Supporting Information

Tin-Free Access to the ABC Core of the Calyciphylline A Alkaloids and Unexpected Formation of a D-Ring-Contracted Tetracyclic Core

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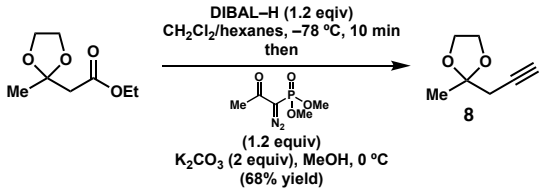
General Information. Unless otherwise specified, all commercially available reagents were purchased from Aldrich, Alfa Aesar, Acros Organics, or Oakwood Chemical and used without further purification. Anhydrous THF, Et_2O, PhH, PhMe, *n*-hexane, ACN, DMF, DMSO, DCM were passed through a commercial solvent purification system (2 columns of alumina) and used without further drying. Triethylamine, diisopropylamine, pyridine, and Hünig's base were distilled over CaH_2 immediately prior to use. Unless otherwise noted, all reactions were performed in flame-dried glassware under 1 atm of pre-purified anhydrous N_2 or Ar gas. All purifications were performed on SiliaFlash® P60 40-63μm (230-400 mesh) 60Å Irregular Silica Gels (SiliCycle cat. # R12030B) or on a Biotage Isolera IV flash purification system using SNAP cartridges (Biotage cat. # FSKO-1107-0XXX–depending on the size). Thin layer chromatography was performed using glass-backed SiliaPlate™ TLC Plates (SiliCycle cat. # TLG-R10011B-323) cut to the desired size. Products and reactants were then visualized with short-wave UV lamps and $KMnO_4$, CAM, PMA, or anisaldehyde stains prepared according to standard recipes.[1] All yields refer to chromatographically and spectroscopically pure products.^{1}H NMR spectra and ^{13}C NMR spectra were recorded on a Varian Mercury 400, Varian MR-400, Agilent MR-400, Varian V-500, or an Agilent DD2-600 MHz instrument with a multinuclear broadband probe at ambient temperature unless otherwise stated. Chemical shifts are reported in parts per million relative to residual solvent peaks.[2] All ^{13}C spectra are recorded with complete proton decoupling. High-resolution mass spectral analyses were performed by the Lumigen Instrument Center, Wayne State University on a Thermofisher scientific LTQ Orbittrap XL mass spectrometer. All spectra were acquired in positive ionization mode unless otherwise noted. The MS survey scan was set from 150 - 1000. The resolution was set to 60000. In all cases only one microscan was used in the analysis. IR data were obtained on a Varian/Digilab Excalibur 3100 High Resolution FT-IR or Shimadzu MIRacle 10 Single Reflection ATR Accessory, and optical rotation data was collected on a Perkin-Elmer 341 automated Polarimeter at the concentration noted.

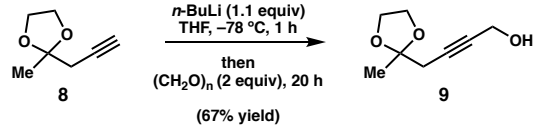
[1] Leonard, J.; Lygo, B.; Procter, G. In *Advanced Practical Organic Chemistry*; CRC Press: Boca Raton, FL, 2013; pp 158. (ISBN: 978-1-4398-6097-7)

[2]Fulmer, G. R.; Miller, A. J.; Sherdan, N. H.; Gottlieb, H. E.; Nudelman, A.; Stoltz, B. M.; Bercaw, J. E.; Goldberg, K. I. NMR Chemical Shifts of Trace Impurities: Common Laboratory Solvents, Organics, and Gases in Deuterated Solvents Relevant to the Organometallic Chemist. *Organometallics*, **2010**, *29*, 2176–2179.

Experimental Procedures and Spectroscopic Data



2-methyl-2-(prop-2-yn-1-yl)-1,3-dioxolane (alkyne 8).[3] To a cooled (–78 °C) solution of ethyl (2-methyl-1,3-dioxolan-2-yl)acetate (10 g, 57.41 mmol, 1 equiv) and DCM (140 mL) was added a solution of DIBAL–H (54.97 g, 68.89 mmol, 1.2 equiv) in hexanes (50 mL) dropwise via positive pressure cannulation. After 10 min, MeOH (25 mL) was added, the flask was opened to air, a solution of dimethyl (1-diazo-2-oxopropyl)phosphonate (13.23 g, 68.89, 1.2 equiv) in MeOH (25 mL) was added followed by K_2CO_3 (15.87 g, 114.8 mmol, 2 equiv), and the flask was placed in 0 °C bath. After 21 h, the reaction was quenched with water (140 mL), the layers were separated, the aqueous layer was extracted with DCM (3 x 100 mL), and the combined organic layers were dried over Na_2SO_4. The solvent was removed under reduced pressure and the crude material was purified by flash chromatography, eluted with 0–5% diethyl ether/pentane. The product was isolated as a light-yellow oil, 4.94 g (68% yield). Spectra are consistent with the literature report.[4]



4-(2-methyl-1,3-dioxolan-2-yl)but-2-yn-1-ol (propargylic alcohol 9). To a cooled (–78 °C) solution of 2-methyl-2-(prop-2-yn-1-yl)-1,3-dioxolane (**8**) (170.0 mg, 1.348 mmol, 1 equiv) in THF (2.2 mL) was added *n*-BuLi (2.3 M in hexanes, 0.645 mL, 1.482 mmol, 1.1 equiv) dropwise. After 1 h, paraformaldehyde (80.94 mg, 2.695 mmol, 2 equiv) was added and reaction was allowed to warm slowly to ambient temperature (24 ± 1 °C) in the dewar overnight. After 20 h, the reaction was quenched with ethyl acetate (5 mL) and water (5 mL). The layers were separated and the aqueous layer was extracted with ethyl acetate (3 x 15 mL). The combined organic layers were washed with brine and then dried over $MgSO_4$. The solvent was removed under reduced pressure and the material was purified by flash chromatography, eluted with ethyl acetate/hexanes (0-60%). The product was isolated as a yellow oil, 138 mg (67% yield). R_f = 0.27 (40% ethyl acetate/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.27 (t, J = 2.18 Hz, 2H), 4.00 (m, 4H), 2.57 (t, J = 2.12 Hz, 2H), 1.46 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 108.69, 81.78, 80.39, 65.22, 51.36, 30.27, 23.87; IR neat 3418, 2986, 2886, 1443, 1381, 1211, 1142, 1096, 1042, 1011, 910, 748 cm^{-1}; HRMS $[M+Na]^+$ m/z ESI calc'd for $[C_8H_{12}O_3Na]^+$ = 179.0679, observed: 179.0674.

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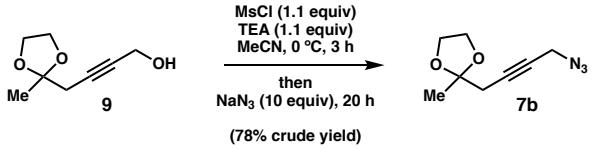
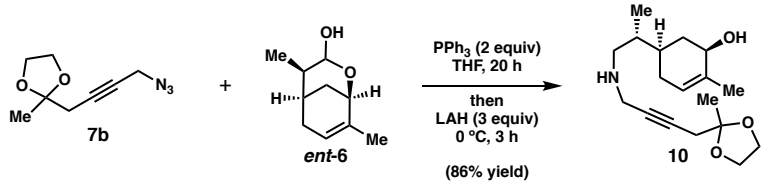
[3] Modified from Dickson, H. D.; Smith, S. C.; Hinkle, K. W. A convenient scalable one-pot conversion of esters and Weinreb amides to terminal alkynes. *Tetrahedron Lett.* **2004**, *45*, 5597–5599.

[4] Spectra for **8** matches specta reported in: Yamasaki, R.; Sotome, I.; Komagawa, S.; Azumaya, I.; Masu, H.; Saito, S. Ni-catalyzed [3+2+2] cycloaddition of ethyl cyclopropylideneacetate and 1,3-diynes. Applications to the three-component cyclozaddition. *Tetrahedron Lett.* **2009**, *50*, 1143–1145.



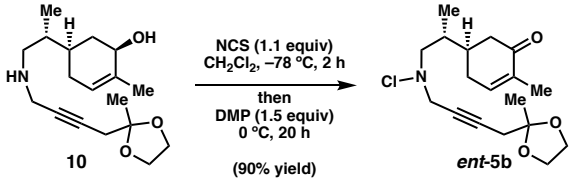
2-(4-azidobut-2-yn-1-yl)-2-methyl-1,3-dioxolane (propargylic azide 7b). To a cooled (0 °C) solution of 4-(2-methyl-1,3-dioxolan-2-yl)but-2-yn-1-ol (**9**) (248.9 mg, 1.590 mmol, 1 equiv) in ACN (3.2 mL) was added MsCl (184.0 mg, 1.606 mmol, 1.1 equiv) and TEA (162.5 mg, 1.606 mmol, 1.1 equiv). The reaction was allowed to warm to ambient temperature (24 ± 1 ° C) over 3 h. After 3 h, sodium azide (2.297 g, 35.33 mmol, 10 equiv) was added and the solution was stirred overnight. **CAUTION:** AZIDES ARE EXPLOSIVE AND SHOULD BE HANDLED IN A FUME HOOD BEHIND A BLAST SHIELD. After 20 h, the reaction was quenched with water (20 mL), the layers were separated, and the aqueous later was extracted with diethyl ether (8 x 10 mL). The combined organic layers were washed with brine and dried over $MgSO_4$ and the solvent was removed under reduced pressure. The resulting red-orange liquid, 225.2 mg (78% crude yield), was used without further purification. R_f = 0.65 (30% ethyl acetate/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.00 (m, 4H), 3.92 (s, 2H), 2.62 (t, J = 2.17 Hz, 2H), 1.47 (s, 3 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 108.37, 83.70, 73.91, 65.14, 40.26, 30.09, 23.79; IR neat 2986, 2091, 1381, 1242, 1211, 1142, 949, 880, 833, 756 cm^{-1}; HRMS [2M+H$^+$] m/z ESI calc'd for $[C_{16}H_{23}N_6O_4]^+$: 363.1775 observed: 363.1765.



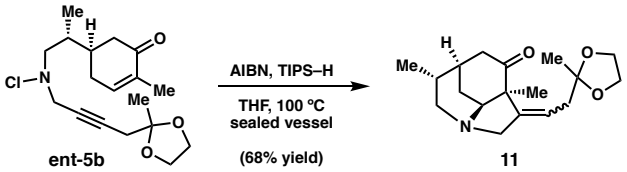
(1*R*,5*R*)-2-methyl-5-((*R*)-1-((4-(2-methyl-1,3-dioxolan-2-yl)but-2-yn-1-yl)amino)propan-2-yl)-cyclohex-2-en-1-ol (allylic alcohol 10). To a solution of (1*R*,4*R*,5*R*)-4,8-dimethyl-2-oxabicyclo[3.3.1]non-7-en-3-ol (***ent*-6**)[5] (1.160 g, 6.91 mmol, 1 equiv) and 2-(4-azidobut-2-yn-1-yl)-2-methyl-1,3-dioxolane (**7b**) (1.313 g, 7.250 mmol, 1.05 equiv) in THF (27.6 mL) was added PPh_3 (3.622 g, 13.81 mmol, 2 equiv) and the reaction was stirred overnight. After 20 h, the reaction was cooled to 0 ºC and LAH (786.0 mg, 20.71 mmol, 3 equiv) was added in 3 equal portions every 15 min. After 3 h, the LAH quenched with ethyl acetate (10 mL, dropwise) and a saturated solution of potassium sodium tartrate was added slowly (20 mL). The resulting suspension was allowed to stir for 3 h. The layers were separated and aqueous layer extracted with DCM (5 x 20 mL). The combined organic layers were dried over Na_2SO_4 and the solvent was removed under reduced pressure. To the crude material was added hexane (10 mL) and the mixture was heated to 70 ºC for 30 min. After 30 min, the flask sealed stored in the –30 ºC freezer overnight. After 16 h, the solids were filtered with hexane and solvent was removed under reduced pressure. The crude material was purified by flash chromatography in a 50 g Biotage SNAP column packed with SiO_2 and eluted with 0–10% MeOH/DCM. The product was isolated as a yellow oil, 1.830 g (86% yield). R_f = 0.22 (7% MeOH/DCM); ^{1}H NMR (400 MHz,

[5] Compound ***ent*-6** was previously reported in Ibrahim, A. A.; Golonka, A. N.; Lopez, A. M.; Stockdill, J. L. *Org. Lett.* **2014**, *16*, 1072–1075.

$CDCl_3$) δ 5.47 (bs, 1H), 4.17 (bs, 1H), 3.99 (m, 4H), 3.41 (t, *J* = 2.09 Hz, 2H), 2.70 (dd, *J* = 11.50, 5.63, 1H), 2.53 (m, 3H), 2.09 (m, 1H), 1.89 (m, 2H), 1.89 (m, 1H) 1.71 (m, 4H), 1.49 (m, 8H), 1.22 (td, *J* = 12.24, 10.31 Hz, 1H), 0.92 (d, *J* = 6.84 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 136.54, 124.30, 108.83, 80.16, 79.19, 71.33, 65.21, 52.60, 39.02, 37.35, 36.37, 35.95, 30.28, 23.89, 18.93, 14.96. IR neat 2970, 2886, 1450, 1381, 1211, 1150, 1049, 910 cm^{-1}; $[\alpha]_D^{22}$ –10.1 (c 0.215, $CHCl_3$); HRMS [M+H$^+$] m/z ESI calc'd for $[C_{18}H_{30}NO_3]^+$: 308.2226 observed: 308.2209.

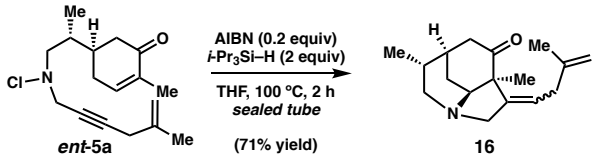


(*R*)-5-((*R*)-1-(chloro(4-(2-methyl-1,3-dioxolan-2-yl)but-2-yn-1-yl)amino)propan-2-yl)-2 methylcyclohex-2-en-1-one (*N*-chloroamine *ent*-5b). To a cooled (–78 °C) solution of (1*R*,5*R*)-2-methyl-5-((*R*)-1-((4-(2-methyl-1,3-dioxolan-2-yl)but-2-yn-1-yl)amino)propan-2-yl)-cyclohex-2-en-1-ol (**10**) (132.0 mg, 0.430 mmol, 1 equiv) in DCM (2.2 mL) was added NCS (63.2 mg, 0.473 mmol, 1.1 equiv). The reaction was allowed to warm to 0 °C slowly in the acetone/dry ice bath over 2 h. After 2 h, DMP (273.5 mg, 0.645 mmol, 1.5 equiv) was added. For this addition, the flask was temporarily opened to air and then it was sealed with a glass stopper. The apparatus was covered in aluminum foil and stirred overnight. After 20 h, the mixture was diluted with hexane (1 mL) and loaded onto a plug of SiO_2. The pure product was eluted with 0-30% ethyl acetate/hexane. The product was isolated as a colorless oil,132.0 mg (90% yield). R_f = 0.64 (40% ethyl acetate/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.75 (dd, *J* = 4.56, 2.67 Hz, 1H), 4.00 (m, 4H), 3.80 (q, *J* = 1.86 Hz, 2H), 2.96 (dd, *J* = 13.05, 6.83 Hz, 1H), 2.75 (dd, *J* = 13.04, 7.06 Hz, 1H), 2.59 (m, 2H), 2.42 (m, 1H), 2.22 (m, 4H), 1.95 (ddt, *J* = 9.80, 6.84, 2.90 Hz, 1H), 1.77 (q, *J* = 1.69 Hz, 3H), 1.48 (s, 3H), 0.93 (d, *J* = 6.88 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 145.36, 135.60, 108.74, 83.20, 75.84, 65.71, 65.29, 53.80, 40.26, 37.81, 35.26, 30.59, 30.32, 24.06, 15.86, 14.14; IR neat 3017, 1721, 1667, 1381, 1211, 1134, 1103, 1049, 748 cm^{-1}; $[\alpha]_D^{22}$ –15.2 (c 0.0025, $CHCl_3$); HRMS [M+H$^+$] m/z ESI calc'd for $[C_{18}H_{27}NO_3Cl]^+$: 340.1679 observed: 340.1661.



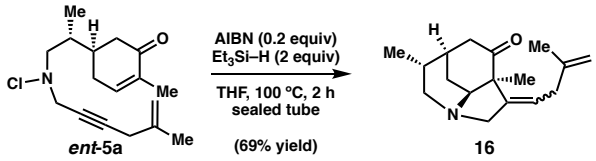
(3a*S*,6*R*,7a*S*,8*R*)-3a,8-dimethyl-3-(2-(2-methyl-1,3-dioxolan-2-yl)ethylidene)hexahydro-6,1-ethanoindol-4(2*H*)-one (tricycle 11). To a Biotage microwave vial was added (*R*)-5-((*R*)-1-(chloro(4-(2-methyl-1,3-dioxolan-2-yl)but-2-yn-1-yl)amino)propan-2-yl)-2-methylcyclohex-2-en-1-one (***ent*-5b**) (49.0 mg, 0.144 mmol, 1 equiv), THF (16 mL), AIBN (4.7 mg, 0.029 mmol, 0.2 equiv), and *i*-Pr_3Si–H (45.7 mg, 0.288 mmol, 2 equiv). The vial was sealed and placed in an oil bath preheated to 100 °C and the solution was stirred for 2 h. **CAUTION:** REACTIONS UNDER PRESSURE SHOULD BE HANDLED IN A FUME HOOD BEHIND A BLAST SHIELD. After 2 h, the solution was allowed to cool to ambient temperature (24 ± 1 °C), then it was transferred to a

round bottom flask, and the solvent removed under reduced pressure. The crude material was dissolved in PhH (3 mL) and the solution was purified on basic alumina. The product was eluted with 0-60% ethyl acetate/hexane. The product was isolated as a yellow oil, 30.0 mg (68% yield). R_f = 0.25 (10% MeOH/ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.82 (ddt, *J* = 7.66, 5.59, 2.62 Hz, 1H), 5.62 (t, *J* = 7.09 Hz, 1H), 3.95 (m, 7H), 3.58 (dd, *J* = 46.93, 15.14 Hz 2H), 3.31 (d, *J* = 15.42 Hz, 1H), 3.12 (d, *J* = 15.22, 1H), 3.09 (s, 1H), 2.93 (dd, *J* = 15.24, 6.88 Hz, 1H), 2.81 (dd, *J* = 15.41, 7.88 Hz, 1H) 2.63 (m, 4H), 2.38 (m, 1H), 2.23 (dd, *J* = 13.21, 4.31 Hz, 1H), 2.06 (s, 1H), 1.90 (s, 1H), 1.85 (m, 3H), 1.41 (s, 2H), 1.37 (s, 2H), 1.34 (s, 3H), 1.27 (d, *J* = 7.09 Hz, 6H), 1.25 (d, *J* = 2.39 Hz, 7H), 0.85 (m, 5H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 215.25, 212.96, 124.87, 108.76, 80.66, 78.61, 77.36, 65.21, 65.17, 64.83, 60.18, 60.07, 50.31, 50.16, 49.13, 47.42, 45.22, 44.88, 41.74, 36.34, 34.53, 34.07, 33.79, 32.03, 30.41, 30.24, 29.81, 29.47, 28.34, 27.62, 23.94, 23.91, 23.36, 22.80, 20.18, 19.66, 17.90, 15.80, 14.30, 14.24; IR neat 3017, 2886, 1721, 1667, 1435, 1381, 1211, 1150, 1103, 1049, 748 cm^{-1}; HRMS [M+H$^+$] m/z ESI calc'd for $[C_{18}H_{28}NO_3]^+$: 306.2064 observed: 306.2069.

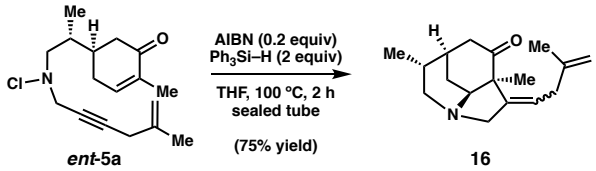


(3a*S*,6*R*,7a*S*,8*R*)-3a,8-dimethyl-3-(3-methylbut-3-en-1-ylidene)hexahydro-6,1-ethanoindol-4(2*H*)-one (tricycle 16).[6] To a Biotage microwave vial was added (*R*)-5-((*R*)-1-(chloro(5-methylhex-5-en-2-yn-1-yl)amino)propan-2-yl)-2-methylcyclohex-2-en-1-one (***ent*-5a**) (27.9 mg, 0.095 mmol, 1 equiv), THF (10.6 mL), AIBN (3.1 mg, 0.019 mmol, 0.2 equiv), and *i*-Pr_3Si–H (30.1 mg, 0.190 mmol, 2 equiv). The vial was sealed and placed in an oil bath preheated to 100 ºC and the solution was stirred for 2 h. **CAUTION:** REACTIONS UNDER PRESSURE SHOULD BE HANDLED IN A FUME HOOD BEHIND A BLAST SHIELD. After 2 h, the solution was allowed to cool to ambient temperature (24 ± 1 ºC), then it was transferred to a round bottom flask, and the solvent removed under reduced pressure. The crude material was purified by flash chromatography in a 10 g Biotage SNAP column packed with SiO_2 and eluted with 0-10% MeOH/DCM. The product was isolated as a yellow oil, 17.0 mg (71% yield). R_f = 0.30 (5% methanol/methylene chloride); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.84 (ddd, *J* = 7.68, 5.48, 2.22 Hz, 1H), 5.62 (t, *J* = 7.66 Hz, 1H), 4.71 (t, *J* = 11.53 Hz, 4H), 3.75 (d, *J* = 13.07 Hz, 1H), 3.62 (d, *J* = 15.65 Hz, 1H), 3.34–3.06 (m, 6H), 2.78–2.62 (m, 5H), 2.49–2.37 (m, 5H), 2.29 (dd, *J* = 13.46, 4.44 Hz, 1H), 2.09 (s, 2H), 1.95–1.81 (m, 5H), 1.76 (s, 3H), 1.71 (s, 3H), 1.42 (s, 3H), 1.33–1.22 (m, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 211.70, 211.04, 145.13, 143.61, 140.46, 135.39, 126.86, 126.03, 110.68, 110.32, 67.27, 65.69, 61.35, 57.37, 55.49, 54.96, 50.59, 49.91, 46.08, 45.59, 37.70, 37.24, 33.24, 33.14, 32.85, 29.68, 23.37, 22.90, 22.64, 21.92, 20.43, 20.36, 18.40, 18.27; IR neat 3077.9, 2958.2, 2929.2, 2901.0, 1702.4, 1674.8, 1448.6, 1375.9 cm^{-1}; HRMS [M+H$^+$] m/z ESI calc'd for $[C_{17}H_{26}NO]^+$: 260.2009 observed: 260.2003.

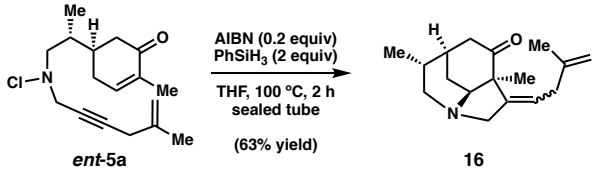
[6] Compounds ***ent*-5a** and **16** were previously reported in Stockdill, J. L.; Lopez, A. M.; Ibrahim, A. A. *Tetrahedron Lett.* **2015**, *56, 3503–3506.*



(3a*S*,6*R*,7a*S*,8*R*)-3a,8-dimethyl-3-(3-methylbut-3-en-1-ylidene)hexahydro-6,1-ethanoindol-4(2*H*)-one (tricycle 16). To a Biotage microwave vial was added (*R*)-5-((*R*)-1-(chloro(5-methylhex-5-en-2-yn-1-yl)amino)propan-2-yl)-2-methylcyclohex-2-en-1-one (***ent*-5a**) (10.3 mg, 0.035 mmol, 1 equiv), THF (3.9 mL), AIBN (1.2 mg, 0.007 mmol, 0.2 equiv), and $Et_3Si–H$ (8.2 mg, 0.070 mmol, 2 equiv). The vial was sealed and placed in an oil bath preheated to 100 ºC and the solution was stirred for 2 h. **CAUTION:** REACTIONS UNDER PRESSURE SHOULD BE HANDLED IN A FUME HOOD BEHIND A BLAST SHIELD. After 2 h, the solution was allowed to cool to ambient temperature (24 ± 1 ºC), then it was transferred to a round bottom flask, and the solvent removed under reduced pressure. The crude material was purified by flash chromatography in a 10 g Biotage SNAP column packed with SiO_2 and eluted with 0-10% MeOH/DCM. The product was isolated as a yellow oil, 6.2 mg (69% yield). Spectral data match the above data for this compound.

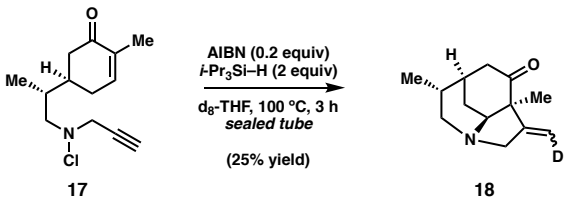


(3a*S*,6*R*,7a*S*,8*R*)-3a,8-dimethyl-3-(3-methylbut-3-en-1-ylidene)hexahydro-6,1-ethanoindol-4(2*H*)-one (tricycle 16). To a Biotage microwave vial was added (*R*)-5-((*R*)-1-(chloro(5-methylhex-5-en-2-yn-1-yl)amino)propan-2-yl)-2-methylcyclohex-2-en-1-one (***ent*-5a**) (10.1 mg, 0.034 mmol, 1 equiv), THF (3.8 mL), AIBN (1.1 mg, 0.007 mmol, 0.2 equiv), and $Ph_3Si–H$ (8.0 mg, 0.069 mmol, 2 equiv). The vial was sealed and placed in an oil bath preheated to 100 ºC and the solution was stirred for 2 h. **CAUTION:** REACTIONS UNDER PRESSURE SHOULD BE HANDLED IN A FUME HOOD BEHIND A BLAST SHIELD. After 2 h, the solution was allowed to cool to ambient temperature (24 ± 1 ºC), then it was transferred to a round bottom flask, and the solvent removed under reduced pressure. The crude material was purified by flash chromatography in a 10 g Biotage SNAP column packed with SiO_2 and eluted with 0-10% MeOH/DCM. The product was isolated as a yellow oil, 6.6 mg (75% yield). Spectral data match the above data for this compound.



(3a*S*,6*R*,7a*S*,8*R*)-3a,8-dimethyl-3-(3-methylbut-3-en-1-ylidene)hexahydro-6,1-ethanoindol-4(2*H*)-one (tricycle 16). To a Biotage microwave vial was added (*R*)-5-((*R*)-1-(chloro(5-methylhex-5-en-2-yn-1-yl)amino)propan-2-yl)-2-methylcyclohex-2-en-1-one (***ent*-5a**) (9.6 mg, 0.033 mmol, 1 equiv), THF (3.6 mL), AIBN (1.1 mg, 0.007 mmol, 0.2 equiv), and $PhSiH_3$ (7.1

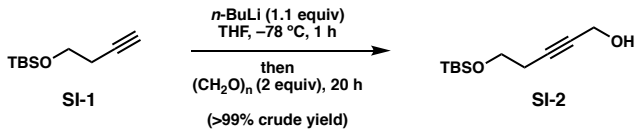
mg, 0.065 mmol, 2 equiv). The vial was sealed and placed in an oil bath preheated to 100 °C and the solution was stirred for 2 h. **CAUTION:** REACTIONS UNDER PRESSURE SHOULD BE HANDLED IN A FUME HOOD BEHIND A BLAST SHIELD. After 2 h, the solution was allowed to cool to ambient temperature (24 ± 1 °C), then it was transferred to a round bottom flask, and the solvent removed under reduced pressure. The crude material was purified by flash chromatography in a 10 g Biotage SNAP column packed with SiO_2 and eluted with 0-10% MeOH/DCM. The product was isolated as a yellow oil, 5.9 mg (63% yield). Spectral data match the above data for this compound.



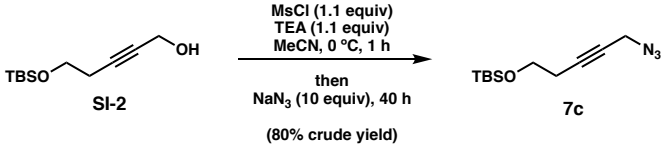
(3a*S*,6*R*,7a*S*,8*R*)-3a,8-dimethyl-3-(methylene-*d*)hexahydro-6,1-ethanoindol-4(2*H*)-one (ketone 18).[7] To a Biotage microwave vial was added (*R*)-5-((*R*)-1-(chloro(prop-2-yn-1-yl)amino)propan-2-yl)-2-methylcyclohex-2-en-1-one (**17**) (17.3 mg, 0.072 mmol, 1 equiv), THF (8 mL), AIBN (2.3 mg, 0.014 mmol, 0.2 equiv), and *i*-Pr_3Si–H (22.9 mg, 0.144 mmol, 2 equiv). The vial was sealed and placed in an oil bath preheated to 100 °C and the solution was stirred for 3 h. **CAUTION:** REACTIONS UNDER PRESSURE SHOULD BE HANDLED IN A FUME HOOD BEHIND A BLAST SHIELD. After 3 h, the solution was allowed to cool to ambient temperature (24 ± 1 °C), then it was transferred to a round bottom flask, and the solvent removed under reduced pressure. The crude material was purified by flash chromatography in a 10 g Biotage SNAP column packed with SiO_2 and eluted with 0-10% MeOH/chloroform. The product was isolated as a yellow oil, 3.7 mg (25% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.39 (dd, *J* = 2.95, 1.81 Hz, 1H), 5.20 (dd, *J* = 2.55, 1.51 Hz, 0.21H), 3.56 (dd, *J* = 15.20, 2.89 Hz, 1H), 3.19 (dd, *J* = 15.44, 1.77 Hz, 1H), 3.05 (s, 1H), 2.64 (dd, *J* = 18.27, 6.01 Hz, 1H), 2.60 (d *J* = 13.30 Hz, 3H), 2.41 (m, 1H), 2.24 (dd, *J* = 13.24, 4.38 Hz, 1H), 2.07 (s, 1H), 1.86 (m, 3H), 1.26 (s, 2H), 1.26 (s, 6H).

Expected Masses (m/z for M+H$^+$)	$[C_{13}H_{20}NO]^+$: 206.15	$[C_{13}H_{19}DNO]^+$: 207.16	$[C_{13}H_{18}D_2NO]^+$: 208.17
Relative Intensities	6.22	100.00	16.32

[7] Compounds **17** and **18** were previously reported in Ibrahim, A. A.; Golonka, A. N.; Lopez, A. M.; Stockdill, J. L. *Org. Lett.* **2014**, *16*, 1072–1075.

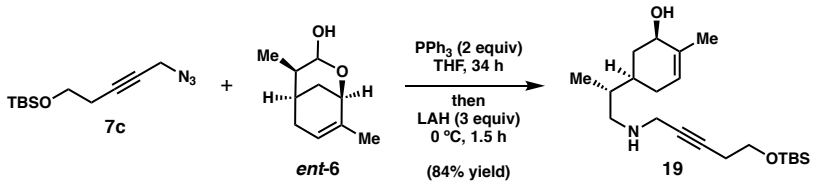


5-((*tert*-butyldimethylsilyl)oxy)pent-2-yn-1-ol (propargylic alcohol SI-2).[8] To a cooled (–78 ºC) solution of 4-(tert-Butyldimethylsilyloxy)-1-butyne (**SI-1**) (21.76 g, 118.0 mmol, 1 equiv) in THF (167 mL) was added *n*-BuLi (2.03 M in hexanes, 51.9 mL, 129.817 mmol, 1.1 equiv) dropwise. After 1 h, paraformaldehyde (8.86 g, 295.0 mmol, 2 equiv) was added and reaction was allowed to warm slowly to ambient temperature (24 ± 1 ºC) in the dewar overnight. After 20 h, the reaction was quenched with ethyl acetate (10 mL) and then water (150 mL). The layers were separated and the aqueous layer was extracted with ethyl acetate (3 x 75 mL). The combined organic layers were washed with brine and then dried over $MgSO_4$. The solvent was removed under reduced pressure and the material, pale yellow oil, 26.0 g (>99% crude yield), was used without further purification. R_f = 0.43 (20% ethyl acetate/hexane); Spectra matched the reported data: ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.24 (m, 2H), 3.72 (t, J = 7.14 Hz, 2H), 2.43 (tt, J = 7.24, 2.08 Hz, 2H), 1.61 (d, J = 1.89 Hz, 1H) 0.90 (s, 9H), 0.07 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 83.52, 79.64, 61.97, 51.46, 26.02, 23.27, 18.48, –5.14; IR neat 3355, 2930, 2858, 1103, 837 cm^{-1}; HRMS [M+Na]$^+$ m/z ESI, calc'd = 237.1281, observed: 237.1277.

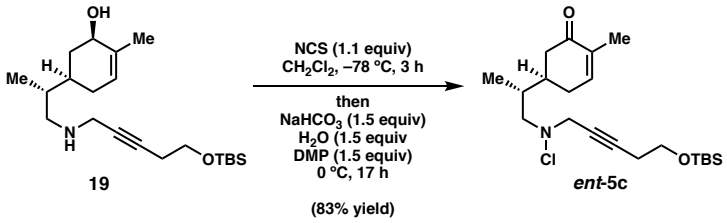


((5-azidopent-3-yn-1-yl)oxy)(*tert*-butyl)dimethylsilane (propargylic azide 7c). To a cooled (0 °C) solution of **5-**((*tert*-butyldimethylsilyl)oxy)pent-2-yn-1-ol (**SI-2**) (25.30 g, 118.0 mmol, 1equiv) in ACN (197 mL) was added MsCl (14.87 g, 129.8 mmol, 1.1 equiv) and TEA (13.14 g, 129.800 mmol, 1.1 equiv). The reaction was allowed to warm to ambient temperature (24 ± 1 º C) over 1 h and then sodium azide (76.71 g, 1180.0 mmol, 10 equiv) was added. **CAUTION:** AZIDES ARE EXPLOSIVE AND SHOULD BE HANDLED IN A FUME HOOD BEHIND A BLAST SHIELD. After 40 h, the reaction was quenched with water (100 mL), the ACN was removed under reduced pressure, and the aqueous later was extracted with diethyl ether (4 x 75 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, and the solvent was removed under reduced pressure. The crude material was purified by flash chromatography, eluted with 0–10% ether/pentanes. The product was isolated as a yellow-green oil, 22.60 g (80% yield). R_f = 0.73 (10% ethyl acetate/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.89 (m, 2H), 3.74 (t, J = 6.98, 2H), 2.47 (tt, J = 7.04, 2.22 Hz, 2H), 0.90 (s, 10H), 0.08 (m, 5H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 85.43, 73.27, 61.88, 40.43, 26.01, 23.22, 18.47,–5.16; IR neat 2956, 2927, 2854, 1253, 1100, 836, 776 cm^{-1}; HRMS [2M+H$^+$] m/z ESI calc'd for $[C_{22}H_{44}N_6O_2Si_2]^+$: 479.2986 observed: 479.2971.

[8] Jensen, T.; Pedersen, H.; Bang-Andersen, B.; Madsen, R.; Jørgensen, M. *Angew. Chem. Int. Ed.* **2008**, *47*, 888–890.

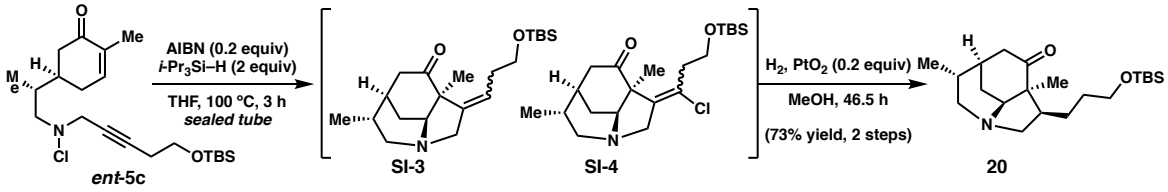


(1*R*,5*R*)-5-((*R*)-1-((5-((*tert*-butyldimethylsilyl)oxy)pent-2-yn-1-yl)amino)propan-2-yl)-2-methylcyclohex-2-en-1-ol (allylic alcohol 19). To a solution of (1*R*,4*R*,5*R*)-4,8-dimethyl-2-oxabicyclo[3.3.1]non-7-en-3-ol (***ent-6***) (2.570 g, 15.24 mmol, 1 equiv) and ((5-azidopent-3-yn-1-yl)oxy)(*tert*-butyl)dimethylsilane (**7c**) (3.695 g, 15.45 mmol, 1.01 equiv) in THF (61.2 mL) was added PPh_3 (8.025 g, 30.60 mmol, 2 equiv) and the reaction was stirred overnight. After 34 h, the reaction was cooled to 0 ºC and LAH (1.742 g, 45.89 mmol, 3 equiv) was added and the reaction was stirred for 1.5 h. After 1.5 h, the LAH quenched with a saturated solution of potassium sodium tartrate and suspension was allowed to stir for 30 min. The layers were separated and aqueous layer extracted with ethyl acetate (4 x 10 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, and then the solvent removed under reduced pressure. The crude material was purified by flash chromatography with a 50 g Biotage SNAP column packed with SiO_2 and eluted with 0-10% MeOH/DCM. The product was isolated as a yellow oil, 4.660 g (84% yield). R_f = 0.38 (5% MeOH/DCM); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.46 (dq, *J* = 5.71, 1.88 Hz, 1H), 4.15 (d, *J* = 9.46 Hz, 1H), 3.70 (m, 2H), 3.37 (qd, *J* = 2.30, 1.19 Hz, 2H), 2.66 (dd, *J* = 11.45, 5.55 Hz, 1H), 2.50 (dd, *J* = 11.52, 7.56 Hz, 1H), 2.40 (tt, *J* = 7.27, 2.22 Hz, 2H), 2.07 (ddt, *J* = 11.74, 5.52, 2.23, 1H), 1.88 (m, 2H), 1.73 (m, 4H), 1.65 (m, 6H), 1.54 (ddd, *J* = 12.69, 7.24, 5.63 Hz, 1H), 1.21 (td, *J* = 12.38, 10.08 Hz, 1H), 0.91 (d, *J* = 7.00 Hz, 4H), 0.89 (d, *J* = 0.69 Hz, 9H), 0.06 (d, *J* = 0.76 Hz, 6H); ^{13}C NMR (121 MHz, $CDCl_3$) δ 136.53, 124.30, 80.63, 79.32, 71.32, 62.22, 52.66, 38.97, 37.34, 36.38, 35.93, 30.26, 30.11, 26.03, 23.27, 18.94, 18.48, 14.90, –5.13; IR neat 3078, 2900, 2754, 1589, 1520, 1404, 1350, 1304, 1165, 1065, 972 cm^{-1}; $[\alpha]_D^{22}$ –7.0 (c 0.0067, $CHCl_3$); HRMS [M+H$^+$] m/z ESI calc'd for $[C_{21}H_{40}NO_2Si]^+$: 366.2828 observed: 366.2813.



(*R*)-5-((*R*)-1-((5-((*tert*-butyldimethylsilyl)oxy)pent-2-yn-1-yl)chloroamino)propan-2-yl)-2-methylcyclohex-2-en-1-one (*N*-chloroamine *ent*-5c). To a cooled (–78 ºC) solution of (1*R*,5*R*)-5-((*R*)-1-((5-((*tert*-butyldimethylsilyl)oxy)pent-2-yn-1-yl)amino)propan-2-yl)-2-methylcyclohex-2-en-1-ol (**19**) (1.032 g, 2.824 mmol, 1 equiv) in DCM (11.4 mL) was added NCS (414.8 mg, 3.106 mmol, 1.1 equiv). The reaction was allowed to warm to 0 ºC slowly in the acetone/dry ice bath over 3 h. After 3 h, $NaHCO_3$ (335.9 mg, 4.236 mmol, 1.5 equiv), water (76 μL, 1.5 equiv), and DMP (1.797 g, 4.236 mmol, 1.5 equiv) were added. For this addition, the flask was temporarily opened to air and then it was sealed with a glass stopper. The apparatus was covered in aluminum foil and stirred overnight. After 17 h, the mixture was diluted with hexane (5 mL) and loaded onto a plug of SiO_2 and the product was eluted with 0-10% ethyl acetate/hexane. The product was isolated as a yellow oil, 929.2 mg (83% yield). R_f = 0.64 (10%

ethyl acetate/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.75 (ddt, *J* = 5.61, 2.82, 1.24 Hz, 1H), 3.77 (t, *J* = 2.14 Hz, 4H), 2.91 (dd, *J* = 13.06, 7.00 Hz, 1H), 2.73 (dd, *J* = 13.06, 6.98 Hz, 1H), 2.46 (tt, *J* = 7.07, 2.14 Hz, 3H), 2.23 (m, 4H), 1.95 (qd, *J* = 6.95, 3.05 Hz, 1H), 1.77 (q, *J* = 1.62, 3H), 1.58 (s, 2H), 0.92 (d, *J* = 6.87 Hz, 4H), 0.90 (s, 9H), 0.07 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 200.35, 145.38, 135.59, 84.63, 75.01, 65.70, 61.97, 53.81, 40.18, 37.70, 35.21, 30.64, 26.03, 23.33, 18.47, 15.87, 14.05, –5.12; IR neat 3017, 2955, 2855, 1667, 1458, 1435, 1381, 1250, 1211, 1103, 903, 841, 748 cm^{-1}; $[\alpha]_D^{22}$ –5.8 (c 0.005, $CHCl_3$); HRMS [M+H$^+$] m/z ESI calc'd for $[C_{21}H_{37}NO_2SiCl]^+$: 398.2282 observed: 398.2264.



(3a*S*,6*R*,7a*S*,8*R*)-3-(3-((*tert*-butyldimethylsilyl)oxy)propylidene)-3a,8-dimethylhexahydro-6,1-ethanoindol-4(2*H*)-one (tricycle SI-3).

> **This procedure was performed in parallel on 1.248 g and 1.641 g of *N*-chloroenone ***ent*-5c**, yielding 420.1 mg + 530.4 mg of **SI-3** and 546.3 mg + 544.0 mg of mixed fractions **SI-3** and **SI-4**. The pure **SI-3** fractions were combined and the mixed fractions were combined, and the hydrogenations were performed as described below. The pure product obtained from each (863.3 mg + 1.0642 mg) was combined to calculate the overall yield (2.8887 g, 7.26 mmol ***ent*-5c** yields 1.9275 g, 5.27 mmol **20** = 73% yield).**

Cyclization A: To a ChemGlass pressure vessel, heavy wall, round bottom (CG-1880-R-13) flask was added (*R*)-5-((*R*)-1-((5-((*tert*-butyldimethylsilyl)oxy)pent-2-yn-1-yl)chloroamino)propan-2-yl)-2-methylcyclohex-2-en-1-one (***ent*-5c**) (1.248 g, 3.135 mmol, 1 equiv), THF (349 mL, total concentration= 0.009 M), AIBN (103.0 mg, 0.627 mmol, 0.2 equiv), and *i*-Pr_3Si–H (992.8 mg, 6.269 mmol, 2 equiv). The vessel was sealed and placed in an oil bath preheated to 120 °C and the temperature was immediately set to 100 °C. **CAUTION:** REACTIONS UNDER PRESSURE SHOULD BE HANDLED IN A FUME HOOD BEHIND A BLAST SHIELD. The solution was stirred for 3 h. After 3 h, the solution was allowed to cool to ambient temperature (24 ± 1 °C), then it was transferred to a round bottom flask, and the solvent removed under reduced pressure. The crude material was purified by flash chromatography with a 25 g Biotage SNAP column packed with SiO_2 and eluted with 0-10% MeOH/chloroform. The product (**SI-3**) was isolated as a brown oil, 420.1 mg. Additionally, a mixture of **SI-3** and (3a*S*,6*R*,7a*S*,8*R*)-3-(3-((*tert*-butyldimethylsilyl)oxy)-1-chloropropylidene)-3a,8-dimethylhexahydro-6,1-ethanoindol-4(2*H*)-one (**SI-4**) was obtained, 546.3 mg, R_f = 0.78 (10% MeOH/chloroform).

Cyclization B: In a separate ChemGlass pressure vessel, heavy wall, round bottom (CG-1880-R-12) flask was added (*R*)-5-((*R*)-1-((5-((*tert*-butyldimethylsilyl)oxy)pent-2-yn-1-yl)chloroamino)propan-2-yl)-2-methylcyclohex-2-en-1-one (***ent*-5c**) (1.641 g, 4.122 mmol, 1 equiv), THF (83 mL, total concentration= 0.05 M), AIBN (135.5 mg, 0.824 mmol, 0.2 equiv), and *i*-Pr_3Si–H (1.306 g, 8.244 mmol, 2 equiv). The vessel was sealed and placed in an oil bath preheated to 120 °C and the temperature was immediately set to 100 °C. The solution was stirred for 3 h. After 3 h, the solution was allowed to cool to ambient temperature (24 ± 1 °C),

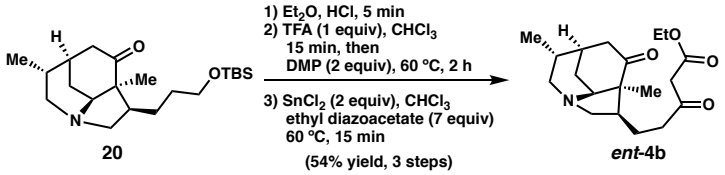
then it was transferred to a round bottom flask, and the solvent removed under reduced pressure. The crude material was purified by flash chromatography with a 25 g Biotage SNAP column packed with SiO_2 and eluted with 0-10% MeOH/chloroform. The product (**SI-3**) was isolated as a brown oil, 530.4 mg. Additionally, a mixture of **SI-3** and **SI-4** was obtained, 544.0 mg, R_f = 0.78 (10% MeOH/chloroform). Pure **SI-3**: R_f = 0.65 (10% MeOH/chloroform); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.84 (m, 1H), 5.70 (t, *J* = 7.49 Hz, 1H), 3.87 (dd, *J* = 37.46, 15.11 Hz, 2H), 3.75 (ddd, *J* = 10.09, 6.75, 5.66 Hz, 1H), 3.66 (m, 3H), 3.43 (d, *J* = 15.11 Hz, 3H), 3.26 (d, *J* = 14.86 Hz, 1H), 2.90 (t, *J* = 12.41 Hz, 2H), 2.70 (m, 4H), 2.48 (m, 4H), 2.19 (m, 5H), 1.95 (d, *J* = 12.87 Hz, 4H), 1.49 (s, 3H), 1.38 (dd, *J* = 7.21, 2.26 Hz, 6H), 1.30 (s, 2H), 0.87 (d, *J* = 1.52Hz, 9H), 0.05 (m, 13H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 210.34, 209.89, 128.21, 126.87, 67.13, 65.78, 62.89, 62.25, 60.84, 57.52, 55.26, 54.85, 50.46, 49.69, 45.89, 45.38, 33.54, 33.08, 33.02, 32.90, 32.53, 32.48, 26.09, 26.05, 23.47, 21.93, 20.05, 19.95, 18.64, 18.51, 18.46, –5.11, –5.14, –5.19; IR neat 2932, 2855, 1712, 1466, 1265, 1096, 910, 725 cm^{-1}; HRMS [M+H$^+$] m/z ESI calc'd for $[C_{21}H_{38}NO_2Si]^+$: 364.2672 observed: 364.2655.

(3*R*,3a*S*,6*R*,7a*S*,8*R*)-3-(3-((*tert*-butyldimethylsilyl)oxy)propyl)-3a,8-dimethylhexahydro-6,1-ethanoindol-4(2*H*)-one (ketone 20).

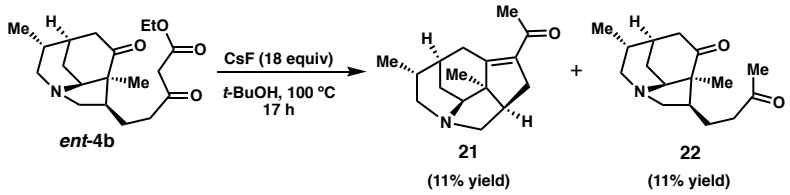
Hydrogenation of pure SI-3: To a flask containing pure **SI-3** (950.5 mg, 2.614 mmol, 1 equiv) and PtO_2 (108.4 mg, 0.478 mmol, 0.18 equiv) was added MeOH (24 mL). The flask was sealed, the atmosphere was evacuated and then purged with H_2 (3x). After 46.5 h, the reaction was filtered through a Whatman® GD/X syringe filter with MeOH. The solvent was removed under reduced pressure and the product was isolated as an orange solid, 863.3 mg.

Hydrogenation of pure SI-3 and SI-4: To a flask containing **SI-3** and **SI-4** (1.090 g, 2.998 mmol, 1 equiv) and PtO_2 (136.2 mg, 0.600 mmol, 0.2 equiv) was added MeOH (30 mL). The flask was sealed, the atmosphere was evacuated and then purged with H_2 (3x). After 46.5 h, the reaction was filtered through a Whatman® GD/X syringe filter with MeOH. The solvent was removed under reduced pressure and the product was isolated as an orange solid, 1.064 g.

Materials from both hydrogenation reactions were combined to afford 1.928 g orange solid (73% yield, 2 steps). R_f = 0.45 (10% MeOH/DCM); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.79 (m, 2H), 3.62 (td, *J* = 6.62, 1.32 Hz, 2H), 3.07 (dd, *J* = 13.89, 9.41 Hz, 1H), 2.73 (dd, *J* = 13.90, 5.23 Hz, 1H), 2.60 (dd *J* = 17.18, 5.22 Hz, 1H), 2.54 (t, *J* = 11.29 Hz, 1H), 2.41 (m, 2H), 2.05 (m, 3H), 1.83 (t, *J* =8.76 Hz, 1H), 1.66 (m, 1H), 1.50 (m, 2H), 1.29 (s, 3H), 1.17 (d, *J* = 6.97 Hz, 3H), 0.89 (s, 9H), 0.05 (s, 6H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 210.93, 65.11, 62.70, 56.66, 55.34, 50.36, 48.96, 47.26, 32.52, 32.37, 29.74, 25.21, 21.58, 21.09, 19.23, 18.47, –5.14; IR neat 2955, 2932, 2855, 2338, 1705, 1466, 1381, 1358, 1250, 1096, 1011, 941, 833, 779 cm^{-1}; $[\alpha]_D^{22}$ –17.2 (c 0.006, $CHCl_3$); HRMS [M+H$^+$] m/z ESI calc'd for $[C_{21}H_{40}NO_2Si]^+$: 366.2828 observed: 366.2810.



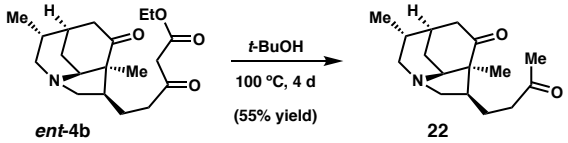
ethyl-5-((3*R*,3a*S*,6*R*,7a*S*,8*R*)-3a,8-dimethyl-4-oxooctahydro-6,1-ethanoindol-3-yl)-3-oxopentanoate (β-keto ester *ent*-4b). To a solution of tricycle **20** (515.8 mg, 1.411 mmol, 1 equiv) in diethyl ether (14 mL) was added HCl (14 mL). After 5 min, the reaction was diluted with water (15 mL) and the aqueous layer was extracted with diethyl ether (1 x 20 mL). The diethyl ether layer was checked for product by LCMS, and no product was observed. To the aqueous layer was added 6 M NaOH until pH ~11, and the basic aqueous layer was extracted with chloroform (10 x 15 mL). The combined organic layers were dried over Na_2SO_4 and the solvent was removed under reduced pressure. The crude material was dissolved in chloroform (14 mL) and TFA (160.9 mg, 1.411 mmol, 1 equiv) was added to the solution. After 15 min, DMP (897.5 mg, 2.116 mmol, 1.5 equiv) as added and the flask was sealed. The apparatus was placed in an oil bath preheated to 60 ºC. At t= 1.5 h, the reaction was incomplete and DMP (310.0 mg, 0.731 mmol, 0.5 equiv) was added. At t= 2 h, the reaction was diluted with saturated $NaHCO_3$ solution (10 mL) and water (10 mL). The aqueous layer was extracted with chloroform (10 x 15 mL), the combined organic layers were dried over Na_2SO_4, and the solvent was removed under reduced pressure. The crude aldehyde was dissolved in chloroform (28 mL) and to the solution was added $SnCl_2$ (535.1 mg, 2.822 mmol, 2 equiv) and ethyl diazoacetate (1.326 g, 9.887 mmol, 7 equiv). The flask was sealed and placed in an oil bath preheated to 60 ºC. At t= 15 min the reaction was diluted with saturated $NaHCO_3$ solution (15 mL) and water (15 mL). The aqueous layer was extracted with chloroform (10 x 15 mL), the combined organic layers were dried over Na_2SO_4, and the solvent was removed under reduced pressure. Crude material was purified by flash chromatography, eluted with 0-20% MeOH/DCM. The product was isolated as a yellow oil, 255.5 mg (54% yield). R_f = 0.48 (10% MeOH/DCM); ^{1}H NMR (600 MHz, $CDCl_3$) δ 4.10 (qd, *J* = 7.15, 2.31 Hz, 2H), 3.35 (s, 2H), 3.30 (dd, *J* = 11.13, 7.63 Hz, 1H), 2.69 (dd, *J* = 13.77, 7.63 Hz, 1H), 2.61 (m, 1H), 2.51 (m, 1H), 2.45 (m, 2H), 2.34 (dd, *J* = 11.07, 8.77 Hz, 1H), 2.26 (dt, *J* = 17.37, 2.55 Hz, 1H), 1.90 (s, 2H), 1.78 (p, *J* = 8.98, 8.24 Hz, 3H), 1.72 (d, *J* = 14.88 Hz, 2H), 1.18 (t, *J* = 7.14, 3H), 1.14 (m, 5H), 1.00 (d, *J* = 7.00 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 213.23, 202.43, 167.24, 128.40, 77.37, 65.40, 61.48, 57.77, 55.59, 51.08, 49.74, 49.29, 47.59, 42.63, 33.01, 31.28, 24.19, 22.39, 21.45, 18.99, 14.20; IR neat 3017, 2932, 1713, 1466, 1265, 1211, 1088, 1018, 934, 748 cm^{-1}; $[\alpha]_D^{22}$ –2.1 (c 0.0014, $CHCl_3$); HRMS [M+H$^+$] m/z ESI calc'd for $[C_{19}H_{30}NO_4]^+$: 336.2175 observed: 336.2162.



1-((3a*R*,7*R*,8*S*,9a*S*,9b*R*)-7,9b-dimethyl-3a,4,6,7,8,9,9a,9b-octahydro-3*H*-1,8-methanocyclopenta[*a*]indolizin-2-yl)ethan-1-one (tetracycle 21) To a Biotage microwave vial containing ***ent*-4b** (54.8 mg, 0.163 mmol, 1 equiv) was added *t*-BuOH (2 mL) and CsF (446.7 mg, 2.941 mmol, 18 equiv). The solution was submerged in an oil bath preheated to 100 ºC and

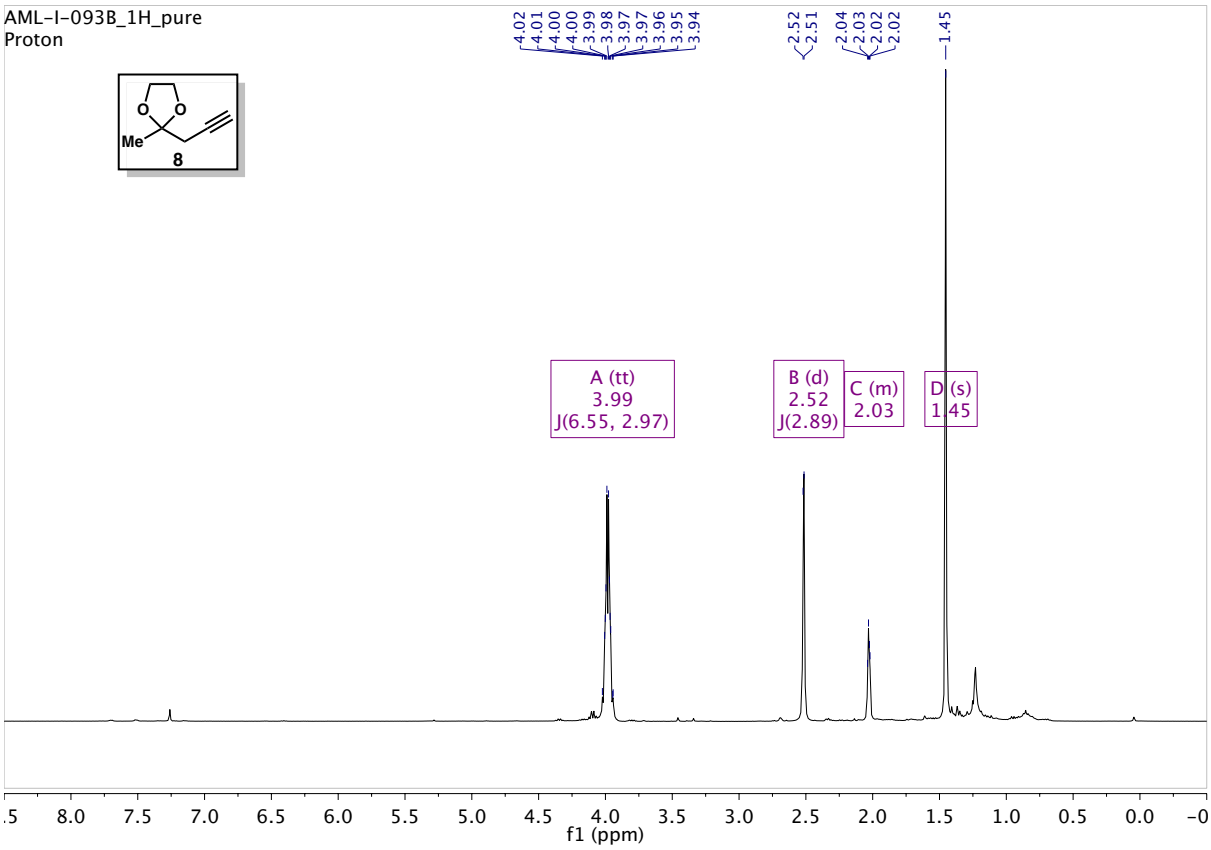
stirred for 17 h. After 17 h, the *t*-BuOH was removed under reduced pressure. The crude material was passed through a pad of Celite 545 with chloroform. The chloroform was removed under reduced pressure and the crude material was dissolved in MeOH (3 mL). The solution was diluted with water, frozen with liquid N_2, and then lyophilized. The crude material was purified by flash chromatography and eluted with 0-10% MeOH/chloroform. The product was isolated as a yellow oil, 4.2 mg (11% yield); R_f = 0.39 (10% MeOH/DCM); ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.44 (dd, *J* = 11.06, 8.91 Hz, 1H), 3.27 (dt, *J* = 14.23, 2.88 Hz, 1H), 3.18 (s, 1H), 2.86 (ttt, *J* = 15.79, 5.16, 3.98 Hz, 1H), 2.58 (dd, *J* = 14.19, 10.47 Hz, 1H), 2.42 (dd, *J* = 14.16, 5.82 Hz, 1H), 2.25 (s, 3H), 2.20, (m, 2H), 2.08 (td, *J* = 3.83, 2.02 Hz, 1H), 1.75 (m, 6H), 1.61 (dt, *J* = 14.18, 2.53 Hz, 1H), 1.47 (m, 1H), 1.06 (s, 3H), 0.83 (d, *J* = 6.88 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 198.48, 160.15, 135.07, 64.14, 60.44, 58.77, 52.94, 46.50, 36.03, 35.10, 33.40, 30.64, 29.70, 29.14, 22.91, 20.29, 18.44; IR neat 3742, 3017, 2955, 2338, 1651, 1604, 1358, 1219, 910 cm^{-1}; $[\alpha]_D^{22}$ –7.3 (c 0.0011, $CHCl_3$); HRMS [M+H$^+$] m/z ESI calc'd for $[C_{16}H_{24}NO]^+$: 246.1852 observed: 246.1840.

4.7 mg of **(3*R*,3a*S*,6*R*,7a*S*,8*R*)-3a,8-dimethyl-3-(3-oxobutyl)hexahydro-6,1-ethanoindol-4(2*H*)-one (methyl ketone 22)** (11% yield) was also isolated. R_f = 0.52 (10% MeOH/DCM); ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.17 (m, 1H), 3.01 (m, 1H), 2.60 (dd, *J* = 13.84, 6.52 Hz, 1H), 2.55 (m, 3H), 2.47 (m, 1H), 2.41 (dd, *J* = 13.73, 5.04 Hz, 1H), 2.33 (m, 3H), 2.22 (m, 2H), 2.12 (s, *J* = 1.12 Hz, 1H), 1.92 (s, 2H), 1.78 (m, 4H), 1.70 (d, *J* = 14.19 Hz, 2H), 1.46 (d, *J* = 1.15 Hz, 1H), 1.29 (m, 1H), 1.17 (d, *J* = 1.11 Hz, 1H), 1.04 (dd, *J* = 7.01, 1.10 Hz, 4H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 214.78, 209.04, 65.73, 58.78, 55.86, 51.70, 50.90, 47.98, 43.81, 33.50, 32.47, 29.98, 28.12, 25.82, 23.05, 21.79, 18.97; IR neat 2878, 2330, 1713, 1697, 1450, 1357, 1219, 949 cm^{-1}; $[\alpha]_D^{22}$ 11.8 (c 0.0011, $CHCl_3$); HRMS [M+H$^+$] m/z ESI calc'd for $[C_{17}H_{26}NO_2]^+$: 264.1964 observed: 264.1947.

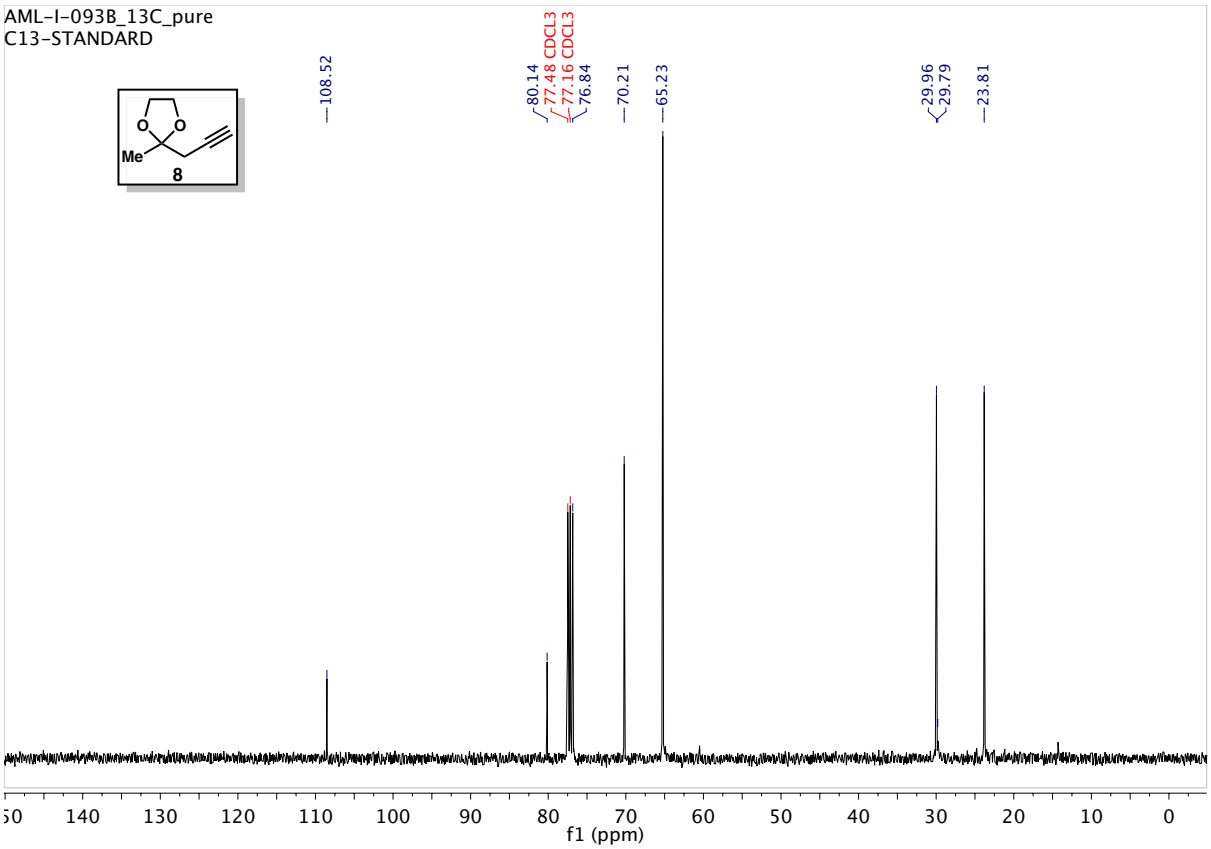


(3*R*,3a*S*,6*R*,7a*S*,8*R*)-3a,8-dimethyl-3-(3-oxobutyl)hexahydro-6,1-ethanoindol-4(2*H*)-one (methyl ketone 22). To a vial containing ***ent*-4b** (53.4 mg, 0.159 mmol) was added *t*-BuOH (2.5 mL). The vial was sealed and placed in an oil bath heated to 100 °C. After 4 d, the was diluted with water and lyophilized. Crude material was purified by flash chromatography and eluted with 0-3% chloroform/MeOH. The product was isolated as a colorless oil, 23.3 mg (55% yield). Spectra matched the above data.

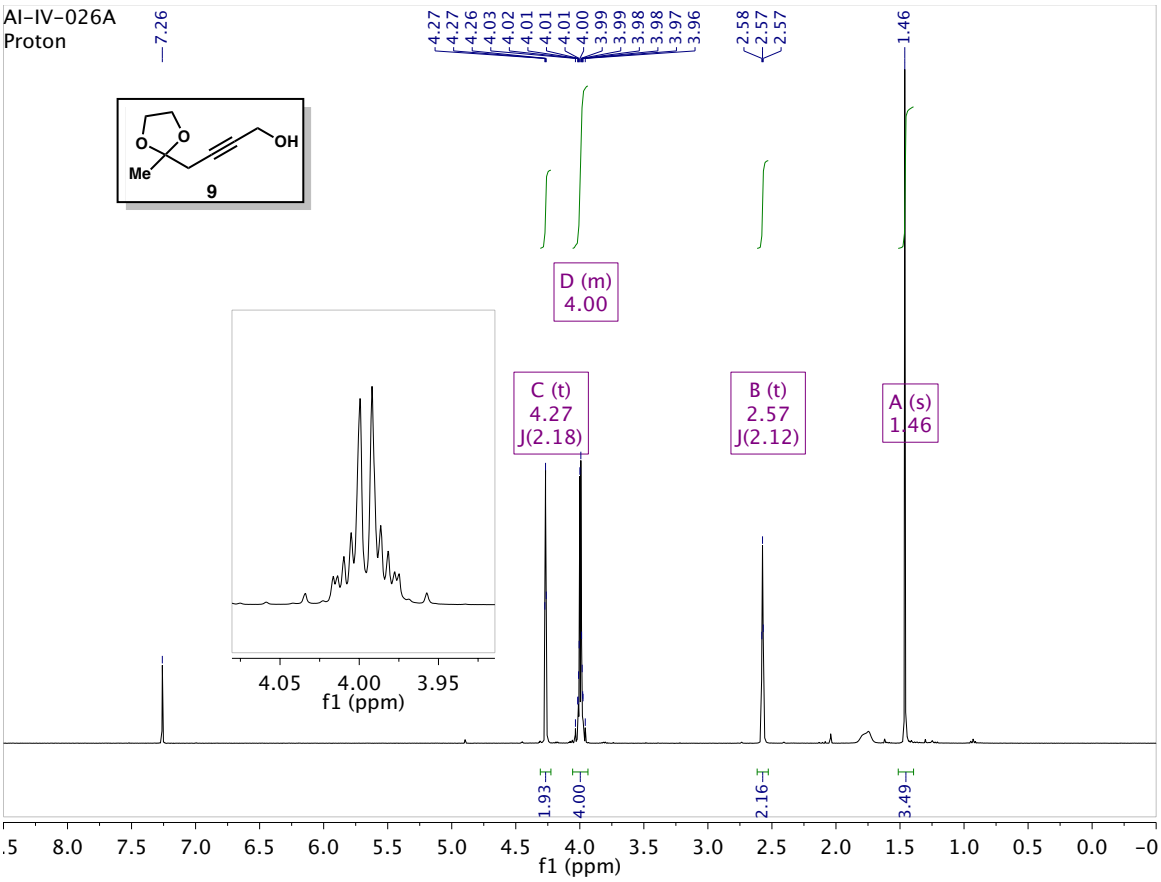
^{1}H, ^{13}C NMR Spectra



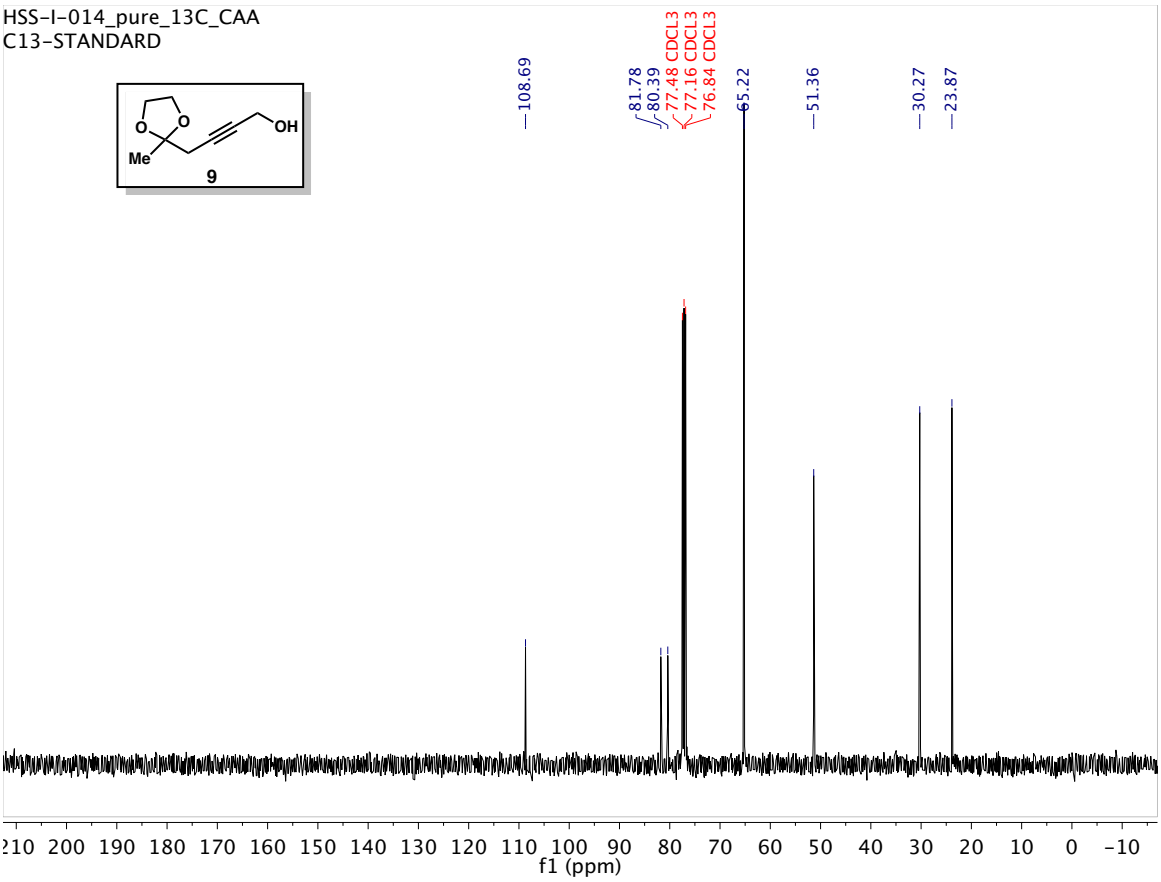
^{1}H NMR (400 MHz, $CDCl_3$) of **alkyne 8**



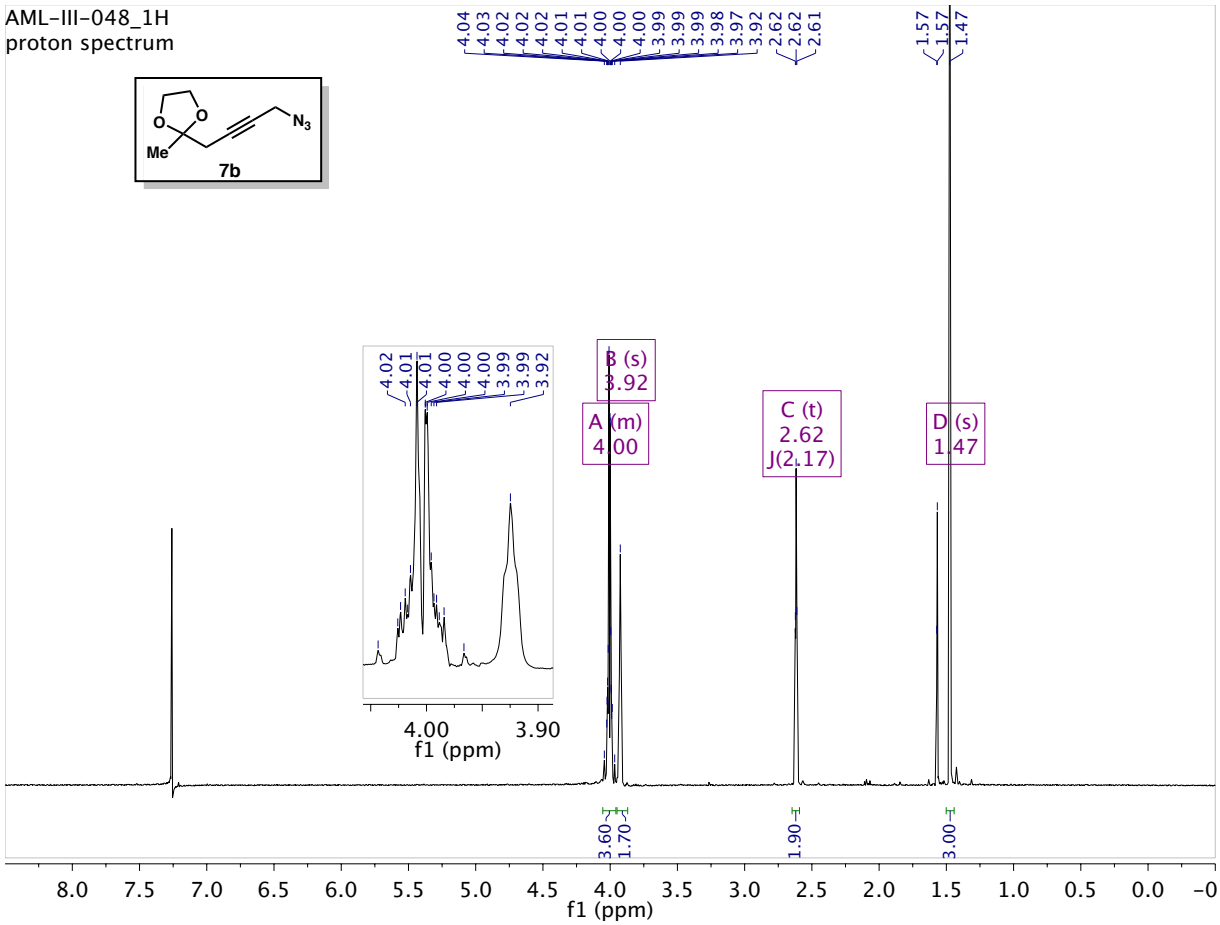
^{13}C NMR (101 MHz, $CDCl_3$) of **alkyne 8**



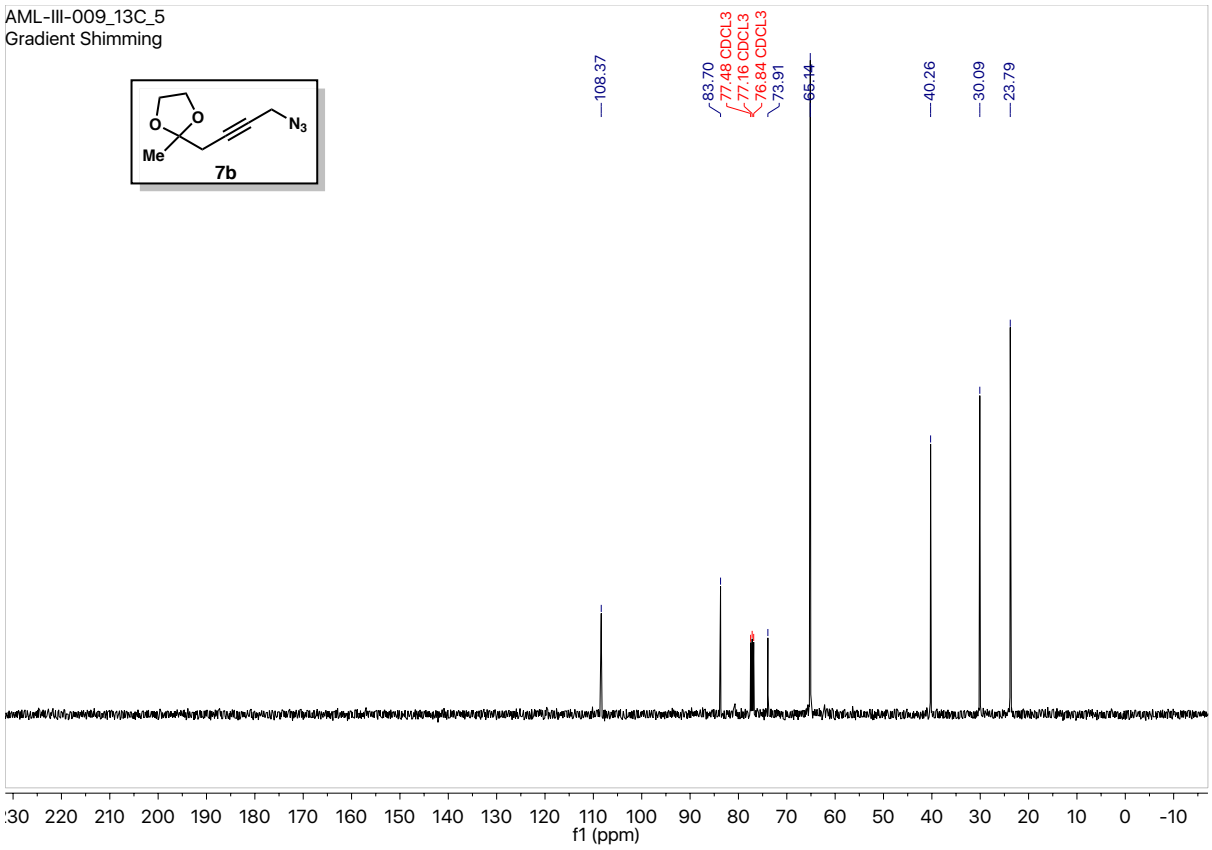
^{1}H NMR (400 MHz, $CDCl_3$) of **propargylic alcohol 9**



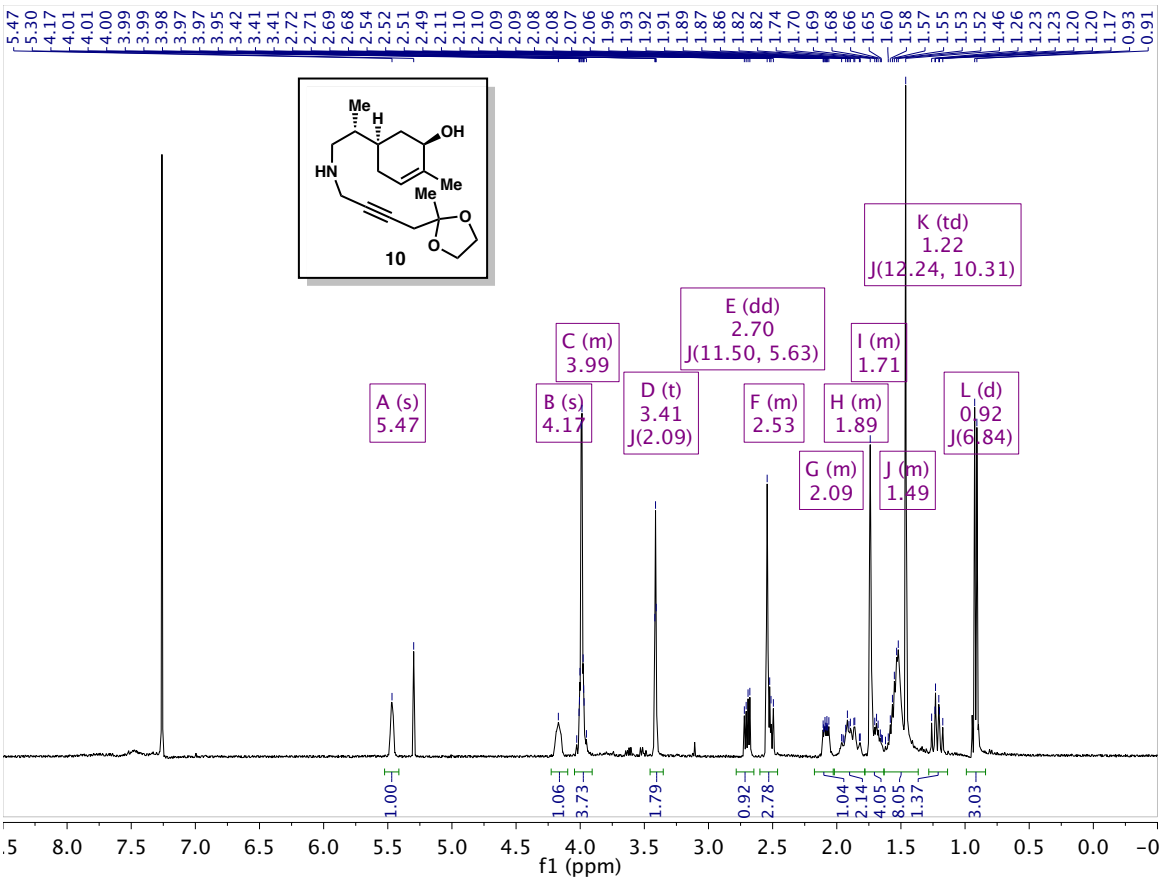
^{13}C NMR (101 MHz, $CDCl_3$) of **propargylic alcohol 9**



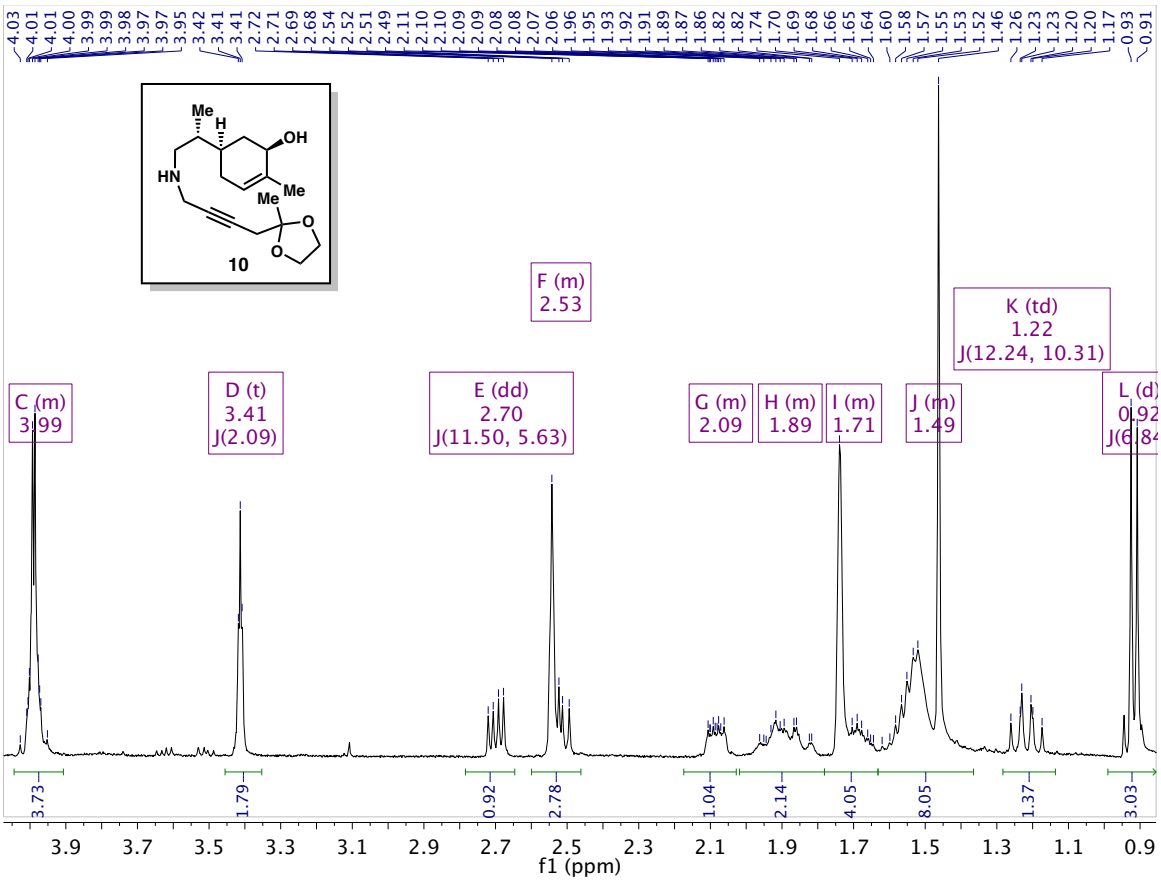
^{1}H NMR (400 MHz, $CDCl_3$) of **propargylic azide 7b**



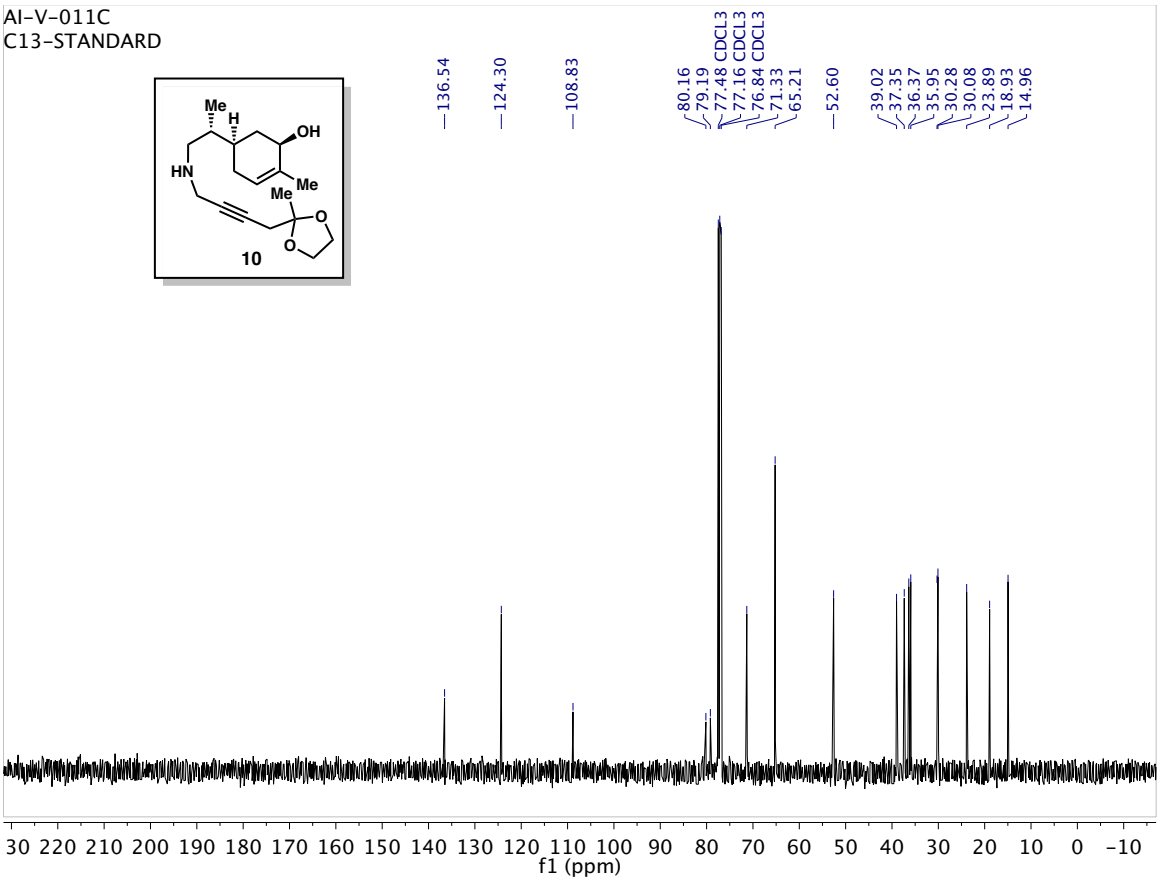
^{13}C NMR (101 MHz, $CDCl_3$) of **propargylic azide 7b**



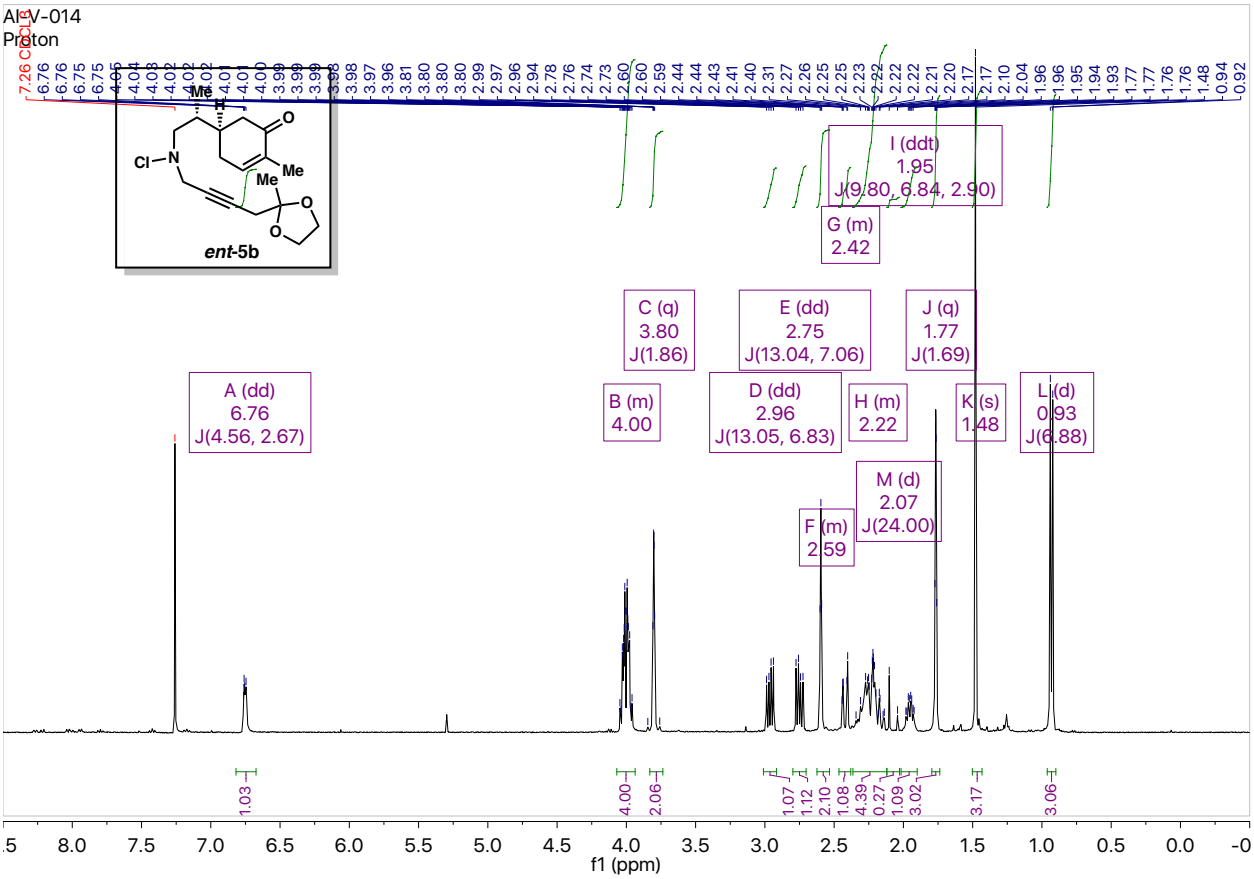
^{1}H NMR (400 MHz, $CDCl_3$) of **allylic alcohol 10**



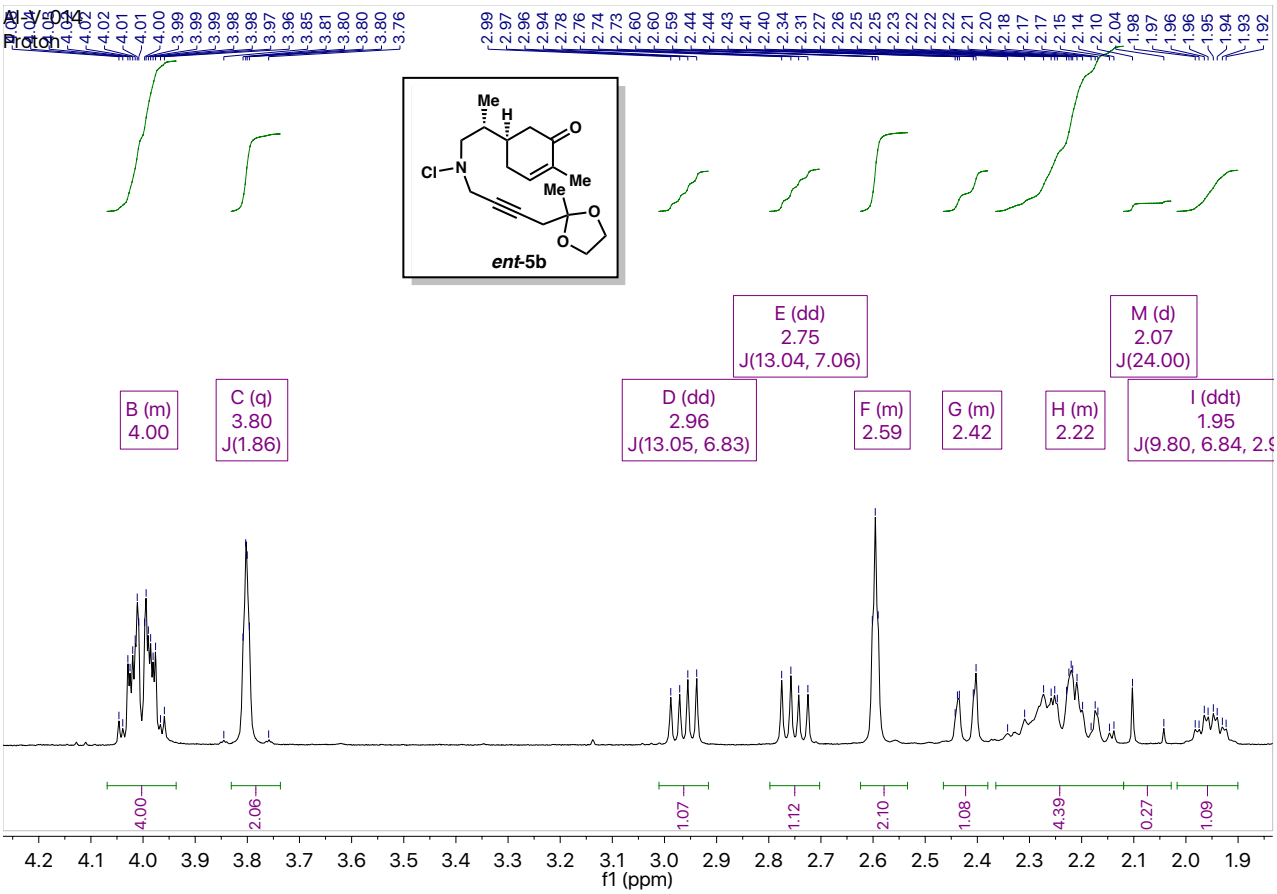
Zoomed in ^{1}H NMR (400 MHz, $CDCl_3$) of **allylic alcohol 10**



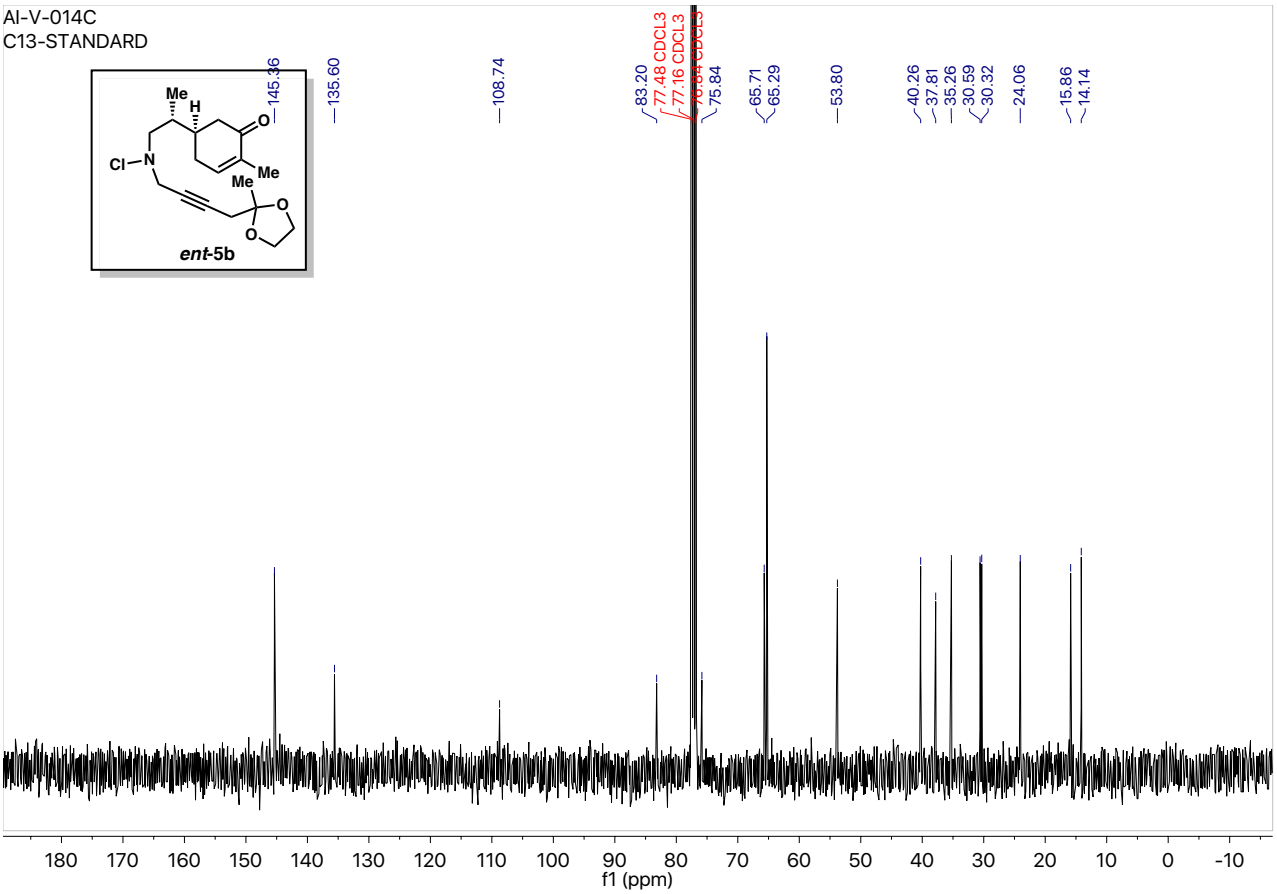
^{13}C NMR (101 MHz, $CDCl_3$) of **allylic alcohol 10**



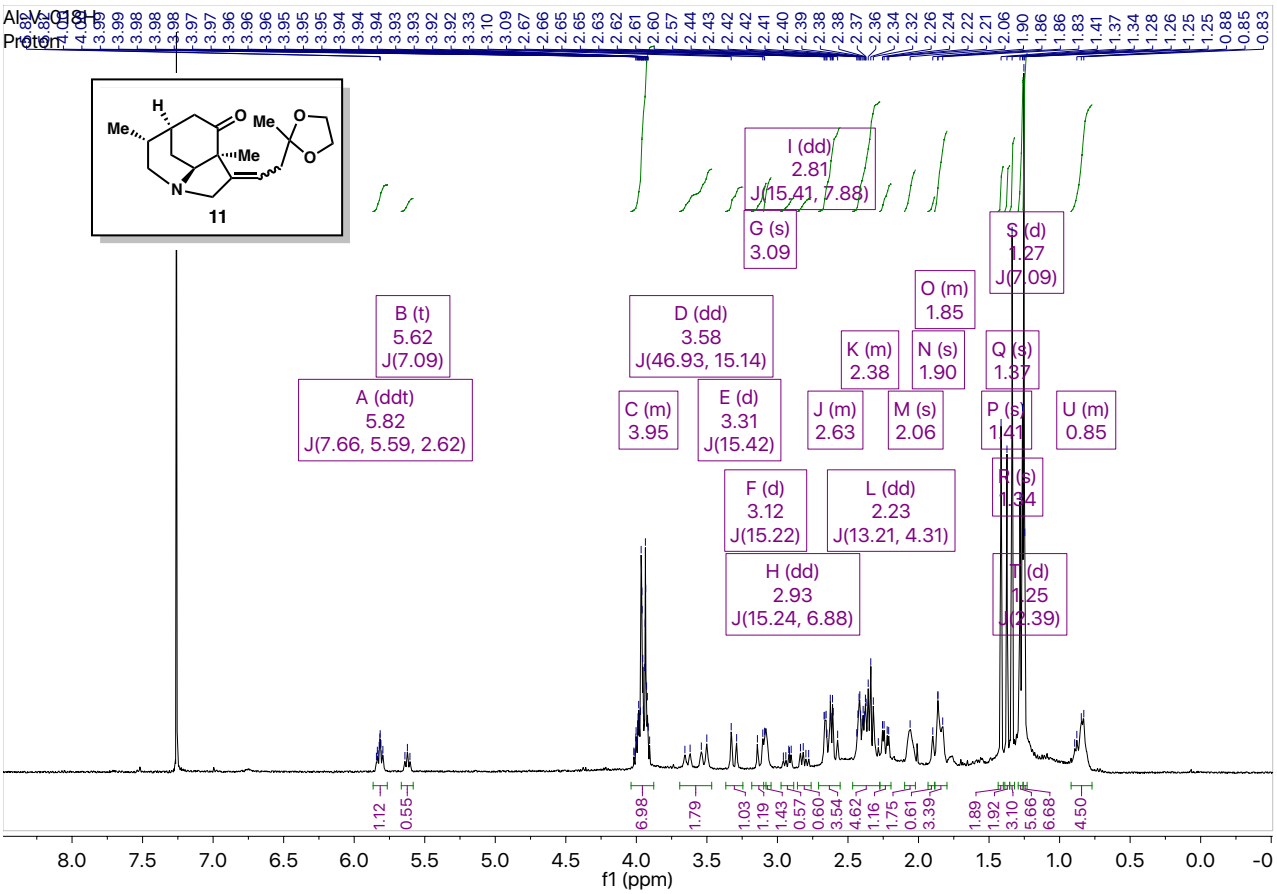
^{1}H NMR (400 MHz, $CDCl_3$) of ***N*-chloroamine *ent*-5b**



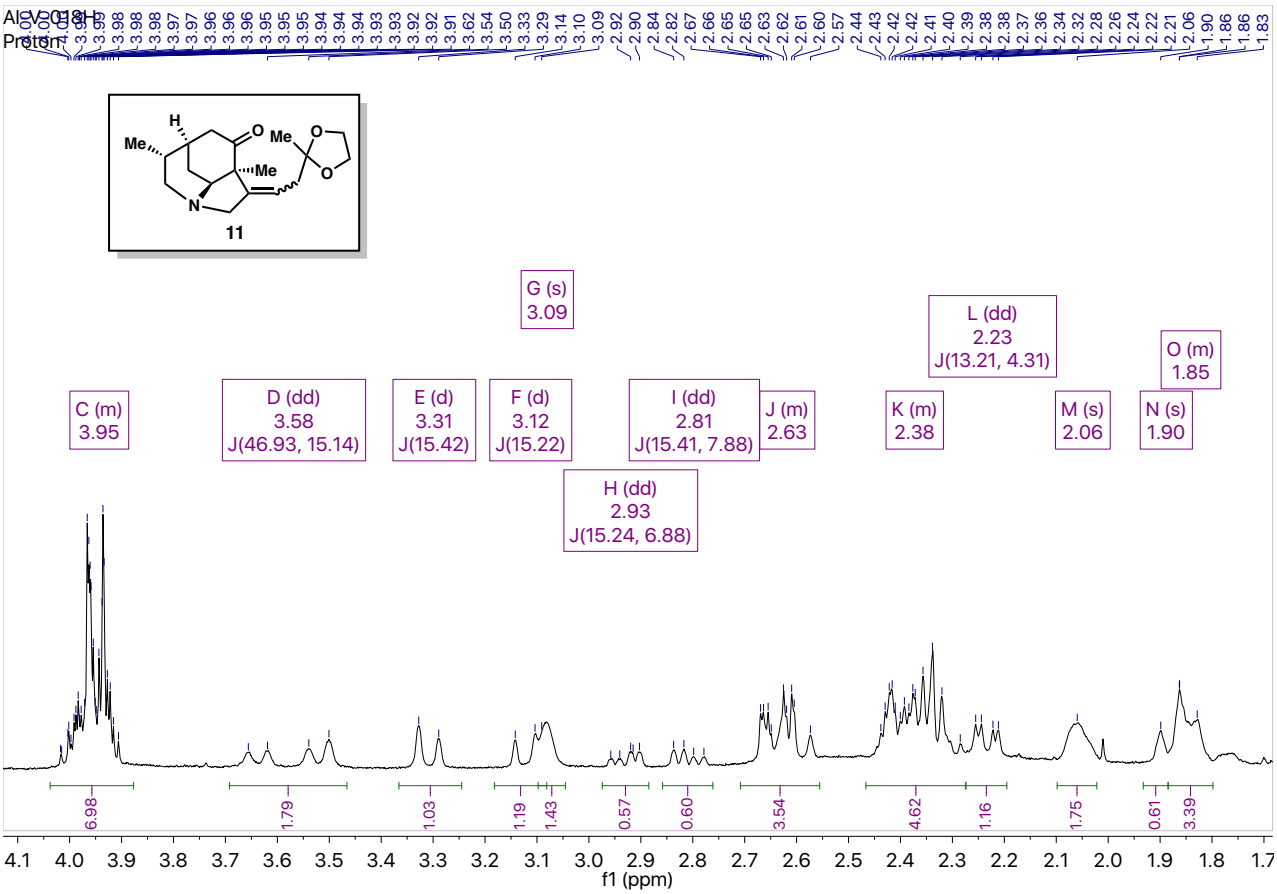
Zoomed in ^{1}H NMR (400 MHz, $CDCl_3$) of ***N*-chloroamine *ent*-5b**



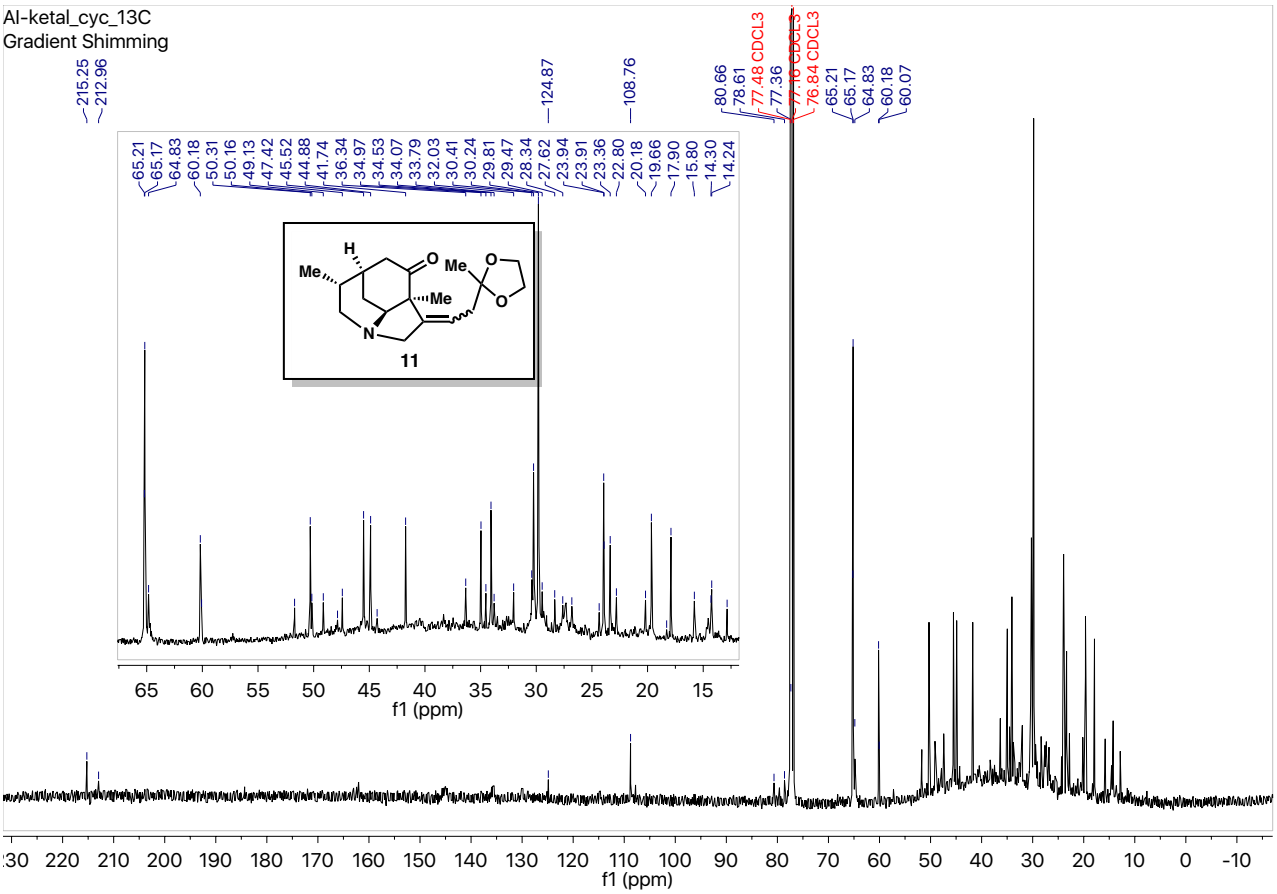
^{13}C NMR (101 MHz, $CDCl_3$) of ***N*-chloroamine *ent*-5b**



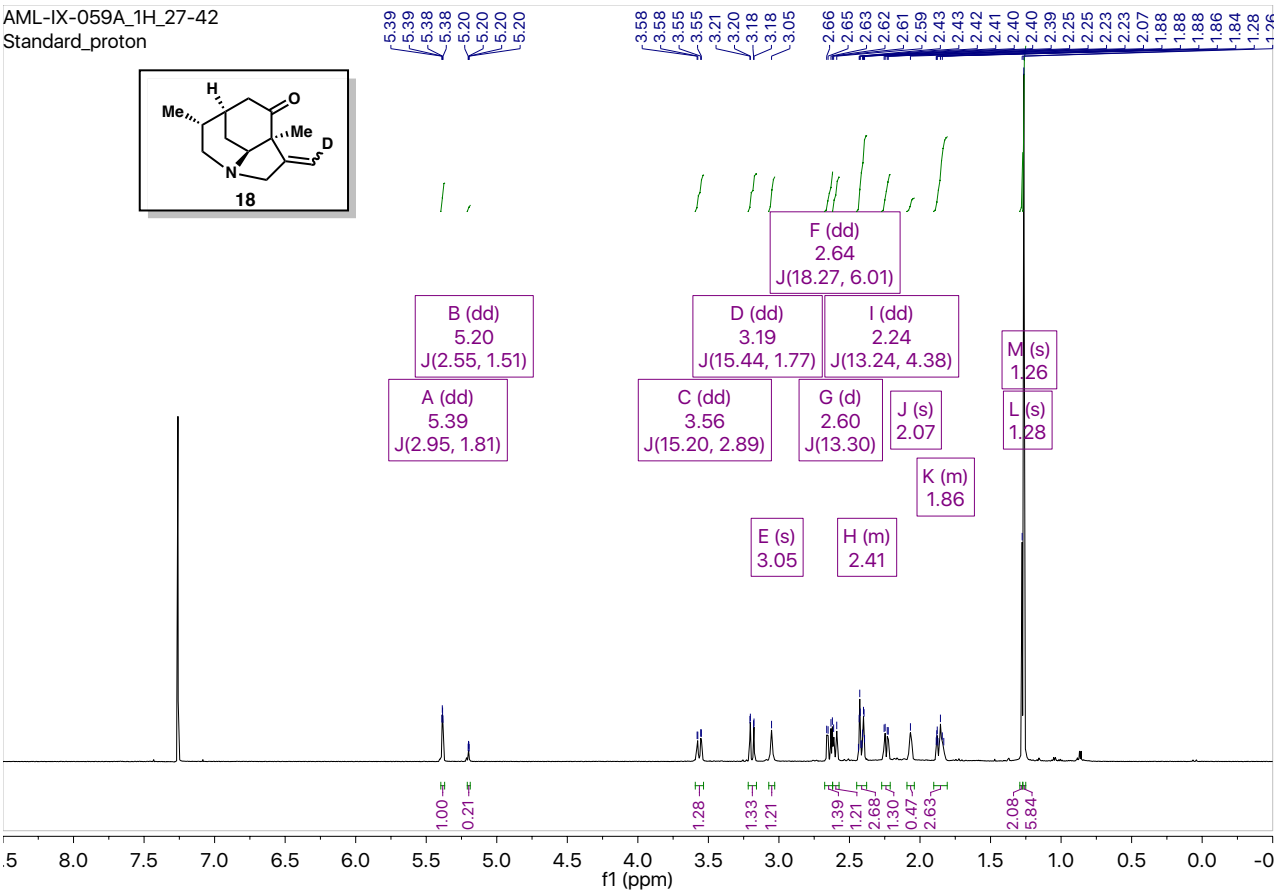
^{1}H NMR (400 MHz, $CDCl_3$) of **tricycle 11**



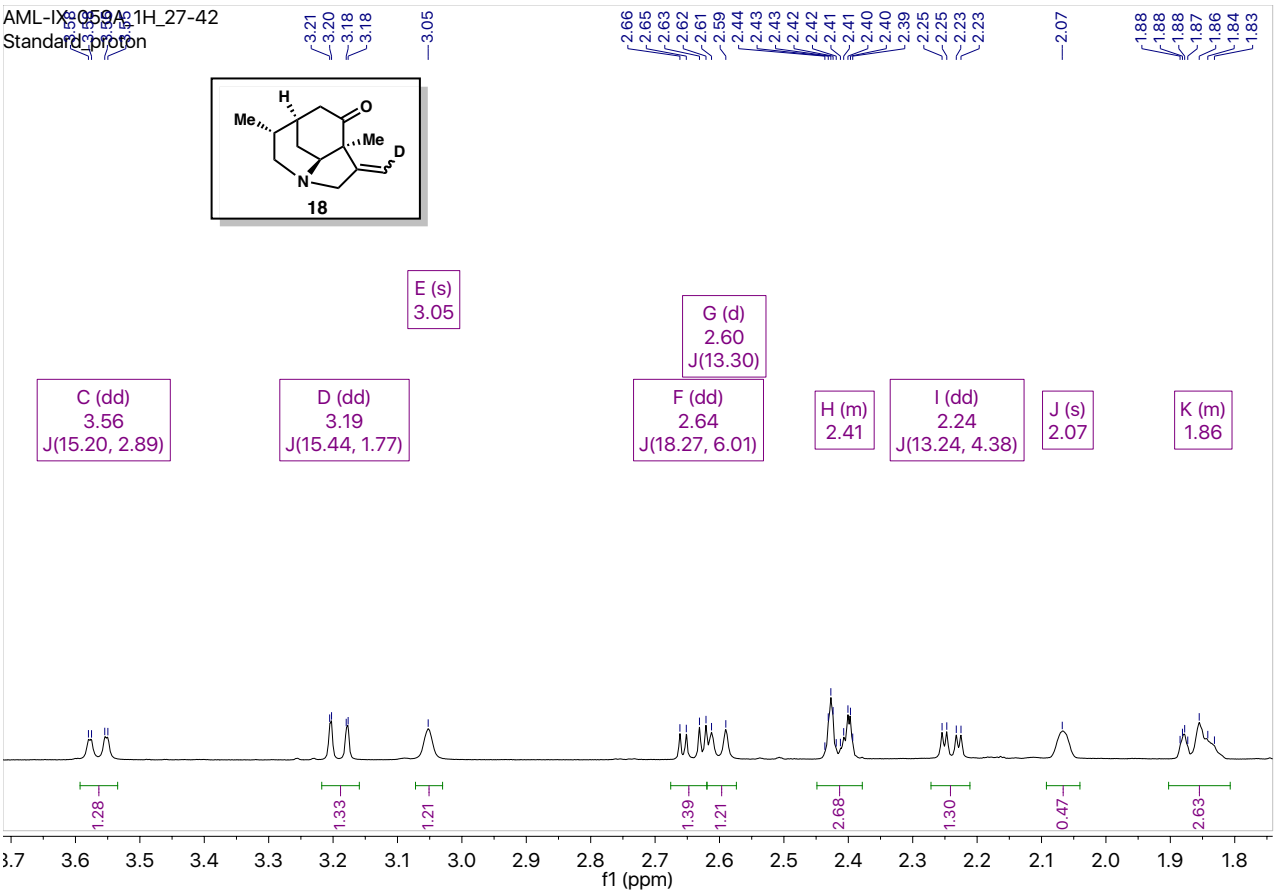
Zoomed in ^{1}H NMR (400 MHz, $CDCl_3$) of **tricycle 11**



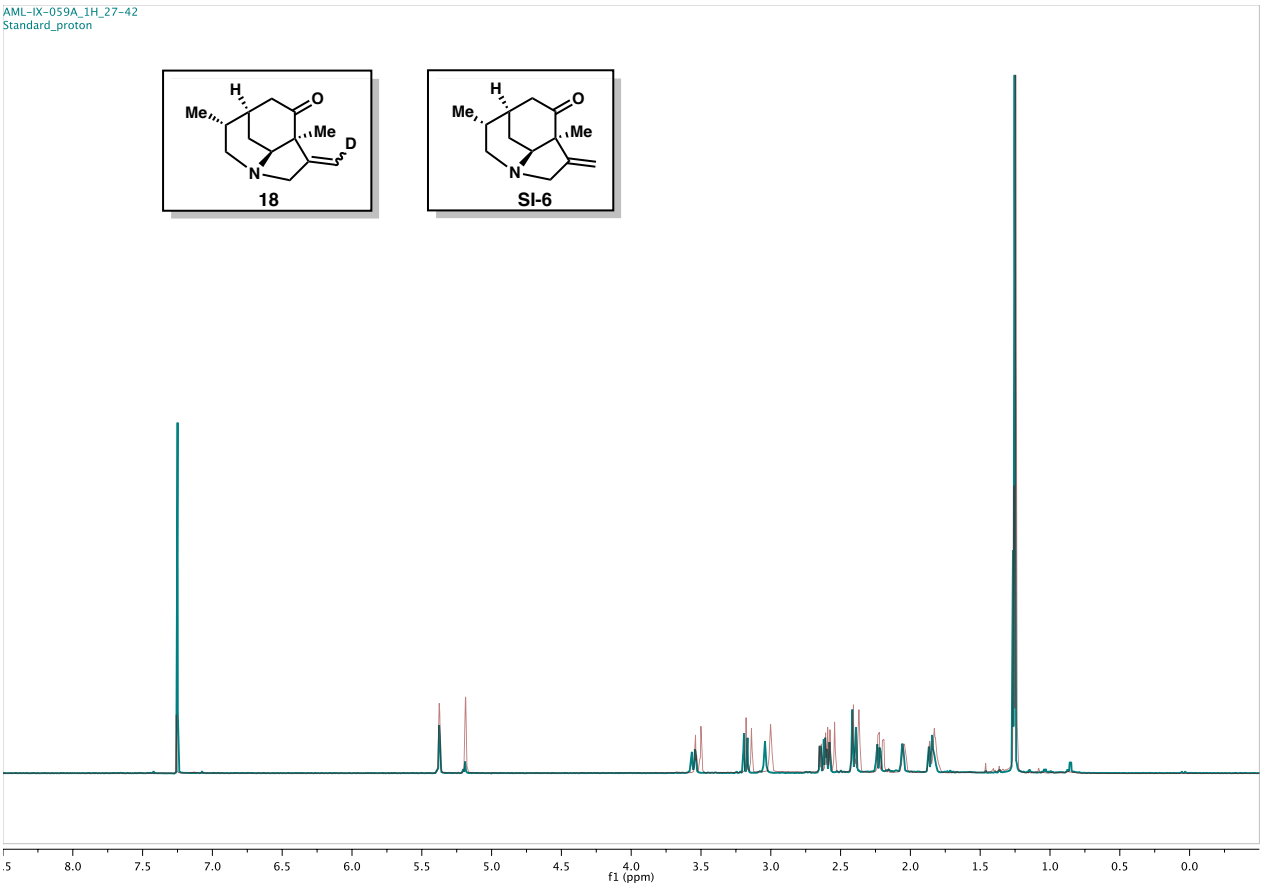
^{13}C NMR (101 MHz, $CDCl_3$) of **tricycle 11**



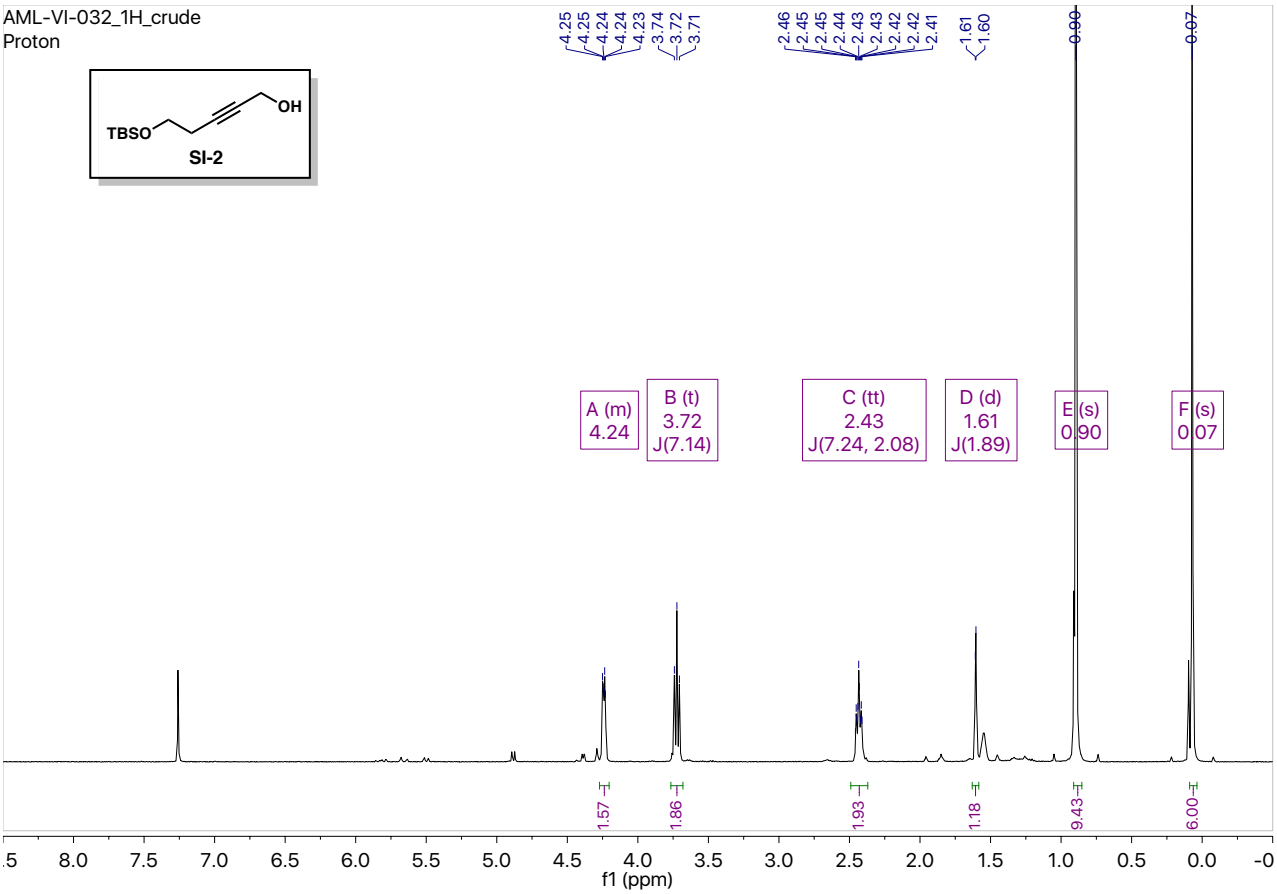
^{1}H NMR (400 MHz, $CDCl_3$) of **tricycle 18**



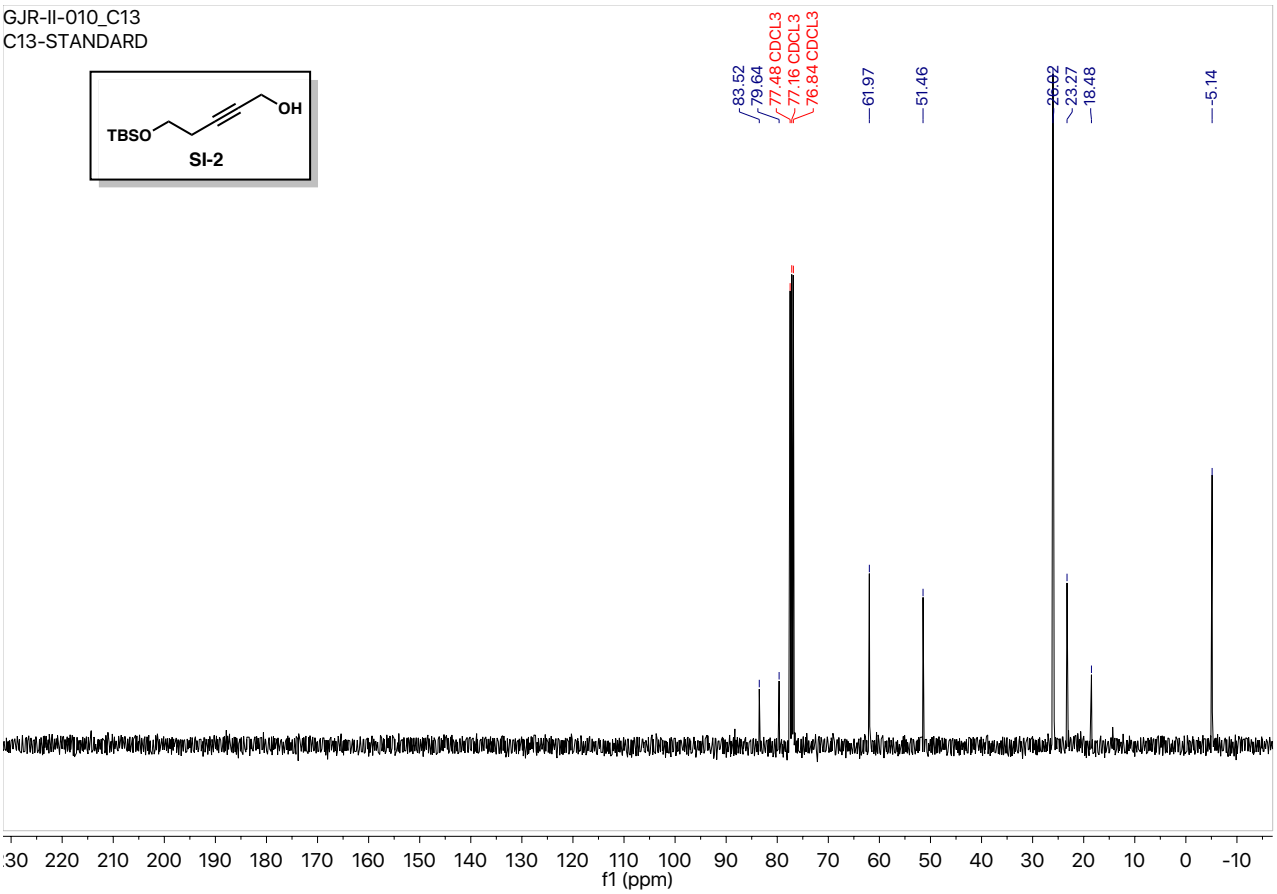
Zoomed in ^{1}H NMR (400 MHz, $CDCl_3$) of **tricycle 18**



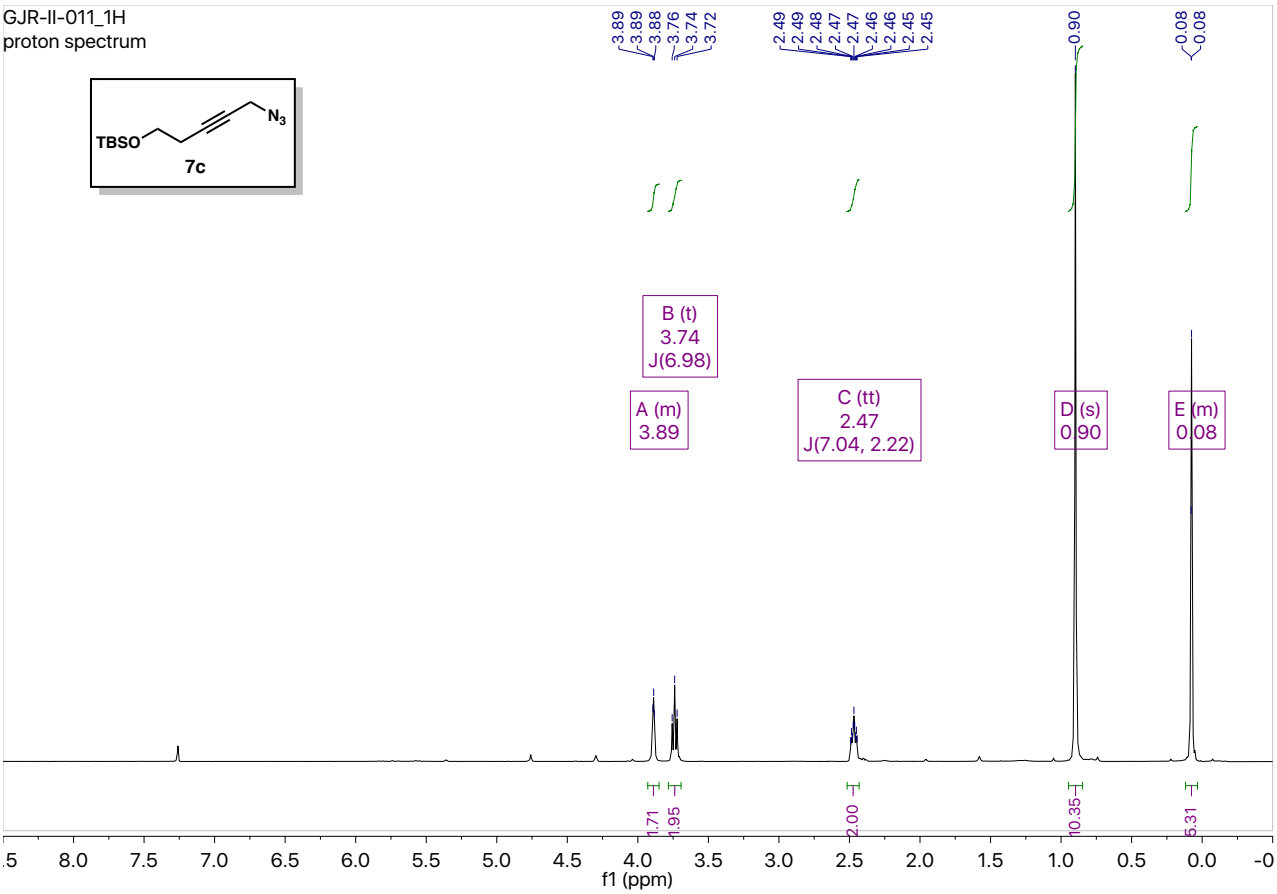
^{1}H NMR (400 MHz, $CDCl_3$) overlay of **tricycle 18** (green) and **tricycle SI-6** (red)



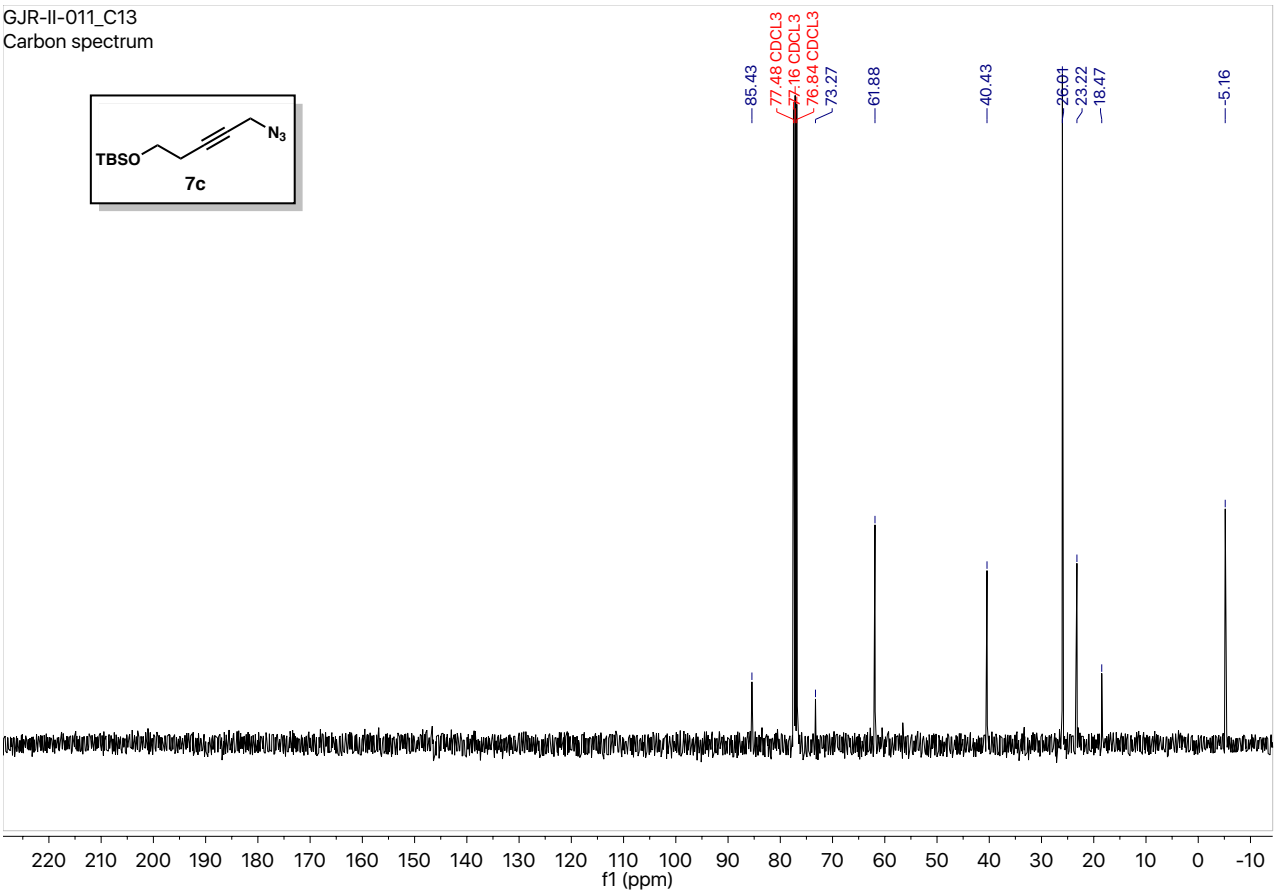
^{1}H NMR (400 MHz, $CDCl_3$) of **propargylic alcohol SI-2**



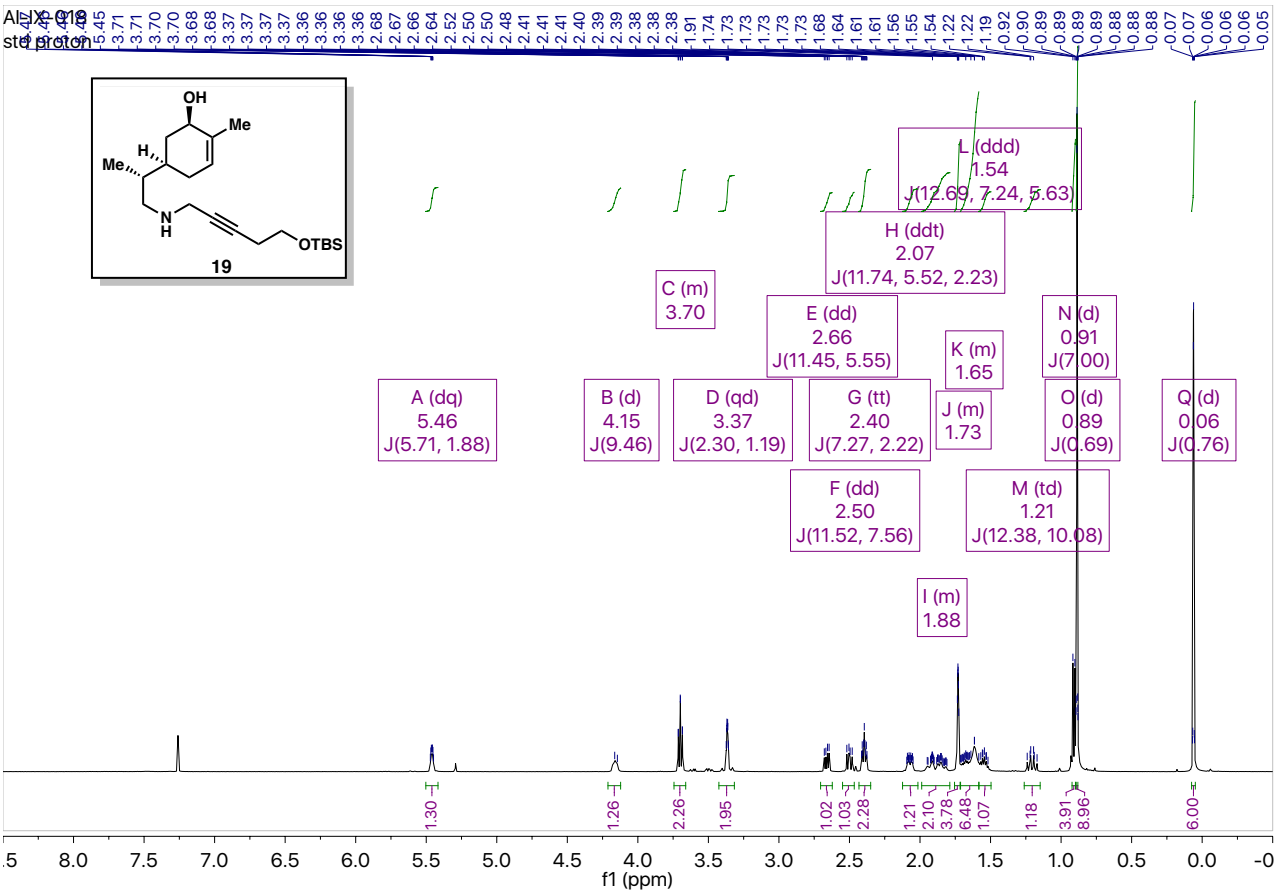
^{13}C NMR (101 MHz, $CDCl_3$) of **propargylic alcohol SI-2**



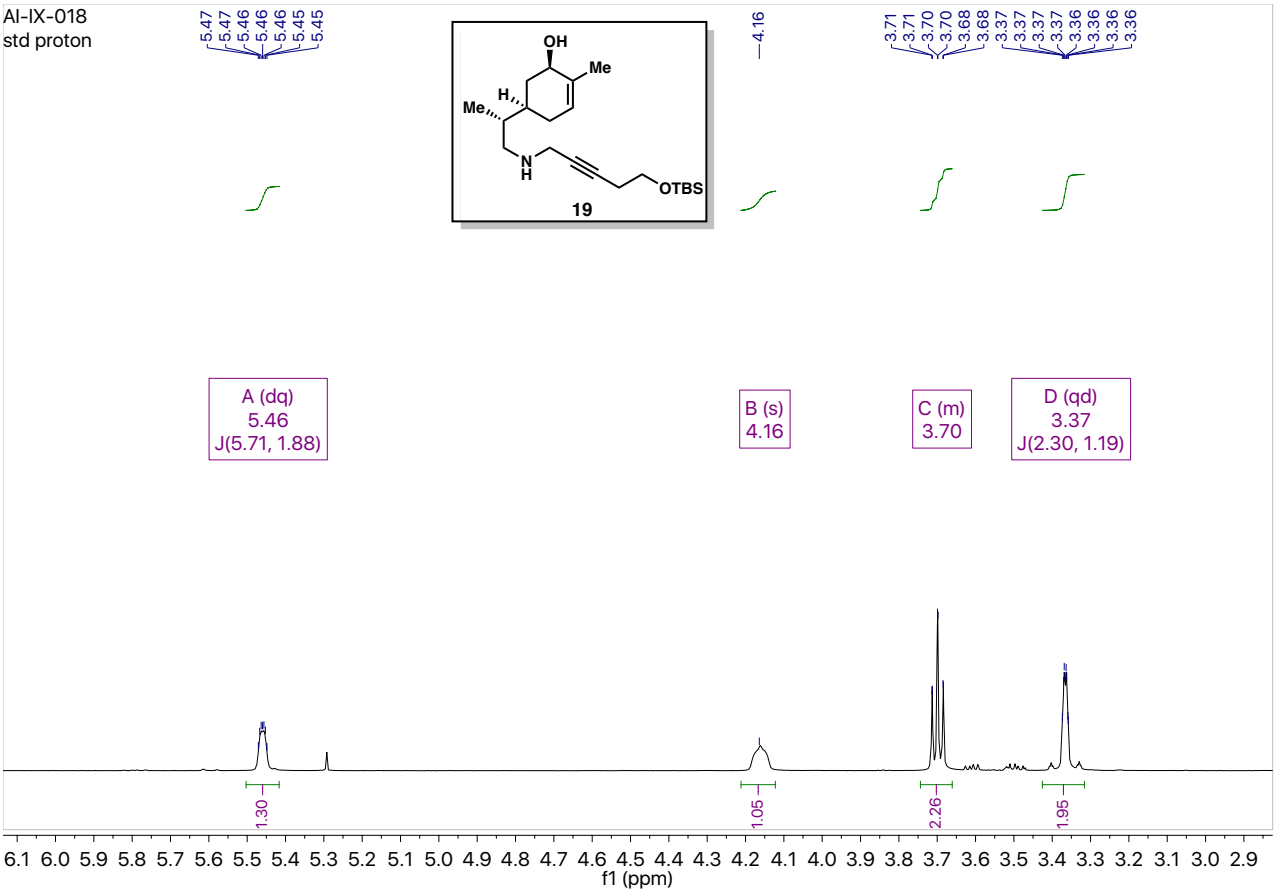
^{1}H NMR (400 MHz, $CDCl_3$) of **propargylic azide 7c**



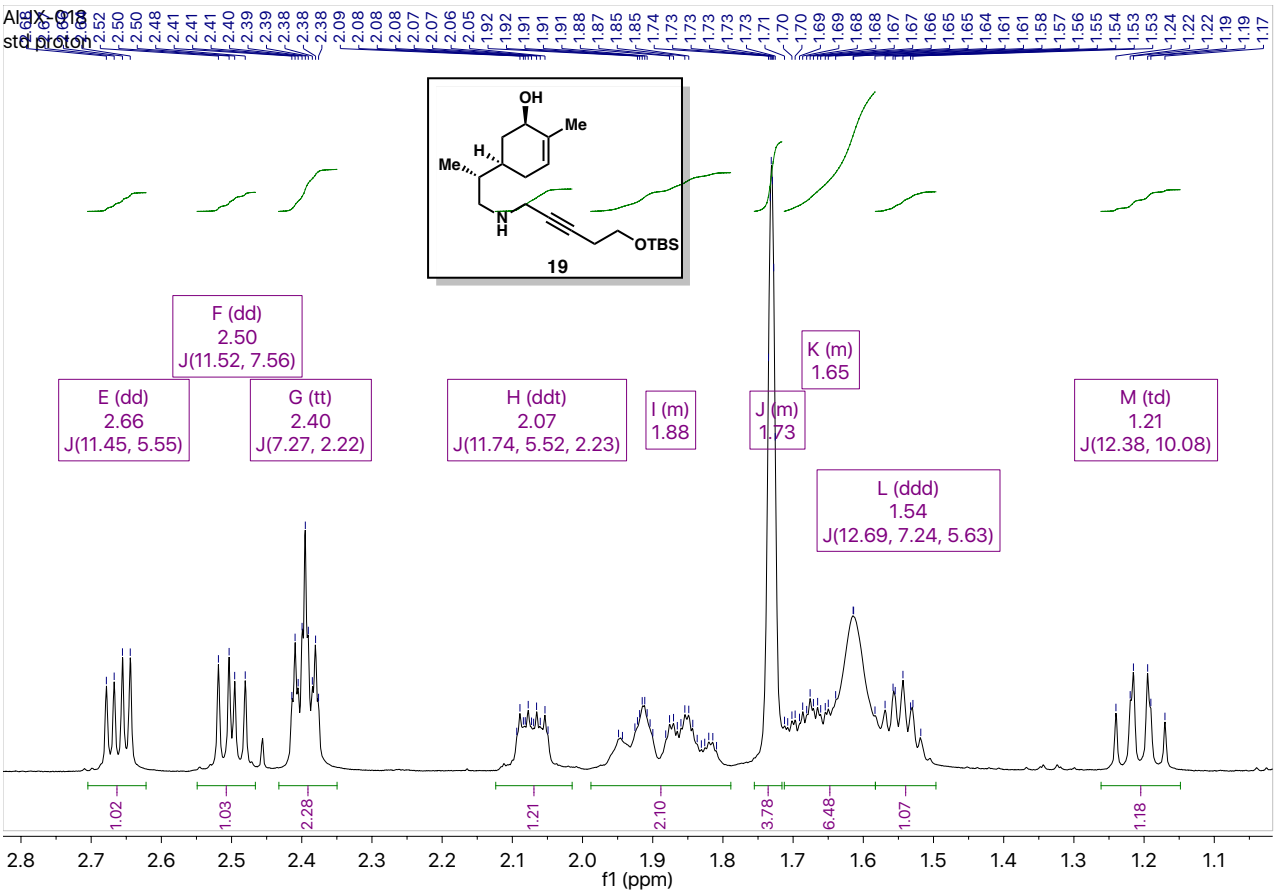
^{13}C NMR (101 MHz, $CDCl_3$) of **propargylic azide 7c**



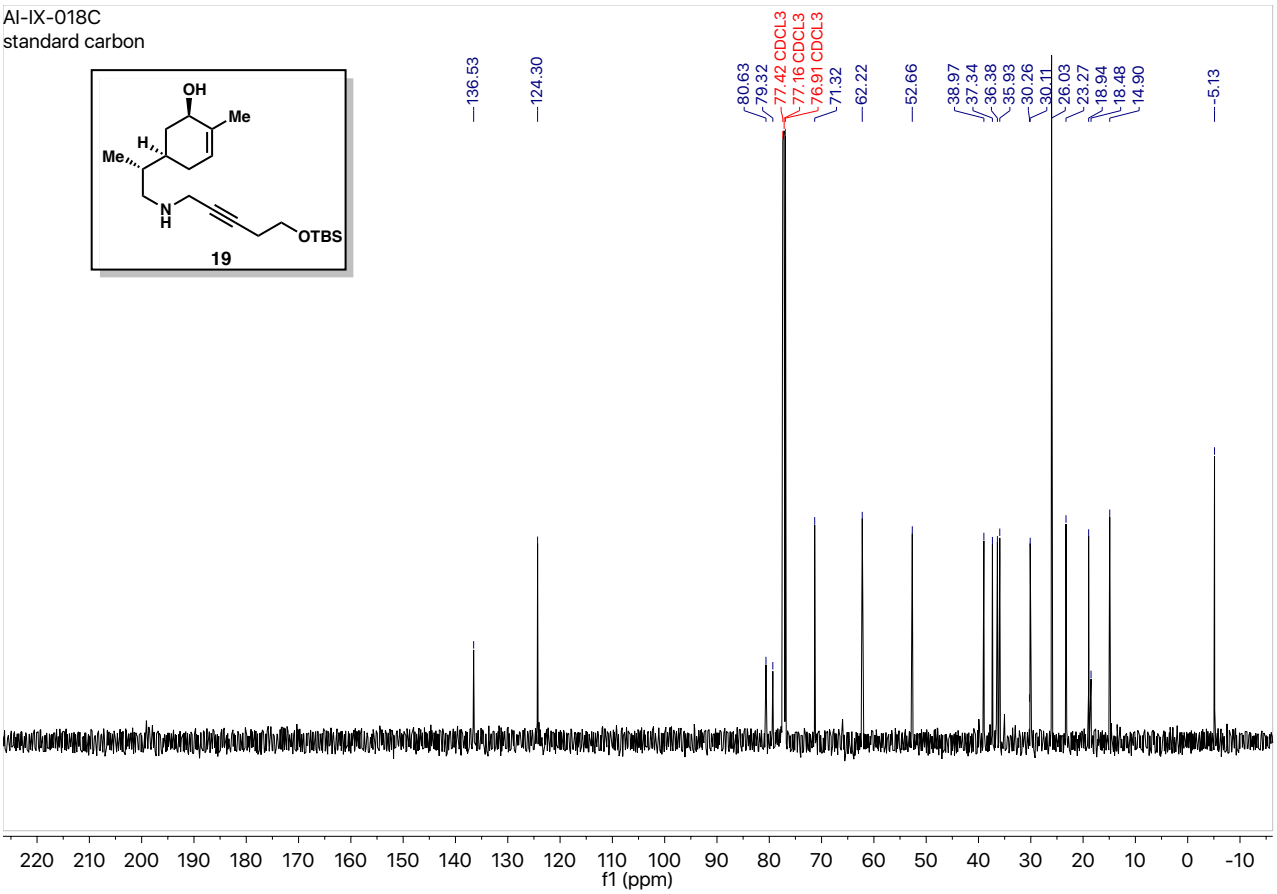
^{1}H NMR (400 MHz, $CDCl_3$) of **allylic alcohol 19**



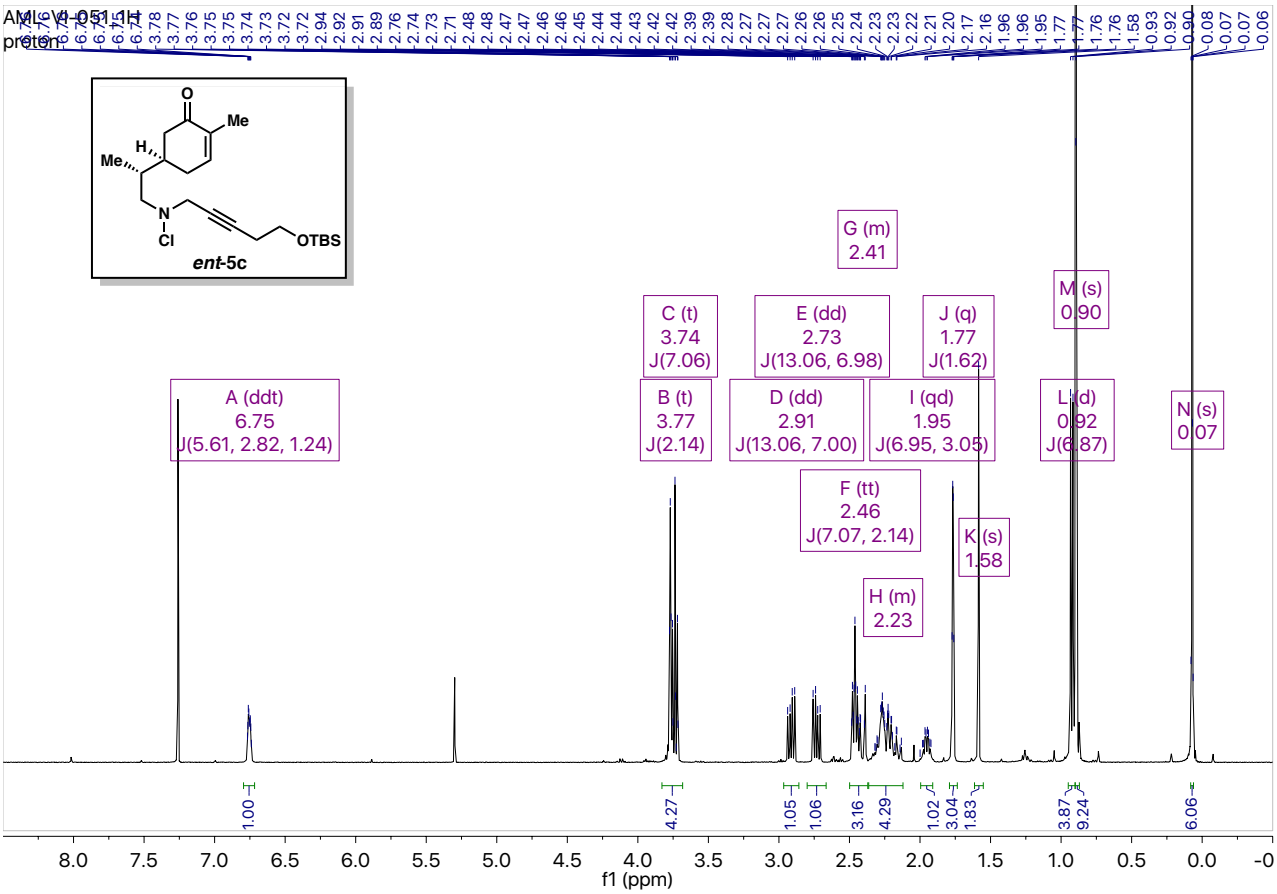
Zoomed in ^{1}H NMR (400 MHz, $CDCl_3$) of **allylic alcohol 19**



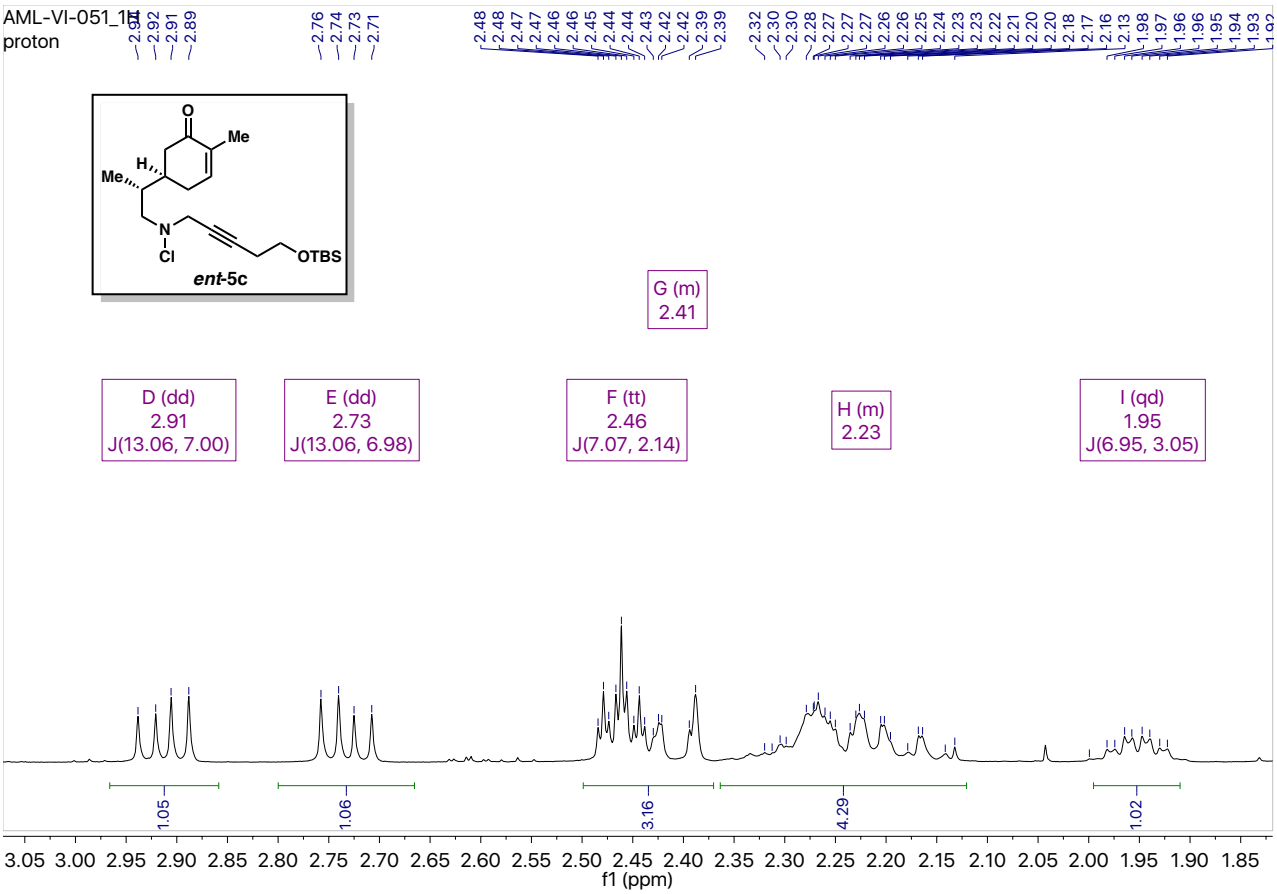
Zoomed in ^{1}H NMR (400 MHz, $CDCl_3$) of **allylic alcohol 19**



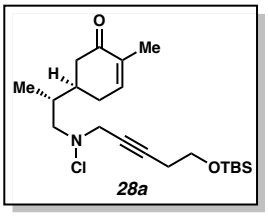
^{13}C NMR (121 MHz, $CDCl_3$) of **allylic alcohol 19**

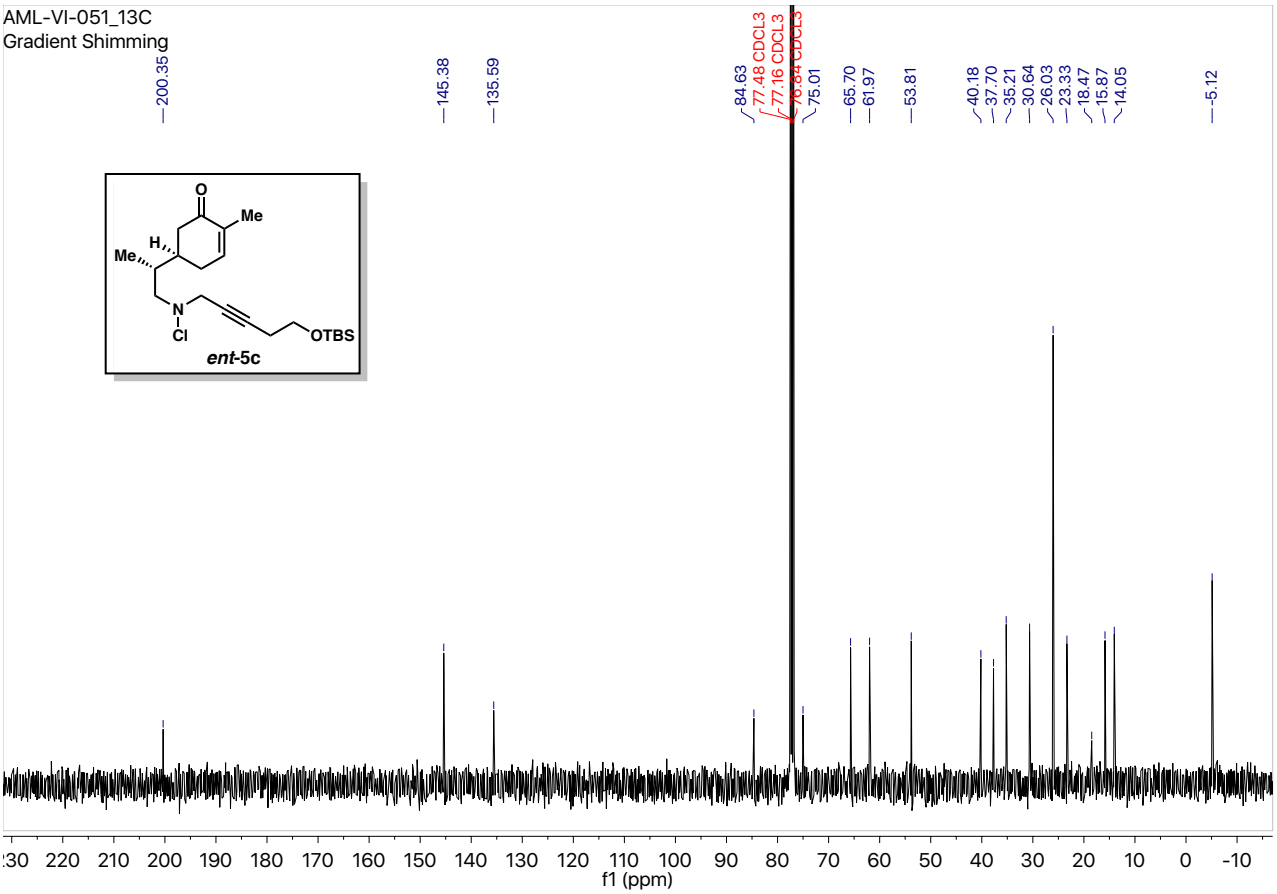


^{1}H NMR (400 MHz, $CDCl_3$) of ***N*-chloroamine *ent*-5c**

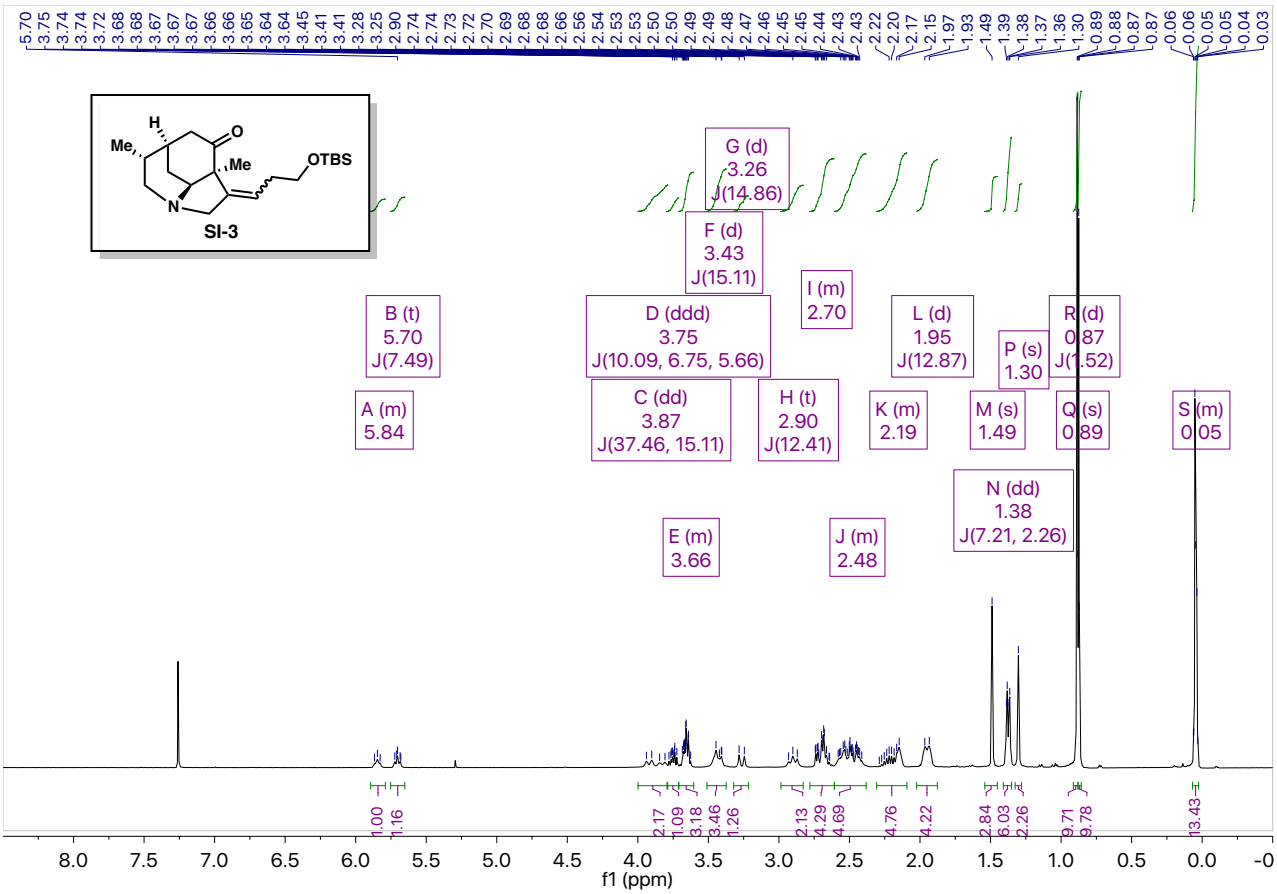


Zoomed in ^{1}H NMR (400 MHz, $CDCl_3$) of ***N*-chloroamine *ent*-5c**

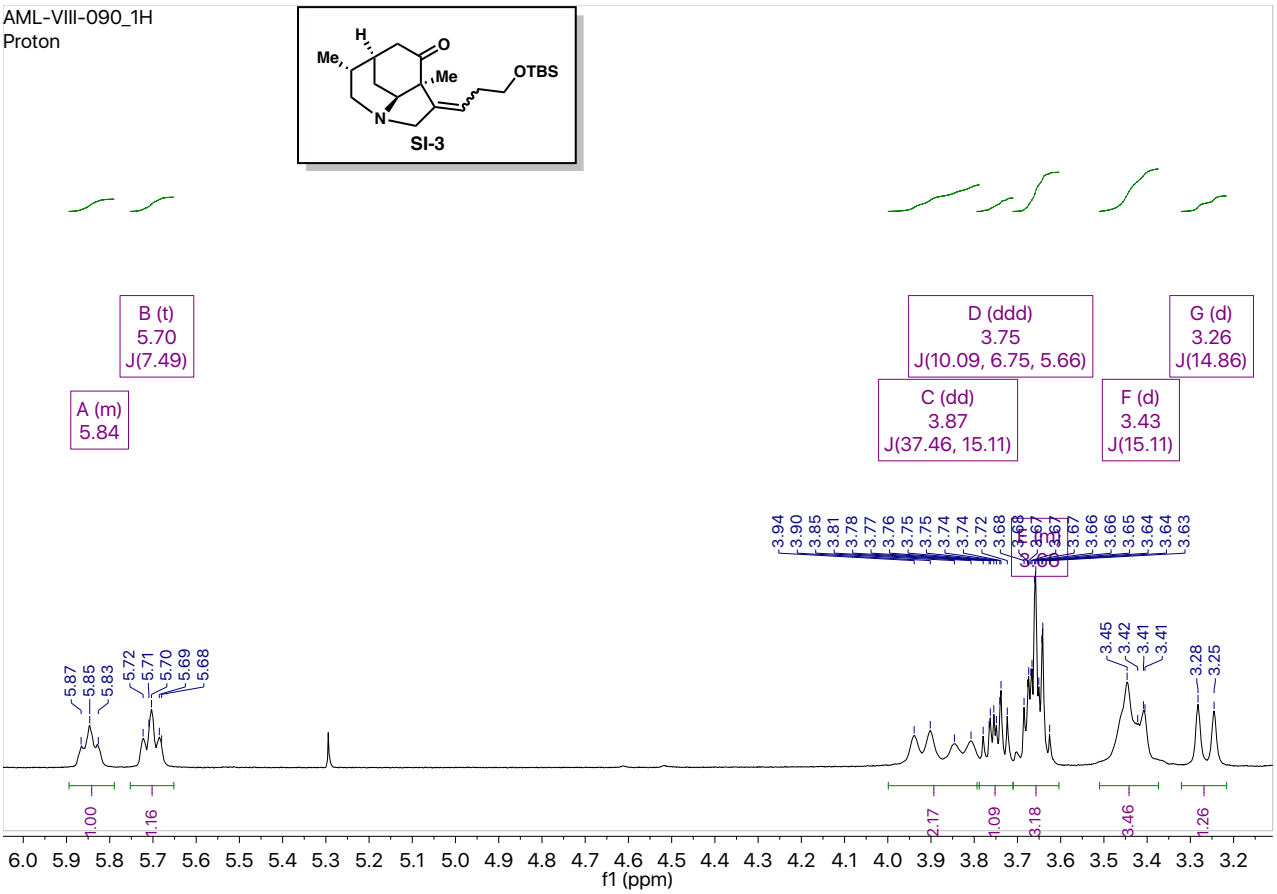




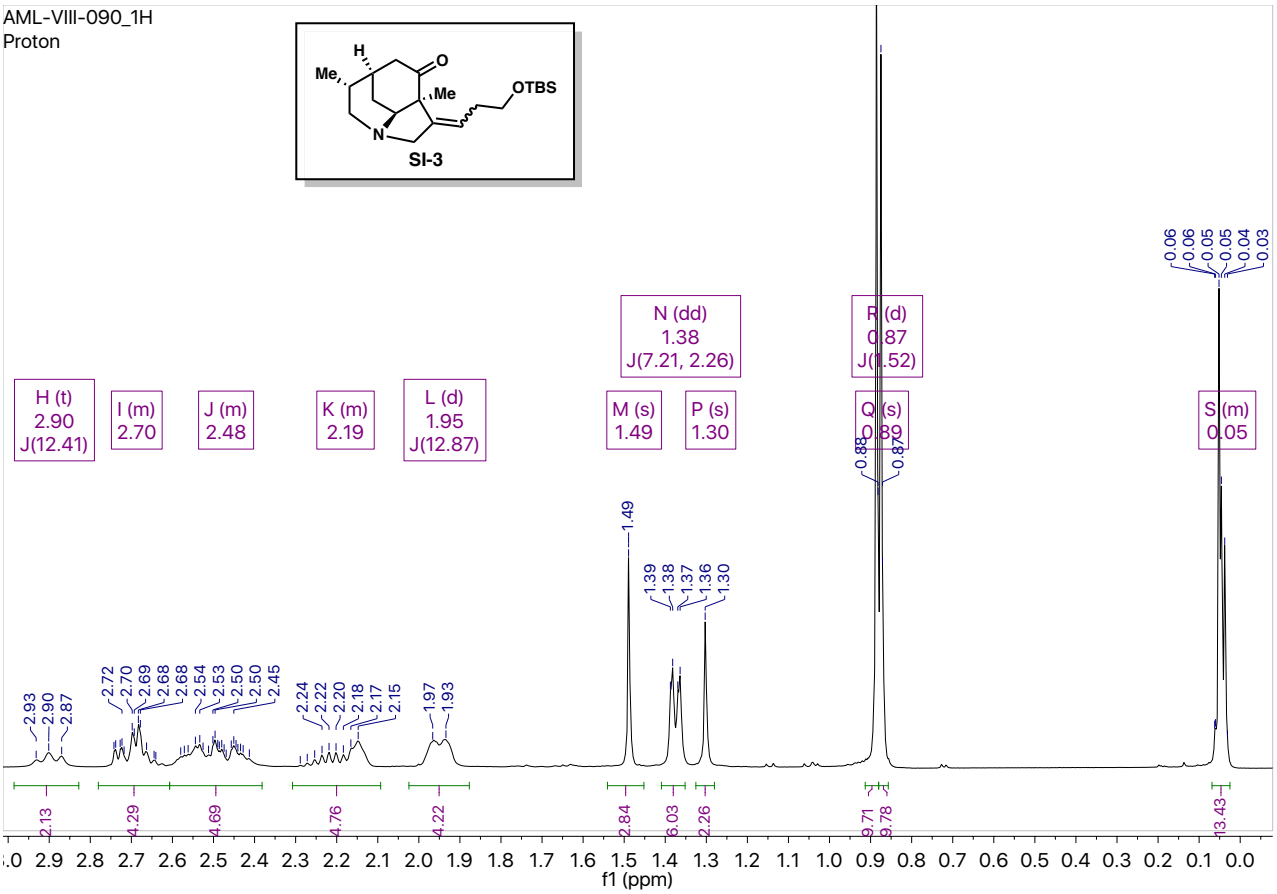
^{13}C NMR (101 MHz, $CDCl_3$) of ***N*-chloroamine *ent*-5c**



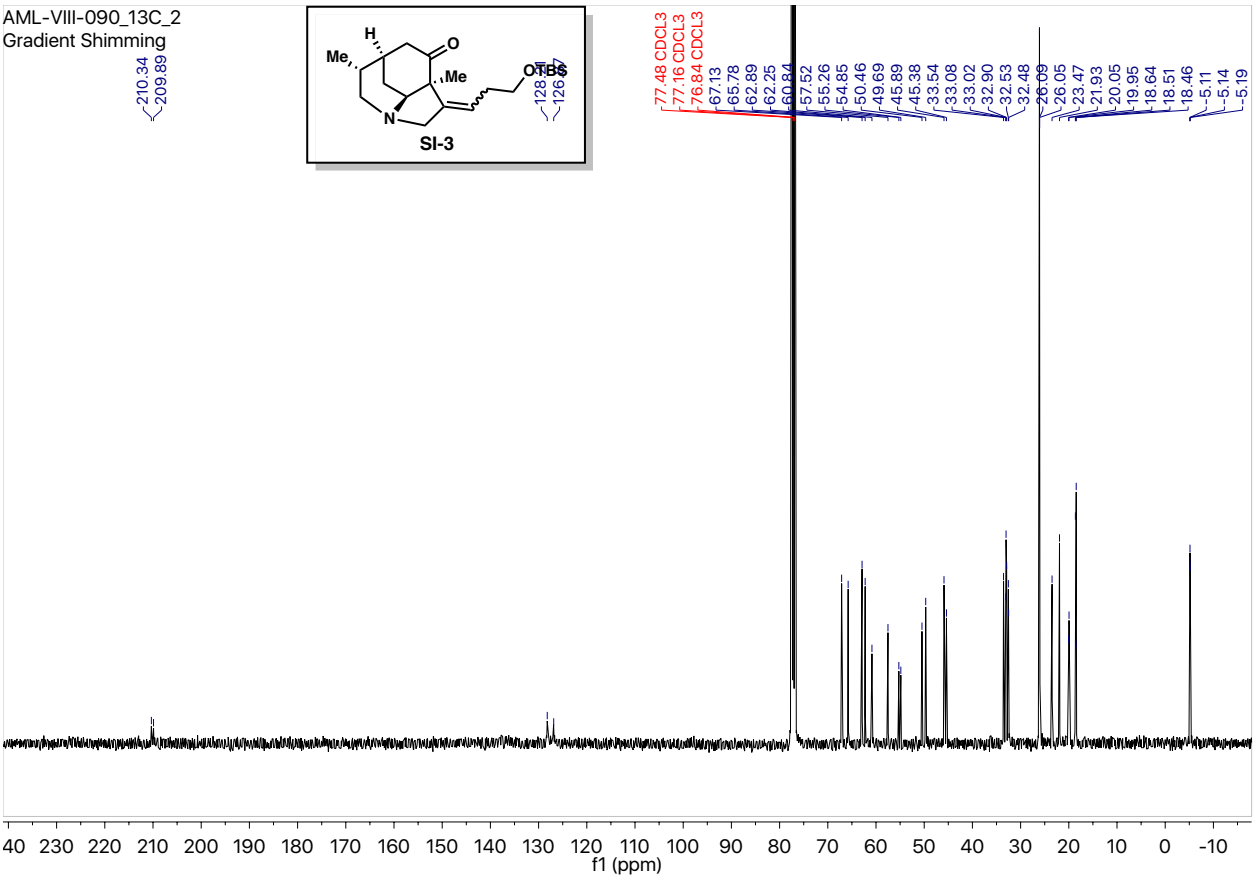
^{1}H NMR (400 MHz, $CDCl_3$) of **tricycle SI-3**



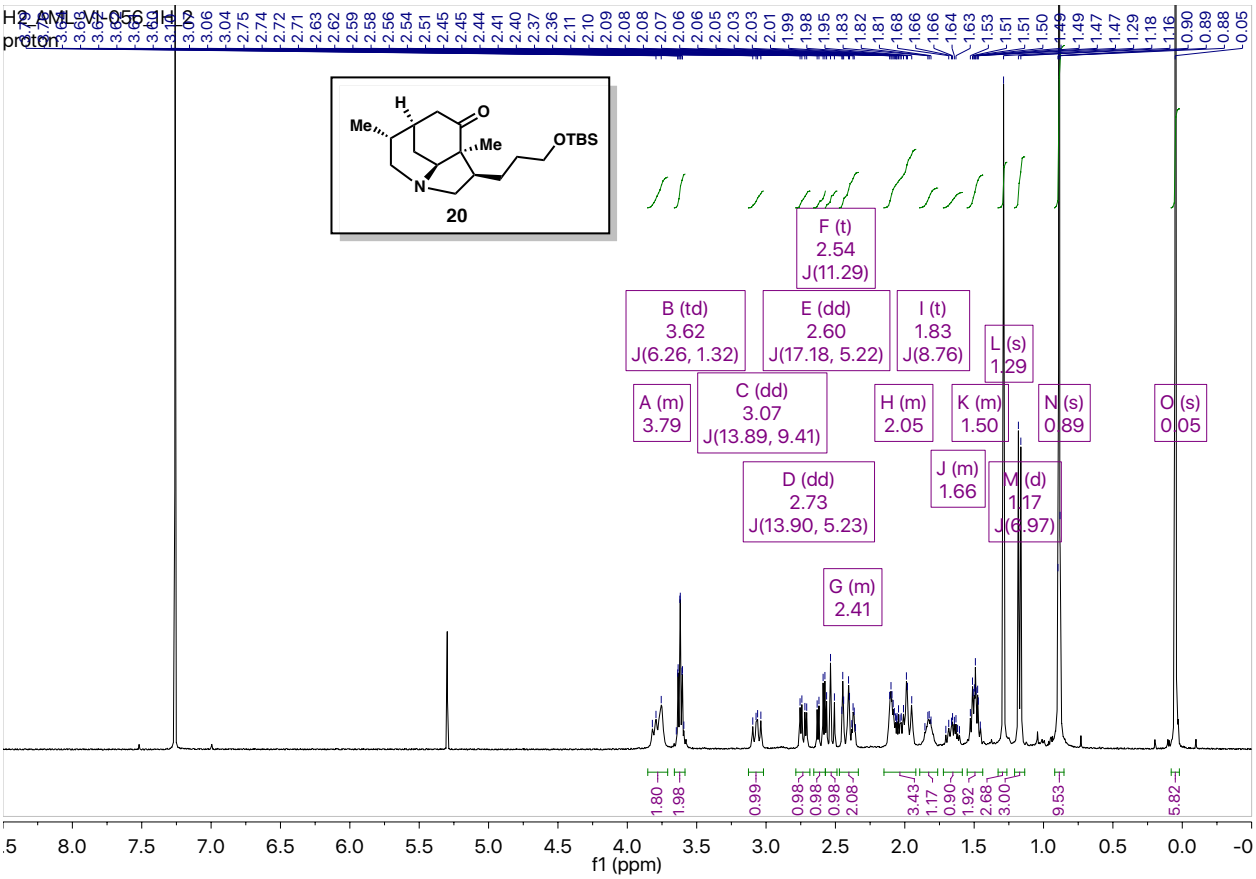
Zoomed in ^{1}H NMR (400 MHz, $CDCl_3$) of **tricycle SI-3**



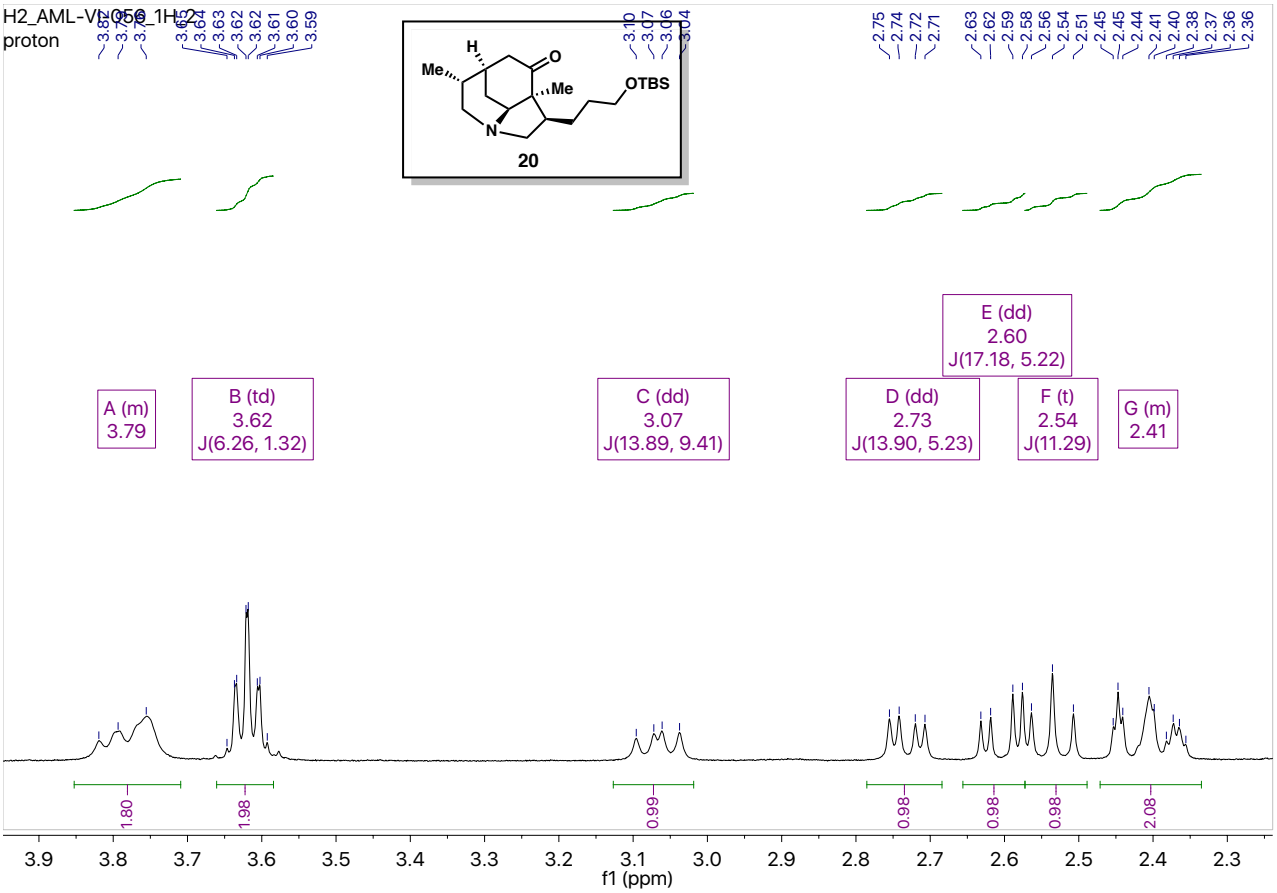
Zoomed in ^{1}H NMR (400 MHz, $CDCl_3$) of **tricycle SI-3**



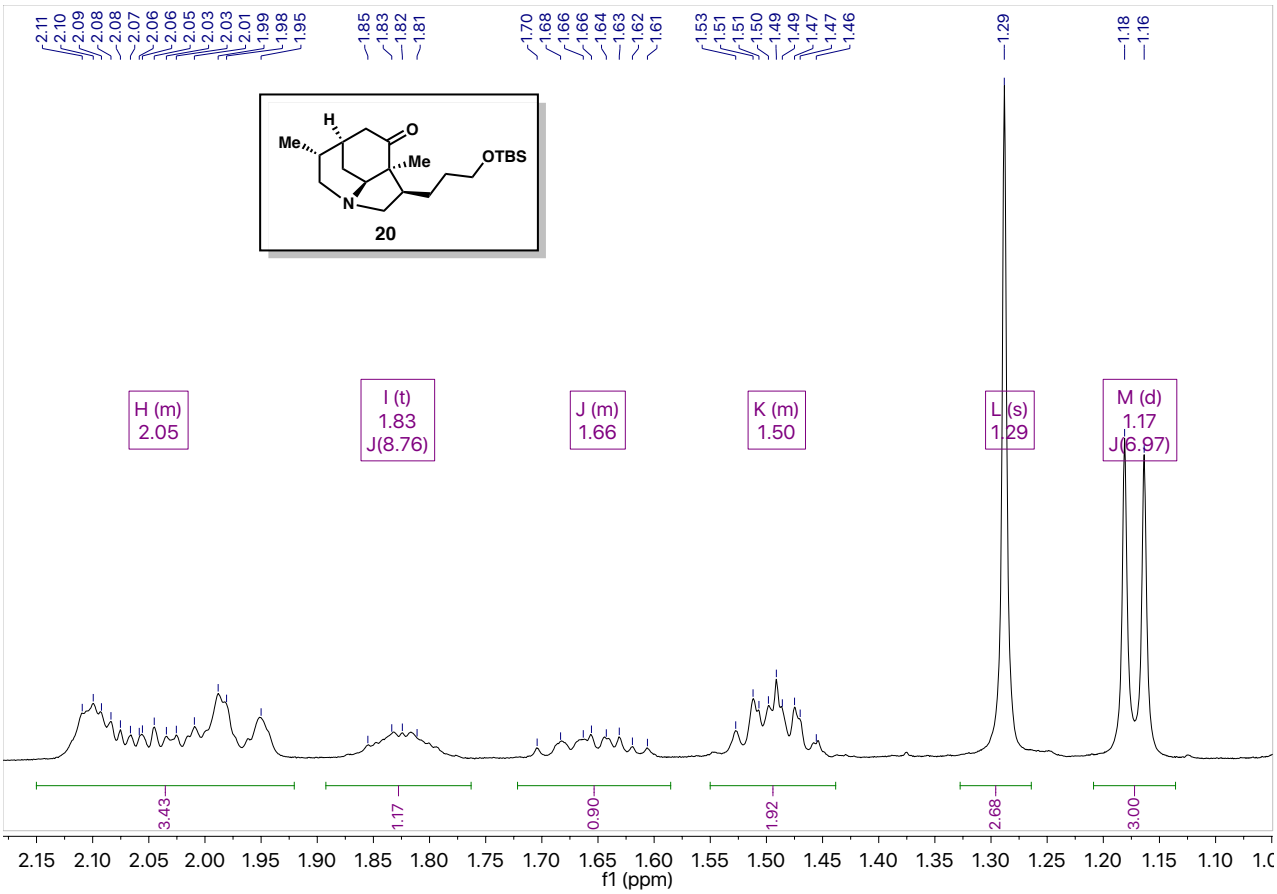
^{13}C NMR (101 MHz, $CDCl_3$) of **tricycle SI-3**



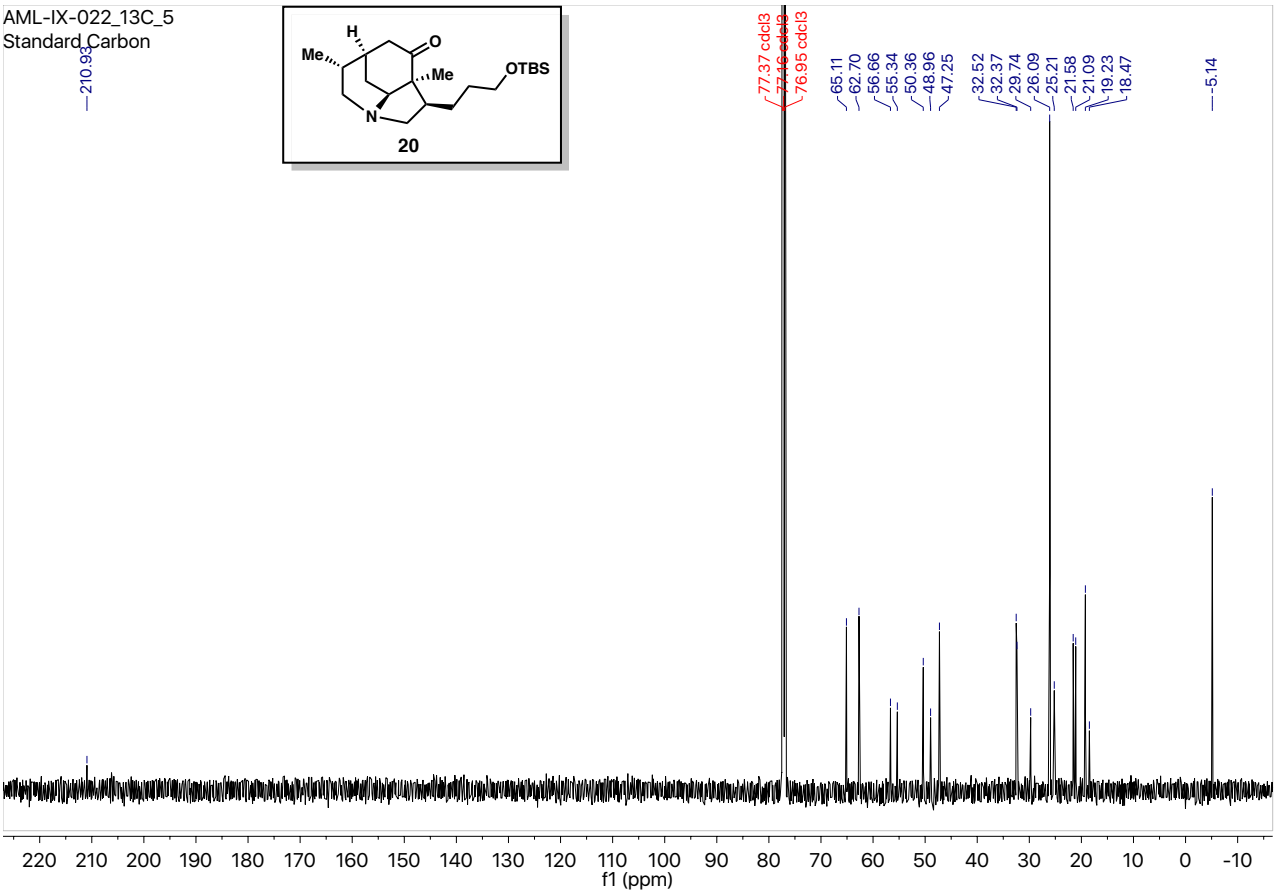
^{1}H NMR (400 MHz, $CDCl_3$) of **ketone 20**



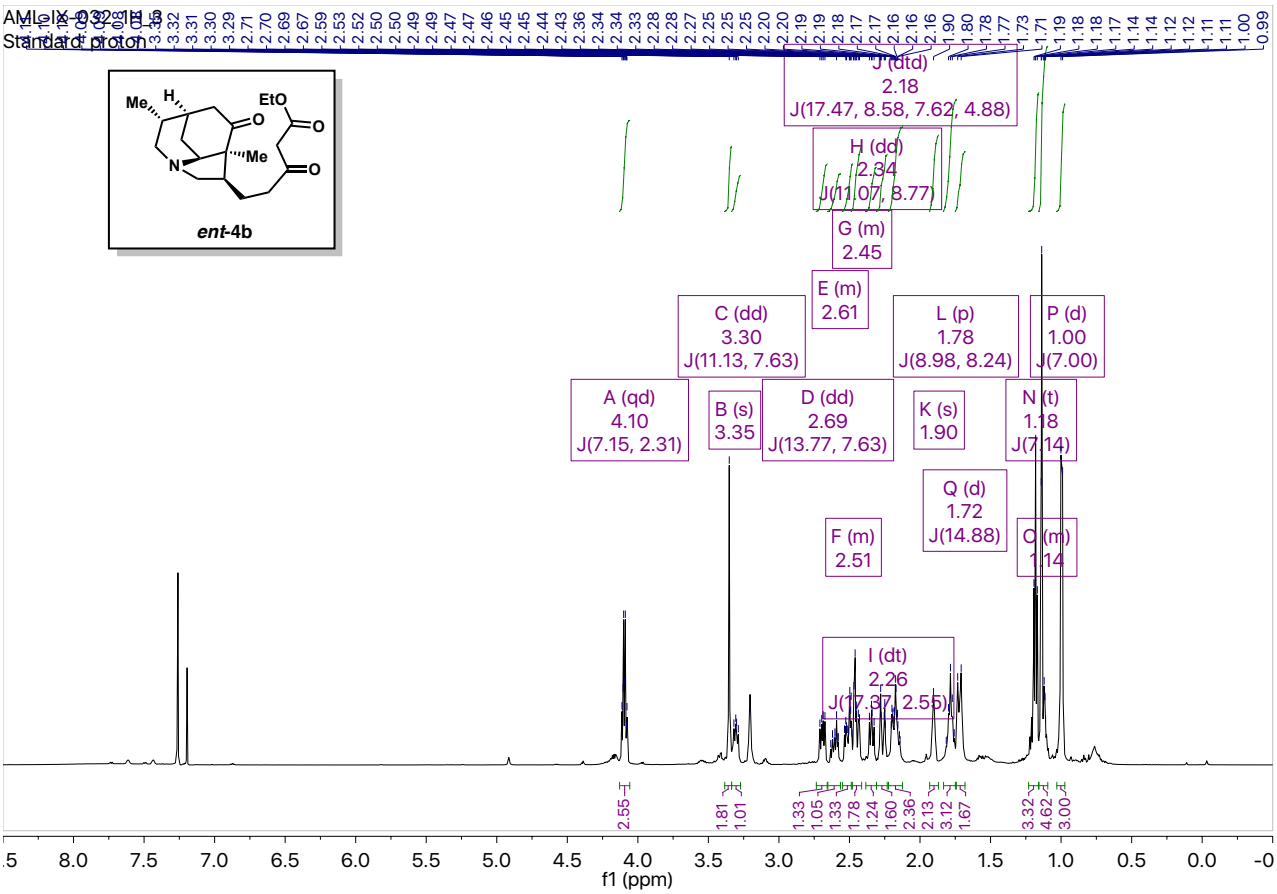
Zoomed in ^{1}H NMR (400 MHz, $CDCl_3$) of **ketone 20**



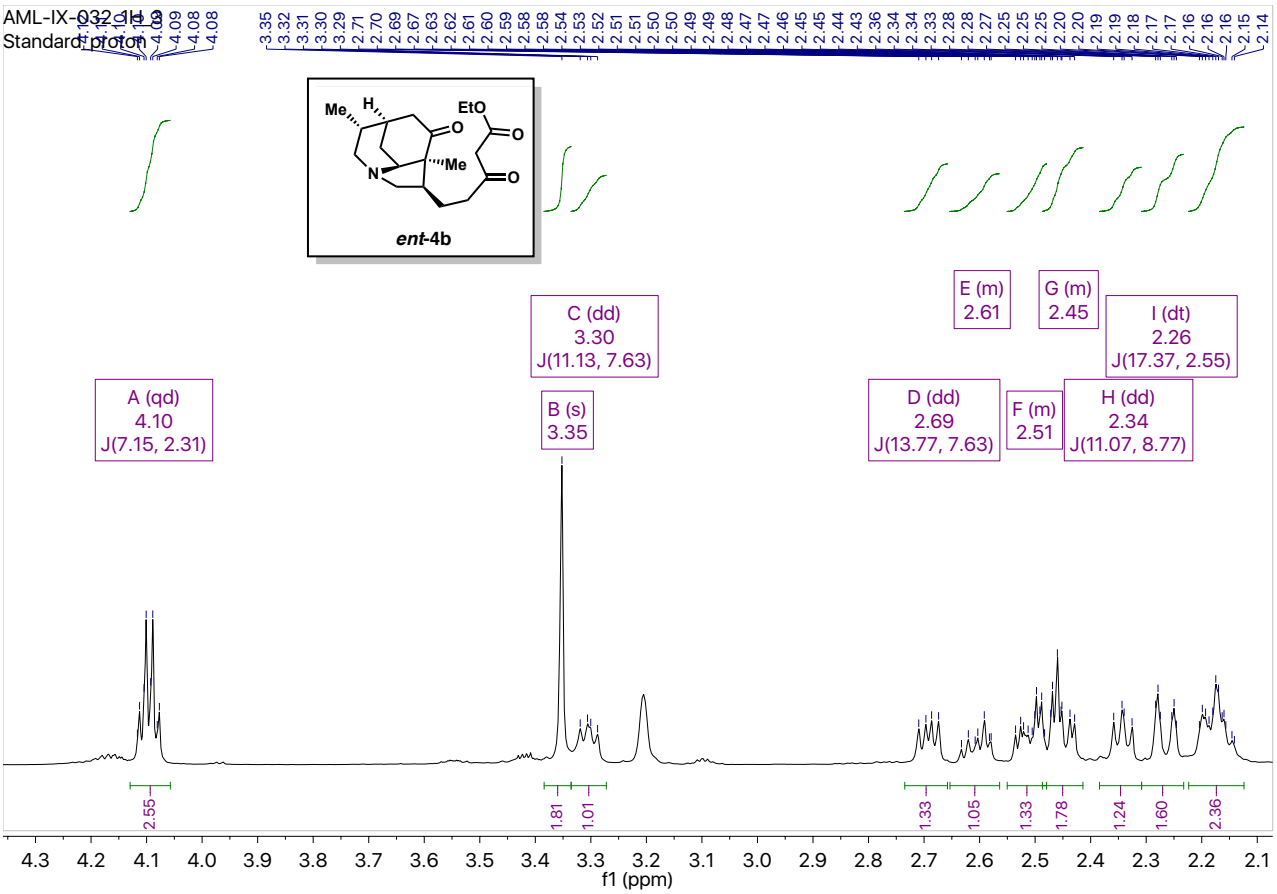
Zoomed in ^{1}H NMR (400 MHz, $CDCl_3$) of **ketone 20**



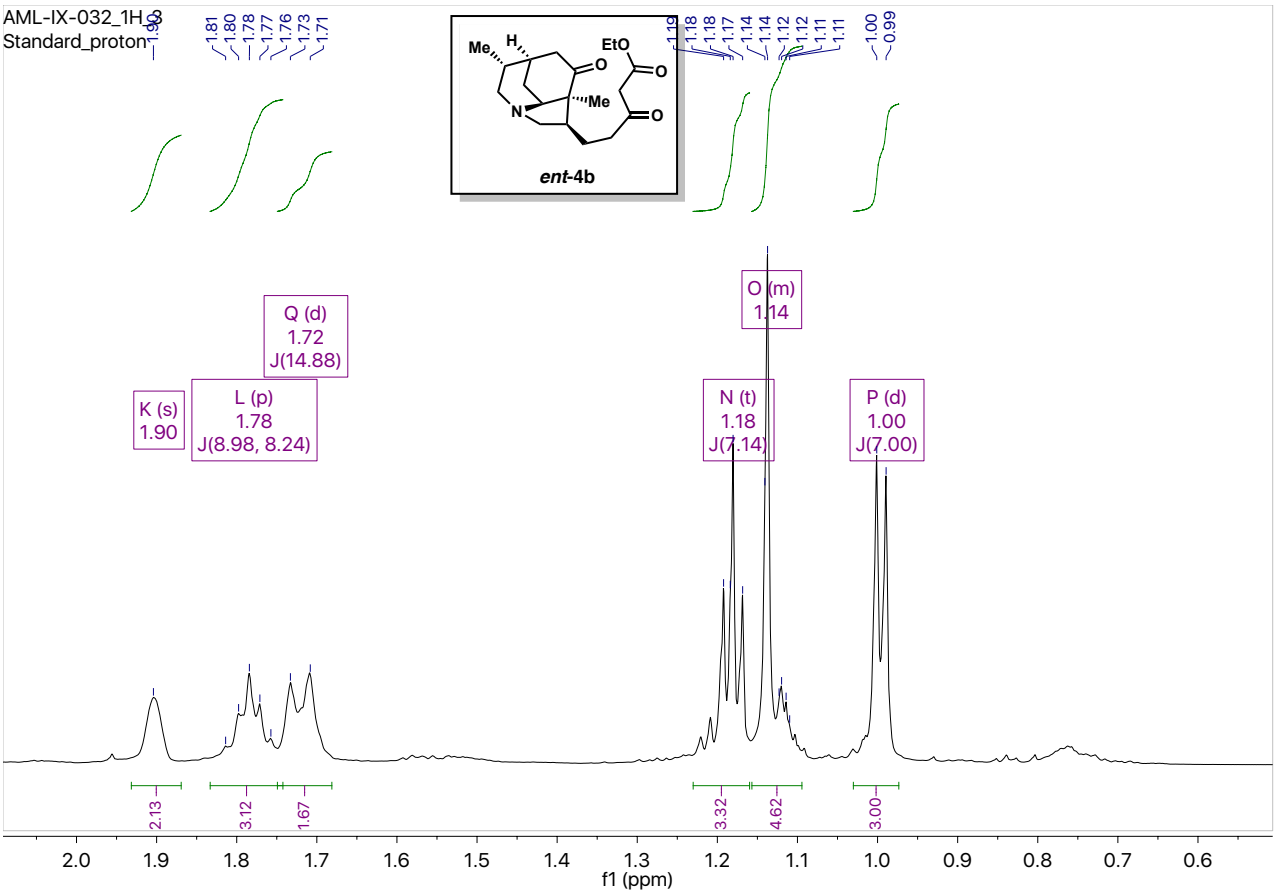
^{13}C NMR (151 MHz, $CDCl_3$) of **ketone 20**



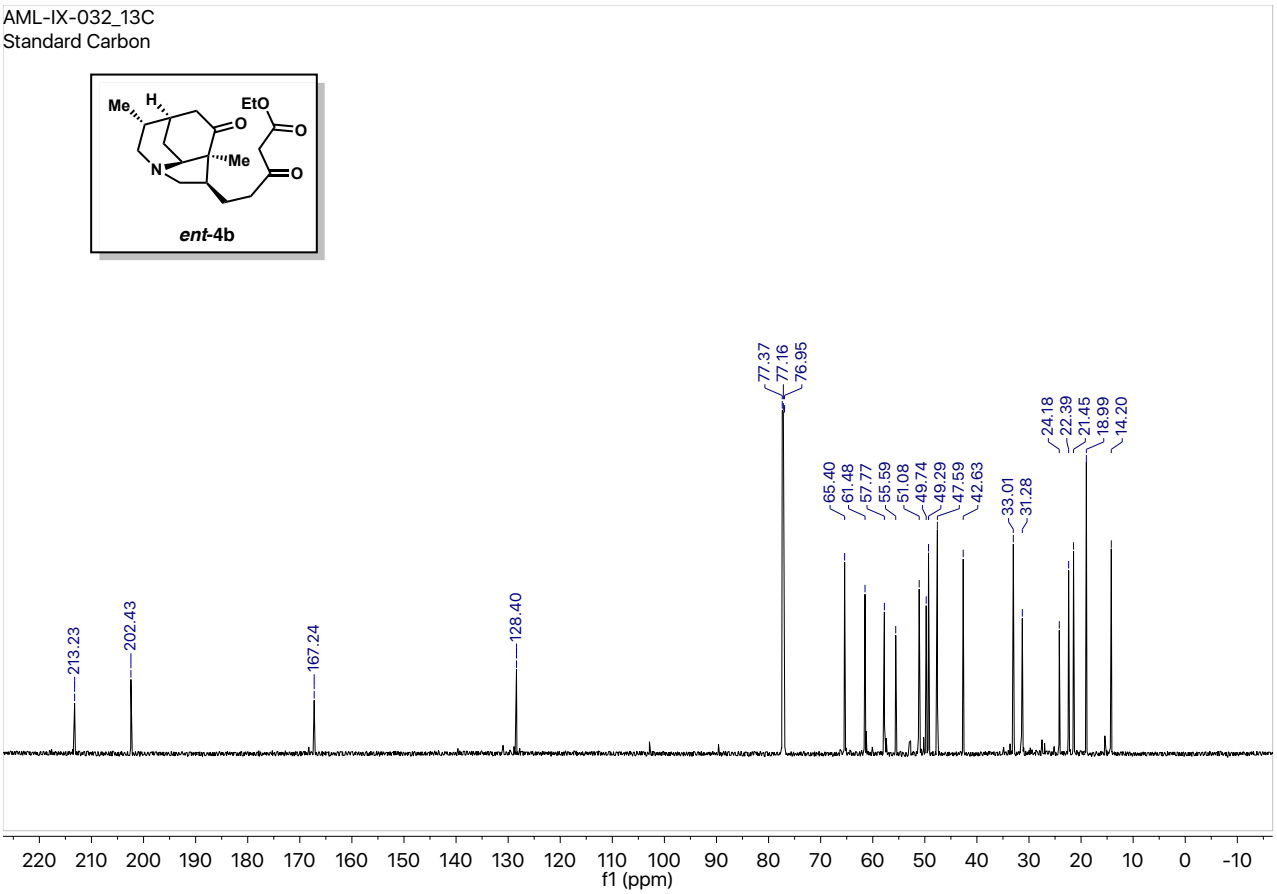
^{1}H NMR (600 MHz, $CDCl_3$) of **β–keto ester *ent*-4b**



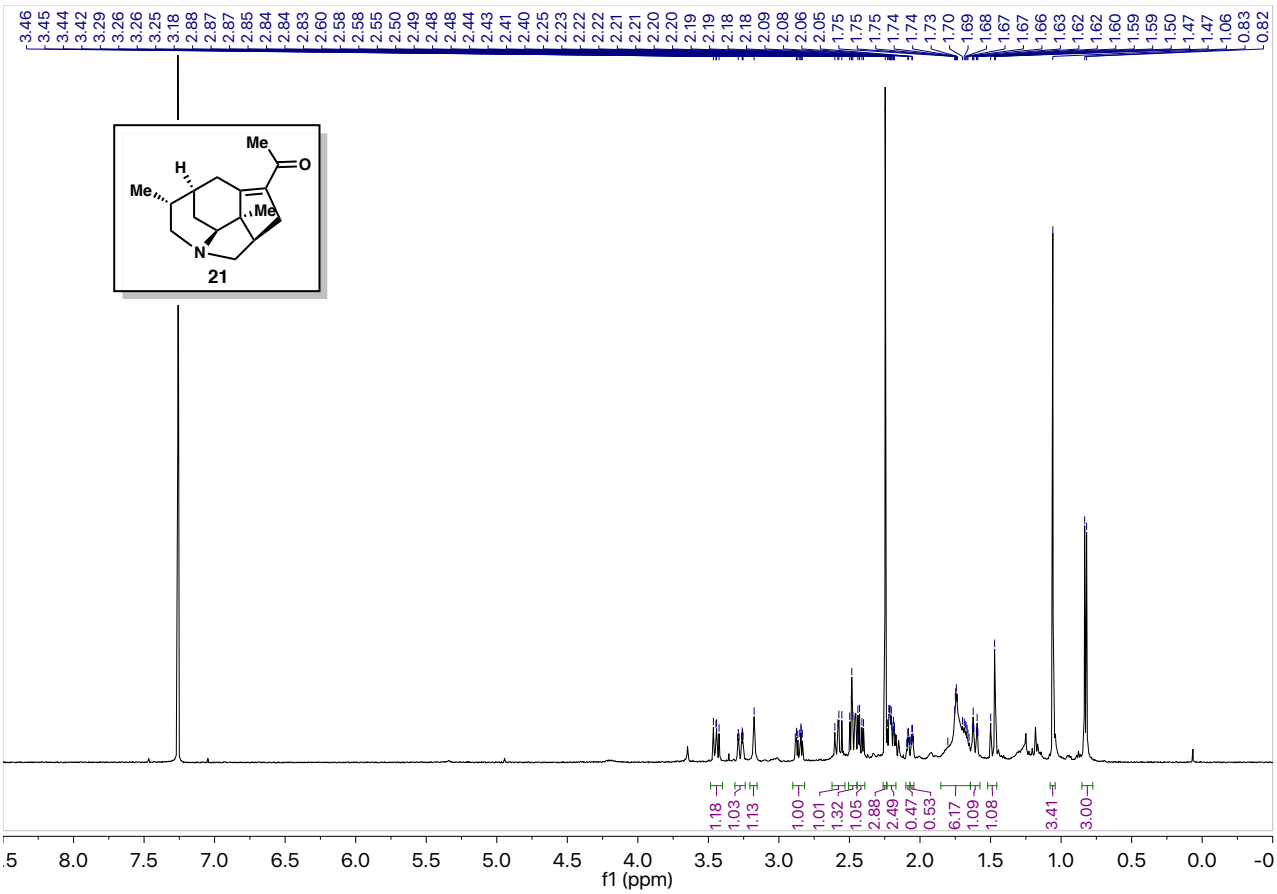
Zoomed in ^{1}H NMR (600 MHz, $CDCl_3$) of **β–keto ester *ent*-4b**



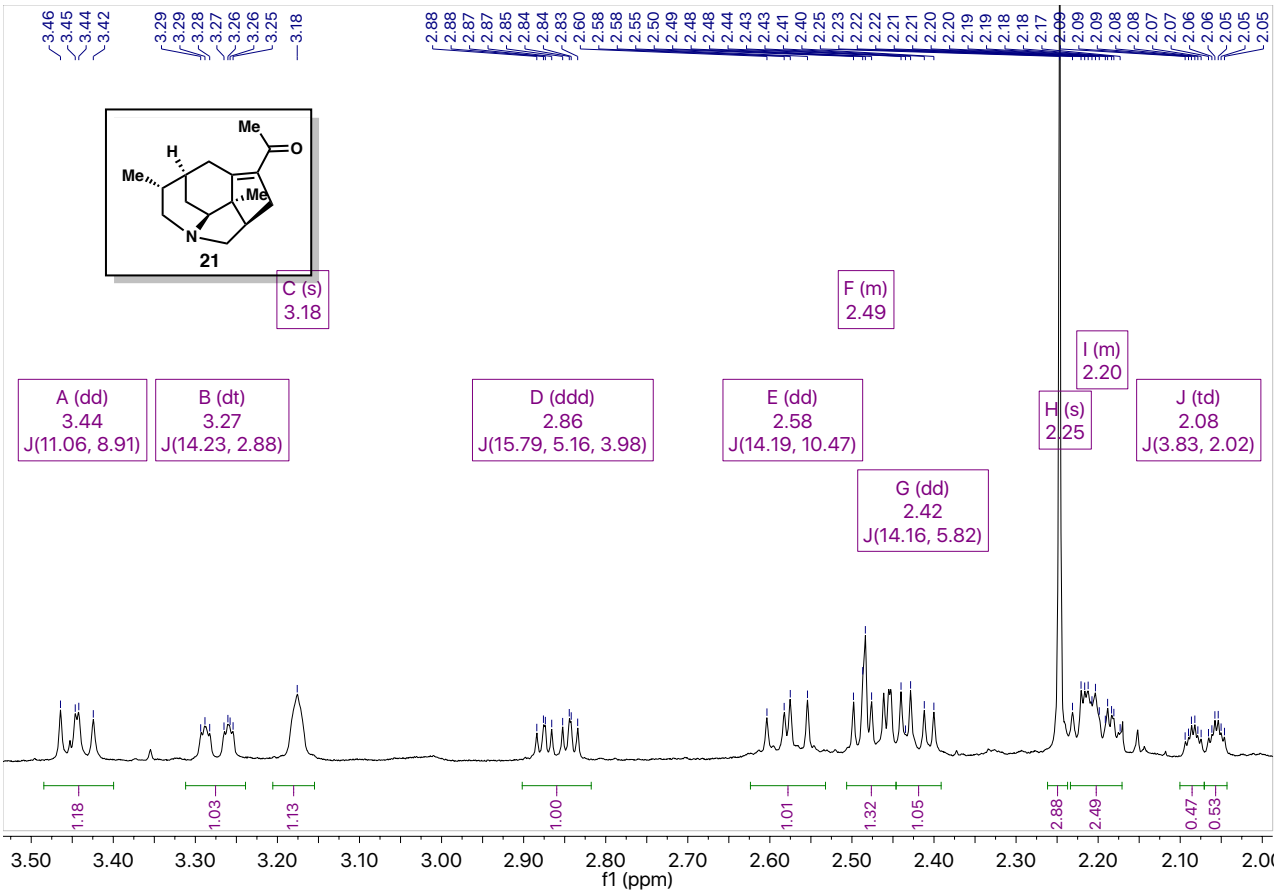
Zoomed in ^{1}H NMR (600 MHz, $CDCl_3$) of **β–keto ester *ent*-4b**



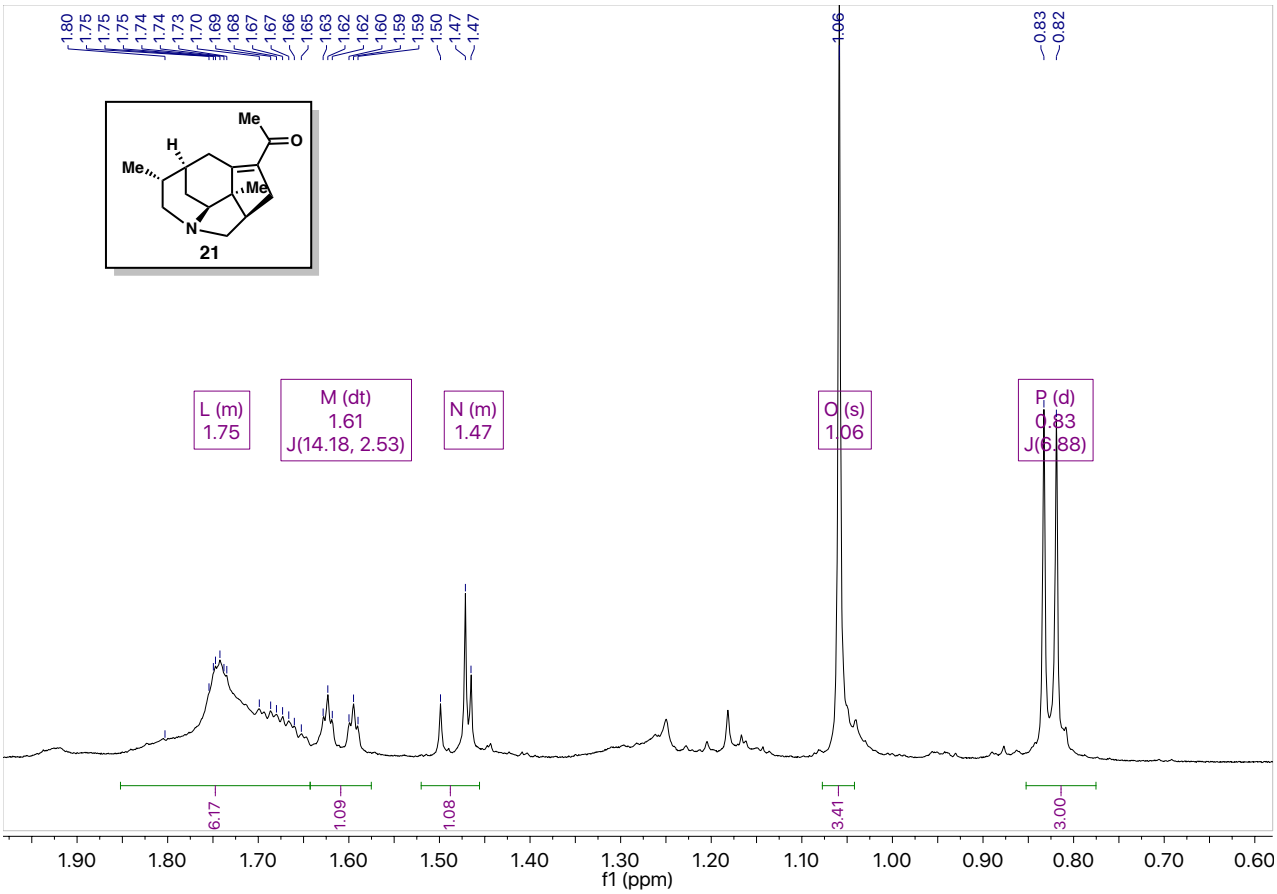
^{13}C NMR (151 MHz, $CDCl_3$) of **β–keto ester *ent*-4b**



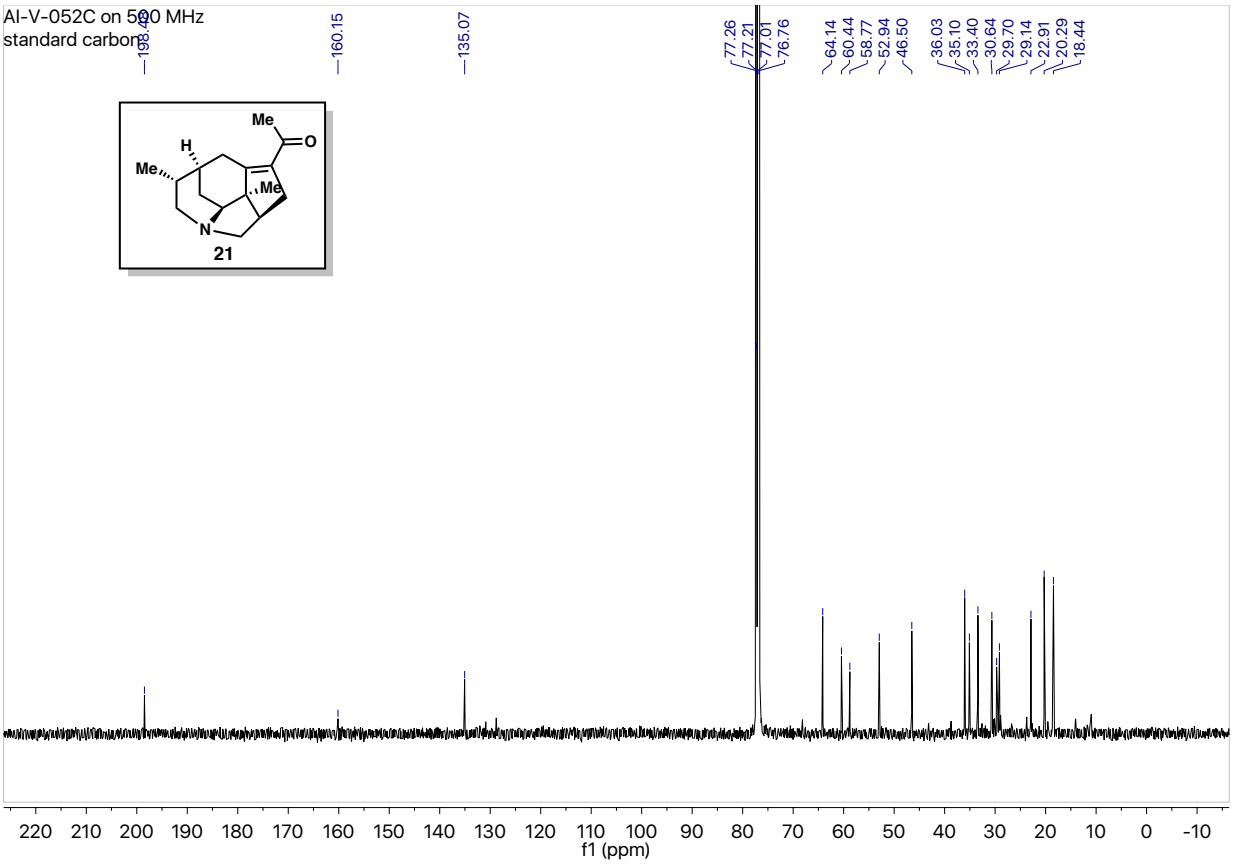
^{1}H NMR (600 MHz, $CDCl_3$) of **tetracycle 21**



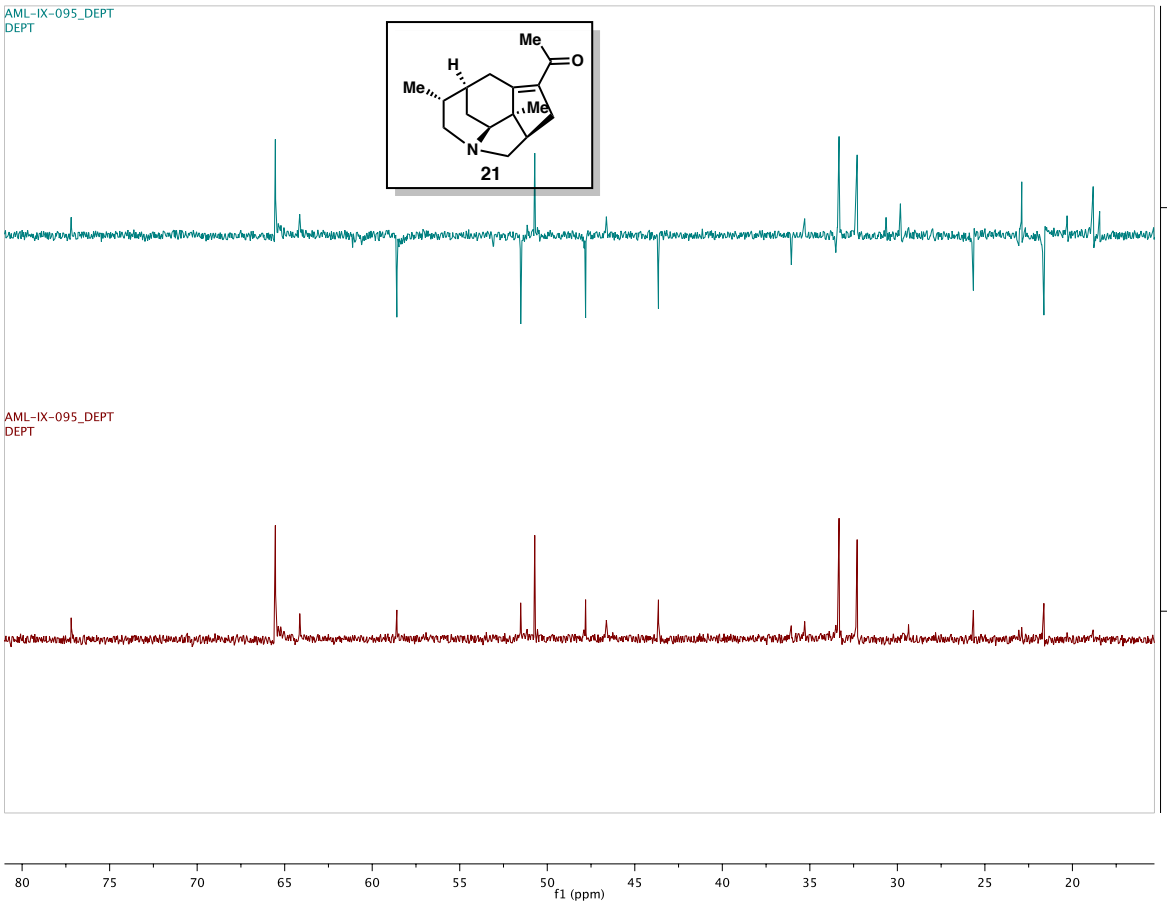
Zoomed in ^{1}H NMR (600 MHz, $CDCl_3$) of **tetracycle 21**



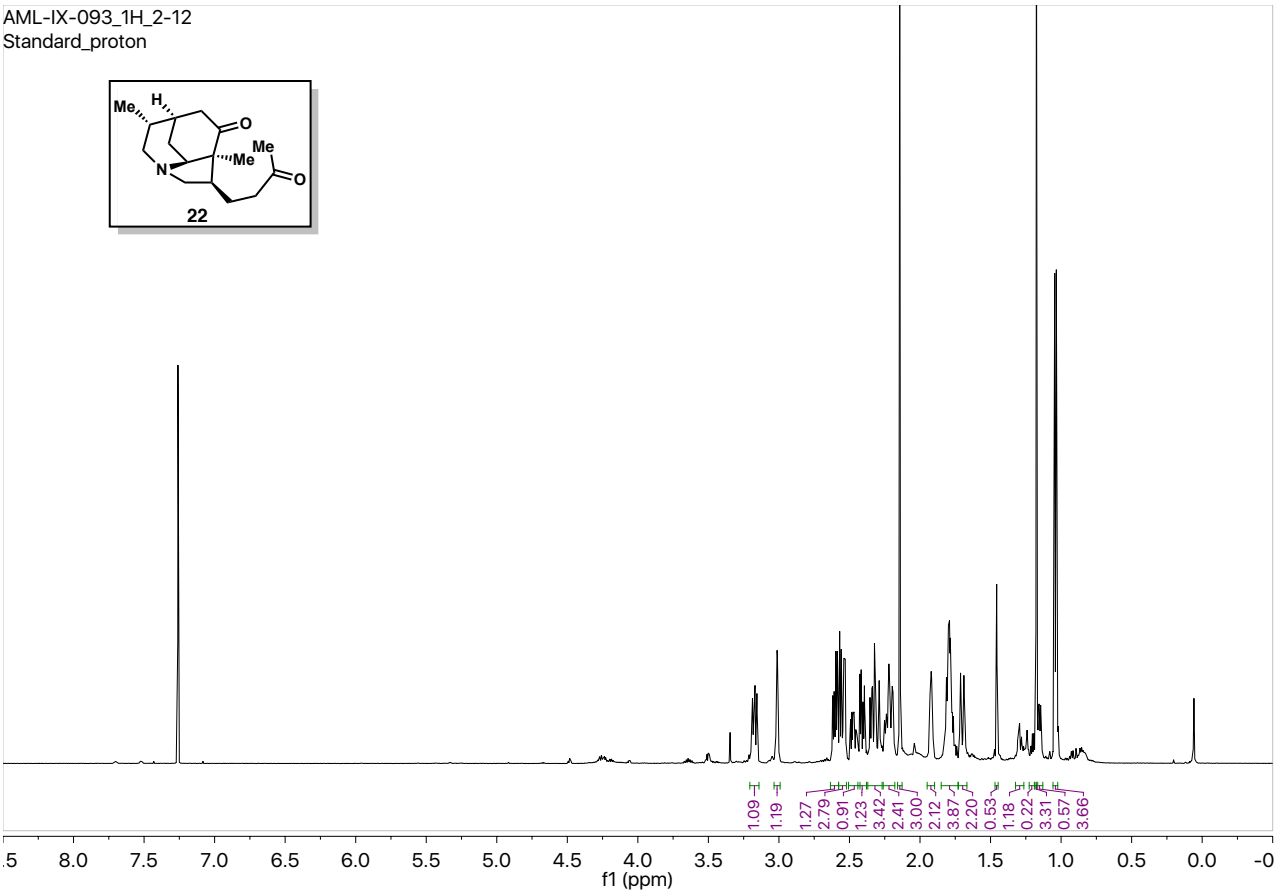
Zoomed in ^{1}H NMR (600 MHz, $CDCl_3$) of **tetracycle 21**



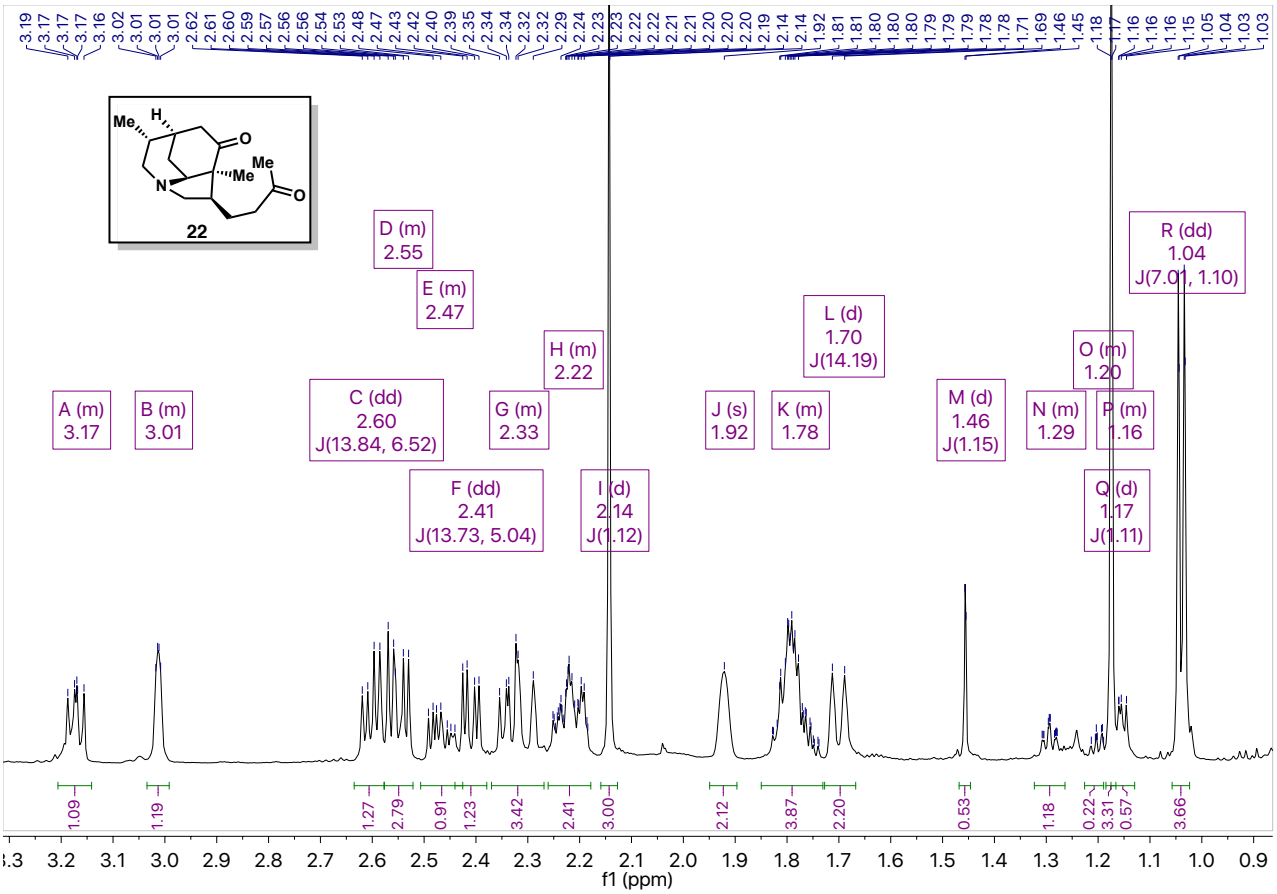
^{13}C NMR (151 MHz, $CDCl_3$) of **tetracycle 21**



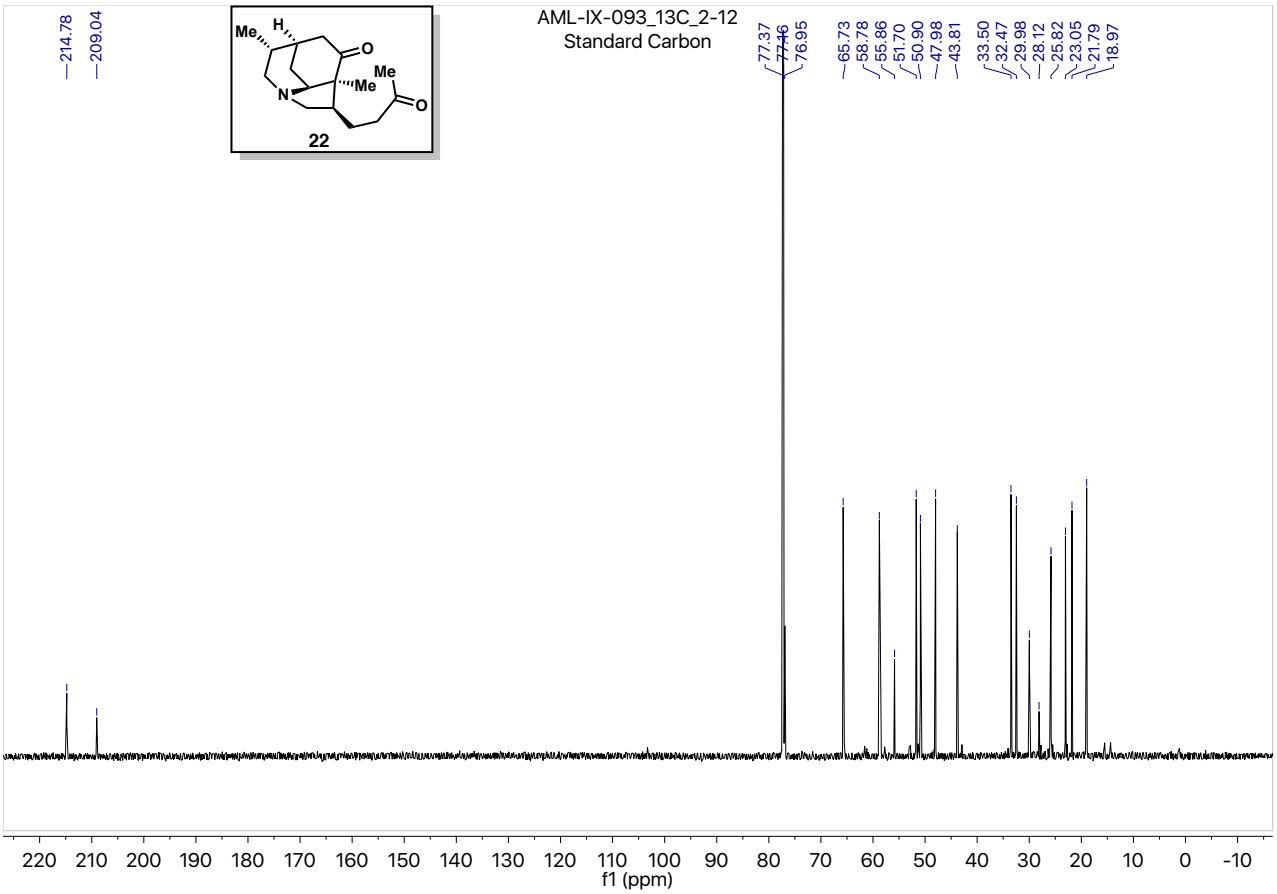
DEPT NMR (151 MHz, $CDCl_3$) of **tetracycle 21**



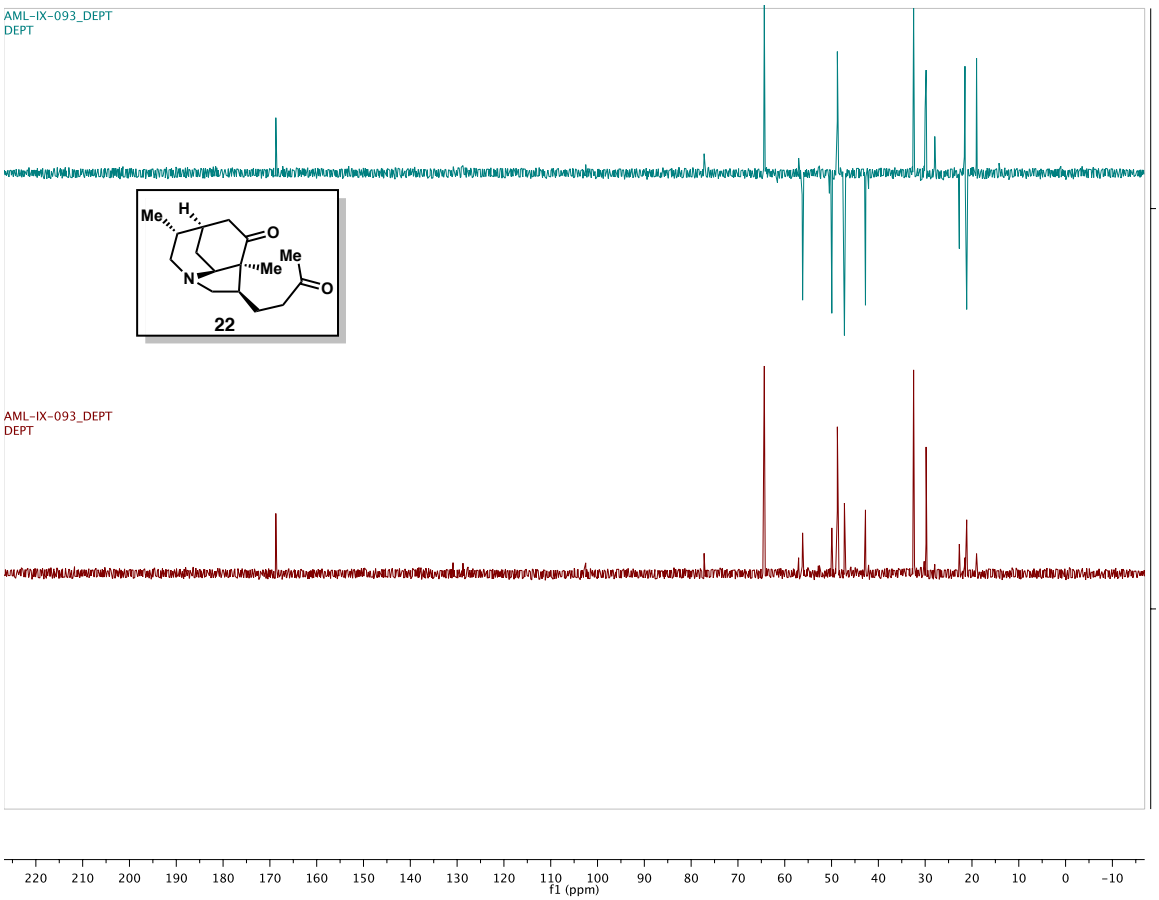
^{1}H NMR (600 MHz, $CDCl_3$) of **methyl ketone 22**



Zoomed in ^{1}H NMR (600 MHz, $CDCl_3$) of **methyl ketone 22**



^{13}C NMR (151 MHz, $CDCl_3$) of **methyl ketone 22**



DEPT NMR (151 MHz, $CDCl_3$) of **methyl ketone 22**