

Supporting Information

Direct observation and characterisation of 3-azido-2*H*-azirines: postulated, but highly elusive intermediates

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[1] General Information

IR spectra were measured on a FT-IR Spectrometer *IFS 28* from BRUKER or on *Nicolet iS5* from THERMO FISCHER SCIENTIFIC. Spectra were measured in suitable organic solvents and are reported in cm^{-1} in decreasing order of wavenumber ($\tilde{\nu}$).

NMR spectra were measured on a *UNITY INOVA 400* FT spectrometer from VARIAN. ^1H NMR spectra were measured at 400 MHz and ^{13}C NMR at 100 MHz. NMR signals were referenced to TMS ($\delta = 0$) or solvent signals and recalculated relative to TMS. DEPT 135 and 2D NMR methods, such as gHSQCAD, etc. were used for assignment of signals, when necessary. Multiplicities of the signals are reported using the standard notations: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br. s = broad singlet, etc.

In situ IR spectra were recorded in real time using a *ReactIR 15* spectrometer (manufactured by METTLER TOLEDO) equipped with a *DS AgX Fiber SiComp* probe.

Mass spectra were obtained from *micrOTOF QII* spectrometer from BRUKER utilizing electrospray-ionisation technique (ESI).

Quantitative elementary analyses were performed on a *Vario Micro Tube* from ELEMENTAR ANALYSENSYSTEME GMBH HANAU.

Thin layer chromatography was performed using *Macherey-Nagel Polygram SIL G/UV₂₅₄* foils.

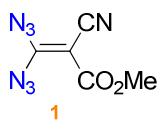
Flash chromatography was performed with Silica gel 60 M (particle-size 0.04–0.063 mm) as the stationary phase from the company *Macherey-Nagel*.

Photolysis experiments were performed utilising a high-pressure Hg-lamp (*TQ 150, Heraeus, Hanau, Germany*).

NOTE: Compounds **1**, **4**, **11** and **12** should be considered highly explosive, and effective safety measures, such as utilisation of blast-shield, thick hand-gloves, etc., must be taken. Special precautions should be taken during the removal of solvents to obtain these compounds in pure state. We highly recommend the use of only dilute solutions, in preferably high boiling solvents.

[2] Experimental procedures

[2a] Synthesis of diazide **1**:

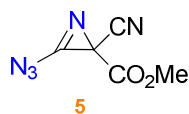


Diazide **1** was synthesised utilising a literature known procedure.^[1] Compound **1** was dissolved in dichloromethane to avoid any untoward incident which is highly possible when handling it in pure state. Generally, 1 mL of this dichloromethane solution had 30 mg of diazide **1** dissolved in it. This diazide was found to be stable even when the above solution was kept in refrigerator ($-23\text{ }^{\circ}\text{C}$) for 15 days. The NMR spectra were in accordance with those published in literature.

$^1\text{H NMR}$ (400 MHz, CDCl_3): $\delta = 3.84$ (s, CH_3).

$^{13}\text{C NMR}$ (100 MHz, CDCl_3): $\delta = 52.88$ (q, CH_3), 80.80 (s, $\text{C}(\text{CN})\text{CO}_2\text{CH}_3$), 113.31 (s, CN), 159.51 (s, $\text{C}(\text{N}_3)_2$), 162.17 (s, CO_2CH_3). Assignment for CO_2Me was confirmed by CIGAR.

[2b] Synthesis of 2H-azirine **5** via photolysis of diazide **1**:

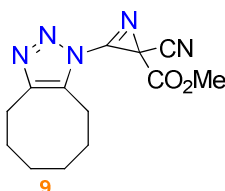


A solution of the diazide **1** (30 mg, 0.18 mmol) in CDCl_3 (0.75 mL) was photolysed, in a normal glass NMR tube, utilising a high-pressure Hg-lamp ($\lambda > 320\text{ nm}$) at $-60\text{ }^{\circ}\text{C}$ for 1 h, and subsequently, NMR measurement at the same temperature indicated the complete consumption of diazide **1** and the formation of azirine **5** in 78% yield ($^1\text{H NMR}$).

$^1\text{H NMR}$ (400 MHz, CDCl_3): $\delta = 3.92$ (s, CH_3).

$^{13}\text{C NMR}$ (100 MHz, CDCl_3): $\delta = 32.78$ (s, $\text{C}(\text{CN})\text{CO}_2\text{CH}_3$), 54.94 (q, CH_3), 114.46 (s, CN), 150.12 (s, CN_3), 164.32 (s, CO_2CH_3). Assignment for CO_2Me was confirmed by CIGAR.

[2c] Synthesis of cycloaddition product **9**:



A solution of diazide **1** (30 mg, 0.18 mmol) in CDCl_3 (0.75 mL) was photolysed, utilising the procedure mentioned in 2b, at $-60\text{ }^{\circ}\text{C}$, and subsequently, the probe was analysed by low-temperature NMR spectroscopy for the complete formation of azirine **5**. Subsequently, cyclooctyne (4 μL , mmol) was added at $-60\text{ }^{\circ}\text{C}$ and the formation of the trapping product **9** could also be seen in the $^1\text{H NMR}$

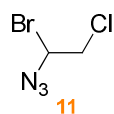
spectrum. Then, the NMR probe was warmed to $-20\text{ }^{\circ}\text{C}$, and more cyclooctyne (4 μL , mmol) was added. At last, the probe was further warmed to $-10\text{ }^{\circ}\text{C}$, and an additional amount of cyclooctyne (12 μL , mmol) was added. This resulted in the complete disappearance of the signals of azirine **5**, and only the signals of 1*H*-1,2,3-triazole **9** could be observed. All together 20 μL of cyclooctyne was added, in a time span of 45 min, to the NMR probe to obtain complete reaction. This solution of cycloaddition product **9** was then warmed to RT, and cyclooctyne as well as CDCl_3 were removed under high-vacuum, thereby, yielding compound **9**, as a straw coloured oil in 57% yield. Triazole **9** was found not be very stable at RT and decomposition can be seen in the ^1H NMR spectrum, which was measured at RT.

^1H NMR (400 MHz, CDCl_3): δ = 1.62 (m, 4H, 2 x CH_2), 1.85 (m, 2H, CH_2), 2.00 (m, 2H, CH_2), 3.05 (m, 2H, CH_2), 3.17 (m, 2H, CH_2), 3.94 (s, 3H, CH_3).

^{13}C NMR (100 MHz, CDCl_3): δ = 21.95 (t, CH_2), 24.08 (t, CH_2), 24.30 (t, CH_2), 25.02 (t, CH_2), 25.89 (t, CH_2), 27.06 (t, CH_2), 30.11 (s, $\text{C}(\text{CN})\text{CO}_2\text{CH}_3$), 54.73 (q, CH_3), 113.91 (s, CN), 137.74 (s, C-9*a*), 146.35 (s, C-3*a*), 147.49 (s, NCN), 163.64 (s, CO_2CH_3).

HR-MS (ESI): m/z calcd. for $\text{C}_{26}\text{H}_{29}\text{N}_{10}\text{Na}_2\text{O}_4$ [$2\text{M} + 2\text{Na} + \text{H}$] $^+$ 655.3420; found: 655.3459; $\text{C}_{26}\text{H}_{30}\text{N}_{10}\text{Na}_2\text{O}_4$ [$2\text{M} + 2\text{Na} + 2\text{H}$] $^+$ 656.3498; found: 656.3480.

[2d] Synthesis of 1-azido-1-bromo-2-chloroethane (**11**):



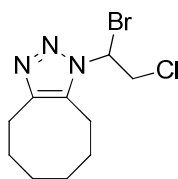
Freshly distilled chloroacetaldehyde (0.33 mL, 0.37 g, 5 mmol) was added dropwise to a solution of $\text{HN}_3/\text{CHCl}_3$ (10 mmol in 5 mL), maintained at $-5\text{ }^{\circ}\text{C}$. After complete addition, the reaction mixture was allowed to warm to RT and stirred for 2 h. Subsequently, the reaction mixture was cooled to $-50\text{ }^{\circ}\text{C}$, and all the volatiles were recondensed at ca. 0.005 mbar. The residue so obtained was α -azido alcohol **10**,^[11] and it was utilised as a permanently cooled substance in the next step.

Compound **10**, so obtained above, was dissolved in cold ($-50\text{ }^{\circ}\text{C}$) CHCl_3 (3 mL), and to this solution was added PBr_3 (1.41 mL, 4.06 g, 15 mmol). This reaction mixture was stirred at this temperature for 1 h, and further 12 h at RT, and at the end, a 1:1 pentane/diethyl ether mixture (25 mL) was added. The resulting solution was washed first with distilled water (25 mL) and subsequently with brine (25 mL). The organic phase was dried over MgSO_4 , and the solvent was removed *in vacuo* leading to a transparent liquid **11** (48%; based on chloroacetaldehyde).

^1H NMR (400 MHz, CDCl_3): δ = 3.81 (dd, $^2J = 11.7\text{ Hz}$, $^3J = 9.0\text{ Hz}$, 1H, 2-*H_a*), 3.92 (dd, $^2J = 11.7\text{ Hz}$, $^3J = 3.6\text{ Hz}$, 1H, 2-*H_b*), 5.70 (dd, $^3J = 9.0\text{ Hz}$, $^3J = 3.6\text{ Hz}$, 1H, CH).

^{13}C NMR (100 MHz, CDCl_3): δ = 46.60 (t, CH_2), 66.80 (d, CH).

[2e] Synthesis of 1H-1,2,3-triazole **13**: trapping reaction with cyclooctyne



13

To a solution of compound **11** (0.92 g, 5.0 mmol) in distilled *n*-hexane (5 mL), maintained at $-20\text{ }^{\circ}\text{C}$, was added, dropwise, a solution of cyclooctyne (0.87 g, 7 mmol, 1.4 eq) in distilled *n*-hexane (5 mL), and the reaction mixture was stirred for 1 h at this temperature. Subsequently, the solvent was removed *in vacuo*, and the crude product was purified by flash chromatography over silica-gel ($\text{CH}_2\text{Cl}_2/\text{Et}_2\text{O}$ 10:1). 1H-1,2,3-triazole **13** was obtained as a white solid in 93% yield.

mp: 79–81 $^{\circ}\text{C}$

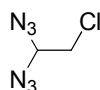
^1H NMR (400 MHz, CDCl_3): δ = 1.37–1.50 (m, 4H, CH_2), 1.68–1.78 (m, 2H, CH_2), 1.78–1.95 (m, 2H, CH_2), 2.75 (m, 2H, CH_2), 2.91 (t, 3J = 6.4 Hz, 2H, CH_2), 4.28 (dd, 2J = 11.6 Hz, 3J = 4.4 Hz, 1H, CH_2Cl), 4.88 (dd, 2J = 11.6 Hz, 3J = 10.4 Hz, 1H, CH_2Cl), 6.21 (dd, 3J = 10.4 Hz, 4.4 Hz, 1H, CH).

^{13}C NMR (100 MHz, CDCl_3): δ = 21.44 (t, CH_2), 24.43 (t, CH_2), 24.57 (t, CH_2), 25.90 (t, CH_2), 25.96 (t, CH_2), 28.20 (t, CH_2), 45.13 (t, CH_2), 54.43 (d, CH), 134.07 (s, C-9a), 145.53 (s, C-3a).

Anal. calcd. for $\text{C}_{10}\text{H}_{15}\text{BrClN}_3$ (292.60): C, 41.05; H, 5.17; N, 14.36; found: C, 41.25; H, 5.21; N, 14.55.

HR-MS (ESI): m/z calcd. for $\text{C}_{10}\text{H}_{16}^{71}\text{Br}^{35}\text{ClN}_3$ $[\text{M} + \text{H}]^+$ 294.0189; found: 294.0188.

[2f] Synthesis of 1,1-diazido-2-chloroethane (**12**):



12

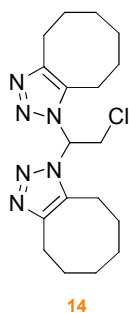
To a solution of 1-azido-1-bromo-2-chloroethane (**11**) (802 mg, 4.35 mmol) in anhydrous CHCl_3 (5 mL) was added, at $0\text{ }^{\circ}\text{C}$, a solution of tetramethylguanidinium azide (TMGA; 1.58 g, 10 mmol, 2.3 eq) in 5 mL anhydrous CHCl_3 . The mixture was allowed to warm to RT and stirred for 12 h. Subsequently, the solvent was removed *in vacuo*, and the crude product was carefully purified by flash chromatography (SiO_2 ; Et_2O), yielding diazide **12** as a transparent liquid in 77% yield.

^1H NMR (400 MHz, CDCl_3): δ = 3.58 (d, 3J = 6.0 Hz, 2H, CH_2), 4.89 (t, 3J = 6.0 Hz, 1H, CH).

^{13}C NMR (100 MHz, CDCl_3): δ = 44.71 (t, CH_2), 76.61 (d, CH).

The characterisation of diazide **12** was limited to NMR spectroscopy owing to the highly explosive nature of this molecule. It is advised to utilise this molecule only in dilute solutions; pure **12** can lead to heavy explosions.

[2g] Synthesis of *bis*-1*H*-1,2,3-triazole **14**: Trapping diazide **4** with cyclooctyne



Compound **12** (72 mg, 0.49 mmol) was dissolved in *n*-hexane (10 mL), and cooled to $-20\text{ }^{\circ}\text{C}$. To this was added, dropwise, cyclooctyne (270 mg, 0.31 mL, 2.5 mmol) as a solution in 5 mL *n*-hexane, and the reaction mixture was stirred for 2 h. Subsequently, all the volatiles (solvent and unreacted cyclooctyne) were removed with a high-vacuum pump. The solid so obtained was recrystallised from *n*-hexane to yield **14** as a white solid (96%).

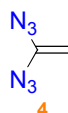
mp: 149–151 $^{\circ}\text{C}$.

^1H NMR (400 MHz, CDCl_3): δ = 1.28–1.42 (m, 8H, CH_2), 1.48–1.57 (m, 4H, CH_2), 1.66–1.75 (m, 4H, CH_2), 2.79–2.89 (m, 8H, CH_2), 4.71 (d, $^3J = 7.5\text{ Hz}$, 2H, CH_2Cl), 7.03 (t, $^3J = 7.5\text{ Hz}$, 1H, CH).

^{13}C NMR (100 MHz, CDCl_3): δ = 21.16 (t, 2 x CH_2), 24.31 (t, 2 x CH_2), 24.85 (t, 2 x CH_2), 25.56 (t, 2 x CH_2), 26.63 (t, 2 x CH_2), 28.22 (t, 2 x CH_2), 41.93 (t, CH_2Cl), 71.17 (d, CH), 134.13 (s, 2 x C), 146.48 (s, 2 x C).

HR-MS (ESI): m/z calcd. for $\text{C}_{18}\text{H}_{28}^{35}\text{ClN}_6$ [$\text{M} + \text{H}$] $^+$ 363.2064; found: 363.2103; $\text{C}_{18}\text{H}_{27}^{35}\text{ClN}_6\text{Na}$ [$\text{M} + \text{Na}$] $^+$ 385.1910; found: 385.1883; $\text{C}_{18}\text{H}_{27}^{35}\text{ClKN}_6$ [$\text{M} + \text{K}$] $^+$ 401.1623; found: 401.1645.

[2h] Synthesis of 1,1-diazidoethene (**4**):



Under nitrogen atmosphere, a solution of 1,1-diazido-2-chloroethane (**12**) (490 mg, 3.35 mmol) in anhydrous Et_2O (25 mL) was cooled to $-20\text{ }^{\circ}\text{C}$, and KO^tBu (790 mg, 7.0 mmol, 2.09 eq) was added very carefully in portions. After, complete addition, the reaction mixture was allowed to warm to $0\text{ }^{\circ}\text{C}$, and stirred for 1 h. Subsequently, the reaction mixture was diluted with anhydrous Et_2O , and filtered, and extracted with more abs. Et_2O . The organic phase was removed *in vacuo* only to an extent wherein small amounts of Et_2O were left, so that compound **4** remained as a solution. Attempts to completely remove the solvent led to violent explosions. A yield of 23% (^1H NMR; based on compound **12**) was obtained; however, diazide **4** always remained in a solution of Et_2O and *tert*-butanol.

^1H NMR (400 MHz, CDCl_3): δ = 4.39 (s, CH_2).

^{13}C NMR (100 MHz, CDCl_3): δ = 85.26 (t, $^1J = 164\text{ Hz}$, CH_2), 139.78 (s, $\text{C}(\text{N}_3)_2$).

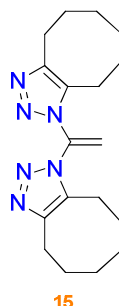
The assignment was further supported by gHSQCAD 2D NMR spectroscopic technique.

IR (CDCl₃; cm⁻¹): $\tilde{\nu}$ = 2977 (C–H), 2120 (N₃; asym.), 1641 (C=C), 1311 (N₃; sym.).

$t_{1/2}$ = 3 h 40 min (40 °C).

Owing to the highly explosive nature of diazide **4**, characterisation was limited to NMR and IR spectroscopic analytical methods. The structure of this diazide was unambiguously confirmed by trapping it with cyclooctyne, as detailed in the next section.

[2i] Synthesis of *bis*-1*H*-1,2,3-triazole **15**: Trapping diazide **4** with cyclooctyne



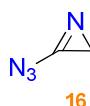
To the above obtained solution of diazide **4** taken in 10 mL distilled *n*-hexane, cooled to –20 °C, was added, dropwise, a solution of cyclooctyne (1.07 mL, 8 mmol, eq) in 5 mL distilled *n*-hexane, and the reaction mixture was stirred for 2 h. Subsequently, the solvent was removed *in vacuo*, and the crude product was purified by flash chromatography over silica-gel (CH₂Cl₂/Et₂O 10:1), to yield **15** as an oil (84%).

¹H NMR (400 MHz, CDCl₃): δ = 1.39–1.41 (m, 8H, CH₂), 1.47–1.53 (m, 4H, CH₂), 1.72–1.77 (m, 4H, CH₂), 2.48 (t, *J* = 5.2 Hz, 4H, CH₂), 2.90 (t, *J* = 5.2 Hz, 4H, CH₂), 5.90 (s, 2H, CH₂).

¹³C NMR (100 MHz, CDCl₃): δ = 21.33 (t, CH₂), 24.33 (t, CH₂), 24.76 (t, CH₂), 25.75 (t, CH₂), 25.91 (t, CH₂), 27.88 (t, CH₂), 114.20 (t, CH₂), 134.24 (s, C), 134.81 (s, C), 145.52 (s, C-3a).

HR-MS (ESI): *m/z* calcd. for C₁₈H₂₇N₆ [M + H]⁺ 327.2292; found: 327.2278; C₁₈H₂₆N₆Na [M + Na]⁺ 349.2111; found: 349.2096; C₁₈H₂₆N₆K [M + K]⁺ 365.1856; found: 365.1840.

[2j] Synthesis of 3-azido-2*H*-azirine (**16**): Photolysis of diazide **4**



The solution of **4**/Et₂O, as obtained in section 2h, was taken in 0.7 mL CDCl₃ in a NMR tube, and this solution was photolysed at –55 °C using a high-pressure Hg-lamp for 30 min. Low-temperature NMR spectroscopy (–55 °C) indicated the formation of 2*H*-azirine **16** in a yield of 34% (¹H NMR; based on diazide **4**).

¹H NMR (400 MHz, CDCl₃): δ = 2.29 (s, CH₂).

^{13}C NMR (100 MHz, CDCl_3): δ = 28.54 (t, CH_2), 162.13 (s, CN_3).

$t_{1/2}$ = 12 min ($-40\text{ }^\circ\text{C}$).

IR (CDCl_3 ; cm^{-1}): $\tilde{\nu}$ = 2148 (N_3), 1756 ($\text{C}=\text{N}$).

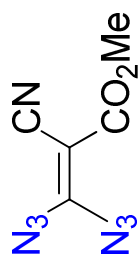
The same reaction was also performed in toluene- d_8 , and similarly, azirine **16** could be identified, but the reaction did not reach completion.

^1H NMR (400 MHz, toluene- d_8): δ = 1.49 (s, CH_2).

^{13}C NMR (100 MHz, toluene- d_8): δ = 27.14 (t, CH_2), 161.25 (s, CN_3).

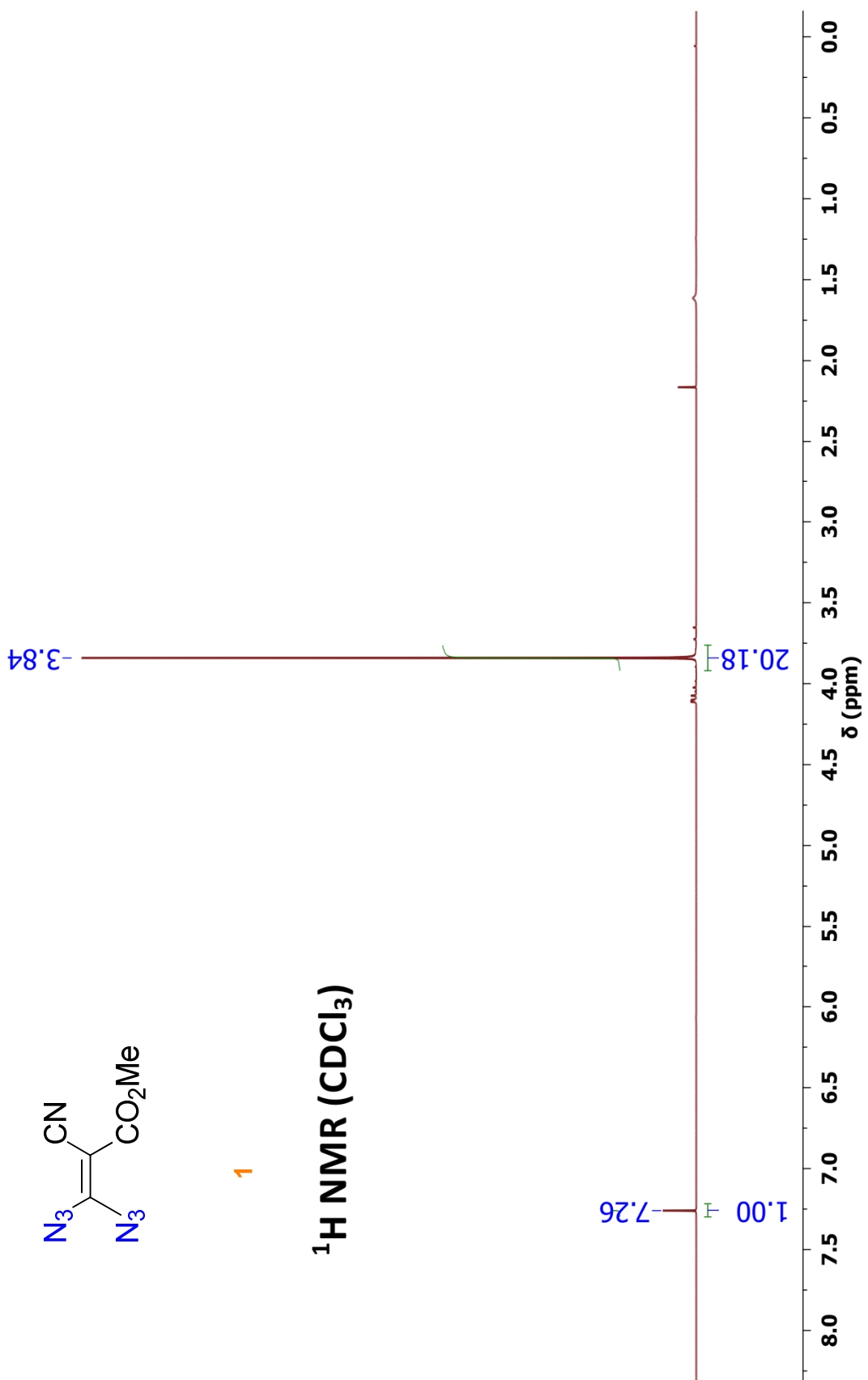
The assignment was further supported by gHSQCAD 2D NMR spectroscopic technique.

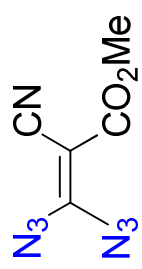
[3] NMR Spectra



1

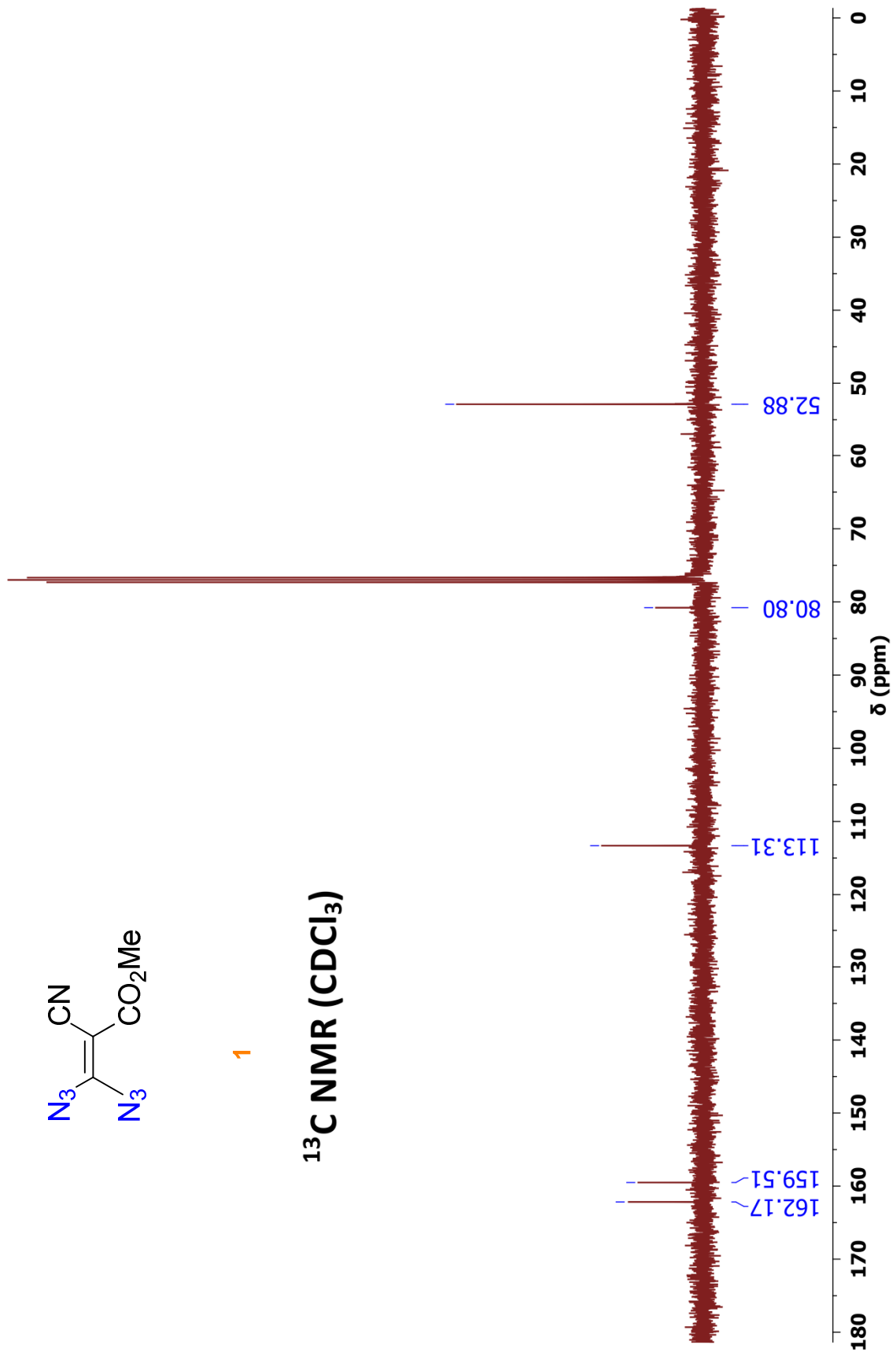
¹H NMR (CDCl₃)

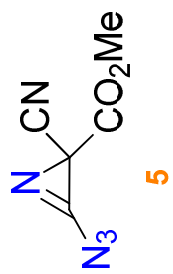




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¹³C NMR (CDCl₃)

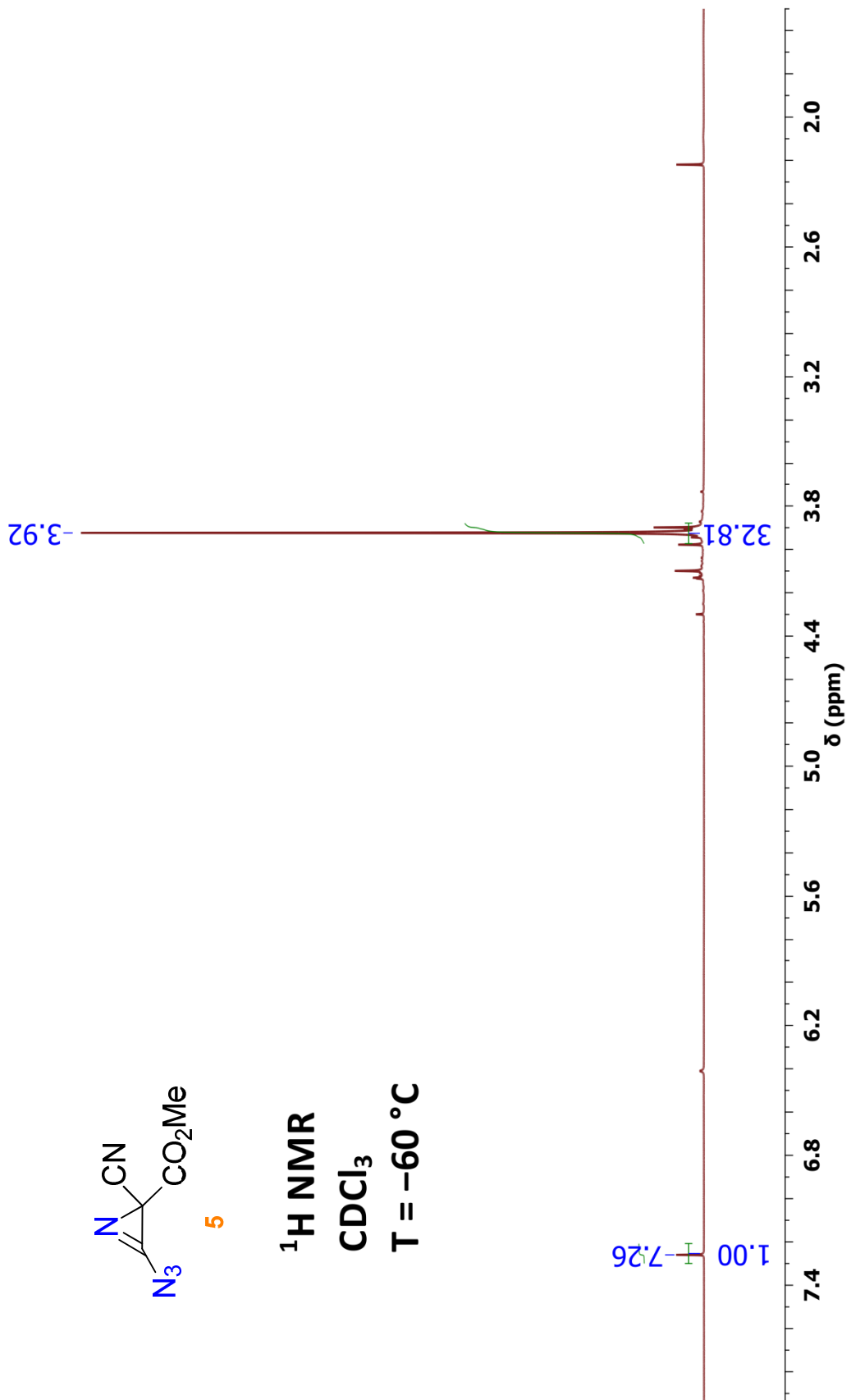


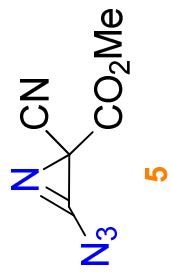


¹H NMR

CDCl₃

T = -60 °C

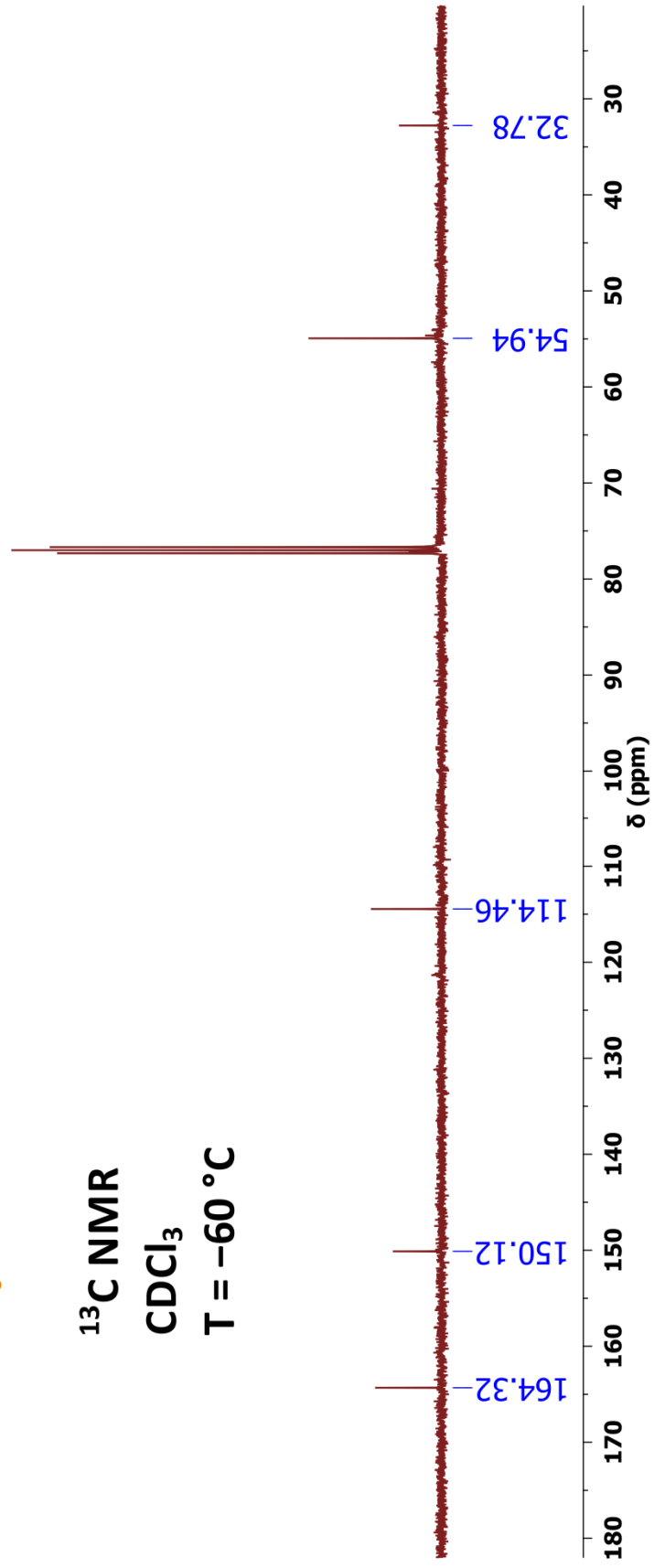


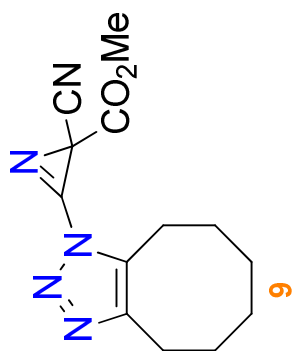


¹³C NMR

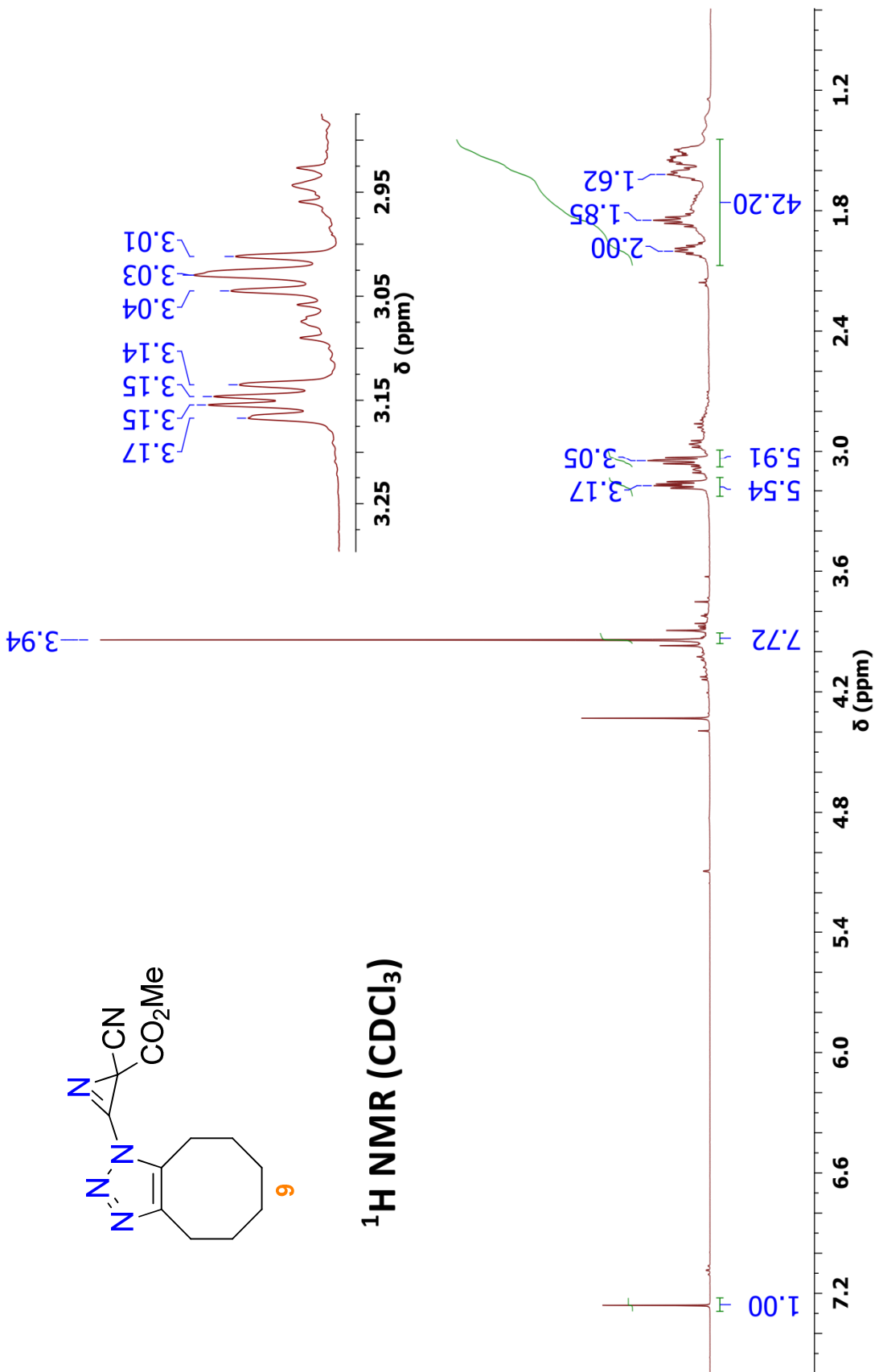
CDCl₃

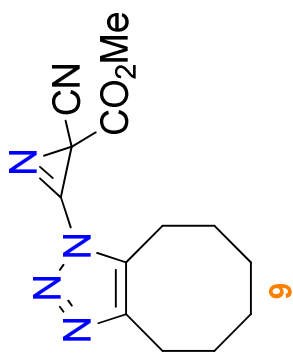
T = -60 °C



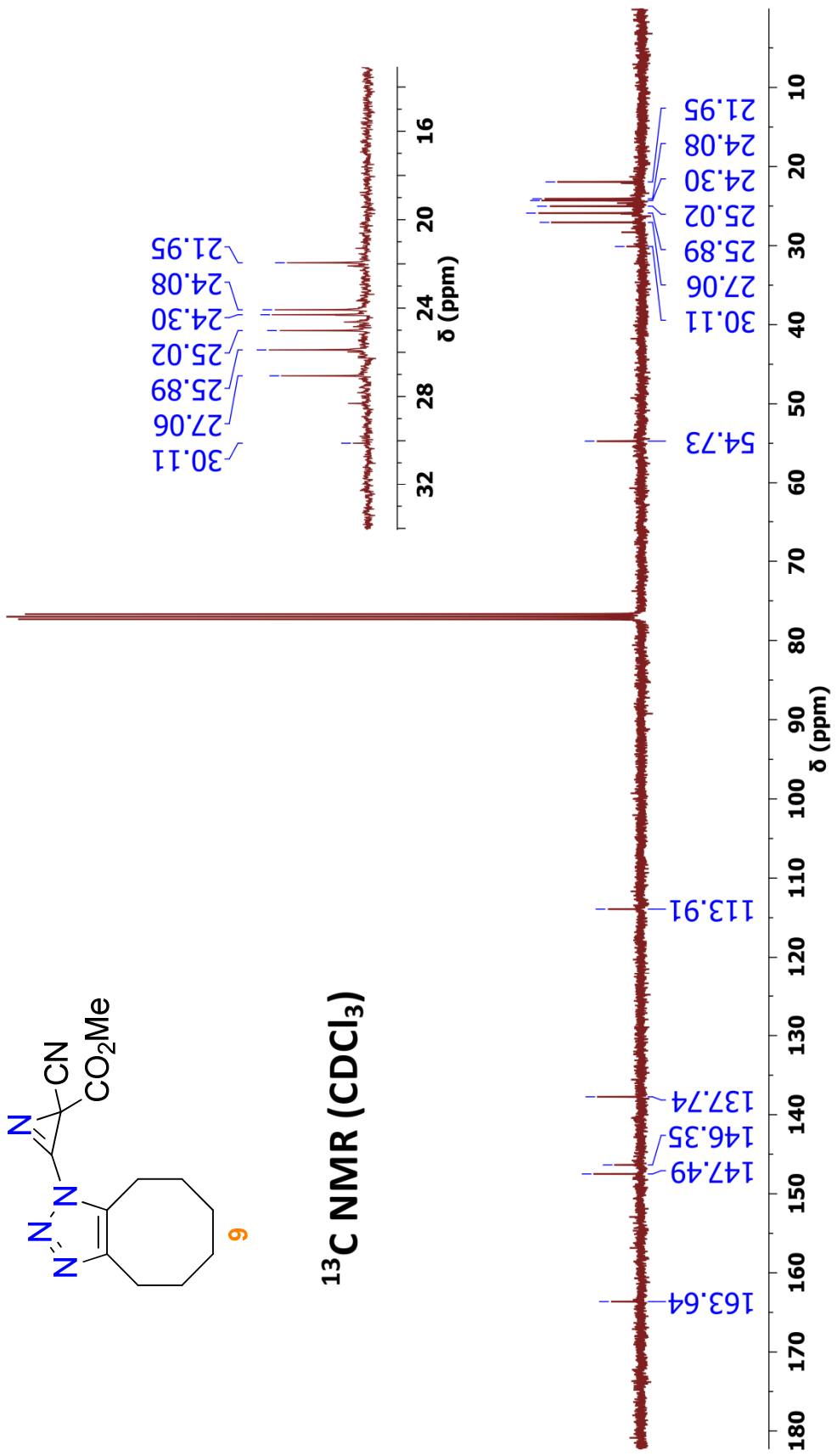


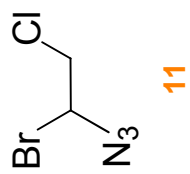
¹H NMR (CDCl₃)



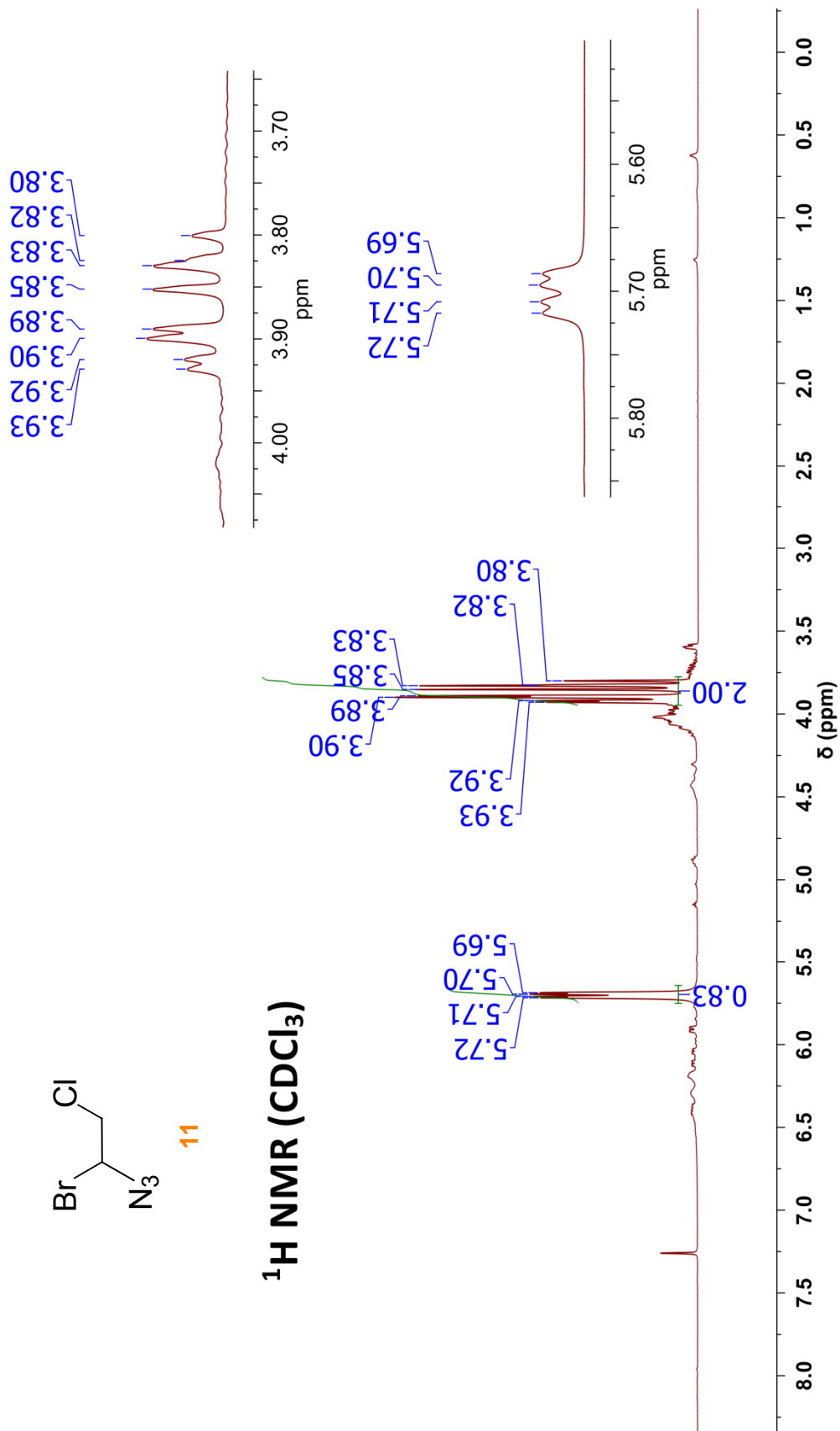


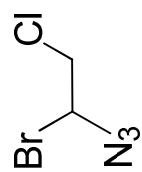
¹³C NMR (CDCl₃)





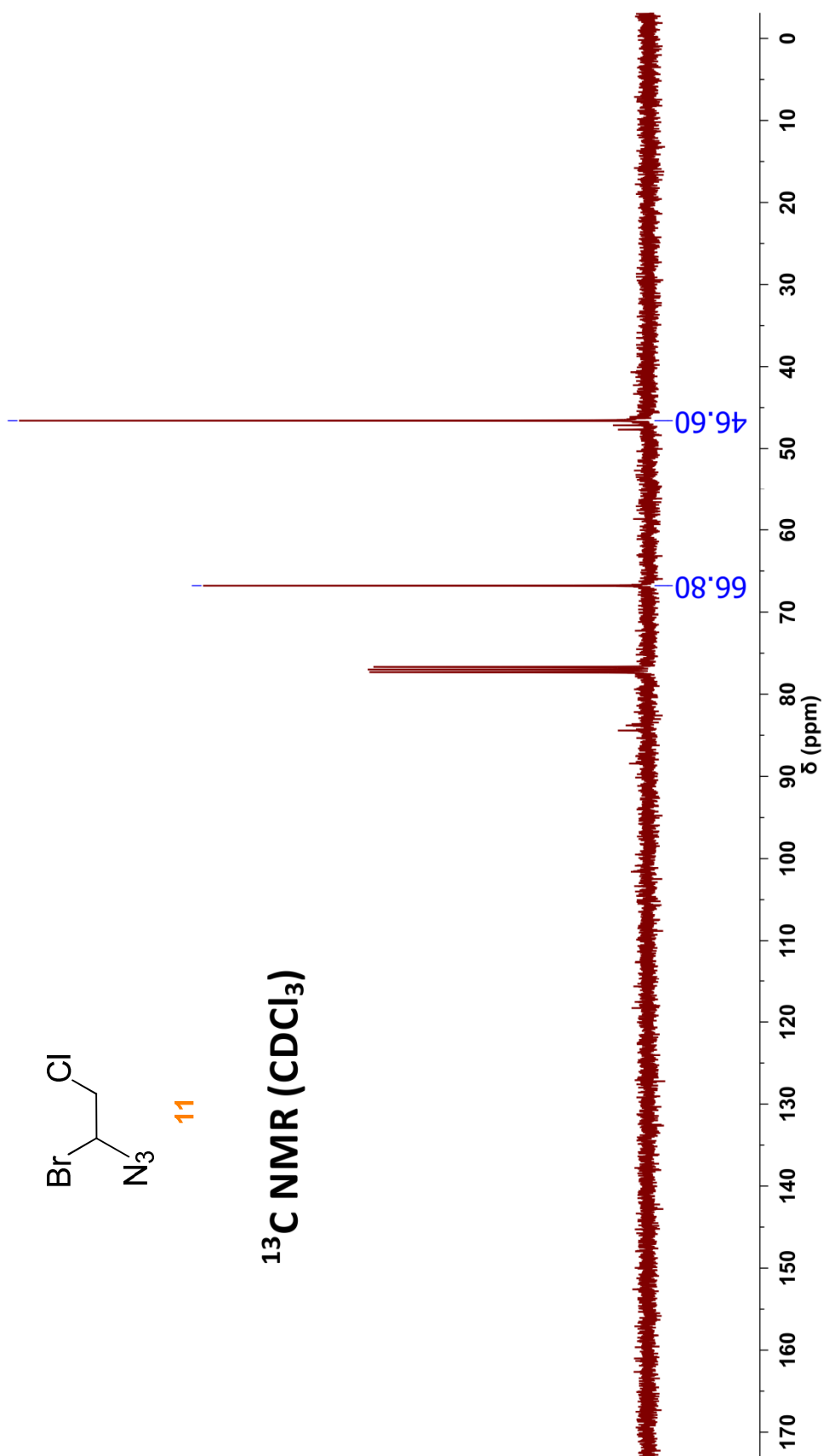
^1H NMR (CDCl_3)

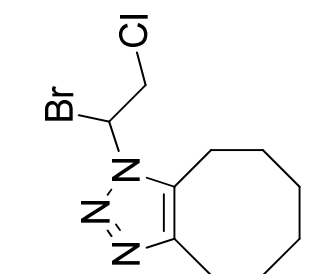




11

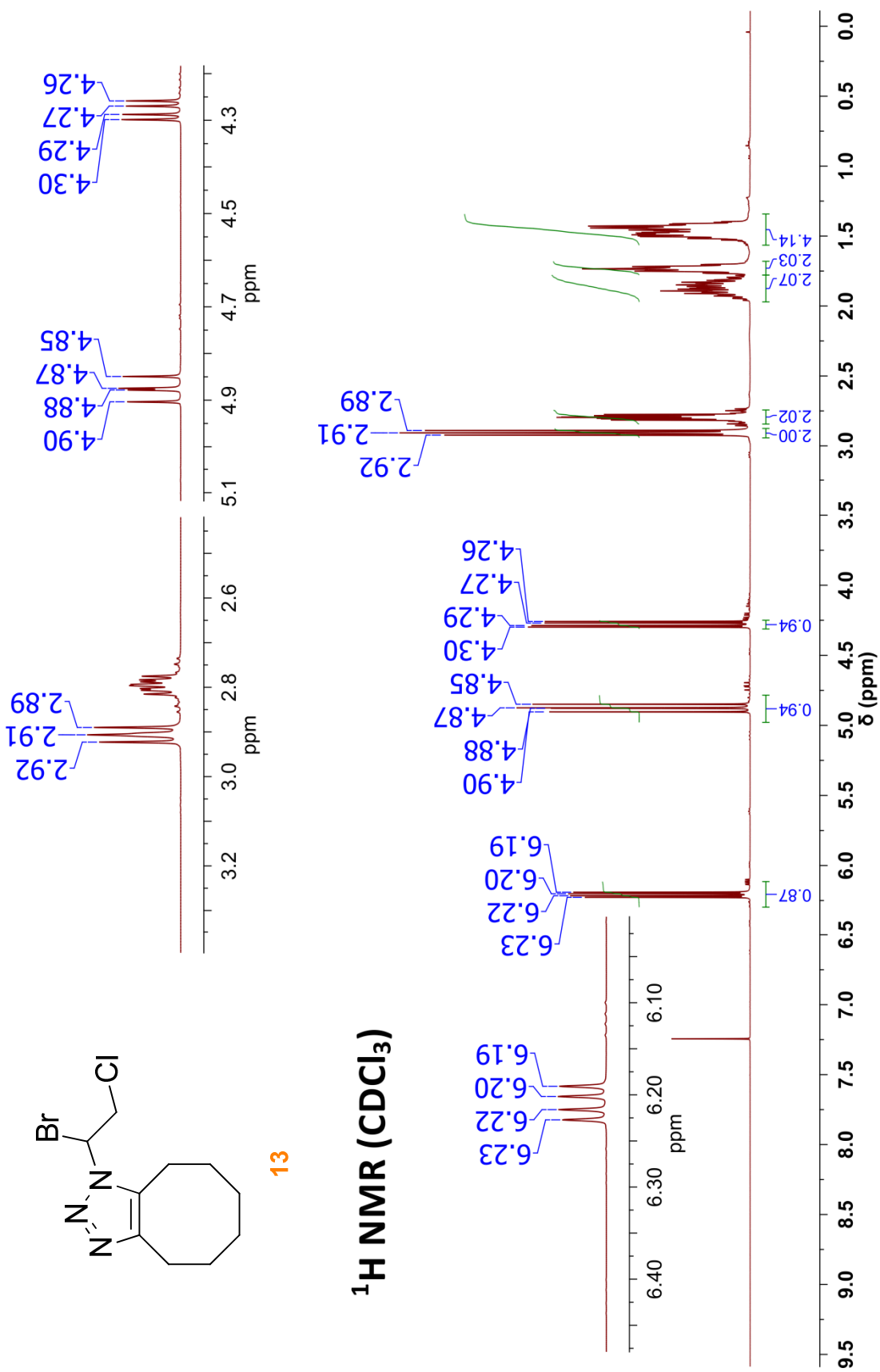
^{13}C NMR (CDCl_3)

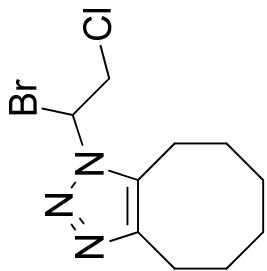




13

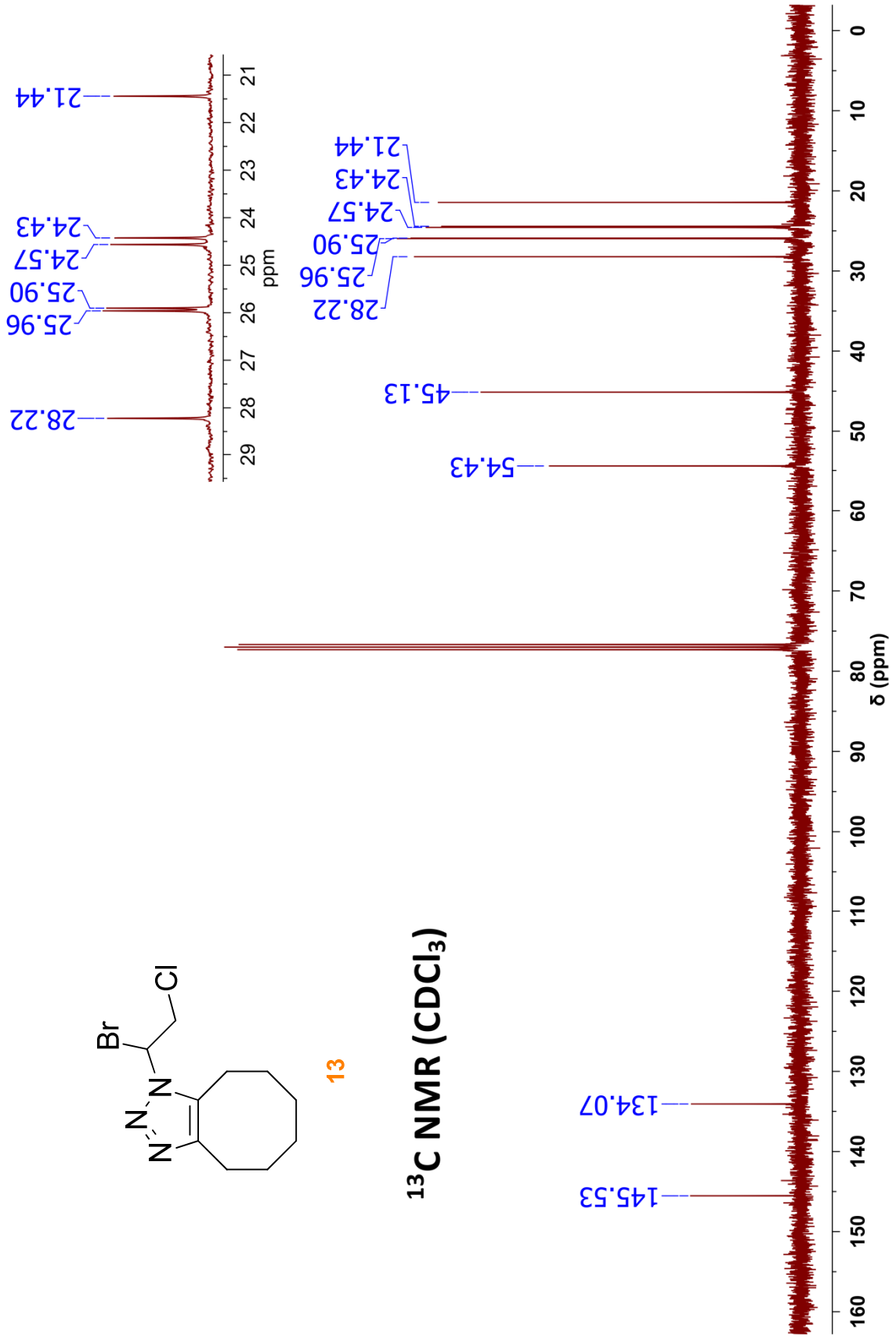
^1H NMR (CDCl_3)

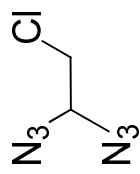




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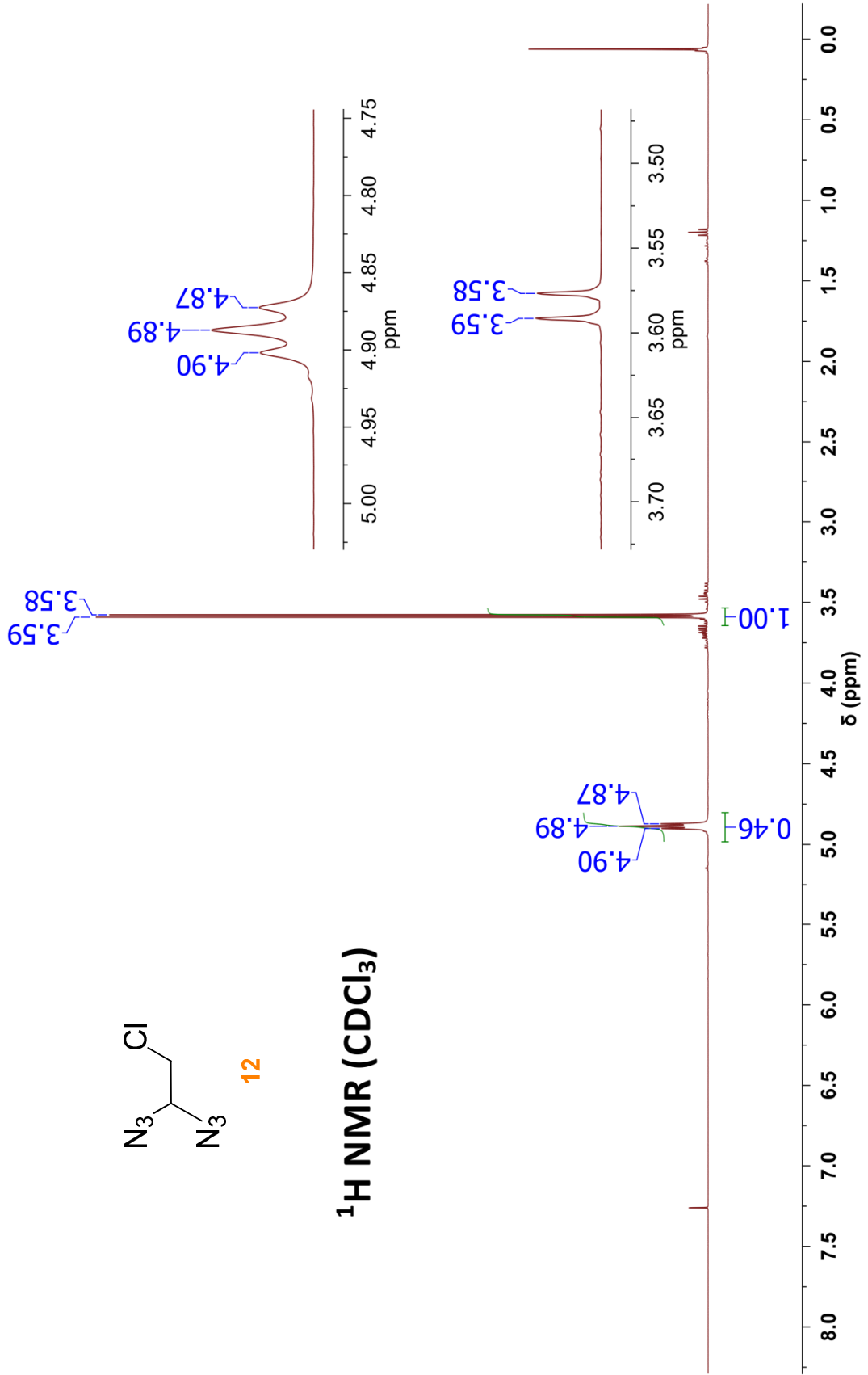
¹³C NMR (CDCl₃)

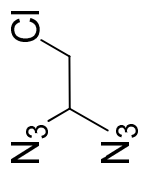




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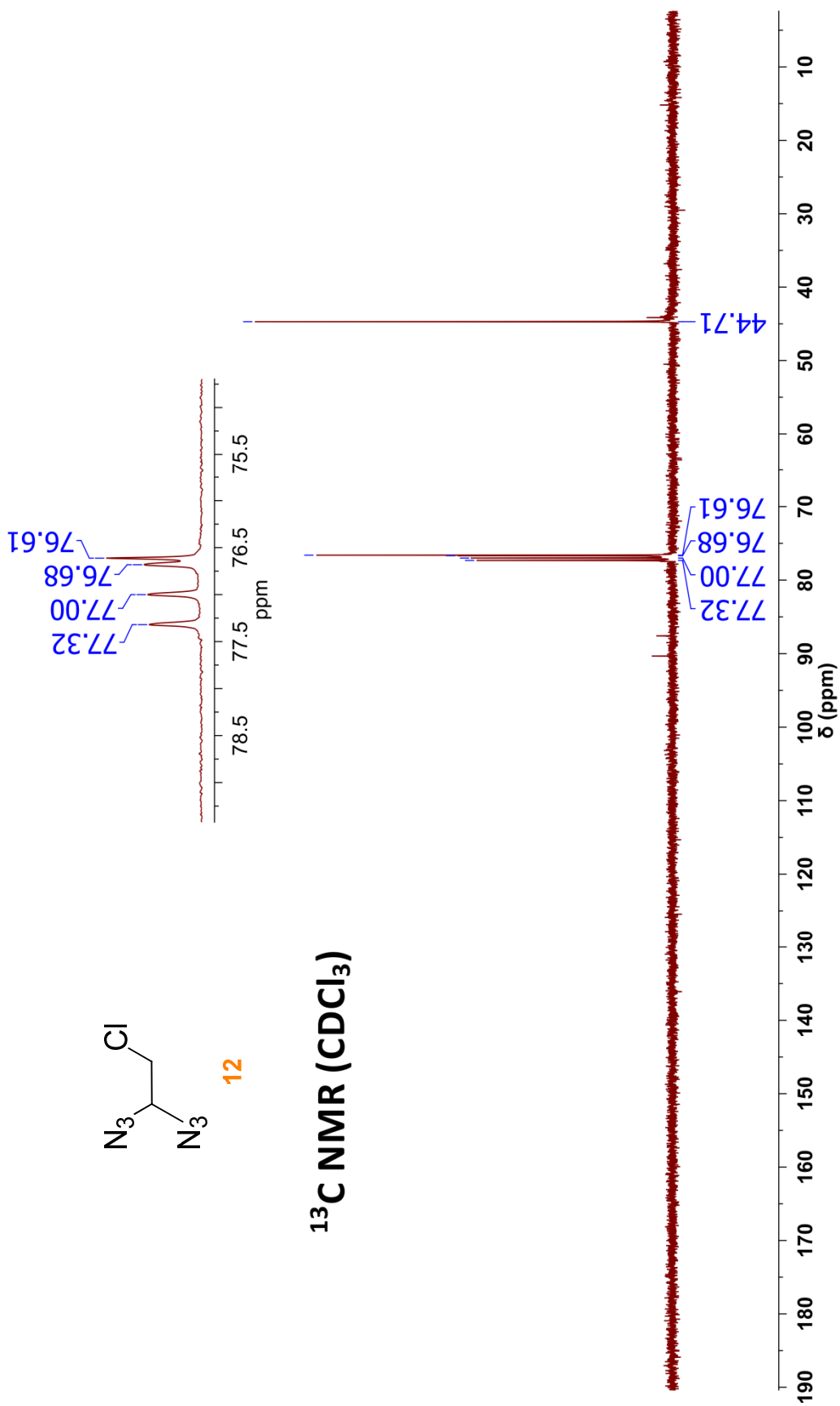
$^1\text{H NMR (CDCl}_3)$

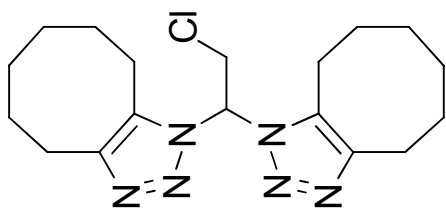




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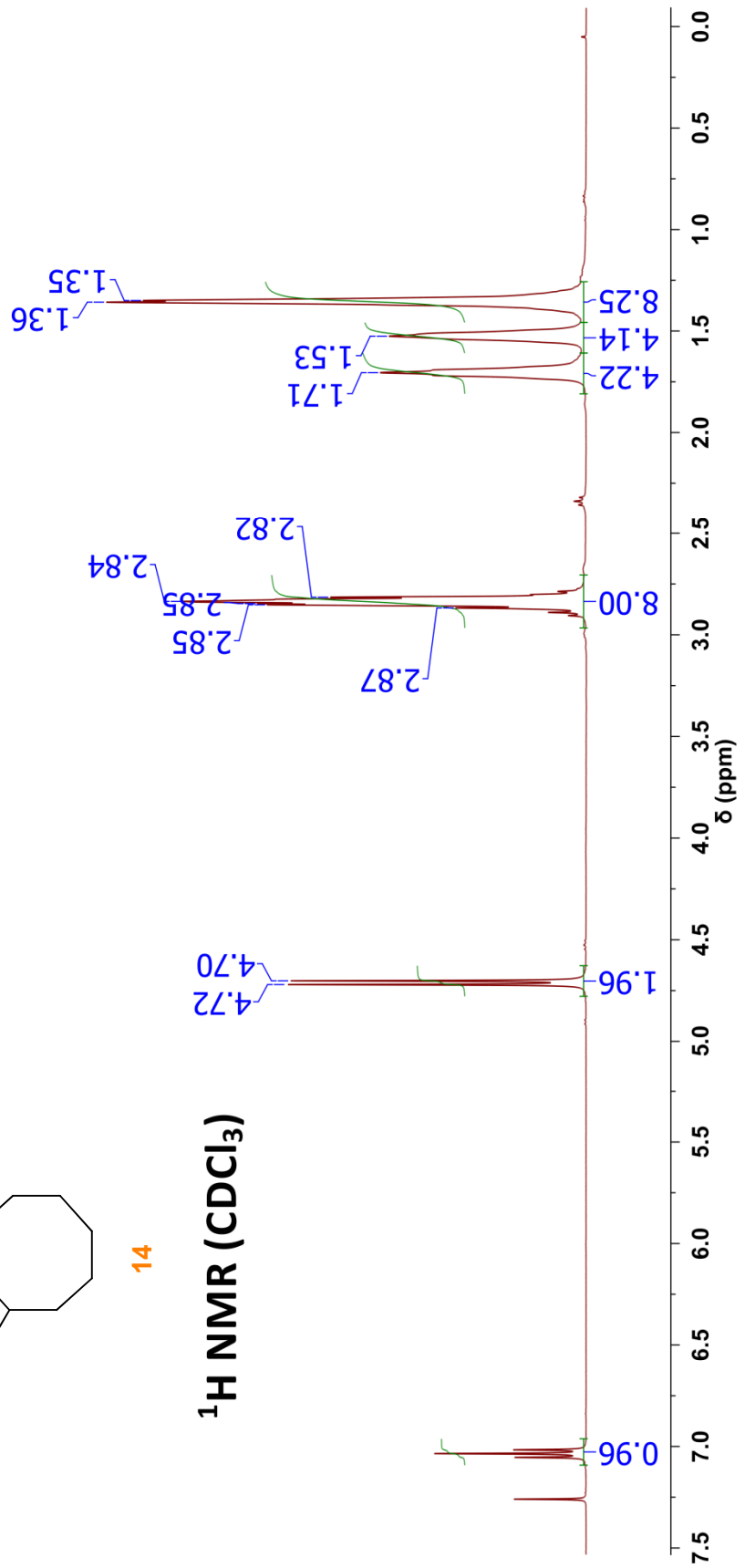
^{13}C NMR (CDCl_3)

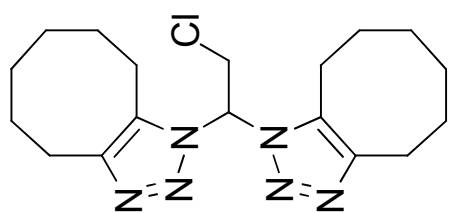




14

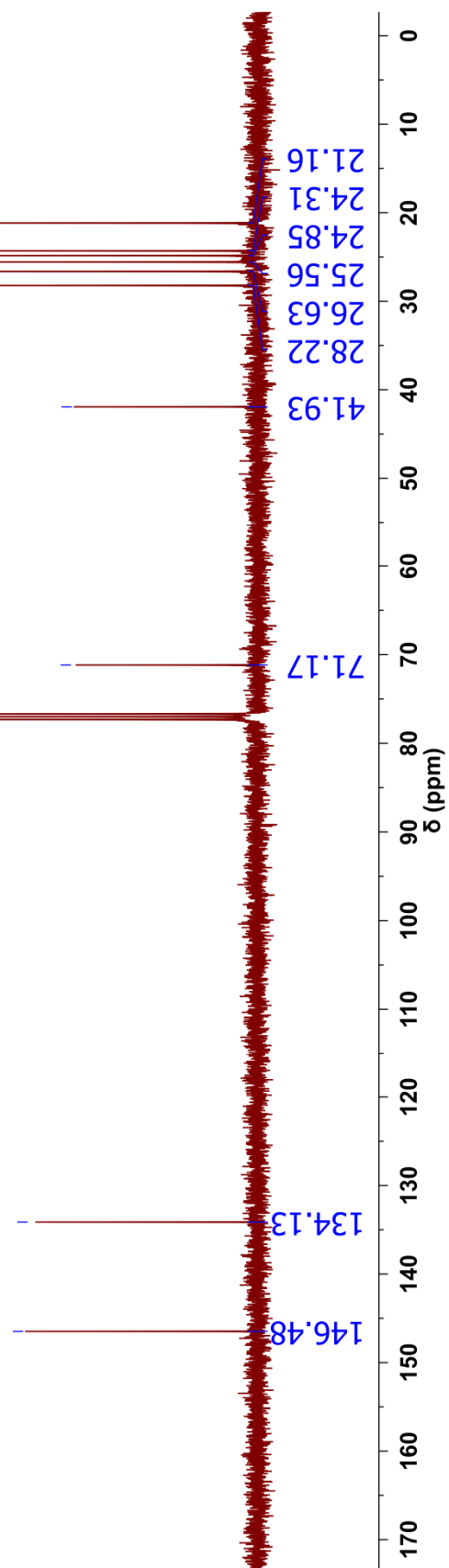
^1H NMR (CDCl_3)

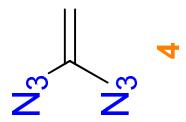




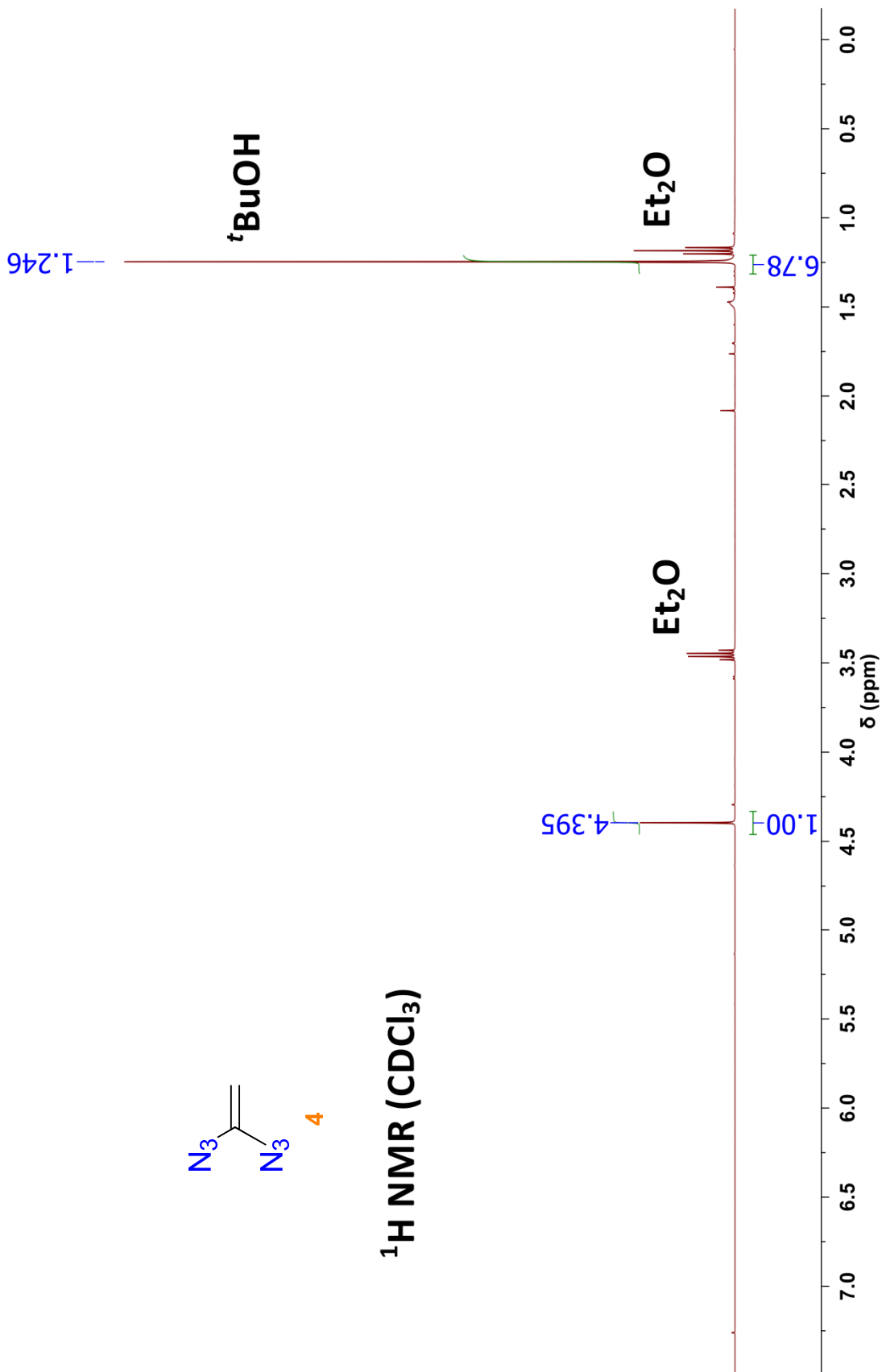
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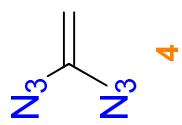
¹³C NMR (CDCl₃)



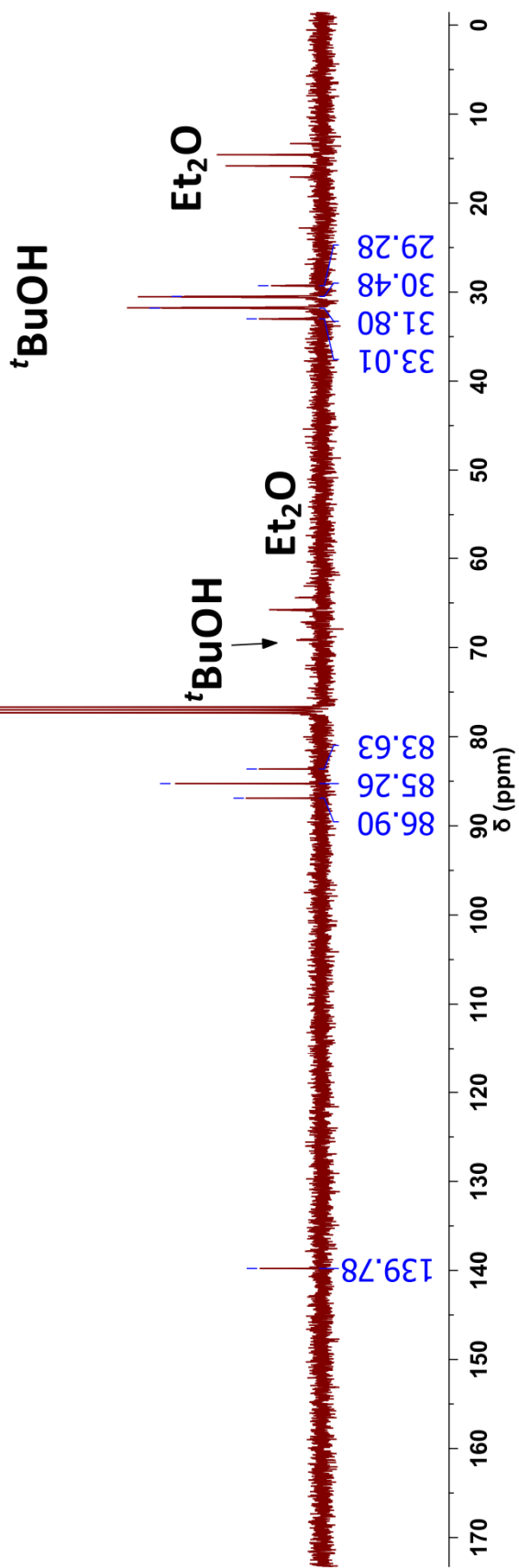


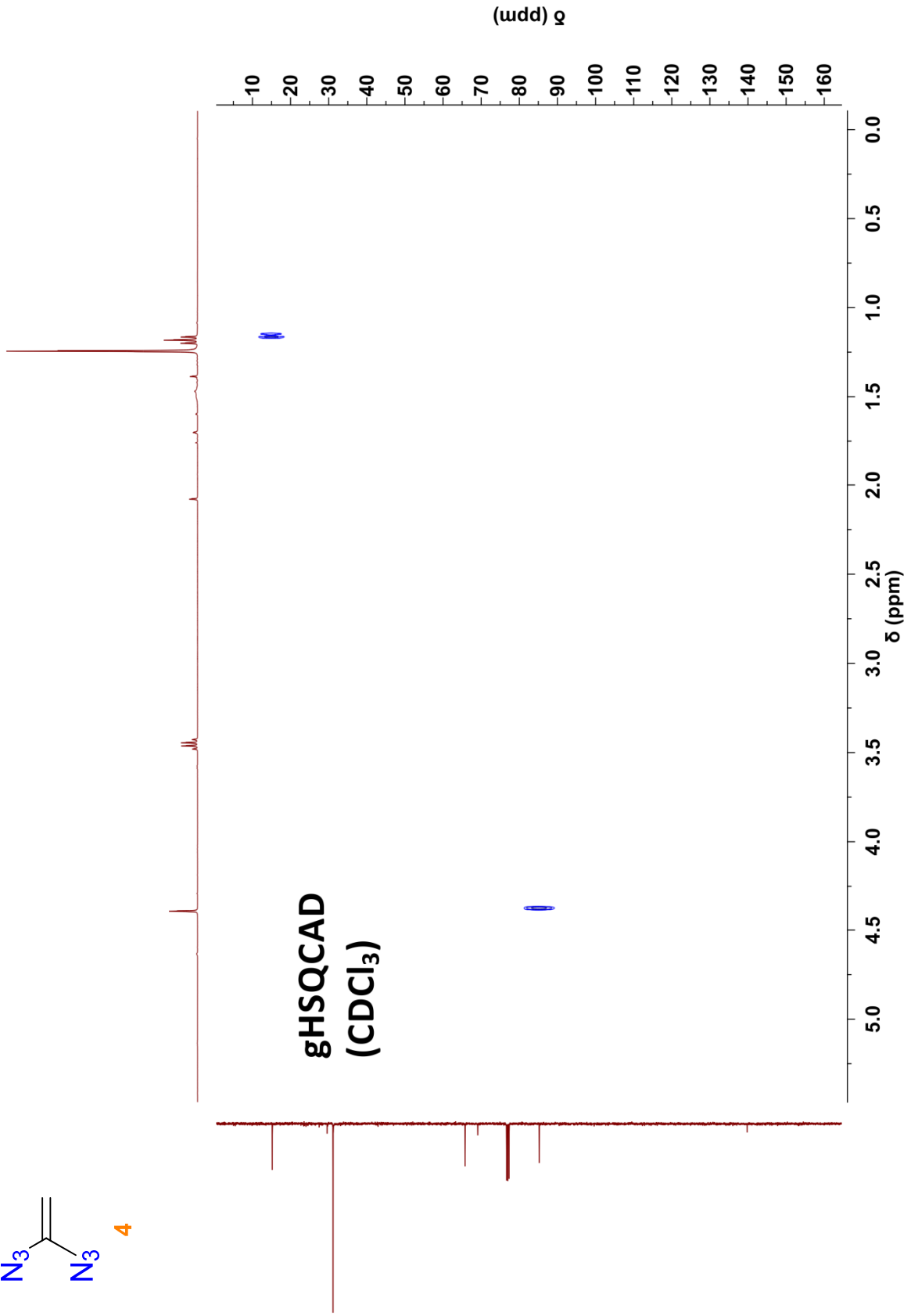
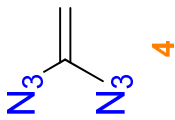
$^1\text{H NMR}$ (CDCl_3)

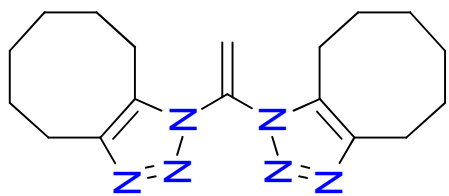




^{13}C NMR (CDCl_3)

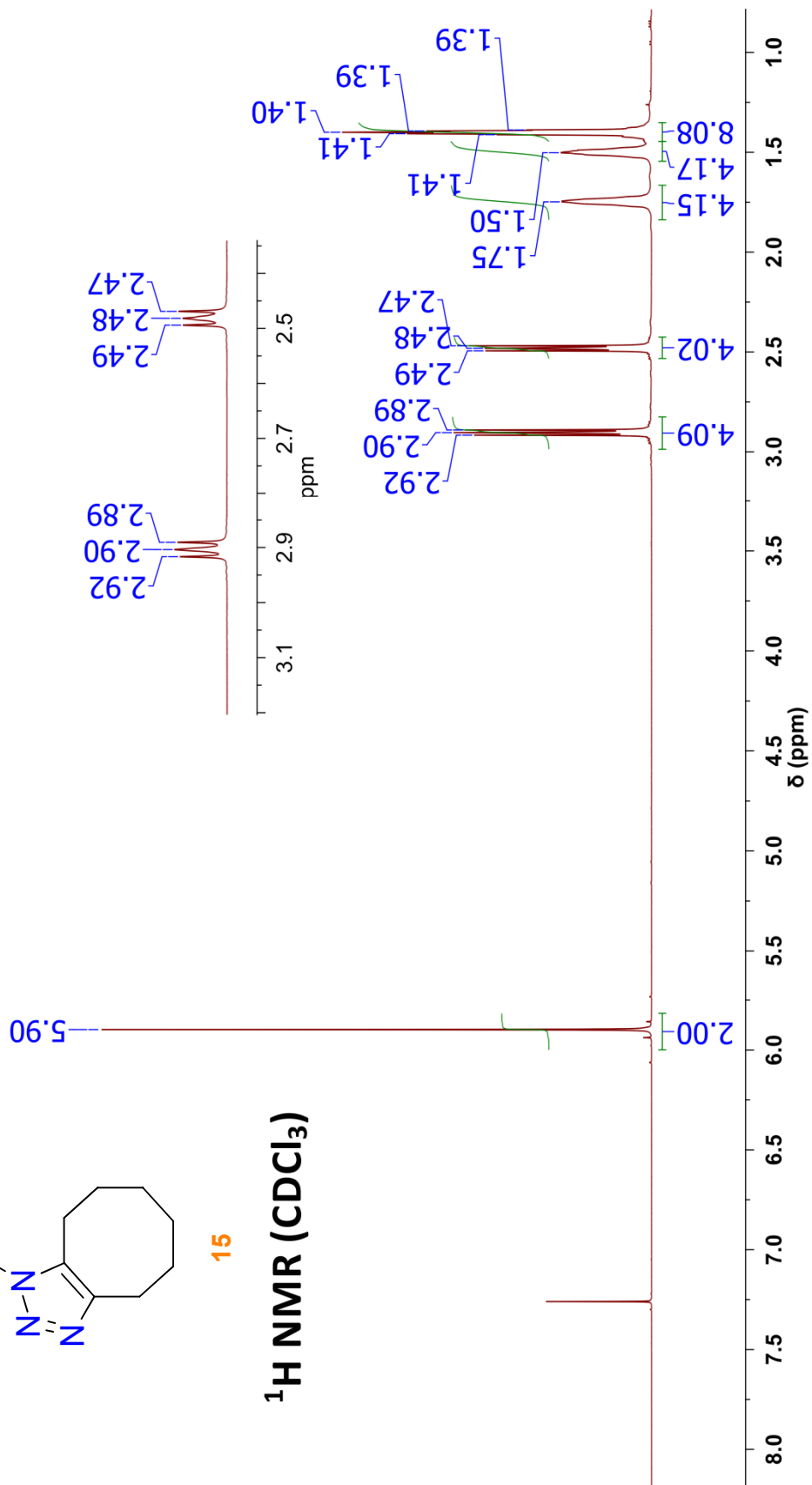


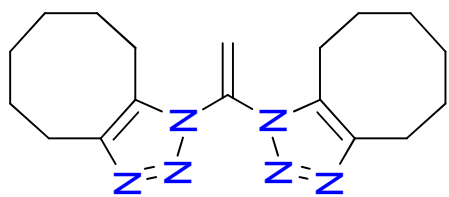




15

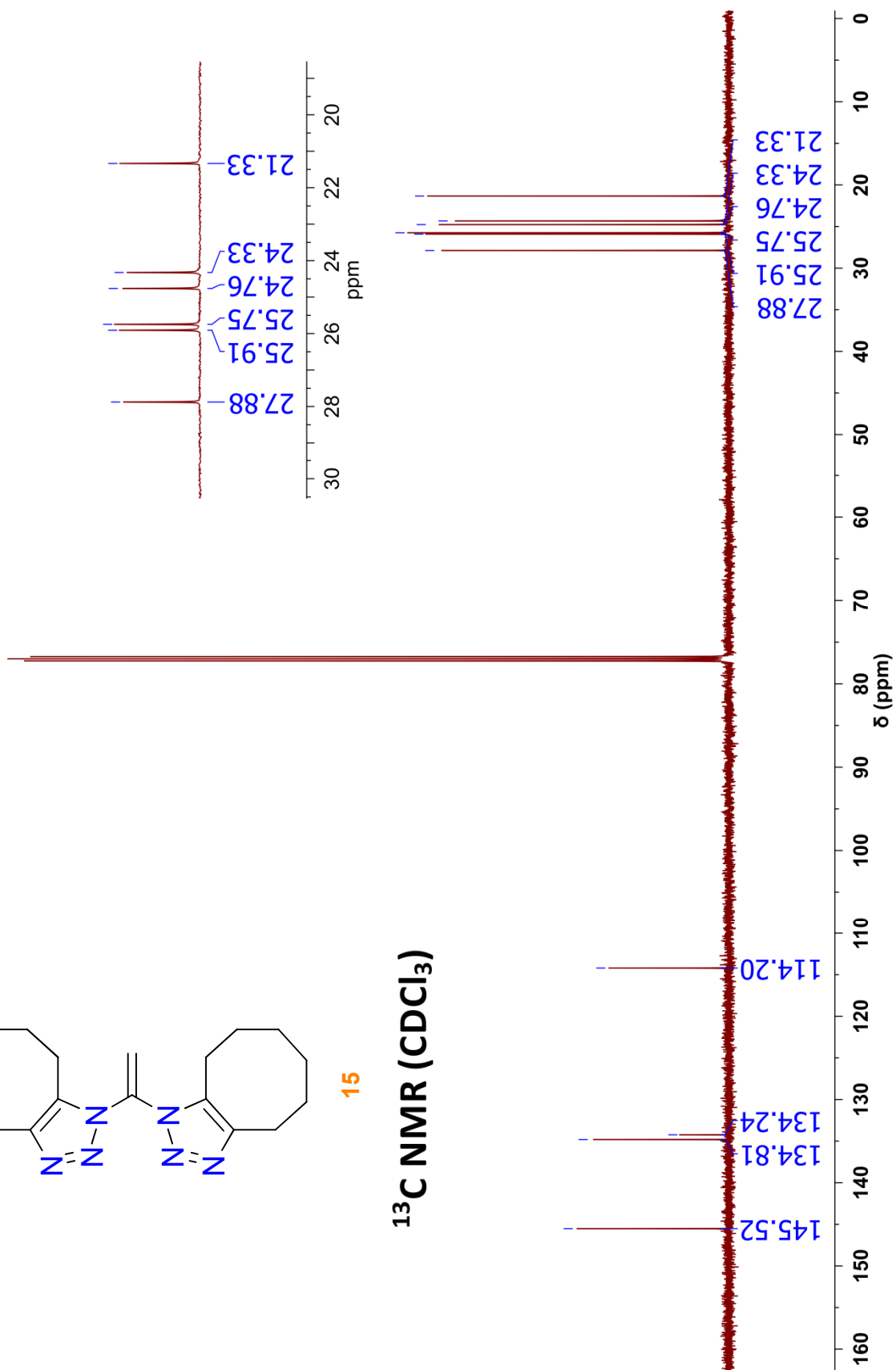
¹H NMR (CDCl₃)

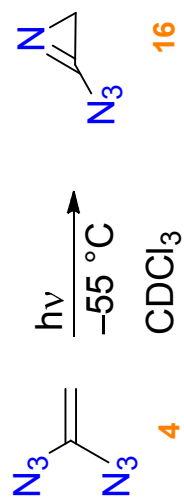




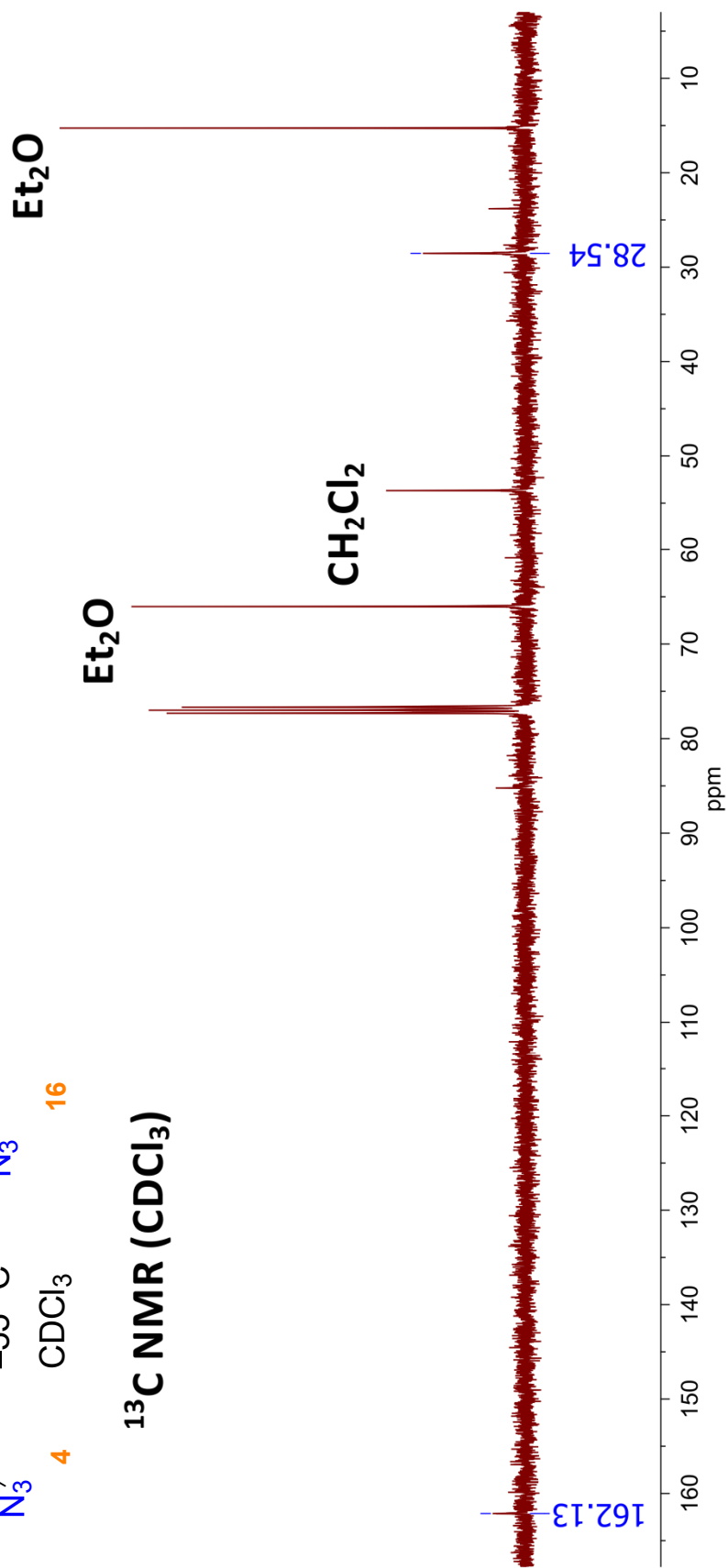
15

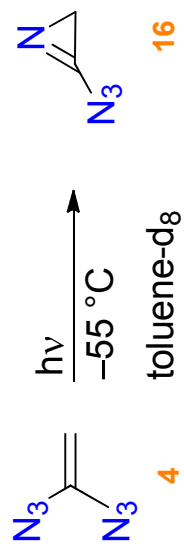
¹³C NMR (CDCl₃)



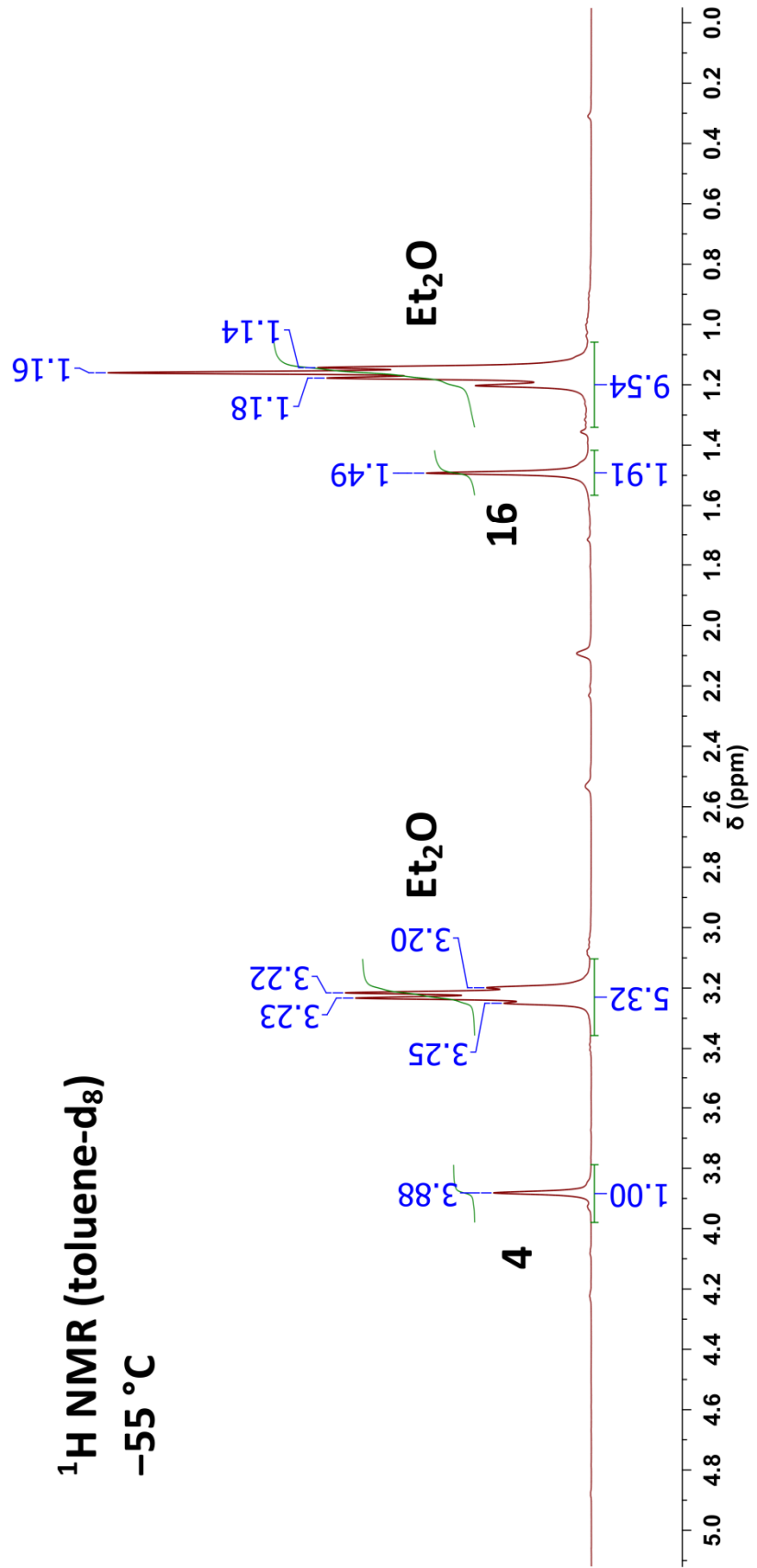


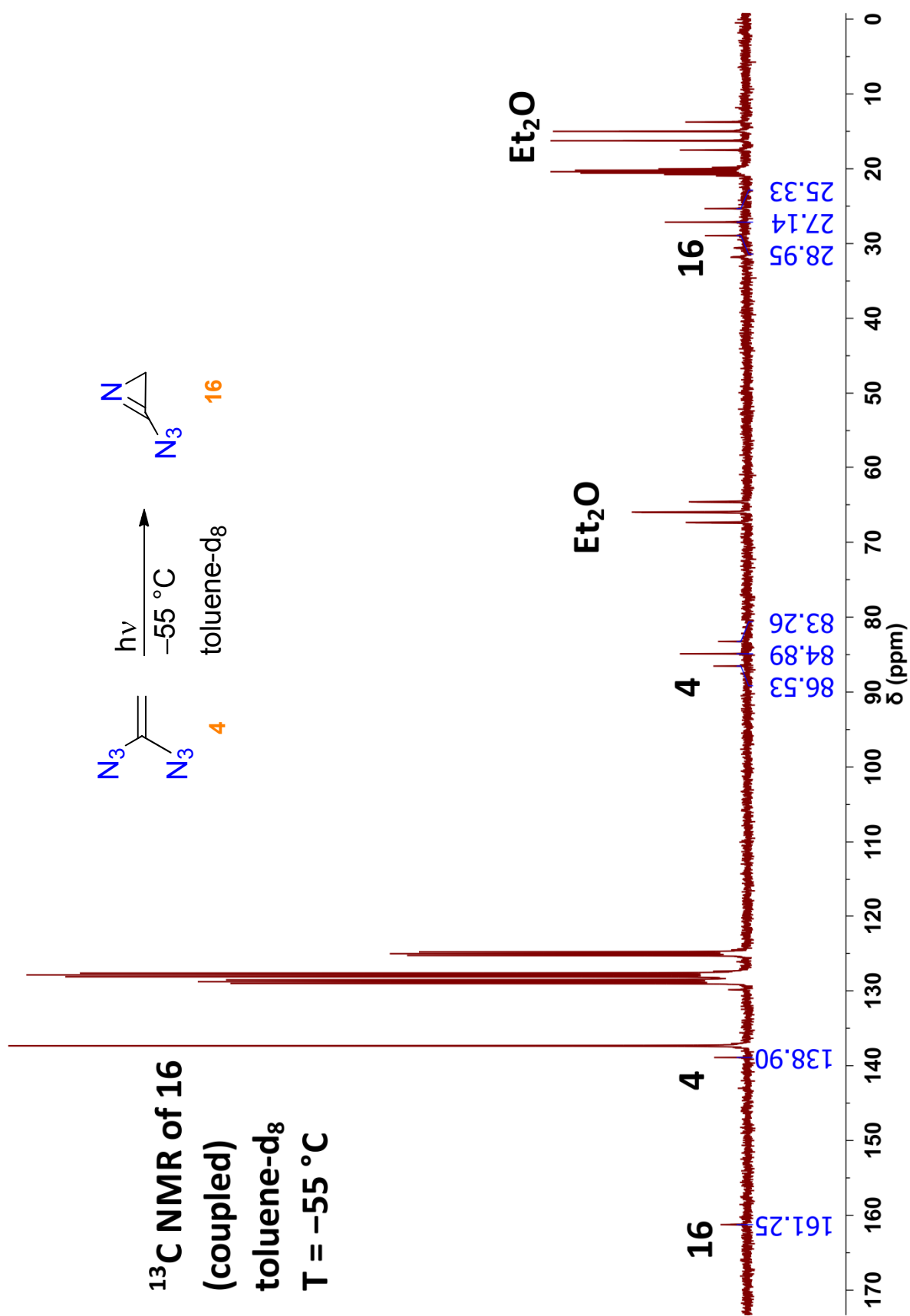
^{13}C NMR (CDCl_3)

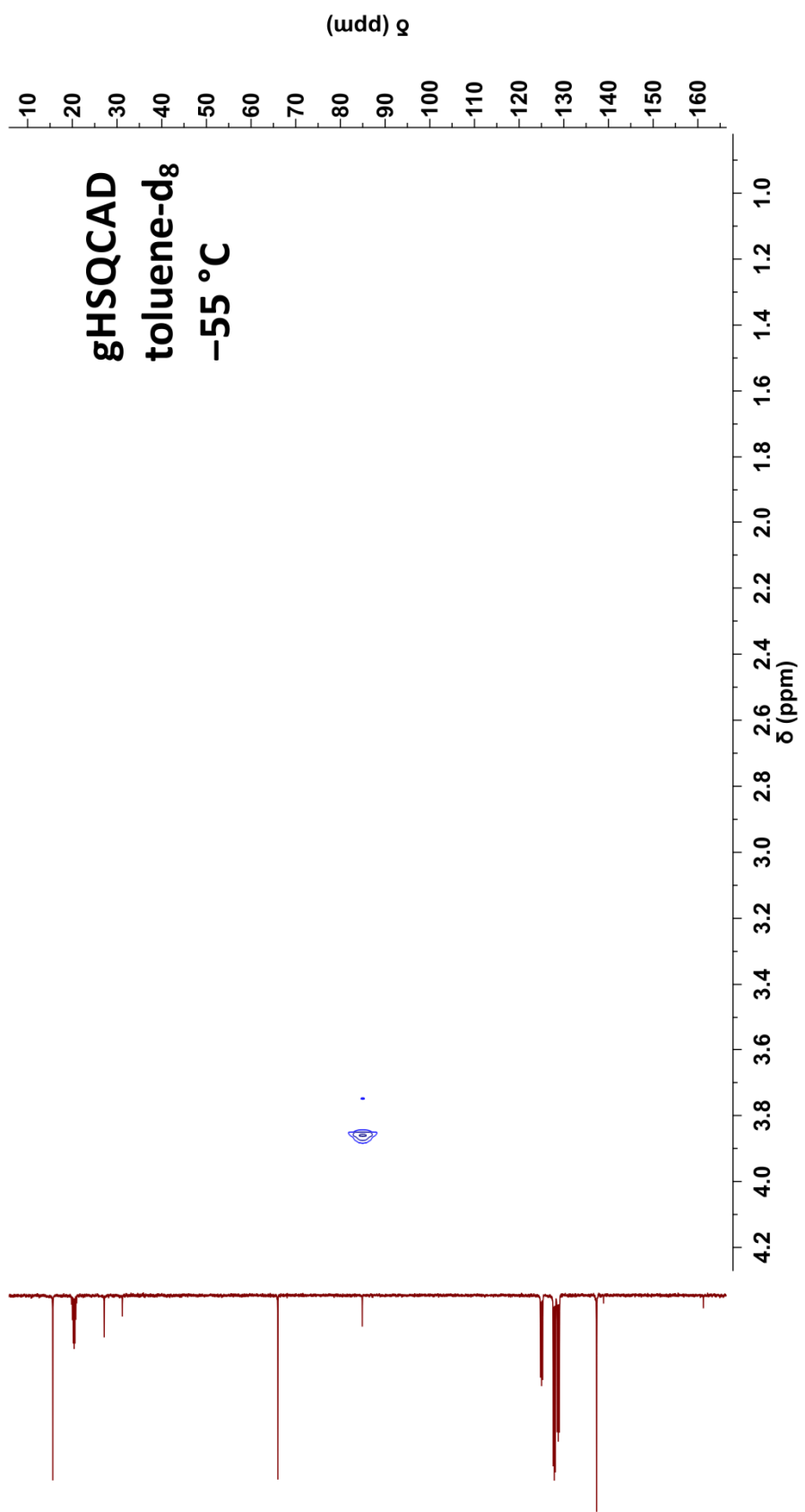
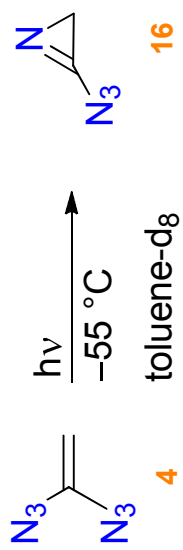




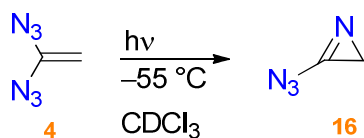
¹H NMR (toluene-d₈)
 -55 °C







[4] Real-time monitoring of the photolysis reaction of diazide **4** by *in situ* IR (ReactIR):



In the IR spectra shown below, the green dotted line represents diazide **4** and the gray or red line represents the 2H-azirine **16**. The temperature has been varied from $-55\text{ }^\circ\text{C}$ to RT.

