

Supporting Information

Synthesis of Geminal Azido-Halo Compounds and α -Azidoalkyl Esters from Aldehydes via α -Azido Alcohols

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1 General experimental details

IR spectra were measured on 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 *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 solvent signals. 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. **Mass spectra** were obtained from *micrOTOF QII* spectrometer from BRUKER utilizing electrospray-ionization 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*.

NOTE:

The following azido-compounds should be considered highly explosive, and effective safety measures, such as utilization 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.

We investigated the equilibrium of **4**/ HN_3 and **5** not only in chloroform, but also in other solvents such as DMSO, acetone, cyclohexane, and benzene. For some solvents, we found higher values of the equilibrium constant K than in the case of the corresponding solutions in chloroform. However, these effects are overcompensated by lower temperatures, which are possible with chloroform, leading to even higher K values. Thus, the latter solvent seems to be an appropriate choice.

2 Experimental procedures

2.1 Synthesis of the 1-azido-1-halo compounds

Freshly distilled aldehyde **4** (1.0 mmol, 1 eq) was added dropwise to a solution of hydrazoic acid (2 eq) in chloroform (1 mL), maintained at $-5\text{ }^{\circ}\text{C}$. After complete addition, the reaction mixture was allowed to warm to room temperature within 2 h (**5g** was stored 5 d at $-30\text{ }^{\circ}\text{C}$). Subsequently, the reaction mixture was cooled to $-50\text{ }^{\circ}\text{C}$ (in case of **5a,b** to $-55\text{ }^{\circ}\text{C}$), and all the volatiles were recondensed at ca. 0.005 mbar. The residue so obtained was α -azido alcohol **5**, and at no point was the substance allowed to warm above $-50\text{ }^{\circ}\text{C}$ in the next step.

Compound **5**, so obtained above, was dissolved in cold ($-50\text{ }^{\circ}\text{C}$) CHCl_3 (5 mL, in case of **5a,b,c** in cold CDCl_3), and to this solution was added PX_3 (3 eq). This reaction mixture was stirred at this temperature for 1 h, and further 12 h at RT (in case of **5a,b,c** stored at $-30\text{ }^{\circ}\text{C}$ for 12 h).

Workup A for **2d,e,f** and **3d,e,f**:

A 1:1 pentane/ Et_2O solvent mixture (25 mL) was added to the reaction mixture, it was washed first three times with ice cold water and subsequently with brine. The organic phase was dried over MgSO_4 , and the solvent was removed *in vacuo* leading to a transparent liquid.

Workup B for **2a,b,c,g** and **3a**:

The reaction mixture was cooled to $-20\text{ }^{\circ}\text{C}$, and the volatiles (product **2a,b,c** or **3a**, CDCl_3 and PX_3) were recondensed at ca. 0.005 mbar. In case of **2g**, the residue was the product, which was diluted in cold CDCl_3 . The yields were calculated against a standard per ^1H NMR spectroscopy.

Synthesis of 2-azido-2-bromo-1,1,1-trichloroethane (**3e**)

Freshly distilled chloral (**4e**, 147 mg, 1 mmol, 0.11 mL) was added dropwise to a solution of hydrazoic acid in chloroform (2M, 1 mL), maintained at $-5\text{ }^{\circ}\text{C}$. After complete addition, the reaction mixture was allowed to warm to room temperature within 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 1-azido-2,2,2-trichloroethanol (**5e**).

The α -azido alcohol **5e** was dissolved in cold ($-50\text{ }^{\circ}\text{C}$) CHCl_3 (5 mL), and to this solution was added PBr_3 (812 mg, 3 mmol, 0.29 mL). This reaction mixture was stirred at this temperature for 1 h, and further 12 h at room temperature. A 1:1 pentane/ Et_2O solvent mixture (10 mL) was added to the reaction mixture, it was washed first three times with ice cold water (10 mL) and subsequently with brine (10 mL). The organic phase was dried over MgSO_4 , and the solvent was removed *in vacuo* leading to 2-azido-2-bromo-1,1,1-trichloroethane (**3e**, 127 mg, 0.5 mmol, 50%).

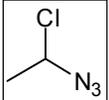
Azidochloromethane (2a)

Yield: 56%. – $^1\text{H NMR}$ (CDCl_3): $\delta = 4.98$ (s, CH_2). – $^{13}\text{C NMR}$ (CDCl_3): $\delta =$  61.2 (t, CH_2). NMR data of **2a**, see also ref. [4].

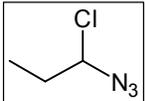
Azidobromomethane (3a)

Yield: 67%. – $^1\text{H NMR}$ (CDCl_3): $\delta = 5.02$ (s, CH_2). – $^{13}\text{C NMR}$ (CDCl_3): $\delta =$  50.0 (t, CH_2). NMR data of **3a**, see also ref. [4].

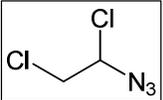
1-Azido-1-chloroethane (2b)

Yield: 66%. – $^1\text{H NMR}$ (CDCl_3): $\delta = 1.73$ (d, $^3J = 6.2$ Hz, 3H, CH_3), 5.51 (q, $^3J = 6.2$ Hz, 1H, CH). – $^{13}\text{C NMR}$ (CDCl_3): $\delta = 25.3$ (q, CH_3), 74.3 (d, CH). 

1-Azido-1-chloropropane (2c)

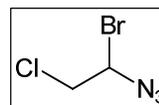
Yield: 65%. – $^1\text{H NMR}$ (CDCl_3): $\delta = 1.05$ (t, $^3J = 7.4$ Hz, 3H, CH_3), 1.95 (m, 2H, CH_2), 5.35 (t, $^3J = 6.1$ Hz, 1H, CH). – $^{13}\text{C NMR}$ (CDCl_3): $\delta = 9.9$ (q, CH_3), 32.1 (t, CH_2), 79.7 (d, CH). 

1-Azido-1,2-dichloroethane (2d)

colorless liquid. – yield: 42%. – $^1\text{H NMR}$ (CDCl_3): $\delta = 3.69$ (dd, $^2J = 11.8$ Hz, $^3J = 7.7$ Hz, 1H, CH_2), 3.79 (dd, $^2J = 11.8$ Hz, $^3J = 4.3$ Hz, 1H, CH_2), 5.53 (dd, $^3J = 7.7$ Hz, $^3J = 4.3$ Hz, 1H, CH). – $^{13}\text{C NMR}$ (CDCl_3): $\delta = 46.5$ (t, CH_2), 75.4 (d, CH). – IR (CDCl_3): $\tilde{\nu}/\text{cm}^{-1} = 2132$ (N_3) – HRMS (ESI): $m/z = 138.9686$ [$\text{C}_2\text{H}_3\text{Cl}_2\text{N}_3$, M, calcd.: 138.9699]. 

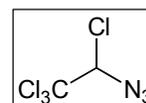
1-Azido-1-bromo-2-chloroethane (3d)

colorless liquid. – **yield:** 48%. – $^1\text{H NMR}$ (CDCl_3): $\delta = 3.81$ (dd, $^2J = 11.7$ Hz, $^3J = 9.0$ Hz, 1H, CH_2), 3.92 (dd, $^2J = 11.7$ Hz, $^3J = 3.6$ Hz, 1H, CH_2), 5.70 (dd, $^3J = 8.9$ Hz, $^3J = 3.6$ Hz, 1H, CH). – $^{13}\text{C NMR}$ (CDCl_3): $\delta = 46.6$ (t, CH_2), 66.8 (d, CH). – **IR** (CDCl_3): $\tilde{\nu}/\text{cm}^{-1} = 2131$ (N_3). NMR data of **3d**, see also ref. [17].



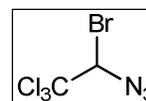
1-Azido-1,2,2,2-tetrachloroethane (2e)

light yellow liquid. – **yield:** 42%. – $^1\text{H NMR}$ (CDCl_3): $\delta = 5.59$ (s, CH). – $^{13}\text{C NMR}$ (CDCl_3): $\delta = 82.6$ (d, CH), 99.1 (s, CCl_3). – **IR** (CDCl_3): $\tilde{\nu}/\text{cm}^{-1} = 2127$ (N_3).



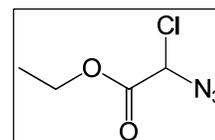
2-Azido-2-bromo-1,1,1-trichloroethane (3e)

colorless liquid. – **yield:** 50%. – $^1\text{H NMR}$ (CDCl_3): $\delta = 5.83$ (s, CH). – $^{13}\text{C NMR}$ (CDCl_3): $\delta = 75.1$ (d, CH), 98.4 (s, CCl_3). – **IR** (CDCl_3): $\tilde{\nu}/\text{cm}^{-1} = 2124$ (N_3).



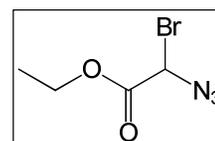
Ethyl 2-azido-2-chloroacetate (2f)

colorless liquid. – **yield:** 49%. – $^1\text{H NMR}$ (CDCl_3): $\delta = 1.32$ (t, $^3J = 7.1$ Hz, 3H, CH_3), 4.30 (m, 2H, CH_2), 5.20 (s, 1H, CH). – $^{13}\text{C NMR}$ (CDCl_3): $\delta = 13.7$ (q, CH_3), 63.2 (t, CH_2), 68.6 (d, CH), 165.2 (s, CO). – **IR** (CDCl_3): $\tilde{\nu}/\text{cm}^{-1} = 2119$ (N_3), 1755 (C=O). – **HRMS (ESI):** $m/z = 186.0048$ [$\text{C}_4\text{H}_6\text{O}_2\text{ClN}_3\text{Na}$, M + Na^+ , calcd.: 186.0041].



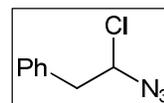
Ethyl 2-azido-2-bromoacetate (3f)

colorless liquid. – **yield:** 54%. – $^1\text{H NMR}$ (CDCl_3): $\delta = 1.33$ (t, $^3J = 7.1$ Hz, 3H, CH_3), 4.31 (m, 2H, CH_2), 5.36 (s, 1H, CH). – $^{13}\text{C NMR}$ (CDCl_3): $\delta = 13.7$ (q, CH_3), 57.9 (d, CH), 63.1 (t, CH_2), 165.5 (s, CO). – **IR** (CDCl_3): $\tilde{\nu}/\text{cm}^{-1} = 2124$ (N_3), 1747 (C=O). – **HRMS (ESI):** $m/z = 331.9863$ [$\text{C}_8\text{H}_9\text{O}_4\text{BrN}_6$, 2M – HBr – 2H, calcd.: 331.9863].



(2-Azido-2-chloroethyl)benzene (2g)

colorless liquid. – **yield:** 90%. – **¹H NMR (CDCl₃):** δ = 3.21 (d, ³J = 6.5 Hz, 2H, CH₂), 5.55 (t, ³J = 6.5 Hz, 1H, CH), 7.20–7.40 (m, 5H, Ar). – **¹³C NMR (CDCl₃):** δ = 44.9 (t, CH₂), 78.0 (d, CH), 127.5 (d, *p*-CH), 128.6 (d, CH, Ar), 129.6 (d, CH, Ar), 134.9 (s, *ipso*-C). – **IR (CDCl₃):** $\tilde{\nu}$ /cm⁻¹ = 2113 (N₃).



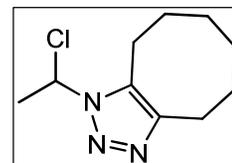
2.2 Consecutive Reactions of 1-azido-1-halo compounds

2.2.1 Reactions of 1-azido-1-halo compounds with cyclooctyne

To a solution of a 1-azido-1-halo compound (1.0 mmol, 1 eq) in distilled dichloromethane (5 mL, in case of **2b,c,g** in CDCl₃), stirred at –20 °C, was added, drop-wise, a solution of cyclooctyne (1.1 eq) in distilled dichloromethane (5 mL). The reaction mixture was stirred for 2 h at this temperature and then warmed to room temperature. Subsequently, the solvent was removed *in vacuo*, and the crude product was purified by flash chromatography over silica-gel (CH₂Cl₂/Et₂O 10:1).

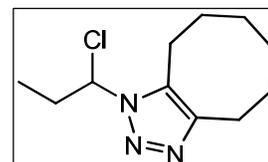
1-(1-Chloroethyl)-4,5,6,7,8,9-hexahydro-1H-cycloocta-1,2,3-triazole (7b)

colorless oil. – **yield:** 14% (based on aldehyde). – **¹H NMR (CDCl₃):** δ = 1.31–1.48 (m, 4H, CH₂), 1.66 (m, 2H, CH₂), 1.81 (m, 2H, CH₂), 2.20 (d, ³J = 6.5 Hz, 3H, CH₃), 2.81 (m, 4H, CCH₂), 6.24 (q, ³J = 6.5 Hz, 1H, CH). – **¹³C NMR (CDCl₃):** δ = 21.4 (t, CH₂), 23.9 (q, CH₃), 24.2 (t, CH₂), 24.4 (t, CH₂), 25.7 (t, CH₂), 25.8 (t, CH₂), 27.9 (t, CH₂), 65.0 (d, CH), 133.3 (s, C, Ar), 145.3 (s, C, Ar). – **HRMS (ESI):** *m/z* = 214.1097 [C₁₀H₁₇ClN₃, M + H⁺, calcd.: 214.1111].



1-(1-Chloropropyl)-4,5,6,7,8,9-hexahydro-1H-cycloocta-1,2,3-triazole (7c)

colorless oil. – **yield:** 48% (based on aldehyde). – **¹H NMR (CDCl₃):** δ = 1.02 (t, ³J = 7.4 Hz, 3H, CH₃), 1.38–1.52 (m, 4H, CH₂), 1.72 (m, 2H, CH₂), 1.84 (m, 2H, CH₂), 2.55 (dq, ²J = 14.6 Hz, ³J = 7.4 Hz, 1H, CH₂CH₃), 2.67 (dq, ²J = 14.6 Hz, ³J = 7.4 Hz, 1H, CH₂CH₃), 2.86 (m, 4H, CCH₂), 6.00 (t, ³J = 7.4 Hz, 1H, CH). – **¹³C NMR (CDCl₃):** δ = 10.9 (q, CH₃), 21.5 (t, CH₂), 24.4 (t, CH₂), 24.7 (t, CH₂), 25.8 (t,

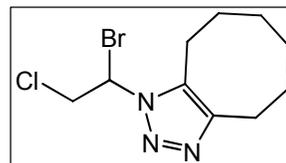


CH₂), 26.3 (t, CH₂), 28.2 (t, CH₂), 31.0 (t, CH₂CH₃), 70.7 (d, CH), 133.5 (s, C, Ar), 145.5 (s, C, Ar). – **HRMS (ESI)**: m/z = 228.1261 [C₁₁H₁₉CIN₃, M + H⁺, calcd.: 228.1268], 250.1094 [C₁₁H₁₈CIN₃Na, M + Na⁺, calcd.: 250.1087], 266.0830 [C₁₁H₁₈CIKN₃, M + K⁺, calcd.: 266.0826].

1-(1-Bromo-2-chloroethyl)-4,5,6,7,8,9-hexahydro-1H-cycloocta-1,2,3-triazole (8d)

white solid. – **yield**: 93%. – **mp.**: 79–81 °C. – **¹H NMR**

(CDCl₃): δ = 1.37–1.52 (m, 4H, CH₂), 1.68–1.78 (m, 2H, CH₂), 1.78–1.95 (m, 2H, CH₂), 2.75 (m, 2H, CH₂), 2.91 (m, 2H, CH₂), 4.28 (dd, ²J = 11.6 Hz, ³J = 4.4 Hz, 1H, CH₂), 4.88



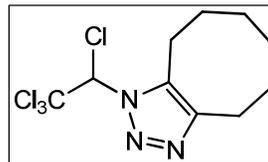
(d, ²J = 11.6 Hz, ³J = 10.4 Hz, 1H, CH₂), 6.21 (dd, ³J = 10.0 Hz, ³J = 4.4 Hz, 1H, CH).

– **¹³C NMR (CDCl₃)**: δ = 21.4 (t, CH₂), 24.4 (t, CH₂), 24.6 (t, CH₂), 25.9 (t, CH₂), 26.0 (t, CH₂), 28.2 (t, CH₂), 45.1 (t, CH₂), 54.4 (d, CH), 134.1 (s, C), 145.5 (s, C). – **Anal. calcd. for C₁₀H₁₅BrClN₃ (292.60)**: C 41.05, H 5.17, N 14.36. Found: C 41.25, H 5.21, N 14.55. – **HRMS (ESI)**: m/z = 294.0188 [C₁₀H₁₆BrClN₃, M + H⁺, calcd.: 294.0189]. NMR data of **8d**, see also ref. [21].

1-(1,2,2,2-Tetrachloroethyl)-4,5,6,7,8,9-hexahydro-1H-cycloocta-1,2,3-triazole (7e)

white solid. – **yield**: 95%. – **mp.**: 120–123 °C. – **¹H NMR**

(CDCl₃): δ = 1.38–1.53 (m, 4H, CH₂), 1.74 (m, 2H, CH₂), 1.88 (m, 2H, CH₂), 2.92 (m, 4H, CCH₂), 6.54 (s, 1H, CH). – **¹³C**

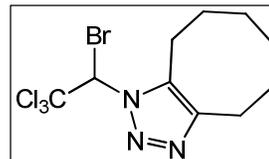


NMR (CDCl₃): δ = 22.2 (t, CH₂), 24.3 (t, CH₂), 24.6 (t, CH₂),

25.8 (t, CH₂), 26.3 (t, CH₂), 28.2 (t, CH₂), 76.4 (d, CH), 97.8 (s, CCl₃), 134.9 (s, C, Ar), 144.8 (s, C, Ar). – **Anal. calcd. for C₁₀H₁₃Cl₄N₃ (317.04)**: C 37.88, H 4.13, N 13.25. Found: C 37.97, H 4.14, N 13.12. – **HRMS (ESI)**: m/z = 317.9921 [C₁₀H₁₄Cl₄N₃, M + H⁺, calcd.: 317.9912], 339.9739 [C₁₀H₁₃Cl₄N₃Na, M + Na⁺, calcd.: 339.9732].

1-(1-Bromo-2,2,2-trichloroethyl)-4,5,6,7,8,9-hexahydro-1H-cycloocta-1,2,3-triazole (8e)

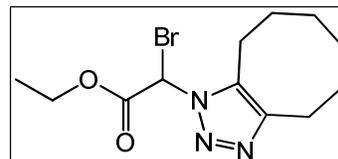
colorless oil. – **yield:** 92%. – **¹H NMR (CDCl₃):** δ = 1.40–1.55 (m, 4H, CH₂), 1.7–1.8 (m, 2H, CH₂), 1.85–1.95 (m, 2H, CH₂), 2.80–2.94 (m, 2H, CH₂), 2.94 (m, 2H, CH₂), 6.66 (s, 1H, CH).



– **¹³C NMR (CDCl₃):** δ = 22.1 (t, CH₂), 24.4 (t, CH₂), 24.5 (t, CH₂), 25.9 (t, CH₂), 26.0 (t, CH₂), 28.1 (t, CH₂), 65.4 (d, CH), 97.6 (s, CCl₃), 134.6 (s, C), 144.6 (s, C). – **HRMS (ESI):** m/z = 361.9403 [C₁₀H₁₄BrCl₃N₃, M + H⁺, calcd.: 361.9409].

Ethyl 2-bromo-2-(4,5,6,7,8,9-hexahydro-1H-cycloocta-1,2,3-triazol-1-yl)acetate (8f)

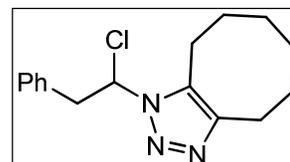
colorless oil. – **yield:** 98%. – **¹H NMR (CDCl₃):** δ = 1.31 (t, ³J = 7.2 Hz, 3H, CH₃), 1.33–1.40 (m, 4H, CH₂), 1.45–1.55 (m, 2H, CH₂), 1.67–1.75 (m, 2H, CH₂), 2.70–2.84 (m, 2H, CH₂), 2.87 (t, ³J = 6.4 Hz, 2H, CH₂), 4.49 (q, ³J = 7.2 Hz,



2H, CH₂), 7.47 (s, 1H, CH). – **¹³C NMR (CDCl₃):** δ = 13.9 (q, CH₃), 21.4 (t, CH₂), 24.4 (t, CH₂), 24.9 (t, CH₂), 25.6 (t, CH₂), 26.3 (t, CH₂), 28.0 (t, CH₂), 63.9 (t, CH₂), 69.9 (d, CH), 135.1 (s, C), 146.1 (s, C), 162.3 (s, CO). – **HRMS (ESI):** m/z = 316.0652 [C₁₂H₁₉BrN₃O₂, M + H⁺, calcd.: 316.0655].

1-(1-Chloro-2-phenylethyl)-4,5,6,7,8,9-hexahydro-1H-cycloocta-1,2,3-triazole (7g)

white solid. – **yield:** 9% (based on used aldehyde). – **mp.:** 70–72 °C – **¹H NMR (CDCl₃):** δ = 1.13–1.45 (m, 5H, CH₂), 1.58–1.78 (m, 3H, CH₂), 2.56 (m, 1H, CCH₂), 2.70 (m, 1H, CCH₂), 2.84 (m, 2H, CCH₂), 3.71 (dd, ²J = 14.0 Hz, ³J = 6.0



Hz, 1H, CH₂CH), 4.13 (dd, ²J = 14.0 Hz, ³J = 8.6 Hz, 1H, CH₂CH), 6.11 (dd, ³J = 8.6 Hz, ³J = 6.0 Hz, 1H, CH), 7.14 (m, 2H, CH, Ph), 7.22 (m, 3H, CH, Ph). – **¹³C NMR (CDCl₃):** δ = 21.3 (t, CH₂), 24.4 (t, CH₂), 24.6 (t, CH₂), 25.7 (t, CH₂), 26.2 (t, CH₂), 28.4 (t, CH₂), 43.9 (t, CH₂CH), 68.8 (d, CH), 127.5 (d, *p*-CH, Ph), 128.7 (d, CH, Ph), 129.4 (d, CH, Ph), 133.8 (s, C, Ar), 135.1 (s, *ipso*-C, Ph), 145.2 (s, C, Ar). – Anal.

calcd. for **C₁₆H₂₀ClN₃ (289.80)**: C 66.31, H 6.96, N 14.50. Found: C 66.29, H 7.05, N 14.23. – **HRMS (ESI)**: m/z = 290.1436 [C₁₆H₂₁ClN₃, M + H⁺, calcd.: 290.1424], 312.1262 [C₁₆H₂₀ClN₃Na, M + Na⁺, calcd.: 312.1243], 328.1011 [C₁₆H₂₀ClKN₃, M + K⁺, calcd.: 328.0983].

2.2.2 Reactions of 1-azido-1-halo compounds with TMGA

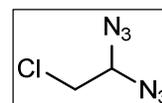
Compound **8d,f** (1.0 mmol, 1 eq), so obtained above, was dissolved in CHCl₃ (2 mL), and to this solution was added TMGA (2 eq) in CHCl₃ (2 mL), maintained at 0 °C. The mixture was allowed to warm up to room temperature and stirred for 12 h. Subsequently, the solvent was removed *in vacuo*, and the crude product was purified by flash chromatography over silica-gel (Et₂O).

Synthesis of 1,1-diazido-2-chloroethane (**9d**)

1-Azido-1-bromo-2-chloroethane (**8d**, 802 mg, 4.35 mmol), so obtained above, was dissolved in CHCl₃ (5 mL), and to this solution was added TMGA (1.58 g, 10 mmol) in CHCl₃ (5 mL), maintained at 0 °C. The mixture was allowed to warm up to room temperature and stirred for 12 h. Subsequently, the solvent was removed *in vacuo*, and the crude product was purified by flash chromatography over silica-gel (Et₂O) to obtain 1,1-diazido-2-chloroethane (**9d**, 490 mg, 3.35 mmol, 77%).

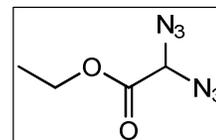
1,1-Diazido-2-chloroethane (**9d**)

colorless liquid. – **yield**: 77%. – **¹H NMR (CDCl₃)**: δ = 3.58 (d, ³J = 6 Hz, 2H, CH₂), 4.89 (t, ³J = 6 Hz, 1H, CH). – **¹³C NMR (CDCl₃)**: δ = 44.72 (t, CH₂), 76.63 (d, CH). – **IR (CCl₄)**: $\tilde{\nu}/\text{cm}^{-1}$ = 2108 (N₃). NMR data of **9d**, see also ref. [21].



Ethyl 2-azido-2-bromoacetate (**9f**)

colorless liquid. – **yield**: 80%. – **¹H NMR (CDCl₃)**: δ = 1.35 (t, ³J = 7.2 Hz, 3H, CH₃), 4.33 (q, ³J = 7.2 Hz, 2H, CH₂), 4.85 (s, 1H, CH). – **¹³C NMR (CDCl₃)**: δ = 13.99 (q, CH₃), 63.14 (t, CH₂), 73.99 (d, CH), 165.06 (s, CO). – **IR (CCl₄)**: $\tilde{\nu}/\text{cm}^{-1}$ = 2110 (N₃), 1761 (C=O). NMR data of **9f**, see also ref. [16].

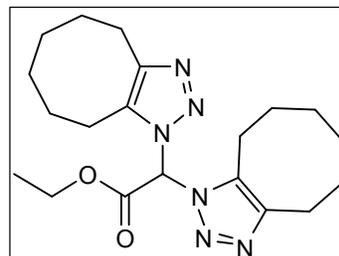


Synthesis of ethyl 2,2-bis(4,5,6,7,8,9-hexahydro-1H-cycloocta-1,2,3-triazol-1-yl)acetate

To a solution of compound **9f** (272 mg, 1.66 mmol) in distilled *n*-hexane (10 mL), stirred at $-20\text{ }^{\circ}\text{C}$, was added, drop-wise, a solution of cyclooctyne (0.4 mL, 3 mmol) in distilled *n*-hexane (5 mL). The reaction mixture was stirred for 2 h at this temperature and then warmed to room 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) to obtain ethyl 2,2-bis(4,5,6,7,8,9-hexahydro-1H-cycloocta-1,2,3-triazol-1-yl)acetate (599 mg, 1.55 mmol, 93%).

Ethyl 2,2-bis(4,5,6,7,8,9-hexahydro-1H-cycloocta-1,2,3-triazol-1-yl)acetate

colorless oil. – $^1\text{H NMR}$ (CDCl_3): δ = 1.31 (t, 3J = 7.2 Hz, 3H, CH_3), 1.33–1.40 (m, 8H, CH_2), 1.45–1.55 (m, 4H, CH_2), 1.67–1.75 (m, 4H, CH_2), 2.74–2.81 (m, 4H, CH_2), 2.87 (m, 4H, CH_2), 4.39 (q, 3J = 7.2 Hz, 2H, CH_2), 7.47 (s, 1H, CH). – $^{13}\text{C NMR}$ (CDCl_3): δ = 13.85 (q, CH_3), 21.40 (t,



CH_2), 24.35 (t, CH_2), 24.87 (t, CH_2), 25.57 (t, CH_2), 26.25 (t, CH_2), 27.98 (t, CH_2), 63.88 (t, CH_2), 69.90 (d, CH), 135.05 (s, C), 146.07 (s, C), 162.31 (s, CO). – **HRMS (ESI)**: m/z = 387.2502 [$\text{C}_{20}\text{H}_{31}\text{N}_6\text{O}_2$, $\text{M} + \text{H}^+$, calcd.: 387.2508], 409.2348 [$\text{C}_{20}\text{H}_{30}\text{N}_6\text{NaO}_2$, $\text{M} + \text{Na}^+$, calcd.: 409.2328], 425.2089 [$\text{C}_{20}\text{H}_{30}\text{KN}_6\text{O}_2$, $\text{M} + \text{K}^+$, calcd.: 425.2067]. – **IR** (CCl_4): $\tilde{\nu}/\text{cm}^{-1}$ = 1771 (C=O).

2.2.3 Reactions of 1-azido-1-halo compounds with Bu_4NSCN

To a solution of tetrabutylammonium thiocyanate (1.33 eq) in distilled CHCl_3 (5 mL), stirred at $-20\text{ }^{\circ}\text{C}$, was added **3e,f** (1.0 mmol, 1 eq) in distilled CHCl_3 (5 mL). The mixture was stirred for 3 h at RT. The solvent was removed *in vacuo*, and the residue was purified by flash chromatography over silica-gel ($\text{Et}_2\text{O}/n$ -pentane 1:5) to obtain **10**.

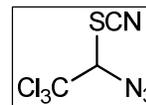
Synthesis of 2-azido-1,1,1-trichloro-2-thiocyanatoethane (**10e**)

To a solution of tetrabutylammonium thiocyanate (370 mg, 1.23 mmol) in distilled CHCl_3 (5 mL), stirred at $-20\text{ }^{\circ}\text{C}$, was added 2-azido-2-bromo-1,1,1-trichloroethane (**3e**, 253 mg, 1 mmol) in distilled CHCl_3 (5 mL). The mixture was stirred for 3 h at RT.

The solvent was removed in *vacuo* and the residue was purified by flash chromatography over silica-gel (Et₂O/*n*-pentane 1:5) to obtain 2-azido-1,1,1-trichloro-2-thiocyanatoethane (**10e**, 62 mg, 0.27 mmol, 27%).

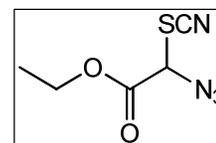
2-Azido-1,1,1-trichloro-2-thiocyanatoethane (**10e**)

yellow liquid. – **yield**: 27% – ¹H NMR (CDCl₃): δ = 5.59 (s, CH). – ¹³C NMR (CDCl₃): δ = 81.79 (d, CH), 97.61 (s, CCl₃), 107.59 (s, SCN). – IR (CDCl₃): $\tilde{\nu}/\text{cm}^{-1}$ = 2163 (SCN), 2124 (N₃).



Ethyl 2-azido-2-thiocyanatoacetate (**10f**)

yellow liquid. – **yield**: 31% – ¹H NMR (CDCl₃): δ = 1.35 (t, ³J = 7.2 Hz, 3H, CH₃), 4.35 (m, 2H, CH₂), 5.14 (s, 1H, CH). – ¹³C NMR (CDCl₃): δ = 14.00 (q, CH₃), 64.21 (t, CH₂), 65.70 (d, CH), 107.91 (s, SCN), 164.01 (s, CO). – IR (CCl₄): $\tilde{\nu}/\text{cm}^{-1}$ = 2163 (SCN), 2113 (N₃), 1755 (C=O).



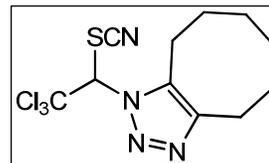
To a solution of **10e,f** (1 mmol, 1 eq) in distilled CH₂Cl₂ (3 mL), stirred at 0 °C, was added, drop-wise, a solution of cyclooctyne (1.1 eq) in distilled CH₂Cl₂ (3 mL). The reaction mixture was stirred for 16 h at RT, and the volatiles were removed *in vacuo*. In the case of **10e**, the residue was the pure product **11e**, and **11f** was isolated by flash chromatography over silica-gel (Et₂O/*n*-hexane 3:1).

Synthesis of 1-(2,2,2-trichloro-1-thiocyanatoethyl)-4,5,6,7,8,9-hexahydro-1H-cycloocta-1,2,3-triazole (**11e**)

To a solution of 2-azido-1,1,1-trichloro-2-thiocyanatoethane (**10e**, 152 mg, 0.66 mmol) in distilled CH₂Cl₂ (2 mL), stirred at 0 °C, was added, drop-wise, a solution of cyclooctyne (79 mg, 0.73 mmol, 91 μL) in distilled CH₂Cl₂ (2 mL). The reaction mixture was stirred for 16 h at RT. 1-(2,2,2-trichloro-1-thiocyanatoethyl)-4,5,6,7,8,9-hexahydro-1H-cycloocta-1,2,3-triazole (**11e**, 221 mg, 0.65 mmol, 99%) was obtained by removing the volatiles *in vacuo*.

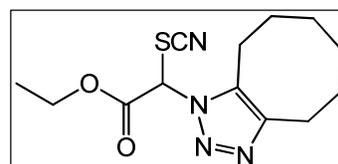
1-(2,2,2-Trichloro-1-thiocyanatoethyl)-4,5,6,7,8,9-hexahydro-1H-cycloocta-1,2,3-triazole (11e)

yellow oil. – **yield:** 99% – **¹H NMR (CDCl₃):** δ = 1.49 (m, 4H, CH₂), 1.76 (m, 2H, CH₂), 1.91 (m, 2H, CH₂), 2.88 (m, 4H, CH₂), 6.24 (s, 1H, CH). – **¹³C NMR (CDCl₃):** δ = 21.99 (t, CH₂), 24.31 (t, CH₂), 24.40 (t, CH₂), 25.87 (t, CH₂), 26.10 (t, CH₂), 27.92 (t, CH₂), 75.47 (d, CH), 96.79 (s, CCl₃), 108.80 (s, SCN), 135.66 (s, C, Ar), 144.61 (s, C, Ar). – **HRMS (ESI):** m/z = 303.0266 [C₁₁H₁₃Cl₃N₄S, M + H⁺ – HCl, calcd.: 303.0238], 325.0087 [C₁₁H₁₂Cl₂N₄NaS, M + Na⁺ – HCl, calcd.: 325.0057], 340.9827 [C₁₁H₁₂Cl₂KN₄S, M + K⁺ – HCl, calcd.: 340.9797]. – **IR (CCl₄):** $\tilde{\nu}/\text{cm}^{-1}$ = 2162 (SCN).



Ethyl 2-(4,5,6,7,8,9-hexahydro-1H-cycloocta-1,2,3-triazol-1-yl)-2-thiocyanatoacetate (11f)

colorless oil. – **yield:** 87% – **¹H NMR (CDCl₃):** δ = 1.19 (t, ³J = 7.2 Hz, 3H, CH₃), 1.32–1.53 (m, 4H, CH₂), 1.68 (m, 2H, CH₂), 1.78 (m, 2H, CH₂), 2.74–2.93 (m, 4H, CH₂), 4.26 (m, 2H, OCH₂), 6.84 (s, 1H, CH). – **¹³C NMR (CDCl₃):** δ = 13.58 (q, CH₃), 21.43 (t, CH₂), 24.12 (t, CH₂), 24.37 (t, CH₂), 25.52 (t, CH₂), 25.98 (t, CH₂), 27.75 (t, CH₂), 62.95 (d, CH), 64.67 (t, OCH₂), 108.43 (s, SCN), 134.44 (s, C, Ar), 145.37 (s, C, Ar), 162.74 (s, C=O). – **HRMS (ESI):** m/z = 295.1225 [C₁₃H₁₉N₄O₂S, M + H⁺, calcd.: 295.1229], 317.1096 [C₁₃H₁₈N₄NaO₂S, M + Na⁺, calcd.: 317.1048], 333.0827 [C₁₃H₁₈KN₄O₂S, M + K⁺, calcd.: 333.0788]. – **IR (CCl₄):** $\tilde{\nu}/\text{cm}^{-1}$ = 2162 (SCN), 1753 (C=O).



2.2.4 HX-elimination reactions of 1-azido-1-halo compounds with *t*-BuOK

Azide **2d**, **2g**, or **3d** (1.0 mmol, 1 eq) was dissolved in anhydrous Et₂O (20 mL). To this solution, stirred at –20 °C, KO^tBu (5 eq) was added in portions and stirred for 2 h at 0 °C. The mixture was filtered over silica-gel and the solid was extracted with Et₂O (20 mL). In the case of **12**, the solvent was removed under reduced pressure to maintain a mixture of **c-12** and **t-12** (74%, 1:9) by flash chromatography (*n*-hexane). The vinyl azides **13**, **14** and **17** were obtained in Et₂O and *t*-BuOH by evaporation. In the case of the 1*H*-cycloocta-1,2,3-triazoles **15**, **16** and **18**, the combined organic phases were treated drop-wise with cyclooctyne (1.1 eq) in Et₂O (5 mL) at –20 °C

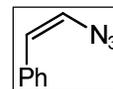
and stirred for 2 h at RT. The volatiles were removed under reduced pressure and the crude product was purified by flash chromatography over silica-gel (Et₂O/*n*-hexane 3:1). In the case of **2d**, 1-(1-chlorovinyl)-4,5,6,7,8,9-hexahydro-1*H*-cycloocta-1,2,3-triazole (**16**) and (*E*)-1-(2-chlorovinyl)-4,5,6,7,8,9-hexahydro-1*H*-cycloocta-1,2,3-triazole (*t*-**15**) were obtained. After the reaction of **3d**, (*Z*)-1-(2-chlorovinyl)-4,5,6,7,8,9-hexahydro-1*H*-cycloocta-1,2,3-triazole (*c*-**15**), (*E*)-1-(2-chlorovinyl)-4,5,6,7,8,9-hexahydro-1*H*-cycloocta-1,2,3-triazole (*t*-**15**) and 1-(1-bromovinyl)-4,5,6,7,8,9-hexahydro-1*H*-cycloocta-1,2,3-triazole (**18**) were isolated.

Synthesis of 1-(1-chlorovinyl)-4,5,6,7,8,9-hexahydro-1*H*-cycloocta-1,2,3-triazole (14**) and (*E*)-1-(2-chlorovinyl)-4,5,6,7,8,9-hexahydro-1*H*-cycloocta-1,2,3-triazole (*t*-**13**)**

1-Azido-1,2-dichloroethane (**2d**, 107 mg, 0.764 mmol) was dissolved in anhydrous Et₂O (20 mL). To this solution, stirred at -20 °C, KO^tBu (450 mg, 4 mmol) was added in portions and stirred for 2 h at 0 °C. The mixture was filtered over silica-gel and the solid was extracted with Et₂O (20 mL). The combined organic phases were treated drop-wise with cyclooctyne (91 mg, 0.84 mmol, 0.1 mL) in Et₂O (5 mL) at -20 °C and stirred for 2 h at RT. The volatiles were removed under reduced pressure and the crude product was purified by flash chromatography over silica-gel (Et₂O/*n*-hexane 3:1) to obtain 1-(1-chlorovinyl)-4,5,6,7,8,9-hexahydro-1*H*-cycloocta-1,2,3-triazole (**16**, 22 mg, 0.104 mmol, 14%) and (*E*)-1-(2-chlorovinyl)-4,5,6,7,8,9-hexahydro-1*H*-cycloocta-1,2,3-triazole (*t*-**15**, 2 mg, 0.009 mmol, 1%).

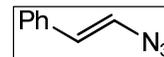
(*Z*)-(2-Azidovinyl)benzene (*c*-12**)**

¹H NMR (CDCl₃): δ = 5.69 (d, ³J = 8.5 Hz, 1H, CH), 6.34 (d, ³J = 8.5 Hz, 1H, CH), 7.19–7.33 (m, 5H, CH, Ph). – IR (CDCl₃): $\tilde{\nu}/\text{cm}^{-1}$ = 2110 (N₃), 1638 (Ph). NMR data of *c*-**12**, see also ref. [23].



(*E*)-(2-Azidovinyl)benzene (*t*-12**)**

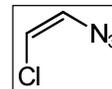
¹H NMR (CDCl₃): δ = 6.27 (d, ³J = 13.8 Hz, 1H, CH), 6.60 (d, ³J = 13.8 Hz, 1H, CH), 7.19–7.33 (m, 5H, CH, Ph). – ¹³C NMR (CDCl₃): δ = 119.77 (d, CH),



125.79 (d, CH), 126.65 (d, CH), 127.36 (d, CH), 128.73 (d, CH), 134.99 (s, C). – IR (CDCl₃): $\tilde{\nu}/\text{cm}^{-1} = 2110$ (N₃), 1638 (Ph). NMR data of *t*-12, see also ref. [23].

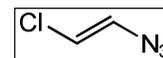
(Z)-1-Azido-2-chloroethene (c-13)

¹H NMR (CDCl₃): $\delta = 5.42$ (d, ³J = 5.6 Hz, 1H, CH), 6.37 (d, ³J = 5.6 Hz, 1H, CH). – ¹³C NMR (CDCl₃): $\delta = 109.56$ (d, CH), 129.59 (d, CH).



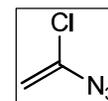
(E)-1-Azido-2-chloroethene (t-13)

¹H NMR (CDCl₃): $\delta = 5.82$ (d, ³J = 12.0 Hz, 1H, CH), 6.31 (d, ³J = 12.0 Hz, 1H, CH). – ¹³C NMR (CDCl₃): $\delta = 107.01$ (d, CH), 126.97 (d, CH).



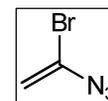
1-Azido-1-chloroethene (14)

¹H NMR (CDCl₃): $\delta = 4.76$ (d, ²J = 2.9 Hz, 1H, CH₂), 4.86 (d, ²J = 2.9 Hz, 1H, CH₂).



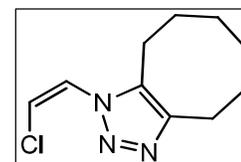
1-Azido-1-bromoethene (17)

¹H NMR (CDCl₃): $\delta = 4.72$ (d, ²J = 2.8 Hz, 1H, CH₂), 5.21 (d, ²J = 2.8 Hz, 1H, CH₂).



(Z)-1-(2-Chlorovinyl)-4,5,6,7,8,9-hexahydro-1H-cycloocta-1,2,3-triazole (c-15)

colorless oil. – yield: 15%. – ¹H NMR (CDCl₃): $\delta = 1.42$ –1.54 (m, 4H, CH₂), 1.72–1.84 (m, 4H, CH₂), 2.73 (m, 2H, CH₂), 2.93 (m, 2H, CH₂), 6.51 (d, ³J = 5.9 Hz, 1H, CH), 7.05 (d, ³J = 5.9 Hz, 1H, CH). – ¹³C NMR (CDCl₃): $\delta = 21.78$ (t, CH₂), 24.31 (t, CH₂), 24.68

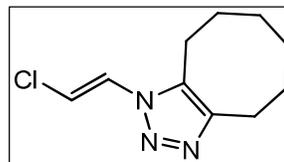


(t, CH₂), 25.90 (t, CH₂), 26.06 (t, CH₂), 27.98 (t, CH₂), 120.25 (d, CH), 123.48 (d, CH), 134.26 (s, C), 144.09 (s, C). – HRMS (ESI): $m/z = 212.0964$ [C₁₀H₁₅ClN₃, M + H⁺, calcd.: 212.0955], 234.0779 [C₁₀H₁₄ClN₃Na, M + Na⁺, calcd.: 234.0774], 250.0547 [C₁₀H₁₄ClKN₃, M + K⁺, calcd.: 250.0513].

(E)-1-(2-Chlorovinyl)-4,5,6,7,8,9-hexahydro-1H-cycloocta-1,2,3-triazole (t-15)

colorless oil. – yield: **2d**→**t-13**: 1%, **3d**→**t-13**: 6%. – ¹H NMR

(CDCl₃): δ = 1.42–1.53 (m, 4H, CH₂), 1.73 (m, 2H, CH₂), 1.84 (m, 2H, CH₂), 2.76 (m, 2H, CH₂), 2.91 (m, 2H, CH₂), 7.10 (d,

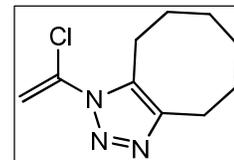


³J = 12.3 Hz, 1H, CH), 7.14 (d, ³J = 12.3 Hz, 1H, CH). – ¹³C NMR (CDCl₃): δ = 21.50 (t, CH₂), 24.40 (t, CH₂), 24.45 (t, CH₂), 25.87 (t, CH₂), 26.03 (t, CH₂), 28.25 (t, CH₂), 115.94 (d, CH), 124.26 (d, CH), 132.62 (s, C), 144.87 (s, C). – HRMS (ESI): m/z = 212.0963 [C₁₀H₁₅ClN₃, M + H⁺, calcd.: 212.0955], 234.0779 [C₁₀H₁₄ClN₃Na, M + Na⁺, calcd.: 234.0774].

1-(1-Chlorovinyl)-4,5,6,7,8,9-hexahydro-1H-cycloocta-1,2,3-triazole (16)

colorless oil. – yield: 14%. – ¹H NMR (CDCl₃): δ = 1.40–1.53 (m,

4H, CH₂), 1.70–1.85 (m, 4H, CH₂), 2.84 (m, 2H, CH₂), 2.88 (m, 2H, CH₂), 5.68 (d, ²J = 2.4 Hz, 1H, C=CH₂), 5.75 (d, ²J = 2.4 Hz,

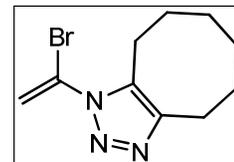


1H, C=CH₂). – ¹³C NMR (CDCl₃): δ = 21.77 (t, CH₂), 24.16 (t, CH₂), 24.94 (t, CH₂), 25.53 (t, CH₂), 26.61 (t, CH₂), 27.80 (t, CH₂), 116.45 (t, C=CH₂), 129.90 (s, CCl), 134.13 (s, C), 144.72 (s, C). – HRMS (ESI): m/z = 212.0967 [C₁₀H₁₅ClN₃, M + H⁺, calcd.: 212.0955], 234.0780 [C₁₀H₁₄ClN₃Na, M + Na⁺, calcd.: 234.0774], 250.0587 [C₁₀H₁₄ClKN₃, M + K⁺, calcd.: 250.0513].

1-(1-Bromovinyl)-4,5,6,7,8,9-hexahydro-1H-cycloocta-1,2,3-triazole (18)

colorless oil. – yield: 13%. – ¹H NMR (CDCl₃): δ = 1.40–1.55 (m,

4H, CH₂), 1.76 (m, 2H, CH₂), 1.83 (m, 2H, CH₂), 2.84 (m, 2H, CH₂), 2.89 (m, 2H, CH₂), 5.99 (d, ²J = 2.4 Hz, 1H, C=CH₂), 6.06



(d, ²J = 2.4 Hz, 1H, C=CH₂). – ¹³C NMR (CDCl₃): δ = 21.98 (t, CH₂), 24.22 (t, CH₂), 24.99 (t, CH₂), 25.59 (t, CH₂), 26.52 (t, CH₂), 27.75 (t, CH₂), 117.03 (s, CBr), 122.20 (t, C=CH₂), 134.12 (s, C), 144.72 (s, C). – HRMS (ESI): m/z = 256.0412 [C₁₀H₁₅BrN₃, M + H⁺, calcd.: 256.0449], 278.0241 [C₁₀H₁₄BrN₃Na, M + Na⁺, calcd.: 278.0269], 293.9984 [C₁₀H₁₄BrKN₃, M + K⁺, calcd.: 294.0008].

2.3 Synthesis of the α -azidoalkyl esters

2.3.1 Method A: Esterification of pure α -azido alcohols with acyl chlorides

The α -azido alcohol **5** (1.0 mmol, 1 eq), as mentioned before, was dissolved in cold ($-50\text{ }^{\circ}\text{C}$) dichloromethane (2 mL), and to this solution was added, drop-wise, acetyl chloride or pivaloyl chloride (1 eq) in dichloromethane (1 mL). The mixture was stirred for 16 h by slow warm-up to room temperature. The suspension was poured into ice water (5 mL) and extracted three times with dichloromethane. The extracts were washed with aqueous sodium bicarbonate (5%) and twice with aqueous saturated sodium chloride. The organic layers were dried over magnesium sulfate, and the solvent was removed *in vacuo* at $0\text{ }^{\circ}\text{C}$ leading to the respective esters, which were recondensed at ca. 0.005 mbar.

2.3.2 Method B: Esterification using the equilibrium mixture of α -azido alcohols and aldehydes/ HN_3

To a solution of hydrazoic acid (2 eq) in chloroform (1 mL), maintained at $-50\text{ }^{\circ}\text{C}$, was carefully added, drop-wise, the respective freshly distilled aldehyde (1.0 mmol, 1 eq) and subsequently acetyl chloride or pivaloyl chloride (1 eq) in chloroform (1 mL) within 10 min. The mixture was stirred for 48 h by slow warm-up to room temperature. The workup was done as mentioned in 2.3.1.

2.3.3 Method C: One-pot synthesis of α -azidoalkyl esters from aldehydes

To a solution of freshly distilled aldehyde (1.0 mmol, 1 eq) and acetyl chloride or pivaloyl chloride (1 eq) in chloroform (2 mL), stirred at $-35\text{ }^{\circ}\text{C}$, was added, drop-wise, sulfuric acid (0.5 eq). Sodium azide (1 eq) was given in portions to the reaction mixture, stirred 1.5 h at the same temperature, warmed to room temperature and stirred for further 48 h. The workup was done as mentioned in 2.3.1.

Synthesis of 1-azidoethyl acetate (**19b**)

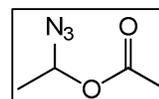
Freshly distilled acetaldehyde (**4b**, 44 mg, 1 mmol, 56 μL) was added drop-wise to a solution of hydrazoic acid in chloroform (2M, 1 mL), stirred at $-5\text{ }^{\circ}\text{C}$. After complete addition, the reaction mixture was allowed to warm to room temperature within 2 h.

Subsequently, the reaction mixture was cooled to $-55\text{ }^{\circ}\text{C}$, and all the volatiles were recondensed at ca. 0.005 mbar. The residue so obtained was α -azido ethanol (**5b**).

The α -azido alcohol **5b** was dissolved in cold ($-50\text{ }^{\circ}\text{C}$) dichloromethane (2 mL), and to this solution was added, drop-wise, acetyl chloride (157 mg, 2 mmol, 0.14 mL) in dichloromethane (1 mL). The mixture was stirred for 16 h by slow warm-up to room temperature. The suspension was poured into ice water (5 mL), extracted three times with dichloromethane (5 mL). The extracts were washed with aqueous sodium bicarbonate (5%, 5 mL) and twice with aqueous saturated sodium chloride (5 mL). The organic layers were dried over magnesium sulfate, and the solvent was removed *in vacuo* at $0\text{ }^{\circ}\text{C}$ leading to 1-azidoethyl acetate (**19b**, 44 mg, 0.34 mmol, 34%) after recondensation at ca. 0.005 mbar.

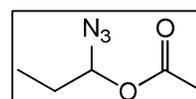
1-Azidoethyl acetate (**19b**)

colorless liquid. – **yield**: 33–44% (based on aldehyde and used method). – **$^1\text{H NMR}$ (CDCl_3)**: $\delta = 1.76$ (d, $^3J = 6.0$ Hz, 3H, CHCH_3), 2.09 (s, 3H, CCH_3), 6.50 (q, $^3J = 6.0$ Hz, 1H, CH). – **$^{13}\text{C NMR}$ (CDCl_3)**: $\delta = 20.7$ (q, CHCH_3), 25.0 (q, CCH_3), 80.6 (dq, $^1J(^{13}\text{C}, ^1\text{H}) = 168.70$ Hz, $^2J(^{13}\text{C}, ^1\text{H}) = 4.5$ Hz, CH), 168.6 (s, CO). – **IR (CCl_4)**: $\tilde{\nu}/\text{cm}^{-1} = 2137$ (N_3 , asym.), 1770 (C=O), 1274 (N_3 , sym.). – **HRMS (ESI)**: $m/z = 169.0456$ [$\text{C}_4\text{H}_8\text{N}_3\text{NaO}_3$, $\text{M} + \text{NaOH}^+$, calcd.: 169.0458].



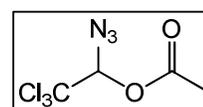
1-Azidopropyl acetate (**19c**)

colorless liquid. – **yield**: 23–54% (based on aldehyde and used method). – **$^1\text{H NMR}$ (CDCl_3)**: $\delta = 1.03$ (t, $J = 7.4$ Hz, 3H, CH_2CH_3), 2.01 (m, 2H, CH_2), 2.11 (s, 3H, CH_3), 6.35 (t, $J = 5.7$ Hz, 1 H, 1-H). – **$^{13}\text{C NMR}$ (CDCl_3)**: $\delta = 9.0$ (q, CH_2CH_3), 20.8 (t, CH_2CH_3), 31.3 (q, CCH_3), 85.1 (d, CH), 168.9 (s, CO). – **IR (CCl_4)**: $\tilde{\nu}/\text{cm}^{-1} = 2103$ (N_3), 1777 (C=O). – **HRMS (ESI)**: $m/z = 183.0605$ [$\text{C}_5\text{H}_{10}\text{N}_3\text{NaO}_3$, $\text{M} + \text{NaOH}^+$, calcd.: 183.0614].



1-Azido-2,2,2-trichloroethyl acetate (**19e**)

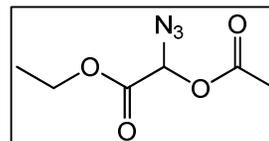
colorless liquid. – **yield**: 70–100% (based on aldehyde and used method). – **$^1\text{H NMR}$ (CDCl_3)**: $\delta = 2.24$ (s, 3H, CH_3), 6.17 (s, 1H, CH). – **$^{13}\text{C NMR}$ (CDCl_3)**: $\delta = 20.4$ (q, CH_3), 88.2 (d, CH), 97.2 (s,



CCl_3), 168.7 (s, CCH_3). – **IR** (CCl_4): $\tilde{\nu}/\text{cm}^{-1} = 2156$ (N_3 , asym.), 1727 ($\text{C}=\text{O}$), 1346 (N_3 , sym.). – **HRMS (ESI)**: $m/z = 270.9280$ [$\text{C}_4\text{H}_5\text{Cl}_3\text{N}_3\text{NaO}_3$, $\text{M} + \text{NaOH}^+$, calcd.: 270.9289].

Ethyl 2-acetoxy-2-azidoacetate (19f)

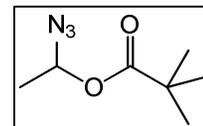
colorless liquid. – **yield**: 79–100% (based on aldehyde and used method). – **$^1\text{H NMR}$** (CDCl_3): $\delta = 1.33$ (t, $^3J = 7.2$ Hz, 3H, CH_2CH_3), 2.20 (s, 3H, CCH_3), 4.30 (q, $^3J = 7.2$ Hz, 2H, CH_2),



5.82 (s, 1 H, CH). – **$^{13}\text{C NMR}$** (CDCl_3): $\delta = 13.9$ (q, CH_2CH_3), 20.5 (q, CCH_3), 62.8 (t, CH_2), 79.7 (d, CH), 164.8 (s, CCH), 169.3 (s, CCH_3). – **IR** (CCl_4): $\tilde{\nu}/\text{cm}^{-1} = 2113$ (N_3 , asym.), 1739 ($\text{C}=\text{O}$), 1719 ($\text{C}=\text{O}$), 1288 (N_3 , sym.). – Anal. calcd. for $\text{C}_6\text{H}_9\text{N}_3\text{O}_4$ (187.15): C 38.51, H 4.85, N 22.45. Found: C 38.44, H 4.91, N 21.98.

1-Azidoethyl pivalate (20b)

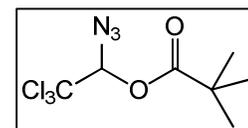
colorless liquid. – **yield**: 10% (based on aldehyde). – **$^1\text{H NMR}$** (CDCl_3): $\delta = 1.16$ (s, 9 H, CCH_3), 1.75 (d, $^3J = 6.4$ Hz, 3H, CHCH_3), 6.48 (q, $^3J = 6.4$ Hz, 1 H, 1-H). – **$^{13}\text{C NMR}$** (CDCl_3): $\delta = 24.9$ (q,



CHCH_3), 26.7 (q, $\text{C}(\text{CH}_3)_3$) 38.5 (s, $\text{C}(\text{CH}_3)_3$), 80.7 (d, CH), 176.4 (s, CO). – **IR** (CCl_4): $\tilde{\nu}/\text{cm}^{-1} = 2117$ (N_3 , asym.), 1730 ($\text{C}=\text{O}$), 1276 (N_3 , sym.). – **HRMS (ESI)**: $m/z = 211.0917$ [$\text{C}_7\text{H}_{14}\text{N}_3\text{NaO}_3$, $\text{M} + \text{NaOH}^+$, calcd.: 211.0927].

1-Azido-2,2,2-trichloroethyl pivalate (20e)

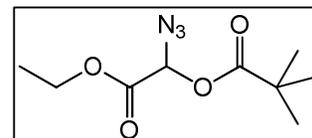
colorless liquid. – **yield**: 12% (based on aldehyde). – **$^1\text{H NMR}$** (CDCl_3): $\delta = 1.30$ (s, 9H, $\text{C}(\text{CH}_3)_3$), 6.11 (s, 1H, CH). – **$^{13}\text{C NMR}$** (CDCl_3): $\delta = 26.8$ (q, CH_3), 38.5 (s, $\text{C}(\text{CH}_3)_3$), 87.7 (d, CH), 97.8



(s, CCl_3), 176.6 (s, CO). – **IR** (CCl_4): $\tilde{\nu}/\text{cm}^{-1} = 2138$ (N_3 , asym.), 1727 ($\text{C}=\text{O}$), 1305 (N_3 , sym.). – **HRMS (ESI)**: $m/z = 312.9751$ [$\text{C}_7\text{H}_{11}\text{Cl}_3\text{N}_3\text{NaO}_3$, $\text{M} + \text{NaOH}^+$, calcd.: 312.9758].

1-Azido-2-ethoxy-2-oxoethyl pivalate (20f)

colorless liquid. – **yield**: 13–15% (based on aldehyde and used method). – **$^1\text{H NMR}$** (CDCl_3): $\delta = 1.26$ (t, $J = 7.2$ Hz, 3H, CH_2CH_3), 1.33 (s, 9H, $\text{C}(\text{CH}_3)_3$), 4.28 (dq, $^2J = 13.1$ Hz,



$^3J = 7.2$ Hz, 1H, CH_2), 4.30 (dq, $^2J = 13.1$ Hz, $^3J = 7.1$ Hz, 1H, CH_2), 5.78 (s, 1H, CH).
– ^{13}C NMR ($CDCl_3$): $\delta = 13.9$ (q, CH_2CH_3), 28.5 (q, $C(CH_3)_3$), 39.0 (s, $C(CH_3)_3$), 62.6 (t, CH_2), 79.7 (d, CH), 165.0 (s, $C(O)CH$), 176.8 (s, $C(O)C(CH_3)_3$). IR (CCl_4): $\tilde{\nu} / cm^{-1} = 2148$ (N_3), 1764 (C=O), 1727 (C=O). – HRMS (ESI): $m/z = 269.0950$ [$C_9H_{16}N_3NaO_5$, M + $NaOH^+$, calcd.: 269.0988].

2.4 Reactions of the α -azidoalkyl esters with cyclooctyne

To a solution of α -azidoalkyl ester (1 eq), which was prepared, as mentioned in 2.3.3, in distilled dichloromethane, stirred at 0 °C, was added, drop-wise, a solution of cyclooctyne (1.1 eq) in distilled dichloromethane (5 mL). The reaction mixture was stirred for 2 h at this temperature and then warmed to room temperature. Subsequently, the solvent was removed *in vacuo*, and the crude product was purified by flash chromatography over silica-gel (Et_2O/n -hexane 1:3 to 1:1).

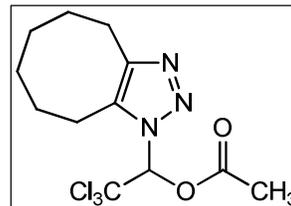
Synthesis of 2,2,2-trichloro-1-(4,5,6,7,8,9-hexahydro-1H-cycloocta-1,2,3-triazol-1-yl)ethyl acetate

To a solution of freshly distilled chloral (**4e**, 1.27 g, 8.61 mmol) and acetyl chloride (676 mg, 8.61 mmol, 0.62 mL) in chloroform (10 mL), stirred at –35 °C, was added, drop-wise, sulfuric acid (422 mg, 4.30 mmol, 0.23 mL). Sodium azide (560 mg, 8.61 mmol) was given in portions to the reaction mixture, stirred 1.5 h at the same temperature, warmed to room temperature and stirred for further 48 h. The suspension was poured into ice water (60 mL), and extracted three times with dichloromethane (30 mL). The extracts were washed with aqueous sodium bicarbonate (5%, 20 mL) and twice with aqueous saturated sodium chloride (25 mL). The organic layers were dried over magnesium sulfate. To this solution of 1-azido-2,2,2-trichloroethyl acetate (**19e**), stirred at 0 °C, was added, drop-wise, a solution of cyclooctyne (1.024 g, 9.47 mmol, 1.18 mL) in distilled dichloromethane (5 mL). The reaction mixture was stirred for 2 h at this temperature and then warmed to room temperature. Subsequently, the solvent was removed *in vacuo*, and the crude product was purified by flash chromatography over silica-gel (Et_2O/n -hexane 1:3 to 1:1) to obtain 2,2,2-trichloro-1-(4,5,6,7,8,9-hexahydro-1H-cycloocta-1,2,3-triazol-1-yl)ethyl acetate (2.61 g, 7.66 mmol, 89%).

2,2,2-Trichloro-1-(4,5,6,7,8,9-hexahydro-1*H*-cycloocta-1,2,3-triazol-1-yl)ethyl acetate

colorless oil. – **yield:** 89% (based on used aldehyde). – **¹H**

NMR (CDCl₃): δ = 1.44 (m, 2H, CH₂), 1.53 (m, 2H, CH₂), 1.75 (m, 2H, CH₂), 1.93 (m, 2H, CH₂), 2.27 (s, 3H, CH₃), 2.95 (m, 2H, CCH₂), 2.99 (m, 2H, CCH₂), 7.02 (s, 1H, CH). – **¹³C NMR**

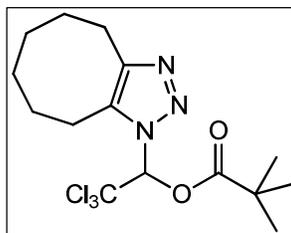


(CDCl₃): δ = 20.4 (q, CH₃), 22.1 (t, CH₂), 24.3 (t, CH₂), 24.4 (t, CH₂), 25.7 (t, CH₂), 26.1 (t, CH₂), 28.1 (t, CH₂), 82.3 (d, CH), 96.0 (s, CCl₃), 135.8 (s, C, Ar), 144.0 (s, C, Ar), 168.4 (s, C=O). – **HRMS (ESI):** 362.0208 [C₁₂H₁₆Cl₃N₃NaO₂, M + Na⁺, calcd.: 362.0206].

2,2,2-Trichloro-1-(4,5,6,7,8,9-hexahydro-1*H*-cycloocta-1,2,3-triazol-1-yl)ethyl pivalate

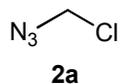
white solid. – **yield:** 9% (based on used aldehyde). – **mp.:**

104–106 °C. – **¹H NMR (CDCl₃):** δ = 1.27 (s, 9H, CH₃), 1.43 (m, 2H, CH₂), 1.53 (m, 2H, CH₂), 1.75 (m, 2H, CH₂), 1.93 (m, 2H, CH₂), 2.90–3.03 (m, 4H, CCH₂), 7.95 (s, 1H, CH). – **¹³C**

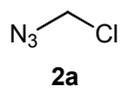
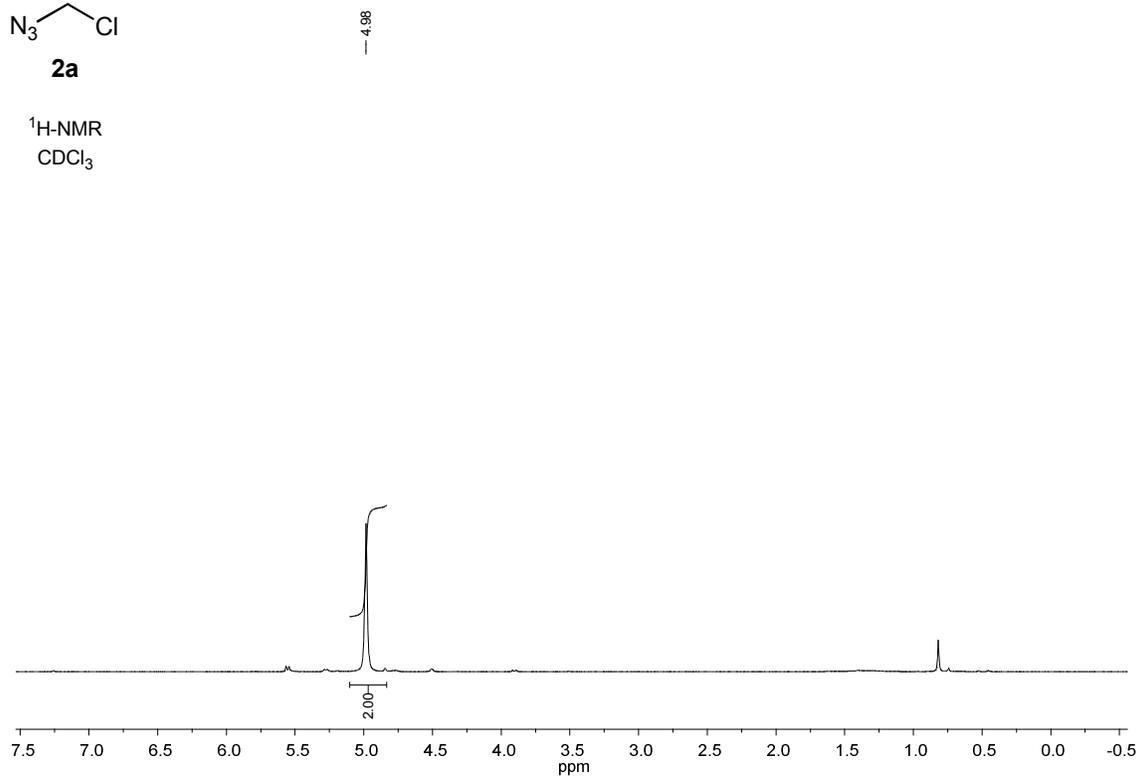


NMR (CDCl₃): δ = 22.1 (t, CH₂), 24.3 (t, CH₂), 24.4 (t, CH₂), 25.7 (t, CH₂), 26.2 (t, CH₂), 26.7 (q, C(CH₃)₃), 28.01 (t, CH₂), 39.1 (s, C(CH₃)₃), 82.4 (d, CH), 96.3 (s, CCl₃), 135.7 (s, C, Ar), 143.8 (s, C, Ar), 175.9 (s, C=O). – **Anal.** calcd. for **C₁₅H₂₂Cl₃N₃O₂ (382.71):** C 47.07, H 5.79, N 10.98. Found: C 47.04, H 5.67, N 10.89. – **HRMS (ESI):** 382.0878 [C₁₅H₂₃Cl₃N₃O₂, M + H⁺, calcd.: 382.0856], 404.0731 [C₁₅H₂₂Cl₃N₃NaO₂, M + Na⁺, calcd.: 404.0675], 420.0455 [C₁₅H₂₂Cl₃KN₃O₂, M + K⁺, calcd.: 420.0415].

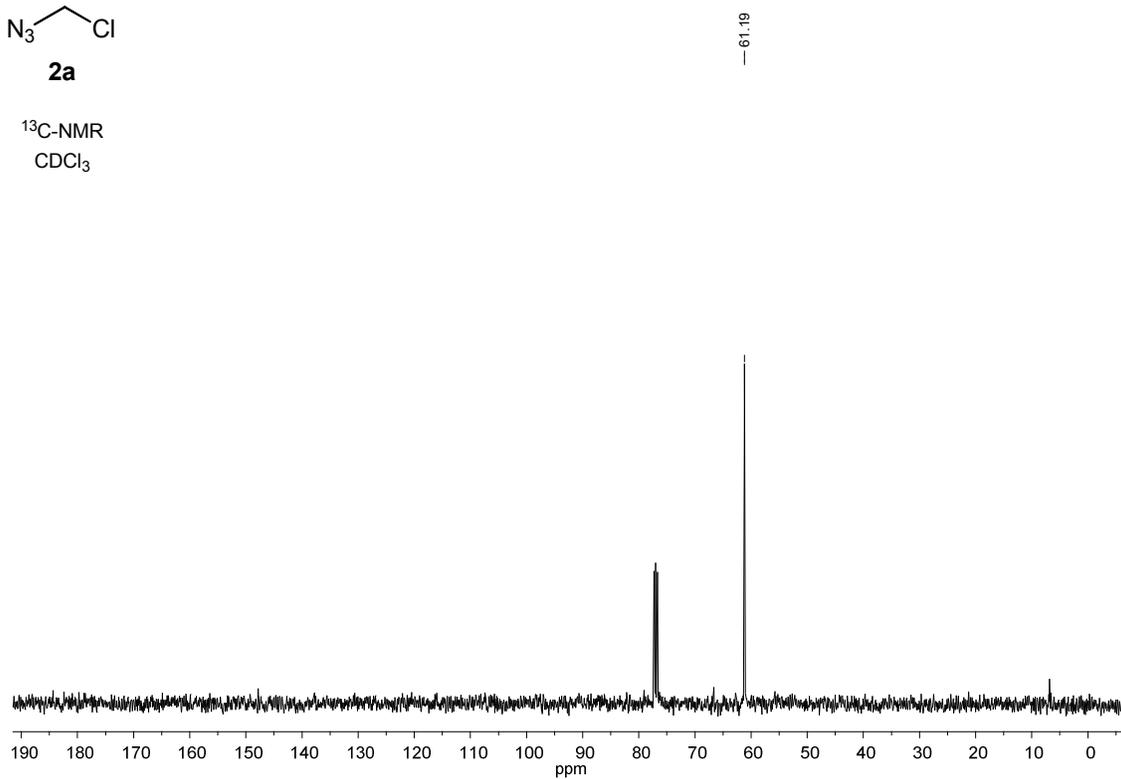
3 NMR Spectra

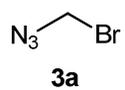


¹H-NMR
CDCl₃

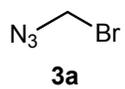
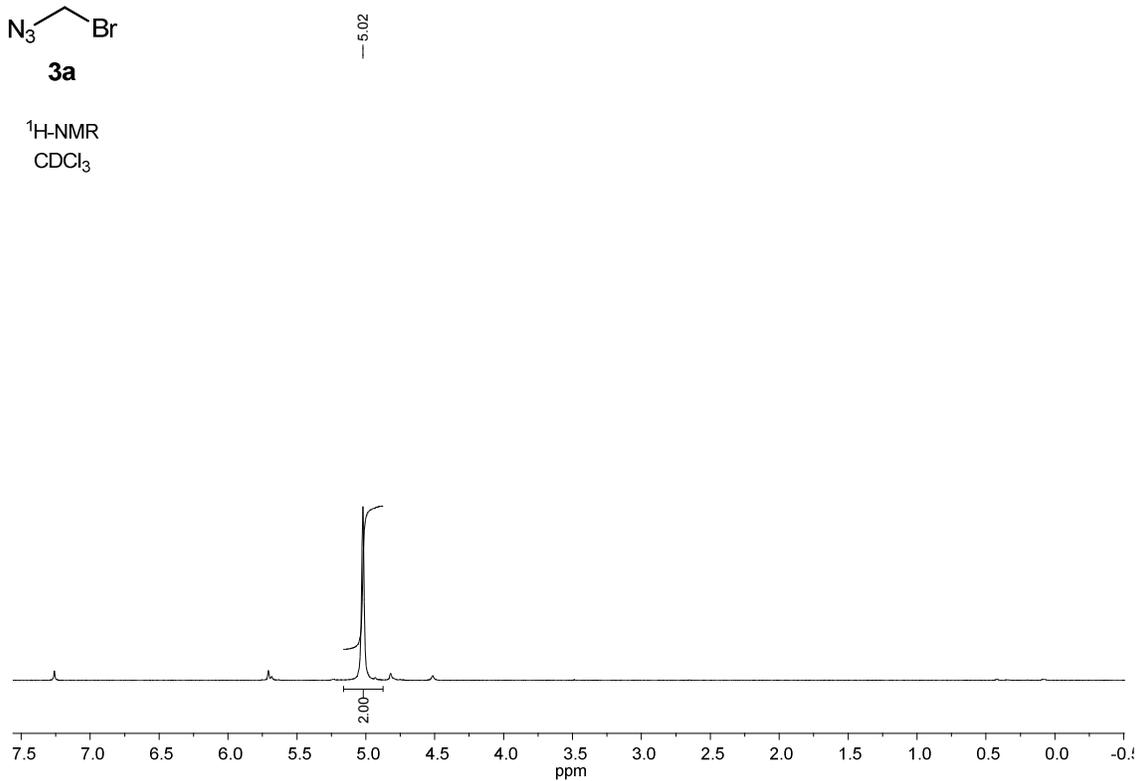


¹³C-NMR
CDCl₃

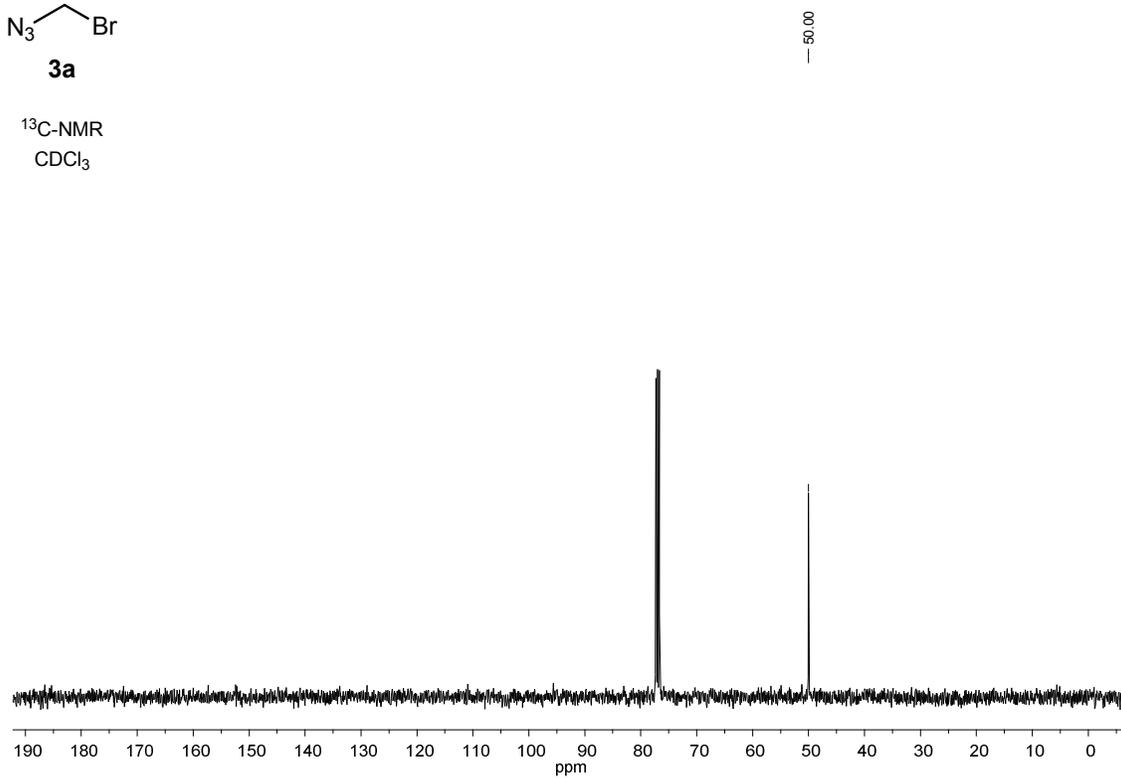


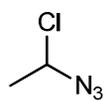


$^1\text{H-NMR}$
 CDCl_3



$^{13}\text{C-NMR}$
 CDCl_3



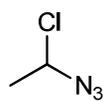
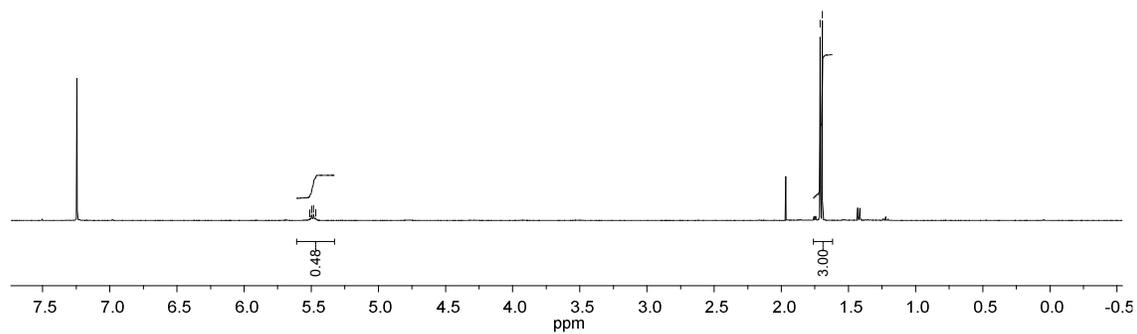


2b

¹H-NMR
CDCl₃

5.51
5.50
5.48
5.47

1.71
1.70

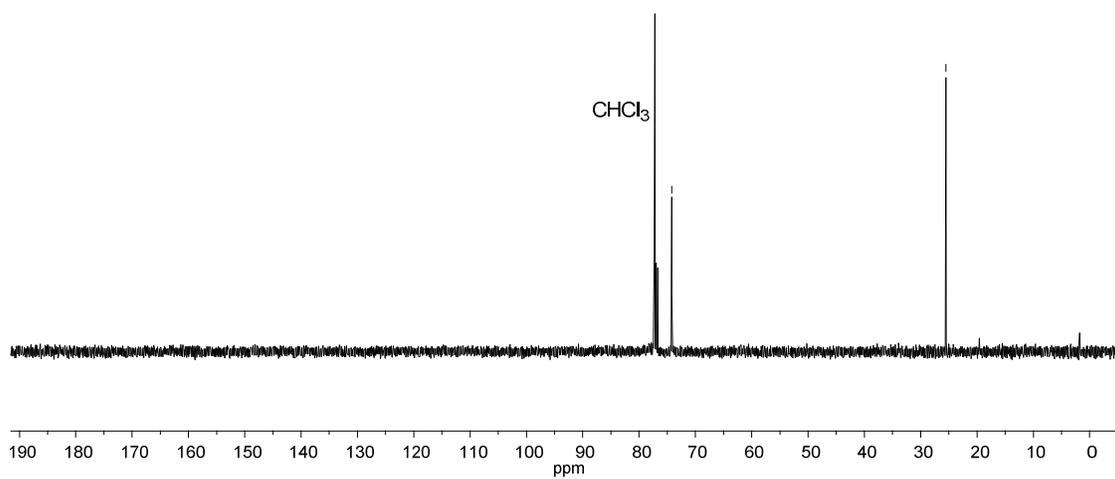


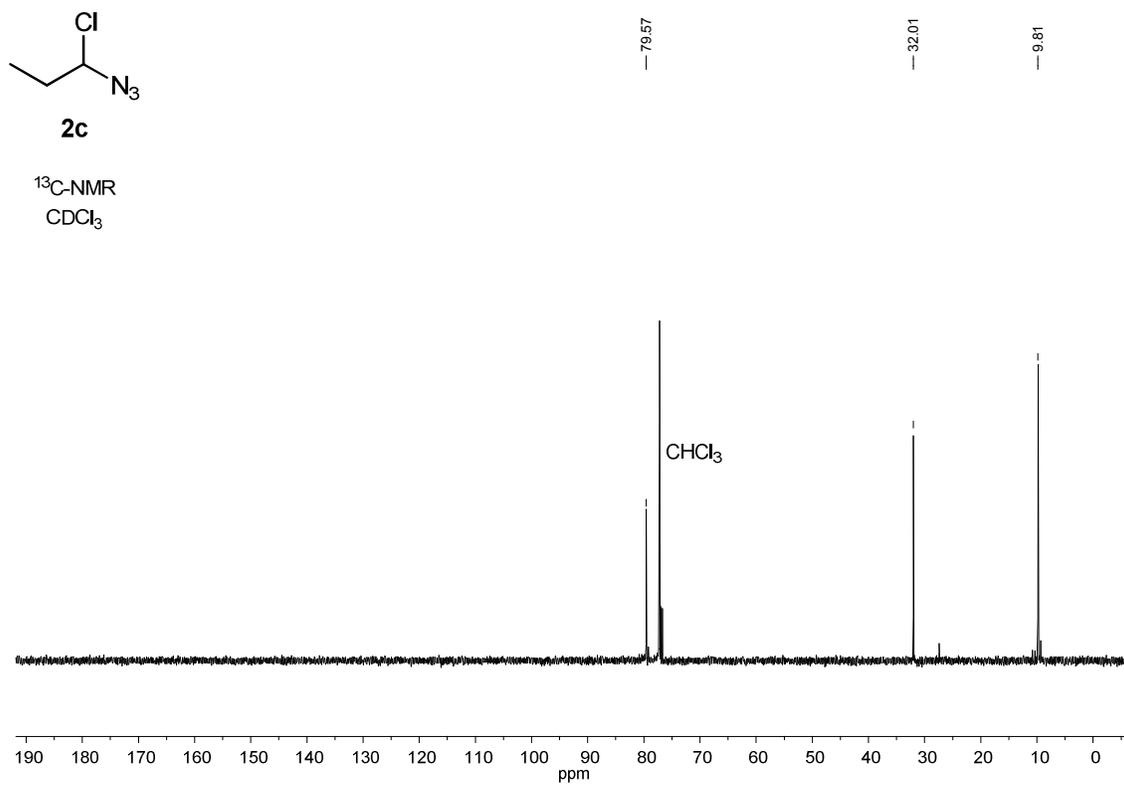
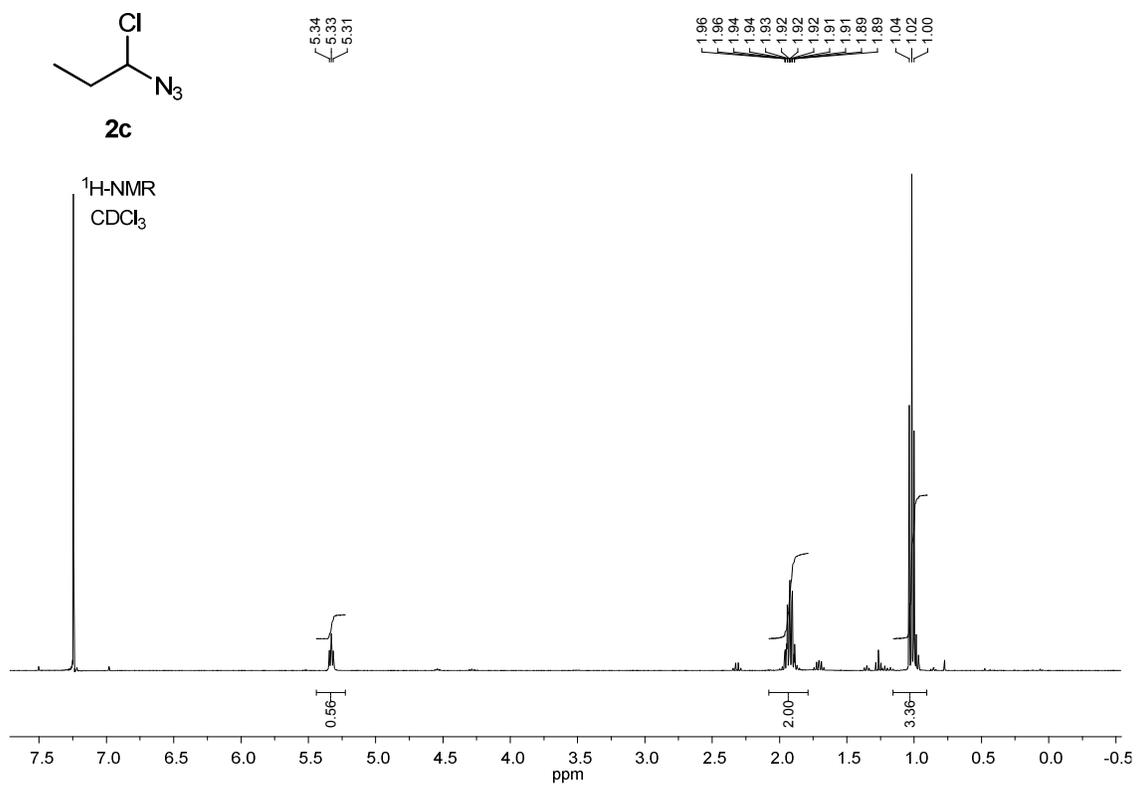
2b

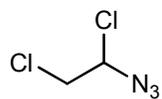
¹³C-NMR
CDCl₃

74.19

25.50

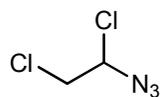
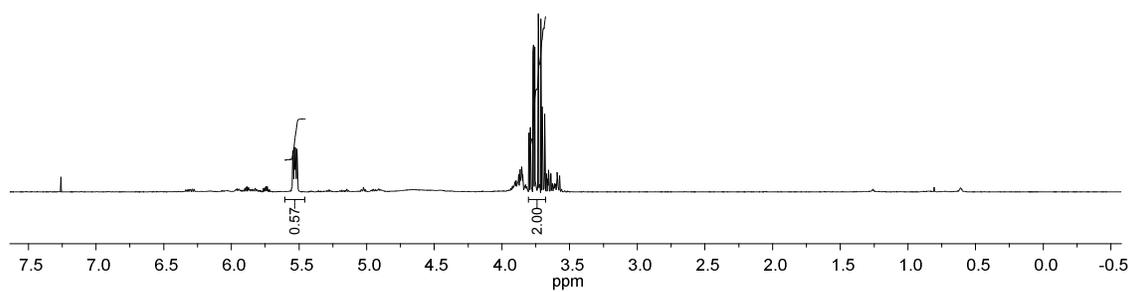
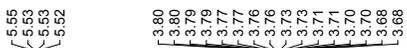






2d

¹H-NMR
CDCl₃

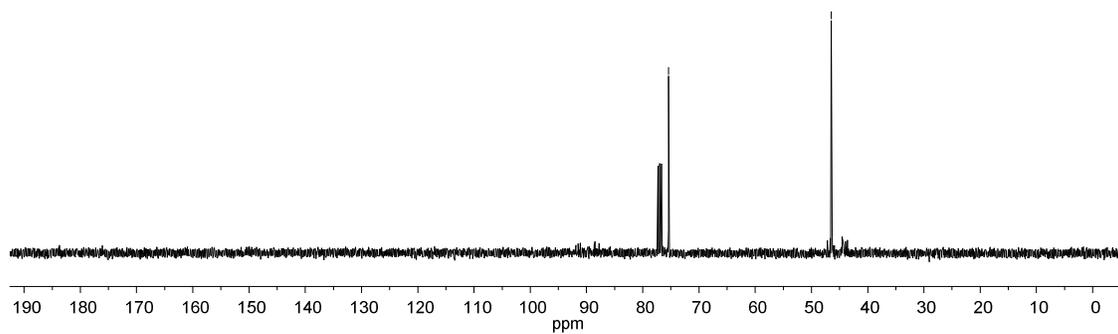


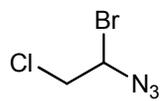
2d

¹H-NMR
CDCl₃

75.39

46.49



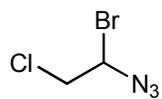
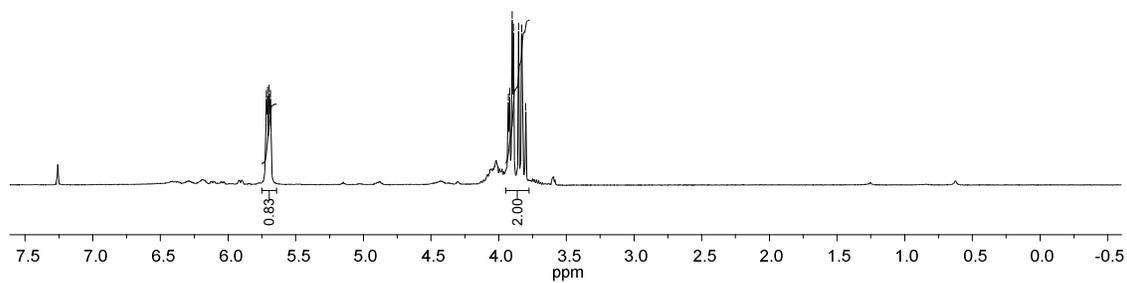


3d

¹H-NMR
CDCl₃

5.72
5.71
5.70
5.69

3.93
3.92
3.90
3.89
3.85
3.83
3.80

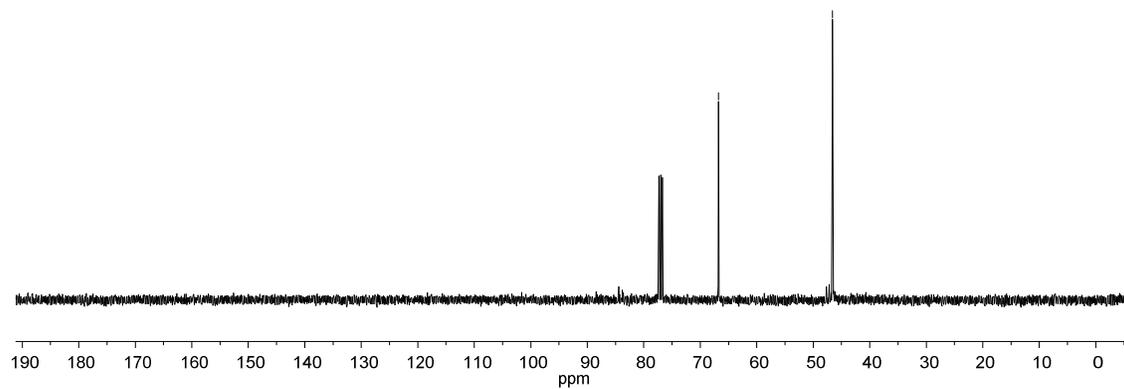


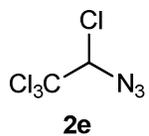
3d

¹³C-NMR
CDCl₃

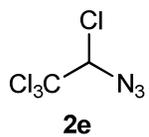
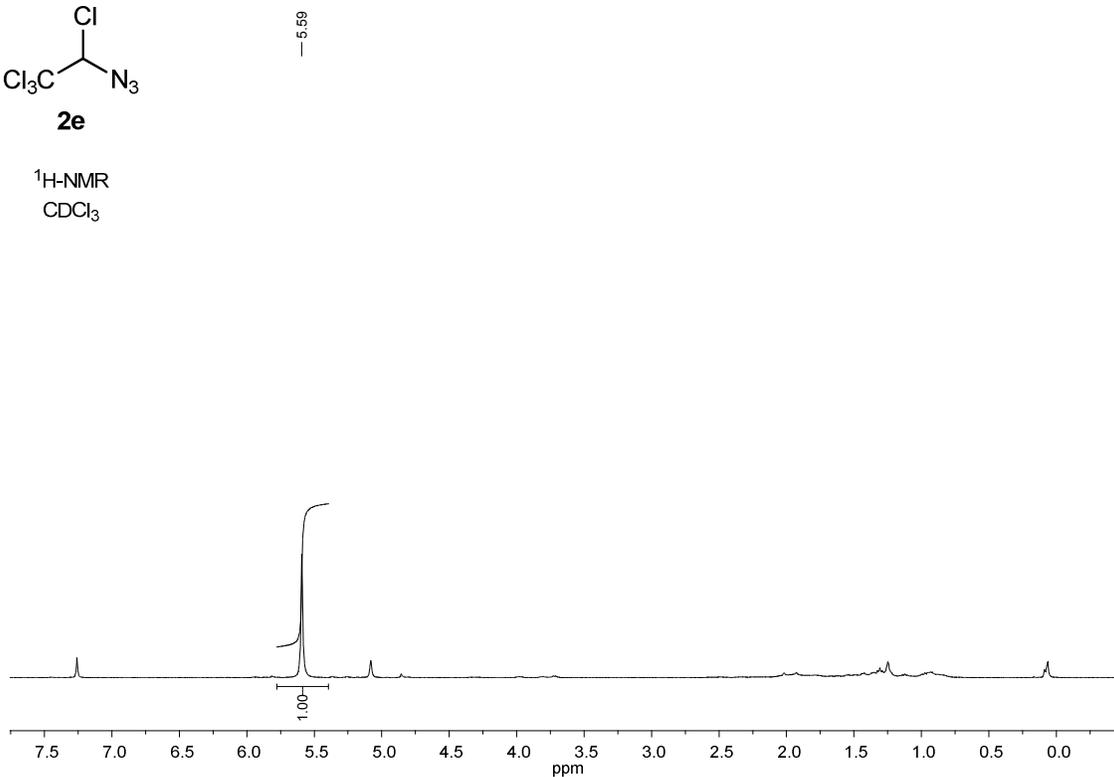
66.80

46.60

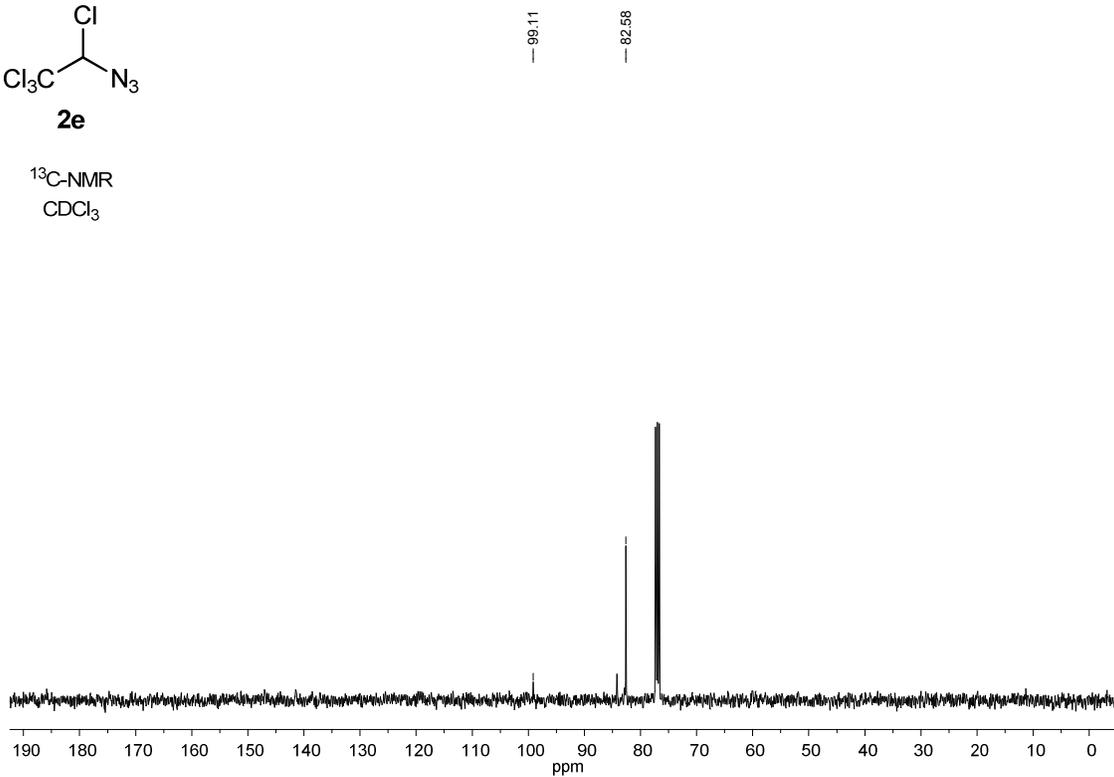


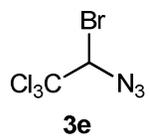


¹H-NMR
CDCl₃

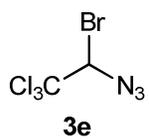
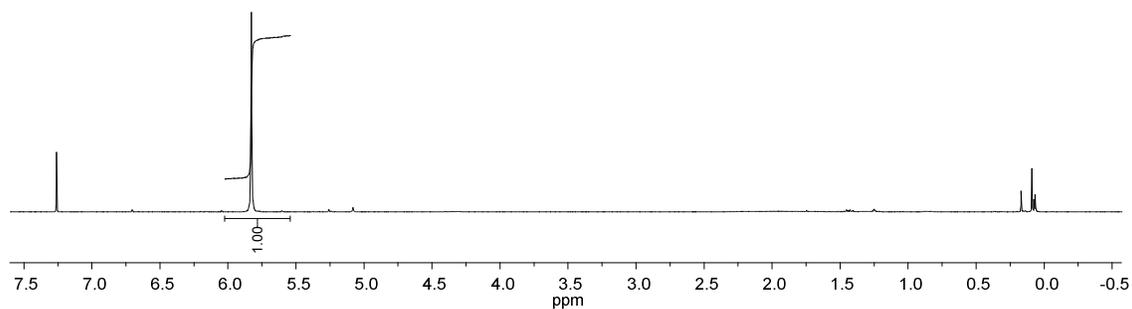


¹³C-NMR
CDCl₃

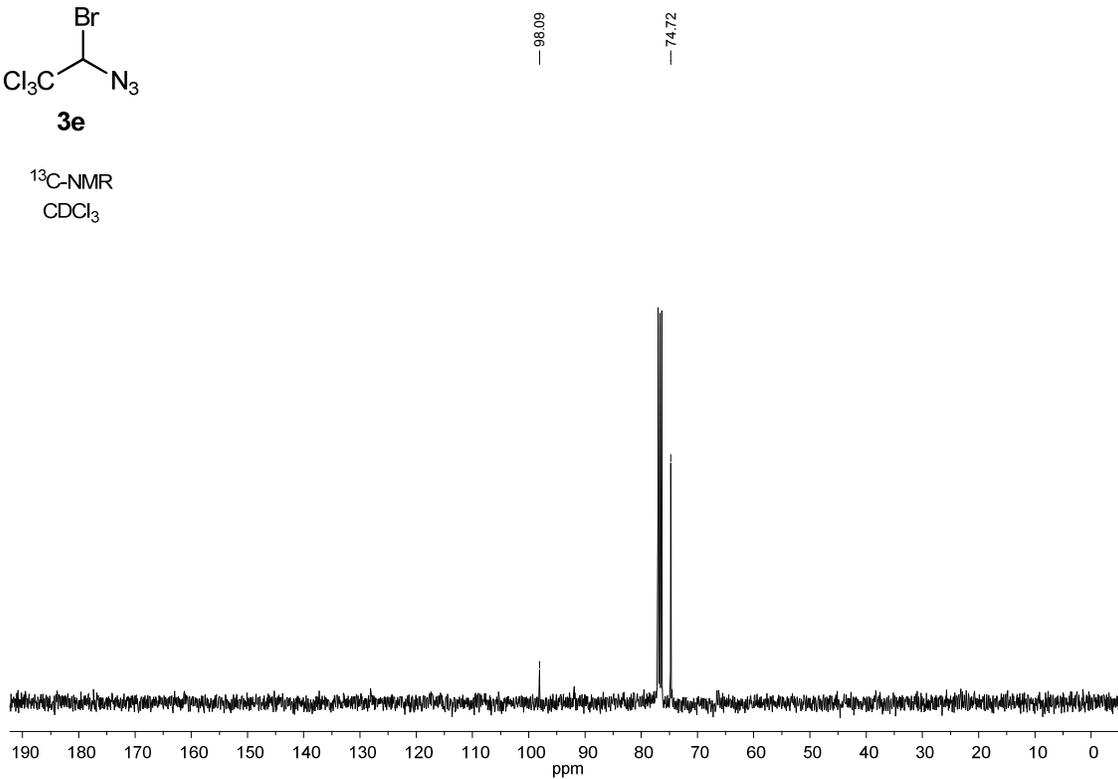


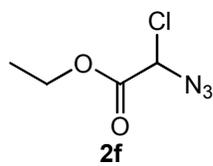


¹H-NMR
CDCl₃

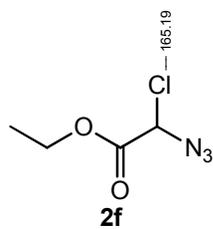
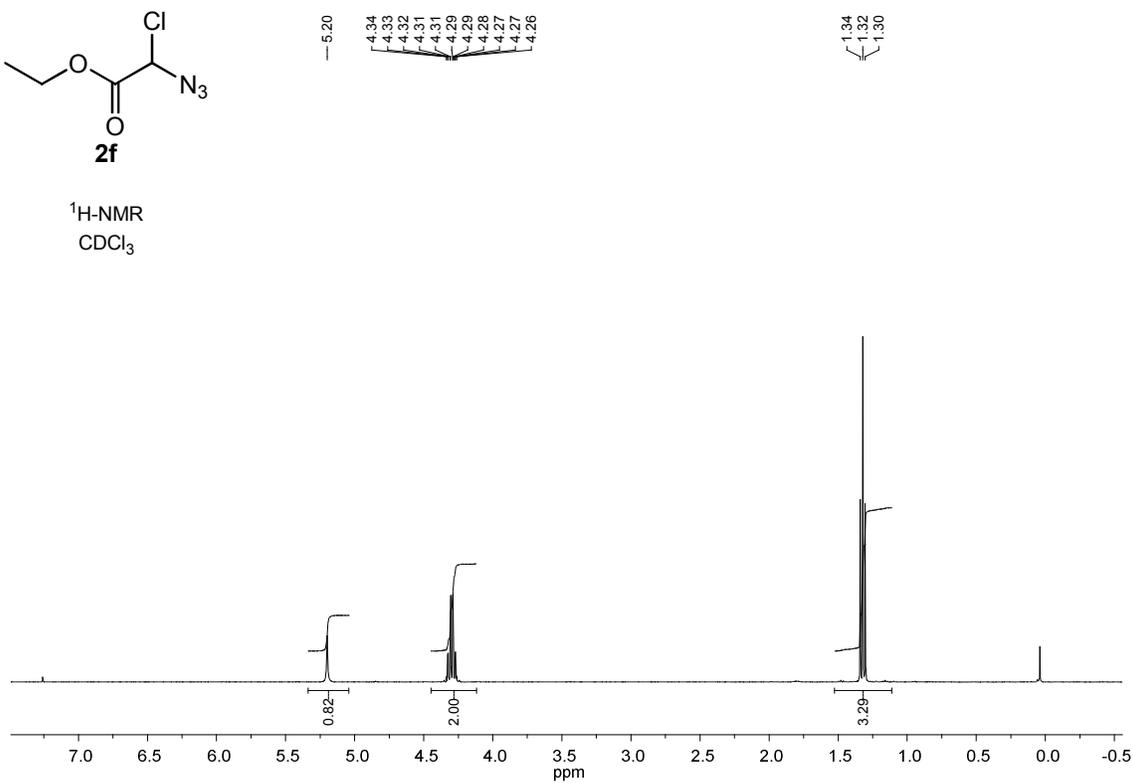


¹³C-NMR
CDCl₃

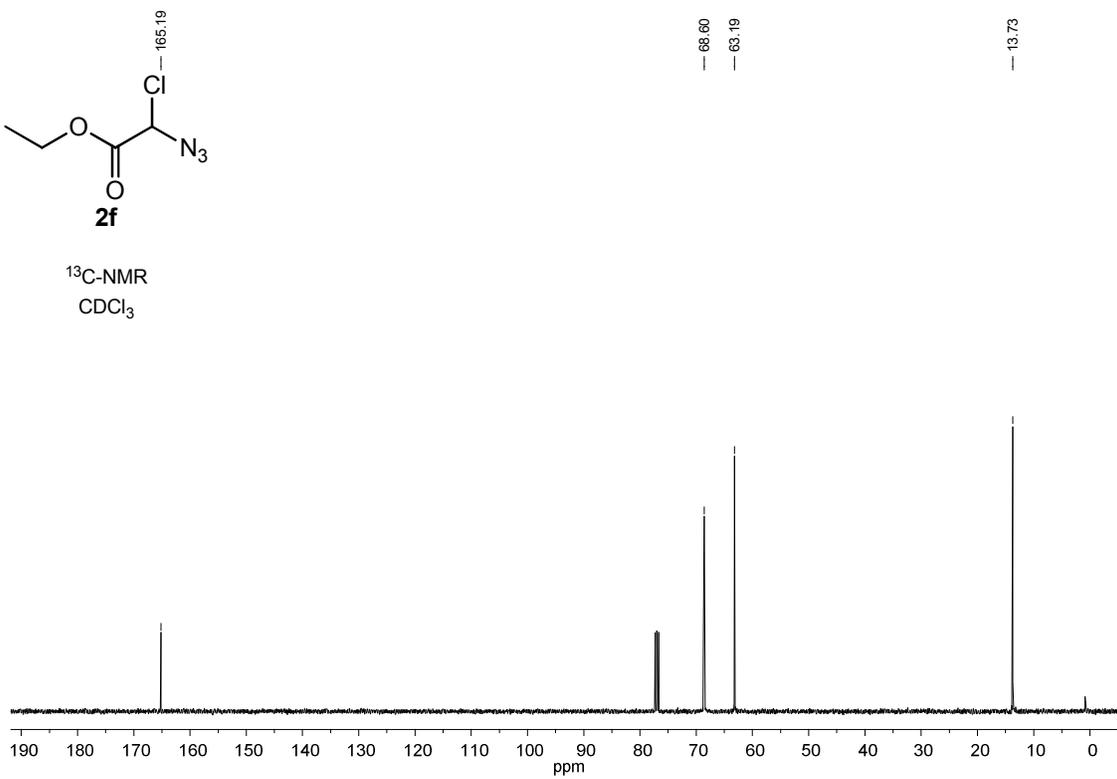


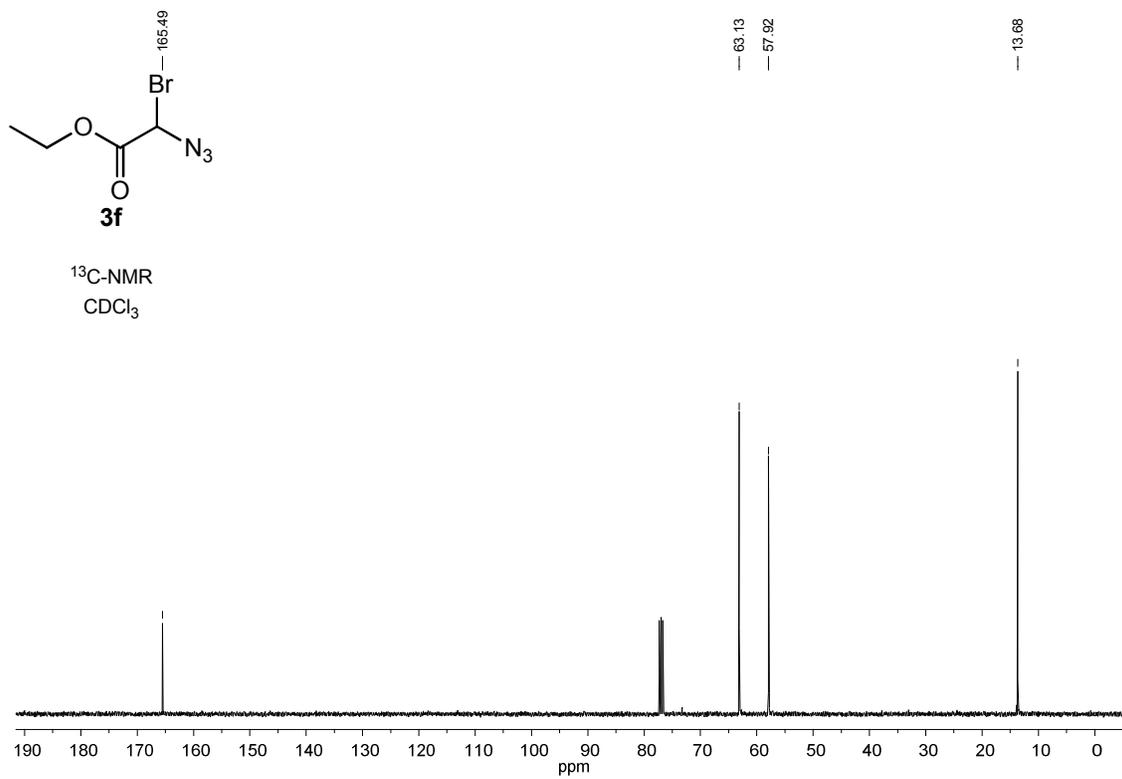
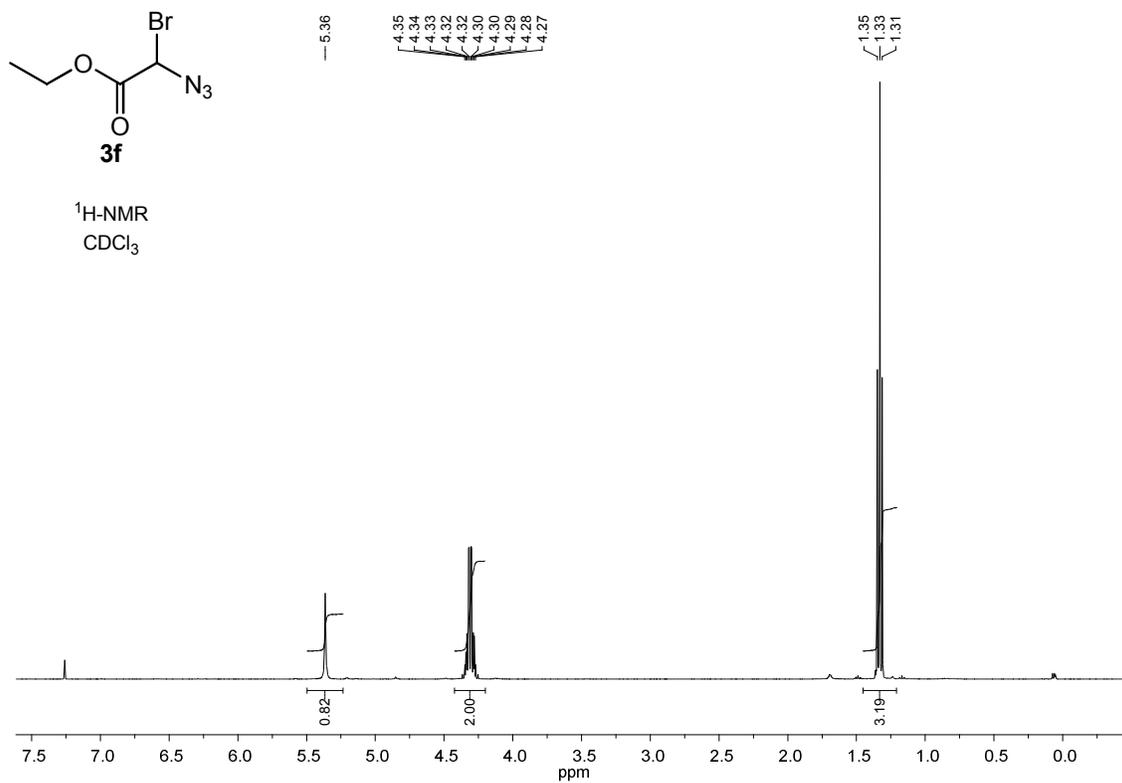


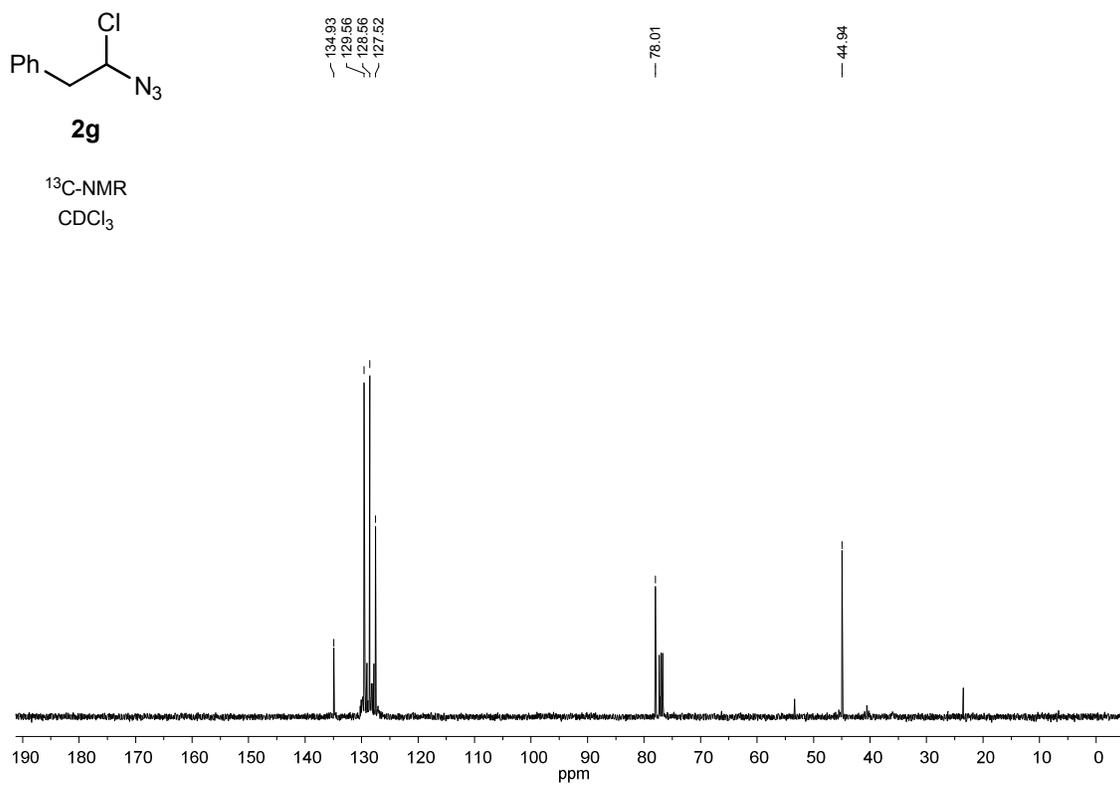
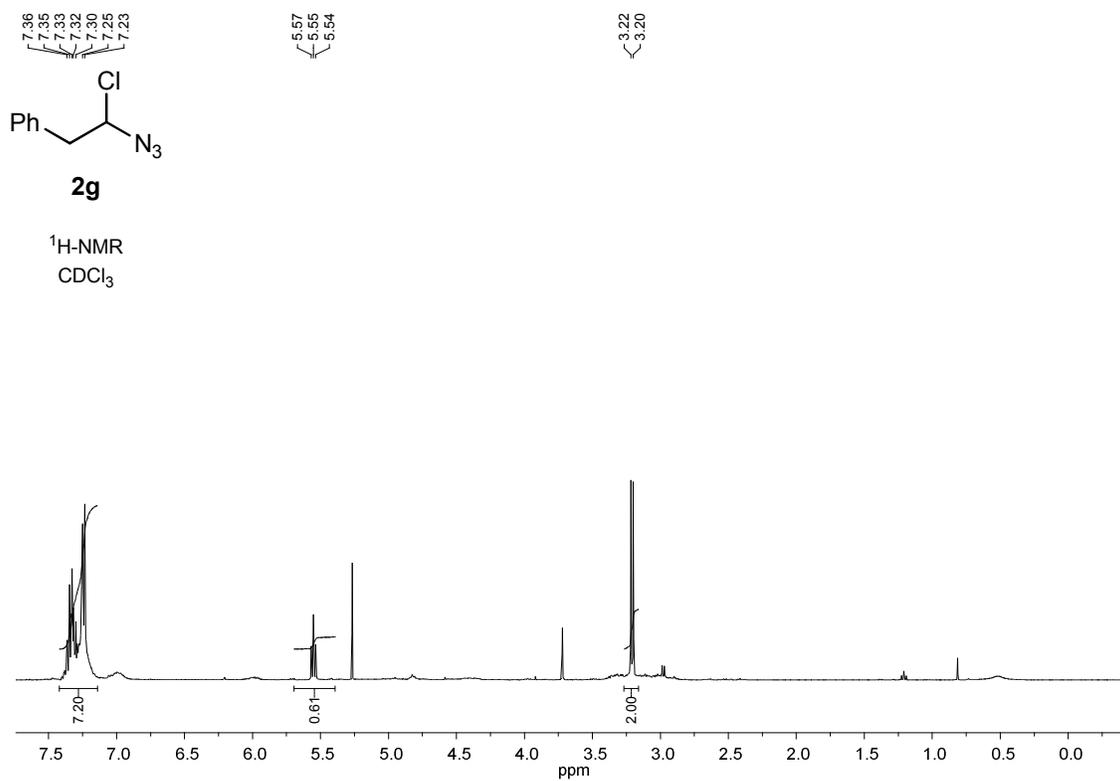
¹H-NMR
CDCl₃

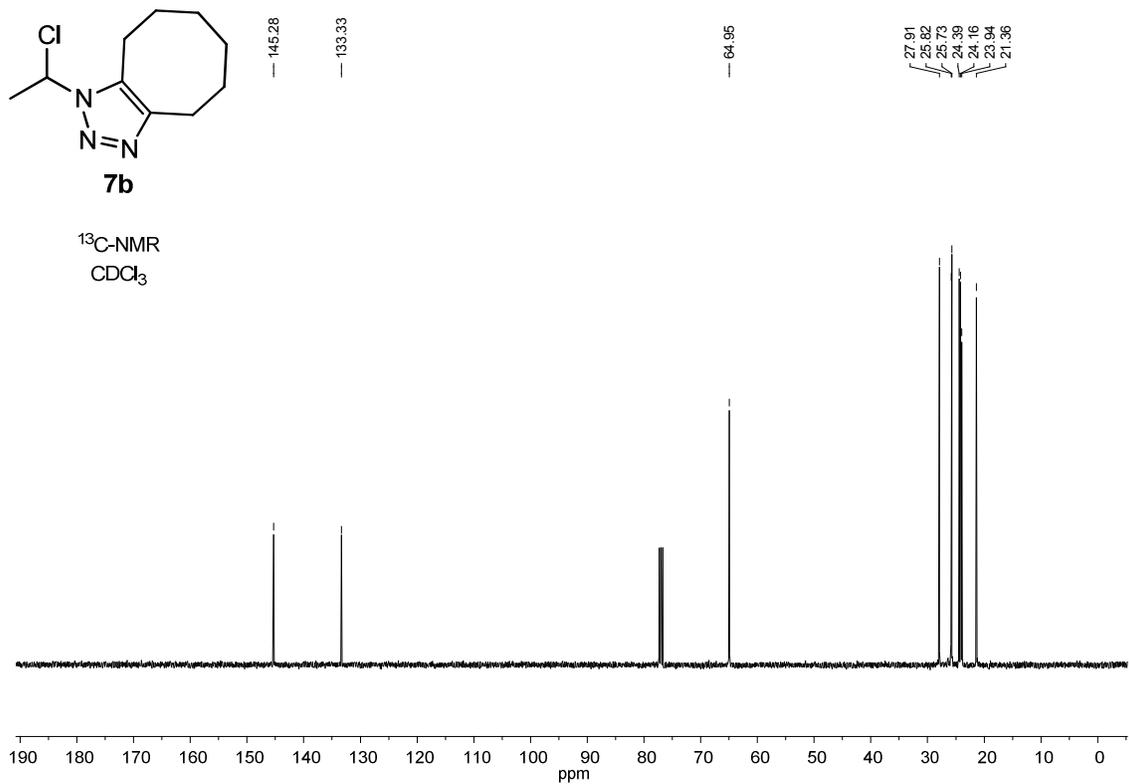
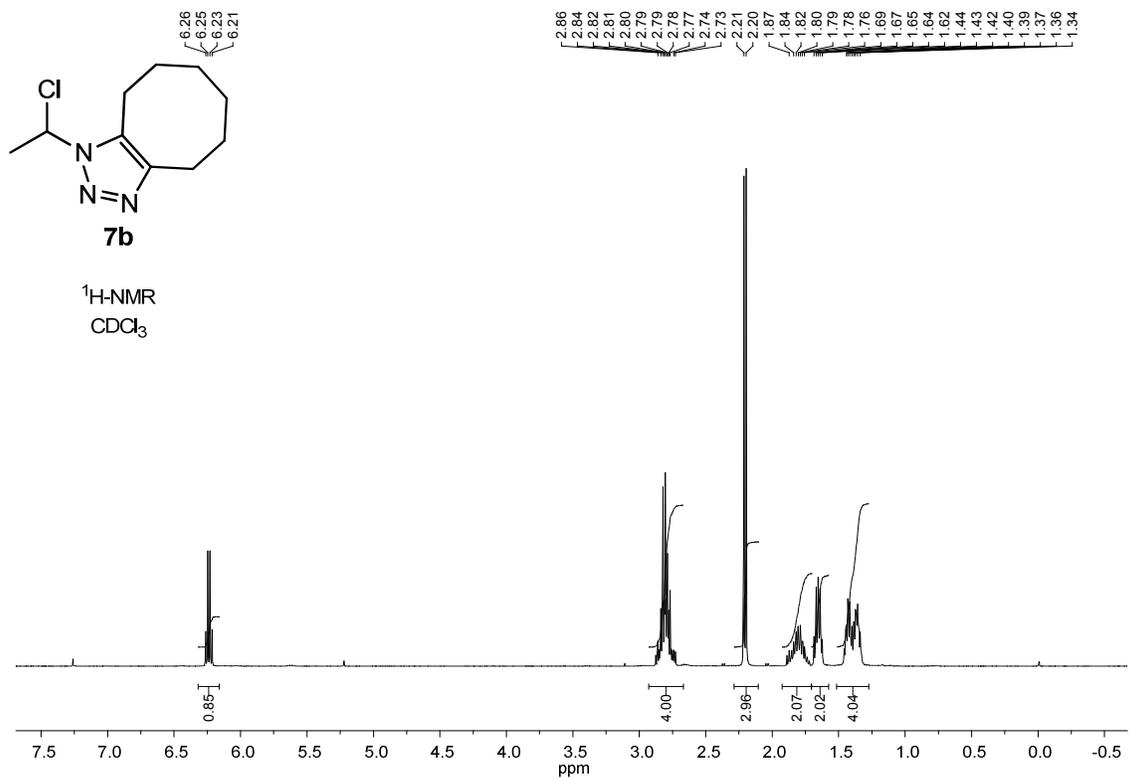


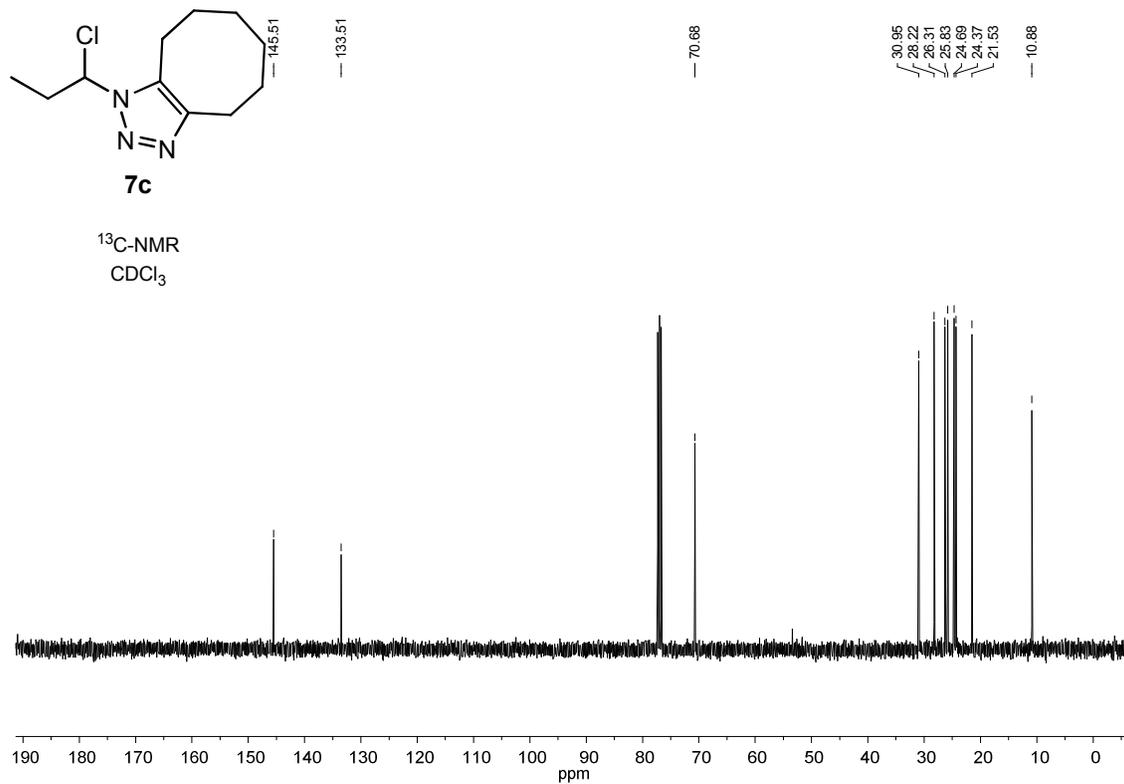
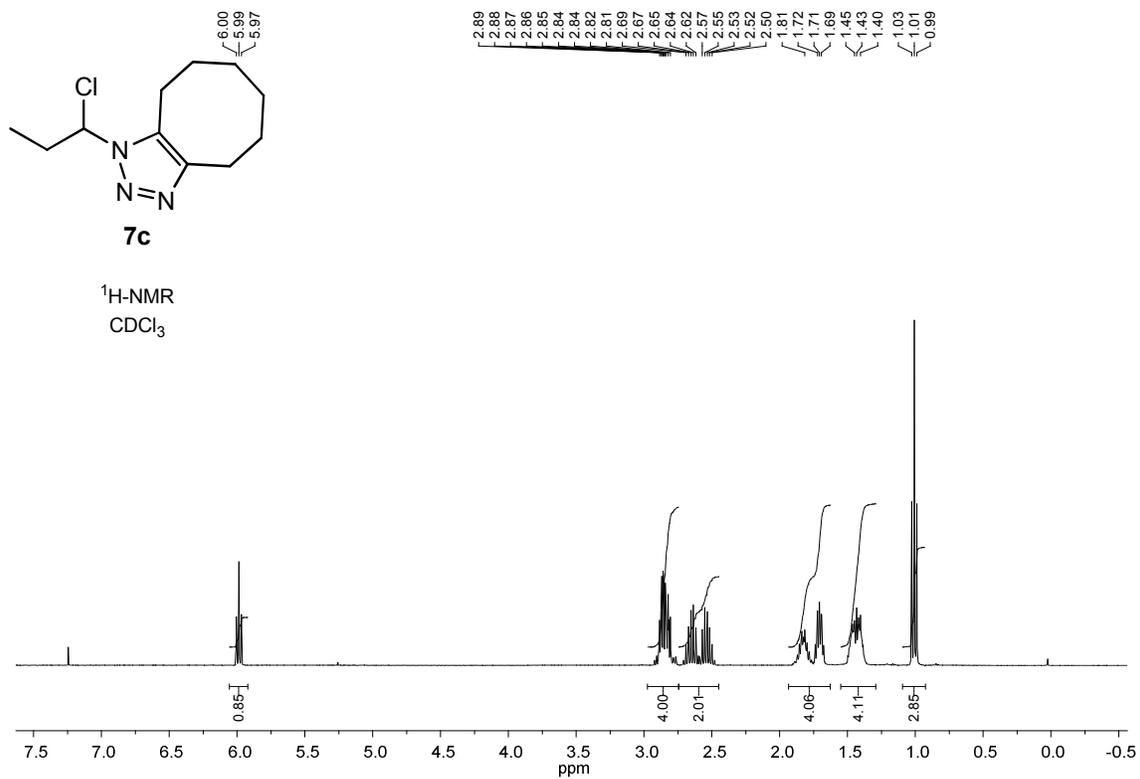
¹³C-NMR
CDCl₃

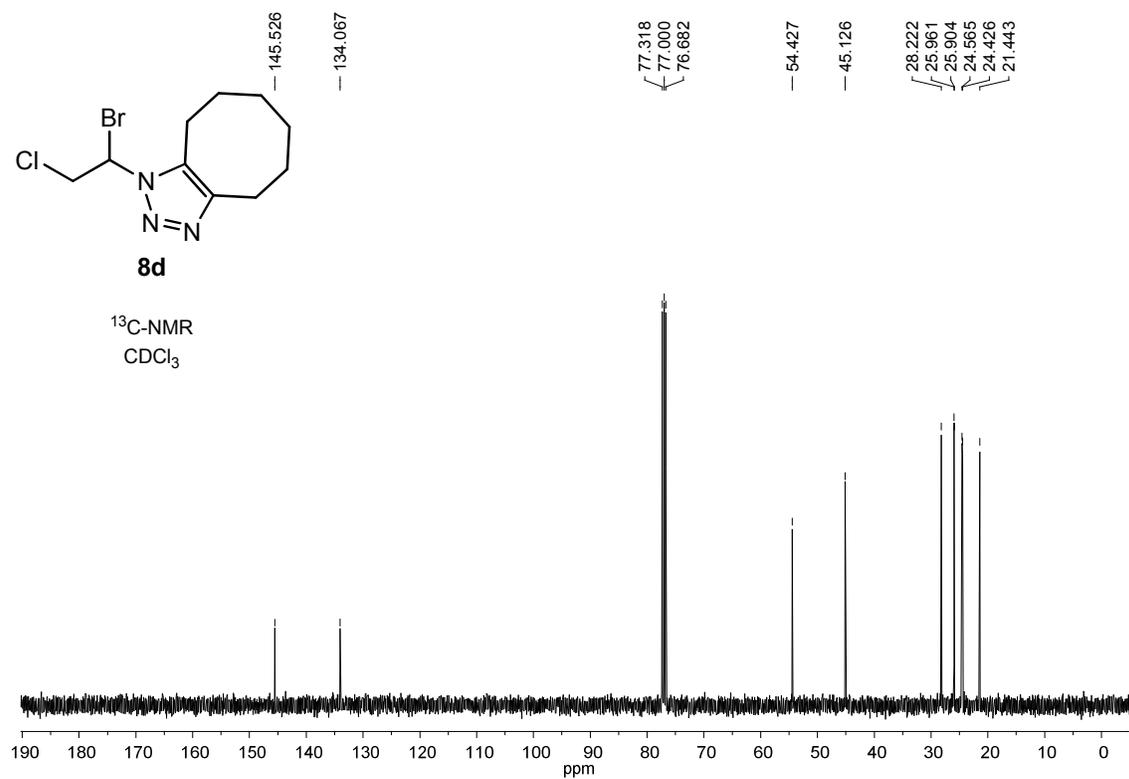
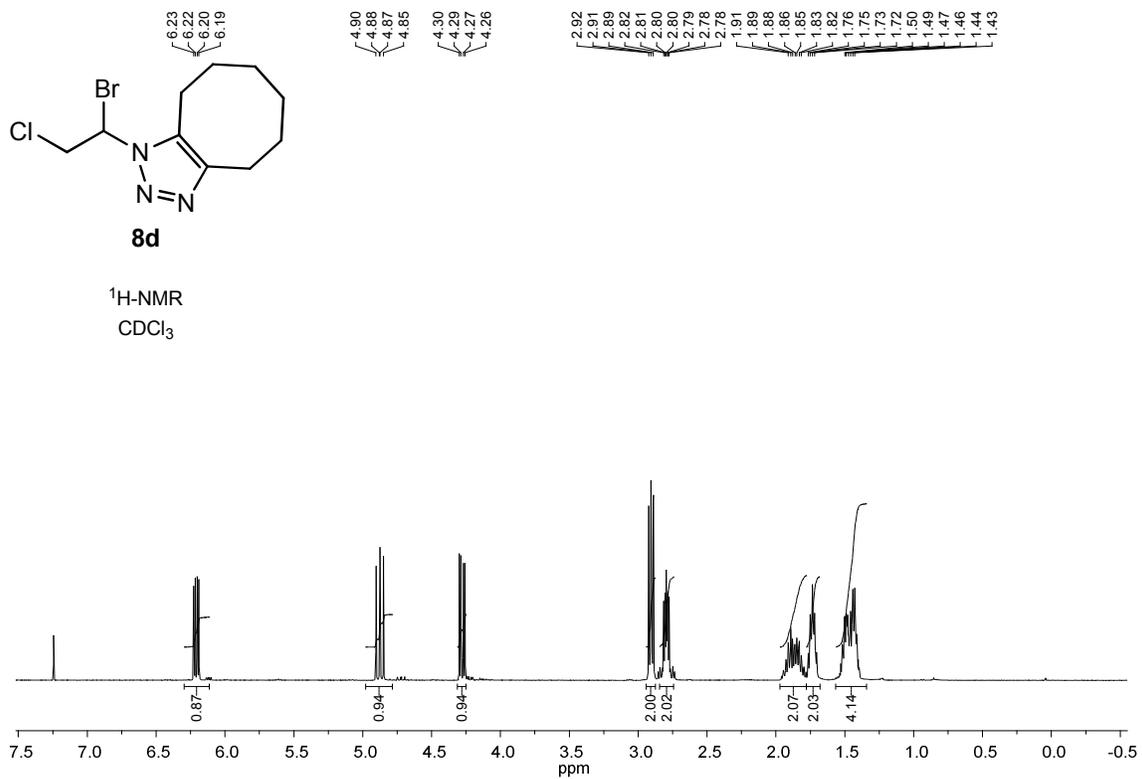


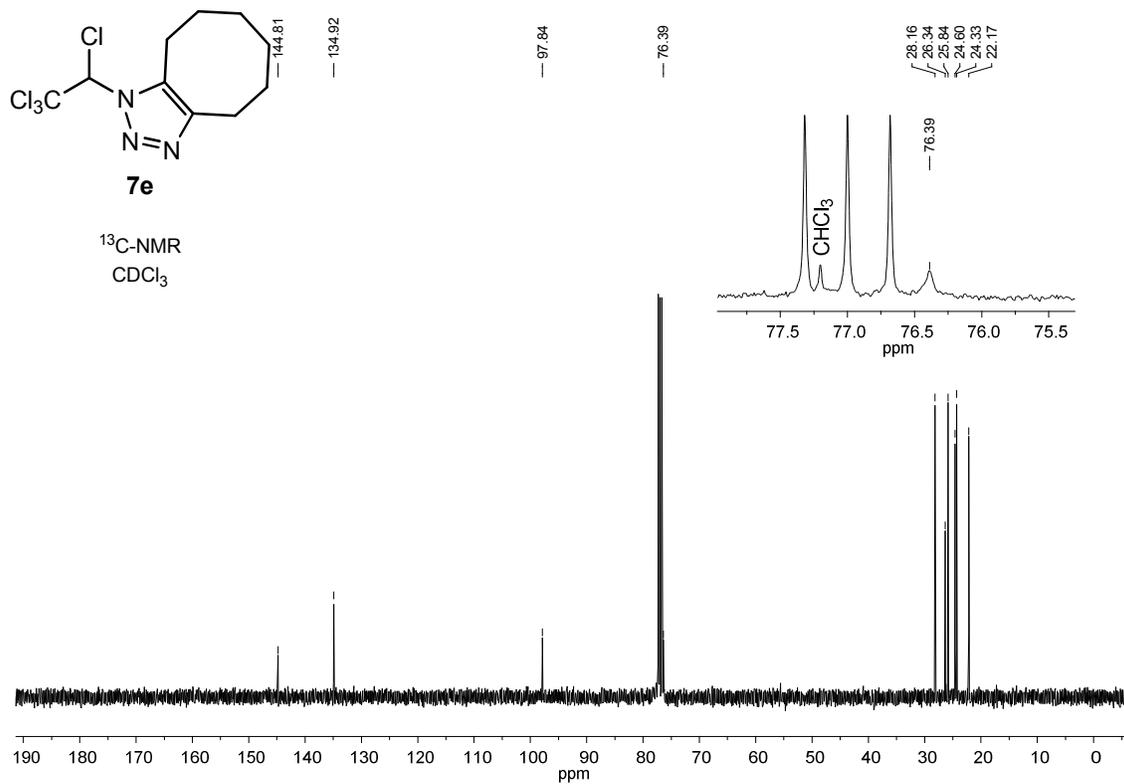
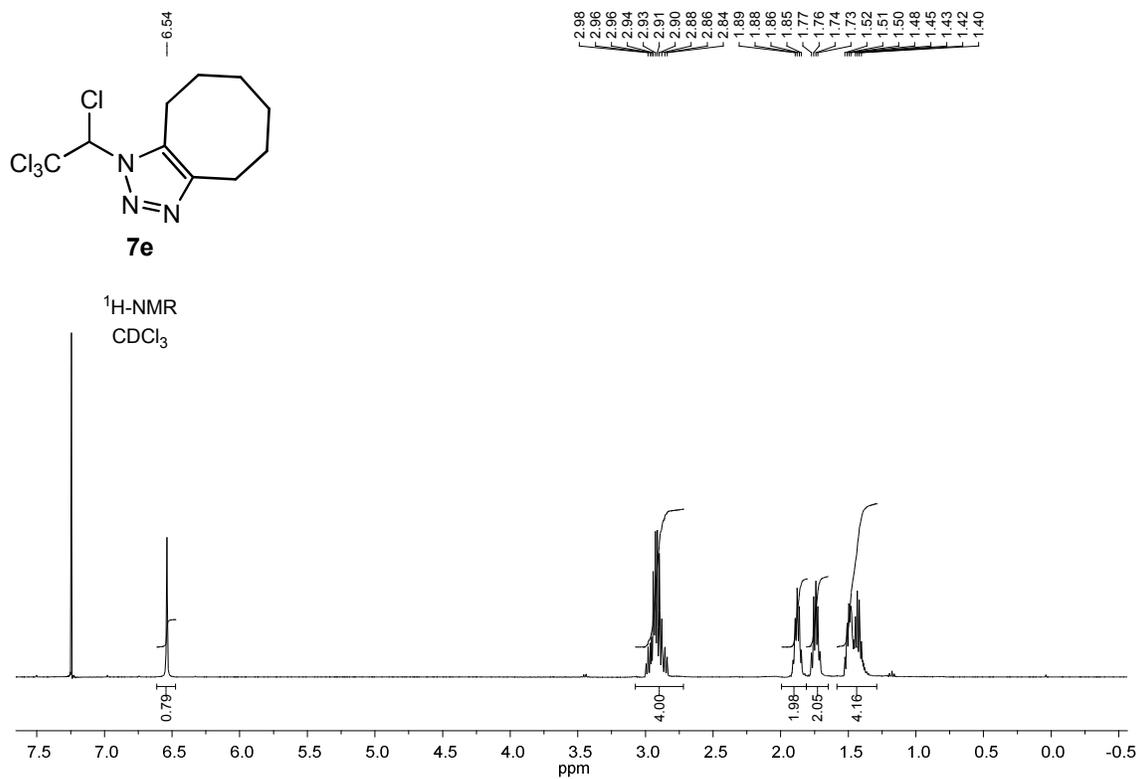


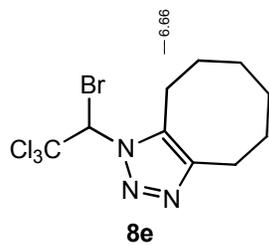




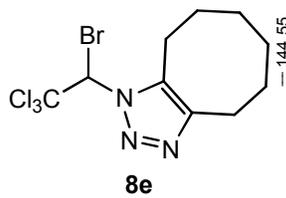
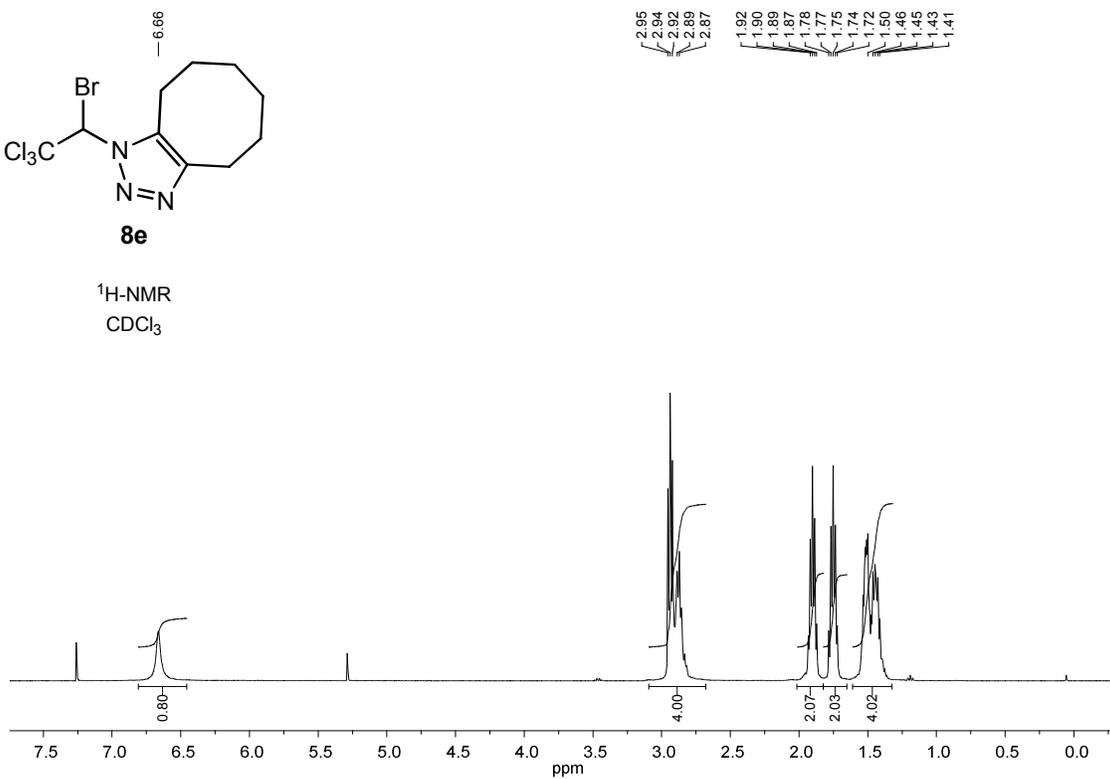




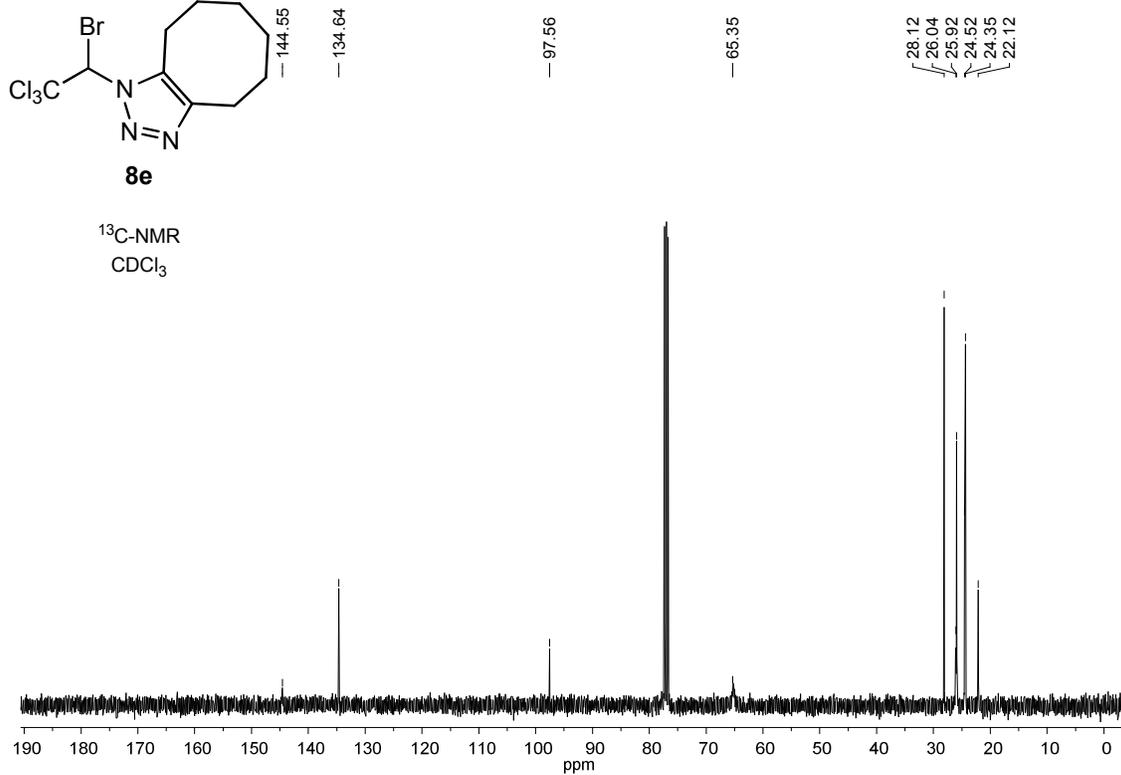


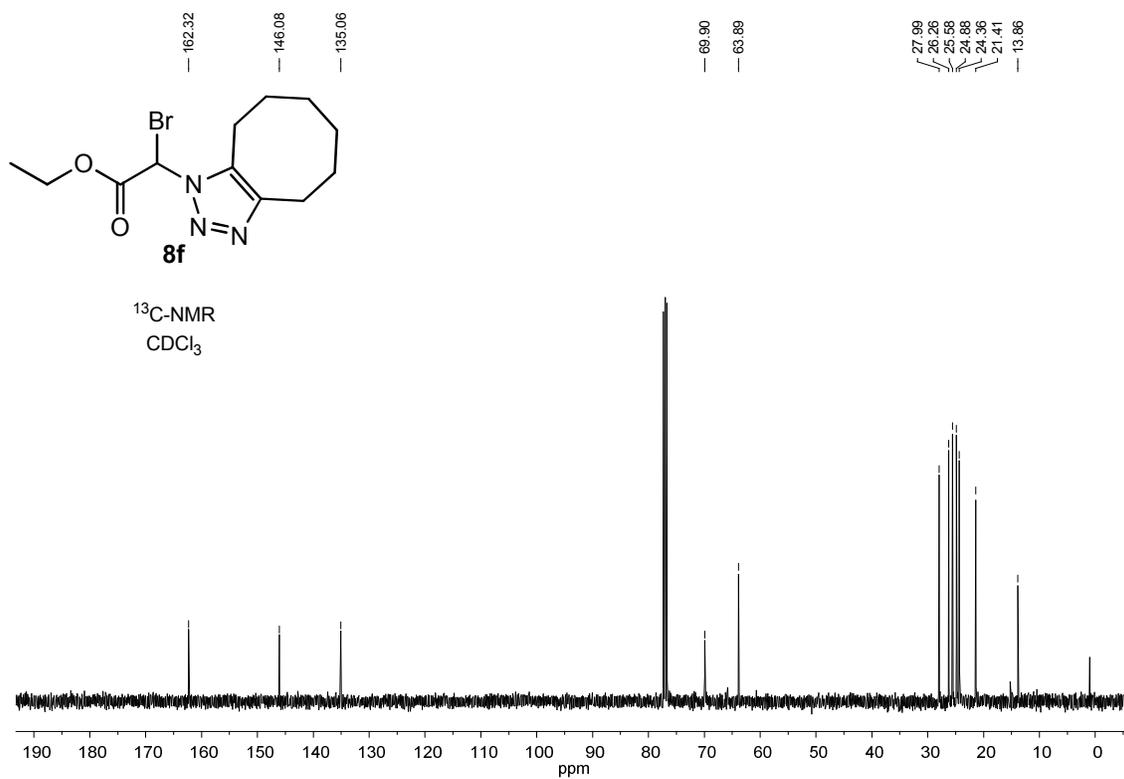
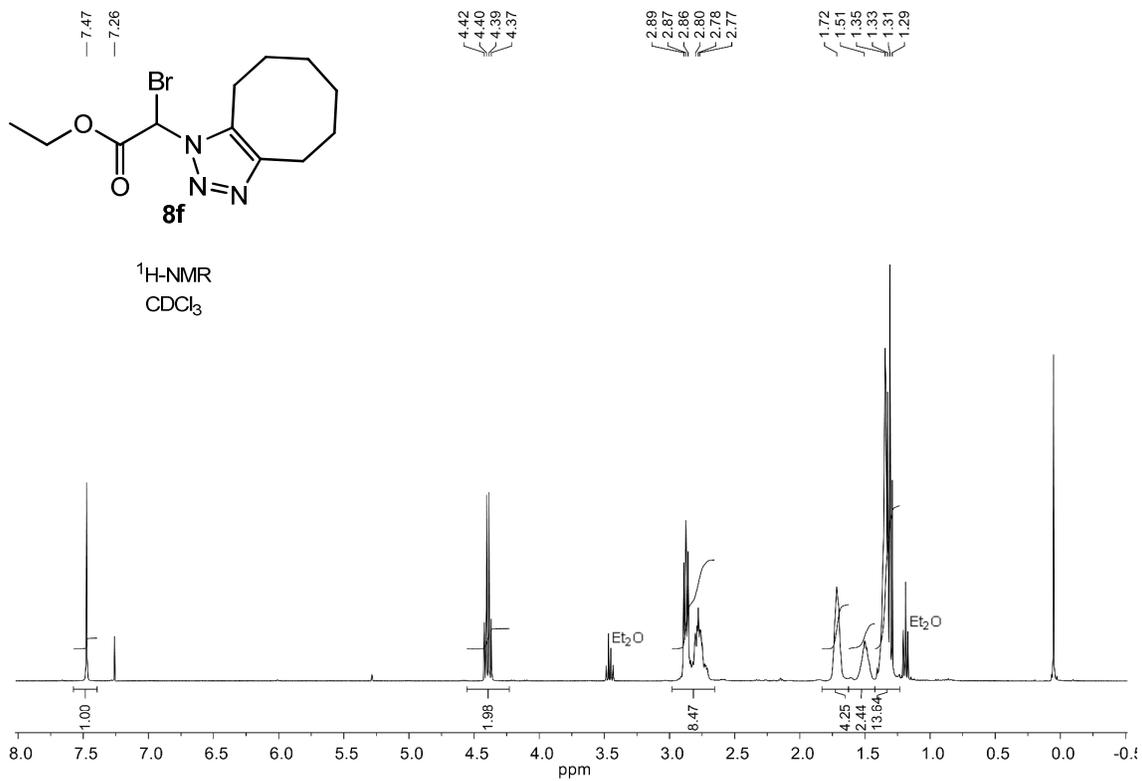


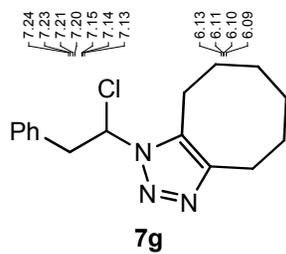
¹H-NMR
CDCl₃



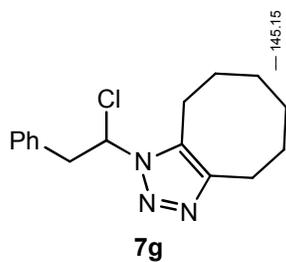
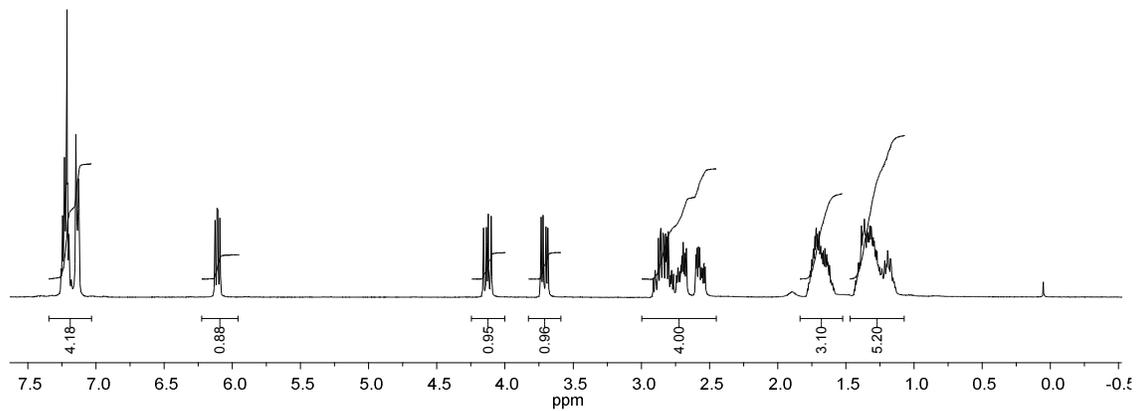
¹³C-NMR
CDCl₃



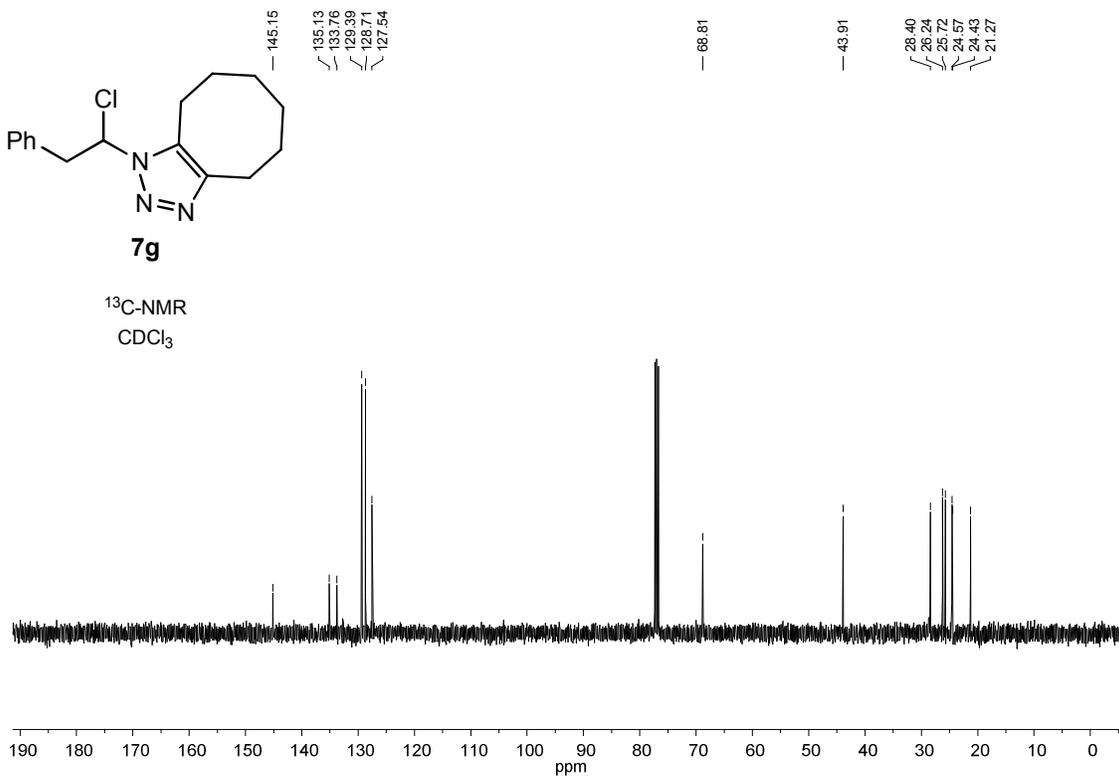


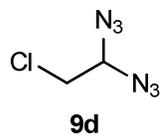


¹H-NMR
CDCl₃

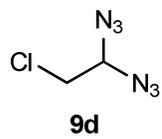
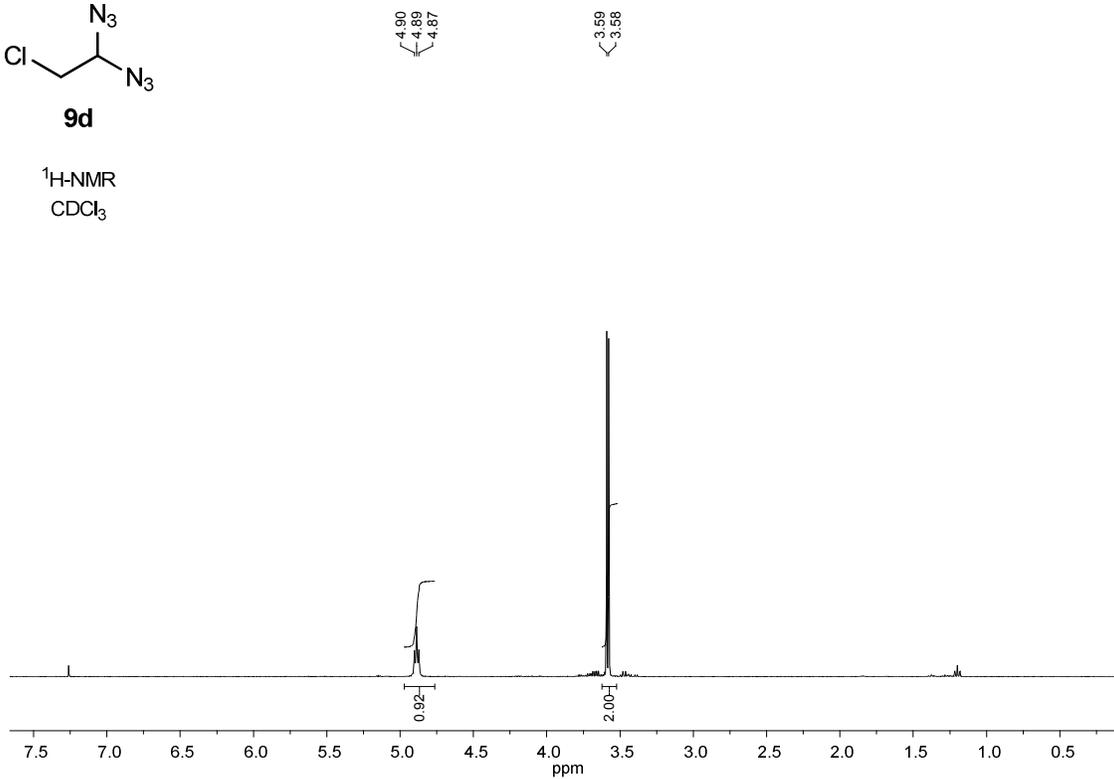


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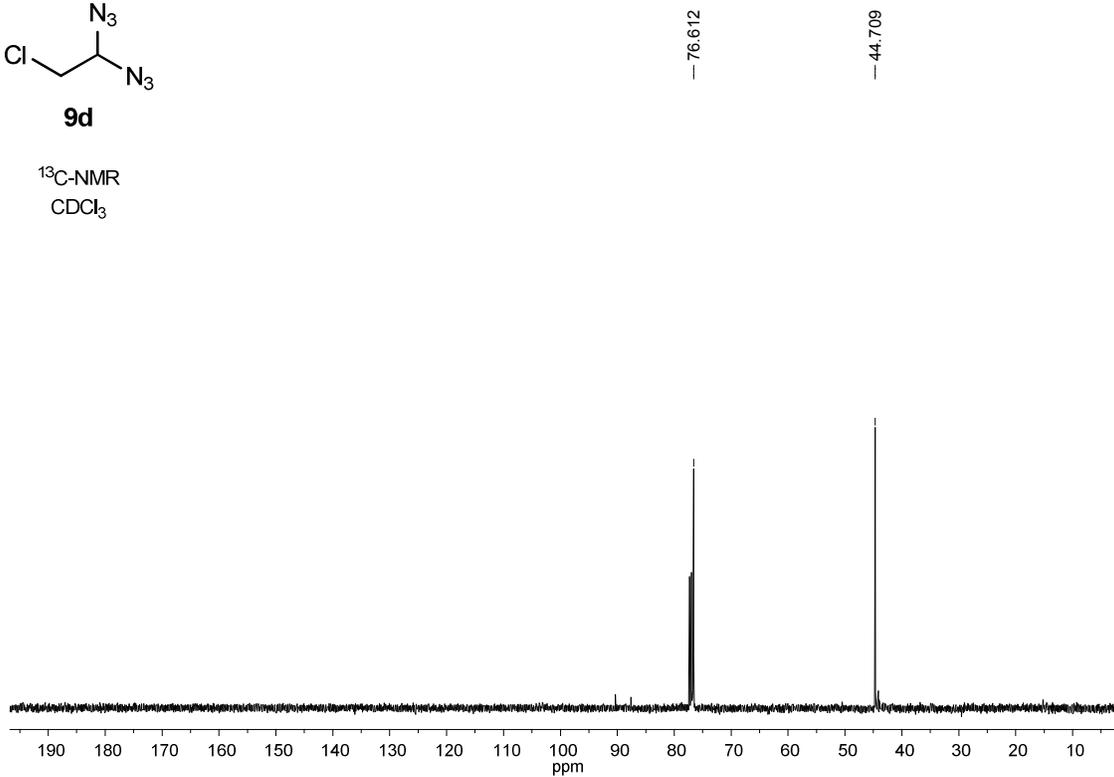


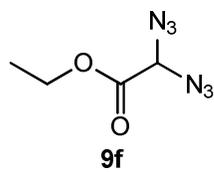


¹H-NMR
CDCl₃

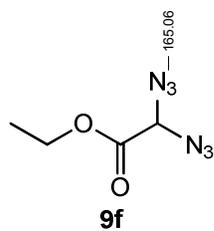
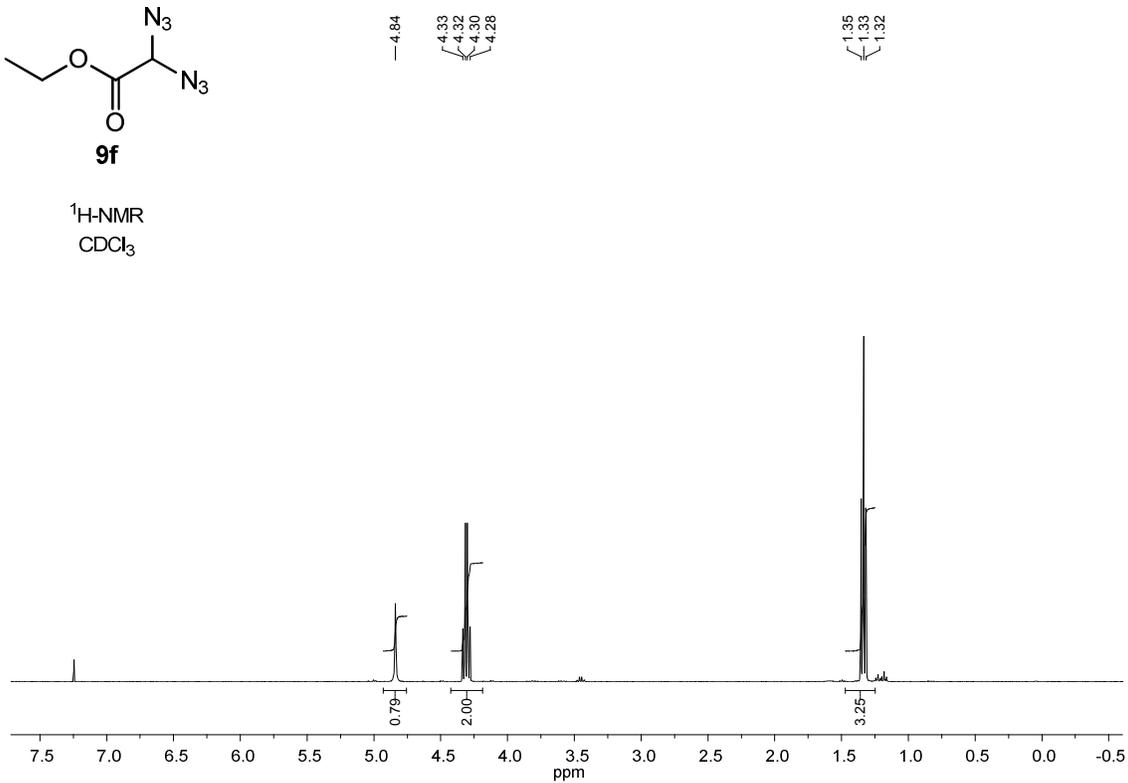


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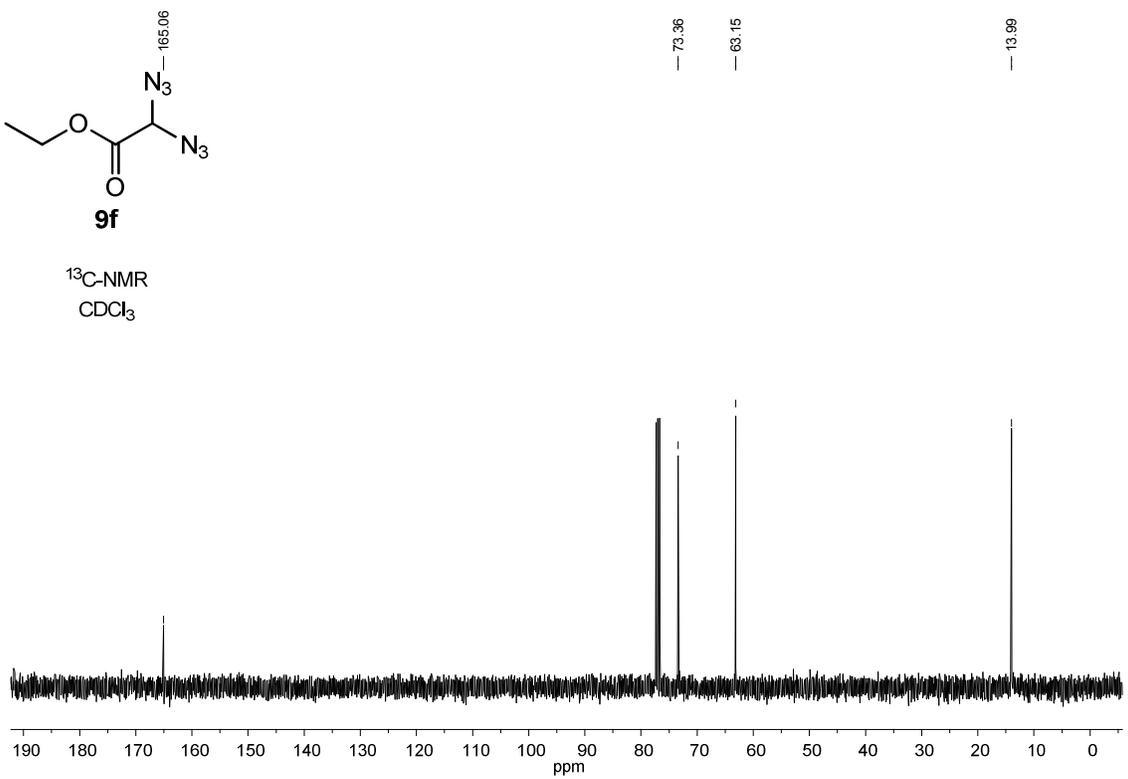


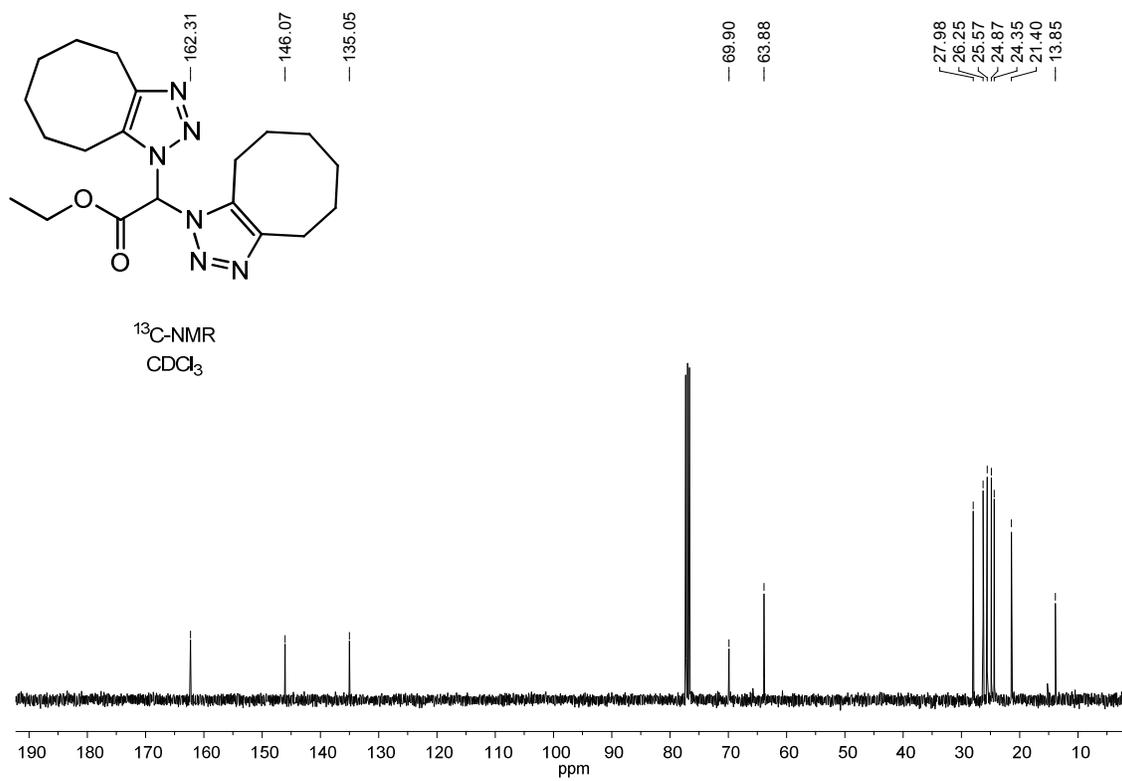
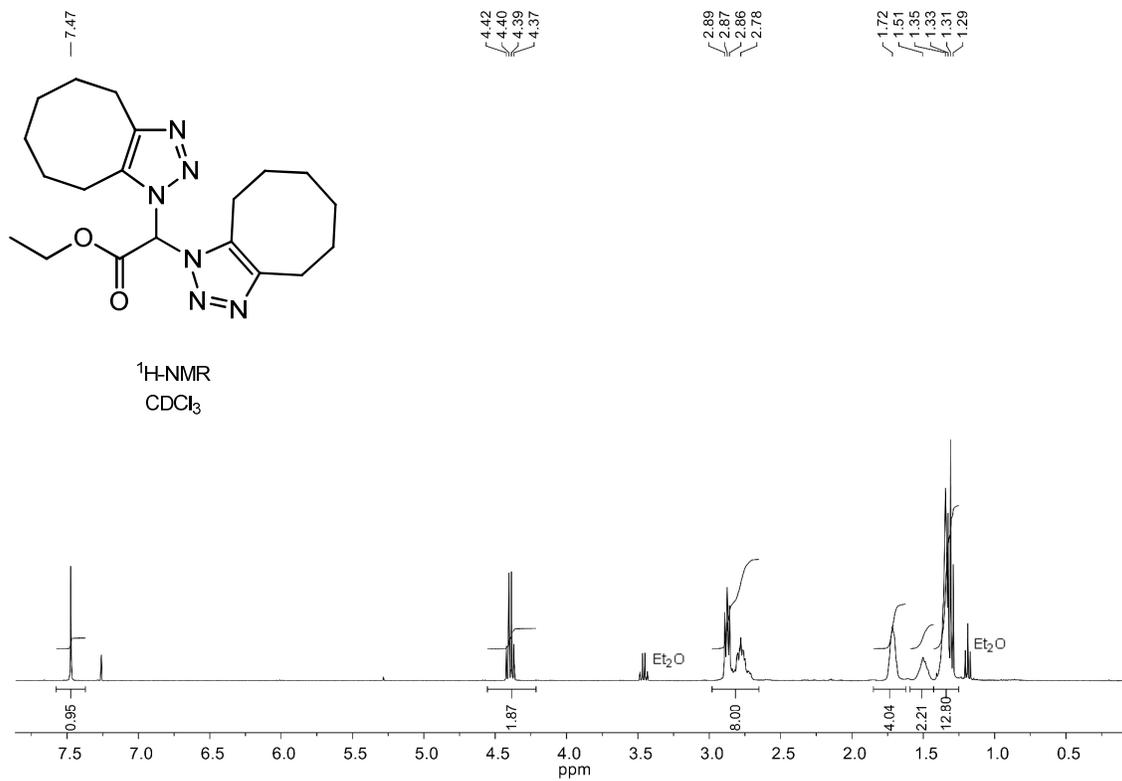


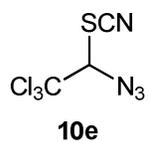
$^1\text{H-NMR}$
 CDCl_3



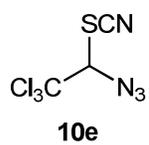
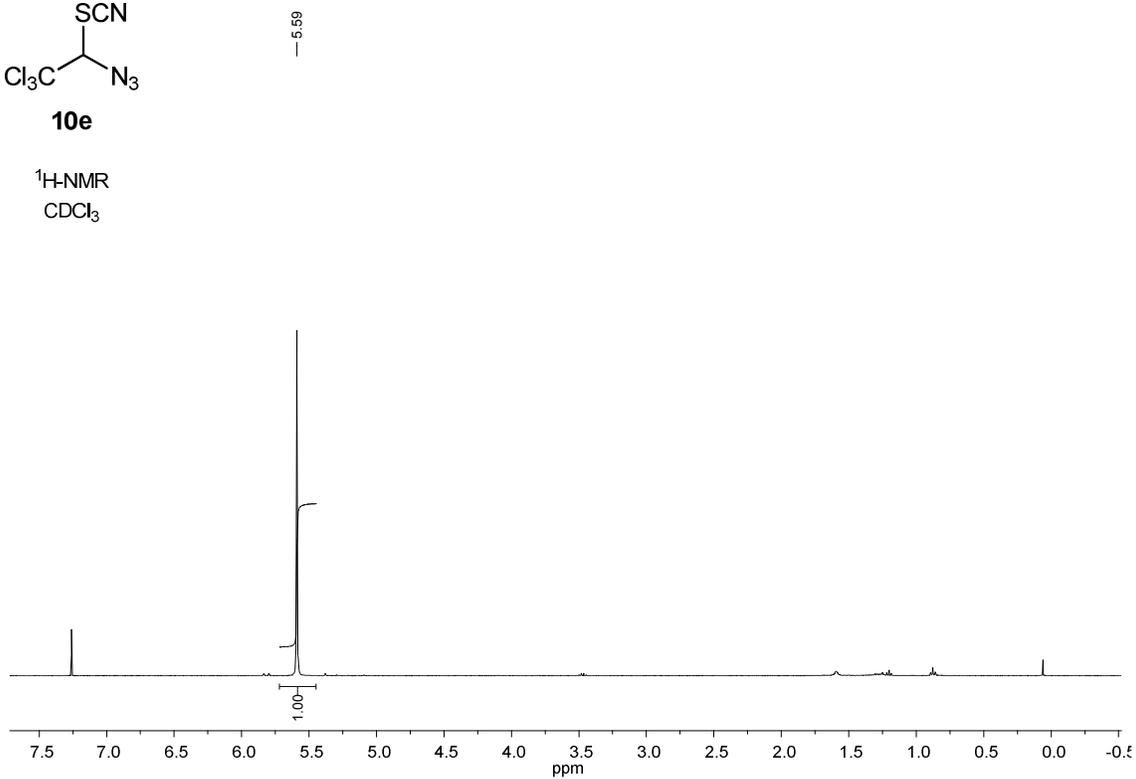
$^{13}\text{C-NMR}$
 CDCl_3



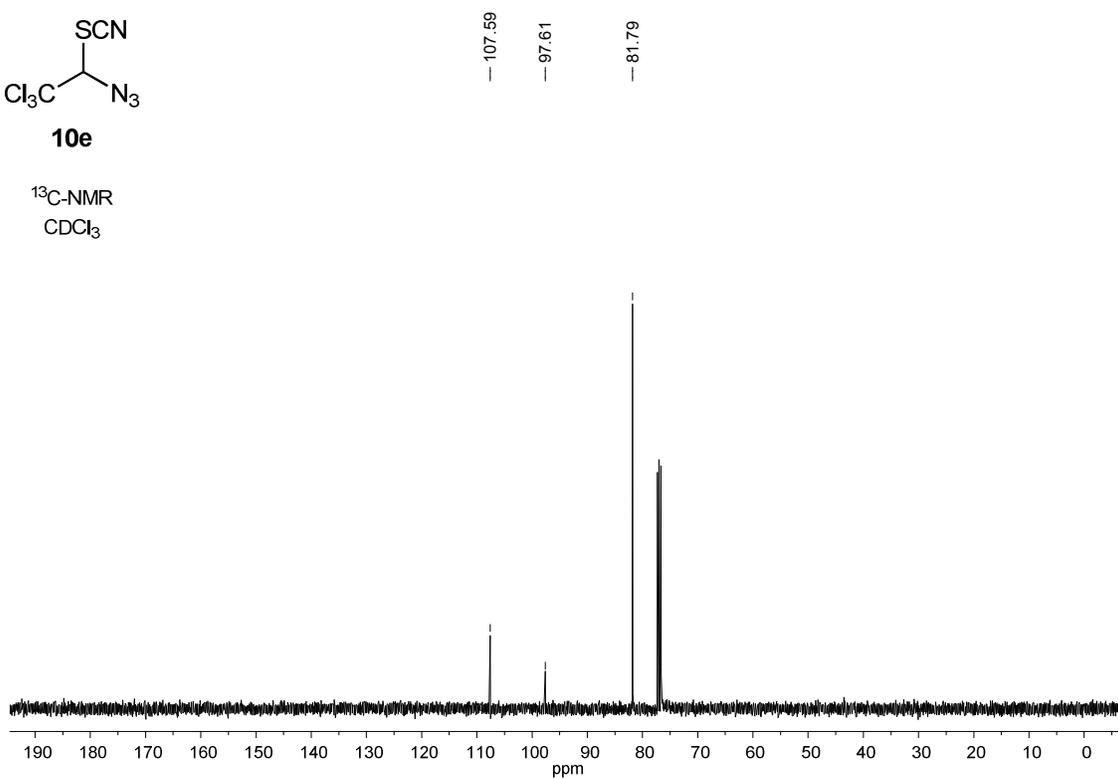


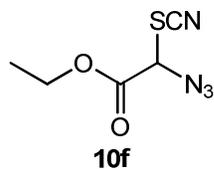


¹H-NMR
CDCl₃

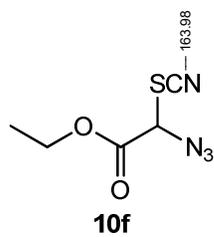
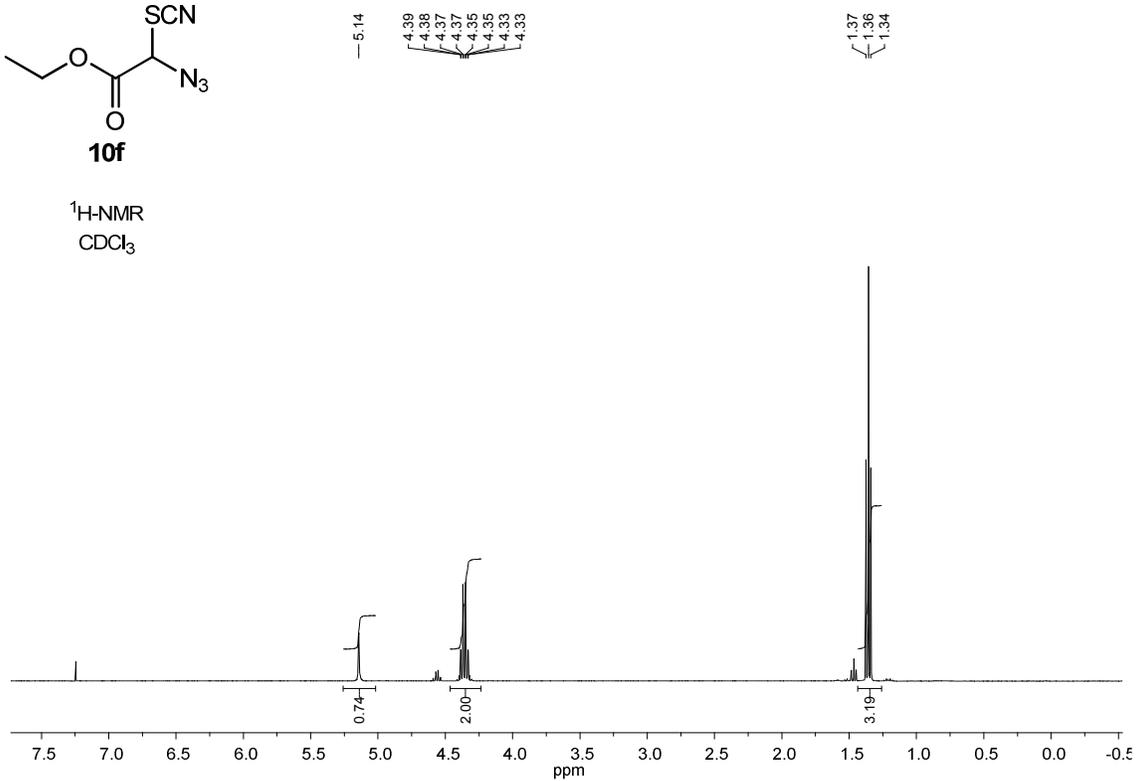


¹³C-NMR
CDCl₃

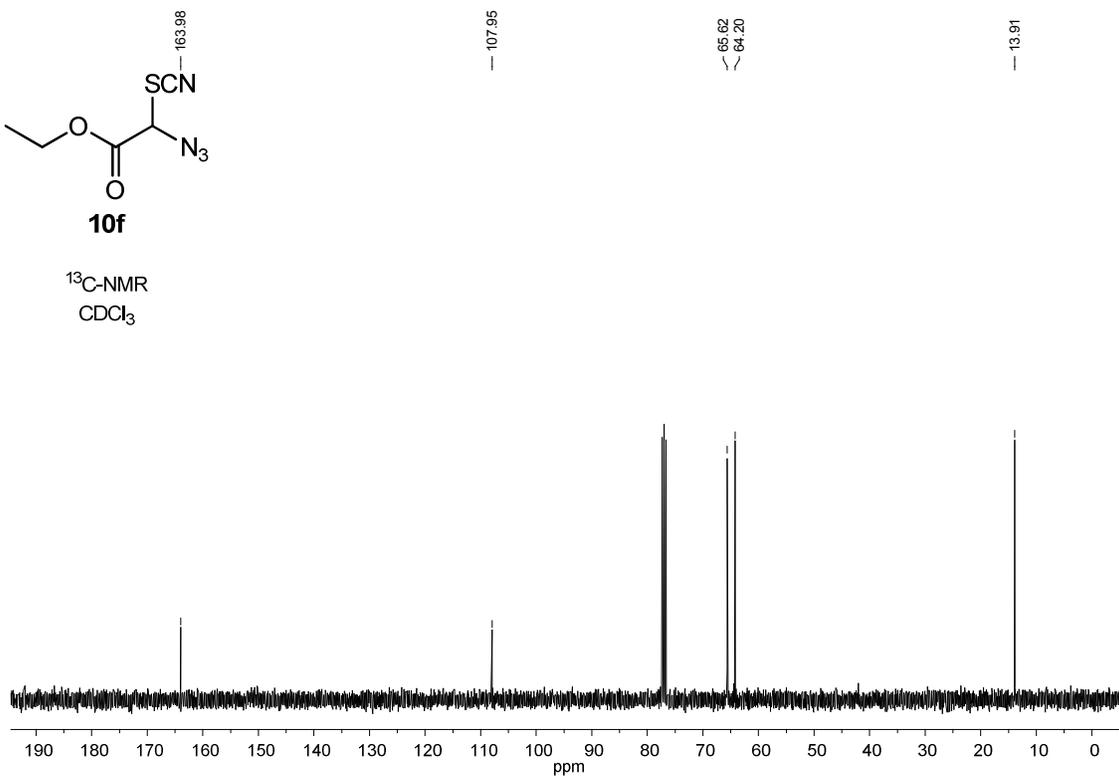


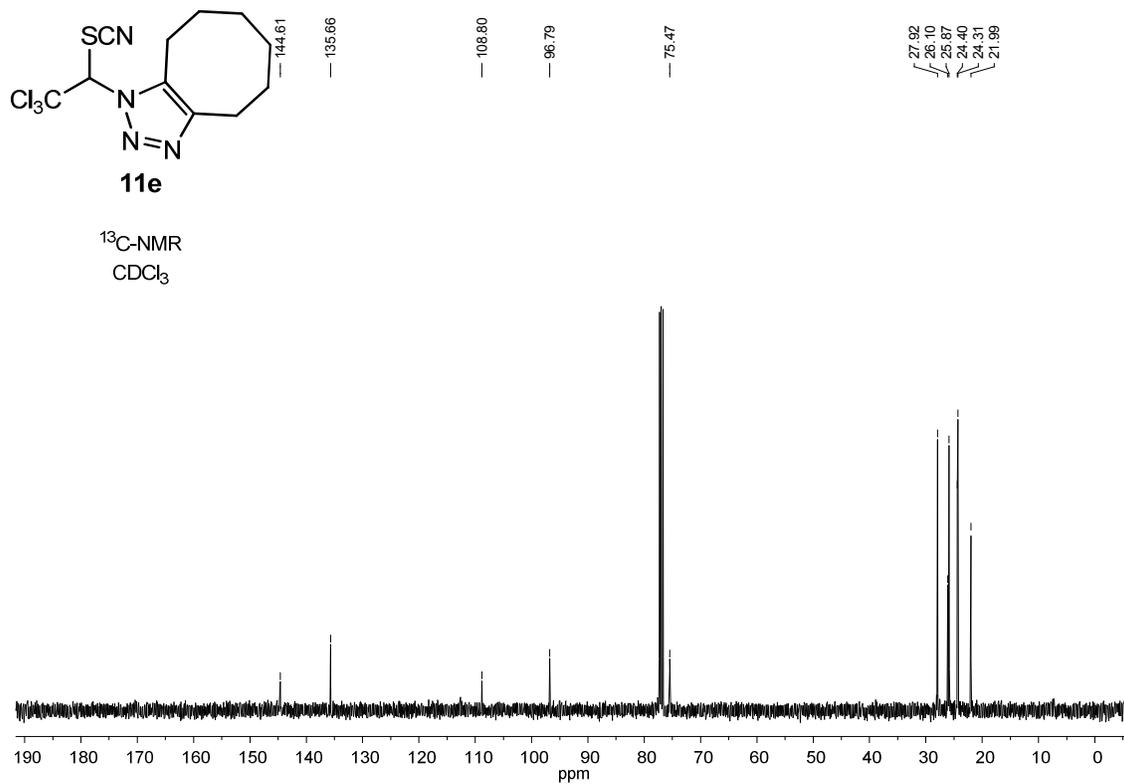
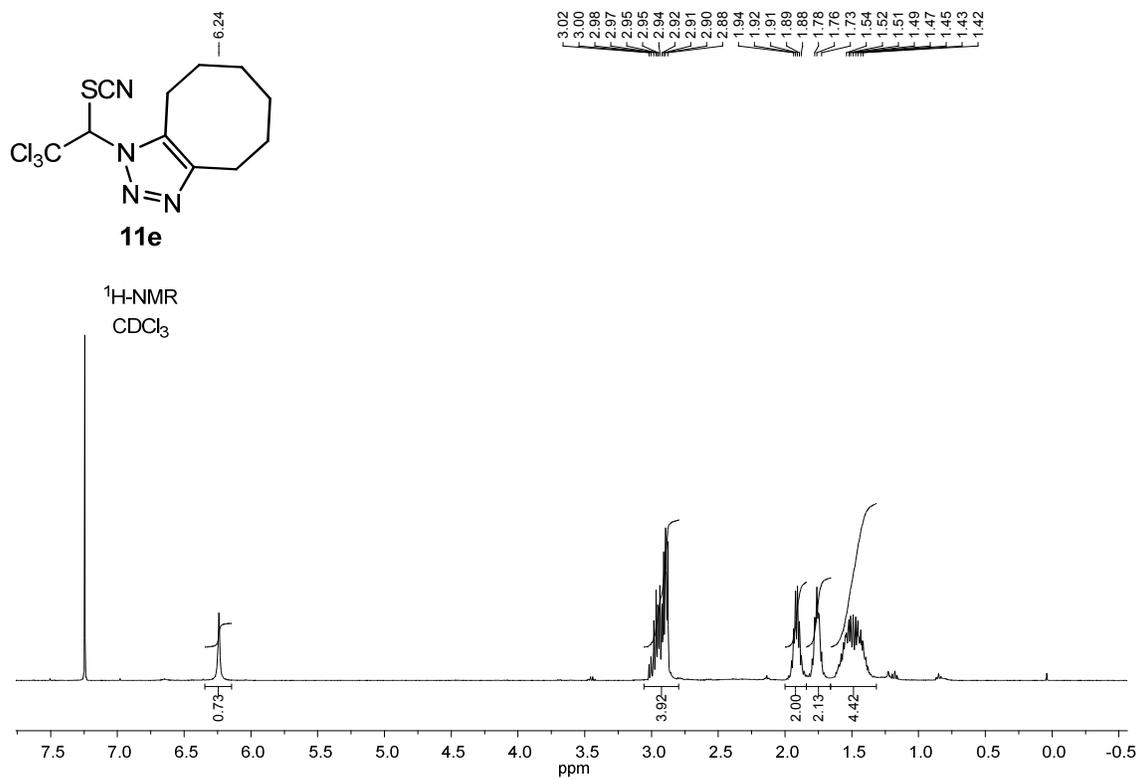


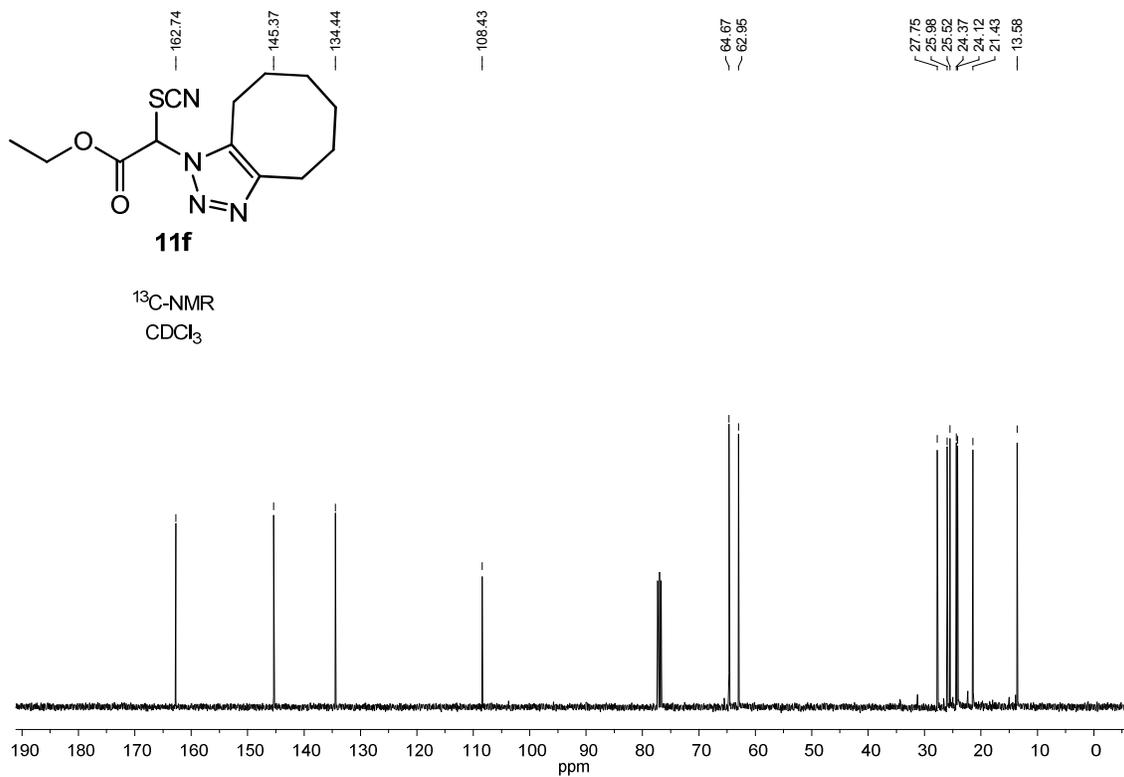
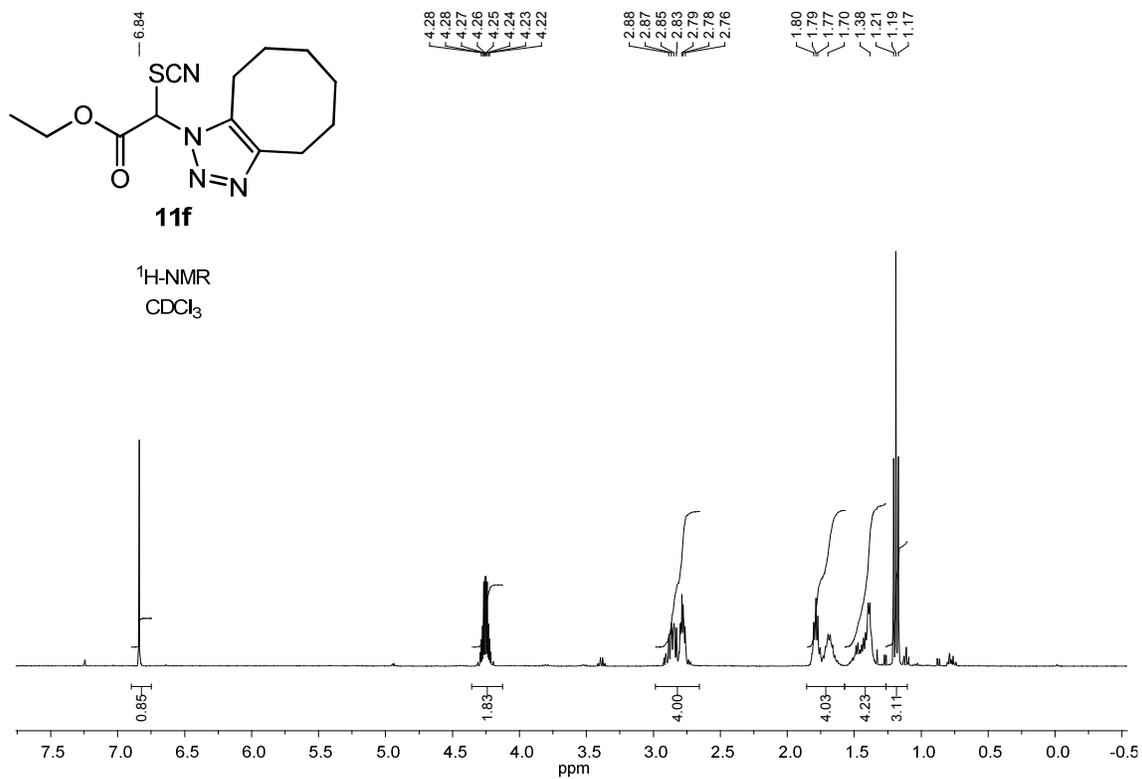
¹H-NMR
CDCl₃

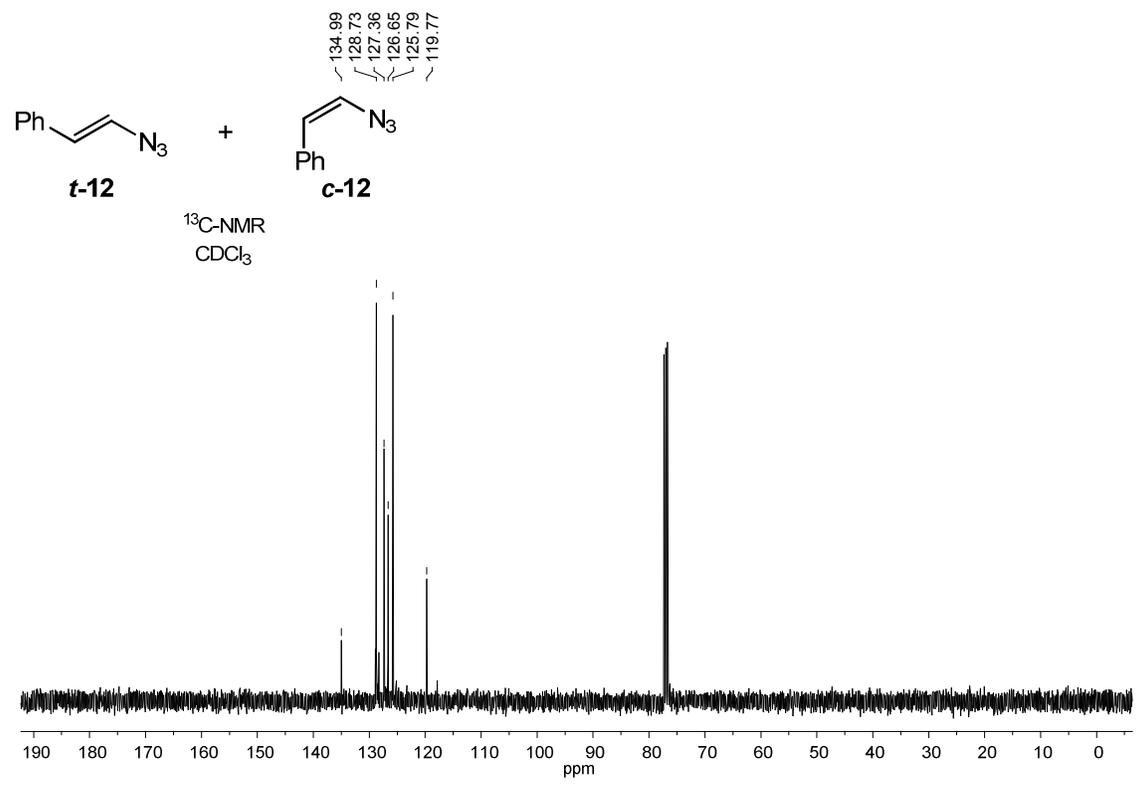
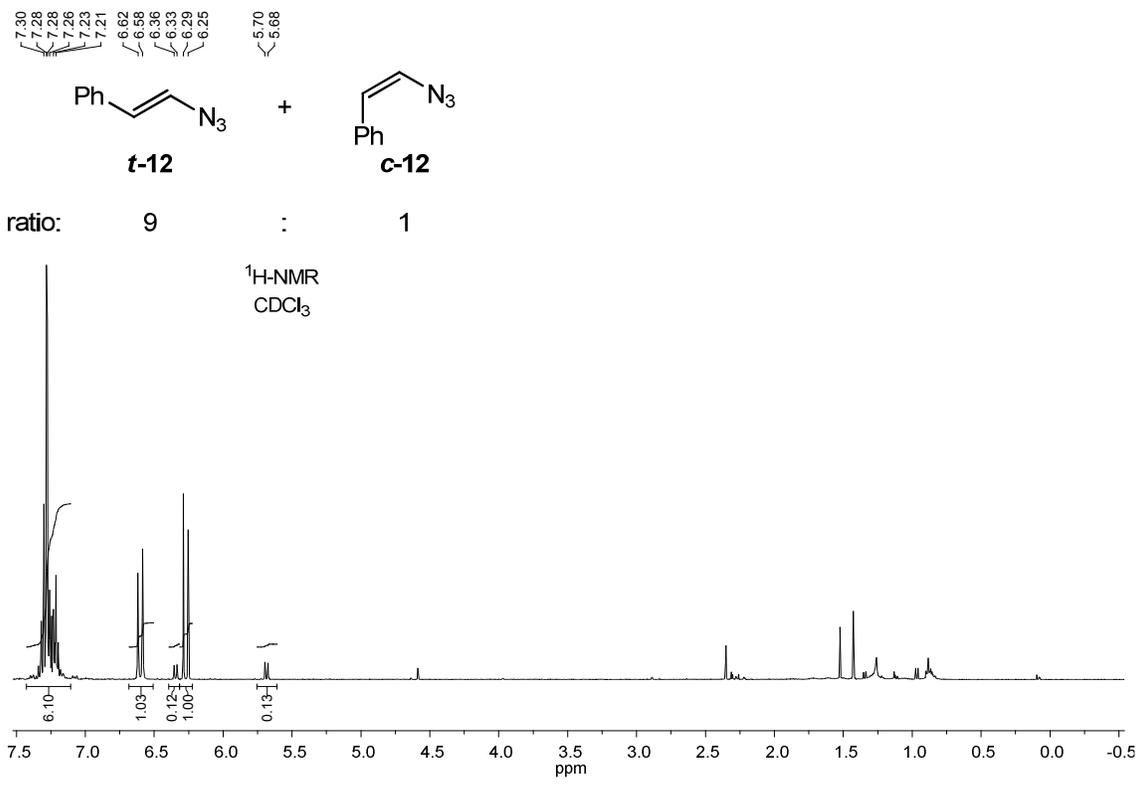


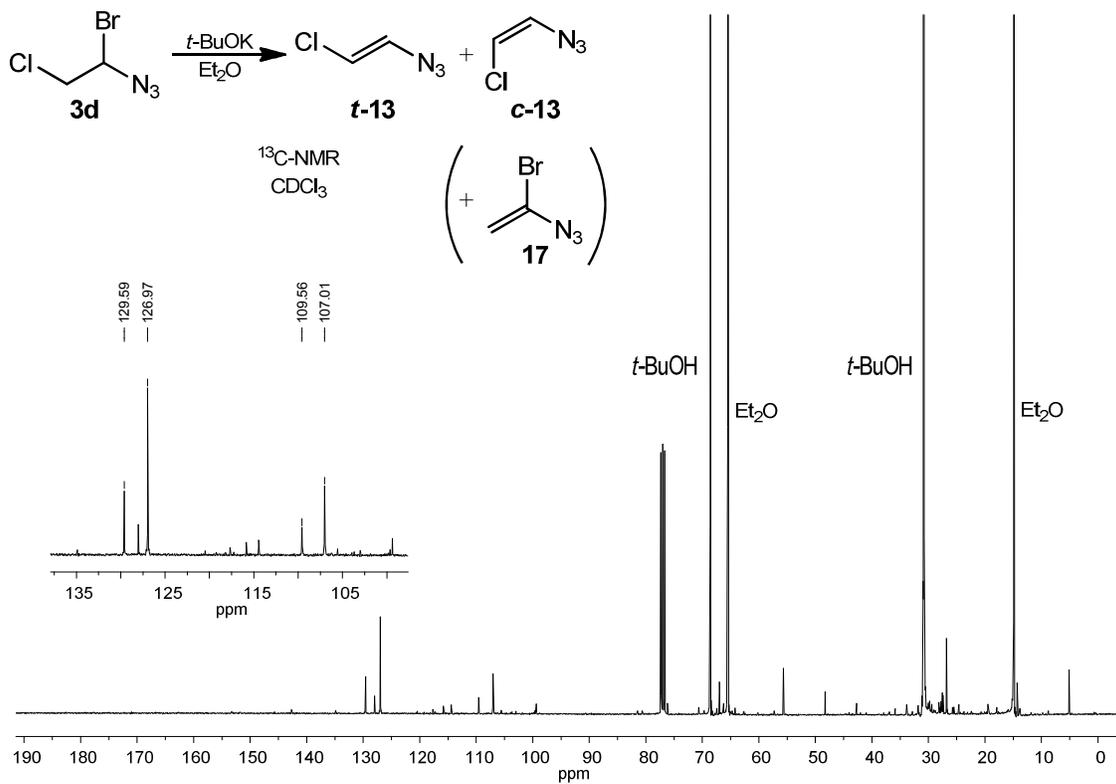
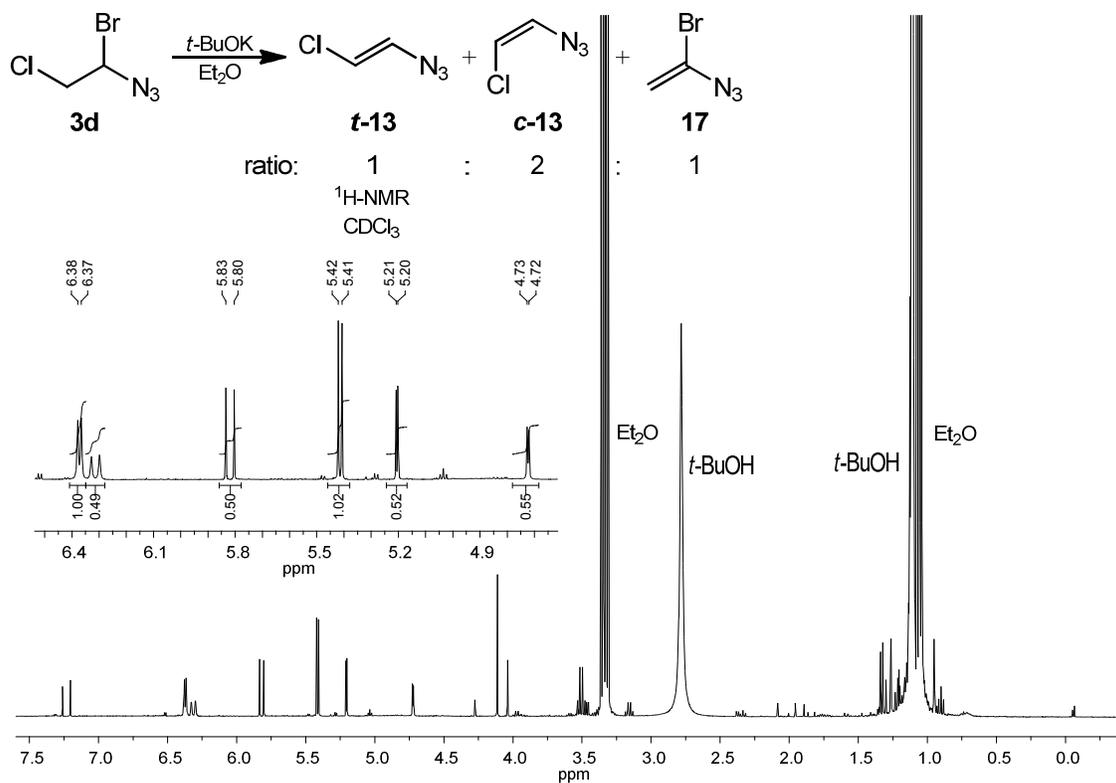
¹³C-NMR
CDCl₃

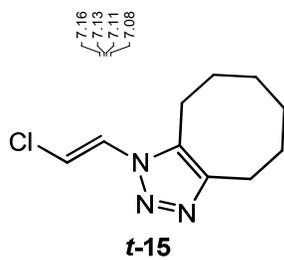




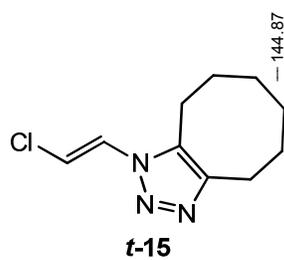
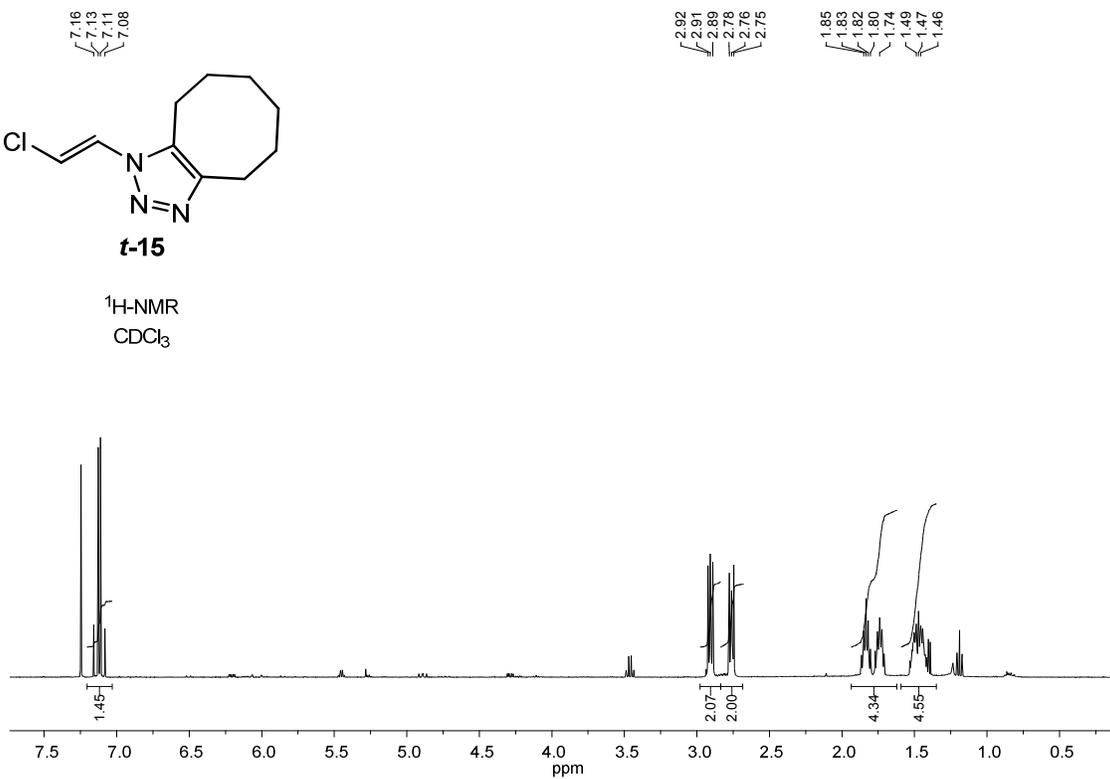




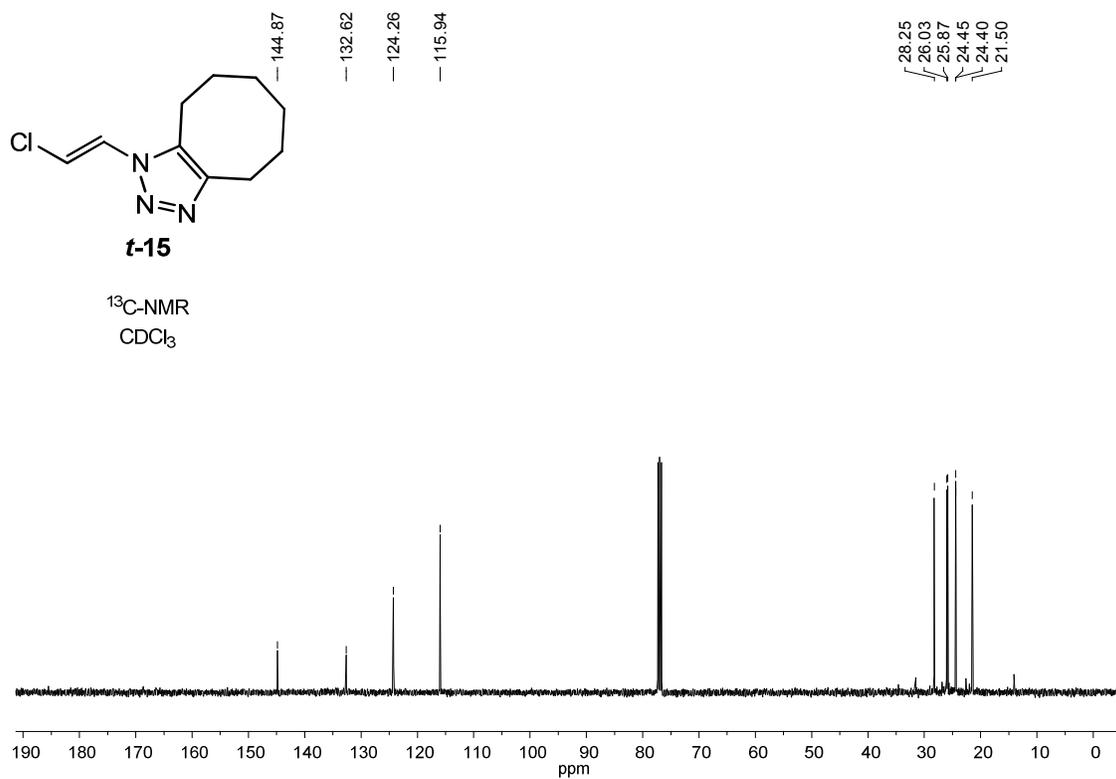


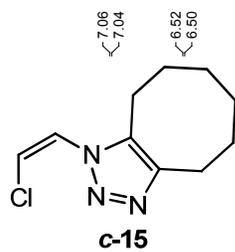


¹H-NMR
CDCl₃

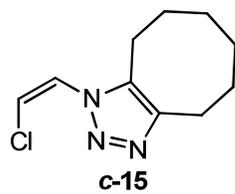
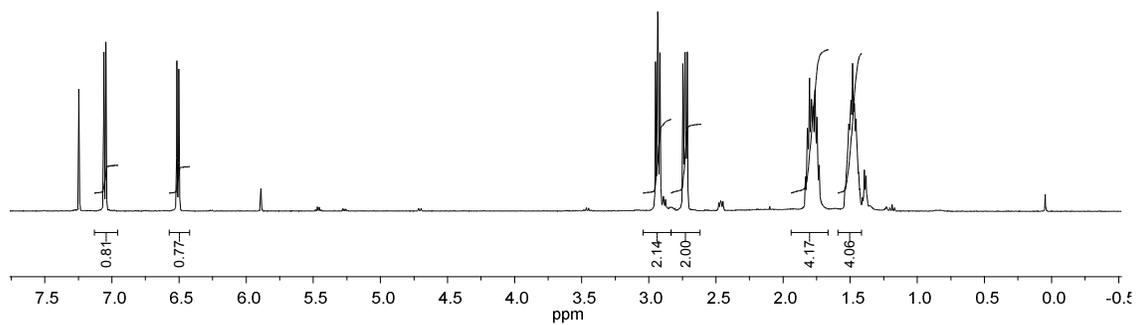


¹³C-NMR
CDCl₃

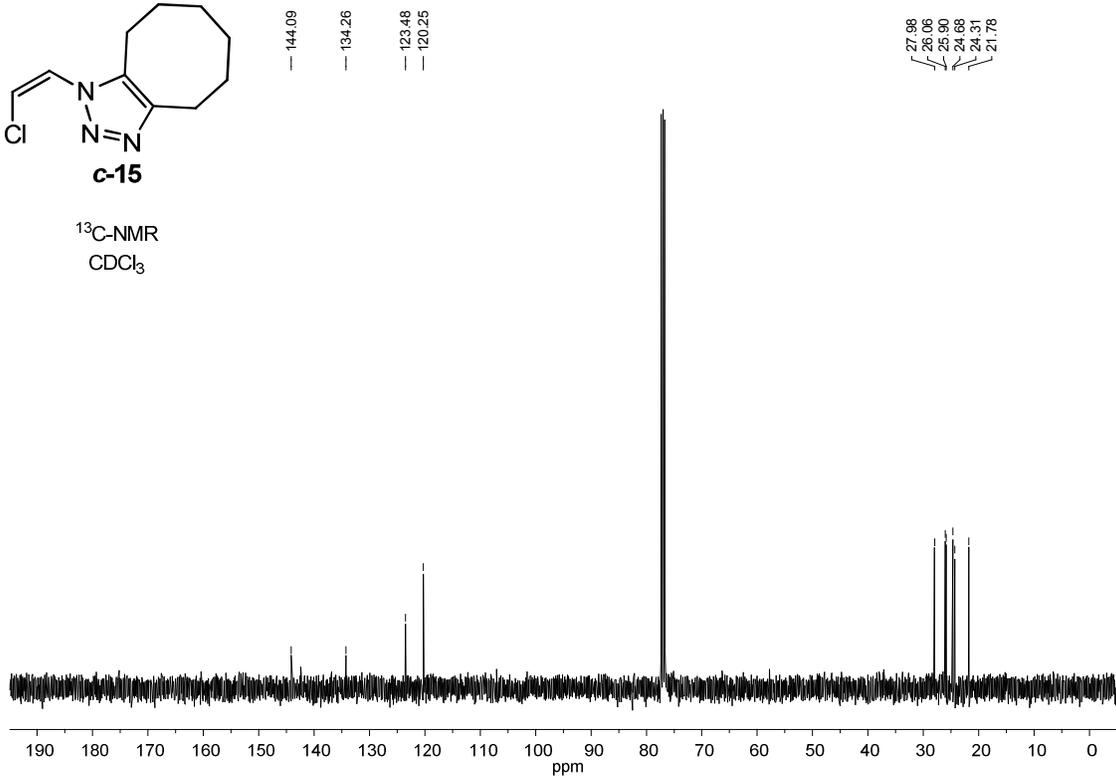


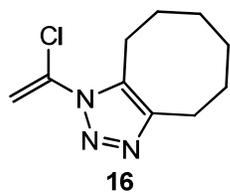


$^1\text{H-NMR}$
 CDCl_3

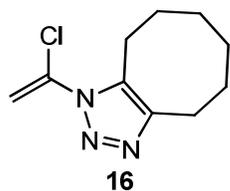
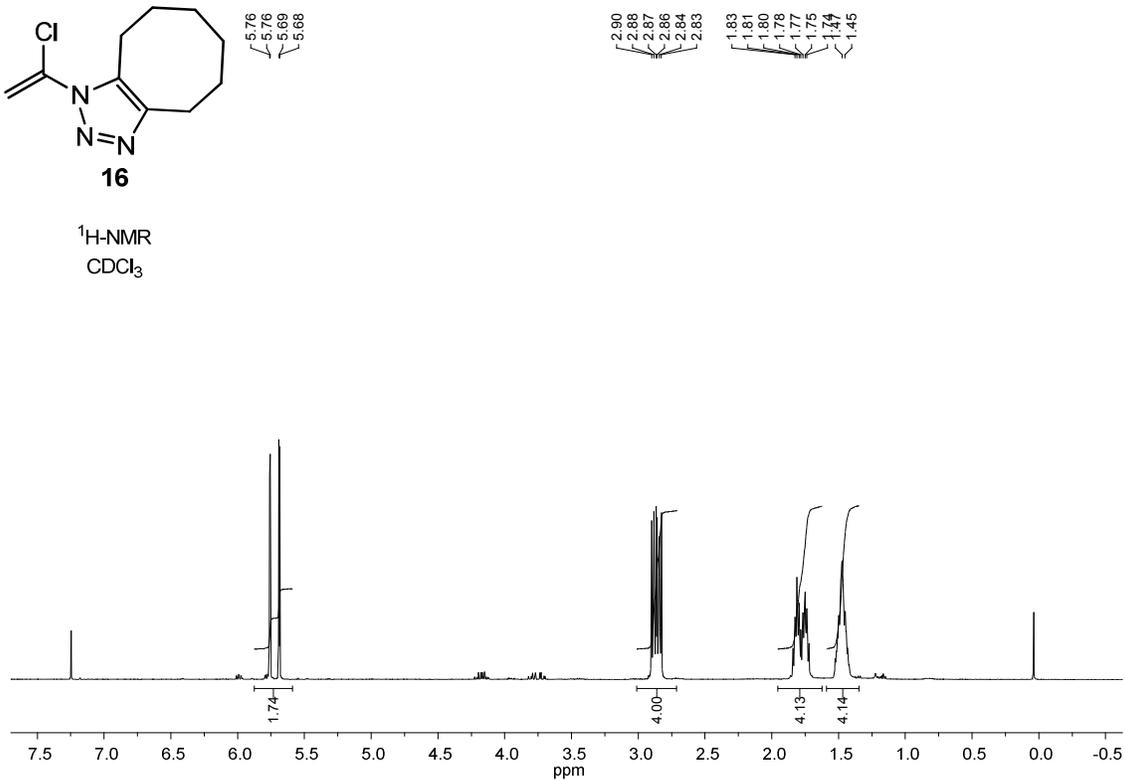


$^{13}\text{C-NMR}$
 CDCl_3

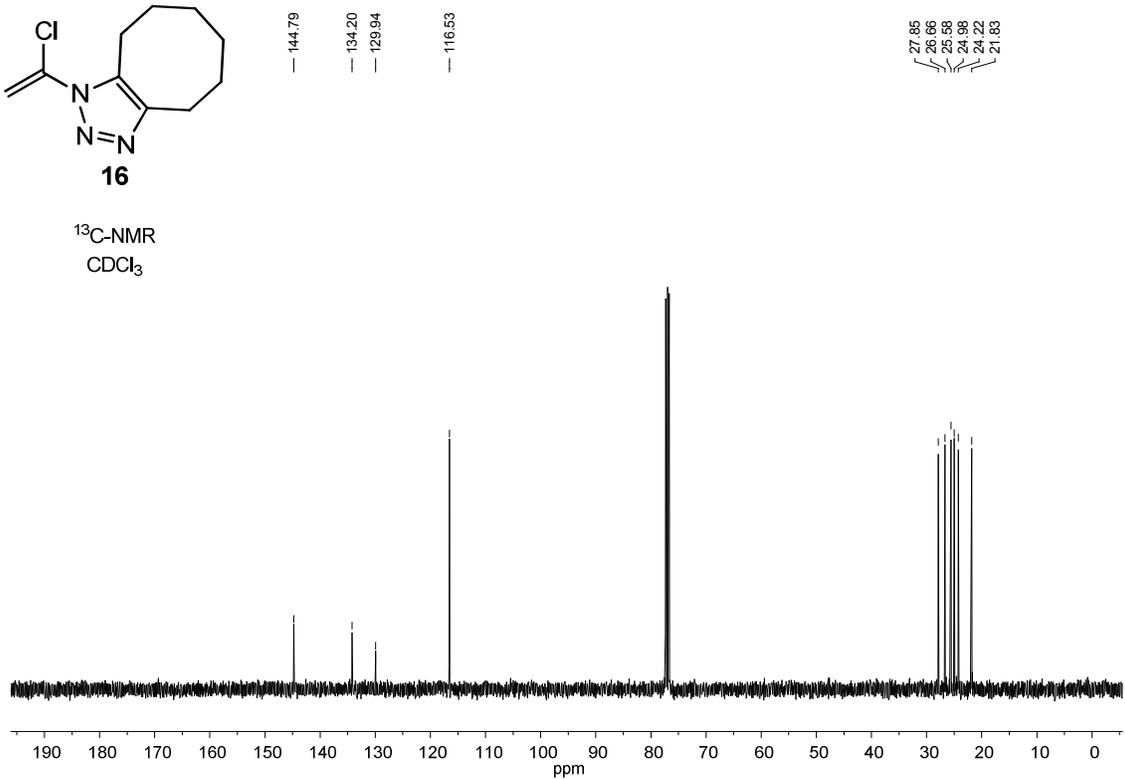


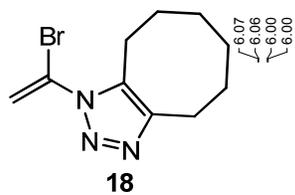


¹H-NMR
CDCl₃

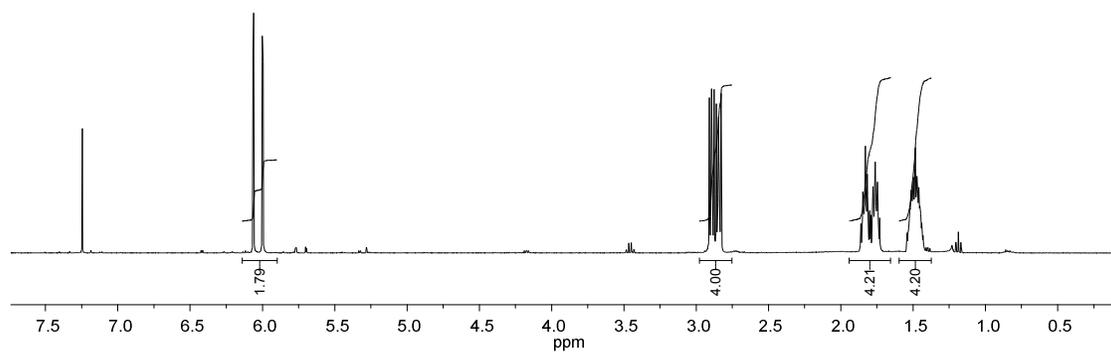


¹³C-NMR
CDCl₃

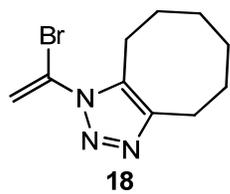




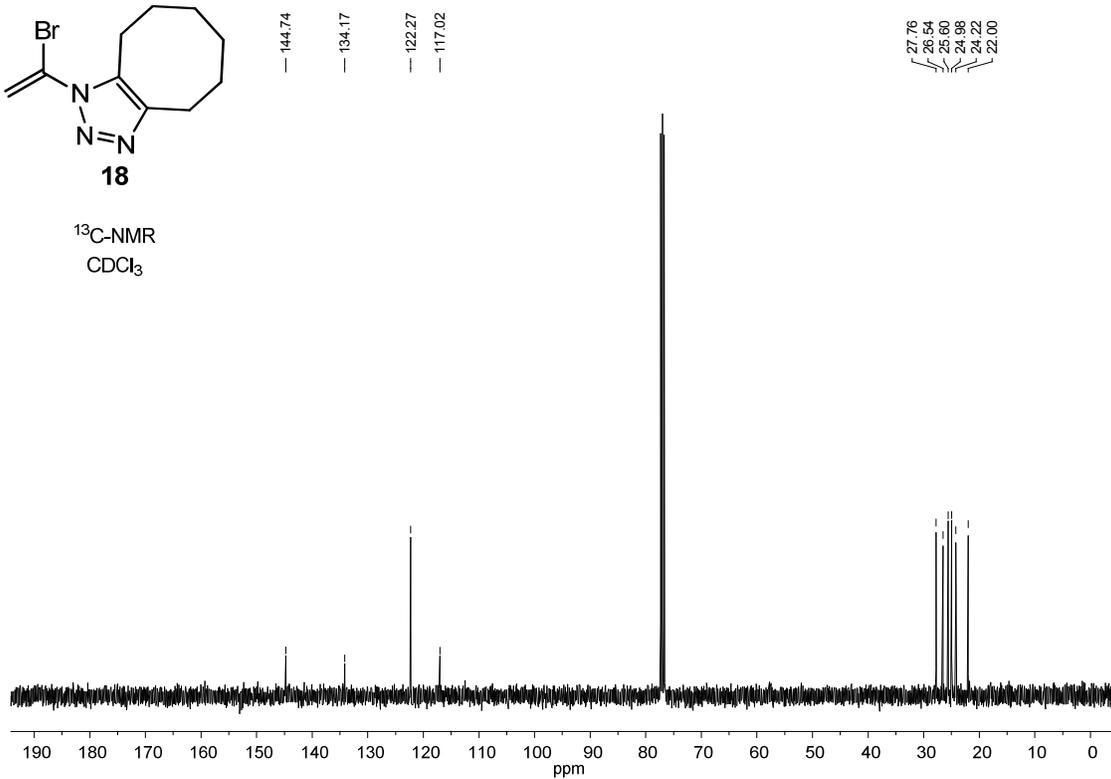
¹H-NMR
CDCl₃



2.91 2.89 2.88 2.86 2.84 2.83
 1.85 1.83 1.82 1.80 1.79 1.78 1.76 1.75 1.49 1.47

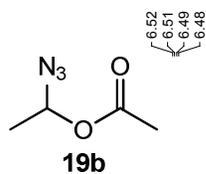


¹³C-NMR
CDCl₃

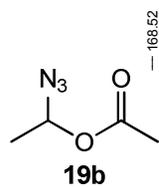
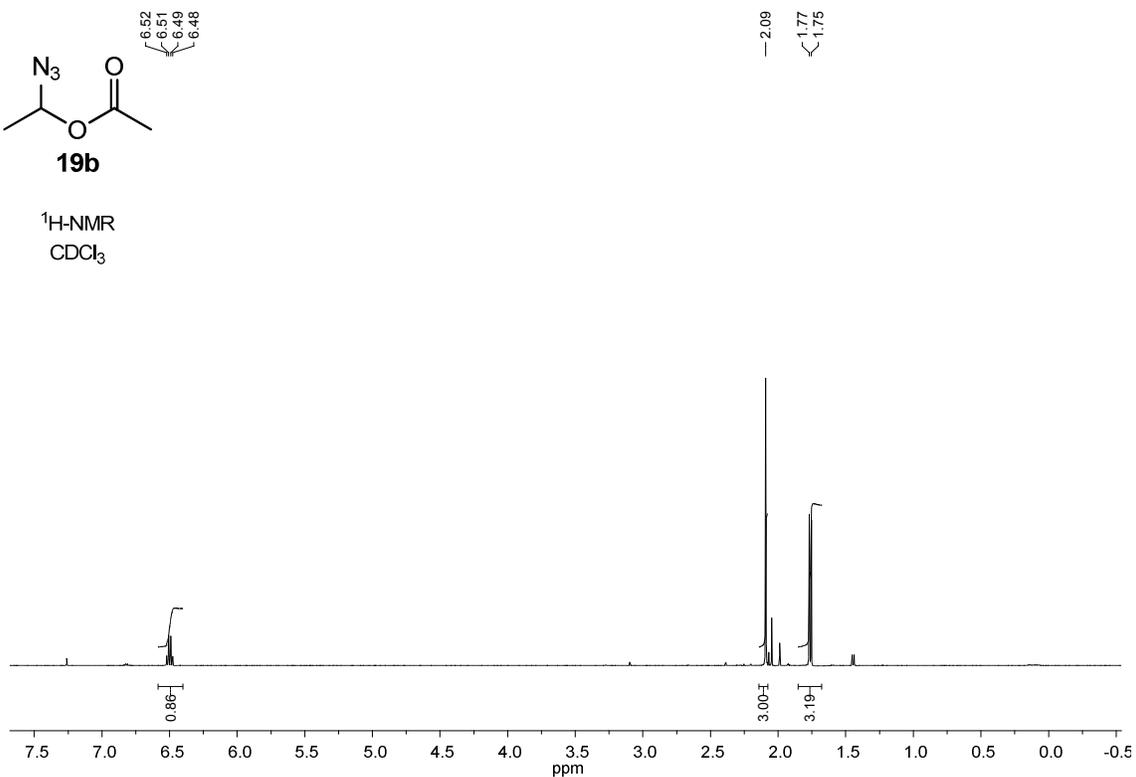


144.74
 134.17
 122.27
 117.02

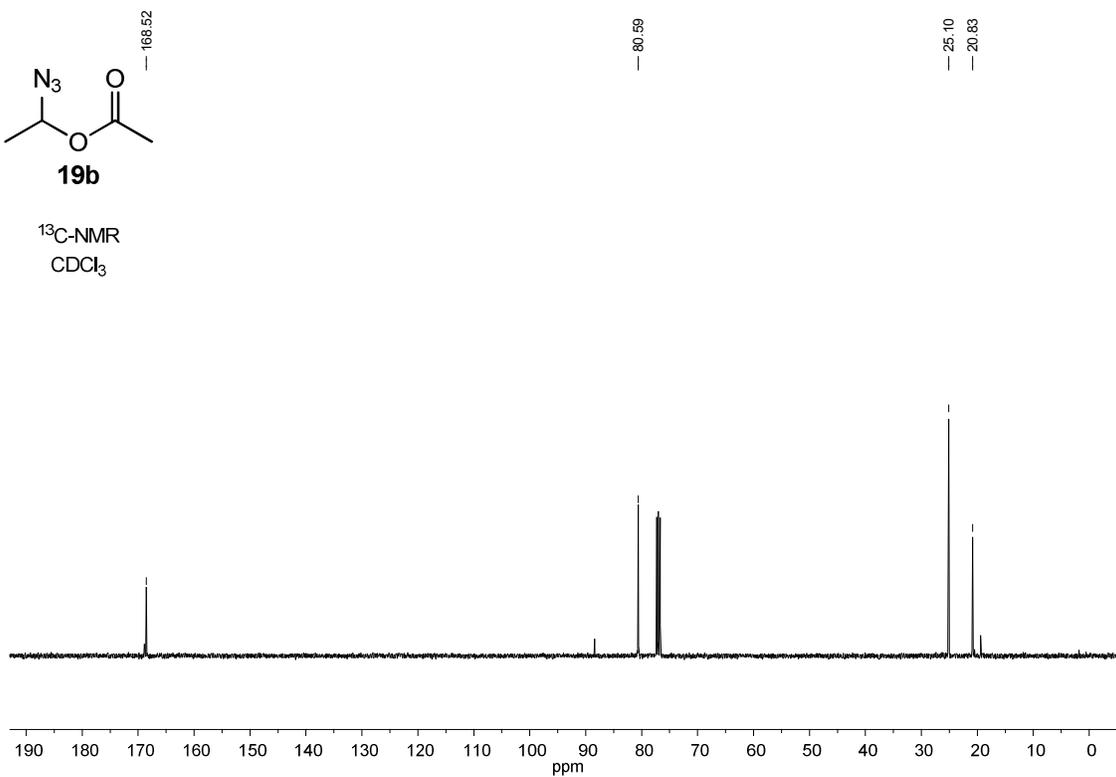
27.76
 26.54
 25.60
 24.98
 24.22
 22.00

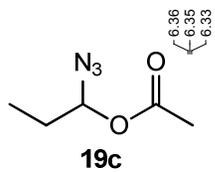


¹H-NMR
CDCl₃

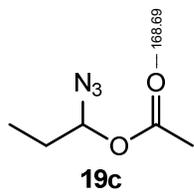
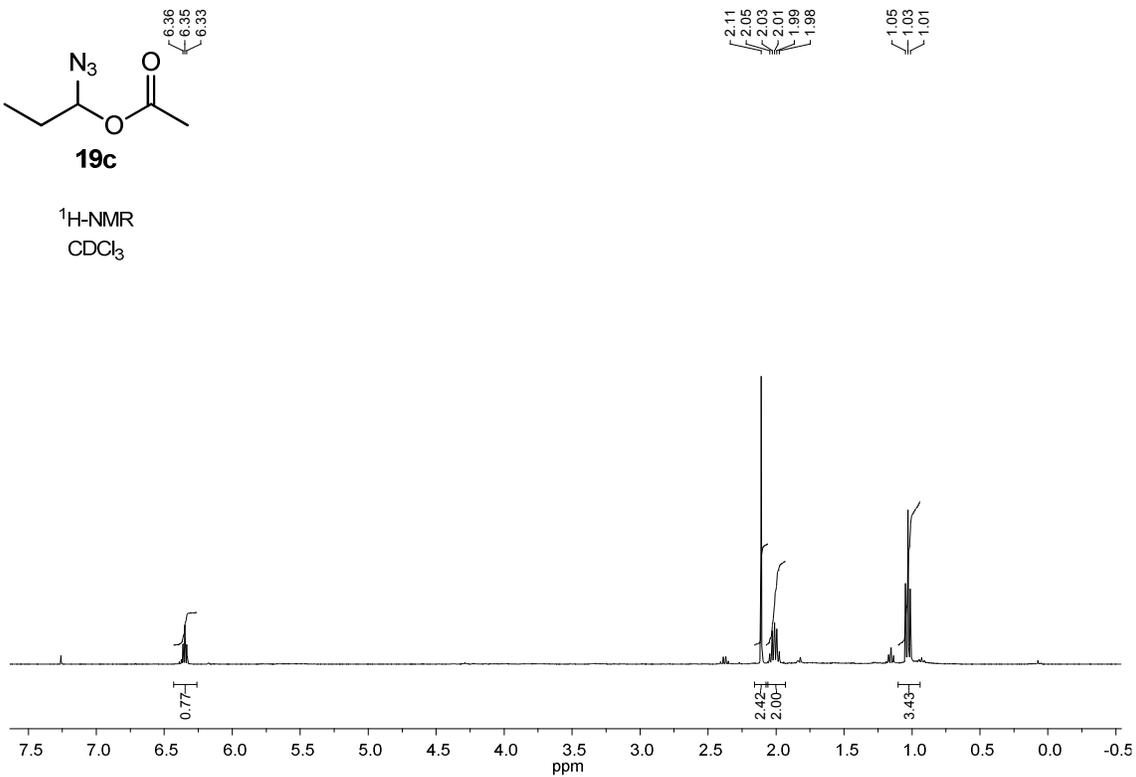


¹³C-NMR
CDCl₃

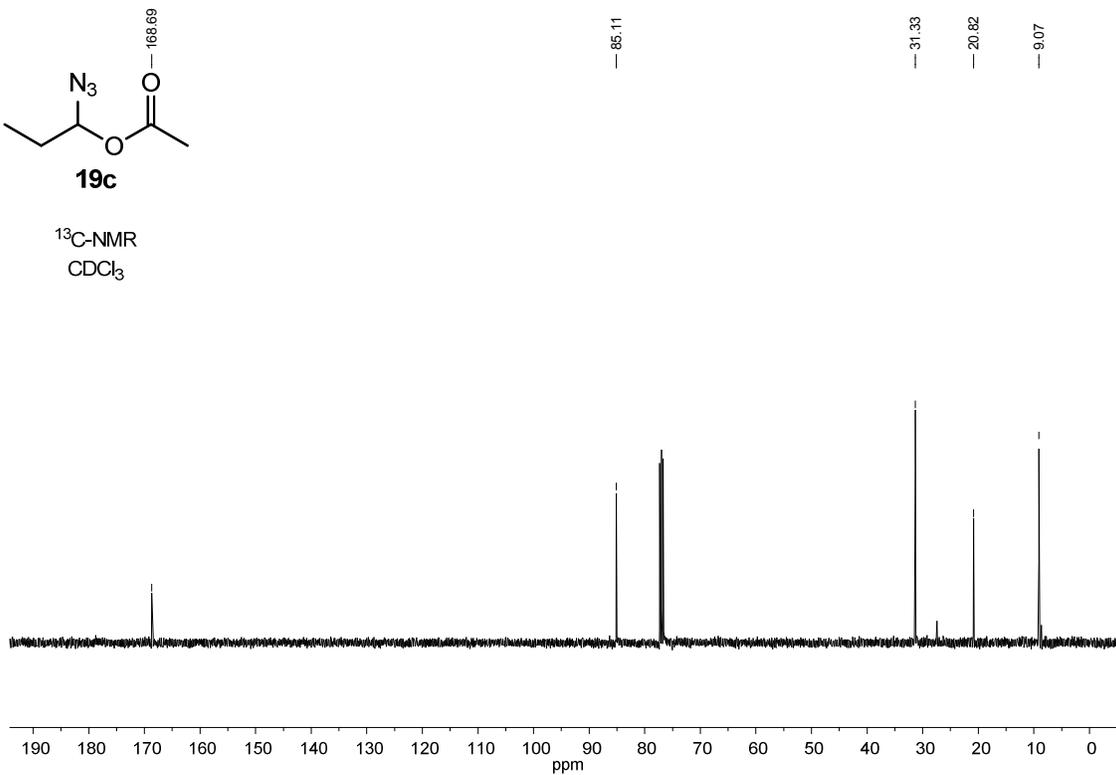


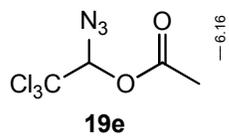


¹H-NMR
CDCl₃

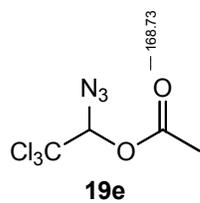
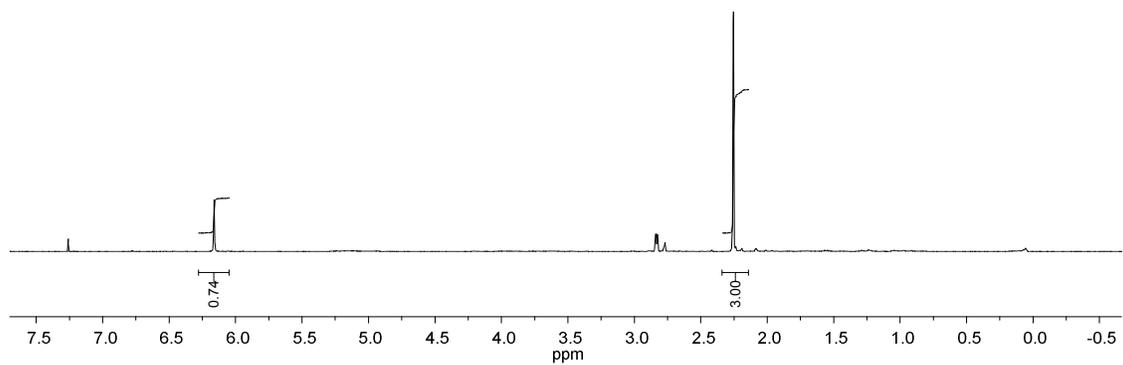


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CDCl₃

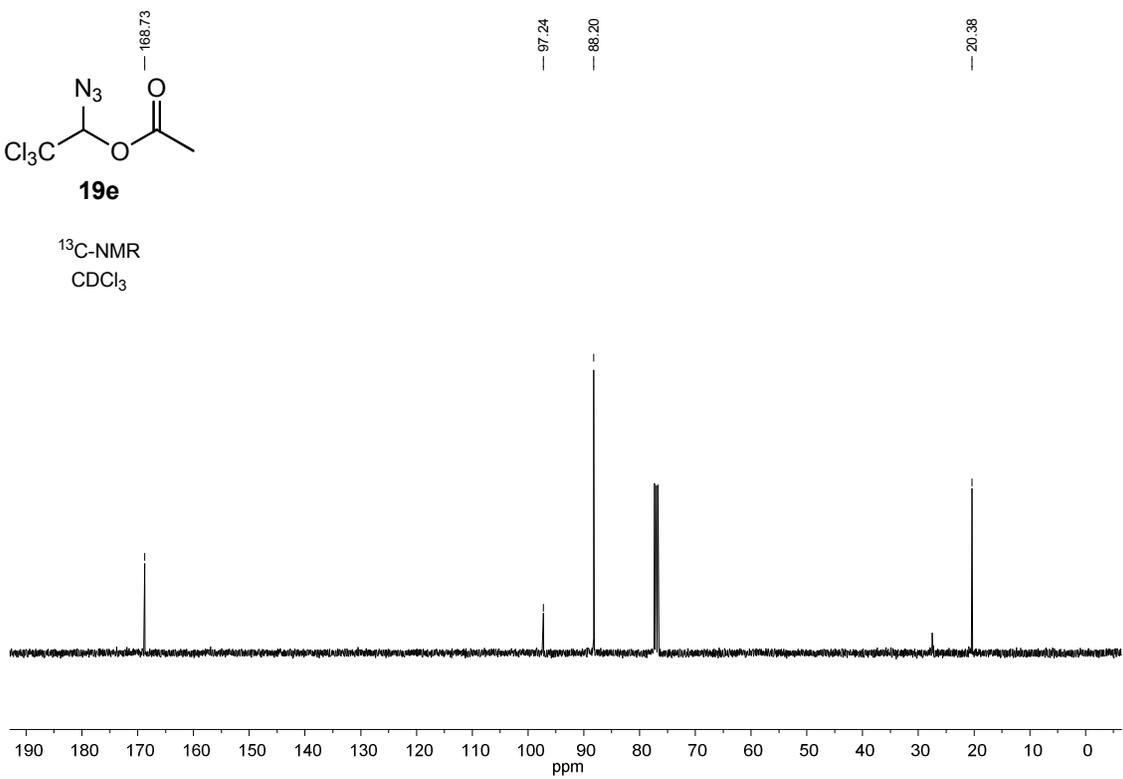


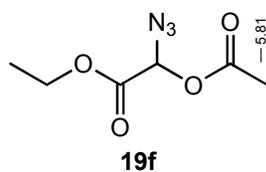


¹H-NMR
CDCl₃

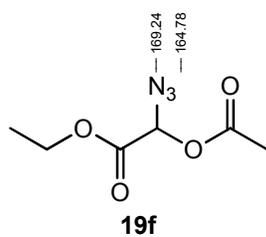
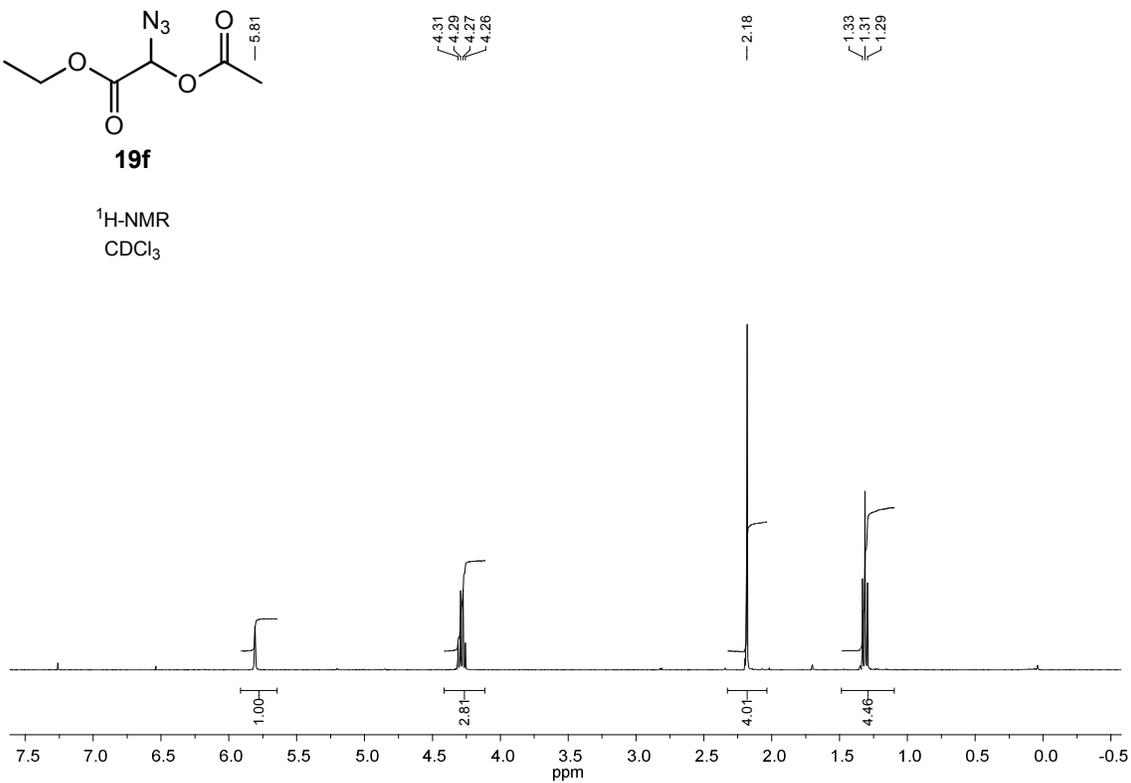


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CDCl₃

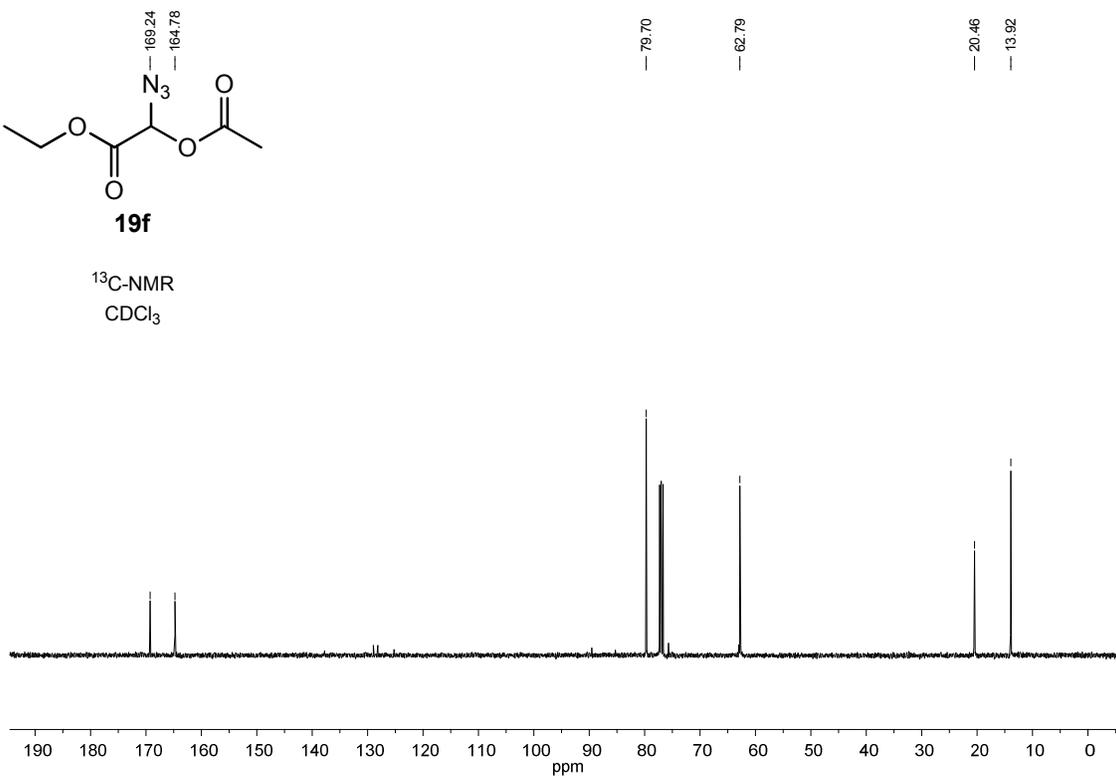


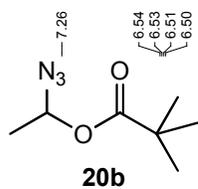


¹H-NMR
CDCl₃

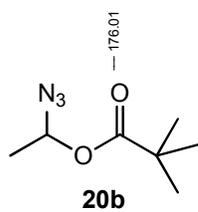
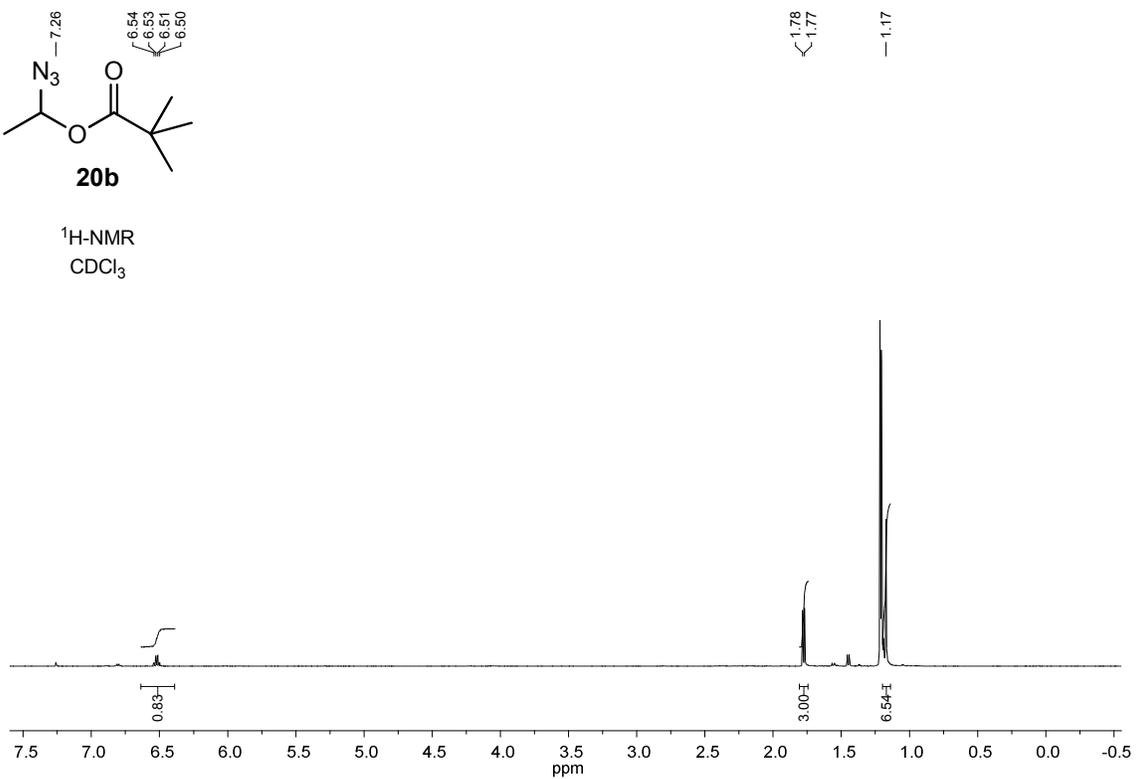


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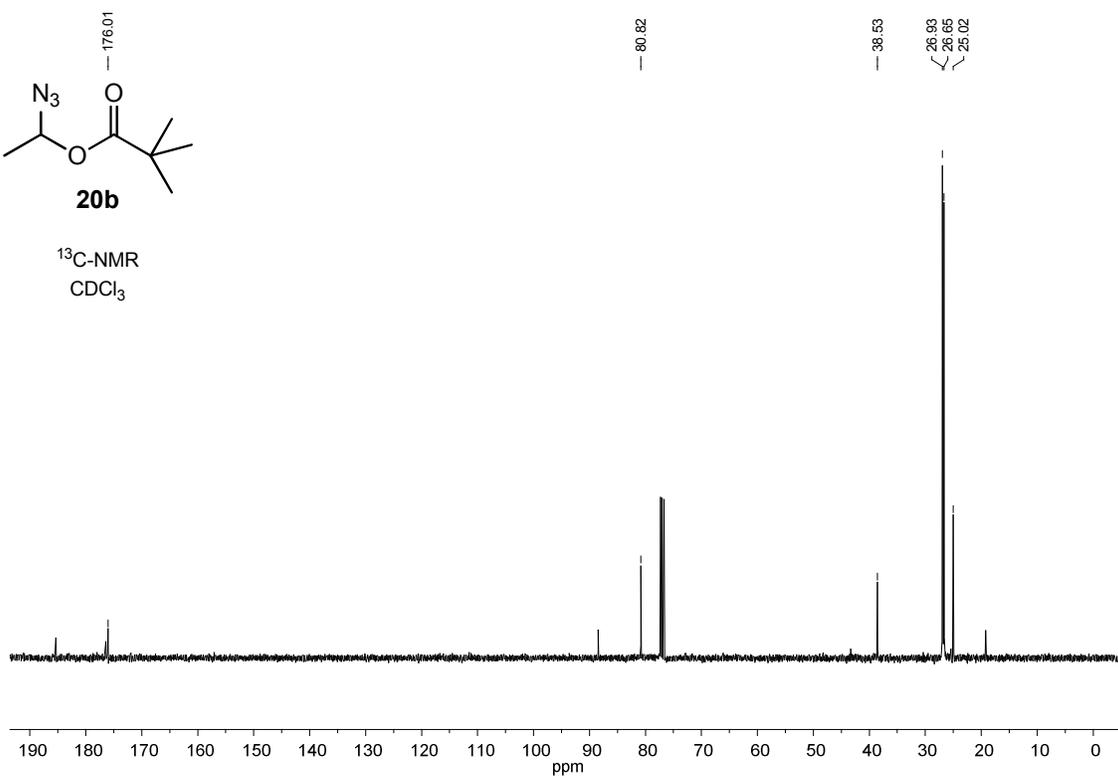


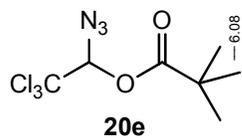


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CDCl₃

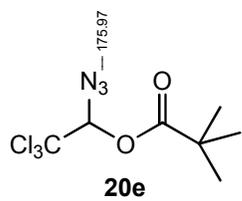
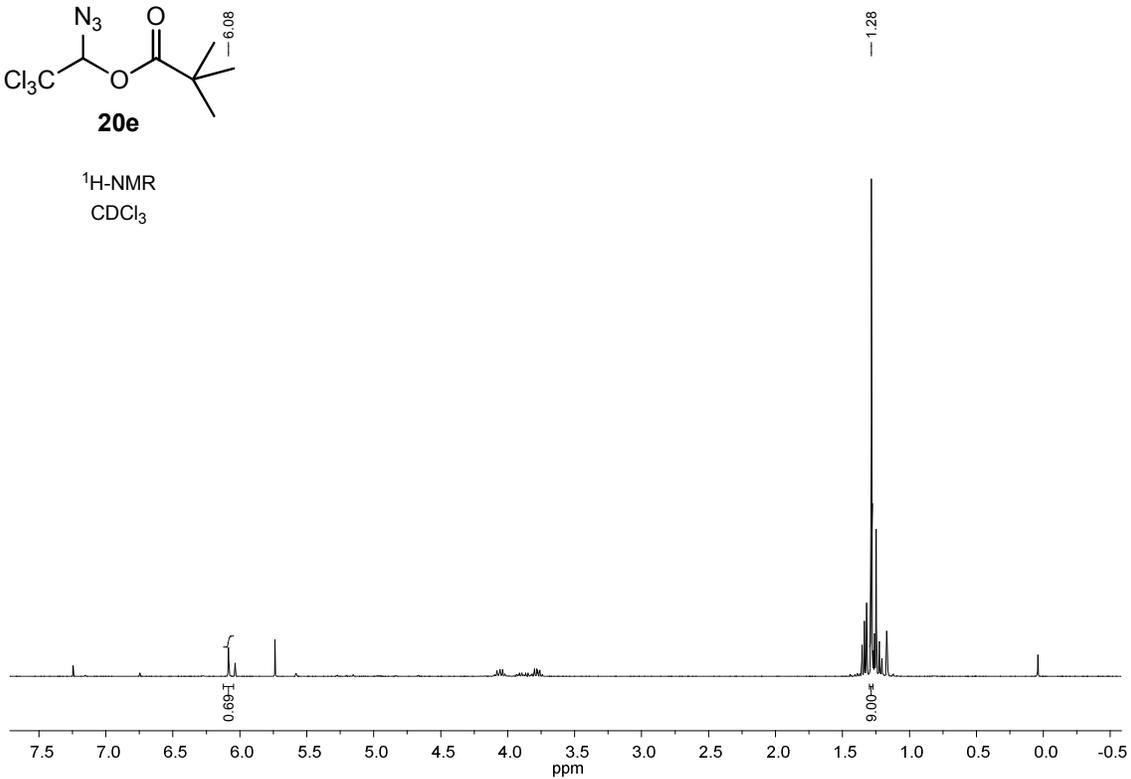


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CDCl₃

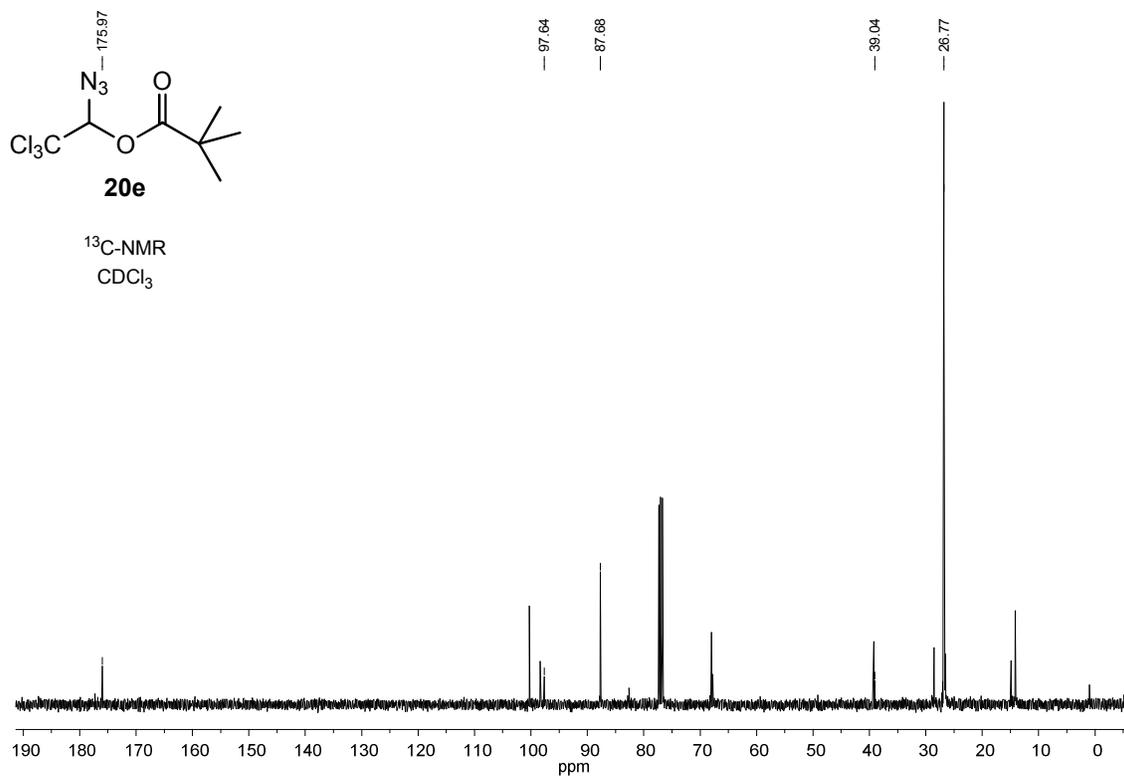


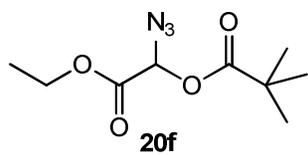


¹H-NMR
CDCl₃

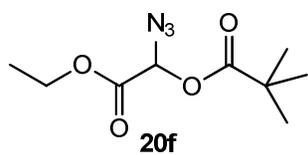
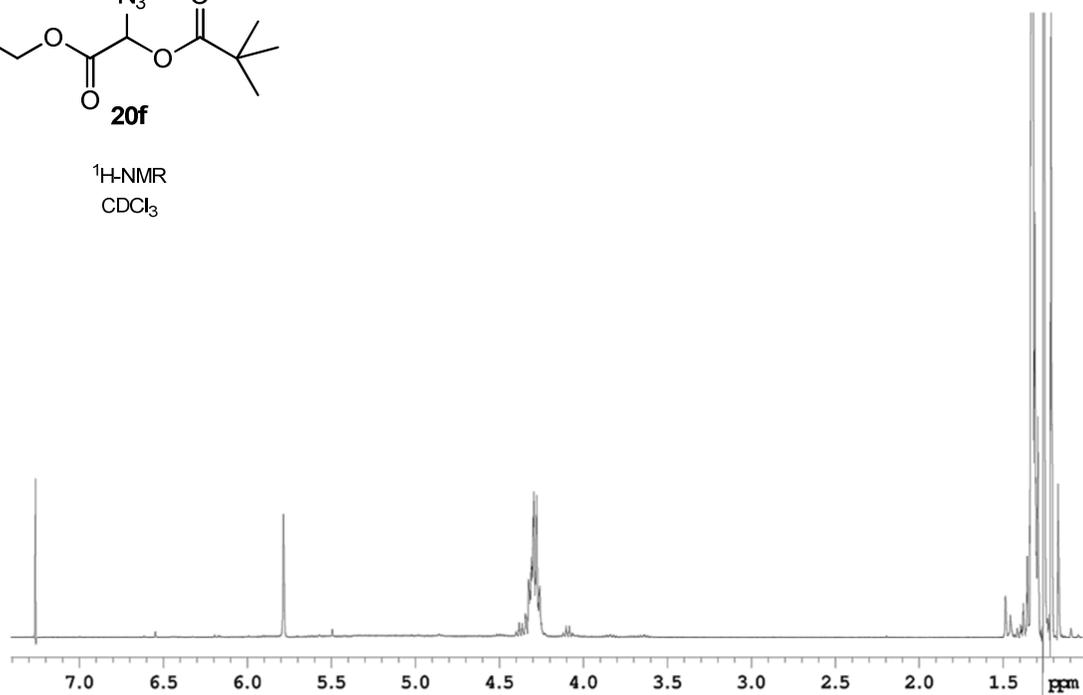


¹³C-NMR
CDCl₃





¹H-NMR
CDCl₃



¹³C-NMR
CDCl₃

