Supplementary Information (SI) for Organic Chemistry Frontiers.

Supporting Information

Synthesis of Noradamantane Building Blocks

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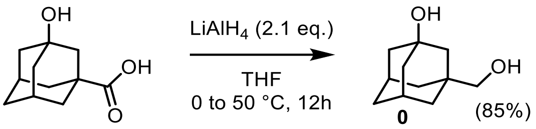
General Information

Unless stated other-wise, reactions with air and moisture sensitive compounds are carried out under an inert atmosphere of argon using an argon/vacuum double manifold Schlenk line, Schlenk tubes and standard Schlenk techniques with anhydrous solvents purchased from commercial sources that were used without further manipulation (exceptions are mentioned with specific compounds in the experimental section). Sealed reactions under high pressure were performed in reinforced glassware with a Teflon coated rubber sealed screw cap (Ace Glass, Inc.). Reactions performed under air were carried out in distilled solvents. Thin layer chromatography (TLC) was performed on Macherey-Nagel POLYGRAM® SIL G/UV$_{254}$ precoated plates and visualised a by 254nm lamp (UV), an ethanolic solution of phosphomolybdic acid (10%w/w) (PMA) or an aqueous solution of $KMnO_4$ ($KMnO_4$ (1 g); Na_2CO_3 (2 g); H_2O (100 mL)). Silica gel column chromatography or reactions requiring the use of silica gel were performed using SiliaFlash® P60 40-63 µm; 230-400 mesh) silica gel. Reactions were also monitored by liquid chromatography mass spectrometry (LCMS) using Shimadzu LCMS-2020 (ESI). Nuclear magnetic resonance (NMR) was measured on Bruker 400 or 600 MHz spectrometers at ambient temperature, unless stated otherwise. ^{1}H-NMR chemical shifts are measured in ppm relative to Me_4Si with the solvent resonance as the internal standard ($CDCl_3$ $\delta = 7.26$ ppm; CD_2Cl_2 $\delta = 5.30$ ppm; MeOD-*d₄* $\delta = 3.31$ ppm; DMSO-d_6 $\delta = 2.50$ ppm; CD_3CN $\delta = 1.94$ ppm). Multiplicities are denoted as follows: s – singlet, d – doublet, t – triplet, q – quartet. ^{13}C-NMR (101 MHz) spectra are measured in ppm relative to Me_4Si with the solvent resonance as a reference ($CDCl_3$ $\delta = 77.16$ ppm; CD_2Cl_2 $\delta = 53.84$ ppm; MeOD-d_4 $\delta = 49.00$ ppm; DMSO-d_6 $\delta = 39.52$ ppm; CD_3CN $\delta = 118.26$ ppm). High resolution mass spectra were obtained using Bruker compact Q-TOF (ESI) or Agilent 7250 GC/QTOF (EI). Infrared (IR) spectra were measured by Thermo Nicolet – Avatar 370 5T-IR and the data reported in wavenumbers (cm^{-1}). X-ray diffraction measurements were conducted using Bruker D8 VENTURE Kappa Duo PHOTON III. Burgess reagent was purchased from TCI and used without further manipulation.

Experimental Section

Synthesis of Adamantane Starting Materials

Compound 0

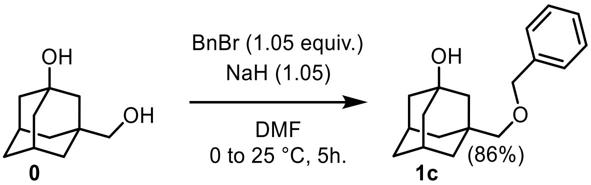


To a cooled suspension of $LiAlH_4$ (1.3 g, 32.1 mmol) to 0 °C in anhydrous THF (80 ml) was added portion-wise 3-hydroxy-1-adamantane carboxylic acid (3 g, 15.3 mmol) under vigorous stirring over 10 minutes. The reaction was transferred to an oil bath, equipped with a condenser and closed with a tube of $CaCl_2$, heated to 50 °C and left stirring overnight. After completion the reaction mixture was cooled down to 0 °C and quenched by the addition of EtOAc (50 ml) followed by distilled water (50 ml). The combined phases were filtered, the filtrate washed with EtOAc and the phases were separated. The aqueous phase was extracted 2x with EtOAc and the combined organic layers were washed with brine, dried over anh. $MgSO_4$ and the solvent was evaporated under reduced pressure. The product was dissolved in a small amount of THF, loaded onto a silica gel column and purified by silica gel column chromatography eluting with pure EtOAc. The product **0** was obtained as a white solid in a yield of 85% (2.37 g).

R$_f$: 0.2 (EtOAc; PMA)
^{1}H NMR (400 MHz, $CDCl_3$) δ 3.28 (s, 2H), 2.26-2.20 (m, 2H), 1.73 – 1.62 (m, 4H), 1.59 – 1.54 (m, 2H), 1.50 – 1.46 (m, 4H), 1.44 – 1.41 (m, 4H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 72.8 (CH_2), 69.0 (C), 46.8 (CH_2), 45.0 ($2CH_2$), 38.9 (C), 37.9 ($2CH_2$), 35.8 (CH_2), 30.5 (2CH).
IR (neat): $\tilde{\nu}$ /cm^{-1} = 3365, 3298, 2914, 2848, 1465, 1340, 1047,646, 596.
HRMS (m/z): Calcd for $C_{11}H_{18}NaO_2^+$: 205.1199 [M+Na]$^+$; Measured: 205.1194.

Notes: If analytical purity of the product is not necessary, it can be used directly in the next step without purification with column chromatography.

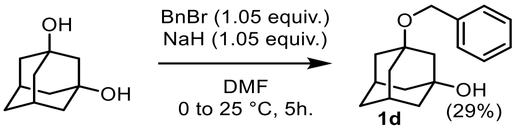
Compound 1c



Starting material **0** (2.3 g, 12.6 mmol) was dissolved in anhydrous DMF (12 ml), the mixture cooled down to 0 °C and NaH (0.53g of 60% dispersion in paraffin, 13.3 mmol) was portion wise and left stirring for 10 minutes. Next, benzyl bromide (2.15 g, 13.3 mmol) was added dropwise and left stirring at 0 °C for an additional 10 minutes. The reaction mixture was removed from the ice bath and gradually warmed up to room temperature while stirring for another 5 h. The reaction was quenched by addition of saturated aqueous NH_4Cl. The phases were partitioned between sat. NH_4Cl and DCM and the aqueous phase extracted 2x with DCM. The combined organic layers were washed with brine, dried over $MgSO_4$ and the solvent evaporated under reduced pressure. The crude mixture was purified by silica gel column chromatography (40% EtOAc:Hex). The product **1c** was obtained as a colourless oil that slowly crystallizes in a yield of 86% (2.96 g).

R$_f$: 0.35 (40% EtOAc:Hex; PMA).
^{1}H NMR (400 MHz, CDCl$_3$) δ 7.38 – 7.26 (m, 5H), 4.51 (s, 2H), 3.12 (s, 2H), 2.25 – 2.19 (m, 2H), 1.74 – 1.64 (m, 4H), 1.59 – 1.54 (m, 4H), 1.51 – 1.46 (m, 5H).
^{13}C NMR (101 MHz, CDCl$_3$) δ 139.0 (C), 128.4 (2CH), 127.5 (CH), 127.4 (2CH), 80.1 (CH$_2$), 73.3 (CH$_2$), 68.9 (C), 47.5 (CH$_2$), 45.0 (2CH$_2$), 38.5 (2CH$_2$), 38.03 (C), 35.8 (CH$_2$), 30.6 (2CH).
IR (neat): $\tilde{\nu}$ /cm^{-1} = 3261, 2902, 2846, 1452, 1115, 1053, 731, 694.
HRMS (m/z): Calcd for $C_{18}H_{24}NaO_2^+$: 295.1669 [M+Na]$^+$; Measured: 295.1668.

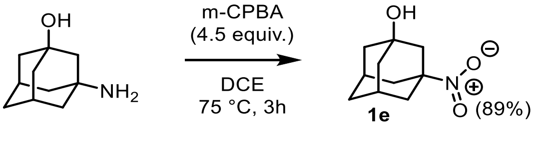
Compound 1d



1,3-dihydroxy adamantane (3 g, 17.9 mmol) was dissolved in anhydrous DMF (18 ml), the mixture cooled down to 0 °C and NaH (0.720 g of 60% dispersion in paraffin, 18.8 mmol) was added portion wise and left stirring for 10 minutes. Next, benzyl bromide (3.05 g (2.1 ml), 18.8 mmol) was added dropwise and the mixture was left stirring at 0 °C for an additional 10 minutes. The reaction mixture was removed from the ice bath and gradually warmed up to room temperature while stirring for another 5 h. The reaction was quenched by addition of saturated aqueous NH$_4$Cl. The phases were partitioned between sat. NH$_4$Cl and DCM and the aqueous phase extracted 2x with DCM. The combined organic layers were washed with brine, dried over anh. MgSO$_4$ and the solvent evaporated under reduced pressure. The crude mixture was purified by silica gel column chromatography (20% EtOAc:Cy). The product **1d** was obtained as a colourless oil that slowly crystallizes in a yield of 1.35 g (29%).

R$_f$: 0.2 (20% EtOAC:Cy; PMA, UV – bottom smaller spot)
^{1}H NMR (400 MHz, CDCl$_3$) δ 7.4 – 7.3 (m, 4H), 7.3 – 7.2 (m, 1H), 4.5 (s, 2H), 2.4 – 2.3 (m, 2H), 1.8 (s, 2H), 1.8 – 1.7 (m, 4H), 1.7 – 1.6 (m, 4H), 1.6 (s, 1H), 1.6 – 1.5 (m, 2H).
^{13}C NMR (101 MHz, CDCl$_3$) δ 139.8 (C), 128.4 (2CH), 127.6 (2CH), 127.3 (CH), 75.1 (C), 70.6 (C), 63.0 (CH$_2$), 49.5 (CH$_2$), 44.4 (2CH$_2$), 40.6 (2CH$_2$), 35.1 (CH$_2$), 31.2 (2CH).
IR (neat): $\tilde{\nu}$ /cm^{-1} = 3209, 2922, 2850, 1699, 1452, 1298, 1134, 1026, 696.
HRMS (m/z): Calcd for $C_{17}H_{22}NaO_2^+$: 281.1512 [M+Na]$^+$; Measured: 281.1513.

Compound 1e

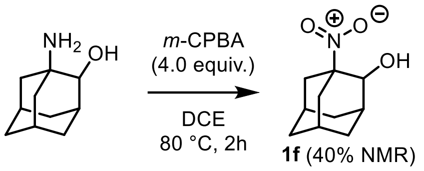


mCPBA (4.83 g of >77% pure, 26.9 mmol) was added to a Schlenk tube, dissolved in anhydrous DCE (30 ml) and heated to 75 °C under N$_2$. A solution of 1-hydroxy-3-amino adamantane (1 g, 6.0 mmol) in hot dry DCE (15 ml) was added dropwise and the reaction mixture was left stirring for 3h at 75 °C. After completion the reaction mixture was cooled down to room temperature and quenched by the addition of aqueous 10% K$_2$CO$_3$. The phases were separated and the organic layer was further washed with aqueous 10% K_2CO_3. The combined aqueous layer was extracted with $CHCl_3$ and the combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 and the solvent was evaporated under reduced pressure. The crude mixture was separated by silica gel column chromatography (10-20% EtOAc:DCM) to give the product **1e** as a white solid (1.05 g; 89%).

R_f : 0.4 (20% EtOAc:DCM; PMA)
^{1}H NMR (400 MHz, $CDCl_3$) δ 2.5 – 2.4 (m, 2H), 2.2 – 2.1 (m, 6H), 1.9 (s, 1H), 1.8 – 1.7 (m, 4H), 1.6 – 1.5 (m, 2H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 86.2 (C), 69.8 (C), 48.1 (CH_2), 43.6 ($2CH_2$), 39.8 ($2CH_2$), 34.2 (CH_2), 30.9 (CH).
IR (neat): $\tilde{\nu}$ /cm^{-1} = 3257, 2925, 2856, 1539, 1369, 1115, 752, 488.
HRMS (m/z): Calcd for $C_{10}H_{15}NNaO_3^+$: 220.0944 [M+Na]$^+$; Measured: 220.0944.

The procedure was adapted from: Schreiner, P. R.; Wurtele, C.; Schwertfeger, H. *Synlett.* **2010**, 3, 493-495.[1] Spectra in accordance with Skrotzki, E. A.; Vandavasi, J. K.; Newman, S. G. *J. Org. Chem.* **2021**, 86, 14169-14176.[2]

Compound 1f



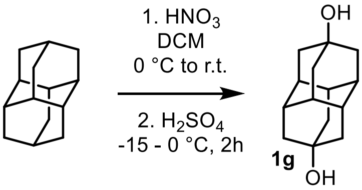
4b (0.7g, 4.2 mmol) and MCPBA (3.0 g, >77% pure, 16.8 mmol) were loaded into a dry Schlenk tube, placed under nitrogen and dissolved in anhydrous DCE (40 ml). The reaction mixture was heated to 80 °C and left stirring for 2h. After completion the reaction mixture was cooled down to room temperature and diluted with DCM. The organic phase was washed with sat. aq. $Na_2S_2O_3$, 3x 10% aq. K_2CO_3, brine and dried over anh. $MgSO_4$. The solvent was evaporated under reduced pressure to give a crude mass of **510 mg**, containing **1f**, that was used in the next step without further purification.

*Notes: The compound **1f** was purified for the purpose of characterization. The bulk was used without further purification. The crude mass is comprised of approx. 40% nitroalcohol **1f** according to NMR.*

R_f : 0.4 (10% EtOAc:$CHCl_3$; PMA)
^{1}H NMR (400 MHz, $CDCl_3$) δ 4.4 – 4.4 (m, 1H), 2.7 – 2.5 (m, 2H), 2.2 – 2.0 (m, 7H), 1.9 – 1.6 (m, 4H), 1.5 – 1.4 (m, 1H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 88.8 (C), 74.0 (CH), 41.2 (CH_2), 35.8 (CH), 35.6 (CH_2), 35.2 (CH_2), 34.2 (CH_2), 29.4 (CH), 29.2 (CH_2), 29.1 (CH).
IR (neat): $\tilde{\nu}$ /cm^{-1} = 3298, 2916, 2864, 1525, 1078, 806, 667.
HRMS (m/z): Calcd for $C_{10}H_{15}NO_2^-$: 197.1057 [M-H]$^-$; Measured: 197.1059.

The procedure was adapted from: Schreiner, P. R.; Wurtele, C.; Schwertfeger, H. *Synlett.* **2010**, 3, 493-495.[1]

Compound 1g

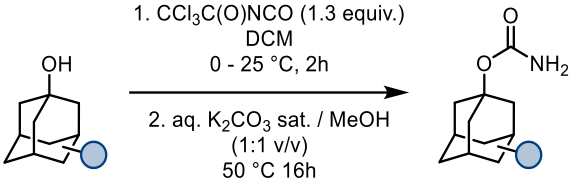


Diamantane (10 g, 53 mmol) was suspended in anhydrous DCM (50 ml) and the flask was placed into a salt-ice-water bath. Fuming 100% HNO_3 was (20 ml) was added dropwise over 10 minutes under vigorous stirring. After the addition was complete the flask was stoppered by a $CaCl_2$ tube and left stirring at 0 °C for an additional 20 minutes. Next the flask was elevated from the bath and left stirring at room temperature for an additional 40 minutes. After completion the reaction mixture was directly placed on a rotary evaporator and the DCM, excess HNO_3 and water were evaporated carefully at ambient temperature (rota bath set to 25 °C). The crude mass was dissolved in a small amount of distilled $CHCl_3$ and solid $NaHCO_3$ was carefully added portion wise with vigorous stirring until the evolution of CO_2 stopped with successive additions. The mixture was left to stir for 20 minutes. The solid was filtered off through a glass frit with a small amount of drying agent and thoroughly washed off with 100 ml of distilled $CHCl_3$. The $CHCl_3$ was evaporated under reduced pressure at ambient temperature (rota bath set to 25 °C) and suspended in a small amount of $CHCl_3$.

The crude mass was added portion wise with a pipette to vigorously stirred concentrated H_2SO_4 (80 ml) that was pre-cooled in a salt-ice-water bath and left stirring for 2 h whilst maintaining the temperature below 0 °C. After completion the reaction mixture was poured onto crushed ice (100 g) and left to cool down. The white precipitate was filtered off through a glass frit, washed with small amounts of water to pH 7, washed with Et_2O and left to dry on air. The dry solid was suspended in $CHCl_3$ and vigorously stirred for 1h at room temperature (to get rid of unwanted soluble diamantanol bi-products). The white solid was retrieved by filtration through a glass frit, washed with a small amount of $CHCl_3$ and dried on air to a stable weight. The product **1g** was obtained as a white powder in a yield of 5.3 g (45%).

The procedure was adapted from: Fokina, N. A.; Tkachenko, B. A.; Merz, A.; Serafin, M.; Dahl, J. E. P.; Carlson, R. M. K.; Fokin, A. A.; Schreiner, P. R. *Eur. J. Org. Chem.* **2007**, 4738-4745.[3]

General procedure A: Carbamate Synthesis

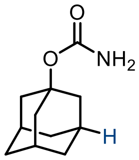


A dry flask was charged with Adamantyl alcohol and dissolved in anhydrous DCM (0.5M). The reaction mixture was cooled to 0 °C and $Cl_3CC(O)NCO$ (1.3 equiv.) was added dropwise. The reaction mixture was allowed to warm up to room temperature and left stirring for an additional 2h. The solvent was evaporated under reduced pressure and a 1:1 (v/v) mixture of saturated aqueous K_2CO_3 and MeOH (0.5M) was added. The reaction mixture was placed into a heating bath and left to stir at 50 °C for 18h. The bulk of the MeOH was evaporated under reduced pressure and the aqueous phase extracted 3x with $CHCl_3$. The combined organic layers were washed with brine, dried over anh. $MgSO_4$ and the solvent evaporated under reduced pressure. The product was purified by silica gel column chromatography.

Any alterations to the general procedure are mentioned with specific compounds.

Notes: If analytical purity of the product is not necessary, it can be used directly in the next step without purification with column chromatography.

Compound 2a



Prepared according to **General procedure A** from adamantan-1-ol (3g, 19.7 mmol). The product **2a** was purified by silica gel column chromatography eluting with 50% EtOAc:Hex and obtained as a white solid (3.73 g, 97%).

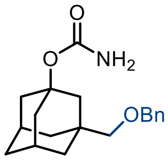
R_f : 0.3 (50% EtOAc:Hex; PMA)

^{1}H NMR (400 MHz, $CDCl_3$): δ 4.71 (s, 2H), 2.13 (s, 3H), 2.09 – 2.05 (m, 6H), 1.67 – 1.57 (m, 6H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 156.3, 79.6, 41.6, 36.3, 30.9.

Spectra are in accordance with published literature: Zonker, B.; Becker, J.; Hrdina, R.; *Org. Biomol. Chem.*, **2021**, 19, 4027.

Compound 2b



Prepared according to **General procedure A** from alcohol **1c** (2.9 g, 10.6 mmol). The product **2b** was purified by silica gel column chromatography eluting with 5-10% EtOAc:DCM and obtained as a white solid (3.19 g, 95%).

R_f : 0.4 (10% EtOAc:DCM).

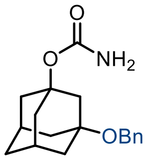
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.31 (m, 4H), 7.30 – 7.25 (m, 1H), 4.73 (s, 2H), 4.50 (s, 2H), 3.11 (s, 2H), 2.27 – 2.20 (m, 2H), 2.13 – 2.02 (m, 4H), 1.94 (s, 2H), 1.68 – 1.62 (m, 1H), 1.60 – 1.48 (m, 5H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 156.2 (C), 138.9 (C), 128.3 (2CH), 127.4 (CH), 127.4 (2CH), 80.0 (C), 79.9 (CH_2), 73.3 (CH_2), 43.6 (CH_2), 41.1 ($2CH_2$), 38.5 ($2CH_2$), 38.0 (C), 35.8 (CH_2), 30.6 (2CH).

IR (neat): $\tilde{\nu}$ /cm^{-1} = 3437, 3325, 3298,3208, 2912, 2850, 1693, 1614, 1356,1053,746, 501.

HRMS (m/z): Calcd for $C_{19}H_{25}NNaO_3^+$: 338.1727 $[M+Na]^+$; Measured: 338.1725.

Compound 2c



Prepared according to ***Altered procedure A*** from alcohol **1d** (1.25 g, 4.8 mmol). Hydrolysis of the intermediate carbamate was performed with a mixture of MeOH and sat. aqueous $NaHCO_3$ (1:1 v/v) at 25 °C for 24h. Extraction was performed with EtOAc. The product **2c** was purified by silica gel column chromatography eluting with 10% EtOAc:DCM. The product was obtained as a white crystalline solid (1.5 g, quant.).

R_f : 0.4 (10% EtOAc:DCM; UV, PMA)

H NMR (400 MHz, $CDCl_3$) δ 7.4 – 7.3 (m, 4H), 7.3 – 7.2 (m, 1H), 4.6 – 4.4 (m, 4H), 2.4 – 2.3 (m, 2H), 2.2 (s, 2H), 2.1 – 2.0 (m, 4H), 1.9 – 1.7 (m, 4H), 1.6 – 1.5 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 155.8 (C), 139.7 (C), 128.4 (2CH), 127.6 (2CH), 127.3 (CH), 80.8 (C), 75.0 (C), 63.0 (CH_2), 45.6 (CH_2), 40.8 ($2CH_2$), 40.6 ($2CH_2$), 35.2 (CH_2), 31.1 (2CH).

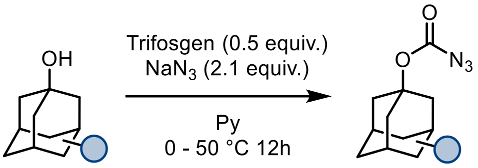
IR (neat): $\tilde{\nu}$ /cm^{-1} = 3510, 3352, 2916, 2850, 1716, 1597, 1346, 1101, 1028, 744, 698.

HRMS (m/z): Calcd for $C_{18}H_{23}NNaO_3^+$: 324.1570 $[M+Na]^+$; Measured: 324.1566

HRMS (m/z): Calcd for $C_{17}H_{21}O^+$: 241.1587 $[M]^+$; Measured: 241.1582 = Artifact from ionization.

Notes: Soluble in warm EtOAc. Handy for preparing a silica slurry for column chromatography.

General procedure B: Carbonazidate Synthesis

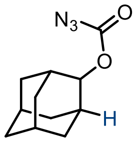


Adamantyl alcohol and sodium azide (2.1 equiv.) were charged into a dry flask under nitrogen, dissolved/suspended in anhydrous pyridine (1M) and the mixture was cooled down to 0 °C with a salt-ice-water bath. A prepared of solution of Trifosgene (0.5 equiv.) in anhydrous DCM (1M) was added dropwise under vigorous stirring (add at a rate to avoid build-up of solid mass) and left stirring at 0 °C for an additional 10 minutes. The reaction mixture elevated from the cold bath and left to stir for 1h at room temperature. Next, the reaction mixture was transferred to a heating bath, heated to 50 °C and stirred overnight. After completion the reaction mixture was allowed to cool down to room temperature, quenched by addition of distilled water and partitioned between distilled water and Et_2O. The organic phase was washed 2x with distilled water and the combined aqueous phases were extracted 2x with Et_2O. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$ and Et_2O with most of the pyridine was evaporated under reduced pressure. The product was purified by a short silica gel column chromatography eluting with pure DCM or $CHCl_3$.

Any alterations to the general procedure are mentioned with specific compounds.

Notes: Completion of the reaction can be also monitored by TLC (pure $CHCl_3$).

Compound 2d



Prepared according to **General procedure B** from adamantan-2-ol (1.0 g, 6.6 mmol). The product **2d** was purified by silica gel column chromatography eluting with pure DCM and obtained as an oil that immediately crystallized to a low melting crystalline solid (1.39 g, 95%).

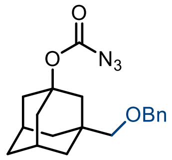
R_f : 0.6 (DCM;UV, PMA)

^{1}H NMR (400 MHz, $CDCl_3$): δ 4.93 – 4.89 (m, 1H), 2.08 (s, 2H), 2.03 – 1.95 (m, 2H), 1.90 – 1.80 (m, 4H), 1.79 – 1.70 (m, 4H), 1.60 – 1.53 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 156.8, 82.2, 37.3, 36.3, 31.8, 31.6, 27.1, 26.9.

Spectra are in accordance with published literature: Lee, J.; Lee, J.; Jung, H.; Kim, D.; Park, J.; Chang, S. *J. Am. Chem. Soc.* **2020**, 142, 28, 12324–12332.

Compound 2e



Prepared according to **General procedure B** from alcohol **1c** (100 mg, 0.37 mmol). The product **2e** was purified by silica gel column chromatography eluting with pure $CHCl_3$ and obtained as a colourless oil (52 mg, 42%).

R$_f$ **:** 0.6 ($CHCl_3$; UV, PMA)

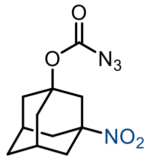
^{1}**H NMR** (400 MHz, $CDCl_3$) δ 7.4 – 7.3 (m, 5H), 4.5 (s, 2H), 3.1 (s, 2H), 2.3 – 2.2 (m, 2H), 2.2 – 2.0 (m, 4H), 2.0 – 1.9 (m, 2H), 1.7 – 1.5 (m, 6H).

^{13}**C NMR** (101 MHz, $CDCl_3$) δ 155.3 (C), 138.9 (C), 128.4 (2CH), 127.6 (CH), 127.5 (2CH), 85.1 (C), 79.7 (CH_2), 73.4 (CH_2), 43.1 (CH_2), 40.6 ($2CH_2$), 38.5 (C), 38.4 ($2CH_2$), 35.6 (CH_2), 30.7 (2CH).

IR (neat): $\tilde{\nu}$ /cm^{-1} = 2912, 2854, 2177, 2131, 1724, 1228, 1146, 999, 750.

HRMS (m/z): Calcd for $C_{19}H_{23}N_3NaO_3^+$: 364.1632 [M+Na]$^+$; Measured: 364.1633.

Compound 2f



Prepared according to **General procedure B** from nitroalcohol **1e** (1.0 g, 5.1 mmol). The product **2f** was purified by silica gel column chromatography eluting with pure $CHCl_3$ and obtained as a low melting colourless crystalline solid (1.25 g, 93%).

R$_f$ **:** 0.5 ($CHCl_3$; UV, PMA)

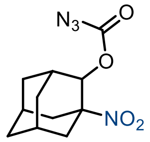
^{1}**H NMR** (400 MHz, $CDCl_3$) δ 2.6 (s, 2H), 2.5 – 2.5 (m, 2H), 2.2 – 2.1 (m, 8H), 1.7 – 1.6 (m, 2H).

^{13}**C NMR** (101 MHz, $CDCl_3$) δ 155.5 (C), 85.7 (C), 83.3 (C), 43.7 (CH_2), 39.7 ($2CH_2$), 39.3 ($2CH_2$), 34.1 (CH_2), 30.8 (2CH).

IR (neat): $\tilde{\nu}$ /cm^{-1} = 2956, 2868, 2407, 2195, 2137, 1707, 1537, 1234, 1065, 756, 480.

HRMS (m/z): Calcd for $C_{11}H_{14}N_4NaO_4^+$: 289.0907 [M+Na]$^+$; Measured: 289.0908.

Compound 2g



Prepared according to ***Altered procedure B*** from nitroalcohol **1f**. The crude mass (510 mg) comprised of approx. 40% nitroalcohol **1f** was used for the reaction. The amount of the reagents necessary were calculated according to 204 mg of nitroalcohol **1f** (1.0 mmol). NaN_3 (142 mg, 2.2 mmol), trifosgen (153 mg, 0.52 mmol). The rest remains identical. The product **2g** was purified by silica gel column chromatography eluting with 0-1% EtOAc:$CHCl_3$ and obtained as a colourless oil (260 mg, 23% over two steps)

R$_f$ **:** 0.5 (1% EtOAc:$CHCl_3$; UV, PMA)

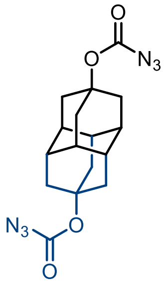
^{1}**H NMR** (400 MHz, $CDCl_3$) δ 5.6 – 5.5 (m, 1H), 2.5 – 2.4 (m, 2H), 2.3 – 2.1 (m, 5H), 1.9 – 1.8 (m, 3H), 1.8 – 1.7 (m, 2H), 1.6 – 1.5 (m, 1H).

^{13}**C NMR** (101 MHz, $CDCl_3$) δ 156.5 (C), 85.5 (C), 79.8 (CH), 42.1 (CH_2), 35.3 (CH_2), 34.8 (CH_2), 34.3 (CH_2), 33.5 (CH), 29.6 (CH_2), 29.1 (CH), 28.7 (CH).

IR (neat): $\tilde{\nu}$ /cm^{-1} = 2935, 2864, 2183, 2139, 1732, 1543, 1242, 1011, 748.

HRMS (m/z): Calcd for $C_{11}H_{18}N_4NaO_4^+$: 289.0907 [M+Na]$^+$; Measured: 289.0906.

Compound 2h



Prepared according to ***Altered procedure B*** from diol **1g** (5.2 g, 23.6 mmol). 50 ml of anhydrous pyridine, NaN$_3$ (4.1 equiv, 6.3 g, 96.8 mmol) and trifosgen (1.0 equiv., 7 g, 23.6 mmol) in 20 ml of anhydrous DCM. After quenching with water at room temperature the reaction mixture was diluted and extracted with CHCl$_3$ and purified according to **General procedure B**. Silica gel column chromatography (slurry dry load) eluting with 1% EtOAc:CHCl$_3$. The final product **2h** was retrieved as a white powder (6.8 g, 81%).

R$_f$: 0.6 (1% EtOAc:CHCl$_3$; UV, PMA)

^{1}H NMR (400 MHz, CDCl$_3$) δ 2.2 (s, 12H), 2.1 (s, 6H).

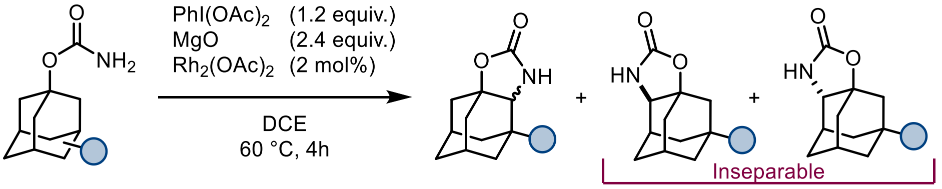
^{13}C NMR (101 MHz, CDCl$_3$) δ 155.5 (2C), 82.8 (2C), 40.0 (6CH), 38.6 (6CH$_2$).

IR (neat): $\tilde{\nu}$ /cm^{-1} = 2902, 2171, 2131, 1724, 1267, 1209, 1070, 999, 912, 754.

HRMS (m/z): Calcd for $C_{16}H_{18}N_6NaO_4^+$: 381.1282 [M+Na]$^+$; Measured: 381.1283.

The procedure was adapted from and the spectra are in accordance with: Zonker, B.; Becker, J.; Hrdina, R.; *Org. Biomol. Chem.,* **2021**, 19, 4027.[4]

General procedure C: Rhodium Catalysed Carbamate Annulation



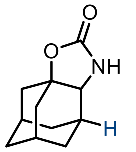
A dry Schlenk tube was charged with carbamate, MgO (2.4 equiv.), PhI(OAc)$_2$ (1.2 equiv.) and Rh$_2$(OAc)$_4$ (2 mol%) and anhydrous DCE (0.17M) was added. The reaction mixture placed into a heating bath, heated to 60 °C and stirred for 4h. Ater completion the reaction mixture was allowed to cool down to room temperature and filtered through a glass frit with a short pad of silica and anhdrous MgSO$_4$ (to eliminate baseline impurities and leftover Rhodium salts) eluting with EtOAc:DCM 1:1. The solvent was evaporated under reduced pressure and repeatedly evaporated from hexane to get rid of as much iodobenzene (side product of the reaction) as possible. The isomers were roughly separated by silica gel column chromatography (EtOAc:Cy). Purification of isomers was performed by additional silica gel column chromatography (EtOAc:DCM).

The procedure was adapted from: Rohde et. al. *J. Med. Chem.* **2007**, 50, 149-164.[5] and Zonker, B.; Becker, J.; Hrdina, R.; *Org. Biomol. Chem.,* **2021**, 19, 4027.[4]

Any alterations to the general procedure are mentioned with specific compounds.

Notes: For practical purposes, minimal purification of the mixture of isomers can be performed (complete removal of iodo-benzene and baseline impurities) without individual separation and can be carried out to the next steps. Both regio-isomers can be easily separated later on.

Compound 3a



Prepared according to **General procedure C** from carbamate **2a** (3.5 g, 17.9 mmol). The product **3a** was purified by silica gel column chromatography eluting with 10% EtOAc:DCM and obtained as a white solid (2.66 g, 77%).

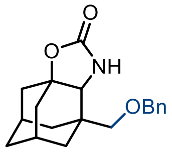
R_f : 0.3 (10% EtOAc:DCM; PMA)

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.10 (s, 1H), 3.63 – 3.60 (m, 1H), 2.29 – 2.19 (m, 2H), 2.13 – 1.93 (m, 4H), 1.86 – 1.52 (m, 7H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 161.6, 80.5, 64.0, 40.0, 37.1, 36.2, 36.2, 31.1, 31.0, 29.2, 29.0.

Spectra are in accordance with published literature: Zonker, B.; Becker, J.; Hrdina, R.; *Org. Biomol. Chem.,* **2021**, 19, 4027.[4]

Compound 3b



Prepared according to **General procedure C** from carbamate **2b** (2.6 g, 8.2 mmol) as a crude mixture together with regio-isomers **3c** in a ratio of 1:2.4 (Crude NMR). The crude mixture was roughly separated by silica gel column chromatography with gradient elution by 30-50% EtOAc. Additional purification with 10% EtOAc:DCM proved to be difficult. The product **3b** was characterized from pure fractions and carried to the next step with impurities (930 mg, estimated yield relative to regio-isomers **3c** is 24%). Pure cyclic carbamate **3b** was obtained as a white crystalline solid.

R_f : 0.45 (50% EtOAc:Cy); 0.45 (10% EtOAc:DCM; UV, PMA)

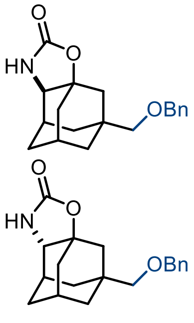
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.27 (m, 5H), 5.36 (s, 1H), 4.47 (q, *J* = 12.1 Hz, 2H), 3.47 (s, 1H), 3.22 – 3.16 (m, 2H), 2.35 – 2.28 (m, 1H), 2.22 – 2.16 (m, 1H), 2.12 – 1.94 (m, 4H), 1.75 – 1.69 (m, 1H), 1.65 – 1.55 (m, 2H), 1.53 – 1.38 (m, 2H), 1.35 – 1.27 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 160.4 (C), 138.0 (C), 128.6 (2CH), 128.0 (CH), 127.6 (2CH), 81.2 (C), 77.9 (CH_2), 73.5 (CH_2), 66.0 (CH), 39.5 (CH_2), 38.9 (CH_2), 38.3 (C), 36.7 (CH_2), 36.0 (CH_2), 32.3 (CH_2), 30.9 (CH), 29.2 (CH).

IR (neat): $\tilde{\nu}$ /cm^{-1} = 3230, 3132, 2912, 2904, 1751, 1294, 957, 746, 695.

HRMS (m/z): Calcd for $C_{19}H_{23}NNaO_3^+$: 336.1570 [M+Na]$^+$; Measured: 336.1568.

Compound 3c



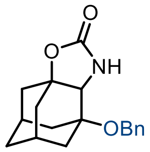
Prepared according to **General procedure C** from carbamate **2b** (2.6 g, 8.3 mmol) as a crude mixture together with regio-isomer **3b** in a ratio of 2.4:1 (Crude NMR). The mixture of regio-isomers **3c** was isolated by silica gel column chromatography with gradient elution 30-50% EtOAc:Cy and obtained as a colourless thick paste (1.5 g, 58%)

R_f : 0.3 (50% EtOAc:Cy); 0.3 (20% EtOAc:DCM; UV, PMA)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.4 – 7.3 (m, 5H), 5.2 (s, 1H), 4.5 – 4.5 (m, 2H), 3.7 – 3.6 (m, 1H), 3.2 – 3.1 (m, 2H), 2.4 – 2.3 (m, 2H), 2.2 – 1.5 (m, 12H).

HRMS (m/z): Calcd for $C_{19}H_{24}NO_3^+$: 314. 1751 [M+H]$^+$; Measured: 314.1748.

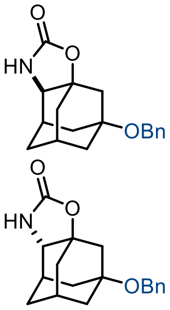
Compound 3d



Prepared according to ***Altered procedure C*** from carbamate **2c** (1.0 g, 3.3 mmol). $PhI(OAc)_2$ (1.8 equiv., 1.92 g, 6 mmol), MgO (3.7 equiv., 490 mg, 12.3 mmol); 87% conversion; 78% combined yield. The crude mixture contained the product **3d** together with regio-isomers **3e** in a ratio of 1:1.3 (Crude NMR). The crude mixture was roughly separated by silica gel column chromatography with gradient elution by 30-50% EtOAc. Additional purification with 10-20% EtOAc:DCM gave product **3d** as a white solid (320 mg, 32%).

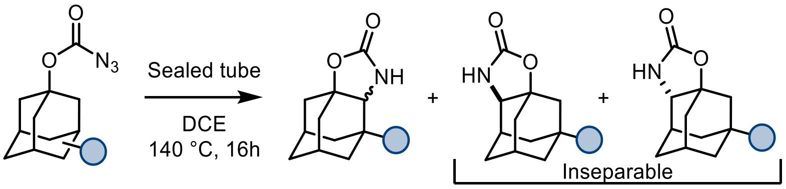
R$_f$: 0.5 (50% EtOAc:Cy); 0.4 (20% EtOAc:DCM; UV, PMA)
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.4 – 7.2 (m, 5H), 5.1 (s, 1H), 4.5 (s, 2H), 3.6 (s, 1H), 2.6 – 2.4 (m, 1H), 2.4 – 2.3 (m, 1H), 2.2 – 1.9 (m, 5H), 1.9 – 1.8 (m, 1H), 1.8 – 1.7 (m, 2H), 1.6 (s, 2H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 160.4 (C), 138.8 (C), 128.6 (2CH), 127.8 (CH), 127.4 (2CH), 82.3 (C), 74.9 (C), 67.1 (CH), 63.7 (CH_2), 40.4 (CH_2), 39.1 (CH_2), 36.7 (CH_2), 35.3 (CH_2), 33.4 (CH_2), 32.4 (CH), 30.6 (CH).
IR (neat): $\tilde{\nu}$ /cm^{-1} = 3242, 2931, 2866, 1743, 1284, 1119, 731, 694.
HRMS (m/z): Calcd for $C_{18}H_{21}NNaO_3^+$: 322.1414 $[M+Na]^+$; Measured: 322.1409.

Compound 3e



Prepared according to ***Altered procedure C*** from carbamate **2c** (1.0 g, 3.3 mmol). $PhI(OAc)_2$ (1.8 equiv., 1.92 g, 6 mmol), MgO (3.7 equiv., 490 mg, 12.3 mmol); 87% conversion; 78% combined yield. The crude mixture contained the cyclic carbamates **3e** together with regio-isomer **3d** in a ratio of 1.3:1 (Crude NMR). The mixture of regio-isomers **3e** was purified by silica gel column chromatography with gradient elution by 30-50% EtOAc:Cy and obtained as a colourless thick paste (460 mg, 46%)
R$_f$: 0.2 (50% EtOAc:Cy); 0.2 (20% EtOAc:DCM; UV, PMA)
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.4 – 7.3 (m, 4H), 7.3 – 7.3 (m, 1H), 5.2 (s, 1H), 4.5 – 4.5 (m, 2H), 3.7 – 3.5 (m, 1H), 2.5 – 2.4 (m, 2H), 2.3 – 1.5 (m, 12H).
HRMS (m/z): Calcd for $C_{19}H_{24}NO_3^+$: 314. 1751 $[M+H]^+$; Measured: 314.1748.

General procedure D: Annulated Carbamate Synthesis from Carbonazidates

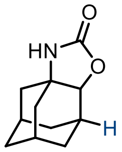


Adamantyl carbonazidate was loaded into a pressure vessel equipped with a magnetic stir bar under a stream of nitrogen and dissolved in anhydrous DCE (0.4M). The DCE was degassed for 5 minutes with bubbling nitrogen, the pressure vessel was sealed, transferred to an oil bath and the reaction mixture was heated to 140 °C and left stirring overnight. The reaction mixture was allowed to cool down to room temperature. The pressure vessel was cooled down in an ice bath and carefully opened. The solvent was evaporated under reduced pressure and the product purified by silica gel column chromatography.

Any alterations to the general procedure are mentioned with specific compounds.

Notes: As aforementioned, minimal or any purification of the mixture of isomers can be performed without individual separation and can be carried out directly to the next steps for practical purposes. Both regio-isomers can be easily separated later on.

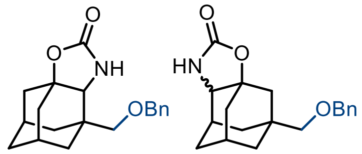
Compound 3f



Prepared according to **General procedure D** from carbonazidate **2d** (1.0 g, 4.5 mmol). The product **3f** was purified by silica gel column chromatography eluting with 30% EtOAc:DCM and obtained as a white solid (633 mg, 73%).
R$_f$: 0.4 (30% EtOAc:DCM; PMA)
^{1}H NMR (400 MHz, $CDCl_3$): δ 5.65 (s, 1H), 4.14 – 4.10 (m, 1H), 2.44 – 2.38 (m, 1H), 2.15 – 2.09 (m, 1H), 2.06 – 2.00 (m, 1H), 1.97 – 1.91 (m, 1H), 1.90 – 1.79 (m, 4H), 1.78 – 1.54 (m, 5H).

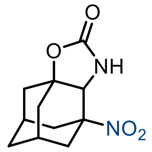
^{13}C NMR (101 MHz, $CDCl_3$): δ 161.2, 85.5, 56.6, 39.7, 39.5, 36.4, 35.9, 30.3, 29.7, 29.6, 27.9.
Spectra are in accordance with published literature: Lee, J.; Lee, J.; Jung, H.; Kim, D.; Park, J.; Chang, S. *J. Am. Chem. Soc.* **2020**, 142, 28, 12324–12332.

Compound 3g



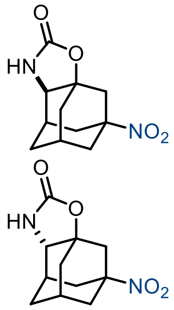
Prepared according to **General procedure D** from carbonazidate **2e** (45 mg, 0.13 mmol) as a crude mixture of regio-isomers **3g** in a ratio of 1:2.3 and an NMR yield of 60% with durene as an internal standard.

Compound 3h



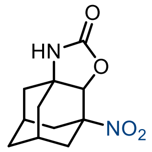
Prepared according to **General procedure D** from carbonazidate **2f** (820 mg, 3.1 mmol) as a mixture of regio-isomers together with **3i** in a ratio of 0.1:1 (according to crude NMR) and purified by silica gel column chromatography eluting with 30% EtOAc:DCM. Product **3h** was obtained as a white powder (30 mg, 4%).
R_f : T = 0.6 (30% EtOAc:DCM)
^{1}H NMR (400 MHz, $CDCl_3$) δ 5.5 (s, 1H), 4.0 (s, 1H), 2.6 (s, 1H), 2.5 – 2.0 (m, 8H), 1.9 – 1.6 (m, 3H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 159.4 (C), 86.1 (C), 81.7 (C), 64.1 (CH), 40.8 (CH_2), 38.5 (CH_2), 36.3 (CH_2), 34.4 (CH_2), 33.5 (CH_2), 31.7 (CH), 30.0 (CH).
IR (neat): $\tilde{\nu}$ /cm^{-1} = 3269, 2937, 2862, 1761, 1533, 13336, 1286, 1070, 775, 706.
HRMS (m/z): Calcd for $C_{11}H_{15}N_2O_4^+$: 239.1026 [M+H]$^+$; Measured: 239.1029

Compound 3i



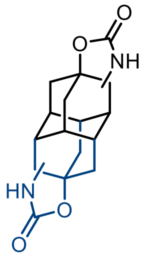
Prepared according to **General procedure D** from carbonazidate **2f** (820 mg, 3.1 mmol) as a mixture of regio-isomers that were purified by silica gel column chromatography eluting with 20-30% EtOAc:DCM. Product **3i** was obtained as a white semisolid (670 mg, 91%).
R_f : 0.4 (30% EtOAc:DCM; PMA)
^{1}H NMR (400 MHz, $CDCl_3$) δ 5.9 – 5.6 (m, 1H), 3.8 – 3.6 (m, 1H), 2.7 – 2.5 (m, 3H), 2.5 – 2.3 (m, 1H), 2.3 – 2.0 (m, 5H), 1.9 – 1.7 (m, 2H), 1.7 – 1.6 (m, 1H).
HRMS (m/z): Calcd for $C_{11}H_{15}N_2O_4^+$: 239.1026 [M+H]$^+$; Measured: 239.1025.

Compound 3j



Prepared according to **General procedure D** from carbonazidate **2g** (250 mg, 0.94 mmol). The product **3j** was purified by silica gel column chromatography eluting with 10-20% EtOAc:DCM and obtained as a white solid (171 mg, 76%).
R_f : 0.4 (20% EtOAc:DCM); 0.6 (30% EtOAc:DCM; PMA, $KMnO_4$)
^{1}H NMR (400 MHz, $CDCl_3$) δ 5.6 (s, 1H), 4.7 (s, 1H), 2.5 – 2.4 (m, 2H), 2.4 – 2.3 (m, 3H), 2.2 – 2.1 (m, 1H), 2.0 – 1.9 (m, 2H), 1.9 – 1.8 (m, 2H), 1.7 – 1.6 (m, 2H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 159.0 (C), 83.7 (C), 83.0 (CH), 59.4 (C), 42.2 (CH_2), 38.3 (CH_2), 38.2 (CH_2), 34.1 (CH_2), 32.3 (CH_2), 31.6 (CH), 29.5 (CH).
IR (neat): $\tilde{\nu}$ /cm^{-1} = 3332, 3251, 2941, 1738, 1535, 1334, 1134, 1063, 922, 769, 648, 550.
HRMS (m/z): Calcd for $C_{11}H_{15}N_2O_4^+$: 239.1026 [M+H]$^+$; Measured: 239.1027.

Compound 3k



Prepared according to ***Altered procedure D*** from carbonazidate **2h** (6.7 g, 18.7 mmol). Anhydrous DCE (140 ml), 24h. After completion the solvent was evaporated under reduced pressure and the off-white solid (**3k**) was used without further purification (5.7 g, quantitative).

^{1}H NMR (400 MHz, MeOD) δ 3.8 – 3.7 (m, 2H), 2.4 – 1.8 (m, 16H).

HRMS (m/z): Calcd for $C_{16}H_{19}N_2O_4^+$: 303.1339 [M+H]$^+$; Measured: 303.1339.

The procedure was adapted and the spectra are in accordance with: Zonker, B.; Becker, J.; Hrdina, R.; *Org. Biomol. Chem.,* **2021**, 19, 4027.[4]

Summary of Rhodium Catalysed and Thermally Initiated Synthesis of Annulated Carbamates

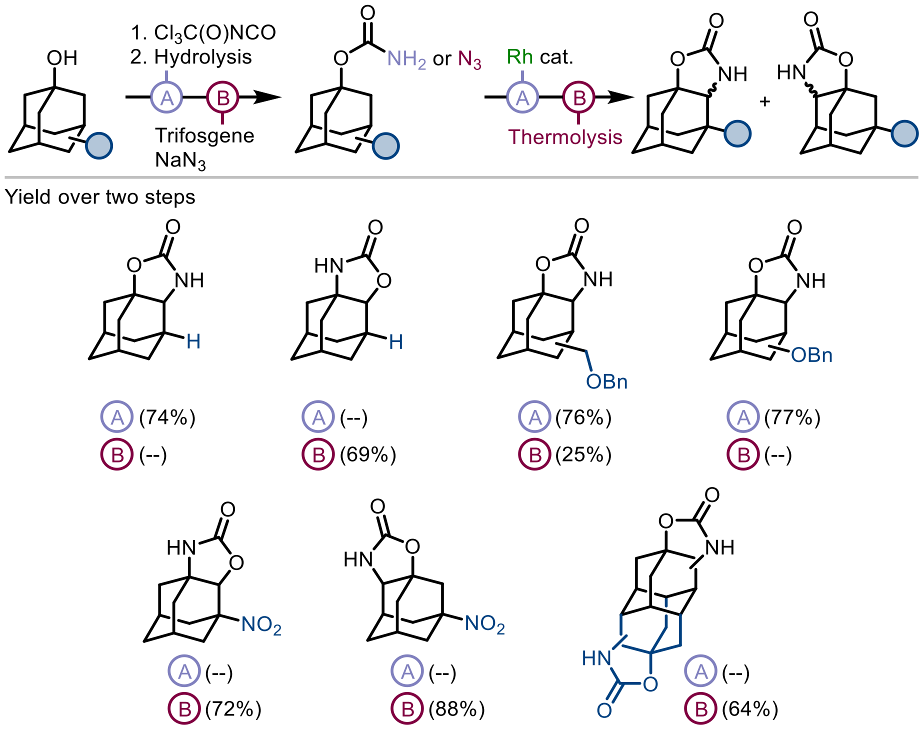
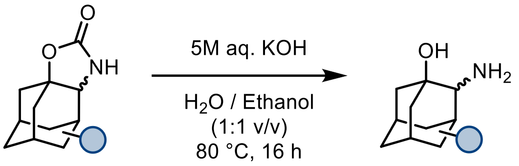


Figure 1: Summary and comparison of yields of annulated carbamates over two steps using method A: Rhodium catalysed nitrenoid insertion, B: Thermal decomposition of carbonazidates.

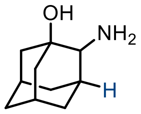
General procedure E: Hydrolysis of Annulated Carbamates



The cyclic carbamate in a round bottom flask was dissolved in a mixture of EtOH and 5M aqueous KOH solution (1:1 v/v; 0.25M) and equipped with a condenser. The reaction mixture was placed into a heating bath, heated to 80 °C and stirred overnight. After completion, the bulk of the EtOH was evaporated under reduced pressure and the aqueous phase diluted with the same amount of brine. The aqueous phase was extracted 3x with $CHCl_3$. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$ and the solvent evaporated under reduced pressure. The aminoalcohols were used without further purification.

Any alterations to the general procedure are mentioned with specific compounds.

Compound 4a



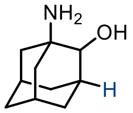
Prepared according to **General procedure E** from cyclic carbamate **3a** (2.0 g, 10.36 mmol). The product **4a** was obtained as a white solid (1.56 g, 90%)

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.77 – 2.75 (m, 1H), 2.12 – 1.90 (m, 4H), 1.86 – 1.55 (m, 10H), 1.50 – 1.41 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 161.6, 80.5, 64.0, 40.0, 37.1, 36.2, 36.2, 31.1, 31.0, 29.2, 29.0.

Spectra are in accordance with published literature: Hrdina, R.; Oksana, M. K.; Císařová, I.; Koucký, F.; Machalický, O. *RSC Adv.* **2022**, 12, 31056-31060.[6]

Compound 4b



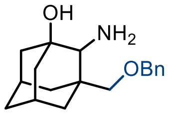
Prepared according to ***Altered procedure E*** from cyclic carbamate **3f** (1.0 g, 5.2 mmol). 1,4-dioxane was used instead of EtOH. Removal of 1,4-dioxane after completion results in a white precipitate that is recovered by filtration, washed with water, dissolved in warm $CHCl_3$ and dried over anhydrous $MgSO_4$. Removal of the solvent under reduced pressure gave the product **4b** as an off-white solid (789 mg, 91%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 3.46 – 3.41 (m, 1H), 2.41 – 1.88 (m, 7H), 1.77 – 1.49 (m, 7H), 1.41 – 1.34 (m, 1H), 1.26 – 1.19 (m, 1H).

^{13}C NMR (101 MHz, MeOD) δ 79.2, 51.5, 44.2, 40.0, 37.6, 37.3, 37.2, 30.8, 30.7, 30.5.

Spectra are in accordance with published literature: Armarego, W. L. F; Tucker, P. G. *Aust. J. Chem.* **1979**, 32, 1805 – 1817.[7]

Compound 4c



Prepared according to **General procedure E** from cyclic carbamate **3b** (930 mg of crude mass). The product **4c** was obtained as a colourless oil (450 mg, 63% over two steps.)

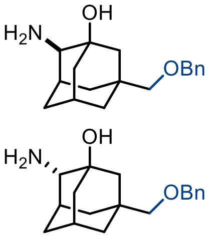
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 – 7.25 (m, 5H), 4.47 (q, 2H), 3.15 (dd, *J* = 74.7, 9.0 Hz, 2H), 2.75 (s, 1H), 2.20 – 1.65 (m, 9H), 1.61 – 1.42 (m, 5H), 1.18 – 1.11 (m, 1H).

^{13}C NMR (101 MHz, MeOD) δ 140.0 (C), 129.3 (2CH), 128.7 (2CH), 128.5 (CH), 77.8 (CH_2), 74.2 (CH_2), 70.6 (C), 61.9 (CH), 45.8 (CH_2), 40.9 (C), 40.8 (CH_2), 38.4 (CH_2), 37.3 (CH_2), 32.8 (CH_2), 31.3 (CH), 30.9 (CH).

IR (neat): $\tilde{\nu}$ /cm^{-1} = 3361, 2904, 2850, 1469, 1092, 796, 692.

HRMS (m/z): Calcd for $C_{18}H_{26}NO_2^+$: 288.1958 [M+H]$^+$; Measured: 288.1955.

Compound 4d

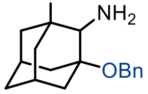


Prepared according to **General procedure E** from a mixture of cyclic carbamates **3c** (1.5 g, 5.2 mmol). The mixture of aminoalcohols **4d** was obtained as a colourless oil (1.24 g, 90%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.4 – 7.3 (m, 5H), 4.5 (s, 2H), 3.1 (s, 1H), 3.1 (s, 1H), 2.8 – 2.7 (m, 1H), 2.2 – 2.1 (m, 1H), 2.0 – 1.9 (m, 1H), 1.8 – 1.3 (m, 13H).

HRMS (m/z): Calcd for $C_{18}H_{26}NO_2^+$: 288.1958 [M+H]$^+$; Measured: 288.1954.

Compound 4e



Prepared according to **General procedure E** from cyclic carbamate **3d** (310 mg, 1.0 mmol). The product **4e** was obtained as a colourless oil (240 mg, 85% over two steps.)

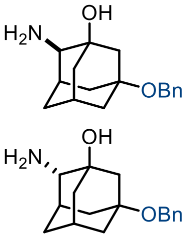
^{1}H NMR (400 MHz, $CDCl_3$δ 7.4 – 7.4 (m, 2H), 7.4 – 7.3 (m, 2H), 7.3 – 7.3 (m, 1H), 7.3 – 7.2 (m, 2H), 7.1 – 7.1 (m, 1H), 4.6 – 4.5 (m, 3H), 4.0 (d, J = 11.8 Hz, 1H), 3.6 (s, 1H), 2.8 (s, 1H), 2.4 – 2.3 (m, 1H), 2.2 – 2.1 (m, 1H), 2.0 – 1.9 (m, 2H), 1.8 – 1.7 (m, 5H), 1.7 – 1.6 (m, 1H), 1.6 – 1.5 (m, 2H), 1.4 – 1.4 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 139.5 (C), 128.5 (2CH), 127.5 (CH), 127.5 (2CH), 76.2 (C), 70.8 (C), 62.8 (CH_2), 62.7 (CH), 43.1 (CH_2), 39.9 (CH_2), 38.4 (CH_2), 35.6 (CH_2), 34.4 (CH_2), 30.7 (CH), 30.1 (CH).

IR (neat): $\tilde{\nu}$ /cm^{-1} = 3369, 2910, 2854, 1452, 1055, 733, 696.

HRMS (m/z): Calcd for $C_{17}H_{24}NO_2^+$: 274.1802 [M+H]$^+$; Measured: 274.1805.

Compound 4f

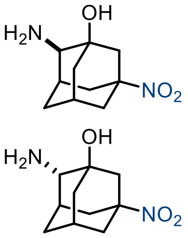


Prepared according to **General procedure E** from a mixture of cyclic carbamates **3e** (440 mg, 1.6 mmol). The mixture of aminoalcohols **4f** was obtained as a colourless thick paste (320 mg, 80%).

^{1}H NMR (400 MHz, CDCl$_3$) δ 7.4 – 7.3 (m, 4H), 7.3 – 7.2 (m, 1H), 4.5 – 4.5 (m, 2H), 2.8 – 2.7 (m, 1H), 2.4 – 1.6 (m, 14H), 1.5 – 1.2 (m, 1H).

HRMS (m/z): Calcd for $C_{17}H_{24}NO_2^+$: 274.1802 [M+H]$^+$; Measured: 274.1799.

Compound 4h

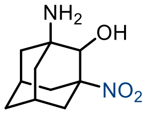


Prepared according to **General procedure E** from a mixture of cyclic carbamates **3i** (650 mg, 2.7 mmol). The mixture of aminoalcohols **4h** was obtained as a white solid (430 mg, 75%).

^{1}H NMR (400 MHz, CDCl$_3$) δ 2.9 – 2.7 (m, 1H), 2.5 – 1.4 (m, 15H).

HRMS (m/z): Calcd for $C_{10}H_{17}N_2O_3^+$: 213.1234 [M+H]$^+$; Measured: 213.1230.

Compound 4i



Prepared according to **General procedure E** from cyclic carbamate **3j** (130 mg, 0.55 mmol). The product **4i** was obtained as an off-white solid (71 mg, 61%)

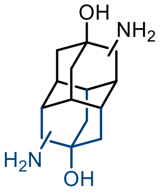
^{1}H NMR (400 MHz, CDCl$_3$) δ 4.0 (s, 1H), 2.6 – 1.2 (m, 15H).

^{13}C NMR (101 MHz, CDCl$_3$) δ 89.2 (C), 77.5 (CH), 52.7 (C), 43.0 (CH$_2$), 41.5 (CH$_2$), 38.5 (CH$_2$), 34.6 (CH$_2$), 32.5 (CH$_2$), 30.3 (CH), 29.3 (CH).

IR (neat): $\tilde{\nu}$ /cm^{-1} = 3066, 2931, 2750, 1529, 1365, 1082, 974, 764.

HRMS (m/z): Calcd for $C_{10}H_{17}N_2O_3^+$: 213.1234 [M+H]$^+$; Measured: 239.1232.

Compound 4j



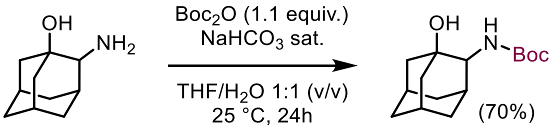
Altered procedure E: The complex mixture of cyclic carbamate isomers **3k** (5.7 g, 18.9 mmol) was loaded into a flask and suspended in a mixture of EtOH and distilled water (4:1 v/v). KOH (5 equiv., 5.32 g, 95 mmol) was added and the reaction vessel was placed into a heating bath, equipped with a condenser and heated to 90 °C while stirring for 24h. After completion the reaction mixture was left to cool down to room temperature and the KOH was neutralized by the addition of approx. 10 ml of conc. HCl. Addition of a small amount of NaHCO$_3$ adjusted the pH from acidic to neutral (pH 7) and the EtOH-water mixture was evaporated under reduced pressure. The aminoalcohol **4j** was characterized from the crude mass that was carried to the next step without further purification due to difficulties of isolation.

^{1}H NMR (400 MHz, MeOD) δ 3.2 – 3.0 (m, 2H), 2.3 – 1.5 (m, 20H).

HRMS (m/z): Calcd for $C_{14}H_{23}N_2O_2^+$: 251.1754 [M+H]$^+$; Measured: 251.1757.

General procedure F: *N*-protection of Aminoalcohols

Compound 5a

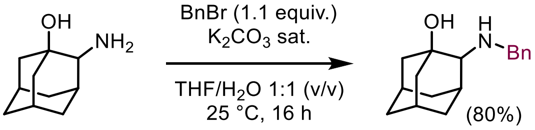


Starting material **4a** (200 mg, 1.2 mmol) was dissolved in a 1:1 mixture of THF (2 ml) and saturated aqueous NaHCO$_3$ (2 ml) and a 1M solution of Boc$_2$O in THF (1.32 ml ,1.32 mmol) was added dropwise.

The reaction mixture was left stirring at room temperature for 24h. The THF was evaporated under reduced pressure and the aqueous phase extracted 3x with $CHCl_3$. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$ and the solvent evaporated under reduced pressure. The product **5a** was purified by silica gel column chromatography (30% EtOAc:DCM) and obtained as a white solid in a yield of 70% (225 mg).

R_f : (30% EtOAc:DCM; PMA)
^{1}H NMR (400 MHz, $CDCl_3$) δ 4.9 – 4.8 (m, 1H), 3.8 – 3.6 (m, 1H), 3.0 (s, 1H), 2.1 – 2.0 (m, 3H), 1.9 – 1.5 (m, 10H), 1.4 (s, 9H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 157.3 (C), 80.0 (C), 69.7 (C), 59.9 (CH), 45.5 (CH_2), 39.0 (CH_2), 36.6 (CH_2), 36.2 (CH_2), 34.8 (CH), 30.8 (CH_2), 30.4 (CH), 29.8 (CH), 28.5 ($3CH_3$).
IR (neat): $\tilde{\nu}$ /cm^{-1} = 3334, 2966, 1674, 1520, 1375, 1167, 1092, 1020, 613.
HRMS (m/z): Calc'd for $C_{15}H_{25}NNaO_3^+$: 290.1727 $[M+Na]^+$; Measured: 290.1724.

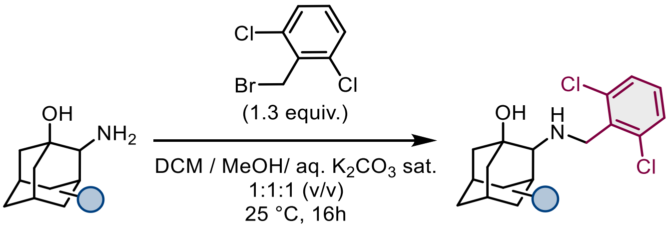
Compound 5b



Starting material **4a** (200 mg, 1.2 mmol) was dissolved in a 1:1 mixture of THF (2 ml) and saturated aqueous K_2CO_3 (2 ml) and benzyl bromide (226 mg, 1.32 mmol) was added dropwise. The reaction mixture was left stirring at room temperature for 24h. The THF was evaporated under reduced pressure and the aqueous phase extracted 3x with $CHCl_3$. The combined organic layers were washed with brine, dried over anh. $MgSO_4$ and the solvent evaporated under reduced pressure. The product **5b** was purified by silica gel column chromatography (50% EtOAc:Hex) and obtained as an amorphous white solid in a yield of 80% (250 mg).

R_f : 0.4 (50% EtOAc:Hex; UV, PMA)
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.31 (m, 4H), 7.28 – 7.23 (m, 1H), 3.80 (dd, *J* = 96.1, 12.9 Hz, 2H), 3.42 (bs, 1H), 2.63 (s, 1H), 2.24 – 2.18 (m, 1H), 2.13 – 2.07 (m, 1H), 2.04 – 1.98 (m, 1H), 1.86 – 1.43 (m, 11H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 140.9 (C), 128.6 (2CH), 128.3 (2CH), 127.2 (CH), 68.5 (C), 66.8 (CH), 52.0 (CH_2), 44.1 (CH_2), 40.4 (CH_2), 37.2 (CH_2), 36.6 (CH_2), 31.5 (CH), 30.5 (CH), 30.0 (CH_2), 29.7 (CH).
IR (neat): $\tilde{\nu}$ /cm^{-1} = 3249, 2906, 2848, 1450, 1113, 1088, 735, 694.
HRMS (m/z): Calc'd for $C_{17}H_{24}NO^+$: 258.1852 $[M+H]^+$; Measured: 258.1849.

2,6-Dichlorobenzyl protection

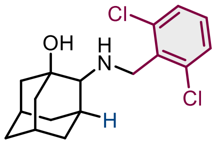


Aminoalcohol and 2,6-dichlorobenzyl bromide (1.3 equiv.) were dissolved in a 1:1:1 (v/v) mixture of DCM, MeOH and aqueous saturated K_2CO_3 (0.5M). The reaction mixture was left to stir for overnight. After completion the reaction mixture was partitioned between brine and DCM and the aqueous layer was extracted 2x with DCM. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$ and the solvent was evaporated under reduced pressure. The product was purified by silica gel column chromatography.

Any alterations to the general procedure are mentioned with specific compounds.

Notes: At this stage, the previously unseparated isomers of the cyclic carbamates can now be easily separated by silica gel column chromatography (EtOAc:$CHCl_3$). It is worth noting that the mixture can be also minimally purified (elimination of excess benzyl bromide and baseline impurities) and easily separated at the stage of noradamantyl carbaldehydes.

Compound 5c



Prepared according to **General procedure F** from aminoalcohol **4a** (300 mg, 1.8 mmol). The product **5c** was purified by silica gel column chromatography eluting with 50% EtOAc:Hex and obtained as a white solid (530 mg, 90%).

R_f : 0.5 (50% EtOAc:Hex; UV, PMA)

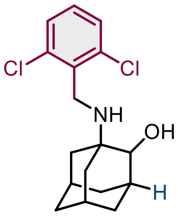
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.3 (d, 2H), 7.1 (t, 1H), 4.1 (dd, J = 101.6, 12.1 Hz, 2H), 3.5 (bs, 1H), 2.7 – 2.6 (m, 1H), 2.2 – 2.0 (m, 2H), 2.0 – 1.9 (m, 1H), 1.8 – 1.4 (m, 11H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 136.2 (C), 136.0 (C), 128.9 (2CH), 128.4 (CH), 68.3 (C), 67.1 (CH), 47.4 (CH_2), 44.0 (CH_2), 40.1 (CH_2), 37.2 (CH_2), 36.4 (CH_2), 32.2 (CH), 30.4 (CH), 30.1 (CH_2), 30.0 (CH).

IR (neat): $\tilde{\nu}$ /cm^{-1} = 3319, 2904, 2846, 1437, 1338, 1086, 758.

HRMS (m/z): Calc'd for $C_{17}H_{22}Cl_2NO^+$: 326.1073 [M+H]$^+$; Measured: 326.1067.

Compound 5d



Prepared according to **General procedure F** from aminoalcohol **4b** (350 mg, 2.1 mmol). The product **5d** was purified by silica gel column chromatography eluting with 20% EtOAc:$CHCl_3$ and obtained as a white solid (525 mg, 77%).

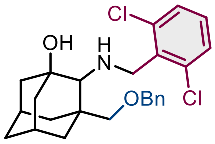
R_f : 0.5 (20% EtOAc:$CHCl_3$; UV, PMA)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.3 (d, J = 8.0 Hz, 2H), 7.2 – 7.1 (m, 1H), 4.0 (dd, J = 11.0 Hz, 2H), 3.8 – 3.7 (m, 1H), 3.4 (s, 1H), 2.2 – 1.9 (m, 5H), 1.9 – 1.8 (m, 1H), 1.8 – 1.7 (m, 2H), 1.7 – 1.6 (m, 3H), 1.4 (bs, J = 14.5 Hz, 1H), 1.4 (d, J = 10.4 Hz, 1H), 1.1 (s, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 136.3 (C), 136.0 (C), 129.0 (CH_2), 128.5 (CH), 73.7 (CH), 54.5 (C), 40.4 (CH_2), 40.2 (CH_2), 37.2 (CH_2), 37.1 (CH_2), 36.0 (CH_2), 33.8 (CH), 30.3 (CH_2), 29.8 (CH), 29.0 (CH).

HRMS (m/z): Calcd for $C_{17}H_{22}Cl_2NO^+$: 326.1073 [M+H]$^+$; Measured: 326.1074.

Compound 5e



Prepared according to **General procedure F** from aminoalcohol **4c** (450 mg, 1.6 mmol). The product **5e** was purified by silica gel column chromatography eluting with 5% EtOAc:$CHCl_3$ and obtained as a colourless oil that slowly crystallizes (620 mg 89%).

R_f : 0.3 (5%EtOAc:$CHCl_3$; UV, PMA)

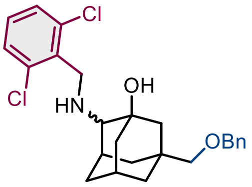
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.4 – 7.3 (m, 7H), 7.1 (t, J = 8.0 Hz, 1H), 4.6 (dd, 2H), 4.3 (d, J = 11.7 Hz, 1H), 4.0 – 3.9 (m, 1H), 3.8 (s, 1H), 3.4 (dd, J = 140.6, 9.0 Hz, 2H), 2.8 – 2.7 (m, 1H), 2.2 – 2.1 (m, 1H), 2.1 – 2.0 (m, 2H), 1.9 – 1.5 (m, 6H), 1.5 – 1.3 (m, 2H), 1.3 – 1.2 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 138.7 (C), 136.4 (C), 136.0 (2C), 129.0 (CH), 128.5 (2CH), 128.4 (2CH), 127.5 (CH), 127.4 (2CH), 76.7 (CH_2), 73.1 (CH_2), 69.3 (C), 67.6 (C), 50.4 (CH_2), 42.8 (CH_2), 41.0 (C), 40.8 (CH_2), 40.3 (CH_2), 36.1 (CH_2), 33.2 (CH_2), 29.7 (CH), 29.3 (CH).

IR (neat): $\tilde{\nu}$ /cm^{-1} = 3460, 2906, 2850, 1562, 1435, 1099, 750, 696, 509.

HRMS (m/z): Calcd for $C_{25}H_{30}Cl_2NO_2^+$: 446.1648 [M+H]$^+$; Measured: 446.1647.

Compound 5f



Prepared according to **General procedure F** from aminoalcohols **4d** (1.1 g, 3.8 mmol). The product **5f** was purified by silica gel column chromatography eluting with 10% EtOAc:$CHCl_3$ and obtained as a colourless oil that slowly crystallizes (1.58 g 82%).

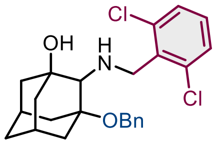
R

R_f : 0.3 (10%EtOAc:$CHCl_3$; UV, PMA)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.4 – 7.3 (m, 7H), 7.2 – 7.1 (m, 1H), 4.5 – 4.5 (m, 2H), 4.2 – 4.2 (m, 1H), 4.0 – 3.9 (m, 1H), 3.5 – 3.3 (m, 1H), 3.1 – 3.0 (m, 2H), 2.7 – 2.6 (m, 1H), 2.3 – 2.0 (m, 2H), 1.8 – 1.3 (m, 12H).

HRMS (m/z): Calcd for $C_{25}H_{30}Cl_2NO_2^+$: 446.1648 [M+H]$^+$; Measured: 446.1648.

Compound 5g



Prepared according to **General procedure F** from aminoalcohol **4e** (220 mg, 0.80 mmol). The product **5g** was purified by silica gel column chromatography eluting with 10% EtOAc:$CHCl_3$ and obtained as a colourless thick paste (275 mg, 79%).

R_f : 0.5 (10% EtOAc: $CHCl_3$)

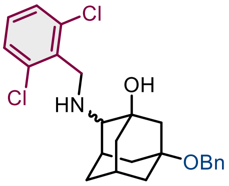
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.4 – 7.4 (m, 2H), 7.4 – 7.3 (m, 2H), 7.3 – 7.2 (m, 3H), 7.1 (dd, 1H), 4.6 – 4.5 (m, 3H), 4.0 (d, *J* = 11.8 Hz, 1H), 3.6 (s, 1H), 2.8 (s, 1H), 2.4 – 2.3 (m, 1H), 2.2 – 2.1 (m, 1H), 2.0 – 1.9 (m, 2H), 1.8 – 1.7 (m, 5H), 1.6 (s, 1H), 1.6 – 1.5 (m, 2H), 1.4 – 1.4 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 139.7 (C), 136.8 (C), 136.2 (2C), 128.9 (CH), 128.4 (2CH), 128.3 (2CH), 127.5 (2CH), 127.3 (CH), 77.3 (C), 71.4 (C), 70.5 (CH), 63.3 (CH_2), 50.7 (CH_2), 42.5 (CH_2), 40.6 (CH_2), 39.4 (CH_2), 35.4 (CH_2), 35.1 (CH_2), 30.7 (CH), 30.0 (CH).

IR (neat): $\tilde{\nu}$ /cm^{-1} = 3425, 2920, 2854, 1435, 1111, 1057, 750, 698.

HRMS (m/z): Calcd for $C_{24}H_{28}Cl_2NO_2^+$: 432.1492 [M+H]$^+$; Measured: 432.1493.

Compound 5h



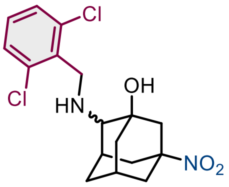
Prepared according to **General procedure F** from aminoalcohols **4f** (300 mg, 1.1 mmol). The product **5h** was purified by silica gel column chromatography eluting with 10% EtOAc:$CHCl_3$ and obtained as a colourless thick paste (438 mg, 92%).

R_f : 0.3 (10%EtOAc:$CHCl_3$; UV, PMA)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.4 – 7.3 (m, 6H), 7.3 – 7.1 (m, 2H), 4.5 – 4.4 (m, 2H), 4.3 – 3.9 (m, 2H), 3.5 – 3.3 (m, 1H), 2.7 – 2.6 (m, 1H), 2.4 – 2.2 (m, 2H), 2.0 – 1.2 (m, 12H).

HRMS (m/z): Calcd for $C_{24}H_{28}Cl_2NO_2^+$: 432.1492 [M+H]$^+$; Measured: 432.1500

Compound 5i



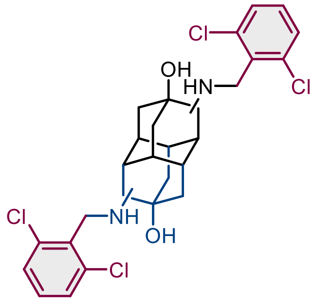
Prepared according to **General procedure F** from aminoalcohols **4h** (415 mg, 2.0 mmol). The product **5i** was purified by silica gel column chromatography eluting with 20% EtOAc:$CHCl_3$ and obtained as a viscous colourless oil (659 mg, 91%).

R_f : 0.4 (20%EtOAc:$CHCl_3$; UV, PMA)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.4 – 7.3 (m, 6H), 7.3 – 7.1 (m, 2H), 4.5 – 4.4 (m, 2H), 4.3 – 3.9 (m, 2H), 3.5 – 3.3 (m, 1H), 2.7 – 2.6 (m, 1H), 2.4 – 2.2 (m, 2H), 2.0 – 1.2 (m, 12H).

HRMS (m/z): Calcd for $C_{17}H_{21}CL_2N_2O_3^+$: 371.0924 [M+H]$^+$; Measured: 371.0923.

Compound 5j



Altered procedure F: The crude mass containing the complex mixture of aminoalcohol isomers was directly suspended (in the same flask) in distilled MeOH (20 ml) and $NaHCO_3$ (6 equiv. relative to **3k**, 9.5 g, 113 mmol) followed by 2,6-dichlorobenzyl bromide (2.5 equiv. relative to **3k**, 11.3 g, 47 mmol) were added. The flask was equipped with a condenser, placed into a heating bath and stirred at 40 °C for 24h. After completion the MeOH was evaporated under reduced pressure. The solid was suspended in $CHCl_3$ and filtered off through a glass frit with drying agent. The solid was washed further with $CHCl_3$ (approx. 100 ml) and the combined organic phases were evaporated under reduced pressure. The crude mixture was separated by silica gel column chromatography by gradient elution 10-40% EtOAc:DCM. The product **5j** was isolated as a complex mixture of protected amino alcohols as a fluffy solid with a light blue haze (6.4 g, 60% over two steps).

Notes: Reaction progress can be monitored by TLC or LCMS. If necessary, additional 2,6-dichlorobenzyl bromide can be added to until at a later stage until complete consumption of starting material.

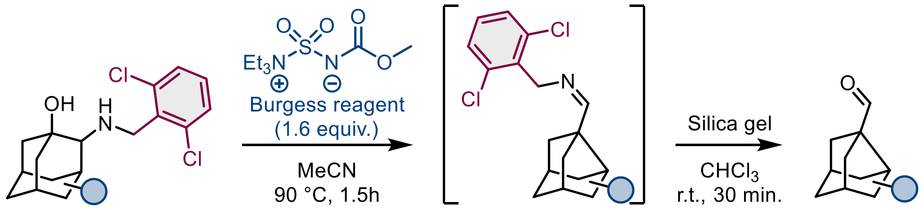
Purification: From the beginning of the elution of the first (most un-polar) mixture of isomers, everything was collected until no more elution occurred, not exceeding the 40% EtOAc:DCM mixture.

R_f : 0.1-0.6 (20% EtOAc:DCM; UV, $KMnO_4$, PMA)

^{1}H NMR δ 7.3 – 7.3 (m, 4H), 7.2 – 7.1 (m, 2H), 4.3 – 3.9 (m, 4H), 3.4 – 3.1 (m, 2H), 2.7 – 2.5 (m, 2H), 2.2 – 2.1 (m, 1H), 2.1 – 1.4 (m, 16H).

HRMS (m/z): Calcd for $C_{28}H_{31}Cl_4N_2O_2^+$: 567.1134 $[M+H]^+$; Measured: 567.1141.

General procedure G: Synthesis of Noradamantyl Carbaldehydes Using Burgess Reagent



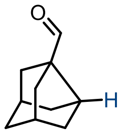
A dry flask under nitrogen equipped with a magnetic stir bar was charged with protected aminoalcohol, Burgess reagent (1.5 equiv.) and dissolved/suspended in anhydrous MeCN (0.1M). The reaction vessel was placed into a **pre-heated to 90 °C** and left to stir for 90 minutes. After completion, the reaction mixture was left to cool down to the touch, aerated and the MeCN was evaporated under reduced pressure (rota bath set to 35 °C). Silica gel (3 equiv. w/w relative to starting material) was added to the crude residue and wet $CHCl_3$ was added to the point of a stirring slurry and left to stir for 30 minutes. The slurry can be either evaporated from chloroform or directly transferred to a short silica gel column eluting with pure $CHCl_3$/DCM to obtain the product. (Caution! The products can be volatile. Evaporate with care.)

Any alterations to the general procedure are mentioned with specific compounds.

Notes: At this stage it is also possible to easily separate the previously unseparated mixture of isomers carried from the previous steps.

The reaction itself can be run on air in a flask stoppered with a $CaCl_2$ tube without any issues.

Compound 6a



Prepared according to **General procedure G** from protected aminoalcohol **5c** (500 mg, 1.53 mmol). The product **6a** was purified by silica gel column chromatography eluting with pure DCM and obtained as a white amorphous solid (217 mg, 94%). (Caution! Volatile.)

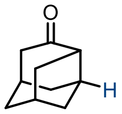
R$_f$: 0.5 (DCM; PMA, $KMnO_4$)

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.69 (s, 1H), 2.58 – 2.51 (m, 1H), 2.35 – 2.29 (m, 2H), 2.02 – 1.94 (m, 2H), 1.74 – 1.54 (m, 8H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 205.1, 60.3, 43.7, 42.03, 37.5, 35.3.

Spectra are in accordance with published literature: Zonker, B.; Becker, J.; Hrdina, R.; *Org. Biomol. Chem.,* **2021**, 19, 4027.[4]

Compound 6b



Prepared according to **General procedure G** from protected aminoalcohol **5d** (100 mg, 0.31 mmol). The product **6b** was purified by silica gel column chromatography eluting with 2% Et_2O:DCM and obtained as a white crystalline solid (30 mg, 65%).

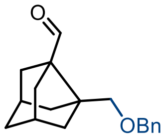
R$_f$: 0.5 (2% Et_2O:DCM)

^{1}H NMR (400 MHz, $CDCl_3$) δ 2.77 – 2.69 (m, 1H), 2.65 – 2.49 (m, 2H), 2.44 – 2.38 (m, 1H), 2.33 – 2.20 (m, 2H), 2.02 – 1.90 (m, 2H), 1.83 – 1.60 (m, 5H), 1.57 – 1.49 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 216.9, 51.3, 45.2, 41.6, 38.3, 37.6, 37.4, 37.3, 35.0, 29.7.

Spectra are in accordance with published literature: Zonker, B.; Becker, J.; Hrdina, R.; *Org. Biomol. Chem.,* **2021**, 19, 4027.

Compound 6c



Prepared according to **General procedure G** from protected aminoalcohol **5e** (200 mg, 0.45 mmol). The product **6c** was purified by silica gel column chromatography eluting with pure $CHCl_3$ and obtained as a colourless oil (102 mg, 84%).

R$_f$: 0.5 ($CHCl_3$); 0.7 (DCM; UV, PMA)

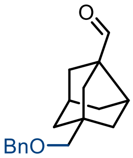
^{1}H NMR (400 MHz, $CDCl_3$) δ 9.71 (s, 1H), 7.36 – 7.24 (m, 5H), 4.43 (s, 2H), 3.38 (s, 2H), 2.40 – 2.35 (m, 2H), 2.22 – 2.14 (m, 2H), 1.90 – 1.83 (m, 2H), 1.73 – 1.62 (m, 2H), 1.60 – 1.53 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 206.6 (CH), 138.5 (C), 128.4 (2CH), 127.6 (2CH, CH), 73.1 (CH_2), 72.5 (CH_2), 59.7 (C), 56.7 (C), 46.0 ($2CH_2$), 44.6 ($2CH_2$), 36.7 (2CH), 35.4 (CH_2).

IR (neat): $\tilde{\nu}$ /cm^{-1} = 2952, 2854, 1707, 1473, 1088, 750, 696.

HRMS (m/z): Calcd for $C_{18}H_{23}O_2^+$: 271.1693 $[M+H]^+$; Measured: 271.1692.

Compound 6d



Prepared according to **General procedure G** from protected aminoalcohols **5f** (200 mg, 0.45 mmol). The product **6d** was purified by silica gel column chromatography eluting with pure DCM and obtained as a colourless oil (87 mg, 72%).

R$_f$: 0.5 (DCM; UV, PMA)

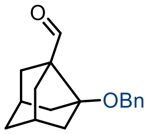
^{1}H NMR (400 MHz, $CDCl_3$) δ 9.73 (s, 1H), 7.37 – 7.27 (m, 5H), 4.50 (s, 2H), 3.29 (s, 2H), 2.66 – 2.60 (m, 1H), 2.46 (s, 1H), 2.04 – 1.95 (m, 2H), 1.77 – 1.66 (m, 4H), 1.65 – 1.58 (m, 2H), 1.55 – 1.48 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 204.8 (CH), 138.9 (C), 128.5 (2CH), 127.6 (CH), 127.5 (2CH), 76.6 (CH_2), 73.4 (CH_2), 60.7 (C), 46.7 (C), 45.6 (CH_2), 45.5 (CH_2), 43.4 (CH_2), 43.2 (CH_2), 42.1 (CH), 37.7 (CH_2), 36.9 (CH).

IR (neat): $\tilde{\nu}$ /cm^{-1} = 2933, 2854, 1712, 1454, 1097, 750, 696.

HRMS (m/z): Calcd for $C_{18}H_{22}NaO_2^+$: 293.1512 $[M+Na]^+$; Measured: 293.1510.

Compound 6e



Prepared according to **General procedure G** from protected aminoalcohol **5g** (200 mg, 0.46 mmol). The product **6e** was purified by silica gel column chromatography eluting with pure DCM and obtained as a colourless oil (49 mg, 41%).

R$_f$: 0.5 (DCM; UV, PMA)

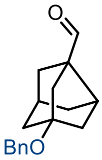
^{1}H NMR (400 MHz, CDCl$_3$) δ 9.7 (s, 1H), 7.4 – 7.2 (m, 5H), 4.5 (s, 2H), 2.5 (s, 2H), 2.4 – 2.3 (m, 2H), 2.1 (s, 4H), 1.7 – 1.5 (m, 4H).

^{13}C NMR (101 MHz, CDCl$_3$) δ 205.0 (CH), 139.0 (C), 128.4 (2CH), 127.4 (CH), 127.0 (2CH), 94.1 (C), 67.0 (CH$_2$), 59.6 (C), 47.8 (2CH$_2$), 43.1 (2CH$_2$), 36.6 (2CH), 34.5 (CH$_2$).

IR (neat): $\tilde{\nu}$ /cm^{-1} = 2927, 2862, 1716, 1454, 1140, 1055, 733, 701.

HRMS (m/z): Calcd for $C_{17}H_{20}NaO_2^+$: 279.1356 [M+Na]$^+$; Measured: 279.1355.

Compound 6f



Prepared according to **General procedure G** from protected aminoalcohols **5h** (210 mg, 0.49 mmol). The product **6f** was purified by silica gel column chromatography eluting with 5%EtOAc:CHCl$_3$ and obtained as a colourless oil (87 mg, 70%).

R$_f$: 0.4 (5% EtOAc:CHCl$_3$; UV, PMA)

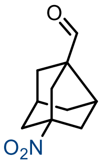
^{1}H NMR (400 MHz, CDCl$_3$) δ 9.7 (s, 1H), 7.4 – 7.2 (m, 5H), 4.5 (s, 2H), 2.7 – 2.5 (m, 2H), 2.4 – 2.3 (m, 1H), 2.1 – 1.9 (m, 4H), 1.8 – 1.5 (m, 5H).

^{13}C NMR (101 MHz, CDCl$_3$) δ 203.5 (CH), 139.3 (C), 128.5 (2CH), 127.6 (2CH), 127.5 (CH), 81.8 (C), 65.9 (CH$_2$), 58.7 (C), 45.7 (CH$_2$), 45.2 (CH$_2$), 43.1 (CH$_2$), 42.6 (CH$_2$), 39.8 (CH), 39.5 (CH$_2$), 37.0 (CH).

IR (neat): $\tilde{\nu}$ /cm^{-1} = 2935, 2868, 1712, 1454, 1097, 733, 698.

HRMS (m/z): Calcd for $C_{17}H_{20}O_2$: 256.1458 [M]; Measured: 256.1458 (source type: APPI).

Compound 6g



Prepared according to ***Altered procedure G:*** from protected aminoalcohols **5i** (200 mg, 0.54 mmol). Complete conversion after 12h at 90 °C (overnight). The product **6g** was purified by silica gel column chromatography eluting with pure DCM and obtained as an amorphous colourless solid (81 mg, 77%).

R$_f$: 0.4 (DCM; PMA)

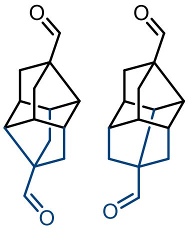
^{1}H NMR (400 MHz, CDCl$_3$) δ 9.7 (s, 1H), 2.8 – 2.7 (m, 2H), 2.7 – 2.7 (m, 1H), 2.5 – 2.4 (m, 1H), 2.4 – 2.2 (m, 2H), 2.1 – 2.0 (m, 3H), 1.8 – 1.8 (m, 1H), 1.7 – 1.6 (m, 2H).

^{13}C NMR (101 MHz, CDCl$_3$) δ 201.5 (CH), 88.4 (C), 58.8 (C), 46.4 (CH$_2$), 45.9 (CH$_2$), 42.8 (CH$_2$), 42.1 (CH$_2$), 40.1 (CH), 38.4 (CH$_2$), 37.3 (CH).

IR (neat): $\tilde{\nu}$ /cm^{-1} = 2952, 2875, 1712, 1365, 804, 696.

HRMS (m/z): Calcd for $C_{10}H_{12}NO_3^-$: 194.0823 [M-H]$^-$; Measured: 194.0819.

Compound 6h



Altered procedure G: A mixture of protected aminoalcohols **5j** (6.26 g, 11.0 mmol) and Burgess reagent (3.2 equiv., 8.47 g, 35.3 mmol) were dissolved/suspended in 100 ml of anhydrous MeCN. With vigorous stirring the reaction mixture was placed into a pre-heated oil bath to 90 °C and stirred for 1.5h (the reaction mixture turned transparent and yellow in colour). Next, the reaction mixture was left to cool down to room temperature and the solvent evaporated under reduced pressure. Once dry, silica gel (10 g) was added together with a mixture of reagent grade 10% MeOH/Chloroform to form a mixing slurry that was stirred at 25 °C for 2h. The slurry was evaporated to dryness under reduced pressure and loaded directly onto a silica gel column for chromatography. The aldehydes **6h** proved to be inseparable and were eluted together (single spot) with 5% EtOAc:CHCl$_3$

and carried directly to the next step (reduction) (In the case of incomplete hydrolysis of imines the process is repeated). The mixture of aldehydes was isolated as a yellowish oil in a ratio of 0.4 : 1 (crude NMR) (1.07 g, 45%). *Note*: *The products are rather unstable on prolonged exposure to air and light (complex mixture of acids and aldehydes). It is advised to carry them to the next step as soon as possible.*

R_f : 0.5 (5% EtOAc:$CHCl_3$) *Stain with $KMnO_4$.*

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.8 – 9.7 (m, 2H), 2.8 – 2.7 (m, 1H), 2.6 – 2.6 (m, 1H), 2.5 – 2.5 (m, 1H), 2.4 – 2.3 (m, 2H), 2.3 – 2.1 (m, 5H), 2.0 – 1.8 (m, 3H), 1.7 – 1.6 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 204.0, 203.5, 64.5, 59.5, 55.8, 52.7, 51.5, 46.3, 43.0, 42.0, 40.9, 40.4.

HRMS (m/z): Calcd for $C_{14}H_{17}O_2^+$: 217.1223 $[M+H]^+$; Measured: 217.1222.

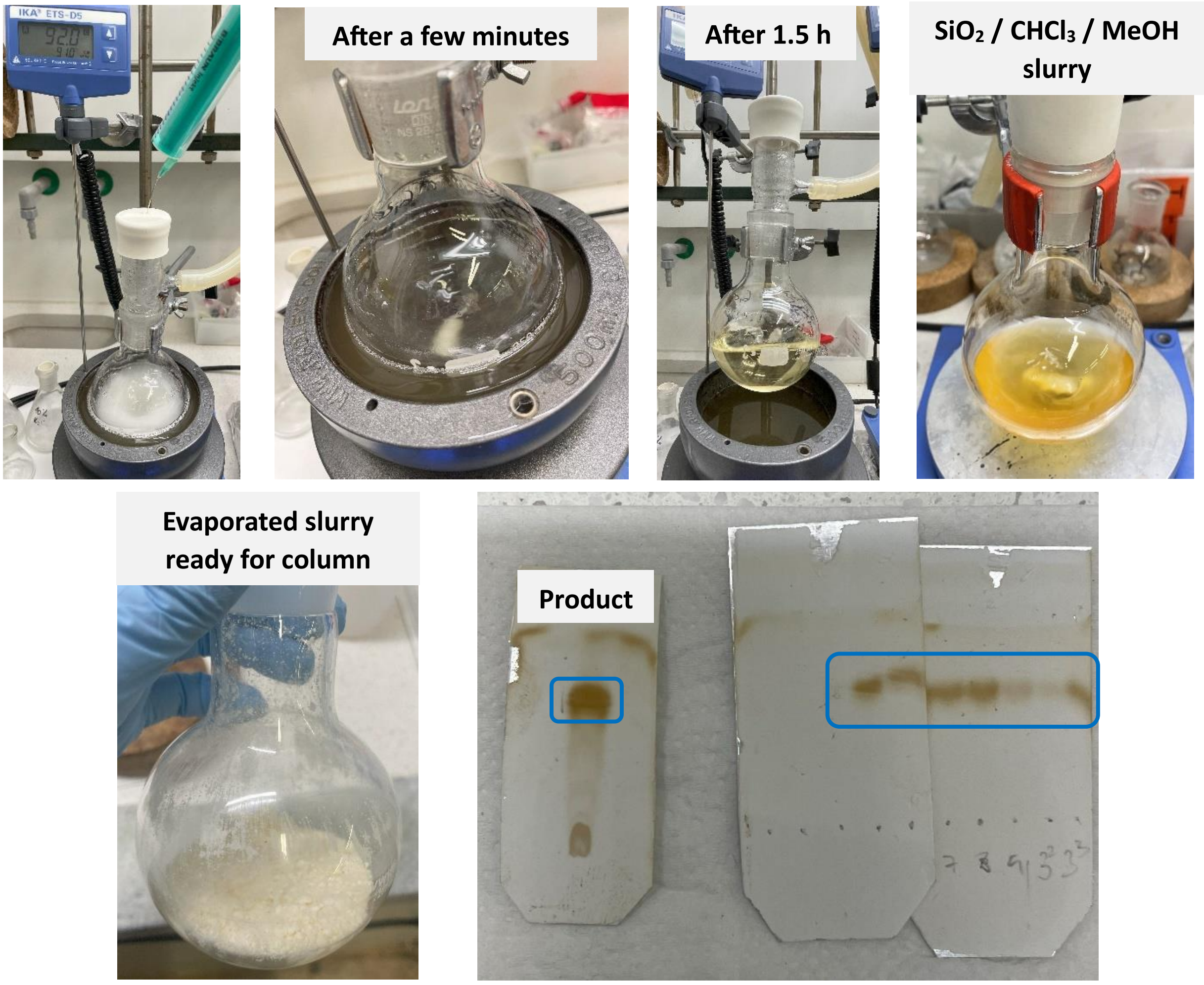
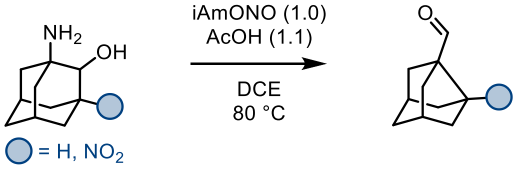


Figure 2: Graphical supporting information for largescale synthesis of **6h** from **5j.**

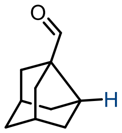
General procedure H: Noradamantyl carbaldehyde synthesis – Deamination procedure



A dry Schlenk tube was charged with aminoalcohol and anhydrous DCE (0.3M) was added. While stirring, iAm-ONO (1 equiv.) was added dropwise followed by dropwise addition of glacial AcOH (1.1 equiv.) and the reaction mixture was left stirring at room temperature for 10 minutes. The vessel was then transferred to an oil bath, heated to 80 °C and stirred for an additional 2h. After completion, the reaction mixture was left to cool down to room temperature and quenched with 10% aqueous K_2CO_3. The phases were separated and the aqueous layer extracted 2x with DCM. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$ and the solvent was removed under reduced pressure. The crude mixture was separated by silica gel column chromatography. (Caution! Volatile.)

Any alterations to the general procedure are mentioned with specific compounds.

Compound 6a.2



Prepared according to **General procedure H** from aminoalcohol **4b** (100 mg, 0.6 mmol). The product **6a.2** was purified by silica gel column chromatography eluting with pure DCM and obtained as a white amorphous solid (63 mg, 69%). (Caution! Volatile.)

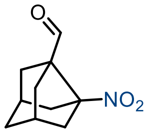
R$_f$: 0.5 (DCM; PMA, $KMnO_4$)

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.69 (s, 1H), 2.58 – 2.51 (m, 1H), 2.35 – 2.29 (m, 2H), 2.02 – 1.94 (m, 2H), 1.74 – 1.54 (m, 8H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 205.1, 60.3, 43.7, 42.03, 37.5, 35.3.

Spectra are in accordance with published literature: Zonker, B.; Becker, J.; Hrdina, R.; *Org. Biomol. Chem.*, **2021**, 19, 4027.[4]

Compound 6i



Prepared according to ***Altered procedure*** **H** from aminoalcohol **4i** (50 mg, 0.24 mmol). Complete conversion was observed after 12h. The product **6i** was purified by silica gel column chromatography eluting with pure DCM and obtained as a white solid (25.3 mg, 55%).

R$_f$: 0.5 (DCM; PMA)

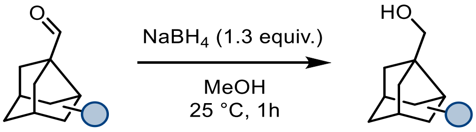
^{1}H NMR (400 MHz, $CDCl_3$) δ 9.5 (s, 1H), 2.7 – 2.6 (m, 4H), 2.5 – 2.4 (m, 2H), 2.2 – 2.2 (m, 2H), 1.8 – 1.6 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 199.6 (C), 98.4 (C), 61.3 (C), 48.8 ($2CH_2$), 44.0 ($2CH_2$), 36.5 (2CH), 33.7 (CH_2).

IR (neat): $\tilde{\nu}$ /cm^{-1} = 2939, 1716, 1527, 1360, 804, 721.

HRMS (m/z): Calcd for $C_{10}H_{14}NO_3^+$: 196.0968 $[M+H]^+$; Measured: 196.0972.

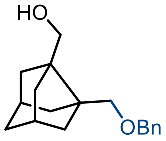
General procedure I: Hydride Reduction of Noradamantyl Carbaldehydes



Noradamantyl carbaldehyde was dissolved in distilled MeOH (0.5M) and $NaBH_4$ (1.3 equiv.) was added portion-wise. The reaction mixture was left to stir at room temperature for 1h. The reaction mixture was quenched by the addition of saturated aqueous NH_4Cl. The reaction mixture was extracted 3x with $CHCl_3$. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$ and the solvent was evaporated under reduced pressure. The product was purified by silica gel column chromatography.

Any alterations to the general procedure are mentioned with specific compounds.

Compound 7a



Prepared according to **General procedure I** from aldehyde **6c** (80 mg, 0.3 mmol). The product **7a** was purified by silica gel column chromatography eluting with 10% EtOAc:Cy and obtained as a colourless oil (75 mg, 93%).

R$_f$: 0.3 (10% EtOAc:Cy; UV, PMA)

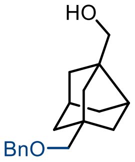
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.4 – 7.3 (m, 5H), 4.6 (s, 2H), 3.5 (s, 2H), 3.5 (s, 2H), 2.2 – 2.2 (m, 2H), 1.8 – 1.7 (m, 4H), 1.7 – 1.6 (m, 2H), 1.5 – 1.4 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 137.5 (C), 128.7 (2CH), 128.02 (CH), 127.95 (2CH), 73.7 (CH_2), 73.4 (CH_2), 65.2 (CH_2), 51.3 (C), 49.5 (C), 46.8 ($2CH_2$), 46.2 ($2CH_2$), 35.9 (CH_2), 34.7 (2CH).

IR (neat): $\tilde{\nu}$ /cm^{-1} = 3440, 2918, 2852, 1454, 1059, 733, 696, 602.

HRMS (m/z): Calcd for $C_{18}H_{24}NaO_2^+$: 295.1669 [M+Na]$^+$; Measured: 295.1667.

Compound 7b



Prepared according to **General procedure I** from aldehyde **6d** (90 mg, 0.33 mmol). The product **7b** was purified by silica gel column chromatography eluting with 50% Et_2O:Cy and obtained as a colourless oil (90 mg, 99%).

R$_f$: 0.2 (50% Et_2O:Cy; UV, PMA)

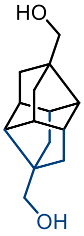
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.4 – 7.2 (m, 5H), 4.5 (s, 2H), 3.6 (s, 2H), 3.3 (s, 2H), 2.3 (s, 1H), 2.2 – 2.1 (m, 1H), 1.7 – 1.5 (m, 8H), 1.5 – 1.4 (m, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 139.1 (C), 128.4 (2CH), 127.47 (CH), 127.44 (2CH), 77.35 (CH_2), 73.35 (CH_2), 69.0 (CH_2), 51.5 (C), 48.0 (CH_2), 46.4 (C), 46.1 (CH_2), 45.5 (CH_2), 43.5 (CH_2), 40.8 (CH), 37.9 (CH_2), 36.8 (CH).

IR (neat): $\tilde{\nu}$ /cm^{-1} = 3367, 2927, 2856, 1454, 1092, 1028, 752, 696.

HRMS (m/z): Calcd for $C_{18}H_{24}NaO_2^+$: 295.1669 [M+Na]$^+$; Measured: 295.1665.

Compound 7c



Prepared according to ***Altered procedure I*** from mixture of aldehydes **6h** (1.05 g, 4.9 mmol). 2.6 equiv. (505 mg, 12.6 mmol) of $NaBH_4$ was used. The product **7c** was purified by silica gel column chromatography eluting with pure Et_2O and obtained as a white solid (185 mg, 17%; recrystallized from distilled EtOAc). *Note: Small impurities, mainly un-cleaved and reduced imines (aminoalcohols), may be carried with the diol during column chromatography. Dissolving in EtOAc and washing with aqueous 1M HCl followed by recrystallization from $CHCl_3$ affords the pure diol **7c**.*

R$_f$: 0.4 (Et_2O)

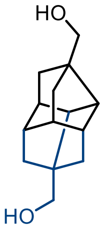
^{1}H NMR (400 MHz, $CDCl_3$) δ 3.6 (s, 4H), 2.2 – 2.2 (m, 4H), 2.1 – 2.1 (m, 2H), 2.0 – 1.9 (m, 4H), 1.8 – 1.7 (m, 4H), 1.4 (bs, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 68.8 ($2CH_2$), 56.2 (2C), 52.7 (2CH), 45.9 (2CH), 43.2 ($4CH_2$).

IR (neat): $\tilde{\nu}$ /cm^{-1} = 3195, 2918, 2852, 1342, 1032, 733.

HRMS (GCQTOF): Calcd for $C_{14}H_{20}O_2$: 220.1463 [M]; Measured: 220.1453.

Compound 7d

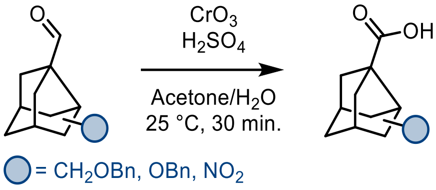


Prepared according to ***Altered procedure I*** from mixture of aldehydes **6h** (1.05 g, 4.9 mmol). 2.6 equiv. (505 mg, 12.6 mmol) of $NaBH_4$ was used. The product **7d** was purified by silica gel column chromatography eluting with pure Et_2O and obtained as a white solid (490 mg, 46%; recrystallized from distilled EtOAc).

R$_f$: 0.3 (Et_2O)

^{1}H NMR (400 MHz, $CDCl_3$) δ 3.6 (s, 4H), 2.4 – 2.3 (m, 4H), 2.0 (s, 2H), 1.8 (s, 4H), 1.7 – 1.6 (m, 2H), 1.5 – 1.5 (m, 2H), 1.4 (s, 2H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 68.8 (2CH_2), 55.8 (2CH), 51.7 (2CH), 50.4 (2C), 44.4 (2CH_2), 43.4 (2CH), 42.6 (2CH_2).
IR (neat): $\tilde{\nu}$ /cm^{-1} = 3327, 2916, 2856, 1437, 1304, 675, 575.
HRMS (GCQTOF): Calcd for $C_{14}H_{20}O_2$: 220.1463 [M]; Measured: 220.1453.

General procedure J: Jones Oxidation of Noradamantyl Carbaldehydes

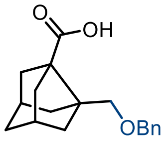


To a stirred solution of aldehyde in reagent grade acetone (0.3M) at room temperature was added drop wise freshly prepared Jones reagent to the point of constant orange colour. Any formed salts were dissolved by the addition of a few drops of distilled water and the mixture was left to stir for 30 minutes at room temperature (Conversion monitored by TLC). The remaining oxidant was quenched with the addition of isopropanol (green colour) and the reaction mixture was diluted with distilled water. The Aqueous phase was extracted 3x with $CHCl_3$ and the combined organic layers were washed with brine, dried over anhydrous $MgSO_4$ and the solvent was evaporated under reduced pressure. If necessary, the product was purified by silica gel column chromatography.

Jones reagent: 1.33 g of CrO_3 was dissolved in 3.75 ml of distilled water and the flask was placed into an ice-bath. Concentrated H_2SO_4 (1.25 ml) was added dropwise and the mixture was left stirring for a few minutes before the addition to a reaction mixture.

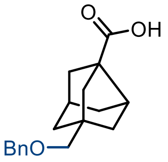
Any alterations to the general procedure are mentioned with specific compounds.

Compound 8a



Prepared according to **General procedure J** from aldehyde **6c** (80 mg, 0.3 mmol). The product **8a** was purified by silica gel column chromatography eluting with 5% EtOAc:DCM and obtained as a colourless oil (44 mg, 52%).
R_f : 0.3 (5% EtOAc:DCM; UV, PMA)
^{1}H NMR (400 MHz, $CDCl_3$) δ 10.9 (s, 1H), 7.4 – 7.2 (m, 5H), 4.4 (s, 2H), 3.6 (s, 2H), 2.4 – 2.3 (m, 2H), 2.3 – 2.2 (m, 2H), 1.9 – 1.9 (m, 2H), 1.7 – 1.6 (m, 6H).
^{13}C NMR (101 MHz, CDCl3) δ 182.8 (C), 138.8 (C), 128.3 (2CH), 127.4 (2CH), 127.3 (CH), 73.7 (CH_2), 73.1 (CH_2), 55.0 (C), 54.4 (C), 47.1 (2CH_2), 46.4 (2CH_2), 36.2 (2CH), 34.6 (CH_2).
IR (neat): $\tilde{\nu}$ /cm^{-1} = 2920, 2850, 1687, 1454, 1294, 1093, 731, 696.
HRMS (m/z): Calcd for $C_{18}H_{22}NaO_3^+$: 309.1461 $[M+Na]^+$; Measured: 309.1459.

Compound 8b



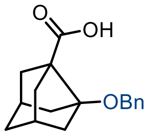
Prepared according to **General procedure J** from aldehyde **6d** (80 mg, 0.3 mmol). The product **8b** was purified by silica gel column chromatography eluting with 10% EtOAc:DCM and obtained as a colourless oil (61 mg, 76%).
R_f : 0.4 (10% EtOAc:DCM; UV, PMA)
^{1}H NMR (400 MHz, $CDCl_3$) δ 10.4 (bs, 1H), 7.4 – 7.3 (m, 5H), 4.5 (s, 2H), 3.3 (s, 2H), 2.8 – 2.7 (m, 1H), 2.5 – 2.4 (m, 1H), 2.1 – 2.0 (m, 2H), 1.9 – 1.7 (m, 3H), 1.7 – 1.6 (m, 4H), 1.5 – 1.5 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 184.1 (C), 138.9 (C), 128.4 (2CH), 127.5 (CH), 127.4 (2CH), 76.8 (CH_2), 73.3(CH_2), 54.0 (C), 48.6 (CH), 46.6 (C), 46.4 (CH_2), 45.7 (CH_2), 44.6 (CH), 43.1 (CH_2), 37.1 (CH_2), 37.0 (CH).

IR (neat): $\tilde{\nu}$ /cm^{-1} = 2922, 2866, 1689, 1454, 1311, 1092, 735, 696.

HRMS (m/z): Calcd for $C_{18}H_{22}NaO_3^+$: 309.1461 [M+Na]$^+$; Measured: 309.1457.

Compound 8c



Prepared according to **General procedure J** from aldehyde **6e** (40 mg, 0.16 mmol). The product **8c** was purified by silica gel column chromatography eluting with 5% EtOAc:DCM and obtained as a low melting crystalline solid (38 mg, 89%).

R$_f$: 0.4 (5% EtOAc:DCM; UV, PMA)

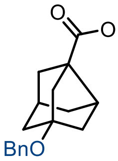
^{1}H NMR (400 MHz, $CDCl_3$) δ 11.2 (bs, 1H), 7.3 – 7.2 (m, 5H), 4.6 (s, 2H), 2.5 – 2.4 (m, 4H), 2.1 – 2.0 (m, 4H), 1.8 (d, *J* = 10.8 Hz, 2H), 1.7 – 1.5 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 178.5 (C), 138.6 (C), 128.4 (2CH), 127.5 (CH), 127.2 (2CH), 91.8 (C), 67.4 (CH_2), 55.4 (C), 47.6 (2CH_2), 46.4 (2CH_2), 35.8 (2CH), 33.6 (CH_2).

IR (neat): $\tilde{\nu}$ /cm^{-1} = 2925, 1687, 1294, 1149, 945, 731, 694.

HRMS (m/z): Calcd for $C_{17}H_{20}NaO_3^+$: 295.1305 [M+Na]$^+$; Measured: 295.1305.

Compound 8d



Prepared according to **General procedure J** from aldehyde **6f** (80 mg, 0.31 mmol). The product **8d** was purified by silica gel column chromatography eluting with 5% EtOAc:DCM and obtained as a colourless oil (75 mg, 88%).

R$_f$: 0.4 (5% EtOAc:DCM; UV, PMA)

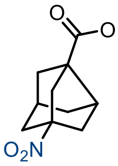
^{1}H NMR (400 MHz, $CDCl_3$) δ 11.2 (bs, 1H), 7.3 – 7.2 (m, 5H), 4.6 (s, 2H), 2.5 – 2.4 (m, 4H), 2.1 – 2.0 (m, 4H), 1.8 (d, *J* = 10.8 Hz, 2H), 1.7 – 1.5 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 178.5 (C), 138.6 (C), 128.4 (2CH), 127.5 (CH), 127.2 (2CH), 91.8 (C), 67.4 (CH_2), 55.4 (C), 47.6 (2CH_2), 46.4 (2CH_2), 35.8 (2CH), 33.6 (CH_2).

IR (neat): $\tilde{\nu}$ /cm^{-1} = 2925, 1687, 1294, 1149, 945, 731, 694.

HRMS (m/z): Calcd for $C_{17}H_{20}NaO_3^+$: 295.1305 [M+Na]$^+$; Measured: 295.1305.

Compound 8e



Prepared according to **General procedure J** from aldehyde **6g** (74 mg, 0.38 mmol). The product **8e** was purified by silica gel column chromatography eluting with 10% EtOAc:DCM and obtained as a colourless oil (70 mg, 88%).

R$_f$: 10% (EtOAc:DCM; PMA, $KMnO_4$)

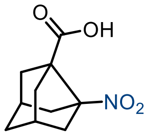
^{1}H NMR (400 MHz, $CDCl_3$) δ 10.5 (bs, 1H), 2.9 – 2.8 (m, 2H), 2.7 – 2.6 (m, 1H), 2.6 – 2.5 (m, 1H), 2.3 – 2.2 (m, 2H), 2.2 – 2.1 (m, 2H), 2.1 – 2.0 (m, 1H), 1.9 – 1.8 (m, 2H), 1.7 – 1.6 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 181.5 (C), 88.4 (C), 52.5 (C), 48.5 (CH_2), 46.4 (CH_2), 45.6 (CH_2), 42.8 (CH), 41.9 (CH_2), 37.8 (CH_2), 37.4 (CH).

IR (neat): $\tilde{\nu}$ /cm^{-1} = 2958, 2638, 1684, 1525, 1257, 941, 806, 698.

HRMS (m/z): Calcd for $C_{10}H_{12}NO_4^-$: 210.0772 [M-H]$^-$; Measured: 210.0771.

Compound 8f

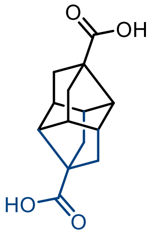


Prepared according to **General procedure J** from aldehyde **6i** (25 mg, 0.13 mmol). The product **8f** was purified by silica gel column chromatography eluting with 20% EtOAc:DCM and obtained as a white solid (21 mg, 78%).

R$_f$: 0.4(20% EtOAC:DCM; PMA, $KMnO_4$)

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.5 (bs, 1H), 2.7 – 2.6 (m, 2H), 2.6 – 2.5 (m, 2H), 2.5 – 2.4 (m, 2H), 2.1 (dd, *J* = 10.5, 3.1 Hz, 2H), 1.9 (dd, *J* = 11.2, 3.1 Hz, 2H), 1.7 – 1.6 (m, 2H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 178.1 (C), 98.1 (C), 58.9 (C), 48.5 ($2CH_2$), 46.4 ($2CH_2$), 36.4 (2CH), 33.2 (CH_2).
IR (neat): $\tilde{\nu}$ /cm^{-1} = 2924, 1703, 1533, 1290, 930, 802, 561, 430.
HRMS (m/z): Calcd for $C_{10}H_{13}NNaO_4^+$: 234.0737 [M+Na]$^+$; Measured: 234.0736.

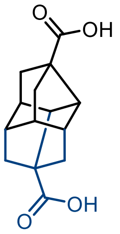
Compound 8g



Prepared according to ***Altered procedure J*** from di-ol **7c** (120 mg, 0.55 mmol). Upon completion the reaction mixture was with water and the pH adjusted to 12 by addition of 2M aqueous NaOH. The aqueous phase was washed with Et_2O, filtered and acidified to pH 1 with concentrated HCl. The aqueous phase was extracted with a large amount of EtOAc. The combined organic layers were dried over anhydrous $MgSO_4$ and evaporated under reduced pressure to give the product **8g** as a white solid. If necessary, the product **8g** can be purified by recrystallization from MeOH:$CHCl_3$ 1:1 and obtained as a colourless crystalline solid (102 mg, 76%).

R$_f$: --
^{1}H NMR (400 MHz, DMSO) δ 12.0 (s, 2H), 2.5 – 2.4 (m, 2H), 2.3 – 2.2 (m, 8H), 1.9 – 1.8 (m, 4H).
^{13}C NMR (101 MHz, DMSO) δ 177.4 (2C), 57.5 (2C), 52.0 (4CH), 47.2 (2CH), 43.5 ($4CH_2$).
IR (neat): $\tilde{\nu}$ /cm^{-1} = 2960, 2885, 2573, 1676,1415, 1323, 1088, 964, 818, 756, 552.
HRMS (m/z): Calcd for $C_{14}H_{15}O_4^-$: 247.0976 [M-H]$^-$; Measured: 247.0978.

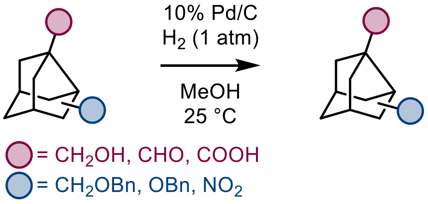
Compound 8h



Prepared according to ***Altered procedure J*** from alcohol **7d** (460 mg, 2.1 mmol). Upon completion the reaction mixture was with water and the pH adjusted to 12 by addition of 2M aqueous NaOH. The aqueous phase was washed with Et_2O, filtered and acidified to pH 1 with concentrated HCl. The aqueous phase was extracted with a EtOAc and the combined organic layers were dried over anhydrous $MgSO_4$ and evaporated under reduced pressure to give product **8h** as a white solid (404 mg, 78%).

R$_f$: --
^{1}H NMR (400 MHz, MeOD) δ 2.9 – 2.8 (m, 2H), 2.5 – 2.4 (m, 2H), 2.3 – 2.0 (m, 8H), 1.8 – 1.7 (m, 2H).
^{13}C NMR (101 MHz, MeOD) δ 180.8 (2C), 59.1 (2CH), 54.4 (2C), 53.0 (2CH), 46.4 ($2CH_2$), 44.1 ($2CH_2$), 43.9 (2CH).
IR (neat): $\tilde{\nu}$ /cm^{-1} = 2918, 2871, 2578, 1682, 1415, 1284, 1196, 937, 744, 555.
HRMS (m/z): Calcd for $C_{14}H_{15}O_4^-$: 247.0976 [M-H]$^-$; Measured: 247.0975.

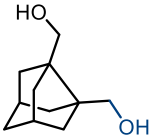
General procedure K: Catalytic hydrogenation of noradamantyl derivatives



A dry vial with containing the desired noradamantyl derivative equipped with a stir bar was charged with 10% Pd/C (10% w/w), sealed with a septum cap, cycled through vacuum and backfilled with nitrogen. Distilled MeOH was added (1 ml per 100 mg) and hydrogen balloon was connected. The nitrogen was displaced by hydrogen and the reaction mixture was left to stir at room temperature for 4h. After completion the reaction vessel was aerated and filtered through a glass frit with a pad of celite. The pad was washed with methanol and the combined solvent evaporated under reduced pressure. If necessary, the product was purified by silica gel column chromatography.

Any alterations to the general procedure are mentioned with specific compounds.

Compound 9a



Prepared according to **General procedure K** from alcohol **7a** (75 mg, 0.28 mmol). The product **9a** was obtained as a white wax (50 mg, quant.).

R$_f$ **:** 0.5 (EtOAc)

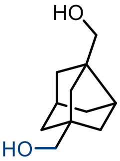
^{1}H NMR (400 MHz, $CDCl_3$) δ 4.1 (s, 2H), 3.6 (s, 4H), 2.2 – 2.2 (m, 2H), 1.8 – 1.7 (m, 4H), 1.7 – 1.7 (m, 2H), 1.5 – 1.4 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 65.1 (2CH_2), 50.9 (2C), 46.2 (4CH_2), 35.9 (CH_2), 34.7 (2CH).

IR (neat): $\tilde{\nu}$ /cm^{-1} = 3242, 2918, 2850, 1458, 1034, 652.

HRMS (m/z): Calcd for $C_{11}H_{18}NaO_2^+$: 205.1199 [M+Na]$^+$; Measured: 205.1197.

Compound 9b



Prepared according to **General procedure K** from alcohol **7b** (90 mg, 0.33 mmol). The product **9b** was obtained as a colourless oil (60 mg, quant.).

R$_f$ **:** 0.3 (EtOAc)

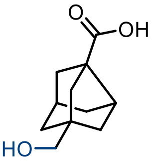
^{1}H NMR (400 MHz, $CDCl_3$) δ 3.6 (s, 2H), 3.4 (s, 2H), 2.4 – 2.3 (m, 3H), 2.2 – 2.1 (m, 1H), 1.7 – 1.6 (m, 1H), 1.6 – 1.5 (m, 7H), 1.4 – 1.3 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 69.7 (CH_2), 68.8 (CH_2), 51.4 (C), 47.3 (C), 47.2 (CH_2), 45.6 (CH_2), 45.3 (CH_2), 43.4 (CH_2), 40.7 (CH), 37.2 (CH_2), 36.7 (CH).

IR (neat): $\tilde{\nu}$ /cm^{-1} = 3315, 2922, 2858, 1436, 1016, 752, 629.

HRMS (m/z): Calcd for $C_{11}H_{18}NaO_2^+$: 205.1199 [M+Na]$^+$; Measured: 205.1196.

Compound 9c



Prepared according to ***Altered procedure K*** from carboxylic acid **8b** (55 mg, 0.19 mmol). 10% Pd/C (20% w/w), EtOH, 25 °C, 24h. The product **9c** was obtained as a colourless oil (36.5 mg, 97%).

R$_f$ **:** 0.5 (EtOAc)

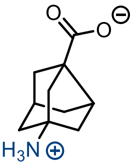
^{1}H NMR (400 MHz, $CDCl_3$) δ 6.3 (bs, 2H), 3.5 (s, 2H), 2.8 – 2.7 (m, 1H), 2.5 – 2.4 (m, 1H), 2.1 – 2.0 (m, 2H), 1.9 – 1.7 (m, 3H), 1.7 – 1.5 (m, 4H), 1.5 – 1.4 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 183.4 (C), 69.4 (CH_2), 54.0 (C), 47.9 (CH_2), 47.5 (C), 46.5 (CH_2), 44.9 (CH_2), 44.5 (CH), 43.1 (CH_2), 36.9 (CH), 36.4 (CH_2).

IR (neat): $\tilde{\nu}$ /cm^{-1} = 3388, 2927, 2860, 1707, 1309. 1018, 731, 552, 511.

HRMS (m/z): Calcd for $C_{11}H_{16}NaO_3^+$: 219.0992 [M+Na]$^+$; Measured: 219.0991.

Compound 9d

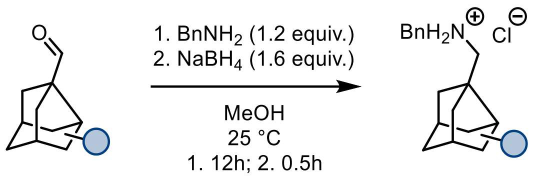


Prepared according to ***Altered procedure K*** from carboxylic acid **8e** (35 mg, 0.17 mmol). 10% Pd/C (20% w/w), MeOH, 50 °C, 24h. The product **9d** was obtained as a white solid (26 mg, 86%).

^{1}H NMR (400 MHz, D_2O) δ 2.7 – 2.6 (m, 1H), 2.5 (s, 1H), 2.3 – 2.2 (m, 1H), 2.1 – 2.0 (m, 1H), 2.0 – 1.7 (m, 7H), 1.6 – 1.5 (m, 1H).

^{13}C NMR (101 MHz, D_2O) δ 185.2 (C), 58.4 (C), 55.4 (C), 48.8 (CH_2), 46.1 (CH_2), 45.3 (CH_2), 42.2 (CH), 41.4 (CH_2), 37.5 (CH_2), 36.5 (CH).
IR (neat): $\tilde{\nu}$ /cm^{-1} = 2960, 2864, 2623, 2567, 2193, 1520, 1392, 777.
HRMS (m/z): Calcd for $C_{10}H_{16}NO_2^+$: 182.1776 [M+H]$^+$; Measured: 182.1778.

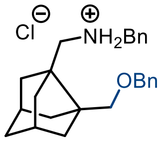
General procedure L: Reductive Amination of Noradamantyl Carbaldehydes



The aldehyde was dissolved in distilled MeOH (0.5M) and benzyl amine (1.2 equiv.) was added. The reaction mixture was left to stir at room temperature overnight. Next, $NaBH_4$ (1.6 equiv.) was added portion-wise and the reaction mixture was left to stir for an additional 30 minutes. The reaction mixture was quenched by addition of 1M aqueous NaOH and partitioned between brine and Et_2O. The aqueous phase was extracted 2x with Et_2O and the combined organic layers were washed with brine, dried over anh. $MgSO_4$ and the solvent evaporated under reduced pressure. The crude mixture was dissolved a small amount of Et_2O and treated with ethereal HCl. The precipitated hydrochloride salt was filtered off, washed with cold Et_2O, dissolved in $CHCl_3$, dried over anhydrous $MgSO_4$ and the solvent was evaporated under reduced pressure to give the final product as its hydrochloride salt.

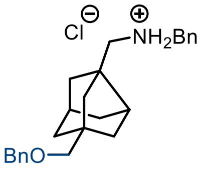
The procedure was adapted from: Abdel-Magid, A. F.; Carson, K. G.; Harris, B. D.; Maryanoff, C. A.; Shah, D. R. *J. Org. Chem.* **1996**, 61, 11.[8]

Compound 10a



Prepared according to **General procedure L** from aldehyde **6c** (51 mg, 0.19 mmol). The product **10a** was obtained as a fluffy white solid (47 mg, 63%).
R_f : 0.3 (10% EtOAc:$CHCl_3$)
^{1}H NMR (400 MHz, $CDCl_3$) δ 9.43 (s, 2H), 7.64 – 7.52 (m, 2H), 7.35 – 7.24 (m, 6H), 7.19 – 7.12 (m, 2H), 4.31 (s, 2H), 4.23 – 4.16 (m, 2H), 3.27 (s, 2H), 3.04 – 2.93 (m, 2H), 2.21 (s, 2H), 2.12 – 2.02 (m, 2H), 1.78 – 1.66 (m, 4H), 1.62 – 1.52 (m, 2H), 1.43 – 1.35 (m, 2H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 137.8 (C), 130.8 (C), 130.5 (2CH), 129.4 (CH), 129.1 (2CH), 128.5 (2CH), 127.7 (CH), 127.5 (2CH), 73.2 (CH_2), 72.7 (CH_2), 51.9 (CH_2), 51.9 (2CH_2), 51.3 (C), 48.0 (2CH_2), 47.7 (C), 46.1 (CH_2), 35.4 (2CH), 34.5 (CH_2).
IR (neat): $\tilde{\nu}$ /cm^{-1} = 2927, 2850, 2789, 1587, 1092, 733, 696.
HRMS (m/z): Calcd for $C_{25}H_{32}NO^+$: 362.2478 [M+H]$^+$; Measured: 362.2476.

Compound 10b

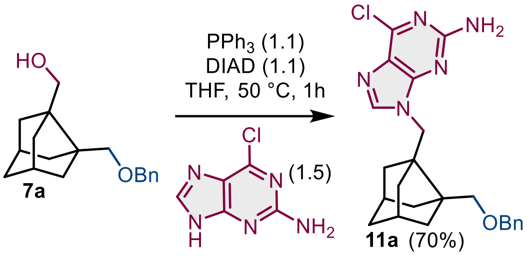


Prepared according to **General procedure L** from aldehyde **6d** (39 mg, 0.14 mmol). The product **10b** was obtained as a fluffy white solid (35 mg, 60%).
R_f : 0.3 (10% EtOAc:$CHCl_3$)
^{1}H NMR (400 MHz, $CDCl_3$) δ 9.62 (s, 2H), 7.72 – 7.63 (m, 2H), 7.45 – 7.33 (m, 3H), 7.33 – 7.19 (m, 5H), 4.38 (s, 2H), 4.24 (s, 2H), 3.21 – 3.14 (m, 2H), 2.82 (s, 2H), 2.31 (s, 1H), 2.29 – 2.22 (m, 1H), 1.85 – 1.66 (m, 5H), 1.65 – 1.39 (m, 5H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 138.9 (C), 130.6 (C), 130.5 (2CH), 129.5 (CH), 129.3 (2CH), 128.4 (2CH), 127.4 (2CH, CH), 76.7 (CH_2), 73.2 (CH_2), 52.9 (CH_2), 51.5 (CH_2), 49.4 (CH_2), 47.7 (C), 46.7 (C, CH_2), 45.6 (CH_2), 43.0 (CH_2), 42.6 (CH), 37.1 (CH_2), 36.9 (CH).

IR (neat): $\tilde{\nu}$ /cm^{-1} = 2933, 2860, 1763, 1585, 1446, 1101, 727, 694.
HRMS (m/z): Calcd for $C_{25}H_{32}NO^+$: 362.2478 [M+H]$^+$; Measured: 362.2477.

Antiviral Analogue Synthesis

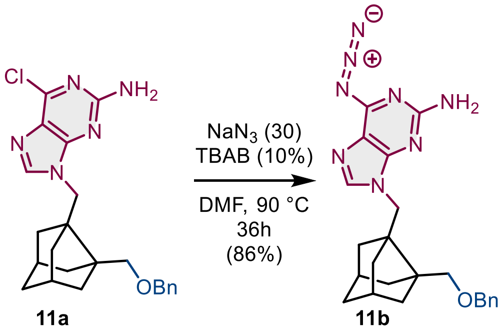
Compound 11a



A vial was charged with noradamantyl alcohol **7a** (50 mg, 0.18 mmol), triphenyl phosphine (1.1 equiv. 53 mg, 0.20 mmol) and 6-chloro-2-amino-purine (1.5 equiv. 47 mg, 0.28 mmol), flushed with argon, sealed with a septum cap and equipped with an argon balloon. 0.5 ml of anhydrous THF was added and the reaction mixture was transferred to a heating bath. The reaction was stirred and the temperature increased to 50 °C, where DIAD (1.1 equiv. 42 µl, 0.20 mmol) was injected in a drop-wise fashion at around 40 °C. The reaction was left to stir at 50 °C for 1 hour. After completion the reaction was cooled down to room temperature and quenched by the addition of brine (1 ml) and diluted with $CHCl_3$. The phases were separated and the aqueous phase extracted with $CHCl_3$. The combined organic layers were dried over anhydrous $MgSO_4$ and the solvent evaporated under vacuo. The crude mixture was separated by silica gel column chromatography (20% EtOAc:DCM). The product **11a** was isolated as a white solid in a yield of 88 mg (70%).

R$_f$: 0.4 (20% EtOAc:DCM; UV, PMA)
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.7 (s, 1H), 7.4 – 7.3 (m, 5H), 5.4 (s, 2H), 4.6 (s, 2H), 4.3 (s, 2H), 3.5 (s, 2H), 2.2 (s, 2H), 1.9 – 1.9 (m, 2H), 1.9 – 1.8 (m, 2H), 1.6 – 1.5 (m, 3H), 1.5 – 1.4 (m, 1H), 1.4 – 1.3 (m, 2H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 159.2 (C), 154.6 (C), 151.2 (C), 143.2 (CH), 138.4 (C), 128.5 (2CH), 127.8 (2CH), 127.8 (CH), 125.0 (C), 73.4 (CH_2), 73.1 (CH_2), 51.0 (C), 50.7 (C), 50.4 (CH_2), 48.6 (2CH_2), 46.7 (2CH_2), 35.6 (2CH), 34.5 (CH_2).
IR (neat): $\tilde{\nu}$ /cm^{-1} = 3402, 3319, 3215, 2927, 2862, 1604, 1560, 1460, 1406, 1070, 912, 731, 698, 501.
HRMS (m/z): Calcd for $C_{23}H_{27}ClN_5O^+$: 424.1899 [M+H]$^+$; Measured: 424.1897.

Compound 11b

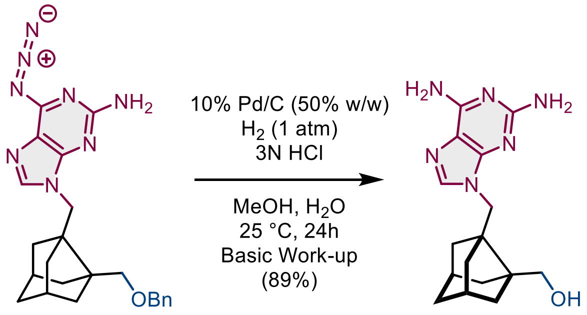


A vial was charged with amine **11a** (50 mg, 0.12 mmol), NaN_3 (30 equiv. 230 mg, 3.55 mmol) and tetrabutylammonium bromide (10 mol%, 4 mg, 0.01 mmol), sealed with a septum cap and placed under nitrogen. Anhydrous DMF (0.5 ml) was added and the mixture was transferred to a heating bath heated to 90 °C and stirred for 36h. The reaction was quenched with brine (2 ml) and the aqueous phase was extracted with $CHCl_3$. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$ and evaporated under reduced pressure with the bulk of DMF. The crude mixture was separated by silica gel column chromatography (10-40% EtOAc:DCM). The product **11b** was obtained as a white solid in a yield of 45 mg (88%).

R_f : 0.3 (30% EtOAc:DCM; UV, PMA)
^{1}H NMR (400 MHz, DMSO-*d*^{6}) δ 8.3 (s, 2H), 8.1 (s, 1H), 7.4 – 7.3 (m, 5H), 4.6 (s, 2H), 4.4 (s, 2H), 3.5 (s, 2H), 2.1 (s, 2H), 2.0 – 1.8 (m, 4H), 1.6 – 1.5 (m, 3H), 1.4 – 1.3 (m, 1H), 1.3 – 1.2 (m, 2H).
^{13}C NMR (101 MHz, DMSO-*d*^{6}) δ 146.5 (C), 145.8 (C), 143.8 (C), 141.3 (CH), 138.9 (C), 128.8 (2CH), 128.1(2CH), 127.9 (CH), 112.0 (C), 73.3 (CH_2), 73.0 (CH_2), 50.8 (C), 50.8 (C), 50.1 (CH_2), 48.4 ($2CH_2$), 46.8 ($2CH_2$), 35.3 (2CH), 34.4 (CH_2).
IR (neat): $\tilde{\nu}$ /cm^{-1} = 3413, 3294, 3195, 3157, 2933, 2844, 1674, 1545, 1119, 1090, 733, 521.
HRMS (m/z): Calcd for $C_{23}H_{27}N_8O^+$: 431.2302 [M+H]$^+$; Measured: 431.2301.

Notes: After evaporation the crude solid is soluble in a 1:1 mixture of MeOH:$CHCl_3$ for ease of manipulation (preparation of silica gel slurry for silica gel column chromatography).

Compound 11c



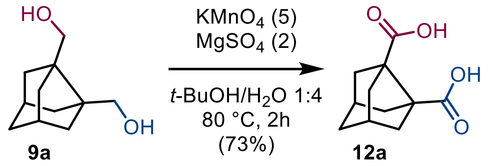
11b **11c**

A vial was charged with Azide **11b** (23 mg 0.05 mmol) and 5% Pd/C (50% w/w, 11 mg), sealed with a septum cap and cycled through vacuum/nitrogen. Distilled MeOH (0.5 ml) was added and the nitrogen was switched for a balloon of hydrogen. After 10 minutes, 3M aqueous HCl (25 µl) was added via a microliter syringe and the reaction mixture was left to stir for 24h at room temperature. After completion the reaction mixture was aerated and 3M aqueous NaOH (approx. 40 µl) was added via a microliter syringe to pH 12 and stirred for additional 10 minutes. The reaction mixture was diluted with $CHCl_3$ (0.5 ml), filtered through a pad of celite and the pad thoroughly washed with a mixture of warm MeOH/$CHCl_3$ (1:1 v/v). The solvent was evaporated under reduced pressure to give a white solid (17.5 mg). Recrystallization from MeOH/$CHCl_3$ (1:1 v/v) gave the final amine product **11c** in a yield of 15 mg (89%).

^{1}H NMR (400 MHz, DMSO) δ 7.6 (s, 1H), 6.6 (s, 2H), 5.7 (s, 2H), 4.8 (t, *J* = 4.6 Hz, 1H), 4.2 (s, 2H), 3.5 (d, *J* = 4.7 Hz, 2H), 2.1 (s, 2H), 1.9 – 1.7 (m, 4H), 1.6 – 1.4 (m, 4H), 1.3 – 1.2 (m, 2H).
^{13}C NMR (101 MHz, DMSO) δ 160.6 (C), 156.5 (C), 152.9 (C), 138.5 (CH), 113.3 (C), 64.3 (CH_2), 51.7 (C), 50.7 (C), 48.8 (CH_2), 48.7 ($2CH_2$), 46.5 ($2CH_2$), 35.3 (2CH), 34.7 (CH_2).
IR (neat): $\tilde{\nu}$ /cm^{-1} = 3329, 3213, 2918, 2850, 1645, 1587, 1377, 1026, 791,741, 623.
HRMS (m/z): Calcd for $C_{16}H_{23}N_6O^+$: 315.1928 [M+H]$^+$; Measured: 315.1930.

Antimicrobial Analogue Synthesis

Compound 12a

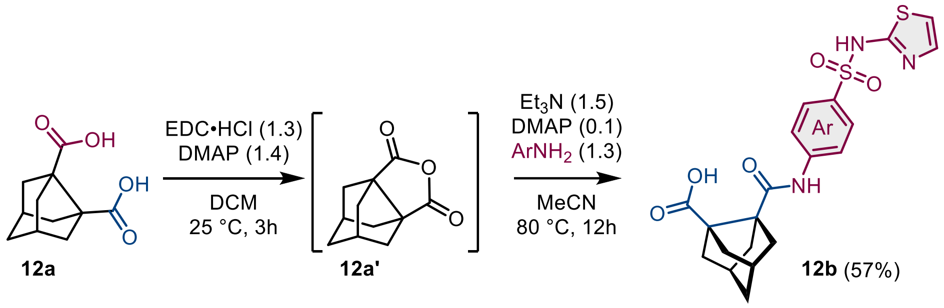


To a vial containing diol **9a** (70 mg, 0.38 mmol) and $MgSO_4$ (2 equiv., 92 mg) was added a mixture of H_2O (0.8 ml) and *t*-BuOH (0.2 ml) (4:1). The stirred solution was placed in a cold heating bath and $KMnO_4$ (5 equiv., 300 mg) was added. The vial was sealed with a septum cap pierced with a syringe (to alleviate built-up pressure) The reaction mixture was heated to 80 °C and vigorously stirred for 2h. After completion the reaction was left to cool down to room temperature and placed in a cold-water bath, quenched with saturated aqueous $Na_2S_2O_3$ and the pH adjusted to 12 with a few drops of 2N aqueous NaOH. The precipitated magnesium oxide was filtered off and the clear aqueous layer acidified to pH 2 with a few drops of concentrated HCl. The aqueous phase was extracted with $CHCl_3$:*i*-PrOH (4:1), the combined organic layers dried over anhydrous $MgSO_4$ and evaporated under reduced pressure. The product was purified by silica gel column chromatography eluting with pure Et_2O to afford the dicarboxylic acid **12a** as a white solid in a yield of 59 mg (73%).

R_f : 0.7 (Et_2O; PMA)
^{1}H NMR (400 MHz, $CDCl_3$) ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.4 (bs, 2H), 2.5 – 2.4 (m, 2H), 2.3 – 2.2 (m, 4H), 1.9 – 1.7 (m, 4H), 1.7 – 1.6 (m, 2H).
^{13}C NMR (101 MHz, $CDCl_3$) ^{13}C NMR (101 MHz, $CDCl_3$) δ 182.4 (2C), 59.7 (2C), 46.6 (4CH_2), 37.0 (2CH), 33.8 (CH_2).
IR (neat): $\tilde{\nu}$ /cm^{-1} = 2924, 1685, 1408, 1282, 1113, 933, 827, 717, 567.
HRMS (m/z): Calcd for $C_{11}H_{13}O_4^-$: 209.0819 [M-H]$^-$; Measured: 209.0818.

The procedure was adapted from: Pustovit, Yu. M.; Ogojko, P. I.; Nazaretian, V. P.; Rozhenko, A. B. *J. Fluor. Chem.* **1993**, 69, 231-236.[9]

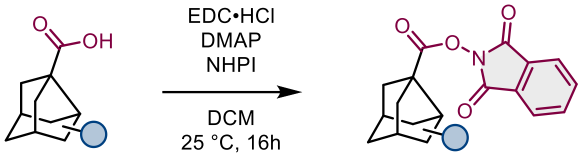
Compound 12b



To a vial containing diacid **12a** (30 mg, 0.14 mmol) was added EDC•HCl (1.3 equiv., 35,5 mg), DMAP (1.4 equiv, 24 mg) and DCM (0.5 ml). The vial was sealed with a cap and the reaction mixture left to stir for 4h at room temperature. After completion the reaction mixture was loaded directly onto a short plug of silica gel and the plug was flushed with pure chloroform. The solvent was evaporated under reduced pressure and to give the anhydride as a white solid that was used without further purification. The anhydride was transferred to a vial and DMAP (relative to acid **12a**, 0.1 equiv., 2 mg)

was added together with sulfathiazole (relative to acid **12a**, 1.3 equiv., 46 mg). The vial was sealed with septum cap and 0.5 ml of anhydrous MeCN was added followed by Et_3N (26 µl, 1.3 equiv., 0.18 mmol). The reaction mixture was heated to 80 °C and left stirring overnight. After completion the reaction mixture was left to cool down to room temperature and the bulk of the solvent evaporated. 0.5 ml of 2M aqueous NaOH was added and the reaction mixture was left to stir for an additional 3 hours (partial hydrolysis of formed di-imide side-product). The aqueous layer was filtered off and acidified with 2M HCl till the point of precipitate formation. The precipitate was filtered off, washed 2x with distilled water, 2x with Et_2O, redissolved in distilled MeOH and the solvents evaporated to dryness under reduced pressure. The final product **12b** was obtained as an off white solid in a yield of 36 mg (56%).
R_f : 0.25 (10% MeOH:$CHCl_3$; UV, PMA)
^{1}H NMR (400 MHz, MeOD) δ 7.8 – 7.8 (m, 2H), 7.7 – 7.7 (m, 2H), 7.1 (d, *J* = 4.6 Hz, 1H), 6.7 (d, *J* = 4.6 Hz, 1H), 2.5 – 2.4 (m, 2H), 2.4 – 2.3 (m, 4H), 1.9 – 1.8 (m, 4H), 1.7 (s, 2H).
^{13}C NMR (101 MHz, MeOD) δ 178.9 (C), 176.5 (C), 171.1 (C), 143.5 (C), 138.3 (C), 128.0 (2CH), 125.0 (CH), 122.1 (2CH), 109.4 (CH), 62.1 (C), 60.5 (C), 47.8 (2CH_2), 47.7 (2CH_2), 38.2 (2CH), 34.9 (CH_2).
IR (neat): $\tilde{\nu}$ /cm^{-1} = 3604, 3276, 3093, 2916, 1711, 1570, 1520, 1400, 1271, 1126, 1068, 935, 690, 584.
HRMS (m/z): Calcd for $C_{20}H_{20}N_3O_5S_2^-$: 446.0850 [M-H]$^-$; Measured: 446.0850.

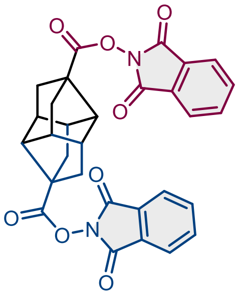
General procedure M: Synthesis of Redox-active Esters



Dicarboxylic acid **XX**, EDC•HCl, DMAP and NHPI were added to a vial equipped with a stir bar and distilled DCM was added. The reaction mixture was left to stir overnight at room temperature. After completion the DCM was evaporated under reduced pressure. Upon the addition of MeOH the product precipitated and was filtered off, washed with MeOH and a small amount of Et_2O and dried on air to a stable weight.

Any alterations to the general procedure are mentioned with specific compounds.

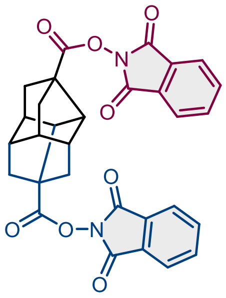
Compound 13a



Prepared according to **General procedure M** from carboxylic acid **8g** (85 mg, 0.34 mmol). EDC•HCl (2.2 equiv., 143 mg), DMAP (2.4 equiv., 100 mg) and NHPI (2.2 equiv, 122 mg). The product **13a** was obtained as a white amorphous solid (100 mg, 54%). *Note!: The compound is practically insoluble (even in DMSO), but very slightly soluble in DCM. Even after measuring prolonged carbon NMR (400 MHz), the carboxylate quaternary carbon (most-likely) wasn't able to be detected.*

R_f : 0.5 (5% EtOAc:$CHCl_3$; UV, PMA)
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.9 – 7.8 (m, 4H), 7.8 – 7.8 (m, 4H), 3.0 – 3.0 (m, 2H), 2.7 – 2.5 (m, 8H), 2.3 – 2.2 (m, 4H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 162.5 (4C), 135.2 (4CH), 129.4 (4C), 124.2 (4CH), 56.5(2C), 52.8 (4CH), 49.1(2CH), 44.1 (4CH_2).
IR (neat): $\tilde{\nu}$ /cm^{-1} = 2935, 1736, 1466, 1360, 1138, 1030, 976, 876, 789, 692, 521.
HRMS (m/z): Calcd for $C_{30}H_{22}N_2NaO_8^+$: 561.1268 [M+Na]$^+$; Measured: 561.1266

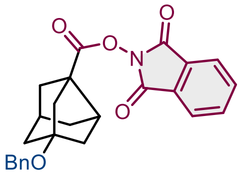
Compound 13b



Prepared according to **General procedure M** from carboxylic acid **8h** (315 mg, 1.27 mmol). EDC•HCl (2.2 equiv, 533 mg), DMAP (2.4 equiv., 370 mg) and NHPI (2.2 equiv., 455 mg). The product **13b** was obtained as a white amorphous solid (430 mg, 63%).

R$_f$: 0.6 (5% EtOAc:CHCl$_3$; UV, PMA)
^{1}H NMR (400 MHz, CDCl$_3$) δ 7.9 – 7.9 (m, 4H), 7.8 – 7.8 (m, 4H), 3.4 – 3.3 (m, 2H), 2.7 – 2.7 (m, 2H), 2.6 – 2.5 (m, 2H), 2.4 – 2.3 (m, 4H), 2.3 (s, 2H), 2.1 – 2.0 (m, 2H).
^{13}C NMR (101 MHz, CDCl$_3$) δ 172.3 (2C), 162.2 (4C), 134.8 (4CH), 129.2 (4C), 124.1 (4CH), 58.0 (2CH), 51.7 (2C), 51.5 (2CH), 45.5 (2CH$_2$), 42.9 (2CH$_2$), 42.3 (2CH).
IR (neat): $\tilde{\nu}$ /cm^{-1} = 2935, 1741, 1464, 1360, 1128, 976, 877, 694, 519.
HRMS (m/z): Calcd for $C_{30}H_{22}N_2NaO_8^+$: 561.1268 [M+Na]$^+$; Measured: 561.1276.

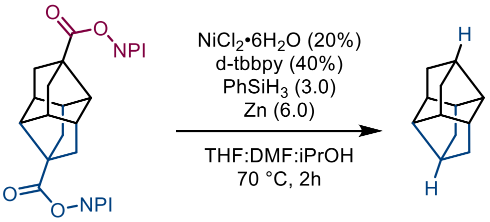
Compound 13c



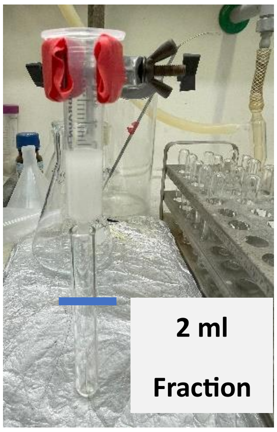
Prepared according to ***Altered procedure M*** from carboxylic acid **8b** (30 mg, 0.11 mmol). EDC•HCl (1.1 equiv., 23 mg), DMAP (1.2 equiv., 16 mg) and NHPI (1.2 equiv., 22 mg). After completion the solvent the bulk of the solvent was evaporated and the crude mixture loaded onto a short column. The product **13c** was purified by silica gel column chromatography eluting with 1% EtOAc:CHCl$_3$ and obtained as an off-white amorphous solid (41 mg, 89%).

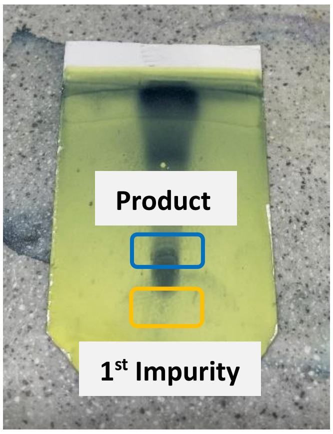
R$_f$: 0.5 (1% EtOAc:CHCl$_3$; UV, PMA)
^{1}H NMR (400 MHz, CDCl$_3$) δ 7.9 – 7.9 (m, 2H), 7.8 – 7.8 (m, 2H), 7.4 – 7.3 (m, 4H), 7.3 – 7.2 (m, 1H), 4.5 (s, 2H), 3.1 – 3.0 (m, 1H), 2.6 – 2.5 (m, 2H), 2.3 – 2.2 (m, 2H), 2.0 – 1.8 (m, 5H), 1.7 – 1.6 (m, 2H).
^{13}C NMR (101 MHz, CDCl$_3$) δ 172.4 (C), 162.2 (2C), 139.2 (2C), 134.8 (2CH), 129.2 (C), 128.5 (2CH), 127.6 (2CH), 127.5 (CH), 124.0 (CH), 81.5 (C), 65.9 (CH$_2$), 50.8 (C), 48.2 (CH$_2$), 46.2 (CH$_2$), 45.6 (CH$_2$), 43.0 (CH), 42.4 (CH$_2$), 38.8 (CH$_2$), 37.1 (CH).
IR (neat): $\tilde{\nu}$ /cm^{-1} = 2954, 1730, 1452, 1375, 1182, 1115, 982, 876, 694, 519.
HRMS (m/z): Calcd for $C_{25}H_{23}NNaO_5^+$: 440.1468 [M+Na]$^+$; Measured: 440.1467.

General procedure N: Nickel Catalysed Barton Decarboxylation



DecarboxylationA schlenk tube equipped with a magnetic stir bar was charged with redox active ester (**13a** or **13b**) and powdered Zinc (6 equiv.). The vial was evacuated, backfilled with nitrogen and anhydrous THF (passed over activated alumina) together with *i*-PrOH were added. A pre-prepared 2M stock solution of NiCl$_2$•6H$_2$O (48 mg) and 4,4’-Di-tert-butyl-bipyridine (108 mg) in anhydrous DMF (1 ml) was taken up into a syringe and added to the reaction mixture without stirring. In immediate succession was added PhSiH$_3$ (3 equiv.), the reaction vessel submerged into a preheated bath to 70 °C and

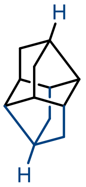




vigorously stirred (1000 rpm) for 2h. After completion, the reaction was quenched by addition of 1:1 (v/v) saturated aqueous NH_4Cl and water and left to stir for 5 minutes. The mixture was extracted with freshly distilled pentane, the combined organic layers dried over anhydrous $MgSO_4$ and carefully evaporated under reduced pressure (450 mbar, rota bath set to 25 °C). The crude mixture was washed/taken up into a small amount of pentane and passed through a short silica gel column (approx. h = 3 cm; d = 1 cm) eluting with distilled pentane. Small fractions were taken to the point of the appearance of the first impurity (TLC-PMA). Fractions leading up to the impurity were collected and the solvent was carefully evaporated under reduced pressure (450 mbar, rota bath set to 25 °C). Traces of pentane were evaporated by flushing the flask with a stream of argon/nitrogen and by slow evaporation from $CDCl_3$.

The procedure was adapted from: Qin, T.; Malins, L. R.; Edwards, J. T.; Merchant, R. R.; Novak, A. J. E.; Zhong, J. Z.; Mills, R. B.; Yan, M.; Yuan, C.; Eastgate, M. D.; Baran, P. S. *Angew. Chem. Int. Ed.* **2017**, 56, 260 -265.[10]

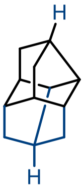
Compound 14a

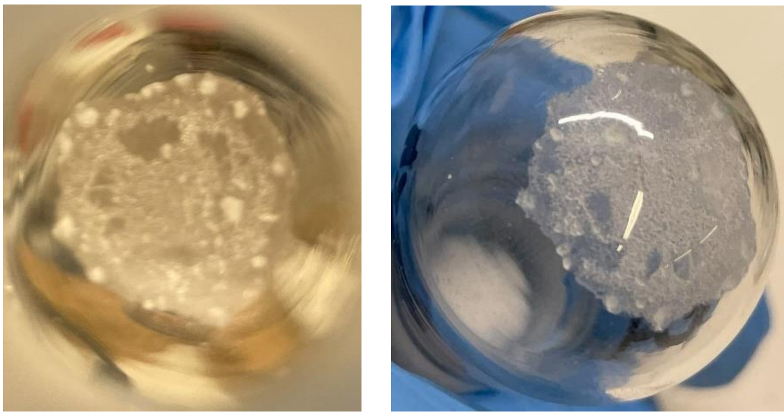


Prepared according to **General procedure N** from redox-active ester **13a** (90 mg, 0.17 mmol). Zinc (powdered 6.0 equiv., 72 mg), anhydrous THF (0.9 ml), *i*-PrOH (0.09 ml), 2M Ni catalyst solution in DMF (0.185 ml), Ph_3SiH (3.0 equiv., 0.16 ml). After the final evaporation out of $CDCl_3$ the hydrocarbon **14a** was obtained as a colourless crystalline solid in a 6 mg yield (22%).

R_f : 1.0 (Pentane; PMA)
^{1}H NMR (400 MHz, $CDCl_3$) δ 2.6 – 2.5 (m, 2H), 2.3 – 2.2 (m, 2H), 2.1 – 2.0 (m, 8H), 1.8 – 1.7 (m, 4H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 52.4 (4CH), 42.9 (2CH), 42.3 (2CH), 41.7 ($4CH_2$).
HRMS (GCQTOF): Calcd for $C_{12}H_{16}$: 160.1252 [M]; Measured 160.1246.

Compound 14b





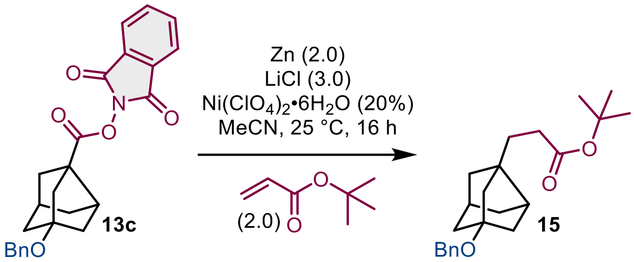
Prepared according to **General procedure M** from redox-active ester **XX** (220 mg, 0.41 mmol). Zinc (powdered 6.0 equiv., 160 mg), anhydrous THF (2.0 ml), *i*-PrOH (0.2 ml), 2M Ni catalyst solution in DMF (0.4 ml), Ph_3SiH (3.0 equiv., 0.36 ml). After the final evaporation out of $CDCl_3$ the hydrocarbon **14b** was obtained as a white amorphous solid in a 13 mg yield (20%).

R_f : 1.0 (Pentane; PMA)

^{1}H NMR (400 MHz, $CDCl_3$) δ 2.5 – 2.4 (m, 2H), 2.4 – 2.3 (m, 2H), 2.1 (bs, 2H), 1.9 – 1.8 (m, 6H), 1.7 – 1.6 (m, 2H), 1.5 – 1.4 (m, 2H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 53.3 (2CH), 51.5 (2CH), 42.9 (2CH_2), 42.8 (2CH), 41.2 (2CH_2), 37.0 (2CH).
HRMS (GCQTOF): Calcd for $C_{12}H_{16}$: 160.1252 [M]; Measured 160.1247.

Nickel Catalysed Giesse Reaction

Compound 15



A vial equipped with a magnetic stir bar was charged with redox active ester **13c** (35 mg, 0.09 mmol), LiCl (3 equiv., 11 mg), powdered Zinc (>2 equiv., 10 mg) and $Ni(ClO_4)_2 6H_2O$ (20 mol%, 7 mg). The vial was sealed with a septum cap, evacuated and backfilled with argon. *Tert*-butyl acrylate (2 equiv., 26 µl) was added *via* a microlitre syringe and MeCN (0.25 ml) was added. The reaction mixture was left stirring at 25 °C overnight. After completion the reaction was quenched by the addition of a mixture of sat. aqueous NH_4Cl and distilled water (1:1 v/v) and extracted with Et_2O. The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 and the solvent evaporated under vacuo. The crude mixture was purified by silica gel column chromatography eluting with pure chloroform to give product **15** as a colourless oil (19.5 mg, 65%).

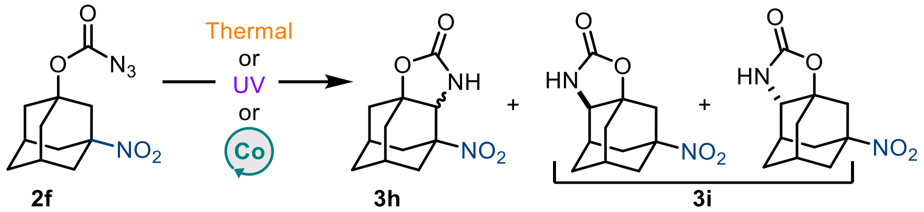
Note: Maintaining the correct dilution is crucial for the reactions success. Excess LiCl or Zn does not harm the reaction in anyway.

The procedure was adapted from: Qin, T.; Malins, L. R.; Edwards, J. T.; Merchant, R. R.; Novak, A. J. E.; Zhong, J. Z.; Mills, R. B.; Yan, M.; Yuan, C.; Eastgate, M. D.; Baran, P. S. *Angew. Chem. Int. Ed.* **2017**, 56, 260 -265.[10]

R_f : 0.6 ($CHCl_3$; UV, PMA)
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.3 – 7.3 (m, 4H), 7.3 – 7.2 (m, 1H), 4.5 (s, 2H), 2.4 – 2.4 (m, 1H), 2.3 – 2.2 (m, 2H), 2.1 – 2.0 (m, 2H), 2.0 – 1.8 (m, 5H), 1.7 – 1.6 (m, 3H), 1.5 – 1.4 (m, 12H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 173.7 (C), 139.7 (C), 128.4 (2CH), 127.6 (2CH), 127.4 (CH), 81.9 (C), 80.2 (C), 65.7 (CH_2), 50.6 (CH_2), 47.3 (CH_2), 47.1 (C), 46.3 (CH_2), 42.7 (CH_2), 41.9 (CH), 39.0 (CH_2), 37.0 (CH), 34.5 (CH_2), 32.4 (CH_2), 28.3 (3CH_3).
IR (neat): $\tilde{\nu}$ /cm^{-1} = 2931, 2862, 1726, 1454, 1365, 1151, 1109, 849, 731, 696.
HRMS (m/z): Calcd for $C_{23}H_{32}NaO_3^+$: 379.2244 $[M+Na]^+$; Measured: 379.2242.

Additional Experiments and Failed Attempts

Irradiation experiment of 2f to form Cyclic Carbamates 3h and 3i



A dry quartz tube was charged with a magnetic stir-bar and compound **2f** (20 mg, 0.08 mmol) and sealed with a septum. The tube was evacuated, backfilled with argon and equipped with an argon balloon. Anhydrous DCM (5 ml) was added and the reaction vessel was illuminated with a 254 nm mercury lamp. Reaction progression was monitored by TLC. Upon completion the solvent was evaporated under reduced pressure and a crude NMR of the mixture was measured to obtain the ratio of products (**3h** 0.05 : 1 **3i**).

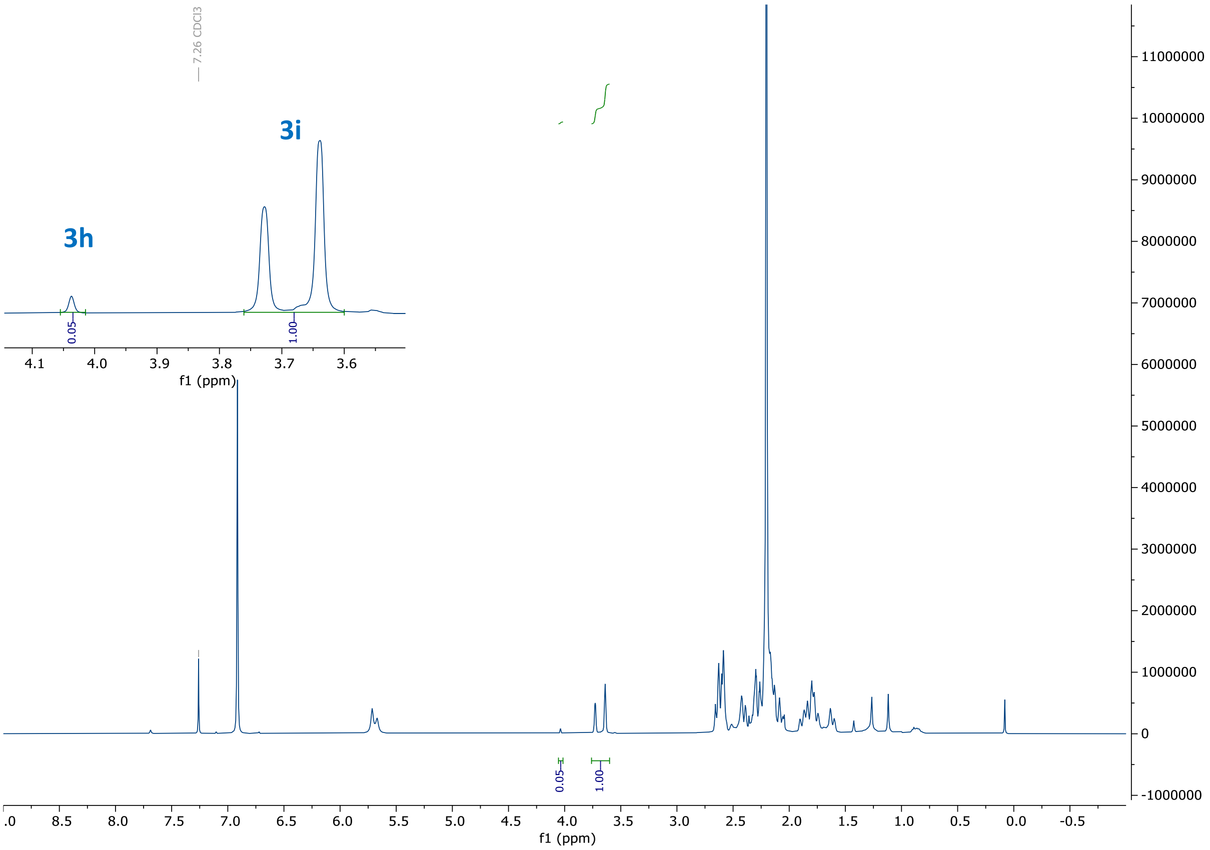
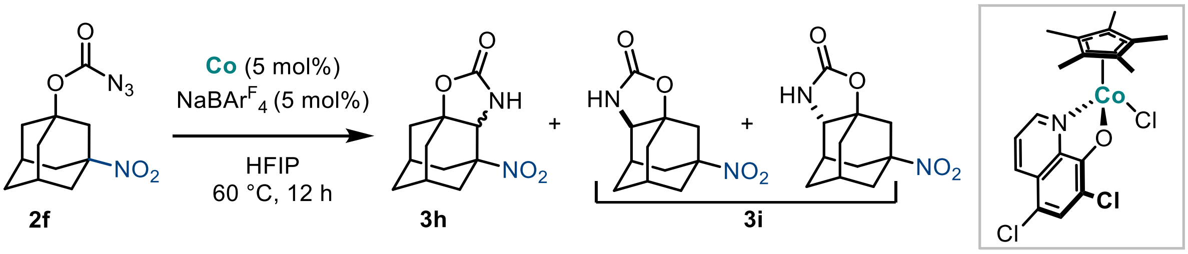


Figure 3: 1H-NMR spectrum of crude mixture after irradiation of 2f with 254 nm lamp with ratio of products.

Sukbok Chang’s Cobalt Catalysed reaction of 2f



The cobalt catalyst (5 mol%, 3 mg) and NaBAr^F (5 mol%, 6 mg) were suspended in HFIP (1 ml) and stirred at room temperature for 1 min. Starting material **2f** (30 mg 0.11 mmol) was added and the reaction vessel was sealed, flushed with nitrogen, connected to a nitrogen balloon and vigorously stirred over night at 60 °C. After completion the reaction mixture was cooled down to room temperature and filtered through a pad of silica gel eluting with EtOAc. The solvent was evaporated under reduced pressure and the sample submitted for NMR. Although the ratio of **3i**-isomers changed, the overall ratio remained the same (**3h** 0.05 : 1 **3i**).

The procedure was adapted from: Lee, J.; Lee, J.; Jung, H.; Kim, D.; Park, J.; Chang, S. *J. Am. Chem. Soc*. **2020**, 142, 28, 12324–12332.[11]

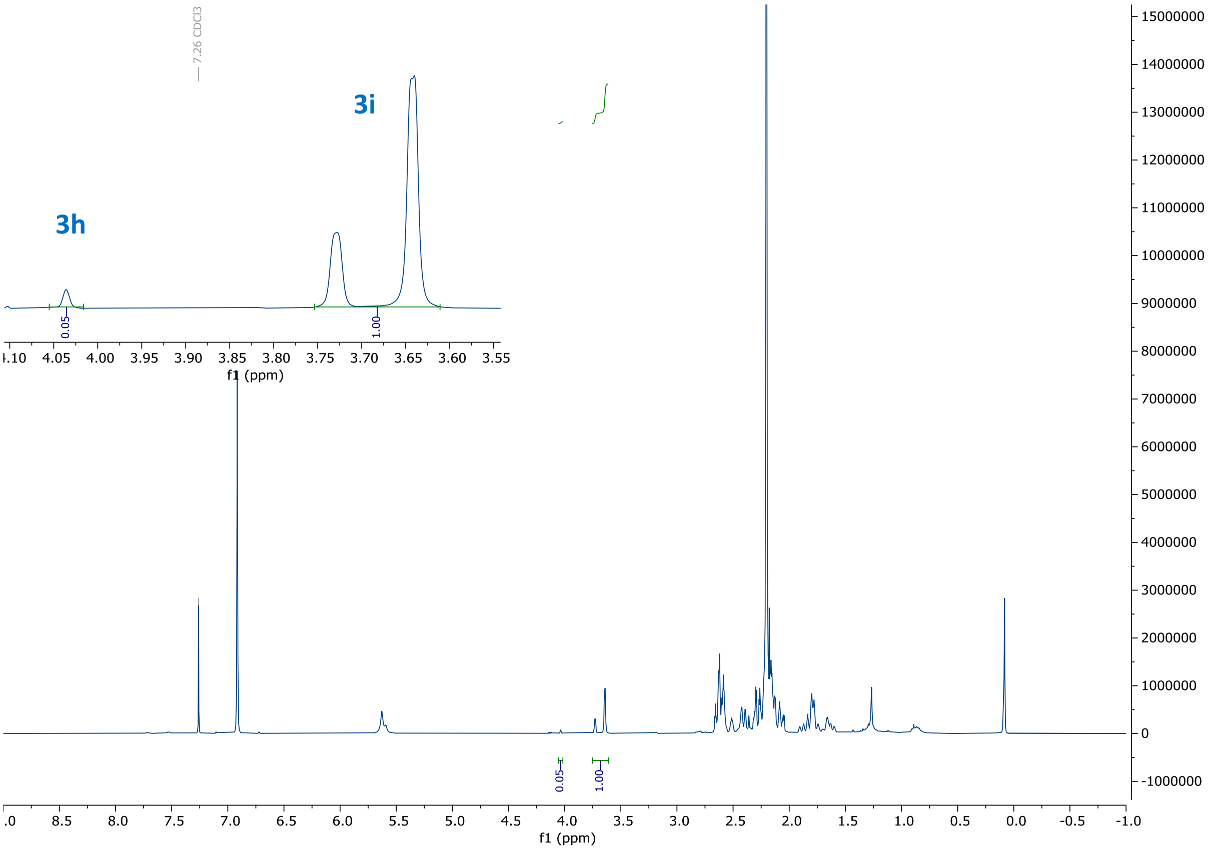
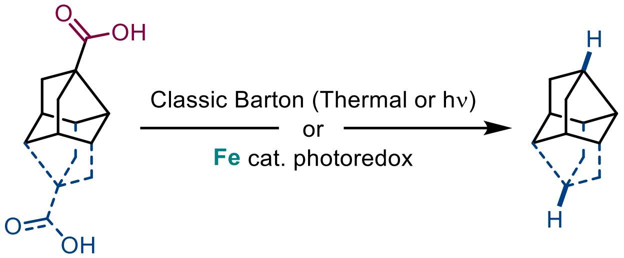


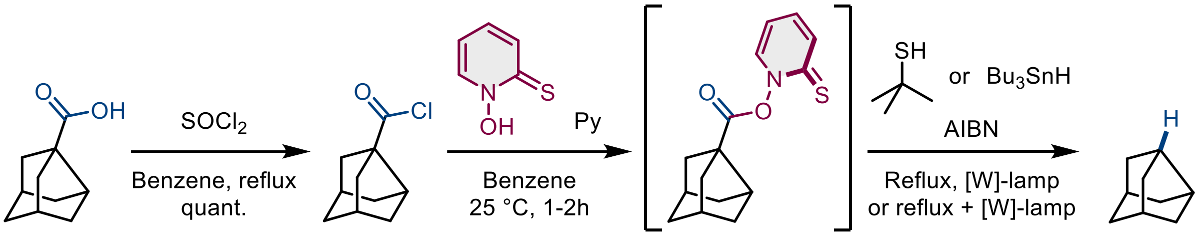
Figure 4:^{1}H-NMR spectrum of crude reaction mixture after cobalt catalysed reaction of **2f** with ratio of products.

Decarboxylation attempts of noradamantane and diamantane carboxylic acids



To avoid losses of precious starting material, investigations were also conducted using noradamantane-3-carboxylic acid as a substrate to scout the reactivity.

Barton Decarboxylation



Refluxing noradamantane carboxylic acid in benzene with a slight excess of thionyl chloride for 2h gave the acyl-chloride quantitatively. The barton ester was prepared easily with excess pyrithione and pyridine mixing in benzene at room temperature. The precipitated pyridinium hydrochloride was filtered off by a syringe filter during the addition of the ester to the reaction mixture.

In general, the reactions gave poor yields (NMR). Using a thiol as the source of hydrogen gave almost no product. Switching to Bu_3SnH gave a maximum NMR yield of 10%. Efforts to speed up the process by illuminating the reaction mixture with a 200W tungsten lamp had no effect, even when combined with refluxing conditions. Nonetheless, the product would be virtually inseparable and purification would be tedious.

The procedure was adapted from: Motherwell, W. B.; Crich, D.; Barton, D. H. R. *Tetrahedron* ***1985**, 41, 3901-3924.*[12]

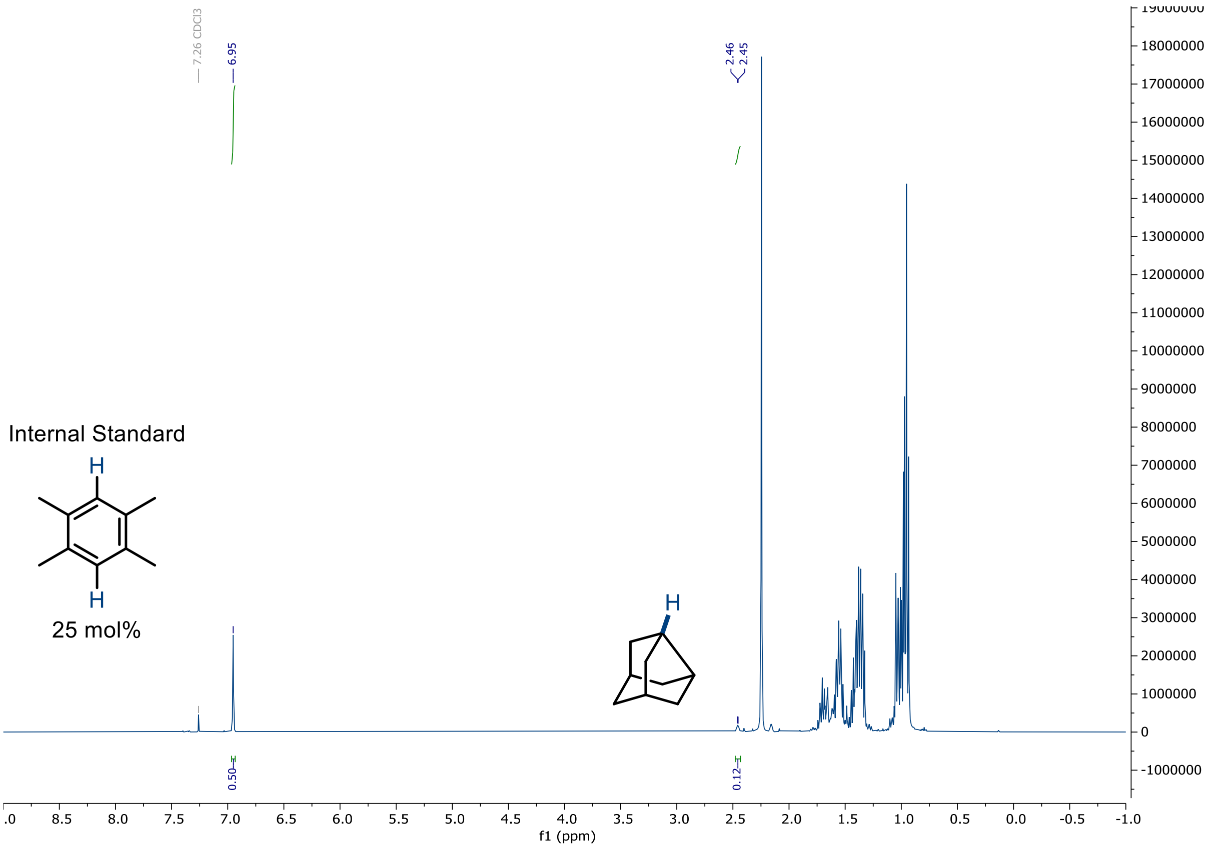
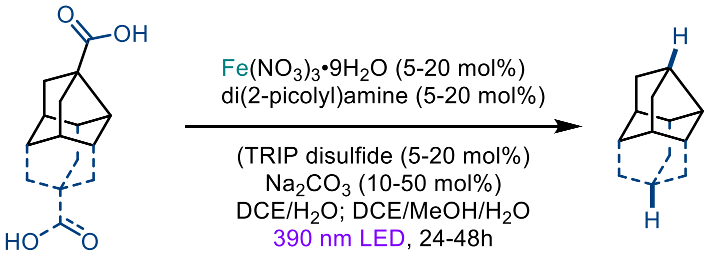
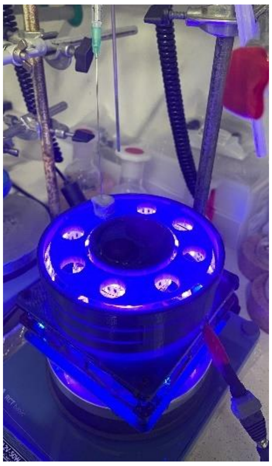


Figure 5: Representative ^{1}H-NMR spectrum of crude reaction mixture of Barton decarboxylation of noradamantane carboxylic acid.

Iron catalysed photochemical decarboxylation



The reactions were setup according to the authors general procedure with a home-made 3D printed photoreactor (390nm LEDs). Initial attempts with adamantane carboxylic acid proceeded without any issues fully converting the starting material to pure adamantane with original conditions within 12h. However, noradamantane gave only yields < 20% (NMR) after prolonged exposure (48h) with higher reagent and catalyst loading. Switching to dicarboxylic acid **8h** proved difficult, mainly due to its reduced solubility in the reaction solvent. To combat this issue adamantane carboxylic acid was successfully decarboxylated in a solvent mixture of DCE/MeOH/H_2O (0.5:0.5:1) and starting material **8h** proved to be also soluble. However even at longer light exposure, higher catalyst loadings and varying the base (Cs_2CO_3) the reaction gave only small amounts (7%) of the desired product.



The procedure was adapted from: Lu, Y.; West, J. G. *Angew. Chem. Int. Ed.* **2023**, 62, e202213055.[13]

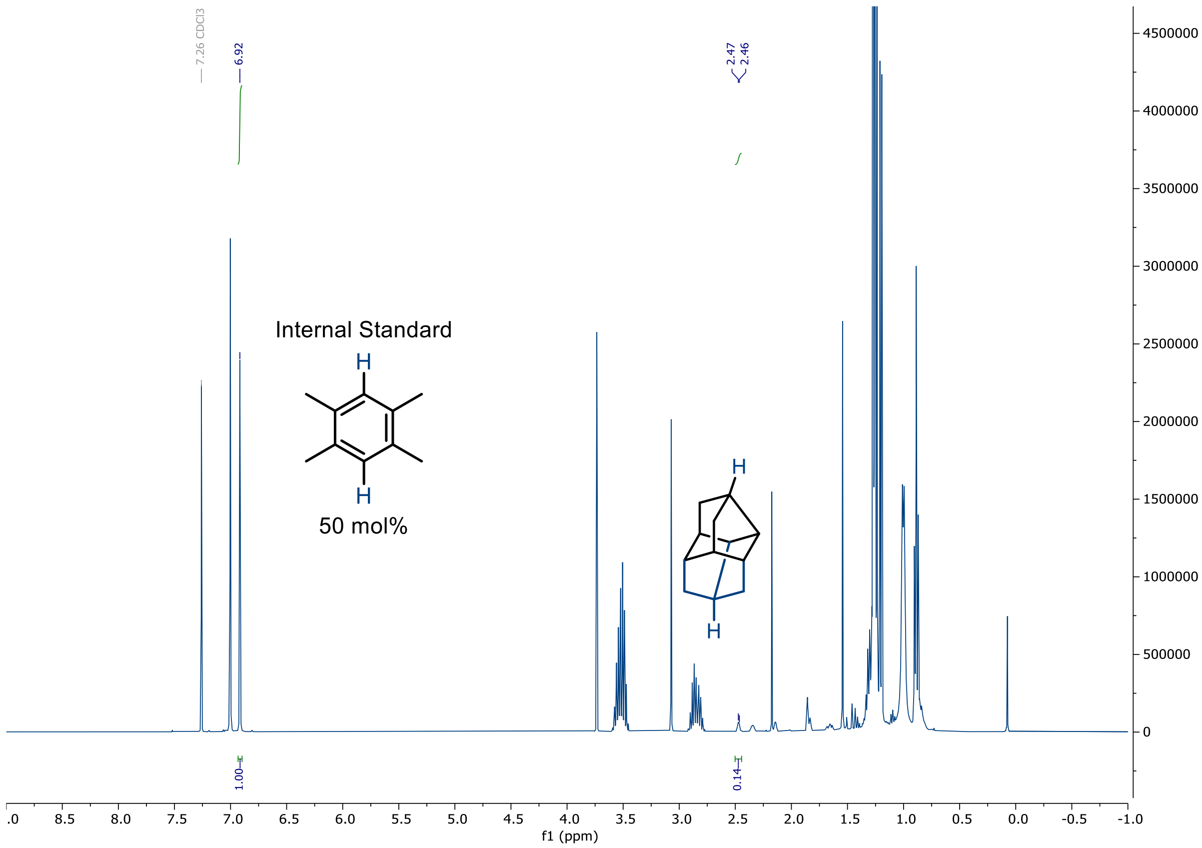
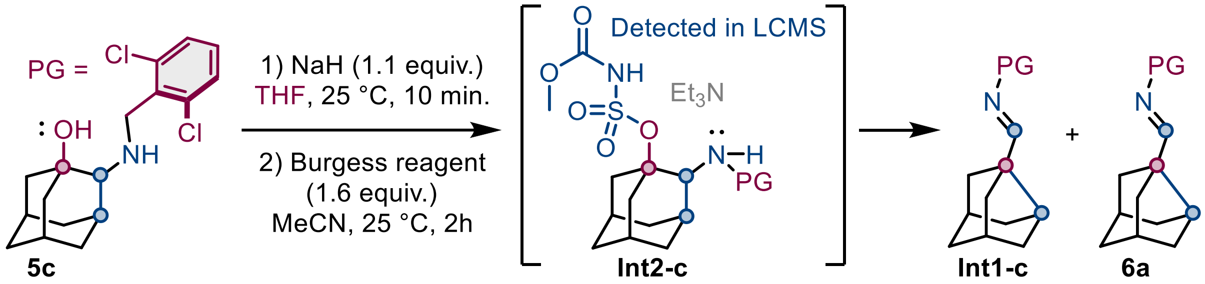


Figure 6: ^{1}H-NMR spectrum of crude reaction mixture after iron catalysed photochemical decarboxylation of **8h**.

Mechanistic investigation control experiment



A vial containing a magnetic stir bar was charged with starting material **5c** (20 mg) and dissolved in anhydrous THF (0.5 ml). To the stirring solution sodium hydride as a 60% dispersion in paraffin oil (1.1 equiv., 3 mg) was added and was left stirring for an additional 10 minutes. After 10 minutes solid Burgess reagent (1.6 equiv., 23 mg) was added and the reaction mixture was left to stir for 1h at 25 °C. After 1h the reaction mixture was quenched with sat. aq. NH_4Cl and extracted with chloroform. The combined organic layers were dried over anhydrous $MgSO_4$ and the solvent was evaporated under reduced pressure at ambient temperature. An internal standard was added to the crude mixture and an NMR sample prepared. NMR analysis showed a 67% combined yield of aldehyde **6a** and imine **Int1-c** and a small amount of remaining starting material (91% conversion).

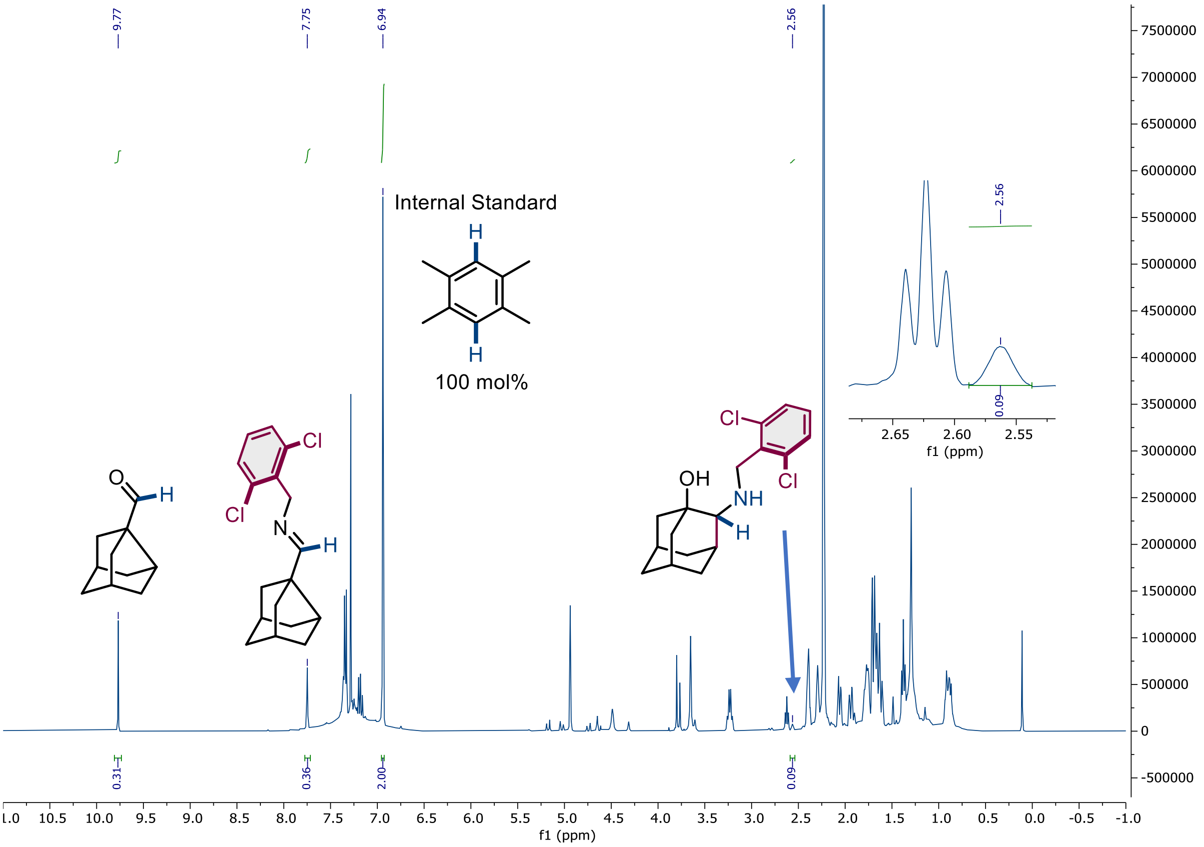


Figure 7: 1H-NMR spectrum of crude reaction mixture after reacting **5c** with sodium hydride followed by addition of Burgess reagent.

The short lived intermediate **Int2-c** could be detected in small amounts when monitoring the reaction with LCMS.

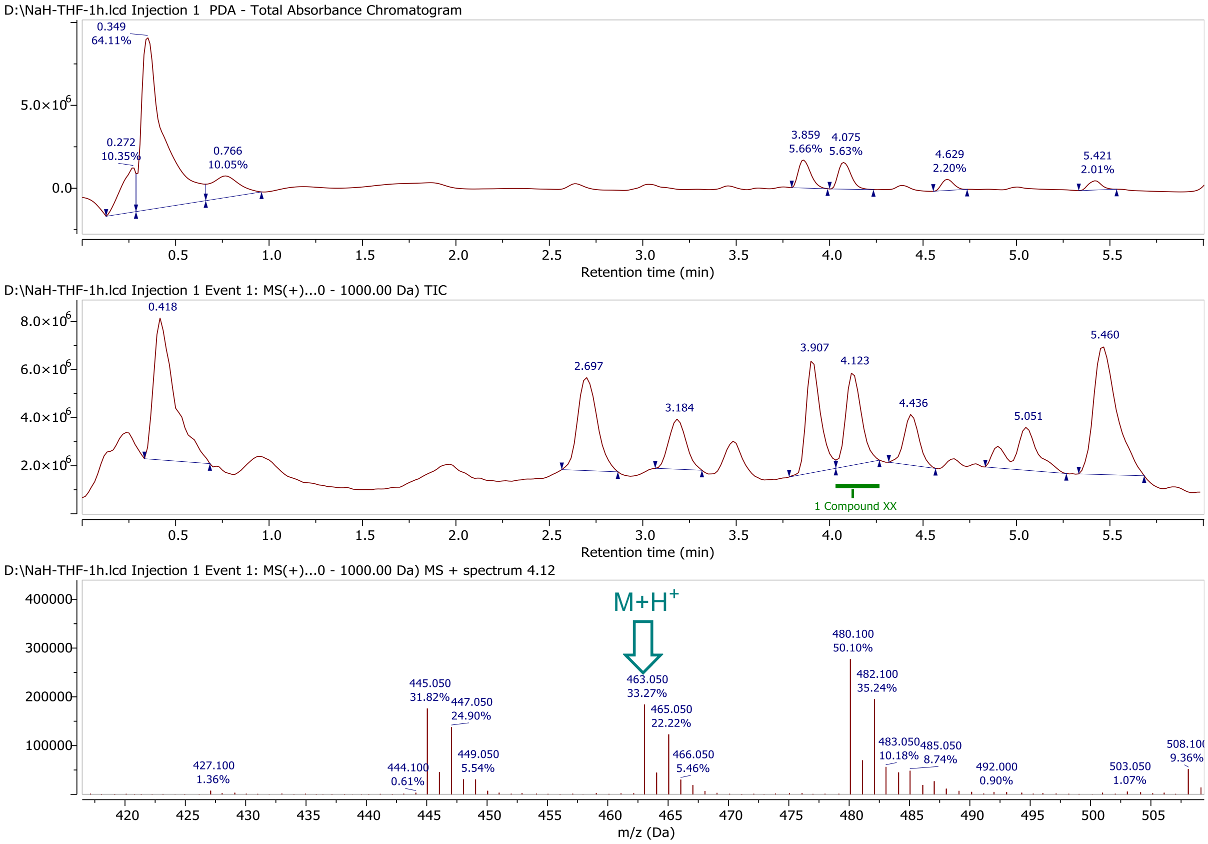
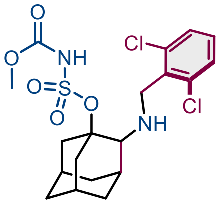


Figure 8: LCMS spectra of reaction mixture of **5c**, sodium hydride and Burgess reagent. UV-VIS (top), TIC (Middle), Mass abundance and detected compound **Int2-c** in highlighted peak (R.T.= 4.12 minutes).

Molecule	Molecule Info		RT	From RT	To RT
	Formula: Label: Monoisotopic Mass:	$C_{19}H_{24}Cl_2N_2O_5S$ Sulfamidate Intermediate **Int2-c** 462.0783	4.12	4.03	4.27

X-Ray Data

X-ray experimental data for structure determination for **14a**, **7c** and **7d** crystals were collected on Bruker D8 VENTURE Kappa Duo PHOTONIII by IµS micro-focus sealed tube at temperature of the samples 120K. The structures were solved by direct methods (XT[14]) and refined by full matrix least squares based on F^2 (SHELXL2014[15]). The hydrogen atoms on carbon were fixed into idealized positions (riding model) and assigned temperature factors H_{iso}(H) = 1.2 U_{eq}(pivot atom). The hydrogen atoms on oxygen were found on difference Fourier map and refined under rigid-body restriction. The absolute structure of **7d** was not determined due to low contribution of anomalous scattering[16] to diffraction pattern.

The details for solution of particular structures: Measured crystal **7c** was refined as non-merohedric twin with ration of two mosaic blocks 0.506:0.494. The real structure of the crystal is farther complicated by disorder of hydrogen atoms in all four -O-H moieties. (two -O-H groups in two symmetrically independent molecule)

X-ray crystallographic data have been deposited with the Cambridge Crystallographic Data Centre (CCDC) under deposition number 2441791-2441793 for **14a**, **7d** and **7c** respectively and can be obtained free of charge from the Centre via its website (www.ccdc.cam.ac.uk/getstructures).

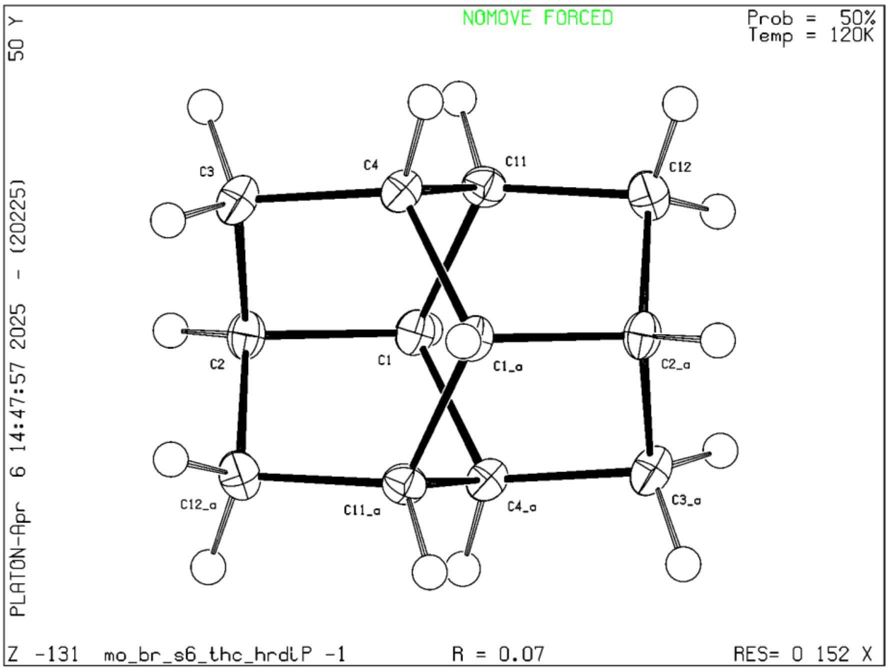


Figure 9: View on molecule of **14a**, the displacement ellipsoids are drawn at 50% probability level. (CCDC: 2441791)

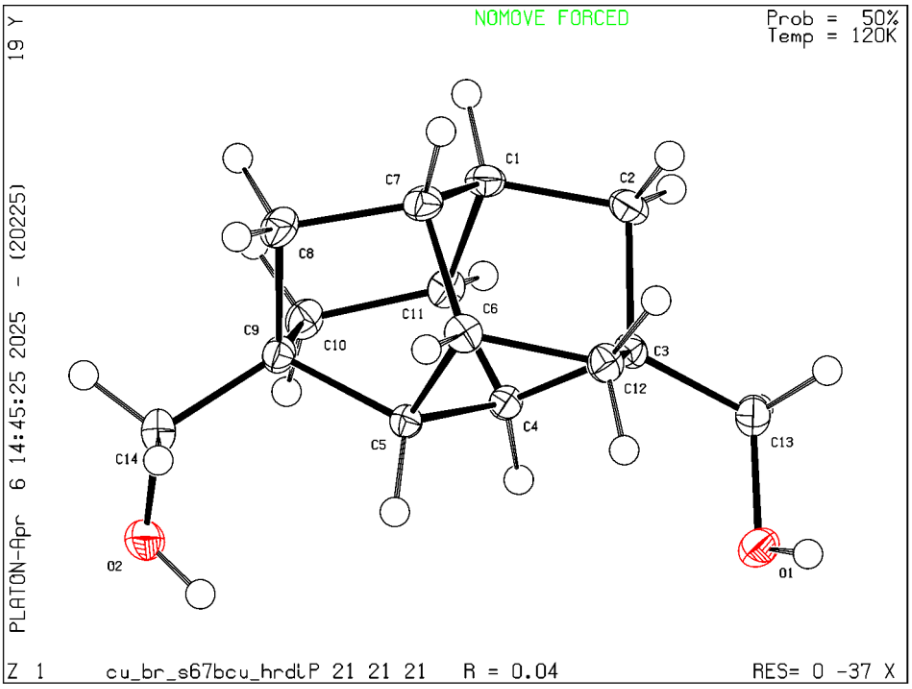


Figure 10: View on molecule of **7d**, the displacement ellipsoids are drawn at 50% probability level. (CCDC: 2441792)

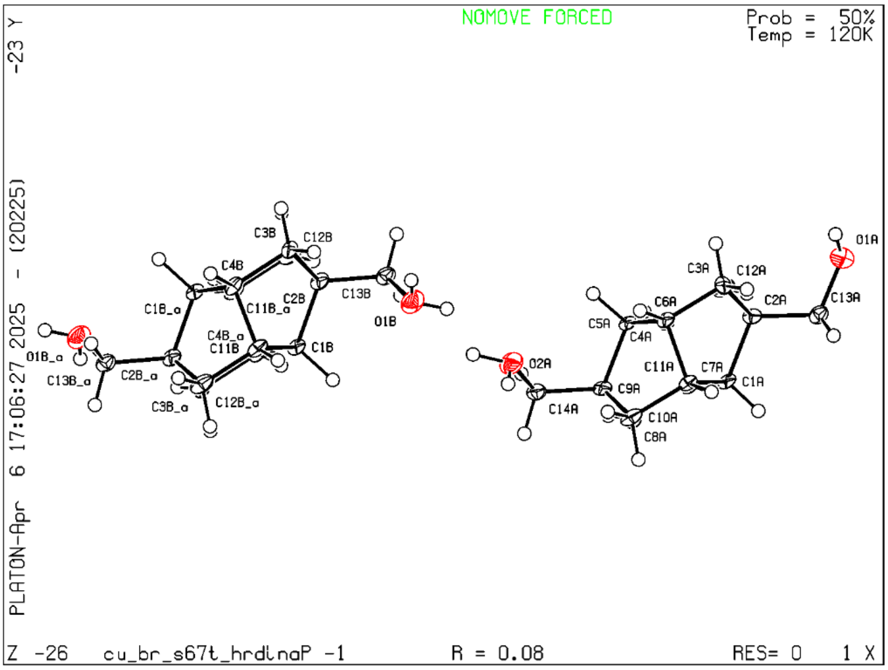


Figure 11: View on one of symmetrically independent molecule of **7c**, (the molecules A and B could be overlapped well except orientation of one -O-H moiety). The displacement ellipsoids are drawn at 30% probability level. The disordered hydrogen atoms are omitted for clarity. (CCDC: 2441793)

Table 1. X-Ray crystallographic data.

Compound	**14a**	**7c**	**7d**
Formula	$C_{12}H_{16}$	$C_{14}H_{20}O_2$	$C_{14}H_{20}O_2$
M.w.	160.25	220.30	220.30
Crystal systém Space group [No.]	Triclinic *P*-1 [No. 2]	Triclinic *P*-1[No. 2]	Orthorhombic $P\ 2_12_12_1$ [No. 19]
a [Å]	6.3269 (7)	9.1061 (7)	8.5091 (6)
b [Å]	6.5017 (6)	10.1614 (8)	10.7402 (8)
c [Å]	6.5027 (6)	11.2863 (8)	12.4070 (9)
α [°]	60.958 (4)	116.664 (3)	90.0
β [°]	83.969 (4)	109.119 (4)	90.0
γ [°]	62.350 (4)	90.243 (4)	90.0
Z	1	3	4
V [Å^3]	204.64 (4)	867.53 (12)	1133.87 (14)
D_x [g cm^{-3}]	1.300	1.265	1.291
Crystal size [mm]	0.64 × 0.18 × 0.14	0.57 × 0.16 × 0.05	0.31 × 0.27 × 0.22
Crystal color, shape	colourless, bar	colourless, plate	colourless, prism
μ [mm^{-1}]	0.07	0.65	0.66
Wavelengh [Å]	0.71073	1.54178	1.54178
T_{min}, T_{max}	0.955, 0.99	0.80, 0.97	0.76, 0.87
Measured reflections	4343	21003	14912
Independent diffract. (R_{int} [a])	940,(0.029)	3086, (0.067)	2443, (0.040)
Observed diffract. [$I > 2\sigma(I)$]	897	2066	2420
No. of parameters	55	218	145
R [b]	0.071	0.082	0.036
$wR(F^2)$ for all data	0.215	0.270	0.097
GOF [c]	1.08	1.09	1.08
Residual electron density [e/Å^3]	0.53, -0.36	0.57, -0.68	0.28, -0.21
Absolute structure parameter			-0.14(10)

[a] $R_{int} = S½F_o^2 - F_{o,mean}^2½/SF_o^2$, [b] $R(F) = S½½F_o½ - ½F_c½½/S½F_o½$, $wR(F^2) = [S(w(F_o^2 - F_c^2)^2)/(Sw(F_o^2)^2)]^{½}$.

[c] $GOF = [S(w(F_o^2 - F_c^2)^2)/(N_{diffrs} - N_{params})]^{½}$.

NMR Kinetic Studies

An NMR tube was charged with solutions of the starting material **5c** or **5i** (0.03 mmol) and burgess reagent (1.6 equiv.) that were pre-dissolved in CD_3CN in separate vials (both 0.25 ml). Burgess reagent decomposition was measured with a 20 mg (0.08 mmol) sample dissolved in CD_3CN (0.5 ml). The samples were transferred to a pre-heated NMR probe to the desired temperature. After quick shimming, ^1H proton spectra were acquired in 30s measurements in specific intervals, that are mentioned with the corresponding experiments. The data was then processed with MestReNova (version 14.1.1-24571) *via* the data analysis tab. In some cases, overlap of compound signals with unwanted compounds or noise introduced slight deviations in the smoothness and quality of the plots. Full conversion of the starting materials **5c** and **5i** does not occur, due to the reactions being monitored at lower concentrations compared to experimental conditions and temperatures.

Burgess Reagent decomposition at 70 °C

Burgess reagent decomposition was measured at **70 °C** every **60s** for **30s** (30s measurement time, 30s downtime).

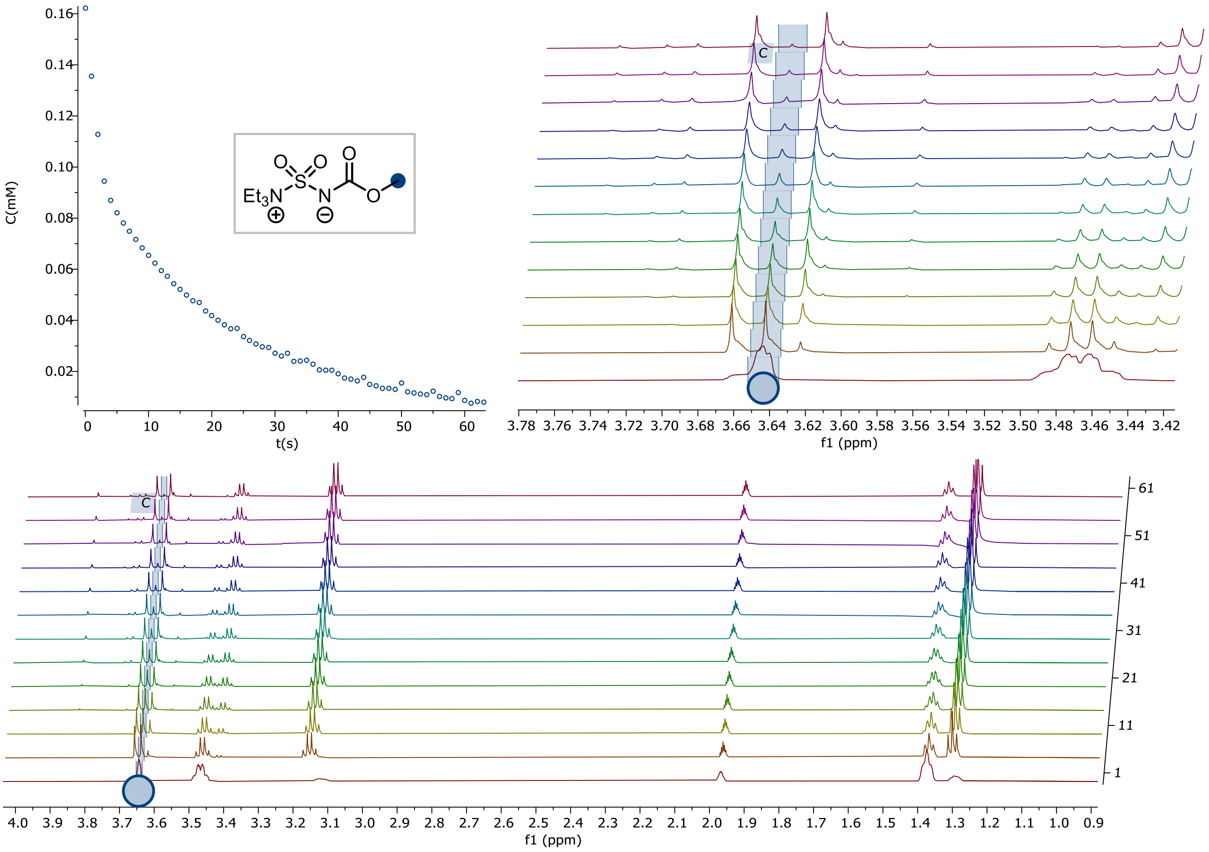
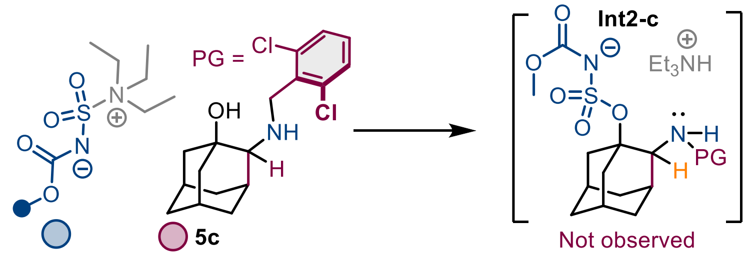
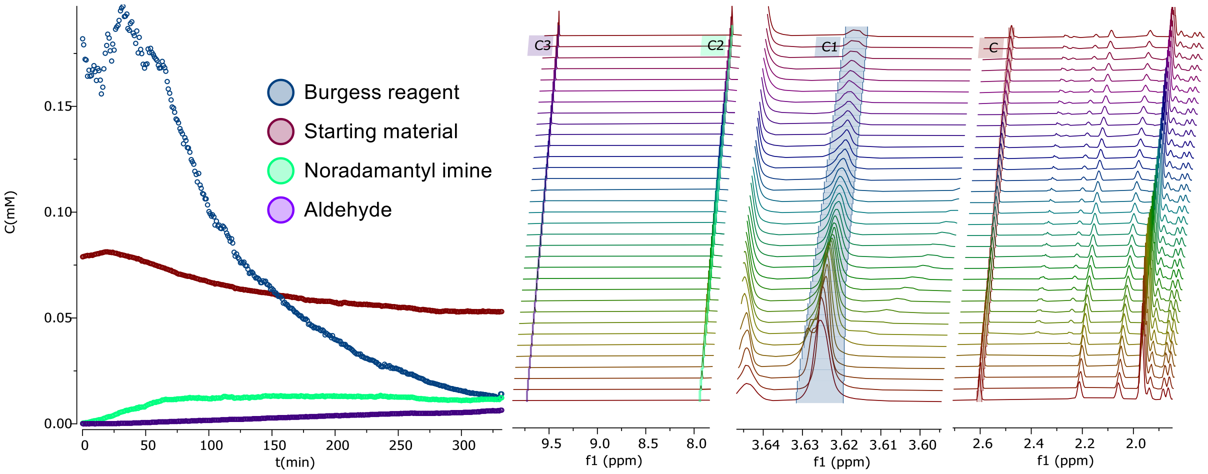


Figure 12: ^1H-NMR spectra of Burgess reagent decomposition measured at 70 °C. Integrated peak (Blue), Plotted relative concentration / time (top-left), Zoomed in peak (top-right), Full spectra (Bottom).



Reaction of 5c at 40 °C

Reaction of **5c** with Burgess reagent (1.6 equiv.) measured at **40 °C** every **60s** for **5h** (30s measurement, 30s downtime).



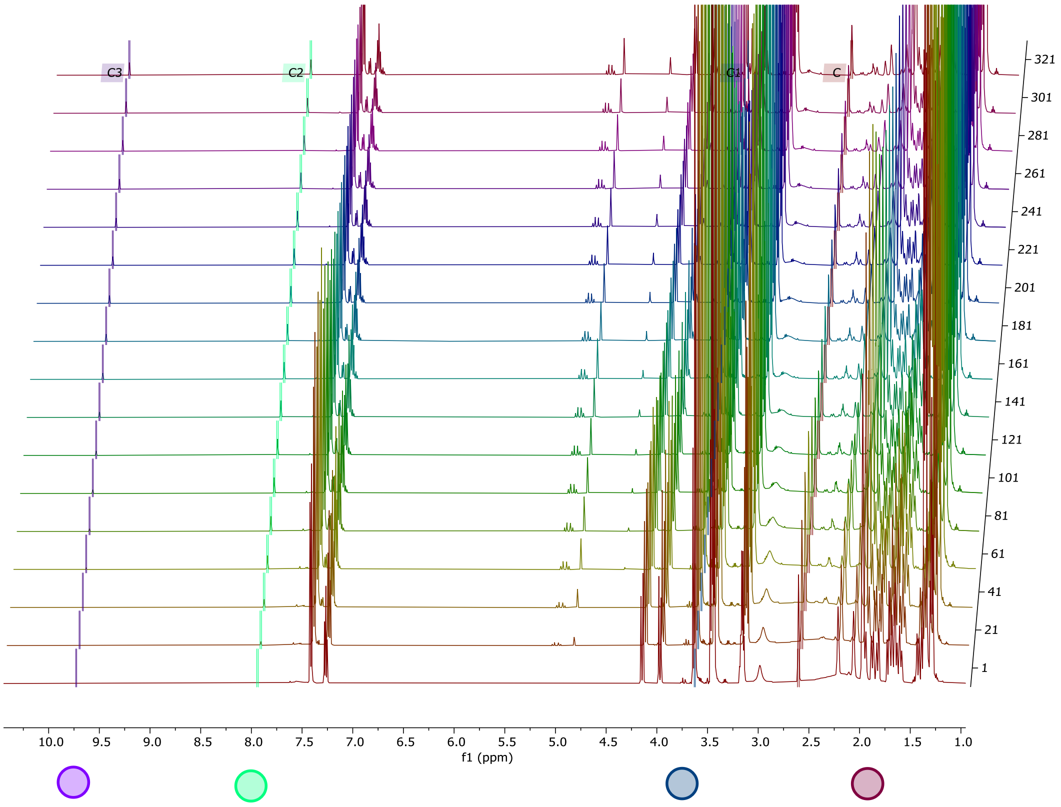


Figure 13: ^{1}H-NMR spectra of reaction of **5c** with Burgess reagent at 40 °C. Plotted relative concentrations / time of Burgess reagent (blue), starting material **5c** (maroon), aldimine **Int1-c** (light green) and carbaldehyde **6a** (violet).

Reaction of 5c at 50 °C

Reaction of **5c** with Burgess reagent (1.6 equiv.) measured at **50 °C** every **60s** for **3h** (30s measurement, 30s downtime).

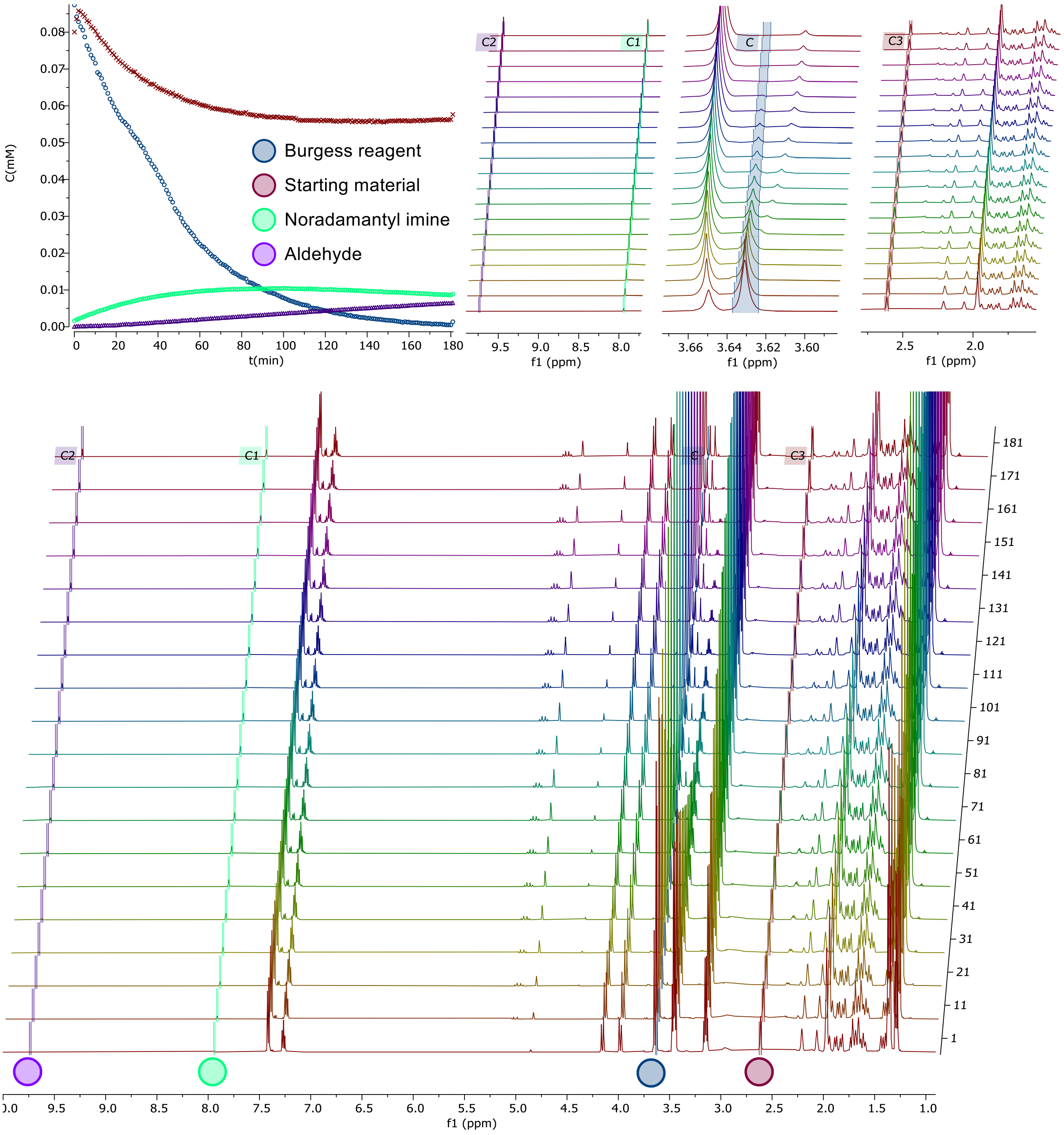


Figure 14: ^{1}H-NMR spectra of reaction of **5c** with Burgess reagent at 50 °C. Plotted relative concentrations / time of Burgess reagent (blue), starting material **5c** (maroon), aldimine **Int1-c** (light green) and carbaldehyde **6a** (violet).

Reaction of 5c at 60 °C

Reaction of **5c** with Burgess reagent (1.6 equiv.) measured at **60 °C** every **60s** for **2h** (30s measurement, 30s downtime).

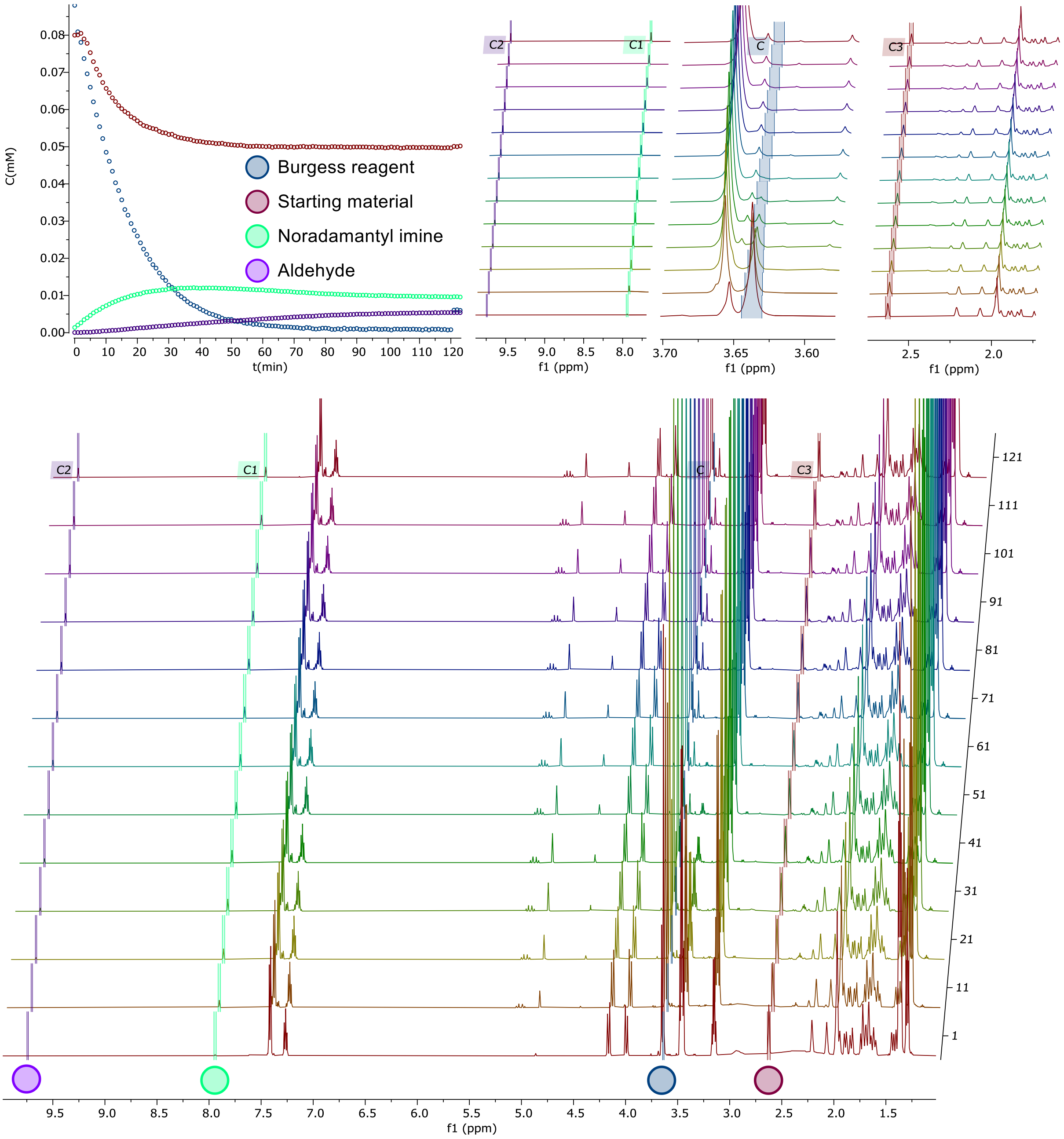


Figure 15: ^{1}H-NMR spectra of reaction of **5c** with Burgess reagent at 60 °C. Plotted relative concentrations / time of Burgess reagent (blue), starting material **5c** (maroon), aldimine **Int1-c** (light green) and carbaldehyde **6a** (violet).

Reaction of 5c at 70 °C

Reaction of **5c** with Burgess reagent (1.6 equiv.) measured at **70 °C** every **60s** for **1h** (30s measurement, 30s downtime).

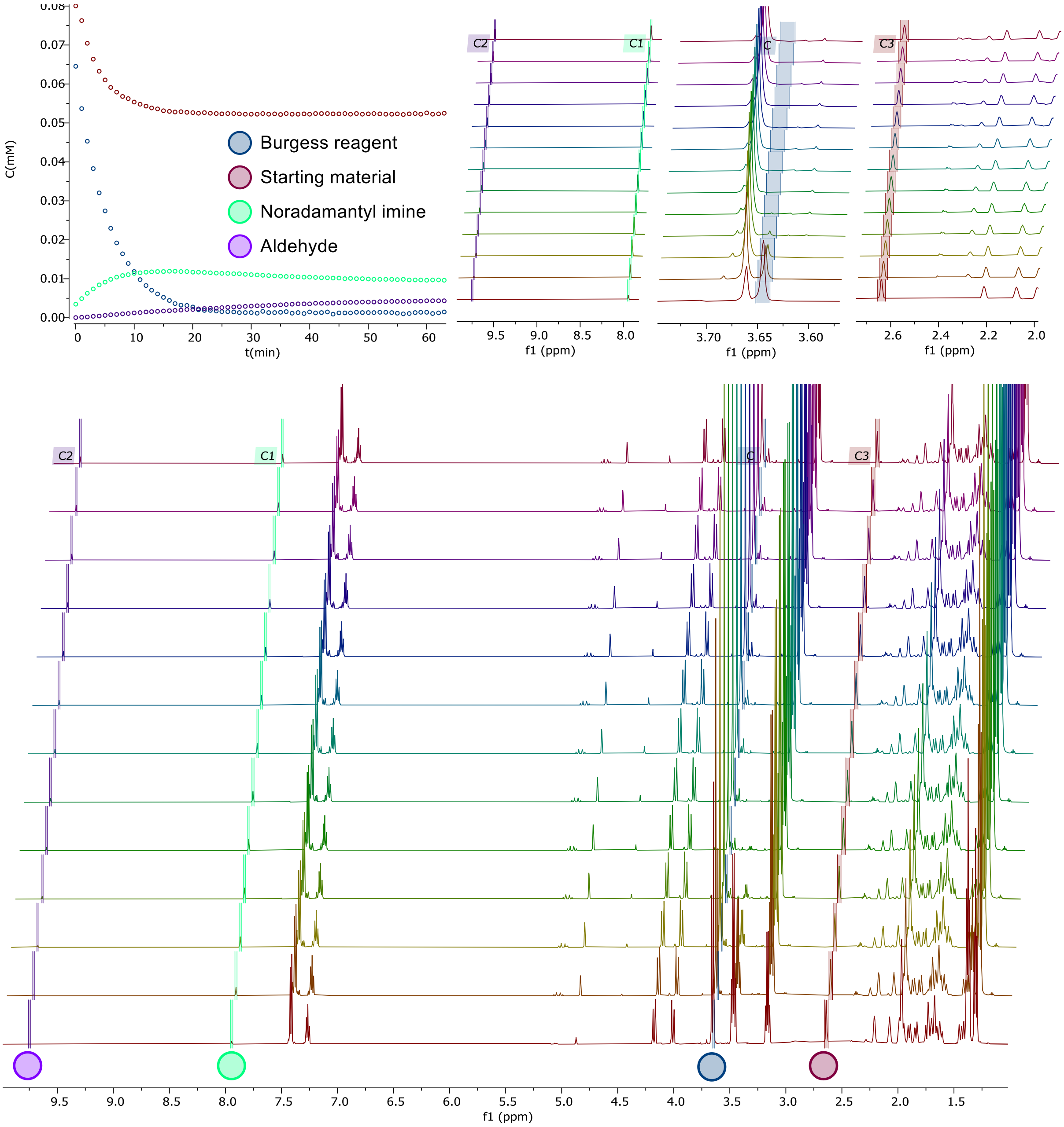


Figure 16: ^{1}H-NMR spectra of reaction of **5c** with Burgess reagent at 70 °C. Plotted relative concentrations / time of Burgess reagent (blue), starting material **5c** (maroon), aldimine **Int1-c** (light green) and carbaldehyde **6a** (violet).

Summary and comparison

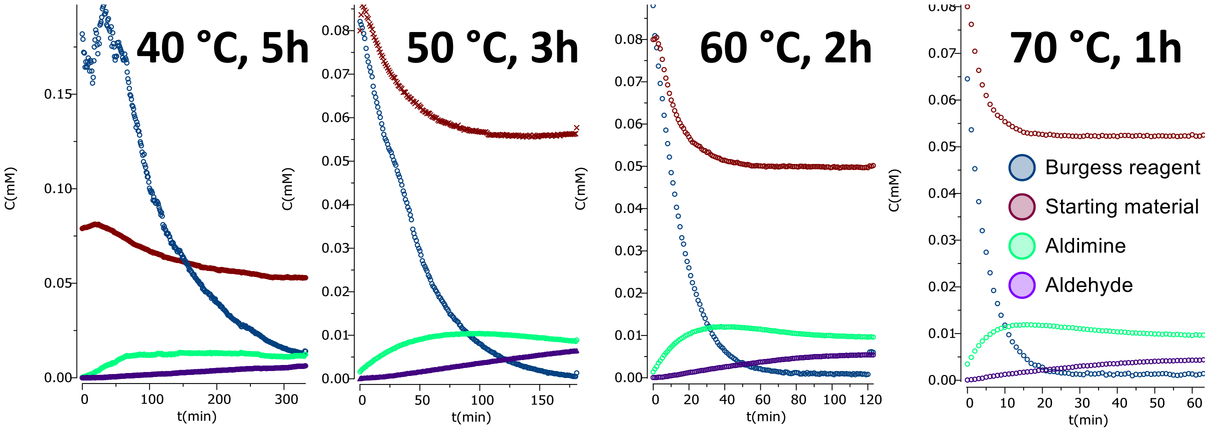
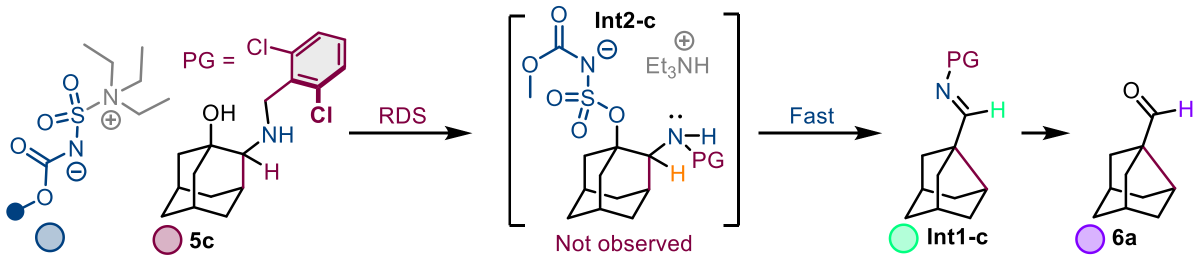


Figure 17: Comparison of plots from above-mentioned kinetic NMR experiments.

It is apparent from the slope and shape of the individual plots, that with increasing temperature (from left to right) the rate of burgess reagent decomposition increases (blue) together with the rate of starting material **5c** consumption (maroon) with the formation of the aldimine product **Int1-c** (light-green). Most likely due to trace amounts of water the aldimine **Int1-c** is then partially hydrolysed to the final aldehyde product **6a** (violet) over time. The reaction halts to a stop upon complete consumption/decomposition of Burgess reagent in the reaction mixture. This would explain the necessity for more than equivalent amounts of the reagent to achieve full conversion as its decomposition competes with the addition to the starting material **5c**. The formation of the intermediate **Int2-c** could not be observed with instantaneous formation of aldimine **Int1-c**. This suggests that the initial nucleophilic substitution of **5c** with the reagent is the rate limiting step (RDS) following 1^{st} order kinetics with the rearrangement to noradamantane being faster (having a lower barrier). Experiments at lower temperatures (40 °C) show that the formation of aldimine **Int1-c** still occurs at the rate of the starting material consumption.

The control experiment (SI page 46, Figure 7) designed based on these findings comports with the NMR kinetic experiments. When the barrier of the initial substitution is lowered by alkoxide formation (with NaH), the rearrangement occurs already at 25 °C with 67% yield and 91% conversion (NMR).



Reaction of 5i at 70 °C

Reaction of **5i** with Burgess reagent (1.6 equiv.) measured at **70 °C** every **5 minutes** for **15h** (30s measurement, 4.5 minutes downtime).

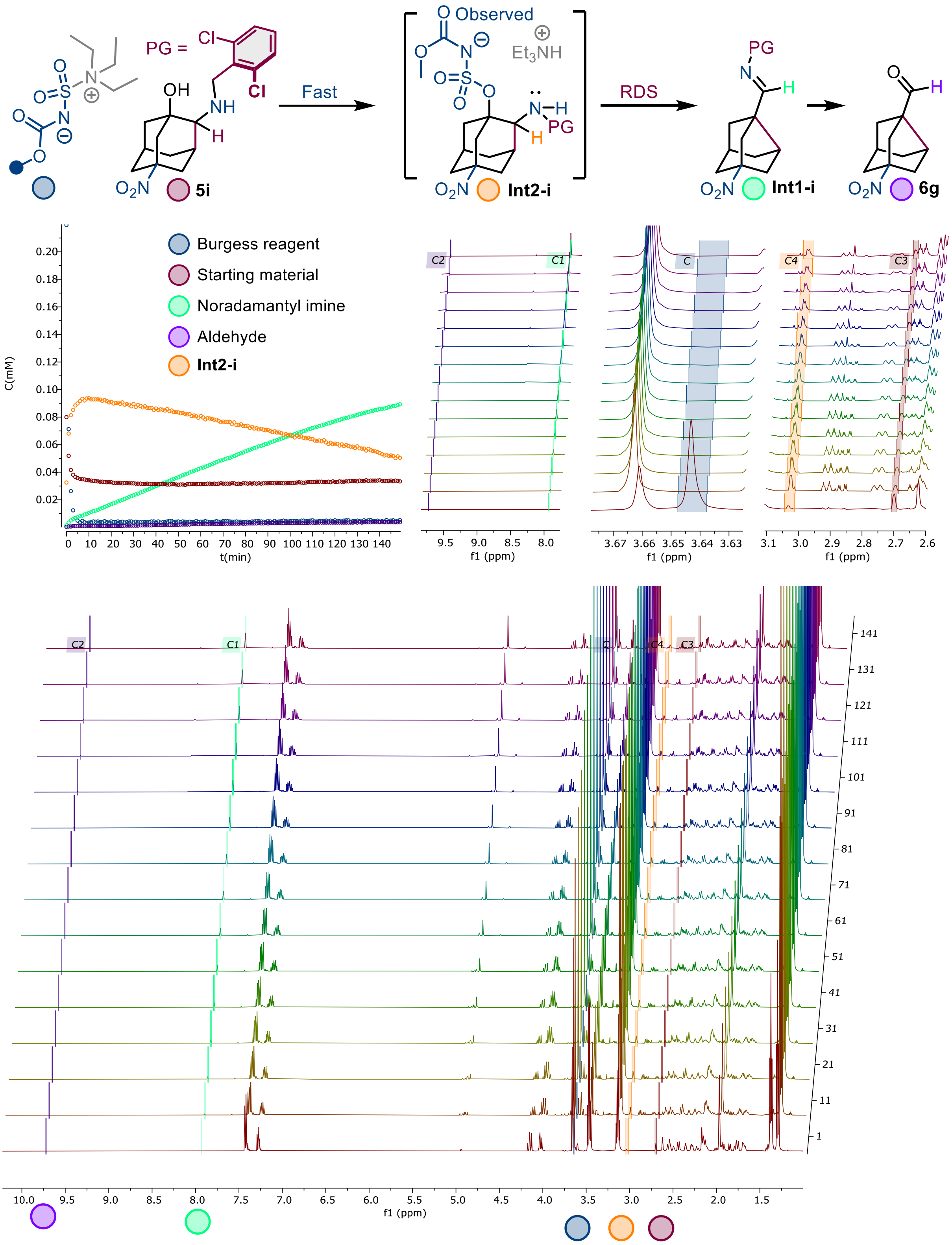


Figure 15: ^{1}H-NMR spectra of reaction of **5i** with Burgess reagent at 70 °C. Plotted relative concentrations / time of Burgess reagent (blue), starting material **5i** (maroon), aldimine **Int1-i** (light green), carbaldehyde **6a** (violet) and sulphonamidate intermediate Int2-i (Orange).

The nitro-derivative **5i** has the rate of the reaction steps reversed. In the first hour the consumption of starting material **5i** proceeds to the point of complete decomposition of burgess reagent and simultaneously the formation of intermediate **Int2-i** (orange) follows, following 1st order kinetics. Due to the deactivation of the adamantane scaffold by the nitro-group, the leaving ability of the leaving group and the formation of the carbocation/rearrangement is diminished, making it the RDS of the reaction. Slow consumption of the intermediate **Int2-i** occurs at the same rate of formation of the corresponding aldimine **Int1-i** following 0 order kinetics.

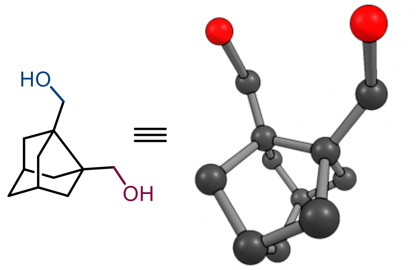
Computational data

Computational Details – Structural Comparison

All structures were computed using the Orca 6.0.0[17] software package. An initial conformer search for the structures global minima was performed by GOAT at the GFN2-xTB level[18]. Geometry optimisations and analytical frequency calculations of the structures were performed at the PBE0-D3BJ/def2-TZVPP level of theory. Visualisation, structural analysis and overlays of the computed structures was performed using Chemcraft.[19]

Computed energies (Hartree) and cartesian coordinates

Structure 9a



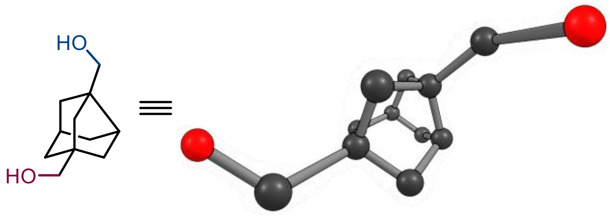
SCF energy: -580.00822909770886 Eh

Free energy (298.15 K, 1 atm): -579.79685253 Eh

O	0.51458482792101	1.78330175408270	-0.69584235485257
C	1.60207637255649	1.76539155846602	0.21861160203923
C	2.90358214088005	2.33640695364394	-0.30535721756821
C	3.39990973566197	1.68944845158017	-1.60674428241229
C	4.39199644964815	2.73621433432699	-2.10316765093144
H	4.77632338241737	2.52082177678073	-3.10255000787854
C	5.54769000145718	2.87974337111108	-1.10097903364358
C	5.03209865666559	3.18060510668119	0.31478341555915
H	5.86518671082703	3.27968689749989	1.01424712937173
C	4.02236245381311	2.11949458214201	0.72801304547190
C	4.11406901555765	4.39562065159115	0.28938121115951
C	2.97049081914581	3.90672694264766	-0.61208289778189
C	1.71110780740319	4.72682079643491	-0.39267610220446
O	0.67455431298780	4.49079063620214	-1.30808582575458
C	3.50027184834348	3.97004840387688	-2.04988390825070
H	0.74785061633618	1.24311722414850	-1.45279987488688

H	1.77930428858897	0.73735228669336	0.55935770942796
H	1.26448635008708	2.33520630061658	1.08651593174048
H	2.59904555254774	1.58330044509934	-2.34687616730615
H	3.83533162643875	0.70191508662226	-1.43479623948585
H	6.21426544260672	3.68404209306922	-1.42674652303573
H	6.14154966210820	1.96040077868046	-1.08611852076017
H	3.66571103395403	2.31612110978986	1.74450013954104
H	4.40900849059708	1.09803945989425	0.70204234720803
H	4.58000245232636	5.30022469330619	-0.10696150877411
H	3.75767791465420	4.61822558192138	1.30088863965804
H	1.97583001484070	5.78395968590669	-0.49314970173325
H	1.36666397784348	4.59292899127239	0.64445336167357
H	0.40186051387367	3.56877170627391	-1.19957356278587
H	4.02736292668340	4.90658417288458	-2.24591425866716
H	2.68074460997488	3.88942817769220	-2.76731890338060

Structure 9b



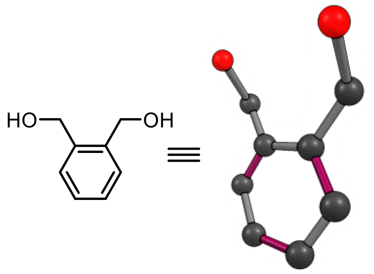
SCF energy: -580.00516119226859 Eh

Free energy (298.15 K, 1 atm): -579.74660839 Eh

O	2.98156622780539	-1.61894056596109	-0.15518799977977
C	2.60428572656799	-0.29254648199663	0.15052050656901
C	2.65273900424744	0.03403855362682	1.62701250020501
C	2.27391620823261	1.49047217974813	1.93217320350636
C	1.81306931044011	1.37688303219164	3.38138701603291
H	1.37990643424012	2.30029180232758	3.77210047964316
C	2.98101207137915	0.91468044519692	4.26569652620478
C	3.63411460413546	-0.38259151301739	3.75024480235736
C	4.01956535722455	-0.20467008553807	2.28063192231002

C	4.77566602951176	-0.83248201659431	4.63802079149294
O	5.83056465953108	0.10246951242024	4.73577273581333
C	2.55648124860374	-1.45501637290782	3.57986579304962
C	1.65875247286713	-0.80708970139424	2.52386941175632
H	1.06271782875426	-1.53073472543468	1.96196551409767
C	0.79979280044667	0.24625787158664	3.23075878345582
H	2.34921070221331	-2.21177985300852	0.25382732594092
H	1.59936026330079	-0.07256667052470	-0.23651434535372
H	3.30492508915766	0.34717540516066	-0.39280408518251
H	1.44834690130557	1.83278668130482	1.29988566222607
H	3.11522399182247	2.17042355585718	1.78434915250177
H	2.62323227090062	0.74940317630376	5.28751637801476
H	3.74323756792922	1.69579610647951	4.32045168131914
H	4.48300012179924	-1.11906629099999	1.89836320466669
H	4.69906591879207	0.63127716037730	2.09486608460201
H	4.41688320330547	-0.98125627245617	5.65986665322293
H	5.14641827430128	-1.80257310512820	4.27633989099490
H	6.22848483949476	0.19476193103796	3.86905371553372
H	2.01725153888392	-1.68569734773854	4.50181404032757
H	3.01456973699640	-2.38030753297736	3.21676123100967
H	0.39526431679112	-0.11843249357205	4.17743478993326
H	-0.03962473642943	0.57244361257177	2.61107661969643

Structure 9a’



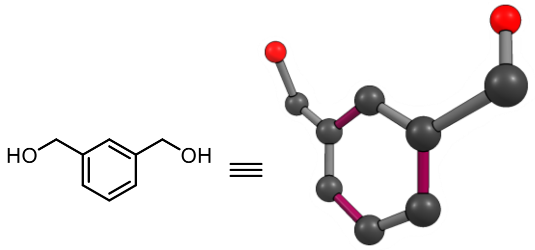
SCF energy: -460.95710809533148 Eh

Free energy (298.15 K, 1 atm): -460.84096606 Eh

O	0.90571300660789	-0.45036242244464	-0.44496486122777

C	2.11590811667088	0.15152504290662	0.01406595804712
C	2.79327214753892	0.97661919434858	-1.03996018028423
C	2.80816837522485	2.36018708376380	-0.91136215044029
C	3.39594479605769	3.16524018575994	-1.87555143417235
C	3.97586973452546	2.58025162702629	-2.98791174217539
C	3.96471686643058	1.19966820789234	-3.12457007814094
C	3.38292446684616	0.38147035370083	-2.16559668153480
C	3.38456962613232	-1.11285805912706	-2.35471300180609
O	2.12695951383498	-1.63948861926488	-2.70797632854444
H	0.34352900573223	0.24712874538241	-0.79000625319318
H	2.74419673130258	-0.68232193499737	0.33151210358651
H	1.91728249415933	0.76930076811818	0.89550627288255
H	2.35618798721008	2.81252863562345	-0.03476001960750
H	3.40057486985111	4.24161341554999	-1.75611845451690
H	4.43801430781137	3.19575186750143	-3.75008750773120
H	4.41942712360058	0.74221971913568	-3.99611156371425
H	3.77248542114719	-1.60034539135898	-1.44846961139611
H	4.06658121828402	-1.36703700495544	-3.16754363137435
H	1.51456419294235	-1.41537141564081	-1.99434082632838

Structure 9b’



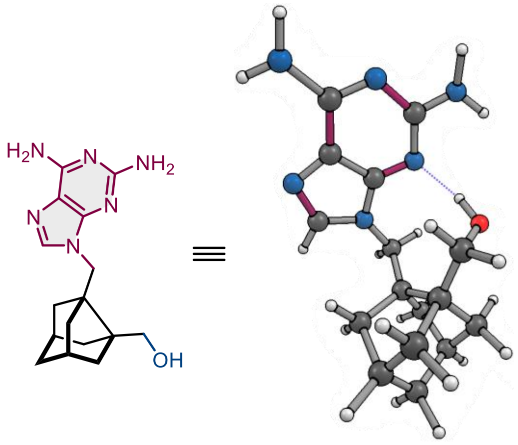
SCF energy: -460.95436420040323 Eh

Free energy (298.15 K, 1 atm): -460.79424266 Eh

O	3.06659149187106	-0.28681505794781	0.84607292780646
C	3.46126963286754	0.17026108272325	-0.42623652165103
C	2.99691664055813	-0.69977568282228	-1.56375401504454
C	2.73064137116454	-0.14048301499402	-2.80830324998918

C	2.33878787985456	-0.94385105434277	-3.86726128633767
C	2.20145182390426	-2.31102045708190	-3.68759551711928
C	2.44645948995055	-2.88408344476848	-2.44488372543928
C	2.25635889365696	-4.36375077558796	-2.24229316936388
O	3.10637490579380	-4.92572263178211	-1.27022311306964
C	2.84773592674295	-2.07084239006990	-1.39172587608366
H	2.11172706580862	-0.37701637685146	0.84915223167612
H	4.55453857551990	0.19076902743321	-0.40087168884217
H	3.12910170897699	1.20165770749111	-0.60179398309200
H	2.83172374009869	0.93043564853667	-2.94806518973092
H	2.13957437980753	-0.50275485972806	-4.83649556350353
H	1.90066111009392	-2.93985823194232	-4.51872576263431
H	2.35797540650905	-4.87636975594862	-3.20757774030748
H	1.24053900595376	-4.55897332405764	-1.88688067558173
H	4.01278071506637	-4.72918697492914	-1.51458825805936
H	3.04704022761346	-2.51202943485567	-0.42252982880077

Structure 11c



SCF energy: -1025.95922747824170 Eh

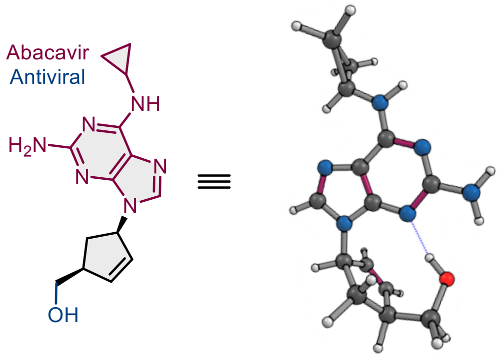
Free energy (298.15 K, 1 atm): -1025.60971889 Eh

N	5.81171137436893	10.18533560096283	2.61252840046952
C	5.25001760799888	8.94669947268964	2.60387472616512
N	4.71819151385270	8.53872910607688	3.76356335649417
C	4.12982528933968	7.34757463064170	3.81153968180540

N	3.60718755059901	6.92666114401049	4.97470501576883
N	5.26761377532567	8.28865490261903	1.44178876630083
C	4.67667594140072	7.09755648300914	1.52479499227671
C	4.08401310030486	6.55566503196351	2.65416730979469
N	3.53991572266224	5.32362923637345	2.38401360581135
C	3.80808046836560	5.13520888016224	1.12550504383434
N	4.51197814711423	6.16476545401576	0.54158437064443
C	4.85577025209060	6.30448769335526	-0.86068750980992
C	6.02715074952784	5.48680951092078	-1.39415084858591
C	6.02400529496801	5.60722399732543	-2.92963343414469
C	7.45463032656502	5.22615859562162	-3.27788682363766
H	7.69383511814465	5.37684274696143	-4.33291513695444
C	7.71532863819804	3.77094822322032	-2.86568635698252
C	7.37504387408652	3.53779707884115	-1.38631697303180
H	7.56280071467641	2.49860052669660	-1.10742240612173
C	5.94769632518970	3.98380576250195	-1.09107760524032
C	8.12369443857191	4.54105848841119	-0.51838564962153
C	7.52706482861634	5.87320041006885	-0.99538322906766
C	7.76193548767208	6.97410803676498	0.01943677161671
O	7.30496721407232	8.23675074174129	-0.39775838149966
C	8.19055189546755	6.17895083701379	-2.34655505406772
H	6.43190355493485	10.41326752235454	1.85684925114121
H	6.01168218066298	10.57572644737885	3.51447025091750
H	3.08457091393377	6.07139737743014	4.99736062155165
H	3.57495608461538	7.56005732726720	5.75101905684235
H	3.51186097048907	4.27170481318583	0.54999163821049
H	5.03498933612864	7.36329988755387	-1.04110453237679
H	3.96894762116779	6.02465828767587	-1.43706881821752
H	5.82652314005154	6.63766033350440	-3.24026892349883
H	5.26461838054341	4.96461887402698	-3.38265476350161
H	8.76609002397564	3.52069585398757	-3.04133923234804

H	7.11946619284218	3.09796416654823	-3.49052130841443
H	5.72597499044220	3.79427495983206	-0.03783040607215
H	5.18464855790361	3.48464897899887	-1.69485058290436
H	9.20818099812176	4.51499630629546	-0.64350347052546
H	7.90313292458196	4.36324165038747	0.53941436811314
H	7.31172691733558	6.69807936931059	0.98057132413630
H	8.84501905519158	7.03083420198207	0.19215381628379
H	6.53831455510144	8.44619359623479	0.17102778664429
H	9.27090118046251	6.02080866019703	-2.30578654339028
H	8.00794673469248	7.21604878942132	-2.63622214604949

Structure 11c’



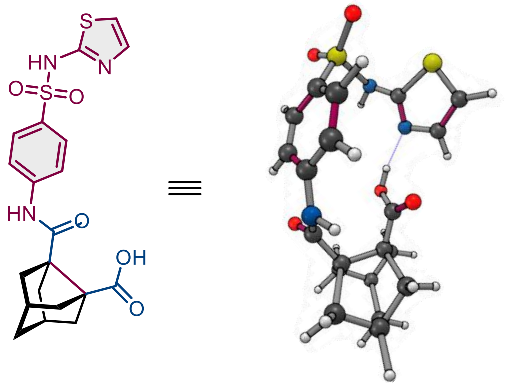
SCF energy: -947.33105204374567 Eh

Free energy (298.15 K, 1 atm): -947.03175053 Eh

O	1.90996036742428	2.57772166335461	0.97748113852215
C	2.91626722129483	2.60844803109755	0.00562843473810
C	4.31172691286313	2.31978191332736	0.56074099867703
H	4.96147017504811	2.13635150309722	-0.30351280646020
C	4.32935058434088	1.13228142193335	1.47437949324815
C	4.84742871854893	1.39547642063916	2.66430807811561
C	5.31957070179801	2.81726514360989	2.77474044622247
H	6.40603900762262	2.84853558116893	2.90236245094300
N	4.79610974392691	3.50780932962650	3.94453799073359
C	5.51000103192519	3.85689747823240	5.06402023938968
N	4.79328598256640	4.41300489147538	5.99311413260056

C	3.51795813413104	4.43806706199312	5.46931529229122
C	3.50511265901545	3.87596520456282	4.19658737162885
N	2.45364243805412	3.74535039220332	3.39369011989357
C	1.33231591973063	4.23077003862842	3.93845036889556
N	0.21911423432290	4.18575191471501	3.16686359730373
N	1.19821070680073	4.77695858382887	5.14889201258415
C	2.26888147054155	4.89800599853525	5.93910237917130
N	2.05465643320549	5.45914783768178	7.13786254116885
C	3.02388189840319	5.69873668329524	8.15229251086412
C	2.92005066681300	6.93081761121100	8.99243433125678
C	2.62839373414837	5.57974567770023	9.58864468922509
C	4.90533515746727	3.45197671675610	1.43012880299530
H	2.24081359936304	2.97477707973468	1.81453633809434
H	2.94405708606612	3.57706295872242	-0.51677494377821
H	2.66559380860910	1.85041003881135	-0.74329391376233
H	3.92963946084683	0.17131679921872	1.17444655646754
H	4.94772572550980	0.69640238612332	3.48505112448821
H	6.57213439339591	3.66926837362084	5.12213516919959
H	0.24401023800357	3.64383593860983	2.32009014113567
H	-0.65977953558711	4.36411078475303	3.61259025912386
H	1.09824117678226	5.73050343044113	7.30068169587577
H	4.00803107594913	5.36022888574223	7.86316120916422
H	2.07678710688986	7.58594613222385	8.81184643084285
H	3.83299871856969	7.44059056840742	9.26987447323607
H	1.59287849982471	5.34449038626301	9.80173435301713
H	3.33790469034499	5.14797872210462	10.28181403280037
H	5.76048623215555	3.92178689854158	0.94567940403321
H	4.16558382742310	4.23265352919612	1.60339303461303

Structure 12b



SCF energy: -2110.34506065467031 Eh

Free energy (298.15 K, 1 atm): -2110.07003744 Eh

O	0.04814094891525	-4.69949349401736	-3.38985241134660
C	1.24150883526981	-4.89689091269848	-3.35939442597867
O	2.11985415801845	-4.12623144456178	-3.98790250873110
C	1.86503045912576	-6.04786894571260	-2.60272418358487
C	3.04832522218418	-5.64460605428518	-1.70957783045694
C	3.75622190448176	-6.98448386540737	-1.53107615128947
H	4.70719561837394	-6.89282060880469	-1.00313381533228
C	2.83886367575462	-7.99229539331776	-0.82417446634101
C	1.49417953681703	-8.13349012897580	-1.55177797606608
H	0.85313643790736	-8.85488856297919	-1.04151335062352
C	0.84749512609483	-6.76589037792213	-1.71086731286869
C	1.71481234355889	-8.47662284401147	-3.02208546467604
C	2.48479265223702	-7.23426068246665	-3.50534870570258
C	2.44194756903655	-7.00559123797927	-4.99805323654407
N	1.17726485306587	-6.76994034216918	-5.50914240066793
C	0.92022180685642	-5.87037774972714	-6.54186203161315
C	1.87955345586687	-5.52452405697042	-7.49620616290030
C	1.67345367814465	-4.41028959652238	-8.28374646848685
C	0.49960762337933	-3.67996673491644	-8.16297812160361
S	0.48480763136462	-2.03036093228521	-8.72198335834820

N	1.08244832892715	-1.22287491237298	-7.36094314800496
C	0.34321229003489	-1.23001413409434	-6.18582951841380
N	0.68500202056278	-1.86120675879382	-5.09485213500630
C	-0.22061125452149	-1.62069844198598	-4.10155713914935
C	-1.26176802517141	-0.81977460613818	-4.43808874192816
S	-1.10457323253003	-0.31517183501916	-6.05999930609853
O	1.49034798120815	-1.84095459560830	-9.71529619799996
O	-0.85722520052322	-1.57456148759442	-8.88825010552194
C	-0.52362262331593	-4.11515607225704	-7.32934584180571
C	-0.31439307444788	-5.21742722809020	-6.53084718941952
O	3.43658926245327	-6.99580347968704	-5.68284773782355
C	3.91999088751043	-7.37454436537781	-2.99261384998287
H	1.65038453779040	-3.40152838431042	-4.46879231081077
H	2.70234105901897	-5.19112264361764	-0.77878666253189
H	3.70157982712335	-4.93517596826737	-2.21842994918820
H	2.65968068642128	-7.67382014739000	0.20701287967105
H	3.33693084362931	-8.96505143309911	-0.77536693010106
H	0.69331705666663	-6.23149712054793	-0.77215613750180
H	-0.12207081542646	-6.84375831624869	-2.20574967083042
H	0.75053179026783	-8.59613712585757	-3.52404165336914
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H	-1.07099554100853	-5.51078511297825	-5.81378179532370
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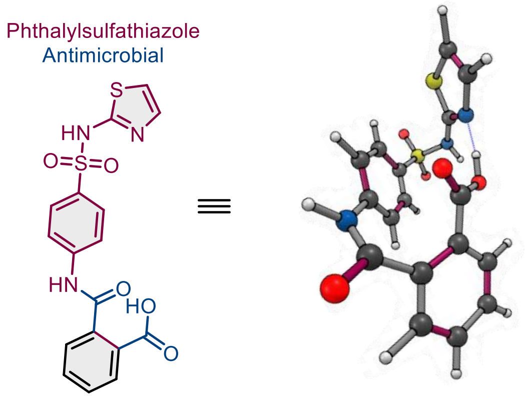
H	4.30130737778686	-8.38432518091682	-3.14841614746502

Structure 12b’



SCF energy: -1991.29606955153372 Eh

Free energy (298.15 K, 1 atm): -1991.04555246 Eh

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C	3.99833760481958	0.76077556390660	1.32135216613547
N	3.85277348794261	2.13207586382535	1.31422631822994
C	2.90443821572819	2.91414068200895	0.66443317403054
C	3.34157514541659	4.03183965325809	-0.04667968118519
C	2.46041421582105	4.75834127603319	-0.81673920316057
C	1.12897468584596	4.36369961860428	-0.87881947222607
S	0.10280233885015	5.03233085726372	-2.12193430891577
N	0.49121050874464	4.09333647021753	-3.46655266580131
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N	2.52326481650521	3.03262175997193	-4.04716877301263
C	3.72798524523053	3.30982234928572	-4.62313639483938
C	3.90885511597275	4.60313098867681	-4.98486242209029
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O	-1.25883206108974	4.70868947004316	-1.85038345643588
O	0.53521889157623	6.35487630174901	-2.43941998669918
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C	2.32324183504072	-0.16170760856913	-0.41583639891949

C	2.83468031829066	0.71679062918758	-1.50389362283121
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C	1.28742387409386	-1.05003347640559	-0.68681497615512
C	0.80680240117208	-1.90243971618297	0.29149898271990
C	1.36258286289154	-1.87309666755583	1.56051931639246
C	2.39339280140276	-0.99205544932798	1.84075055431961
H	4.73757925547072	2.57885770625886	1.50442564189997
H	4.39425699778929	4.28637107142088	-0.04454706445523
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H	2.26039843601481	1.62703539609308	-3.08883793167157
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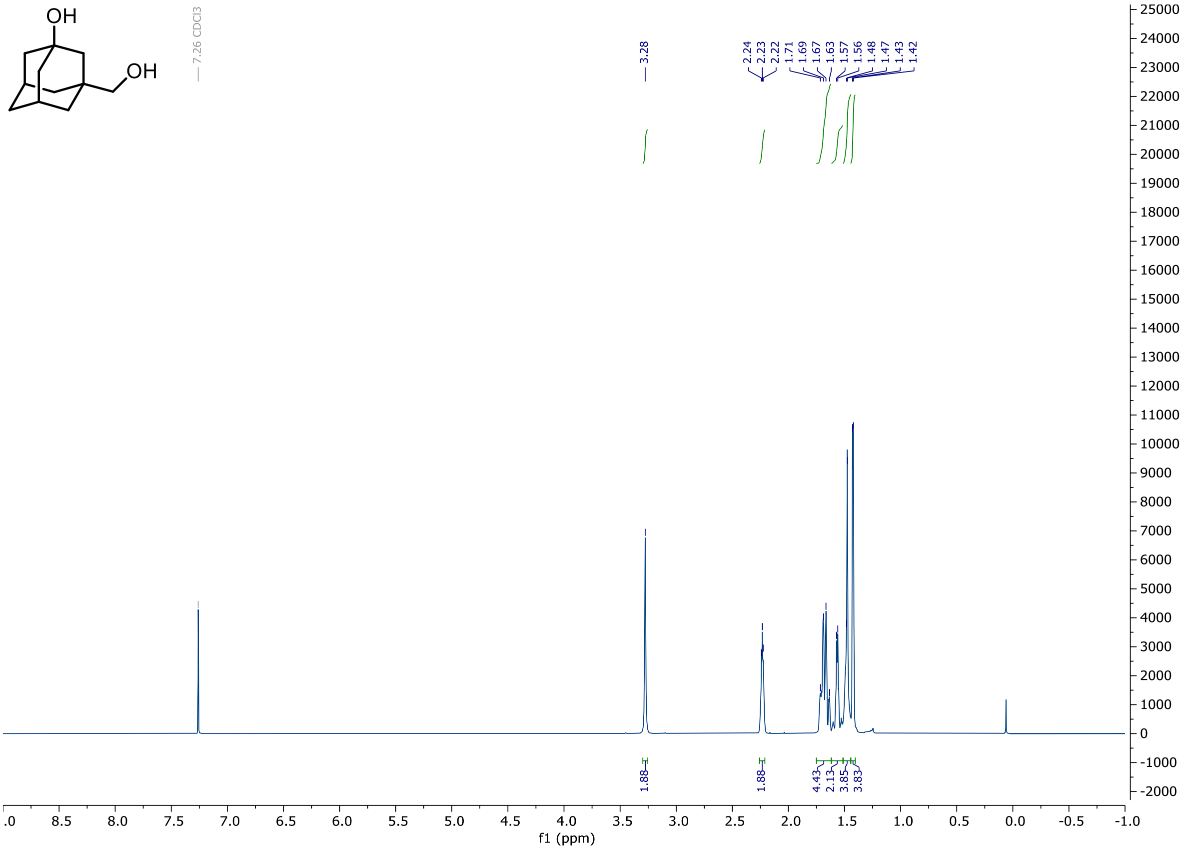
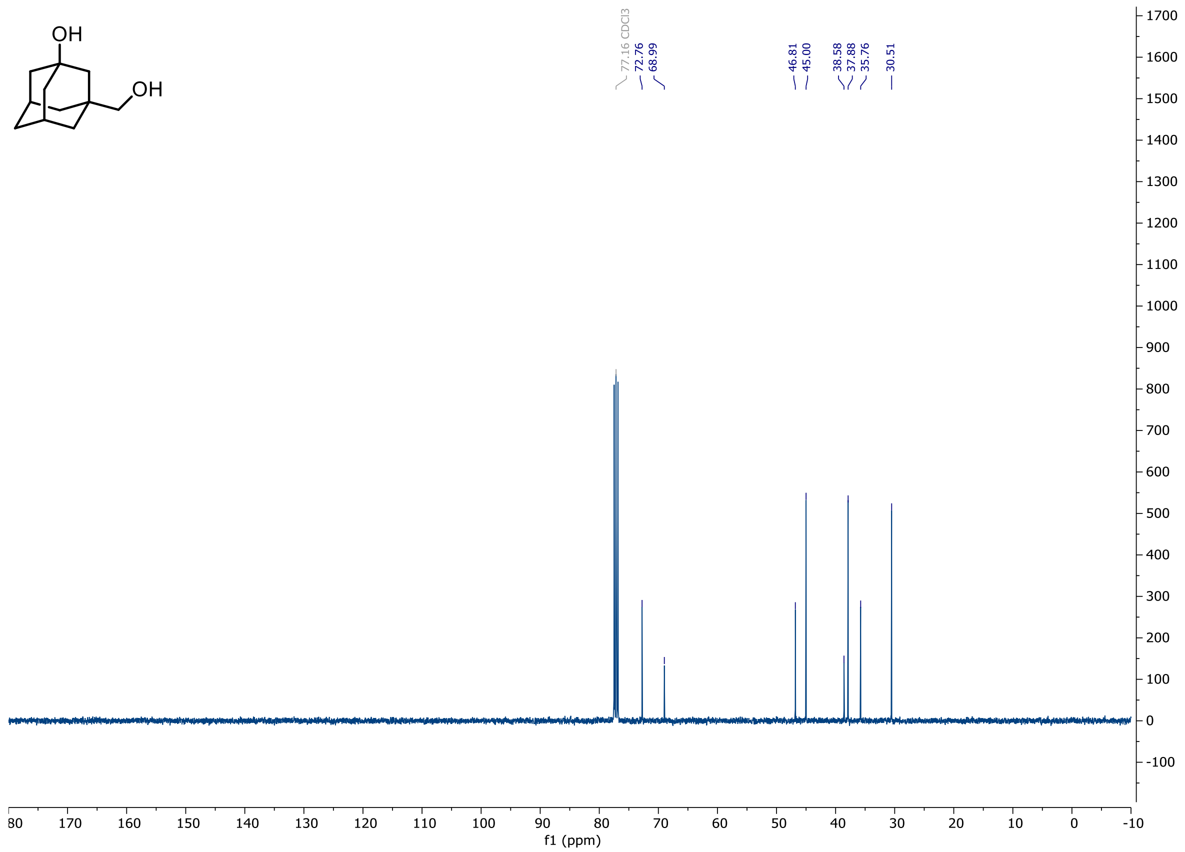
NMR Spectra

Starting Materials

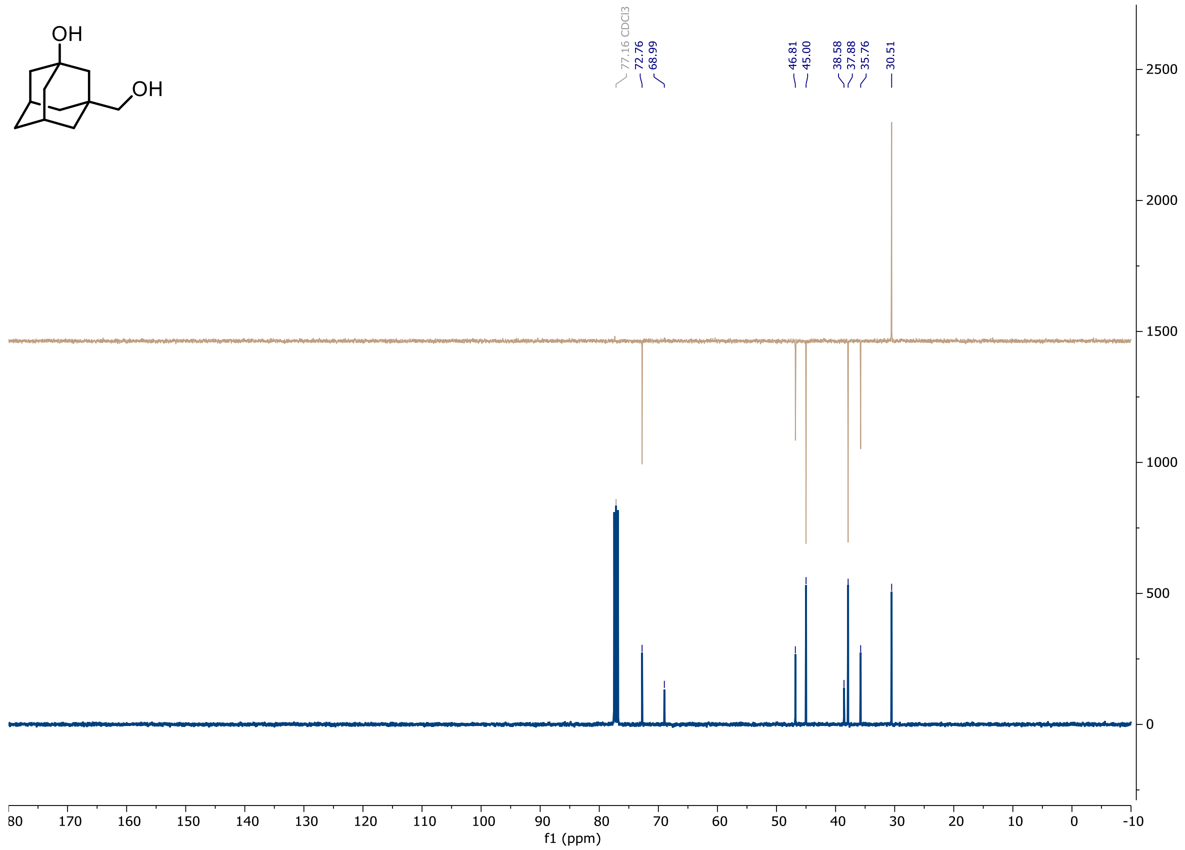
Compound 0: ^{1}H NMR (400 MHz, $CDCl_3$)



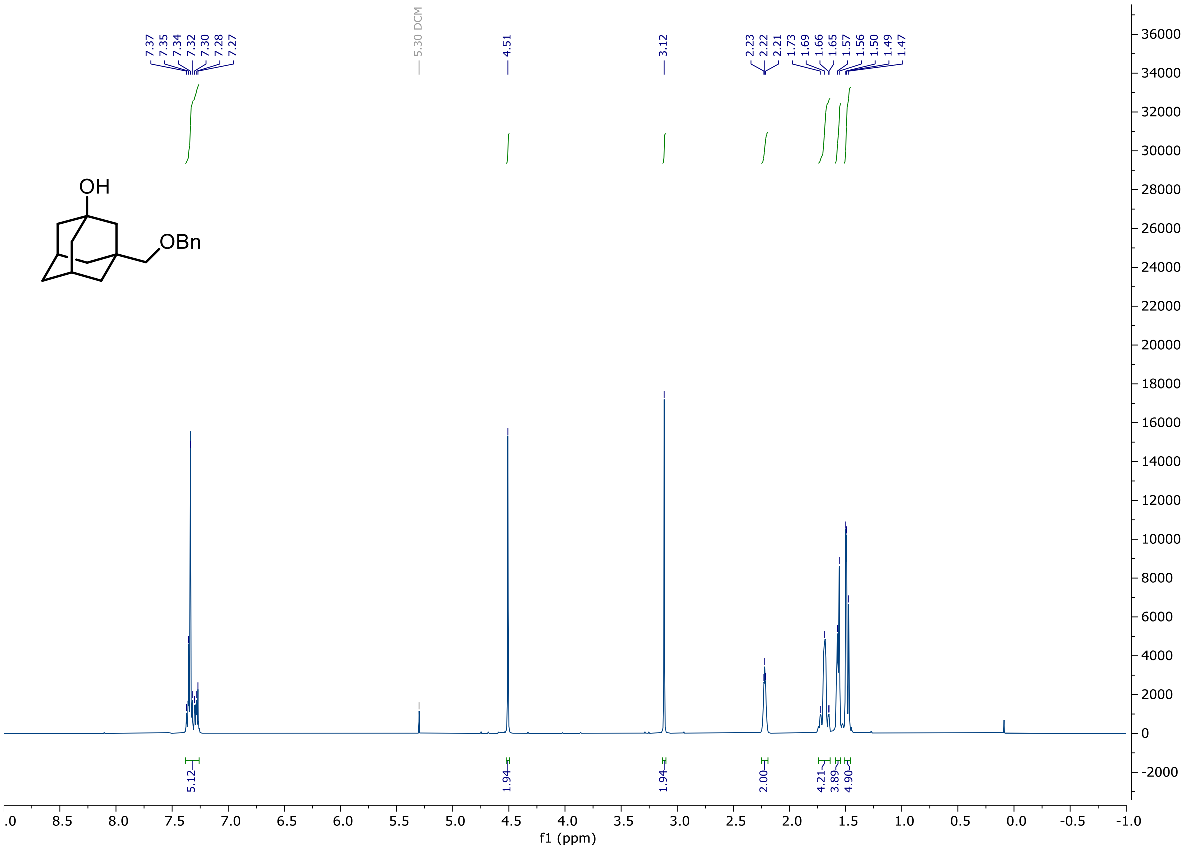
Compound 0: ^{13}C NMR (101 MHz, $CDCl_3$)



Compound 0: ^{13}C NMR-DEPT (101 MHz, $CDCl_3$)



Compound 1c: ^{1}H NMR (400 MHz, CDCl$_3$)



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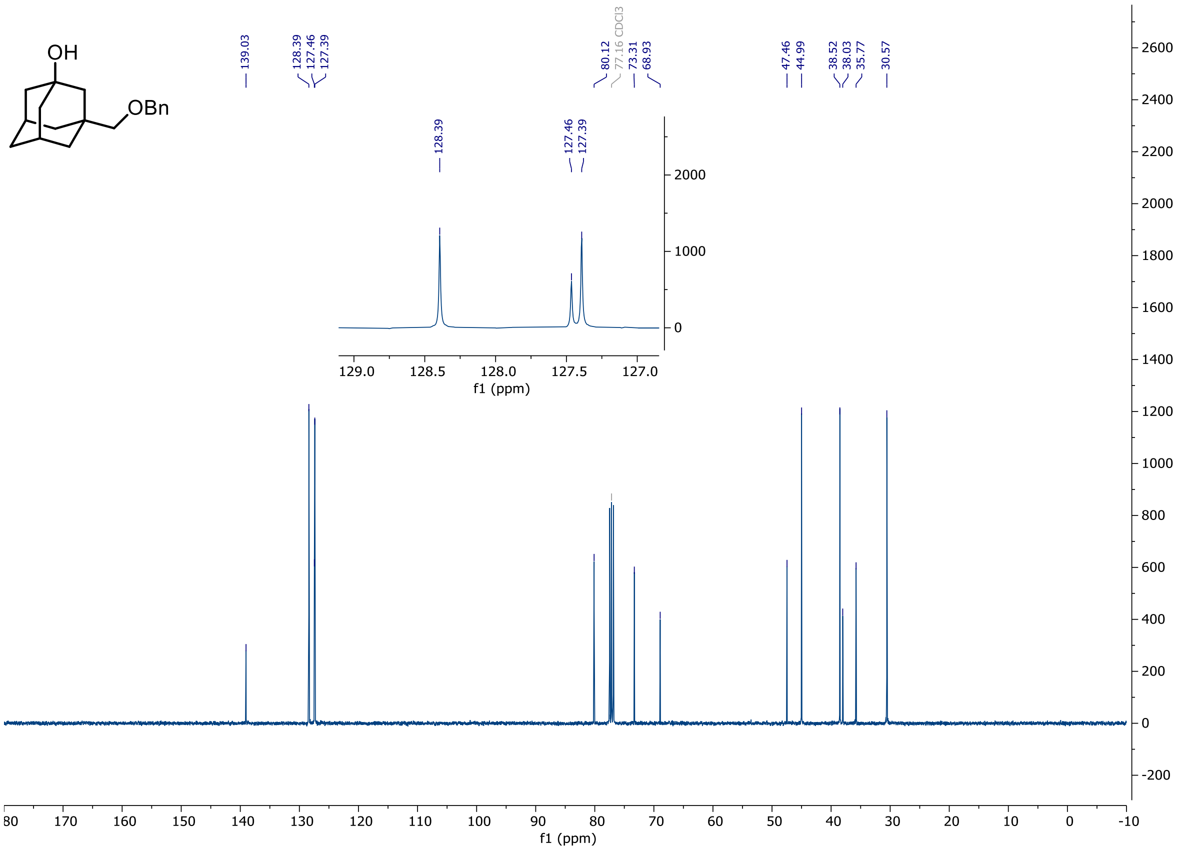
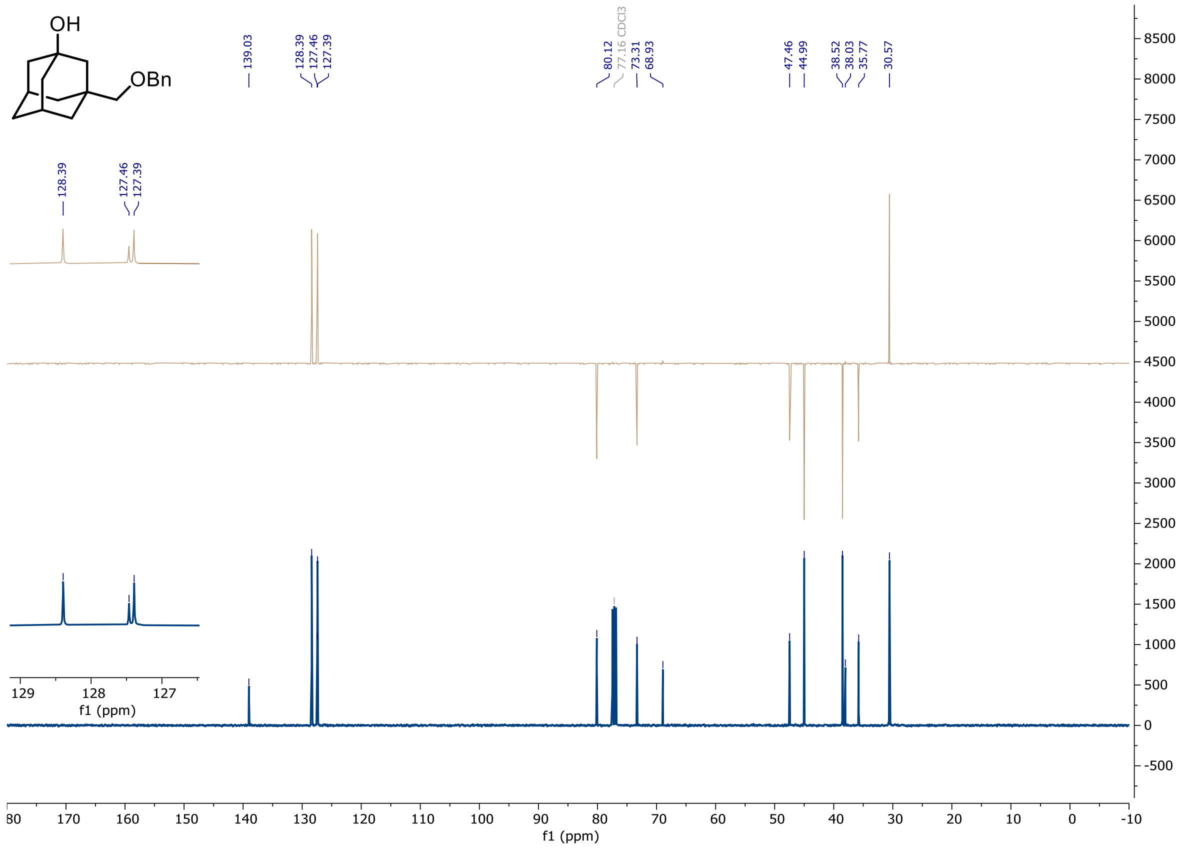


Compound 1c: ^{13}C NMR-DEPT (101 MHz, CDCl$_3$)



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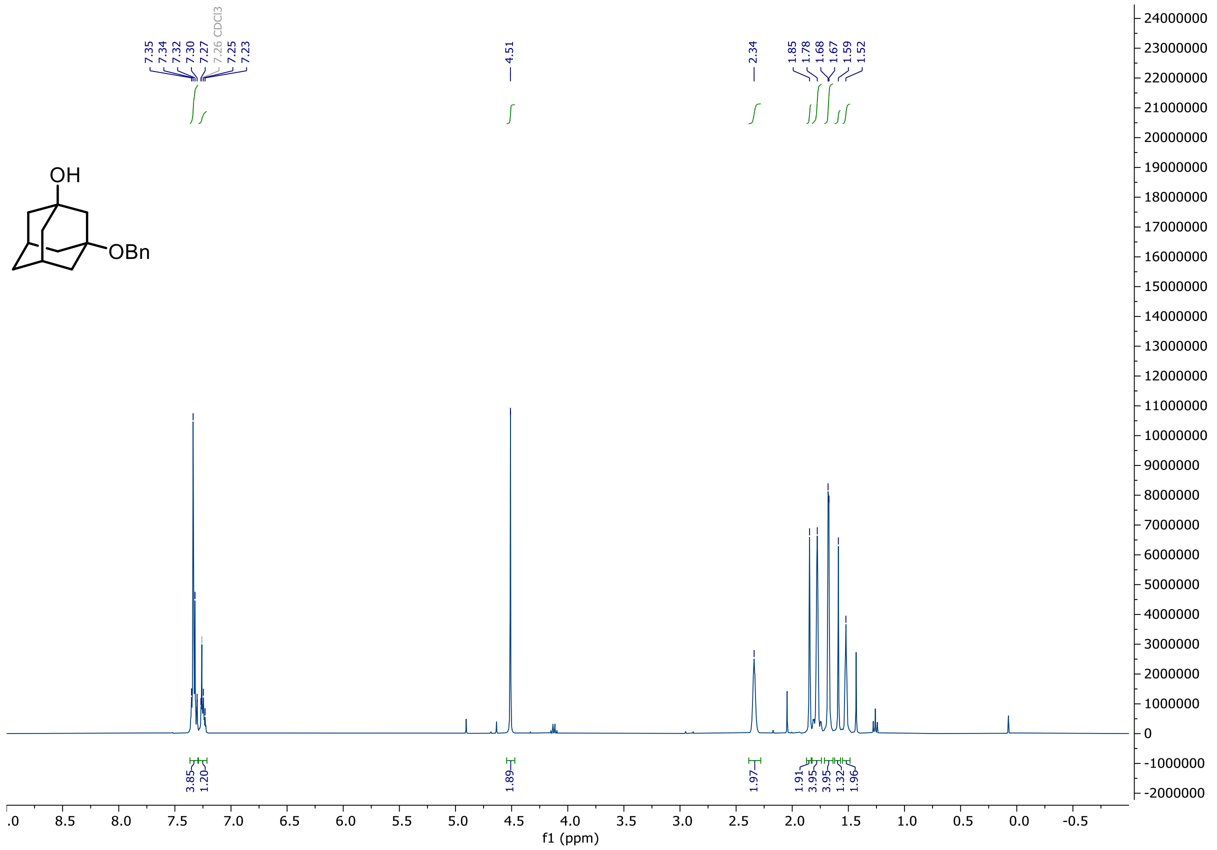

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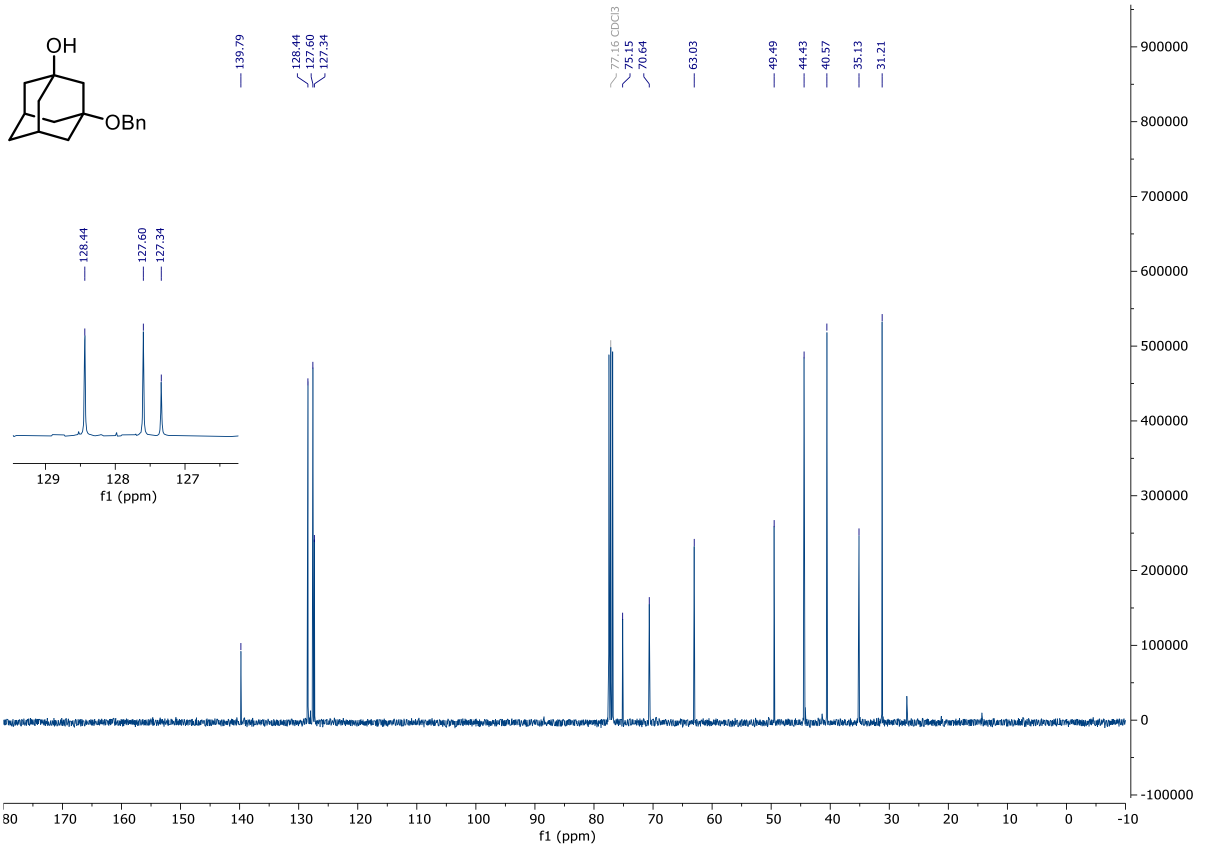

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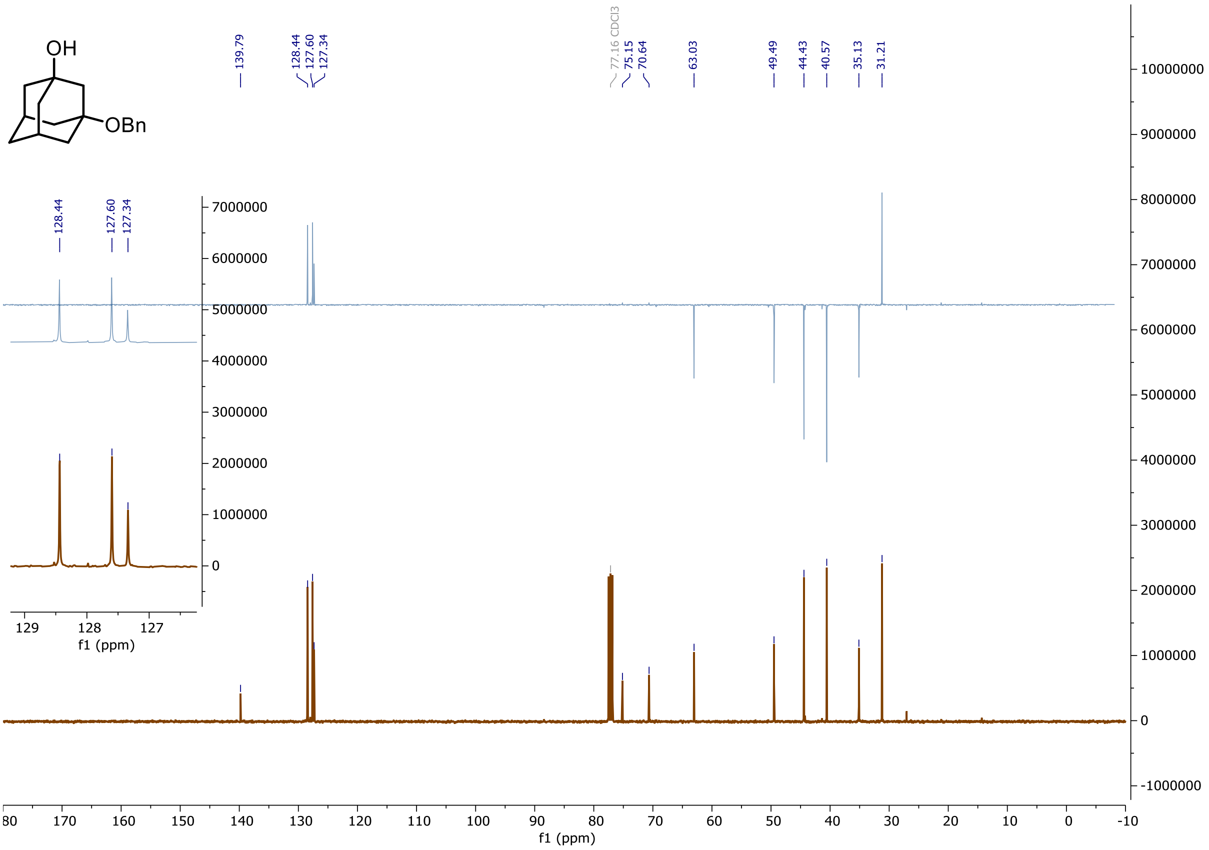

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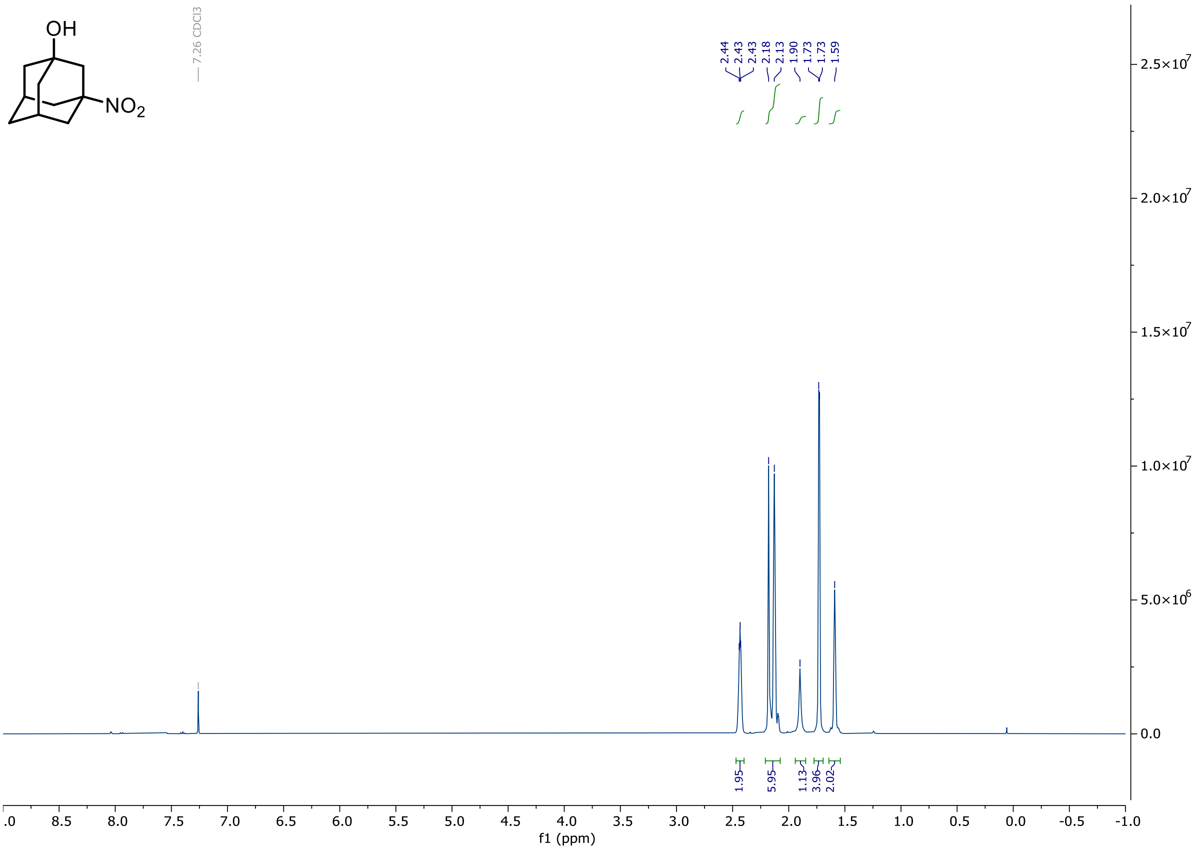

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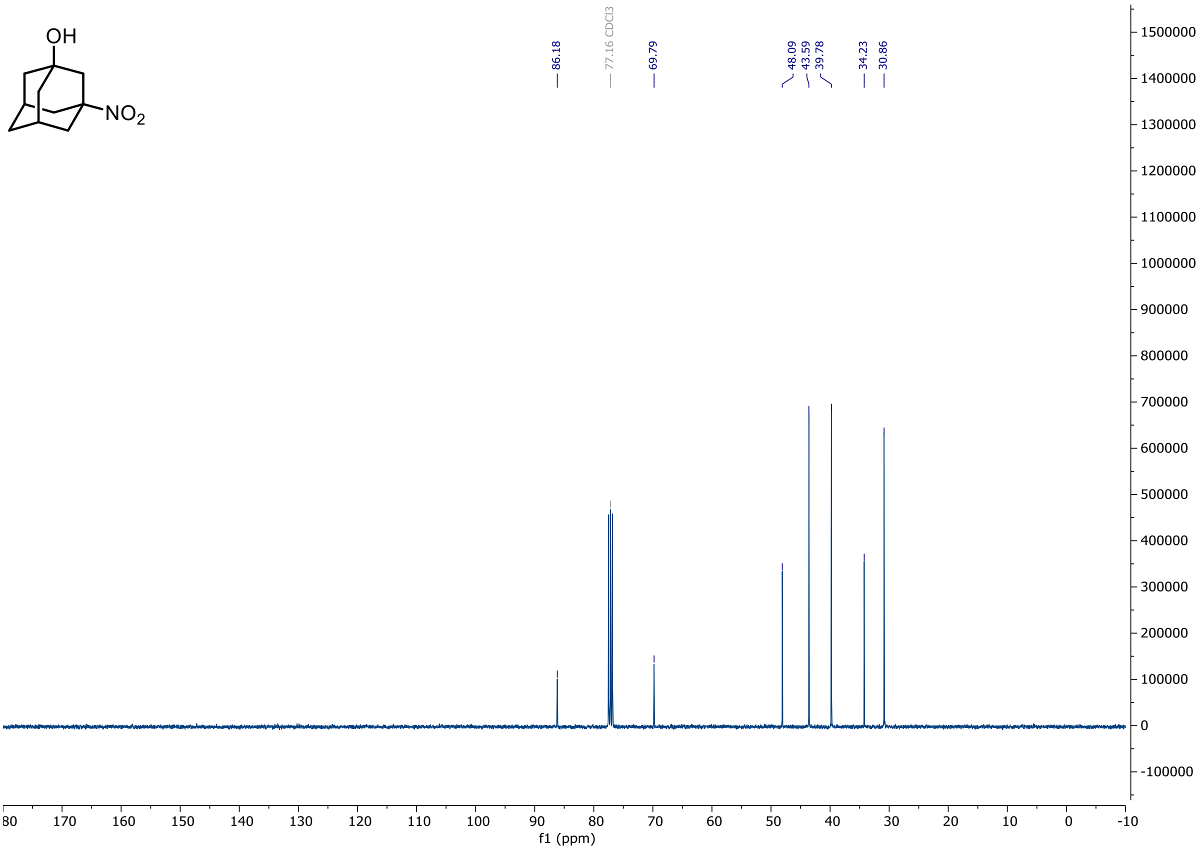
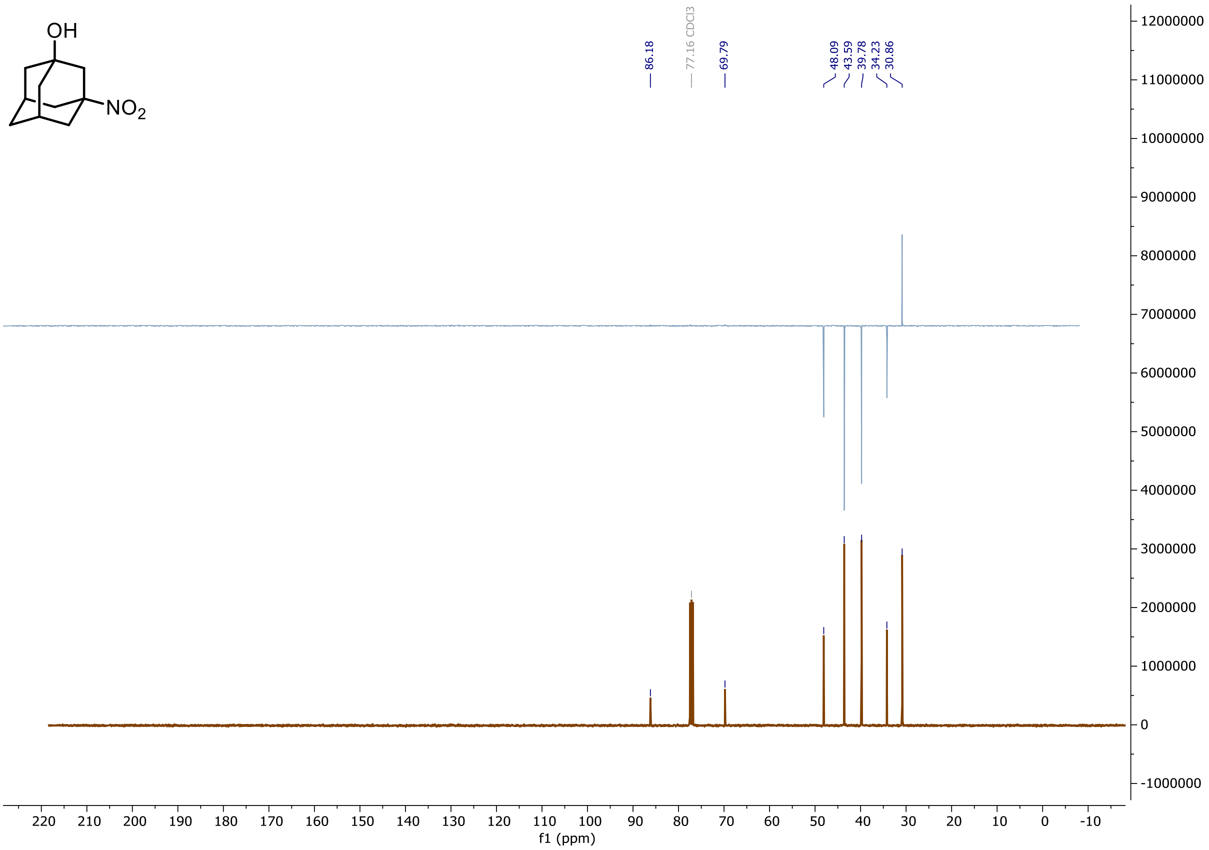
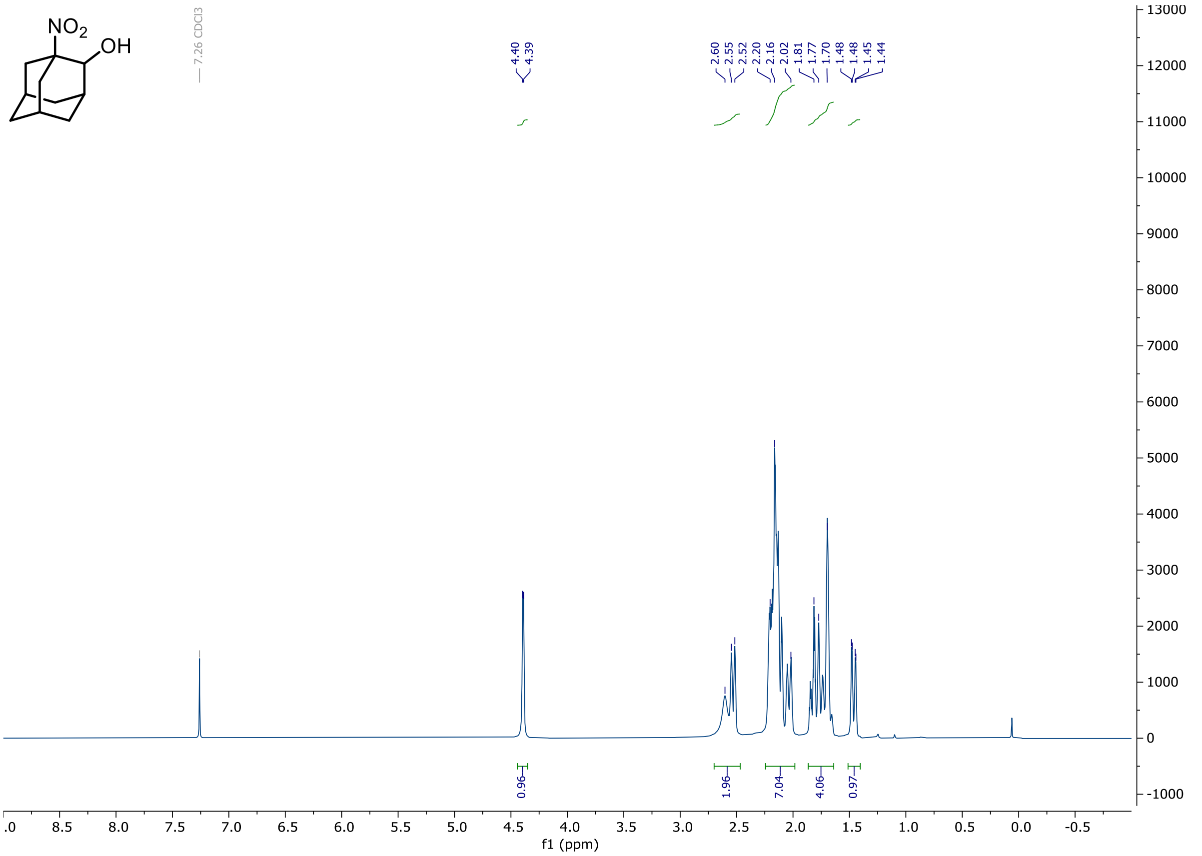


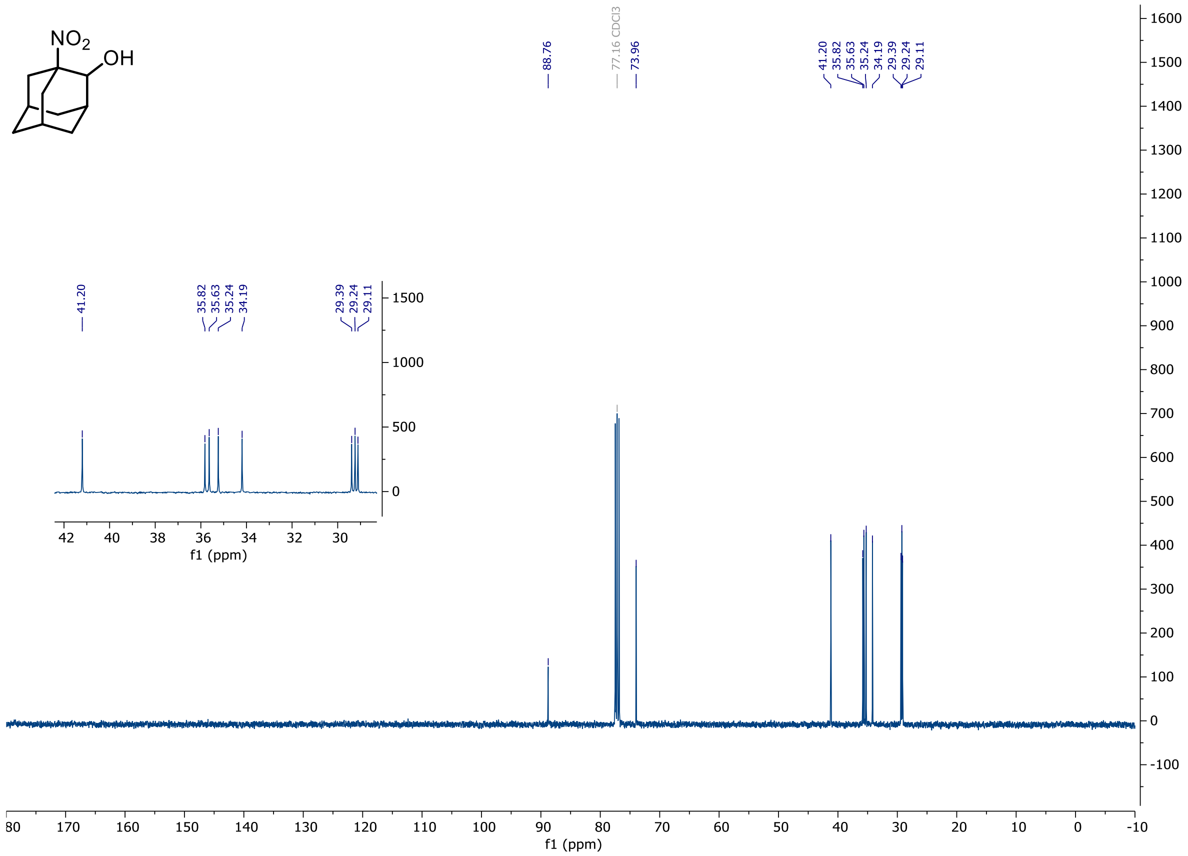
Compound 1e: ^{13}C NMR-DEPT (101 MHz, $CDCl_3$)



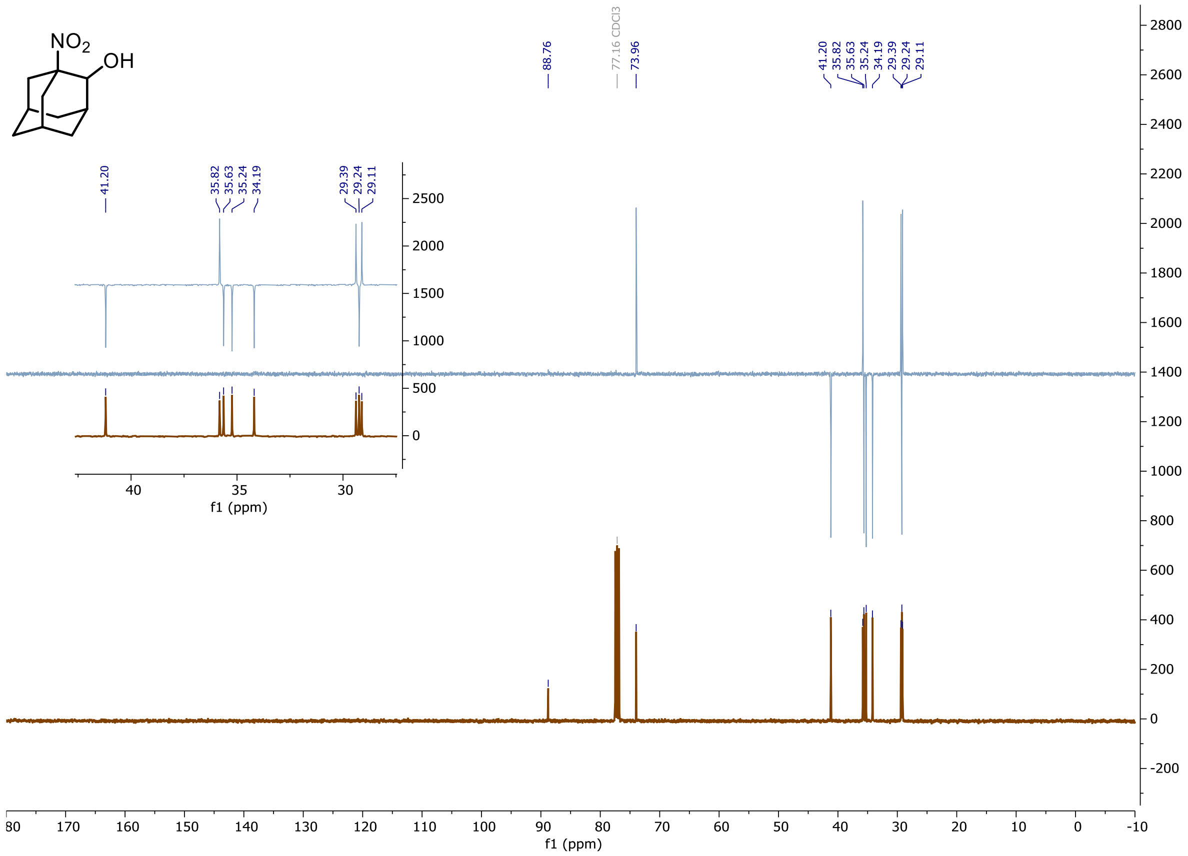
Compound 1f: ^{1}H NMR (400 MHz, $CDCl_3$)



Compound 1f: ^{13}C NMR (101 MHz, CDCl$_3$)

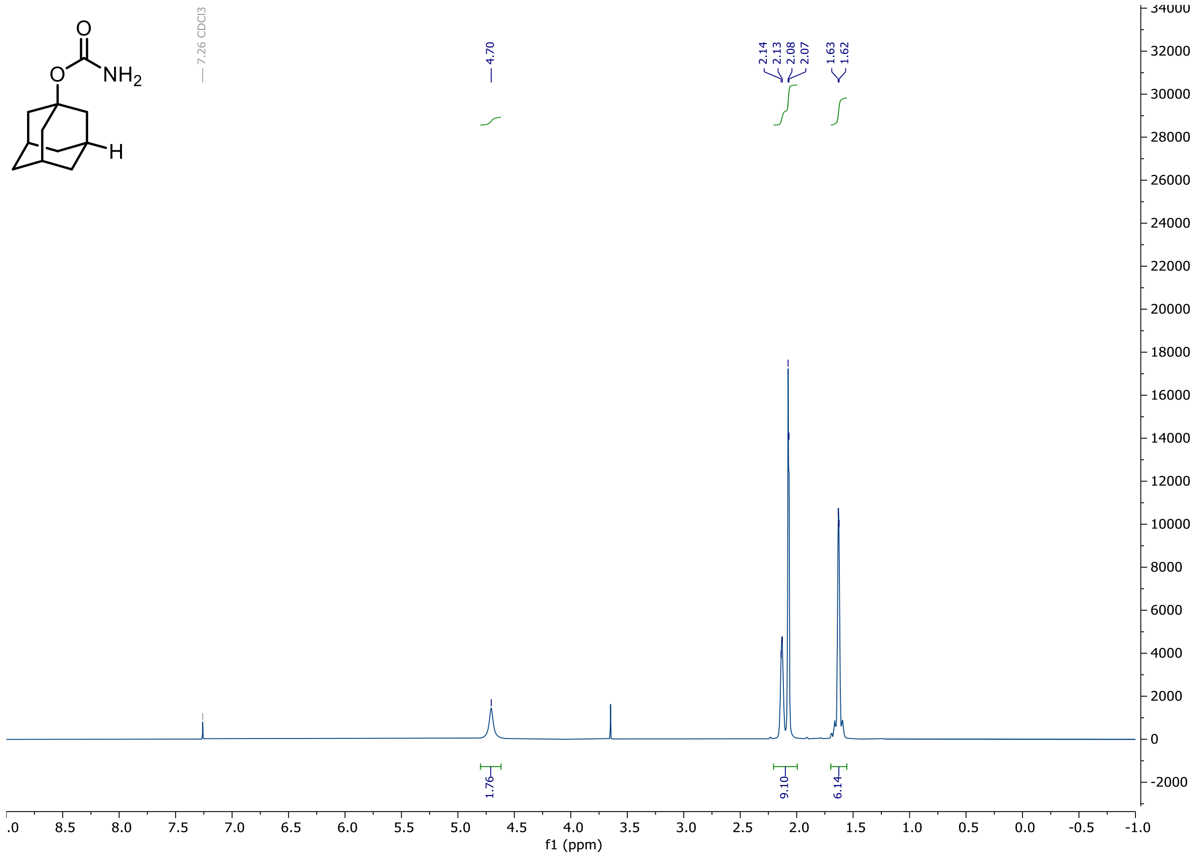


Compound 1f: ^{13}C NMR-DEPT (101 MHz, CDCl$_3$)

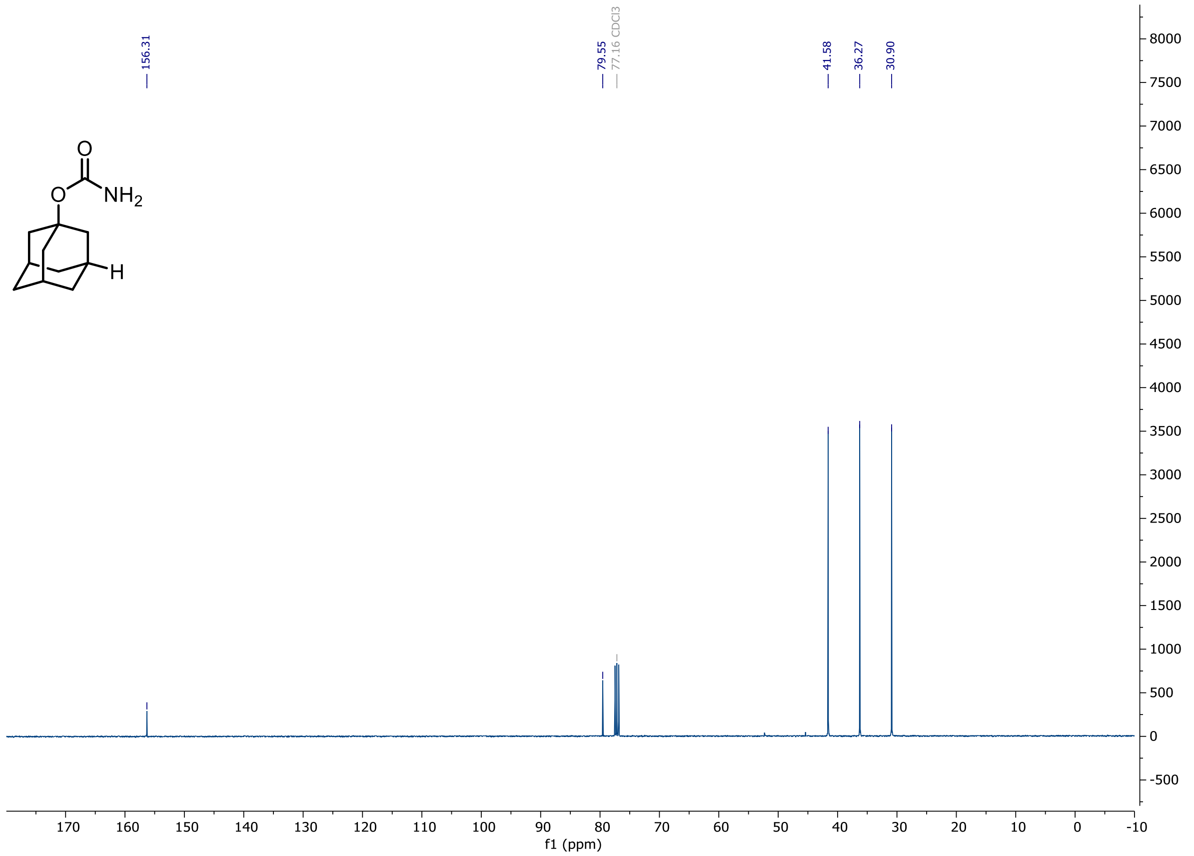


Acyclic Carbamates and Carbonazidates

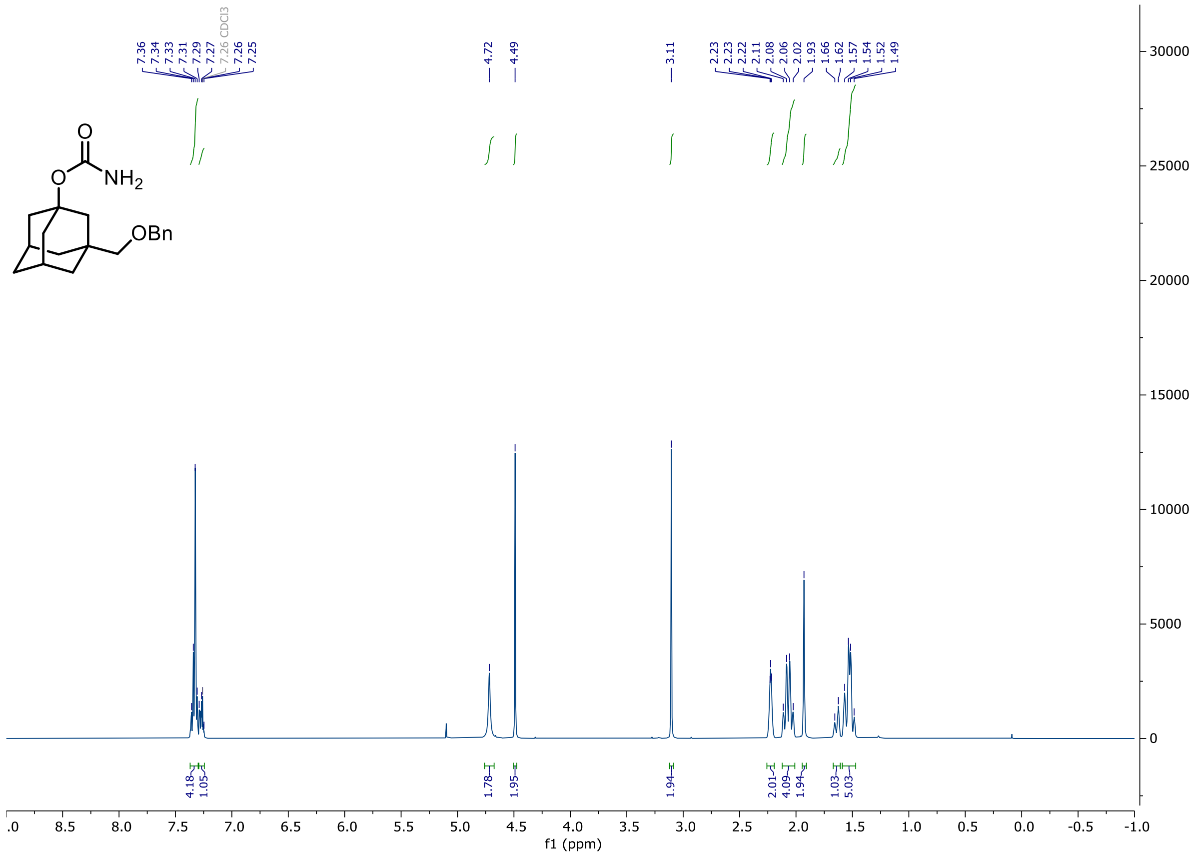
Compound 2a: ^{1}H NMR (400 MHz, CDCl$_3$)



Compound 2a: ^{13}C NMR (101 MHz, $CDCl_3$)



Compound 2b: ^{1}H NMR (400 MHz, $CDCl_3$)



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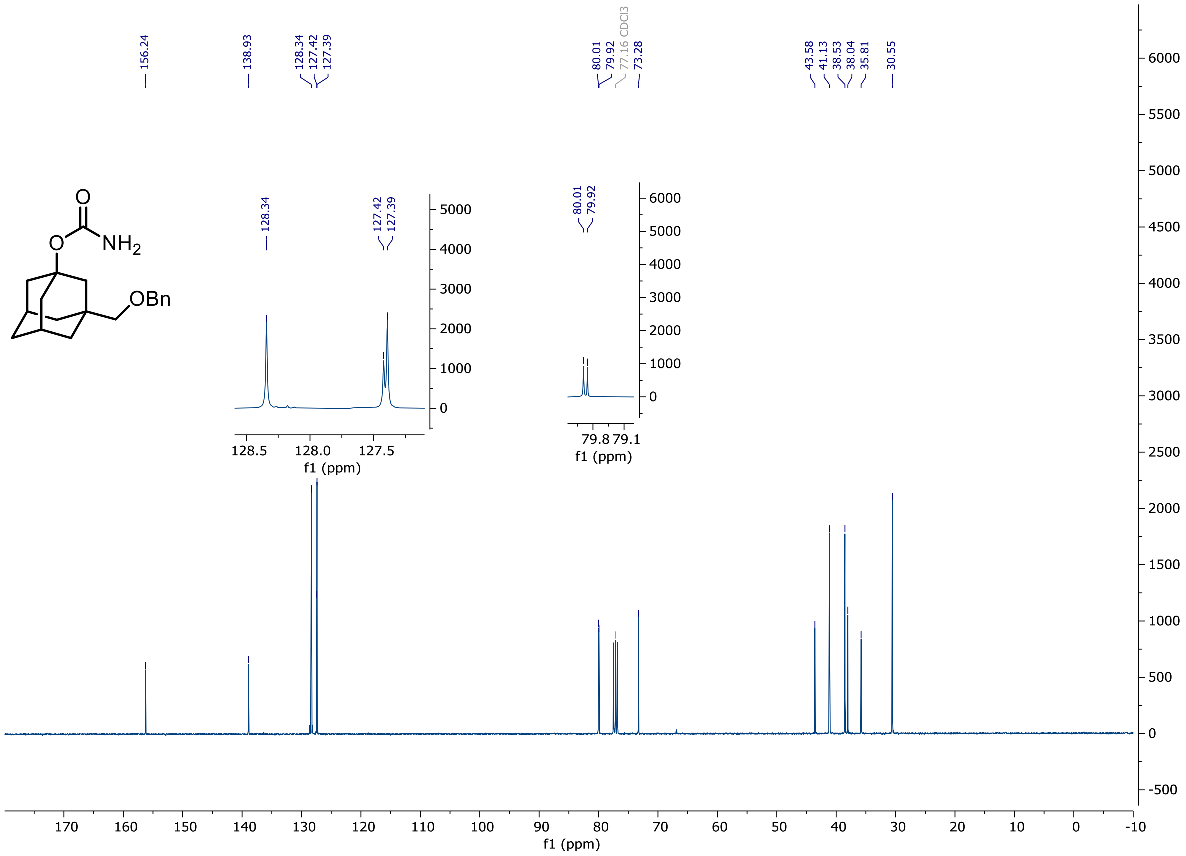

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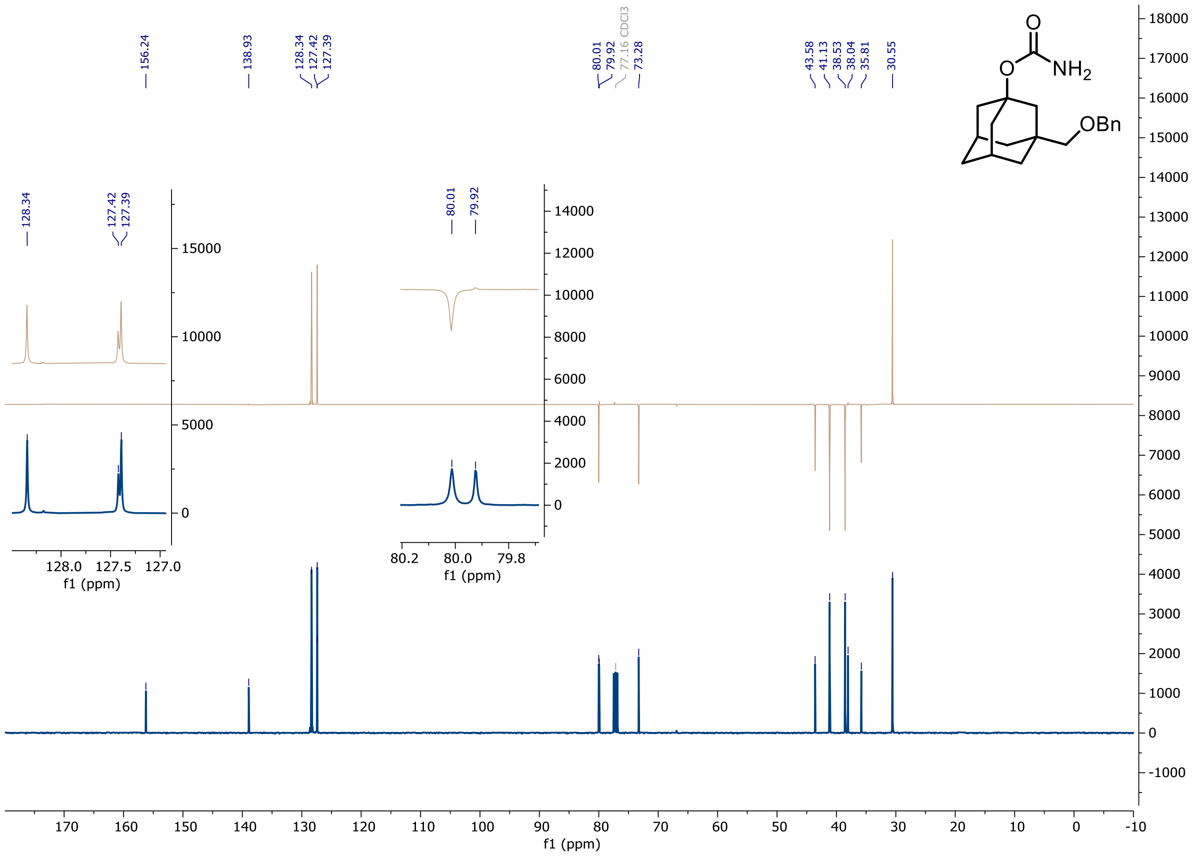
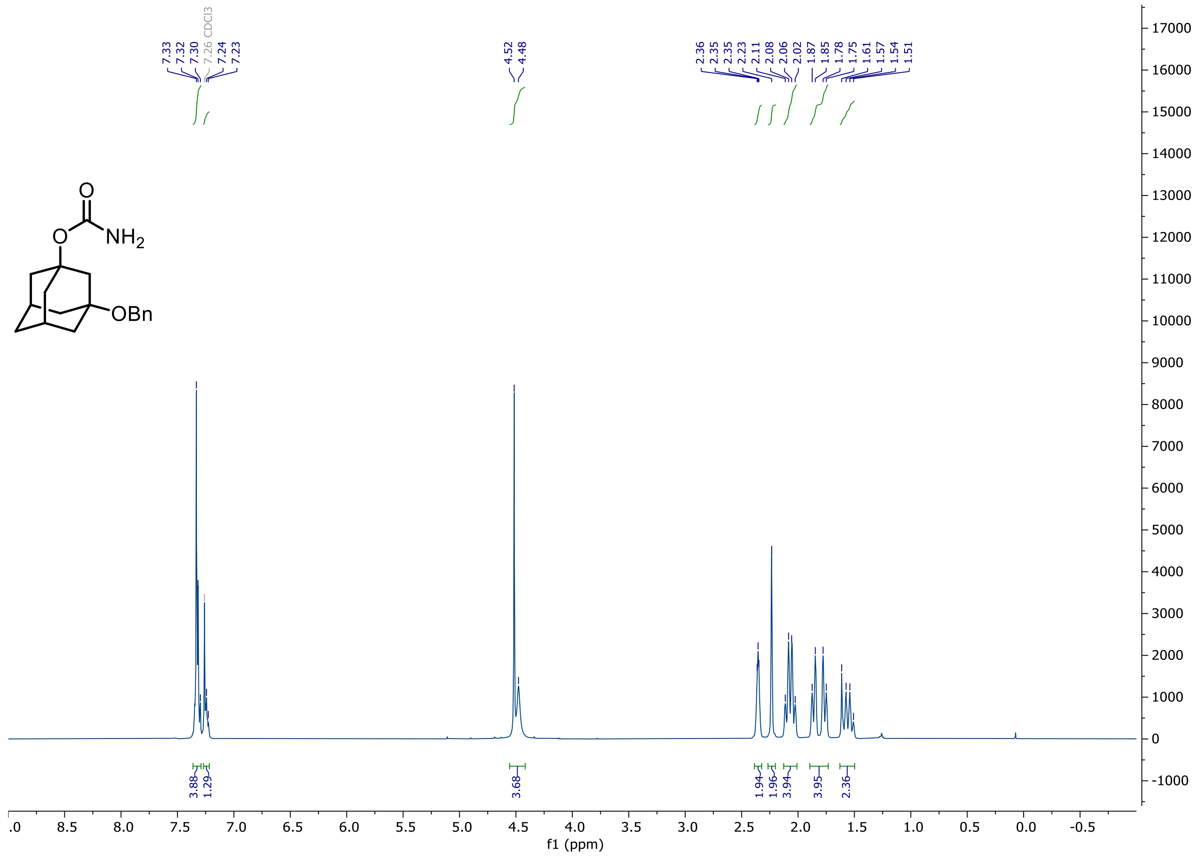
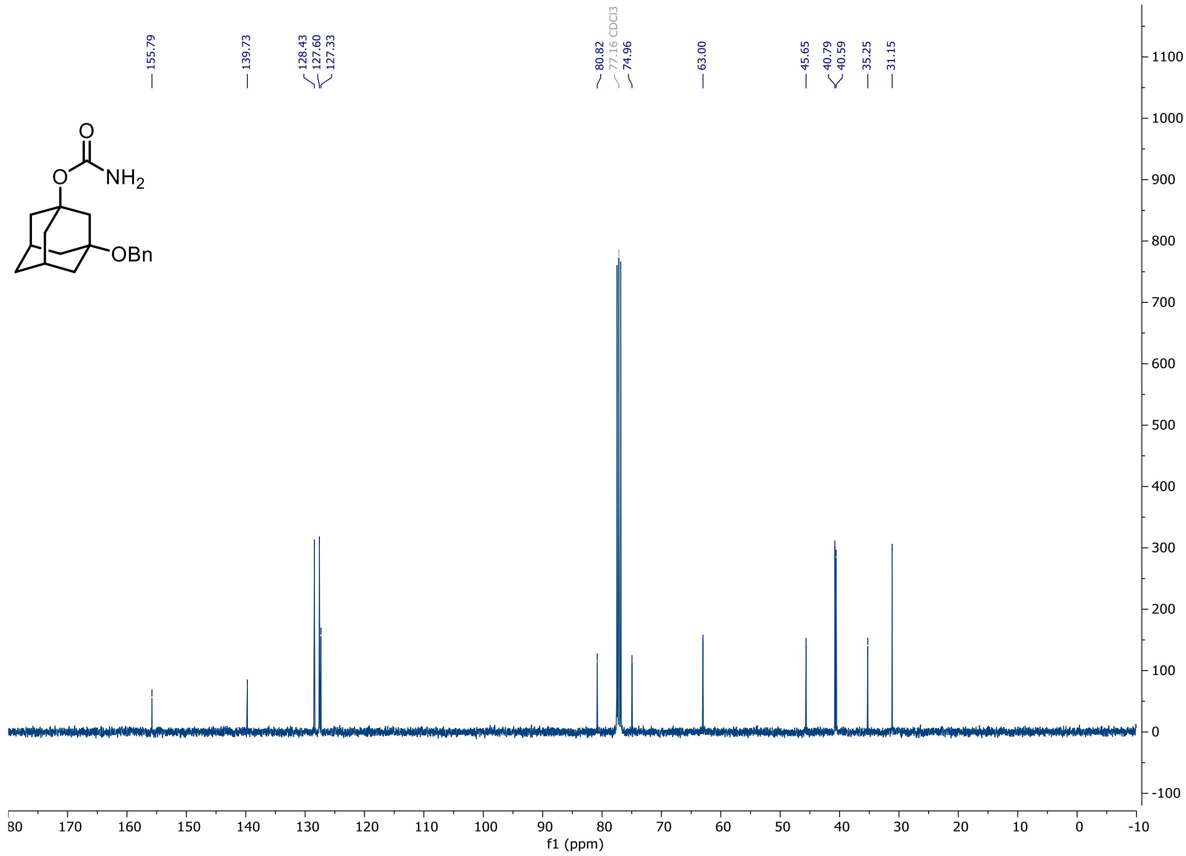


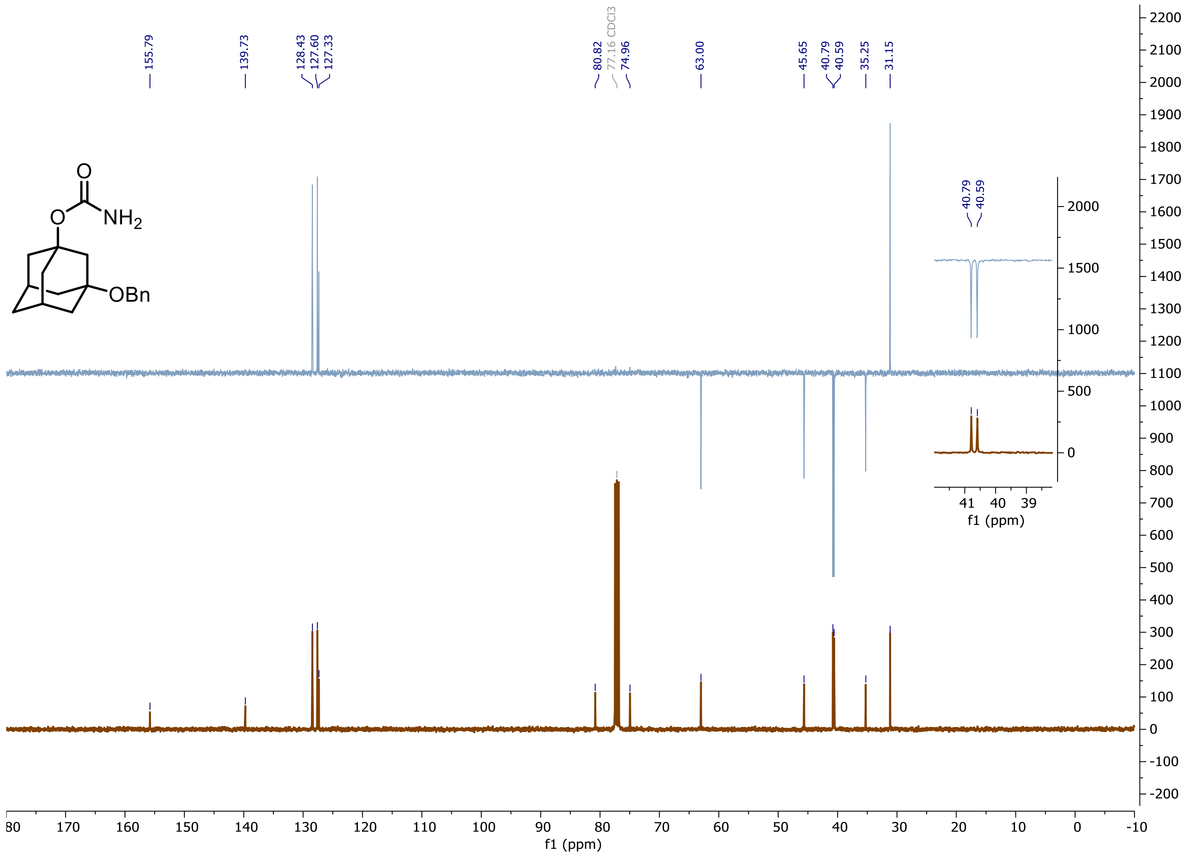
Compound 2c: ^{1}H NMR (400 MHz, $CDCl_3$)



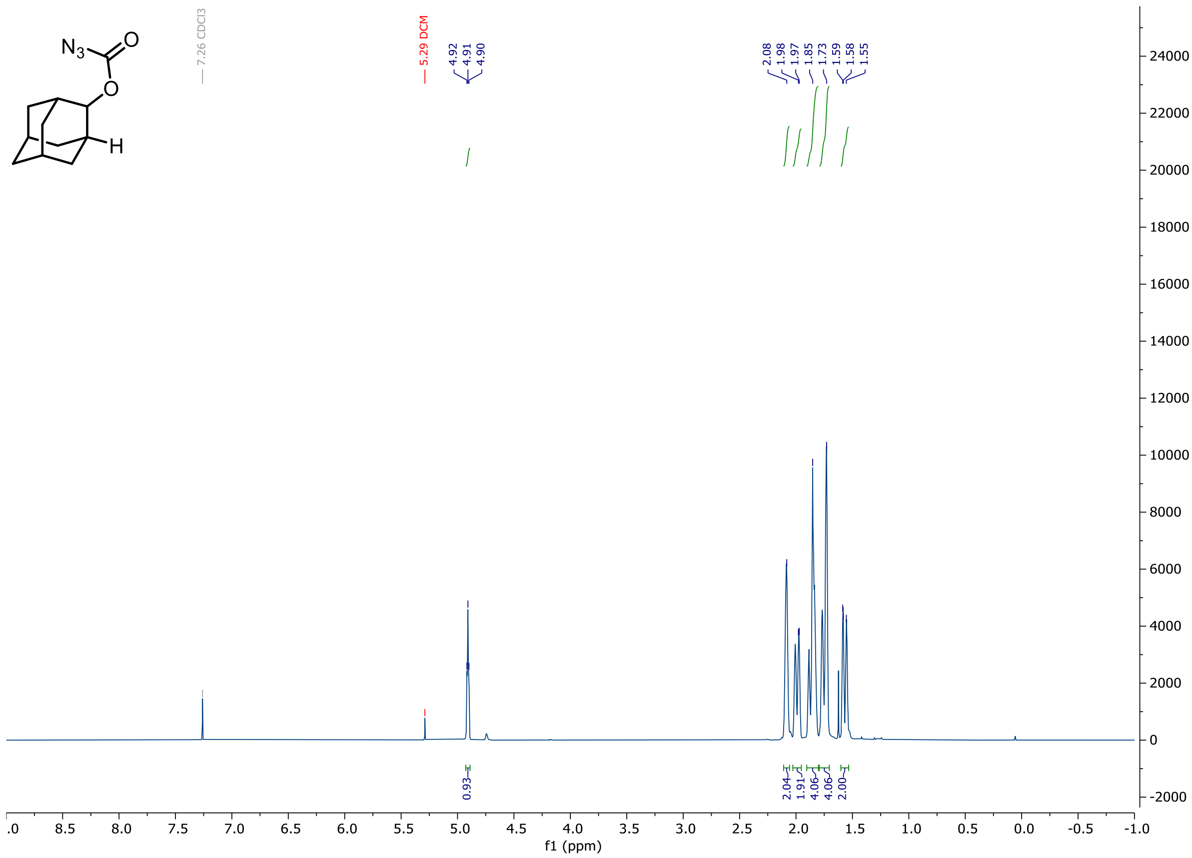
Compound 2c: ^{13}C NMR (101 MHz, $CDCl_3$)



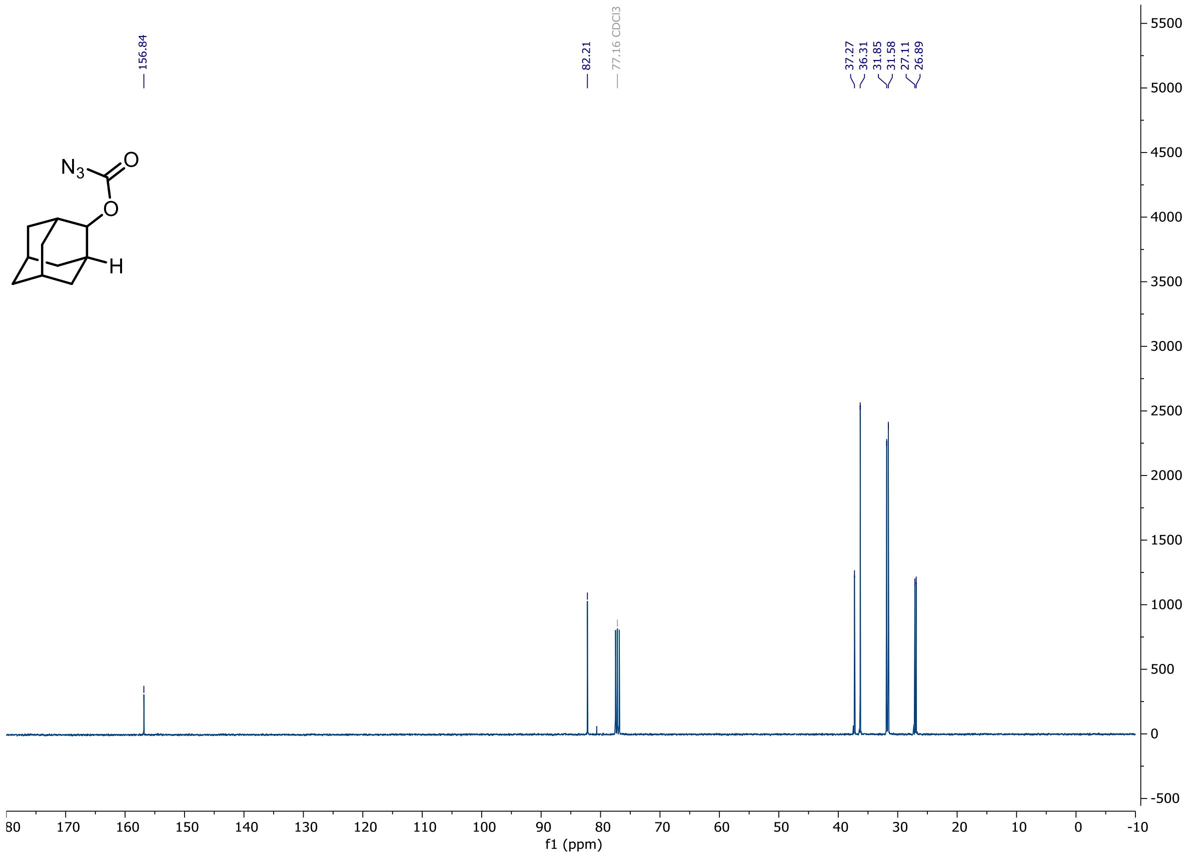
Compound 2c: ^{13}**C NMR-DEPT** (101 MHz, $CDCl_3$)



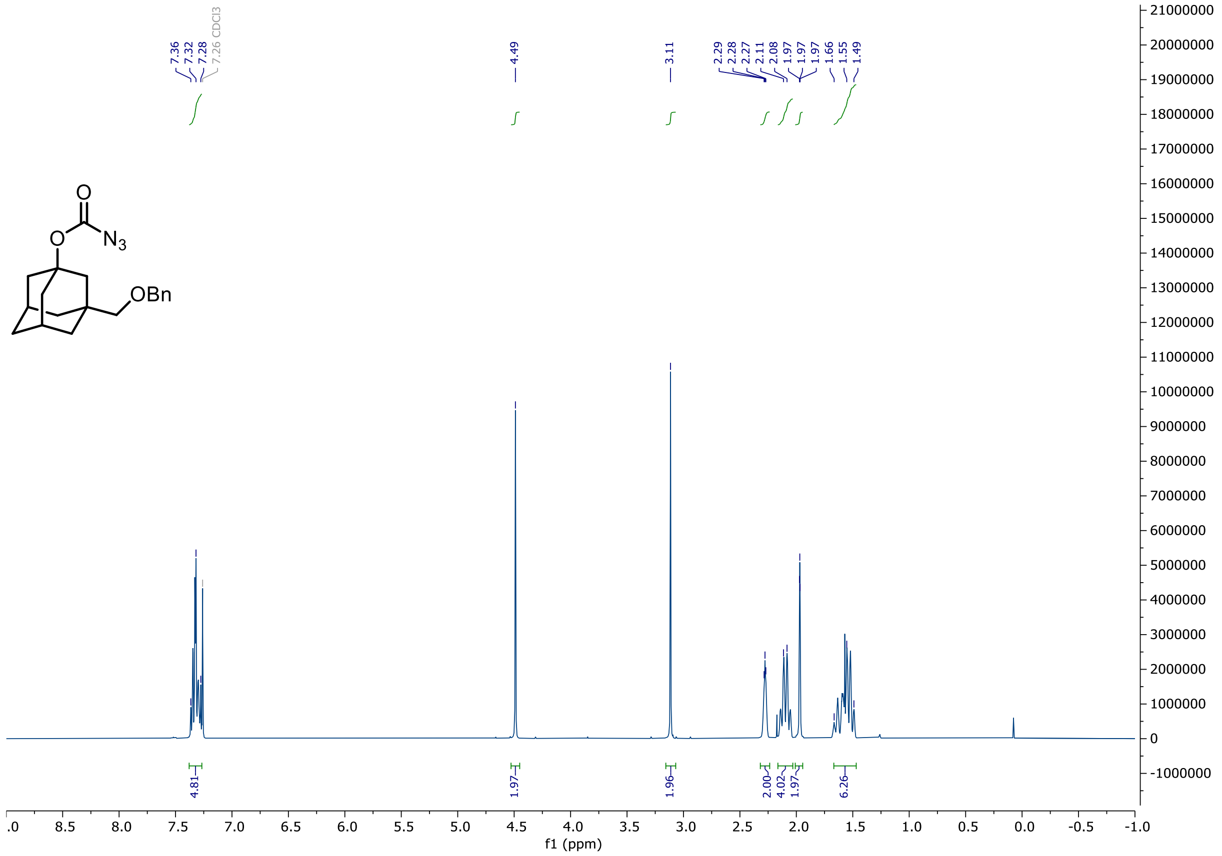
Compound 2d: ^{1}**H NMR** (400 MHz, $CDCl_3$)



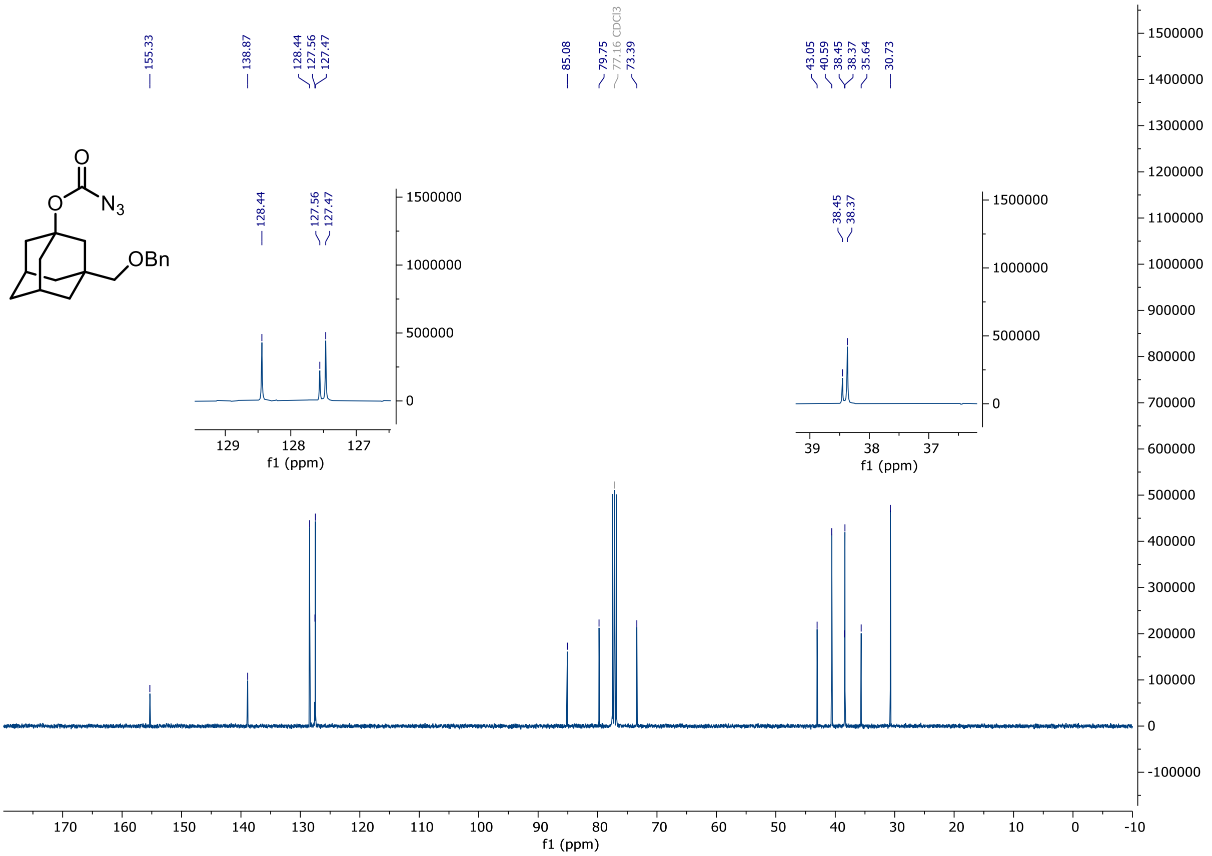
Compound 2d: ^{13}C NMR (101 MHz, $CDCl_3$)



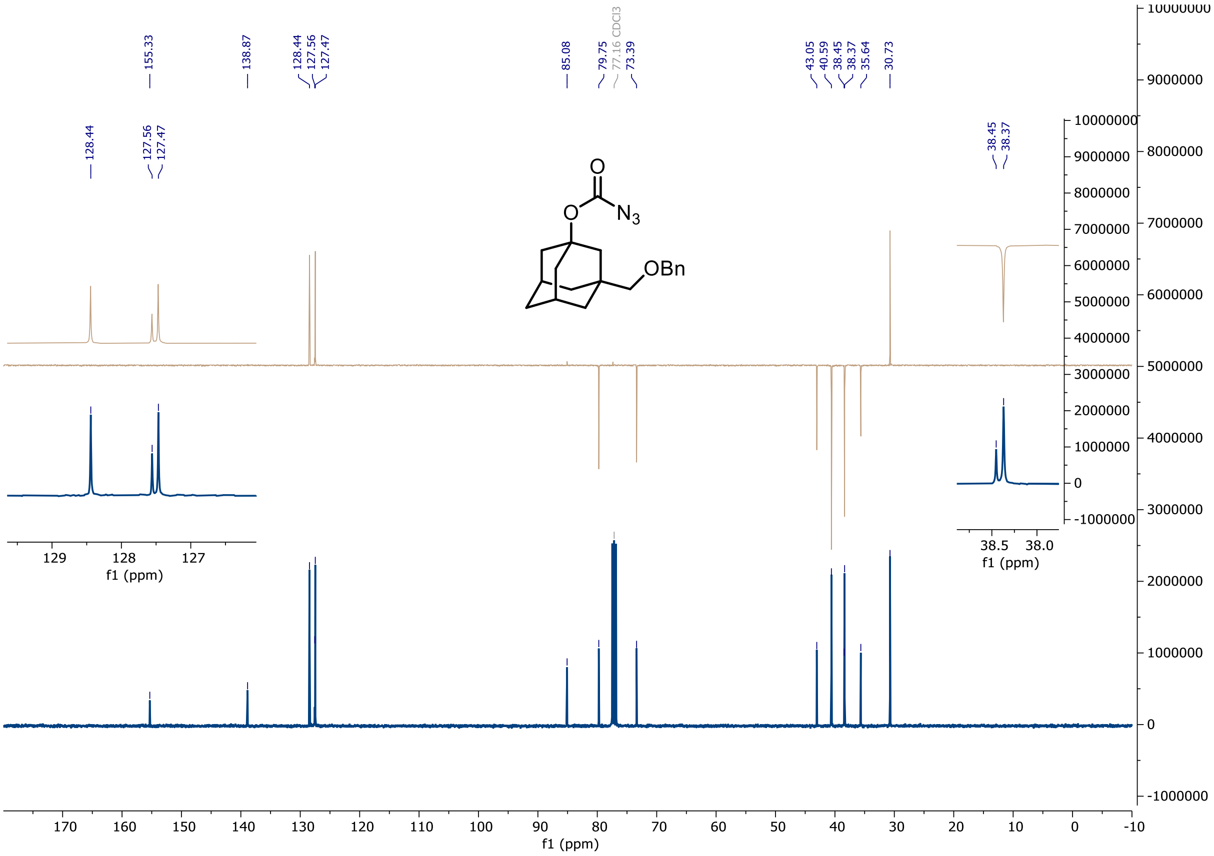
Compound 2e: ^{1}H NMR (400 MHz, $CDCl_3$)



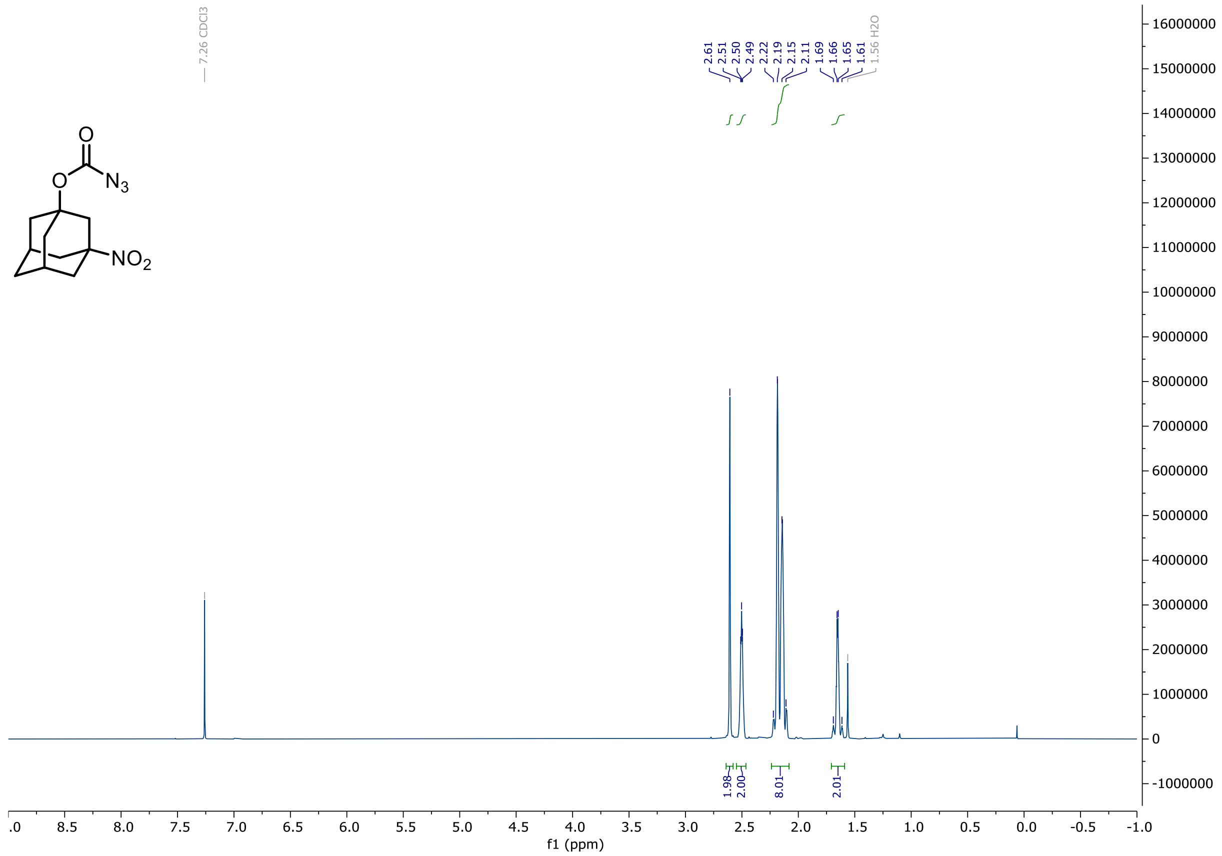
Compound 2e: ^{13}C NMR (101 MHz, $CDCl_3$)



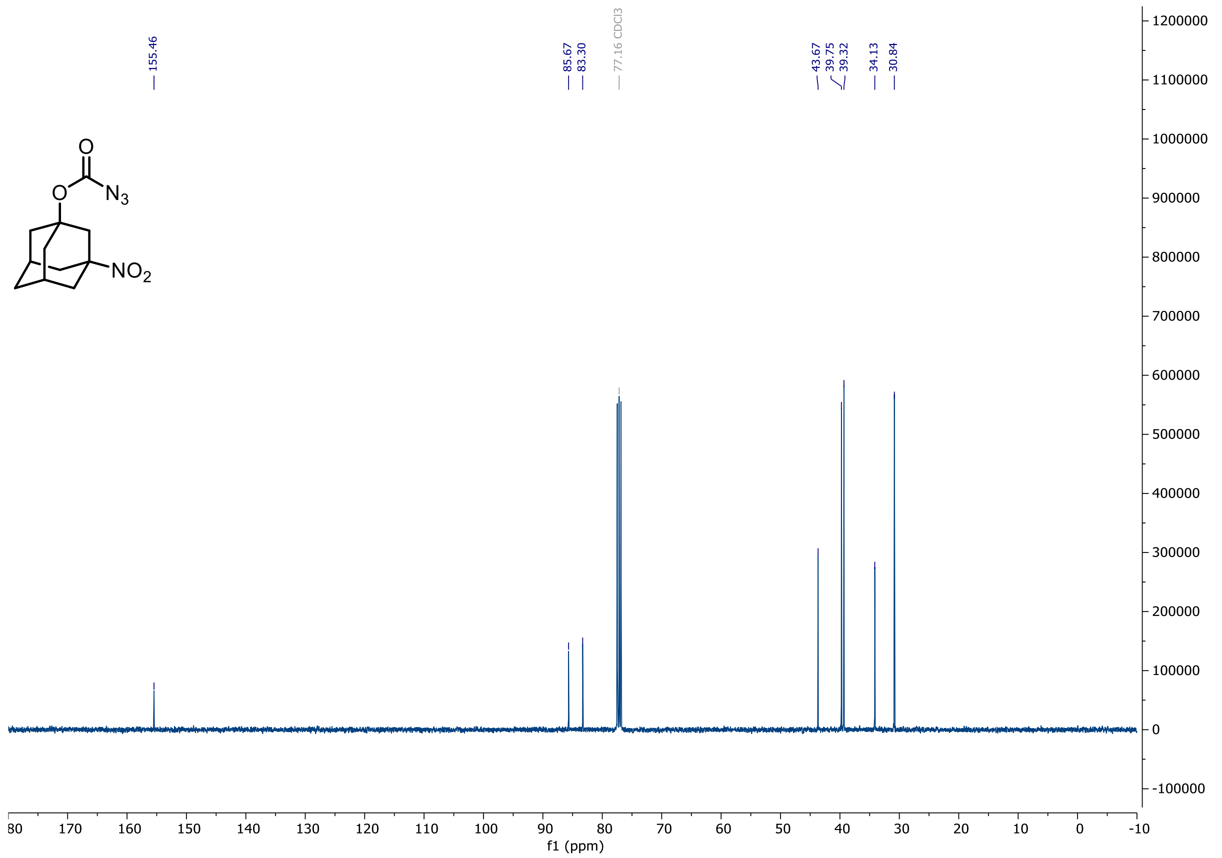
Compound 2e: ^{13}C NMR-DEPT (101 MHz, $CDCl_3$)



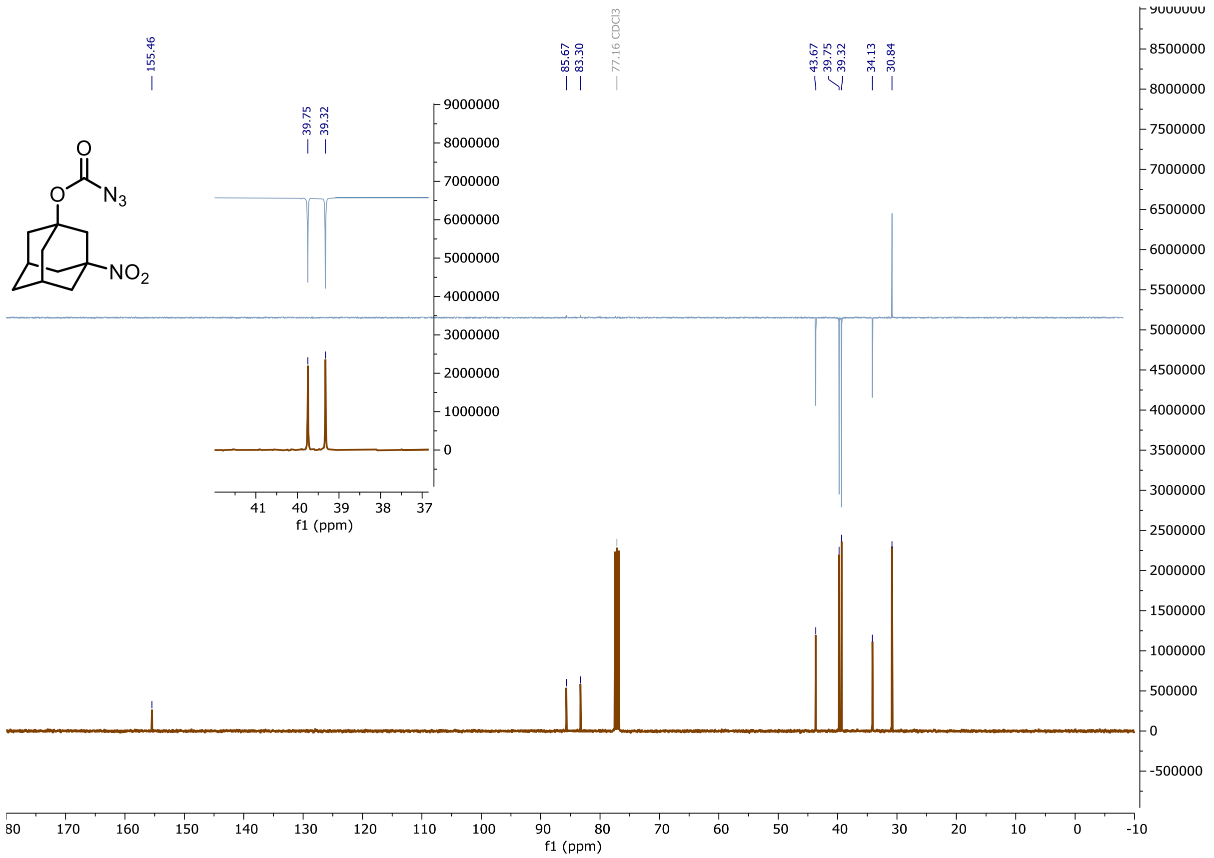
Compound 2f: ^{1}H NMR (400 MHz, $CDCl_3$)



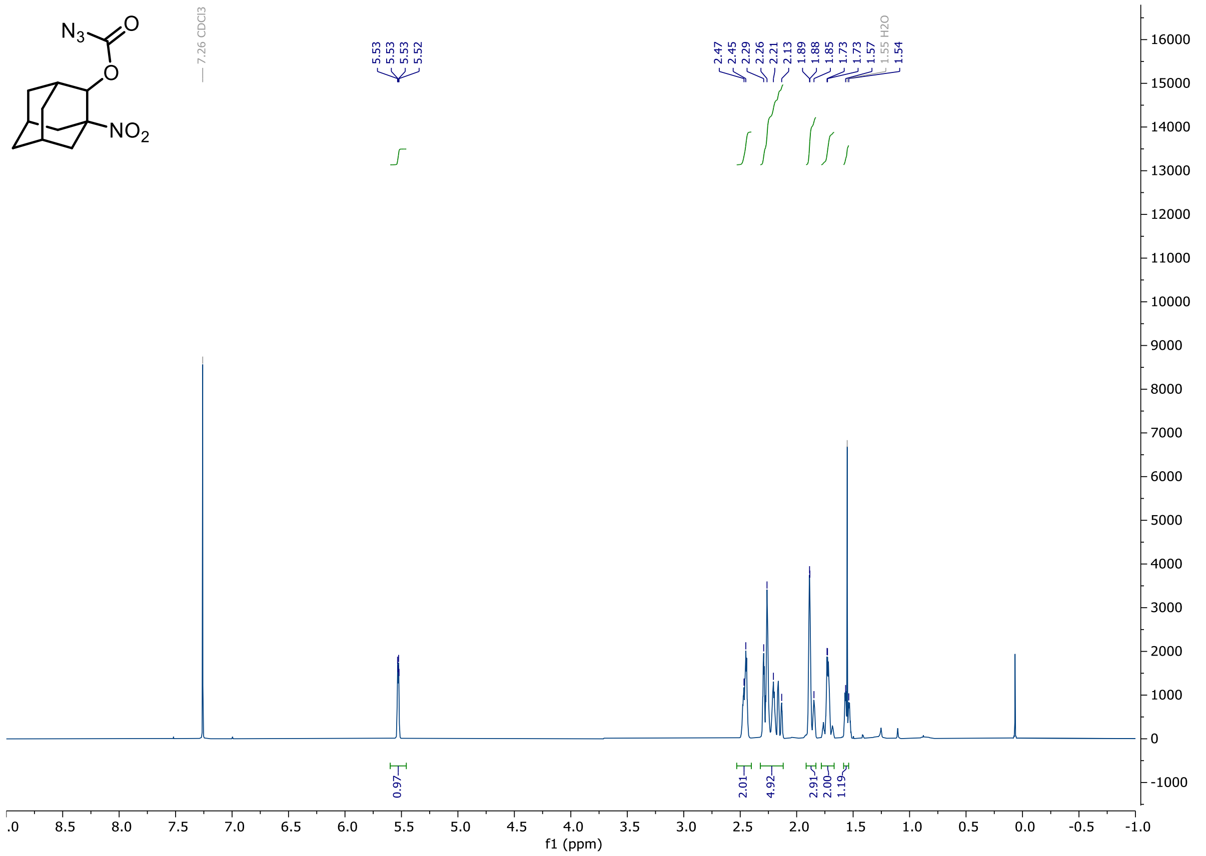
Compound 2f: ^{13}C NMR (101 MHz, $CDCl_3$)



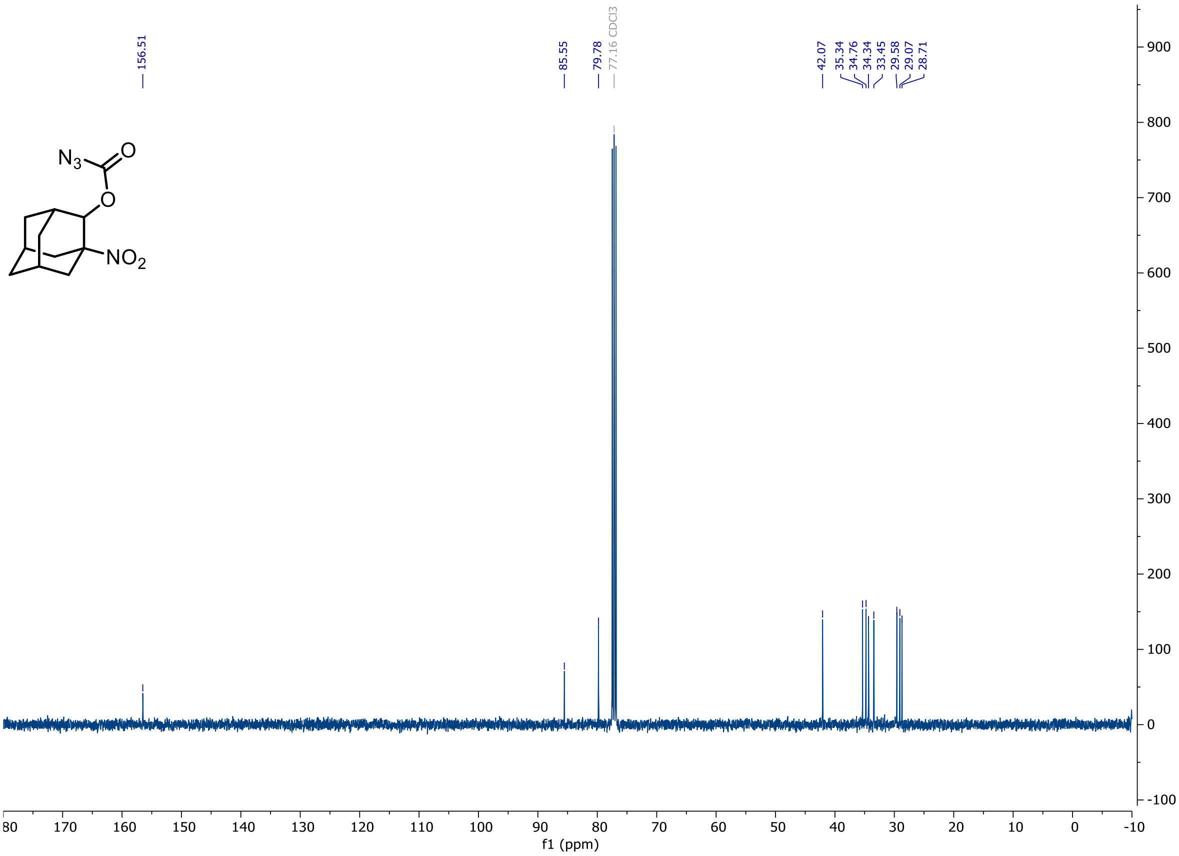
Compound 2f: ^{13}C NMR-DEPT (101 MHz, $CDCl_3$)



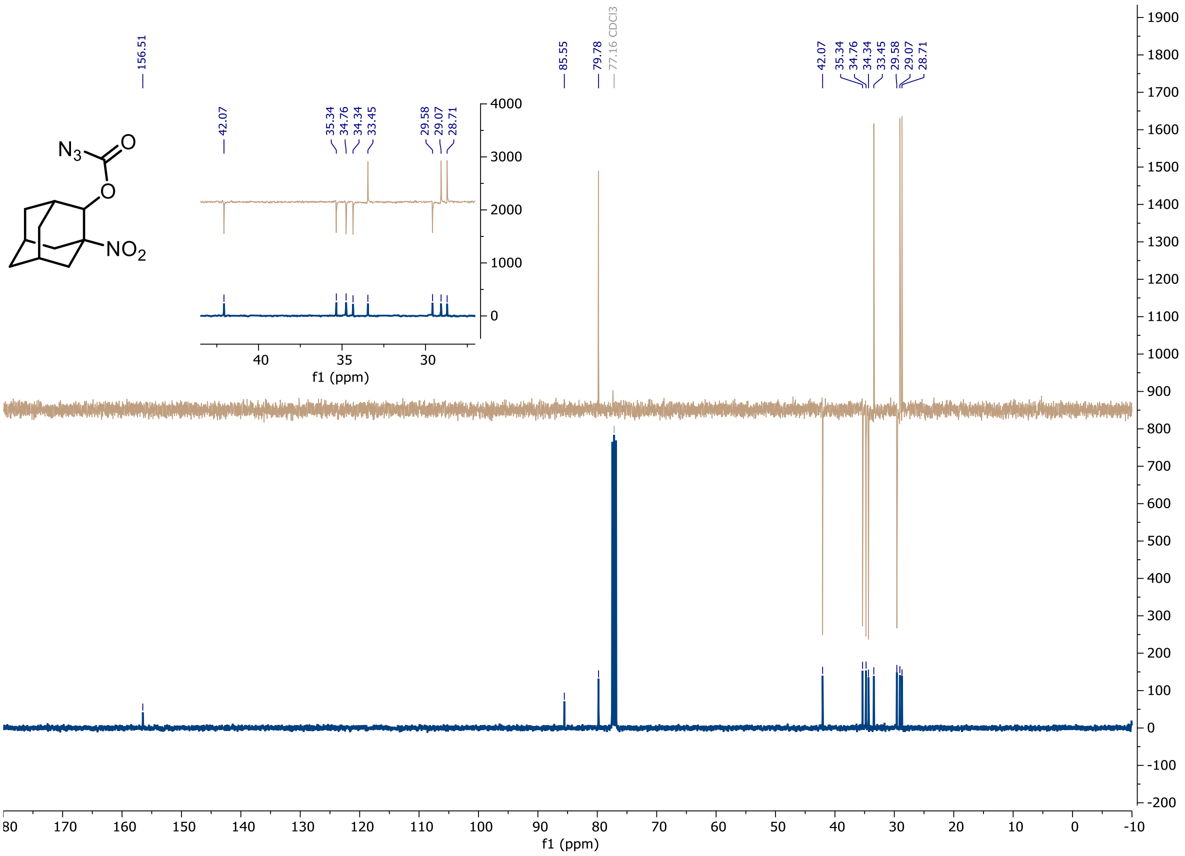
Compound 2g: ^{1}H NMR (400 MHz, $CDCl_3$)



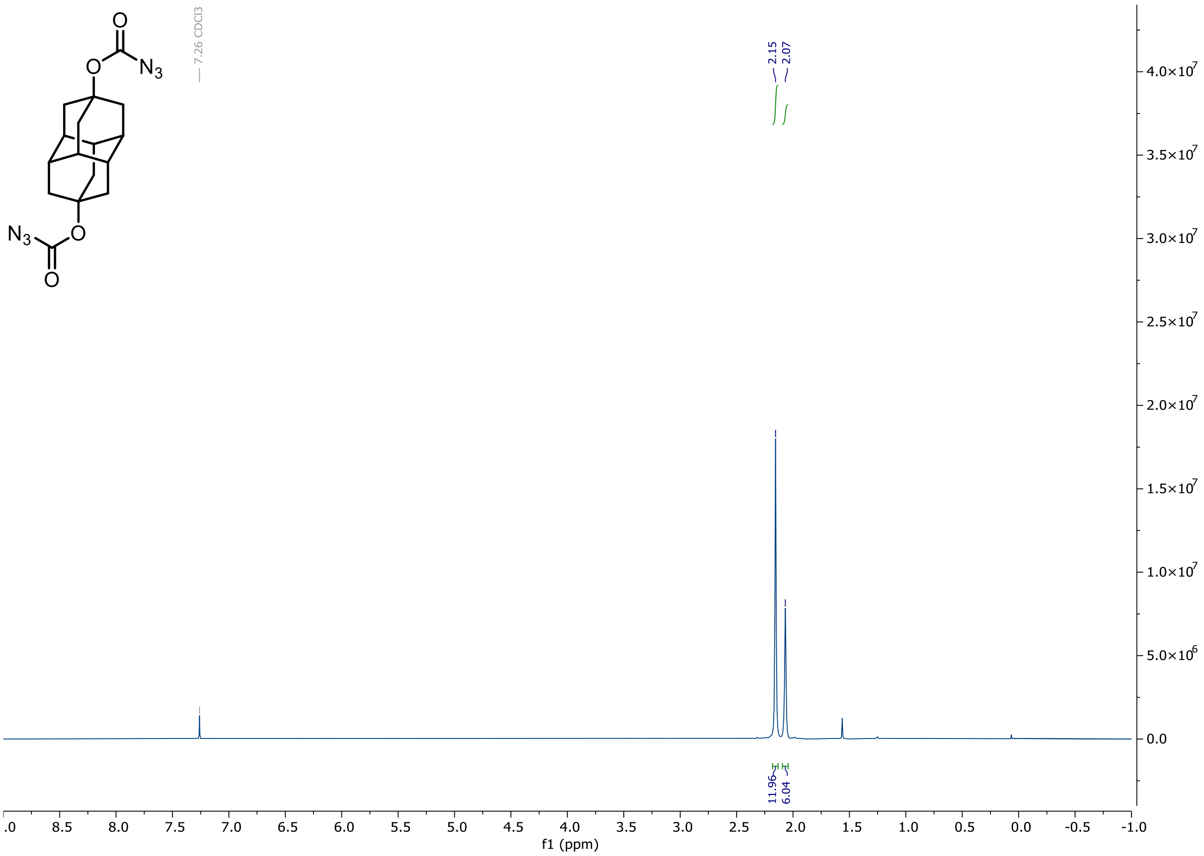
Compound 2g: ^{13}C NMR (101 MHz, $CDCl_3$)



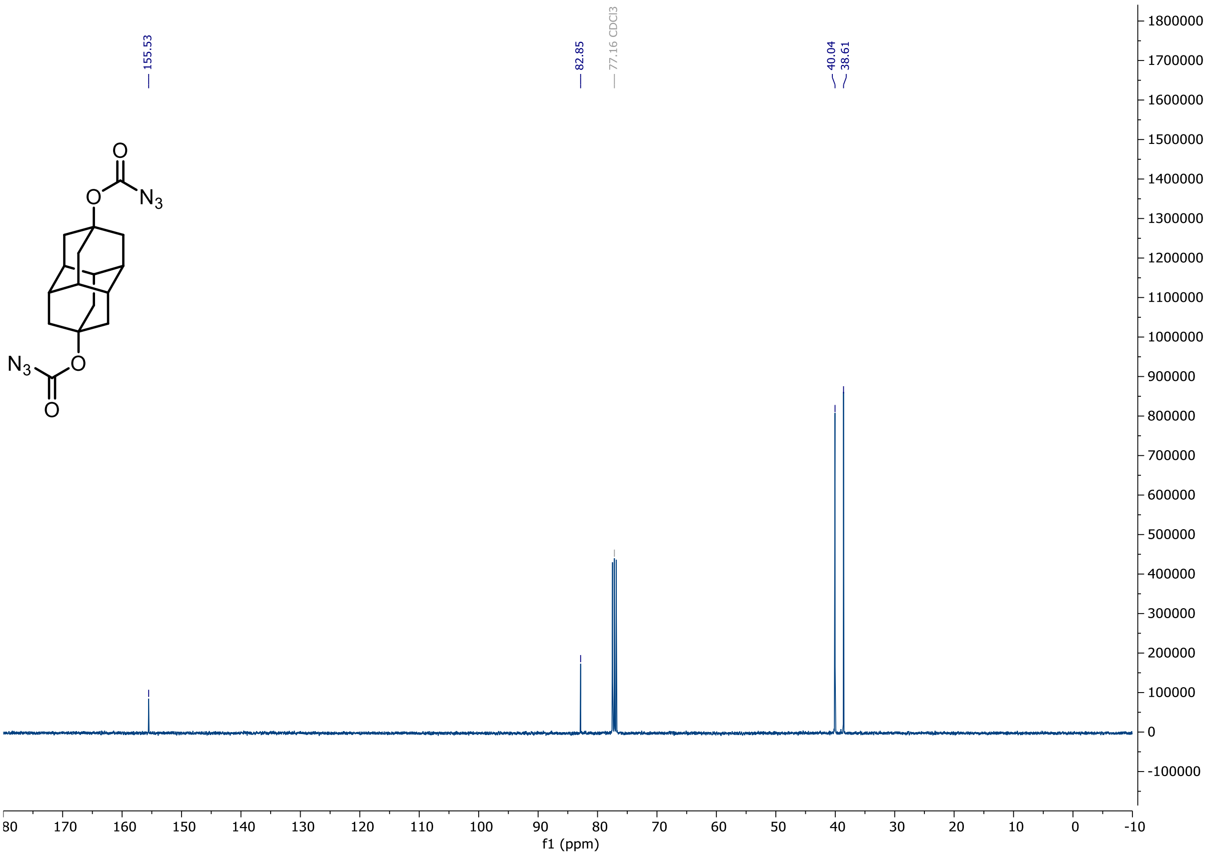
Compound 2g: ^{13}C NMR-DEPT (101 MHz, $CDCl_3$)



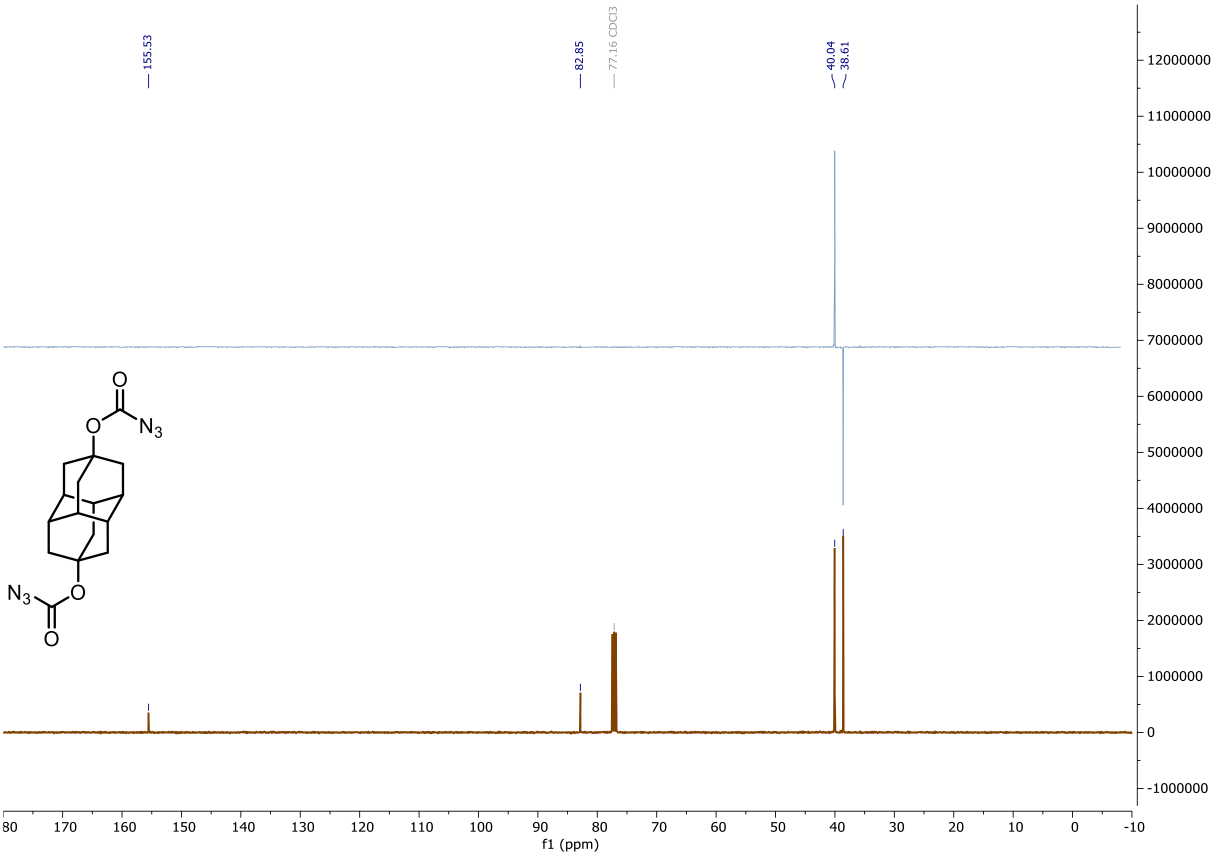
Compound 2h: ^{1}H NMR (400 MHz, $CDCl_3$)



Compound 2h: ^{13}C NMR (101 MHz, $CDCl_3$)

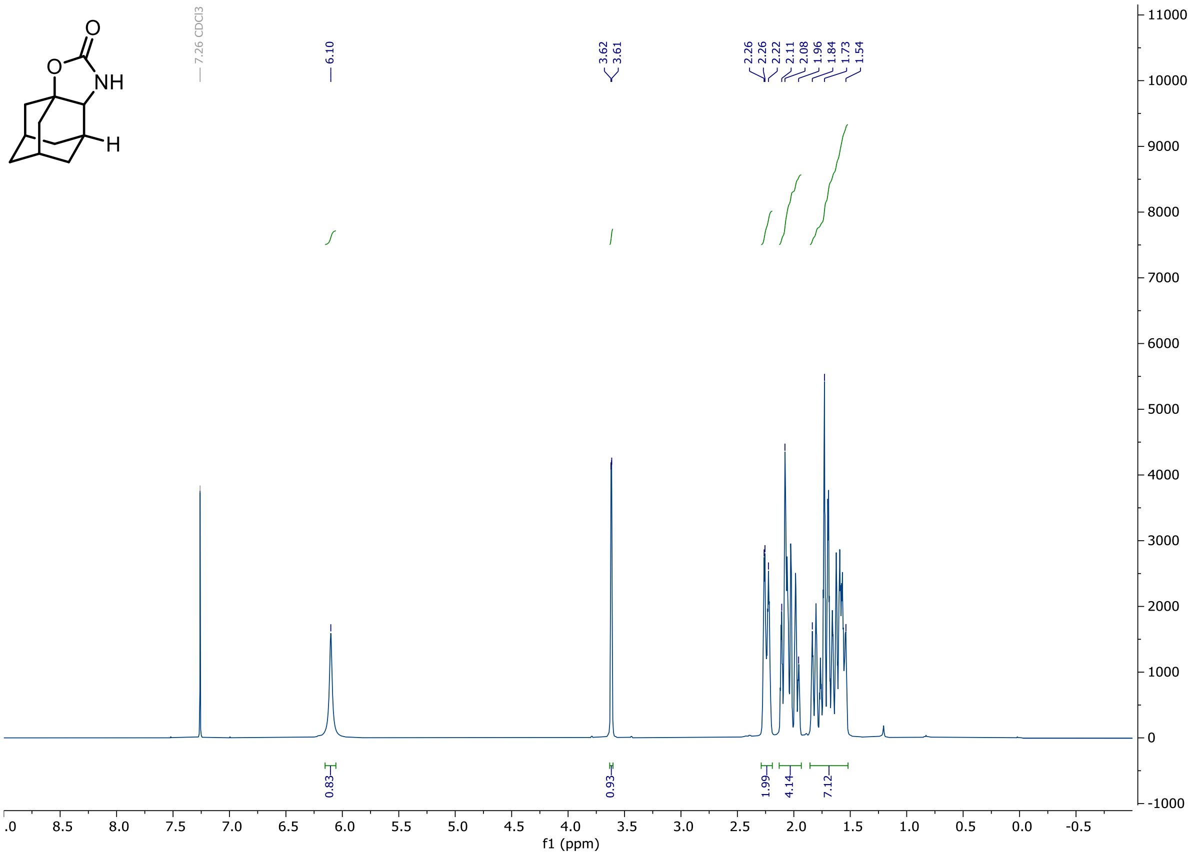


Compound 2h: ^{13}C NMR-DEPT (101 MHz, CDCl$_3$)

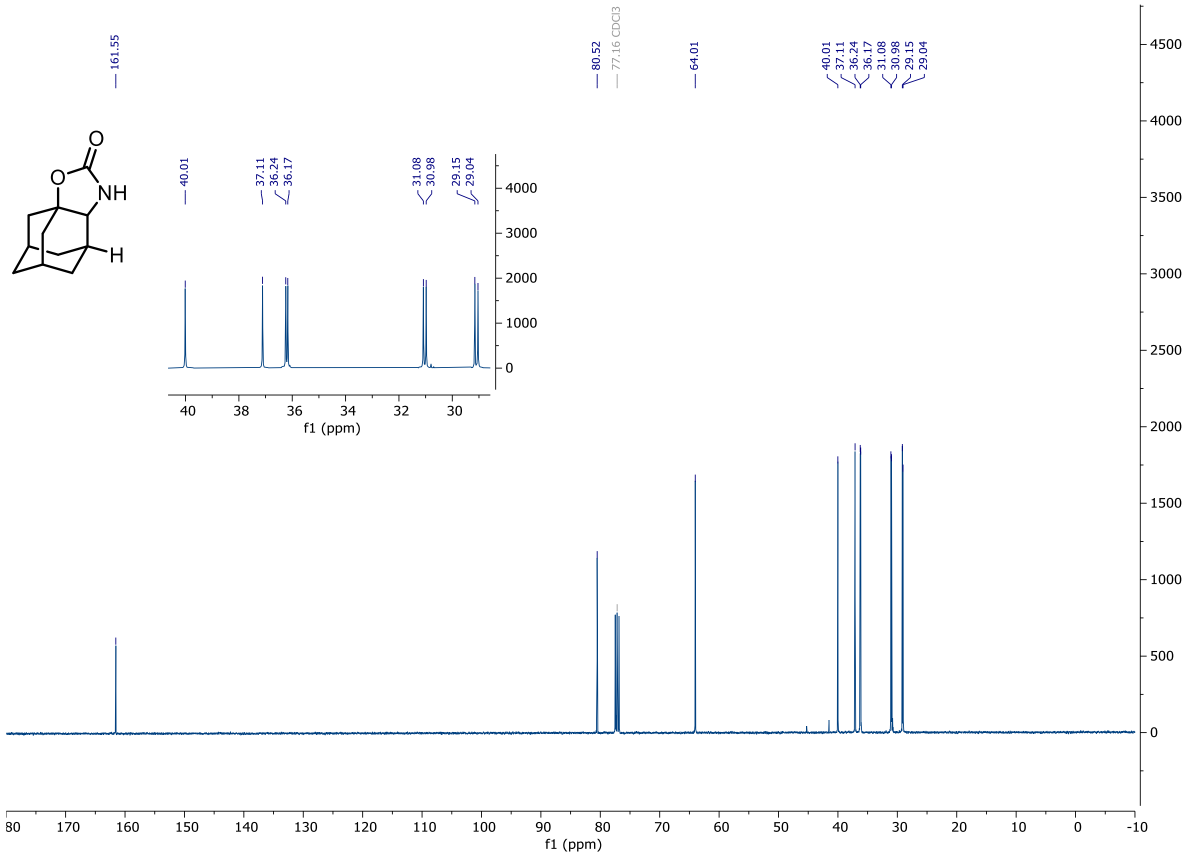


Annulated Carbamates

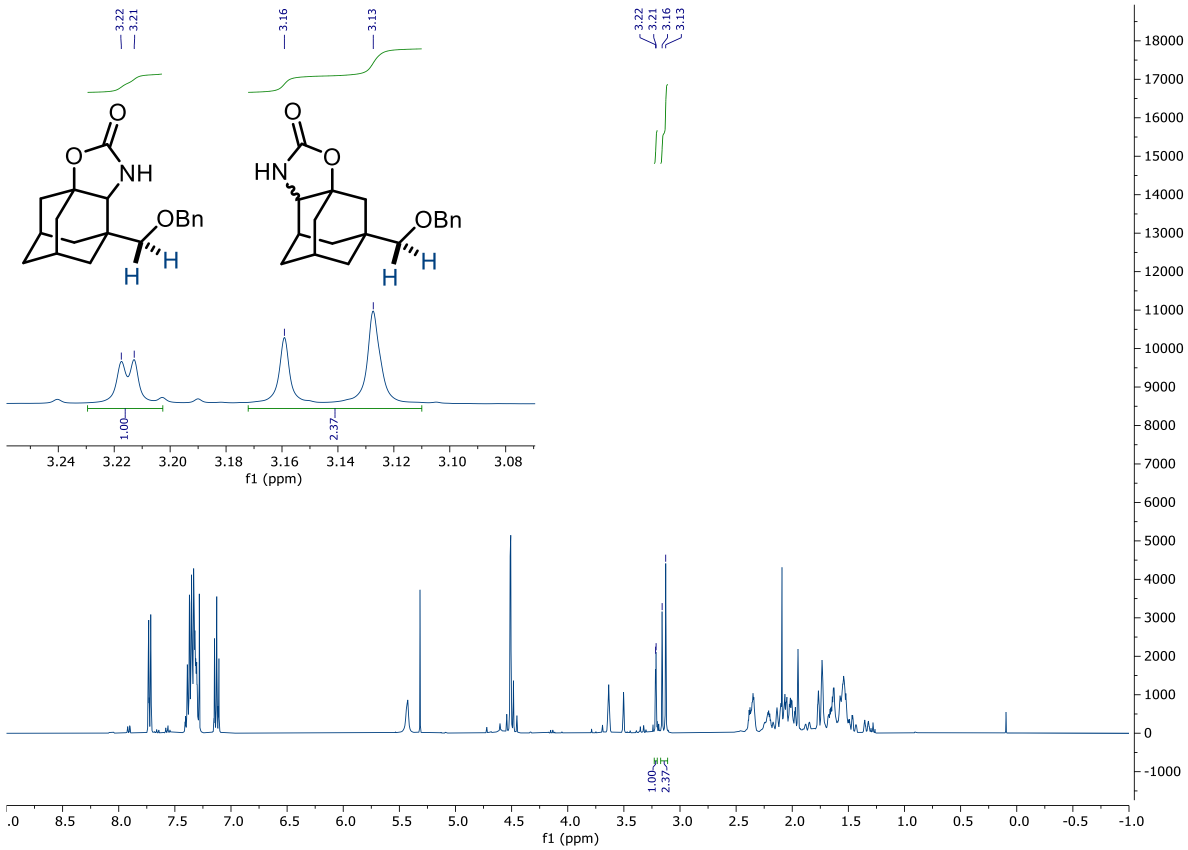
Compound 3a: ^{1}H NMR (400 MHz, $CDCl_3$)



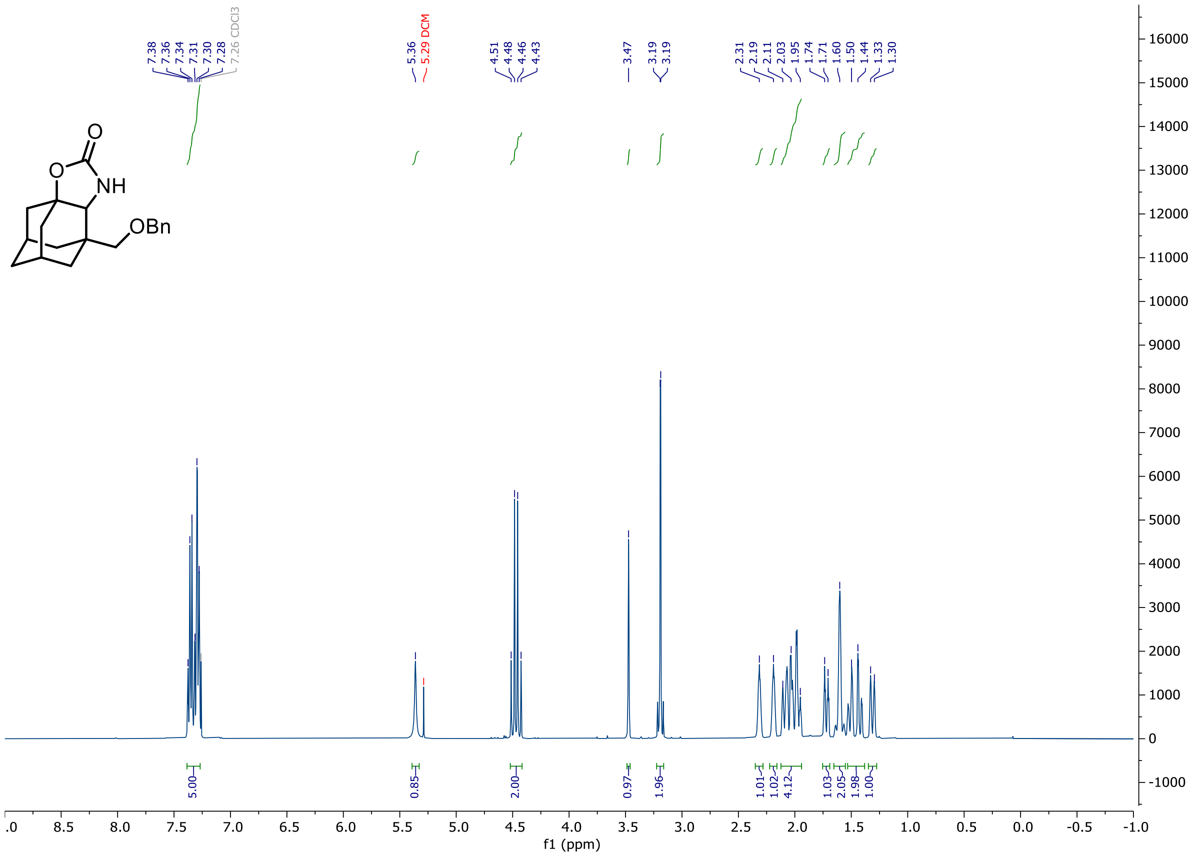
Compound 3a: ^{13}C NMR (101 MHz, CDCl$_3$)



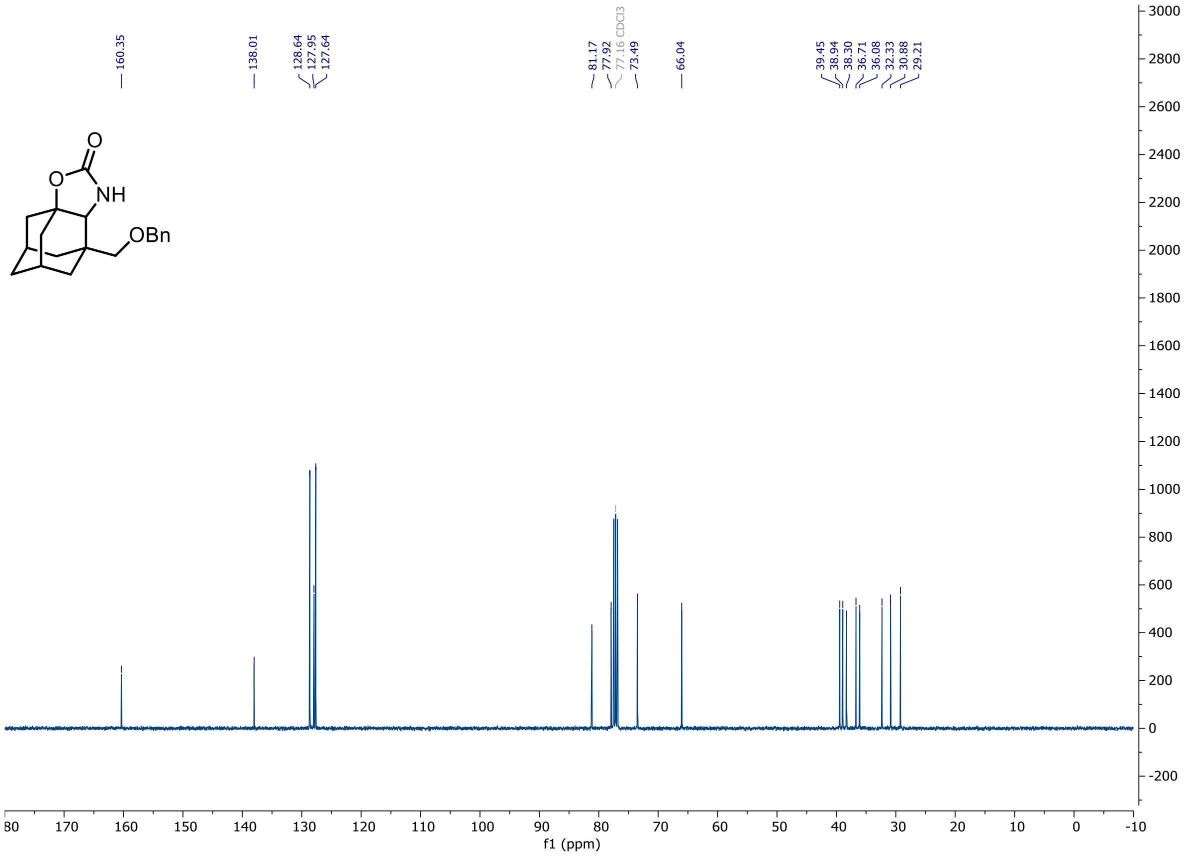
Compound 3b and 3c (Crude reaction mixture): ^{1}H NMR (400 MHz, CDCl$_3$)



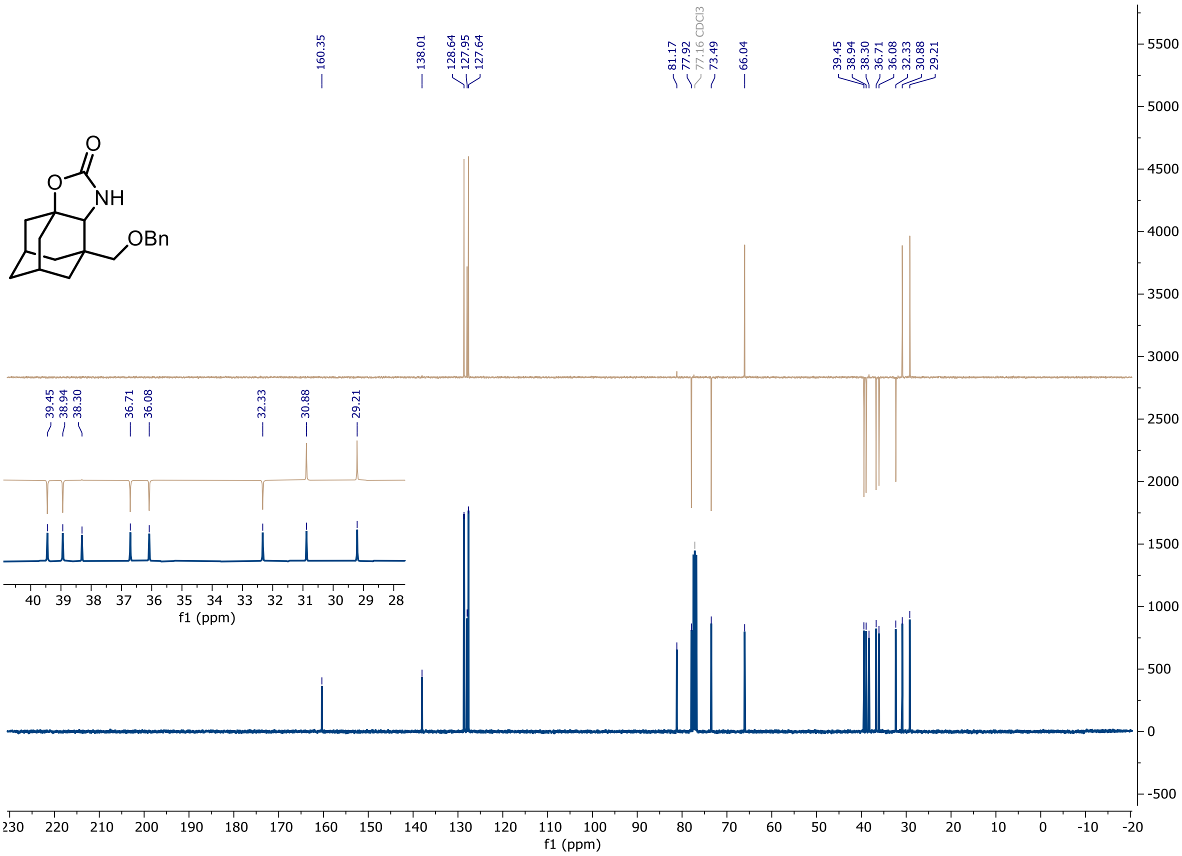
Compound 3b: ^{1}H NMR (400 MHz, $CDCl_3$)



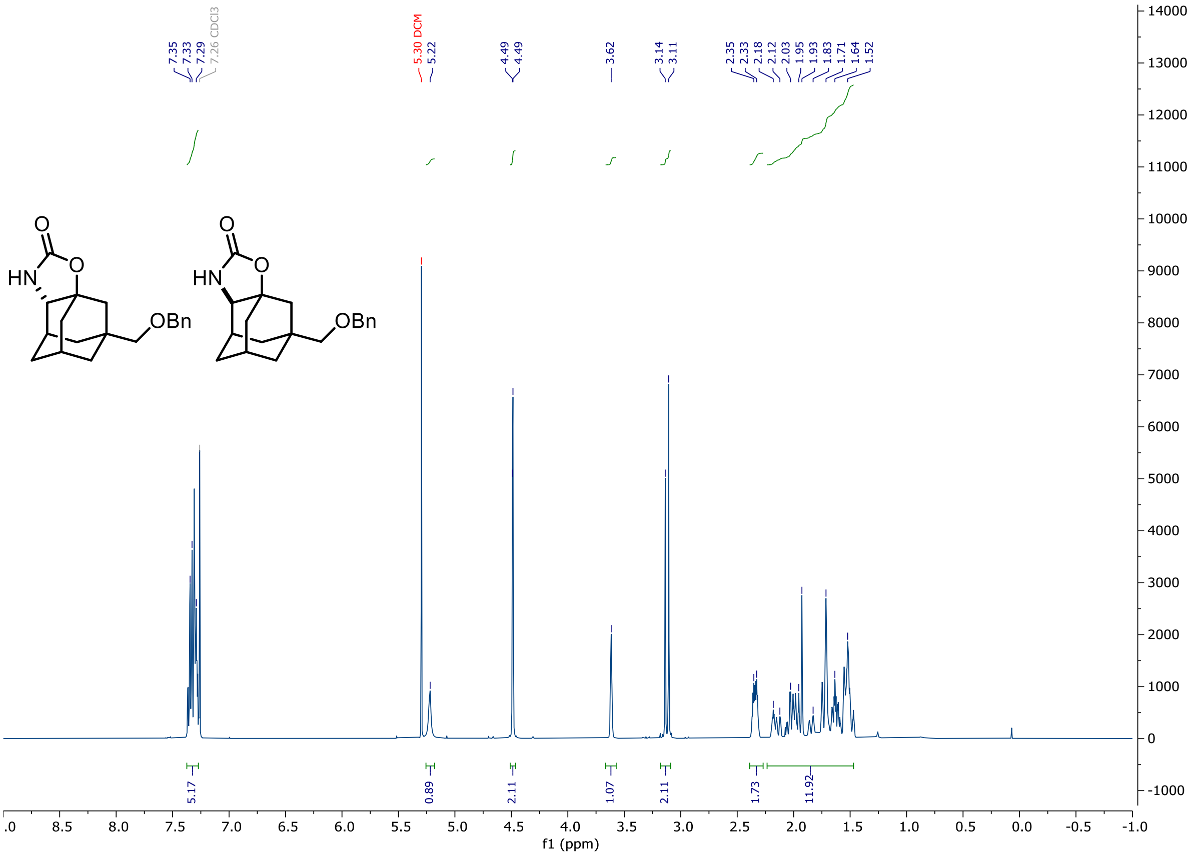
Compound 3b: ^{13}C NMR (101 MHz, $CDCl_3$)



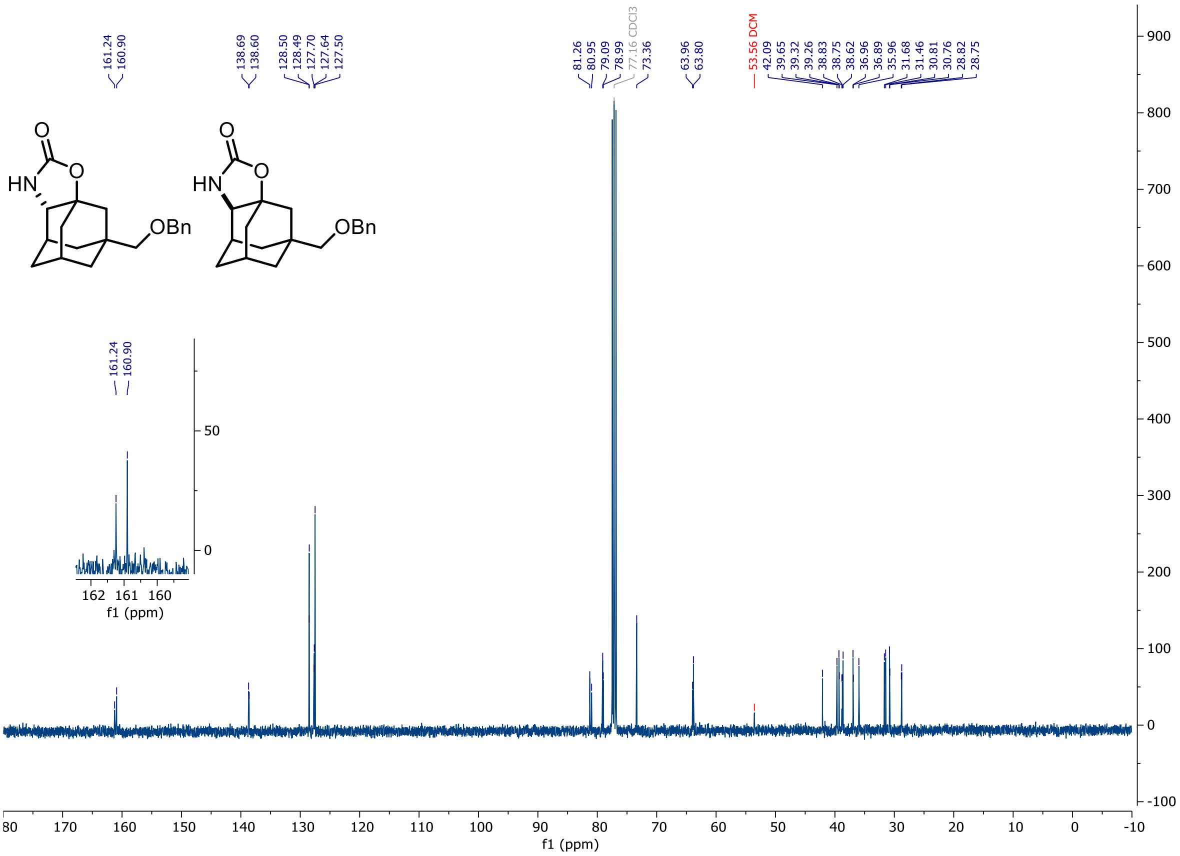
Compound 3b: ^{13}C NMR-DEPT (101 MHz, CDCl$_3$)



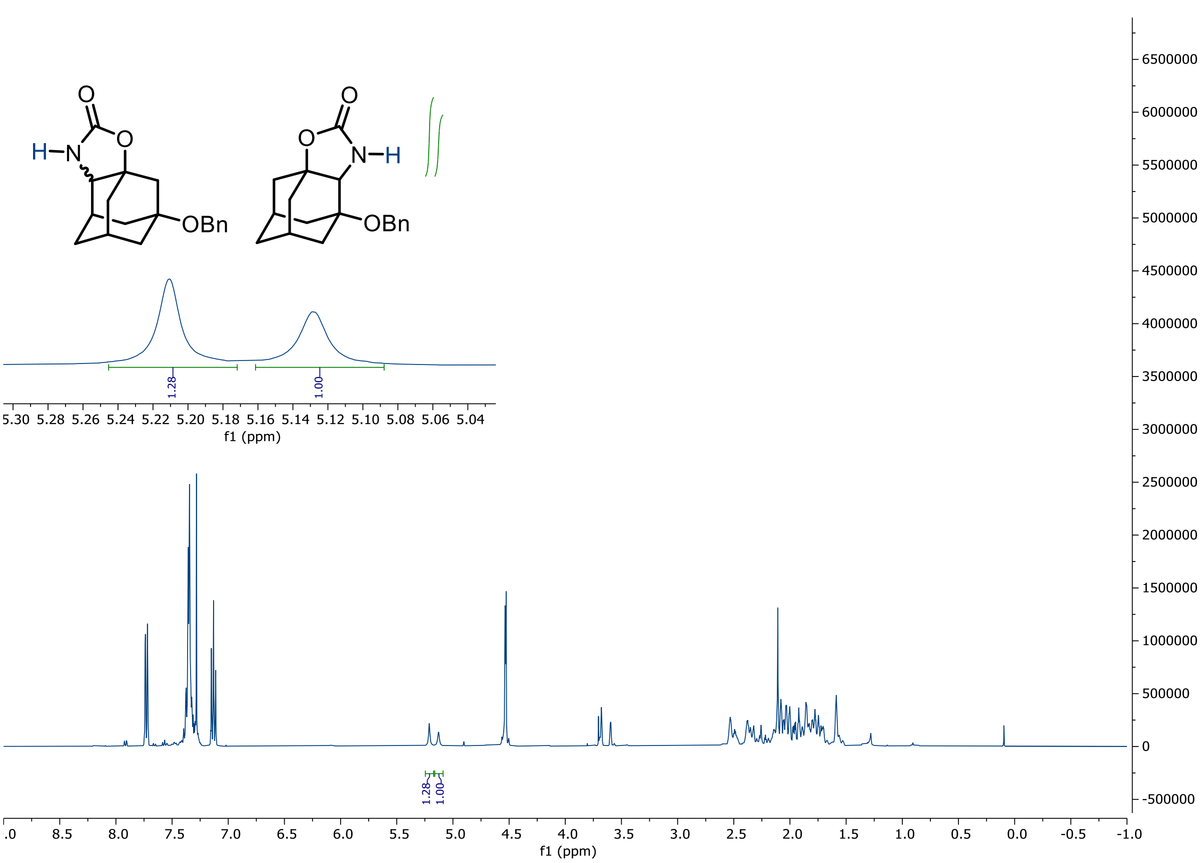
Compound 3c: ^{1}H NMR (400 MHz, CDCl$_3$)



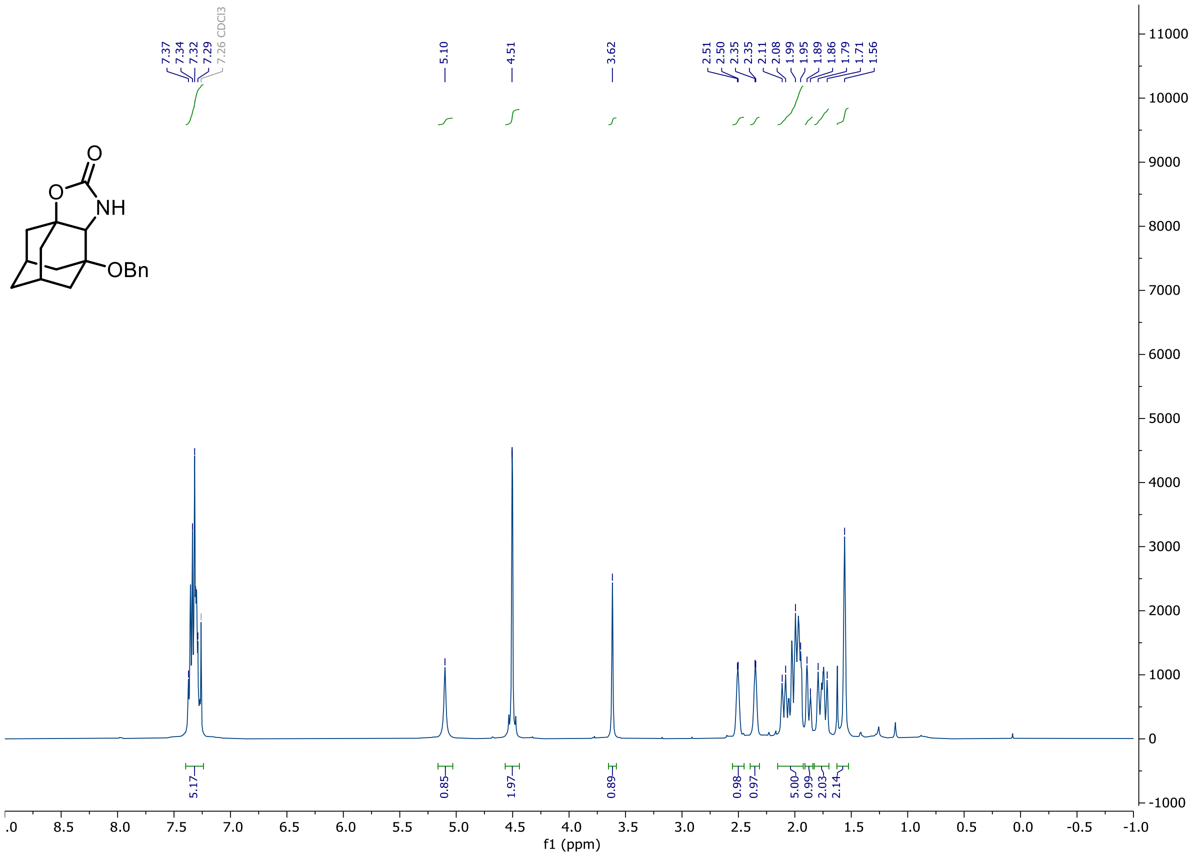
Compound 3c: ^{13}C NMR (101 MHz, $CDCl_3$)



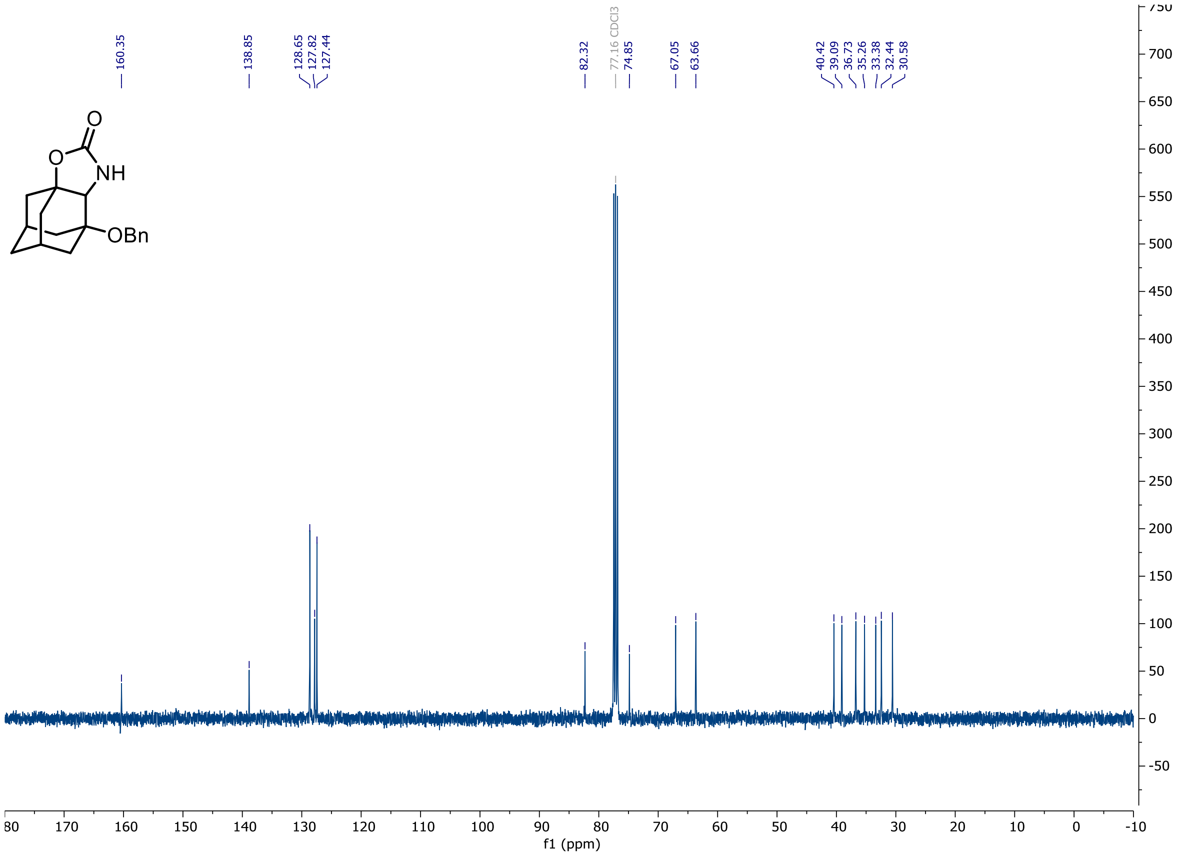
Compound 3d and 3e (Crude reaction mixture): ^{1}H NMR (400 MHz, $CDCl_3$)



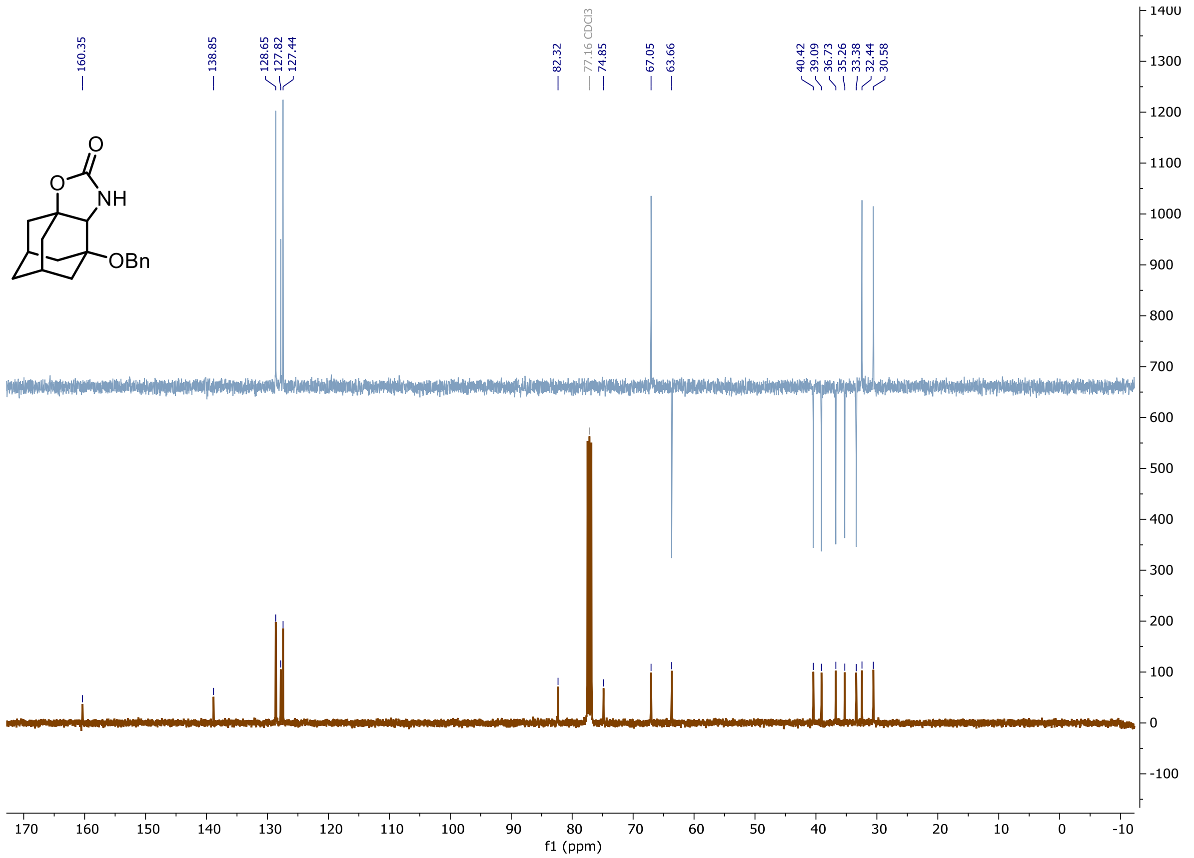
Compound 3d: ^{1}H NMR (400 MHz, CDCl$_3$)



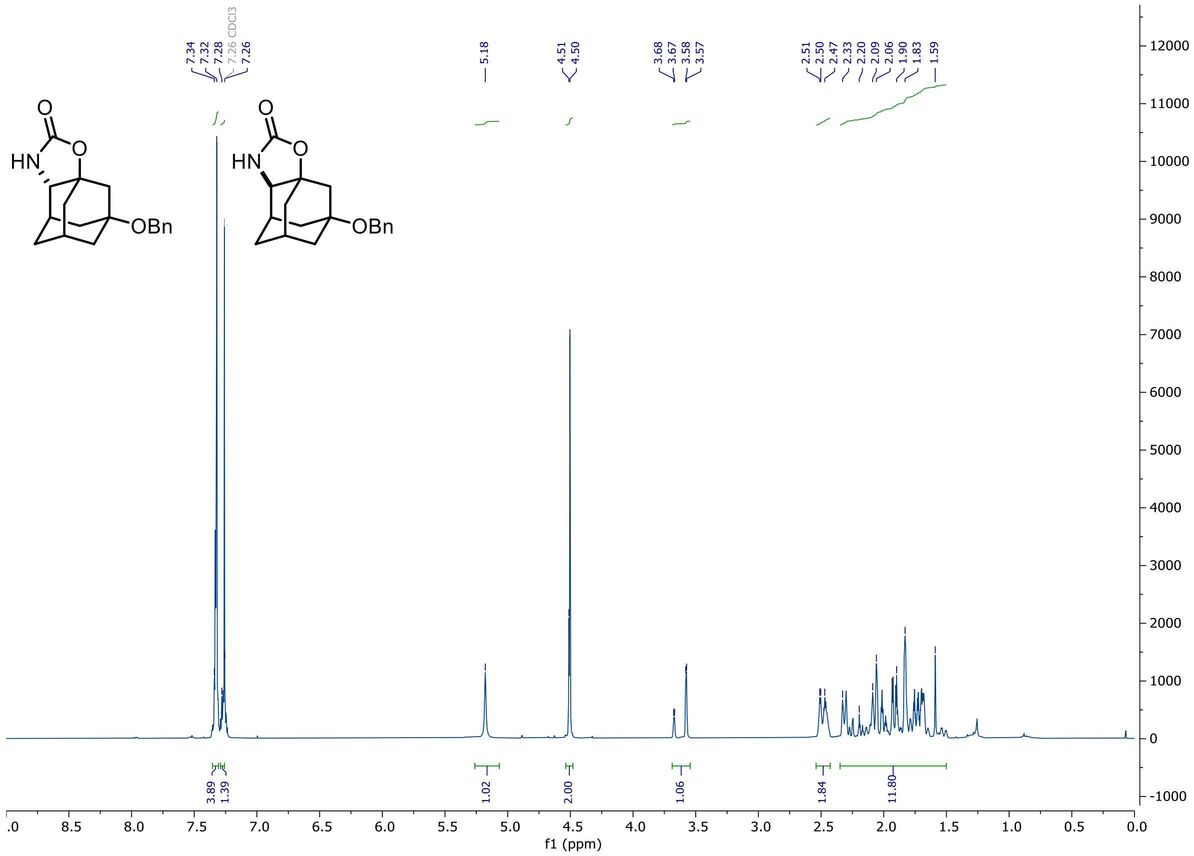
Compound 3d: ^{13}C NMR (101 MHz, CDCl$_3$)



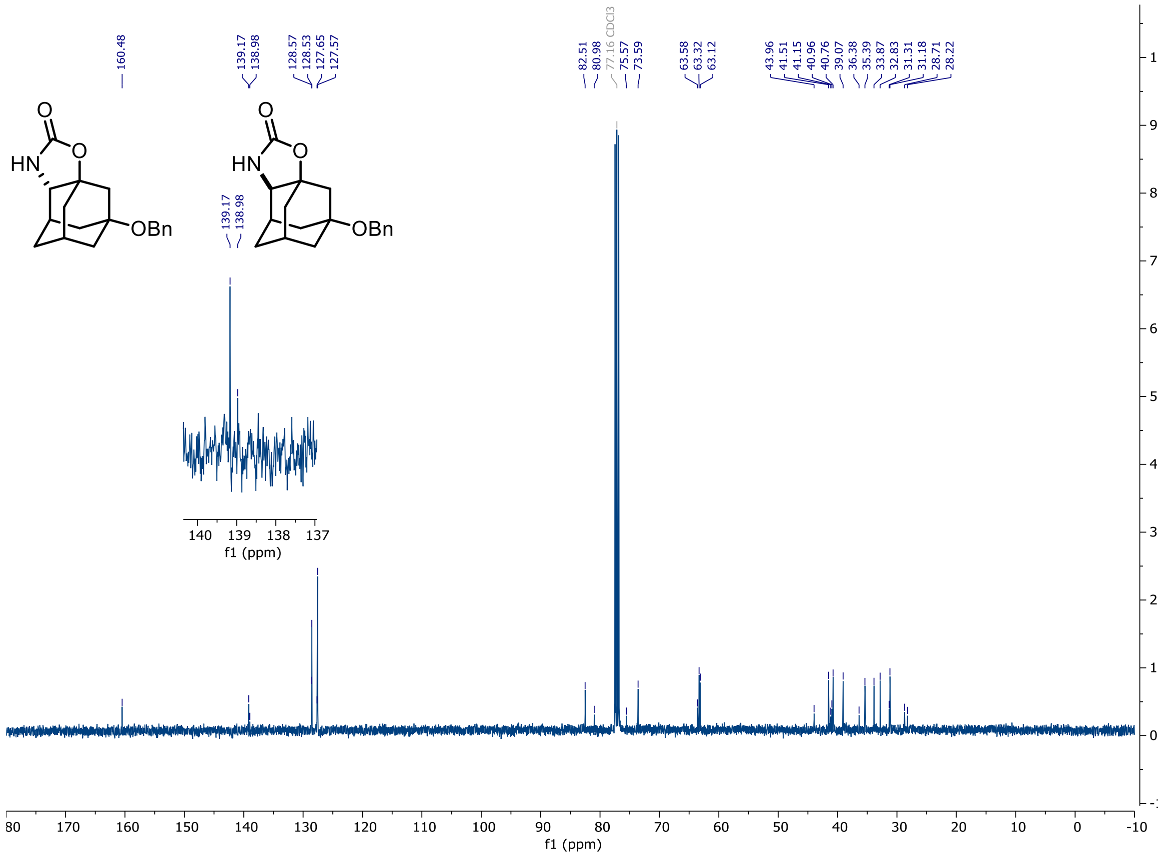
Compound 3d: ^{13}C NMR-DEPT (101 MHz, CDCl$_3$)



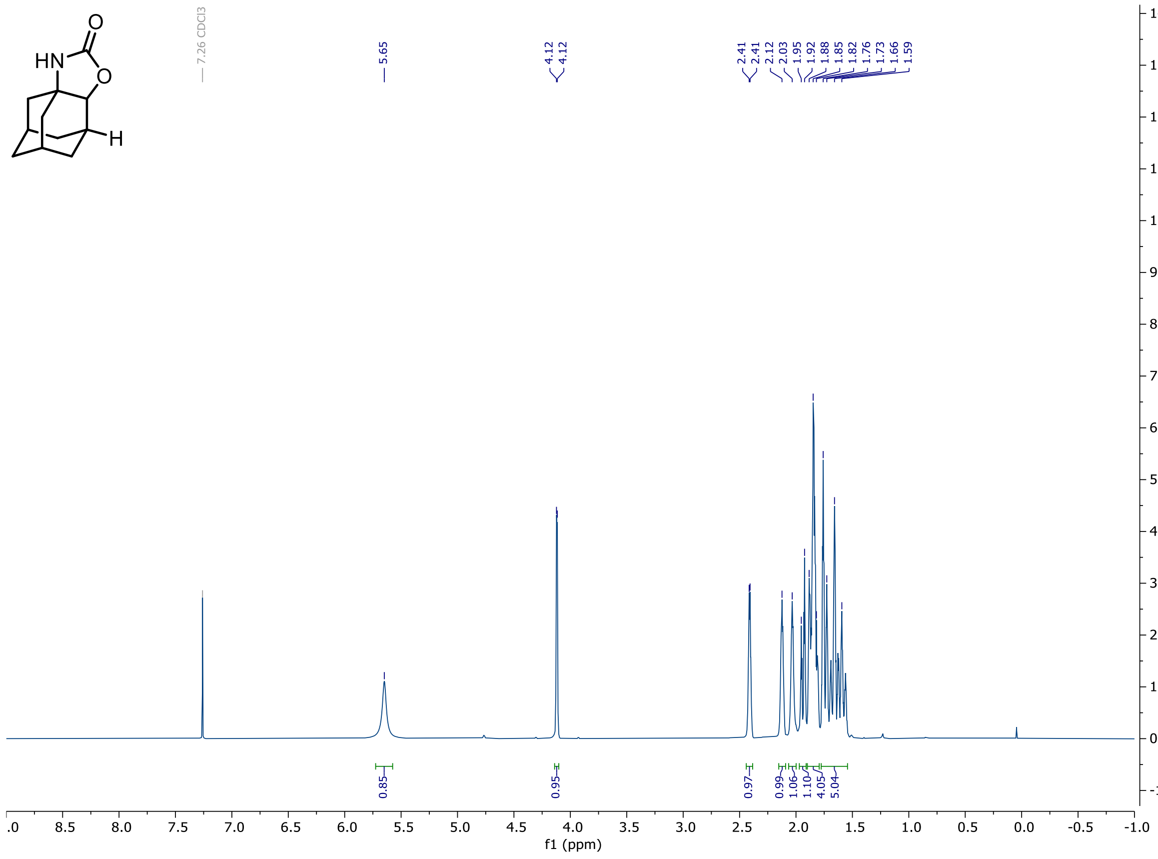
Compound 3e: ^{1}H NMR (400 MHz, CDCl$_3$)



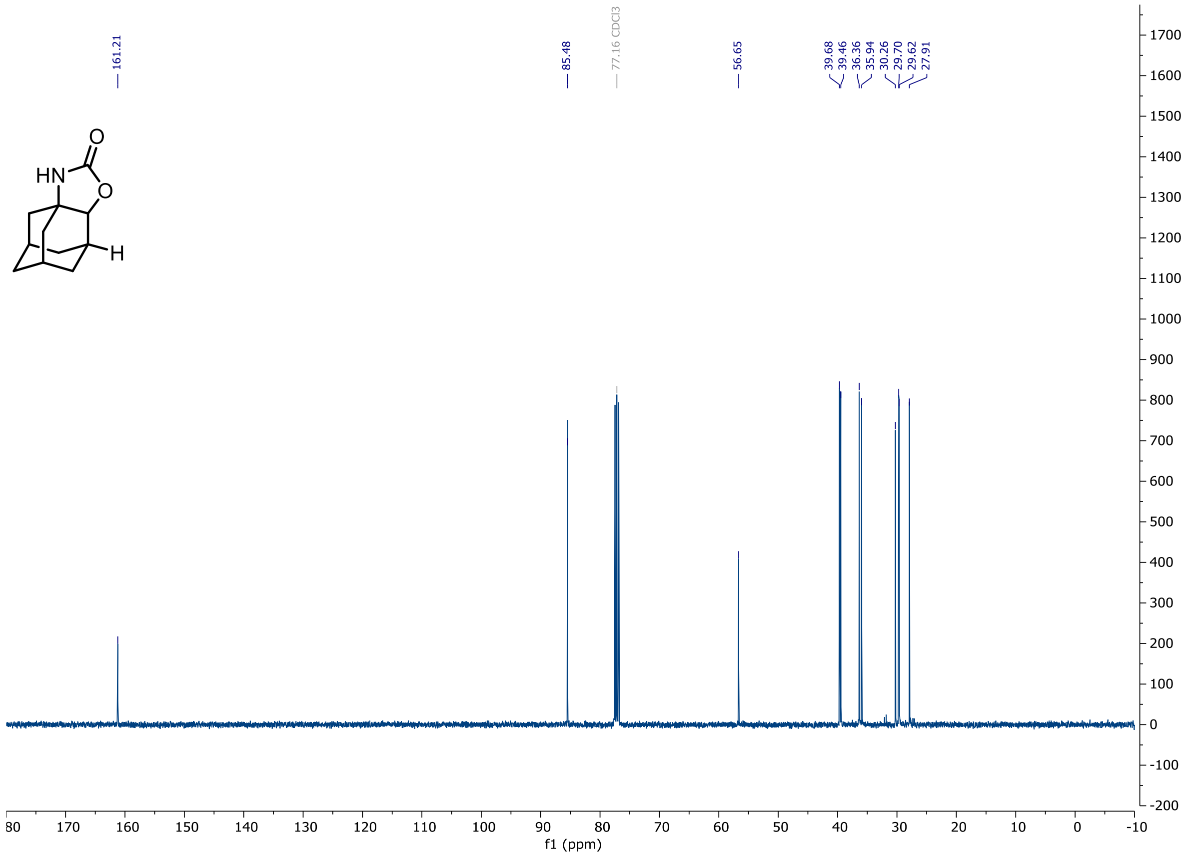
Compound 3e: ^{13}C NMR (101 MHz, CDCl$_3$)



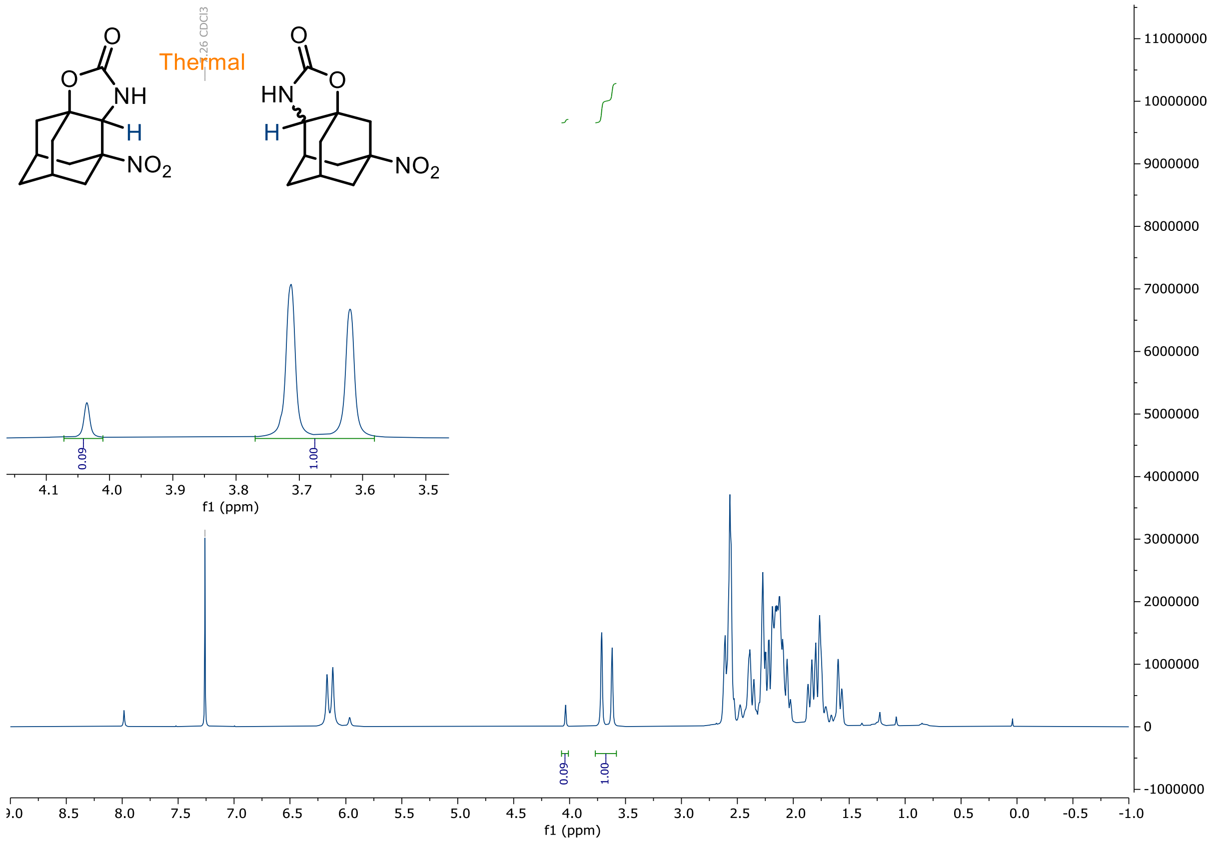
Compound 3f: ^{1}H NMR (400 MHz, CDCl$_3$)



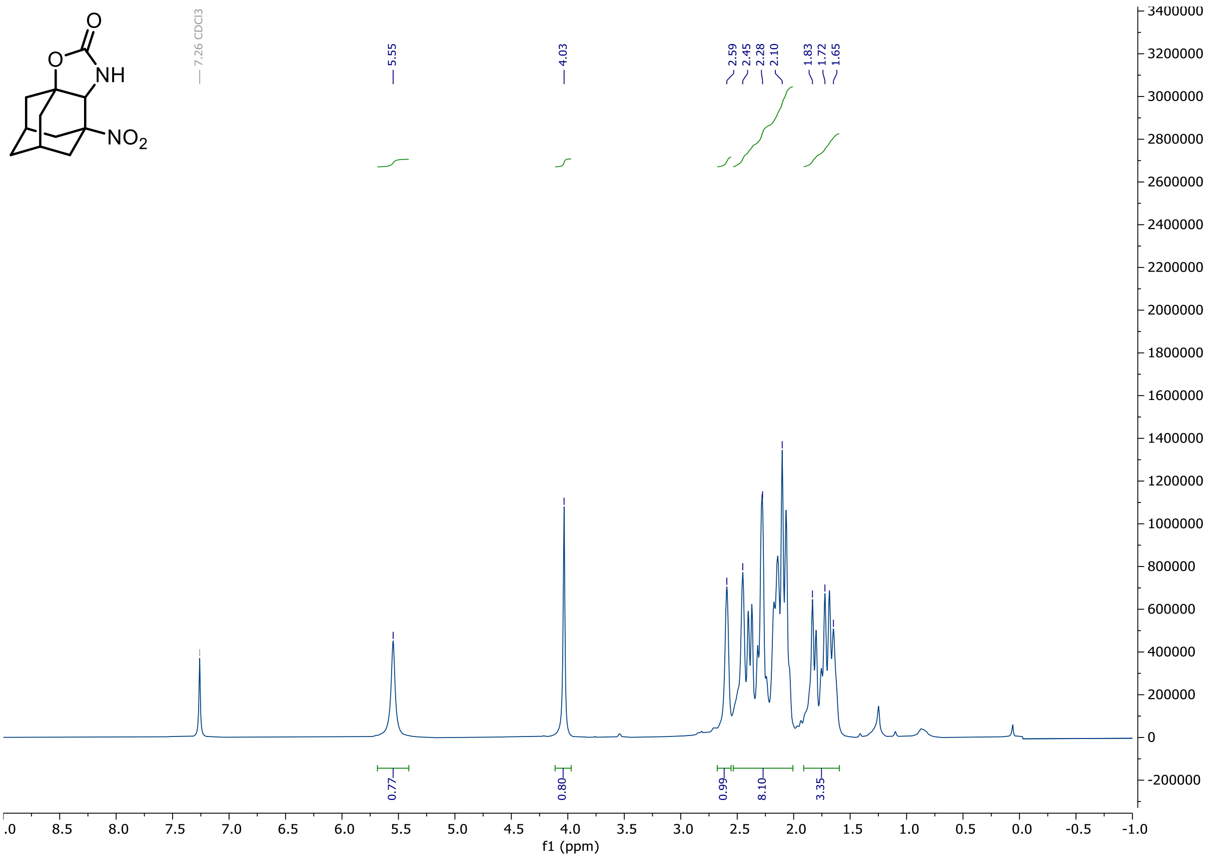
Compound 3f: ^{13}C NMR (101 MHz, CDCl$_3$)



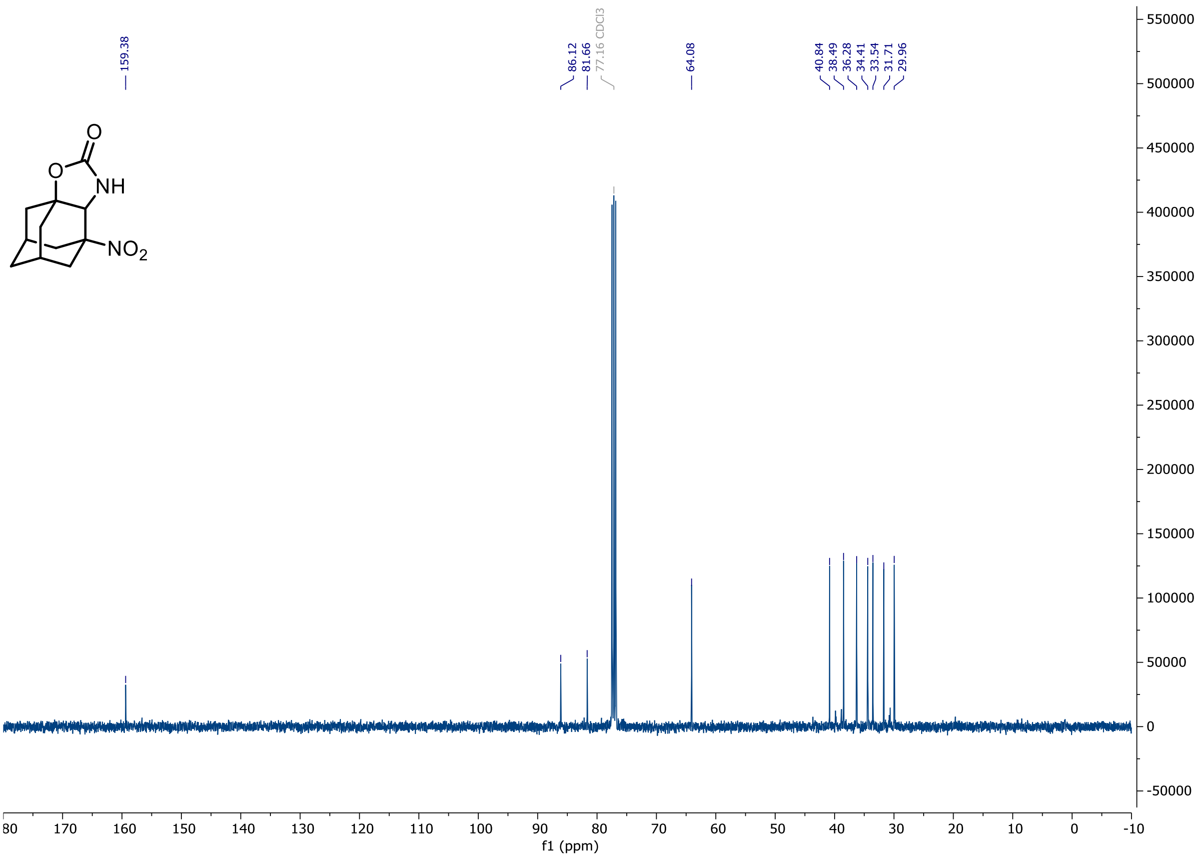
Compound 3h and 3i (Crude reaction mixture): ^{1}H NMR (400 MHz, CDCl$_3$)



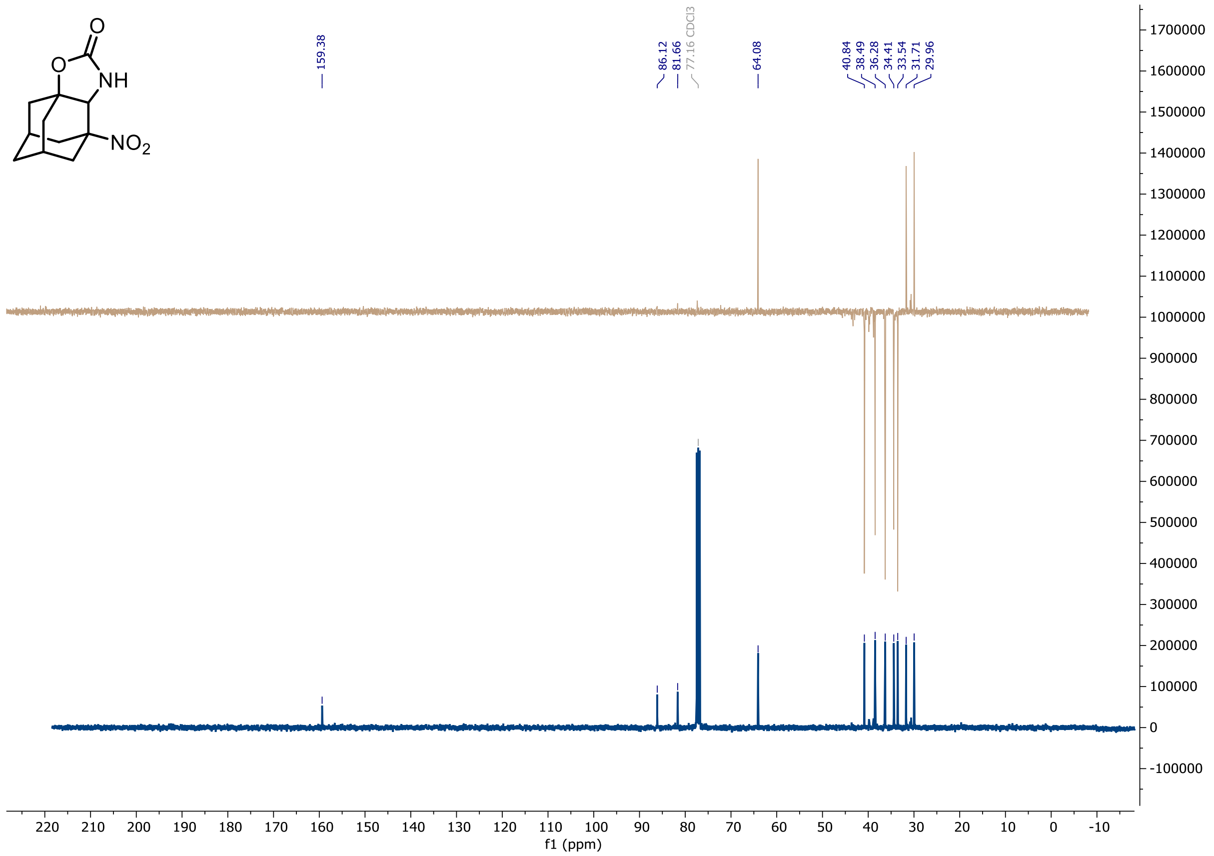
Compound 3h: ^{1}H NMR (400 MHz, $CDCl_3$)



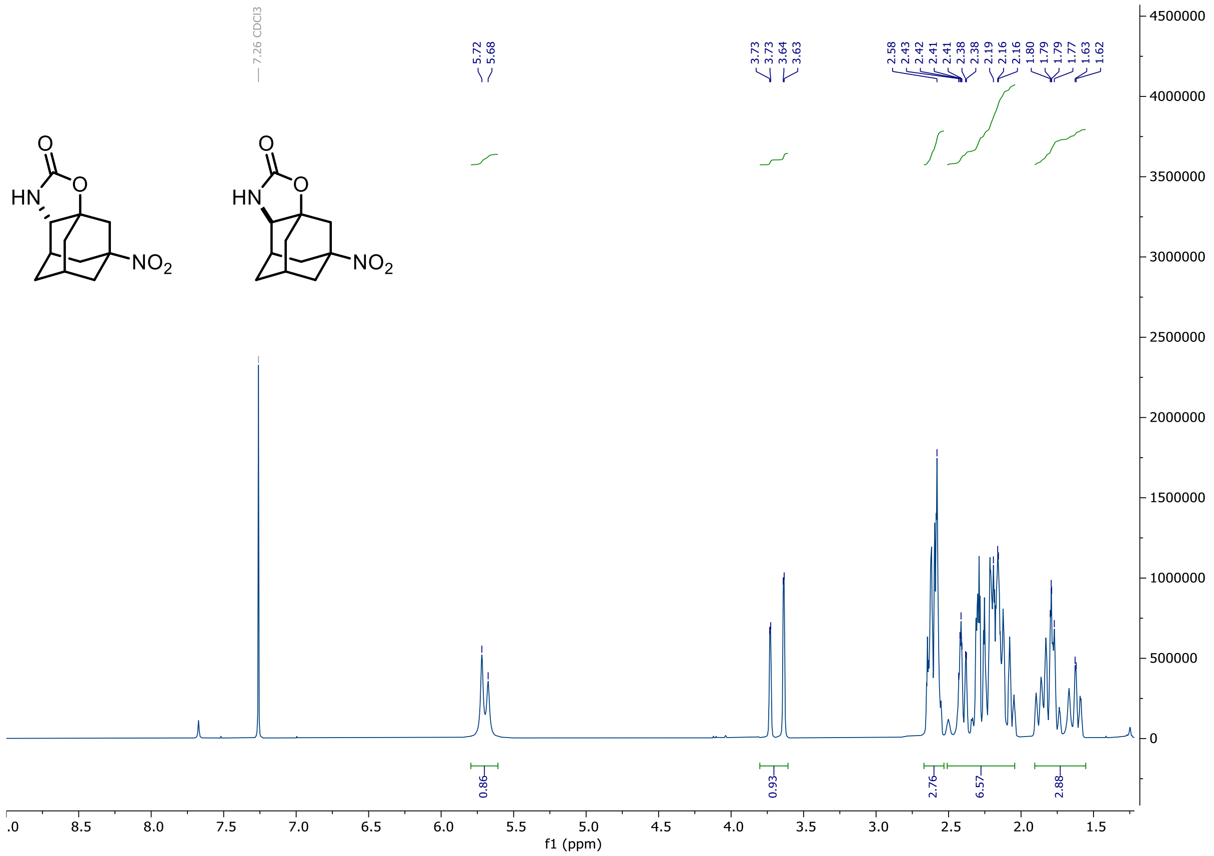
Compound 3h: ^{13}C NMR (101 MHz, $CDCl_3$)



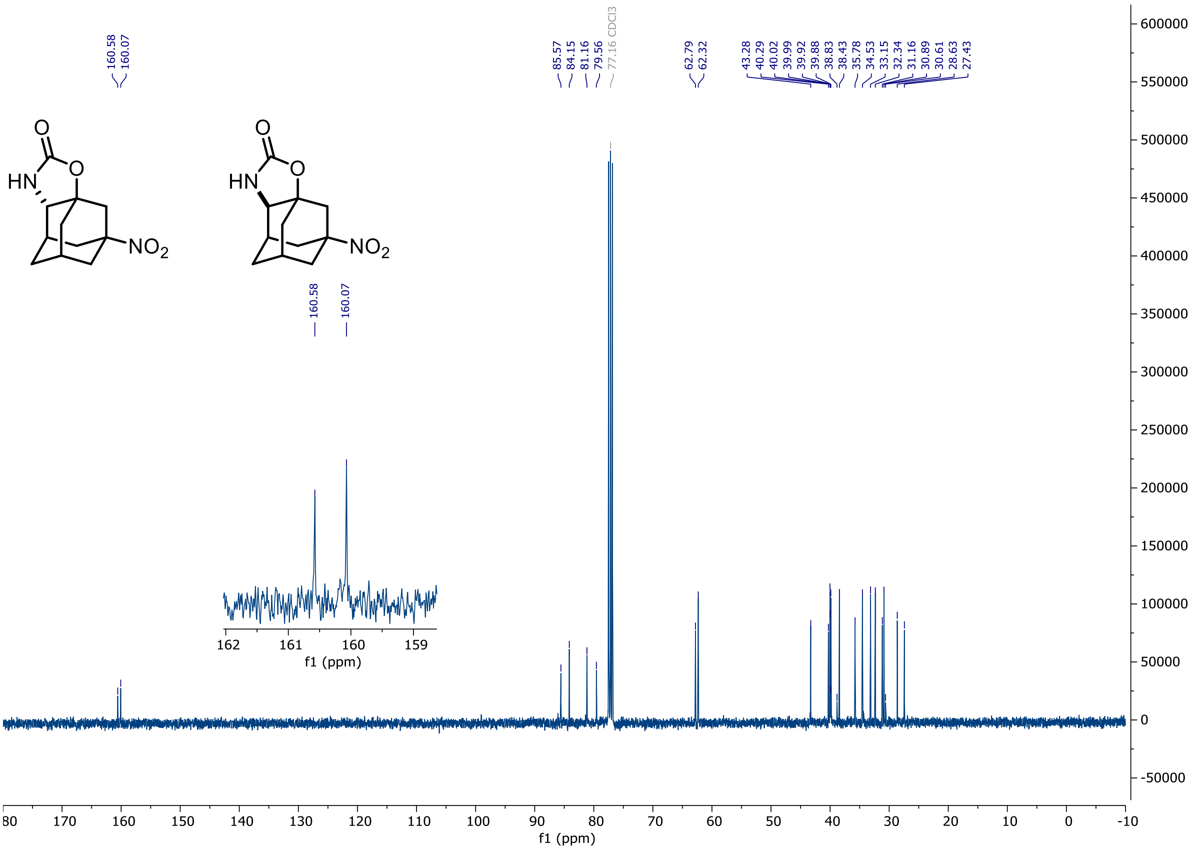
Compound 3h: ^{13}C NMR-DEPT (101 MHz, $CDCl_3$)



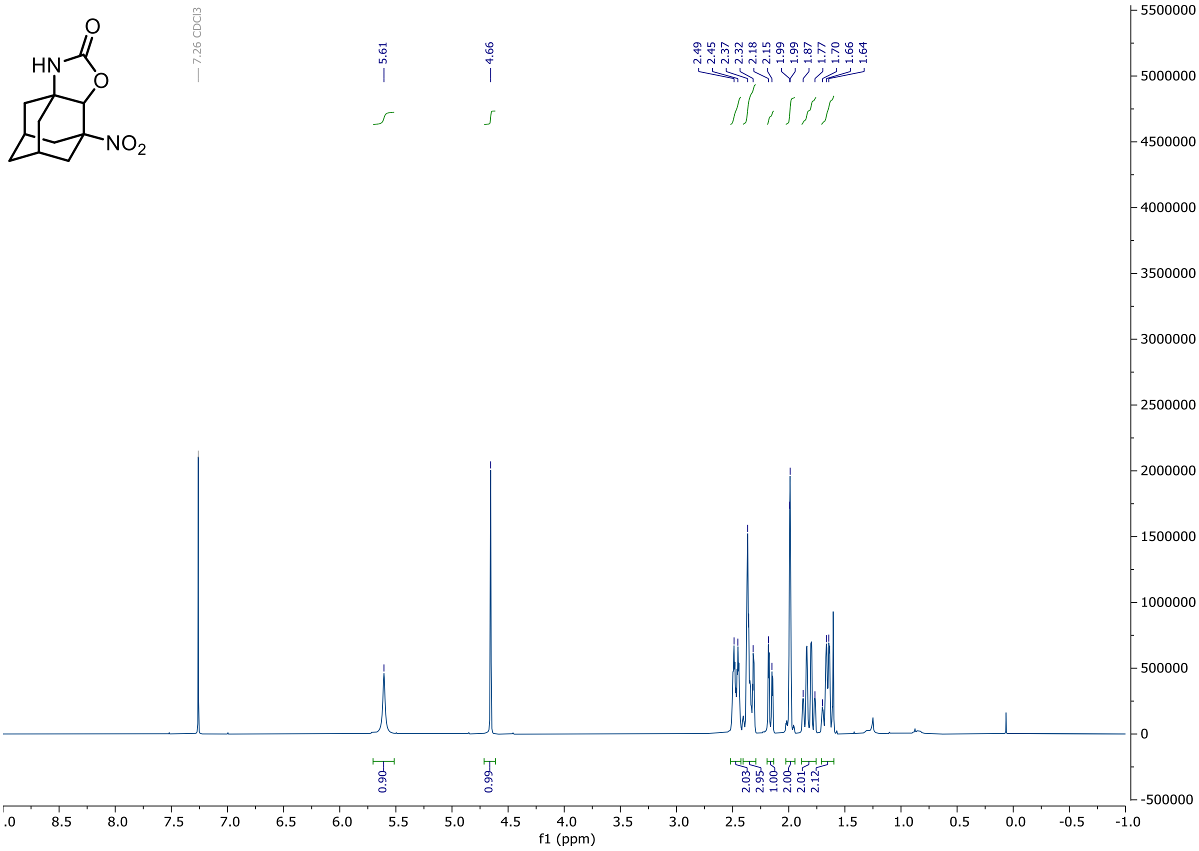
Compound 3i: ^{1}H NMR (400 MHz, $CDCl_3$)



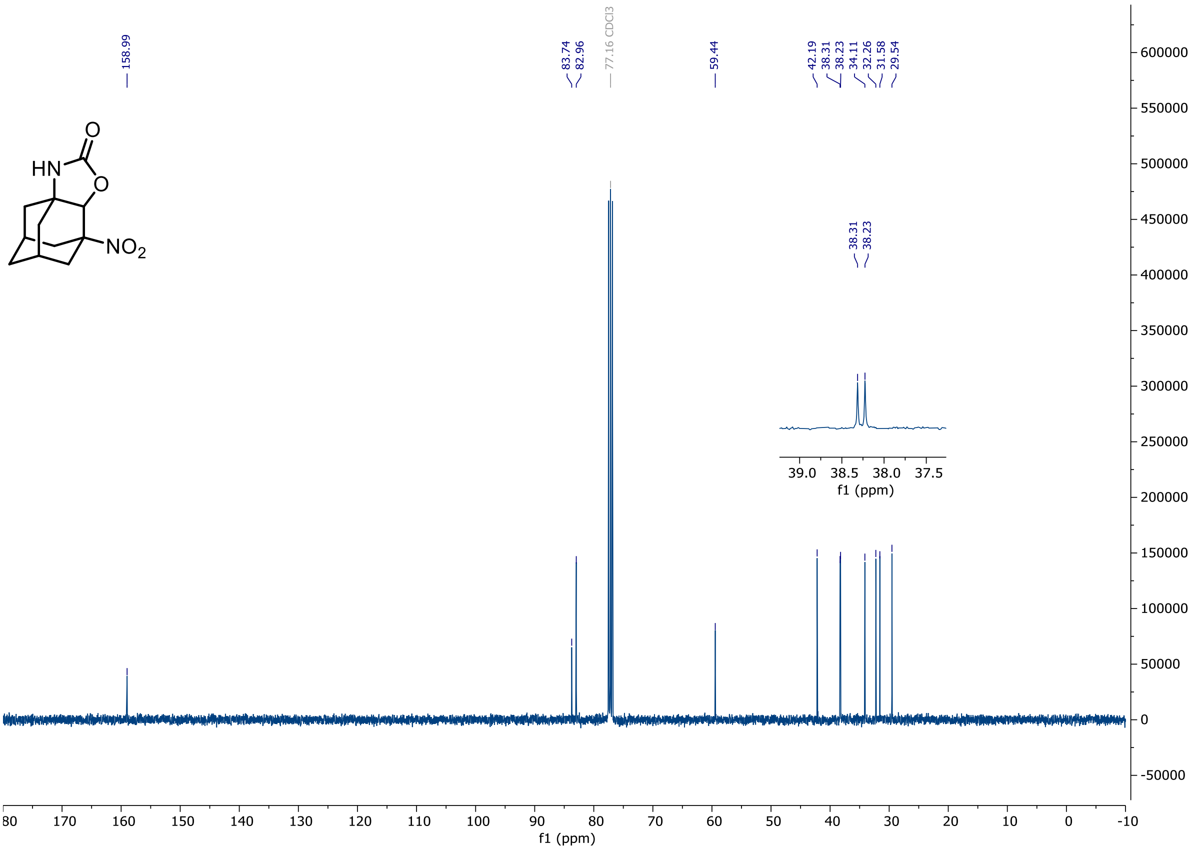
Compound 3i: ^{13}C NMR (101 MHz, CDCl$_3$)



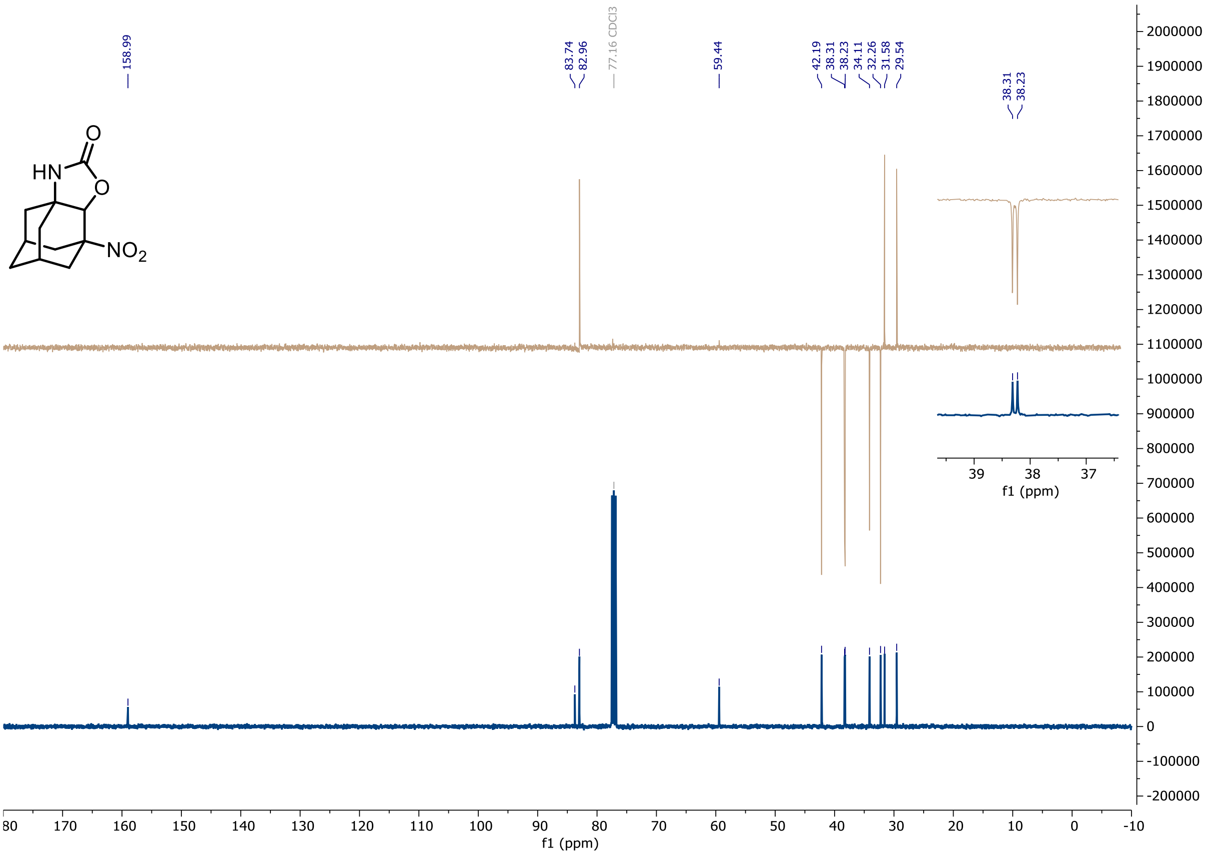
Compound 3j: ^{1}H NMR (400 MHz, CDCl$_3$)



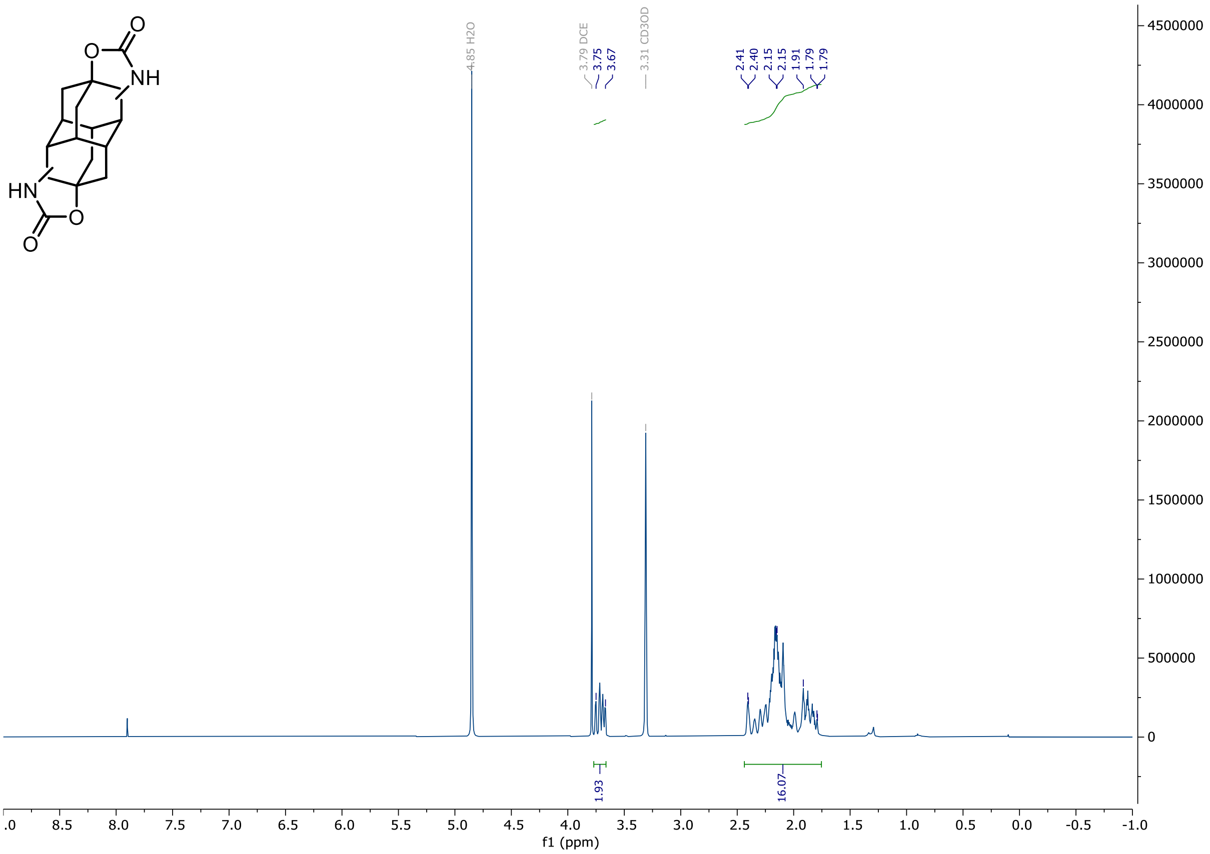
Compound 3j: ^{13}C NMR (101 MHz, CDCl$_3$)



Compound 3j: ^{13}C NMR-DEPT (101 MHz, CDCl$_3$)

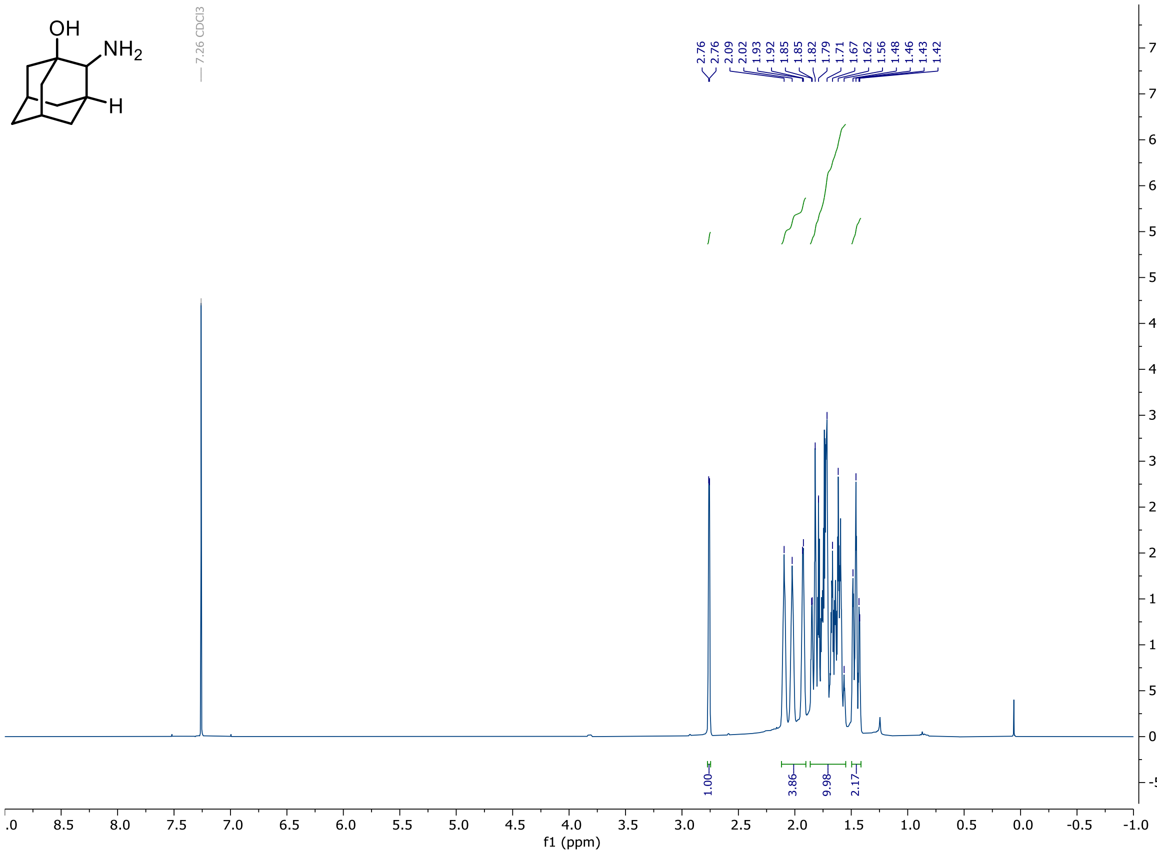


Compound 3k: $\mathbf{^1H}$ **NMR** (400 MHz, MeOD-d_4)

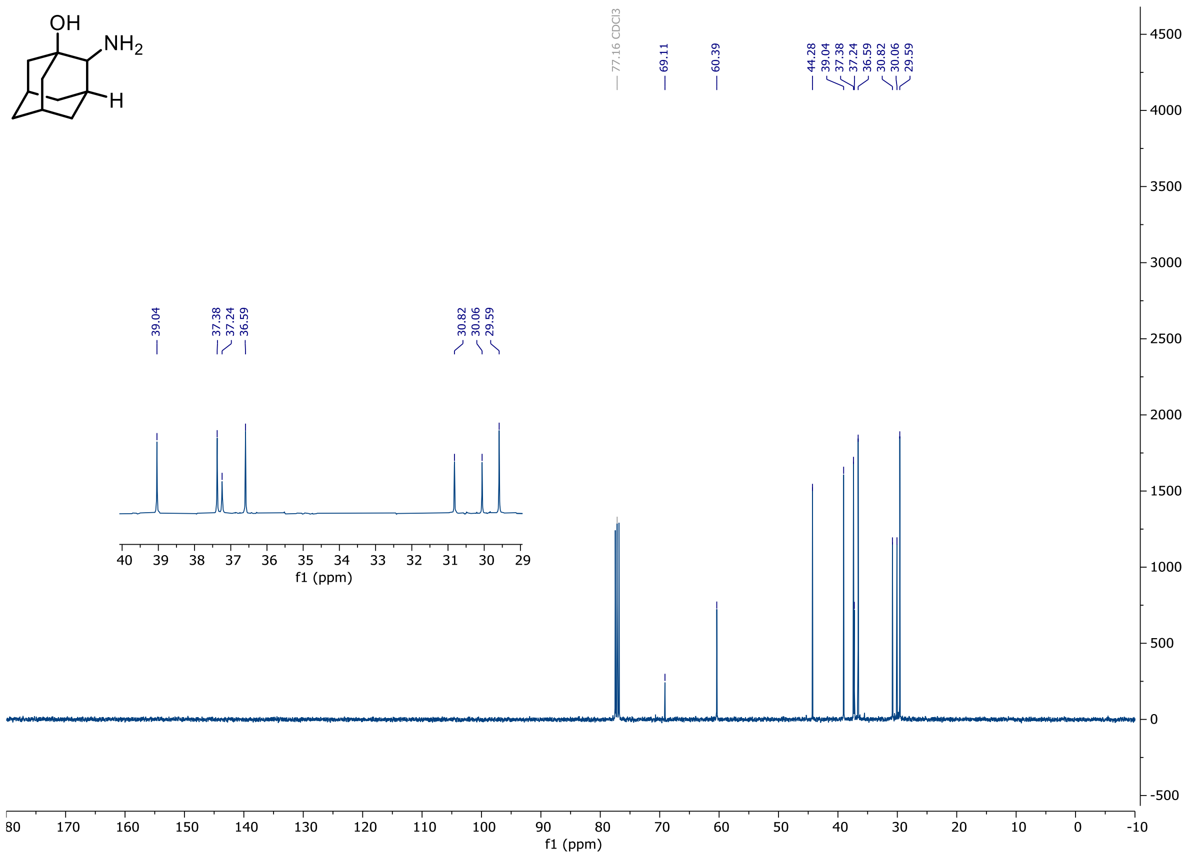


Aminoalcohols

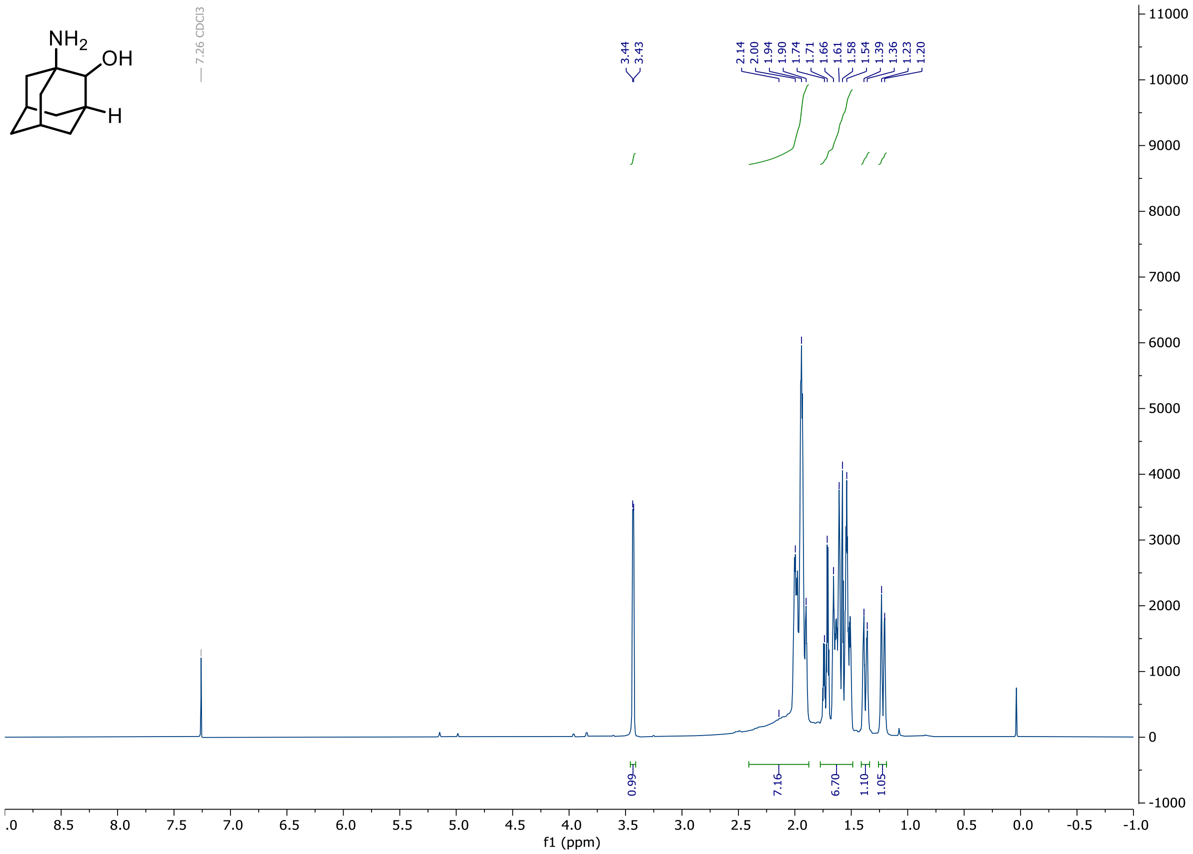
Compound 4a: ^{1}H NMR (400 MHz, $CDCl_3$)



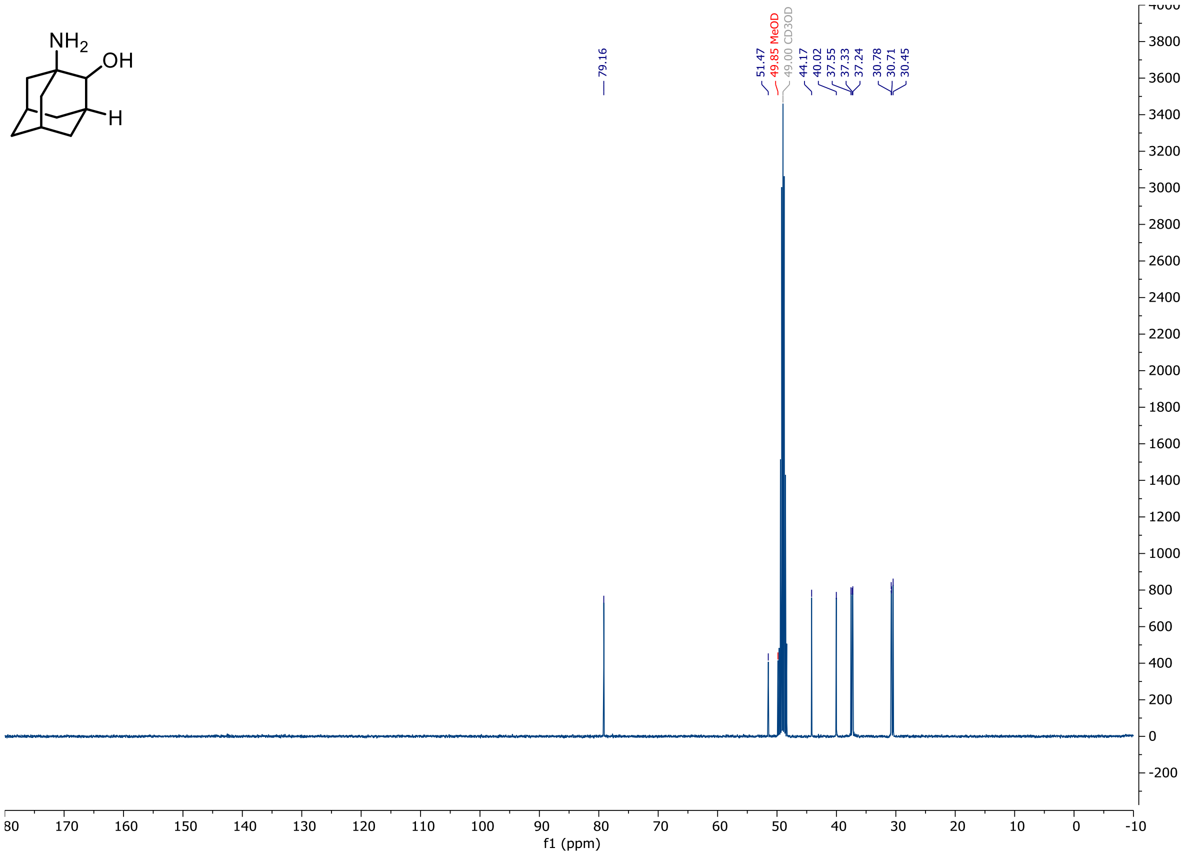
Compound 4a: ^{13}C **NMR** (101 MHz, $CDCl_3$)



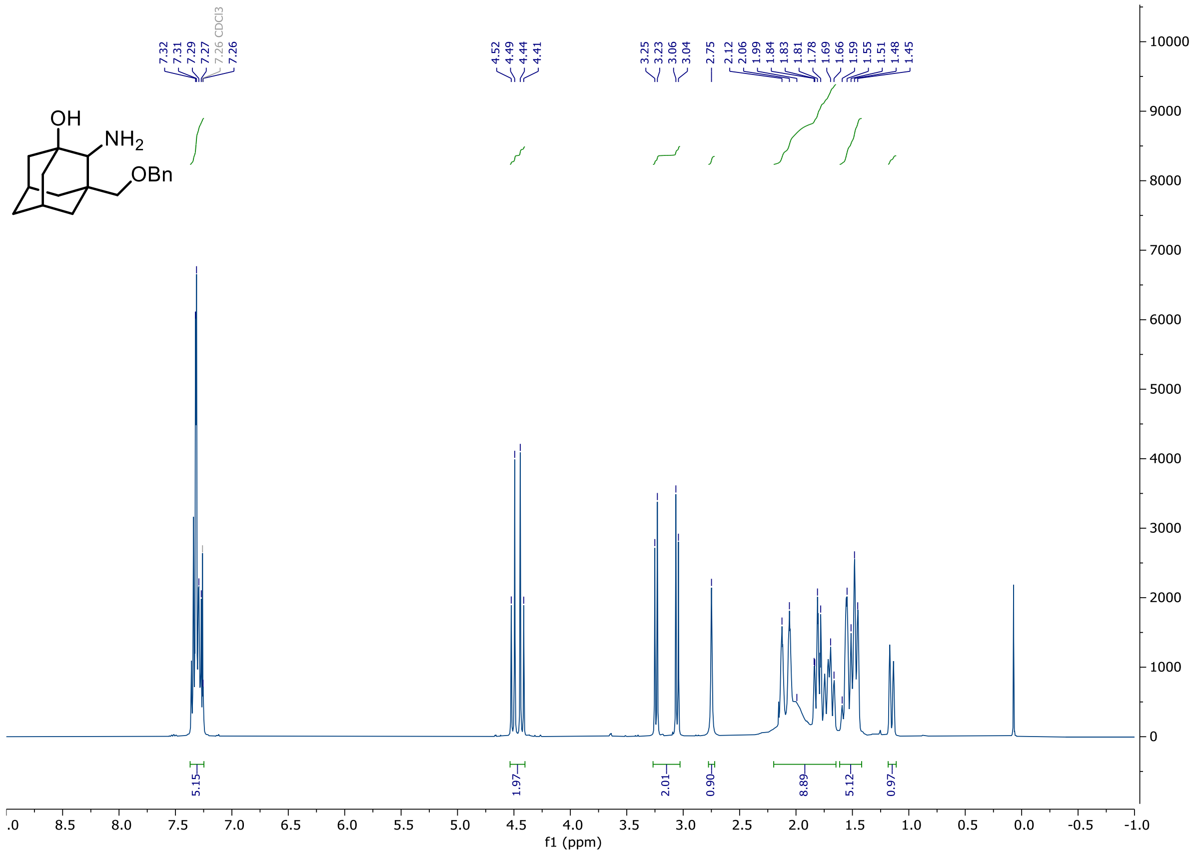
Compound 4b: ^{1}H **NMR** (400 MHz, $CDCl_3$)



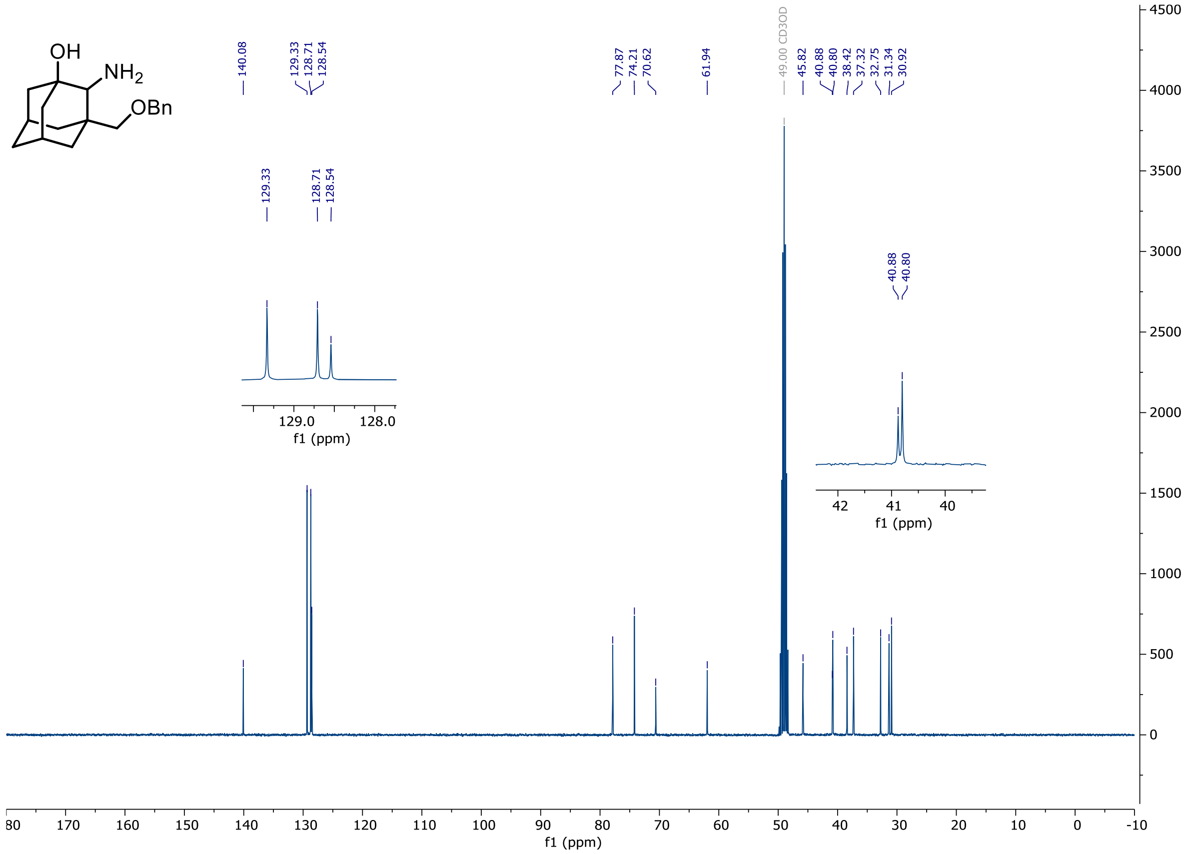
Compound 4b: ^{13}C NMR (101 MHz, MeOD-d_4)



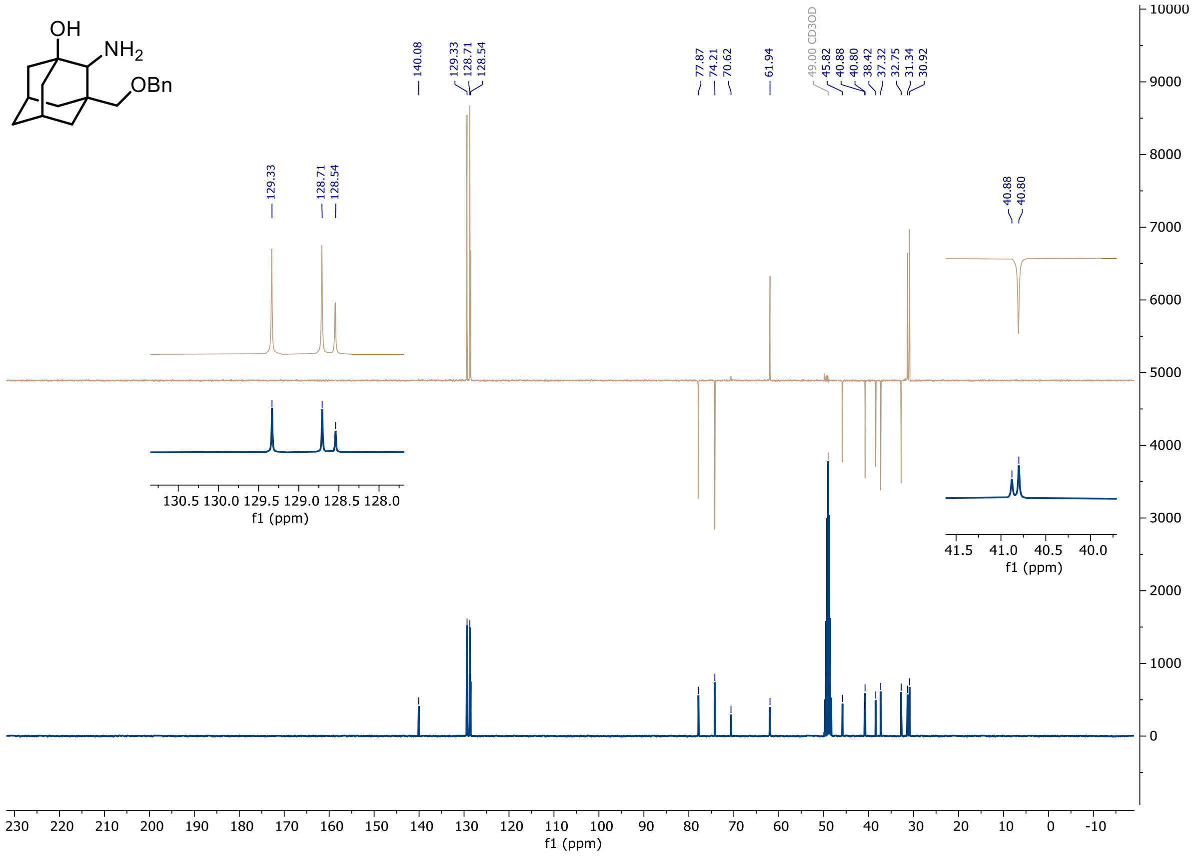
Compound 4c: ^{1}H NMR (400 MHz, CDCl$_3$)



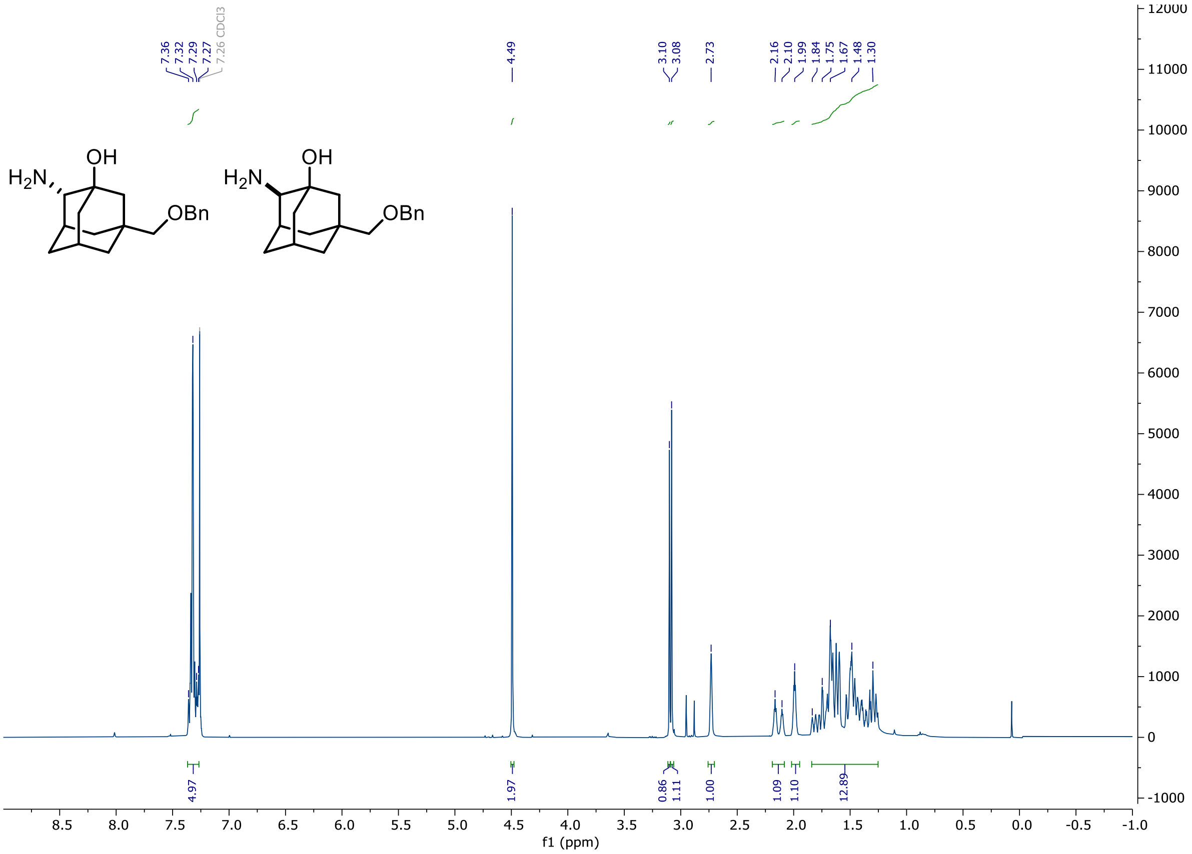
Compound 4c: ^{13}C NMR (101 MHz, MeOD-*d$_4$*)



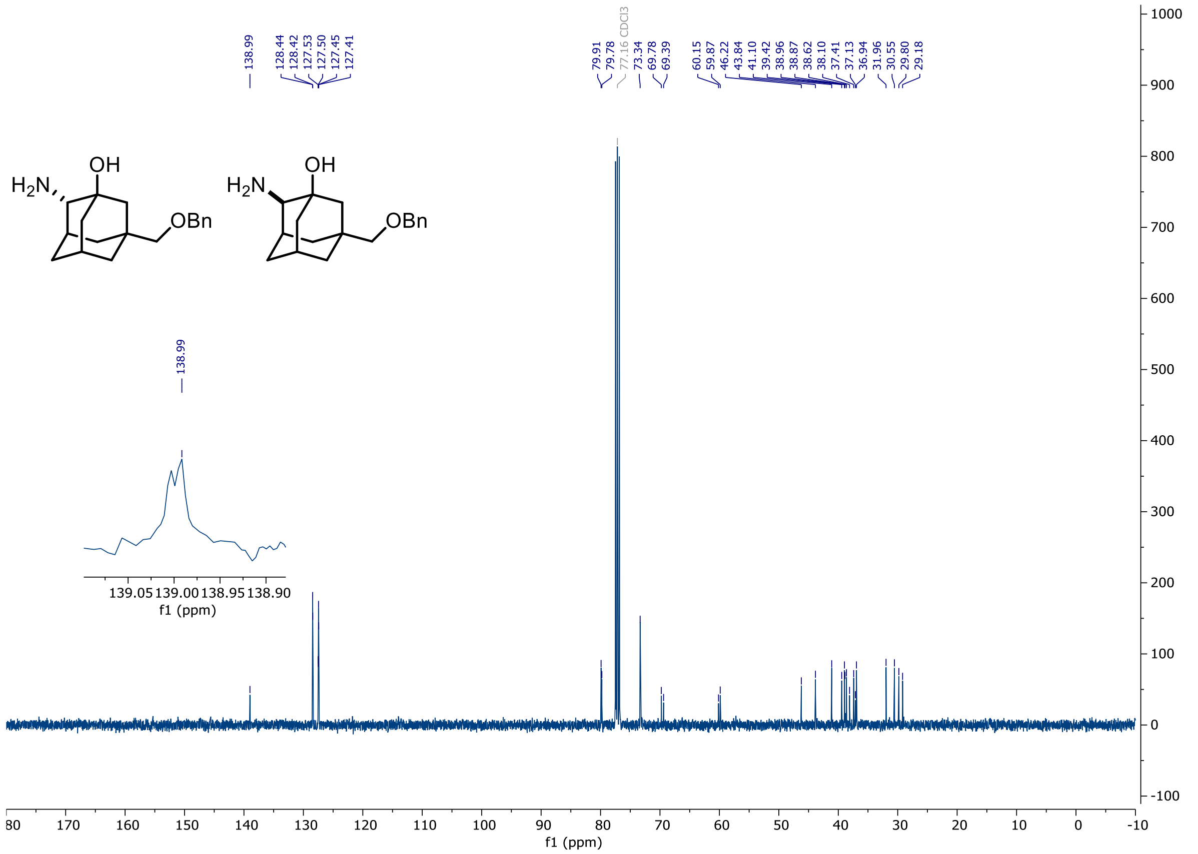
Compound 4c: ^{13}C NMR-DEPT (101 MHz, MeOD-*d$_4$*)



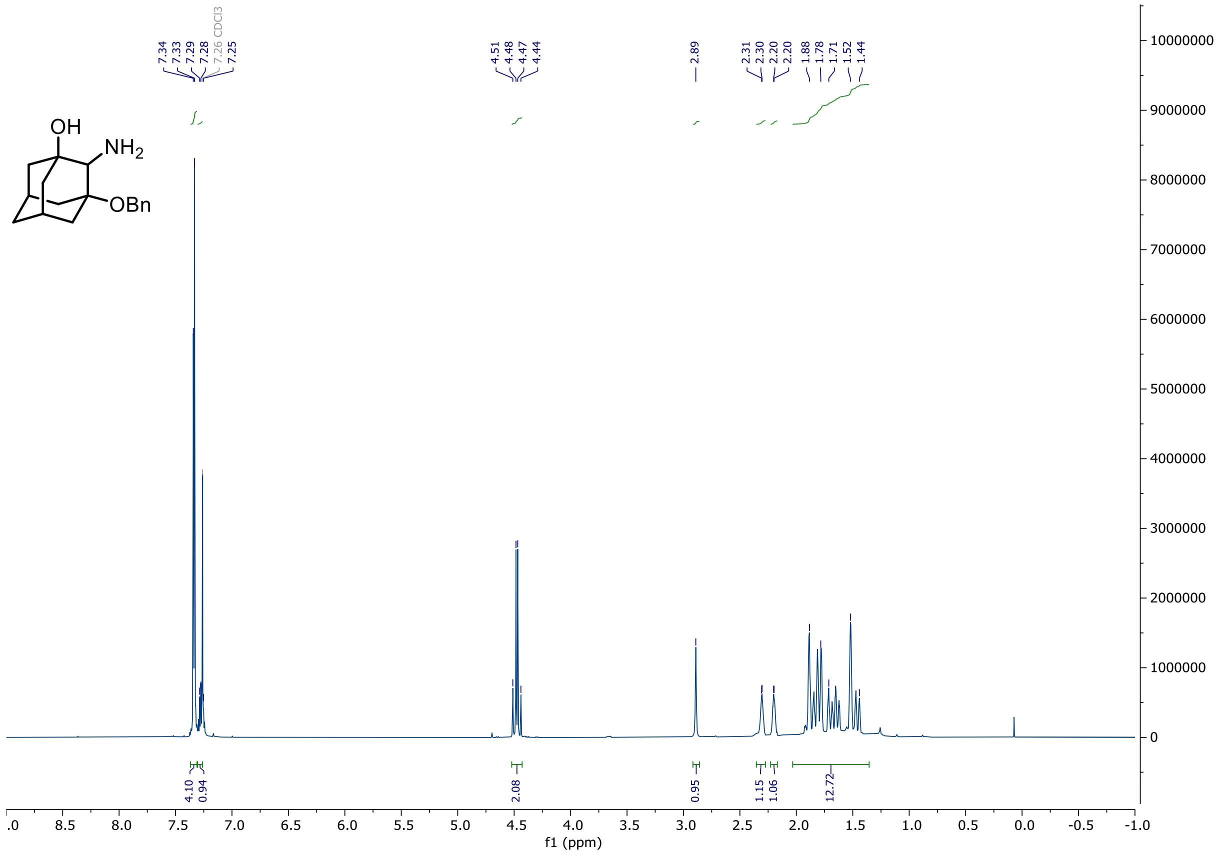
Compound 4d: ^{1}H NMR (400 MHz, $CDCl_3$)



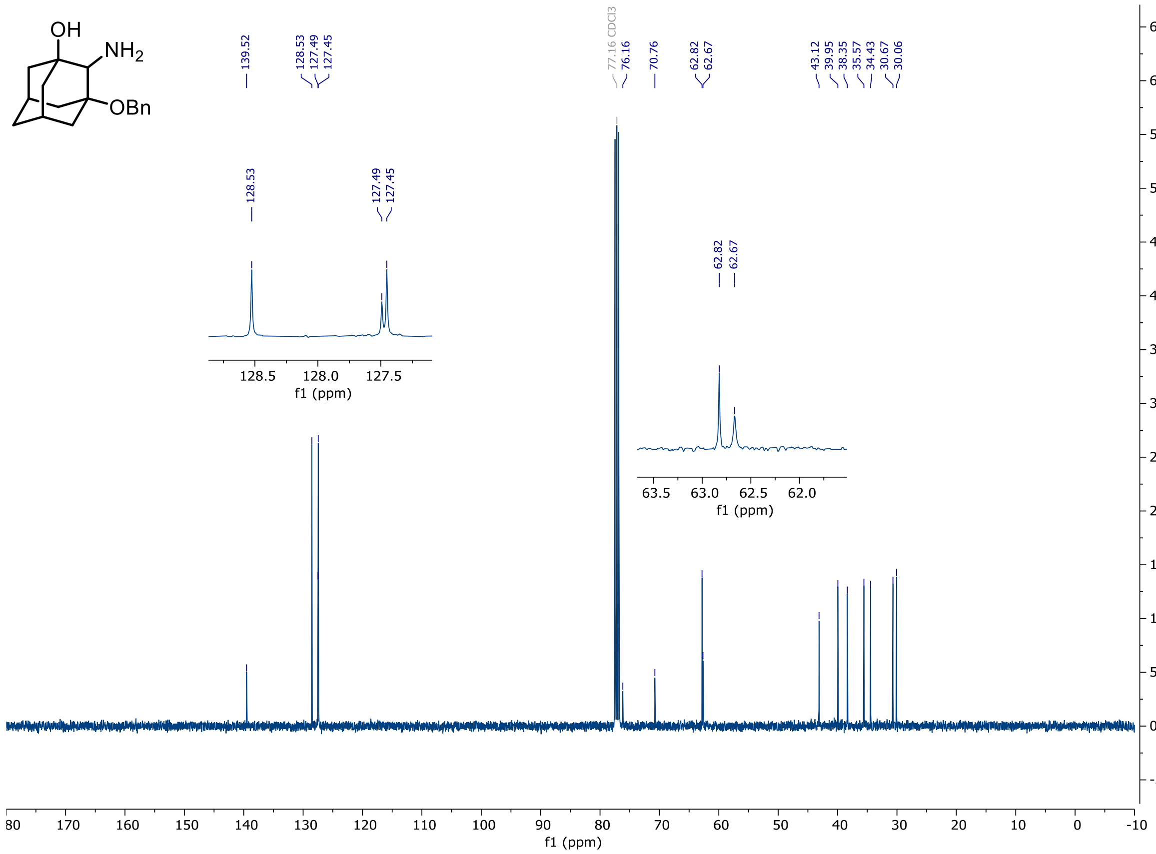
Compound 4d: ^{13}C NMR (101 MHz, $CDCl_3$)



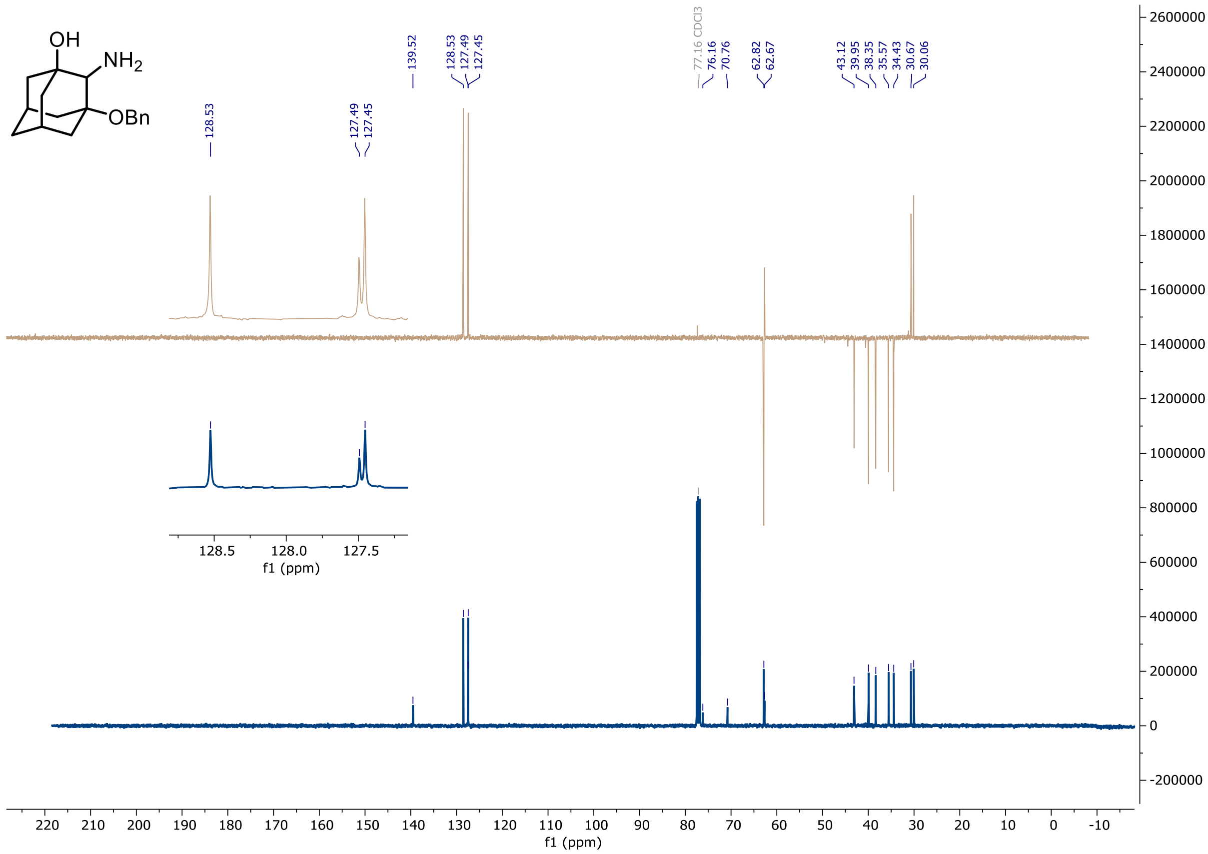
Compound 4e: ^{1}H NMR (400 MHz, $CDCl_3$)



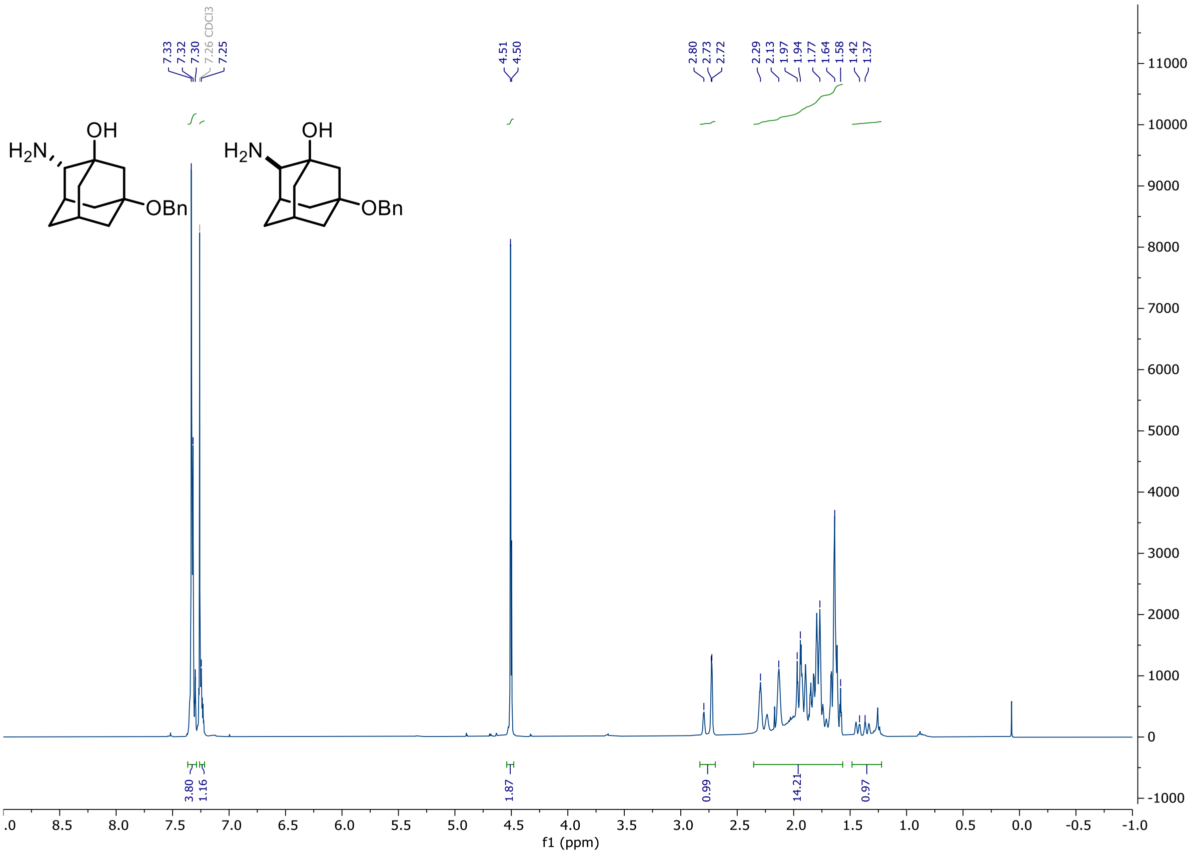
Compound 4e: ^{13}C NMR (101 MHz, CDCl$_3$)



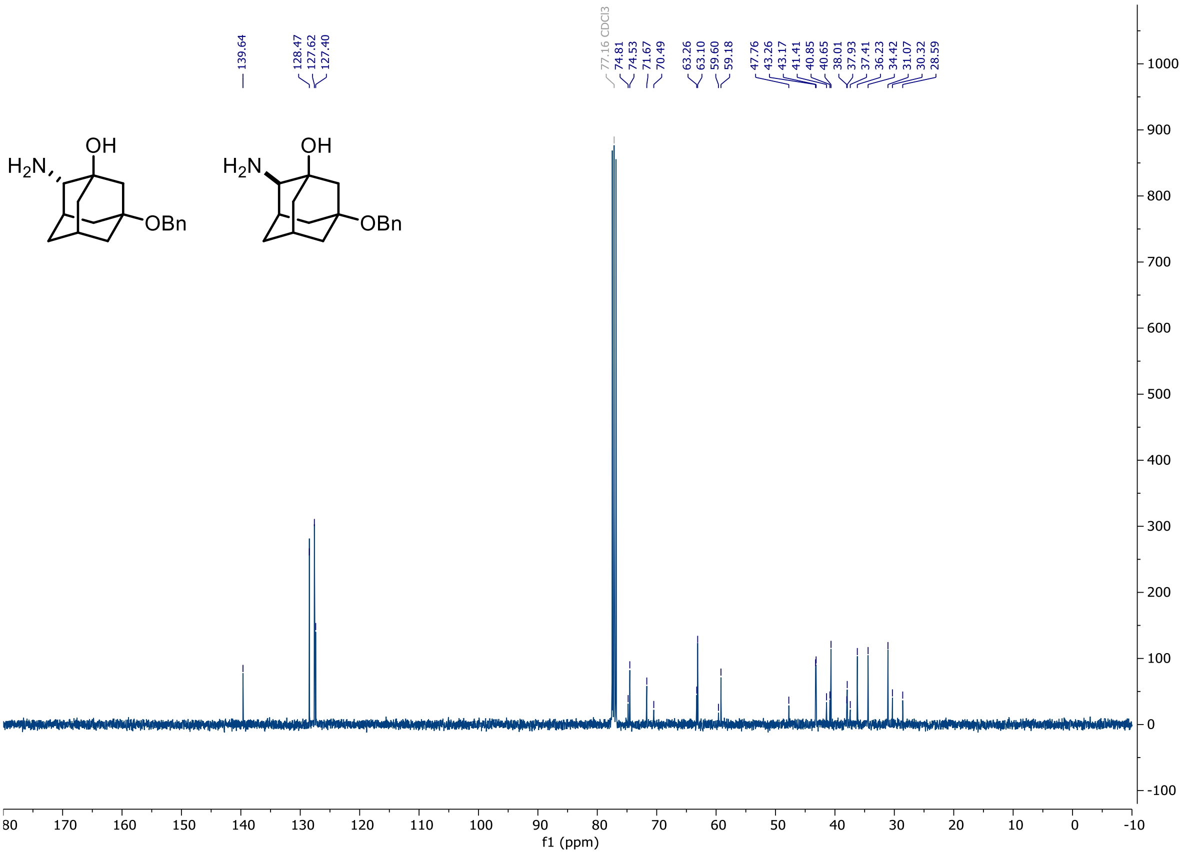
Compound 4e: ^{13}C NMR-DEPT (101 MHz, CDCl$_3$)



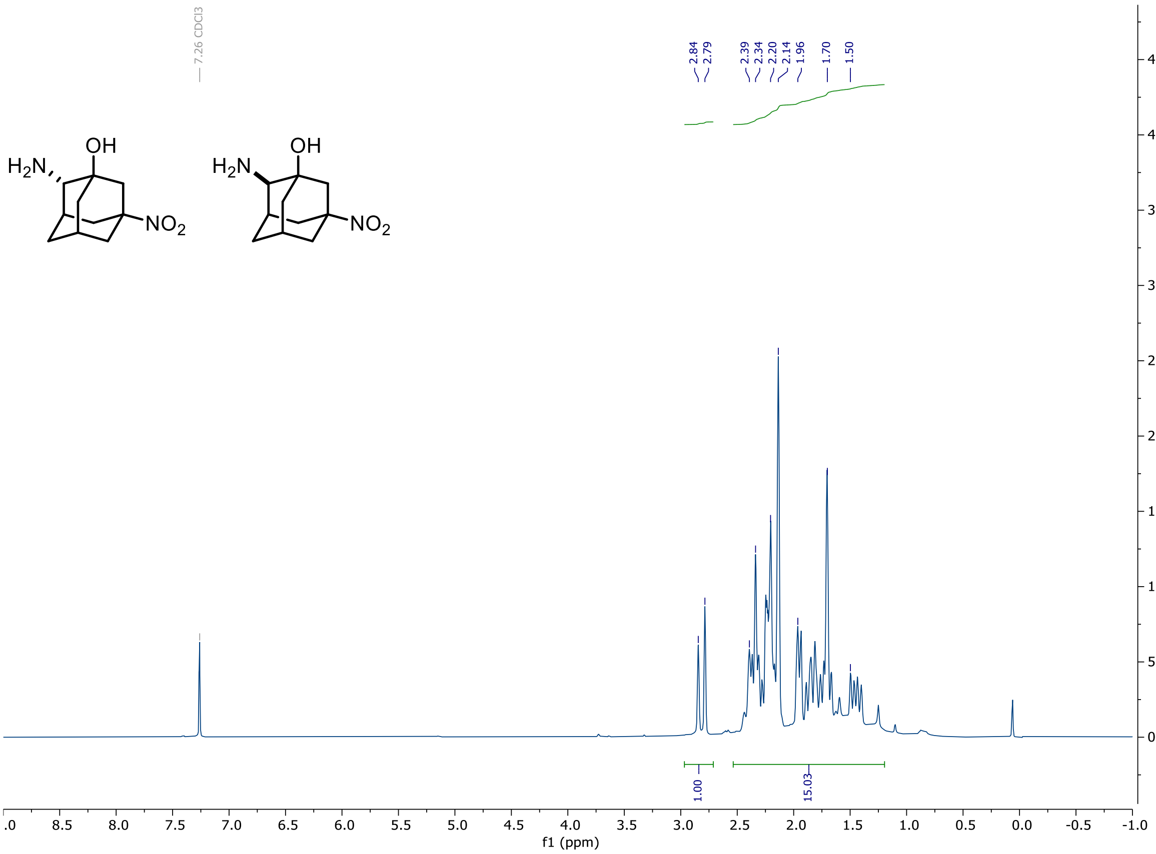
Compound 4f: ^{1}H NMR (400 MHz, CDCl$_3$)



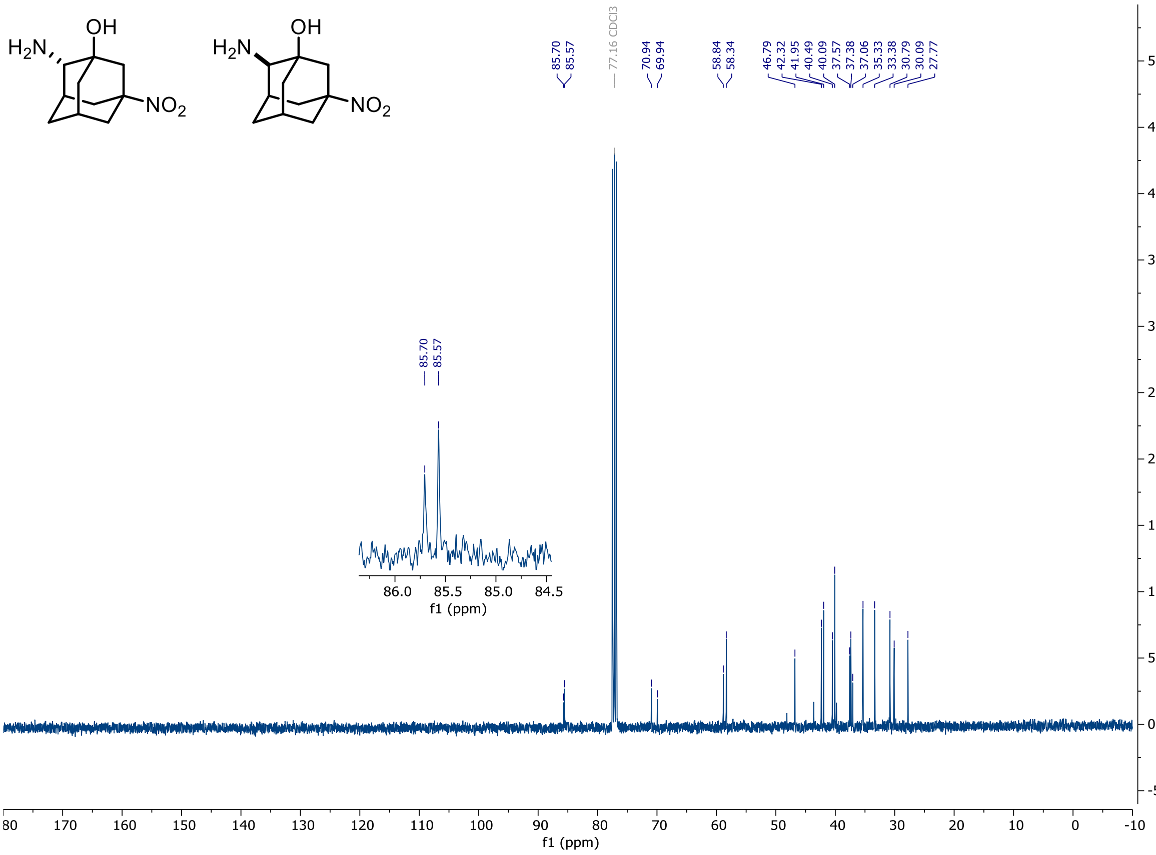
Compound 4f: ^{13}**C NMR** (101 MHz, $CDCl_3$)



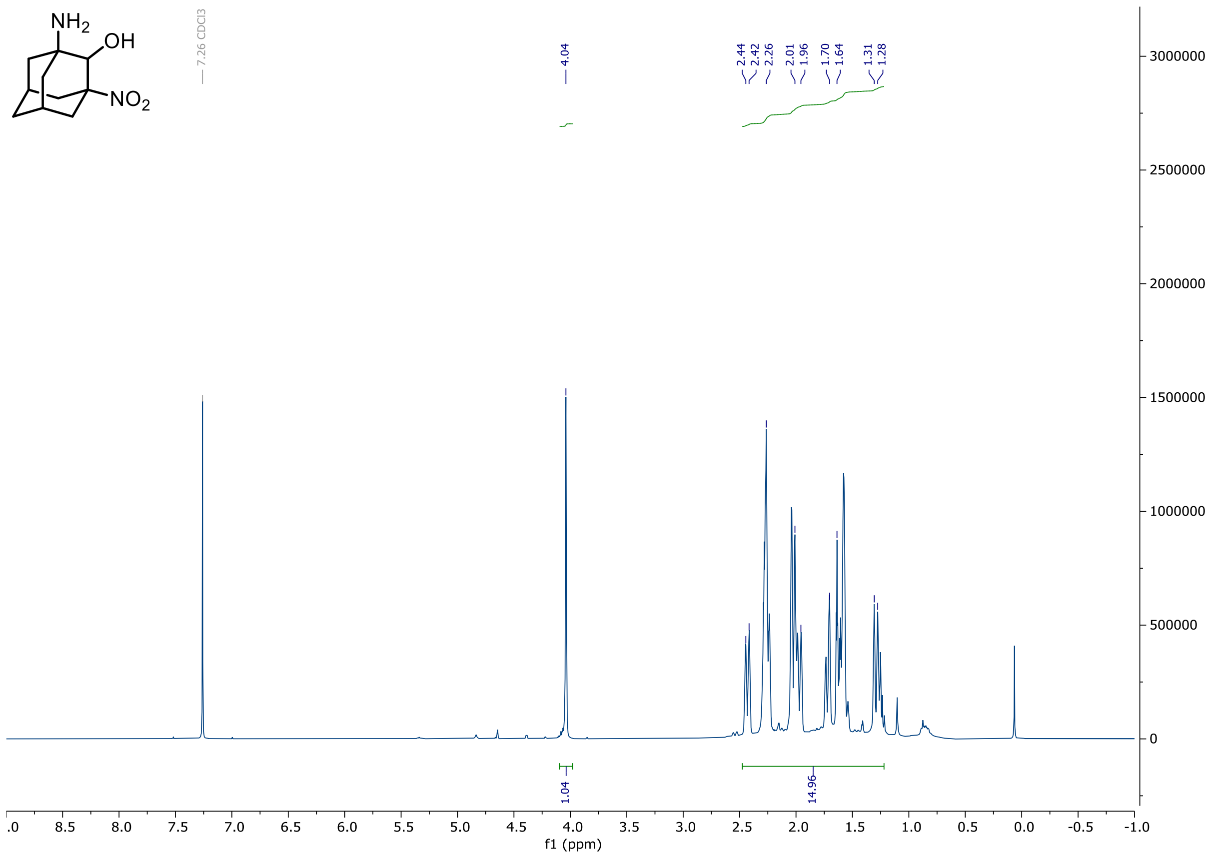
Compound 4h: ^{1}**H NMR** (400 MHz, $CDCl_3$)



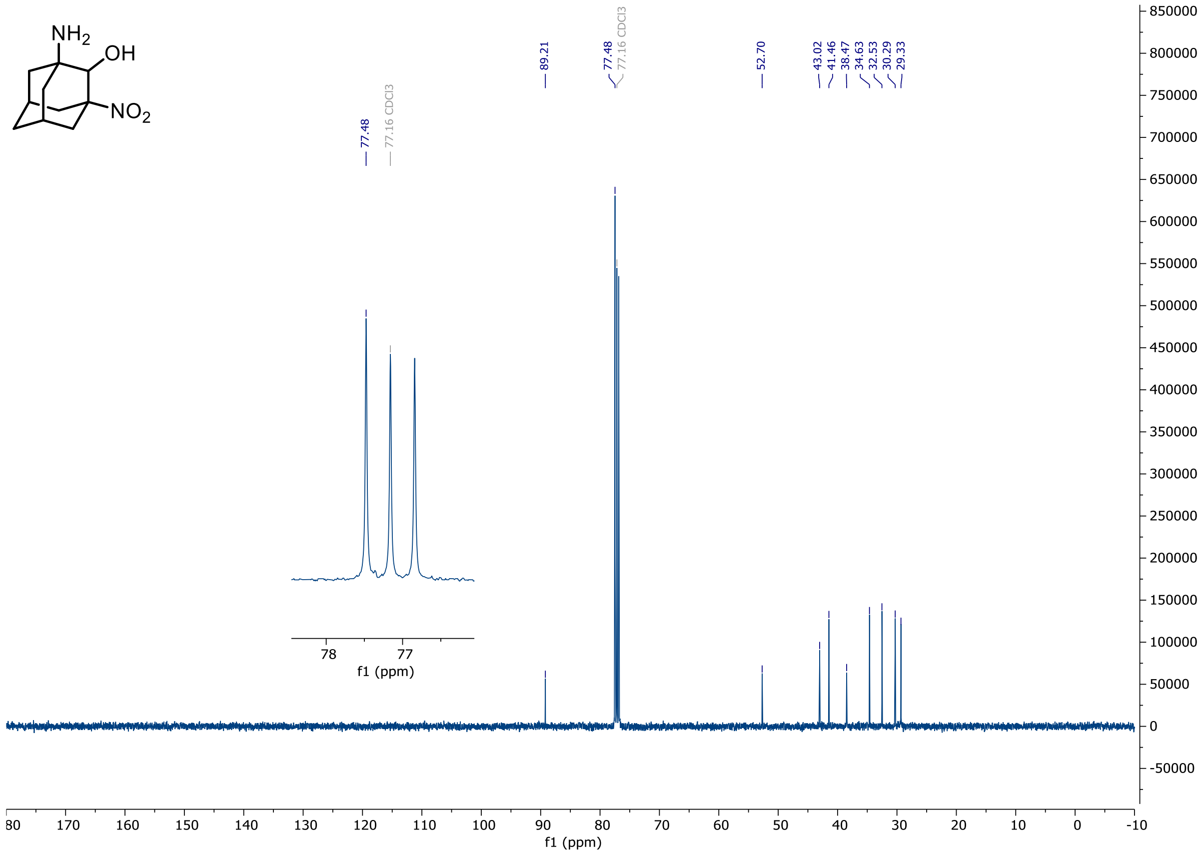
Compound 4h: ^{13}C NMR (101 MHz, CDCl$_3$)



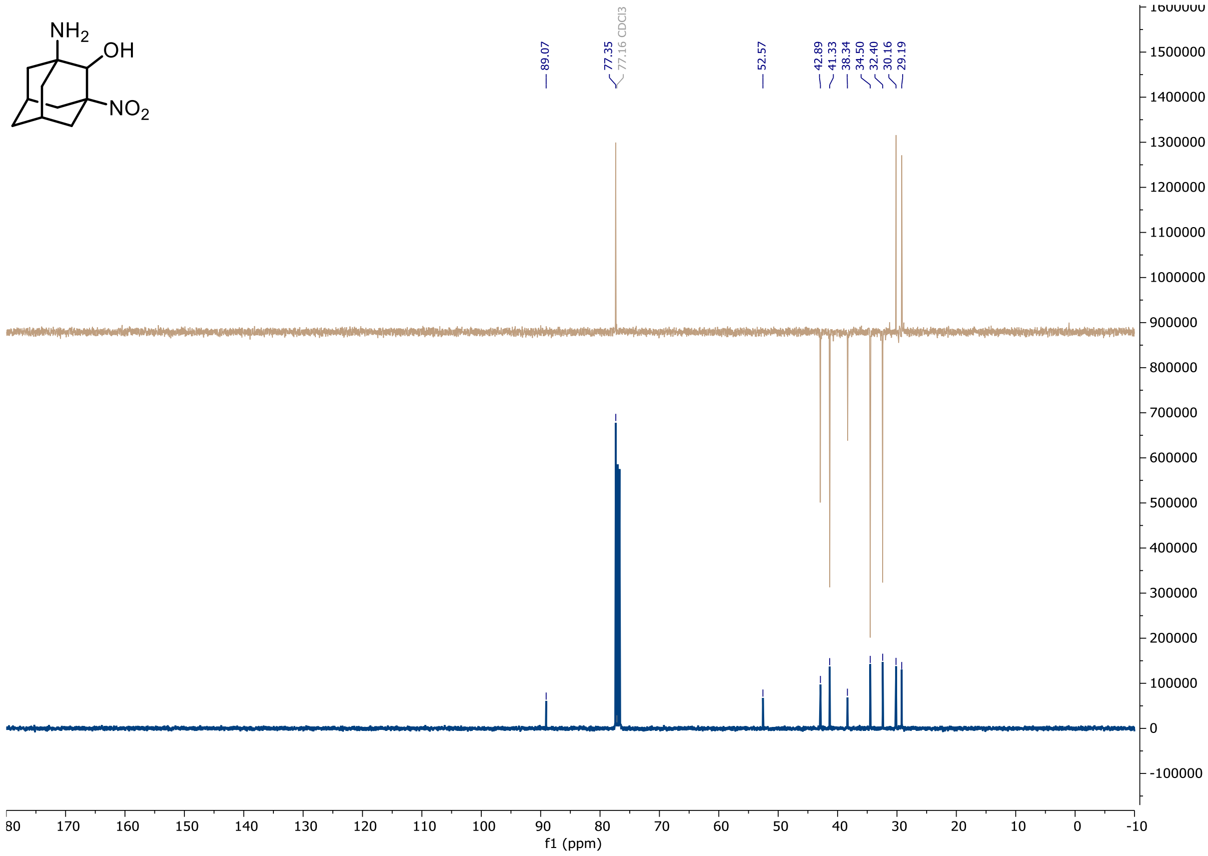
Compound 4i: ^{1}**H NMR** (400 MHz, $CDCl_3$)



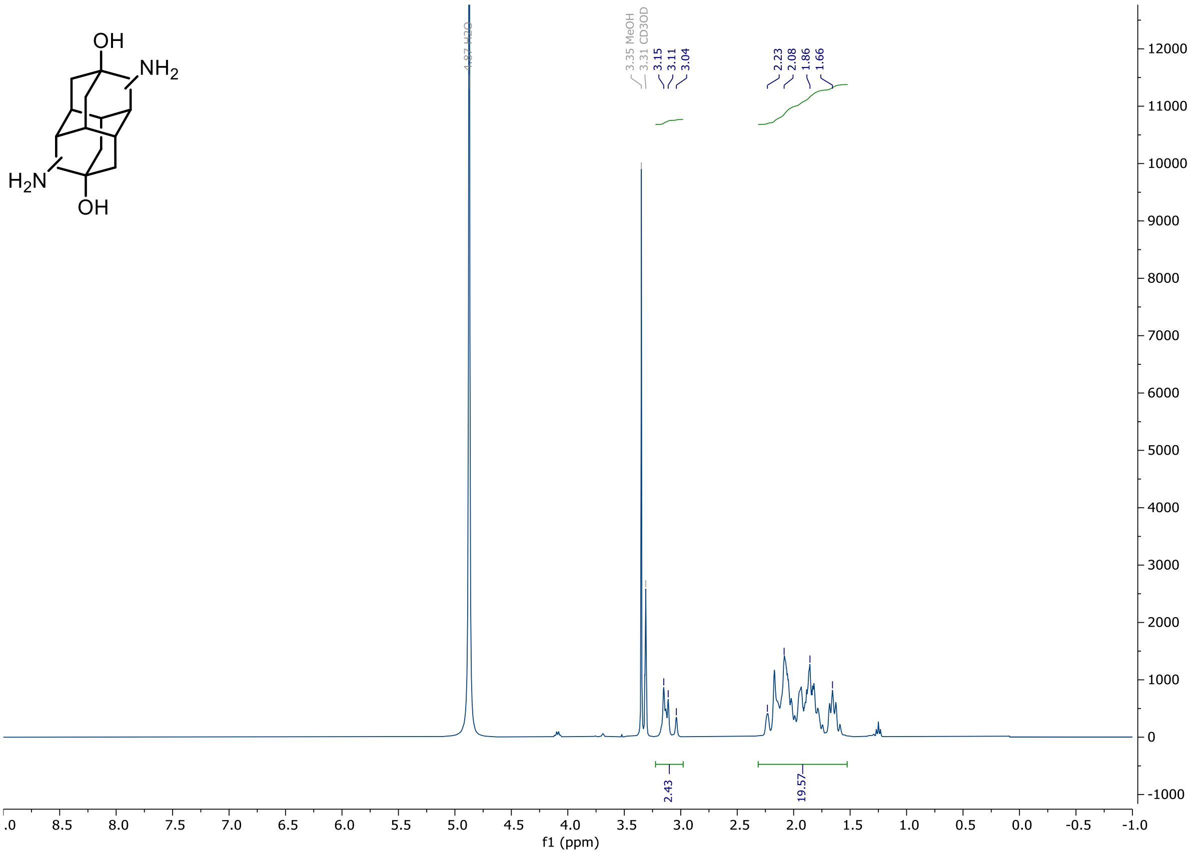
Compound 4i: ^{13}**C NMR** (101 MHz, $CDCl_3$)



Compound 4i: ^{13}C NMR-DEPT (101 MHz, CDCl$_3$)

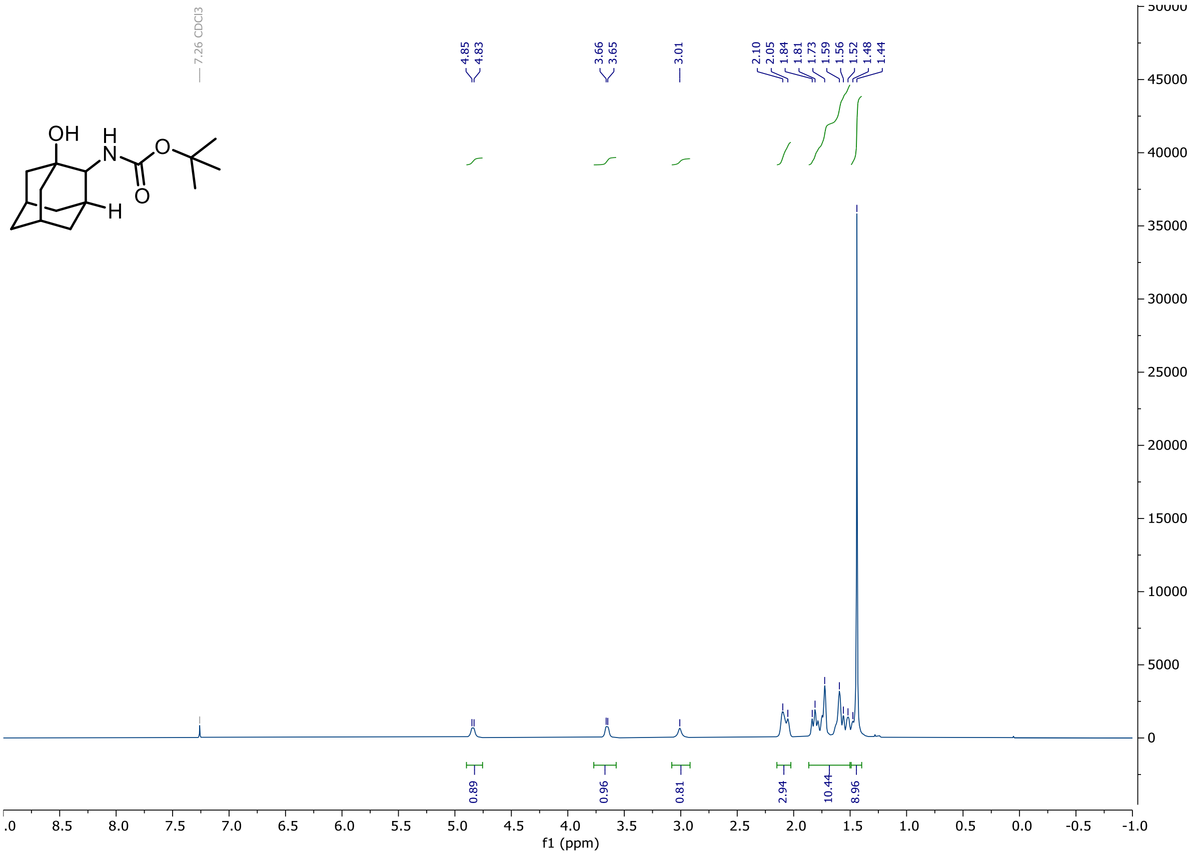


Compound 4j: ^{1}**H NMR** (400 MHz, MeOD-d_4)

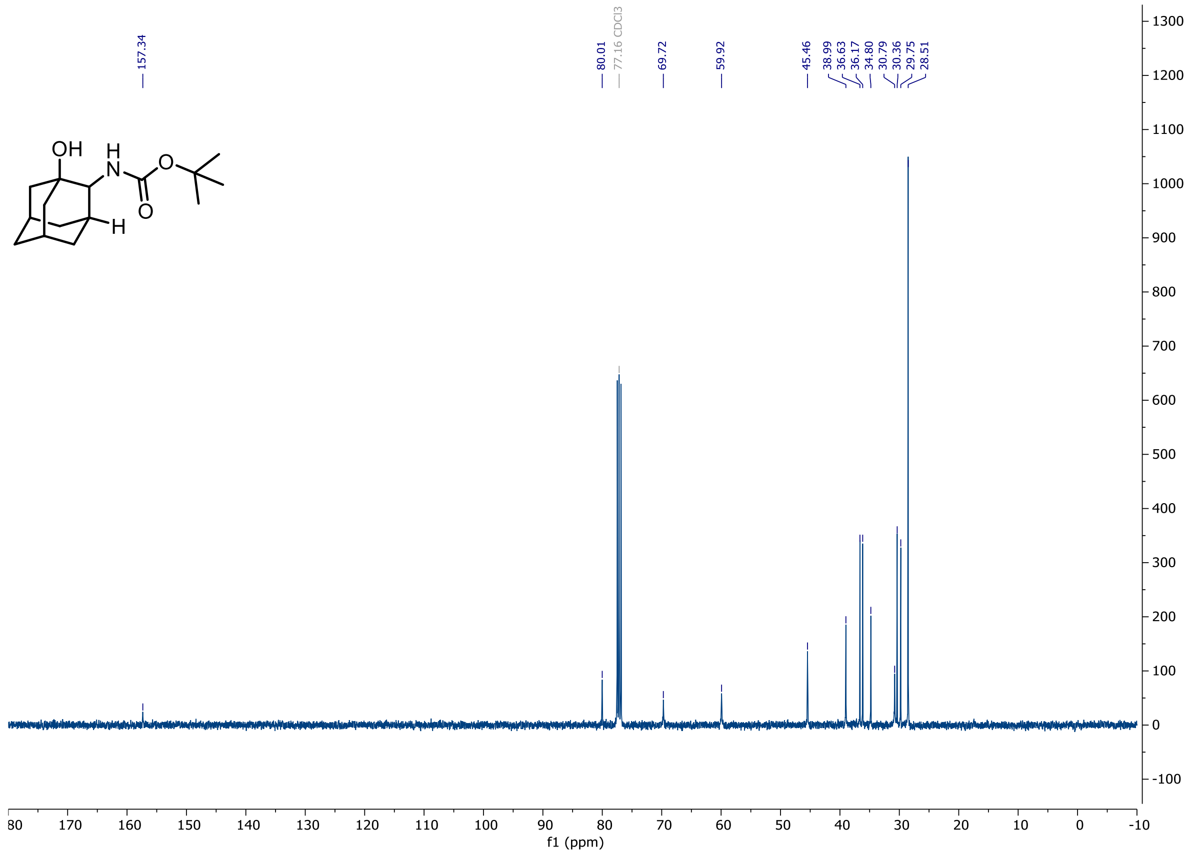


N-protected Aminoalcohols

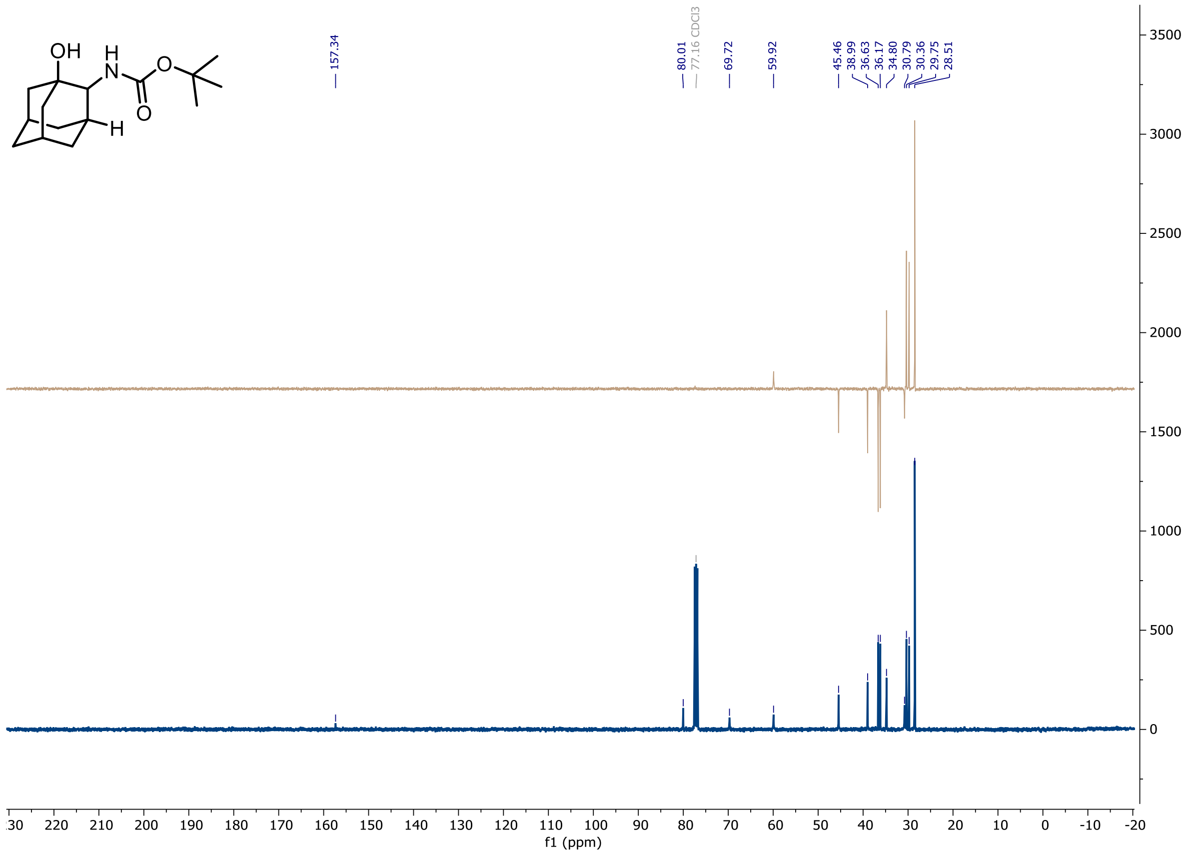
Compound 5a: ^{1}H NMR (400 MHz, $CDCl_3$)



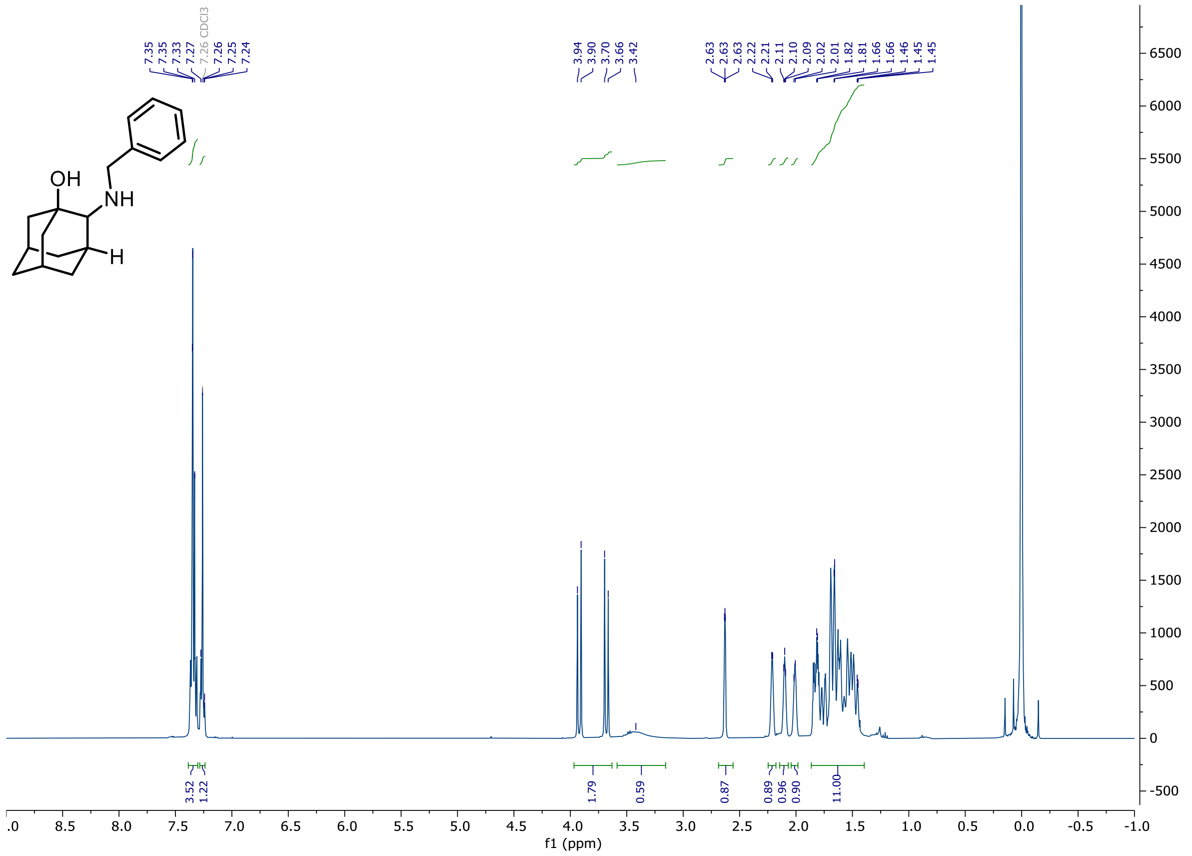
Compound 5a: ^{13}C NMR (101 MHz, $CDCl_3$)



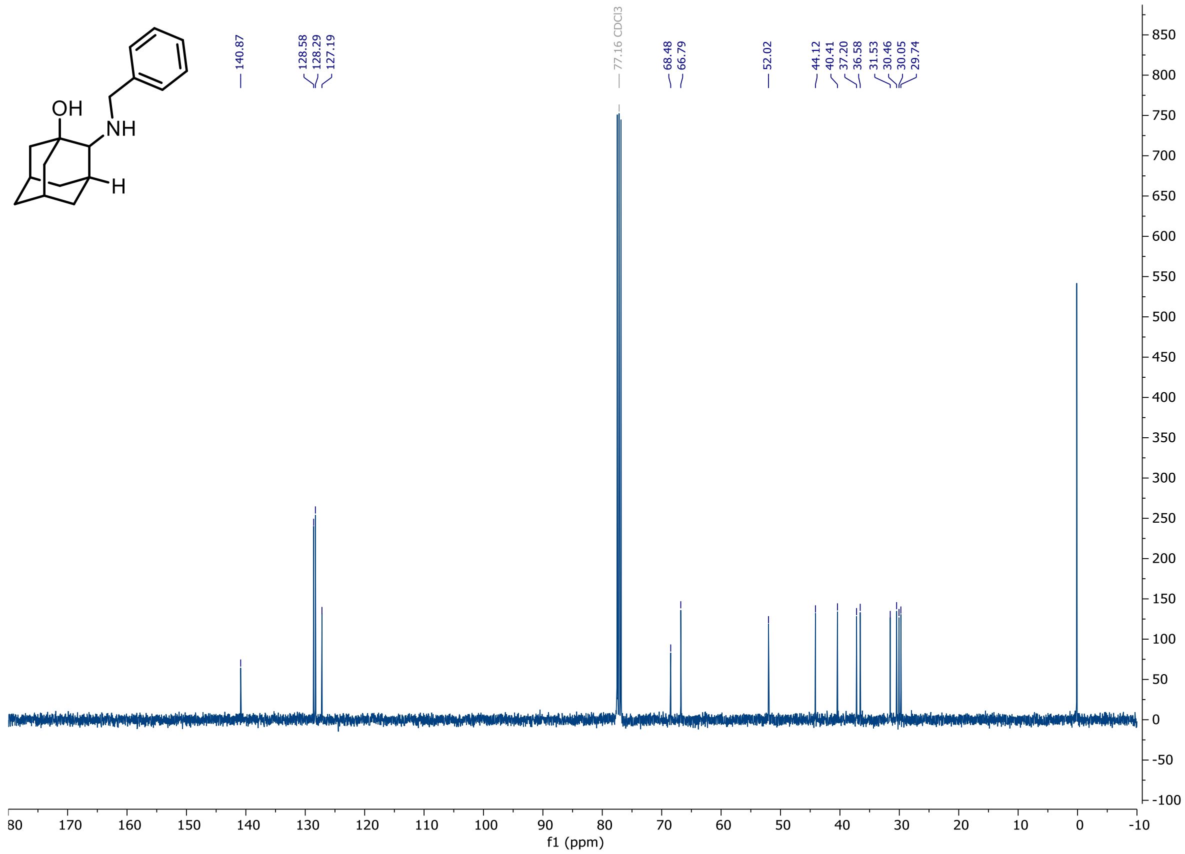
Compound 5a: ^{13}C NMR-DEPT (101 MHz, $CDCl_3$)



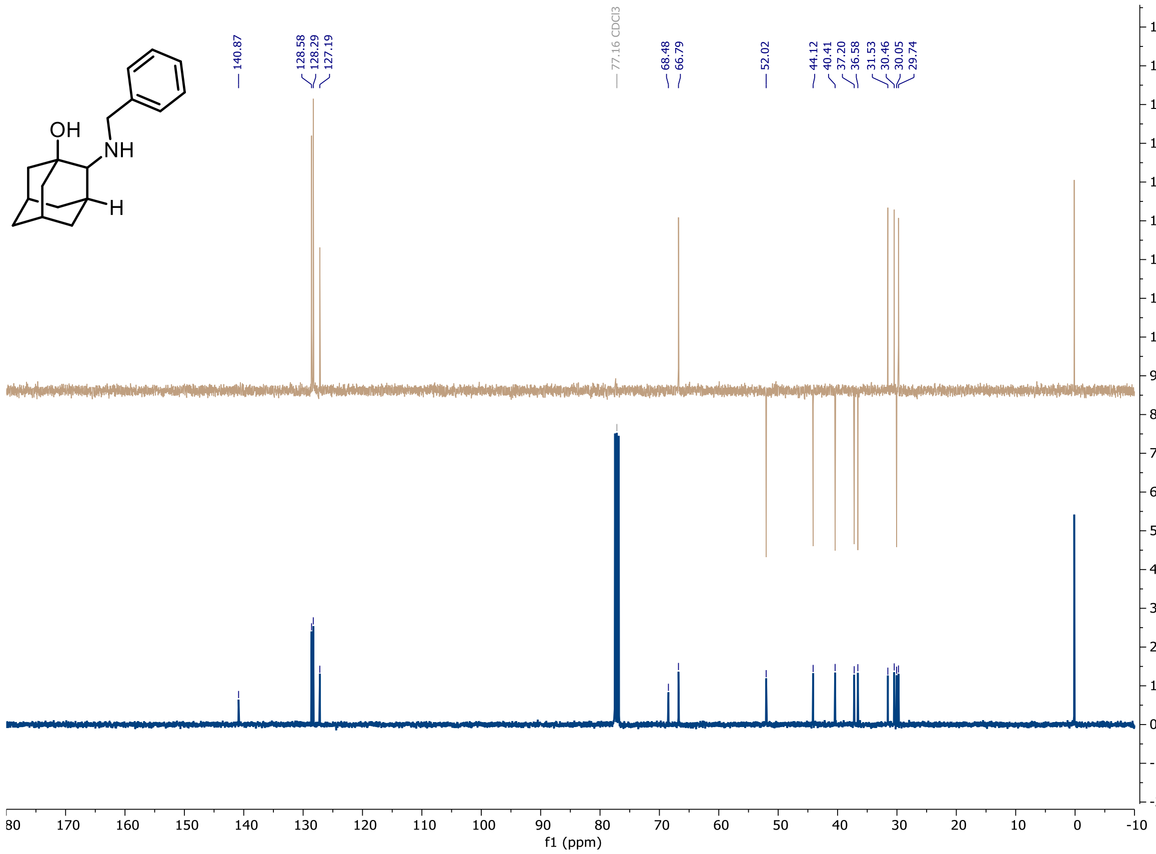
Compound 5b: ^{1}H NMR (400 MHz, CDCl$_3$)



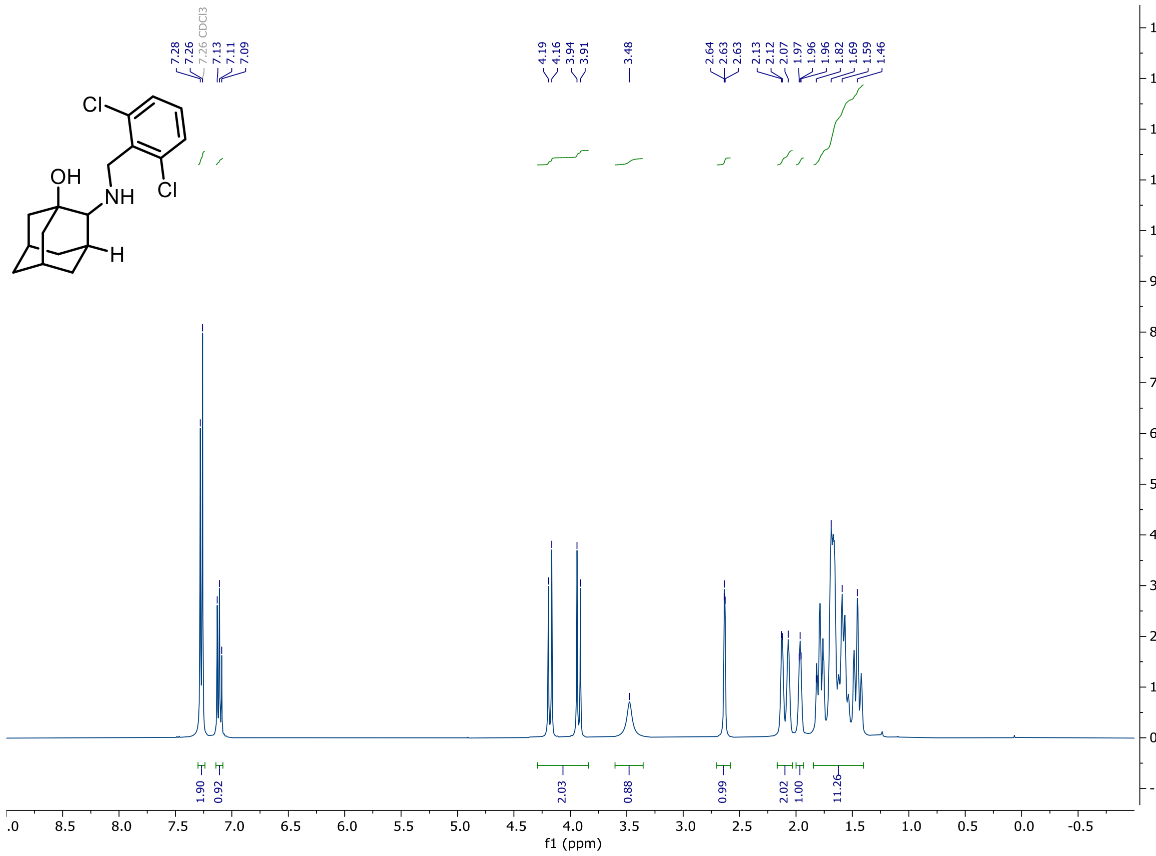
Compound 5b: ^{13}C NMR (101 MHz, $CDCl_3$)



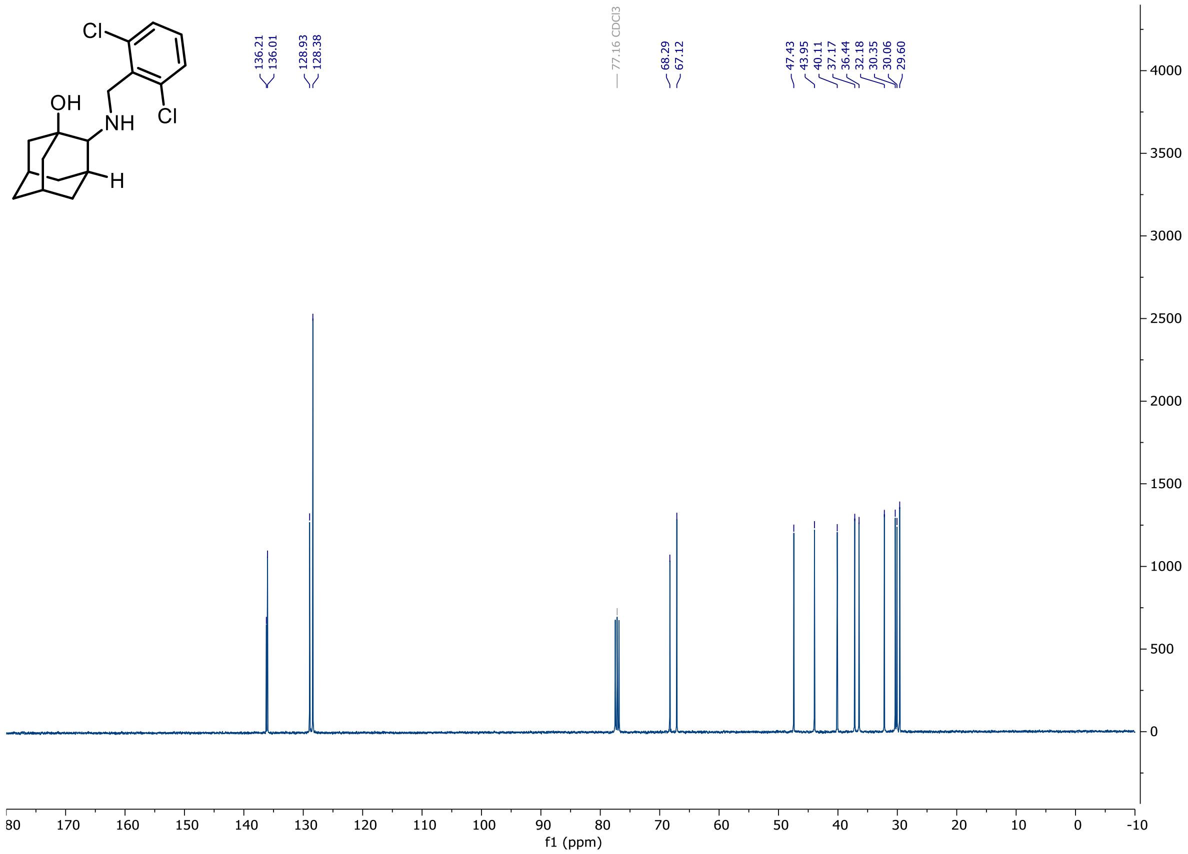
Compound 5b: ^{13}C NMR-DEPT (101 MHz, $CDCl_3$)



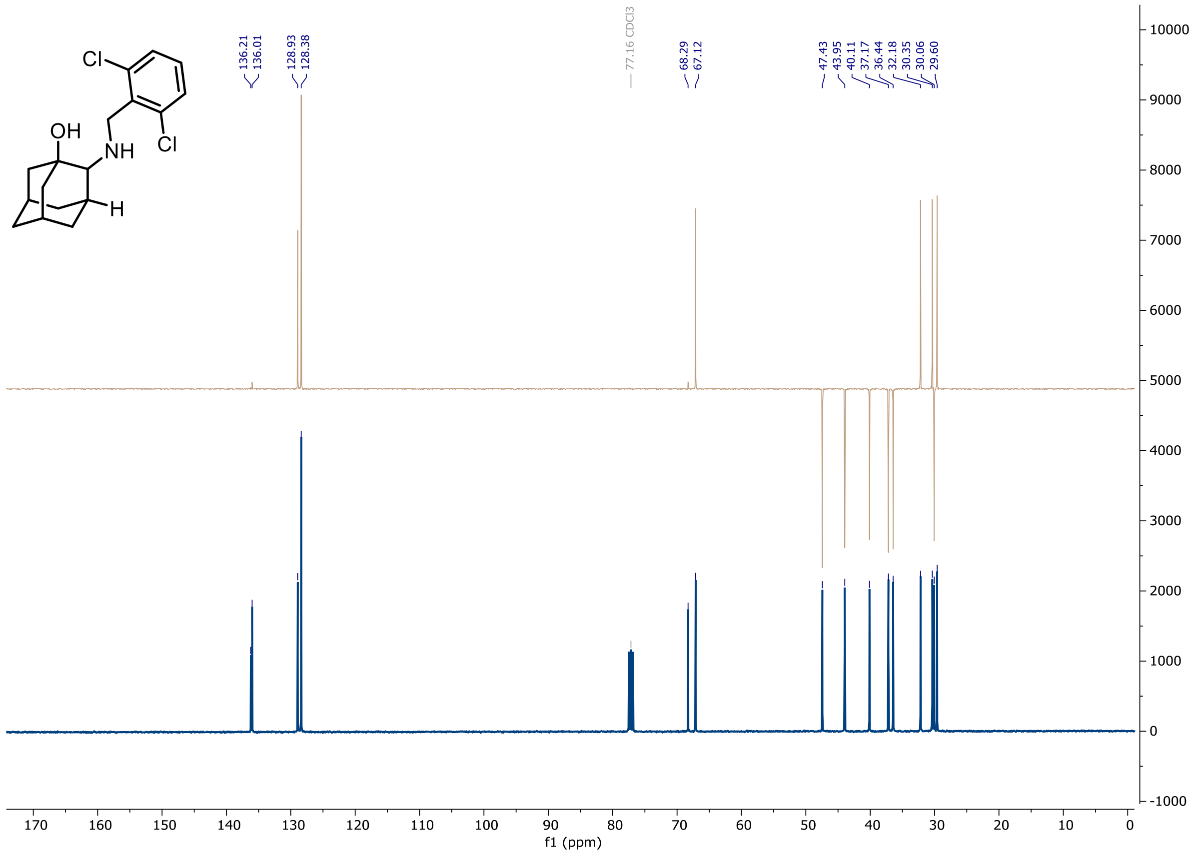
Compound 5c: ^{1}H NMR (400 MHz, $CDCl_3$)



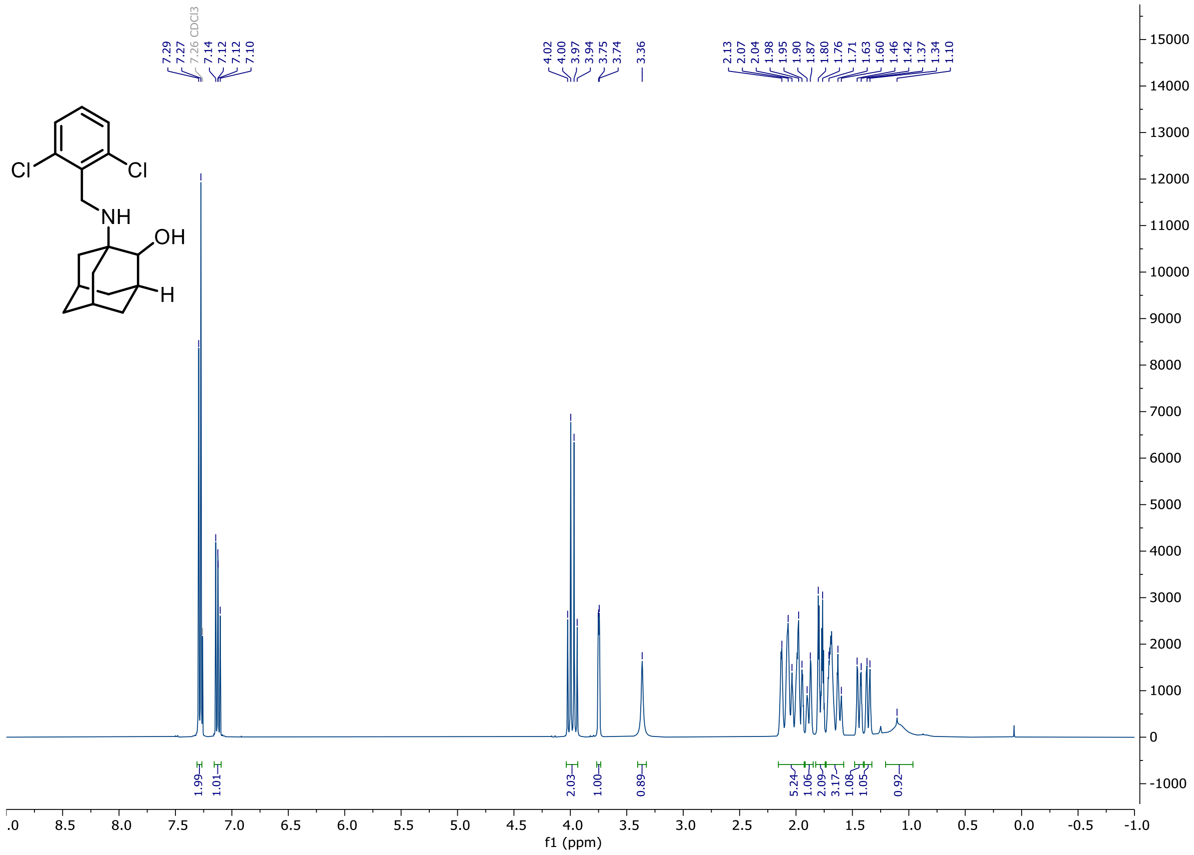
Compound 5c: ^{13}C NMR (101 MHz, CDCl$_3$)



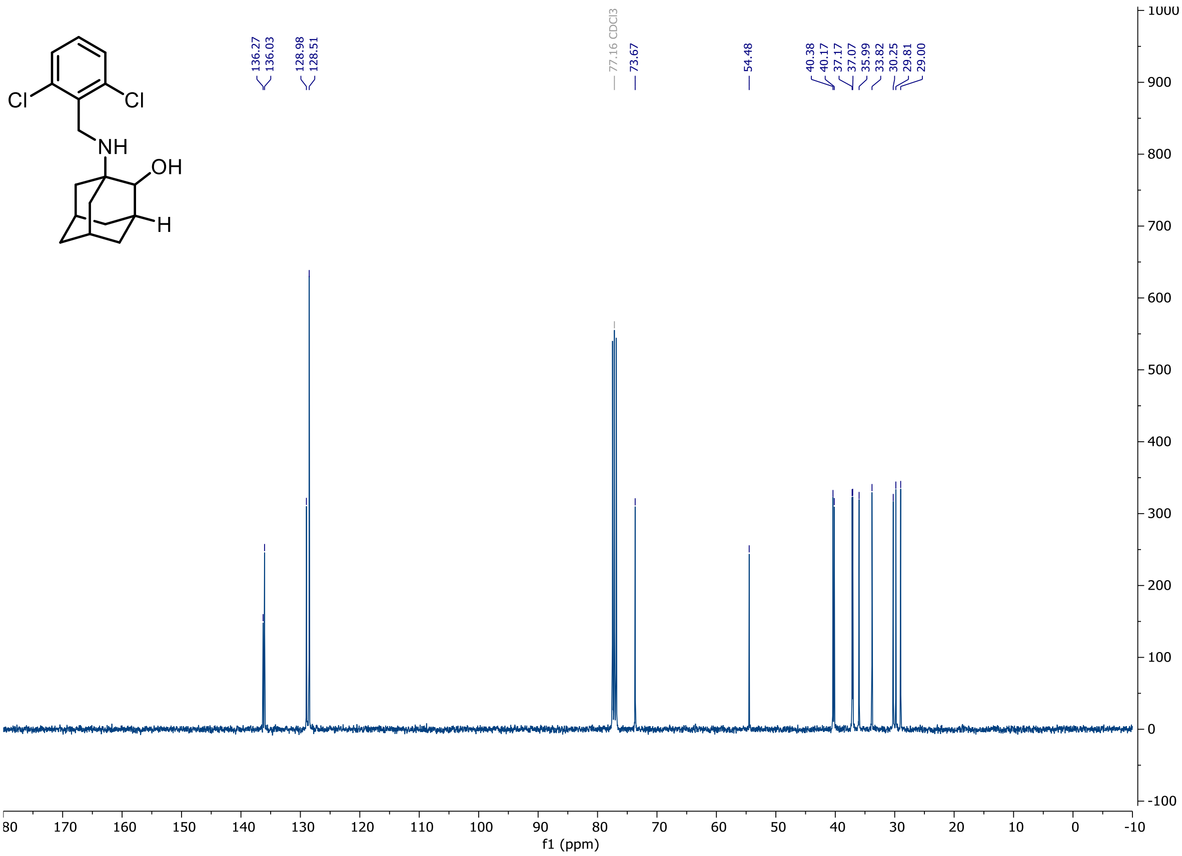
Compound 5c: ^{13}C NMR-DEPT (101 MHz, CDCl$_3$)



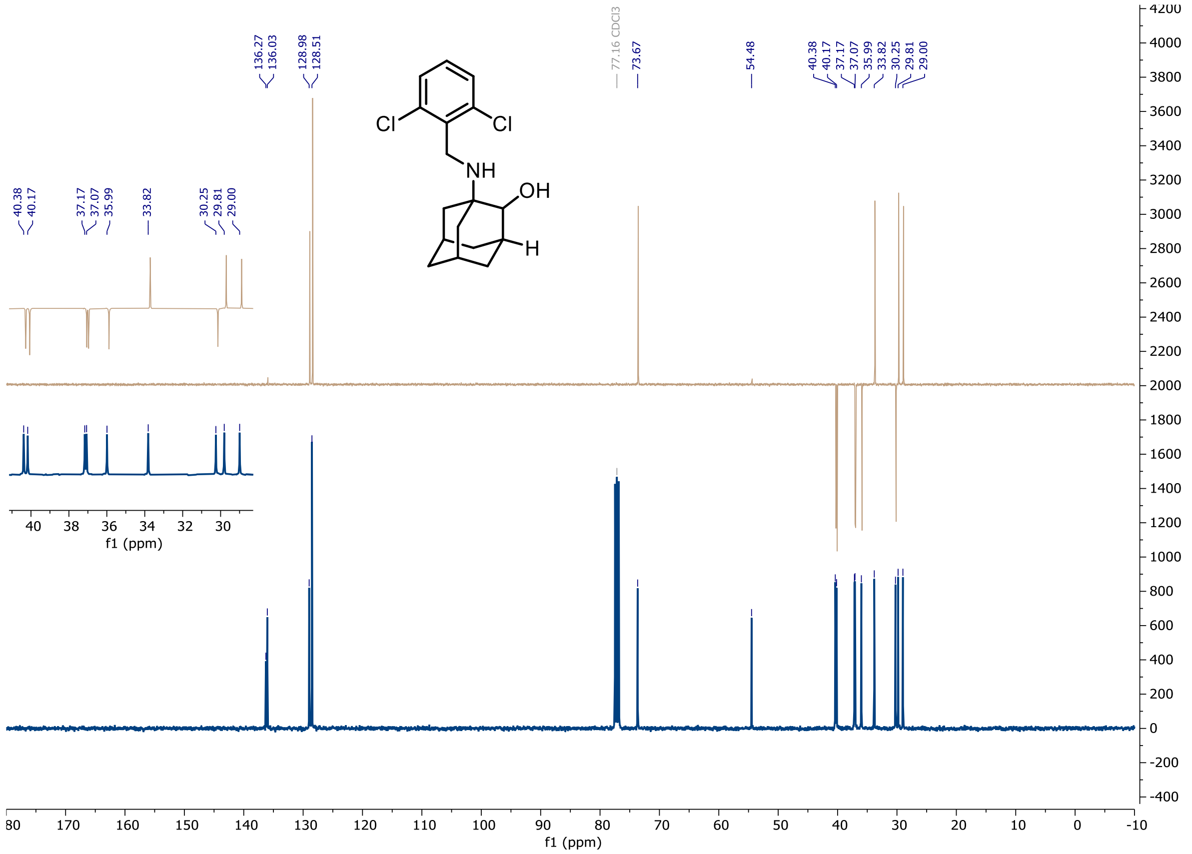
Compound 5d: ^{1}H NMR (400 MHz, $CDCl_3$)



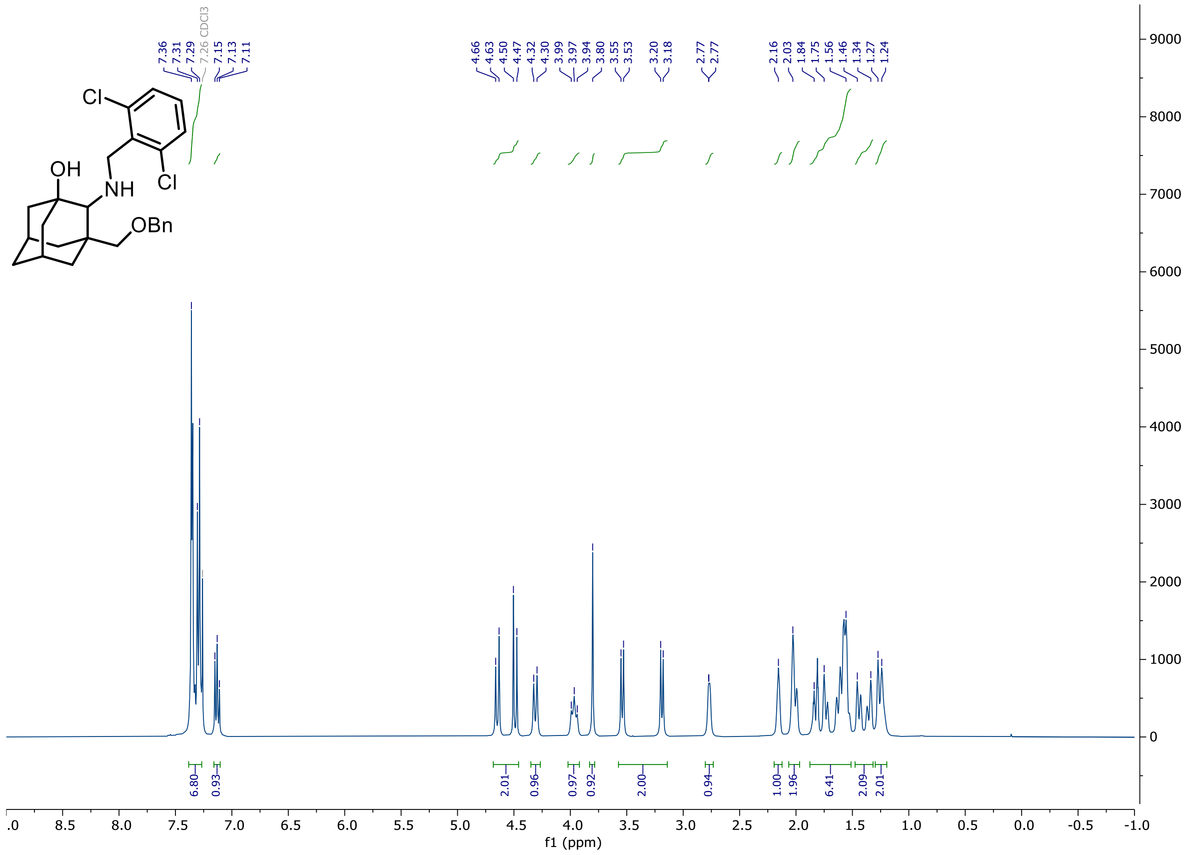
Compound 5d: ^{13}C NMR (101 MHz, CDCl$_3$)



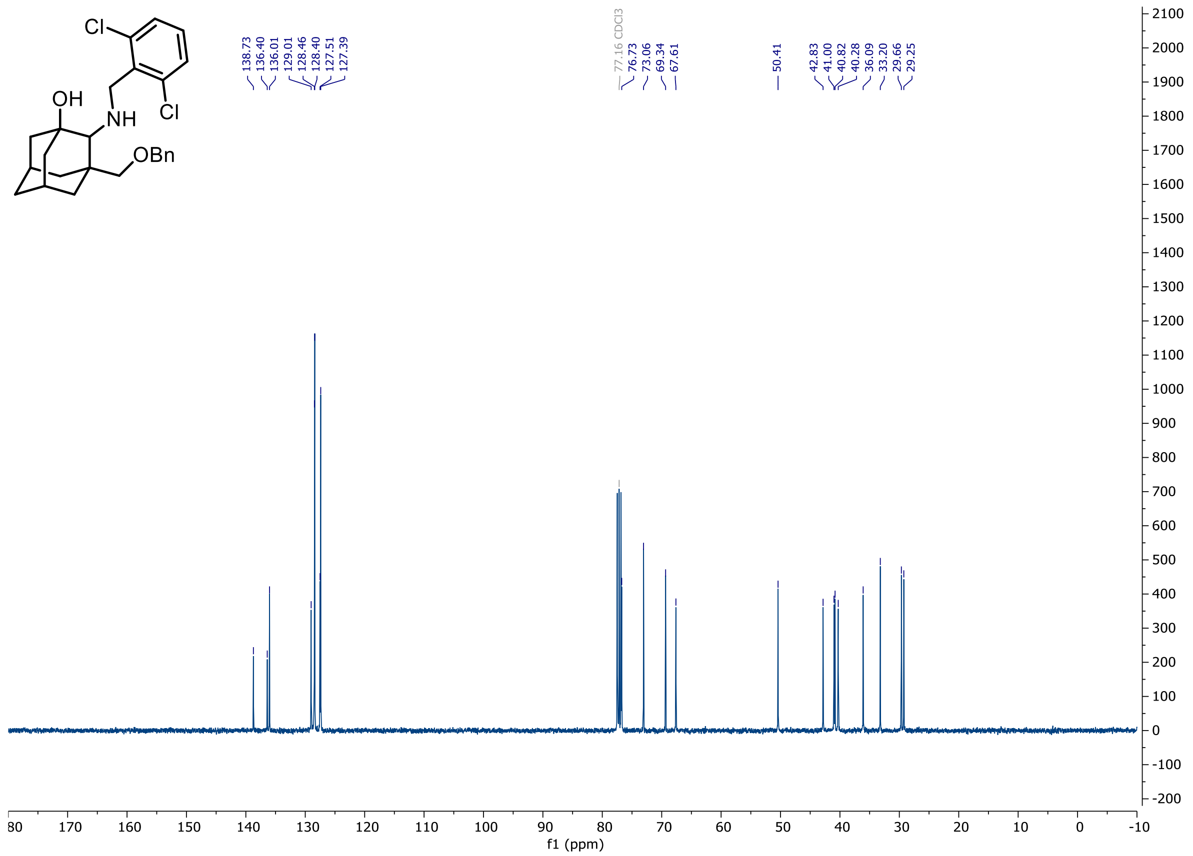
Compound 5d: ^{13}C NMR-DEPT (101 MHz, CDCl$_3$)



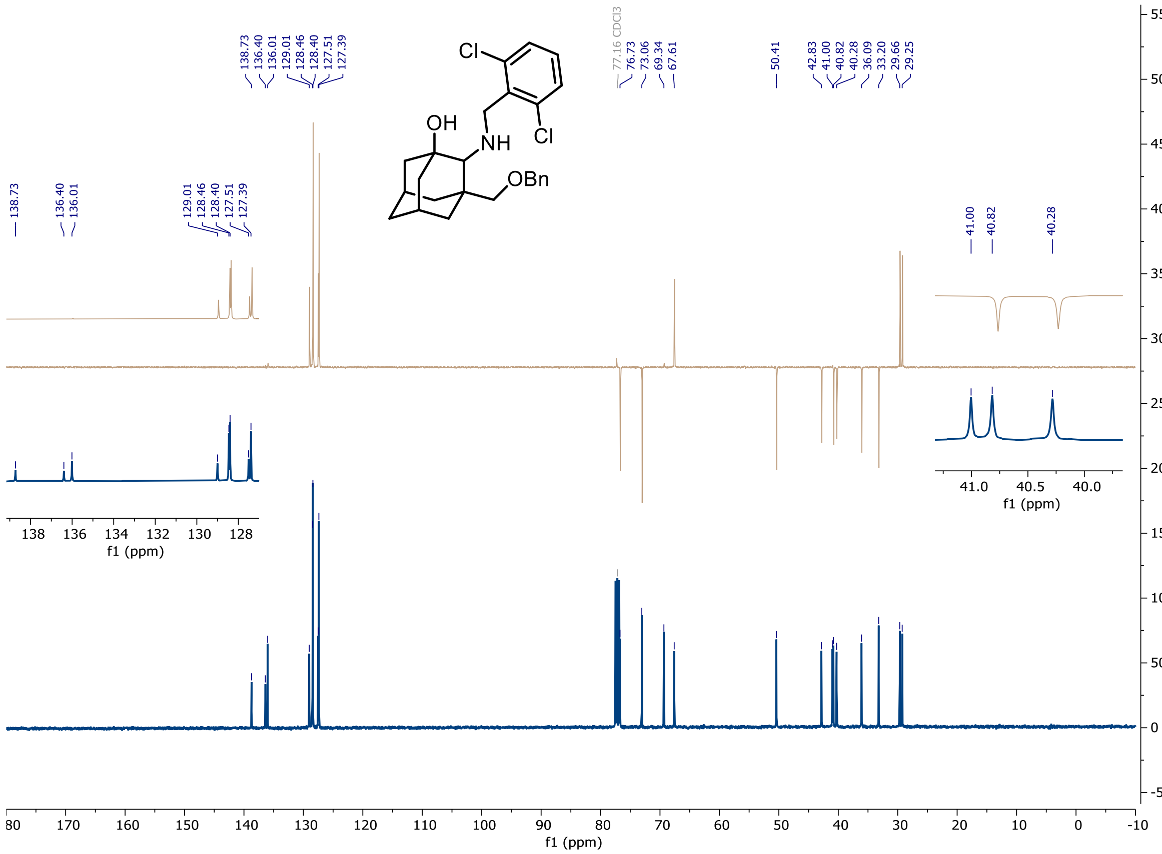
Compound 5e: ^{1}H NMR (400 MHz, CDCl$_3$)



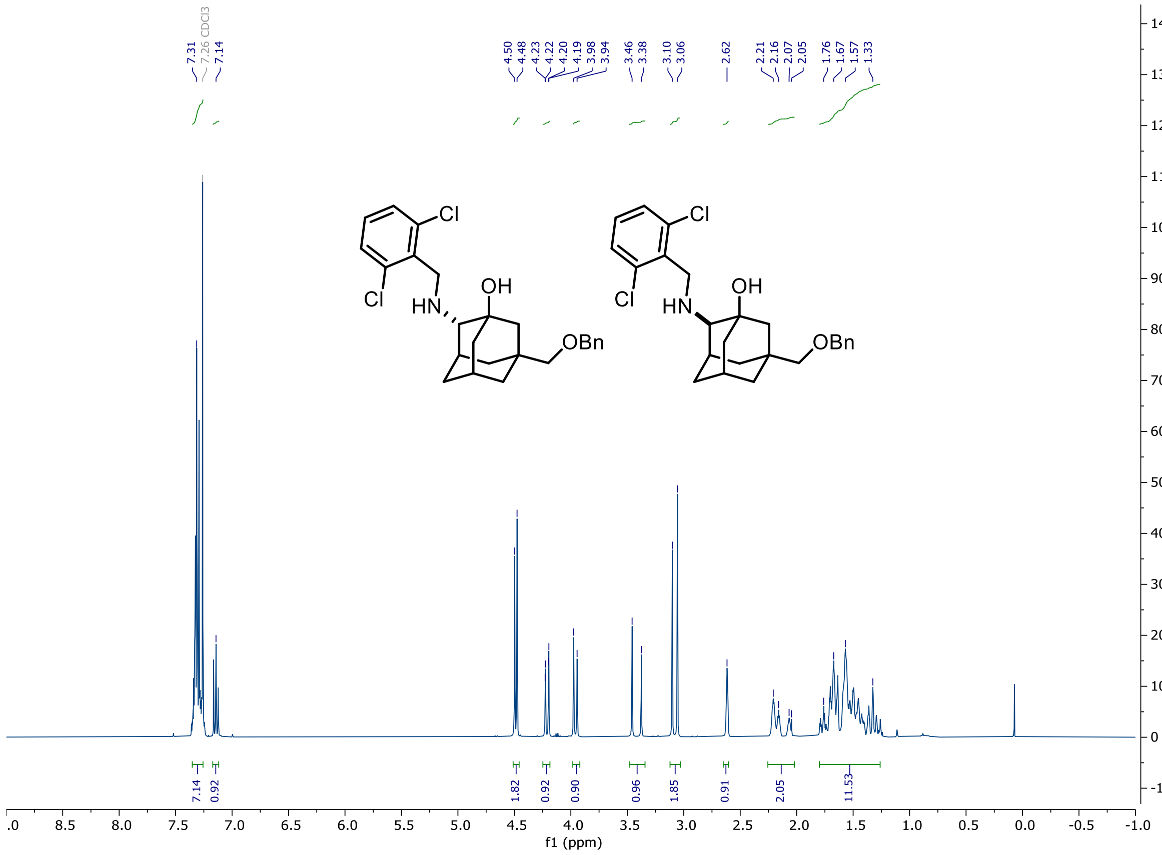
Compound 5e: ^{13}C NMR (101 MHz, $CDCl_3$)



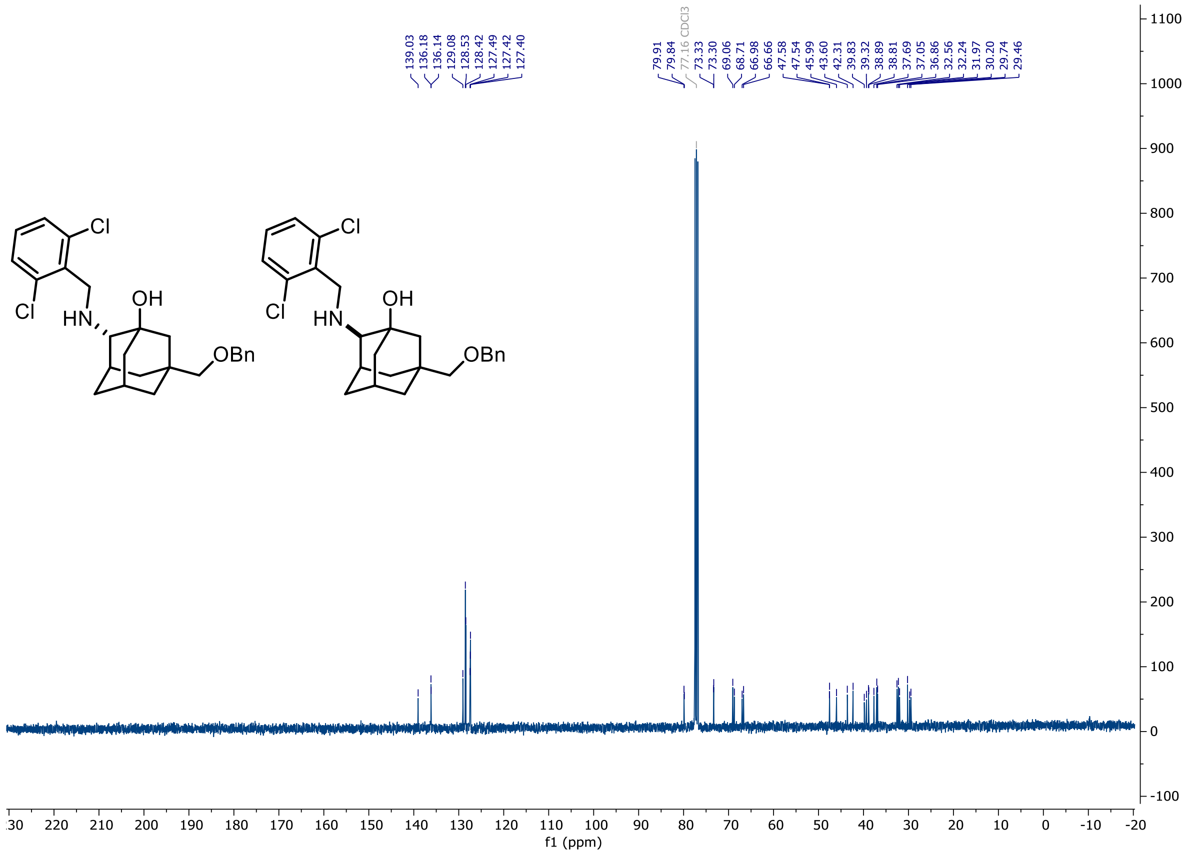
Compound 5e: ^{13}C NMR-DEPT (101 MHz, $CDCl_3$)



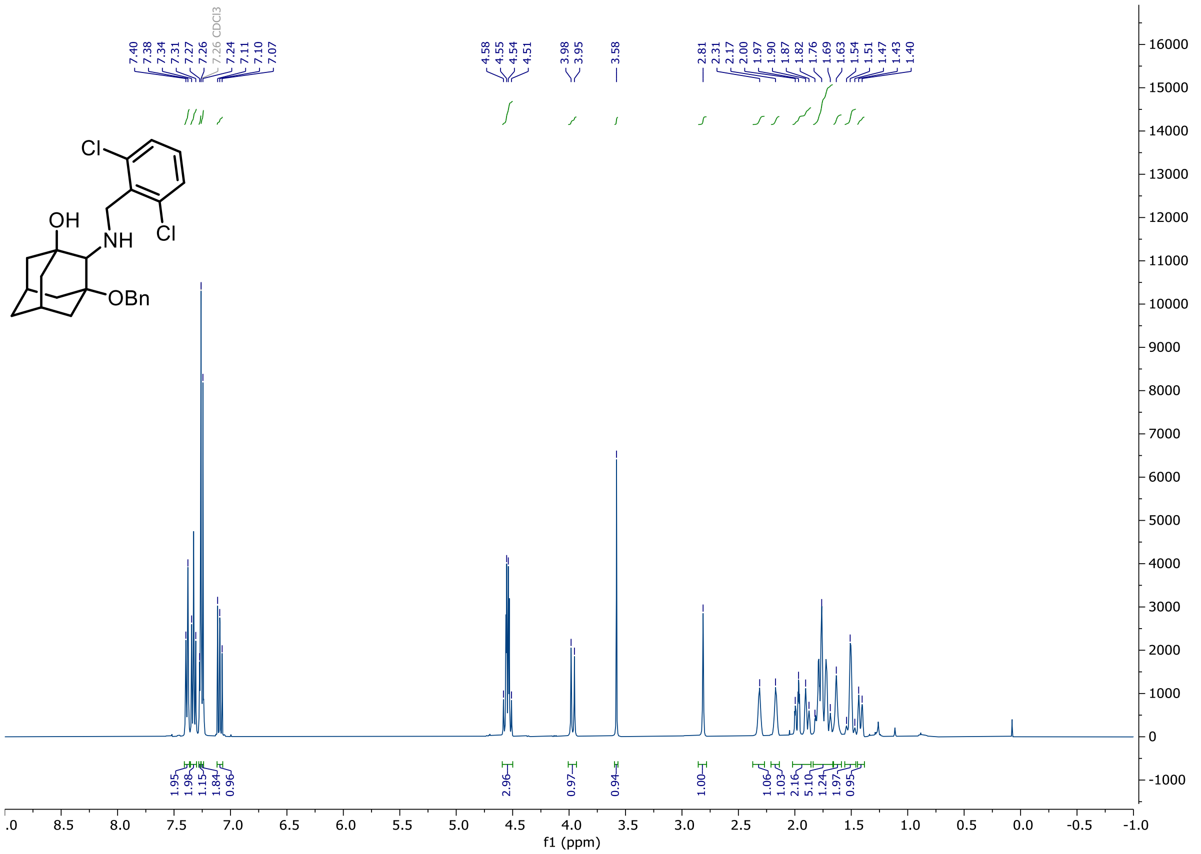
Compound 5f: ^{1}H NMR (400 MHz, CDCl$_3$)



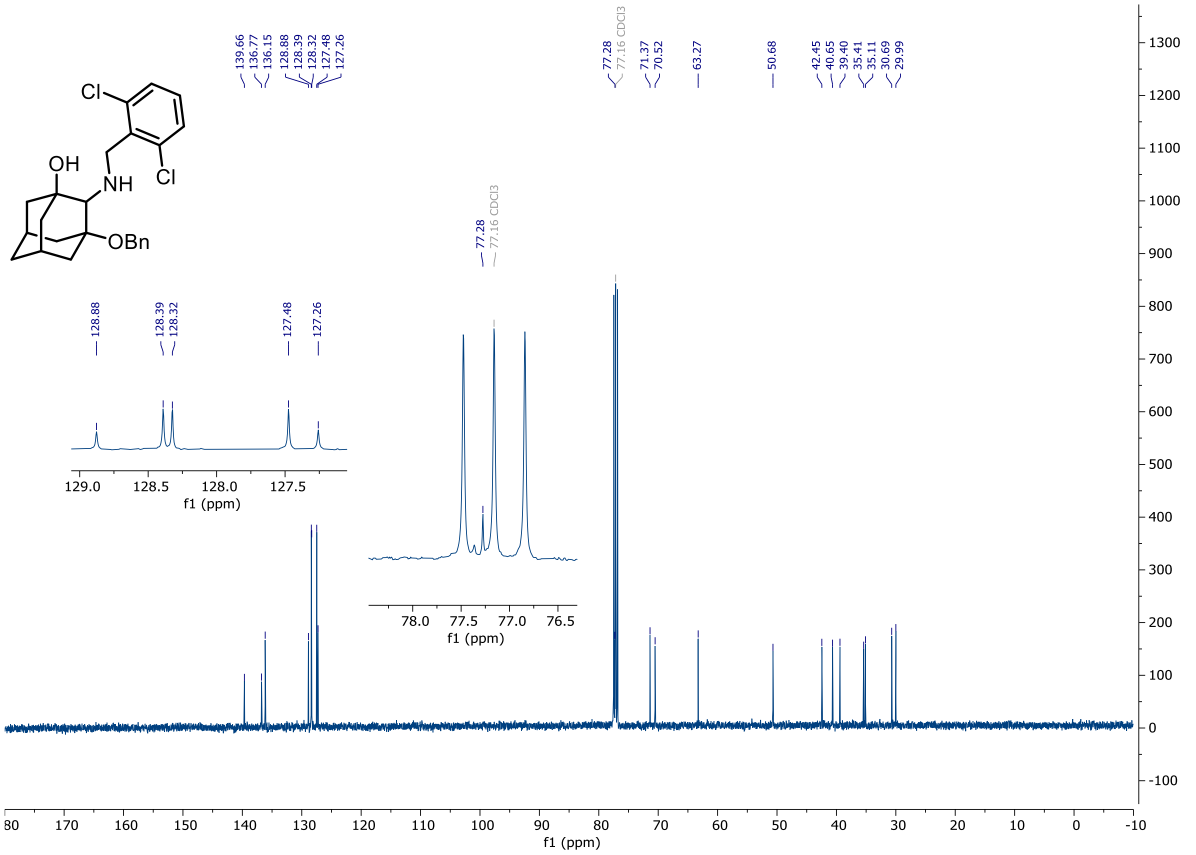
Compound 5f: ^{13}C NMR (101 MHz, CDCl$_3$)



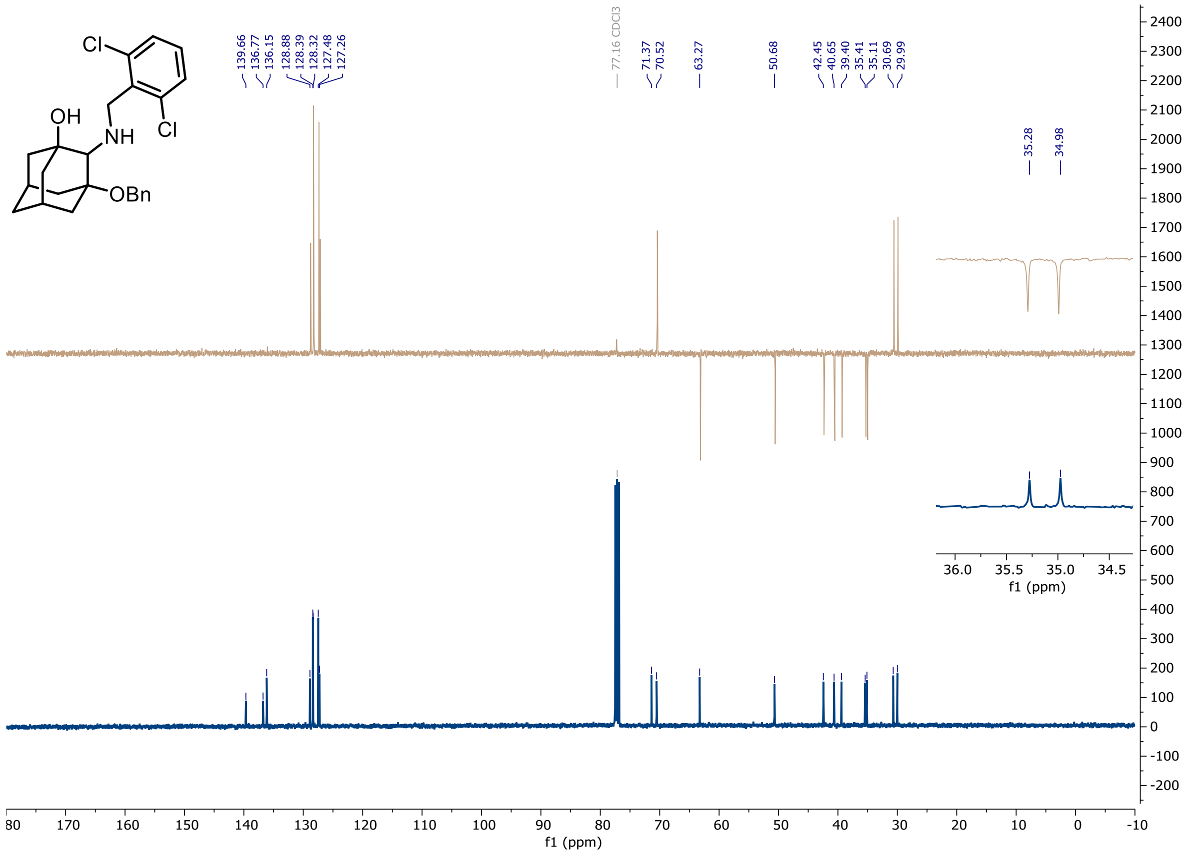
Compound 5g: ^{1}H NMR (400 MHz, CDCl$_3$)



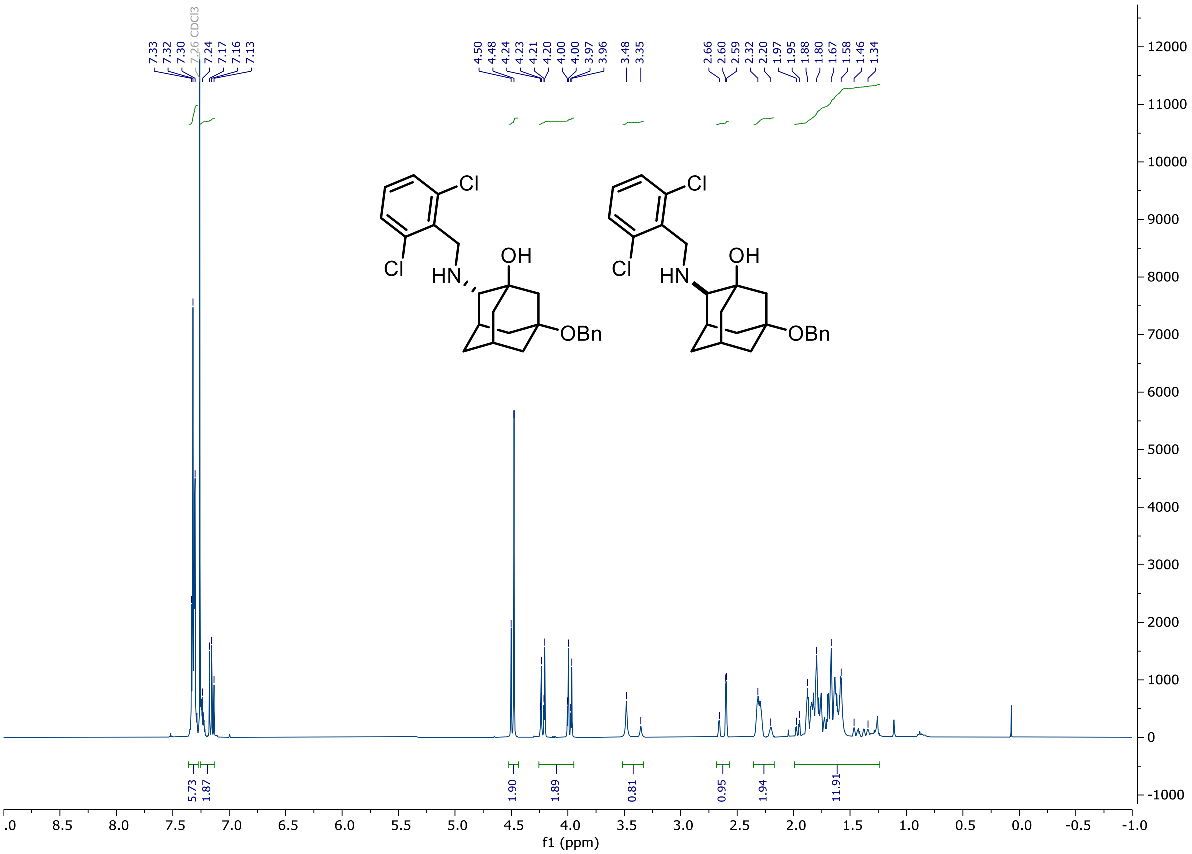
Compound 5g: ^{13}C NMR (101 MHz, $CDCl_3$)



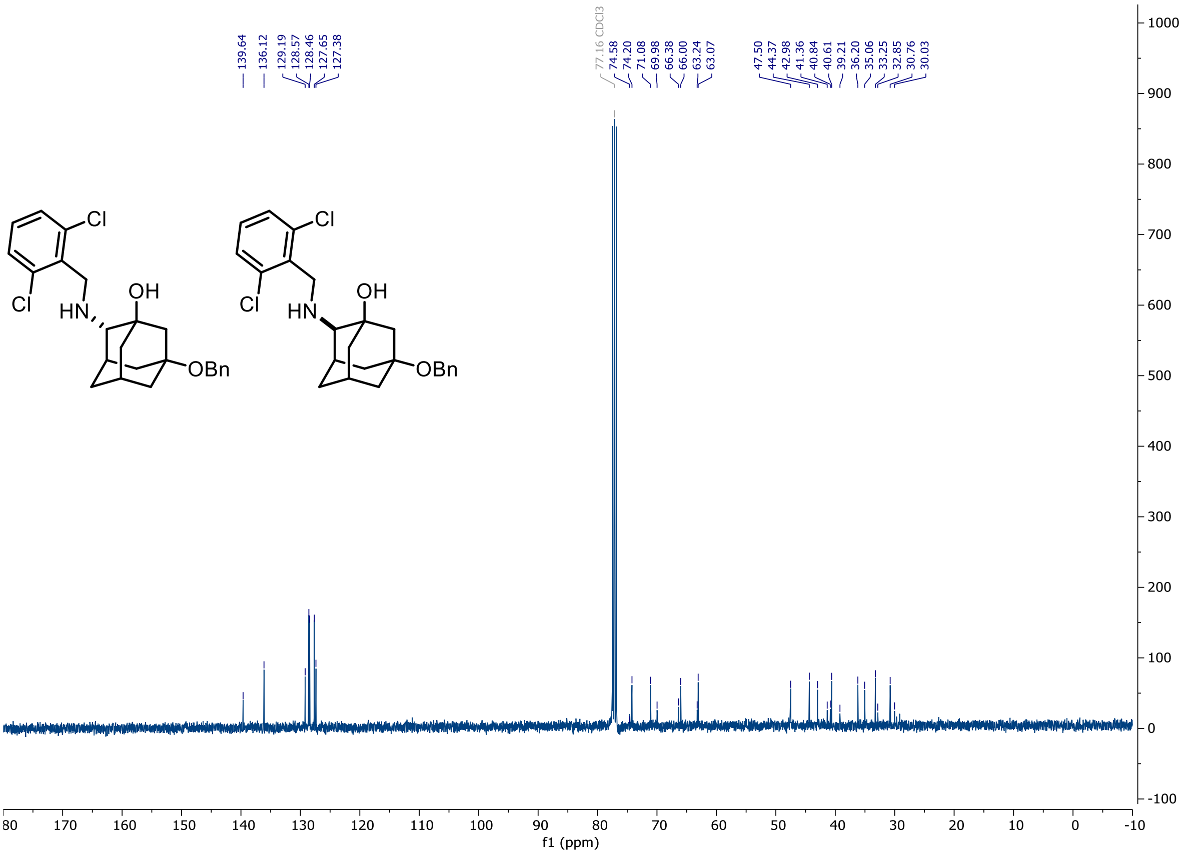
Compound 5g: ^{13}C NMR-DEPT (101 MHz, CDCl$_3$)



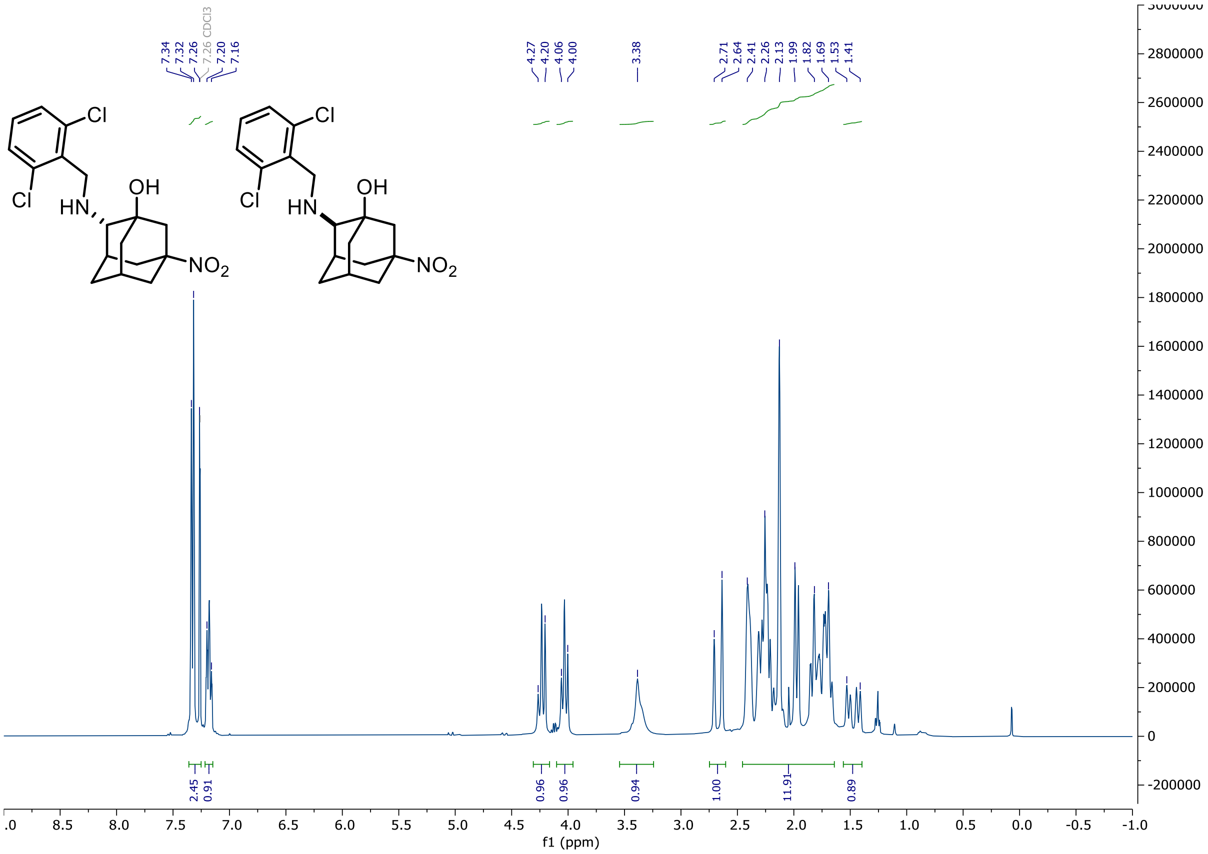
Compound 5h: ^{1}H NMR (400 MHz, CDCl$_3$)



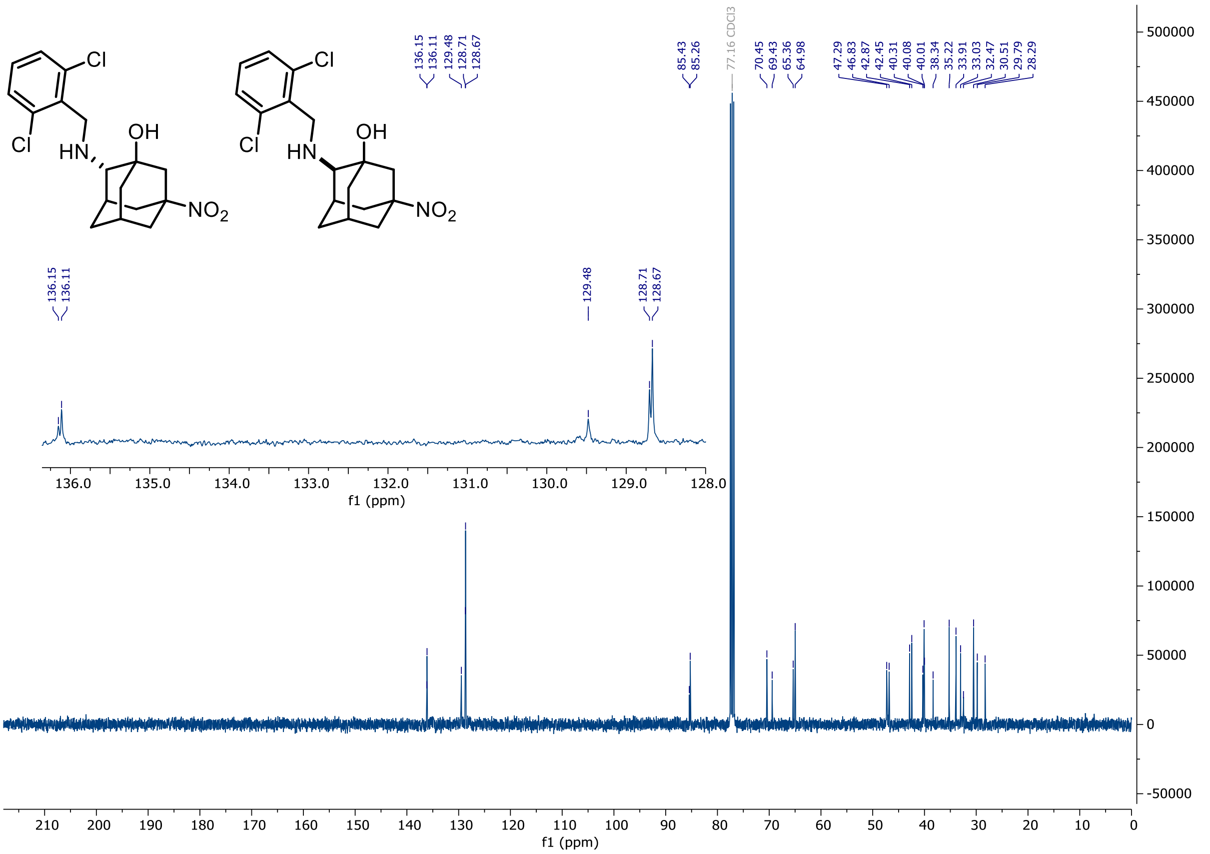
Compound 5h: ^{13}C NMR (101 MHz, CDCl$_3$)



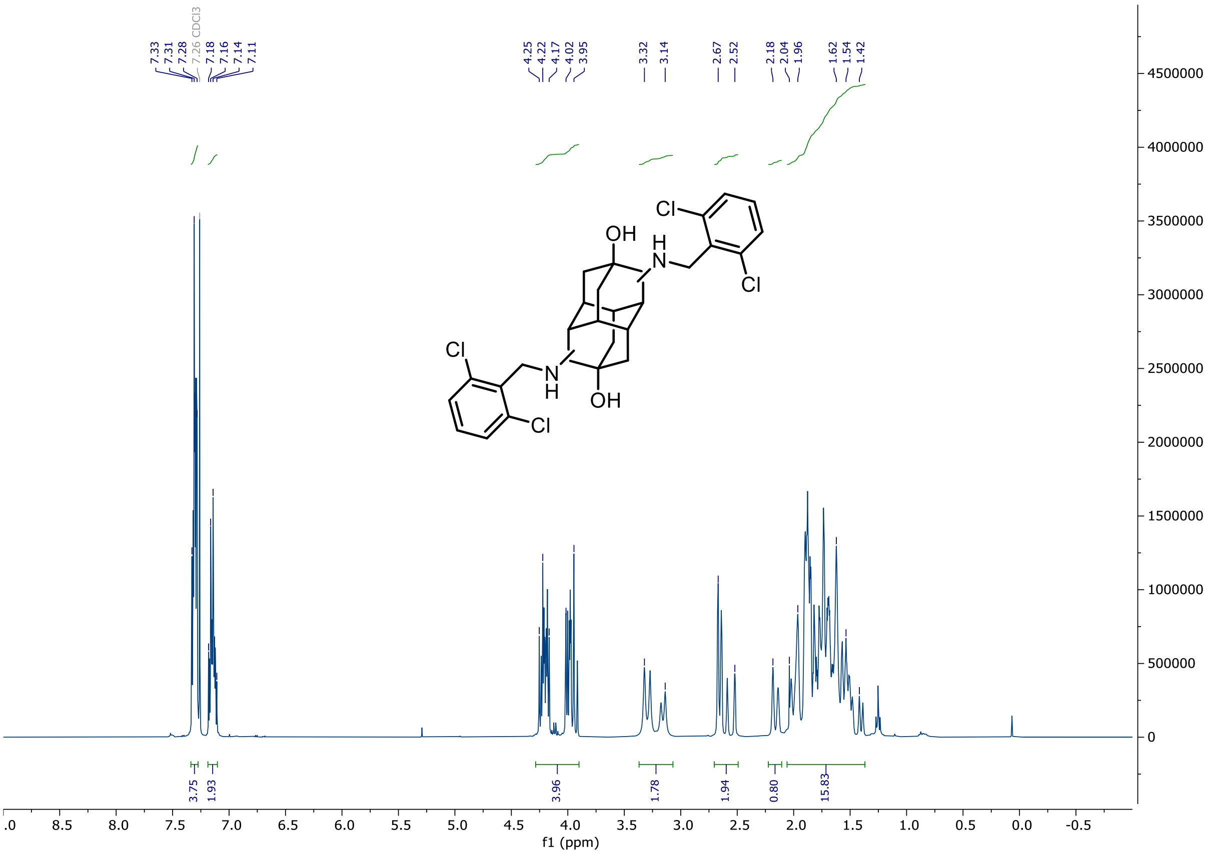
Compound 5i: ^{1}H NMR (400 MHz, CDCl$_3$)



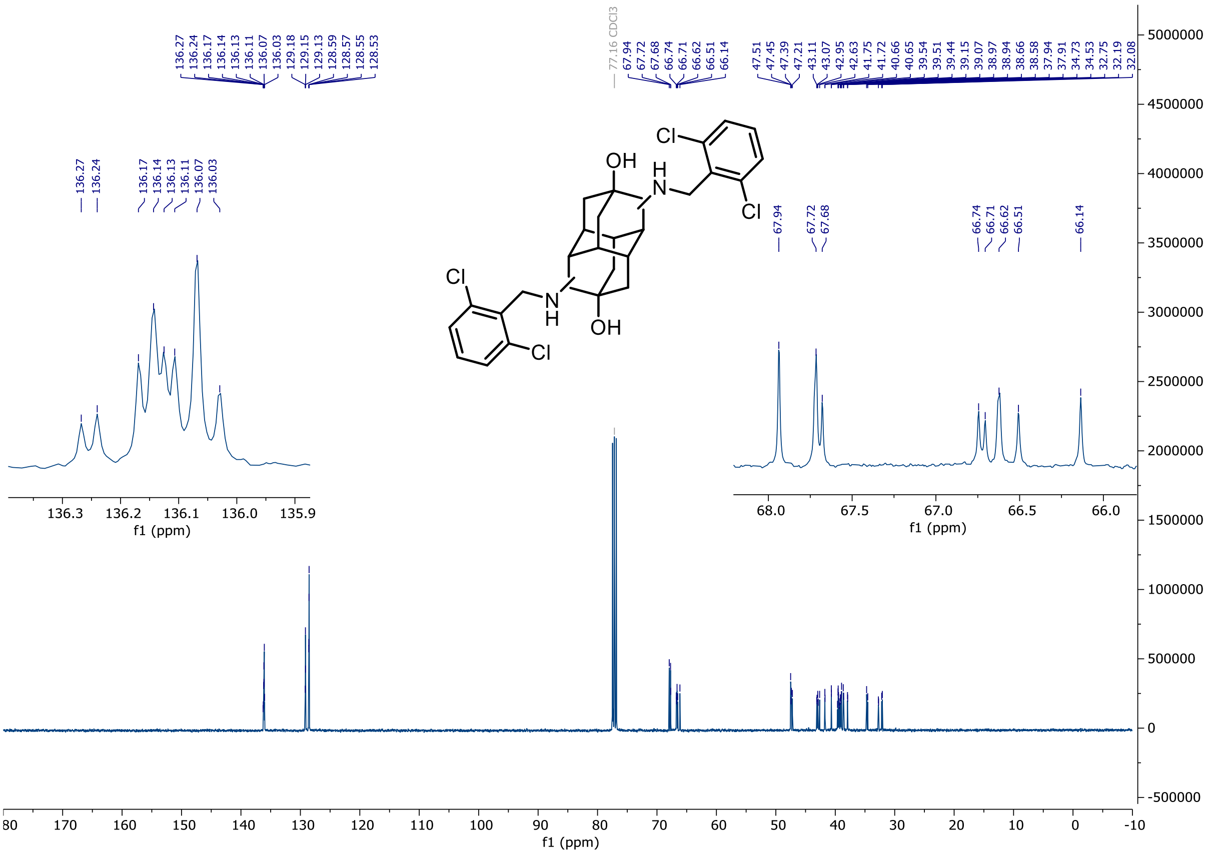
Compound 5i: ^{13}C NMR (101 MHz, CDCl$_3$)



Compound 5j: ^{1}H NMR (400 MHz, $CDCl_3$)

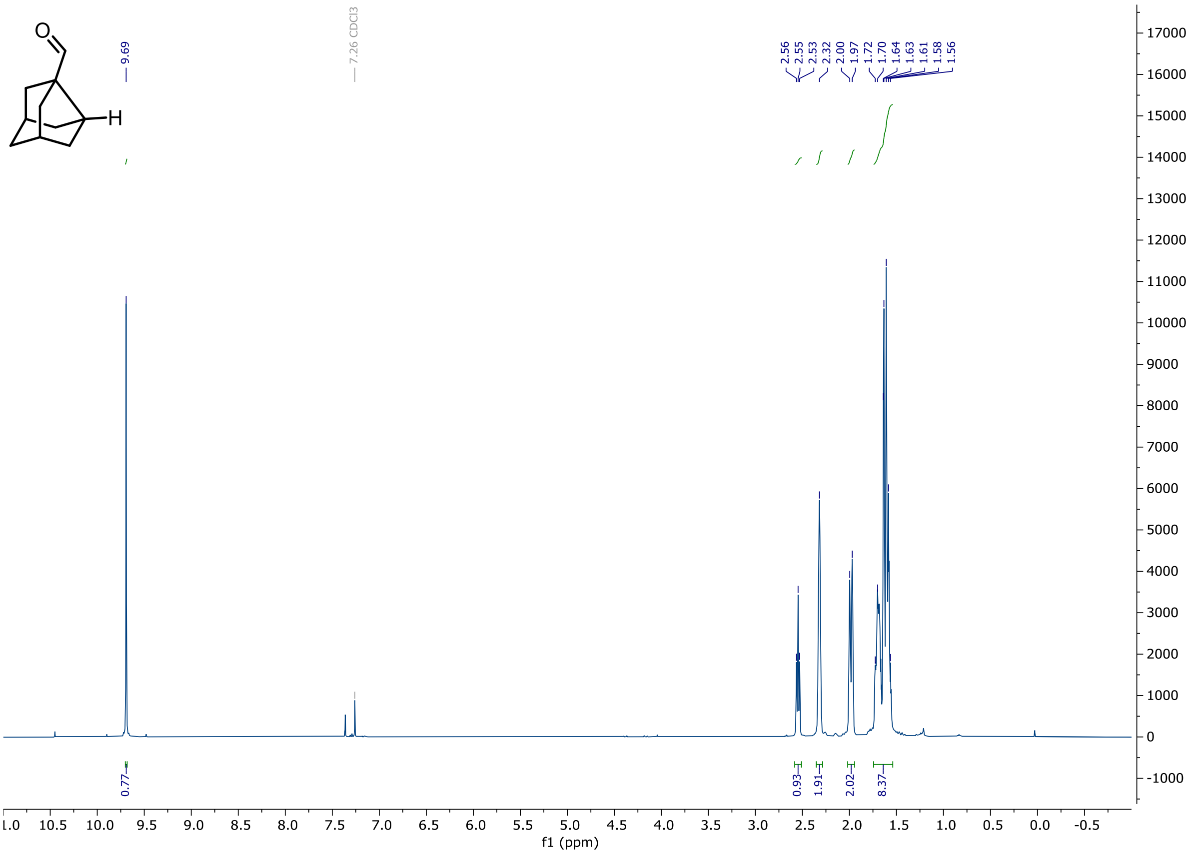


Compound 5j: ^{13}C NMR (101 MHz, $CDCl_3$)

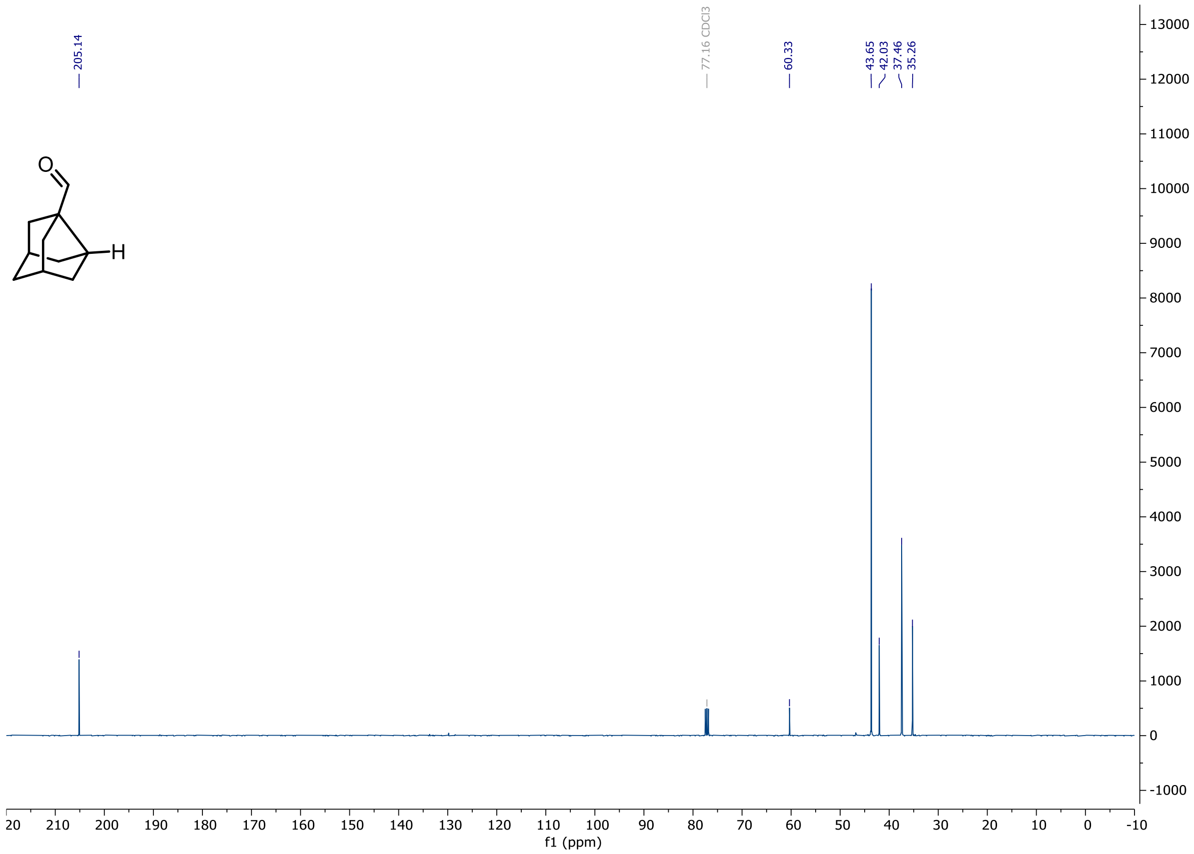


Noradamantyl Carbaldehydes

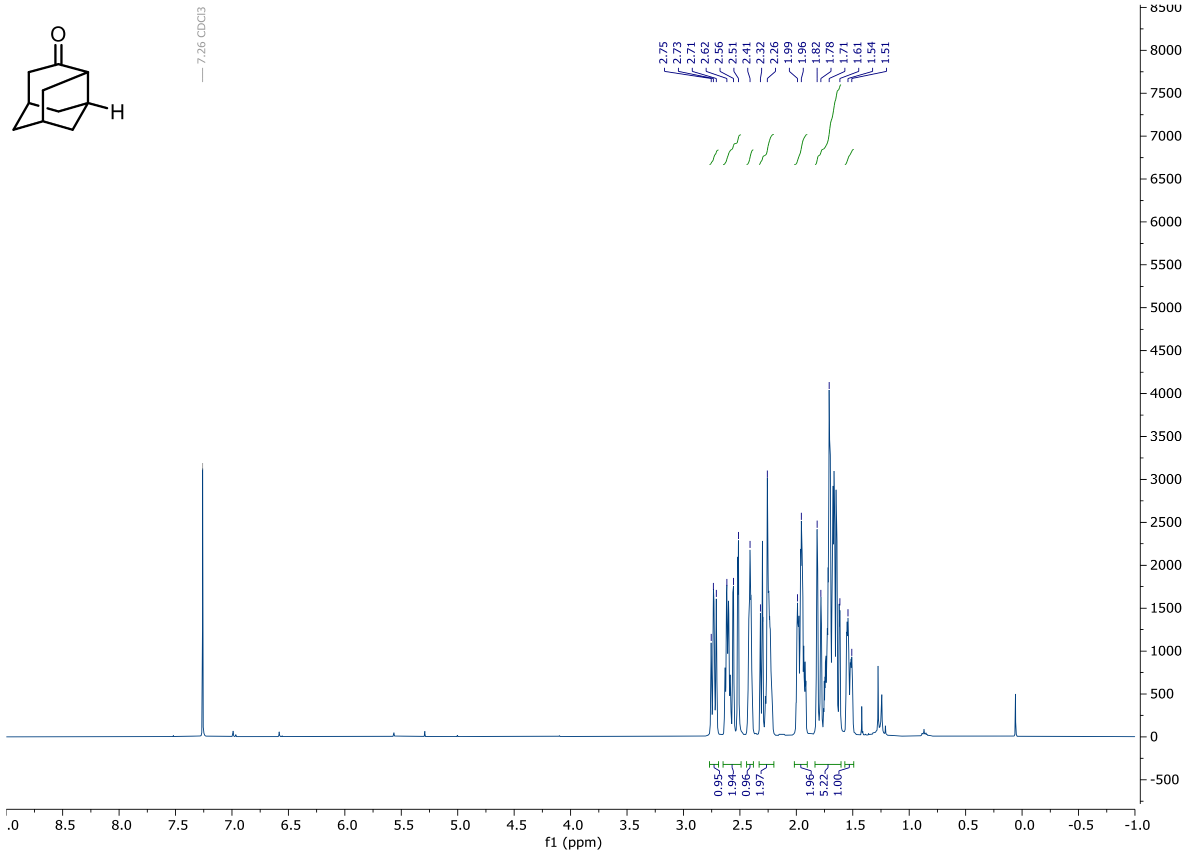
Compound 6a: ^{1}H NMR (400 MHz, $CDCl_3$)



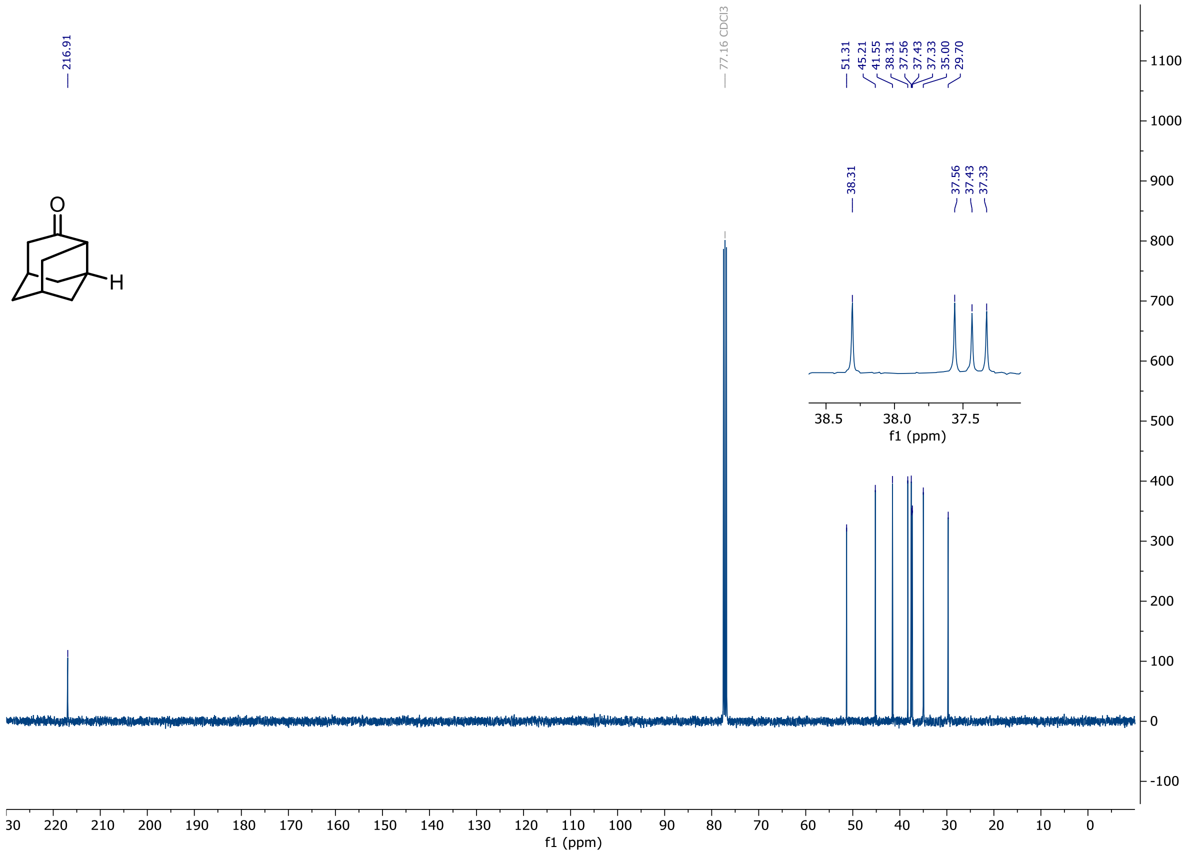
Compound 6a: ^{13}C NMR (101 MHz, $CDCl_3$)



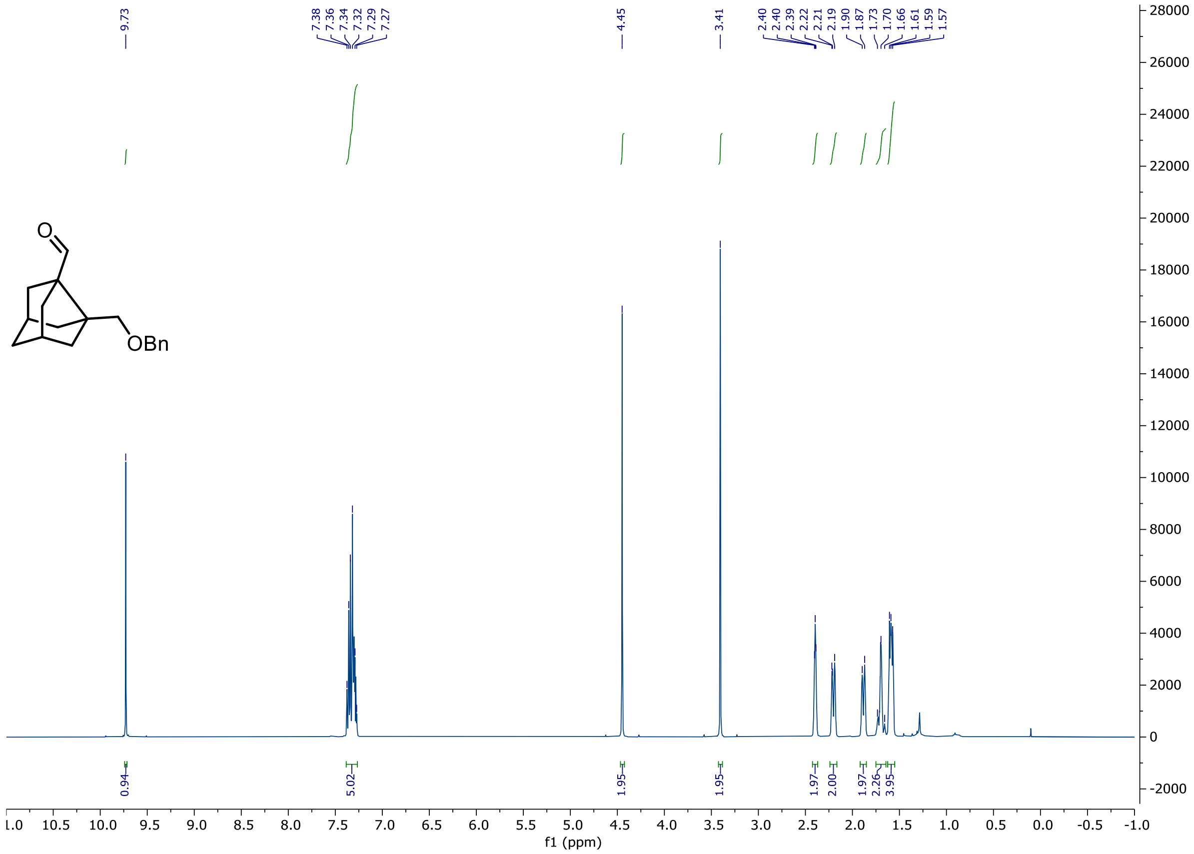
Compound 6b: ^{1}H NMR (400 MHz, $CDCl_3$)



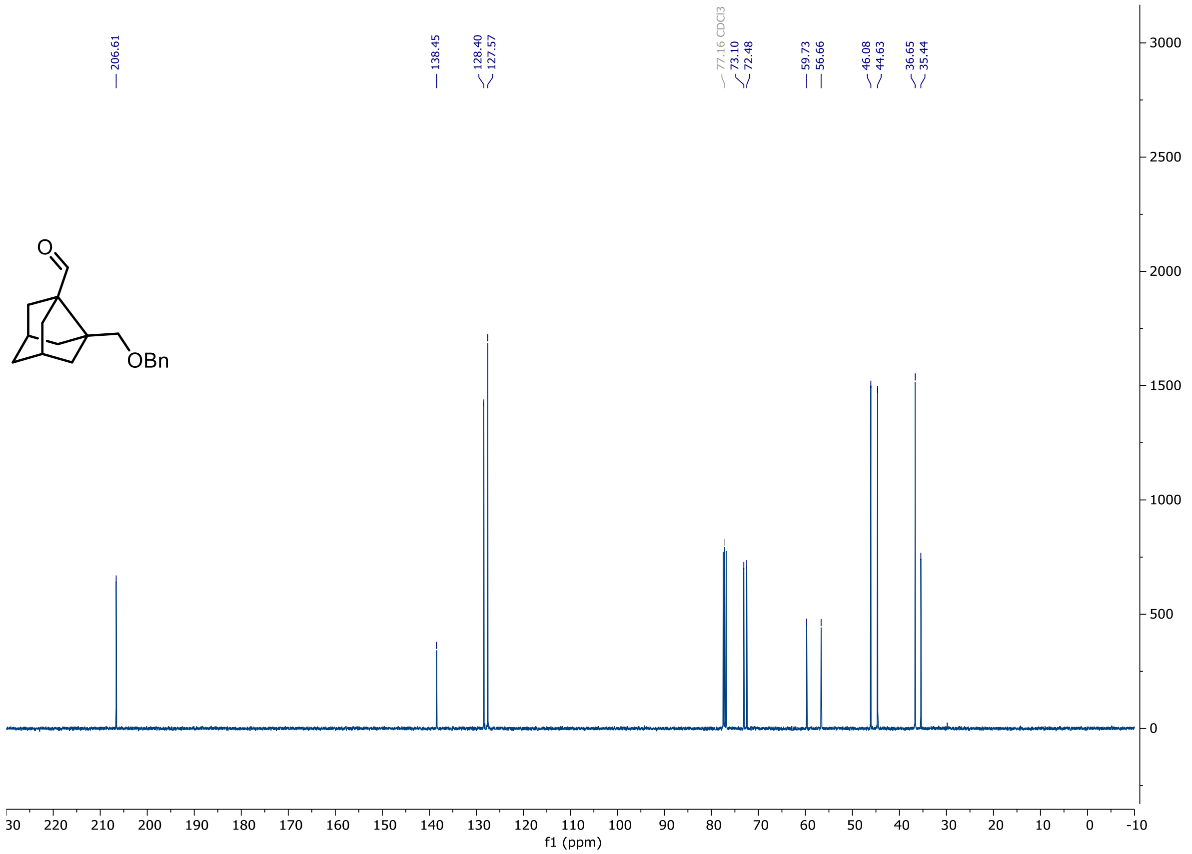
Compound 6b: ^{13}C NMR (101 MHz, CDCl$_3$)



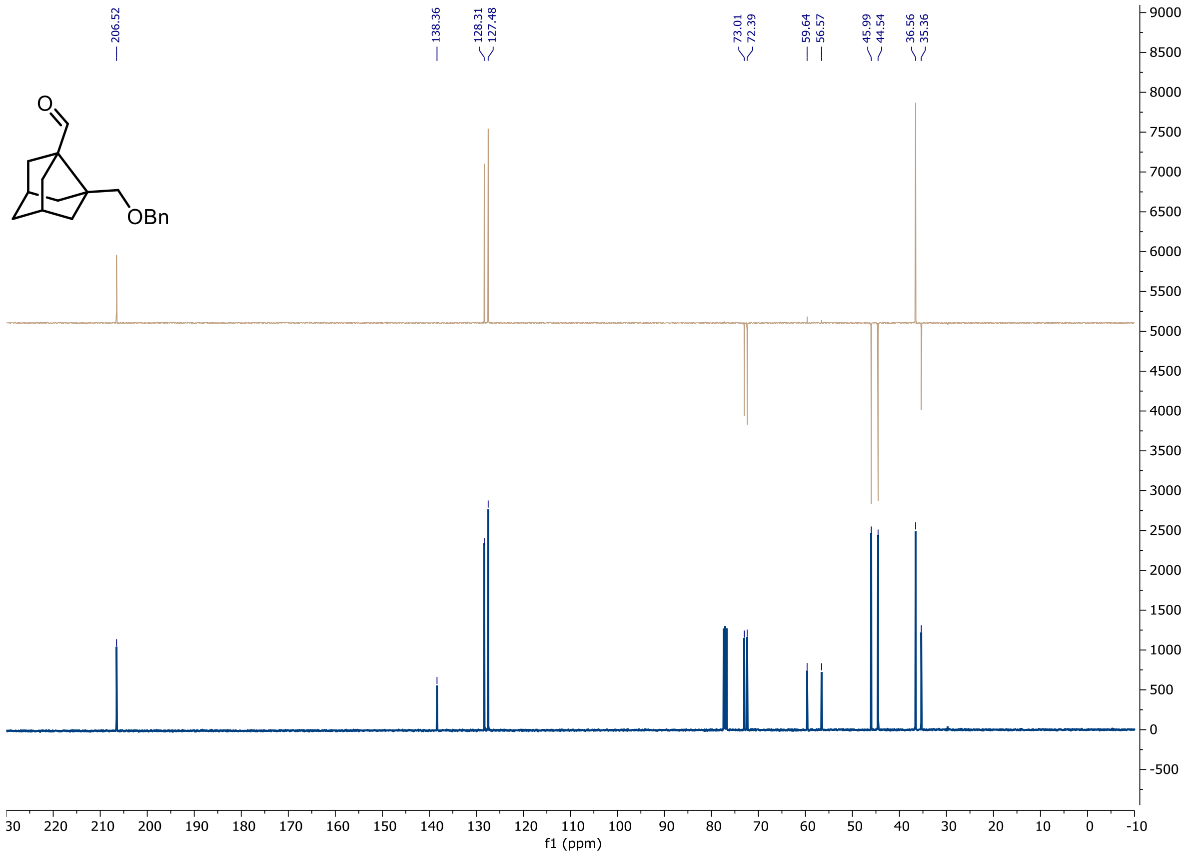
Compound 6c: ^{1}H NMR (400 MHz, CDCl$_3$)



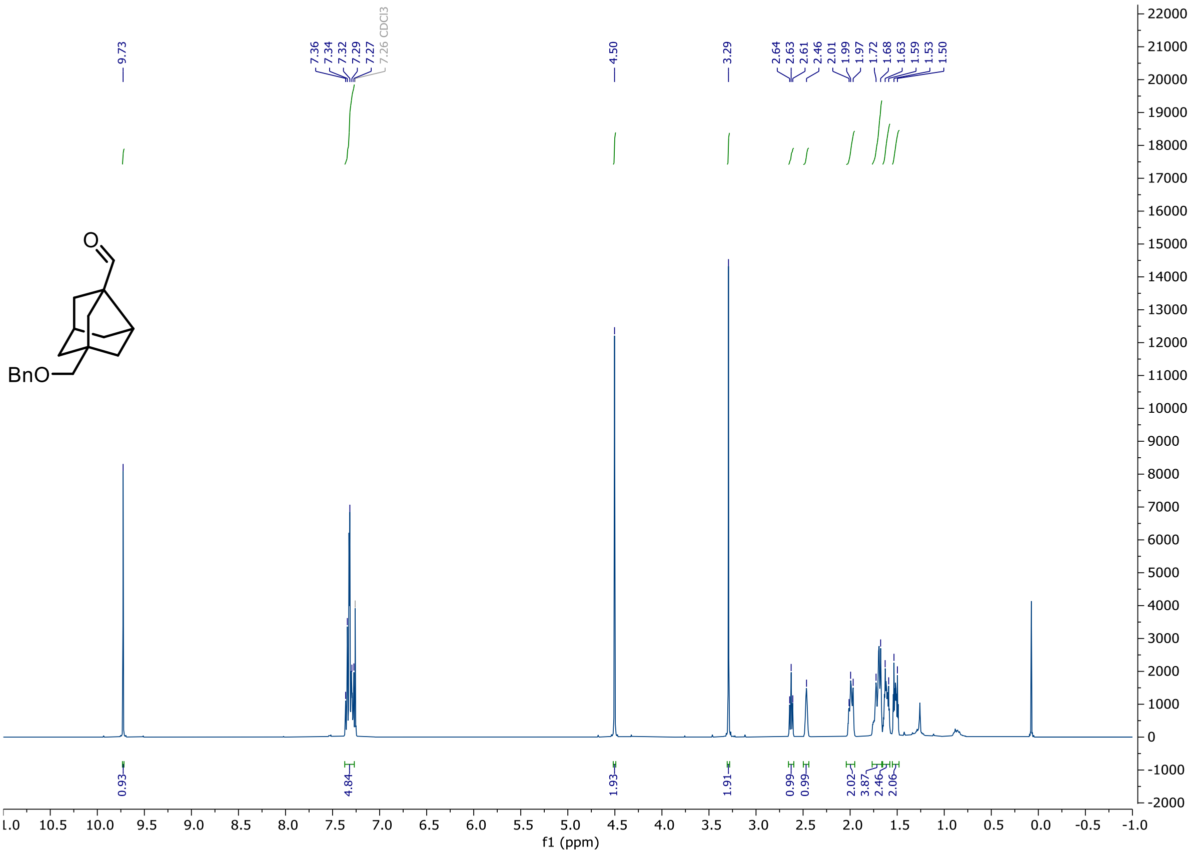
Compound 6c: ^{13}C NMR (101 MHz, CDCl$_3$)



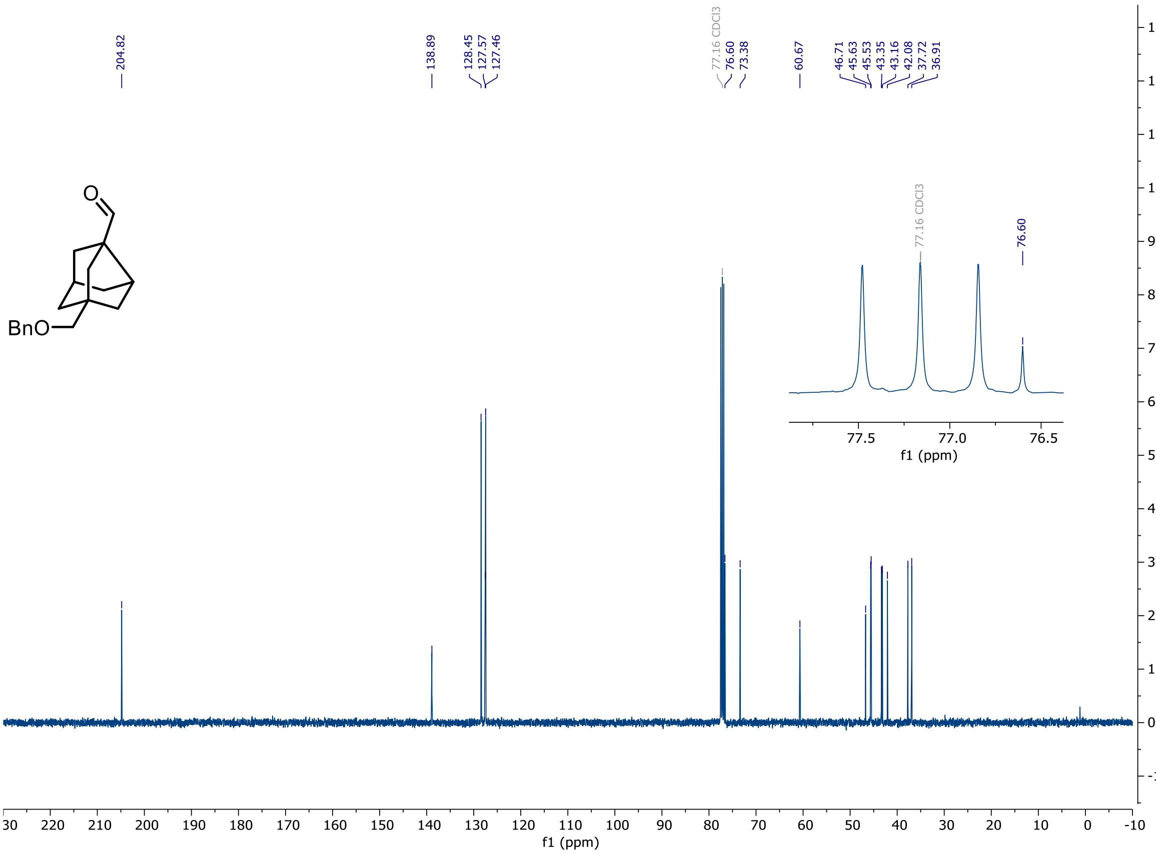
Compound 6c: ^{13}C NMR-DEPT (101 MHz, CDCl$_3$)



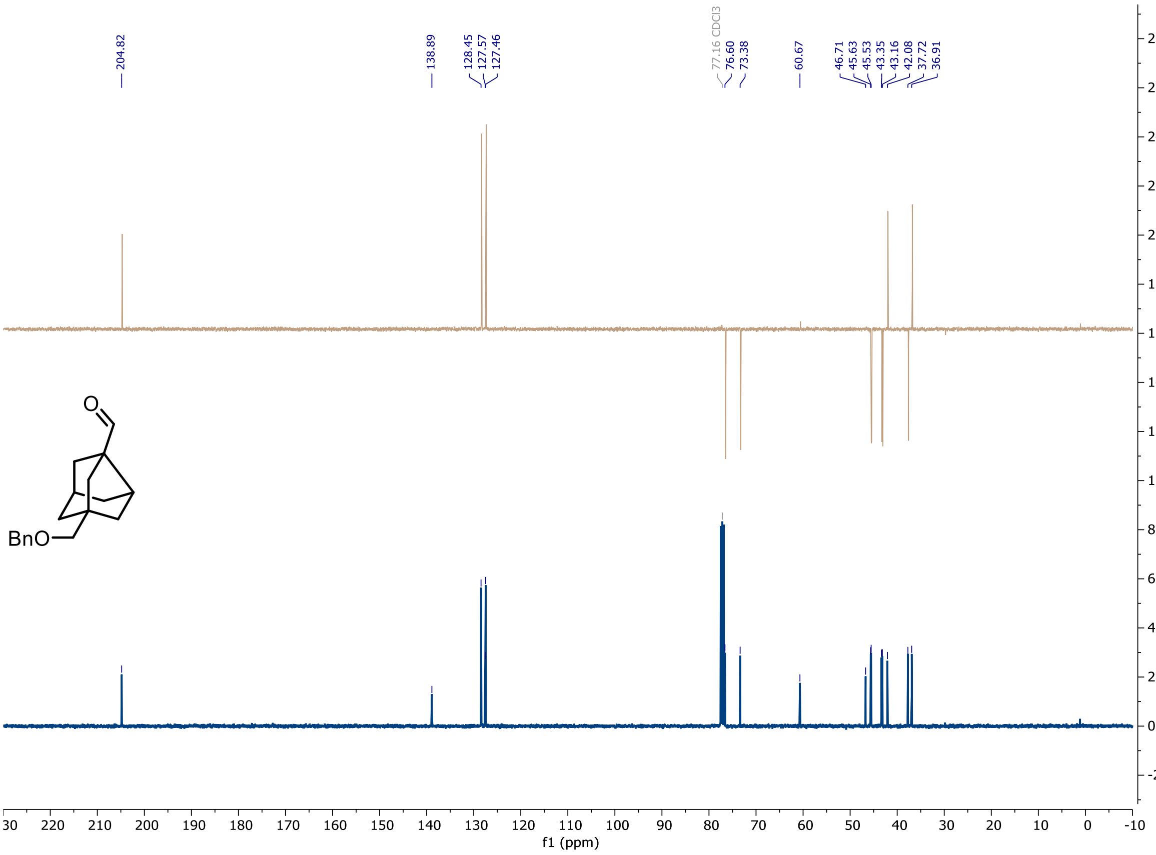
Compound 6d: ^{1}H NMR (400 MHz, $CDCl_3$)



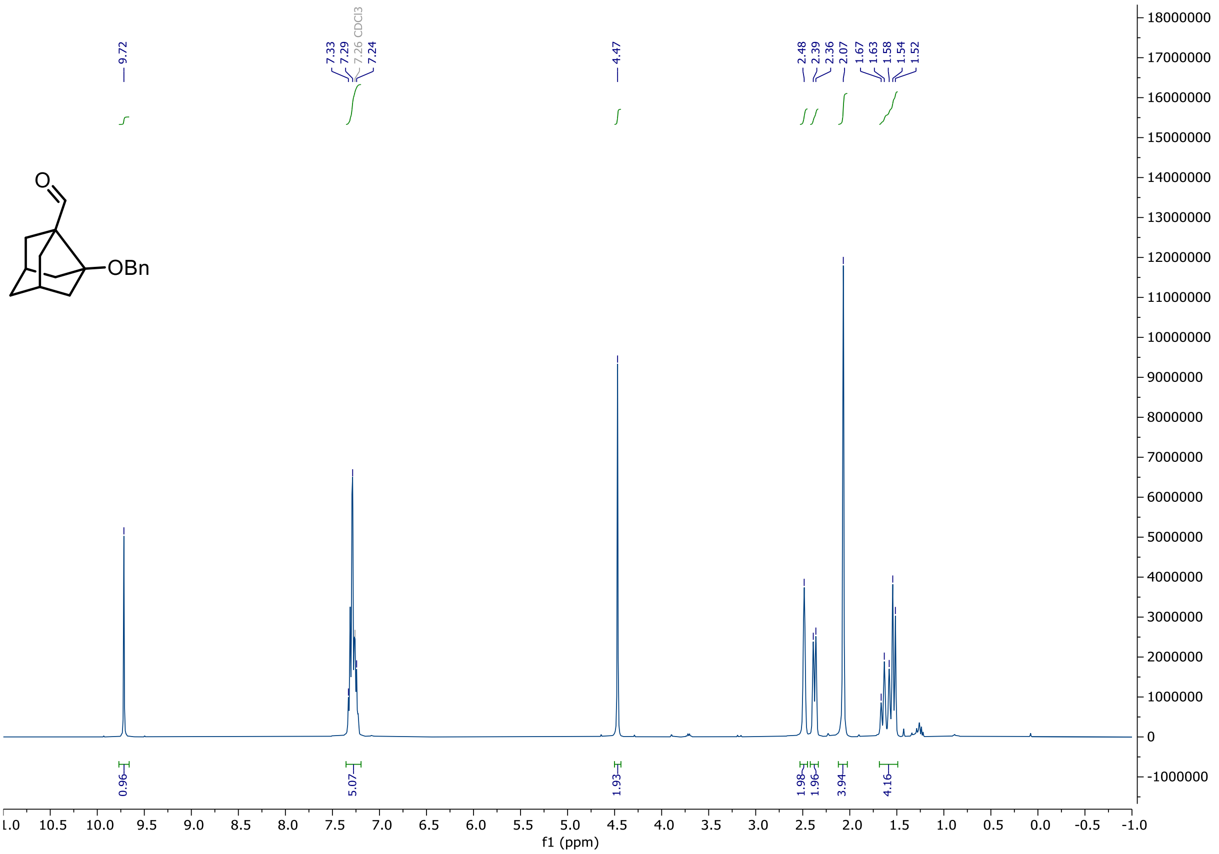
Compound 6d: ^{13}C NMR (101 MHz, $CDCl_3$)



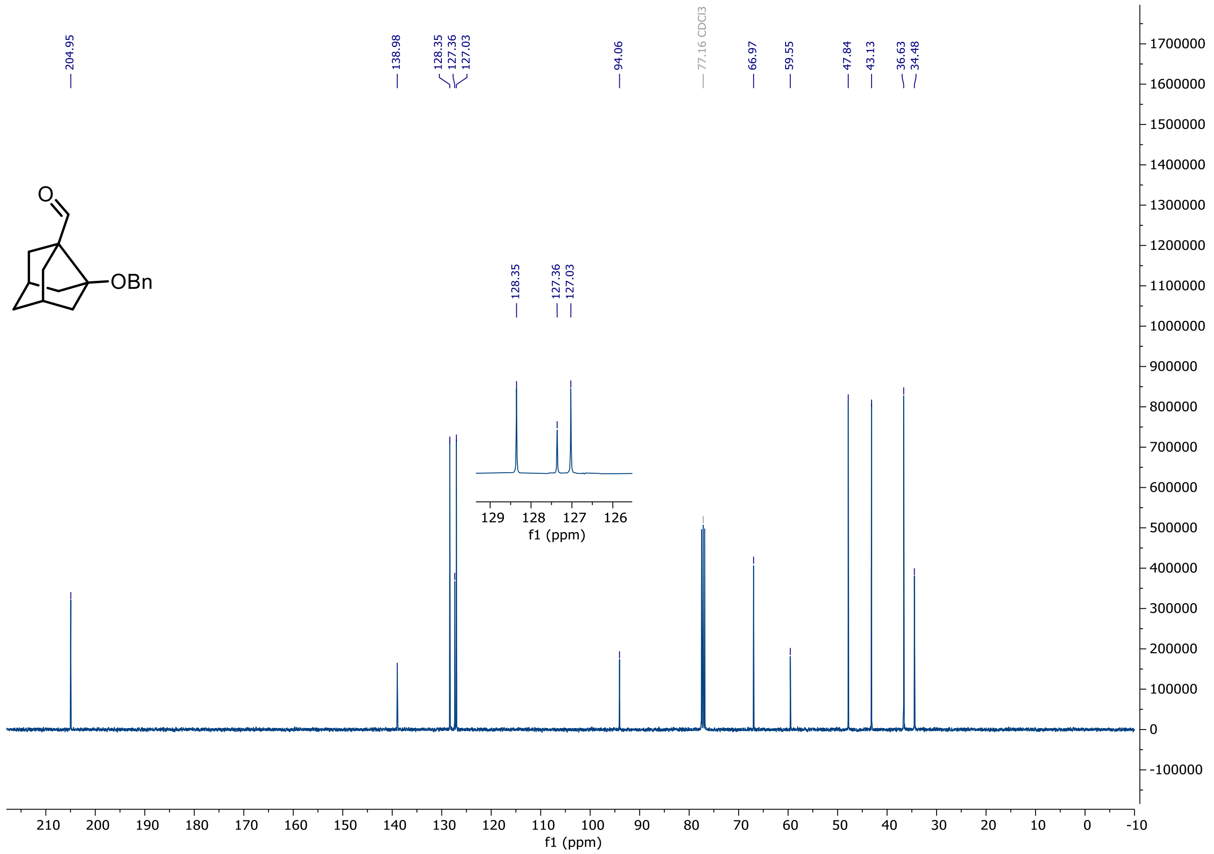
Compound 6d: ^{13}C NMR-DEPT (101 MHz, $CDCl_3$)



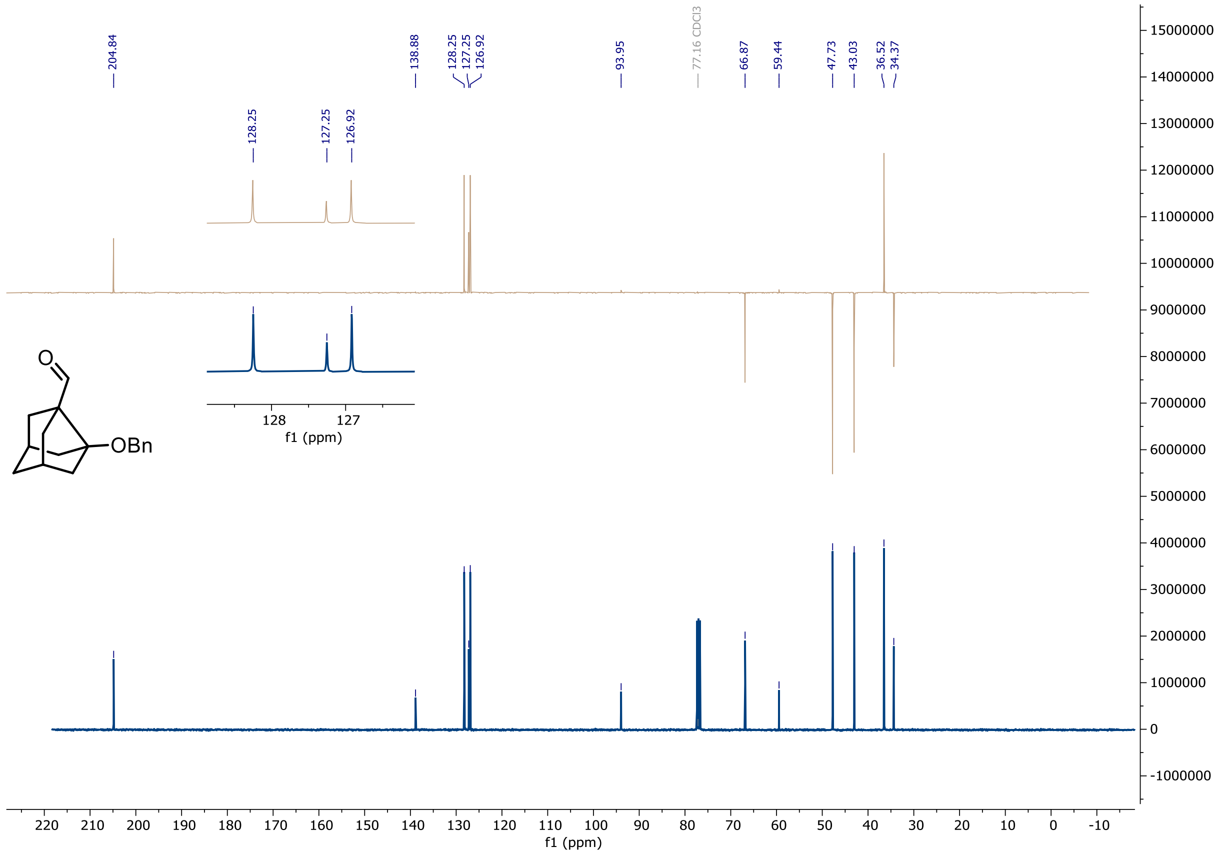
Compound 6e: ^{1}H NMR (400 MHz, CDCl$_3$)



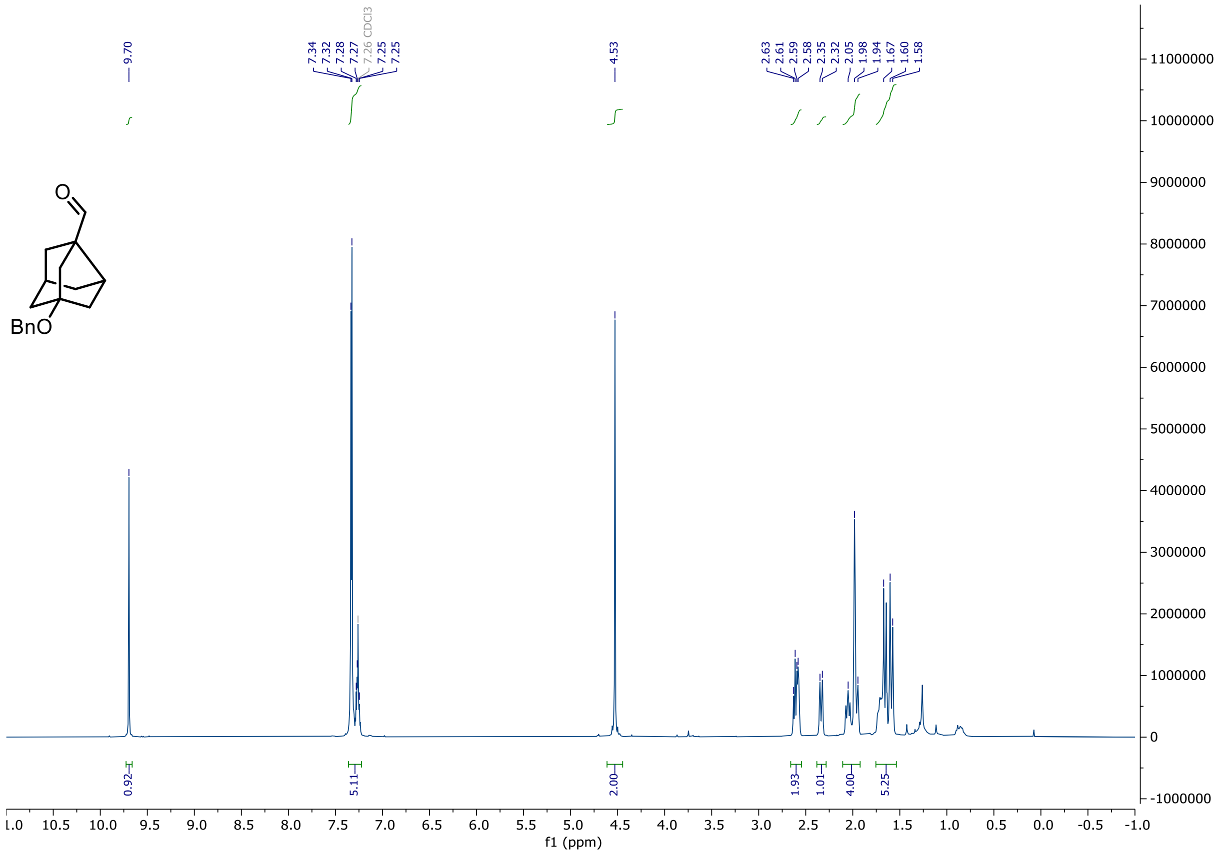
Compound 6e: ^{13}C NMR (101 MHz, CDCl$_3$)



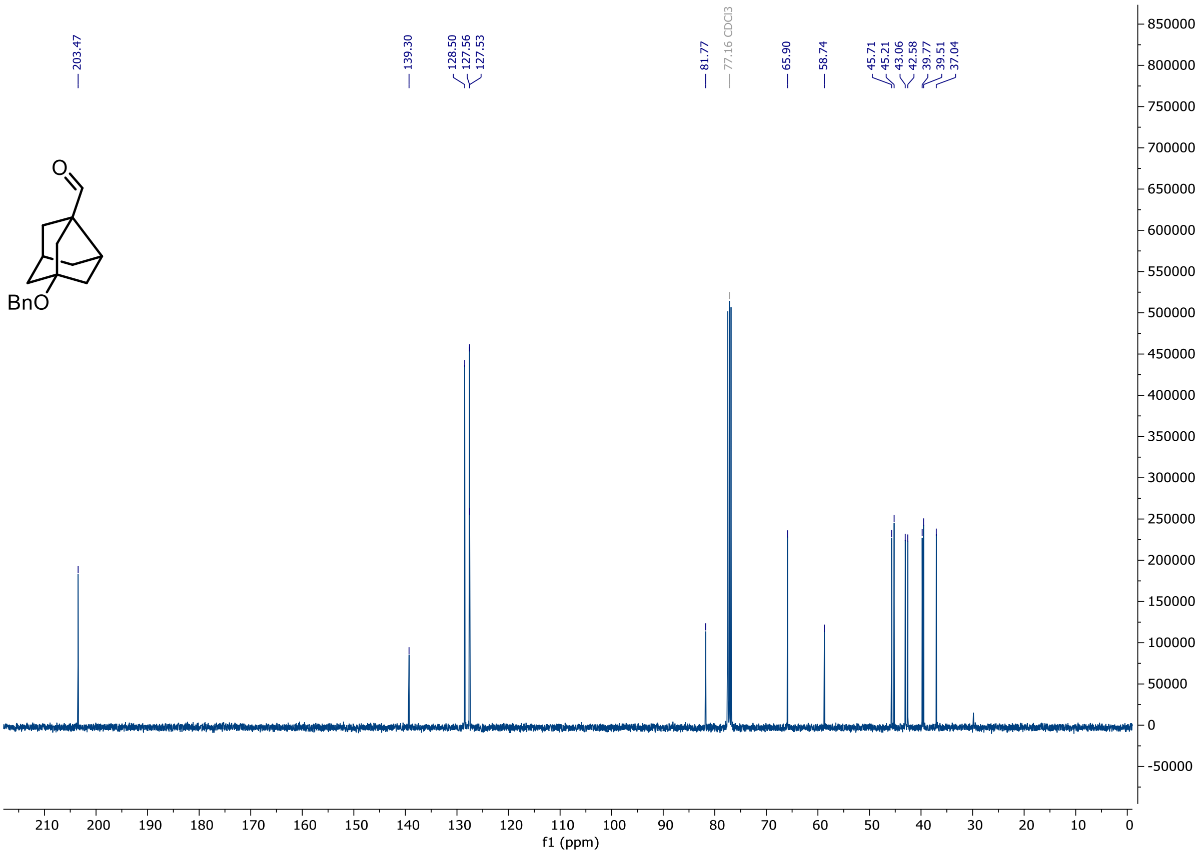
Compound 6e: ^{13}C NMR-DEPT (101 MHz, $CDCl_3$)



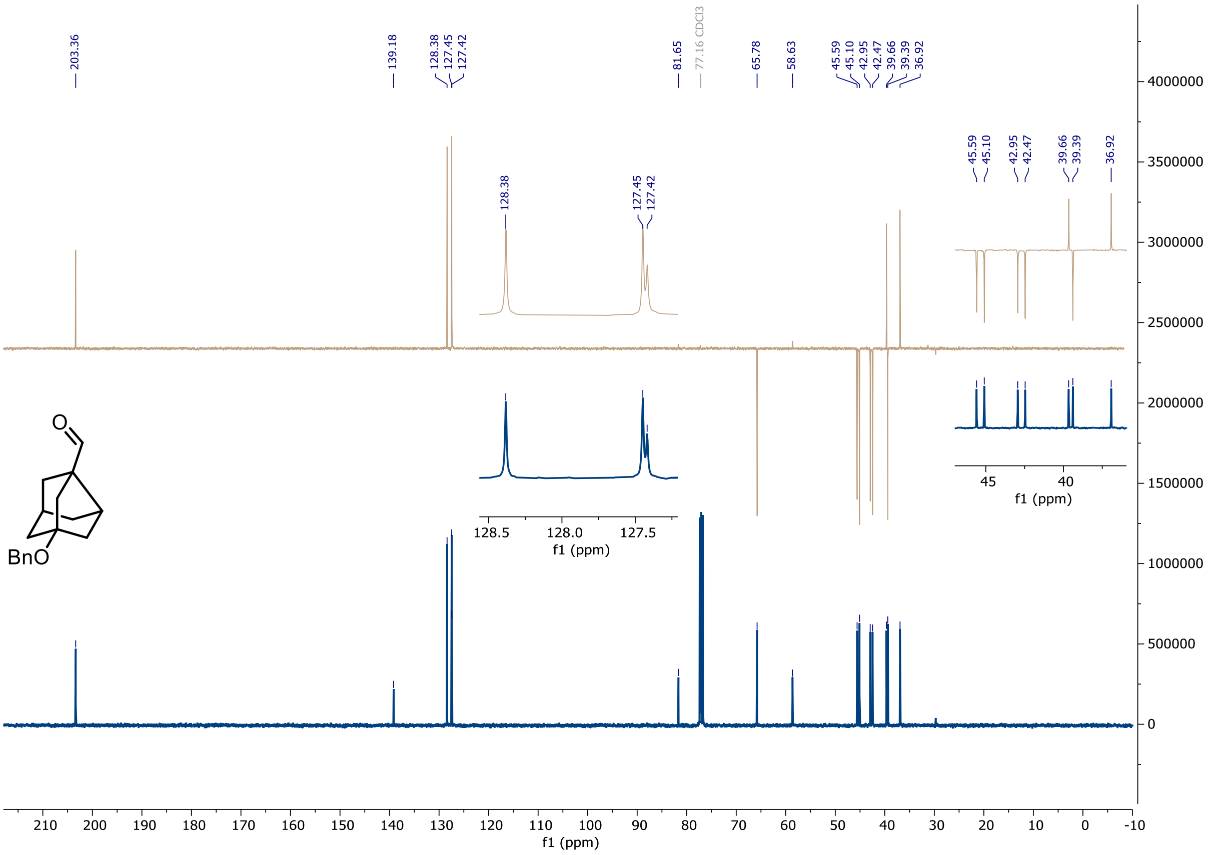
Compound 6f: ^{1}H NMR (400 MHz, CDCl$_3$)



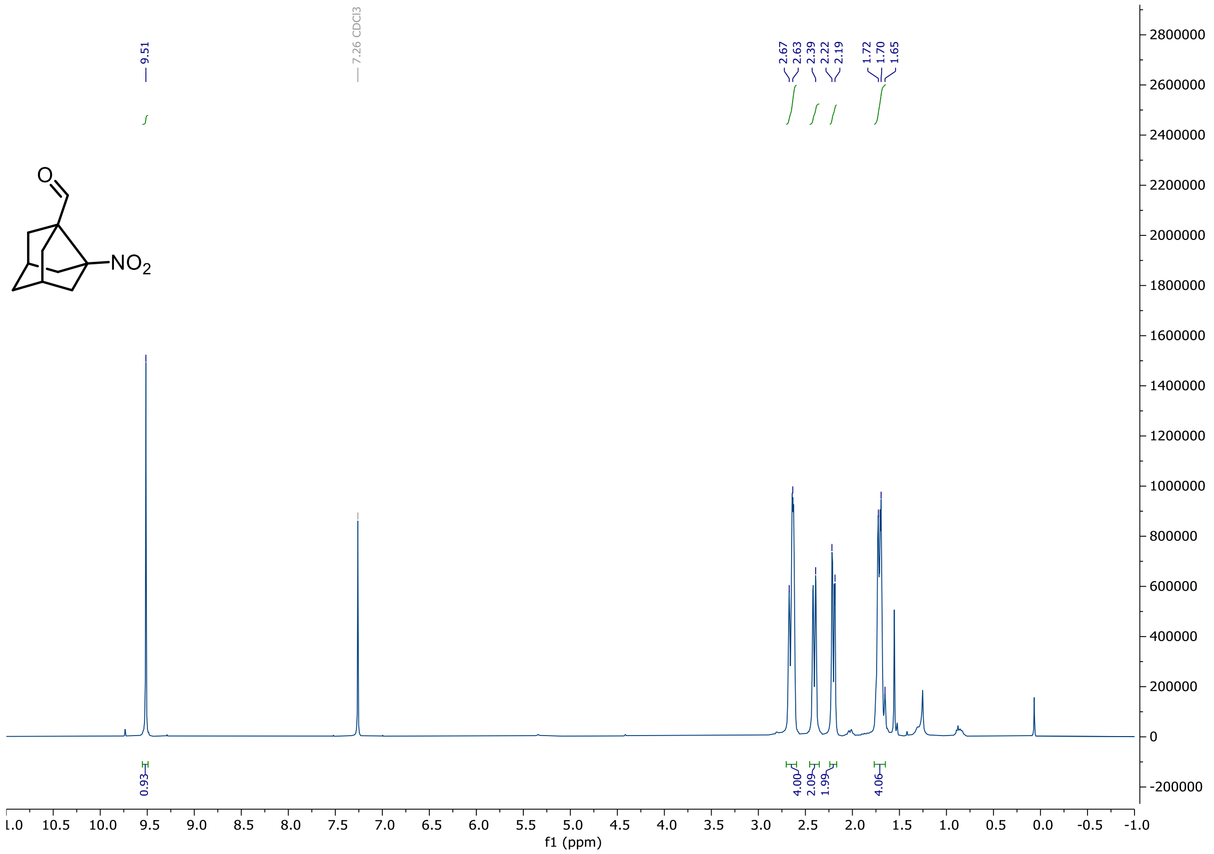
Compound 6f: ^{13}C NMR (101 MHz, CDCl$_3$)



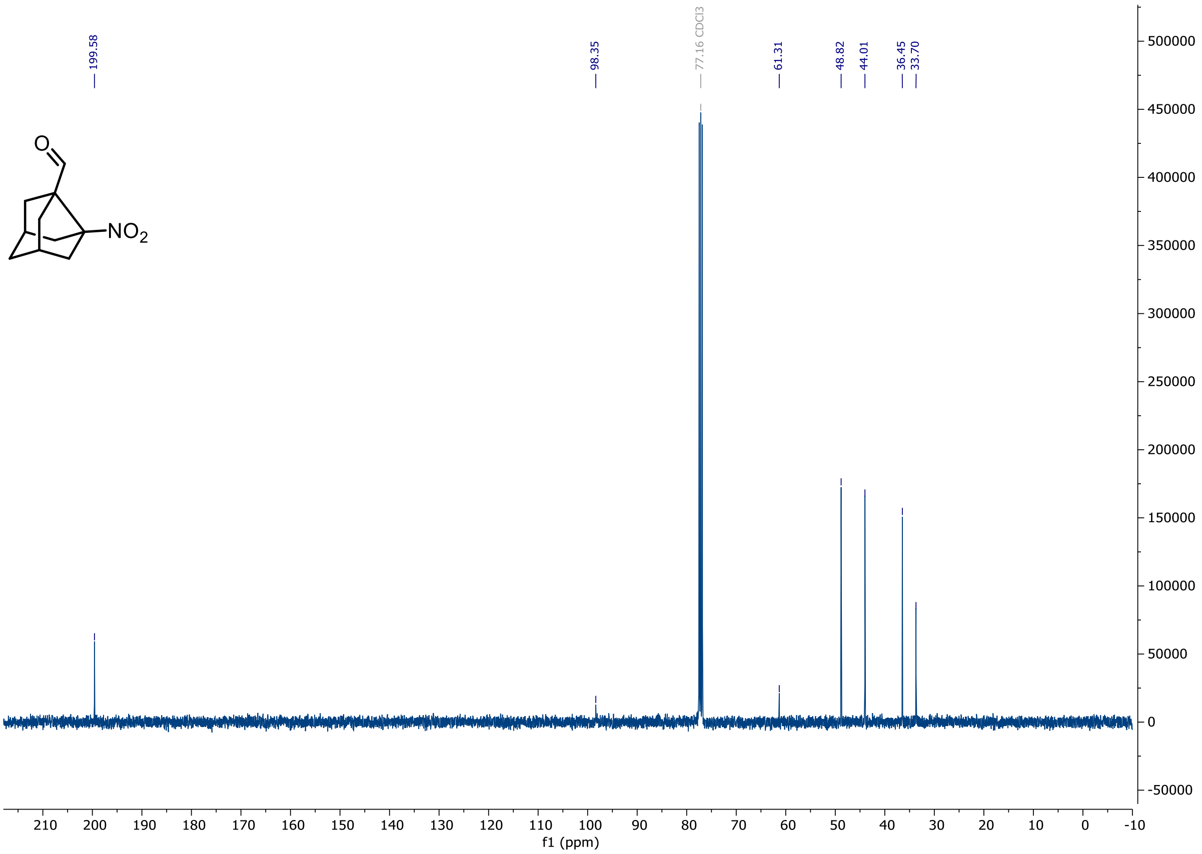
Compound 6f: ^{13}C NMR-DEPT (101 MHz, CDCl$_3$)



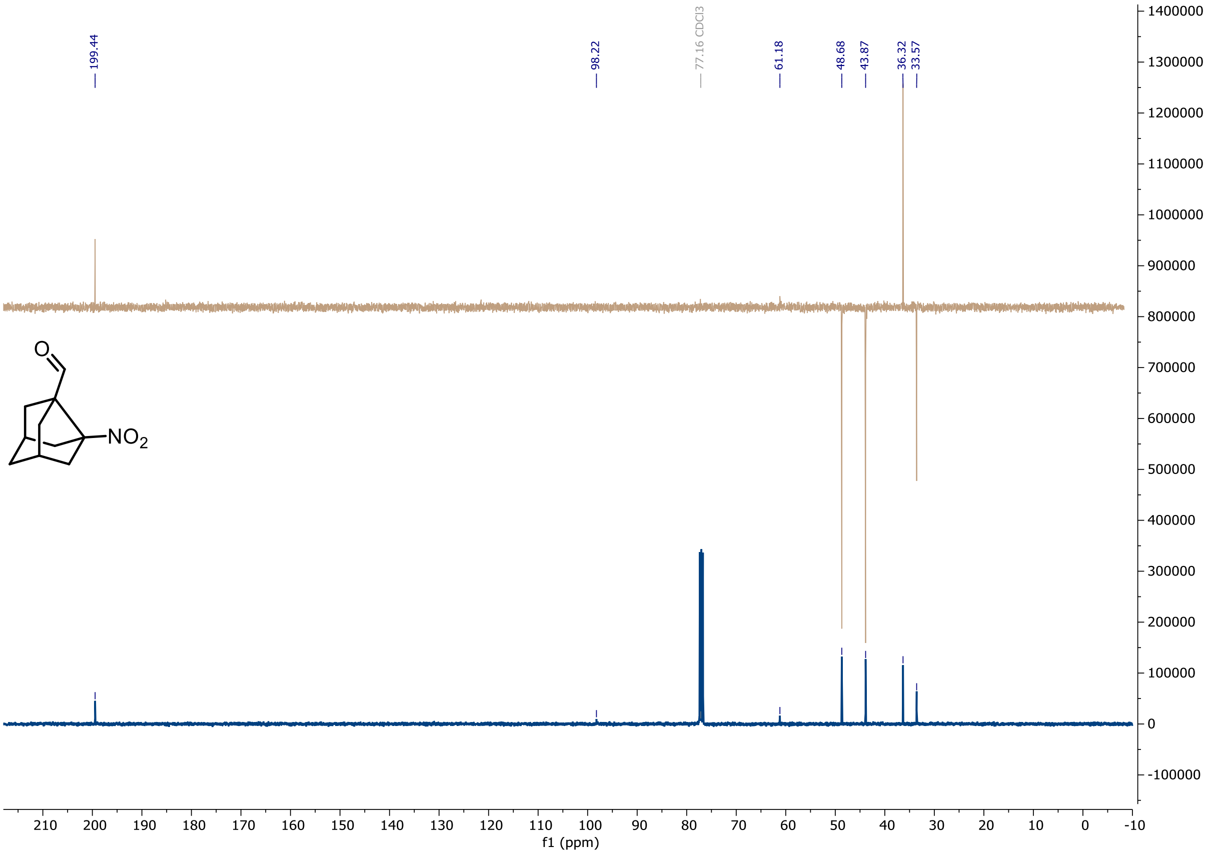
Compound 6i: ^{1}H NMR (400 MHz, CDCl$_3$)



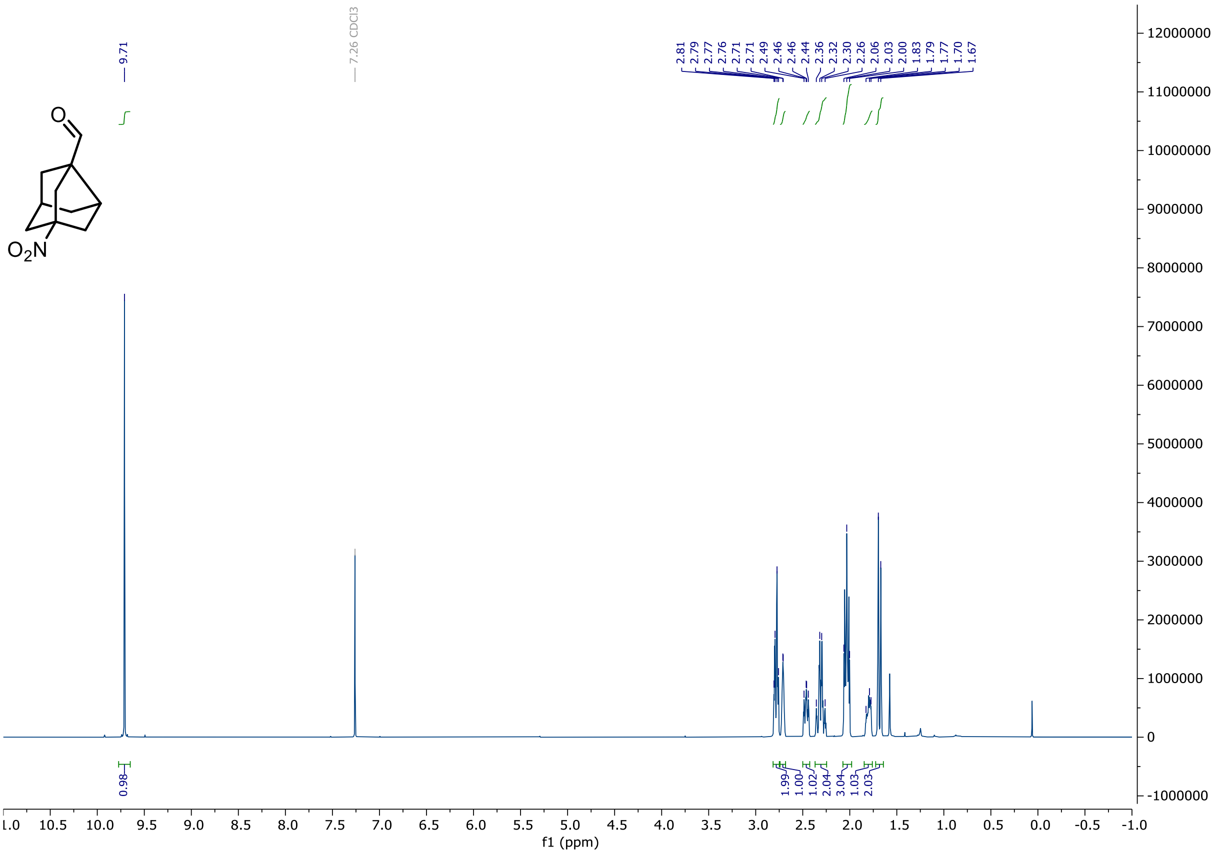
Compound 6i: ^{13}C NMR (101 MHz, CDCl$_3$)



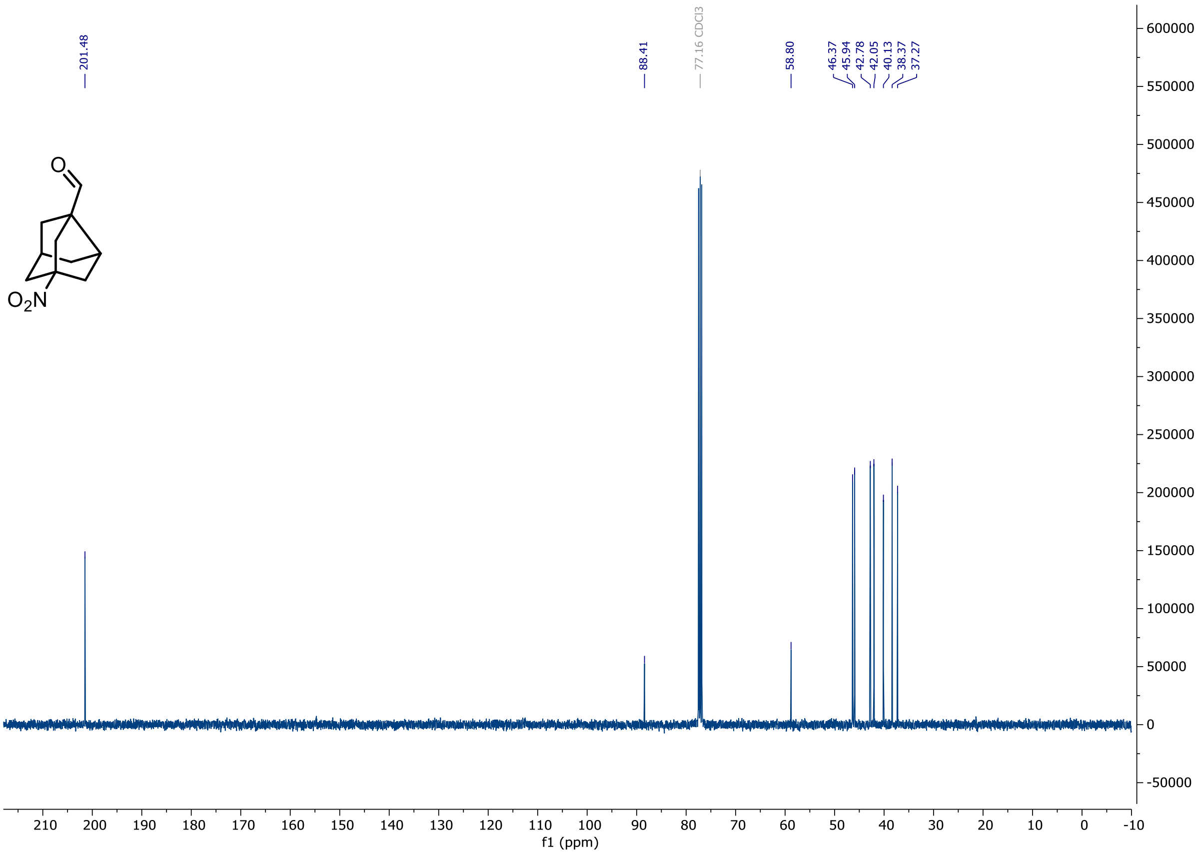
Compound 6i: ^{13}C NMR-DEPT (101 MHz, CDCl$_3$)



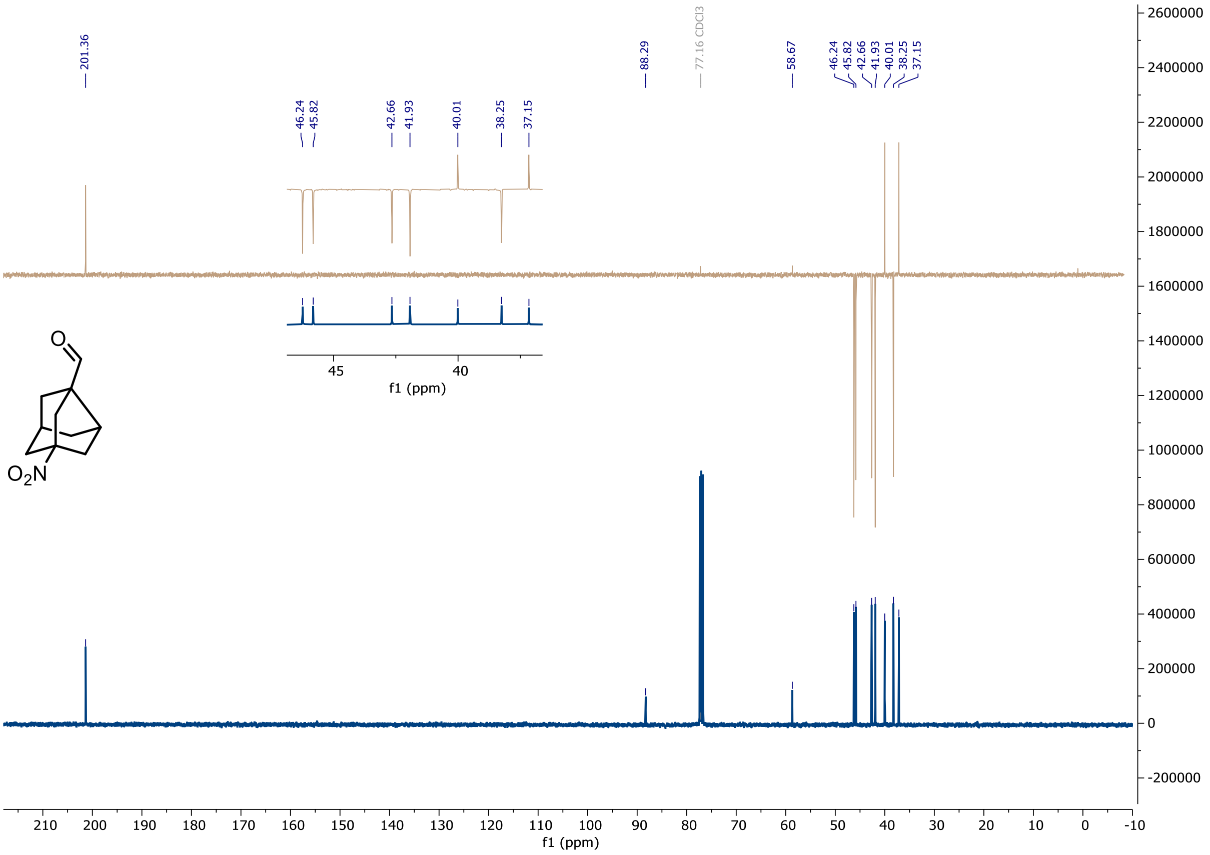
Compound 6g: ¹H NMR (400 MHz, $CDCl_3$)



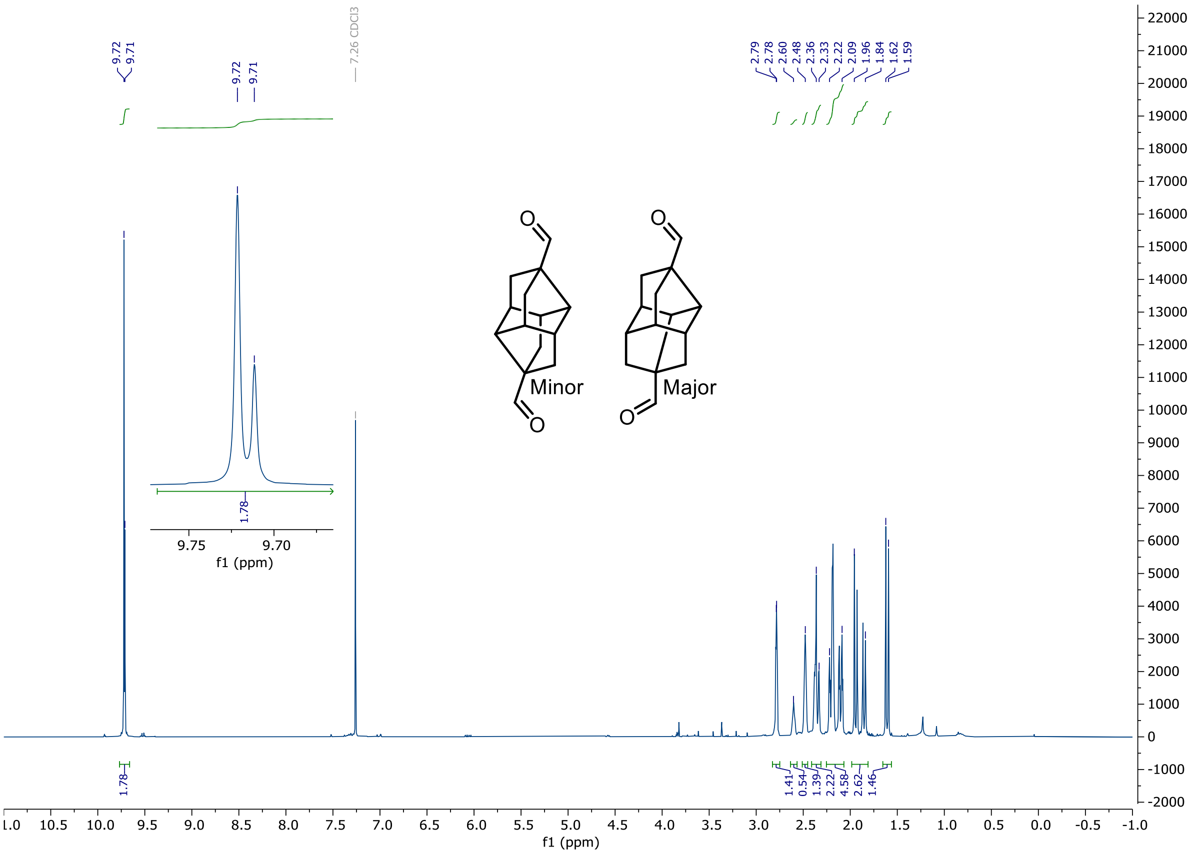
Compound 6g: ¹³C NMR (101 MHz, $CDCl_3$)



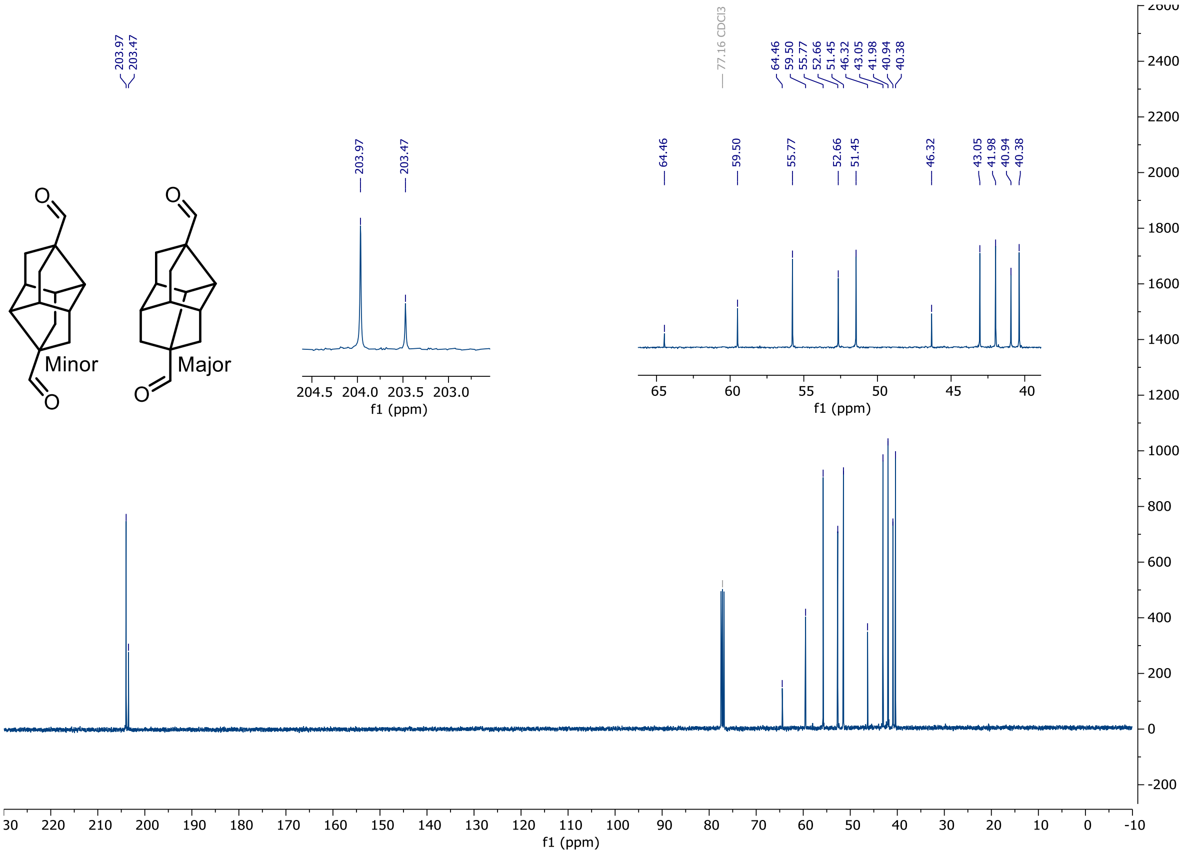
Compound 6g: ^{13}C NMR-DEPT (101 MHz, $CDCl_3$)



Compound 6h: ^{1}H NMR (400 MHz, CDCl$_3$)

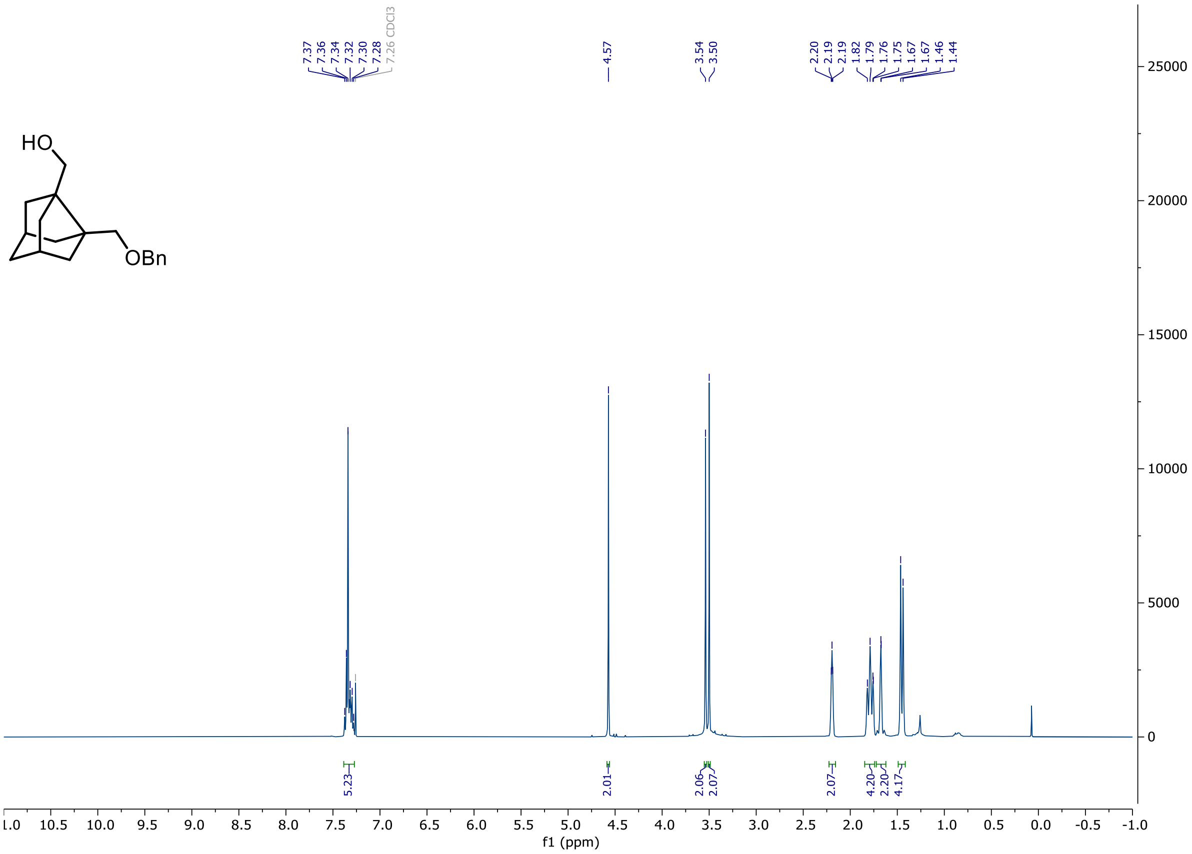


Compound 6h: ^{13}C NMR (101 MHz, CDCl$_3$)

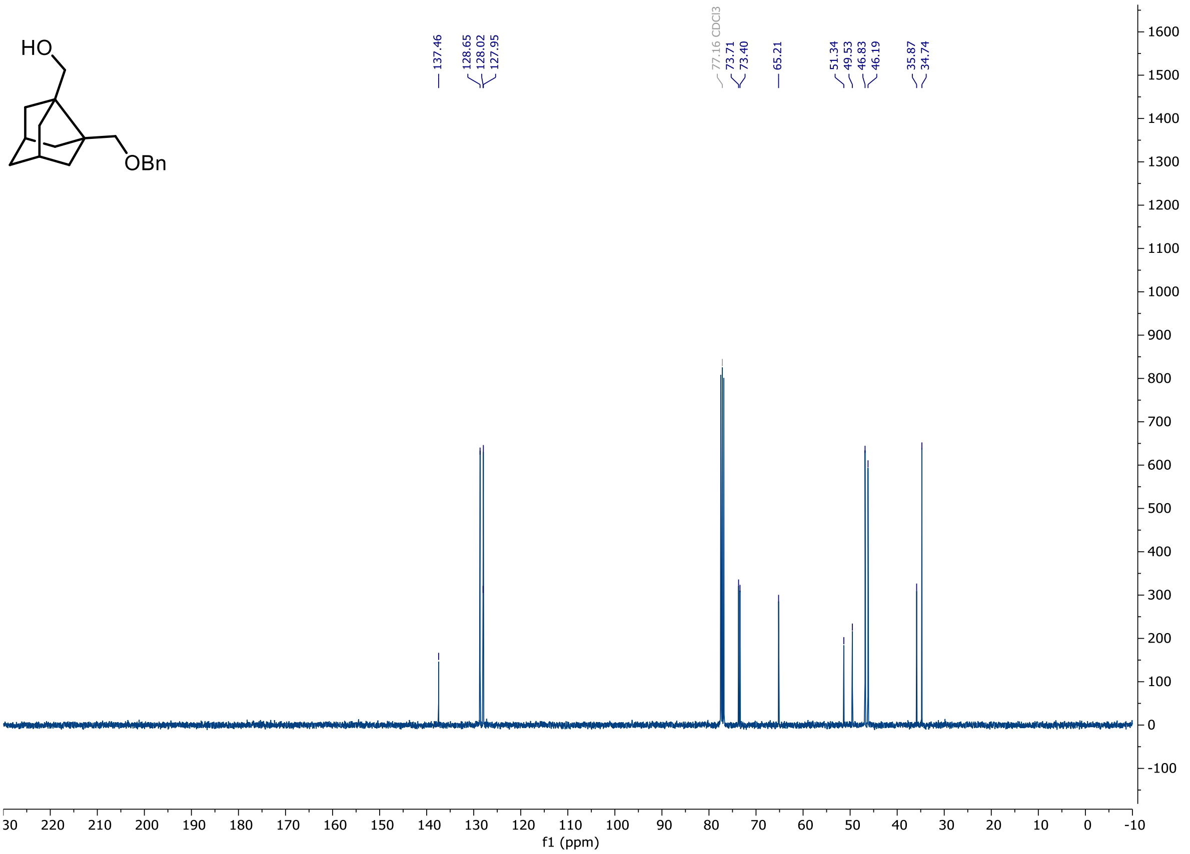

Minor
Major
203.97
203.47
77.16 CDCl3
64.46
59.50
55.77
52.66
51.45
46.32
43.05
41.98
40.94
40.38
204.5 204.0 203.5 203.0
f1 (ppm)
65 60 55 50 45 40
f1 (ppm)
2600 2400 2200 2000 1800 1600 1400 1200 1000 800 600 400 200 0 -200
30 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

Noradamantyl Methylene Alcohols

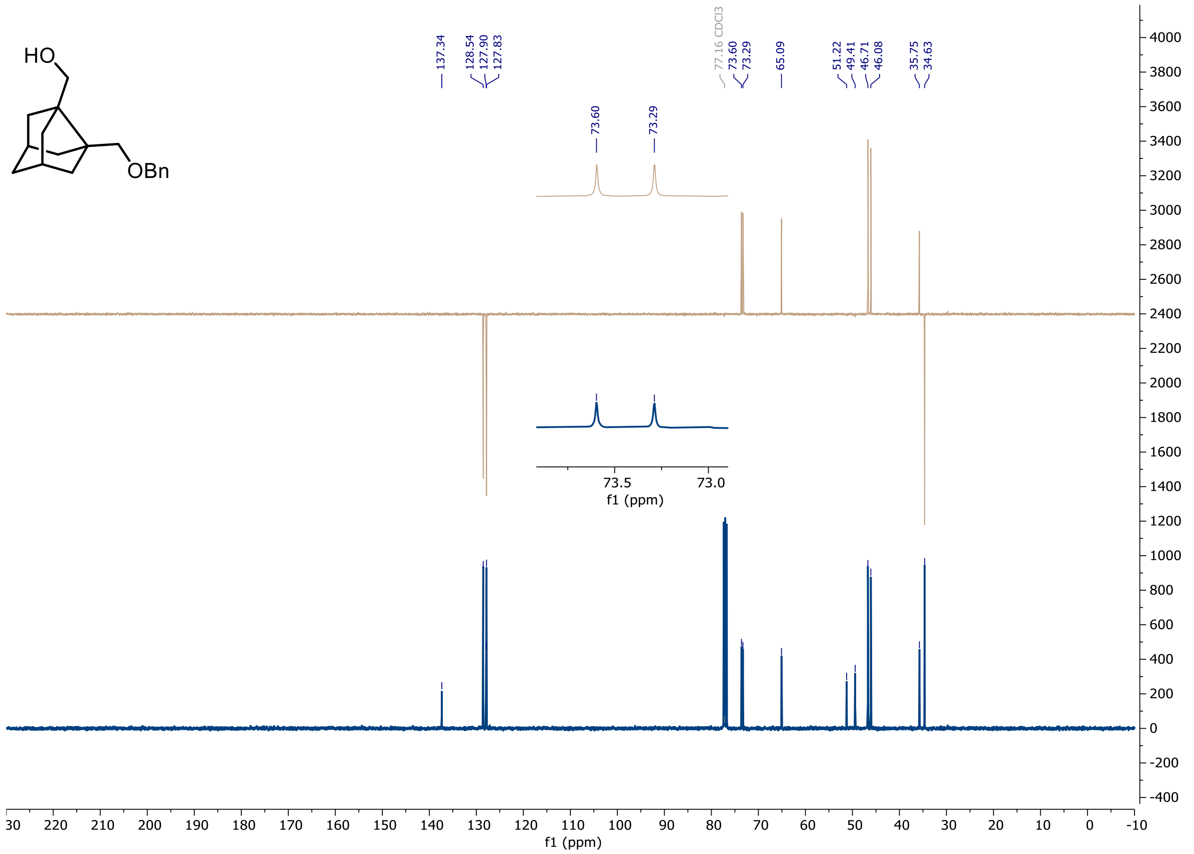
Compound 7a: ^{1}H NMR (400 MHz, CDCl$_3$)



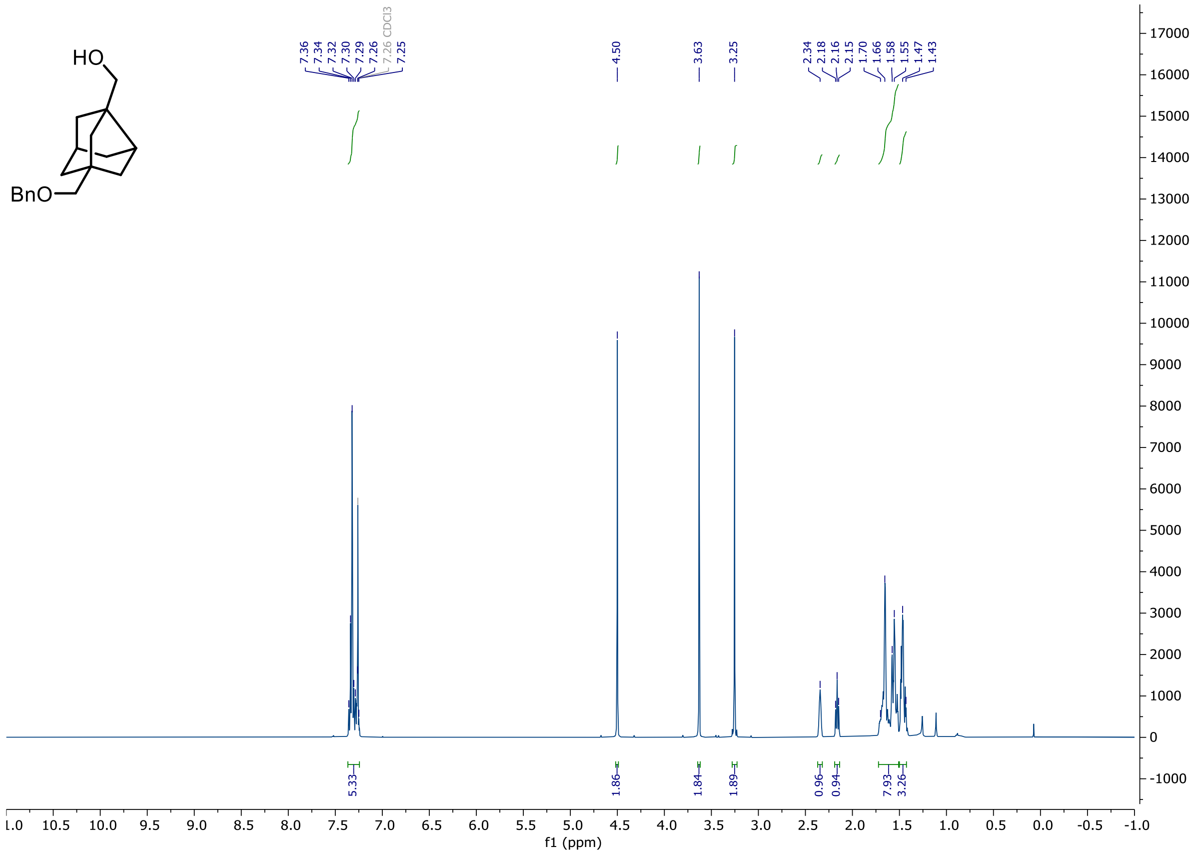
Compound 7a: ^{13}C NMR (101 MHz, CDCl$_3$)



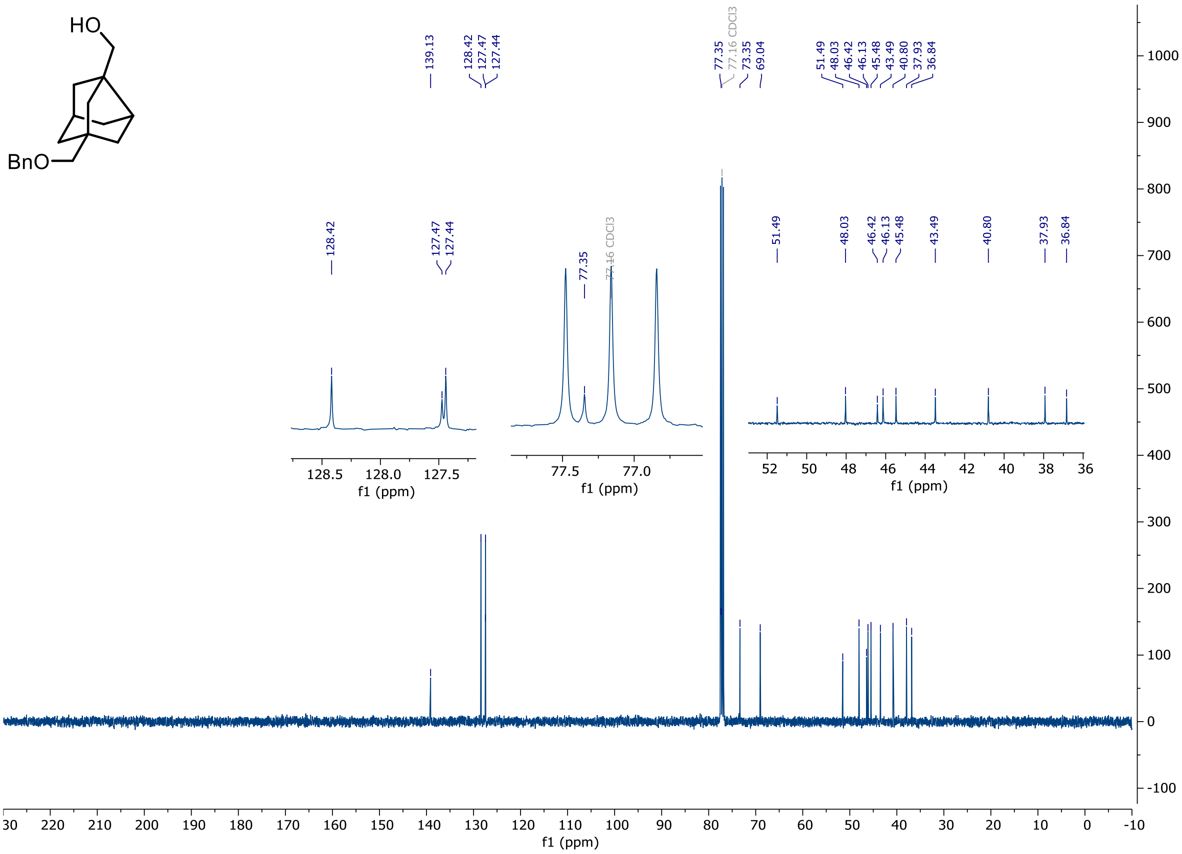
Compound 7a: ^{13}C NMR-DEPT (101 MHz, CDCl$_3$)



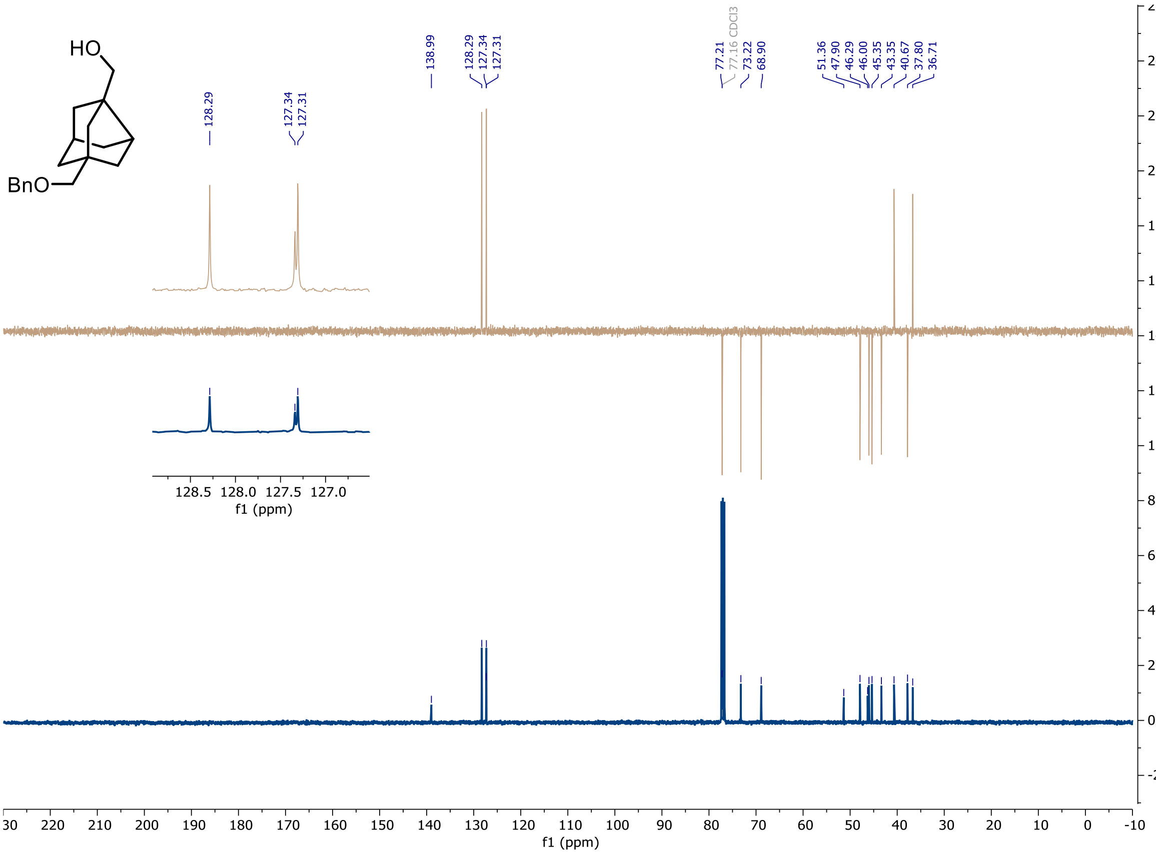
Compound 7b: ^{1}H NMR (400 MHz, CDCl$_3$)



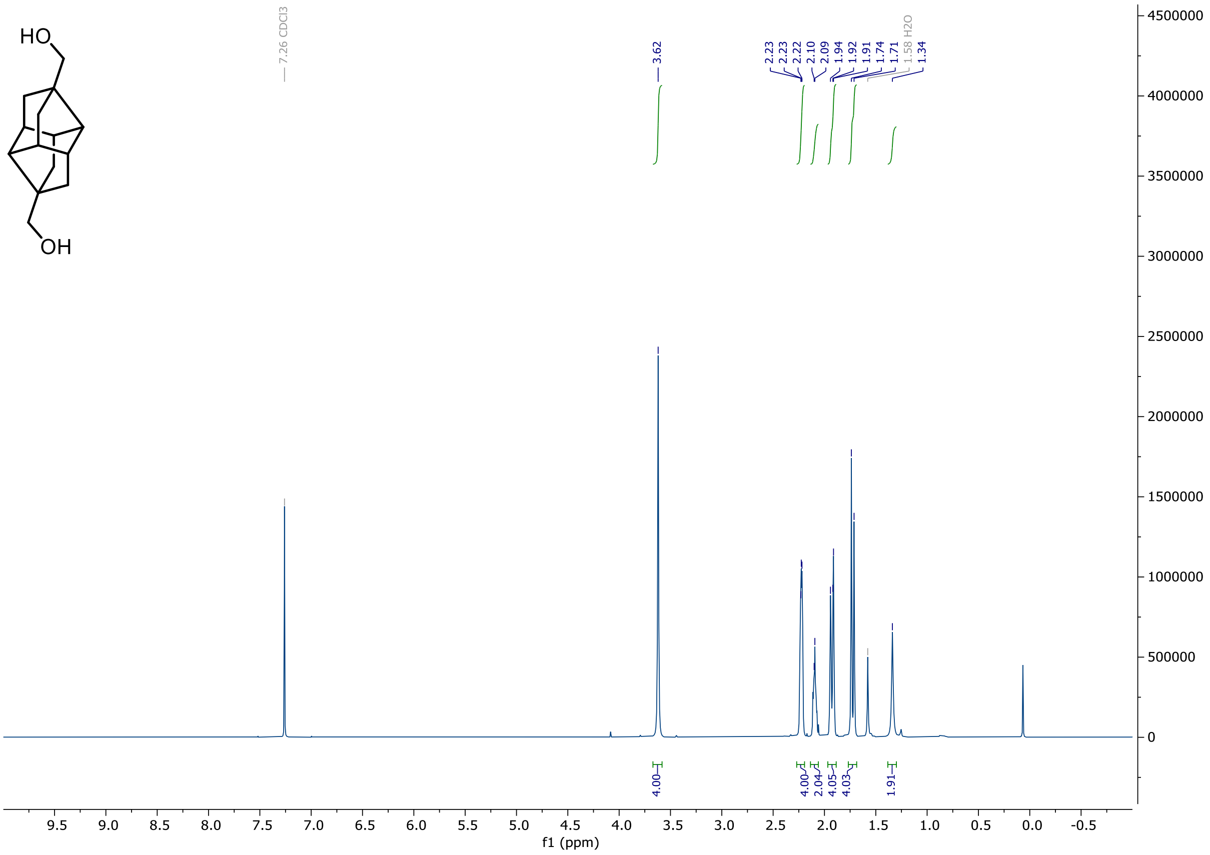
Compound 7b: ^{13}C NMR (101 MHz, CDCl$_3$)



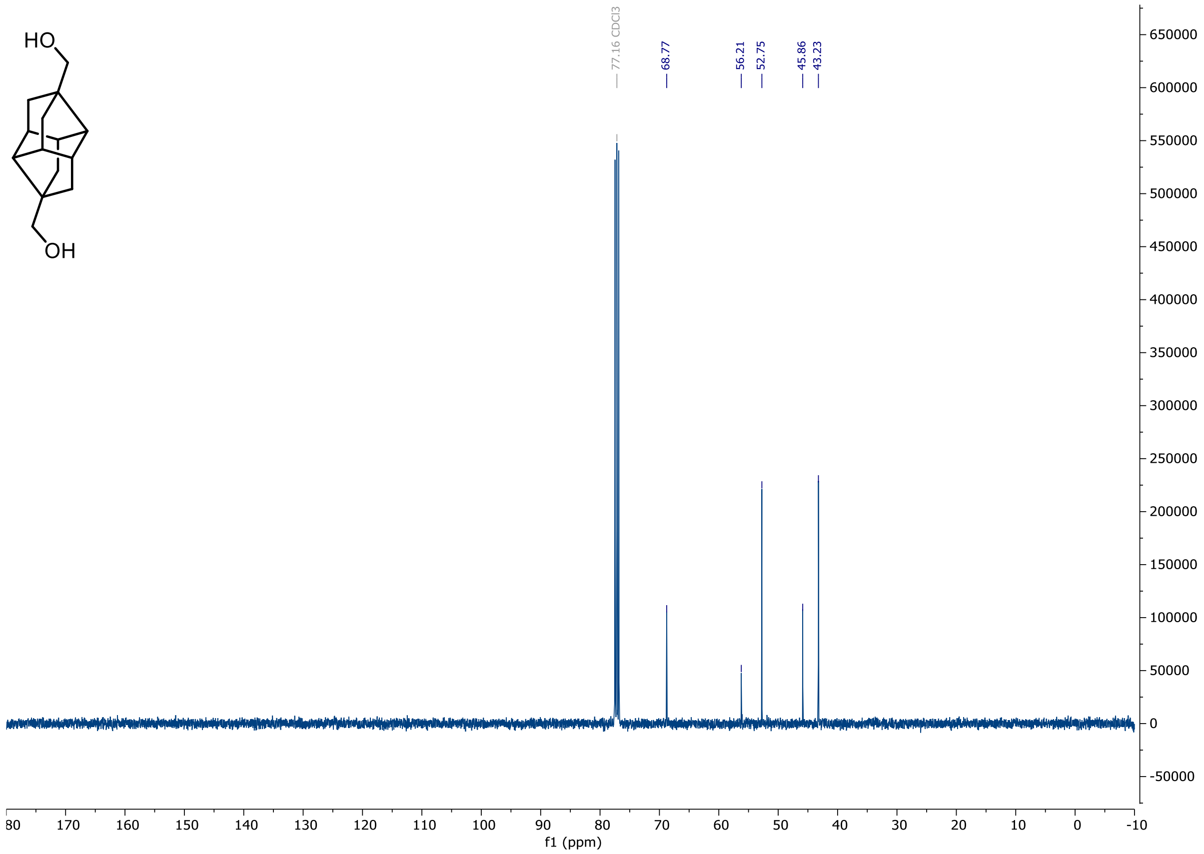
Compound 7b: ^{13}C NMR-DEPT (101 MHz, CDCl$_3$)



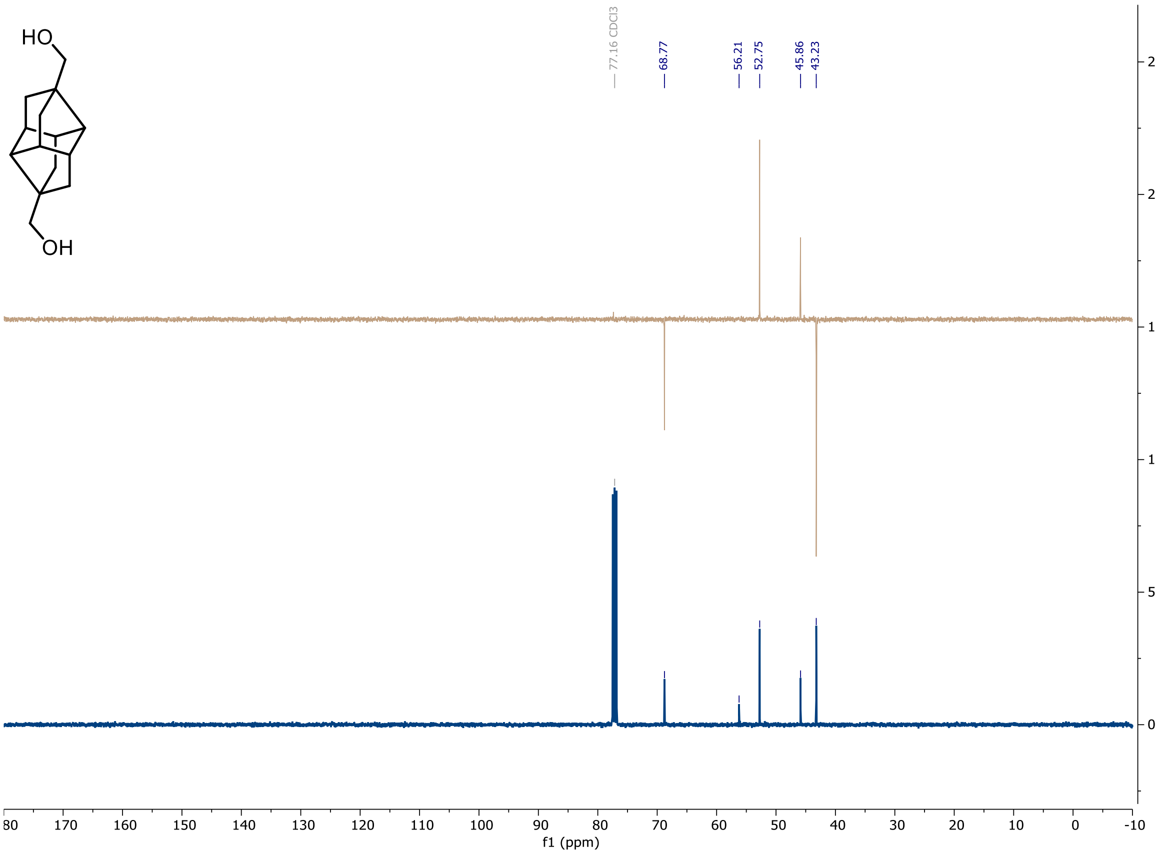
Compound 7c: ^{1}H NMR (400 MHz, CDCl$_3$)



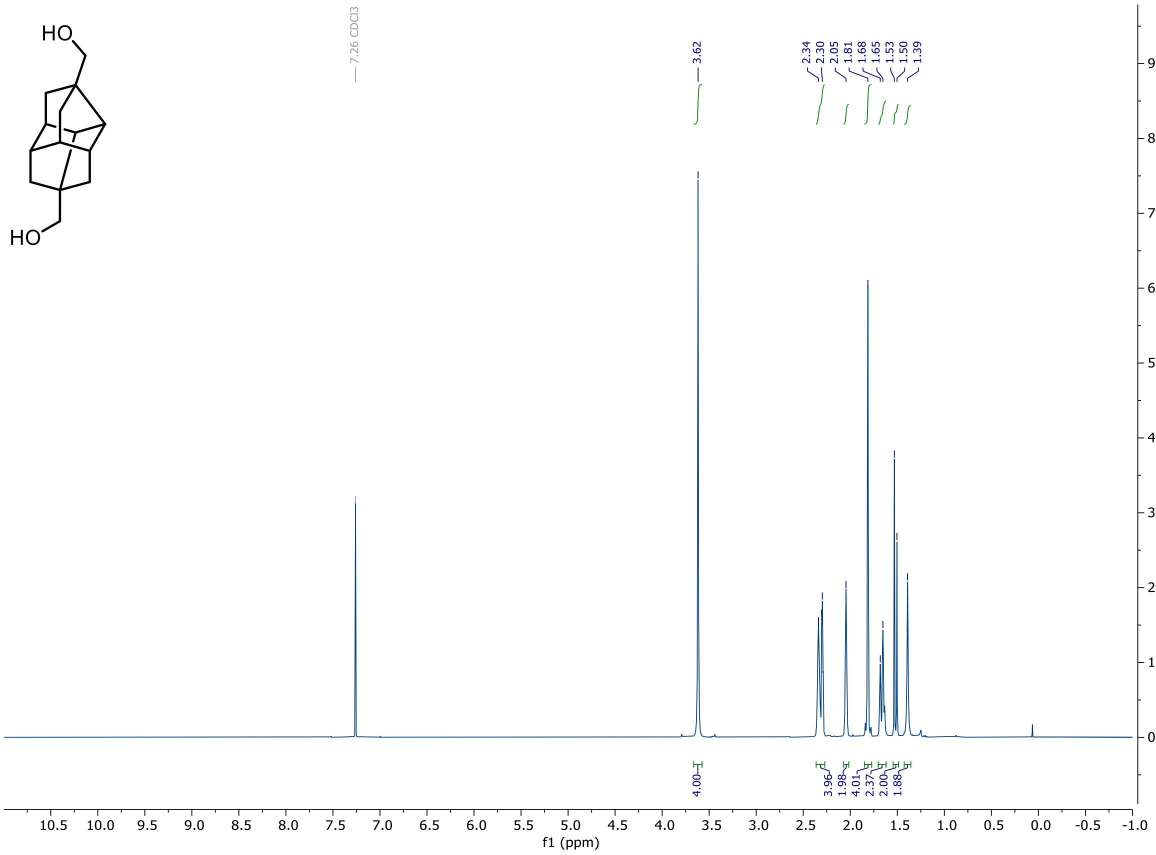
Compound 7c: ^{13}C NMR (101 MHz, $CDCl_3$)



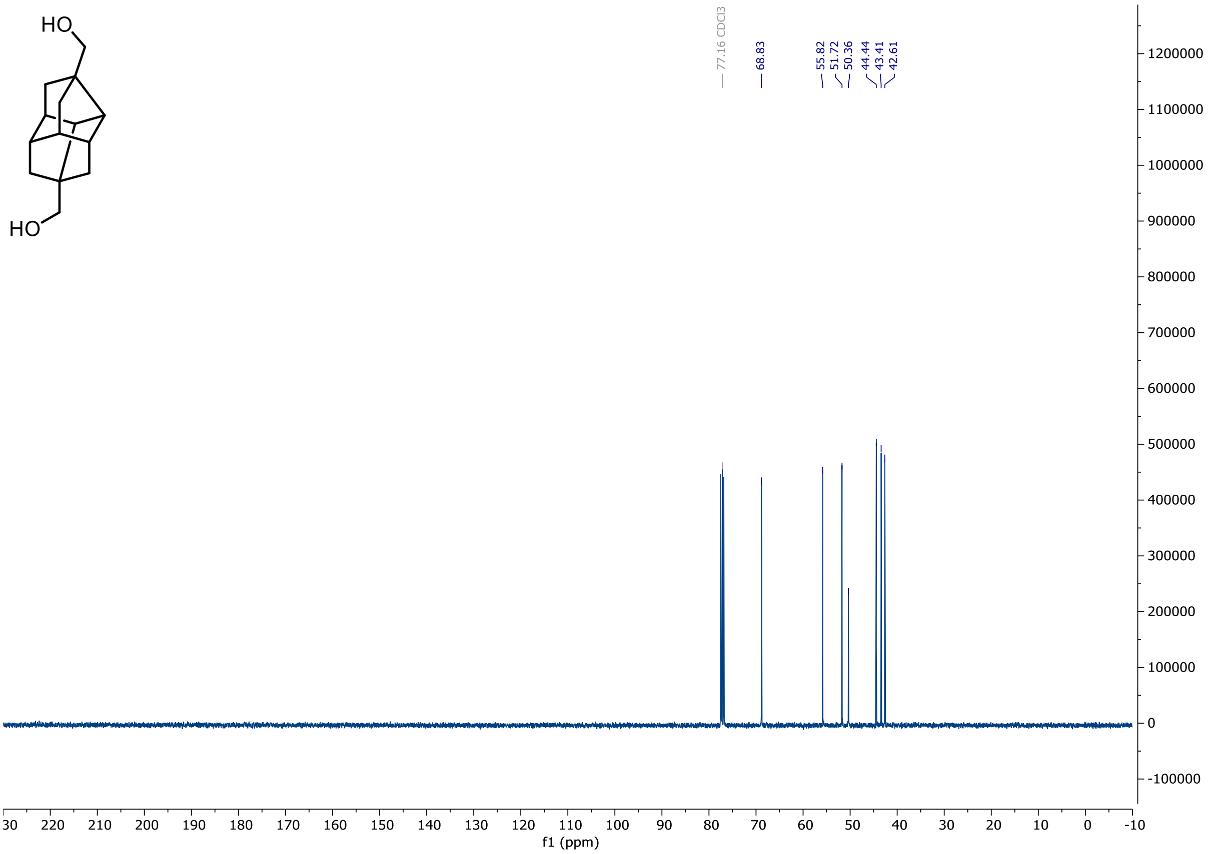
Compound 7c: ^{13}C NMR-DEPT (101 MHz, $CDCl_3$)



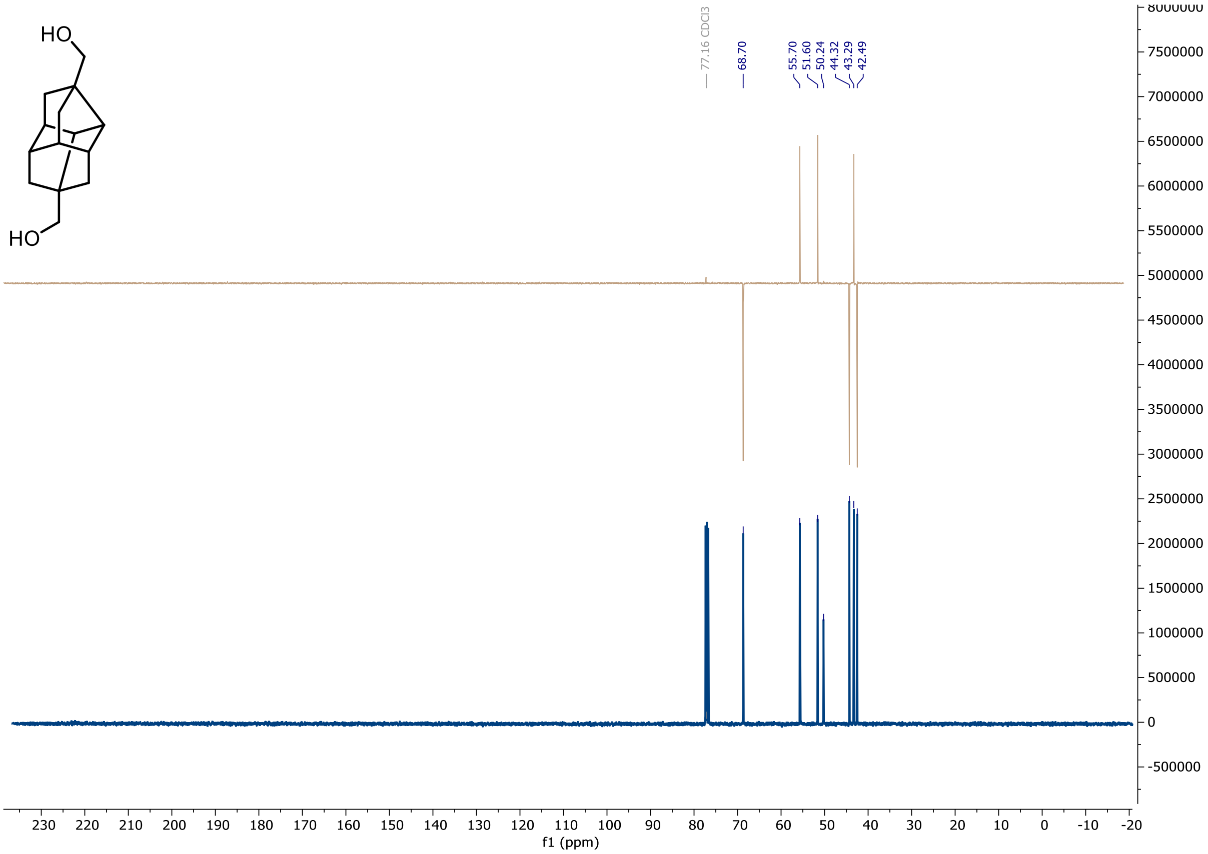
Compound 7d: ^{1}H NMR (400 MHz, CDCl$_3$)



Compound 7d: ^{13}C NMR (101 MHz, CDCl$_3$)

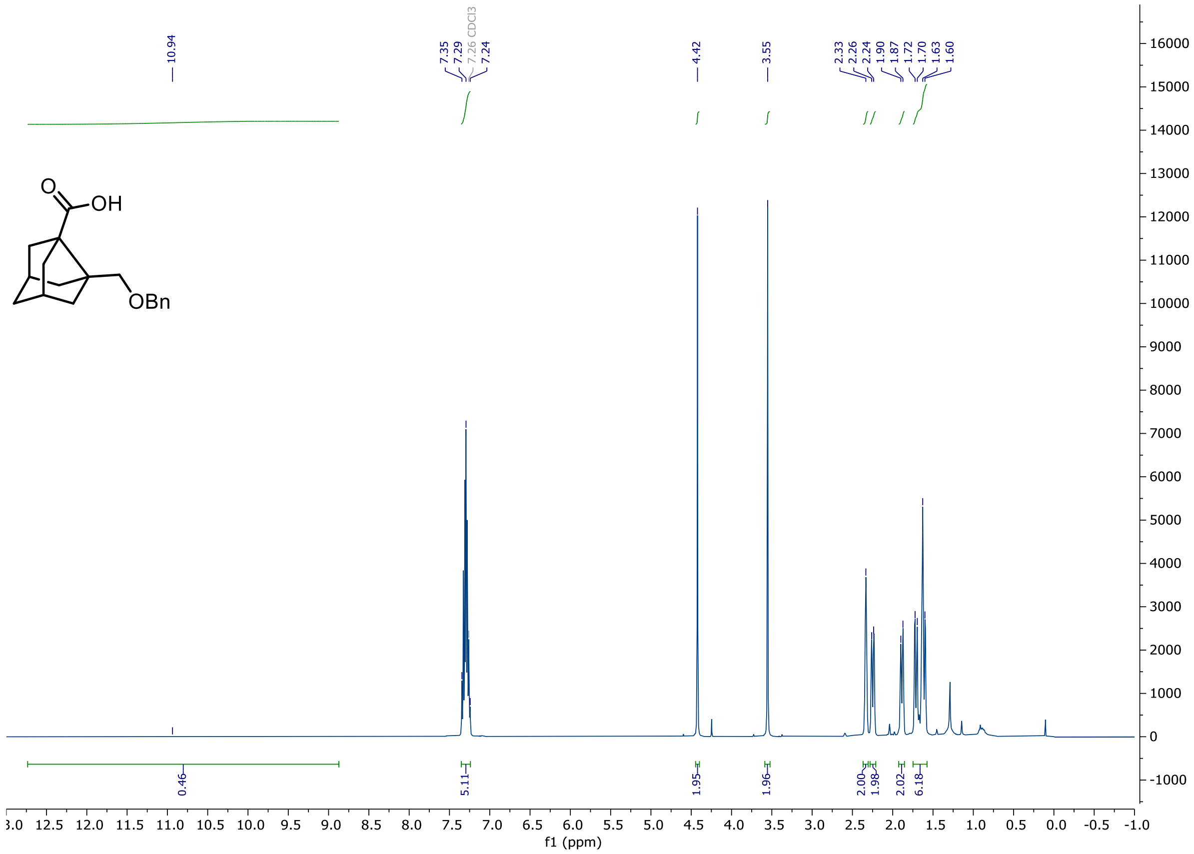


Compound 7d: ^{13}C NMR-DEPT (101 MHz, CDCl$_3$)

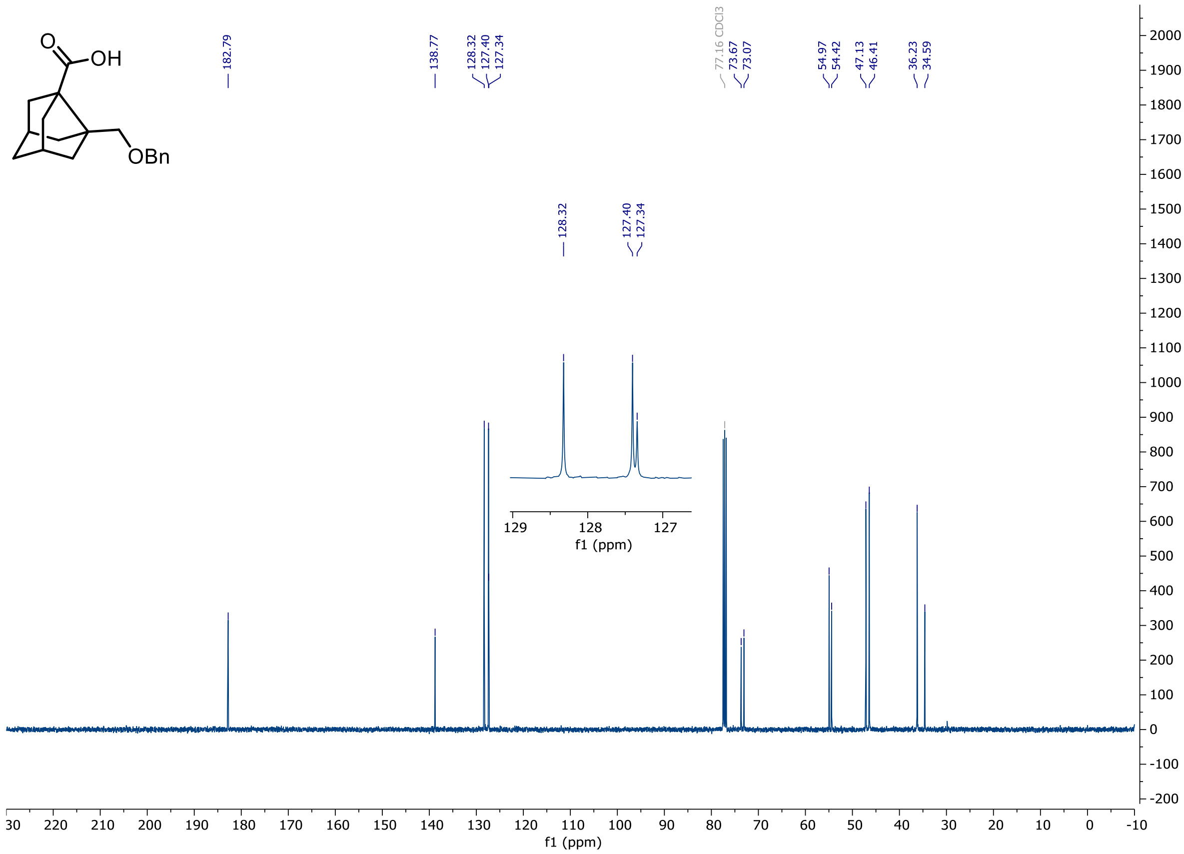

HO
HO
77.16 CDCl3
68.70
55.70
51.60
50.24
44.32
43.29
42.49
8000000
7500000
7000000
6500000
6000000
5500000
5000000
4500000
4000000
3500000
3000000
2500000
2000000
1500000
1000000
500000
0
-500000
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)

Noradamantyl Carboxylic Acids

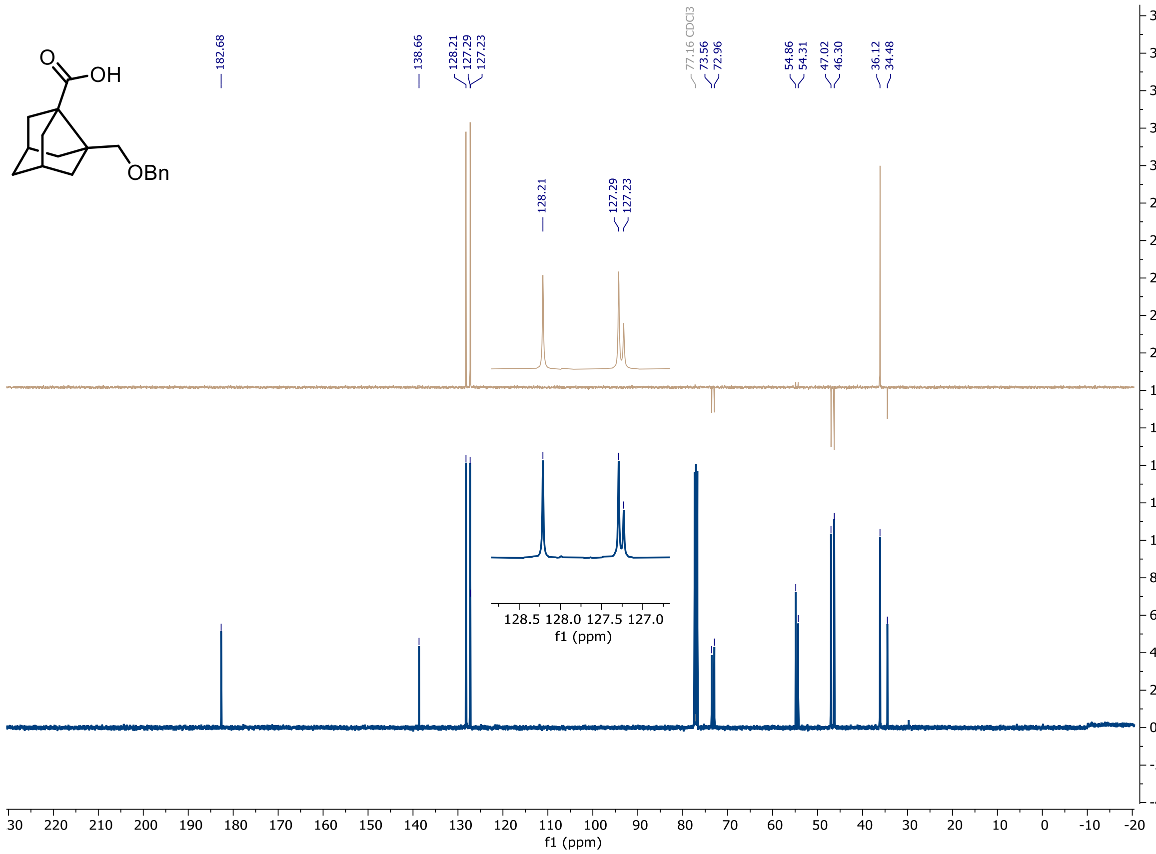
Compound 8a: ^{1}H NMR (400 MHz, $CDCl_3$)



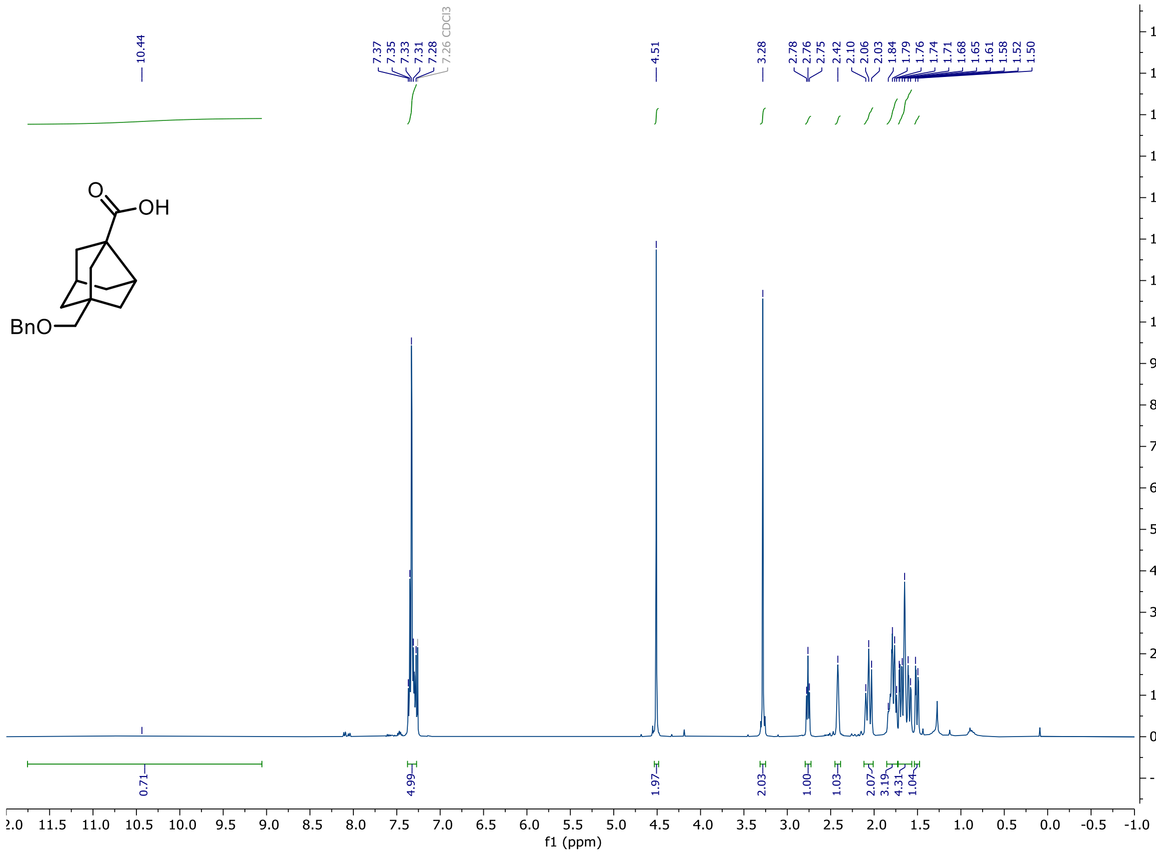
Compound 8a: ^{13}C NMR (101 MHz, $CDCl_3$)



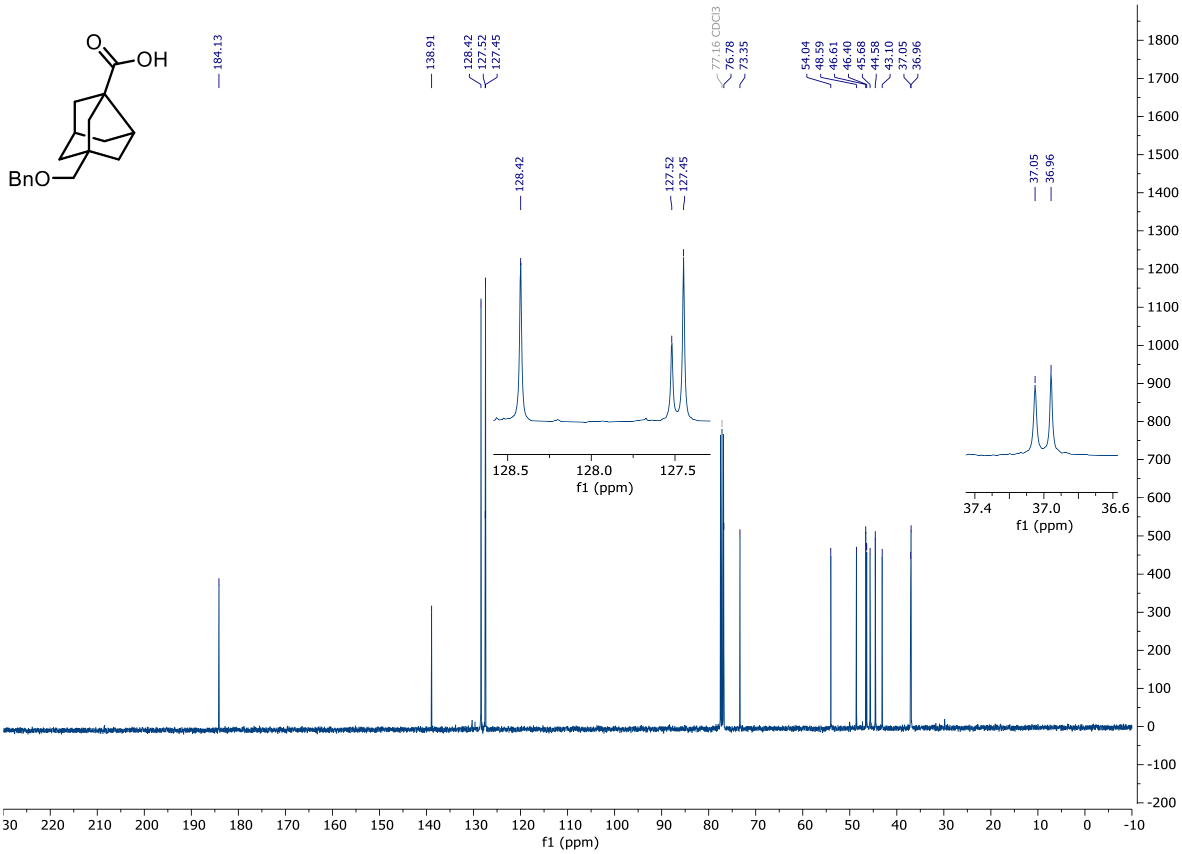
Compound 8a: ^{13}C NMR-DEPT (101 MHz, $CDCl_3$)



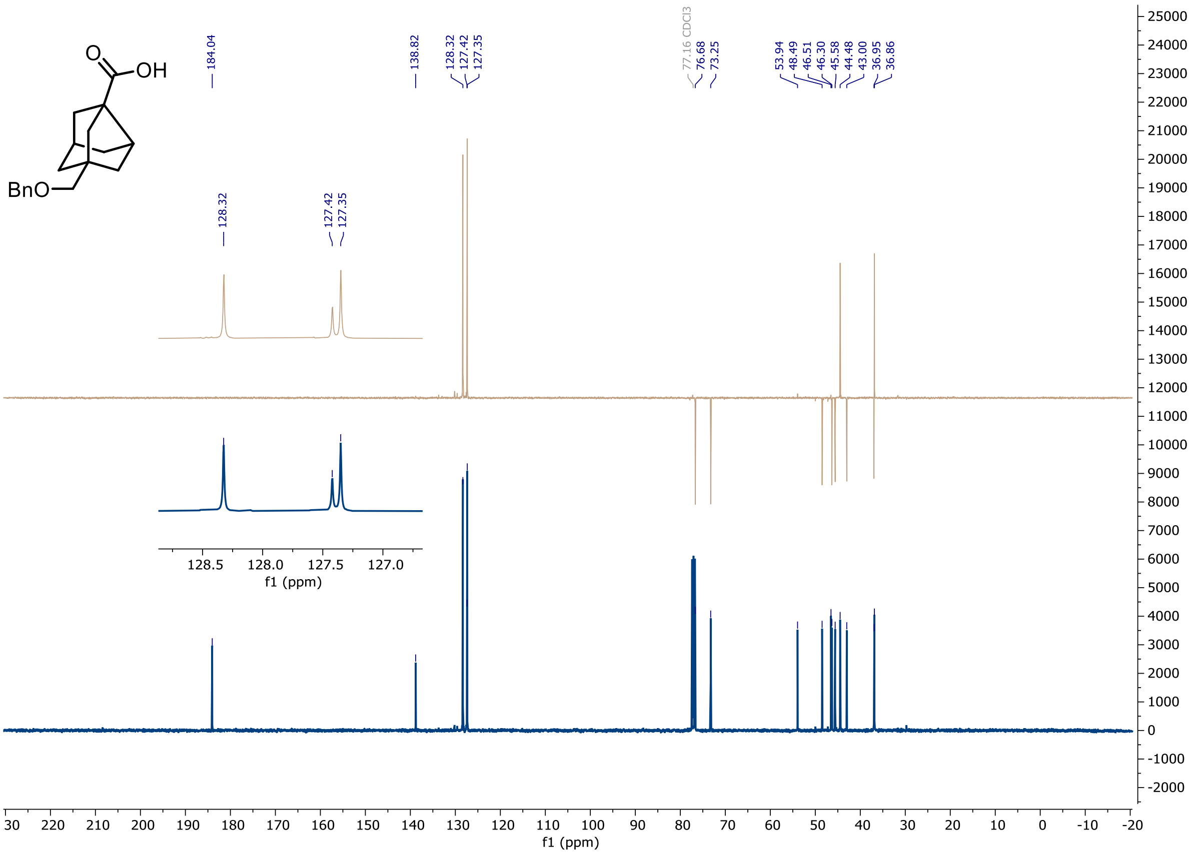
Compound 8b: ^{1}H NMR (400 MHz, CDCl$_3$)



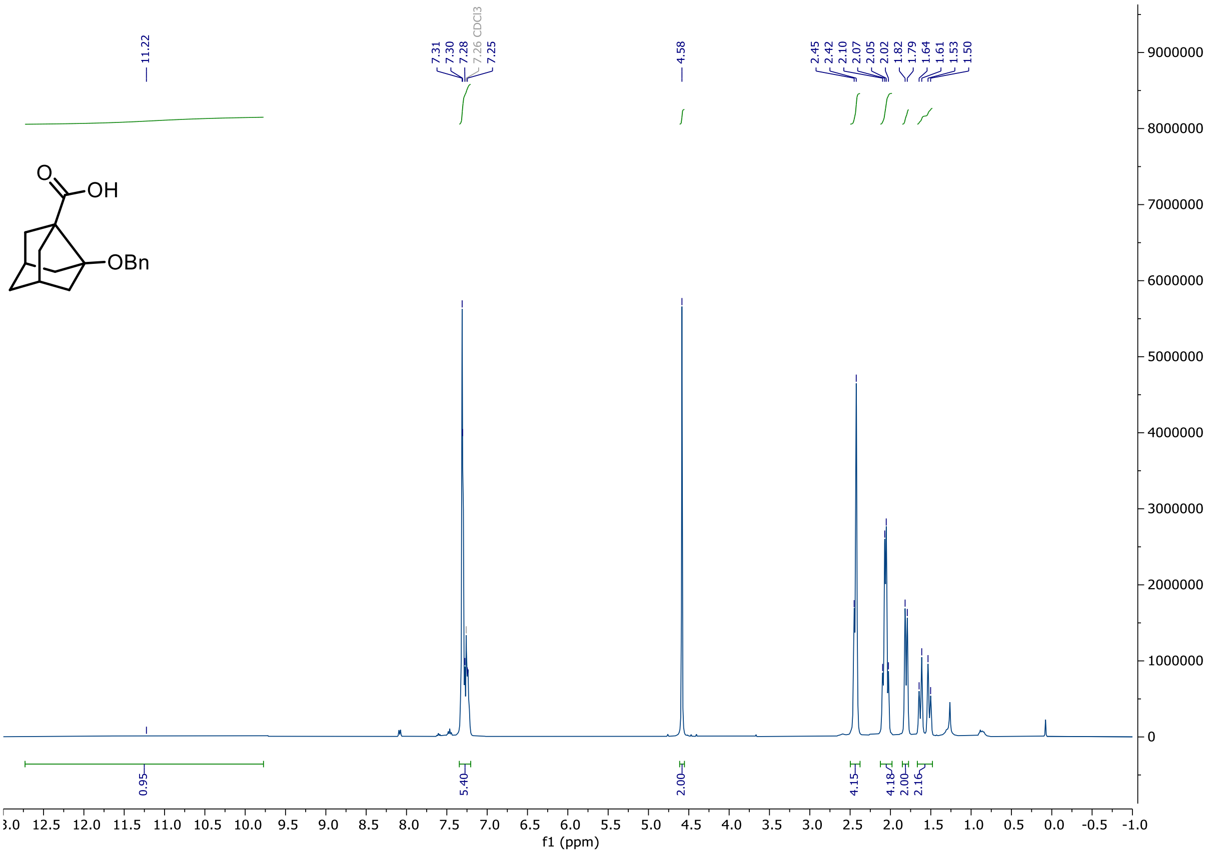
Compound 8b: ^{13}C NMR (101 MHz, CDCl$_3$)



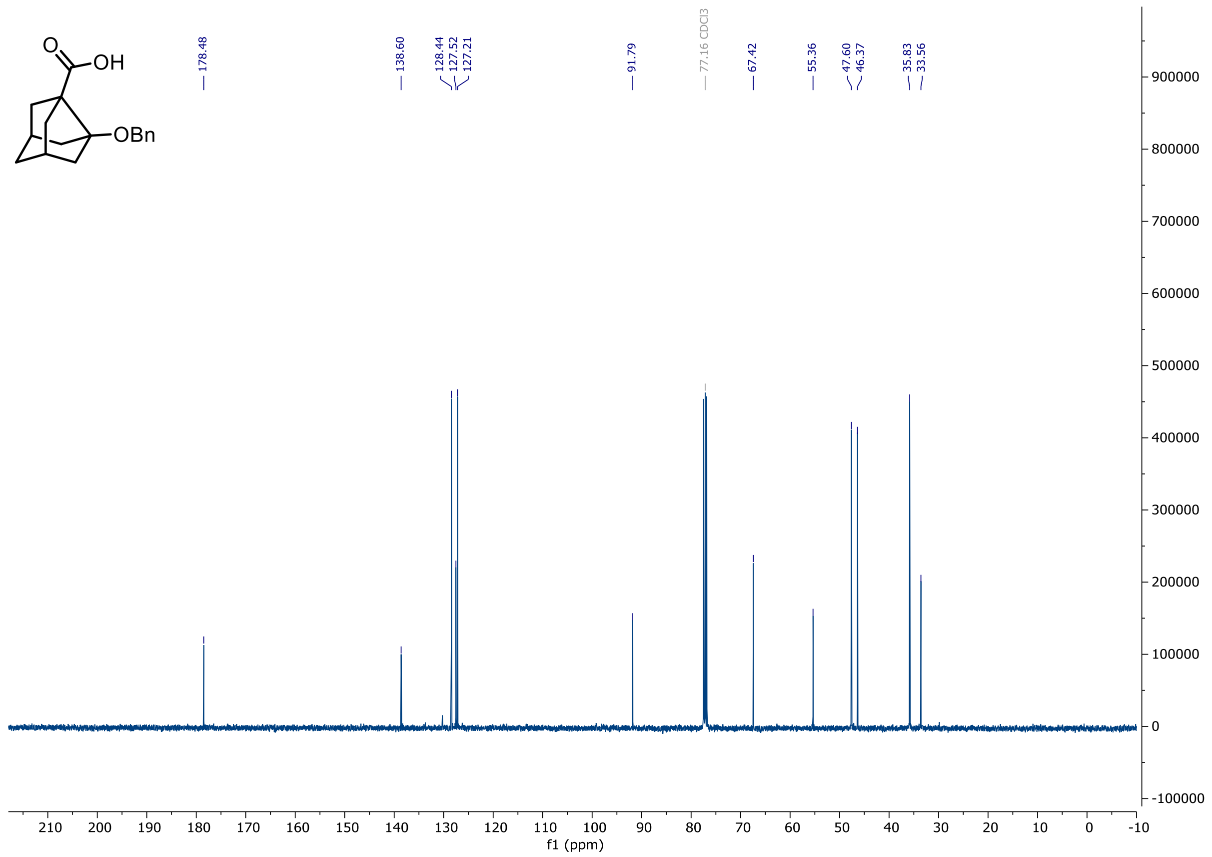
Compound 8b: ^{13}C NMR-DEPT (101 MHz, CDCl$_3$)



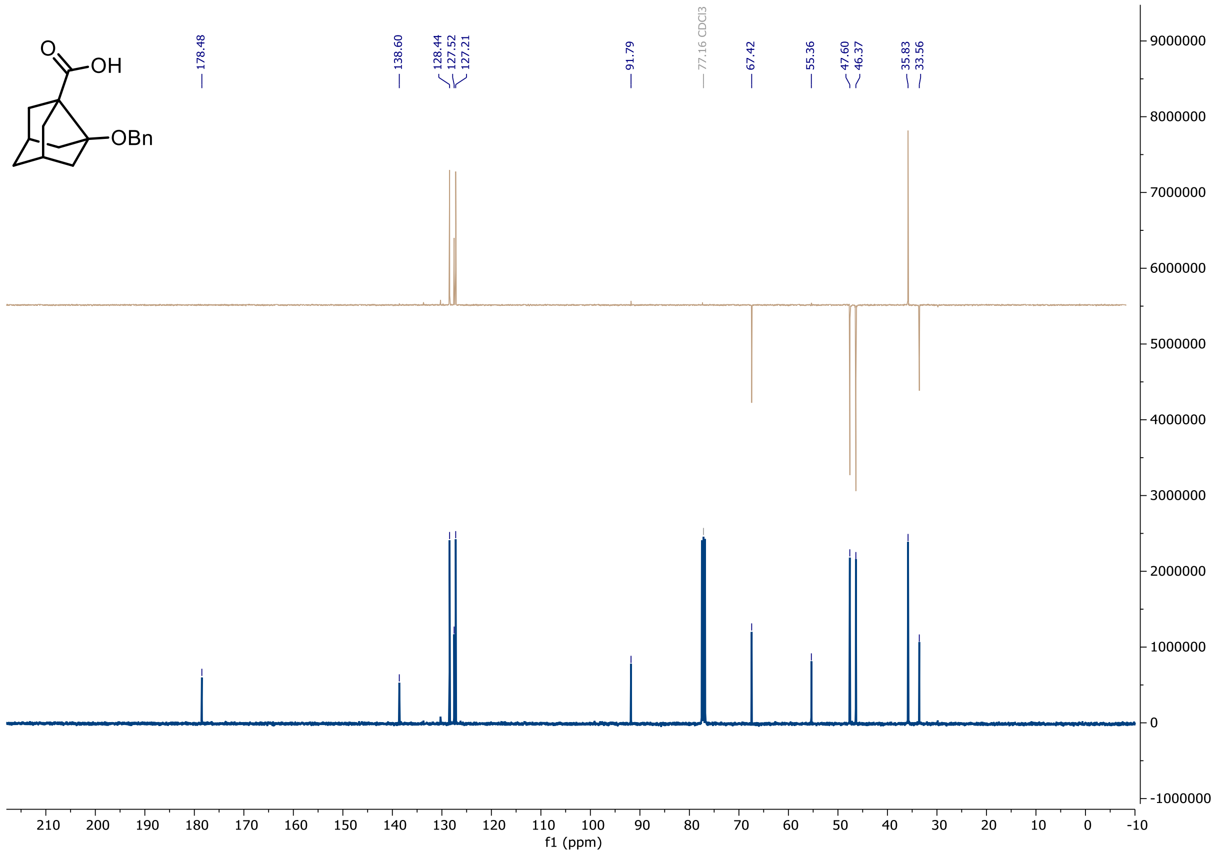
Compound 8c: ^{1}H NMR (400 MHz, $CDCl_3$)



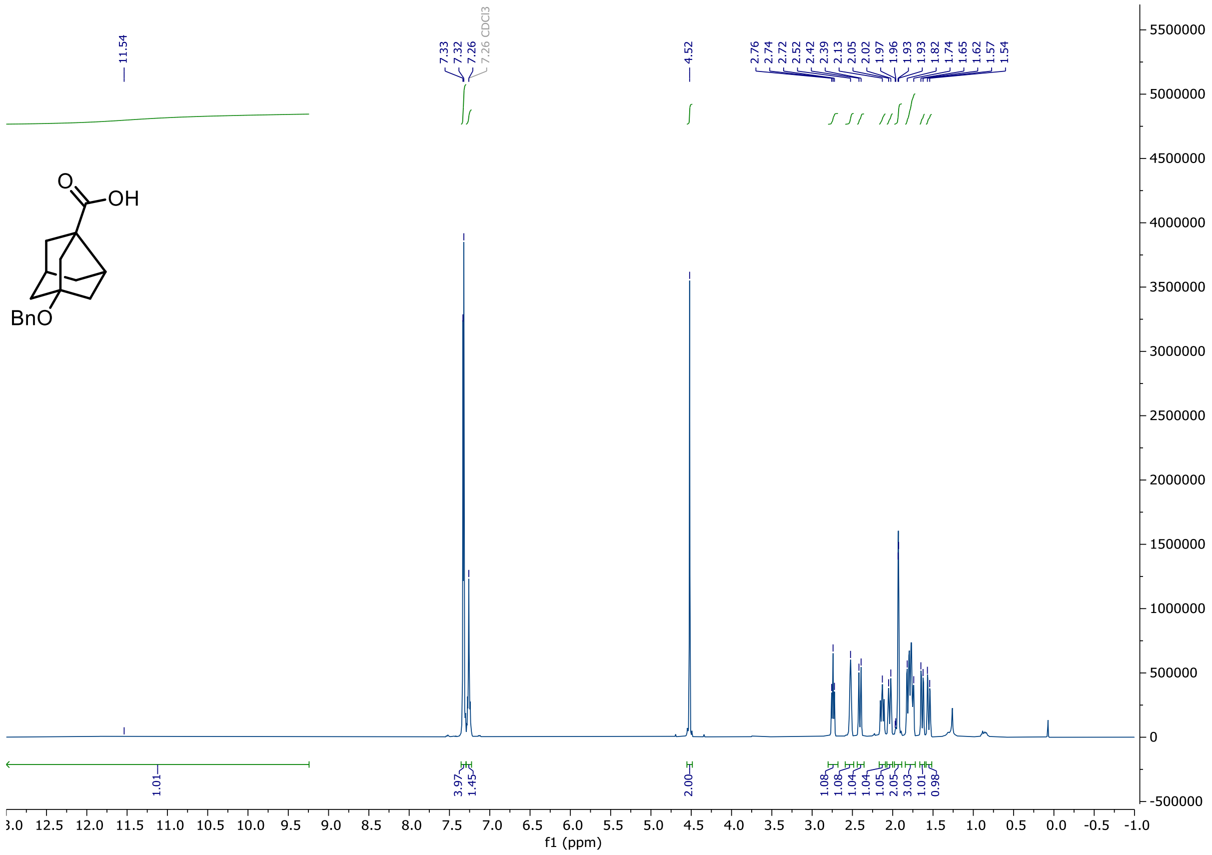
Compound 8c: ^{13}C NMR (101 MHz, $CDCl_3$)



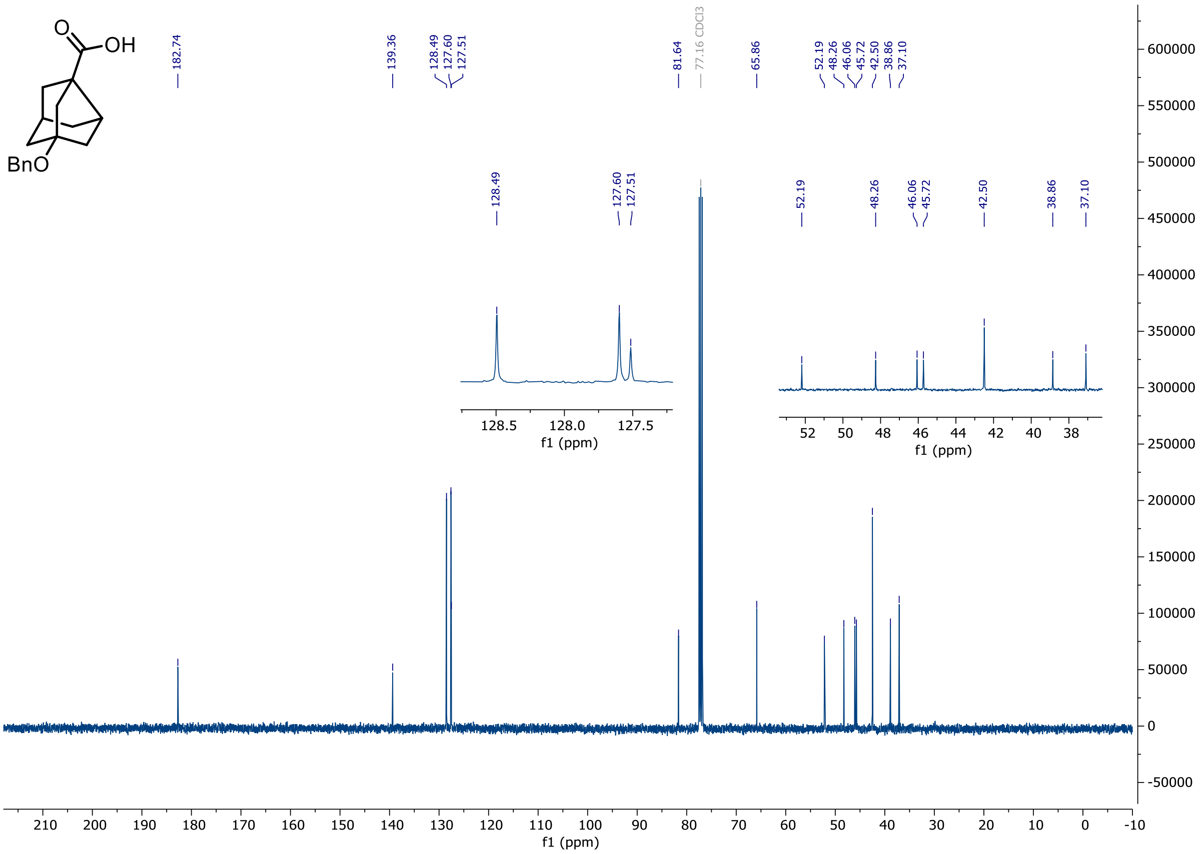
Compound 8c: ^{13}C NMR-DEPT (101 MHz, $CDCl_3$)



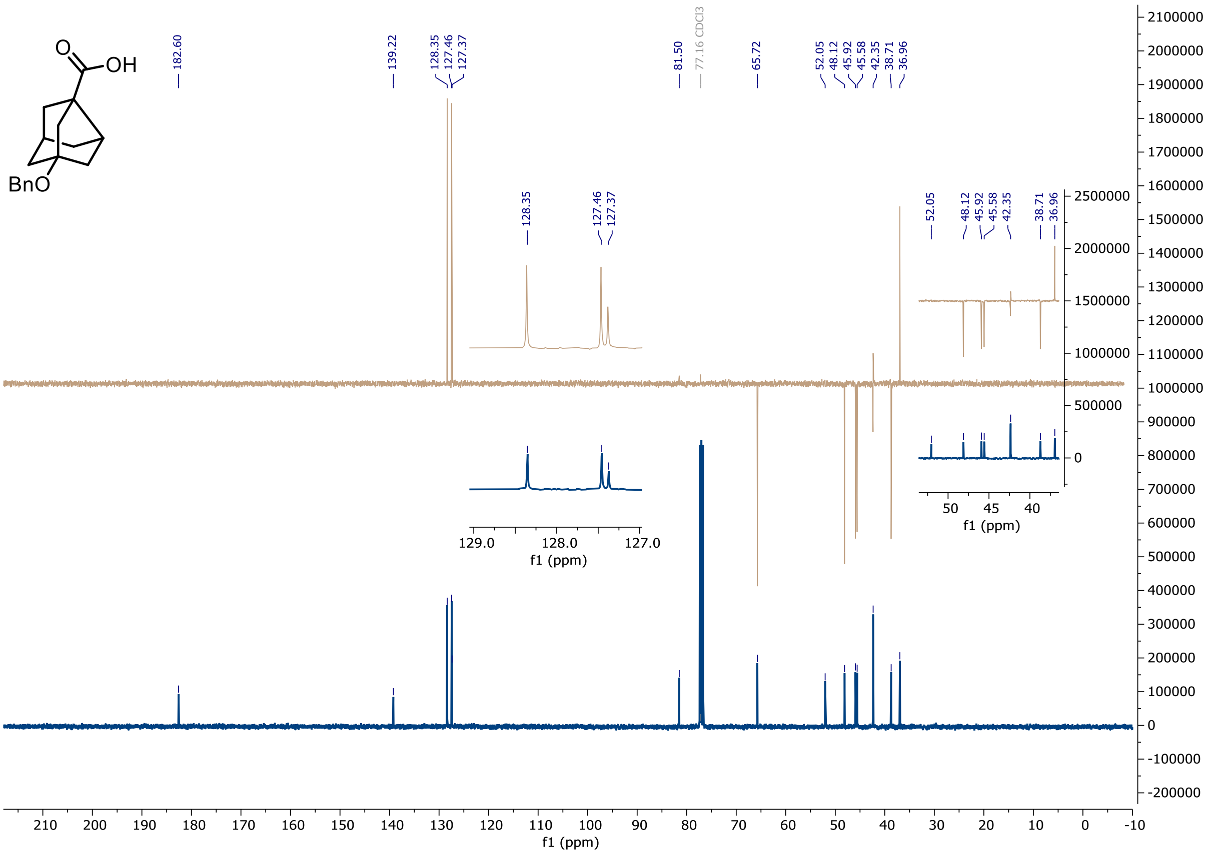
Compound 8d: ^{1}H NMR (400 MHz, CDCl$_3$)



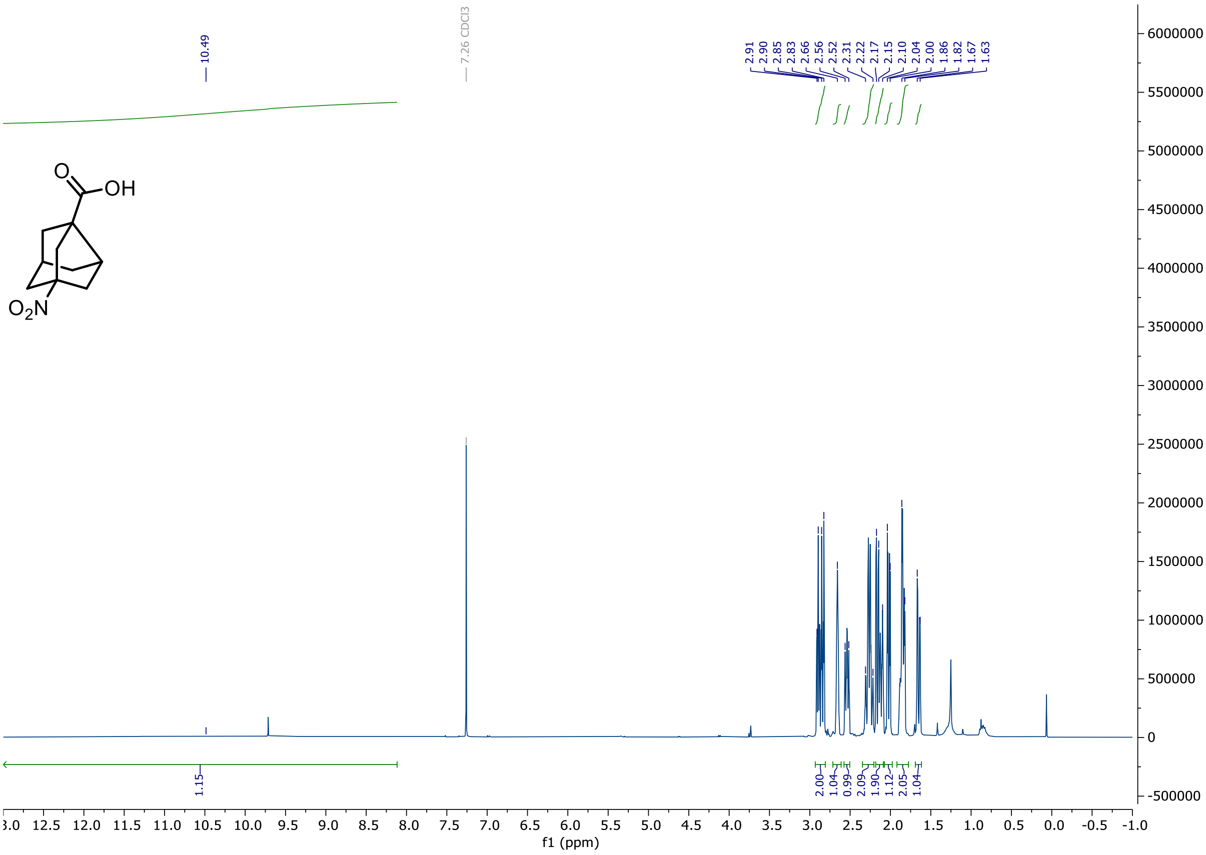
Compound 8d: ^{13}C NMR (101 MHz, $CDCl_3$)



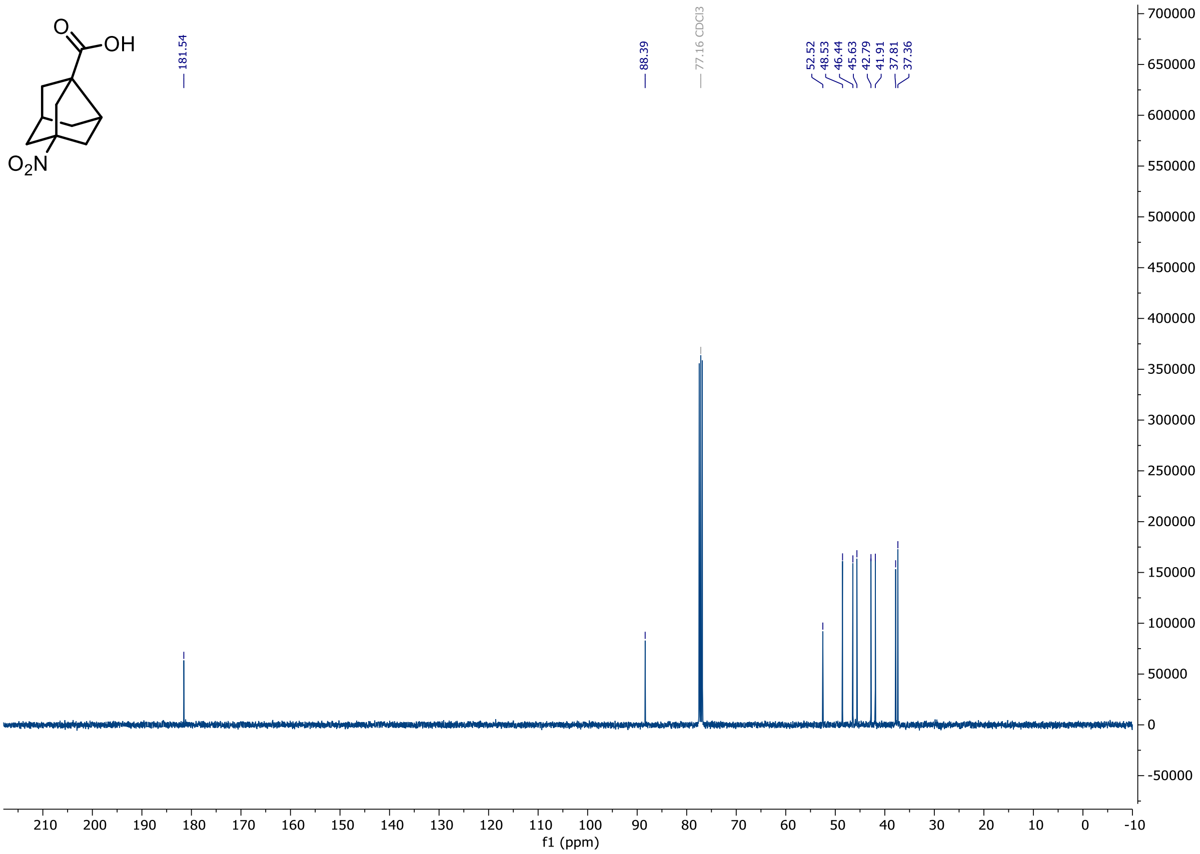
Compound 8d: ^{13}C NMR-DEPT (101 MHz, $CDCl_3$)



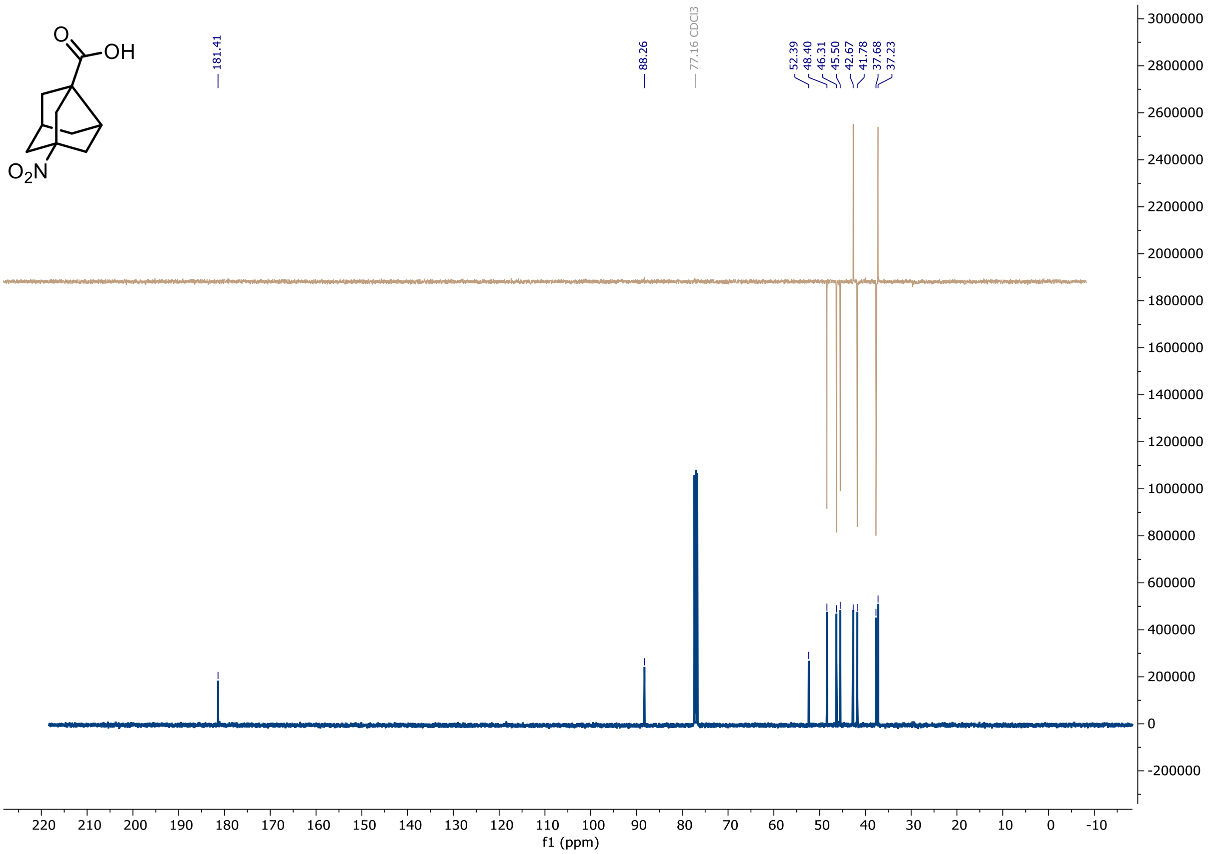
Compound 8e: ^{1}H NMR (400 MHz, CDCl$_3$)



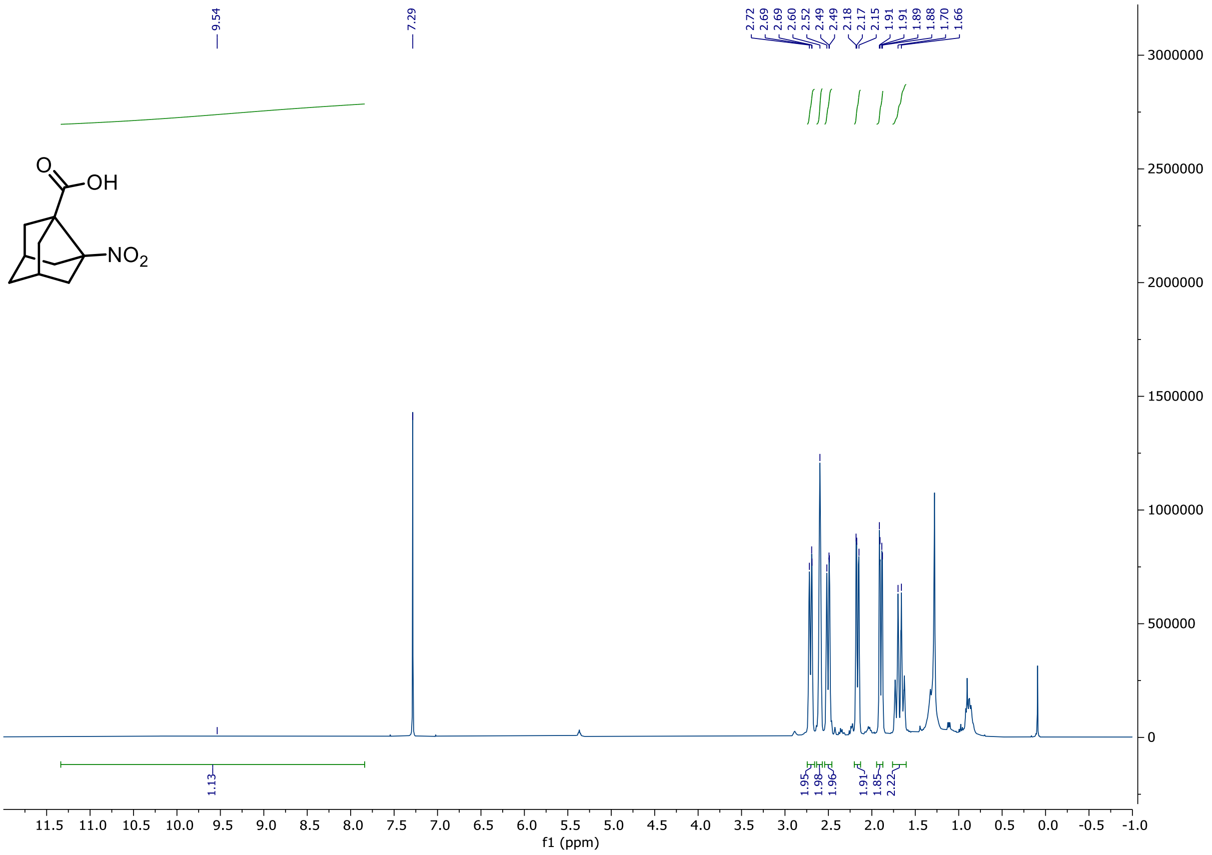
Compound 8e: ^{13}C NMR (101 MHz, $CDCl_3$)



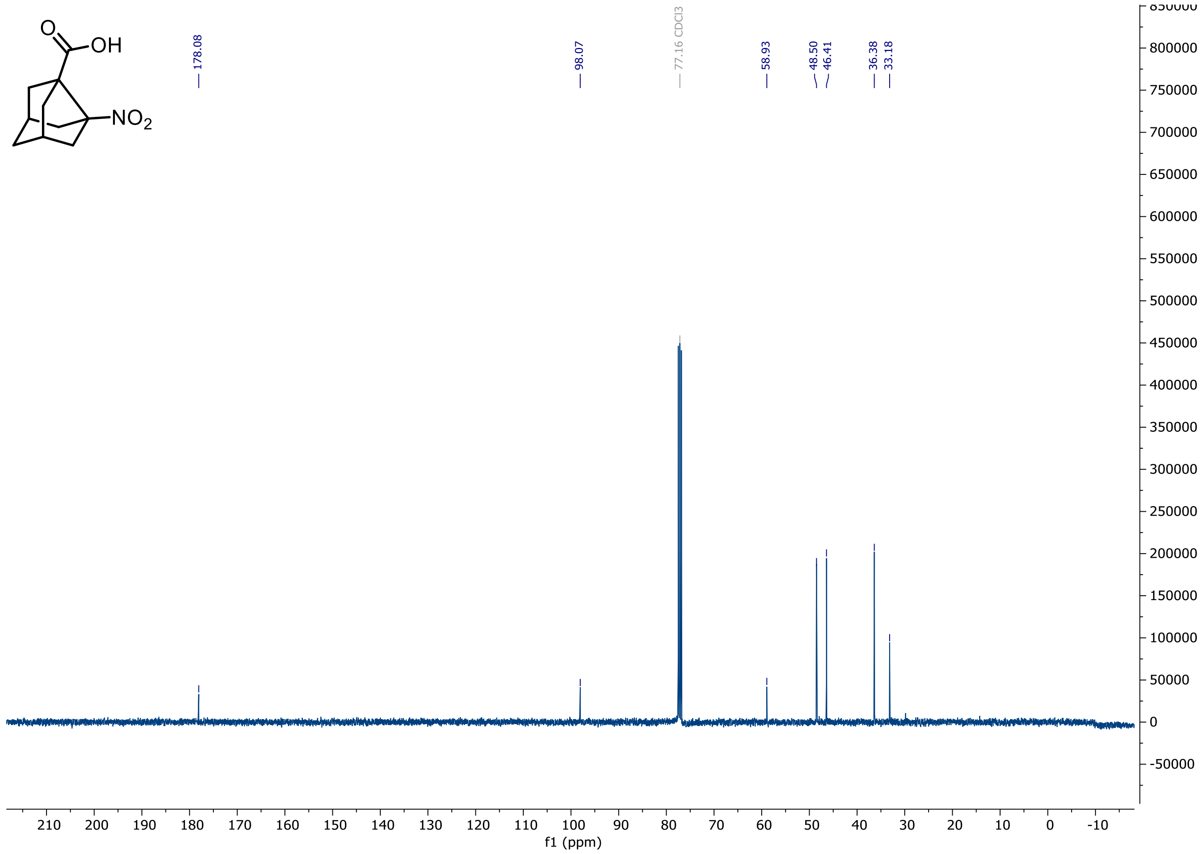
Compound 8e: ^{13}C NMR-DEPT (101 MHz, $CDCl_3$)



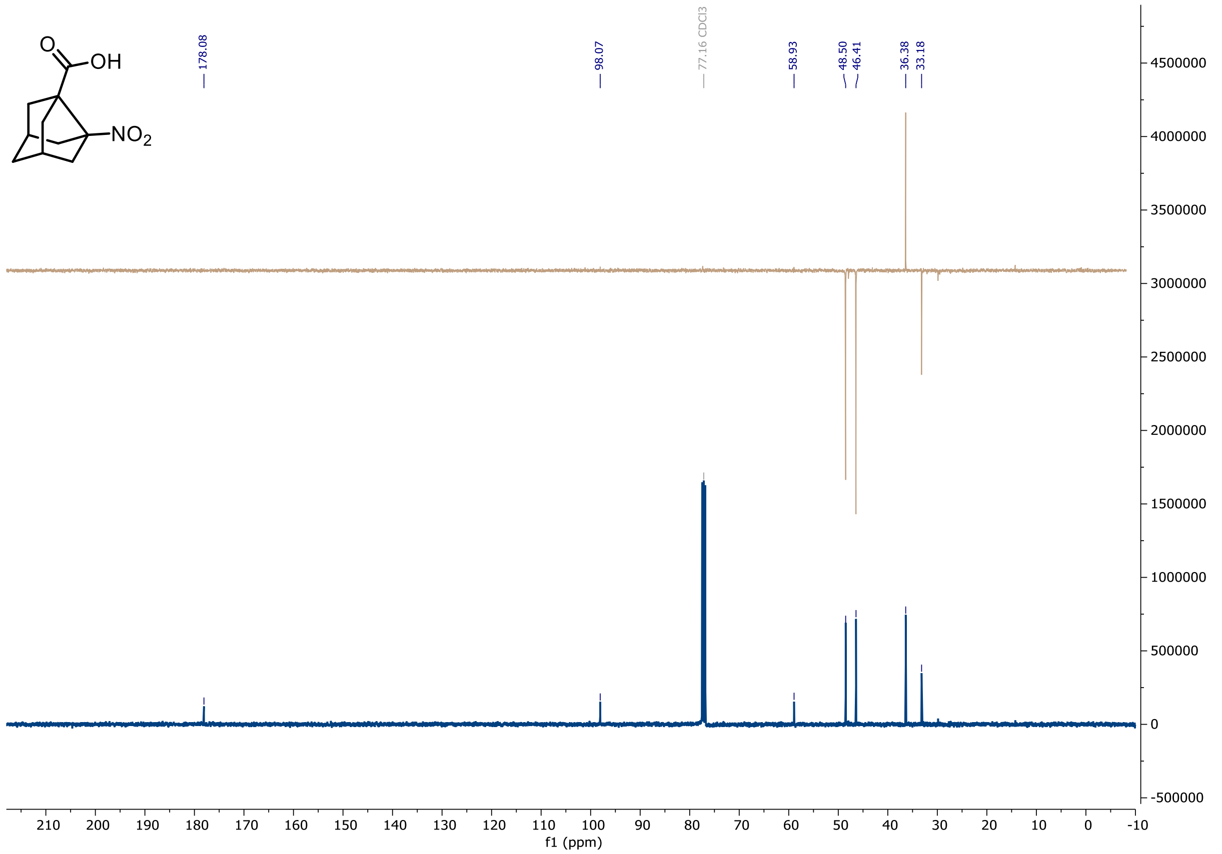
Compound 8f: ^{1}H NMR (400 MHz, CDCl$_3$)



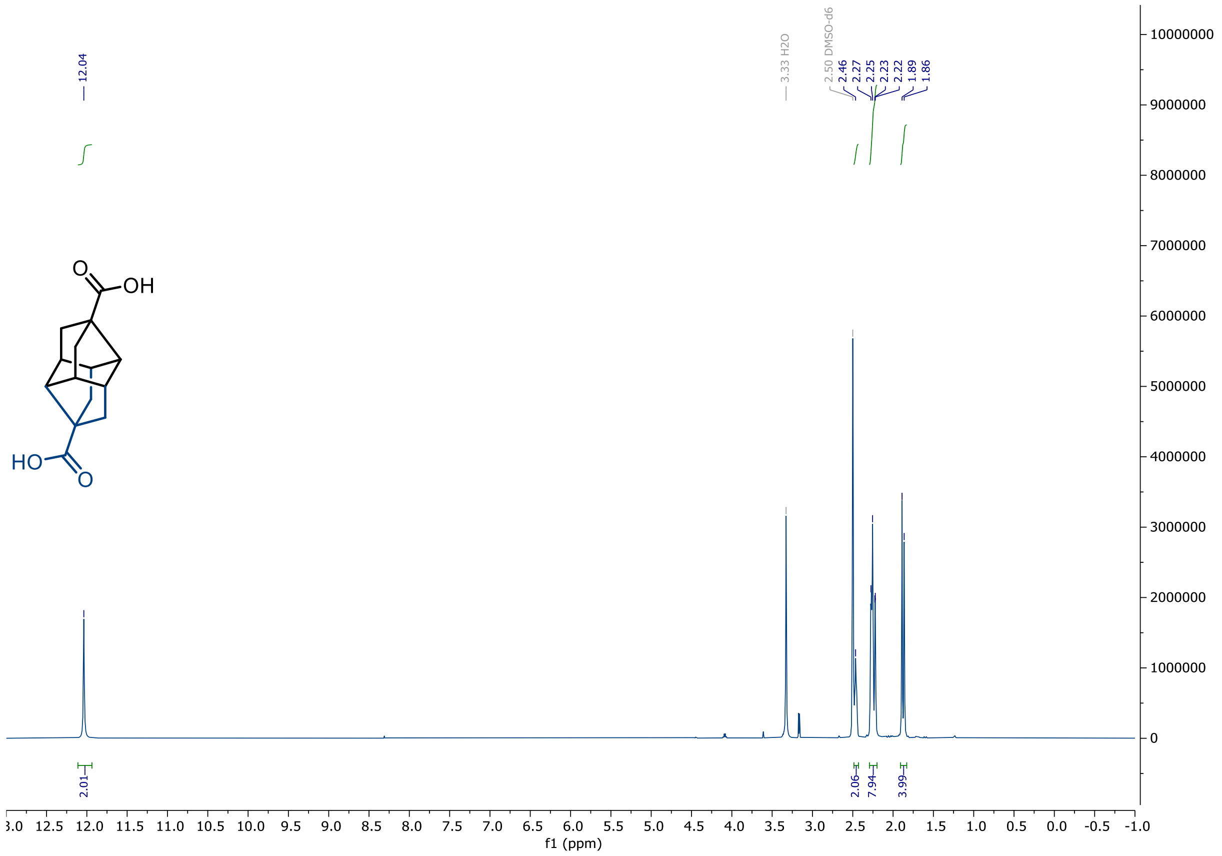
Compound 8f: ^{13}**C NMR** (101 MHz, $CDCl_3$)



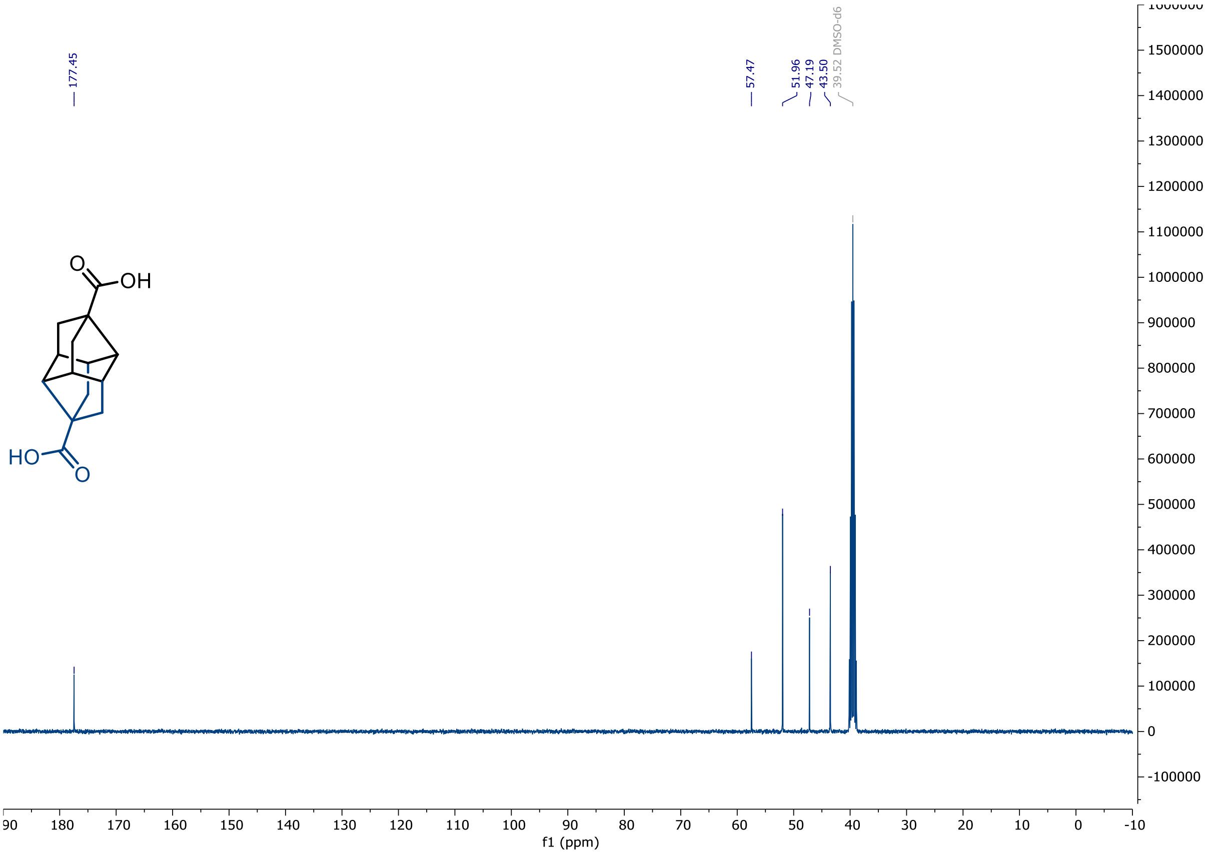
Compound 8f: ^{13}**C NMR-DEPT** (101 MHz, $CDCl_3$)



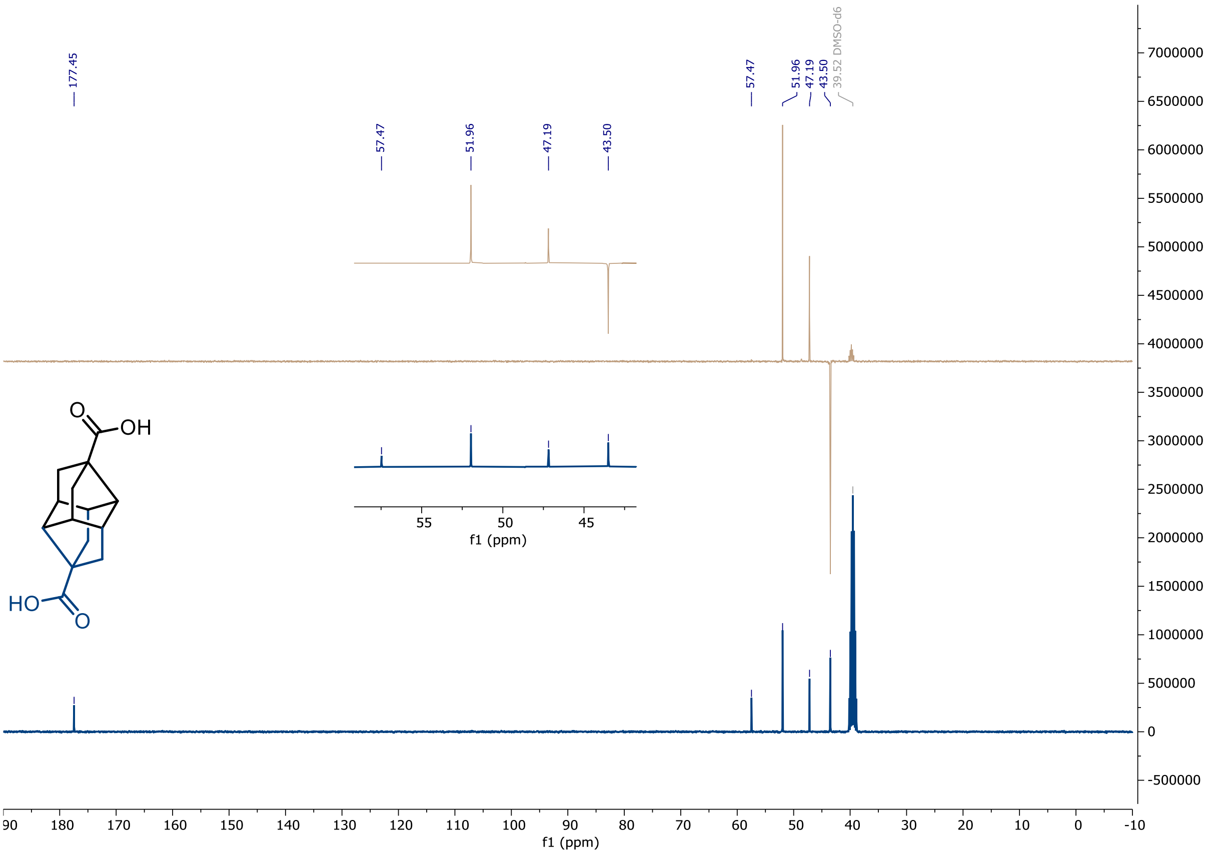
Compound 8g: ^{1}H NMR (400 MHz, DMSO-d^6)



Compound 8g: ^{13}C NMR (101 MHz, DMSO-*d*^{6})



Compound 8g: ^{13}C NMR-DEPT (101 MHz, DMSO-*d*^{6})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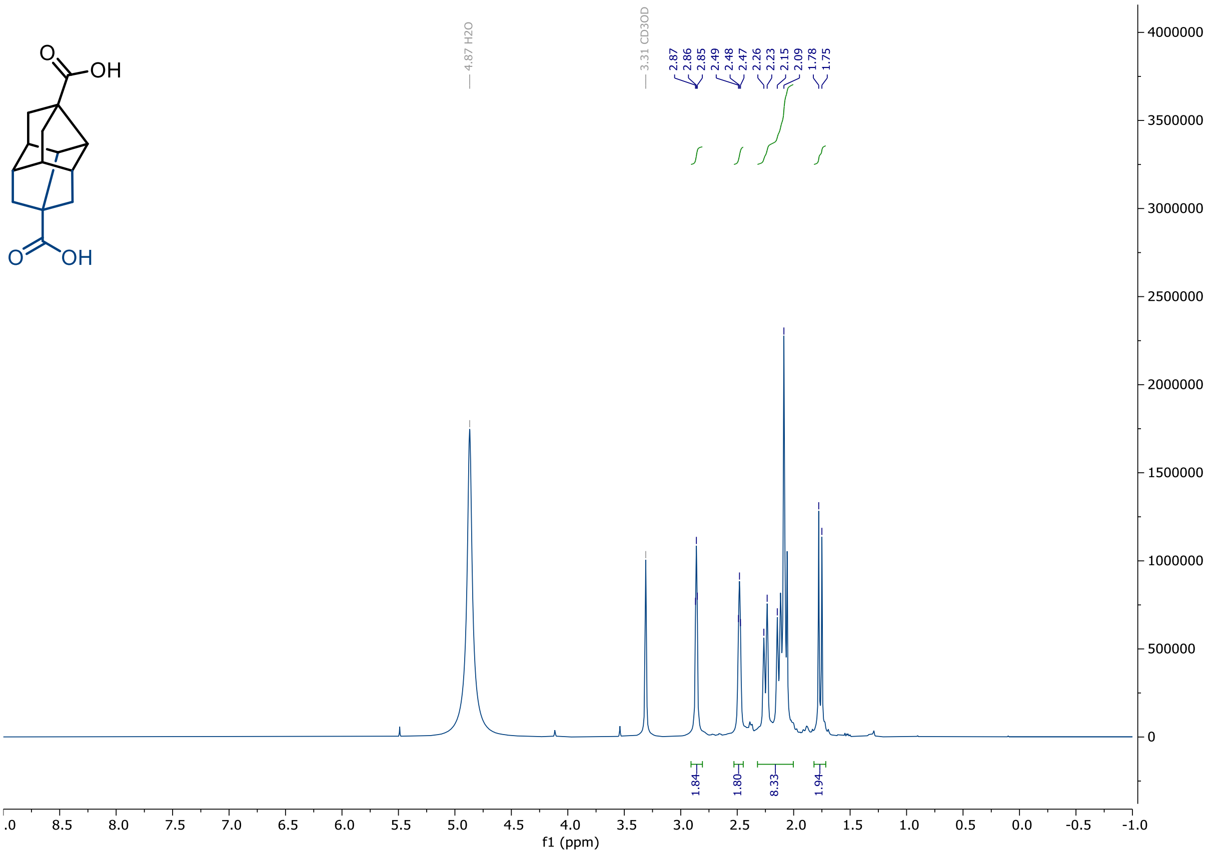
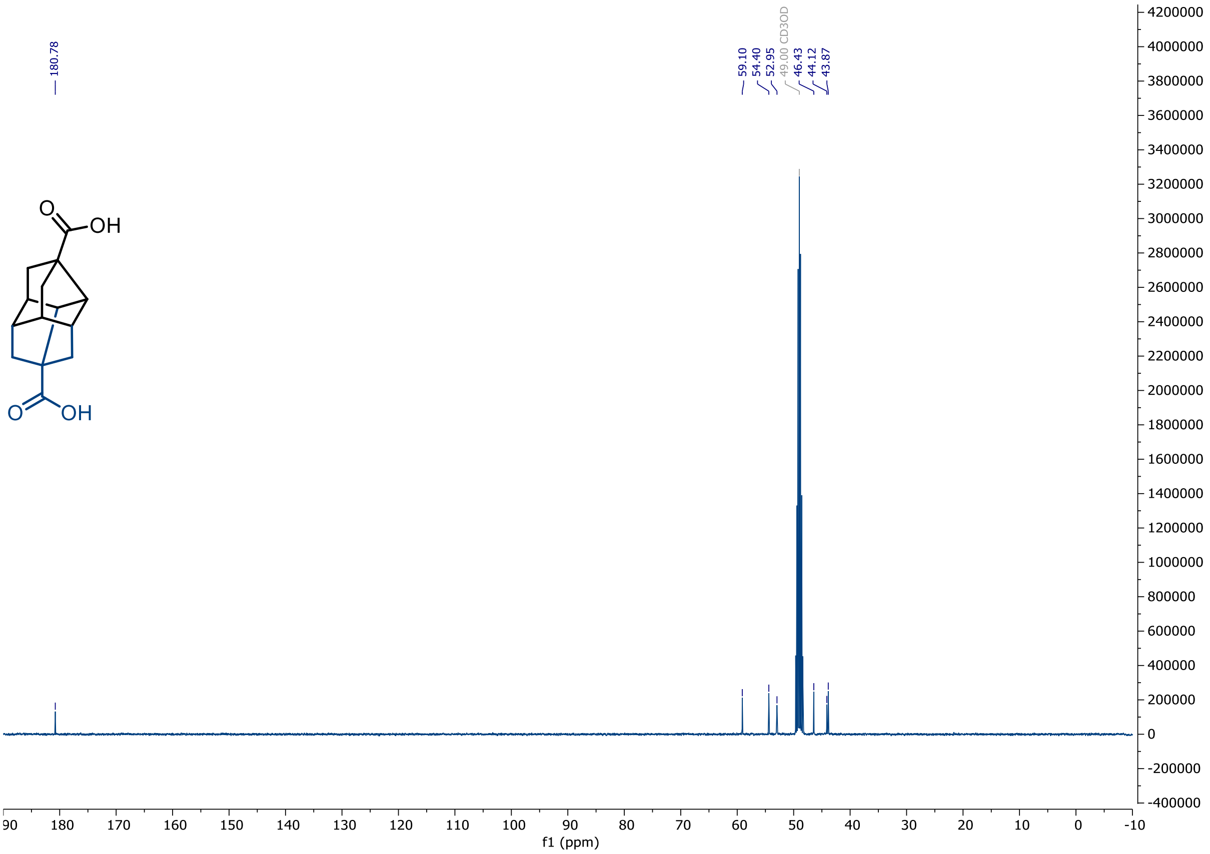
57.47
51.96
47.19
43.50
39.52 DMSO-d6
57.47
51.96
47.19
43.50
55
50
45
f1 (ppm)
O
OH
HO
O
7000000
6500000
6000000
5500000
5000000
4500000
4000000
3500000
3000000
2500000
2000000
1500000
1000000
500000
0
-500000
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

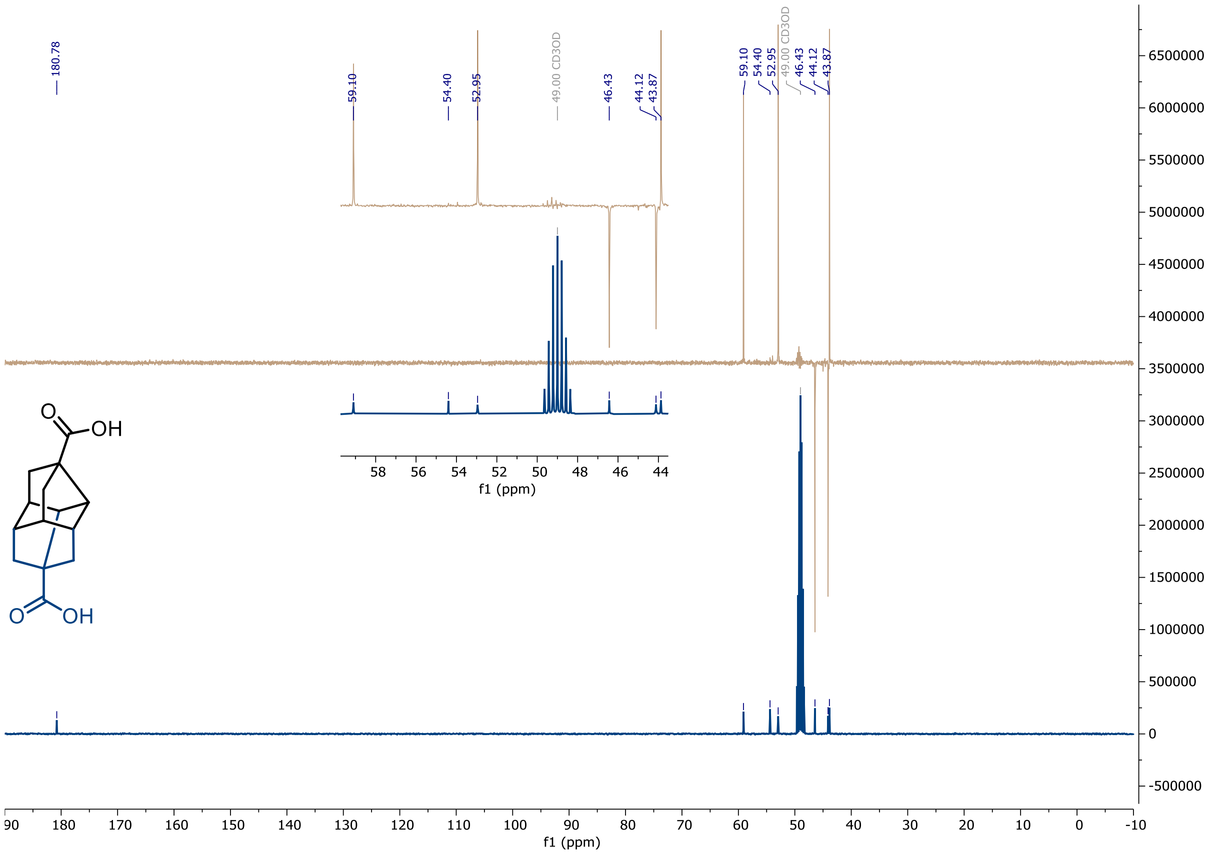
Compound 8h: ^{1}H NMR (400 MHz, MeOD)



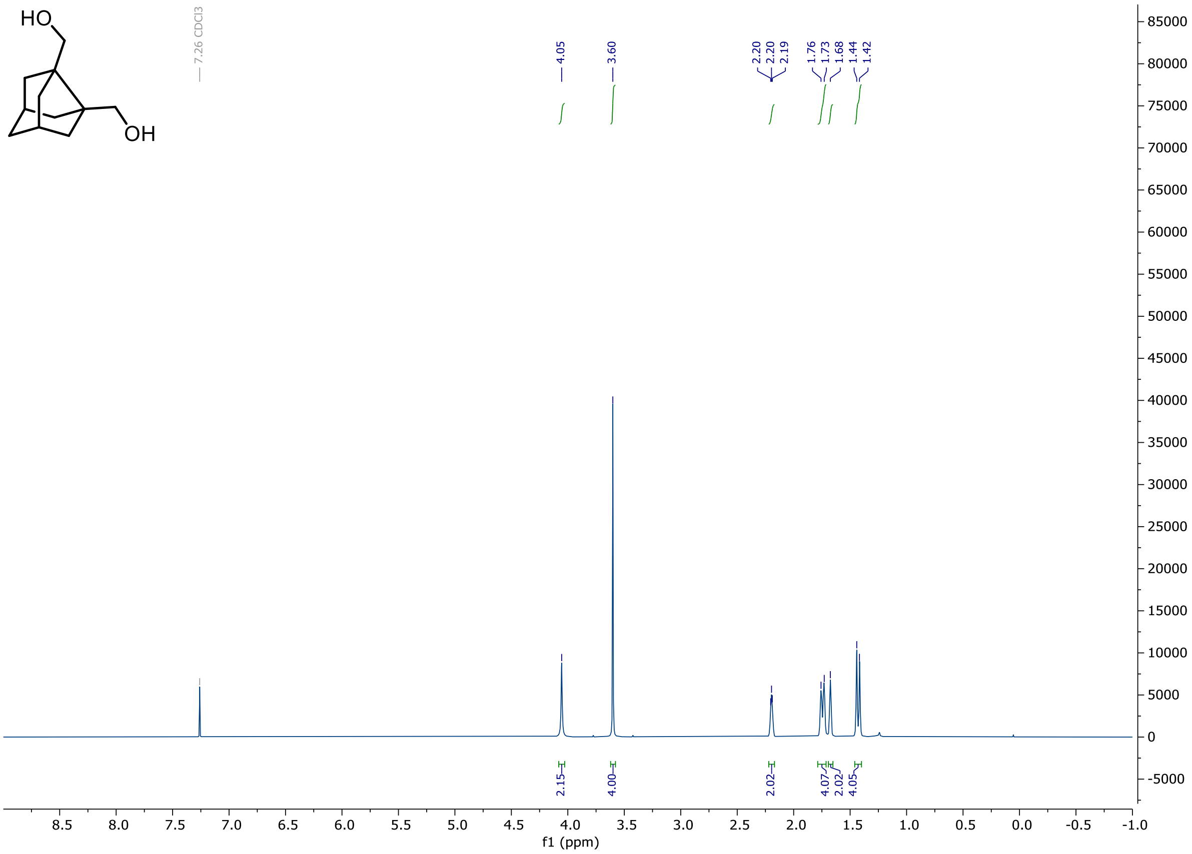
Compound 8h: ^{13}C NMR (101 MHz, MeOD)



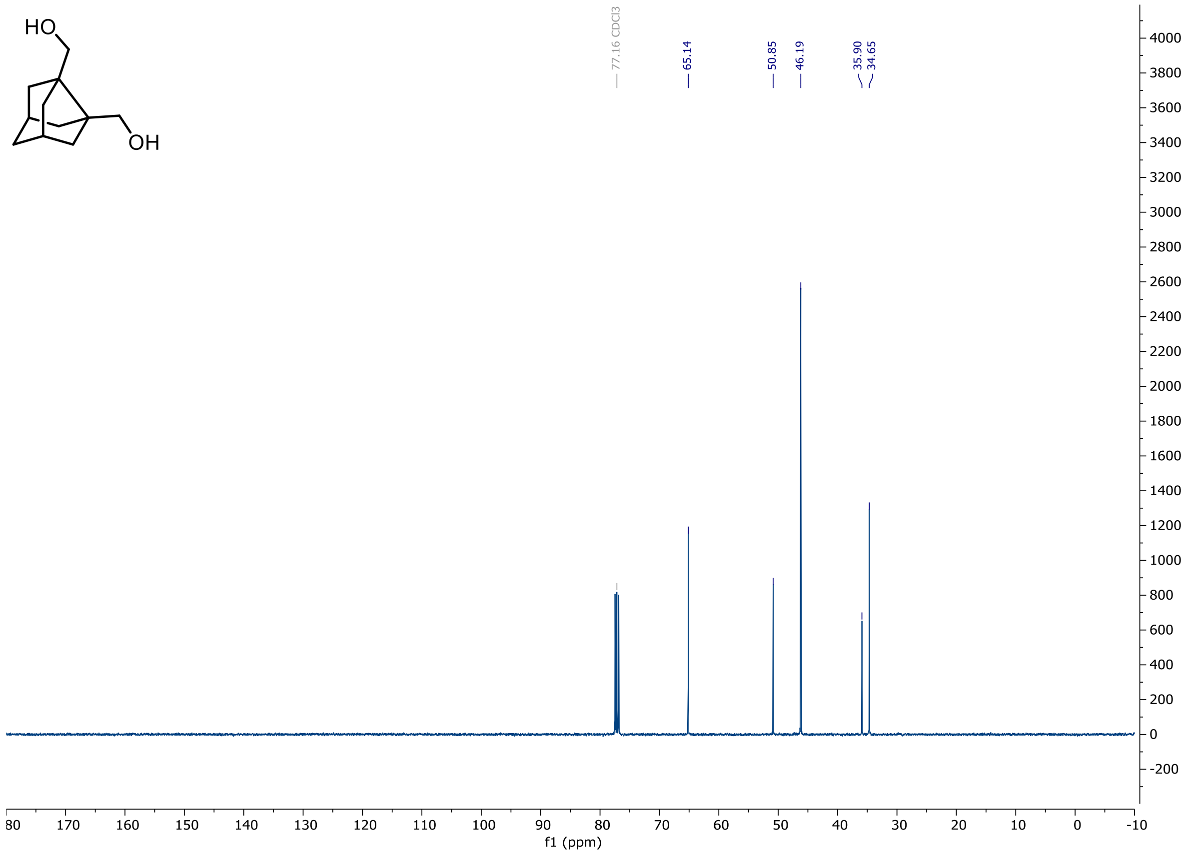
Compound 8h: ^{13}C NMR-DEPT (101 MHz, MeOD)



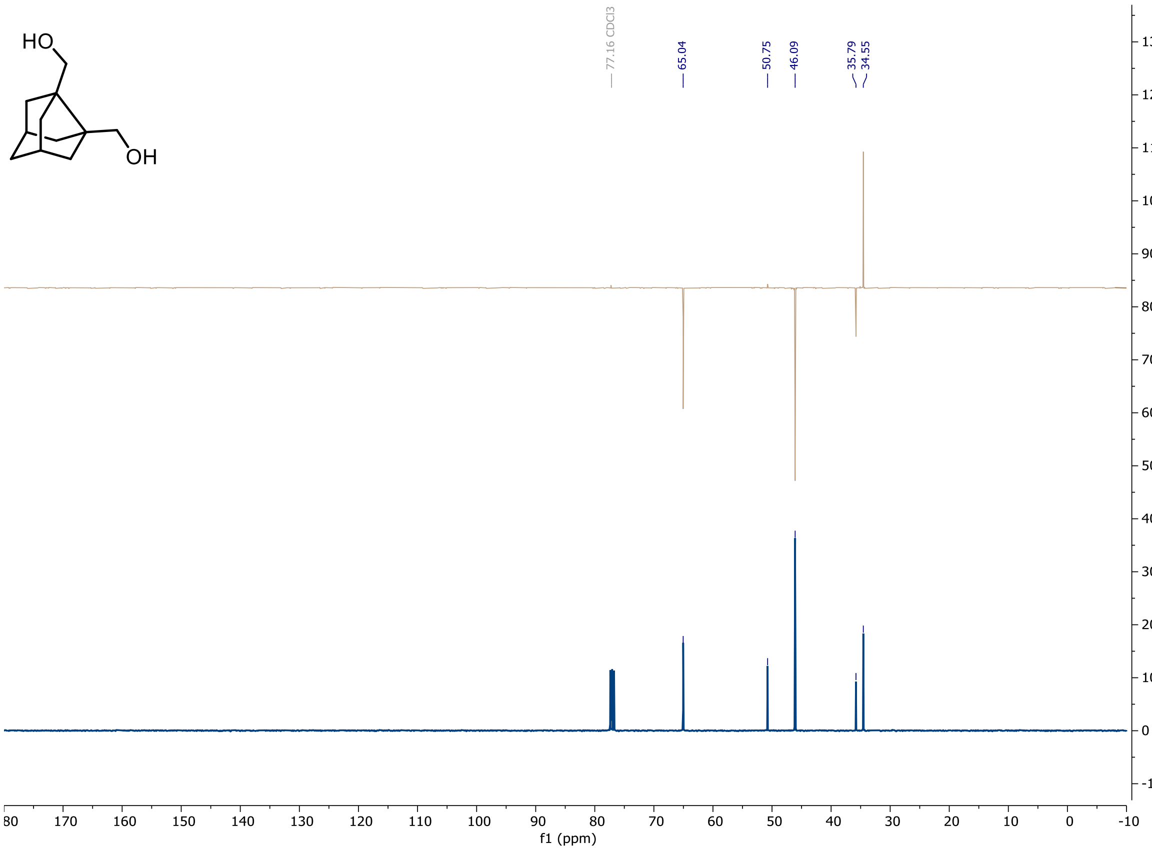
Compound 9a: ^{1}H NMR (400 MHz, $CDCl_3$)



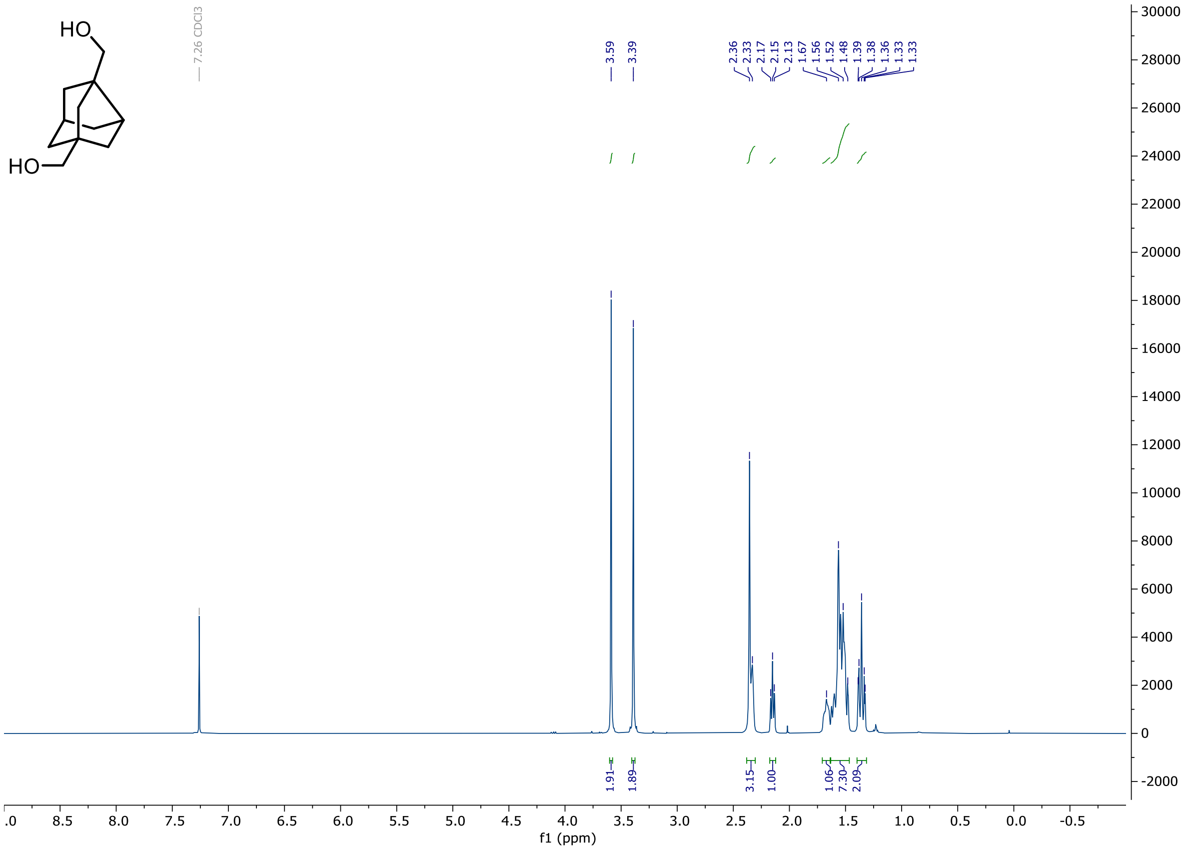
Compound 9a: ^{13}C NMR (101 MHz, $CDCl_3$)



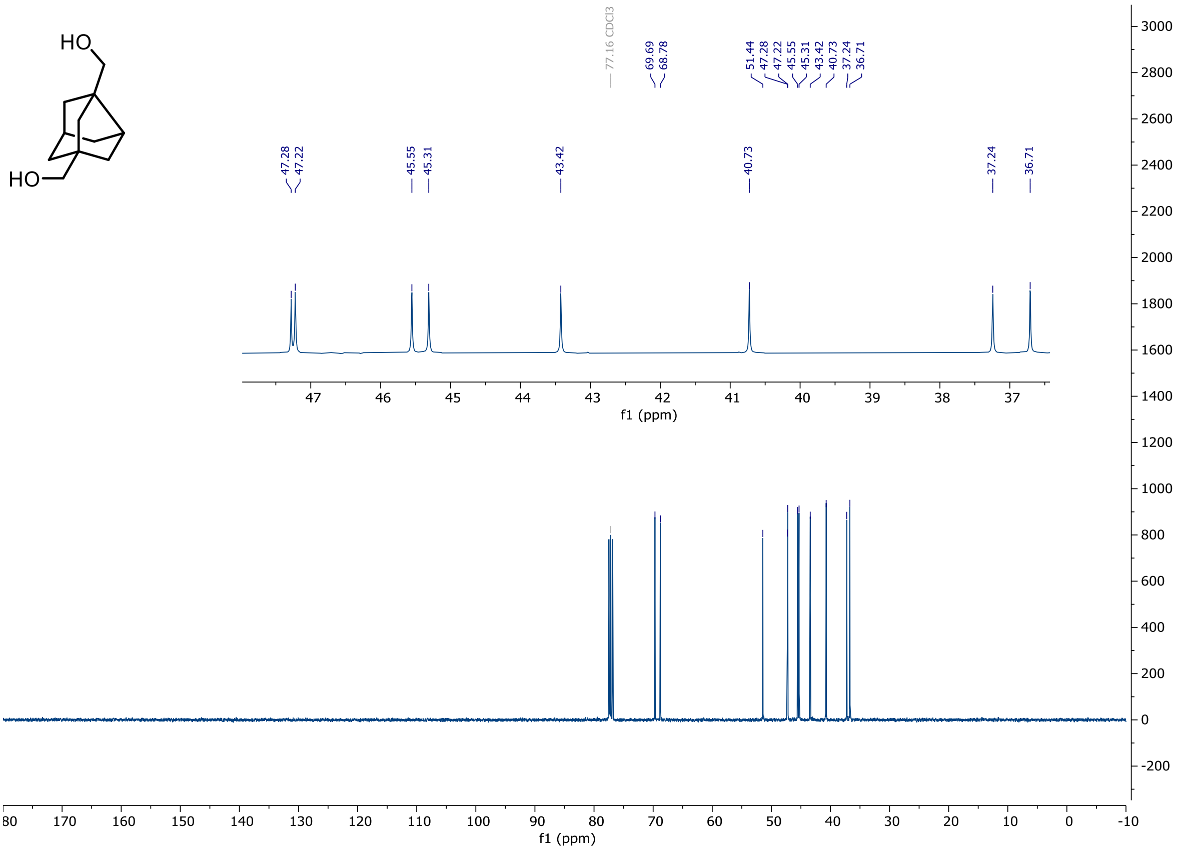
Compound 9a: ^{13}C NMR-DEPT (101 MHz, $CDCl_3$)



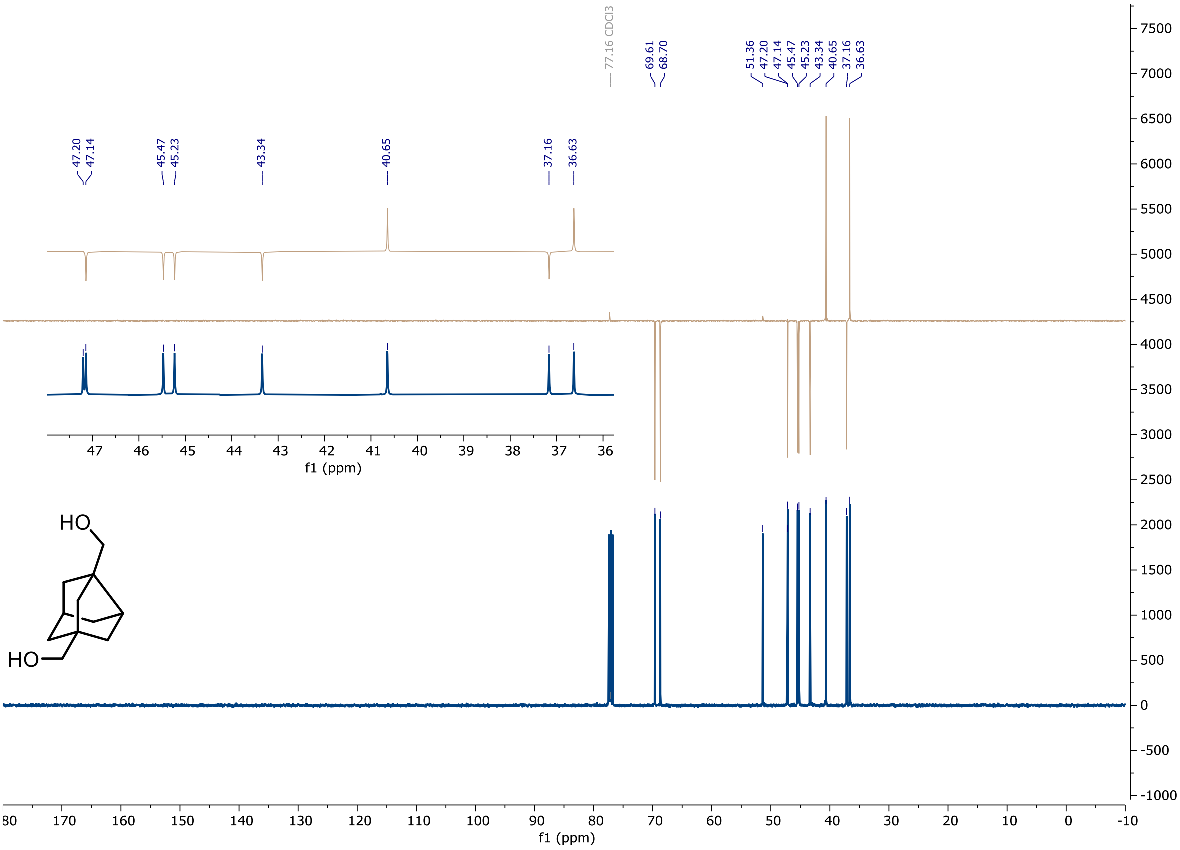
Compound 9b: ^{1}H NMR (400 MHz, $CDCl_3$)



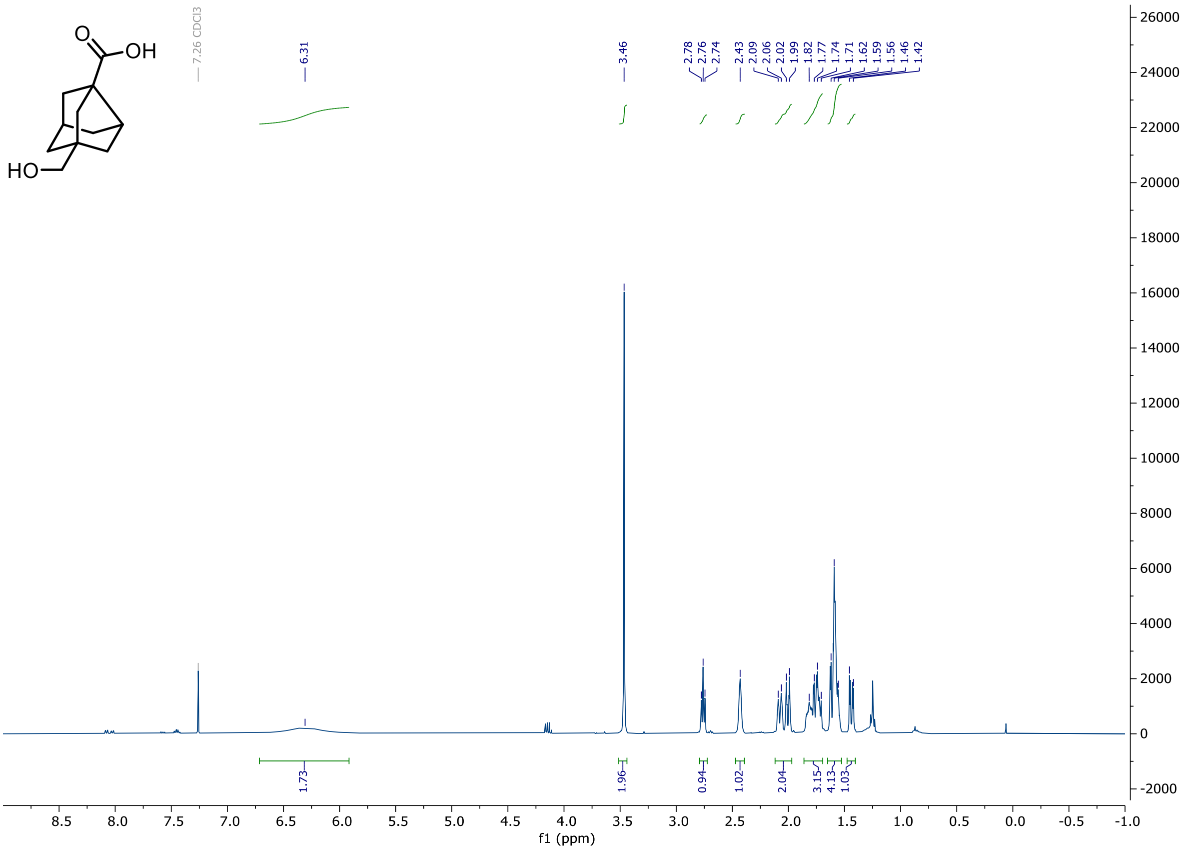
Compound 9b: ^{13}C NMR (101 MHz, $CDCl_3$)



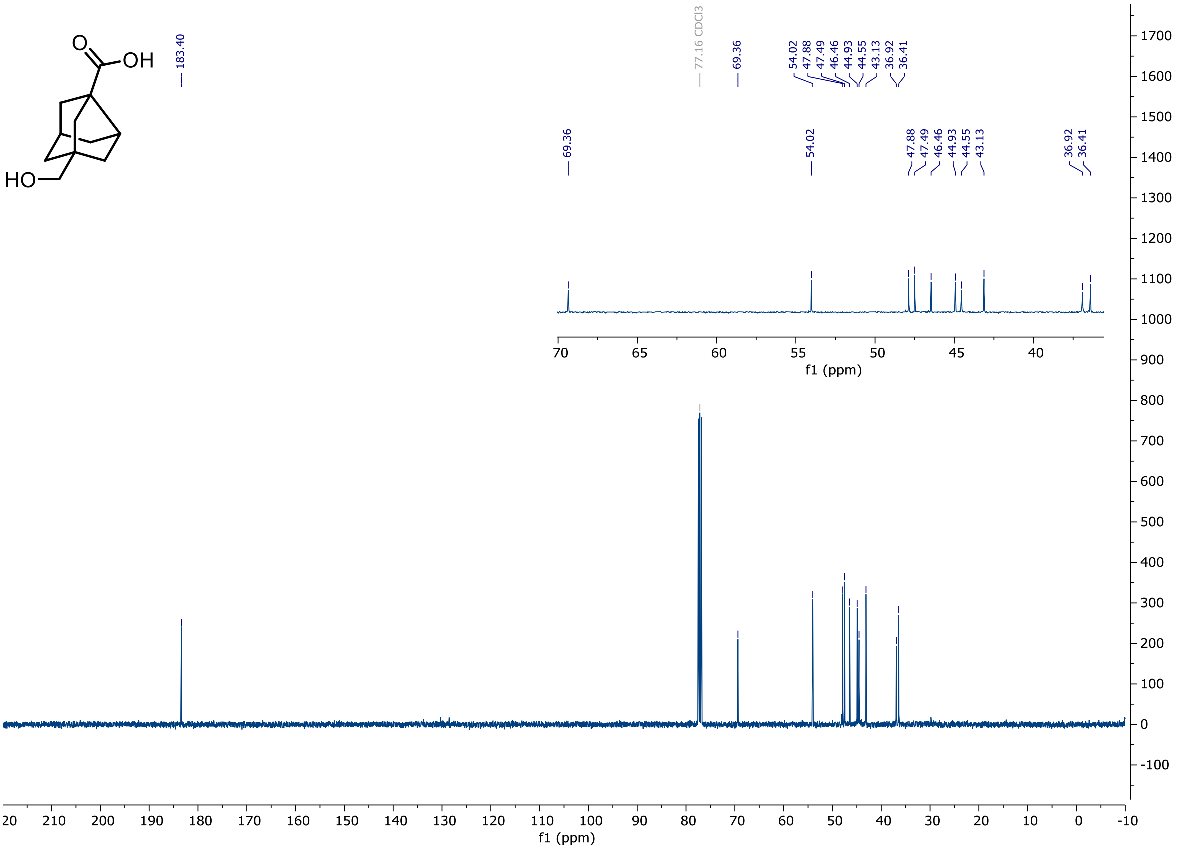
Compound 9b: ^{13}C NMR-DEPT (101 MHz, CDCl$_3$)



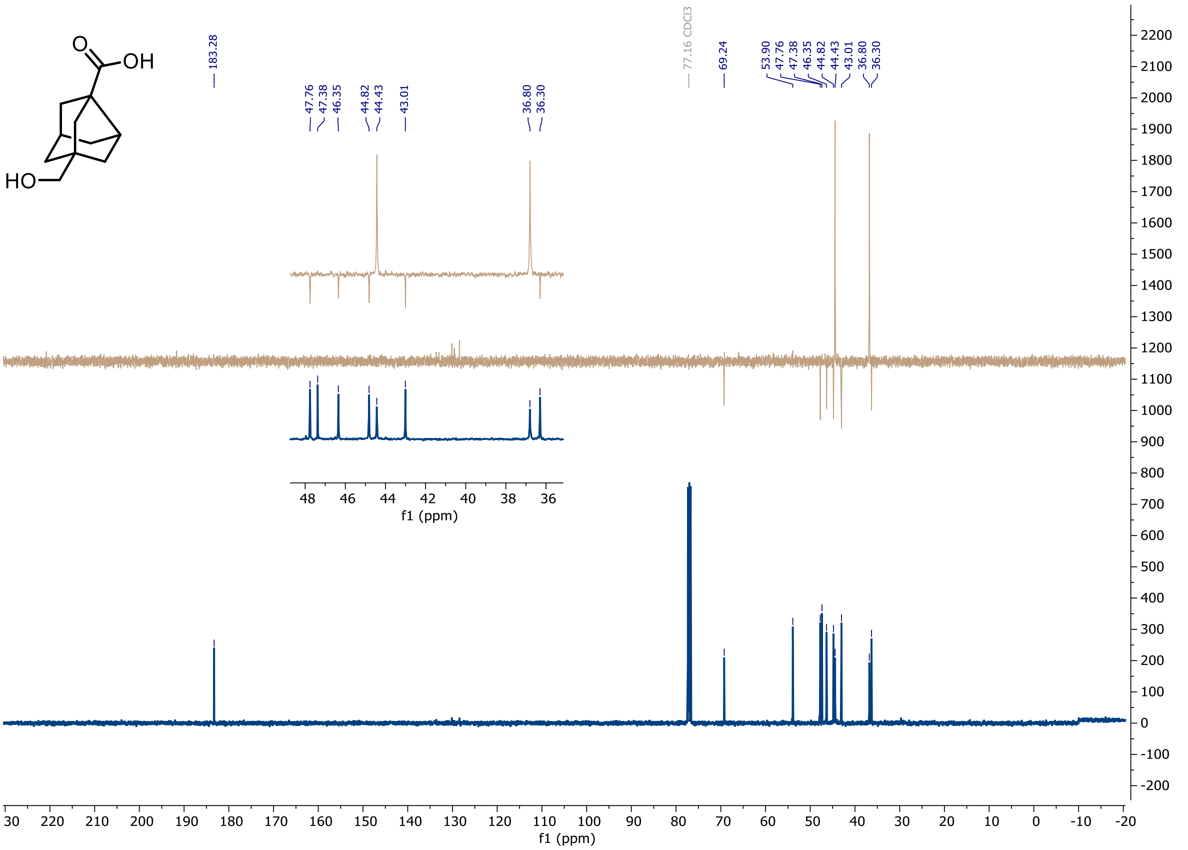
Compound 9c: ^{1}H NMR (400 MHz, CDCl$_3$)



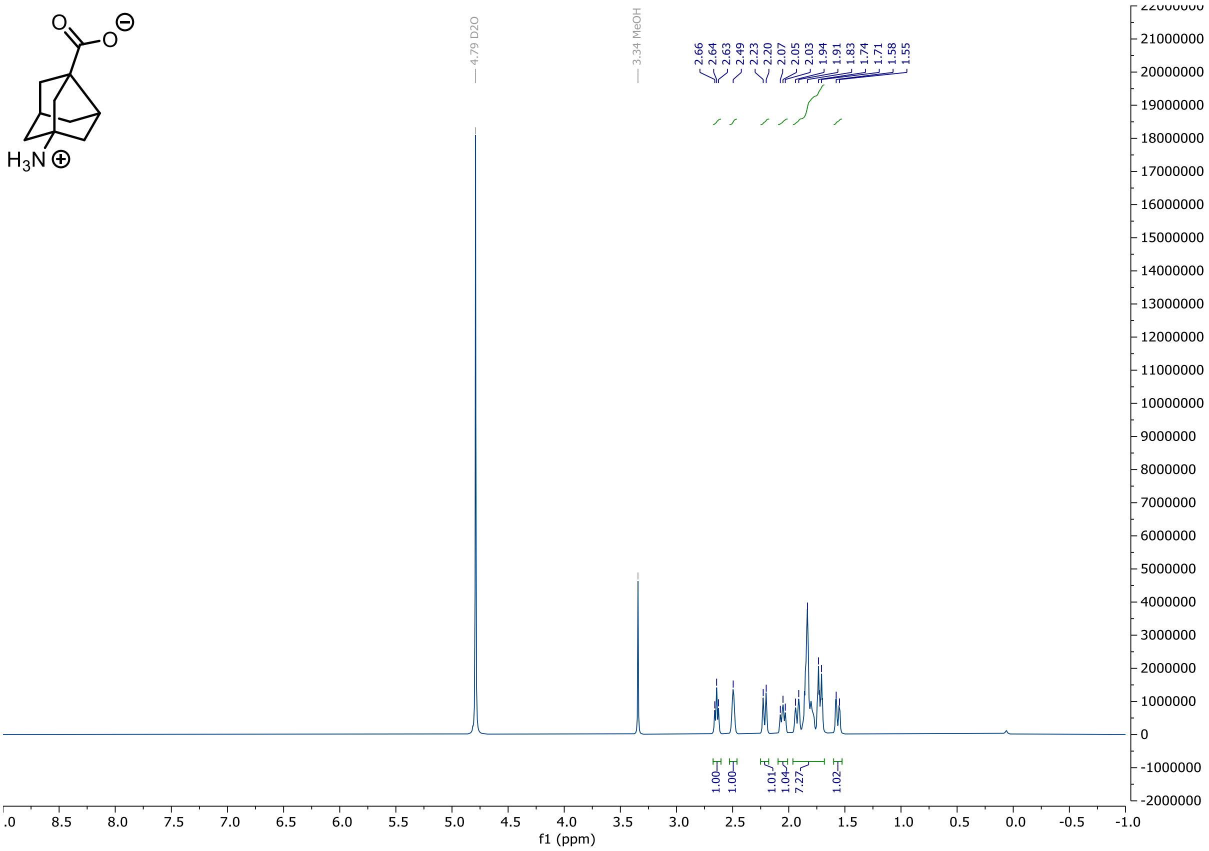
Compound 9c: ^{13}C NMR (101 MHz, $CDCl_3$)



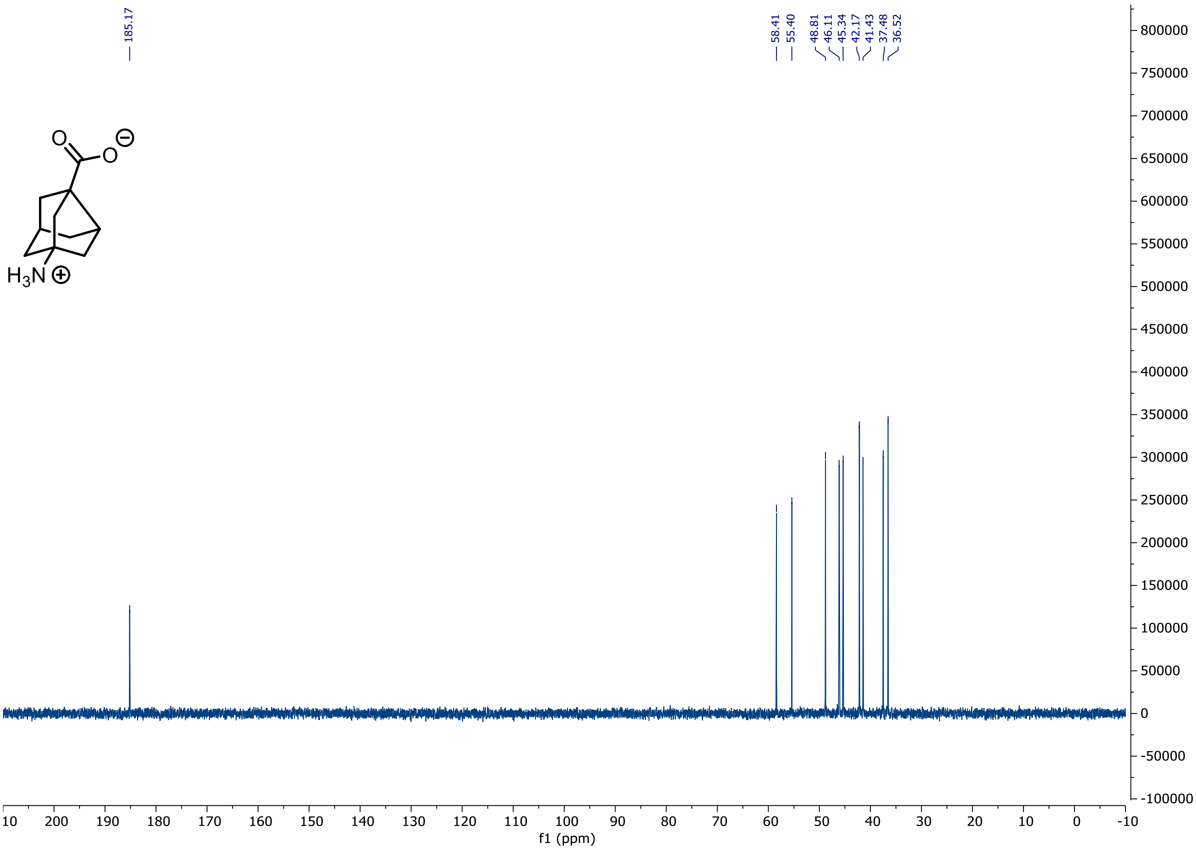
Compound 9c: ^{13}C NMR-DEPT (101 MHz, $CDCl_3$)



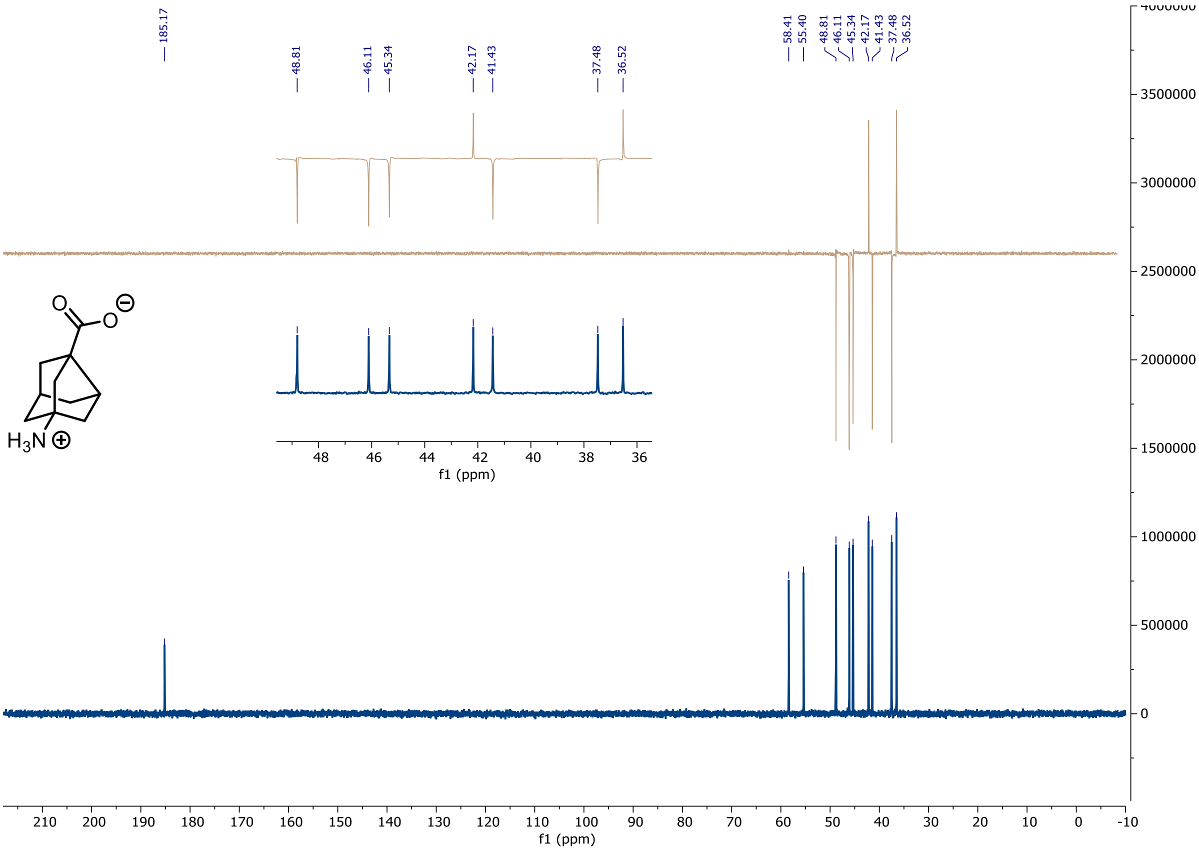
Compound 9d: ^{1}H NMR (400 MHz, D_2O)



Compound 9d: ^{13}C NMR (101 MHz, D_2O)

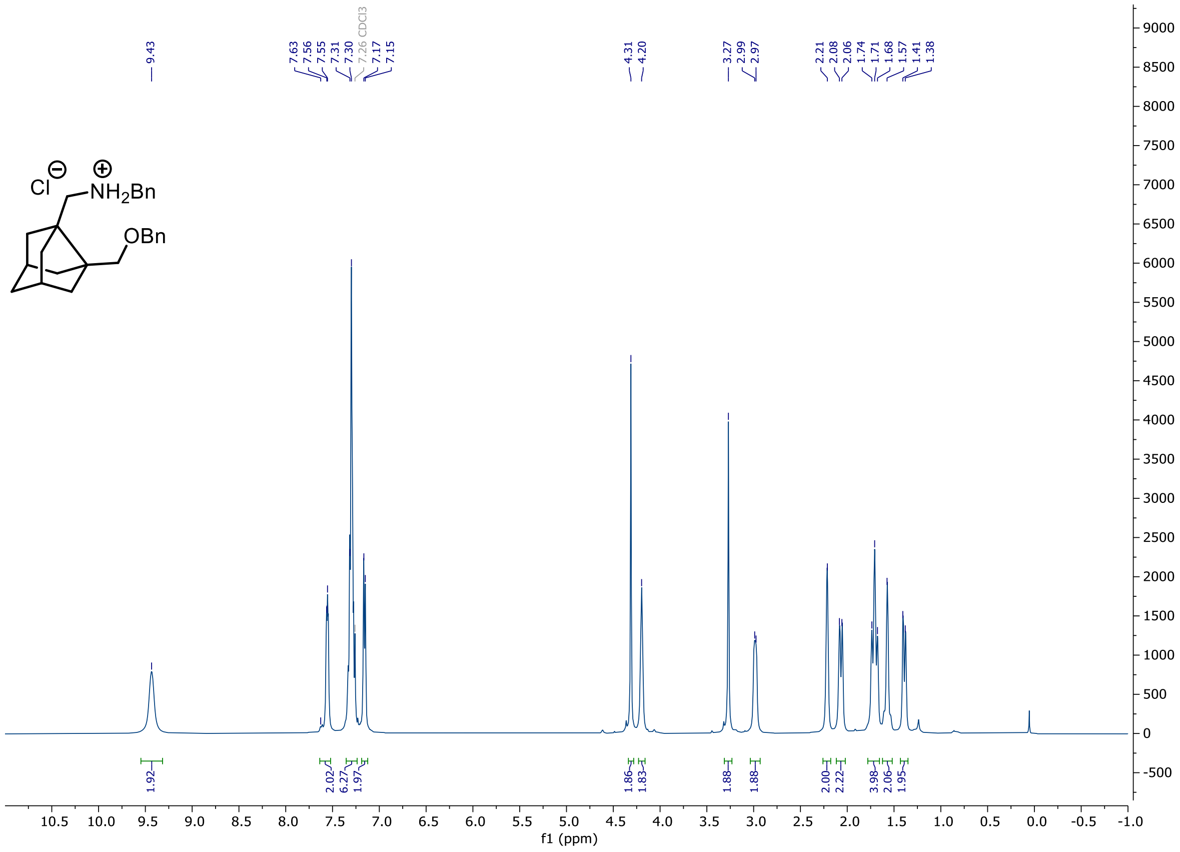


Compound 9d: ^{13}**C NMR-DEPT** (101 MHz, D_2O)

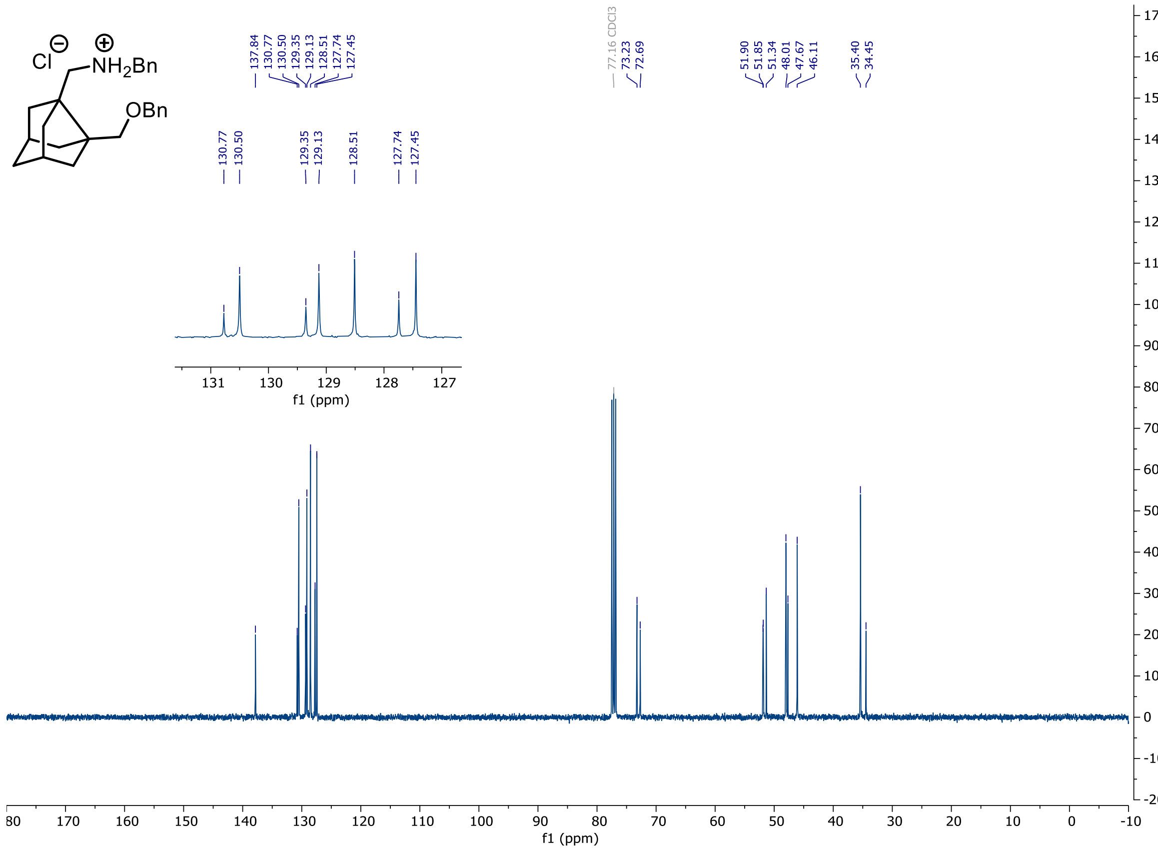


Reductive Amination of Noradamantyl Carbaldehydes

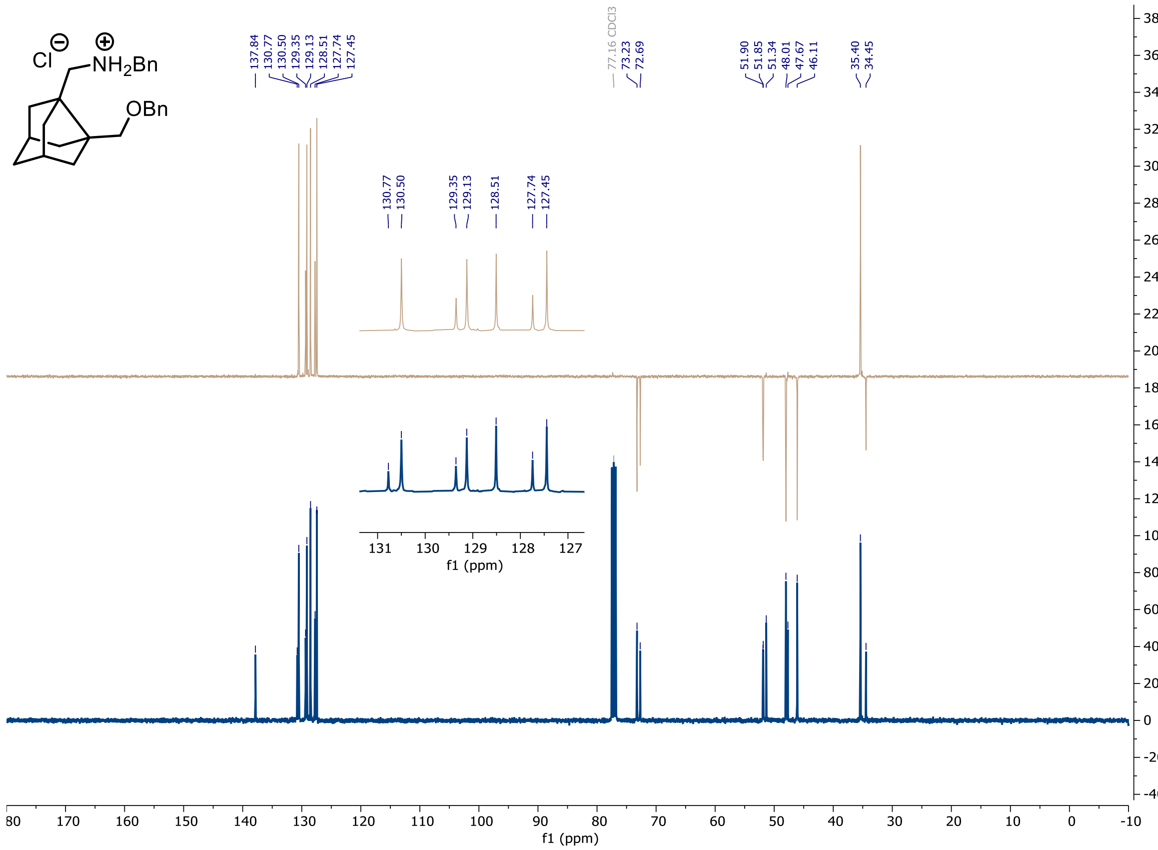
Compound 10a: ^{1}H NMR (400 MHz, $CDCl_3$)



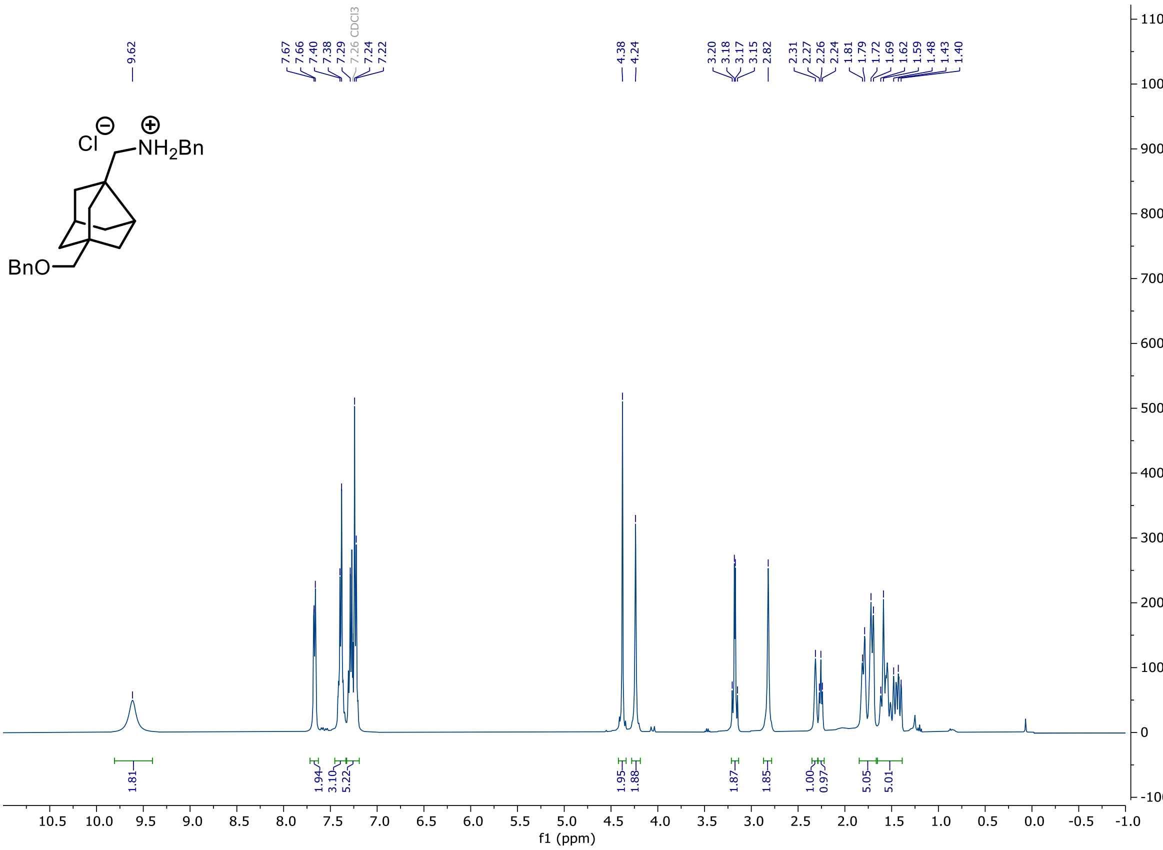
Compound 10a: ^{13}C NMR (101 MHz, CDCl$_3$)



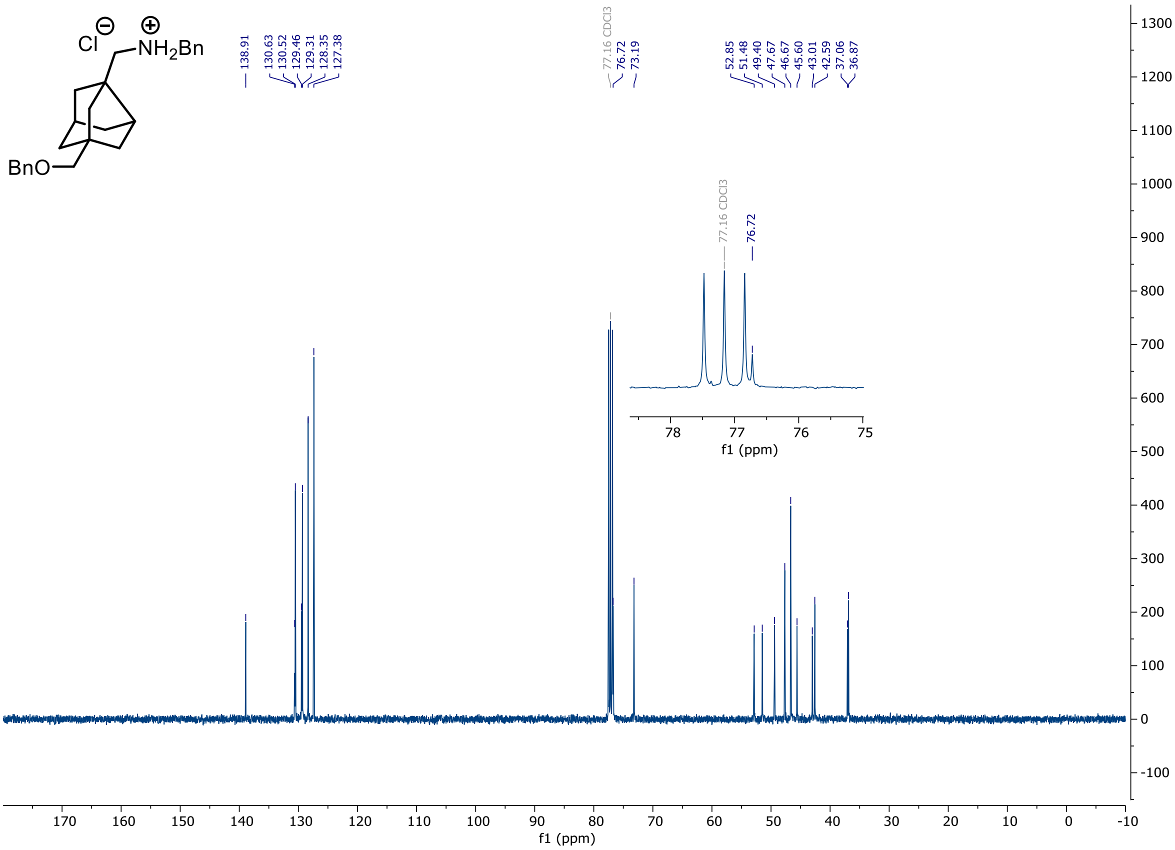
Compound 10a: ^{13}C NMR-DEPT (101 MHz, CDCl$_3$)



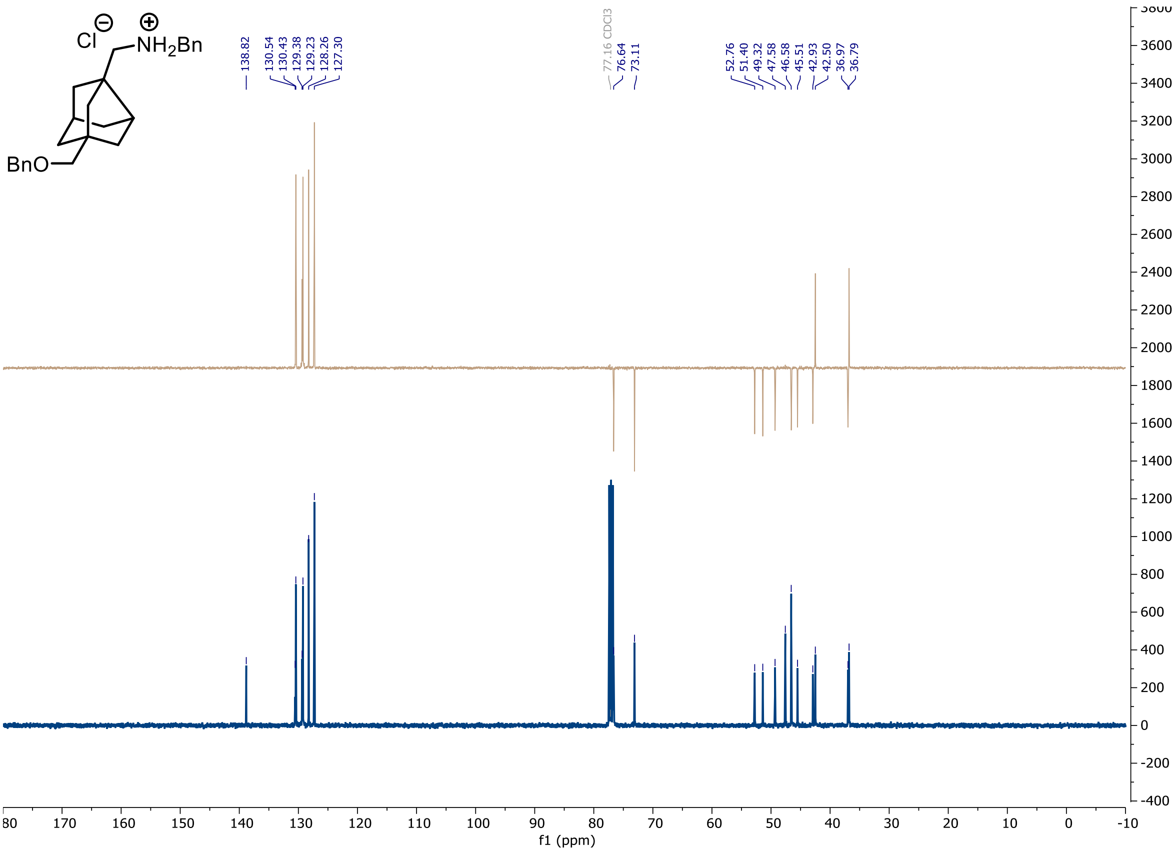
Compound 10b: ^{1}H NMR (400 MHz, $CDCl_3$)



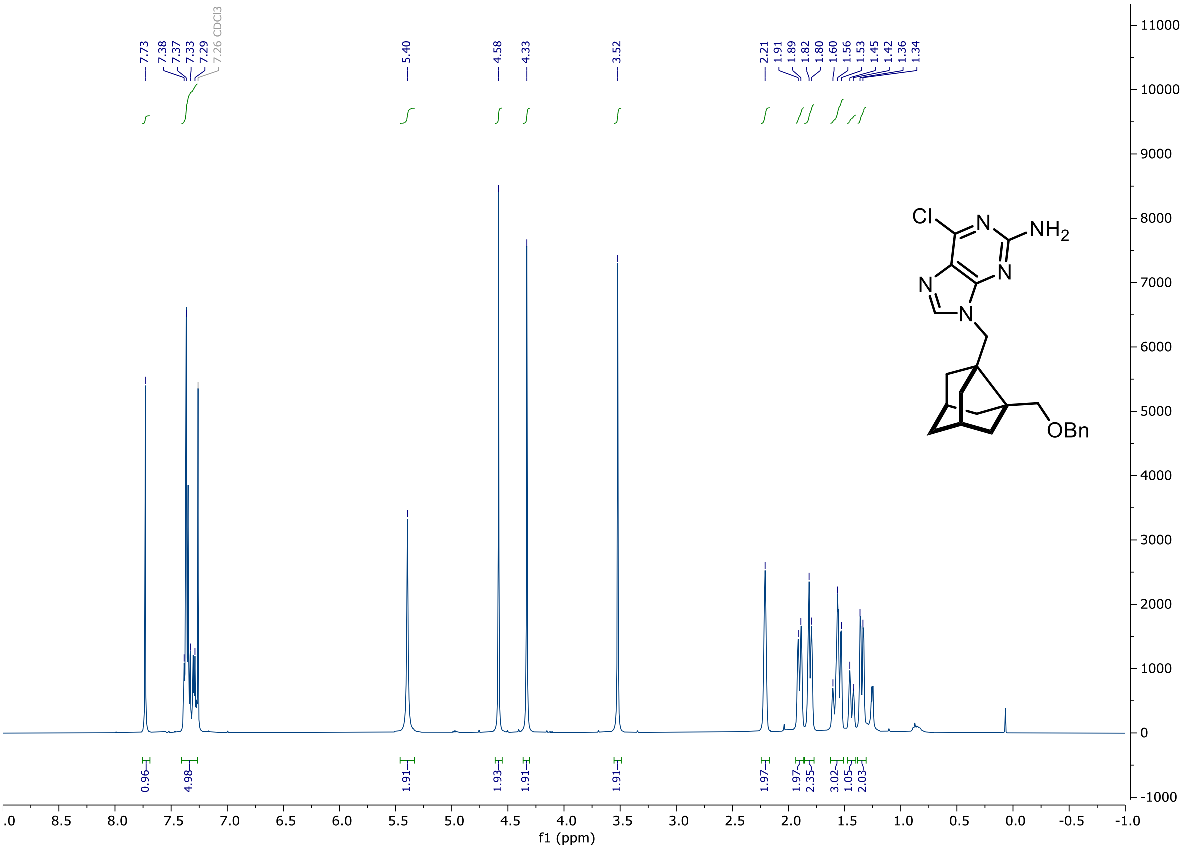
Compound 10b: ^{13}C NMR (101 MHz, $CDCl_3$)



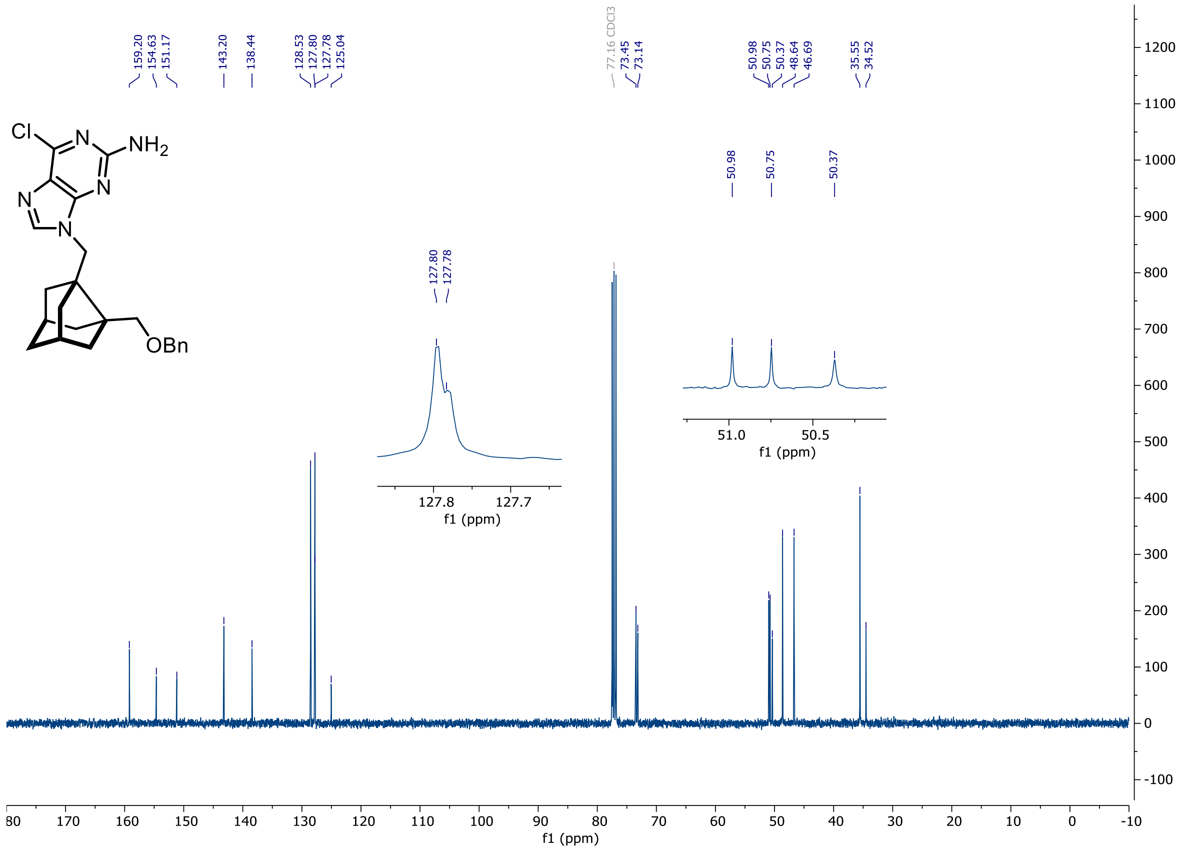
Compound 10b: ^{13}**C NMR-DEPT** (101 MHz, CDCl$_3$)



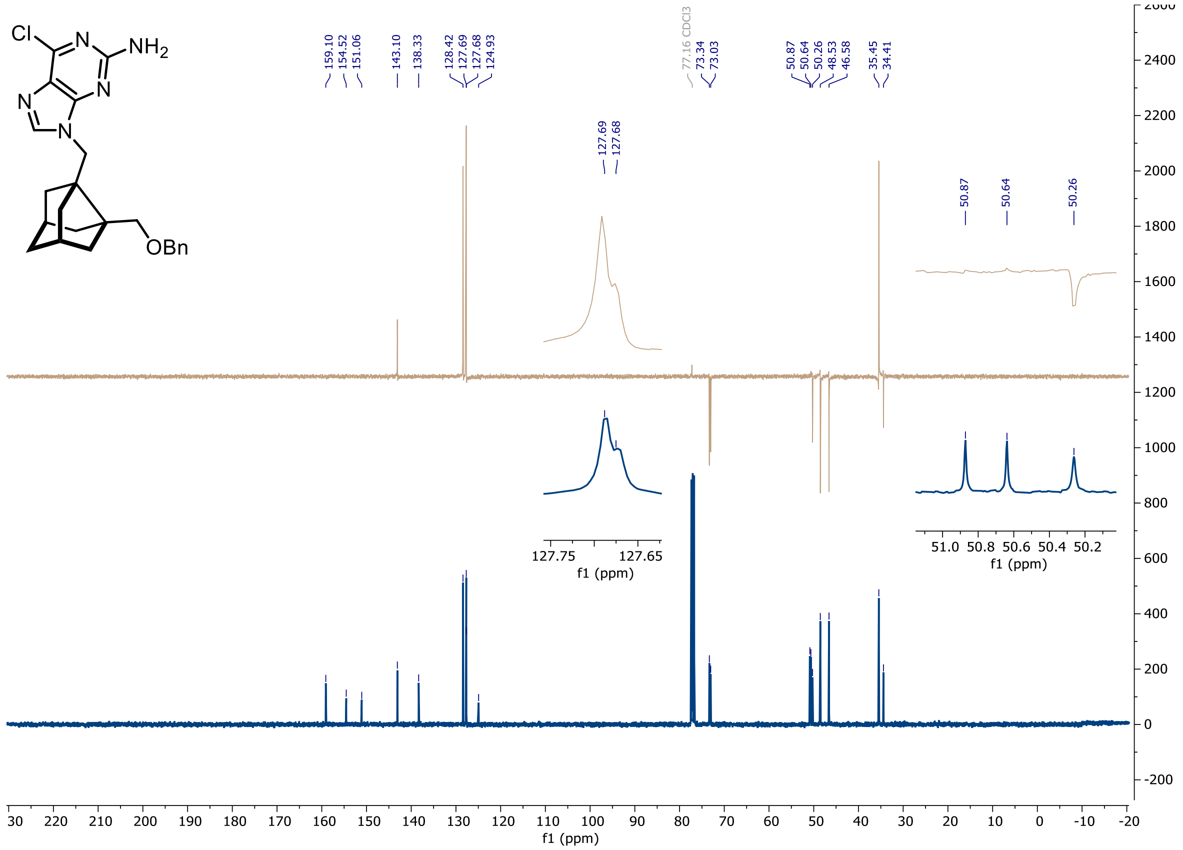
Compound 11a: ^{1}**H NMR** (400 MHz, $CDCl_3$)



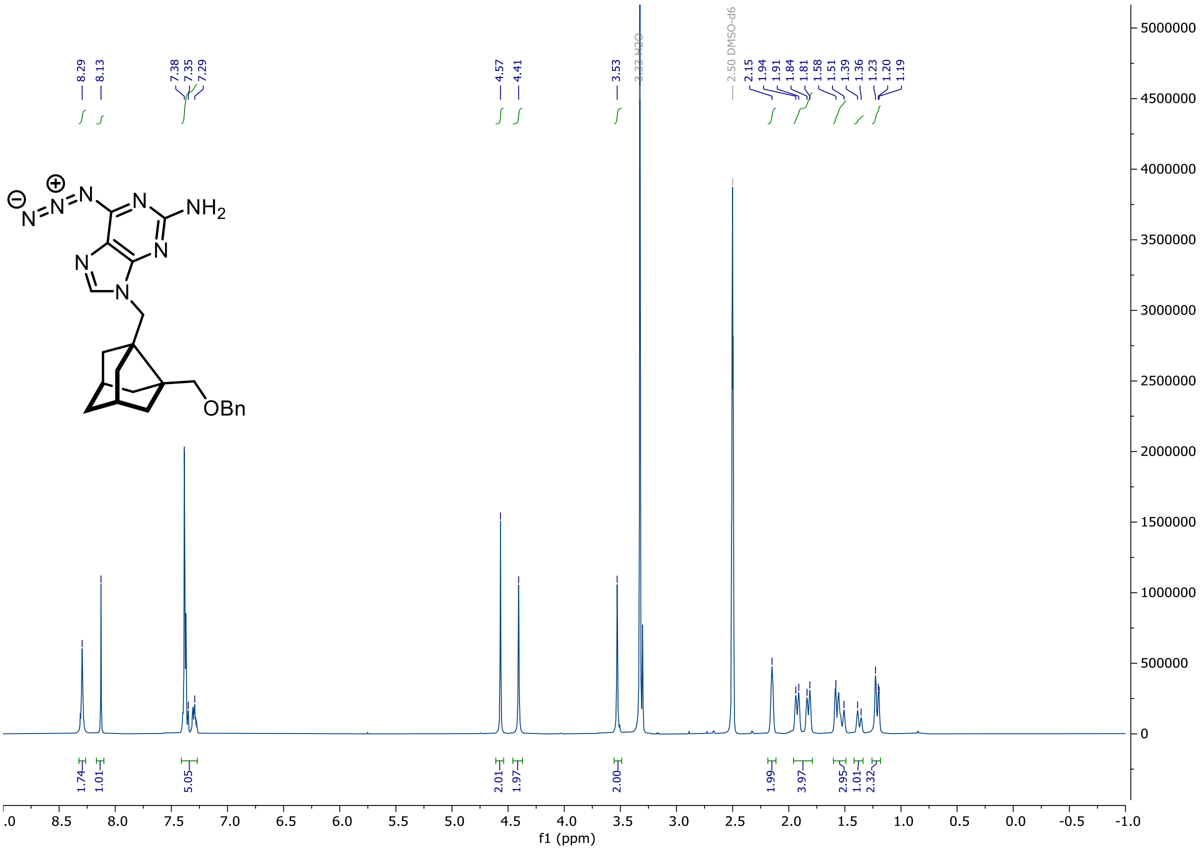
Compound 11a: ^{13}C NMR (101 MHz, $CDCl_3$)



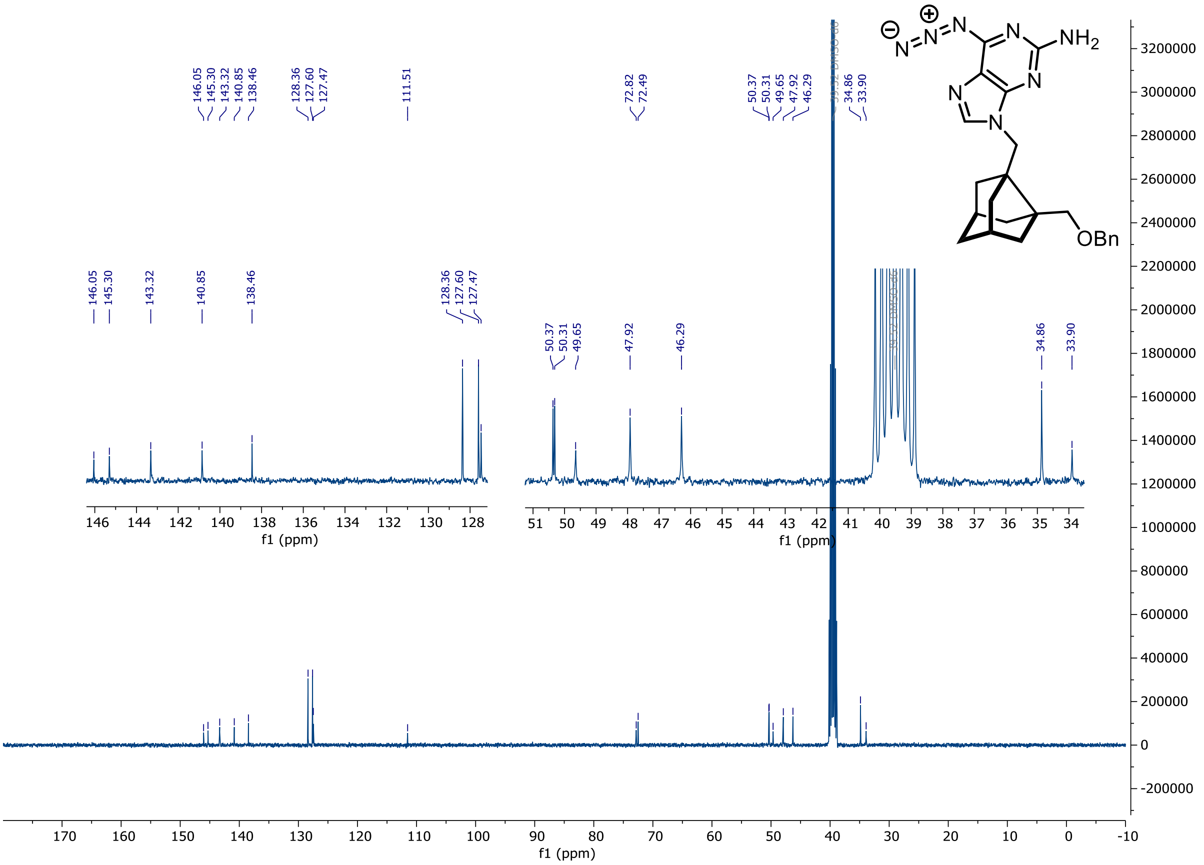
Compound 11a: ^{13}C NMR-DEPT (101 MHz, $CDCl_3$)



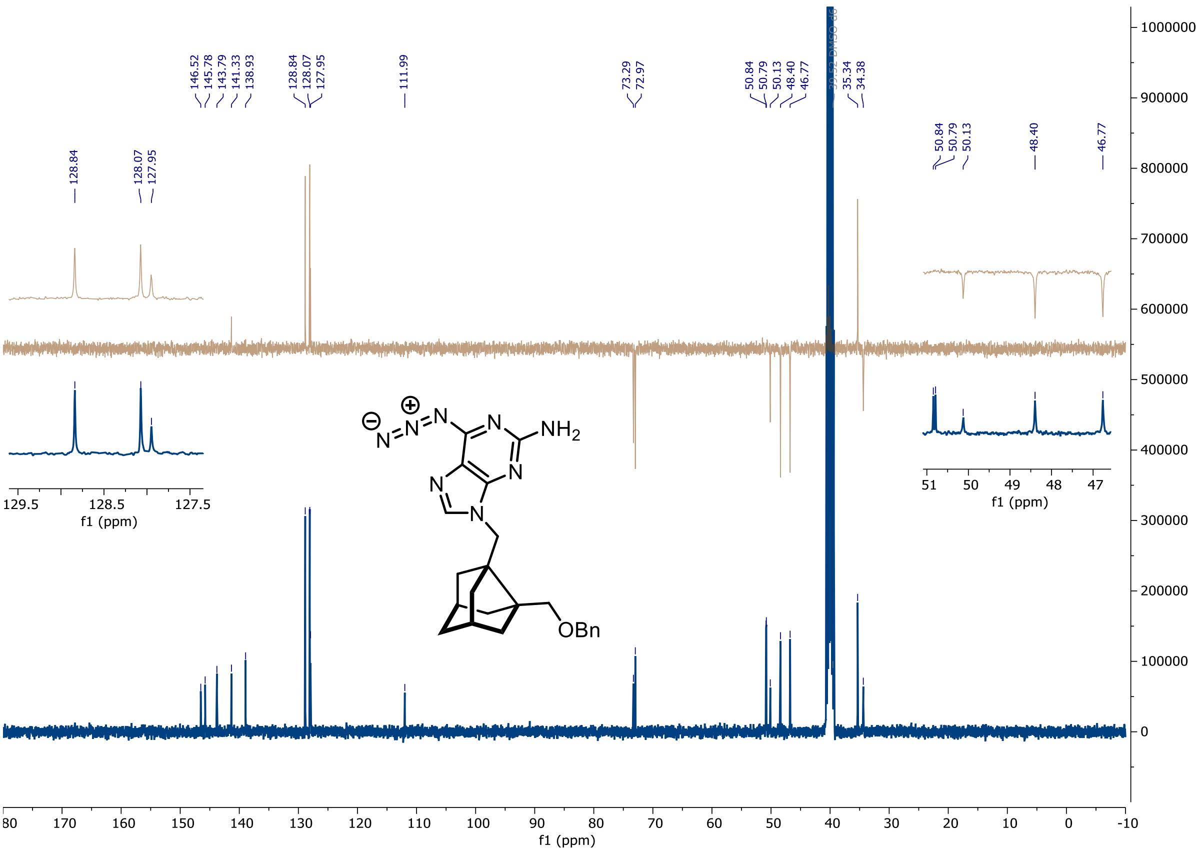
Compound 11b: ^{1}H NMR (400 MHz, DMSO-d_6)



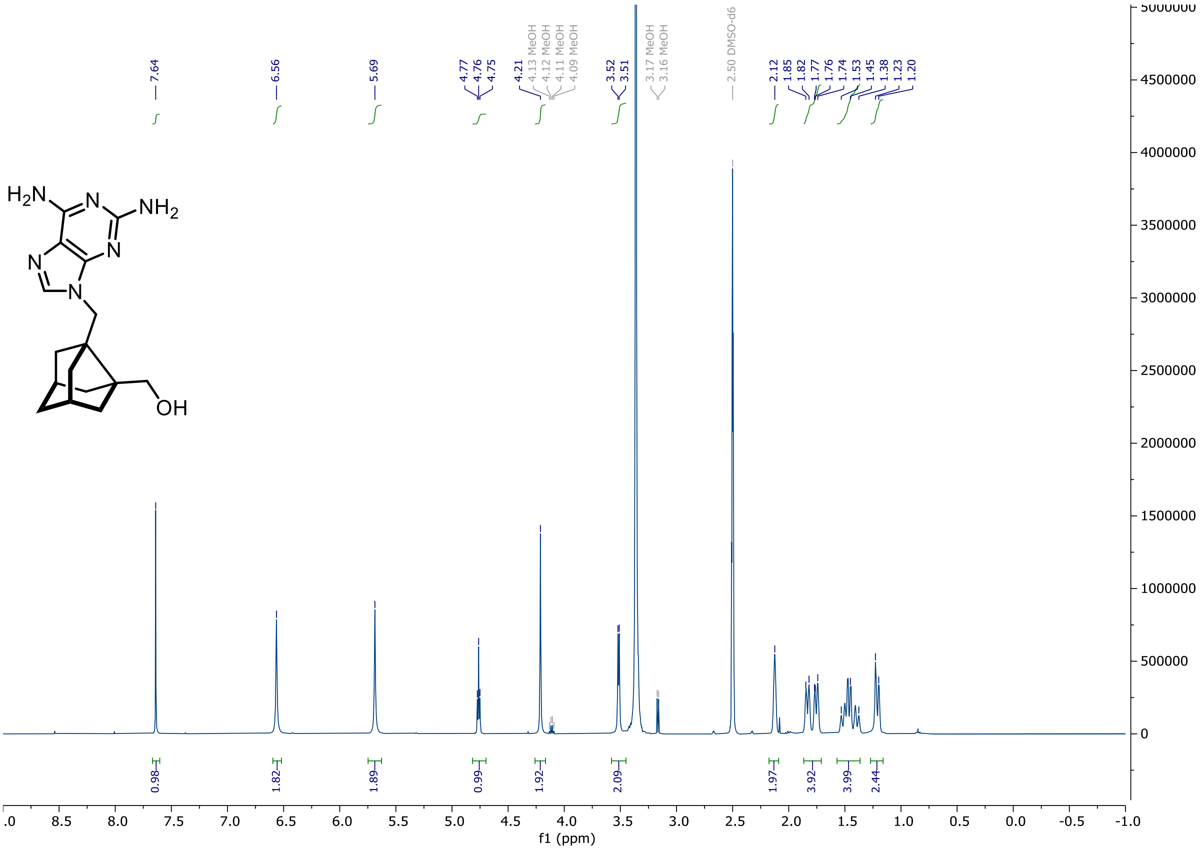
Compound 11b: ^{13}C NMR (101 MHz, DMSO-d_6)



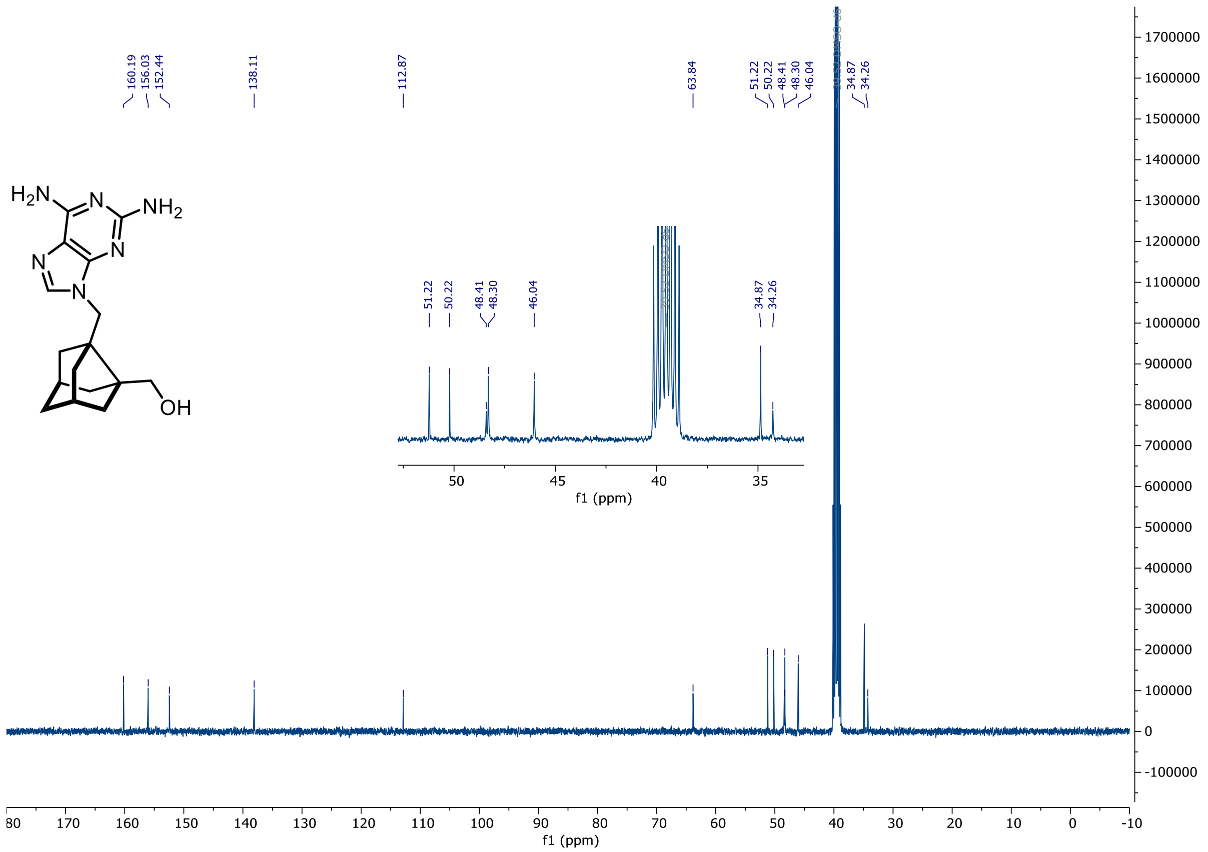
Compound 11c: ^{13}C NMR-DEPT (101 MHz, DMSO-d_6)



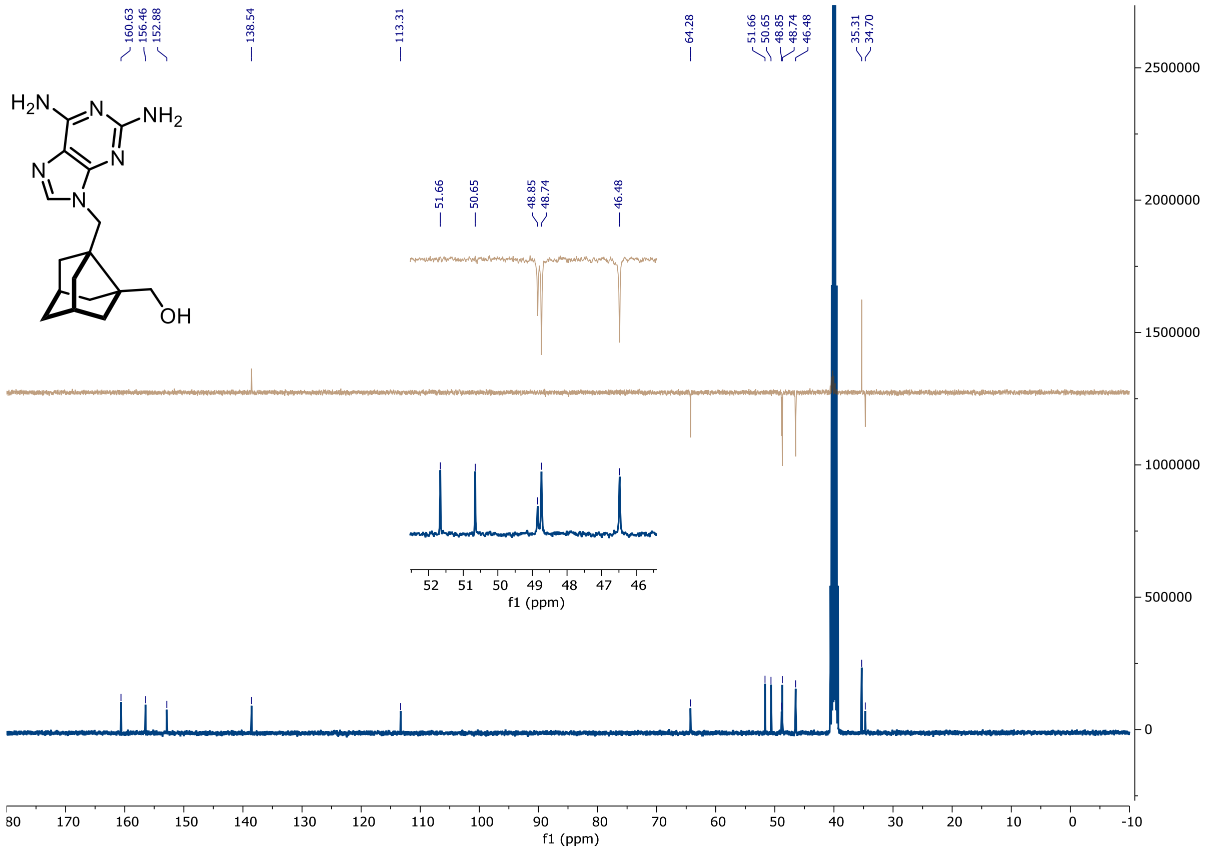
Compound 11d: ^{1}H NMR (400 MHz, DMSO-d_6)



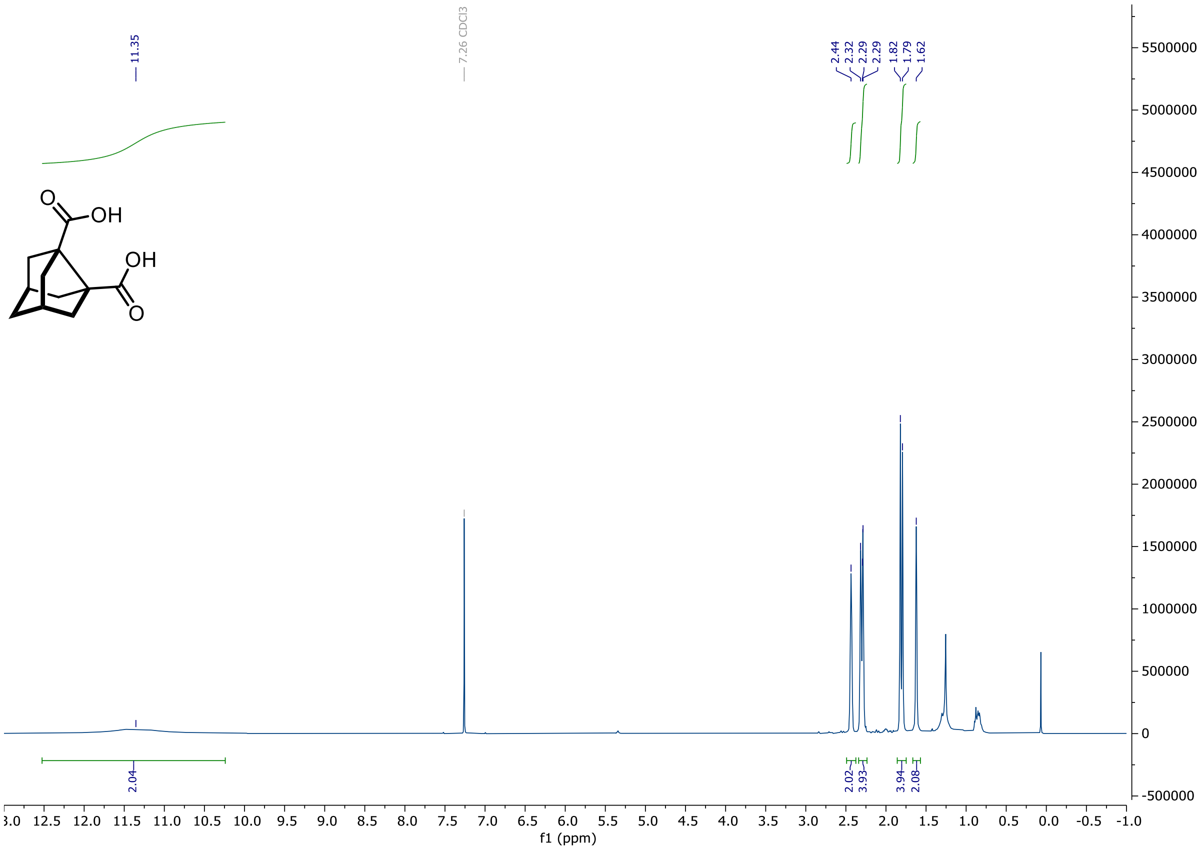
Compound 11d: ^{13}C NMR (101 MHz, DMSO-d_6)



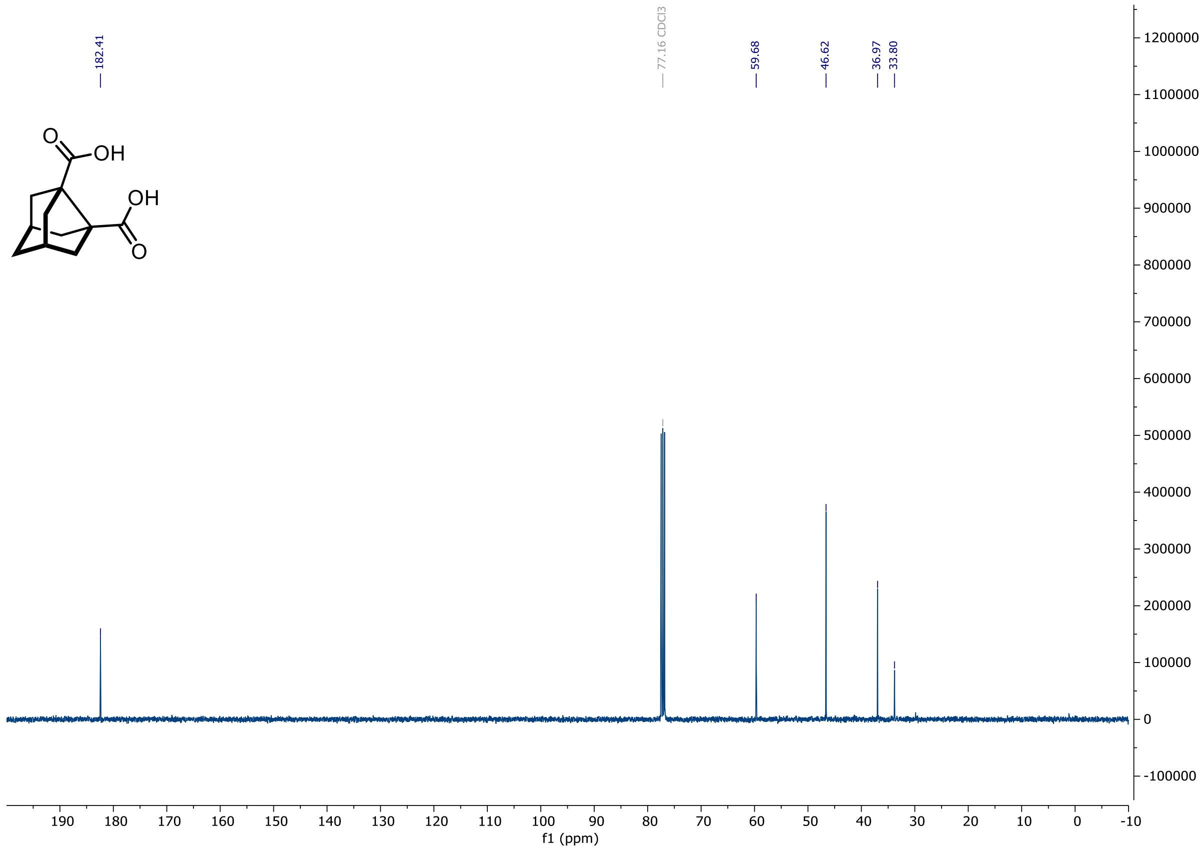
Compound 11d: ^{13}C NMR-DEPT (101 MHz, DMSO-d_6)



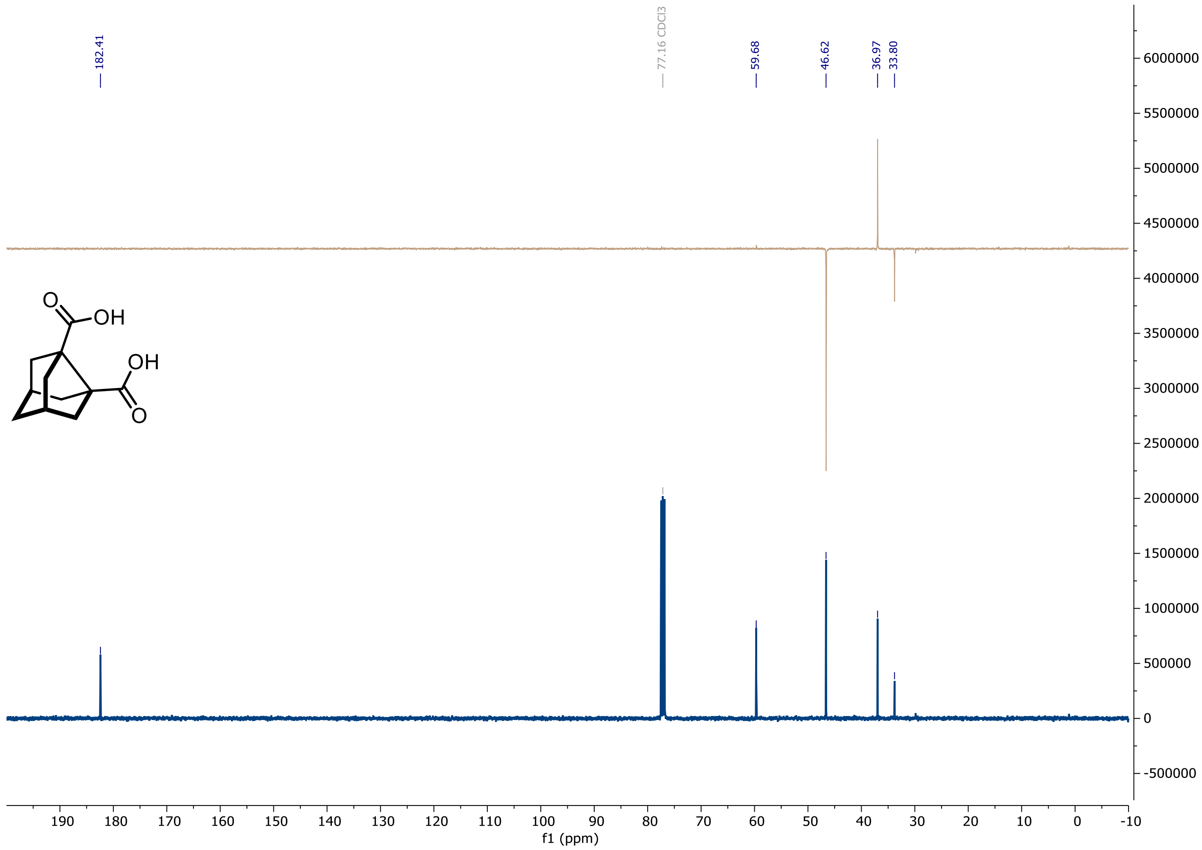
Compound 12a: **^{1}H NMR** (400 MHz, $CDCl_3$)



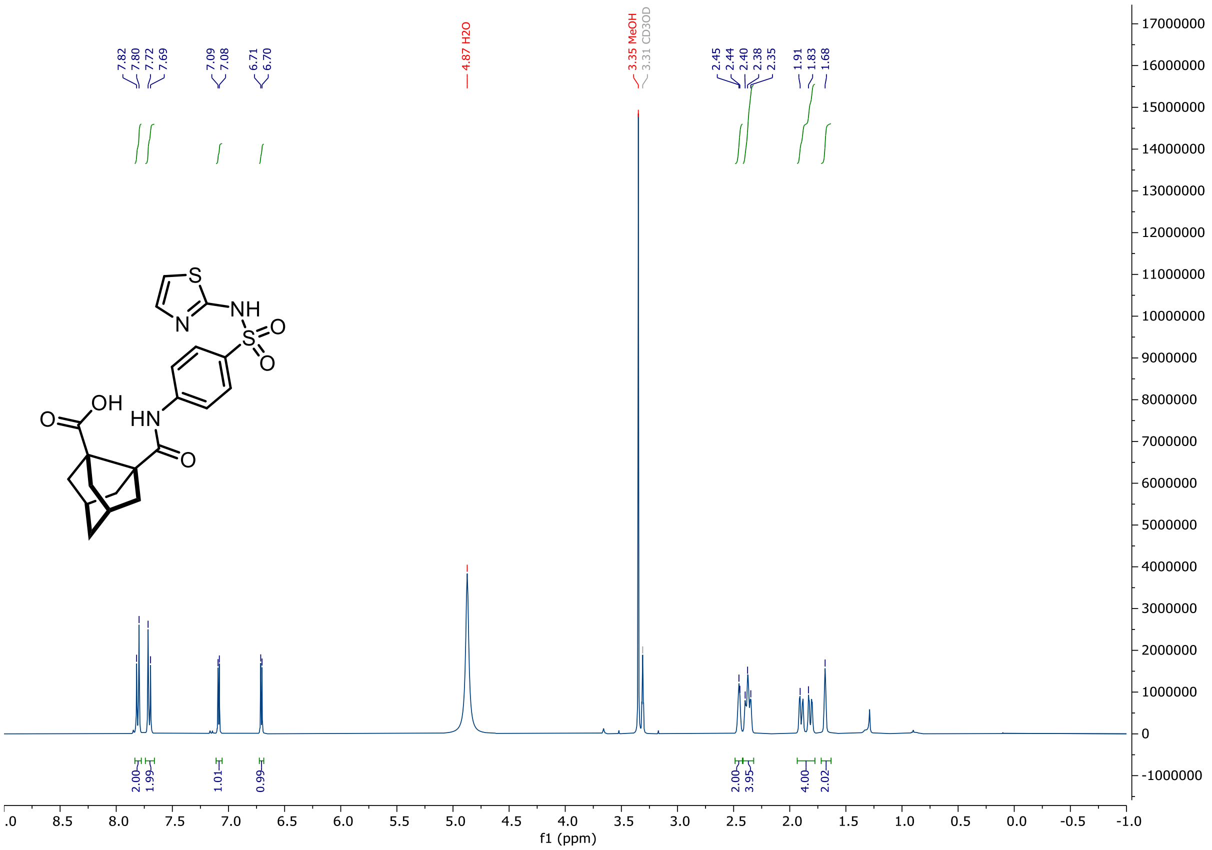
Compound 12a: ^{13}C NMR (101 MHz, CDCl$_3$)



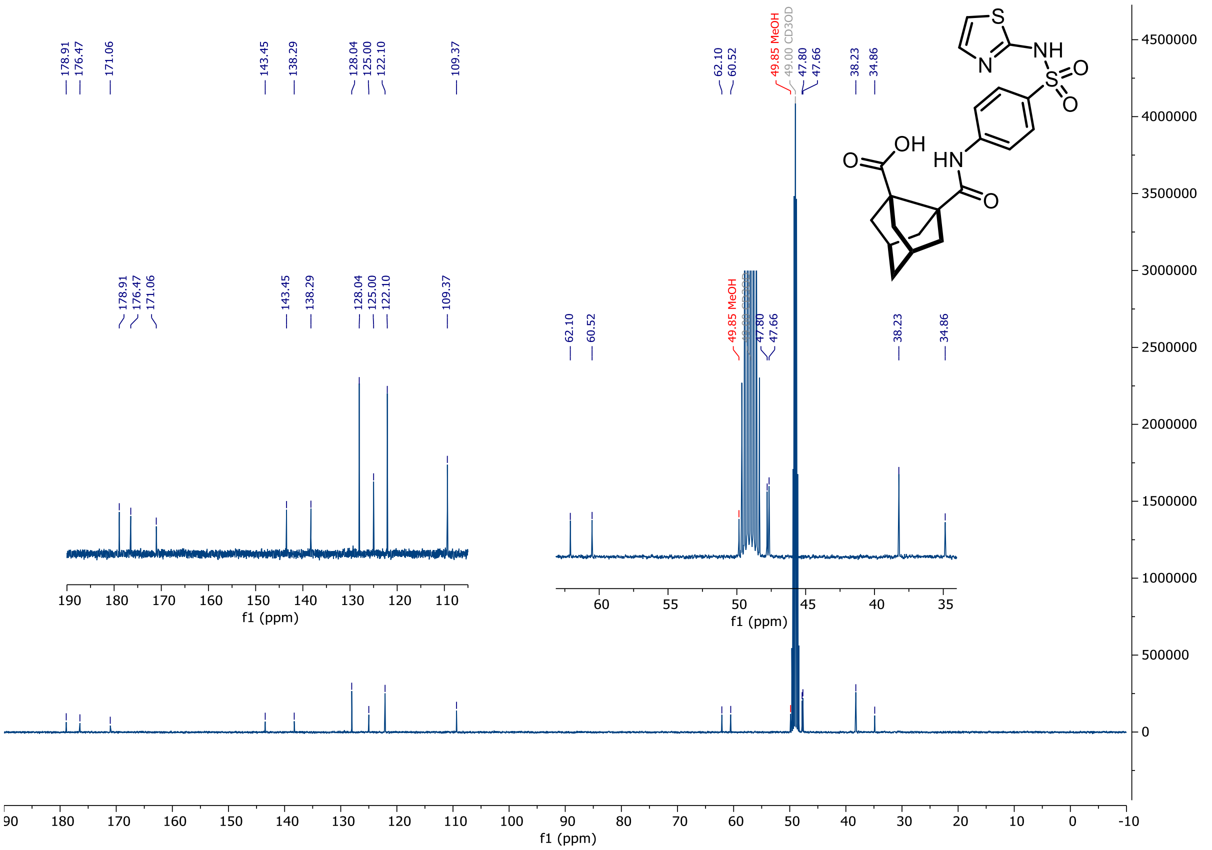
Compound 12a: ^{13}C NMR-DEPT (101 MHz, CDCl$_3$)



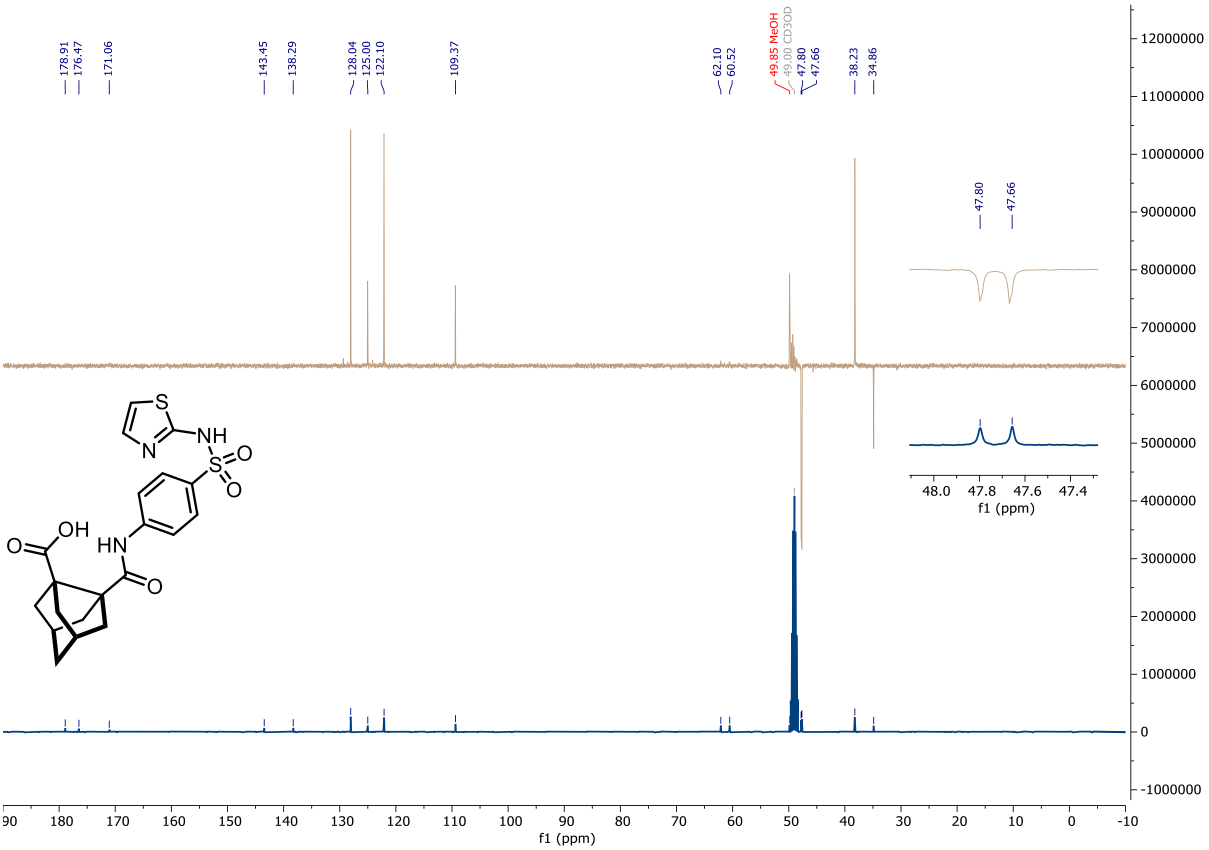
Compound 12b: ^{1}H NMR (400 MHz, MeOD)



Compound 12b: ^{13}C NMR (101 MHz, MeOD)

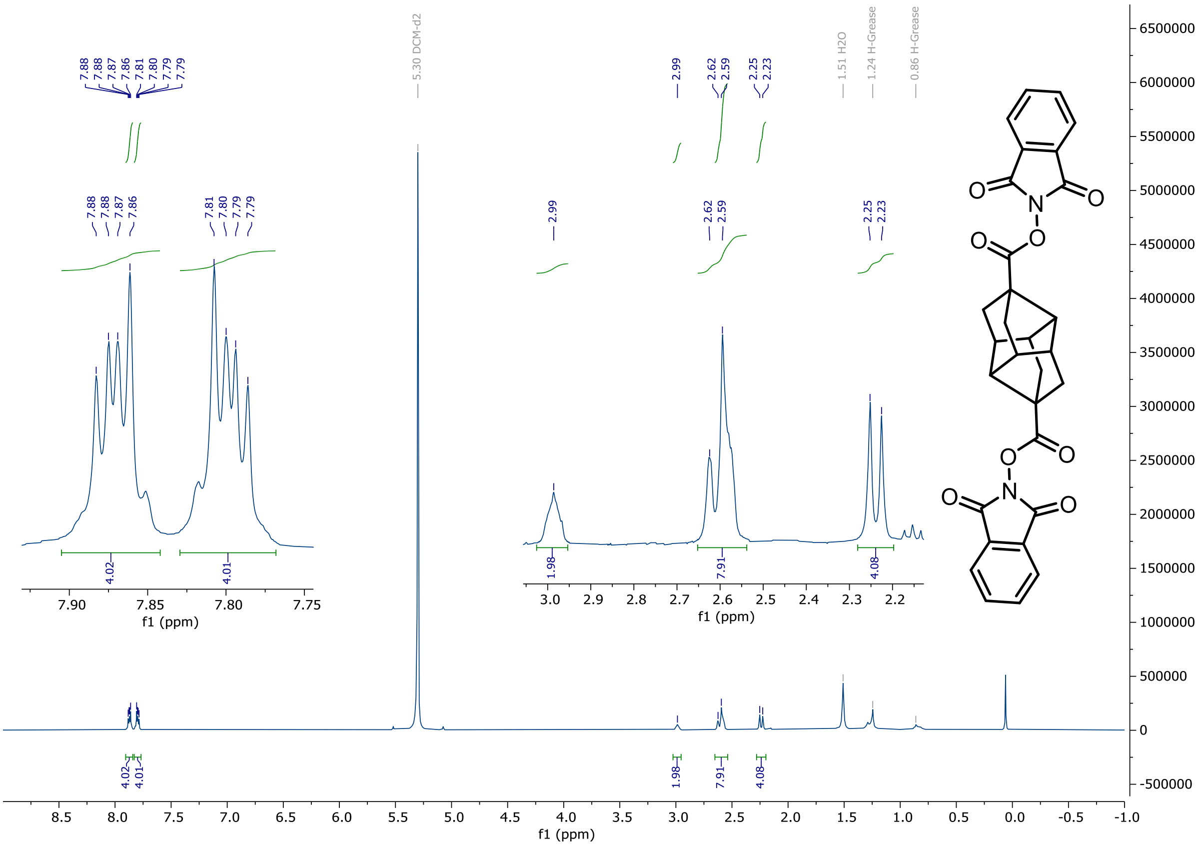


Compound 12b: ^{13}C NMR-DEPT (101 MHz, MeOD)

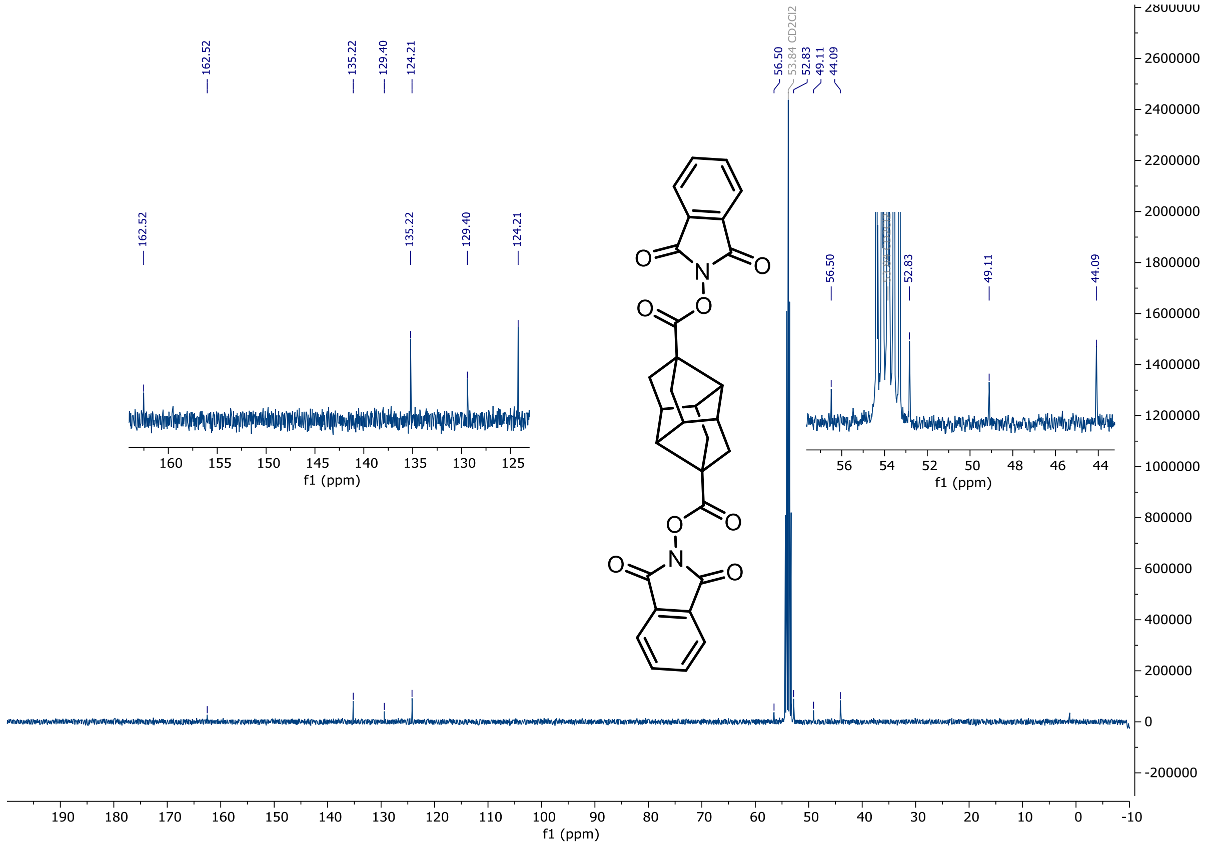


Redox-active Esters

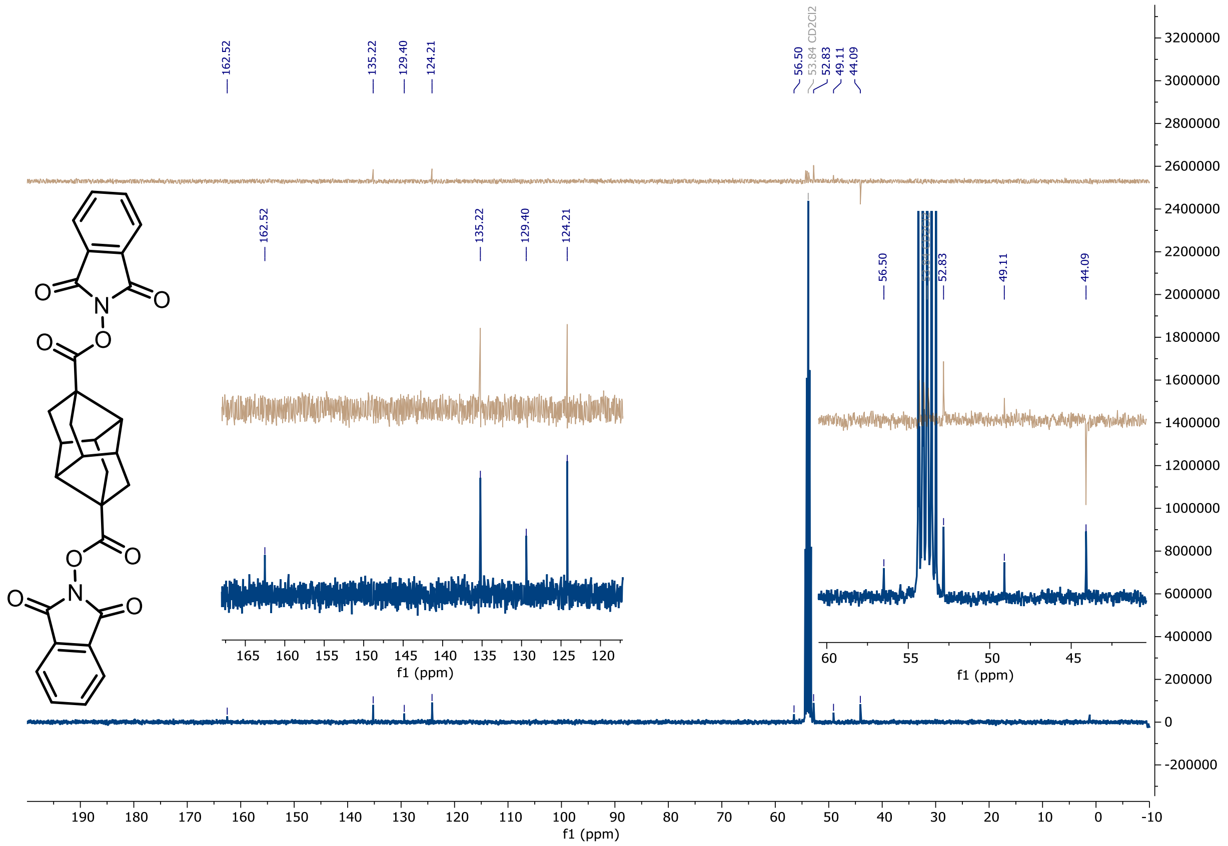
Compound 13a: ^{1}H NMR (400 MHz, CD_2Cl_2)



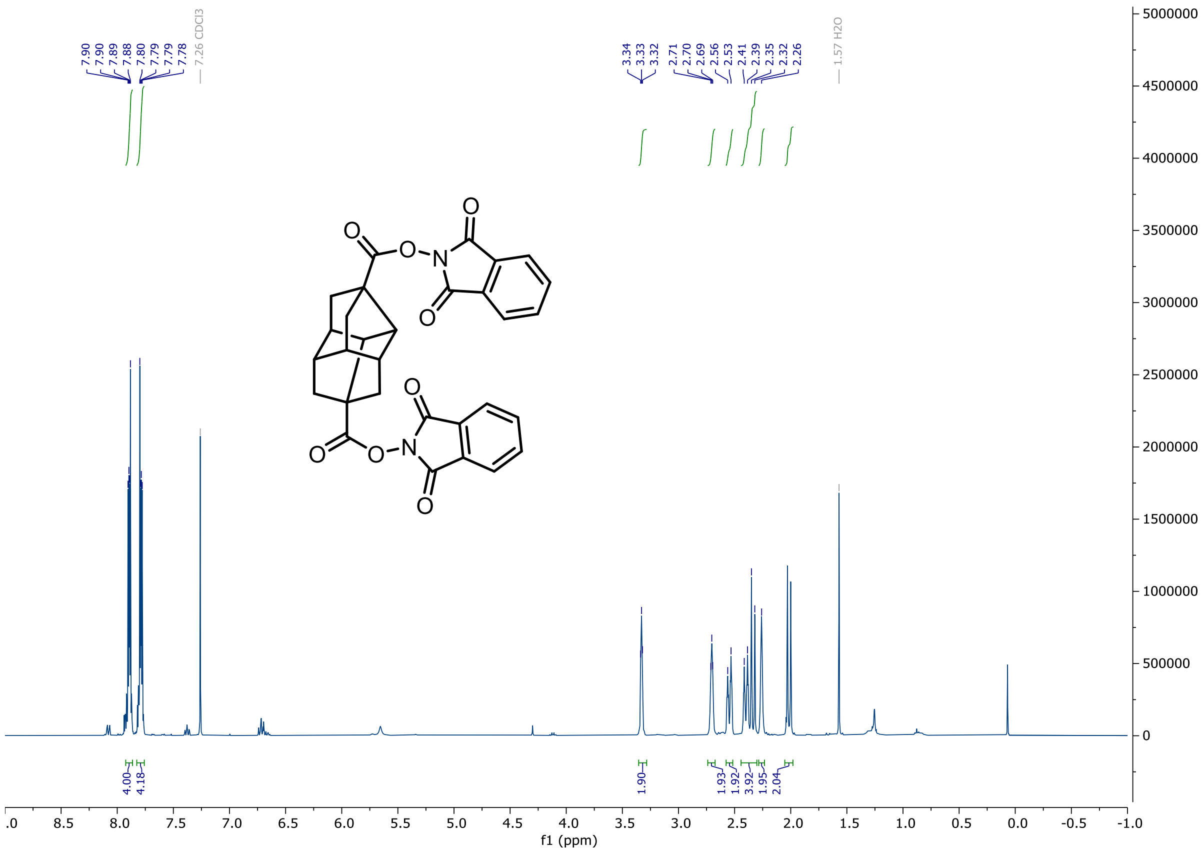
Compound 13a: ^{13}C NMR (101 MHz, CD$_2$Cl$_2$)



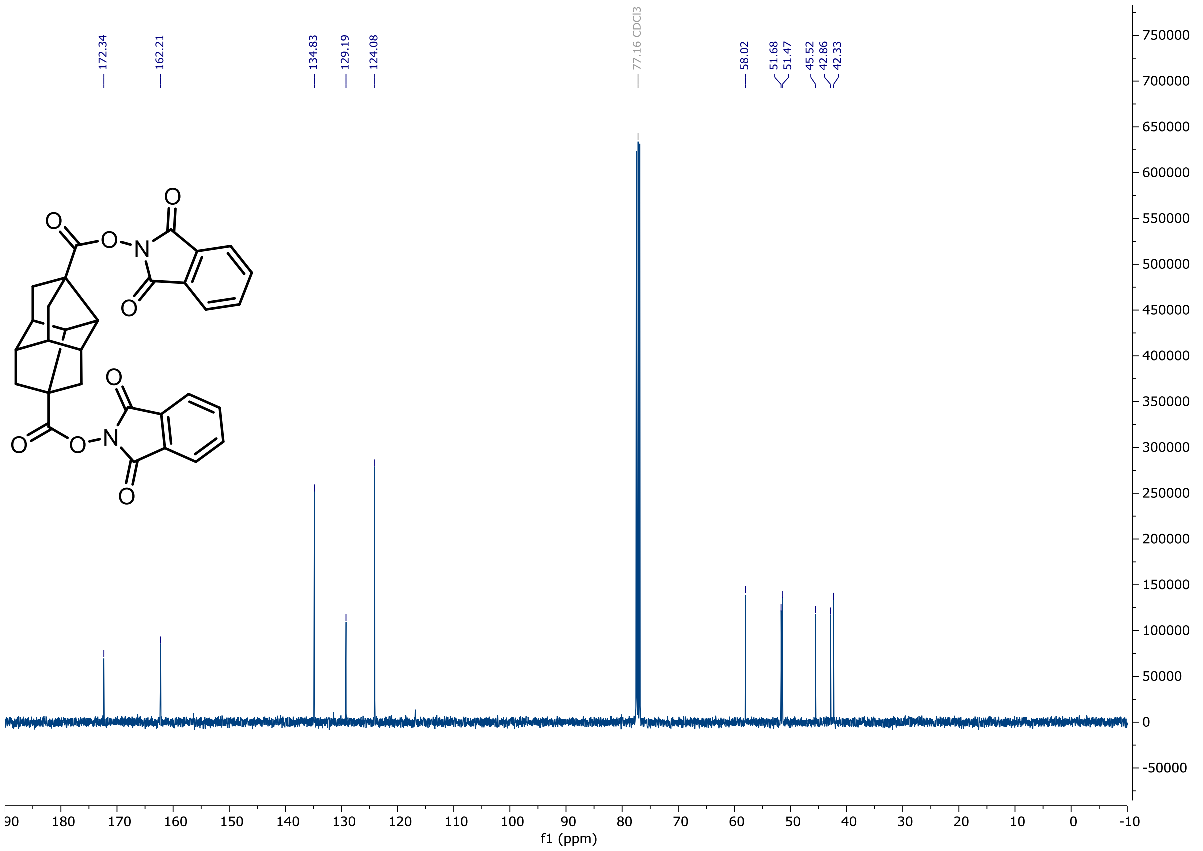
Compound 13a: ^{13}C NMR-DEPT (101 MHz, CD$_2$Cl$_2$)



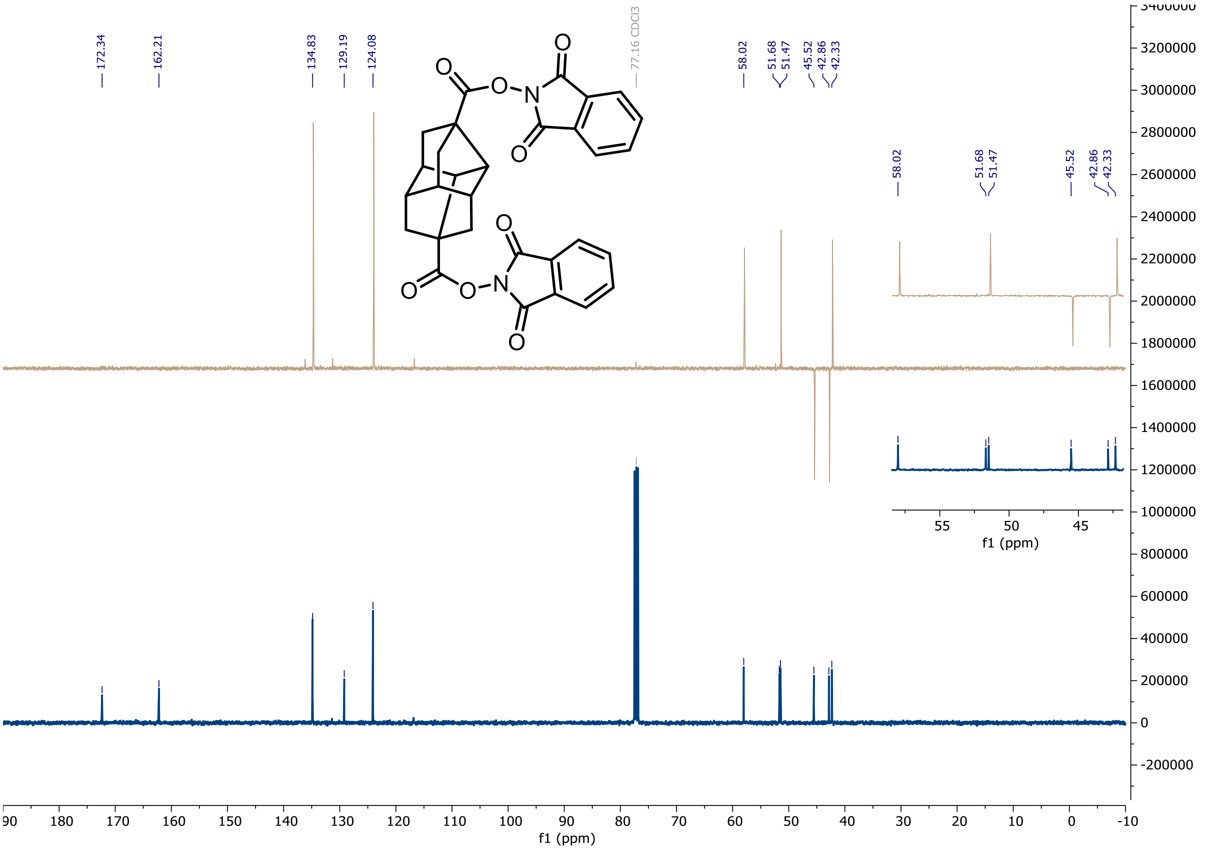
Compound 13b: ^{1}H NMR (400 MHz, CDCl$_3$)



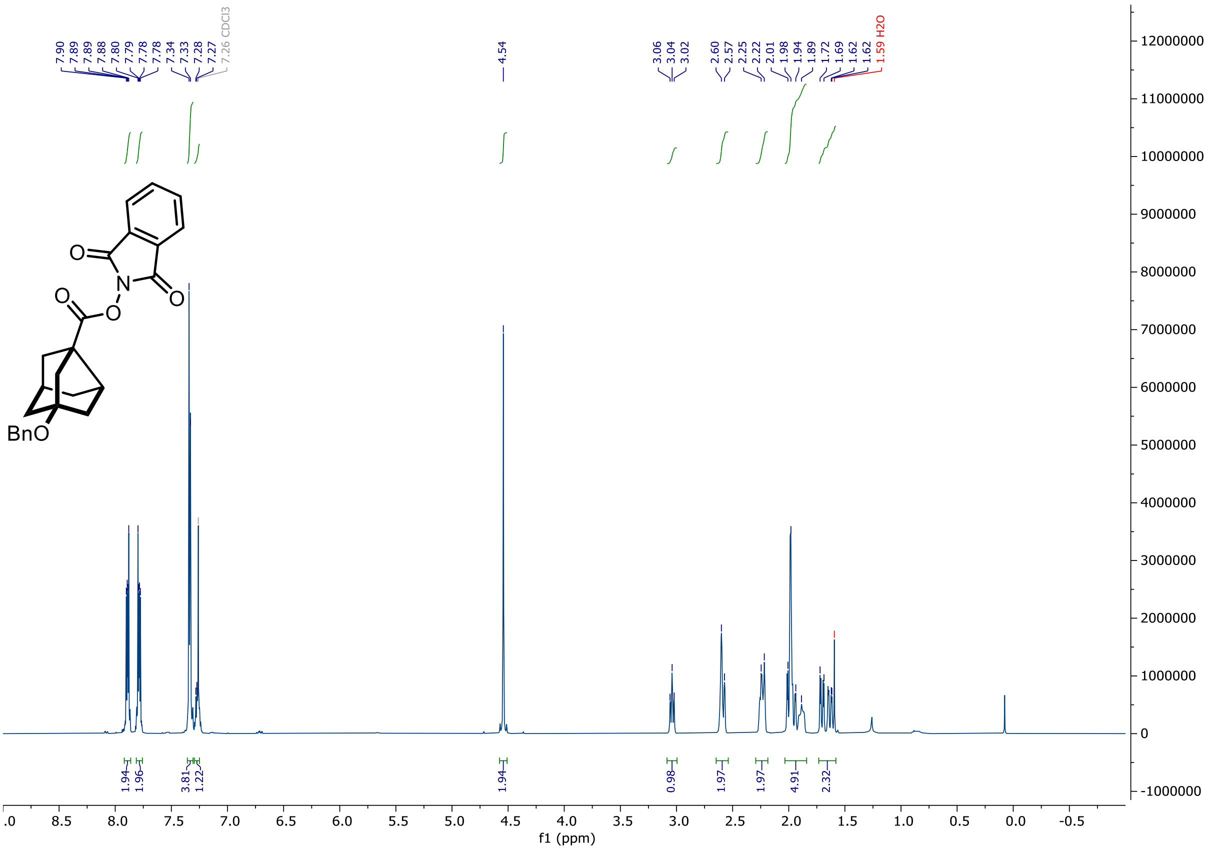
Compound 13b: ^{13}C NMR (101 MHz, CDCl$_3$)



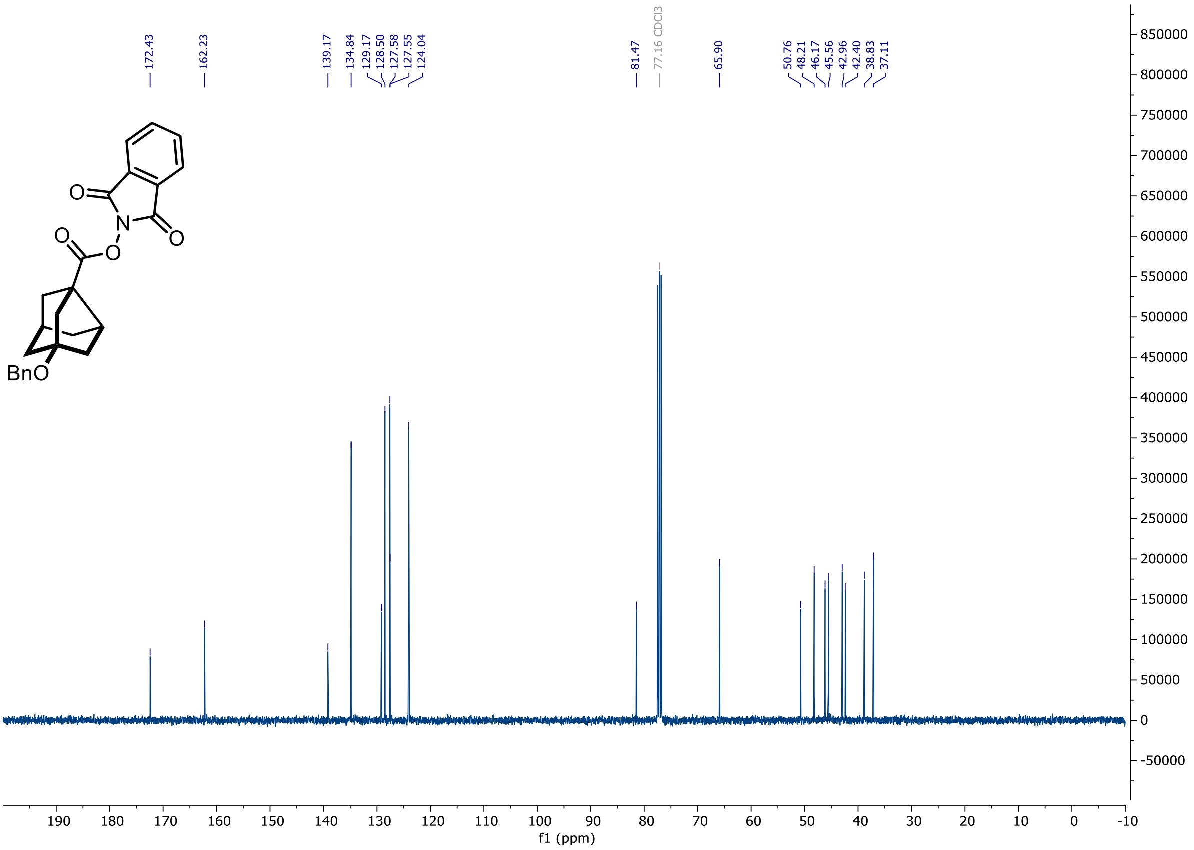
Compound 13b: ^{13}C NMR-DEPT (101 MHz, CDCl$_3$)



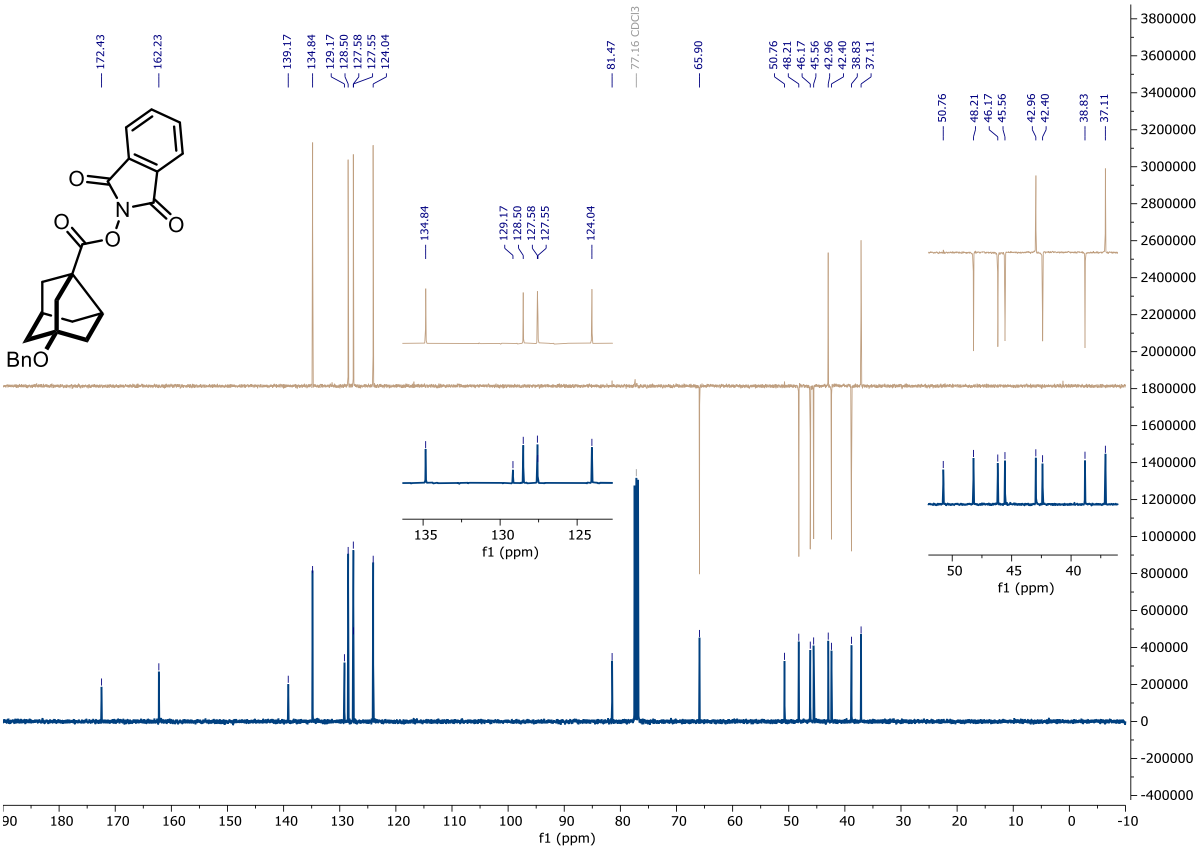
Compound 13c: ^{1}H NMR (400 MHz, CDCl$_3$)



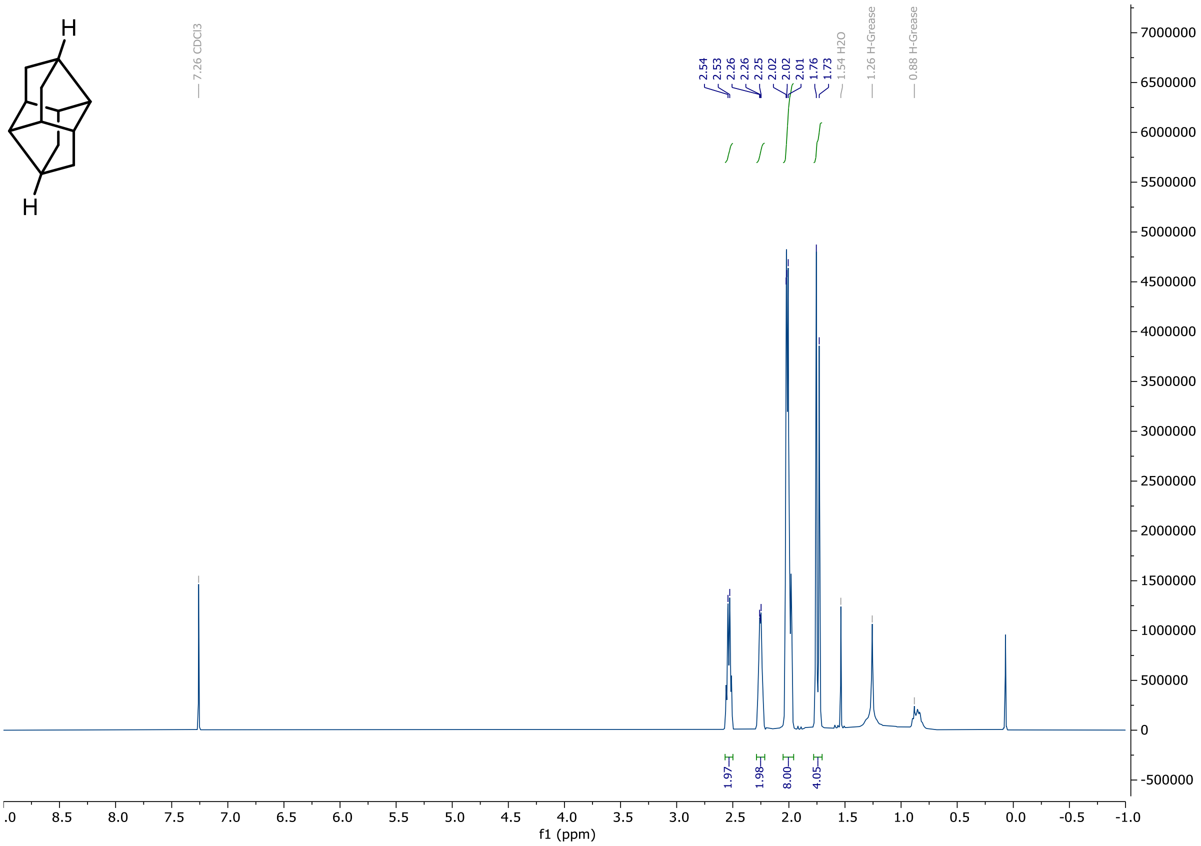
Compound 13c: ^{13}C NMR (101 MHz, CDCl$_3$)



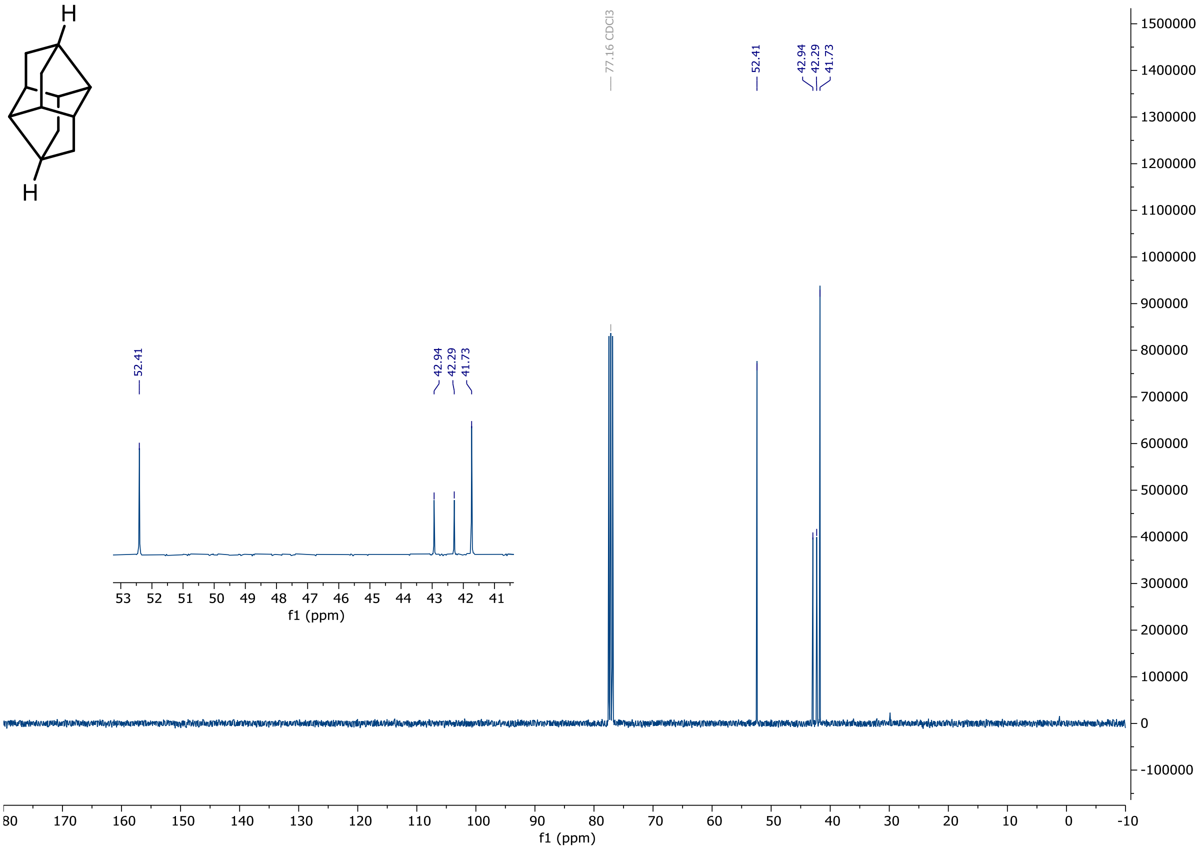
Compound 13c: ^{13}C NMR-DEPT (101 MHz, CDCl$_3$)



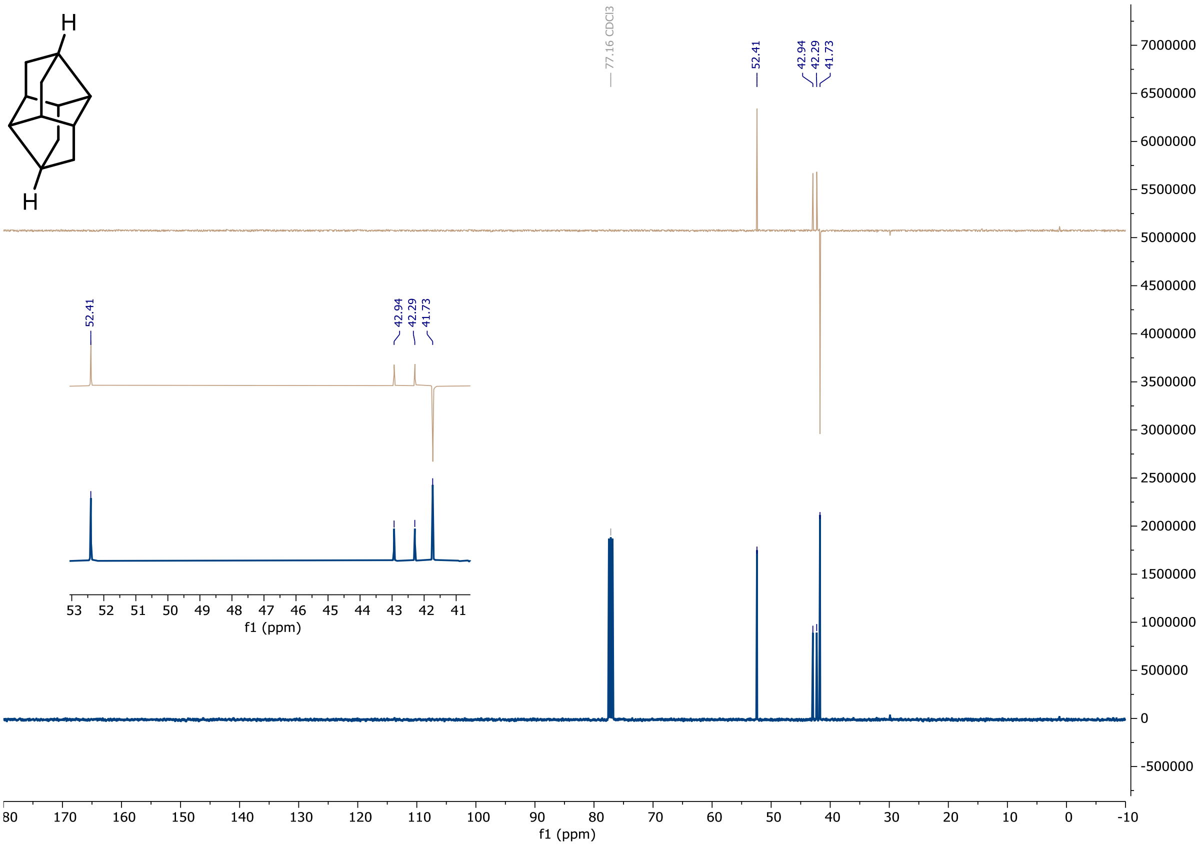
Compound 14a: ^{1}H NMR (400 MHz, $CDCl_3$)



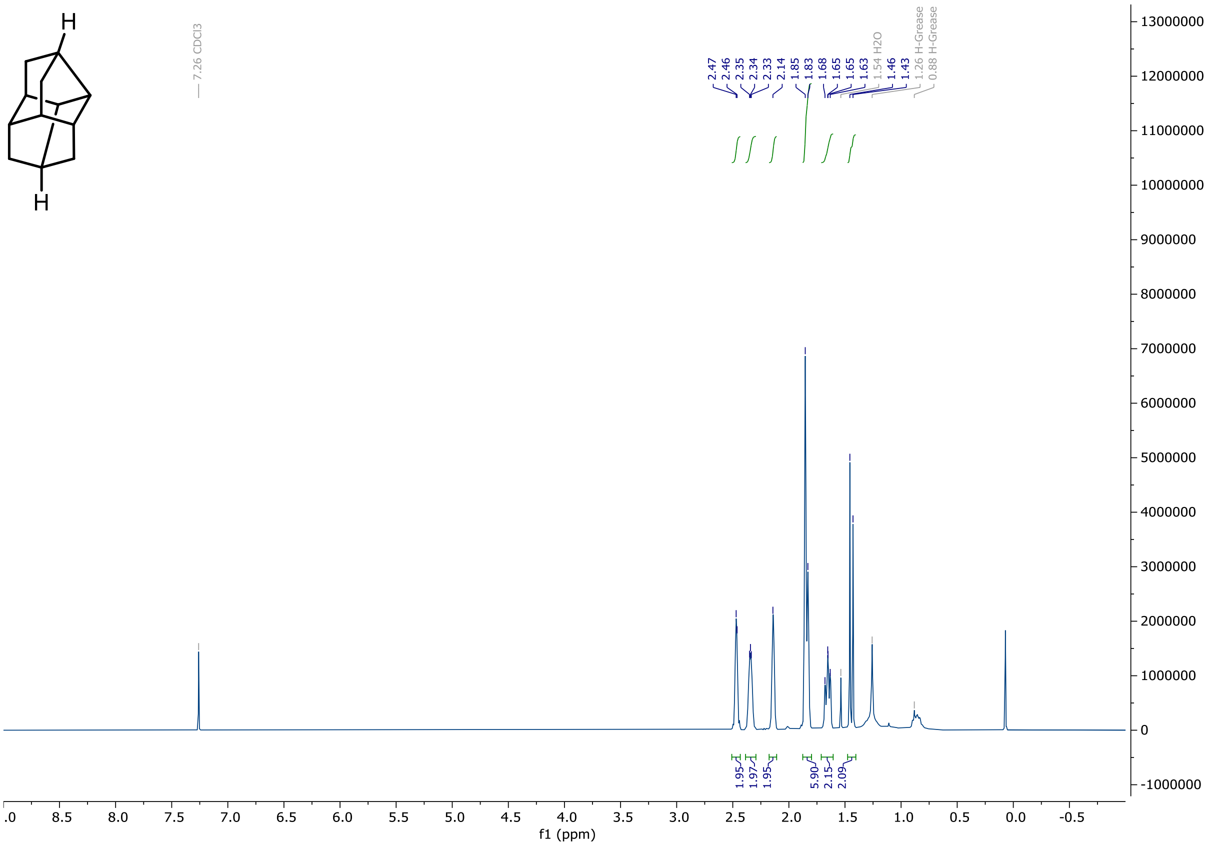
Compound 14a: ^{13}C NMR (101 MHz, $CDCl_3$)



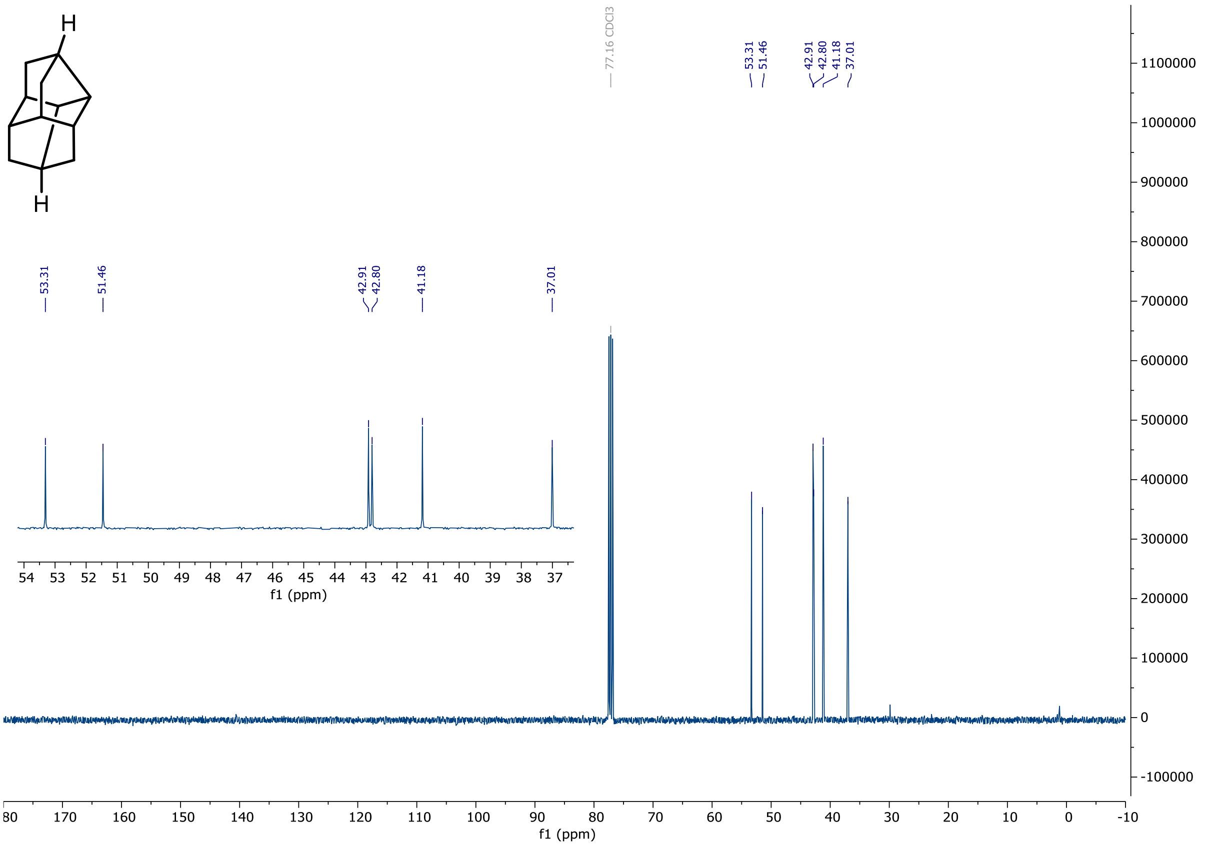
Compound 14a: ^{13}C NMR-DEPT (101 MHz, $CDCl_3$)



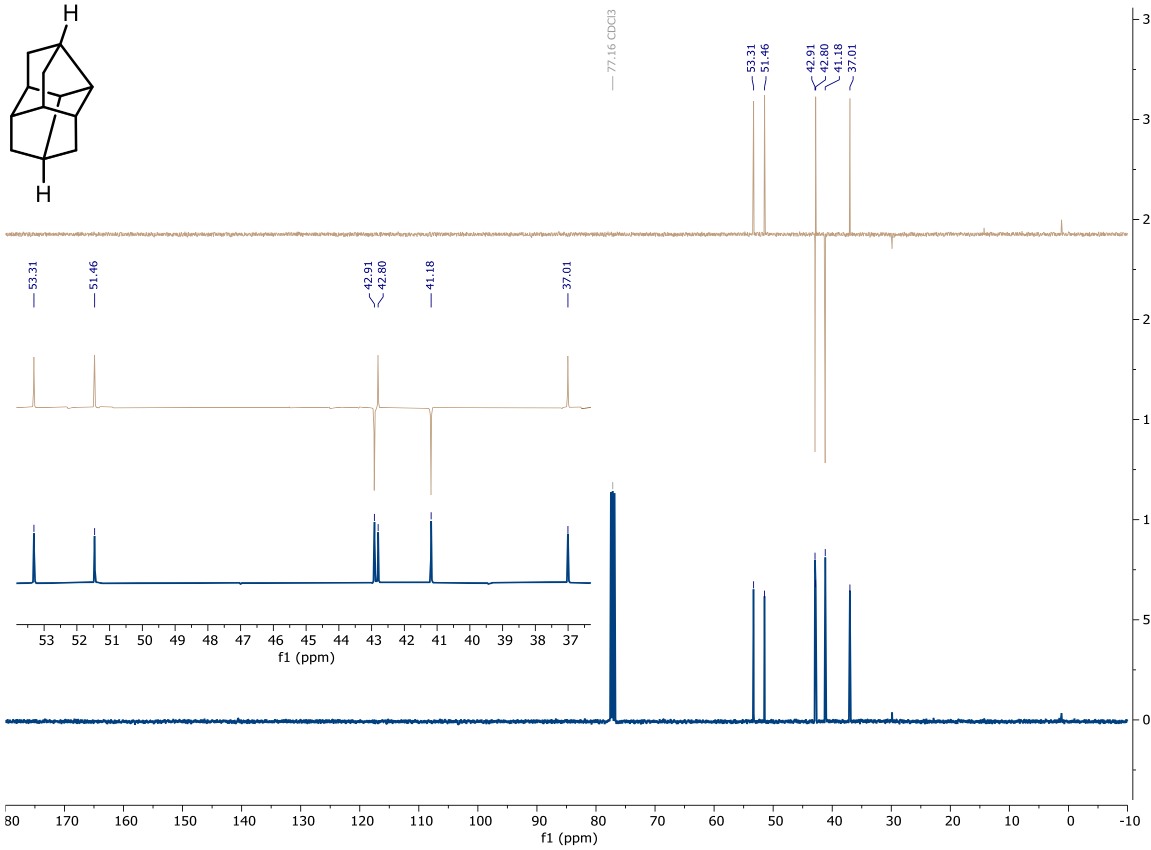
Compound 14b: ^{1}H NMR (400 MHz, CDCl$_3$)



Compound 14b: ^{13}C NMR (101 MHz, CDCl$_3$)

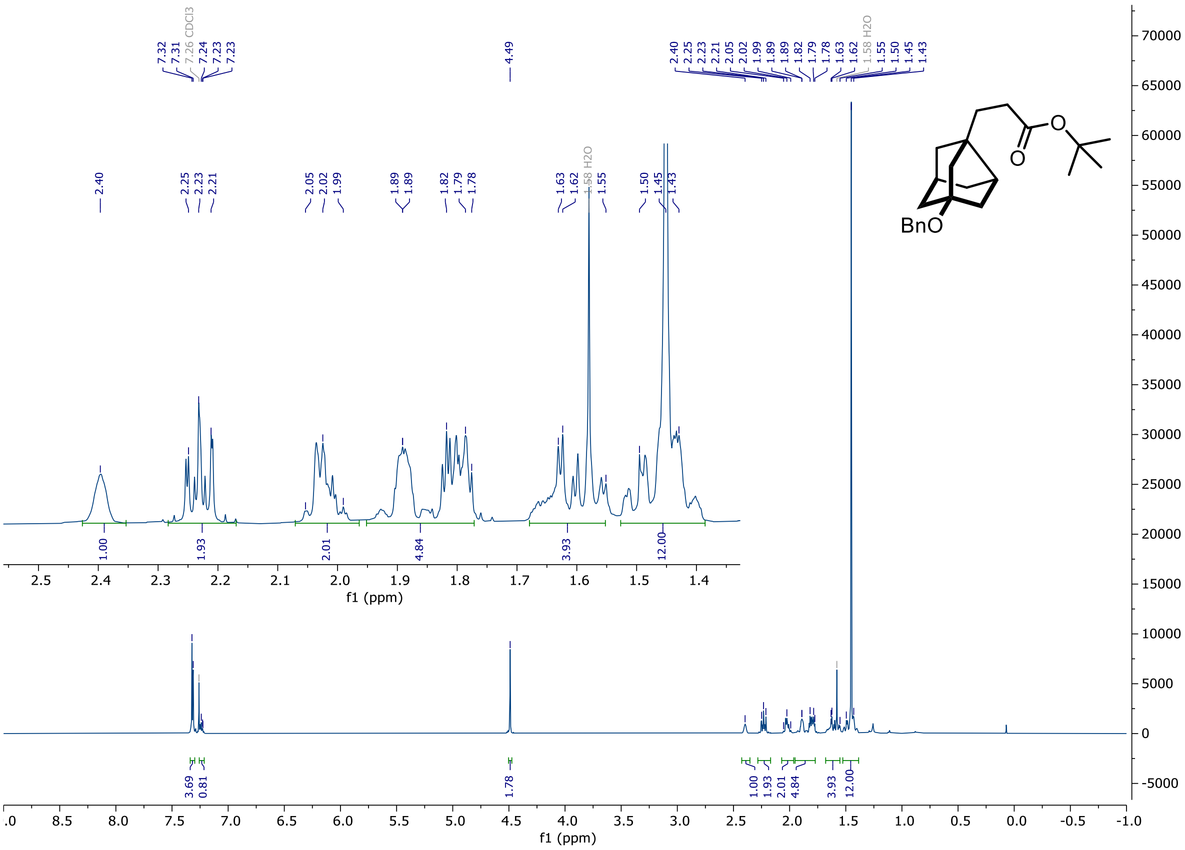


Compound 14b: ^{13}C NMR-DEPT (101 MHz, $CDCl_3$)

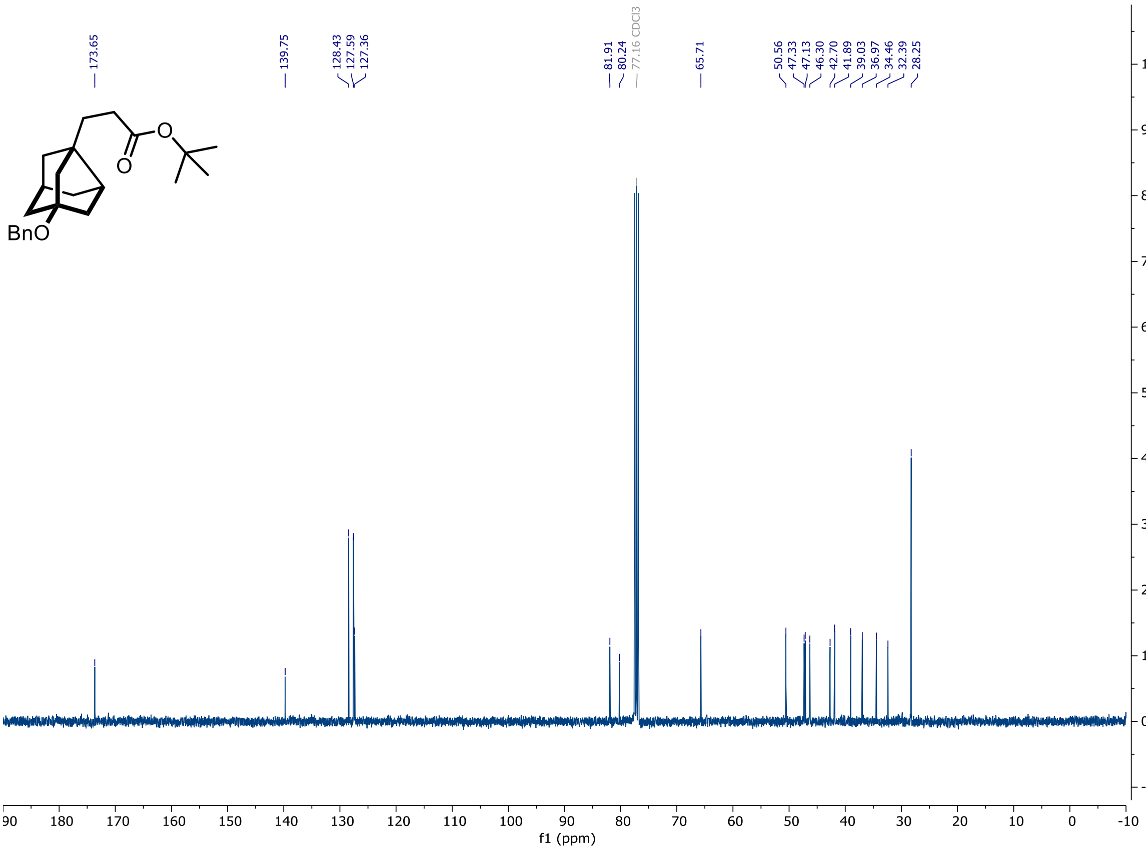


Giesse Reaction

Compound 15: ^{1}H NMR (400 MHz, CDCl$_3$)



Compound 15: ^{13}C NMR (101 MHz, CDCl$_3$)



Compound 15: ^{13}C NMR-DEPT (101 MHz, CDCl$_3$)