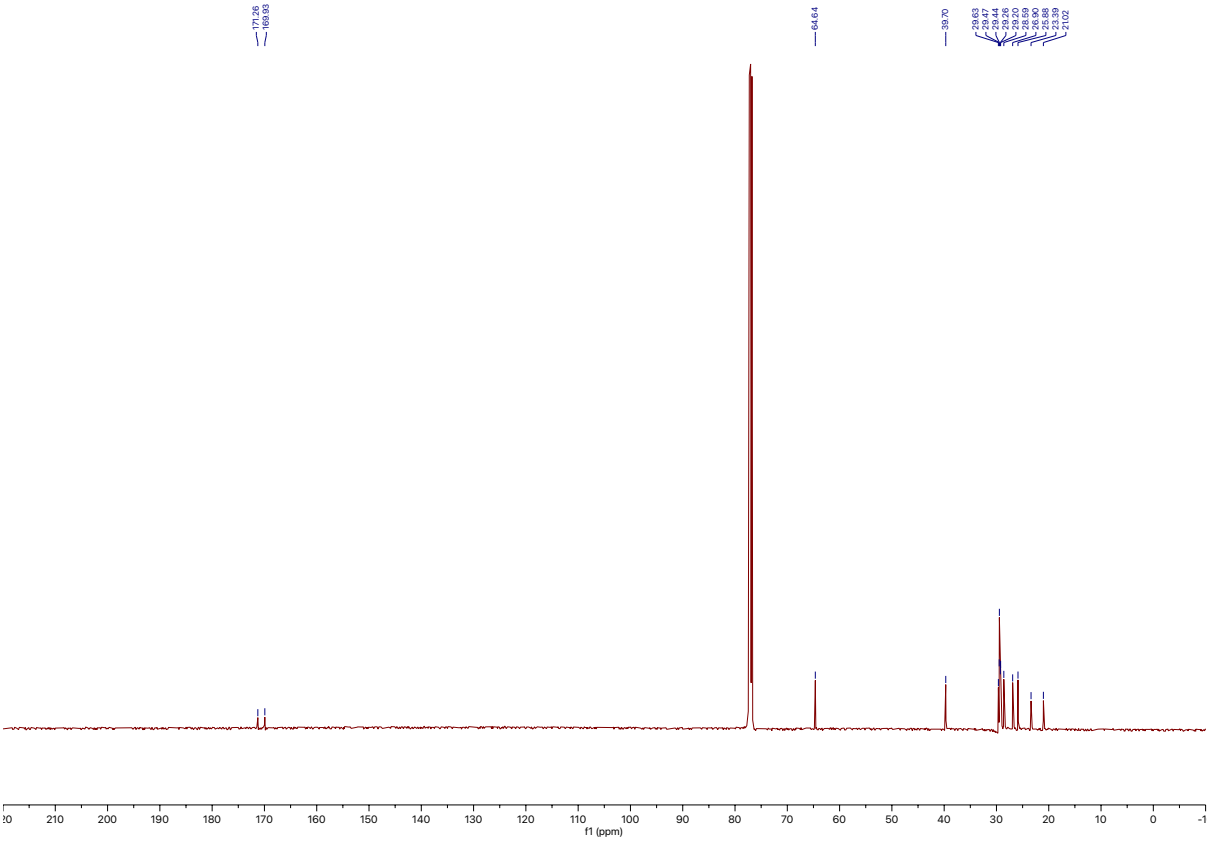

H
N
O
OBn
f1 (ppm)

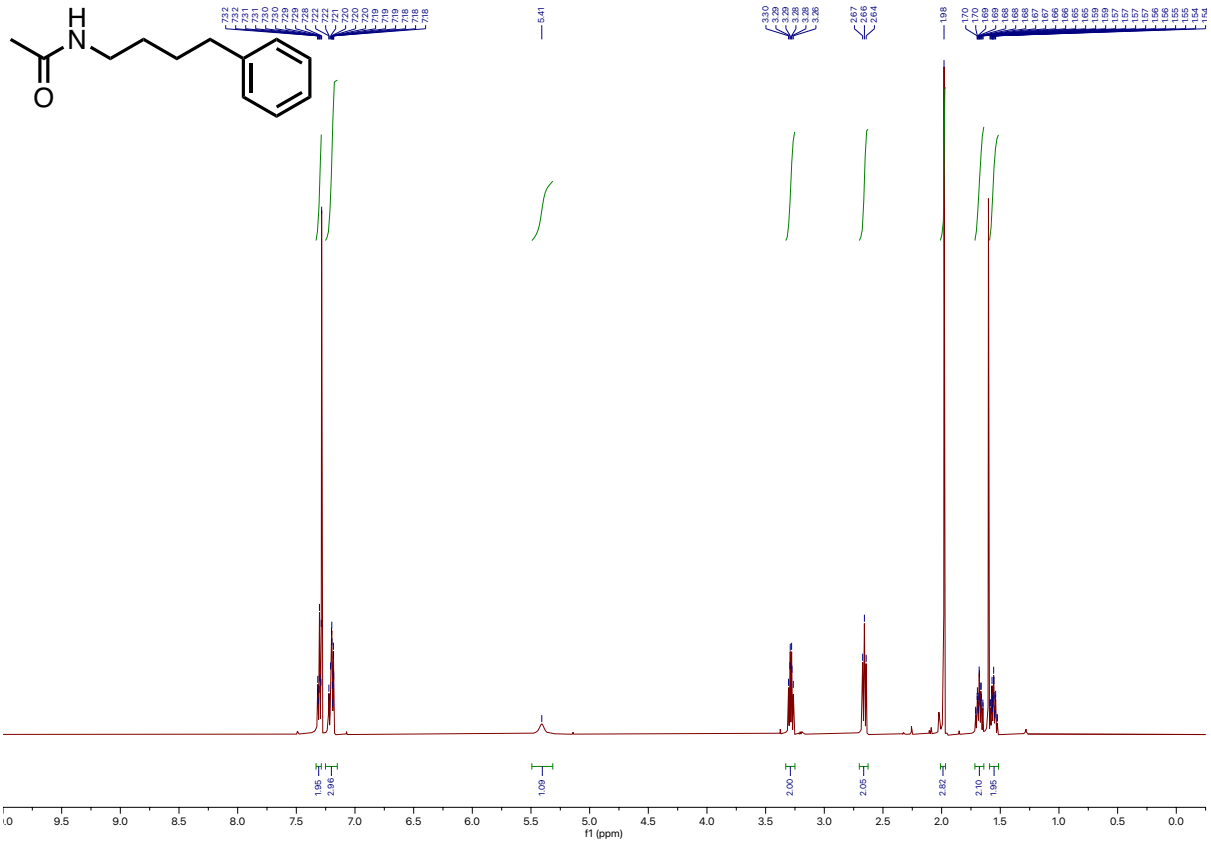

f1 (ppm)

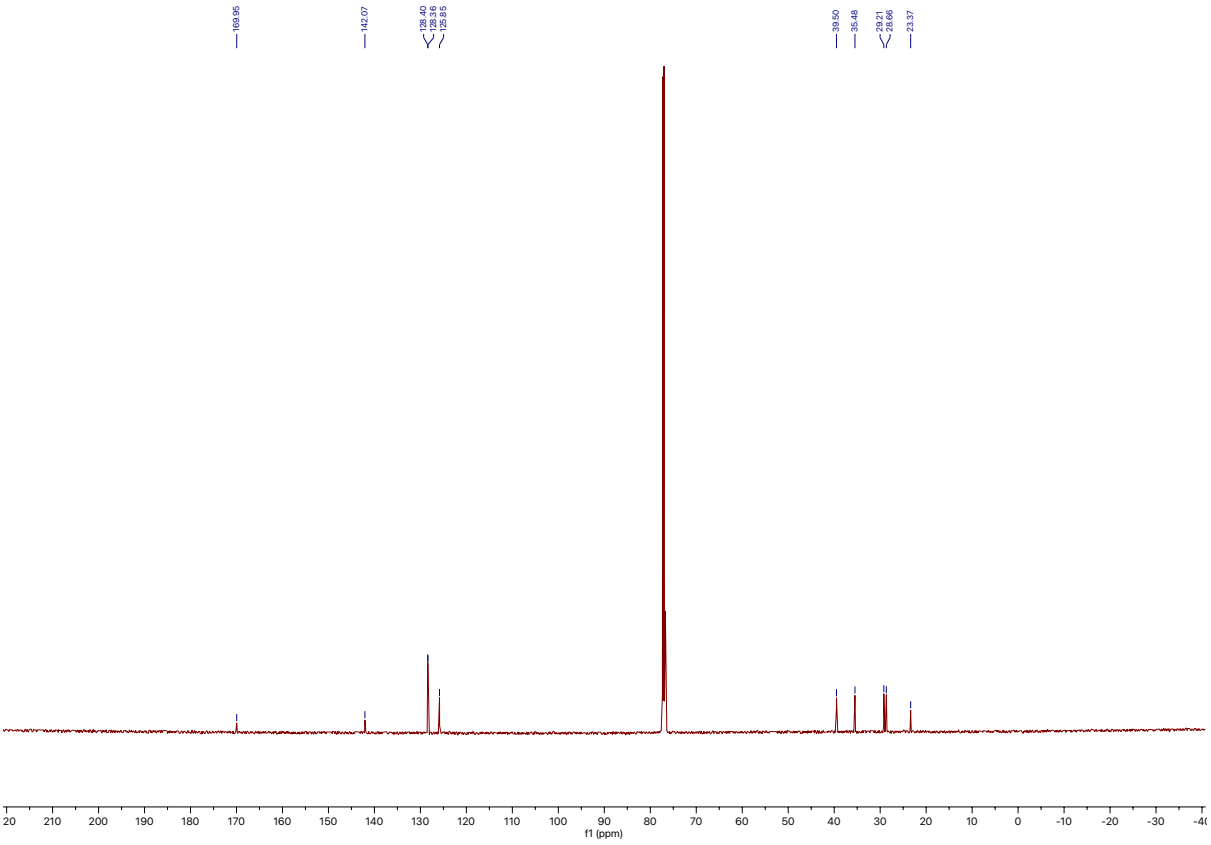

NPhth
f1 (ppm)

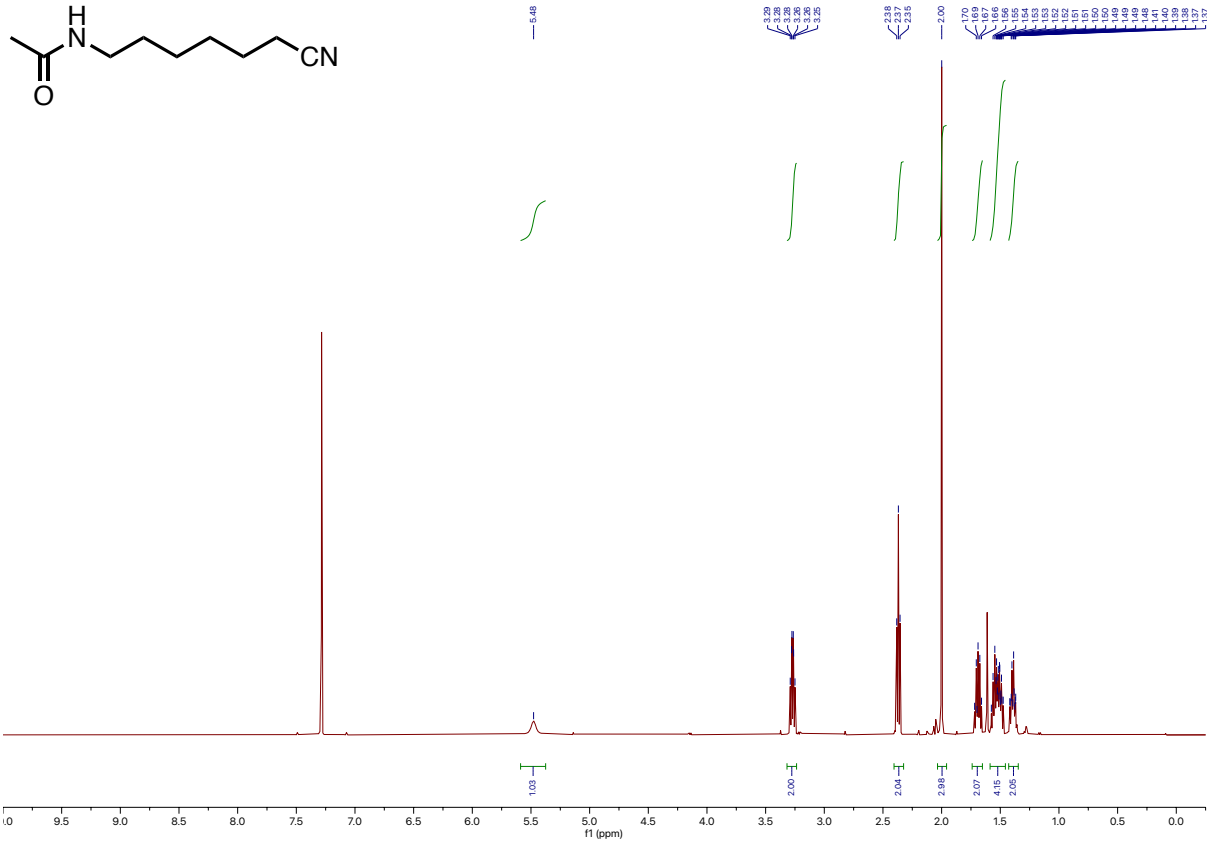

f1 (ppm)

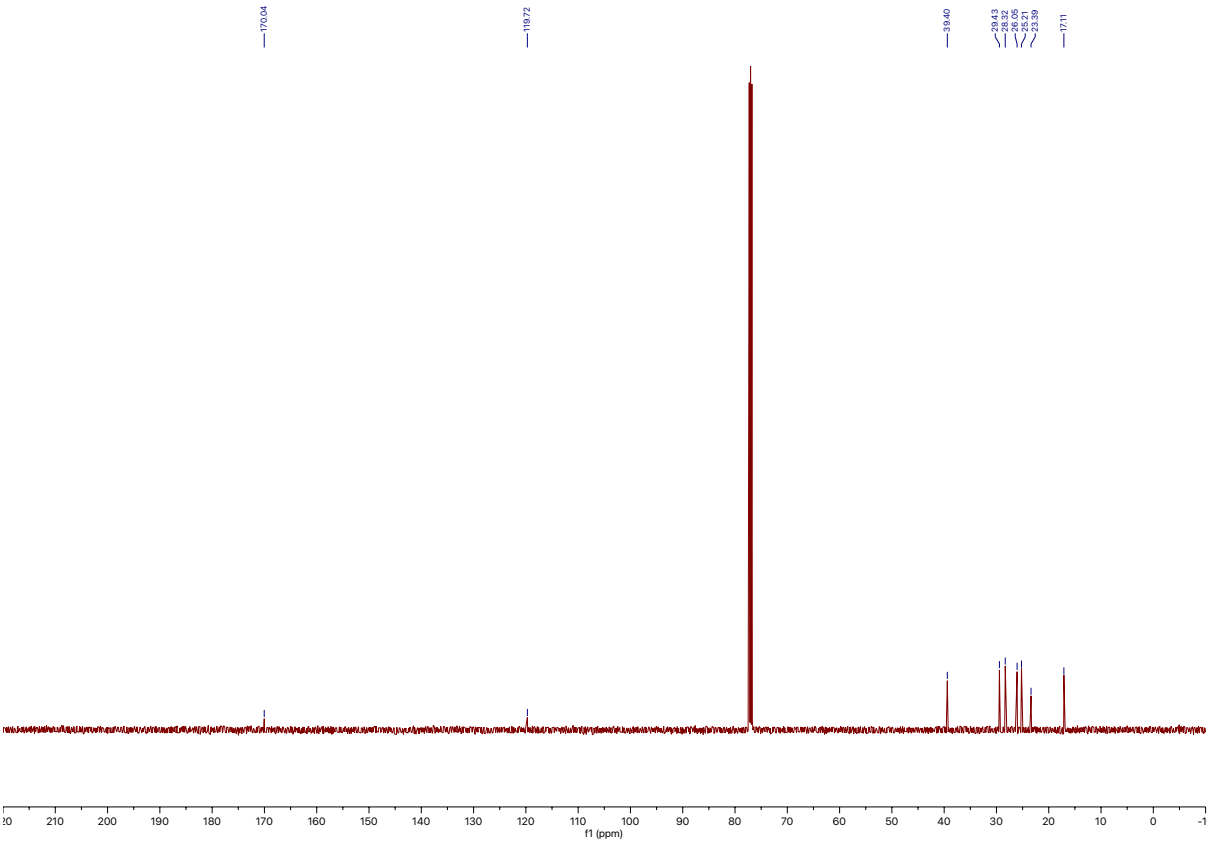

H
N
O
OAc
f1 (ppm)

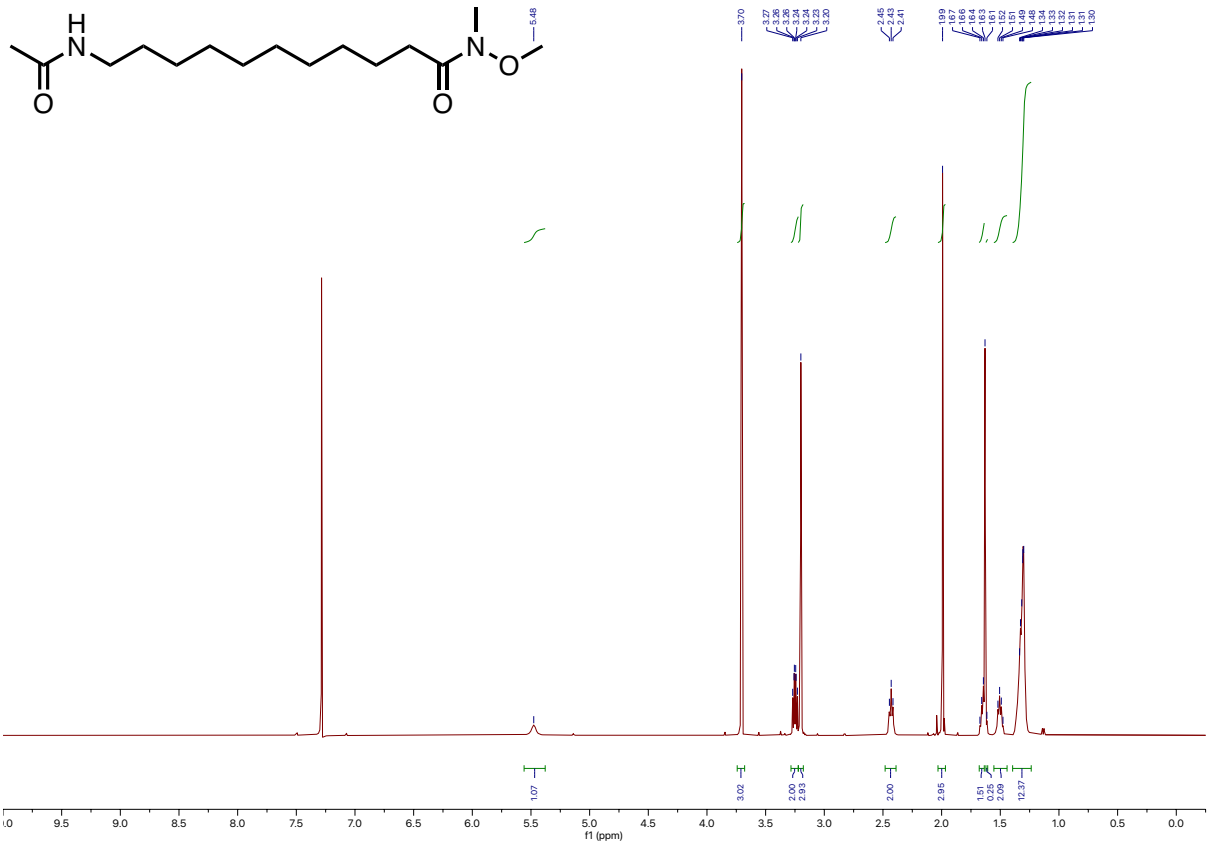

f1 (ppm)

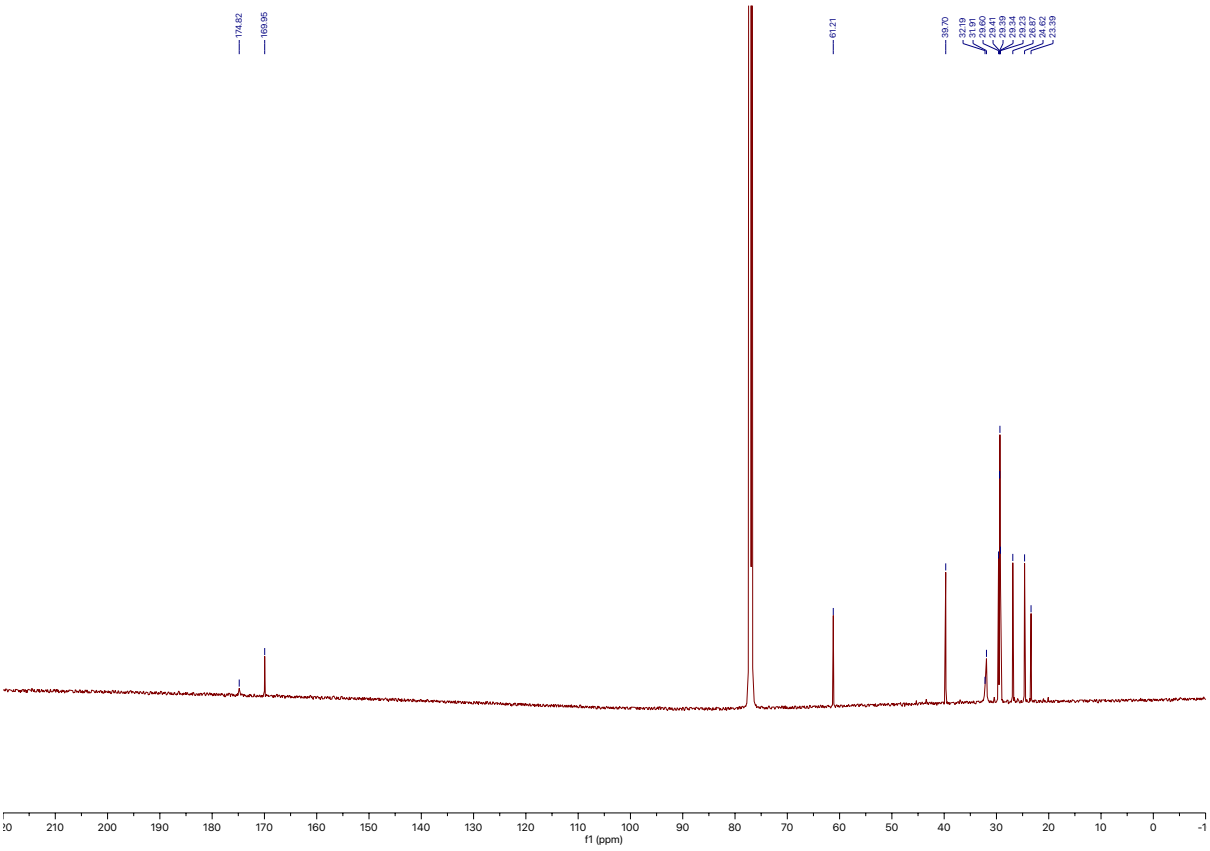

7.32
7.32
7.31
7.31
7.30
7.30
7.29
7.29
7.28
7.22
7.22
7.21
7.20
7.20
7.19
7.19
7.19
7.18
7.18
7.18
5.41
3.30
3.29
3.29
3.28
3.28
3.26
3.26
2.67
2.66
2.64
1.98
1.70
1.70
1.69
1.69
1.68
1.68
1.68
1.68
1.67
1.67
1.67
1.66
1.66
1.65
1.65
1.59
1.59
1.57
1.57
1.57
1.57
1.56
1.56
1.55
1.55
1.54
1.54
1.95
2.96
1.09
2.00
2.05
2.82
2.10
1.95
f1 (ppm)

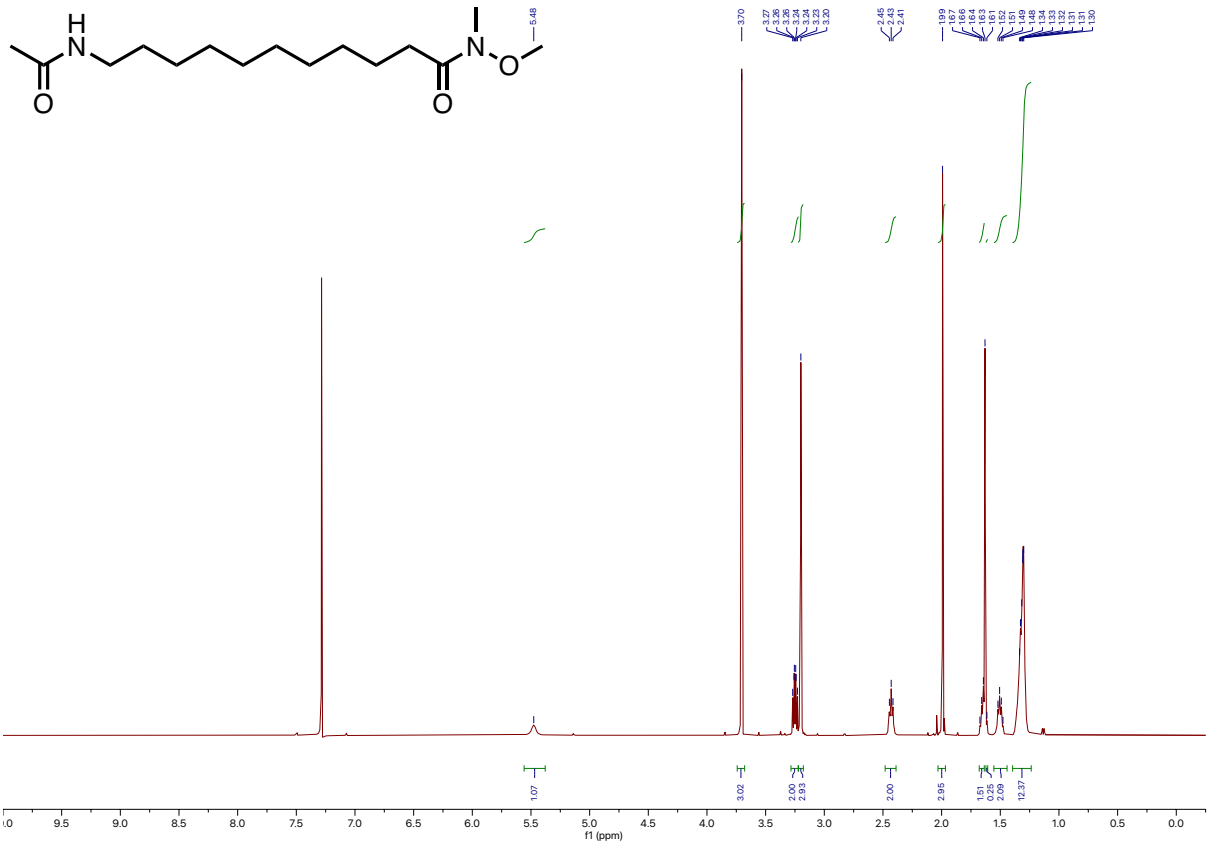

169.95
142.07
128.40
128.36
125.85
39.50
35.48
29.21
28.66
23.37
f1 (ppm)

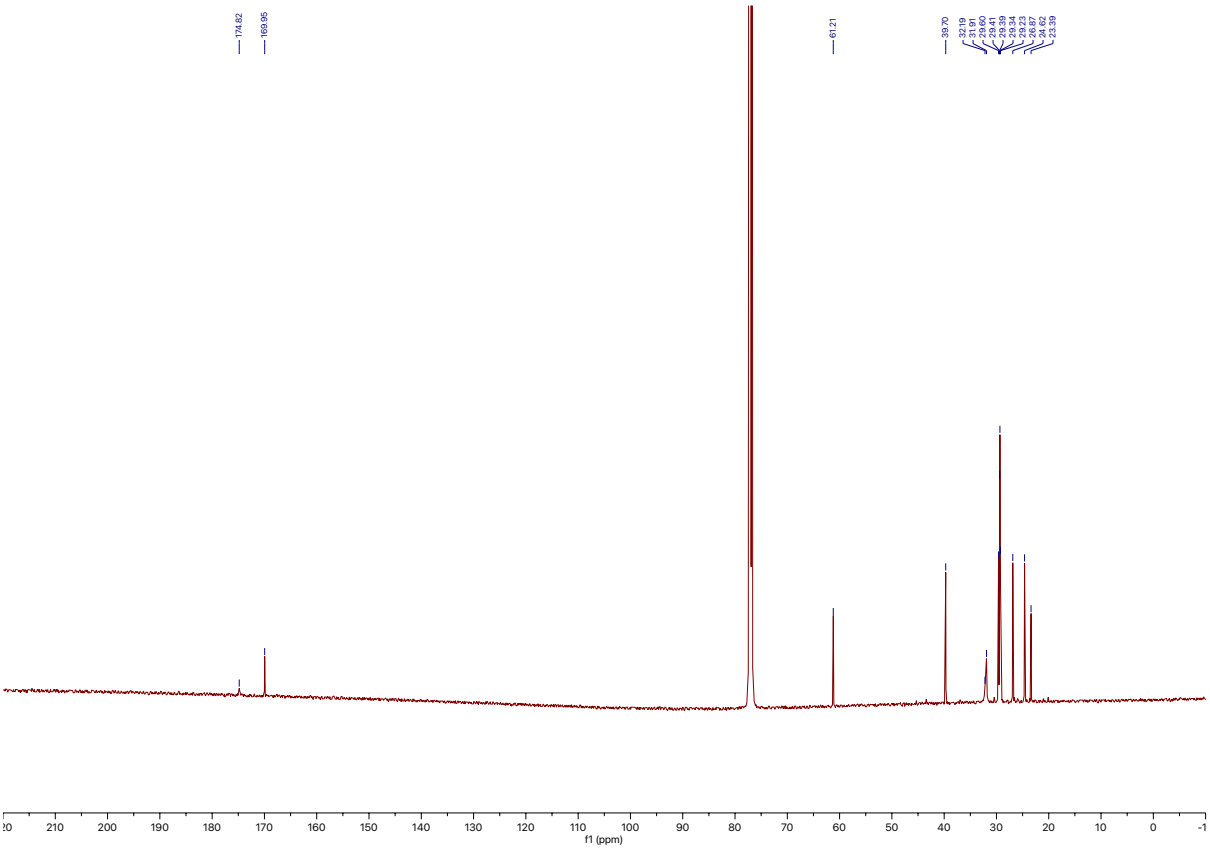

H
N
O
CN
5.48
3.29
3.28
3.26
3.25
2.38
2.37
2.35
2.00
1.03
2.00
2.04
2.98
2.07
4.15
2.05
f1 (ppm)

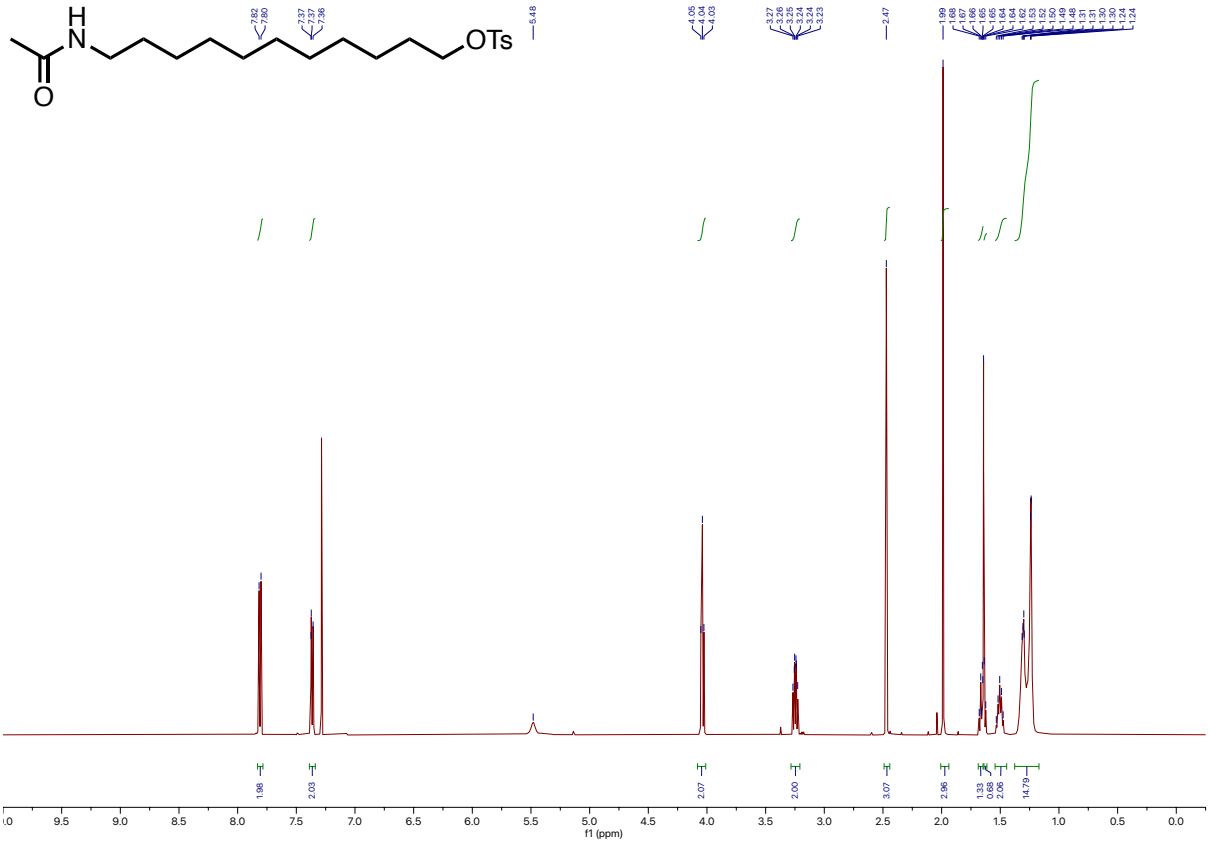

170.04
119.72
39.40
29.43
28.32
25.65
25.21
23.39
17.11
f1 (ppm)

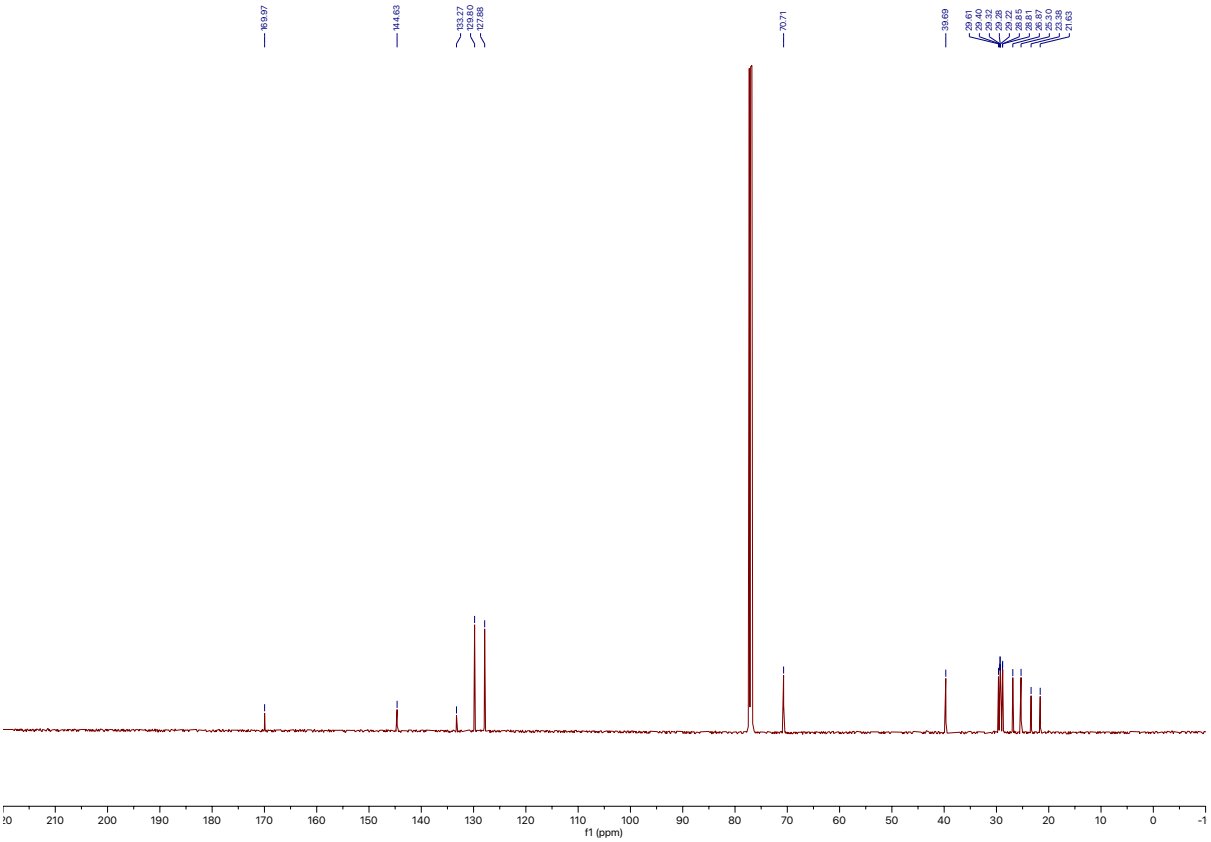

H
N
O
N
O
O
5.48
3.70
3.27
3.26
3.26
3.24
3.24
3.22
3.20
2.45
2.43
2.41
1.99
1.67
1.66
1.64
1.63
1.61
1.52
1.51
1.50
1.49
1.48
1.34
1.34
1.33
1.32
1.31
1.31
1.30
1.07
3.02
2.00
2.93
2.00
2.95
1.51
0.25
2.09
12.37
f1 (ppm)

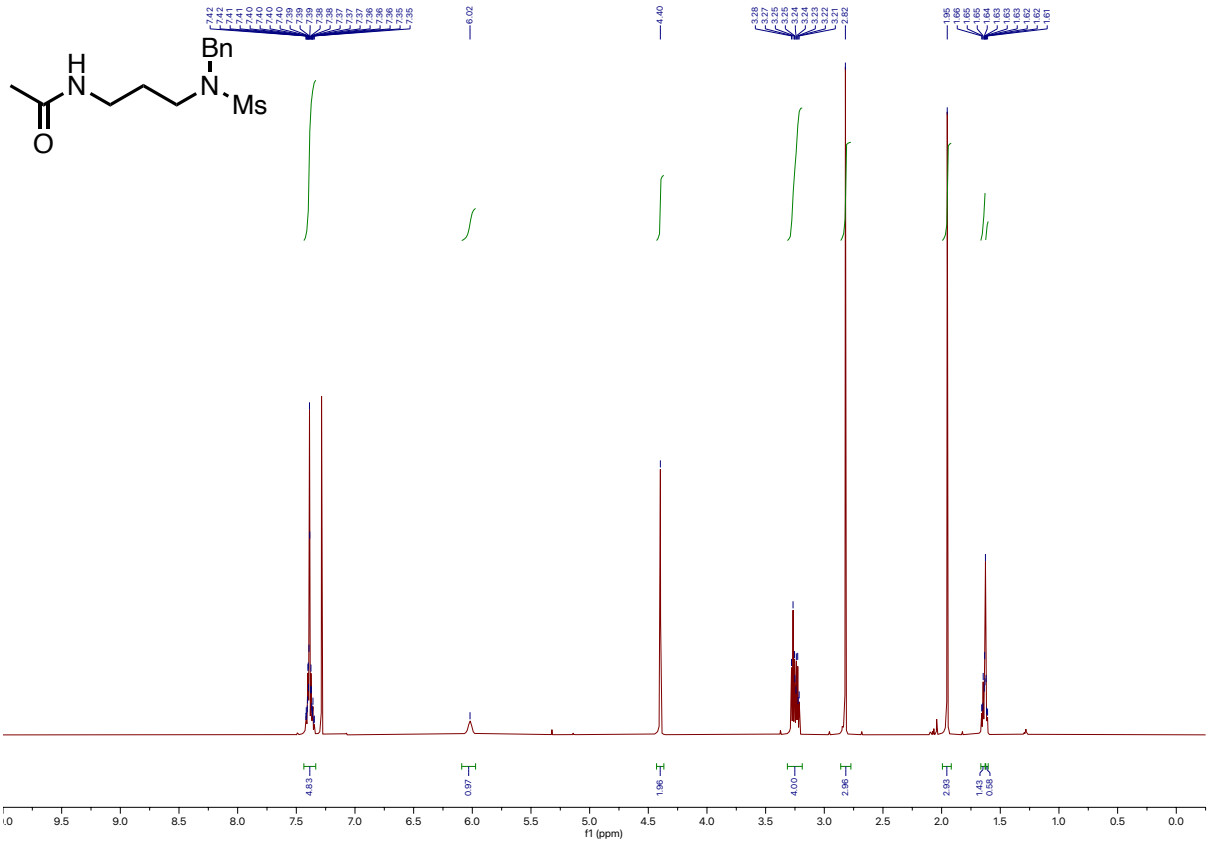

174.62
169.95
61.21
39.70
32.19
31.91
29.60
29.41
29.39
29.34
29.23
26.87
25.62
23.39
f1 (ppm)

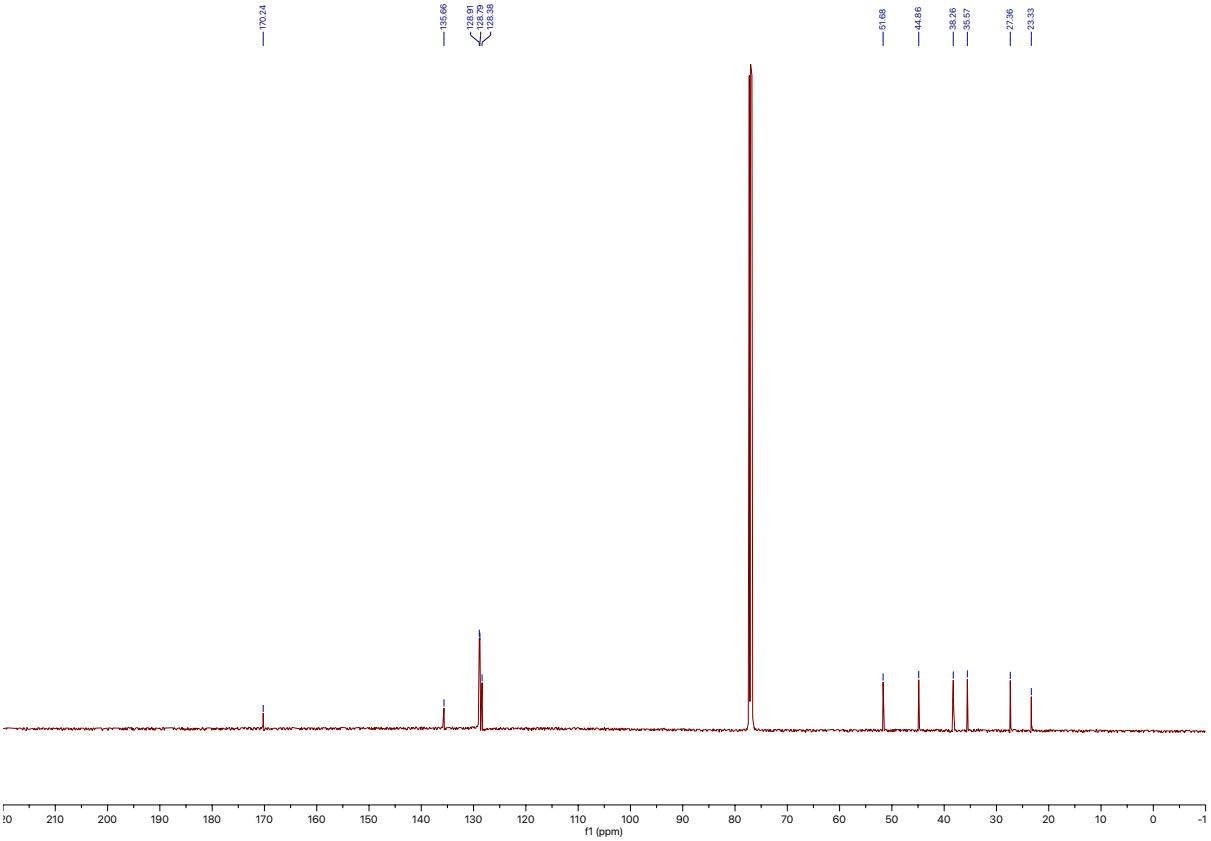

5.48
3.70
3.27
3.26
3.26
3.24
3.24
3.22
3.20
2.45
2.43
2.41
1.99
1.67
1.66
1.64
1.63
1.61
1.52
1.51
1.50
1.49
1.48
1.34
1.33
1.32
1.31
1.31
1.30
1.07
3.02
2.00
2.93
2.00
2.95
1.51
0.25
2.09
12.37
f1 (ppm)

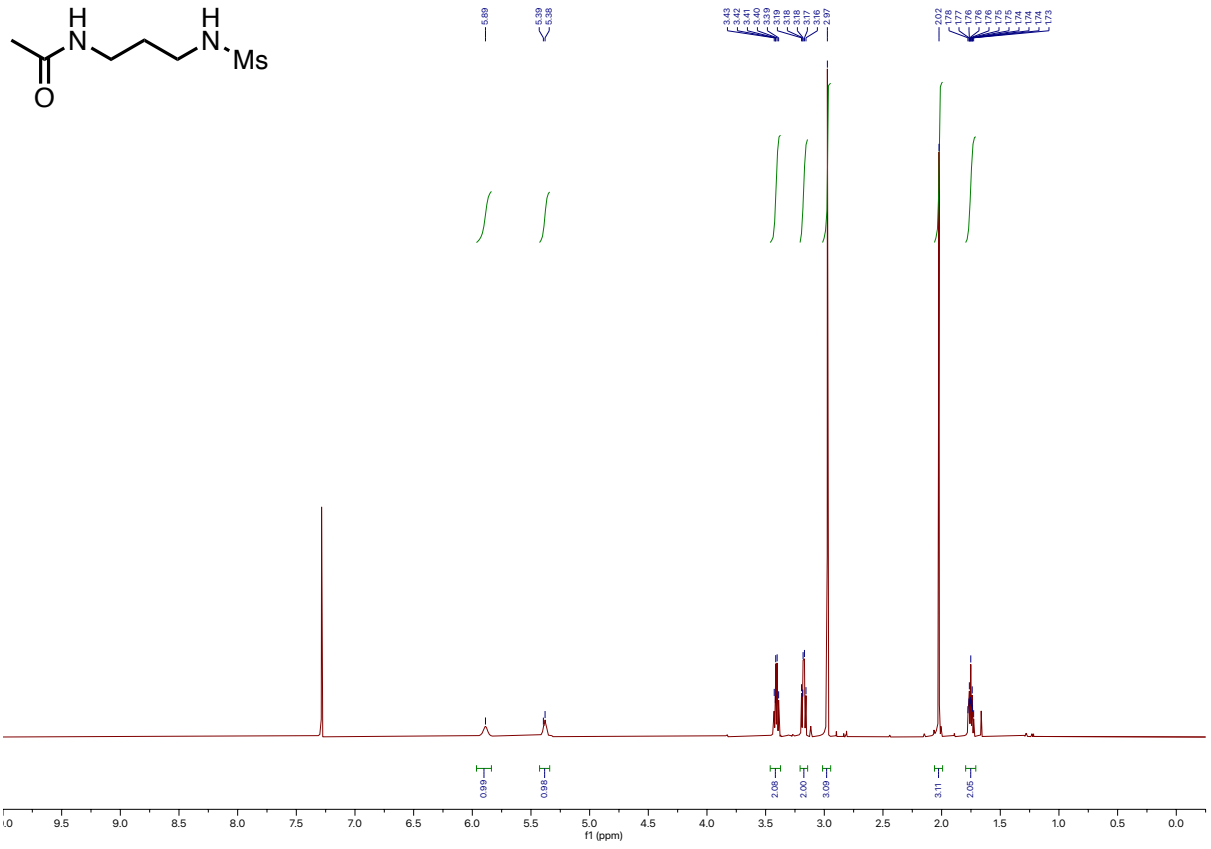

174.62
169.95
61.21
39.70
32.19
31.91
29.60
29.41
29.39
29.34
29.23
26.87
25.62
23.39
f1 (ppm)

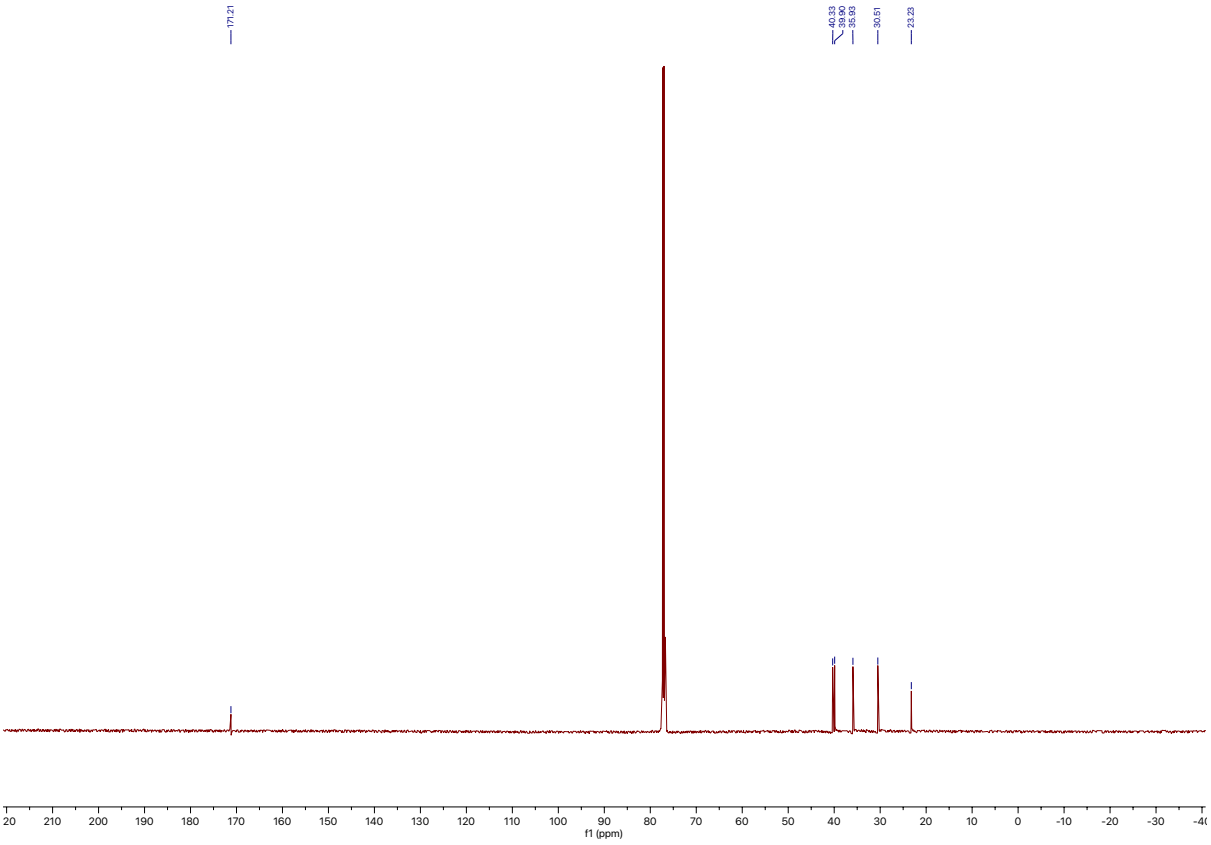

H
N
O
OTs
7.82
7.80
7.37
7.37
7.36
5.48
4.05
4.04
4.03
3.27
3.26
3.25
3.24
3.24
3.23
2.47
1.99
1.68
1.67
1.66
1.65
1.65
1.64
1.64
1.62
1.53
1.52
1.50
1.49
1.48
1.31
1.31
1.30
1.30
1.24
1.24
1.98
2.03
2.07
2.00
3.07
2.96
1.33
0.68
2.06
14.79
f1 (ppm)

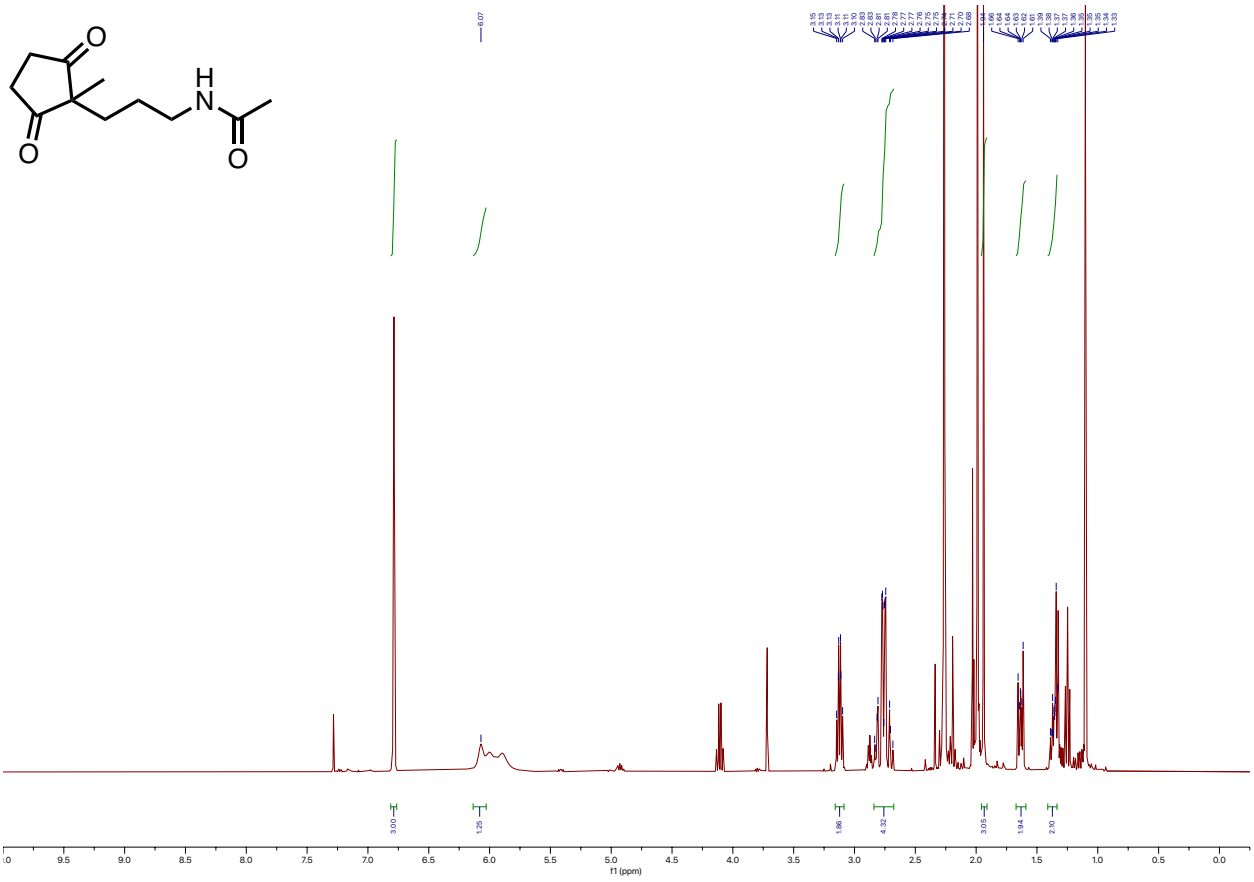

169.97
144.63
133.27
129.80
127.88
70.71
39.69
29.61
29.40
29.32
29.28
29.22
28.85
28.81
26.67
25.30
23.38
21.63
f1 (ppm)

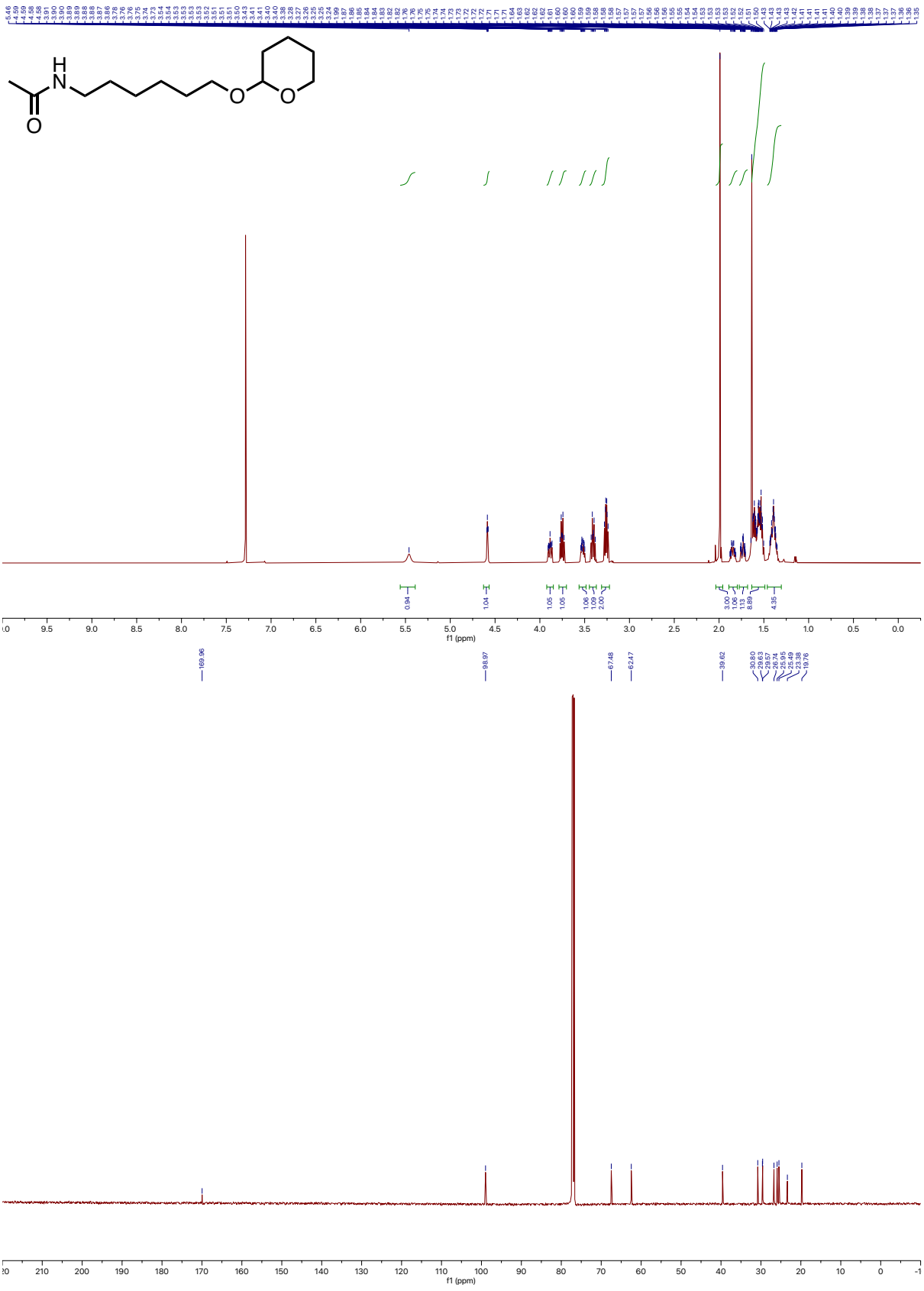

Bn
H
N
N
Ms
O
f1 (ppm)

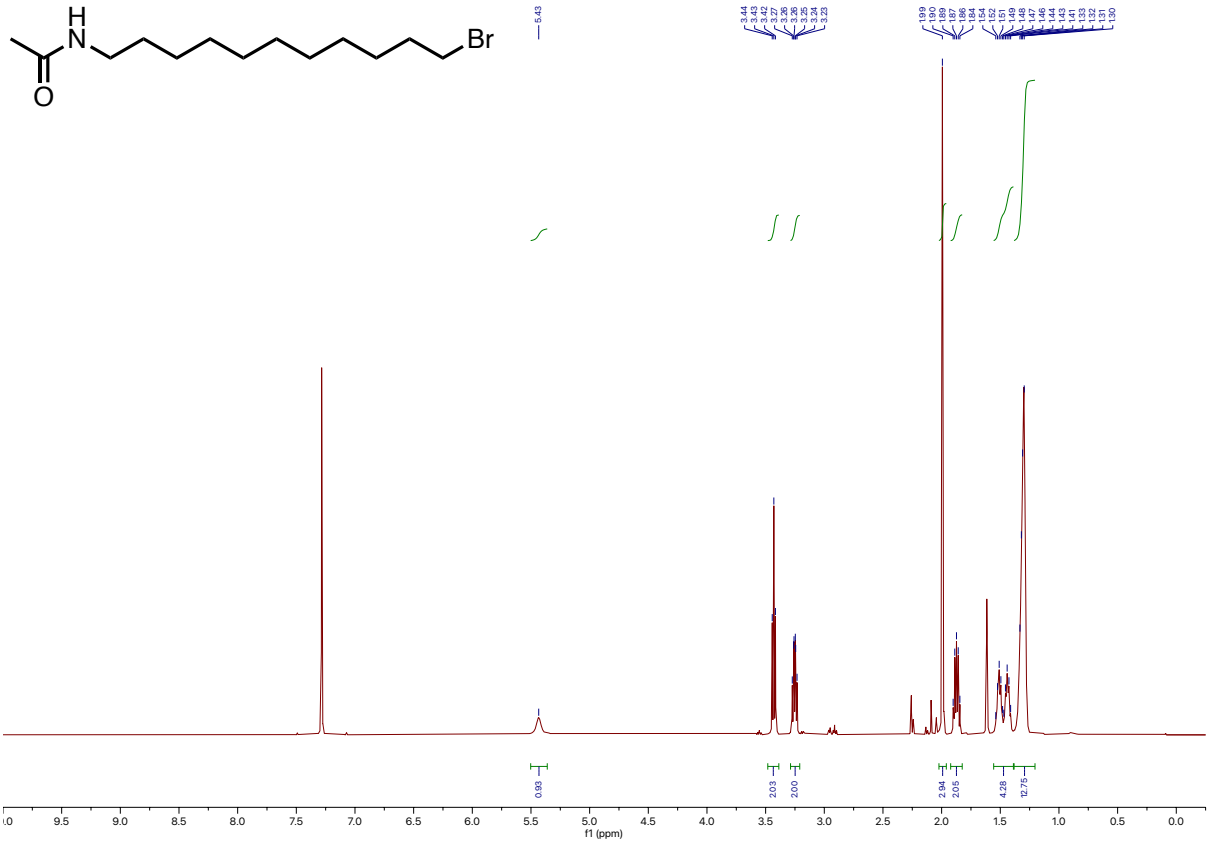

f1 (ppm)

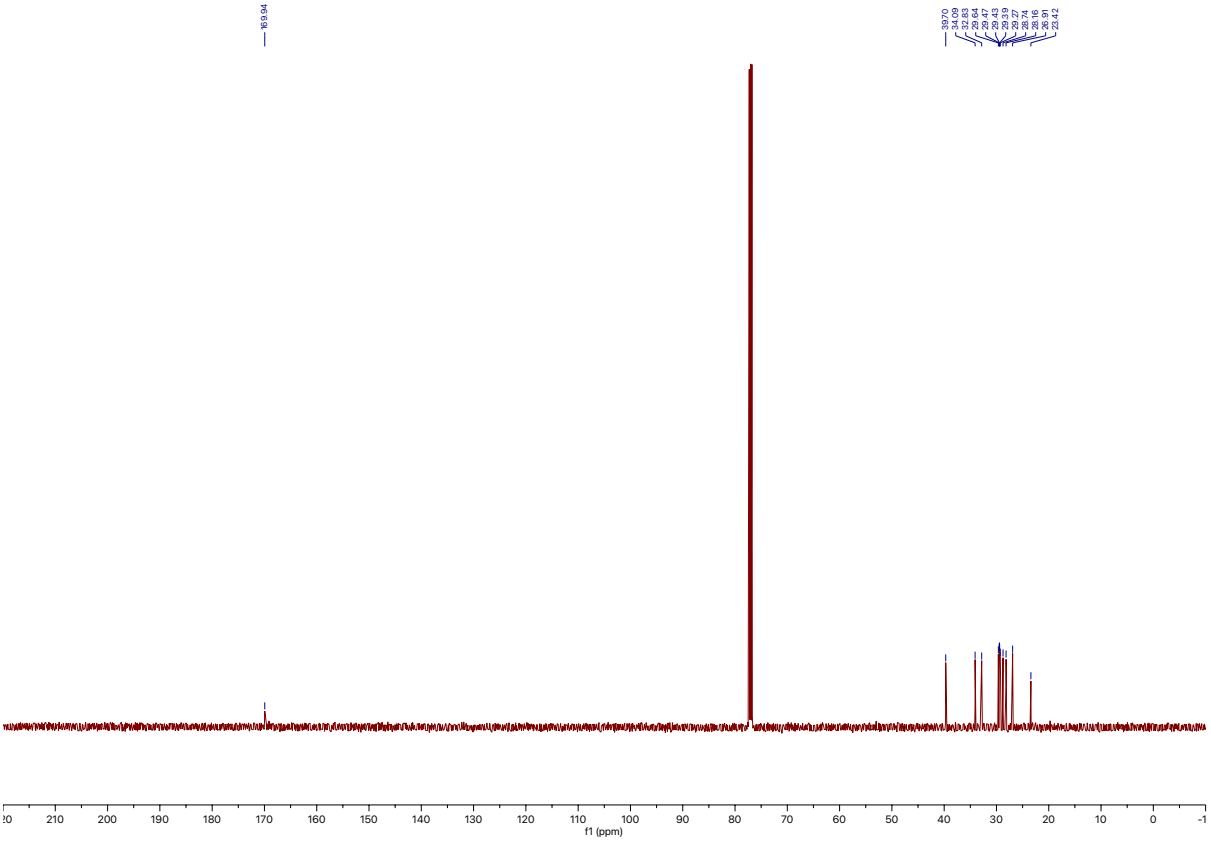

5.89
5.39
5.38
3.43
3.42
3.41
3.40
3.39
3.39
3.18
3.17
3.16
2.97
2.02
1.78
1.77
1.77
1.76
1.76
1.76
1.75
1.75
1.74
1.74
1.74
1.73
0.99
0.98
2.08
2.00
3.09
3.11
2.05
f1 (ppm)

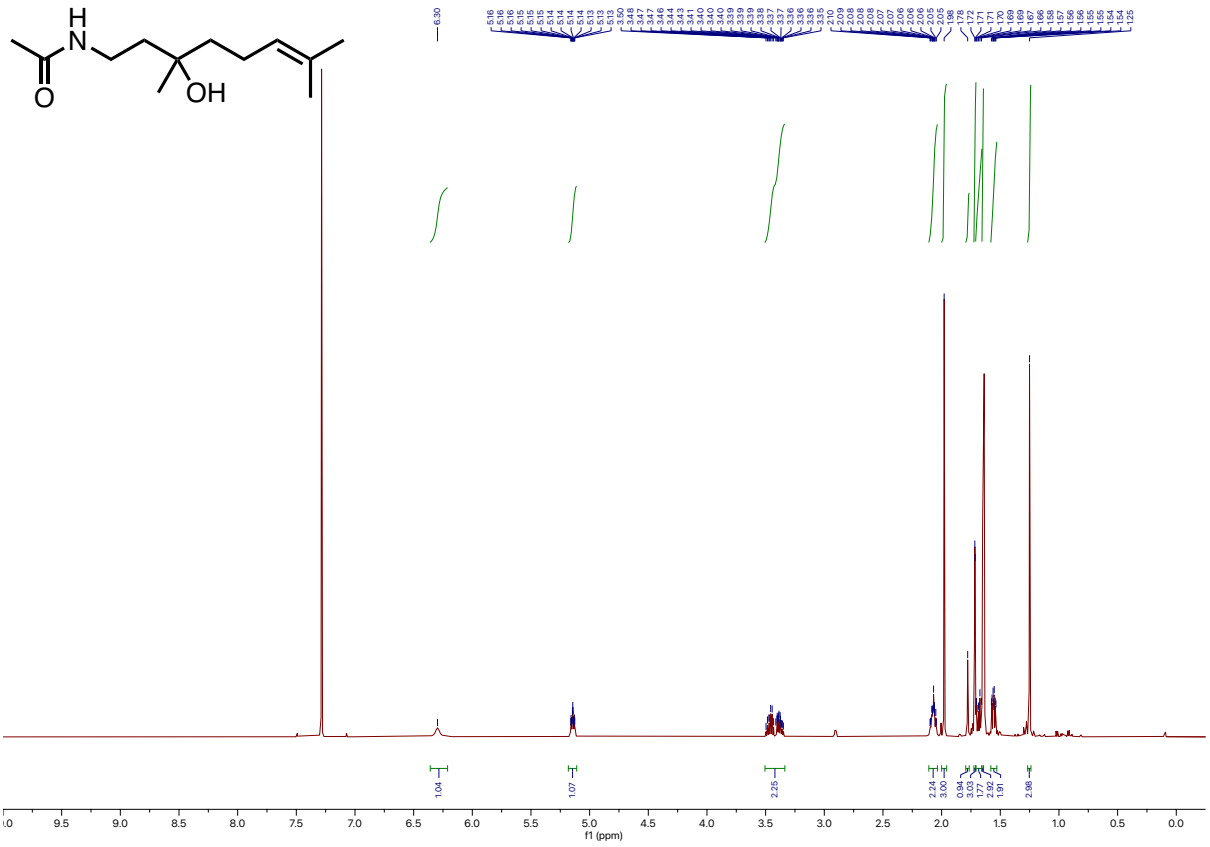

171.21
40.33
39.90
35.93
30.51
23.23
f1 (ppm)

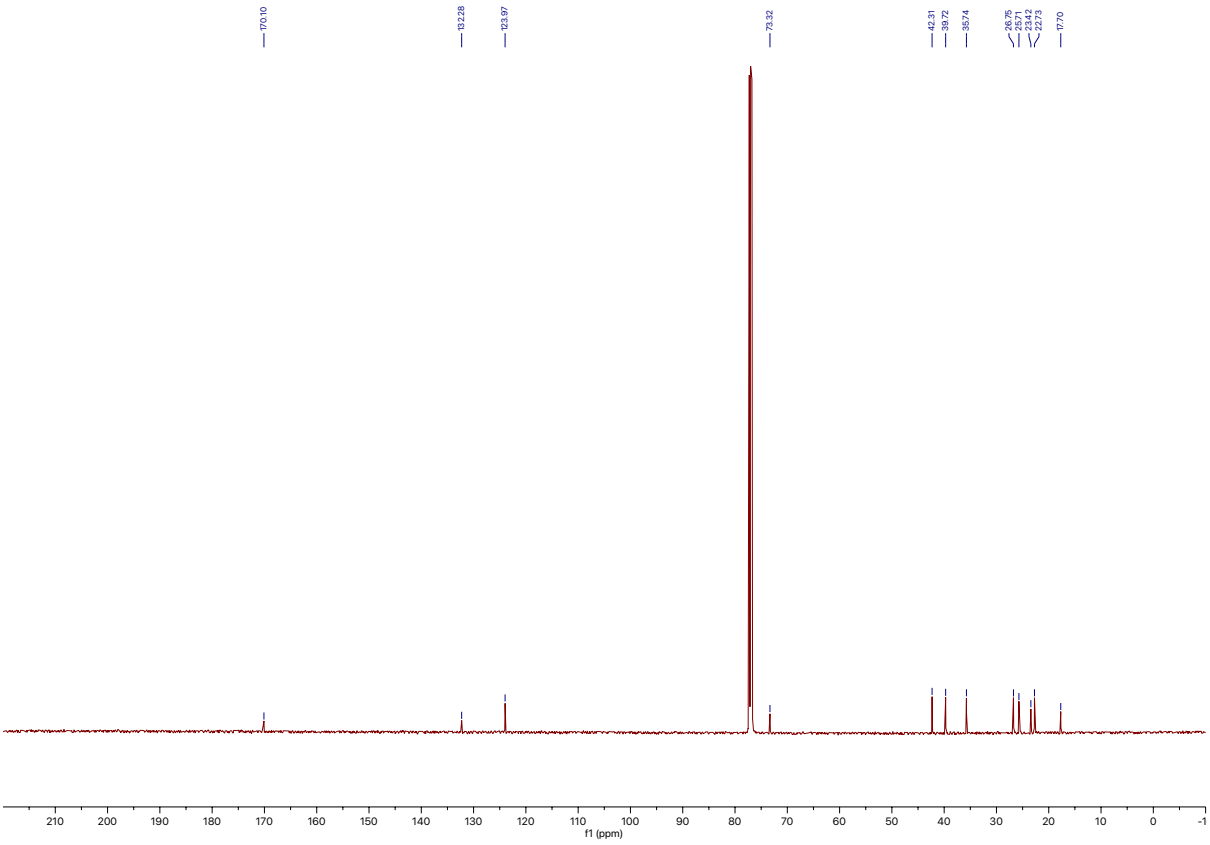

O
O
H
N
O
6.07
3.00
1.25
1.86
4.32
3.05
1.94
2.10
f1 (ppm)

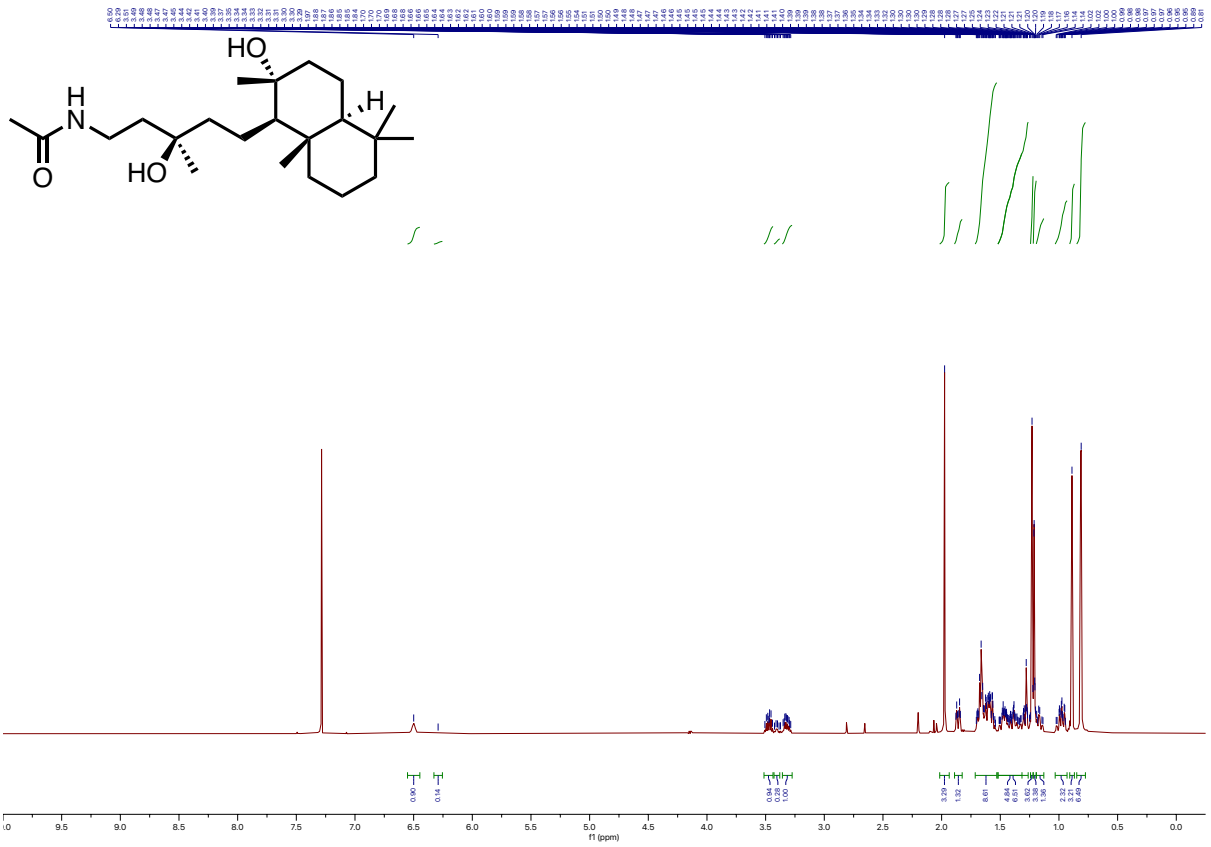

H
N
O
O
O
f1 (ppm)
169.96
98.97
67.48
62.47
39.62
30.60
29.63
29.57
29.34
25.95
25.49
23.38
19.76
f1 (ppm)


H
N
O
Br
5.43
3.44
3.43
3.42
3.27
3.26
3.25
3.24
3.23
1.99
1.90
1.89
1.87
1.86
1.84
1.54
1.52
1.51
1.49
1.48
1.47
1.46
1.44
1.43
1.41
1.33
1.32
1.31
1.30
0.93
2.03
2.00
2.94
2.05
4.28
12.75
f1 (ppm)

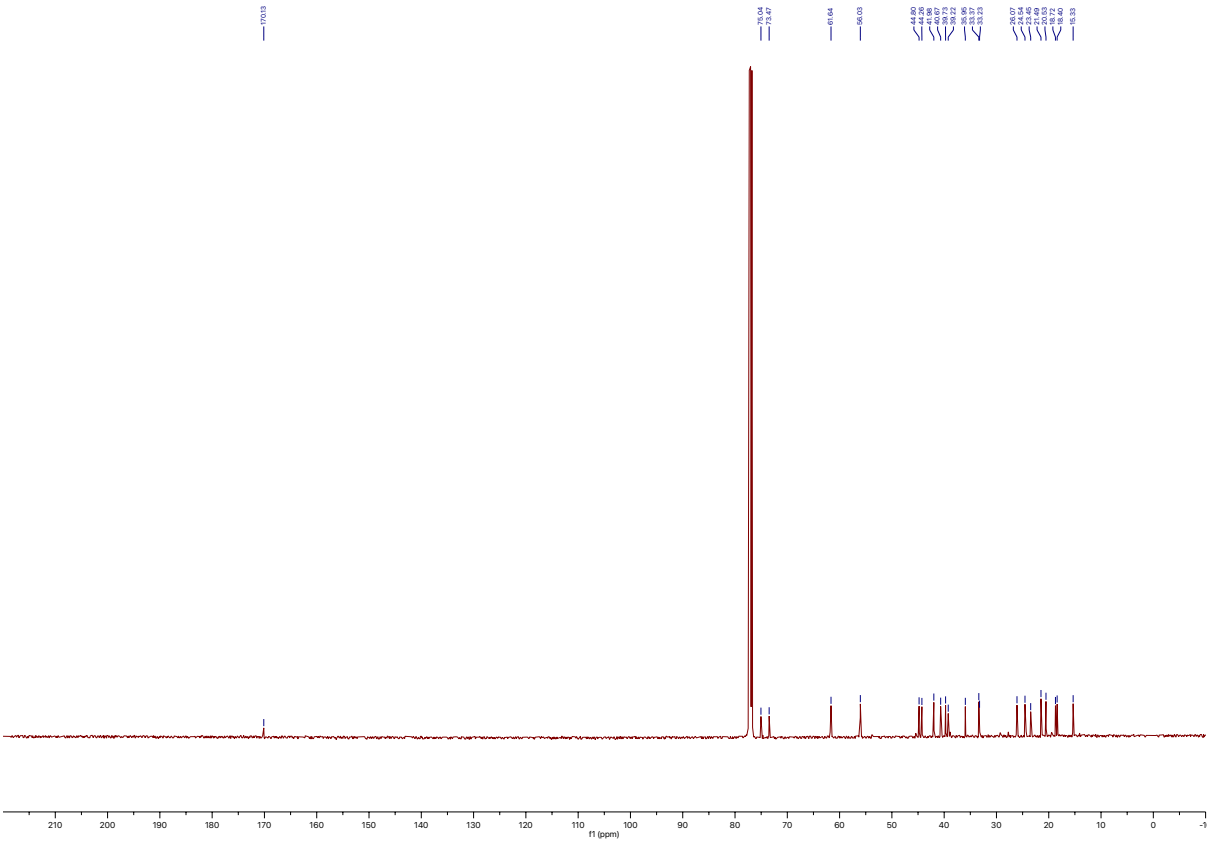

169.94
39.70
34.09
32.83
29.64
29.47
29.43
29.39
29.27
28.74
28.16
26.91
25.42
f1 (ppm)

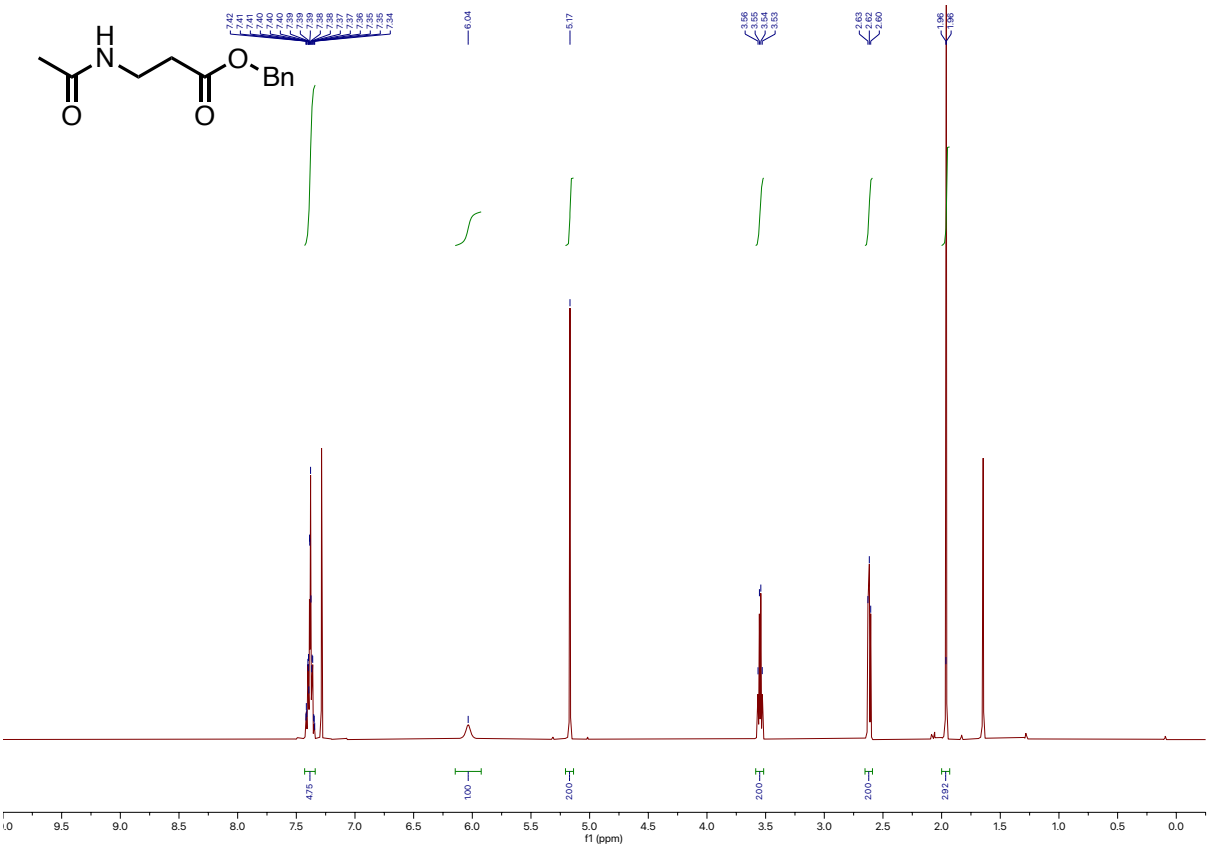

H
N
O
OH
f1 (ppm)

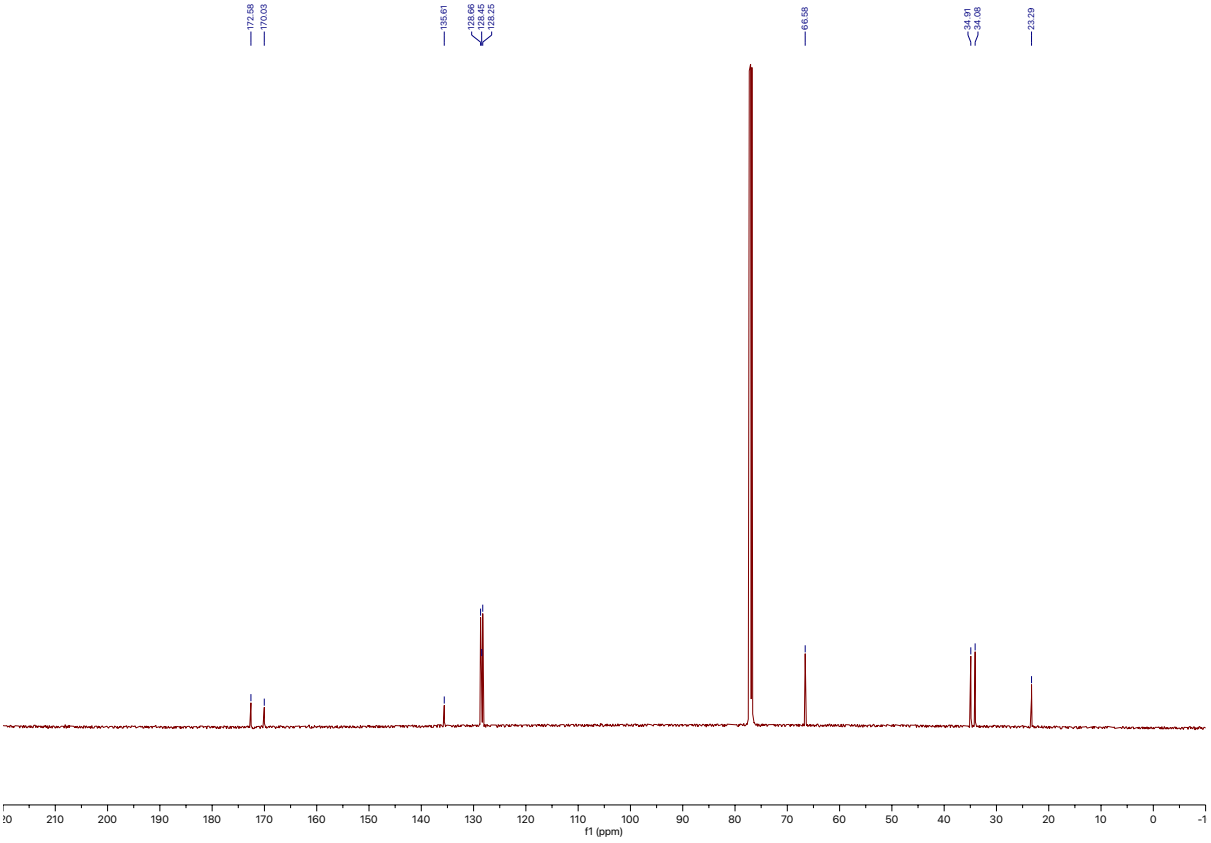

f1 (ppm)

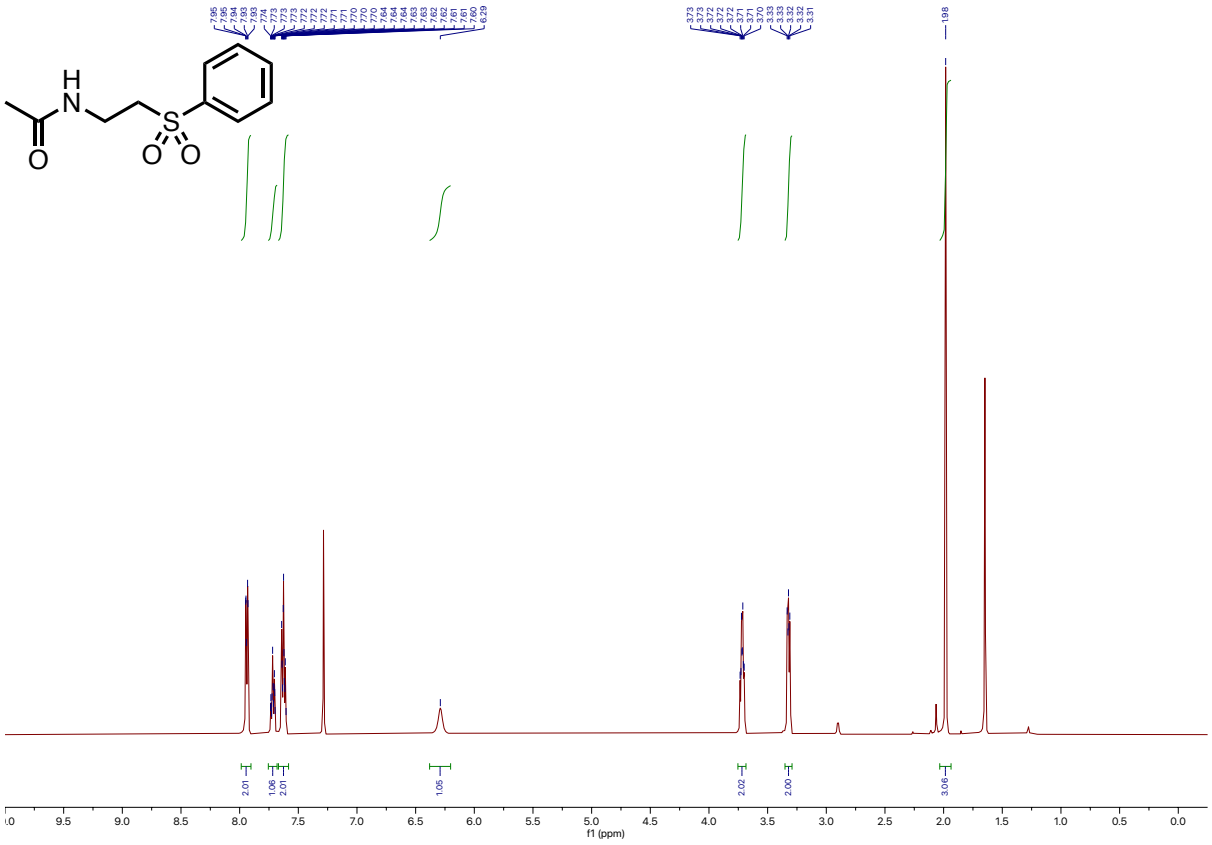

HO
H
N
O
HO
H

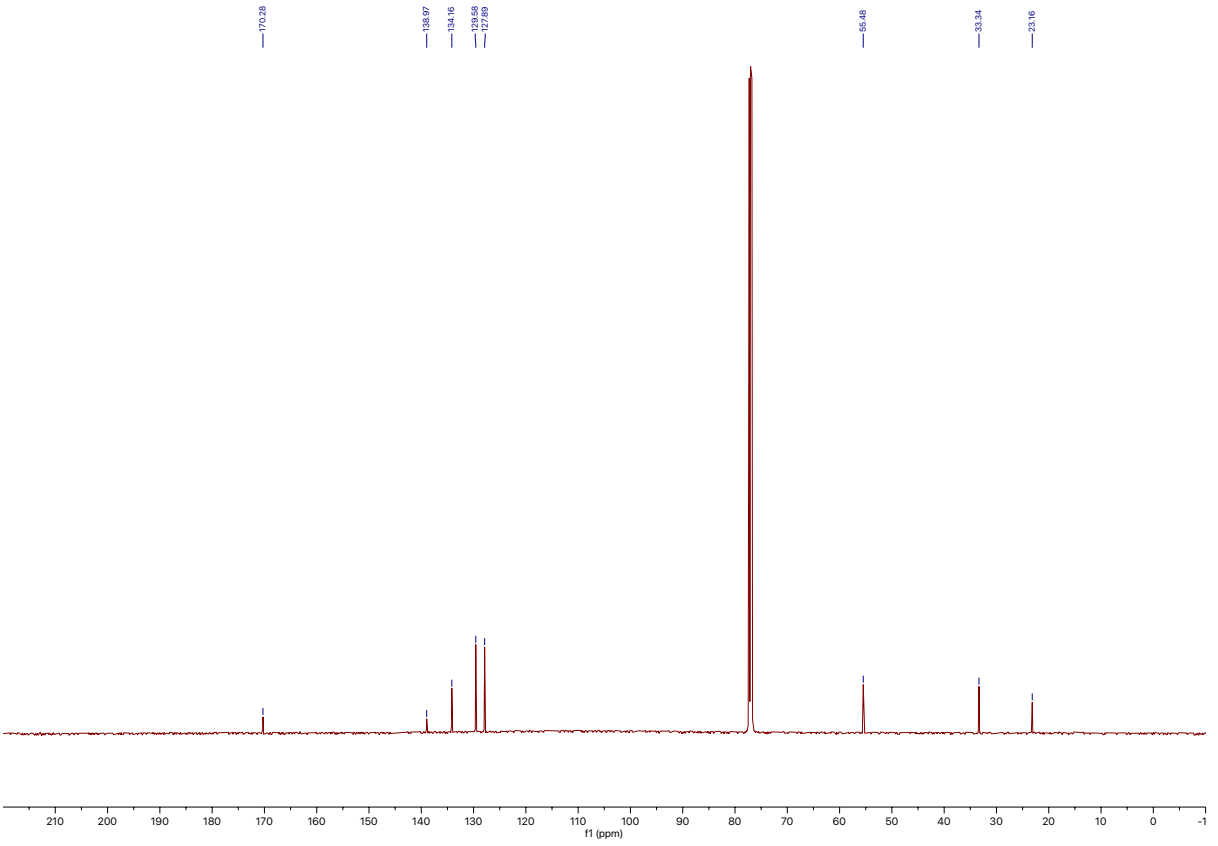
f1 (ppm)

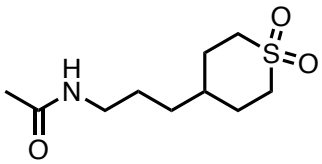

f1 (ppm)


7.42
7.41
7.41
7.40
7.40
7.40
7.39
7.39
7.39
7.38
7.38
7.37
7.37
7.36
7.35
7.35
7.34
6.04
5.17
3.56
3.55
3.54
3.53
2.63
2.62
2.60
1.96
1.96
4.75
1.00
2.00
2.00
2.00
2.92
f1 (ppm)

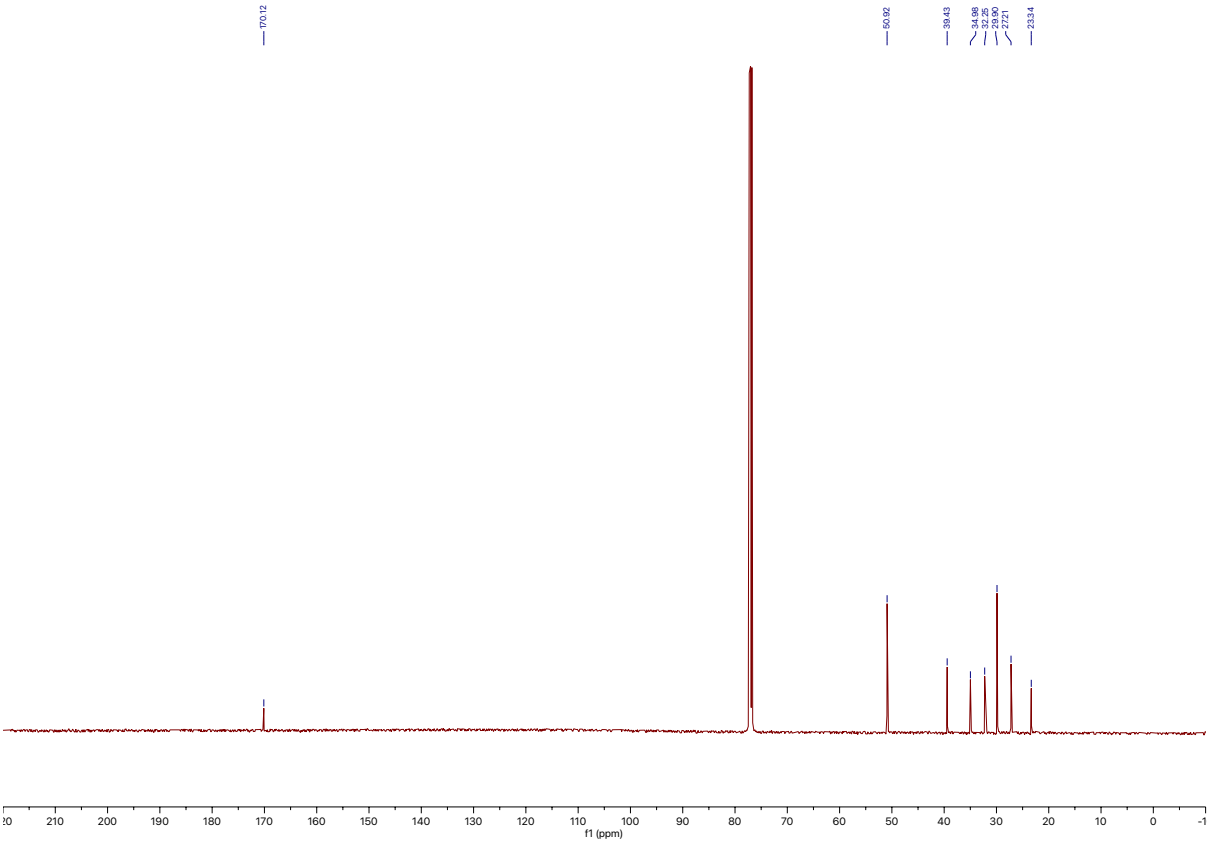

172.58
170.03
135.61
128.66
128.45
128.25
66.58
34.91
34.08
23.29
f1 (ppm)

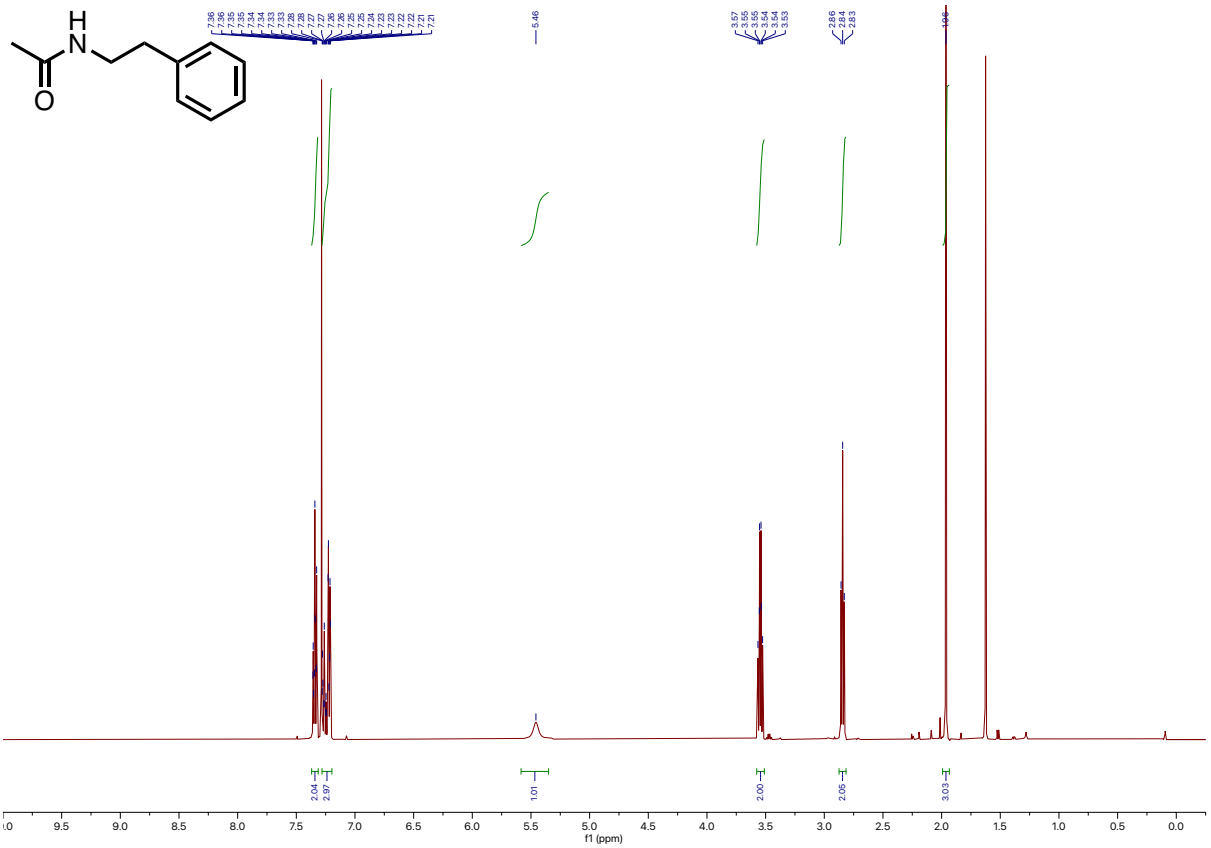

7.96
7.95
7.94
7.93
7.93
7.74
7.73
7.73
7.72
7.72
7.71
7.71
7.70
7.70
7.70
7.70
7.64
7.64
7.64
7.63
7.63
7.62
7.62
7.61
7.61
7.60
6.29
3.73
3.73
3.72
3.72
3.72
3.71
3.71
3.70
3.33
3.33
3.32
3.32
3.31
1.98
2.01
1.06
2.01
1.05
2.02
2.00
3.06
f1 (ppm)

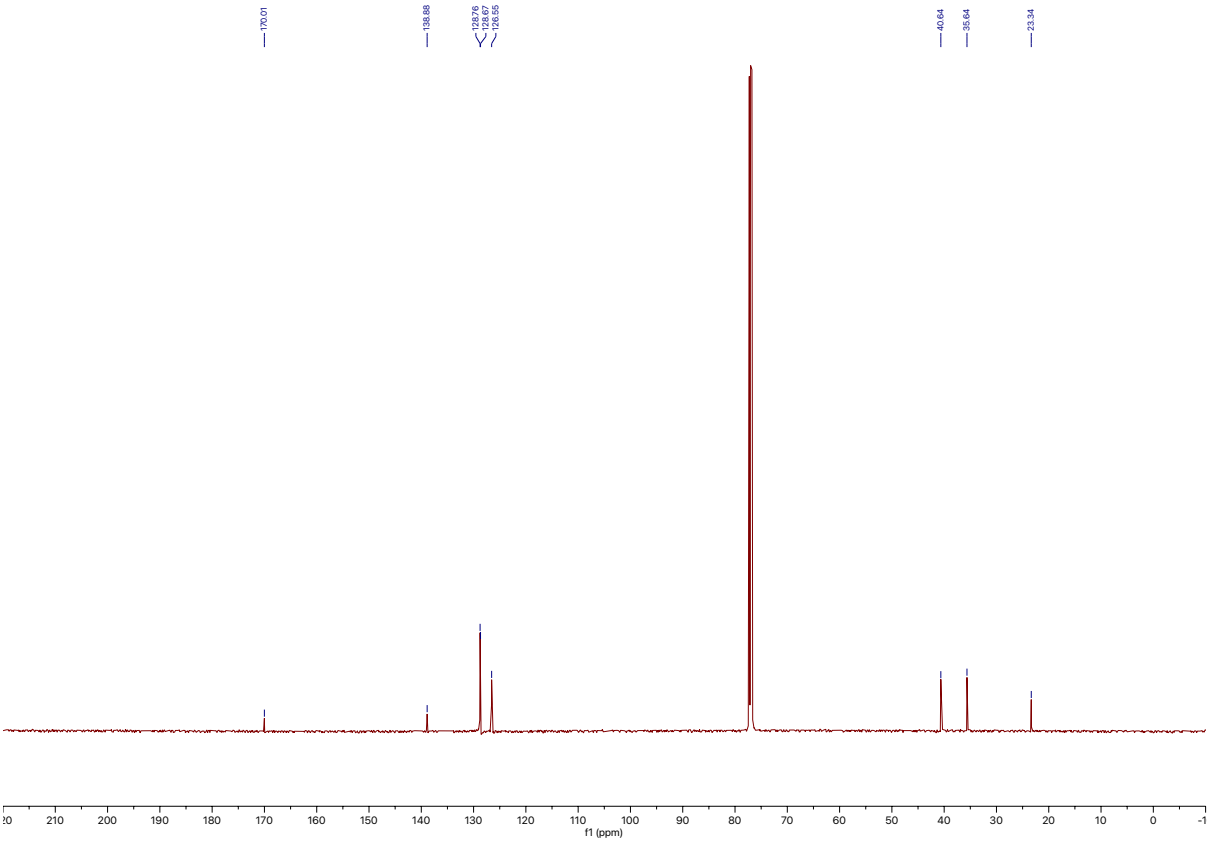

170.28
138.97
134.16
129.58
127.89
55.48
33.34
23.16
f1 (ppm)

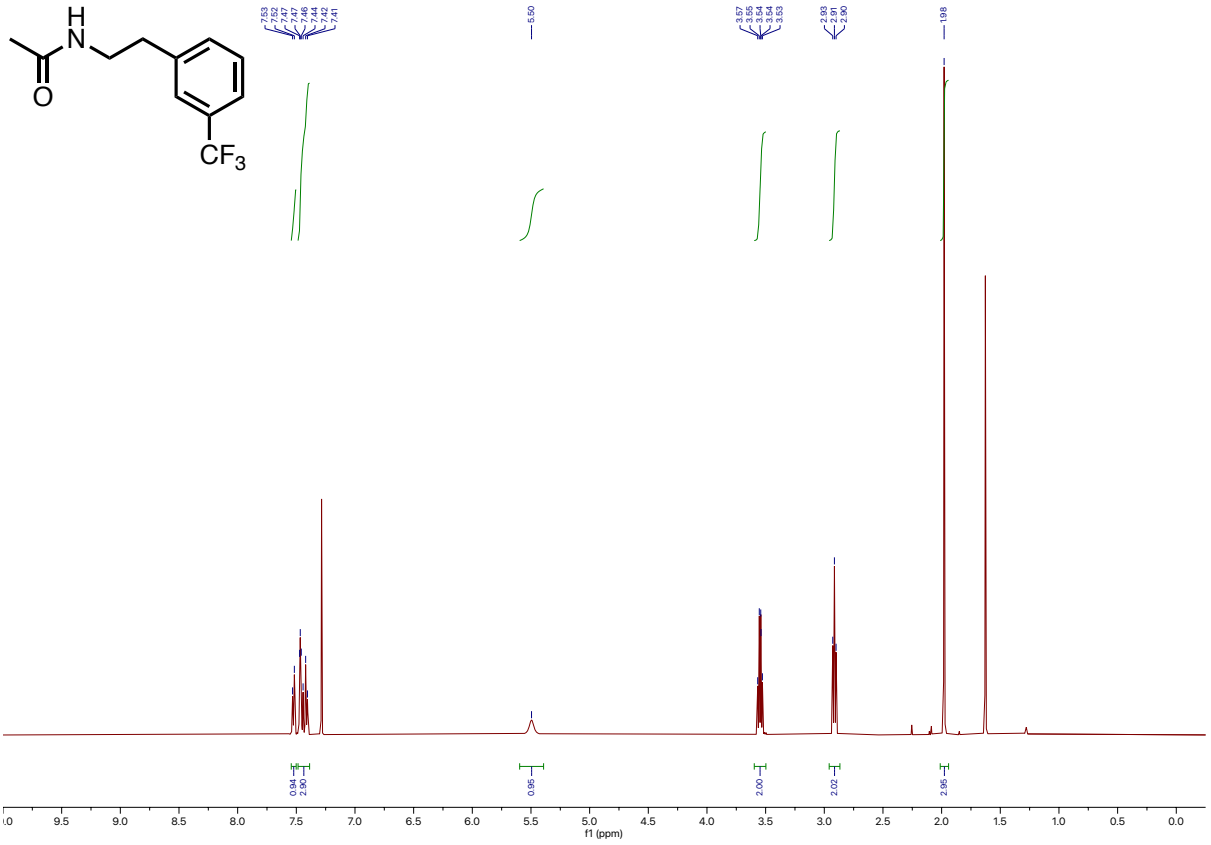

O
S
O
H
N
O

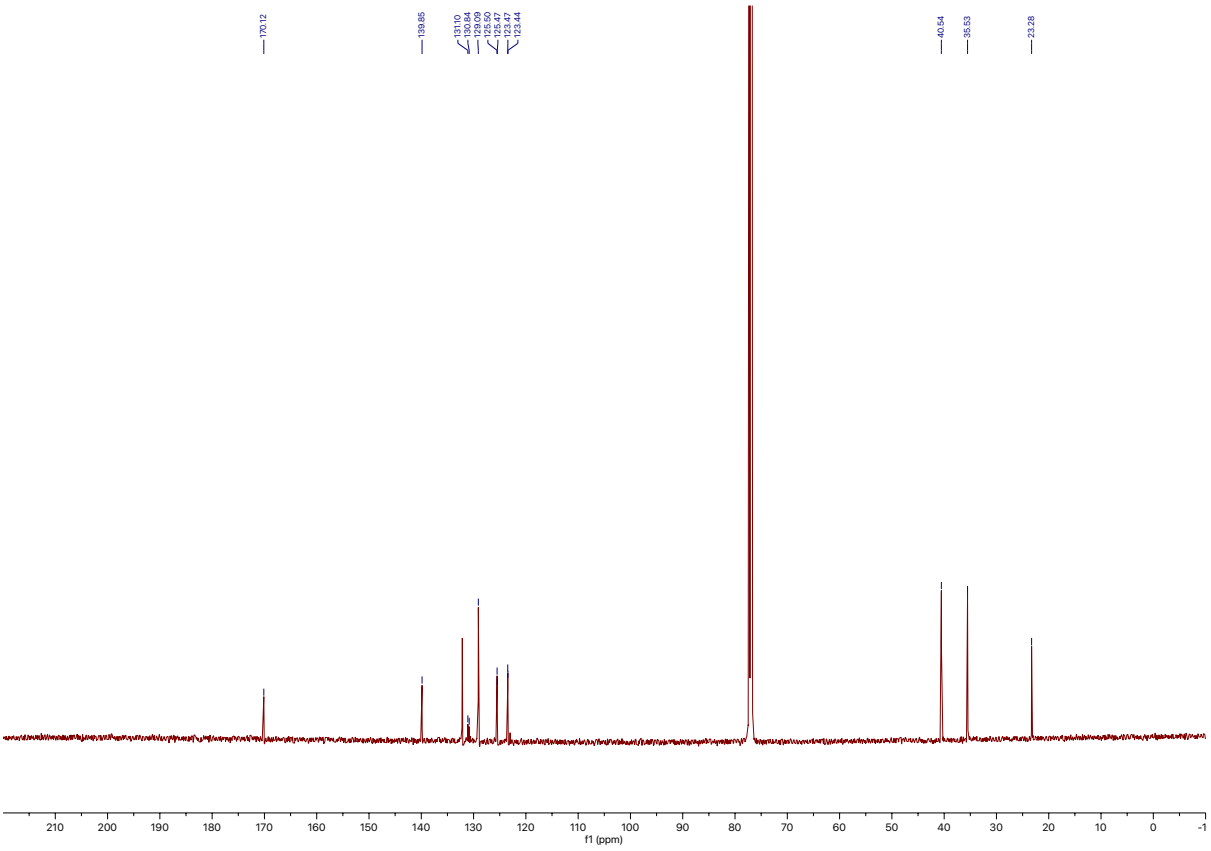
0.95
2.00
2.06
2.09
2.08
2.07
2.09
3.09
2.09
f1 (ppm)

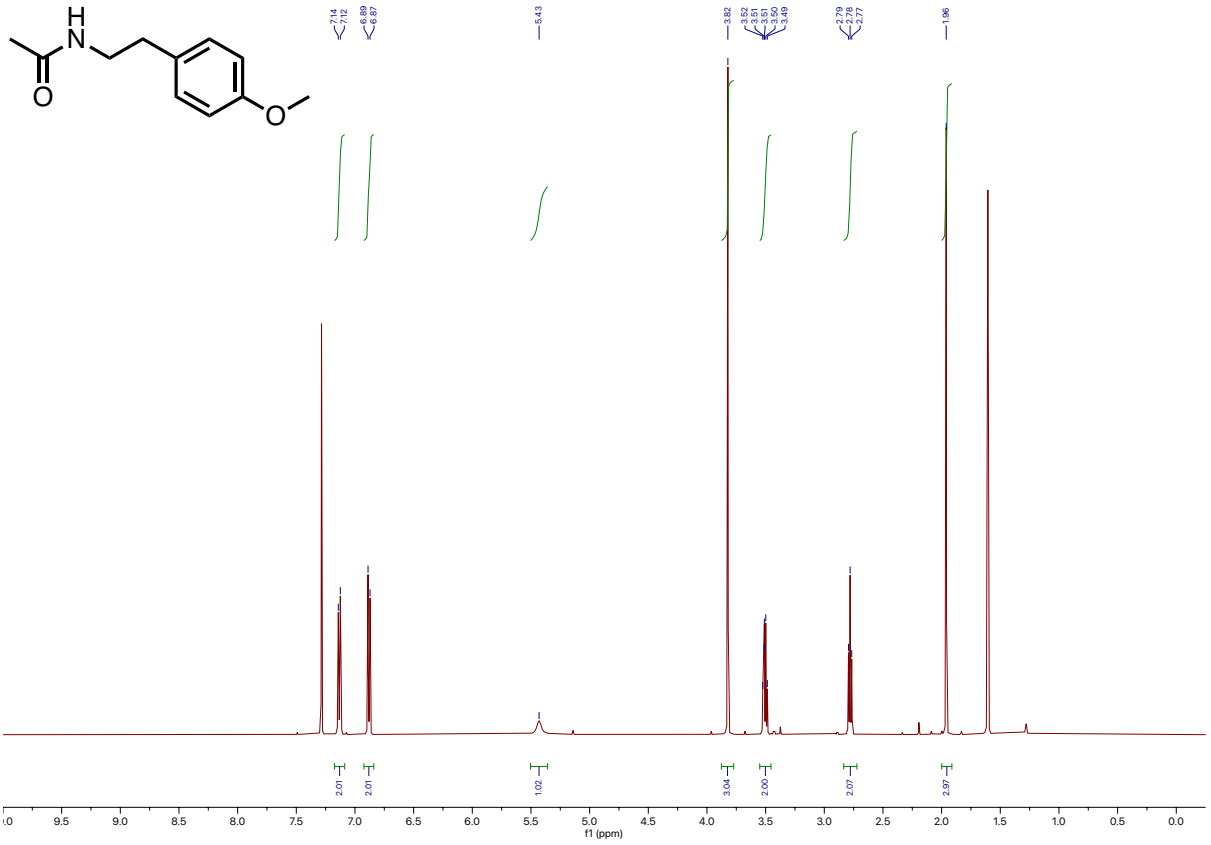

170.12
50.92
39.43
34.98
32.45
29.90
27.21
23.34
f1 (ppm)

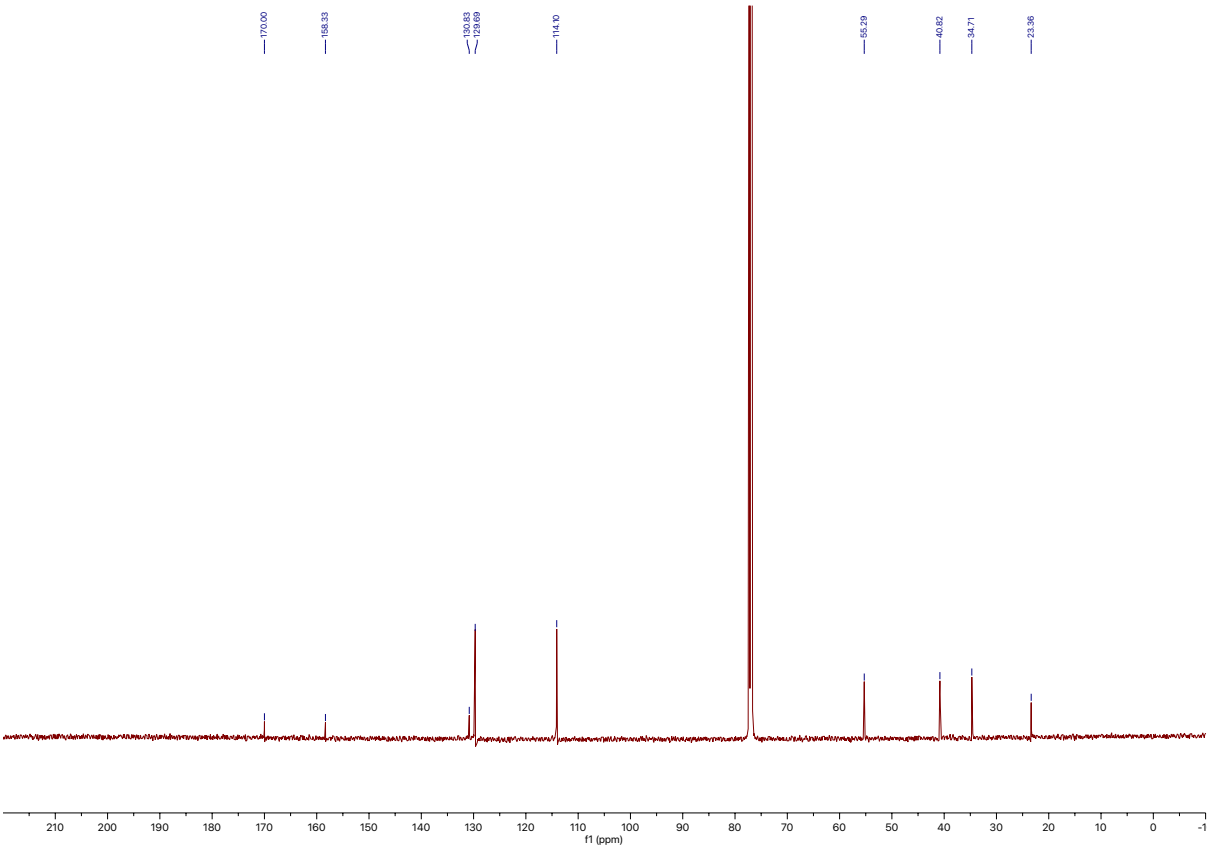

H
N
O
7.36
7.36
7.35
7.35
7.35
7.34
7.34
7.33
7.33
7.28
7.28
7.27
7.27
7.26
7.26
7.25
7.25
7.24
7.23
7.23
7.22
7.22
7.21
7.21
5.46
3.57
3.55
3.55
3.54
3.54
3.53
2.86
2.84
2.83
1.96
2.04
2.97
1.01
2.00
2.05
3.03
f1 (ppm)

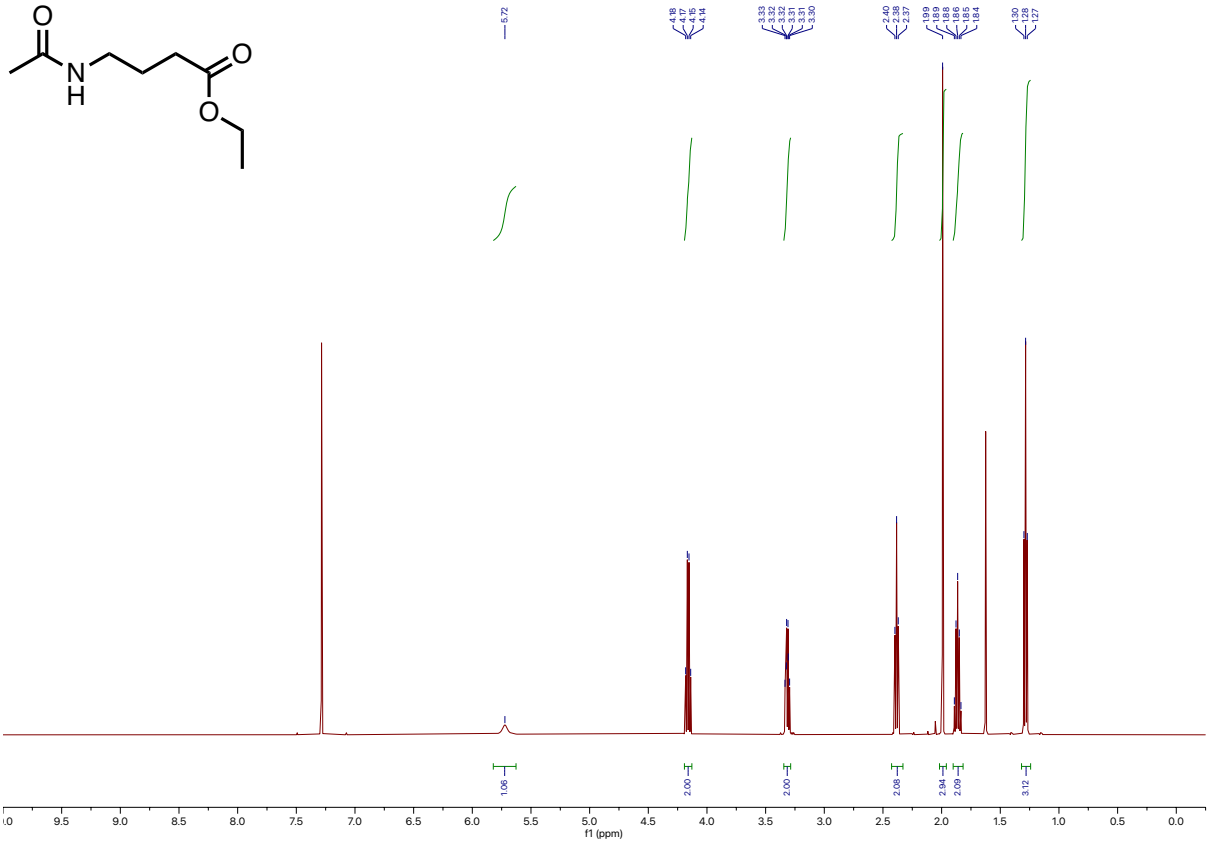

170.01
138.88
128.76
128.67
126.55
40.64
35.64
23.34
f1 (ppm)

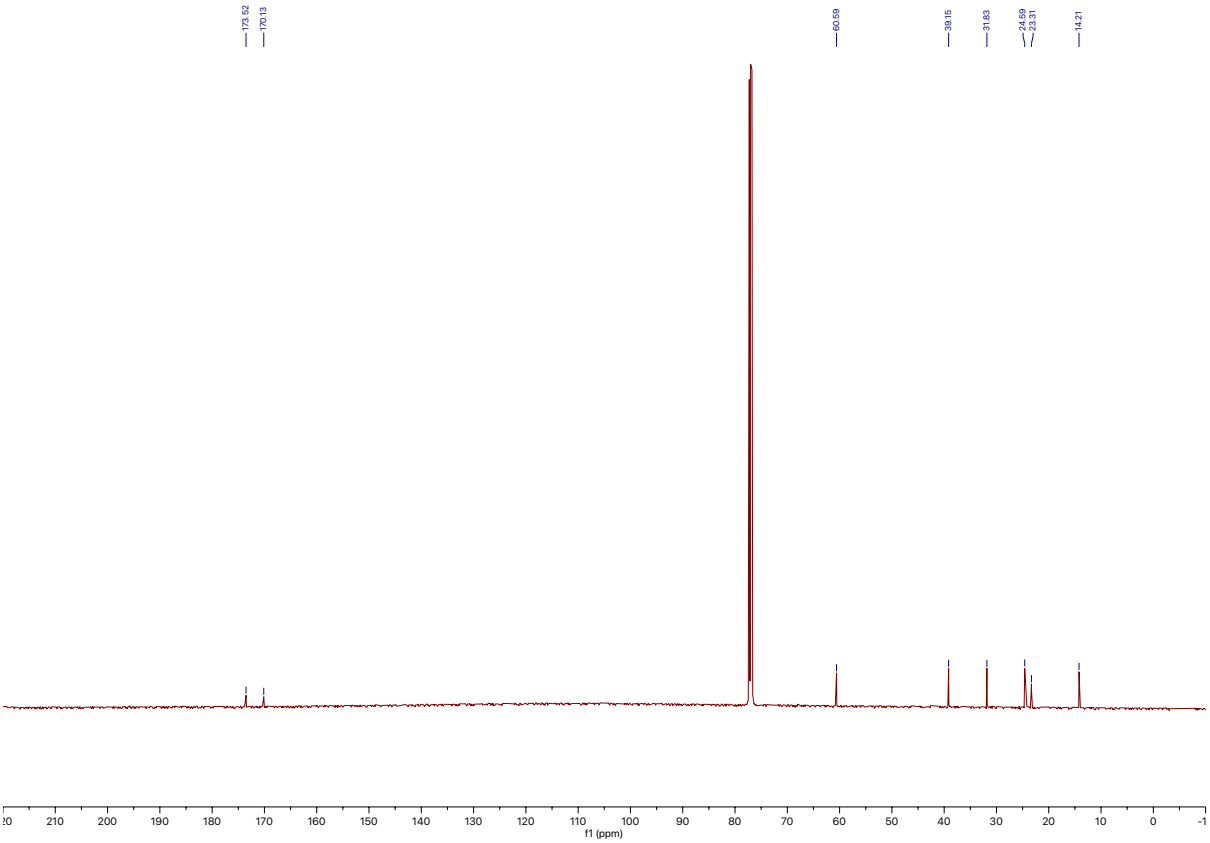

7.53
7.52
7.47
7.47
7.46
7.44
7.42
7.41
5.50
3.57
3.55
3.54
3.54
3.53
2.93
2.91
2.90
1.98
0.94
2.90
0.95
2.00
2.02
2.95
f1 (ppm)

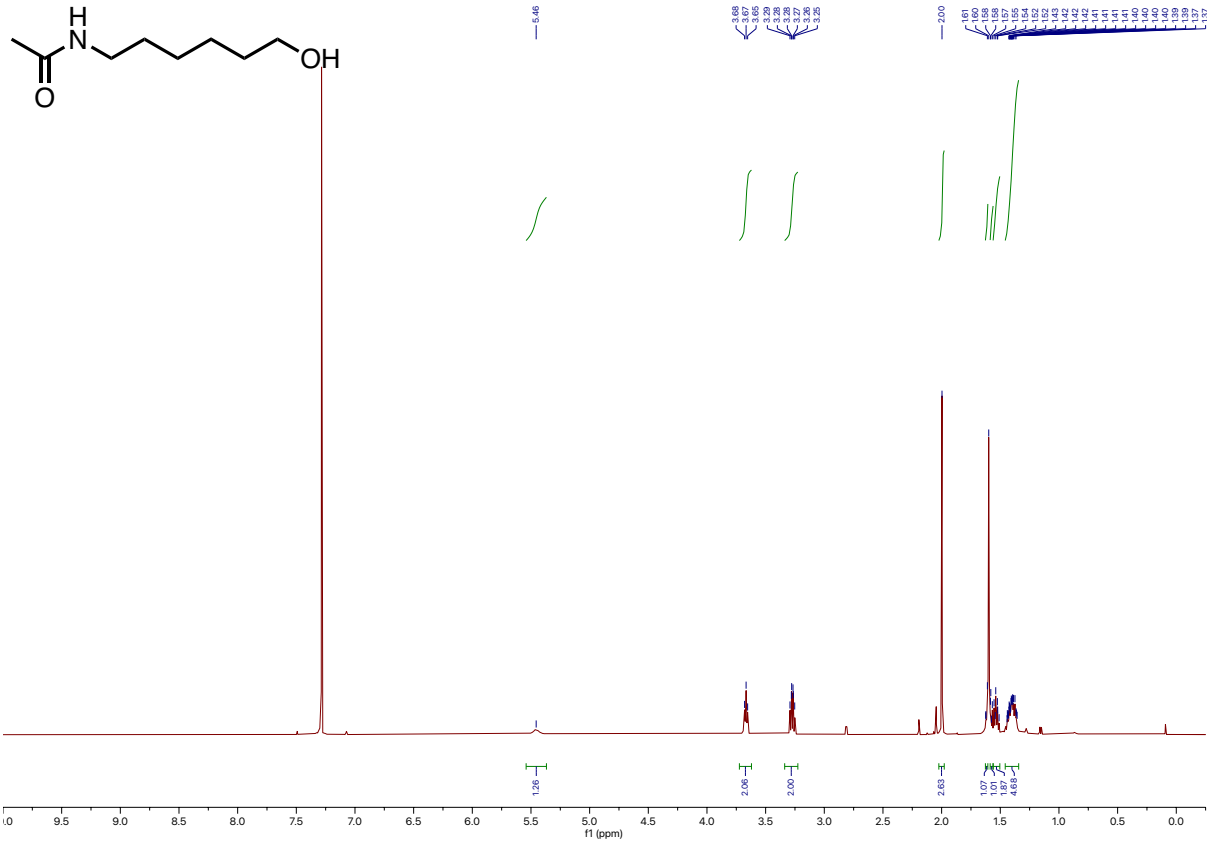

170.12
139.85
131.10
130.84
129.09
125.50
125.47
123.47
123.44
40.54
35.53
23.28
f1 (ppm)

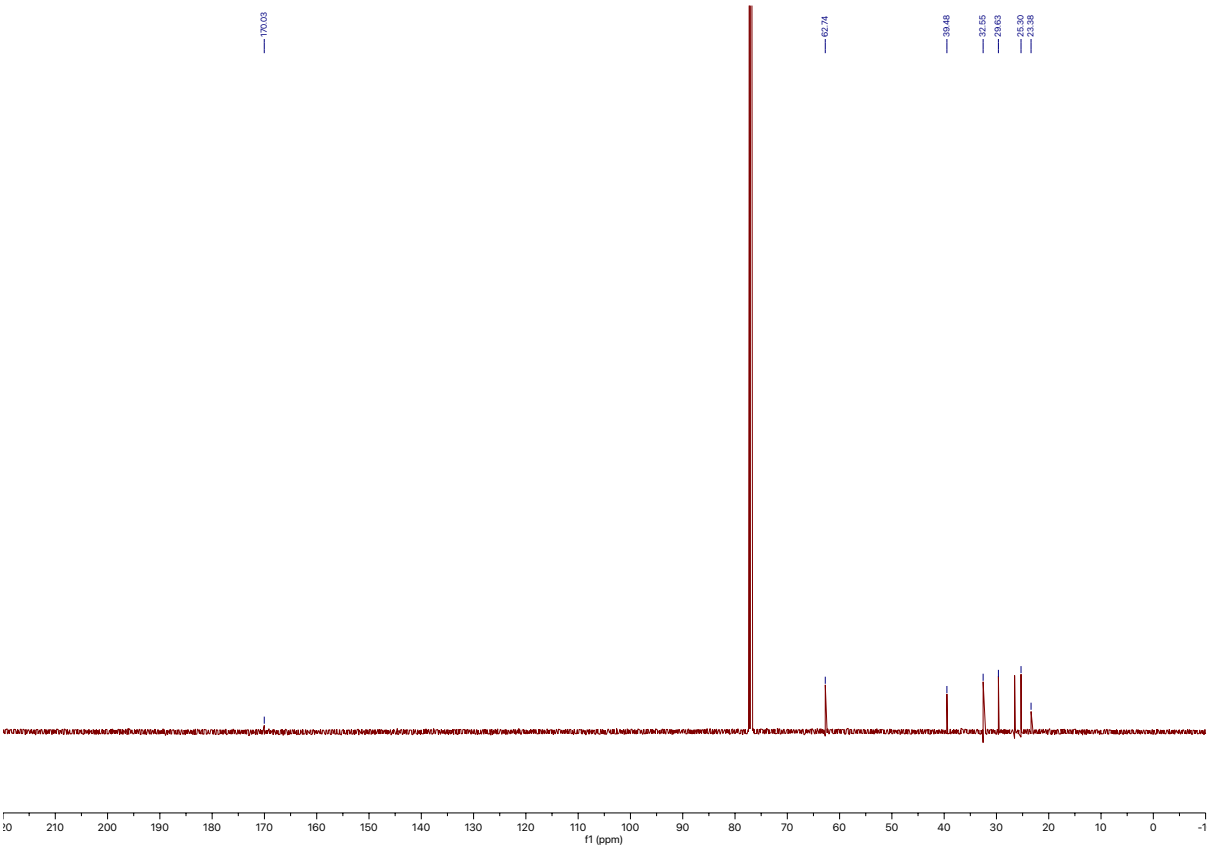

7.14
7.12
6.89
6.87
5.43
3.82
3.52
3.51
3.51
3.50
3.49
2.79
2.78
2.77
1.96
2.01
2.01
1.02
3.04
2.00
2.07
2.97
f1 (ppm)

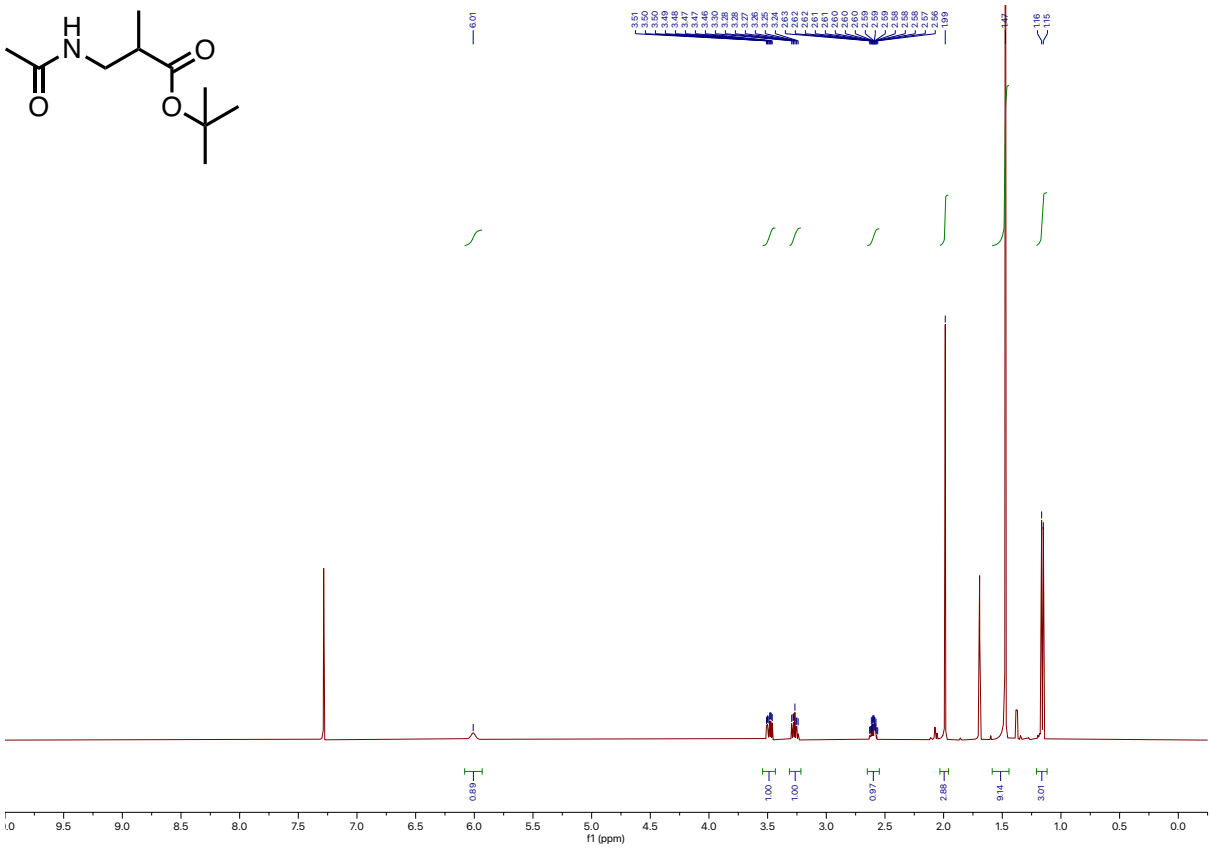

170.00
158.33
130.83
129.69
114.10
55.29
40.82
34.71
23.36
f1 (ppm)

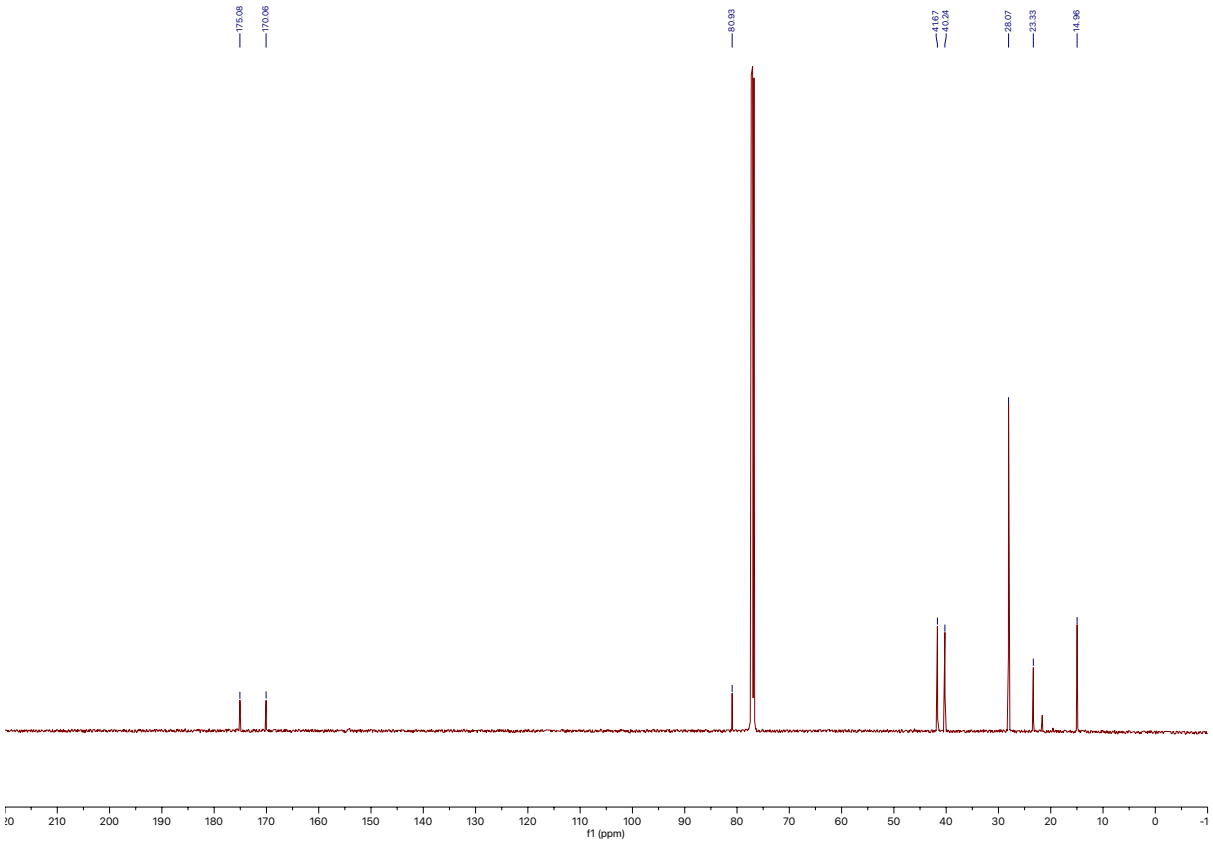

O
N
H
O
O
5.72
4.18
4.17
4.15
4.14
3.33
3.32
3.32
3.31
3.31
3.30
2.40
2.38
2.37
1.99
1.89
1.88
1.86
1.85
1.84
1.30
1.28
1.27
1.06
2.00
2.00
2.08
2.94
2.09
3.12
f1 (ppm)

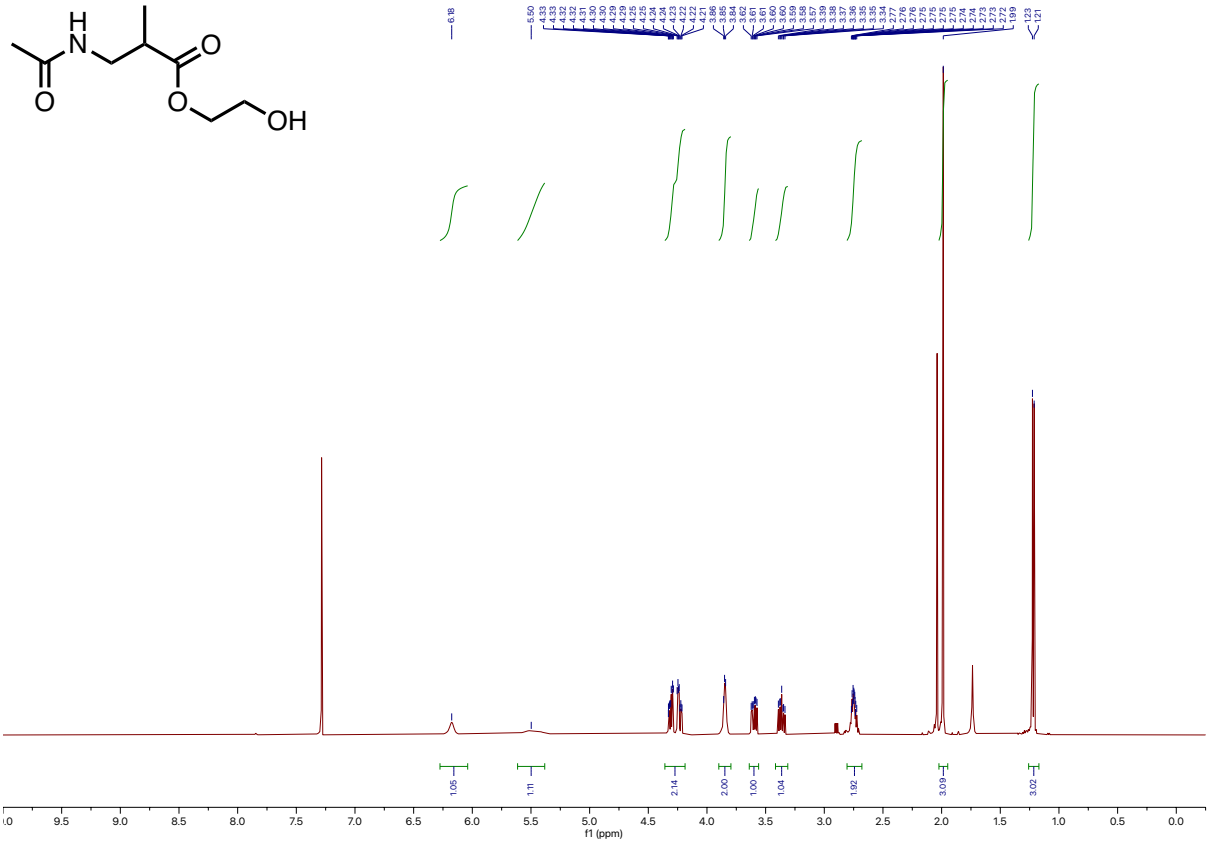

173.52
170.13
60.59
39.15
31.83
24.59
23.31
14.21
f1 (ppm)

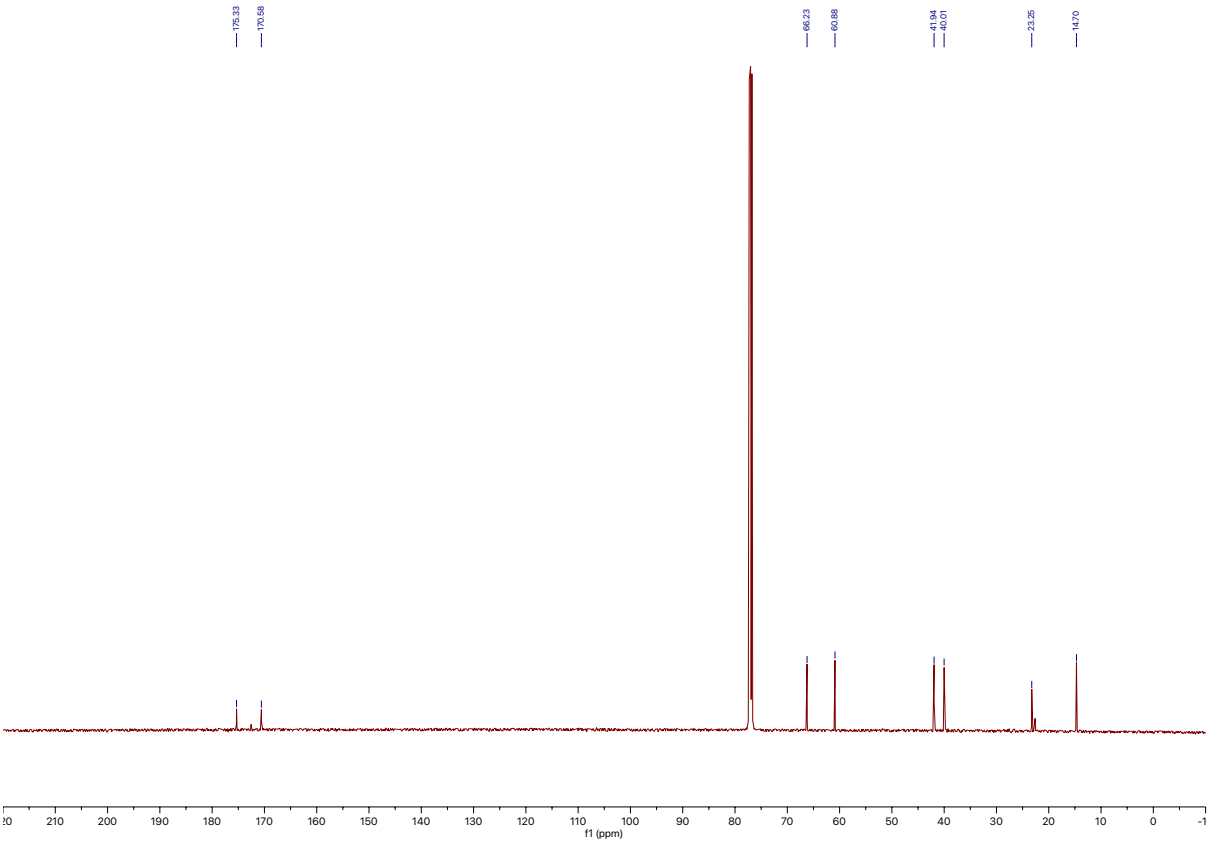

H
N
O
OH
5.46
3.68
3.67
3.65
3.29
3.28
3.28
3.27
3.26
3.25
2.00
1.61
1.60
1.59
1.58
1.57
1.56
1.55
1.54
1.52
1.52
1.44
1.43
1.42
1.42
1.41
1.41
1.41
1.41
1.40
1.40
1.40
1.40
1.39
1.39
1.37
1.37
1.26
2.06
2.00
2.63
1.07
1.01
1.87
4.68
f1 (ppm)

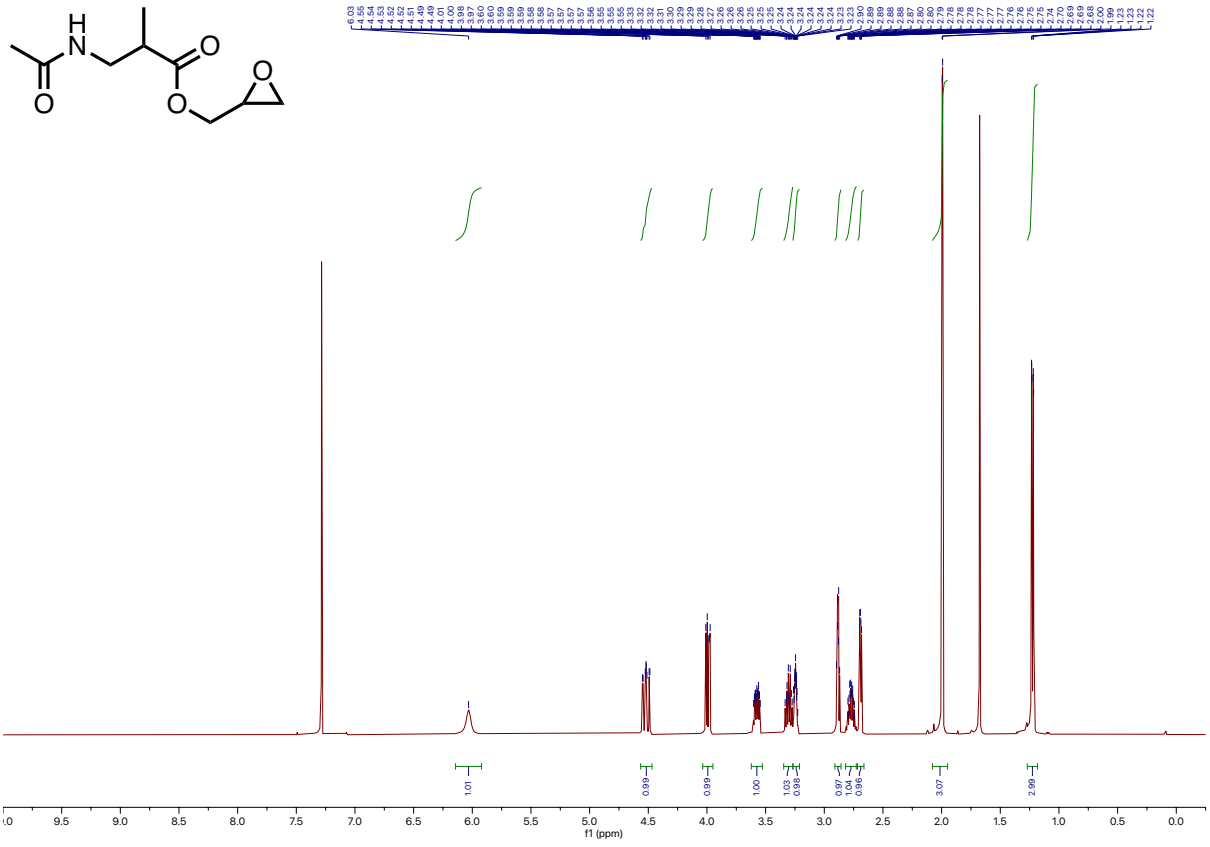

170.03
62.74
39.48
32.55
29.63
25.30
23.38
f1 (ppm)

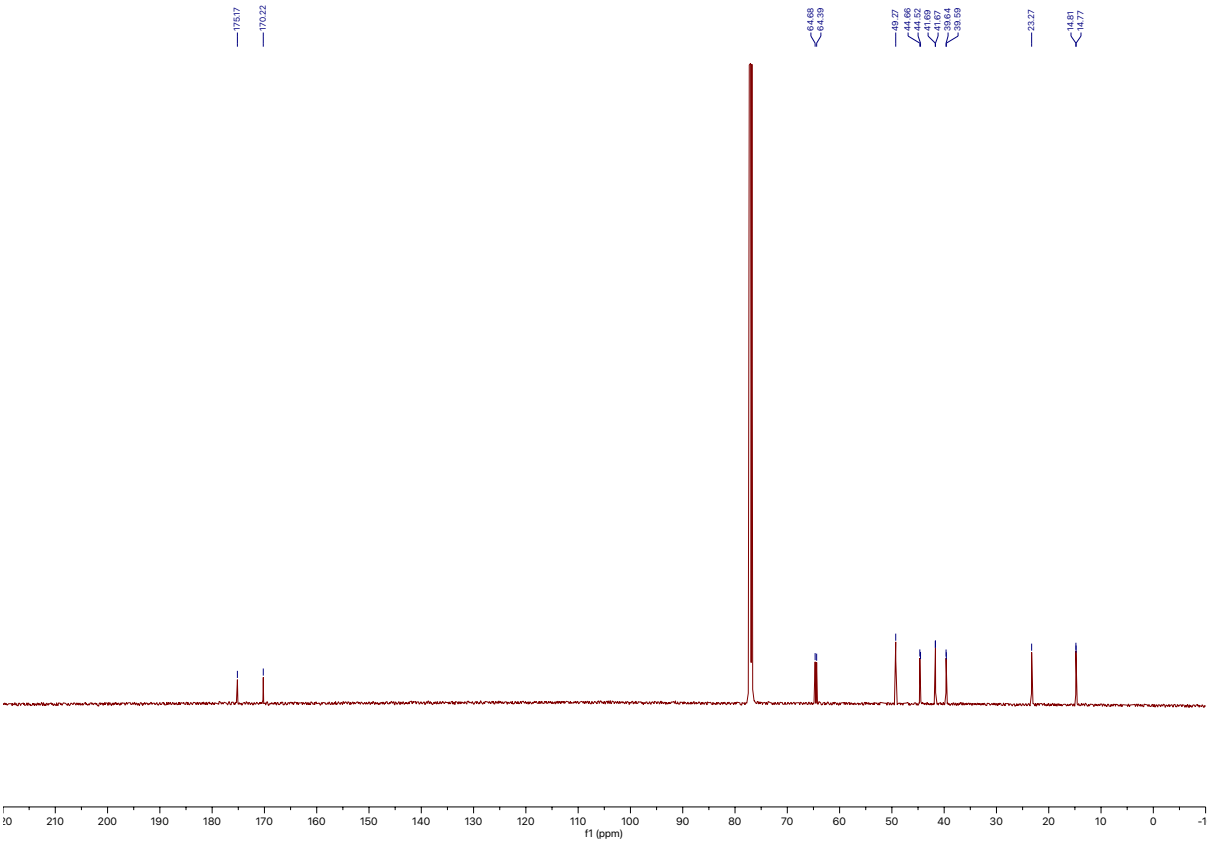

6.01
3.51
3.50
3.50
3.49
3.48
3.47
3.47
3.46
3.30
3.28
3.27
3.26
3.25
3.24
2.63
2.62
2.61
2.61
2.60
2.60
2.60
2.59
2.59
2.59
2.58
2.58
2.57
2.56
1.99
1.47
1.16
1.15
0.89
1.00
1.00
0.97
2.88
9.14
3.01
f1 (ppm)

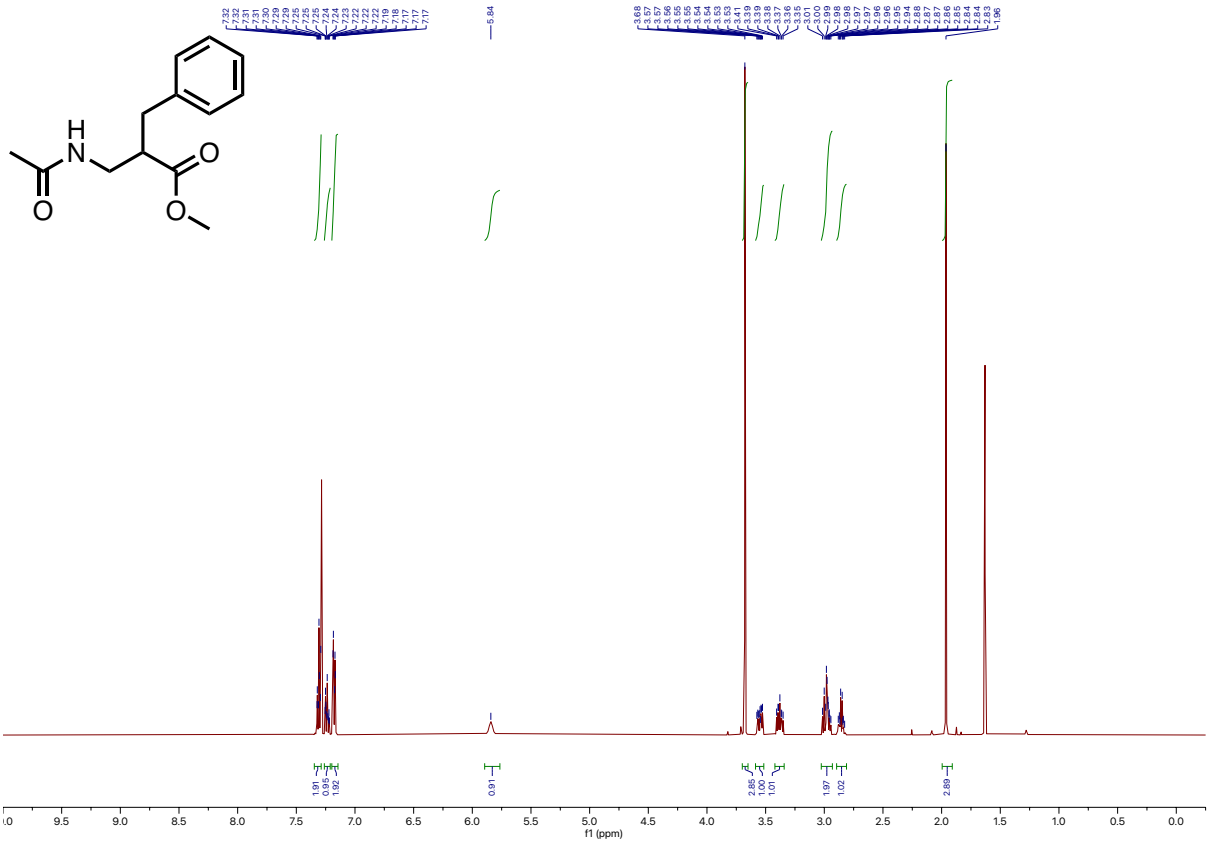

175.08
170.06
80.93
41.67
40.24
28.07
23.33
14.96
f1 (ppm)

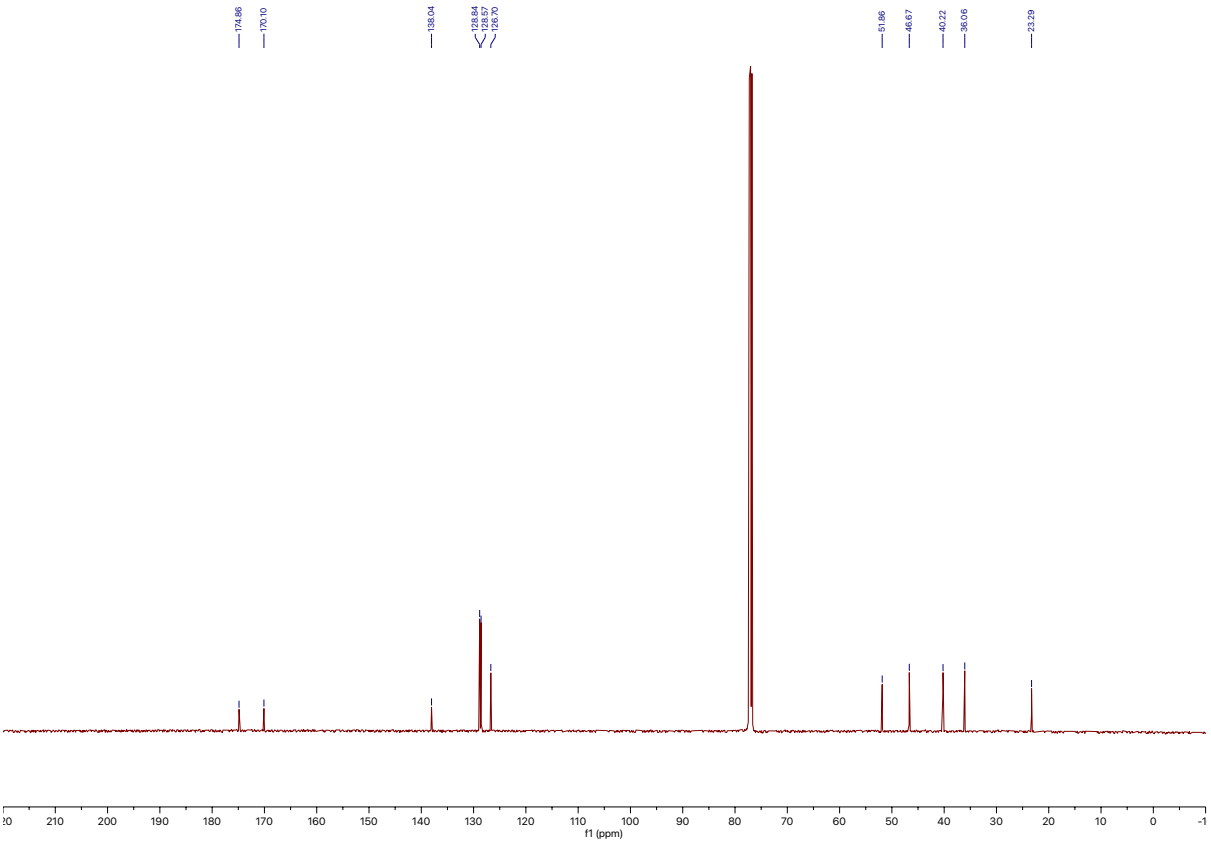

H
N
O
O
O
OH
6.18
5.50
1.05
1.11
2.14
2.00
1.00
1.04
1.92
3.09
3.02
f1 (ppm)

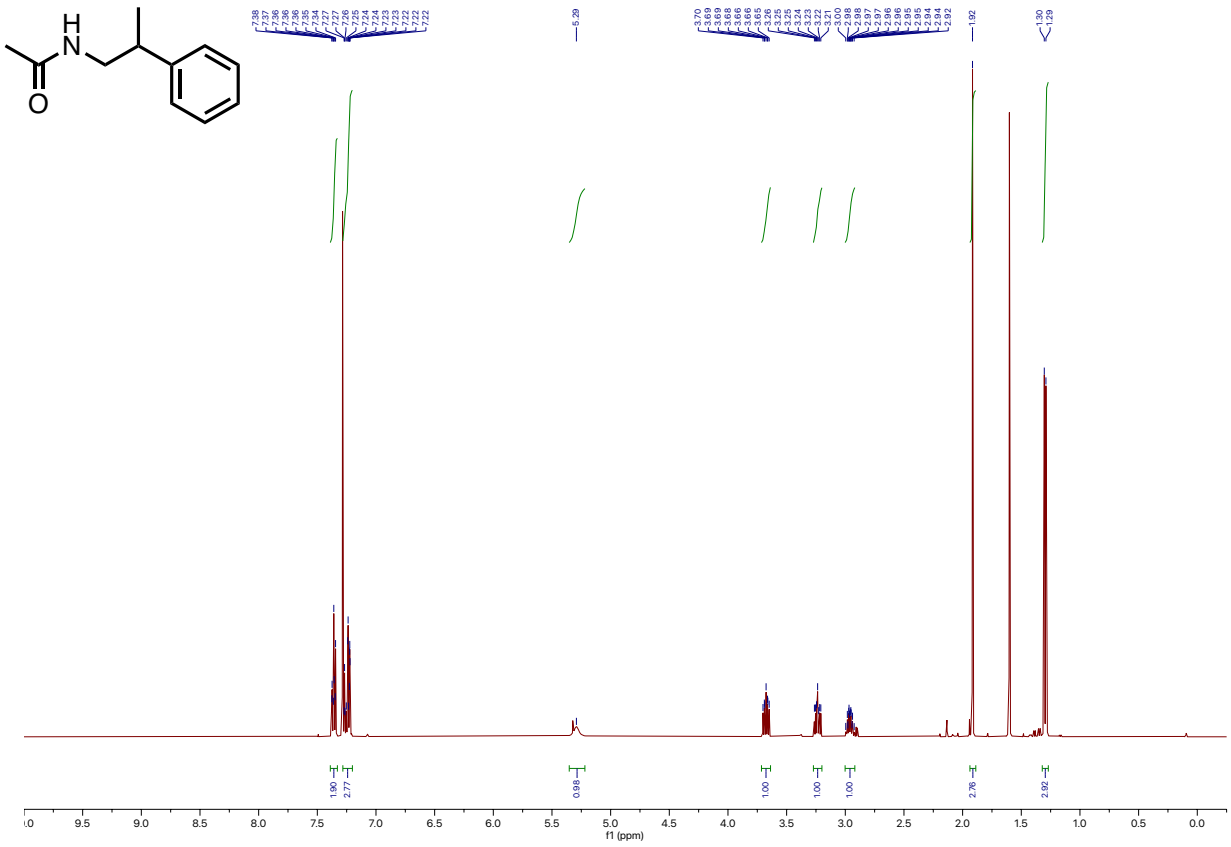

175.33
170.58
66.23
60.88
41.94
40.01
23.25
14.70
f1 (ppm)

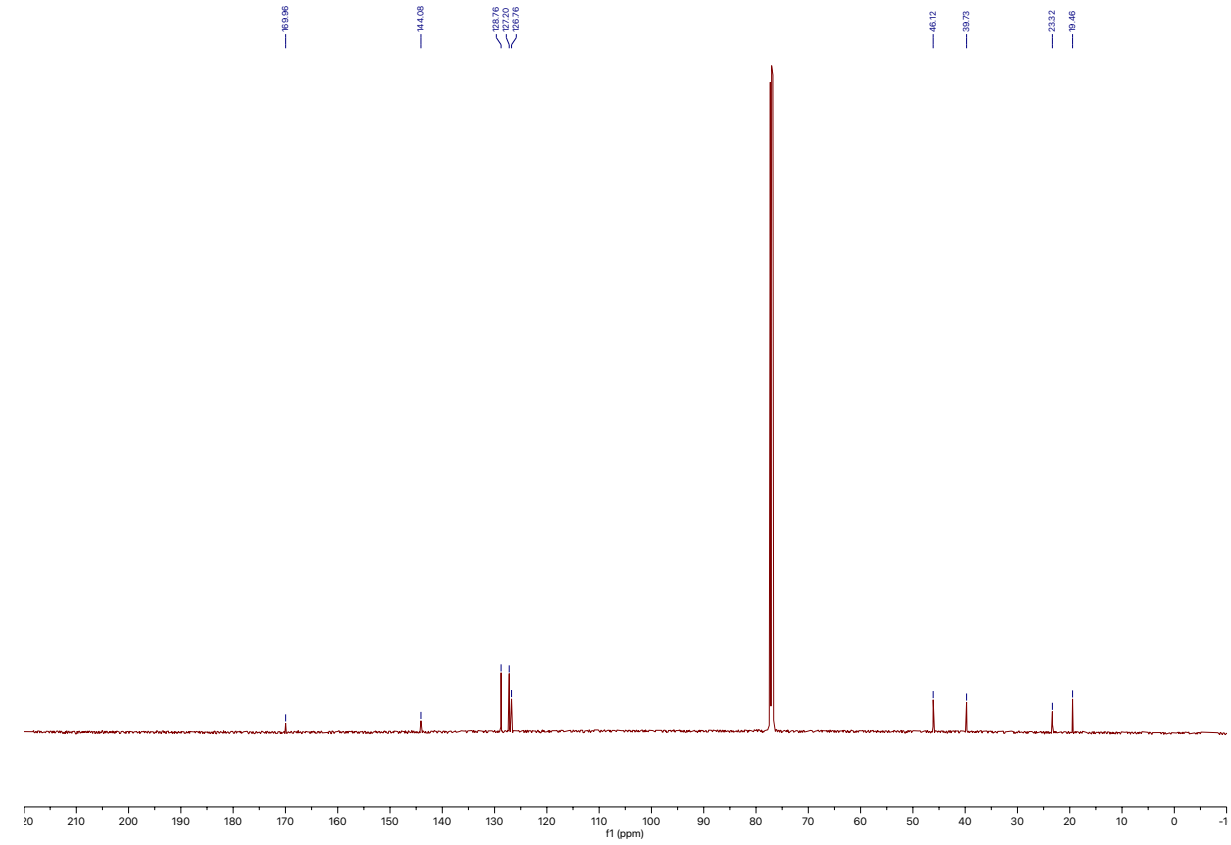

f1 (ppm)

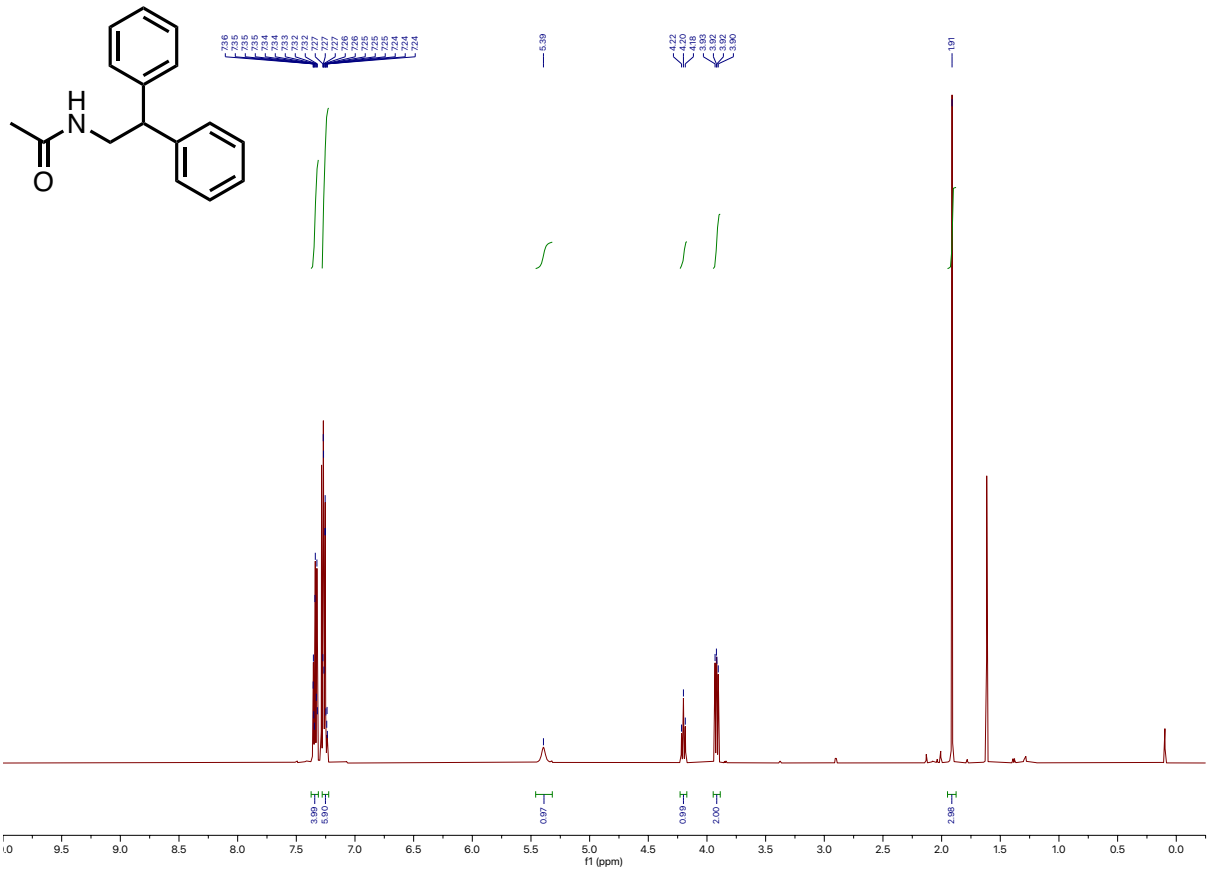

f1 (ppm)

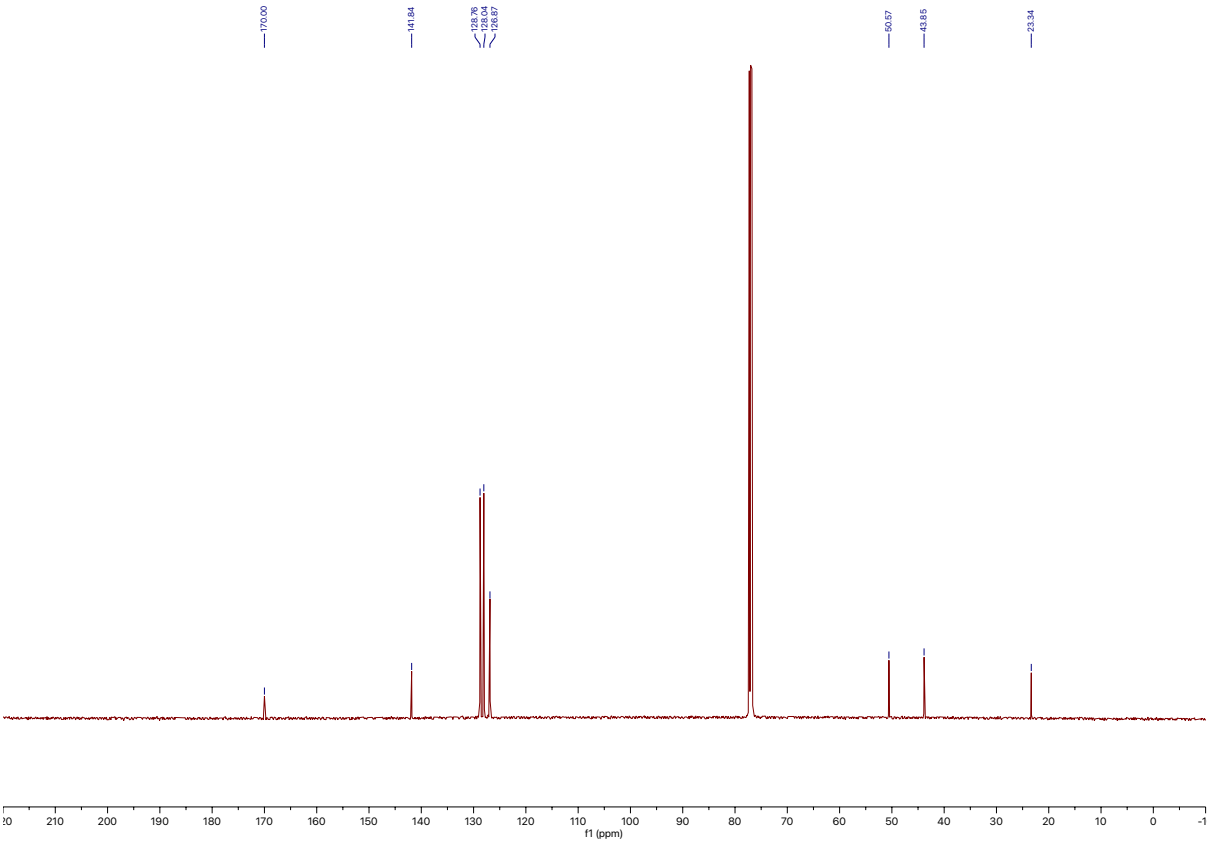

7.32
7.32
7.31
7.31
7.30
7.29
7.29
7.25
7.25
7.24
7.24
7.23
7.22
7.22
7.22
7.19
7.18
7.17
7.17
7.17
5.84
3.68
3.57
3.57
3.56
3.55
3.55
3.54
3.54
3.53
3.53
3.41
3.39
3.39
3.38
3.37
3.36
3.35
3.01
3.00
2.99
2.98
2.98
2.97
2.97
2.96
2.96
2.95
2.94
2.88
2.87
2.86
2.85
2.84
2.84
2.83
1.96
1.91
0.95
1.92
0.91
2.85
1.00
1.01
1.97
1.02
2.89
f1 (ppm)

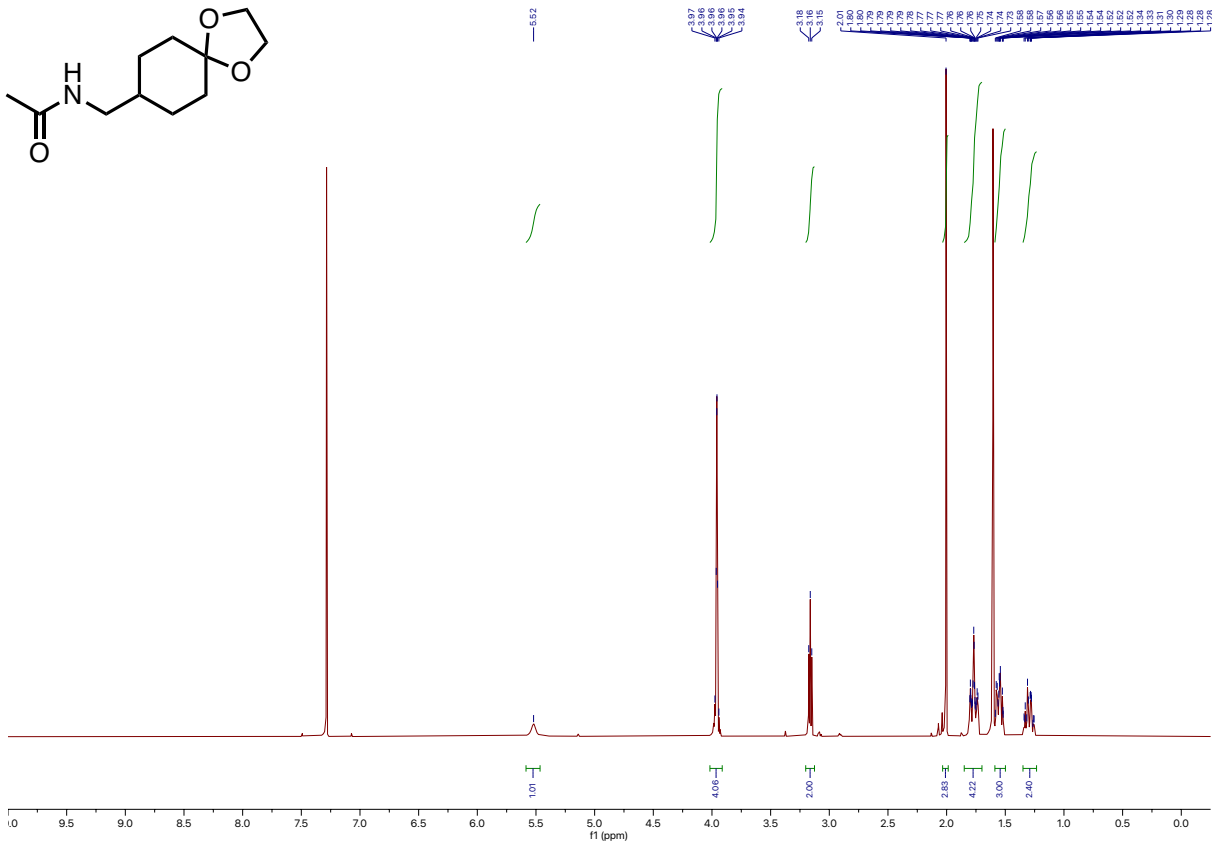

174.86
170.10
138.04
128.84
128.57
126.70
51.86
46.67
40.22
36.06
23.29
f1 (ppm)

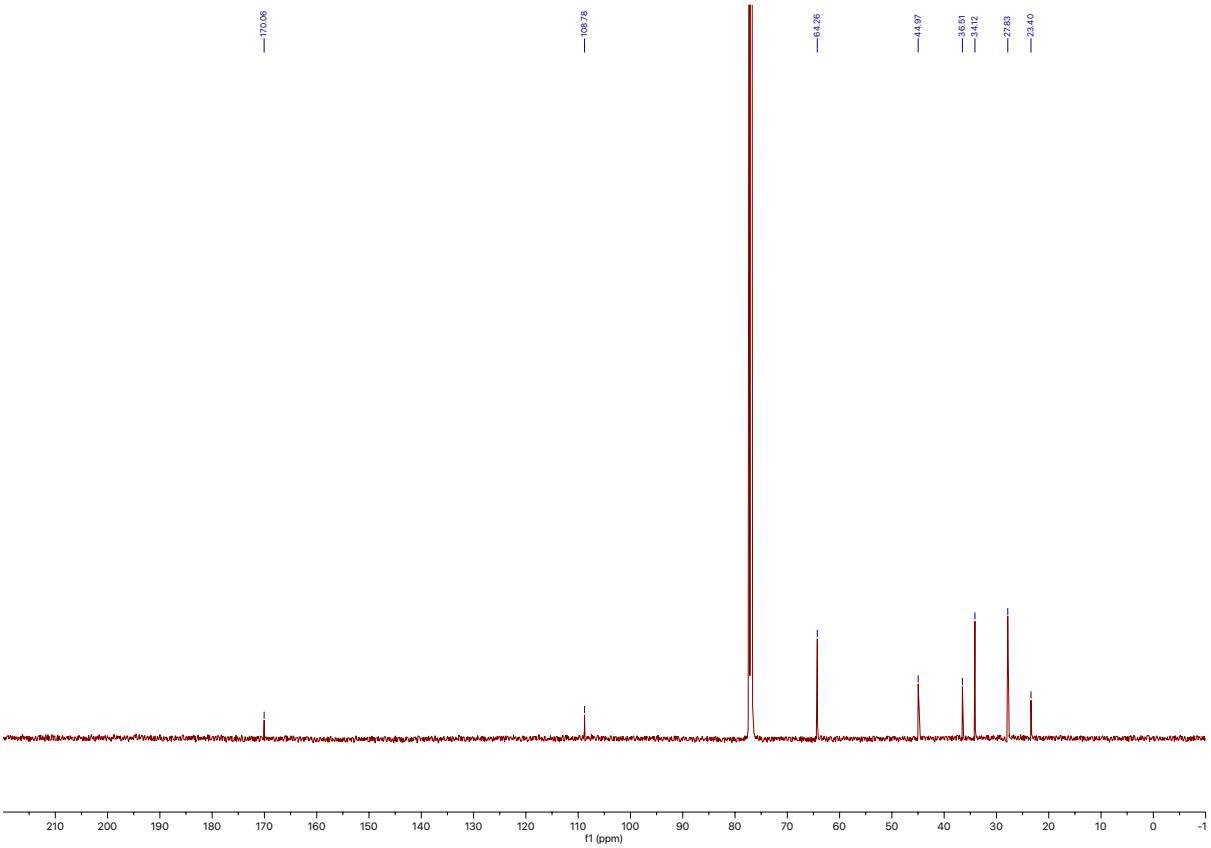

7.38
7.37
7.36
7.36
7.36
7.35
7.34
7.27
7.27
7.26
7.25
7.24
7.24
7.23
7.23
7.22
7.22
7.22
5.29
3.70
3.69
3.69
3.68
3.66
3.66
3.65
3.26
3.25
3.24
3.24
3.23
3.22
3.21
3.00
2.98
2.97
2.97
2.96
2.96
2.95
2.95
2.94
2.94
2.92
1.92
1.30
1.29
1.90
2.77
0.98
1.00
1.00
1.00
2.76
2.92
f1 (ppm)

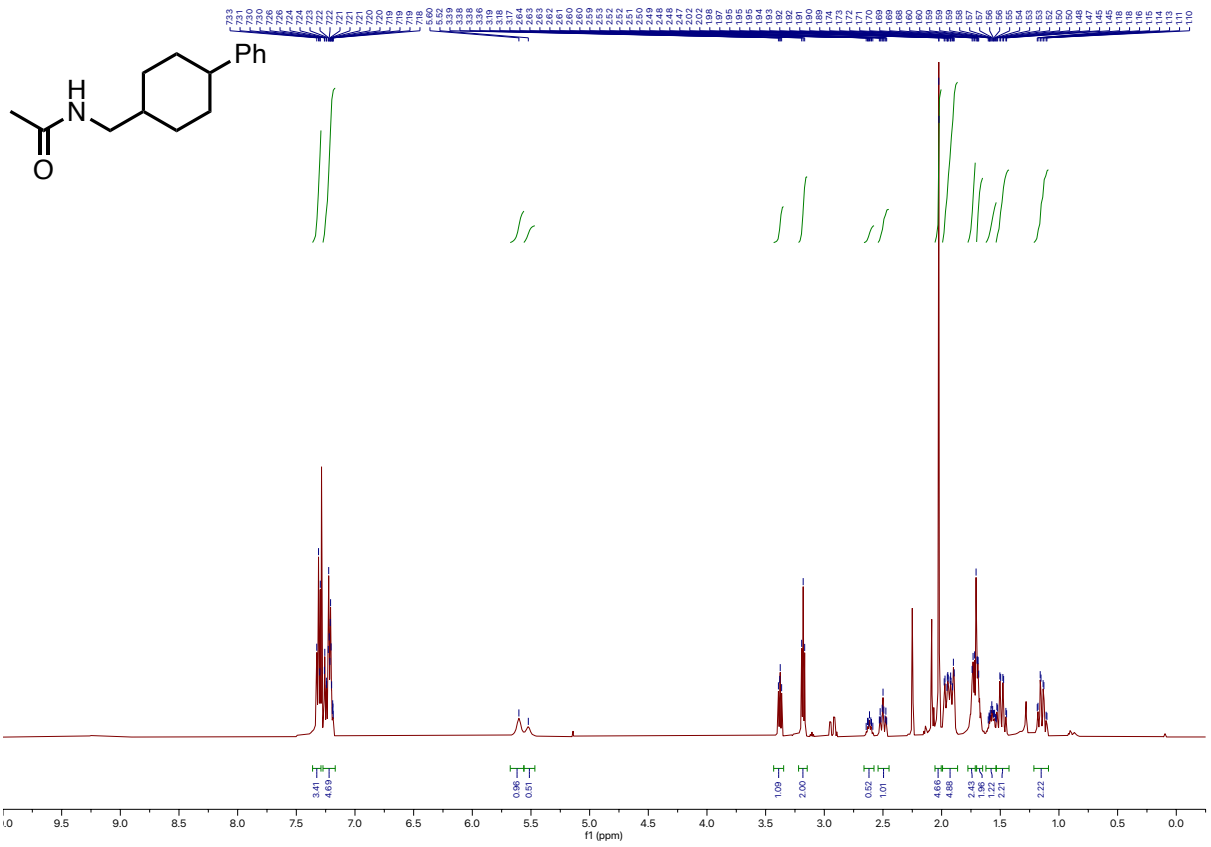

169.96
144.08
128.76
127.20
126.76
46.12
39.73
23.32
19.46
f1 (ppm)

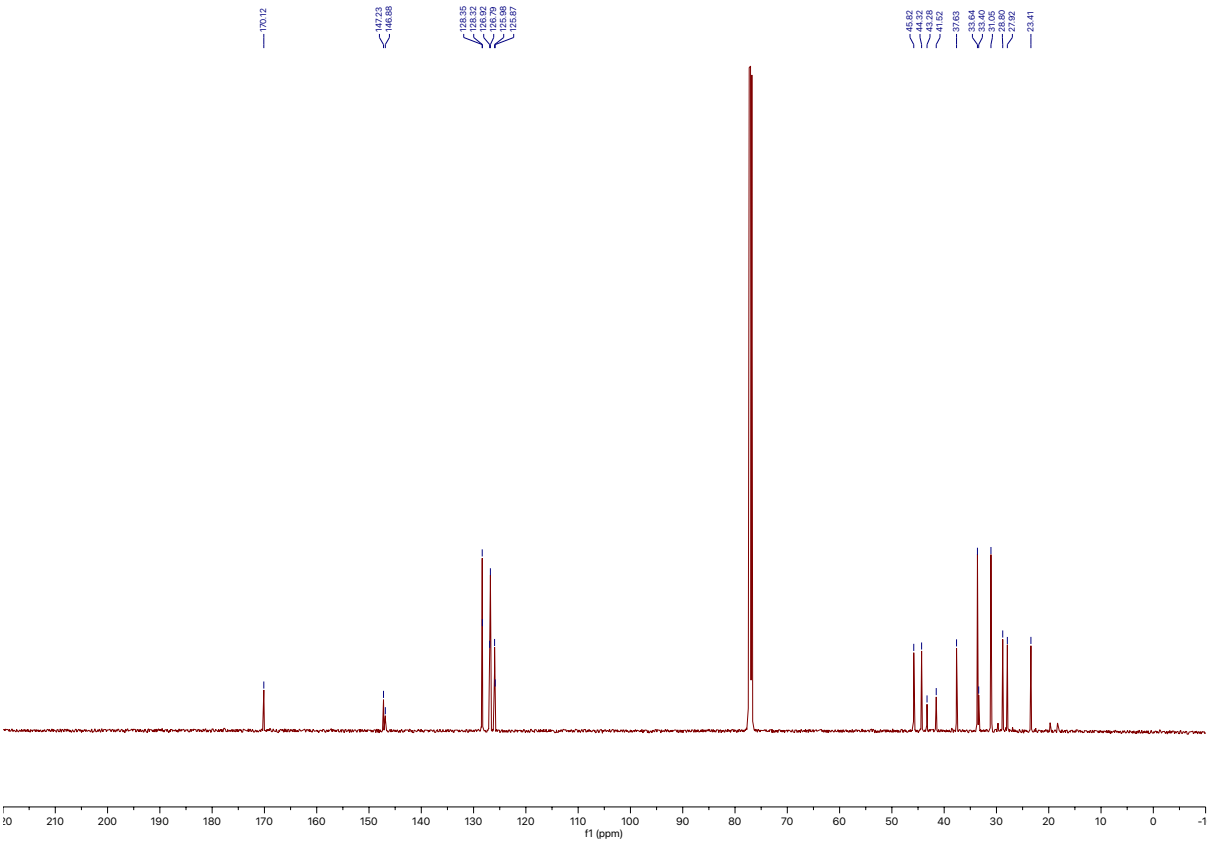

H
N
O
7.36
7.35
7.35
7.35
7.34
7.34
7.33
7.33
7.32
7.27
7.27
7.27
7.26
7.26
7.25
7.25
7.25
7.24
7.24
7.24
5.39
4.22
4.20
4.16
3.93
3.92
3.92
3.90
1.91
3.99
5.90
0.97
0.99
2.00
2.98
f1 (ppm)

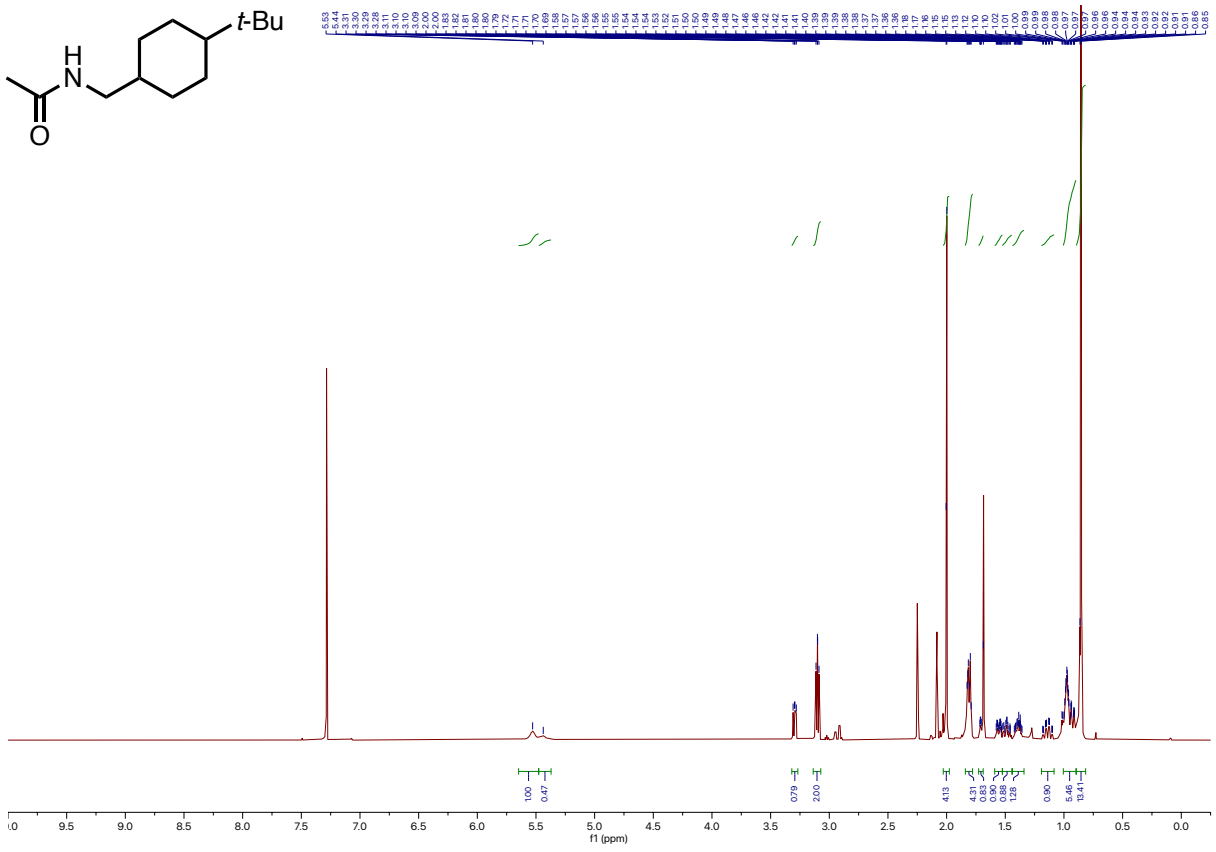

170.00
141.84
128.76
128.04
126.97
50.57
43.85
23.34
f1 (ppm)

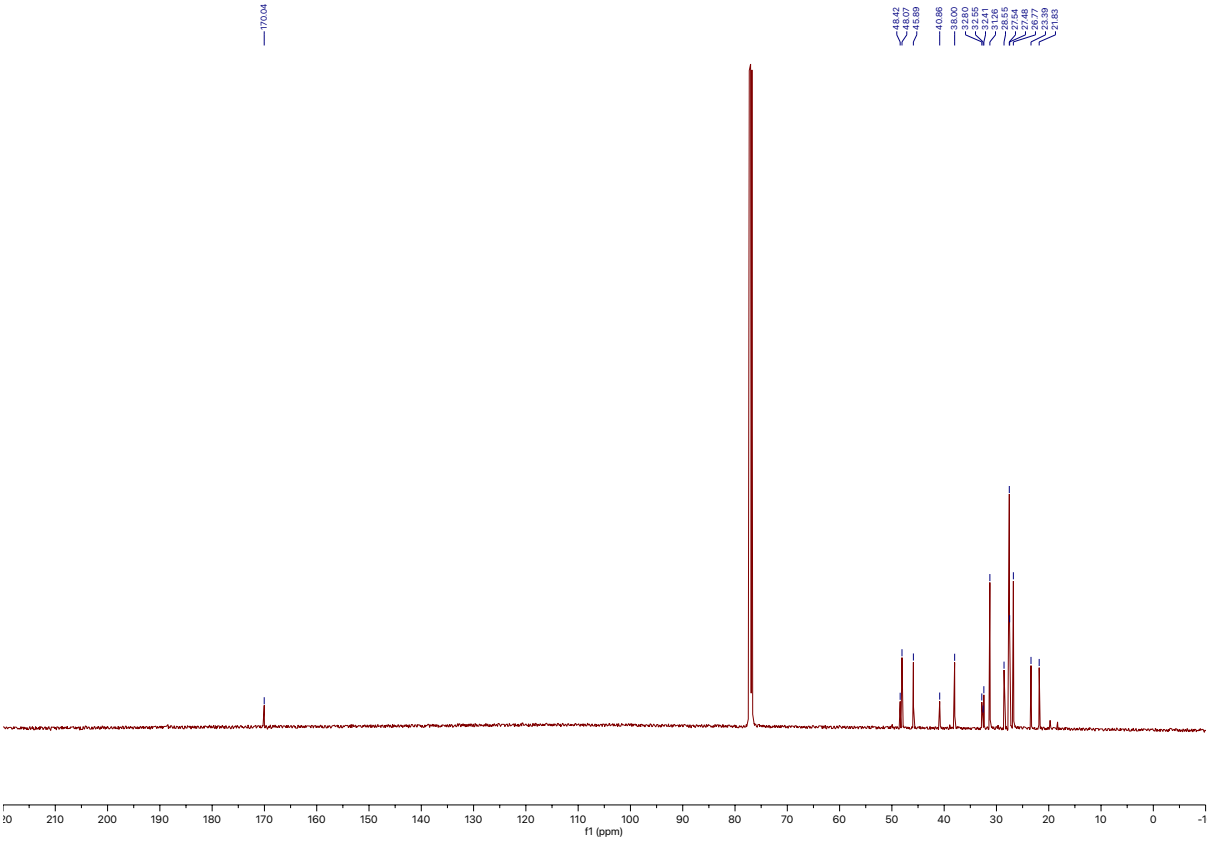

5.52
3.97
3.96
3.96
3.95
3.95
3.94
3.18
3.16
3.15
2.01
1.80
1.80
1.79
1.79
1.79
1.79
1.78
1.78
1.77
1.77
1.77
1.77
1.76
1.76
1.76
1.75
1.74
1.74
1.73
1.58
1.58
1.57
1.57
1.56
1.56
1.55
1.55
1.55
1.54
1.54
1.53
1.52
1.52
1.34
1.33
1.33
1.31
1.30
1.29
1.29
1.28
1.28
1.01
4.06
2.00
2.83
4.22
3.00
2.40
f1 (ppm)

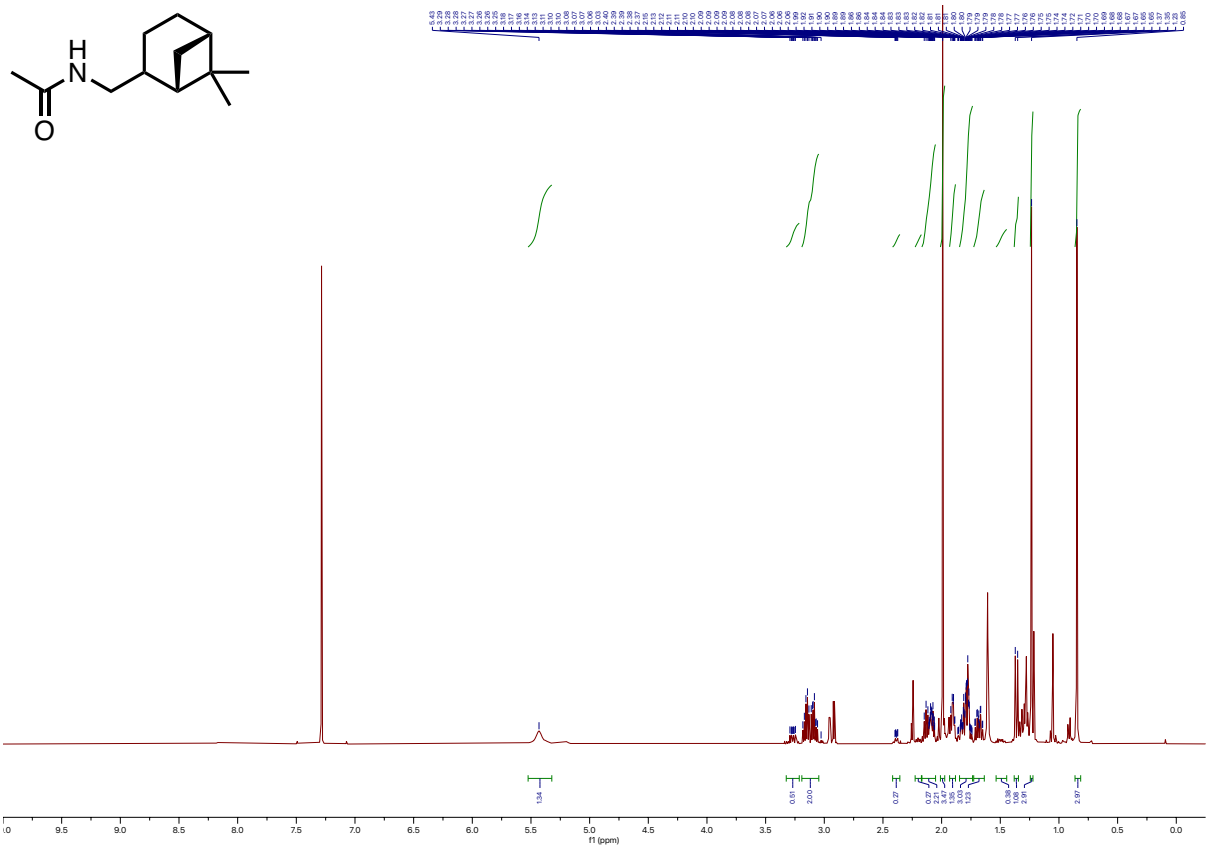

170.06
108.78
64.26
44.97
36.51
34.12
27.83
23.40
f1 (ppm)

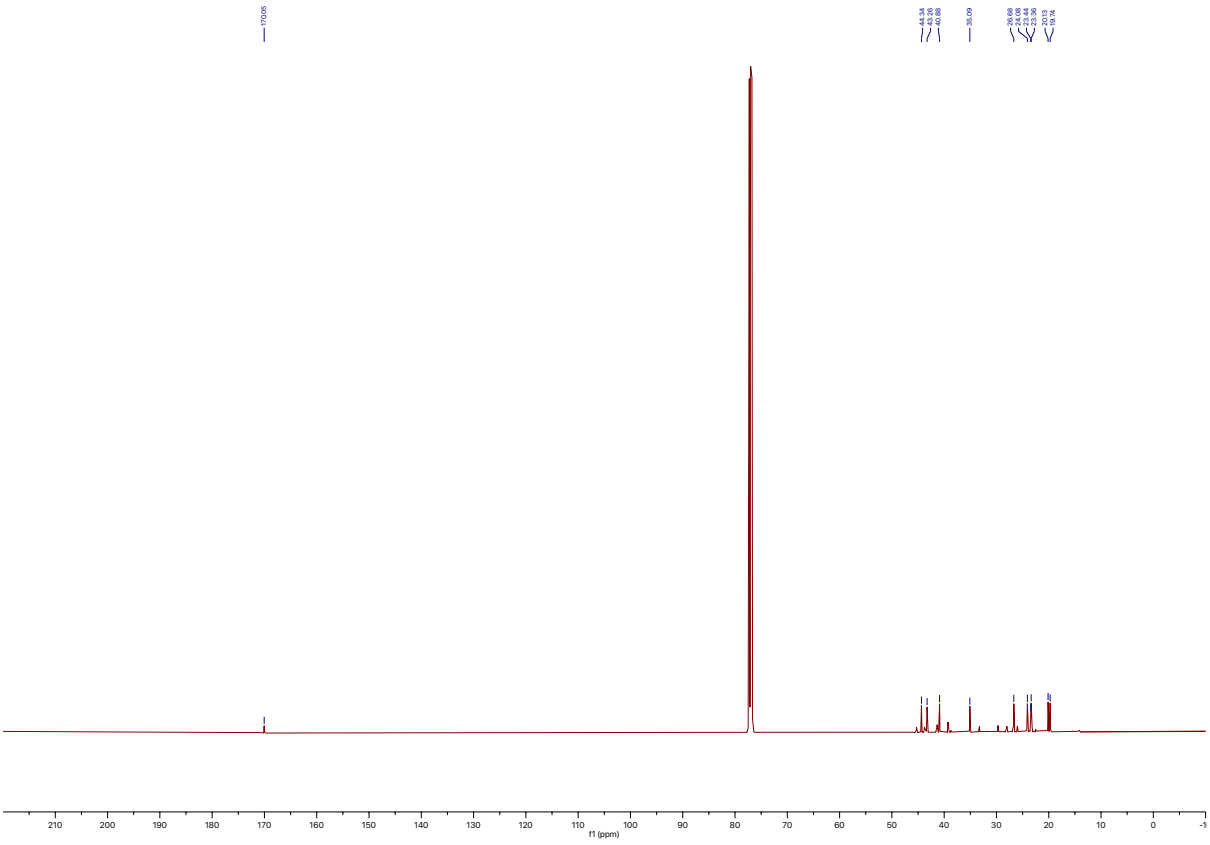

Ph
H
N
O
f1 (ppm)

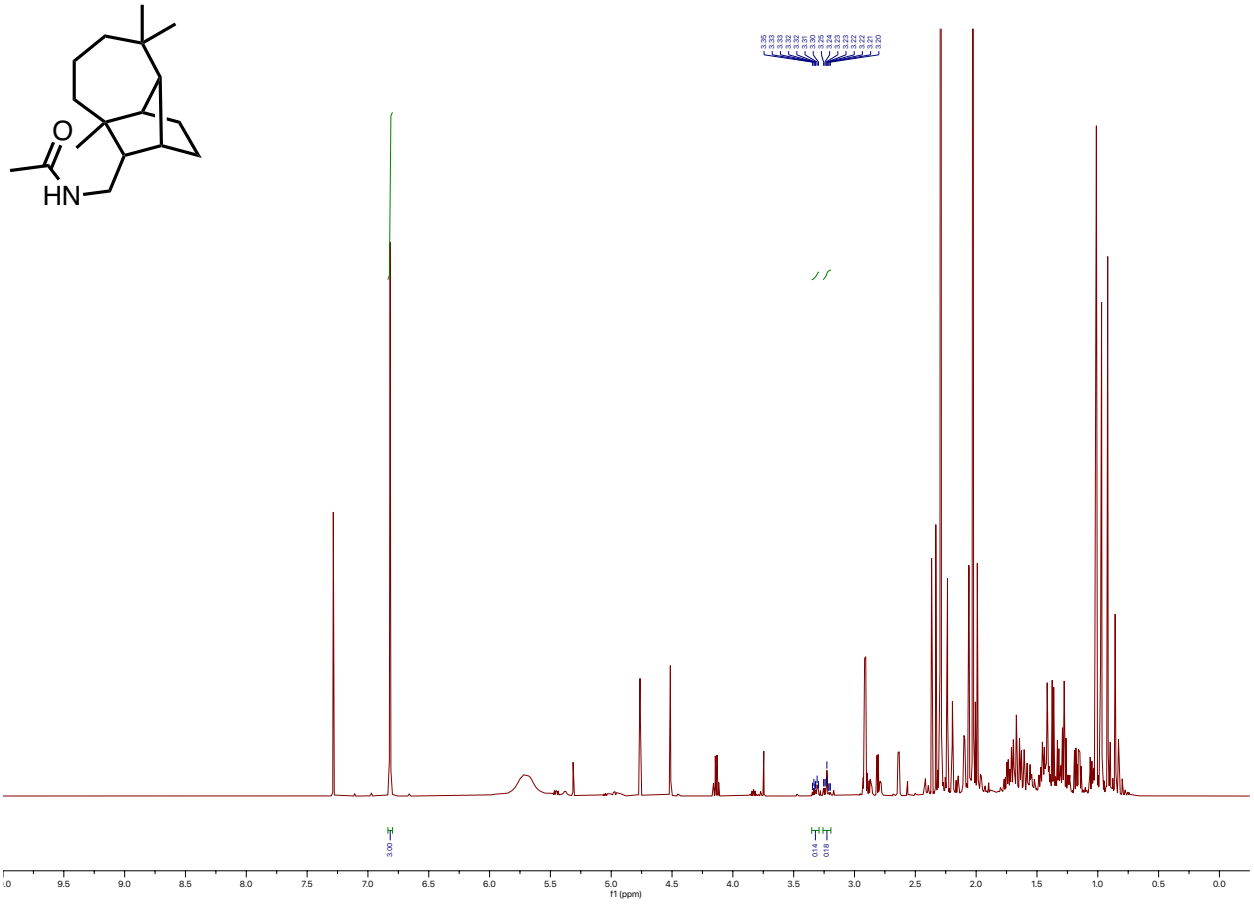

f1 (ppm)

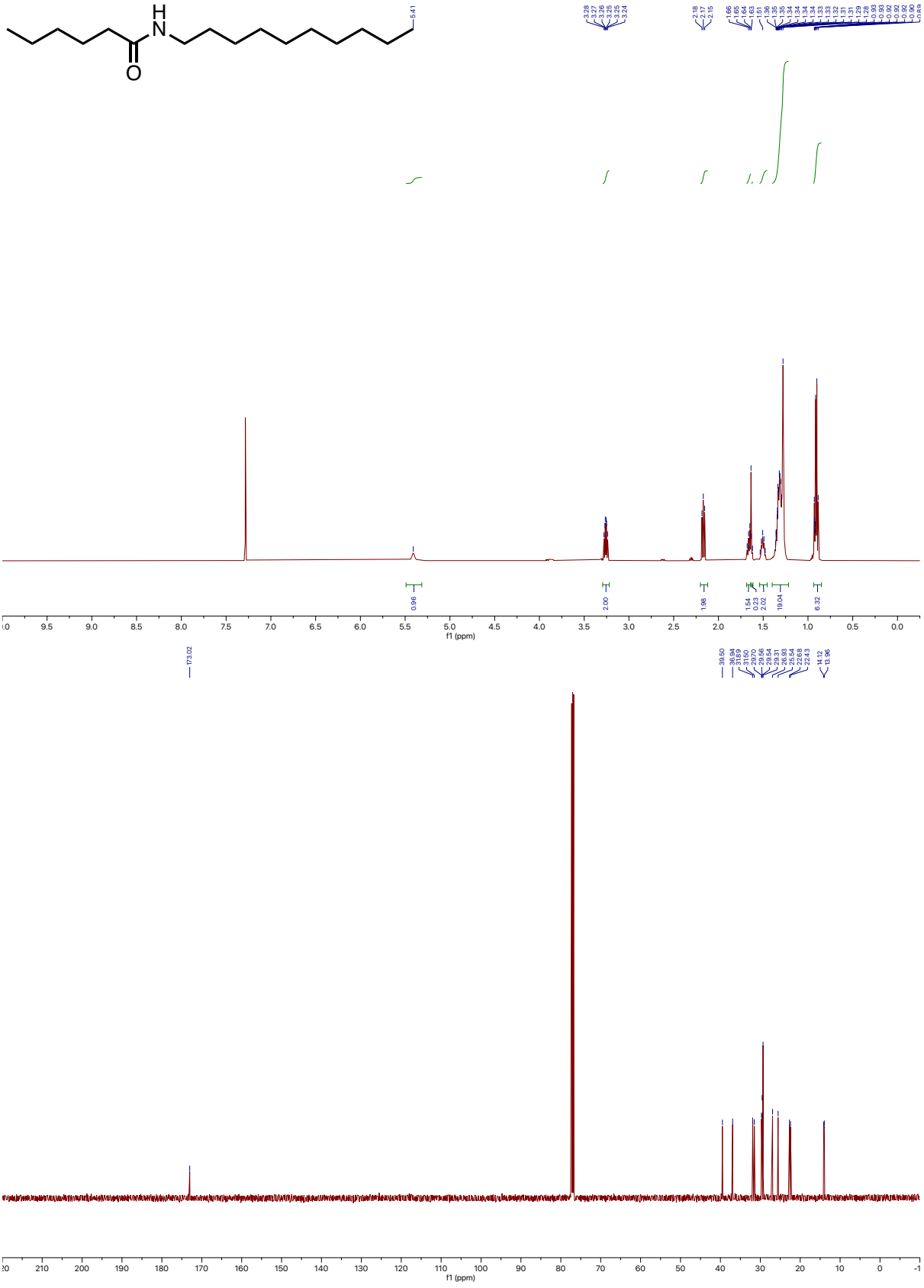

t-Bu
H
N
O
f1 (ppm)

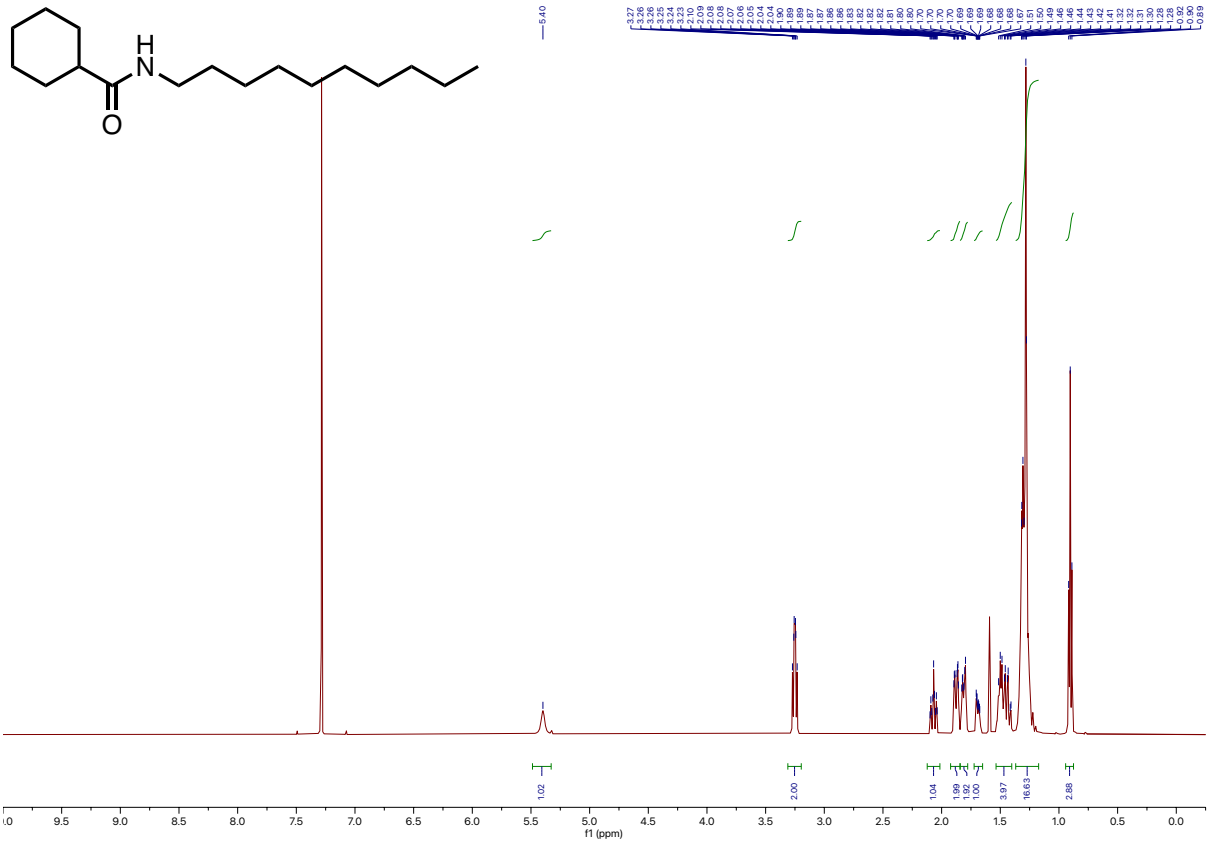

170.04
48.42
48.07
45.99
40.86
38.00
32.80
32.55
31.41
31.26
28.55
28.54
27.64
27.48
26.77
23.89
21.83
f1 (ppm)

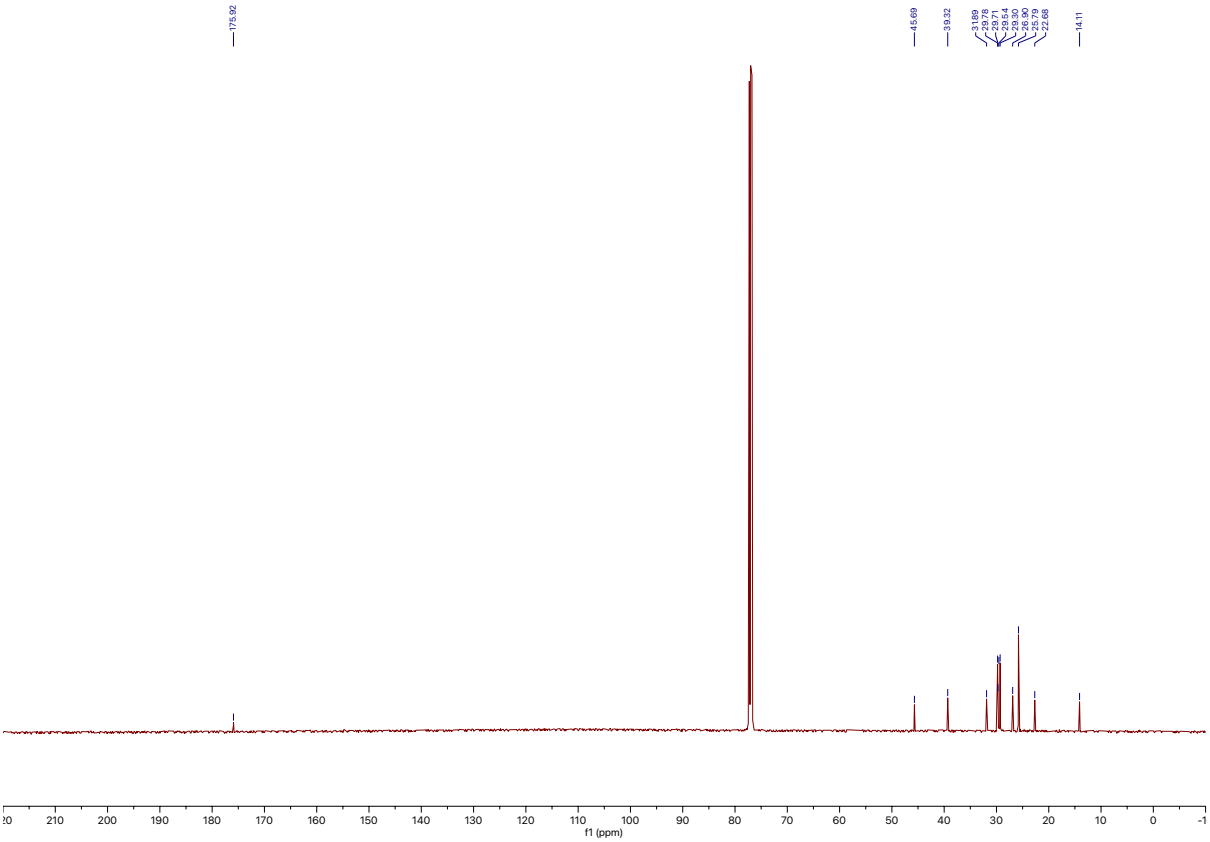

H
N
O
f1 (ppm)

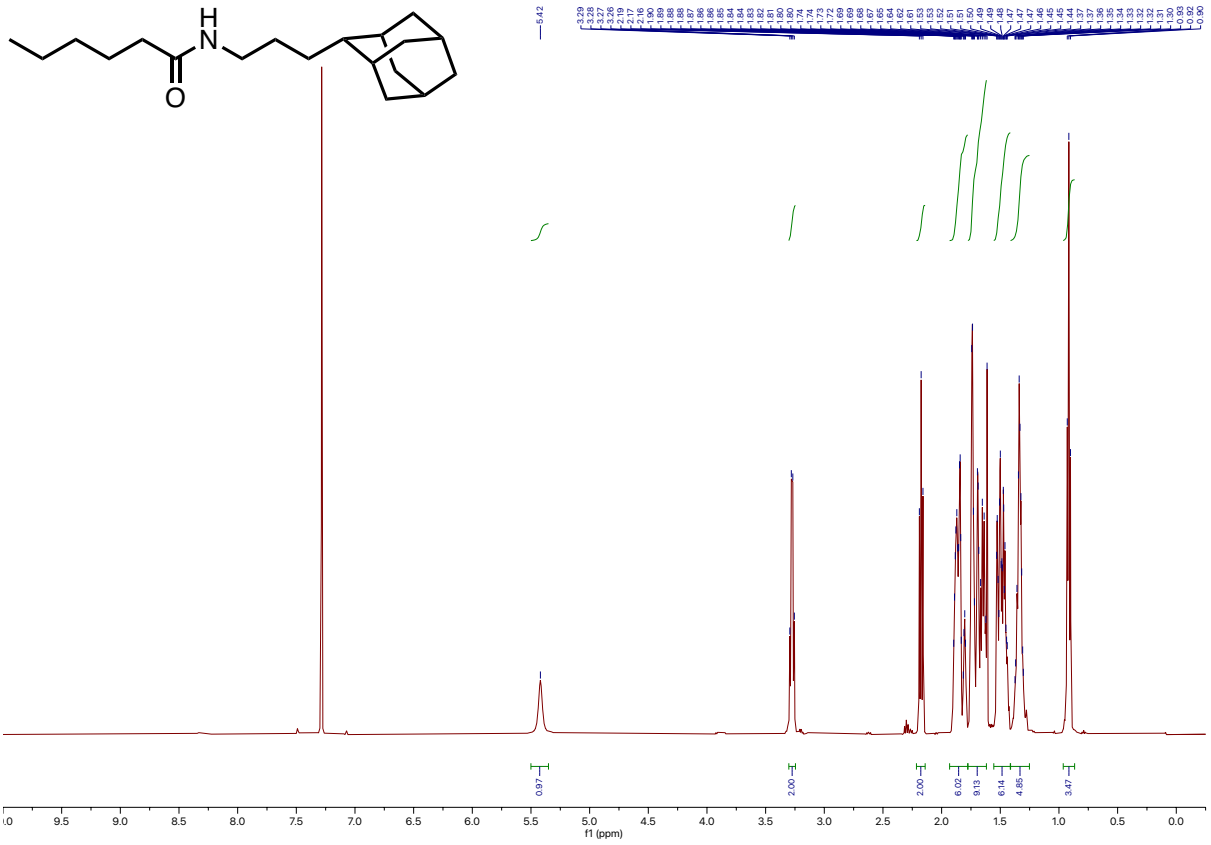

170.05
44.34
43.36
40.88
35.09
26.68
24.08
23.44
23.36
20.53
19.24
f1 (ppm)

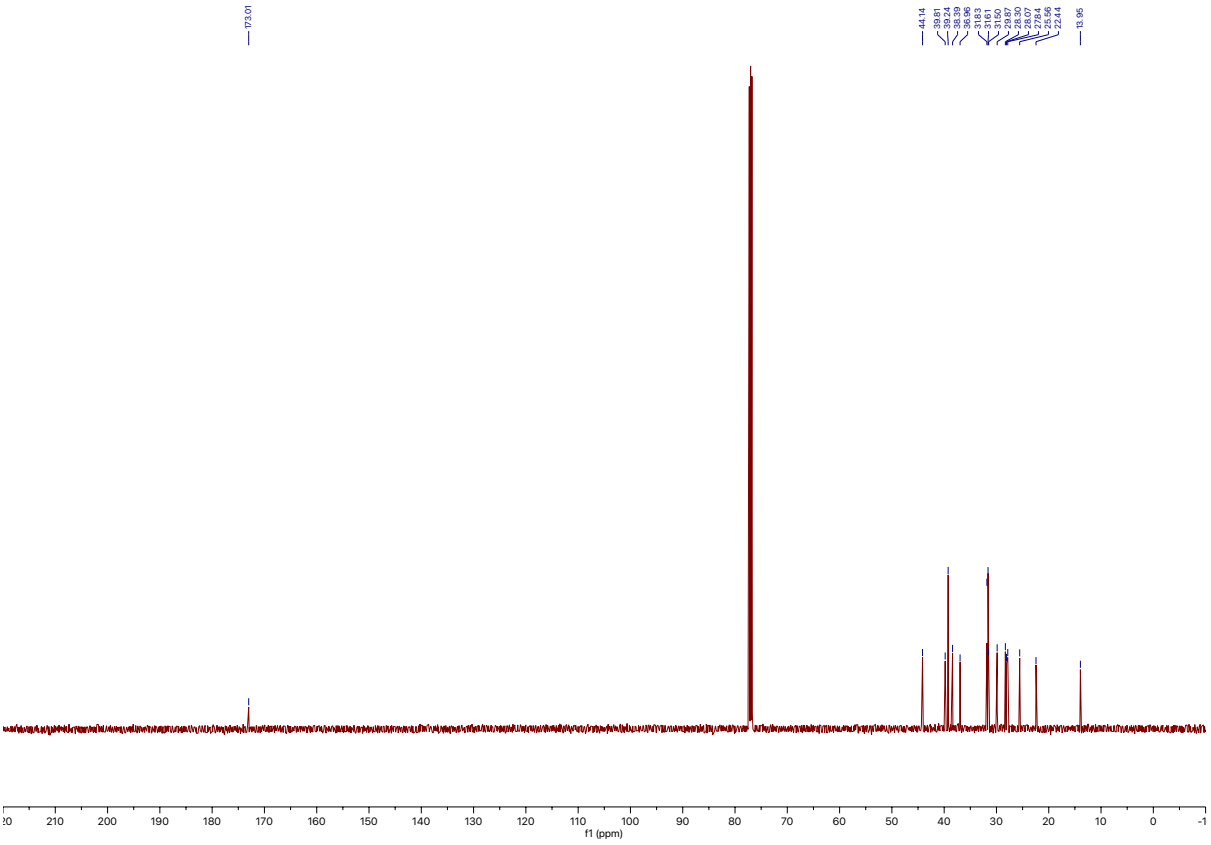

O
HN
3.00
0.14
0.18
f1 (ppm)

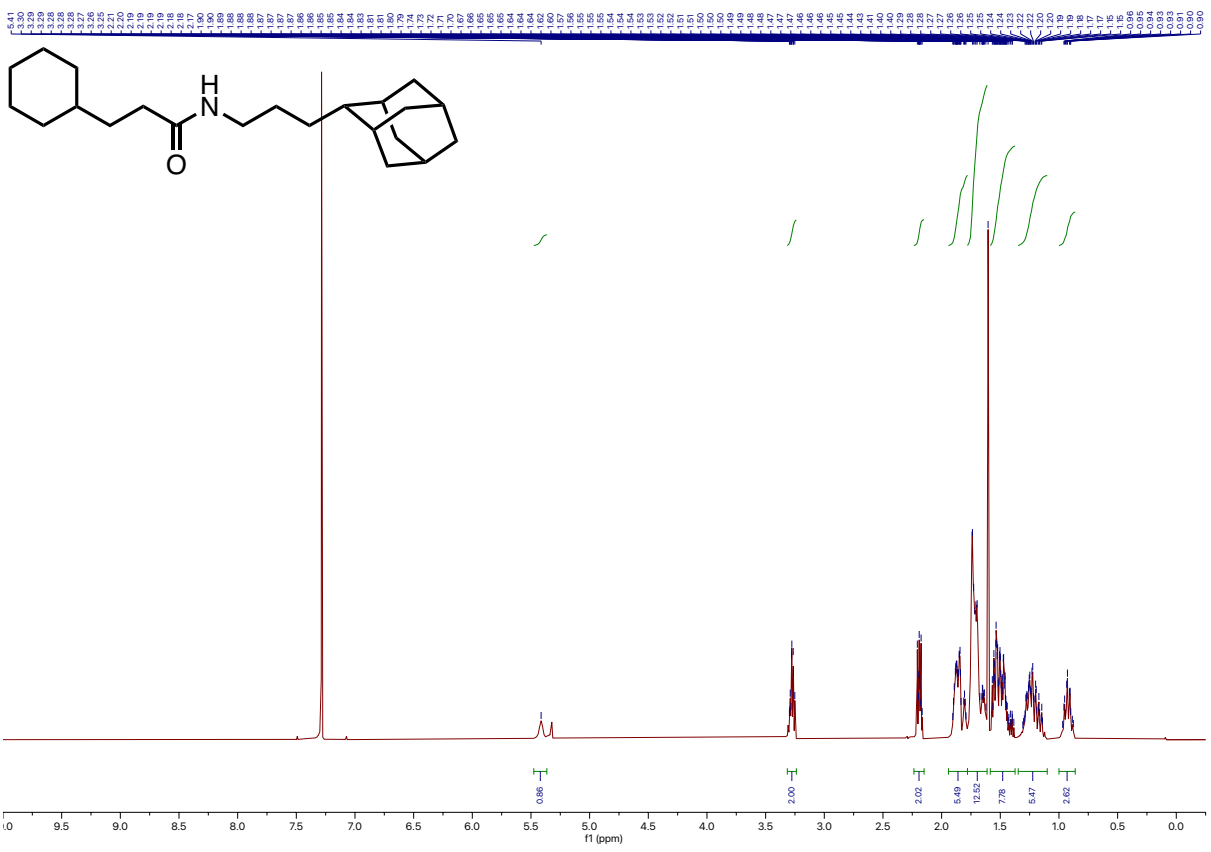

H
N
O
f1 (ppm)
f1 (ppm)

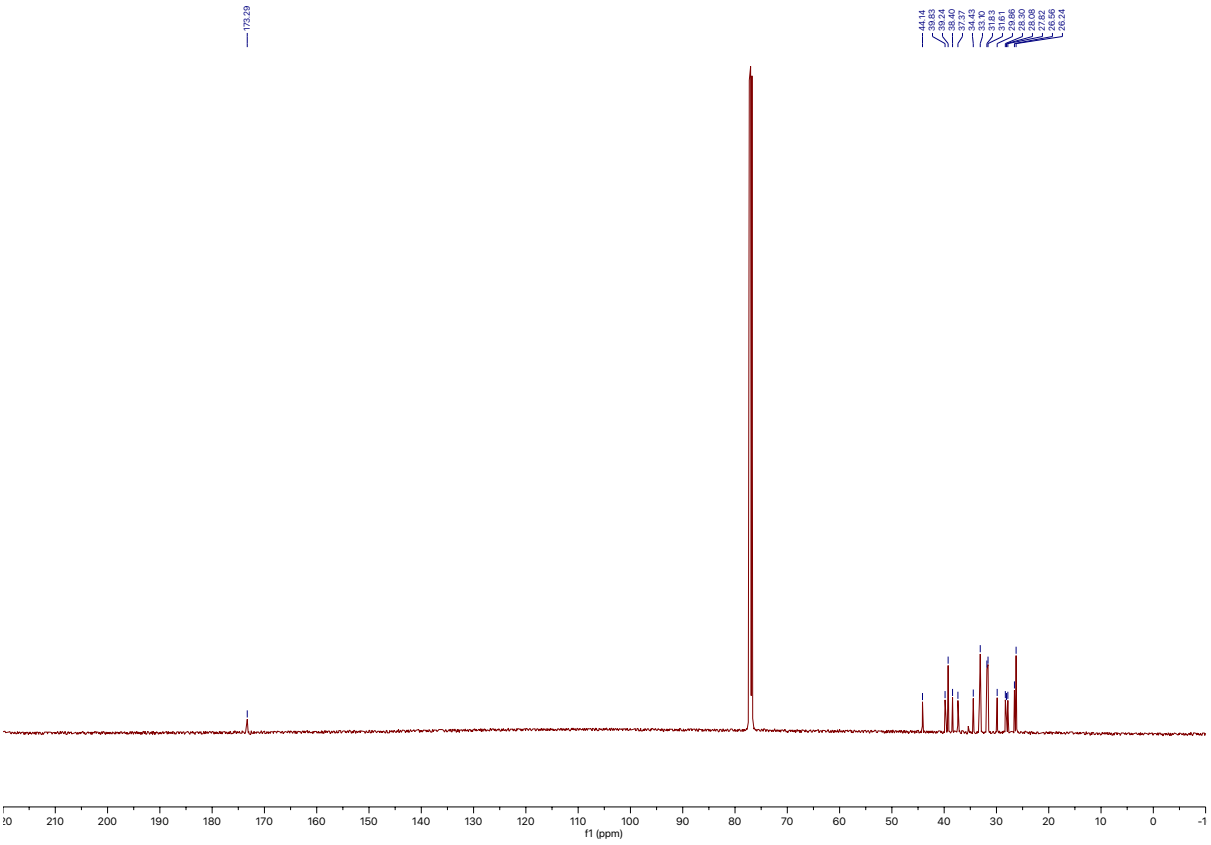

H
N
O
5.40
1.02
2.00
1.04
1.99
1.92
1.00
3.97
16.63
2.86
f1 (ppm)

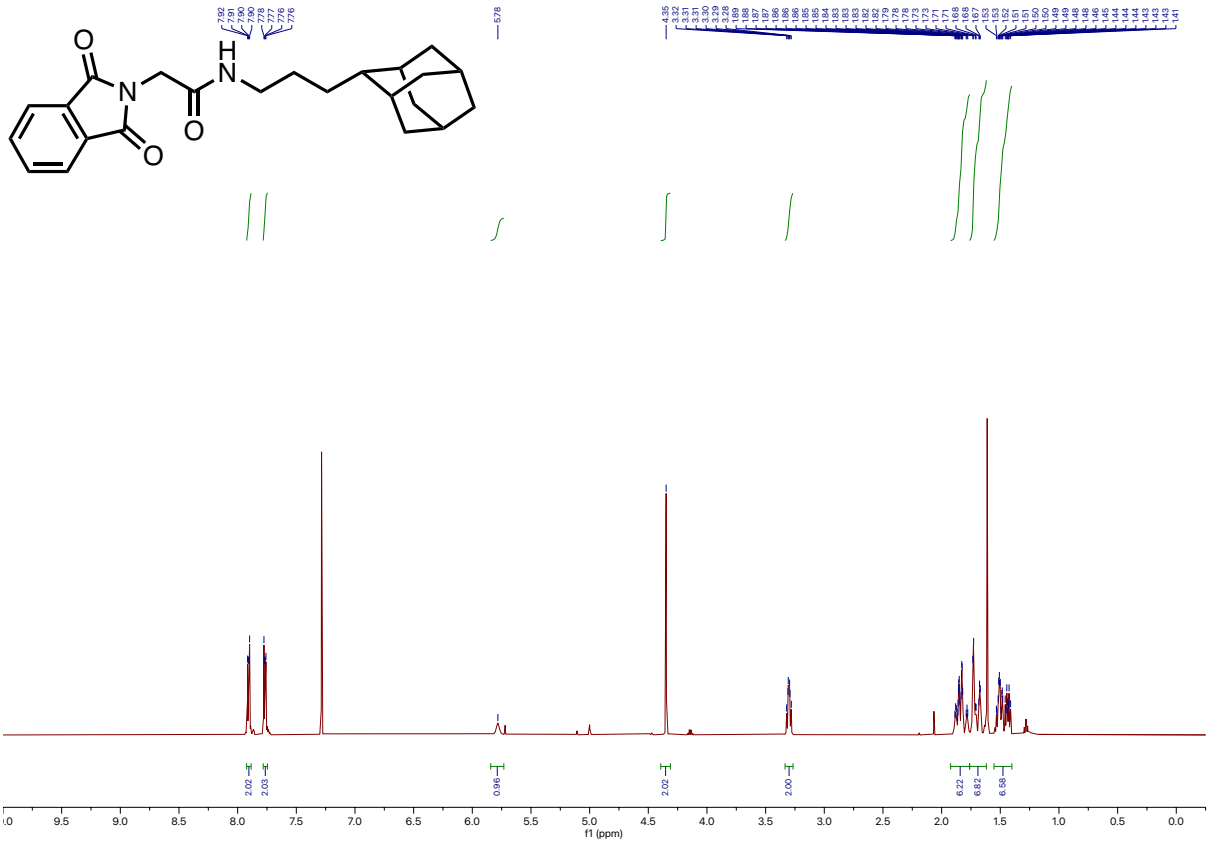

175.92
45.69
39.32
31.89
29.54
29.71
29.90
26.90
25.79
22.68
14.11
f1 (ppm)

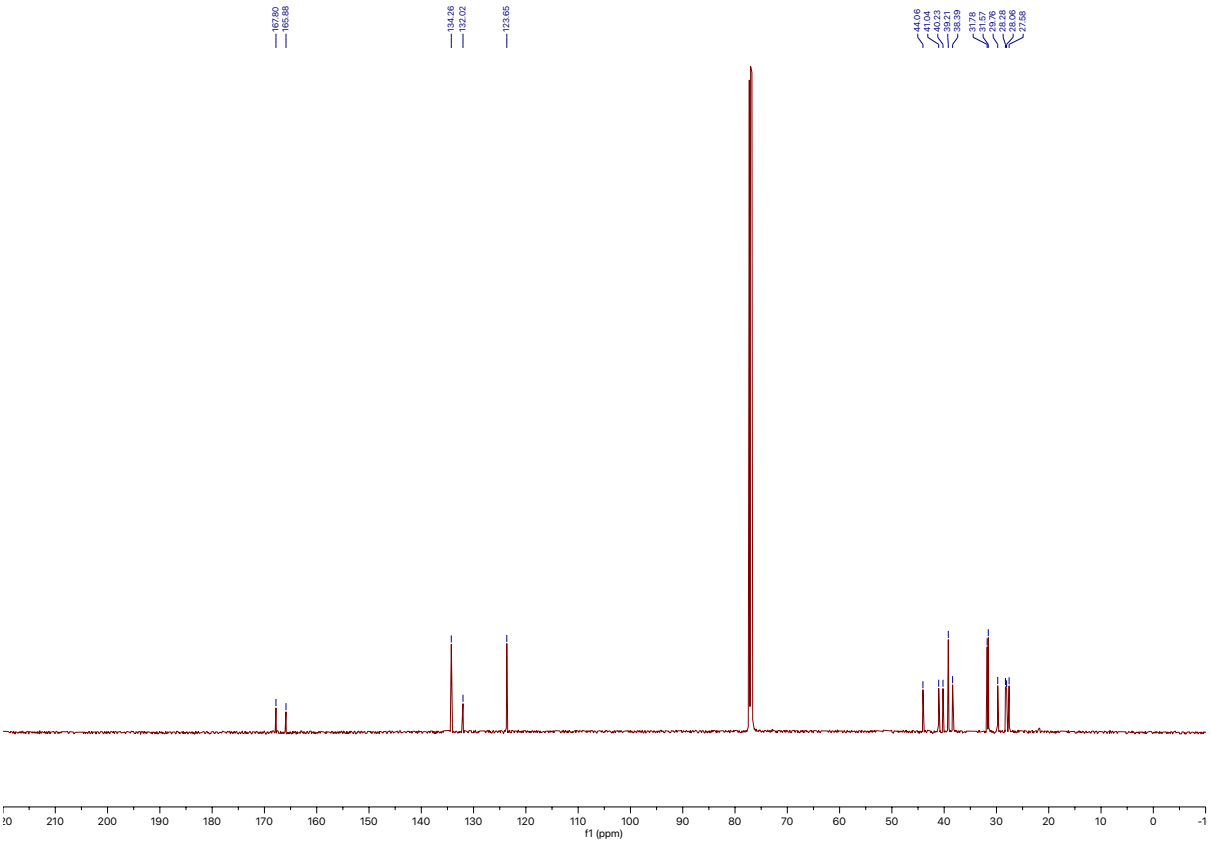

H
N
O
f1 (ppm)

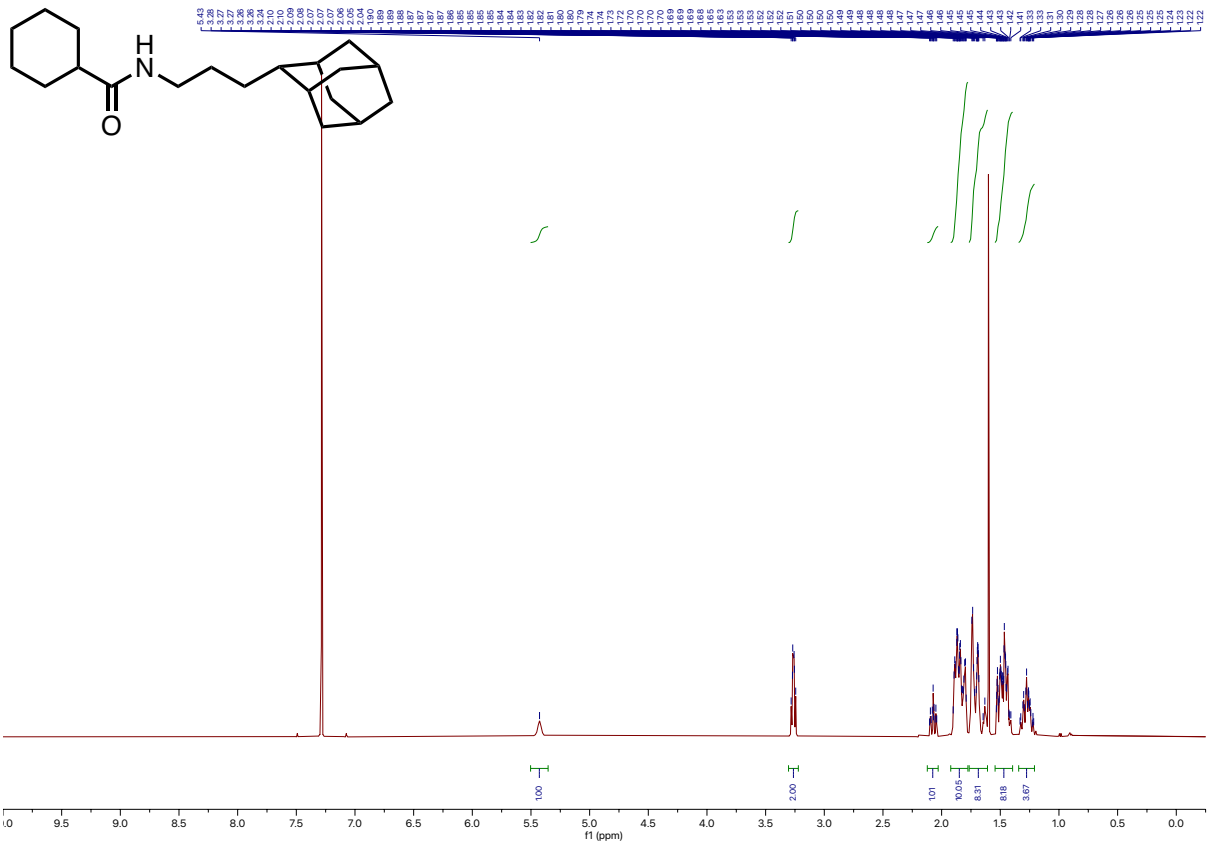

f1 (ppm)

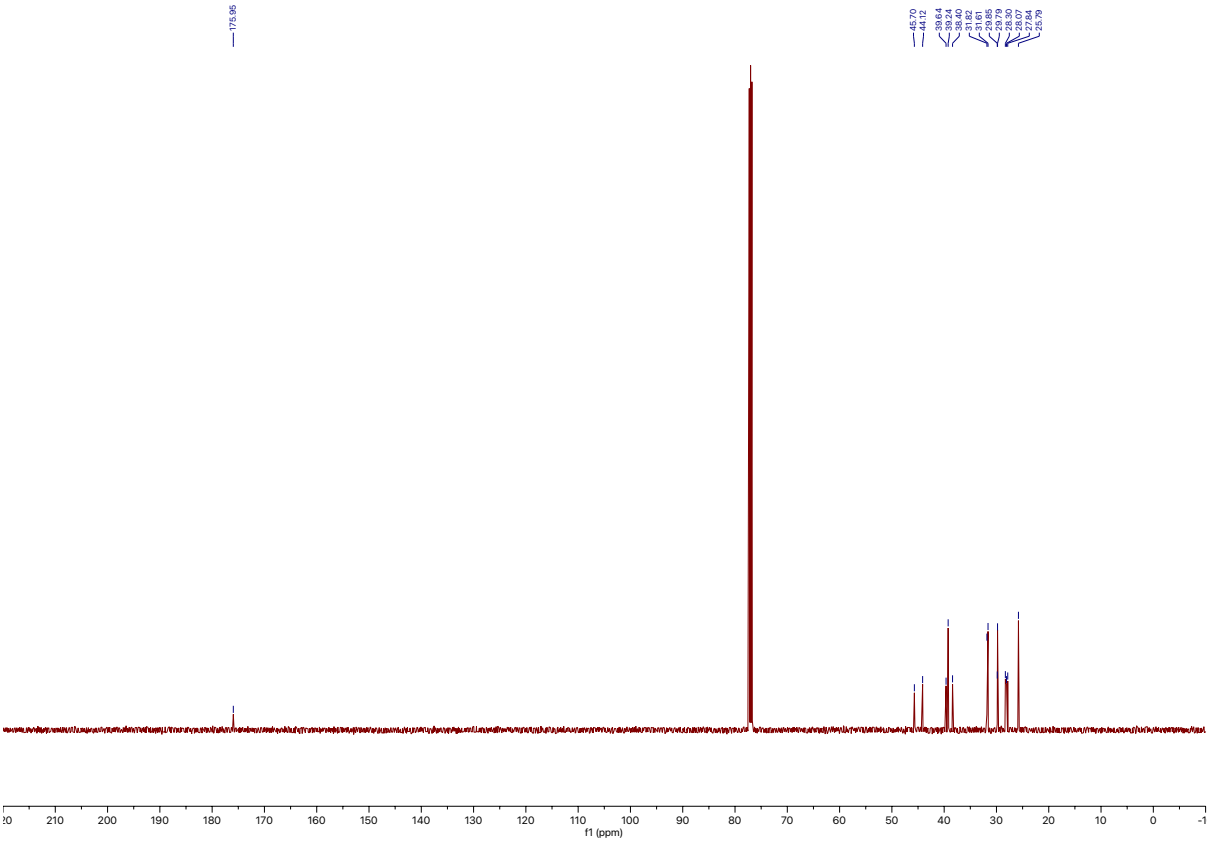

H
N
O
0.86
2.00
2.02
5.49
12.52
7.78
5.47
2.62
f1 (ppm)

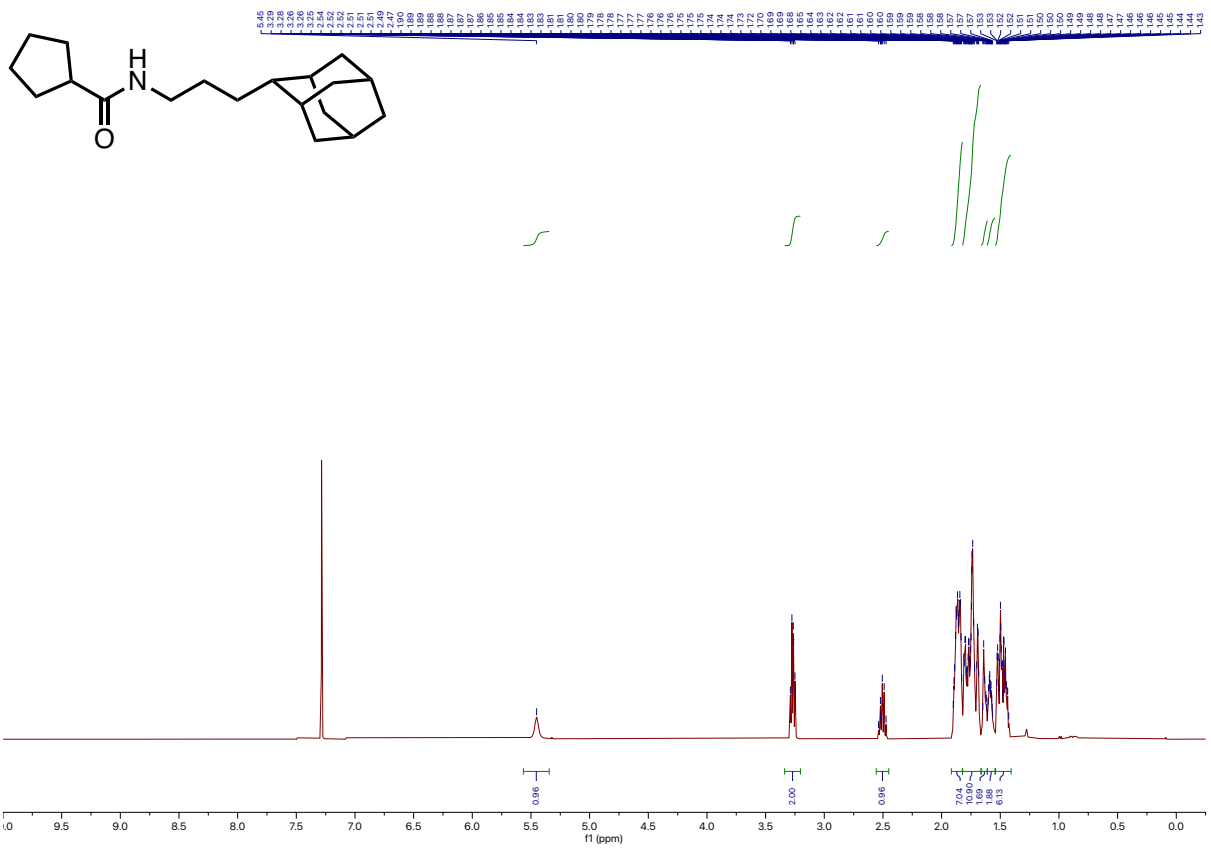

173.29
44.14
39.93
39.24
38.40
37.37
34.45
33.10
31.83
31.61
29.86
28.30
28.08
26.62
26.56
26.24
f1 (ppm)

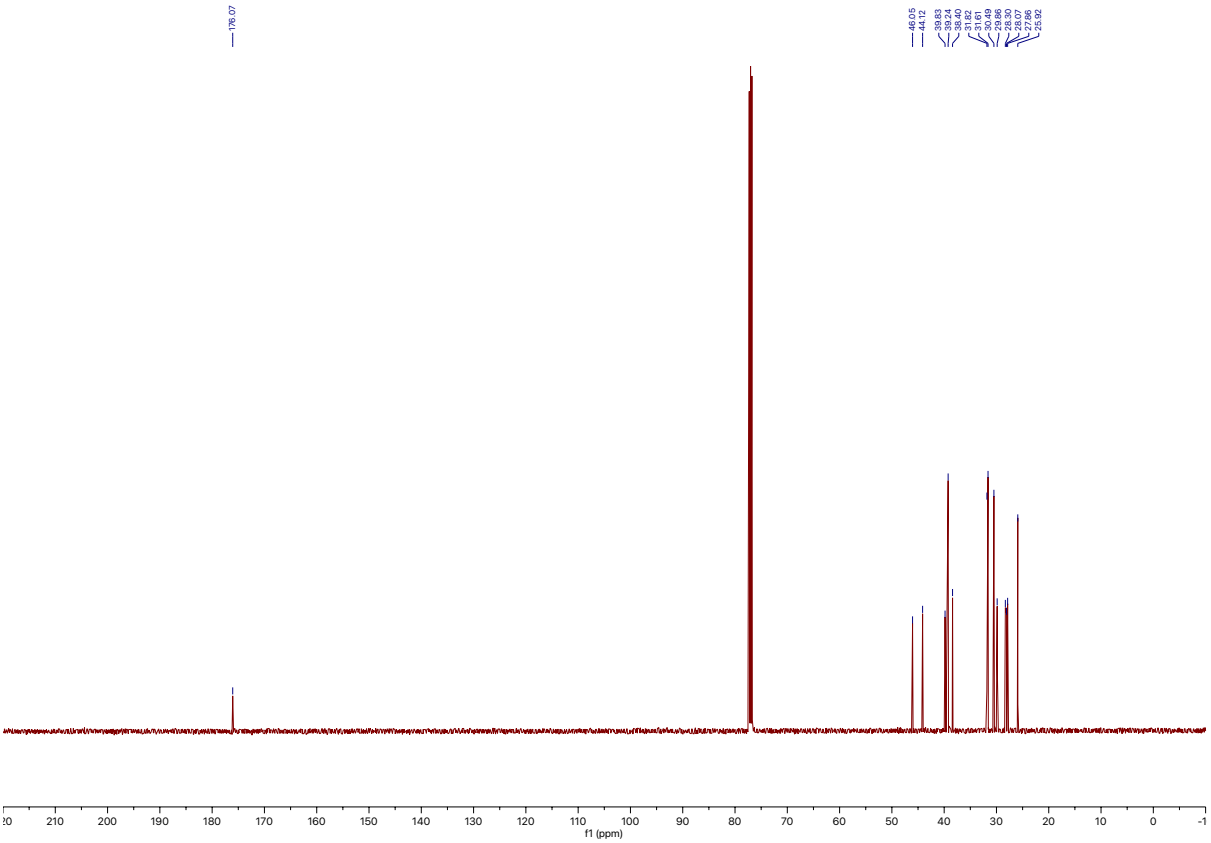

f1 (ppm)

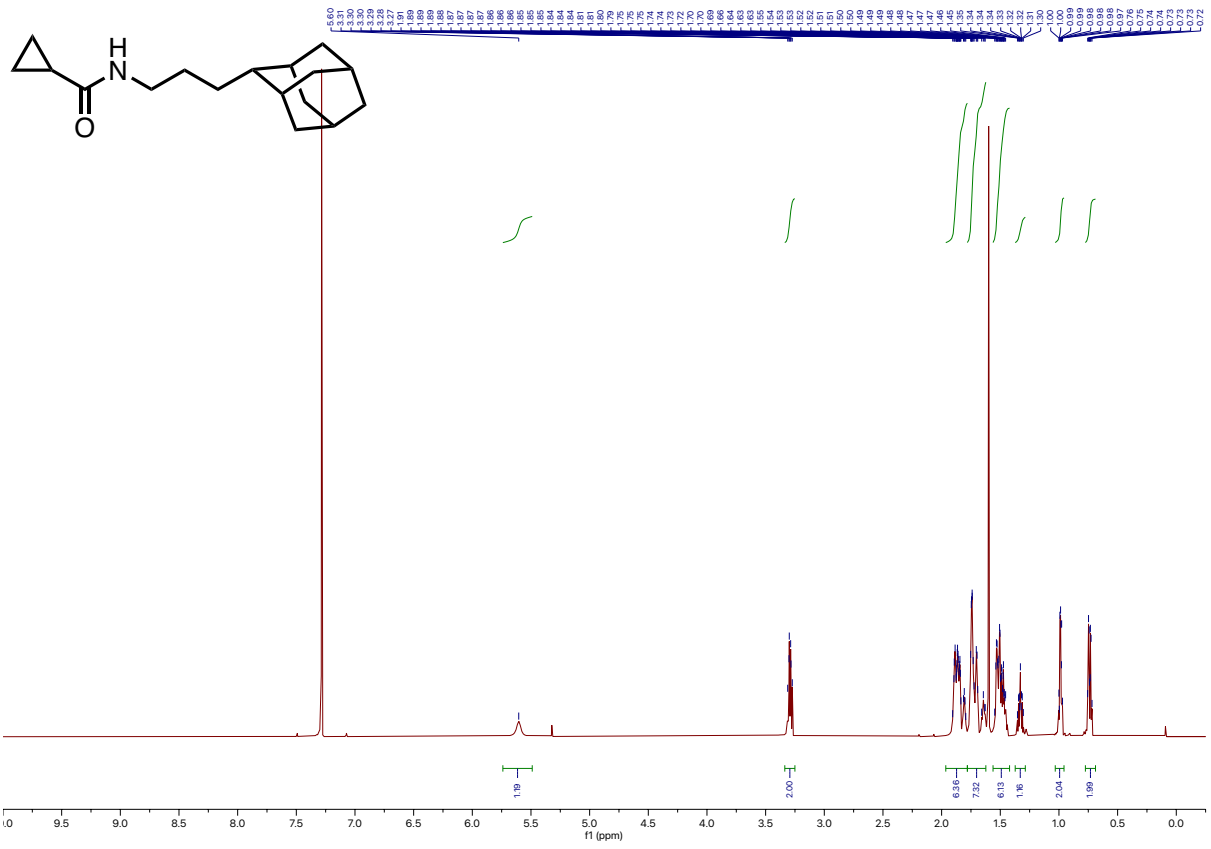

f1 (ppm)

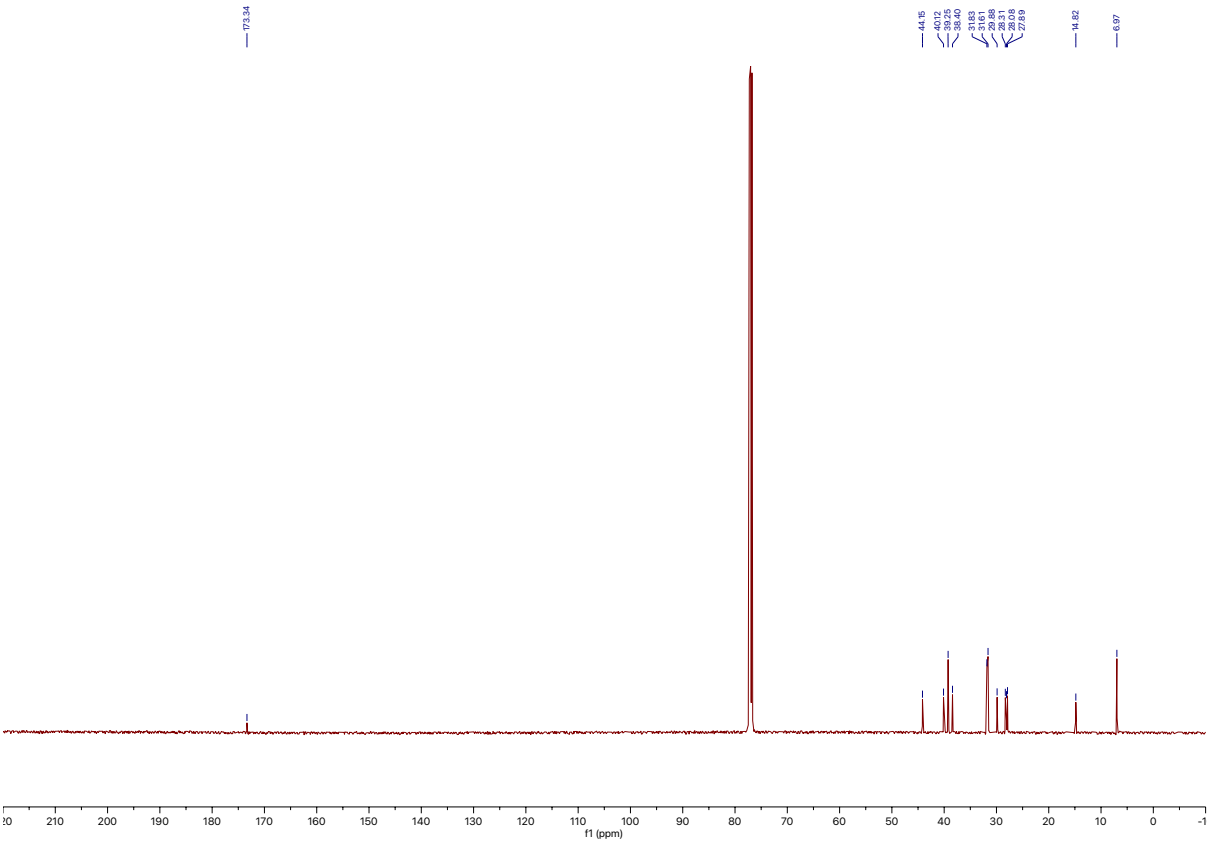

H
N
O
1.00
2.00
1.01
10.05
8.31
8.18
3.67
f1 (ppm)

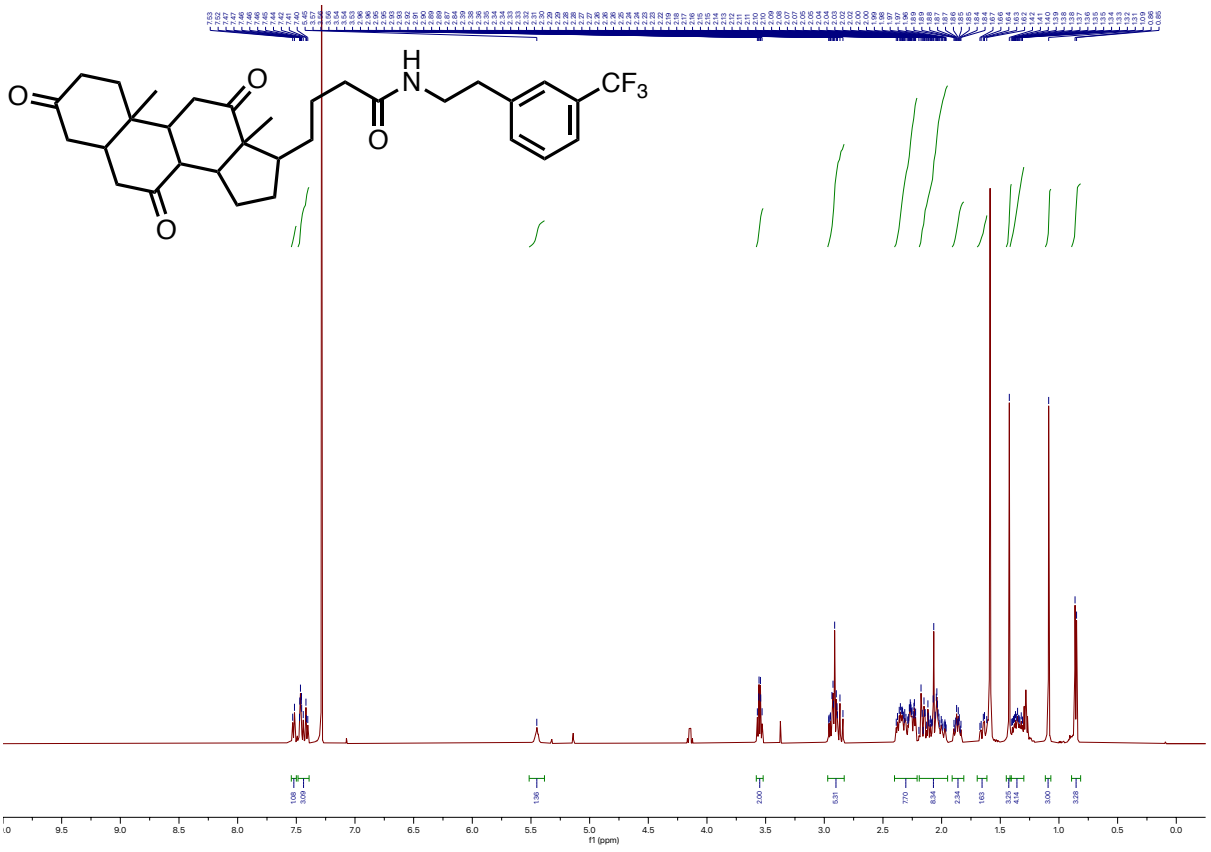

175.95
45.70
44.12
39.64
39.24
38.40
31.82
31.61
29.95
29.75
28.30
28.07
27.84
25.79
f1 (ppm)

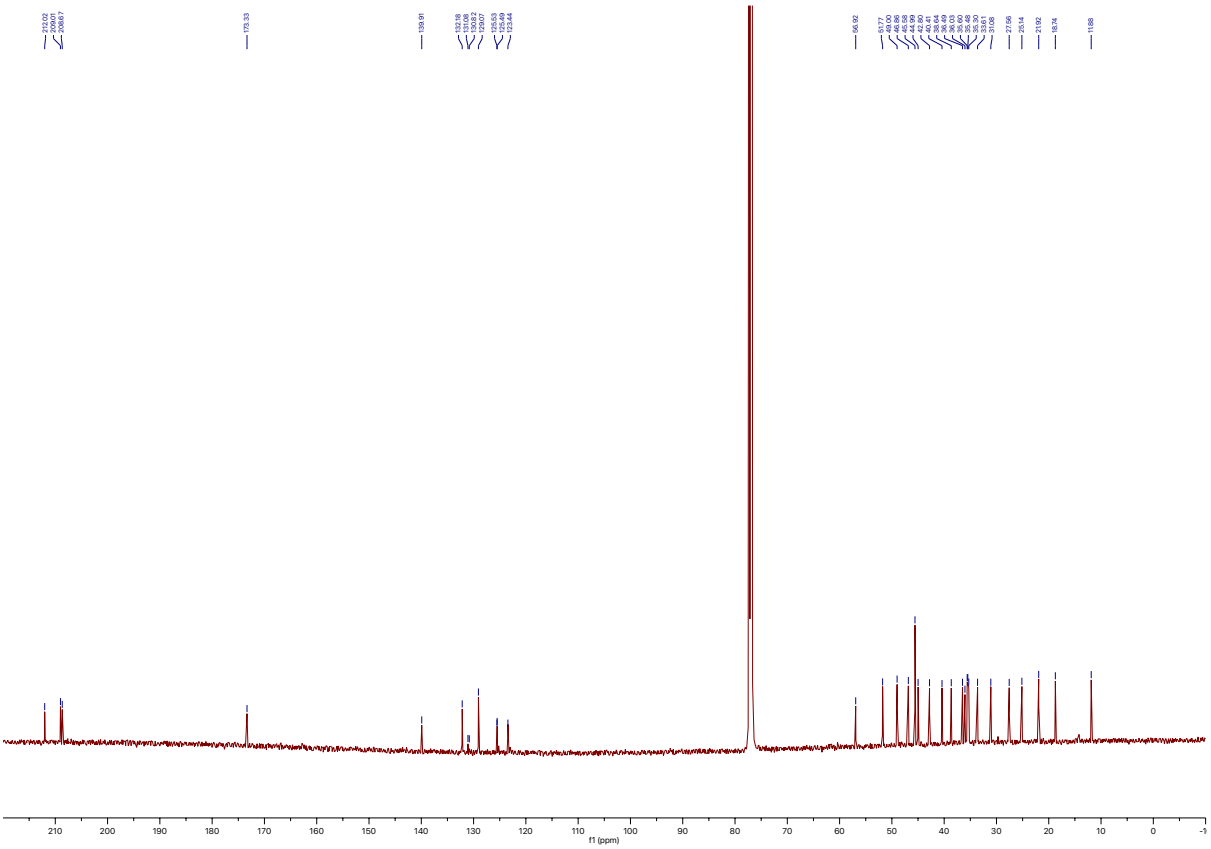

H
N
O
0.96
2.00
0.96
7.04
10.90
1.69
1.88
6.15
f1 (ppm)


176.07
46.05
44.12
39.83
39.24
38.40
31.82
31.61
30.49
29.98
28.30
28.07
26.96
25.92
f1 (ppm)


H
N
O
f1 (ppm)


173.34
44.15
40.12
39.25
38.40
31.83
31.61
29.88
29.71
28.01
27.89
14.82
6.97
f1 (ppm)


O
O
O
O
H
N
CF3
f1 (ppm)


f1 (ppm)