Supporting Information

Ruthenium-Catalyzed Cycloisomerization-6π-Cyclization: A Novel Route to Pyridines

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Experimental Section

All reactions were performed under an argon atmosphere unless otherwise noted. Catalyst $[CpRu(CH_3CN)_3]PF_6$ (**1**) was prepared according to literature procedures.[1] Diynol substrates were also prepared according to known literature protocols. The procedures outlined bellow for the ruthenium-catalyzed cycloisomerization are based on those previously reported.[2] All ruthenium-catalyzed cycloisomerization reactions were done as described in the procedures, unless otherwise stated. Dry acetone was distilled over drierite. All other solvents were purified on an alumina column purification system. The water used in all reactions was deionized water. Commercially available chemicals were distilled prior to use. Analytical thin-layer chromatography (TLC) was performed on 0.2 mm coated silica gel plates (EM 60-F_{254}). Visualization was accomplished with UV light and exposure to anisaldehyde or aqueous ceric ammonium molybdate solution followed by heating. Flash chromatography was performed using Silicycle silica gel (230-400 mesh). All microwave reactions were carried out in sealed vials using a Smith Synthesizer microwave reactor. Proton and broad band decoupled ^{13}C NMR data were acquired on a Varian Mercury 400, or Inova Unity 500 spectrometer as indicated. Chemical shifts are reported in ppm relative to the residual solvent peak. All IR spectra were obtained on sodium chloride plates with a Perkin Elmer Paragon 500 FT-IR spectrometer. Melting points were obtained on a Thomas-Hoover apparatus in open capillary tubes and are uncorrected.

Cycloisomerization Reactions: General Procedure A (secondary alcohols)

To a solution of diynol (0.20 mmol) in acetone (2.0 mL, 0.1M) and water (8 μL, 2 equiv.) was added catalyst **1** (0.02 mmol, 8.9 mg). The orange solution was then stirred at room temperature until consumption of starting material was complete as judged by TLC (generally 2-16 h). The crude reaction mixture was then diluted with hexanes (5 mL) and stirred for an additional 15-30 minutes until the catalyst could be seen precipitating out of solution. The reaction mixture was then filtered through a plug of celite, the solvent removed in vacuo, and the crude product further purified via silica gel chromatography.

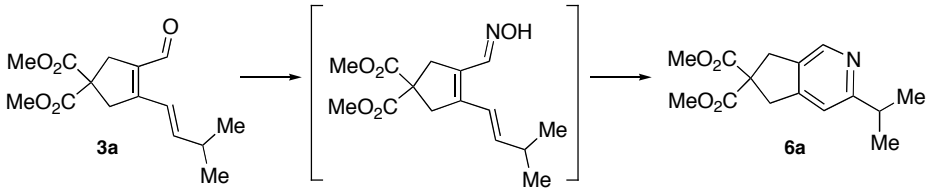
Cycloisomerization Reactions: General Procedure B (primary alcohols)

To vial containing diynol (0.200 mmol), malonic acid (21 mg, 0.20 mmol), acetone (1.8 mL), and water (0.2 mL) was added catalyst **1**. The resulting yellow-orange solution was then capped and heated in an oil bath at 50 °C until consumption of starting material was complete as judged by TLC (generally 0.5-2 h). The reaction was then cooled to room temperature, diluted with hexanes, and stirred for an additional 15-30 minutes. The reaction mixture was then filtered through a plug of celite, the solvent removed in vacuo, and the crude product further purified via silica gel chromatography.

One-Pot Protocol: General Procedure C

To a solution of diynol (0.200 mmol) in dichloromethane (1.6 mL), DMF (0.4 mL, 20 vol%), and water (8 μL, 2 equiv.) in a microwave reaction vial was added catalyst **1** (11 mg, 0.024 mmol). The orange solution was then stirred at room temperature until consumption of starting material was complete as judged by TLC (generally 2-16 h). To the crude reaction was then added hydroxylamine hydrochloride (42 mg, 0.600 mmol) and sodium acetate (0.300 mmol, 25 mg). The sealed suspension was microwaved at 150°C for 1.5h, diluted with $CHCl_3$, and washed with aqueous sodium hydroxide (5x). The organic phases were then dried, diluted with hexanes, and stirred for an additional 15-30 minutes. The reaction mixture was then filtered through a plug of celite, the solvent removed in vacuo, and the crude product further purified via silica gel chromatography.

6a



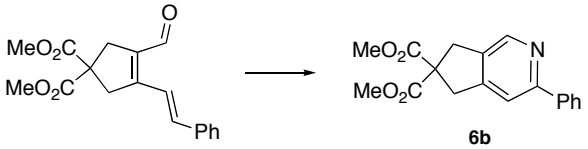
Known aldehyde **3a** was prepared via Procedure A as reported previously.[1]

To a flask containing aldehyde **3a** (119 mg, 0.426 mmol) in methanol (30 ml) was added $NH_2OH{\cdot}HCl$ (36 mg, 0.510 mmol) and NaOAc (21 mg, 0.255 mmol), and the solution heated to reflux for 6 h. The reaction was cooled to rt, extracted with ether (3 x 50 mL), and the organic layers dried ($MgSO_4$). The solvent evaporated in vacuo to yield crude oxime, which was made into a stock solution and carried on without further purification.

A solution of the crude oxime (20 mg, 0.068 mmol) in trifluorotoluene (3 mL) was prepared and transferred to a sealed, dry microwave vial. The solution was heated to 220 °C for 40 minutes. The solvent was then removed in vacuo, and the crude product purified via filtration through a silica gel column (40 → 100% EtOAc/hexanes), to yield the title compound (18 mg, 96%, two steps) as a brown oil.

$\mathbf{R}_f$ = 0.2 (20% EtOAc/hexanes). **IR**(thin film): 2956, 2926, 2849, 1738, 1610, 1435, 1264, 1201, 1162, 1073 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$): 8.38 (d, *J* = 0.8 Hz, 1H), 7.04 (s, 1H), 3.77 (s, 6H), 3.60 (s, 2H), 3.58 (s, 2H), 3.05 (septet, *J* = 6.8 Hz, 1H), 1.29 (d, *J* = 6.8 Hz, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$): 171.7, 166.0, 150.1, 144.6, 133.4, 116.5, 53.4, 53.3, 40.4, 38.1, 36.2, 29.8, 22.8, 20.5. **HRMS** (EI, $[M]^+$) Calc'd for $C_{15}H_{19}NO_4$: 277.1314. Found: 277.1310.

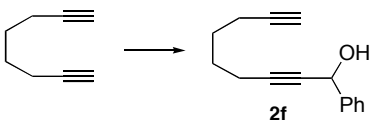
6b



To a capped vial was added 30 mg (0.096 mmol), of aldehyde **3b** (prepared via the ruthenium-catalyzed cycloisomerization as reported[1]), ethanol (1 mL), $NH_2OH{\cdot}HCl$ (8 mg, 0.115 mmol), and NaOAc (5 mg, 0.057 mmol). The sealed vial was heated to 90 °C for 24 h. The vial was cooled to rt, saturated aqueous sodium bicarbonate added, and the mixture extracted with ethyl acetate. The organic layers were dried (Na_2SO_4), the solvent removed in vacuo, and the crude product further purified via column chromatography (25% EtOAc/hexanes), providing the title compound (24 mg, 80%) as a cream solid.

$\mathbf{R}_f$ = 0.4 (25% EtOAc/hexanes). **mp**: 104-106 °C. **IR**(thin film): 2917, 2849, 1738, 1434, 1263, 1264, 1200, 1163, 1072 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$): 8.54 (s, 1H), 7.93 (m, 2H), 7.59 (s, 1H), 7.48-7.37 (comp m, 3H), 3.79 (s, 6H), 3.674 (s, 2H), 3.67 (s, 2H). **^{13}C NMR** (100 MHz, $CDCl_3$): 171.6, 150.6, 145.3,139.5, 134.7, 128.8, 127.0, 116.7, 60.3, 53.3, 40.5, 38.2. **HRMS** (EI, $[M]^+$) Calc'd for $C_{18}H_{17}NO_4$: 311.1158. Found: 311.1158.

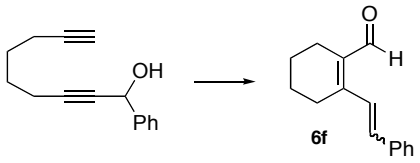
2f



A flame-dried flask containing 1,7-octadiyne (3.75 mL, 28.25 mmol) was charged with dry THF (280 mL). The solution was cooled to -78 °C, and freshly prepared LiHMDS (28.3 mL, 1M in THF) was added. The solution was stirred for 15 min at -78 °C, and benzaldehyde (3.0 mL, 5.65 mmol) was added dropwise. After 20 minutes, the reaction was quenched with saturated aqueous NH_4Cl, warmed to rt, extracted with Et_2O and EtOAc, washed with brine, and the organic layer dried over $MgSO_4$. The solvent was removed in vacuo to give the crude product, which was further purified via column chromatography (20% Et_2O/hexanes) to yield **2f** (3.22 g, 54%) as a light yellow oil.

R_f = 0.3 (20% Et_2O/hexanes). **IR**(thin film): 3295, 2945, 1455, 1002, 699 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$): 7.55-7.53 (m, 3H), 7.40-7.31 (m, 2H), 5.46 (d, *J* = 6.0 Hz, 1H), 2.34-2.30 (m, 2H), 2.25-2.21 (m, 2H), 2.10 (d, *J* = 6.4 Hz, 1H), 1.96 (t, *J* = 2.0 Hz, 1H), 1.69-1.64 (m, 4H). **^{13}C NMR** (100 MHz, $CDCl_3$): 141.2, 128.5, 128.2, 126.6, 86.9, 86.8, 84.1, 80.4, 68.6, 64.7, 27.5, 27.4. **HRMS** (EI, $[M]^+$) Calc'd for $C_{15}H_{16}O$: 212.1201. Found: 211.1121.

6f

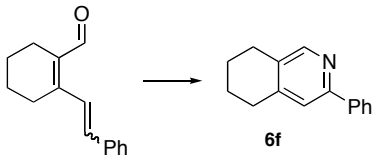


Aldehyde **3f** was prepared from diynol **2f** (210 mg, 0.99 mmol) according to Procedure A. Purification via silica gel chromatography (30% Et_2O/hexanes) produced **3f**, as an inseparable 7:1 E/Z mixture of geometrical isomers, (188 mg, 90%) as a light yellow oil.

Only the major trans isomer was characterized.

R_f = 0.5 (30% Et_2O/hexanes). **IR**(thin film): 2933, 2862, 1658, 1615, 1582, 1149, 955, 750, 692 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$): 10.47 (s, 1H), 7.76 (d, *J* = 16.0 Hz, 1H), 7.48 (m, 2H), 7.37 (m, 2H), 7.32 (m, 1H), 6.87 (d, *J* = 16.0 Hz, 1H), 2.57 (t, *J* = Hz, 2H), 2.37 (t, *J* = 6.0 Hz, 2H), 1.74 (m, 2H), 1.66 (m, 2H). **^{13}C NMR** (100 MHz, $CDCl_3$): 190.6, 151.7, 136.7, 135.8, 133.5, 129.8, 129.1, 128.9, 127.1, 123.4, 27.6, 23.4, 22.1. **HRMS** (El, [M+]) Calc'd for $C_{15}H_{16}O$: 212.1201. Found: 212.1198.

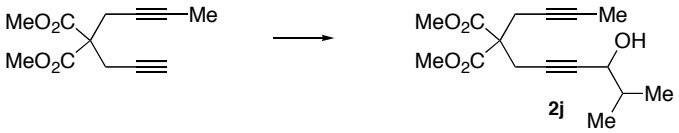
6f



A capped vial containing aldehyde **3f** (22 mg, 0.106 mmol), ethanol (1 mL), water (0.3 mL), $NH_2OH{\cdot}HCl$ (5 mg, 0.127 mmol), and NaOAc (9 mg, 0.064 mmol) was heated in a 90 °C oil bath for 16 h. The vial was cooled to rt, saturated aqueous sodium bicarbonate added, and the mixture extracted with ethyl acetate. The organic layers were concentrated and and extracted with 1M aqueous HCl (3x). The aqueous phases were then combined and basified (pH >7) with $NaHCO_3$. The aqueous phase was then extracted with chloroform (4x), dried (Na_2SO_4), and the solvent removed in vacuo. The crude product was further purified via column chromatography (20% EtOAc/hexanes), providing the title compound[3] (19 mg, 84%) as a yellow oil.

$\mathbf{R}_f$ = 0.6 (20% EtOAc/hexanes). **IR**(thin film): 2932, 2860, 1599, 1558, 1475, 1446, 1392, 1308, 777, 694 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$): 8.38 (s, 1H), 7.94 (m, 1H), 7.93 (m, 1H), 7.42 (m, 4H), 2.80 (m, 4H), 1.85 (m, 4H). **^{13}C NMR** (100 MHz, $CDCl_3$): 154.5, 150.3, 146.8, 139.8, 131.8, 128.7, 128.4, 126.8, 120.8, 29.0, 26.1, 22.8, 22.6. **HRMS** (El, $[M^+]$) Calc'd for $C_{15}H_{15}N$: 209.1204. Found: 209.1197.

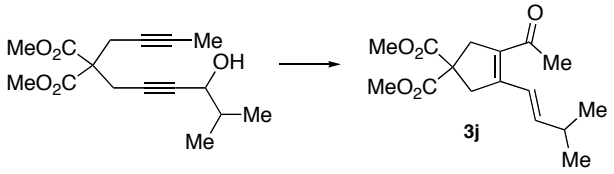
2j



To a solution of dimethyl 2-(but-2-ynyl)-2-(prop-2-ynyl)malonate (615 mg, 2.77 mmol) in THF (27 mL) at -78 °C was added n-BuLi (2.5M in hexanes; 1.9 mL; 4.2 mmol). The reaction was stirred for 30 minutes, and isobutyrylaldehyde (275 μL, 3.1 mmol) was added, dropwise. and the reaction was stirred for an additional 30 minutes. Saturated ammonium chloride was added at -78 °C, the reaction warmed to room temperature, and the mixture extracted with ether (2 x 60 mL) and ethyl acetate (1 x 60 mL). The organic layers were combined and washed once with brine, dried ($MgSO_4$), and the solvent removed in vacuo to yield a yellow oil which was further purified by column chromatography to yield **2j** (331 mg, 40%) as a clear oil.

$\mathbf{R}_f$ = 0.5 (50% Et_2O/hexanes). **IR**(thin film): 3520, 2959, 2926, 2349, 1741, 1437, 1384, 1327, 1295, 1247, 1214, 1151, 1055, 1030, 951, 899, 836 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$): 4.12 (s, 1H), 3.74 (s, 6H), 3.01 (d, J = 2 Hz, 2H), 2.90 (q, J = 6.4 Hz, 2H), 1.76 (t, J = 2.4 Hz, 3H), 0.96 (t, J = 6.8 Hz, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$): 169.6, 83.2, 80.3, 79.4, 72.9, 68.0, 57.0, 53.1, 34.5, 23.2, 23.0, 18.1, 17.3. **HRMS** (EI, $[M_{C_{13}H_{22}O_5}$-(i-Pr)$]^+$) Calc'd for $C_{13}H_{15}O_5$: 251.0919. Found: 251.0919.

3j



Ketone **3j** was prepared from **2j** (332 mg, 1.13 mmol) according to Procedure A. Crude material was purified via column chromatography (20% EtOAc/hexanes) to yield 246 mg (74%) of the title compound as a yellow oil.

$\mathbf{R}_f$ = 0.6 (50% Et_2O/hexanes). **IR**(thin film): 2959, 1738, 1629, 1580, 1436, 1363, 1264, 1201, 1167 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$): 7.08 (d, J = 16.0 Hz, 1H), 6.02 (dd, J = 16.0 Hz, J = 7.2 Hz, 1H), 3.77 (s, 6H), 3.41 (s, 2H), 3.37 (d, J = 0.8 Hz, 2H), 2.46 (q, J = 6.7 Hz, 1H), 2.28 (s, 3H), 1.05 (d, J = 6.8 Hz, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$): 197.1, 172.1, 148.4, 147.5, 131.6, 122.3, 56.7, 53.4, 42.4, 42.1, 32.2, 31.0. **HRMS** (EI, $[M_{C_{16}H_{22}O_5}$ + H$]^+$) Calc'd for $C_{16}H_{23}O_5$: 295.1545. Found: 295.1554.

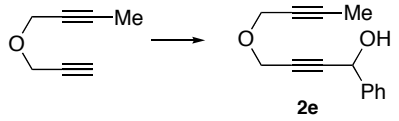
6j

An oven-dried flask was charged with ketone **3j** (19 mg, 0.063 mmol), methanol (10 mL), $NH_2OH{\cdot}HCl$ (4 mg, 0.063 mmol), and NaOAc (3 mg, 0.038 mmol). The solution was heated to reflux for 1 h. The rose-colored solution was then cooled to rt and extracted with ether (3 x 15 mL). The organic layer was dried ($MgSO_4$), and the solvent evaporated in vacuo to yield crude oxime, which was carried on without purification.

The crude oxime was then dissolved in triflourotolulene (3 mL) and transferred into a flame-dried vial containing 4Å molecular sieves. The vial was heated to 230 °C in a microwave reactor (high absorption) and monitored via TLC until the starting material was consumed (4.25 h). The solvent was removed in vacuo and the crude oils purified via column chromatography (50% EtOAc/hexanes) to yield pyridine **6j** (18 mg, 98%) as a dark orange oil.

$\mathbf{R}_f$ = 0.5 (50% EtOAc/hexanes). **IR**(thin film): 2959, 2927, 2871, 1737, 1604, 1580, 1435.4, 1580, 1435, 1405, 1381, 1268, 1200, 1167, 1073, 962, 929, 878 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$): 6.89 (s, 1H), 3.77 (s, 6H), 3.58 (s, 2H), 3.53 (s, 2H), 3.02 (sept., J = 7.0 Hz, 1H), 2.45 (s, 3H), 1.26 (d, J = 6.8 Hz, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$): 171.9, 165.9,152.7, 131.5, 113.6, 59.6, 53.2, 40.7, 38.6, 36.2, 22.9, 22.0. **HRMS** (EI, $[M]^+$) Calc'd for $C_{16}H_{21}NO_4$: 291.1471. Found: 291.1466.

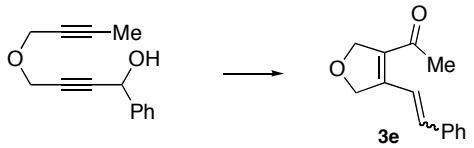
2e



To a flame-dried flask containing 1-(prop-2-ynyloxy)but-2-yne (1.0 g, 9.25 mmol) in THF (92.5 mL) at -78 °C was added LiHMDS (13.9 mmol, 1M solution in THF, 13.9 mL). After stirring for 30 minutes, benzaldehyde (14.88 mmol, 1.5 mL) was added dropwise. The reaction was stirred for 20 minutes at -78 °C, quenched with saturated aqueous NH_4Cl, and warmed to room temperature. The reaction was then extracted with ether (2x) and ethyl acetate (1x). The organic layers were then combined and washed once with brine, dried ($MgSO_4$), and the solvent removed in vacuo. The crude reaction mixture was purified via column chromatography to yield dinyol **2e** (1.4g, 71%) as a yellow oil.

$\mathbf{R}_f$ (50% Et_2O/hexanes): 0.3. **IR**(thin film): 3405, 3032, 2855, 1454, 1351, 1264, 1121, 1072, 920 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$): 7.56-7.53 (m, 1H), 7.42-7.32 (m, 3H), 5.52 (s, 1H), 4.34 (d, J = 1.6 Hz, 2H), 4.22 (q, J = 4.4 Hz, 2H), 2.25 (s, 1H), 1.87 (t, J = 2.4 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): 140.4, 128.7, 238.6, 126.7, 86.4, 83.4, 82.3, 74.3, 64.7, 57.4, 56.7, 3.7. **HRMS** (EI, $[M_{C_{14}H_{14}O_2} - H]^+$) Calc'd for $C_{14}H_{13}O_2$: 213.0916. Found: 213.0916.

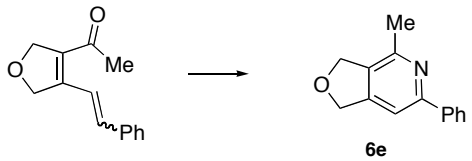
3e



Cycloisomerization product **XX** was obtained from diynol **XX** (400.0 mg, 1.87 mmol) according to Procedure A. The crude reaction mixture was purified via column chromatography (50% Et_2O/hexanes) to yield the title compound (240 mg, 60%) as an inseparable 5:1 mixture of E/Z geometrical isomers.

R_f = 0.4 (50% Et_2O/hexanes). **IR** (thin film): 3059, 2847, 2363, 1672, 1648, 1617, 1585, 1278, 1231, 1070, 753, 691 cm^{-1}. **^{1}H NMR (major *E*-isomer)** (400 MHz, $CDCl_3$): 7.82 (d, *J* = 16.4 Hz, 1H), 7.52 (dt, *J* = 6.8, 1.6 Hz, 2H), 7.40-7.31 (m, 3H), 6.64 (d, *J* = 16.4 Hz, 1H), 5.10-5.08 (m, 2H), 5.04-5.02 (m, 2H), 2.32 (s, 3H). **^{1}H NMR (minor *Z*-isomer)** (400 MHz, $CDCl_3$): 7.52 (dt, *J* = 6.8, 1.6 Hz, 2H), 7.40-7.31 (m, 3H), 6.88 (d, *J* = 12Hz, 1H), 6.74 (dt, *J* = 12, 1.6 Hz, 1H), 4.90 (td, *J* = 4.4, 1.6 Hz, 2H), 4.53 (td, *J* = 4.8, 1.6 Hz, 2H), 2.33 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): 194.4, 145.8, 138.0, 136.8, 132.1, 129.4, 128.9, 128.54, 128.46, 128.39, 127.4, 121.3, 119.7, 76.4, 75.9, 30.9, 30.4. **HRMS** (EI, $[M]^+$) Calc'd for $C_{14}H_{14}O_2$: 214.0994. Found: 214.0995.

6e

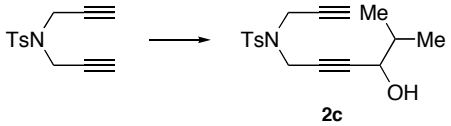


6e

A capped vial containing ketone **3e** (49 mg, 0.227 mmol) was added ethanol (2.3 mL), water (0.3 mL) NH_2OMe•HCl (23 mg, 0.272 mmol), and NaOAc (11 mg, 0.136 mmol) was heated at 90 °C in an oil bath for 5 h, followed by heating at 110 °C for 1 h. The reaction was cooled to rt, diluted with dichloromethane, and extracted with 1M aqueous HCl (3x). The aqueous phases were then combined and basified (pH >7) with $NaHCO_3$. The aqueous phase was then extracted with dichloromethane (4x), dried (Na_2SO_4), and the solvent removed in vacuo. The crude product was further purified via column chromatography (40% EtOAc/hexanes) to yield pyridine **6e** (85 %) as a yellow-white solid.

R_f = 0.8 (60% EtOAc/hexanes). **mp:** 70-76 °C. **IR**(thin film): 3031, 2852, 1609, 1574, 1450, 1388, 1052, 903, 886, 778, 734, 695 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$): 7.98 (t, *J* = 1.6 Hz, 1H), 7.96-7.95 (m, 1H), 7.49-7.38 (m, 4H), 5.16-5.14 (m, 4H), 2.54 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): 156.7, 151.4, 149.5, 139.7, 132.0, 128.8, 127.1, 110.9, 73.6, 72.1, 22.6. **HRMS** (EI, $[M]^+$) Calc'd for $C_{14}H_{13}NO$: 211.0997. Found: 211.0991.

2c

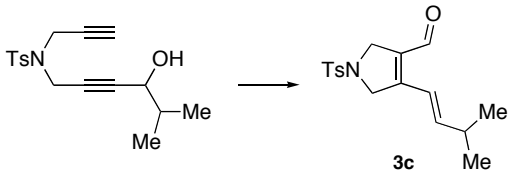


2c

To a flame-dried flask containing 4-methyl-*N*,*N*-di(prop-2-ynyl)benzenesulfonamide[4] (1.0 g, 4.1 mmol) and dry THF (40 mL) was added freshly prepared Li-HMDS (4.1 mmol, 4.1 mL, 1M in THF) at -78 °C. After 15 min, isobutyraldehyde (371 μL, 4.1 mmol) was added dropwise. The solution was stirred for 30 min, quenched with saturated NH_4Cl_4, warmed to rt, extracted with Et_2O (1x 40 mL), and ethyl acetate (2 x 40 mL), and dried over $MgSO_4$. The solvent was removed in vacuo, to yield crude **XX** as a cream solid. The crude solid was further purified via silica gel chromatography to yield the title compound (759 mg, 60 %) as a crystalline white solid.

R_f = 0.5 (60% Et_2O/hexanes). **IR**(thin film): 3520, 3288, 2963, 1598, 1494, 1469, 1435, 1350, 1163, 1094, 1031, 897, 815, 753, 663, 578, 543 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$): 7.72 (d, *J* = 8.0 Hz, 2H), 7.32 (d, *J* = 7.6 Hz, 2H), 4.23 (d, *J* = 1.6 Hz, 2H), 4.15 (d, *J* = 1.6 Hz, 2H), 4.00 (tt, *J* = 5.6 Hz, *J* = 1.6 Hz, 1H), 2.43 (s, 3H), 2.16 (t, *J* = 2.4 Hz, 1H), 1.72 (m, 1H), 1.52 (s, 1H), 0.87 (dd, *J* = 6.4, 1.2 Hz, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$): 144.1, 135.2, 129.7, 127.9, 85.8, 77.7, 76.3, 74.1, 67.6, 36.5, 36.4, 34.2, 21.6, 18.0, 17.4. **HRMS** (EI, [M+]) Calc'd for $C_{17}H_{21}NO_3S$: 319.1242. Found: 319.1120.

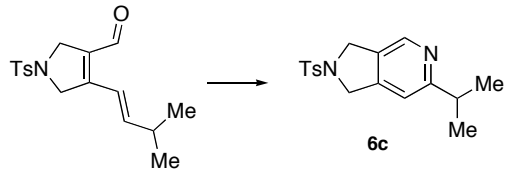
3c



Compound **3c** was obtained from the cycloisomerization of diynol **2c** using a modified version of Procedure A. To a vial containing **2c** (150 mg, 0.500 mmol), acetone (5 mL), and water (45 μL, 2.5 mmol), was added catalyst **1** (21 mg, 0.05 mmol) and camphor sulfonic acid (11 mg, 0.05 mmol). The reaction was stirred at room temperature for 10 hours, then sealed and heated to 45 °C for two hours, after which it was filtered through a pad of silica with ether as the eluent. The solvent was then removed in vacuo to give the crude product which was further purified on silica (50% Et_2O/hexanes) to yield 105 mg of **3c** (70%) as a yellow oil.

R_f = 0.5 (50% Et_2O/hexanes). **^{1}H NMR** (400 MHz, $CDCl_3$): 10.00 (s, 1H), 7.75 (d, *J* = 8.4 Hz, 2H), 7.34 (d, *J* = 8.0 Hz), 6.73 (d, *J* = 16.0 Hz, 1H), 5.97 (dd, *J* = 16.0, *J* = 7.2 Hz, 1H), 4.47 (t, *J* = 3.2 Hz, 2H), 4.30 (t, *J* = 3.6 Hz, 2H), 2.43 (s, 3H), 1.07 (d, *J* = 6.4 Hz, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$): 185.0, 150.1, 149.8, 144.0, 133.6, 131.3, 130.0, 127.7, 116.4, 56.0, 53.5, 32.2, 21.8, 21.6. **HRMS** (El, $[M-H]^+$) Calc'd for $C_{17}H_{20}NO_3S$: 319.1164. Found: 318.1164.

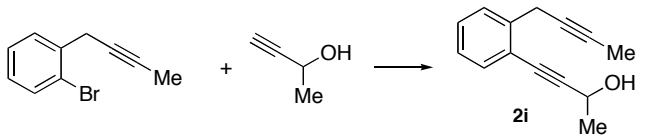
6c



To a vial containing aldehyde **3c** (21 mg, 0.067 mmol) was added ethanol (0.7mL), $NH_2OH{\cdot}HCl$ (6 mg, 0.080 mmol), and NaOAc (3 mg, 0.040 mmol). The vial was capped and heated in a 95 °C oil bath for 24 h. The vial was cooled to rt, saturated aqueous sodium bicarbonate added, the mixture extracted with ethyl acetate, and the organic layers concentrated in vacuo. The crude product was further purified via column chromatography (10% MeOH/CH_2Cl_2), providing the title compound (8 mg, 40%) as a white solid.

R_f = 0.5 (60% Et_2O/hexanes. **mp:** 110-115 °C. **^{1}H NMR** (400 MHz, $CDCl_3$): 8.37, (s, 1H), 7.77 (d, *J* = 8.4 Hz, 2H), 7.33 (d, *J* = 8.0 Hz, 2H), 7.01 (s, 4H), 4.60 (dd, *J* = 9.6, 1.6 Hz, 4H), 3.03 (sept., *J* = 7.0 Hz, 1H), 2.41 (s, 3H), 1.25 (d, *J* = 7.0, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$): 166.9, 144.1, 143.5, 130.0, 127.7, 114.7, 94.5, 53.4, 51.7, 36.3, 22.7, 21.6. **HRMS** (EI, [M]+) Calc'd for $C_{17}H_{20}N_2O_2S$: 316.1245. Found: 316.124.

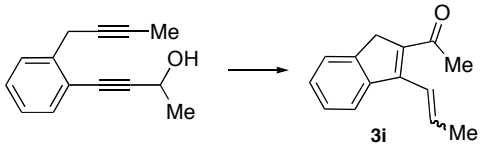
2i



To a flask containing1-bromo-2-(but-2-ynyl)benzene (300 mg, 1.44 mmol) under argon was added DIPA (14.4 ml). After the solution was degassed (bubbling Ar), $Pd(PPh_3)_4$ (166 mg, 0.144 mmol) was added, followed by CuTC (114 mg, 0.58 mmol). After further degassing, 3-butyn-2-ol (226 μL, 22.86 mmol) was added. The septa was then replaced by an airtight screw-cap, and the solution heated to 90°C for 60h. The crude reaction mixture was then filtered through celite with ether as the eluent. The solvent was then removed in vacuo, and the product was further purified via column chromatography (40% EtOAc, 2% Et_3N/hexanes) to yield 73% of **2i**.

R_f = 0.5 (40% EtOAc/hexanes). **IR**(thin film): 3362, 3067, 2981, 2919, 2359, 1714, 1600, 1483, 1450, 1371, 1326, 1275, 1181, 1110, 1088, 1032, 936, 858, 758, 724, 695 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$): 7.56 (dd, *J* = 7.6, 0.4 Hz, 1H), 7.40 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.32 (td, *J* = 7.6, 1.6, 1H), 7.21-7.17 (m, 1H), 4.82-4.76 (m, 1H), 3.68 (q, *J* = 2.7, 2H), 1.90 (d, *J* = 5.2 Hz), 1.87 (t, *J* = 2.4 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): 139.4, 132.0, 128.8, 128.0, 126.5, 121.5, 96.0, 82.1, 78.4, 76.1, 59.0, 24.6, 24.0, 3.7. **HRMS** (EI, $[M_{C_{14}H_{14}O} -(CH_3)]^+$) Calc'd for $C_{13}H_{11}O$: 183.0810. Found: 183.0809.

3i



Ketone **3i** was prepared from diynol **3i** (200 mg, 1.01 mmol) according to Procedure A. Crude material was purified via silica gel chromatography (0 → 20% EtOAc/hexanes) to yield the title compound (120 mg, 60%) as a yellow oil.

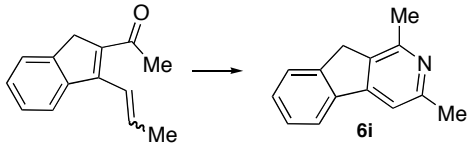
Compound characterized as a 2:1 E/Z mixture of double bond isomers.

R_f = 0.5 (20% EtOAc). **IR**(thin film): 2917, 2360, 2342, 1644, 1533, 1362, 1239, 1189, 975, 748, 720, 668 cm^{-1}. **^{13}C NMR** (100 MHz, $CDCl_3$): 196.8, 148.9, 143.8, 143.5, 137.2, 134.8, 131.3, 128.2, 128.0, 126.8, 125.3, 124.4, 124.3, 123.7, 123.5, 123.3, 39.2, 38.8, 30.5, 29.9, 19.5, 15.7. **HRMS** (EI, $[M]^+$) Calc'd for $C_{14}H_{14}O$: 195.1048. Found: 195.1040.

^{1}H NMR (*E*-isomer) (400 MHz, $CDCl_3$): 7.75-7.72 (m, 1H), 7.54-7.51 (m, 1H), 7.43-7.33 (m, 2H), 7.11-7.05 (dm, *J* = 16 Hz, 1H), 6.54-6.43 (m, 1H), 3.75 (s, 2H), 2.47 (s, 3H), 2.04-2.02 (m, 3H).

^{1}H NMR (*Z*-isomer) (400 MHz, $CDCl_3$): 7.54-7.51 (m, 1H), 7.43-7.33 (m, 3H), 6.54-6.43 (m, 1H), 6.16-6.08 (m, 1H), 3.77 (d, *J* = 2.8 Hz, 2H), 2.48 (s, 3H), 1.62 (dd, *J* = 8.0, 1.6 Hz, 3H).

6i



A suspension of ketone **6i** (30 mg, 0.151 mmol), ethanol (1.5 mL), $NH_2OH{\cdot}HCl$ (15 mg, 0.181 mmol), and NaOAc (7 mg, 0.091 mmol) in a capped vial was heated in an oil bath at 95 °C for 24 h. The vial was cooled to rt, diluted with $CHCl_3$, and extracted with 1M aqueous HCl (3x). The aqueous phases were then combined and basified (pH > 7) by slow addition of $NaHCO_3$. The aqueous phase was then extracted with $CHCl_3$ (5x), dried (Na_2SO_4), and the solvent removed in vacuo. The crude product was purified via column chromatography (20% EtOAc/hexanes) to yield pyridine **6i** (25 mg, 85 %) as a yellow-white solid. Spectral data matched that reported previously.[5,6]

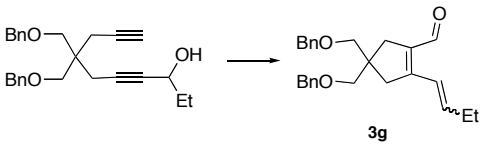
R_f = 0.3 (50% EtOAc/hexanes). **IR**(thin film): 2919, 1568, 1431, 774, 744 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$): 7.85-7.81 (m, 1H), 7.64-7.595 (m, 1H), 7.44-7.42 (comp m, 2H), 7.41 (s, 1H), 3.85 (s, 2H), 2.64 (s, 3H), 2.62 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): 156.3, 153.4, 149.8, 144.3, 140.0, 133.2, 128.9, 127.1, 125.5, 121.5, 112.2, 35.3, 24.7, 22.0. **HRMS** (EI, $[M]^+$) Calc'd for $C_{14}H_{13}N$: 195.1048. Found: 195.1049.

2g

To a flame-dried flask containing (2,2-di(prop-2-ynyl)propane-1,3-diyl)bis(oxy)bis(methylene)dibenzene[7] (407 mg, 1.22 mmol) and dry THF (11 mL) was added freshly prepared Li-HMDS (1.22 mmol, 1M in THF) at -78 °C. After 15 min, propionaldehyde (88 μL, 1.22 mmol) was added dropwise. The reaction was stirred for 30 min, quenched with saturated aqueous NH_4Cl_4, warmed to rt, extracted with Et_2O (1x 20mL), and ethyl acetate (2x 20mL), and dried over $MgSO_4$. The solvent was removed in vacuo, and the crude oil purified via column chromatography (10→20% EtOAc/hexanes) to yield the title compound (156 mg, 33%) as a colorless oil.

R_f = 0.5 (20% EtOAc/hexanes). **IR** (thin film): 3417, 2864, 2244, 2117, 1496, 1454, 1366, 1270, 1206, 1096, 1008, 963, 909, 831, 737, 698, 639 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$): 7.35-7.25 (m, 10H), 4.51 (s, 4H), 4.24 (m, 1H), 3.48 (s, 4H), 2.44 (d, J = 2.0 Hz, 2H), 2.41 (d, J = 2.4 Hz, 2H), 1.95 (d, J = 2.4 Hz, 1H), 1.71-1.56 (m, 3H), 0.95 (t, J = 7.6 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$):138.7, 128.3, 127.54, 127.52, 83.4, 81.7, 80.9, 73.4, 71.2, 70.6, 63.9, 42.2, 31.2, 22.4, 22.2, 9.5. **HRMS** (EI, $[M]^+$) Calc'd for $C_{25}H_{30}O_3$: 390.2195. Found: 390.2183.

3g

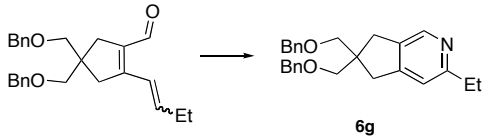


Aldehyde **3g** was prepared from **2j** (39 mg, 0.100 mmol) according to Procedure A. Crude material was purified via silica gel chromatography (15% EtOAc/hexanes) to yield the title compound (21 mg, 54%) as a light oil.

Compound characterized as an 8:1 E/Z mixture of double bond isomers.

$\mathbf{R}_f$ = 0.5 (30% EtOAc/hexanes). **IR** (thin film): 2924, 2852, 2360, 1659, 1454, 1362, 1216, 1100, 1028, 961, 737, 698 cm^{-1}. **^{1}H NMR (major, *E*-isomer)** (400 MHz, $CDCl_3$): 10.14 (s, 1H), 7.34-7.25 (m, 10H), 6.44 (d, *J* = 11.6 Hz, 1H), 5.76 (dt, *J* = 12.0, 7.6 Hz, 1H), 4.51 (s, 4H), 3.42 (q, *J* = 3.6 Hz, 4H), 2.76 (s, 2H), 2.52 (s, 2H), 2.24 (app. quintet, *J* = 7.2 Hz, 2H), 1.07 (t, *J* = 8.0 Hz, 3H). **^{1}H NMR (minor, *Z*-isomer)** (400 MHz, $CDCl_3$): 9.96 (s, 1H), 7.34-7.25 (m, 10H), 6.92 (d, *J* = 15.6 Hz, 1H), 6.09 (dt, *J* = 15.2 Hz, 1H), 4.51 (s, 4H), 3.42 (q, *J* = 4.0 Hz, 4H), 2.71 (s, 2H), 2.57 (s, 2H), 2.24 (app. quintet, *J* = 7.2 Hz, 2H), 1.01 (t, *J* = 7.6 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): 187.8, 142.4, 138.7, 135.8, 128.4, 127.5, 121.4, 73.7, 73.3, 44.7, 41.0, 26.6,13.2. **HRMS** (EI, $[M_{C_{26}H_{30}O_3}$ - Et$]^+$) Calc'd for $C_{24}H_{25}O_3$: 361.1804. Found: 361.1804.

6g

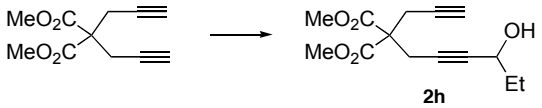


6g

A vial was charged with aldehyde **3g** (56 mg, 0.143 mmol), ethanol (0.5 mL), $NH_2OH{\cdot}HCl$ (13 mg, 0.143 mmol) and NaOAc (7 mg, 0.086 mmol). The solution was heated in an oil bath at 90 °C overnight (16 h). The solution was then cooled to rt, sat'd aqueous $NaHCO_3$ added, and the solution extracted several times with CH_2Cl_2 (3 x 10 mL). The organic layer was dried (Na_2SO_4), and the solvent evaporated in vacuo. Purification via column chromatography (gradient 20-40% EtOAc/hexanes, w/2%Et_3N) provided the title compound (40 mg, 73%) as a clear oil.

$\mathbf{R}_f$ = 0.6 (40% EtOAc/hexanes). **IR** (thin film): 2928, 2853, 1609, 1563, 1454, 1363, 1101, 736, 698 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$): 8.30 (s, 1H), 7.34-7.24 (comp m, 10H), 6.98 (s, 1H), 4.51 (s, 4H), 3.51-2.46, m, 4H), 2.86 (s, 4H), 2.77 (q, *J* = 7.6 Hz, 2H), 1.28 (t, *J* = 8.0 Hz, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$): 161.2, 152.8, 145.2, 138.6, 135.7, 128.4, 127.6, 127.5, 118.6, 73.32, 73.28, 48.7, 48.5, 38.8, 36.3, 31.2, 22.8,14.3. **HRMS** (EI, $[M]^+$) Calc'd for $C_{26}H_{29}NO_2$: 387.2198. Found: 387.2197.

2h

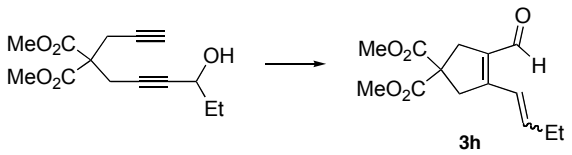


2h

To a flame-dried flask containing 2,2-di-prop-2-ynyl-malonic acid dimethyl ester (800 mg, 3.84 mmol) in dry THF (40 mL) was added Li-HMDS (3.84 mL, 1M in THF, 3.84 mmol) at -78°C. After 15 minutes, propionaldehyde (277 μL, 3.84 mmol) was added slowly. After 30 min, the reaction was quenched with saturated aq. NH_4Cl, warmed to rt, extracted with ether, washed with brine, and dried over $MgSO_4$. The drying salts were filtered, the solvent removed in vacuo, and the crude product was purified via column chromatography (50% Et_2O/hexanes) to yield 50% of the desired product as a colorless oil.

$\mathbf{R}_f$ = 0.7 (60% Et_2O/hexanes). **IR**(thin film): 3417, 3289, 2960, 1741, 1437, 1326, 1297, 1215, 1057, 986, 854 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$): 4.27 (s, 1H), 3.76 (s, 6H), 3.02 (d, *J* = 2 Hz, 2H), 2.97 (d, *J* = 2.4 Hz, 2H), 2.04 (t, *J* = 2.8 Hz, 1H), 1.90 (s, 1H), 1.67 (m, 2H), 0.97 (t, *J* = 7.6 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): 169.2, 84.8, 79.2, 78.4, 71.9, 63.7, 56.7, 53.2, 31.0, 23.0, 22.8, 9.4. **HRMS** (EI, $[M_{C_{12}H_{13}O_5}$ - (Et)$]^+$) Calc'd for $C_{12}H_{13}O_5$: 237.0763. Found: 237.0761.

3h

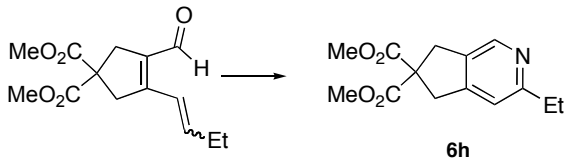


Aldehyde **3h** was prepared from diynol **2h** (70 mg, 0.26 mmol) according to Procedure A. The reaction mixture was concentrated in vacuo and purified via column chromatography (40% EtO/hexanes) to yield **3h** (49 mg, 70%) as a colorless oil.

Compound characterized as an 12:1 E/Z mixture of geometric isomers; only the major E-isomer was fully characterized.

$\mathbf{R}_f$ = 0.5 (15% EtOAc). **IR**(thin film): 2958, 1736, 1663, 1632, 1435, 1267, 1201, 1075, 967, 865, 823 cm^{-1}. **^{1}H NMR (major, *E*-isomer)** (400 MHz, $CDCl_3$)10.11 (s, 1H), 6.89 (d, *J* = 15.6 Hz, 1H), 6.17 (dt, *J* = 15.2, 6.4 Hz, 1H), 3.75 (s, 6H), 3.43 (s, 2H), 3.31(s, 2), 2.27 (m, 2H), 1.08 (t, *J* = 7.6 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): 187.8, 186.7, 171.8, 171.7, 154.4, 154.1, 143.6, 141.8, 129.1, 128.3, 125.3, 120.4, 119.4, 57.2, 56.4, 53.2, 53.0, 45.6, 42.4, 40.5.

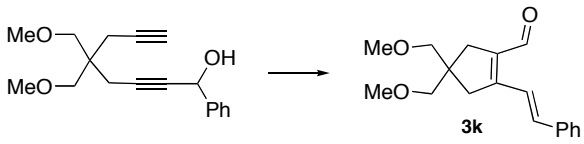
6h



A capped vial containing aldehyde **3h** (29 mg, 0.110 mmol), ethanol (1.1 mL), $NH_2OH{\cdot}HCl$ (9 mg, 0.132 mmol), and NaOAc (5 mg, 0.066 mmol) was heated in an oil bath at 95 °C for 24h. The vial was cooled to rt, diluted with $CHCl_3$, washed with sat'd aqueous $NaHCO_3$, and extracted with 1M aqueous HCl (3x). The aqueous phases were then combined and basified (pH >7) by slow addition of $NaHCO_3$. The aqueous phase was then extracted with $CHCl_3$ (5x), dried (Na_2SO_4), and the solvent removed in vacuo to yield pyridine **6h** (28 mg, 97 %) as a light oil.

$\mathbf{R}_f$ = 0.3 (40% EtOAc/hexanes). **IR**(thin film): 2957, 1737, 1611, 1567, 1435, 1276, 1248, 1202, 1162, 1071, 910, 883 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$): 8.35 (s, 1H), 7.03 (s, 1H), 3.76 (s, 6H), 3.59 (s, 2H), 2.78 (q, *J* = 15.2 Hz, 2H), 1.28 (t, *J* = 7.6 Hz, 3H). **^{13}C NMR** (100 MHz, C_6D_6): 171.5, 162.2, 149.6, 145.3, 133.6, 117.9, 145.3, 133.4, 117.9, 60.4, 52.5, 40.5, 38.2, 31.5, 14.2. **HRMS** (EI, $[M]^+$) Calc'd for $C_{14}H_{17}NO_4$: 263.1158. Found: 263.1150.

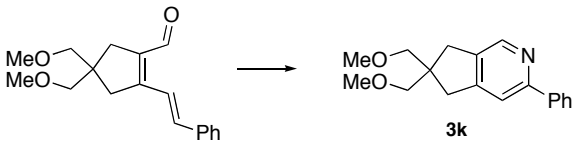
3k



Aldehyde **3k** was prepared from **2k** (100 mg, 0.35 mmol) according to Procedure A. Crude material was purified via silica gel chromatography (30% EtOAc/hexanes) to yield the title compound (70 mg, 70%) as a white solid.

$\mathbf{R}_f$ = 0.5 (40% EtOAc/hexanes). **mp**: 94-96 °C. **IR** (thin film): 2919, 1654, 1618, 1198, 1107, 959, 751, 691 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$): 10.31 (s, 1H), 7.65 (d, *J* = 16 Hz, 1H), 7.51-7.48 (m, 2H), 7.40-7.33 (m, 3H), 6.87 (d, *J* = 16 Hz, 1H), 3.37 (s, 6H), 3.34 (s, 2H), 3.33 (s, 2H), 2.85 (s, 2H), 2.61 (s, 2H). **^{13}C NMR** (100 MHz, $CDCl_3$): 187.5, 155.8, 137.8, 137.0, 136.2, 129.2, 129.0, 127.3, 119.9, 76.4, 59.4, 44.6, 40.6, 37.6.

3k

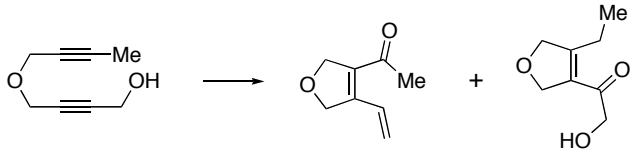


3k

A microwave reaction vial was charged with aldehyde **3k** (18 mg, 0.061 mmol), ethanol (2 mL), $NH_2OH{\cdot}HCl$ (5 mg, 0.073 mmol) and NaOAc (3 mg, 0.037 mmol), and heated under microwave irradiation at 150 °C for 1.5h. The reaction was quenched with saturated $NaHCO_3$, and the mixture extracted with $CHCl_3$ (4 x 10 mL). The organic layer was dried (Na_2SO_4), filtered, and the solvent evaporated in vacuo. Purification via column chromatography (30% EtOAc/hexanes) provided the title compound (15 mg, 87%) as a clear oil.

$\mathbf{R}_f$ = 0.5 (30% EtOAc/hexanes). **IR** (thin film): 2924, 2890, 1606, 1477, 1384, 1200, 1113, 960, 891, 778, 737, 695 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$): 8.49 (s, 1H), 7.96-7.93 (m, 2H), 7.56 (s, 1H), 7.48-7.44 (m, 2H), 7.41-7.37 (m, 1H), 3.39 (s, 4H), 3.38 (s, 6H), 2.91 (s, 2H), 2.90 (s, 2H). **^{13}C NMR** (125 MHz, C_6D_6): 155.6, 152.9, 146.2, 137.3, 117.0, 75.8, 58.8, 48.6, 38.8, 36.3. **HRMS** (EI, $[M]^+$) Calc'd for $C_{18}H_{21}NO_2$: 283.1572. Found: 283.1571.

3d



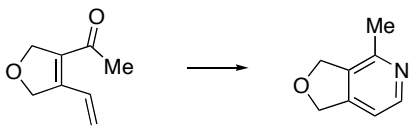
3d **7**

Ketone **3d** was prepared from 4-(but-2-ynyloxy)but-2-yn-1-ol [8] 54 mg, 0.390 mmol) according to Procedure B. Crude material was purified via silica gel chromatography (30% Et_2O/hexanes) to yield **3d** (37 mg, 68%) along with **7** (15 mg, 24%), both as clear oils.

3d: $\mathbf{R}_f$ = 0.5 (30% EtOAc/hexanes). **IR** (thin film): 2917, 2850, 1681, 1582, 1276, 1240, 931 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$): 7.28 (dd, *J* = 17.6, 10.8 Hz, 1H), 5.55 (dd, *J* = 10.8, 0.8, 1H), 5.35 (dd, *J* = 17.6, 0.8 Hz, 1H), 4.70 (s, 4H), 2.29 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): 194.5, 145.3, 132.8, 128.1, 123.4, 77.0, 76.4, 30.8. **HRMS** (EI, $[M]^+$) Calc'd for $C_8H_{10}O_2$: 138.0681. Found: 138.0687.

7: $\mathbf{R}_f$ = 0.3 (30% EtOAc/hexanes). **IR** (thin film): 3448, 2920, 1686, 1274, 1104 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$): 4.91-4.88 (m, 2H), 4.80 (t, *J* = 4.4 Hz, 2H), 4.33 (d, *J* = 4.8 Hz, 2H), 3.43 (t, *J* = 4.8 Hz, 1H), 2.65-2.59 (comp m, 2H), 1.14 (t, *J* = 7.6 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): 194.7, 78.8, 75.4, 67.8, 20.8, 12.3. **HRMS** (EI, $[M]^+$) Calc'd for $C_8H_{12}O_3$: 156.0786. Found: 156.0786.

6d



6d

A capped microwave reaction vial containing a suspension of **3d** (26 mg, 0.189 mmol), ethanol (2 mL), $NH_2OMe{\cdot}HCl$ (19 mg, 0.227 mmol), and NaOAc (9 mg, 0.113 mmol) was heated in the microwave at 150 °C for 1h. The vial was cooled to rt, diluted with $CHCl_3$, washed with aqueous $NaHCO_3$ (2x 5mLs), and extracted with 1M aqueous HCl (3x). The aqueous phases were then combined and basified (pH >7) by slow addition of $NaHCO_3$. The aqueous phase was then extracted with $CHCl_3$ (5x), dried (Na_2SO_4), and the solvent removed in vacuo to yield pyridine **6d** (13 mg, 58 %) as a light oil.

$\mathbf{R_f}$ = 0.3 (50% EtOAc/hexanes). **IR** (thin film): 2922, 2851, 2360, 1053, 756 cm^{-1}. **^{1}H NMR** (400 MHz, $CDCl_3$): 8.40 (d, *J* = 4 Hz, 1H), 7.05 (d, *J* = 4Hz, 1H), 5.11 (d, *J* = 2.4 Hz, 4H), 2.47 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): 148.2, 114.2, 73.6, 72.2, 22.3. **HRMS** (EI, $[M]^+$) Calc'd for C_8H_9NO: 135.1632. Found: 135.0683.

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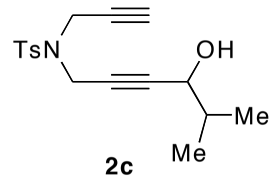

2c

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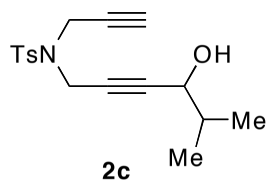

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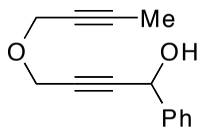

2e

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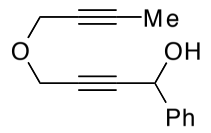
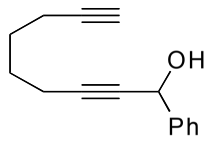


2e

^{13}C: 100 MHz, $CDCl_3$

180 160 140 120 100 80 60 40 20 ppm



2f

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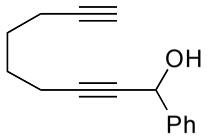

2f

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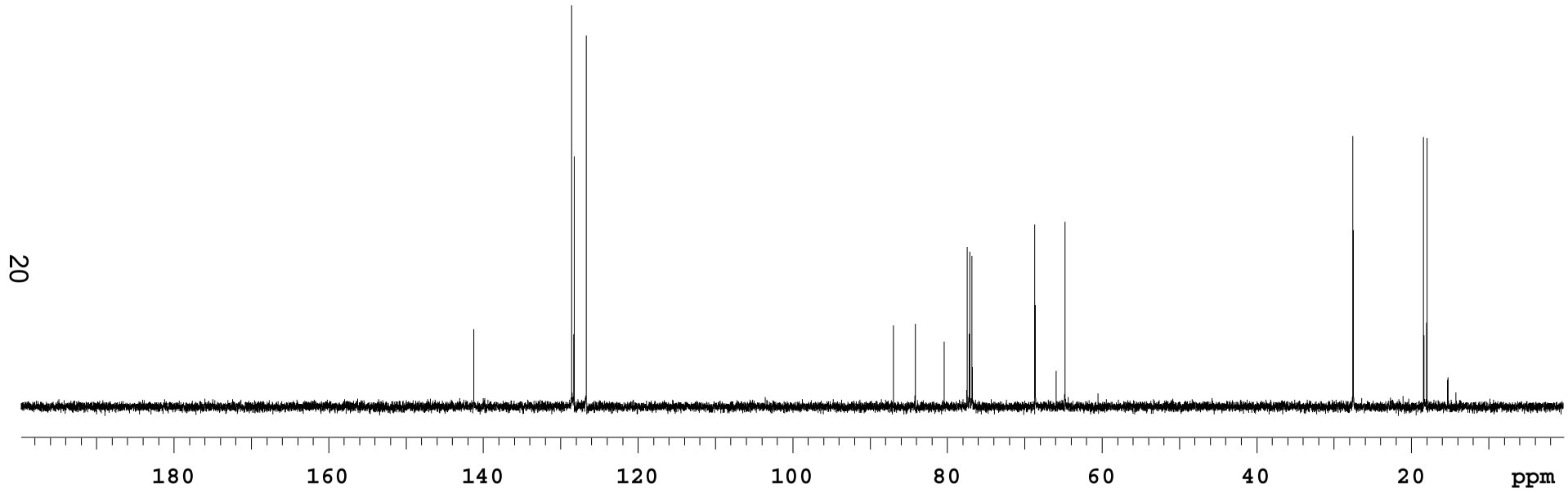

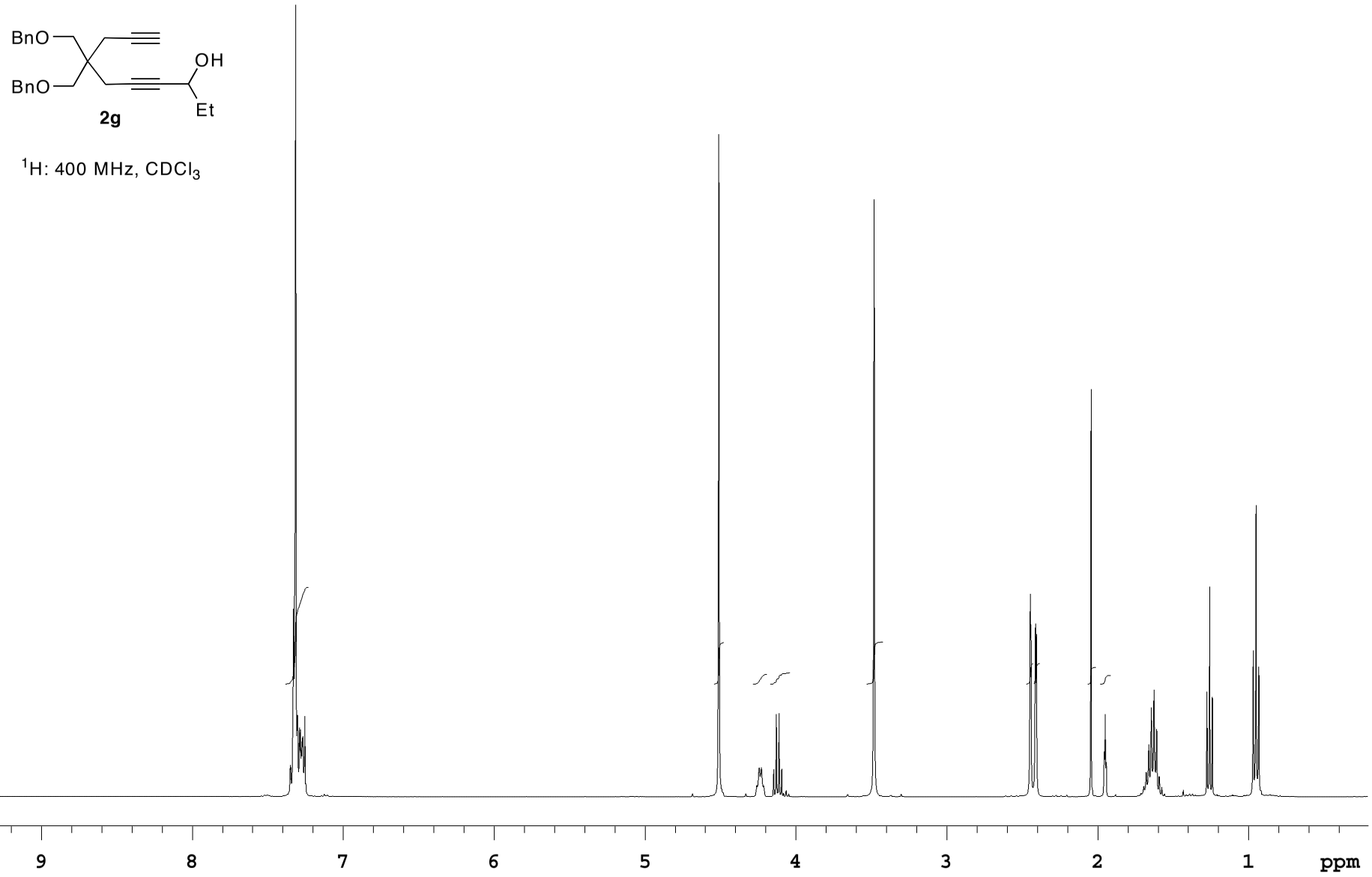
BnO
BnO
OH
Et
2g
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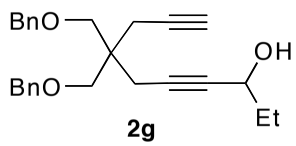
21
9
8
7
6
5
4
3
2
1
ppm



2g

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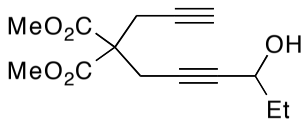

2h

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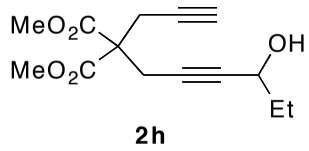

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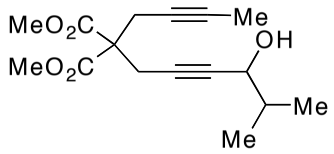

2j

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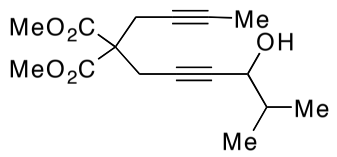

2j

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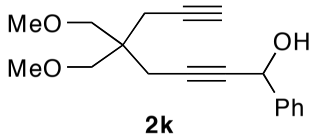

2k

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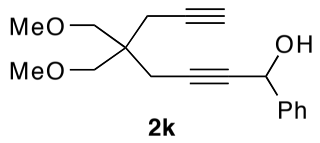

2k

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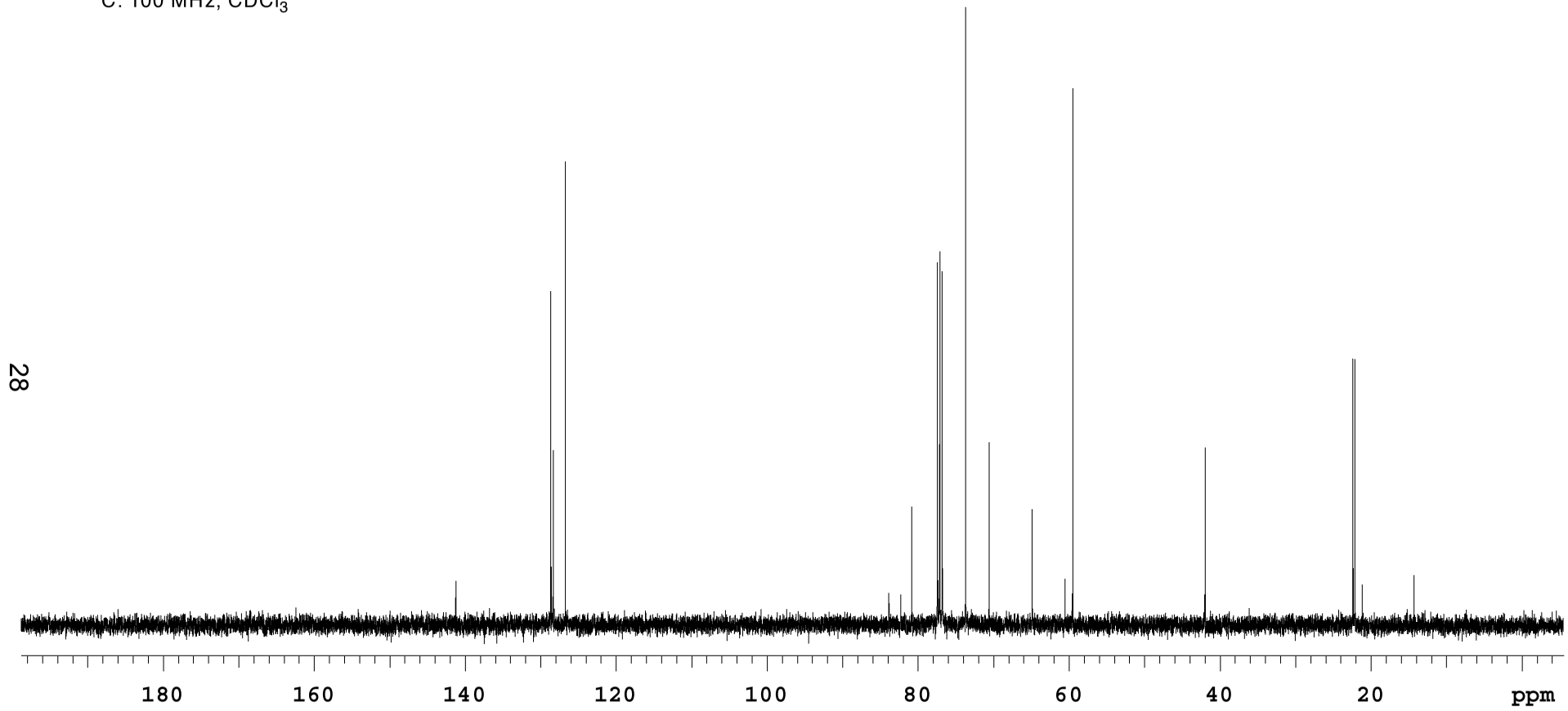

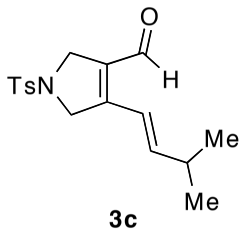

3c

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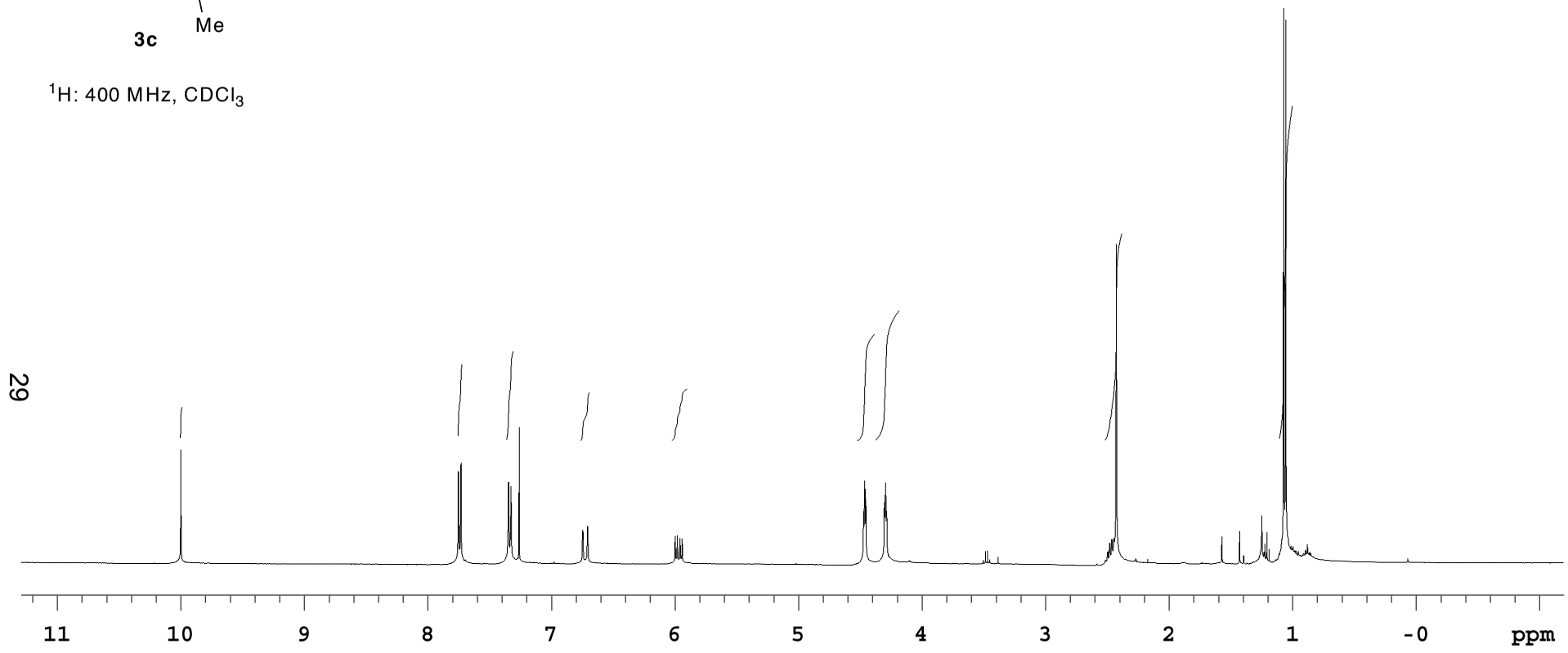

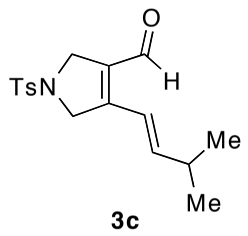

3c

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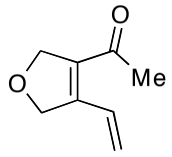

3d

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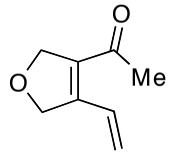

3d

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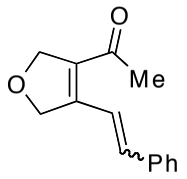

3e

E/Z = 5:1

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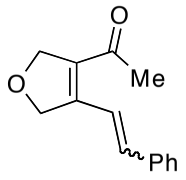

3e

E/Z = 5:1

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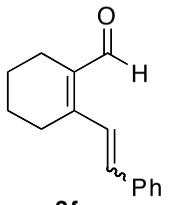

3f

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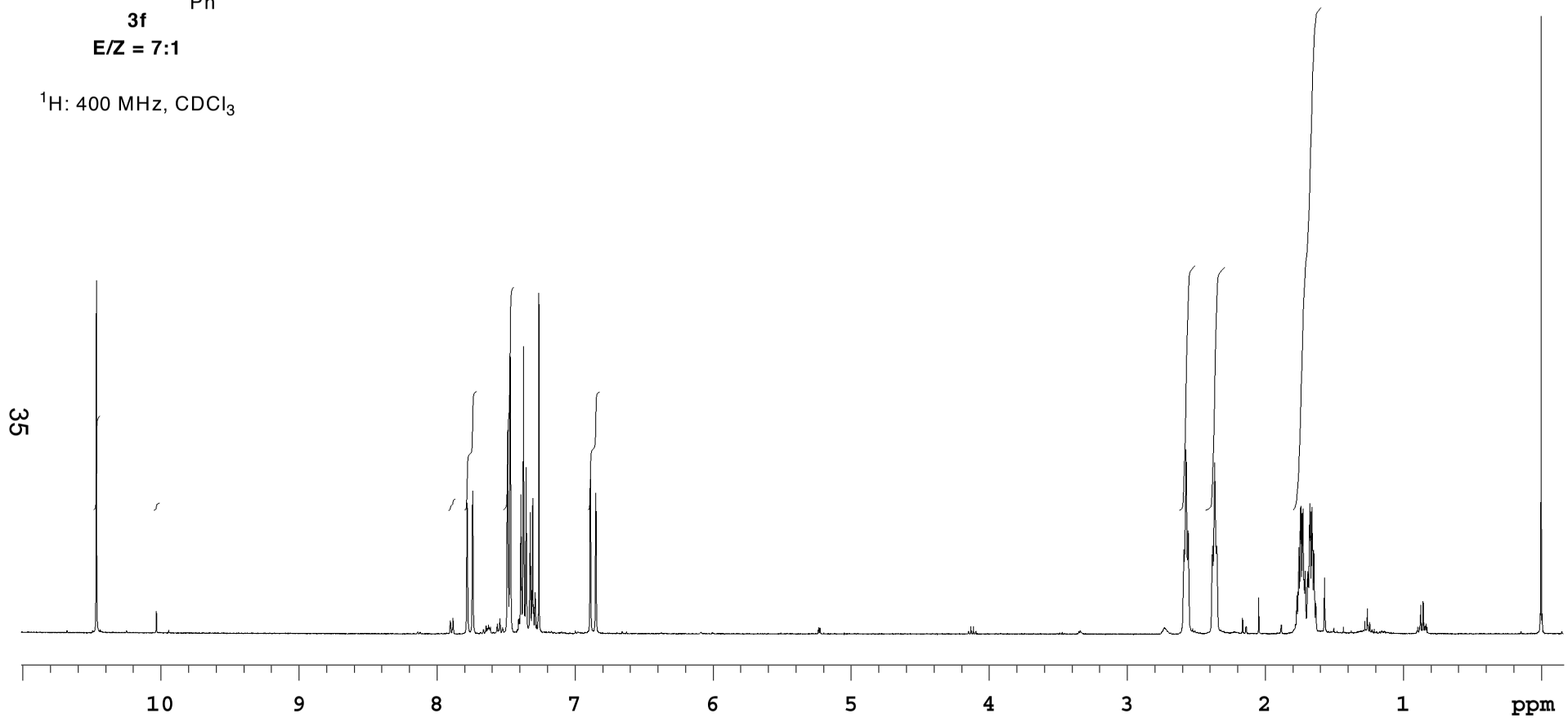

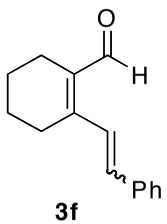

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E/Z = 7:1

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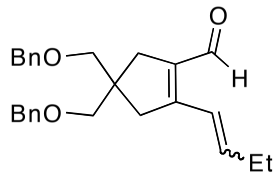
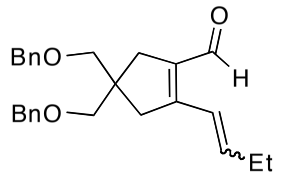


3g

^{1}H: 400 MHz, $CDCl_3$

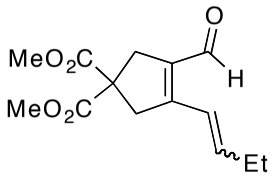
37

11 10 9 8 7 6 5 4 3 2 1 -0 ppm



3g

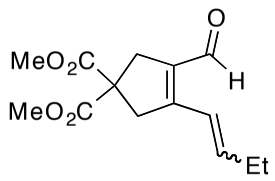
^{13}C: 100 MHz, $CDCl_3$



3h

E/Z = 12:1

^{1}H: 400 MHz, $CDCl_3$



3h

E/Z = 12:1

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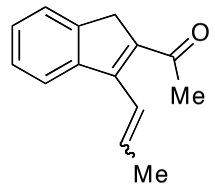

3i

E/Z = 2:1

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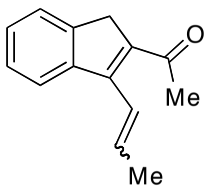

3i
E/Z = 2:1

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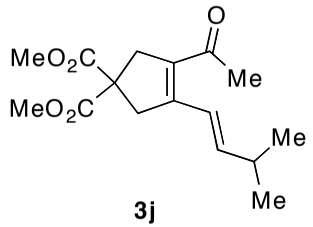

3j

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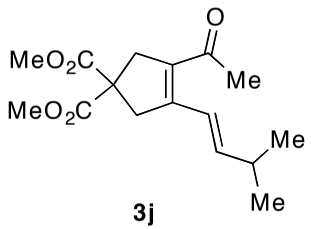
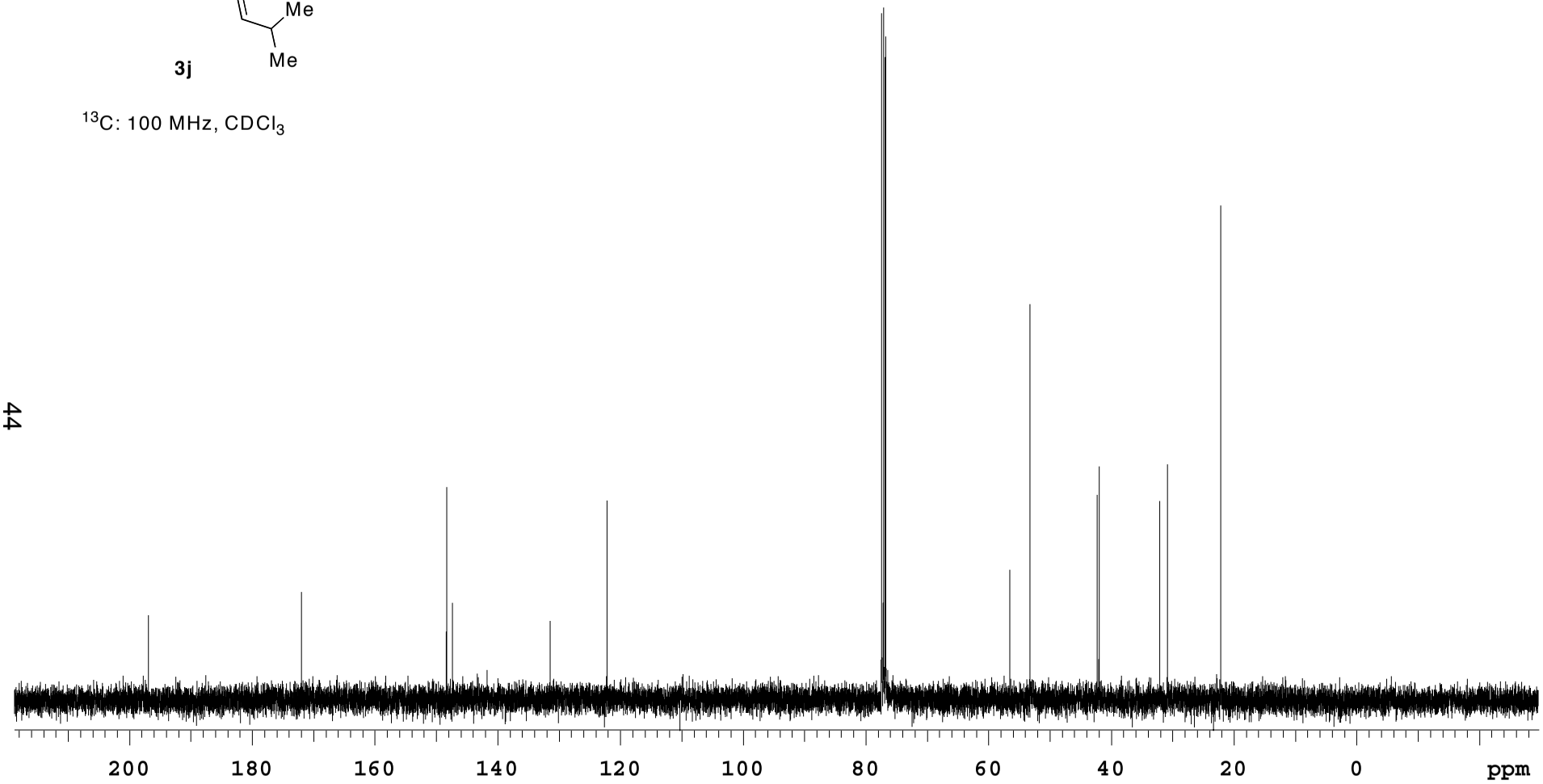
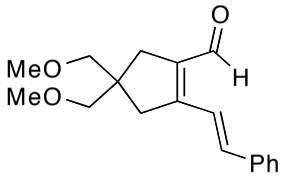


3j

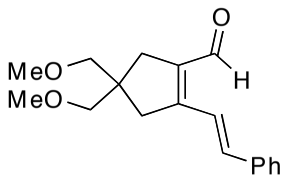
^{13}C: 100 MHz, $CDCl_3$





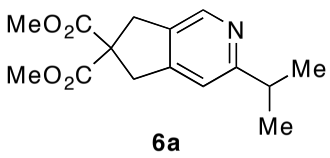
3k

^{1}H: 400 MHz, $CDCl_3$



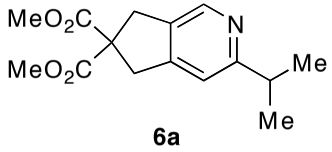
3k

^{13}C: 100 MHz, $CDCl_3$



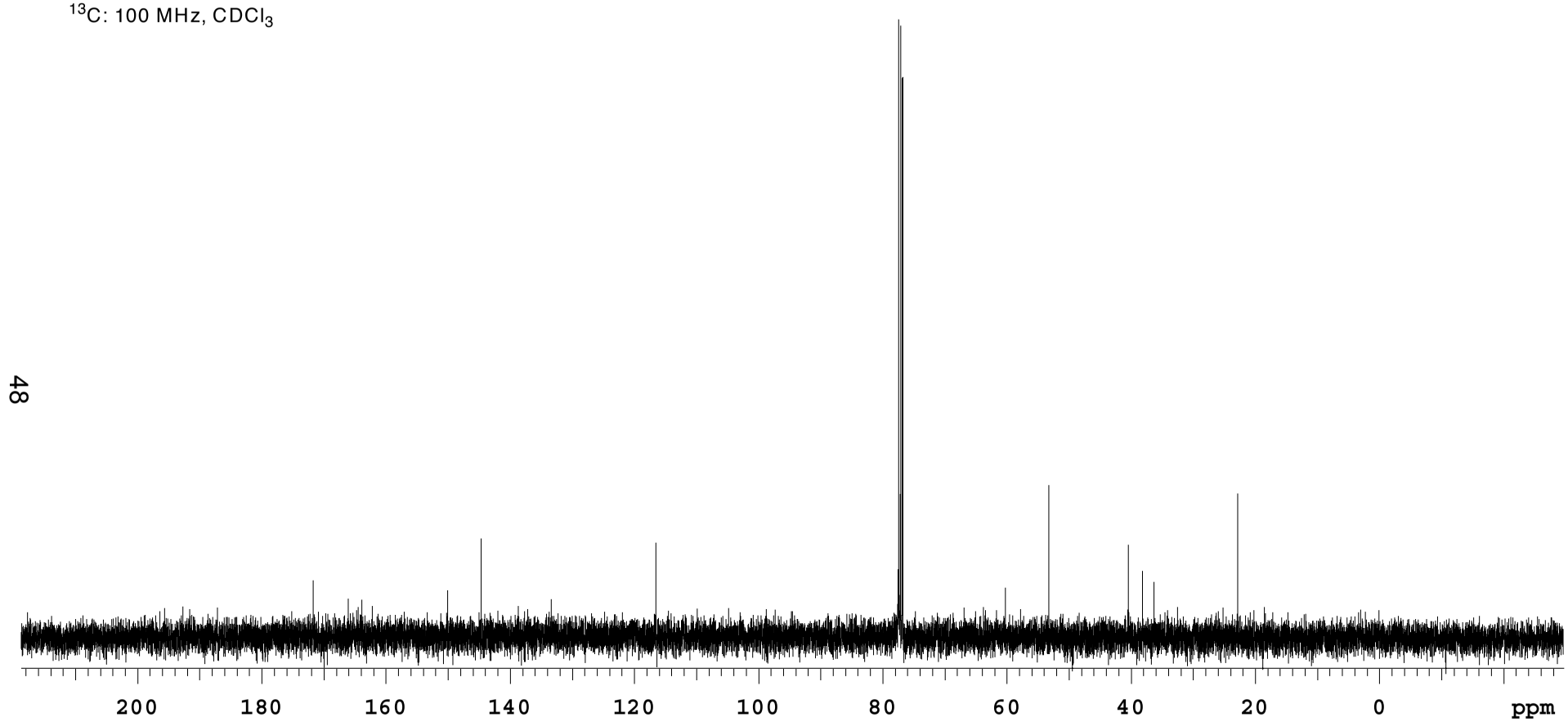
6a

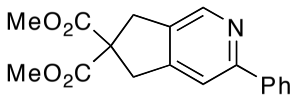
^{1}H: 400 MHz, CDCl3



6a

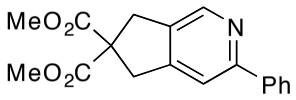
^{13}C: 100 MHz, $CDCl_3$





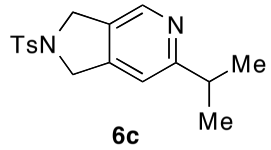
6b

^{1}H: 400 MHz, $CDCl_3$



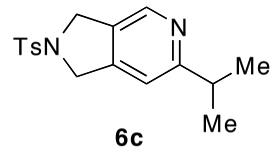
6b

^{13}C: 100 MHz, $CDCl_3$



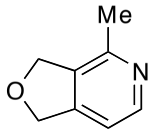
6c

^{1}H: 400 MHz, $CDCl_3$



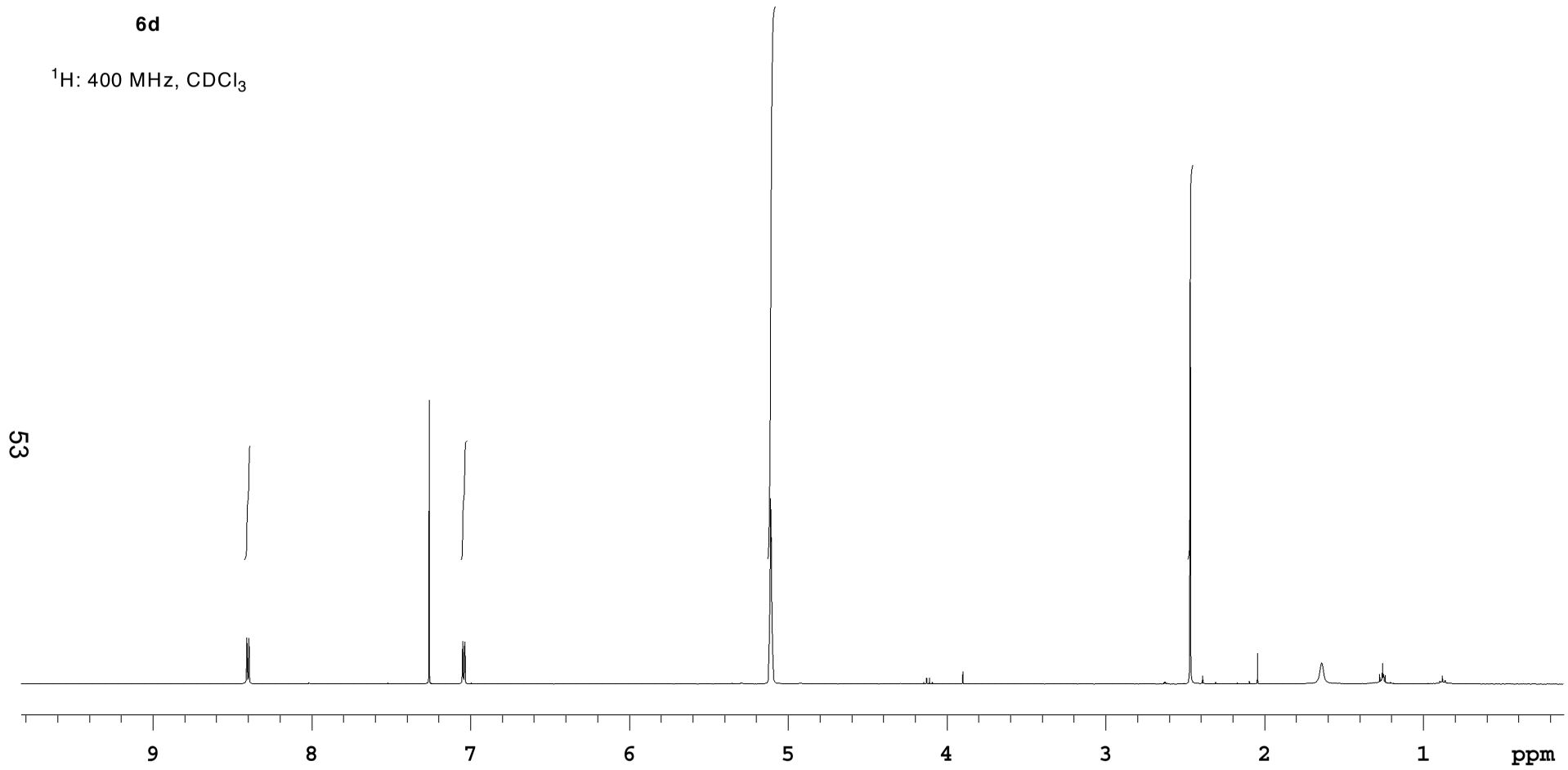
6c

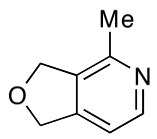
^{13}C: 100 MHz, $CDCl_3$



6d

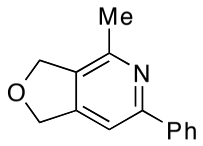
^{1}H: 400 MHz, $CDCl_3$





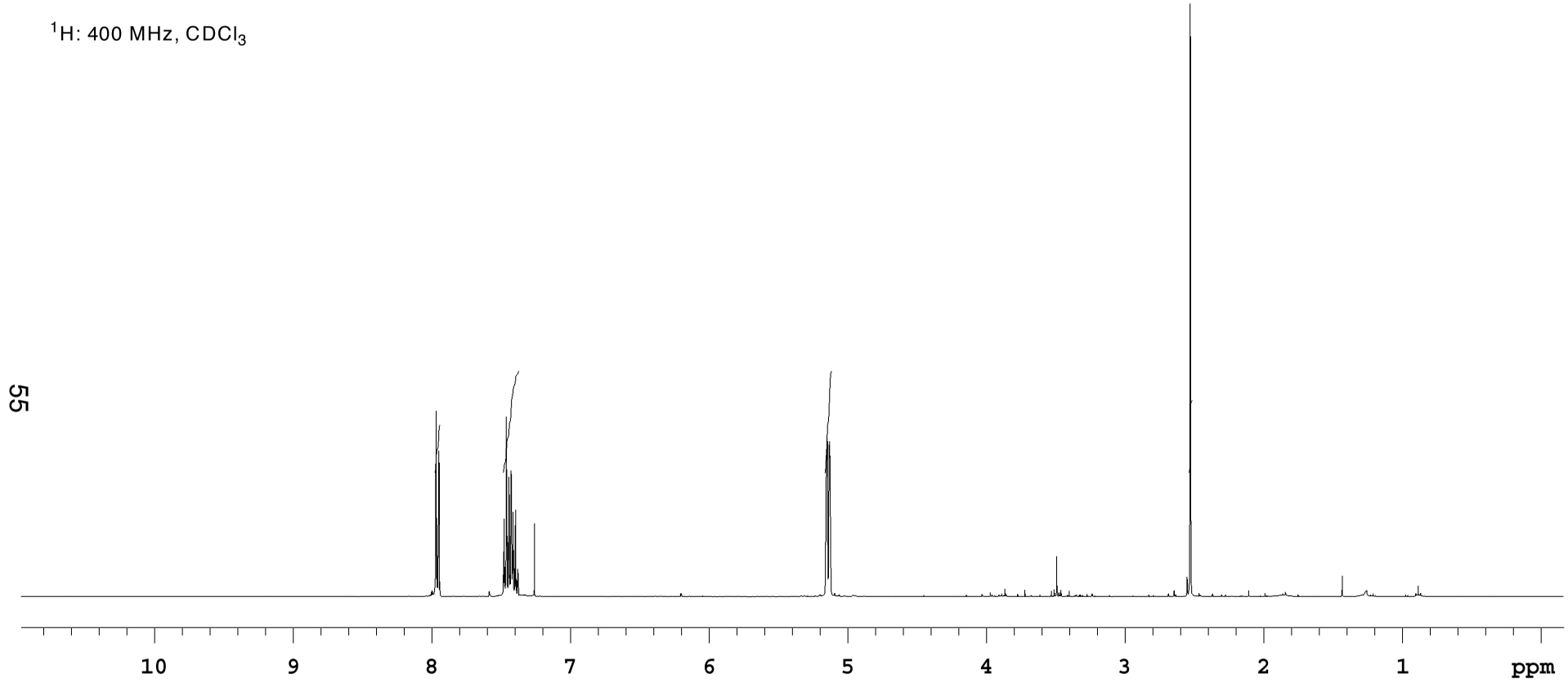
6d

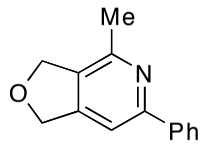
^{13}C: 100 MHz, $CDCl_3$



6e

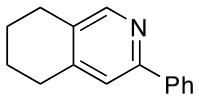
^{1}H: 400 MHz, $CDCl_3$





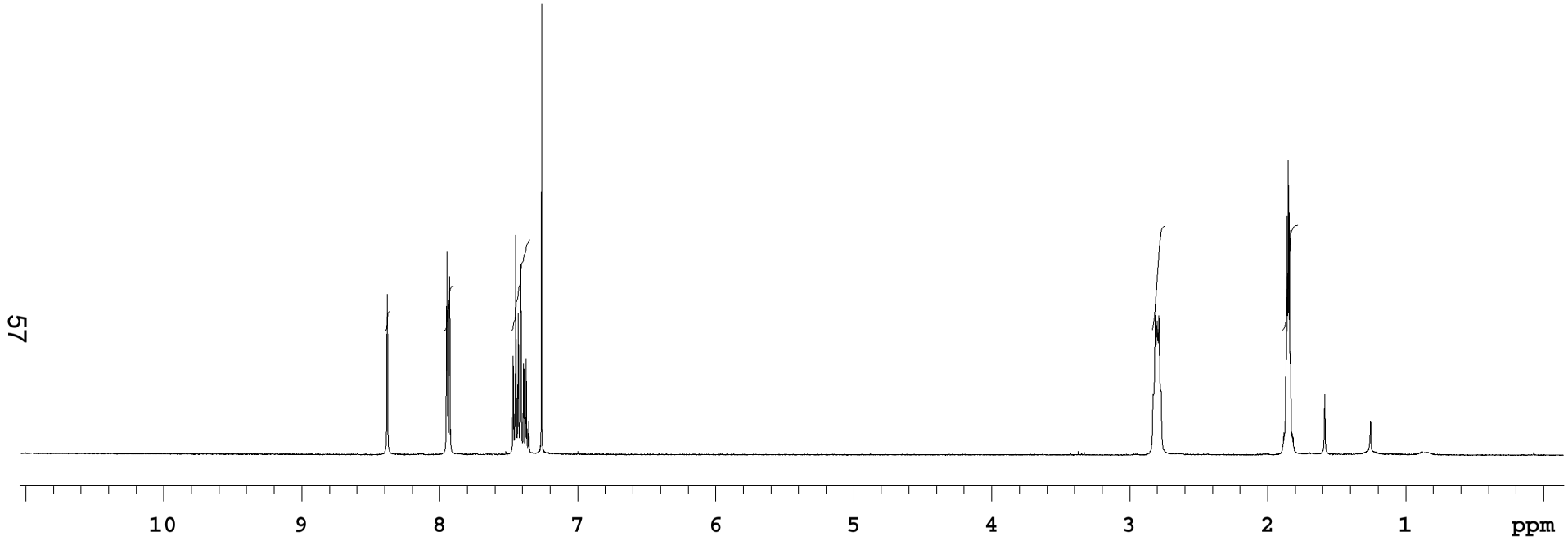
6e

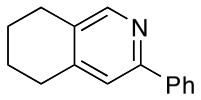
^{13}C: 100 MHz, $CDCl_3$



6f

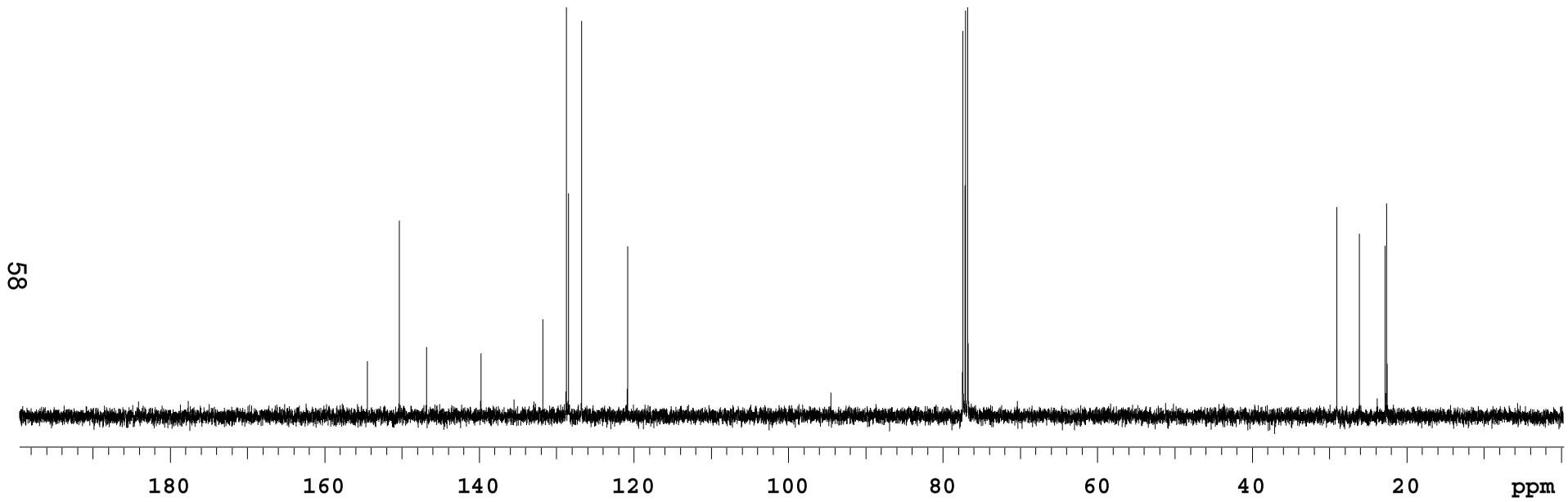
^{1}H: 400 MHz, $CDCl_3$

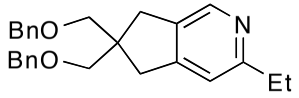




6f

^{13}C: 100 MHz, $CDCl_3$



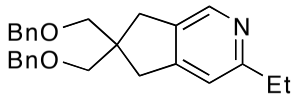


6g

^{1}H: 400 MHz, $CDCl_3$

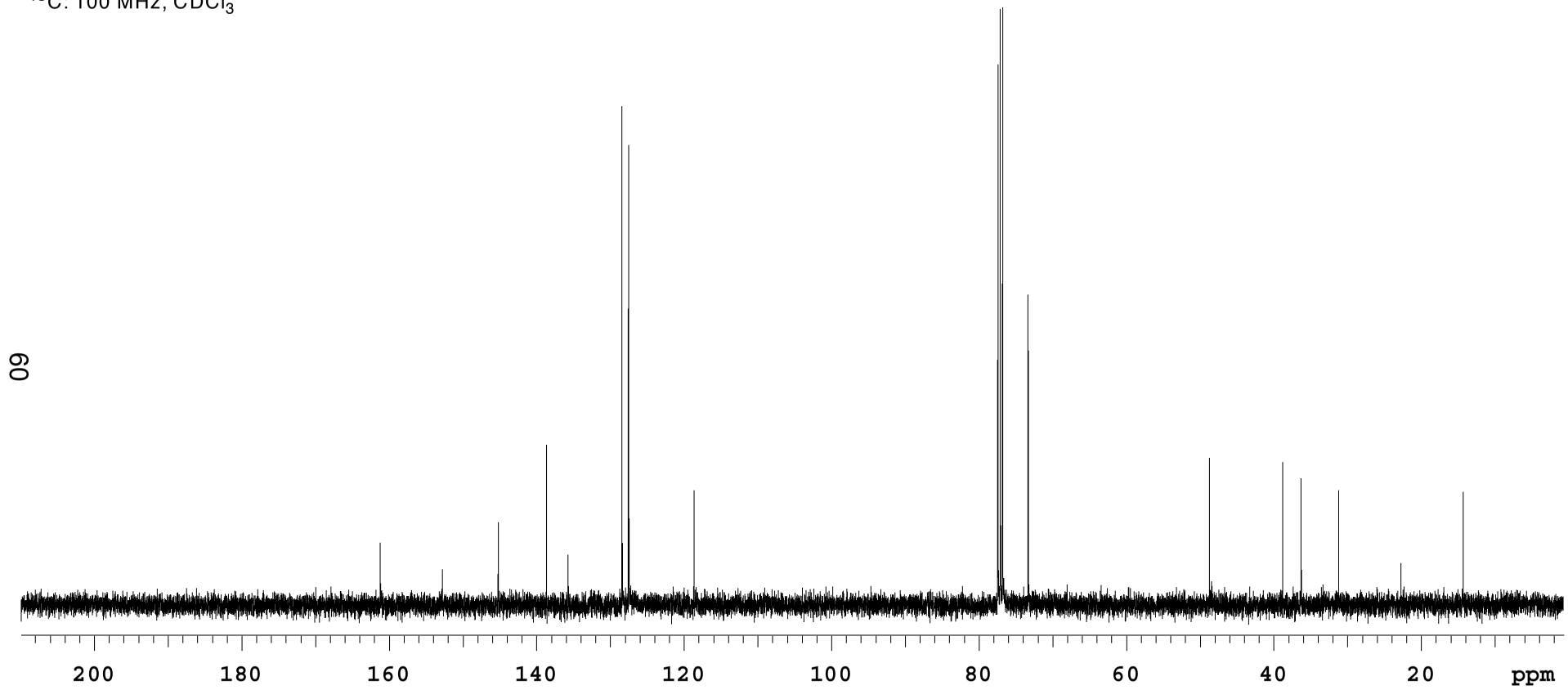
59

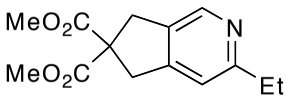
11 10 9 8 7 6 5 4 3 2 1 -0 ppm



6g

^{13}C: 100 MHz, $CDCl_3$

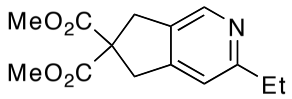




6h

^{1}H: 400 MHz, $CDCl_3$

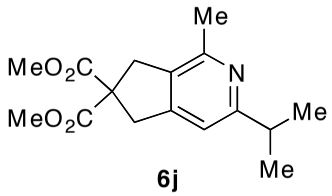
61



6h

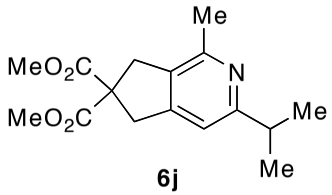
^{13}C: 100 MHz, C_6D_6

62



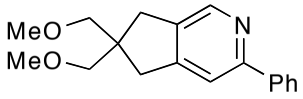
6j

^{1}H: 400 MHz, $CDCl_3$



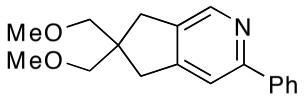
6j

^{13}C: 100 MHz, $CDCl_3$



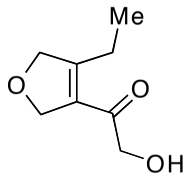
6k

^{1}H: 400 MHz, $CDCl_3$



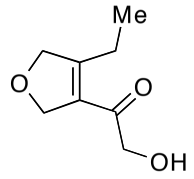
6k

^{13}C: 100 MHz, $CDCl_3$



7

^{1}H: 400 MHz, C_6D_6



7

^{13}C: 100 MHz, $CDCl_3$