

A catalytic alkene insertion approach to bicyclo[2.1.1]hexane bioisosteres

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1. General Information

All experiments were performed under a nitrogen atmosphere unless stated otherwise.

All solvents were purchased at the highest commercial grade and used as received or after distillation from sodium/benzophenone under nitrogen (THF). Diiodoethane was washed with diethyl ether and sodium thiosulfate before use. All other chemicals were purchased at the highest commercial grade and used as received.

^1H NMR spectra were recorded on NMR spectrometers at 400 MHz and 500 MHz and ^{13}C NMR at 101 MHz and 126 MHz. ^1H NMR chemical shifts (δH) and ^{13}C NMR chemical shifts (δC) are quoted in parts per million (ppm) downfield from trimethylsilane (TMS) and coupling constants (J) are quoted in Hertz (Hz). Abbreviations for NMR data are s (singlet), d (doublet), t (triplet), q (quartet), quin (quintet), sxt (sextet).

Infrared (IR) spectra were recorded on a FTIR spectrometer and mass spectra were obtained using positive or negative electrospray ionization (ESI), atmospheric pressure chemical ionization (APCI), electron impact ionization (EI) or chemical ionization (CI) techniques.

Specific rotations were measured on a Rudolph Research Analytical Autopol I Automatic Polarimeter.

^1H NMR and ^{13}C NMR spectra were assigned with the aid of COSY, HSQC, HMBC, DEPT 135 and nOe NMR techniques and stereochemistry assigned with the aid of X-ray crystallography.

Chromatography was carried out using silica gel 60 Angstrom ($\text{\AA}$), 100–200 mesh. Thin layer chromatography (TLC) was performed on aluminium sheets pre-coated with silica gel, 0.20 mm (Macherey-Nagel, Polygram@ Sil G/UV254). TLC plates were visualized by UV absorption or potassium permanganate solution and heating.

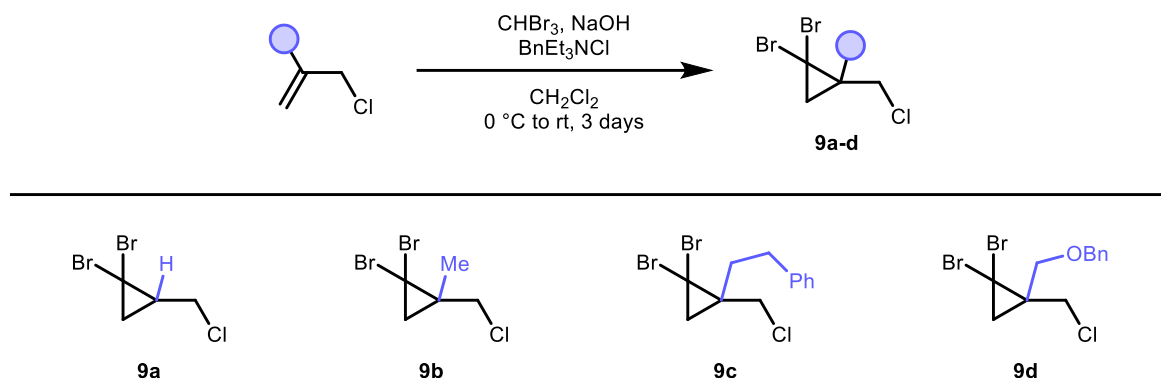
2. Preparation of SmI_2

An oven-dried round bottom flask, equipped with a stirrer bar, was flushed with a strong flow of N_2 for 30 min. Subsequently, the flask was loaded with samarium metal (~40 mesh, 1.4 eq.) and washed with diiodoethane (1 eq.). It was then flushed for another 30 min, before freshly distilled and degassed THF (0.1 M) was added followed by continuous stirring overnight at room temperature. Finally, the mixture was allowed to settle for at least one hour, and the characteristic inky-blue solution of SmI_2 was titrated prior to use.¹

UV-vis Absorption spectrum (λ_{max}) 555, 618 nm.

3. Starting Material Preparation

3.1. Synthesis of 1,1-dibromo cyclopropanes 9a-d

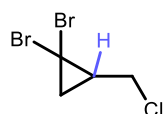


Scheme S1. Synthesis of 1,1-dibromo cyclopropanes

General Procedure A (compounds 9a-d):

A 500 mL round bottom flask was fitted with a reflux condenser and an elliptical-shaped stirrer bar under a nitrogen atmosphere. The flask was charged with sodium hydroxide powder (or freshly ground pellets) (56.0 g, 1.40 mol, 8.75 equiv.) The reaction flask was cooled in an ice/water bath and CH_2Cl_2 (1.23 M, 130 mL) was added. Allyl chloride (19.6 mL, 0.24 mol, 1.5 equiv.), bromoform (14.0 mL, 0.16 mol, 1 equiv.) and benzyltriethylammonium chloride (66 mg, catalytic) were added sequentially. The reaction was allowed to warm slowly to room temperature and stirring was maintained for 3 days (or until full consumption of bromoform). The reaction mixture was poured into a 500 mL beaker containing 250 mL of pentane. The mixture was gently stirred with a glass stick and sonicated for 10 minutes and then left for 20 min. The supernatant pentane was passed through a silica plug and the filtrate collected (**!! Extra attention should be paid to avoid pouring the black precipitate or the water phase over the filter !!**). The black precipitate was washed two times with 250 mL of pentane repeating the stirring-sonication-plug procedure. The solvent was then evaporated, and the resulting residue was dissolved in 300 mL of pentane. The mixture was filtered through a thin layer of silica and the silica was washed with 200 mL of pentane. Evaporation of the solvent led to a turbid liquid, which was passed through a syringe containing a small amount of MgSO_4 to afford the desired compounds (**!! The compounds were kept under a nitrogen atmosphere in the freezer at $-20\text{ }^\circ\text{C}$ and in the dark !!**).

1,1-Dibromo-2-(chloromethyl)cyclopropane (9a)



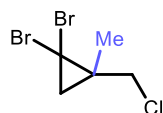
Prepared by following the **general procedure A** from allyl chloride (0.24 mol) and bromoform (0.16 mol), **9a** (13.7 g, 55.2 mmol, 34% yield) was obtained as a colourless liquid.

^1H NMR (400 MHz, CDCl_3) δ 3.65 (d, J = 7.5 Hz, 2H, ClCH_2CH), 2.04 (dq, J = 10.3, 7.4, 0.9 Hz, 1H, ClCH_2CH), 1.93 (ddd, J = 10.2, 7.6, 1.0 Hz, 1H, CBr_2CH_2), 1.53 – 1.40 (m, 1H, CBr_2CH_2).

^{13}C NMR (101 MHz, CDCl_3) δ 46.3 (ClCH_2CH), 32.2 (CBr_2CH_2), 29.0 (ClCH_2CH), 25.8 (CBr_2).

These data match with those previously reported in the literature.³

1,1-Dibromo-2-(chloromethyl)-2-methylcyclopropane (**9b**)



Prepared by following the **general procedure A** from 3-chloro-2-methylprop-1-ene (0.12 mol) and bromoform (0.80 mol), **9b** (6.85 g, 26.1 mmol, 32% yield) was obtained as a colourless liquid.

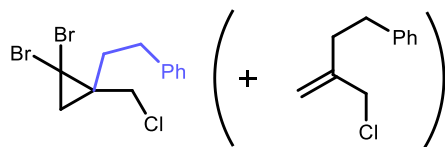
^1H NMR (500 MHz, CDCl_3) δ 3.81 (d, J = 11.3 Hz, 1H, CH_2Cl), 3.69 (d, J = 11.4 Hz, 1H, CH_2Cl), 1.68 (d, J = 7.7 Hz, 1H, CH_2CBr_2), 1.60 (d, J = 7.8 Hz, 1H, CH_2CBr_2), 1.55 (s, 3H, C^qCH_3).

^{13}C NMR (126 MHz, CDCl_3) δ 52.9 (CH_2Cl), 35.6 (C^qCH_3), 34.8 (CH_2CBr_2), 30.7 (C^qBr_2), 21.4 (C^qCH_3).

GC/MS (EI): m/z 259.9, 261.9, 263.9, 265.8.

These data match with those previously reported in the literature.³

(2-(2,2-Dibromo-1-(chloromethyl)cyclopropyl)ethyl)benzene (**9c**)



Prepared by following the **general procedure A** from (3-(chloromethyl)but-3-en-1-yl)benzene **S1** (21.0 mmol) and bromoform (14.0 mmol), a mixture of **9c** (1.87 g, 5.31 mmol, 38% yield) and alkene starting material **S1** (610 mg, 3.37 mmol, 16% recovery) was obtained as a colourless liquid (overall 2.49 g).

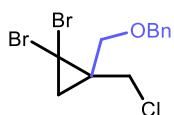
^1H NMR (400 MHz, CDCl_3) δ 7.34 – 7.27 (m, 2.6H, $\text{ArCH}^{9c + S1}$), 7.26 – 7.17 (m, 4H, $\text{ArCH}^{9c + S1}$), 5.17 – 5.15 (m, 1H, $\text{CH}_2=\text{C}^q S1$), 5.06 – 4.96 (m, 1H, $\text{CH}_2=\text{C}^q S1$), 4.06 (d, J = 1.0 Hz, 2H, $\text{CH}_2\text{Cl}^{S1}$), 3.87 (d, J = 11.9 Hz, 1H, $\text{CH}_2\text{Cl}^{9c}$), 3.83 (d, J = 11.8 Hz, 1H, $\text{CH}_2\text{Cl}^{9c}$), 2.89 (ddd, J = 13.3, 10.7, 5.7 Hz, 1H, $\text{CH}_2\text{Ph}^{9c}$), 2.83 – 2.78 (m, 2H, $\text{CH}_2\text{Ph}^{S1}$), 2.74 (ddd, J = 13.3, 10.8, 6.4 Hz, 1H, $\text{CH}_2\text{Ph}^{9c}$), 2.51 (ddd, J = 9.2, 6.9, 1.3 Hz, 2H, $\text{CH}_2\text{C}^q S1$), 2.17 (dt, J = 14.3, 11.1, 7.5 Hz, 2H, $\text{CH}_2\text{C}^q 9c$), 1.66 (d, J = 7.9 Hz, 1H, $\text{CH}_2\text{CBr}_2^{9c}$), 1.58 (d, J = 7.9 Hz, 1H, $\text{CH}_2\text{CBr}_2^{9c}$).

3.2. Synthesis of 1,1-dibromo cyclopropane **9d**

Similar to **general procedure A**, using sodium hydroxide (8.75 equiv.), CH_2Cl_2 (1 M), alkene (1 equiv.), bromoform (5 equiv.) and benzyltriethylammonium chloride (6 mg, catalytic). After 3 days, the mixture was diluted with water and Et_2O . The suspension was filtered through a pad of Celite and rinsed with Et_2O . The filtrate was transferred into a separating funnel. The aqueous layer was extracted three times with Et_2O and

the combined organic layers were washed with brine, dried over MgSO_4 , filtered and concentrated in vacuo. The residue was purified by column chromatography to afford the desired compound **9d**.

(((2,2-Dibromo-1-(chloromethyl)cyclopropyl)methoxy)methyl)benzene (**9d**)

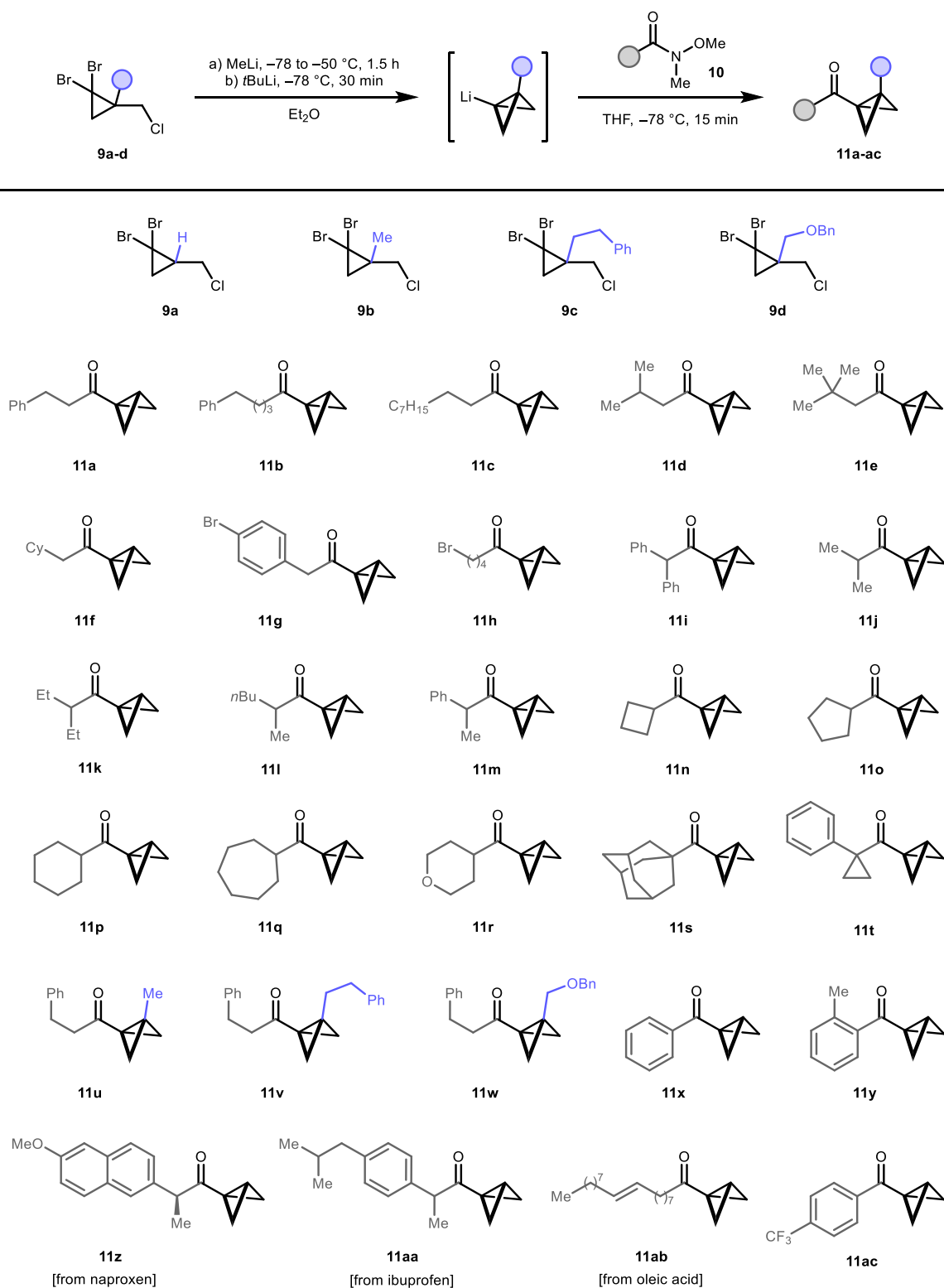


Prepared from (((2-(chloromethyl)allyl)oxy)methyl)benzene (15.4 mmol) and bromoform (77.0 mmol), **9d** (3.21 g, 8.70 mmol, 56% yield) was obtained after purification by column chromatography (0-2% EtOAc in hexane) as a yellow liquid.

^1H NMR (400 MHz, CDCl_3) δ 7.53 – 7.32 (m, 5H, ArCH), 4.60 (s, 2H, PhCH_2), 4.06 – 3.87 (m, 2H, $\text{CH}_2\text{--O}$), 3.86 – 3.72 (m, 2H, CH_2Cl), 1.80 – 1.66 (m, 2H, CH_2CBr_2).

^{13}C NMR (101 MHz, CDCl_3) δ 137.9 (ArC^q), 128.6 ($2 \times \text{ArCH}$), 128.0 (ArCH), 127.9 ($2 \times \text{ArCH}$), 73.6 ($\text{CH}_2\text{--O}$), 71.3 ($\text{CH}_2\text{--O}$), 48.4 ($\text{CH}_2\text{--Cl}$), 34.3 (C^qBr_2), 32.4 (CH_2CBr_2), 32.1 (C^q).

3.3. Synthesis of BCB ketones 11a-ac

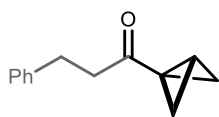


Scheme S2. Synthetic route for BCB ketone starting materials

General procedure B (compounds 11a-11ac):

A round bottom flask under N₂ was charged with 1,1-dibromo cyclopropane **9a-d** (4.80 mmol, 1.2 equiv.) and Et₂O (0.16 M). The solution was cooled to -78 °C then methyl lithium (1.6 M in Et₂O, 4.80 mmol, 1.2 equiv.) was added dropwise. The reaction was allowed to stir for 30 min at -78 °C followed by 30 min at -50 °C. High vacuum was applied to the round bottom flask for 10 min in order to remove most of the methyl bromide formed during the reaction. The solution was then cooled to -78 °C and *tert*-butyl lithium (1.7 M in pentane, 4.80 mmol, 1.2 equiv.) was added dropwise, and the resulting solution stirred for 30 min at the same temperature. The corresponding Weinreb amide **10** (4.00 mmol, 1 equiv.) in THF (1 M) was added dropwise and the reaction mixture was stirred at -78 °C for 15 min. Subsequently, the reaction mixture was quenched with saturated aqueous NH₄Cl solution and the aqueous layer extracted with EtOAc (3 × 20 mL). The organic layers were collected, dried over MgSO₄, and concentrated in vacuo (!! at room temperature !!). The desired compounds **11a-11ac** were isolated by column chromatography on silica gel using hexane and EtOAc as eluent (!! The products should be stored at -20 °C to avoid degradation !!).

1-(Bicyclo[1.1.0]butan-1-yl)-3-phenylpropan-1-one (**11a**)



Prepared following **general procedure B** (2 mmol scale), **11a** (417 mg, 2.24 mmol, 56% yield) was obtained after purification by column chromatography (30-50% CH₂Cl₂ in hexane) as a colourless liquid.

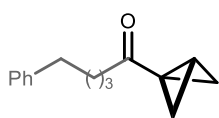
¹H NMR (400 MHz, CDCl₃) δ 7.32 – 7.24 (m, 2H, ArCH), 7.24 – 7.14 (m, 3H, ArCH), 2.93 (t, *J* = 7.7 Hz, 2H, PhCH₂), 2.75 (dd, *J* = 8.4, 6.9 Hz, 2H, C(O)CH₂), 2.40 (d, *J* = 3.4 Hz, 2H, BCB CH₂), 2.00 (p, *J* = 3.2 Hz, 1H, BCB CH), 1.26 – 1.12 (m, 2H, BCB CH₂).

¹³C NMR (101 MHz, CDCl₃) δ 205.8 (C=O), 141.3 (ArC^q), 128.6 (2 × ArCH), 128.5 (2 × ArCH), 126.3 (ArCH), 40.6 (C(O)CH₂), 35.9 (2 × BCB CH₂), 30.6 (PhCH₂), 19.9 (BCB CH), 18.7 (C(O)C^q).

IR (neat, cm⁻¹): 3027, 2935, 1663, 1603, 1495, 1453, 1402, 1180, 1031, 983, 912, 817, 770, 747, 714, 697.

HRMS (ESI⁺): calculated for C₁₃H₁₅O (M+H⁺): 187.1117; found: 187.1115.

1-(Bicyclo[1.1.0]butan-1-yl)-5-phenylpentan-1-one (**11b**)



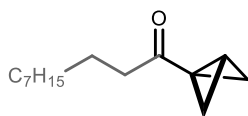
Prepared following **general procedure B** (4 mmol scale), **11b** (303 mg, 1.42 mmol, 36% yield) was obtained after purification by column chromatography (30-40% CH₂Cl₂ in hexane) as a colourless liquid.

¹H NMR (400 MHz, CDCl₃) δ 7.30 – 7.24 (m, 2H, ArCH), 7.18 (dd, *J* = 7.7, 5.5 Hz, 3H, ArCH), 2.62 (t, *J* = 7.0 Hz, 2H, COCH₂), 2.47 – 2.39 (m, 4H, CH₂ and BCB CH₂), 2.12 (p, *J* = 3.2 Hz, 1H, BCB CH), 1.71 – 1.59 (m, 4H, 2 × CH₂), 1.19 (dd, *J* = 2.7, 1.2 Hz, 2H, BCB CH₂).

^{13}C NMR (101 MHz, CDCl_3) δ 206.7 ($\text{C}=\text{O}$), 142.4 (ArC^q), 128.5 ($2 \times \text{ArCH}$), 128.4 ($2 \times \text{ArCH}$), 125.9 (ArCH), 38.8 (COCH_2), 35.9 (CH_2), 35.8 ($2 \times \text{BCB CH}_2$), 31.2 (CH_2), 24.3 (CH_2), 19.8 (BCB CH), 18.5 (C(O)C^q).

HRMS (ESI $^+$): calculated for $\text{C}_{15}\text{H}_{18}\text{ONa}$ ($\text{M}+\text{Na}^+$): 237.1250; found: 237.1241.

1-(Bicyclo[1.1.0]butan-1-yl)decan-1-one (**11c**)



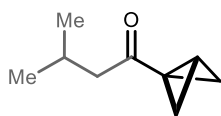
Prepared following **general procedure B** (4 mmol scale), **11c** (148 mg, 0.71 mmol, 18% yield) was obtained after purification by column chromatography (30%-40% CH_2Cl_2 in hexane) as a colourless liquid.

^1H NMR (400 MHz, CDCl_3) δ 2.45 – 2.38 (m, 4H, COCH_2 and BCB CH_2), 2.14 (p, J = 3.1 Hz, 1H, BCB CH), 1.59 (q, J = 6.6 Hz, 2H, COCH_2CH_2), 1.29 – 1.23 (m, 12H, CH_2), 1.19 (d, J = 2.8 Hz, 2H, BCB CH_2), 0.87 (t, J = 6.7 Hz, 3H, CH_3).

^{13}C NMR (101 MHz, CDCl_3) δ 207.1 ($\text{C}=\text{O}$), 39.1 (COCH_2), 35.8 ($2 \times \text{BCB CH}_2$), 32.0 (CH_2), 29.6 (CH_2), 29.6 (CH_2), 29.5 (CH_2), 29.4 (CH_2), 24.7 (CH_2), 22.8 (CH_2), 19.8 (BCB CH), 18.5 (C(O)C^q), 14.3 (CH_3).

HRMS (ESI $^+$): calculated for $\text{C}_{14}\text{H}_{24}\text{ONa}$ ($\text{M}+\text{Na}^+$): 231.1719; found: 231.1714.

1-(Bicyclo[1.1.0]butan-1-yl)-3-methylbutan-1-one (**11d**)



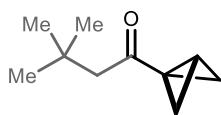
Prepared following **general procedure B** (4 mmol scale), **11d** (167 mg, 1.21 mmol, 30% yield) was obtained after purification by column chromatography (30%-50% CH_2Cl_2 in hexane) as a colourless liquid.

^1H NMR (400 MHz, CDCl_3) δ 2.43 (dt, J = 3.5, 1.1 Hz, 2H, BCB CH_2), 2.29 (d, J = 6.9 Hz, 2H, COCH_2), 2.20 – 2.11 (m, 2H, BCB CH and CH_3CH), 1.19 (dt, J = 2.6, 1.1 Hz, 2H, BCB CH_2), 0.93 (d, J = 6.6 Hz, 6H, $2 \times \text{CH}_3$).

^{13}C NMR (101 MHz, CDCl_3) δ 206.7 ($\text{C}=\text{O}$), 47.9 (COCH_2), 35.8 ($2 \times \text{BCB CH}_2$), 25.4 ($2 \times \text{CH}_3$), 22.8 (CH_3CH), 19.6 (BCB CH), 18.9 (C(O)C^q).

HRMS (ESI $^+$): calculated for $\text{C}_9\text{H}_{15}\text{O}$ ($\text{M}+\text{H}^+$): 139.1117; found: 139.1114.

1-(Bicyclo[1.1.0]butan-1-yl)-3,3-dimethylbutan-1-one (**11e**)



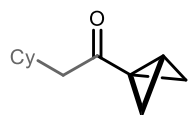
Prepared following **general procedure B** (4 mmol scale), **11e** (128 mg, 0.84 mmol, 21% yield) was obtained after purification by column chromatography (30%-40% CH_2Cl_2 in hexane) as a colourless liquid.

^1H NMR (400 MHz, CDCl_3) δ 2.43 (dt, J = 3.5, 1.1 Hz, 2H, BCB CH_2), 2.29 (s, 2H, COCH), 2.20 – 2.14 (m, 1H, BCB CH), 1.19 (dt, J = 2.9, 1.1 Hz, 2H, BCB CH_2), 1.04 (s, 9H, $t\text{-Bu}$).

¹³C NMR (101 MHz, CDCl₃) δ 206.7 (C=O), 51.1 (COCH₂), 36.1 (2 × BCB CH₂), 31.6 (C^q), 30.1 (3 × CH₃), 20.1 (C(O)C^q), 19.7 (BCB CH).

HRMS (ESI⁺): calculated for C₁₀H₁₆ONa (M+Na⁺): 175.1093; found: 175.1091.

1-(Bicyclo[1.1.0]butan-1-yl)-2-cyclohexylethan-1-one (**11f**)



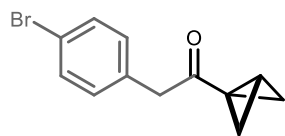
Prepared following **general procedure B** (4 mmol scale), **11f** (163 mg, 0.91 mmol, 23% yield) was obtained after purification by column chromatography (30%-50% CH₂Cl₂ in hexane) as a colourless liquid.

¹H NMR (500 MHz, CDCl₃) δ 2.42 (dt, *J* = 3.4, 1.2 Hz, 2H, BCB CH₂), 2.28 (d, *J* = 6.9 Hz, 2H, COCH₂), 2.13 (p, *J* = 3.2 Hz, 1H, BCB CH), 2.01 – 1.78 (m, 1H cyclohexyl CH), 1.74 – 1.56 (m, 5H, cyclohexyl CH), 1.27 (qt, *J* = 14.3, 4.4 Hz, 2H, cyclohexyl CH), 1.19 (dt, *J* = 2.6, 1.1 Hz, 2H, BCB CH₂), 1.17 – 1.05 (m, 1H, cyclohexyl CH), 0.99 – 0.84 (m, 2H, cyclohexyl CH).

¹³C NMR (126 MHz, CDCl₃) δ 206.7 (C=O), 46.7 (COCH₂), 35.9 (2 × BCB CH₂), 34.8 (cyclohexyl CH), 33.4 (cyclohexyl CH₂), 26.4 (cyclohexyl CH₂), 26.3 (cyclohexyl CH₂), 19.6 (BCB CH), 19.1 (C(O)C^q).

HRMS (ESI⁺): calculated for C₁₂H₁₈ONa (M+Na⁺): 201.1200; found: 201.1200.

1-(Bicyclo[1.1.0]butan-1-yl)-2-(4-bromophenyl)ethan-1-one (**11g**)



Prepared following **general procedure B** (2 mmol scale), **11g** (91.7 mg, 0.37 mmol, 18% yield) was obtained after purification by column chromatography (30-35% CH₂Cl₂ in hexane) as a white solid.

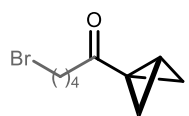
¹H NMR (400 MHz, CDCl₃) δ 7.56 – 7.40 (m, 2H, ArCH), 7.18 – 7.04 (m, 2H, ArCH), 3.70 (s, 2H, C(O)CH₂), 2.46 (dt, *J* = 3.5, 1.2 Hz, 2H, BCB CH₂), 2.21 (p, *J* = 3.2 Hz, 1H, BCB CH), 1.23 (dd, *J* = 2.8, 1.4 Hz, 2H, BCB CH₂).

¹³C NMR (101 MHz, CDCl₃) δ 203.4 (C=O), 133.7 (ArC^q), 131.9 (2 × ArCH), 131.1 (2 × ArCH), 121.1 (ArC^q), 45.5 (C(O)CH₂), 36.2 (2 × BCB CH₂), 21.2 (BCB CH), 18.8 (C(O)C^q).

IR (neat, cm⁻¹): 2929, 2904, 2860, 1701, 1696, 1659, 1485, 1388, 1316, 1104, 1068, 1057, 1009, 839, 798, 759, 690, 625.

HRMS (ESI⁺): calculated for C₁₂H₁₁OB⁺Na (M+Na⁺): 272.9885; found: 272.9876.

1-(Bicyclo[1.1.0]butan-1-yl)-5-bromopentan-1-one (**11h**)



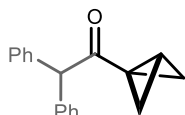
Prepared following **general procedure B** (4 mmol scale), **11h** (153 mg, 0.71 mmol, 18% yield) was obtained after purification by column chromatography (30%-50% CH₂Cl₂ in hexane) as a colourless liquid.

¹H NMR (400 MHz, CDCl₃) δ 3.40 (t, *J* = 6.6 Hz, 2H, COCH₂), 2.49 – 2.41 (m, 4H, CH₂ and BCB CH₂), 2.16 (p, *J* = 3.2 Hz, 1H, BCB CH), 1.99 – 1.81 (m, 2H, CH₂), 1.75 (dtd, *J* = 9.6, 7.0, 5.0 Hz, 2H, CH₂), 1.20 (dd, *J* = 2.7, 1.4 Hz, 2H, BCB CH₂).

¹³C NMR (101 MHz, CDCl₃) δ 206.0 (C=O), 37.8 (COCH₂), 35.8 (2 × BCB CH₂), 33.4 (CH₂), 32.2 (CH₂), 23.1 (CH₂), 20.1 (BCB CH), 18.5 (C(O)C^q).

HRMS (APCI⁺): calculated for C₉H₁₄OBr (M+H⁺): 217.0223; found: 217.0224.

1-(Bicyclo[1.1.0]butan-1-yl)-2,2-diphenylethan-1-one (**11i**)



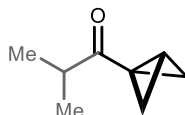
Prepared following **general procedure B** (4 mmol scale), **11i** (184 mg, 0.74 mmol, 19% yield) was obtained after purification by column chromatography (30%-50% CH₂Cl₂ in hexane) as a yellow solid.

¹H NMR (400 MHz, CDCl₃) δ 7.35 – 7.29 (m, 4H, ArCH), 7.25 (tt, *J* = 8.0, 1.4 Hz, 6H, ArCH), 5.31 (s, 1H, COCH), 2.50 – 2.41 (m, 2H, BCB CH₂), 2.14 (p, *J* = 3.2 Hz, 1H, BCB CH), 1.24 – 1.13 (m, 2H, BCB CH₂).

¹³C NMR (101 MHz, CDCl₃) δ 204.6 (C=O), 139.1 (ArC^q), 129.1 (2 × ArCH), 128.8 (2 × ArCH), 127.3 (ArCH), 60.3 (COCH), 36.2 (2 × BCB CH₂), 22.4 (BCB CH), 19.5 (C(O)C^q).

HRMS (ESI⁺): calculated for C₁₈H₁₆ONa (M+Na⁺): 271.1093; found: 271.1091.

1-(Bicyclo[1.1.0]butan-1-yl)-2-methylpropan-1-one (**11j**)



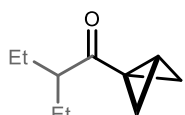
Prepared following **general procedure B** (4 mmol scale), **11j** (41.0 mg, 0.33 mmol, 8% yield) was obtained after purification by column chromatography (30%-40% CH₂Cl₂ in hexane) as a colourless liquid. Low yield was observed due to the volatility of the compound.

¹H NMR (400 MHz, CDCl₃) δ 2.75 (h, *J* = 6.9 Hz, 1H, (C(O)CH), 2.43 (dt, *J* = 3.5, 1.1 Hz, 2H, BCB CH₂), 2.17 (p, *J* = 3.2 Hz, 1H, BCB CH), 1.19 (dt, *J* = 2.6, 1.1 Hz, 2H, BCB CH₂), 1.11 (d, *J* = 6.8 Hz, 6H, 2 × CH₃).

¹³C NMR (101 MHz, CDCl₃) δ 210.8 (C=O), 36.7 (C(O)CH), 35.5 (BCB, CH₂), 20.2 (BCB CH), 19.2 (2 × CH₃), 17.5 (C(O)C^q).

HRMS (ESI⁺): calculated for C₈H₁₃O (M+H⁺): 125.0961; found: 125.0962.

1-(Bicyclo[1.1.0]butan-1-yl)-2-ethylbutan-1-one (**11k**)



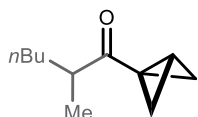
Prepared following **general procedure B** (4 mmol scale), **11k** (315 mg, 2.07 mmol, 26% yield) was obtained after purification by column chromatography (30-40% CH₂Cl₂ in hexane) as a colourless liquid.

¹H NMR (500 MHz, CDCl₃) δ 2.58 – 2.37 (m, 3H, C(O)CH, BCB CH₂), 2.16 (p, *J* = 3.1 Hz, 1H, BCB CH), 1.82 – 1.60 (m, 2H, CH₂CH₃), 1.53 – 1.38 (m, 2H, CH₂CH₃), 1.20 (dt, *J* = 2.9, 1.1 Hz, 2H, BCB CH₂), 0.85 (t, *J* = 7.4 Hz, 6H, 2 × CH₂CH₃).

¹³C NMR (126 MHz, CDCl₃) δ 210.4 (C=O), 50.7 (C(O)CH), 35.7 (2 × BCB CH₂), 24.9 (2 × CH₂CH₃), 19.5 (C(O)C^q), 19.1 (BCB CH), 12.1 (2 × CH₂CH₃).

HRMS (ESI⁺): calculated for C₁₀H₁₆ONa (M+Na⁺): 175.1093; found: 175.1091.

1-(Bicyclo[1.1.0]butan-1-yl)-2-methylhexan-1-one (**11l**)



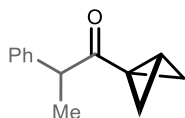
Prepared following **general procedure B** (4 mmol scale), **11l** (173 mg, 1.04 mmol, 26% yield) was obtained after purification by column chromatography (30% CH₂Cl₂ in hexane) as a colourless liquid.

¹H NMR (500 MHz, CDCl₃) δ 2.66 (h, *J* = 6.9 Hz, 1H, (C(O)CH), 2.43 (dt, *J* = 3.4, 1.0 Hz, 2H, BCB CH₂), 2.16 (p, *J* = 3.2 Hz, 1H, BCB CH), 1.69 (ddt, *J* = 13.2, 8.1, 6.7 Hz, 1H, CH₂), 1.38 – 1.21 (m, 5H, CH₂), 1.19 (ddt, *J* = 5.3, 2.4, 1.1 Hz, 2H, BCB CH₂), 1.08 (d, *J* = 6.9 Hz, 3H, CHCH₃), 0.88 (t, *J* = 7.1 Hz, 3H, CH₂CH₃).

¹³C NMR (126 MHz, CDCl₃) δ 210.8 (C=O), 41.9 (C(O)CH), 35.6 (BCB, CH₂), 35.5 (BCB CH₂), 33.4 (CH₂), 29.7 (CH₂), 22.9 (CH₂), 19.8 (BCB CH), 18.2 (C(O)C^q), 17.4 (CHCH₃), 14.1 (CH₂CH₃).

HRMS (ESI⁺): calculated for C₁₁H₁₈ONa (M+Na⁺): 189.1250; found: 189.1247.

1-(Bicyclo[1.1.0]butan-1-yl)-2-phenylpropan-1-one (**11m**)



Prepared following **general procedure B** (4 mmol scale), **11m** (298 mg, 1.60 mmol, 40% yield) was obtained after purification by column chromatography (30%-60% CH₂Cl₂ in hexane) as a colourless solid.

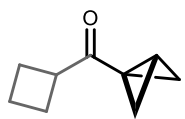
¹H NMR (400 MHz, CDCl₃) δ 7.35 – 7.28 (m, 2H, ArCH), 7.26 – 7.19 (m, 3H, ArCH), 3.95 (q, *J* = 6.9 Hz, 1H, COCH), 2.39 (dt, *J* = 3.4, 1.1 Hz, 2H, BCB CH₂), 1.97 (p, *J* = 3.2 Hz, 1H, BCB CH), 1.39 (d, *J* = 6.9 Hz, 3H, CH₃), 1.09 (ddt, *J* = 9.7, 2.7, 1.2 Hz, 2H, BCB CH₂).

¹³C NMR (101 MHz, CDCl₃) δ 206.9 (C=O), 141.7 (ArC^q), 129.0 (2 × ArCH), 127.8 (2 × ArCH), 127.1 (ArCH), 49.2 (COCH), 35.8 (BCB CH₂), 35.7 (BCB CH₂), 21.5 (BCB CH), 19.1 (CH₃), 18.5 (C(O)C^q).

IR (neat, cm⁻¹): 2985, 2930, 1646, 1614, 1369, 1029, 972, 919, 906, 857, 829, 771, 743, 712.

HRMS (ESI⁺): calculated for C₁₃H₁₄ONa (M+Na⁺): 209.0937; found: 209.0933.

Bicyclo[1.1.0]butan-1-yl(cyclobutyl)methanone (**11n**)



Prepared following **general procedure B** (4 mmol scale), **11n** (174 mg, 1.27 mmol, 32% yield) was obtained after purification by column chromatography (30%-40% CH₂Cl₂ in hexane) as a colourless liquid.

¹H NMR (400 MHz, CDCl₃) δ 3.36 (p, *J* = 8.5 Hz, 1H, COCH), 2.38 (dd, *J* = 3.5, 1.1 Hz, 2H, BCB CH₂), 2.30 (dq, *J* = 11.5, 8.9 Hz, 2H, cyclobutyl CH₂), 2.17 – 2.04 (m, 3H,

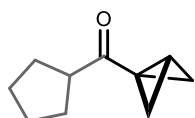
cyclobutyl CH_2 and BCB CH), 1.97 (dq, $J = 11.0, 8.5$ Hz, 1H, cyclobutyl CH_2), 1.89 – 1.75 (m, 1H, cyclobutyl CH_2), 1.16 (dd, $J = 2.8, 1.3$ Hz, 2H, BCB CH_2).

^{13}C NMR (101 MHz, CDCl_3) δ 207.9 ($\text{C}=\text{O}$), 42.5 (COCH), 35.5 ($2 \times$ BCB CH_2), 25.1 ($2 \times$ cyclobutyl CH_2), 19.8 (BCB CH), 18.2 (cyclobutyl CH_2), 17.0 ($\text{C}(\text{O})\text{C}^q$).

IR (neat, cm^{-1}): 2940, 1658, 1398, 1180, 1115, 1077, 980, 902, 858, 792, 733, 712.

HRMS (ESI^+): calculated for $\text{C}_9\text{H}_{12}\text{ONa}$ ($\text{M}+\text{Na}^+$): 159.0780; found: 159.0778.

Bicyclo[1.1.0]butan-1-yl(cyclopentyl)methanone (**11o**)



Prepared following **general procedure B** (2 mmol scale), **11o** (94.5 mg, 0.63 mmol, 31% yield) was obtained after purification by column chromatography (30%-40% CH_2Cl_2 in hexane) as a colourless liquid.

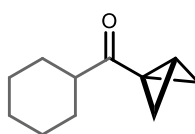
^1H NMR (400 MHz, CDCl_3) δ 2.96 (p, $J = 7.9$ Hz, 1H, COCH), 2.44 (d, $J = 3.4$ Hz, 2H, BCB CH_2), 2.15 (p, $J = 3.1$ Hz, 1H, BCB CH), 1.88 – 1.73 (m, 4H, cyclopentyl CH_2), 1.73 – 1.62 (m, 2H, cyclopentyl CH_2), 1.62 – 1.50 (m, 2H, cyclopentyl CH_2), 1.18 (d, $J = 2.8$ Hz, 2H, BCB CH_2).

^{13}C NMR (101 MHz, CDCl_3) δ 209.4 ($\text{C}=\text{O}$), 47.3 (COCH), 35.6 ($2 \times$ BCB CH_2), 29.8 ($2 \times$ cyclopentyl CH_2), 26.2 ($2 \times$ cyclopentyl CH_2), 19.8 (BCB CH), 18.2 ($\text{C}(\text{O})\text{C}^q$).

IR (neat, cm^{-1}): 2950, 2868, 1659, 1489, 1449, 1394, 1182, 1104, 1077, 1048, 1030, 1001, 893, 856, 803, 737.

HRMS (ESI^+): calculated for $\text{C}_{10}\text{H}_{15}\text{O}$ ($\text{M}+\text{H}^+$): 151.1117; found: 151.1116.

Bicyclo[1.1.0]butan-1-yl(cyclohexyl)methanone (**11p**)



Prepared following **general procedure B** (4 mmol scale), **11p** (174 mg, 1.06 mmol, 27% yield) was obtained after purification by column chromatography (30%-50% CH_2Cl_2 in hexane) as a colourless liquid.

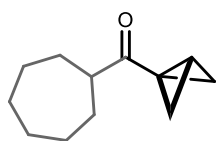
^1H NMR (400 MHz, CDCl_3) δ 2.47 (tt, $J = 11.7, 3.3$ Hz, 1H, COCH), 2.42 (dt, $J = 3.5, 1.1$ Hz, 2H, BCB CH_2), 2.16 (p, $J = 3.1$ Hz, 1H, BCB CH), 1.84 – 1.71 (m, 4H, cyclohexyl CH), 1.69 – 1.62 (m, 1H, cyclohexyl CH), 1.53 – 1.36 (m, 2H, cyclohexyl CH), 1.34 – 1.20 (m, 3H, cyclohexyl CH), 1.18 (dd, $J = 2.7, 1.3$ Hz, 2H, BCB CH_2).

^{13}C NMR (101 MHz, CDCl_3) δ 210.1 ($\text{C}=\text{O}$), 46.8 (COCH), 35.5 ($2 \times$ BCB CH_2), 29.4 (cyclohexyl CH_2), 26.0 (cyclohexyl CH_2), 25.9 (cyclohexyl CH_2), 20.1 (BCB CH), 17.6 ($\text{C}(\text{O})\text{C}^q$).

IR (neat, cm^{-1}): 2927, 2852, 1660, 1487, 1448, 1404, 1350, 1141, 1102, 1065, 988, 876, 835, 790, 720.

HRMS (APCI^+): calculated for $\text{C}_{11}\text{H}_{17}\text{O}$ ($\text{M}+\text{H}^+$): 165.1274; found: 165.1268.

Bicyclo[1.1.0]butan-1-yl(cycloheptyl)methanone (**11q**)



Prepared following **general procedure B** (2 mmol scale), **11q** (74.6 mg, 0.42 mmol, 21% yield) was obtained after purification by column chromatography (30% CH₂Cl₂ in hexane) as a colourless liquid.

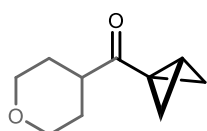
¹H NMR (500 MHz, CDCl₃) δ 2.64 (tt, *J* = 9.7, 4.1 Hz, 1H, C(O)CH), 2.41 (dt, *J* = 3.4, 1.1 Hz, 2H, BCB CH₂), 2.15 (p, *J* = 3.1 Hz, 1H, BCB CH), 1.88 – 1.79 (m, 2H, CH₂), 1.74 (ddq, *J* = 16.7, 6.9, 3.3 Hz, 2H, CH₂), 1.68 – 1.50 (m, 6H, CH₂), 1.45 (dtdd, *J* = 10.2, 8.7, 5.5, 3.3 Hz, 2H, CH₂), 1.17 (dd, *J* = 2.7, 1.3 Hz, 2H, BCB CH₂).

¹³C NMR (126 MHz, CDCl₃) δ 210.7 (C=O), 48.2 (C(O)CH), 35.4 (2 × BCB CH₂), 30.8 (2 × CH₂), 28.5 (2 × CH₂), 26.8 (2 × CH₂), 20.0 (BCB CH), 17.5 (C(O)C^q).

IR (neat, cm⁻¹): 2921, 2854, 1660, 1459, 1445, 1401, 1390, 1364, 1101, 1071, 1048, 994, 940, 859, 829, 798, 719.

HRMS (ESI⁺): calculated for C₁₂H₁₈ONa (M+Na⁺): 201.1250; found: 201.1245.

Bicyclo[1.1.0]butan-1-yl(tetrahydro-2H-pyran-4-yl)methanone (**11r**)



Prepared following **general procedure B** (4 mmol scale), **11r** (218 mg, 1.31 mmol, 33% yield) was obtained after purification by column chromatography (6% EtOAc in hexane) as a colourless liquid.

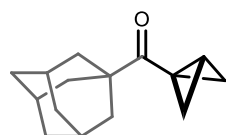
¹H NMR (400 MHz, CDCl₃) δ 4.00 (ddd, *J* = 11.6, 4.4, 2.4 Hz, 2H, O-CH₂), 3.43 (td, *J* = 11.6, 2.4 Hz, 2H O-CH₂), 2.70 (tt, *J* = 11.2, 4.0 Hz, 1H, COCH), 2.44 (d, *J* = 3.2 Hz, 2H, BCB CH₂), 2.22 (p, *J* = 3.2 Hz, 1H, BCB CH), 1.90 – 1.72 (m, 2H, O-CH₂CH₂), 1.67 (dt, *J* = 12.3, 2.4 Hz, 2H, O-CH₂CH₂), 1.36 – 1.13 (m, 2H, BCB CH₂).

¹³C NMR (101 MHz, CDCl₃) δ 207.9 (C=O), 67.3 (2 × O-CH₂), 43.8 (COCH), 35.6 (2 × BCB CH₂), 29.0 (2 × O-CH₂CH₂), 20.7 (BCB CH), 17.5 (C(O)C^q).

IR (neat, cm⁻¹): 2949, 1655, 1444, 1403, 1385, 1356, 1114, 1103, 1088, 1021, 993, 983, 890, 846.

HRMS (APCI⁺): calculated for C₁₀H₁₅O₂ (M+H⁺): 167.1067; found: 167.1068.

Adamantan-1-yl(bicyclo[1.1.0]butan-1-yl)methanone (**11s**)



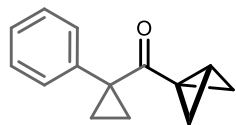
Prepared following **general procedure B** (4 mmol scale), **11s** (167 mg, 0.77 mmol, 20% yield) was obtained after purification by column chromatography (30%-40% CH₂Cl₂ in hexane) as a white solid

¹H NMR (400 MHz, CDCl₃) δ 2.53 (d, *J* = 3.3 Hz, 2H, BCB CH₂), 2.28 (p, *J* = 2.9 Hz, 1H, BCB CH), 2.03 (q, *J* = 3.2 Hz, 3H, 3 × adamantyl CH), 1.88 (d, *J* = 3.0 Hz, 6H, 3 × adamantyl CH₂), 1.78 – 1.65 (m, 6H, 3 × adamantyl CH₂), 1.10 (d, *J* = 2.6 Hz, 2H, BCB CH₂).

¹³C NMR (101 MHz, CDCl₃) δ 211.1 (C=O), 47.2 (C(O)C^q), 38.8 (3 × adamantyl CH₂), 36.8 (2 × BCB CH₂), 36.1 (3 × adamantyl CH₂), 28.3 (3 × adamantyl CH), 20.4 (BCB CH), 15.2 (C(O)C^q).

HRMS (ESI⁺): calculated for C₁₅H₂₀ONa (M+Na⁺): 239.1406; found: 239.1398.

Bicyclo[1.1.0]butan-1-yl(1-phenylcyclopropyl)methanone (11t**)**



Prepared following **general procedure B** (4 mmol scale), **11t** (221 mg, 1.12 mmol, 28% yield) was obtained after purification by column chromatography (30-35% CH₂Cl₂ in hexane) as a white solid.

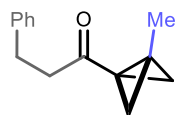
¹H NMR (500 MHz, CDCl₃) δ 7.29 – 7.21 (m, 4H, ArCH), 7.21 – 7.17 (m, 1H, ArCH), 2.06 (p, *J* = 3.1 Hz, 1H, BCB CH), 1.91 (dt, *J* = 3.4, 1.1 Hz, 2H, BCB CH₂), 1.49 (d, *J* = 4.0 Hz, 1H, CH₂), 1.48 (d, *J* = 3.8 Hz, 1H, CH₂), 1.09 (d, *J* = 3.8 Hz, 1H, CH₂), 1.08 (d, *J* = 3.9 Hz, 1H, CH₂), 0.85 (dd, *J* = 2.8, 1.3 Hz, 2H, BCB CH₂).

¹³C NMR (126 MHz, CDCl₃) δ 205.9 (C=O), 141.3 (ArC^q), 129.6 (2 × ArCH), 128.7 (2 × ArCH), 127.2 (ArCH), 36.8 (2 × BCB CH₂), 36.1 (C^q), 22.8 (BCB CH), 18.3 (C^q), 17.4 (2 × CH₂).

IR (neat, cm⁻¹): 2960, 2934, 2871, 1648, 1497, 1384, 1251, 1102, 1065, 1047, 1023, 1006, 914, 836, 755, 739, 696, 652.

HRMS (APCI⁺): calculated for C₁₄H₁₅O (M+H⁺): 199.1117; found: 199.1115.

1-(3-Methylbicyclo[1.1.0]butan-1-yl)-3-phenylpropan-1-one (11u**)**



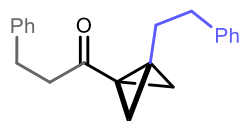
Prepared following **general procedure B** (4 mmol scale), **11u** (339 mg, 1.69 mmol, 42% yield) was obtained after purification by column chromatography (30-35% CH₂Cl₂ in hexane) as a colourless liquid.

¹H NMR (400 MHz, CDCl₃) δ 7.43 – 7.24 (m, 2H, ArCH), 7.23 – 7.15 (m, 3H, ArCH), 2.94 (t, *J* = 7.8 Hz, 2H, CH₂), 2.74 – 2.58 (m, 2H, CH₂), 2.28 (d, *J* = 1.1 Hz, 2H, BCB CH₂), 1.50 – 1.43 (m, 3H, CH₃), 1.27 (d, *J* = 1.1 Hz, 2H, BCB CH₂).

¹³C NMR (101 MHz, CDCl₃) δ 204.4 (C=O), 141.3 (ArC^q), 128.2 (2 × ArCH), 128.2 (2 × ArCH), 125.8 (ArCH), 41.8 (C(O)CH₂), 38.4 (2 × BCB CH₂), 32.5 (C^q), 29.8 (PhCH₂), 22.5 (C^q), 12.4 (CH₃).

HRMS (ESI⁺): calculated for C₁₄H₁₆ONa (M+Na⁺): 223.1093; found: 223.1083.

1-(3-Phenethylbicyclo[1.1.0]butan-1-yl)-3-phenylpropan-1-one (11v**)**



Prepared following **general procedure B** (4.42 mmol scale), **11v** (419 mg, 1.44 mmol, 33% yield) was obtained after purification by column chromatography (30-40% CH₂Cl₂ in hexane) as a colourless liquid.

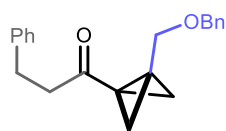
¹H NMR (400 MHz, CDCl₃) δ 7.36 – 7.26 (m, 2H, ArCH), 7.26 – 7.07 (m, 8H, ArCH), 2.92 (t, *J* = 7.7 Hz, 2H, CH₂), 2.83 – 2.68 (m, 2H, CH₂), 2.66 (dd, *J* = 8.4, 7.0 Hz, 2H, CH₂), 2.34 – 2.23 (m, 2H, BCB CH₂), 2.15 – 1.89 (m, 2H, CH₂), 1.22 (s, 2H, BCB CH₂).

¹³C NMR (101 MHz, CDCl₃) δ 204.7 (C=O), 141.5 (ArC^q), 141.0 (ArC^q), 128.6 (2 × ArCH), 128.6 (2 × ArCH), 128.5 (2 × ArCH), 128.5 (2 × ArCH), 126.3 (ArCH), 126.2 (ArCH), 42.2 (CH₂), 37.6 (2 × BCB CH₂), 36.0 (C^q), 34.9 (CH₂), 30.2 (CH₂), 29.6 (CH₂), 23.0 (C^q).

IR (neat, cm⁻¹): 2929, 2856, 1657, 1603, 1495, 1453, 1410, 1365, 1100, 1067, 1030, 984, 799, 746, 696.

HRMS (APCI⁺): calculated for C₂₁H₂₃O (M+H⁺): 291.1743; found: 291.1733.

1-(3-((Benzyloxy)methyl)bicyclo[1.1.0]butan-1-yl)-3-phenylpropan-1-one (**11w**)



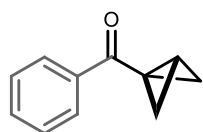
Prepared following **general procedure B** (4 mmol scale), **11w** (85.0 mg, 0.28 mmol, 7% yield) was obtained after purification by column chromatography (0-10% EtOAc in hexane) as a yellow liquid. Low yield was observed due to decomposition during the reaction.

¹H NMR (400 MHz, CDCl₃) δ 7.37 – 7.22 (m, 5H, ArCH), 7.24 – 7.20 (m, 2H, ArCH), 7.19 – 7.12 (m, 1H, ArCH), 7.13 – 7.03 (m, 2H, ArCH), 4.47 (s, 2H, PhCH₂-O), 3.81 (s, 2H, CH₂-O), 3.01 – 2.80 (m, 2H, CH₂), 2.78 – 2.69 (m, 2H, CH₂), 2.52 (d, *J* = 1.0 Hz, 2H, BCB CH₂), 1.31 (d, *J* = 1.0 Hz, 2H, BCB CH₂).

¹³C NMR (101 MHz, CDCl₃) δ 204.7 (C=O), 141.6 (ArC^q), 137.8 (ArC^q), 128.6 (2 × ArCH), 128.5 (2 × ArCH), 128.5 (2 × ArCH), 127.9 (ArCH), 127.8 (2 × ArCH), 126.1 (ArCH), 73.2 (PhCH₂-O), 67.0 (CH₂-O), 42.0 (CH₂), 36.8 (2 × BCB CH₂), 33.0 (C^q), 30.2 (CH₂), 22.1 (C^q).

HRMS (ESI⁺): calculated for C₂₁H₂₂O₂Na (M+Na⁺): 329.1512; found: 329.1498.

Bicyclo[1.1.0]butan-1-yl(phenyl)methanone (**11x**)



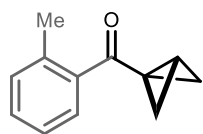
Prepared following **general procedure B** (4 mmol scale), **11x** (261 mg, 1.65 mmol, 41% yield) was obtained after purification by column chromatography (30%-50% CH₂Cl₂ in hexane) as a colourless liquid.

¹H NMR (400 MHz, CDCl₃) δ 7.88 – 7.82 (m, 2H, ArCH), 7.58 – 7.50 (m, 1H, ArCH), 7.48 – 7.37 (m, 2H, ArCH), 2.67 – 2.54 (m, 2H, BCB CH₂), 2.21 (p, *J* = 3.3 Hz, 1H, BCB CH), 1.48 (dt, *J* = 3.2, 1.1 Hz, 2H, BCB CH₂).

¹³C NMR (101 MHz, CDCl₃) δ 200.1 (C=O), 137.9 (ArC^q), 132.3 (ArCH), 128.9 (ArCH), 128.3 (ArCH), 38.0 (2 × BCB CH₂), 21.6 (BCB CH), 17.2 (C(O)C^q).

Characterization data matches that in the literature.⁴

Bicyclo[1.1.0]butan-1-yl(o-tolyl)methanone (**11y**)



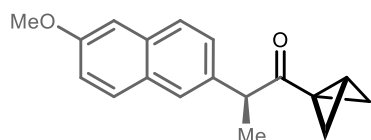
Prepared following **general procedure B** (4 mmol scale), **11y** (256 mg, 1.48 mmol, 37% yield) was obtained after purification by column chromatography (30%-60% CH₂Cl₂ in hexane) as a colourless liquid.

¹H NMR (500 MHz, CDCl₃) δ 7.42 (d, *J* = 7.5 Hz, 1H, ArCH), 7.30 (t, *J* = 7.5 Hz, 1H, ArCH), 7.19 (d, *J* = 7.6 Hz, 2H, ArCH), 2.42 – 2.40 (m, 2H, BCB CH₂), 2.40 (s, 3H, *o*-CH₃), 2.24 (p, *J* = 3.6 Hz, 1H, BCB CH), 1.41 (dd, *J* = 3.1, 1.3 Hz, 2H, BCB CH₂).

¹³C NMR (126 MHz, CDCl₃) δ 203.4 (C=O), 138.3 (ArC^q), 136.2 (ArC^q), 131.0 (ArCH), 130.2 (ArCH), 128.4 (ArCH), 125.2 (ArCH), 37.6 (2 × BCB CH₂), 21.8 (BCB CH), 20.0 (CH₃), 19.9 (C(O)C^q).

HRMS (ESI⁺): calculated for C₁₂H₁₂ONa (M+Na⁺): 195.0780; found: 195.0778.

(S)-1-(Bicyclo[1.1.0]butan-1-yl)-2-(6-methoxynaphthalen-2-yl)propan-1-one (**11z**)



Prepared following **general procedure B** (4 mmol scale), **11z** (307 mg, 1.15 mmol, 29% yield) was obtained after purification by column chromatography (30-40% CH₂Cl₂ in hexane) as a white solid.

¹H NMR (500 MHz, CDCl₃) δ 7.69 (dd, *J* = 8.6, 2.6 Hz, 2H, ArCH), 7.58 (d, *J* = 1.8 Hz, 1H, ArCH), 7.31 (dd, *J* = 8.5, 1.9 Hz, 1H, ArCH), 7.14 (dd, *J* = 8.9, 2.6 Hz, 1H, ArCH), 7.11 (d, *J* = 2.5 Hz, 1H, ArCH), 4.08 (q, *J* = 6.9 Hz, 1H, C(O)CH), 3.91 (s, 3H, OCH₃), 2.42 (t, *J* = 1.1 Hz, 1H, BCB CH₂), 2.42 (t, *J* = 1.1 Hz, 1H, BCB CH₂), 1.97 (p, *J* = 3.2 Hz, 1H, BCB CH), 1.46 (d, *J* = 7.0 Hz, 3H, CHCH₃), 1.10 (dd, *J* = 2.8, 1.3 Hz, 1H, BCB CH₂), 1.07 (dd, *J* = 2.8, 1.4 Hz, 1H, BCB CH₂).

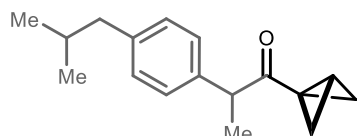
¹³C NMR (126 MHz, CDCl₃) δ 207.1 (C=O), 157.8 (ArC^q), 136.9 (ArC^q), 133.7 (ArC^q), 129.3 (ArCH), 129.2 (ArC^q), 127.6 (ArCH), 126.4 (ArCH), 126.2 (ArCH), 119.2 (ArCH), 105.7 (ArCH), 55.5 (OCH₃), 49.1 (C(O)CH), 35.8 (BCB CH₂), 35.7 (BCB CH₂), 21.7 (CHCH₃), 19.1 (BCB CH), 18.6 (C(O)C^q).

IR (neat, cm⁻¹): 2968, 2933, 2871, 1650, 1602, 1482, 1388, 1369, 1261, 1226, 1193, 1109, 981, 889, 856, 843, 817, 806, 786, 715, 673.

HRMS (ESI⁺): calculated for C₁₈H₁₈O₂Na (M+Na⁺): 289.1199; found: 289.1189.

[α]_D²¹ = +185 ° (c = 0.2 g/100 mL, CHCl₃)

1-(Bicyclo[1.1.0]butan-1-yl)-2-(4-isobutylphenyl)propan-1-one (**11aa**)



Prepared following **general procedure B** (4 mmol scale), **11aa** (246 mg, 1.02 mmol, 25% yield) was obtained after purification by column chromatography (30%-60% CH₂Cl₂ in hexane) as a colourless liquid.

¹H NMR (400 MHz, CDCl₃) δ 7.11 (d, *J* = 8.2 Hz, 2H, ArCH), 7.07 (d, *J* = 8.2 Hz, 2H, ArCH), 3.92 (q, *J* = 6.9 Hz, 1H, CO-CH-CH₃), 2.43 (d, *J* = 7.2 Hz, 2H, CH₂), 2.39 (dt,

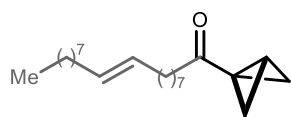
$J = 3.5, 1.1$ Hz, 2H, BCB CH_2), 1.94 (p, $J = 3.1$ Hz, 1H, BCH CH), 1.84 (dp, $J = 13.5, 6.8$ Hz, 1H, $\text{CH}-\text{CH}_2$), 1.38 (d, $J = 6.9$ Hz, 3H, $\text{CO}-\text{CH}-\text{CH}_3$), 1.15 – 1.03 (m, 2H, BCB CH_2), 0.89 (d, $J = 6.6$ Hz, 6H, $2 \times \text{CH}_3$).

^{13}C NMR (101 MHz, CDCl_3) δ 207.2 ($\text{C}=\text{O}$), 140.5 (ArC^q), 138.9 (ArC^q), 129.7 ($2 \times \text{ArCH}$), 127.4 ($2 \times \text{ArCH}$), 48.7 ($\text{CO}-\text{CH}-\text{CH}_3$), 45.2 (CH_2), 35.7 (BCB CH_2), 35.7 (BCB CH_2), 30.3 ($\text{CO}-\text{CH}-\text{CH}_3$), 22.5 ($2 \times \text{CH}_3$), 21.4 (BCB CH), 19.0 ($\text{CH}-\text{CH}_2$), 18.4 ($\text{C}(\text{O})\text{C}^q$).

IR (neat, cm^{-1}): 2955, 2930, 1662, 1508, 1465, 1452, 1216, 1110, 1076, 1034, 1020, 749, 666.

HRMS (APCI $^+$): calculated for $\text{C}_{17}\text{H}_{23}\text{O}$ ($\text{M}+\text{H}^+$): 243.1743; found: 243.1738.

(*E*)-1-(Bicyclo[1.1.0]butan-1-yl)octadec-9-en-1-one (**11ab**)



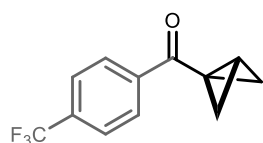
Prepared following **general procedure B** (4 mmol scale), **11ab** (285 mg, 0.89 mmol, 23% yield) was obtained after purification by column chromatography (30%-40% CH_2Cl_2 in hexane) as a colourless liquid.

^1H NMR (400 MHz, CDCl_3) δ 5.48 – 5.22 (m, 2H, $\text{CH}=\text{CH}$), 2.45 – 2.38 (m, 4H, CH_2 and BCB CH_2), 2.13 (p, $J = 3.2$ Hz, 1H, BCB CH), 2.04 – 1.93 (m, 4H, $2 \times \text{CH}_2$), 1.60 (dd, $J = 13.6, 6.4$ Hz, 2H, CH_2), 1.37 – 1.23 (m, 20H, $10 \times \text{CH}_2$), 1.19 (d, $J = 2.8$ Hz, 2H, BCB CH_2), 0.87 (t, $J = 6.7$ Hz, 3H, CH_3).

^{13}C NMR (101 MHz, CDCl_3) δ 207.1 ($\text{C}=\text{O}$), 130.2 ($\text{CH}=\text{CH}$), 130.0 ($\text{CH}=\text{CH}$), 39.1 (COCH_2), 35.8 ($2 \times \text{BCB CH}_2$), 32.1 (CH_2), 30.0 (CH_2), 29.9 (CH_2), 29.7 (CH_2), 29.5 ($3 \times \text{CH}_2$), 29.5 (CH_2), 29.3 (CH_2), 27.4 (CH_2), 27.4 (CH_2), 24.8 (CH_2), 22.9 (CH_2), 19.8 (BCB CH), 18.5 ($\text{C}(\text{O})\text{C}^q$), 14.3 (CH_3).

HRMS (ESI $^+$): calculated for $\text{C}_{22}\text{H}_{39}\text{O}$ ($\text{M}+\text{H}^+$): 319.2995; found: 319.2987.

Bicyclo[1.1.0]butan-1-yl(4-(trifluoromethyl)phenyl)methanone (**11ac**)



Prepared following **general procedure B** (4 mmol scale), **11ac** (258 mg, 1.14 mmol, 28% yield) was obtained after purification by column chromatography (30% CH_2Cl_2 in hexane) as a yellow solid.

^1H NMR (500 MHz, CDCl_3) δ 7.95 (d, $J = 8.0$ Hz, 2H, ArCH), 7.70 (d, $J = 8.1$ Hz, 2H, ArCH), 2.62 (dt, $J = 3.6, 1.2$ Hz, 2H, BCB CH_2), 2.30 (p, $J = 3.4$ Hz, 1H, BCB CH), 1.53 (dt, $J = 3.2, 1.2$ Hz, 2H, BCB CH_2).

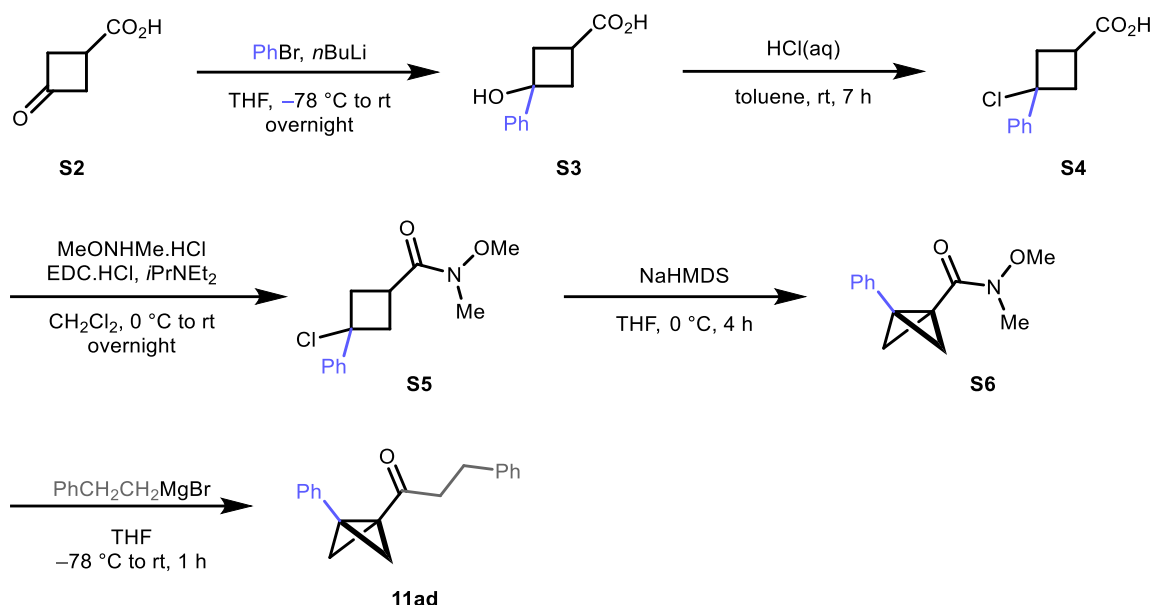
^{19}F NMR (376 MHz, CDCl_3) δ -63.00 (s).

^{13}C NMR (126 MHz, CDCl_3) δ 199.0 ($\text{C}=\text{O}$), 140.8 (ArC^q), 133.7 (q, $J = 32.3$ Hz, ArC^q), 129.1 ($2 \times \text{ArCH}$), 125.4 (q, $J = 3.9$ Hz, $2 \times \text{ArCH}$), 123.8 (q, $J = 271.9$ Hz, CF_3), 38.2 ($2 \times \text{BCB CH}_2$), 22.8 (BCB CH), 17.6 ($\text{C}(\text{O})\text{C}^q$).

IR (neat, cm^{-1}): 2962, 2939, 2855, 1636, 1410, 1318, 1165, 1131, 1108, 1062, 1014, 982, 974, 850, 762, 700, 680.

HRMS (APCI⁺): calculated for C₁₂H₁₀OF₃ (M+H⁺): 227.0678; found: 227.0673.

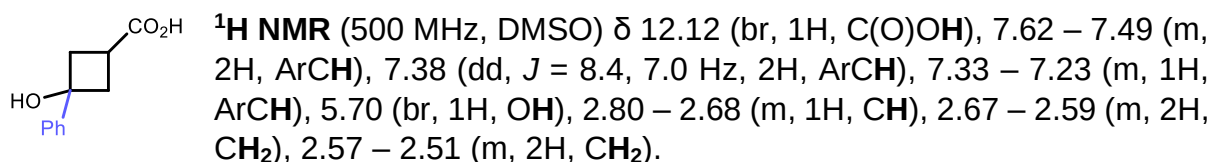
3.4. Synthesis of substituted BCB ketone 11ad



Scheme S3. Synthetic route for substituted BCB ketone starting material

Prepared according to a modified procedure from the literature.⁵

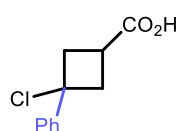
Step-1: To bromobenzene (5.02 mL, 48.0 mmol, 2 equiv.) in THF (0.44 M, 54.5 mL) was added *n*-butyllithium (2.5 M in hexane, 26.9 mL, 67.2 mmol, 2.8 equiv.) dropwise at -78 °C. The reaction was stirred for 2 h before 3-oxocyclobutane-1-carboxylic acid **S2** (2.74 g, 24.0 mmol, 1 equiv.) in THF (1.75 M, 13.7 mL) was added dropwise at -78 °C. The reaction was allowed to warm to room temperature and was stirred overnight. The reaction mixture was quenched with saturated NH₄Cl solution (100 mL) and basified with 4 M NaOH solution (250 mL) and washed with ethyl acetate (350 mL). The layers were separated, and the aqueous layer was acidified with 2 M HCl solution (400 mL). The aqueous layer was extracted with ethyl acetate (500 mL) which was then dried over MgSO₄ and evaporated under reduced pressure to afford 3-hydroxy-3-phenylcyclobutane-1-carboxylic acid **S3** (3.01 g, 15.6 mmol, 65%) as a white solid. The product was used in the next step without further purification.



¹³C NMR (126 MHz, DMSO) δ 175.9 (C(O)OH), 146.7 (ArC^q), 128.1 (2 × ArCH), 126.7 (ArCH), 125.0 (2 × ArCH), 70.9 (C^q), 40.9 (2 × CH₂), 28.7 (CH–C(O)OH).

These data match with those previously reported in the literature.⁵

Step-2: To a solution of 3-hydroxy-3-phenylcyclobutane-1-carboxylic acid **S3** (3.00 g, 15.6 mmol, 1 equiv.) in toluene (0.48 M, 32.5 mL) was added concentrated HCl (37% in water, 0.48 M, 32.5 mL). The resulting mixture was stirred at room temperature for 7 h. The two layers were separated, and the aqueous layer was extracted with toluene. The organic layers were combined and washed with water and brine. The solution was then dried with MgSO₄ and the solvent was removed under vacuum to afford 3-chloro-3-phenylcyclobutane-1-carboxylic acid **S4** (2.49 g, 11.8 mmol, 75%) as a yellowish solid. The product was used in the next step without further purification.

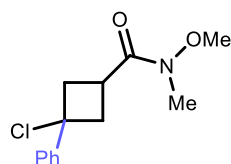


¹H NMR (400 MHz, DMSO) δ 12.42 (br, 1H, C(O)OH), 7.49 – 7.28 (m, 5H, ArCH), 3.53 (p, *J* = 8.7 Hz, 1H, CH), 2.95 (d, *J* = 8.8 Hz, 4H, 2 × CH₂).

¹³C NMR (101 MHz, DMSO) δ 174.8 (C(O)OH), 144.9 (ArC^q), 128.6 (2 × ArCH), 128.0 (ArCH), 126.0 (2 × ArCH), 69.4 (C^q), 41.3 (2 × CH₂), 32.2 (CH–C(O)OH).

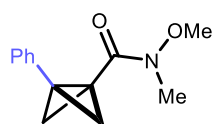
These data match with those previously reported in the literature.⁵

Step-3: To an ice-cooled suspension of *N,O*-dimethylhydroxylamine hydrochloride (988 mg, 10.1 mmol, 1.05 equiv.) and 3-chloro-3-phenylcyclobutane-1-carboxylic acid **S4** (2.03 g, 9.65 mmol, 1 equiv.) in CH₂Cl₂ (0.4 M, 24.1 mL) was added *i*PrNEt₂ (3.36 mL, 19.3 mmol, 2 equiv.). After stirring for 5 min, EDC.HCl (2.03 g, 10.6 mmol, 1.1 equiv.) was added in one portion and the reaction mixture was stirred overnight while allowing it to warm to room temperature. The mixture was diluted with CH₂Cl₂ (25 mL) and was transferred to a separating funnel. The organic layer was washed with saturated aqueous NaHCO₃ (2×25 mL), water (1×50 mL), brine (50 mL), dried (MgSO₄) and concentrated. Column chromatography on silica gel (0-40% EtOAc in hexane) afforded 3-chloro-*N*-methoxy-*N*-methyl-3-phenylcyclobutane-1-carboxamide **S5** (1.72 g, 6.77 mmol, 70%) as a colourless liquid.



¹H NMR (400 MHz, CDCl₃) δ 7.38 – 7.27 (m, 5H, ArCH), 3.73 (s, 3H, CH₃), 3.60 (s, 1H, CH), 3.18 (s, 3H, CH₃), 3.12 – 3.03 (m, 2H, CH₂), 3.01 – 2.89 (m, 2H, CH₂).

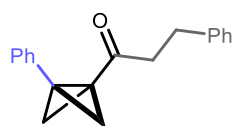
Step-4: A round bottom flask under N₂ atmosphere was charged with 3-chloro-*N*-methoxy-*N*-methyl-3-phenylcyclobutane-1-carboxamide **S5** (1.71 g, 6.75 mmol, 1 equiv.) and THF (0.34 M, 19.8 mL). The solution was cooled to 0 °C and NaHMDS (2 M in THF, 4.05 mL, 8.10 mmol, 1.2 equiv.) was added dropwise and the reaction mixture was stirred at 0 °C for 4 h. The reaction mixture was diluted with CH₂Cl₂ and washed with water. The organic layer was dried with MgSO₄ and the solvent was removed in vacuo. *N*-methoxy-*N*-methyl-3-phenylbicyclo[1.1.0]butane-1-carboxamide **S6** (1.19 g, 5.48 mmol, 81%) was obtained as a yellow solid and used in the next step without further purification.



¹H NMR (400 MHz, CDCl₃) δ 7.37 – 7.27 (m, 4H, ArCH), 7.24 – 7.18 (m, 1H, ArCH), 3.64 (s, 3H, CH₃), 3.10 (s, 3H, CH₃), 2.99 (s, 2H, BCB H₂), 1.59 (s, 2H, BCB CH₂).

Step-5: A round bottom flask under N₂ atmosphere was charged with *N*-methoxy-*N*-methyl-3-phenylbicyclo[1.1.0]butane-1-carboxamide **S6** (217 mg, 1.00 mmol, 1 equiv.) in THF (0.1 M, 10 mL). The solution was cooled to -78 °C and PhCH₂CH₂MgBr (1 M in THF, 3 mL, 3 mmol, 3 equiv.) was added dropwise and the resulting solution was stirred at -78 °C for 15 min and 30 min at room temperature. The reaction was quenched with saturated NH₄Cl solution (10 mL) and then extracted with EtOAc (3×10 mL). The combined organic layers were dried (MgSO₄) and concentrated. The residue was subjected to column chromatography on silica gel (0-10% EtOAc in hexane) to afford the desired product, 3-phenyl-1-(3-phenylbicyclo[1.1.0]butan-1-yl)propan-1-one **11ad** (60.5 mg, 0.23 mmol, 23%) as a white solid.

3-Phenyl-1-(3-phenylbicyclo[1.1.0]butan-1-yl)propan-1-one (**11ad**)



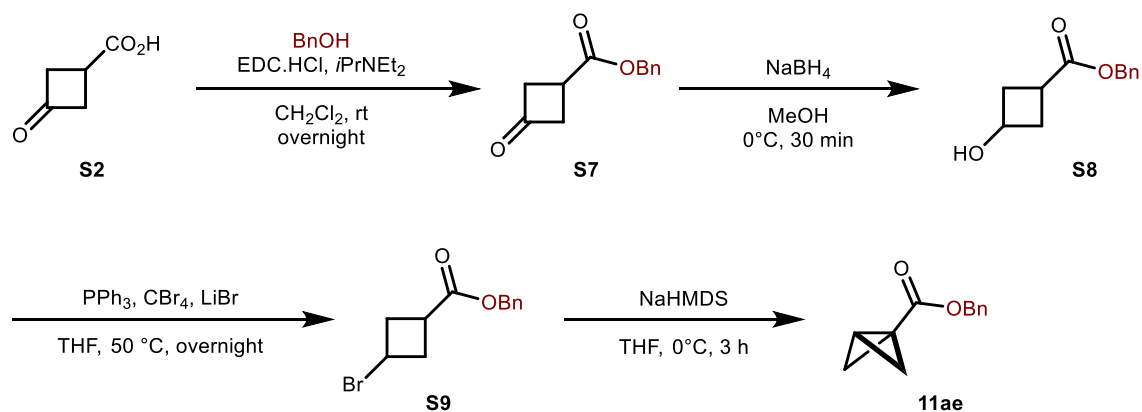
Prepared in 6% yield over 5 steps.

¹H NMR (500 MHz, CDCl₃) δ 7.37 – 7.22 (m, 5H, ArCH), 7.23 – 7.16 (m, 2H, ArCH), 7.16 – 7.10 (m, 1H, ArCH), 7.02 – 6.92 (m, 2H, ArCH), 3.03 (t, *J* = 1.3 Hz, 2H, BCB CH₂), 2.64 (dd, *J* = 8.5, 7.1 Hz, 2H, CH₂), 2.38 (dd, *J* = 8.5, 7.0 Hz, 2H, CH₂), 1.65 (t, *J* = 1.3 Hz, 2H, BCB CH₂).

¹³C NMR (126 MHz, CDCl₃) δ 201.8 (C=O), 141.3 (ArC^q), 133.2 (ArC^q), 128.9 (2 × ArCH), 128.5 (2 × ArCH), 128.3 (2 × ArCH), 127.4 (ArCH), 126.0 (ArCH), 125.7 (2 × ArCH), 41.2 (C(O)CH₂), 37.3 (C^q), 35.7 (2 × BCB CH₂), 32.6 (C^q), 29.5 (PhCH₂).

HRMS (APCI⁺): calculated for C₁₉H₁₉O (M+H⁺): 263.1430; found: 263.1418.

3.5. Synthesis of BCB-ester **11ae**

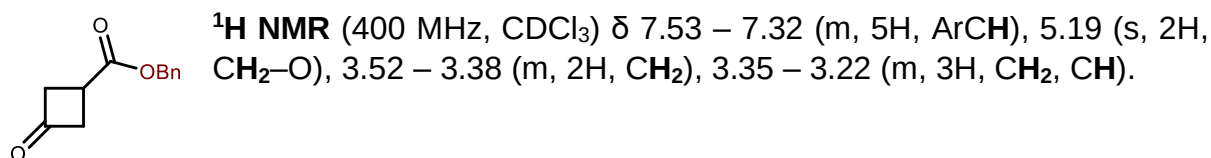


Scheme S4. Synthetic route for BCB-ester starting material

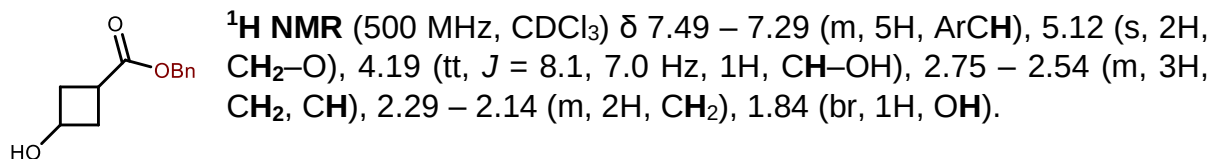
Prepared according to a modified procedure from the literature.⁶

Step-1: To a stirred solution of 3-oxocyclobutane-1-carboxylic acid **S2** (1.88 g, 16.5 mmol, 1.1 equiv.) and EDC.HCl (3.45 g, 18.0 mmol, 1.2 equiv.) in dry CH₂Cl₂ (0.4 M, 37.5 mmol) was added benzyl alcohol (1.56 mL, 15.0 mmol, 1 equiv.) and DMAP (366

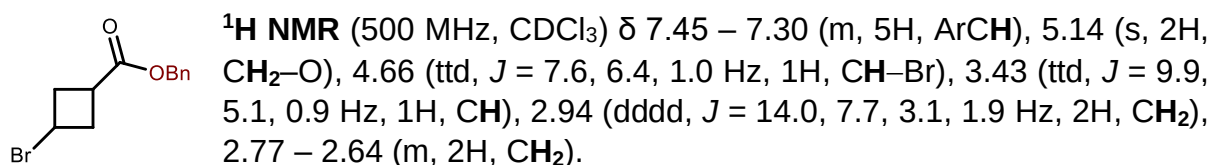
mg, 3.00 mmol, 20 mol%). The resulting mixture was stirred overnight at room temperature then diluted with CH₂Cl₂ and saturated NH₄Cl solution. The separated aqueous layer was extracted twice with CH₂Cl₂, and the combined organic layers were washed with brine, dried (MgSO₄) and concentrated to give benzyl 3-oxocyclobutane-1-carboxylate **S7** as a colourless oil (3.06 g, 15.00 mmol, 100%), which was used in the next step without further purification.



Step-2: To a stirred solution of the above ester **S7** (15.0 mmol, 1 equiv.) in MeOH (3 M, 5 mL) was added NaBH₄ (284 mg, 7.50 mmol, 0.5 equiv.) portionwise at 0 °C. The resulting solution was stirred for 30 min at 0 °C then diluted with saturated NH₄Cl solution. The aqueous layer was extracted three times with CH₂Cl₂, and the combined organic layers were washed with brine, dried over MgSO₄ and concentrated in vacuo. The residue was purified by column chromatography on silica gel (20-40% EtOAc in hexane) to give the desired product, benzyl 3-hydroxycyclobutane-1-carboxylate **S8** as a colourless liquid (2.60 g, 12.6 mmol, 84%).



Step-3: To a stirred solution of the above hydroxy-ester **S8** (2.60 g, 12.6 mmol, 1 equiv.) and PPh₃ (5.95 g, 22.7 mmol, 1.8 equiv.) in dry THF (0.3 M, 42 mL) was added CBr₄ (7.53 g, 22.7 mmol, 1.8 equiv.) and LiBr (2.08 g, 24.0 mmol, 1.9 equiv.) and the resulting mixture was stirred overnight at 50 °C. The reaction mixture was then diluted with Et₂O and solid materials were removed by filtration through a pad of celite. The filtrate was washed with water and brine, dried over MgSO₄ and concentrated in vacuo. The residue was purified by column chromatography on silica gel (0-5% EtOAc in hexane) to give the desired product, benzyl 3-bromocyclobutane-1-carboxylate **S9** as a colourless liquid (2.19 g, 8.14 mmol, 64%).

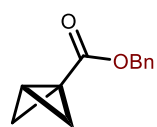


These data match with those previously reported in the literature.⁶

Step-4: To a stirred solution of the above bromo-ester **S9** (606 mg, 2.25 mmol, 1 equiv.) in dry THF (0.2 M, 11.2 mL) was added NaHMDS (2 M in THF, 1.16 mL, 2.32 mmol, 1.03 equiv.) dropwise at 0 °C and the resulting mixture was stirred for 3 h at 0 °C. The reaction was then quenched with saturated NH₄Cl solution and the aqueous phase was extracted three times with Et₂O. The combined organic layers were washed

with brine, dried over MgSO_4 and concentrated in vacuo (at room temperature). The residue was purified by column chromatography on silica gel (0-4% EtOAc in hexane) to give the desired product, benzyl bicyclo[1.1.0]butane-1-carboxylate **11ae**, as a colourless liquid (289 mg, 1.54 mmol, 68%).

Benzyl bicyclo[1.1.0]butane-1-carboxylate (**11ae**)



Prepared in 36% yield over 4 steps.

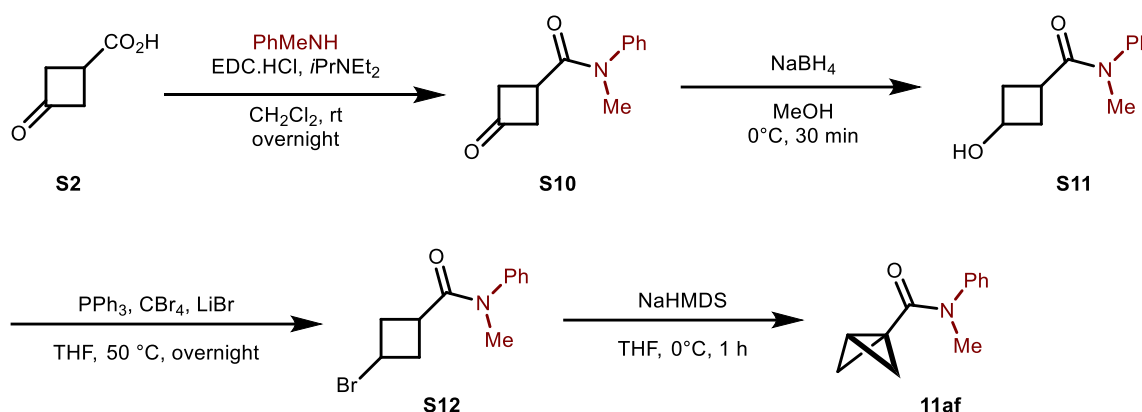
^1H NMR (500 MHz, CDCl_3) δ 7.42 – 7.29 (m, 5H, ArCH), 5.15 (s, 2H, $\text{CH}_2\text{—O}$), 2.39 (dt, $J = 3.5, 1.0$ Hz, 2H, BCB CH_2), 2.10 (p, $J = 3.1$ Hz, 1H, BCB CH), 1.17 (dt, $J = 2.9, 1.0$ Hz, 2H, BCB CH_2).

^{13}C NMR (126 MHz, CDCl_3) δ 173.1 (C(O)O), 136.4 (ArC^q), 128.7 (2 $\times$ ArCH), 128.3 (ArCH), 128.1 (2 $\times$ ArCH), 66.5 ($\text{CH}_2\text{—O}$), 35.8 (2 $\times$ BCB CH_2), 17.0 (BCB CH), 9.3 (BCB C^q).

IR (neat, cm^{-1}): 2944, 2894, 1705, 1497, 1455, 1405, 1359, 1191, 1131, 1179, 1019, 846, 827, 747, 695.

HRMS (APCI⁺): calculated for $\text{C}_{12}\text{H}_{13}\text{O}_2$ ($\text{M}+\text{H}^+$): 189.0910; found: 189.0905.

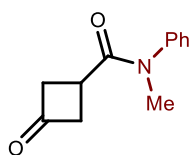
3.6. Synthesis of BCB-amide **11af**



Scheme S5. Synthetic route for BCB-amide starting material

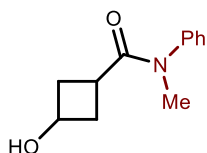
Prepared according to a modified procedure from the literature.⁶

Step-1: To a stirred solution of 3-oxocyclobutane-1-carboxylic acid **S2** (1.88 g, 16.5 mmol, 1.1 equiv.) and EDC.HCl (3.45 g, 18.0 mmol, 1.2 equiv.) in dry CH_2Cl_2 (0.4 M, 37.5 mmol) was added *N*-methylaniline (1.63 mL, 15.0 mmol, 1 equiv.) and DMAP (366 mg, 3 mmol, 20 mol%). The resulting mixture was stirred overnight at room temperature then diluted with CH_2Cl_2 and saturated NH_4Cl solution. The separated aqueous layer was extracted twice with CH_2Cl_2 and the combined organic layers were washed with brine, dried (MgSO_4) and concentrated to give the desired product, *N*-methyl-3-oxo-*N*-phenylcyclobutane-1-carboxamide **S10** as a colourless oil (3.05 g, 15.0 mmol, 100%), which was used in the next step without further purification.



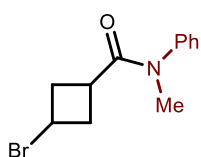
¹H NMR (400 MHz, CDCl₃) δ 7.45 (t, *J* = 7.8 Hz, 2H, ArCH), 7.42 – 7.34 (m, 1H, ArCH), 7.21 – 7.14 (m, 2H, ArCH), 3.55 – 3.43 (m, 2H, CH₂), 3.33 (s, 3H, CH₃), 3.11 – 2.98 (m, 1H, CH), 2.96 – 2.78 (m, 2H, CH₂).

Step-2: To a stirred solution of the above amide **S10** (15.0 mmol, 1 equiv.) in MeOH (3 M, 5 mL) was added NaBH₄ (284 mg, 7.50 mmol, 0.5 equiv.) portionwise at 0 °C. The resulting solution was stirred for 30 min at 0 °C then diluted with saturated NH₄Cl solution. The aqueous layer was extracted three times with CH₂Cl₂ and the combined organic layers were washed with brine, dried over MgSO₄ and concentrated in vacuo. The residue was purified by column chromatography on silica gel (5-30% acetone in CH₂Cl₂) to give the desired product, 3-hydroxy-*N*-methyl-*N*-phenylcyclobutane-1-carboxamide **S11** as a white solid (2.49 g, 12.1 mmol, 81%).



¹H NMR (500 MHz, CDCl₃) δ 7.46 – 7.39 (m, 2H, ArCH), 7.37 – 7.32 (m, 1H, ArCH), 7.15 – 7.09 (m, 2H, ArCH), 3.96 (p, *J* = 7.1 Hz, 1H, CH–OH), 3.27 (s, 3H, CH₃), 2.49 (p, *J* = 8.1 Hz, 1H, CH), 2.33 – 2.12 (m, 5H, 2 × CH₂, OH).

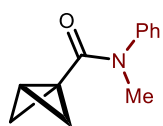
Step-3: To a stirred solution of the above hydroxy-amide **S11** (2.49 g, 12.1 mmol, 1 equiv.) and PPh₃ (5.73 g, 21.8 mmol, 1.8 equiv.) in dry THF (0.3 M, 40.4 mL) was added CBr₄ (7.24 g, 21.8 mmol, 1.8 equiv.) and LiBr (2.00 g, 23.1 mmol, 1.9 equiv.) and the resulting mixture was stirred overnight at 50 °C. The reaction mixture was then diluted with Et₂O and solid materials were removed by filtration through a pad of celite. The filtrate was washed with water and brine, dried over MgSO₄ and concentrated in vacuo. The residue was purified by column chromatography on silica gel (0-30% EtOAc in hexane) to give the desired product, 3-bromo-*N*-methyl-*N*-phenylcyclobutane-1-carboxamide **S12** as a yellow liquid (2.19 g, 8.14 mmol, 64%).



¹H NMR (400 MHz, CDCl₃) δ 7.47 – 7.38 (m, 2H, ArCH), 7.38 – 7.31 (m, 1H, ArCH), 7.11 – 7.05 (m, 2H, ArCH), 4.66 (ttd, *J* = 7.7, 5.6, 0.8 Hz, 1H, CH–Br), 3.35 – 3.27 (m, 1H, CH), 3.27 (s, 3H, CH₃), 2.94 (dddd, *J* = 15.3, 7.3, 3.1, 1.5 Hz, 2H, CH₂), 2.43 – 2.28 (m, 2H, CH₂).

Step-4: To a stirred solution of the above bromo-amide **S12** (1.07 g, 4.00 mmol, 1 equiv.) in dry THF (0.2 M, 20 mL) was added NaHMDS (2 M in THF, 2.06 mL, 4.12 mmol, 1.03 equiv.) dropwise at 0 °C and the resulting mixture was stirred for 1 h at 0 °C. The reaction was then quenched with saturated NH₄Cl solution and the aqueous phase was extracted three times with Et₂O. The combined organic layers were washed with brine, dried over MgSO₄ and concentrated in vacuo (at room temperature). The residue was purified by column chromatography on silica gel (0-30% EtOAc in hexane) to give the desired product, *N*-methyl-*N*-phenylbicyclo[1.1.0]butane-1-carboxamide **11af**, as a colourless liquid (544 mg, 2.91 mmol, 73%).

N-Methyl-*N*-phenylbicyclo[1.1.0]butane-1-carboxamide (**11af**)



Prepared in 38% yield over 4 steps.

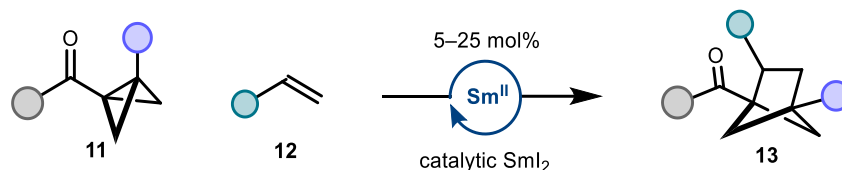
¹H NMR (500 MHz, CDCl₃) δ 7.41 – 7.34 (m, 2H, ArCH), 7.29 – 7.21 (m, 3H, ArCH), 3.35 (s, 3H, CH₃), 2.03 (ddd, *J* = 5.8, 3.3, 2.5 Hz, 1H, BCB CH), 1.82 (d, *J* = 3.3 Hz, 2H, BCB CH₂), 0.78 (d, *J* = 2.4 Hz, 2H, BCB CH₂).

¹³C NMR (126 MHz, CDCl₃) δ 171.9 (C(O)N), 145.3 (ArC^q), 129.3 (2 × ArCH), 127.0 (2 × ArCH), 126.6 (ArCH), 38.1 (N–CH₃), 37.2 (2 × BCB CH₂), 17.0 (BCB CH), 10.2 (C^q).

These data match with those previously reported in the literature.⁶

4. SmI₂-catalyzed intermolecular coupling

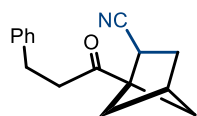
4.1. General Procedure C



An oven-dried microwave reaction vial was charged with a magnetic stirring-bar and BCB-ketone **11a-11af** (0.1 mmol, 1 equiv.). The vial was sealed and flushed with N₂. After 15 min, alkene **12a-12w** (0.25 mmol, 2.5 equiv.) and THF (0.2 M, 0.5 mL) were sequentially added by syringe and the vial was placed at -10 °C in a cold bath. Freshly prepared SmI₂ (0.1 M, typically 25 mol%, 0.25 mL) was added dropwise and the reaction mixture was stirred at -10 °C for 15 min. The reaction mixture was then filtered through a silica gel pad washing with CH₂Cl₂ (3 × 5 mL) or EtOAc (3 × 5 mL). Excess solvent was removed in vacuo and the desired compounds **13a-aaa** were obtained without further purification. In some cases, the final products were purified by column chromatography using silica gel.

4.2. Characterization Data

rac-1-(3-Phenylpropanoyl)bicyclo[2.1.1]hexane-2-carbonitrile (**13a**)



Prepared by following the **general procedure C** from **11a** (0.10 mmol), **12a** (0.25 mmol), and SmI₂ (25 mol%). The reaction mixture was filtered through a silica gel pad and concentrated in vacuo. The crude product was purified by column chromatography (0-6% EtOAc in hexane) to afford **13a** (19.1 mg, 0.08 mmol, 80% yield) as a white solid.

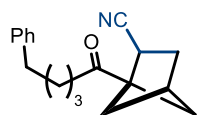
¹H NMR (500 MHz, CDCl₃) δ 7.32 – 7.27 (m, 2H, ArCH), 7.23 – 7.17 (m, 3H, ArCH), 3.04 (ddd, *J* = 9.2, 3.9, 1.9 Hz, 1H, CH–CN), 2.98 – 2.82 (m, 4H, CH₂), 2.59 (tt, *J* = 2.9, 1.4 Hz, 1H, BCH CH), 2.26 (dddd, *J* = 11.6, 9.2, 2.5, 1.4 Hz, 1H, BCH CH₂), 2.05 (ddt, *J* = 3.1, 2.0, 1.3 Hz, 1H, BCH CH₂), 2.04 – 2.01 (m, 1H, BCH CH₂), 1.94 (dt, *J* = 7.4, 2.9 Hz, 1H, BCH CH₂), 1.68 (dd, *J* = 9.9, 7.8 Hz, 1H, BCH CH₂), 1.32 (dd, *J* = 9.9, 7.5 Hz, 1H, BCH CH₂).

¹³C NMR (126 MHz, CDCl₃) δ 206.9 (C=O), 140.9 (ArC^q), 128.7 (2 × ArCH), 128.5 (2 × ArCH), 126.4 (ArCH), 121.7 (C≡N), 62.8 (C^q), 43.0 (C(O)CH₂), 41.7 (BCH CH₂), 39.2 (BCH CH₂), 36.4 (BCH CH), 34.9 (BCH CH₂), 29.8 (CH–CN), 29.4 (PhCH₂).

IR (neat, cm⁻¹): 2986, 2954, 2237, 1697, 1496, 1453, 1367, 1269, 749, 699.

HRMS (ESI⁺): calculated for C₁₆H₁₇ONNa (M+Na⁺): 262.1202; found: 262.1201.

rac-1-(5-Phenylpentanoyl)bicyclo[2.1.1]hexane-2-carbonitrile (**13b**)



Prepared by following the **general procedure C** from **11b** (0.10 mmol), **12a** (0.25 mmol), and SmI_2 (25 mol%). The reaction mixture was filtered through a silica gel pad and concentrated in vacuo. The crude product was purified by column chromatography (0-6% EtOAc in hexane) to afford **13b** (20.0 mg, 0.074 mmol, 74% yield) as a colourless liquid.

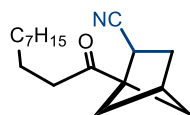
^1H NMR (400 MHz, CDCl_3) δ 7.31 – 7.25 (m, 2H, ArCH), 7.18 (dt, J = 7.6, 3.2 Hz, 3H, ArCH), 3.04 (ddd, J = 9.2, 3.9, 1.9 Hz, 1H, CH–CN), 2.66 – 2.54 (m, 5H, BCH CH, COCH₂, and PhCH₂), 2.27 (ddt, J = 11.3, 9.3, 1.9 Hz, 1H, BCH CH₂), 2.11 – 2.01 (m, 2H, BCH CH₂), 1.97 (dt, J = 7.4, 2.9 Hz, 1H, BCH CH₂), 1.70 (dd, J = 9.9, 7.8 Hz, 1H, BCH CH₂), 1.68 – 1.61 (m, 4H, PhCH₂CH₂CH₂), 1.35 (dd, J = 9.9, 7.4 Hz, 1H, BCH CH₂).

^{13}C NMR (101 MHz, CDCl_3) δ 207.7 (C=O), 142.3 (ArC^q), 128.5 (2 × ArCH), 128.4 (2 × ArCH), 125.9 (ArCH), 121.8 (C≡N), 62.7 (C(O)C^q), 43.1 (BCH CH₂), 39.8 (COCH₂), 39.2 (BCH CH₂), 36.3 (BCH CH), 35.9 (PhCH₂), 35.0 (BCH CH₂), 31.0 (CH₂), 29.9 (CH–CN), 22.8 (CH₂).

IR (neat, cm^{-1}): 2987, 2935, 2883, 2238, 1697, 1495, 1453, 1372, 749, 699.

HRMS (ESI⁺): calculated for $\text{C}_{18}\text{H}_{22}\text{NO}$ ($\text{M}+\text{H}^+$): 268.1696; found: 268.1690.

rac-1-Decanoylbicyclo[2.1.1]hexane-2-carbonitrile (**13c**)



Prepared by following the **general procedure C** from **11c** (0.10 mmol), **12a** (0.25 mmol), and SmI_2 (17 mol%). The reaction mixture was filtered through a silica gel pad and concentrated in vacuo. The crude product was purified by column chromatography (0-4% EtOAc in hexane) to afford **13c** (23.0 mg, 0.088 mmol, 88% yield) as a colourless liquid.

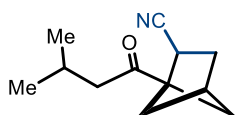
^1H NMR (400 MHz, CDCl_3) δ 3.05 (ddd, J = 9.2, 3.9, 1.9 Hz, 1H, CH–CN), 2.60 (t, J = 3.1 Hz, 1H, BCH CH), 2.58 – 2.50 (m, 2H, COCH₂), 2.27 (ddt, J = 11.1, 9.2, 1.9 Hz, 1H, BCH CH₂), 2.09 (dq, J = 7.7, 2.5 Hz, 1H, BCH CH₂), 2.07 – 2.02 (m, 1H, BCH CH₂), 1.99 (dt, J = 7.4, 2.9 Hz, 1H, BCH CH₂), 1.71 (dd, J = 9.9, 7.8 Hz, 1H, BCH CH₂), 1.58 (p, J = 7.0 Hz, 2H, CH₂), 1.37 (dd, J = 9.9, 7.4 Hz, 1H, BCH CH₂), 1.33 – 1.15 (m, 12H, 6 × CH₂), 0.87 (t, J = 6.7 Hz, 3H, CH₃).

^{13}C NMR (101 MHz, CDCl_3) δ 208.0 (C=O), 121.8 (C≡N), 62.8 (C(O)C^q), 43.1 (BCH CH₂), 40.0 (COCH₂), 39.2 (BCH CH₂), 36.3 (BCH CH), 35.0 (BCH CH₂), 32.0 (CH₂), 29.9 (CH–CN), 29.6 (2 × CH₂), 29.4 (CH₂), 29.3 (CH₂), 23.2 (CH₂), 22.8 (CH₂), 14.2 (CH₃).

IR (neat, cm^{-1}): 2953, 2923, 2853, 2238, 1699, 1457, 1375, 1269.

HRMS (ESI⁺): calculated for $\text{C}_{17}\text{H}_{27}\text{ONa}$ ($\text{M}+\text{Na}^+$): 284.1985; found: 284.1973.

rac-1-(3-Methylbutanoyl)bicyclo[2.1.1]hexane-2-carbonitrile (**13d**)



Prepared by following the **general procedure C** from **11d** (0.10 mmol), **12a** (0.25 mmol), and Sml_2 (25 mol%). The reaction mixture was filtered through a silica gel pad and concentrated in vacuo.

The crude product was purified by column chromatography (0-4% EtOAc in hexane) to afford **13d** (14.1 mg, 0.074 mmol, 74% yield) as a colourless liquid.

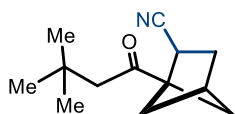
^1H NMR (400 MHz, CDCl_3) δ 3.05 (ddt, J = 9.2, 3.6, 1.5 Hz, 1H, CH–CN), 2.60 (td, J = 3.0, 1.5 Hz, 1H, BCH CH), 2.46 – 2.38 (m, 2H, COCH_2), 2.31 – 2.23 (m, 1H, BCH CH_2), 2.23 – 2.14 (m, 1H, COCH_2CH), 2.11 – 2.01 (m, 2H, BCH CH_2), 2.01 – 1.95 (m, 1H, BCH CH_2), 1.73 – 1.67 (m, 1H, BCH CH_2), 1.39 – 1.33 (m, 1H, BCH CH_2), 0.93 (d, J = 4.8 Hz, 3H, CH_3), 0.92 (d, J = 3.8 Hz, 3H, CH_3).

^{13}C NMR (101 MHz, CDCl_3) δ 207.7 ($\text{C}=\text{O}$), 121.7 ($\text{C}\equiv\text{N}$), 63.0 ($\text{C}(\text{O})\text{C}^q$), 48.7 (COCH_2), 43.0 (BCH CH_2), 39.1 (BCH CH_2), 36.3 (BCH CH), 35.0 (BCH CH_2), 29.8 (CH–CN), 24.1 (COCH_2CH), 22.7 (CH_3), 22.7 (CH_3).

IR (neat, cm^{-1}): 2956, 2873, 2238, 1696, 1467, 1367, 1156, 1046, 752.

HRMS (ESI^+): calculated for $\text{C}_{12}\text{H}_{18}\text{ON}$ ($\text{M}+\text{H}^+$): 192.1383; found: 192.1381.

rac-1-(3,3-Dimethylbutanoyl)bicyclo[2.1.1]hexane-2-carbonitrile (**13e**)



Prepared by following the **general procedure C** from **11e** (0.10 mmol), **12a** (0.25 mmol), and Sml_2 (10 mol%). The reaction mixture was filtered through a silica gel pad and concentrated in vacuo.

The crude product was purified by column chromatography (0-4% EtOAc in hexane) to afford **13e** (18.0 mg, 0.086 mmol, 86% yield) as a colourless liquid.

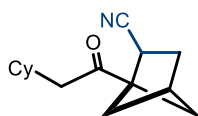
^1H NMR (400 MHz, CDCl_3) δ 3.04 (dtd, J = 9.5, 3.8, 1.8 Hz, 1H, CH–CN), 2.59 (dq, J = 3.0, 1.5 Hz, 1H, BCH CH), 2.51 – 2.35 (m, 2H, COCH_2), 2.32 – 2.18 (m, 1H, BCH CH_2), 2.20 – 1.84 (m, 3H, BCH CH_2 and BCH CH_2), 1.69 (ddd, J = 9.7, 7.8, 3.5 Hz, 1H, BCH CH_2), 1.34 (ddd, J = 10.6, 7.3, 3.6 Hz, 1H, BCH CH_2), 1.03 (s, 9H, 3 $\times$ CH_3).

^{13}C NMR (101 MHz, CDCl_3) δ 207.7 ($\text{C}=\text{O}$), 121.8 ($\text{C}\equiv\text{N}$), 63.7 ($\text{C}(\text{O})\text{C}^q$), 51.2 (COCH_2), 43.0 (BCH CH_2), 39.3 (BCH CH_2), 36.3 (BCH CH), 35.0 (BCH CH_2), 31.2 (CH–CN), 29.8 ($\text{C}^q(\text{CH}_3)_3$), 29.7 (3 $\times$ CH_3).

IR (neat, cm^{-1}): 2953, 2906, 2883, 2238, 1698, 1464, 1363, 1267, 1216.

HRMS (ESI^+): calculated for $\text{C}_{13}\text{H}_{19}\text{ONNa}$ ($\text{M}+\text{Na}^+$): 228.1359; found: 228.1350.

rac-1-(2-Cyclohexylacetyl)bicyclo[2.1.1]hexane-2-carbonitrile (**13f**)



Prepared by following the **general procedure C** from **11f** (0.10 mmol), **12a** (0.25 mmol), and Sml_2 (25 mol%). The reaction mixture was filtered through a silica gel pad and concentrated in vacuo. The

crude product was purified by column chromatography (0-5% EtOAc in hexane) to afford **13f** (17.0 mg, 0.074 mmol, 74% yield) as a colourless liquid.

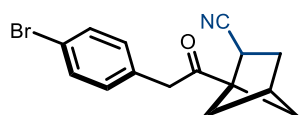
¹H NMR (400 MHz, CDCl₃) δ 3.05 (ddd, *J* = 9.1, 3.9, 1.9 Hz, 1H, CH–CN), 2.60 (tt, *J* = 2.9, 1.4 Hz, 1H, BCH CH), 2.41 (d, *J* = 6.7 Hz, 2H, COCH₂), 2.27 (ddt, *J* = 11.3, 9.4, 1.7 Hz, 1H, BCH CH₂), 2.08 (dq, *J* = 7.9, 2.6 Hz, 1H, BCH CH₂) 2.06 – 2.01 (m, 1H, BCH CH₂), 1.98 (dt, *J* = 7.4, 2.9 Hz, 1H, BCH CH₂), 1.88 (tdq, *J* = 13.4, 6.7, 3.3 Hz, 1H, cyclohexyl CH), 1.73 – 1.60 (m, 6H, 3 × cyclohexyl CH₂), 1.35 (dd, *J* = 9.9, 7.4 Hz, 1H, BCH CH₂), 1.26 (ddt, *J* = 13.2, 7.1, 3.1 Hz, 2H, BCH CH₂ and cyclohexyl CH₂), 1.19 – 1.06 (m, 1H, cyclohexyl CH₂), 0.99 – 0.85 (m, 2H, cyclohexyl CH₂).

¹³C NMR (101 MHz, CDCl₃) δ 207.7 (C=O), 121.8 (C≡N), 63.1 (C(O)C^q), 47.4 (COCH₂), 43.0 (BCH CH₂), 39.1 (BCH CH₂), 36.3 (BCH CH), 35.0 (BCH CH₂), 33.3 (cyclohexyl CH₂), 33.3 (cyclohexyl CH₂), 29.8 (CH–CN), 26.3 (cyclohexyl CH₂), 26.2 (cyclohexyl CH₂), 26.2 (cyclohexyl CH₂). cyclohexyl CH not observed.

IR (neat, cm⁻¹): 2921, 2850, 2238, 1696, 1448, 1376, 1359, 753.

HRMS (ESI⁺): calculated for C₁₅H₂₁ONNa (M+Na⁺): 254.1515; found: 254.1505.

rac-1-(2-(4-Bromophenyl)acetyl)bicyclo[2.1.1]hexane-2-carbonitrile (**13g**)



Prepared by following the **general procedure C** from **11g** (0.10 mmol), **12a** (0.25 mmol), and Sml₂ (25 mol%). The reaction mixture was filtered through a silica gel pad and concentrated in vacuo. The crude product was purified by

column chromatography (0-12% EtOAc in hexane) to afford **13g** (21.3 mg, 0.07 mmol, 70% yield) as a colourless liquid.

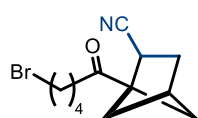
¹H NMR (500 MHz, CDCl₃) δ 7.54 – 7.42 (m, 2H, ArCH), 7.15 – 7.02 (m, 2H, ArCH), 3.84 (s, 2H, C(O)CH₂), 3.04 (ddd, *J* = 9.1, 3.9, 1.9 Hz, 1H, CH–CN), 2.61 (tt, *J* = 2.9, 1.4 Hz, 1H, BCH CH), 2.27 (dddd, *J* = 11.5, 9.1, 2.5, 1.3 Hz, 1H, BCH CH₂), 2.09 (dq, *J* = 7.6, 2.5 Hz, 1H, BCH CH₂), 2.07 – 2.03 (m, 1H, BCH CH₂), 2.00 (dt, *J* = 7.5, 2.9 Hz, 1H, BCH CH₂), 1.72 (dd, *J* = 9.9, 7.8 Hz, 1H, BCH CH₂), 1.36 (dd, *J* = 9.9, 7.5 Hz, 1H, BCH CH₂).

¹³C NMR (126 MHz, CDCl₃) δ 204.6 (C=O), 132.1 (ArC^q), 131.9 (2 × ArCH), 131.4 (2 × ArCH), 121.6 (ArC^q–Br), 121.4 (C≡N), 62.7 (C(O)C^q), 46.3 (C(O)CH₂), 43.4 (BCH CH₂), 39.6 (BCH CH₂), 36.4 (BCH CH), 34.9 (BCH CH₂), 30.2 (CH–CN).

IR (neat, cm⁻¹): 2989, 2956, 2883, 2238 (C≡N), 1700 (C=O), 1488, 1340, 1070, 1011, 757.

HRMS (ESI⁺): calculated for C₁₅H₁₄ONBrNa (M+Na⁺): 326.0151; found: 326.0143

rac-1-(5-Bromopentanoyl)bicyclo[2.1.1]hexane-2-carbonitrile (**13h**)



Prepared by following the **general procedure C** from **11h** (0.10 mmol), **12a** (0.25 mmol), and Sml₂ (25 mol%). The reaction mixture was filtered through a silica gel pad and concentrated in vacuo. The

crude product was purified by column chromatography (0-10% EtOAc in hexane) to afford **13h** (18.0 mg, 0.067 mmol, 67% yield) as a colourless liquid.

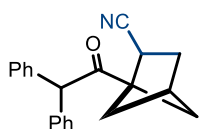
¹H NMR (400 MHz, CDCl₃) δ 3.41 (t, *J* = 6.5 Hz, 2H, BrCH₂), 3.06 (ddd, *J* = 9.2, 3.9, 1.9 Hz, 1H, CH–CN), 2.65 – 2.54 (m, 3H, BCH CH, C(O)CH₂), 2.34 – 2.22 (m, 1H, BCH CH₂), 2.13 – 2.02 (m, 2H, BCH CH₂, BCH CH₂), 2.00 (dt, *J* = 7.4, 2.9 Hz, 1H, BCH CH₂), 1.93 – 1.82 (m, 2H, BCH CH₂ and CH₂), 1.81 – 1.67 (m, 3H, CH₂ and CH₂), 1.38 (dd, *J* = 9.9, 7.4 Hz, 1H, BCH CH₂).

¹³C NMR (101 MHz, CDCl₃) δ 207.2 (C=O), 121.7 (C≡N), 62.7 (C(O)C^q), 43.1 (BCH CH₂), 39.3 (BCH CH₂), 38.9 (COCH₂), 36.3 (BCH CH), 35.0 (BCH CH₂), 33.3 (CH₂Br), 32.1 (CH₂CH₂Br), 29.9 (CH–CN), 21.8 (COCH₂CH₂).

IR (neat, cm⁻¹): 2987, 2955, 2883, 2237, 1697, 1455, 1374, 1269, 1251, 750.

HRMS (ESI⁺): calculated for C₁₂H₁₆ONBrNa (M+Na⁺): 292.0307; found: 292.0295.

rac-1-(2,2-Diphenylacetyl)bicyclo[2.1.1]hexane-2-carbonitrile (**13i**)



Prepared by following the **general procedure C** from **11i** (0.10 mmol), **12a** (0.25 mmol), and Sml₂ (17 mol%). The reaction mixture was filtered through a silica gel pad and concentrated in vacuo. The crude product was purified by column chromatography (0-8% EtOAc in hexane) to afford **13i** (27.2 mg, 0.09 mmol, 90% yield) as a white solid.

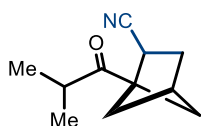
¹H NMR (400 MHz, CDCl₃) δ 7.34 (td, *J* = 7.4, 3.4 Hz, 4H, ArCH), 7.31 – 7.20 (m, 6H, ArCH), 5.45 (s, 1H, COCH), 3.03 (ddd, *J* = 9.2, 3.9, 1.9 Hz, 1H, CH–CN), 2.58 – 2.49 (m, 1H, BCH CH), 2.21 (tt, *J* = 8.9, 2.2 Hz, 1H, BCH CH₂), 2.02 – 1.90 (m, 3H, BCH CH₂ and BCH CH₂), 1.57 (dd, *J* = 9.9, 8.0 Hz, 1H, BCH CH₂), 1.33 – 1.25 (m, 1H, BCH CH₂).

¹³C NMR (101 MHz, CDCl₃) δ 205.4 (C=O), 137.7 (ArC^q), 137.4 (ArC^q), 129.2 (2 × ArCH), 129.2 (2 × ArCH), 129.0 (2 × ArCH), 128.9 (2 × ArCH), 127.6 (ArCH), 127.6 (ArCH), 121.6 (C≡N), 63.1 (C(O)C^q), 61.5 (COCH), 44.1 (BCH CH₂), 39.7 (BCH CH₂), 36.3 (BCH CH), 34.9 (BCH CH₂), 30.5 (CH–CN).

IR (neat, cm⁻¹): 2989, 2955, 2237, 1698, 1494, 1452, 1044, 1032, 735, 698, 615.

HRMS (ESI⁺): calculated for C₂₁H₁₉ONNa (M+Na⁺): 324.1359; found: 324.1350.

rac-1-Isobutyrylbicyclo[2.1.1]hexane-2-carbonitrile (**13j**)



Prepared by following the **general procedure C** from **11j** (0.10 mmol), **12a** (0.25 mmol), and Sml₂ (7.5 mol%). The reaction mixture was filtered through a silica gel pad and concentrated in vacuo to afford the final product **13j** (15.0 mg, 0.084 mmol, 84% yield) as a colourless liquid.

¹H NMR (400 MHz, CDCl₃) δ 3.11 (ddd, *J* = 9.1, 3.8, 1.9 Hz, 1H, CH–CN), 2.97 (p, *J* = 6.8 Hz, 1H, COCH), 2.62 (dq, *J* = 3.0, 1.4 Hz, 1H, BCH CH), 2.33 – 2.22 (m, 1H, BCH CH₂), 2.15 (dq, *J* = 7.6, 2.5 Hz, 1H, BCH CH₂), 2.09 – 1.98 (m, 2H, BCH CH₂),

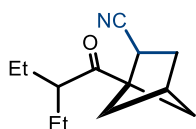
1.74 (dd, $J = 9.8, 7.8$ Hz, 1H, BCH CH₂), 1.39 (dd, $J = 9.8, 7.4$ Hz, 1H, BCH CH₂), 1.10 (d, $J = 6.8$ Hz, 3H, CH₃), 1.09 (d, $J = 6.9$ Hz, 3H, CH₃).

¹³C NMR (101 MHz, CDCl₃) δ 211.7 (C=O), 121.8 (C $\equiv$ N), 62.6 (C(O)C^q), 43.6 (BCH CH₂), 39.3 (BCH CH₂), 37.4 (COCH), 36.6 (BCH CH), 34.9 (BCH CH₂), 30.1 (CH–CN), 18.4 (CH₃), 18.3 (CH₃).

IR (neat, cm⁻¹): 2971, 2934, 2881, 2238, 1697, 1465, 1383, 1034, 1012, 954.

HRMS (ESI⁺): calculated for C₁₁H₁₆ON (M+H⁺): 178.1226; found: 178.1223.

rac-1-(2-Ethylbutanoyl)bicyclo[2.1.1]hexane-2-carbonitrile (**13k**)



Prepared by following the **general procedure C** from **11k** (0.10 mmol), **12a** (0.25 mmol), and Sml₂ (15 mol%). The reaction mixture was filtered through a silica gel pad and concentrated in vacuo to afford the final product **13k** (20.3 mg, 0.099 mmol, 99% yield) as a colourless liquid.

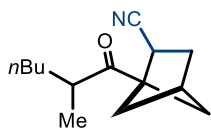
¹H NMR (400 MHz, CDCl₃) δ 3.11 (ddd, $J = 9.2, 3.8, 1.9$ Hz, 1H, CH–CN), 2.72 (tt, $J = 7.5, 5.7$ Hz, 1H, COCH), 2.64 (dp, $J = 2.8, 1.4$ Hz, 1H, BCH CH), 2.27 (tdd, $J = 9.1, 2.6, 1.4$ Hz, 1H, BCH CH₂), 2.21 – 2.14 (m, 1H, BCH CH₂), 2.10 – 1.99 (m, 2H, BCH CH₂), 1.78 – 1.58 (m, 3H, BCH CH₂ and COCHCH₂), 1.51 – 1.38 (m, 2H, COCHCH₂), 1.34 (dd, $J = 9.9, 7.2$ Hz, 1H, BCH CH₂), 0.88 (t, $J = 6.6$ Hz, 3H, CH₃), 0.84 (t, $J = 6.4$ Hz, 3H, CH₃).

¹³C NMR (101 MHz, CDCl₃) δ 211.3 (C=O), 121.9 (C $\equiv$ N), 63.6 (C(O)C^q), 51.4 (COCH), 43.0 (BCH CH₂), 39.1 (BCH CH₂), 36.9 (BCH CH), 34.9 (BCH CH₂), 29.6 (CH–CN), 24.5 (COCHCH₂), 24.0 (COCHCH₂), 12.2 (CH₃), 11.9 (CH₃).

IR (neat, cm⁻¹): 2962, 2878, 2238, 1692, 1458, 1384, 1270, 818.

HRMS (ESI⁺): calculated for C₁₃H₁₉ONNa (M+Na⁺): 228.1359; found: 228.1368.

rac-1-(2-Methylhexanoyl)bicyclo[2.1.1]hexane-2-carbonitrile (**13l**)



Prepared by following the **general procedure C** from **11l** (0.10 mmol), **12a** (0.25 mmol), and Sml₂ (10 mol%). The reaction mixture was filtered through a silica gel pad and concentrated in vacuo to afford **13l** (21.2 mg, 0.096 mmol, 96% yield, d.r. 1:1) as a colourless liquid.

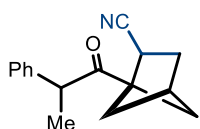
¹H NMR (500 MHz, CDCl₃) δ 3.13 – 3.10 (m, 1H, CH–CN^{d1}), 3.10 – 3.07 (m, 1H, CH–CN^{d2}), 2.86 (p, $J = 7.1$ Hz, 1H, C(O)CH^{d1d2}), 2.68 – 2.60 (m, 1H, BCH CH^{d1d2}), 2.31 – 2.25 (m, 1H, BCH CH₂^{d1d2}), 2.17 – 2.11 (m, 1H, BCH CH₂^{d1d2}), 2.09 – 1.99 (m, 2H, BCH CH₂^{d1d2}), 1.73 (dddd, $J = 10.0, 8.8, 7.7, 1.2$ Hz, 1H, BCH CH₂^{d1d2}), 1.37 (dddd, $J = 10.0, 7.5, 3.9, 1.3$ Hz, 1H, CH₂^{d1d2}), 1.34 – 1.24 (m, 4H, BCH CH₂, CH₂^{d1d2}), 1.24 – 1.14 (m, 2H, CH₂^{d1d2}), 1.07 (ddd, $J = 6.9, 5.6, 1.2$ Hz, 3H, CH₃^{d1d2}), 1.04 (ddd, $J = 7.0, 4.5, 1.2$ Hz, 1H, CH₂^{d1}), 0.88 (td, $J = 7.2, 1.3$ Hz, 3H, CH₃^{d1d2}).

¹³C NMR (126 MHz, CDCl₃) δ 211.7 (C=O)^{d1}, 211.7 (C=O)^{d2}, 121.8 (C≡N)^{d1d2}, 63.0 (C(O)C^q)^{d1}, 63.0 (C(O)C^q)^{d2}, 43.5 (BCH CH₂)^{d1}, 43.2 (BCH CH₂)^{d2}, 42.8 (C(O)CH)^{d1}, 42.7 (C(O)CH)^{d2}, 39.2 (CH₂)^{d1}, 39.1 (CH₂)^{d2}, 36.7 (BCH CH)^{d1}, 36.7 (BCH CH)^{d2}, 34.9 (BCH CH₂)^{d1}, 34.9 (BCH CH₂)^{d2}, 32.8 (CH₂)^{d1}, 32.7 (CH₂)^{d2}, 29.9 (CH–CN)^{d1}, 29.9 (BCH CH₂)^{d1}, 29.8 (CH–CN)^{d2}, 29.6 (BCH CH₂)^{d2}, 22.9 (CH₂CH₃)^{d1}, 22.9 (CH₂CH₃)^{d2}, 16.7 (CHCH₃)^{d1}, 16.7 (CHCH₃)^{d2}, 14.1 (CH₂CH₃)^{d1}, 14.0 (CH₂CH₃)^{d2}.

IR (neat, cm⁻¹): 2957, 2931, 2859, 2238 (C≡N), 1695 (C=O), 1457, 1376, 1266, 951.

HRMS (APCI⁺): calculated for C₁₄H₂₂ON (M+H⁺): 220.1696; found: 220.1690.

rac-1-(2-Phenylpropanoyl)bicyclo[2.1.1]hexane-2-carbonitrile (**13m**)



Prepared by following the **general procedure C** from **11m** (0.10 mmol), **12a** (0.25 mmol), and Sml₂ (20 mol%). The reaction mixture was filtered through a silica gel pad and concentrated in vacuo. The crude product was purified by column chromatography (0-7% EtOAc in hexane) to afford **13m** (24.0 mg, 0.099 mmol, 99% yield) as a white solid and as a 1:1 mixture of diastereomers.

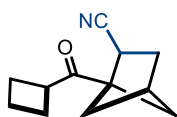
¹H NMR (400 MHz, CDCl₃) δ 7.37 – 7.24 (m, 3H, ArCH^{d1d2}), 7.24 – 7.16 (m, 2H, ArCH^{d1d2}), 4.04 (p, *J* = 6.8 Hz, 1H, COCH^{d1d2}), 3.05 (ddd, *J* = 9.2, 3.7, 1.9 Hz, 1H, CH–CN^{d1}), 2.75 (ddd, *J* = 9.1, 4.0, 1.9 Hz, 1H, CH–CN^{d2}), 2.50 – 2.38 (m, 1H, BCH CH^{d1d2}), 2.20 – 2.07 (m, 1H, BCH CH₂^{d1d2}), 1.99 – 1.86 (m, 2H, BCH CH₂^{d1d2}), 1.84 (dq, *J* = 7.7, 2.5 Hz, 1H, BCH CH₂^{d1}), 1.72 – 1.61 (m, 1H, BCH CH₂^{d1d2}), 1.39 (d, *J* = 6.9 Hz, 3H, CH₃^{d1}), 1.38 (d, *J* = 6.8 Hz, 3H, CH₃^{d2}), 1.31 (dd, *J* = 9.9, 8.0 Hz, 1H, BCH CH₂^{d2}), 1.19 (dd, *J* = 9.8, 7.5 Hz, 1H, BCH CH₂^{d1}), 1.07 (dd, *J* = 9.9, 7.3 Hz, 1H, BCH CH₂^{d2}), 1.39 (d, *J* = 6.9 Hz, 3H, CH₃^{d1}), 1.38 (d, *J* = 6.8 Hz, 3H, CH₃^{d2}).

¹³C NMR (101 MHz, CDCl₃) δ 208.2 (C=O)^{d1}, 206.5 (C=O)^{d2}, 140.2 (ArC^q)^{d1}, 139.5 (ArC^q)^{d2}, 129.2 (2 × ArCH)^{d1}, 129.2 (2 × ArCH)^{d2}, 128.1 (2 × ArCH)^{d1}, 128.1 (2 × ArCH)^{d2}, 127.5 (ArCH)^{d1}, 127.5 (ArCH)^{d2}, 121.6 (C≡N)^{d1d2}, 63.0 (C(O)C^q)^{d1}, 62.4 (C(O)C^q)^{d2}, 50.7 (COCH)^{d1}, 50.4 (COCH)^{d2}, 44.8 (BCH CH₂)^{d1}, 43.4 (BCH CH₂)^{d2}, 39.8 (BCH CH₂)^{d1}, 39.3 (BCH CH₂)^{d2}, 36.3 (BCH CH)^{d1}, 36.1 (BCH CH)^{d2}, 34.8 (BCH CH₂)^{d1}, 34.7 (BCH CH₂)^{d2}, 31.3 (CH–CN)^{d1}, 29.6 (CH–CN)^{d2}, 18.8 (CH₃)^{d1}, 18.7 (CH₃)^{d2}.

IR (neat, cm⁻¹): 2978, 2931, 2883, 2238, 1695, 1452, 1064, 1028, 930, 742, 700.

HRMS (ESI⁺): calculated for C₁₆H₁₇ONNa (M+Na⁺): 262.1202; found: 262.1193.

rac-1-(Cyclobutanecarbonyl)bicyclo[2.1.1]hexane-2-carbonitrile (**13n**)



Prepared by following the **general procedure C** from **11n** (0.10 mmol), **12a** (0.25 mmol), and Sml₂ (5 mol%). The reaction mixture was filtered through a silica gel pad and concentrated in vacuo. The crude product was purified by column chromatography (0-5% EtOAc in hexane) to afford **13n** (17.0 mg, 0.09 mmol, 90% yield) as a colourless liquid.

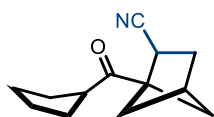
¹H NMR (400 MHz, CDCl₃) δ 3.62 – 3.45 (m, 1H, COCH), 3.07 (ddd, *J* = 9.2, 3.9, 1.9 Hz, 1H, CH–CN), 2.60 (t, *J* = 1.5 Hz, 1H, BCH CH), 2.42 – 2.20 (m, 3H, BCH CH₂ and cyclobutyl CH₂), 2.20 – 2.08 (m, 2H, cyclobutyl CH₂ and BCH CH₂), 2.08 – 1.95 (m, 4H, cyclobutyl CH₂ and BCH CH₂), 1.91 – 1.78 (m, 1H, cyclobutyl CH₂), 1.66 (dd, *J* = 9.9, 7.8 Hz, 1H, BCH CH₂), 1.34 (dd, *J* = 9.9, 7.3 Hz, 1H, BCH CH₂).

¹³C NMR (101 MHz, CDCl₃) δ 208.0 (C=O), 121.9 (C≡N), 61.9 (C(O)C^q), 43.6 (BCH CH₂), 43.1 (cyclobutyl CH), 39.1 (BCH CH₂), 36.7 (BCH CH), 34.8 (BCH CH₂), 29.9 (CH–CN), 24.4 (cyclobutyl CH₂), 24.2 (cyclobutyl CH₂), 17.9 (cyclobutyl CH₂).

IR (neat, cm⁻¹): 2985, 2949, 1689, 1359, 1266, 1215, 1148, 1118, 753.

HRMS (ESI⁺): calculated for C₁₂H₁₆ON (M+H⁺): 190.1226; found: 190.1223.

rac-1-(Cyclopentanecarbonyl)bicyclo[2.1.1]hexane-2-carbonitrile (**13o**)



Prepared by following the **general procedure C** from **11o** (0.10 mmol), **12a** (0.25 mmol), and Sml₂ (17 mol%). The reaction mixture was filtered through a silica gel pad and concentrated in vacuo. The crude product was purified by column chromatography (0-5% EtOAc in hexane) to afford **13o** (18.0 mg, 0.089 mmol, 89% yield) as a colourless liquid.

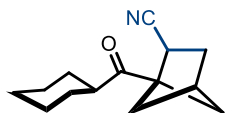
¹H NMR (400 MHz, CDCl₃) δ 3.22 – 3.06 (m, 2H, CH–CN and cyclopentyl CH), 2.62 (tt, *J* = 3.0, 1.4 Hz, 1H, BCH CH), 2.27 (ddt, *J* = 11.0, 9.2, 1.9 Hz, 1H, BCH CH₂), 2.13 (dq, *J* = 7.6, 2.5 Hz, 1H, BCH CH₂), 2.07 – 1.98 (m, 2H, BCH CH₂), 1.88 – 1.76 (m, 3H, cyclopentyl CH₂ and CH₂), 1.74 – 1.65 (m, 4H, 2 × cyclopentyl CH₂), 1.59 (tdt, *J* = 8.9, 5.2, 2.4 Hz, 2H, cyclopentyl CH₂ and BCH CH₂), 1.37 (dd, *J* = 9.9, 7.4 Hz, 1H, BCH CH₂).

¹³C NMR (101 MHz, CDCl₃) δ 210.3 (C=O), 121.9 (C≡N), 62.9 (C(O)C^q), 48.0 (cyclopentyl CH), 43.5 (BCH CH₂), 39.3 (BCH CH₂), 36.6 (BCH CH), 34.9 (BCH CH₂), 30.0 (CH–CN), 29.3 (cyclopentyl CH₂), 29.2 (cyclopentyl CH₂), 26.5 (cyclopentyl CH₂), 26.3 (cyclopentyl CH₂).

IR (neat, cm⁻¹): 2954, 2869, 2238, 1692, 1451, 1367, 1266, 1214, 1155, 753.

HRMS (ESI⁺): calculated for C₁₃H₁₇ONNa (M+Na⁺): 226.1202; found: 226.1194.

rac-1-(Cyclohexanecarbonyl)bicyclo[2.1.1]hexane-2-carbonitrile (**13p**)



Prepared by following the **general procedure C** from **11p** (0.20 mmol), **12a** (0.50 mmol), and Sml₂ (25 mol%). The reaction mixture was filtered through a silica gel pad and concentrated in vacuo. The crude product was purified by column chromatography (0-4% EtOAc in hexane) to afford **13p** (32.0 mg, 0.147 mmol, 74% yield) as a colourless liquid.

¹H NMR (400 MHz, CDCl₃) δ 3.09 (ddd, *J* = 9.1, 3.9, 1.9 Hz, 1H, CH–CN), 2.68 (tt, *J* = 11.2, 3.0 Hz, 1H, COCH), 2.61 (t, *J* = 2.4 Hz, 1H, BCH CH), 2.31 – 2.22 (m, 1H, BCH CH₂), 2.12 (dq, *J* = 7.7, 2.5 Hz, 1H, BCH CH₂), 2.07 – 1.97 (m, 2H, BCH CH₂), 1.83 –

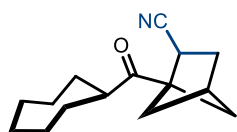
1.65 (m, 6H, 3 × cyclohexyl CH₂), 1.43 (td, *J* = 12.4, 3.2 Hz, 1H, BCH CH₂), 1.37 (dd, *J* = 9.8, 7.4 Hz, 1H, BCH CH₂), 1.33 – 1.16 (m, 4H, 2 × cyclohexyl CH₂).

¹³C NMR (101 MHz, CDCl₃) δ 210.9 (C=O), 121.8 (C≡N), 62.7 (C(O)C^q), 47.6 (COCH), 43.5 (BCH CH₂), 39.2 (BCH CH₂), 36.5 (BCH CH), 34.9 (BCH CH₂), 30.0 (CH–CN), 28.4 (cyclohexyl CH₂), 28.3 (cyclohexyl CH₂), 25.8 (cyclohexyl CH₂), 25.7 (cyclohexyl CH₂), 25.5 (cyclohexyl CH₂).

IR (neat, cm⁻¹): 2929, 2854, 2237, 1691, 1448, 1375, 1151, 955, 767.

HRMS (ESI⁺): calculated for C₁₄H₂₀ON (M+H⁺): 218.1539; found: 218.1529.

rac-1-(Cycloheptanecarbonyl)bicyclo[2.1.1]hexane-2-carbonitrile (**13q**)



Prepared by following the **general procedure C** from **11q** (0.10 mmol), **12a** (0.25 mmol), and Sml₂ (5 mol%). The reaction mixture was filtered through a silica gel pad and concentrated in vacuo to afford **13q** (22.0 mg, 0.095 mmol, 95% yield) as a colourless liquid.

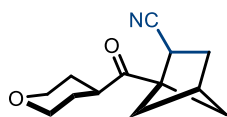
¹H NMR (500 MHz, CDCl₃) δ 3.10 (ddd, *J* = 9.2, 3.9, 2.0 Hz, 1H, CH–CN), 2.84 (tt, *J* = 9.6, 3.8 Hz, 1H, C(O)CH), 2.62 (tt, *J* = 3.0, 1.4 Hz, 1H, CH, BCH CH), 2.31 – 2.22 (m, 1H, BCH CH₂), 2.12 (dq, *J* = 7.6, 2.5 Hz, 1H, BCH CH₂), 2.07 – 1.97 (m, 2H, BCH CH₂), 1.82 – 1.69 (m, 5H, BCH CH₂, 2 × CH₂), 1.66 – 1.41 (m, 8H, 4 × CH₂), 1.37 (dd, *J* = 9.8, 7.3 Hz, 1H, BCH CH₂).

¹³C NMR (126 MHz, CDCl₃) δ 211.1 (C=O), 121.8 (C≡N), 62.7 (C(O)C^q), 48.6 (C(O)CH), 43.6 (BCH CH₂), 39.2 (CH₂), 36.6 (BCH CH), 34.9 (BCH CH₂), 30.1 (CH–CN), 29.9 (BCH CH₂), 29.6 (CH₂), 28.4 (CH₂), 28.3 (CH₂), 26.8 (CH₂), 26.8 (CH₂).

IR (neat, cm⁻¹): 2922, 2854, 2238 (C≡N), 1692 (C=O), 1457, 1270, 922.

HRMS (ESI⁺): calculated for C₁₅H₂₁ONNa (M+Na⁺): 254.1515; found: 254.1504.

rac-1-(Tetrahydro-2H-pyran-4-carbonyl)bicyclo[2.1.1]hexane-2-carbonitrile (**13r**)



Prepared by following the **general procedure C** from **11r** (0.10 mmol), **12a** (0.25 mmol), and Sml₂ (17 mol%). The reaction mixture was filtered through a silica gel pad and concentrated in vacuo. The crude product was purified by column chromatography (0-15% EtOAc in hexane) to afford **13r** (17.0 mg, 0.078 mmol, 78% yield) as a colourless liquid.

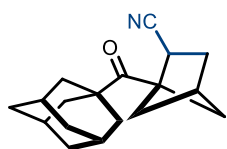
¹H NMR (400 MHz, CDCl₃) δ 4.01 (dp, *J* = 11.6, 4.0, 3.2 Hz, 2H, O–CH₂), 3.44 (td, *J* = 11.6, 2.6 Hz, 2H, O–CH₂), 3.11 (ddd, *J* = 9.3, 3.8, 1.9 Hz, 1H, CH–CN), 2.94 (ddd, *J* = 15.1, 10.5, 4.2 Hz, 1H, COCH), 2.64 (t, *J* = 2.9 Hz, 1H, BCH CH), 2.29 (td, *J* = 10.5, 2.4 Hz, 1H, BCH CH₂), 2.14 (dq, *J* = 7.7, 2.5 Hz, 1H, BCH CH₂), 2.08 – 1.92 (m, 2H, BCH CH₂), 1.89 – 1.59 (m, 5H, 2 × O–CH₂CH₂ and BCH CH₂), 1.40 (dd, *J* = 9.9, 7.3 Hz, 1H, BCH CH₂).

¹³C NMR (101 MHz, CDCl₃) δ 209.0 (C=O), 121.8 (C≡N), 67.2 (O–CH₂), 67.1 (O–CH₂), 62.5 (C(O)C^q), 44.7 (COCH), 43.6 (BCH CH₂), 39.4 (BCH CH₂), 36.7 (BCH CH), 34.9 (BCH CH₂), 30.3 (CH–CN), 28.2 (O–CH₂CH₂), 27.9 (O–CH₂CH₂).

IR (neat, cm⁻¹): 2953, 2848, 2237, 1692, 1240, 1111, 1085, 1015, 985, 960.

HRMS (ESI⁺): calculated for C₁₃H₁₈O₂N (M+H⁺): 220.1332; found: 220.1325.

rac-1-(Adamantane-1-carbonyl)bicyclo[2.1.1]hexane-2-carbonitrile (**13s**)



Prepared by following the **general procedure C** from **11s** (0.10 mmol), **12a** (0.25 mmol), and Sml₂ (7.5 mol%). The reaction mixture was filtered through a silica gel pad and concentrated in vacuo. The crude product was purified by column chromatography (0-6% EtOAc in hexane) to afford **13s** (22.4 mg, 0.083 mmol, 83% yield) as a white solid

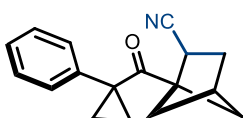
¹H NMR (400 MHz, CDCl₃) δ 3.23 (ddd, *J* = 8.9, 4.0, 2.1 Hz, 1H, CH–CN), 2.57 (tt, *J* = 3.0, 1.4 Hz, 1H, BCH CH), 2.33 – 2.18 (m, 2H, BCH CH₂), 2.09 – 1.97 (m, 5H, BCH CH₂ and 3 × adamantyl CH), 1.96 – 1.84 (m, 6H, 3 × adamantyl CH₂), 1.80 – 1.66 (m, 7H, 3 × adamantyl CH₂ and BCH CH₂), 1.51 (dd, *J* = 9.8, 7.4 Hz, 1H BCH CH₂).

¹³C NMR (101 MHz, CDCl₃) δ 212.1 (C=O), 121.8 (C≡N), 61.7 (C(O)C^q), 47.6 (adamantyl C^q), 45.4 (BCH CH₂), 40.6 (BCH CH₂), 37.9 (3 × adamantyl CH₂), 36.6 (3 × adamantyl CH₂), 36.4 (BCH CH), 34.4 (BCH CH₂), 32.5 (CH–CN), 28.0 (3 × adamantyl CH).

IR (neat, cm⁻¹): 2993, 2930, 2903, 2879, 2850, 2237, 1672, 1294, 1269, 1162.

HRMS (ESI⁺): calculated for C₁₈H₂₄ON (M+H⁺): 270.1852; found: 270.1840.

rac-1-(1-Phenylcyclopropane-1-carbonyl)bicyclo[2.1.1]hexane-2-carbonitrile (**13t**)



Prepared by following the **general procedure C** from **11t** (0.10 mmol), **12a** (0.25 mmol), and Sml₂ (15 mol%). The reaction mixture was filtered through a silica gel pad and concentrated in vacuo to afford **13t** (23.1 mg, 0.092 mmol, 92% yield) as a colourless liquid.

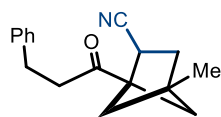
¹H NMR (500 MHz, CDCl₃) δ 7.42 – 7.37 (m, 2H, ArCH), 7.36 – 7.28 (m, 3H, ArCH), 2.70 (ddd, *J* = 9.1, 4.0, 1.9 Hz, 1H, CH–CN), 2.30 (tt, *J* = 2.9, 1.4 Hz, 1H, BCH CH), 1.95 (dddd, *J* = 11.8, 9.1, 2.7, 1.3 Hz, 1H, BCH CH₂), 1.84 (dddd, *J* = 11.2, 4.0, 2.6, 1.4 Hz, 1H, BCH CH₂), 1.81 – 1.69 (m, 3H, CH₂, BCH CH₂), 1.63 (ddd, *J* = 9.8, 7.0, 3.7 Hz, 1H, CH₂), 1.38 (dd, *J* = 9.8, 8.2 Hz, 1H, BCH CH₂), 1.30 (ddd, *J* = 9.4, 6.9, 3.7 Hz, 1H, CH₂), 1.11 (ddd, *J* = 9.3, 6.9, 3.4 Hz, 1H, CH₂), 0.70 (dd, *J* = 9.8, 7.4 Hz, 1H, BCH CH₂).

¹³C NMR (126 MHz, CDCl₃) δ 206.4 (C=O), 139.4 (ArC^q), 130.8 (2 × ArCH), 128.8 (2 × ArCH), 128.1 (ArCH), 121.5 (C≡N), 63.5 (C(O)C^q), 45.2 (BCH CH₂), 39.4 (BCH CH₂), 36.7 (C(O)C^q–Ar), 35.0 (BCH CH), 34.7 (BCH CH₂), 31.2 (CH–CN), 18.8 (CH₂), 18.7 (CH₂).

IR (neat, cm⁻¹): 2989, 2957, 2883, 2238 (C≡N), 1675 (C=O), 1497, 1445, 1308, 1038, 1000, 959, 702.

HRMS (APCI⁺): calculated for C₁₇H₁₈ON (M+H⁺): 252.1383; found: 252.1374.

rac-4-Methyl-1-(3-phenylpropanoyl)bicyclo[2.1.1]hexane-2-carbonitrile (**13u**)



Prepared by following the **general procedure C** from **11u** (0.10 mmol), **12a** (0.25 mmol), and Sml₂ (10 mol%). The reaction mixture was filtered through a silica gel pad and concentrated in vacuo to afford the final product **13u** (25.3 mg, 0.10 mmol, 100% yield) as a colourless liquid.

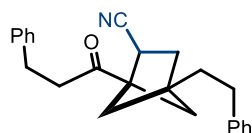
¹H NMR (400 MHz, CDCl₃) δ 7.28 (dd, *J* = 8.3, 6.3 Hz, 2H, ArCH), 7.22 – 7.15 (m, 3H, ArCH), 3.09 (ddd, *J* = 9.1, 4.0, 1.8 Hz, 1H, CH–CN), 2.94 – 2.80 (m, 4H, C(O)CH₂CH₂), 2.07 (ddd, *J* = 11.5, 9.1, 2.4 Hz, 1H, BCH CH₂), 1.86 (dt, *J* = 11.3, 3.4 Hz, 1H, BCH CH₂), 1.82 – 1.74 (m, 2H, BCH CH₂), 1.70 (dd, *J* = 7.3, 2.9 Hz, 1H, BCH CH₂), 1.43 – 1.36 (m, 1H, BCH CH₂), 1.22 (s, 3H, CH₃).

¹³C NMR (101 MHz, CDCl₃) δ 206.8 (C=O), 140.9 (ArC^q), 128.7 (2 × ArCH), 128.5 (2 × ArCH), 126.3 (ArCH), 121.6 (C≡N), 59.9 (C(O)C^q), 47.3 (COCH₂), 45.4 (CH₃C^q), 43.6 (BCH CH₂), 41.6 (BCH CH₂), 40.1 (BCH CH₂), 31.5 (CH–CN), 29.4 (PhCH₂), 18.6 (CH₃).

IR (neat, cm⁻¹): 2952, 2925, 2873, 2237, 1697, 1453, 1382, 1369, 1329, 1127, 741, 698.

HRMS (ESI⁺): calculated for C₁₇H₂₀ON (M+H⁺): 254.1539; found: 254.1530.

rac-4-Phenethyl-1-(3-phenylpropanoyl)bicyclo[2.1.1]hexane-2-carbonitrile (**13v**)



Prepared by following the **general procedure C** from **11v** (0.10 mmol), **12a** (0.25 mmol), and Sml₂ (10 mol%). The reaction mixture was filtered through a silica gel pad and concentrated in vacuo. The crude product was purified by column chromatography

(0-8% EtOAc in hexane) to afford **13v** (34.0 mg, 0.099 mmol, 99% yield) as a colourless liquid.

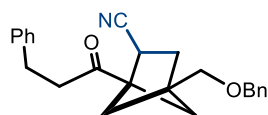
¹H NMR (400 MHz, CDCl₃) δ 7.34 – 7.26 (m, 4H, ArCH), 7.23 – 7.13 (m, 6H, ArCH), 3.09 (ddd, *J* = 9.1, 4.0, 1.9 Hz, 1H, CH–CN), 2.97 – 2.89 (m, 2H, CH₂), 2.85 (ddd, *J* = 10.6, 5.9, 3.1 Hz, 2H, CH₂), 2.68 – 2.57 (m, 2H, CH₂), 2.13 (ddd, *J* = 11.5, 9.1, 2.6 Hz, 1H, BCH CH₂), 1.99 – 1.87 (m, 3H, BCH CH₂, CH₂), 1.83 (dt, *J* = 7.6, 2.3 Hz, 1H, BCH CH₂), 1.78 – 1.69 (m, 2H, BCH CH₂), 1.35 (dd, *J* = 9.6, 7.3 Hz, 1H, BCH CH₂).

¹³C NMR (101 MHz, CDCl₃) δ 206.8 (C=O), 141.5 (ArC^q), 140.9 (ArC^q), 128.7 (2 × ArCH), 128.6 (2 × ArCH), 128.5 (2 × ArCH), 128.2 (2 × ArCH), 126.4 (ArCH), 126.3 (ArCH), 121.6 (C≡N), 59.7 (C(O)C^q), 49.1 (C^qCH₂), 45.6 (C(O)CH₂), 41.9 (BCH CH₂), 41.7 (C^qCH₂), 38.0 (BCH CH₂), 34.2 (BCH CH₂), 32.1 (PhCH₂), 31.1 (CH–CN), 29.4 (PhCH₂).

IR (neat, cm⁻¹): 2930, 2877, 2855, 2238 (C≡N), 1697 (C=O), 1602, 1496, 1453, 1370, 1320, 1126, 1029, 697.

HRMS (APCI⁺): calculated for C₂₄H₂₆ON (M+H⁺): 344.2009; found: 344.2003.

rac-4-((Benzyloxy)methyl)-1-(3-phenylpropanoyl)bicyclo[2.1.1]hexane-2-carbonitrile (**13w**)



Prepared by following the **general procedure C** from **11w** (0.10 mmol), **12a** (0.25 mmol), and Sml₂ (25 mol%). The reaction mixture was filtered through a silica gel pad and concentrated in vacuo. The crude product was purified by column chromatography (0-10% EtOAc in hexane) to afford **13w** (15.6 mg, 0.043 mmol, 43% yield) as a colourless liquid.

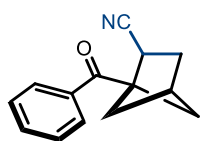
¹H NMR (400 MHz, CDCl₃) δ 7.40 – 7.33 (m, 2H, ArCH), 7.29 (qd, *J* = 4.8, 3.4 Hz, 5H, ArCH), 7.20 (td, *J* = 7.3, 1.6 Hz, 3H, ArCH), 4.51 (s, 2H, CH₂–O), 3.50 (s, 2H, CH₂–O), 3.11 (ddd, *J* = 9.2, 3.9, 2.0 Hz, 1H, CH–CN), 3.00 – 2.81 (m, 4H, 2 × CH₂), 2.28 – 2.12 (m, 1H, BCH CH₂), 2.04 (dt, *J* = 7.6, 2.3 Hz, 1H, BCH CH₂), 2.00 – 1.91 (m, 2H, BCH CH₂), 1.77 (dd, *J* = 9.8, 7.6 Hz, 1H, BCH CH₂), 1.40 (dd, *J* = 9.7, 7.2 Hz, 1H, BCH CH₂).

¹³C NMR (101 MHz, CDCl₃) δ 206.7 (C=O), 140.9 (ArC^q), 138.2 (ArC^q), 128.7 (2 × ArCH), 128.6 (2 × ArCH), 128.5 (2 × ArCH), 127.9 (ArCH), 127.6 (2 × ArCH), 126.4 (ArCH), 121.5 (C≡N), 73.4 (CH₂–O), 70.1 (CH₂–O), 59.9 (C(O)C^q), 49.0 (C^qCH₂), 44.0 (C(O)CH₂), 41.7 (BCH CH₂), 40.4 (BCH CH₂), 36.3 (BCH CH₂), 30.7 (CH–CN), 29.4 (CH₂Ph).

IR (neat, cm⁻¹): 2951, 2921, 2881, 2857, 2238 (C≡N), 1699 (C=O), 1496, 1453, 1364, 1129, 1090, 739, 698.

HRMS (APCI⁺): calculated for C₂₄H₂₆O₂N (M+H⁺): 360.1958; found: 360.1947.

rac-1-Benzoylbicyclo[2.1.1]hexane-2-carbonitrile (**13x**)



Prepared by following the **general procedure C** from **11x** (0.10 mmol), **12a** (0.25 mmol), and Sml₂ (25 mol%). The reaction mixture was filtered through a silica gel pad and concentrated in vacuo. The crude product was purified by column chromatography (0-7% EtOAc in hexane) to afford **13x** (10.2 mg, 0.048 mmol, 48% yield) as a colourless liquid.

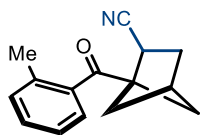
¹H NMR (400 MHz, CDCl₃) δ 7.88 – 7.82 (m, 2H, ArCH), 7.63 – 7.53 (m, 1H, ArCH), 7.51 – 7.39 (m, 2H, ArCH), 3.24 (ddd, *J* = 9.0, 3.8, 1.9 Hz, 1H, CH–CN), 2.66 (tt, *J* = 2.9, 1.4 Hz, 1H, BCH CH), 2.47 – 2.35 (m, 1H, BCH CH₂), 2.30 – 2.24 (m, 1H, BCH CH₂), 2.23 – 2.12 (m, 2H, BCH CH₂), 1.97 (dd, *J* = 9.8, 8.0 Hz, 1H, BCH CH₂), 1.73 (dd, *J* = 9.8, 7.4 Hz, 1H, BCH CH₂).

¹³C NMR (101 MHz, CDCl₃) δ 199.2 (C=O), 136.4 (ArC^q), 133.5 (ArCH), 128.9 (2 × ArCH), 128.6 (2 × ArCH), 121.3 (C≡N), 61.9 (C(O)C^q), 45.0 (BCH CH₂), 40.6 (BCH CH₂), 36.0 (BCH CH), 35.5 (BCH CH₂), 32.5 (CH–CN).

IR (neat, cm⁻¹): 2956, 2237, 1663, 1597, 1446, 1322, 1300, 1268, 1217, 1168, 782, 712, 690.

HRMS (ESI⁺): calculated for C₁₄H₁₄ON (M+H⁺): 212.1056; found: 212.1063.

rac-1-(2-Methylbenzoyl)bicyclo[2.1.1]hexane-2-carbonitrile (**13y**)



Prepared by following the **general procedure C** from **11y** (0.10 mmol), **12a** (0.25 mmol), and Sml₂ (25 mol%). The reaction mixture was filtered through a silica gel pad and concentrated in vacuo. The crude product was purified by column chromatography (0-7% EtOAc in hexane) to afford **13y** (15.0 mg, 0.068 mmol, 68% yield) as a colourless liquid.

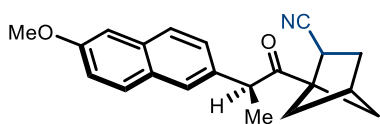
¹H NMR (400 MHz, CDCl₃) δ 7.39 – 7.26 (m, 3H, ArCH), 7.23 (t, *J* = 7.5 Hz, 1H, ArCH), 3.17 (ddd, *J* = 9.2, 3.9, 1.9 Hz, 1H, CH–CN), 2.62 (tt, *J* = 3.0, 1.4 Hz, 1H, BCH CH), 2.39 (s, 3H, CH₃), 2.33 (dddd, *J* = 10.7, 9.3, 2.6, 1.4 Hz, 1H, BCH CH₂), 2.21 – 2.05 (m, 3H, BCH CH₂ and BCH CH₂), 1.80 (dd, *J* = 9.9, 7.9 Hz, 1H, BCH CH₂), 1.60 (dd, *J* = 9.9, 7.2 Hz, 1H, BCH CH₂).

¹³C NMR (101 MHz, CDCl₃) δ 203.2 (C=O), 137.9 (ArC^q), 136.8 (ArC^q), 131.8 (ArCH), 130.8 (ArCH), 126.3 (ArCH), 125.5 (ArCH), 121.6 (C≡N), 63.6 (C(O)C^q), 44.7 (BCH CH₂), 39.4 (BCH CH₂), 36.5 (BCH CH), 35.2 (BCH CH₂), 30.8 (CH–CN), 20.1 (CH₃).

IR (neat, cm⁻¹): 2988, 2957, 2237, 1677, 1455, 1307, 1269, 1216, 919, 763, 734.

HRMS (APCI⁺): calculated for C₁₅H₁₆NO (M+H⁺): 226.1226; found: 226.1223.

1-((*S*)-2-(6-Methoxynaphthalen-2-yl)propanoyl)bicyclo[2.1.1]hexane-2-carbonitrile (**13z**)



Prepared by following the **general procedure C** from **11z** (0.10 mmol), **12a** (0.25 mmol), and Sml₂ (5 mol%). The reaction mixture was filtered through a silica gel pad and concentrated in vacuo. The crude product was purified by column chromatography (0-10% EtOAc in hexane) to afford **13z** (31.5 mg, 0.099 mmol, 99% yield, d.r. 1:1) as a white solid.

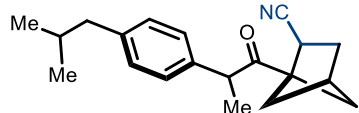
¹H NMR (400 MHz, CDCl₃) δ 7.82 – 7.67 (m, 2H, ArCH^{d1d2}), 7.59 (d, *J* = 1.8 Hz, 1H, ArCH^{d1}), 7.56 (d, *J* = 1.8 Hz, 1H, ArCH^{d2}), 7.37 – 7.21 (m, 1H, ArCH^{d1d2}), 7.20 – 7.13 (m, 1H, ArCH^{d1d2}), 7.13 – 7.08 (m, 1H, ArCH^{d1d2}), 4.18 (q, *J* = 6.8 Hz, 1H, C(O)CH^{d1}), 4.17 (q, *J* = 6.8 Hz, 1H, C(O)CH^{d2}), 3.92 (s, 3H, OCH₃^{d1}), 3.91 (s, 3H, OCH₃^{d2}), 3.07 (ddd, *J* = 9.1, 3.9, 1.9 Hz, 1H, CH–CN^{d1}), 2.76 (ddd, *J* = 9.2, 4.0, 1.9 Hz, 1H, CH–CN^{d2}), 2.48 – 2.35 (m, 1H, BCH CH^{d1d2}), 2.16 – 2.05 (m, 1H, BCH CH₂^{d1d2}), 1.98 – 1.88 (m, 2H, BCH CH₂^{d1d2}), 1.86 – 1.81 (m, 1H, BCH CH₂^{d1}), 1.68 (dd, *J* = 7.7, 3.3 Hz, 1H, BCH CH₂^{d1}), 1.67 (dd, *J* = 7.8, 3.5 Hz, 1H, BCH CH₂^{d2}), 1.46 (d, *J* = 6.8 Hz, 3H, CHCH₃^{d1}), 1.45 (d, *J* = 6.9 Hz, 3H, CHCH₃^{d2}), 1.28 (dd, *J* = 10.0, 8.1 Hz, 1H, BCH CH₂^{d2}), 1.19 (dd, *J* = 9.8, 7.5 Hz, 1H, BCH CH₂^{d1}), 1.05 (dd, *J* = 10.0, 7.3 Hz, 1H; BCH CH₂^{d2}).

¹³C NMR (101 MHz, CDCl₃) δ 208.5 (C=O)^{d1}, 206.7 (C=O)^{d2}, 158.0 (ArC^q)^{d1}, 158.0 (ArC^q)^{d2}, 135.3 (ArC^q)^{d1}, 134.7 (ArC^q)^{d2}, 133.9 (ArC^q)^{d1}, 133.8 (ArC^q)^{d2}, 129.4 (ArCH)^{d1}, 129.4 (ArCH)^{d2}, 129.2 (ArC^q)^{d1}, 129.2 (ArC^q)^{d2}, 127.9 (ArCH)^{d1d2}, 126.8 (ArCH)^{d1}, 126.7 (ArCH)^{d2}, 126.5 (ArCH)^{d1}, 126.5 (ArCH)^{d2}, 121.8 (C≡N)^{d1}, 121.7 (C≡N)^{d2}, 119.5 (ArCH)^{d1}, 119.4 (ArCH)^{d2}, 105.8 (ArCH)^{d1}, 105.7 (ArCH)^{d2}, 63.1 (C(O)C^q)^{d1}, 62.5 (C(O)C^q)^{d2}, 55.5 (OCH₃)^{d1}, 55.5 (OCH₃)^{d2}, 50.7 (C(O)CH)^{d1}, 50.4 (C(O)CH)^{d2}, 44.9 (BCH CH₂)^{d1}, 43.5 (BCH CH₂)^{d2}, 39.9 (BCH CH₂)^{d1}, 39.4 (BCH CH₂)^{d2}, 36.3 (BCH CH)^{d1}, 36.1 (BCH CH)^{d2}, 34.8 (BCH CH₂)^{d1}, 34.7 (BCH CH₂)^{d2}, 31.4 (CH–CN)^{d1}, 29.6 (CH–CN)^{d2}, 18.9 (CHCH₃)^{d1}, 18.7 (CHCH₃)^{d2}.

IR (neat, cm⁻¹): 2974, 2935, 2883, 2238 (C≡N), 1695 (C=O), 1631, 1604 (C=C), 1483, 1391, 1265, 1227, 1029, 854, 749.

HRMS (ESI⁺): calculated for C₂₁H₂₁O₂NNa (M+Na⁺): 342.1465; found: 342.1454.

***rac*-1-(2-(4-Isobutylphenyl)propanoyl)bicyclo[2.1.1]hexane-2-carbonitrile (**13aa**)**



Prepared by following the **general procedure C** from **11aa** (0.10 mmol), **12a** (0.25 mmol), and Sml₂ (15 mol%). The reaction mixture was filtered through a silica gel pad and concentrated in vacuo. The crude product was

purified by column chromatography (0-10% EtOAc in hexane) to afford **13aa** (26.0 mg, 0.088 mmol, 88% yield) as a colourless liquid and as a 1:1 mixture of diastereomers.

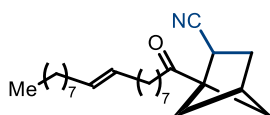
¹H NMR (400 MHz, CDCl₃) δ 7.09 (d, *J* = 8.6 Hz, 4H, ArCH), 4.07 – 3.93 (m, 1H, CO–CH–CH₃), 3.04 (ddd, *J* = 9.3, 3.7, 1.9 Hz, 1H, CH–CN^{d1}), 2.72 (ddd, *J* = 9.1, 4.0, 1.9 Hz, 1H, CH–CN^{d2}), 2.54 – 2.37 (m, 3H, BCH CH^{d1d2} and CH₂^{d1d2}), 2.19 – 2.04 (m, 1H, BCH CH₂^{d1d2}), 2.01 – 1.76 (m, 3H, BCH CH₂^{d1d2} and BCH CH₂^{d1d2}), 1.70 – 1.63 (m, 1H, BCH CH₂^{d1d2}), 1.37 (d, *J* = 6.8 Hz, 3H, CO–CH–CH₃^{d1}), 1.37 (d, *J* = 6.8 Hz, 3H, CO–CH–CH₃^{d2}), 1.34 – 1.27 (m, 1H, CH–CH₂), 1.18 (dd, *J* = 9.8, 7.5 Hz, 1H, BCH CH₂^{d1}), 1.03 (dd, *J* = 9.9, 7.4 Hz, 1H, BCH CH₂^{d2}), 0.98 – 0.78 (m, 6H, 2 × CH₃).

¹³C NMR (101 MHz, CDCl₃) δ 208.4 (C=O)^{d1}, 206.6 (C=O)^{d2}, 141.1 (ArC^q)^{d1}, 141.0 (ArC^q)^{d2}, 137.3 (ArC^q)^{d1}, 136.8 (ArC^q)^{d2}, 129.9 (2 × ArCH)^{d1}, 129.9 (2 × ArCH)^{d2}, 127.9 (2 × ArCH)^{d1}, 127.8 (2 × ArCH)^{d2}, 121.7 (C≡N)^{d1d2}, 63.0 (C(O)C^q)^{d1}, 62.4 (C(O)C^q)^{d2}, 50.4 (CO–CH–CH₃)^{d1}, 50.1 (CO–CH–CH₃)^{d2}, 45.1 (CH₂)^{d1}, 45.1 (CH₂)^{d2}, 44.9 (BCH CH₂)^{d1}, 43.4 (BCH CH₂)^{d2}, 39.8 (BCH CH₂)^{d1}, 39.3 (BCH CH₂)^{d2}, 36.3 (BCH CH)^{d1}, 36.0 (BCH CH)^{d2}, 34.8 (BCH CH₂)^{d1}, 34.7 (BCH CH₂)^{d2}, 31.3 (CO–CH–CH₃)^{d1}, 30.3 (CH–CN)^{d1}, 30.3 (CH–CN)^{d2}, 29.6 (CO–CH–CH₃)^{d2}, 22.5 (2 × CH₃)^{d1}, 22.4 (2 × CH₃)^{d2}, 18.8 (CH–CH₂)^{d1}, 18.6 (CH–CH₂)^{d2}.

IR (neat, cm⁻¹): 2954, 2926, 2884, 2868, 2238, 1696, 1454, 847, 754.

HRMS (APCI⁺): calculated for C₂₀H₂₆NO (M+H⁺): 296.2009; found: 296.2003.

rac-(*E*)-1-(Octadec-9-enoyl)bicyclo[2.1.1]hexane-2-carbonitrile (**13ab**)



Prepared by following the **general procedure C** from **11ab** (0.10 mmol), **12a** (0.25 mmol), and Sml_2 (25 mol%). The reaction mixture was filtered through a silica gel pad and concentrated in vacuo. The crude product was purified by column chromatography (0-6% EtOAc in hexane) to afford **13ab** (31.0 mg, 0.084 mmol, 84% yield) as a colourless liquid.

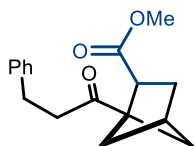
^1H NMR (400 MHz, CDCl_3) δ 5.40 – 5.26 (m, 2H, $\text{CH}=\text{CH}$), 3.05 (dd, J = 9.0, 5.1 Hz, 1H, $\text{CH}-\text{CN}$), 2.60 (d, J = 3.3 Hz, 1H, BCH CH), 2.54 (t, J = 7.3 Hz, 2H, COCH_2), 2.27 (td, J = 10.2, 8.8, 2.4 Hz, 1H, BCH CH_2), 2.14 – 1.92 (m, 7H, BCH CH_2 , BCH CH_2 and $2 \times \text{CH}_2$), 1.71 (dd, J = 9.9, 7.8 Hz, 1H, BCH CH_2), 1.64 – 1.52 (m, 2H, CH_2), 1.40 – 1.33 (m, 1H, BCH CH_2), 1.27 (d, J = 11.6 Hz, 20H, $10 \times \text{CH}_2$), 0.87 (t, J = 6.7 Hz, 3H, CH_3).

^{13}C NMR (101 MHz, CDCl_3) δ 208.0 ($\text{C}=\text{O}$), 130.1 ($\text{CH}=\text{CH}$), 129.9 ($\text{CH}=\text{CH}$), 121.8 ($\text{C}\equiv\text{N}$), 62.8 ($\text{C}(\text{O})\text{C}^q$), 43.1 (CH_2), 39.9 (CH_2), 39.2 (BCH CH_2), 36.3 (BCH CH), 35.0 (BCH CH_2), 32.0 (CH_2), 29.9 (CH_2), 29.9 ($\text{CH}-\text{CN}$), 29.8 (CH_2), 29.6 (CH_2), 29.4 ($2 \times \text{CH}_2$), 29.2 ($2 \times \text{CH}_2$), 27.3 (CH_2), 27.3 (CH_2), 23.2 (CH_2), 22.8 (CH_2), 14.2 (CH_3).

IR (neat, cm^{-1}): 2922, 2857, 2238, 1700, 1457, 1375, 722.

HRMS (ESI^+): calculated for $\text{C}_{25}\text{H}_{42}\text{NO}$ ($\text{M}+\text{H}^+$): 372.3261; found: 372.3247.

rac-Methyl 1-(3-phenylpropanoyl)bicyclo[2.1.1]hexane-2-carboxylate (**13ac**)



Prepared by following the **general procedure C** from **11a** (0.10 mmol), **12b** (0.25 mmol), and Sml_2 (25 mol%). The reaction mixture was filtered through a silica gel pad and concentrated in vacuo. The crude product was purified by column chromatography (0-6% EtOAc in hexane) to afford **13ac** (24.6 mg, 0.09 mmol, 90% yield) as a colourless liquid.

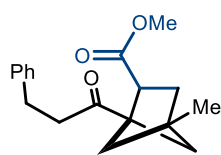
^1H NMR (500 MHz, CDCl_3) δ 7.28 (ddd, J = 8.3, 6.9, 1.2 Hz, 2H, ArCH), 7.23 – 7.16 (m, 3H, ArCH), 3.61 (d, J = 1.1 Hz, 3H, OCH_3), 3.19 (ddt, J = 9.4, 4.1, 1.4 Hz, 1H, $\text{CH}-\text{C}(\text{O})\text{O}$), 2.93 – 2.74 (m, 4H, $2 \times \text{CH}_2$), 2.44 (tq, J = 2.8, 1.3 Hz, 1H, BCH CH), 2.13 (dddt, J = 10.7, 9.4, 2.5, 1.2 Hz, 1H, BCH CH_2), 1.97 (dddt, J = 11.3, 4.1, 2.6, 1.2 Hz, 1H, BCH CH_2), 1.88 (ddq, J = 7.3, 3.0, 1.4 Hz, 1H, BCH CH_2), 1.79 (dtd, J = 6.8, 2.8, 1.1 Hz, 1H, BCH CH_2), 1.60 (ddd, J = 9.8, 7.4, 1.0 Hz, 1H, BCH CH_2), 1.43 (ddd, J = 9.7, 6.7, 1.1 Hz, 1H, BCH CH_2).

^{13}C NMR (126 MHz, CDCl_3) δ 209.2 ($\text{C}=\text{O}$), 174.7 ($\text{C}(\text{O})\text{O}$), 141.5 (ArC^q), 128.6 ($2 \times \text{ArCH}$), 128.5 ($2 \times \text{ArCH}$), 126.2 (ArCH), 62.1 ($\text{C}(\text{O})\text{C}^q$), 51.9 (OCH_3), 45.6 ($\text{CH}-\text{C}(\text{O})\text{O}$), 45.1 ($\text{C}(\text{O})\text{CH}_2$), 41.2 (BCH CH_2), 37.4 (BCH CH_2), 35.4 (BCH CH), 32.8 (BCH CH_2), 29.4 (PhCH_2).

IR (neat, cm^{-1}): 2951, 2923, 1731 ($\text{C}=\text{O}$), 1698 ($\text{C}=\text{O}$), 1453, 1435, 1363, 1196, 1173, 1041, 749, 698.

HRMS (ESI^+): calculated for $\text{C}_{17}\text{H}_{20}\text{O}_3\text{Na}$ ($\text{M}+\text{Na}^+$): 295.1305; found: 295.1291.

rac-Methyl 4-methyl-1-(3-phenylpropanoyl)bicyclo[2.1.1]hexane-2-carboxylate (**13ad**)



Prepared by following the **general procedure C** from **11u** (0.10 mmol), **12b** (0.25 mmol), and Sml_2 (17 mol%). The reaction mixture was filtered through a silica gel pad and concentrated in vacuo to afford the final product **13ad** (29.0 mg, 0.10 mmol, 100% yield) as a colourless liquid.

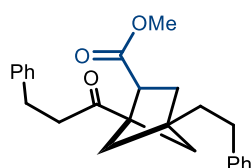
^1H NMR (400 MHz, CDCl_3) δ 7.37 (dd, $J = 8.6, 6.2$ Hz, 2H, ArCH), 7.33 – 7.26 (m, 3H, ArCH), 3.70 (s, 3H, OCH_3), 3.34 (ddd, $J = 9.3, 4.3, 1.7$ Hz, 1H, CH–C(O)O), 3.03 – 2.81 (m, 4H, PhCH_2CH_2), 2.04 (ddd, $J = 11.7, 9.3, 2.6$ Hz, 1H, BCH CH_2), 1.93 (ddd, $J = 11.1, 4.3, 2.7$ Hz, 1H, BCH CH_2), 1.79 (dd, $J = 9.0, 7.2$ Hz, 1H, BCH CH_2), 1.76 – 1.68 (m, 1H, BCH CH_2), 1.68 – 1.57 (m, 2H, BCH CH_2), 1.28 (s, 1H, CH_3).

^{13}C NMR (101 MHz, CDCl_3) δ 209.1 (C=O), 174.5 ($\text{O}=\text{C}(\text{O})$), 141.6 (ArC^q), 128.5 ($2 \times \text{ArCH}$), 128.5 ($2 \times \text{ArCH}$), 126.1 ($p\text{-ArCH}$), 59.3 ($\text{C}(\text{O})\text{C}^q$), 51.9 (OCH_3), 49.4 ($\text{C}(\text{O})\text{CH}_2$), 47.5 (CH–C(O)O), 44.0 (C^qCH_3), 41.9 (BCH CH_2), 41.1 (BCH CH_2), 38.4 (BCH CH_2), 29.4 (PhCH_2), 18.9 (C^qCH_3).

IR (neat, cm^{-1}): 2950, 2869, 1731, 1698, 1452, 1435, 1214, 1196, 1175, 698.

HRMS (ESI^+): calculated for $\text{C}_{18}\text{H}_{22}\text{O}_3\text{Na}$ ($\text{M}+\text{Na}^+$): 309.1461; found: 309.1447.

rac-Methyl 4-phenethyl-1-(3-phenylpropanoyl)bicyclo[2.1.1]hexane-2-carboxylate (**13ae**)



Prepared by following the **general procedure C** from **11v** (0.10 mmol), **12b** (0.25 mmol), and Sml_2 (10 mol%). The reaction mixture was filtered through a silica gel pad and concentrated in vacuo. The crude product was purified by column chromatography (0–8% EtOAc in hexane) to afford **13ae** (35.2 mg, 0.093 mmol, 93% yield) as a colourless liquid.

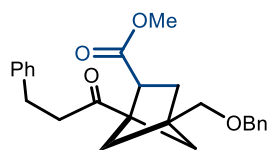
^1H NMR (400 MHz, CDCl_3) δ 7.33 – 7.23 (m, 4H, ArCH), 7.23 – 7.12 (m, 6H, ArCH), 3.62 (s, 3H, OCH_3), 3.25 (ddd, $J = 9.3, 4.3, 1.2$ Hz, 1H, CH–C(O)O), 2.96 – 2.71 (m, 4H, $2 \times \text{CH}_2$), 2.67 – 2.56 (m, 2H, CH_2), 2.01 (ddd, $J = 11.3, 9.2, 1.9$ Hz, 1H, BCH CH_2), 1.96 – 1.82 (m, 3H, CH_2 , BCH CH_2), 1.73 – 1.65 (m, 2H, BCH CH_2), 1.60 – 1.56 (m, 1H, BCH CH_2), 1.54 – 1.42 (m, 1H, BCH CH_2).

^{13}C NMR (101 MHz, CDCl_3) δ 209.1 (C=O), 174.5 ($\text{C}(\text{O})\text{O}$), 142.2 (ArC^q), 141.5 (ArC^q), 128.6 ($2 \times \text{ArCH}$), 128.5 ($4 \times \text{ArCH}$), 128.3 ($2 \times \text{ArCH}$), 126.2 (ArCH), 126.0 (ArCH), 59.1 ($\text{C}(\text{O})\text{C}^q$), 51.9 (OCH_3), 47.7 (C^qCH_2), 47.7 ($\text{C}(\text{O})\text{CH}_2$), 47.0 (CH–C(O)O), 41.1 (BCH CH_2), 40.1 (C^qCH_2), 36.1 (BCH CH_2), 34.7 (BCH CH_2), 32.2 (PhCH_2), 29.4 (PhCH_2).

IR (neat, cm^{-1}): 2949, 2930, 2874, 2854, 1731 (C=O), 1697 (C=O), 1496, 1453, 1434, 1197, 1174, 748, 697.

HRMS (APCI^+): calculated for $\text{C}_{25}\text{H}_{29}\text{O}_3$ ($\text{M}+\text{H}^+$): 377.2111; found: 377.2102.

rac-Methyl 4-((benzyloxy)methyl)-1-(3-phenylpropanoyl)bicyclo[2.1.1]hexane-2-carboxylate (**13af**)



Prepared by following the **general procedure C** from **11w** (0.10 mmol), **12b** (0.25 mmol), and Sml_2 (25 mol%). The reaction mixture was filtered through a silica gel pad and concentrated in vacuo. The crude product was purified by column chromatography (0-8% EtOAc in hexane) to afford **13af** (20.9 mg, 0.053 mmol, 53% yield) as a colourless liquid.

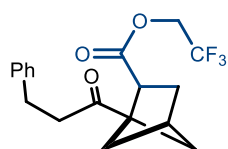
^1H NMR (500 MHz, CDCl_3) δ 7.38 – 7.26 (m, 7H, ArCH), 7.22 – 7.16 (m, 3H, ArCH), 4.52 (s, 2H, O–CH₂), 3.61 (s, 3H, OCH₃), 3.50 (s, 2H, O–CH₂), 3.27 (ddd, J = 9.5, 4.2, 1.8 Hz, 1H, CH–C(O)O), 3.04 – 2.73 (m, 4H, 2 $\times$ CH₂), 2.08 (ddd, J = 11.0, 9.4, 2.6 Hz, 1H, BCH CH₂), 2.00 – 1.83 (m, 2H, BCH CH₂), 1.78 (dd, J = 6.6, 2.9 Hz, 1H, BCH CH₂), 1.70 (dd, J = 9.5, 7.2 Hz, 1H, BCH CH₂), 1.52 (dd, J = 9.5, 6.6 Hz, 1H, BCH CH₂).

^{13}C NMR (126 MHz, CDCl_3) δ 209.0 (C=O), 174.4 (C(O)O), 141.5 (ArC^q), 138.5 (ArC^q), 128.6 (2 $\times$ ArCH), 128.5 (2 $\times$ ArCH), 128.5 (2 $\times$ ArCH), 127.7 (ArCH), 127.5 (2 $\times$ ArCH), 126.2 (ArCH), 73.3 (O–CH₂), 70.9 (O–CH₂), 59.2 (C(O)C^q), 52.0 (OCH₃), 47.7 (C^qCH₂), 46.6 (CH–C(O)O), 46.1 (C(O)CH₂), 41.2 (BCH CH₂), 38.7 (BCH CH₂), 34.4 (BCH CH₂), 29.4 (PhCH₂).

IR (neat, cm^{-1}): 2950, 2876, 2856, 1731 (C=O), 1698 (C=O), 1453, 1361, 1200, 1088, 738, 696.

HRMS (APCI⁺): calculated for $\text{C}_{25}\text{H}_{29}\text{O}_4$ ($\text{M}+\text{H}^+$): 393.2060; found: 393.2048.

rac-2,2,2-Trifluoroethyl 1-(3-phenylpropanoyl)bicyclo[2.1.1]hexane-2-carboxylate (**13ag**)



Prepared by following the **general procedure C** from **11a** (0.10 mmol), **12c** (0.25 mmol), and Sml_2 (25 mol%). The reaction mixture was filtered through a silica gel pad and concentrated in vacuo. The crude product was purified by column chromatography (0-6% EtOAc in hexane) to afford **13ag** (29.0 mg, 0.085 mmol, 85% yield) as a colourless liquid.

^1H NMR (500 MHz, CDCl_3) δ 7.31 – 7.26 (m, 2H, ArCH), 7.24 – 7.15 (m, 3H, ArCH), 4.50 (dq, J = 12.7, 8.5 Hz, 1H, O–CH₂), 4.35 (dq, J = 12.7, 8.5 Hz, 1H, O–CH₂), 3.28 (ddd, J = 9.5, 4.2, 1.7 Hz, 1H, CH–C(O)O), 2.95 – 2.75 (m, 4H, 2 $\times$ CH₂), 2.49 (tt, J = 2.9, 1.4 Hz, 1H, BCH CH), 2.20 (dddd, J = 11.0, 9.4, 2.5, 1.4 Hz, 1H, BCH CH₂), 2.03 – 1.90 (m, 2H, BCH CH₂), 1.85 (dt, J = 6.8, 2.8 Hz, 1H, BCH CH₂), 1.62 (dd, J = 9.8, 7.5 Hz, 1H, BCH CH₂), 1.43 (dd, J = 9.8, 6.9 Hz, 1H, BCH CH₂).

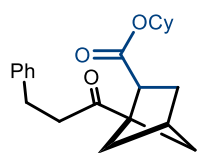
^{13}C NMR (126 MHz, CDCl_3) δ 208.6 (C=O), 172.8 (C(O)O), 141.4 (ArC^q), 128.6 (2 $\times$ ArCH), 128.5 (2 $\times$ ArCH), 126.2 (ArCH), 123.01 (q, J = 277.6 Hz, CF₃), 62.3 (C(O)C^q), 60.5 (q, J = 37.6 Hz, O–CH₂), 45.0 (C(O)CH₂), 44.9 (CH–C(O)O), 41.4 (BCH CH₂), 37.7 (BCH CH₂), 35.6 (BCH CH), 33.1 (BCH CH₂), 29.4 (PhCH₂).

^{19}F NMR (471 MHz, CDCl_3) δ -73.69 (t, J = 8.2 Hz, CF₃).

IR (neat, cm^{-1}): 3028, 2959, 1753, 1699, 1277, 1156, 1073, 981, 699.

HRMS (ESI⁺): calculated for C₁₈H₁₉O₃F₃Na (M+Na⁺): 363.1179; found: 363.1172.

rac-Cyclohexyl 1-(3-phenylpropanoyl)bicyclo[2.1.1]hexane-2-carboxylate (**13ah**)



Prepared by following the **general procedure C** from **11a** (0.10 mmol), **12d** (0.25 mmol), and Sml₂ (25 mol%). The reaction mixture was filtered through a silica gel pad and concentrated in vacuo. The crude product was purified by column chromatography (0-6% EtOAc in hexane) to afford **13ah** (30.3 mg, 0.089 mmol, 89% yield) as a colourless liquid.

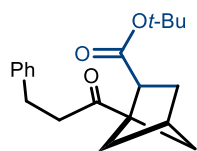
¹H NMR (500 MHz, CDCl₃) δ 7.28 (dd, *J* = 8.1, 6.9 Hz, 2H, ArCH), 7.23 – 7.16 (m, 3H, ArCH), 4.73 (dt, *J* = 9.2, 4.8 Hz, 1H, CH–O), 3.18 (ddd, *J* = 9.3, 4.1, 1.8 Hz, 1H, CH–C(O)O), 2.96 – 2.71 (m, 4H, 2 × CH₂), 2.43 (tt, *J* = 3.0, 1.4 Hz, 1H, BCH CH), 2.19 – 2.08 (m, 1H, BCH CH₂), 2.00 (dddd, *J* = 11.3, 4.1, 2.7, 1.4 Hz, 1H, BCH CH₂), 1.86 (dq, *J* = 7.2, 2.4 Hz, 1H, BCH CH₂), 1.84 – 1.78 (m, 2H, CH₂), 1.76 (dt, *J* = 6.6, 2.8 Hz, 1H, BCH CH₂), 1.73 – 1.63 (m, 2H, CH₂), 1.59 – 1.48 (m, 2H, CH₂, BCH CH₂), 1.43 (dd, *J* = 9.6, 6.6 Hz, 1H, BCH CH₂), 1.39 – 1.30 (m, 5H, CH₂).

¹³C NMR (126 MHz, CDCl₃) δ 209.1 (C=O), 173.5 (C(O)O), 141.6 (ArC^q), 128.6 (2 × ArCH), 128.5 (2 × ArCH), 126.2 (ArCH), 73.3 (CH–O), 62.2 (C(O)C^q), 46.1 (CH–C(O)O), 45.4 (C(O)CH₂), 41.0 (BCH CH₂), 37.0 (BCH CH₂), 35.2 (BCH CH), 32.8 (BCH CH₂), 31.7 (CH₂), 31.7 (CH₂), 29.5 (PhCH₂), 25.4 (CH₂), 23.9 (CH₂), 23.8 (CH₂).

IR (neat, cm⁻¹): 2927, 2856, 1723 (C=O), 1701 (C=O), 1452, 1184, 1040, 750, 698.

HRMS (ESI⁺): calculated for C₂₂H₂₈O₃Na (M+Na⁺): 363.1931; found: 363.1913.

rac-*tert*-Butyl 1-(3-phenylpropanoyl)bicyclo[2.1.1]hexane-2-carboxylate (**13ai**)



Prepared by following the **general procedure C** from **11a** (0.10 mmol), **12e** (0.25 mmol), and Sml₂ (25 mol%). The reaction mixture was filtered through a silica gel pad and concentrated in vacuo. The crude product was purified by column chromatography (0-6% EtOAc in hexane) to afford **13ai** (22.0 mg, 0.07 mmol, 70% yield) as a white crystalline solid.

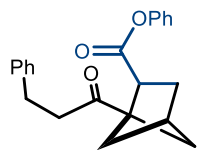
¹H NMR (400 MHz, CDCl₃) δ 7.31 – 7.25 (m, 2H, ArCH), 7.19 (ddt, *J* = 7.5, 3.1, 1.9 Hz, 3H, ArCH), 3.11 (ddd, *J* = 8.9, 4.4, 1.7 Hz, 1H, CH–CO₂*t*-Bu), 2.96 – 2.72 (m, 4H, PhCH₂CH₂), 2.40 (tt, *J* = 2.9, 1.4 Hz, 1H, BCH CH), 2.13 – 1.96 (m, 2H, BCH CH₂), 1.83 (dq, *J* = 7.2, 2.3 Hz, 1H, BCH CH₂), 1.76 – 1.71 (m, 1H, BCH CH₂), 1.50 (dd, *J* = 9.6, 7.2 Hz, 1H, BCH CH₂), 1.43 (d, *J* = 6.6 Hz, 1H, BCH CH₂), 1.40 (s, 9H, 3 × CH₃).

¹³C NMR (101 MHz, CDCl₃) δ 209.1 (C=O), 173.1 (O=C(O)*t*-Bu), 141.6 (ArC^q), 128.6 (2 × ArCH), 128.5 (2 × ArCH), 126.2 (*p*-ArCH), 81.1 [O–C(CH₃)₃], 62.4 (C(O)C^q), 46.8 (CH–CO₂*t*-Bu), 45.6 (COCH₂), 40.7 (BCH CH₂), 36.6 (BCH CH₂), 35.0 (BCH CH), 32.5 (BCH CH₂), 29.5 (PhCH₂), 28.1 (3 × CH₃).

IR (neat, cm⁻¹): 2976, 2930, 2881, 1724, 1701, 1453, 1366, 1232, 1215, 1151, 747, 699.

HRMS (ESI⁺): calculated for C₂₀H₂₆O₃Na (M+Na⁺): 337.1774; found: 337.1765.

rac-Phenyl 1-(3-phenylpropanoyl)bicyclo[2.1.1]hexane-2-carboxylate (**13aj**)



Prepared by following the **general procedure C** from **11a** (0.10 mmol), **12f** (0.25 mmol), and Sml_2 (25 mol%). The reaction mixture was filtered through a silica gel pad and concentrated in vacuo. The crude product was purified by column chromatography (0-8% EtOAc in hexane) to afford **13aj** (25.7 mg, 0.077 mmol, 77% yield) as a colourless liquid.

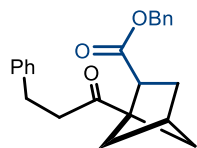
^1H NMR (400 MHz, CDCl_3) δ 7.40 – 7.34 (m, 2H, ArCH), 7.28 – 7.21 (m, 3H, ArCH), 7.17 (tt, J = 6.5, 1.4 Hz, 3H, ArCH), 7.07 – 7.01 (m, 2H, ArCH), 3.44 (ddd, J = 9.3, 4.2, 1.7 Hz, 1H, CH–C(O)O–), 2.93 – 2.87 (m, 4H, PhCH₂CH₂), 2.52 (tt, J = 3.0, 1.4 Hz, 1H, BCH CH), 2.30 – 2.20 (m, 1H, BCH CH₂), 2.16 – 2.08 (m, 1H, BCH CH₂), 1.94 (dq, J = 7.4, 2.5 Hz, 1H, BCH CH₂), 1.88 (dt, J = 6.8, 2.8 Hz, 1H, BCH CH₂), 1.74 (dd, J = 9.8, 7.4 Hz, 1H, BCH CH₂), 1.51 (dd, J = 9.7, 6.8 Hz, 1H, BCH CH₂).

^{13}C NMR (101 MHz, CDCl_3) δ 209.1 (C=O), 173.0 (C(O)O), 150.7 (ArC^q), 141.4 (ArC^q), 129.6 (2 $\times$ ArCH), 128.6 (2 $\times$ ArCH), 128.5 (2 $\times$ ArCH), 126.2 (ArCH), 126.0 (ArCH), 121.7 (2 $\times$ ArCH), 62.6 (C(O)C^q), 45.6 (CH–C(O)O), 45.1 (COCH₂), 41.3 (BCH CH₂), 37.6 (BCH CH₂), 35.5 (BCH CH), 33.0 (BCH CH₂), 29.5 (PhCH₂).

IR (neat, cm^{-1}): 2954, 2922, 1753, 1698, 1593, 1492, 1454, 1365, 1194, 1162, 1135, 1069, 1025, 741, 698.

HRMS (APCI⁺): calculated for $\text{C}_{22}\text{H}_{23}\text{O}_3$ ($\text{M}+\text{H}^+$): 335.1642; found: 335.1653.

rac-Benzyl 1-(3-phenylpropanoyl)bicyclo[2.1.1]hexane-2-carboxylate (**13ak**)



Prepared by following the **general procedure C** from **11a** (0.10 mmol), **12g** (0.25 mmol), and Sml_2 (25 mol%). The reaction mixture was filtered through a silica gel pad and concentrated in vacuo. The crude product was purified by column chromatography (0-6% EtOAc in hexane) to afford **13ak** (30.3 mg, 0.087 mmol, 87% yield) as a colourless liquid.

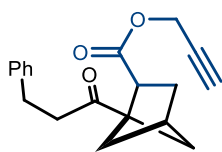
^1H NMR (500 MHz, CDCl_3) δ 7.43 – 7.30 (m, 5H, ArCH), 7.29 – 7.22 (m, 2H, ArCH), 7.21 – 7.15 (m, 1H, ArCH), 7.13 – 7.06 (m, 2H, ArCH), 5.11 (d, J = 12.2 Hz, 1H, O–CH₂Ph), 5.04 (d, J = 12.2 Hz, 1H, O–CH₂Ph), 3.25 (ddd, J = 9.3, 4.2, 1.7 Hz, 1H, CH–C(O)O), 2.86 – 2.69 (m, 4H, 2 $\times$ CH₂), 2.45 (tt, J = 2.8, 1.4 Hz, 1H, BCH CH), 2.19 – 2.11 (m, 1H, BCH CH₂), 2.01 (dddd, J = 11.3, 4.1, 2.7, 1.4 Hz, 1H, BCH CH₂), 1.89 (dq, J = 7.3, 2.4 Hz, 1H, BCH CH₂), 1.79 (dt, J = 6.7, 2.8 Hz, 1H, BCH CH₂), 1.60 (dd, J = 9.7, 7.4 Hz, 1H, BCH CH₂), 1.43 (dd, J = 9.7, 6.8 Hz, 1H, BCH CH₂).

^{13}C NMR (126 MHz, CDCl_3) δ 209.1 (C=O), 174.0 (C(O)O), 141.5 (ArC^q), 135.8 (ArC^q), 128.7 (2 $\times$ ArCH), 128.5 (2 $\times$ ArCH), 128.5 (2 $\times$ ArCH), 128.5 (2 $\times$ ArCH), 128.4 (ArCH), 126.1 (ArCH), 66.8 (O–CH₂Ph), 62.2 (C(O)C^q), 45.7 (CH–C(O)O), 45.3 (C(O)CH₂), 41.2 (BCH CH₂), 37.3 (BCH CH₂), 35.4 (BCH CH), 32.8 (BCH CH₂), 29.3 (PhCH₂).

IR (neat, cm^{-1}): 2954, 2923, 1730 (C=O), 1698 (C=O), 1453, 1205, 1028, 748, 696.

HRMS (ESI⁺): calculated for $\text{C}_{23}\text{H}_{24}\text{O}_3\text{Na}$ ($\text{M}+\text{Na}^+$): 371.1618; found: 371.1600

rac-Prop-2-yn-1-yl 1-(3-phenylpropanoyl)bicyclo[2.1.1]hexane-2-carboxylate (**13al**)



Prepared by following the **general procedure C** from **11a** (0.10 mmol), **12h** (0.25 mmol), and Sml_2 (25 mol%). The reaction mixture was filtered through a silica gel pad and concentrated in vacuo. The crude product was purified by column chromatography (0-8% EtOAc in hexane) to afford **13al** (28.0 mg, 0.094 mmol, 94% yield) as a colourless liquid.

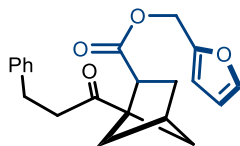
^1H NMR (400 MHz, CDCl_3) δ 7.27 – 7.21 (m, 2H, ArCH), 7.16 (d, J = 7.4 Hz, 3H, ArCH), 4.79 – 4.41 (m, 2H, OCH_2), 3.19 (ddd, J = 9.4, 4.2, 1.7 Hz, 1H $\text{CH}-\text{C}(\text{O})\text{O}-$), 3.02 – 2.69 (m, 4H, PhCH_2CH_2), 2.53 – 2.33 (m, 2H, BCH CH, alkyne CH), 2.12 (tt, J = 9.4, 1.8 Hz, 1H, BCH CH_2), 1.95 (dt, J = 11.6, 3.4 Hz, 1H, BCH CH_2), 1.86 (dt, J = 7.3, 2.3 Hz, 1H, BCH CH_2), 1.77 (dt, J = 6.2, 2.8 Hz, 1H, BCH CH_2), 1.59 (dd, J = 9.7, 7.4 Hz, 1H, BCH CH_2), 1.39 (dd, J = 9.7, 6.8 Hz, 1H, BCH CH_2).

^{13}C NMR (101 MHz, CDCl_3) δ 209.0 ($\text{C}=\text{O}$), 173.5 ($\text{O}=\text{C}(\text{O})-$), 141.5 (ArC^q), 128.6 (2 $\times$ ArCH), 128.5 (2 $\times$ ArCH), 126.1 (ArCH), 77.6 (alkyne CH), 75.1 (OCH_2C), 62.2 ($\text{C}(\text{O})\text{C}^q$), 52.2 (OCH_2), 45.3 ($\text{CH}-\text{C}(\text{O})\text{O}-$), 45.1 (COCH_2), 41.3 (BCH CH_2), 37.5 (BCH CH_2), 35.4 (BCH CH), 32.9 (BCH CH_2), 29.4 (PhCH_2).

IR (neat, cm^{-1}): 3280, 2954, 1736, 1697, 1370, 1163, 1039, 749, 698.

HRMS (ESI^+): calculated for $\text{C}_{19}\text{H}_{20}\text{O}_3\text{Na}$ ($\text{M}+\text{Na}^+$): 319.1305; found: 319.1289.

rac-Furan-2-ylmethyl 1-(3-phenylpropanoyl)bicyclo[2.1.1]hexane-2-carboxylate (**13am**)



Prepared by following the **general procedure C** from **11a** (0.10 mmol), **12i** (0.25 mmol), and Sml_2 (20 mol%). The reaction mixture was filtered through a silica gel pad and concentrated in vacuo. The crude product was purified by column chromatography (0-12% EtOAc in hexane) to afford **13am** (29.0 mg, 0.088 mmol, 88% yield) as a colourless liquid.

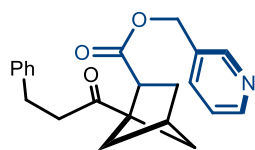
^1H NMR (400 MHz, CDCl_3) δ 7.46 (d, J = 1.8 Hz, 1H, furan CH), 7.40 – 7.32 (m, 2H, ArCH), 7.30 – 7.20 (m, 3H, ArCH), 6.46 (d, J = 3.2 Hz, 1H, furan CH), 6.42 (t, J = 2.6 Hz, 1H, furan CH), 5.14 (d, J = 13.1 Hz, 1H, $\text{CH}_2-\text{O}-\text{CO}$), 5.07 (d, J = 13.1 Hz, 1H, $\text{CH}_2-\text{O}-\text{CO}$), 3.34 – 3.24 (m, 1H, $\text{CH}-\text{C}(\text{O})\text{O}-$), 3.08 – 2.68 (m, 4H, PhCH_2CH_2), 2.51 (d, J = 3.1 Hz, 1H, BCH CH), 2.20 (td, J = 10.4, 9.6, 2.2 Hz, 1H, BCH CH_2), 2.06 (dt, J = 11.3, 3.4 Hz, 1H, BCH CH_2), 1.94 (dq, J = 7.4, 2.4 Hz, 1H, BCH CH_2), 1.85 (dt, J = 6.3, 2.9 Hz, 1H, BCH CH_2), 1.65 (dd, J = 9.7, 7.4 Hz, 1H, BCH CH_2), 1.49 (dd, J = 9.7, 6.7 Hz, 1H, BCH CH_2).

^{13}C NMR (101 MHz, CDCl_3) δ 209.1 ($\text{C}=\text{O}$), 173.8 ($\text{O}=\text{C}(\text{O})-$), 149.4 (furan: ArC^q), 143.4 (furan: ArCH), 141.6 (ArC^q), 128.5 (2 $\times$ ArCH), 128.5 (2 $\times$ ArCH), 126.1 (ArCH), 110.8 (furan: ArCH), 110.7 (furan: ArCH), 62.2 ($\text{C}(\text{O})\text{C}^q$), 58.4 ($\text{CH}_2-\text{O}-\text{CO}$), 45.6 ($\text{CH}-\text{C}(\text{O})\text{O}-$), 45.2 (COCH_2), 41.1 (BCH CH_2), 37.3 (BCH CH_2), 35.3 (BCH CH), 32.8 (BCH CH_2), 29.4 (PhCH_2).

IR (neat, cm^{-1}): 2955, 2920, 1731, 1696, 1370, 1230, 1167, 1077, 1030, 746, 699.

HRMS (ESI^+): calculated for $\text{C}_{21}\text{H}_{23}\text{O}_4$ ($\text{M}+\text{H}^+$): 339.1591; found: 339.1580.

rac-Pyridin-3-ylmethyl 1-(3-phenylpropanoyl)bicyclo[2.1.1]hexane-2-carboxylate (**13an**)



Prepared by following the **general procedure C** from **11a** (0.10 mmol), **12j** (0.25 mmol), and Sml_2 (25 mol%). The reaction mixture was filtered through a silica gel pad and concentrated in vacuo. The crude product was purified by column chromatography (0-30% EtOAc in hexane) to afford **13an** (23.4 mg, 0.067 mmol, 67% yield) as a colourless liquid.

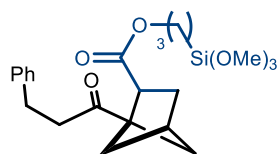
^1H NMR (500 MHz, CDCl_3) δ 8.68 – 8.52 (m, 2H, ArCH), 7.65 (dt, J = 7.8, 2.0 Hz, 1H, ArCH), 7.40 – 7.22 (m, 3H, ArCH), 7.21 – 7.15 (m, 1H, ArCH), 7.14 – 7.07 (m, 2H, ArCH), 5.11 (d, J = 12.6 Hz, 1H, O-CH₂), 5.05 (d, J = 12.5 Hz, 1H, O-CH₂), 3.23 (ddd, J = 9.4, 4.2, 1.7 Hz, 1H, CH-C(O)O), 2.93 – 2.68 (m, 4H, PhCH₂CH₂), 2.45 (tt, J = 2.9, 1.4 Hz, 1H, BCH CH), 2.23 – 2.09 (m, 1H, BCH CH₂), 1.97 (dddd, J = 11.3, 4.2, 2.7, 1.3 Hz, 1H, BCH CH₂), 1.89 (dq, J = 7.4, 2.5 Hz, 1H, BCH CH₂), 1.80 (dt, J = 6.8, 2.8 Hz, 1H, BCH CH₂), 1.60 (dd, J = 9.7, 7.4 Hz, 1H, BCH CH₂), 1.42 (dd, J = 9.7, 6.8 Hz, 1H, BCH CH₂).

^{13}C NMR (126 MHz, CDCl_3) δ 208.9 (C=O), 174.0 (C(O)O), 149.2 (ArCH), 149.2 (ArCH), 141.4 (ArC^q), 136.8 (ArCH), 131.9 (ArC^q), 128.6 (2 × ArCH), 128.5 (2 × ArCH), 126.2 (ArCH), 123.8 (ArCH), 63.9 (O-CH₂), 62.3 (C(O)C^q), 45.4 (CH-C(O)O), 45.1 (C(O)CH₂), 41.1 (BCH CH₂), 37.5 (BCH CH₂), 35.5 (BCH CH), 32.9 (BCH CH₂), 29.3 (PhCH₂).

IR (neat, cm^{-1}): 3026, 2953, 1731, 1697, 1371, 1166, 1026, 699.

HRMS (ESI⁺): calculated for $\text{C}_{22}\text{H}_{23}\text{O}_3\text{NNa}$ ($\text{M}+\text{Na}^+$): 372.1570; found: 372.1560.

rac-3-(Trimethoxysilyl)propyl 1-(3-phenylpropanoyl)bicyclo[2.1.1]hexane-2-carboxylate (**13ao**)



Prepared by following the **general procedure C** from **11a** (0.10 mmol), **12k** (0.25 mmol), and Sml_2 (25 mol%). The reaction mixture was filtered through a silica gel pad and concentrated in vacuo (78% NMR yield). The crude product was purified by column chromatography (0-6% EtOAc in hexane) to afford **13ao** (6.20 mg, 0.015 mmol, 15% yield) as a colourless liquid.

^1H NMR (500 MHz, CDCl_3) δ 7.31 – 7.26 (m, 2H, ArCH), 7.23 – 7.16 (m, 3H, ArCH), 4.10 – 3.94 (m, 2H, O-CH₂), 3.57 (d, J = 1.5 Hz, 9H, 3 × OCH₃), 3.20 (ddt, J = 9.3, 4.0, 1.5 Hz, 1H, CH-C(O)O), 2.96 – 2.74 (m, 4H, PhCH₂CH₂), 2.44 (dh, J = 2.9, 1.4 Hz, 1H, BCH CH), 2.13 (tdd, J = 10.9, 2.5, 1.3 Hz, 1H, BCH CH₂), 1.97 (dddd, J = 11.3, 4.2, 2.8, 1.4 Hz, 1H, BCH CH₂), 1.88 (dtt, J = 7.2, 2.8, 1.7 Hz, 1H, BCH CH₂), 1.77 (dh, J = 5.6, 1.4 Hz, 1H, BCH CH₂), 1.75 – 1.66 (m, 2H, CH₂), 1.62 – 1.54 (m, 1H, BCH CH₂), 1.42 (ddd, J = 9.7, 6.7, 1.4 Hz, 1H, BCH CH₂), 0.69 – 0.59 (m, 2H, CH₂-Si).

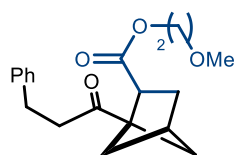
^{13}C NMR (126 MHz, CDCl_3) δ 209.1 (C=O), 174.2 (C(O)O), 141.6 (ArC^q), 128.6 (2 × ArCH), 128.5 (2 × ArCH), 126.2 (ArCH), 66.8 (O-CH₂), 62.1 (C(O)C^q), 50.7 (OCH₃),

45.8 (CH–C(O)O), 45.3 (C(O)CH₂), 41.2 (BCH CH₂), 37.3 (BCH CH₂), 35.4 (BCH CH), 32.9 (BCH CH₂), 29.5 (PhCH₂), 22.1 (CH₂), 5.5 (CH₂–Si).

IR (neat, cm⁻¹): 2954, 2931, 2883, 1726 (C=O), 1697 (C=O), 1231, 1107 (Si–O–C), 1071 (Si–O–C), 1030 (Si–O–C), 905, 749, 698.

HRMS (ESI⁺): calculated for C₂₂H₃₂O₆NaSi (M+Na⁺): 443.1860; found: 443.1847.

rac-2-Methoxyethyl 1-(3-phenylpropanoyl)bicyclo[2.1.1]hexane-2-carboxylate (**13ap**)



Prepared by following the **general procedure C** from **11a** (0.10 mmol), **12l** (0.25 mmol), and Sml₂ (20 mol%). The reaction mixture was filtered through a silica gel pad and concentrated in vacuo. The crude product was purified by column chromatography (0-12% EtOAc in hexane) to afford **13ap** (31.0 mg, 0.098 mmol, 98% yield) as a colourless liquid.

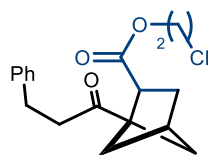
¹H NMR (400 MHz, CDCl₃) δ 7.27 – 7.19 (m, 2H, ArCH), 7.16 (d, *J* = 7.5 Hz, 3H, ArCH), 4.21 – 4.10 (m, 2H, CH₂–O–CO), 3.54 – 3.45 (m, 2H, CH₂–O–CH₃), 3.31 (s, 3H, OCH₃), 3.20 (ddd, *J* = 9.4, 4.2, 1.7 Hz, 1H, CH–C(O)O–), 2.92 – 2.71 (m, 4H, PhCH₂CH₂), 2.40 (dt, *J* = 3.0, 1.5 Hz, 1H, BCH CH), 2.10 (ddt, *J* = 11.1, 9.1, 2.0 Hz, 1H, BCH CH₂), 2.00 – 1.91 (m, 1H, BCH CH₂), 1.84 (dq, *J* = 7.2, 2.4 Hz, 1H, BCH CH₂), 1.75 (dt, *J* = 6.1, 2.8 Hz, 1H, BCH CH₂), 1.57 (dd, *J* = 9.7, 7.4 Hz, 1H, BCH CH₂), 1.39 (dd, *J* = 9.7, 6.7 Hz, 1H, BCH CH₂).

¹³C NMR (101 MHz, CDCl₃) δ 209.2 (C=O), 174.2 (O=C(O)–), 141.6 (ArC^q), 128.6 (2 × ArCH), 128.5 (2 × ArCH), 126.1 (ArCH), 70.5 (CH₂–O–CO), 63.7 (CH₂–O–CH₃), 62.2 (C(O)C^q), 59.0 (OCH₃), 45.6 (CH–C(O)O–), 45.2 (COCH₂), 41.1 (BCH CH₂), 37.3 (BCH CH₂), 35.3 (BCH CH), 32.9 (BCH CH₂), 29.4 (PhCH₂).

IR (neat, cm⁻¹): 2952, 2881, 1729, 1698, 1180, 1127, 1078, 1048, 1030, 749, 699.

HRMS (ESI⁺): calculated for C₁₉H₂₄O₄Na (M+Na⁺): 339.1567; found: 339.1552.

rac-2-Chloroethyl 1-(3-phenylpropanoyl)bicyclo[2.1.1]hexane-2-carboxylate (**13aq**)



Prepared by following the **general procedure C** from **11a** (0.10 mmol), **12m** (0.25 mmol), and Sml₂ (25 mol%). The reaction mixture was filtered through a silica gel pad and concentrated in vacuo. The crude product was purified by column chromatography (0-10% EtOAc in hexane) to afford **13aq** (28.0 mg, 0.088 mmol, 88% yield) as a colourless liquid.

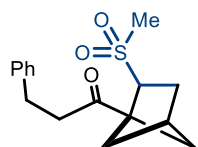
¹H NMR (400 MHz, CDCl₃) δ 7.32 – 7.24 (m, 2H, ArCH), 7.20 (d, *J* = 7.3 Hz, 3H, ArCH), 4.28 (t, *J* = 5.7 Hz, 2H, CH₂–O–CO), 3.60 (t, *J* = 5.7 Hz, 2H, CH₂–Cl), 3.39 – 3.16 (m, 1H, CH–C(O)O–), 3.03 – 2.71 (m, 4H, PhCH₂CH₂), 2.46 (t, *J* = 2.6 Hz, 1H, BCH CH), 2.16 (t, *J* = 10.4 Hz, 1H, BCH CH₂), 2.00 (dt, *J* = 11.6, 3.3 Hz, 1H, BCH CH₂), 1.94 – 1.83 (m, 1H, BCH CH₂), 1.81 (dd, *J* = 6.5, 3.1 Hz, 1H, BCH CH₂), 1.60 (dd, *J* = 9.7, 7.4 Hz, 1H, BCH CH₂), 1.43 (dd, *J* = 9.7, 6.7 Hz, 1H, BCH CH₂).

¹³C NMR (101 MHz, CDCl₃) δ 209.0 (C=O), 173.9 (O=C(O)–), 141.5 (ArC^q), 128.6 (2 × ArCH), 128.5 (2 × ArCH), 126.2 (ArCH), 64.3 (CH₂-O-CO), 62.2 (C(O)C^q), 45.4 (CH–C(O)O–), 45.2 (COCH₂), 41.7 (BCH CH₂), 41.1 (CH₂Cl), 37.4 (BCH CH₂), 35.4 (BCH CH), 32.9 (BCH CH₂), 29.4 (PhCH₂).

IR (neat, cm⁻¹): 2955, 1733, 1697, 1167, 1079, 1033, 747, 698, 663.

HRMS (ESI⁺): calculated for C₁₈H₂₁O₃ClNa (M+Na⁺): 343.1071; found: 343.1058.

rac-1-(2-(Methylsulfonyl)bicyclo[2.1.1]hexan-1-yl)-3-phenylpropan-1-one (**13ar**)



Prepared by following the **general procedure C** from **11a** (0.10 mmol), **12n** (0.25 mmol), and Sml₂ (20 mol%). The reaction mixture was filtered through a silica gel pad and concentrated in vacuo. The crude product was purified by column chromatography (0-15% EtOAc in hexane) to afford **13ar** (19.0 mg, 0.065 mmol, 65% yield) as a white crystalline solid.

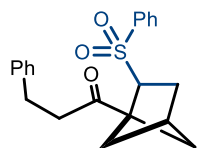
¹H NMR (400 MHz, CDCl₃) δ 7.31 – 7.25 (m, 2H, ArCH), 7.20 (d, *J* = 7.4 Hz, 3H, ArCH), 3.89 (ddd, *J* = 9.3, 4.6, 1.5 Hz, 1H, CH–SO₂–), 2.95 – 2.89 (m, 4H, PhCH₂CH₂), 2.87 (s, 3H, SO₂–CH₃), 2.57 – 2.46 (m, 1H, BCH CH), 2.34 (dddd, *J* = 12.0, 4.5, 3.0, 1.3 Hz, 1H, BCH CH₂), 2.29 – 2.17 (m, 1H, BCH CH₂), 2.09 (dd, *J* = 9.7, 7.7 Hz, 1H, BCH CH₂), 2.02 (dt, *J* = 7.7, 2.2 Hz, 1H, BCH CH₂), 1.94 (dt, *J* = 7.0, 3.0 Hz, 1H, BCH CH₂), 1.51 (dd, *J* = 9.7, 7.1 Hz, 1H, BCH CH₂).

¹³C NMR (101 MHz, CDCl₃) δ 208.6 (C=O), 141.1 (ArC^q), 128.6 (2 × ArCH), 128.6 (2 × ArCH), 126.3 (ArCH), 64.4 (CH–SO₂–), 62.6 (C(O)C^q), 47.3 (COCH₂), 43.1 (SO₂–CH₃), 42.2 (BCH CH₂), 37.0 (BCH CH₂), 34.4 (BCH CH), 30.9 (BCH CH₂), 29.3 (PhCH₂).

IR (neat, cm⁻¹): 2956, 2926, 1700, 1310, 1289, 1134, 758, 700.

HRMS (ESI⁺): calculated for C₁₆H₂₁O₃S (M+Na⁺): 293.1206; found: 293.1199.

rac-3-Phenyl-1-(2-(phenylsulfonyl)bicyclo[2.1.1]hexan-1-yl)propan-1-one (**13as**)



Prepared by following the **general procedure C** from **11a** (0.10 mmol), **12o** (0.25 mmol), and Sml₂ (17 mol%). The reaction mixture was filtered through a silica gel pad and concentrated in vacuo. The crude product was purified by column chromatography (0-20% EtOAc in hexane) to afford **13as** (28.4 mg, 0.08 mmol, 80% yield) as a colourless liquid.

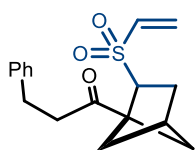
¹H NMR (500 MHz, CDCl₃) δ 7.91 – 7.81 (m, 2H, ArCH), 7.71 – 7.63 (m, 1H, ArCH), 7.61 – 7.52 (m, 2H, ArCH), 7.35 – 7.26 (m, 2H, ArCH), 7.24 – 7.10 (m, 3H, ArCH), 3.96 (ddd, *J* = 8.9, 4.4, 1.6 Hz, 1H, CH–SO₂–), 2.95 – 2.79 (m, 3H, CH₂, CH₂), 2.77 – 2.68 (m, 1H, CH₂), 2.47 (tt, *J* = 2.9, 1.4 Hz, 1H, BCH CH), 2.35 (dddd, *J* = 11.8, 4.4, 3.0, 1.4 Hz, 1H, BCH CH₂), 2.19 – 2.06 (m, 2H, BCH CH₂), 1.88 (dtd, *J* = 7.4, 2.7, 1.6 Hz, 1H, BCH CH₂), 1.80 (dt, *J* = 7.1, 3.0 Hz, 1H, BCH CH₂), 1.44 (dd, *J* = 9.8, 7.2 Hz, 1H, BCH CH₂).

¹³C NMR (126 MHz, CDCl₃) δ 207.9 (C=O), 141.4 (ArC^q), 139.9 (ArC^q), 133.9 (ArCH), 129.4 (2 × ArCH), 128.6 (2 × ArCH), 128.5 (2 × ArCH), 126.2 (ArCH), 66.8 (CH–SO₂), 62.4 (C(O)C^q), 47.3 (C(O)CH₂), 41.6 (BCH CH₂), 35.7 (BCH CH₂), 34.4 (BCH CH), 31.8 (BCH CH₂), 29.4 (PhCH₂).

IR (neat, cm⁻¹): 2984, 2955, 2924, 1700 (C=O), 1446, 1306, 1287, 1144, 1085, 738, 716, 699, 688.

HRMS (ESI⁺): calculated for C₂₁H₂₂O₃NaS (M+Na⁺): 377.1182; found: 377.1175.

rac-3-Phenyl-1-(2-(vinylsulfonyl)bicyclo[2.1.1]hexan-1-yl)propan-1-one (**13at**)



Prepared by following the **general procedure C** from **11a** (0.1 mmol), **12p** (0.25 mmol), and Sml₂ (17 mol%). The reaction mixture was filtered through a silica gel pad and concentrated in vacuo. The crude product was purified by column chromatography (0-20% EtOAc in hexane) to afford **13at** (24.3 mg, 0.08 mmol, 80% yield) as a brown viscous liquid.

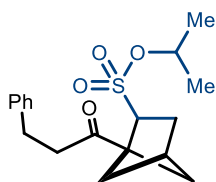
¹H NMR (400 MHz, CDCl₃) δ 7.31 – 7.25 (m, 2H, ArCH), 7.22 – 7.18 (m, 3H, ArCH), 6.58 (dd, *J* = 16.6, 9.8 Hz, 1H, CH=CH₂), 6.32 (d, *J* = 16.6 Hz, 1H, CH=CH₂), 6.02 (d, *J* = 9.9 Hz, 1H, CH=CH₂), 3.82 (ddd, *J* = 9.1, 4.6, 1.6 Hz, 1H, CH–SO₂), 2.95 – 2.82 (m, 4H, PhCH₂CH₂), 2.50 (dq, *J* = 2.9, 1.4 Hz, 1H, BCH CH), 2.30 (dddd, *J* = 12.0, 4.5, 2.9, 1.3 Hz, 1H, BCH CH₂), 2.21 (dddd, *J* = 11.8, 9.0, 2.5, 1.4 Hz, 1H, BCH CH₂), 2.12 (dd, *J* = 9.9, 7.7 Hz, 1H, BCH CH₂), 1.94 (dq, *J* = 7.5, 2.4 Hz, 1H, BCH CH₂), 1.89 (dt, *J* = 7.2, 3.0 Hz, 1H, BCH CH₂), 1.49 (dd, *J* = 9.9, 7.1 Hz, 1H, BCH CH₂).

¹³C NMR (101 MHz, CDCl₃) δ 208.2 (C=O), 141.2 (ArC^q), 137.3 (CH=CH₂), 129.7 (CH=CH₂), 128.6 (2 × ArCH), 128.6 (2 × ArCH), 126.3 (ArCH), 64.4 (CH–SO₂), 62.2 (C(O)C^q), 47.2 (COCH₂), 42.1 (BCH CH₂), 36.6 (BCH CH₂), 34.4 (BCH CH), 31.0 (BCH CH₂), 29.3 (PhCH₂).

IR (neat, cm⁻¹): 2955, 2920, 2851, 1697, 1452, 1286, 1267, 1206, 1128, 1076, 1040, 699.

HRMS (ESI⁺): calculated for C₁₇H₂₀O₃SNa (M+Na⁺): 327.1025; found: 327.1013.

rac-Isopropyl 1-(3-phenylpropanoyl)bicyclo[2.1.1]hexane-2-sulfonate (**13au**)



Prepared by following the **general procedure C** from **11a** (0.10 mmol), **12q** (0.25 mmol), and Sml₂ (25 mol%). The reaction mixture was filtered through a silica gel pad and concentrated in vacuo. The crude product was purified by column chromatography (0-6% EtOAc in hexane) to afford **13au** (19.4 mg, 0.058 mmol, 58% yield) as a colourless liquid.

¹H NMR (500 MHz, CDCl₃) δ 7.33 – 7.26 (m, 2H, ArCH), 7.23 – 7.16 (m, 3H, ArCH), 4.97 (hept, *J* = 6.3 Hz, 1H, O–CH), 3.89 (ddd, *J* = 8.7, 4.7, 1.5 Hz, 1H, CH–SO₃), 2.97 – 2.84 (m, 4H, PhCH₂CH₂), 2.48 (tt, *J* = 2.9, 1.4 Hz, 1H, BCH CH), 2.29 (dddd, *J* = 11.1, 8.7, 2.4, 1.4 Hz, 1H, BCH CH₂), 2.24 (dddd, *J* = 11.9, 4.5, 2.8, 1.3 Hz, 1H, BCH CH₂), 2.12 (dd, *J* = 9.9, 7.7 Hz, 1H, BCH CH₂), 1.85 (ddt, *J* = 7.9, 4.5, 2.2 Hz, 1H, BCH CH₂).

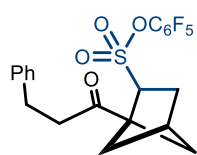
CH₂), 1.82 (dt, *J* = 7.2, 2.9 Hz, 1H, BCH CH₂), 1.49 (dd, *J* = 9.9, 7.2 Hz, 1H, BCH CH₂), 1.39 (d, *J* = 6.3 Hz, 6H, CH(CH₃)₂).

¹³C NMR (126 MHz, CDCl₃) δ 208.0 (C=O), 141.3 (ArC^q), 128.6 (2 × ArCH), 128.5 (2 × ArCH), 126.2 (ArCH), 77.1 (O–CH), 62.7 (CH–SO₃), 61.9 (C(O)C^q), 46.4 (C(O)CH₂), 41.7 (BCH CH₂), 35.7 (BCH CH₂), 34.3 (BCH CH), 32.2 (BCH CH₂), 29.4 (PhCH₂), 23.4 (CH₃), 23.3 (CH₃).

IR (neat, cm⁻¹): 2983, 2958, 2935, 1702 (C=O), 1453, 1331 (SO₂), 1167 (SO₂), 1094, 905, 876, 748, 698.

HRMS (ESI⁺): calculated for C₁₈H₂₄O₄NaS (M+Na⁺): 359.1288; found: 359.1276.

Perfluorophenyl 1-(3-phenylpropanoyl)bicyclo[2.1.1]hexane-2-sulfonate (**13av**)



Prepared by following the **general procedure C** from **11a** (0.10 mmol), **12r** (0.25 mmol), and Sml₂ (25 mol%). The reaction mixture was filtered through a silica gel pad and concentrated in vacuo. The crude product was purified by column chromatography (0-6% EtOAc in hexane) to afford **13av** (29.8 mg, 0.065 mmol, 65% yield) as a colourless liquid.

¹H NMR (400 MHz, CDCl₃) δ 7.31 – 7.21 (m, 2H, ArCH), 7.21 – 7.11 (m, 3H, ArCH), 4.32 (ddd, *J* = 8.5, 4.5, 1.5 Hz, 1H, CH–SO₃), 2.97 – 2.84 (m, 4H, PhCH₂CH₂), 2.58 (dq, *J* = 2.9, 1.5 Hz, 1H, BCH CH), 2.48 (ddt, *J* = 10.2, 8.6, 1.9 Hz, 1H, BCH CH₂), 2.41 (dddd, *J* = 12.2, 4.4, 2.9, 1.3 Hz, 1H, BCH CH₂), 2.11 (dd, *J* = 10.0, 8.0 Hz, 1H, BCH CH₂), 1.98 (dq, *J* = 7.9, 2.5 Hz, 1H, BCH CH₂), 1.93 (dt, *J* = 7.4, 2.9 Hz, 1H, BCH CH₂), 1.58 (dd, *J* = 9.9, 7.4 Hz, 1H, BCH CH₂).

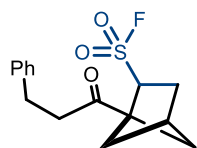
¹³C NMR (101 MHz, CDCl₃) δ 206.6 (C=O), 141.1 (ArC^q), 128.6 (2 × ArCH), 128.6 (2 × ArCH), 126.2 (ArCH), 64.8 (CH–SO₃), 62.4 (C(O)C^q), 46.4 (C(O)CH₂CH₂), 41.8 (BCH CH₂), 36.1 (BCH CH₂), 34.7 (BCH CH), 32.8 (BCH CH₂), 29.3 (PhCH₂). ArC^q and ArCF not observed.

¹⁹F NMR (376 MHz, CDCl₃) δ -148.62 – -151.97 (m, ArCF), -155.28 (td, *J* = 21.8, 1.7 Hz, ArCF), -158.78 – -162.53 (m, ArCF).

IR (neat, cm⁻¹): 2989, 2962, 2931, 1706 (C=O), 1516, 1379 (SO₂), 1184, 994, 700.

HRMS (ESI⁺): calculated for C₂₁H₁₇O₄F₅NaS (M+Na⁺): 483.0660; found: 483.0649.

rac-1-(3-Phenylpropanoyl)bicyclo[2.1.1]hexane-2-sulfonyl fluoride (**13aw**)



Prepared by following the **general procedure C** from **111a** (0.10 mmol), **12s** (0.25 mmol), and Sml₂ (20 mol%). The reaction mixture was filtered through a silica gel pad and concentrated in vacuo. The crude product was purified by column chromatography (0-12% EtOAc in hexane) to afford **13aw** (18.0 mg, 0.062 mmol, 62% yield) as a white crystalline solid.

¹H NMR (400 MHz, CDCl₃) δ 7.29 (t, *J* = 7.4 Hz, 2H, ArCH), 7.20 (t, *J* = 8.3 Hz, 3H, ArCH), 4.21 (dd, *J* = 9.0, 4.4 Hz, 1H, CH–SO₂–), 3.02 – 2.74 (m, 4H, PhCH₂CH₂), 2.59

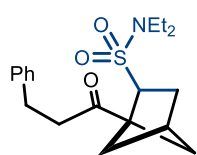
(s, 1H, BCH CH), 2.51 – 2.40 (m, 1H, BCH CH₂), 2.33 (dt, *J* = 12.3, 3.7 Hz, 1H, BCH CH₂), 2.01 (d, *J* = 6.0 Hz, 2H, BCH CH₂), 1.93 (dq, *J* = 8.0, 2.7 Hz, 1H, BCH CH₂), 1.58 – 1.47 (m, 1H, BCH CH₂).

¹³C NMR (101 MHz, CDCl₃) δ 206.3 (C=O), 140.9 (ArC^q), 128.7 (2 × ArCH), 128.5 (2 × ArCH), 126.4 (ArCH), 62.8 (d, *J*² = 15.2, CH–SO₂–), 62.3 (C(O)C^q), 46.1 (d, *J* = 3.0, COCH₂), 41.7 (BCH CH₂), 36.3 (BCH CH₂), 34.7 (BCH CH), 32.6 (BCH CH₂), 29.3 (PhCH₂).

IR (neat, cm⁻¹): 3332, 2954, 2917, 1071, 1399, 1208, 1110, 1051, 1028, 986.

HRMS (ESI⁺): calculated for C₁₅H₁₈O₃FS (M+H⁺): 297.0955; found: 297.0949.

rac-*N,N*-Diethyl-1-(3-phenylpropanoyl)bicyclo[2.1.1]hexane-2-sulfonamide (**13ax**)



Prepared by following the **general procedure C** from **11a** (0.10 mmol), **12t** (0.25 mmol), and Sml₂ (25 mol%). The reaction mixture was filtered through a silica gel pad and concentrated in vacuo. The crude product was purified by column chromatography (0-10% EtOAc in hexane) to afford **13ax** (16.7 mg, 0.048 mmol, 48% yield) as a colourless liquid.

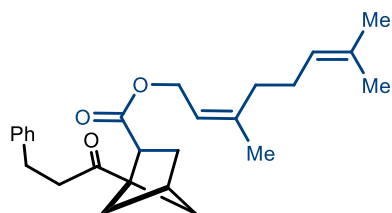
¹H NMR (400 MHz, CDCl₃) δ 7.33 – 7.23 (m, 2H, ArCH), 7.23 – 7.15 (m, 3H, ArCH), 3.84 (ddd, *J* = 8.6, 4.5, 1.5 Hz, 1H, CH–SO₂N), 3.32 – 3.21 (m, 4H, PhCH₂CH₂), 3.00 – 2.81 (m, 4H, 2 × N–CH₂CH₃), 2.46 (tt, *J* = 2.9, 1.4 Hz, 1H, BCH CH), 2.22 (dddd, *J* = 11.5, 4.4, 2.9, 1.4 Hz, 1H, BCH CH₂), 2.17 (dt, *J* = 8.8, 2.0 Hz, 1H, BCH CH₂), 2.11 (dd, *J* = 9.8, 7.5 Hz, 1H, BCH CH₂), 1.84 (dq, *J* = 7.3, 2.1 Hz, 1H, BCH CH₂), 1.78 (dt, *J* = 7.0, 2.8 Hz, 1H, BCH CH₂), 1.45 (dd, *J* = 9.8, 7.1 Hz, 1H, BCH CH₂), 1.19 (t, *J* = 7.1 Hz, 6H, 2 × N–CH₂CH₃).

¹³C NMR (101 MHz, CDCl₃) δ 208.8 (C=O), 141.6 (ArC^q), 128.6 (2 × ArCH), 128.6 (2 × ArCH), 126.1 (ArCH), 64.2 (CH–SO₂N), 62.1 (C(O)C^q), 46.6 (C(O)CH₂), 42.1 (BCH CH₂), 41.6 (2 × N–CH₂CH₃), 35.9 (BCH CH₂), 34.8 (BCH CH), 32.5 (BCH CH₂), 29.4 (PhCH₂), 14.6 (2 × N–CH₂CH₃).

IR (neat, cm⁻¹): 2973, 2924, 1701 (C=O), 1325 (SO₂), 1201, 1137 (SO₂), 1017, 934, 749, 696.

HRMS (ESI⁺): calculated for C₁₉H₂₇ONNaS (M+Na⁺): 372.1604; found: 372.1596.

rac-(*Z*)-3,7-Dimethylocta-2,6-dien-1-yl 1-(3-phenylpropanoyl)bicyclo[2.1.1]hexane-2-carboxylate (**13ay**)



Prepared by following the **general procedure C** from **11a** (0.10 mmol), **12u** (0.25 mmol), and Sml₂ (25 mol%). The reaction mixture was filtered through a silica gel pad and concentrated in vacuo. The crude product was purified by column chromatography (0-6% EtOAc in hexane) to afford **13ay** (35.1 mg, 0.089 mmol, 89% yield) as a colourless liquid.

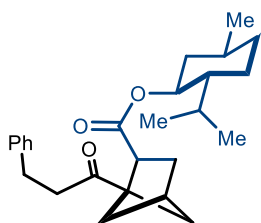
¹H NMR (500 MHz, CDCl₃) δ 7.31 – 7.24 (m, 2H, ArCH), 7.22 – 7.16 (m, 3H, ArCH), 5.29 (tq, *J* = 7.2, 1.4 Hz, 1H, CH=C^q), 5.07 (tdt, *J* = 6.9, 2.9, 1.5 Hz, 1H, CH=C^q), 4.59 (dd, *J* = 12.4, 7.1 Hz, 1H, CH₂–O), 4.53 (dd, *J* = 12.4, 7.1 Hz, 1H, CH₂–O), 3.20 (ddd, *J* = 9.4, 4.2, 1.7 Hz, 1H, CH–C(O)O), 2.94 – 2.71 (m, 4H, PhCH₂CH₂), 2.43 (tt, *J* = 2.9, 1.4 Hz, 1H, BCH CH), 2.20 – 2.06 (m, 3H, BCH CH₂, CH₂), 2.05 – 2.00 (m, 2H, CH₂), 1.98 (dddd, *J* = 11.2, 4.2, 2.7, 1.4 Hz, 1H, CH₂), 1.87 (dq, *J* = 7.3, 2.4 Hz, 1H, BCH CH₂), 1.77 (dt, *J* = 6.7, 2.8 Hz, 1H, BCH CH₂), 1.70 – 1.65 (m, 6H, C^q(CH₃)₂), 1.62 – 1.56 (m, 4H, BCH CH₂, CH₃), 1.42 (dd, *J* = 9.7, 6.7 Hz, 1H, BCH CH₂).

¹³C NMR (126 MHz, CDCl₃) δ 209.2 (C=O), 174.2 (C(O)O), 142.6 (C^q=CH), 141.6 (ArC^q), 132.0 (C^q=CH), 128.6 (2 × ArCH), 128.5 (2 × ArCH), 126.1 (ArCH), 123.9 (C^q=CH), 118.2 (C^q=CH), 62.2 (C(O)C^q), 61.7 (CH₂–O), 45.8 (CH–C(O)O), 45.2 (C(O)CH₂), 41.2 (BCH CH₂), 39.6 (CH₂), 37.2 (BCH CH₂), 35.3 (BCH CH), 32.8 (BCH CH₂), 29.5 (PhCH₂), 26.4 (CH₂), 25.8 (CH₃), 17.8 (CH₃), 16.6 (CH₃).

IR (neat, cm⁻¹): 2974, 2882, 1728 (C=O), 1698 (C=O), 1452, 1375, 1178, 1030, 750, 698.

HRMS (ESI⁺): calculated for C₂₆H₃₄O₃Na (M+Na⁺): 417.2400; found: 417.2388.

(1*S*,2*R*,5*S*)-2-Isopropyl-5-methylcyclohexyl 1-(3-phenylpropanoyl)bicyclo[2.1.1]hexane-2-carboxylate (**13az**)



Prepared by following the **general procedure C** from **11a** (0.10 mmol), **12v** (0.25 mmol), and Sml₂ (25 mol%). The reaction mixture was filtered through a silica gel pad and concentrated in vacuo. The crude product was purified by column chromatography (0–3% EtOAc in hexane) to afford **13az** (34.5 mg, 0.087 mmol, 87% yield, d.r. 1:1) as a colourless liquid.

¹H NMR (500 MHz, CDCl₃) δ 7.31 – 7.26 (m, 2H, ArCH ^{d1d2}), 7.22 – 7.16 (m, 3H, ArCH ^{d1d2}), 4.72 – 4.61 (m, 1H, CH–O ^{d1d2}), 3.21 (dd, *J* = 4.2, 1.8 Hz, 1H, CH–C(O)O ^{d1}), 3.19 (dd, *J* = 4.1, 1.8 Hz, 1H, CH–C(O)O ^{d2}), 2.95 – 2.75 (m, 4H, PhCH₂CH₂ ^{d1d2}), 2.49 – 2.40 (m, 1H, BCH CH ^{d1d2}), 2.22 – 2.09 (m, 1H, CH₂ ^{d1d2}), 2.00 (dddd, *J* = 11.2, 4.1, 2.7, 1.3 Hz, 1H, aliphatic ^{d1}), 1.96 – 1.90 (m, 2H, aliphatic ^{d1d2}), 1.88 (dq, *J* = 7.1, 2.4 Hz, 1H, aliphatic ^{d2}), 1.86 – 1.79 (m, 1H, aliphatic ^{d1d2}), 1.78 – 1.74 (m, 1H, aliphatic ^{d1d2}), 1.70 – 1.63 (m, 2H, aliphatic ^{d1d2}), 1.55 (dd, *J* = 9.7, 7.3 Hz, 1H, BCH CH₂ ^{d1}), 1.51 (dd, *J* = 9.7, 7.3 Hz, 1H, BCH CH₂ ^{d2}), 1.49 – 1.38 (m, 2H, BCH CH₂ ^{d1d2}), 1.37 – 1.27 (m, 1H, CH₂ ^{d1d2}), 1.08 – 0.98 (m, 1H, CH₂ ^{d1d2}), 0.96 – 0.85 (m, 8H, 2 × CH₃, CH₂ ^{d1d2}), 0.74 (d, *J* = 5.8 Hz, 3H, CH₃ ^{d1}), 0.73 (d, *J* = 5.8 Hz, 3H, CH₃ ^{d2}).

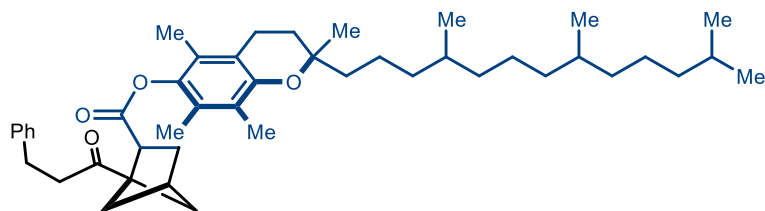
¹³C NMR (126 MHz, CDCl₃) δ 209.0 (C=O) ^{d1}, 208.8 (C=O) ^{d2}, 173.9 (C(O)O) ^{d1}, 173.7 (C(O)O) ^{d2}, 141.6 (ArC^q) ^{d1}, 141.6 (ArC^q) ^{d2}, 128.6 (2 × ArCH) ^{d1}, 128.6 (2 × ArCH) ^{d2}, 128.5 (2 × ArCH) ^{d1}, 128.5 (2 × ArCH) ^{d2}, 126.2 (ArCH) ^{d1}, 126.1 (ArCH) ^{d2}, 74.8 (CH–O) ^{d1}, 74.7 (CH–O) ^{d2}, 62.1 (C(O)C^q) ^{d1}, 61.9 (C(O)C^q) ^{d2}, 47.1 (CH–C(O)O) ^{d1}, 47.0 (CH–C(O)O) ^{d2}, 46.0 (CH) ^{d1}, 46.0 (CH) ^{d2}, 45.4 (C(O)CH₂) ^{d1d2}, 41.2 (CH₂) ^{d1}, 41.1 (CH₂) ^{d2}, 41.0 (CH₂) ^{d1}, 40.9 (CH₂) ^{d2}, 37.3 (CH₂) ^{d1}, 37.0 (CH₂) ^{d2}, 35.4 (BCH CH) ^{d1}, 35.3 (BCH CH) ^{d2}, 34.3 (CH₂) ^{d1d2}, 33.3 (CH₂) ^{d1}, 32.8 (CH₂) ^{d2}, 31.5 (CH) ^{d1}, 31.5

(CH)^{d2}, 29.5 (PhCH₂)^{d1d2}, 26.3 (CH)^{d1}, 26.0 (CH)^{d2}, 23.4 (CH₂)^{d1}, 23.2 (CH₂)^{d2}, 22.1 (CH₃)^{d1}, 22.1 (CH₃)^{d2}, 21.0 (CH₃)^{d1d2}, 16.2 (CH₃)^{d1}, 16.1 (CH₃)^{d2}.

IR (neat, cm⁻¹): 2953, 2927, 2869, 1723 (C=O), 1701 (C=O), 1453, 1368, 1179, 1030, 750, 697.

HRMS (ESI⁺): calculated for C₂₆H₃₆O₃Na (M+Na⁺): 419.2557; found: 419.2544.

(*R*)-2,5,7,8-Tetramethyl-2-((4*R*,8*R*)-4,8,12-trimethyltridecyl)chroman-6-yl 1-(3-phenylpropanoyl)bicyclo[2.1.1]hexane-2-carboxylate (**13aaa**)



Prepared by following the **general procedure C** from **11a** (0.10 mmol), **12w** (0.25 mmol), and Sml₂ (25 mol%). The reaction mixture was filtered through a silica gel

pad and concentrated in vacuo. The crude product was purified by column chromatography (0-5% EtOAc in hexane) to afford **13aaa** (27.0 mg, 0.04 mmol, 40% yield) as a colourless liquid.

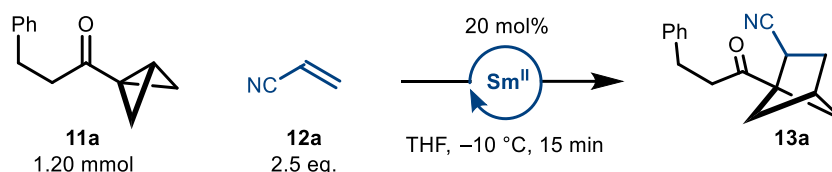
¹H NMR (400 MHz, CDCl₃) δ 7.26 – 7.20 (m, 2H, ArCH), 7.18 – 7.12 (m, 3H, ArCH), 3.58 – 3.51 (m, 1H, CH–C(O)O–), 3.01 – 2.83 (m, 4H, PhCH₂CH₂), 2.62 – 2.51 (m, 3H, CH₂, BCH CH), 2.39 – 2.30 (m, 1H, BCH CH₂), 2.17 – 2.11 (m, 1H, BCH CH₂), 2.10 – 2.08 (m, 3H, CH₃), 2.05 – 2.01 (m, 1H, aliphatic), 1.99 – 1.97 (m, 3H, CH₃), 1.96 – 1.90 (m, 3H, CH₃), 1.89 – 1.69 (m, 4H, aliphatic), 1.55 – 1.51 (m, 1H, aliphatic), 1.50 – 1.47 (m, 1H, aliphatic), 1.45 – 1.33 (m, 4H, aliphatic), 1.31 – 1.20 (m, 11H, aliphatic, CH₃), 1.18 – 1.02 (m, 8H, aliphatic), 0.90 – 0.80 (m, 12H, 4 × CH₃).

¹³C NMR (101 MHz, CDCl₃) δ 208.9 (C=O), 173.1 (O=C(O)–), 149.6 (ArC^q), 141.5 (ArC^q), 140.5 (ArC^q), 131.4 (ArC^q), 128.6 (ArC^q), 128.5 (2 × ArCH), 128.5 (2 × ArCH), 126.1 (ArCH), 75.2 (O–C^q), 62.0 (C(O)C^q), 45.6 (CH–C(O)O), 45.4 (COCH₂), 41.6 (CH₂), 39.5 (CH₂), 37.8 (CH₂), 37.6 (CH₂), 37.6 (CH₂), 37.5 (CH₂), 37.4 (CH₂), 35.8 (BCH CH), 33.3 (CH₂), 32.9 (CH₃), 32.9 (CH), 29.5 (PhCH₂), 28.1 (CH₃), 25.0 (CH₂), 24.6 (CH₂), 22.9 (CH₃), 22.8 (CH₃), 21.2 (CH₂), 20.8 (CH₂), 19.9 (CH₃), 19.8 (CH₃), 19.8 (CH), 19.7 (CH), 12.3 (CH₃), 12.0 (CH₃) “2 × ArC^q missing”.

IR (neat, cm⁻¹): 2923, 2866, 1747, 1701, 1454, 1375, 1152, 1106, 1076, 697.

HRMS (APCI⁺): calculated for C₄₅H₆₇O₄ (M+H⁺): 671.5034; found: 671.5020.

5. Larger-scale reaction



To an oven-dried round bottom flask was charged with a magnetic stir-bar and BCB-ketone **11a** (223 mg, 1.20 mmol, 1 equiv.). The flask was sealed and flushed with N_2 . After 15 min, acrylonitrile **12a** (0.20 mL, 3.00 mmol, 2.5 equiv.) and THF (0.25 mL/mmol) were sequentially introduced by syringe. The flask was placed in a cold bath at $-10\text{ }^{\circ}\text{C}$, followed by the dropwise addition of freshly prepared SmI_2 (20 mol%, 0.1 M). The reaction mixture was stirred at $-10\text{ }^{\circ}\text{C}$ for 15 min. After completion, the reaction mixture was diluted with CH_2Cl_2 followed by saturated aqueous sodium thiosulphate solution. The mixture was poured into a saturated aqueous solution of sodium potassium tartrate and the aqueous layer was extracted three times with CH_2Cl_2 . The combined organic layer was dried over MgSO_4 and concentrated in vacuo to give the crude product. The crude product was then purified by column chromatography (silica gel 100-200 mesh size; hexane/ethyl acetate) to afford the final product **13a** (273 mg, 1.14 mmol, 95% yield) as a white solid.

5.1. Reaction Colour Study

The colour of the above larger-scale reaction (Section 5) was monitored. The reaction was over after 15 min (with 95% product formation) and the mixture was still deep blue. The persistence of the blue colour (associated with SmI_2) is supportive of the proposed catalytic process in which SmI_2 is regenerated.



Reaction time: 0 min
(Before SmI_2 addition)



Reaction time: 1 min



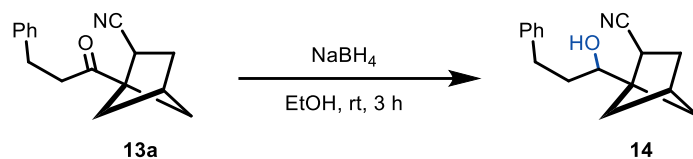
Reaction time: 10 min



Reaction time: 15 min
(End of the reaction)

6. Product Manipulations

6.1. Carbonyl reduction



To an oven-dried reaction vial containing a magnetic stir-bar, nitrile **13a** (23.9 mg, 0.10 mmol) and sodium borohydride (18.0 mg, 0.50 mmol, 5 eq.) were added. Ethanol (1 mL) was then introduced by syringe and the reaction mixture was stirred for 3 h at room temperature. After completion, the reaction was quenched with dilute HCl carefully and the aqueous layer was extracted with Et₂O (3 × 3 mL). The combined organic layer was dried over MgSO₄ and concentrated in vacuo. After removal of the solvent, final alcohol product **14** obtained as a colorless oil (24.0 mg, 0.10 mmol, 100%) and as a 1:1 mixture of diastereomers.

rac-1-(1-hydroxy-3-phenylpropyl)bicyclo[2.1.1]hexane-2-carbonitrile (**14**)

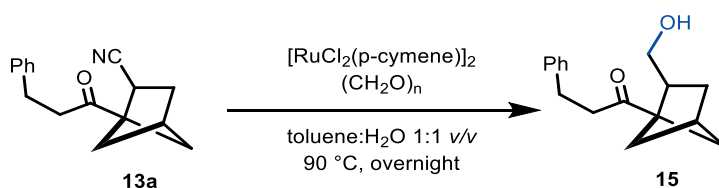
¹H NMR (400 MHz, CDCl₃) δ 7.34 – 7.27 (m, 2H, ArCH), 7.25 – 7.18 (m, 3H, ArCH), 3.94 (t, *J* = 3.3 Hz, 1H, CH–CN^{d1}), 3.91 (t, *J* = 3.3 Hz, 1H, CH–CN^{d2}), 3.00 – 2.86 (m, 1H, CH–OH), 2.78 – 2.63 (m, 1H, CH₂), 2.59 – 2.46 (m, 1H, BCH CH), 2.33 – 2.12 (m, 1H, CH₂), 2.09 – 1.94 (m, 1H BCH CH₂), 1.92 – 1.67 (m, 4H, CH₂ and BCH CH₂), 1.66 – 1.60 (m, 1H, BCH CH₂), 1.52 – 1.35 (m, 1H, BCH CH₂), 1.13 – 0.96 (m, 1H, BCH CH₂).

¹³C NMR (101 MHz, CDCl₃) δ 141.8 (ArC^q^{d1}), 141.8 (ArC^q^{d2}), 128.7 (2 × ArCH)^{d1}, 128.6 (2 × ArCH)^{d2}, 128.5 (2 × ArCH)^{d1d2}, 126.2 (ArCH)^{d1}, 126.2 (ArCH)^{d2}, 122.8 (C≡N)^{d1}, 122.5 (C≡N)^{d2}, 70.4 (CH–OH)^{d1}, 70.2 (CH–OH)^{d2}, 60.2 (C(O)C^q)^{d1}, 59.9 (C(O)C^q)^{d2}, 38.2 (BCH CH₂)^{d1}, 38.1 (BCH CH₂)^{d2}, 37.8 (PhCH₂CH₂)^{d1}, 37.4 (PhCH₂CH₂)^{d2}, 36.5 (BCH CH₂)^{d1}, 35.9 (BCH CH₂)^{d2}, 35.6 (CH–CN)^{d1}, 35.3 (CH–CN)^{d2}, 35.0 (BCH CH₂)^{d1}, 34.7 (BCH CH₂)^{d2}, 32.8 (PhCH₂)^{d1}, 32.5 (PhCH₂)^{d2}, 29.3 (BCH CH)^{d1}, 29.2 (BCH CH)^{d2}.

IR (neat, cm⁻¹): 3434, 2979, 2949, 2879, 2235, 1454, 1279, 1081, 1064, 1030, 748, 699.

HRMS (ESI⁺): calculated for C₁₆H₁₉ONNa (M+Na⁺): 264.1359; found: 264.1346.

6.2. Selective nitrile reduction



According to a related procedure from the literature:⁷ To an oven-dried microwave reaction vial containing a magnetic stir-bar, nitrile **13a** (23.9 mg, 0.10 mmol, 1 equiv.),

paraformaldehyde (27.0 mg, 0.90 mmol, 9 equiv.) and $[\text{RuCl}_2(\text{p-cymene})]_2$ (1.20 mg, 2 mol%) were introduced and the vial was sealed (to avoid any leakage) under air. Toluene (0.5 M, 0.2 mL) and water (0.5 M, 0.2 mL) were added by syringe and the vial was placed in a pre-heated oil bath at 90 °C. The reaction mixture was vigorously stirred (750 rpm) at 90 °C overnight. Then the reaction mixture was allowed to reach room temperature, the cap was slowly opened to guarantee a slow gas release. The crude mixture was neutralized using a saturated aqueous Na_2CO_3 solution and extracted three times with CH_2Cl_2 . The combined organic layers were dried over MgSO_4 , filtered and concentrated under vacuum. The crude residue was purified by column chromatography (30% EtOAc in hexane) to afford **15** (9.60 mg, 0.039 mmol, 39% yield) as a colourless liquid.

rac-1-(2-(Hydroxymethyl)bicyclo[2.1.1]hexan-1-yl)-3-phenylpropan-1-one (**15**)

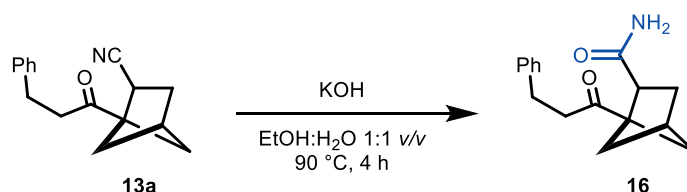
^1H NMR (400 MHz, CDCl_3) δ 7.34 – 7.24 (m, 2H, ArCH), 7.23 – 7.15 (m, 3H, ArCH), 3.66 – 3.50 (m, 2H, CH_2OH), 2.94 – 2.75 (m, 4H, CH_2 , BCH CH_2), 2.60 – 2.45 (m, 2H, CH_2), 2.38 (tt, $J = 2.9, 1.4$ Hz, 1H, BCH CH), 1.96 (ddt, $J = 11.0, 9.0, 2.0$ Hz, 1H, BCH CH_2), 1.84 (p, $J = 2.9$ Hz, 1H, BCH CH_2), 1.76 (dt, $J = 5.6, 2.8, 1.4$ Hz, 1H, BCH CHCH_2OH), 1.54 – 1.38 (m, 2H, BCH CH_2), 1.18 (dddd, $J = 11.2, 4.2, 2.7, 1.4$ Hz, 1H, BCH CH_2).

^{13}C NMR (101 MHz, CDCl_3) δ 190.8 (C=O), 141.5 (ArC^q), 128.6 (2 × ArCH), 128.5 (2 × ArCH), 126.2 (ArCH), 64.8 (CH_2OH), 44.8 (C(O) CH_2), 44.3 (CHCH_2OH), 41.2 (BCH CH_2), 36.8 (BCH CH_2), 35.3 (BCH CH), 32.0 (BCH CH_2), 29.6 (Ph CH_2). C(O)C^q not observed.

IR (neat, cm^{-1}): 3428 (O-H), 2951, 2874, 1696 (C=O), 1496, 1453, 1368, 1063, 748, 698.

HRMS (APCI⁺): calculated for $\text{C}_{16}\text{H}_{21}\text{O}_2$ ($\text{M}+\text{H}^+$): 245.1536; found: 245.1528.

6.3. Hydration of nitrile



According to a related procedure from the literature:⁸ To a microwave reaction vial containing a magnetic stir-bar, nitrile **13a** (23.9 mg, 0.10 mmol, 1 equiv.) and KOH (25.3 mg, 0.45 mmol, 4.5 equiv.) were introduced under air. Ethanol (0.5 M, 0.2 mL) and water (0.5 M, 0.2 mL) were added by syringe and the vial was placed in a pre-heated oil bath at 90 °C. The reaction mixture was vigorously stirred (750 rpm) at 90 °C for 4 h. Then the reaction mixture was allowed to reach room temperature and the cap was opened. The crude mixture was neutralized using a 1 M HCl solution and extracted three times with CH_2Cl_2 . The combined organic layers were dried over MgSO_4 , filtered and concentrated under vacuum. The crude residue was purified by

column chromatography (0-10% acetone in CH₂Cl₂) to afford **16** (15.5 mg, 0.06 mmol, 60% yield) as a white solid.

rac-1-(3-Phenylpropanoyl)bicyclo[2.1.1]hexane-2-carboxamide (**16**)

¹H NMR (400 MHz, CDCl₃) δ 7.32 – 7.23 (m, 2H, ArCH), 7.22 – 7.15 (m, 3H, ArCH), 5.75 (br, 1H, NH₂), 5.30 (br, 1H, NH₂), 3.09 (ddd, *J* = 8.8, 4.4, 1.6 Hz, 1H, CH–C(O)NH₂), 2.97 – 2.74 (m, 4H, PhCH₂CH₂), 2.46 (tt, *J* = 2.9, 1.4 Hz, 1H, BCH CH), 2.14 – 1.99 (m, 2H, BCH CH₂), 1.95 – 1.84 (m, 2H, BCH CH₂), 1.79 (dd, *J* = 9.6, 7.1 Hz, 1H, BCH CH₂), 1.43 (dd, *J* = 9.6, 6.7 Hz, 1H, BCH CH₂).

¹³C NMR (101 MHz, CDCl₃) δ 211.0 (C=O), 175.8 (C(O)NH₂), 141.3 (ArC^q), 128.6 (2 × ArCH), 128.5 (2 × ArCH), 126.3 (ArCH), 62.7 (C(O)C^q), 46.4 (C(O)CH₂), 45.4 (CH–C(O)NH₂), 42.0 (BCH CH₂), 37.2 (BCH CH₂), 35.8 (BCH CH), 32.4 (BCH CH₂), 29.4 (PhCH₂).

¹H NMR (500 MHz, MeOH-*d*₄) δ 7.30 – 7.21 (m, 2H, ArCH), 7.21 – 7.16 (m, 2H, ArCH), 7.16 – 7.12 (m, 1H, ArCH), 3.15 (ddd, *J* = 9.5, 4.3, 1.7 Hz, 1H, CH–C(O)NH₂), 2.99 – 2.77 (m, 4H, PhCH₂CH₂), 2.39 (tt, *J* = 2.9, 1.4 Hz, 1H, BCH CH), 2.18 (dddd, *J* = 10.9, 9.4, 2.5, 1.4 Hz, 1H, BCH CH₂), 1.90 (dtd, *J* = 7.1, 2.7, 1.7 Hz, 1H, BCH CH₂), 1.83 (dddd, *J* = 10.9, 4.1, 2.6, 1.3 Hz, 1H, BCH CH₂), 1.79 – 1.71 (m, 2H, BCH CH₂), 1.39 (dd, *J* = 9.6, 6.6 Hz, 1H, BCH CH₂).

¹³C NMR (126 MHz, MeOH-*d*₄) δ 212.4 (C=O), 179.3 (C(O)NH₂), 142.8 (ArC^q), 129.4 (4 × ArCH), 127.0 (ArCH), 63.4 (C(O)C^q), 47.4 (CH–C(O)NH₂), 46.0 (C(O)CH₂), 42.3 (BCH CH₂), 38.3 (BCH CH₂), 36.2 (BCH CH), 34.7 (BCH CH₂), 30.4 (PhCH₂).

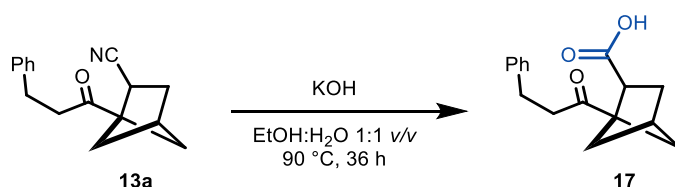
IR (neat, cm⁻¹): 3379 (N–H), 3286 (N–H), 2967, 2942, 2915, 2876, 2550, 2415, 1693 (C=O), 1632 (C=O), 1451, 1374, 751, 734, 693.

HRMS (ESI⁺): calculated for C₁₆H₁₉O₂NNa (M+Na⁺): 280.1308; found: 280.1300.

HRMS (APCI⁺): calculated for C₁₆H₂₀O₂N (M+H⁺): 258.1489; found: 258.1483.

HRMS (APCI⁻): calculated for C₁₆H₁₈O₂N (M-H⁺): 256.1343; found: 256.1331.

6.4. Hydrolysis of nitrile



According to a related procedure from the literature:⁸ To a microwave reaction vial containing a magnetic stir-bar, nitrile **13a** (23.9 mg, 0.10 mmol, 1 equiv.) and KOH (25.3 mg, 0.90 mmol, 9 equiv.) were introduced under air. Ethanol (0.5 M, 0.2 mL) and water (0.5 M, 0.2 mL) were added by syringe and the vial was placed in a pre-heated oil bath at 90 °C. The reaction mixture was vigorously stirred (750 rpm) at 90 °C for 36 h. Then the reaction mixture was allowed to reach room temperature and the cap was opened. The crude mixture was diluted with a 2 N KOH solution and washed with

CH₂Cl₂. The aqueous layer was then neutralized using a 4 M HCl solution and extracted three times with CH₂Cl₂. The combined organic layers were dried over MgSO₄, filtered and concentrated under vacuum to afford **17** (24.1 mg, 0.093 mmol, 93% yield) as a white solid.

rac-1-(3-Phenylpropanoyl)bicyclo[2.1.1]hexane-2-carboxylic acid (**17**)

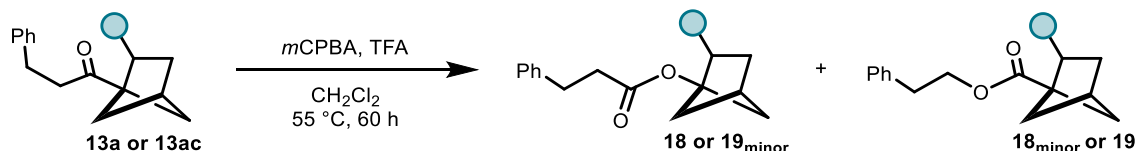
¹H NMR (500 MHz, MeOD-*d*₄) δ 7.30 – 7.21 (m, 2H, ArCH), 7.21 – 7.12 (m, 3H, ArCH), 3.23 (ddd, *J* = 9.5, 4.2, 1.8 Hz, 1H, CH–COOH), 2.95 – 2.80 (m, 4H, PhCH₂CH₂), 2.40 (tt, *J* = 2.9, 1.4 Hz, 1H, BCH CH), 2.16 (dddd, *J* = 11.0, 9.4, 2.5, 1.4 Hz, 1H, BCH CH₂), 1.94 (dddd, *J* = 11.1, 4.2, 2.7, 1.4 Hz, 1H, BCH CH₂), 1.89 (dtd, *J* = 7.2, 2.7, 1.8 Hz, 1H, BCH CH₂), 1.75 (dt, *J* = 6.5, 2.8 Hz, 1H, BCH CH₂), 1.51 (dd, *J* = 9.7, 7.1 Hz, 1H, BCH CH₂), 1.44 (dd, *J* = 9.7, 6.5 Hz, 1H, BCH CH₂).

¹³C NMR (126 MHz, MeOD-*d*₄) δ 212.0 (C=O), 177.6 (C(O)OH), 142.7 (ArC^q), 129.4 (2 × ArCH), 129.4 (2 × ArCH), 127.0 (ArCH), 63.3 (C(O)C^q), 47.0 (CH–C(O)OH), 46.1 (C(O)CH₂), 41.8 (BCH CH₂), 37.8 (BCH CH₂), 36.3 (BCH CH), 33.8 (BCH CH₂), 30.4 (PhCH₂).

HRMS (ESI⁺): calculated for C₁₆H₁₈O₃Na (M+Na⁺): 281.1148; found: 281.1136.

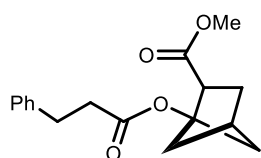
HRMS (ESI⁻): calculated for C₁₆H₁₇O₃ (M-H⁺): 257.1183; found: 257.1179.

6.5. Baeyer-Villiger oxidation



General procedure D: A flame-dried microwave vial with magnetic stir bar was charged with ketone **13a** or **13ac** (0.10 mmol), *m*-CPBA (≤77%, 172 mg, 1.00 mmol), and CH₂Cl₂ (2 mL). The vial was sealed with a rubber septum and purged three times with nitrogen. The vial was then placed in an ice bath, followed by the addition of trifluoroacetic acid (32 μL, 0.40 mmol). The vial was then covered in aluminium foil, and stirred for 60 h at 55 °C. After completion, the reaction was quenched by washing with saturated aqueous Na₂SO₃. The aqueous layer was extracted three times with CH₂Cl₂ (3 × 5 mL). The combined organics were washed one more time with brine, dried over MgSO₄, and concentrated under vacuo to give the crude product. The crude product was then purified by column chromatography (silica gel 100-200 mesh size; hexane/ethyl acetate) to afford the desired product.

Methyl 1-((3-phenylpropanoyl)oxy)bicyclo[2.1.1]hexane-2-carboxylate (**18**)



Prepared by following the **general procedure D** from **13ac** (27.2 mg, 0.10 mmol). The crude product was purified by column chromatography (silica gel 100-200 mesh size; hexane/ethyl

acetate) to afford **18** (12.0 mg, 0.042 mmol, 42% yield) as a light-yellow solid.

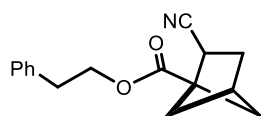
¹H NMR (400 MHz, CDCl₃) δ 7.36 – 7.27 (m, 2H, ArCH), 7.24 – 7.17 (m, 3H, ArCH), 3.62 (s, 3H, OCH₃), 3.28 (ddd, *J* = 9.0, 4.2, 1.4 Hz, 1H, CH–CO–OCH₃), 3.05 – 2.85 (m, 2H, O–C(O)CH₂), 2.71 – 2.53 (m, 2H, PhCH₂), 2.35 (tt, *J* = 3.3, 1.5 Hz, 1H, BCH CH), 2.09 (dq, *J* = 11.1, 2.2 Hz, 1H, BCH CH₂), 2.04 (dd, *J* = 9.4, 6.6 Hz, 1H, BCH CH₂), 2.00 – 1.92 (m, 1H, BCH CH₂), 1.89 – 1.80 (m, 2H, BCH CH₂), 1.76 – 1.68 (m, 1H, BCH CH₂).

¹³C NMR (101 MHz, CDCl₃) δ 174.1 (–CO–OCH₃), 172.0 (–O–C=O), 140.6 (ArC^q), 128.6 (2 × ArCH), 128.4 (2 × ArCH), 126.4 (ArCH), 82.4 (O–C^q), 51.8 (OCH₃), 45.9 (O–C(O)CH₂), 41.5 (CH–CO–OCH₃), 39.6 (BCH CH₂), 36.1 (BCH CH₂), 32.8 (BCH CH₂), 30.9 (PhCH₂), 29.1 (BCH CH).

IR (neat, cm⁻¹): 2953, 1732, 1435, 1363, 1274, 1242, 1205, 1145, 751, 698.

HRMS (ESI⁺): calculated for C₁₇H₂₀O₄Na (M+Na⁺): 311.1254; found: 311.1259.

Phenethyl 2-cyanobicyclo[2.1.1]hexane-1-carboxylate (**19**)



Prepared by following the **general procedure D** from **13a** (47.8 mg, 0.20 mmol). The crude products were purified by column chromatography (silica gel 100-200 mesh size; hexane/ethyl acetate) to afford **19** (32.0 mg, 0.12 mmol, 62% yield) as a light-yellow solid and **19**_{minor} (8.00 mg, 0.03 mmol, 16% yield) as a light-yellow solid.

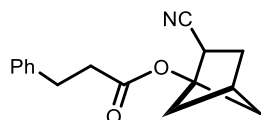
¹H NMR (400 MHz, CDCl₃) δ 7.34 – 7.28 (m, 2H, ArCH), 7.26 – 7.19 (m, 3H, ArCH), 4.38 (tt, *J* = 7.0, 3.8 Hz, 2H, O–CH₂), 3.04 (ddd, *J* = 9.2, 3.9, 1.9 Hz, 1H, CH–CN), 2.99 (t, *J* = 7.0 Hz, 2H, PhCH₂), 2.56 (t, *J* = 1.5 Hz, 1H, BCH CH), 2.40 – 2.17 (m, 1H, BCH CH₂), 2.14 – 1.92 (m, 3H, BCH CH₂ and BCH CH₂), 1.68 (dd, *J* = 9.9, 7.8 Hz, 1H, BCH CH₂), 1.33 (dd, *J* = 9.9, 7.1 Hz, 1H, BCH CH₂).

¹³C NMR (101 MHz, CDCl₃) δ 169.7 (–O–C=O), 137.6 (ArC^q), 129.1 (2 × ArCH), 128.6 (2 × ArCH), 126.8 (ArCH), 121.7 (C≡N), 65.7 (O–CH₂), 55.9 (C(O)C^q), 43.0 (BCH CH₂), 39.5 (BCH CH₂), 36.4 (CH–CN), 35.1 (BCH CH₂), 35.1 (PhCH₂), 30.1 (BCH CH).

IR (neat, cm⁻¹): 2957, 2239, 1728, 1454, 1310, 1269, 1217, 1167, 1126, 1101, 1069, 748, 699

HRMS (ESI⁺): calculated for C₁₆H₁₇O₂NNa (M+Na⁺): 278.1152; found: 278.1139.

2-Cyanobicyclo[2.1.1]hexan-1-yl 3-phenylpropanoate (**19**_{minor})



¹H NMR (400 MHz, CDCl₃) δ 7.34 – 7.27 (m, 2H, ArCH), 7.24 – 7.18 (m, 3H, ArCH), 3.32 (ddd, *J* = 9.3, 4.0, 1.9 Hz, 1H, CH–CN), 2.96 (t, *J* = 7.8 Hz, 2H, O–C(O)CH₂), 2.68 (td, *J* = 7.6, 2.7 Hz, 2H, PhCH₂), 2.47 (tt, *J* = 3.4, 1.6 Hz, 1H, BCH CH), 2.26 – 2.14 (m, 1H, BCH CH₂), 2.07 – 2.00 (m, 1H, BCH CH₂), 1.95 (ddd, *J* = 5.4, 4.0, 2.5 Hz, 1H, BCH CH₂), 1.93 – 1.89 (m, 2H, BCH CH₂), 1.78 (dd, *J* = 9.5, 7.2 Hz, 1H, BCH CH₂).

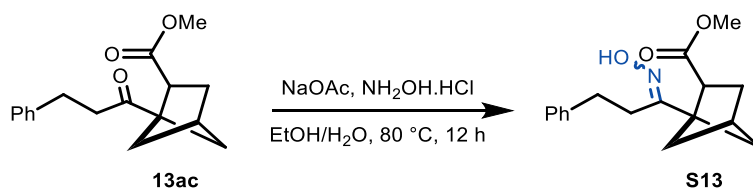
^{13}C NMR (101 MHz, CDCl_3) δ 172.1 ($-\text{O}-\text{C}=\text{O}$), 140.2 (ArC^q), 128.7 ($2 \times \text{ArCH}$), 128.4 ($2 \times \text{ArCH}$), 126.5 (ArCH), 121.0 ($\text{C}\equiv\text{N}$), 81.5 ($\text{O}-\text{C}^q$), 43.3 ($\text{O}-\text{C}(\text{O})\text{CH}_2$), 41.3 (BCH CH_2), 36.0 (BCH CH_2), 35.2 (BCH CH_2), 30.9 (PhCH_2), 29.8 ($\text{CH}-\text{CN}$), 28.7 (BCH CH).

IR (neat, cm^{-1}): 2961, 2926, 2240, 1740, 1271, 1228, 1194, 1149, 1070, 752, 698.

HRMS (ESI^+): calculated for $\text{C}_{16}\text{H}_{17}\text{O}_2\text{NNa}$ ($\text{M}+\text{Na}^+$): 278.1152; found: 278.1139.

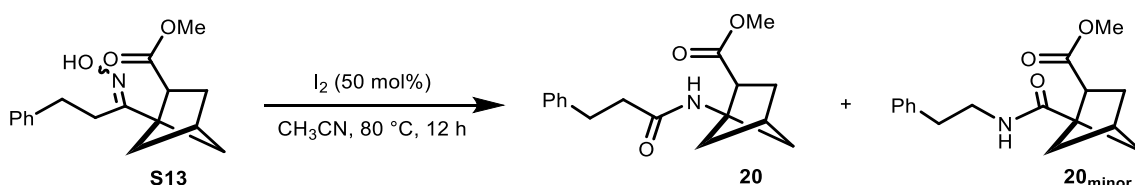
6.6. Beckmann rearrangement

Oxime synthesis:



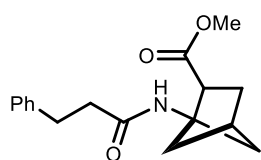
Ketone **13ac** (82.0 mg, 0.30 mol) and hydroxylamine hydrochloride (31.0 mg, 0.45 mol) were dissolved in EtOH (2 mL) and H_2O (4 mL). To the mixture was added NaOAc (49.2 mg, 0.60 mol) and the reaction was heated under reflux for 12 h. After completion of the reaction, the reaction mixture was cooled to room temperature, and 1 M HCl (15 mL) and water (50 mL) were added. The aqueous layer was extracted three times with EtOAc (3×15 mL). The combined organics were washed with brine, dried over MgSO_4 , and concentrated under vacuo to give the **S13** product (86.0 mg, 0.30 mmol, 100%, E:Z ~ 5:1) as a colourless sticky solid.

Beckmann rearrangement:



In an oven-dried microwave reaction vial, to the corresponding **S13** (57.4 mg, 0.20 mmol, E:Z ~ 5:1) in anhydrous acetonitrile (2 mL) was added I_2 (25.0 mg, 50 mol%) and the reaction mixture was stirred vigorously for 12 h at 80 °C. The solvent was removed under reduced pressure and the mixture was treated with saturated aqueous $\text{Na}_2\text{S}_2\text{O}_3$ (10 mL). The aqueous layer was extracted with EtOAc (3×10 mL), and the combined extracts were washed with brine (1×10 mL). The combined organic extracts were dried over MgSO_4 and concentrated in vacuo to give the crude product. The product was purified by column chromatography on silica gel (hexane/ethyl acetate) to afford **20** (41.0 mg, 0.14 mmol, 72% yield) as a light-yellow crystalline solid and **20_{minor}** (13.0 mg, 0.04 mmol, 23% yield) as a white solid.

Methyl 1-(3-phenylpropanamido)bicyclo[2.1.1]hexane-2-carboxylate (**20**)



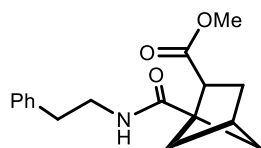
^1H NMR (400 MHz, CDCl_3) δ 7.35 – 7.22 (m, 2H, ArCH), 7.19 (d, J = 7.4 Hz, 3H, ArCH), 6.18 (s, 1H, CONH), 3.65 (s, 3H, O-CH₃), 3.04 (dd, J = 9.2, 4.5 Hz, 1H, CH-CO-OCH₃), 2.93 (t, J = 7.8 Hz, 2H, NHCOCH₂), 2.43 (t, J = 7.9 Hz, 2H, PhCH₂), 2.40 – 2.24 (m, BCH CH), 2.15 (dt, J = 4.9, 2.5 Hz, 1H, BCH CH₂), 2.08 – 1.90 (m, 2H, BCH CH₂), 1.90 – 1.82 (m, 1H, BCH CH₂), 1.71 – 1.55 (m, 2H, BCH CH₂).

^{13}C NMR (101 MHz, CDCl_3) δ 175.0 (-CO-OCH₃), 172.3 (CONH), 141.0 (ArC^q), 128.6 (2 × ArCH), 128.5 (2 × ArCH), 126.3 (ArCH), 62.3 (CONH-C^q), 51.8 (O-CH₃), 44.7 (NHCOCH₂), 43.8 (CH-CO-OCH₃), 39.4 (BCH CH₂), 38.9 (BCH CH₂), 32.6 (BCH CH₂), 32.4 (BCH CH), 31.7 (PhCH₂).

IR (neat, cm^{-1}): 3285, 2988, 2952, 1730, 1649, 1536, 1497, 1434, 1364, 1287, 1194, 1174, 699.

HRMS (ESI⁺): calculated for C₁₇H₂₂O₃N (M+H⁺): 288.1594; found: 288.1583.

Methyl 1-(phenethylcarbamoyl)bicyclo[2.1.1]hexane-2-carboxylate (**20**_{minor})



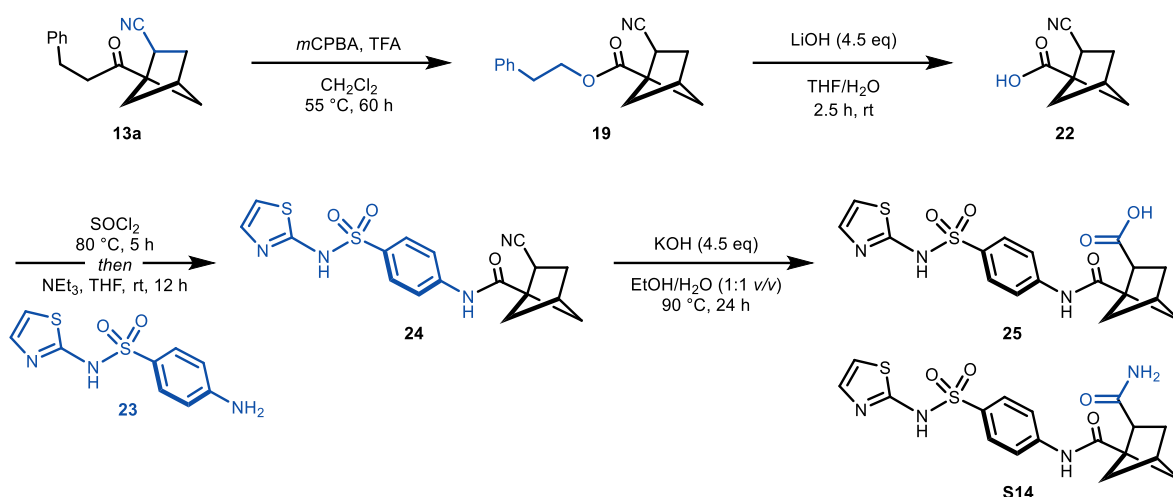
^1H NMR (400 MHz, CDCl_3) δ 7.31 (t, J = 7.4 Hz, 2H, ArCH), 7.21 (t, J = 6.5 Hz, 3H, ArCH), 5.92 (s, 1H, CONH), 3.64 (s, 3H, O-CH₃), 3.50 (q, J = 6.8 Hz, 2H, CH₂NH), 3.13 (dd, J = 9.5, 4.2 Hz, 1H, CH-CO-OCH₃), 2.81 (td, J = 6.9, 4.3 Hz, 2H, PhCH₂), 2.43 – 2.26 (s, 1H, BCH CH), 2.17 (t, J = 10.3 Hz, 1H, BCH CH₂), 1.91 – 1.77 (m, 2H, BCH CH₂), 1.72 (p, J = 6.8 Hz, 2H, BCH CH₂), 1.45 (dd, J = 9.0, 7.0 Hz, 1H, BCH CH₂).

^{13}C NMR (101 MHz, CDCl_3) δ 175.7 (-CO-OCH₃), 172.2 (CONH), 139.1 (ArC^q), 128.9 (2 × ArCH), 128.7 (2 × ArCH), 126.6 (ArCH), 56.7 (NHC(O)-C^q), 51.9 (O-CH₃), 44.9 (CH-CO-OCH₃), 44.2 (CH₂NH), 40.6 (BCH CH₂), 38.0 (BCH CH₂), 35.9 (BCH CH₂), 34.6 (BCH CH), 33.7 (PhCH₂).

IR (neat, cm^{-1}): 3308, 2951, 2880, 1730, 1636, 1531, 1434, 1232, 1196, 1169, 748, 699

HRMS (ESI⁺): calculated for C₁₇H₂₂O₃N (M+H⁺): 288.1594; found: 288.1600.

7. Synthesis of drug analogue 25

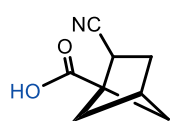


Scheme S6. Synthetic route for the drug analogue

Step-1: **19** was synthesized following the procedure described in the [section 6.5](#).

Step-2: To an oven-dried reaction vial containing a magnetic stir-bar was added **19** (178 mg, 0.70 mmol), THF (7 mL) and water (2 mL). Lithium hydroxide (132 mg, 3.15 mmol, 4.5 eq.) was then introduced and the reaction mixture was stirred for 3 h at room temperature. After completion, the reaction was quenched with 2 M HCl and the aqueous layer was extracted with EtOAc (3 × 10 mL). The combined organics were washed with brine, dried over MgSO₄, and concentrated under vacuo. The product was purified by column chromatography on silica gel (hexane/ethyl acetate) to afford **22** (88.0 mg, 0.58 mmol, 83% yield) as a white crystalline solid.

2-cyanobicyclo[2.1.1]hexane-1-carboxylic acid (**22**)



¹H NMR (400 MHz, CDCl₃) δ 3.12 (ddd, *J* = 9.1, 3.9, 1.9 Hz, 1H, CH–CN), 2.62 (tt, *J* = 2.9, 1.4 Hz, 1H, BCH CH), 2.30 (dddd, *J* = 10.6, 9.1, 2.6, 1.3 Hz, 1H, BCH CH₂), 2.16 (ddt, *J* = 16.3, 7.3, 2.7 Hz, 2H, BCH CH₂), 2.08 (dddd, *J* = 11.5, 4.1, 2.8, 1.4 Hz, 1H, BCH CH₂), 1.74 (dd, *J* = 9.9, 7.8 Hz, 1H, BCH CH₂), 1.43 (dd, *J* = 9.9, 7.3 Hz, 1H, BCH CH₂).

¹³C NMR (101 MHz, CDCl₃) δ 175.0 (C(O)OH), 121.5 (C≡N), 55.8 (OH(O)C–C^q) 43.2 (BCH CH₂), 39.5 (BCH CH₂), 36.7 (CH–CN), 35.1 (BCH CH₂), 30.0 (BCH CH).

IR (neat, cm⁻¹): 2995, 2960, 2888, 2597, 2242, 1703, 1313, 1270, 1223, 1174.

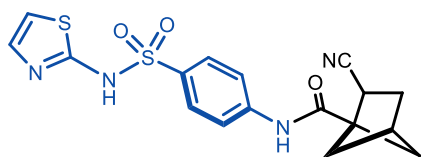
GCMS: calculated for C₈H₉NO₂: 151.06; found: 151.

Step-3: To an oven-dried microwave vial containing a magnetic stir-bar, was added acid **22** (15.1 mg, 0.10 mmol) and SOCl₂ (1.5 mL). The vial was sealed with a septum and stirred for 5 h at 80 °C. Solvent was removed under reduced pressure (toxic

waste!) and the solid crude material was dissolved in THF (1 mL) and used in the following step.

In an oven-dried reaction vial containing a magnetic stir-bar, was added sulfathiazole **23** (25 mg, 0.1 mmol), THF (1 mL), NEt₃ (28 µL, 0.2 mmol, 0.2 eq.). The vial was placed in an ice-cold bath and the crude material from the previous step (acid chloride) was added dropwise. The reaction mixture was stirred overnight at room temperature. After completion, THF was removed under reduced pressure and the crude material was treated with 2 (M) HCl. The aqueous layer was extracted with EtOAc (3 × 10 mL) and the combined layers were dried over MgSO₄. The crude product was purified by column chromatography on silica gel (CH₂Cl₂/MeOH: 20:1) to afford **24** (24.4 mg, 0.063 mmol, 63% yield) as a white powder.

2-cyano-*N*-(4-(*N*-(thiazol-2-yl)sulfamoyl)phenyl)bicyclo[2.1.1]hexane-1-carboxamide (**24**)



¹H NMR (400 MHz, DMSO-*d*₆) δ 9.93 (s, 1H, CONH), 7.81 (d, *J* = 8.8 Hz, 2H, ArCH), 7.76 (d, *J* = 8.9 Hz, 2H, ArCH), 7.23 (d, *J* = 4.6 Hz, 1H, CH–N(thiazole)), 6.80 (d, *J* = 4.6 Hz, 1H, CH–S(thiazole)), 3.39 (dt, *J* = 8.9, 2.6 Hz, 1H, CH–CN), 2.52 – 2.49 (m, 1H, BCH CH), 2.29 – 2.15 (m, 2H, BCH CH₂), 2.06 (dt, *J* = 6.4, 2.8 Hz, 1H, BCH CH₂), 1.88 (dt, *J* = 11.3, 3.3 Hz, 1H, BCH CH₂), 1.54 (dd, *J* = 9.7, 7.3 Hz, 1H, BCH CH₂), 1.46 (dd, *J* = 9.8, 6.8 Hz, 1H, BCH CH₂).

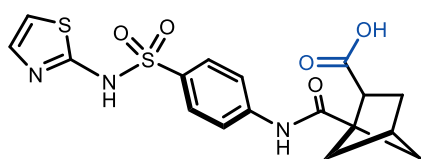
¹³C NMR (101 MHz, DMSO-*d*₆) δ 168.8 (CONH), 168.8 (thiazole ArC^q), 141.8 (ArC^q), 136.9 (ArC^q), 126.9 (2 × ArCH), 124.5 (CH–N(thiazole)), 122.2 (C≡N), 119.6 (2 × ArCH), 108.2 (CH–S(thiazole)), 57.7 (NHC(O)–C^q), 42.0 (CH–CN), 38.9 (BCH CH₂), 35.3 (BCH CH₂), 34.2 (BCH CH), 30.0 (BCH CH₂).

IR (neat, cm^{–1}): 2956, 2918, 2849, 2234, 1531, 1504, 1463, 1397, 1251, 1144, 1087, 934.

HRMS (ESI⁺): calculated for C₁₇H₁₇O₃N₄S₂ (M+H⁺): 389.0737; found: 389.0728.

Step-4: To a microwave reaction vial under air containing a magnetic stir-bar, nitrile **24** (37.5 mg, 0.096 mmol, 1 equiv.) and KOH (24.4 mg, 0.434 mmol, 4.5 equiv.) were introduced. Ethanol (0.2 M, 0.5 mL) and water (0.2 M, 0.5 mL) were added by syringe and the vial was placed in a pre-heated oil bath at 90 °C. The reaction mixture was vigorously stirred (750 rpm) at 90 °C for 24 h. Then the reaction mixture was allowed to reach room temperature and the cap was opened. The crude mixture was neutralized using a 1 M HCl solution and extracted three times with EtOAc. The combined organic layers were dried over MgSO₄, filtered and concentrated under vacuum. The crude residue was analysed by ¹H NMR and NMR yields were determined using CH₂Br₂ as an internal standard (**25**: 58% yield, **S14**: 19% yield). The residue was then purified by column chromatography (0-20% MeOH in CH₂Cl₂) to afford pure **25** as a colourless oil for analysis.

1-((4-(*N*-(thiazol-2-yl)sulfamoyl)phenyl)carbamoyl)bicyclo[2.1.1]hexane-2-carboxylic acid (**25**)



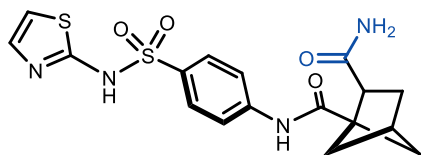
¹H NMR (600 MHz, DMSO-*d*₆) δ 12.39 (bs, 2H, NH, C(O)OH), 9.70 (bs, 1H, NH), 7.83 – 7.75 (m, 2H, ArCH), 7.74 – 7.68 (m, 2H, ArCH), 7.21 (d, *J* = 4.5 Hz, 1H, Het ArCH), 6.77 (d, *J* = 4.6 Hz, 1H, Het ArCH), 3.21 (ddd, *J* = 9.5, 4.2, 1.6 Hz, 1H, CH–C(O)OH), 2.38 – 2.36 (m, 1H, BCH CH), 2.08 (dd, *J* = 11.3, 9.0 Hz, 1H, BCH CH₂), 2.01 – 1.94 (m, 1H, BCH CH₂), 1.86 (dt, *J* = 6.0, 2.8 Hz, 1H, BCH CH₂), 1.84 – 1.78 (m, 1H, BCH CH₂), 1.56 (dd, *J* = 9.7, 6.9 Hz, 1H, BCH CH₂), 1.51 (dd, *J* = 9.6, 6.3 Hz, 1H, BCH CH₂).

¹³C NMR (151 MHz, DMSO-*d*₆) δ 175.3 (C(O)OH), 170.7 (C(O)NH), 168.8 (Het ArC^q), 142.2 (ArC^q), 136.6 (ArC^q), 126.7 (2 × ArCH, 1 Het ArCH), 119.1 (2 × ArCH), 108.0 (Het ArCH), 57.0 (C(O)C^q), 44.7 (CH–C(O)OH), 44.2 (BCH CH₂), 37.2 (BCH CH₂), 34.1 (BCH CH), 32.4 (BCH CH₂).

IR (neat, cm⁻¹): 3442, 2252, 2125, 1662, 1052, 1024, 1004, 821, 758, 623.

HRMS (ESI⁻): calculated for C₁₇H₁₆O₅N₃S₂ (M-H⁺): 406.0537; found: 406.0521.

N-(4-(*N*-(thiazol-2-yl)sulfamoyl)phenyl)bicyclo[2.1.1]hexane-1,2-dicarboxamide (**S14**)



¹H NMR (500 MHz, DMSO-*d*₆) δ 12.68 (br, 1H, NH), 9.68 (s, 1H, NH), 7.78 (d, *J* = 8.8 Hz, 2H, 2 × ArCH), 7.71 (d, *J* = 8.8 Hz, 2H, 2 × ArCH), 7.28 (br, 1H, C(O)NH₂), 7.23 (d, *J* = 4.6 Hz, 1H, ArCH), 6.85 (br, 1H, C(O)NH₂), 6.80 (d, *J* = 4.6 Hz, 1H, ArCH), 3.05 (dd, *J* = 9.5, 4.2 Hz, 1H, CH–C(O)NH₂), 2.35 – 2.32 (m, 1H, BCH CH), 2.06 (t, *J* = 10.0 Hz, 1H, BCH CH₂), 1.95 – 1.90 (m, 1H, BCH CH₂), 1.86 – 1.77 (m, 2H, BCH CH₂), 1.75 – 1.70 (m, 1H, BCH CH₂), 1.42 (dd, *J* = 9.6, 6.5 Hz, 1H, BCH CH₂).

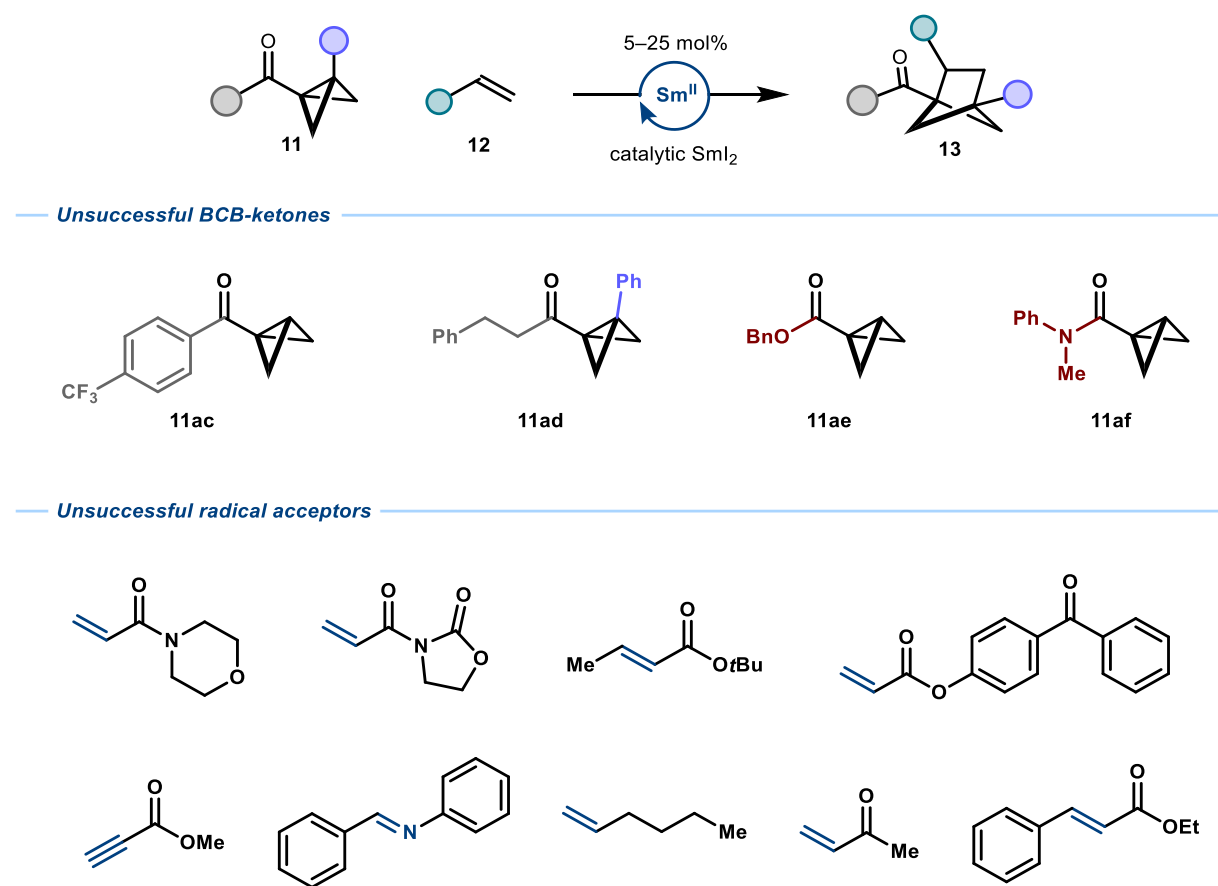
¹³C NMR (126 MHz, DMSO-*d*₆) δ 175.7 (C(O)NH₂), 171.2 (C(O)NH), 168.7 (ArC^q), 142.2 (ArC^q), 136.3 (ArC^q), 126.7 (2 × ArCH), 124.7 (ArCH), 119.2 (2 × ArCH), 108.1 (ArCH), 57.1 (C(O)C^q), 45.0 (CH–C(O)NH₂), 44.3 (BCH CH₂), 37.4 (BCH CH₂), 33.8 (BCH CH), 33.3 (BCH CH₂).

IR (neat, cm⁻¹): 3342, 2955, 2924, 2853, 1667, 1589, 1524, 1399, 1327, 1279, 1142, 1090, 1024, 1003, 688, 639.

HRMS (ESI⁻): calculated for C₁₇H₁₇O₄N₄S₂ (M-H⁺): 405.0697; found: 405.0696

HRMS (ESI⁺): calculated for C₁₇H₁₈O₄N₄S₂Na (M+Na⁺): 429.0662; found: 429.0656

8. Unsuccessful Substrates



Scheme S7. Unsuccessful substrates

Discussion: ester **11ae**, and amide **11af** were unreactive in the SmI_2 -catalyzed protocol. This is likely due to the higher reduction potential of these more electron-rich carbonyl groups. Thus, ketyl radicals (*c.f.* structure **I** in Figure 1) are not formed in the presence of catalytic amounts of SmI_2 reductant under our standard conditions.

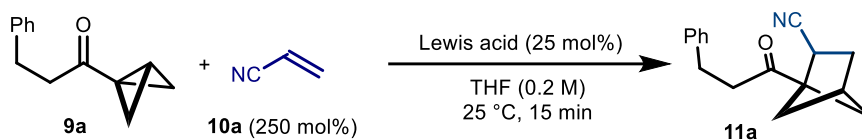
Interestingly, electron-deficient aromatic BCB ketone **11ac** may be ineffective as a substrate due to destabilisation of the ketyl radical – formed upon SET reduction by SmI_2 – by the sigma electron-withdrawing effect of the CF_3 group. This destabilization may favour back electron-transfer to $\text{Sm}(\text{III})$ and the return of starting BCB ketone.

Conversely, for BCB **11ad**, we believe that the formation of a stable tertiary benzylic radical (*c.f.* structure **II** in Figure 1) – upon fragmentation of the BCB ring – slows down the intermolecular addition of the radical intermediate to the alkene partner. Thus, we believe that the benzylic radical undergoes intramolecular re-addition to the Sm -enolate to return starting BCB ketone.

On the other hand, the successful participation of alkenes in the SmI_2 -catalyzed BCH formation process seems to be influenced both by electronic factors (electron-deficient alkenes are currently required), sterics (beta-substitution on electron-deficient alkenes is not currently tolerated) and the stability of the alkenes to the catalytic conditions. In the majority of the unsuccessful experiments, degradation of the alkene partners was observed, even if the alkenes were present in superstoichiometric amounts.

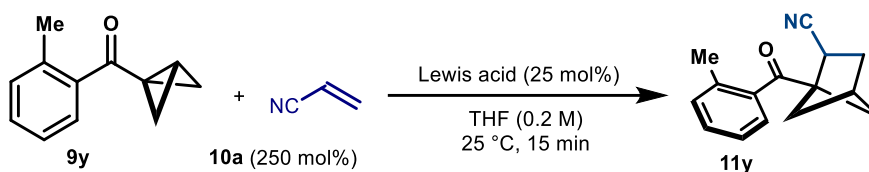
The use of the alkyne partner, methyl propiolate, was unsuccessful. This is most likely due to an unfavourable radical rebound step to generate a highly-strained unsaturated BCH scaffold.

9. Control experiments with Lewis acids



entry	Lewis acid	conversion	yield 11a
1	Sm(OTf) ₃	100%	0
2	La(OTf) ₃	100%	0
3	Yb(OTf) ₃	100%	0
4	Al(OTf) ₃	100%	0
5	standard condition with 25 mol% SmI ₂	100%	88

Table S1. Lewis acid experiments with substrate **9a**



entry	Lewis acid	conversion	yield 11y
1	Sm(OTf) ₃	100%	0
2	La(OTf) ₃	100%	0
3	Yb(OTf) ₃	100%	0
4	Al(OTf) ₃	100%	0
5	standard condition with 25 mol% SmI ₂	100%	68

Table S2. Lewis acid experiments with substrate **9y**

10. Effect of SmI_2 -catalyst loading

The amount of SmI_2 catalyst used was determined on a case-by-case basis: the catalytic reactions were usually set up using approximately 17-25 mol% of SmI_2 – as inferred upon determination of the concentration of a freshly prepared solution of SmI_2 in THF, by titration. For reactions that delivered BCH analogues **13** in high yield, the catalysis was repeated using lower loadings of SmI_2 , in order to test the efficiency of the process and to identify the most cost-effective and sustainable reaction conditions.

As a comparative study, we have re-performed the SmI_2 -catalyzed procedures to make BCHs **13c**, **13e** and **13n** at different catalyst loadings (ranging from 5 mol% to 20 mol%, see Scheme below).

Reaction scheme: Ketone **11** + Alkene **12a** $\xrightarrow[\text{catalytic } \text{SmI}_2]{5-20 \text{ mol\%}}$ BCH **13**

BCH 13c			BCH 13e		
entry	SmI_2 loading	yield 13c	entry	SmI_2 loading	yield 13e
1	5 mol%	30	1	5 mol%	73
2	10 mol%	51	2	7.5 mol%	78
3	15 mol%	75	3	10 mol%	86
2	17 mol%	88	2	15 mol%	86
2	20 mol%	90			

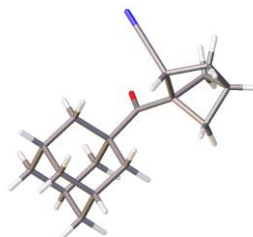
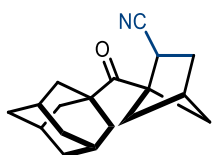
Chemical structure of BCH **13n**

entry	SmI_2 loading	yield 13n
1	5 mol%	90
2	7.5 mol%	89
3	10 mol%	92
2	15 mol%	87

Table S3. Efficiency of the SmI_2 -catalyzed alkene insertion reaction, delivering BCHs **13c**, **13e** and **13n**, at different catalyst loadings

11. X-ray Structures

11.1. X-ray structure of **13s**



CCDC 2129464

Crystal data and structure refinement of **13s**

Bond precision: C-C = 0.0030 Å Wavelength=0.71073
Cell: a=10.0176(8) b=12.8217(9) c=11.5215(8)
alpha=90 beta=106.552(7) gamma=90
Temperature: 100 K

	Calculated	Reported
Volume	1418.53(19)	1418.53(19)
Space group	P 21/c	P 1 21/c 1
Hall group	-P 2ybc	-P 2ybc
Moiety formula	C ₁₈ H ₂₃ N O	C ₁₈ H ₂₃ N O
Sum formula	C ₁₈ H ₂₃ N O	C ₁₈ H ₂₃ N O
Mr	269.37	269.37
D _x , g cm ⁻³	1.261	1.261
Z	4	4
Mu (mm ⁻¹)	0.077	0.077
F ₀₀₀	584.0	584.0
F ₀₀₀ '	584.22	
h, k, lmax	13,17,15	13,17,15
Nref	3810	3239
Tmin, Tmax	0.977,0.985	0.926,1.000
Tmin'	0.977	

Correction method= # Reported T Limits: Tmin=0.926 Tmax=1.000

AbsCorr = MULTI-SCAN

Data completeness= 0.850

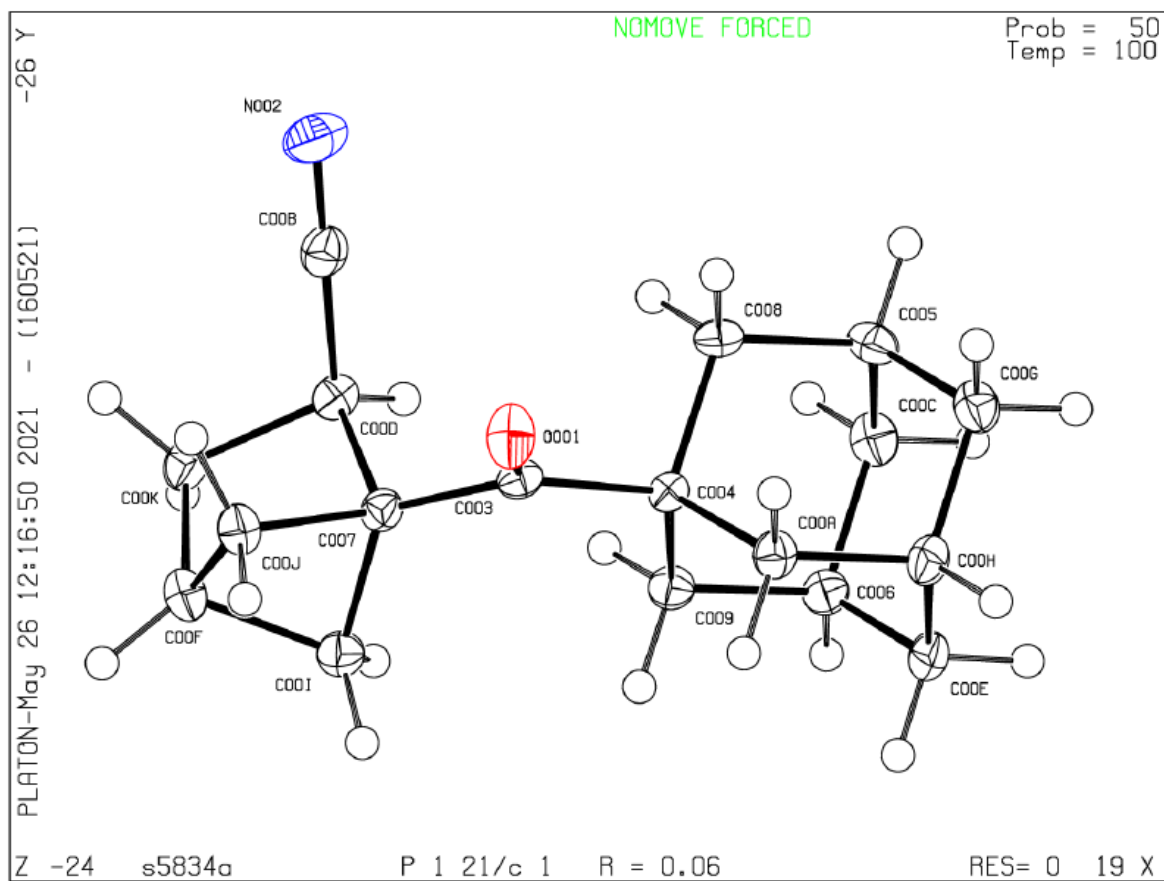
Theta(max)= 29.065

R(reflections)= 0.0626(2326)

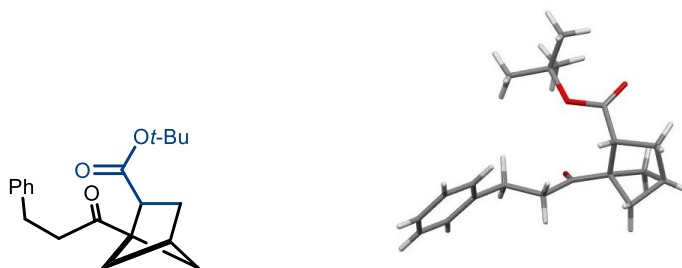
wR2(reflections)= 0.1549(3239)

S = 1.038

Npar= 181



11.2. X-ray structure of 13ai



CCDC 2129466

Crystal data and structure refinement of **13ai**

Bond precision: C-C = 0.0023 Å Wavelength=1.54184
Cell: a=5.7376(4) b=11.1536(7) c=13.4854(8)
 alpha=89.133(5) beta=84.473(5) gamma=88.911(5)
Temperature: 100 K

	Calculated	Reported
Volume	858.75(10)	858.75(10)
Space group	P -1	P -1
Hall group	-P 1	-P 1
Moiety formula	C ₂₀ H ₂₆ O ₃	C ₂₀ H ₂₆ O ₃
Sum formula	C ₂₀ H ₂₆ O ₃	C ₂₀ H ₂₆ O ₃
Mr	314.41	314.41
Dx, g cm ⁻³	1.216	1.216
Z	2	2
Mu (mm ⁻¹)	0.635	0.635
F ₀₀₀	340.0	340.0
F ₀₀₀ '	340.98	
h, k, lmax	7,14,16	6,14,16
Nref	3593	6068
Tmin, Tmax	0.987,0.997	0.716,1.000
Tmin'	0.910	

Correction method= # Reported T Limits: Tmin=0.716 Tmax=1.000

AbsCorr = MULTI-SCAN

Data completeness= 1.689

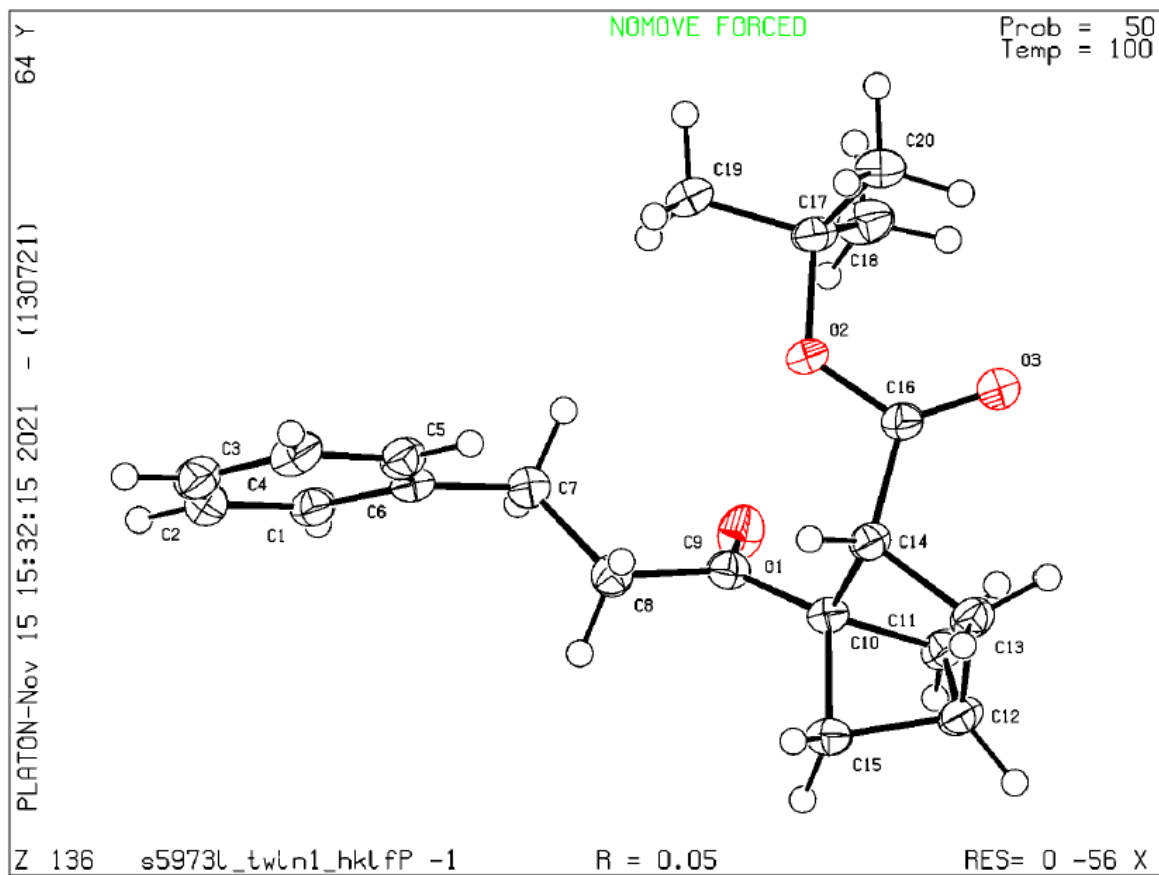
Theta(max)= 76.389

R(reflections)= 0.0453(4238)

wR2(reflections)=0.1250(6068)

S = 0.980

Npar= 212



11.3. X-ray structure of 13aw



CCDC 2129467

Crystal data and structure refinement of 13aw

Bond precision: C-C = 0.0030 Å Wavelength=1.54184
Cell: a=11.4393(3) b=11.1812(3) c=10.9094(2)
 alpha=90 beta=98.768(2) gamma=90
Temperature: 100 K

	Calculated	Reported
Volume	1379.06(6)	1379.06(6)
Space group	P 21/c	P 1 21/c 1
Hall group	-P 2ybc	-P 2ybc
Moiety formula	C ₁₅ H ₁₇ F O ₃ S	C ₁₅ H ₁₇ F O ₃ S
Sum formula	C ₁₅ H ₁₇ F O ₃ S	C ₁₅ H ₁₇ F O ₃ S
Mr	296.35	296.34
D _x , g cm ⁻³	1.427	1.427
Z	4	4
Mu (mm ⁻¹)	2.245	2.245
F ₀₀₀	624.0	624.0
F ₀₀₀ '	627.25	
h, k, lmax	14,14,13	13,13,13
N _{ref}	2890	2770
T _{min} , T _{max}	0.968,0.982	0.756,1.000
T _{min} '	0.853	

Correction method= # Reported T Limits: T_{min}=0.756 T_{max}=1.000

AbsCorr = MULTI-SCAN

Data completeness= 0.958

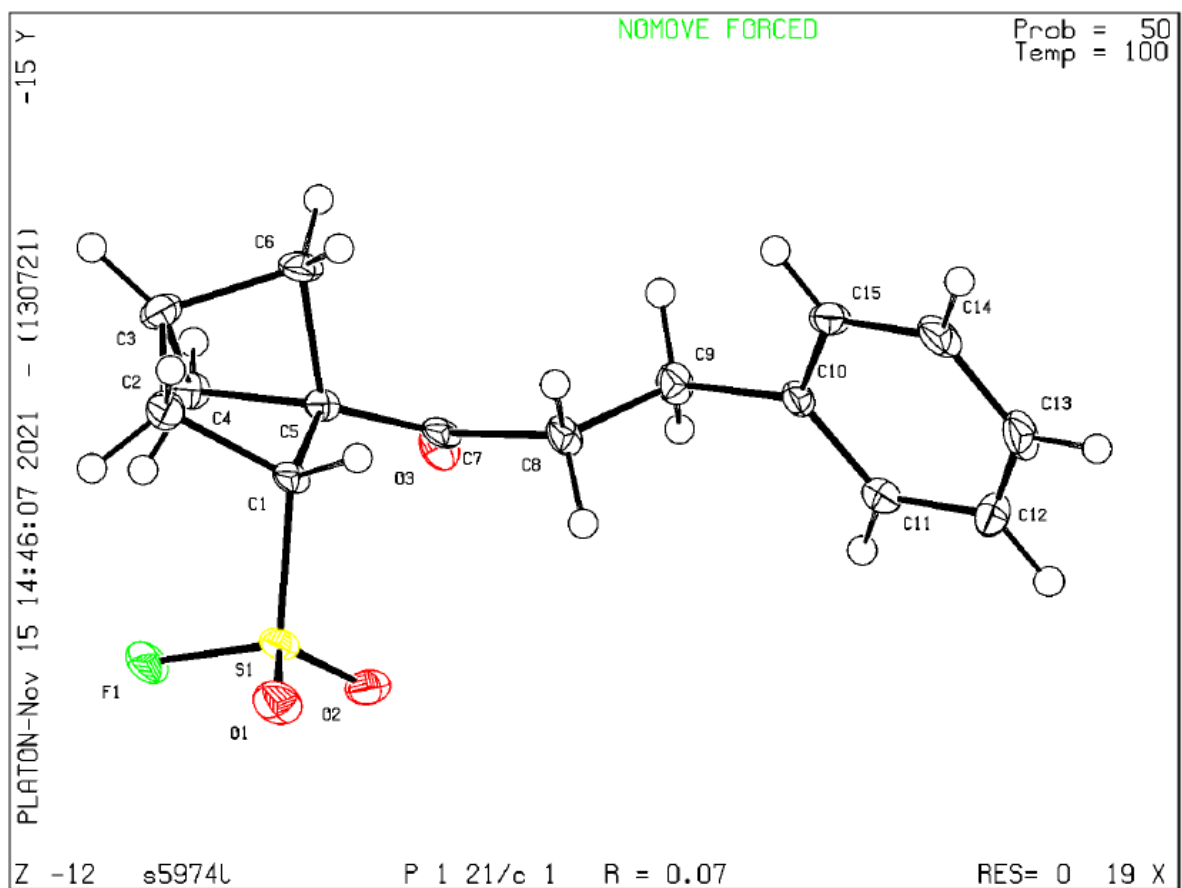
Theta(max)= 76.158

R(reflections)= 0.0689(2389)

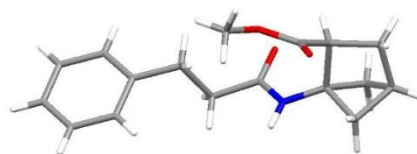
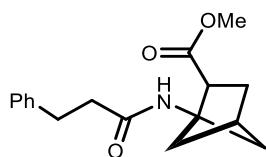
wR2(reflections)=0.1875(2770)

S = 1.033

N_{par}= 181



11.4. X-ray structure of 20



CCDC 2129468

Crystal data and structure refinement of 20

Bond precision: C-C = 0.0032 Å Wavelength=0.71073
Cell: a=8.4886(10) b=9.6125(11) c=37.350(4)
 alpha=90 beta=90 gamma=90
Temperature: 100 K

	Calculated	Reported
Volume	3047.6(6)	3047.6(6)
Space group	P b c a	P b c a
Hall group	-P 2ac 2ab	-P 2ac 2ab
Moiety formula	C ₁₇ H ₂₁ N O ₃	C ₁₇ H ₂₁ N O ₃
Sum formula	C ₁₇ H ₂₁ N O ₃	C ₁₇ H ₂₁ N O ₃
Mr	287.35	287.36
D _x , g cm ⁻³	1.253	1.253
Z	8	8
Mu (mm ⁻¹)	0.085	0.085
F ₀₀₀	1232.0	1232.8
F ₀₀₀ '	1232.58	
h, k, lmax	12,13,53	11,13,52
Nref	4679	3803
Tmin, Tmax	0.992,0.992	0.628,1.000
Tmin'	0.992	

Correction method= # Reported T Limits: Tmin=0.628 Tmax=1.000

AbsCorr = MULTI-SCAN

Data completeness= 0.813

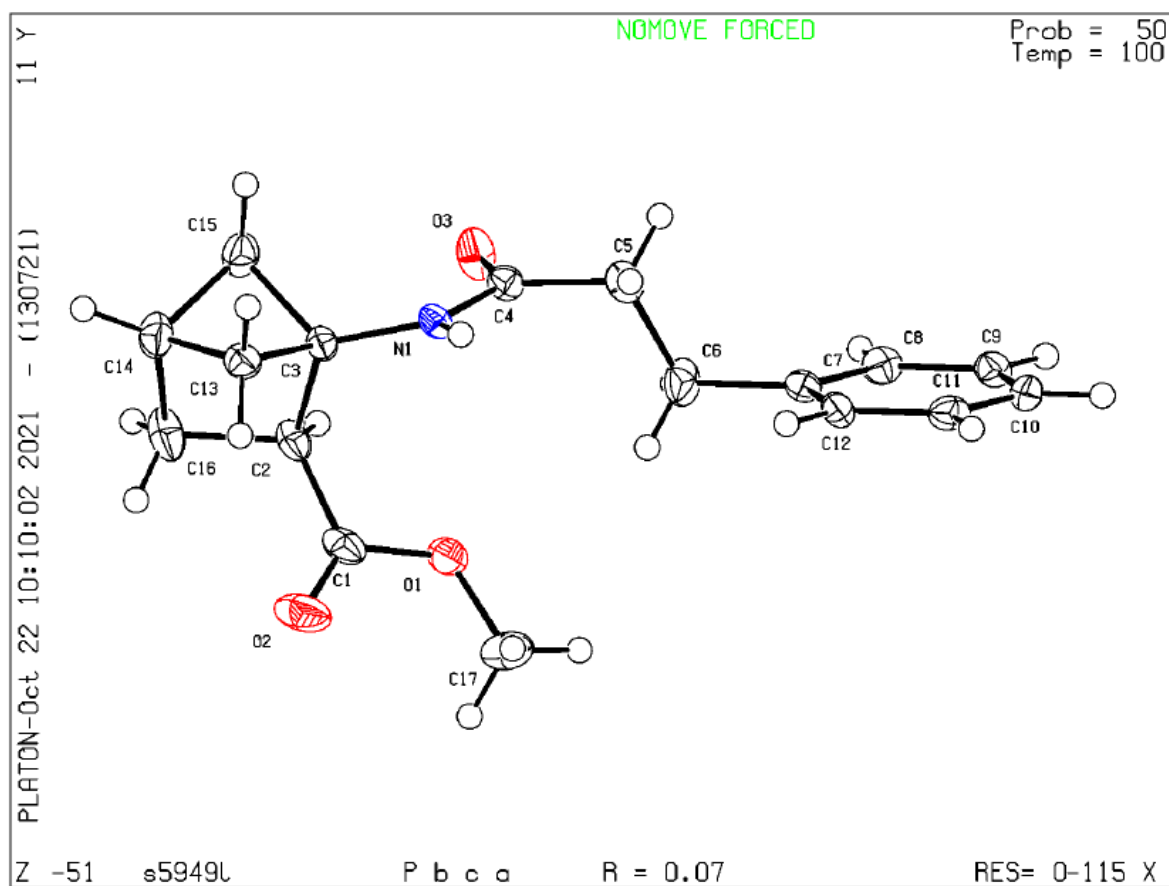
Theta(max)= 30.580

R(reflections)= 0.0694(2241)

wR2(reflections)=0.1845(3803)

S = 0.980

Npar= 191



12. DFT Studies

12.1. Cyclopropyl Ketones

12.1.1. Background

The computational method used in our previous study of cyclopropyl ketones¹⁸ has been modified to that described in 12.1.2 for use in this study. We here recalculate our data for species **1a** in Figure 3 and Table S.1 of reference 18, to assess the effects of the methodological changes. Those changes are principally that we here use different basis sets from our previous work, and include dispersion corrections throughout the geometry optimisations, not just as single point energy corrections at previously optimised structures. We note that in the present work, application of wavefunction stability checks yielded no lower energy solutions, whereas these checks were often required to obtain the data provided in reference 18.

12.1.2. Computational Details

Geometry optimisations were performed using Gaussian 16, Revision C.01.,⁹ employing the PBE0 functional¹⁰ and Dunning's correlation-consistent double-zeta + polarisation basis sets for C, H and O.¹¹ For Samarium and Iodine, Stuttgart-Köln effective core potentials and associated valence basis sets were used.¹⁶ The geometry optimisations were run with dispersion corrections from Grimme's D3 model¹² with Becke-Johnson damping factors.¹³ Harmonic vibrational frequencies calculations were performed, to confirm the stationary points as true minima or transition states and to provide thermodynamic corrections to the SCF energies. Further single point energy calculations using Dunning's correlation-consistent triple-zeta + polarisation basis sets for C, H and O¹⁴ and corrections for solvation (PCM in THF ($\epsilon = 7.6$)¹⁵) were then run on the optimised geometries. The ball and stick structures in the main text were created using GaussView 6.1.1.¹⁷

Our previous calculations¹⁸ on systems of this type suggest that reactivity takes place *via* the quintet spin state, with antiparallel coupling of ligand radical anion to Sm(III) 4f⁵ metal centre. Hence all calculations have been performed with a spin multiplicity of 5.

12.1.3. Breakdown of Energy Contributions

Table S4: *Breakdown of energy contributions detailing the evolution of relative energies as the successive corrections to the initial SCF energy are included. This is data calculated for species **1a** in Figure 3 and Table S.1 of reference 18, using the computational method detailed in 12.1.2. Energies in kcal mol⁻¹:*

ΔE: SCF energy computed from the PBE0/cc-pVDZ/GD3BJ geometry optimisations

ΔH: Enthalpy at 298.15K

ΔG: Free energy at 298.15 K and 1 atm

$\Delta G_{\text{cc-pVTZ}}$: Free energy from cc-pVTZ single point calculations, with thermodynamic corrections from the cc-pVDZ frequencies calculations (298.15 K).

$\Delta G_{\text{Finalcc-pVTZ+Solv}}$: Free energy from cc-pVTZ single point calculations (with corrections for THF solvent), with thermodynamic corrections from the cc-pVDZ frequencies calculations (298.15 K). Data in italics are from reference 18, species **1a** in Figure 3 and Table S.1.

Label	ΔE	ΔH	ΔG	$\Delta G_{\text{cc-pVTZ}}$	$\Delta G_{\text{Finalcc-pVTZ+Solv}}$
1a	0.0	0.0	0.0	0.0	0.0 0.0
Ia	+16.5	+15.7	+19.2	+19.9	+22.4 +20.0
TS(I-II)a	+31.3	+29.4	+34.2	+34.5	+37.3 +35.7
IIa	+23.1	+21.6	+24.9	+25.5	+28.3 +26.5
TS(II-III)a	+16.7	+12.6	+26.9	+33.9	+38.7 +37.5
IIIa	-21.9	-24.1	-8.2	+0.9	+6.5 +4.5
TS(III-IV)a	-17.9	-20.9	-4.9	+4.6	+9.3 +8.9
IVa	-58.5	-59.4	-40.4	-29.2	-24.9 -26.0
3a	-72.1	-72.2	-55.8	-45.2	-42.9 -45.2

12.1.4. Conclusion

The data in the final column of Table S4 show that there is little difference between the results from our previous and present methodology. Specifically, the mean absolute difference between the two sets of data is only 1.6 kcal/mol, with the largest single difference being 2.4 kcal/mol (for **Ia**). This close agreement gives us confidence that we can reliably compare our computational results for the previous and present catalytic cycles.

12.1.5. Cartesian Coordinates (Å) and computed energies (in Hartrees) for all optimised structures in Table S4

	C	5.323571	-3.032094	-0.994339
	C	5.966524	-1.867862	-0.571085
	C	5.227902	-0.817981	-0.036481
	C	3.831455	-0.919250	0.073257
1a	C	3.193011	-2.089732	-0.366194
SCF Energy = -2150.3396663	C	3.935780	-3.139338	-0.890888
Free Energy (298.15 K)= -2149.727258	C	3.004475	0.182446	0.607564
Free Energy (cc-pVTZ, PCM(THF), 298.15 K) = -2150.135328	C	3.670449	1.312679	1.278842

C	2.880011	2.487786	1.799659	H	-2.442843	-1.432980	-2.612114
C	3.714527	2.691341	0.581655	H	-4.107689	1.891329	-3.517417
C	5.018789	3.437307	0.707940	H	-5.531178	1.443444	-2.547951
O	1.773115	0.153928	0.462583	H	-4.465407	-0.445541	-4.206900
Sm	-0.654526	0.055046	0.097979	H	-4.832728	-0.928449	-2.531044
O	-0.282673	-0.791184	2.546685	H	-1.004332	1.872019	-3.214990
C	0.700388	-0.236421	3.423143	H	0.069368	2.849897	-2.177995
C	1.751491	-1.336495	3.618004	H	2.365989	0.209549	-2.396998
C	1.049233	-2.612334	3.113027	H	1.110977	-1.015661	-2.759114
C	-0.391767	-2.167029	2.914105	H	1.931909	2.595952	-3.717160
I	-1.020778	3.104713	0.922533	H	0.596376	2.582103	-4.895567
I	-0.584212	-3.045388	-0.882551	H	2.256431	0.417232	-4.821992
O	-2.539543	0.391788	-1.662763	H	0.499826	0.113813	-4.831264
C	-3.624279	1.322040	-1.481785	H	-2.530331	0.029793	3.169262
C	-4.475034	1.205795	-2.736458	H	-3.487163	1.262489	2.306292
C	-4.233821	-0.242512	-3.152092	H	-4.601524	-1.140961	0.160914
C	-2.759282	-0.404605	-2.836655	H	-3.228836	-2.275004	0.381843
O	0.398369	0.811806	-2.127900	H	-5.516750	-0.040131	2.484557
C	0.034529	1.991957	-2.864951	H	-4.724069	-0.619723	3.967657
C	1.016750	2.064028	-4.022457	H	-5.397048	-2.458120	2.062756
C	1.321508	0.588885	-4.270915	H	-3.755731	-2.544345	2.755762
C	1.374879	0.047821	-2.854615	H	1.078462	0.681416	2.958112
O	-2.958904	-0.408585	1.203516	H	0.210080	0.026599	4.377726
C	-3.356769	0.181371	2.457690	H	-0.979897	-2.242751	3.849178
C	-4.623295	-0.553071	2.875514	H	-0.909652	-2.693246	2.101128
C	-4.455128	-1.906936	2.190793	H	2.045736	-1.412461	4.674486
C	-3.831553	-1.496420	0.871638	H	2.661354	-1.131390	3.037017
H	-4.177775	1.025143	-0.575912	H	1.131249	-3.456215	3.811826
H	-3.198592	2.320261	-1.306909	H	1.463356	-2.931367	2.145468
H	-2.129553	-0.014383	-3.657913	H	5.738177	0.094047	0.276099

H	2.105608	-2.172945	-0.301601	O	-1.544450	0.375131	0.184022
H	7.050647	-1.777613	-0.661482	Sm	0.558233	0.020986	0.029424
H	3.421310	-4.042756	-1.223913	O	-0.403184	-1.779671	-1.367154
H	5.907422	-3.856123	-1.409847	C	-1.295736	-1.531576	-2.476388
H	4.591219	1.056181	1.805048	C	-2.255489	-2.703411	-2.473117
C	3.018642	2.857287	-0.745312	C	-1.353228	-3.841731	-2.005745
H	3.222581	2.923247	2.740432	C	-0.504579	-3.160333	-0.947055
H	1.795886	2.463914	1.655975	I	0.850001	1.745036	-2.507899
H	2.755919	3.916228	-0.895490	I	0.804437	-1.807252	2.494666
H	3.675885	2.547056	-1.574801	O	2.901783	0.917370	0.617380
H	2.087301	2.279135	-0.793986	C	3.896447	1.405425	-0.306246
H	5.738943	3.113747	-0.061566	C	4.934408	2.100705	0.553942
H	4.852548	4.518664	0.574801	C	4.886080	1.270922	1.832441
H	5.480777	3.287855	1.695254	C	3.399645	1.003527	1.970518

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SCF Energy = -2150.3133369

Free Energy (298.15 K) = -2149.696661

Free Energy (cc-pVTZ, PCM(THF),
298.15 K) = -2150.099561

C	-5.124405	-3.055143	1.166043	O	0.465475	1.933678	1.609936
C	-5.696346	-2.082286	0.337037	C	0.748330	3.292845	1.228891
C	-4.965864	-0.978589	-0.075399	C	-0.381889	4.105600	1.826819
C	-3.608123	-0.811670	0.316590	C	-0.641961	3.363629	3.134964
C	-3.055397	-1.792968	1.184221	C	-0.442667	1.908575	2.739757
C	-3.800586	-2.887429	1.591754	O	2.375850	-1.483843	-0.955981
C	-2.821679	0.277689	-0.154654	C	2.481222	-1.793063	-2.360730
C	-3.402920	1.306321	-1.051769	C	3.892418	-2.313776	-2.539395
C	-2.737934	2.642992	-1.213065	C	4.104429	-3.066253	-1.229793
C	-4.052156	2.571027	-0.489440	C	3.426668	-2.151156	-0.224485
C	-5.281909	3.085117	-1.193928	H	4.324743	0.541966	-0.844117
				H	3.393129	2.049728	-1.038715
				H	2.879444	1.832309	2.477700
				H	3.142652	0.067028	2.484051
				H	4.628519	3.139394	0.758965
				H	5.923692	2.124784	0.076612

H 5.300003 1.784544 2.711047
 H 5.438275 0.326267 1.699124
 H 1.726957 3.583142 1.652864
 H 0.807752 3.332034 0.131604
 H -1.369163 1.425834 2.396106
 H 0.010112 1.285017 3.522725
 H -1.266689 4.060835 1.173848
 H -0.109751 5.160678 1.967498
 H -1.646610 3.542049 3.542225
 H 0.093123 3.664304 3.898330
 H 1.732495 -2.563637 -2.610347
 H 2.250631 -0.876648 -2.921020
 H 4.116899 -1.381722 0.158064
 H 2.971948 -2.665565 0.632826
 H 4.602568 -1.475256 -2.625682
 H 3.996376 -2.943490 -3.433679
 H 5.160773 -3.242523 -0.984460
 H 3.596422 -4.043382 -1.265350
 H -1.767601 -0.554356 -2.317074
 H -0.690015 -1.485441 -3.397475
 H 0.515305 -3.560968 -0.853856
 H -0.985625 -3.183321 0.041337
 H -2.701424 -2.877476 -3.462025
 H -3.062716 -2.529523 -1.745633
 H -0.726162 -4.204984 -2.836586
 H -1.908114 -4.695314 -1.593604
 H -5.438128 -0.228853 -0.712069
 H -2.032337 -1.666988 1.541043
 H -6.734466 -2.188302 0.012396
 H -3.344594 -3.621631 2.260906

H -5.706536 -3.920543 1.487609
 H -3.908987 0.910450 -1.940575
 C -4.063938 2.745518 1.007635
 H -2.707121 3.083693 -2.210825
 H -1.829765 2.791631 -0.627976
 H -4.120719 3.813322 1.278525
 H -4.929936 2.233699 1.457956
 H -3.159607 2.320810 1.465227
 H -6.191741 2.589701 -0.815561
 H -5.403812 4.170233 -1.037999
 H -5.226722 2.908438 -2.278898

TS(I-II)a

SCF Energy = -2150.2898155

Free Energy (298.15 K) = -2149.672768

Free Energy (cc-pVTZ, PCM(THF),
298.15 K) = -2150.075881

Imaginary mode = 520.1 i cm⁻¹

C -3.644789 -1.728722 0.670609
 O -2.727991 -0.740053 1.178930
 C -3.200087 -0.237484 2.448760
 C -4.327633 -1.168489 2.853904
 C -4.904073 -1.566255 1.499309
 Sm -0.505099 -0.038188 0.114764
 O 0.289402 0.952325 -2.014386
 C -0.055392 2.226818 -2.598478
 C 1.067604 2.545562 -3.571463
 C 1.548906 1.155508 -3.978314
 C 1.464438 0.407545 -2.664762
 O 1.582707 0.103401 0.431786
 C 2.901487 0.149999 0.663484

C	3.448484	1.105640	1.514309	H	-3.027515	1.459516	-4.364933
C	2.723596	2.286347	2.071264	H	-4.434719	0.472834	-3.946200
C	3.424755	3.050829	1.008783	H	-1.020572	2.112570	-3.116158
C	2.748085	3.288037	-0.295496	H	-0.175390	2.956711	-1.785302
C	3.735821	-0.855899	0.007567	H	2.337558	0.594690	-2.021871
C	5.132930	-0.704504	-0.123553	H	1.316636	-0.676902	-2.756500
C	5.904890	-1.684939	-0.733370	H	1.874150	3.092142	-3.060380
C	5.313292	-2.842848	-1.244964	H	0.719905	3.157127	-4.415492
C	3.930801	-2.997947	-1.140176	H	2.566011	1.147762	-4.392843
C	3.153808	-2.021630	-0.527285	H	0.869455	0.709854	-4.723164
H	5.612244	0.208719	0.232877	H	-2.348959	-0.224053	3.141743
C	4.700650	3.758319	1.311058	H	-3.543243	0.798491	2.300434
O	-0.203664	-1.156410	2.337093	H	-3.772220	-1.552538	-0.404912
C	0.877981	-0.835941	3.228176	H	-3.194070	-2.726719	0.794878
C	1.804832	-2.047547	3.181488	H	-5.052930	-0.677822	3.517174
C	0.897305	-3.191380	2.683586	H	-3.931416	-2.055507	3.374100
C	-0.477397	-2.545161	2.569075	H	-5.531028	-0.753629	1.097481
I	-1.177248	2.741830	1.244430	H	-5.506431	-2.484600	1.525633
I	-0.635028	-2.797579	-1.278562	H	1.334336	0.094980	2.877545
O	-2.499580	0.447349	-1.461655	H	0.448215	-0.682100	4.234009
C	-3.678354	1.199421	-1.159177	H	-1.057892	-2.632391	3.506428
C	-3.940694	1.976901	-2.433512	H	-1.072409	-2.915308	1.725281
C	-3.549214	0.973049	-3.528552	H	2.238096	-2.250167	4.170853
C	-2.653485	-0.043912	-2.802710	H	2.630677	-1.869894	2.479740
H	-4.509022	0.504494	-0.932339	H	0.880611	-4.055853	3.361655
H	-3.457605	1.817606	-0.280029	H	1.223395	-3.541153	1.693942
H	-1.645320	-0.151492	-3.220224	H	2.074551	-2.159106	-0.462023
H	-3.107410	-1.047482	-2.762524	H	6.983632	-1.537597	-0.825435
H	-3.289608	2.863710	-2.456097	H	3.443477	-3.889642	-1.541636
H	-4.981803	2.318701	-2.513077	H	5.923520	-3.608009	-1.728725

H 4.487294 0.979910 1.819587
H 2.996232 2.553926 3.100735
H 1.634600 2.243557 1.952102
H 3.469204 3.299158 -1.130943
H 1.993893 2.513237 -0.490573
H 2.219875 4.262394 -0.303643
H 5.391777 3.757024 0.451316
H 4.514839 4.821604 1.568126
H 5.223876 3.312780 2.171559

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SCF Energy = -2150.3028924

Free Energy (298.15 K)= -2149.687585

Free Energy (cc-pVTZ, PCM(THF),
298.15 K) = -2150.090172

C -4.549144 -3.868775 0.928578
C -5.166650 -3.097948 -0.057403
C -4.661675 -1.843503 -0.388317
C -3.530814 -1.329691 0.263348
C -2.917507 -2.113055 1.250330
C -3.423958 -3.367455 1.581922
C -2.941006 -0.013081 -0.094138
C -3.679979 0.990726 -0.623300
C -3.138007 2.324837 -1.023665
C -3.883443 3.494916 -0.454331
C -3.823827 4.804590 -1.160812
O -1.636146 0.105333 0.144297
Sm 0.470491 -0.019842 0.024737
O -0.222132 -2.124858 -1.089364
C -1.173777 -2.168563 -2.177880
C -1.818196 -3.538269 -2.085106

C -0.681620 -4.388159 -1.525795
C -0.051249 -3.440621 -0.522896
I 0.551099 1.362123 -2.729299
I 0.837931 -1.439144 2.740146
O 2.707032 1.162492 0.512052
C 3.628044 1.662353 -0.475934
C 4.489196 2.666969 0.262801
C 4.590012 2.026948 1.643618
C 3.193307 1.461524 1.839270
O 0.145431 2.133842 1.216444
C 0.480942 3.441518 0.708485
C -0.540332 4.383161 1.320205
C -0.840540 3.704559 2.653356
C -0.858624 2.243154 2.253988
O 2.484496 -1.411191 -0.763395
C 2.676590 -1.857603 -2.121328
C 4.127219 -2.291619 -2.190798
C 4.343355 -2.857519 -0.790950
C 3.570055 -1.872022 0.066766
H 4.229920 0.818787 -0.858537
H 3.039024 2.071941 -1.307257
H 2.505393 2.192396 2.293928
H 3.154097 0.540127 2.436267
H 3.975895 3.640326 0.322431
H 5.461539 2.823822 -0.224106
H 4.867644 2.731152 2.439897
H 5.336692 1.216375 1.633753
H 1.506130 3.684587 1.036935
H 0.458025 3.400585 -0.390058
H -1.825315 1.938900 1.824966

H -0.582369 1.540597 3.051985
 H -1.447591 4.414783 0.698233
 H -0.153879 5.406703 1.420774
 H -1.792443 4.021198 3.101253
 H -0.035616 3.900984 3.380215
 H 1.992431 -2.701060 -2.313660
 H 2.407812 -1.026661 -2.787918
 H 4.187916 -1.001086 0.341745
 H 3.140726 -2.295890 0.984953
 H 4.781550 -1.421155 -2.361164
 H 4.308551 -3.017600 -2.995230
 H 5.399795 -2.925887 -0.497034
 H 3.902819 -3.864737 -0.713626
 H -1.873561 -1.332170 -2.054873
 H -0.615367 -2.026364 -3.117831
 H 1.024034 -3.597826 -0.357859
 H -0.563445 -3.469658 0.450476
 H -2.187963 -3.887198 -3.059048
 H -2.661386 -3.515043 -1.378927
 H 0.036970 -4.650003 -2.320115
 H -1.024813 -5.317818 -1.051702
 H -5.131076 -1.265920 -1.186715
 H -2.031388 -1.729300 1.759279
 H -6.041572 -3.483873 -0.585292
 H -2.930986 -3.955915 2.359294
 H -4.942192 -4.855496 1.182225
 H -4.752065 0.826066 -0.754097
 C -4.362302 3.478304 0.956219
 H -3.138522 2.414212 -2.126876
 H -2.063301 2.357908 -0.751026

H -4.714659 5.421534 -0.953278
 H -2.949579 5.414520 -0.844047
 H -3.735788 4.678036 -2.251246
 H -5.360947 3.940732 1.052923
 H -4.416621 2.454185 1.354708
 H -3.699394 4.063576 1.629031

TS(II-III)a

SCF Energy = -2458.3662097

Free Energy (298.15 K)= -2457.649797

Free Energy (cc-pVTZ, PCM(THF),
298.15 K) = -2458.128112

Imaginary mode = 266.8i cm⁻¹

C -6.125036 0.838058 -1.003677
 C -5.329131 0.565789 0.126397
 C -4.937635 -0.765170 0.375395
 C -5.336850 -1.784347 -0.481598
 C -6.127758 -1.505930 -1.598006
 C -6.518455 -0.189778 -1.852726
 C -4.960487 1.602630 1.021389
 C -4.600936 2.503590 1.770744
 C -2.572248 3.717345 1.136030
 C -1.792953 3.538036 2.395891
 C -2.117923 2.947180 -0.071197
 C -0.815043 3.493827 -0.576156
 C 0.330857 2.781549 -0.697244
 C 1.618246 3.427087 -1.065531
 C 1.934016 4.727619 -0.645936
 C 3.162398 5.300619 -0.965286
 C 4.101994 4.582844 -1.706076
 C 3.799668 3.287055 -2.123848

C	2.572457	2.713443	-1.802640	H	-2.620721	-3.675084	0.088406
O	0.392428	1.465935	-0.504620	H	-2.145830	-5.357067	0.431763
Sm	0.767955	-0.554029	-0.004027	H	-2.157886	-4.214136	-2.171508
O	-0.021871	-2.976255	-0.326267	H	-1.137039	-5.592897	-1.735626
C	-0.564893	-3.861065	0.658366	H	-2.533085	-1.837556	-1.824528
C	-1.808324	-4.410745	-0.012668	H	-2.386877	-0.547092	-0.597024
C	-1.371779	-4.549566	-1.480579	H	-0.259506	1.087557	-2.829175
C	-0.112221	-3.674508	-1.579489	H	0.210586	-0.404490	-3.705287
O	2.152493	-2.103773	1.466533	H	-2.918249	1.172261	-2.190780
C	2.909733	-3.252932	1.029167	H	-3.918921	-0.143265	-2.849518
C	3.292767	-4.017013	2.297266	H	-2.041686	0.985386	-4.483856
C	2.357282	-3.436059	3.355815	H	-2.104063	-0.795063	-4.410086
C	2.237057	-1.999675	2.895847	H	3.129584	-1.408797	3.169691
O	-0.802532	-0.701026	-1.934062	H	1.333821	-1.480868	3.242243
C	-2.219582	-0.794124	-1.654623	H	2.259692	-3.826473	0.354283
C	-2.889571	0.160870	-2.621682	H	3.774672	-2.905281	0.446769
C	-1.942227	0.119130	-3.815627	H	1.368246	-3.919606	3.320182
C	-0.589989	0.082522	-3.133135	H	3.187445	-5.103637	2.172828
O	2.289410	0.701783	1.516517	H	4.340696	-3.813401	2.566213
C	1.822425	1.816643	2.313080	H	1.165431	2.433297	1.682922
C	3.075967	2.561083	2.737554	H	1.231266	1.409980	3.145356
C	4.025621	2.283738	1.576445	H	4.248191	0.134405	1.895300
C	3.700546	0.840893	1.246157	H	3.877059	0.567179	0.196308
I	-1.316496	-0.575784	2.301494	H	3.477379	2.145175	3.675913
I	2.908097	-1.241815	-2.117234	H	2.881701	3.631241	2.892036
C	-3.219672	5.042769	0.907690	H	5.084917	2.421812	1.833395
H	0.170538	-4.660318	0.872141	H	3.786603	2.930457	0.719508
H	-0.756172	-3.272714	1.564165	H	1.216392	5.281429	-0.037254
H	-0.141090	-2.914179	-2.366509	H	2.355172	1.691959	-2.119002
H	0.801683	-4.278406	-1.708020	H	3.394210	6.310483	-0.619500

H	4.525517	2.709224	-2.700181	C	-4.206168	2.742233	1.277065
H	5.068329	5.029752	-1.948764	C	-2.924282	3.489369	0.938288
H	-0.773130	4.558408	-0.819196	C	-2.025373	3.474995	2.178142
H	-1.990940	1.885493	0.189858	C	-2.214816	2.811679	-0.251273
H	-2.902069	3.012195	-0.847895	C	-0.920060	3.447028	-0.631355
H	-2.344014	3.912266	3.275049	C	0.264644	2.794631	-0.708115
H	-1.537629	2.480446	2.562800	C	1.531613	3.509591	-1.014051
H	-0.841025	4.106675	2.355039	C	1.777585	4.804556	-0.536299
H	-3.741455	5.406134	1.808632	C	2.986631	5.443238	-0.801993
H	-2.469369	5.819209	0.650177	C	3.973433	4.797508	-1.547277
H	-3.944656	5.003720	0.079729	C	3.739246	3.507396	-2.023310
H	-4.587048	3.175262	2.609517	C	2.532571	2.867463	-1.754327
H	-4.313130	-0.978069	1.244615	O	0.385561	1.482493	-0.525185
H	-5.032208	-2.812162	-0.270671	Sm	0.762323	-0.532114	-0.009420
H	-6.443789	-2.311373	-2.263782	O	0.093817	-2.991214	-0.383027
H	-7.139531	0.037343	-2.721802	C	-0.489451	-3.873832	0.592596
H	-6.433019	1.866479	-1.197958	C	-1.260192	-4.892508	-0.220261
H	2.747559	-3.524510	4.379095	C	-0.343315	-5.071533	-1.426115

IIIa

SCF Energy = -2458.4276158

Free Energy (298.15 K) = -2457.705674

Free Energy (cc-pVTZ, PCM(THF),
298.15 K) = -2458.179289

C	-6.241428	0.698537	-0.932573	O	0.165967	-3.658070	-1.665449
C	-5.307400	0.581446	0.142906	O	2.210755	-2.082038	1.414140
C	-5.009638	-0.730028	0.627931	C	3.031036	-3.164839	0.925530
C	-5.602950	-1.840755	0.054952	C	3.817107	-3.654084	2.129268
C	-6.509672	-1.706931	-1.005782	C	2.861848	-3.347958	3.277931
C	-6.823143	-0.427748	-1.486128	C	2.298823	-2.007521	2.852139
C	-4.693614	1.691015	0.678666	O	-0.964807	-0.734649	-1.774635
				C	-2.330191	-1.135055	-1.515542
				C	-3.175903	-0.338160	-2.488871
				C	-2.225058	-0.162253	-3.667758
				C	-0.910873	0.096222	-2.959654
				O	2.260428	0.740595	1.527402

C	1.771310	1.842102	2.329043	H	1.119385	2.462475	1.696556
C	3.012703	2.590096	2.778675	H	1.171044	1.418241	3.145422
C	3.965749	2.359905	1.610256	H	4.236591	0.204412	1.849580
C	3.662827	0.922229	1.236040	H	3.827573	0.690666	0.174045
I	-1.279068	-0.594694	2.324481	H	3.417749	2.151263	3.705123
I	2.879923	-1.043613	-2.209932	H	2.804397	3.652606	2.964308
C	-3.313428	4.932060	0.597589	H	5.023249	2.506052	1.870165
H	0.319856	-4.352974	1.173386	H	3.716569	3.028667	0.773501
H	-1.097534	-3.263607	1.272964	H	1.020072	5.302169	0.072809
H	-0.466604	-3.093247	-2.366549	H	2.363551	1.851565	-2.114866
H	1.203161	-3.604715	-2.023618	H	3.165039	6.447878	-0.412159
H	-2.233178	-4.474936	-0.526281	H	4.503152	2.987478	-2.605660
H	-1.445061	-5.822113	0.335565	H	4.923694	5.296154	-1.749421
H	-0.849708	-5.482844	-2.310115	H	-0.914281	4.512053	-0.873451
H	0.490079	-5.745531	-1.170694	H	-2.039867	1.754895	0.001573
H	-2.408987	-2.220916	-1.697366	H	-2.919190	2.827604	-1.105196
H	-2.556931	-0.936379	-0.460046	H	-2.536577	3.932536	3.040319
H	-0.815245	1.145010	-2.638841	H	-1.747068	2.444422	2.444713
H	-0.012518	-0.193795	-3.521299	H	-1.102469	4.043653	1.983649
H	-3.427876	0.638937	-2.051653	H	-3.884566	5.388392	1.421728
H	-4.115955	-0.849713	-2.733626	H	-2.420545	5.553821	0.430976
H	-2.503219	0.665152	-4.334802	H	-3.937164	4.970469	-0.309287
H	-2.169830	-1.085209	-4.268192	H	-4.765348	3.163843	2.130553
H	2.974500	-1.178692	3.120946	H	-4.295814	-0.833374	1.446825
H	1.294252	-1.785360	3.236804	H	-5.360420	-2.833711	0.441112
H	2.362820	-3.945501	0.526771	H	-6.974574	-2.589491	-1.448500
H	3.645561	-2.782253	0.099886	H	-7.535437	-0.315491	-2.306631
H	2.059806	-4.102389	3.327251	H	-6.482934	1.693546	-1.309569
H	4.086455	-4.716007	2.045846	H	3.350729	-3.303366	4.260872
H	4.747391	-3.074661	2.242641				

TS(III-IV)a

SCF Energy = -2458.4212662

Free Energy (298.15 K) = -2457.700513

Free Energy (cc-pVTZ, PCM(THF),
298.15 K) = -2458.174851Imaginary mode = 202.0i cm⁻¹

C 3.138427 4.722050 -0.630496
C 3.619876 3.996790 -1.722277
C 3.287637 2.654753 -1.877769
C 2.470183 2.000193 -0.940174
C 1.989852 2.741928 0.149423
C 2.321642 4.084808 0.303014
C 2.090064 0.577389 -1.074232
C 2.849168 -0.310113 -1.785292
C 2.471138 -1.732248 -2.035072
C 3.678950 -2.678506 -2.110864
C 4.618610 -2.346171 -0.968949
C 4.431368 -1.310812 -0.179141
C 4.808656 -0.575691 0.964134
O 1.000363 0.202430 -0.415956
Sm -1.059474 -0.050403 0.046803
O -1.110858 1.873053 -1.512151
C -0.510306 1.844053 -2.827666
C -0.164450 3.288470 -3.134284
C -1.274052 4.040964 -2.407138
C -1.408735 3.233667 -1.130236
I -1.497286 -1.957211 -2.338148
I -1.217787 1.869110 2.466818
O -2.732451 -1.577322 1.252448
C -3.745264 -2.407607 0.644871
C -4.311824 -3.249331 1.774795

C -4.135603 -2.329160 2.978151
C -2.784324 -1.707296 2.688939
O 0.052960 -1.648428 1.570174
C 0.209441 -3.038170 1.209920
C 1.527677 -3.469719 1.830821
C 1.618420 -2.553284 3.046615
C 1.120271 -1.249192 2.464134
O -3.460331 0.744151 -0.391426
C -4.018393 0.908035 -1.710360
C -5.517488 0.933046 -1.496296
C -5.618870 1.674903 -0.167435
C -4.438958 1.109412 0.605438
C 3.205577 -4.128893 -1.999685
H -4.508053 -1.746300 0.200768
H -3.278218 -2.980613 -0.166733
H -1.957656 -2.361682 3.011764
H -2.630478 -0.709116 3.121473
H -3.715962 -4.166884 1.906267
H -5.353669 -3.545463 1.590443
H -4.155768 -2.853695 3.943353
H -4.921106 -1.555954 2.993758
H -0.647939 -3.592740 1.628824
H 0.177193 -3.125214 0.113690
H 1.897421 -0.737990 1.873958
H 0.691337 -0.544862 3.188216
H 2.360340 -3.257593 1.140984
H 1.540008 -4.541087 2.074056
H 2.631926 -2.459556 3.455523
H 0.948390 -2.900980 3.850273
H -3.657227 1.860918 -2.133398

H -3.650357 0.078862 -2.329889
 H -4.712451 0.198403 1.161888
 H -3.969206 1.813908 1.305270
 H -5.907838 -0.093306 -1.400901
 H -6.050831 1.426817 -2.320229
 H -6.571605 1.519143 0.357169
 H -5.492274 2.757933 -0.325995
 H 0.355562 1.169983 -2.794109
 H -1.253783 1.429677 -3.528592
 H -2.413164 3.245684 -0.684172
 H -0.681067 3.545863 -0.366161
 H -0.134438 3.486041 -4.214624
 H 0.815557 3.543690 -2.703439
 H -2.210256 4.011230 -2.988916
 H -1.028539 5.092036 -2.203060
 H 3.646364 2.113226 -2.754897
 H 1.354758 2.251680 0.888010
 H 4.250356 4.485679 -2.468372
 H 1.937538 4.634019 1.165693
 H 3.395975 5.776627 -0.513069
 H 3.705785 0.091278 -2.329068
 C 4.434759 -2.498905 -3.433492
 H 1.888053 -1.824704 -2.969509
 H 1.794403 -2.057834 -1.231813
 H 5.330396 -3.139639 -3.464887
 H 3.792504 -2.771620 -4.286238
 H 4.766789 -1.458839 -3.571067
 H 4.051088 -4.832340 -2.065414
 H 2.691054 -4.303121 -1.042112
 H 2.500092 -4.368645 -2.811208

C 5.097255 0.807133 0.884448
 C 5.376191 1.538182 2.029914
 C 5.378492 0.923792 3.284834
 C 5.107025 -0.443374 3.380770
 C 4.822044 -1.184910 2.242355
 H 5.075712 1.298309 -0.088267
 H 5.581565 2.607133 1.943976
 H 5.588785 1.506904 4.183164
 H 5.120124 -0.935278 4.356337
 H 4.617641 -2.254981 2.311937
 H 5.517245 -2.978821 -0.867010

IVa

SCF Energy = -2458.4860649

Free Energy (298.15 K) = -2457.757004

Free Energy (cc-pVTZ, PCM(THF),
298.15 K) = -2458.229331

C -2.479194 2.509555 1.375600
 C -3.163960 1.182815 0.997522
 C -3.511923 1.430220 -0.470811
 C -3.440941 2.739151 -0.755121
 C -3.046313 3.585310 0.429484
 C -2.308120 -0.024950 1.271881
 C -2.754007 -1.174719 1.990071
 C -4.064002 -1.305027 2.532822
 C -4.461306 -2.460507 3.187089
 C -3.582396 -3.537780 3.346154
 C -2.281478 -3.422474 2.842485
 C -1.872837 -2.275534 2.182938
 H -3.712066 3.179470 -1.717980
 H -1.407097 2.386871 1.165633

O	-1.074593	0.002827	0.794234	H	6.087157	2.093989	1.327943
Sm	0.913377	-0.067787	0.026834	H	6.073085	0.847439	0.058692
O	-0.054060	-2.076368	-1.027606	H	2.439445	3.233931	1.451328
C	-1.358095	-2.017809	-1.657193	H	0.870693	3.380923	0.604717
C	-1.946516	-3.396084	-1.453977	H	-0.467833	1.292662	3.068882
C	-0.707721	-4.279465	-1.558964	H	1.108371	0.559267	3.496028
C	0.336413	-3.453316	-0.828918	H	-0.267080	4.029902	2.632842
I	0.210660	1.857276	-2.255815	H	1.330328	4.734723	2.985412
I	2.169174	-1.982603	2.112033	H	0.318123	2.899790	4.733273
O	3.235524	1.094458	0.011247	H	2.011590	2.705724	4.213909
C	3.781218	1.855649	-1.084386	H	1.420410	-2.143616	-3.093804
C	4.950189	2.618983	-0.493912	H	1.768563	-0.425778	-3.450359
C	5.470371	1.631600	0.545091	H	4.544323	-0.874465	-1.253266
C	4.183735	1.046006	1.099436	H	3.741643	-2.235897	-0.415138
O	1.102458	1.686538	1.770936	H	4.092386	-0.930767	-3.992948
C	1.350863	3.089539	1.549779	H	3.310799	-2.411221	-4.602196
C	0.798366	3.796614	2.775264	H	5.240828	-2.694051	-2.695725
C	0.967611	2.738643	3.862193	H	3.707427	-3.566559	-2.455966
C	0.618276	1.465930	3.117142	H	-1.922990	-1.210456	-1.181832
O	2.528085	-1.126909	-1.665773	H	-1.215335	-1.775252	-2.723353
C	2.191868	-1.357210	-3.050309	H	1.360070	-3.578016	-1.211153
C	3.485322	-1.803903	-3.703478	H	0.347221	-3.652004	0.252897
C	4.157234	-2.566465	-2.566345	H	-2.719664	-3.624391	-2.198422
C	3.818824	-1.697150	-1.369727	H	-2.393814	-3.467399	-0.450155
H	4.107683	1.154214	-1.872034	H	-0.425570	-4.420958	-2.615329
H	2.976580	2.478009	-1.496364	H	-0.833384	-5.271235	-1.103212
H	3.780609	1.645922	1.932176	H	-4.779381	-0.485867	2.443549
H	4.262396	0.005085	1.439997	H	-0.848888	-2.198344	1.820256
H	4.598628	3.543206	-0.006990	H	-5.476594	-2.523589	3.586010
H	5.694233	2.896964	-1.253039	H	-1.568560	-4.240076	2.975952

H	-3.902519	-4.443839	3.863307	C	3.501524	-2.725650	-0.112646
H	-4.105392	1.077792	1.559823	C	3.344043	-3.073128	1.345597
C	-3.936925	0.377181	-1.399433	C	2.519891	0.555897	0.906331
C	-3.634650	0.471526	-2.767640	C	2.912650	1.869568	1.440887
C	-4.048765	-0.513314	-3.658419	C	4.223891	2.175999	1.847555
C	-4.770349	-1.617442	-3.202250	C	4.535689	3.443975	2.325031
C	-5.066532	-1.728427	-1.844493	C	3.545667	4.423083	2.417306
C	-4.648402	-0.746153	-0.950650	C	2.237794	4.126805	2.028141
H	-3.032929	1.311184	-3.119098	C	1.923923	2.866490	1.540374
H	-3.796603	-0.423220	-4.717366	H	3.622878	-3.490503	-0.882459
H	-5.094730	-2.390857	-3.901927	H	1.778923	-1.670816	1.852797
H	-5.623837	-2.590783	-1.472350	O	1.383808	0.404328	0.428331
H	-4.881297	-0.856450	0.108526	Sm	-0.942897	-0.021850	-0.092918
H	-2.604837	2.762742	2.440032	O	-0.218656	1.523768	-2.040077
C	-4.293059	4.251459	1.025728	C	1.098906	1.545834	-2.597302
C	-2.012699	4.648515	0.066211	C	1.658871	2.920126	-2.236601
H	-2.438555	5.393714	-0.625109	C	0.399865	3.777381	-1.992371
H	-1.672054	5.190076	0.964634	C	-0.751671	2.824202	-2.294646
H	-1.141639	4.191660	-0.427708	I	-0.301244	-2.832983	-1.422150
H	-4.780101	4.909722	0.288848	I	-2.012019	2.713192	1.310858
H	-5.032875	3.500084	1.342836	O	-3.163821	-1.084276	0.806846
H	-4.027454	4.864979	1.902556	C	-3.810095	-2.202223	0.169111

3a

SCF Energy = -2458.5077556

Free Energy (298.15 K)= -2457.781557

Free Energy (cc-pVTZ, PCM(THF),
298.15 K) = -2458.258062

C	2.875312	-1.719127	1.917700
C	3.442137	-0.640488	0.969339
C	3.555236	-1.405448	-0.340445

C	-5.355583	-1.188117	1.643946
C	-3.985207	-0.578139	1.871495
O	-0.585323	-0.912196	2.300533
C	-0.890395	-2.254464	2.716636
C	-0.341164	-2.371787	4.126835
C	-0.524502	-0.949402	4.649590
C	-0.164908	-0.122339	3.428636

O	-2.844057	0.183928	-1.843091	H	1.018734	1.413296	-3.691211
C	-2.676722	-0.181459	-3.227790	H	-1.059791	2.877865	-3.356640
C	-3.957496	0.254039	-3.923645	H	-1.623128	2.965532	-1.642839
C	-4.414030	1.424074	-3.056269	H	2.295049	3.310681	-3.042700
C	-4.060847	0.922384	-1.669676	H	2.274481	2.859917	-1.328579
H	-4.130284	-1.885268	-0.837582	H	0.360381	4.675068	-2.625108
H	-3.070057	-3.005669	0.049466	H	0.341612	4.099268	-0.942683
H	-3.557288	-0.904687	2.837282	H	5.014376	1.427558	1.784359
H	-3.951658	0.519497	1.835790	H	0.896368	2.638502	1.249716
H	-4.681193	-3.238436	1.861332	H	5.559430	3.670178	2.628842
H	-5.809056	-3.026216	0.500748	H	1.450289	4.878730	2.107852
H	-5.948917	-1.245793	2.567033	H	3.794294	5.416282	2.796813
H	-5.922761	-0.592275	0.910321	H	4.443620	-0.329072	1.302256
H	-1.984634	-2.387363	2.693925	C	3.761430	-0.749067	-1.633967
H	-0.443868	-2.947430	1.989974	C	3.294801	-1.345088	-2.817168
H	0.924674	0.038606	3.357234	C	3.499354	-0.730157	-4.047416
H	-0.671775	0.851339	3.367816	C	4.163347	0.495262	-4.123505
H	0.727981	-2.636066	4.101848	C	4.617970	1.103303	-2.954779
H	-0.868218	-3.132765	4.718896	C	4.415031	0.489306	-1.721270
H	0.107083	-0.712247	5.516731	H	2.723931	-2.273191	-2.754439
H	-1.575209	-0.776129	4.933555	H	3.119160	-1.204015	-4.954757
H	-1.792290	0.353726	-3.608394	H	4.317254	0.979048	-5.090210
H	-2.474924	-1.261001	-3.275499	H	5.132104	2.065558	-3.000831
H	-4.842803	0.243858	-1.281127	H	4.777220	0.979881	-0.815533
H	-3.876688	1.710692	-0.925184	H	3.176109	-1.565720	2.965366
H	-4.707159	-0.553209	-3.896698	C	4.701620	-3.483534	1.930203
H	-3.788719	0.523195	-4.975474	C	2.318365	-4.180439	1.573281
H	-5.481446	1.662947	-3.161095	H	2.685917	-5.141789	1.180561
H	-3.832879	2.330396	-3.290783	H	2.120480	-4.315872	2.649612
H	1.654655	0.698942	-2.182683	H	1.375084	-3.947787	1.056375

H 5.100330 -4.370165 1.412903
H 5.443748 -2.676152 1.828022

H 4.606170 -3.732084 2.999912

12.2. BCB Ketones

12.2.1. Computational Details

Geometry optimisations were performed using Gaussian 16, Revision C.01.,⁹ employing the PBE0 functional¹⁰ and Dunning's correlation-consistent double-zeta + polarisation basis sets for C, H, O and N.¹¹ For Samarium and Iodine, Stuttgart-Köln effective core potentials and associated valence basis sets were used.¹⁶ The geometry optimisations were run with dispersion corrections from Grimme's D3 model¹² with Becke-Johnson damping factors.¹³ Harmonic vibrational frequencies calculations were performed, to confirm the stationary points as true minima or transition states and to provide thermodynamic corrections to the SCF energies. Further single point energy calculations using Dunning's correlation-consistent triple-zeta + polarisation basis sets for C, H, O and N¹⁴ and corrections for solvation (PCM in THF ($\epsilon = 7.6$)¹⁵) were then run on the optimised geometries. The ball and stick structures in the main text were created using GaussView 6.1.1.¹⁷

Our previous calculations¹⁸ on systems of this type suggest that reactivity takes place *via* the quintet spin state, with antiparallel coupling of ligand radical anion to Sm(III) 4f⁵ metal centre. Hence all calculations have been performed with a spin multiplicity of 5.

12.2.2. Breakdown of Energy Contributions

Table S5: Breakdown of energy contributions detailing the evolution of relative energies as the successive corrections to the initial SCF energy are included. Energies in kcal mol⁻¹:

ΔE : SCF energy computed from the PBE0/cc-pVDZ/GD3BJ geometry optimisations

ΔH : Enthalpy at 298.15 K

ΔG : Free energy at 298.15 K and 1 atm

$\Delta G_{\text{cc-pVTZ}}$: Free energy from cc-pVTZ single point calculations, with thermodynamic corrections from the cc-pVDZ frequencies calculations (298.15 K).

$\Delta G_{\text{Finalcc-pVTZ+Solv}}$: Free energy from cc-pVTZ single point calculations (with corrections for THF solvent), with thermodynamic corrections from the cc-pVDZ frequencies calculations (298.15 K). Data in italics are free energies at 263.15 K – these are the data used in the main article.

Label	ΔE	ΔH	ΔG	$\Delta G_{\text{cc-pVTZ}}$	$\Delta G_{\text{Finalcc-pVTZ+Solv}}$
Sm(II)-11j	0.0	0.0	0.0	0.0	0.0 0.0

Int I	+24.4	+23.3	+27.2	+28.4	+33.0	+32.5
TS 1	+24.6	+22.9	+29.4	+30.7	+34.9	+34.1
Int II	+15.3	+13.6	+18.2	+19.6	+24.3	+23.8
TS 2	+8.6	+7.8	+25.5	+27.9	+33.7	+31.7
Int III	-28.7	-26.9	-8.5	-4.2	+1.9	-0.3
TS 3	-25.0	-23.6	-2.2	+2.2	+8.4	+5.9
Int IV	-42.2	-39.4	-18.4	-13.0	-5.7	-8.1
Sm(II)-13j	-57.7	-54.1	-38.3	-34.2	-32.1	-34.0

12.2.3 Cartesian Coordinates (Å) and computed energies (in Hartrees) for all optimised structures in Table S5

Sm(II)-11j

SCF Energy = -1996.810522

Free Energy (298.15 K) = -1996.243397

Free Energy (cc-pVTZ, PCM(THF), 298.15 K) = -1996.619637

Free Energy (cc-pVTZ, PCM(THF), 263.15 K) = -1996.604353

C -3.345097 0.180969 -0.307482

O -2.125884 0.009063 -0.261774

Sm 0.355042 0.004070 -0.116489

O -0.208475 -2.117520 -1.537587

C -1.191965 -2.131060 -2.570928

C -2.329020 -3.005739 -2.036449

C -1.658340 -3.842608 -0.926682

C -0.189418 -3.441982 -1.008455

I 0.551596 1.784569 -2.749568

I 0.183949 -1.797899 2.587136

O 2.404728 1.259726 0.890332

C 3.504237 1.744131 0.099383

C 4.482820 2.350176 1.092626

C 4.230031 1.506923 2.339671

C 2.723573 1.334328 2.286883

O -0.452640 2.027129 1.294693

C -0.044332 3.381704 1.035369

C -0.790035 4.236934 2.049002

C -0.988733 3.262526 3.207345

C -1.274020 1.970552 2.465489

O 2.562595 -1.231579 -0.771831

C 2.899052 -1.566044 -2.132526

C 4.091613 -2.508721 -2.043157

C 3.900829 -3.144352 -0.668414

C 3.394825 -1.963256 0.136188

H 3.940060 0.886613 -0.439187

H 3.108836 2.449625 -0.645471

H 2.206707 2.208063 2.725733

H 2.343325 0.423596 2.772114

H 4.231142 3.405048 1.289392

H 5.520777 2.311280 0.734108

H 4.569122 1.980737 3.271294

H 4.728676 0.527962 2.251809

H 1.048105 3.436673 1.170897
 H -0.270113 3.620801 -0.013818
 H -2.335653 1.915962 2.158523
 H -1.016670 1.052426 3.013437
 H -1.765855 4.551122 1.645035
 H -0.230928 5.142176 2.323380
 H -1.800140 3.548220 3.891202
 H -0.062321 3.164677 3.796324
 H 2.016849 -2.047195 -2.582174
 H 3.099131 -0.634667 -2.681981
 H 4.232014 -1.317669 0.463661
 H 2.786694 -2.227220 1.013886
 H 5.037160 -1.943404 -2.070197
 H 4.110119 -3.235196 -2.867337
 H 4.818915 -3.581354 -0.251821
 H 3.130361 -3.931363 -0.707452
 H -1.460494 -1.089087 -2.784133
 H -0.741311 -2.567787 -3.481188
 H 0.375486 -4.095823 -1.700769
 H 0.314587 -3.406987 -0.033097
 H -2.758044 -3.627972 -2.834560
 H -3.138407 -2.390506 -1.620248
 H -1.795767 -4.924561 -1.060746
 H -2.054463 -3.570126 0.061311
 C -3.930483 1.308872 -1.128075
 H -4.993002 1.420031 -0.859373
 C -3.190284 2.616774 -0.871524
 H -3.628424 3.420459 -1.481700
 H -3.254827 2.916728 0.185634
 H -2.130495 2.516055 -1.148998

C -3.840178 0.909199 -2.605523
 H -2.783794 0.855103 -2.911648
 H -4.321545 -0.062408 -2.797615
 H -4.336252 1.666269 -3.230745
 C -4.224569 -0.741336 0.393007
 C -4.642039 -0.552620 1.850590
 H -4.365520 0.301664 2.464723
 C -3.799232 -1.711575 1.464113
 H -2.744208 -1.692592 1.760366
 H -4.270290 -2.702265 1.446243
 C -5.674734 -0.621242 0.786442
 H -6.282666 -1.531279 0.708797
 H -6.202928 0.302498 0.535596

Int I

SCF Energy = -1996.7715685

Free Energy (298.15 K) = -1996.20002

Free Energy (cc-pVTZ, PCM(THF),
298.15 K) = -1996.567096

Free Energy (cc-pVTZ, PCM(THF),
263.15 K) = -1996.552527

C -3.208952 0.135224 -0.507612
 O -1.884339 0.028020 -0.357484
 Sm 0.203167 -0.018593 -0.098150
 O -0.113950 -2.019811 -1.557749
 C -1.166731 -2.052767 -2.534646
 C -2.182048 -3.055368 -1.991971
 C -1.363933 -3.916422 -1.006673
 C 0.055620 -3.381742 -1.145335
 I 0.748994 1.862677 -2.470567
 I 0.195149 -1.884763 2.391479

O	2.264949	1.091334	1.018869	H	-0.917306	3.095750	3.862429
C	3.327806	1.762427	0.313436	H	2.105218	-1.962483	-2.616150
C	4.076597	2.546893	1.373211	H	2.907162	-0.370138	-2.611566
C	3.938143	1.635208	2.587551	H	4.039370	-1.035841	0.567124
C	2.515282	1.127414	2.439500	H	2.754366	-2.211070	0.982418
O	-0.414633	1.852038	1.402866	H	5.031229	-1.328378	-1.956576
C	-0.051958	3.237813	1.235072	H	4.395792	-2.712289	-2.876670
C	-1.157037	4.029099	1.912643	H	5.041122	-3.105407	-0.253713
C	-1.613905	3.070257	3.008751	H	3.462205	-3.713309	-0.817031
C	-1.540498	1.731642	2.301124	H	-1.547642	-1.032896	-2.644776
O	2.433805	-1.142663	-0.749593	H	-0.726212	-2.383802	-3.491905
C	2.868095	-1.348664	-2.113589	H	0.623821	-3.913725	-1.931295
C	4.208202	-2.058947	-2.013549	H	0.626098	-3.381943	-0.208259
C	4.078167	-2.808217	-0.691407	H	-2.624451	-3.647719	-2.805075
C	3.344073	-1.790012	0.156701	H	-2.992331	-2.529992	-1.469504
H	3.970695	1.000055	-0.159336	H	-1.413147	-4.991524	-1.228472
H	2.876463	2.370295	-0.481624	H	-1.713413	-3.764197	0.024089
H	1.782919	1.810859	2.900977	C	-3.742194	1.223333	-1.398895
H	2.343858	0.120729	2.843449	H	-4.841800	1.154323	-1.363119
H	3.580627	3.513717	1.557903	C	-3.332167	2.614108	-0.905845
H	5.117750	2.748671	1.086015	H	-3.720056	3.402983	-1.570143
H	4.100310	2.145235	3.547085	H	-3.715259	2.805612	0.109287
H	4.653787	0.799597	2.521943	H	-2.234261	2.699295	-0.891584
H	0.923675	3.397842	1.724235	C	-3.307470	1.034188	-2.855034
H	0.054598	3.437855	0.159276	H	-2.211918	1.103744	-2.943022
H	-2.438622	1.525647	1.699528	H	-3.633925	0.055591	-3.239952
H	-1.345280	0.873301	2.958743	H	-3.740566	1.815720	-3.499854
H	-1.977674	4.219166	1.205028	C	-4.063460	-0.725247	0.260307
H	-0.799742	4.995636	2.293797	C	-4.577963	-0.704187	1.740133
H	-2.623452	3.285614	3.384994	H	-4.345906	0.059586	2.478175

C -3.706885 -1.805518 1.236142
H -2.667363 -1.828167 1.577979
H -4.163775 -2.801136 1.108591
C -5.520636 -0.621719 0.584369
H -6.172058 -1.487114 0.383305
H -6.004432 0.343486 0.398635

TS 1

SCF Energy = -1996.7713691

Free Energy (298.15 K) = -1996.19653

Free Energy (cc-pVTZ, PCM(THF),
298.15 K) = -1996.564096

Free Energy (cc-pVTZ, PCM(THF),
263.15 K) = -1996.550007

Imaginary mode = 334.0i cm⁻¹

C -3.241089 -1.965811 -0.394867
O -2.377410 -1.349040 0.579447
C -2.845516 -1.643857 1.911941
C -3.859978 -2.758231 1.739213
C -4.464530 -2.416148 0.381489
Sm -0.203484 -0.065763 0.083464
O 0.413253 1.965757 -1.206726
C 0.014947 3.325429 -0.935446
C 1.148027 4.189203 -1.458452
C 1.673339 3.354072 -2.622901
C 1.575982 1.946321 -2.067953
O 0.171745 -2.195807 1.345032
C 1.225202 -2.329083 2.312169
C 2.246648 -3.264765 1.668328
C 1.442328 -3.997149 0.574248
C 0.016866 -3.502219 0.776321

I -0.900129 1.581521 2.584349
I -0.186605 -1.606166 -2.594609
O -2.289479 1.071515 -0.948650
C -3.469086 1.473962 -0.246320
C -3.829909 2.797965 -0.887947
C -3.498335 2.551532 -2.365915
C -2.485483 1.395387 -2.334999
H -4.265284 0.720863 -0.399493
H -3.212445 1.533279 0.819073
H -1.499001 1.641683 -2.745858
H -2.852666 0.499268 -2.860739
H -3.194746 3.590419 -0.463989
H -4.879128 3.078234 -0.721438
H -3.088666 3.447006 -2.854260
H -4.397112 2.257872 -2.927400
H -0.924911 3.522680 -1.477132
H -0.170497 3.417722 0.144157
H 2.447937 1.676527 -1.454105
H 1.414245 1.164361 -2.822923
H 1.925501 4.306210 -0.689159
H 0.802393 5.189138 -1.754826
H 2.699790 3.611720 -2.918077
H 1.024518 3.469093 -3.506301
H -1.972450 -1.909257 2.521325
H -3.296877 -0.730102 2.330895
H -3.444508 -1.231444 -1.185016
H -2.704781 -2.811362 -0.854672
H -4.593621 -2.784394 2.556459
H -3.356418 -3.737571 1.697049
H -5.185686 -1.588856 0.483673

H -4.976641 -3.259360 -0.101854
 H 1.602036 -1.325337 2.529337
 H 0.786614 -2.762495 3.228632
 H -0.544549 -4.129622 1.493645
 H -0.552739 -3.398042 -0.155260
 H 2.671908 -3.953565 2.411675
 H 3.068353 -2.685281 1.227159
 H 1.505718 -5.091525 0.649895
 H 1.790447 -3.703047 -0.425987
 O 1.876975 0.009410 0.408022
 C 3.196431 0.110859 0.604063
 C 3.679500 1.115492 1.617014
 C 4.075042 -0.661789 -0.189829
 H 4.780359 1.063066 1.622247
 C 3.267653 2.539793 1.236522
 C 3.186799 0.785515 3.027958
 C 3.745619 -1.509564 -1.377728
 C 5.535672 -0.485288 -0.459570
 H 3.617676 3.268430 1.985078
 H 3.687202 2.828290 0.259476
 H 2.170005 2.612978 1.185739
 H 2.087069 0.824747 3.073564
 H 3.520452 -0.216831 3.338342
 H 3.573688 1.513459 3.758813
 H 2.722811 -1.445010 -1.764390
 H 4.153988 -2.533709 -1.399668
 H 6.185673 -1.368580 -0.352116
 H 6.011096 0.435453 -0.102753
 C 4.708303 -0.410048 -1.707778
 H 4.448939 0.512221 -2.224157

Int II

SCF Energy = -1996.7861406

Free Energy (298.15 K) = -1996.214418

Free Energy (cc-pVTZ, PCM(THF),
298.15 K) = -1996.58092

Free Energy (cc-pVTZ, PCM(THF),
263.15 K) = -1996.566476

O -1.844696 0.175498 -0.415520
 Sm 0.231899 -0.000645 -0.101713
 O -0.127695 -1.906752 -1.688339
 C -1.163059 -1.845679 -2.680075
 C -2.242358 -2.790786 -2.166909
 C -1.461698 -3.795649 -1.292519
 C -0.020594 -3.296064 -1.351859
 I 0.904026 1.965630 -2.373821
 I 0.041756 -2.028055 2.252235
 O 2.281372 0.974923 1.133146
 C 3.392138 1.642794 0.502075
 C 4.171688 2.282004 1.636086
 C 3.937503 1.292552 2.772887
 C 2.484290 0.913380 2.559434
 O -0.368939 1.792001 1.508332
 C 0.032089 3.172771 1.404888
 C -1.046052 3.962604 2.126541
 C -1.530067 2.964385 3.174610
 C -1.498686 1.660678 2.401423
 O 2.434438 -1.171967 -0.749576
 C 2.906107 -1.329290 -2.107787
 C 4.180157 -2.155298 -2.009124
 C 3.963871 -2.939613 -0.718685
 C 3.287349 -1.899861 0.150124

H 3.992507 0.887584 -0.032895
 H 2.989827 2.346460 -0.238705
 H 1.798317 1.631601 3.039764
 H 2.214405 -0.096398 2.896736
 H 3.745050 3.266080 1.889799
 H 5.231331 2.426547 1.384295
 H 4.116439 1.713743 3.771718
 H 4.586975 0.410050 2.654043
 H 1.014929 3.282128 1.894170
 H 0.139871 3.423229 0.339654
 H -2.406183 1.509072 1.796587
 H -1.326454 0.766987 3.016537
 H -1.861884 4.214054 1.432680
 H -0.657986 4.897320 2.554228
 H -2.531793 3.190893 3.564646
 H -0.831002 2.926615 4.025941
 H 2.113718 -1.841614 -2.673565
 H 3.047983 -0.329736 -2.541505
 H 4.026071 -1.204709 0.588751
 H 2.657973 -2.303738 0.955067
 H 5.060534 -1.500076 -1.910636
 H 4.330476 -2.790330 -2.892958
 H 4.892285 -3.322889 -0.273339
 H 3.285168 -3.790906 -0.888620
 H -1.472413 -0.800504 -2.772516
 H -0.733342 -2.186097 -3.639518
 H 0.558709 -3.799569 -2.147929
 H 0.514352 -3.370067 -0.397088
 H -2.779910 -3.273213 -2.995021
 H -2.970477 -2.231647 -1.563028

H -1.540020 -4.830368 -1.654176
 H -1.819180 -3.769749 -0.253730
 C -3.650468 1.478458 -1.377592
 H -4.750891 1.485378 -1.306368
 C -3.127481 2.835821 -0.910734
 H -3.481882 3.642145 -1.571838
 H -3.469145 3.059626 0.112128
 H -2.026569 2.846756 -0.929527
 C -3.261839 1.225978 -2.832606
 H -2.167491 1.259588 -2.951669
 H -3.629363 0.247520 -3.179535
 H -3.688708 2.000673 -3.488600
 C -3.163521 0.373742 -0.465732
 C -4.015361 -0.361179 0.273432
 C -5.530540 -0.374288 0.436551
 C -3.821628 -1.485665 1.276320
 H -6.113265 -0.639288 -0.468854
 H -5.983628 0.551581 0.845589
 H -3.364061 -2.414446 0.880923
 H -3.232385 -1.230368 2.178857
 C -5.317610 -1.489320 1.425612
 H -6.004254 -2.075856 2.037234

TS 2

SCF Energy = -2167.4338252

Free Energy (298.15 K) = -2166.814775

Free Energy (cc-pVTZ, PCM(THF),
298.15 K) = -2167.229922

Free Energy (cc-pVTZ, PCM(THF),
263.15 K) = -2167.214341

Imaginary mode = 140.8i cm⁻¹

Sm -0.624427 -0.024476 0.101880	H -5.161490 -0.377596 -2.377880
O 0.314964 -1.965882 1.368344	H -2.443896 3.176529 -1.202349
C 1.361810 -1.753898 2.328459	H -1.467161 3.337976 0.288394
C 2.624441 -2.193371 1.605059	H 1.311996 2.458505 -1.682024
C 2.121790 -3.266596 0.615891	H 0.315585 1.626722 -2.915599
C 0.603208 -3.245129 0.788848	H 0.110769 4.811825 -0.798060
I -1.561756 1.327083 2.696840	H -1.360526 5.285789 -1.684650
I -0.116846 -1.541518 -2.569878	H 0.757575 4.347943 -3.125004
O -2.954798 0.520398 -0.866167	H -0.854900 3.682896 -3.488823
C -4.142487 0.746470 -0.080671	H -1.773592 -2.701538 2.394897
C -5.153687 1.336489 -1.045646	H -3.021300 -1.438573 2.553477
C -4.771659 0.653036 -2.354568	H -3.985493 -2.090932 -0.681132
C -3.256823 0.644934 -2.270350	H -2.415778 -2.766760 -1.214683
O -0.670077 2.109349 -1.172566	H -4.770851 -2.929656 1.789576
C -1.419004 3.286060 -0.808582	H -3.718987 -4.138554 2.562529
C -0.688191 4.446305 -1.460211	H -4.284046 -4.441523 -0.090602
C -0.090237 3.791567 -2.702378	H -2.579970 -4.589740 0.413706
C 0.325191 2.433788 -2.170109	H 1.343275 -0.699126 2.618532
O -2.386186 -1.836860 0.623070	H 1.143671 -2.380131 3.212158
C -2.700482 -2.302941 1.955828	H 0.258846 -4.025749 1.491624
C -3.762859 -3.374764 1.774058	H 0.046788 -3.320997 -0.153424
C -3.446377 -3.909481 0.380997	H 3.385687 -2.564440 2.304605
C -3.081740 -2.634334 -0.350990	H 3.045614 -1.335702 1.064507
H -4.480645 -0.222298 0.324450	H 2.528547 -4.266333 0.824309
H -3.873575 1.395293 0.763601	H 2.380878 -3.000209 -0.418985
H -2.821302 1.589941 -2.637059	O 1.372939 0.634370 0.306090
H -2.768688 -0.186281 -2.796848	C 2.558071 1.243247 0.258935
H -5.017176 2.427094 -1.127505	C 2.854017 2.258587 1.341130
H -6.189419 1.147060 -0.731845	C 3.446934 0.990486 -0.721603
H -5.136823 1.174224 -3.250166	H 3.893162 2.591417 1.184064

C	1.934173	3.471809	1.211265	Sm	0.621238	-0.018533	-0.104571
C	2.756431	1.648296	2.736660	O	-0.221461	-1.945418	-1.462474
C	4.827717	1.540055	-1.046773	C	-1.220946	-1.729653	-2.470151
C	3.453276	0.064986	-1.923999	C	-2.511767	-2.199465	-1.819269
H	2.154410	4.214392	1.994112	C	-2.042990	-3.289831	-0.831873
H	2.060964	3.962282	0.232975	C	-0.517713	-3.240632	-0.924353
H	0.881143	3.170650	1.324827	I	1.572729	1.416348	-2.649575
H	1.719750	1.347468	2.953841	I	0.098514	-1.622385	2.510670
H	3.423595	0.779003	2.838001	O	2.909809	0.576219	0.926395
H	3.049989	2.387364	3.498147	C	4.107880	0.857338	0.175127
H	5.604634	1.420546	-0.267603	C	5.078414	1.452245	1.178186
H	4.855106	2.601054	-1.366446	C	4.686266	0.726089	2.460874
H	3.329360	-1.013929	-1.713017	C	3.174774	0.676561	2.340061
H	2.717431	0.300124	-2.716835	O	0.571914	2.081332	1.222459
C	4.856523	0.550396	-2.187714	C	1.282923	3.292213	0.895298
H	5.424336	0.579996	-3.121682	C	0.506667	4.410330	1.568205
C	6.344221	-1.274418	-1.158784	C	-0.086594	3.703373	2.783668
H	6.234568	-1.826481	-2.092688	C	-0.452135	2.349383	2.207775
H	7.074616	-0.465540	-1.127406	O	2.448014	-1.772096	-0.617086
C	5.718153	-1.700731	-0.042347	C	2.812889	-2.201176	-1.949236
H	5.029646	-2.548384	-0.070017	C	3.917597	-3.227576	-1.759531
C	5.852041	-1.048084	1.214505	C	3.588224	-3.803758	-0.386193
N	5.937518	-0.530092	2.254683	C	3.149680	-2.560653	0.360173

Int III

SCF Energy = -2167.4932

Free Energy (298.15 K) = -2166.86883

Free Energy (cc-pVTZ, PCM(THF),
298.15 K) = -2167.280662

Free Energy (cc-pVTZ, PCM(THF),
263.15 K) = -2167.265219

H	3.839108	1.519376	-0.658875
H	2.703373	1.599920	2.717283
H	2.698860	-0.180568	2.835356
H	4.907953	2.536084	1.282905
H	6.126321	1.300645	0.884968
H	5.014983	1.235484	3.377127

H 5.105543 -0.293148 2.468995	C -2.026387 3.419177 -1.208063
H 2.307235 3.207114 1.296343	C -2.766572 1.592914 -2.768738
H 1.339439 3.374305 -0.199478	C -4.897120 1.345289 0.959947
H -1.429421 2.359846 1.700270	C -3.490847 -0.064775 1.858668
H -0.434026 1.522373 2.930804	H -2.258553 4.165125 -1.984268
H -0.295020 4.768477 0.905239	H -2.182617 3.891857 -0.225402
H 1.148683 5.264333 1.824338	H -0.962912 3.152089 -1.309814
H -0.956881 4.221415 3.209327	H -1.715818 1.339100 -2.977523
H 0.670628 3.596253 3.577537	H -3.392957 0.696156 -2.890526
H 1.915704 -2.634034 -2.416722	H -3.083086 2.328555 -3.524227
H 3.108191 -1.313548 -2.525512	H -5.607389 1.360553 0.116737
H 4.020097 -1.986867 0.726226	H -4.955733 2.322711 1.469718
H 2.466300 -2.738800 1.201672	H -3.130634 -1.091952 1.691952
H 4.904427 -2.737446 -1.738849	H -2.950217 0.318044 2.740843
H 3.929219 -3.976256 -2.563492	C -5.026429 0.160078 1.956217
H 4.435446 -4.308989 0.097661	H -5.396830 0.432190 2.956177
H 2.753351 -4.519774 -0.455666	C -5.884734 -1.002055 1.434202
H -1.201477 -0.669480 -2.740192	H -5.871217 -1.813335 2.180286
H -0.949756 -2.335861 -3.353216	H -6.926554 -0.654155 1.339952
H -0.124702 -4.001147 -1.623577	C -5.419475 -1.559362 0.130531
H -0.009058 -3.327093 0.043726	H -4.677472 -2.360264 0.114022
H -3.236663 -2.564043 -2.559774	C -5.817341 -1.059452 -1.103560
H -2.966920 -1.359035 -1.279269	N -6.147037 -0.639863 -2.150713
H -2.422827 -4.289518 -1.085519	
H -2.358680 -3.055927 0.195317	TS 3
O -1.391804 0.586461 -0.332549	SCF Energy = -2167.4872736
C -2.592375 1.164096 -0.289398	Free Energy (298.15 K)= -2166.858861
C -2.905687 2.179191 -1.366706	Free Energy (cc-pVTZ, PCM(THF),
C -3.482906 0.884682 0.684835	298.15 K) = -2167.270326
H -3.956520 2.478223 -1.220743	Free Energy (cc-pVTZ, PCM(THF),
	263.15 K) = -2167.255413

Imaginary mode = 411.9i cm⁻¹

C	2.696467	1.077378	0.641566	H	-6.083970	1.403709	-0.316441
O	1.458194	0.668760	0.441216	H	-5.035791	2.276869	-2.680626
Sm	-0.524345	0.008627	0.031403	H	-5.118339	0.520560	-2.405125
O	0.499737	-2.163898	0.578456	H	-2.379702	3.500795	-0.169084
C	1.389946	-2.299433	1.719664	H	-1.495736	3.045326	1.322264
C	1.848120	-4.051770	0.202800	H	1.382104	2.927396	-0.704912
C	0.595740	-3.333633	-0.260725	H	0.449468	2.646904	-2.206929
I	-1.448110	0.453931	2.929682	H	0.172499	4.760990	0.960661
I	-0.013253	-0.553336	-2.961081	H	-1.247912	5.597316	0.280600
O	-2.865705	0.784958	-0.698254	H	0.910636	5.230650	-1.342702
C	-4.051339	0.732855	0.120194	H	-0.691805	4.796446	-1.990416
C	-5.042817	1.657289	-0.558772	H	-1.712444	-3.294921	1.414889
C	-4.688402	1.463188	-2.029319	H	-2.855689	-2.034823	1.946861
C	-3.173850	1.373726	-1.980089	H	-3.767802	-1.697044	-1.417816
O	-0.618106	2.447948	-0.453784	H	-2.222706	-2.345904	-2.038746
C	-1.381535	3.417454	0.294400	H	-4.705841	-3.084604	0.779872
C	-0.602131	4.714262	0.180126	H	-3.782965	-4.545737	1.203996
C	0.040545	4.575988	-1.196807	H	-4.288839	-4.073412	-1.436671
C	0.421766	3.108840	-1.210462	H	-2.624421	-4.509607	-0.977043
O	-2.243017	-1.904797	-0.024144	H	2.219872	-1.596987	1.581093
C	-2.599558	-2.711095	1.120186	H	0.823932	-2.017615	2.618283
C	-3.739196	-3.597898	0.650356	H	-0.305911	-3.950681	-0.101900
C	-3.424269	-3.765627	-0.832631	H	0.619263	-2.997606	-1.306555
C	-2.928690	-2.380349	-1.198034	H	2.864982	-3.829261	2.141481
H	-4.416998	-0.308300	0.141867	H	1.814885	-5.127070	-0.020527
H	-3.770827	1.022160	1.141795	H	2.739490	-3.627755	-0.284026
H	-2.698628	2.367515	-2.023363	C	3.056305	1.595459	2.013296
H	-2.725447	0.744211	-2.760391	H	4.121627	1.876167	1.976356
H	-4.866244	2.701315	-0.253158	C	2.867484	0.566457	3.126402
				H	3.148810	1.007031	4.095866

H 1.812557 0.260949 3.194951
 H 3.495174 -0.321715 2.962384
 C 2.233682 2.854597 2.302983
 H 1.159915 2.609813 2.313326
 H 2.495012 3.271720 3.287814
 H 2.411869 3.633978 1.544447
 C 3.633180 0.999846 -0.379664
 C 5.070479 1.483361 -0.471325
 C 3.520689 1.081907 -1.896927
 C 5.053703 0.869464 -1.895041
 H 5.125839 2.584200 -0.510296
 H 5.810402 1.103039 0.249605
 H 2.878758 0.377633 -2.444100
 H 3.261454 2.110845 -2.198125
 C 5.265214 -0.634577 -1.713635
 H 5.667940 1.322418 -2.685836
 H 5.104365 -1.167275 -2.665291
 H 6.290931 -0.850089 -1.377545
 C 1.865718 -3.737744 1.695617
 H 1.167213 -4.394354 2.239253
 C 4.658635 -1.641150 0.537547
 N 4.951820 -2.077074 1.586295
 C 4.251393 -1.069388 -0.678655
 H 3.275415 -1.412333 -1.033187

Int IV

SCF Energy = -2167.514776

Free Energy (298.15 K) = -2166.884686

Free Energy (cc-pVTZ, PCM(THF),
298.15 K) = -2167.292699

Free Energy (cc-pVTZ, PCM(THF),
263.15 K) = -2167.277716

C 2.742839 -0.911802 -0.787031
 O 1.498545 -0.486069 -0.556202
 Sm -0.489429 -0.005043 -0.060882
 O 0.235206 2.234712 -0.794068
 C 1.037351 2.403827 -1.994038
 C 1.446469 4.224274 -0.526346
 C 0.256222 3.442774 -0.010384
 I -1.621631 -0.641125 -2.852028
 I 0.289319 0.712243 2.855310
 O -2.696329 -0.902217 0.950617
 C -3.953689 -0.969853 0.252170
 C -4.791380 -1.958774 1.039221
 C -4.318598 -1.694597 2.465280
 C -2.829270 -1.470491 2.269594
 O -0.412239 -2.435827 0.472718
 C -1.202524 -3.474571 -0.139612
 C -0.345300 -4.724293 -0.066683
 C 0.438718 -4.494198 1.222154
 C 0.732610 -3.008620 1.143449
 O -2.375395 1.769376 0.107091
 C -2.949626 2.455485 -1.024793
 C -4.127332 3.234963 -0.467609
 C -3.659351 3.547132 0.950344
 C -2.952445 2.260063 1.330638
 H -4.411419 0.034679 0.251539
 H -3.748141 -1.257734 -0.787970
 H -2.261001 -2.414955 2.294201
 H -2.371986 -0.776993 2.988408
 H -4.552727 -2.991377 0.737265

H -5.869205 -1.802803 0.894098
 H -4.527543 -2.518339 3.161554
 H -4.796455 -0.784758 2.863399
 H -2.134058 -3.588220 0.441440
 H -1.454342 -3.154452 -1.160353
 H 1.623972 -2.793683 0.536278
 H 0.832984 -2.507023 2.115886
 H 0.338012 -4.766018 -0.928244
 H -0.948958 -5.642228 -0.058710
 H 1.356950 -5.093783 1.289819
 H -0.185301 -4.723378 2.101312
 H -2.179088 3.118054 -1.452450
 H -3.211008 1.703453 -1.781411
 H -3.662741 1.505717 1.712220
 H -2.144975 2.375581 2.066563
 H -5.030535 2.603705 -0.442241
 H -4.355618 4.127964 -1.065380
 H -4.476100 3.795872 1.641853
 H -2.948333 4.388843 0.945279
 H 1.900741 1.733372 -1.908885
 H 0.423303 2.095517 -2.852060
 H -0.688914 3.988913 -0.177874
 H 0.323841 3.155258 1.048194
 H 2.435459 3.994130 -2.472779
 H 1.348658 5.302265 -0.336989
 H 2.374245 3.872068 -0.052665
 C 3.049675 -1.541626 -2.115994
 H 4.119095 -1.811747 -2.106289
 C 2.814725 -0.567871 -3.276683
 H 3.082602 -1.033423 -4.238805

H 1.750937 -0.287434 -3.325026
 H 3.415976 0.346175 -3.156433
 C 2.231378 -2.818627 -2.334354
 H 1.154993 -2.589469 -2.282330
 H 2.433412 -3.255515 -3.325302
 H 2.467666 -3.579342 -1.573011
 C 3.747735 -0.603384 0.251333
 C 5.247084 -0.973844 0.154171
 C 3.792870 -1.300901 1.656525
 C 3.838721 0.887341 0.721097
 C 5.226299 -0.737699 1.682116
 H 5.386435 -2.034521 -0.097365
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 H 3.773421 -2.394090 1.546656
 C 4.968642 0.766504 1.784837
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 H 0.713125 4.475862 -2.557505
 C 4.166780 1.783876 -0.374601
 N 4.428358 2.483975 -1.265456

Sm(II)-13j

SCF Energy = -2167.5394442

Free Energy (298.15 K) = -2166.91642

Free Energy (cc-pVTZ, PCM(THF),
298.15 K) = -2167.334865

Free Energy (cc-pVTZ, PCM(THF),
263.15 K) = -2167.31891

C 2.896582 -0.605948 -0.435050
O 1.762637 -0.141198 -0.411257
Sm -0.742446 0.055775 -0.117833
O -0.012324 2.160557 -1.496938
C 0.839093 2.082858 -2.643446
C 2.164222 2.740496 -2.229069
C 1.838750 3.410568 -0.881466
C 0.319547 3.383184 -0.841419
I -1.347647 -1.536204 -2.805672
I -0.218899 1.598100 2.682514
O -2.869352 -1.007378 0.938895
C -4.058973 -1.307648 0.185793
C -5.042245 -1.882101 1.192609
C -4.629436 -1.171469 2.478771
C -3.118446 -1.157779 2.343914
O -0.103249 -2.199642 1.012854
C -0.748921 -3.440629 0.669253
C -0.099913 -4.490768 1.553464
C 0.235971 -3.682344 2.803566
C 0.684326 -2.363780 2.199774
O -2.809138 1.574859 -0.564148
C -3.184257 2.040307 -1.875996
C -4.248784 3.104184 -1.646952
C -3.895666 3.620651 -0.254648
C -3.487738 2.337739 0.442157
H -4.425045 -0.368351 -0.259949
H -3.785288 -1.989494 -0.632069
H -2.680212 -2.114713 2.684018
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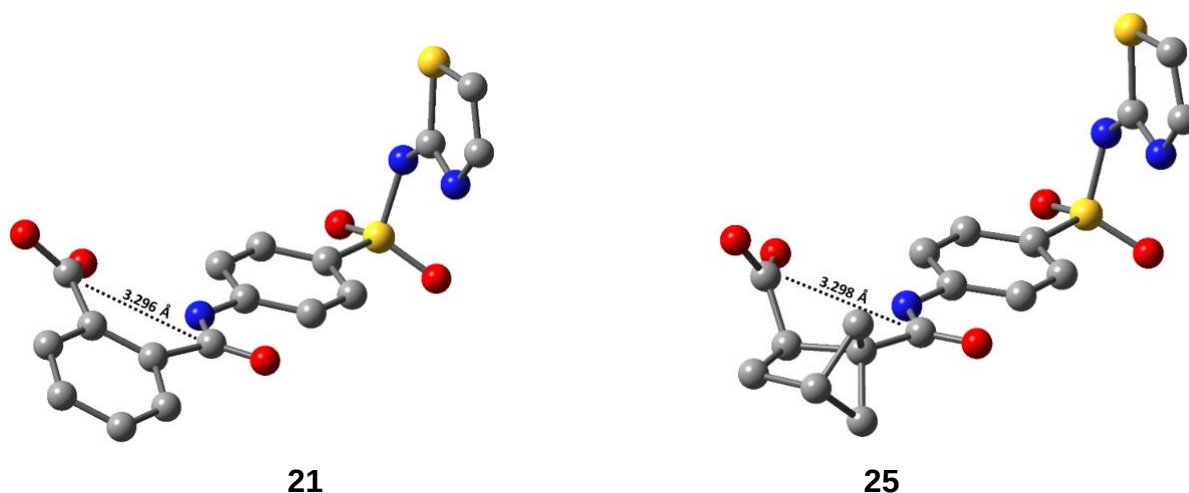
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H -1.826146 -3.335283 0.878645
H -0.626862 -3.603578 -0.410830
H 1.750959 -2.404477 1.912315
H 0.523774 -1.484007 2.840726
H 0.821992 -4.872117 1.085605
H -0.763775 -5.345166 1.744247
H 1.009399 -4.141502 3.434797
H -0.664711 -3.533273 3.420824
H -2.279892 2.449268 -2.351745
H -3.524964 1.178129 -2.467416
H -4.374625 1.773938 0.788909
H -2.798606 2.469316 1.289227
H -5.254360 2.653499 -1.639092
H -4.233964 3.881094 -2.423816
H -4.725274 4.134167 0.250706
H -3.038820 4.312272 -0.302341
H 0.914029 1.025477 -2.925885
H 0.360799 2.630887 -3.474478
H -0.121974 4.229384 -1.402701
H -0.099470 3.348359 0.173824
H 2.488459 3.472391 -2.982312
H 2.968300 1.997538 -2.133333
H 2.247131 4.426525 -0.790562
H 2.214325 2.810358 -0.038731
C 3.302383 -1.651239 -1.446969
H 4.399147 -1.748078 -1.412763

C	2.865745	-1.255813	-2.853942	H	4.379408	-1.944216	1.747981
H	3.191089	-2.023222	-3.571272	H	5.797969	-1.412851	0.761210
H	1.769111	-1.179467	-2.912645	H	3.116942	1.406094	2.055334
H	3.318680	-0.300850	-3.159545	H	2.827482	-0.306058	2.480989
C	2.670626	-2.985309	-1.029984	C	5.695143	1.165156	1.404319
H	1.574517	-2.897635	-1.039966	H	5.369564	-0.011601	3.294499
H	2.963528	-3.770716	-1.741911	H	5.606496	2.180958	1.812482
H	2.994071	-3.299986	-0.025549	H	6.757977	0.946563	1.232292
C	3.902978	-0.141364	0.570232	C	4.849592	1.004546	0.100107
C	4.894795	-1.084801	1.298016	H	4.263087	1.907597	-0.124065
C	3.508572	0.383231	1.968187	C	5.635013	0.676301	-1.081378
C	4.999864	0.113317	2.269809	N	6.251312	0.399327	-2.025972

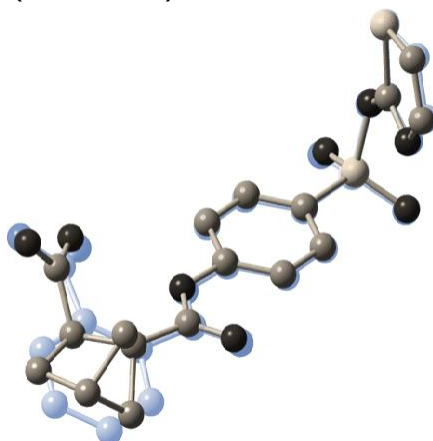
12.3. Lowest energy conformations of phthalylsulfathiazole and its BCH analogue

12.3.1. Background/Results

The lowest energy conformations of phthalylsulfathiazole **21** and its BCH analogue **25** were calculated, in order to establish whether the latter could act as a saturated analogue of the former. Geometry optimisations located several true minimum energy conformations. Thermodynamic corrections from subsequent harmonic vibrational frequency calculations were then used to identify the lowest energy conformations of phthalylsulfathiazole and the BCH analogue as **21** and **25**, respectively (see below).



In order for the BCH analogue to effectively mimic phthalylsulfathiazole, it would be expected that the distance between the carbon atoms of the ortho substituents be similar in both compounds. This key distance was found to be 3.3 Å in both structures, differing by only 0.002 Å. Superimposing the lowest energy conformations further emphasizes their similarity (see below).



12.3.2. Computational Details

In this study, geometry optimisation calculations were performed (using Gaussian 16, Revision C.01.)⁹ using the PBE0 functional¹⁰ and Dunning's correlation-consistent double-zeta + polarisation basis sets for C, H, O, N and S.¹¹ The geometry optimisation calculations were run with the Grimme's D3 model¹² with Becke-Johnson damping factors.¹³ Harmonic vibrational frequencies calculations were performed, to confirm the stationary points as true minima and to provide thermodynamic corrections to the SCF energies. Further single point energy calculations using Dunning's correlation-consistent triple-zeta + polarisation basis sets for C, H, O, N and S¹⁴ were then run on the optimised geometries.

12.3.3. Cartesian Coordinates (Å) and computed energies (in Hartrees) for the lowest energy conformations of phthalylsulfathiazole 21 and BCH analogue 25

Phthalylsulfathiazole 21

SCF Energy = -1990.8973034

Free Energy (298.15 K) = -1990.665604

Free Energy (cc-pVTZ, 298.15 K) = -1991.048785

C -0.032923 -1.579793 -0.645927

C 1.323508 -1.853024 -0.619243

C 2.101339 -1.306752 0.401787

C 1.538157 -0.513502 1.398039

C 0.176614 -0.238131 1.371444

H -0.660318 -1.995188 -1.437417

H 1.784687 -2.496759 -1.368883

H 2.176301 -0.109880 2.182701

H -0.284694 0.382437 2.134372

C -0.619200 -0.770104 0.344551

N -1.992102 -0.561885 0.234481

C -2.776776 0.244773 0.994995

H -2.448474 -1.010822 -0.566030

O -2.370463 0.887284 1.952100

C -4.261932 0.295345 0.661214
 C -4.943916 0.091292 -0.566671
 C -5.021662 0.696988 1.766978
 C -6.332046 0.301501 -0.621800
 C -6.399042 0.861475 1.706439
 H -4.475425 0.893990 2.688797
 C -7.062765 0.663594 0.500638
 H -6.839665 0.163225 -1.574916
 H -6.949330 1.156542 2.601660
 H -8.142899 0.798772 0.426452
 C -4.332011 -0.355759 -1.848581
 O -3.350768 -1.065135 -1.989605
 O -5.014979 0.062558 -2.918782
 H -4.565276 -0.332047 -3.684857
 S 3.834100 -1.657768 0.430396
 O 4.336016 -1.509458 1.794886
 O 4.095651 -2.850598 -0.391490
 N 4.549516 -0.426484 -0.532545
 H 4.703610 -0.755901 -1.480362
 C 4.340665 0.920867 -0.336904
 S 4.742041 2.063914 -1.605602
 C 3.796718 2.809509 0.629841
 C 4.218541 3.339578 -0.549720
 H 3.416597 3.394014 1.467456
 H 4.264204 4.379803 -0.861133
 N 3.865322 1.443958 0.751790

BCH analogue 25

SCF Energy = -1993.2766302

Free Energy (298.15 K) = -1992.998239

Free Energy (cc-pVTZ, 298.15 K) = -1993.384532

C 0.006158 -1.524709 0.772163
 C -1.348779 -1.808480 0.764763
 C -2.128833 -1.345380 -0.294734
 C -1.570351 -0.624098 -1.347052
 C -0.211002 -0.337512 -1.339518
 H 0.636159 -1.876254 1.592441
 H -1.806397 -2.397998 1.559816
 H -2.210625 -0.284281 -2.159708
 H 0.247865 0.232063 -2.143113
 C 0.585878 -0.786740 -0.275255
 N 1.959465 -0.559564 -0.190225
 C 2.734340 0.221841 -1.000762
 H 2.402523 -0.934807 0.650271
 O 2.320968 0.839127 -1.969184
 S -3.858969 -1.710318 -0.298827
 O -4.359990 -1.666172 -1.671007
 O -4.112928 -2.841694 0.607925
 N -4.584930 -0.417159 0.570710
 H -4.737417 -0.677502 1.540049
 C -4.384788 0.913715 0.277519
 S -4.794924 2.143433 1.459359
 C -3.852666 2.730501 -0.824117
 C -4.279038 3.342255 0.313546
 H -3.475850 3.254956 -1.702013
 H -4.332288 4.402090 0.548176
 N -3.911994 1.359276 -0.846235
 C 4.209906 0.285616 -0.670512
 C 4.905303 1.667800 -0.531675
 C 5.189245 0.053500 -1.853815

C 4.909641 -0.545063 0.446778
C 6.153023 0.872567 -0.974982
H 4.538331 2.356072 -1.302882
H 4.908061 2.147544 0.458278
H 5.453030 -0.987000 -2.100686
H 4.834311 0.590922 -2.741405
C 6.373749 -0.078863 0.204220
H 7.041660 1.366750 -1.386198
H 7.025102 -0.925065 -0.057553
H 6.796110 0.424234 1.083005
H 4.769829 -1.618961 0.252842
C 4.350285 -0.311890 1.824744
O 3.356690 -0.871148 2.250022
O 5.014794 0.580047 2.563565
H 4.525417 0.647888 3.401983

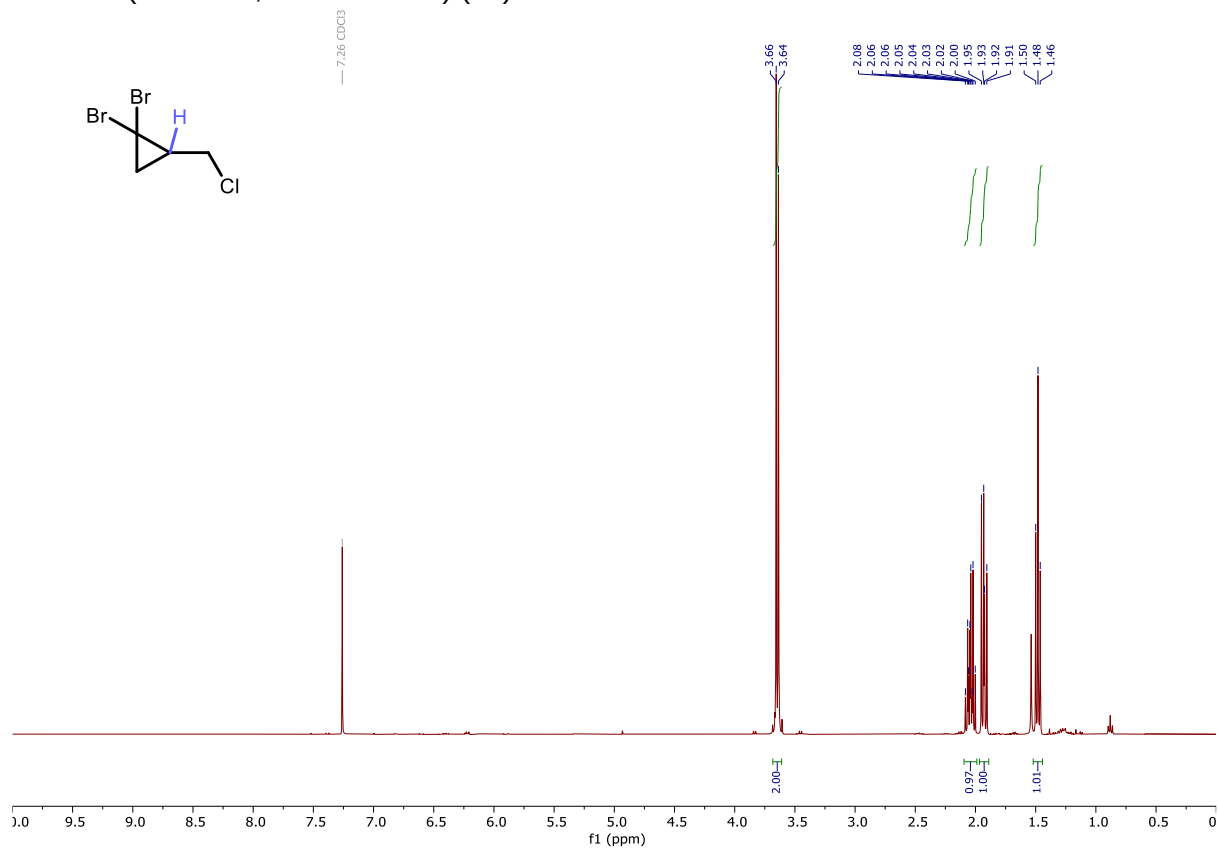
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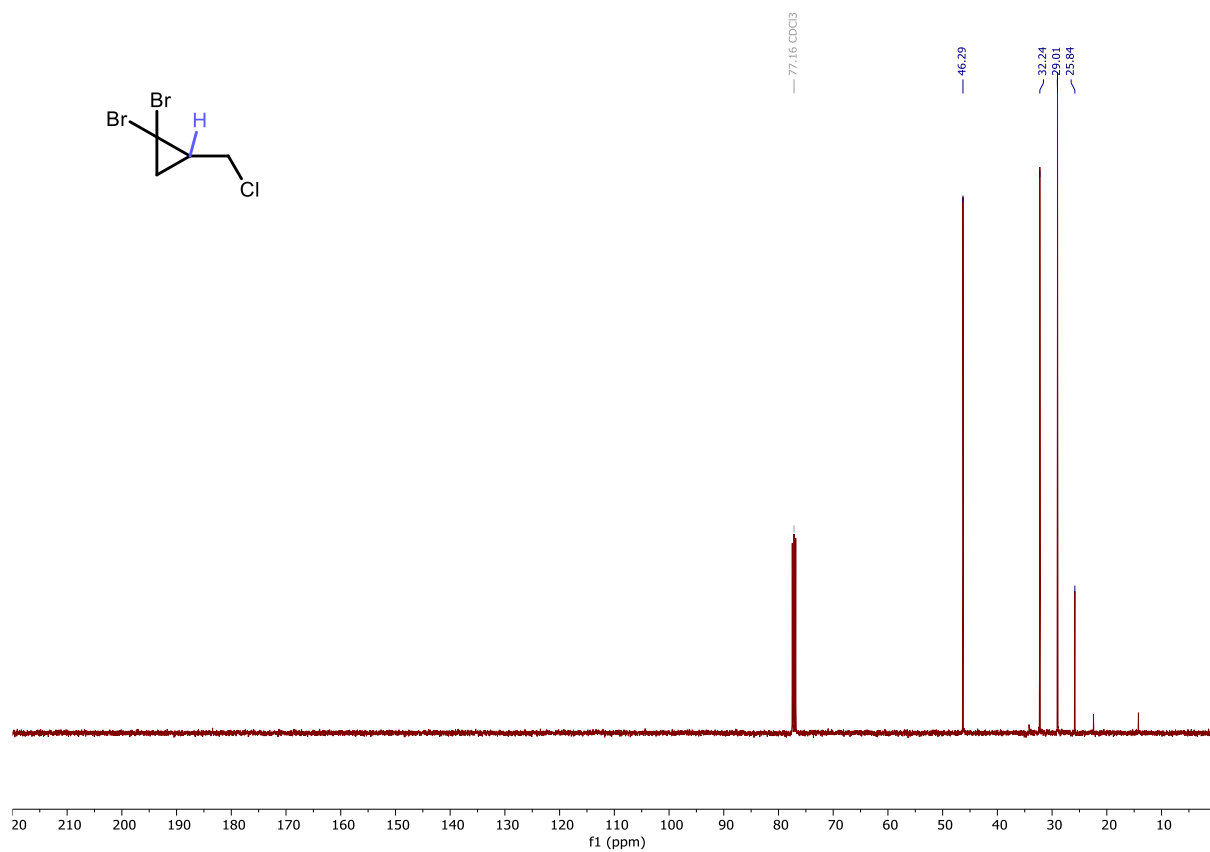
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(b) for I: J. M. L. Martin, A. Sundermann, *J. Chem. Phys.* **2001**, *114*, 3408–3420.
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14. NMR Spectra

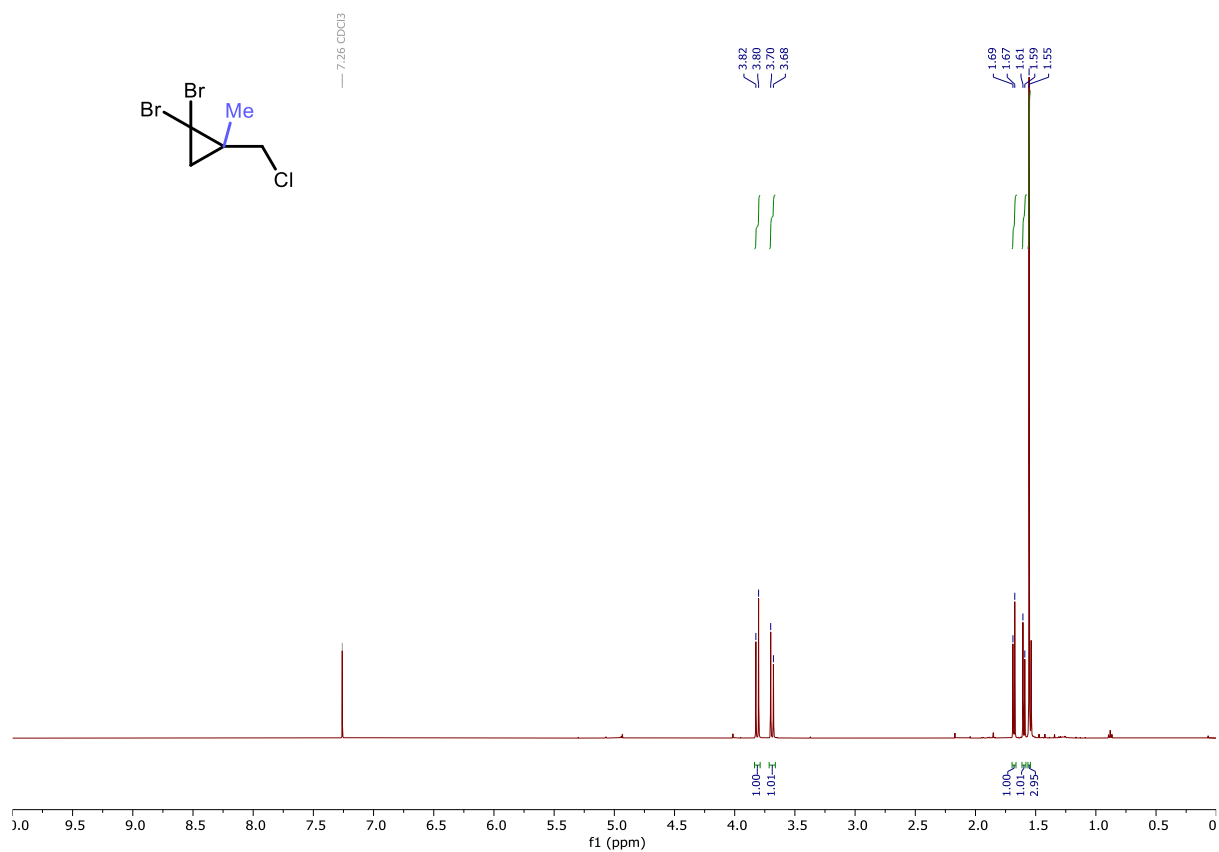
^1H NMR (400 MHz, Chloroform-*d*) (**9a**):



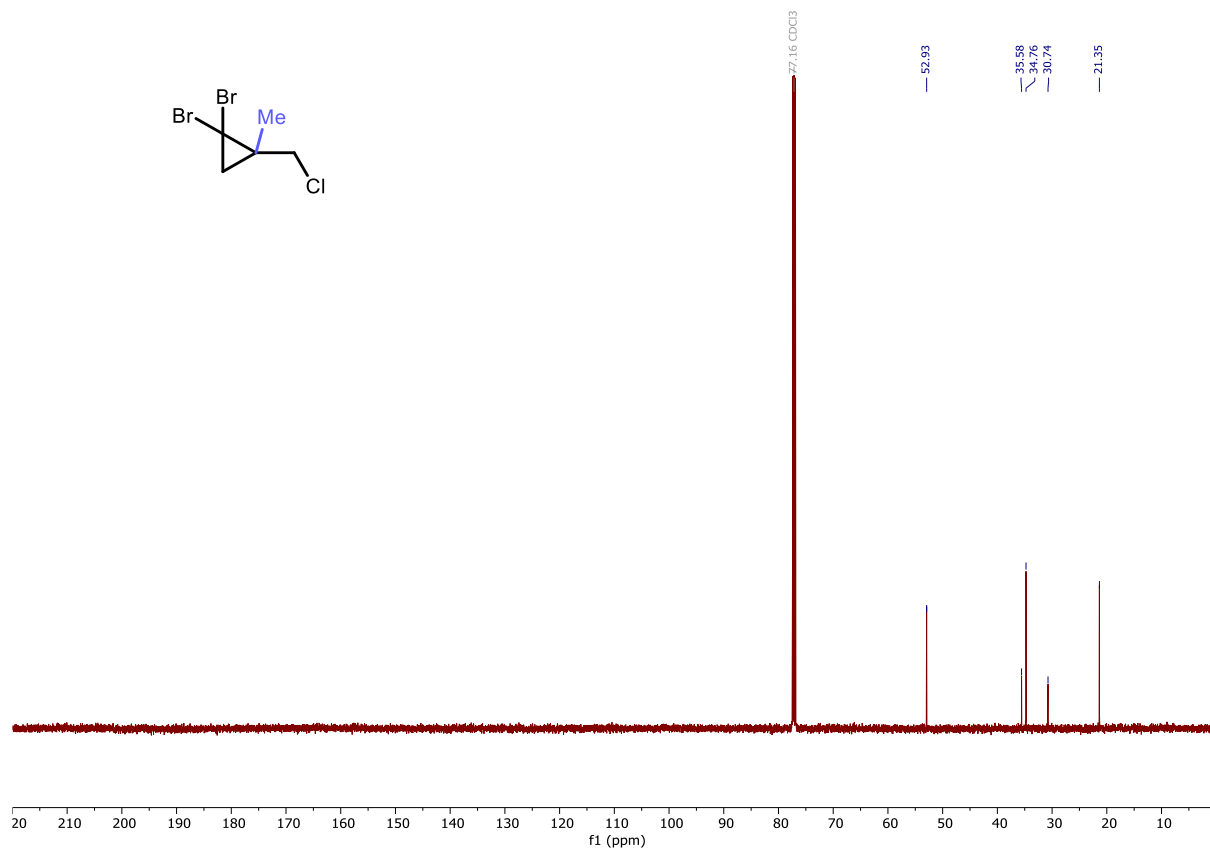
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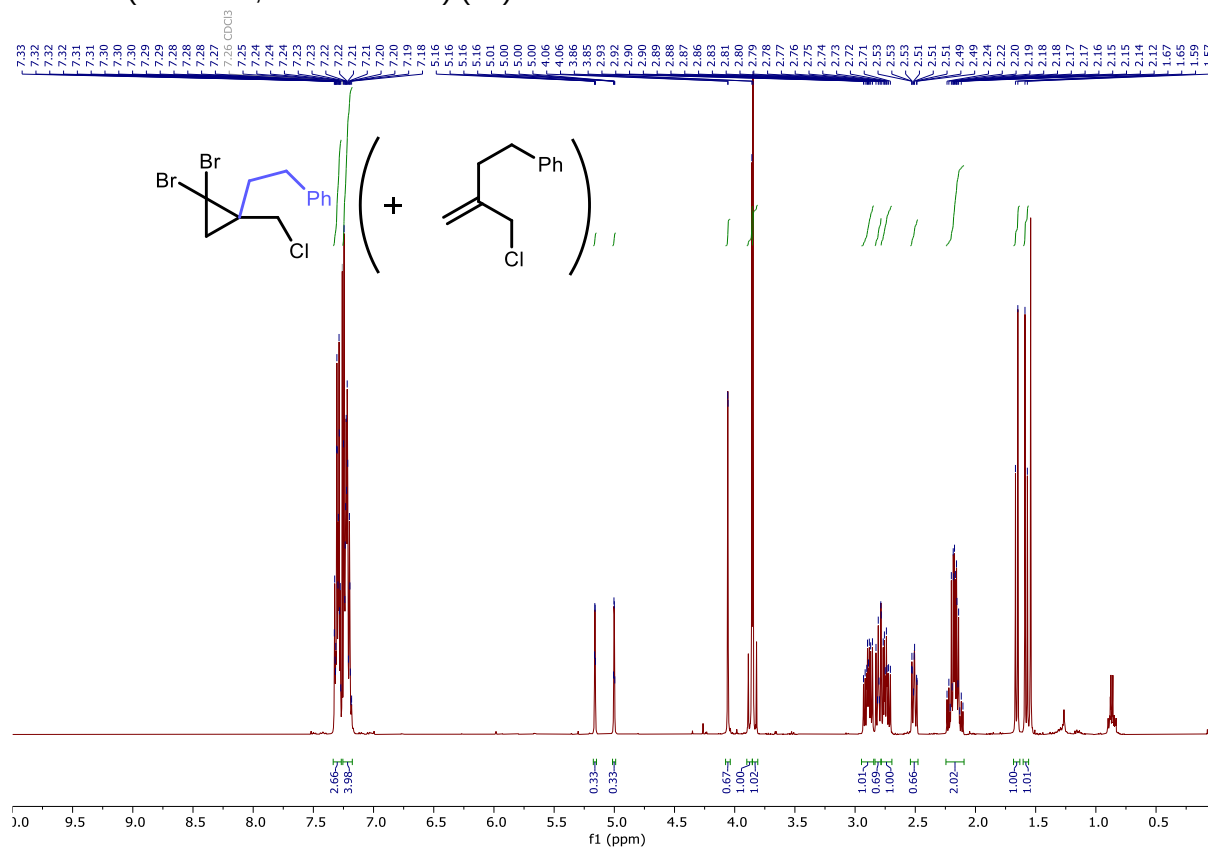
^1H NMR (400 MHz, Chloroform-*d*) (**9b**):



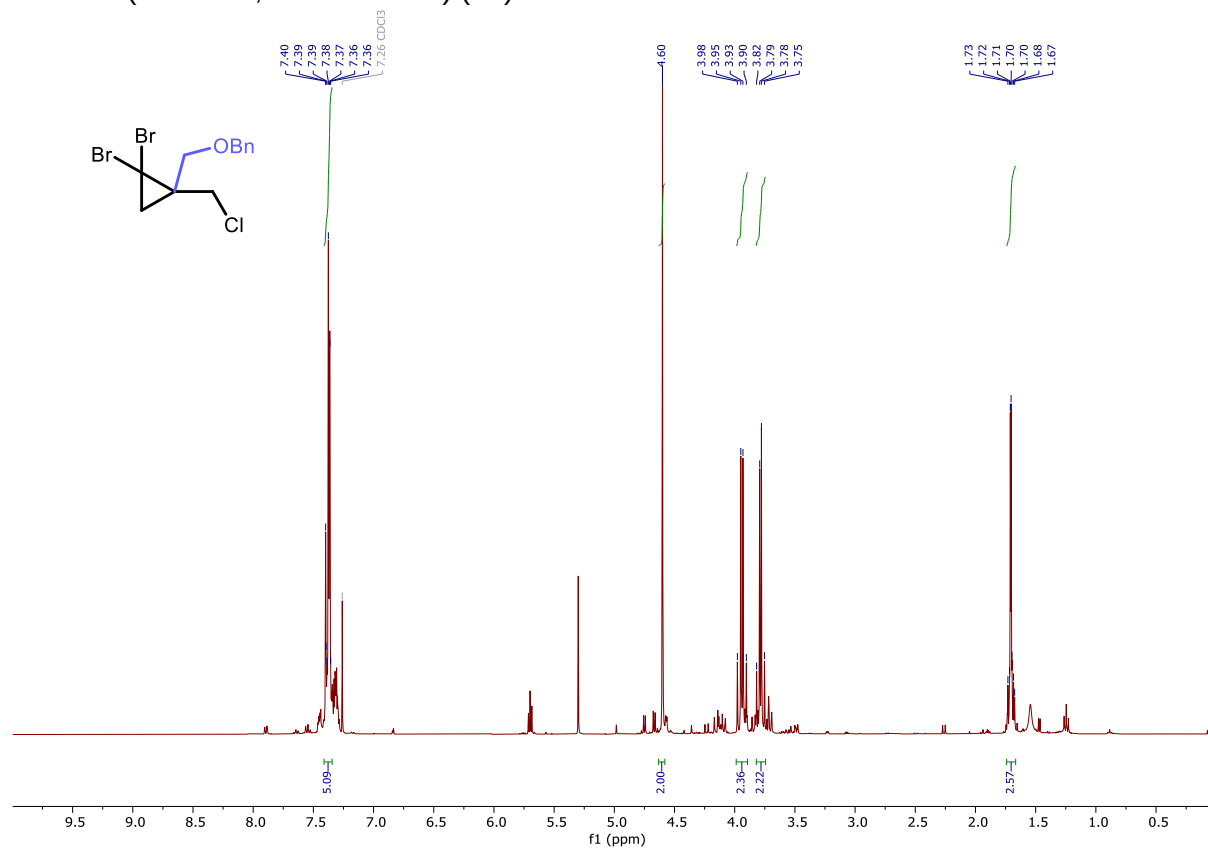
^{13}C NMR (126 MHz, Chloroform-*d*) (**9b**):



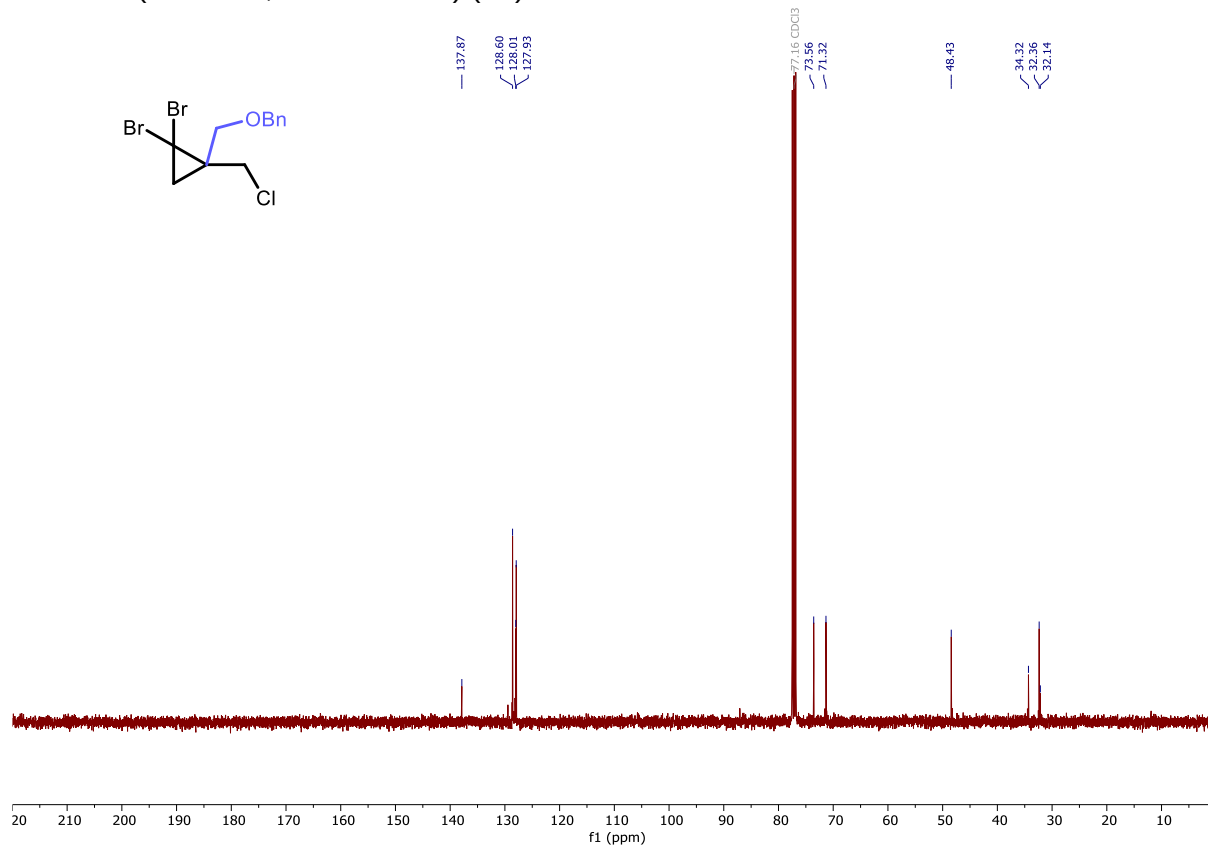
¹H NMR (400 MHz, Chloroform-*d*) (9c):



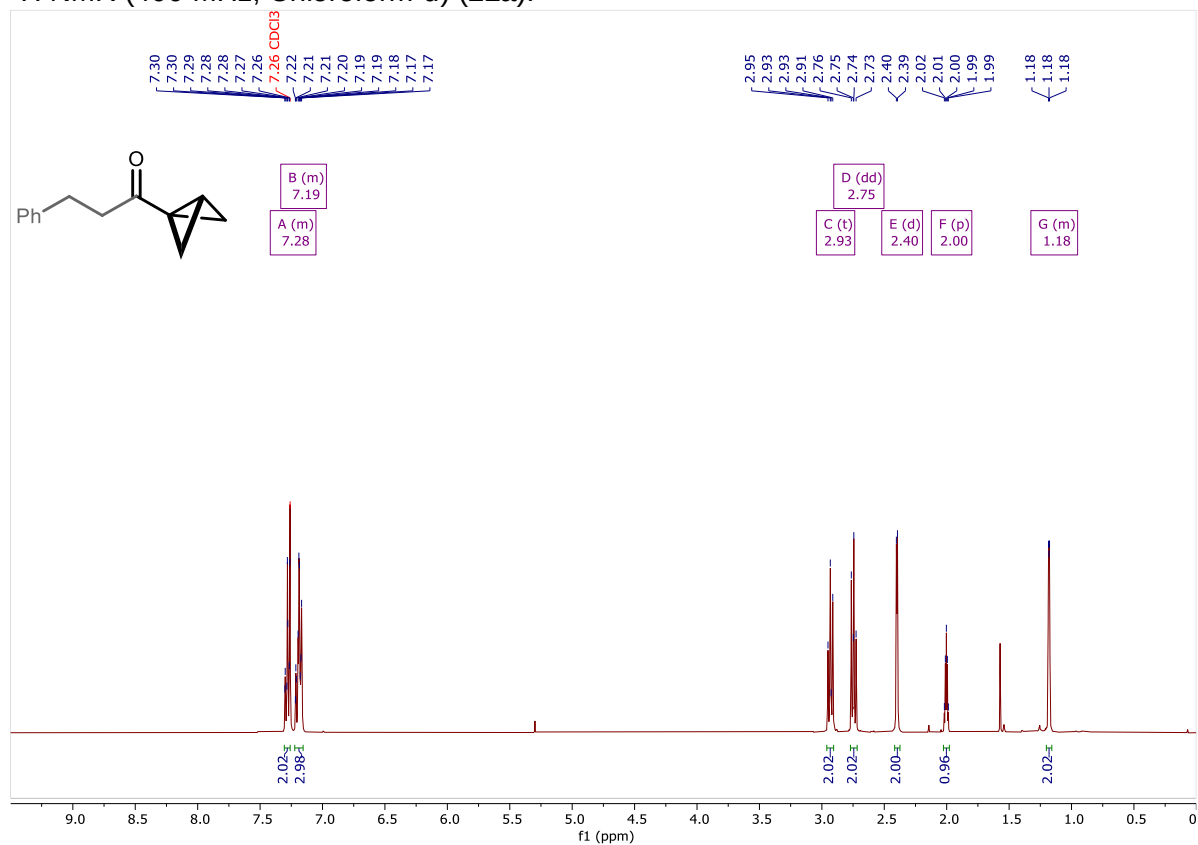
^1H NMR (400 MHz, Chloroform-*d*) (**9d**):



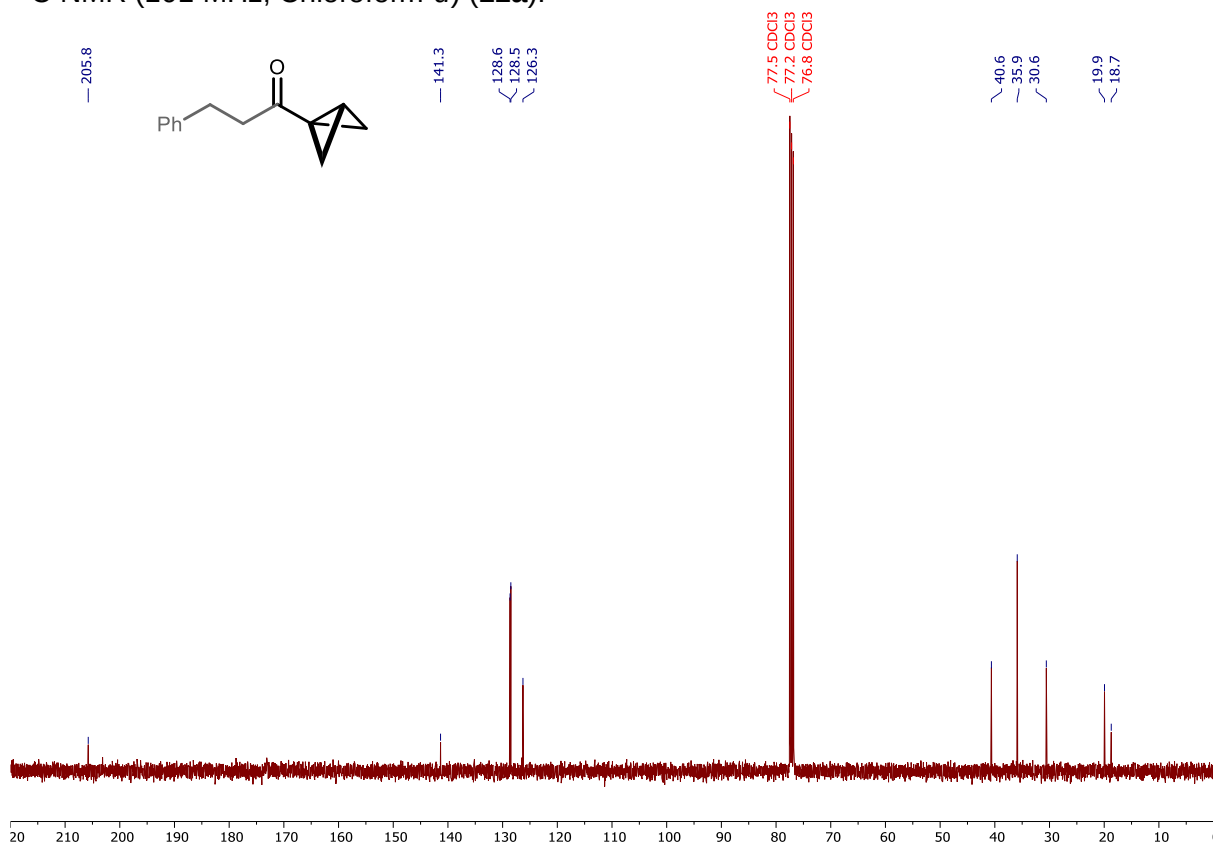
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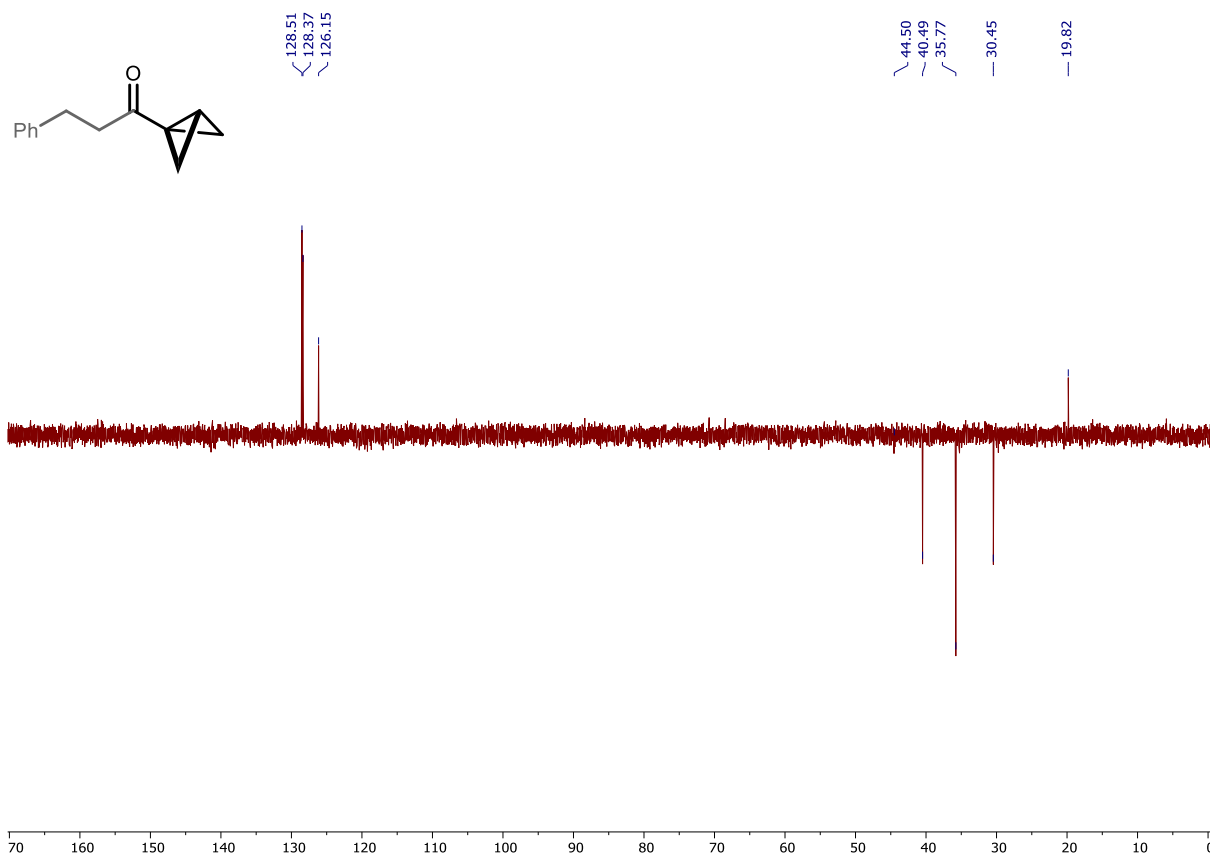
¹H NMR (400 MHz, Chloroform-*d*) (**11a**):



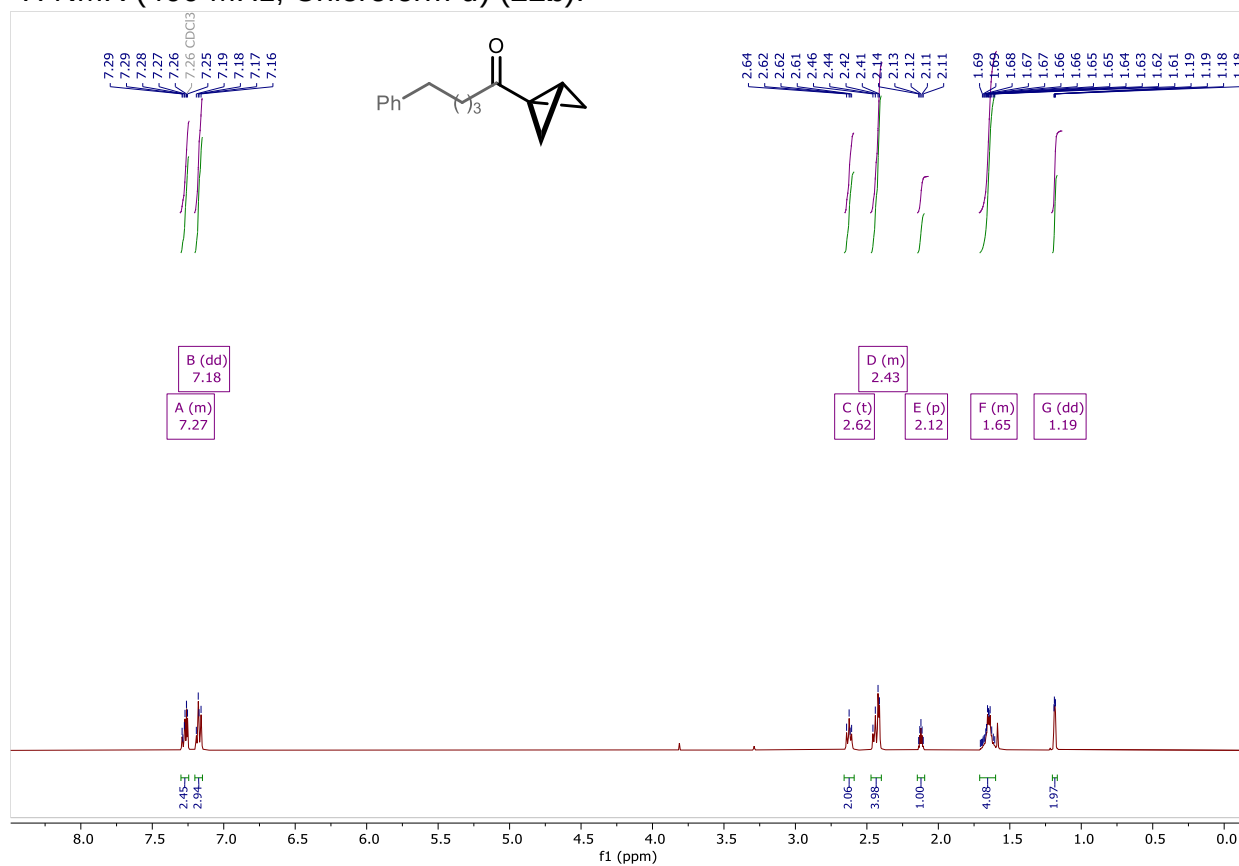
¹³C NMR (101 MHz, Chloroform-*d*) (**11a**):



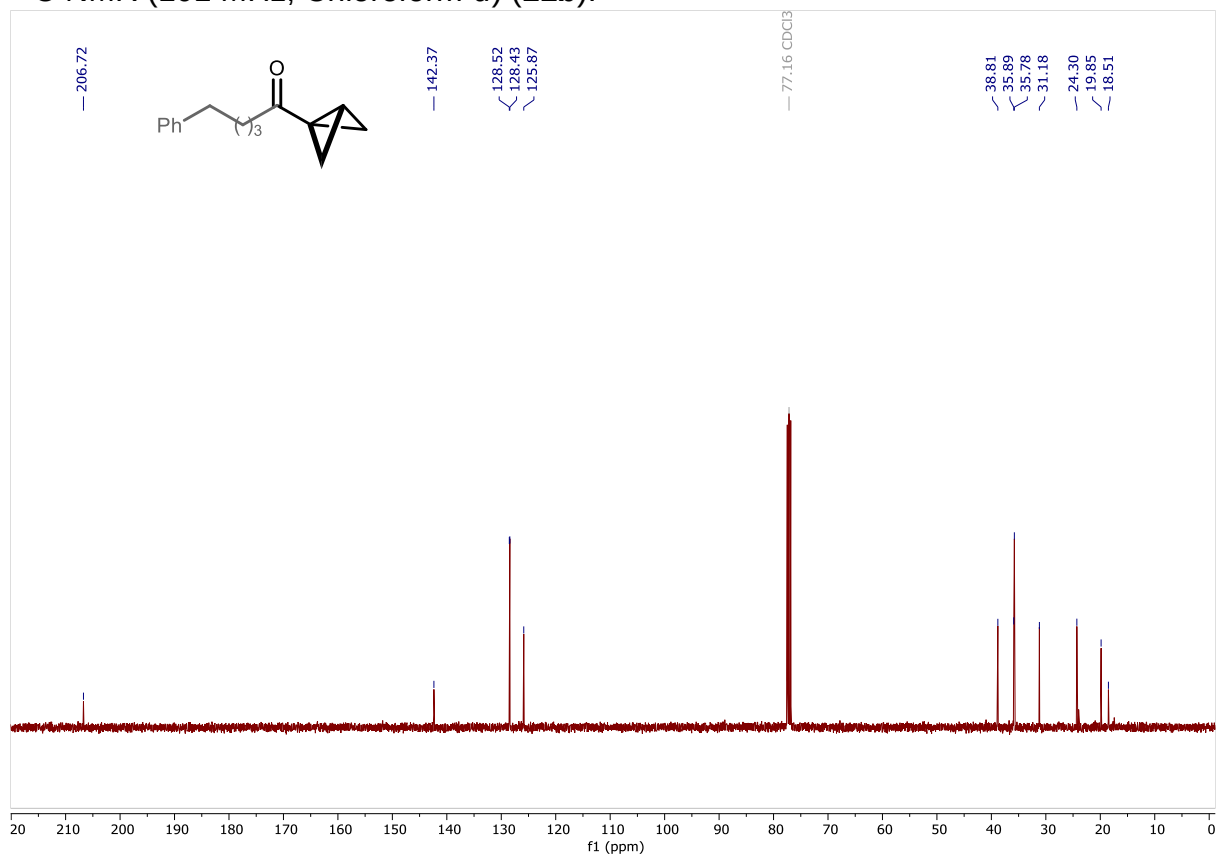
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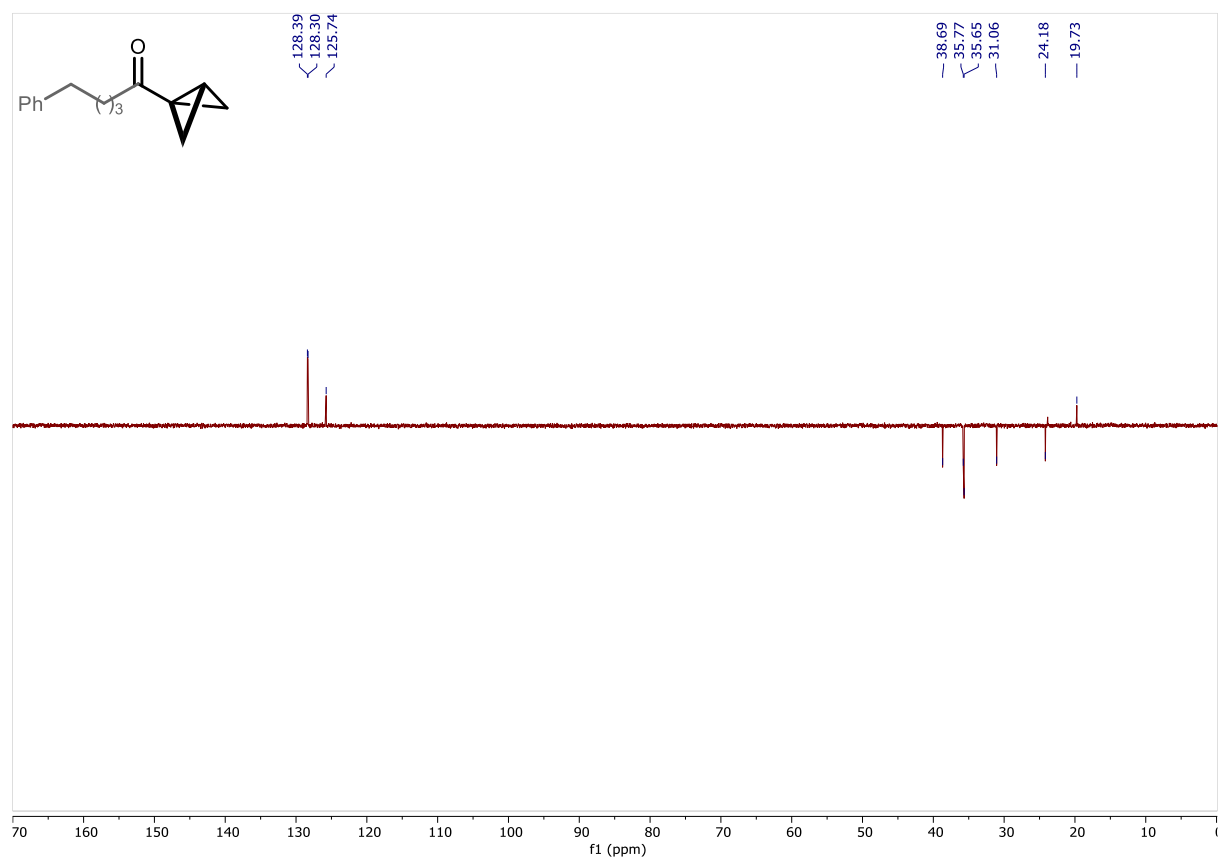
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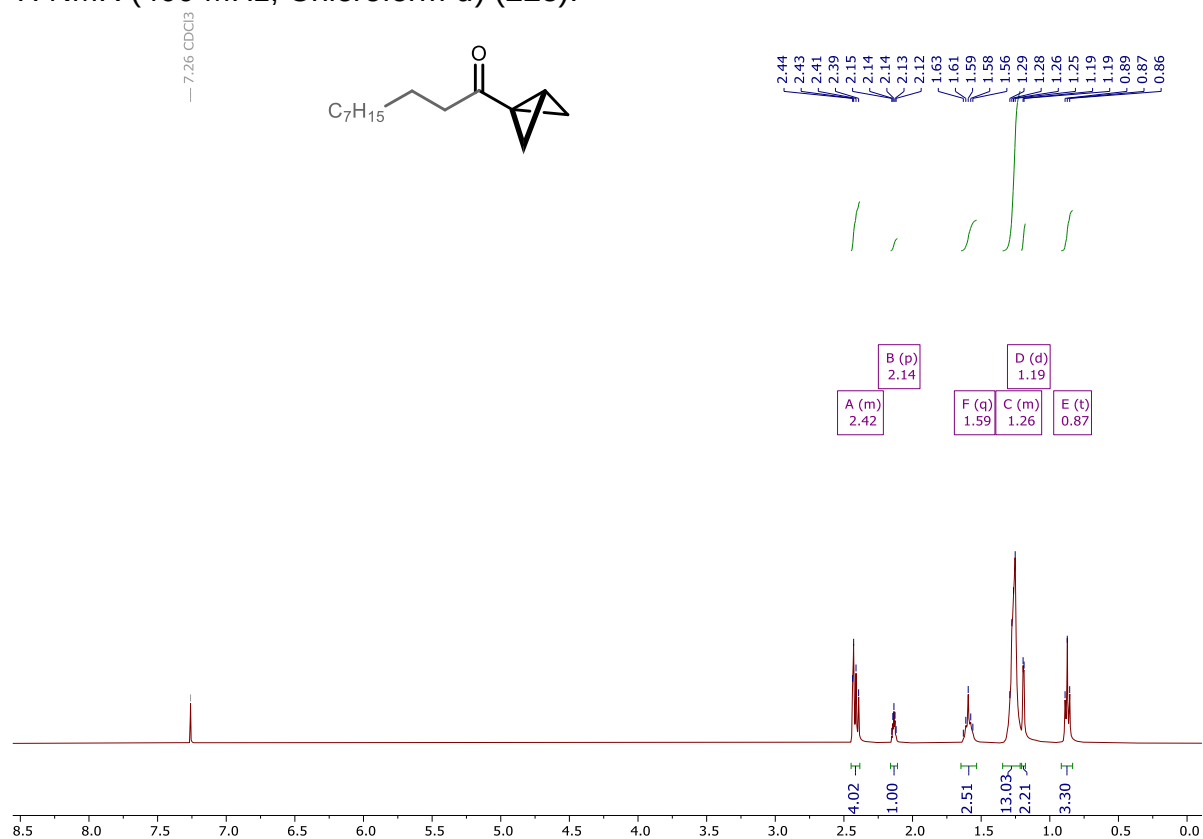
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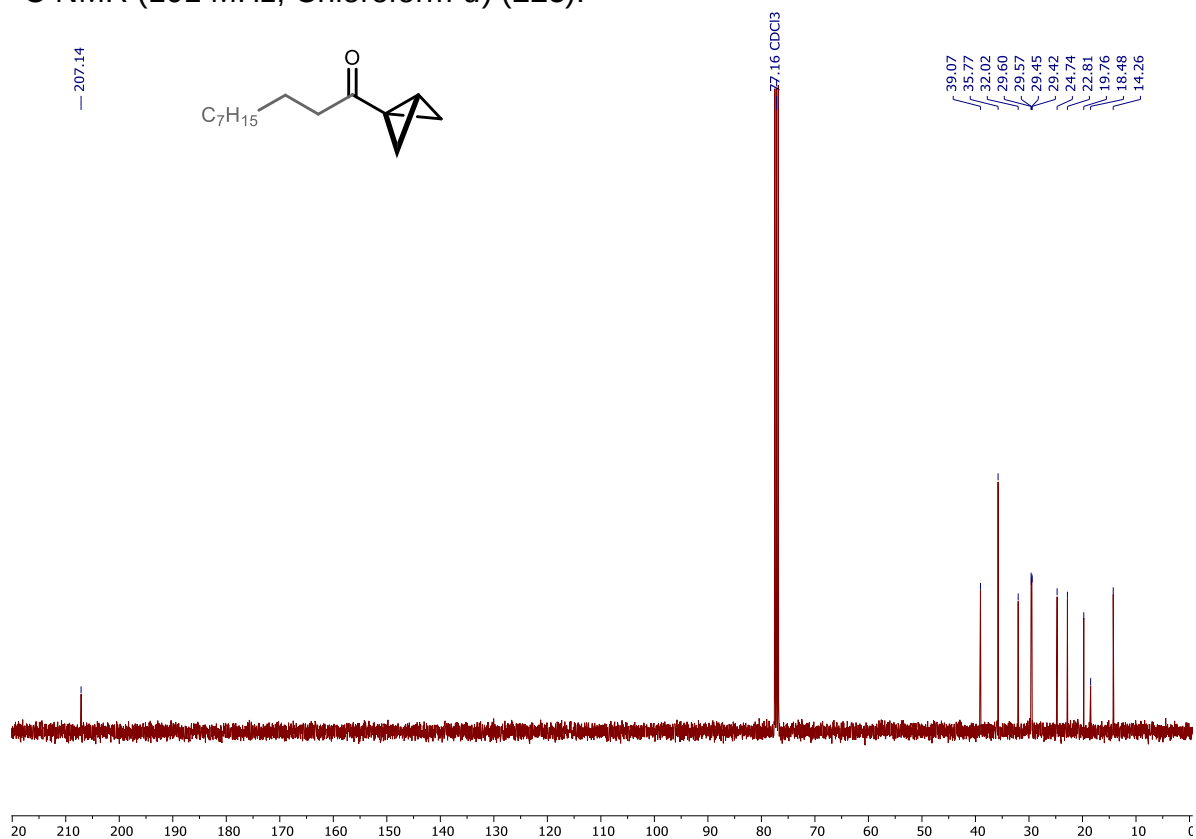
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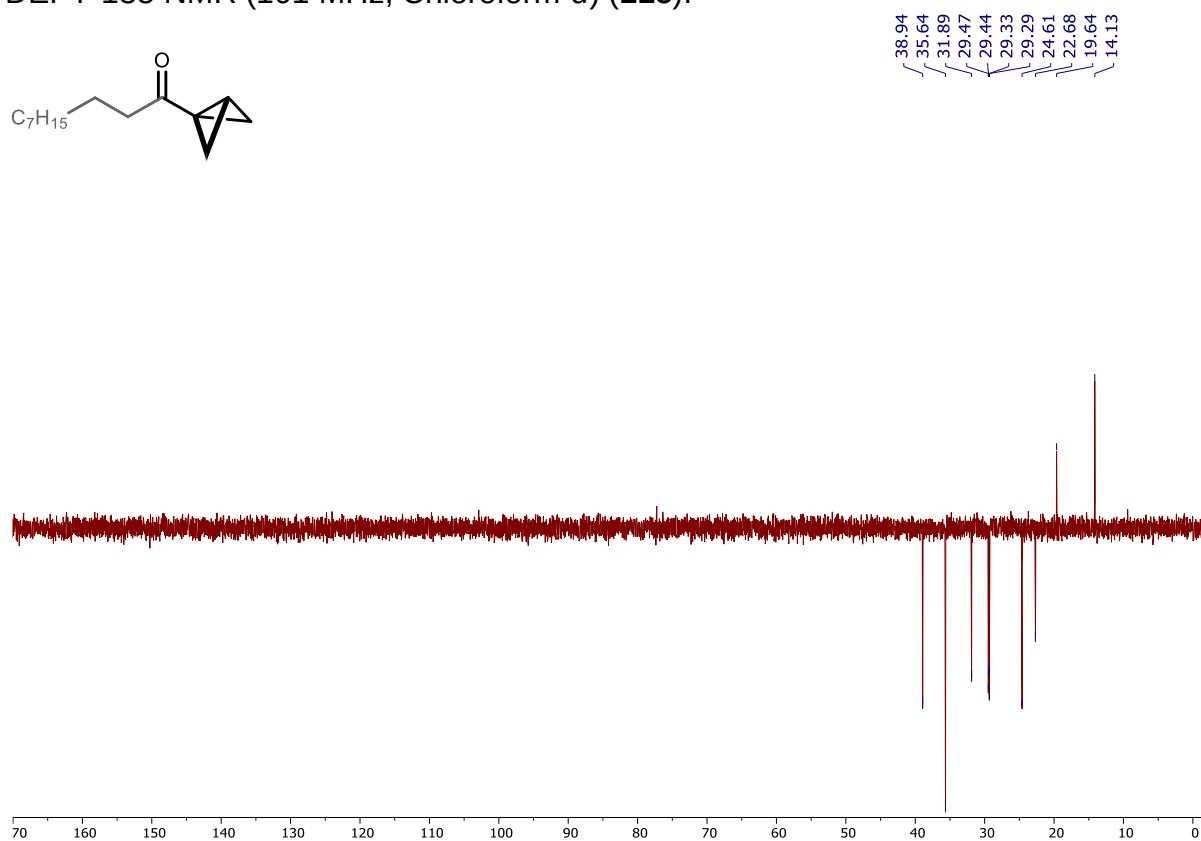
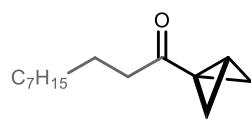
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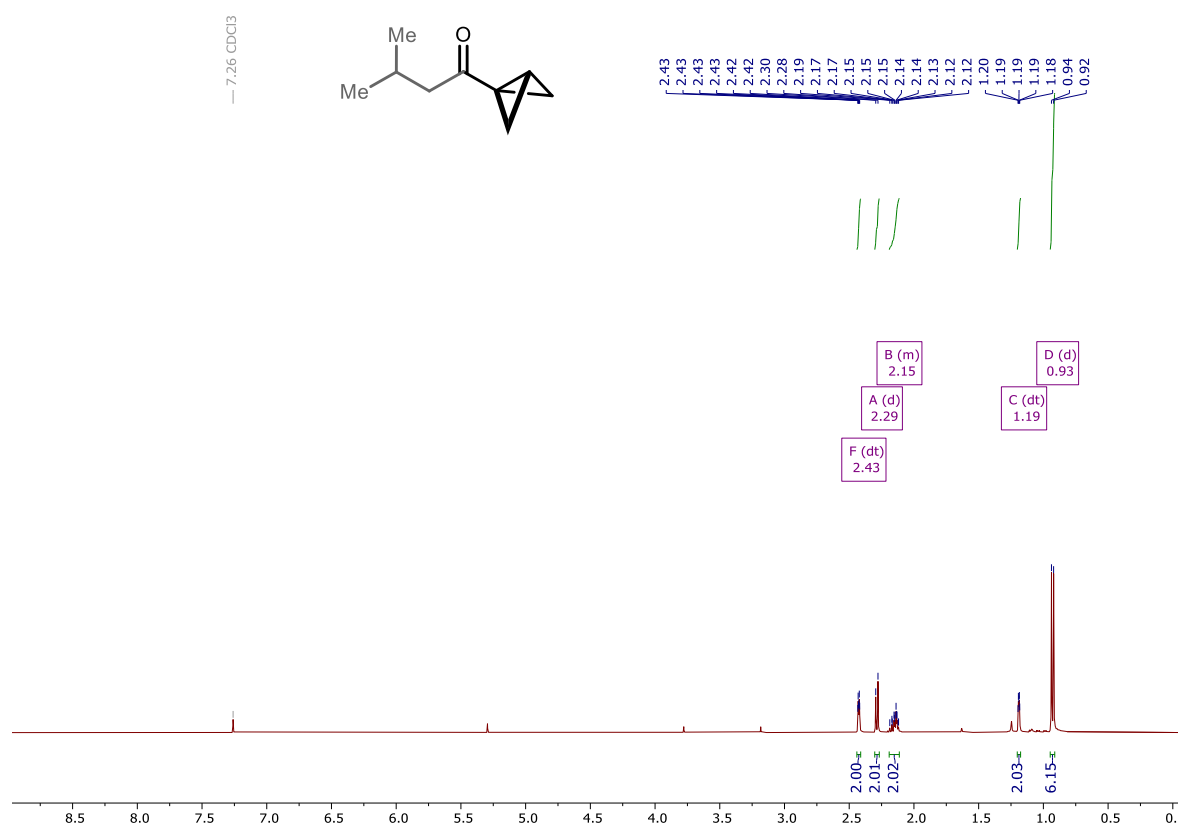
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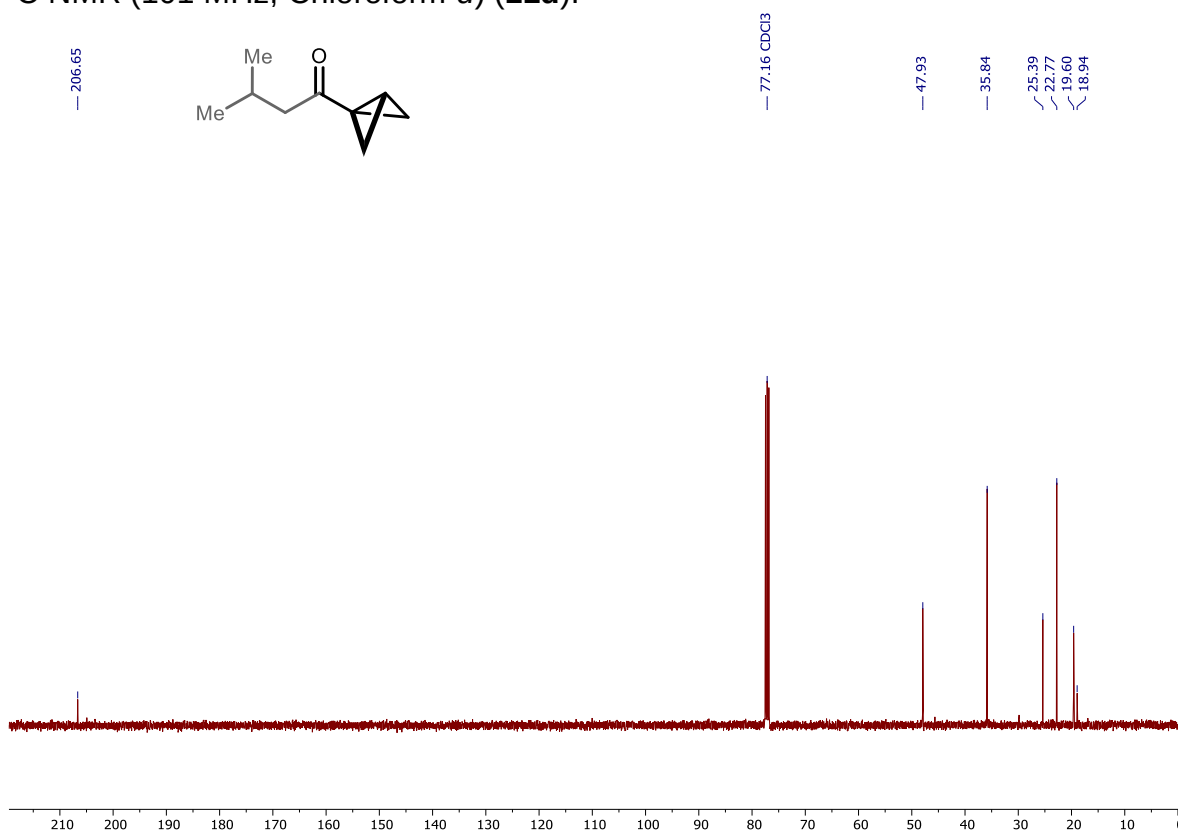
DEPT-135 NMR (101 MHz, Chloroform-*d*) (**11c**):



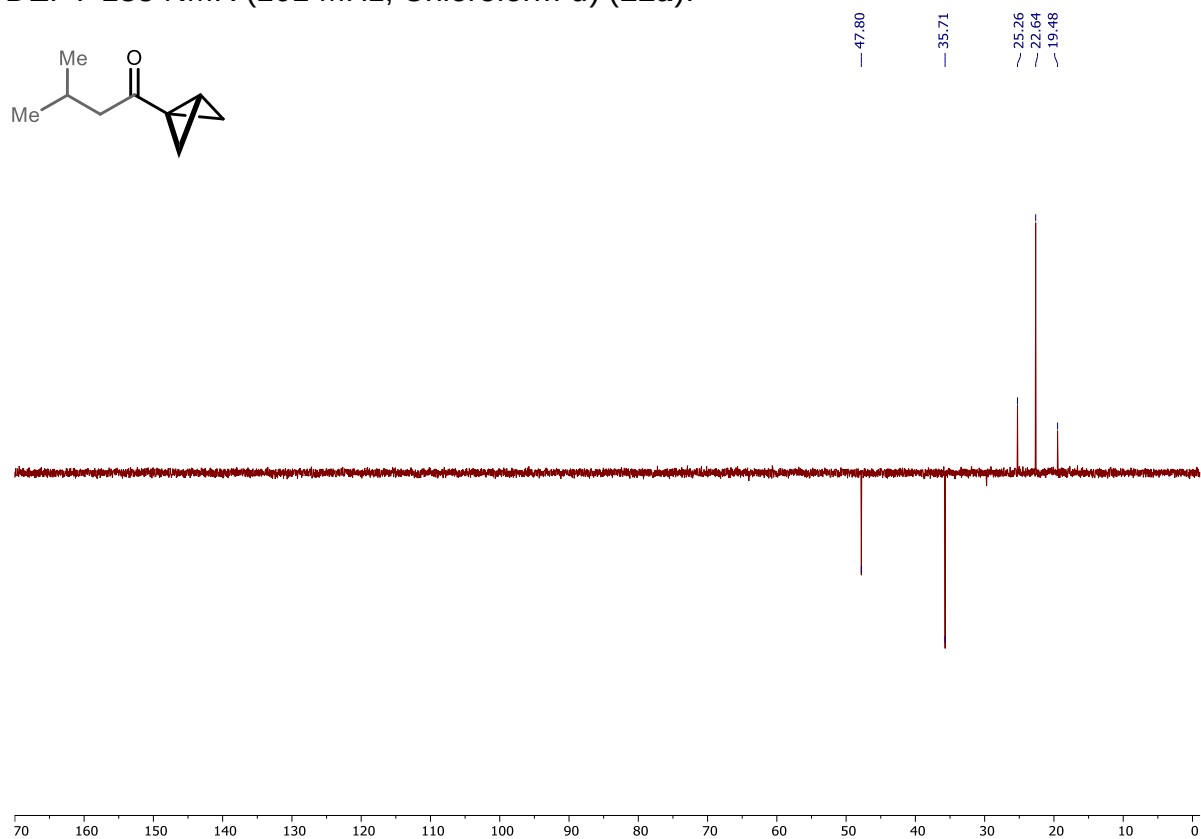
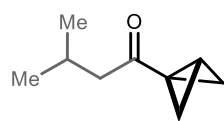
^1H NMR (400 MHz, Chloroform-*d*) (**11d**):



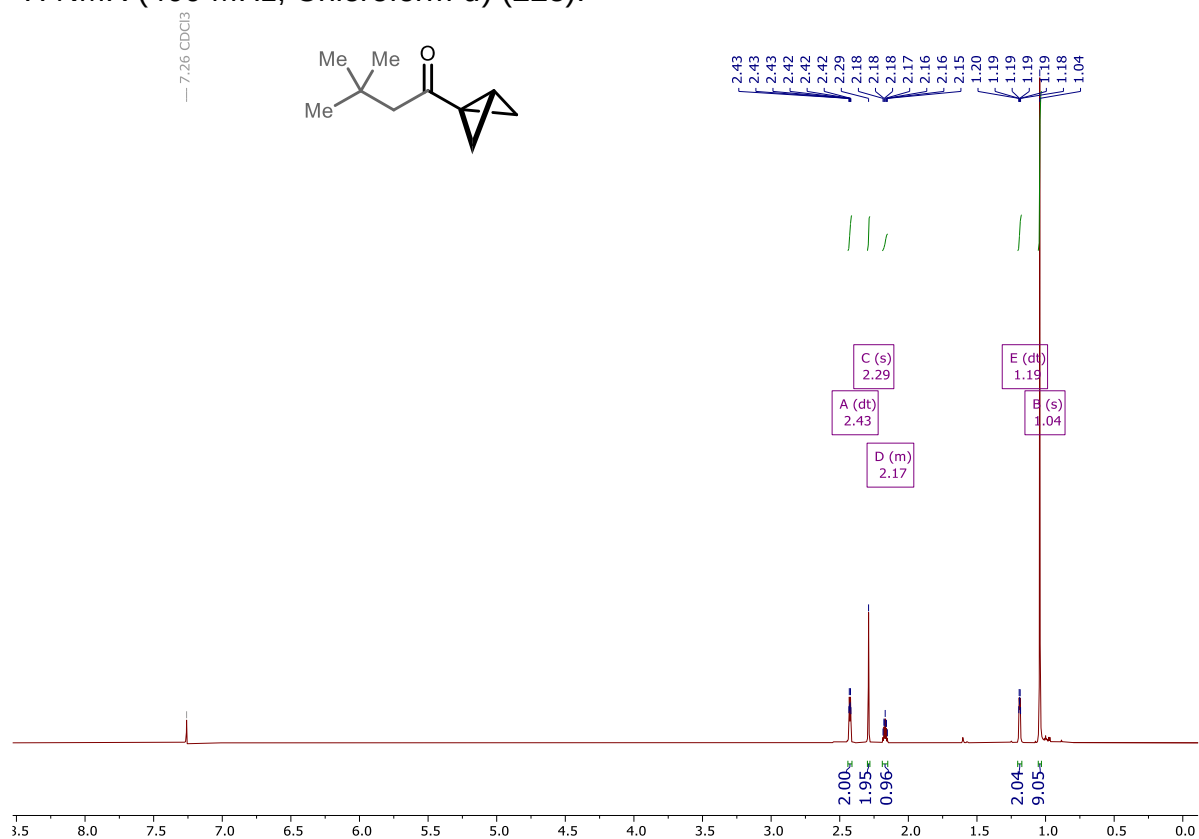
^{13}C NMR (101 MHz, Chloroform-*d*) (**11d**):



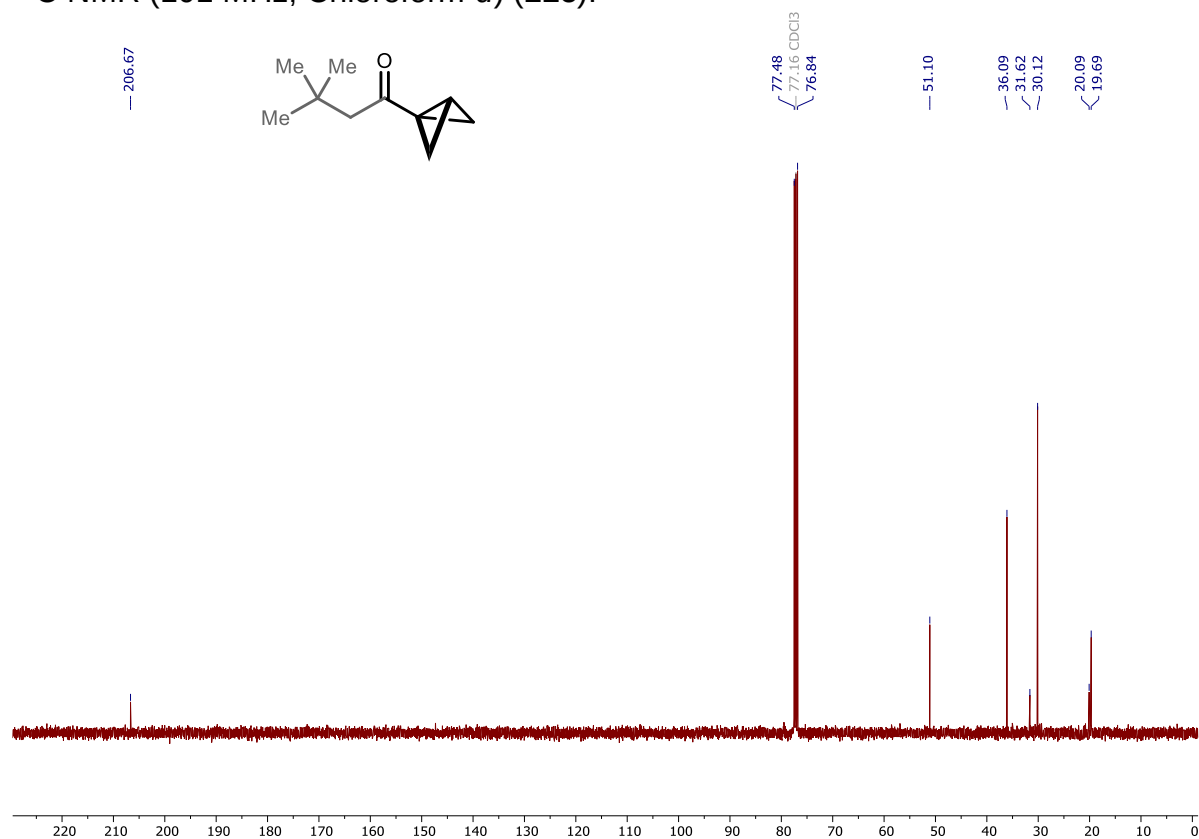
DEPT-135 NMR (101 MHz, Chloroform-*d*) (**11d**):



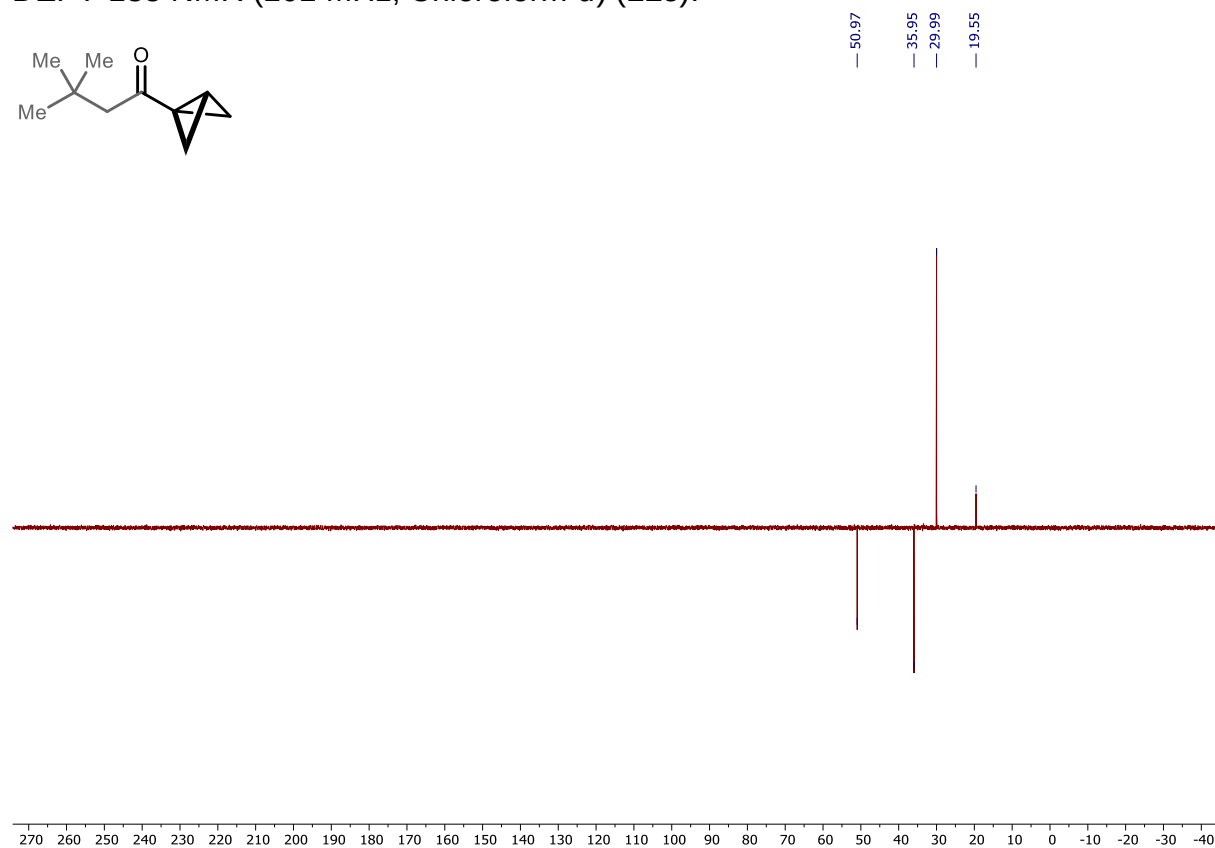
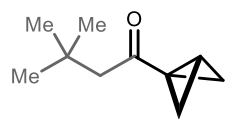
^1H NMR (400 MHz, Chloroform-*d*) (**11e**):



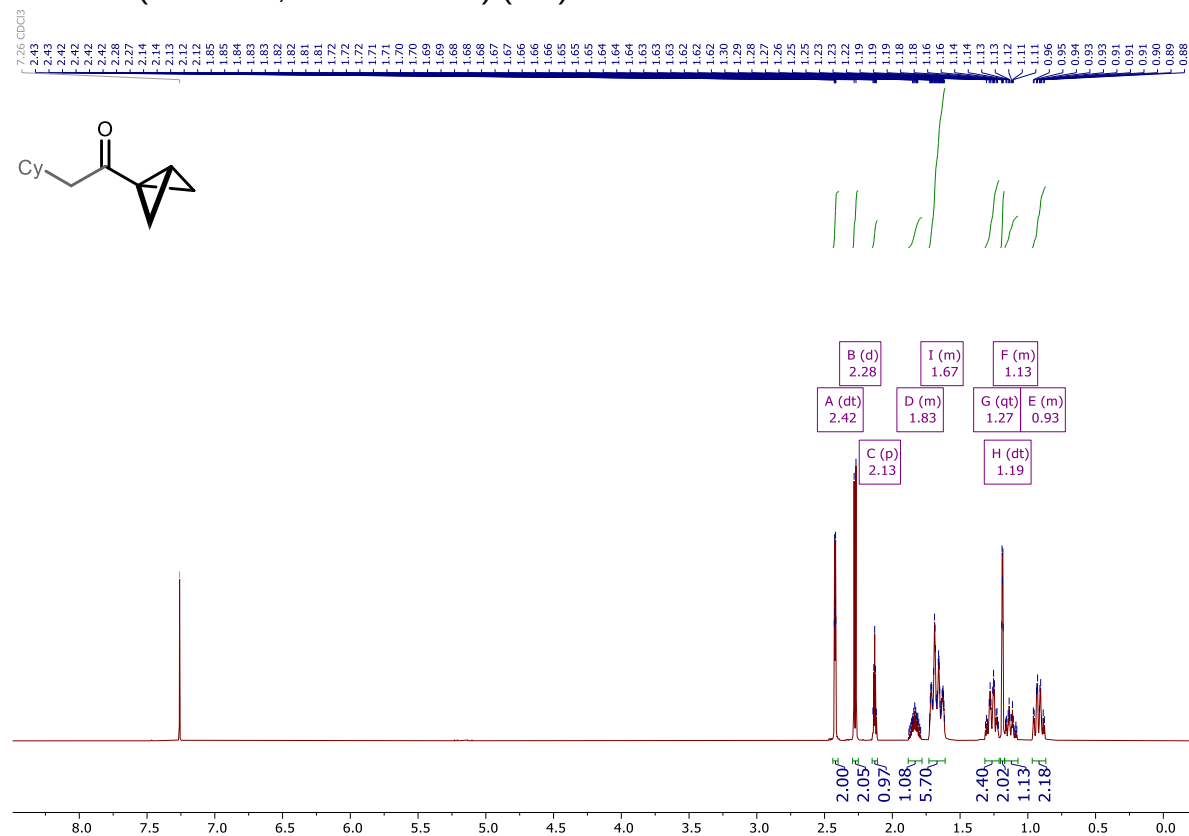
^{13}C NMR (101 MHz, Chloroform-*d*) (**11e**):



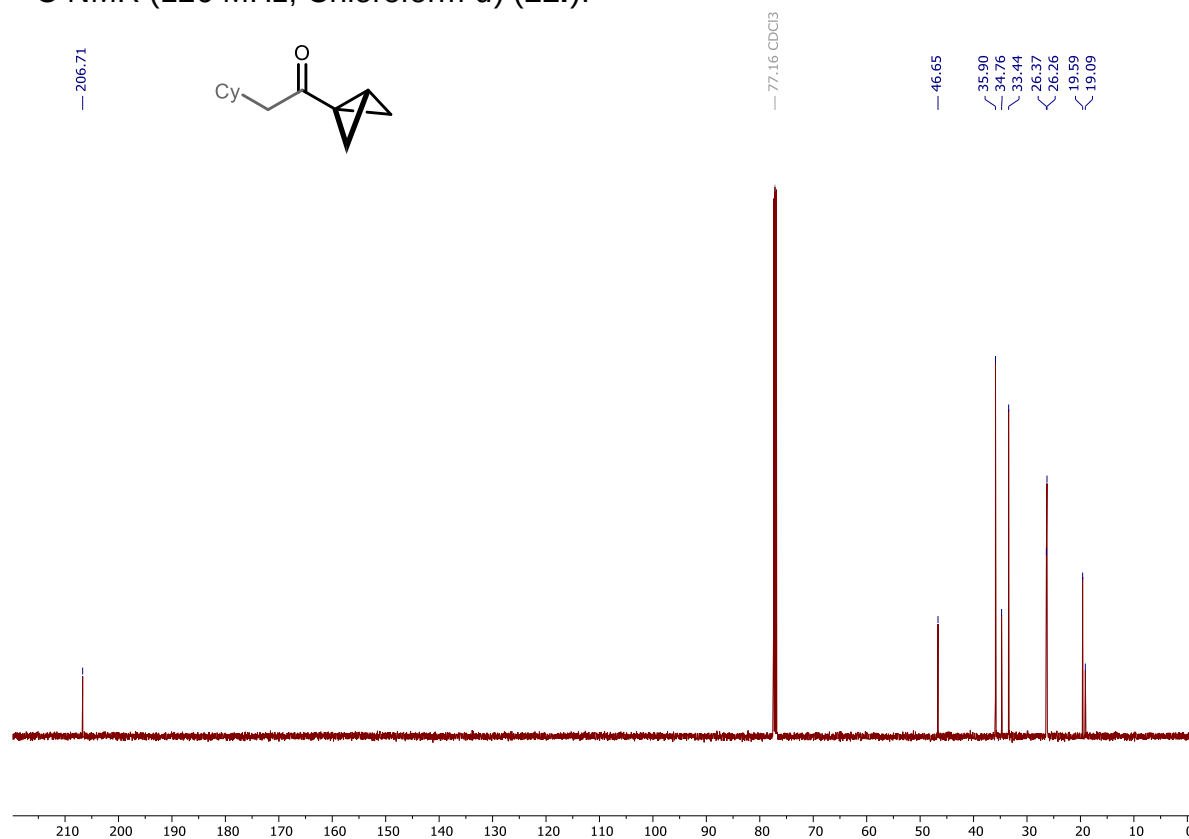
DEPT-135 NMR (101 MHz, Chloroform-*d*) (**11e**):



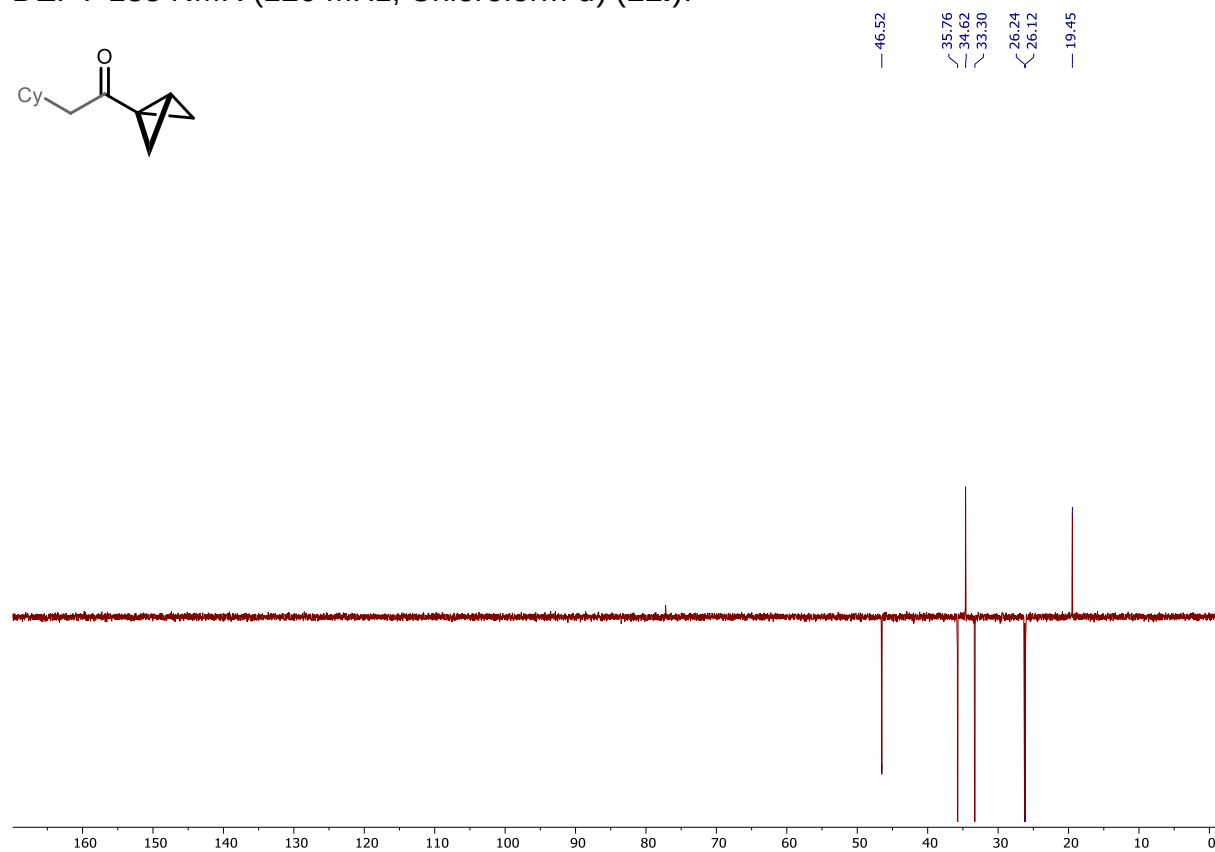
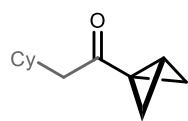
¹H NMR (500 MHz, Chloroform-*d*) (**11f**):



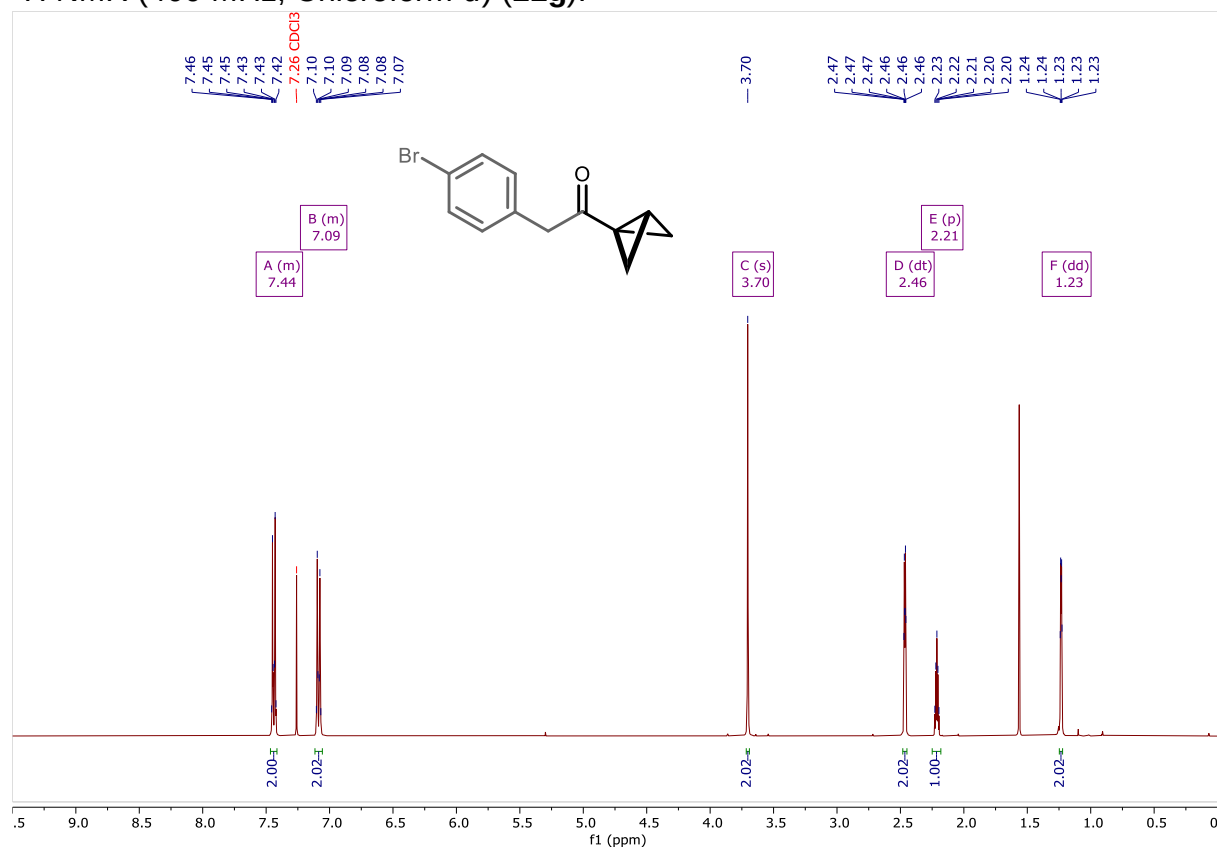
¹³C NMR (126 MHz, Chloroform-*d*) (**11f**):



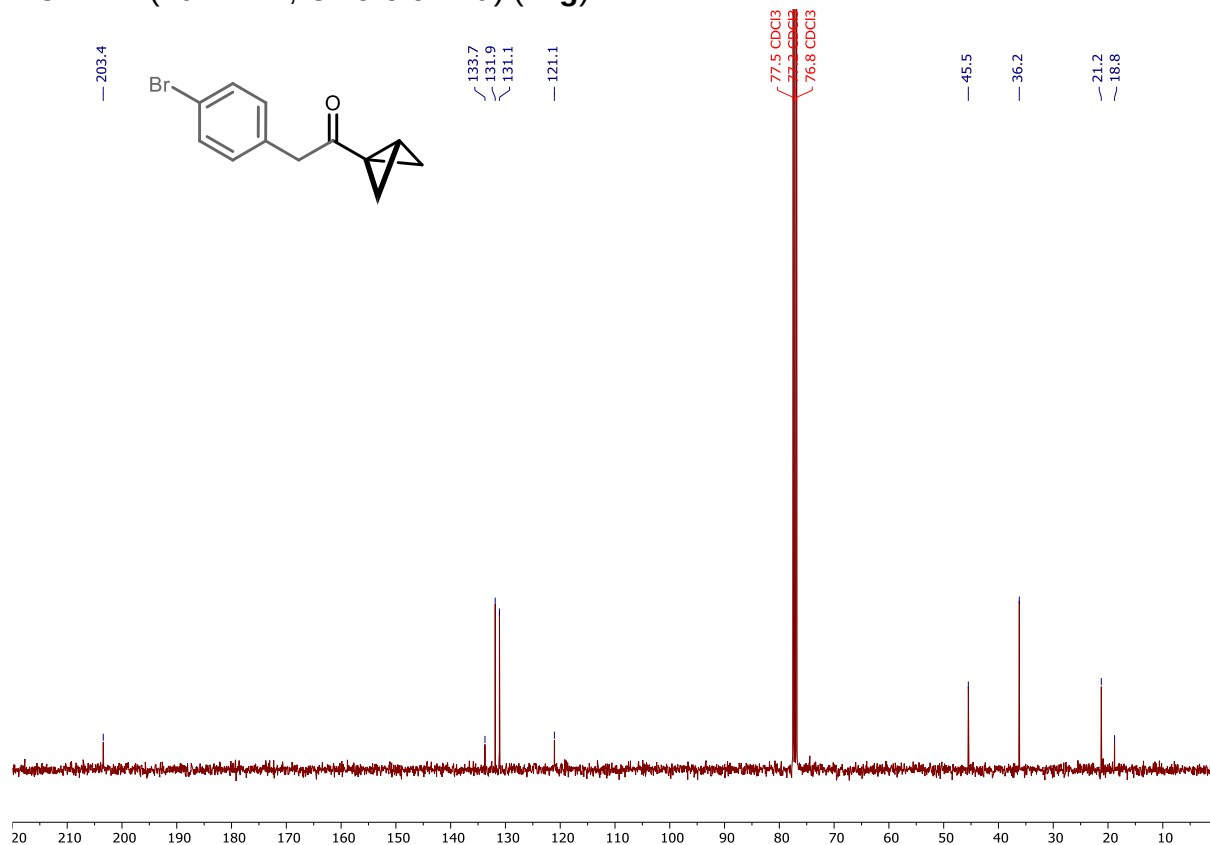
DEPT-135 NMR (126 MHz, Chloroform-*d*) (**11f**):



^1H NMR (400 MHz, Chloroform-*d*) (**11g**):



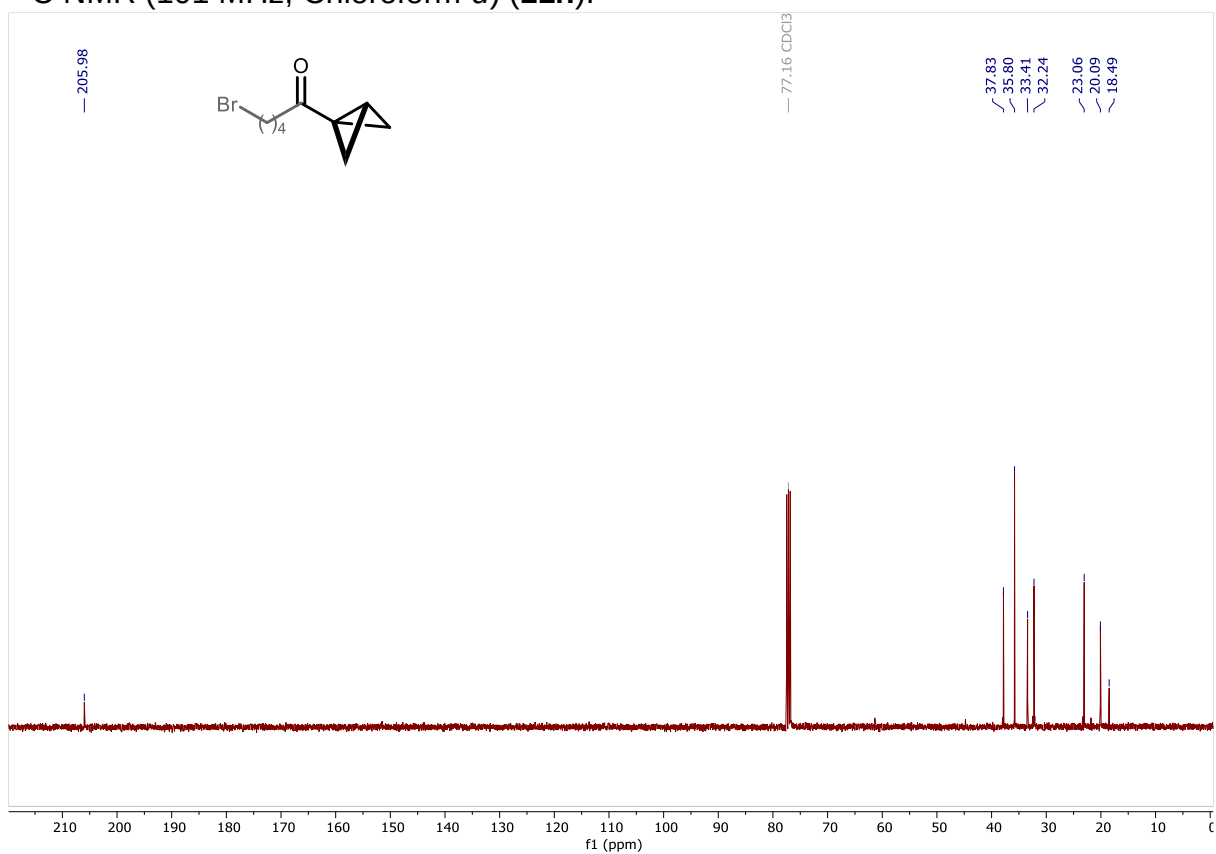
^{13}C NMR (101 MHz, Chloroform-*d*) (**11g**):



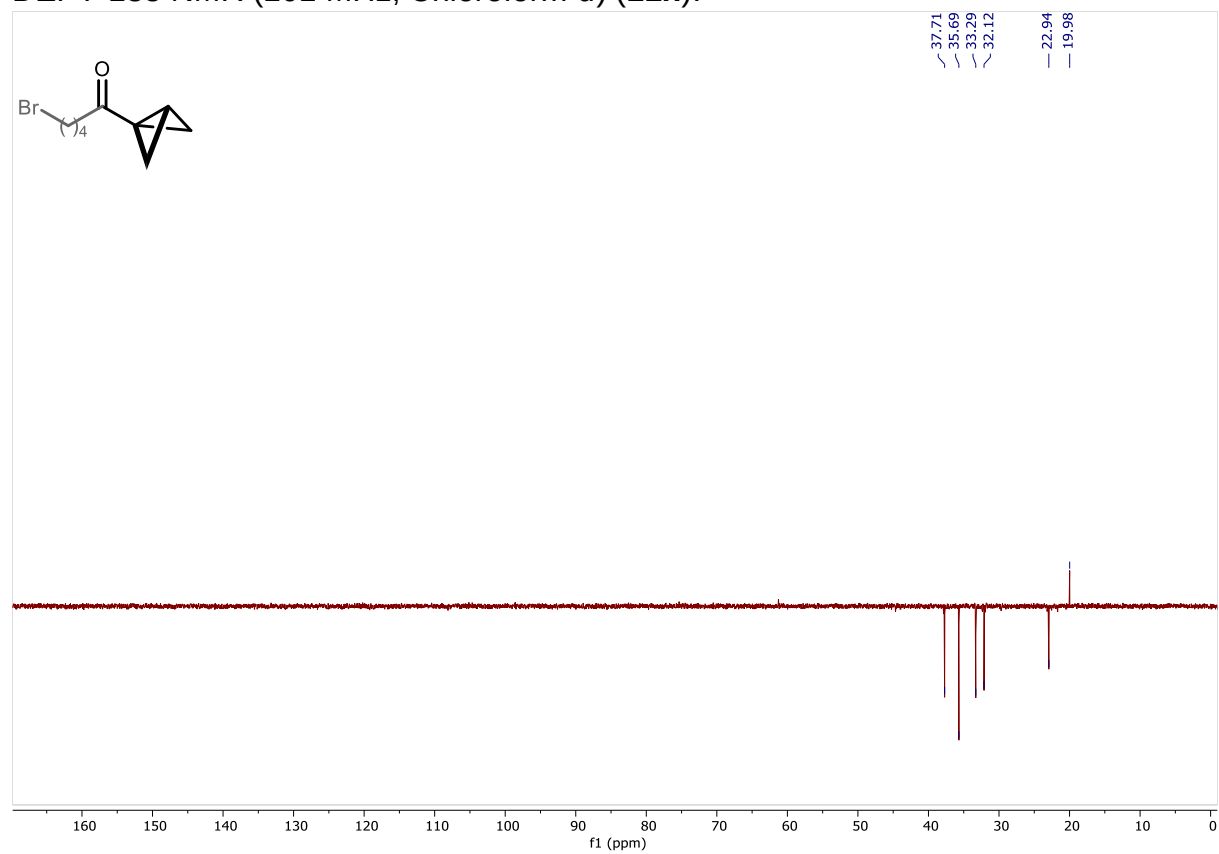
^1H NMR (400 MHz, Chloroform-*d*) (**11h**):



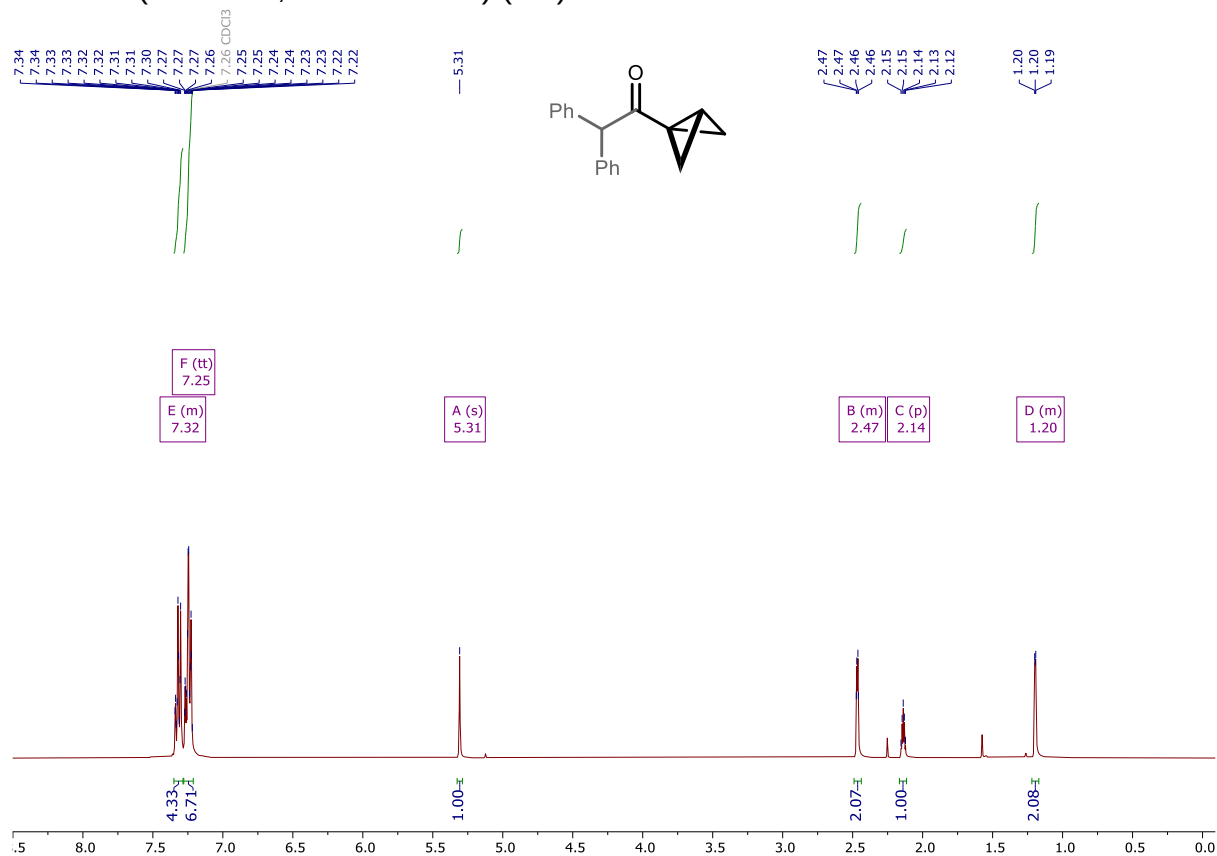
^{13}C NMR (101 MHz, Chloroform-*d*) (**11h**):



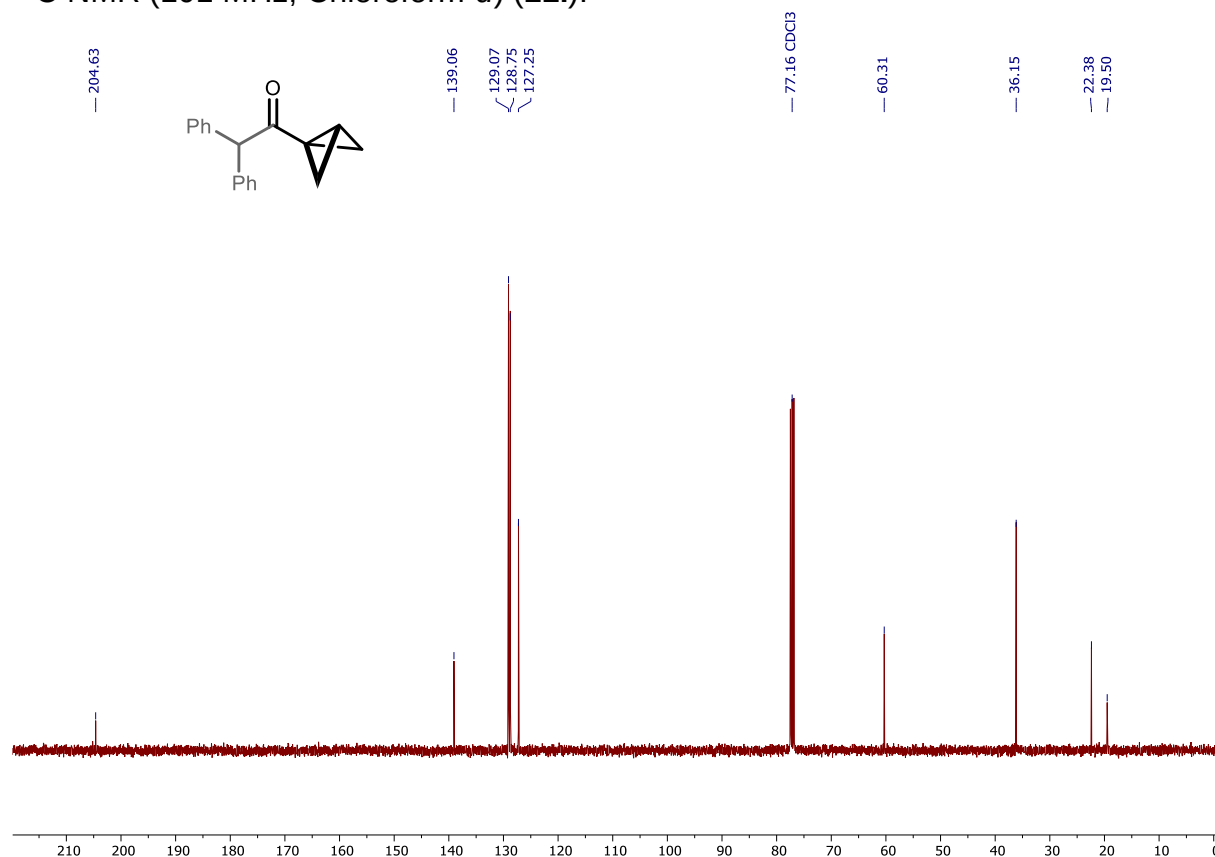
DEPT-135 NMR (101 MHz, Chloroform-*d*) (**11h**):



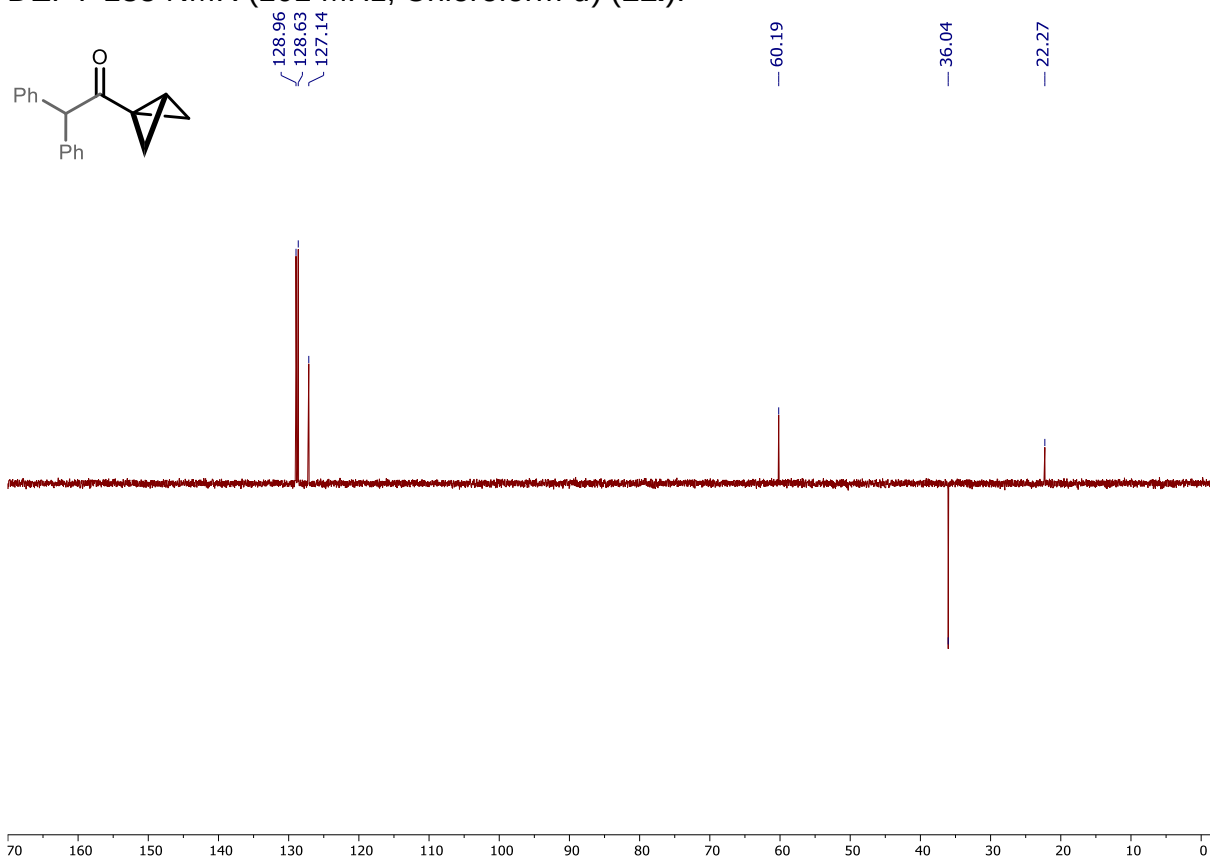
¹H NMR (400 MHz, Chloroform-*d*) (**11i**):



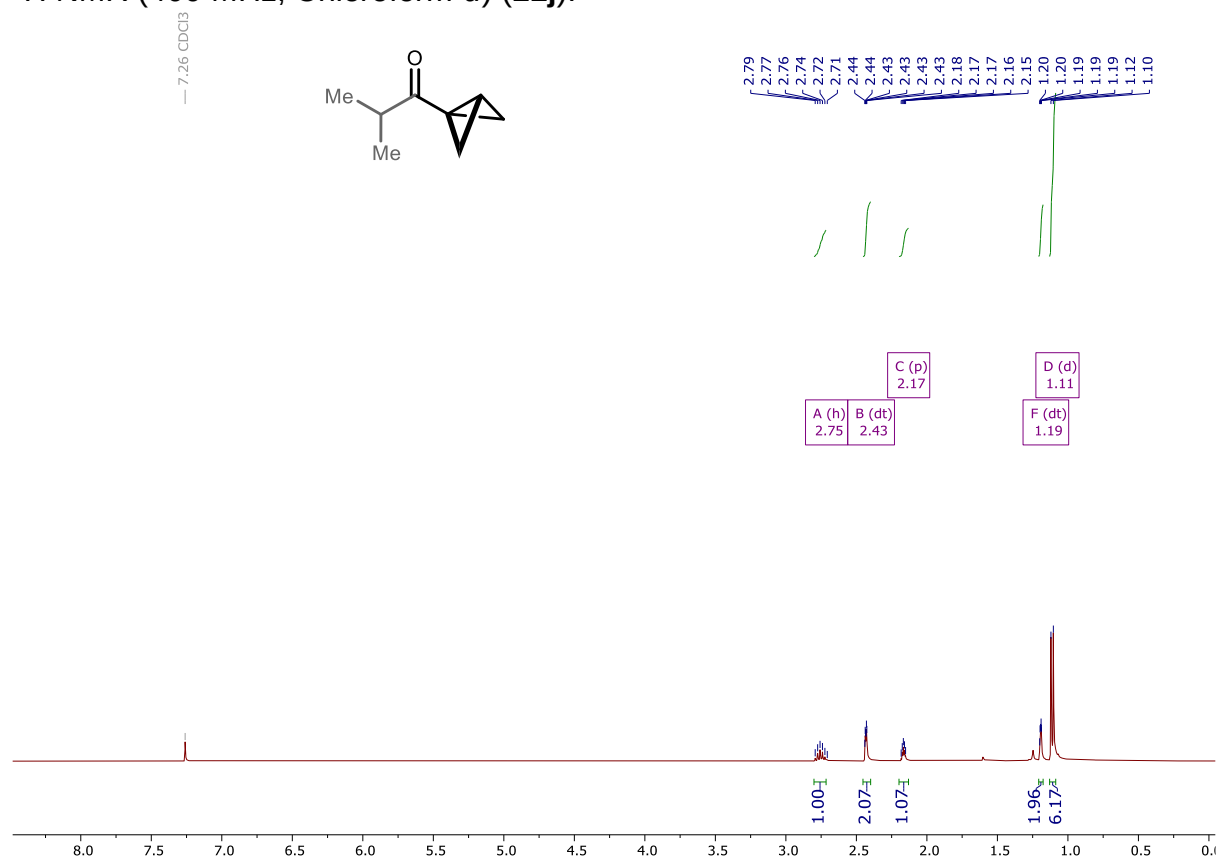
¹³C NMR (101 MHz, Chloroform-*d*) (**11i**):



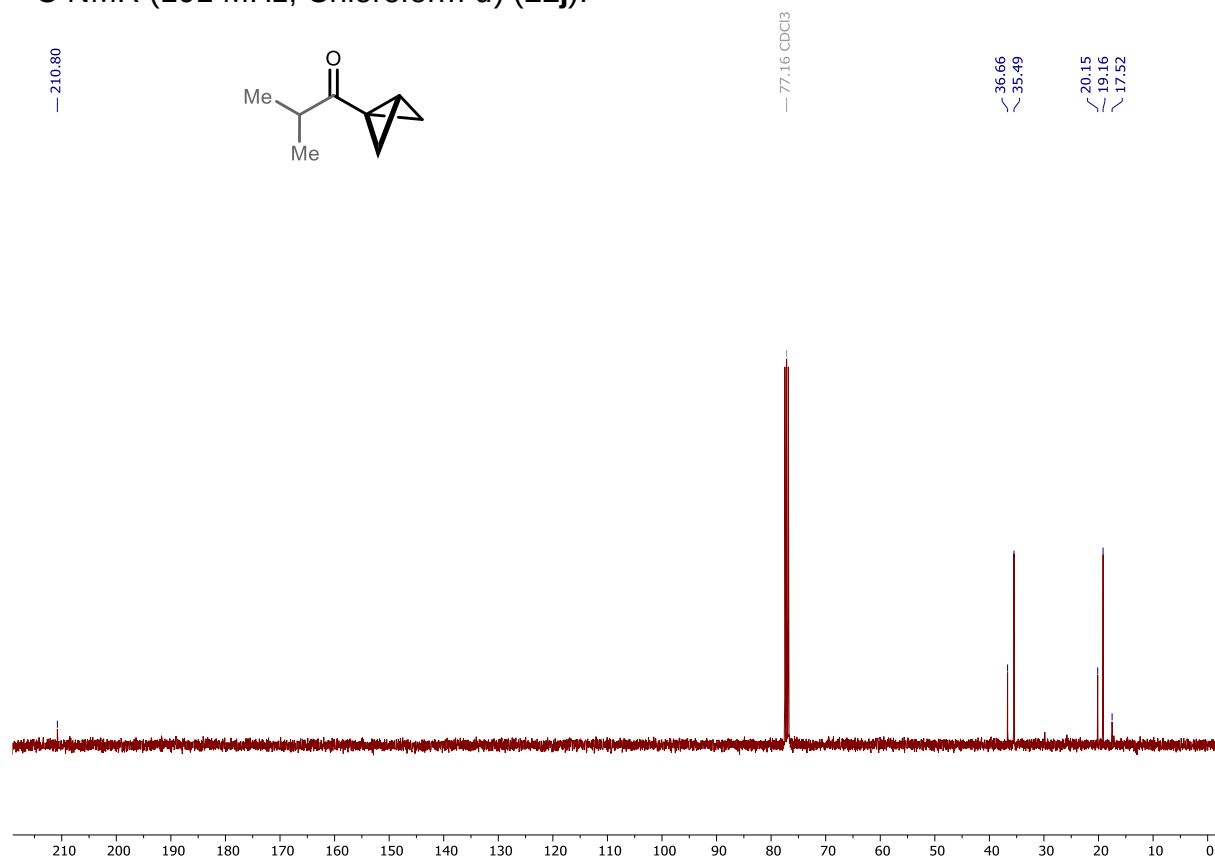
DEPT-135 NMR (101 MHz, Chloroform-*d*) (**11i**):



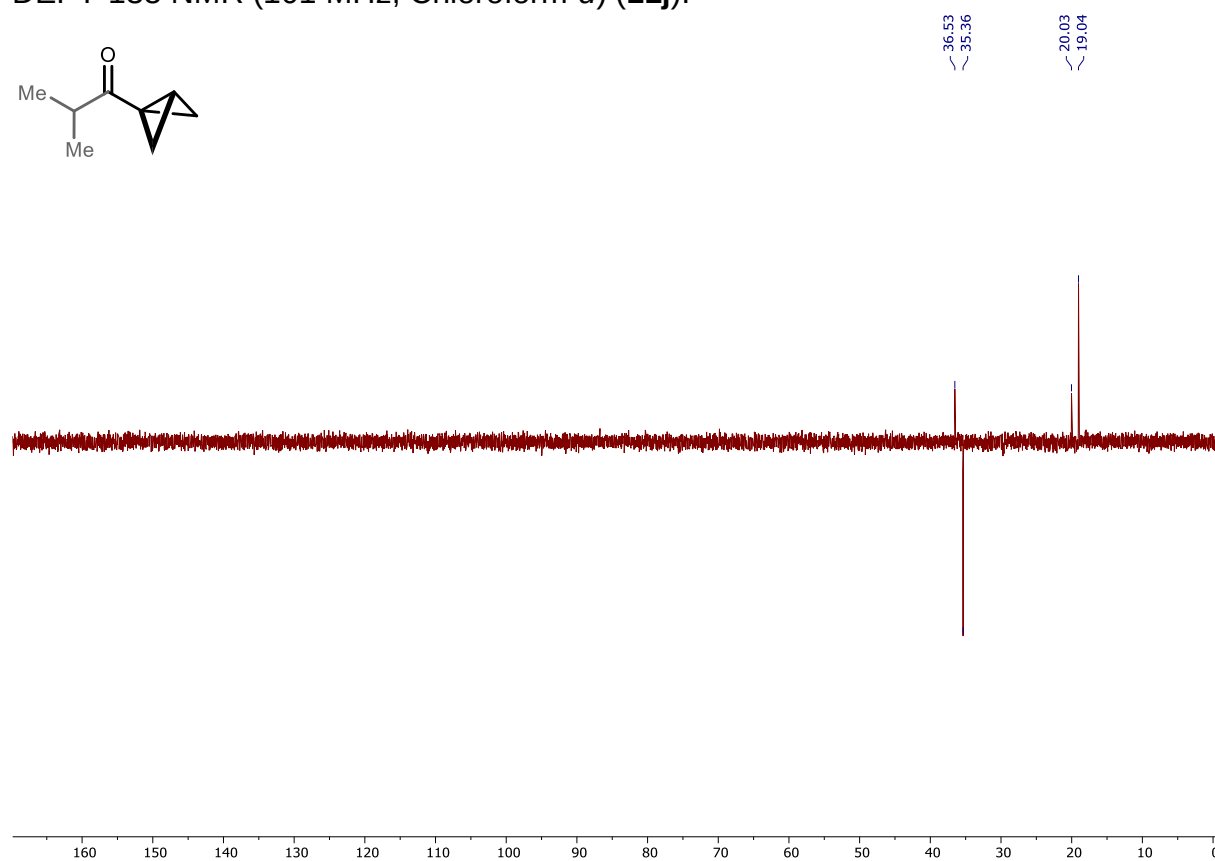
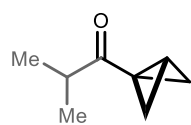
^1H NMR (400 MHz, Chloroform-*d*) (**11j**):



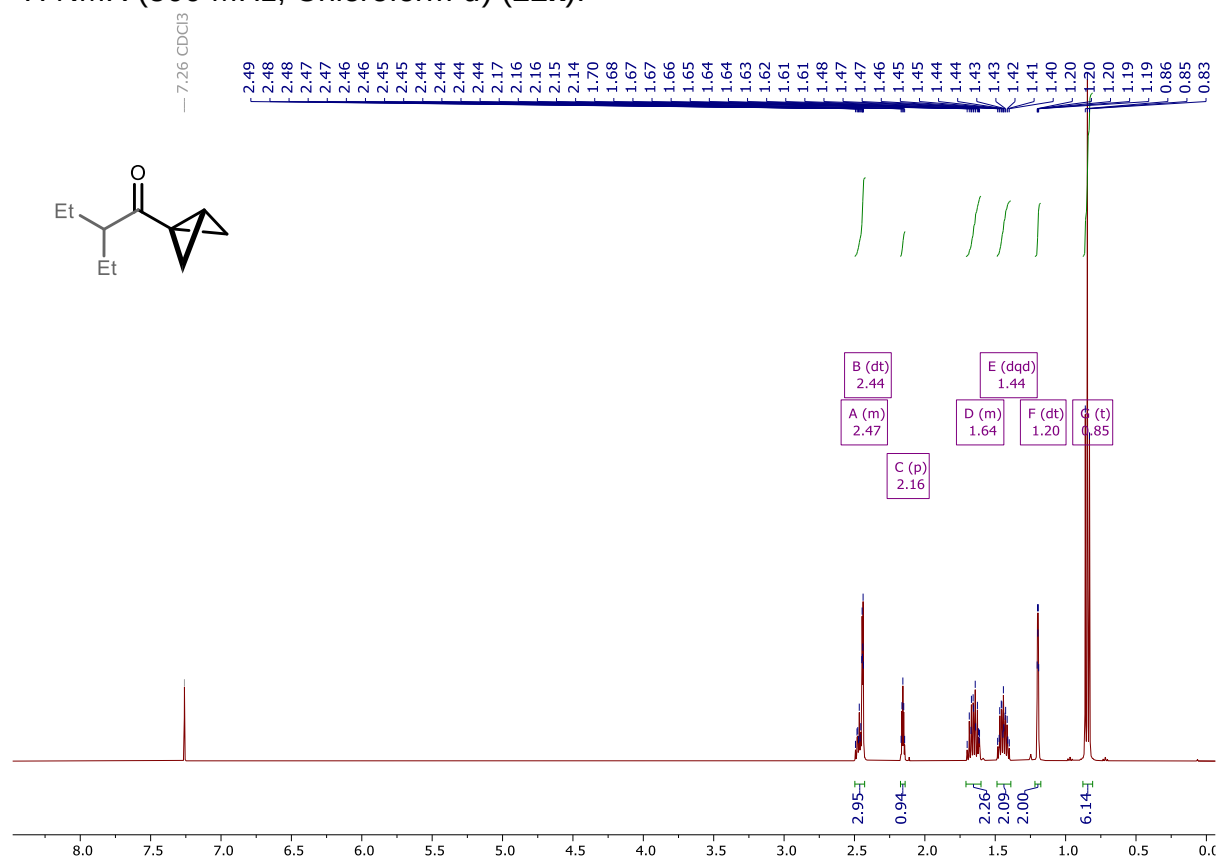
^{13}C NMR (101 MHz, Chloroform-*d*) (**11j**):



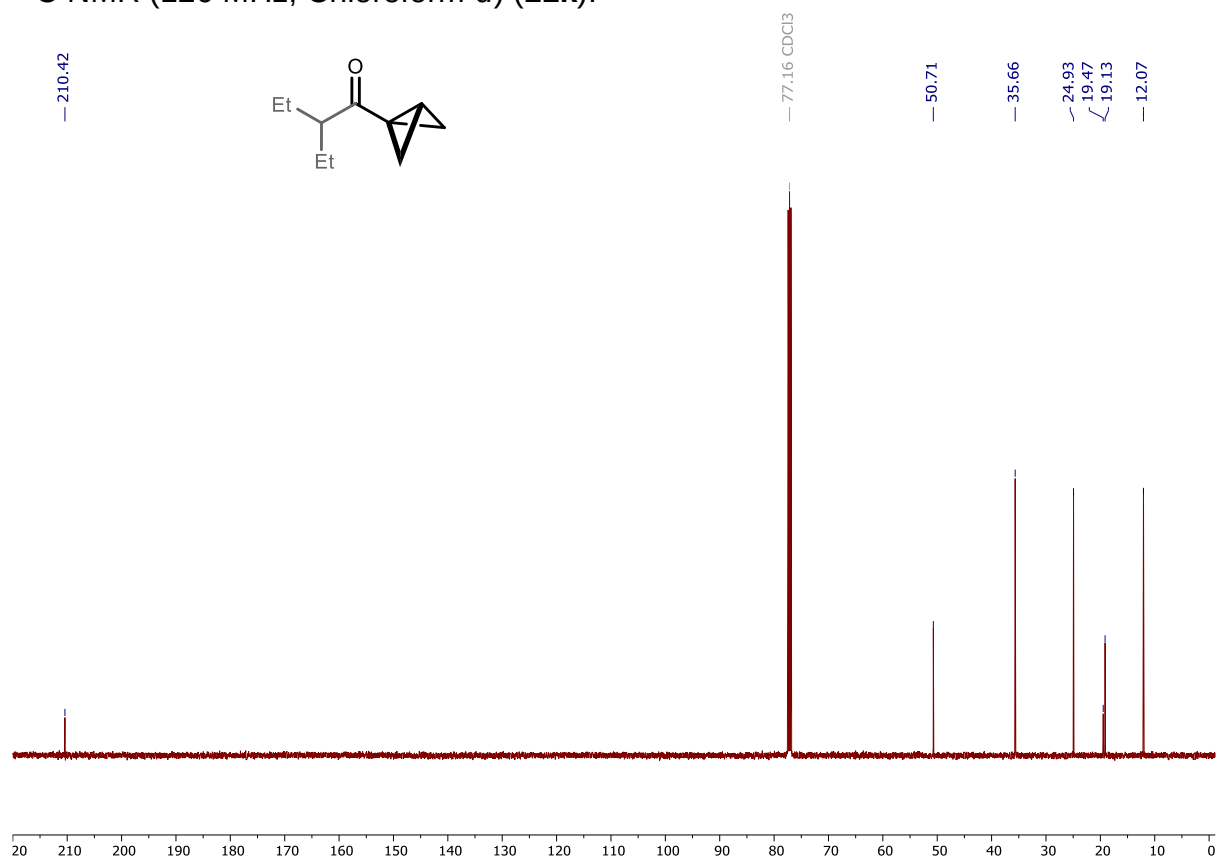
DEPT-135 NMR (101 MHz, Chloroform-*d*) (**11j**):



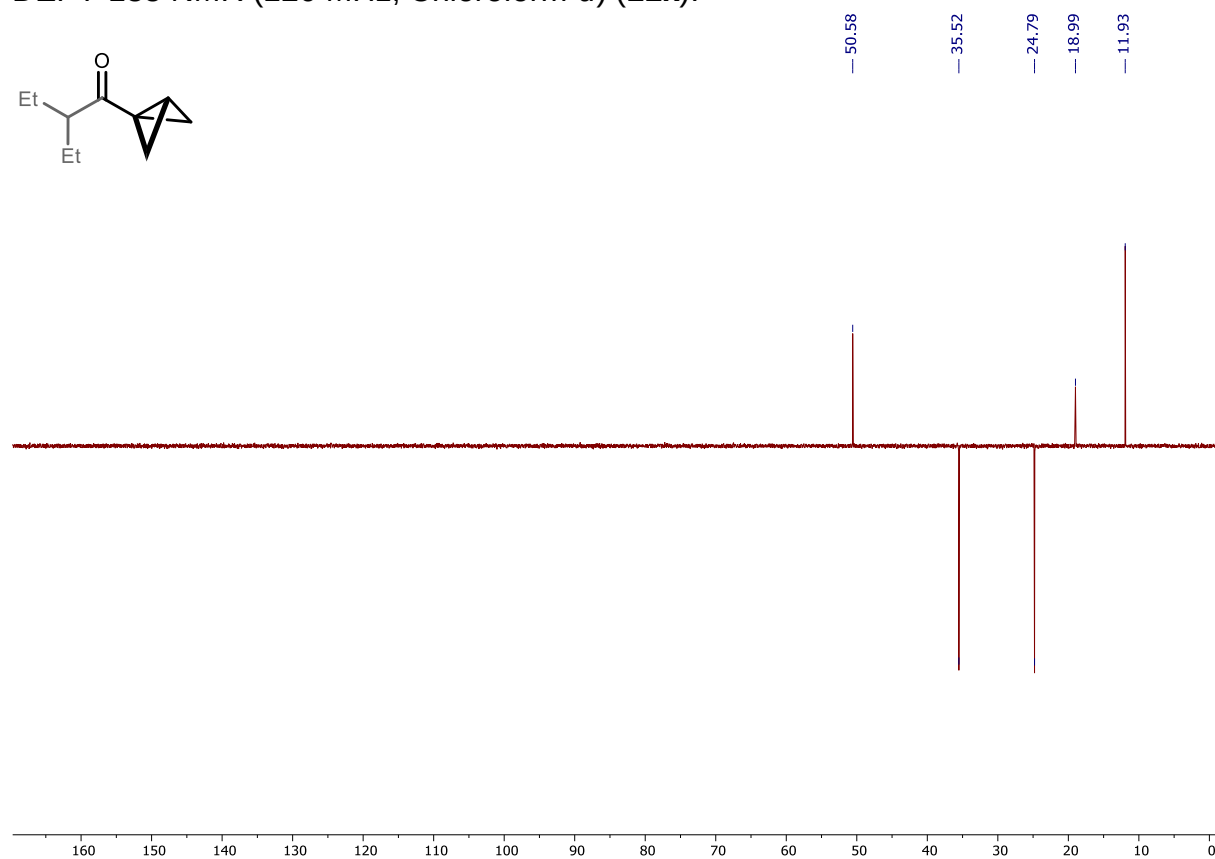
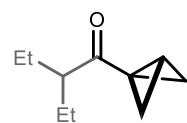
^1H NMR (500 MHz, Chloroform-*d*) (**11k**):



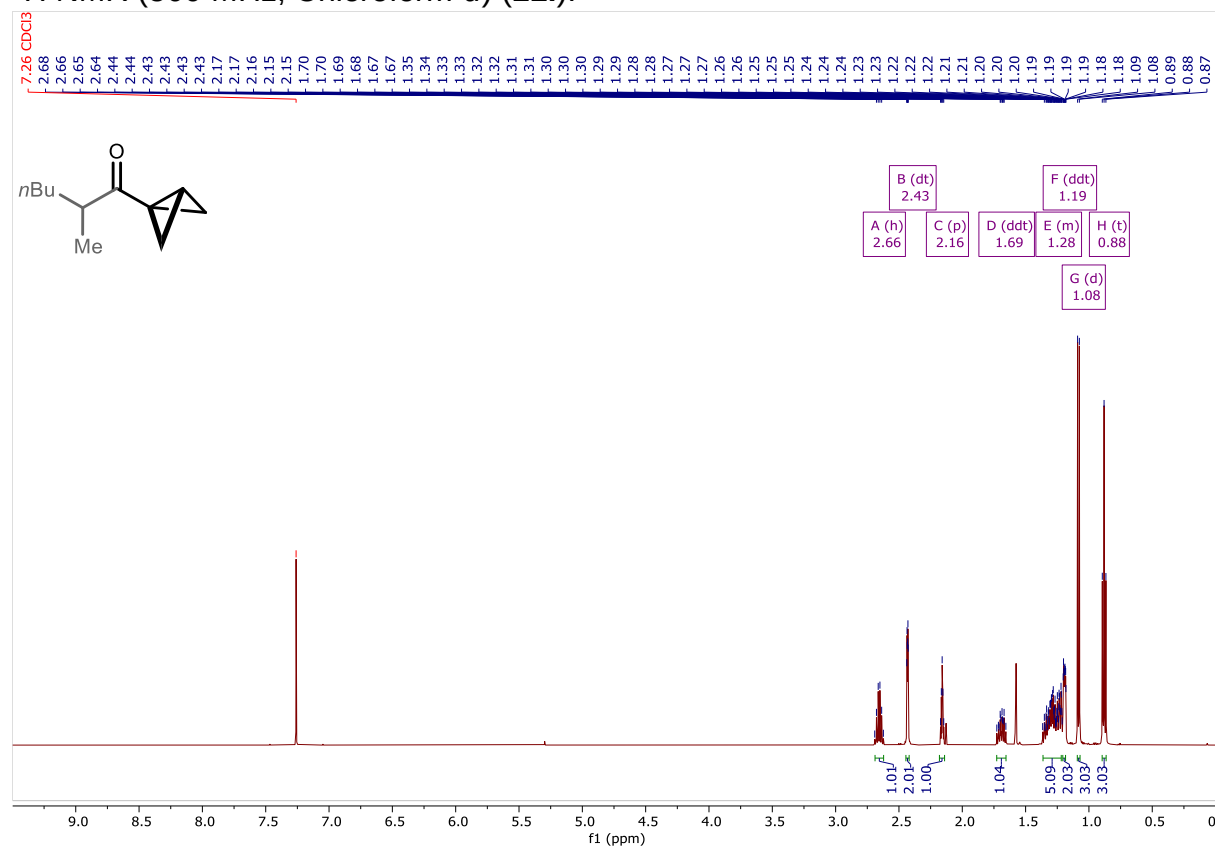
^{13}C NMR (126 MHz, Chloroform-*d*) (**11k**):



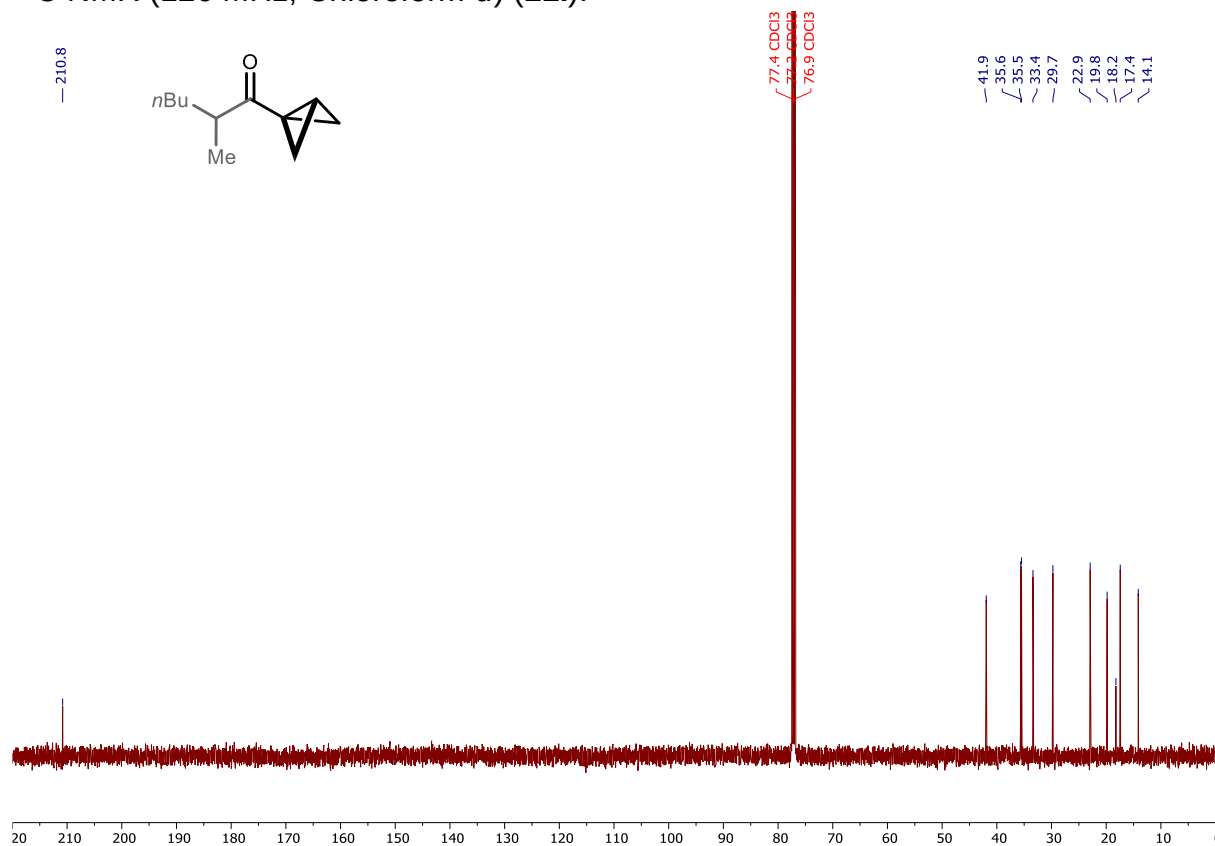
DEPT-135 NMR (126 MHz, Chloroform-*d*) (**11k**):



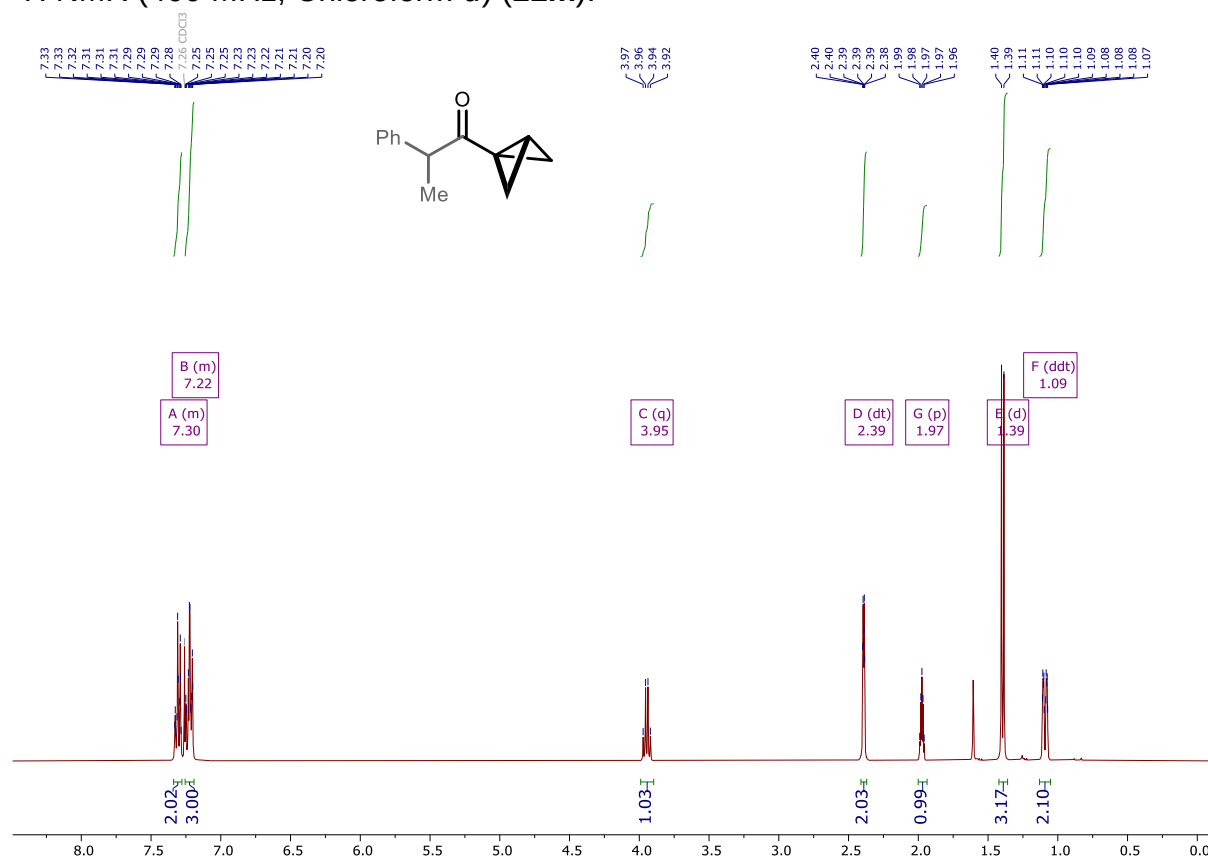
¹H NMR (500 MHz, Chloroform-*d*) (**11I**):



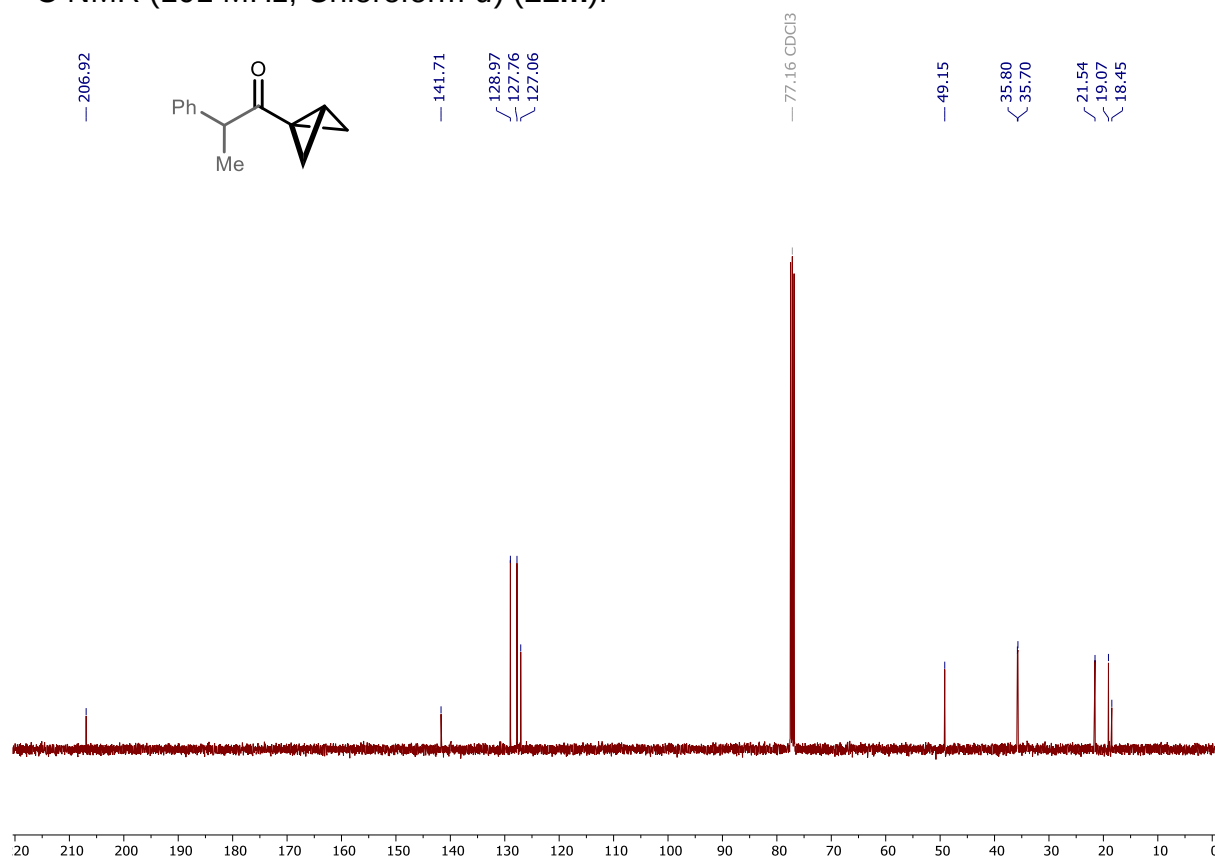
¹³C NMR (126 MHz, Chloroform-*d*) (**11I**):



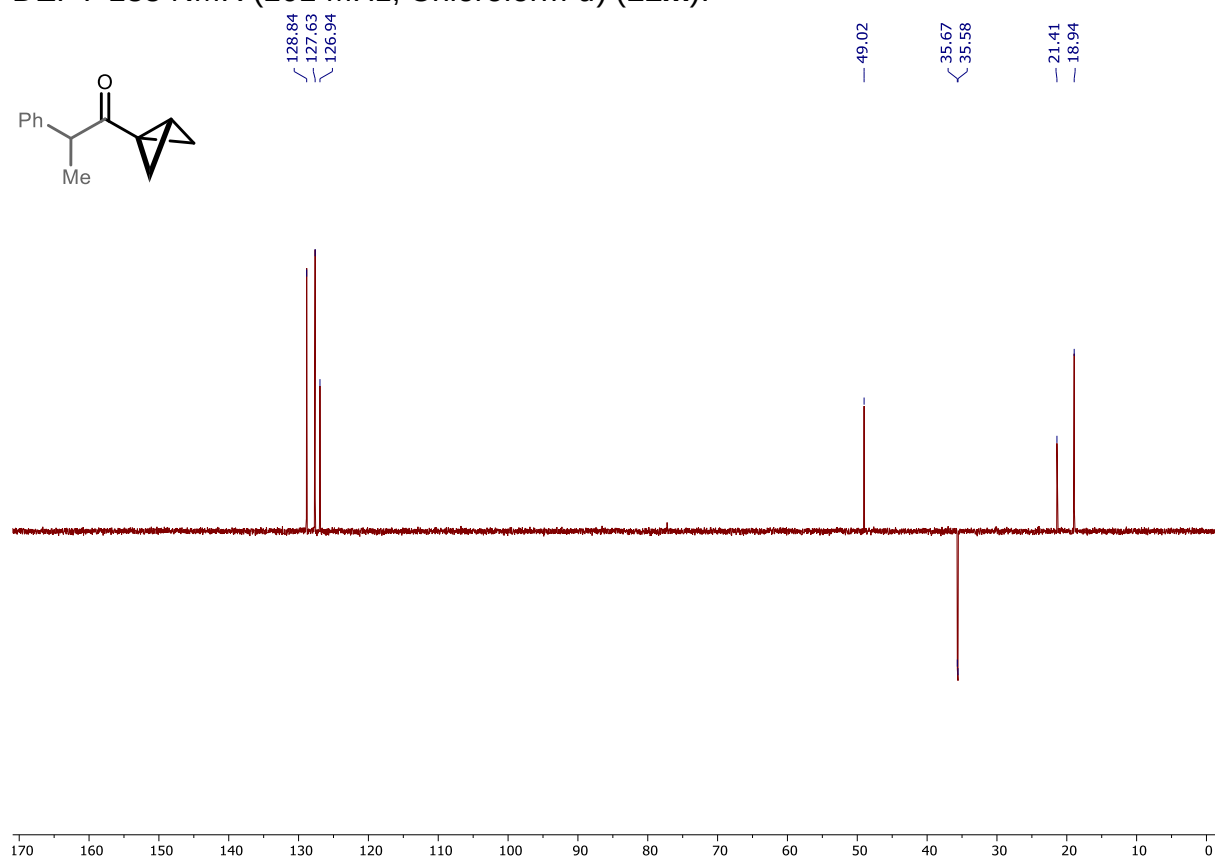
¹H NMR (400 MHz, Chloroform-*d*) (**11m**):



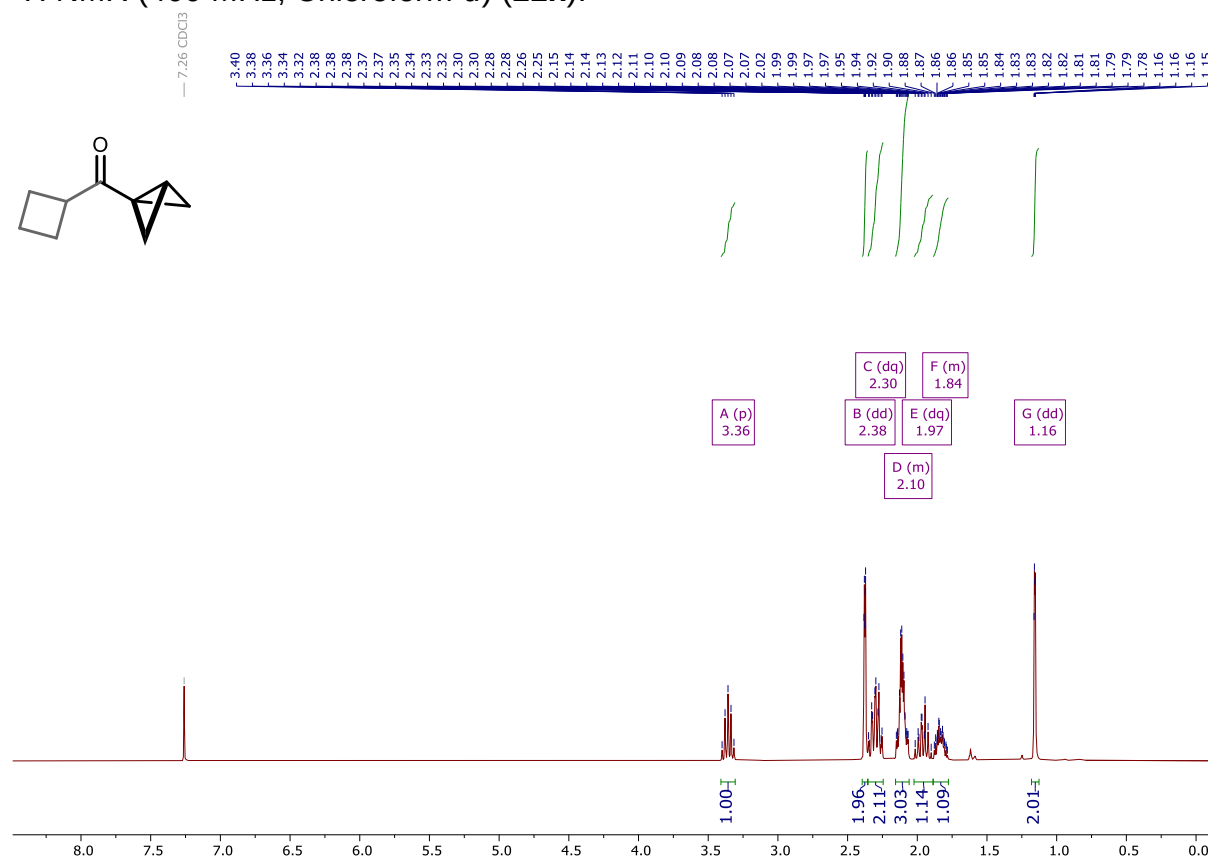
¹³C NMR (101 MHz, Chloroform-*d*) (**11m**):



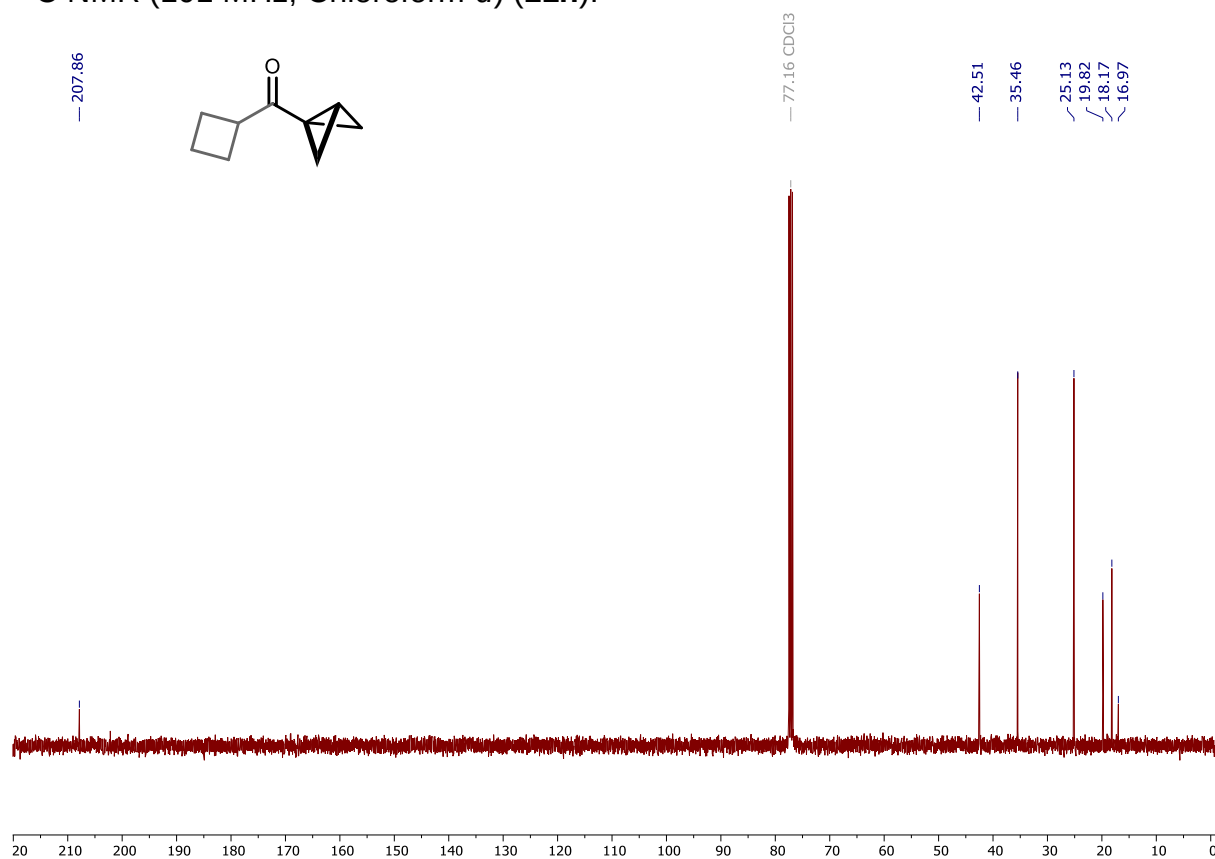
DEPT-135 NMR (101 MHz, Chloroform-*d*) (**11m**):



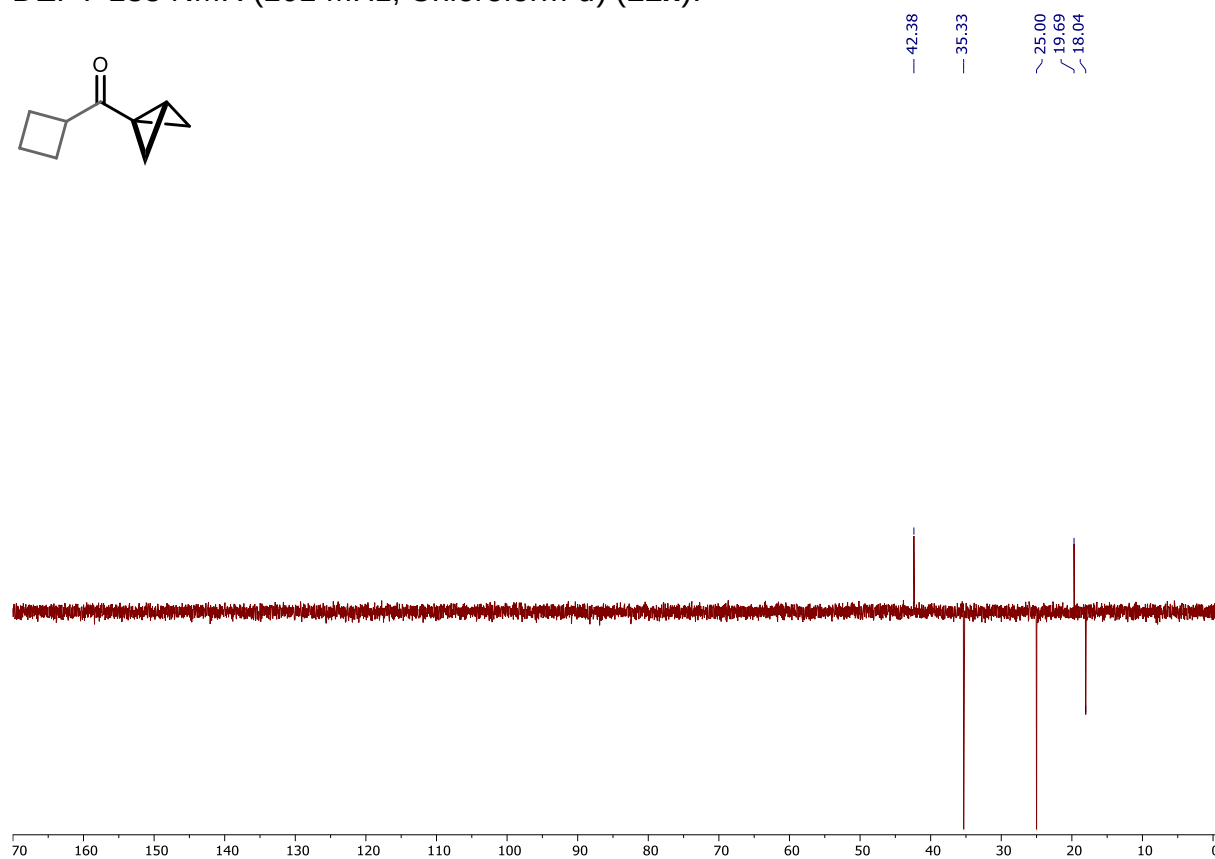
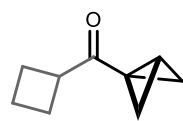
^1H NMR (400 MHz, Chloroform-*d*) (**11n**):



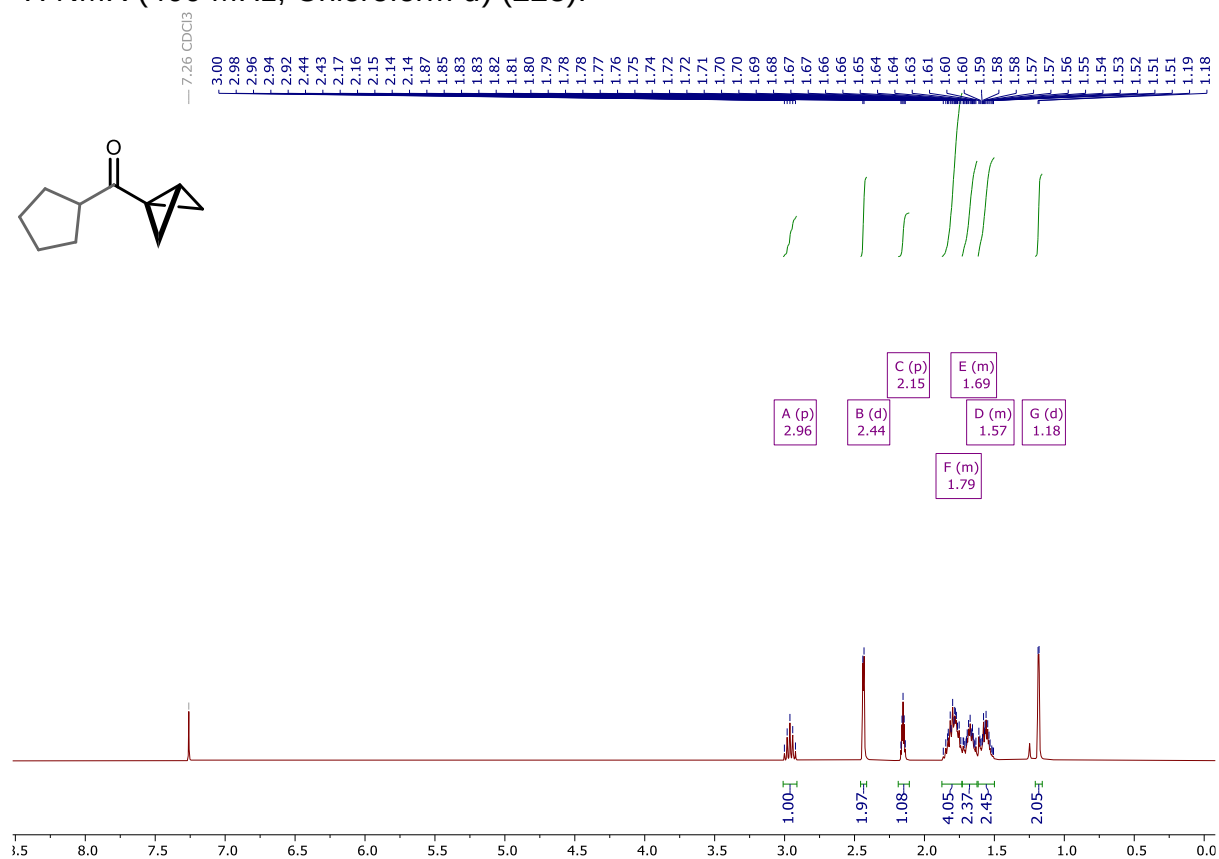
^{13}C NMR (101 MHz, Chloroform-*d*) (**11n**):



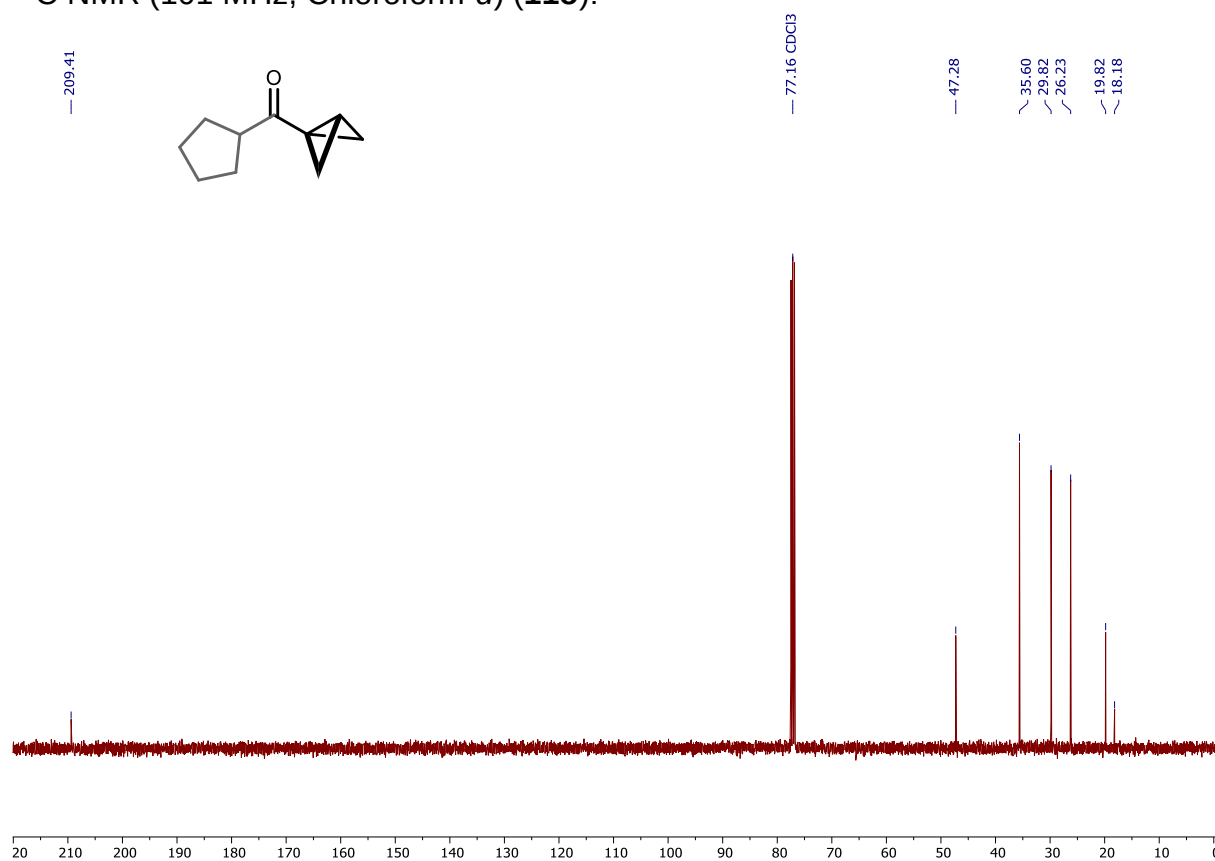
DEPT-135 NMR (101 MHz, Chloroform-*d*) (**11n**):



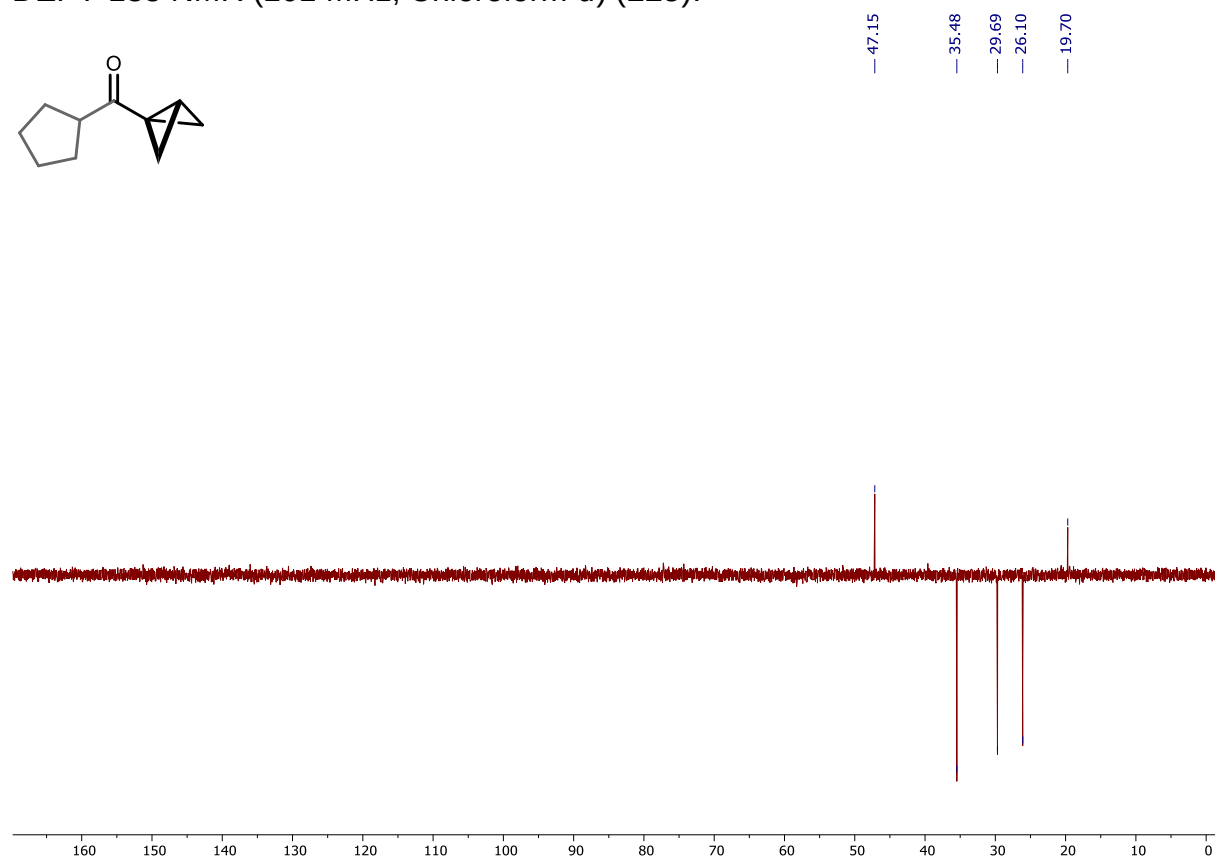
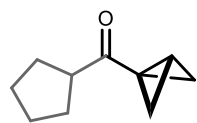
^1H NMR (400 MHz, Chloroform- d) (**11o**):



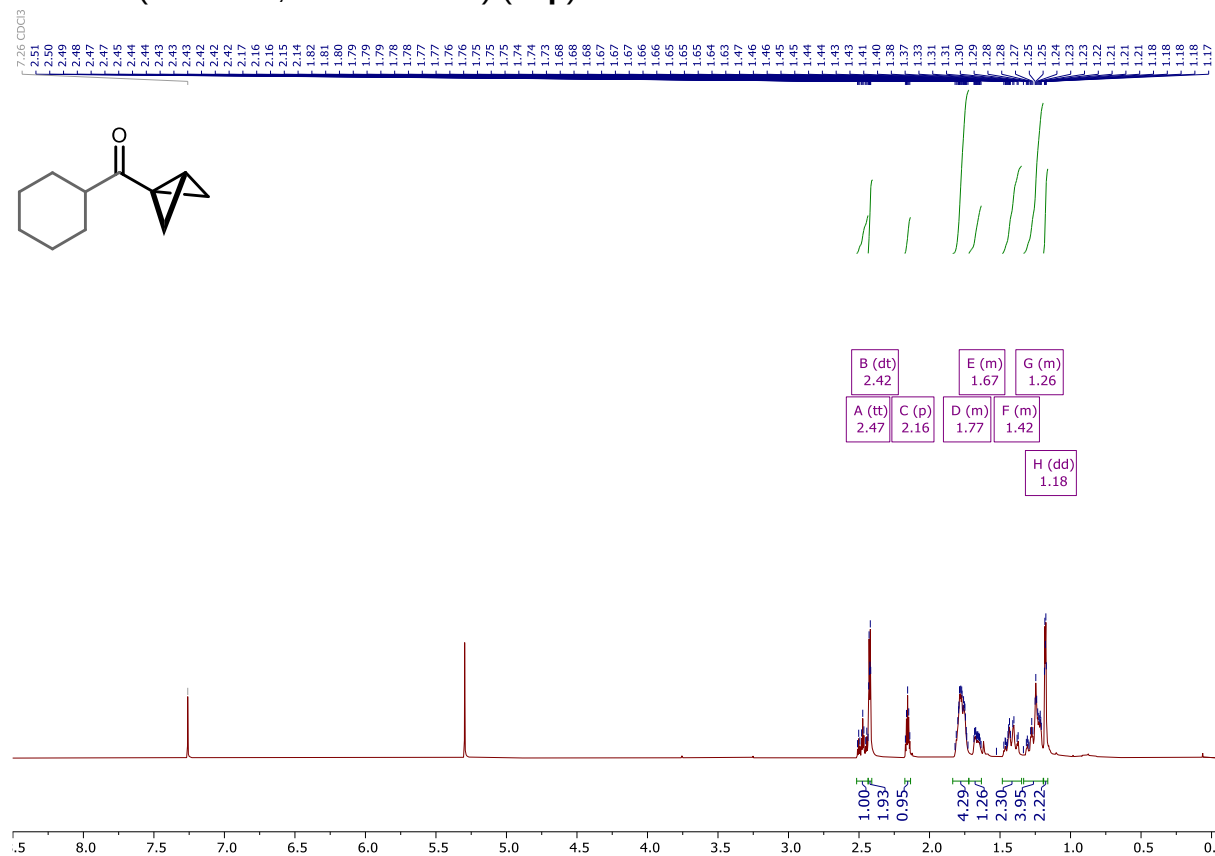
^{13}C NMR (101 MHz, Chloroform- d) (**11o**):



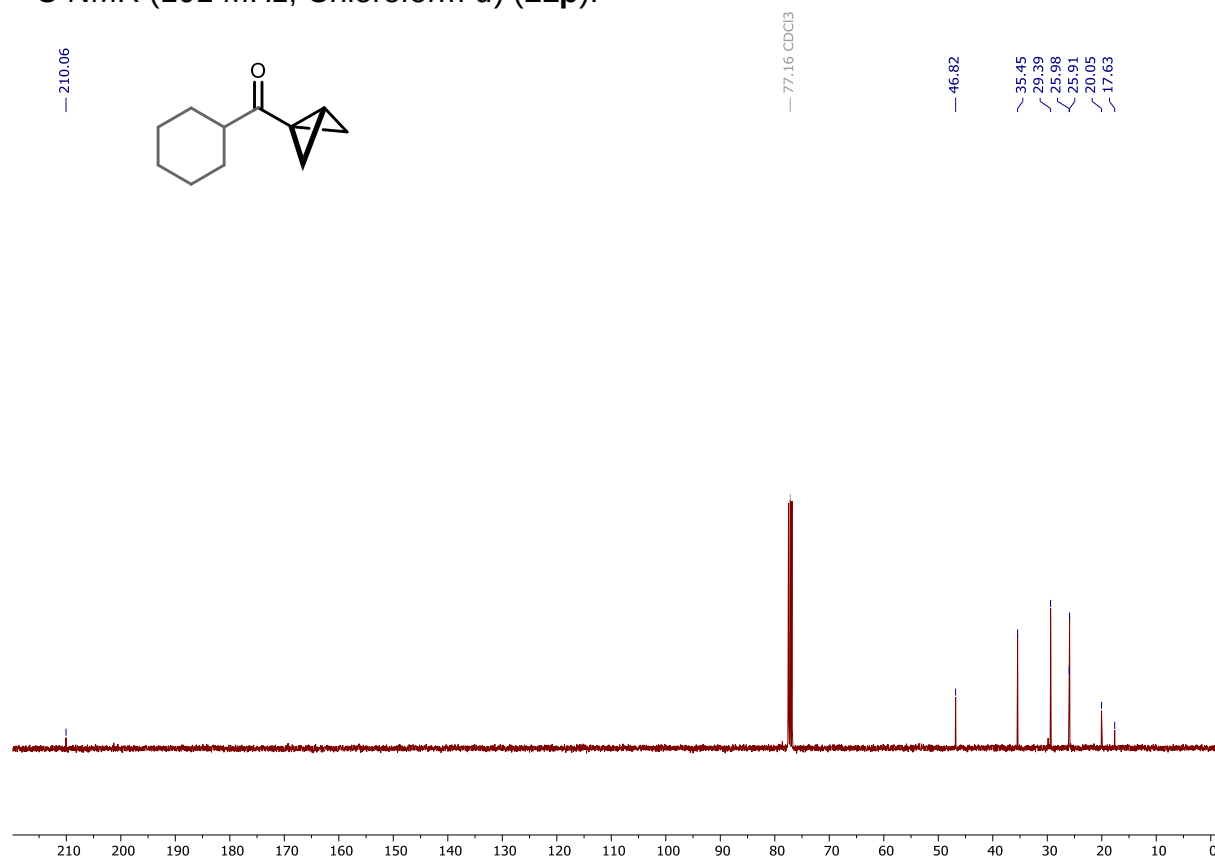
DEPT-135 NMR (101 MHz, Chloroform-*d*) (**11o**):



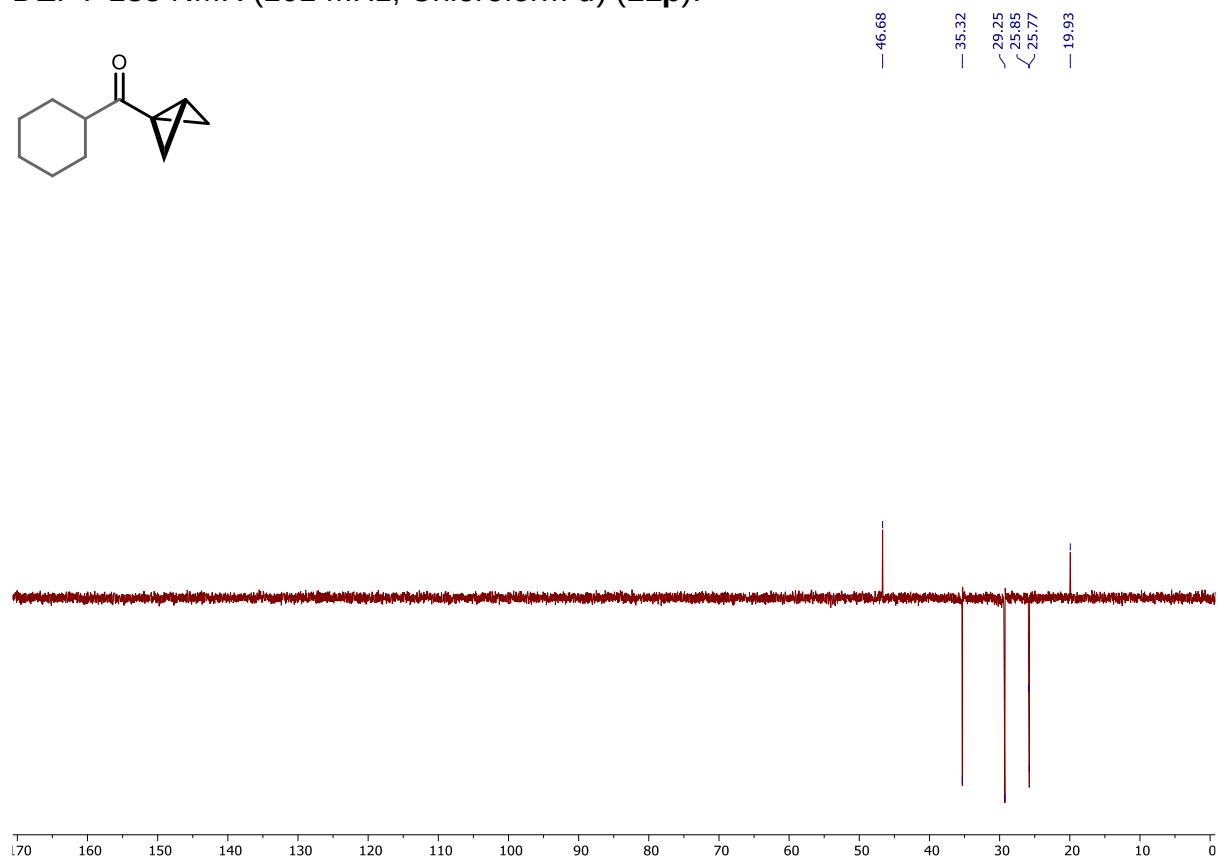
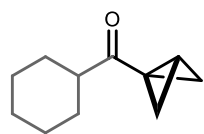
¹H NMR (400 MHz, Chloroform-*d*) (**11p**):



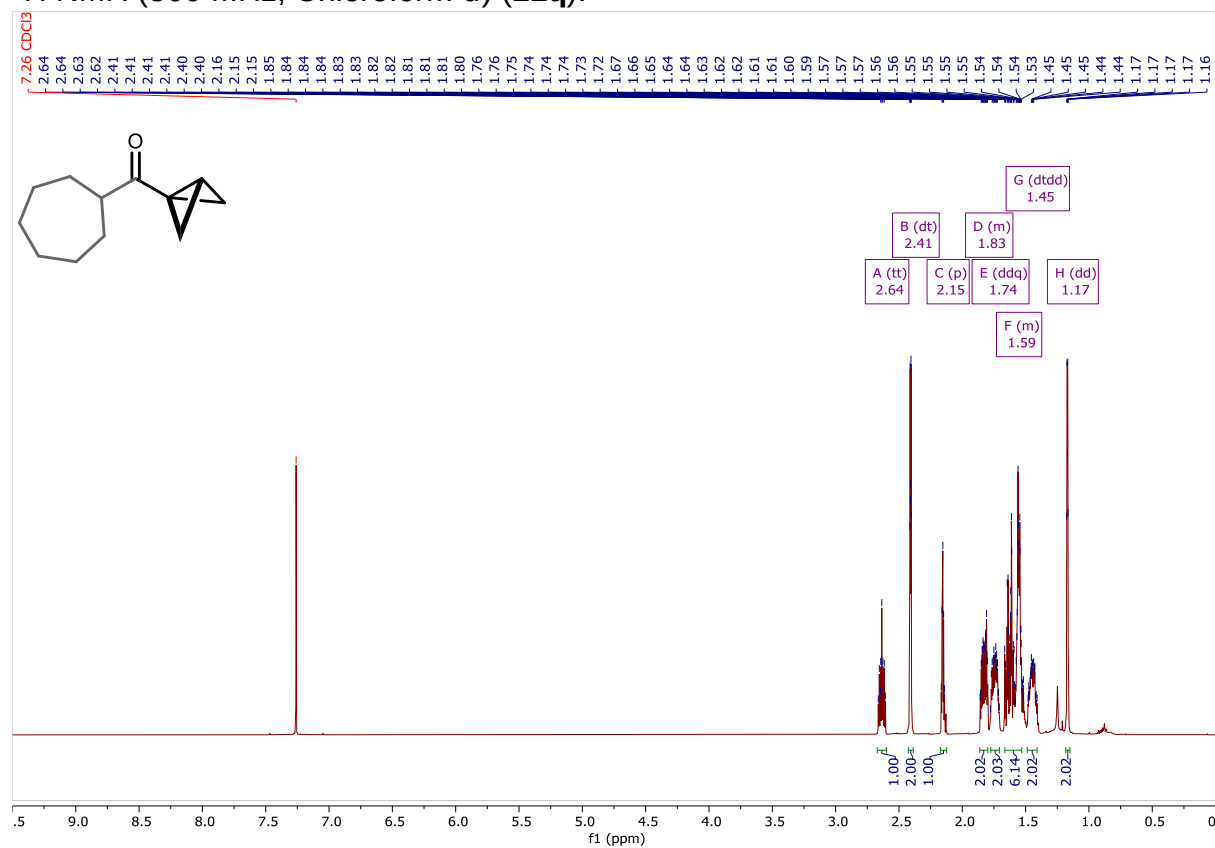
¹³C NMR (101 MHz, Chloroform-*d*) (**11p**):



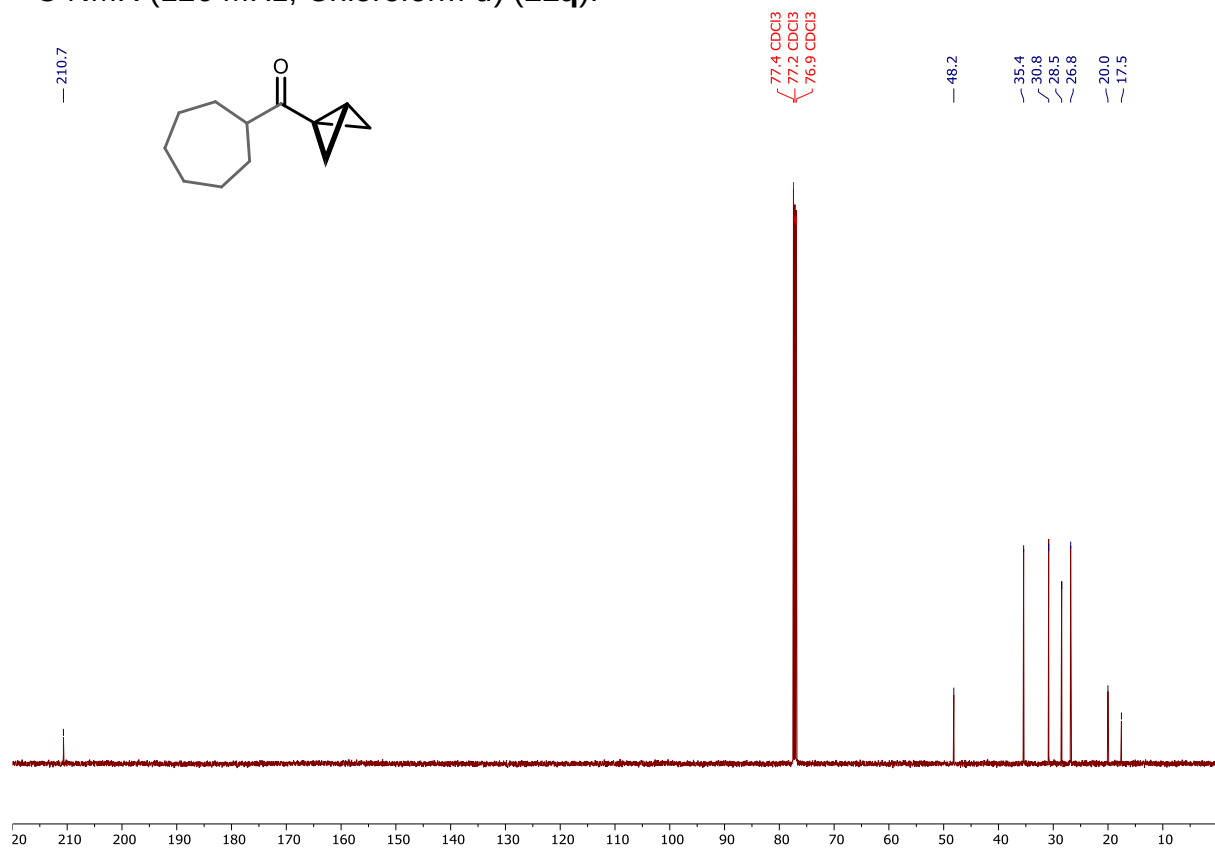
DEPT-135 NMR (101 MHz, Chloroform-*d*) (**11p**):



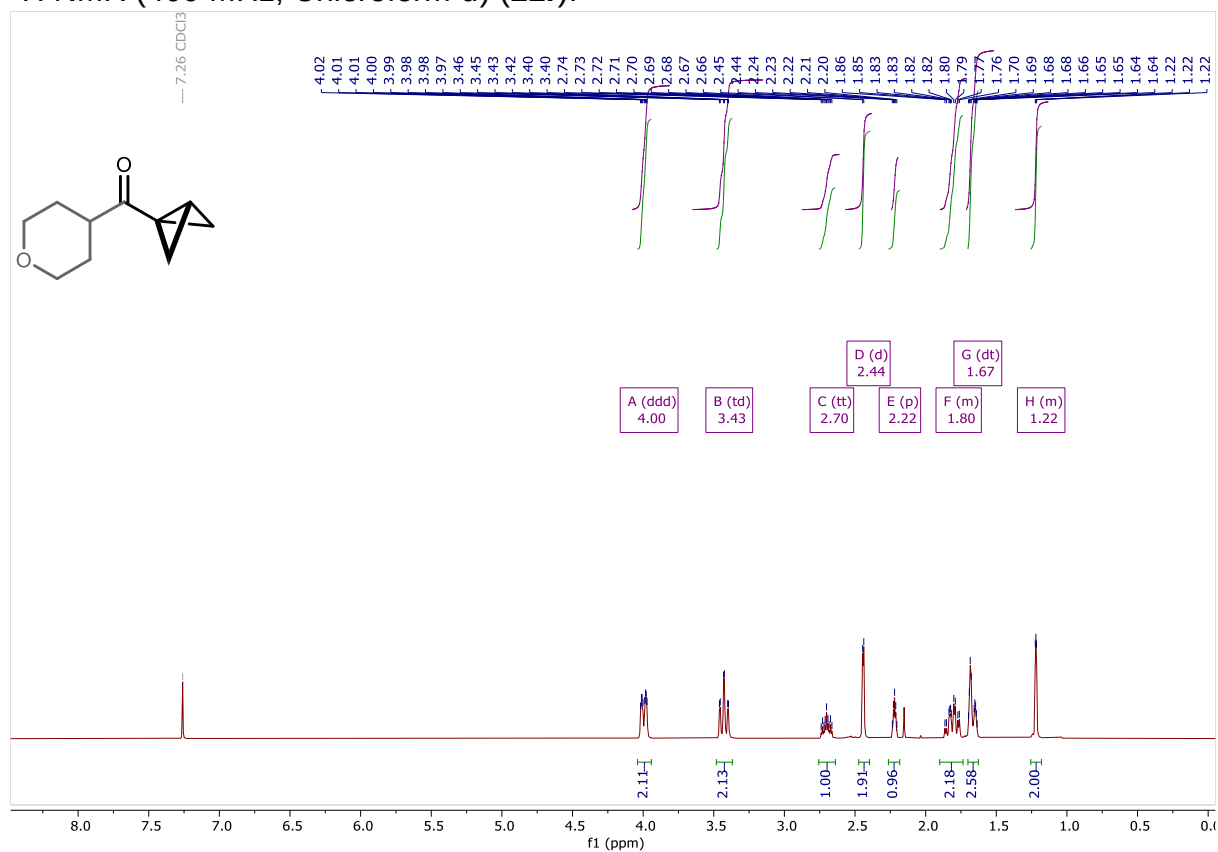
¹H NMR (500 MHz, Chloroform-*d*) (**11q**):



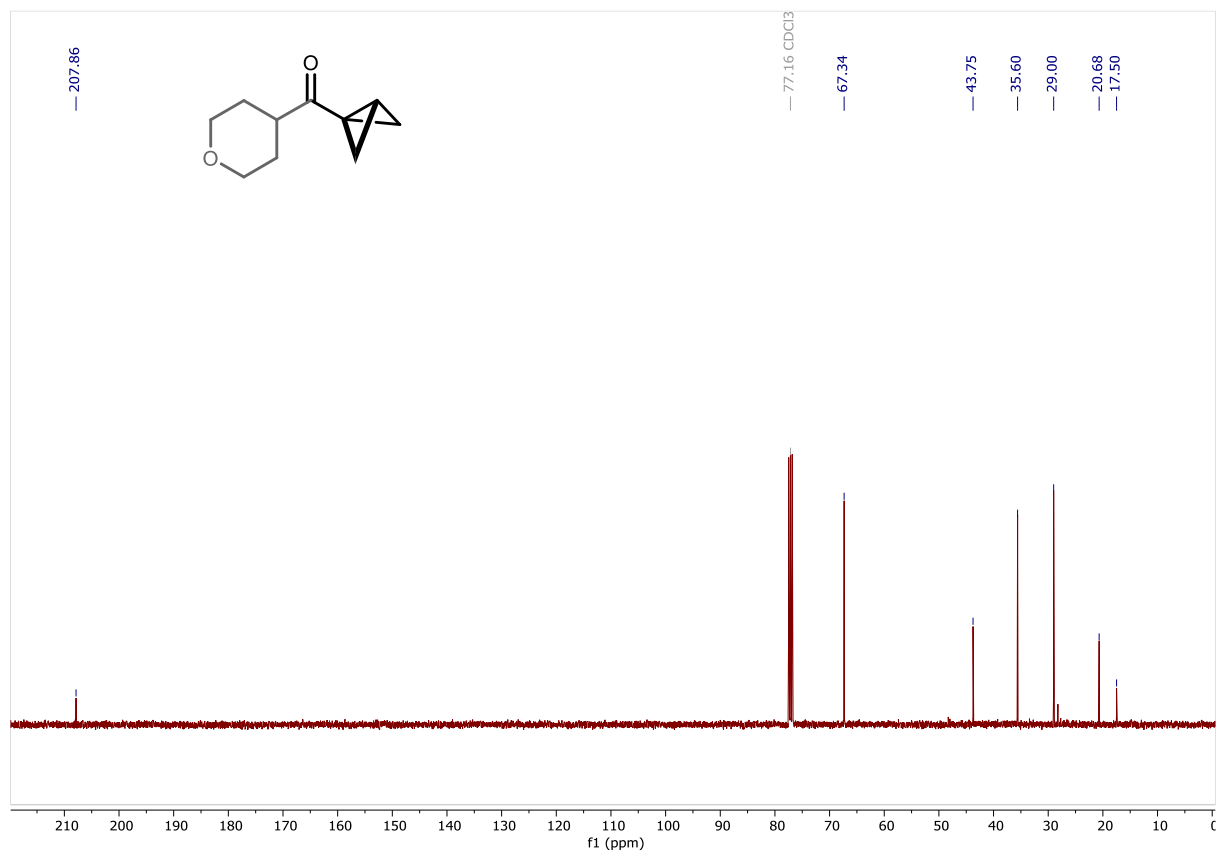
¹³C NMR (126 MHz, Chloroform-*d*) (**11q**):



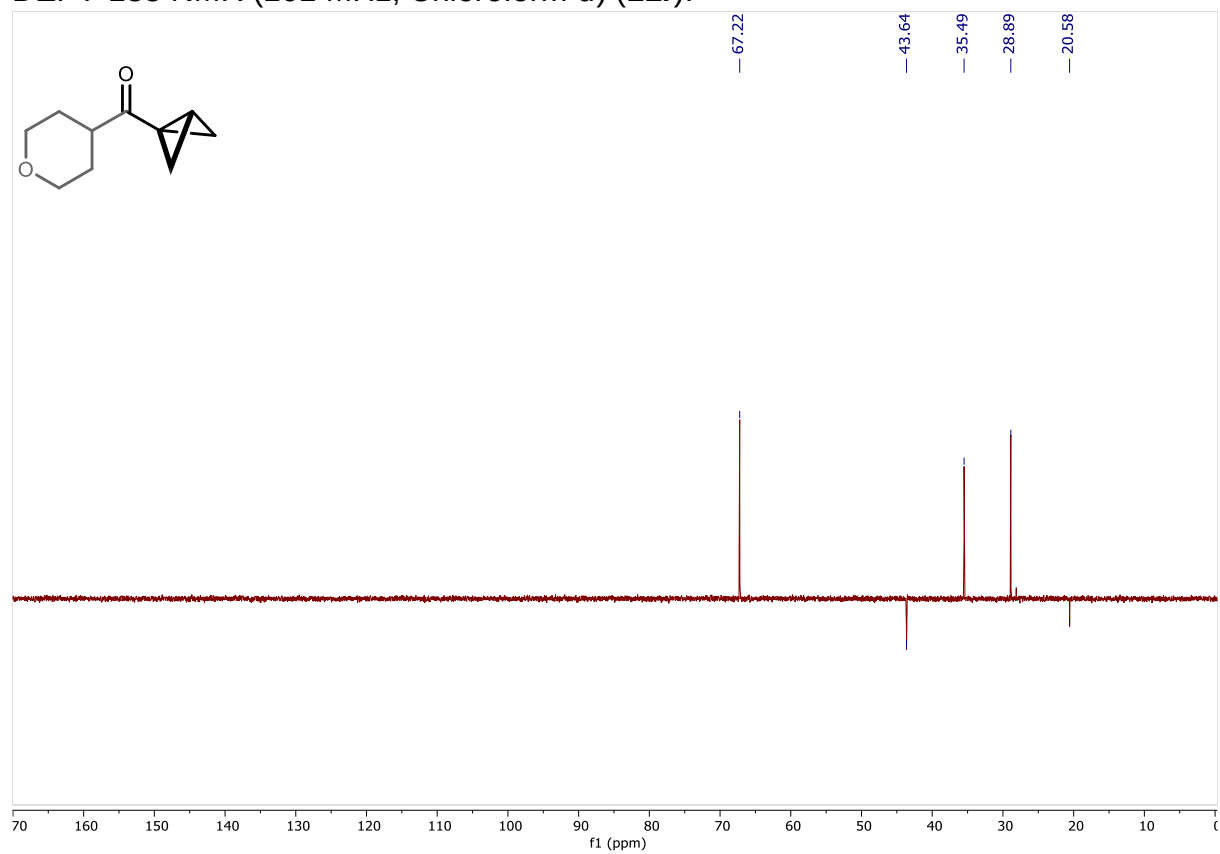
¹H NMR (400 MHz, Chloroform-*d*) (**11r**):



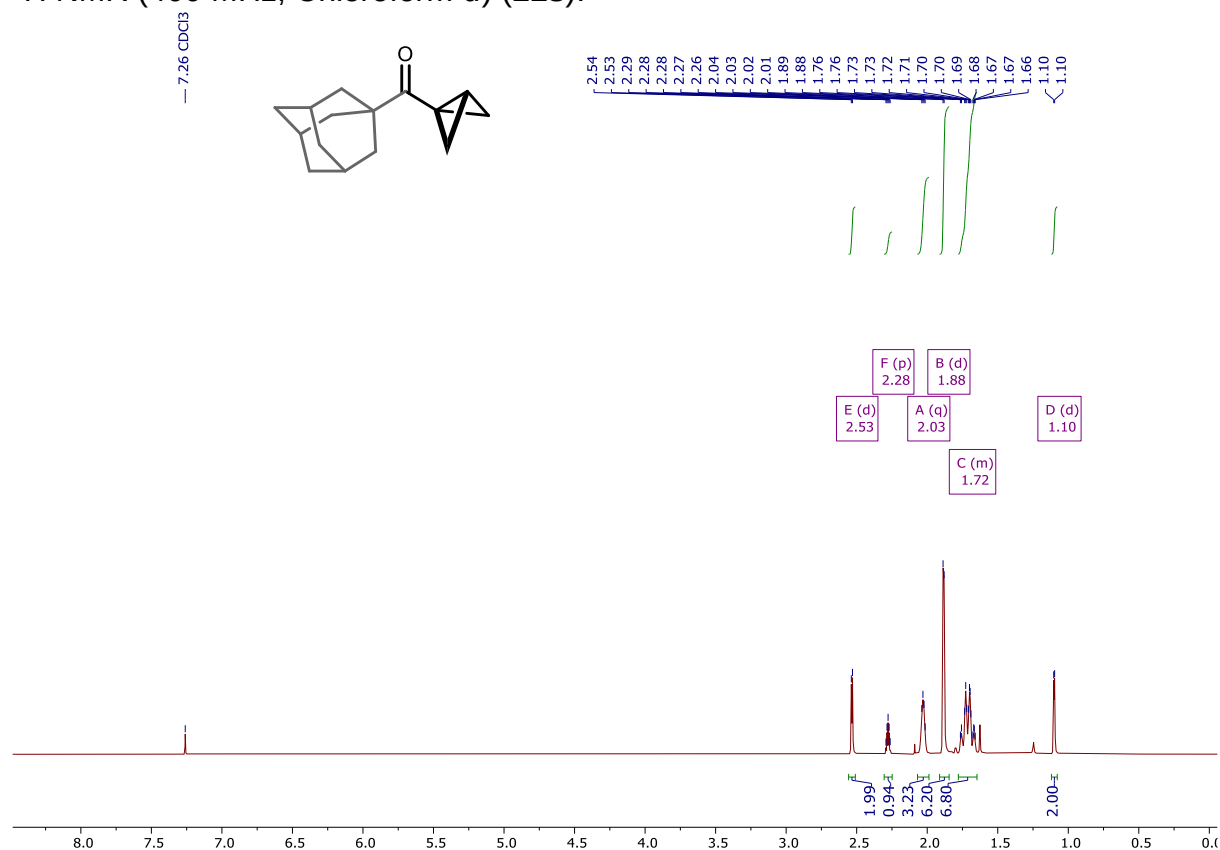
¹³C NMR (101 MHz, Chloroform-*d*) (**11r**):



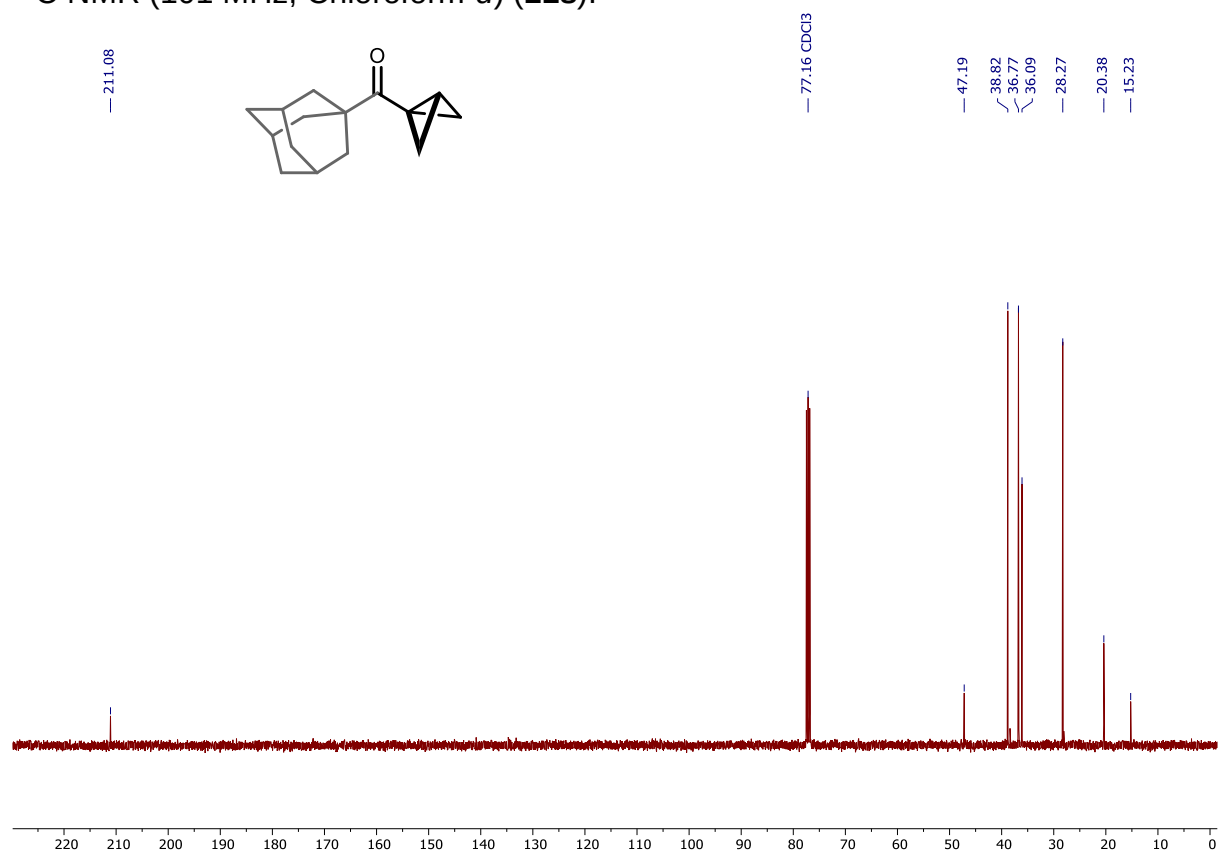
DEPT-135 NMR (101 MHz, Chloroform-*d*) (**11r**):



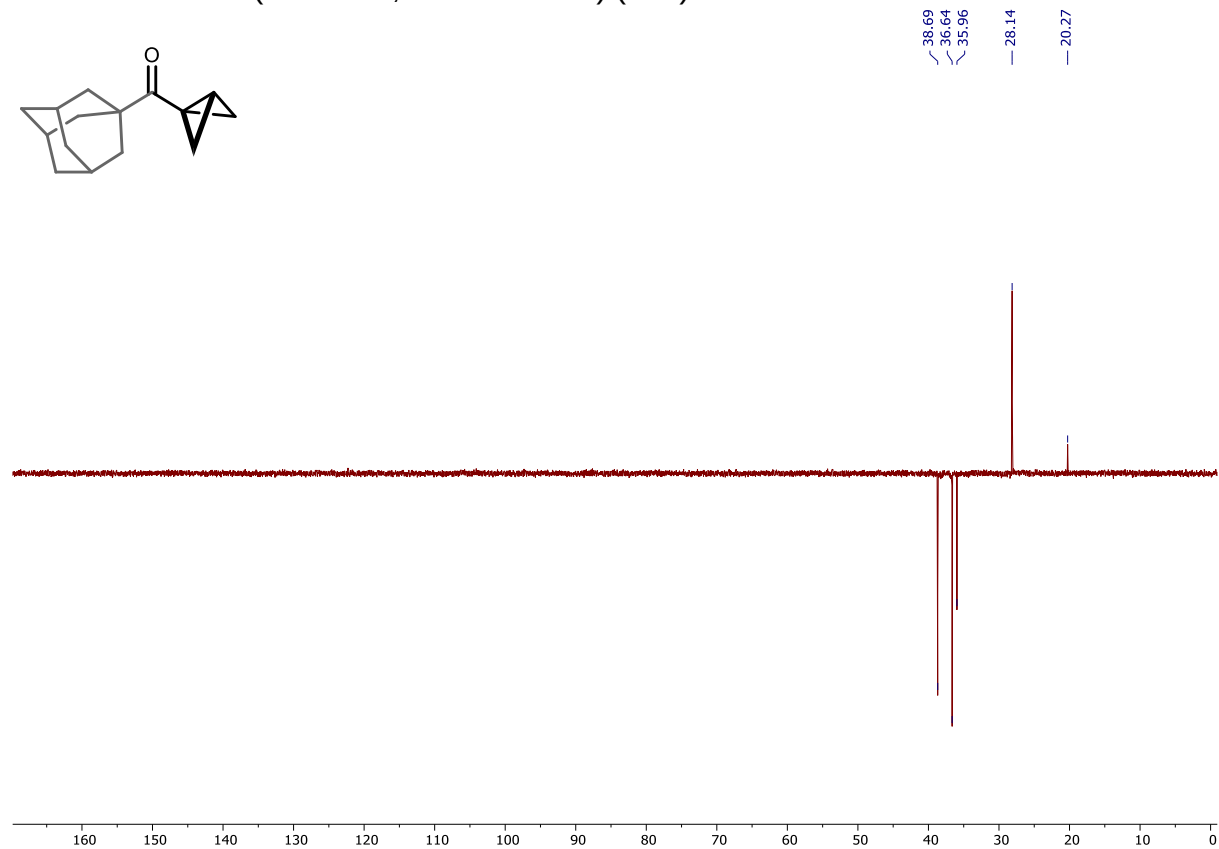
^1H NMR (400 MHz, Chloroform-*d*) (**11s**):



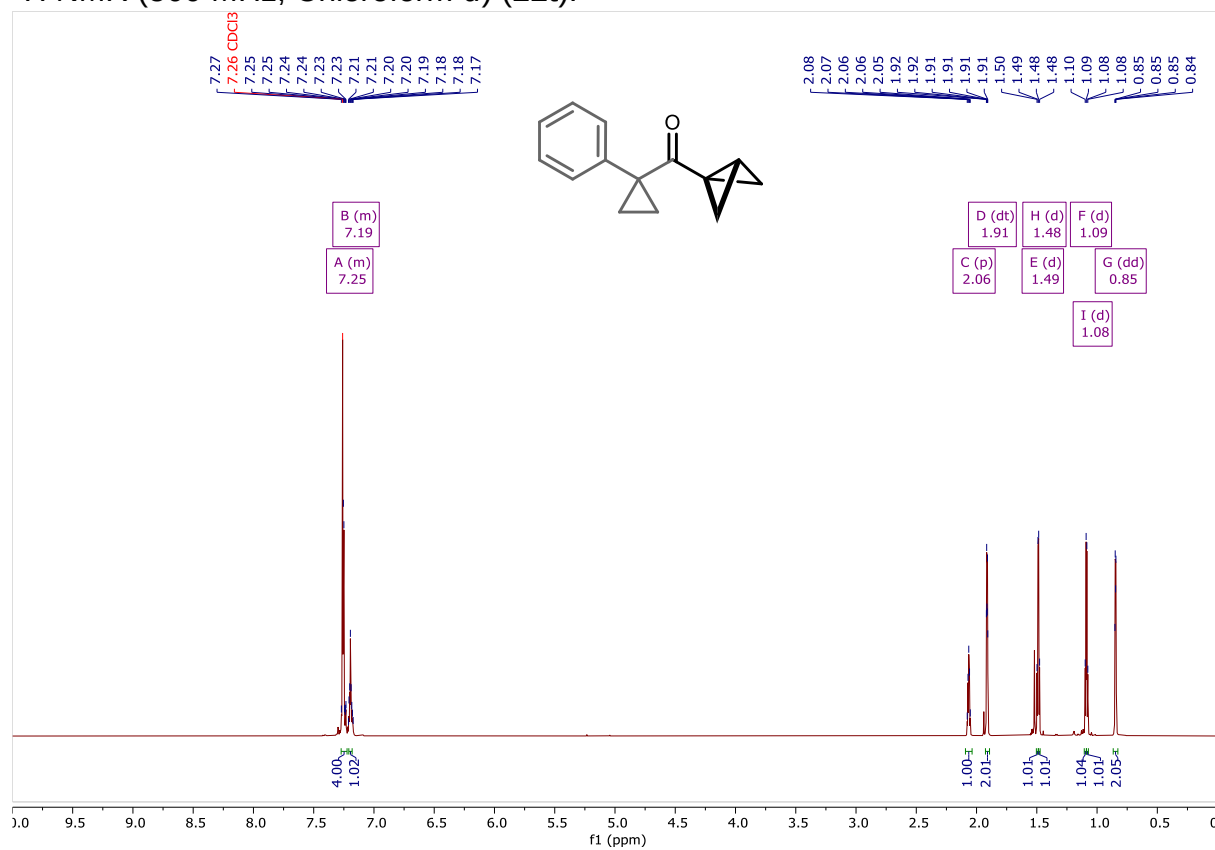
^{13}C NMR (101 MHz, Chloroform-*d*) (**11s**):



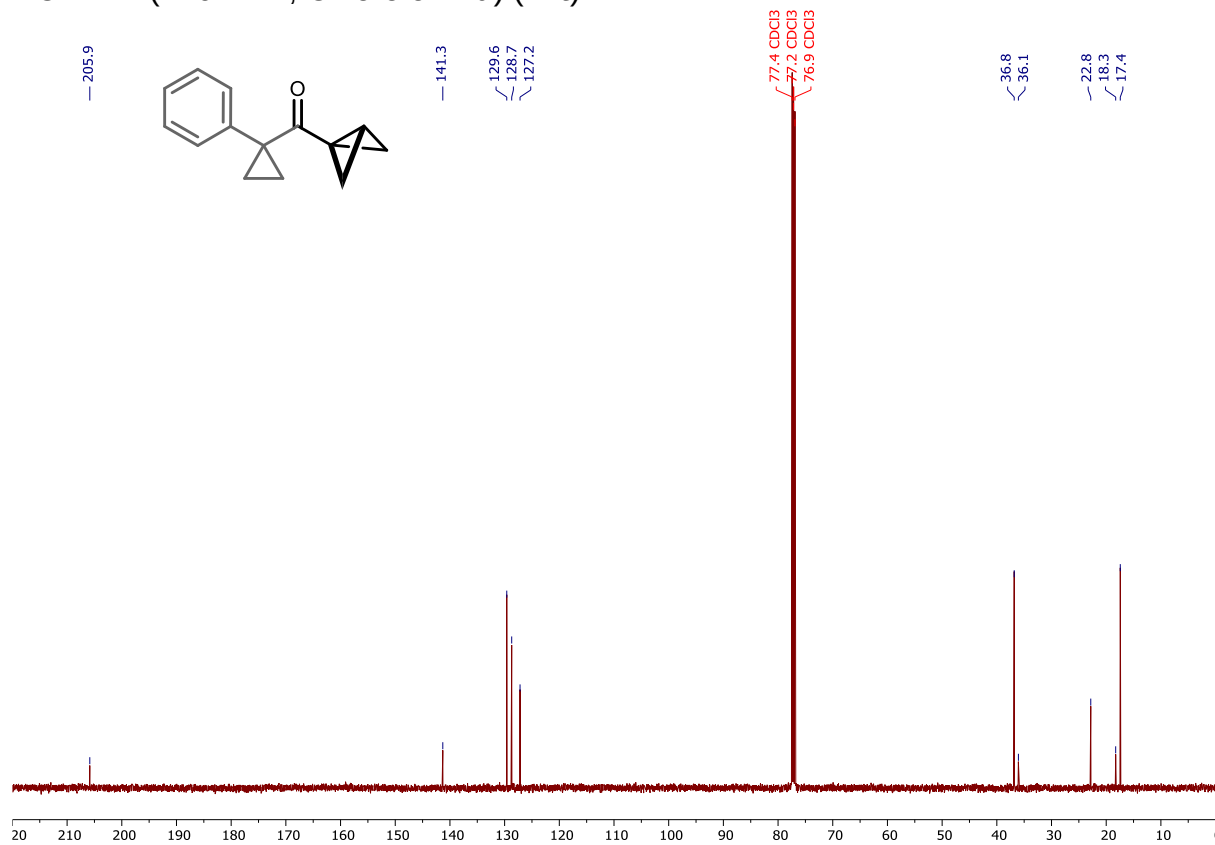
DEPT-135 NMR (101 MHz, Chloroform-*d*) (**11s**):



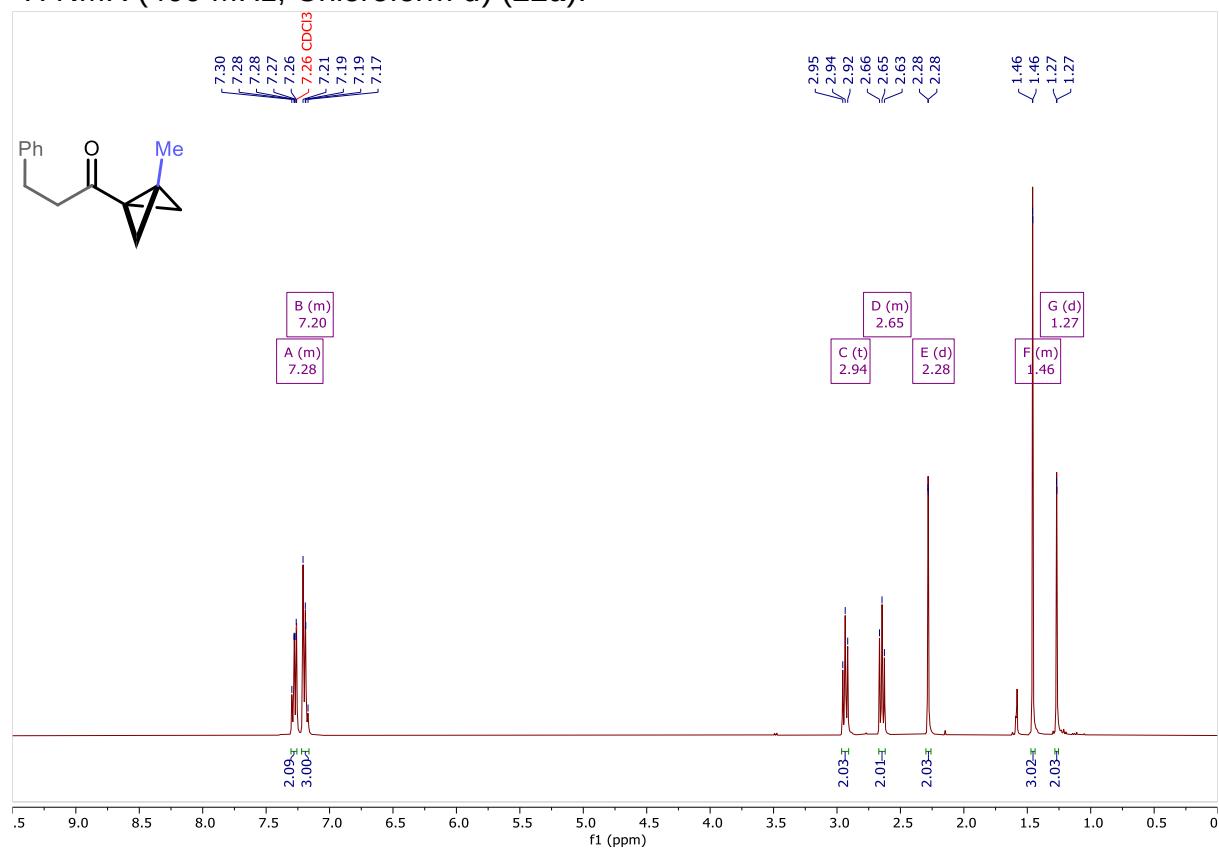
^1H NMR (500 MHz, Chloroform-*d*) (**11t**):



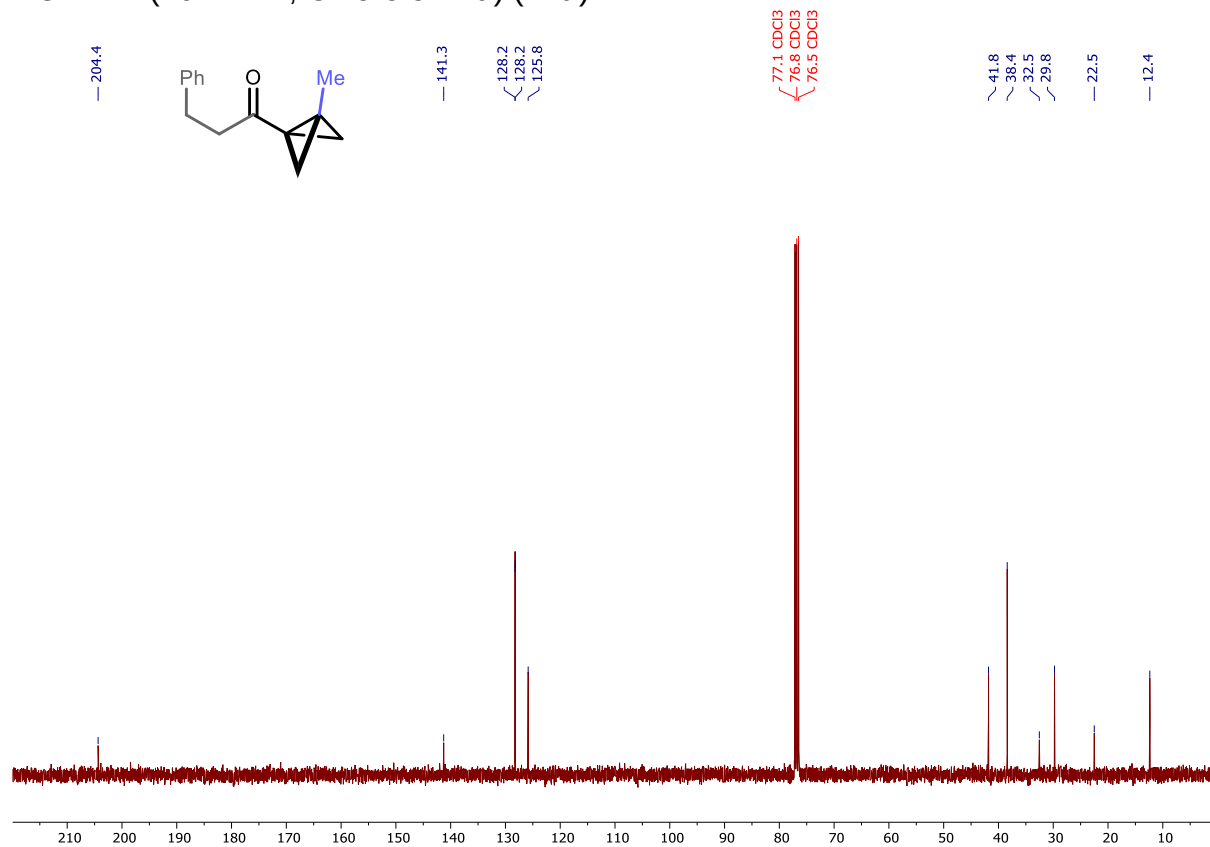
^{13}C NMR (126 MHz, Chloroform-*d*) (**11t**):



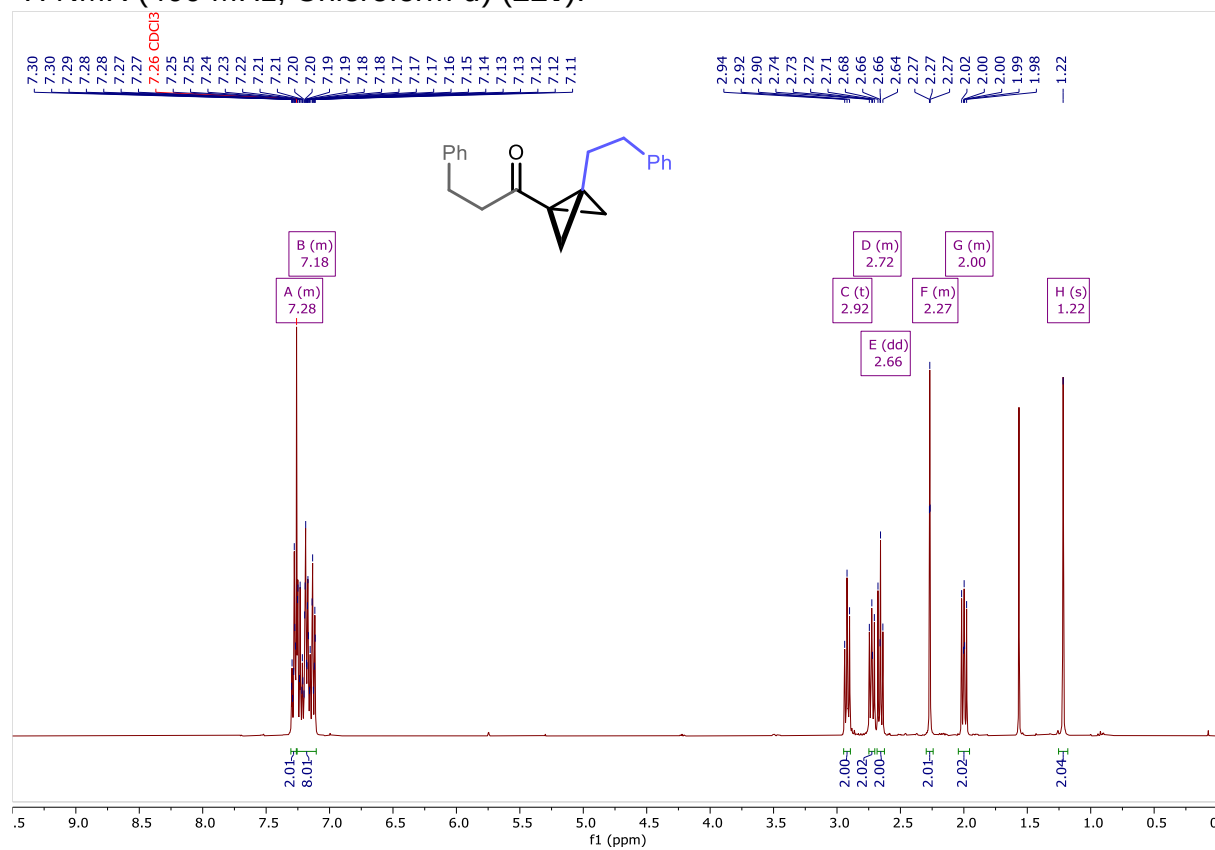
¹H NMR (400 MHz, Chloroform-*d*) (**11u**):



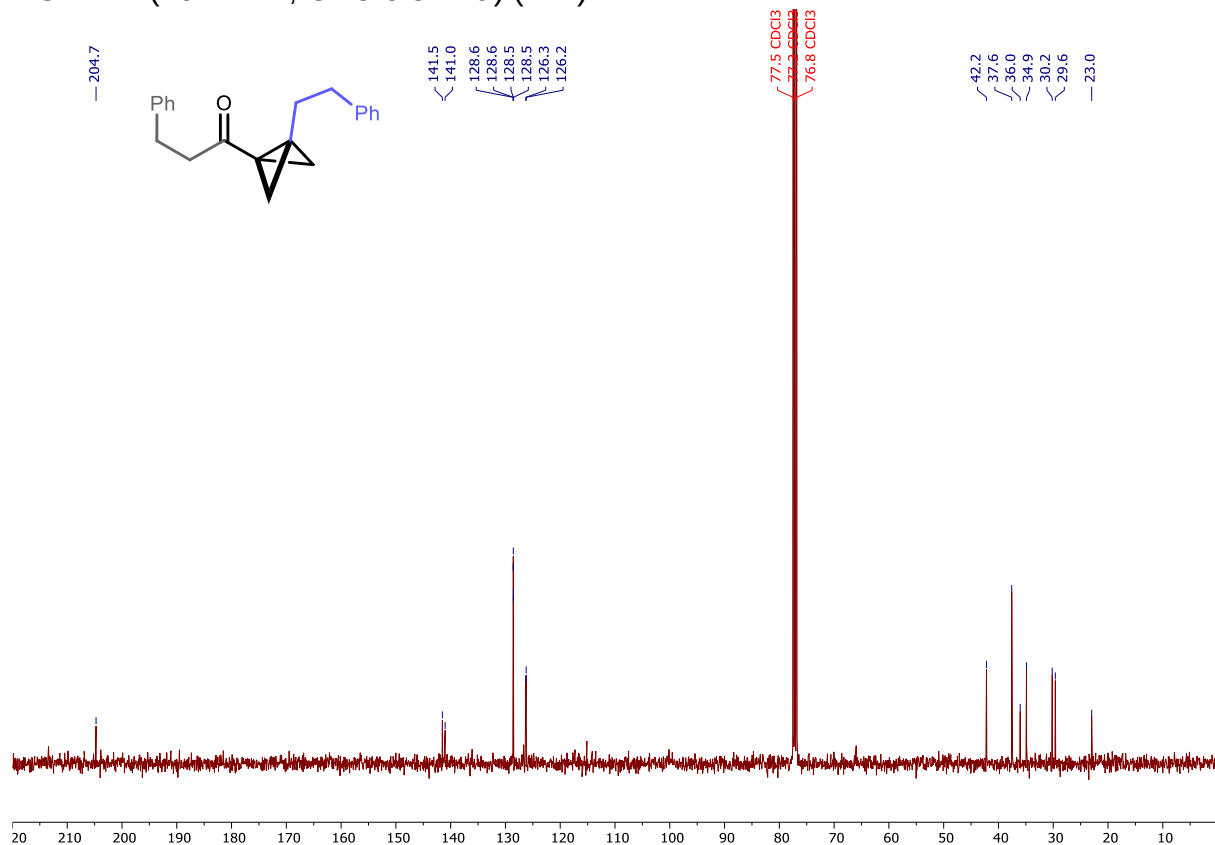
¹³C NMR (101 MHz, Chloroform-*d*) (**11u**):



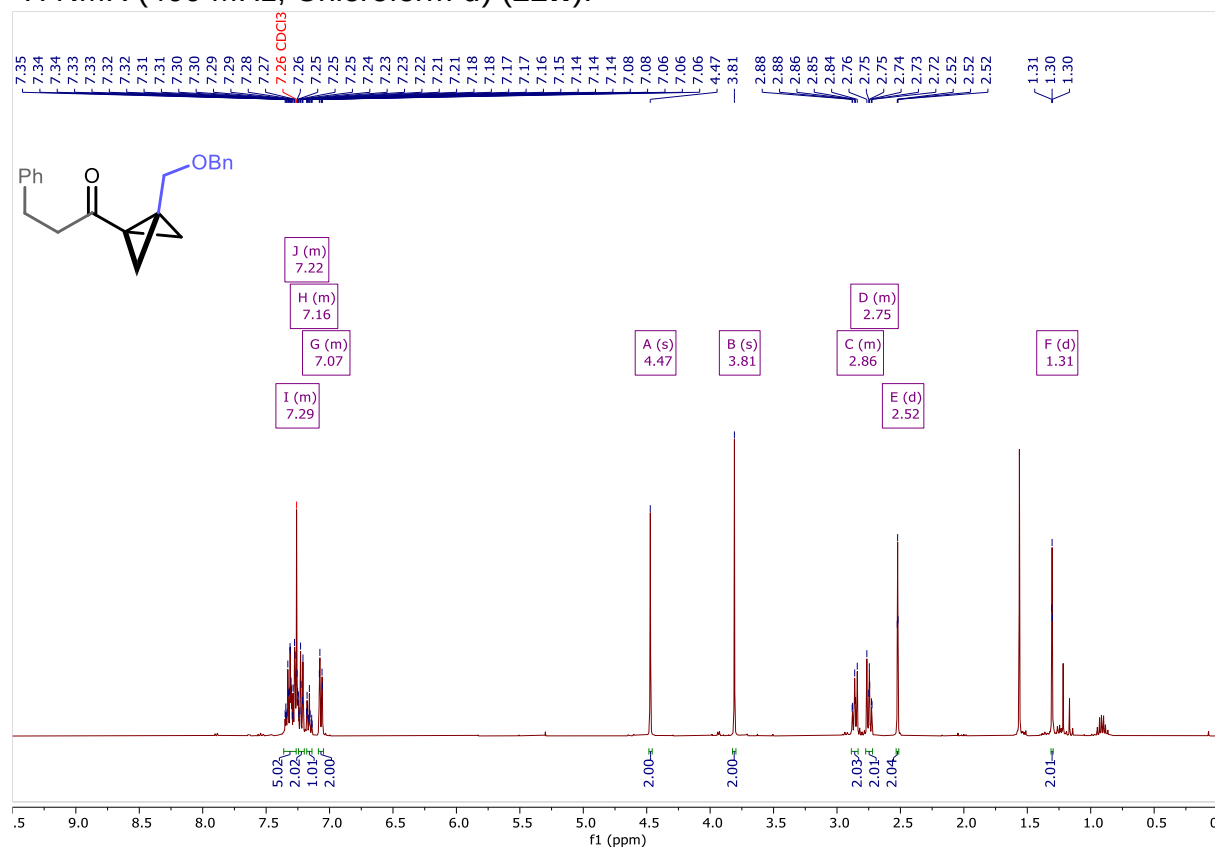
^1H NMR (400 MHz, Chloroform-*d*) (**11v**):



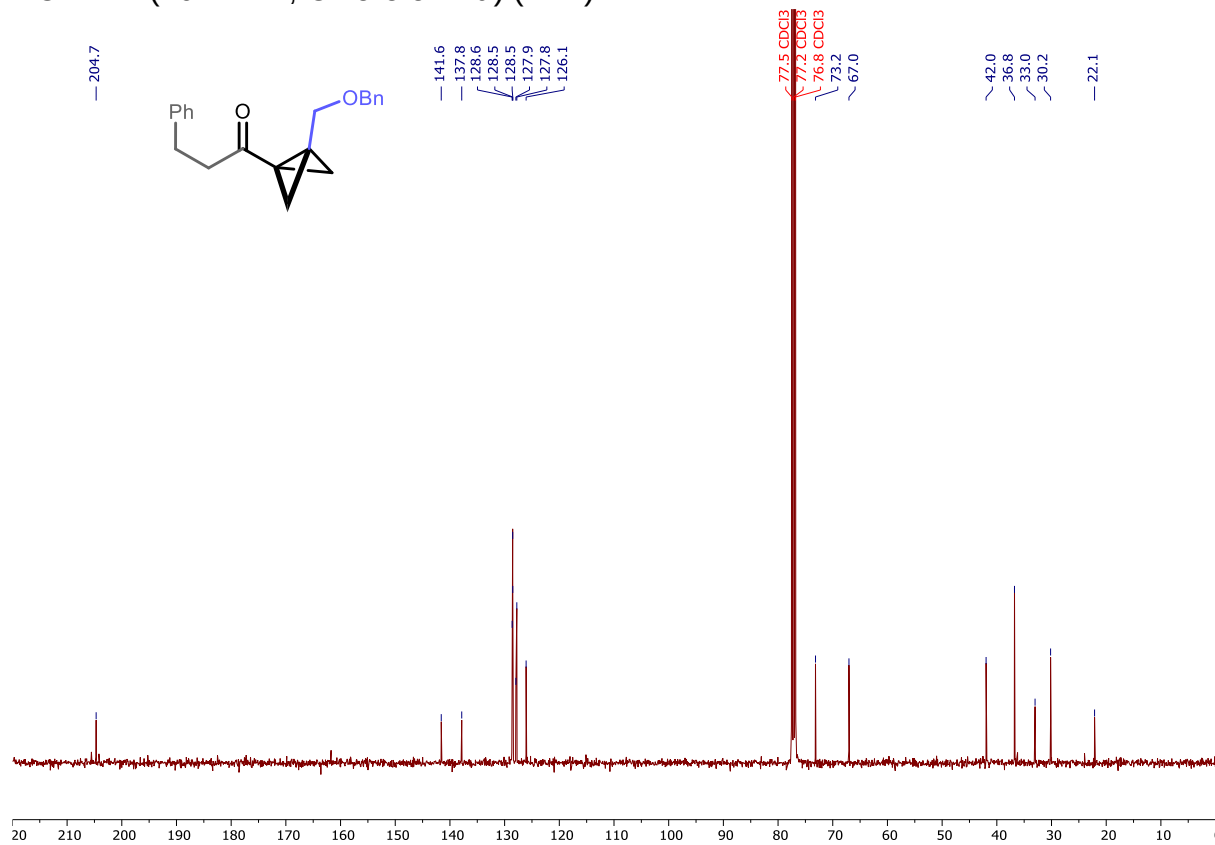
^{13}C NMR (101 MHz, Chloroform-*d*) (**11v**):



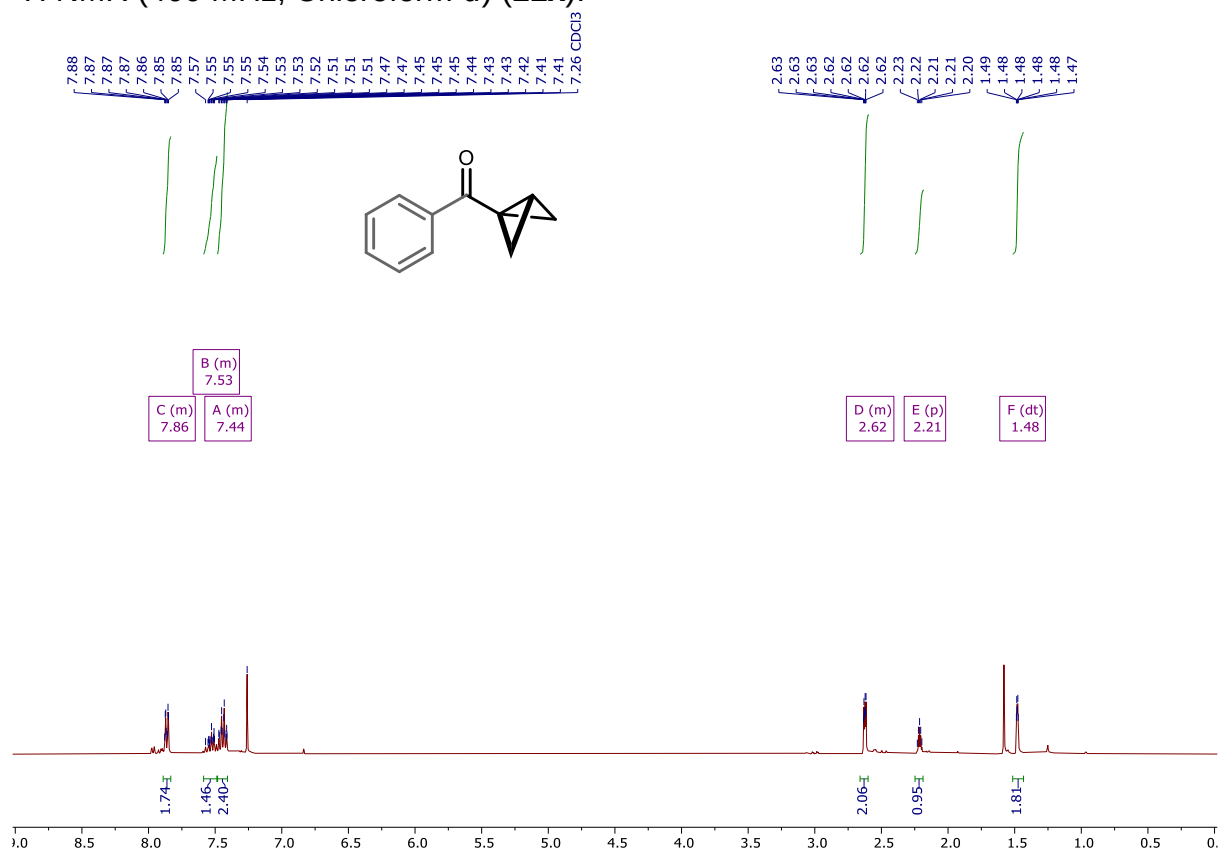
¹H NMR (400 MHz, Chloroform-*d*) (**11w**):



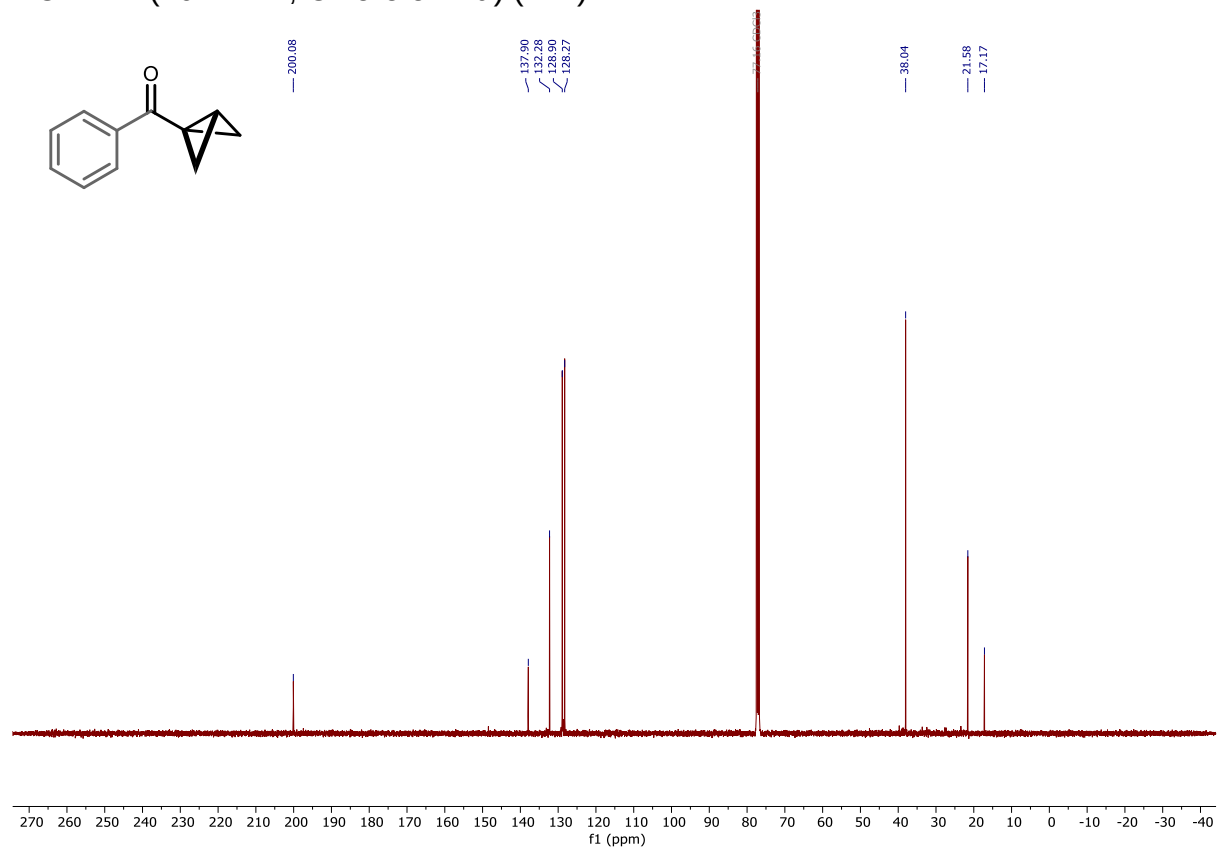
¹³C NMR (101 MHz, Chloroform-*d*) (**11w**)



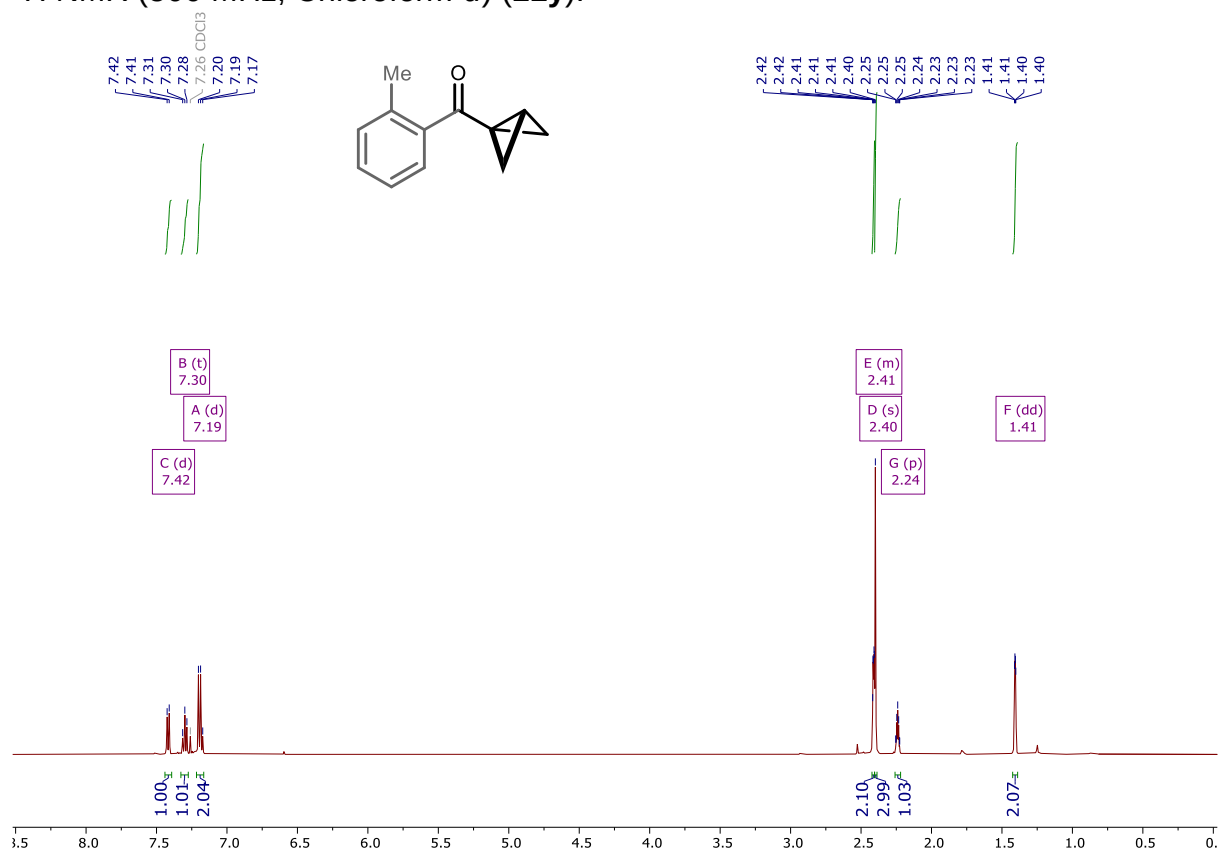
^1H NMR (400 MHz, Chloroform-*d*) (**11x**):



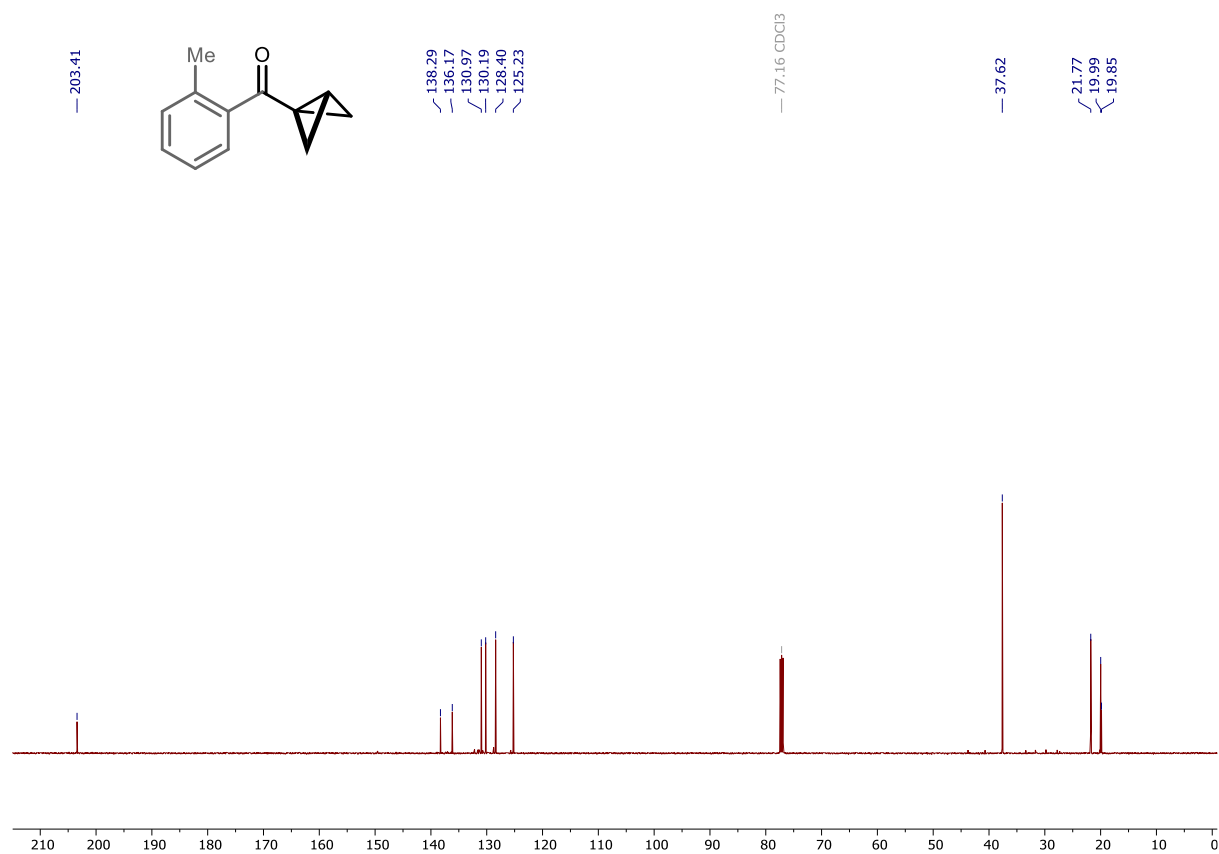
^{13}C NMR (101 MHz, Chloroform-*d*) (**11x**)



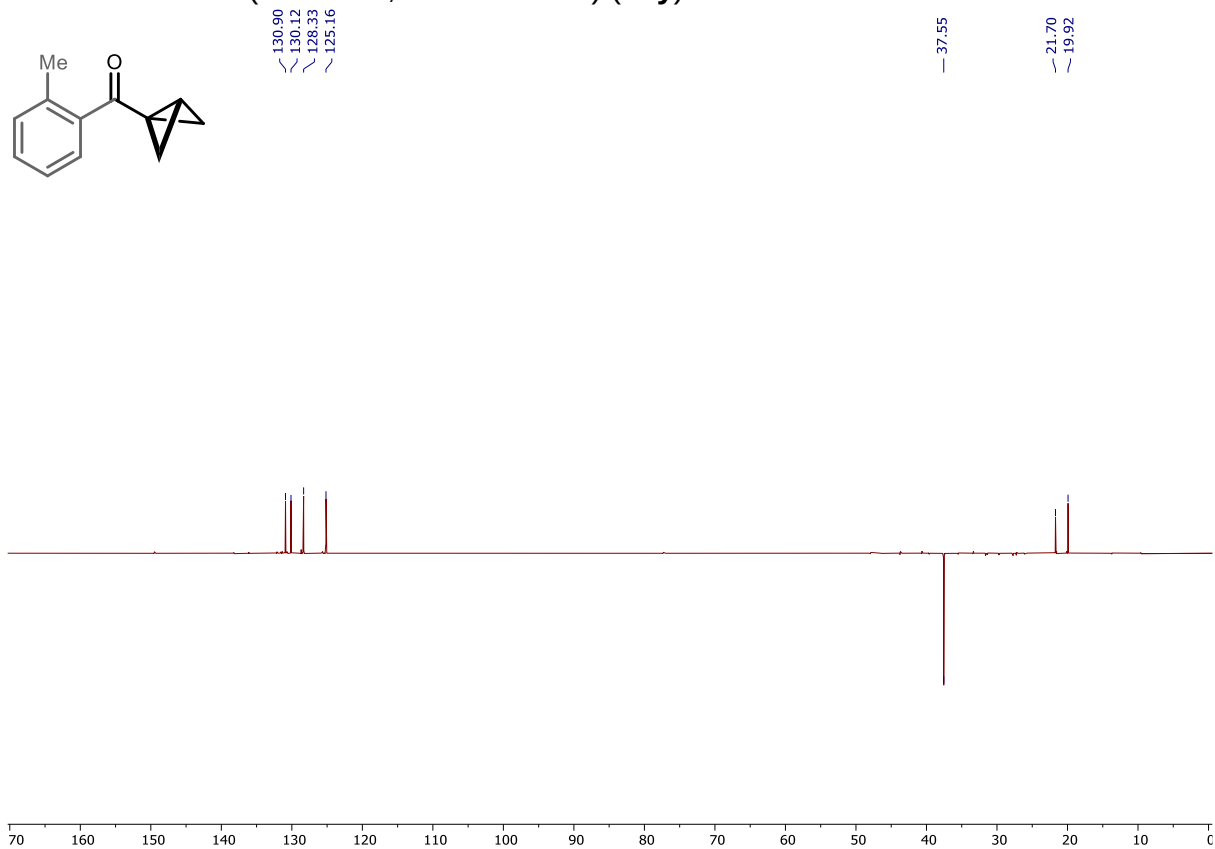
^1H NMR (500 MHz, Chloroform-*d*) (**11y**):



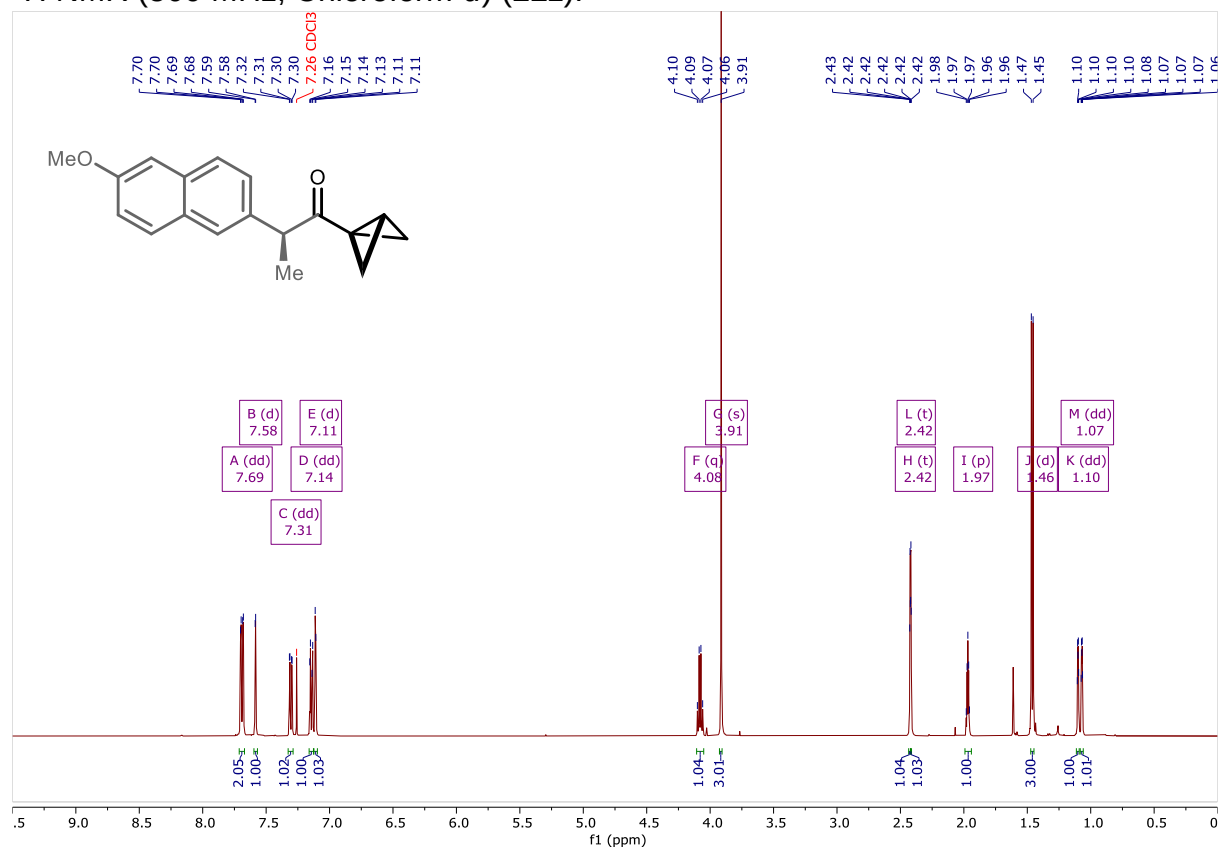
^{13}C NMR (126 MHz, Chloroform-*d*) (**11y**):



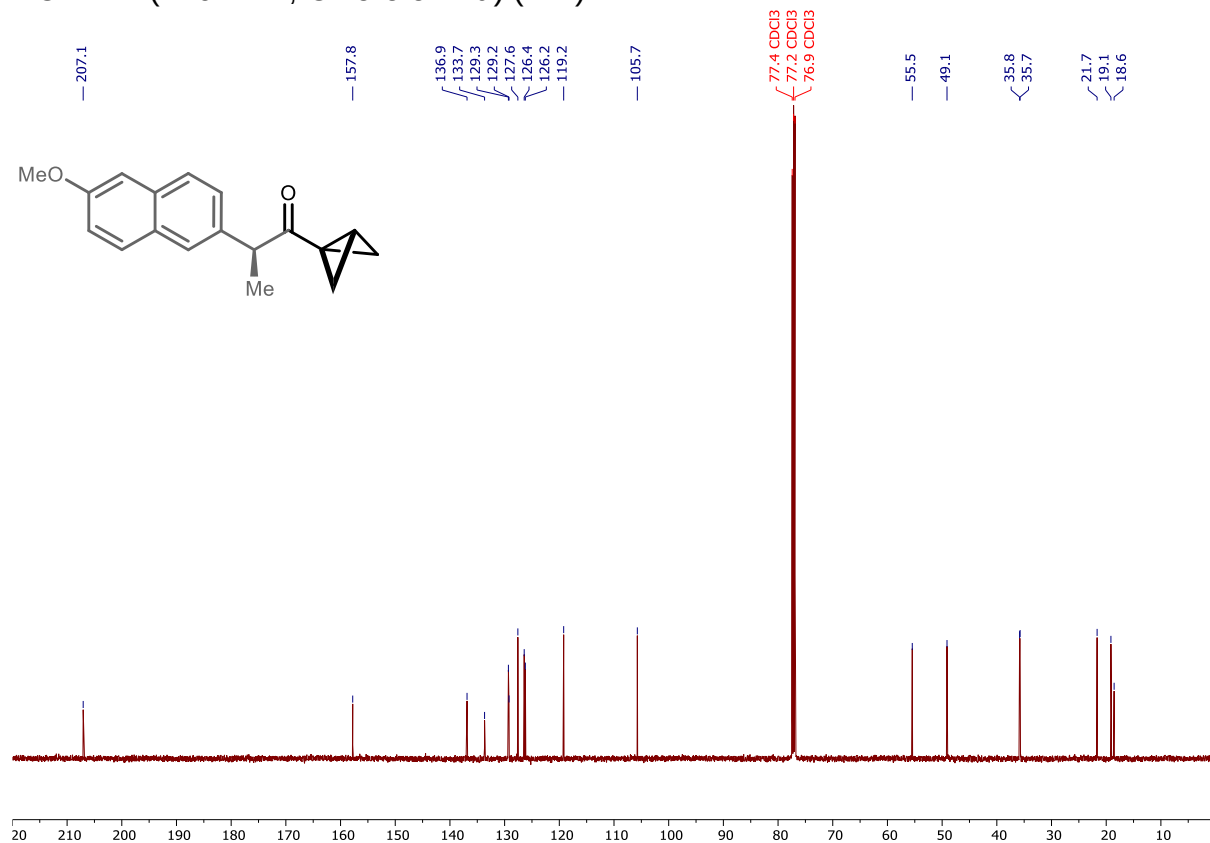
DEPT-135 NMR (126 MHz, Chloroform-*d*) (**11y**):



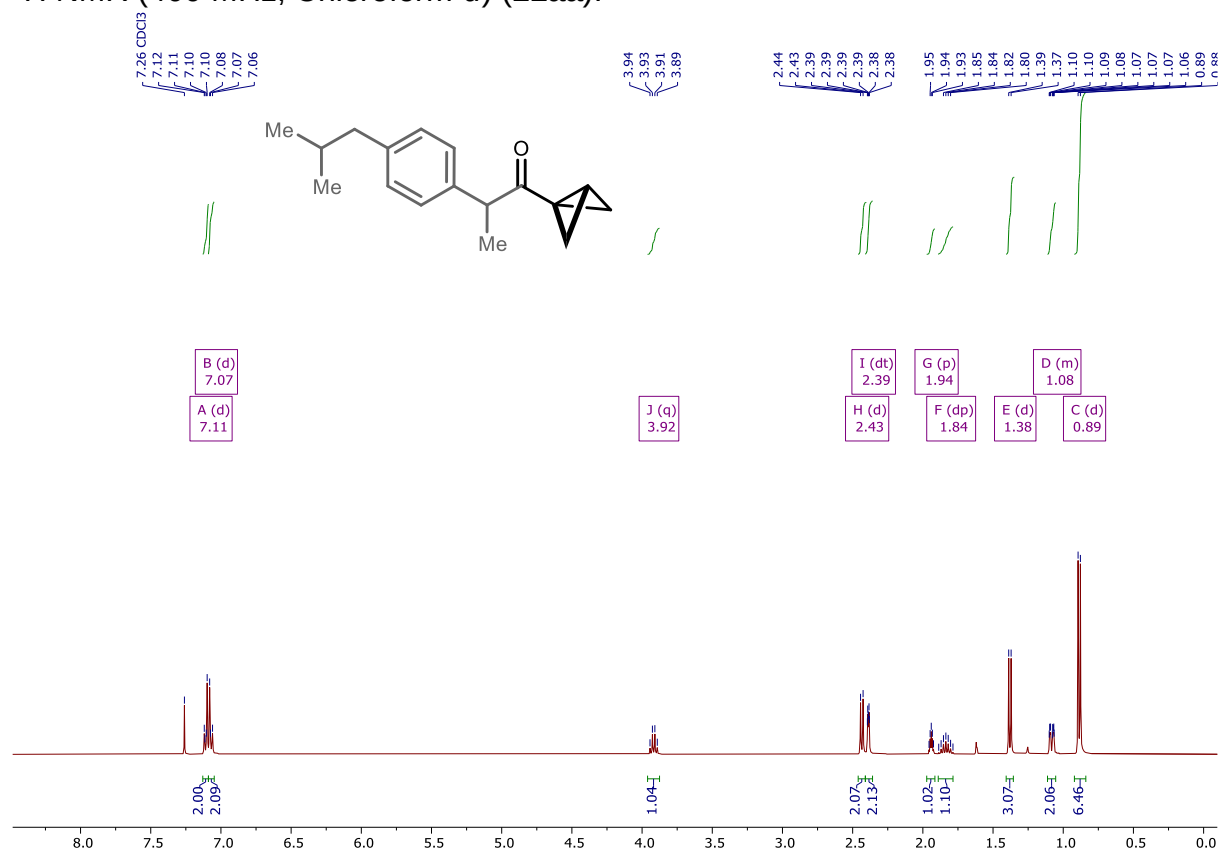
¹H NMR (500 MHz, Chloroform-*d*) (**11z**):



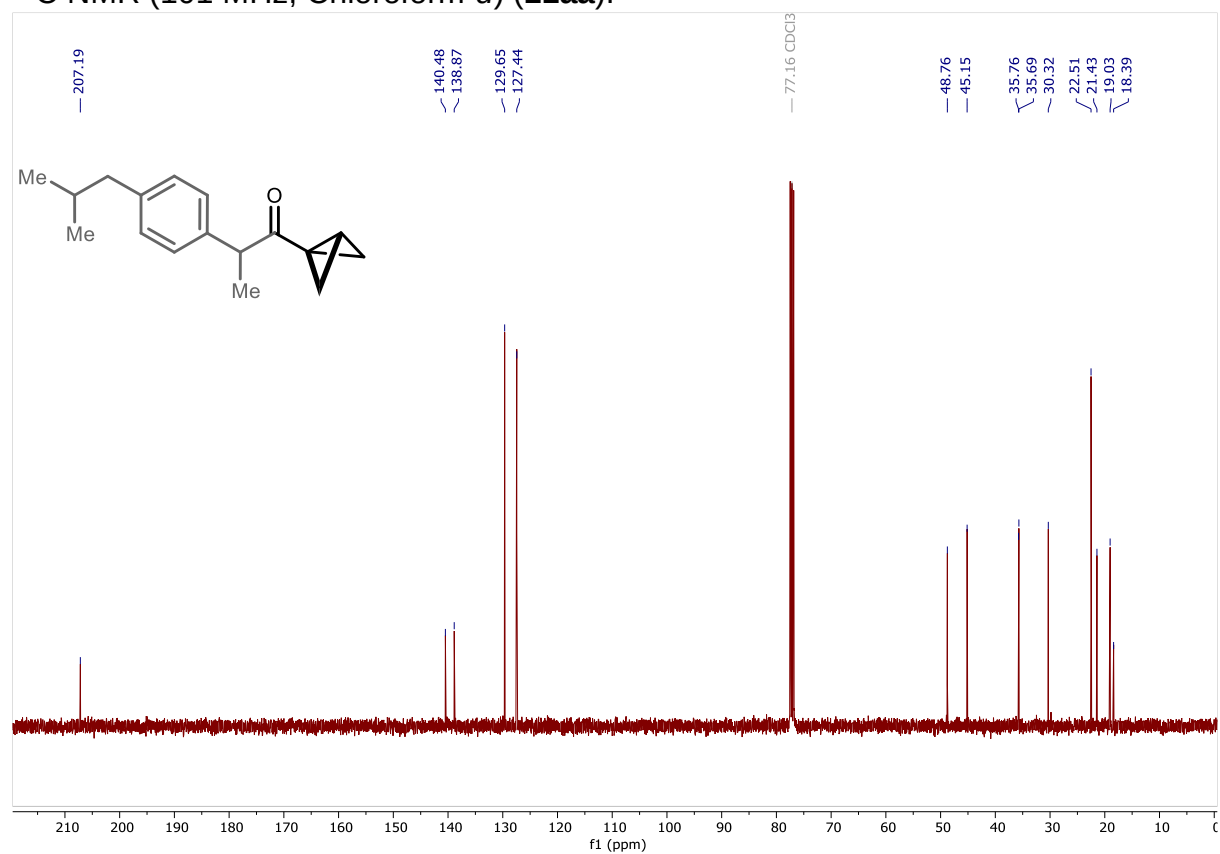
¹³C NMR (126 MHz, Chloroform-*d*) (**11z**):



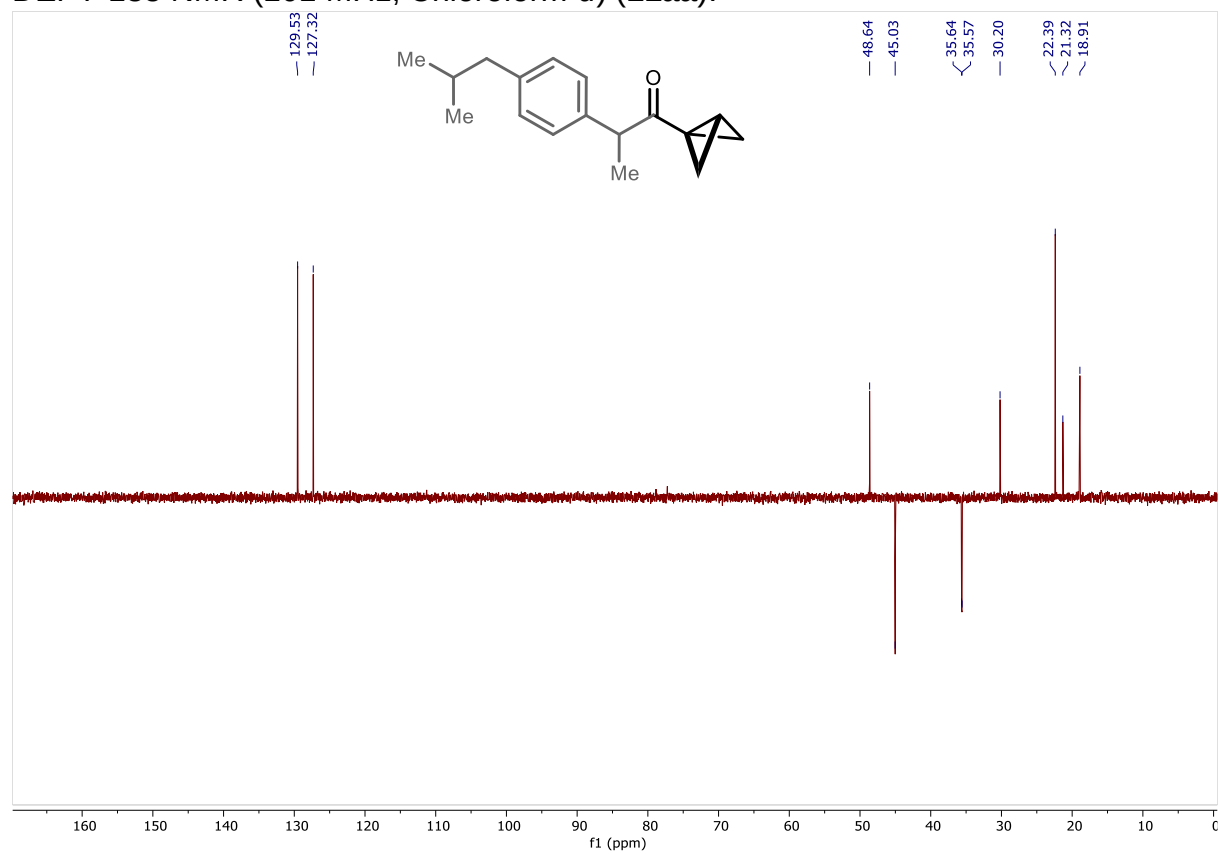
^1H NMR (400 MHz, Chloroform-*d*) (**11aa**):



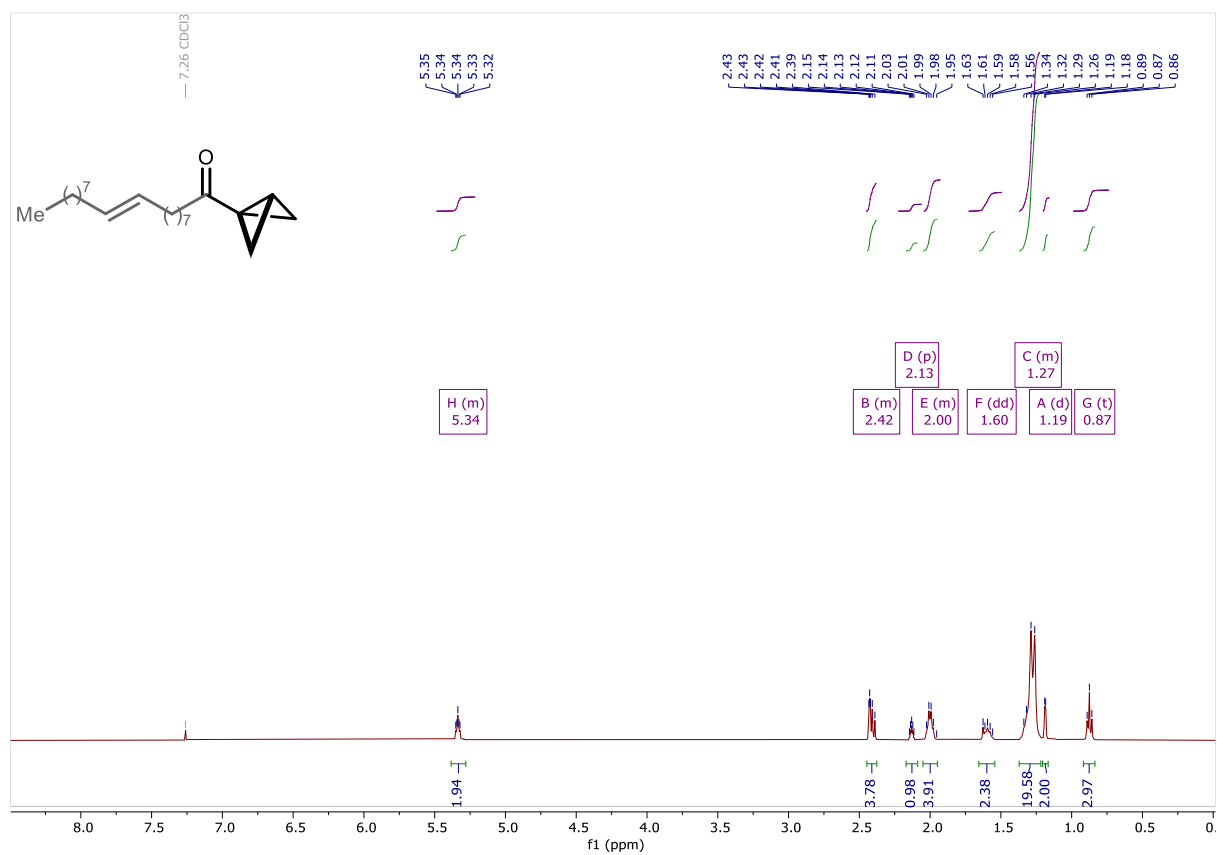
^{13}C NMR (101 MHz, Chloroform-*d*) (**11aa**):



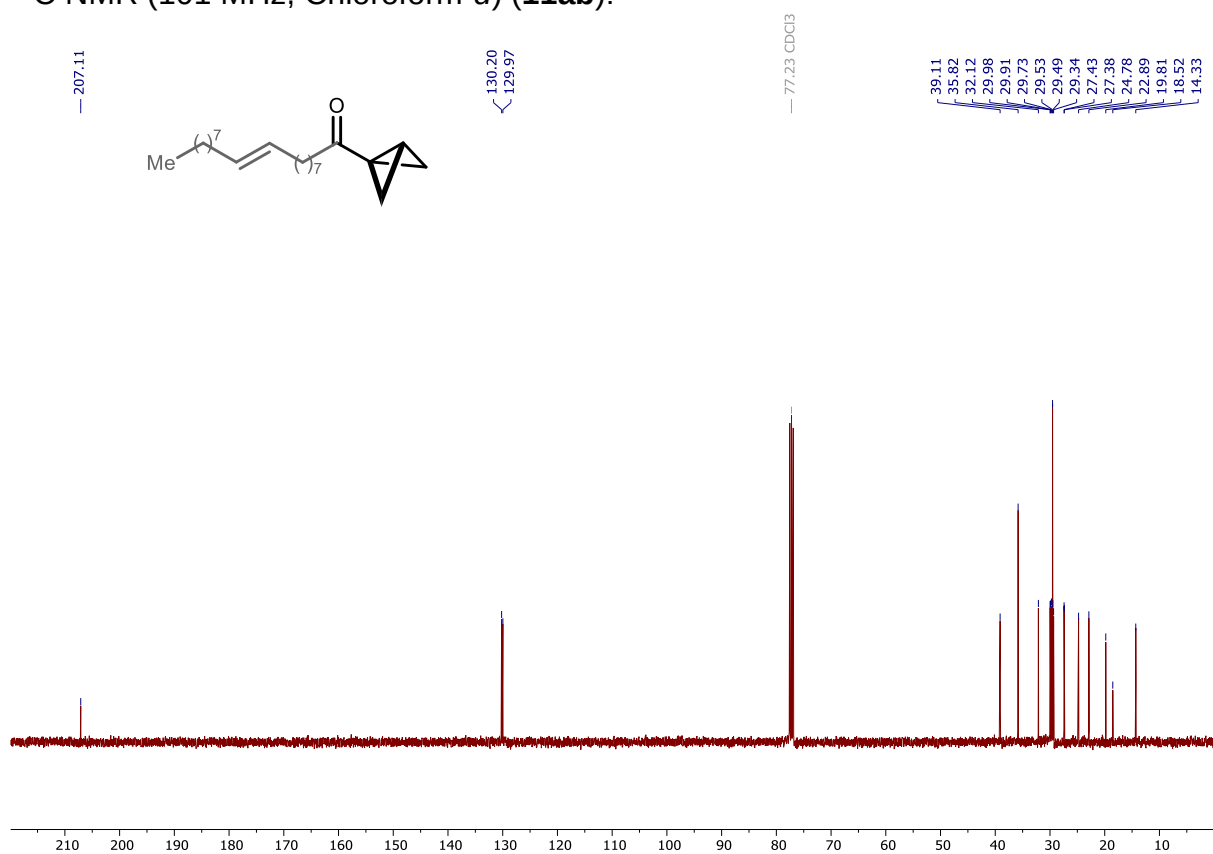
DEPT-135 NMR (101 MHz, Chloroform-*d*) (**11aa**):



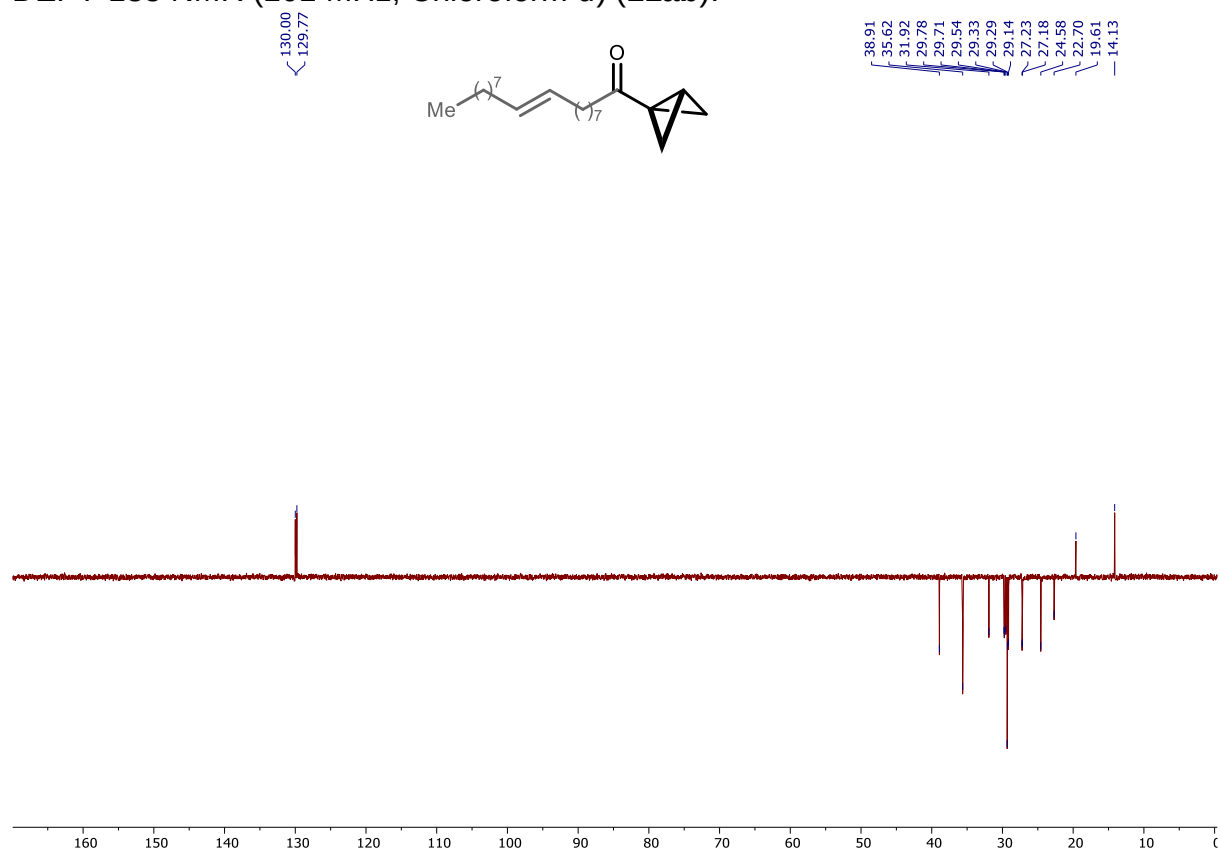
^1H NMR (400 MHz, Chloroform-*d*) (**11ab**):



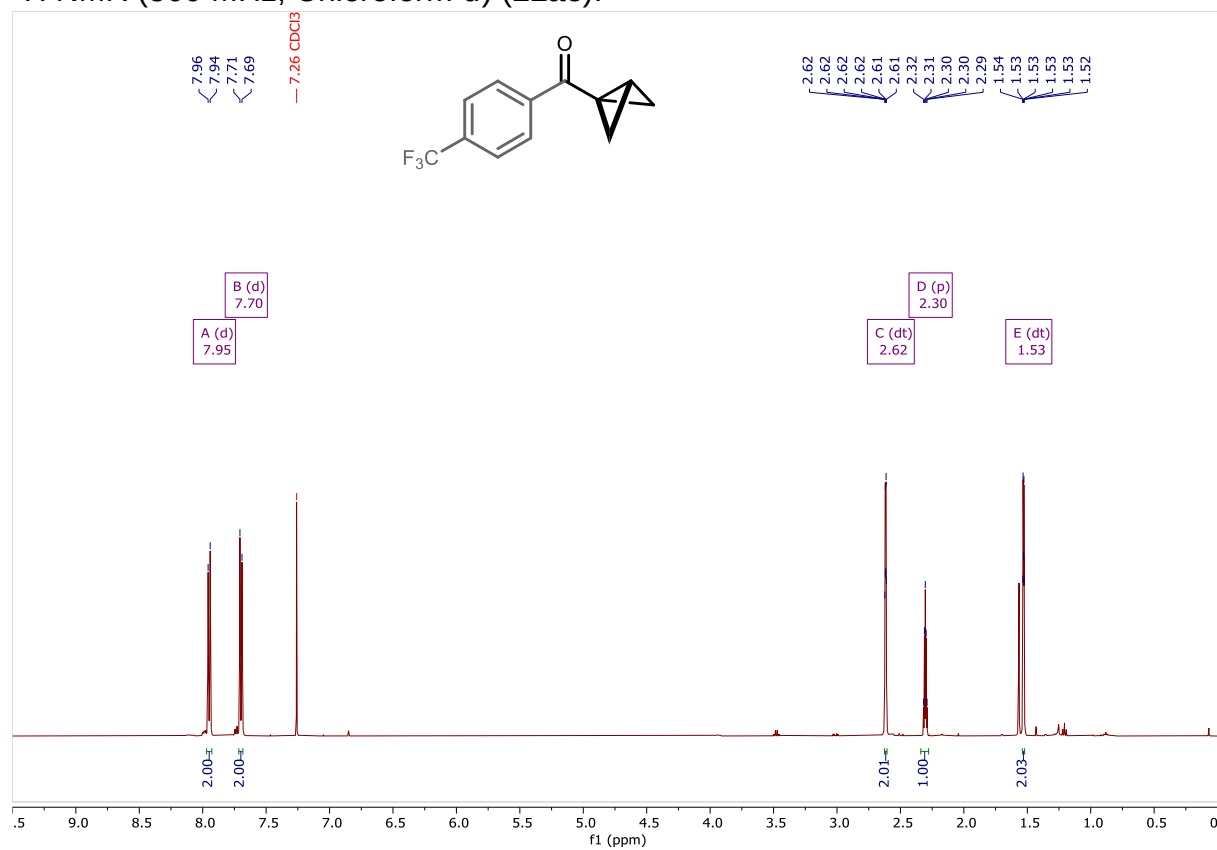
^{13}C NMR (101 MHz, Chloroform-*d*) (**11ab**):



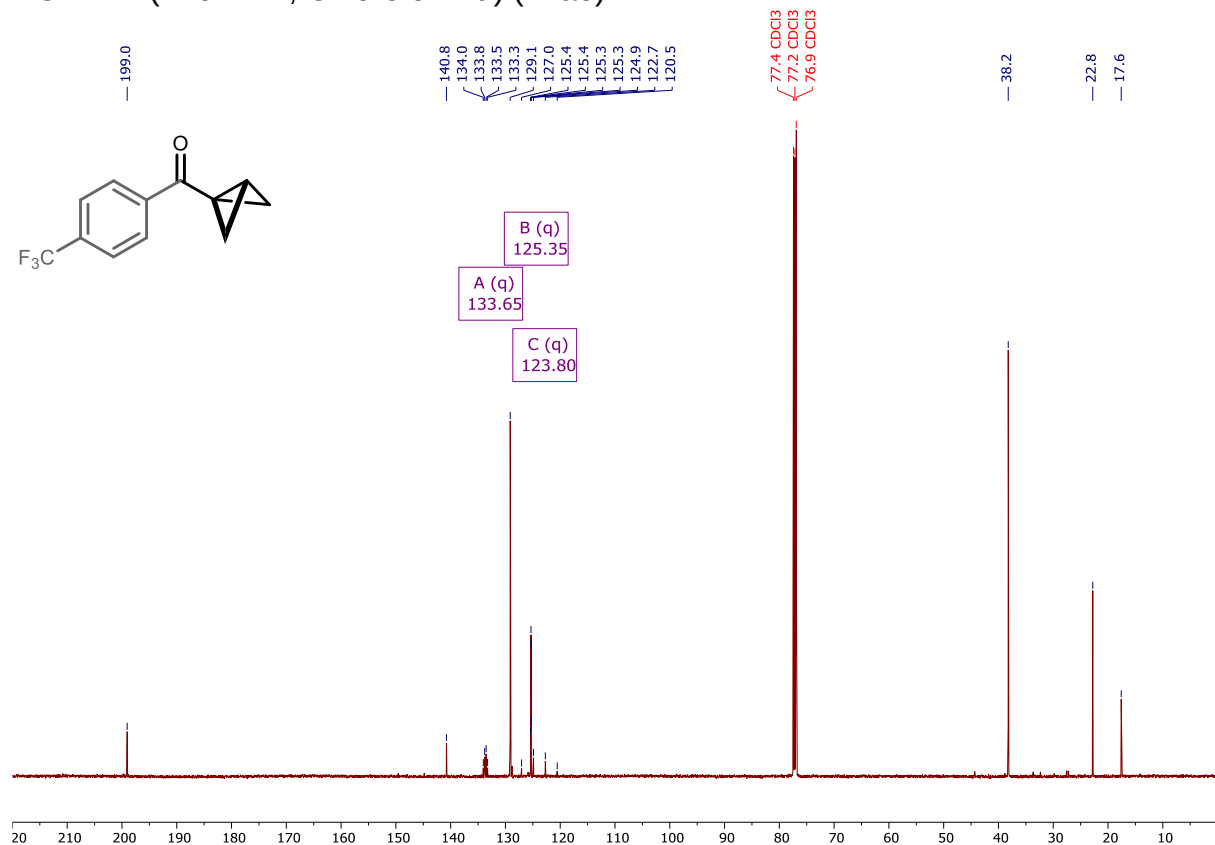
DEPT-135 NMR (101 MHz, Chloroform-*d*) (**11ab**):



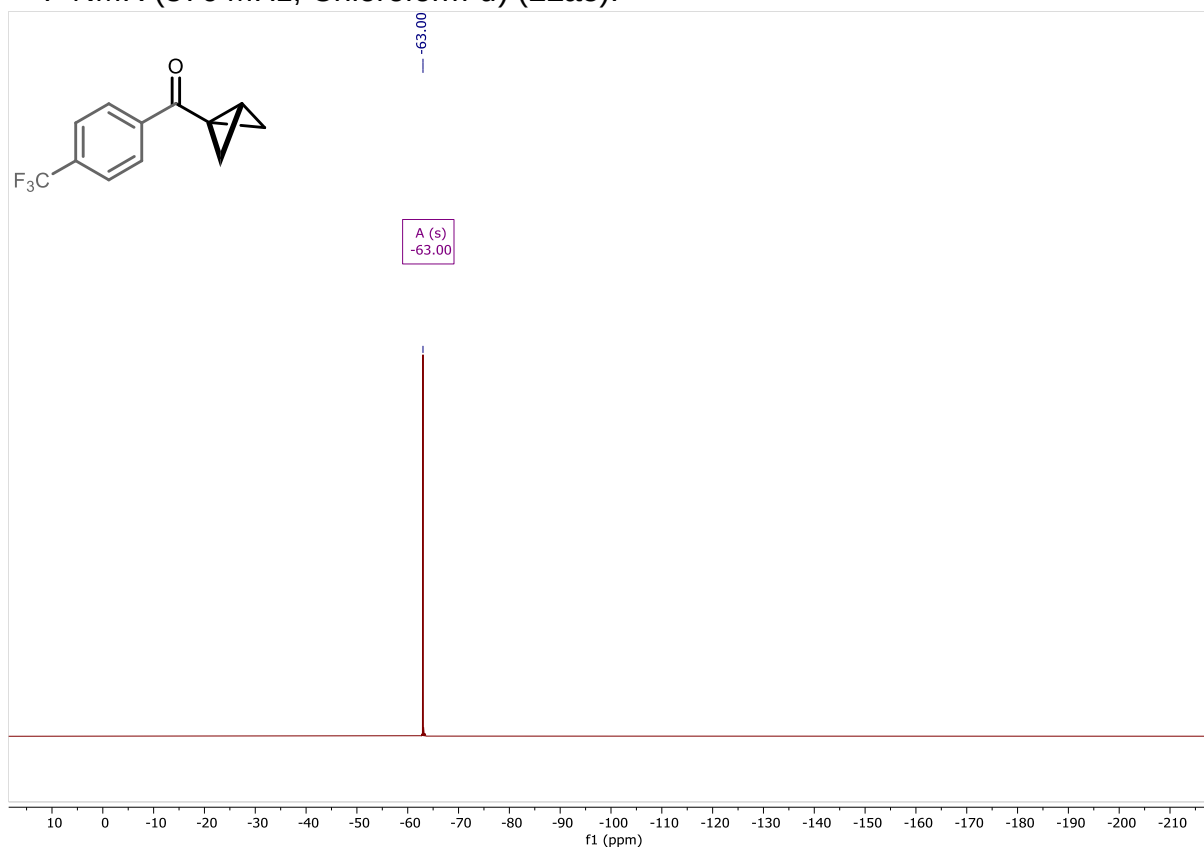
^1H NMR (500 MHz, Chloroform-*d*) (**11ac**):



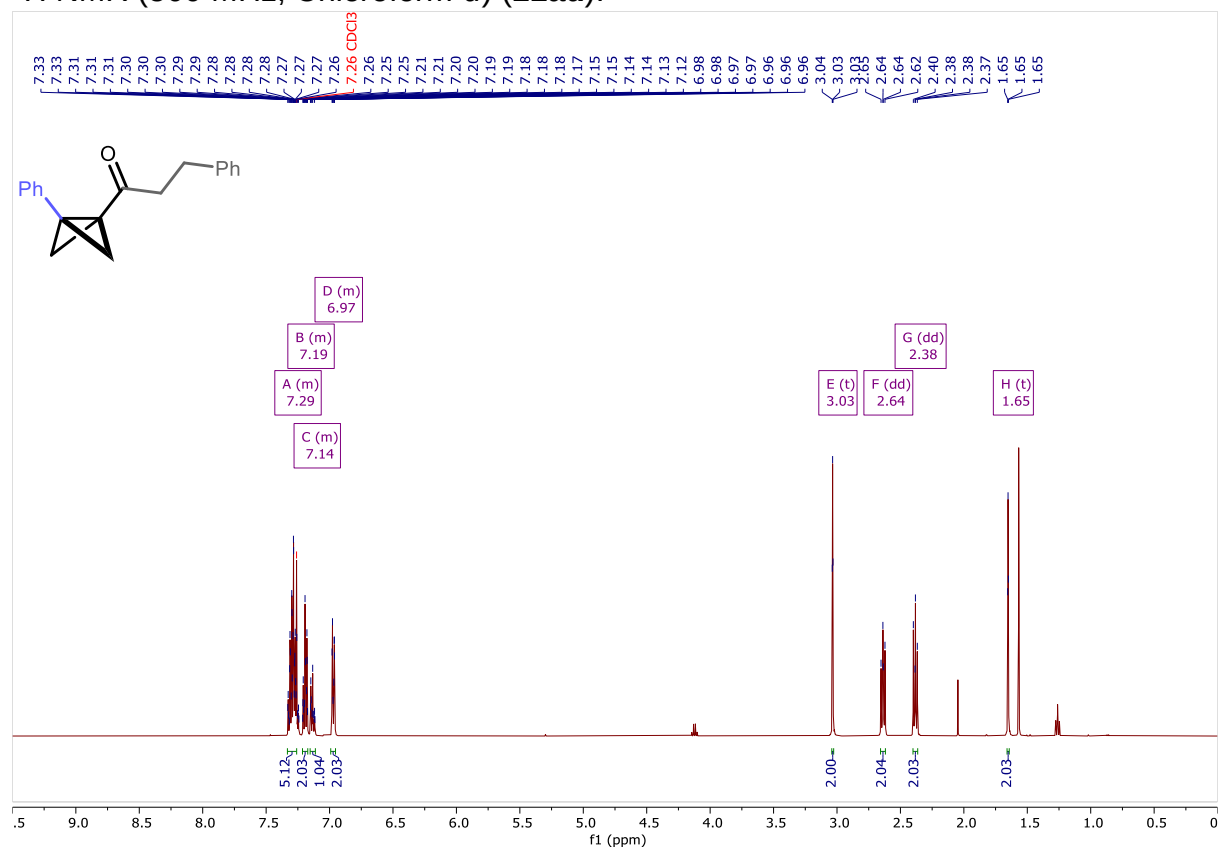
^{13}C NMR (126 MHz, Chloroform-*d*) (**11ac**):



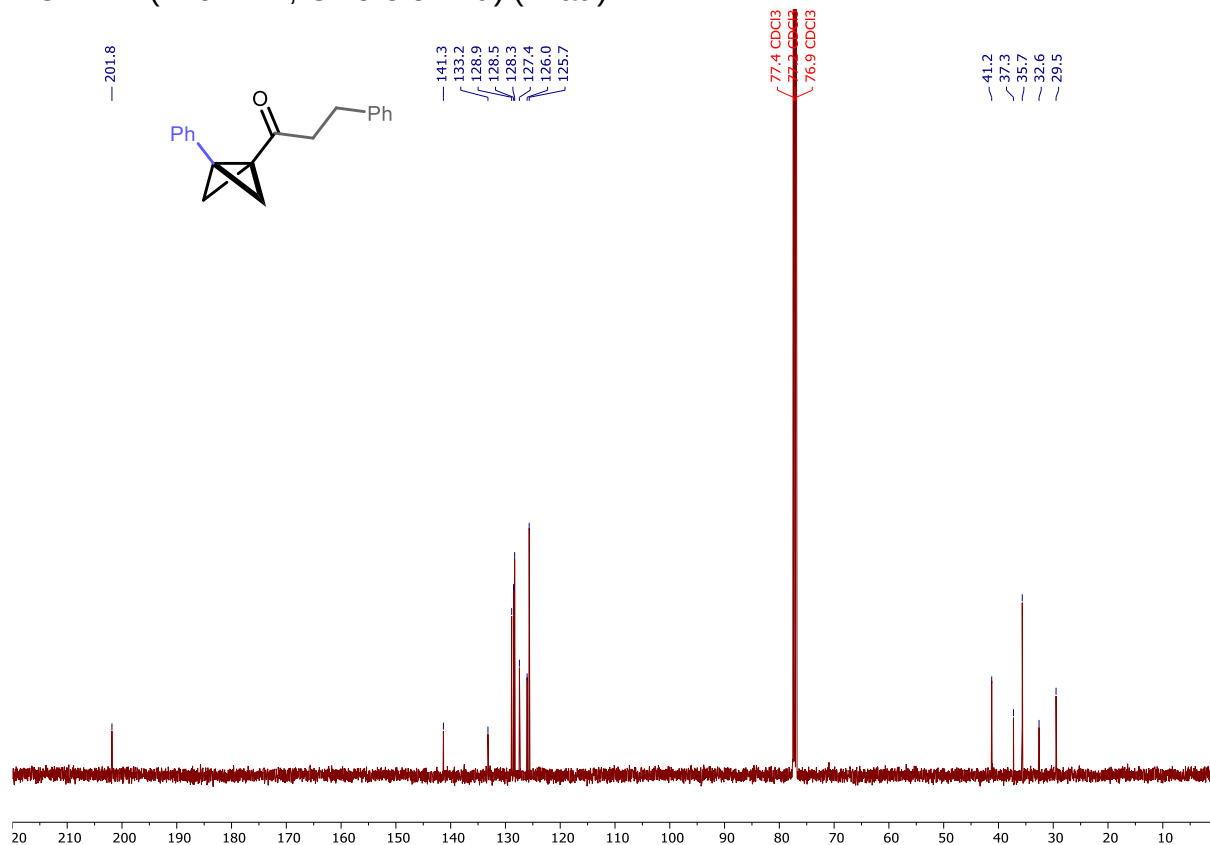
^{111}F NMR (376 MHz, Chloroform-*d*) (**11ac**):



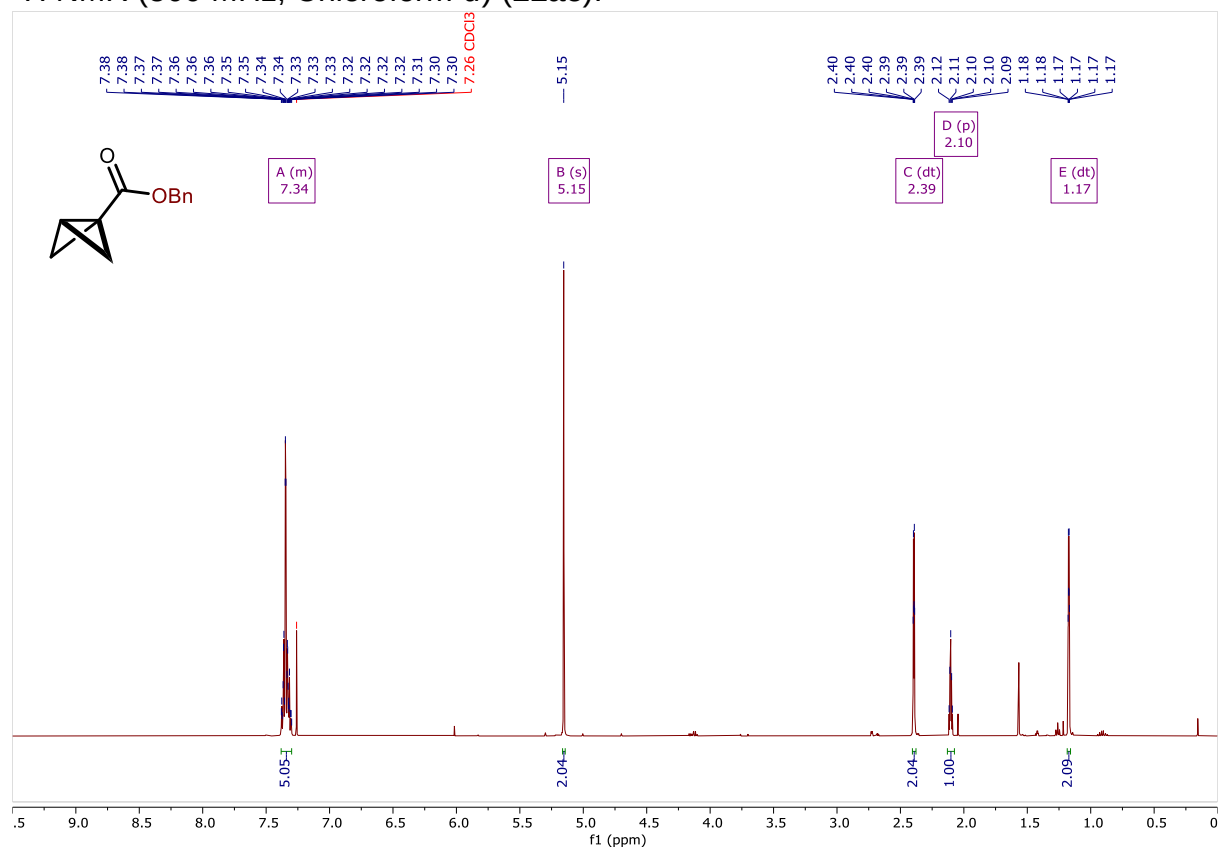
¹H NMR (500 MHz, Chloroform-*d*) (**11ad**):



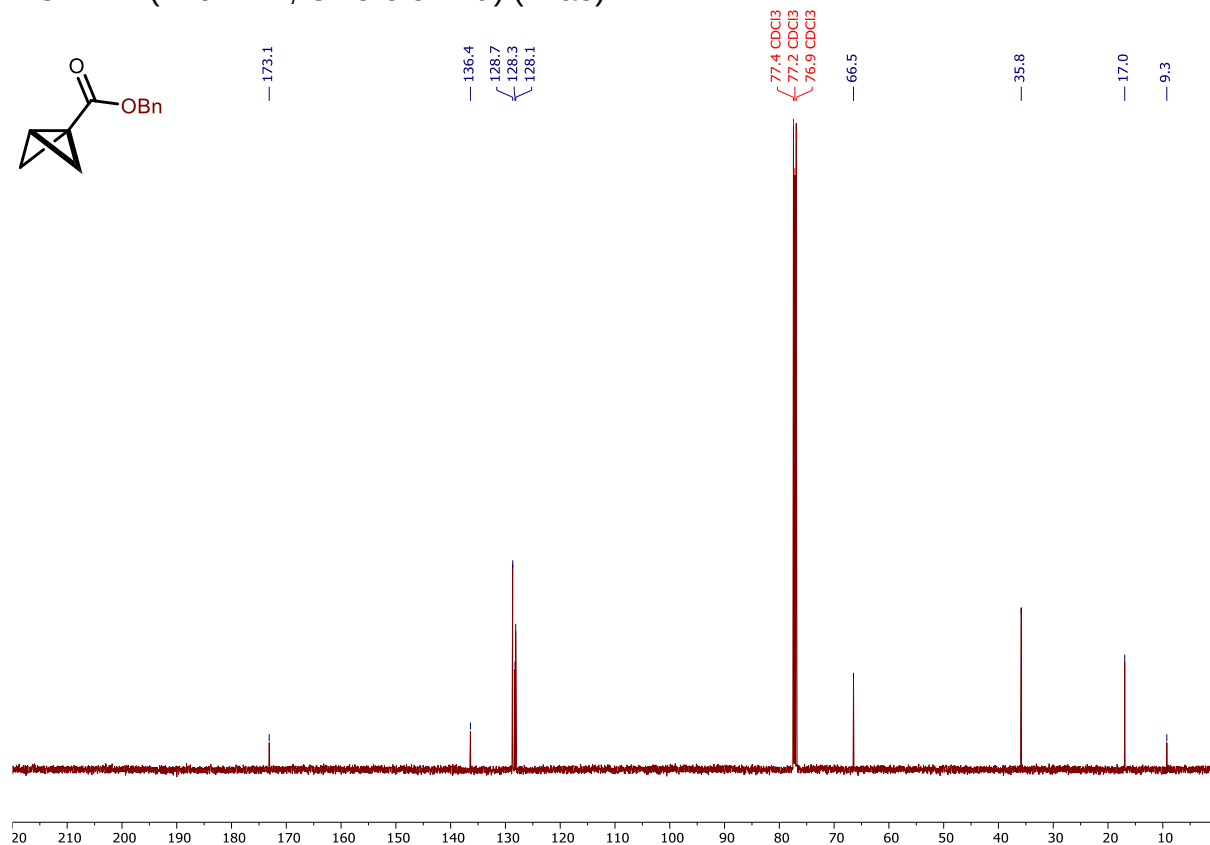
¹³C NMR (126 MHz, Chloroform-*d*) (**11ad**):



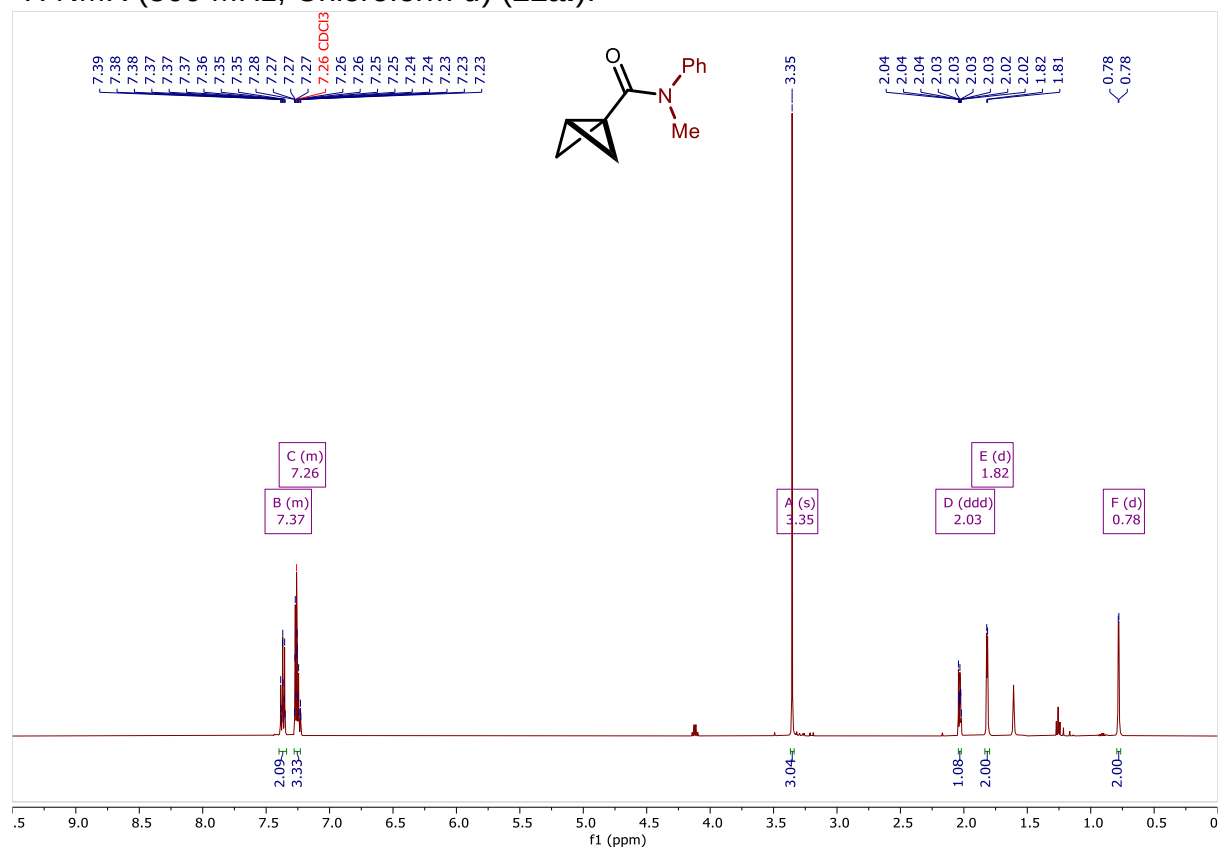
¹H NMR (500 MHz, Chloroform-*d*) (**11ae**):



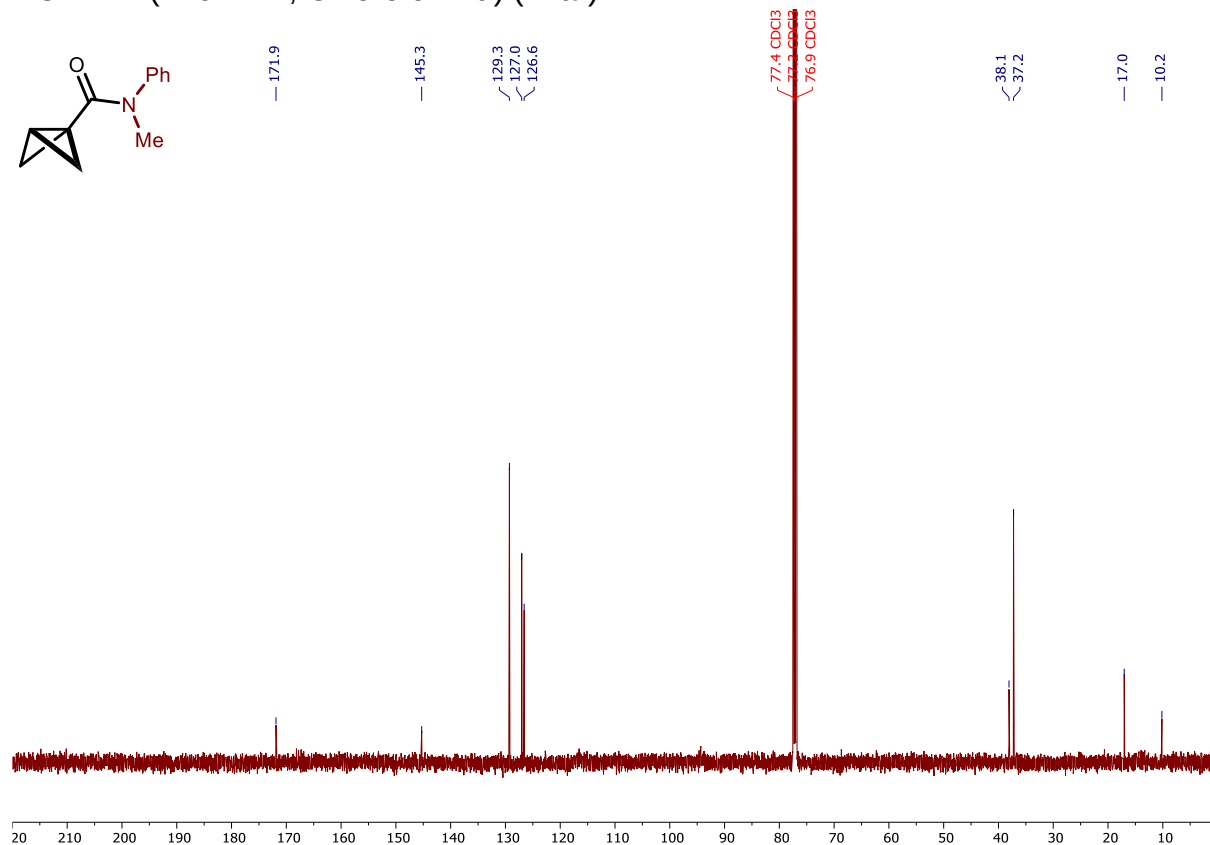
¹³C NMR (126 MHz, Chloroform-*d*) (**11ae**):



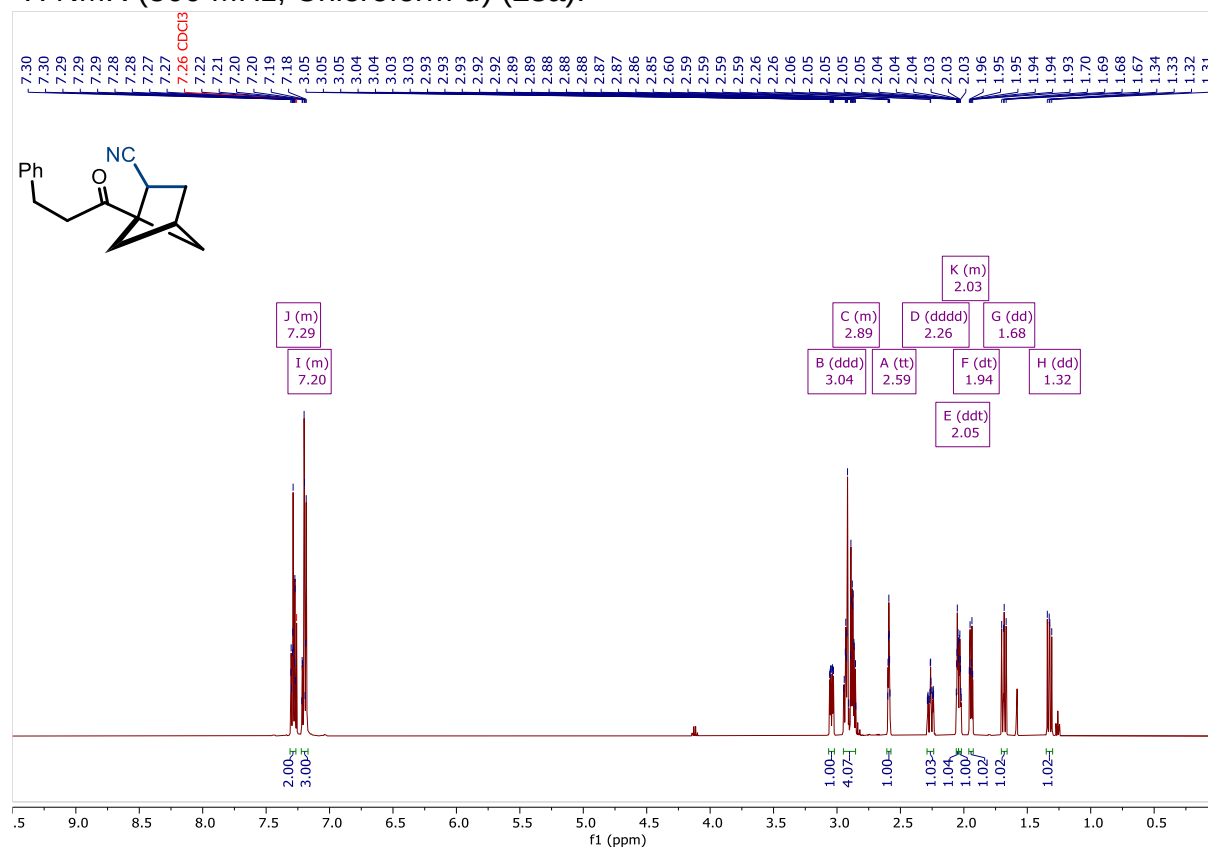
¹H NMR (500 MHz, Chloroform-*d*) (**11af**):



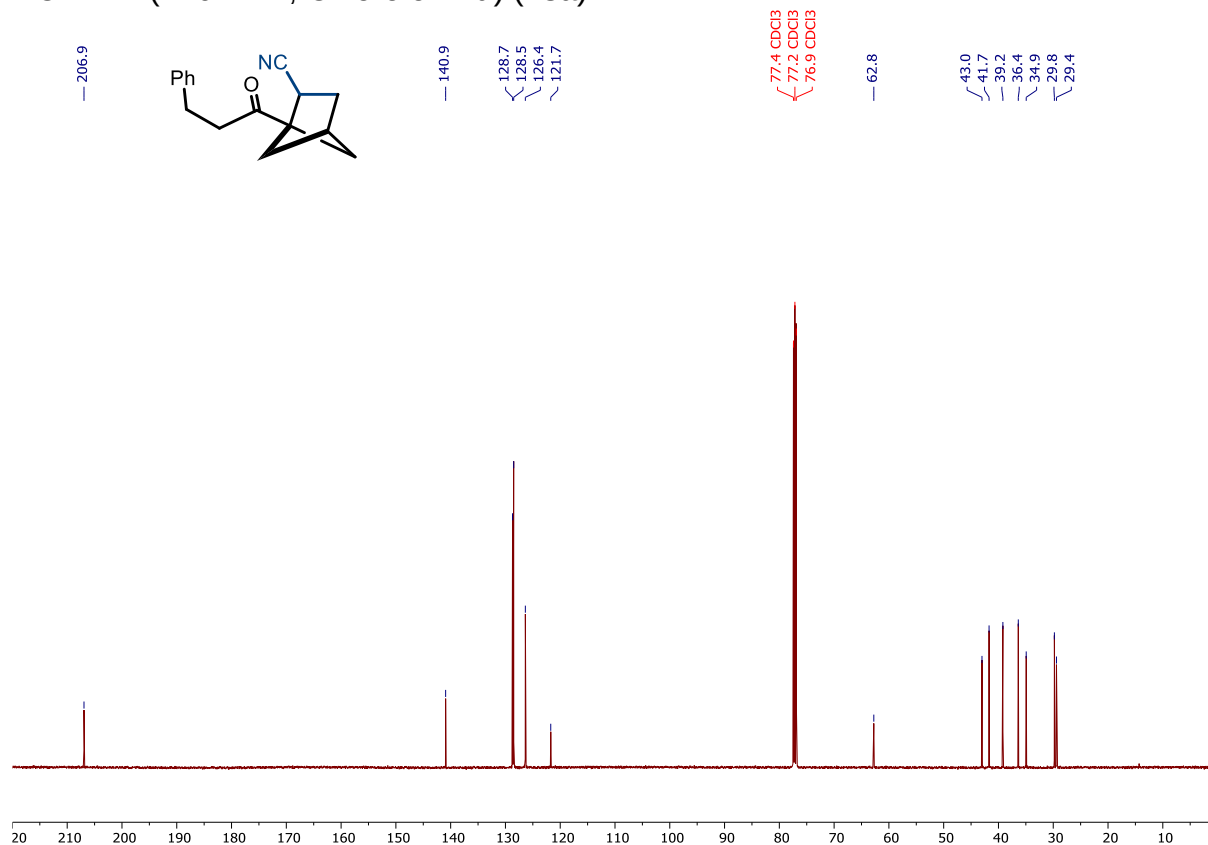
¹³C NMR (126 MHz, Chloroform-*d*) (**11af**):



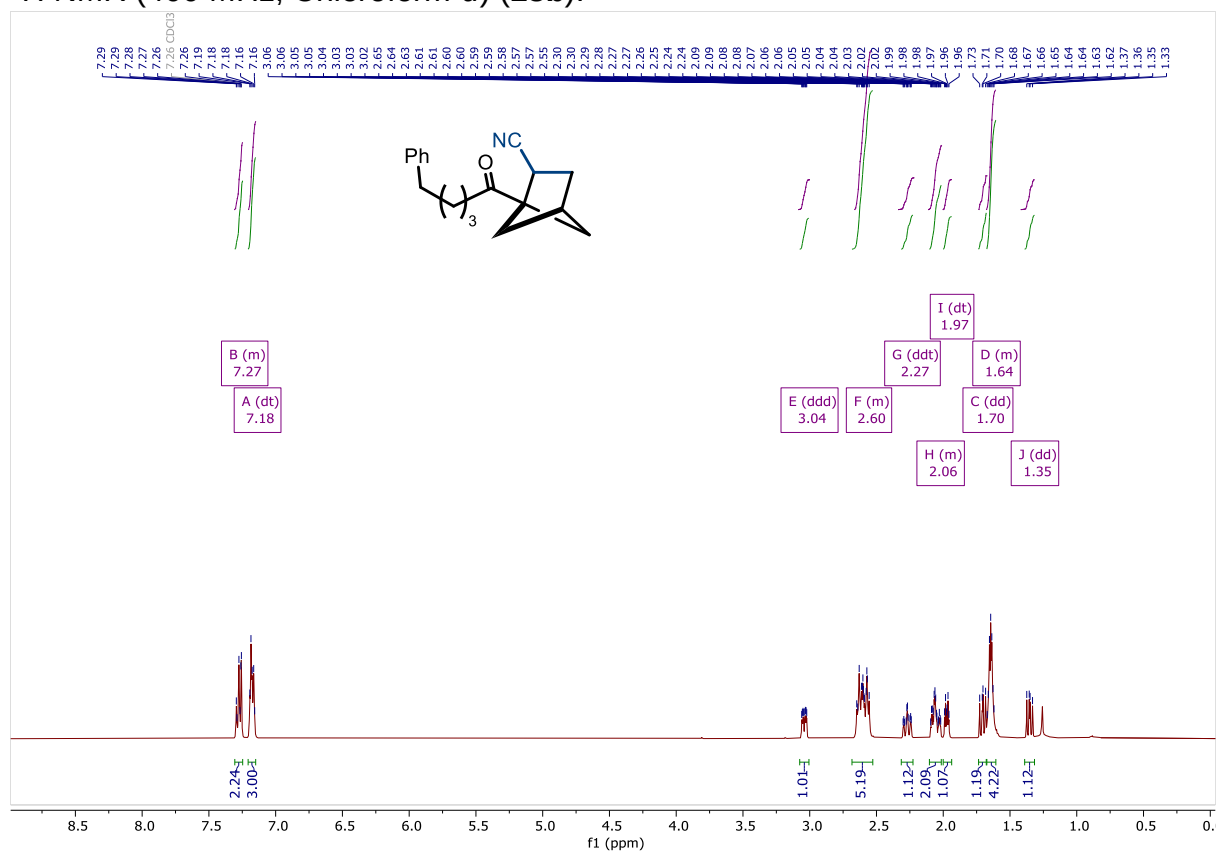
¹H NMR (500 MHz, Chloroform-*d*) (**13a**):



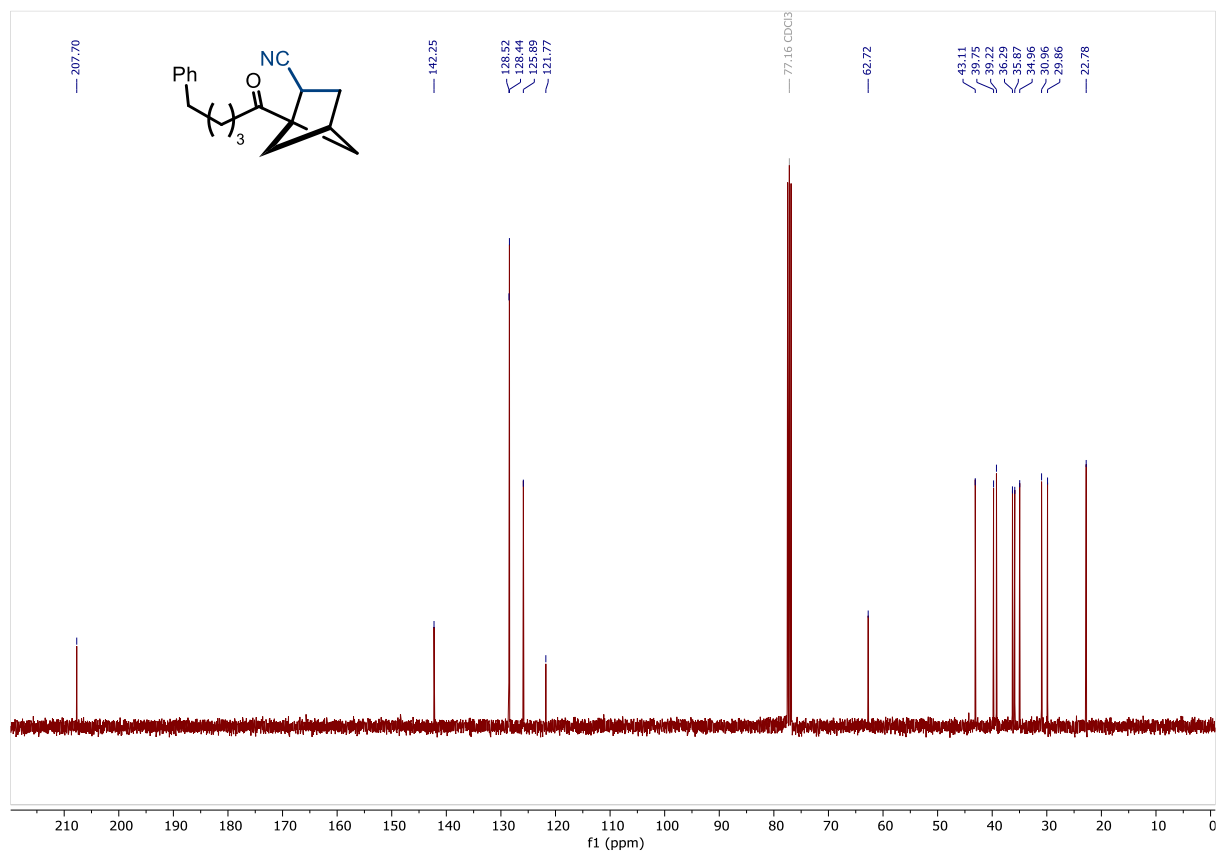
¹³C NMR (126 MHz, Chloroform-*d*) (**13a**):



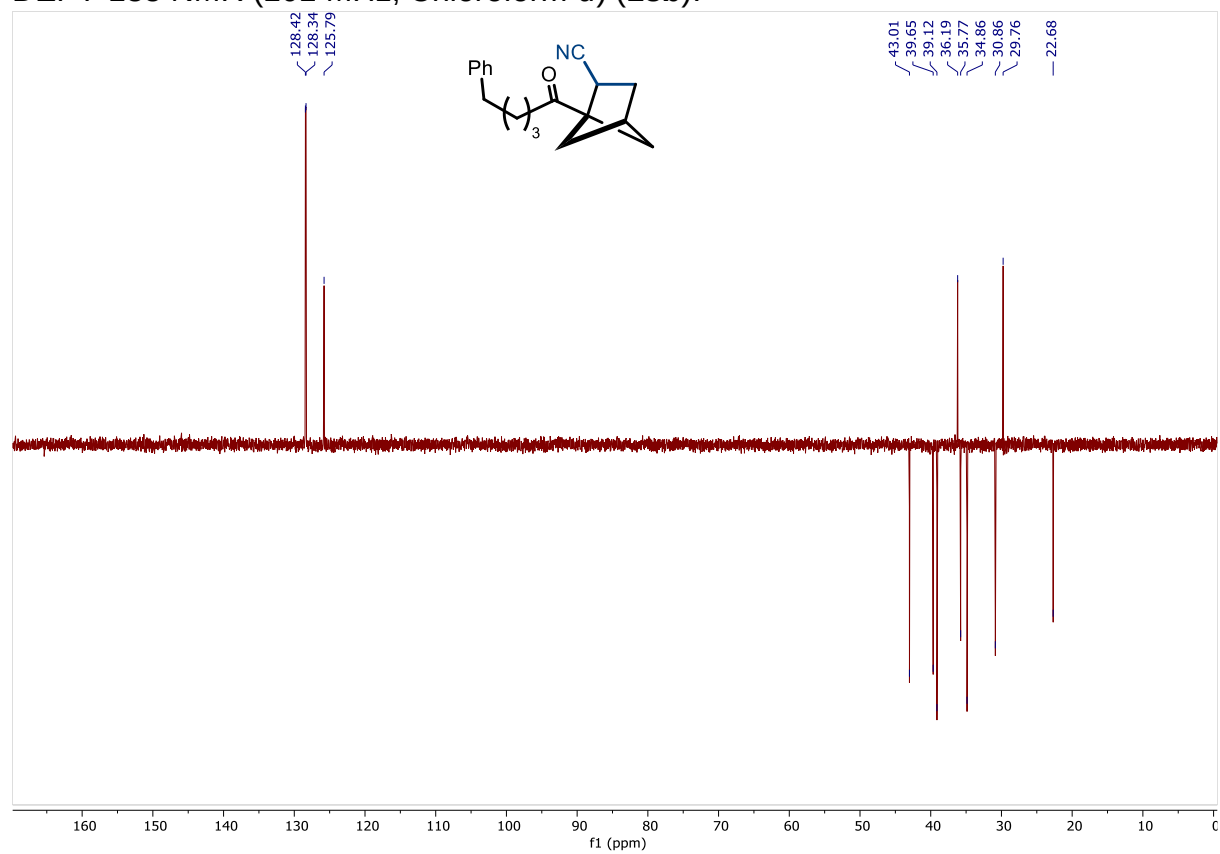
¹H NMR (400 MHz, Chloroform-*d*) (**13b**):



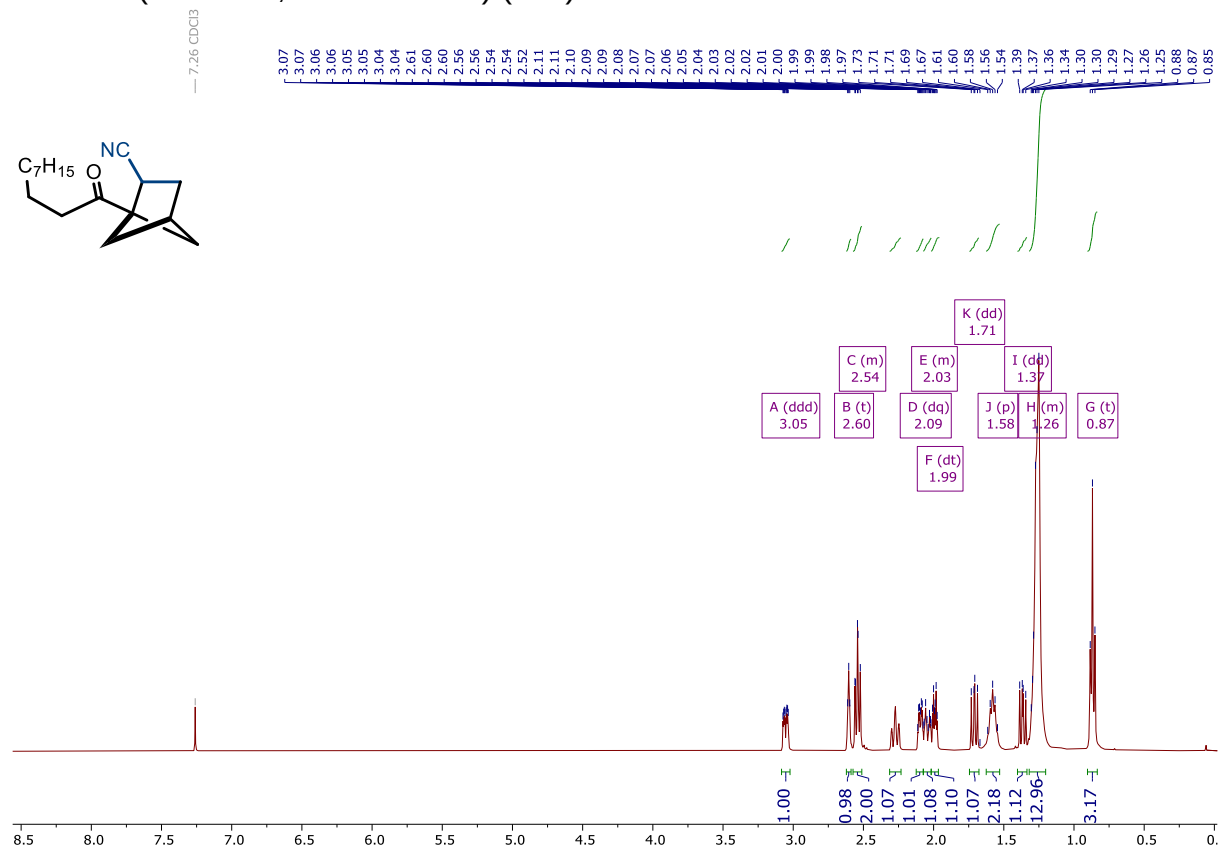
¹³C NMR (101 MHz, Chloroform-*d*) (**13b**):



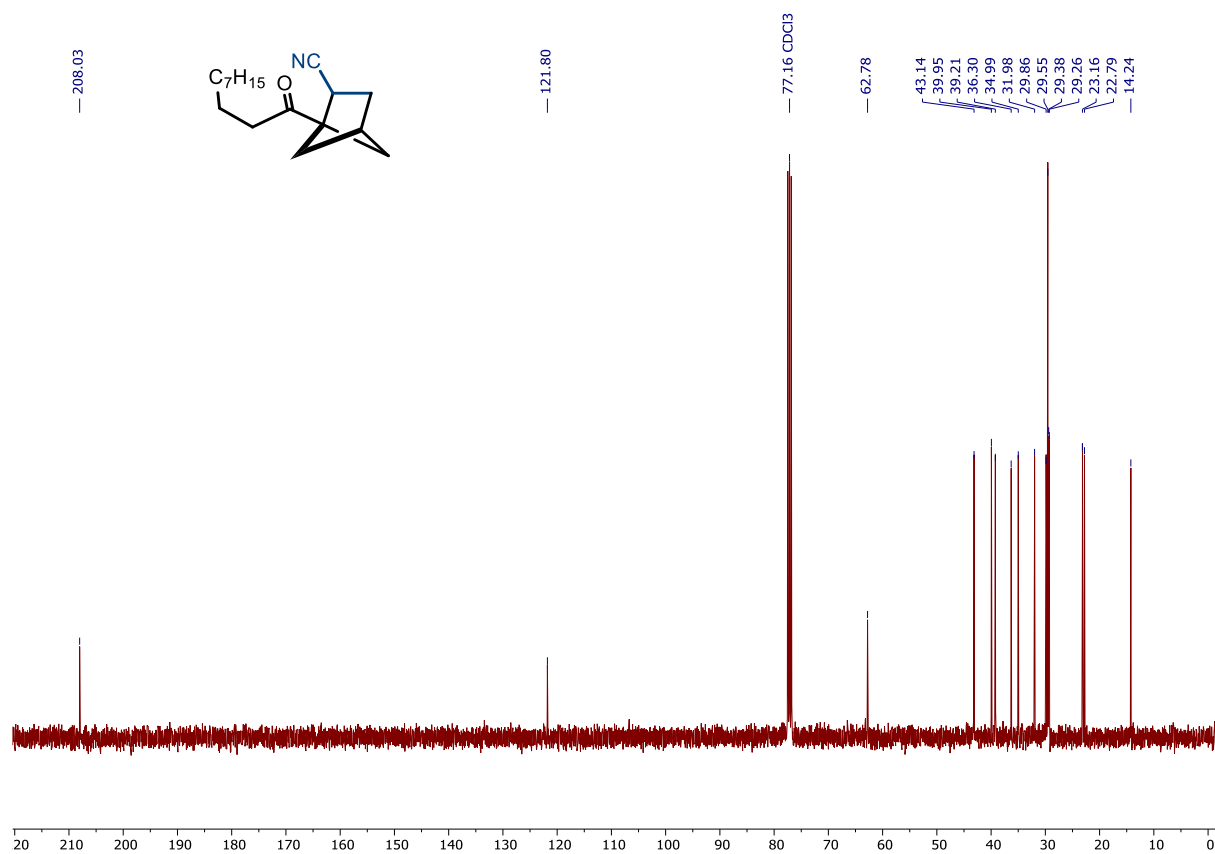
DEPT-135 NMR (101 MHz, Chloroform-*d*) (**13b**):



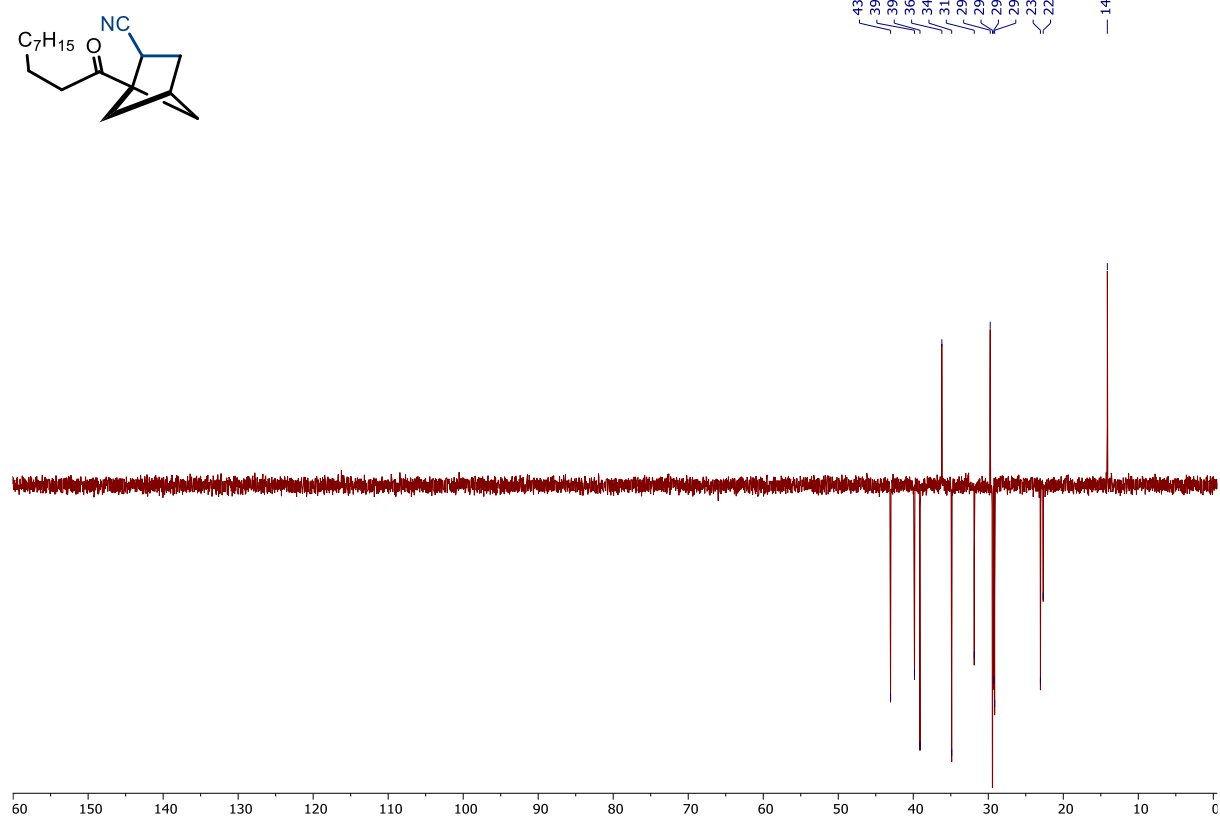
^1H NMR (400 MHz, Chloroform-*d*) (**13c**):



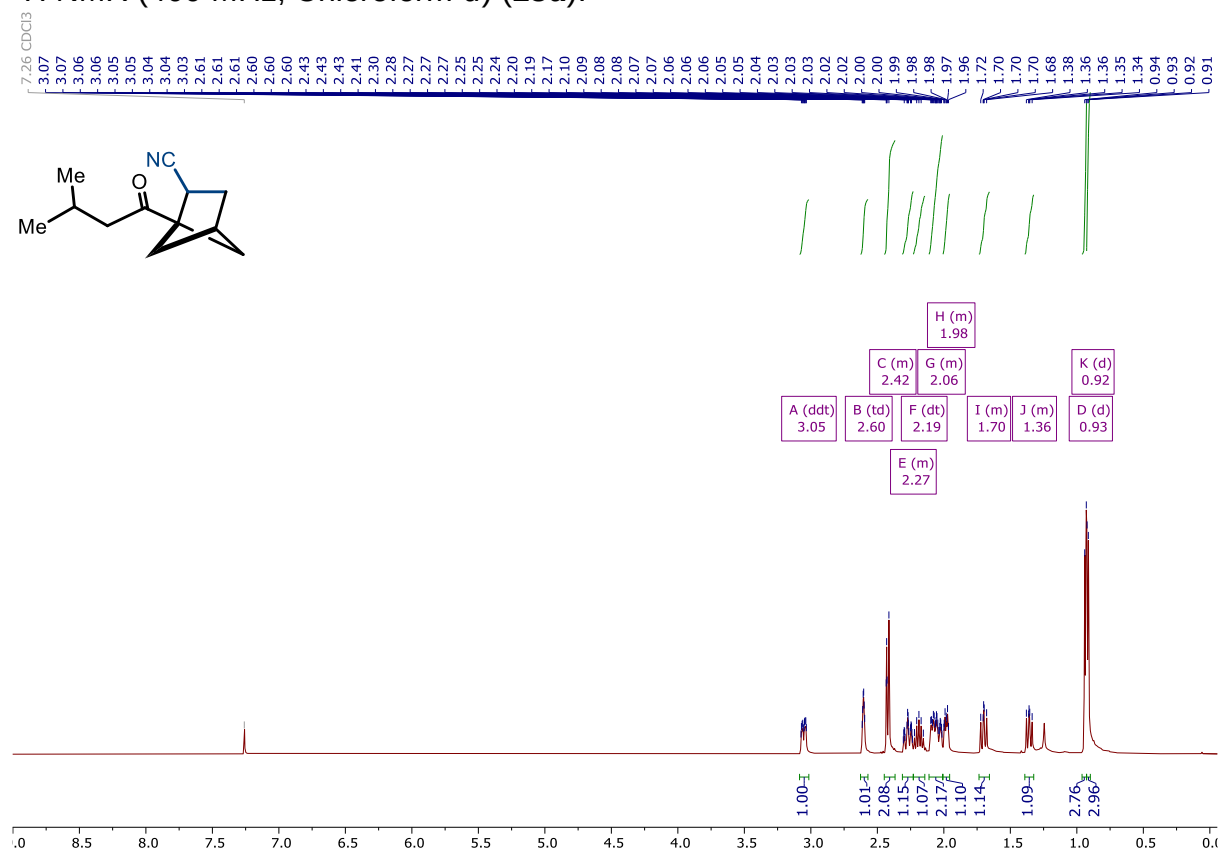
^{13}C NMR (101 MHz, Chloroform-*d*) (**13c**):



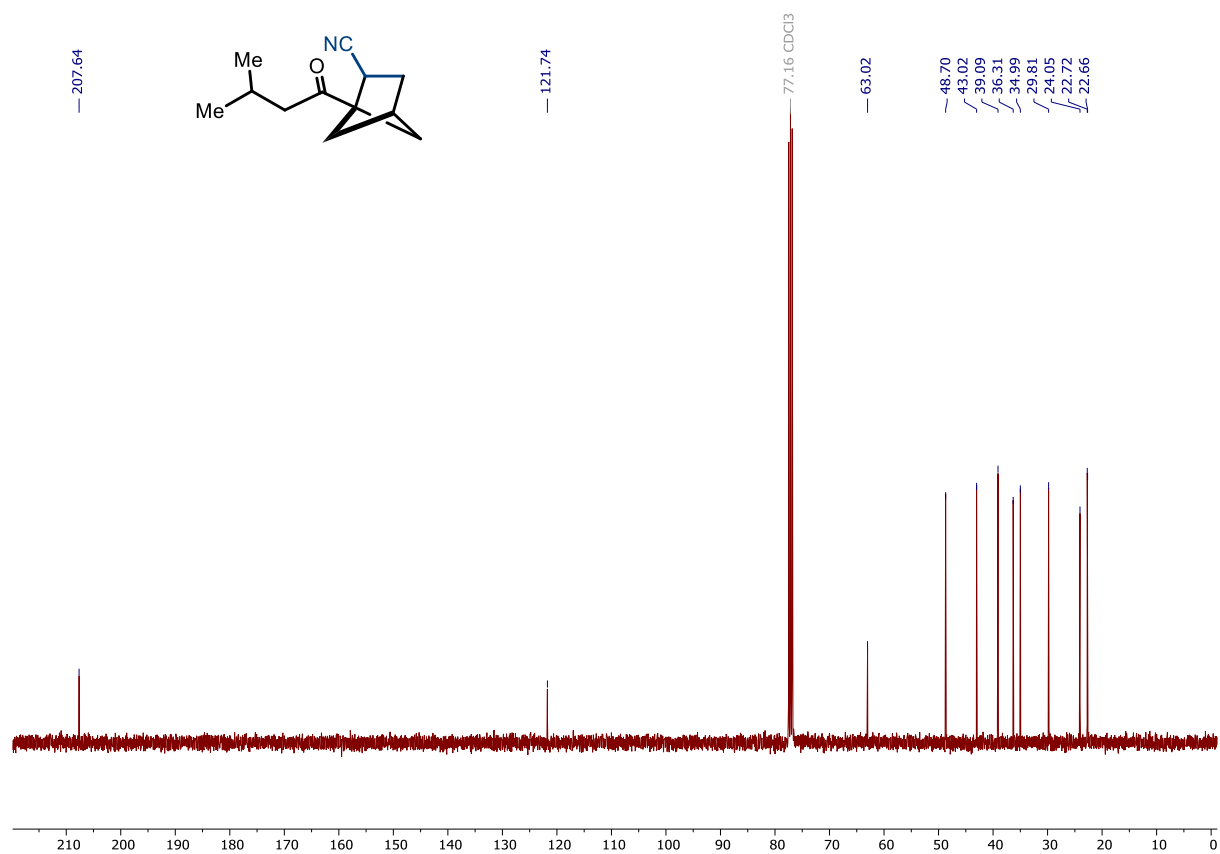
DEPT-135 NMR (101 MHz, Chloroform-*d*) (**13c**):



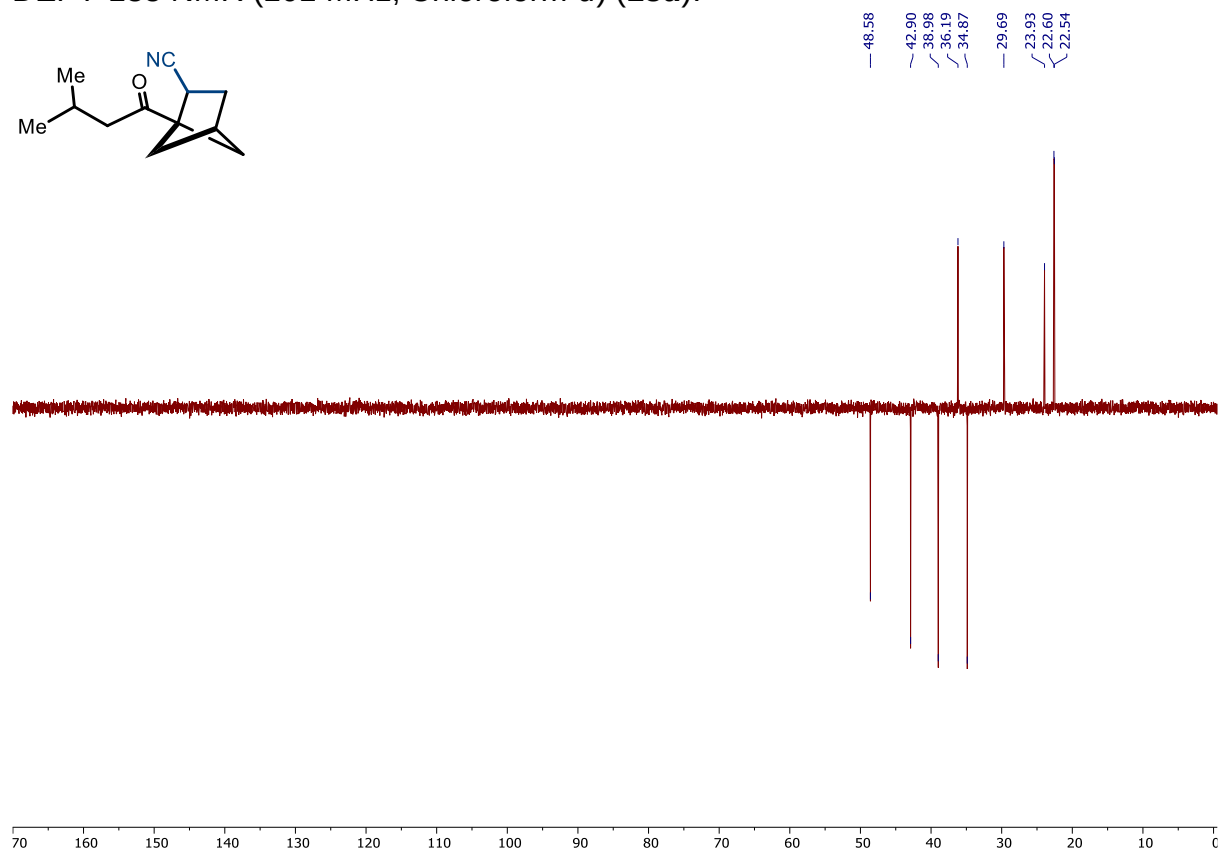
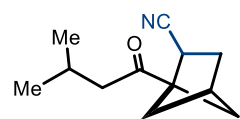
¹H NMR (400 MHz, Chloroform-*d*) (**13d**):



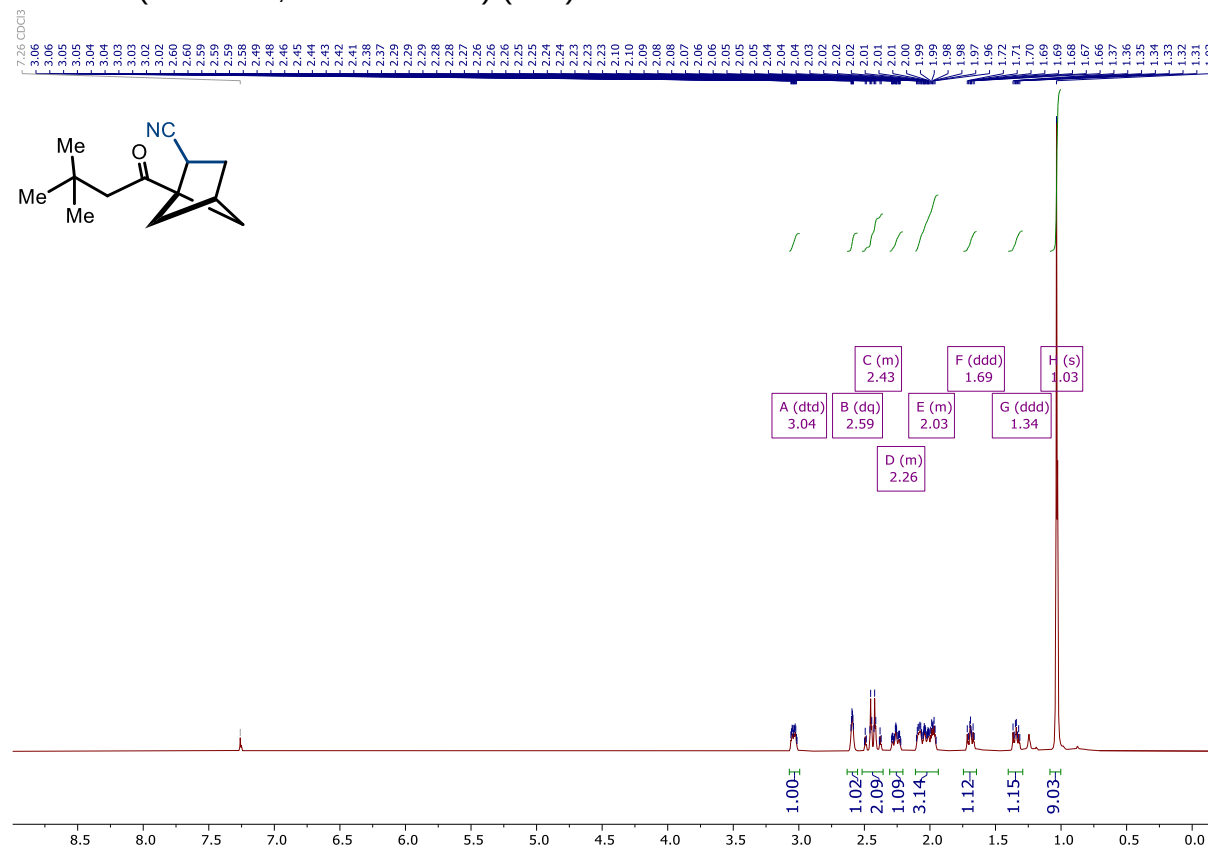
¹³C NMR (101 MHz, Chloroform-*d*) (**13d**):



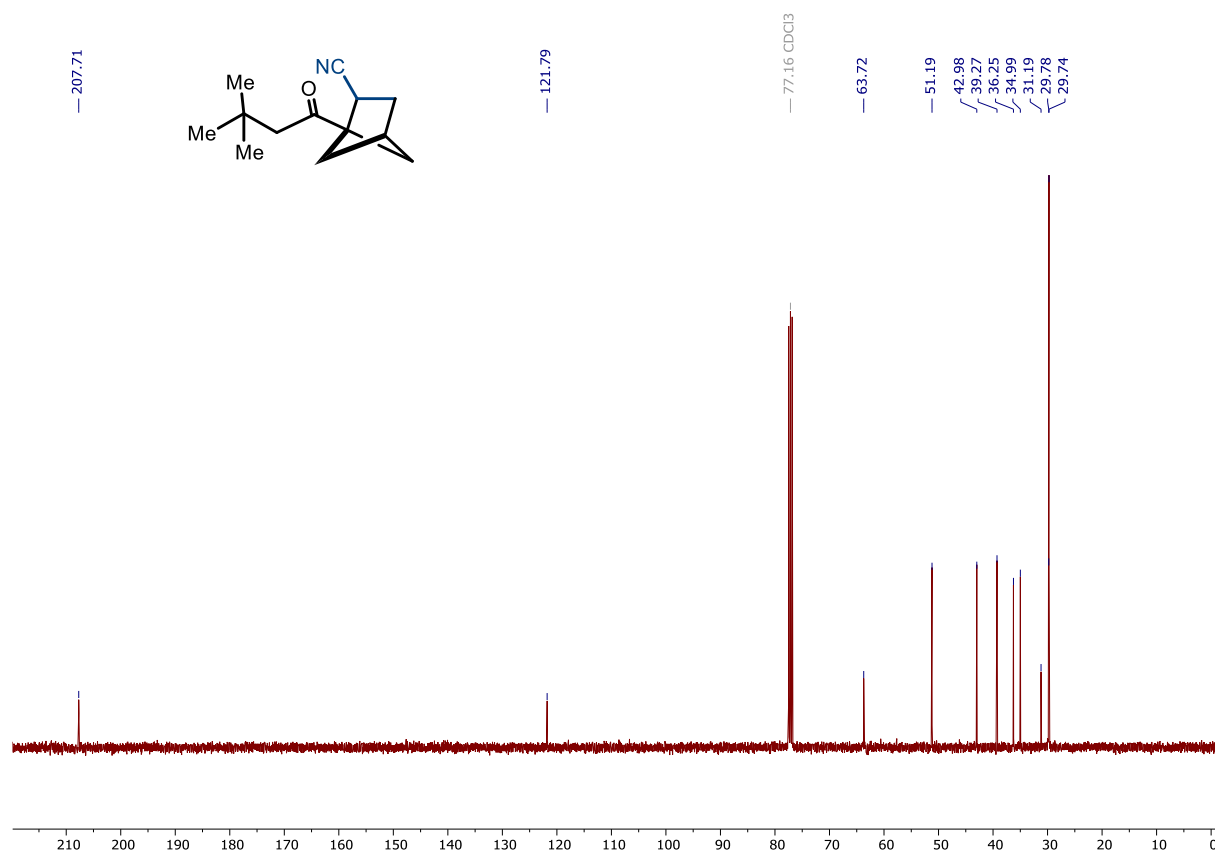
DEPT-135 NMR (101 MHz, Chloroform-*d*) (**13d**):



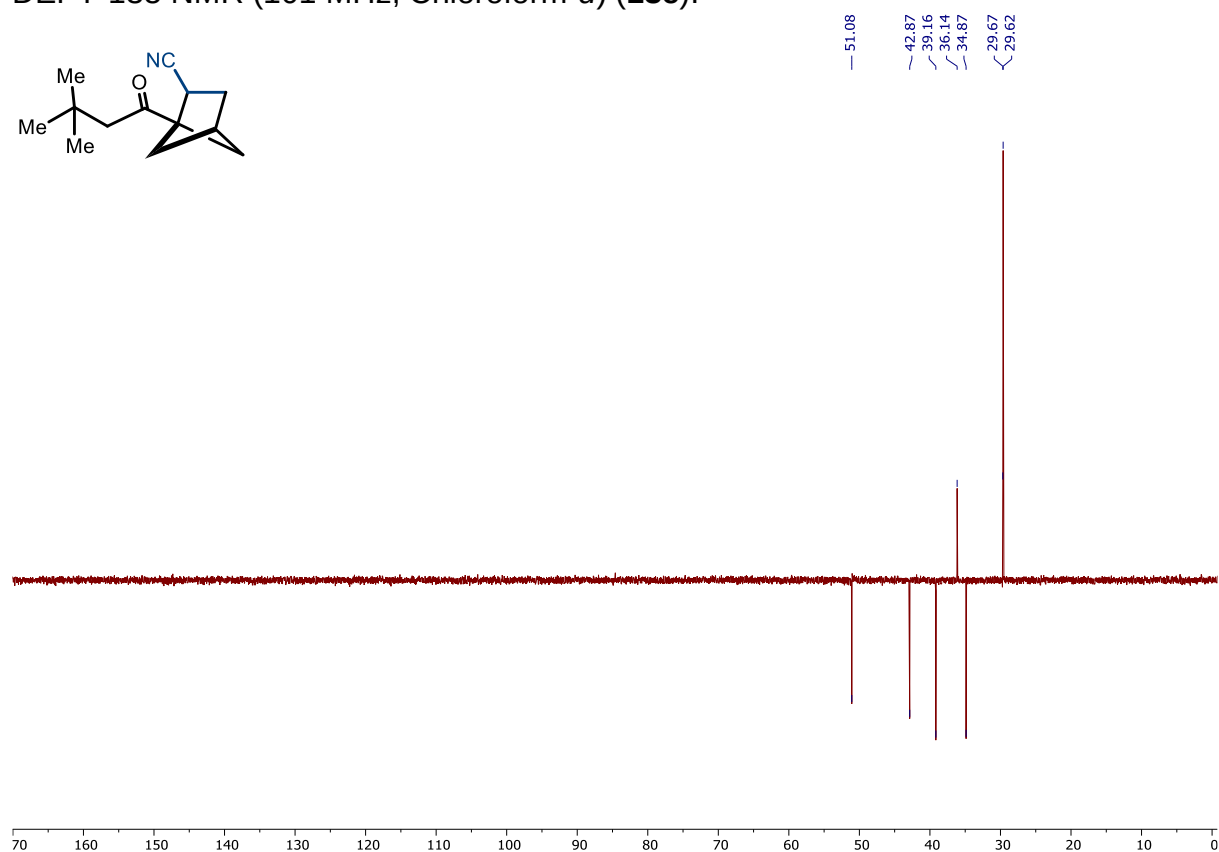
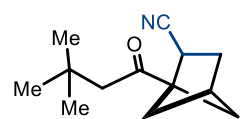
¹H NMR (400 MHz, Chloroform-*d*) (**13e**):



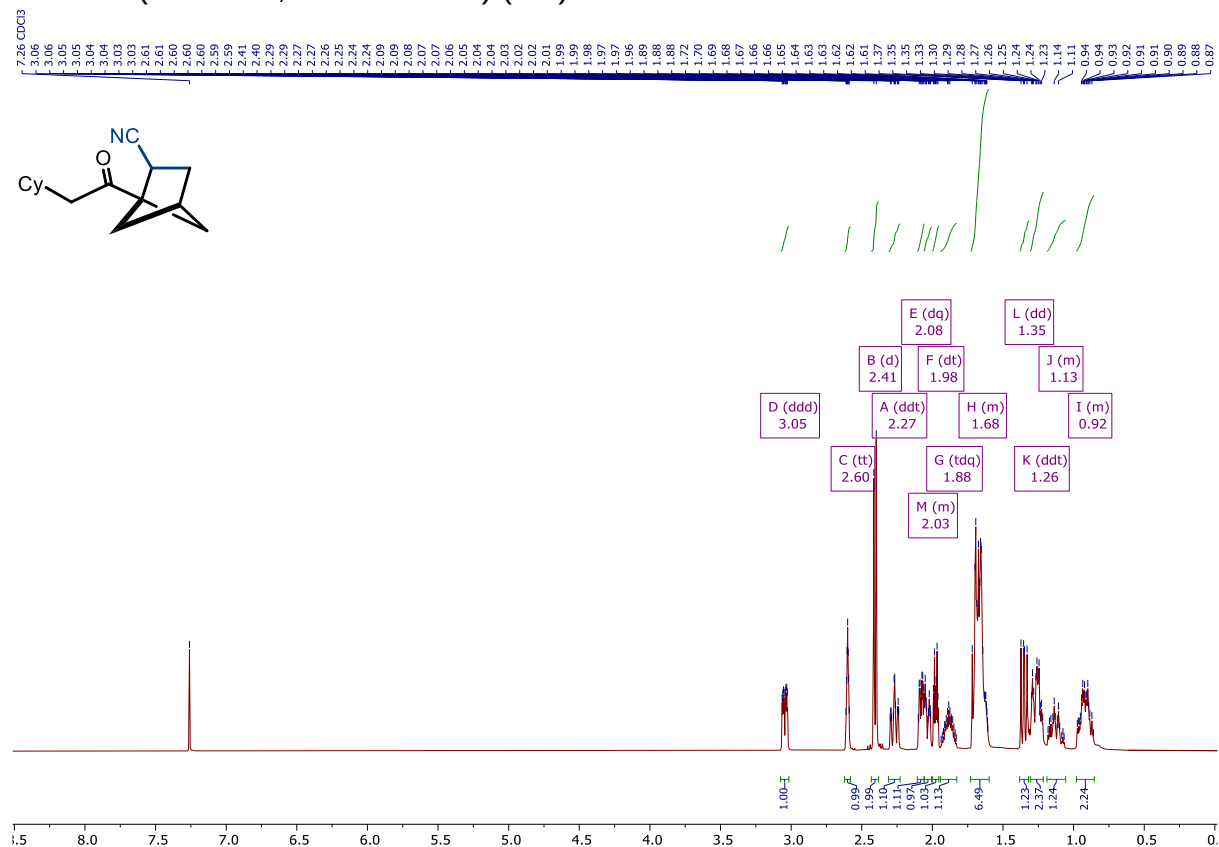
¹³C NMR (101 MHz, Chloroform-*d*) (**13e**):



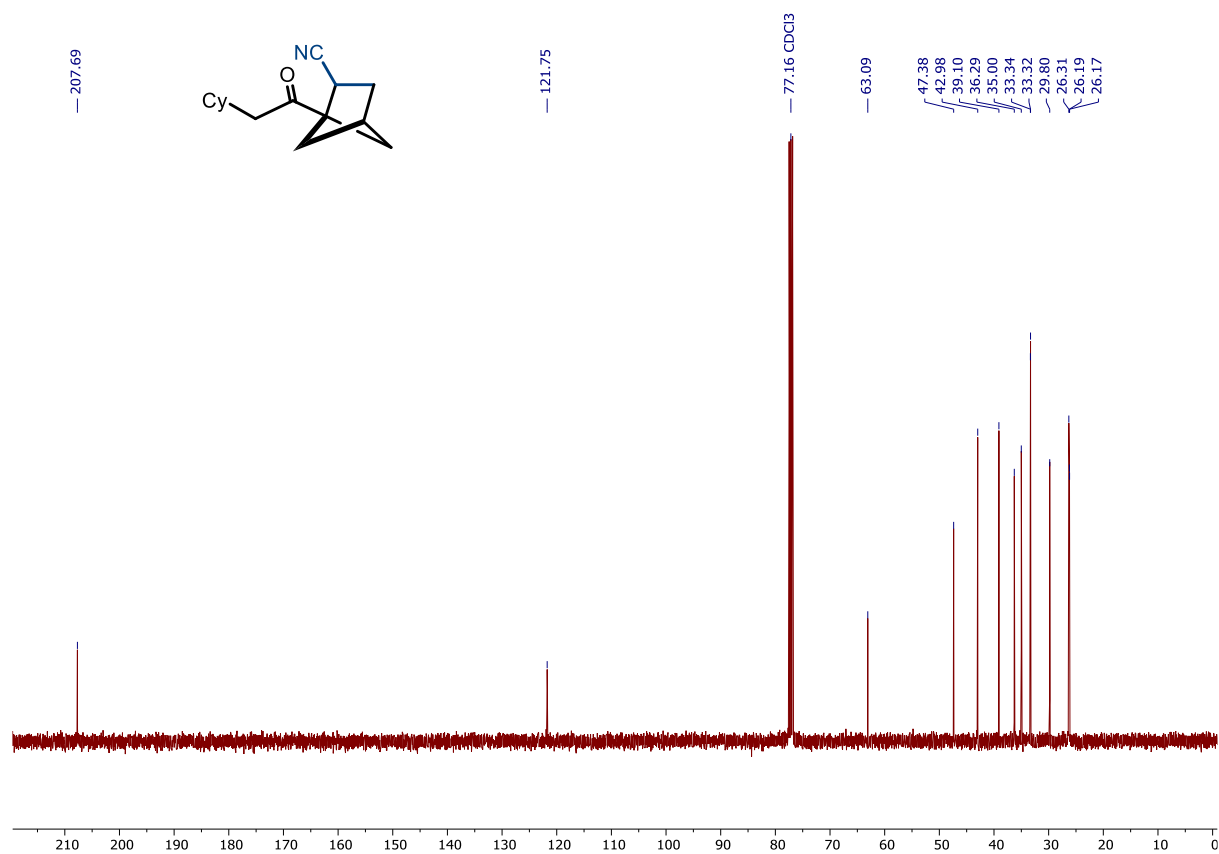
DEPT-135 NMR (101 MHz, Chloroform-*d*) (**13e**):



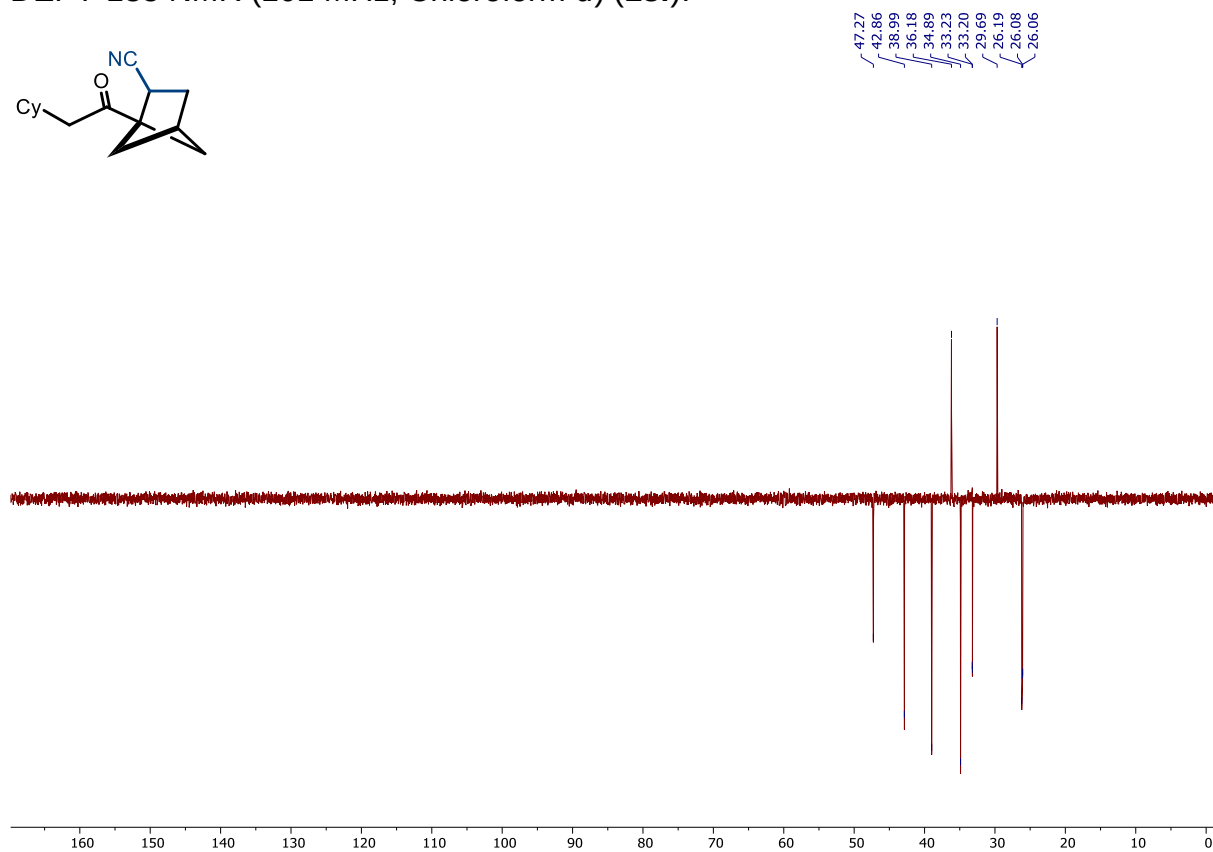
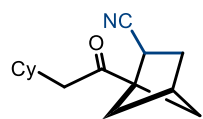
¹H NMR (400 MHz, Chloroform-*d*) (**13f**):



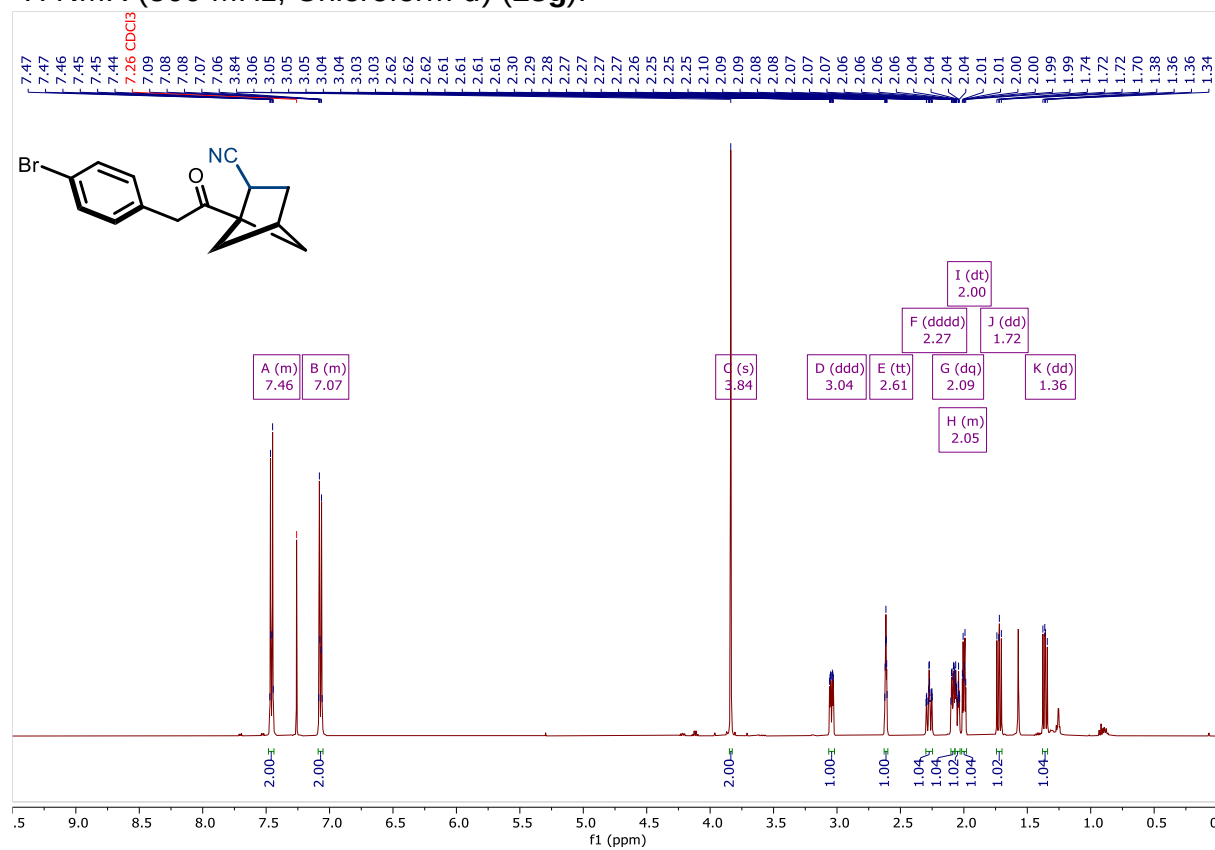
¹³C NMR (101 MHz, Chloroform-*d*) (**13f**):



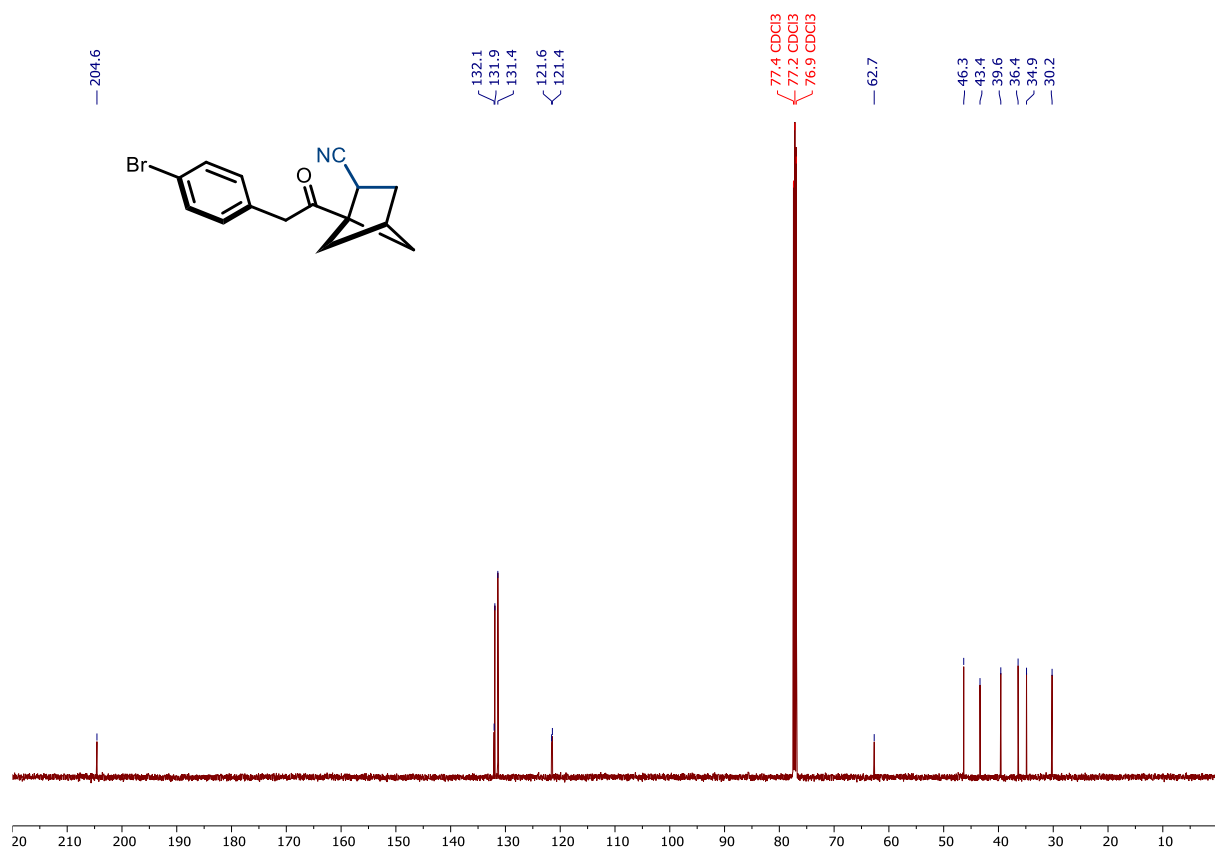
DEPT-135 NMR (101 MHz, Chloroform-*d*) (**13f**):



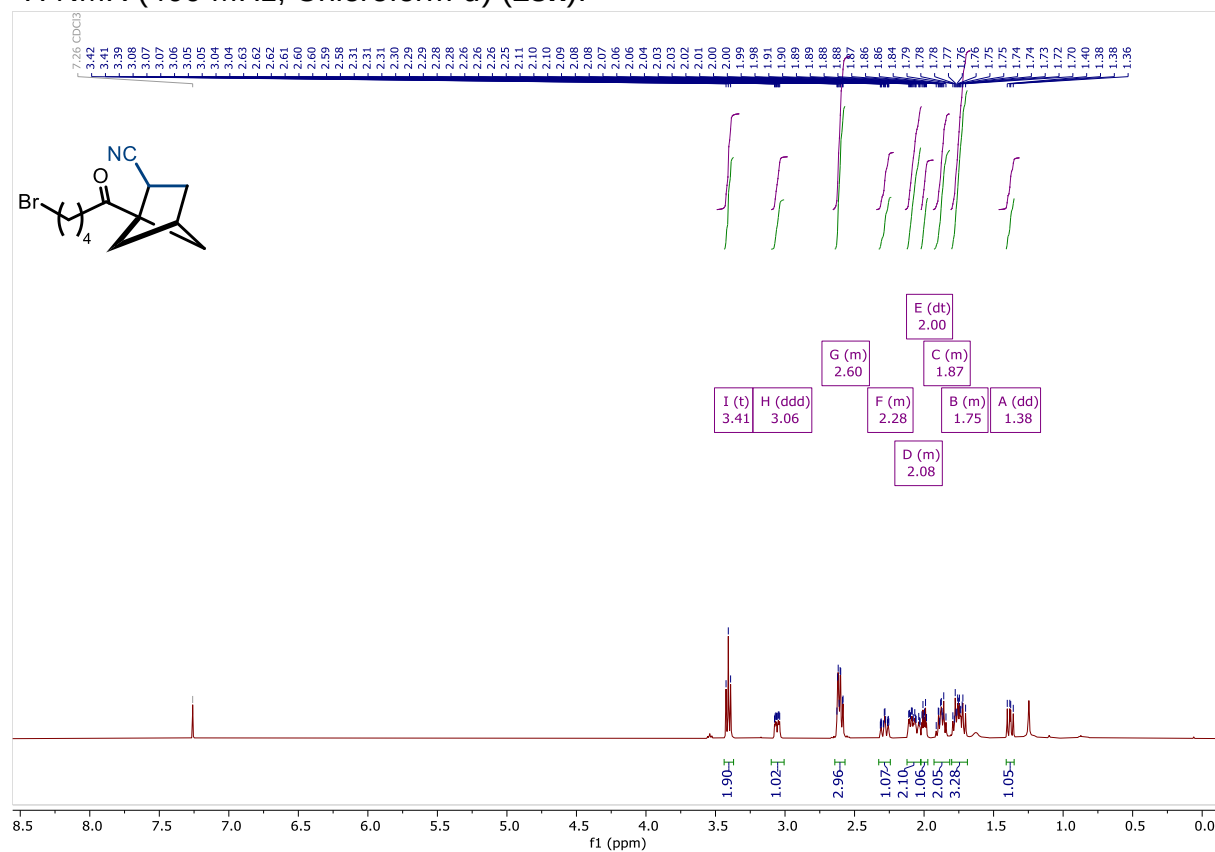
¹H NMR (500 MHz, Chloroform-*d*) (**13g**):



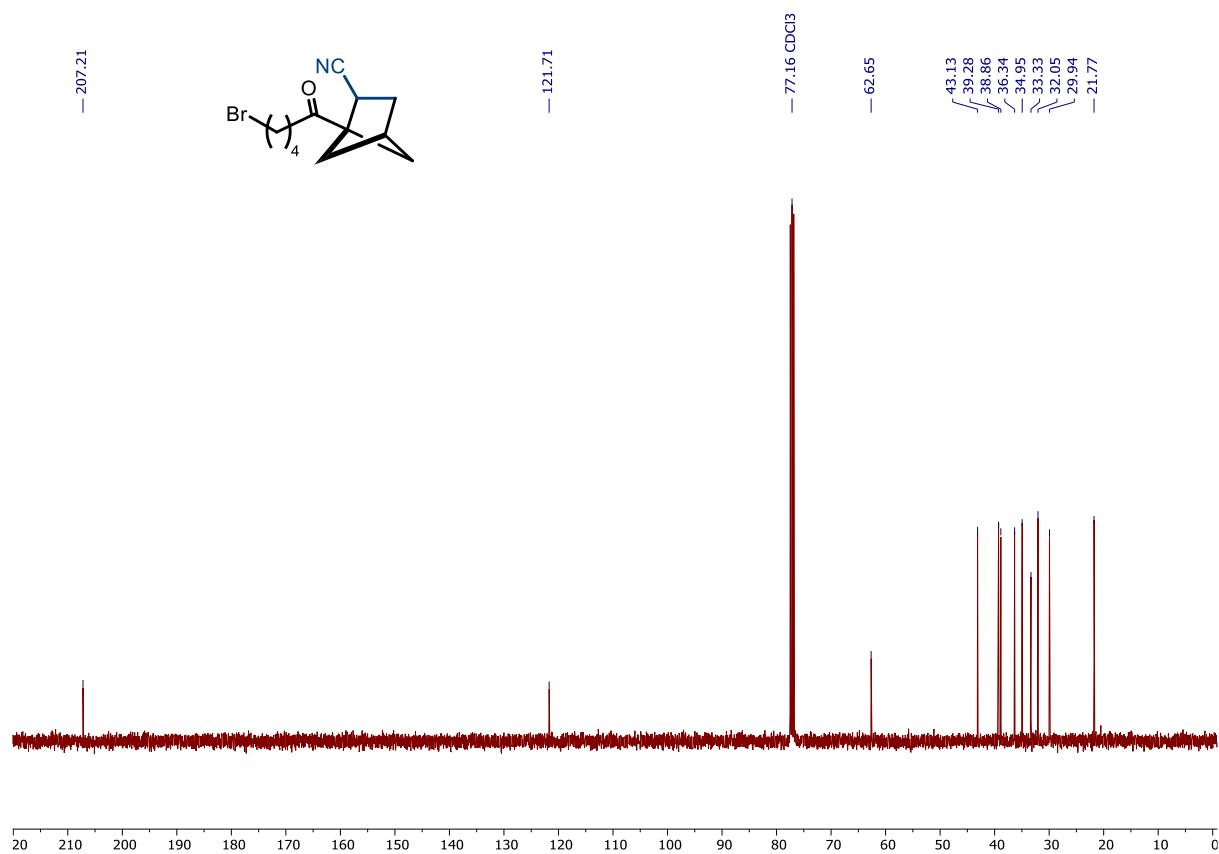
¹³C NMR (126 MHz, Chloroform-*d*) (**13g**):



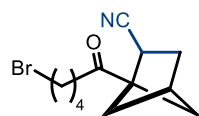
¹H NMR (400 MHz, Chloroform-*d*) (**13h**):



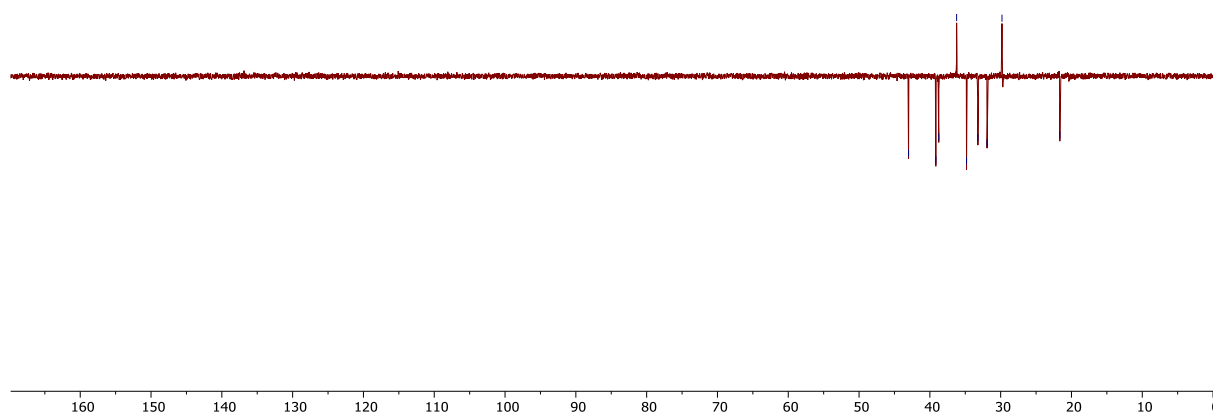
¹³C NMR (101 MHz, Chloroform-*d*) (**13h**):



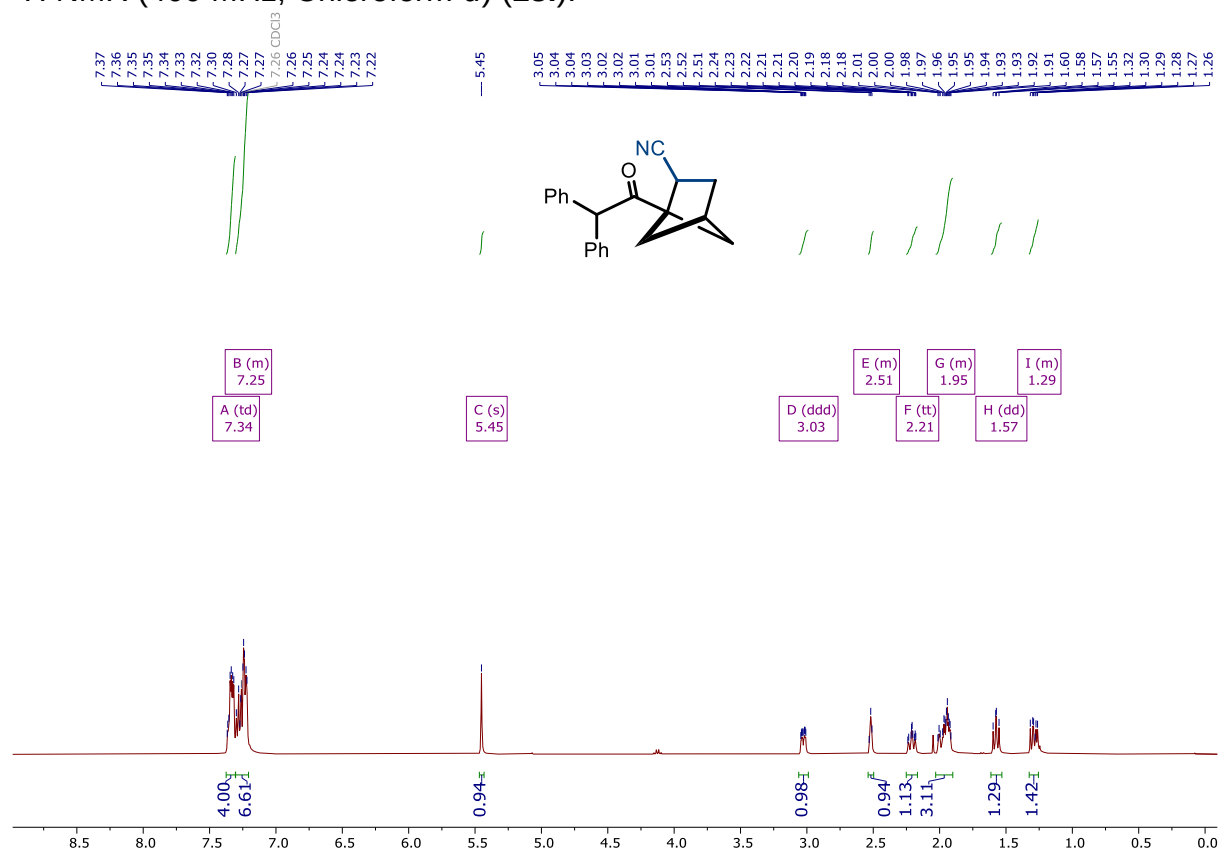
DEPT-135 NMR (101 MHz, Chloroform-*d*) (**13h**):



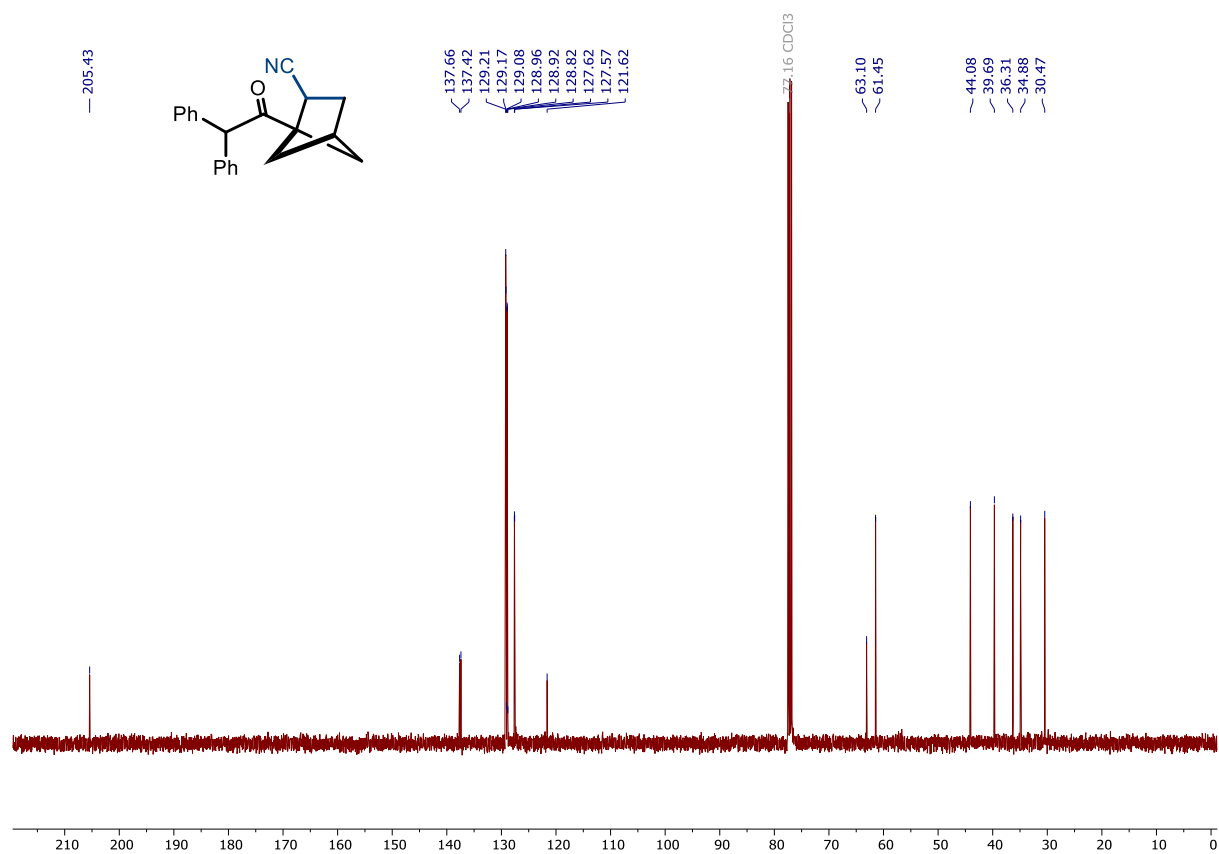
43.01
39.16
38.74
36.22
36.22
34.82
33.22
31.92
29.81
— 21.64



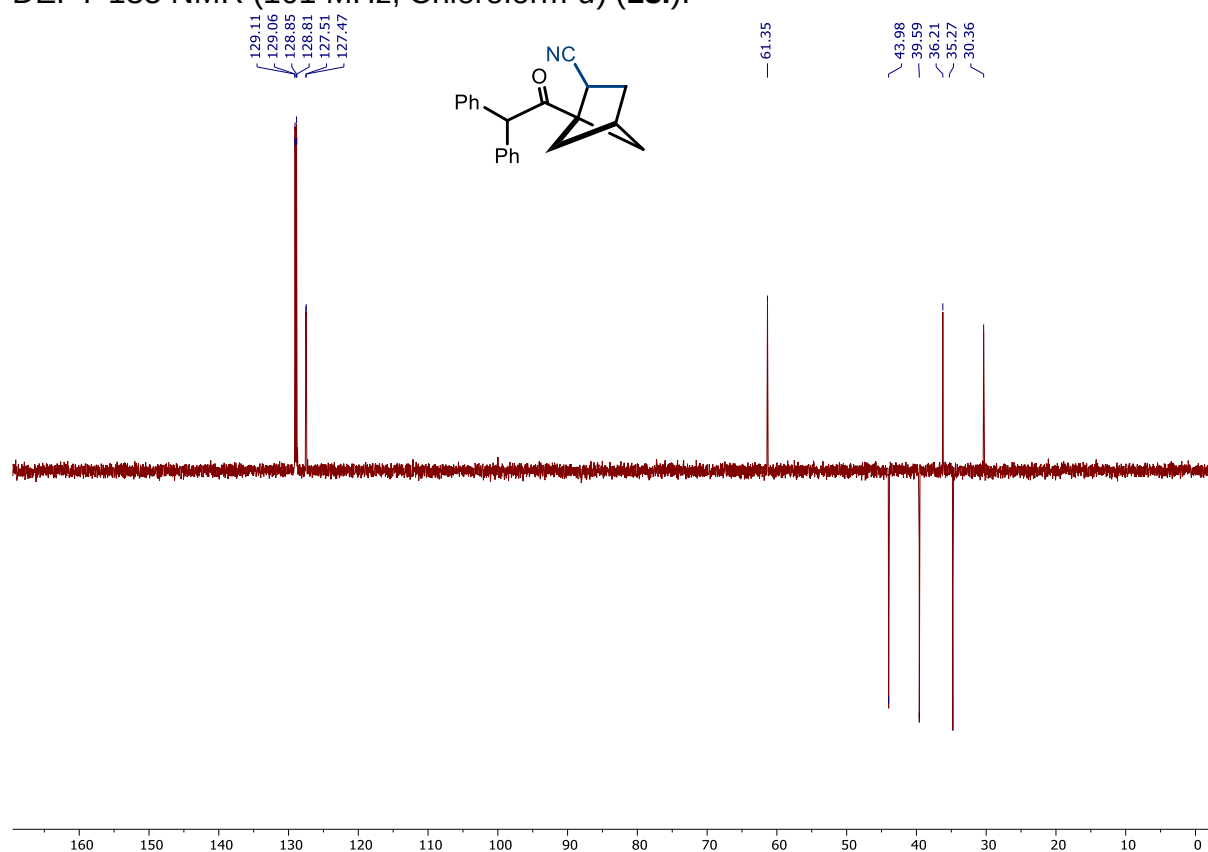
^1H NMR (400 MHz, Chloroform-*d*) (**13i**):



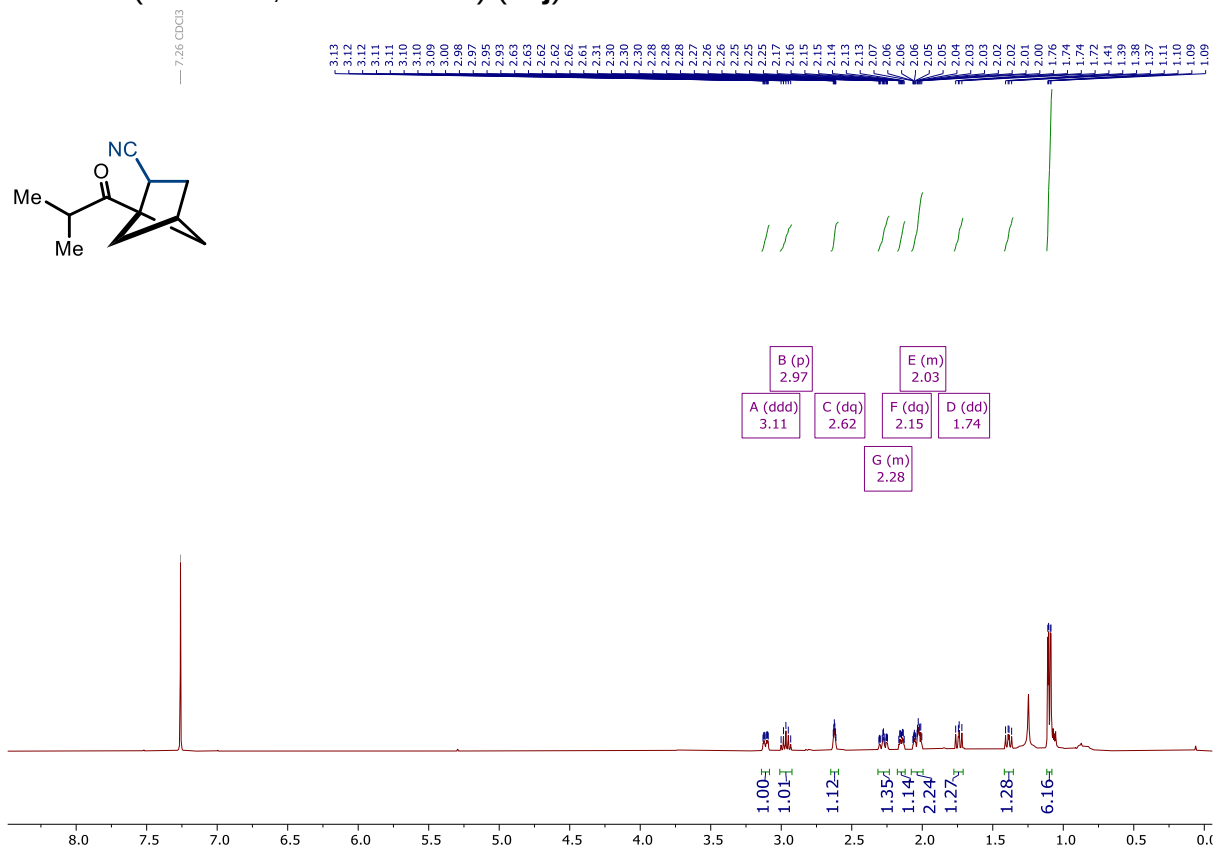
^{13}C NMR (101 MHz, Chloroform-*d*) (**13i**):



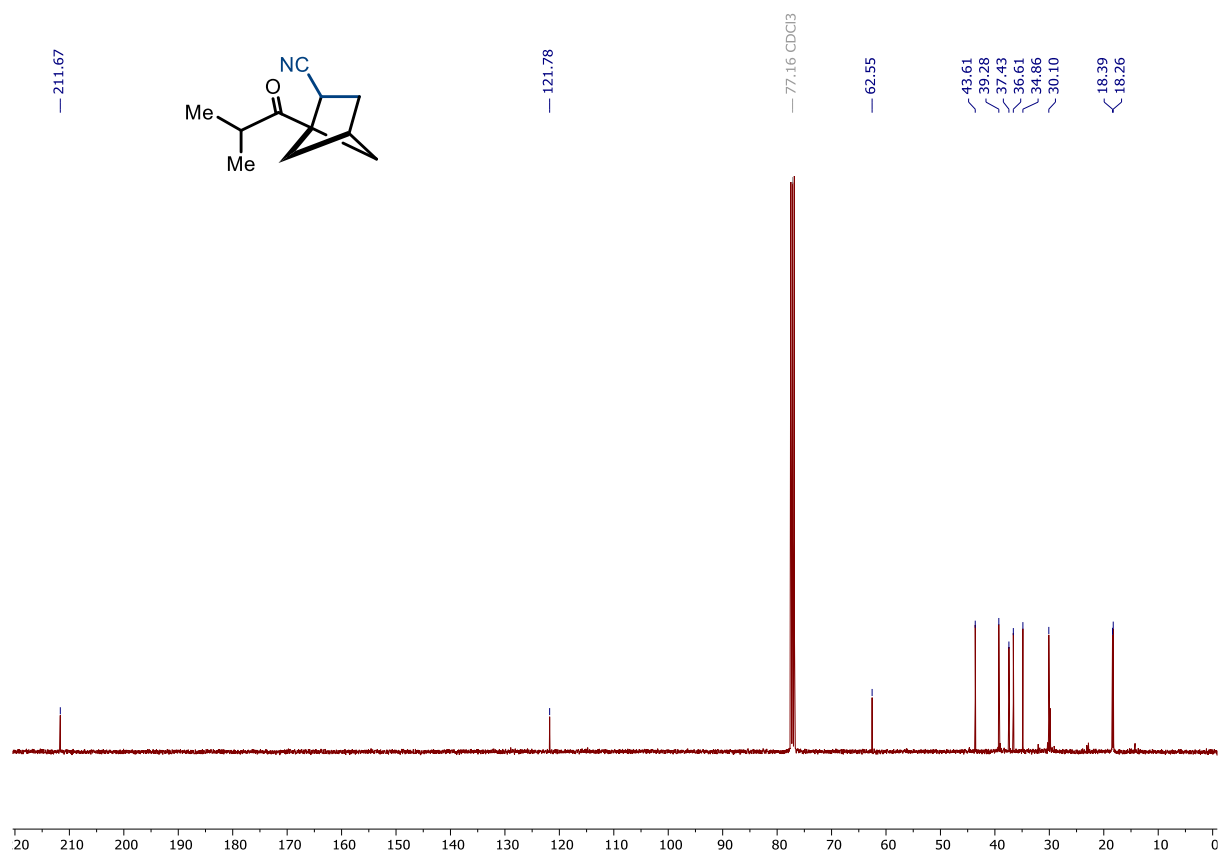
DEPT-135 NMR (101 MHz, Chloroform-*d*) (**13i**):



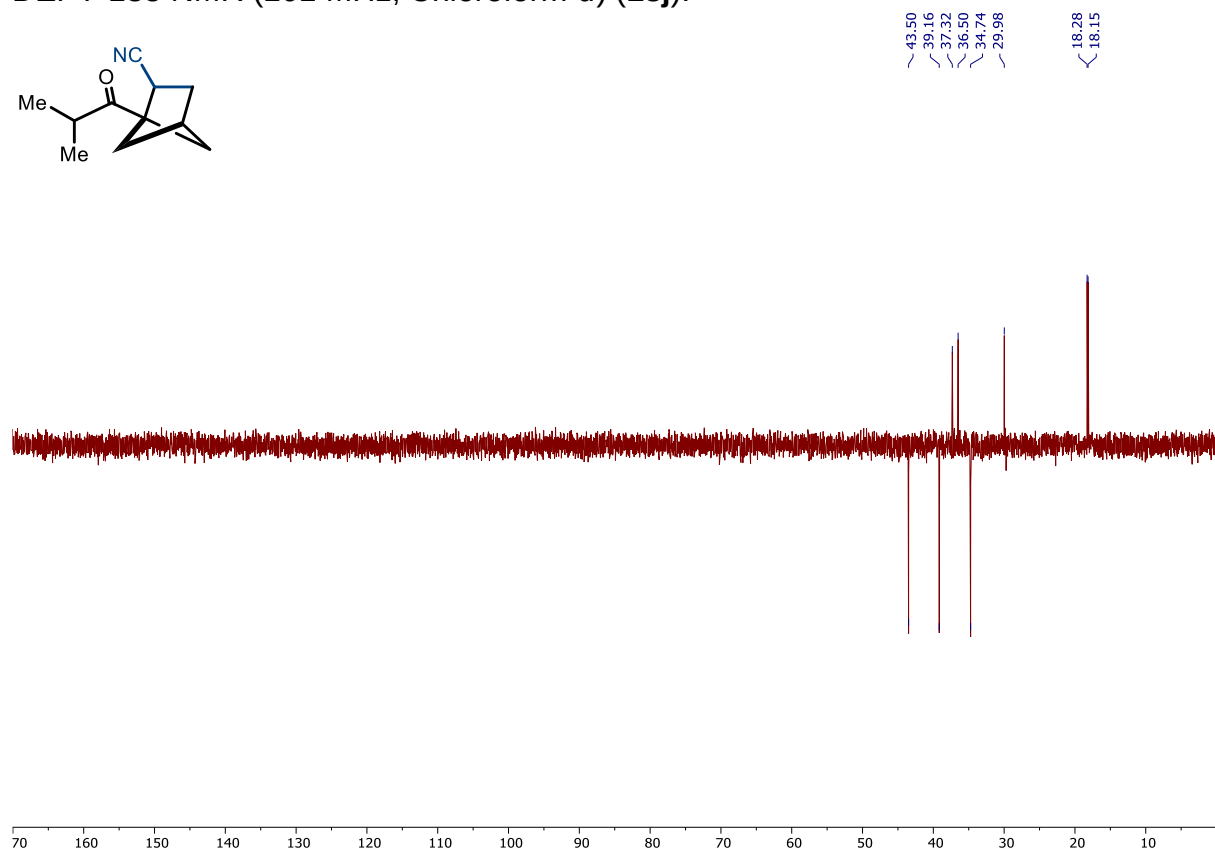
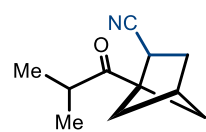
¹H NMR (400 MHz, Chloroform-*d*) (**13j**):



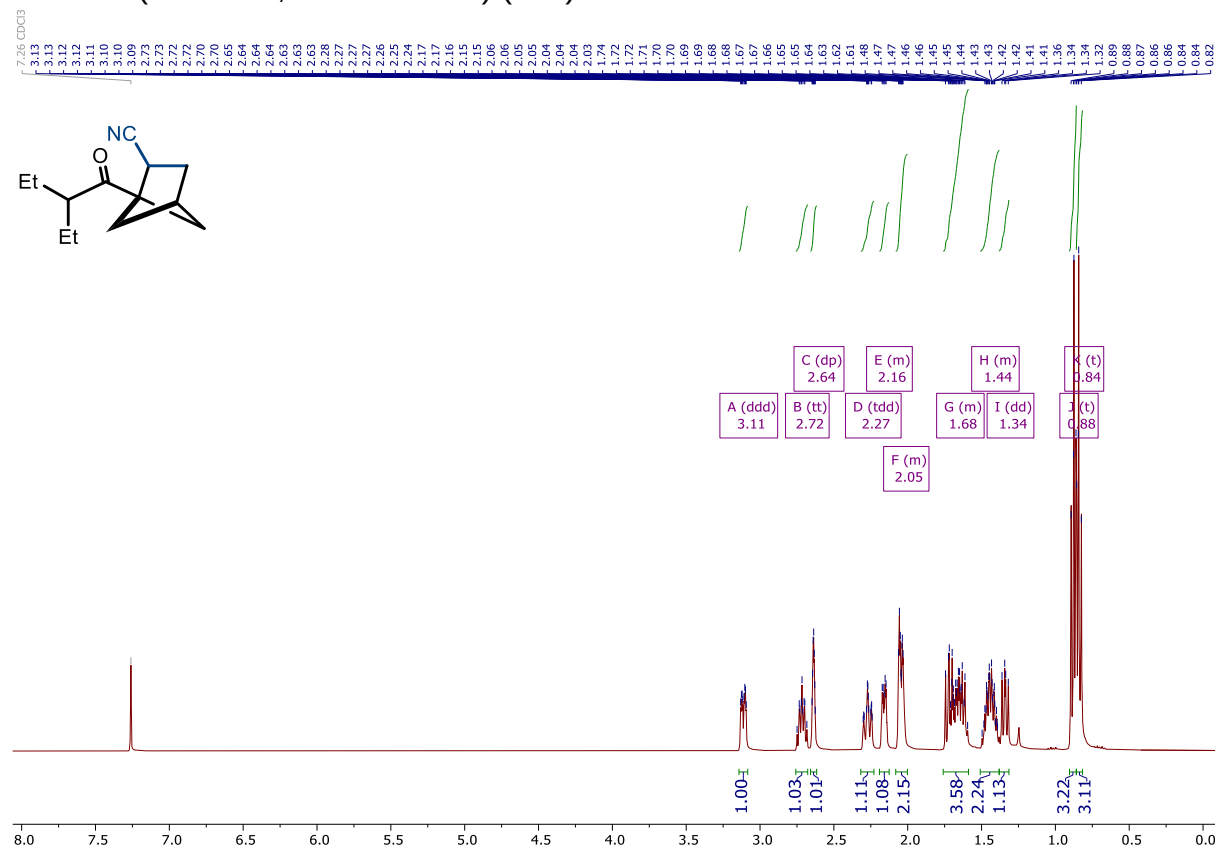
¹³C NMR (101 MHz, Chloroform-*d*) (**13j**):



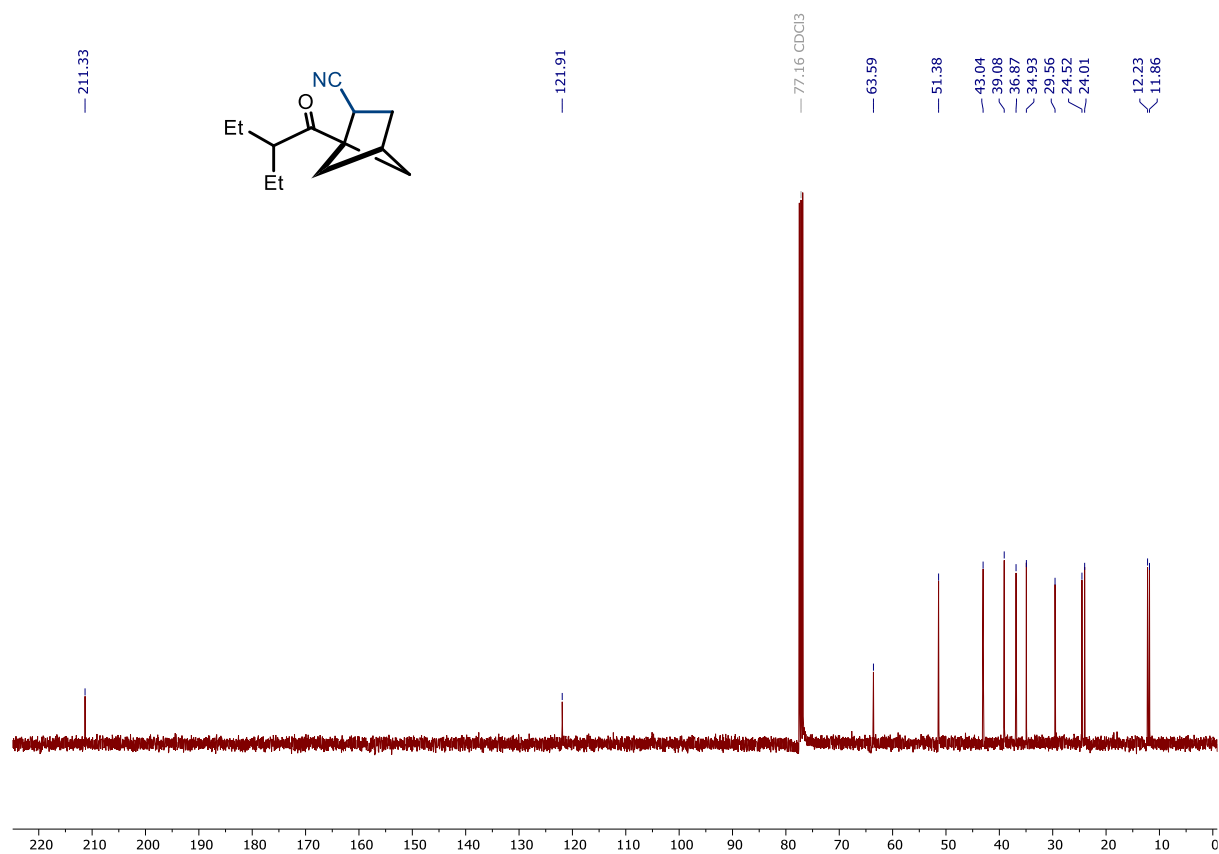
DEPT-135 NMR (101 MHz, Chloroform-*d*) (**13j**):



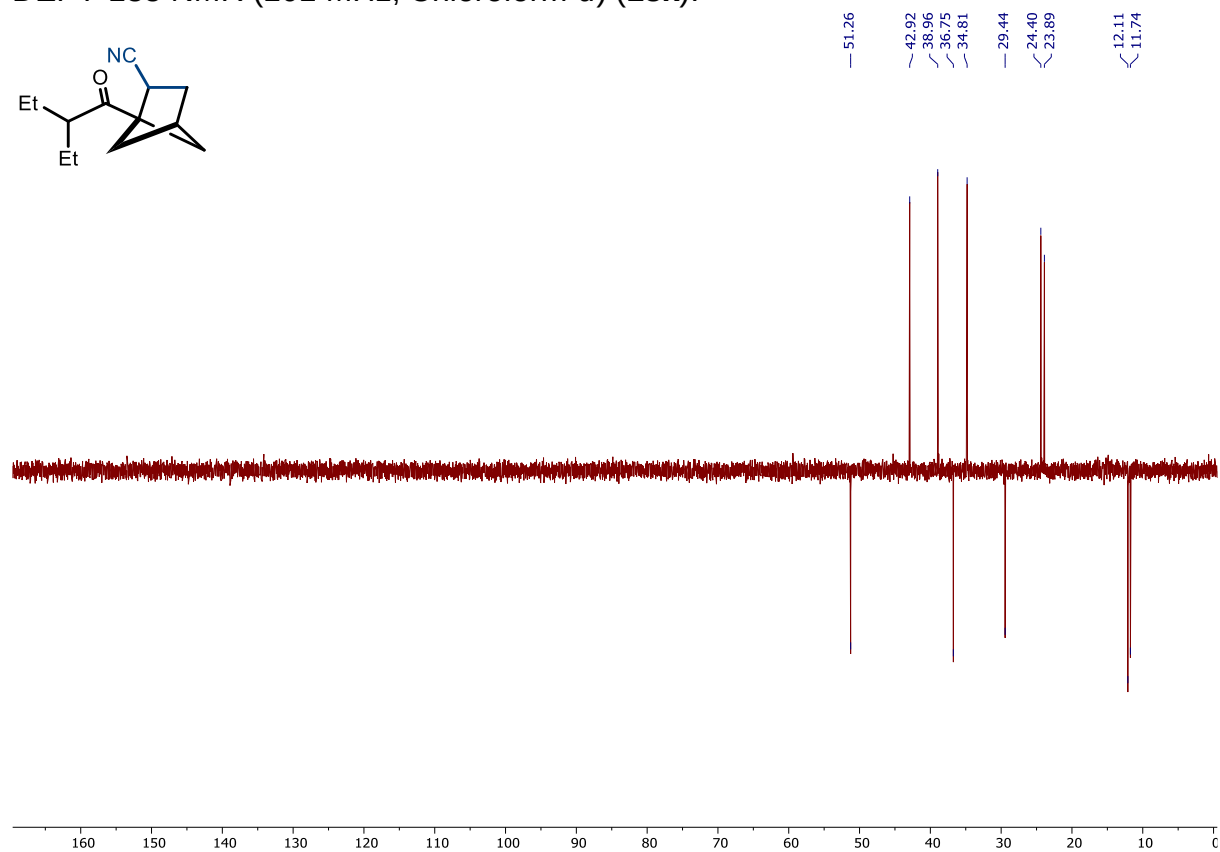
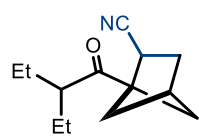
¹H NMR (400 MHz, Chloroform-*d*) (**13k**):



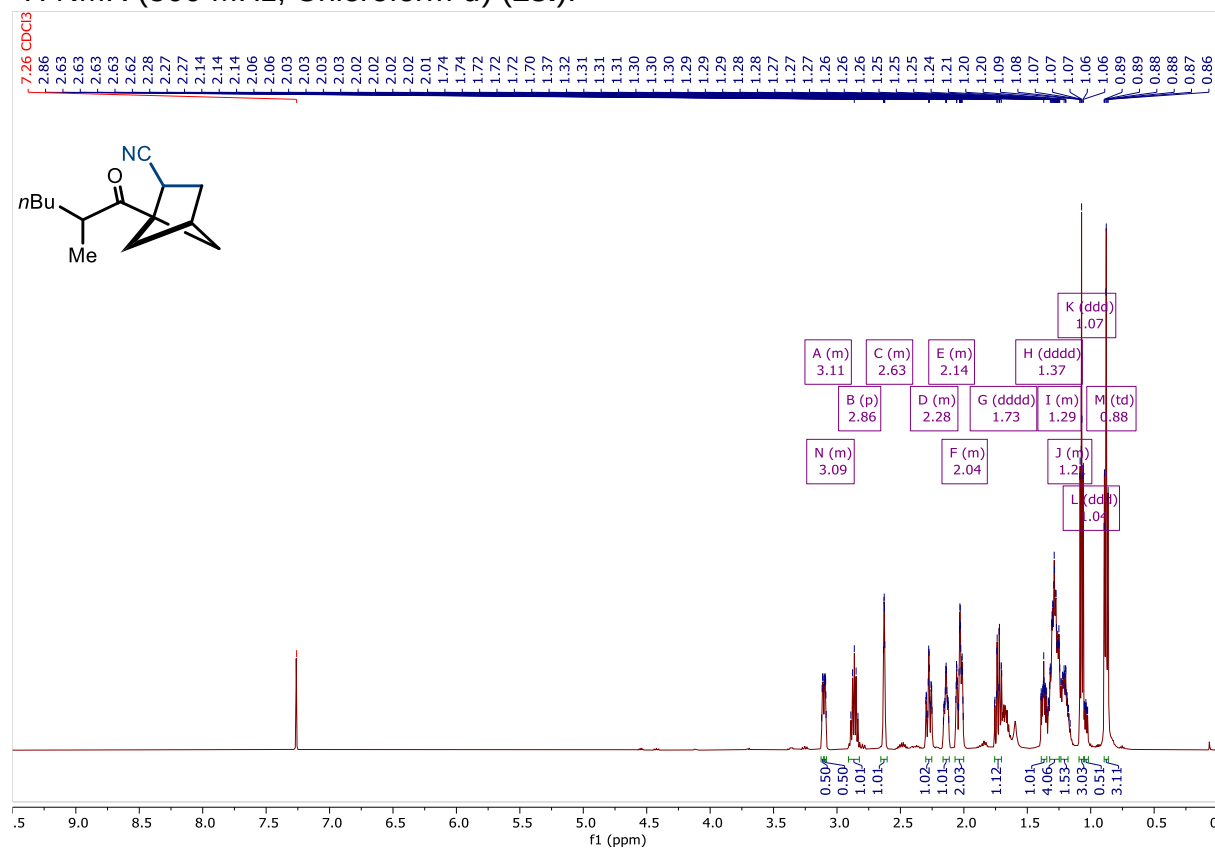
¹³C NMR (101 MHz, Chloroform-*d*) (**13k**):



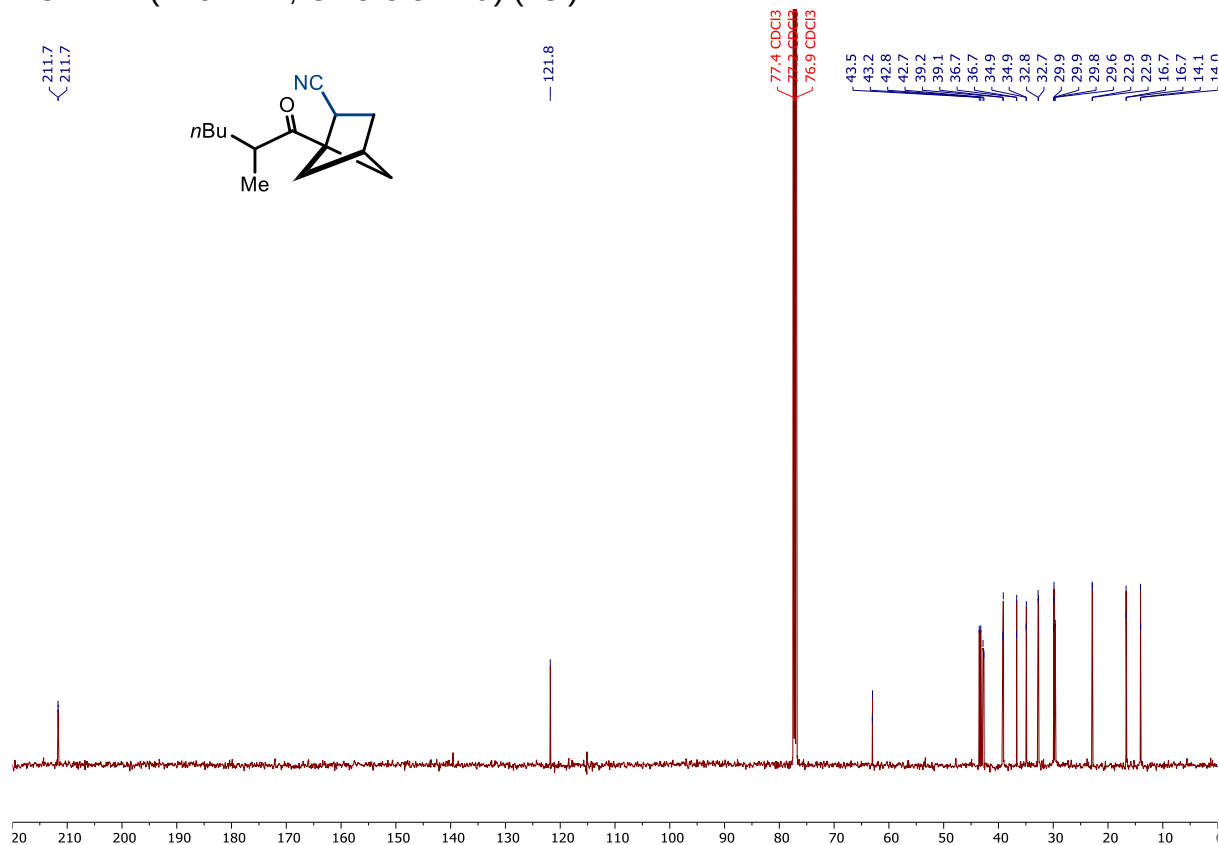
DEPT-135 NMR (101 MHz, Chloroform-*d*) (**13k**):



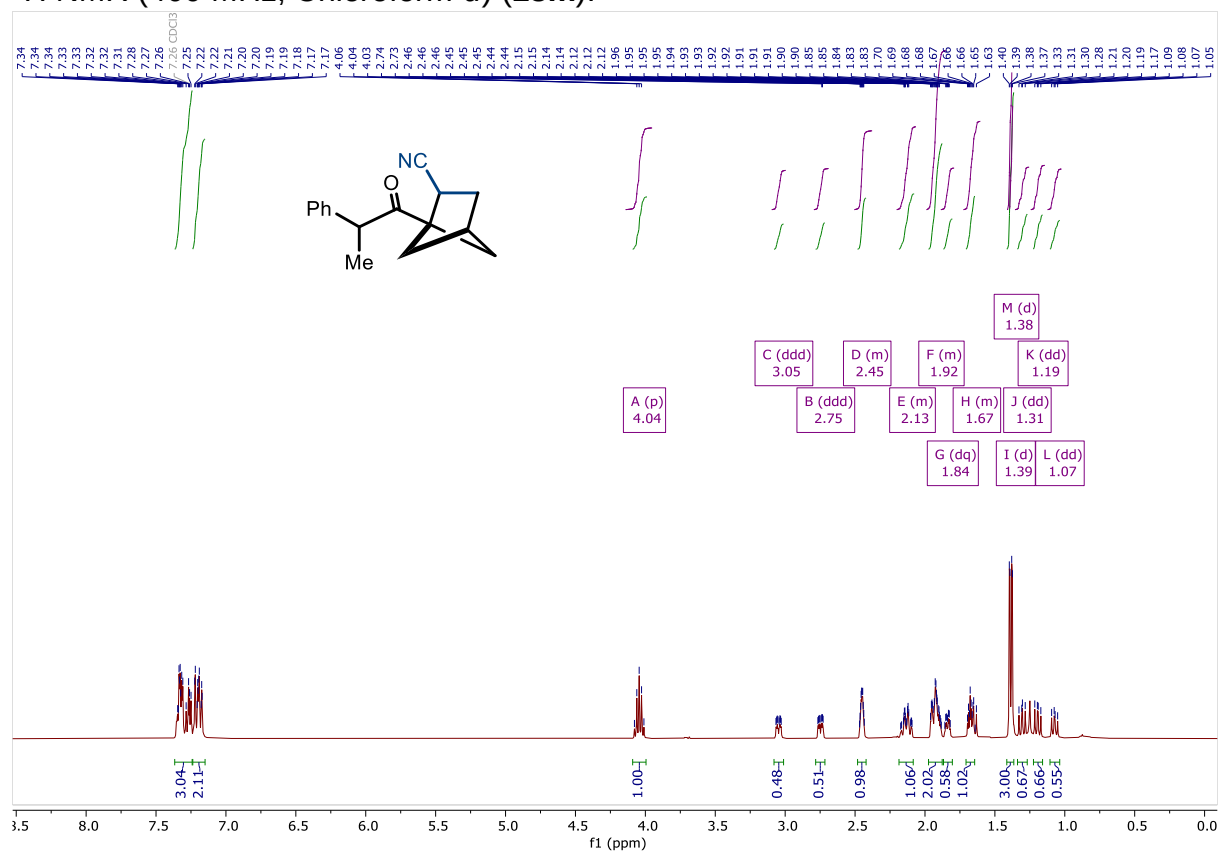
¹H NMR (500 MHz, Chloroform-*d*) (**13l**):



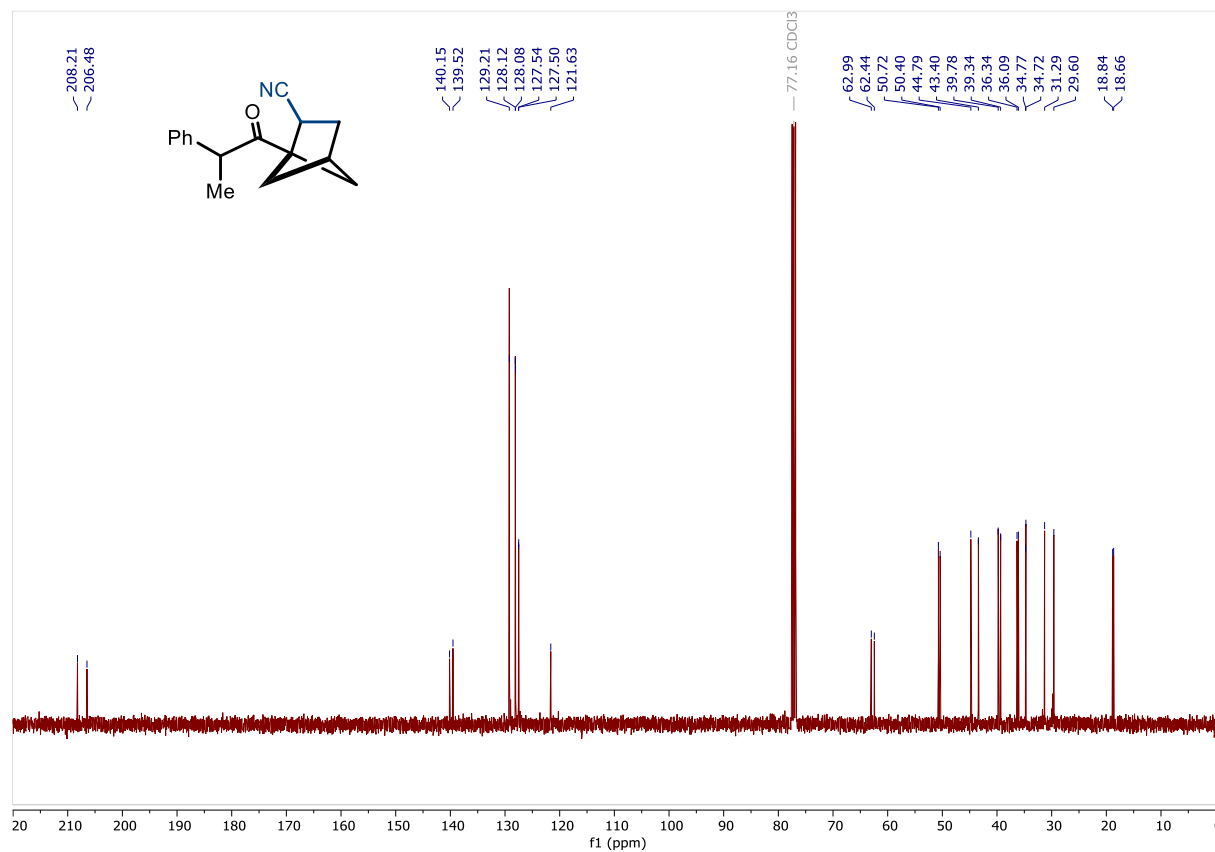
¹³C NMR (126 MHz, Chloroform-*d*) (**13l**):



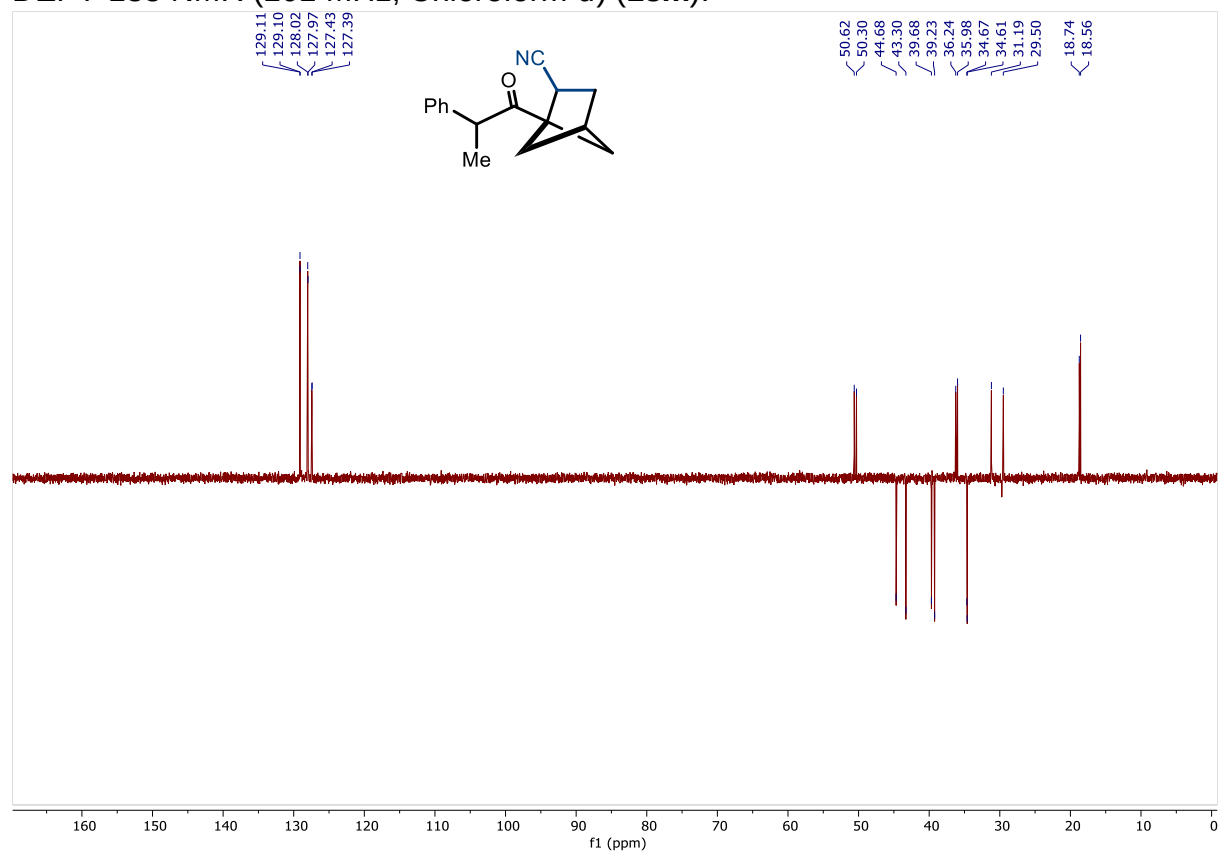
¹H NMR (400 MHz, Chloroform-*d*) (**13m**):



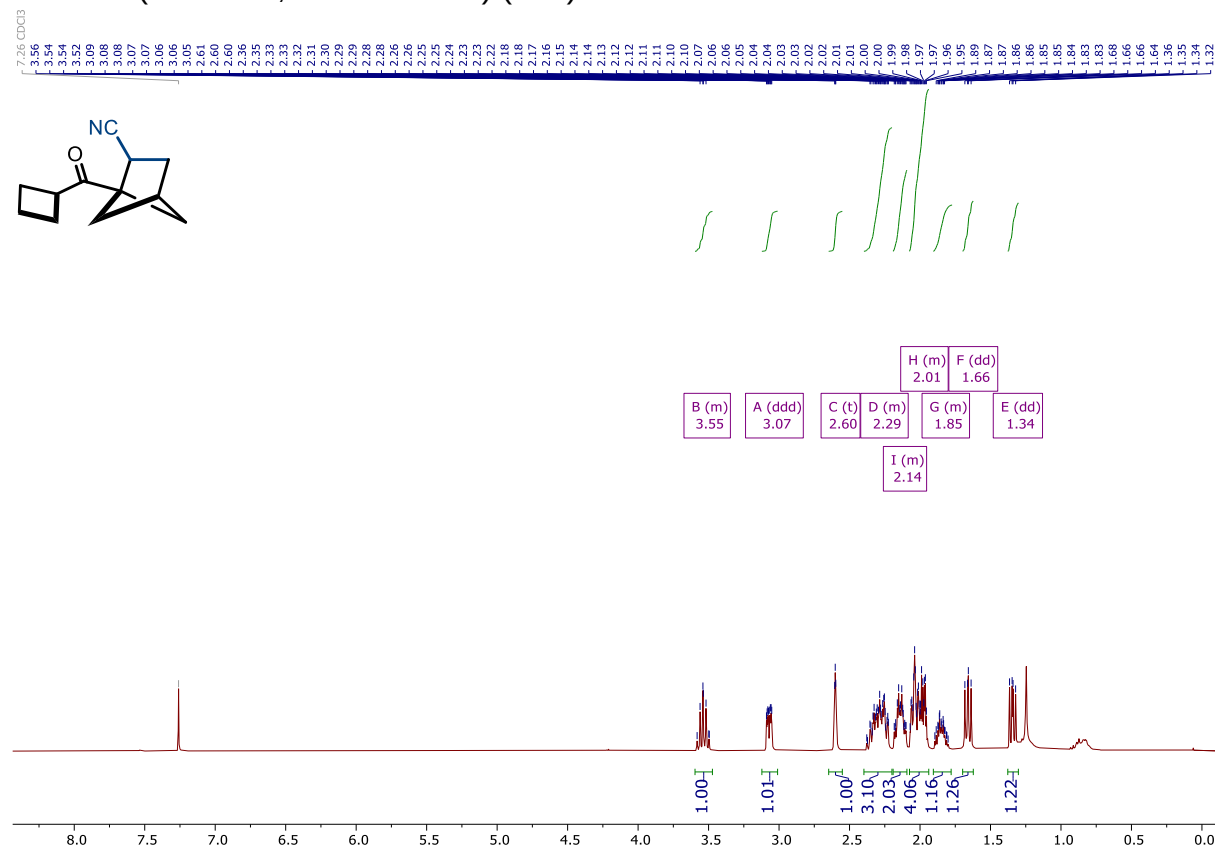
¹³C NMR (101 MHz, Chloroform-*d*) (**13m**):



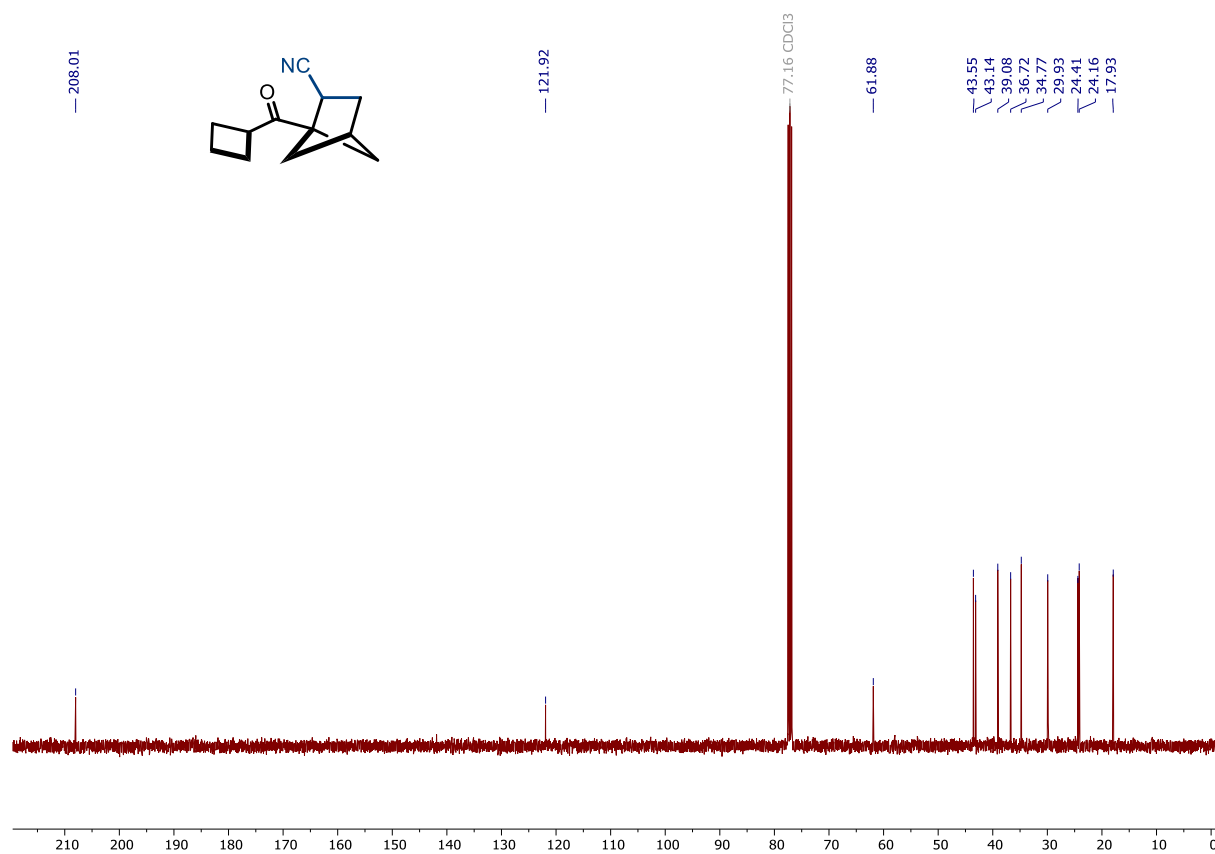
DEPT-135 NMR (101 MHz, Chloroform-*d*) (**13m**):



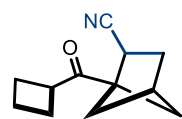
¹H NMR (400 MHz, Chloroform-*d*) (**13n**):



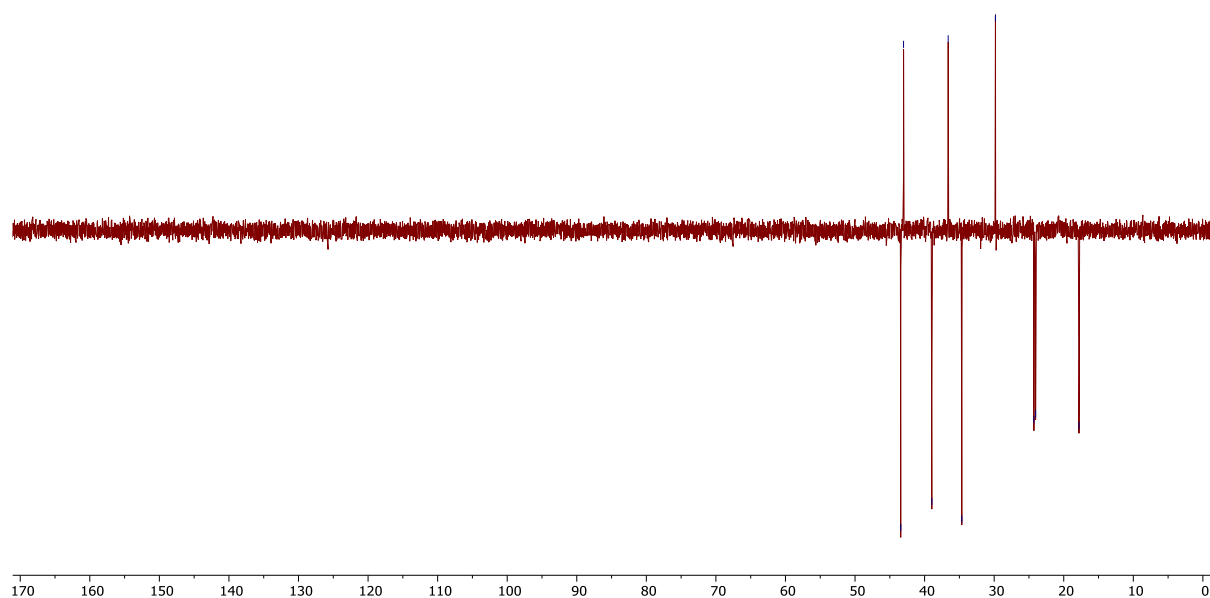
¹³C NMR (101 MHz, Chloroform-*d*) (**13n**):



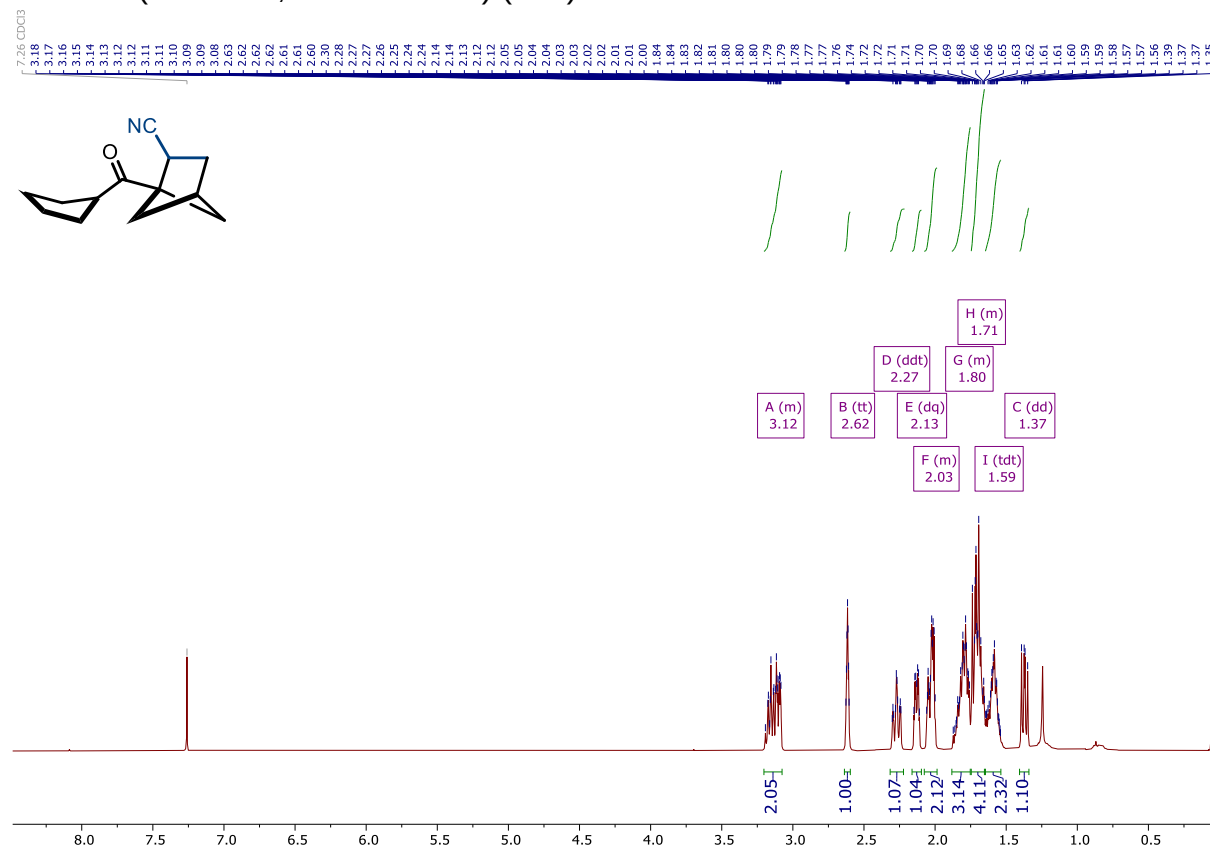
DEPT-135 NMR (101 MHz, Chloroform-*d*) (**13n**):



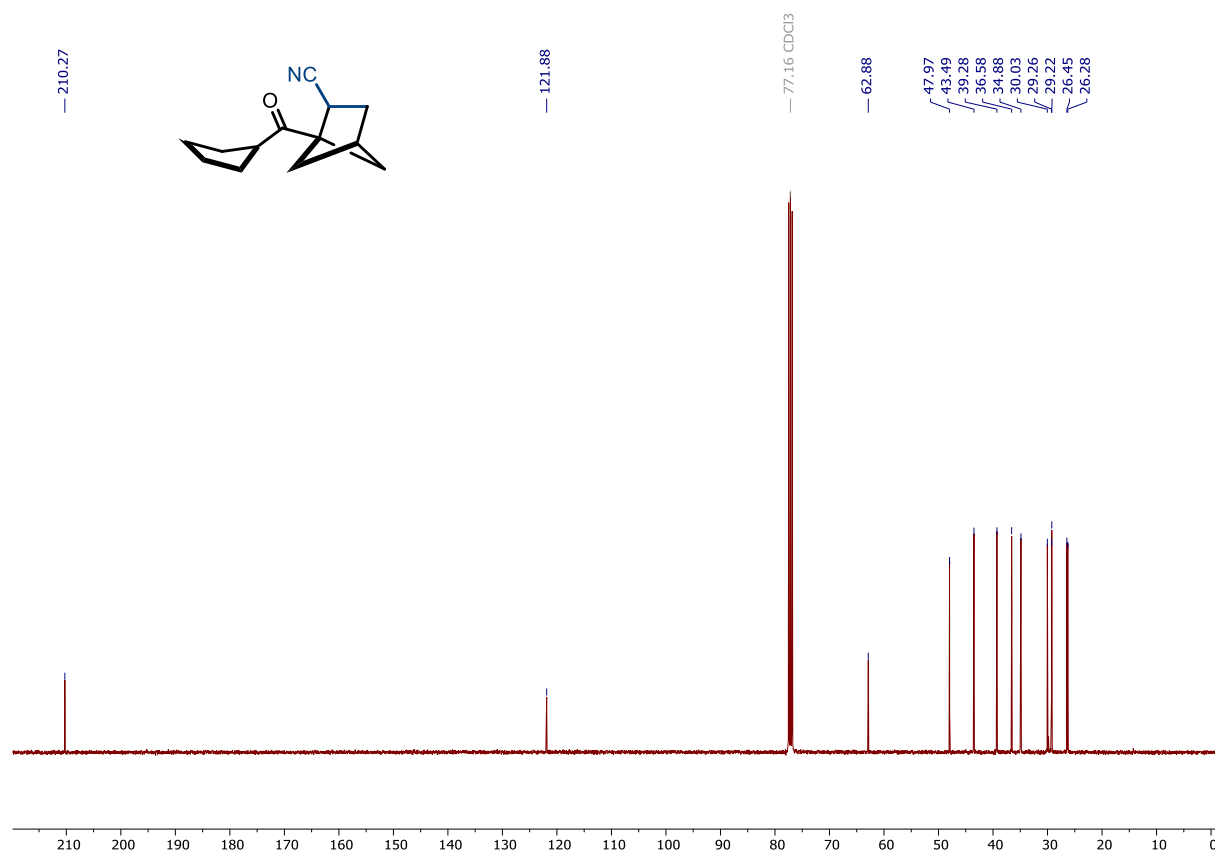
43.43
43.03
38.96
36.61
34.66
29.82
24.29
24.05
17.81



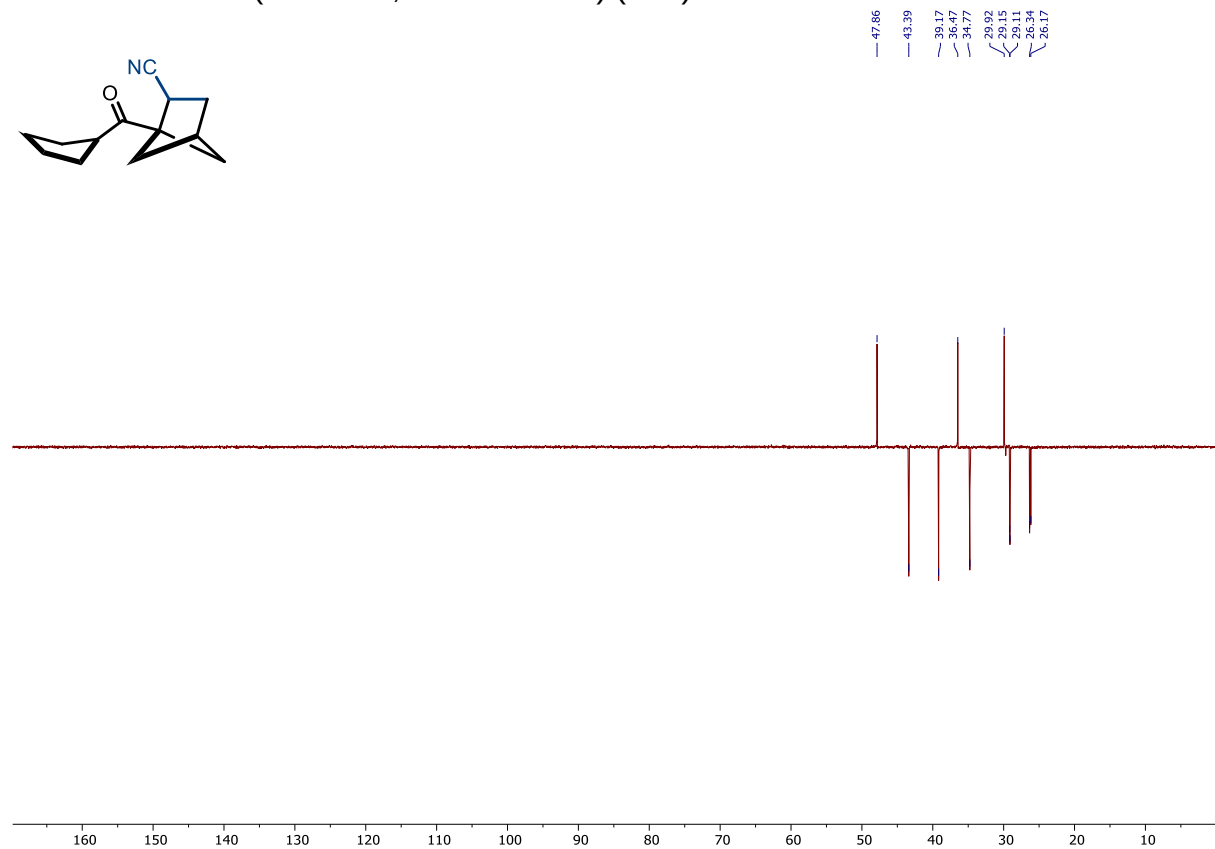
¹H NMR (400 MHz, Chloroform-*d*) (**13o**):



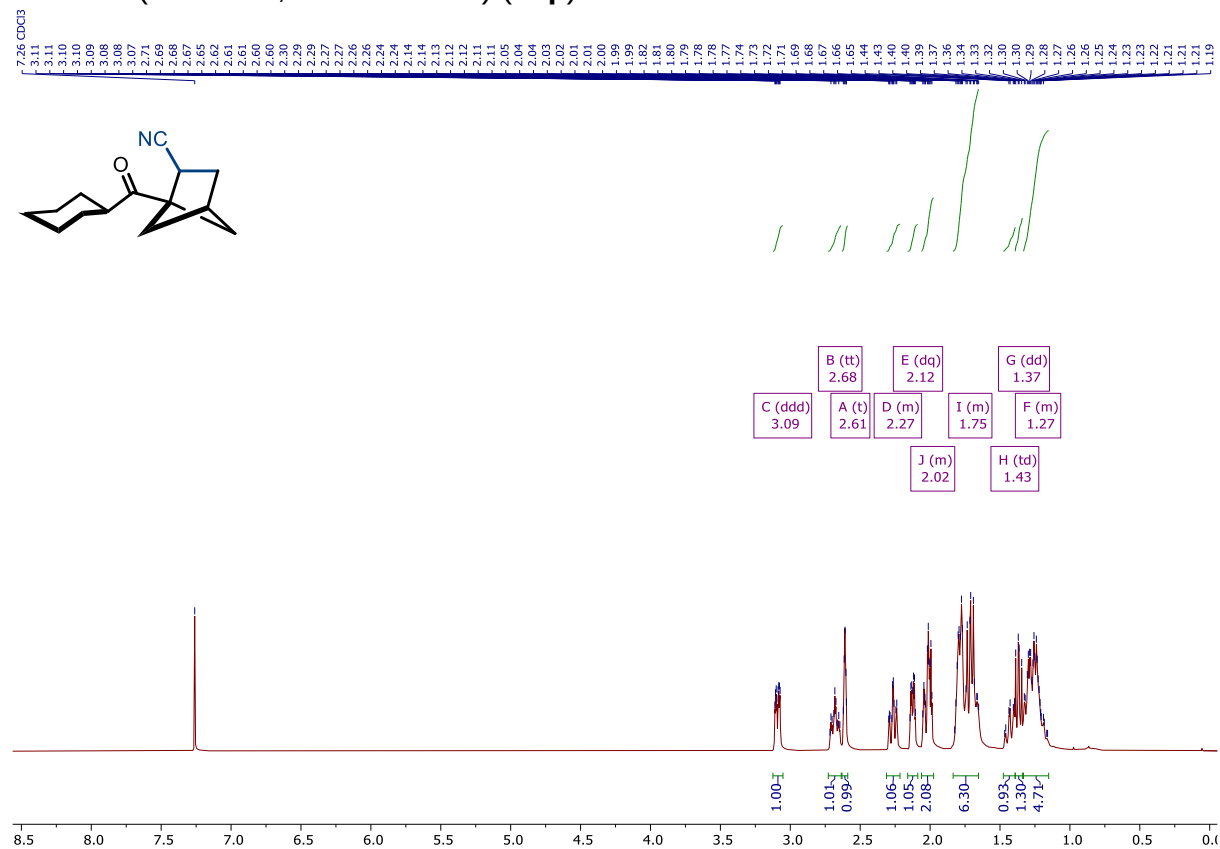
¹³C NMR (101 MHz, Chloroform-*d*) (**13o**):



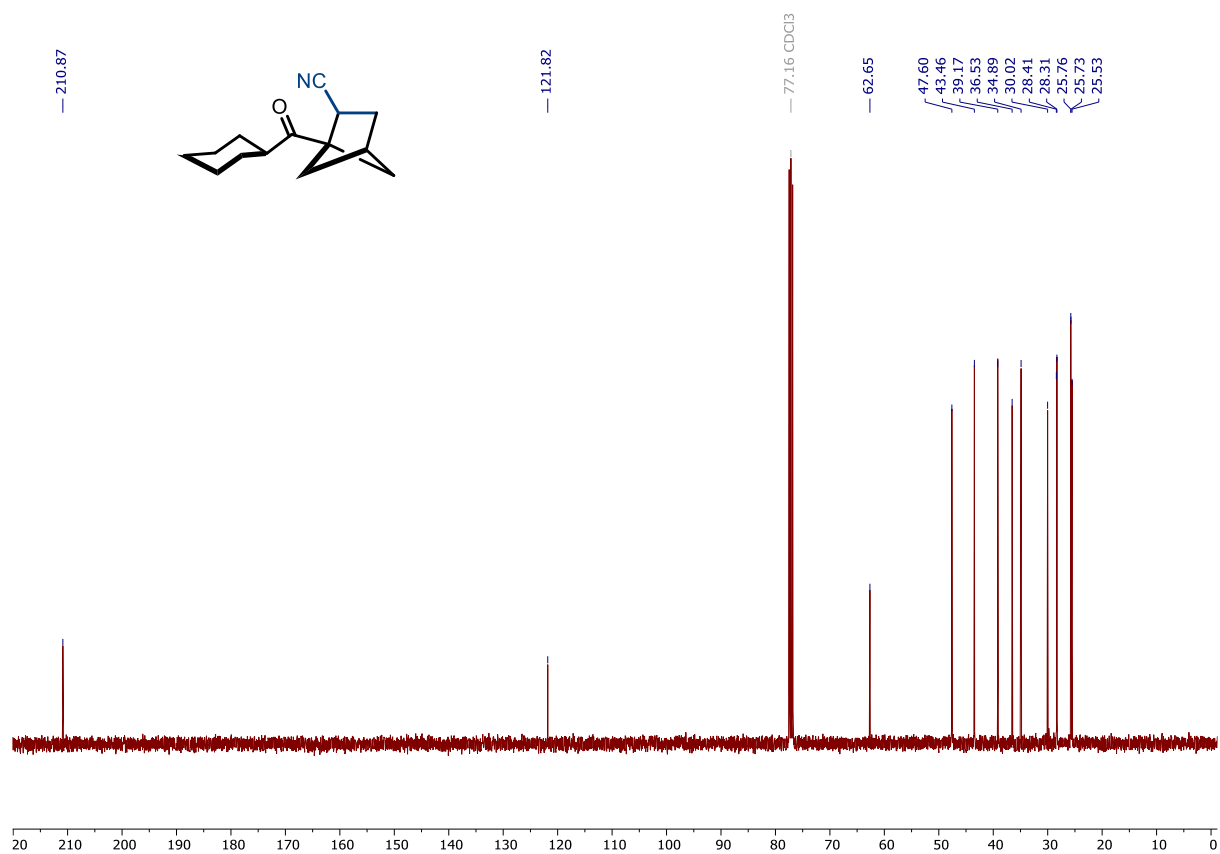
DEPT-135 NMR (101 MHz, Chloroform-*d*) (**13o**):



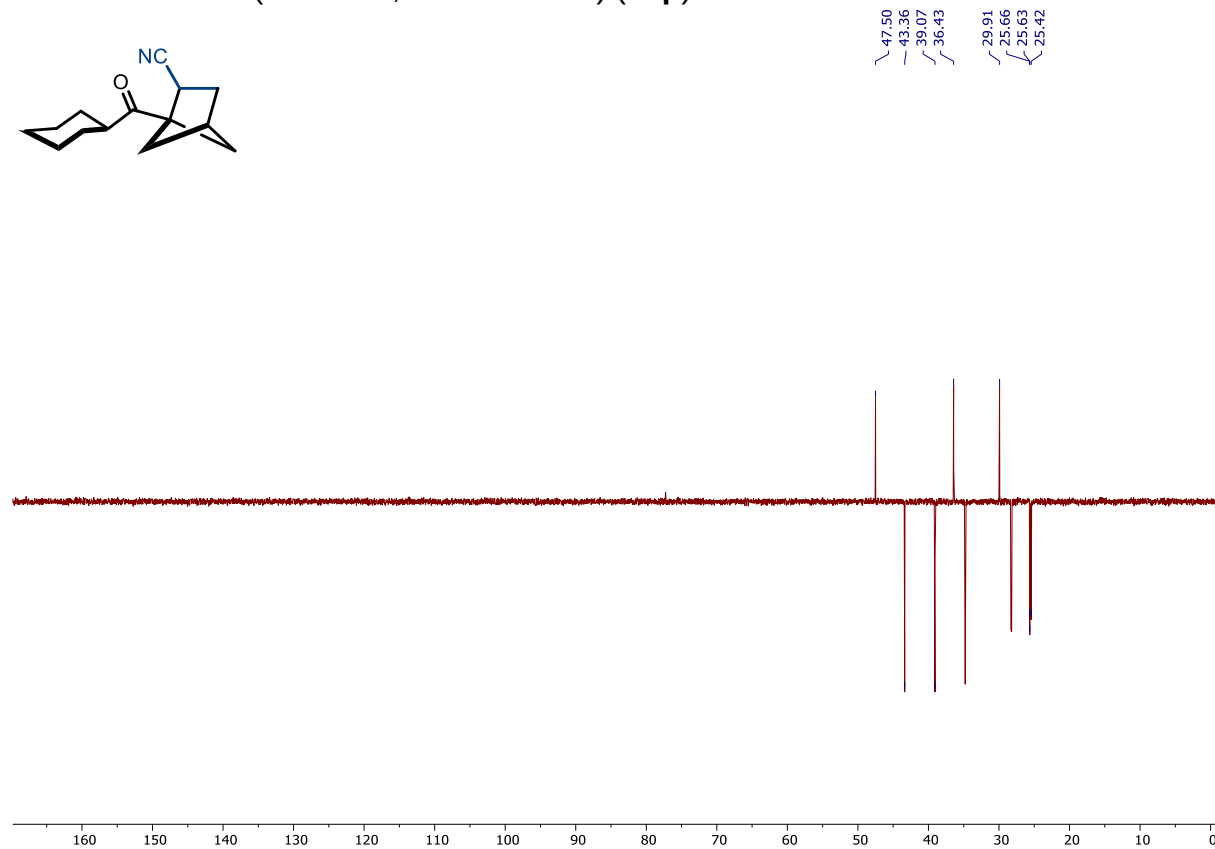
¹H NMR (400 MHz, Chloroform-*d*) (**13p**):



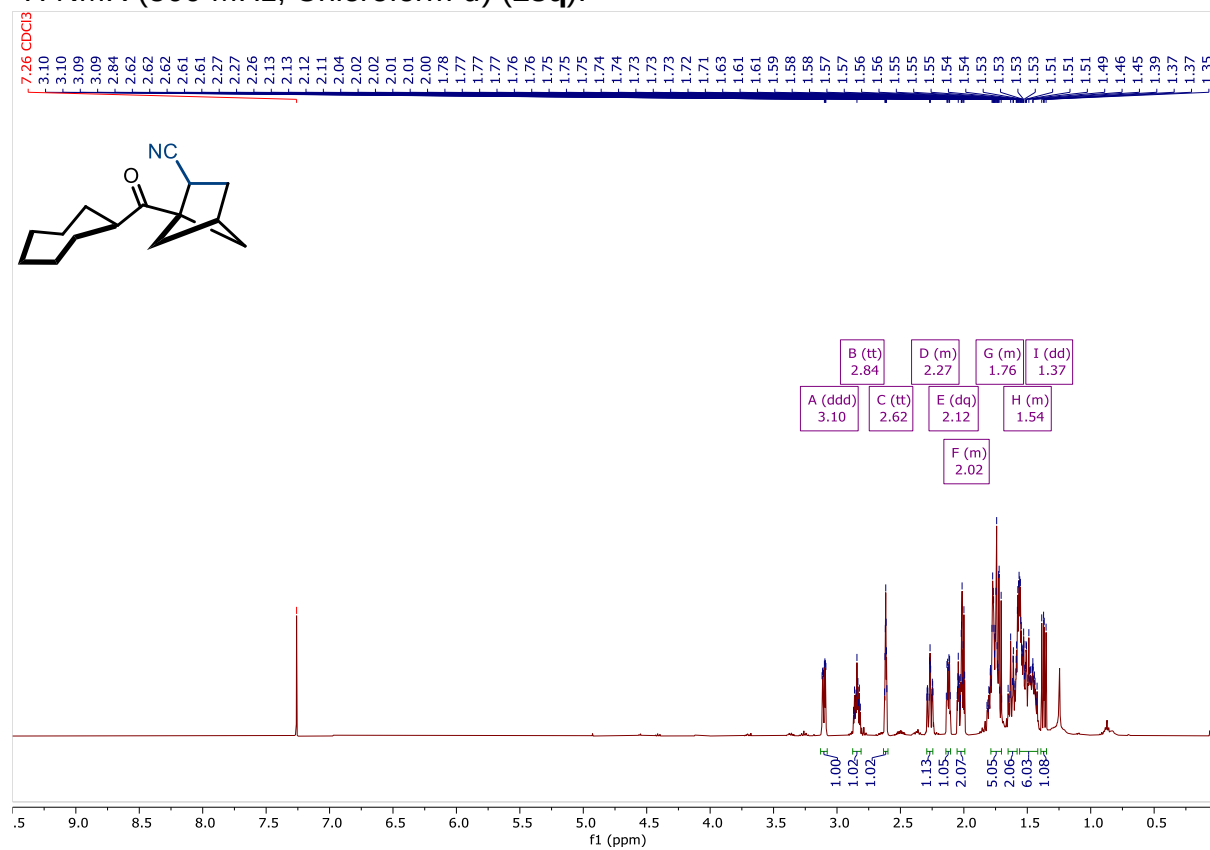
¹³C NMR (101 MHz, Chloroform-*d*) (**13p**):



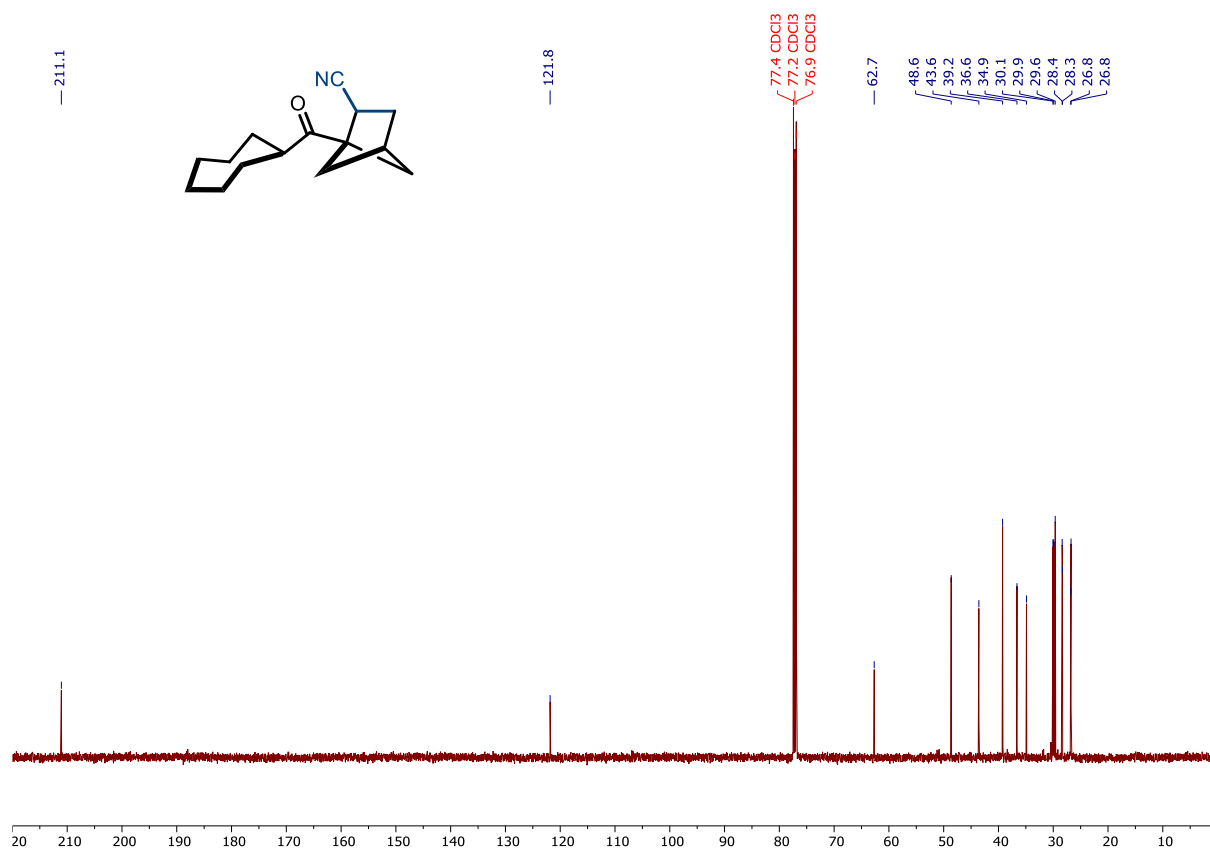
DEPT-135 NMR (101 MHz, Chloroform-*d*) (**13p**):



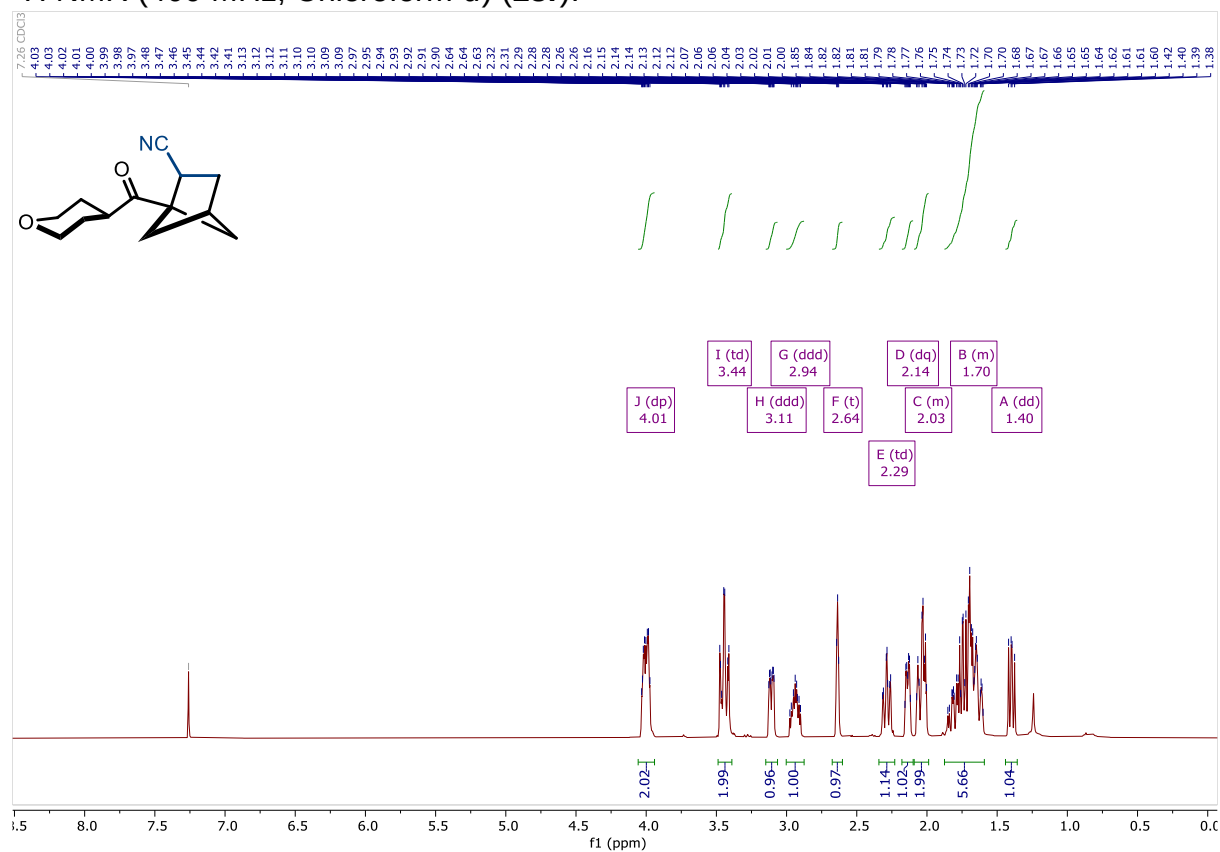
¹H NMR (500 MHz, Chloroform-*d*) (**13q**):



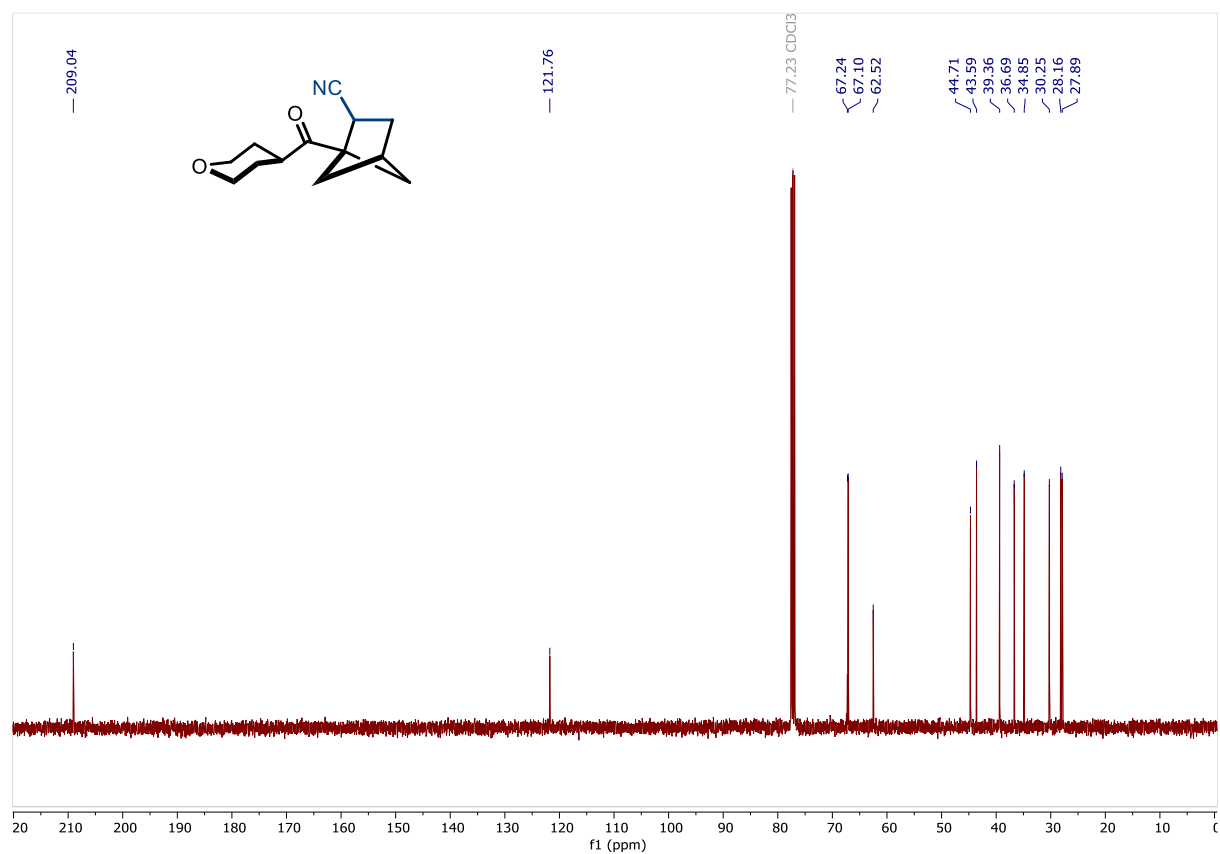
¹³C NMR (126 MHz, Chloroform-*d*) (**13q**):



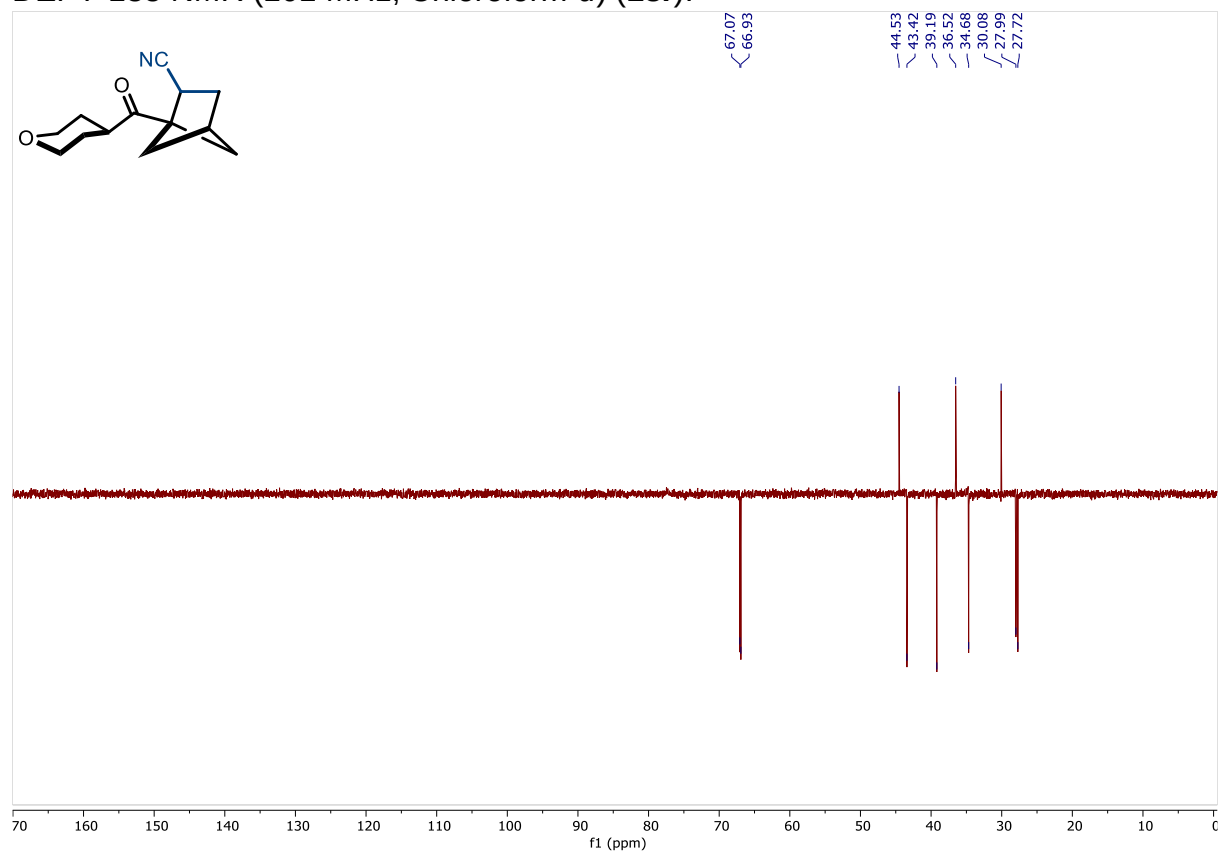
¹H NMR (400 MHz, Chloroform-*d*) (**13r**):



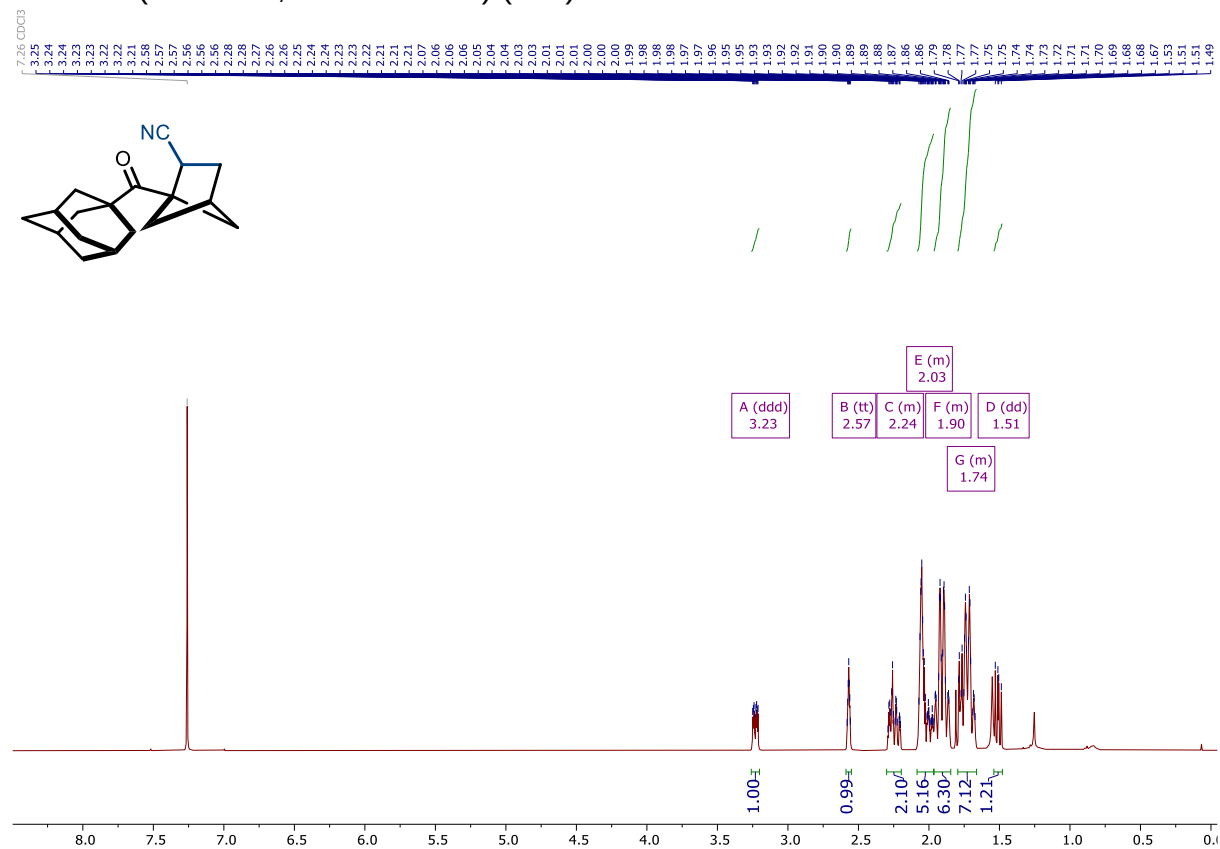
¹³C NMR (101 MHz, Chloroform-*d*) (**13r**):



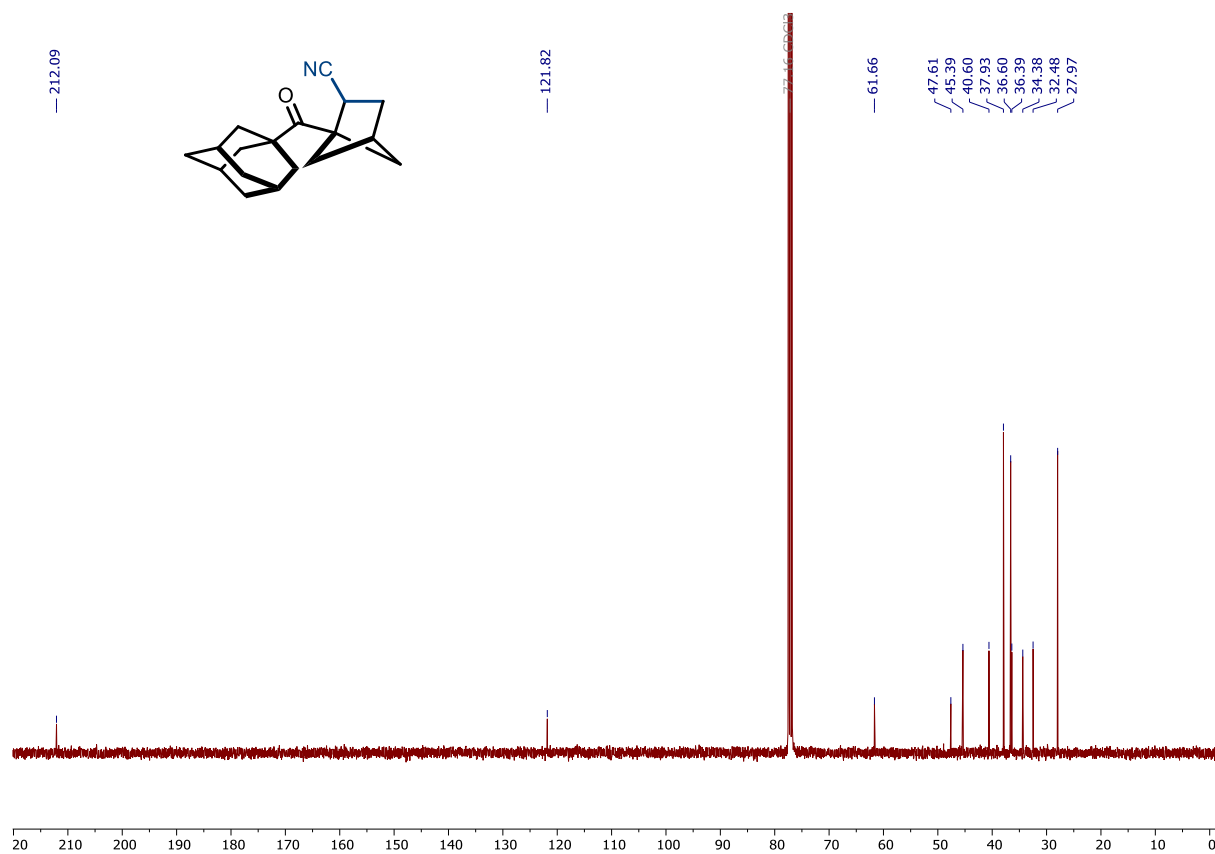
DEPT-135 NMR (101 MHz, Chloroform-*d*) (**13r**):



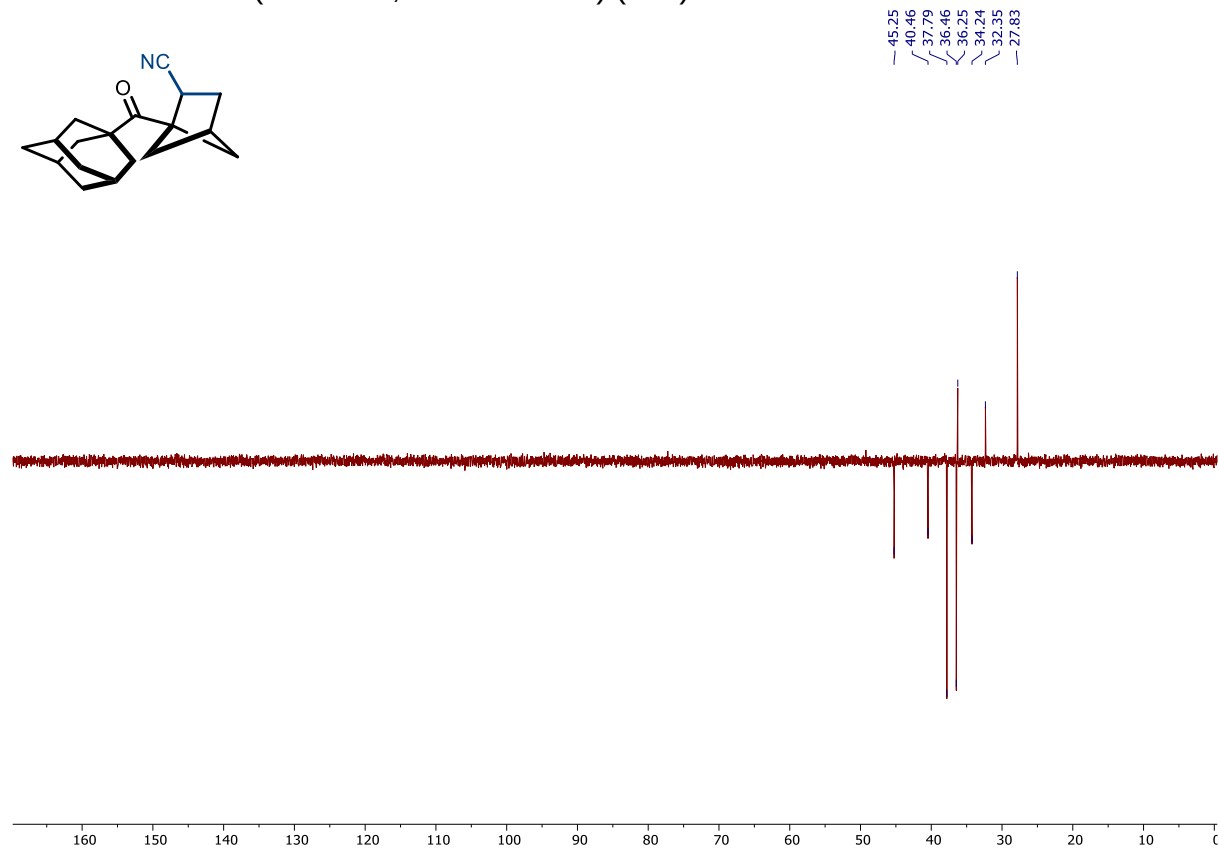
¹H NMR (400 MHz, Chloroform-*d*) (**13s**):



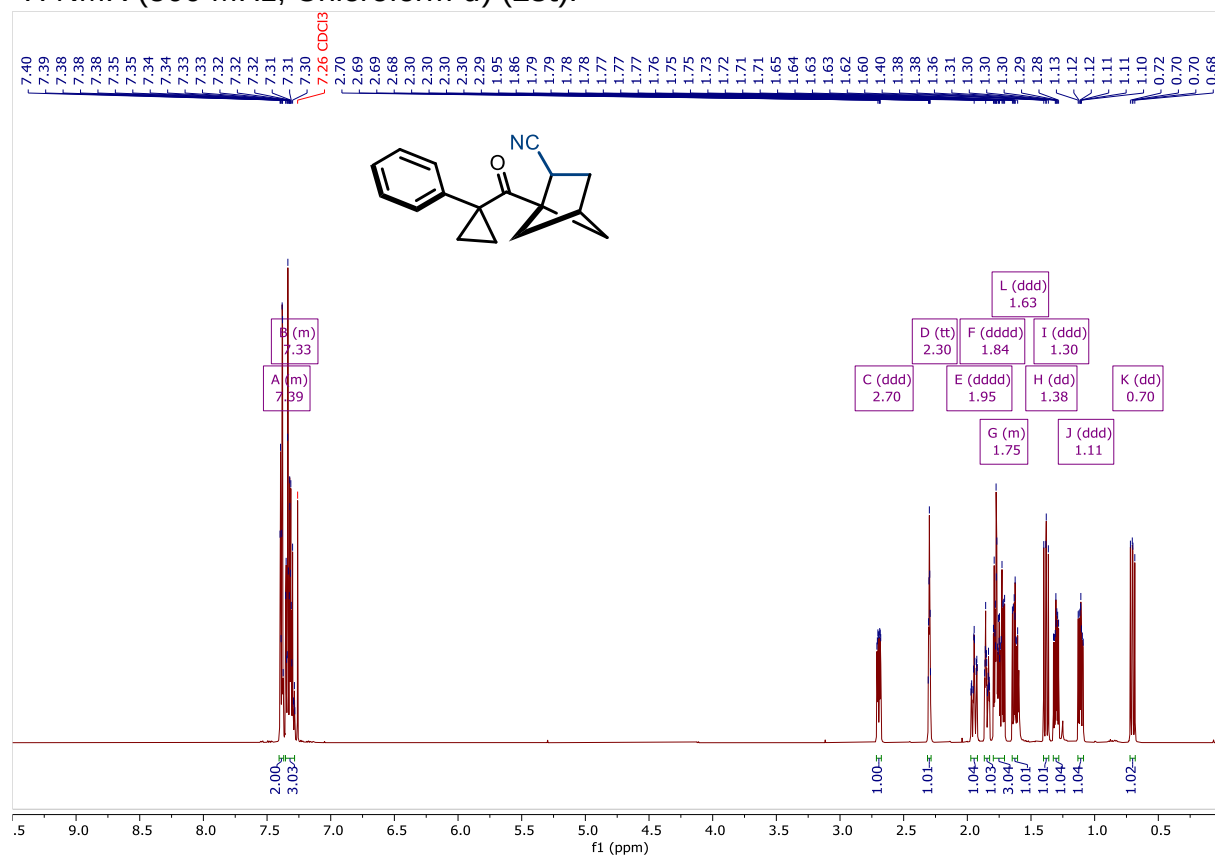
¹³C NMR (101 MHz, Chloroform-*d*) (**13s**):



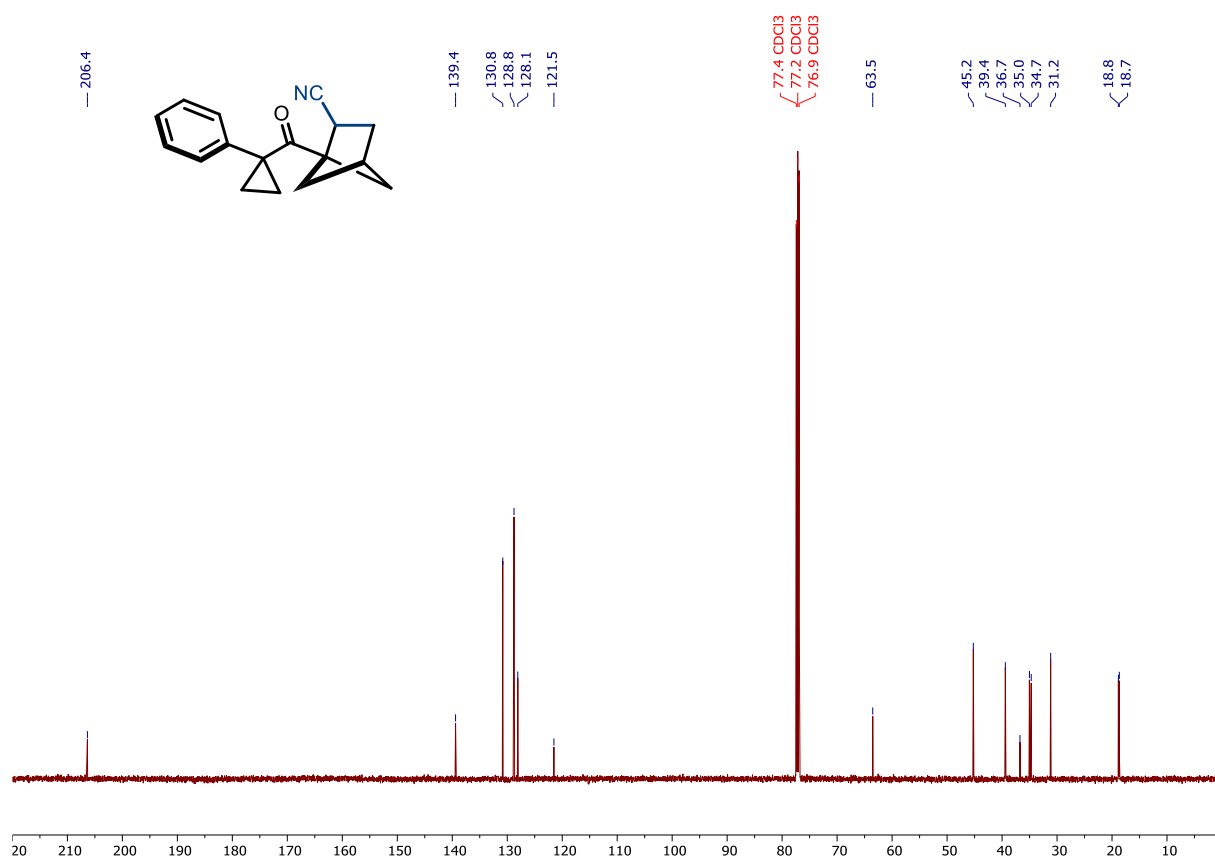
DEPT-135 NMR (101 MHz, Chloroform-*d*) (**13s**):



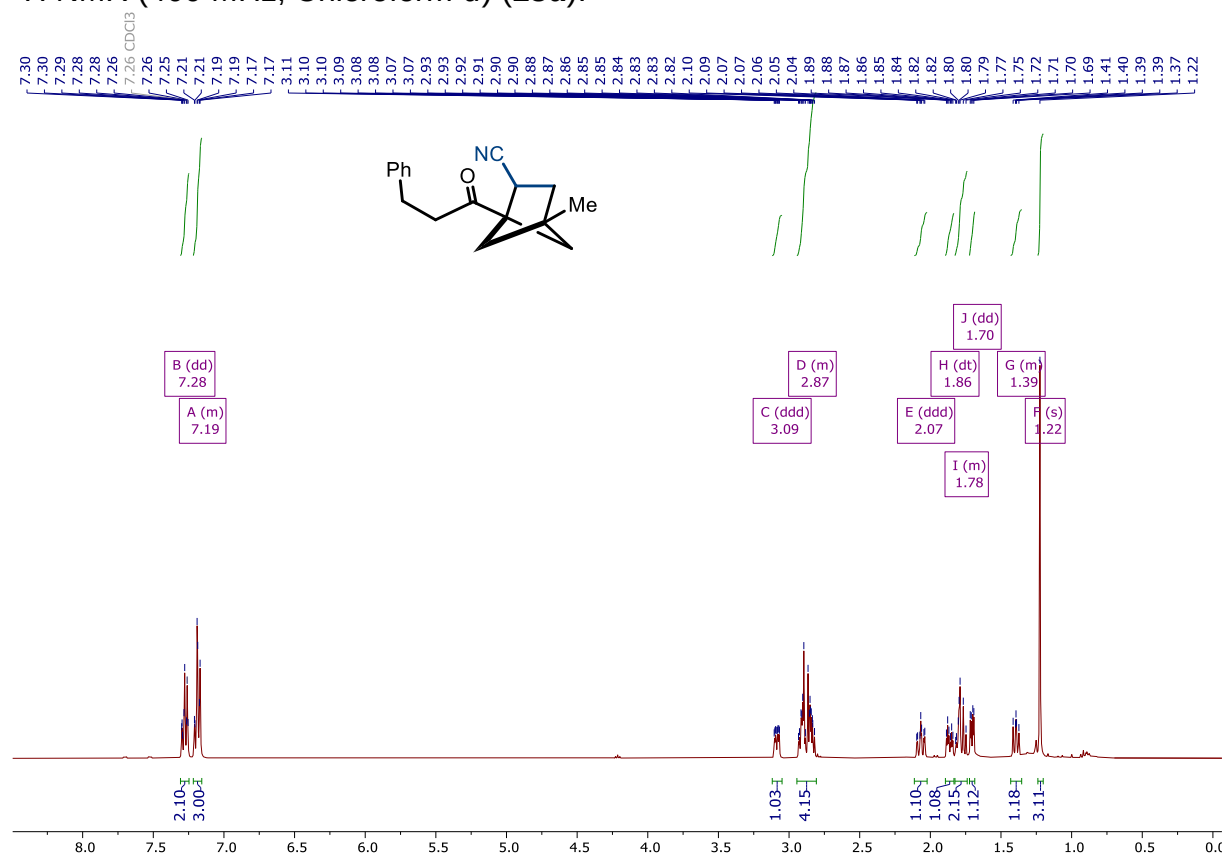
¹H NMR (500 MHz, Chloroform-*d*) (**13t**):



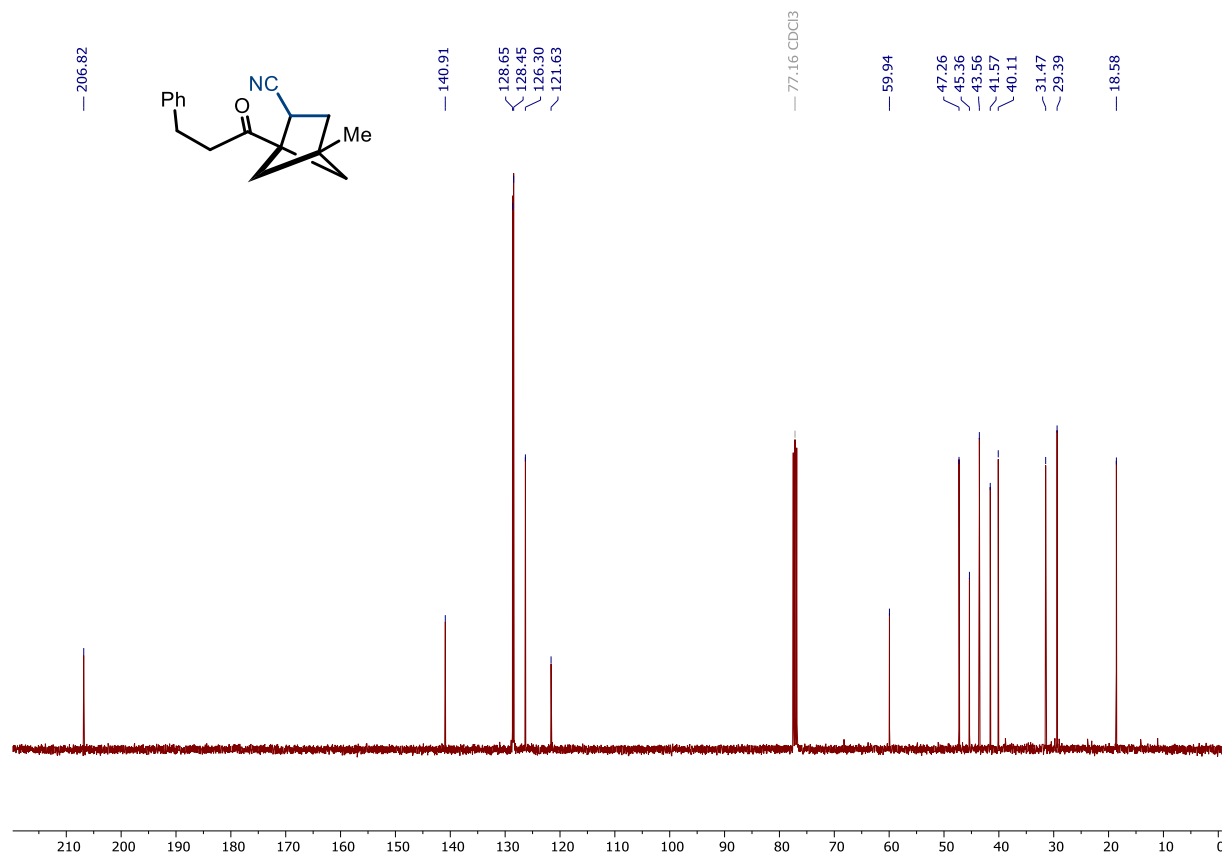
¹³C NMR (126 MHz, Chloroform-*d*) (**13t**):



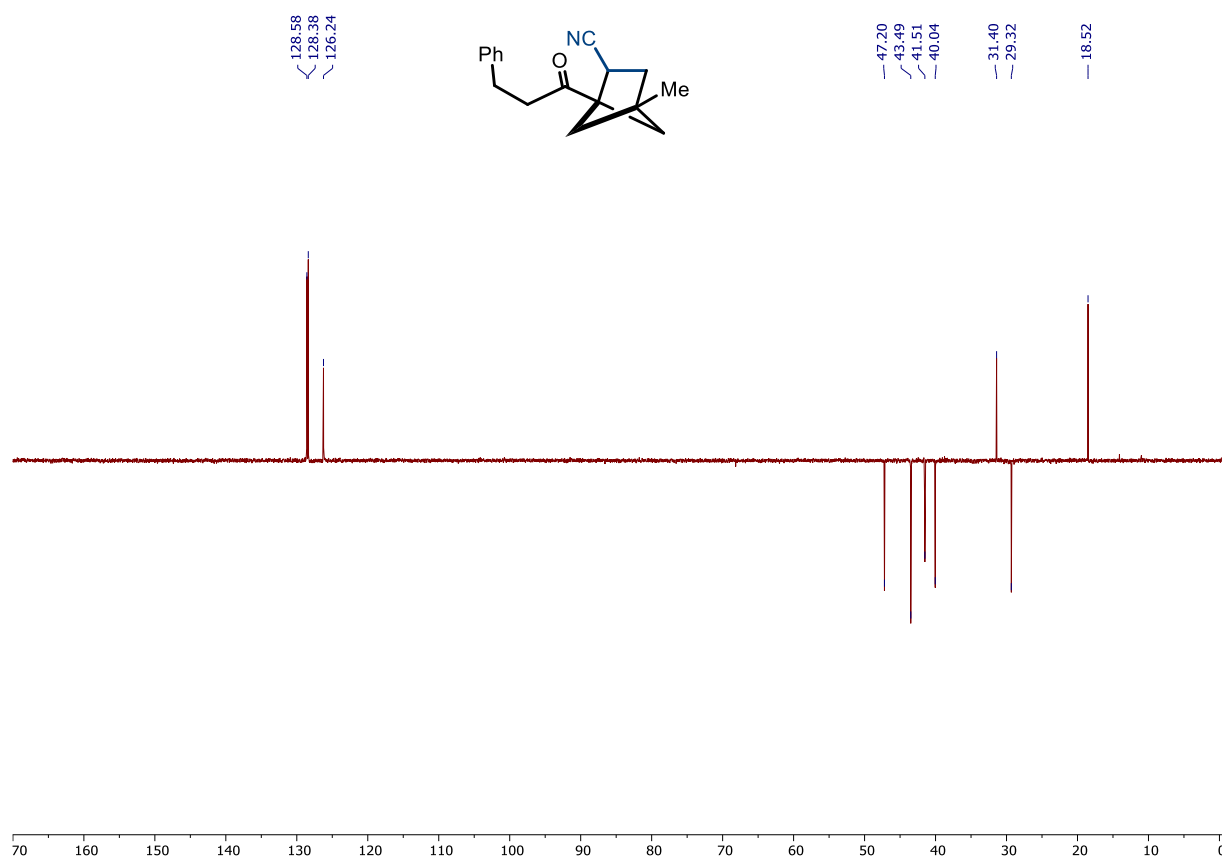
^1H NMR (400 MHz, Chloroform- d) (**13u**):



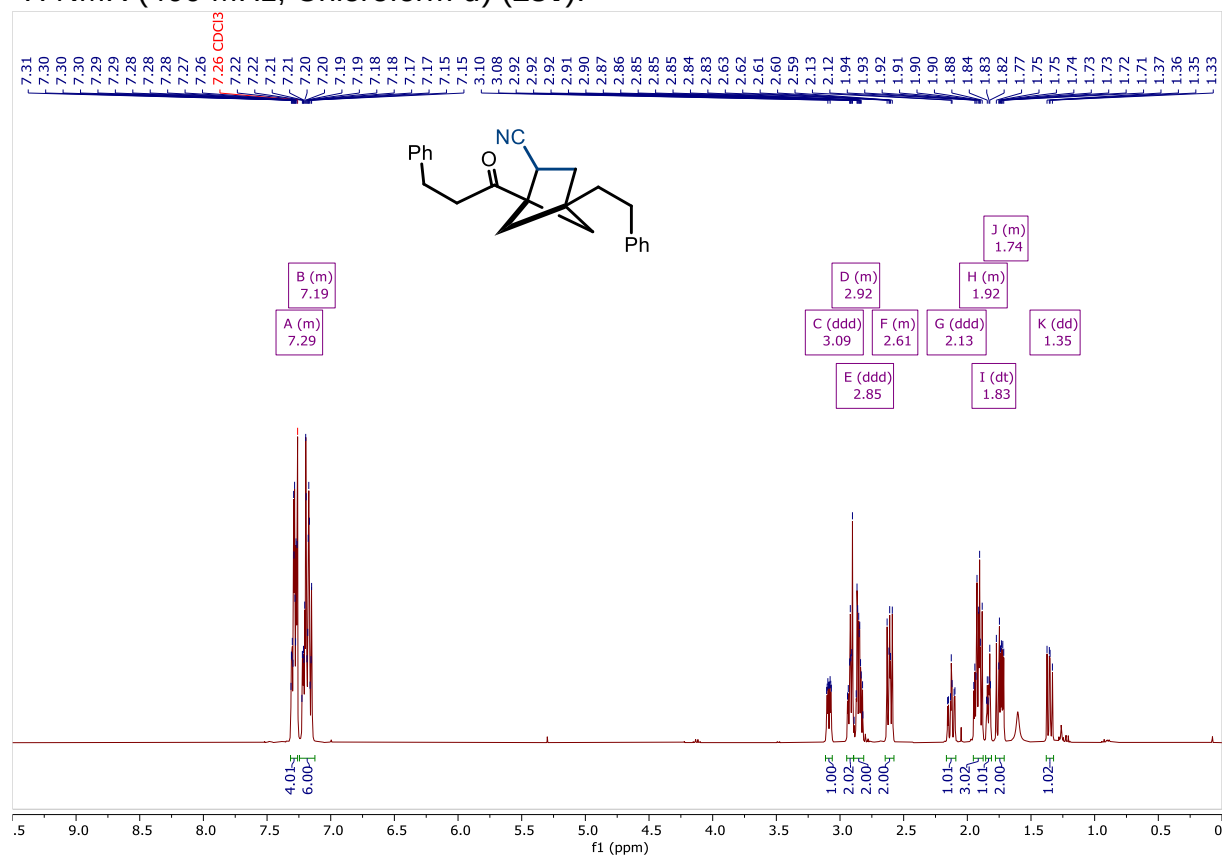
^{13}C NMR (101 MHz, Chloroform- d) (**13u**):



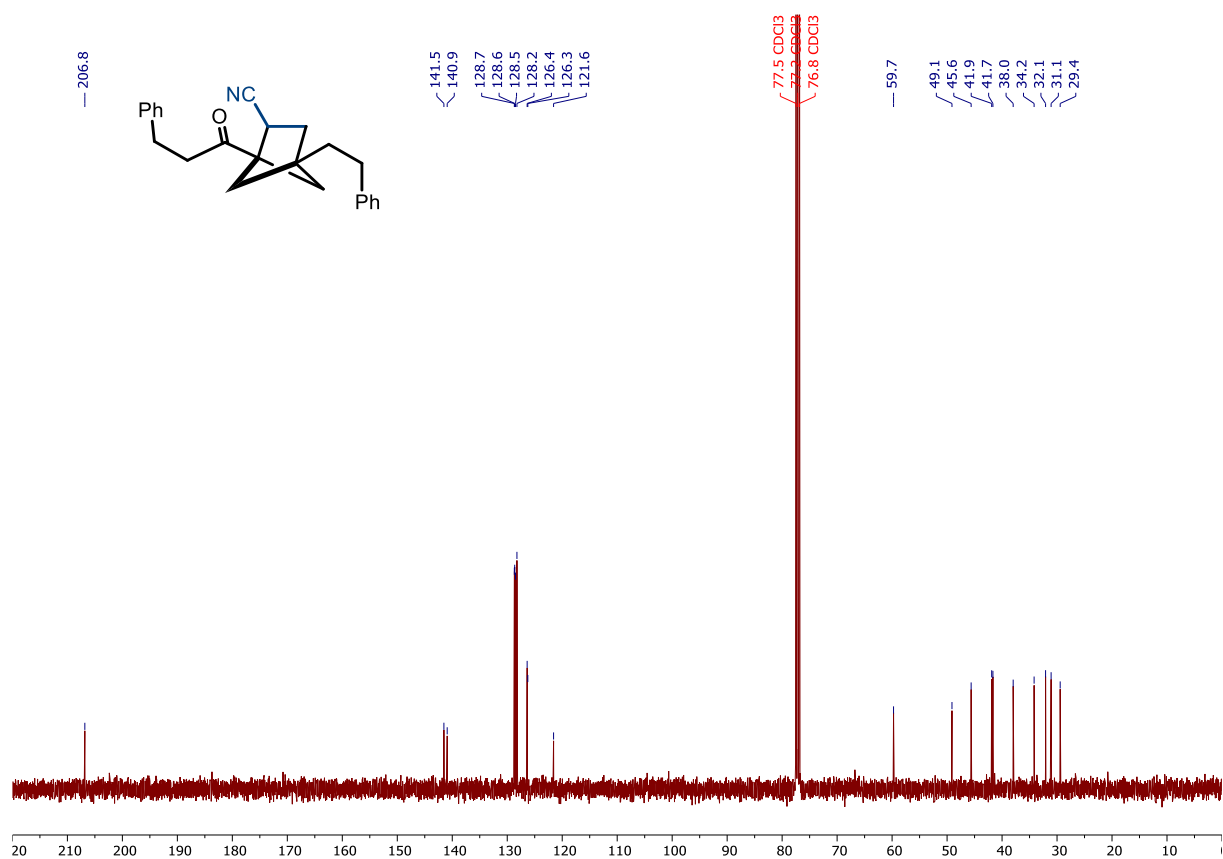
DEPT-135 NMR (101 MHz, Chloroform-*d*) (**13u**):



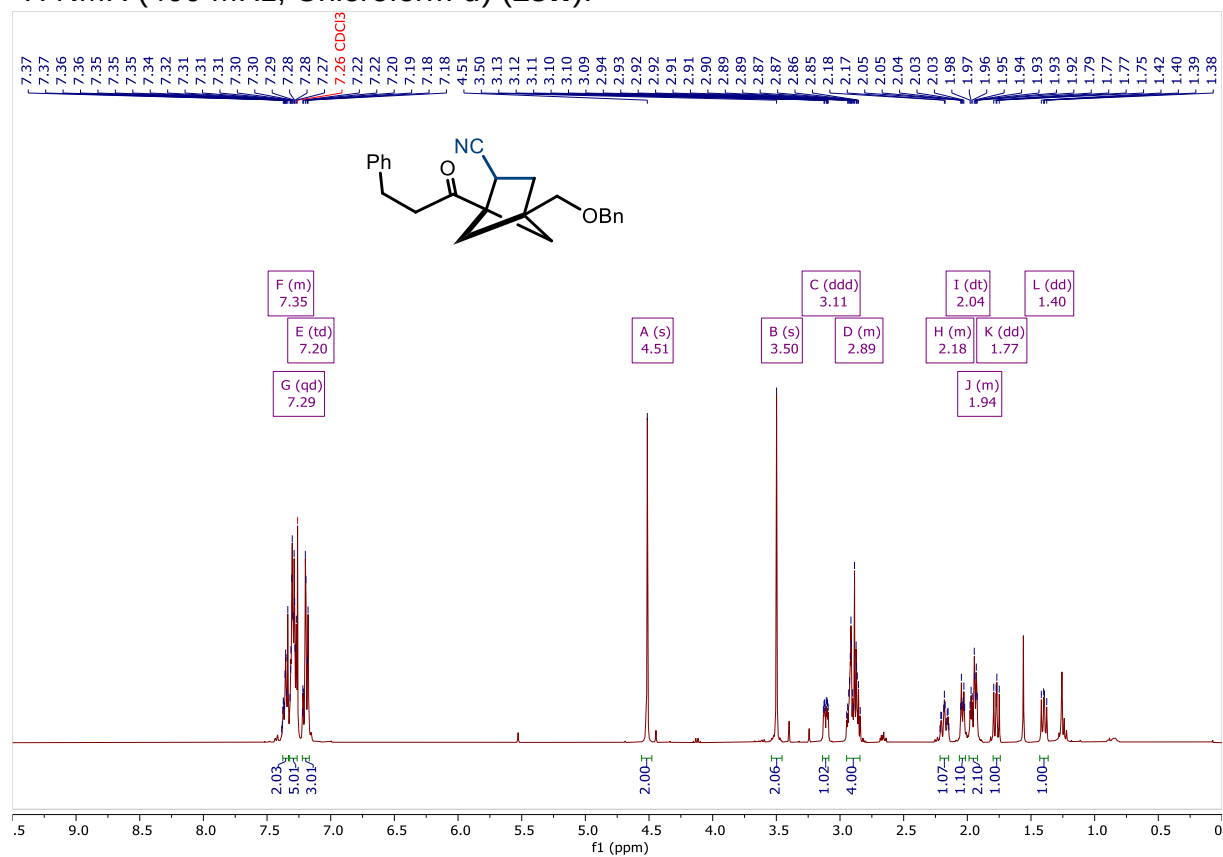
¹H NMR (400 MHz, Chloroform-*d*) (**13v**):



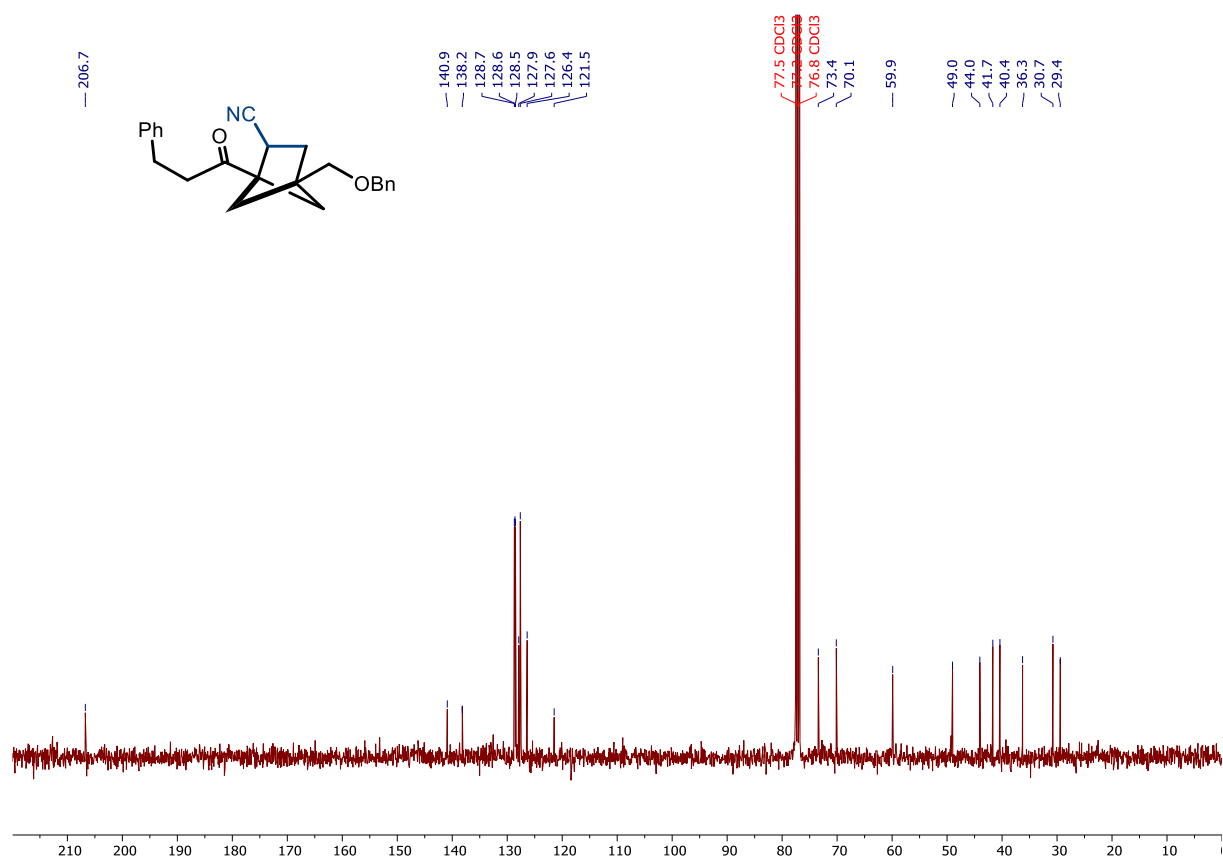
¹³C NMR (101 MHz, Chloroform-*d*) (**13v**):



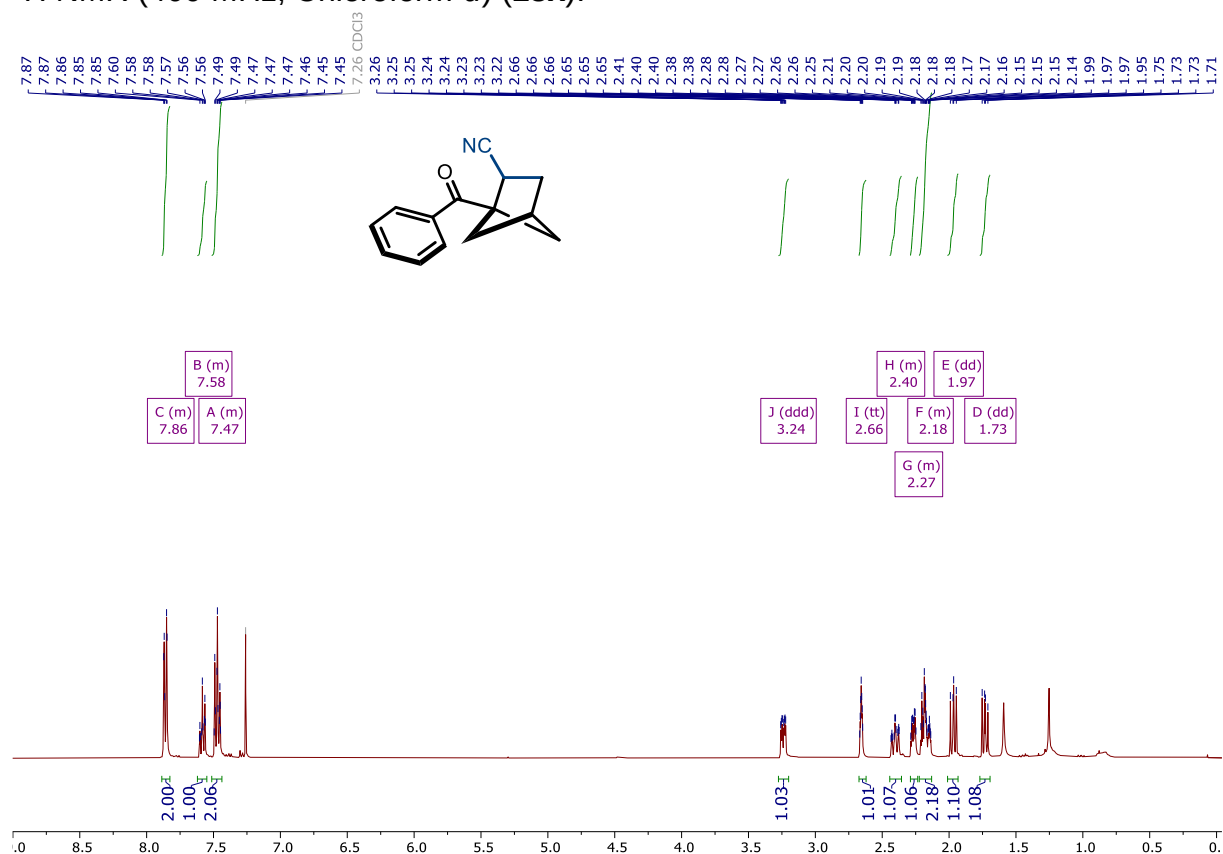
¹H NMR (400 MHz, Chloroform-*d*) (**13w**):



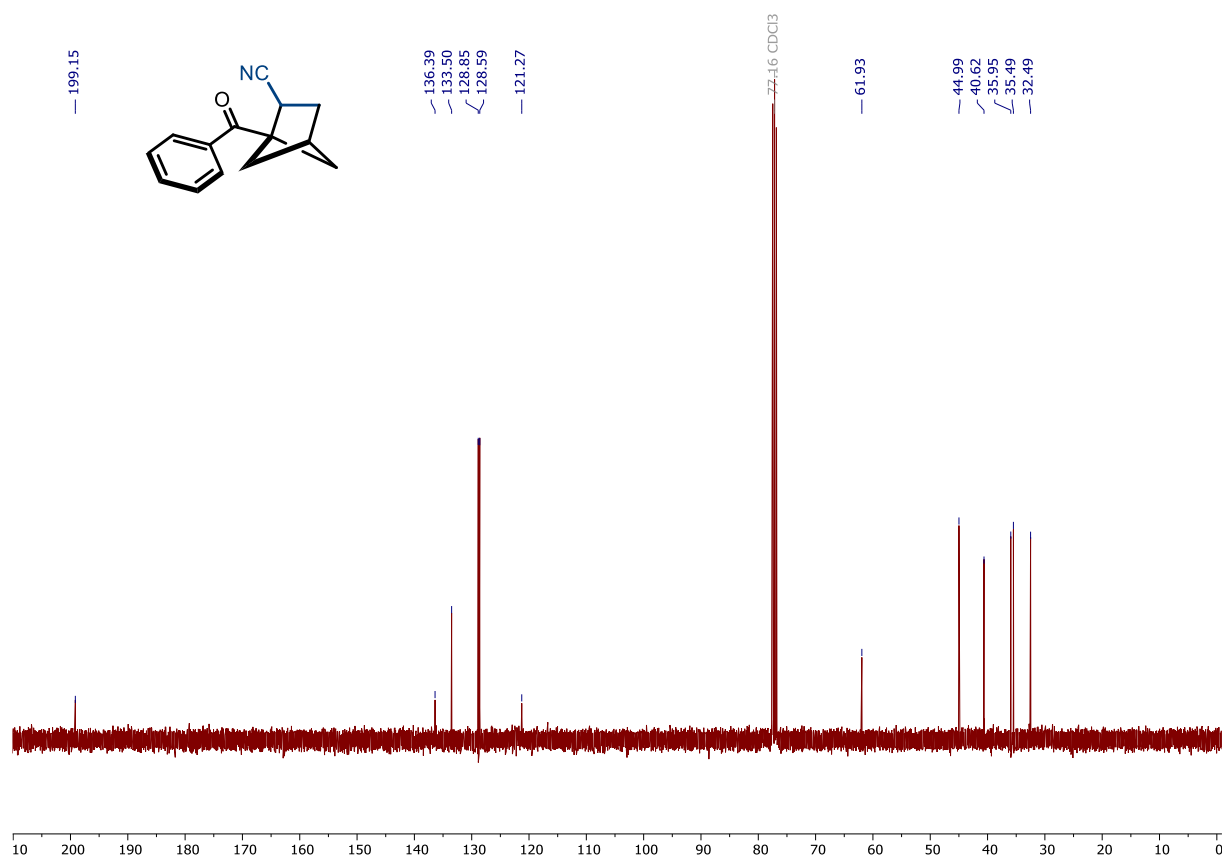
¹³C NMR (101 MHz, Chloroform-*d*) (**13w**):



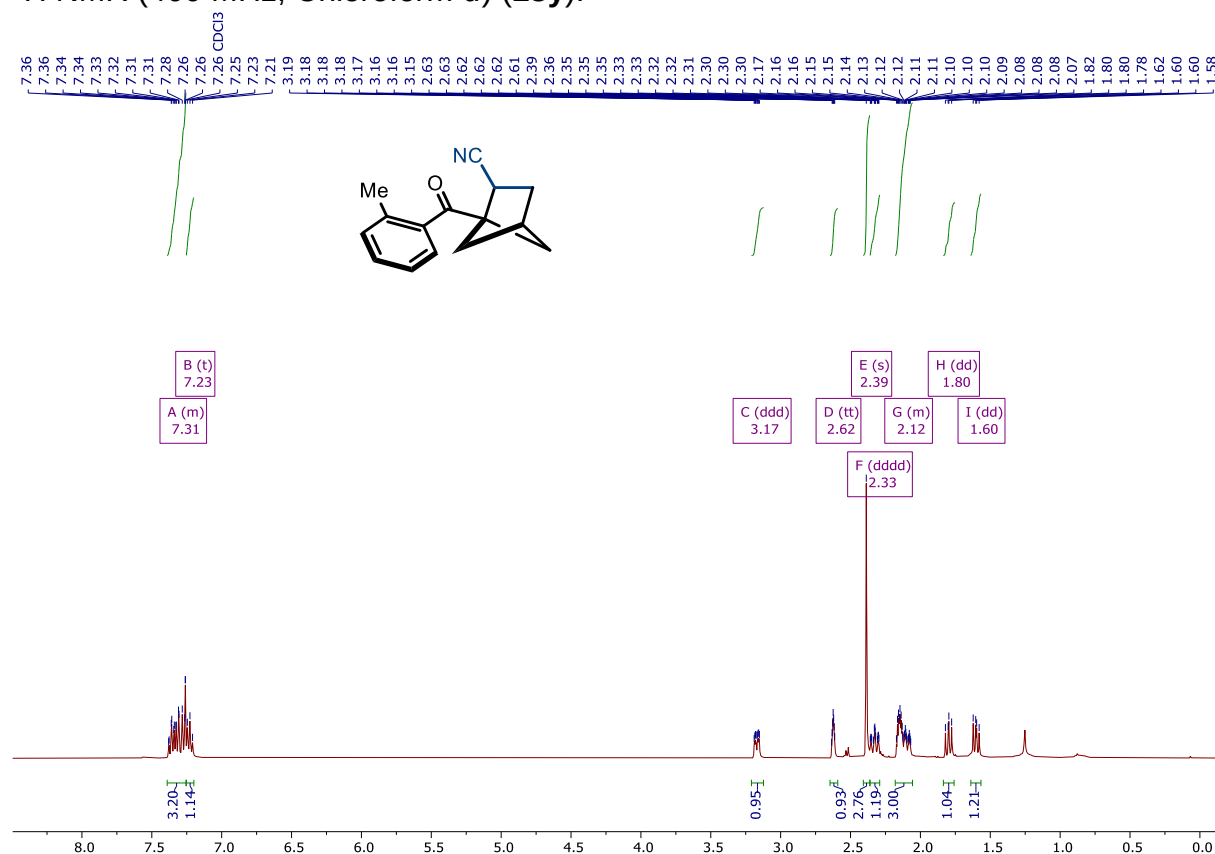
^1H NMR (400 MHz, Chloroform-*d*) (**13x**):



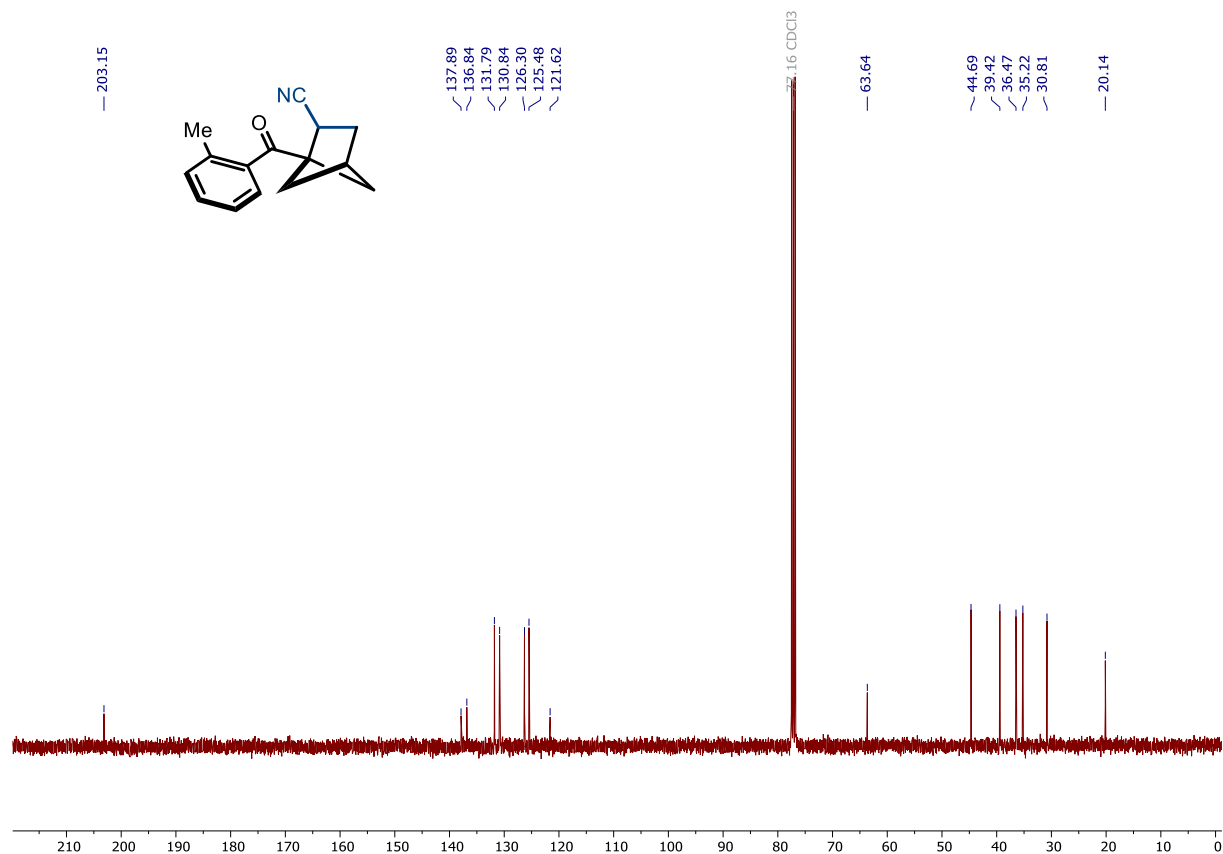
^{13}C NMR (101 MHz, Chloroform-*d*) (**13x**):



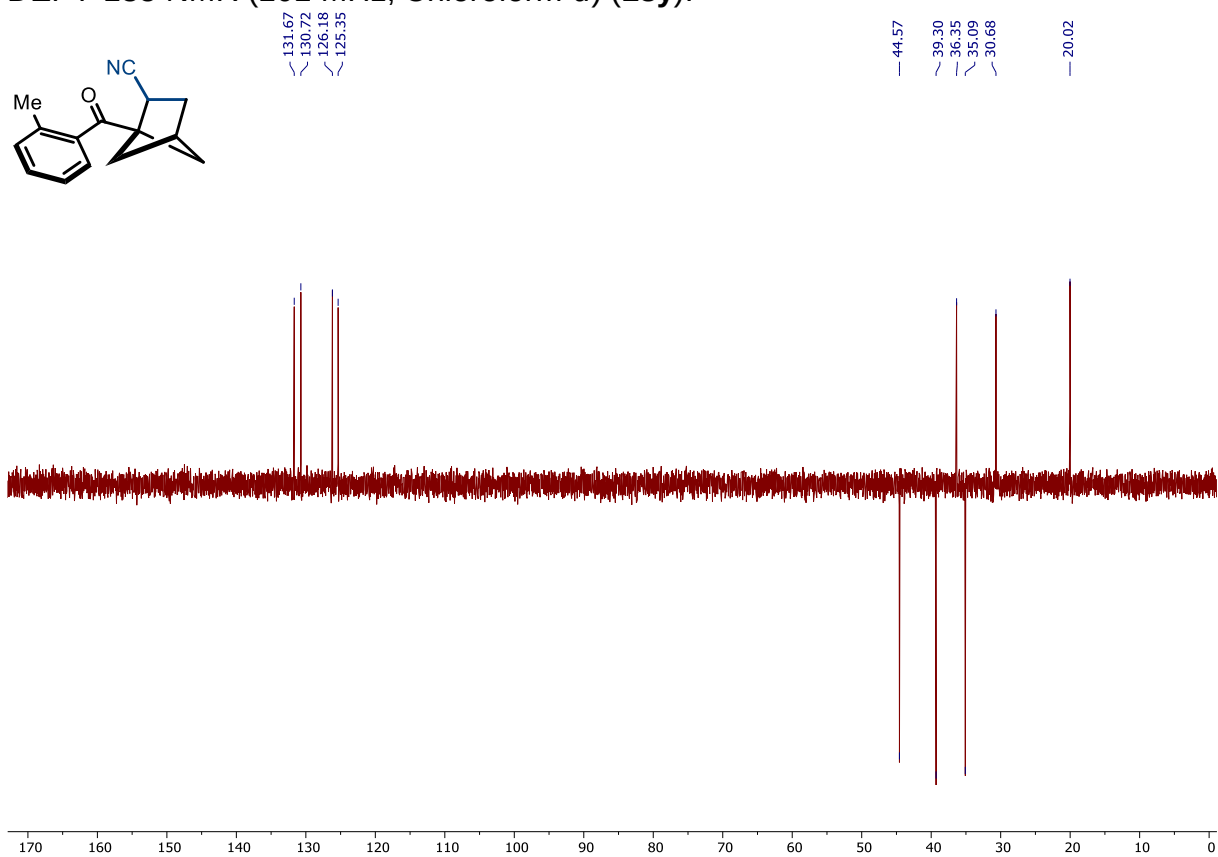
^1H NMR (400 MHz, Chloroform-*d*) (**13y**):



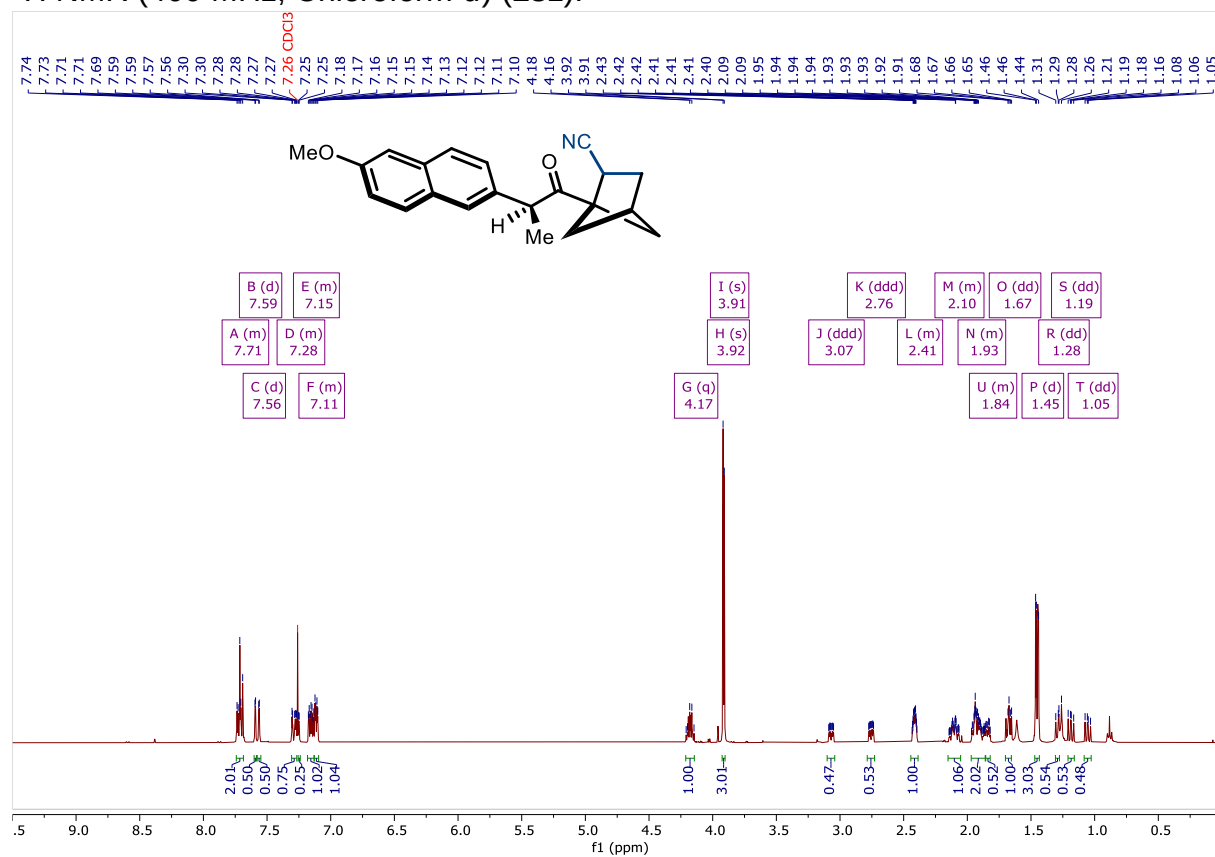
^{13}C NMR (101 MHz, Chloroform-*d*) (**13y**):



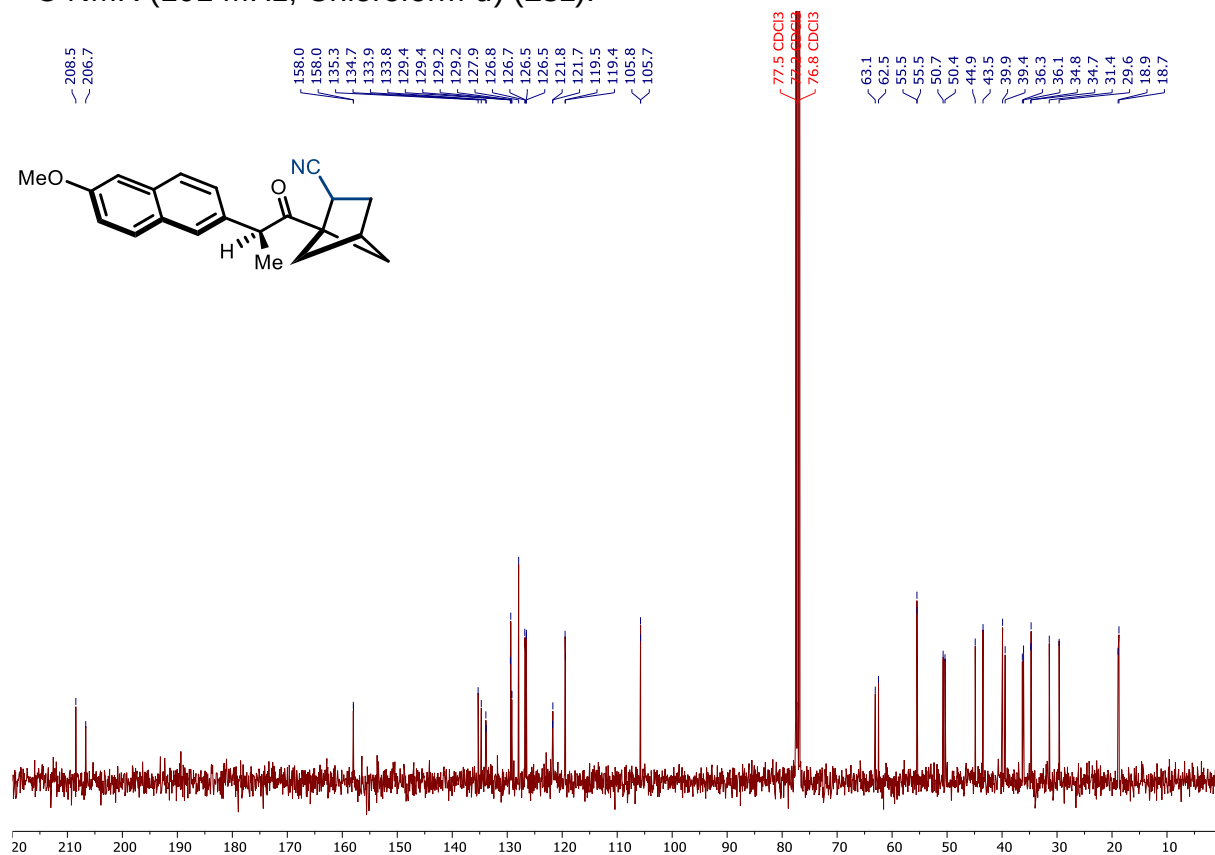
DEPT-135 NMR (101 MHz, Chloroform-*d*) (**13y**):



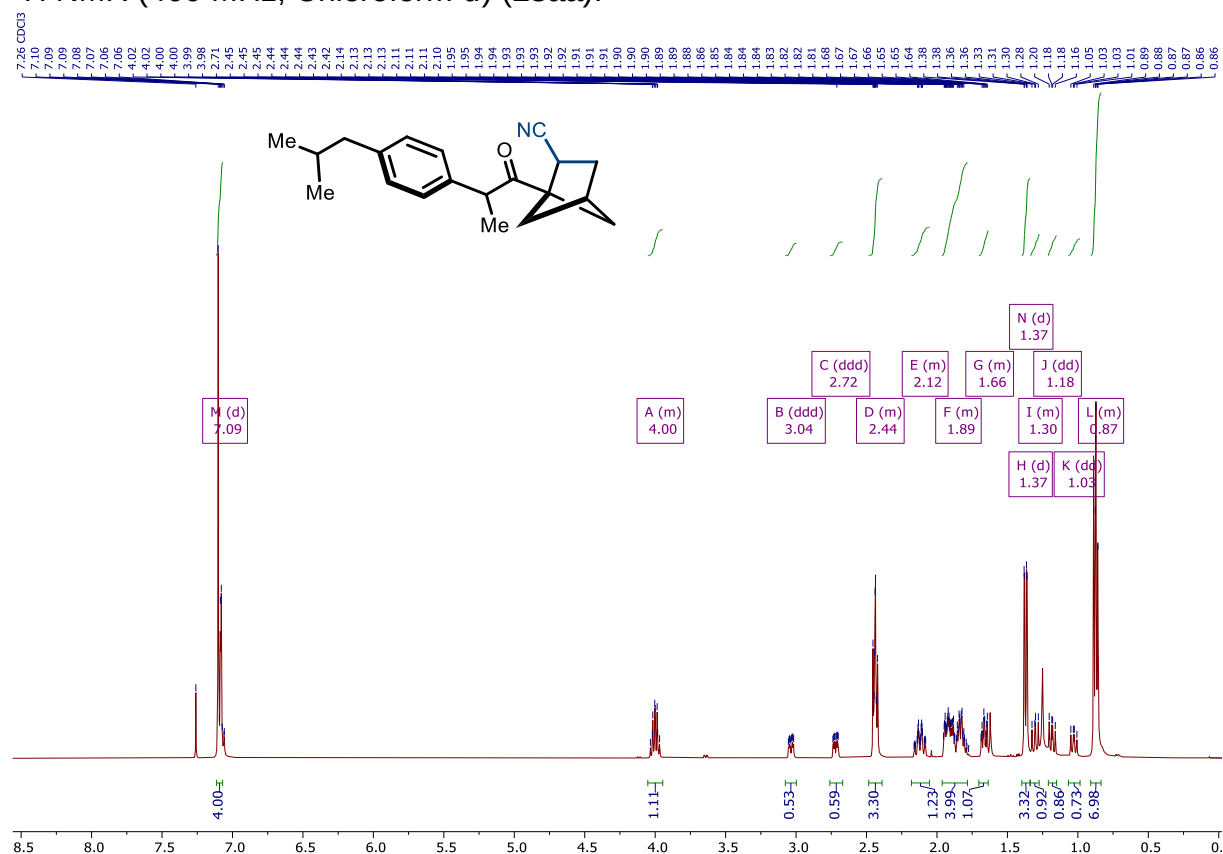
¹H NMR (400 MHz, Chloroform-*d*) (**13z**):



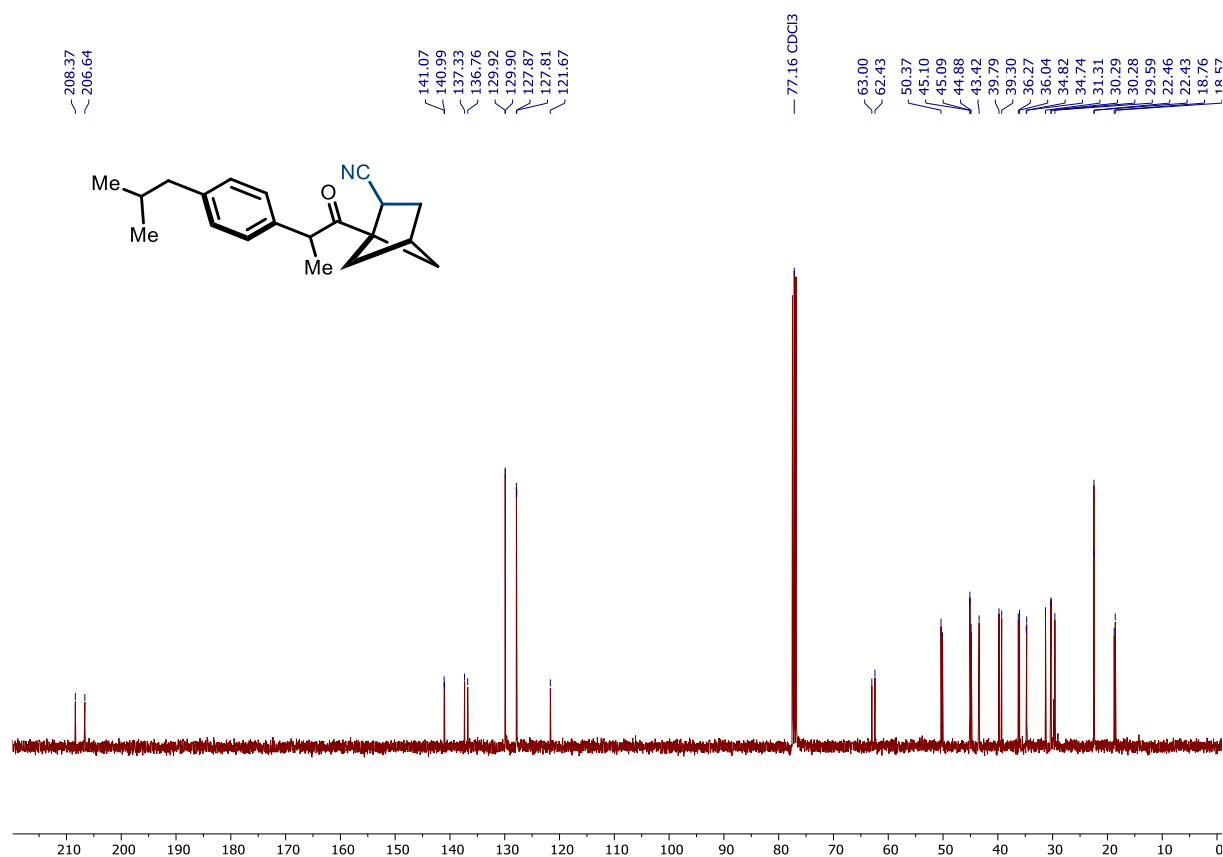
¹³C NMR (101 MHz, Chloroform-*d*) (**13z**):



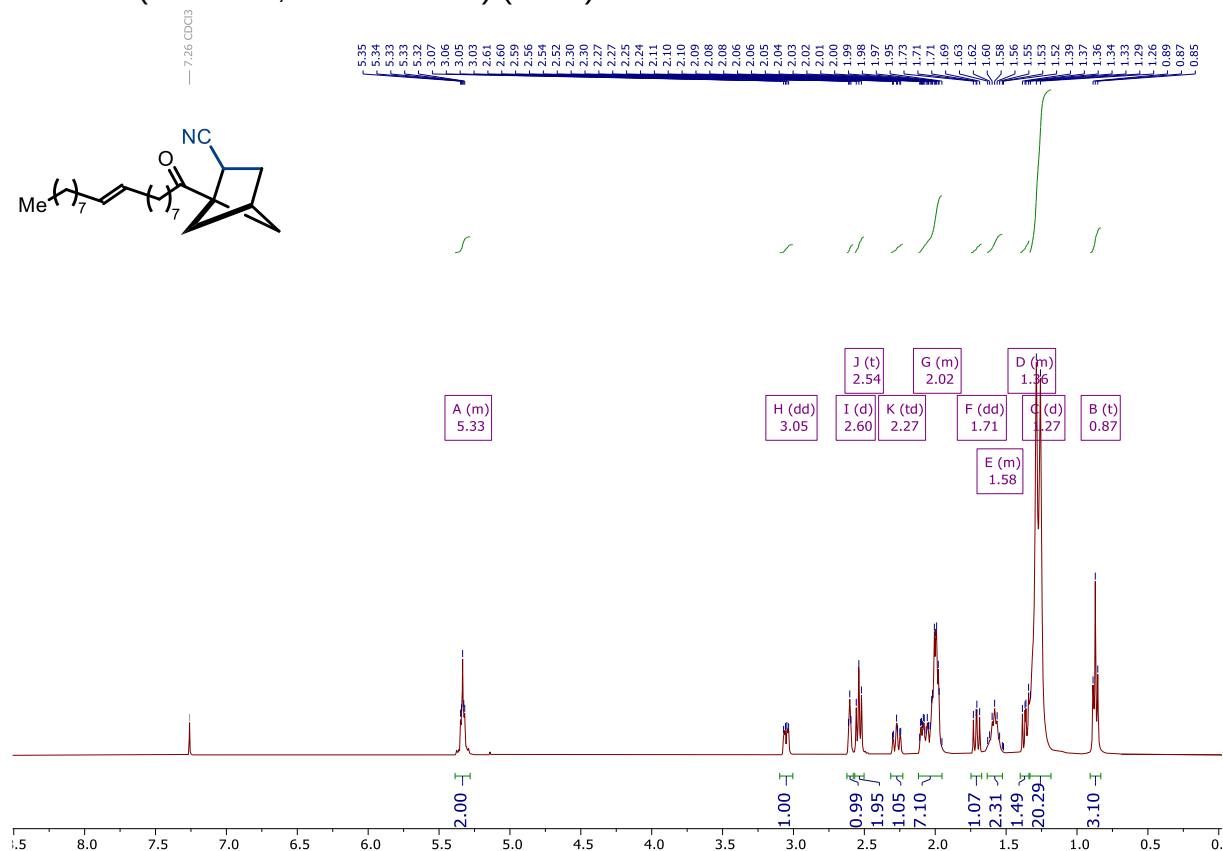
¹H NMR (400 MHz, Chloroform-*d*) (**13aa**):



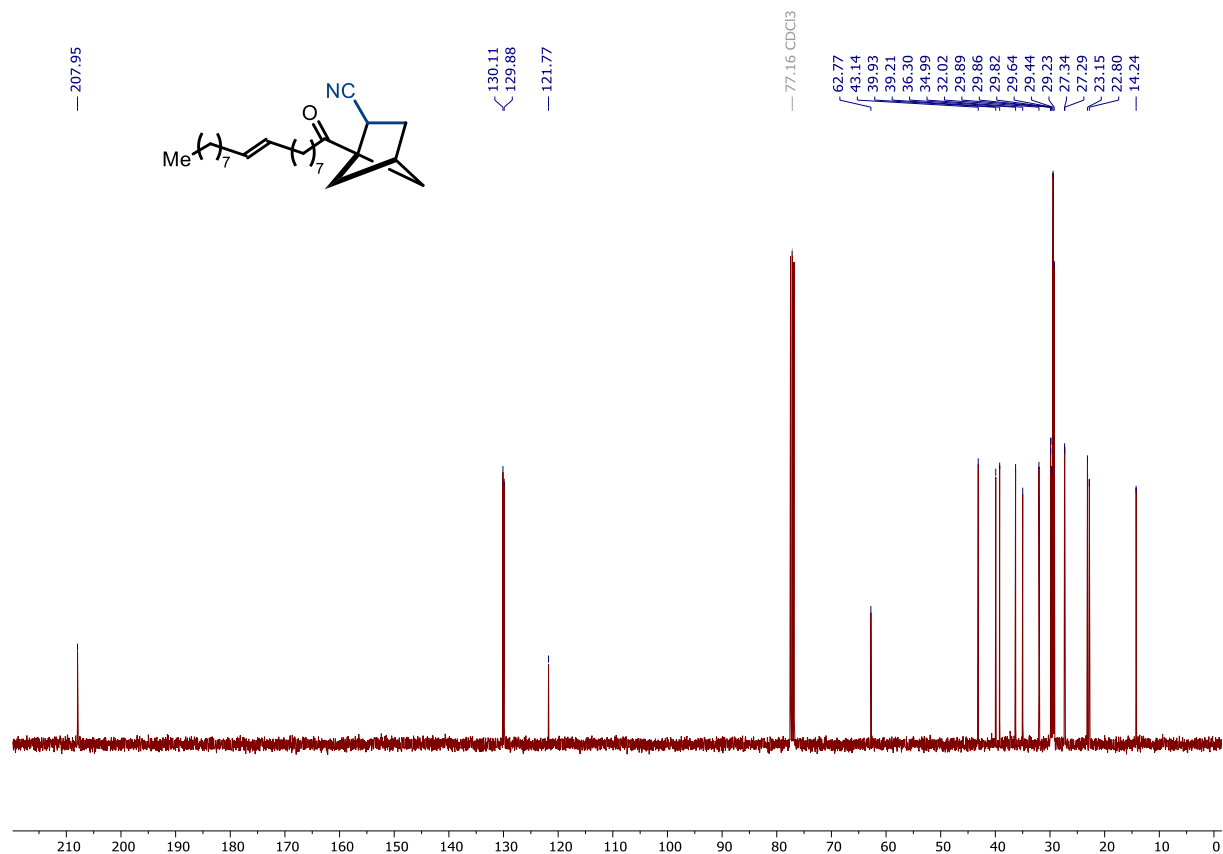
¹³C NMR (101 MHz, Chloroform-*d*) (**13aa**):



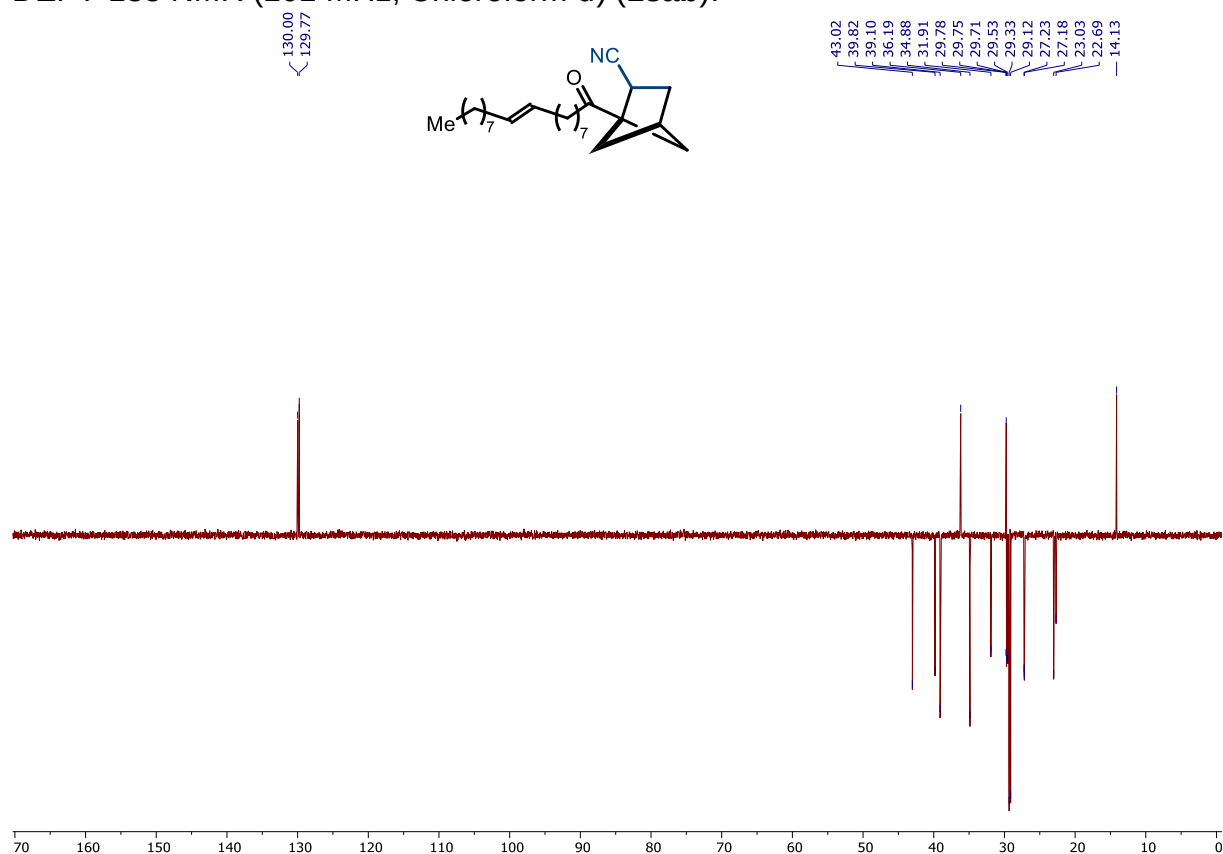
^1H NMR (400 MHz, Chloroform-*d*) (**13ab**):



^{13}C NMR (101 MHz, Chloroform-*d*) (**13ab**):



DEPT-135 NMR (101 MHz, Chloroform-*d*) (**13ab**):



Chemical structure: 1-(2-phenylethyl)-2-methoxy-2-oxobicyclo[2.2.1]heptane

¹H NMR spectrum (CDCl₃) showing peaks labeled A through L and the solvent peak (CDCl₃).

Label	Chemical Shift (ppm)	Integration
A (ddd)	7.28	2.08
B (m)	7.19	3.00
C (d)	3.61	3.00
D (ddt)	3.19	1.00
E (m)	2.85	4.06
F (tq)	2.44	1.01
G (dddt)	2.13	1.05
H (dddt)	1.97	1.05
I (ddq)	1.88	1.02
J (dtd)	1.79	1.04
K (ddd)	1.60	-
L (ddd)	1.43	-

Solvent peak: CDCl₃ (7.26 ppm)

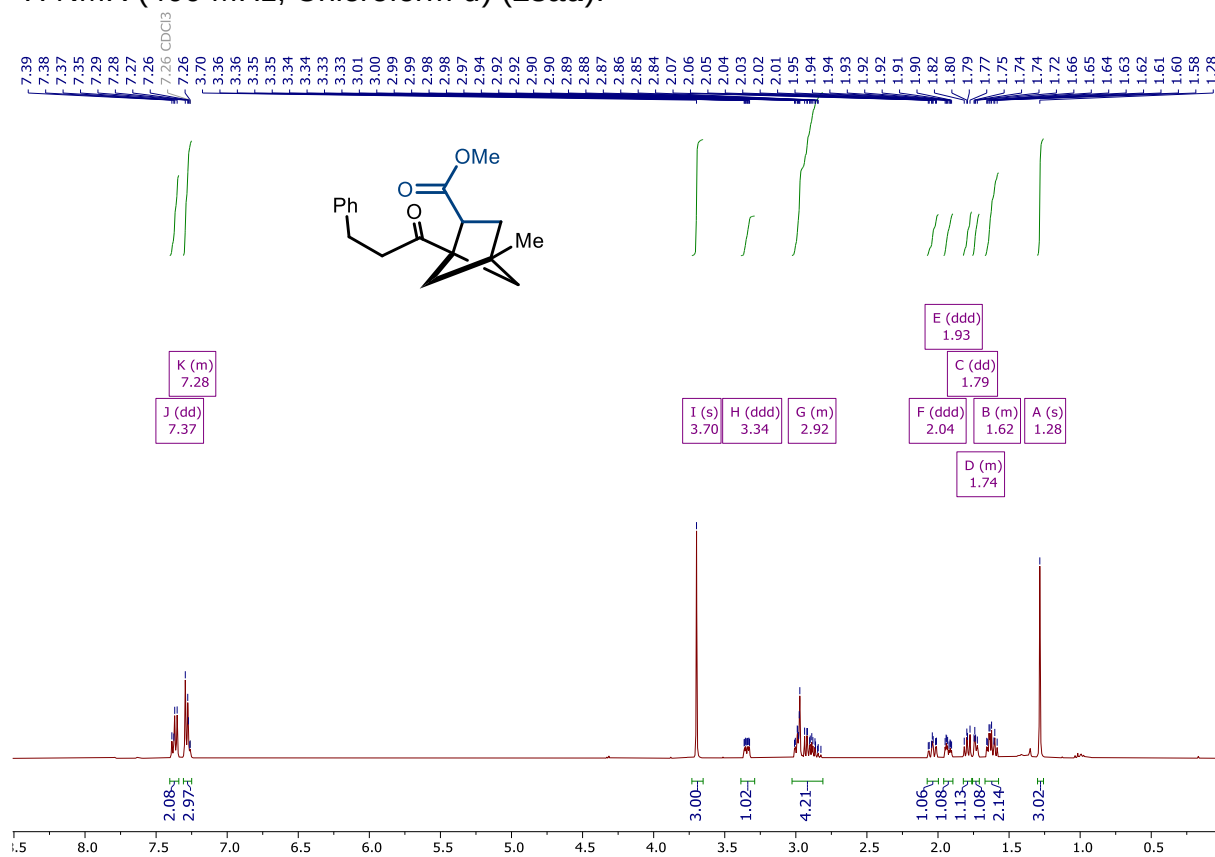
Chemical structure of the compound is shown above the spectrum. The structure is a bicyclic ketone with a phenyl group and a methoxy group.

The spectrum displays the following chemical shifts (ppm):

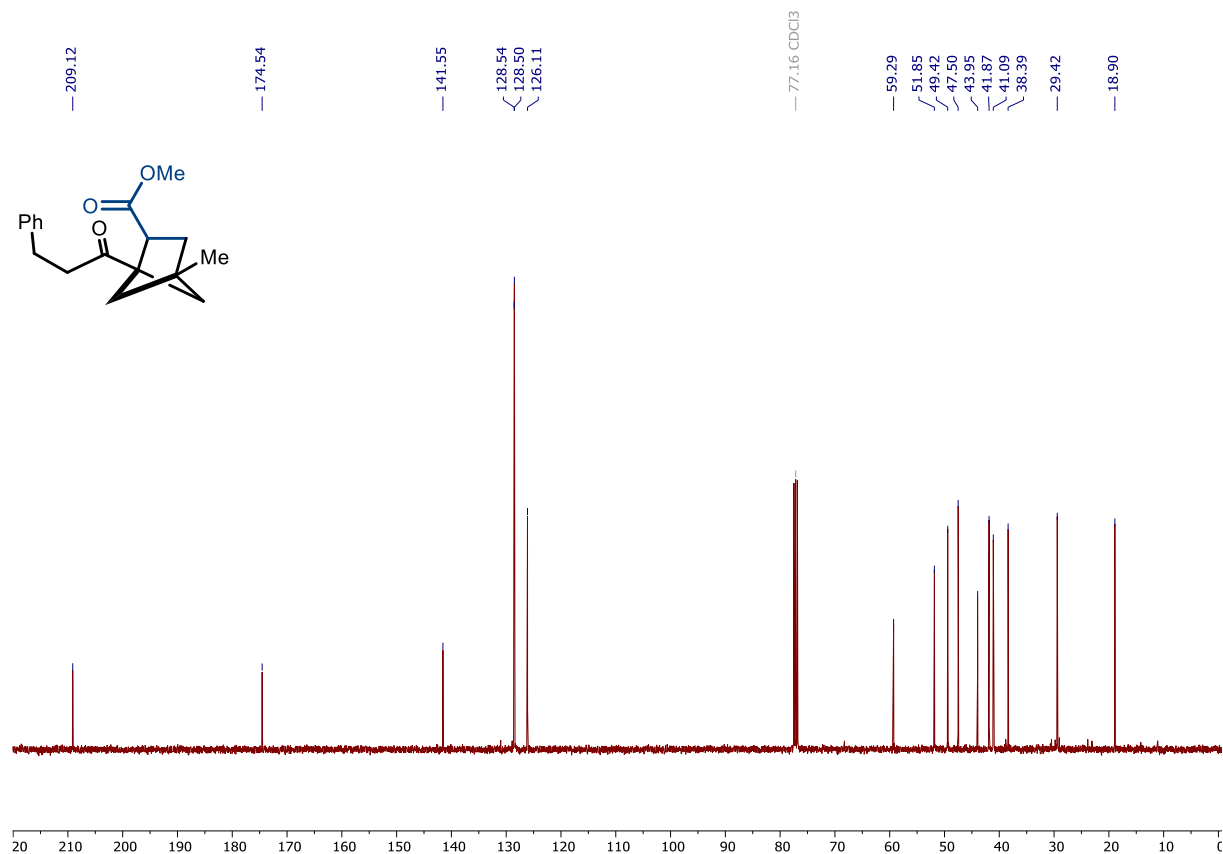
- 209.2
- 174.7
- 141.5
- 128.6
- 128.5
- 126.2
- 77.4 CDCl₃
- 77.2 CDCl₃
- 76.9 CDCl₃
- 62.1
- 51.9
- 45.6
- 45.1
- 41.2
- 37.4
- 35.4
- 32.8
- 29.4

13C NMR spectrum (CDCl₃) of the compound. The spectrum shows peaks at 209.2, 174.7, 141.5, 128.6, 128.5, 126.2, 77.4, 77.2, 76.9, 62.1, 51.9, 45.6, 45.1, 41.2, 37.4, 35.4, 32.8, and 29.4 ppm. The peaks at 77.4, 77.2, and 76.9 ppm are labeled as CDCl₃ solvent peaks.

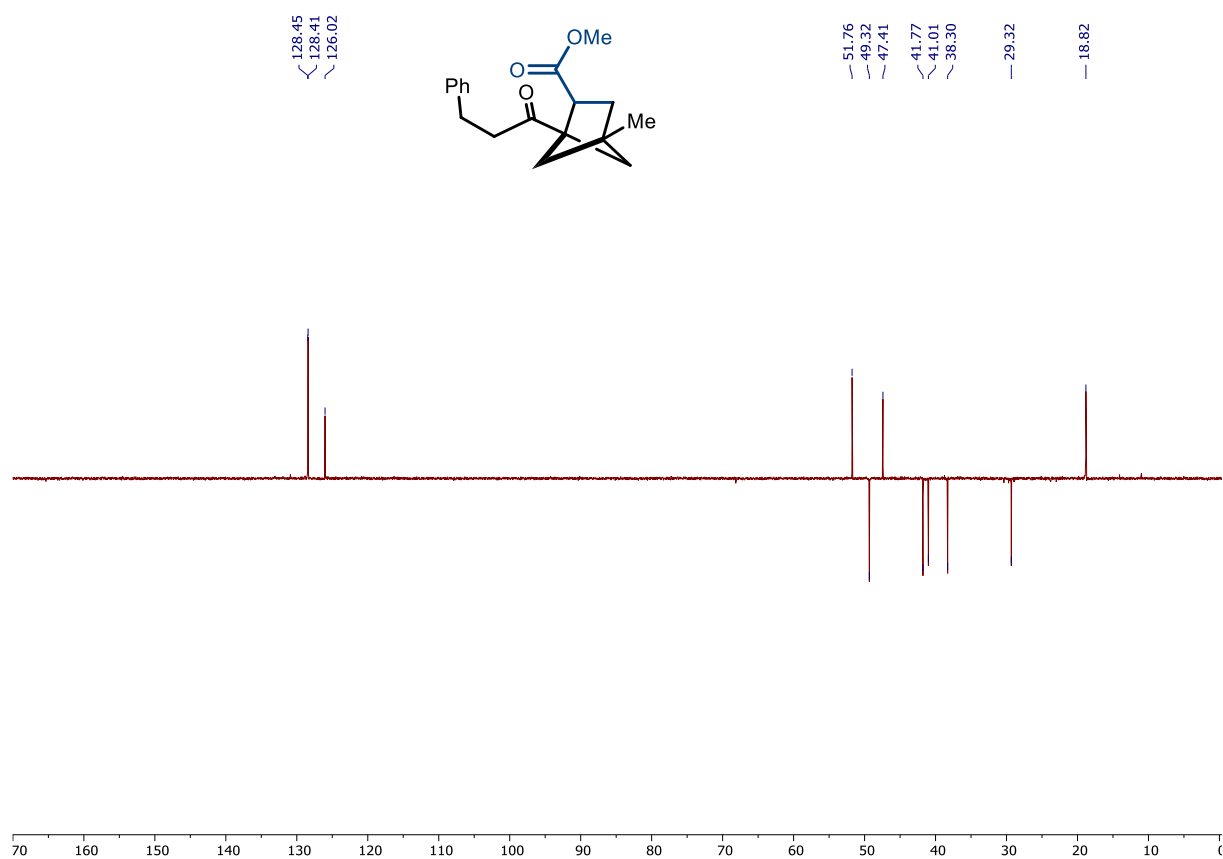
^1H NMR (400 MHz, Chloroform-*d*) (**13ad**):



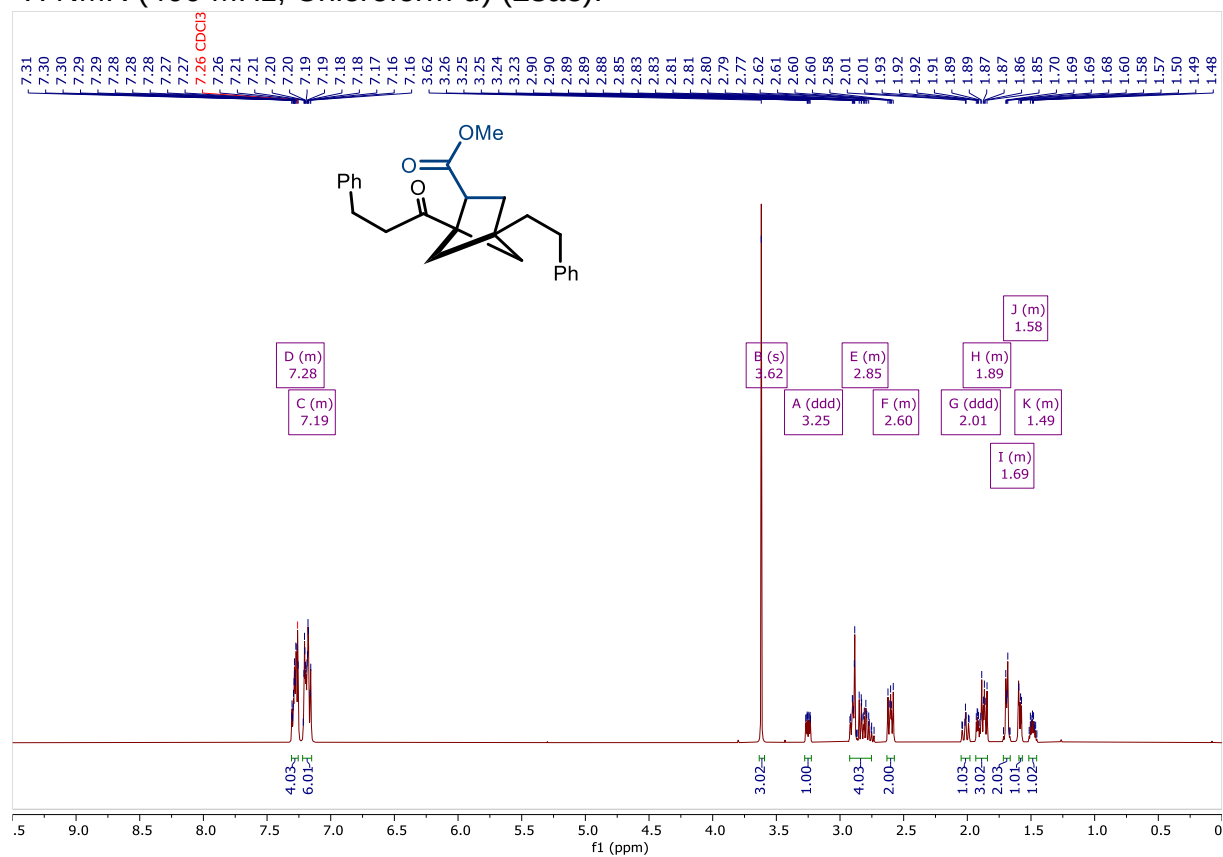
^{13}C NMR (101 MHz, Chloroform-*d*) (**13ad**):



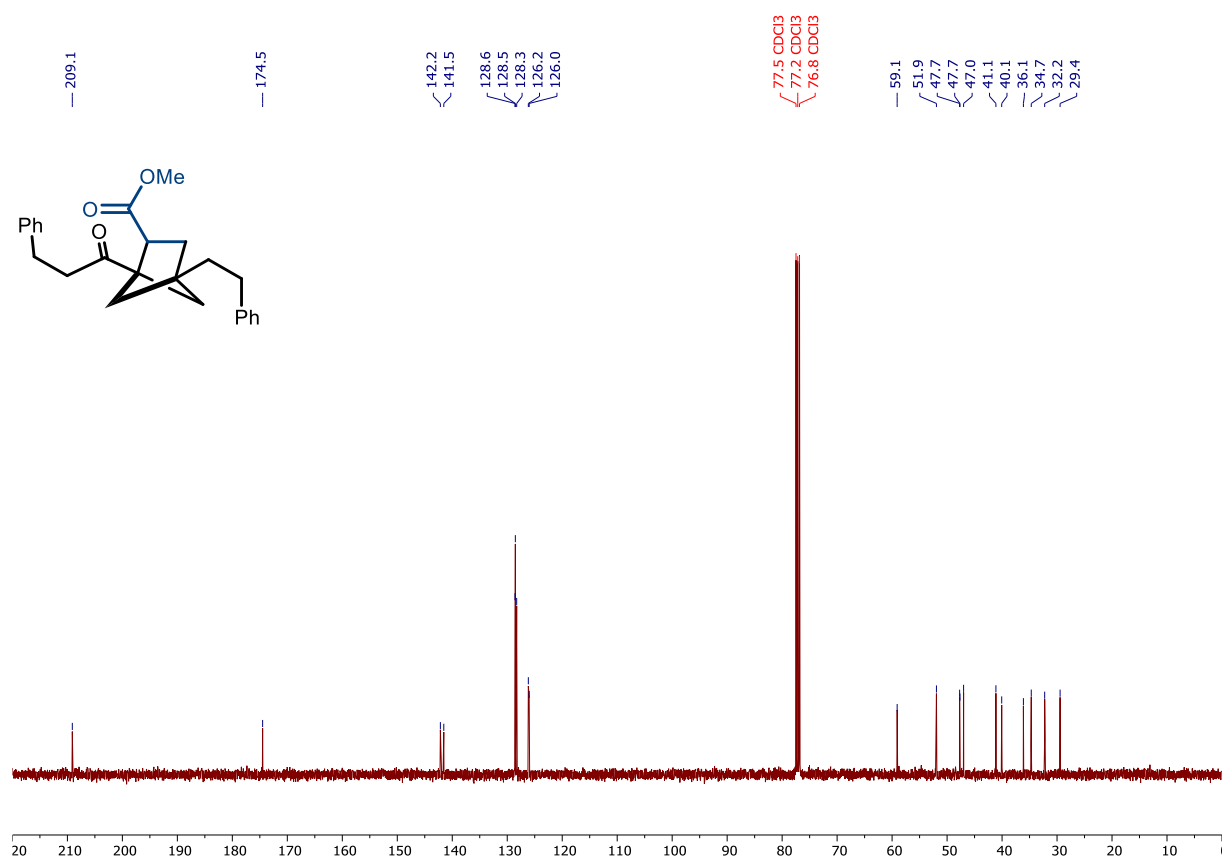
DEPT-135 NMR (101 MHz, Chloroform-*d*) (**13ad**):



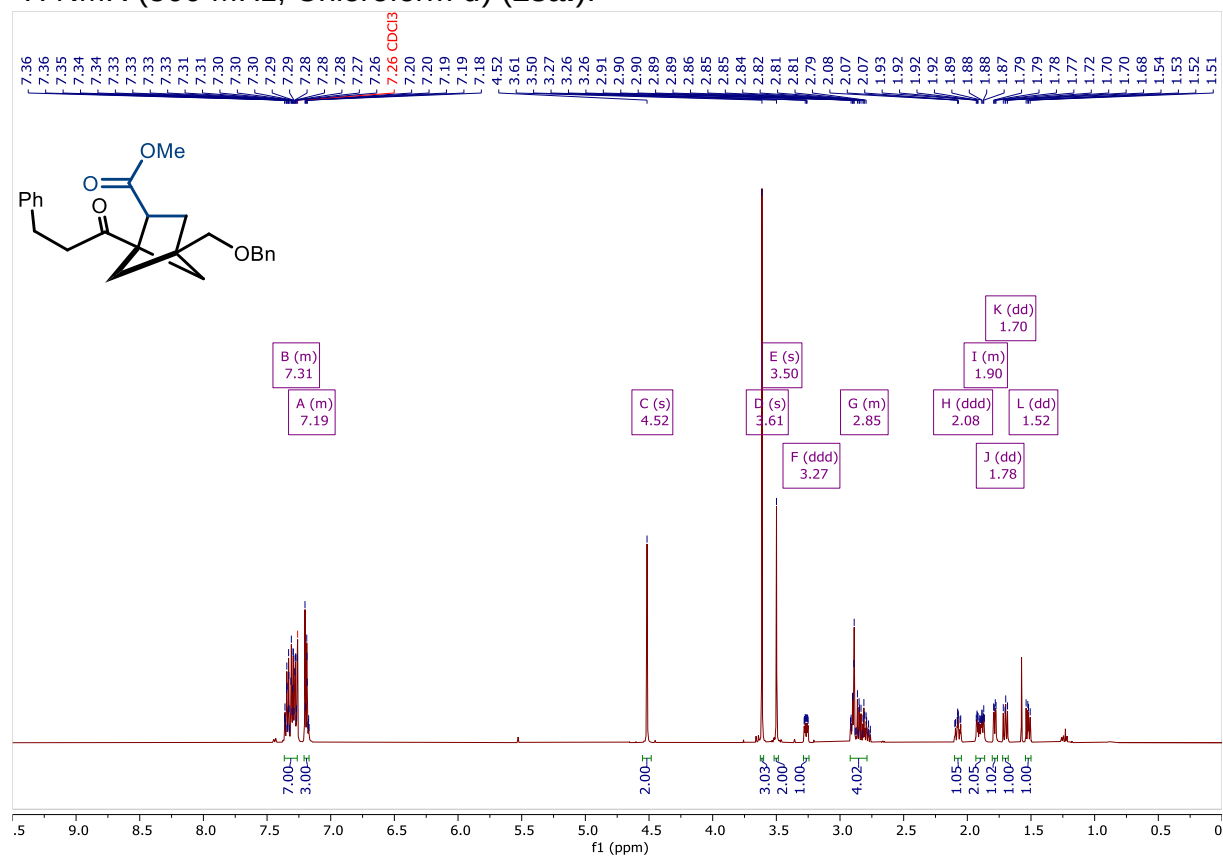
¹H NMR (400 MHz, Chloroform-*d*) (**13ae**):



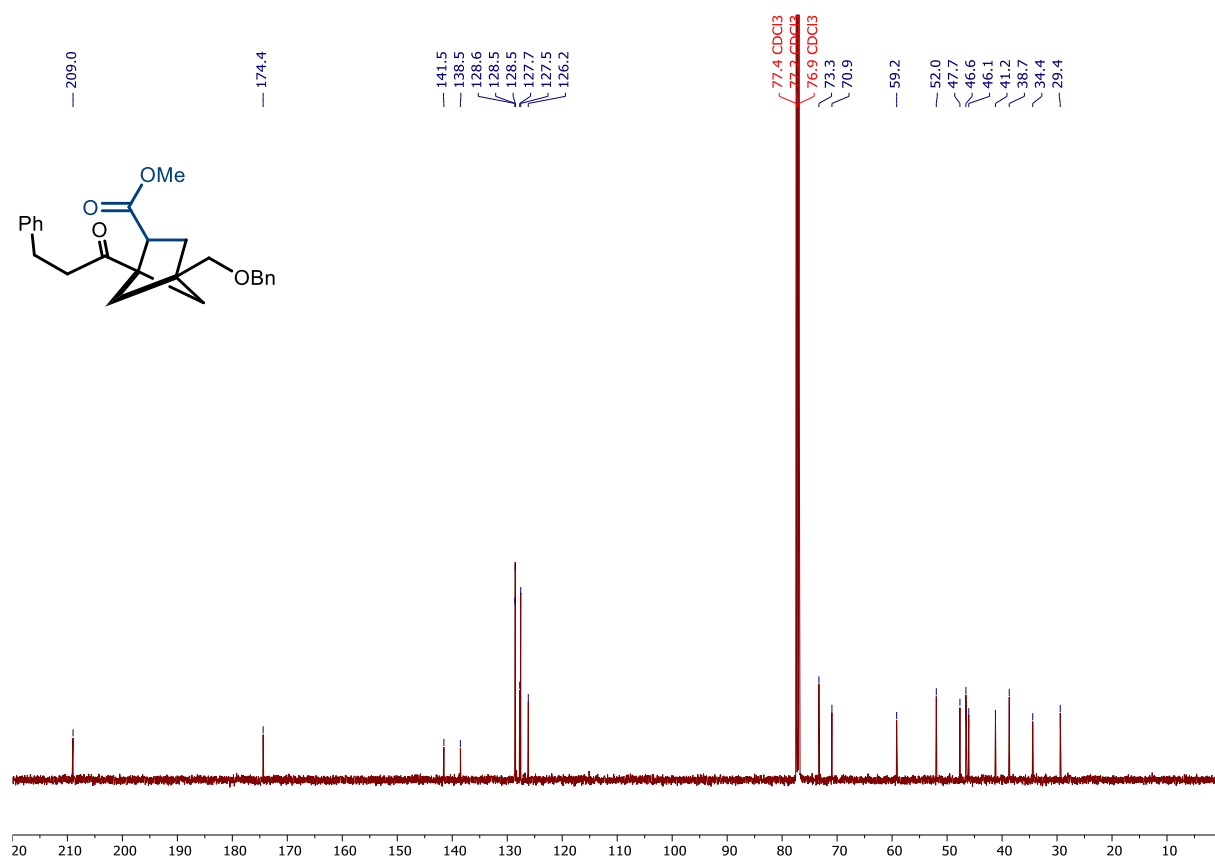
¹³C NMR (101 MHz, Chloroform-*d*) (**13ae**):



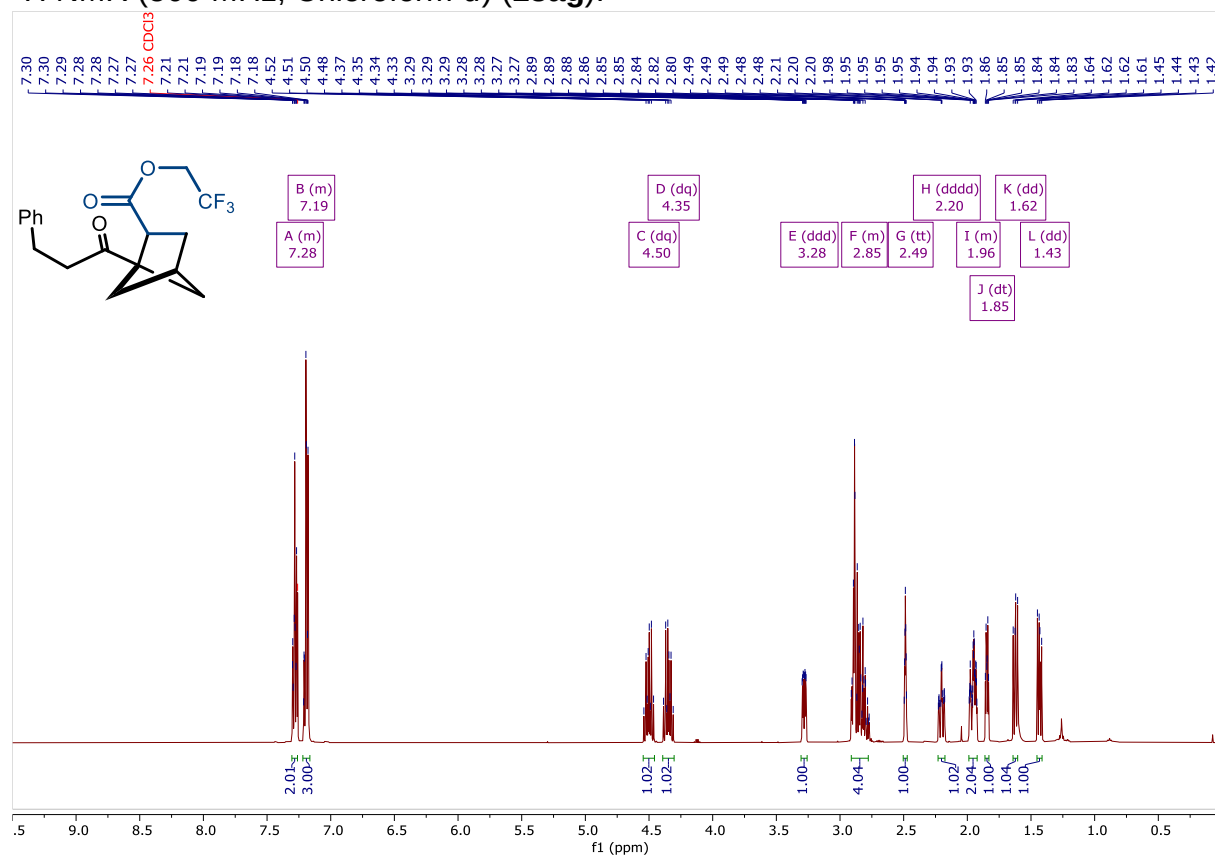
¹H NMR (500 MHz, Chloroform-*d*) (**13af**):



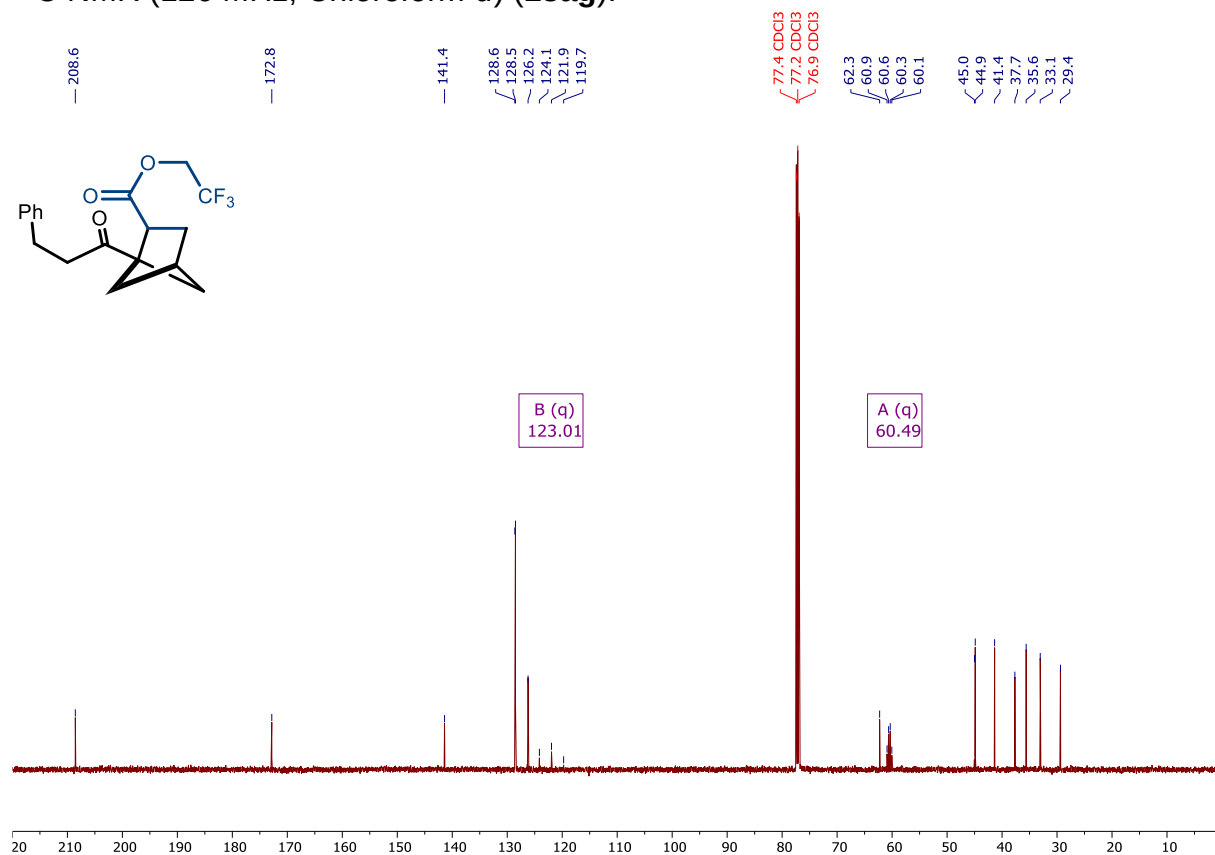
¹³C NMR (126 MHz, Chloroform-*d*) (**13af**):



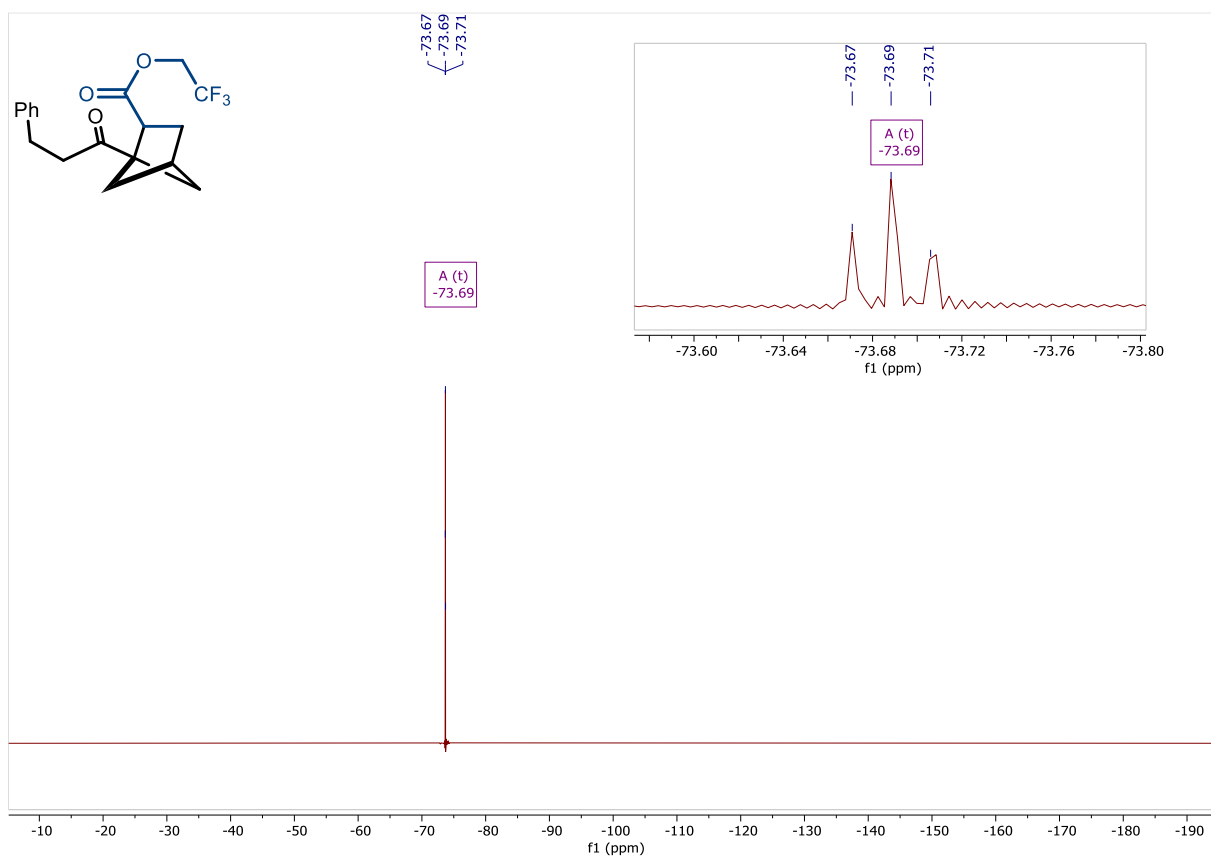
¹H NMR (500 MHz, Chloroform-*d*) (**13ag**):



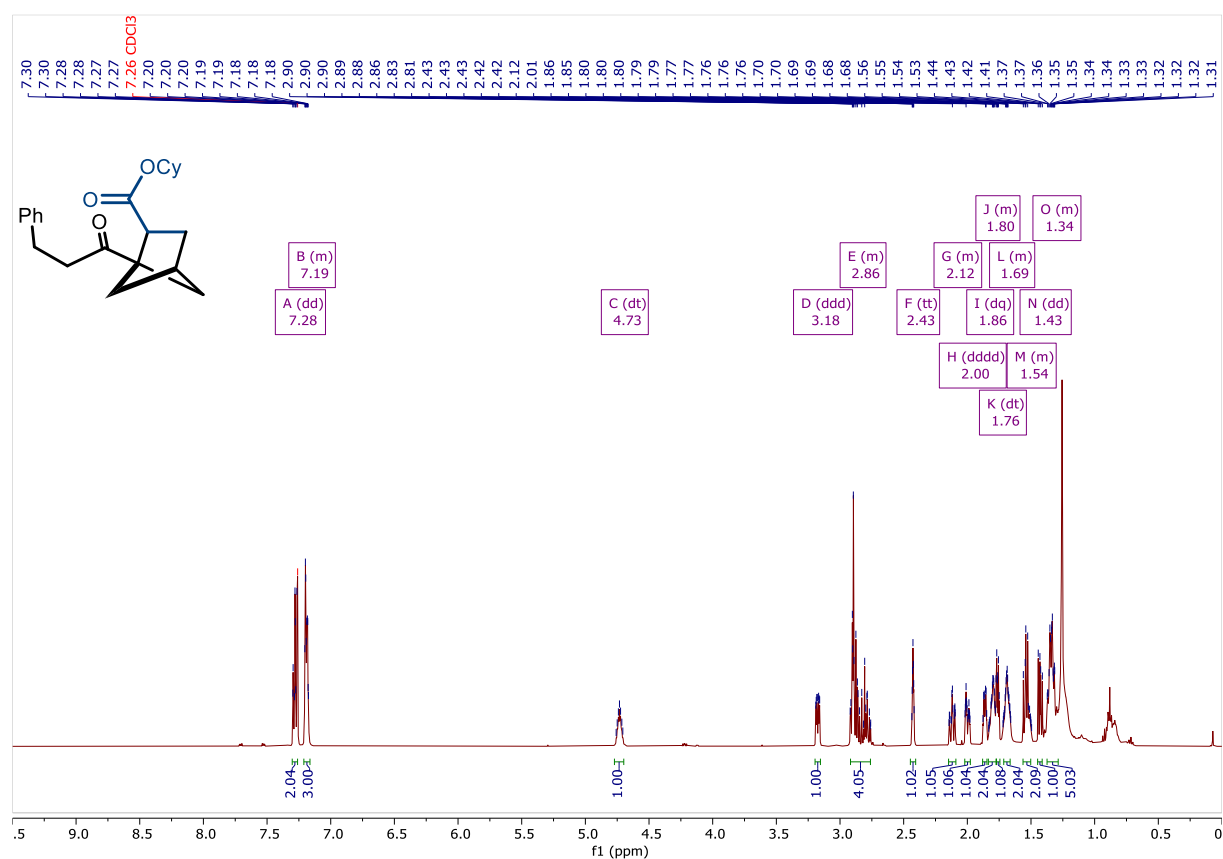
¹³C NMR (126 MHz, Chloroform-*d*) (**13ag**):



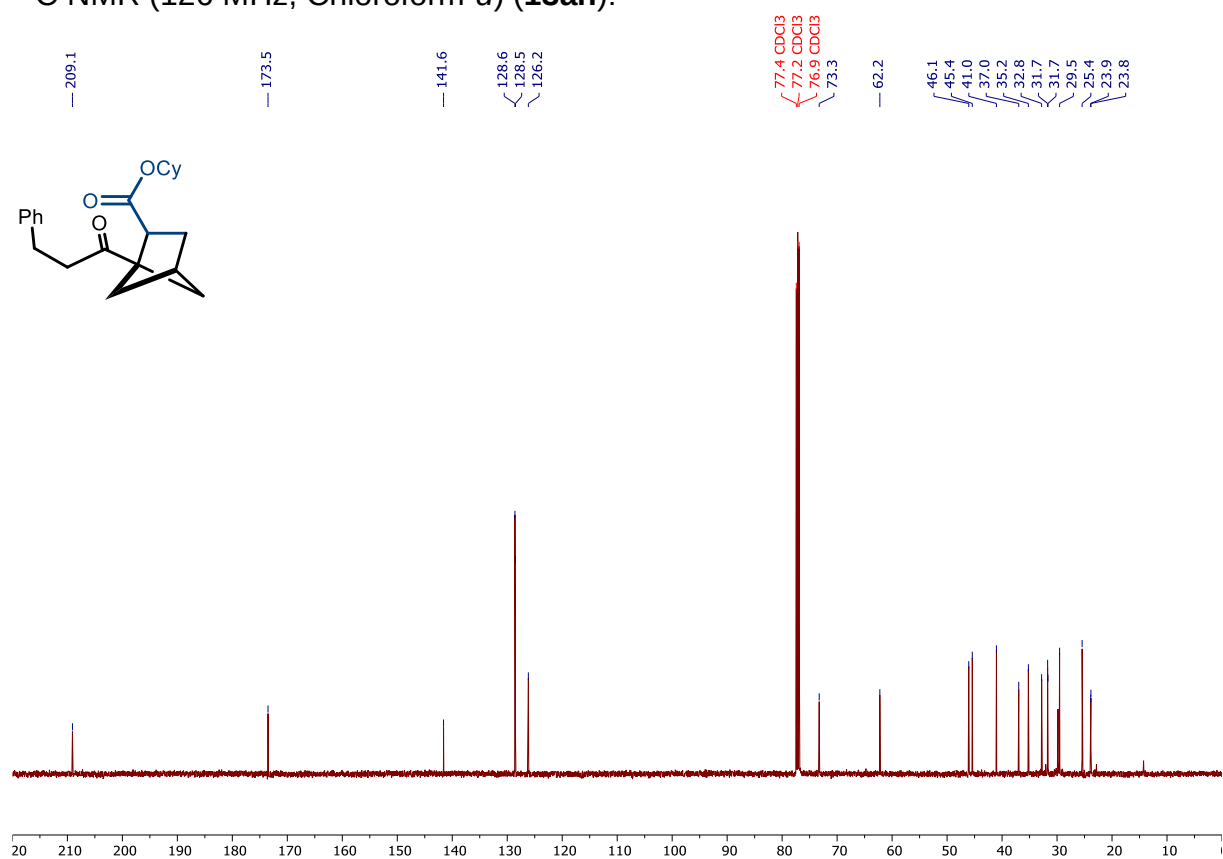
^{19}F NMR (471 MHz, Chloroform- d) (**13ag**):



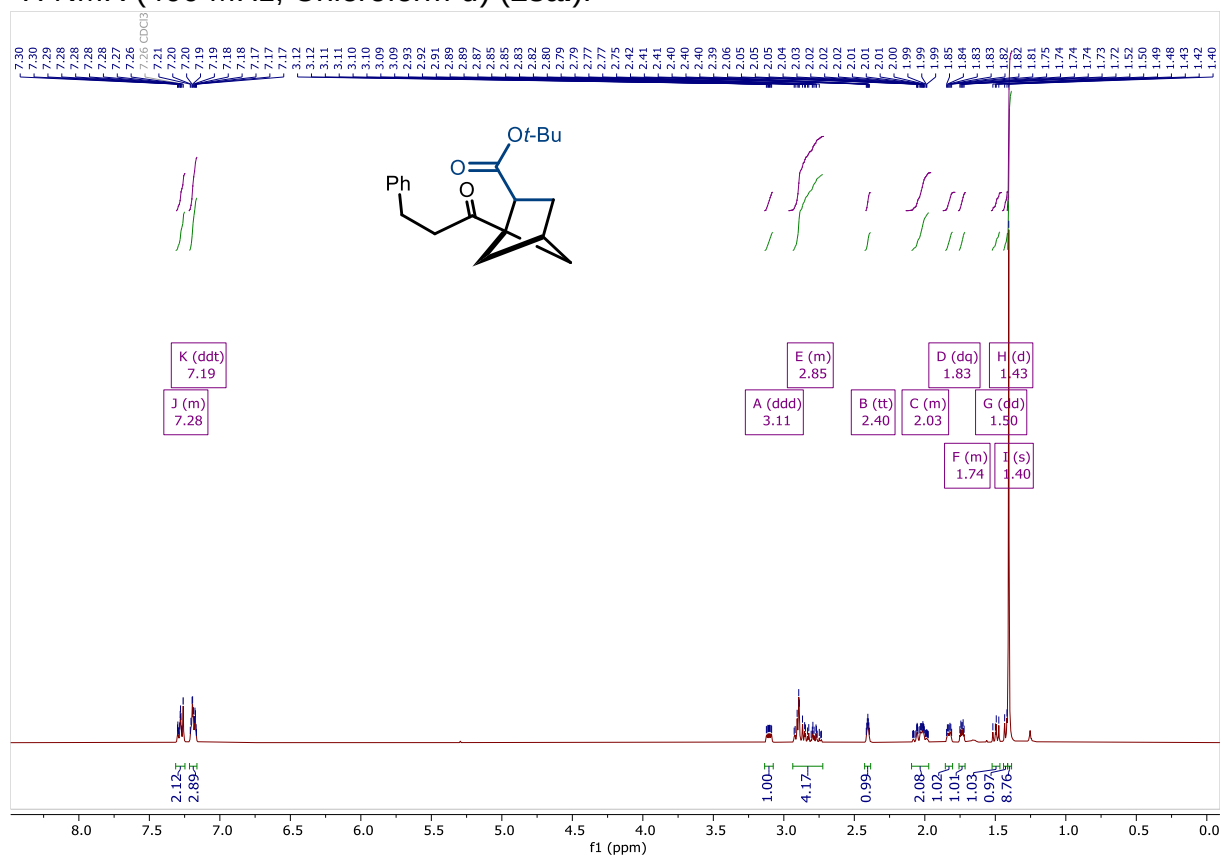
^1H NMR (500 MHz, Chloroform-*d*) (**13ah**):



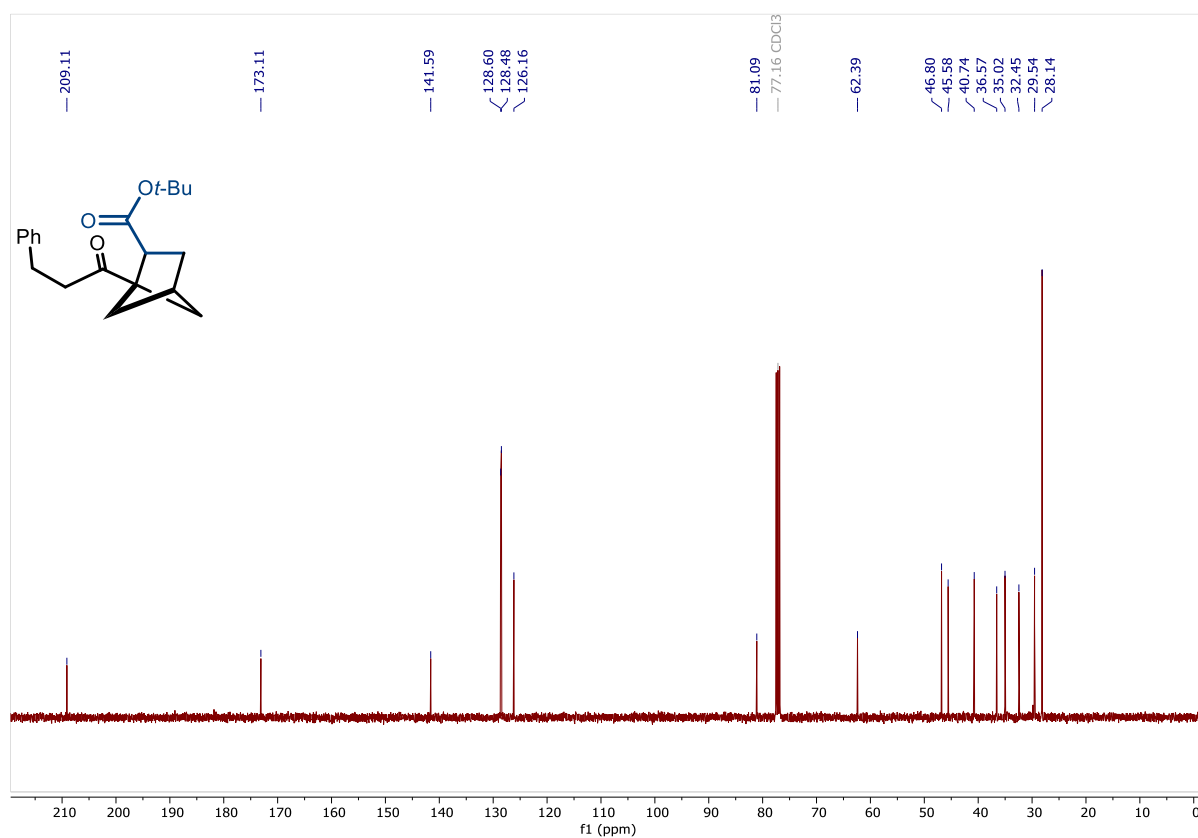
^{13}C NMR (126 MHz, Chloroform-*d*) (**13ah**):



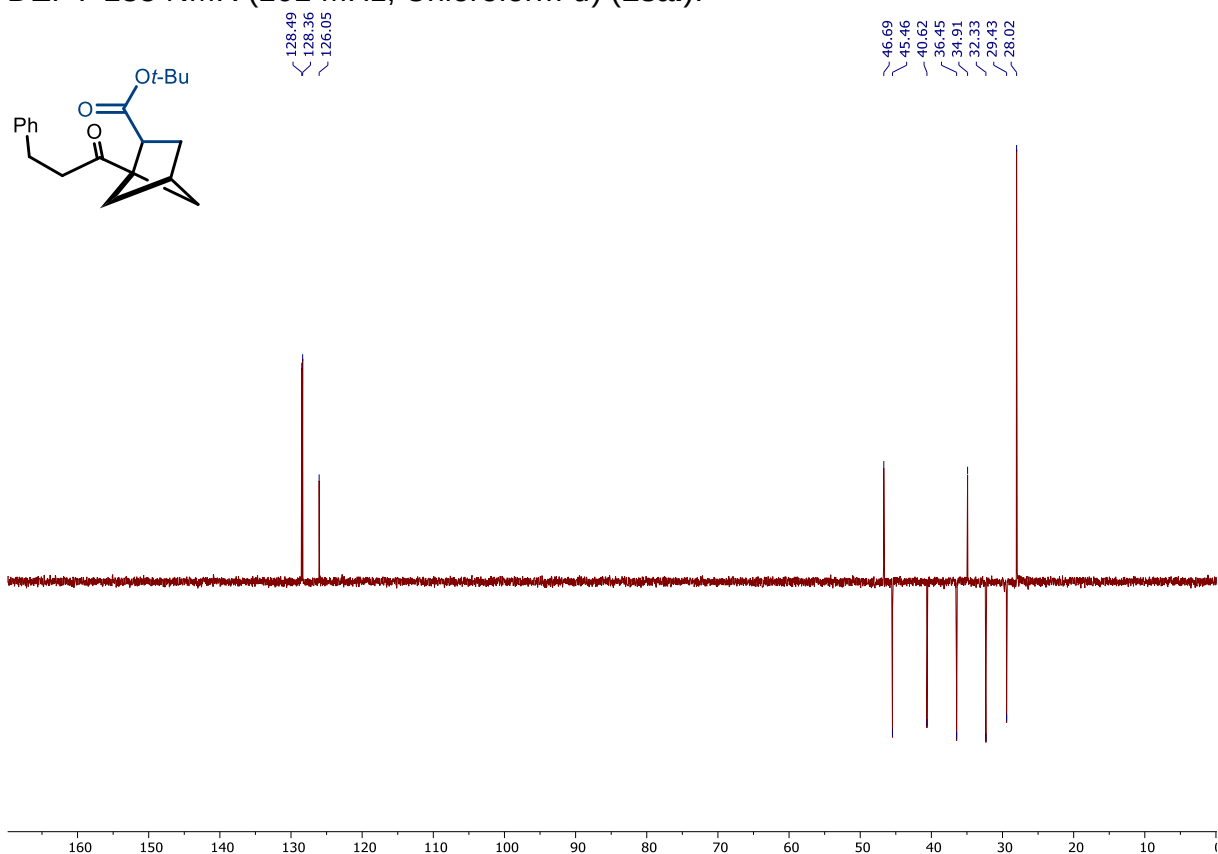
¹H NMR (400 MHz, Chloroform-*d*) (**13ai**):



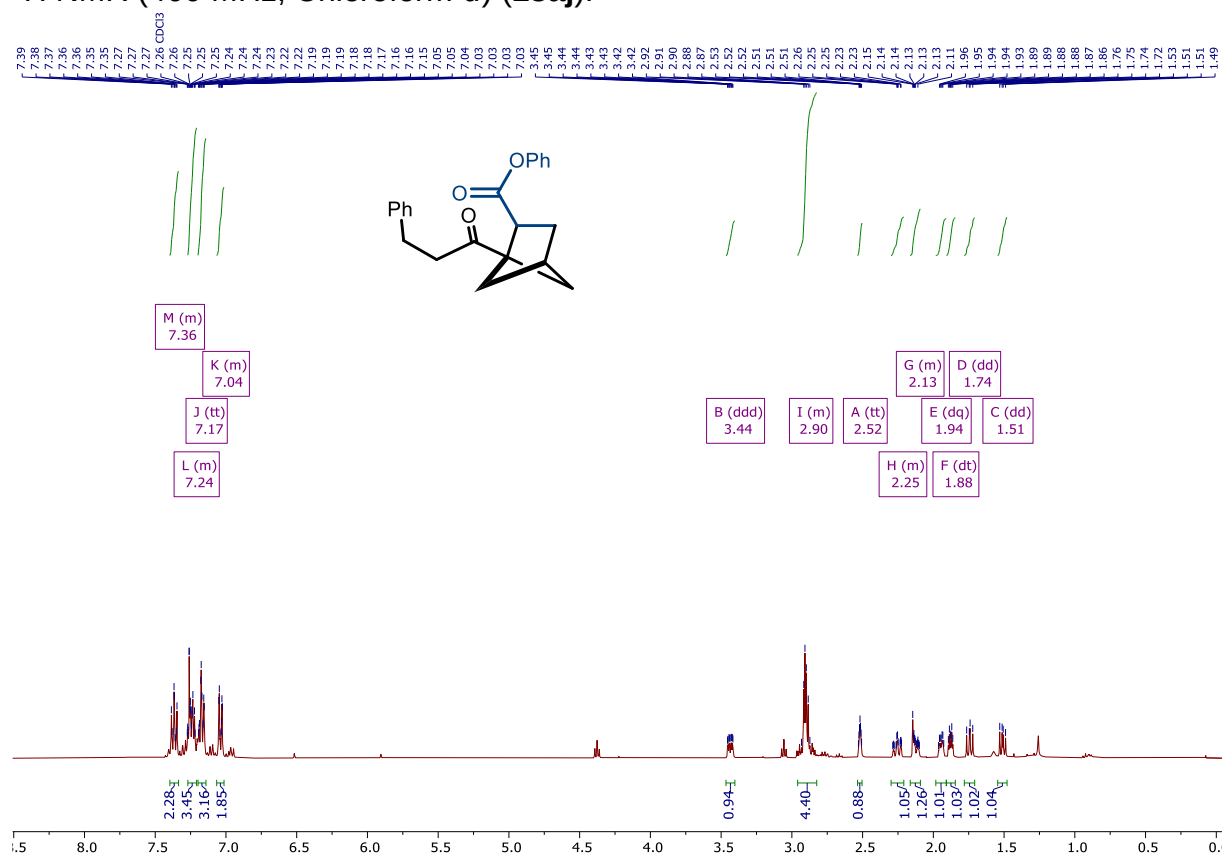
¹³C NMR (101 MHz, Chloroform-*d*) (**13ai**):



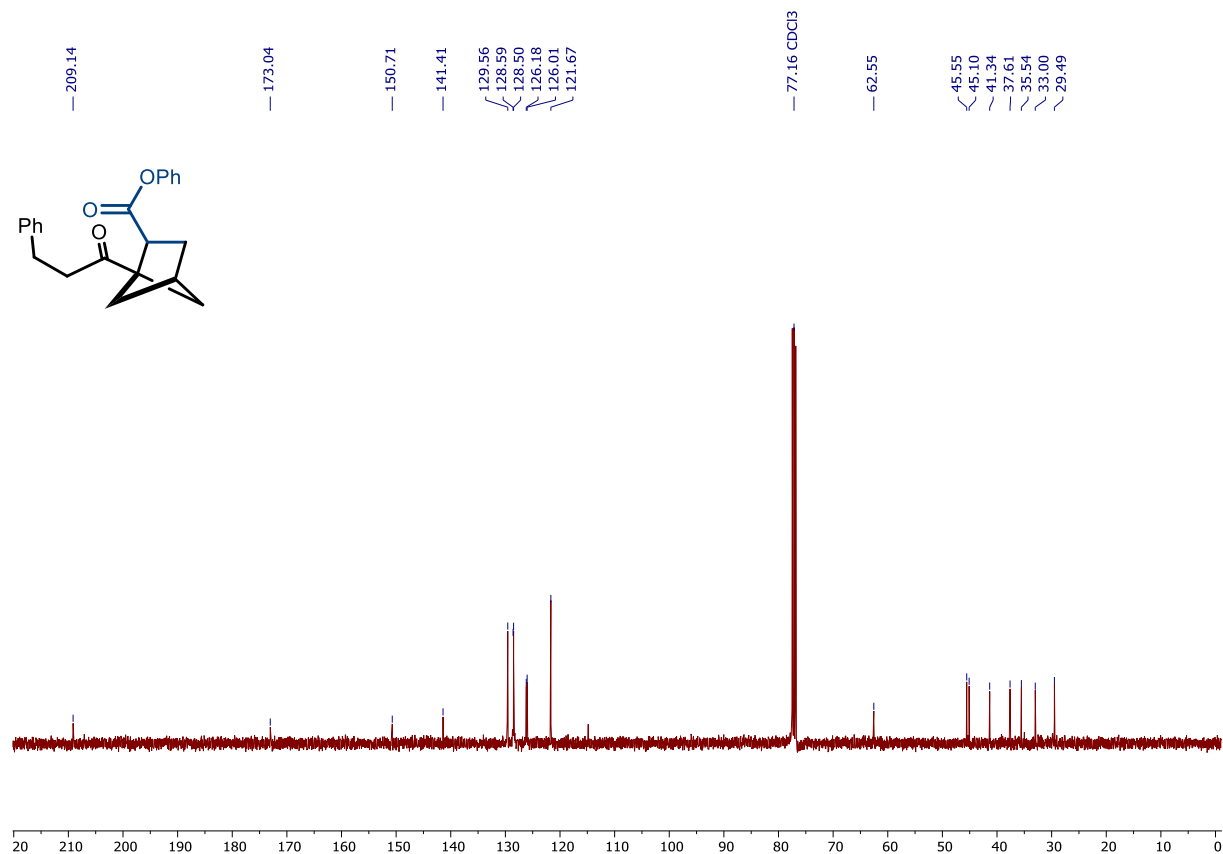
DEPT-135 NMR (101 MHz, Chloroform-*d*) (**13ai**):



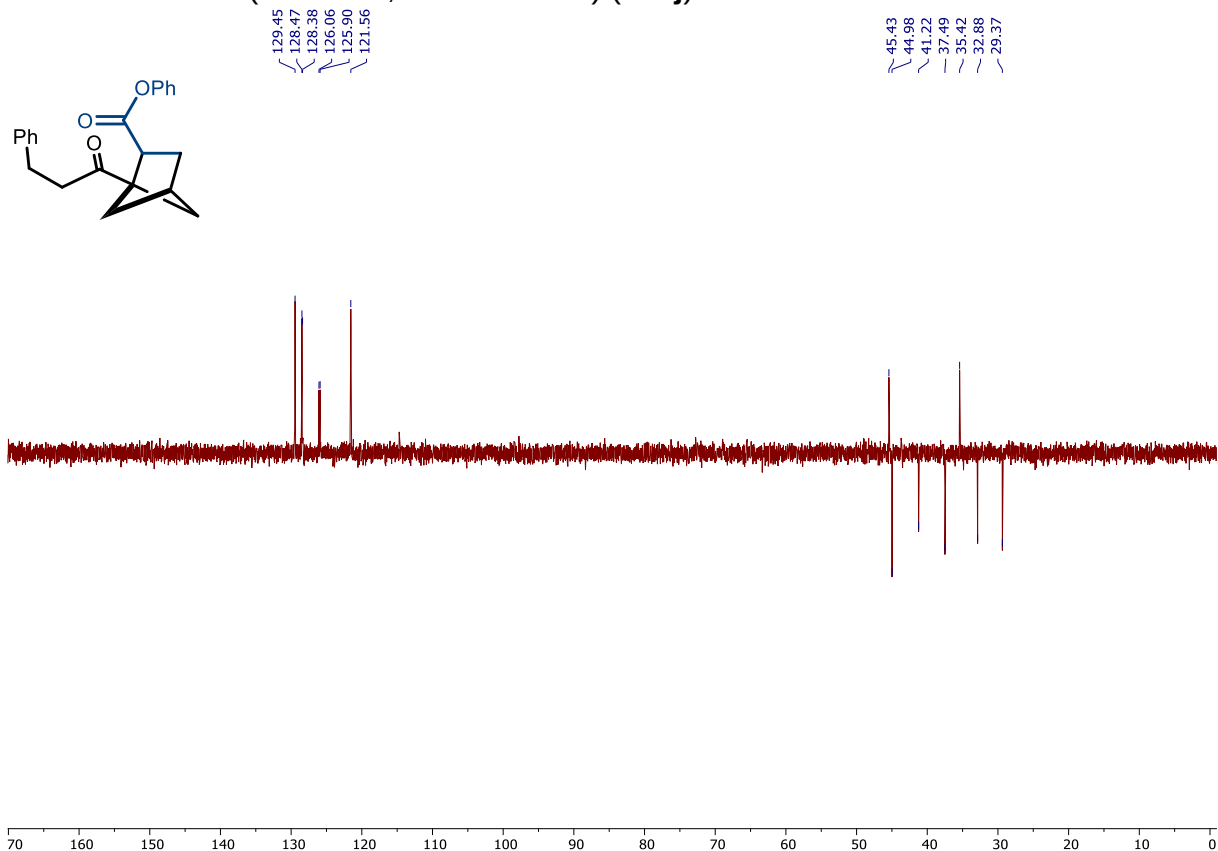
¹H NMR (400 MHz, Chloroform-*d*) (**13aj**):



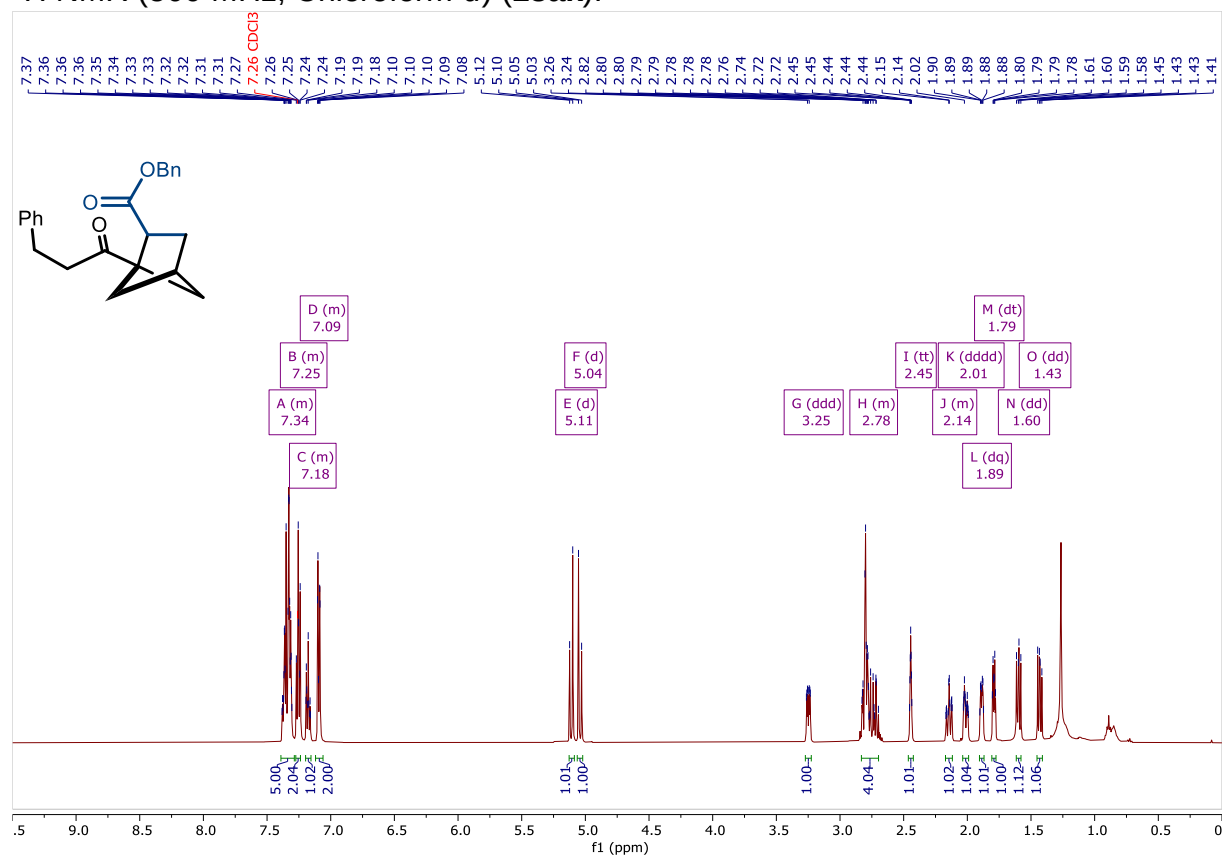
¹³C NMR (101 MHz, Chloroform-*d*) (**13aj**):



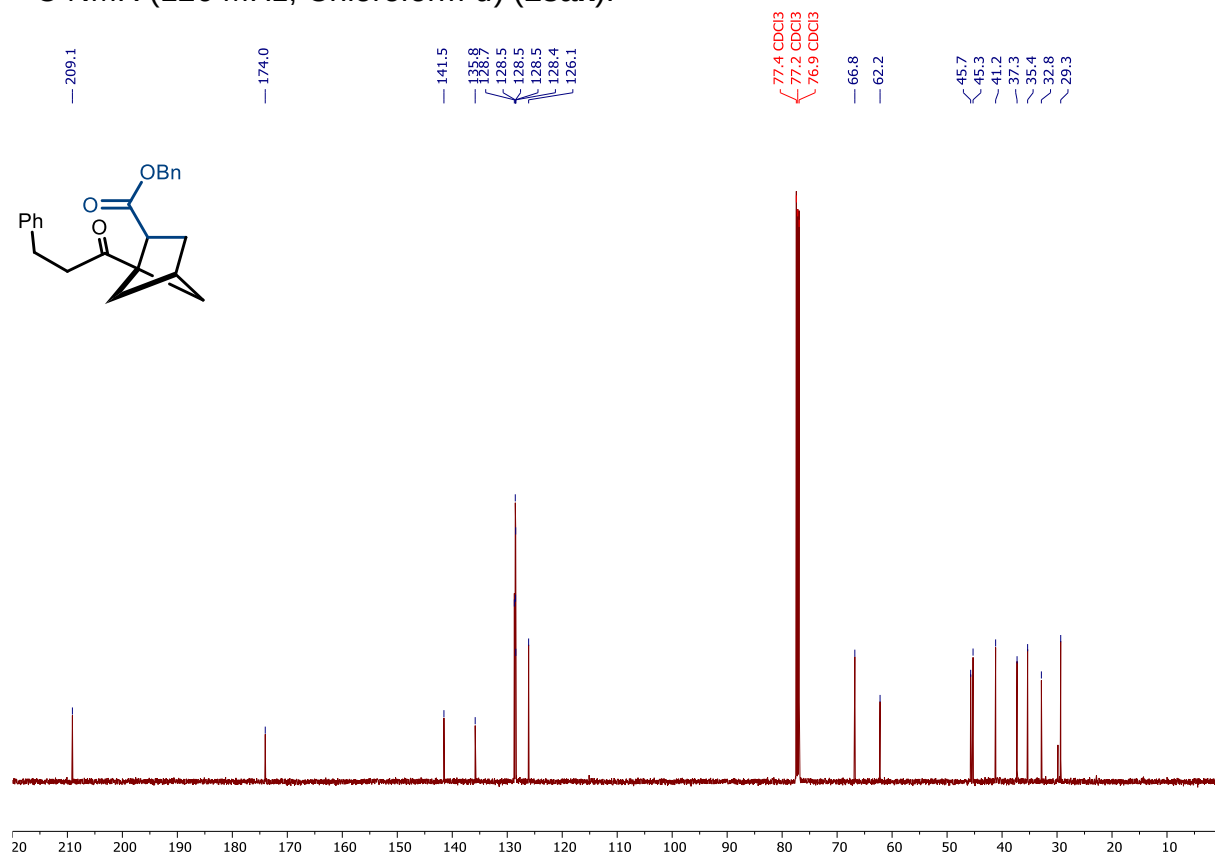
DEPT-135 NMR (101 MHz, Chloroform-*d*) (**13aj**):



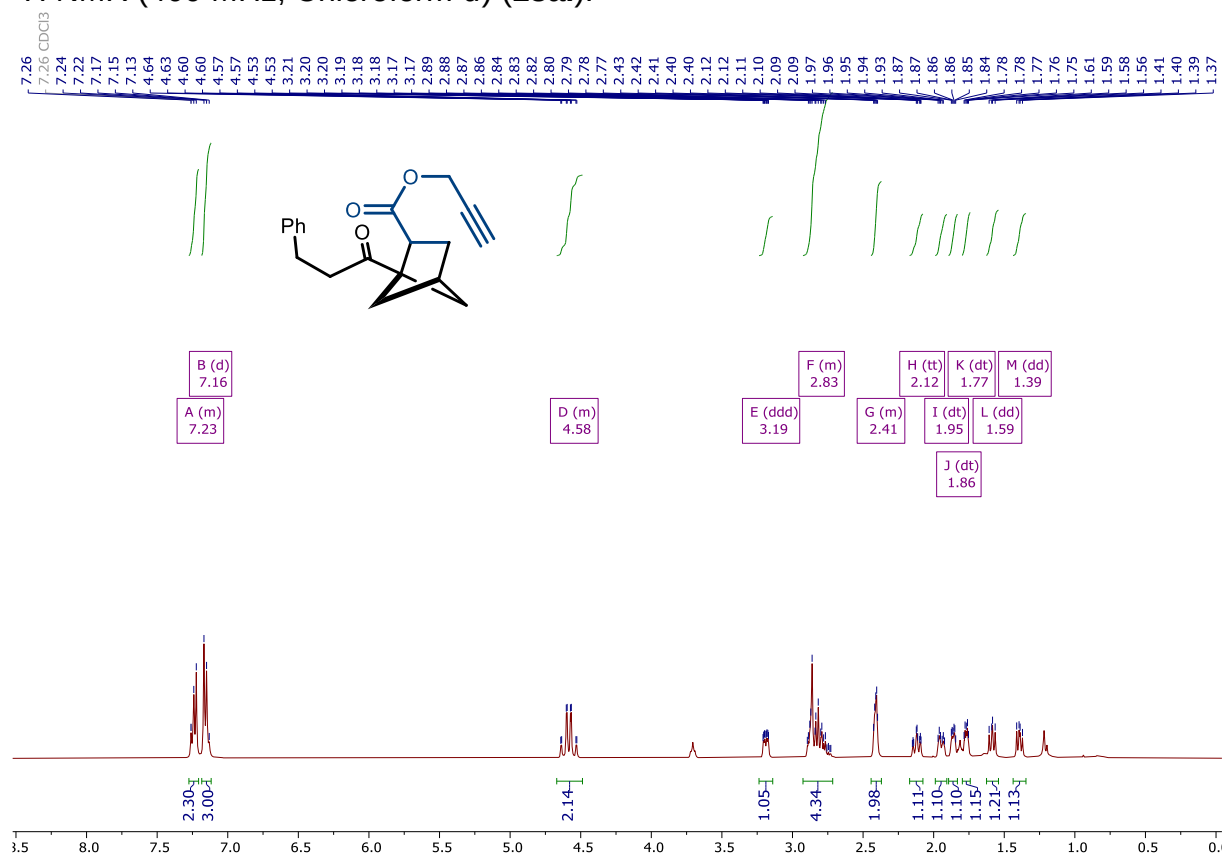
¹H NMR (500 MHz, Chloroform-*d*) (**13ak**):



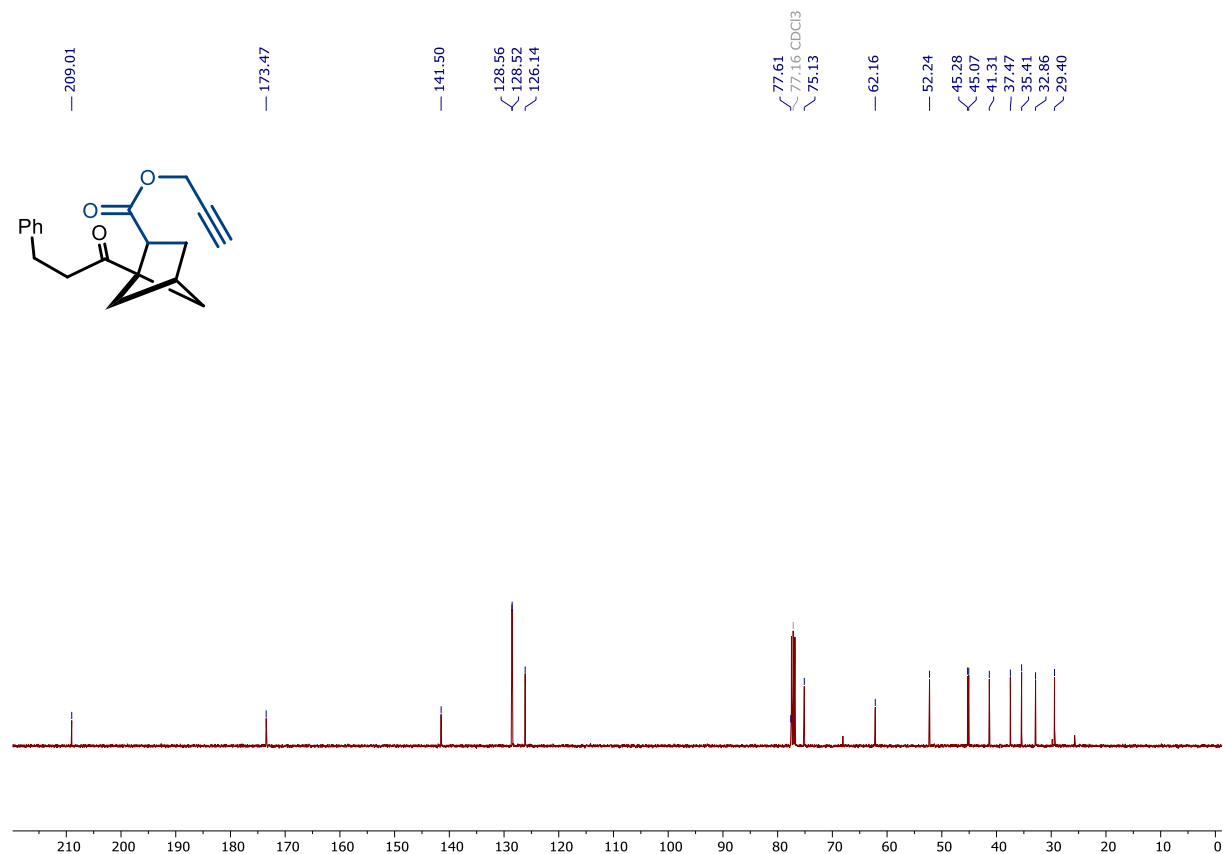
¹³C NMR (126 MHz, Chloroform-*d*) (**13ak**):



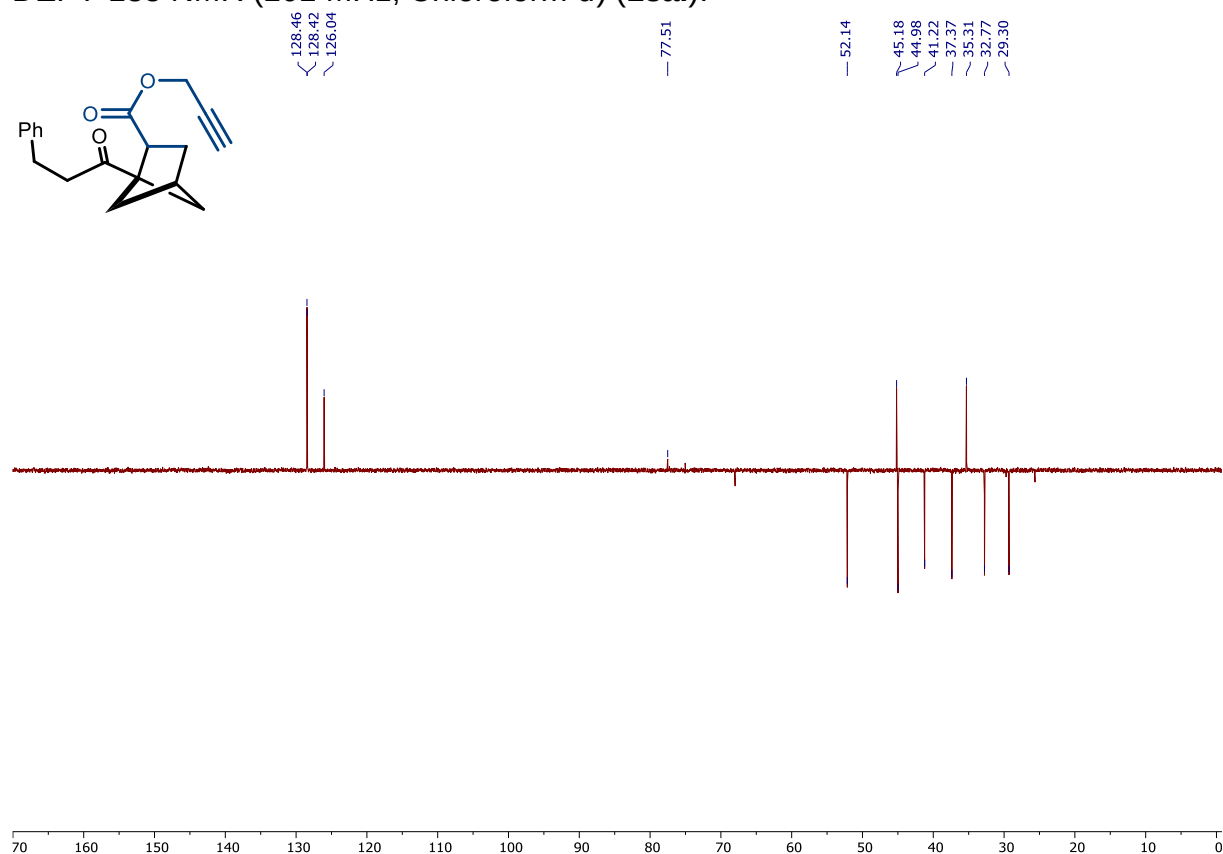
¹H NMR (400 MHz, Chloroform-*d*) (**13al**):



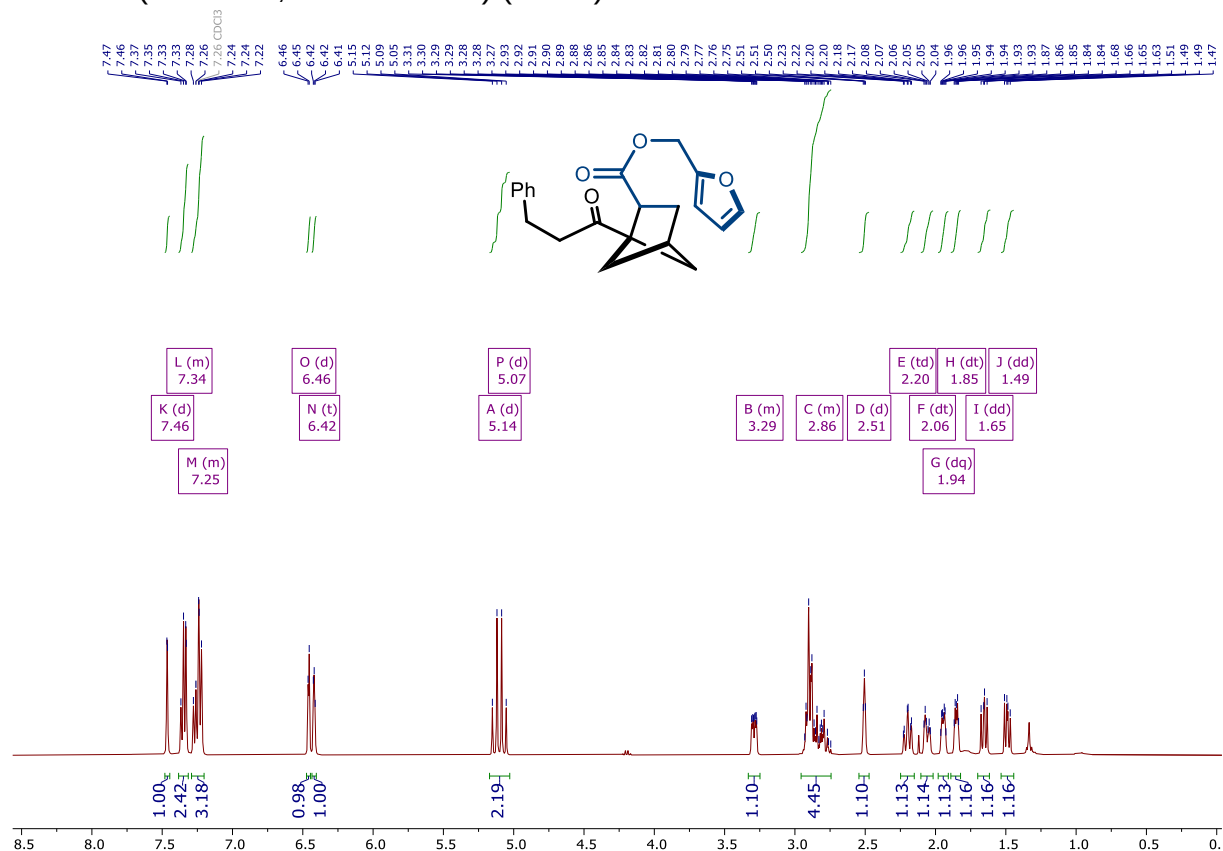
¹³C NMR (101 MHz, Chloroform-*d*) (**13al**):



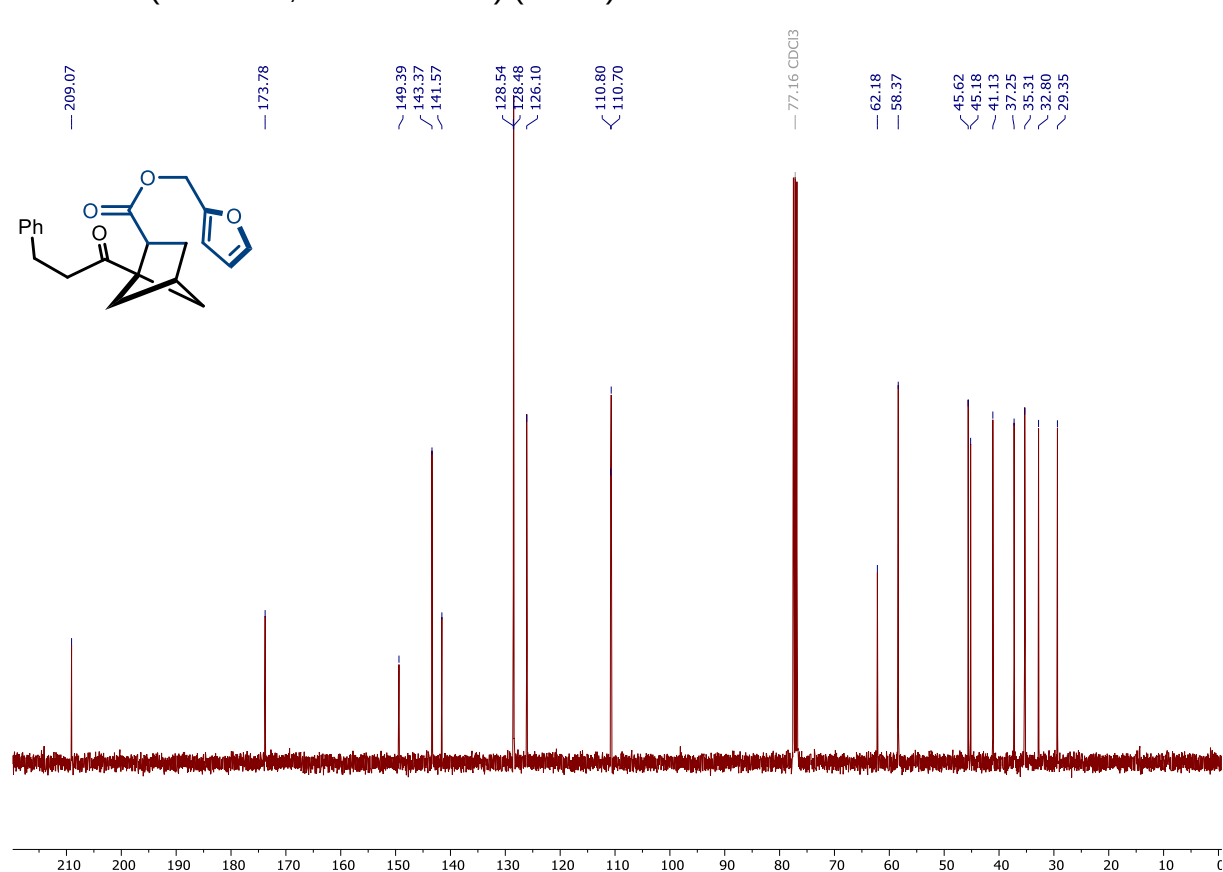
DEPT-135 NMR (101 MHz, Chloroform-*d*) (**13al**):



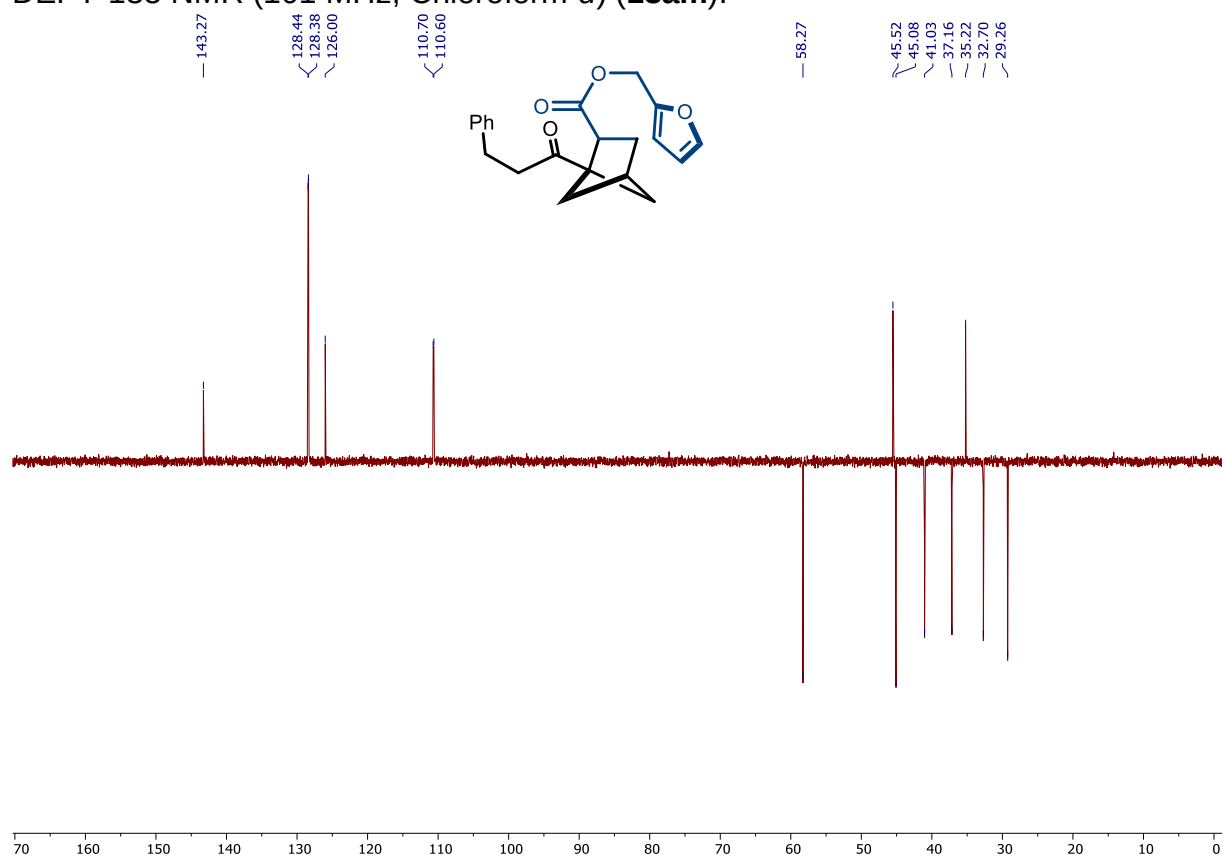
¹H NMR (400 MHz, Chloroform-*d*) (**13am**):



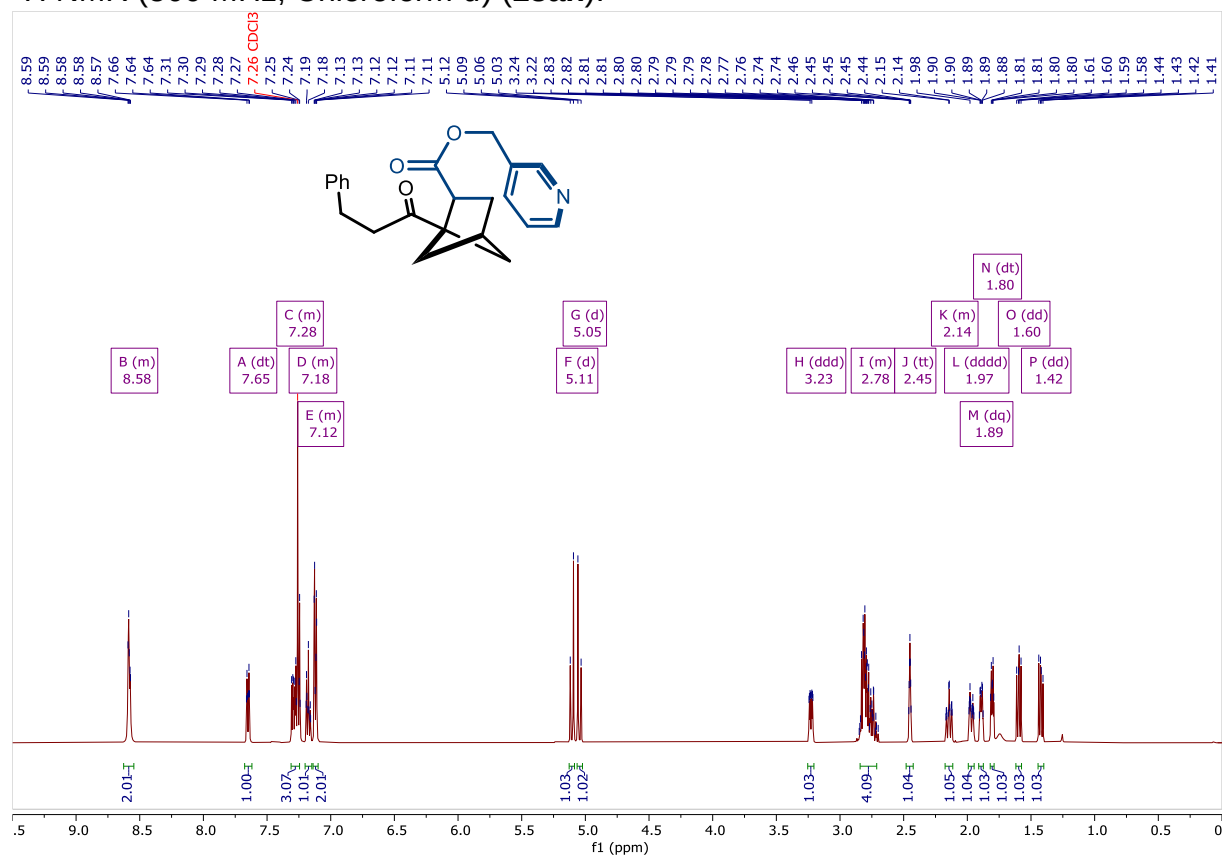
¹³C NMR (101 MHz, Chloroform-*d*) (**13am**):



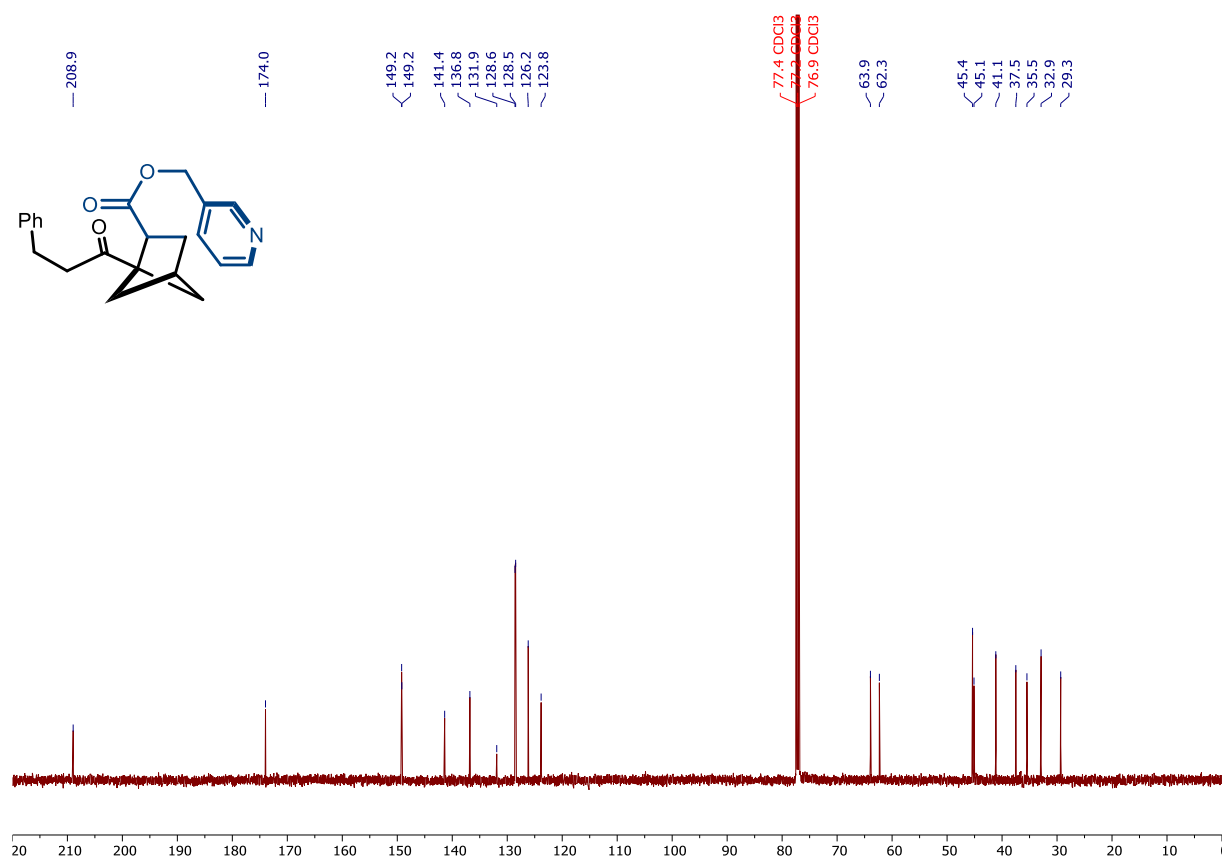
DEPT-135 NMR (101 MHz, Chloroform-*d*) (**13am**):



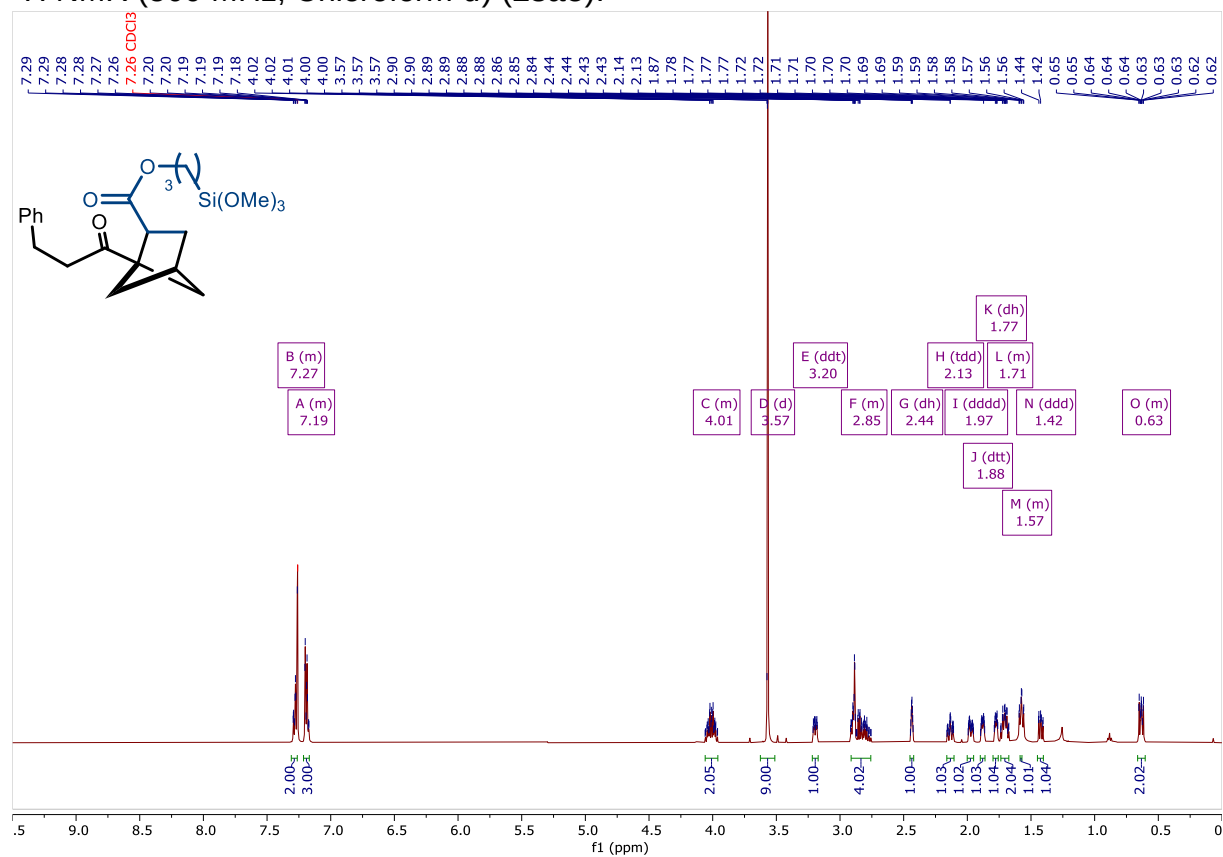
¹H NMR (500 MHz, Chloroform-*d*) (**13an**):



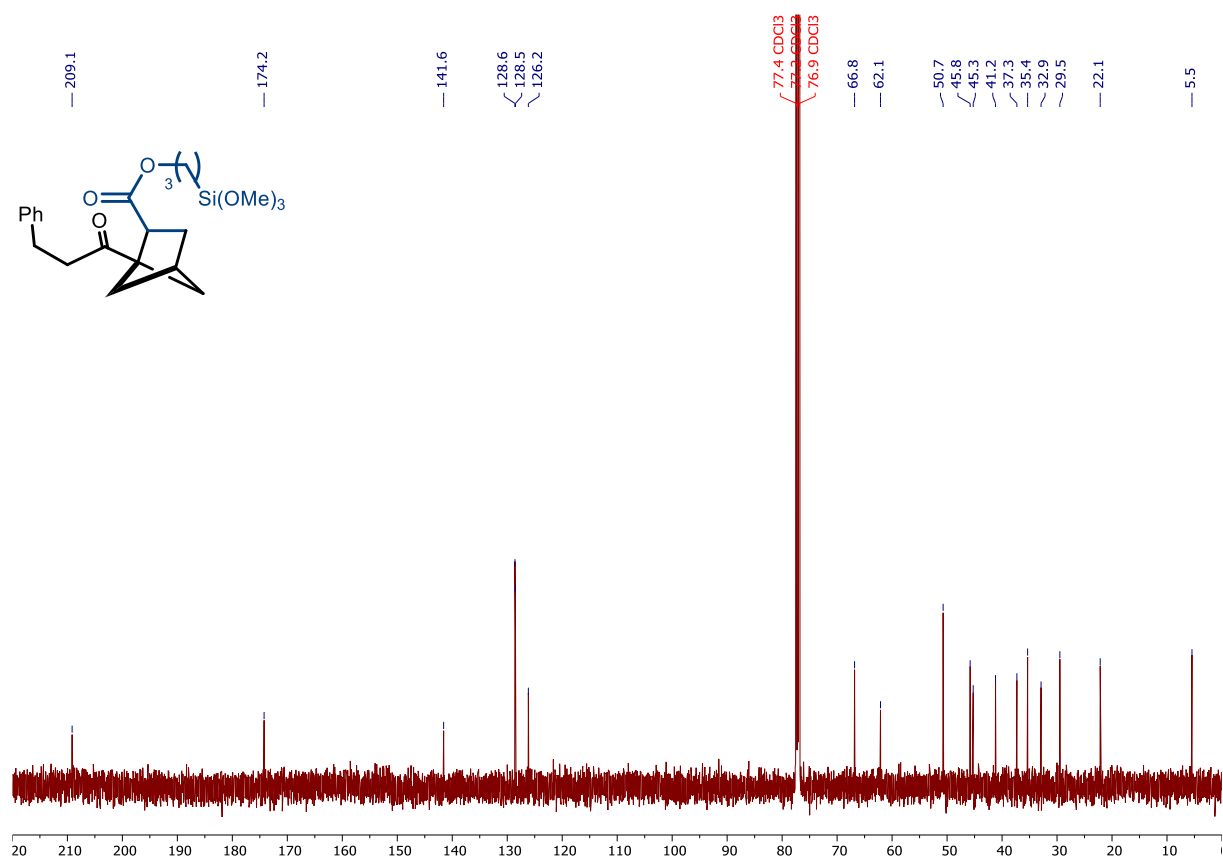
¹³C NMR (126 MHz, Chloroform-*d*) (**13an**):



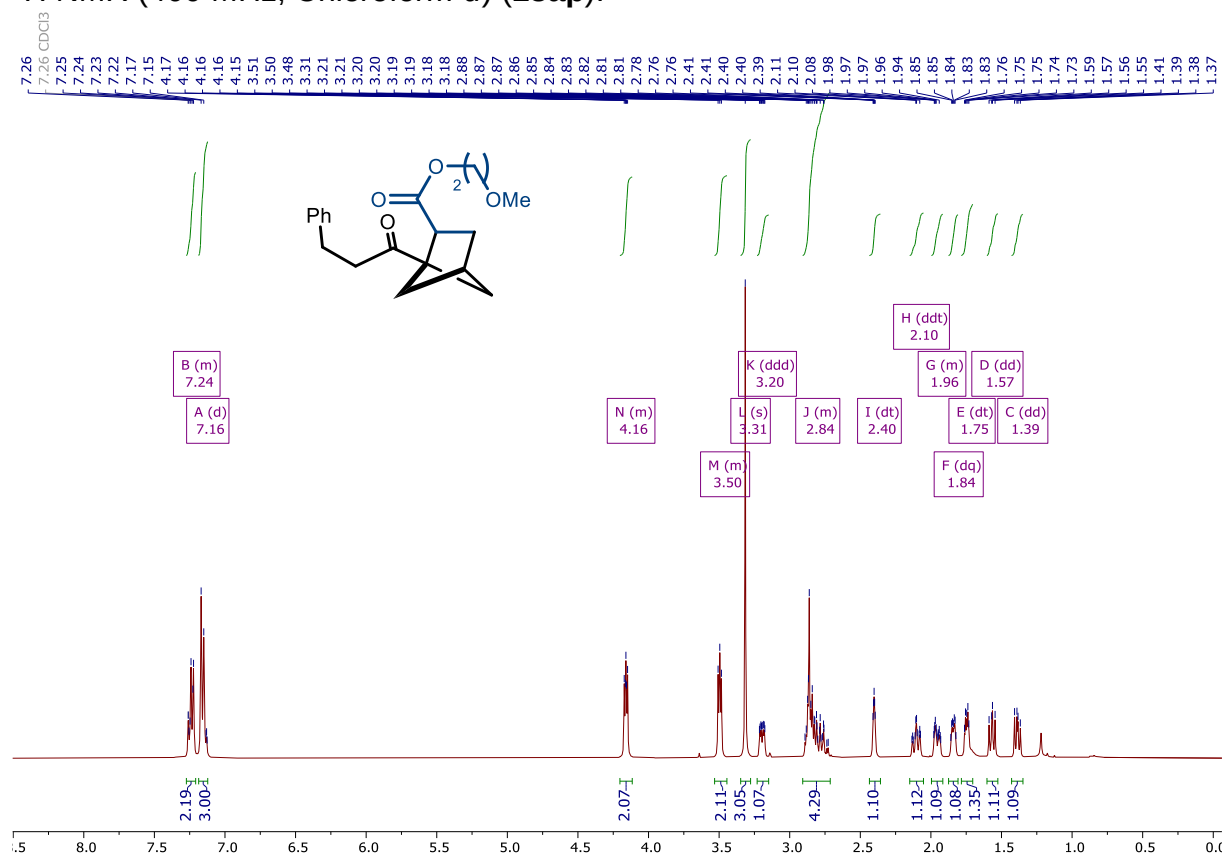
¹H NMR (500 MHz, Chloroform-*d*) (**13ao**):



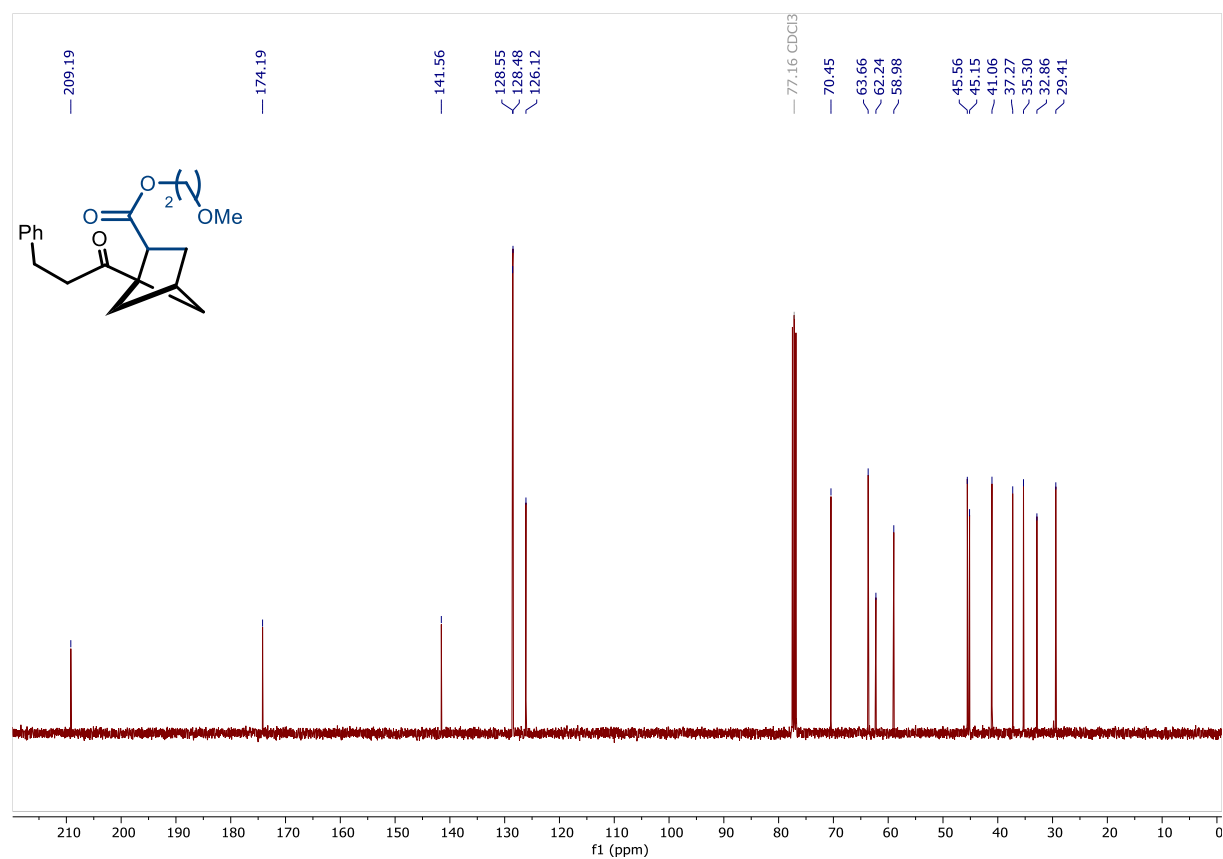
¹³C NMR (126 MHz, Chloroform-*d*) (**13ao**):



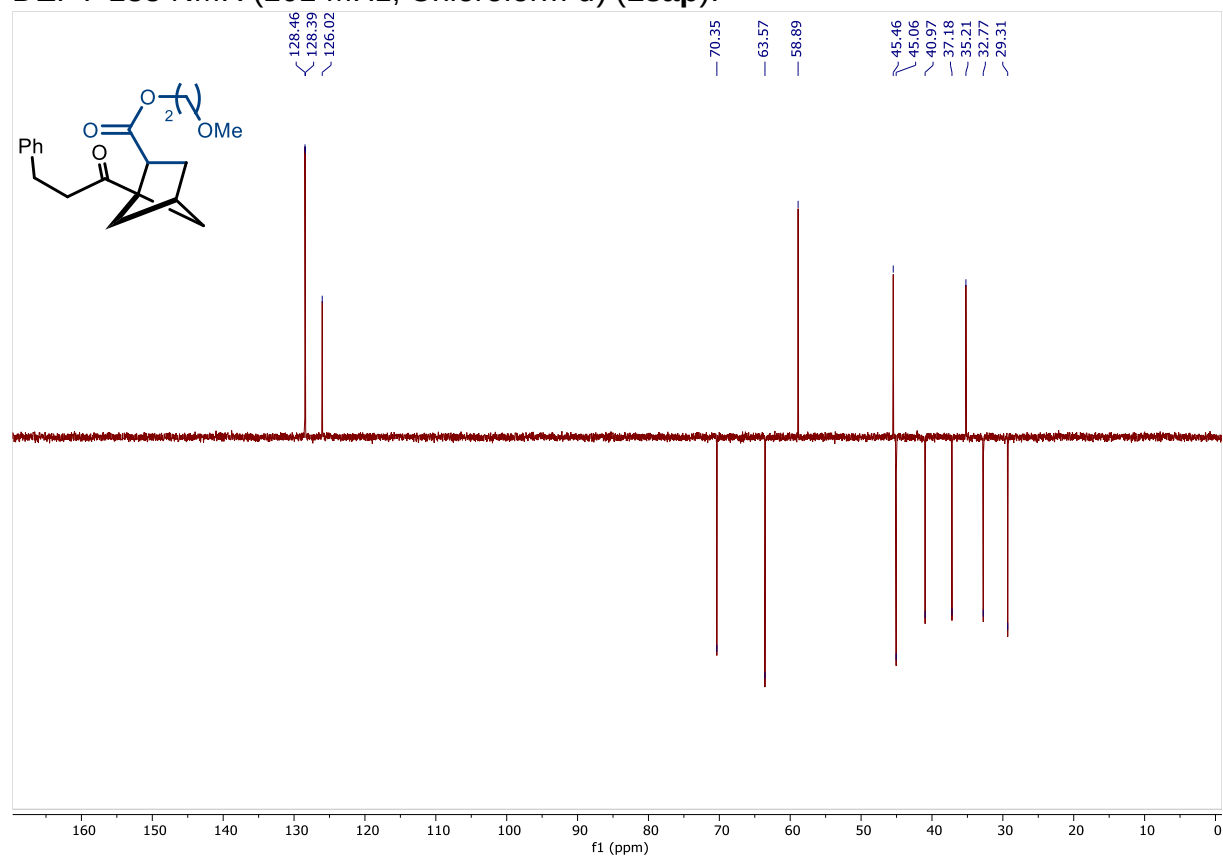
¹H NMR (400 MHz, Chloroform-*d*) (**13ap**):



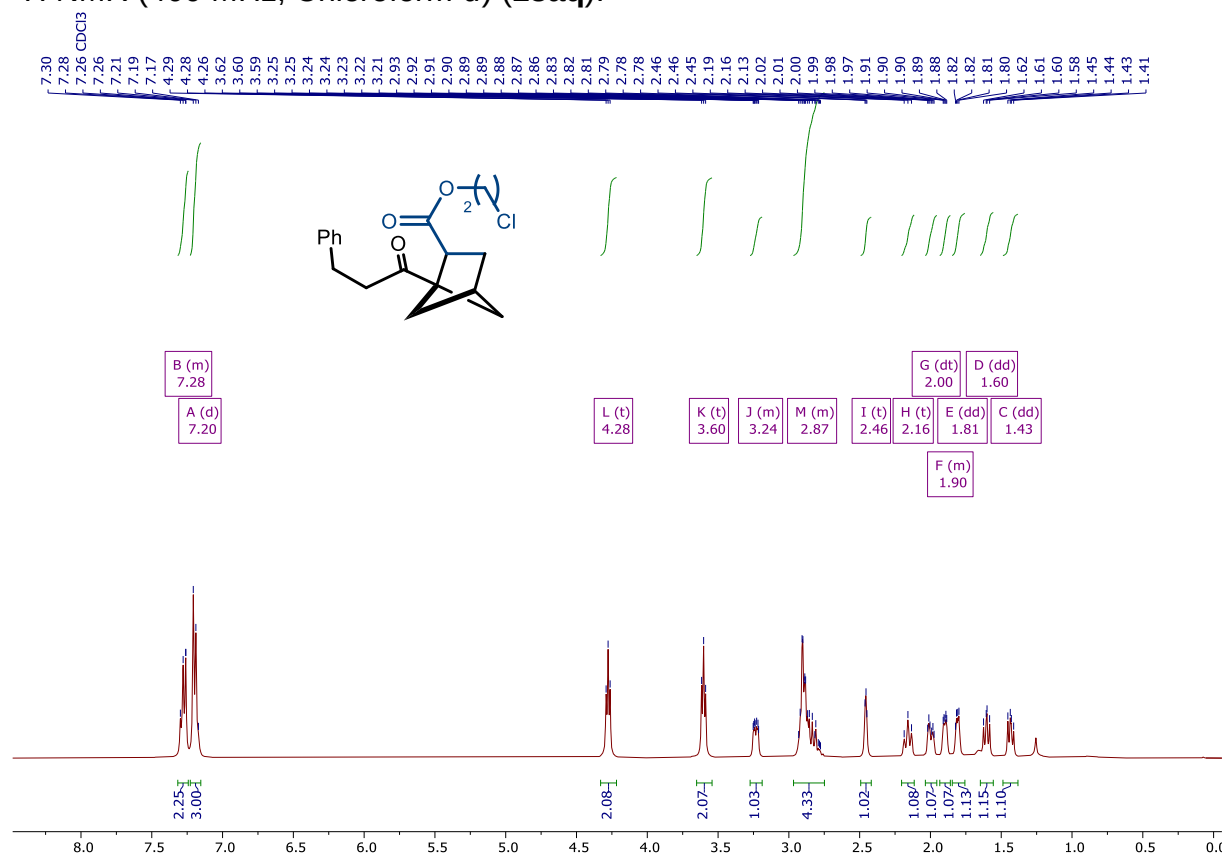
¹³C NMR (101 MHz, Chloroform-*d*) (**13ap**):



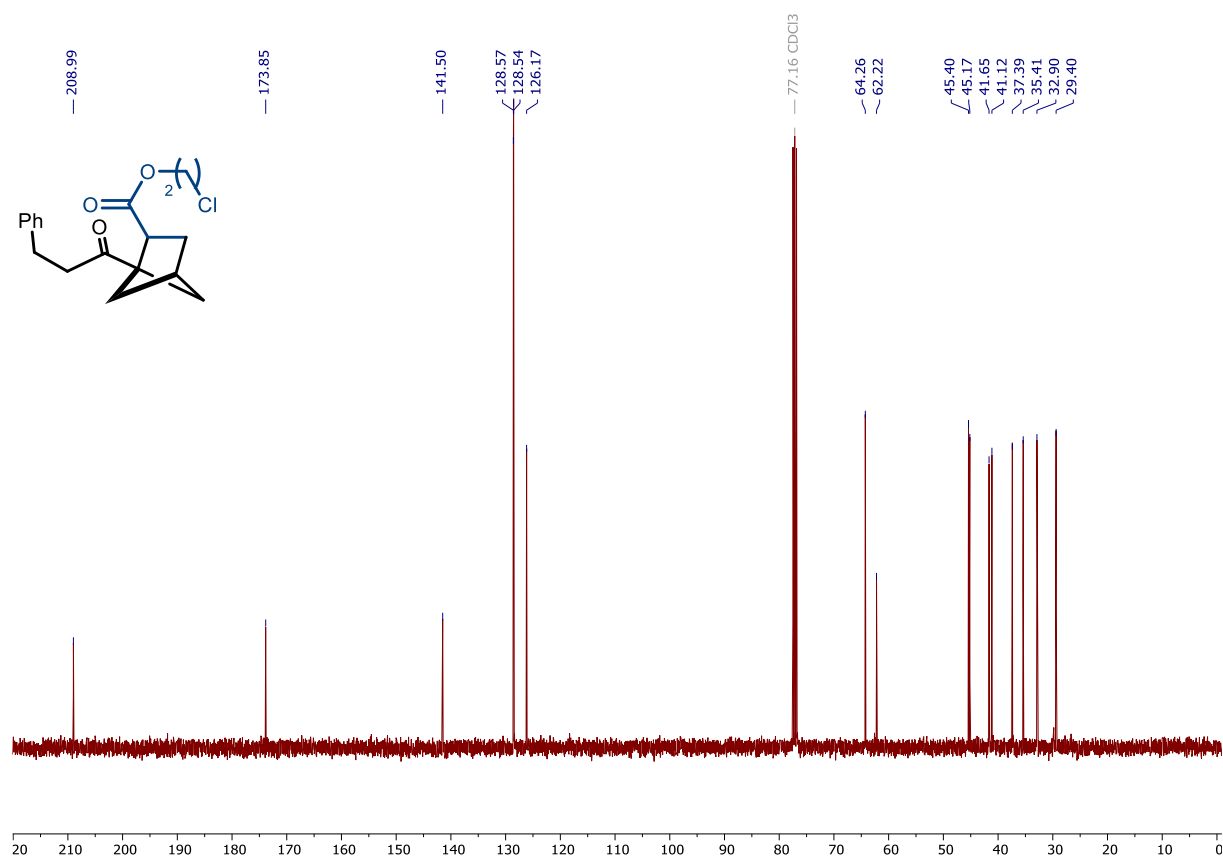
DEPT-135 NMR (101 MHz, Chloroform-*d*) (**13ap**):



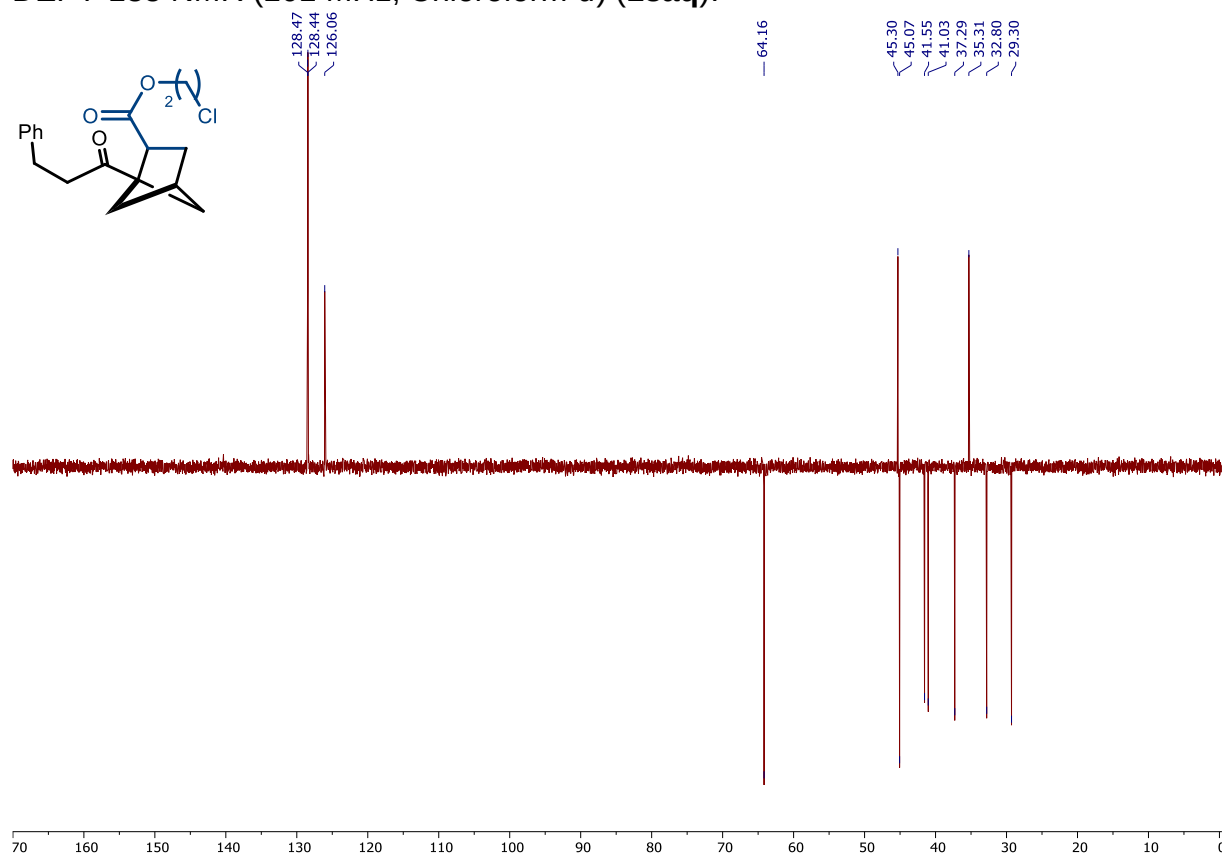
^1H NMR (400 MHz, Chloroform-*d*) (**13aq**):



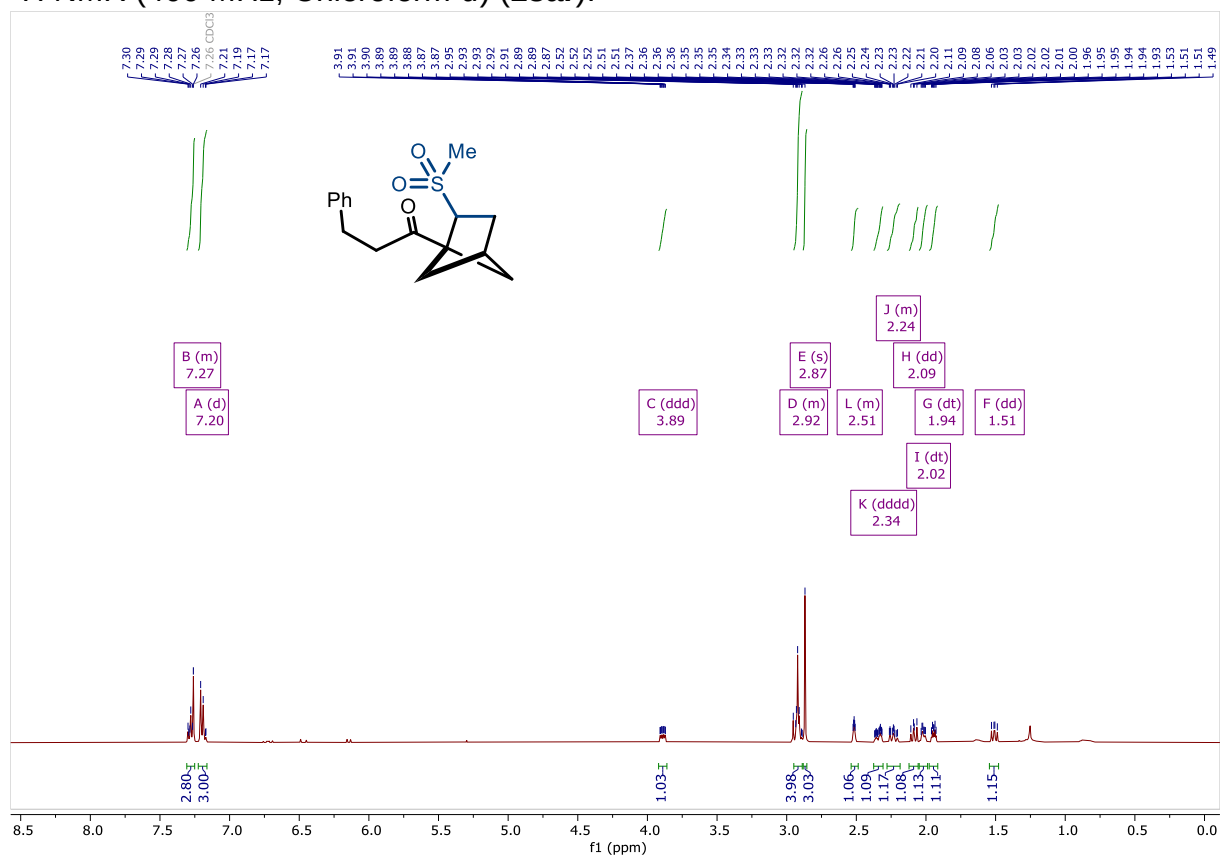
^{13}C NMR (101 MHz, Chloroform-*d*) (**13aq**):



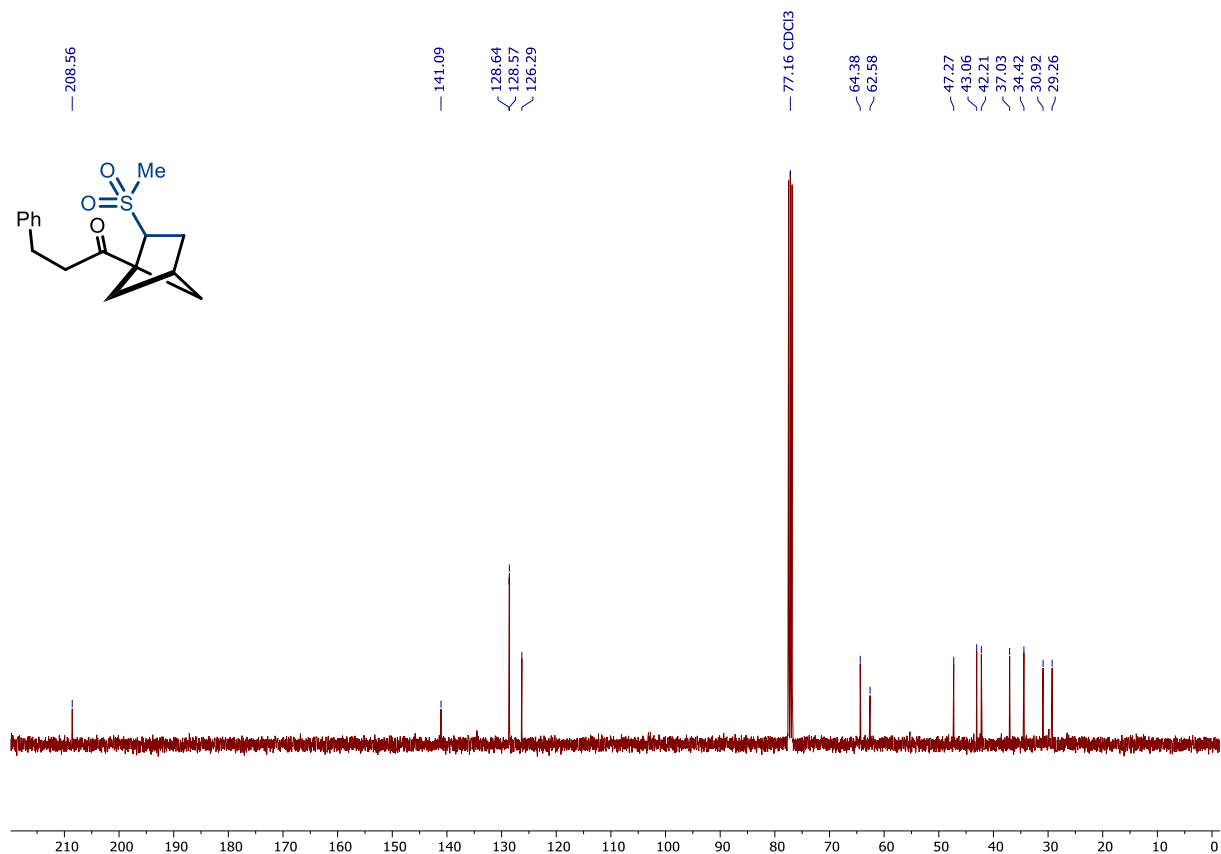
DEPT-135 NMR (101 MHz, Chloroform-*d*) (**13aq**):



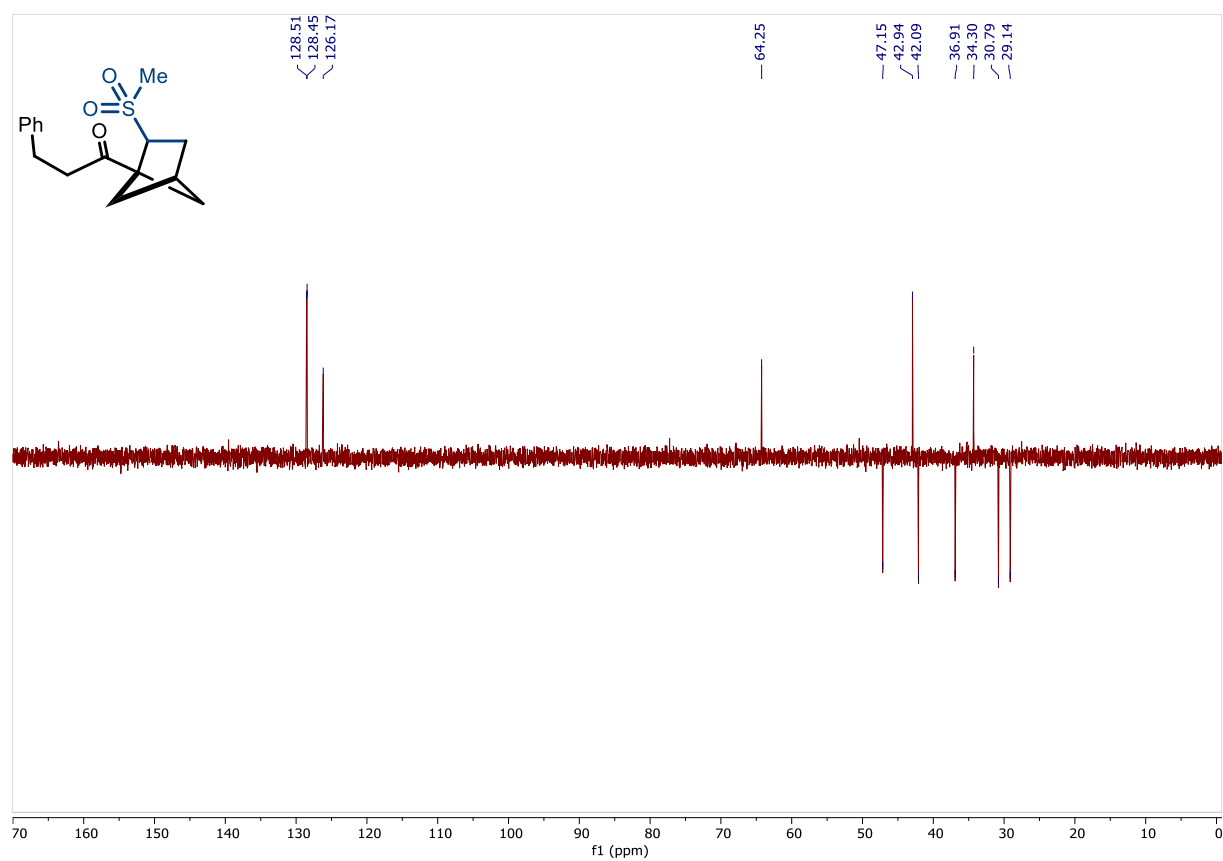
¹H NMR (400 MHz, Chloroform-*d*) (**13ar**):



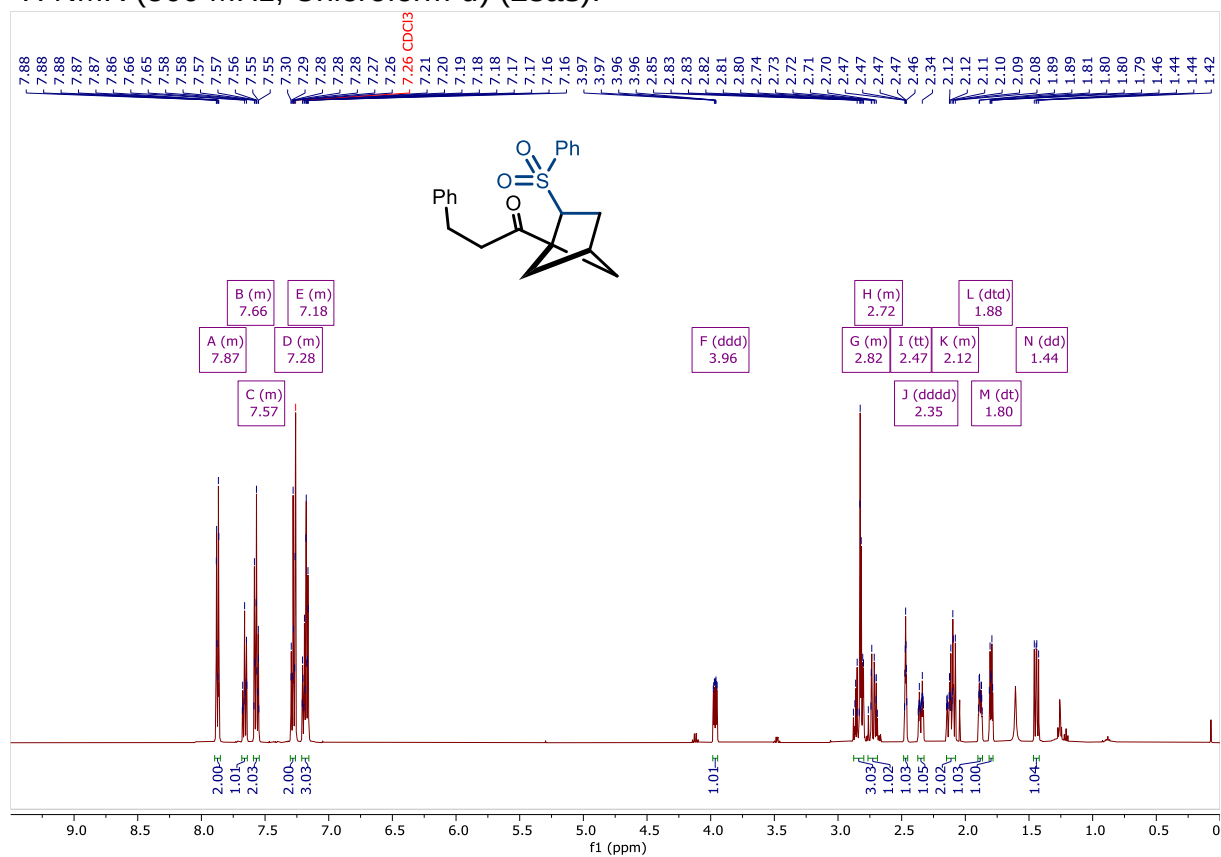
¹³C NMR (101 MHz, Chloroform-*d*) (**13ar**):



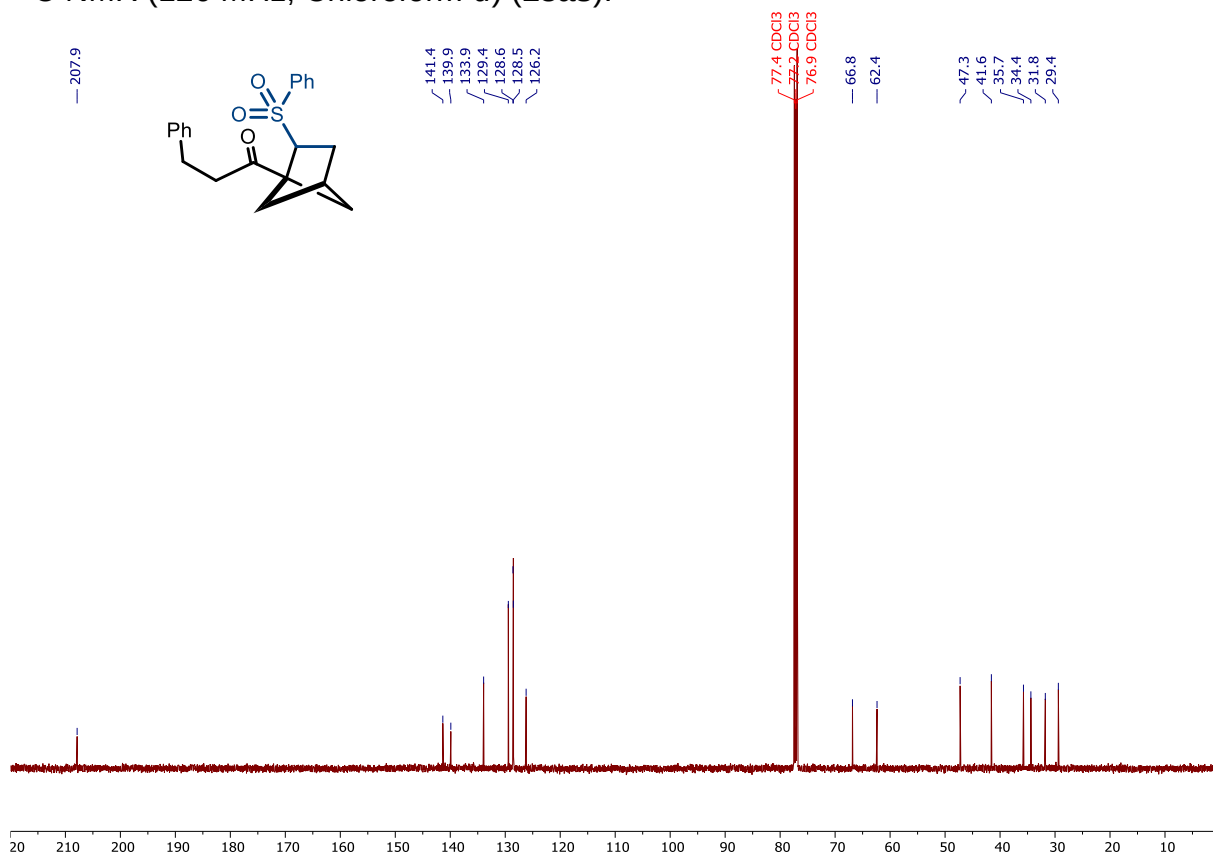
DEPT-135 NMR (101 MHz, Chloroform-*d*) (**13ar**):



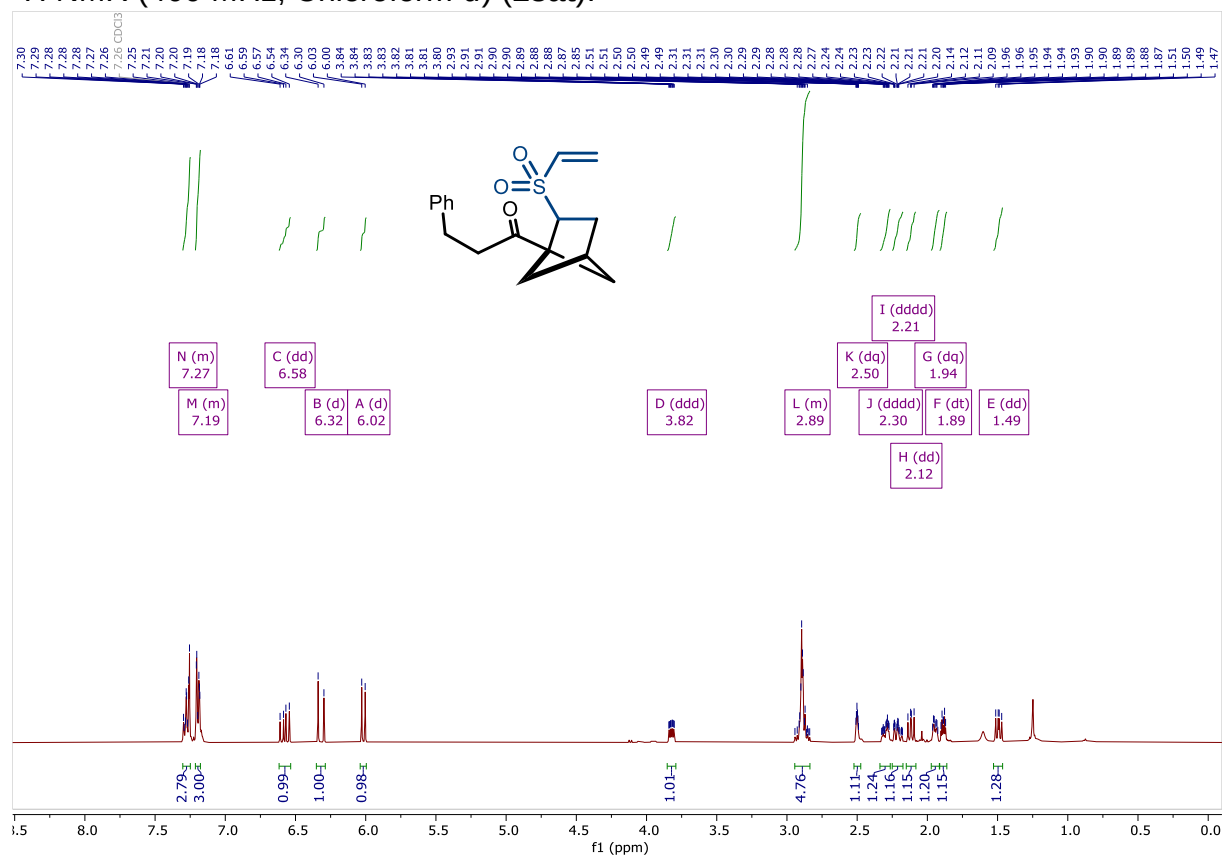
¹H NMR (500 MHz, Chloroform-*d*) (**13as**):



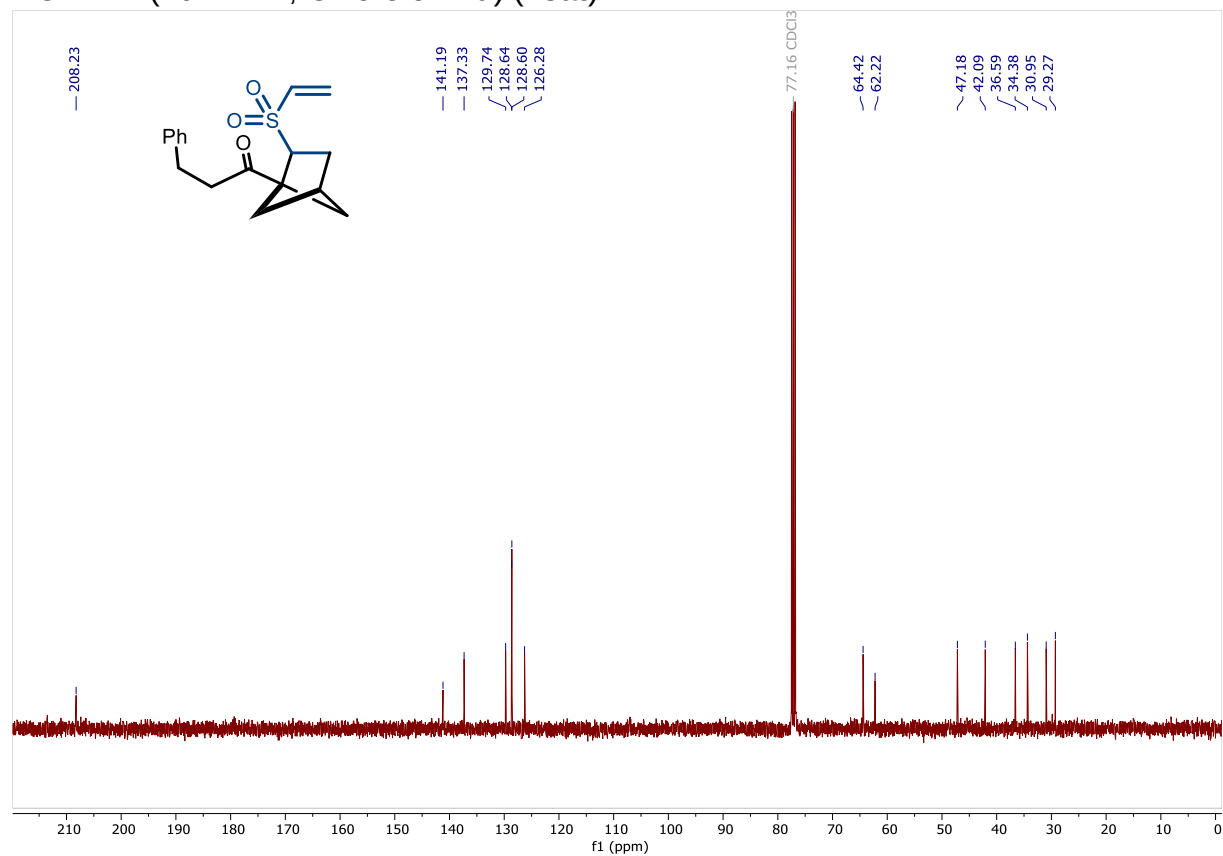
¹³C NMR (126 MHz, Chloroform-*d*) (**13as**):



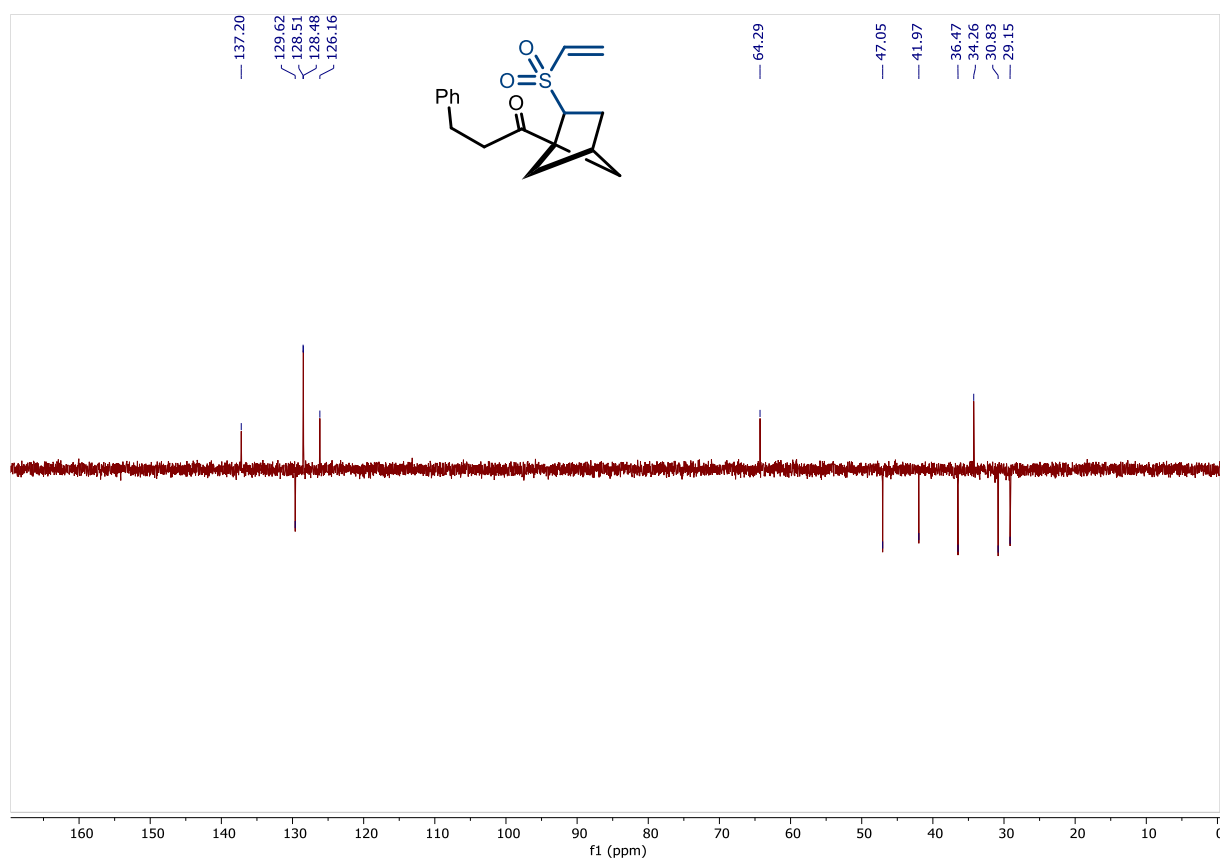
¹H NMR (400 MHz, Chloroform-*d*) (**13at**):



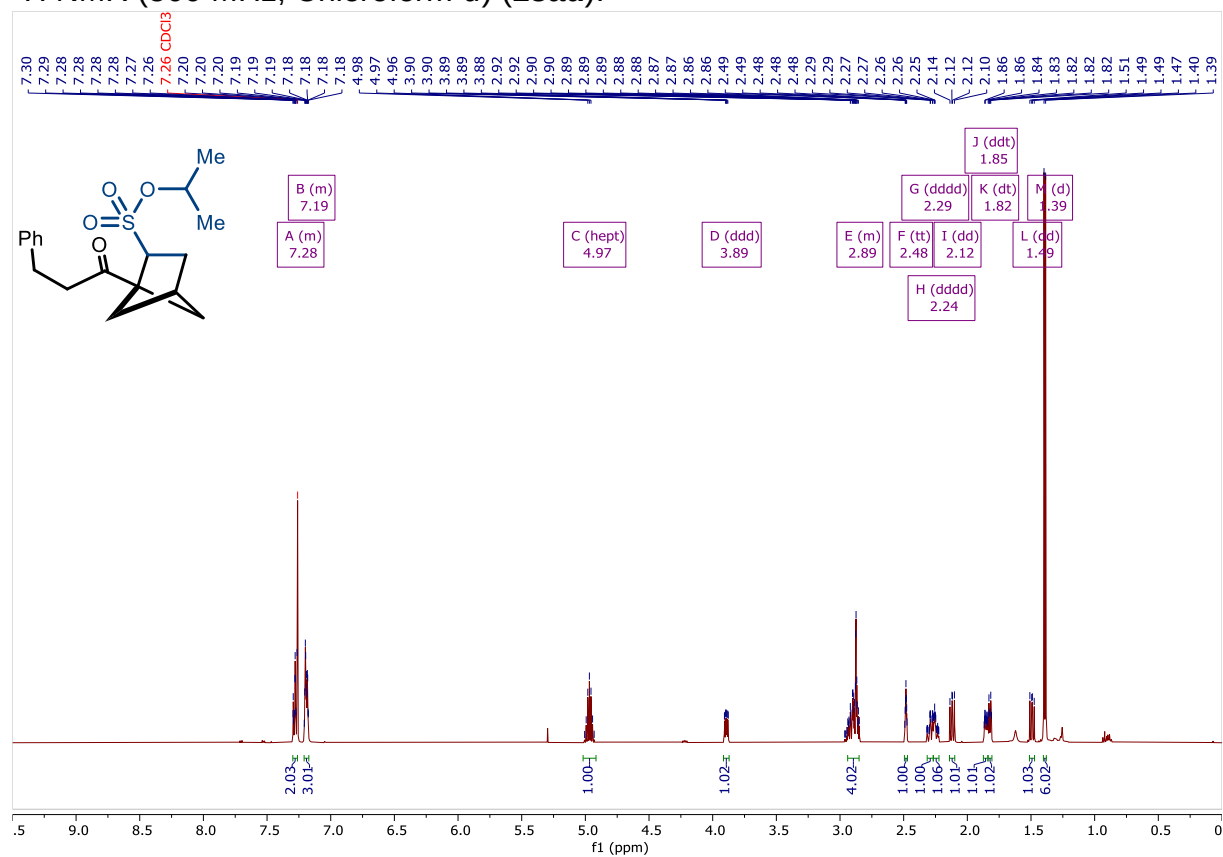
¹³C NMR (101 MHz, Chloroform-*d*) (**13at**):



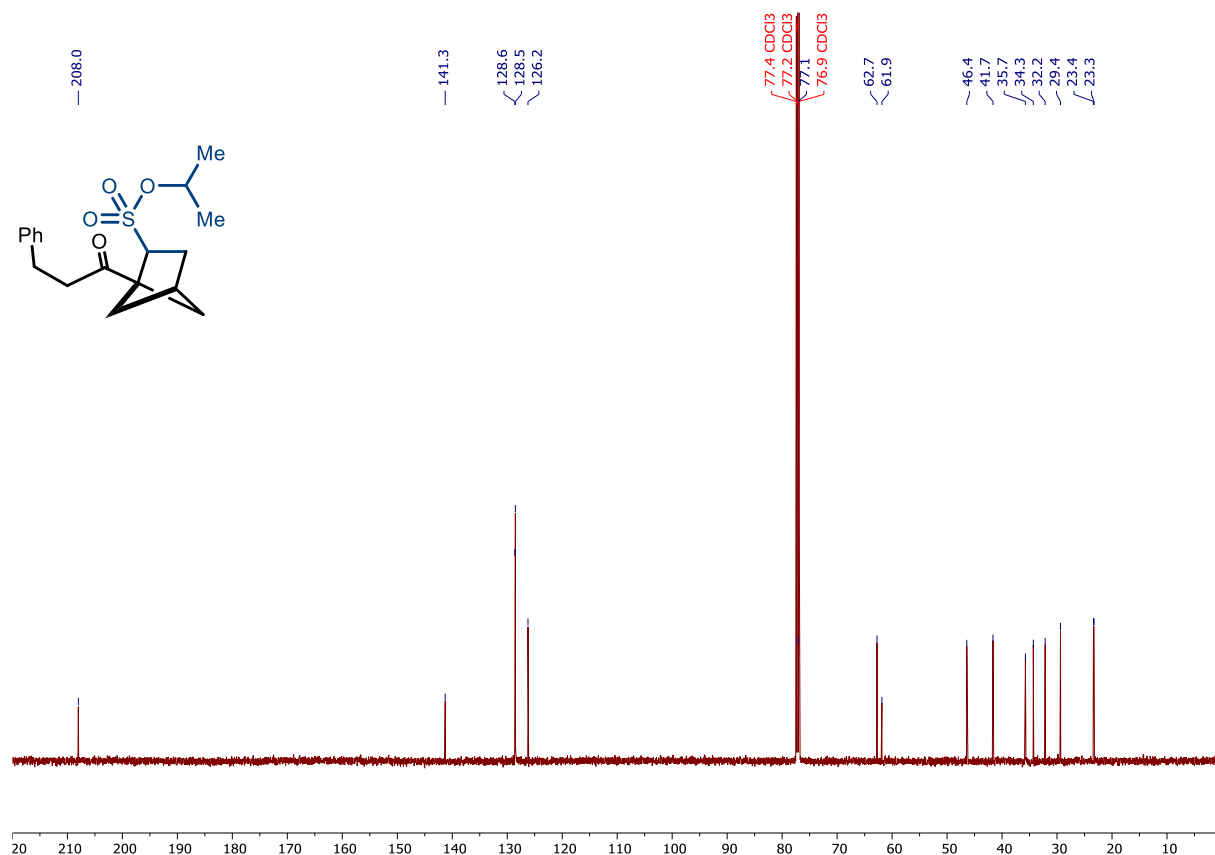
DEPT-135 NMR (101 MHz, Chloroform-*d*) (**13at**):



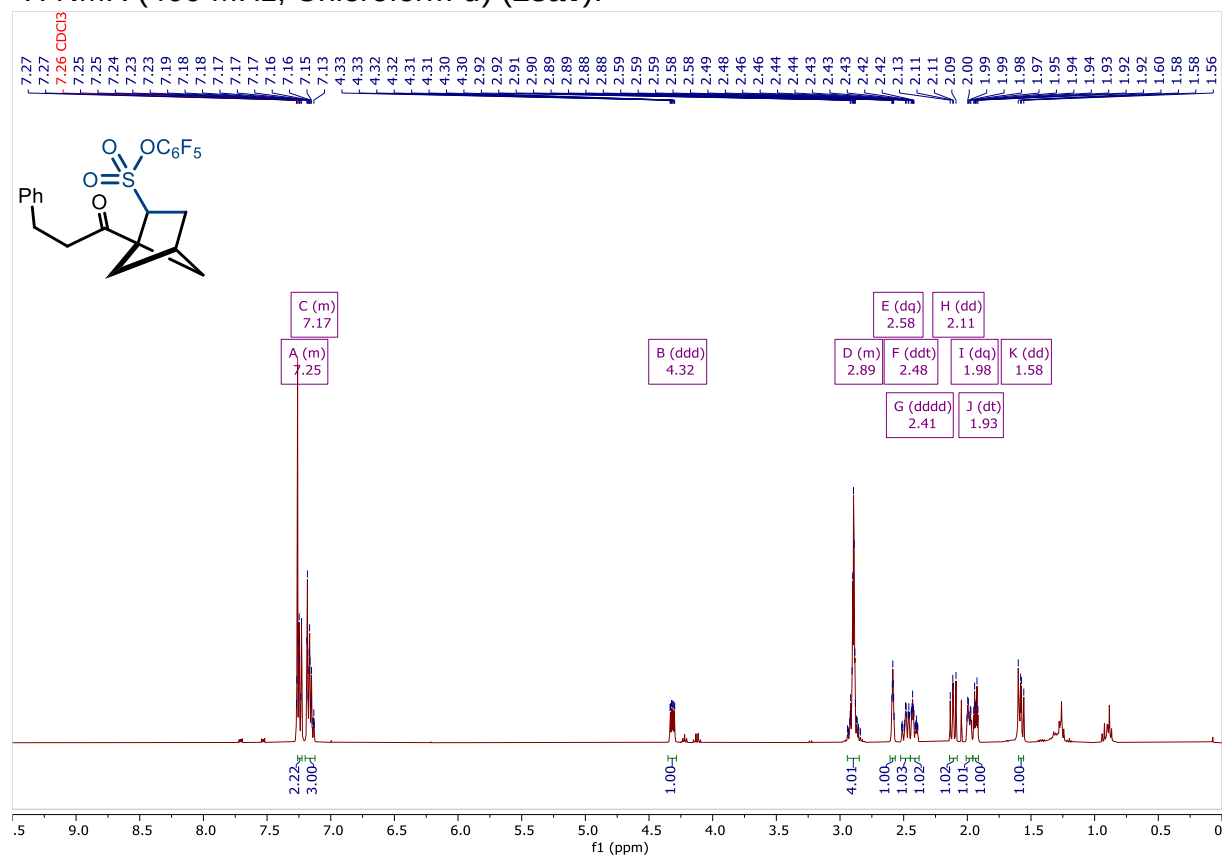
¹H NMR (500 MHz, Chloroform-*d*) (**13au**):



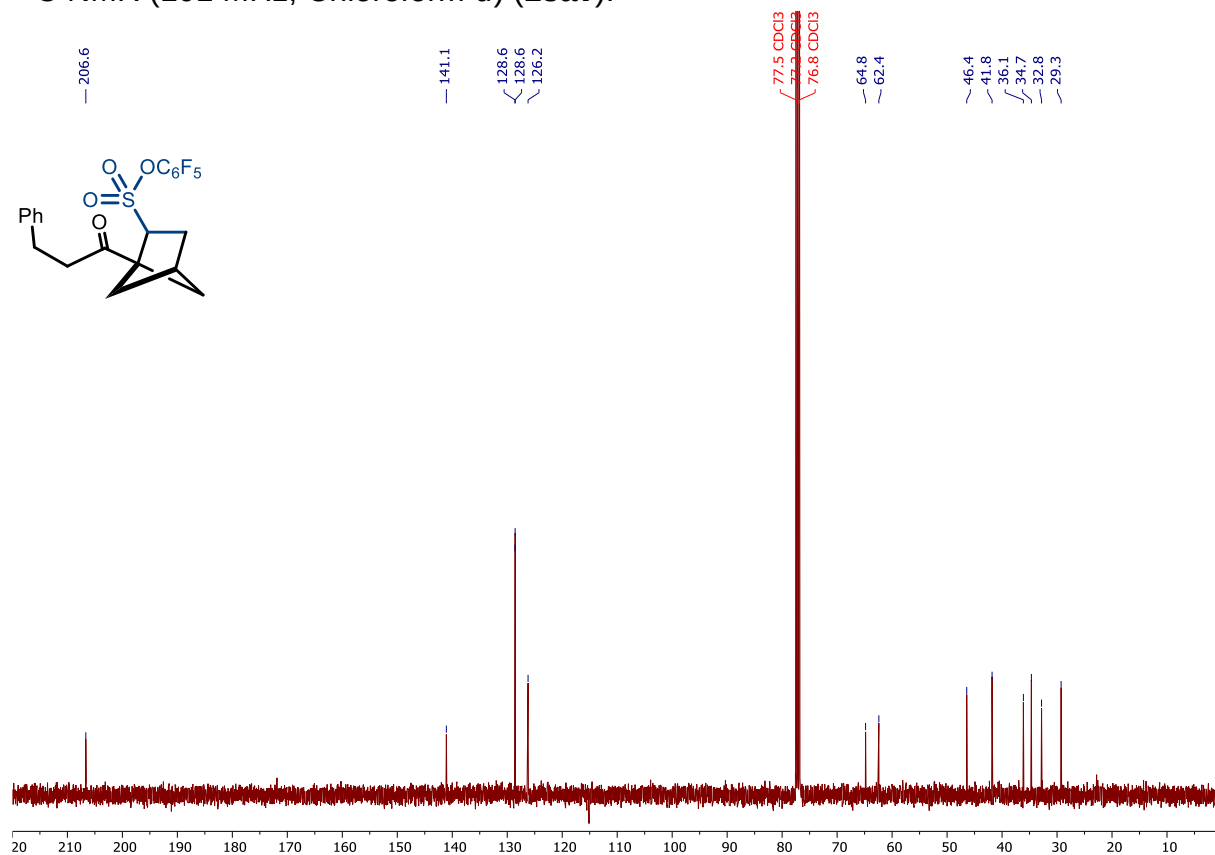
¹³C NMR (126 MHz, Chloroform-*d*) (**13au**):



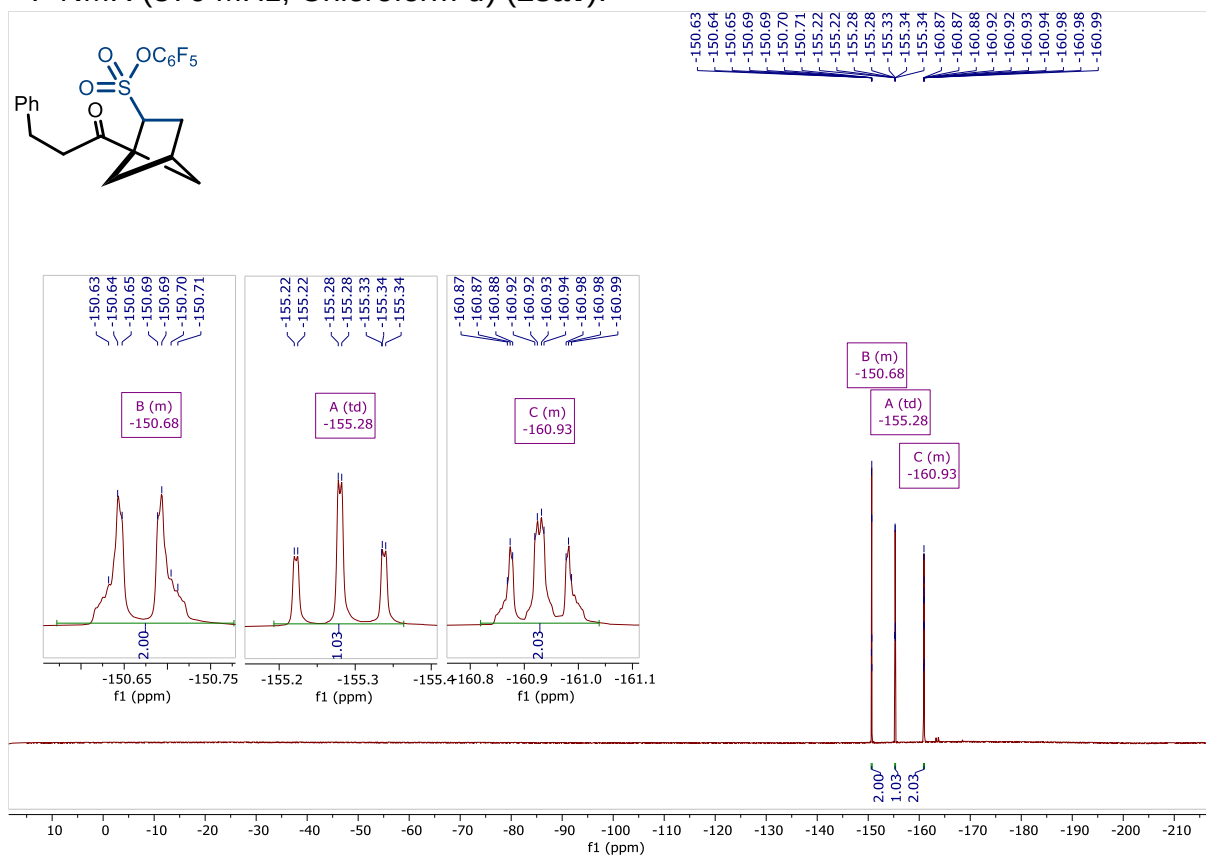
¹H NMR (400 MHz, Chloroform-*d*) (**13av**):



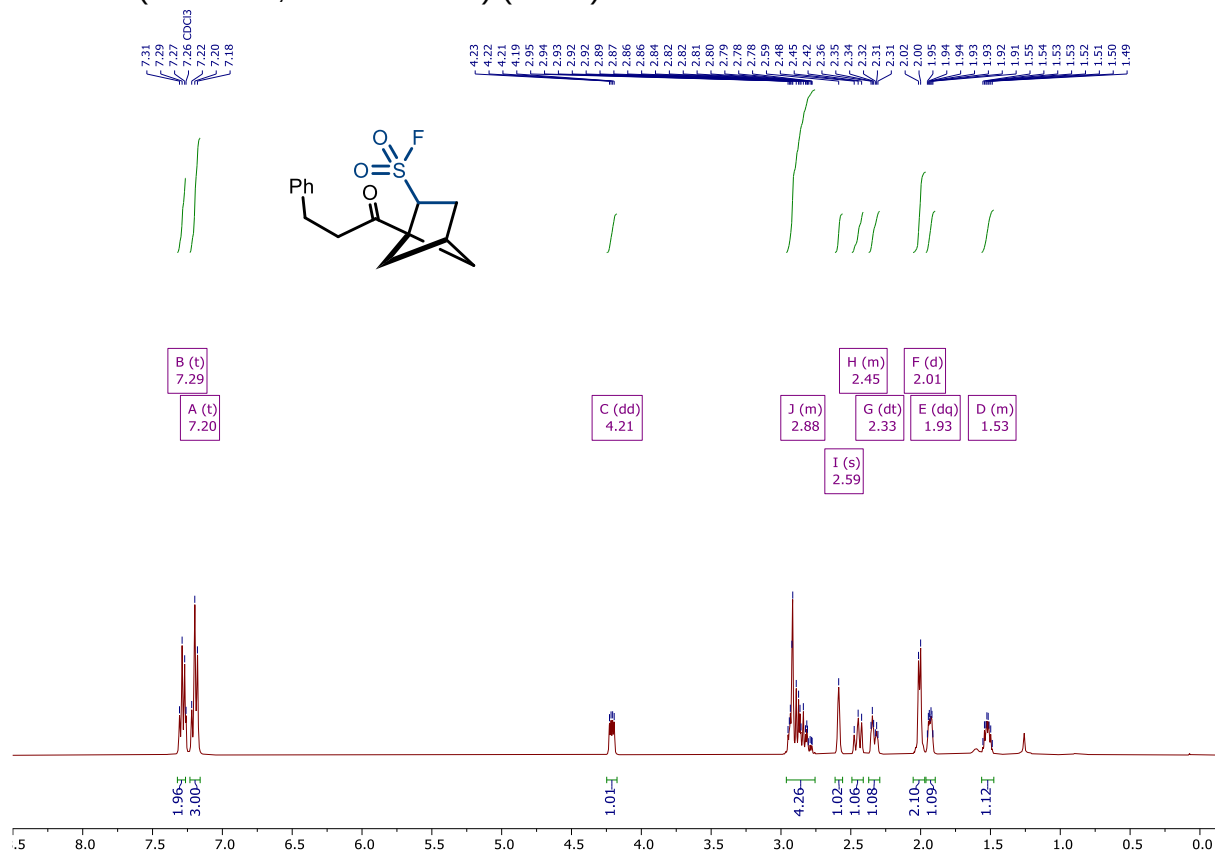
¹³C NMR (101 MHz, Chloroform-*d*) (**13av**):



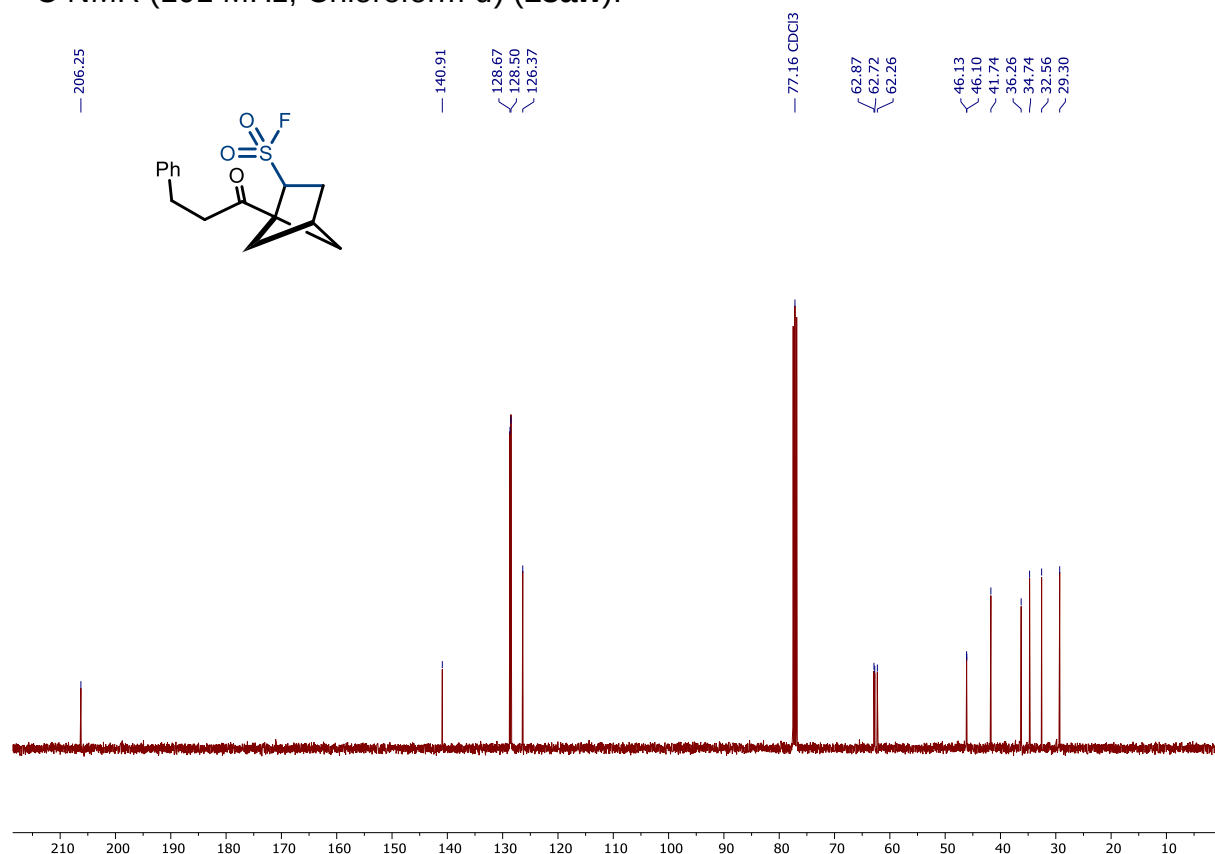
^{19}F NMR (376 MHz, Chloroform- d) (**13av**):



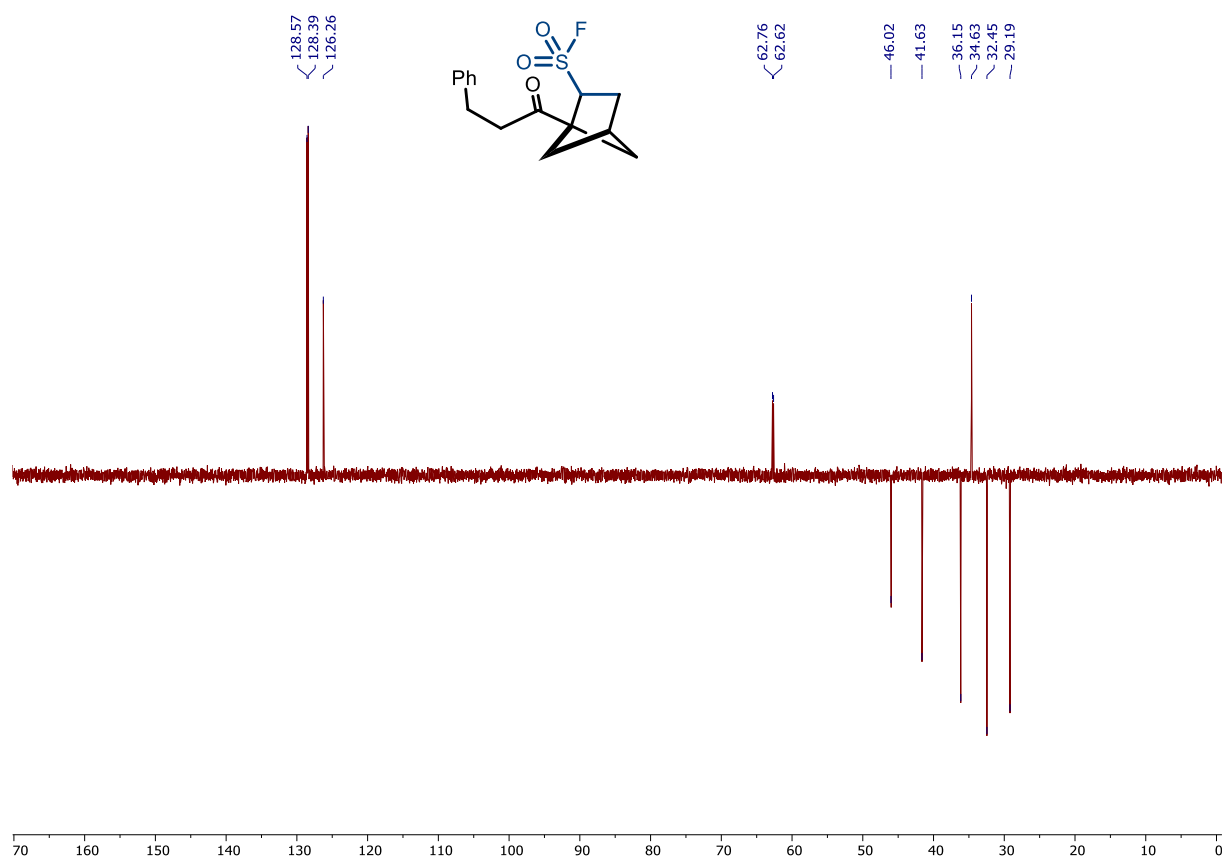
^1H NMR (400 MHz, Chloroform-*d*) (**13aw**):



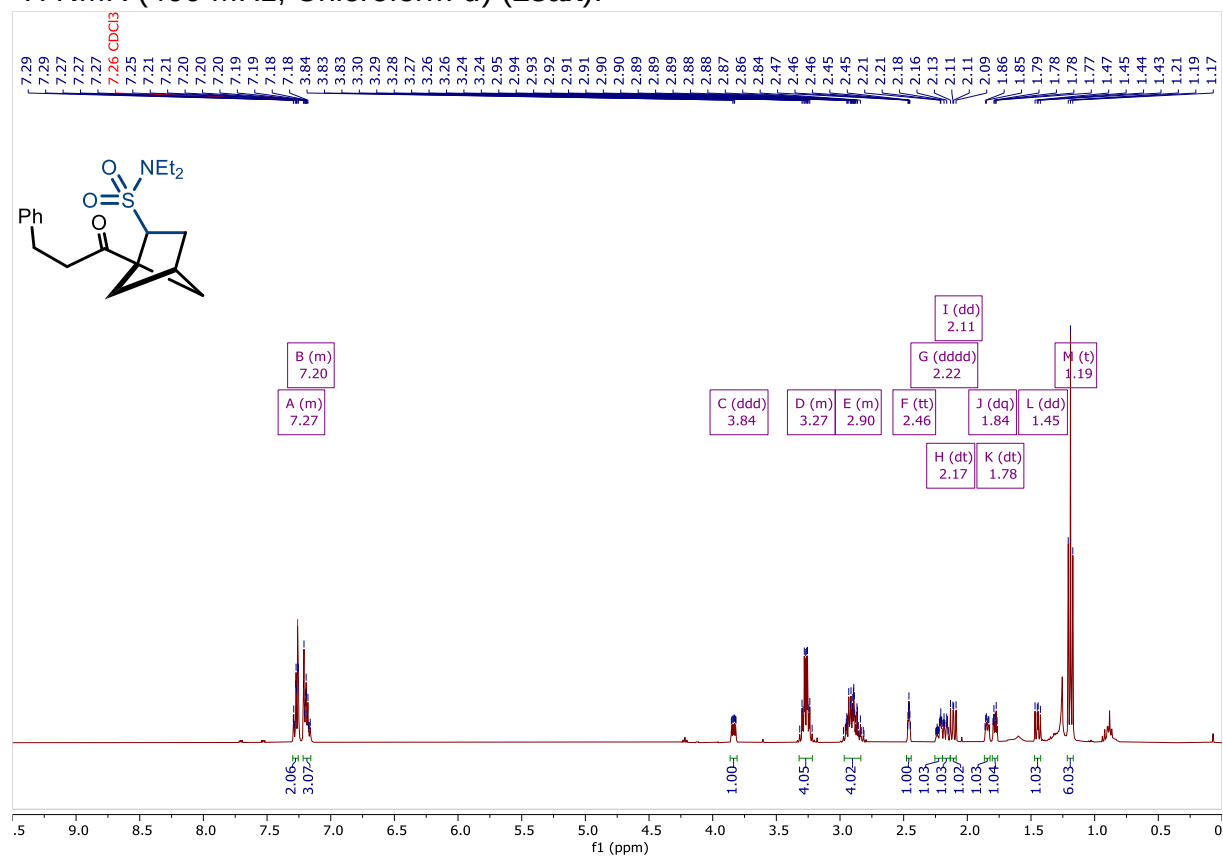
^{13}C NMR (101 MHz, Chloroform-*d*) (**13aw**):



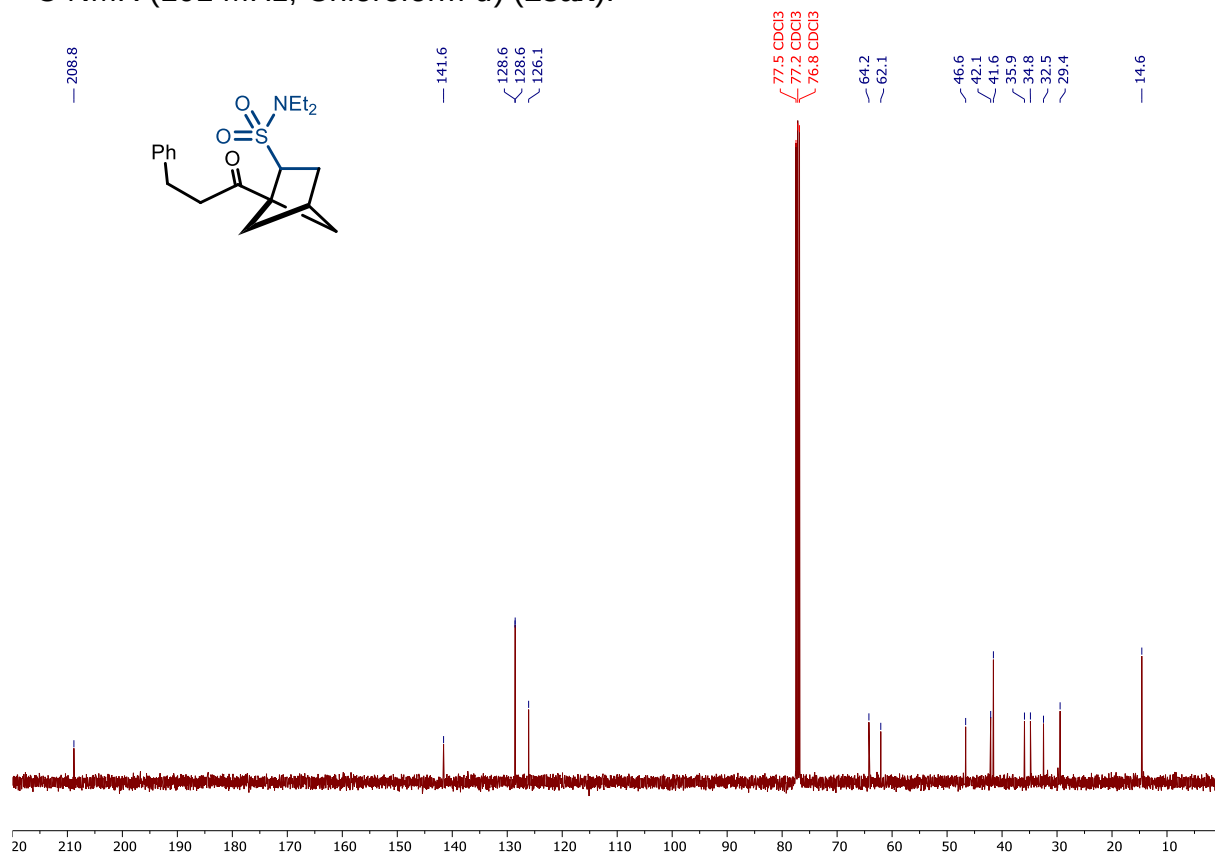
DEPT-135 NMR (101 MHz, Chloroform-*d*) (**13aw**):



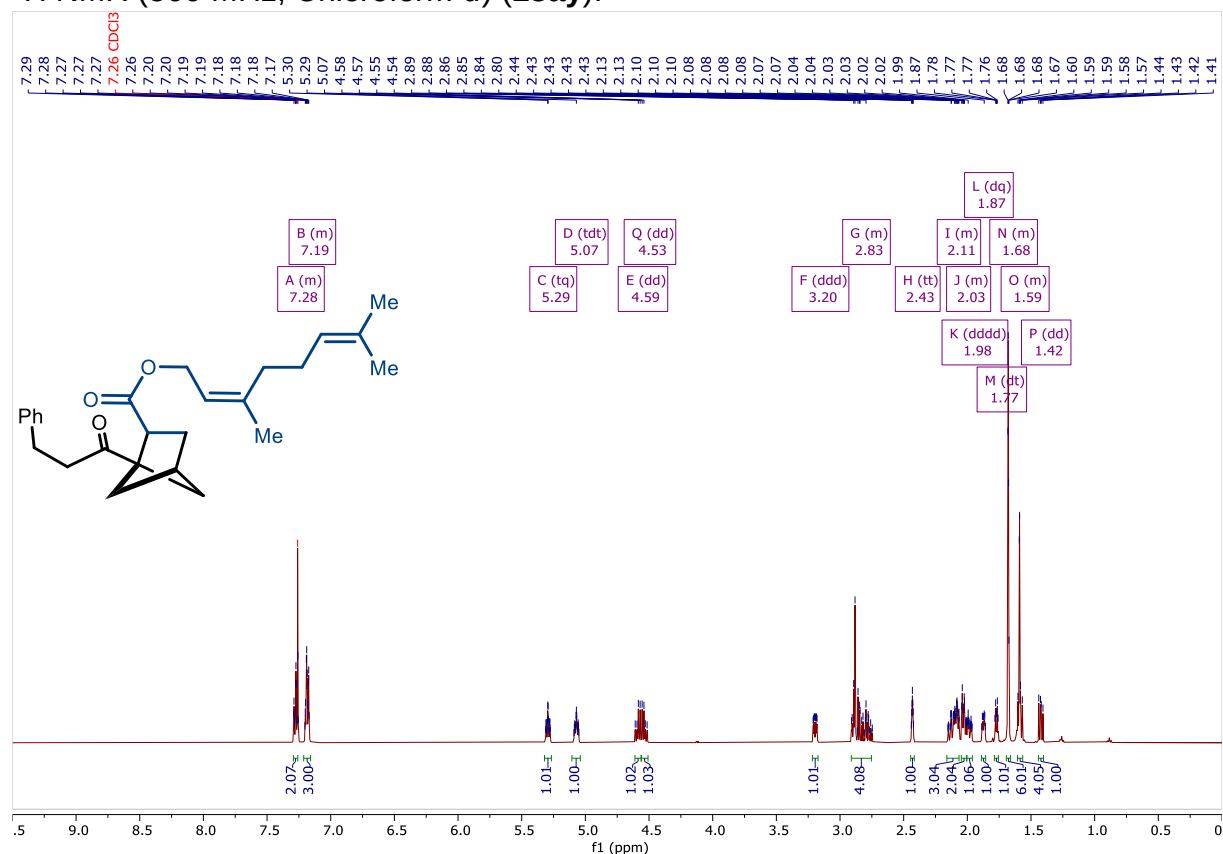
¹H NMR (400 MHz, Chloroform-*d*) (**13ax**):



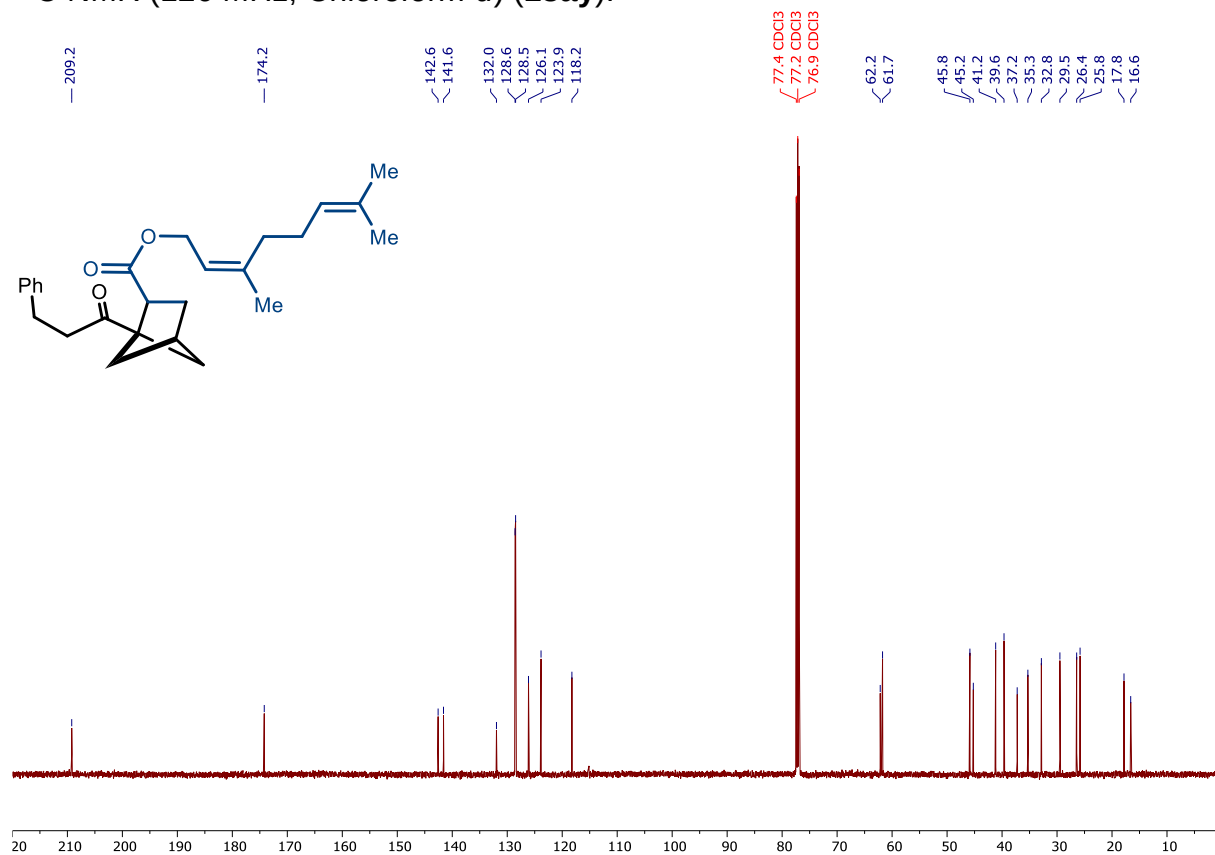
¹³C NMR (101 MHz, Chloroform-*d*) (**13ax**):

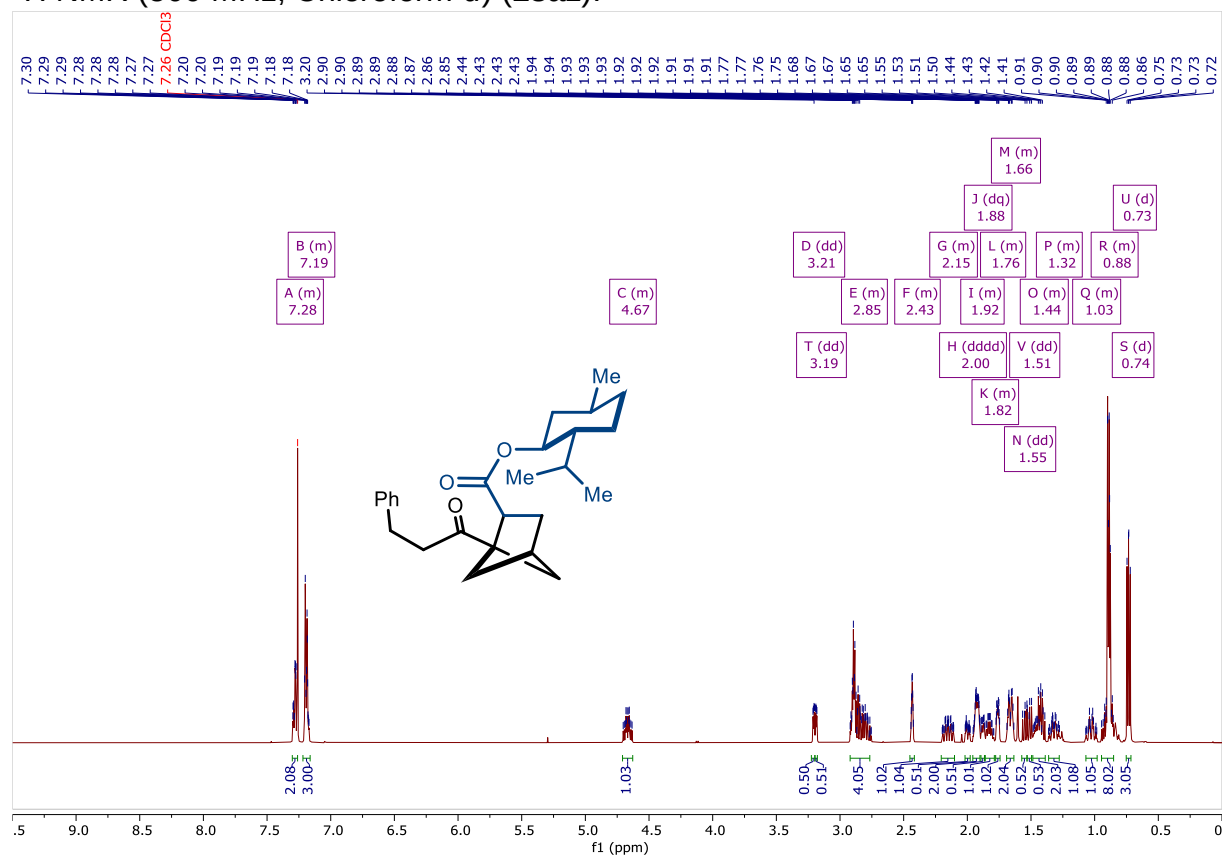


¹H NMR (500 MHz, Chloroform-*d*) (**13ay**):

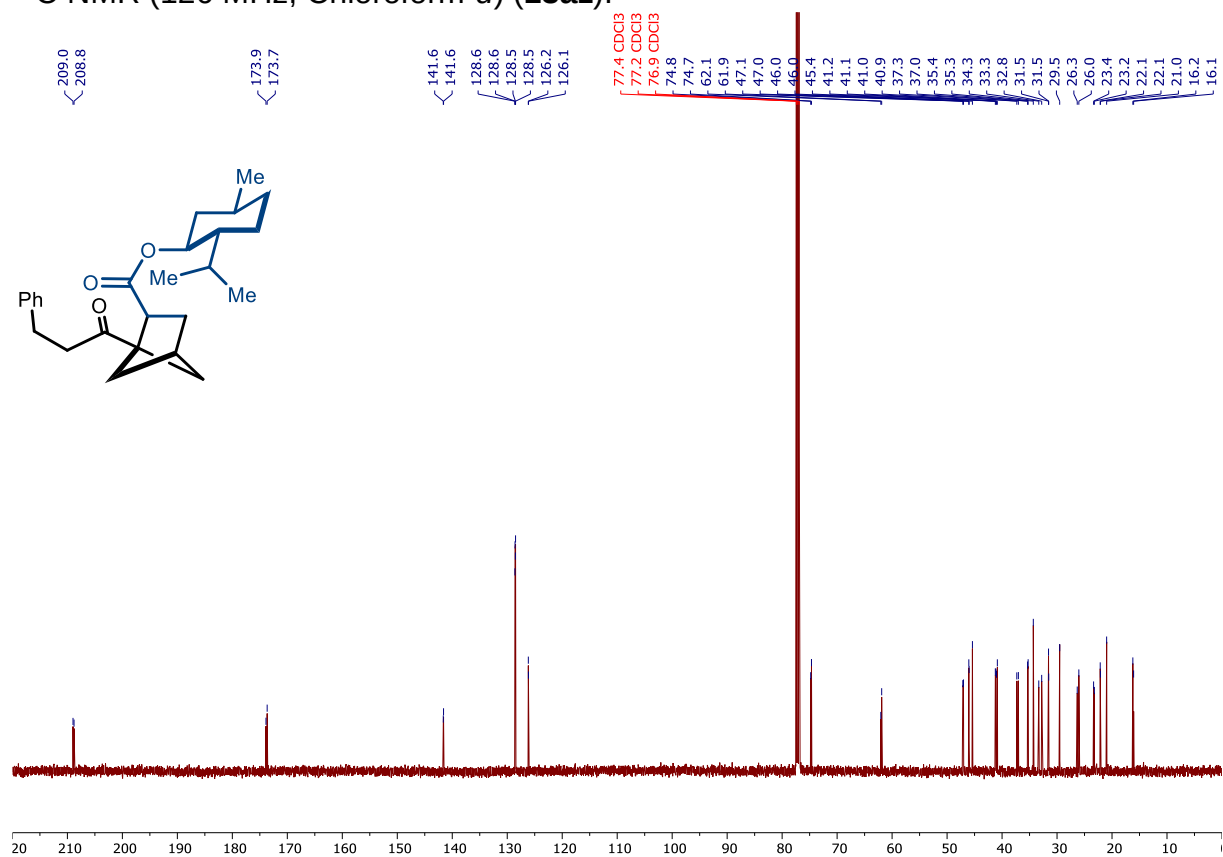


¹³C NMR (126 MHz, Chloroform-*d*) (**13ay**):

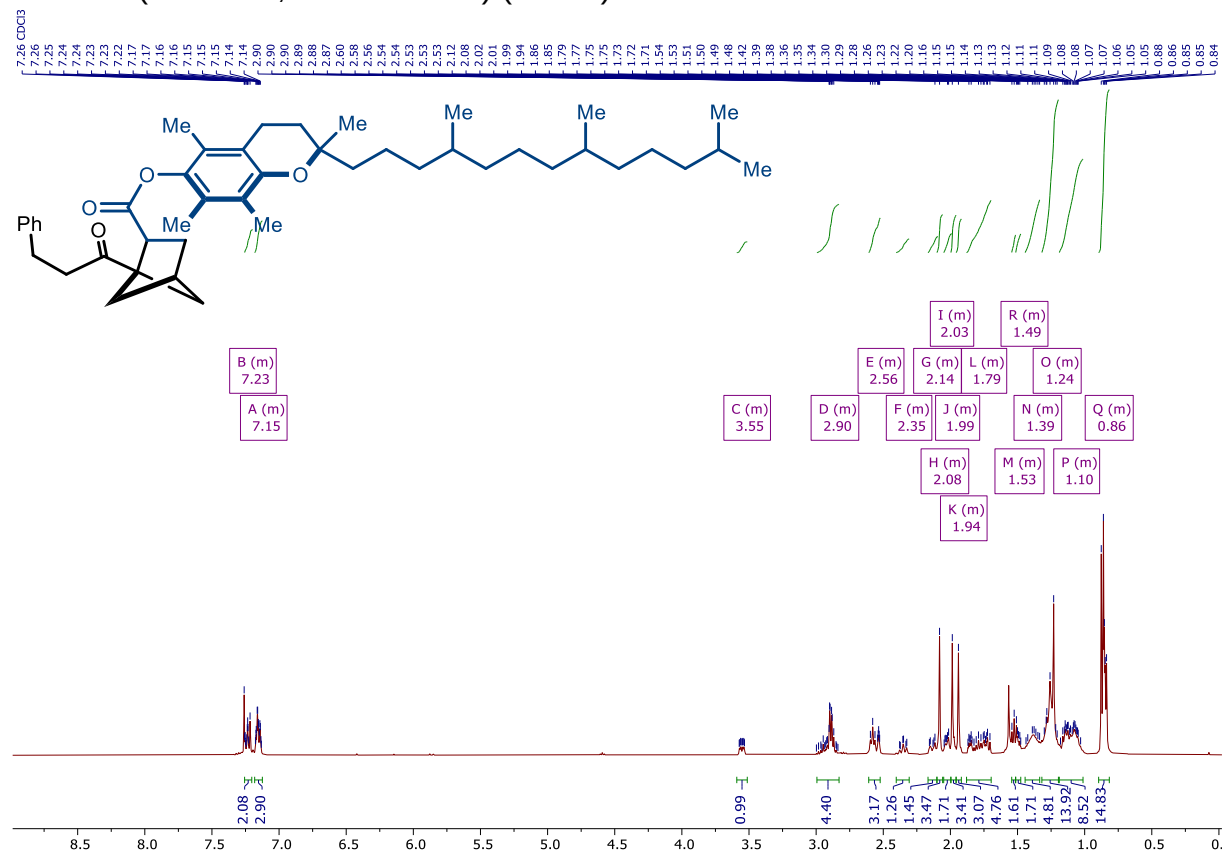


¹H NMR (500 MHz, Chloroform-*d*) (**13az**):

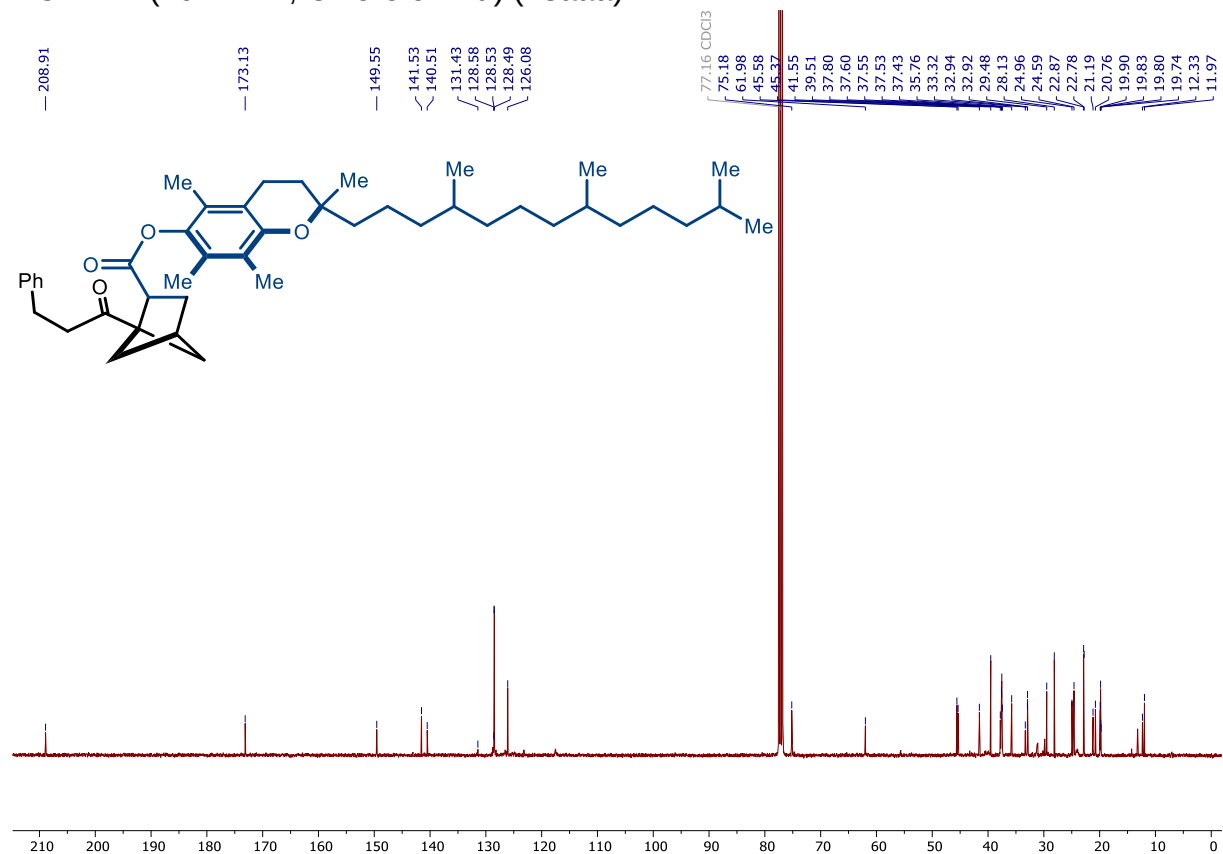
¹³C NMR (126 MHz, Chloroform-*d*) (**13az**):



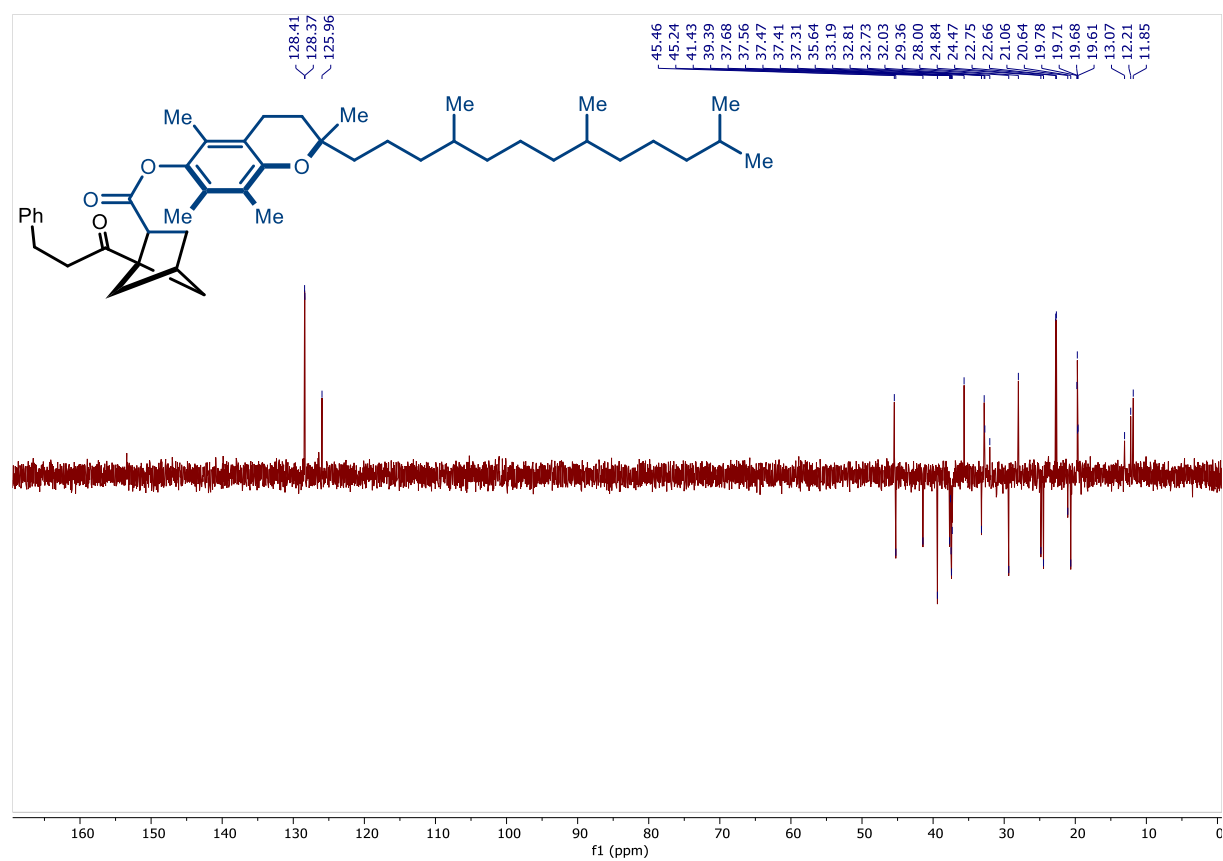
¹H NMR (400 MHz, Chloroform-*d*) (**13aaa**):



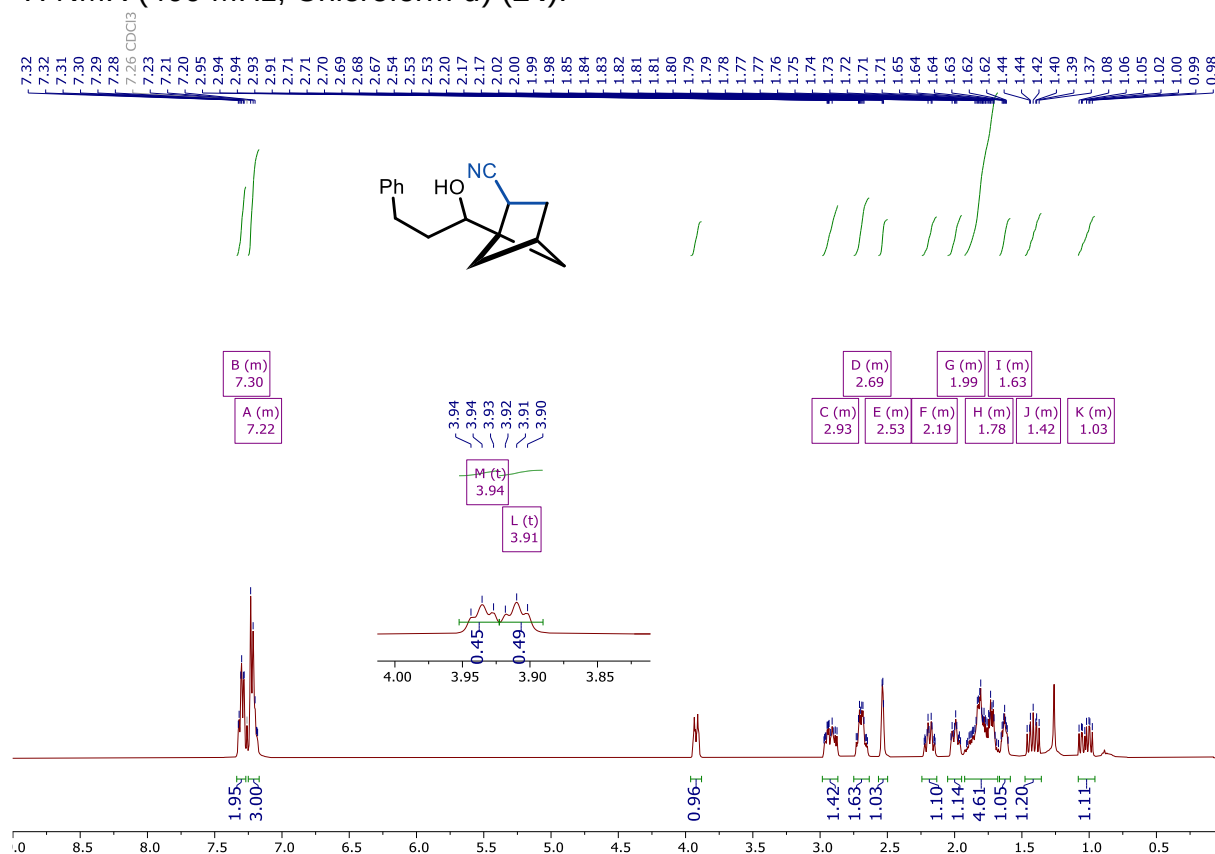
¹³C NMR (101 MHz, Chloroform-*d*) (**13aaa**):



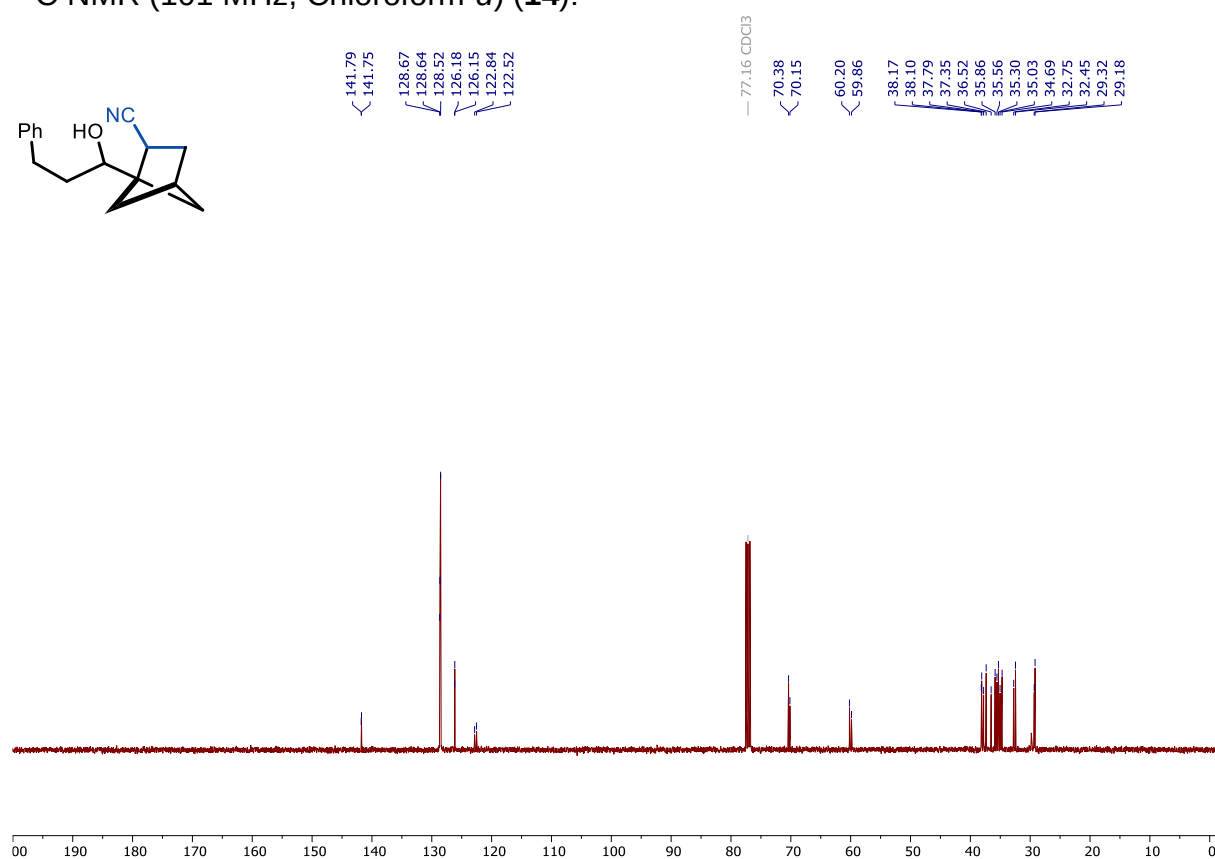
DEPT-135 NMR (101 MHz, Chloroform-*d*) (**13aaa**):



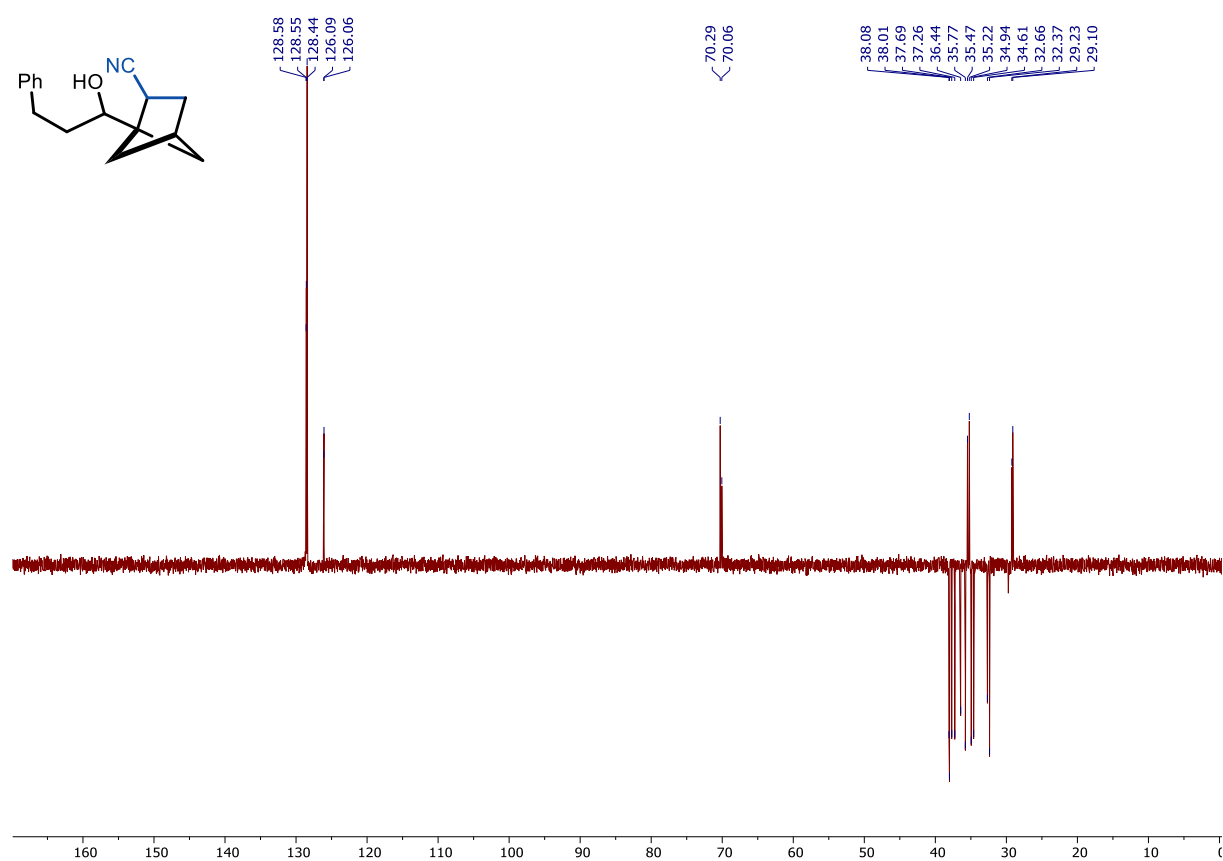
¹H NMR (400 MHz, Chloroform-*d*) (**14**):



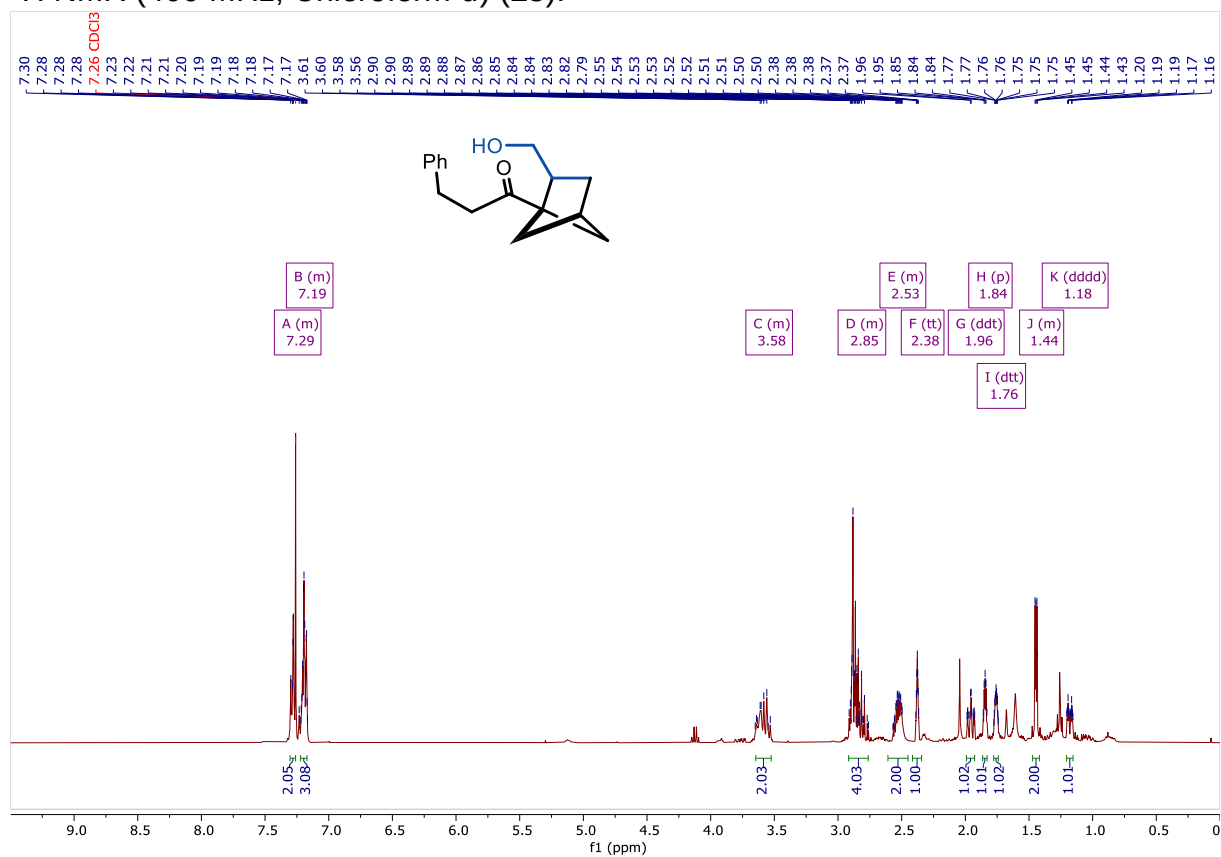
¹³C NMR (101 MHz, Chloroform-*d*) (**14**):



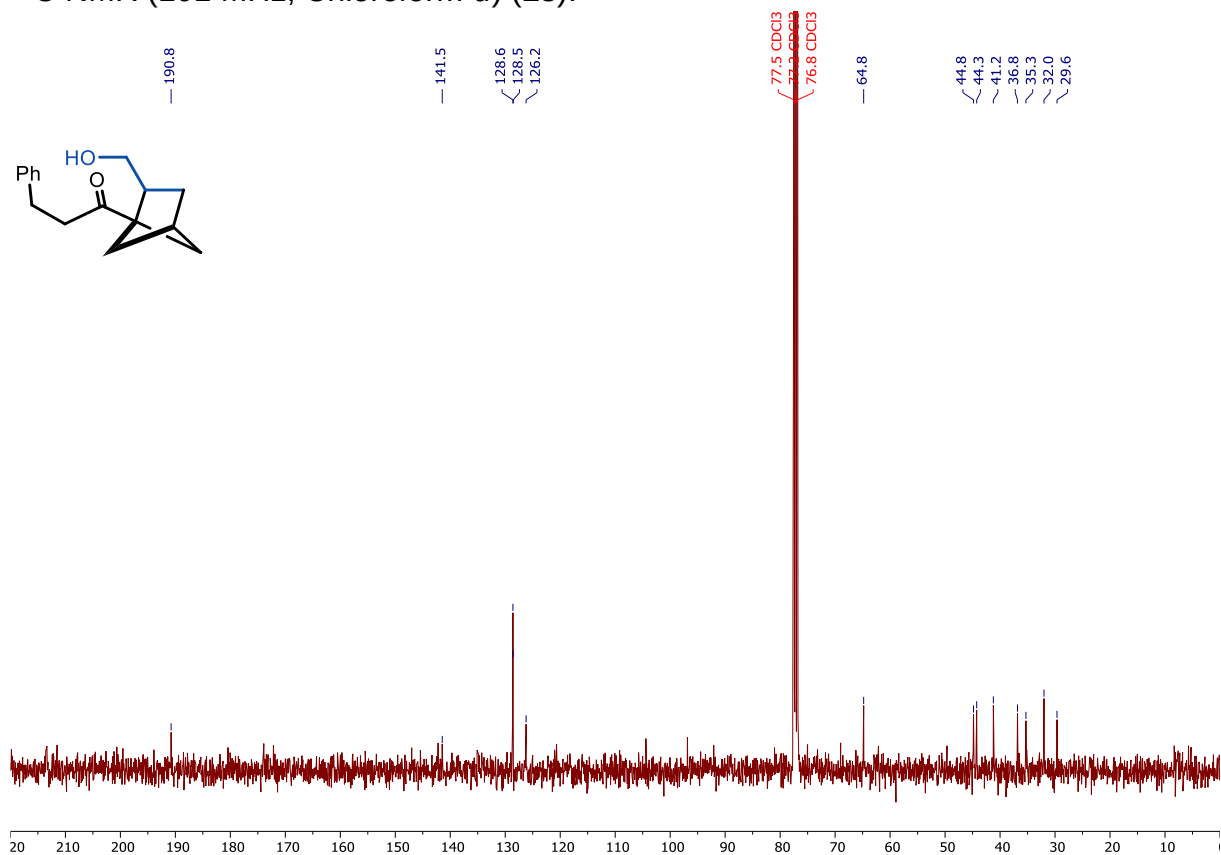
DEPT-135 NMR (101 MHz, Chloroform-*d*) (**14**):



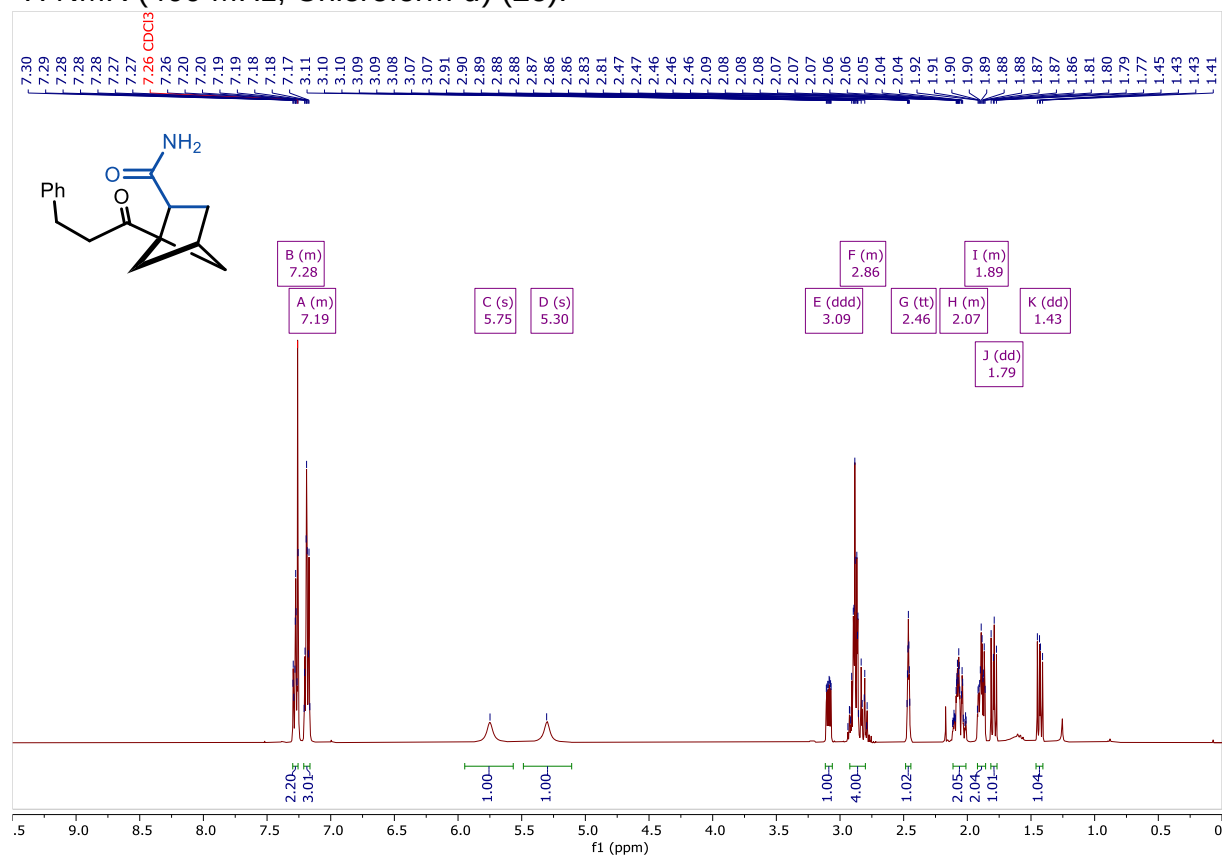
¹H NMR (400 MHz, Chloroform-*d*) (**15**):



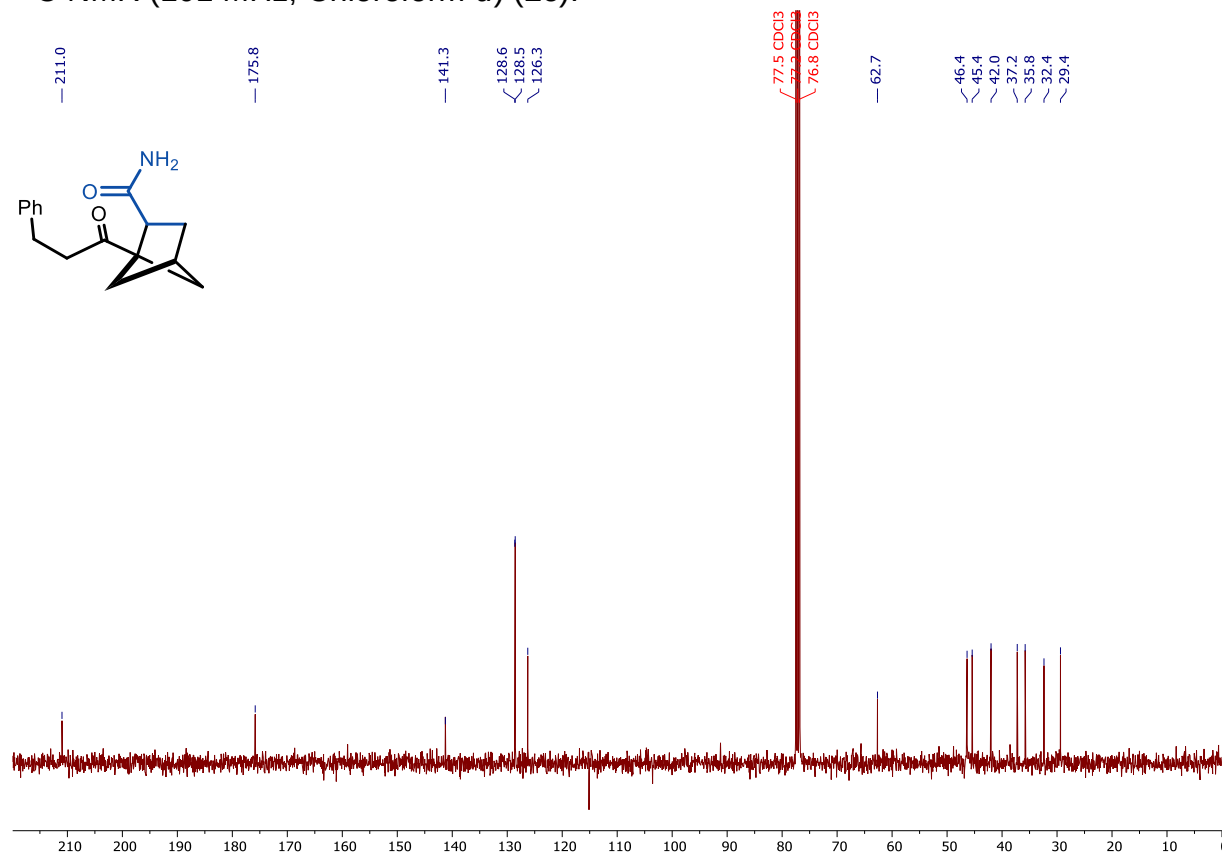
¹³C NMR (101 MHz, Chloroform-*d*) (**15**):



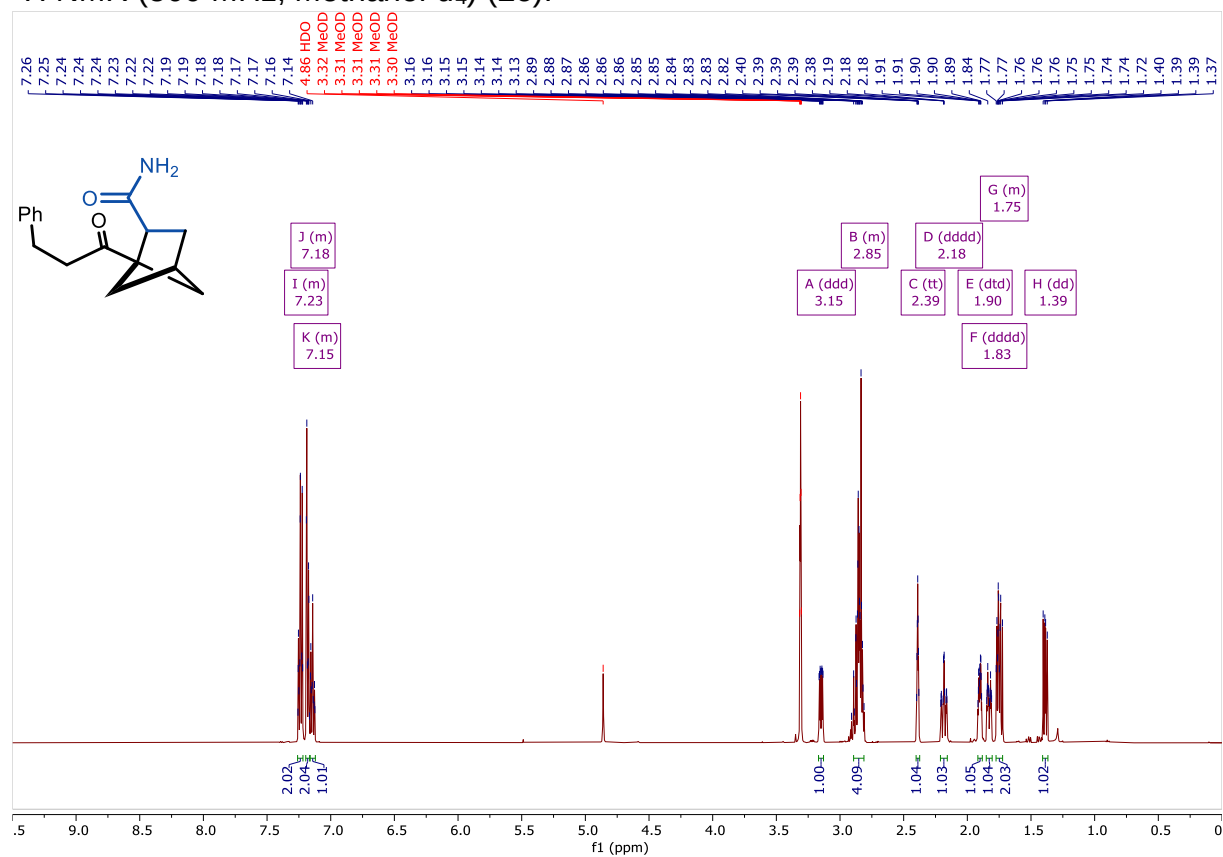
¹H NMR (400 MHz, Chloroform-*d*) (**16**):



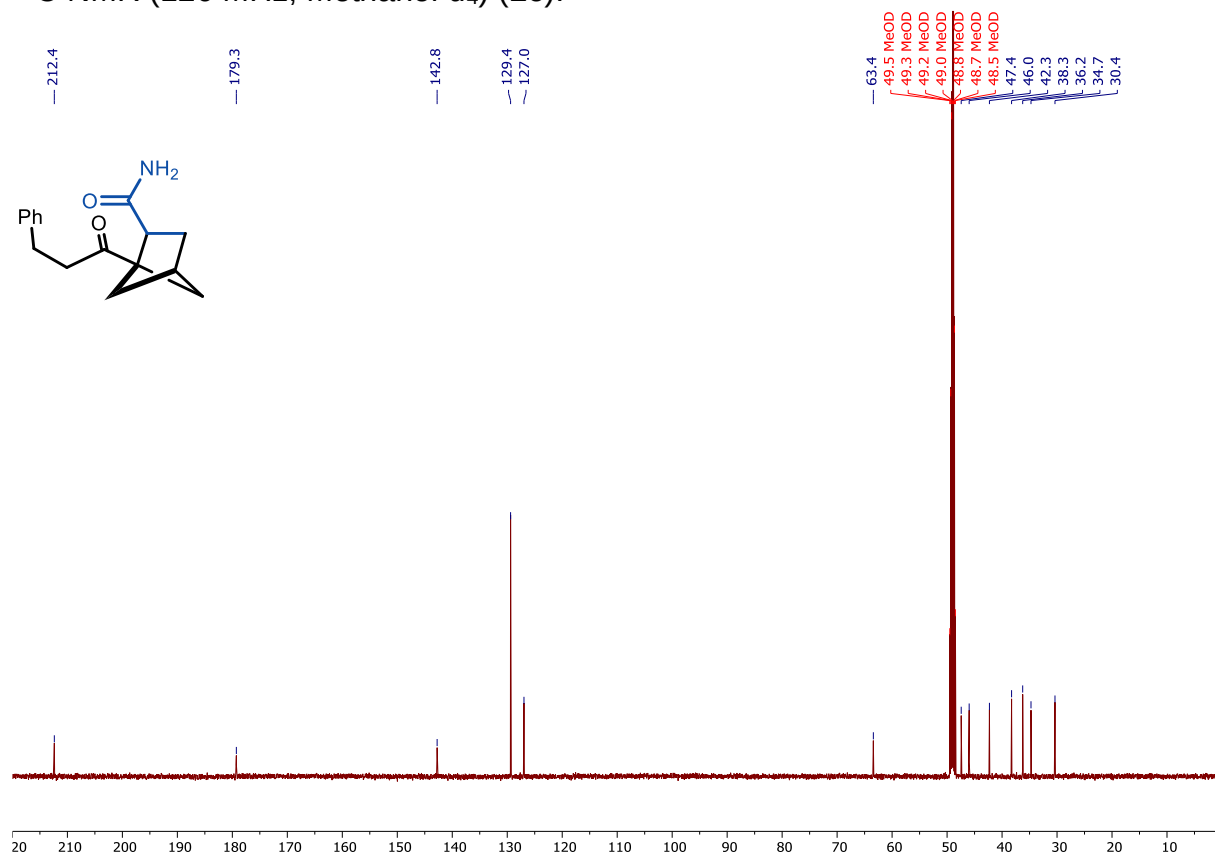
¹³C NMR (101 MHz, Chloroform-*d*) (**16**):



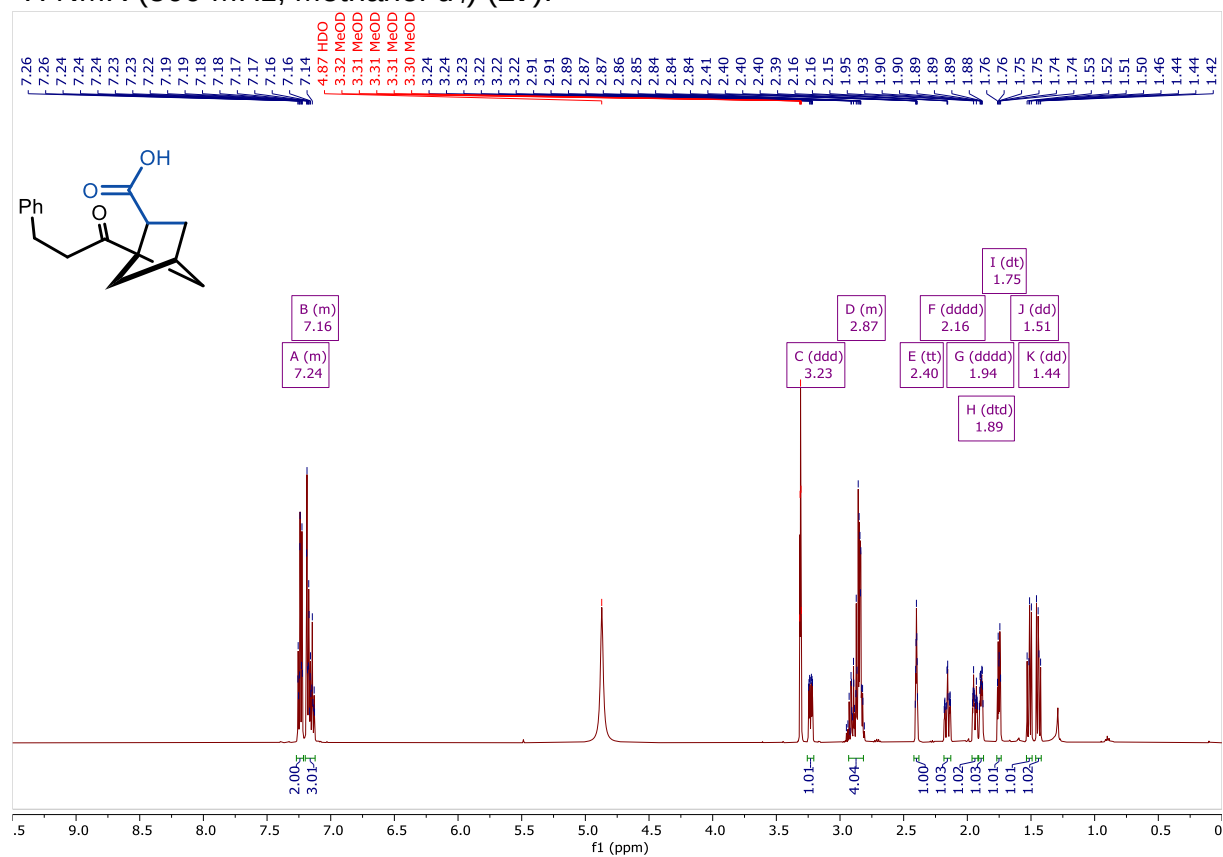
¹H NMR (500 MHz, Methanol-*d*₄) (**16**):



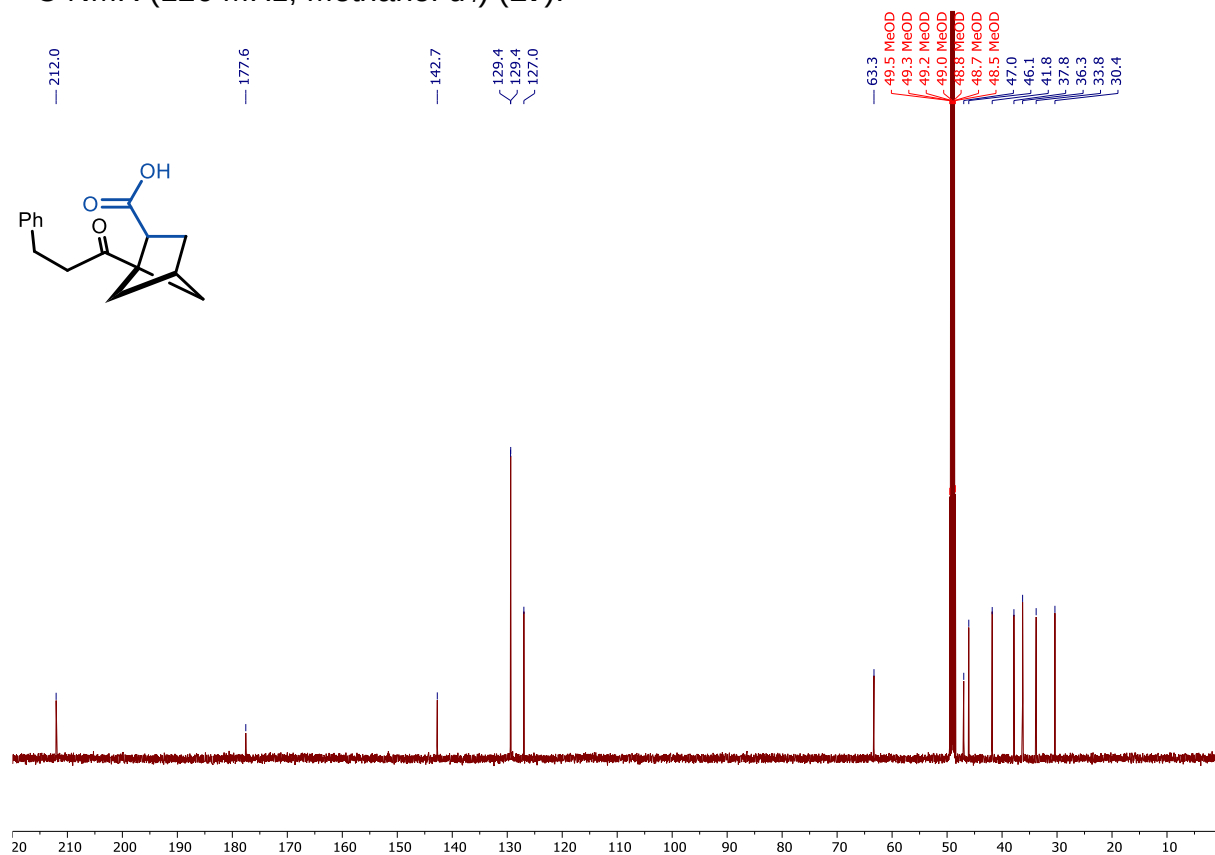
¹³C NMR (126 MHz, Methanol-*d*₄) (**16**):



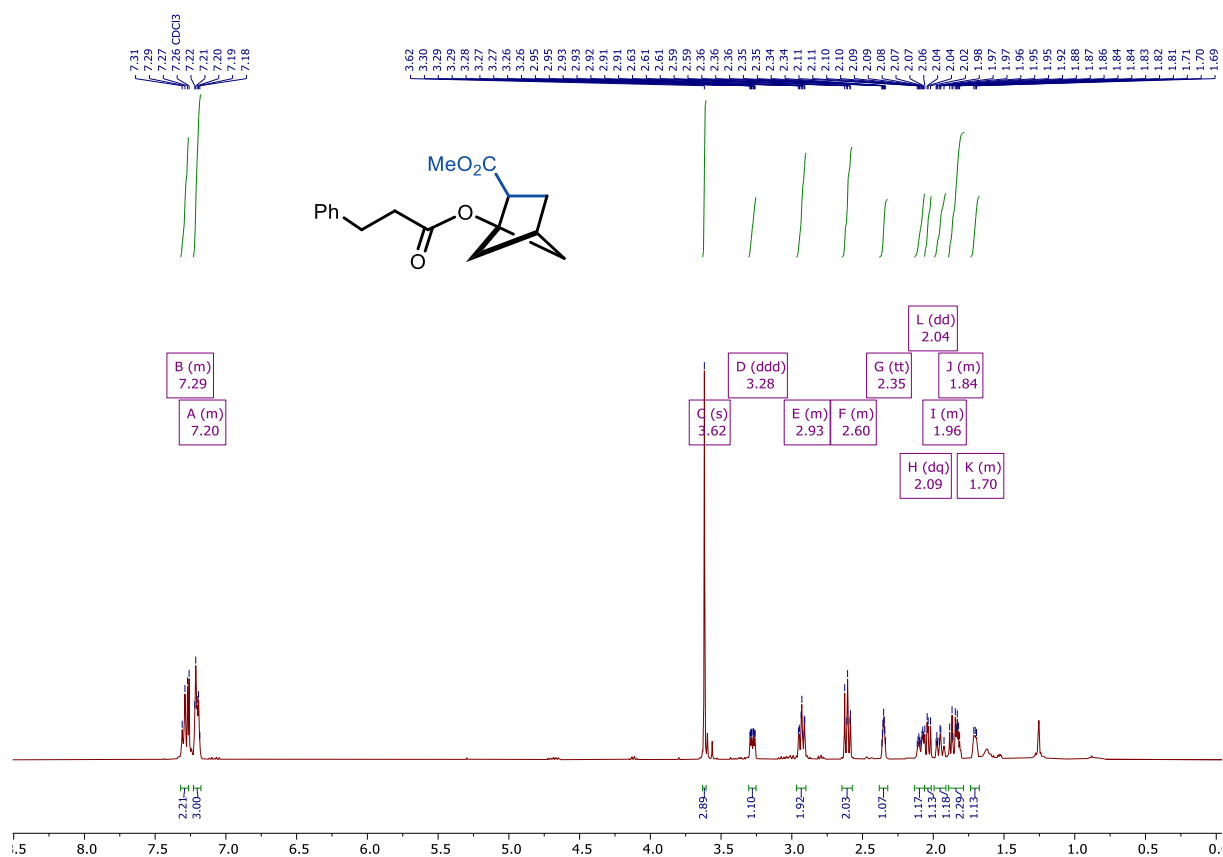
¹H NMR (500 MHz, Methanol-*d*₄) (**17**):



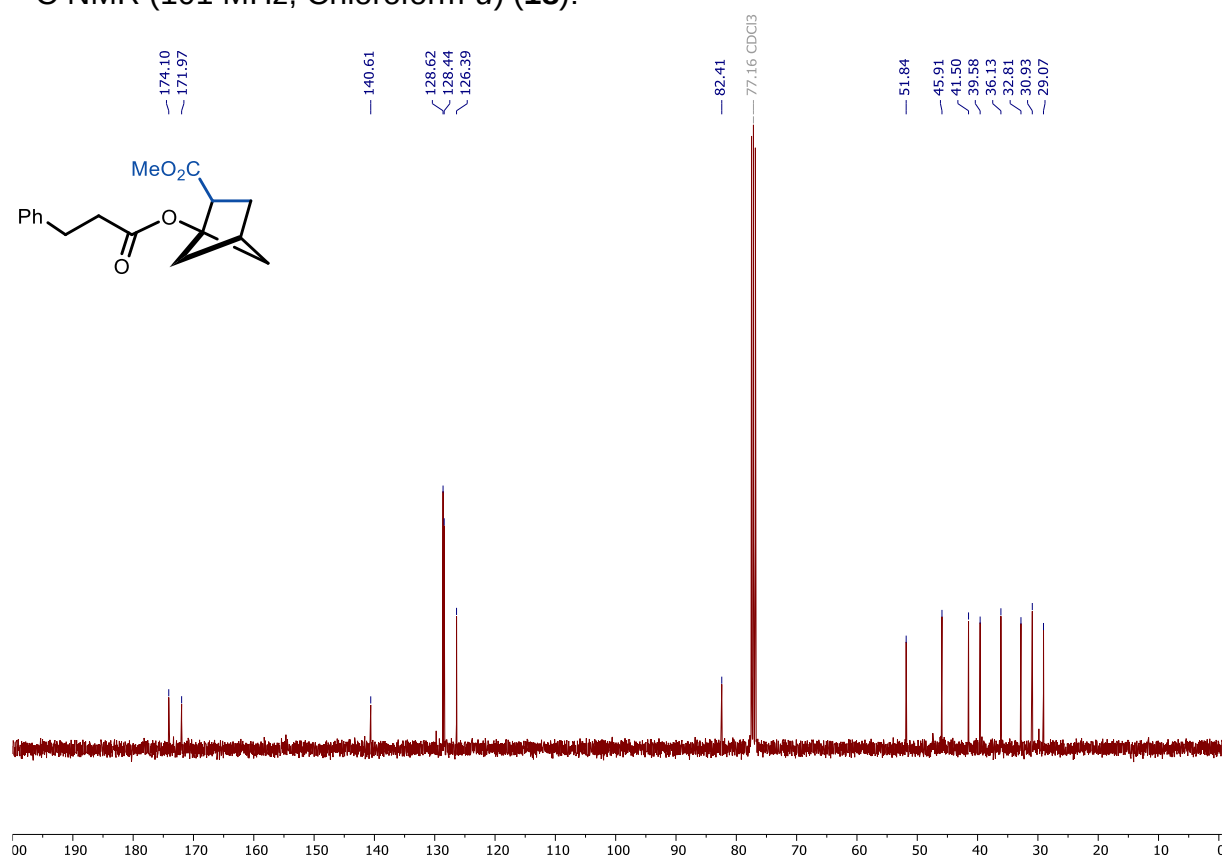
¹³C NMR (126 MHz, Methanol-*d*₄) (**17**):



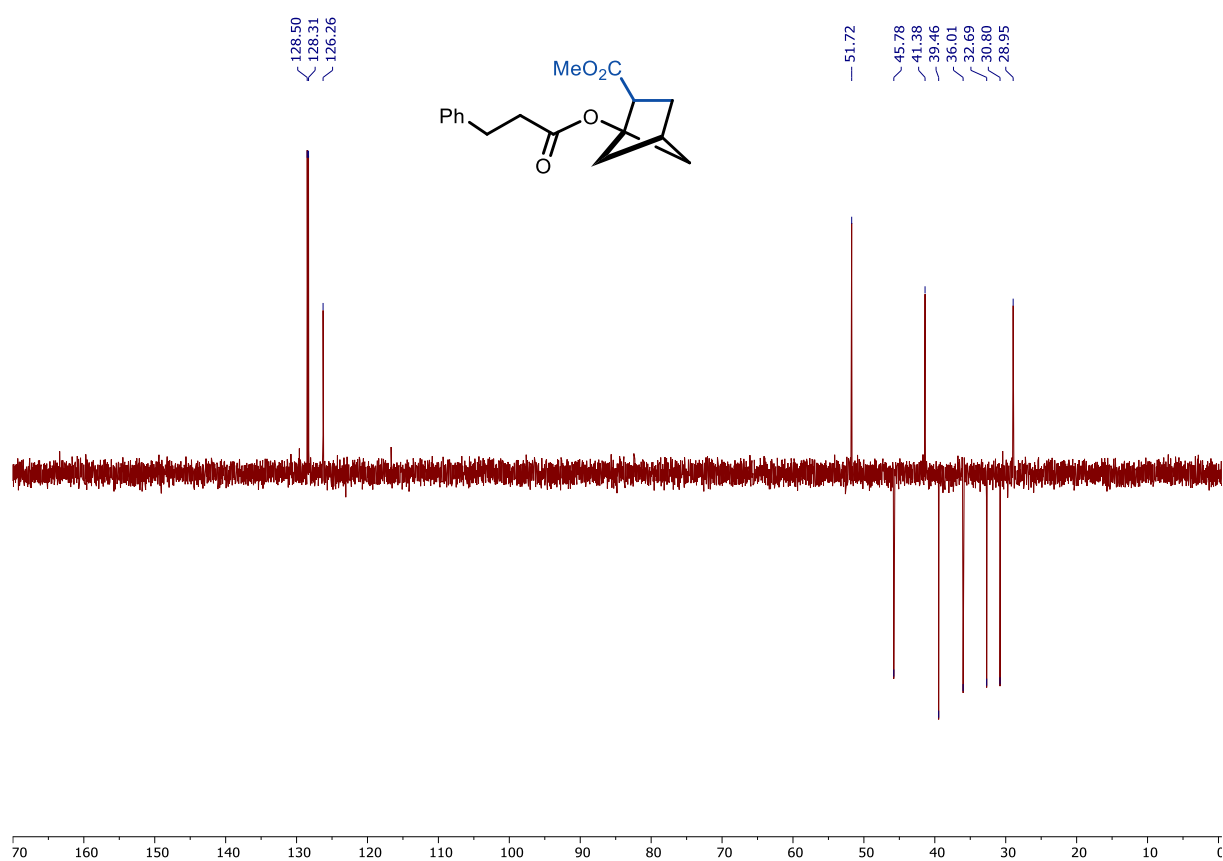
^1H NMR (400 MHz, Chloroform-*d*) (**18**):

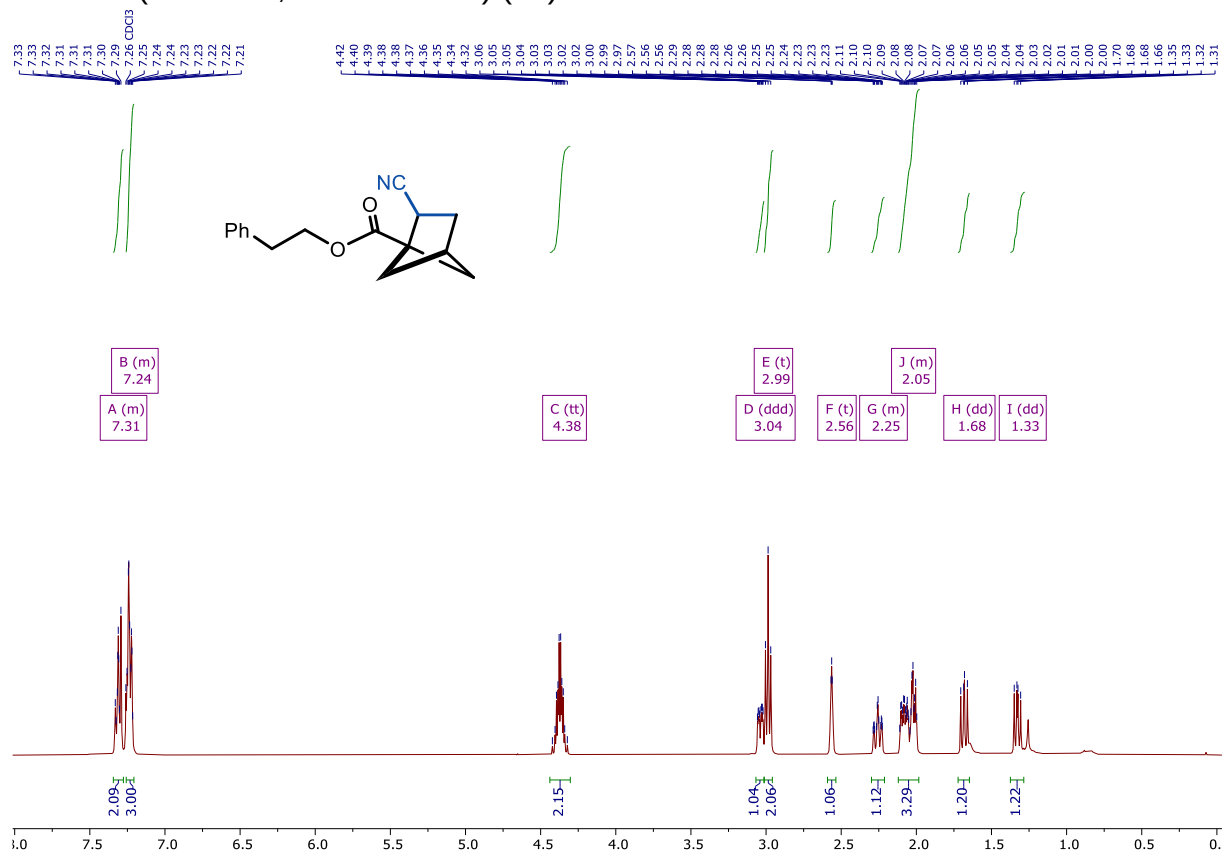


^{13}C NMR (101 MHz, Chloroform-*d*) (**18**):

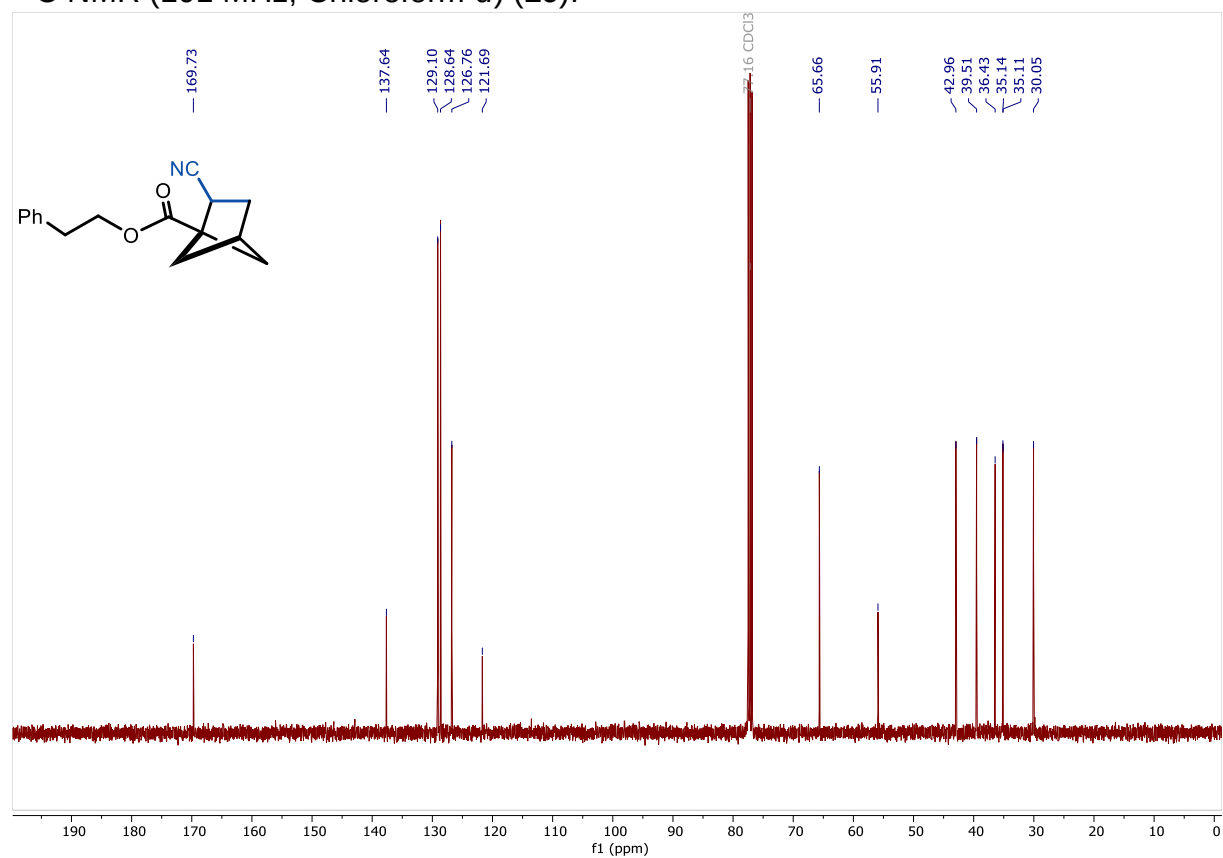


DEPT-135 NMR (101 MHz, Chloroform-*d*) (**18**):

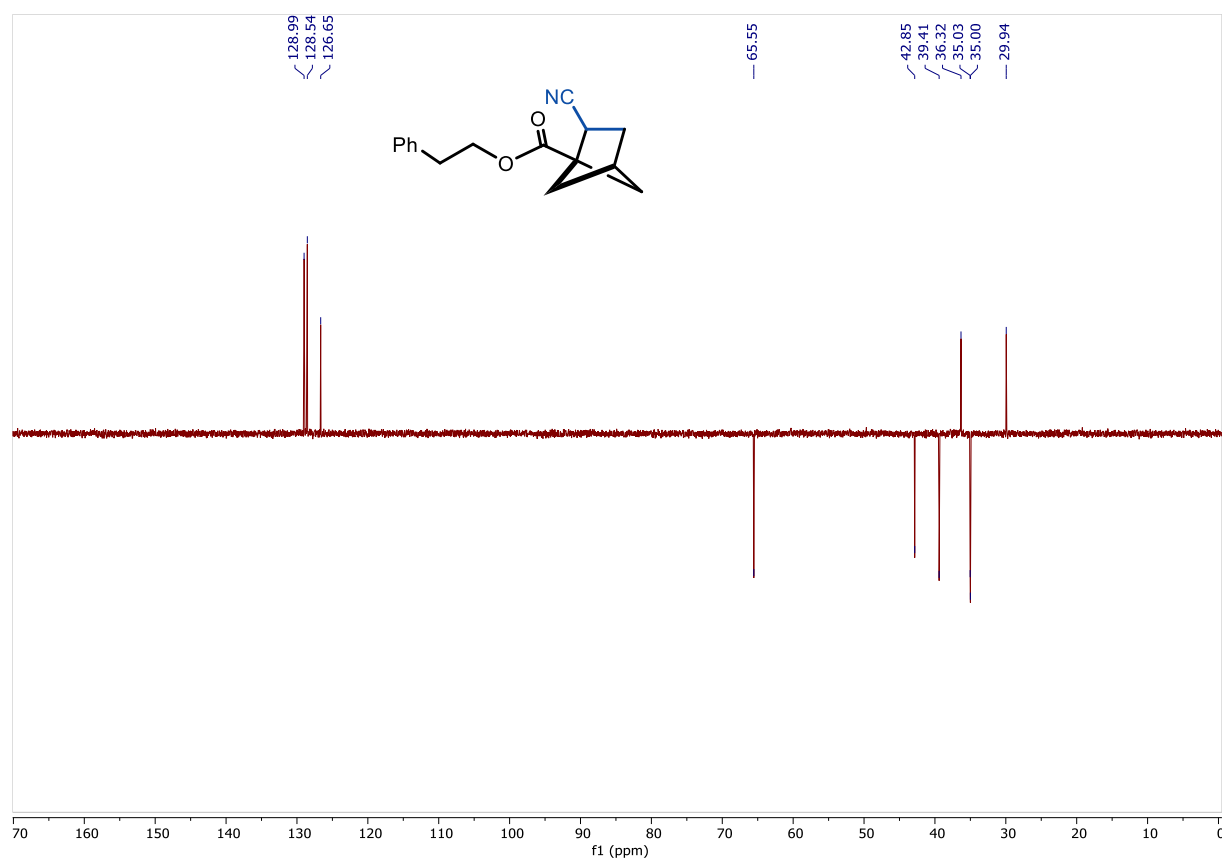


¹H NMR (400 MHz, Chloroform-*d*) (**19**):

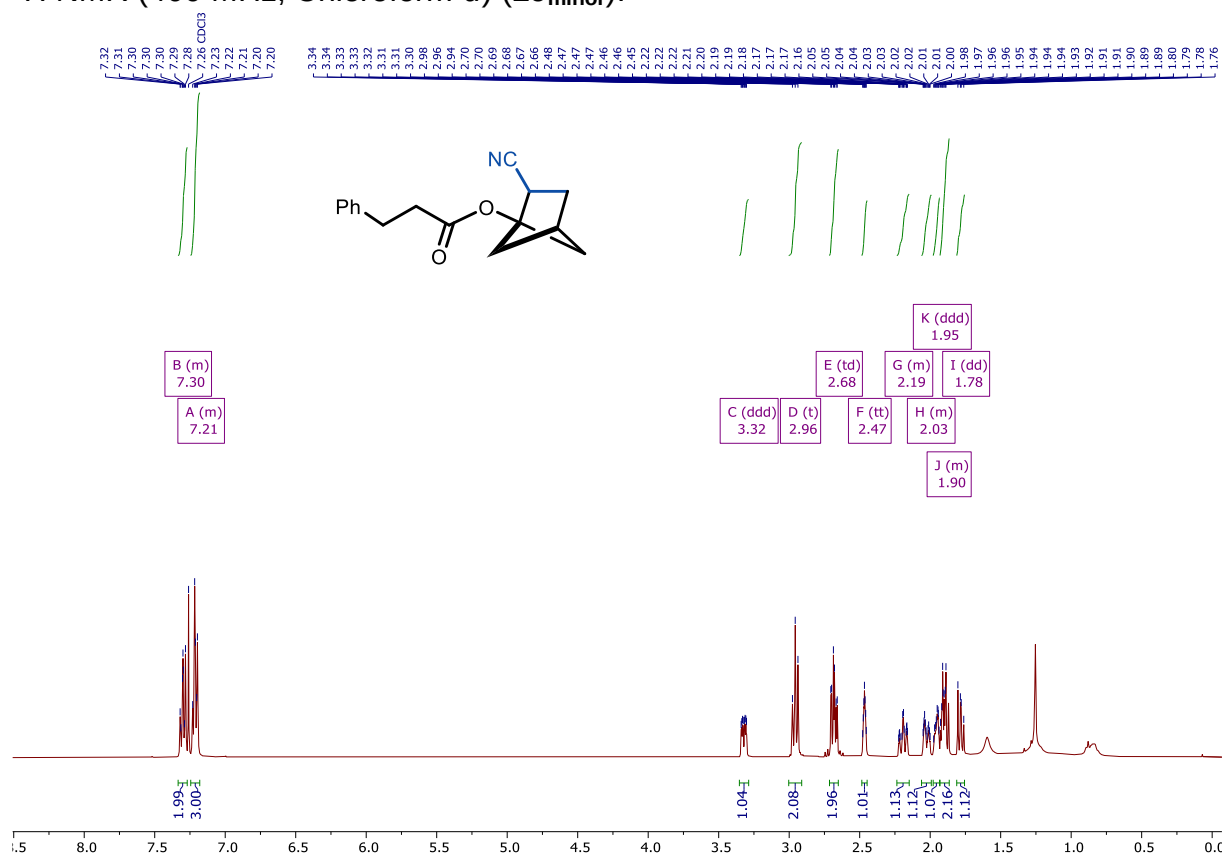
¹³C NMR (101 MHz, Chloroform-*d*) (**19**):



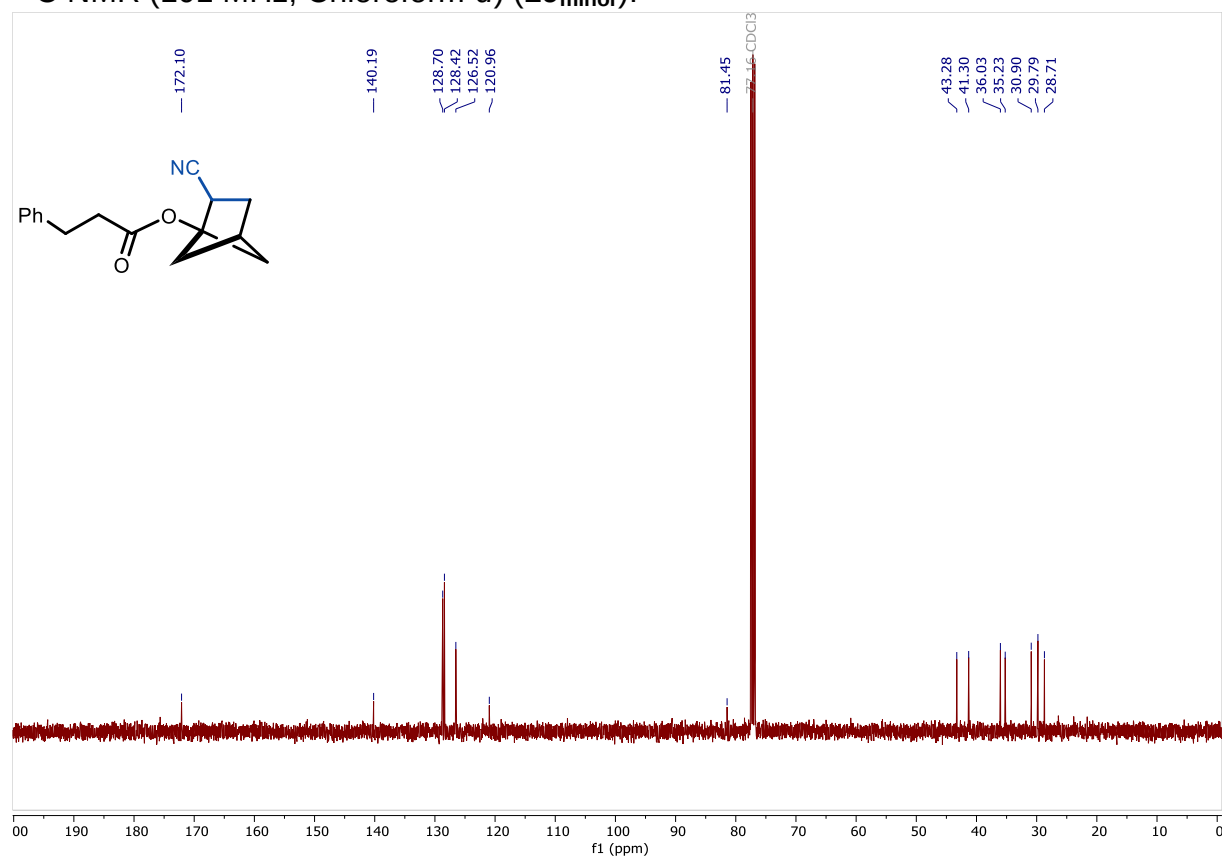
DEPT-135 NMR (101 MHz, Chloroform-*d*) (**19**):



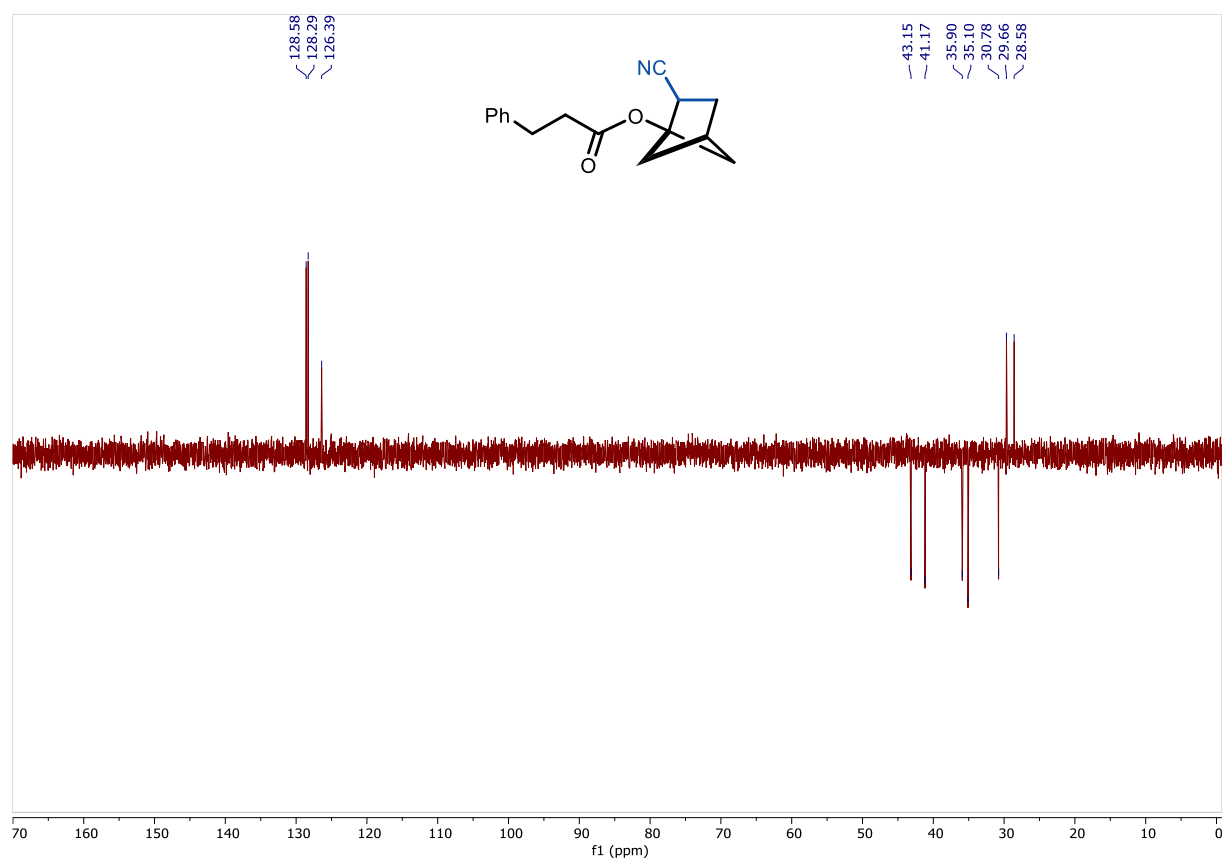
^1H NMR (400 MHz, Chloroform- d) (**19**_{minor}):



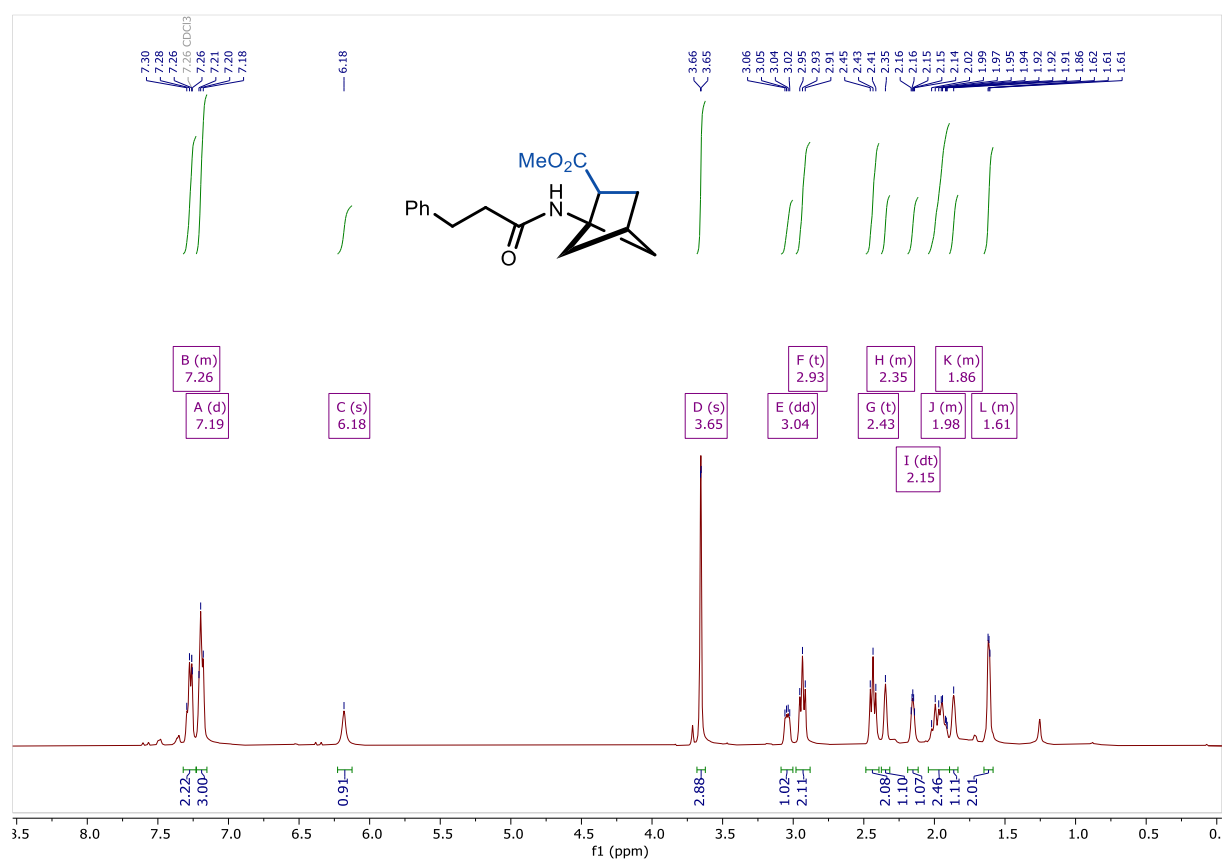
^{13}C NMR (101 MHz, Chloroform- d) (**19**_{minor}):



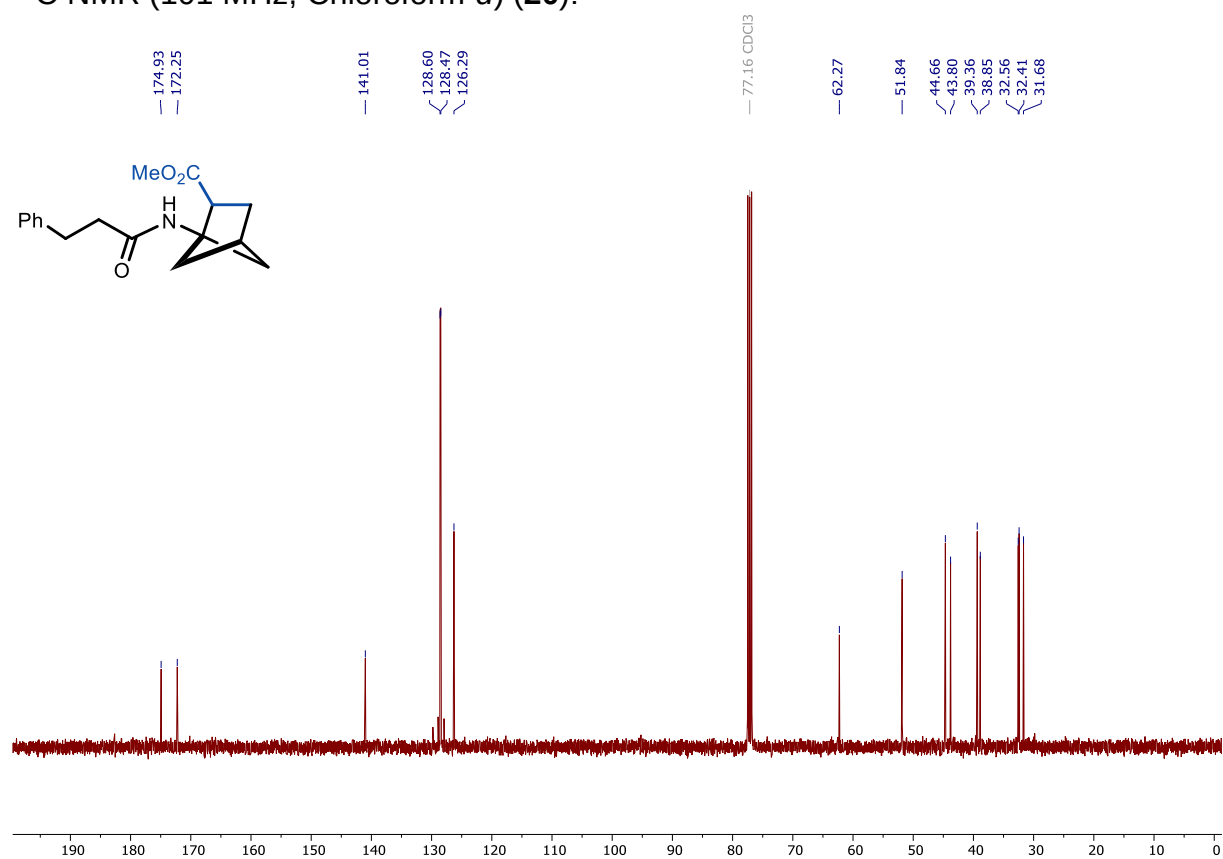
DEPT-135 NMR (101 MHz, Chloroform-*d*) (**19**_{minor}):



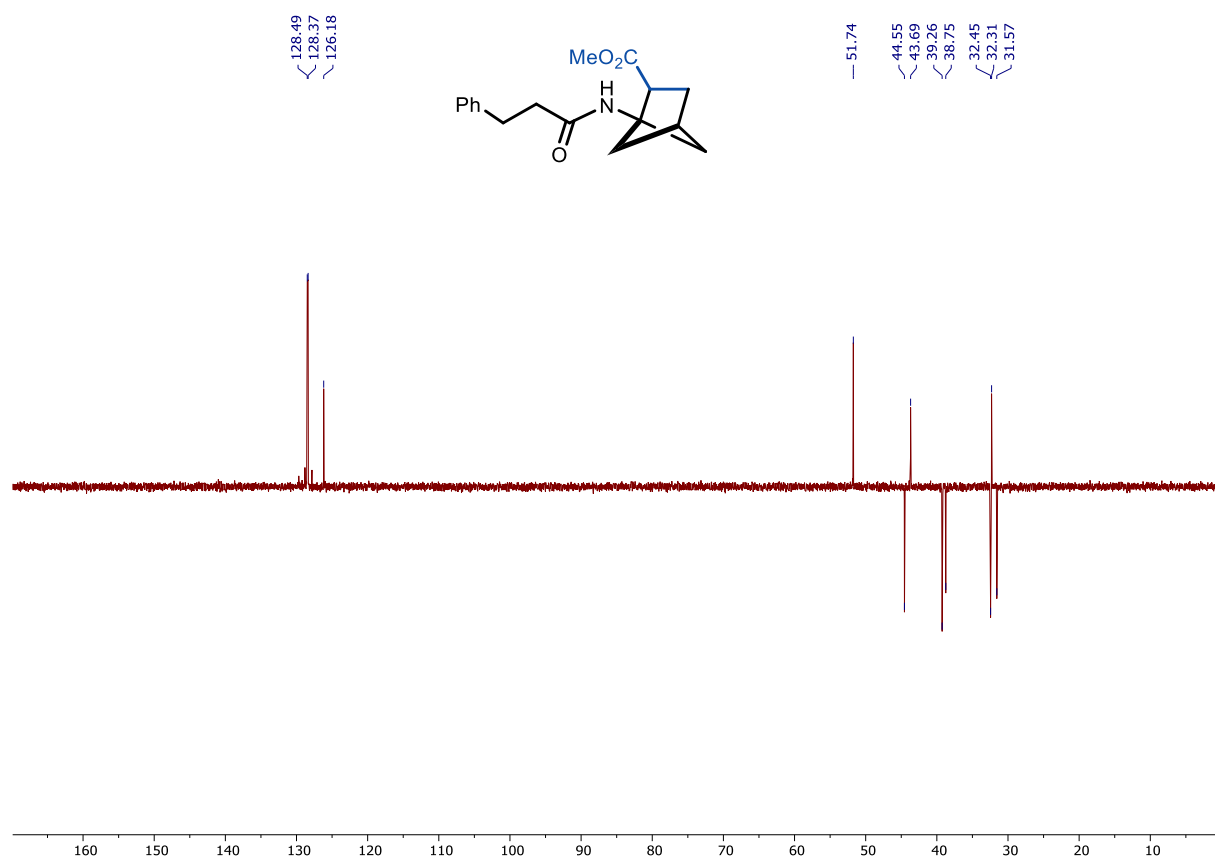
¹H NMR (400 MHz, Chloroform-*d*) (**20**):



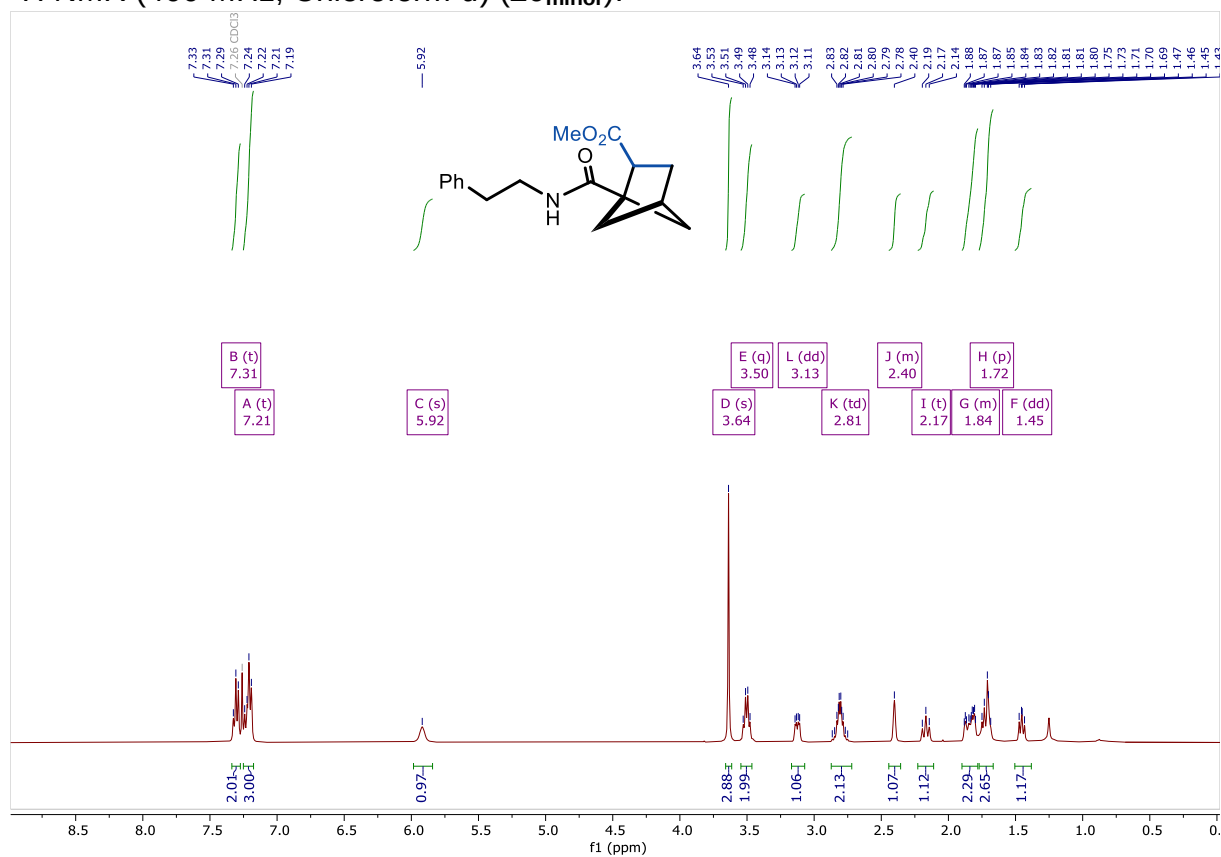
¹³C NMR (101 MHz, Chloroform-*d*) (**20**):



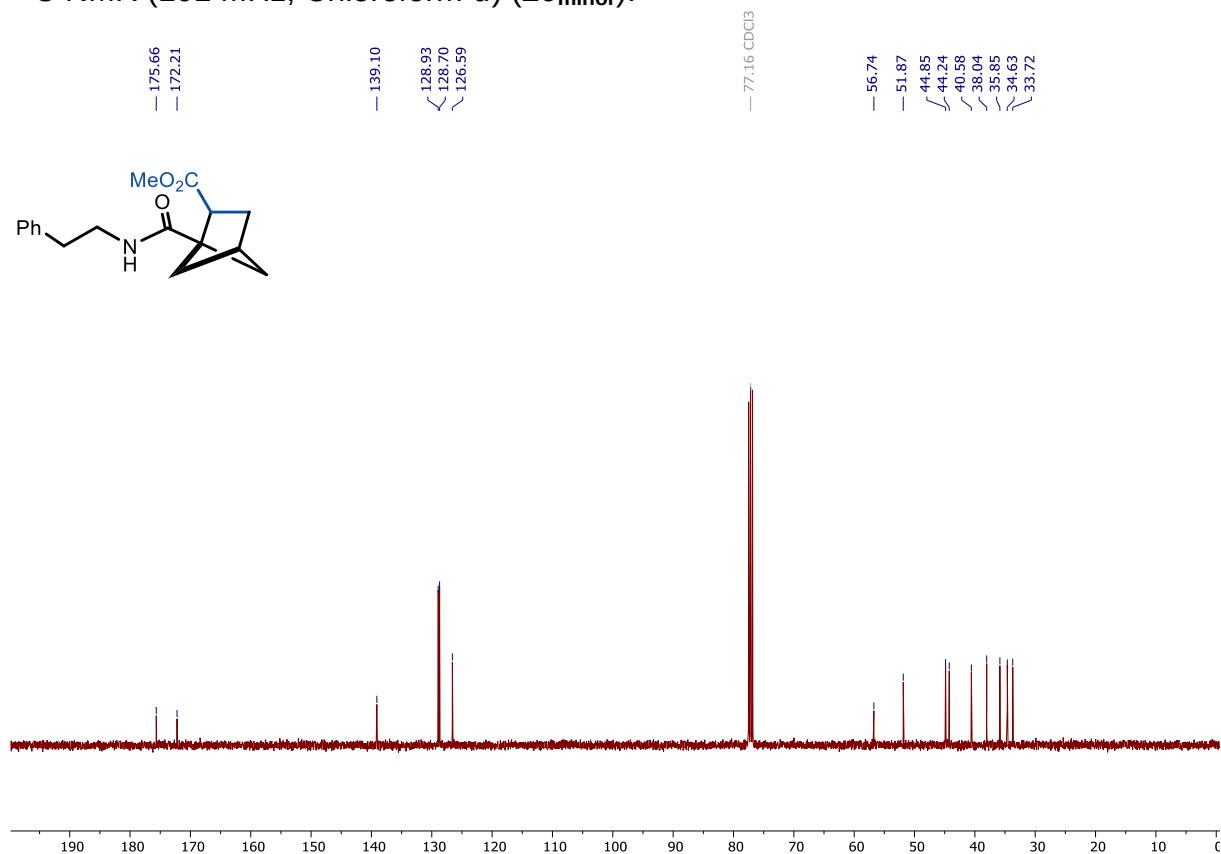
DEPT-135 NMR (101 MHz, Chloroform-*d*) (**20**):



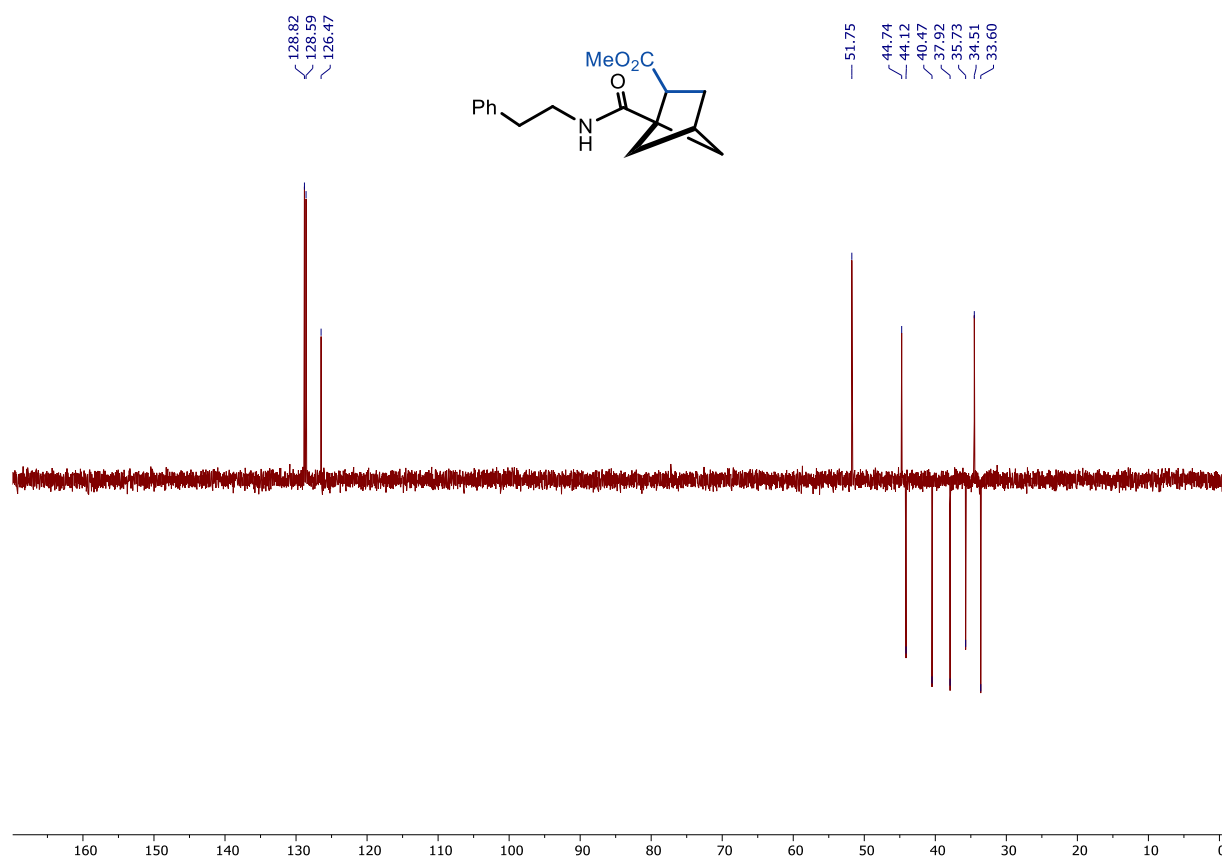
^1H NMR (400 MHz, Chloroform-*d*) (**20**_{minor}):



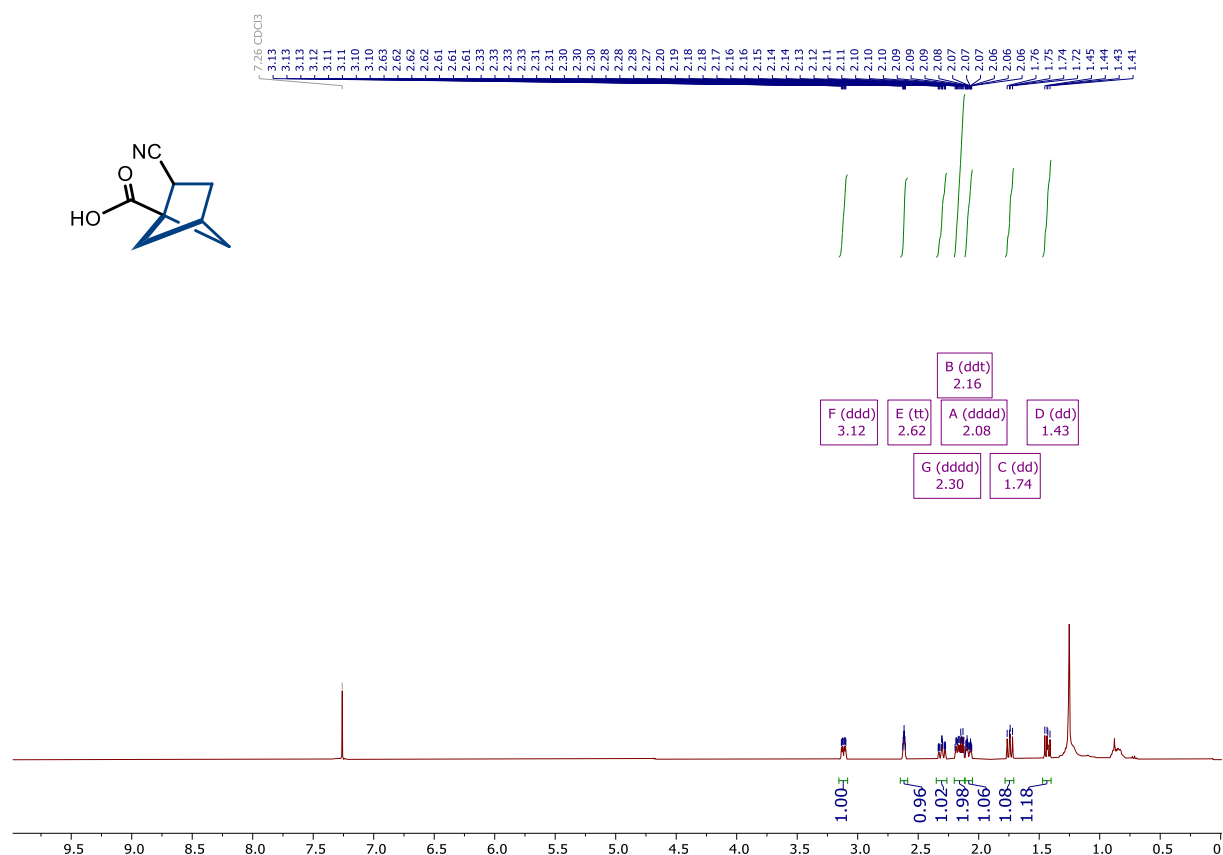
^{13}C NMR (101 MHz, Chloroform-*d*) (**20**_{minor}):



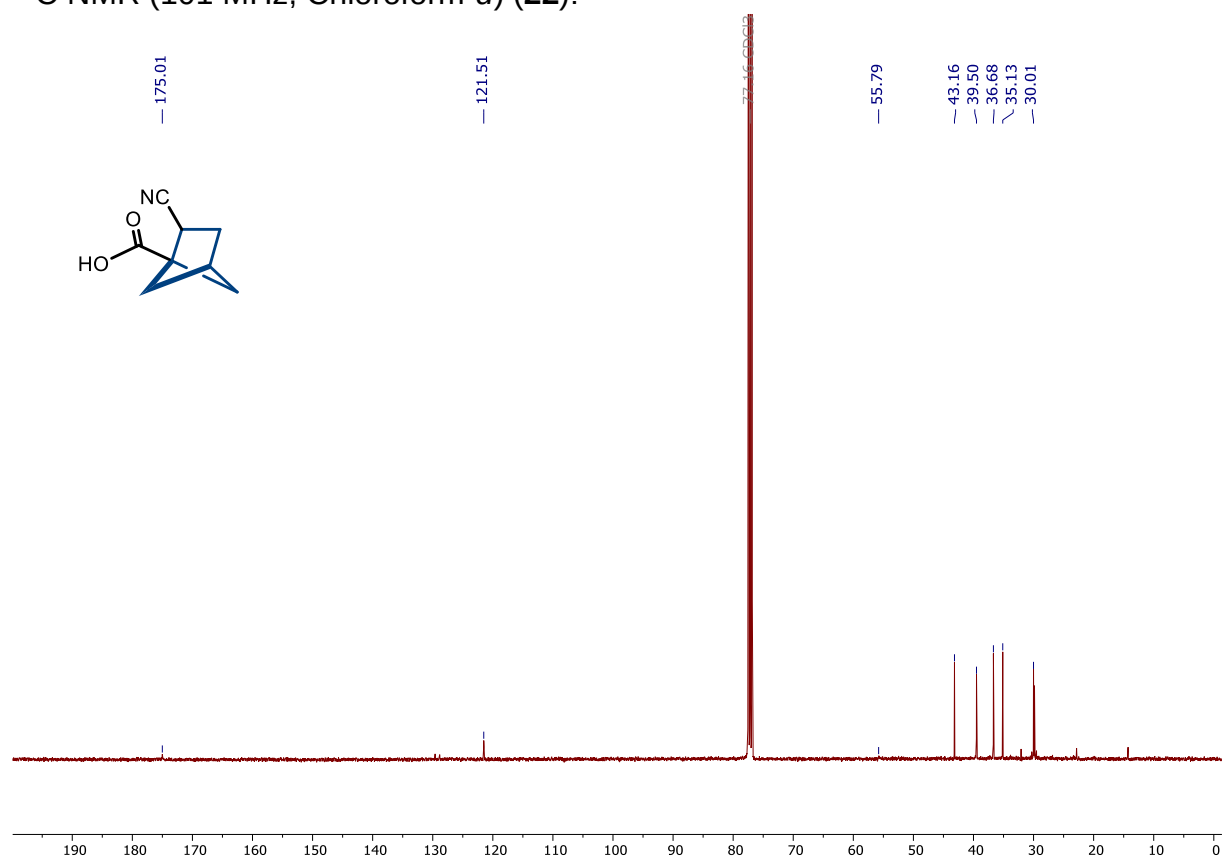
DEPT-135 NMR (101 MHz, Chloroform-*d*) (**20**_{minor}):



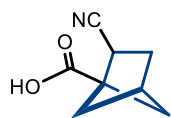
^1H NMR (400 MHz, Chloroform-*d*) (**22**):



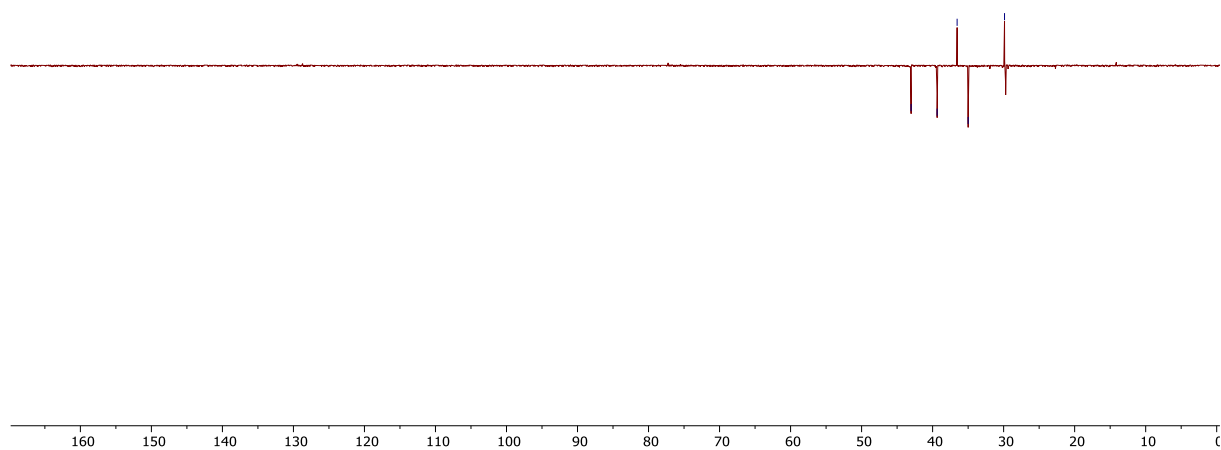
^{13}C NMR (101 MHz, Chloroform-*d*) (**22**):



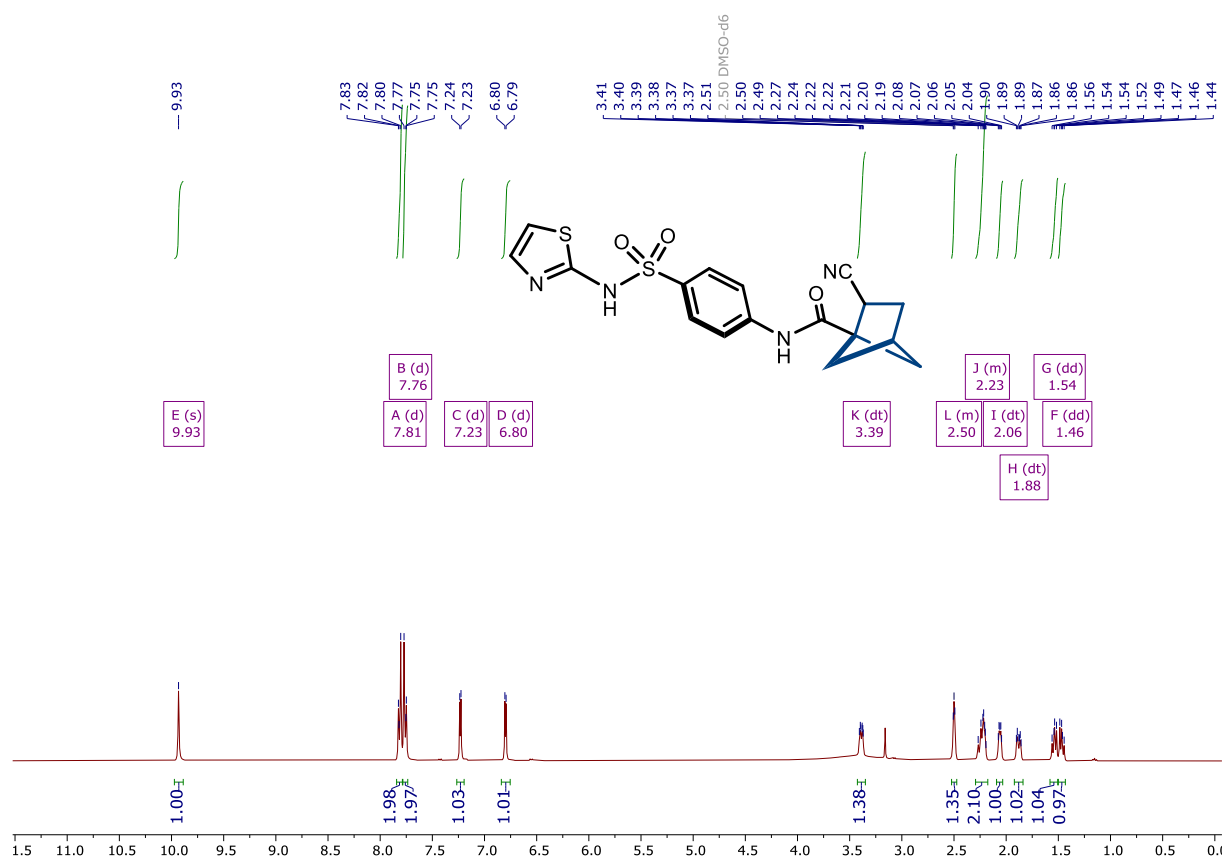
DEPT-135 NMR (101 MHz, Chloroform-*d*) (**22**):



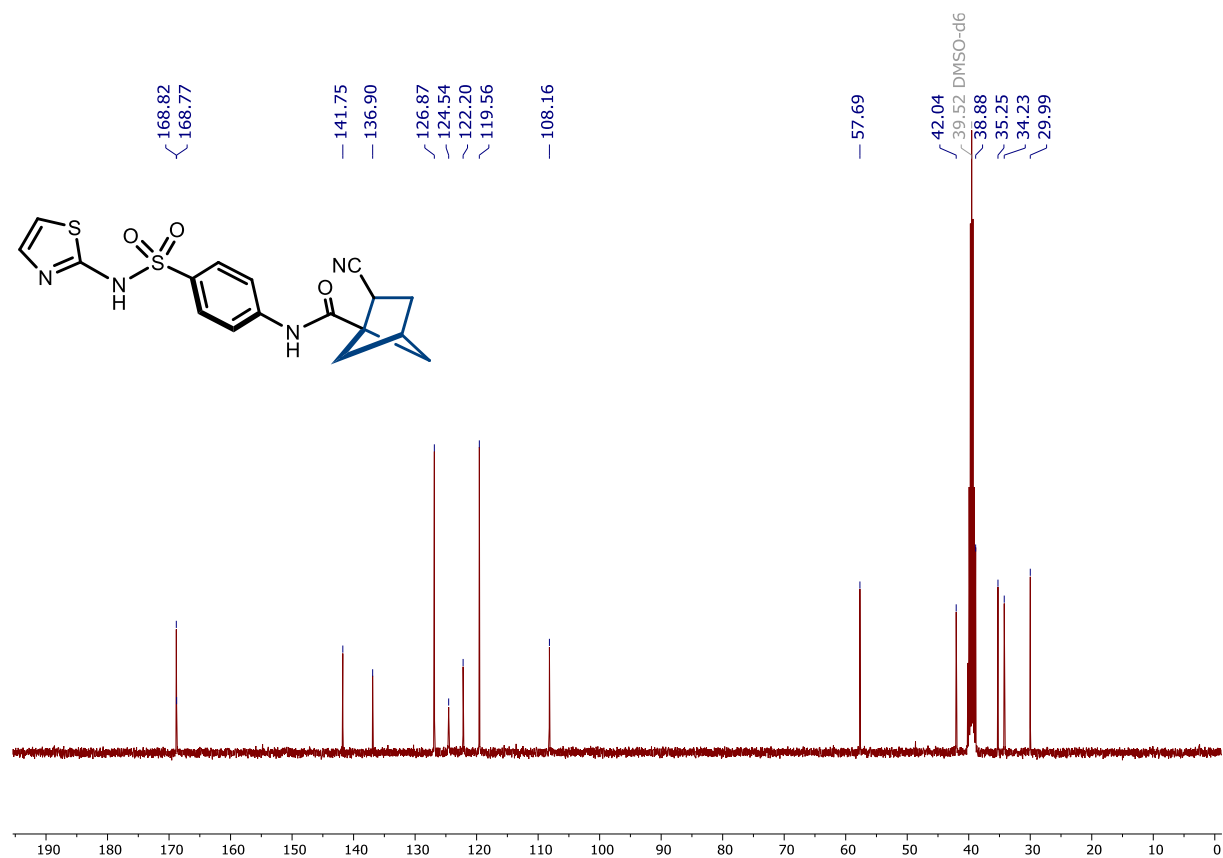
43.03
39.36
36.55
34.99
29.88



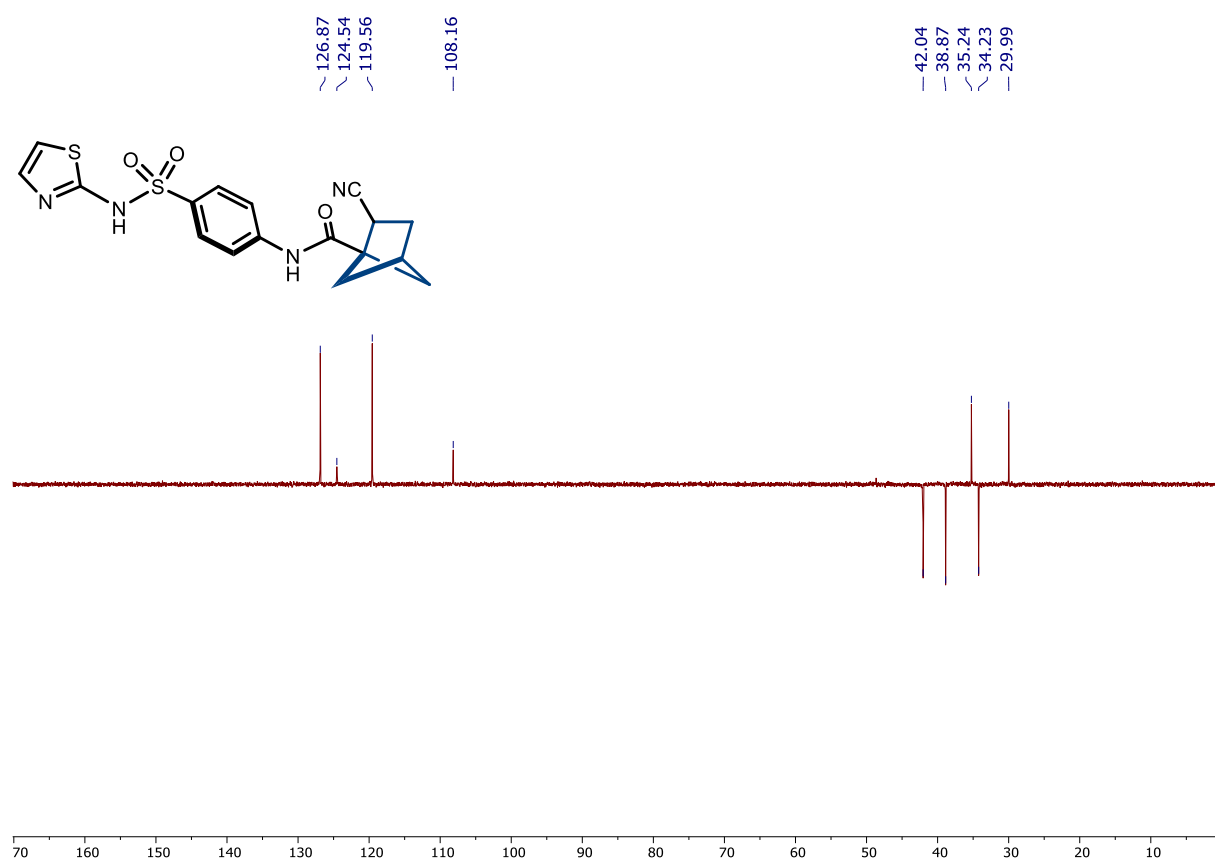
^1H NMR (400 MHz, $\text{DMSO}-d_6$) (**24**):



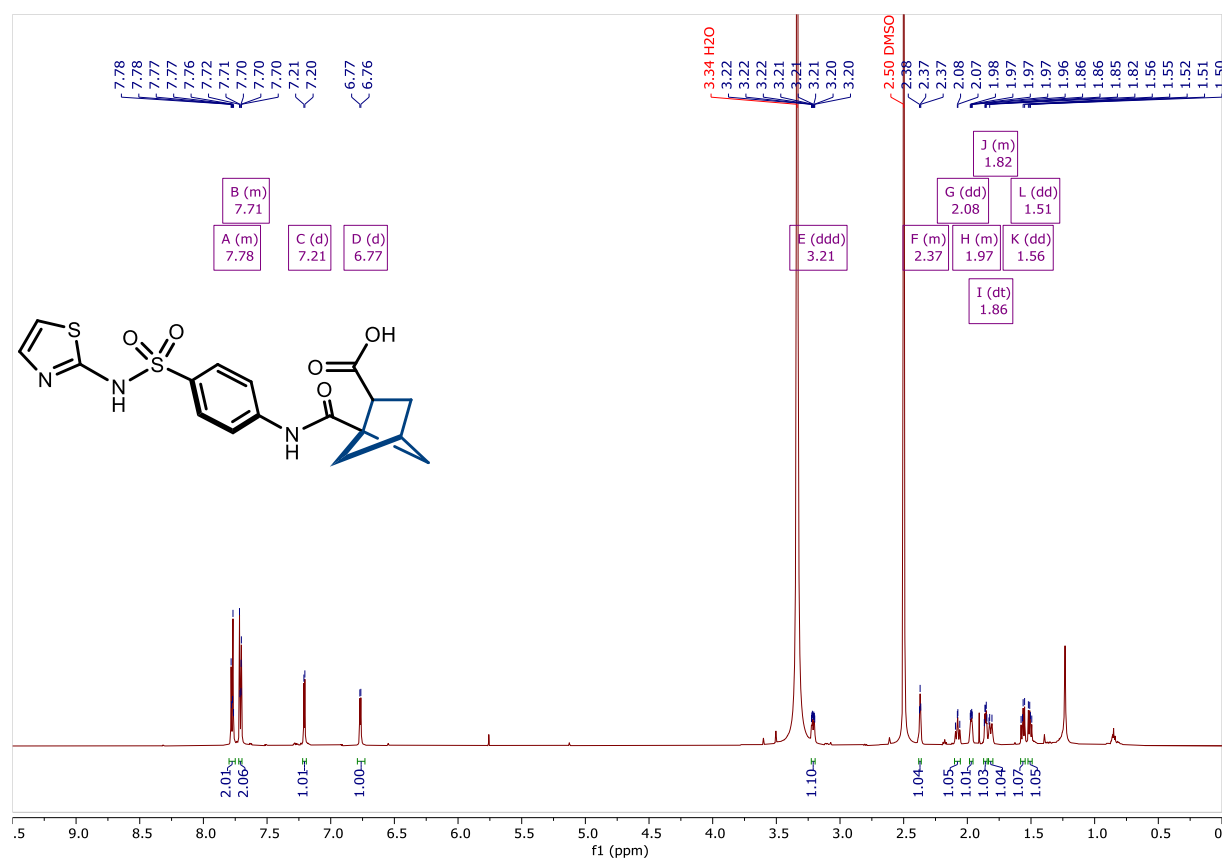
^{13}C NMR (101 MHz, $\text{DMSO}-d_6$) (**24**):



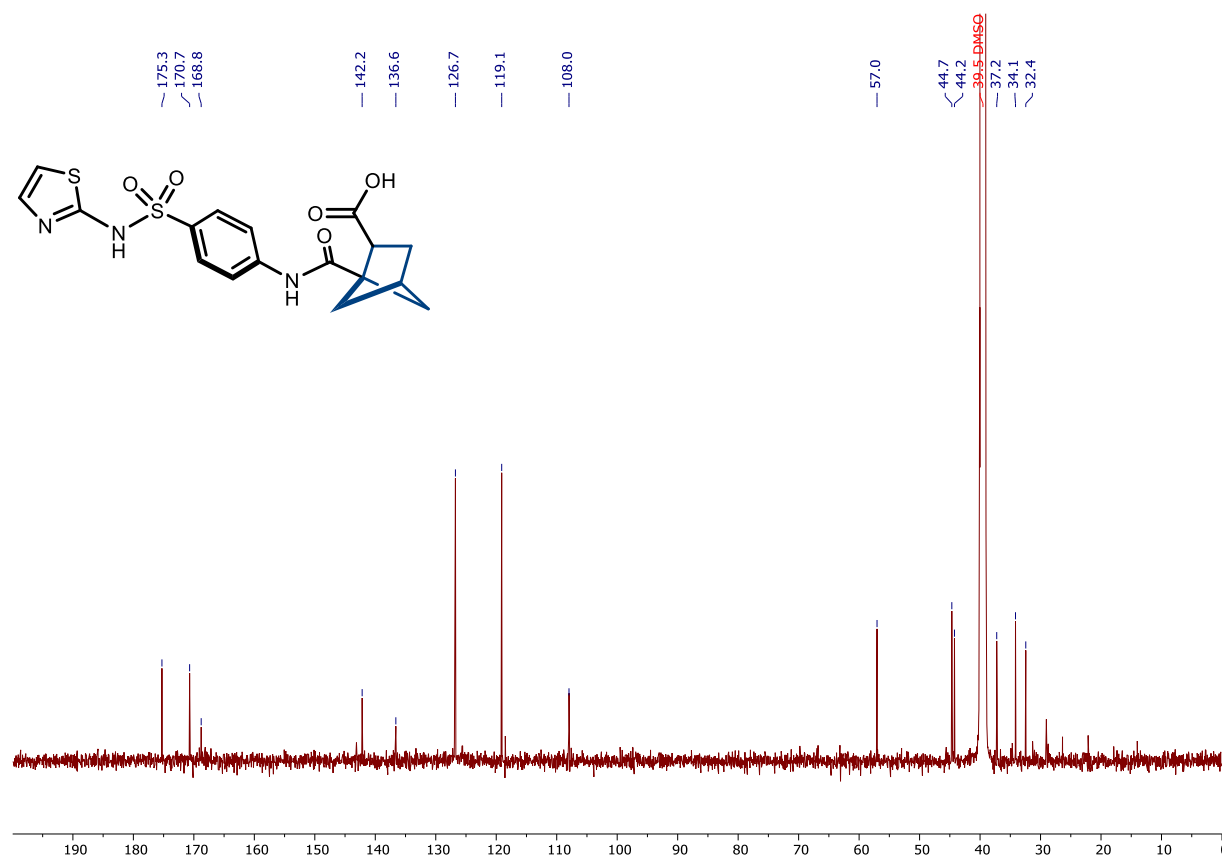
DEPT-135 NMR (101 MHz, DMSO-*d*₆) (**24**):

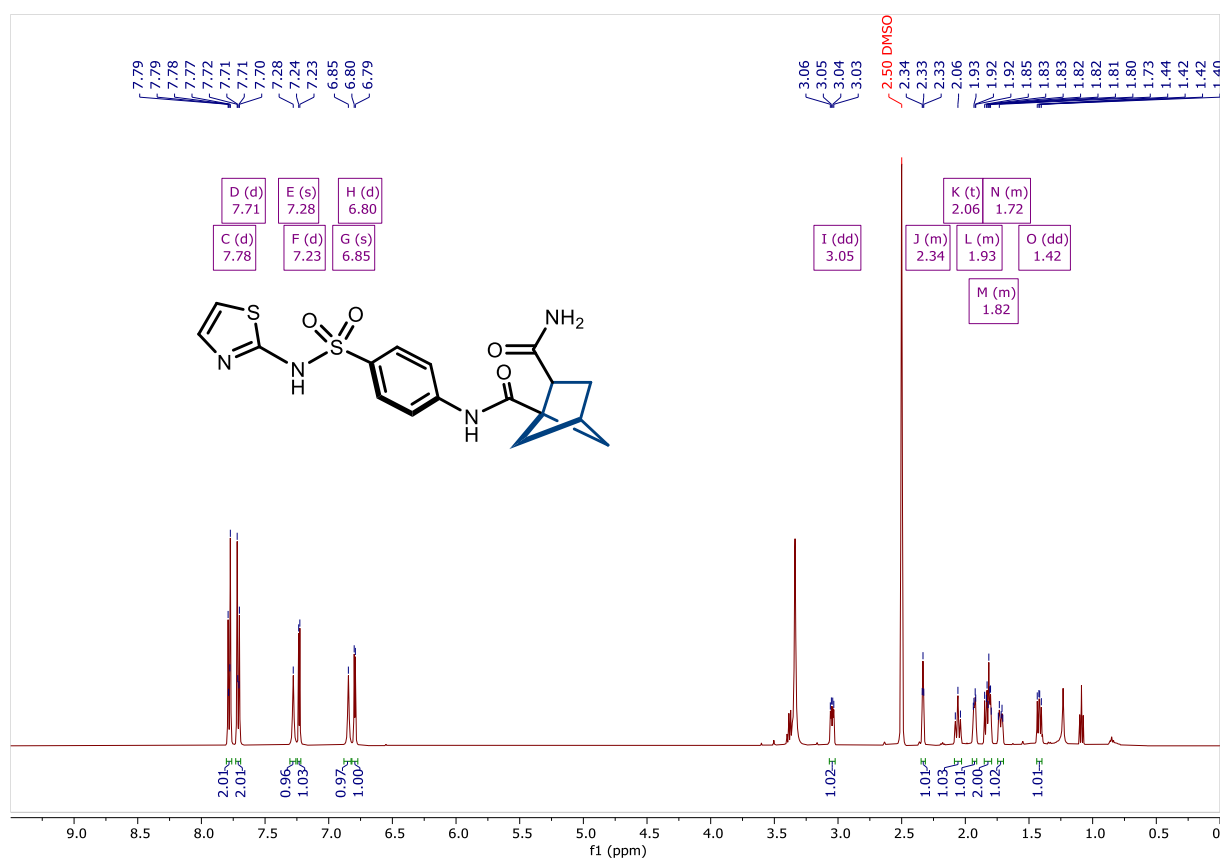


^1H NMR (600 MHz, $\text{DMSO}-d_6$) (**25**):



^{13}C NMR (151 MHz, $\text{DMSO}-d_6$) (**25**):



^1H NMR (600 MHz, DMSO- d_6) (**S14**):

¹³C NMR (151 MHz, DMSO-*d*₆) (**S14**):

