Synthesis of Quinolinone Alkaloids via Aryne Insertions into Unsymmetric Imides in Flow

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Supporting Information

General Methods

Analytical data were obtained with the help of the following equipment:

NMR spectroscopy: ^{1}H and ^{13}C NMR spectra were acquired on a JEOL ECX 400 (400 MHz), JEOL ECP 500 (500 MHz) and a Bruker Avance 700 (700 MHZ) in the reported deuterated solvents. The chemical shifts were reported relative to the deuterated solvents' residual shifts. The multiplicities of the signals are reported using the following abbreviations: s = singlet, d = doublet, t = triplet, q = quartet, p = quintet, br = broad.
The spectra were processed with the software MestRec 9.0.

Mass spectra were obtained on a ESI-FTICR-MS: Ionspec QFT-7 (Agilent/Varian), or a HR-EI-MS: Autospec Premier (Waters).

GC-MS were recorded on a GC system Agilent Technologies 7890-A series/Mass selective detector, Agilent Technologies 5975 C (column: HP-5MS (J&W Scientific, Agilent); 30 m, 0.250 mm i.D., Film 0.25 µm).

IR spectroscopy: IR Spectra were recorded on a JASCO FT/IR-4100 spectrometer. Characteristic absorption bands are reported in wavelengths $\tilde{\nu}$ in cm^{-1} and were analyzed with the software Spectral Manager from JASCO.

Melting points were measured on a Thermovar (Reichert) and are not corrected.

Chromatography: Reaction progress was monitored by thin layer chromatography (silica gel 60 F 254, E. Merck) using UV light (λ = 254 nm) for visualization or vanillin staining agent (170 mL methanol, 20.0 ml conc. acetic acid, 10.0 mL conc. sulfuric acid, 1.0 g vanillin).
Flash column chromatography was performed using silica gel M60 from Macherey & Nagel (particle size: 40–63 µm).

HPLC was conducted on a modular Knauer HPLC system with a UV detector at 254 nm and differential refractometer on a 4 x 250 mm column packed with Nucleosil 50-5 from Machery-Nagel.

Flow Reactions: Flow reactions were performed in 1/16 inch PTFE tubing with an inner diameter of 1.0 mm. The tubing was embedded in an aluminum block from ThalesNano and heated with an IKA stirring plate. A stainless steel T-piece from Vici or a static mixer from Upchurch Scientific was used for mixing. Fittings were either coned 10/32 stainless steel fittings from Upchurch scientific or flat bottom 1/4-28 gripper fittings from Dibafit. A kdScientific syringe pump (model no. KDS 200CE) was used to pump the reagents through the reactor.

Reagents and Solvents: Reactions with air or moisture sensitive substances were carried out under an argon atmosphere with the help of the Schlenk technique. All other reagents and solvents were used as purchased from commercial suppliers unless otherwise noted. Anhydrous solvents were purified with the solvent purification system MB-SPS-800 (Braun). Dry acetonitrile was purchased from Acros Organics in AcroSeal©-bottles under argon atmosphere with molecular sieves (4 Å). HPLC-grade acetonitrile was purchased from Fischer Scientific. The solvents used for column chromatography (ethyl acetate, pentane) and work up were purified from commercially available technical grade solvents by

distillation under reduced pressure with the help of rotatory evaporators (Heidolph or IKA) at 40 °C bath temperature.

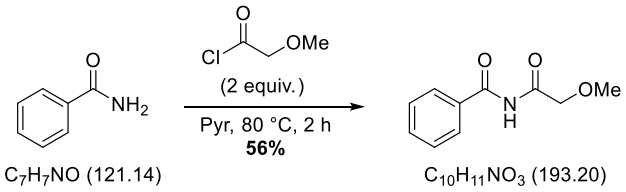
Benzamides,[1] benzyloxy acetic acid,[2] benzyloxyacetyl chloride[3] and 3-hydroxy-2-(trimethylsilyl)phenyl triflate[4] were prepared according to literature procedures.

Compound names are derived from Chemdraw and are not necessarily identical with the IUPAC nomenclature.

Room temperature refers to 23 °C.

Synthesis of Compounds

N-(2-Methoxyacetyl)-benzamide (4a)

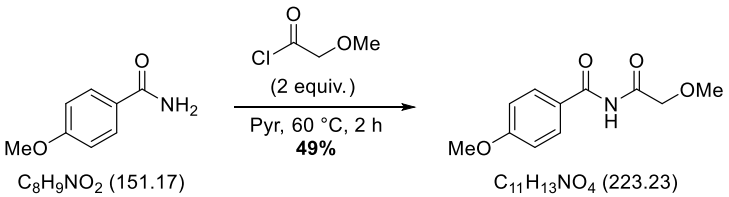


C_7H_7NO (121.14) $C_{10}H_{11}NO_3$ (193.20)

Benzamide (2.00 g, 16.5 mmol, 1 equiv.) was dissolved in anhydrous pyridine (26 mL) and 2-methoxyacetyl chloride (3.01 mL, 33.0 mmol, 2 equiv.) was added in one portion at room temperature. The yellow mixture was stirred in a sealed tube at 80 °C for 2 hours. After cooling to room temperature, the mixture was concentrated under reduced pressure to 1/4 of its original volume and diluted with NH_4Cl (sat. aq., 50 mL) and EtOAc (50 mL). The organic layer was separated and the aqueous layer was extracted with EtOAc (3 × 50 mL). The combined organic layers were washed with NH_4Cl (sat. aq., 3 × 150 mL) and NaCl (sat. aq., 100 mL), dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The crude product was purified by column chromatography (silica gel, *n*-pentane/EtOAc = 1:1) affording the title compound (**4a**, 1.77 g, 9.17 mmol, 56%) as a colorless solid.

R_f = 0.41 (*n*-pentane/EtOAc = 1:1); **m.p.:** 103 **°C -** 105 °C; **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 9.44 (s, 1H), 7.86 (d, *J* = 7.4 Hz, 2H), 7.58 (t, *J* = 7.4 Hz, 1H), 7.48 (t, *J* = 7.7 Hz, 2H), 4.38 (s, 2H), 3.49 (s, 3H) ppm; **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 171.1, 165.2, 133.4, 132.5, 129.0, 127.9, 73.1, 59.5 ppm; **IR** (neat): $\tilde{\nu}$ = 3378, 3280, 3168, 3071, 2990, 2963, 2938, 2920, 2825, 2748, 2600, 1909, 1771, 1709, 1685, 1636, 1602, 1584, 1555, 1508, 1465, 1448, 1396, 1384, 1346, 1327, 1310, 1287, 1250, 1239, 1196, 1169, 1120, 1090, 1069, 1031, 1012, 1002, 973, 933, 907, 842, 818, 805, 751, 701 cm^{-1}; **HRMS** (ESI): m/z calculated for $C_{10}H_{11}NNaO_3^+$ ($[M+Na]^+$): 216.0631; found: 216.0641.

4-Methoxy-*N*-(2-methoxyacetyl)-benzamide (4b)



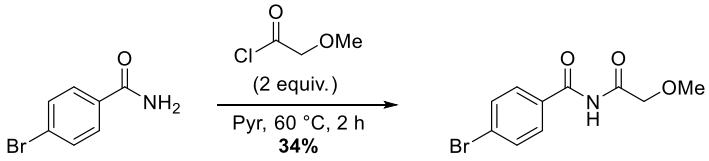
$C_8H_9NO_2$ (151.17) $C_{11}H_{13}NO_4$ (223.23)

4-Methoxybenzamide (2.00 g, 13.2 mmol, 1 equiv.) was dissolved in anhydrous pyridine (20 mL) and 2-methoxyacetyl chloride (1.50 mL, 16.5 mmol, 2 equiv.) was added at room temperature. The orange mixture was stirred in a sealed tube at 60 °C for 2 hours. After cooling to room temperature, the solvent was removed under reduced pressure. The residue was suspended in $NaHCO_3$ (sat. aq., 250 mL) and EtOAc (250 mL). The organic layer was separated and the aqueous layer was extracted with EtOAc (3 × 100 mL). The combined organic layers were washed with NaCl (sat. aq., 2 × 400 mL), dried (Na_2SO_4), filtered and concentrated under reduced pressure. The crude product was recrystallized from hot EtOAc affording the title compound (**4b**, 1.45 g, 6.48 mmol, 49%) as a colorless solid.

R_f = 0.42 (*n*-pentane/EtOAc = 1:2); **m.p.:** 153 °C - 156 °C; **^{1}H NMR** (400 MHz, DMSO-d_6): δ = 11.00 (s, 1H), 7.94 (d, *J* = 8.8 Hz, 2H), 7.03 (d, *J* = 8.9 Hz, 2H), 4.44 (s, 2H), 3.83 (s, 3H), 3.34 (s, 3H) ppm; **^{13}C NMR** (101 MHz, DMSO-d_6): δ = 172.9, 165.7, 163.0, 130.7, 124.6, 113.8, 72.8, 58.5, 55.6 ppm; **IR** (neat):

$\tilde{\nu}$ = 3390, 3291, 3169, 3094, 3080, 3014, 2970, 2942, 2843, 1769, 1710, 1685, 1645, 1618, 1607, 1574, 1517, 1458, 1422, 1394, 1311, 1254, 1182, 1146, 1124, 1025, 849, 809, 764 cm^{-1}; **HRMS** (ESI): m/z calculated for $C_{11}H_{13}NNaO_4^+$ ([M+Na]$^+$): 246.0737; found 246.0738.

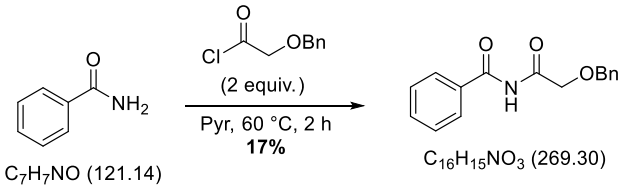
4-bromo-*N*-(2-methoxyacetyl)-benzamide (4c)



4-Bromobenzamide (150 mg, 0.992 mmol, 1 equiv.) was dissolved in anhydrous pyridine (1.6 mL) and 2-methoxyacetyl chloride (0.181 mL, 1.99 mmol, 2 equiv.) was added at room temperature. The orange mixture was stirred in a sealed tube at 60 °C for 2 hours. After cooling to room temperature, the solvent was removed under reduced pressure. The residue was suspended in $NaHCO_3$ (sat. aq., 20 mL) and EtOAc (20 mL). The organic layer was separated and the aqueous layer was extracted with EtOAc (3 × 20 mL). The combined organic layers were washed with NaCl (sat. aq., 2 × 50 mL), dried (Na_2SO_4), filtered, and concentrated under reduced pressure. The crude product was purified by column chromatography (silica gel, *n*-pentane/EtOAc 2:1) to afford the title compound (**4c**, 74.0 mg, 0.332 mmol, 34%) as a colorless solid.

R_f = 0.30 (*n*-pentane/EtOAc = 1:2); **m.p.:** 139 °C - 141 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ = 9.37 (s, 1H), 7.73 (d, *J* = 8.1 Hz, 2H), 7.64 (d, *J* = 8.2 Hz, 2H), 4.35 (s, 2H), 3.51 (s, 3H) ppm; **^{13}C NMR** (126 MHz, $CDCl_3$) δ = 170.7, 164.5, 132.4, 131.5, 129.5, 128.6, 73.0, 59.6 ppm; **IR** (neat): $\tilde{\nu}$ = 3240, 3196, 3160, 2970, 2952, 2926, 2823, 1731, 16696, 1591, 1524, 1502, 1479, 1400, 1386, 1257, 1232, 1202, 1136, 1110, 1069, 1012, 939, 907, 840, 818, 772, 763, 744, 717, 684, 661 cm^{-1}; **HRMS** (ESI): m/z calculated for $C_{10}H_{10}BrNO_3Na^+$ ([M+Na]$^+$): 293.9736; found: 293.9745.

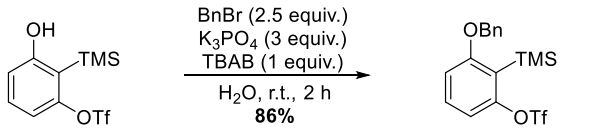
***N*-(2-(Benzyloxy)acetyl)benzamide (4d)**



Benzamide (800 mg, 6.60 mmol, 1 equiv.) was dissolved in anhydrous pyridine (11 mL). Benzyloxyacetyl chloride (2.44 g, 13.2 mmol, 2 equiv.) was added and the mixture was stirred in a sealed tube at 60 °C for 2 hours. After cooling to room temperature, the solvent was removed under reduced pressure. The residue was dissolved in EtOAc (10 mL) and $NaHCO_3$ (sat. aq., 10 mL), the layers were separated, and the aqueous layer was extracted with EtOAc (3 x 10 mL). The combined organic layers were washed with NaCl (sat. aq., 2 x 10 mL) and dried ($MgSO_4$). The solvents were removed under reduced pressure. The crude product was recrystallized from boiling EtOAc affording the title compound (**4d**, 300 mg, 1.10 mmol, 17%) as colorless crystals.

m.p.: 109 °C **-** 113 °C; **^{1}H NMR** (700 MHz, $CDCl_3$) δ = 9.32 (s, 1H), 7.82 – 7.80 (m, 2H), 7.60 (td, *J* = 7.3, 1.3 Hz, 1H), 7.50 – 7.47 (m, 2H), 7.39 (s, 2H), 7.38 (d, *J* = 1.6 Hz, 2H), 7.36 – 7.33 (m, 1H), 4.70 (s, 2H), 4.43 (s, 2H) ppm; **^{13}C NMR** (176 MHz, $CDCl_3$) δ = 170.5, 165.0, 136.8, 133.5, 132.6, 129.2, 128.8, 128.5, 128.2, 127.8, 73.9, 70.5 ppm; **IR** (neat): $\tilde{\nu}$ = 3284, 2951, 2922, 2868, 1712, 1688, 1599, 1582, 1500, 1469, 1406, 1390, 1373, 1324, 1304, 1244, 1216, 1115, 1102, 1072, 1028, 1001, 975, 949, 933, 908, 872, 862, 841, 822, 800, 785, 757, 702, 657 cm^{-1}; **HRMS** (ESI): *m/z* calculated for $C_{16}H_{15}NNaO_3^+$ ([M+Na]$^+$): 292.0944; found: 292.0951.

3-(Benzyloxy)-2-(trimethylsilyl)phenyl trifluoromethanesulfonate (**3b**)

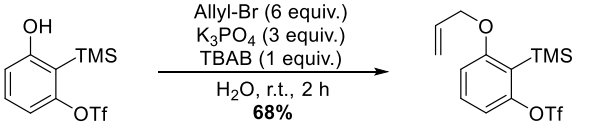


$C_{10}H_{13}F_3O_4SSi$ (314.35) $C_{17}H_{19}F_3O_4SSi$ (404.48)

3-Hydroxy-2-(trimethylsilyl)phenyl trifluoromethanesulfonate (500 mg, 1.59 mmol, 1 equiv.) was suspended in water (15 mL) and benzyl bromide (0.472 mL, 3.98 mmol, 2.5 equiv.), tetrabutylammonium bromide (513 mg, 1.59 mmol, 1 equiv.) and K_3PO_4 (1.01 g, 4.77 mmol, 3 equiv.) were added at room temperature. The suspension was stirred vigorously for 2 hours, diluted with water, and extracted with EtOAc (3 x 50 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated under reduced pressure. The crude product was purified by column chromatography (silica gel, *n*-pentane/EtOAc = 20:1) to afford the title compound (**3b**, 555 mg, 1.37 mmol, 86%) as a colorless oil.

R_f = 0.83 (*n*-pentane/EtOAc = 10:1); **^{1}H NMR** (500 MHz, $CDCl_3$) δ = 7.41 (m, 4H), 7.39 – 7.32 (m, 2H), 6.97 (d, *J* = 8.4 Hz, 1H), 6.89 (d, *J* = 8.4 Hz, 1H), 5.09 (s, 2H), 0.34 (s, 9H) ppm; **^{13}C NMR** (126 MHz, $CDCl_3$) δ = 164.8, 154.9, 136.2, 131.7, 128.8, 128.4, 127.9, 121.2, 118.8 (q, *J* = 320.6 Hz), 113.1, 110.6, 71.1, 1.1 ppm; **^{19}F NMR** (376 MHz, $CDCl_3$) δ = -73.98 ppm; **IR** (neat): $\tilde{\nu}$ = 3067, 3036, 2954, 2901, 2876, 1594, 1565, 1434, 1417, 1247, 1207, 1160, 1137, 1116, 1024, 934, 842, 826, 785, 735 cm^{-1}; **HRMS** (ESI): m/z calculated for $C_{17}H_{19}F_3O_4SSiK$ ([M+K]$^+$): 443.0357, found 443.0378.

3-(Allyloxy)-2-(trimethylsilyl)phenyl trifluoromethanesulfonate (**3c**)



$C_{10}H_{13}F_3O_4SSi$ (314.35) $C_{13}H_{17}F_3O_4SSi$ (354.42)

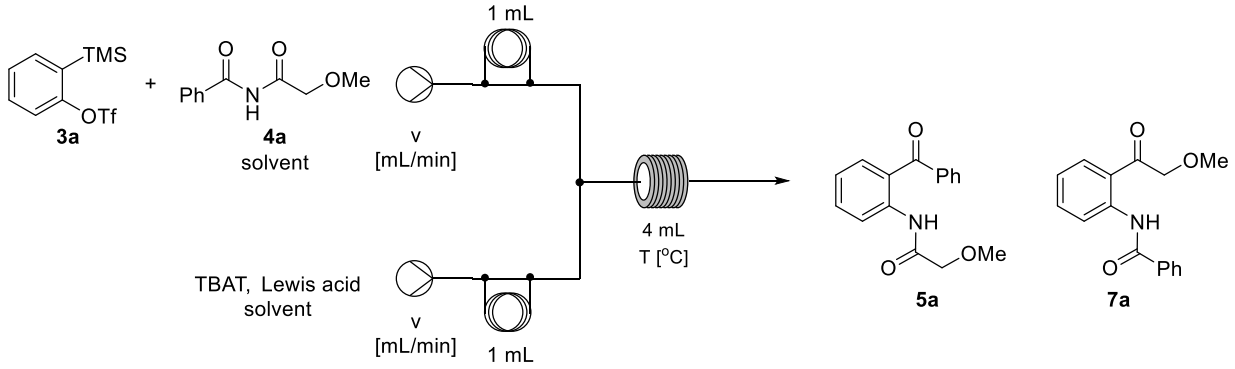
3-Hydroxy-2-(trimethylsilyl)phenyl trifluoromethanesulfonate (1.47 g, 4.66 mmol, 1 equiv.) was suspended in water (150 mL). Allyl bromide (2.42 mL, 28.0 mmol, 6.0 equiv.), tetrabutylammonium bromide (1.50 g, 4.66 mmol, 1.0 equiv.) and K_3PO_4 (2.97 g, 14.0 mmol, 3 equiv.) were added at room temperature. The suspension was stirred vigorously for 1 hour, diluted with water (50 mL), and extracted with EtOAc (3 x 50 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated under reduced pressure. The crude product was purified by column chromatography (silica gel, *n*-pentane) to afford the title compound (**3c**, 1.12 g, 3.16 mmol, 68%) as a colorless oil.

R_f = 0.65 (*n*-pentane); **^{1}H NMR** (500 MHz, $CDCl_3$) δ = 7.34 (t, *J* = 8.4 Hz, 1H), 6.94 (d, *J* = 8.4 Hz, 1H), 6.81 (d, *J* = 8.3 Hz, 1H), 6.09 – 5.98 (m, 1H), 5.45 – 5.35 (m, 1H), 5.34 – 5.30 (m, 1H), 4.56 (d, *J* = 5.4 Hz, 2H), 0.38 (s, 9H) ppm; **^{13}C NMR** (126 MHz, $CDCl_3$) δ = 164.6, 154.8, 132.7, 131.7, 121.2, 118.8 (q, *J* = 320.6 Hz), 118.5, 113.0, 110.6, 69.7, 1.1 ppm; **^{19}F NMR** (376 MHz, $CDCl_3$) δ = -72.77 ppm; **IR** (neat): $\tilde{\nu}$ = 3089, 2988, 2955, 2901, 2865, 1595, 1565, 1436, 1420, 1362, 1247, 1206, 1160, 1140, 1117, 1057, 1034, 996, 939, 924, 894, 837, 787, 769, 738, 712, 693, 668 cm^{-1}; **HRMS** (ESI): m/z calculated for $C_{13}H_{17}F_3O_4SSiNa^+$ ([M+Na]$^+$): 377.0461, found: 377.0461.

General Procedure for the Optimization of the Aryne Insertion in Flow

A stock solution of **3a** and **4a** at the indicated concentrations was loaded onto a 1 mL sample loop. A second stock solution of tetrabutylammonium difluorotriphenylsilicate at the indicated concentration was loaded on a second 1 mL sample loop. Both loops were connected to two syringes in a syringe pump and the stock solutions were combined at a T-piece or static mixer, as indicated in table S1. The reaction was pushed through a 4 mL reaction coil at the reported flow rate and temperature and collected afterwards. The results are summarized in Table S1.

Table S1. Analysis of main parameters for the synthesis of benzophenone **5a** and acetophenone **7a**

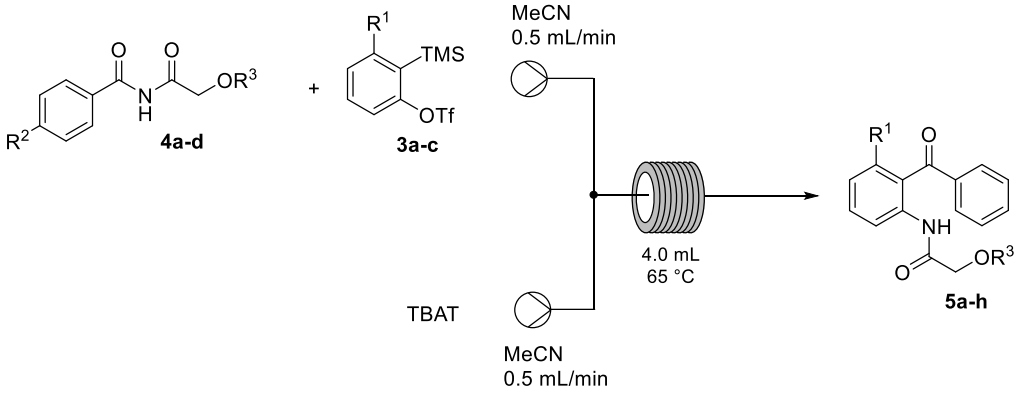


Entry	v [ml/min]	Residence time [min]	Lewis acid	C_{Imid} [mol/L]	C_{Arin} [mol/L]	C_{TBAT} [mol/L]	T [°C]	**5a : 7a**[a]	Solvent/cond.	**5a**[a] [%]
1	0.5	4	none	0.05	0.06	0.10	55	-	no workup	32
2	0.5	4	none	0.05	0.06	0.10	55	-	aq. workup	42
3	0.5	4	none	0.05	0.06	0.10	55	-	wet MeCN, no workup, static mixer	31
4	0.5	4	none	0.05	0.06	0.10	55	-	static mixer, dry MeCN	36
5	0.2	10	none	0.05	0.06	0.10	55	-	wet MeCN, no workup, static mixer	32
6	0.2	10	none	0.05	0.06	0.10	65	-	wet MeCN, no workup, static mixer	32
7	0.2	10	none	0.05	0.08	0.10	55	-	wet MeCN, no workup, static mixer	26

8	0.2	10	none	0.09	0.05	0.10	55	-	wet MeCN, no workup, static mixer	24
9	0.5	4	none	0.05	0.08	0.10	80	-	wet MeCN, no workup, static mixer	42
10	0.5	4	none	0.025	0.04	0.05	55	2.7 : 1	PhMe/MeCN (1:1)	31
11	0.5	4	none	0.025	0.04	0.05	80	4.2 : 1	PhMe/MeCN (1:1); 40 psi BPR[d]	42
12	0.2	10	none	0.025	0.04	0.05	65	3.1 : 1	PhMe/MeCN (1:1), static mixer	32
13	0.5	4	none	0.05	0.08	0.1	55	2.5 : 1	THF	20
14	0.5	4	none	0.04	0.08	0.1	80	4.1 : 1	wet MeCN; 40 psi BPR	36
15	0.5	4	none	0.04	0.08	0.1	90	4.2 : 1	wet MeCN; 40 psi BPR	35
16	0.5	4	none	0.04	0.08	0.1	100	4.0 : 1	wet MeCN; 40 psi BPR	40
17	0.5	4	$Sc(OTf)_3$	0.1	0.15	0.18	65	-	dry MeCN	<5[b]
18	0.5	4	$MgCl_2$	0.1	0.15	0.18	65	-	dry MeCN	<5[b]
19	0.5	4	$BF_3{\cdot}OEt_2$	0.1	0.15	0.18	65	-	dry MeCN	<5[b]
20	0.5	4	$AlCl_3$	0.1	0.15	0.18	65	-	dry MeCN	<5[b]
21	0.5	4	$Ti(OiPr)_4$	0.1	0.15	0.18	65	-	dry MeCN	<5[b]
22	0.5	4	$Ti(OiPr)_4$	0.1	0.15	0.18	65	-	dry MeCN	<5[b]
23	0.5	4	none	0.1	0.15	0.18	65	2.9 : 1[c]	wet MeCN	52[c]
24	0.2	10	none	0.05	0.06	0.075	65	3.3 : 1[b]	dry MeCn	42[c]
25	0.2	10	none	0.05	0.06	0.075	80	3.8 : 1[b]	dry MeCN	39[c]

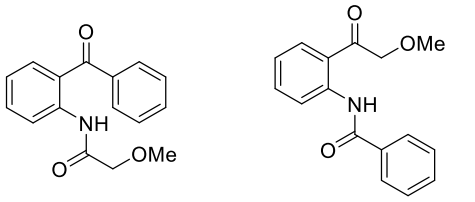
[a]The ratio of **5a**:**7a** as well as the yield of **5a** were determined via GC-MS with acetanilide as standard. An aliquot of the reactor output (100 µL or 500 µL) was taken, diluted to yield a volume of 900 µL, and treated with a solution of acetanilide (100 µL, 0.05 M). [b]Determined by ^{1}H NMR integration. [c]Isolated yield. [d]BPR: back pressure regulator.

General Procedure for the Aryne Insertion in Flow (GP1)



A stock solution of aryne precursor (**3a**–**c**, 0.150 M in acetonitrile, 1.5 equiv.) and imide (**4a**–**d**, 0.100 M in acetonitrile, 1.0 equiv.) were pumped simultaneously with a stock solution of tetrabutylammonium difluorotriphenylsilicate (0.180 M in acetonitrile, 1.8 equiv.), both at a rate of 0.5 mL/min. The stock solutions were combined at a T-piece to react in a 4.0 mL PTFE coil, preheated to 65 °C. The reaction mixture was collected, concentrated under reduced pressure, and purified by column chromatography to afford the *ortho*-aminobenzophenones **5a**–**h**. The constitutional isomer ratio was deduced by ^{1}H NMR integration of the crude reaction product.

***N*-(2-Benzoylphenyl)-2-methoxyacetamide (5a)**



5a $C_{16}H_{15}NO_3$ (269.30) **7a** $C_{16}H_{15}NO_3$ (269.30)

Compound **5a** was prepared according to **GP1** starting from **3a** (127 mg, 0.427 mmol, 1.5 equiv.) and **4a** (55.0 mg, 0.285 mmol, 1 equiv.). Column chromatography (silica gel, *n*-pentane/EtOAc = 4:1) afforded the title compound (**5a**, 40.0 mg, 0.148 mmol, 52%) as a colorless oil that solidified in the fridge and compound **7** (14.5 mg, 0.054 mmol, 19%) as a colorless solid. The isomeric ratio was determined as 2.9:1 (**5a**:**7a**).

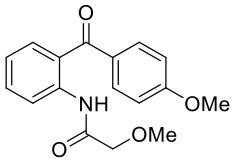
5a:

R_f = 0.40 (*n*-pentane/EtOAc = 3:1); **^{1}H NMR** (700 MHz, $CDCl_3$): δ = 11.39 (s, 1H), 8.69 (d, *J* = 8.3 Hz, 1H), 7.73 – 7.70 (m, 2H), 7.60 – 7.54 (m, 3H), 7.47 (t, *J* = 7.8 Hz, 2H), 7.11 (td, *J* = 7.6, 1.2 Hz, 1H), 4.04 (s, 2H), 3.55 (s, 3H) ppm; **^{13}C NMR** (176 MHz, $CDCl_3$): δ 199.1, 169.2, 139.4, 138.7, 134.1, 133.5, 132.5, 130.0, 128.4, 124.3, 122.6, 121.7, 72.7, 59.8 ppm; **IR** (neat): $\tilde{\nu}$ = 3286, 3060, 3033, 2996, 2934, 2828, 2756, 2249, 1832, 1692, 1639, 1598, 1577, 1515, 1446, 1432, 1362, 1317, 1293, 1263, 1196, 1180, 1158, 1114, 1076, 1048, 1028, 987, 959, 935, 917, 880, 852, 805, 752, 728 cm^{-1}; **HRMS** (ESI): m/z calculated for $C_{16}H_{15}NNaO_3^+$ ([M+Na]$^+$): 292.0944; found: 292.0959.

7a:

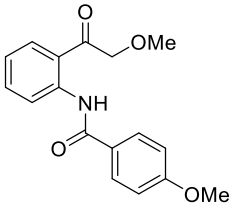
R_f = 0.35 (*n*-pentane/EtOAc = 3:1); **m.p.:** 138–139 °C; **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 12.57 (s, 1H), 9.02 (dd, J = 8.6, 1.1 Hz, 1H), 8.12 – 8.08 (m, 2H), 7.82 (dd, J = 8.0, 1.4 Hz, 1H), 7.64 (ddd, J = 8.7, 7.3, 1.5 Hz, 1H), 7.58 – 7.54 (m, 1H), 7.53 – 7.49 (m, 2H), 7.14 (t, J = 8.2 Hz, 1H), 4.81 (s, 2H), 3.55 (s, 3H) ppm; **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 200.2, 166.2, 141.8, 135.9, 134.6, 132.2, 129.6, 129.0, 127.7, 122.6, 121.3, 119.7, 75.5, 59.7 ppm; **IR** (neat): $\tilde{\nu}$ = 3268, 3236, 3130, 3062, 2995, 2942, 2829, 1672, 1653, 1610, 1585, 1559, 1537, 1507, 1496, 1448, 1368, 1322, 1311, 1258, 1216, 1196, 1139, 1120, 1029, 978, 925, 699, 661 cm^{-1}; **HRMS** (ESI): m/z calculated for $C_{16}H_{15}NNaO_3^+$ ([M+Na]$^+$): 292.0944; found: 292.0944.

2-Methoxy-*N*-(2-(4-methoxybenzoyl)phenyl)acetamide (5b)



5b

$C_{17}H_{17}NO_4$ (299.33)



7b

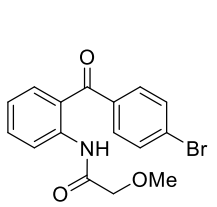
$C_{17}H_{17}NO_4$ (299.33)

Compound **5b** was prepared according to **GP1** starting from **3a** (90.4 mg, 0.303 mmol, 1.5 equiv., 0.015 M) and **4b** (45.0 mg, 0.202 mmol, 1 equiv., 0.010 M). Column chromatography (silica gel, *n*-pentane/EtOAc = 3:1) afforded the title compound (**5b**, 32.8 mg, 0.122 mmol, 60%) as a slightly yellow oil. The isomeric ratio was determined as 4.6:1 (**5b**:**7b**).

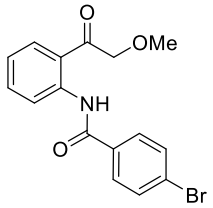
5b:

R_f = 0.21 (*n*-pentane/EtOAc = 3:1); **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 11.09 (s, 1H), 8.62 (dt, *J* = 8.1, 1.0 Hz, 1H), 7.78 – 7.72 (m, 2H), 7.58 – 7.52 (m, 2H), 7.16 – 7.09 (m, 1H), 6.99 – 6.93 (m, 2H), 4.03 (s, 2H), 3.89 (s, 3H), 3.53 (s, 3H) ppm; **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 197.3, 169.1, 163.5, 138.8, 133.4, 132.8, 132.7, 131.1, 125.3, 122.7, 121.9, 113.7, 72.7, 59.8, 55.7 ppm; **IR** (neat): $\tilde{\nu}$ = 3310, 3006, 2931, 2840, 1687, 1633, 1597, 1578, 1510, 1447, 1419, 1315, 1306, 1293, 1253, 1196, 1172, 1154, 1110, 1026, 986, 925, 844, 788, 760, 739, 696 cm^{-1}; **HRMS** (ESI): m/z calculated for $C_{17}H_{17}NNaO_4^+$ ([M+Na]$^+$): 322.1050; found: 322.1062.

***N*-(2-(4-Bromobenzoyl)phenyl)-2-methoxyacetamide (5c)**



5c
$C_{16}H_{14}BrNO_3$ (348.20)



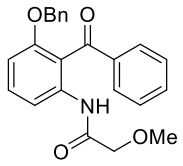
7c
$C_{16}H_{14}BrNO_3$ (348.20)

Compound **5c** was prepared according to **GP1** starting from **3a** (44.8 mg, 0.150 mmol, 1.5 equiv.) **4c** (27.2 mg, 0.100 mmol, 1 equiv.). Column chromatography (silica gel, *n*-pentane/EtOAc 3:1) afforded the title compound (**5c**, 8.10 mg, 0.023 mmol, 23%) as a slightly yellow oil. The isomeric ratio was determined as 4.5:1 (**5c**:**7c**).

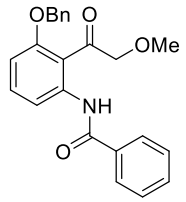
5c:

R_f = 0.33 (*n*-pentane/EtOAc = 3:1); **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 11.31 (s, 1H), 8.68 (dd, *J* = 8.4, 1.0 Hz, 1H), 7.67 – 7.54 (m, 5H), 7.52 (dd, *J* = 7.9, 1.6 Hz, 1H), 7.15 – 7.11 (m, 1H), 4.05 (s, 2H), 3.56 (s, 3H) ppm; **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 197.9, 169.2, 139.5, 137.5, 134.4, 133.2, 131.8, 131.6, 127.7, 124.0, 122.8, 121.9, 72.7, 59.9 ppm; **IR** (neat): $\tilde{\nu}$ = 3298, 3081, 3033, 2995, 2932, 2827, 1692, 1641, 1601, 1577, 1515, 1483, 1446, 1432, 1394, 1361, 1314, 1293, 1262, 1196, 1178, 1167, 1157, 1114, 1068, 1051, 1010, 987, 959, 921, 880, 841, 783, 758, 725, 675, 654 cm^{-1}; **HRMS** (ESI): m/z calculated for $C_{16}H_{14}BrNNaO_3^+$ ($[M+Na]^+$): 370.0049; found: 370.0063.

***N*-(2-Benzoyl-3-(benzyloxy)phenyl)-2-methoxyacetamide (5d)**



5d
$C_{23}H_{21}NO_4$ (375.42)



7d
$C_{23}H_{21}NO_4$ (375.42)

Compound **5d** was prepared according to **GP1** starting from **3b** (273 mg, 0.675 mmol, 1.5 equiv.) and **4a** (87.0 mg, 0.450 mmol, 1 equiv.). Column chromatography (silica gel, *n*-pentane/EtOAc = 4:1) afforded the title compound (**5d**, 59.0 mg, 0.082 mmol, 35%) as a slightly yellow oil. Additionally, **7d** (14.6 mg, 0.038 mmol, 9%) was isolated as a colorless oil. The isomeric ratio was determined as 4.9:1 (**5d**:**7d**).

5d:

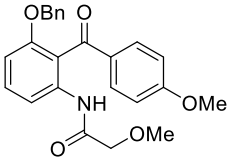
R_f = 0.24 (*n*-pentane/EtOAc = 4:1); **^{1}H NMR** (700 MHz, $CDCl_3$): δ = 9.51 (s, 1H), 8.03 (dd, *J* = 8.4, 0.8 Hz, 1H), 7.80 – 7.77 (m, 2H), 7.55 (tt, *J* = 8.7, 1.3 Hz, 1H), 7.47 – 7.41 (m, 3H), 7.21 – 7.17 (m, 1H), 7.16 – 7.13 (m, 2H), 6.81 (dd, *J* = 8.4, 0.8 Hz, 1H), 6.77 (d, *J* = 7.5 Hz, 2H), 4.90 (s, 2H), 3.93 (s, 2H), 3.41 (s, 3H) ppm; **^{13}C NMR** (176 MHz, $CDCl_3$): δ = 197.1, 168.6, 157.4, 139.4, 137.1, 136.1, 133.1,

132.5, 129.4, 128.5, 128.4, 127.8, 126.8, 118.8, 115.2, 108.5, 72.4, 70.4, 59.6 ppm; **IR** (neat): $\tilde{\nu}$ = 3359, 3061, 3031, 3003, 2929, 2829, 1802, 1693, 1646, 1597, 1581, 1523, 1497, 1466, 1460, 1450, 1428, 1381, 1313, 1275, 1256, 1196, 1178, 1146, 1112, 1087, 1071, 1028, 986, 925, 875, 865, 846, 807, 782, 739 cm^{-1}; **HRMS** (ESI): m/z calculated for $C_{23}H_{21}NNaO4^+$ ([M+Na]$^+$): 398.1363; found: 398.1367.

7d:

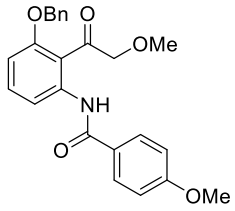
R_f = 0.37 (*n*-pentane/EtOAc = 4:1); **^{1}H NMR** (700 MHz, $CDCl_3$): δ = 12.22 (s, 1H), 8.52 (dd, *J* = 8.5, 0.9 Hz, 1H), 8.07 – 8.03 (m, 2H), 7.56 – 7.53 (m, 1H), 7.53 – 7.48 (m, 3H), 7.46 – 7.42 (m, 4H), 7.41 – 7.38 (m, 1H), 6.80 (dd, *J* = 8.4, 1.0 Hz, 1H), 5.17 (s, 2H), 4.56 (s, 2H), 3.31 (s, 3H) ppm; **^{13}C NMR** (176 MHz, $CDCl_3$): δ = 202.6, 166.2, 160.2, 142.1, 135.5, 135.3, 134.8, 132.2, 129.0, 128.9, 128.9, 128.3, 127.7, 114.5, 113.3, 107.2, 80.3, 71.6, 59.2 ppm; **IR** (neat): $\tilde{\nu}$ = 3065, 3031, 2925, 2822, 1680, 1648, 1604, 1579, 1525, 1492, 1458, 1408, 1382, 1271, 1187, 1124, 1098, 1053, 1024, 1001, 986, 910, 847, 787, 741 cm^{-1}; **HRMS** (ESI): m/z calculated for $C_{23}H_{21}NNaO4^+$ ([M+Na]$^+$): 398.1363; found: 398.1382.

N-(3-(Benzyloxy)-2-(4-methoxybenzoyl)phenyl)-2-methoxyacetamide (5e)



5e

$C_{24}H_{23}NO_5$ (405.45)



7e

$C_{24}H_{23}NO_5$ (405.45)

Compound **5e** was prepared according to **GP1** starting from **3b** (571 mg, 1.41 mmol, 1.5 equiv., 0.015 M) and **4b** (210 mg, 0.941 mmol, 1 equiv., 0.010 M). Column chromatography (silica gel, *n*-pentane/EtOAc = 3:1) afforded the title compound (**5e**, 90.6 mg, 0.122 mmol, 24%) as a slightly yellow oil. Additionally, **7e** (38.1 mg, 0.094 mmol, 10%) was isolated as a colorless oil. The isomeric ratio was determined as 2.8:1 (**5e**:**7e**).

5e:

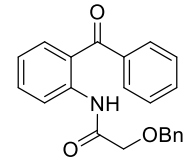
R_f = 0.18 (*n*-pentane/EtOAc = 3:1); **^{1}H NMR** (700 MHz, CD_3CN): δ = 8.96 (s, 1H), 7.87 (dd, *J* = 8.3, 0.8 Hz, 1H), 7.76 – 7.73 (m, 2H), 7.47 (t, *J* = 8.3 Hz, 1H), 7.24 – 7.18 (m, 3H), 6.99 – 6.96 (m, 3H), 6.95 – 6.93 (m, 2H), 4.98 (s, 2H), 3.85 (s, 3H), 3.84 (s, 2H), 3.30 (s, 3H) ppm; **^{13}C NMR** (176 MHz, CD_3CN): δ = 195.8, 169.1, 165.2, 157.6, 137.4, 137.3, 132.6, 132.5, 132.2, 129.2, 128.7, 128.1, 120.7, 115.9, 114.9, 109.8, 72.7, 71.1, 59.7, 56.4 ppm; **IR** (neat): $\tilde{\nu}$ = 3360, 3062, 3034, 3009, 2935, 2840, 1691, 1645, 1593, 1509, 1461, 1382, 1280, 1254, 1173, 1145, 1111, 1070, 1028, 986, 927, 844, 793, 735, 696, 668 cm^{-1}; **HRMS** (ESI): m/z calculated for $C_{24}H_{23}NNaO_5^+$ ([M+Na]$^+$): 428.1468; found: 428.1461.

7e:

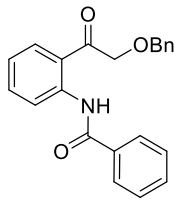
R_f = 0.30 (*n*-pentane/EtOAc = 5:2); **^{1}H NMR** (700 MHz, $CDCl_3$): δ = 12.16 (s, 1H), 8.51 (d, *J* = 8.5 Hz, 1H), 8.03 (d, *J* = 8.7 Hz, 2H), 7.49 (td, *J* = 8.5, 1.9 Hz, 1H), 7.46 – 7.37 (m, 5H), 7.00 – 6.96 (m, 2H),

6.78 (d, *J* = 8.3 Hz, 1H), 5.16 (s, 2H), 4.56 (s, 2H), 3.87 (d, *J* = 2.1 Hz, 3H), 3.31 (d, *J* = 2.0 Hz, 3H) ppm; **^{13}C NMR** (176 MHz, $CDCl_3$): δ = 202.6, 165.7, 162.8, 160.2, 142.4, 135.5, 135.3, 129.6, 129.0, 128.9, 128.3, 127.1, 114.4, 114.1, 111.6, 106.8, 80.3, 71.6, 59.2, 55.6 ppm; **IR** (neat): $\tilde{\nu}$ = 3194, 2953, 2925, 2844, 2818, 1675, 1647, 1604, 1579, 1531, 1507, 1457, 1420, 1404, 1380, 1308, 1253, 1174, 1124, 1052, 1027, 983, 907, 844, 787, 760, 744 cm^{-1}; **HRMS** (ESI): m/z calculated for $C_{24}H_{23}NNaO_5^+$ ($[M+Na]^+$): 428.1468; found: 428.1476.

N-(2-Benzoylphenyl)-2-(benzyloxy)acetamide (5f)



5f
$C_{22}H_{19}NO_3$ (345.40)



7f
$C_{22}H_{19}NO_3$ (345.40)

Compound **5f** was prepared according to **GP1** starting from **3a** (199 mg, 0.668 mmol, 1.5 equiv.) and **4d** (120 mg, 0.446 mmol, 1 equiv.). Column chromatography (silica gel, *n*-pentane/EtOAc 6:1) afforded the title compound (**5f**, 63.0 mg, 0.180 mmol, 40%) as a colorless oil. Additionally, compound **7f** (19.1 mg, 0.058 mmol, 13%) was isolated as colorless oil. The isomer ratio was determined as 4.3:1 (**5f**:**7f**).

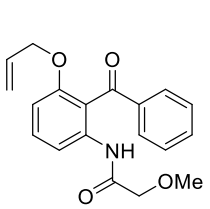
5f:

R_f = 0.23 (*n*-pentane/EtOAc = 6:1); **^{1}H NMR** (700 MHz, $CDCl_3$): δ = 11.46 (s, 1H), 8.67 (dd, *J* = 8.4, 1.1 Hz, 1H), 7.77 – 7.74 (m, 2H), 7.62 – 7.55 (m, 3H), 7.52 – 7.45 (m, 4H), 7.37 – 7.33 (m, 2H), 7.32 – 7.28 (m, 1H), 7.15 – 7.10 (m, 1H), 4.73 (s, 2H), 4.10 (s, 2H) ppm; **^{13}C NMR** (176 MHz, $CDCl_3$): δ = 198.8, 169.2, 139.3, 138.7, 136.9, 134.0, 133.3, 132.6, 130.2, 128.7, 128.4, 128.2, 128.1, 124.6, 122.7, 121.8, 73.8, 69.8 ppm; **IR** (neat): $\tilde{\nu}$ = 3300, 3061, 3029, 2955, 2924, 2867, 1694, 1641, 1599, 1578, 1519, 1447, 1397, 1373, 1317, 1293, 1265, 1207, 1163, 1099, 1027, 1000, 974, 936, 921, 852, 805, 75 cm^{-1}; **HRMS** (ESI): m/z calculated for $C_{22}H_{19}NNaO_3^+$ ($[M+Na]^+$): 368.1257; found: 368.1263.

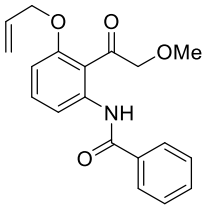
7f:

R_f = 0.25 (*n*-pentane/EtOAc = 6:1); **^{1}H NMR** (700 MHz, $CDCl_3$): δ = 12.51 (s, 1H), 9.02 – 9.00 (m, 1H), 8.13 – 8.09 (m, 2H), 7.81 – 7.79 (m, 1H), 7.65 – 7.61 (m, 1H), 7.60 – 7.54 (m, 1H), 7.54 – 7.51 (m, 2H), 7.41 – 7.38 (m, 2H), 7.38 – 7.35 (m, 2H), 7.33 – 7.30 (m, 1H), 7.12 (ddd, *J* = 8.0, 7.3, 1.2 Hz, 1H), 4.82 (s, 2H), 4.75 – 4.72 (m, 2H) ppm; **^{13}C NMR** (176 MHz, $CDCl_3$): δ = 200.3, 166.3, 141.8, 137.1, 135.8, 134.8, 132.2, 130.0, 129.0, 128.8, 128.3, 128.2, 127.7, 122.6, 121.3, 120.0, 73.8, 73.0 ppm; **IR** (neat): $\tilde{\nu}$ = 3276, 3243, 3062, 3030, 2925, 2857, 1664, 1607, 1583, 1525, 1496, 1450, 1365, 1305, 1256, 1213, 1188, 1168, 1144, 1121, 1094, 1053, 1028, 976, 946, 896, 869, 798, 751 cm^{-1}; **HRMS** (ESI): m/z calculated for $C_{22}H_{19}NNaO_3^+$ ($[M+Na]^+$): 368.1257; found: 368.1260.

***N*-(3-(Allyloxy)-2-benzoylphenyl)-2-methoxyacetamide (5g)**



5g
$C_{19}H_{19}NO_4$ (325.36)



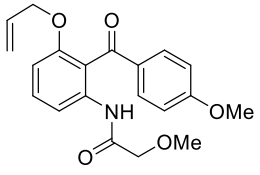
7g
$C_{19}H_{19}NO_4$ (325.36)

Compound **5g** was prepared according to **GP1** starting from **3c** (107 mg, 0.303 mmol, 1.5 equiv.) and **4a** (45.0 mg, 0.202 mmol, 1 equiv.). Column chromatography (silica gel, *n*-pentane/EtOAc = 3:1) afforded the title compound (**5g**, 12.0 mg, 0.0371 mmol, 18%) as a slightly yellow oil. The isomeric ratio was determined as 3.0:1 (**5g**:**7g**).

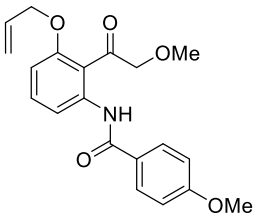
5g:

R_f = 0.29 (*n*-pentane/EtOAc = 3:1); **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 9.52 (s, 1H), 8.01 (dd, *J* = 8.4, 0.8 Hz, 1H), 7.80 – 7.73 (m, 2H), 7.56 – 7.51 (m, 1H), 7.47 – 7.38 (m, 3H), 6.73 (dd, *J* = 8.4, 0.9 Hz, 1H), 5.53 (ddt, *J* = 17.2, 10.7, 4.9 Hz, 1H), 4.97 (dq, *J* = 10.7, 1.5 Hz, 1H), 4.87 (dq, *J* = 17.3, 1.7 Hz, 1H), 4.35 (dt, *J* = 5.0, 1.7 Hz, 2H), 3.93 (s, 2H), 3.40 (s, 3H) ppm; **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 197.1, 168.6, 157.4, 139.3, 137.1, 133.1, 132.5, 132.1, 129.3, 128.4, 118.6, 117.1, 115.1, 108.6, 72.4, 69.3, 59.6 ppm; **IR** (neat): $\tilde{\nu}$ = 3356, 3066, 2951, 2922, 2850, 1696, 1648, 1597, 1584, 1522, 1468, 1422, 1370, 1362, 1314, 1277, 1197, 1178, 1145, 1114, 1076, 986, 926, 853, 808, 782, 746, 718, 702, 671, 661 cm^{-1}; **HRMS** (ESI): m/z calculated for $C_{19}H_{19}NNaO_4^+$ ([M+Na]$^+$): 348.1206; found: 348.1207.

***N*-(3-(Allyloxy)-2-(4-methoxybenzoyl)phenyl)-2-methoxyacetamide (5h)**



5h
$C_{20}H_{21}NO_5$ (355.39)



7h
$C_{20}H_{21}NO_5$ (355.39)

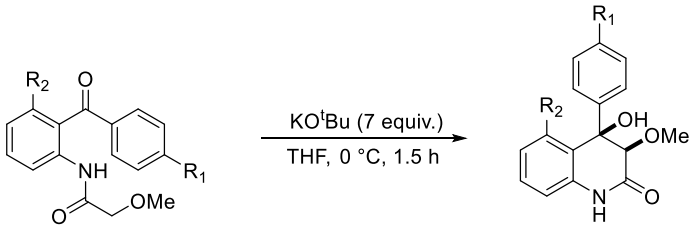
Compound **5h** was prepared according to **GP1** starting from **3c** (198 mg, 0.555 mmol, 1.5 equiv., 0.015 M) and **4b** (83.0 mg, 0.370 mmol, 1 equiv., 0.010 M). Column chromatography (silica gel, *n*-pentane/EtOAc = 2:1) afforded the title compound (**5h**, 39.3 mg, 0.111 mmol, 30%) as a slightly yellow oil. The isomeric ratio was determined as 4.2:1 (**5h**:**7h**).

5h:

R_f = 0.32 (*n*-pentane/EtOAc = 2:1); **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 9.25 (s, 1H), 7.95 (d, *J* = 7.8 Hz, 1H), 7.78 (d, *J* = 8.5 Hz, 2H), 7.40 (t, *J* = 8.3 Hz, 1H), 6.89 (d, *J* = 8.2 Hz, 2H), 6.74 (d, *J* = 9.1 Hz, 1H), 5.65 (ddt, *J* = 17.2, 10.6, 4.9 Hz, 1H), 5.02 (dq, *J* = 10.7, 1.5 Hz, 1H), 4.96 (dq, *J* = 17.3, 1.7 Hz, 1H), 4.40 (dt, *J* = 4.8, 1.7 Hz, 2H), 3.90 (s, 2H), 3.86 (s, 3H), 3.37 (s, 3H) ppm; **^{13}C NMR** (126 MHz, $CDCl_3$):

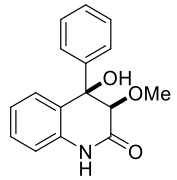
δ = 195.1, 168.5, 164.0, 156.8, 136.5, 132.4, 132.0, 131.8, 131.6, 119.5, 117.1, 115.2, 113.7, 108.7, 72.3, 69.3, 59.6, 55.7 ppm; **IR** (neat): $\tilde{\nu}$ = 3359, 3075, 2931, 2840, 1810, 1693, 1646, 1594, 1522, 1509, 1467, 1421, 1382, 1362, 1315, 1281, 1256, 1196, 1173, 1146, 1113, 1073, 1026, 986, 929, 880, 846, 817, 792, 768, 734, 709, 693, 672, 663 cm^{-1}; **HRMS** (ESI): m/z calculated for $C_{20}H_{21}NNaO_5^+$ ($[M+Na]^+$): 378.1312; found: 378.1331.

General Procedure for the Aldol Reaction (GP2)



The *ortho*-aminobenzophenone (**5a**–**h**, 1 equiv.) was dissolved in anhydrous THF (50 mL/mmol substrate) and a solution of KO^{t}Bu (7 equiv., 1 M in THF) was added dropwise at 0 °C. Upon addition of KO^{t}Bu, the solution turned bright yellow. After stirring at 0 °C for 1.5 hours, water (50 mL/mmol substrate) was added to the reaction mixture. The organic layer was separated and the aqueous layer was extracted with EtOAc (3 x 50 mL/mmol substrate). The combined organic layers were dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The crude products were purified by column chromatography to afford the quinolinones **6a**–**g**.

(±)–6-Deoxyaflaquinolone E (6a)

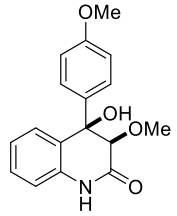


$C_{16}H_{15}NO_3$ (269.30)

6-Deoxyaflaquinolone E was prepared according to **GP2** starting from **5a** (20 mg, 0.075 mmol, 1 equiv.) and KO^{t}Bu (59 mg, 0.53 mmol, 7 equiv.). The crude product was purified by column chromatography (silica gel, CH_2Cl_2/MeOH = 100:3) to afford the title compound (**6a**, 18 mg, 0.068 mmol, 92%) as a colorless solid.

R_f = 0.21 (*n*-pentane/EtOAc = 1:1); **m.p.:** 160–165 °C; **^{1}H NMR** (700 MHz, DMSO-d_6): δ = 10.21 (s, 1H), 7.33 (m, 4H), 7.28 (dt, *J* = 8.5, 4.2 Hz, 1H), 7.24 – 7.20 (m, 1H), 6.93 – 6.90 (m, 2H), 6.88 (dd, *J* = 7.5, 1.6 Hz, 1H), 5.81 (s, 1H), 4.18 (s, 1H), 3.34 (s, 3H) ppm; **^{13}C NMR** (176 MHz, DMSO-d_6): δ = 168.4, 142.3, 136.8, 129.2, 128.7, 127.8, 127.5, 127.3, 126.7, 122.1, 115.1, 83.9, 76.7, 59.1 ppm; **IR** (neat): $\tilde{\nu}$ = 3446, 3361, 3211, 3085, 3022, 2993, 2931, 2845, 2831, 1681, 1609, 1593, 1559, 1486, 1446, 1433, 1397, 1318, 1285, 1263, 1246, 1226, 1203, 1181, 1157, 1142, 1119, 1097, 1069, 1048, 1020, 1001, 953, 940, 910, 871, 858, 824, 791, 762, 752, 704, 674, 658 cm^{-1}; **HRMS** (ESI): m/z calculated for $C_{16}H_{15}NNaO_3^+$ ([M+Na]$^+$): 292.0944; found: 292.0945. The NMR data match those reported for 6-deoxyaflaquinolone E.[5]

(±)–Quinolinone A (6b)

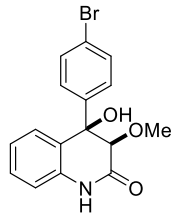


$C_{17}H_{17}NO_4$ (299.33)

Quinolinone A was prepared according to **GP2** starting from **5b** (20 mg, 0.067 mmol, 1 equiv.) and KO*t*Bu (53 mg, 0.47 mmol, 7 equiv.). The crude product was purified by column chromatography (silica gel, CH_2Cl_2/MeOH = 100:3) to afford the title compound (**6b**, 16.7 mg, 0.056 mmol, 84%) as a colorless solid.

R_f = 0.22 (*n*-pentane/EtOAc = 1:1); **m.p.:** 172–175 °C; **^{1}H NMR** (500 MHz, acetone-d_6): δ = 9.29 (s, 1H), 7.35 – 7.20 (m, 4H), 7.07 – 6.97 (m, 2H), 6.91 – 6.81 (m, 2H), 4.61 (s, 1H), 3.93 (s, 1H), 3.76 (s, 3H), 3.45 (s, 3H) ppm; **^{13}C NMR** (126 MHz, acetone-d_6): δ = 168.2, 160.3, 137.6, 134.5, 129.6, 129.0, 128.4, 123.6, 115.9, 115.9, 114.2, 85.7, 77.3, 59.4, 55.5 ppm; **IR** (neat): $\tilde{\nu}$ = 3249, 3081, 3002, 2931, 2836, 1687, 1611, 1595, 1512, 1483, 1463, 1379, 1306, 1252, 1173, 1146, 1106, 1081, 1033, 991, 942, 903, 860, 833, 812, 757 cm^{-1}; **HRMS** (ESI): m/z calculated for $C_{17}H_{17}NNaO_4^+$ ([M+Na]$^+$): 322.1050; found: 322.1047. The NMR data match those reported for Quinolinone A.[6]

***cis*-4-(4-Bromophenyl)-4-hydroxy-3-methoxy-3,4-dihydroquinolin-2(1*H*)-one (6c)**

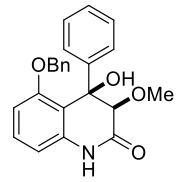


$C_{16}H_{14}BrNO_3$ (348.20)

Compound **6c** was prepared according to **GP2** starting from **5c** (8.0 mg, 0.021 mmol, 1 equiv.) and KO*t*Bu (16 mg, 0.15 mmol, 7 equiv.). The crude product was purified by column chromatography (silica gel, CH_2Cl_2/MeOH = 100:3) to afford the title compound (**6c**, 7.2 mg, 0.019 mmol, 90%) as a colorless oil.

R_f = 0.21 (*n*-pentane/EtOAc = 1:1); **^{1}H NMR** (700 MHz, CD_3OD): δ = 7.51 (d, *J* = 8.8 Hz, 2H), 7.36 – 7.33 (m, 2H), 7.28 (ddd, *J* = 8.0, 5.8, 3.0 Hz, 1H), 7.00 – 6.98 (m, 2H), 6.95 (dt, *J* = 7.9, 0.8 Hz, 1H), 4.23 (s, 1H), 3.40 (s, 3H) ppm; **^{13}C NMR** (176 MHz, $CDCl_3$): δ = 170.9, 142.4, 138.0, 132.2, 130.5, 130.2, 129.7, 129.1, 124.3, 122.7, 116.8, 85.4, 78.4, 60.6 ppm; **IR** (neat): $\tilde{\nu}$ = 3241, 3069, 2954, 2927, 2853, 2358, 1685, 1607, 1592, 1488, 1467, 1394, 1309, 1205, 1173, 1143, 989, 802, 759 cm^{-1}; **HRMS** (ESI): m/z calculated for $C_{16}H_{14}BrNO_3Na^+$ ([M+Na]$^+$): 370.0049; found: 370.0051.

***cis*-5-(Benzyloxy)-4-hydroxy-3-methoxy-4-phenyl-3,4-dihydroquinolin-2(1*H*)-one (6d)**

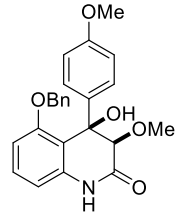


$C_{23}H_{21}NO_4$ (375.42)

Compound **6d** was prepared according to **GP2** starting from **5d** (28 mg, 0.075 mmol, 1 equiv.) and KO^{t}Bu (59 mg, 0.53 mmol, 7 equiv.). The crude product was purified by column chromatography (silica gel, CH_2Cl_2/MeOH = 100:2) to afford the title compound (**6d**, 23 mg, 0.062 mmol, 84%) as a colorless oil.

R_f = 0.25 (*n*-pentane/EtOAc = 1:1); **^{1}H NMR** (700 MHz, $CDCl_3$): δ = 8.58 (s, 1H), 7.28 – 7.21 (m, 9H), 7.07 (dd, *J* = 7.6, 1.9 Hz, 2H), 6.73 (dd, *J* = 8.5, 0.9 Hz, 1H), 6.57 (dd, *J* = 8.0, 0.9 Hz, 1H), 5.29 (s, 1H), 5.05 (d, *J* = 11.5 Hz, 1H), 4.96 (d, *J* = 11.6 Hz, 1H), 3.85 (d, *J* = 1.4 Hz, 1H), 3.61 (s, 3H) ppm; **^{13}C NMR** (176 MHz, $CDCl_3$): δ = 168.0, 158.0, 142.0, 137.2, 135.7, 130.1, 128.7, 128.7, 128.4, 128.3, 127.5, 126.2, 115.2, 109.6, 108.8, 85.0, 78.4, 71.1, 59.8 ppm; **IR** (neat): $\tilde{\nu}$ = 3503, 3232, 3062, 3031, 2930, 2829, 2248, 1691, 1595, 1498, 1471, 1448, 1383, 1315, 1277, 1259, 1222, 1176, 1138, 1102, 1059, 1028, 993, 910, 846, 783, 730, 697, 654 cm^{-1}; **HRMS** (ESI): m/z calculated for $C_{23}H_{21}NNaO_4^+$ ([M+Na]$^+$): 398.1363; found: 398.1368.

***cis*-5-(benzyloxy)-4-hydroxy-3-methoxy-4-(4-methoxyphenyl)-3,4-dihydroquinolin-2(1*H*)-one (6e)**

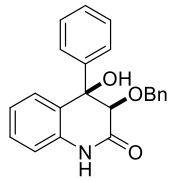


$C_{24}H_{23}NO_5$ (405.45)

Compound **6e** was prepared according to **GP2** starting from **5e** (30 mg, 0.080 mmol, 1 equiv.) and KO^{t}Bu (63 mg, 0.56 mmol, 7 equiv.). The crude product was purified by column chromatography (silica gel, CH_2Cl_2/MeOH = 100:3) to afford the title compound (**6e**, 25 mg, 0.067 mmol, 84%) as a colorless oil.

R_f = 0.25 (*n*-pentane/EtOAc = 1:1); **^{1}H NMR** (700 MHz, $CDCl_3$): δ = 8.33 (s, 1H), 7.29 – 7.23 (m, 3H), 7.21 (t, *J* = 7.8 Hz, 1H), 7.16 (d, *J* = 7.5 Hz, 2H), 7.11 – 7.08 (m, 2H), 6.79 (d, *J* = 7.5 Hz, 2H), 6.71 (d, *J* = 8.4 Hz, 1H), 6.52 (d, *J* = 8.0 Hz, 1H), 5.28 (s, 1H), 5.05 (d, *J* = 11.5 Hz, 1H), 4.97 (d, *J* = 11.5 Hz, 1H), 3.80 (s, 1H), 3.76 (s, 3H), 3.59 (s, 3H) ppm; **^{13}C NMR** (176 MHz, $CDCl_3$): δ = 168.0, 159.7, 158.1, 137.1, 135.7, 133.6, 129.9, 128.8, 128.4, 127.6, 127.5, 115.4, 114.1, 109.5, 108.8, 85.2, 78.2, 71.1, 59.7, 55.4 ppm; **IR** (neat): $\tilde{\nu}$ = 3502, 3237, 3066, 3034, 2999, 2930, 2834, 1693, 1596, 1508, 1471, 1388, 1302, 1280, 1253, 1231, 1172, 1103, 1061, 1031, 993, 913, 895, 834, 778, 734, 698, 656 cm^{-1}; **HRMS** (ESI): m/z calculated for $C_{24}H_{23}NNaO_5^+$ ([M+Na]$^+$): 428.1468; found: 428.1467.

cis-3-(Benzyloxy)-4-hydroxy-4-phenyl-3,4-dihydroquinolin-2(1*H*)-one (6f)

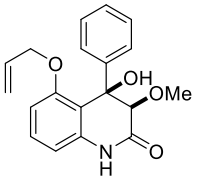


$C_{22}H_{19}NO_3$ (345.40)

Compound **6f** was prepared according to **GP2** starting from **5f** (14 mg, 0.043 mmol, 1 equiv.) and KO*t*Bu (34 mg, 0.30 mmol, 7 equiv.). The crude product was purified by column chromatography (silica gel, CH_2Cl_2/MeOH = 100:3) to afford the title compound (**6f**, 12 mg, 0.031 mmol, 72%) as a colorless oil.

R_f = 0.23 (Pentane/EtOAc = 1:1); **^{1}H NMR** (500 MHz, CD_3OD): δ = 7.40 – 7.32 (m, 5H), 7.27 (ddd, *J* = 7.9, 6.3, 2.6 Hz, 1H), 7.20 – 7.15 (m, 3H), 7.03 – 6.99 (m, 2H), 6.99 – 6.93 (m, 3H), 4.81 (d, *J* = 11.5 Hz, 1H), 4.50 (s, 1H), 4.45 (d, *J* = 11.5 Hz, 1H) ppm; **^{13}C NMR** (176 MHz, $CDCl_3$): δ = 168.5, 140.7, 136.7, 135.7, 129.7, 128.8, 128.6, 128.6, 128.5, 128.5, 128.2, 128.1, 126.8, 124.1, 115.5, 81.1, 73.8 ppm; **IR** (neat): $\tilde{\nu}$ = 3263, 3087, 3060, 3029, 2923, 2854, 1692, 1610, 1595, 1485, 1448, 1375, 1296, 1265, 1241, 1211, 1174, 1143, 1125, 1096, 1070, 1044, 1028, 989, 936, 907, 853, 811, 753 cm^{-1}; **HRMS** (ESI): m/z calculated for $C_{22}H_{19}NO_3K^+$ ([M+K^+]): 384.0997; found: 384.1002.

cis-5-(Allyloxy)-4-hydroxy-3-methoxy-4-phenyl-3,4-dihydroquinolin-2(1*H*)-one (6g)

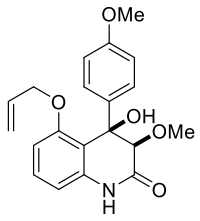


$C_{19}H_{19}NO_4$ (325.36)

Compound **6g** was prepared according to **GP2** starting from **5g** (35 mg, 0.11 mmol, 1 equiv.) and KO*t*Bu (86 mg, 0.77 mmol, 7 equiv.). The crude product was purified by column chromatography (silica gel, CH_2Cl_2/MeOH = 100:2) to afford the title compound (**6g**, 27 mg, 0.072 mmol, 67%) as a colorless oil.

R_f = 0.23 (*n*-pentane/EtOAc = 1:1); **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 8.07 (s, 1H), 7.29 – 7.26 (m, 5H), 7.22 (t, *J* = 8.2 Hz, 1H), 6.65 (dd, *J* = 8.4, 1.0 Hz, 1H), 6.52 (dd, *J* = 8.0, 0.9 Hz, 1H), 5.78 (ddt, *J* = 17.2, 10.6, 5.4 Hz, 1H), 5.34 (s, 1H), 5.21 – 5.15 (m, 2H), 4.52 – 4.41 (m, 2H), 3.84 (d, *J* = 1.4 Hz, 1H), 3.58 (s, 3H) ppm; **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 167.7, 158.0, 141.9, 137.2, 132.1, 130.0, 128.7, 128.5, 126.1, 118.8, 115.0, 109.4, 108.7, 85.1, 78.4, 69.8, 59.8 ppm; **IR** (neat): $\tilde{\nu}$ = 3494, 3249, 3235, 3083, 3002, 2928, 2829, 1692, 1596, 1502, 1473, 1447, 1421, 1391, 1324, 1313, 1278, 1259, 1224, 1179, 1103, 1059, 1028, 992, 930, 887, 824, 784, 750, 731, 699, 674, 665, 654 cm^{-1}; **HRMS** (ESI): m/z calculated for $C_{19}H_{19}NO_4Na^+$ ([M+Na]$^+$): 348.1206; found: 348.1195.

***cis*-5-(Allyloxy)-4-hydroxy-3-methoxy-4-(4-methoxyphenyl)-3,4-dihydroquinolin-2(1*H*)-one (6h)**

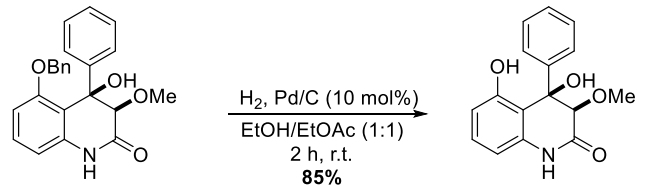


$C_{20}H_{21}NO_5$ (355.39)

Compound **6h** was prepared according to **GP2** starting from **5h** (43 mg, 0.12 mmol, 1 equiv.) and KO^{t}Bu (94 mg, 0.84 mmol, 7 equiv.). The crude product was purified by column chromatography (silica gel CH_2Cl_2/MeOH = 100:3) to afford the title compound (**6h**, 25 mg, 0.070 mmol, 58%) as a colorless oil.

R_f = 0.23 (*n*-pentane/EtOAc = 1:1); **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 8.34 (s, 1H), 7.21 (t, *J* = 8.2 Hz, 1H), 7.18 – 7.15 (m, 2H), 6.81 – 6.77 (m, 2H), 6.65 (d, *J* = 8.5 Hz, 1H), 6.51 (dd, *J* = 8.0, 0.8 Hz, 1H), 5.83 (ddt, *J* = 17.0, 10.4, 5.3 Hz, 1H), 5.40 (s, 1H), 5.25 – 5.16 (m, 2H), 4.54 – 4.44 (m, 2H), 3.81 (d, *J* = 1.5 Hz, 1H), 3.74 (s, 3H), 3.59 (s, 3H) ppm; **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 167.9, 159.7, 158.0, 137.0, 133.6, 132.1, 129.8, 127.5, 118.8, 115.2, 114.1, 109.5, 108.7, 85.2, 78.2, 69.8, 59.6, 55.3 ppm; **IR** (neat): $\tilde{\nu}$ = 3697, 3251, 3237, 3196, 3101, 3087 3039, 2997, 2932, 2833, 2246, 1691, 1595, 1508, 1471, 1442, 1417, 1392, 1303, 1280, 1251, 1224, 1172, 1101, 993, 928, 912, 893, 833, 809, 779, 729, 693, 670, 661cm^{-1}; **HRMS** (ESI): m/z calculated for $C_{20}H_{21}NNaO_5^+$ ([M+Na]$^+$): 378.1312; found: 378.1317.

(±)–Aflaquinolone E (9)



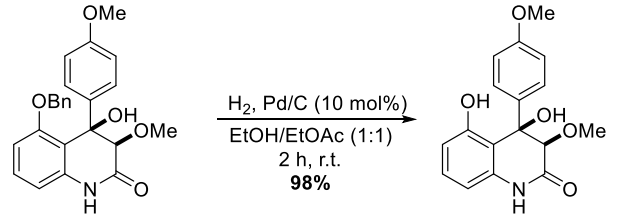
6d
$C_{23}H_{21}NO_4$ (375.42)

9
$C_{16}H_{15}NO_4$ (285.30)

To a solution of **6d** (23 mg, 0.060 mmol, 1 equiv.) in EtOH/EtOAc (1:1, 1 mL) was added Pd/C (6.4 mg, 0.0061 mmol, 10 w% Pd, 10 mol%) and the atmosphere was changed from Ar to H_2 by short evacuation and backfilling with H_2. The reaction mixture was then stirred vigorously at room temperature for 2 hours under an atmosphere of H_2. The reaction mixture was then filtered through a short pad of Celite® and concentrated under reduced pressure. The crude product was purified by column chromatography (silica gel, CH_2Cl_2/MeOH = 50:1) to afford the title compound (**9**, 15 mg, 0.051 mmol, 85%) as a colorless solid.

R_f = 0.21 (*n*-pentane/EtOAc = 3:1); **m.p.:** 143–148 °C; **^{1}H NMR** (700 MHz, CD_3OD): δ = 7.32 – 7.29 (m, 3H), 7.29 – 7.26 (m, 2H), 7.15 (t, *J* = 8.1 Hz, 1H), 6.54 (dd, *J* = 8.3, 1.1 Hz, 1H), 6.46 (dd, *J* = 8.0, 1.1 Hz, 1H), 3.66 (s, 1H), 3.53 (s, 3H) ppm; **^{13}C NMR** (176 MHz, CD_3OD): δ = 169.1, 159.1, 140.9, 138.1, 131.0, 129.8, 129.6, 127.5, 113.2, 113.0, 108.2, 86.3, 79.9, 59.2 ppm; **IR** (neat): $\tilde{\nu}$ = 3281, 3061, 2998, 2935, 2832, 1681, 1620, 1595, 1475, 1448, 1387, 1243, 1207, 1169, 1099, 1021, 879, 791, 745, 725, 698, 659 cm^{-1}; **HRMS** (ESI): m/z calculated for $C_{16}H_{15}NNaO_4^+$ ($[M+Na]^+$): 308.0893; found: 308.0900. The NMR data match those reported for Aflaquinolone E.[7]

(±)–Quinolinone B (10)



6e
$C_{24}H_{23}NO_5$ (405.45)

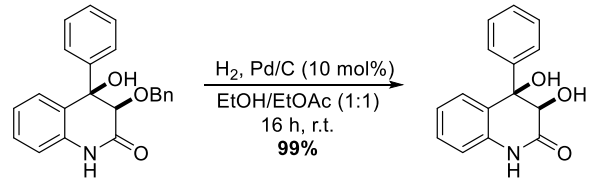
10
$C_{17}H_{17}NO_5$ (315.33)

To a solution of **6e** (12 mg, 0.028 mmol, 1 equiv.) in EtOAc/EtOH (1:1, 1 mL) was added Pd/C (3.0 mg, 0.0029 mmol, 10 w% Pd, 10 mol%) and the atmosphere was changed from Ar to H_2 by short evacuation and backfilling with H_2. The reaction mixture was then stirred vigorously at room temperature for 2 hours under an atmosphere of H_2. The reaction mixture was then filtered through a short pad of Celite® and concentrated under reduced pressure. The crude product was purified by column chromatography (silica gel CH_2Cl_2/MeOH = 50:1) to afford the title compound (**10**, 8.8 mg, 0.028 mmol, 98%) as a colorless oil.

R_f = 0.60 (CH_2Cl_2/MeOH = 50:1); **^{1}H NMR** (700 MHz, acetone-d_6): δ = 9.28 (s, 1H), 9.16 (s, 1H), 7.22 (d, *J* = 8.9 Hz, 2H), 7.16 (t, *J* = 8.1 Hz, 1H), 6.88 (d, *J* = 8.9 Hz, 2H), 6.55 (dd, *J* = 8.0, 1.1 Hz, 1H), 6.49 (dd, *J* = 8.2, 1.1 Hz, 1H), 6.14 (s, 1H), 3.77 (s, 3H), 3.67 (d, *J* = 1.6 Hz, 1H), 3.50 (s, 3H) ppm; **^{13}C NMR** (176 MHz, acetone-d_6): δ = 166.5, 161.0, 159.2, 138.1, 131.9, 130.7, 128.8, 114.7, 112.5, 112.4, 107.4,

85.8, 79.6, 58.9, 55.5. ppm; **IR** (neat): $\tilde{\nu}$ = 3294, 3066, 2993, 2932, 2837, 1685, 1626, 1595, 1510, 1439, 1379, 1305, 1253, 1207, 1170, 1103, 1076, 1051, 1025, 989, 936, 884, 834, 783, 756, 716 cm^{-1}; **HRMS** (ESI): m/z calculated for $C_{17}H_{17}NNaO_5^+$ ([M+Na]$^+$): 338.0999; found: 338.1006. The NMR data match those reported for Quinolinone B.[6]

(±)–Aflaquinolone F (11)



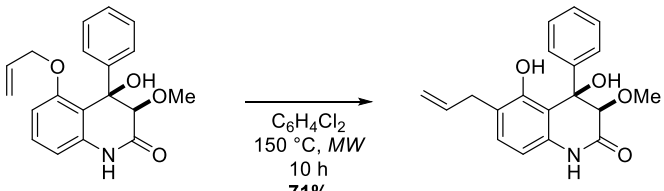
6f
$C_{22}H_{19}NO_3$ (345.40)

11
$C_{15}H_{13}NO_3$ (255.27)

To a solution of **6f** (12 mg, 0.034 mmol, 1 equiv.) in EtOAc/EtOH (1:1, 1 mL) was added Pd/C (3.6 mg, 0.0031 mmol, 10 w% Pd, 10 mol%) and the atmosphere was changed from Ar to H_2 by short evacuation and backfilling with H_2. The reaction mixture was then stirred vigorously at room temperature for 16 hours under an atmosphere of H_2. The reaction mixture was filtered through a short pad of Celite® and concentrated under reduced pressure. The crude product was purified by column chromatography (silica gel, CH_2Cl_2/MeOH = 100:3) to afford the title compound (**11**, 8.7 mg, 0.034 mmol, 99%) as a colorless oil.

R_f = 0.30 (CH_2Cl_2/MeOH = 50:1); **^{1}H NMR** (700 MHz, CD_3OD): δ = 7.53 – 7.49 (m, 2H), 7.39 (t, *J* = 7.6 Hz, 2H), 7.34 – 7.31 (m, 1H), 7.26 (td, *J* = 7.6, 1.2 Hz, 1H), 6.96 (dd, *J* = 7.9, 1.2 Hz, 1H), 6.91 (td, *J* = 7.6, 1.1 Hz, 1H), 6.73 (d, *J* = 7.8 Hz, 1H), 4.76 (s, 1H) ppm; **^{13}C NMR** (176 MHz, CD_3OD): δ = 172.6, 143.1, 138.3, 130.6, 130.1, 129.0, 128.4, 128.3, 124.0, 117.0, 78.6, 75.8 ppm; **IR** (neat): $\tilde{\nu}$ = 3294, 2954, 2922, 2853, 1727, 1707, 1606, 1464, 1376, 1282, 1248, 1116, 1031, 824, 762, 722 cm^{-1}; **HRMS** (ESI): m/z calculated for $C_{15}H_{13}NNaO_3^+$ ([M+Na]$^+$): 278.0787; found: 278.0795. The NMR data match those reported for Aflaquinolone F.[7]

***cis*-6-Allyl-4,5-dihydroxy-3-methoxy-4-phenyl-3,4-dihydroquinolin-2(1*H*)-one (12a)**



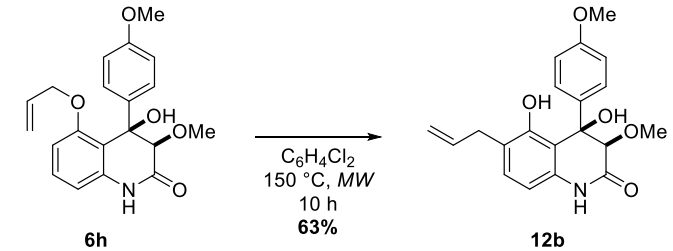
6g
$C_{19}H_{19}NO_4$ (325.36)

12a
$C_{19}H_{19}NO_4$ (325.36)

6g (14 mg, 0.040 mmol, 1 equiv.) was dissolved in 1,2-dichlorobenzene (1 mL) and heated in a microwave at 150 °C for 10 hours. The solvent was removed under reduced pressure and the crude product was purified by column chromatography (silica gel, *n*-pentane/EtOAc = 1:2) to afford the title compound (**12a**, 9.9 mg, 0.030 mmol, 71%) as a colorless oil.

R_f = 0.32 (CH_2Cl_2/MeOH = 50:1); **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 8.90 (d, *J* = 0.5 Hz, 1H), 7.85 (s, 1H), 7.33 – 7.29 (m, 3H), 7.28 – 7.25 (m, 2H), 7.05 (d, *J* = 8.0 Hz, 1H), 6.32 (d, *J* = 8.0 Hz, 1H), 5.97 (ddt, *J* = 16.8, 10.1, 6.6 Hz, 1H), 5.07 – 5.02 (m, 2H), 4.60 (s, 1H), 3.69 (d, *J* = 1.5 Hz, 1H), 3.62 (s, 3H), 3.31 (qdt, *J* = 15.7, 6.7, 1.7 Hz, 2H) ppm; **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 165.7, 155.7, 137.7, 136.9, 133.8, 130.8, 129.3, 129.0, 126.5, 124.4, 115.7, 110.5, 106.5, 84.3, 79.1, 59.1, 33.7 ppm; **IR** (neat): $\tilde{\nu}$ = 3465, 3290, 3074, 2954, 2924, 2869, 1683, 1638, 1622, 1602, 1505, 1493, 1463, 1449, 1421, 1378, 1346, 1272, 1223, 1174, 1102, 1077, 1036, 1027, 992, 947, 916, 892, 856, 846, 815, 754, 697, 673, 666 cm^{-1}; **HRMS** (ESI): *m/z* calculated for $C_{19}H_{19}NNaO_4^+$ ($[M+Na]^+$): 348.1206; found: 348.1216.

***cis*-6-Allyl-4,5-dihydroxy-3-methoxy-4-(4-methoxyphenyl)-3,4-dihydroquinolin-2(1*H*)-one (12b)**



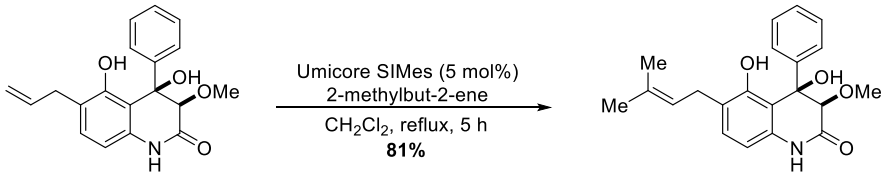
6h
$C_{20}H_{21}NO_5$ (355.39)

12b
$C_{20}H_{21}NO_5$ (355.39)

6h (39 mg, 0.11 mmol, 1 equiv.) was dissolved in 1,2-dichlorobenzene (1 mL) and heated in a microwave at 150 °C for 10 hours. The solvent was removed under reduced pressure and the crude product was purified by column chromatography (SiO_2, *n*-pentane/EtOAc = 1:2) to afford the title compound (**12b**, 25 mg, 0.070 mmol, 63%) as a colorless oil.

R_f = 0.32 (*n*-Pentane/EtOAc = 1:1); **^{1}H NMR** (400 MHz, acetone-d_6): δ= 9.45 (s, 1H), 9.25 (s, 1H), 7.28 – 7.15 (m, 2H), 7.04 (dt, *J* = 8.1, 0.7 Hz, 1H), 6.93 – 6.82 (m, 2H), 6.51 (d, *J* = 8.5 Hz, 1H), 6.23 (s, 1H), 6.01 – 5.89 (m, 1H), 5.08 – 5.00 (m, 1H), 4.96 (ddtd, *J* = 10.1, 2.0, 1.4, 0.5 Hz, 1H), 3.76 (s, 3H), 3.65 (dd, *J* = 1.5, 0.5 Hz, 1H), 3.50 (s, 3H), 3.33 – 3.20 (m, 2H) ppm; **^{13}C NMR** (126 MHz, acetone-d_6): δ = 166.4, 161.0, 156.6, 138.1, 136.3, 131.9, 130.8, 128.8, 123.2, 115.4, 114.7, 112.0, 107.1, 85.8, 79.7, 58.8, 55.5, 34.2. ppm; **IR** (neat): $\tilde{\nu}$ = 3280, 3069, 2955, 2924, 2853, 1683, 1638, 1623, 1603, 1509, 1463, 1418, 1379, 1306, 1253, 1224, 1172, 1103, 1077, 1028, 993, 944, 909, 891, 860, 830, 812, 798, 765, 754, 730, 709, 701, 687, 681, 666 cm^{-1}; **HRMS** (ESI): *m/z* calculated for $C_{20}H_{21}NNaO_5^+$ ($[M+Na]^+$): 378.1312; found: 378.1328.

(±)–Aniduquinolone C (13a)



$C_{19}H_{19}NO_4$ (325.36)

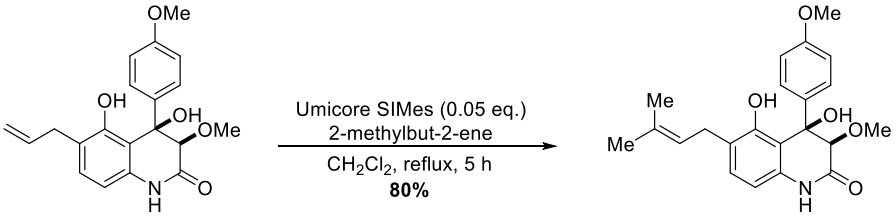
$C_{21}H_{23}NO_4$ (353.42)

12a (9.9 mg, 0.030 mmol, 1 equiv.) and Umicore M71 SIMes (1.1 mg, 0.0015 mmol, 5 mol%) were dissolved in CH_2Cl_2 (0.5 mL). 2-Methylbut-2-ene (0.030 mL, 0.30 mmol, 10 equiv.) was added and the reaction mixture was heated to reflux for 5 hours in a sealed tube. After cooling to room temperature,

the reaction mixture was filtered through a short pad of silica gel. All volatiles were removed under reduced pressure and the crude product was purified by HPLC (EtOH/*n*-pentane = 1:10, 1 mL/min, t_r = 7.00 min) to afford the title compound (**13a**, 8.0 mg, 0.024 mmol, 81%) as a colorless oil.

R_f = 0.35 (CH_2Cl_2/MeOH 50:1); **^{1}H NMR** (700 MHz, DMSO-d_6): δ = 10.15 (s, 1H), 9.59 (s, 1H), 7.37 – 7.28 (m, 3H), 7.19 (dd, *J* = 5.8, 3.6 Hz, 2H), 6.95 (d, *J* = 7.9 Hz, 1H), 6.37 (d, *J* = 7.9 Hz, 1H), 5.24 (t, *J* = 7.4 Hz, 1H), 3.58 (s, 1H), 3.43 (s, 3H), 3.19 (dd, *J* = 15.4, 7.4 Hz, 1H), 3.08 (dd, *J* = 15.4, 7.3 Hz, 1H), 1.68 (s, 3H), 1.65 (s, 3H) ppm; **^{13}C NMR** (176 MHz, DMSO-d_6): δ = 166.1, 155.0, 140.0, 135.0, 131.3, 129.2, 128.6, 126.2, 123.0, 122.8, 110.9, 106.3, 84.4, 78.7, 58.3, 27.5, 25.6, 17.7 ppm; **IR** (neat): $\tilde{\nu}$ = 3218, 3142, 3062, 2912, 2832, 2255, 1685, 1623, 1602, 1506, 1493, 1447, 1422, 1375, 1274, 1224, 1174, 1105, 1076, 1024, 1003, 943, 902, 867, 818, 767, 734 cm^{-1}; **HRMS** (ESI): *m/z* calculated for $C_{21}H_{23}NNaO_4^+$ ([M+Na]$^+$): 376.1519; found: 376.1513. The NMR data match those reported for Aniduquinolone C.[5]

(±)–Peniprequinolone (**13b**)



$C_{20}H_{21}NO_5$ (355.39) → $C_{22}H_{25}NO_5$ (383.44)

12b (11 mg, 0.030 mmol, 1 equiv.) and Umicore M71 SIMes (1.1 mg, 0.0015 mmol, 5 mol%) were dissolved in CH_2Cl_2 (0.5 mL). 2-Methylbut-2-ene (0.030 mL, 0.30 mmol, 10 equiv.) was added and the reaction mixture was heated to reflux for 5 hours in a sealed tube. After cooling to room temperature, the reaction mixture was filtered through a short pad of silica gel. All volatiles were removed under reduced pressure and the crude product was purified by HPLC (EtOH/*n*-pentane = 1:10, 1 mL/min, t_r = 8.60 min) to afford the title compound (**13b**, 9.0 mg, 0.024 mmol, 80%) as a colorless solid.

R_f = 0.40 (CH_2Cl_2/MeOH 50:1); **m.p.:** 55 **°C -** 59°C; **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 8.91 (s, 1H), 7.91 (s, 1H), 7.19 – 7.14 (m, 2H), 7.03 (d, J = 8.0 Hz, 1H), 6.84 – 6.78 (m, 2H), 6.28 (d, J = 8.0 Hz, 1H), 5.30 – 5.26 (m, 1H), 4.54 (s, 1H), 3.76 (s, 3H), 3.68 (d, J = 1.5 Hz, 1H), 3.60 (s, 3H), 3.29 (dd, J = 16.0, 7.5 Hz, 1H), 3.20 (dd, J = 16.0, 7.2 Hz, 1H), 1.74 (s, 3H), 1.68 (s, 3H) ppm; **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 166.0, 160.3, 155.7, 133.3, 132.8, 130.1, 129.5, 128.0, 125.8, 122.4, 114.4, 110.5, 106.4, 84.5, 78.9, 59.0, 55.4, 27.8, 25.9, 17.9 ppm; **IR** (neat): $\tilde{\nu}$ = 3277, 3059, 2954, 2923, 2869, 2853, 1684, 1621, 1603, 1510, 1462, 1419, 1377, 1306, 1254, 1221, 1188, 1172, 1105, 1079, 1032, 989, 974, 940, 929, 903, 867, 829, 810, 767, 755, 734, 707, 698, 974, 661, 652 cm^{-1}; **HRMS** (ESI): *m/z* calculated for $C_{22}H_{25}NNaO_5^+$ ([M+Na]$^+$): 406.1625; found: 406.1627. The NMR data match those reported for Peniprequinolone.[6]

References

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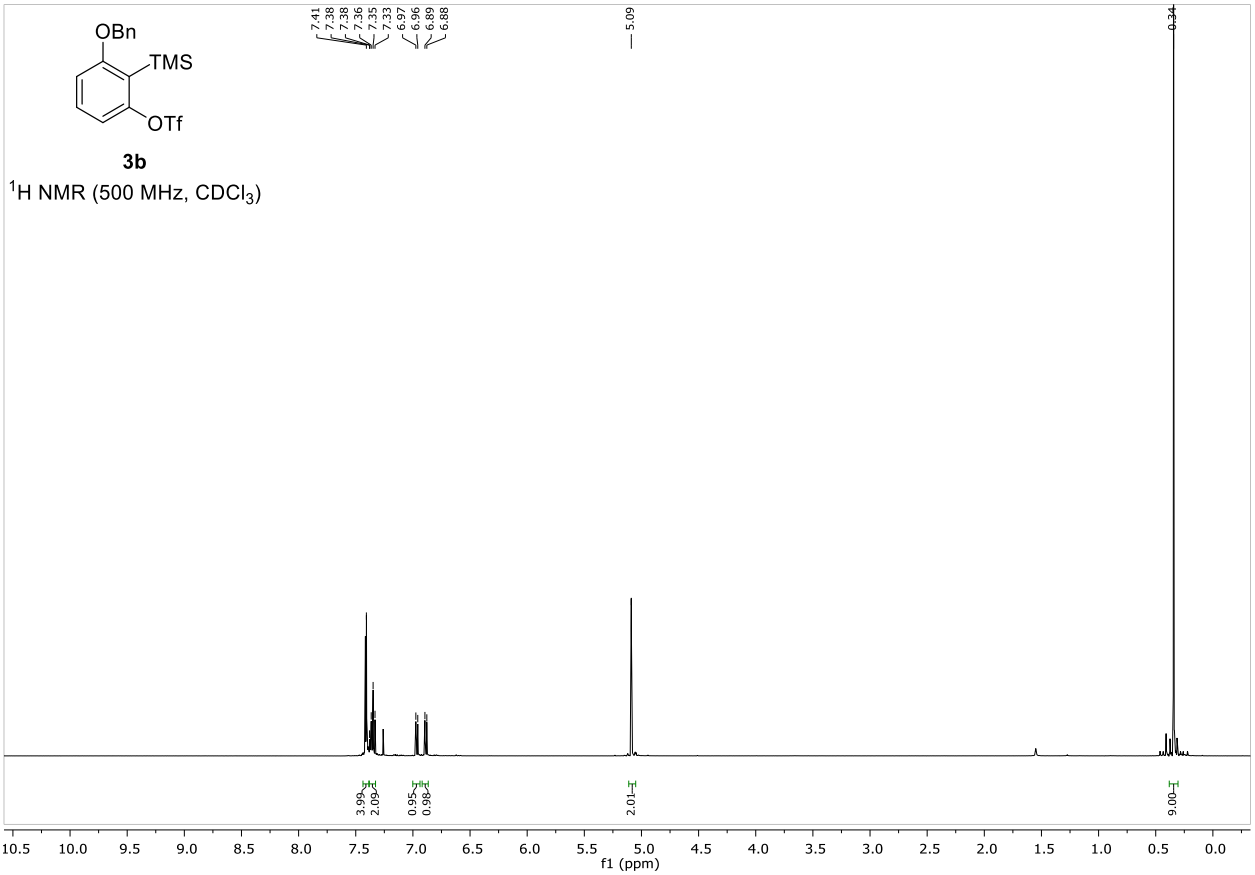
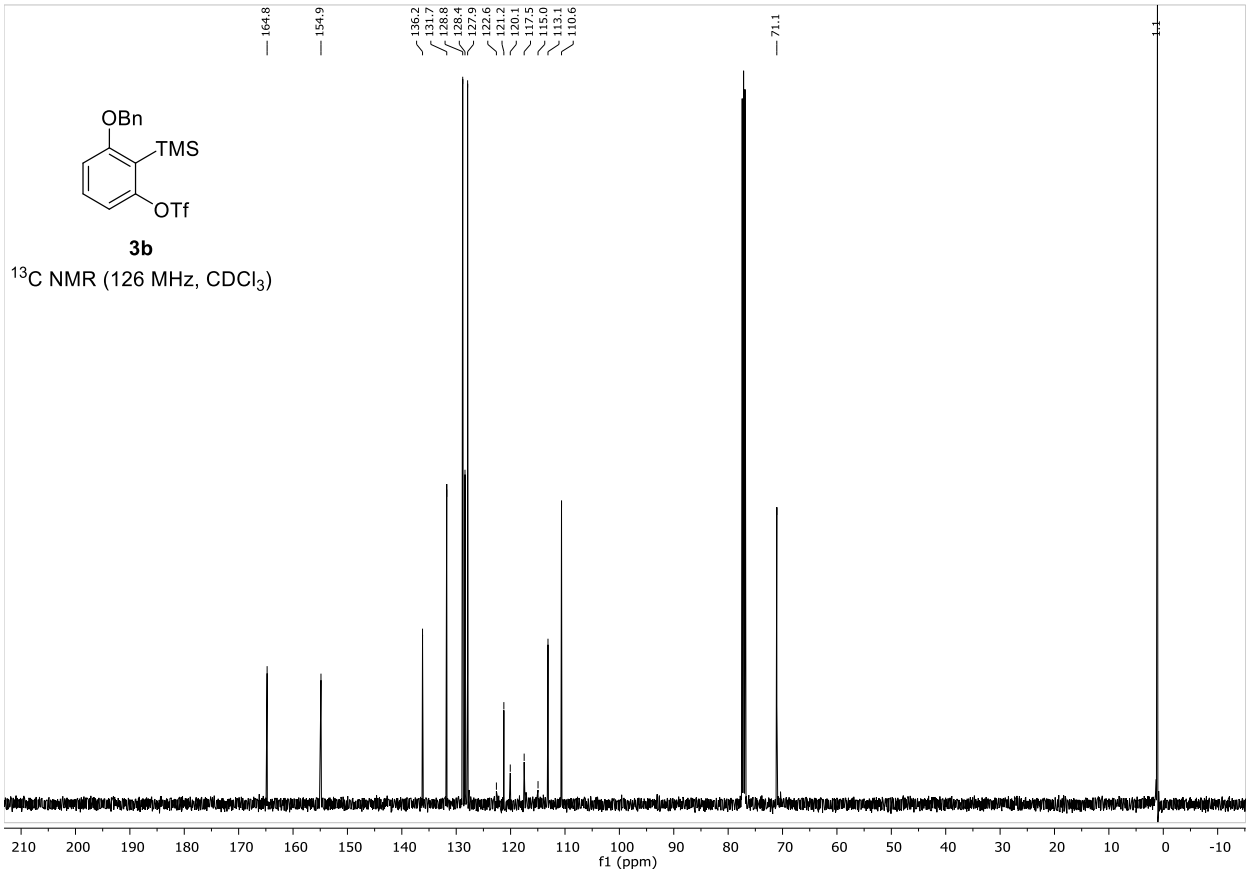
Appendix



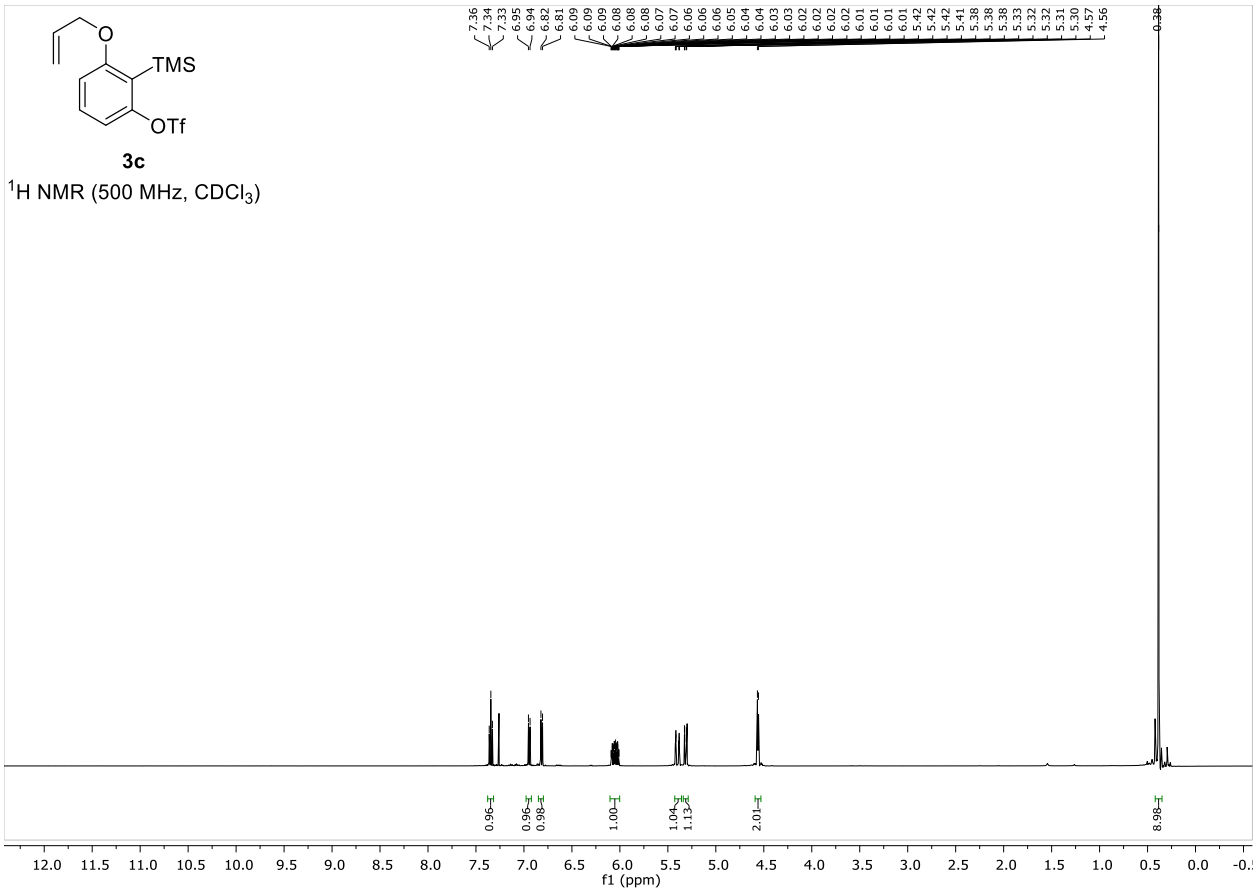
3b

^{1}H NMR (500 MHz, $CDCl_3$)



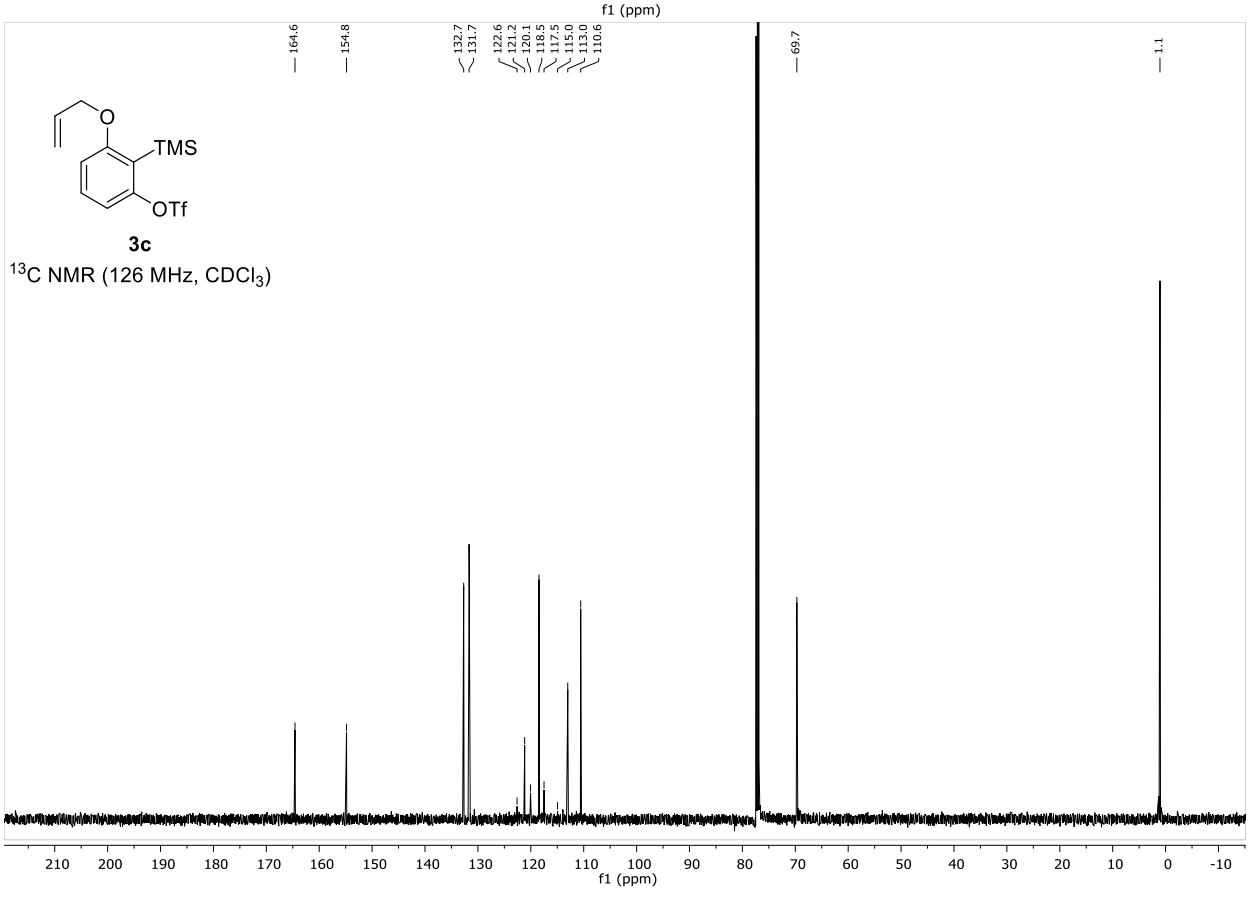
3b

^{13}C NMR (126 MHz, $CDCl_3$)



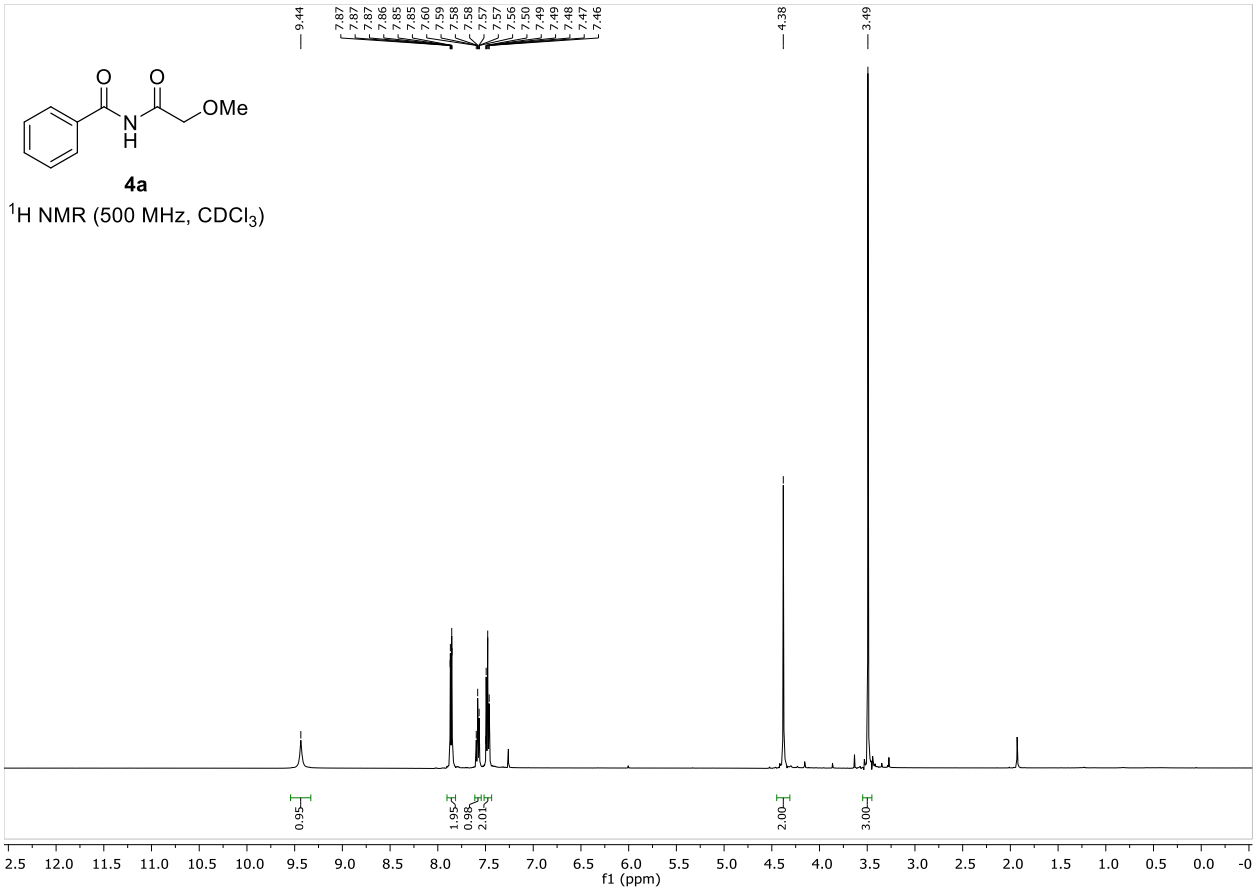
3c

^{1}H NMR (500 MHz, $CDCl_3$)



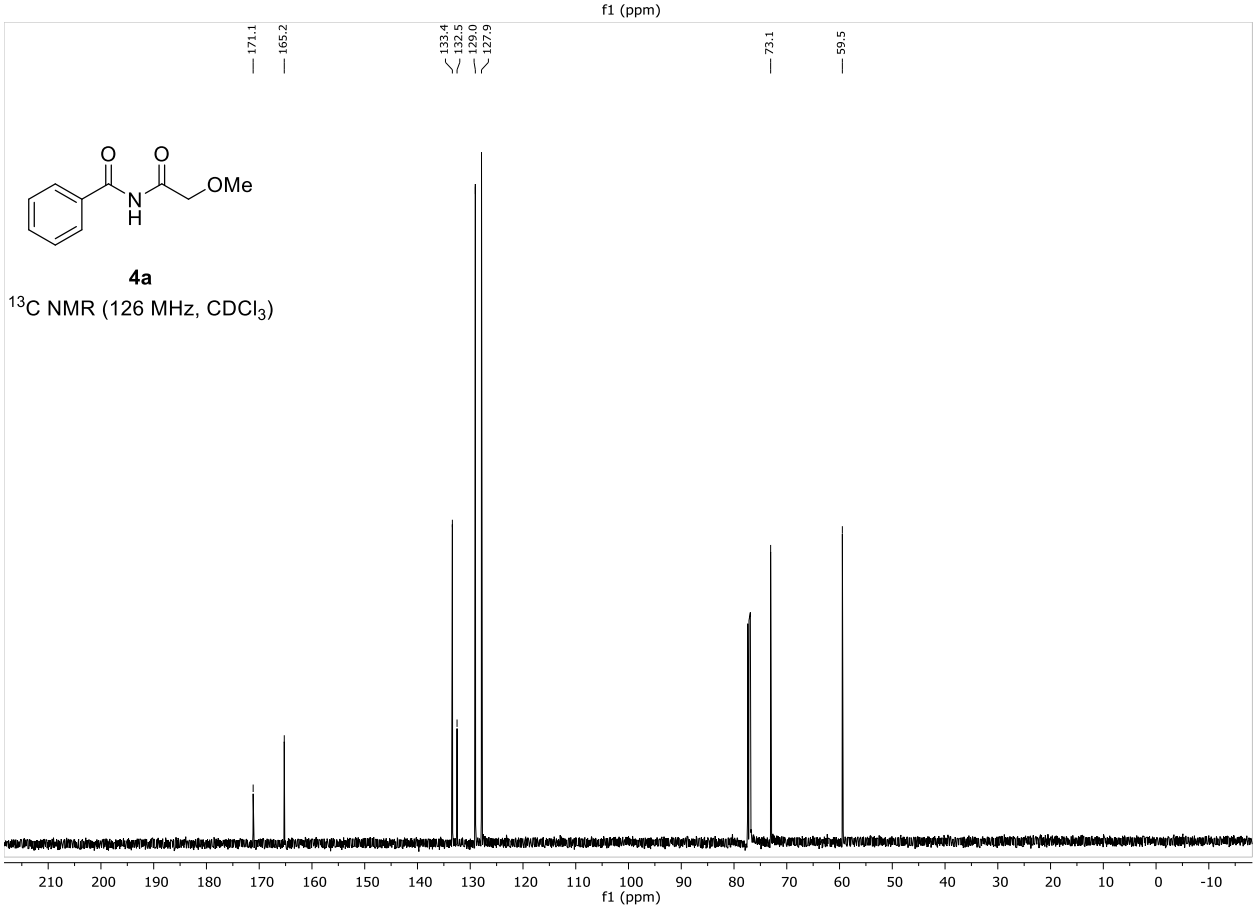
3c

^{13}C NMR (126 MHz, $CDCl_3$)



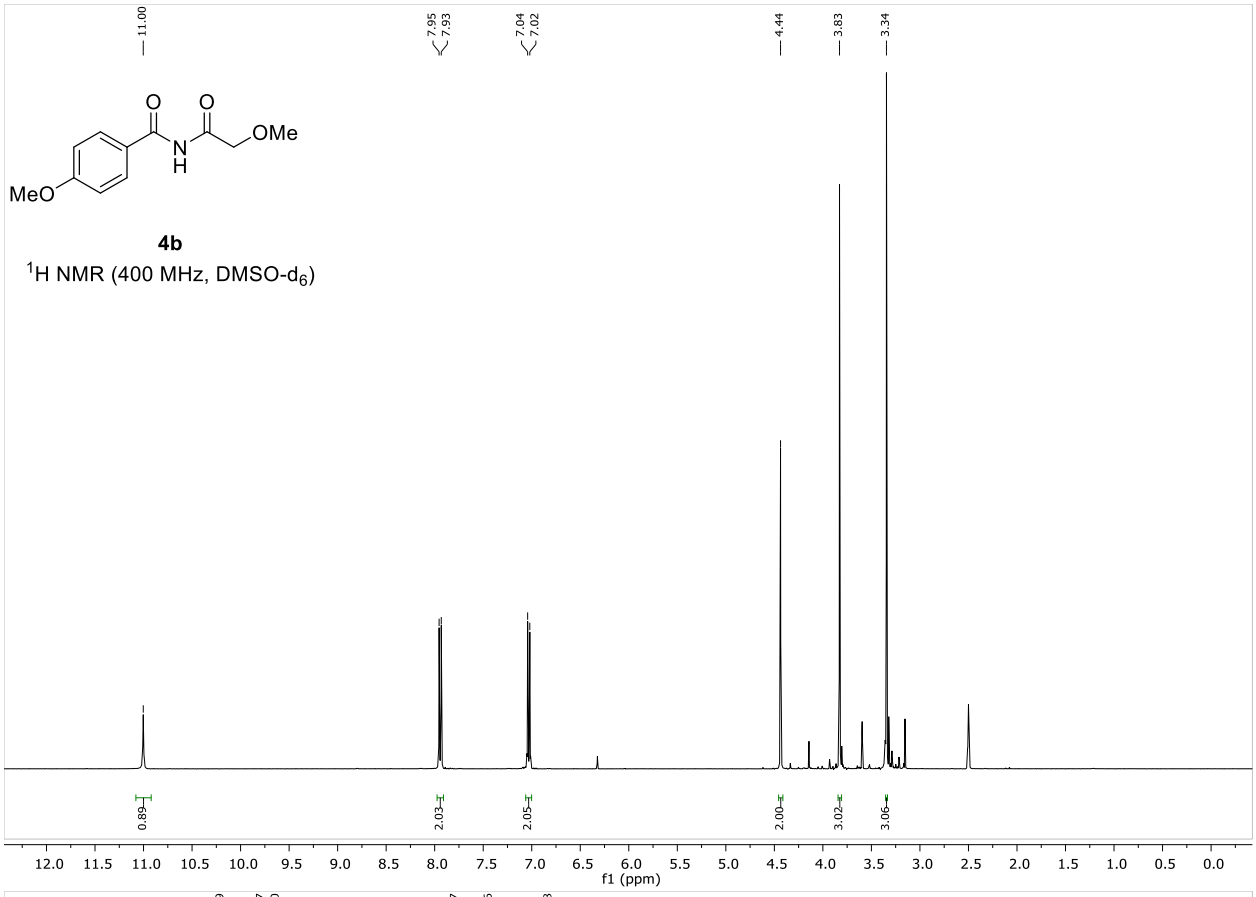
4a

^{1}H NMR (500 MHz, $CDCl_3$)



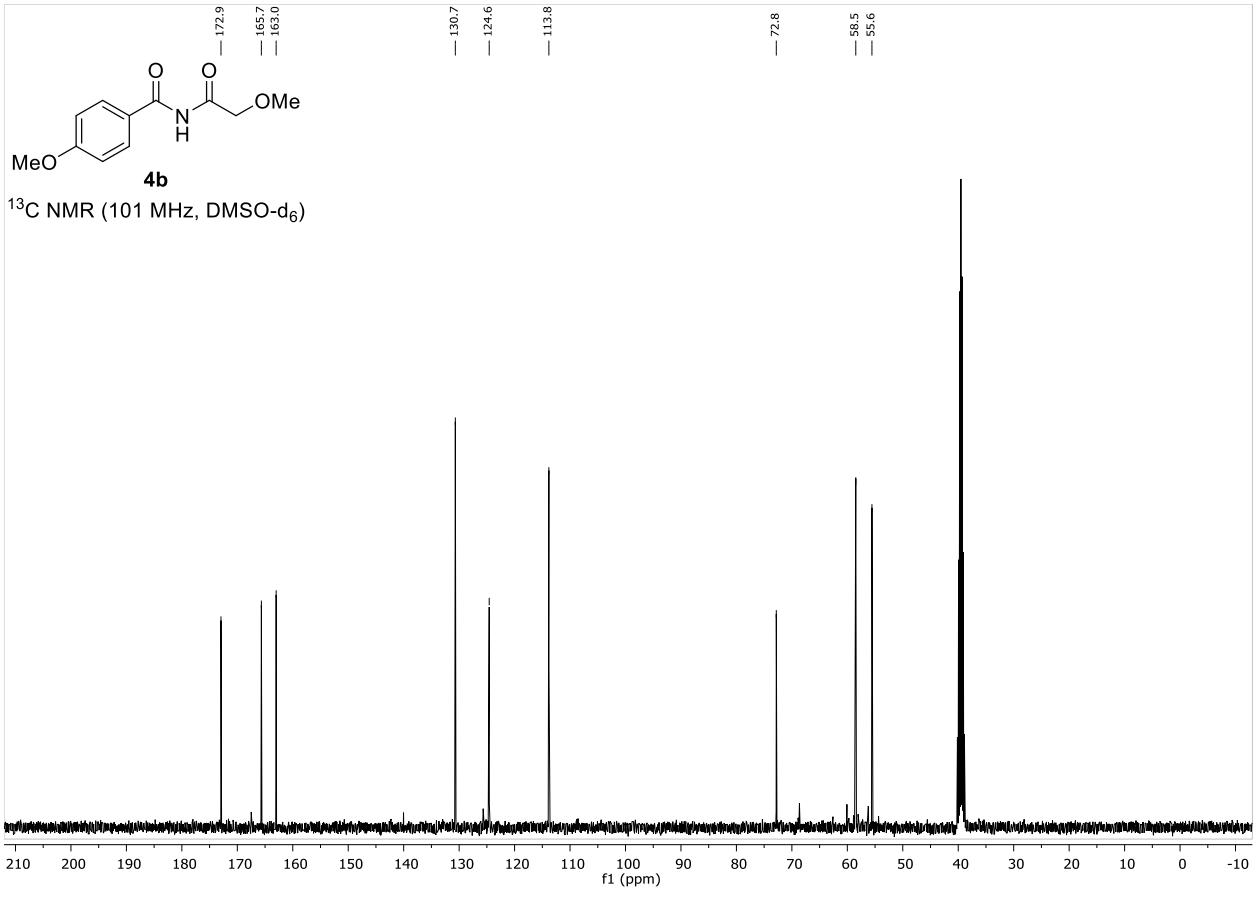
4a

^{13}C NMR (126 MHz, $CDCl_3$)



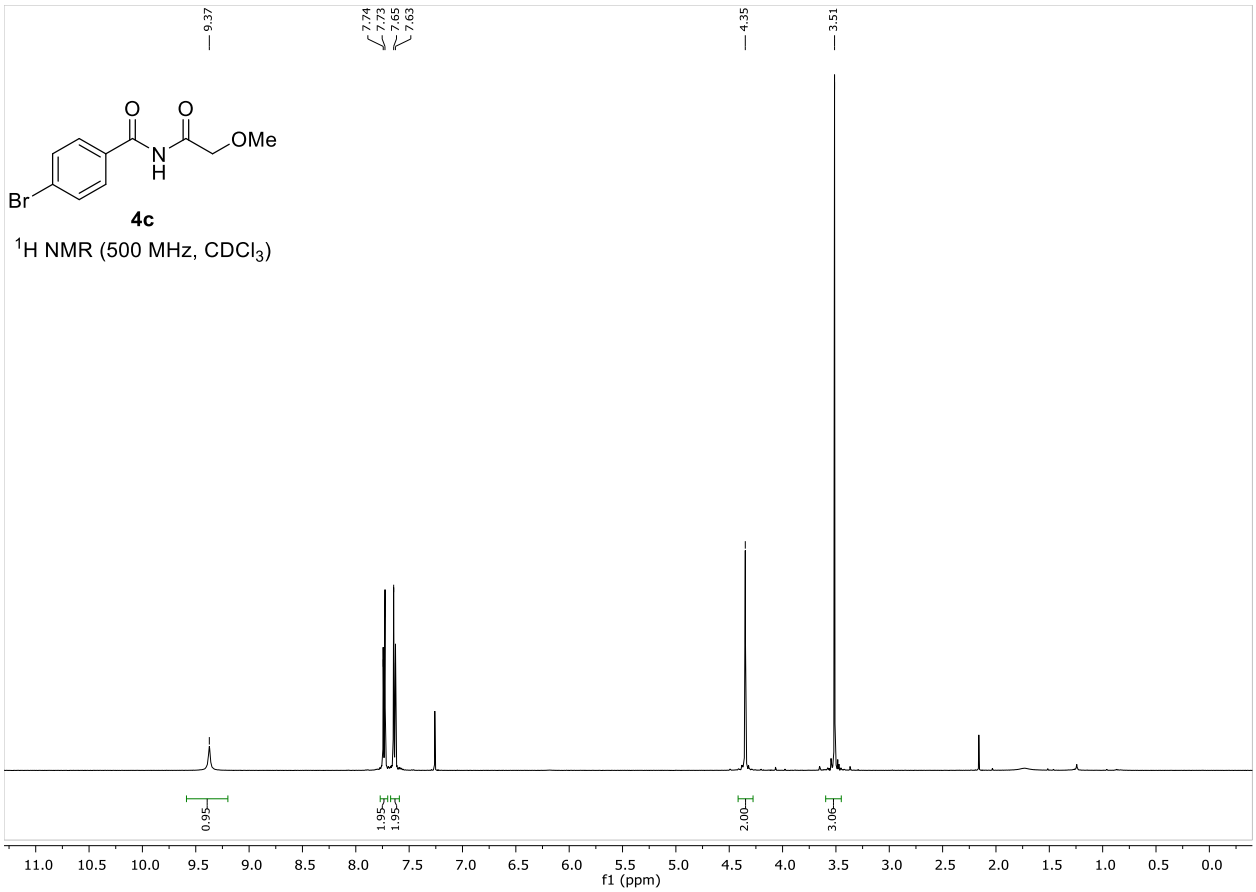
4b

^{1}H NMR (400 MHz, DMSO-d_6)



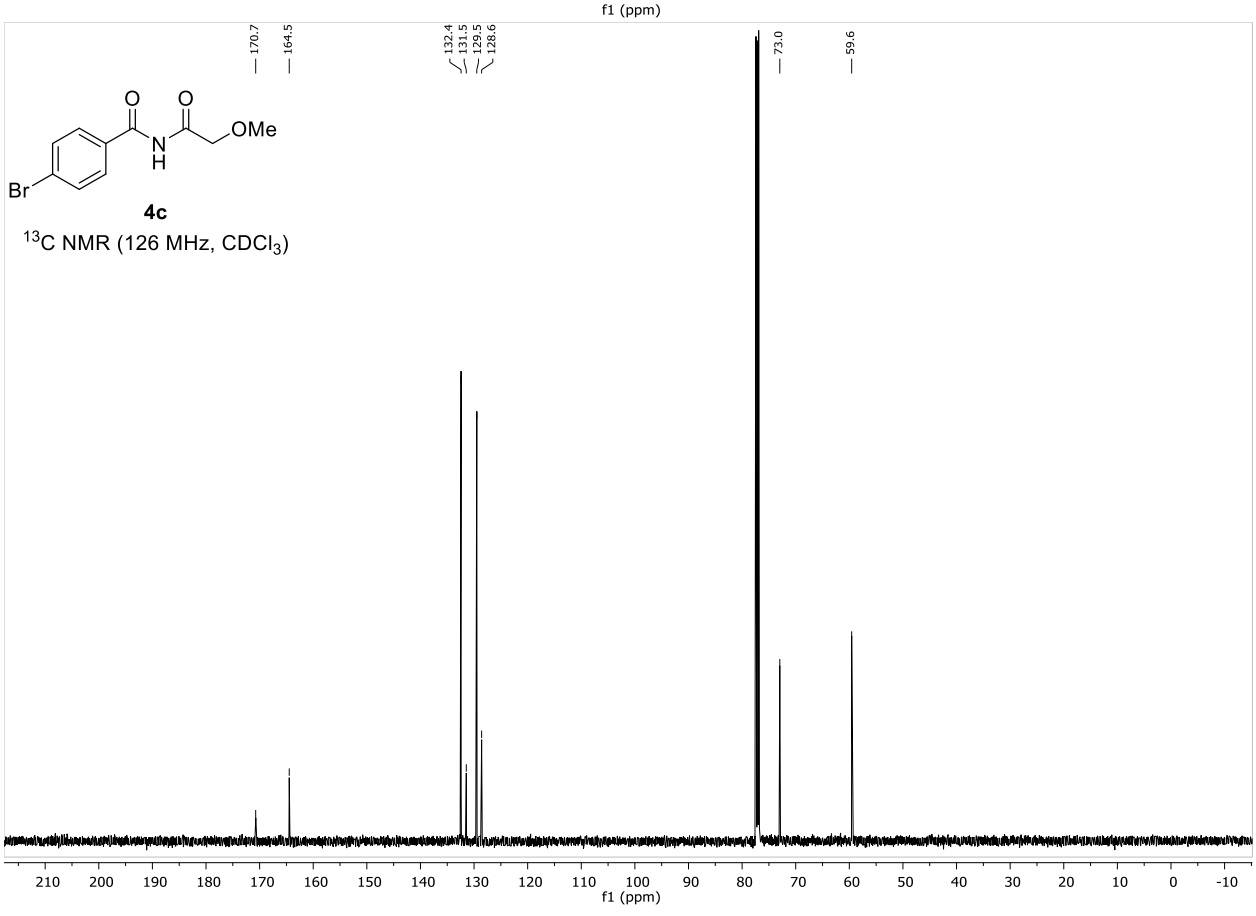
4b

^{13}C NMR (101 MHz, DMSO-d_6)



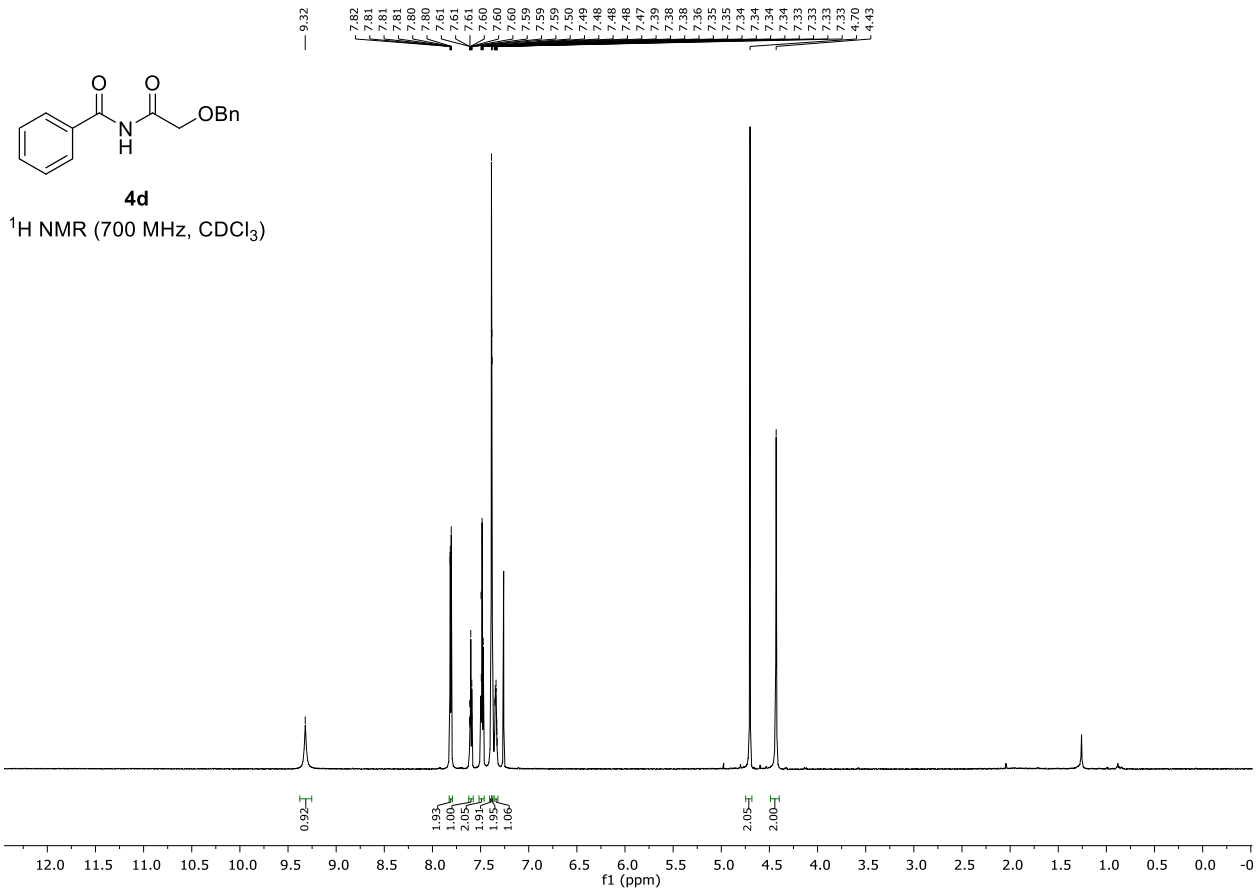
4c

^{1}H NMR (500 MHz, $CDCl_3$)



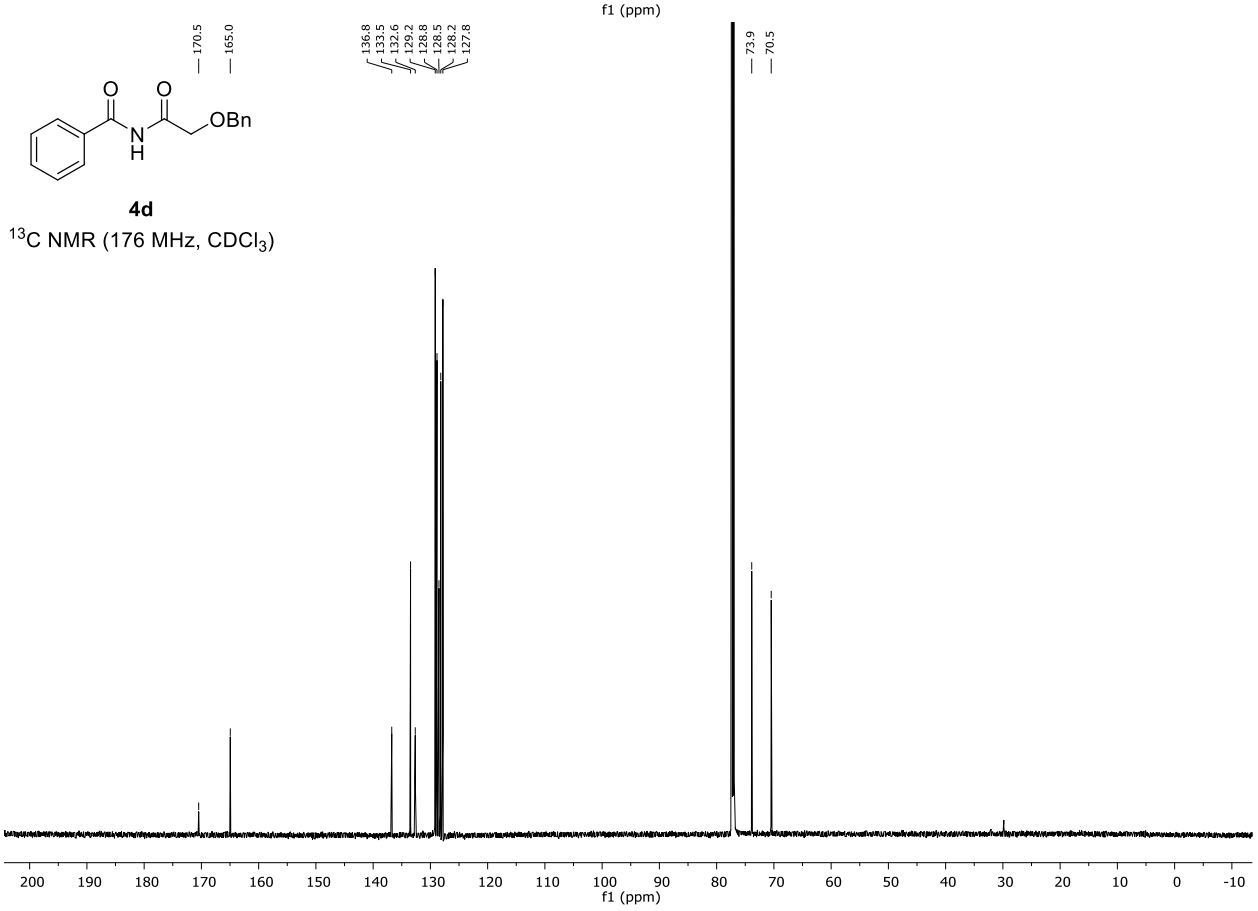
4c

^{13}C NMR (126 MHz, $CDCl_3$)



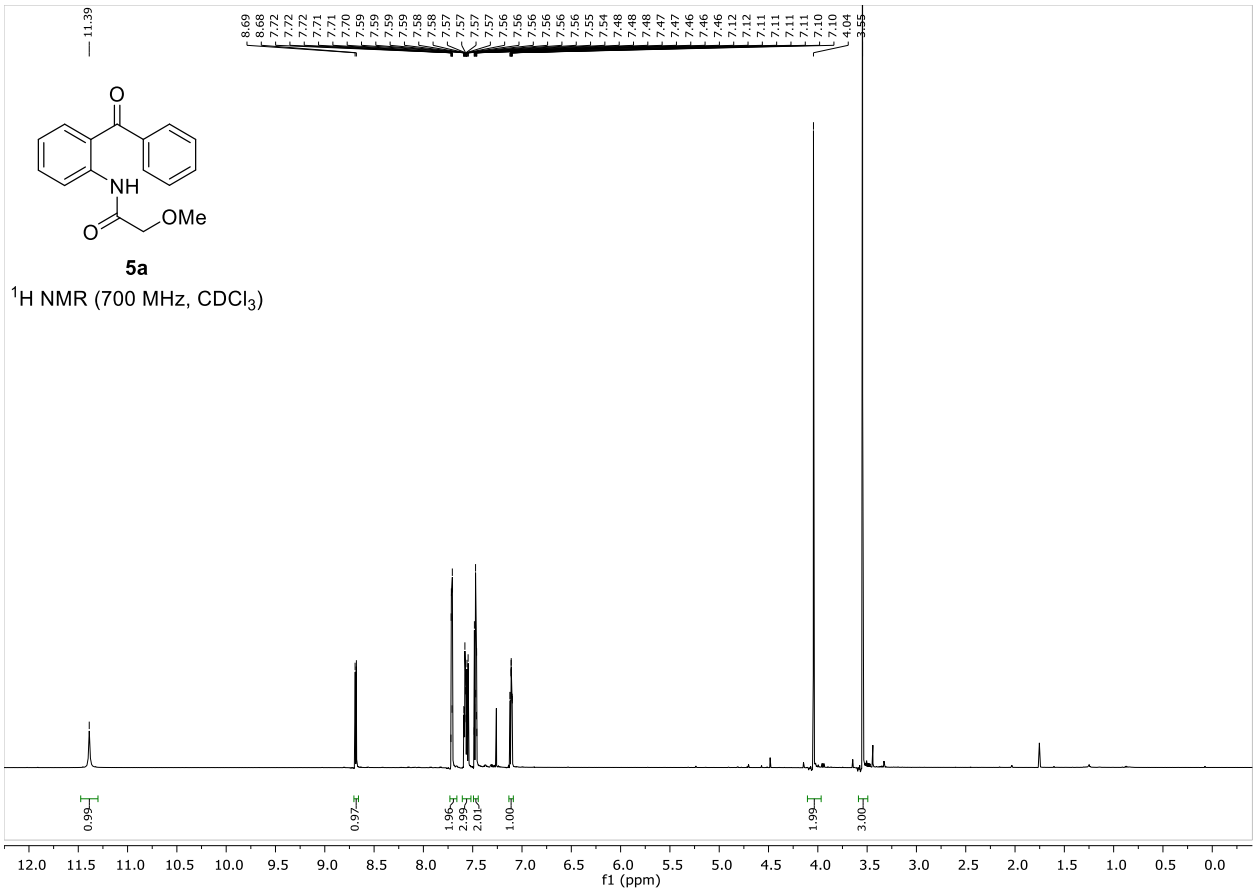
4d

^{1}H NMR (700 MHz, $CDCl_3$)



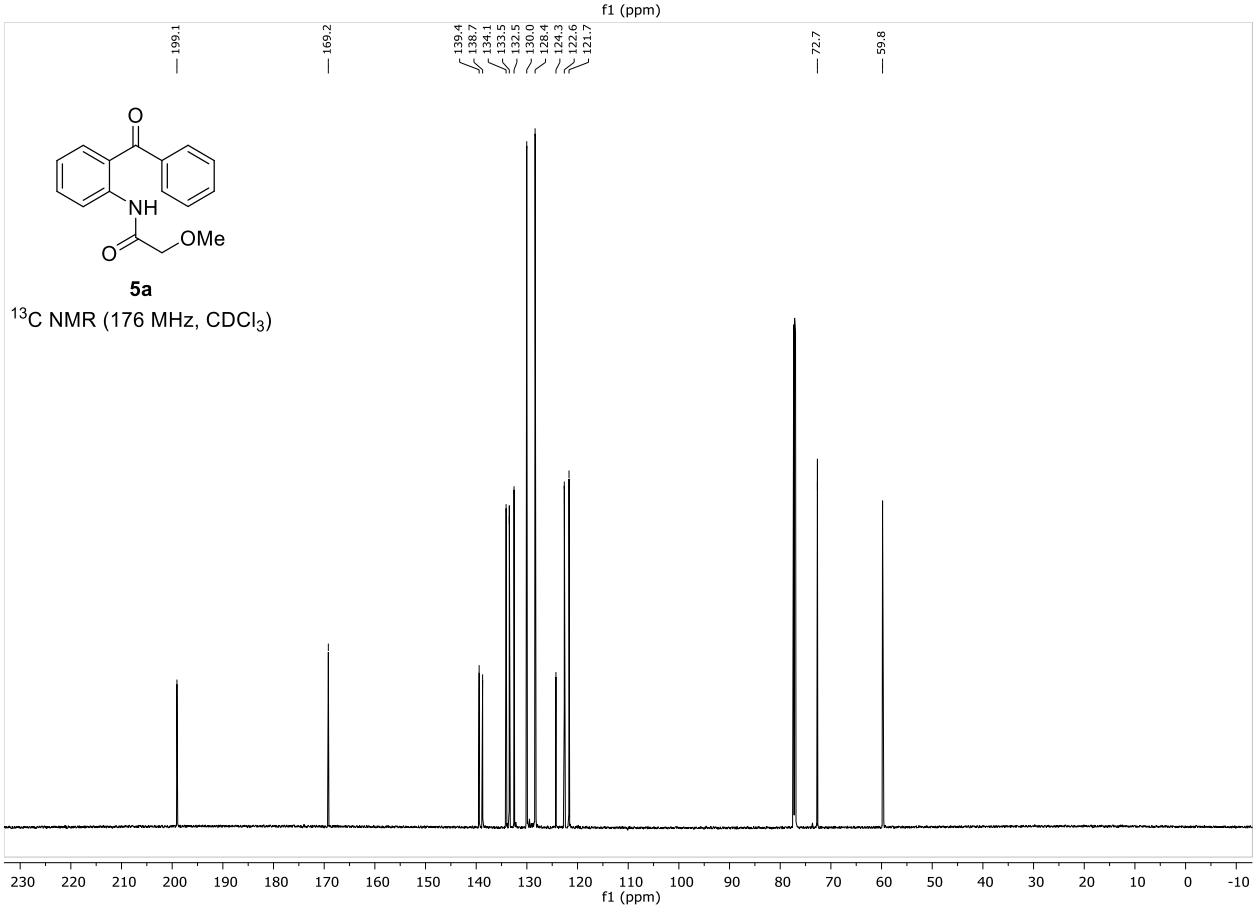
4d

^{13}C NMR (176 MHz, $CDCl_3$)



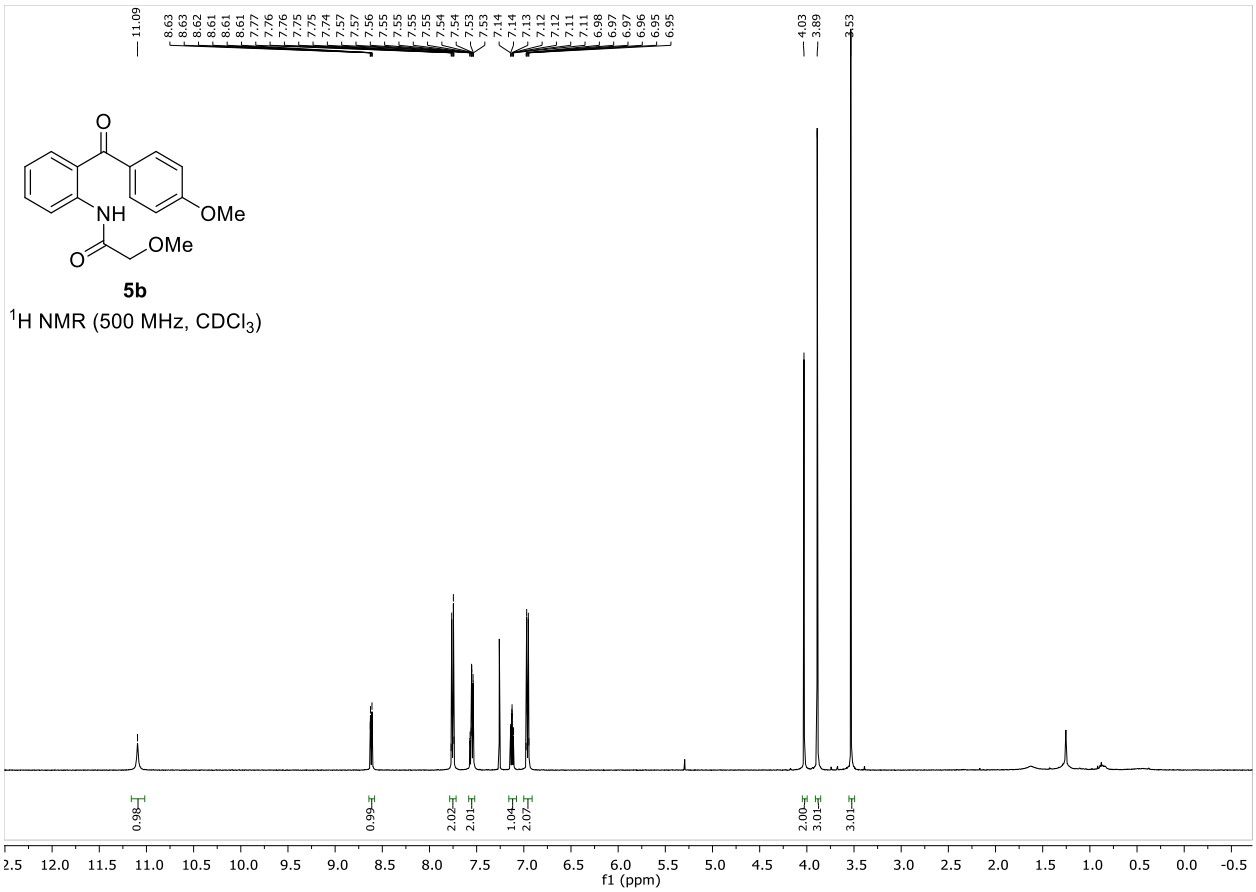
5a

^{1}H NMR (700 MHz, $CDCl_3$)



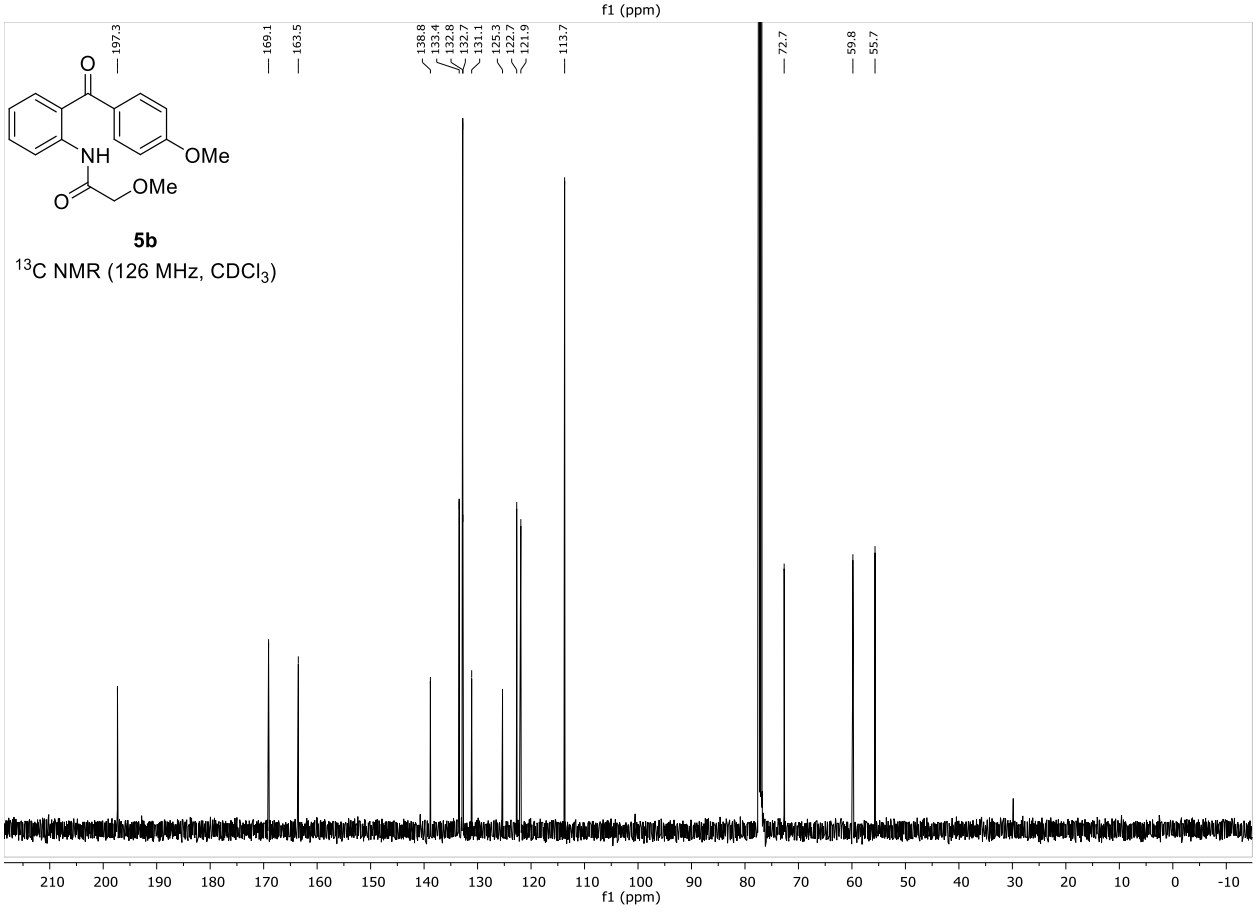
5a

^{13}C NMR (176 MHz, $CDCl_3$)



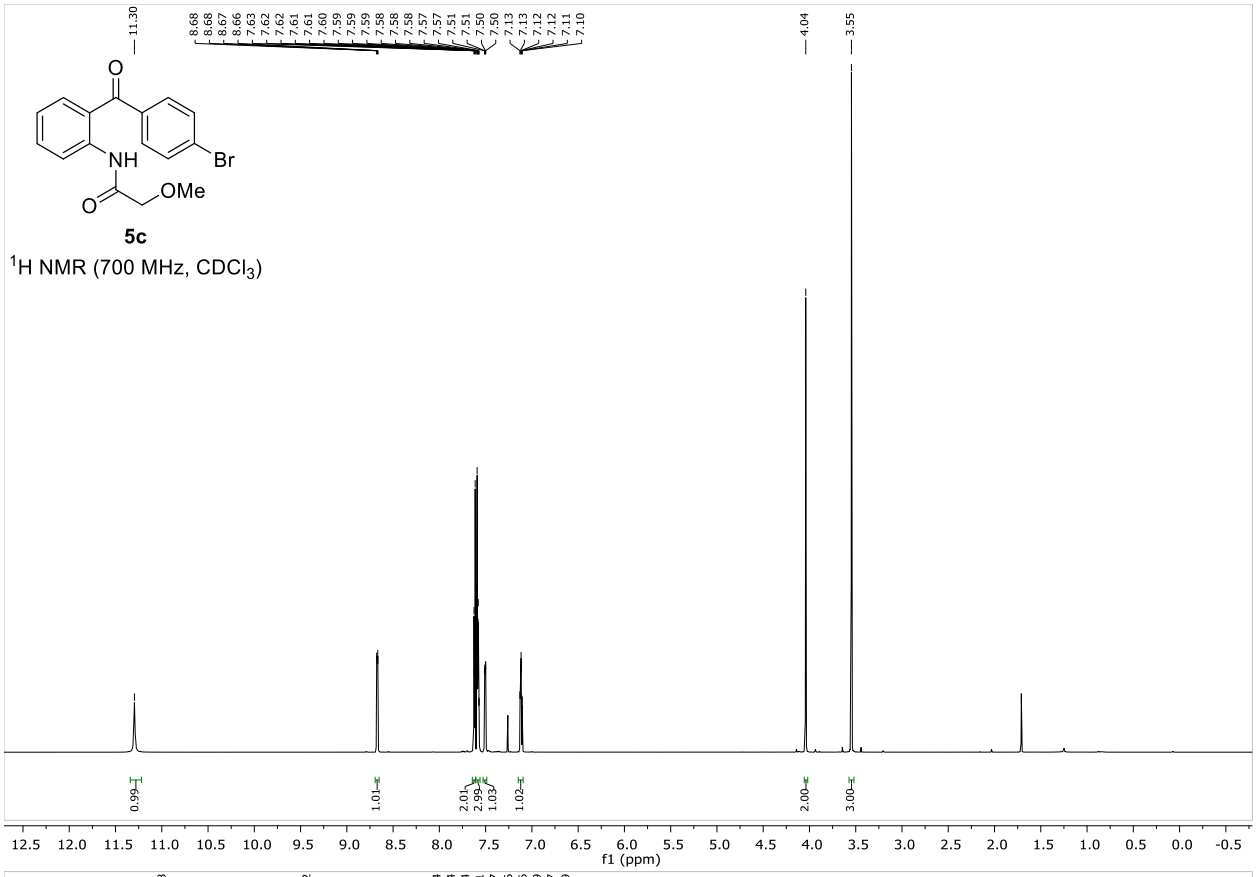
5b

^{1}H NMR (500 MHz, $CDCl_3$)



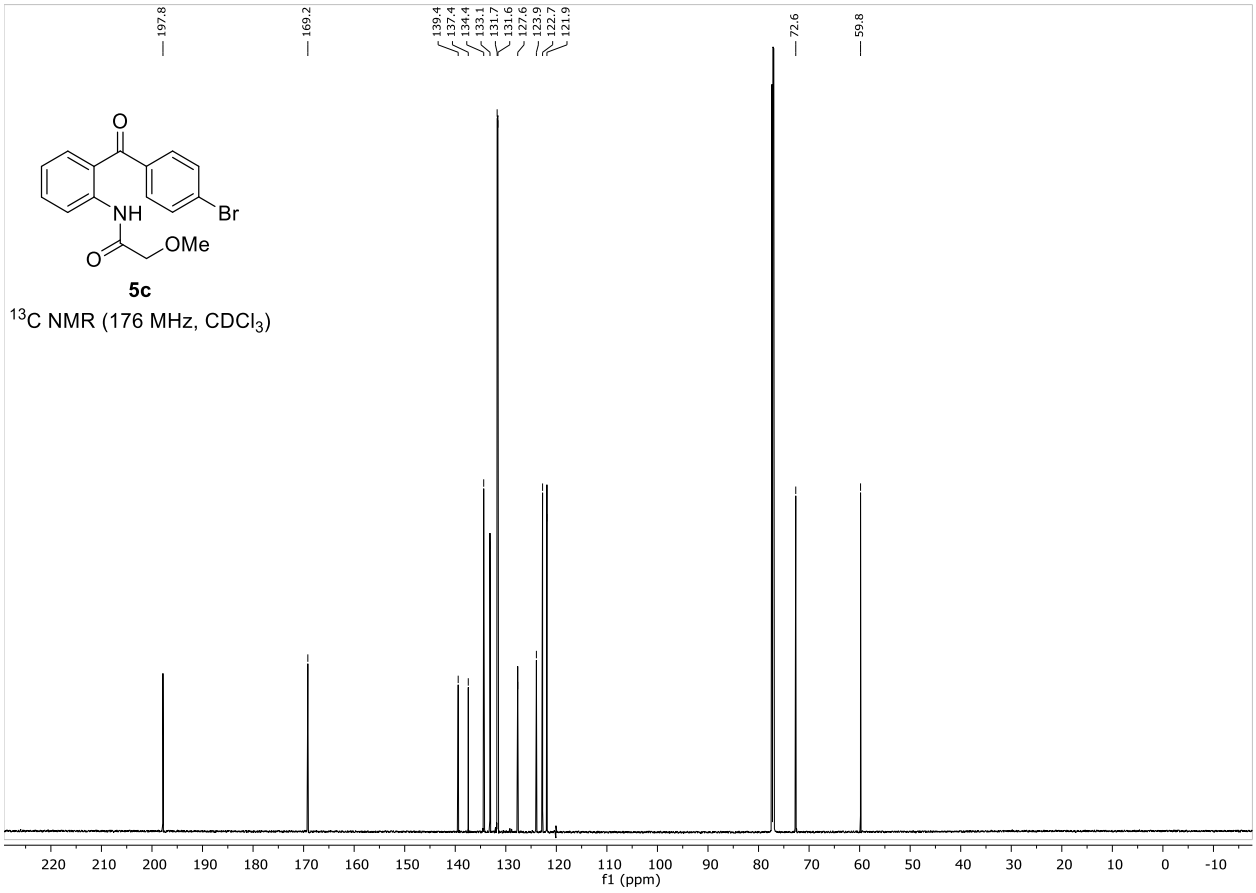
5b

^{13}C NMR (126 MHz, $CDCl_3$)



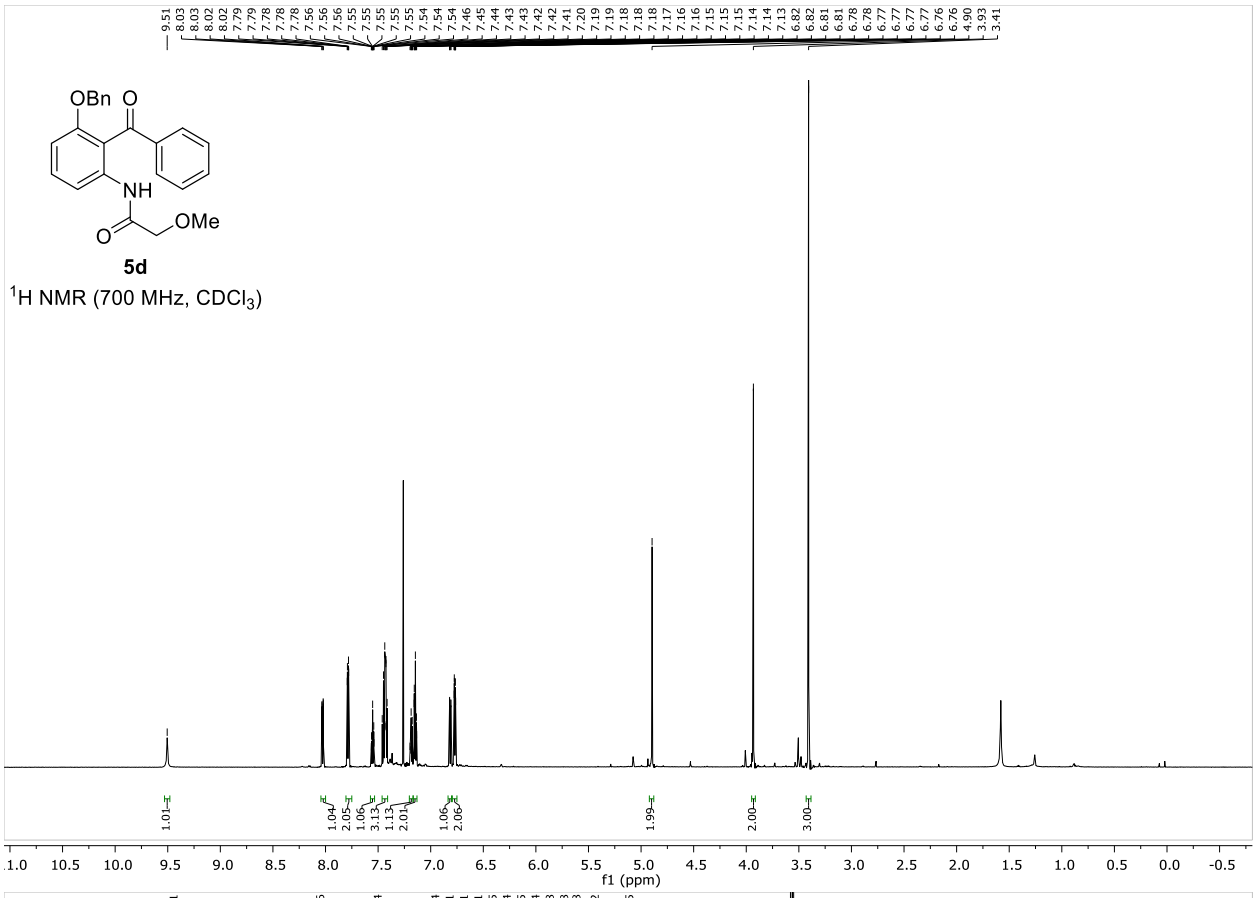
5c

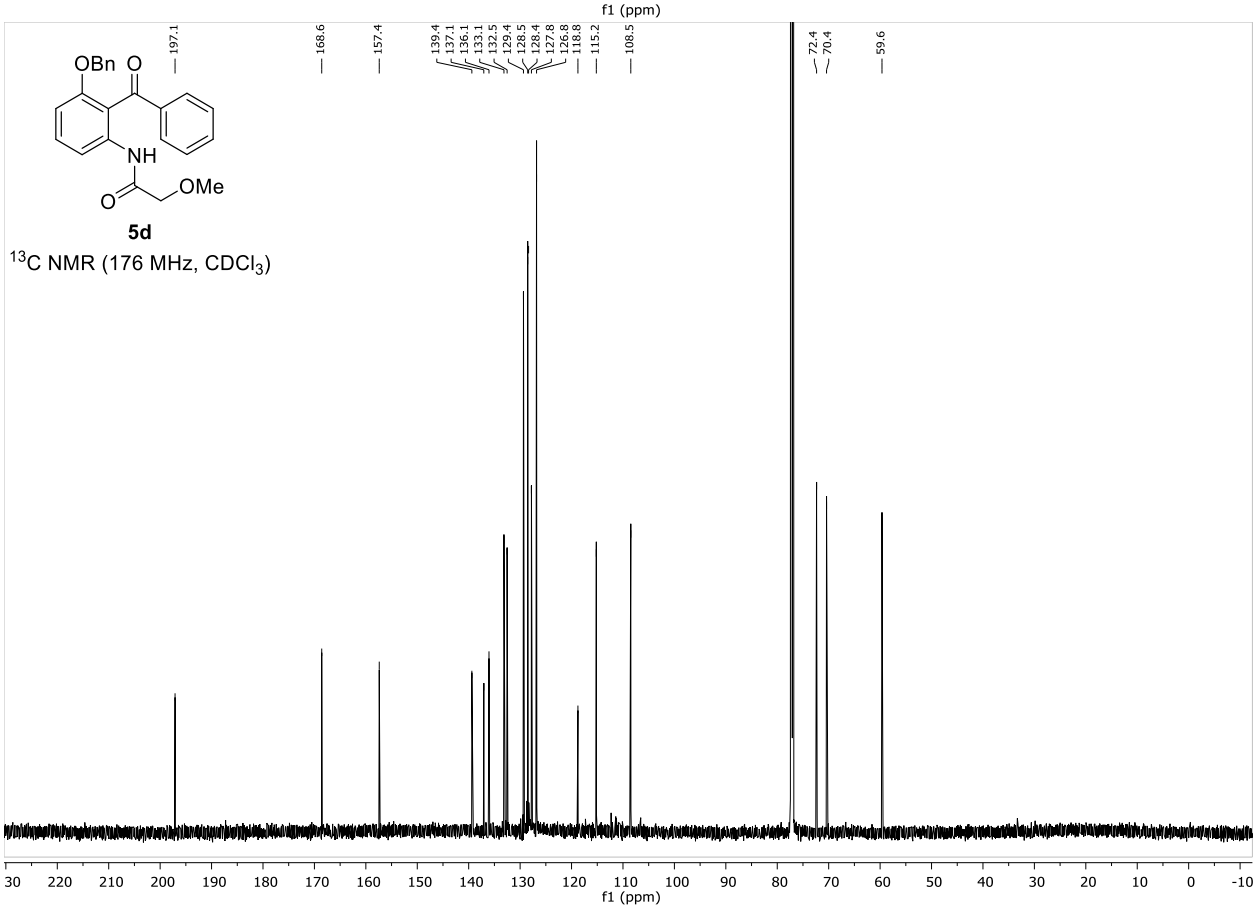
^{1}H NMR (700 MHz, $CDCl_3$)

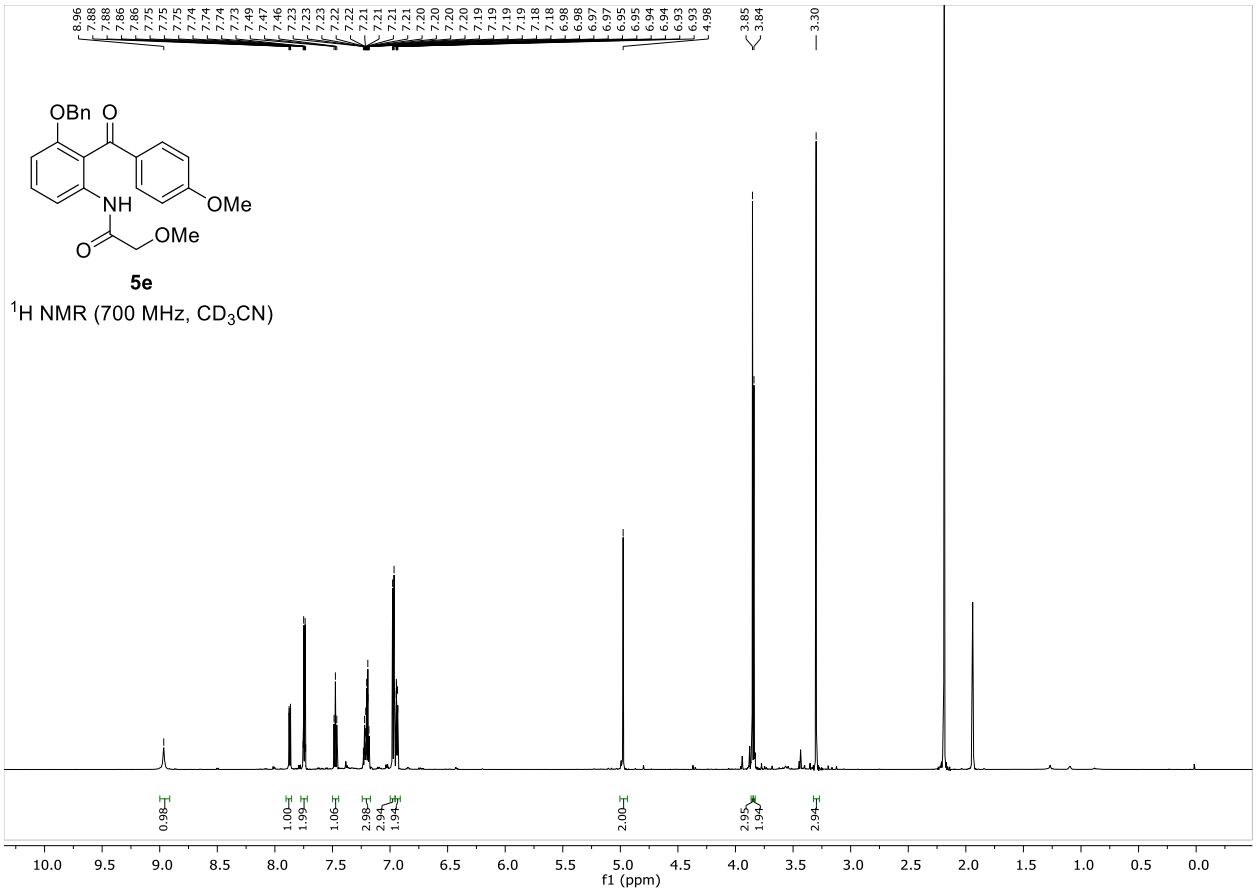


5c

^{13}C NMR (176 MHz, $CDCl_3$)

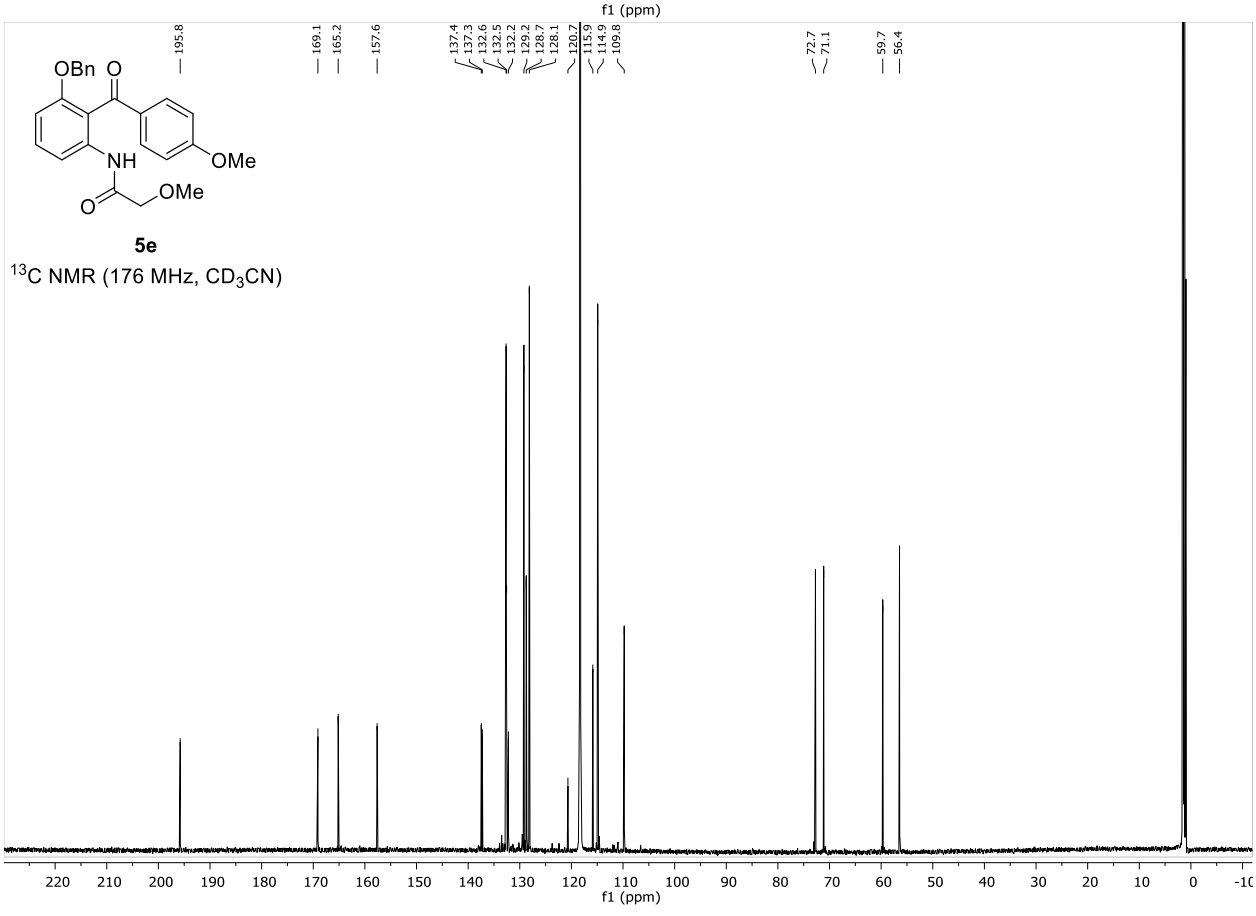

OBn O
NH
OMe
O
5d
1H NMR (700 MHz, CDCl3)
f1 (ppm)


OBn O
NH
OMe
O
5d
13C NMR (176 MHz, CDCl3)
f1 (ppm)



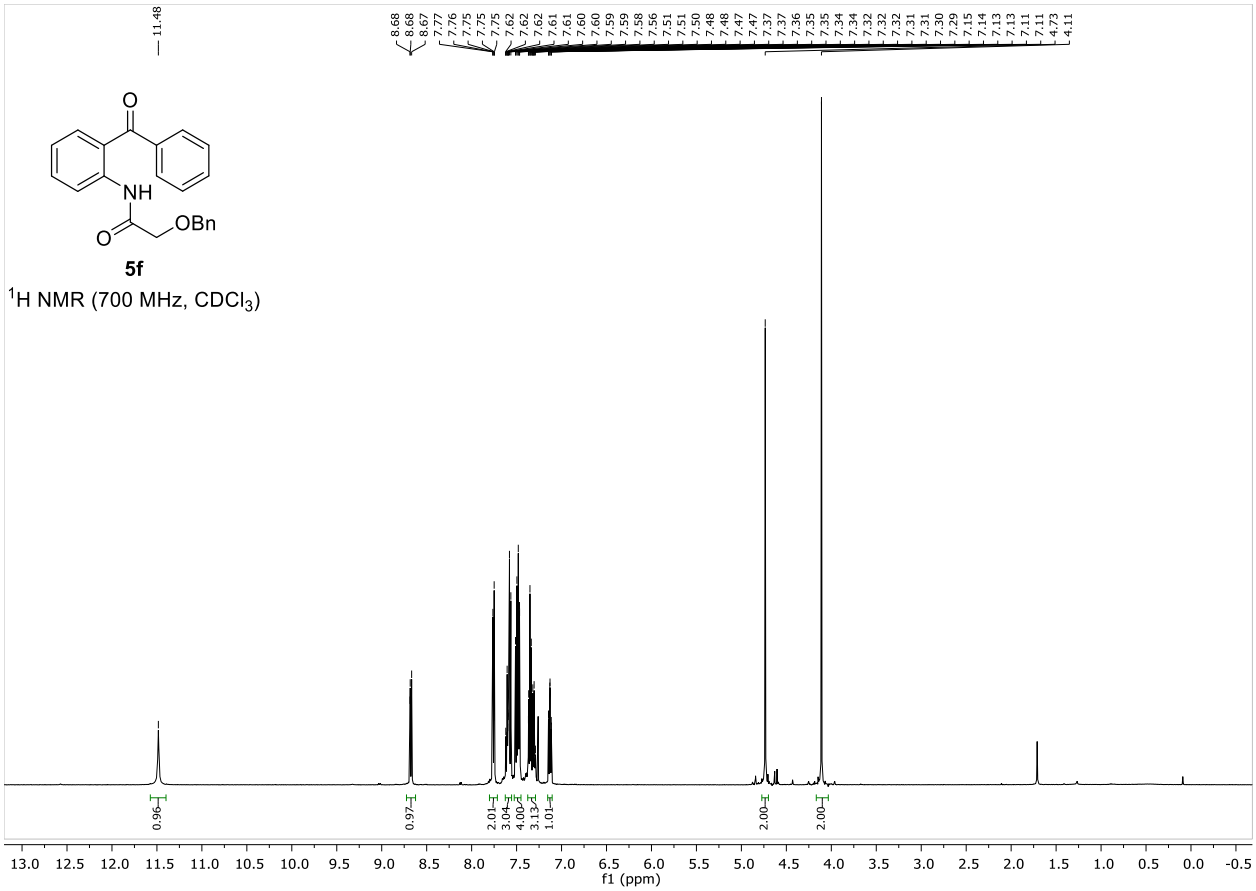
5e

^{1}H NMR (700 MHz, CD_3CN)



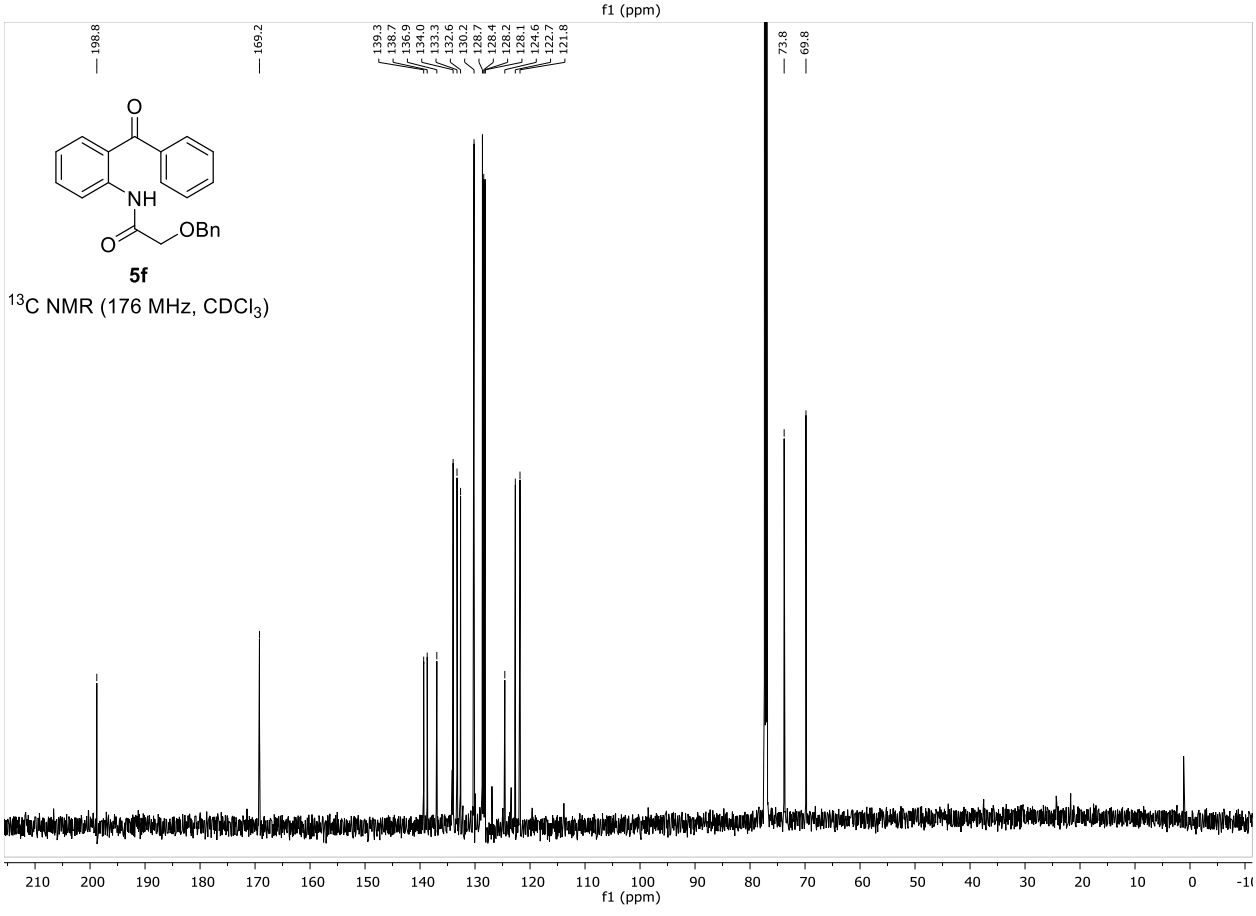
5e

^{13}C NMR (176 MHz, CD_3CN)



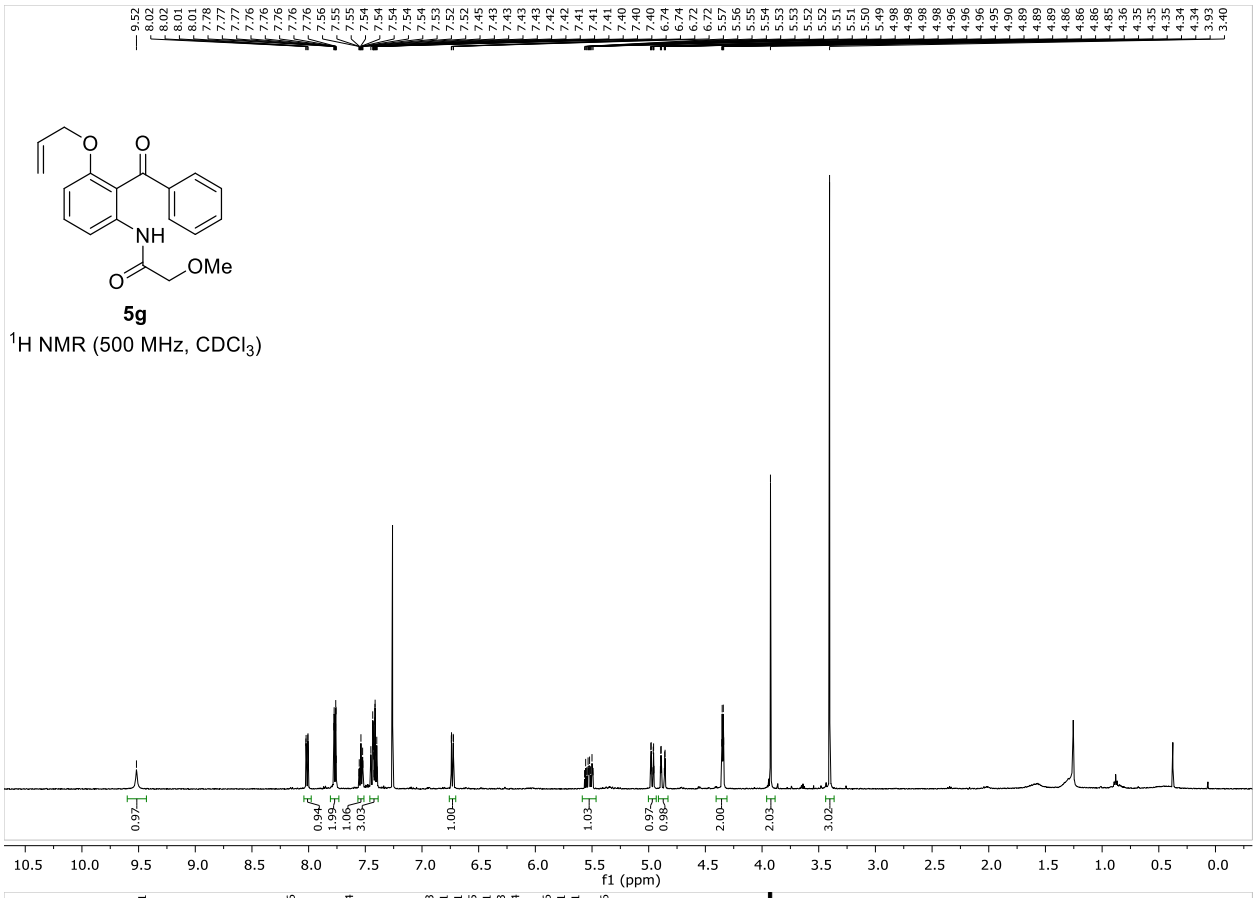
5f

^{1}H NMR (700 MHz, $CDCl_3$)



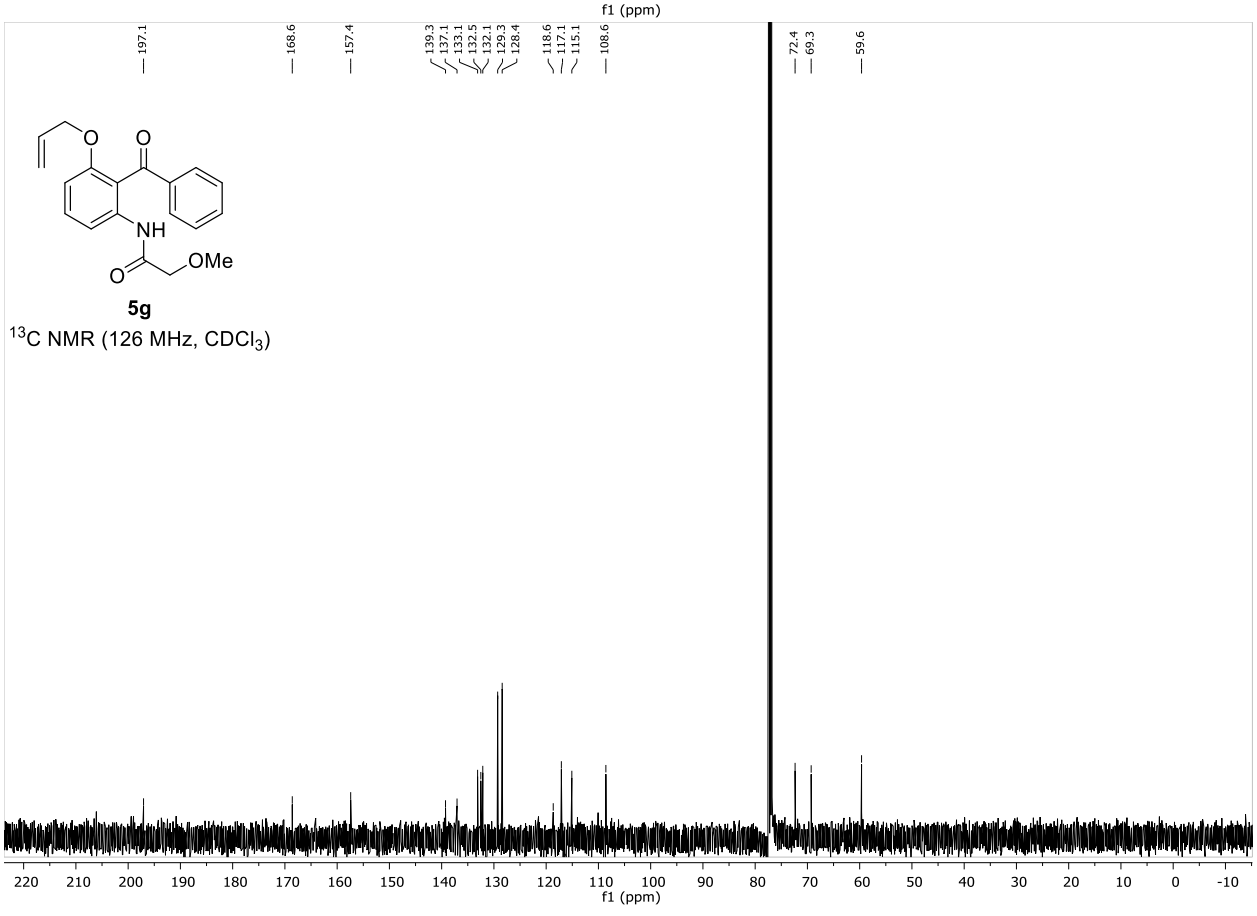
5f

^{13}C NMR (176 MHz, $CDCl_3$)



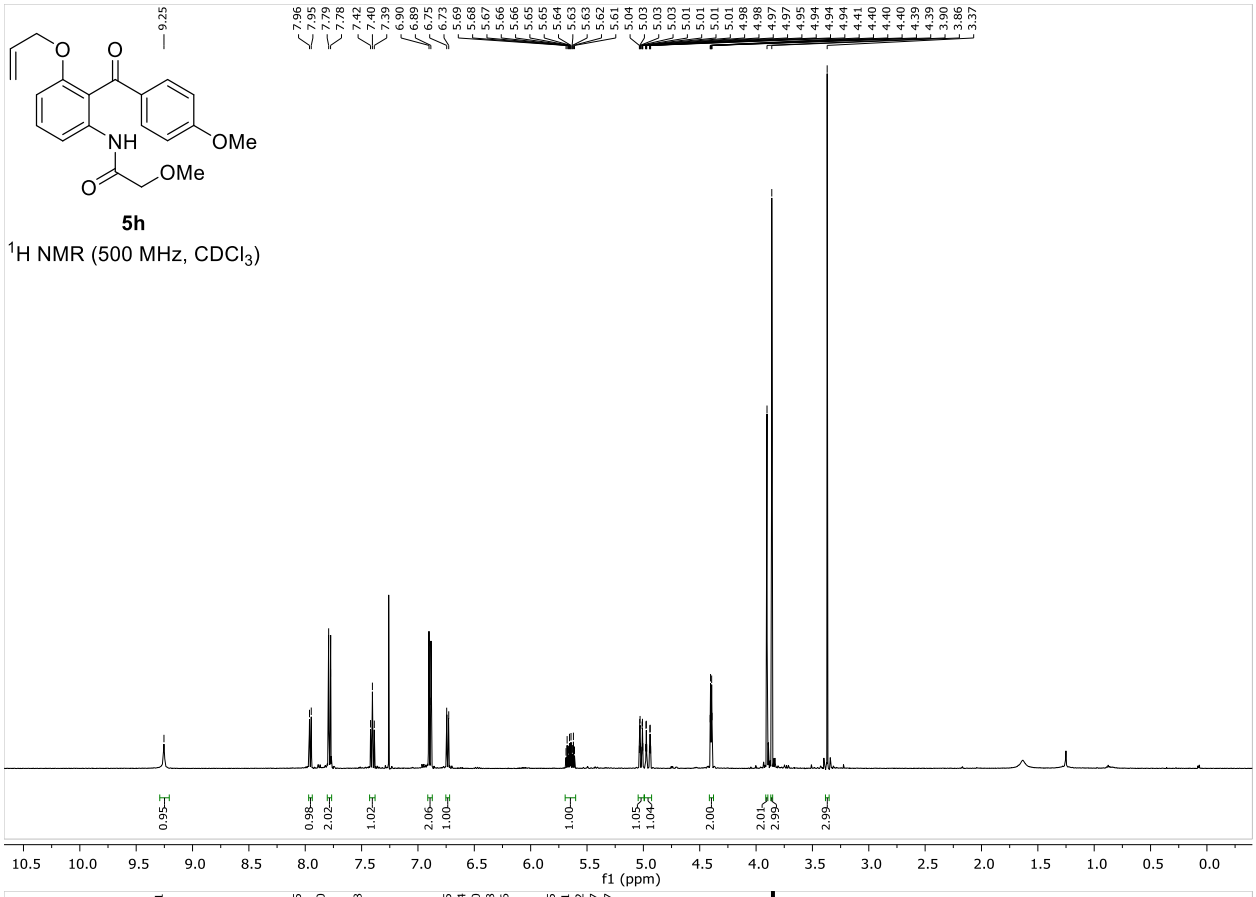
5g

^{1}H NMR (500 MHz, $CDCl_3$)



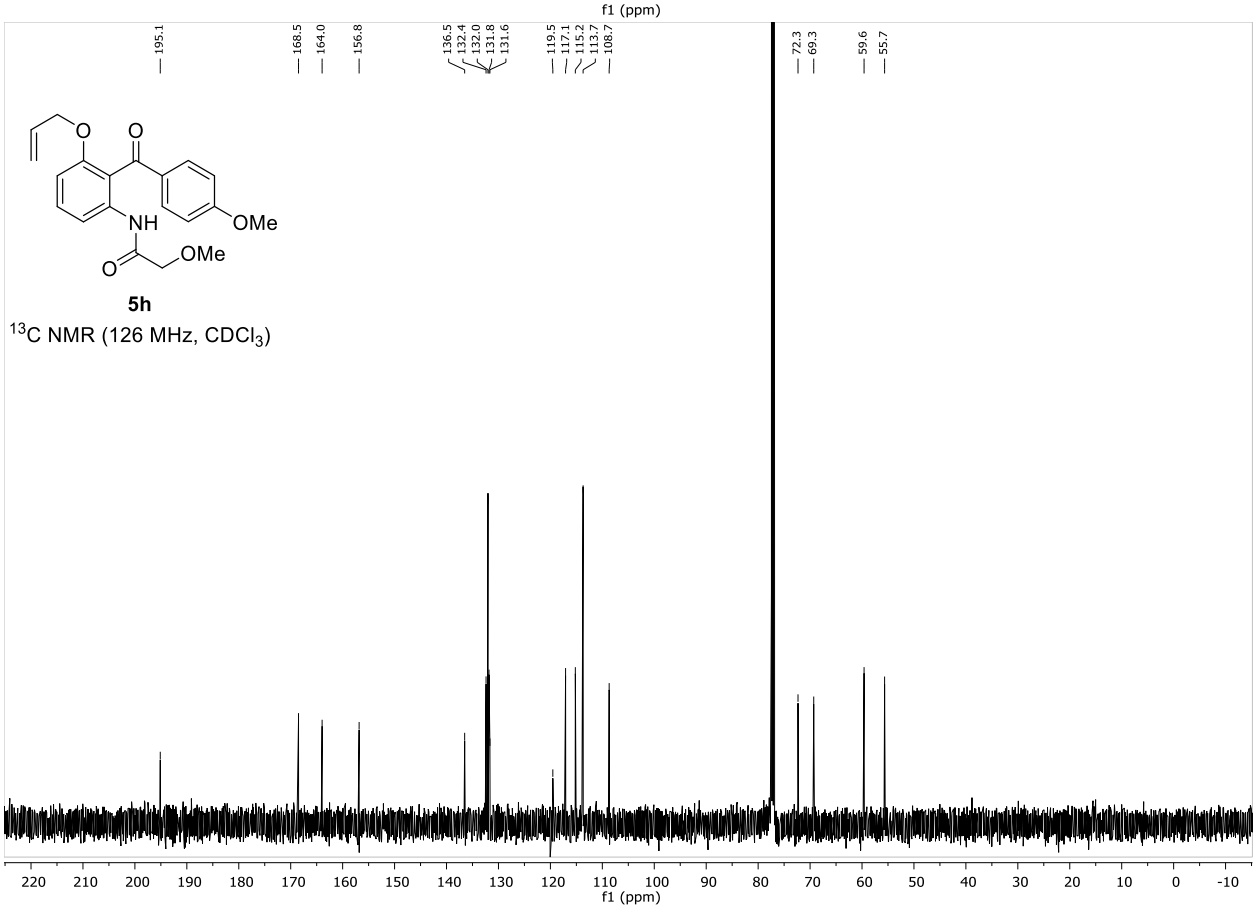
5g

^{13}C NMR (126 MHz, $CDCl_3$)



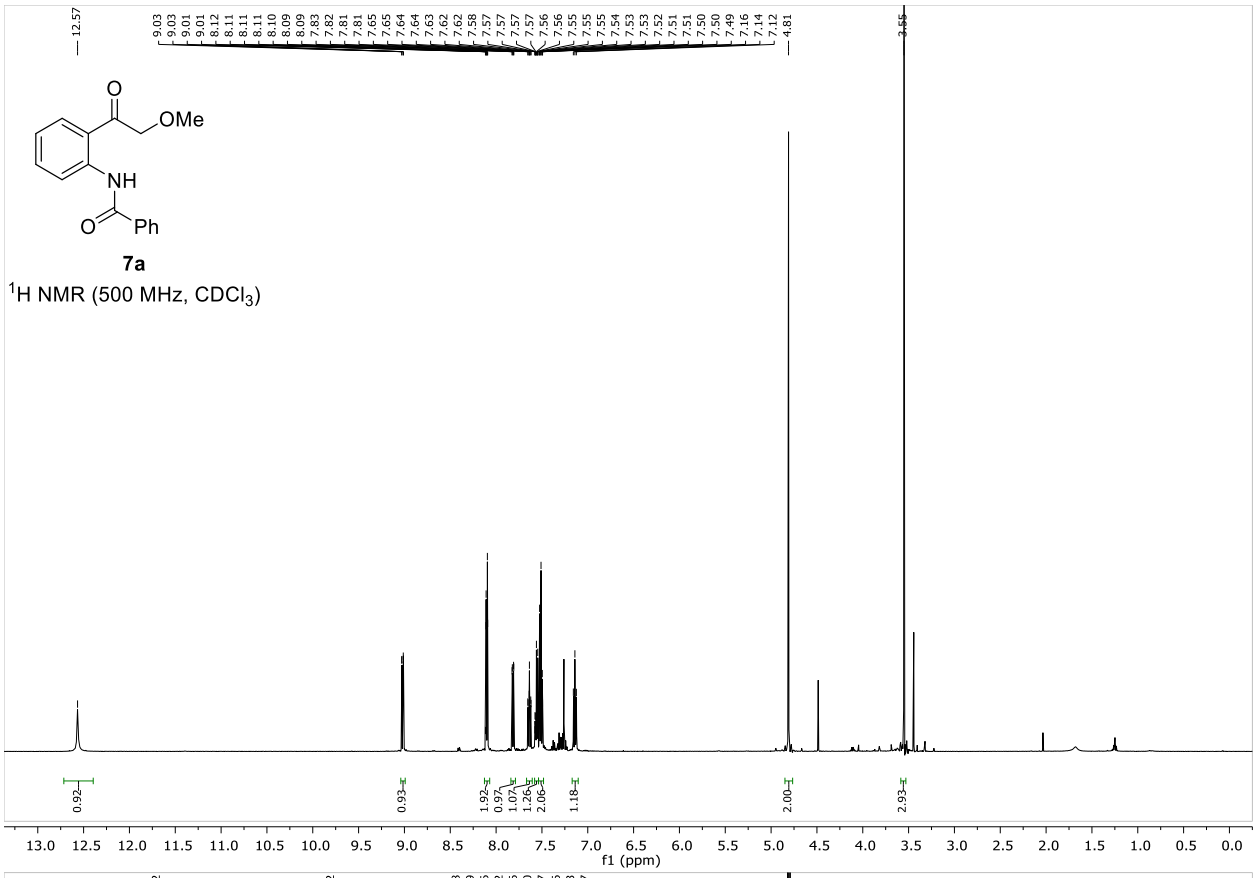
5h

^{1}H NMR (500 MHz, $CDCl_3$)



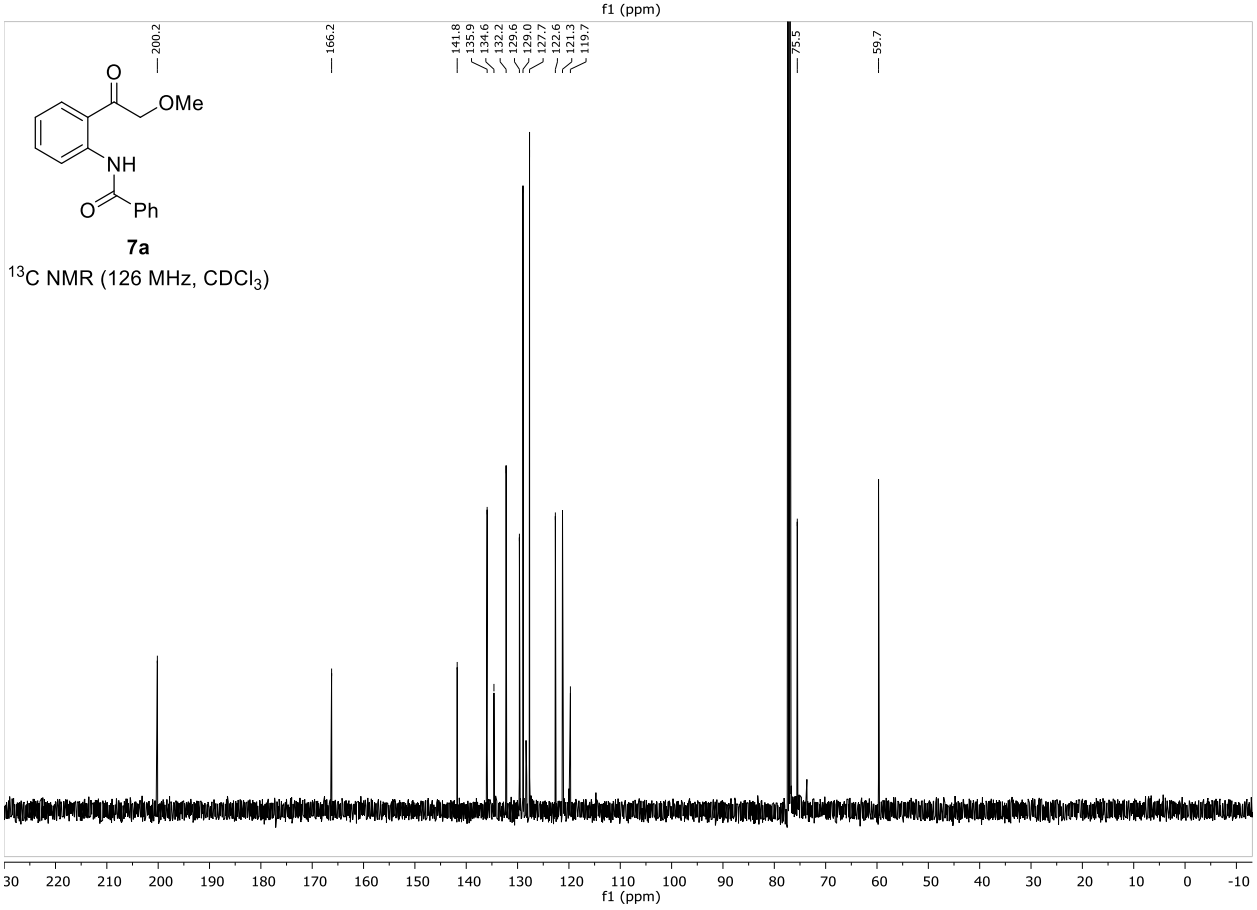
5h

^{13}C NMR (126 MHz, $CDCl_3$)



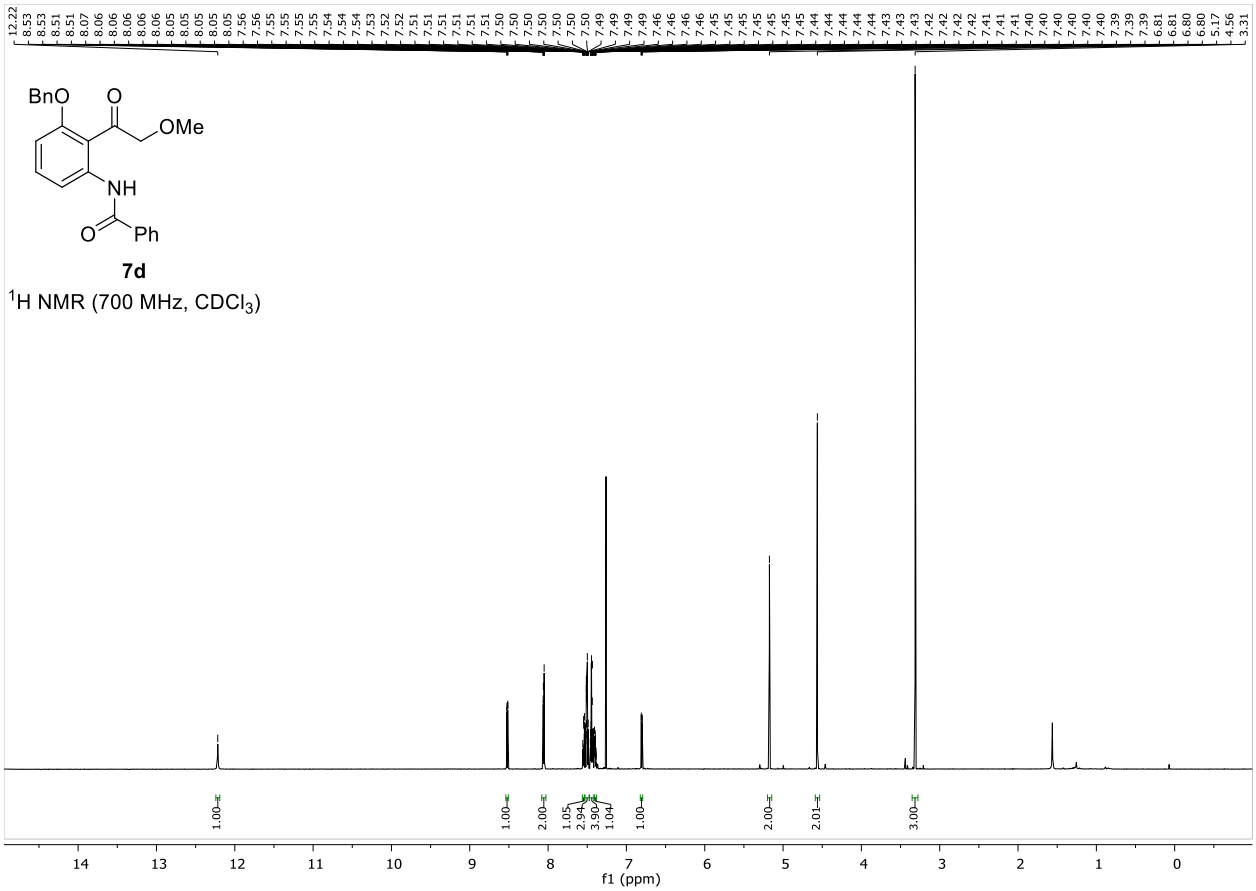
7a

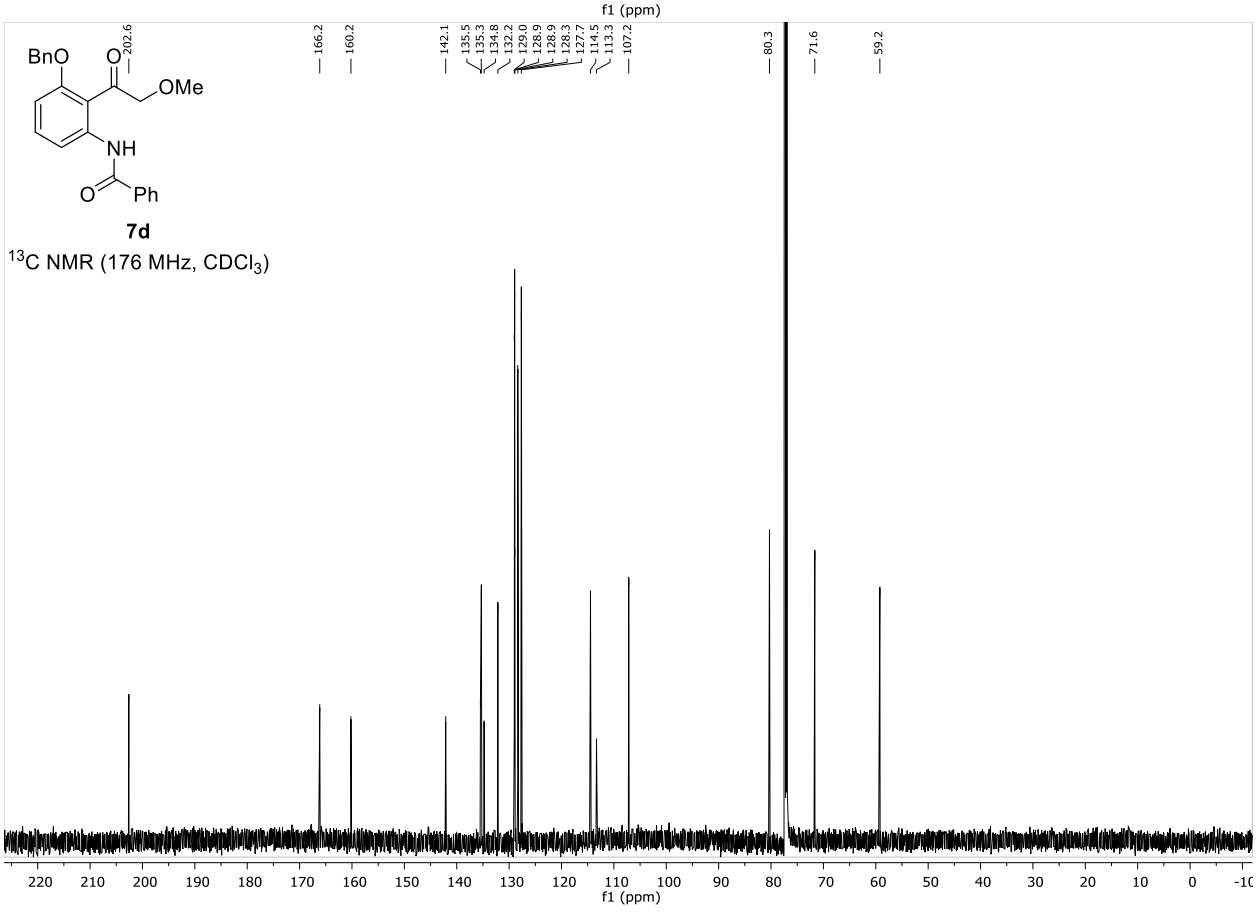
^{1}H NMR (500 MHz, $CDCl_3$)

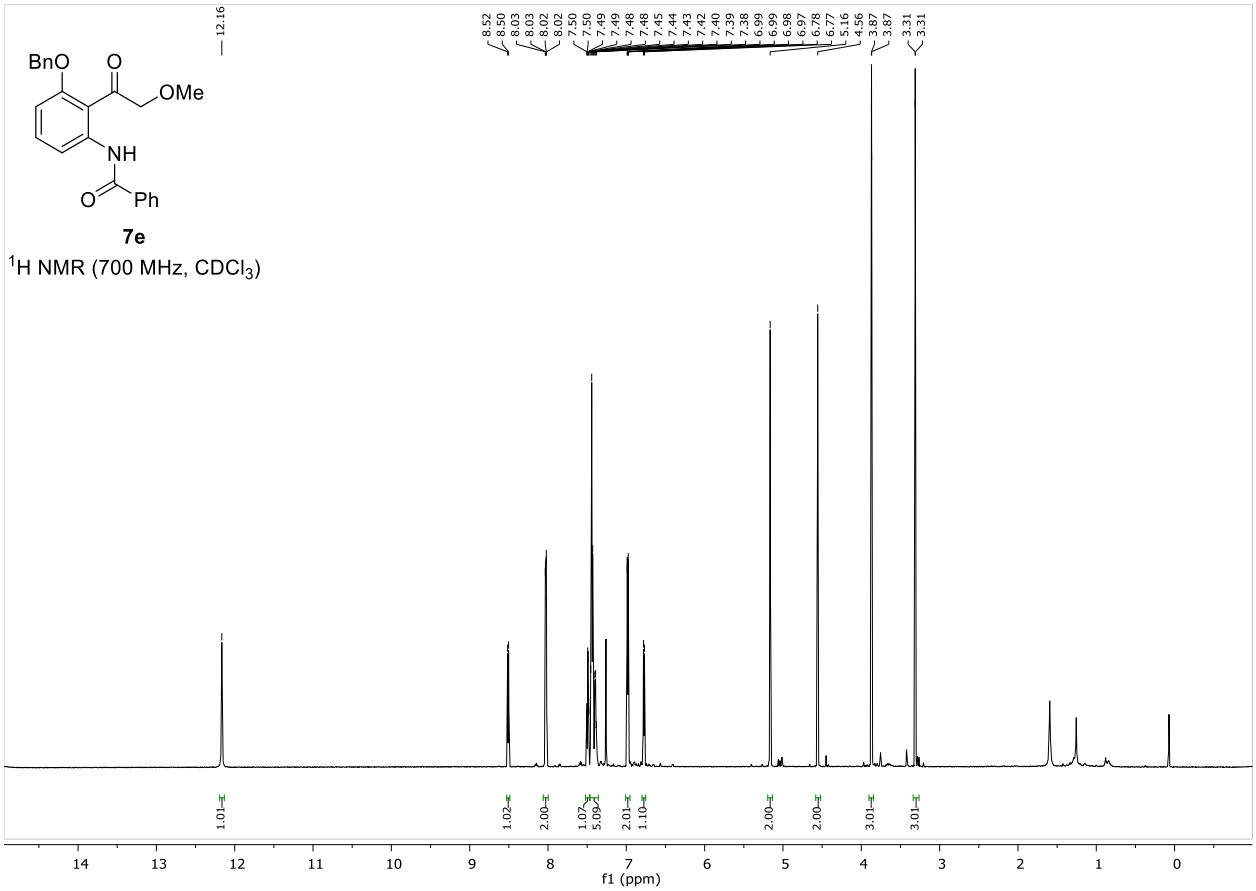


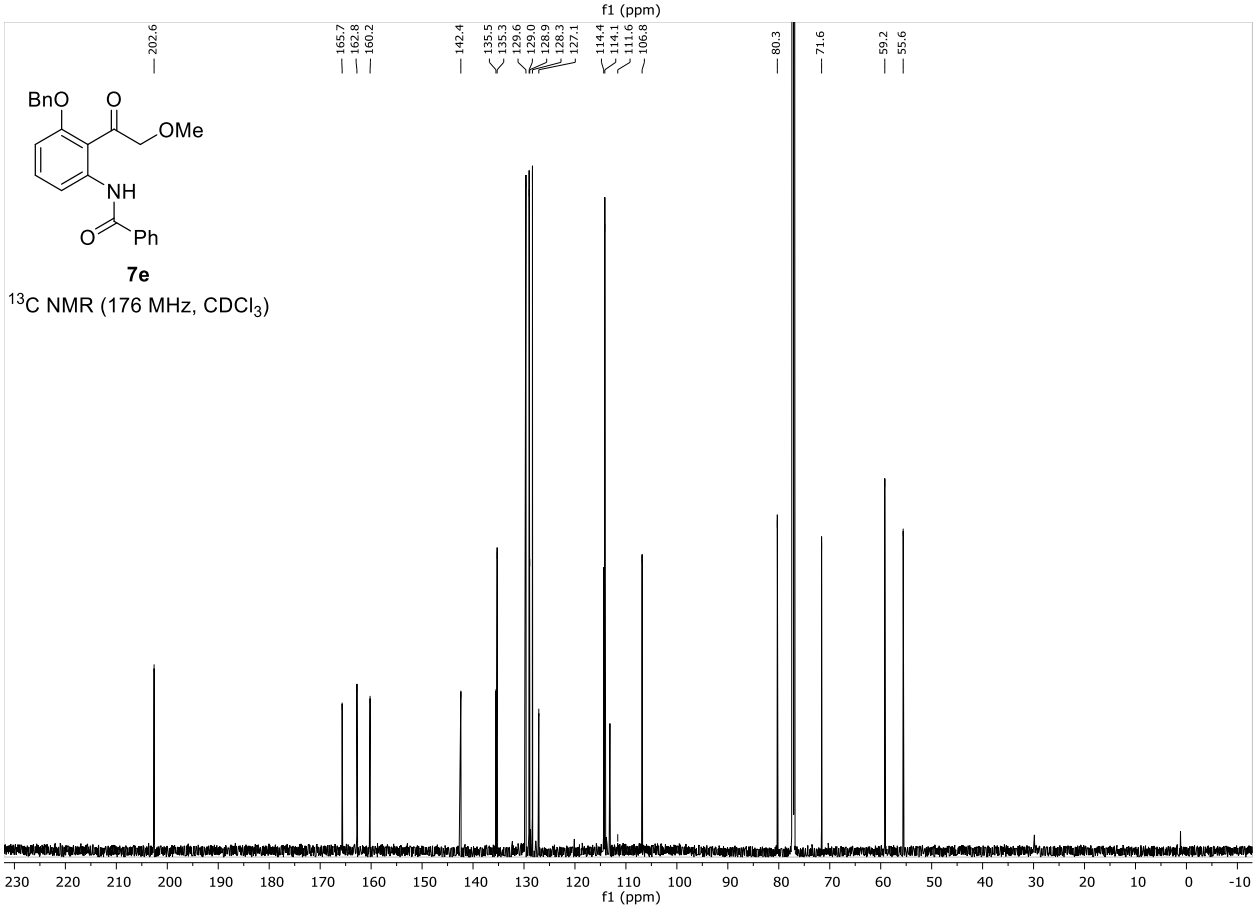
7a

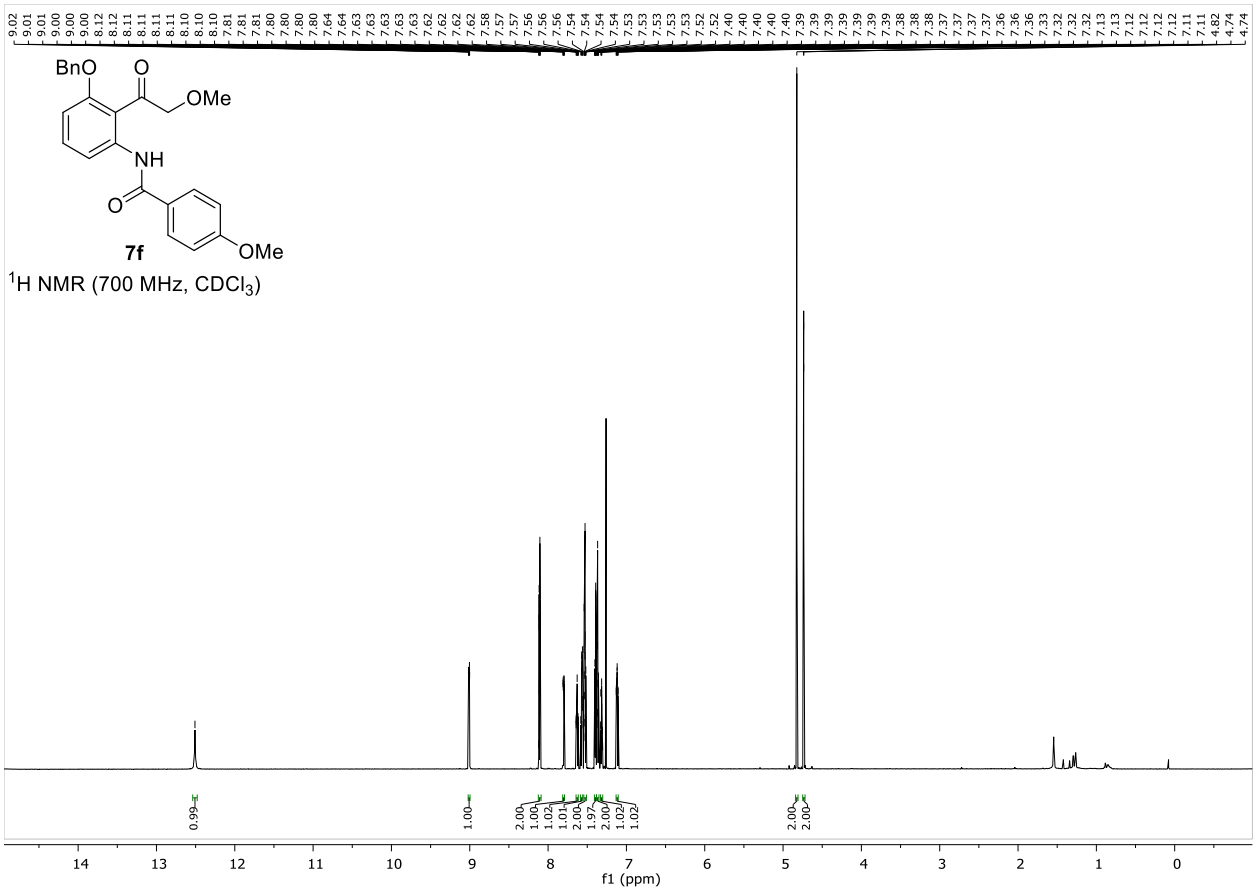
^{13}C NMR (126 MHz, $CDCl_3$)


BnO
O
OMe
NH
O
Ph
7d
1H NMR (700 MHz, CDCl3)
f1 (ppm)

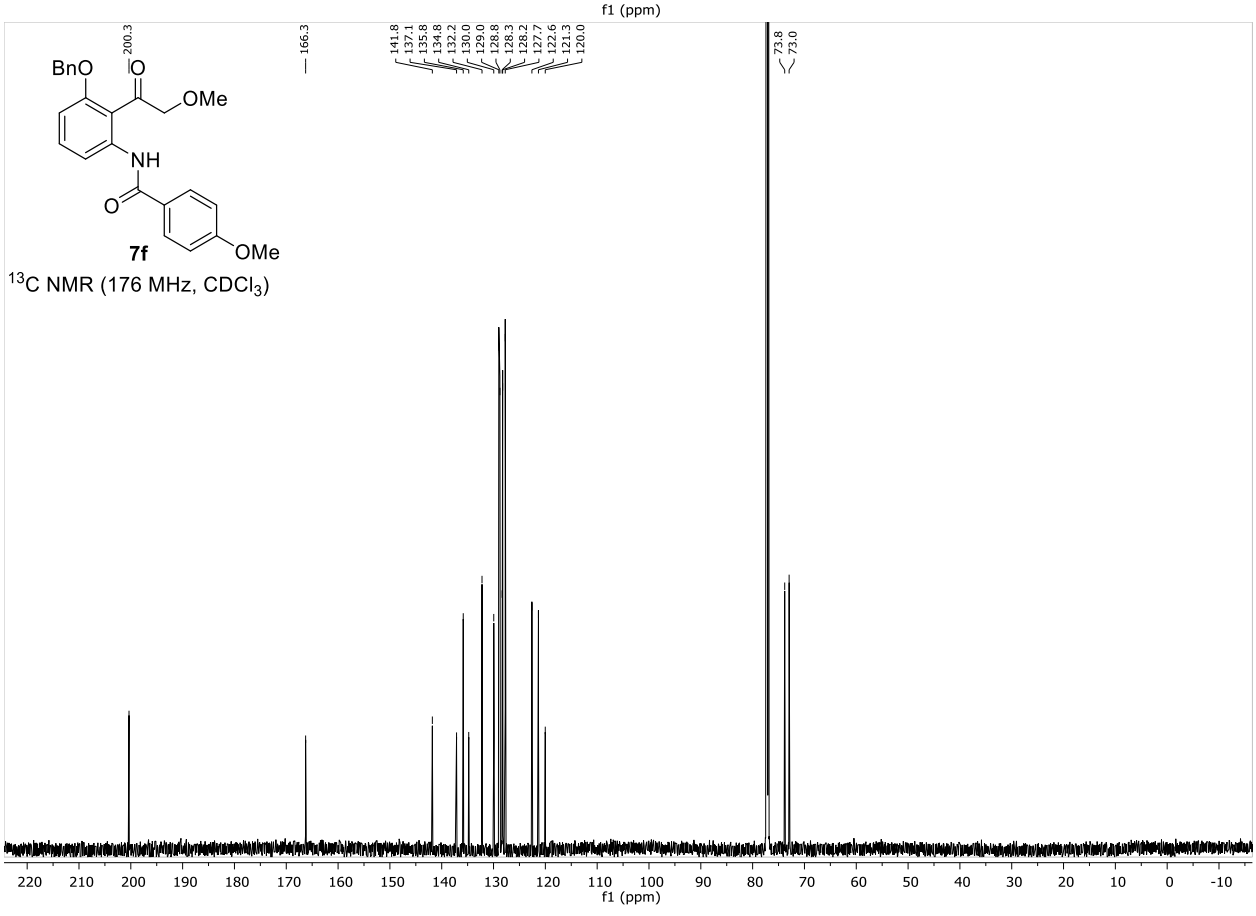

BnO
O
OMe
NH
O
Ph
7d
13C NMR (176 MHz, CDCl3)
f1 (ppm)


BnO
O
OMe
NH
O
Ph
7e
1H NMR (700 MHz, CDCl3)
f1 (ppm)

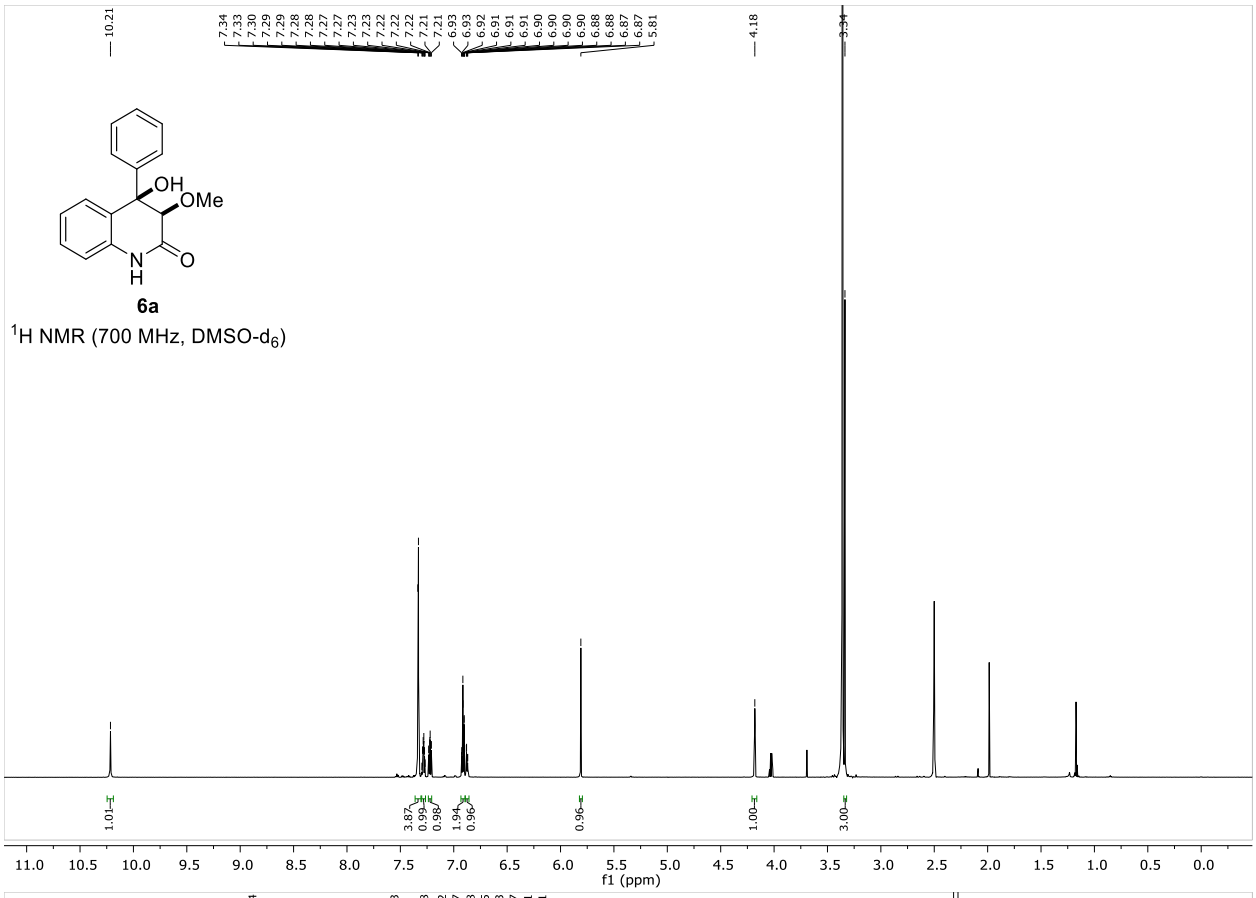

BnO
O
OMe
NH
O
Ph
7e
13C NMR (176 MHz, CDCl3)
f1 (ppm)



^{1}H NMR (700 MHz, $CDCl_3$)

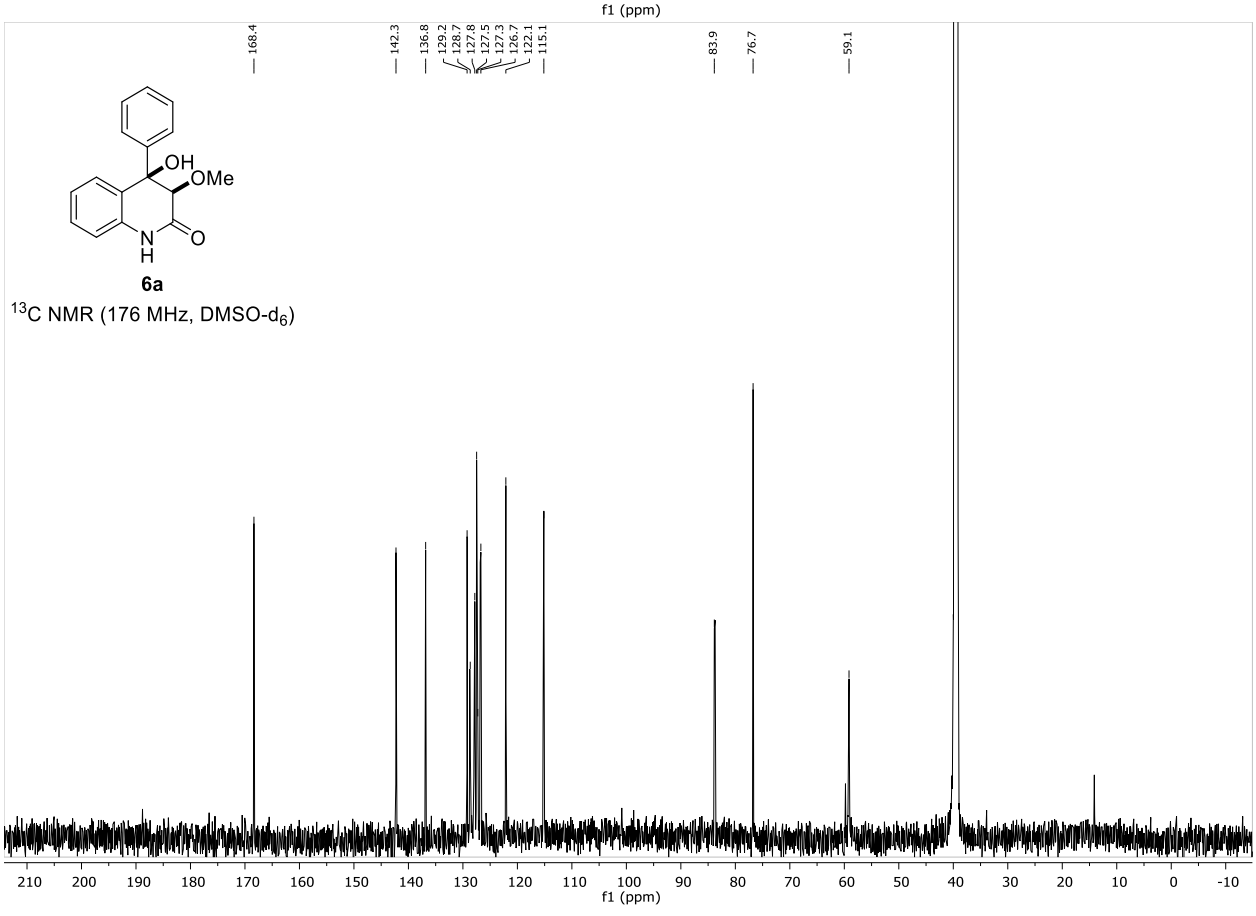


^{13}C NMR (176 MHz, $CDCl_3$)



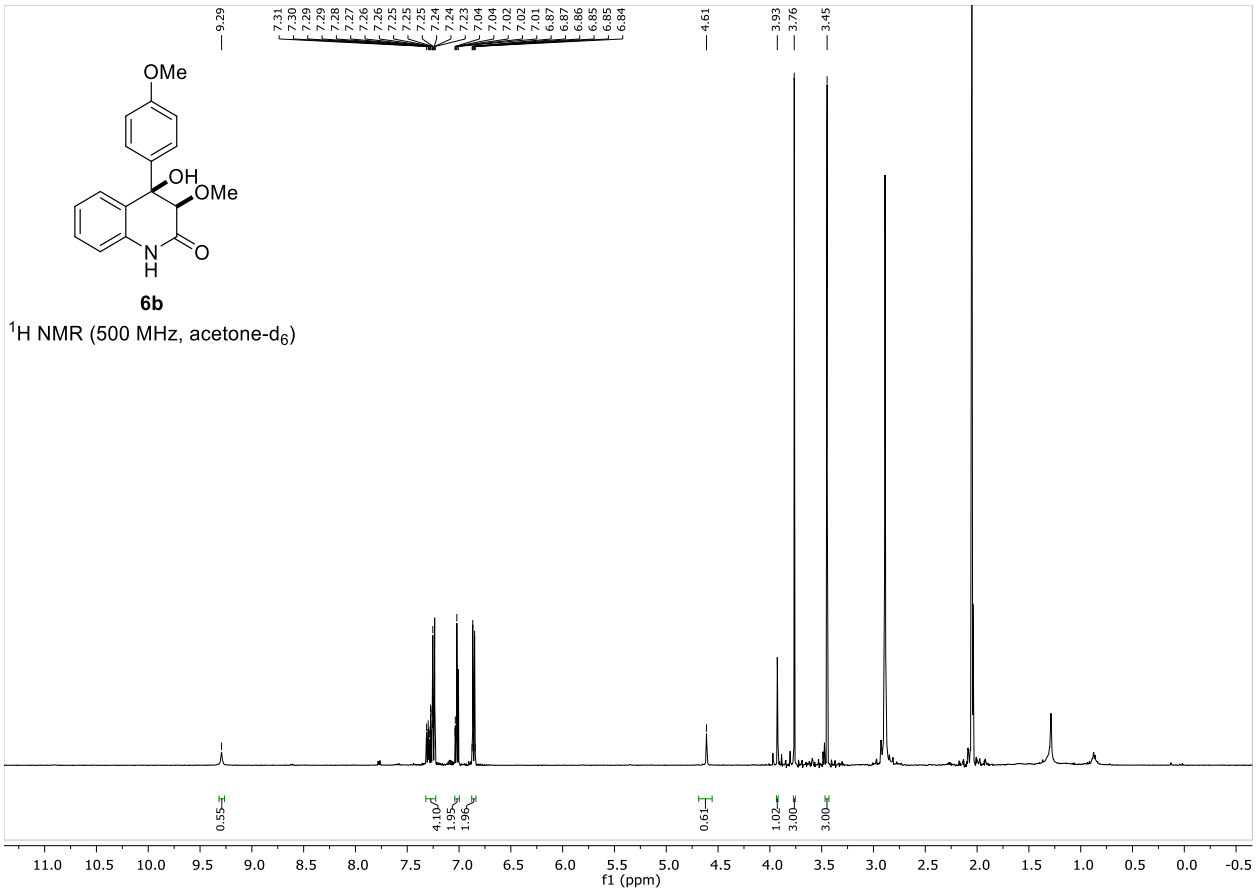
6a

^{1}H NMR (700 MHz, DMSO-d_6)



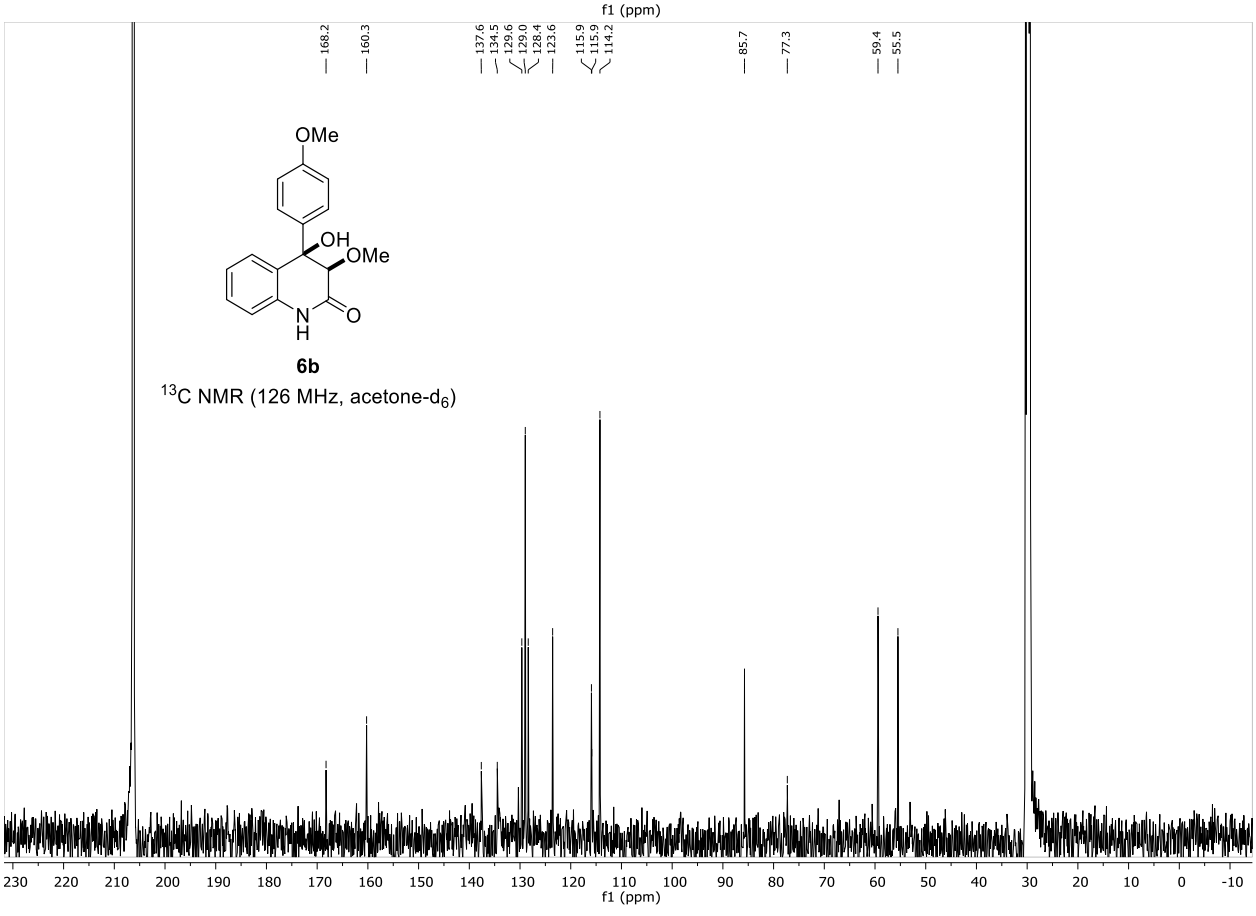
6a

^{13}C NMR (176 MHz, DMSO-d_6)



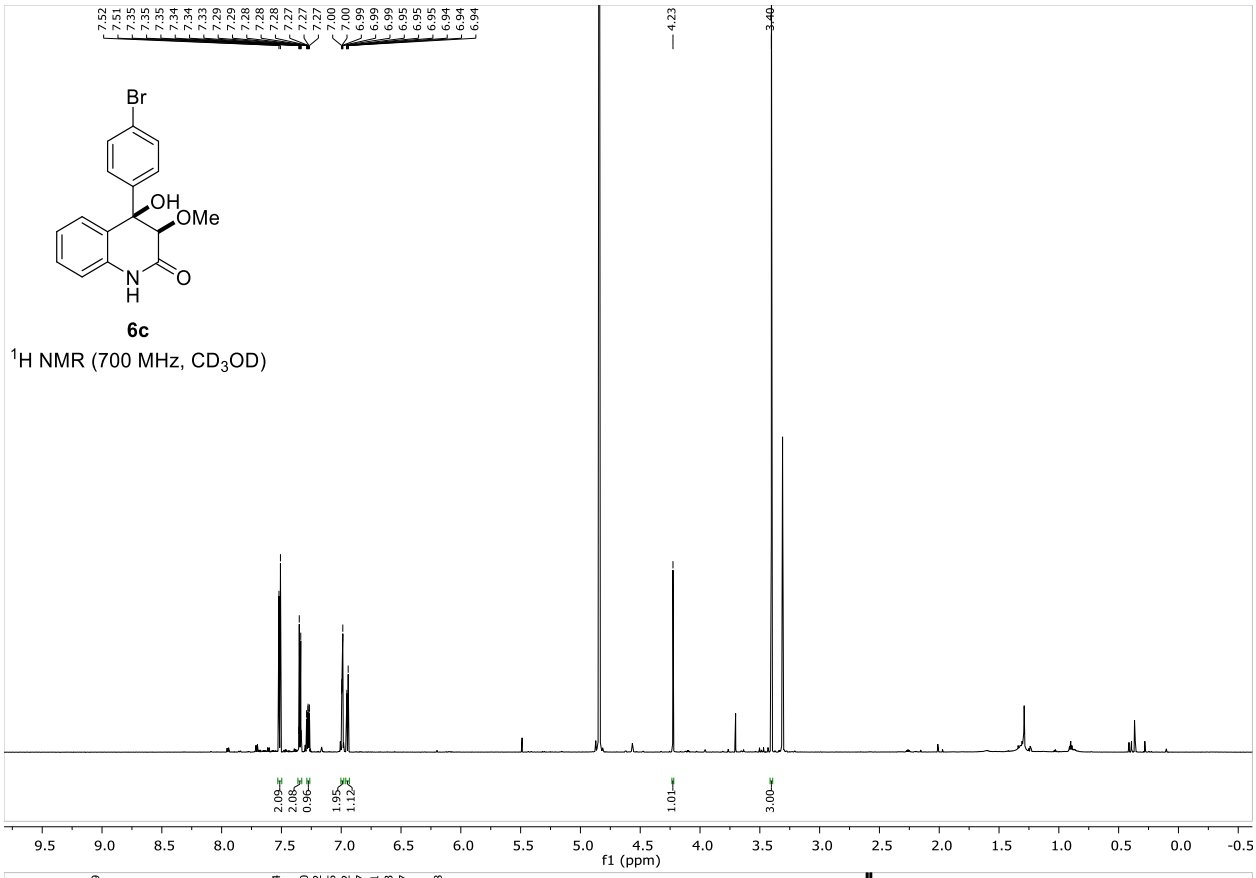
6b

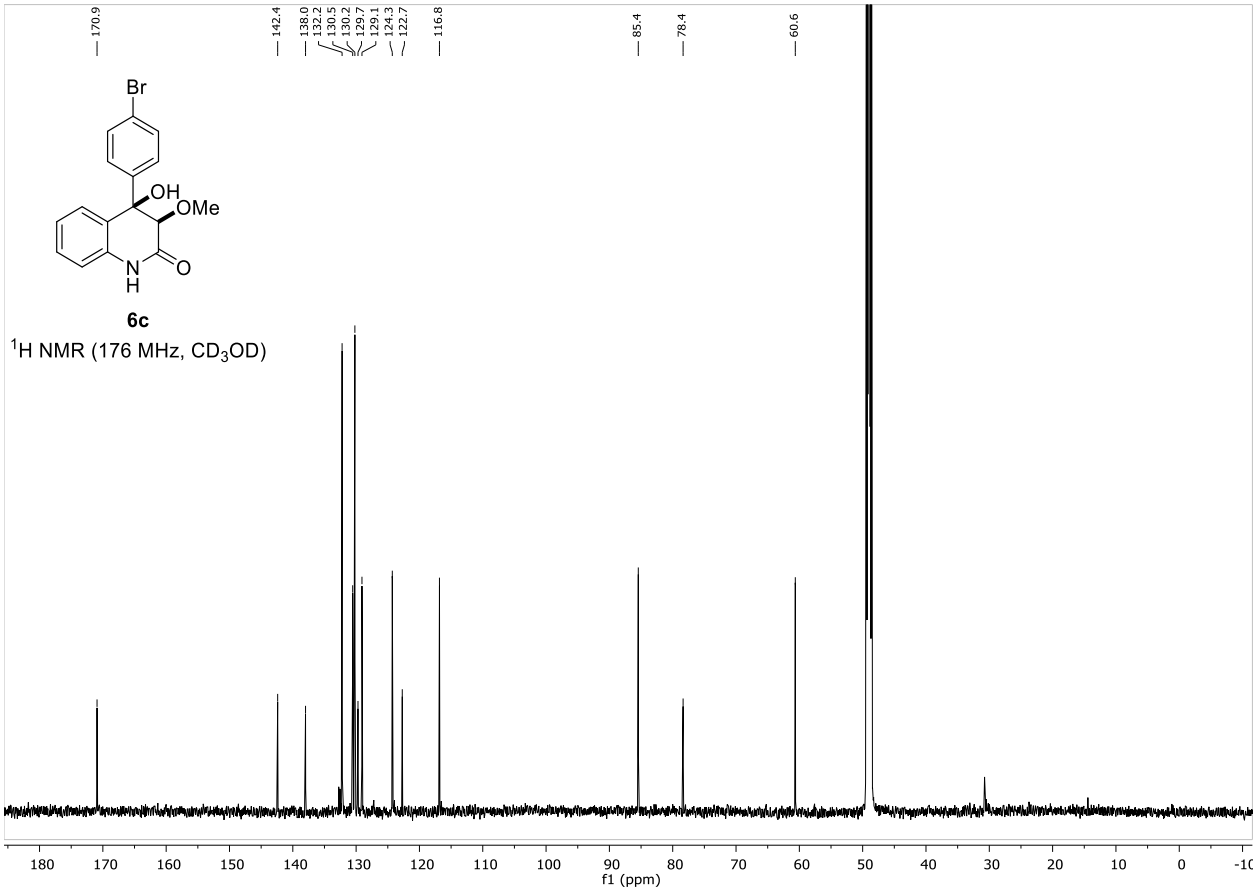
^{1}H NMR (500 MHz, acetone-d_6)

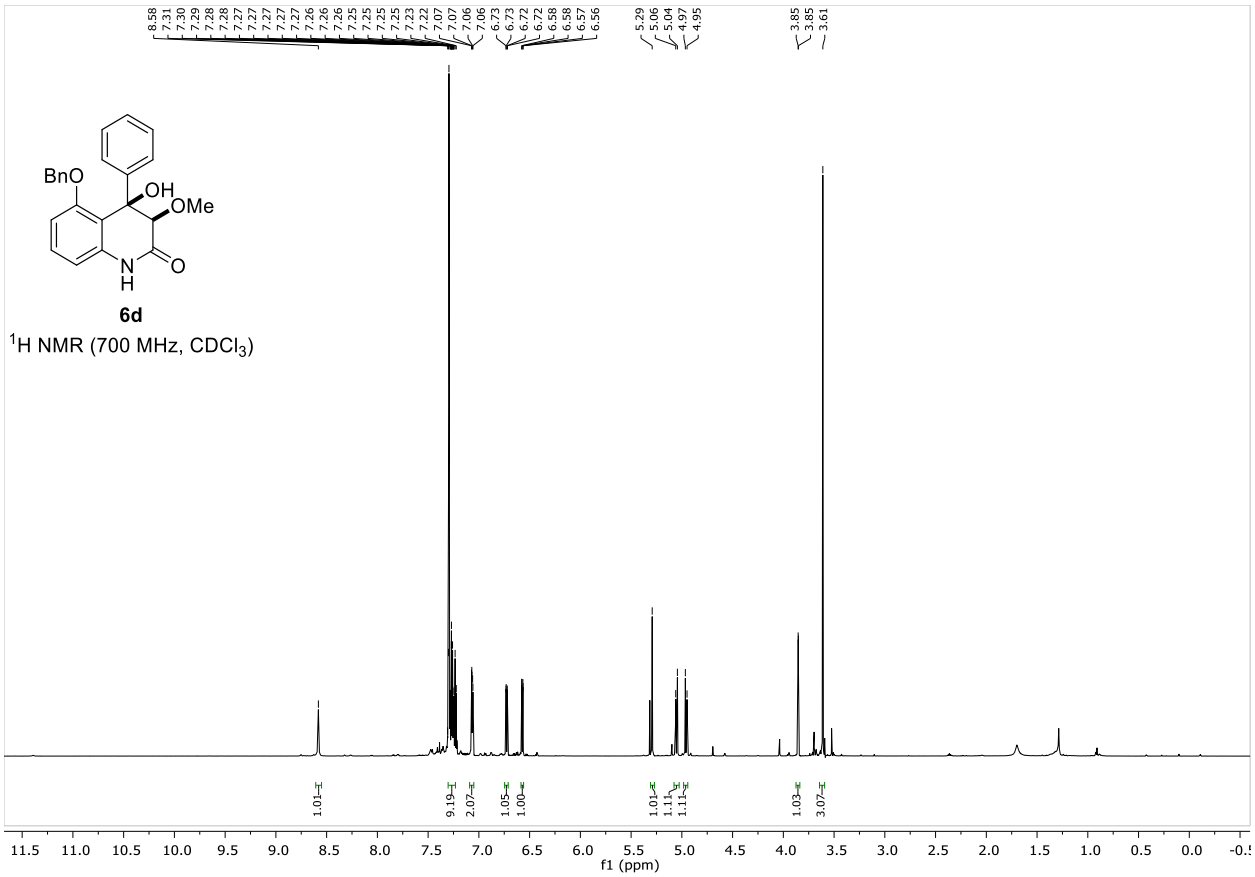


6b

^{13}C NMR (126 MHz, acetone-d_6)

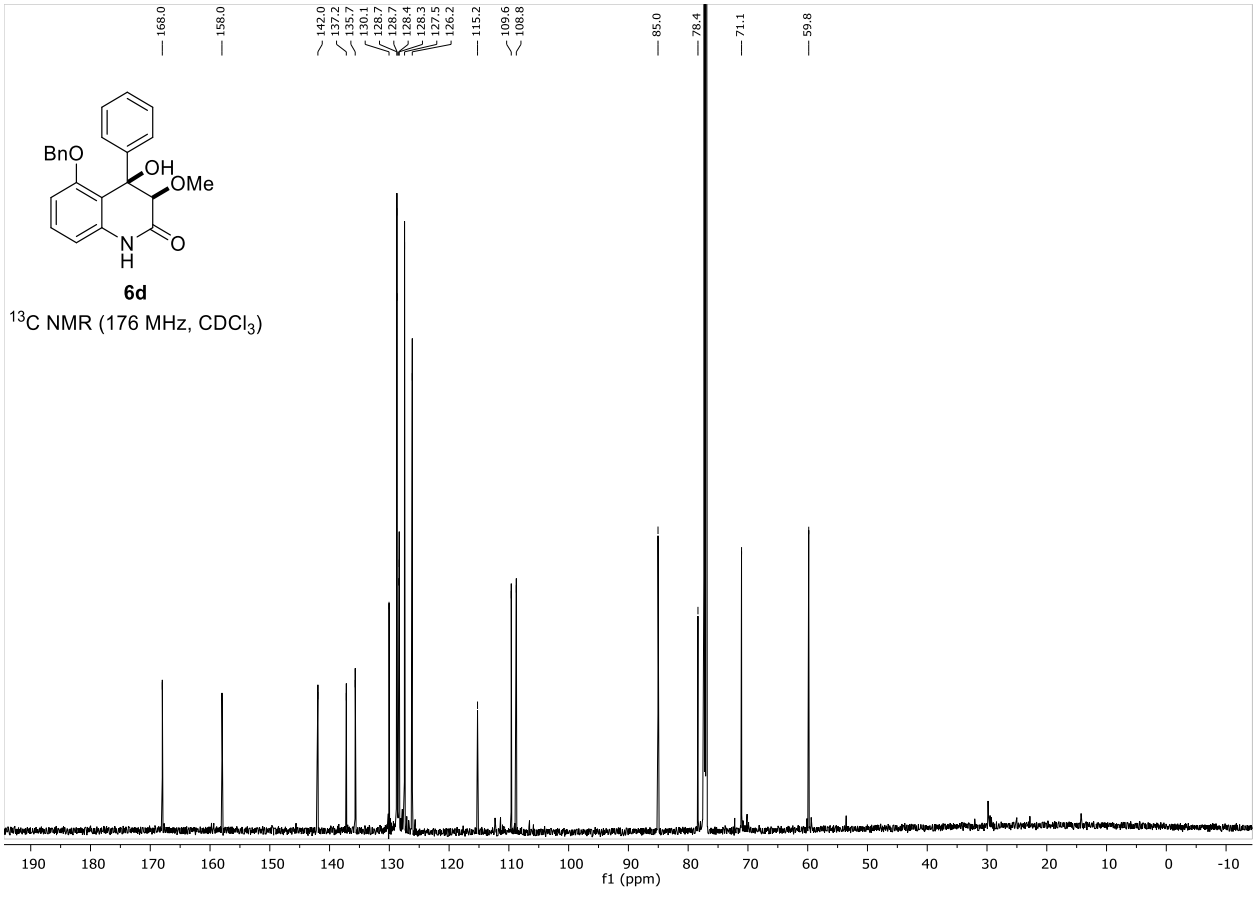

Br
OH
OMe
N
H
O
6c
1H NMR (700 MHz, CD3OD)
f1 (ppm)


Br
OH
OMe
N
H
O
6c
1H NMR (176 MHz, CD3OD)
f1 (ppm)



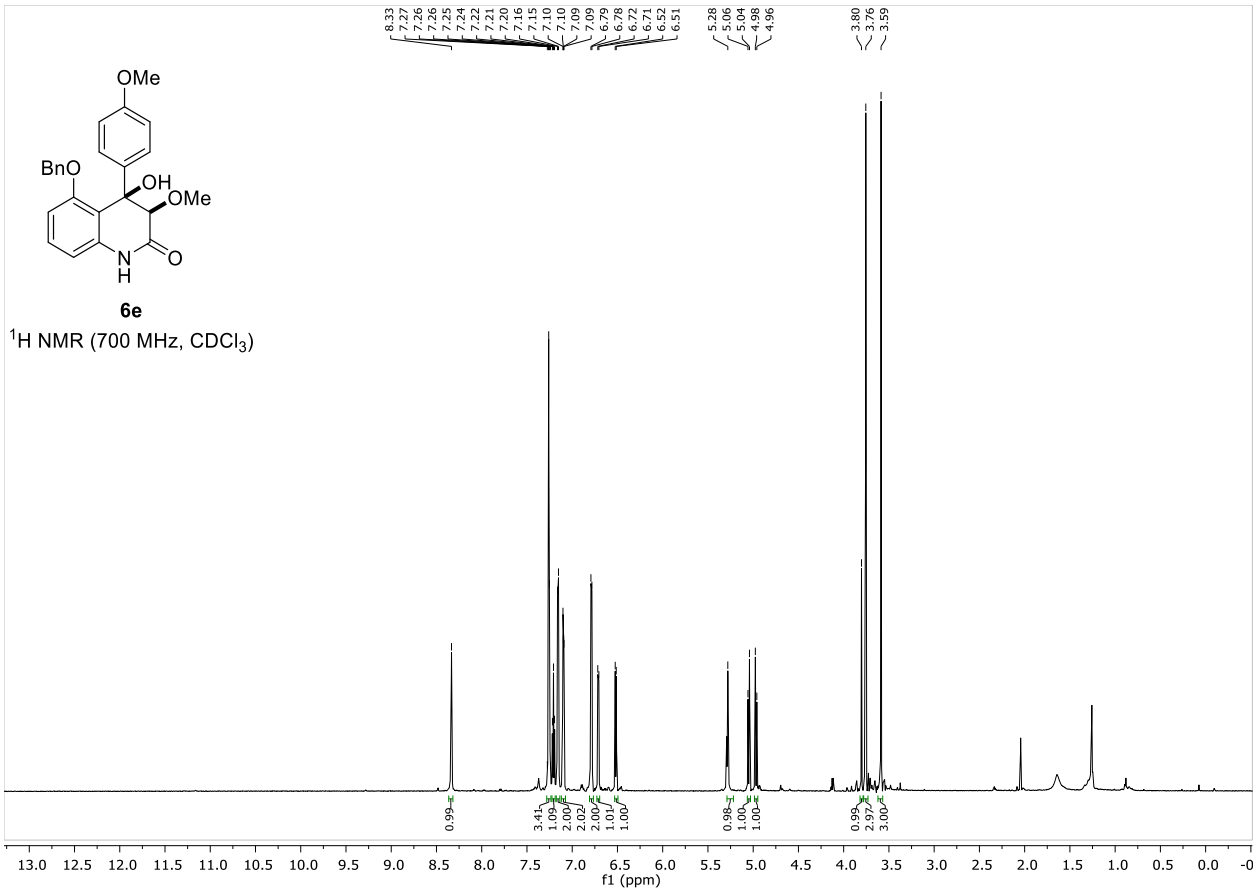
6d

^{1}H NMR (700 MHz, $CDCl_3$)



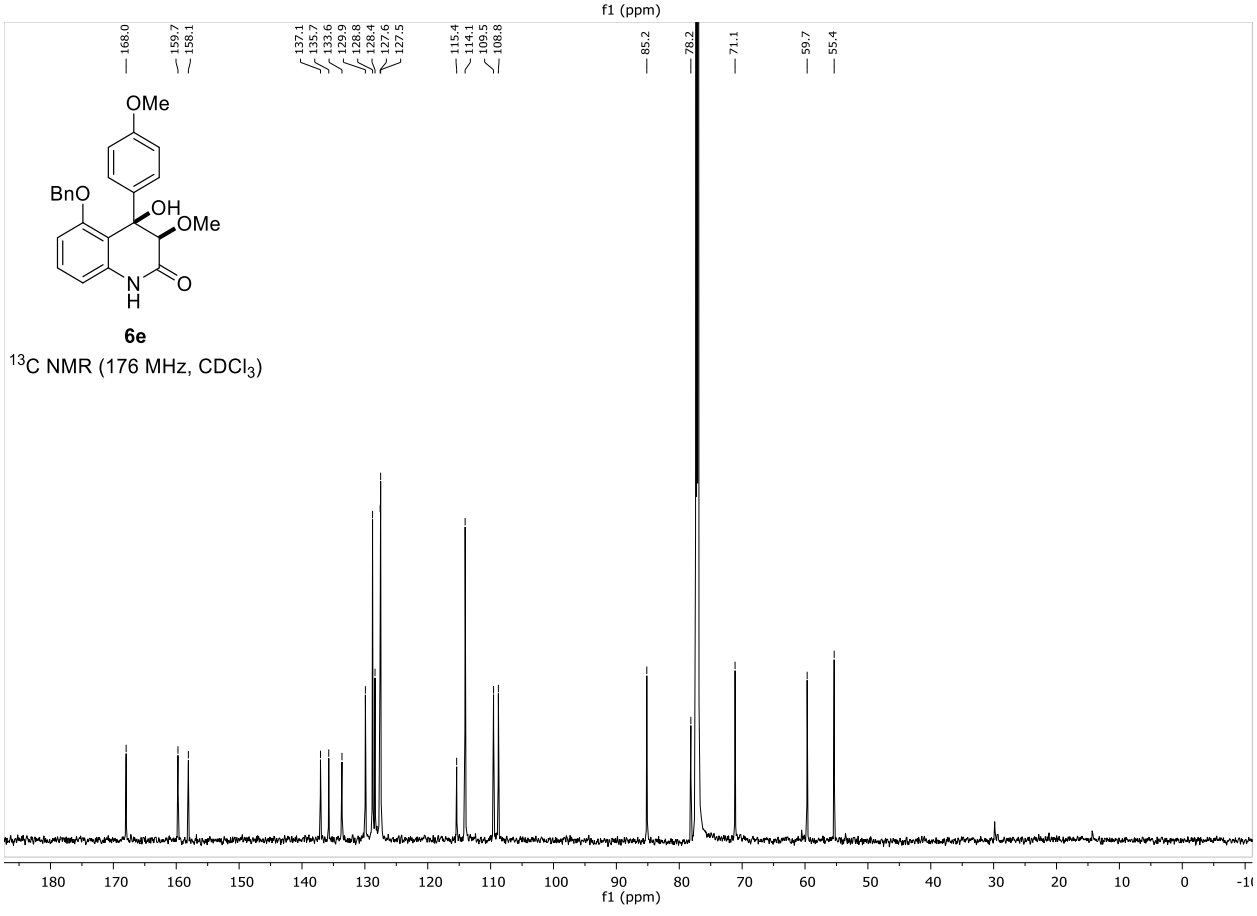
6d

^{13}C NMR (176 MHz, $CDCl_3$)



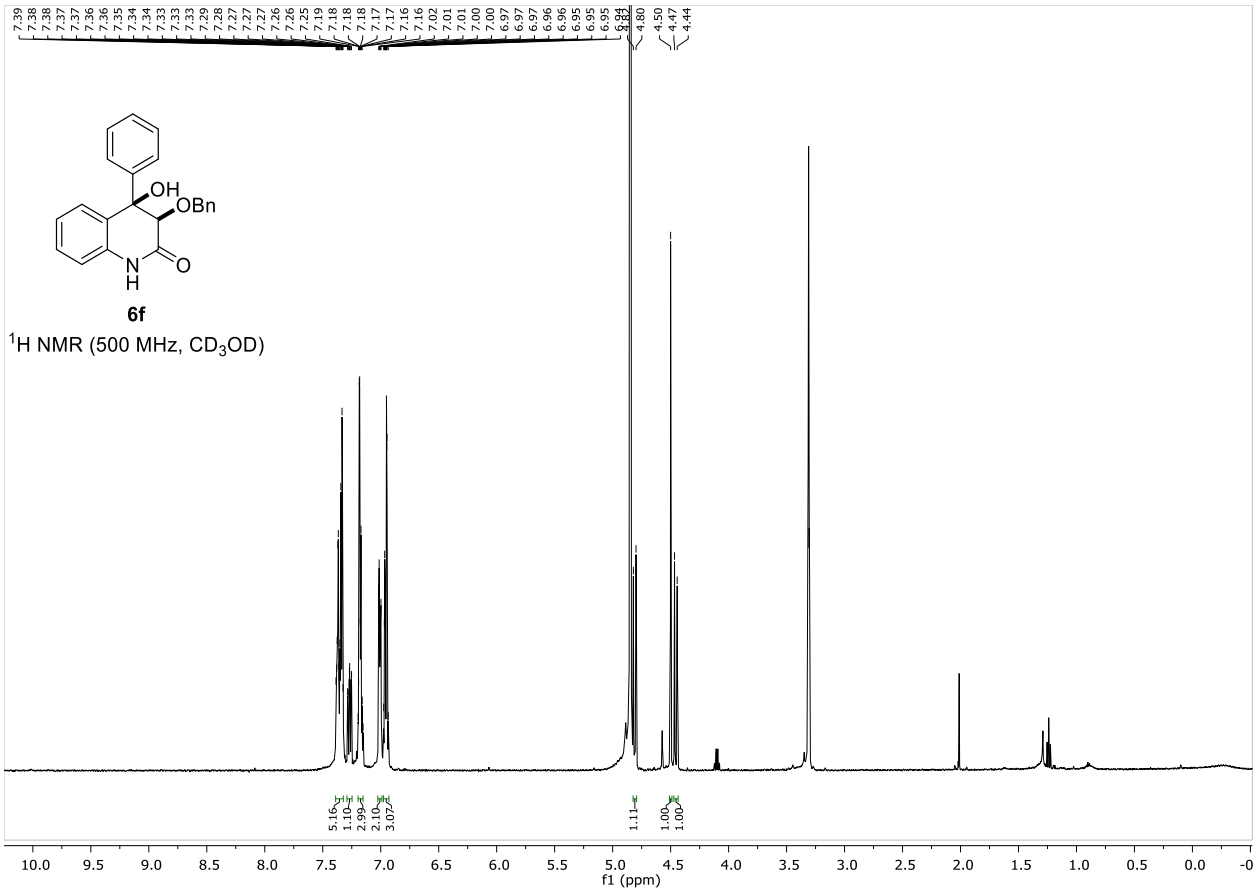
6e

^{1}H NMR (700 MHz, $CDCl_3$)



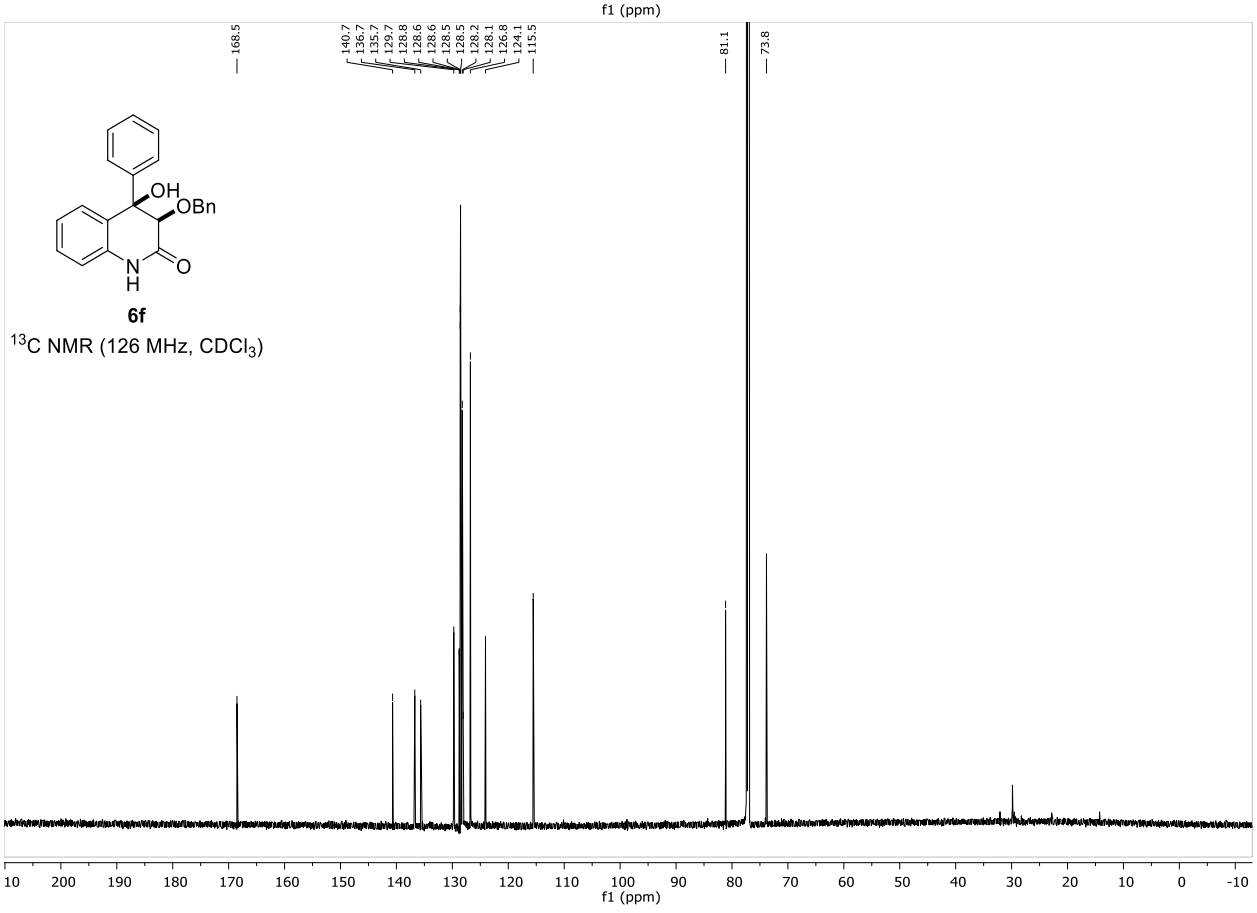
6e

^{13}C NMR (176 MHz, $CDCl_3$)



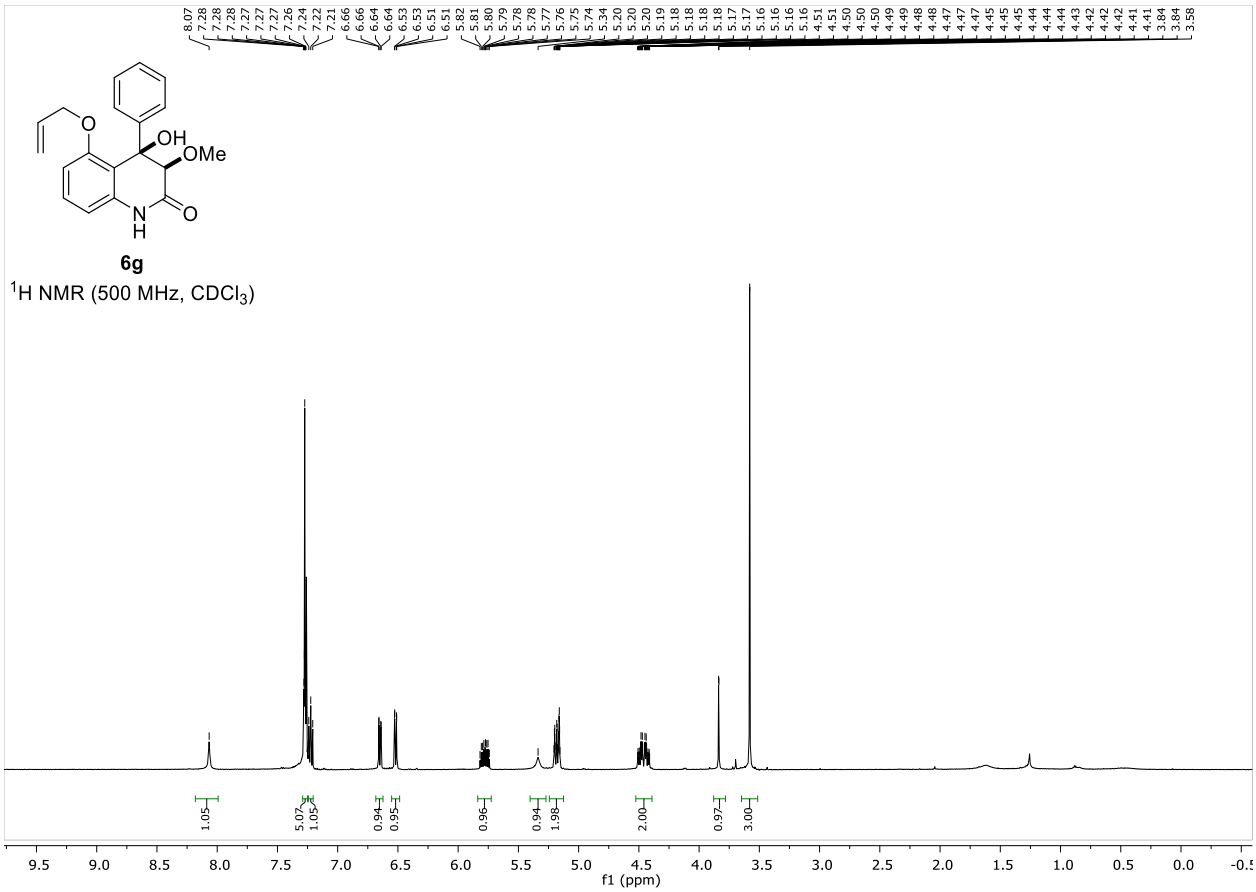
6f

^{1}H NMR (500 MHz, CD_3OD)



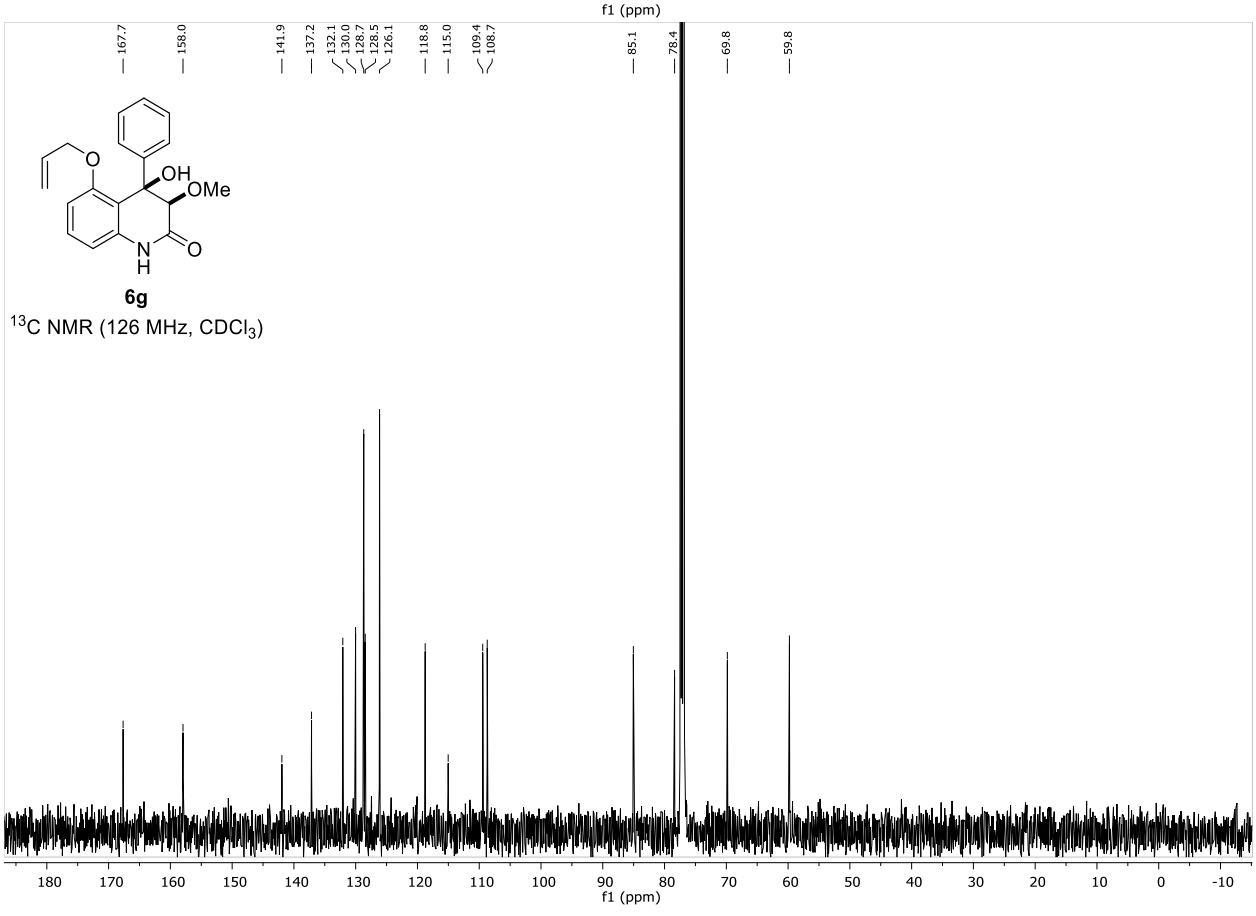
6f

^{13}C NMR (126 MHz, $CDCl_3$)



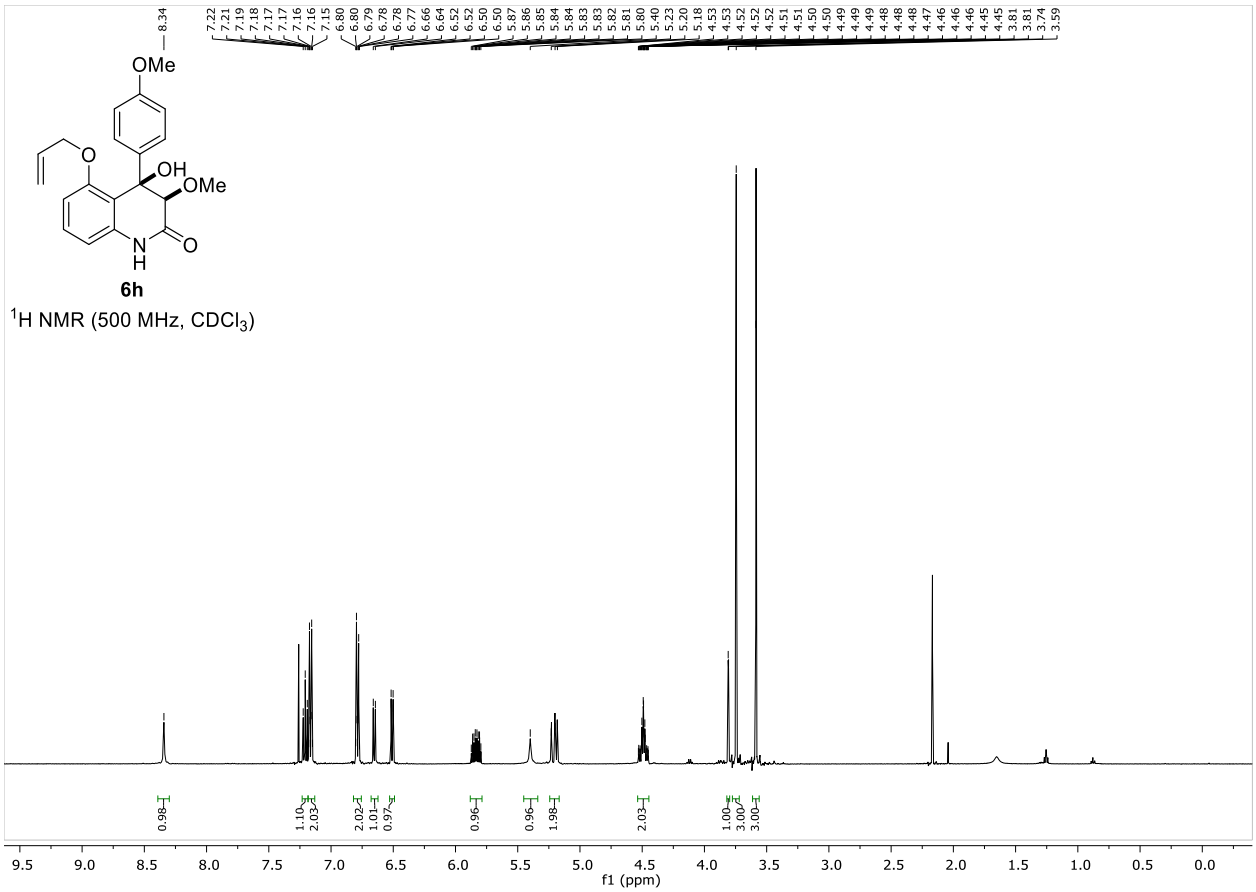
6g

^{1}H NMR (500 MHz, $CDCl_3$)



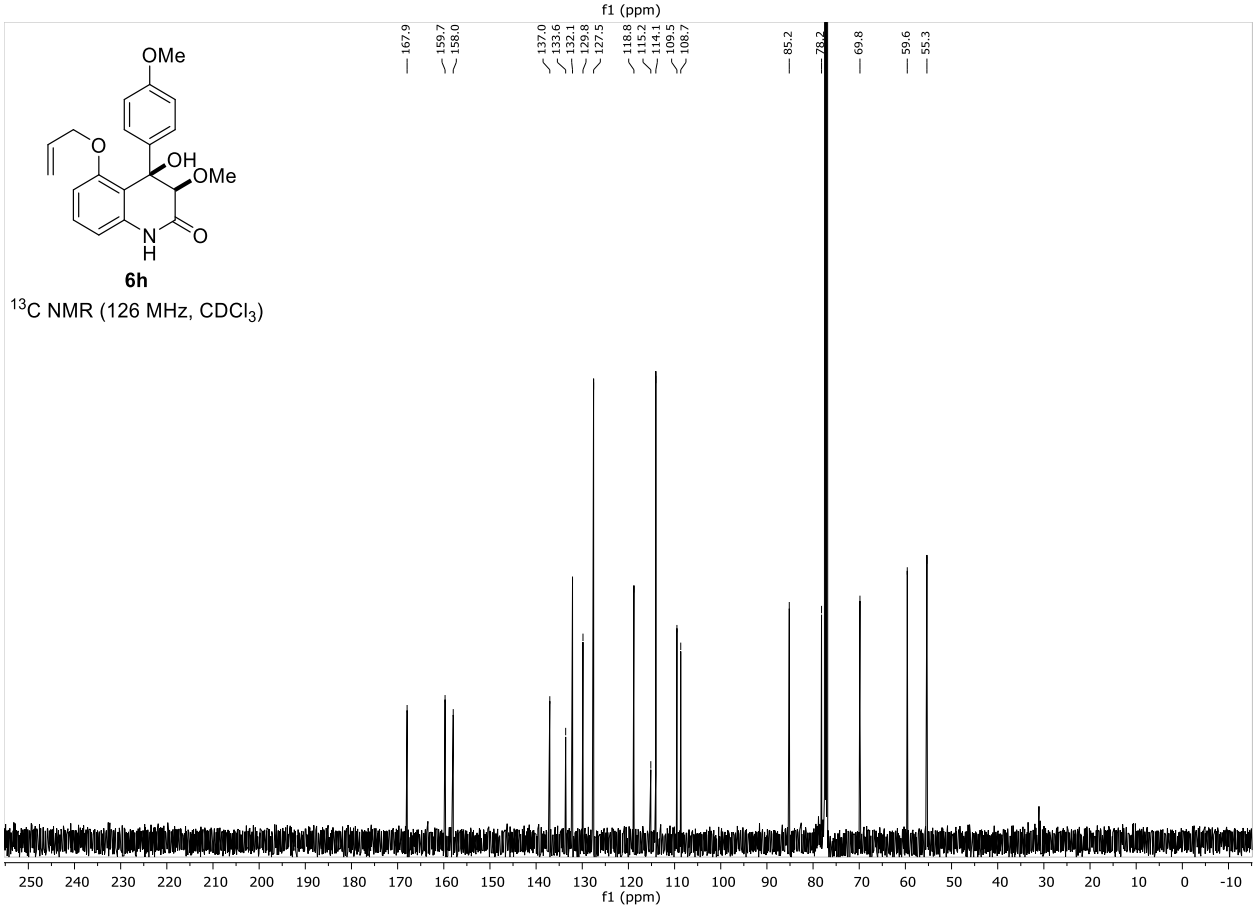
6g

^{13}C NMR (126 MHz, $CDCl_3$)



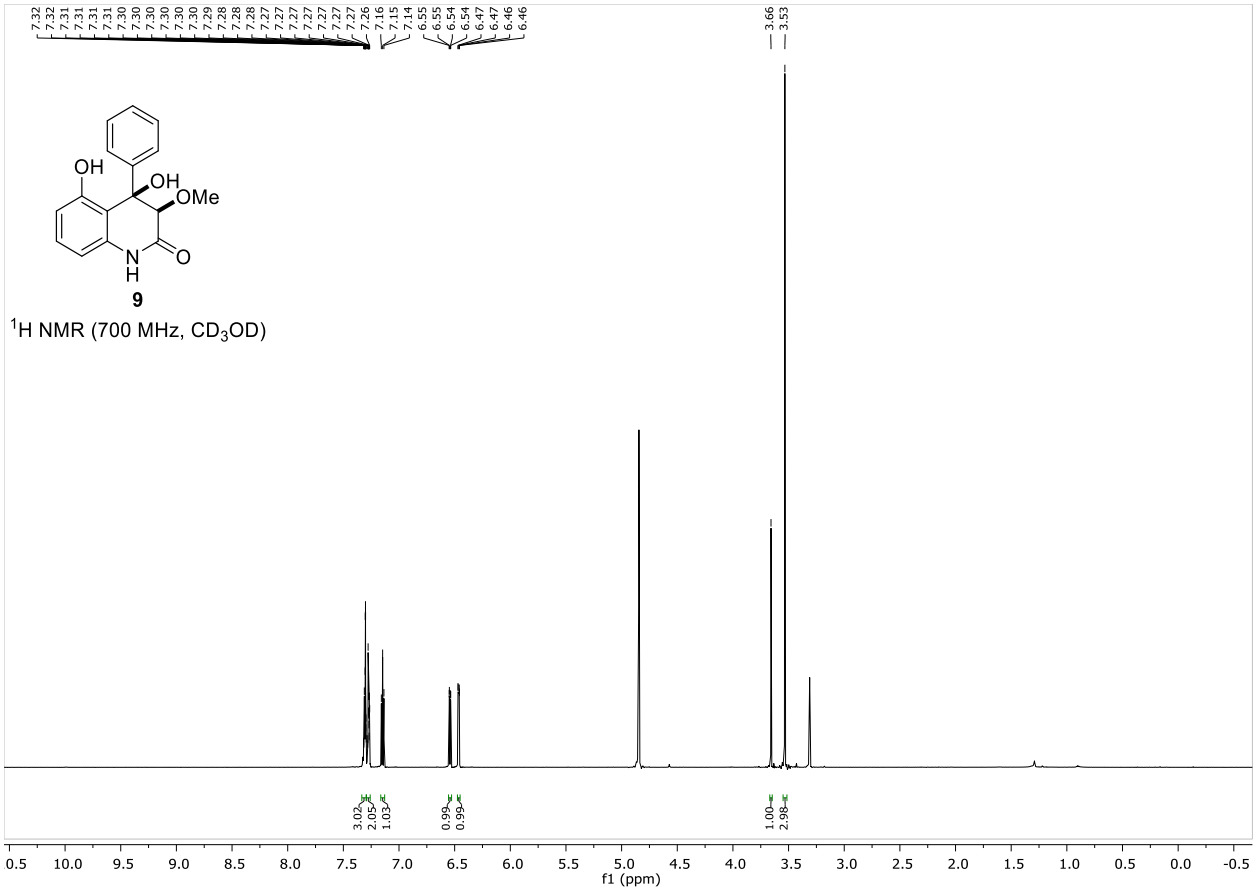
6h

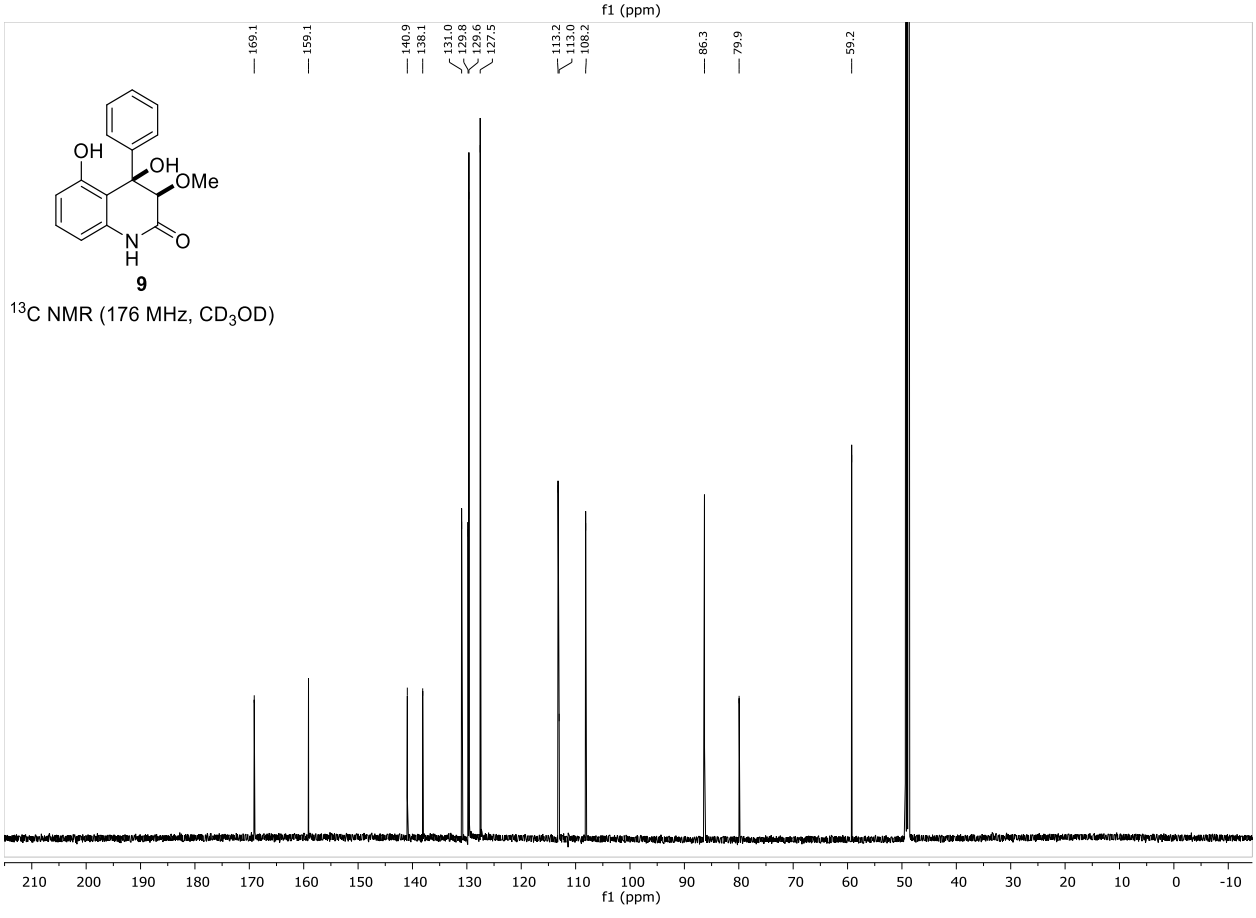
^{1}H NMR (500 MHz, $CDCl_3$)

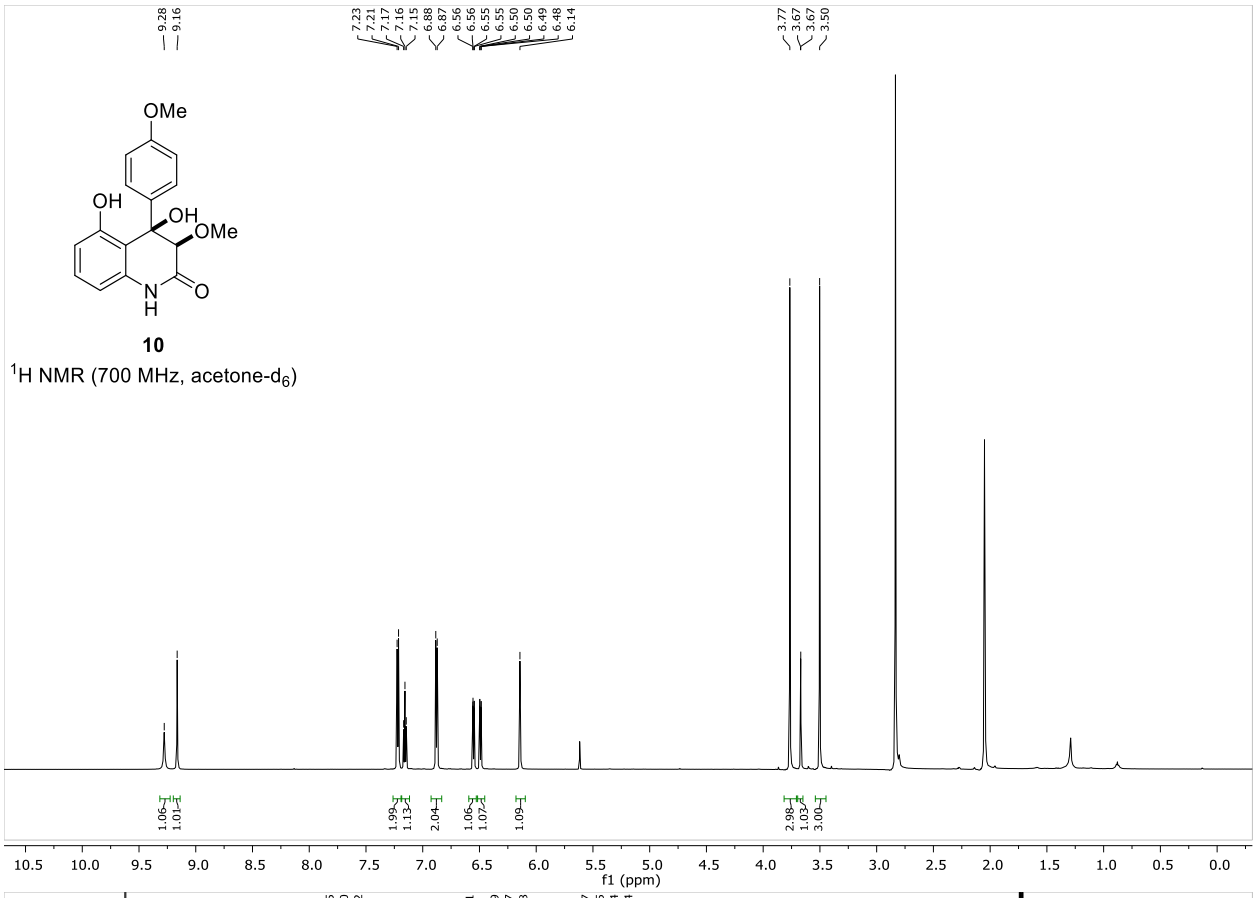


6h

^{13}C NMR (126 MHz, $CDCl_3$)

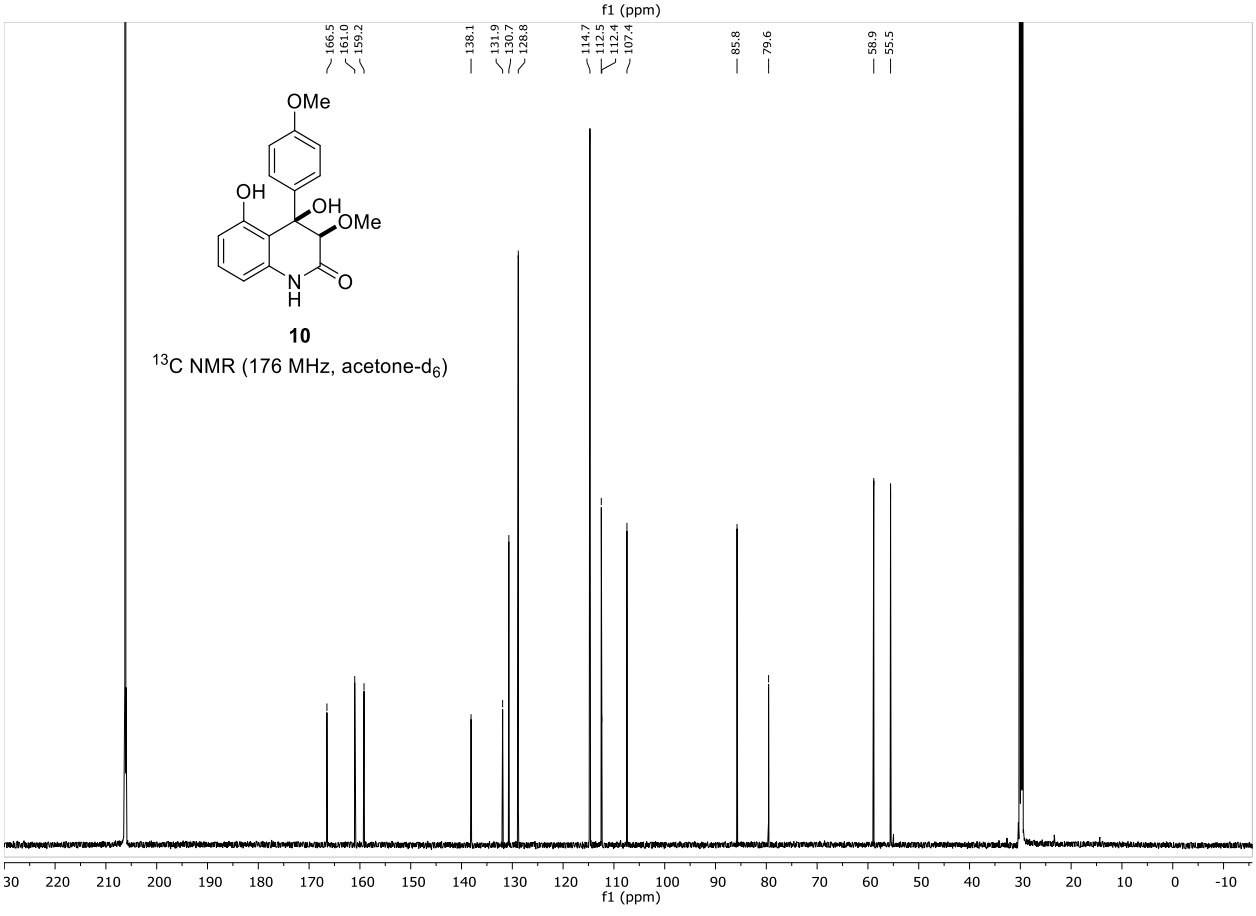

OH
OH
OMe
N
H
O
9
^{1}H NMR (700 MHz, CD_3OD)
f1 (ppm)


OH
OH
OMe
N
H
O
9
^{13}C NMR (176 MHz, CD_3OD)
f1 (ppm)



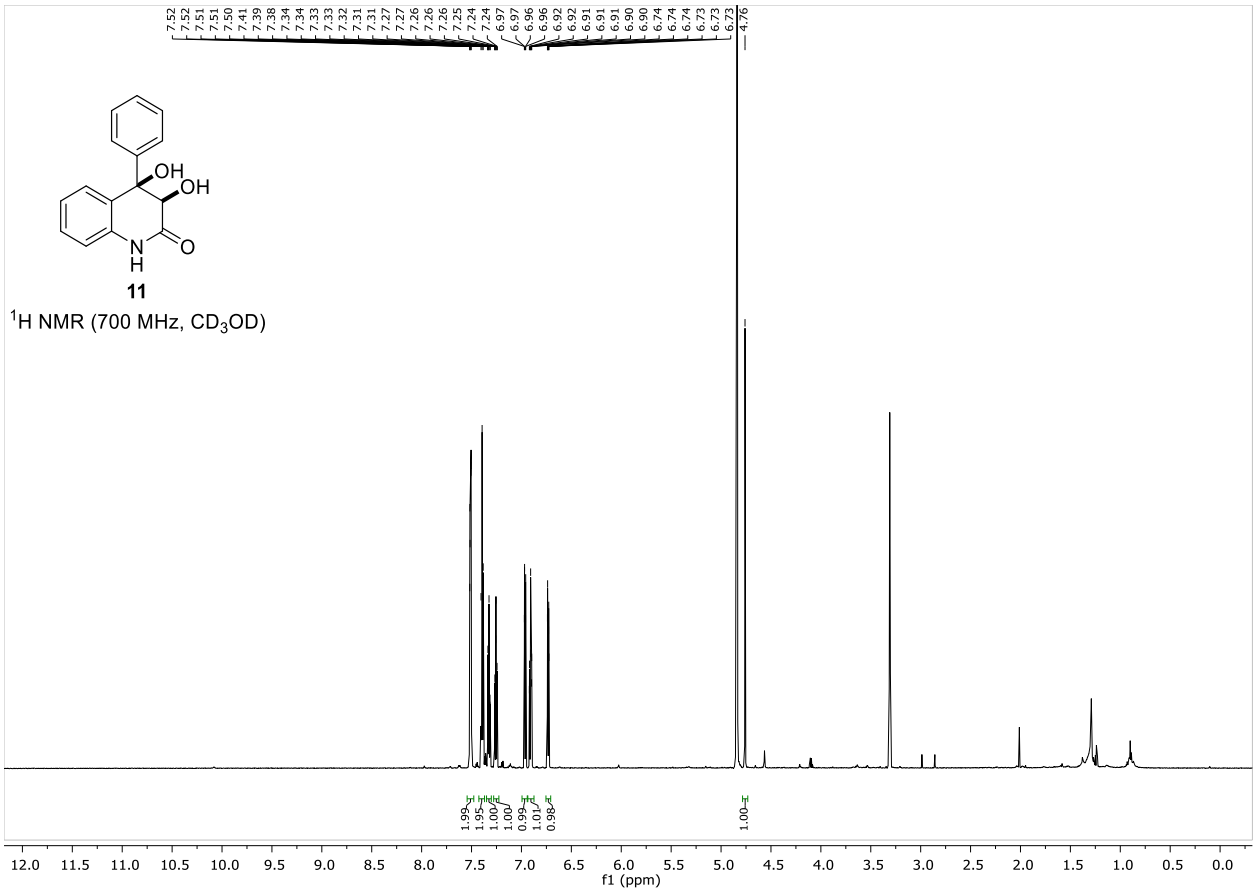
10

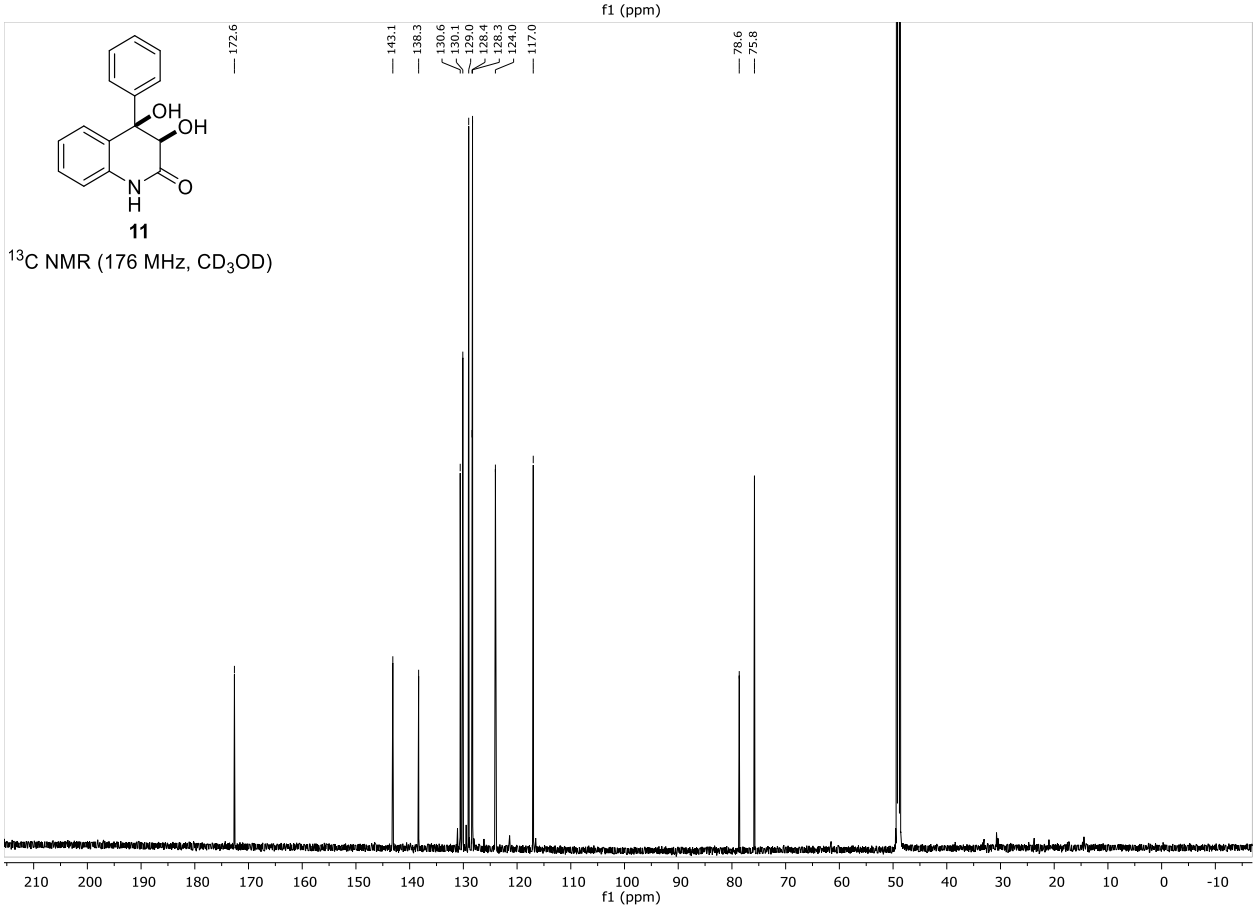
^{1}H NMR (700 MHz, acetone-d_6)

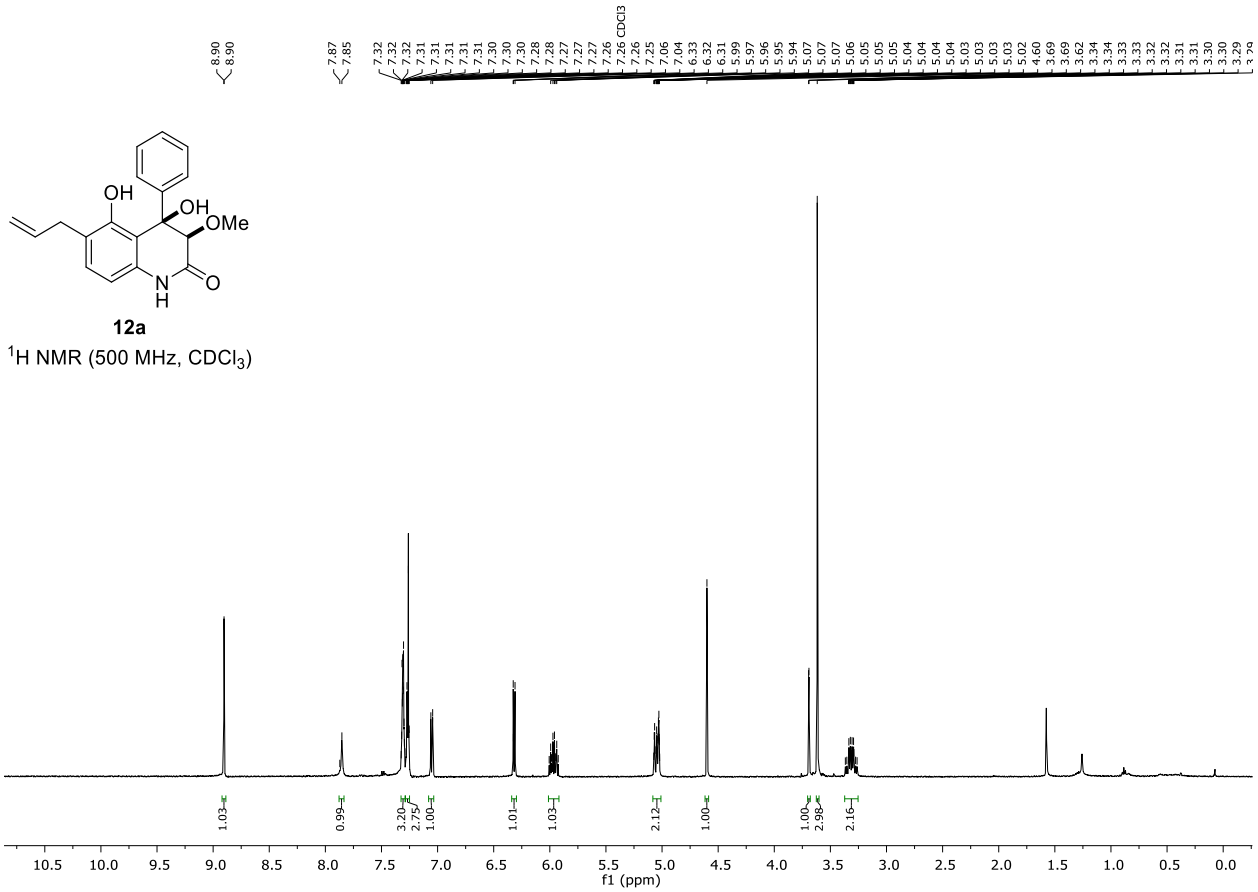


10

^{13}C NMR (176 MHz, acetone-d_6)

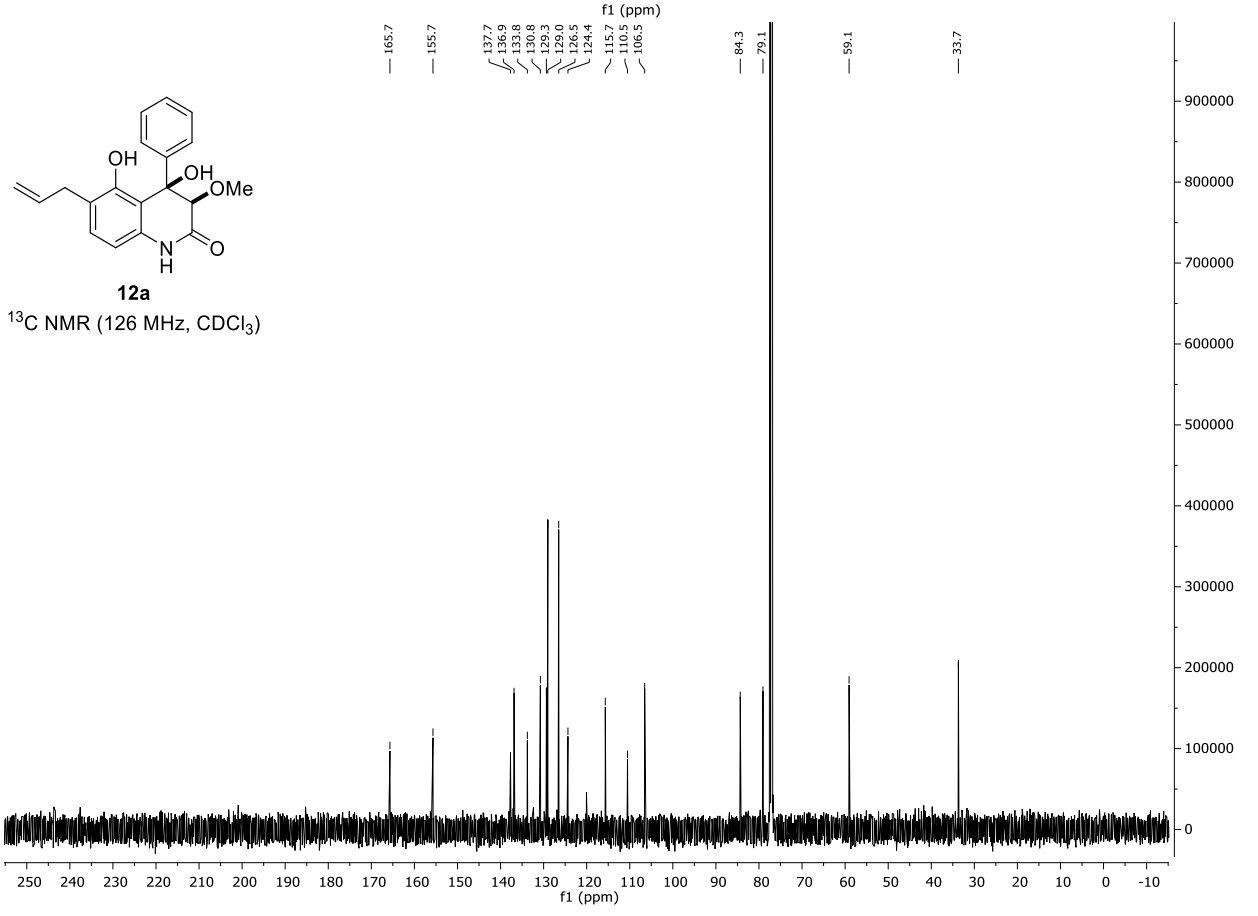

OH
OH
N
H
O
11
1H NMR (700 MHz, CD3OD)
f1 (ppm)


OH
OH
N
H
O
11
13C NMR (176 MHz, CD3OD)
f1 (ppm)



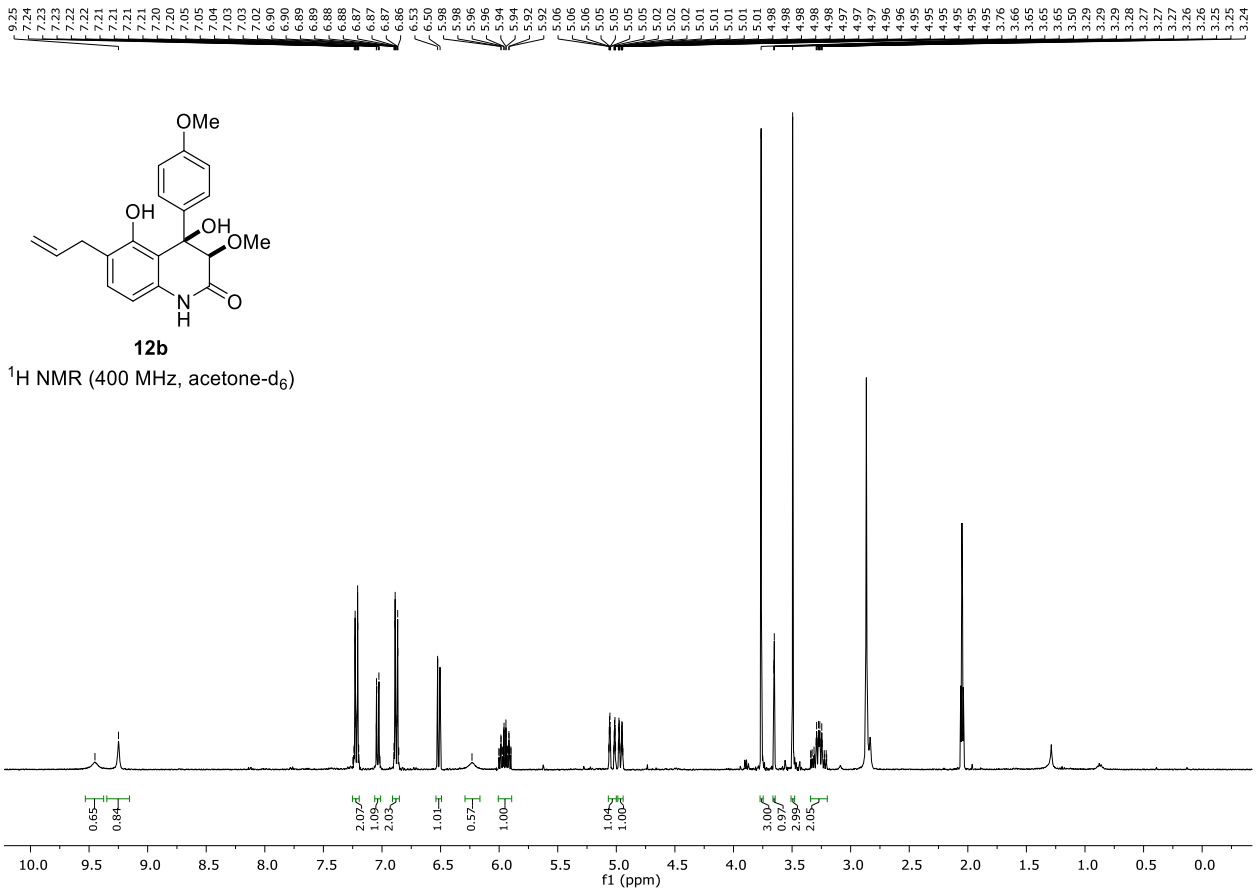
12a

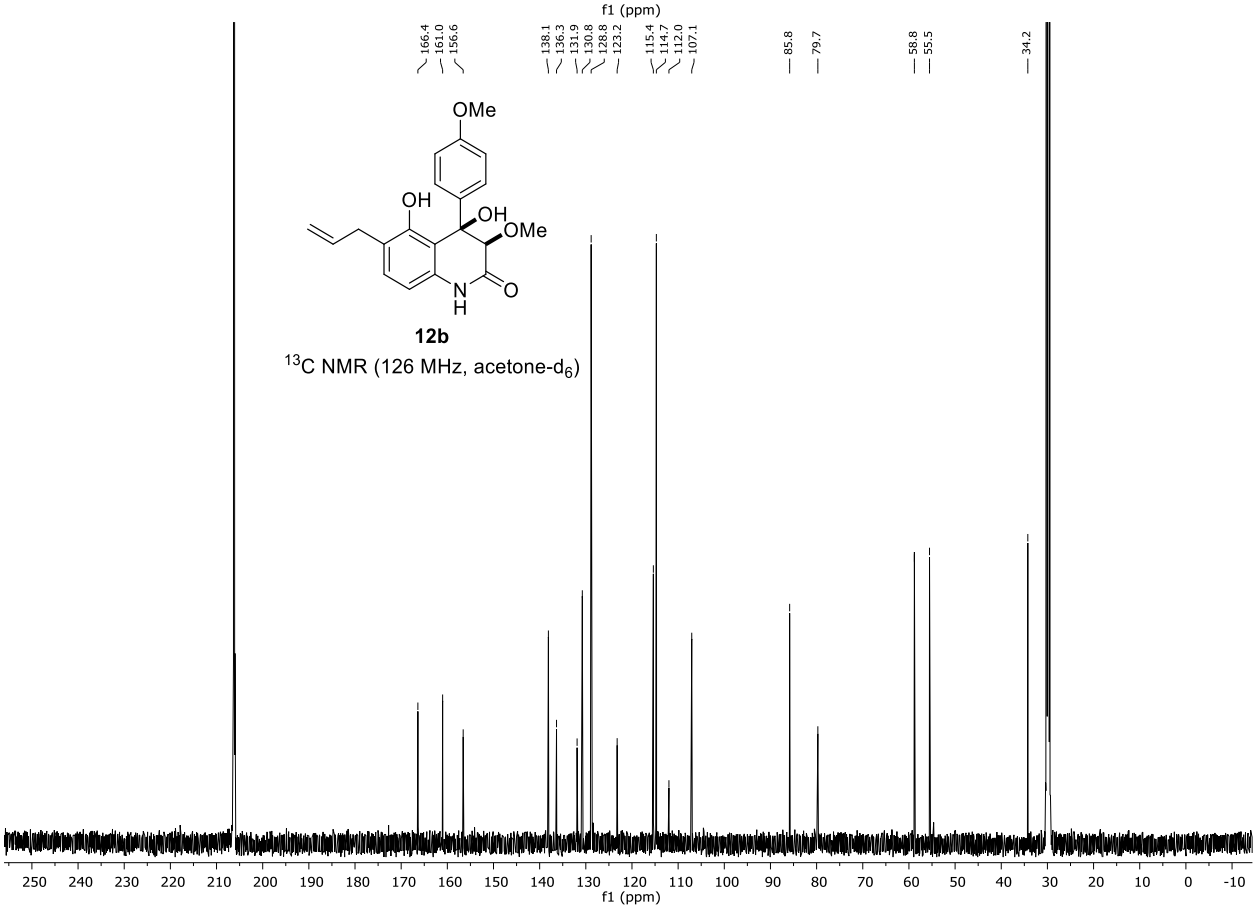
^{1}H NMR (500 MHz, $CDCl_3$)

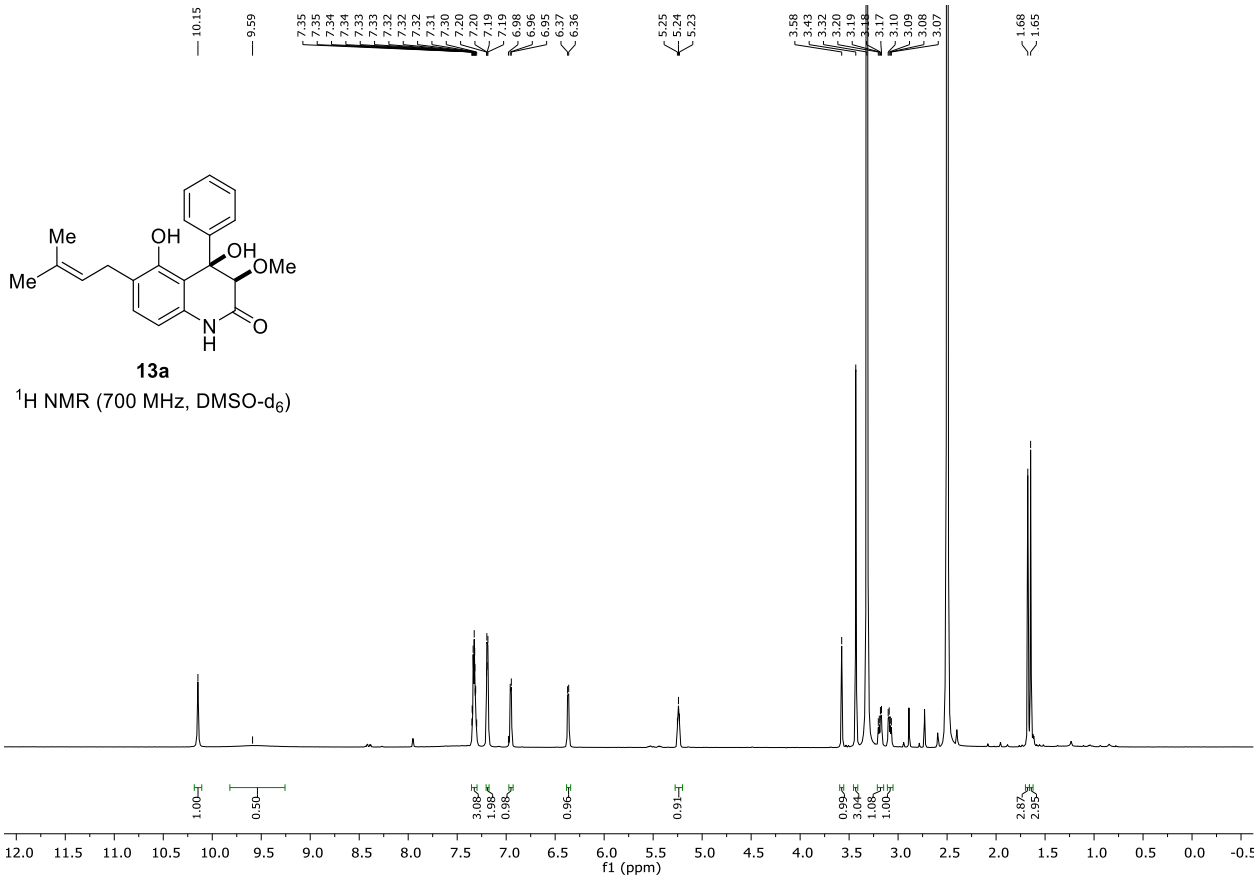


12a

^{13}C NMR (126 MHz, $CDCl_3$)

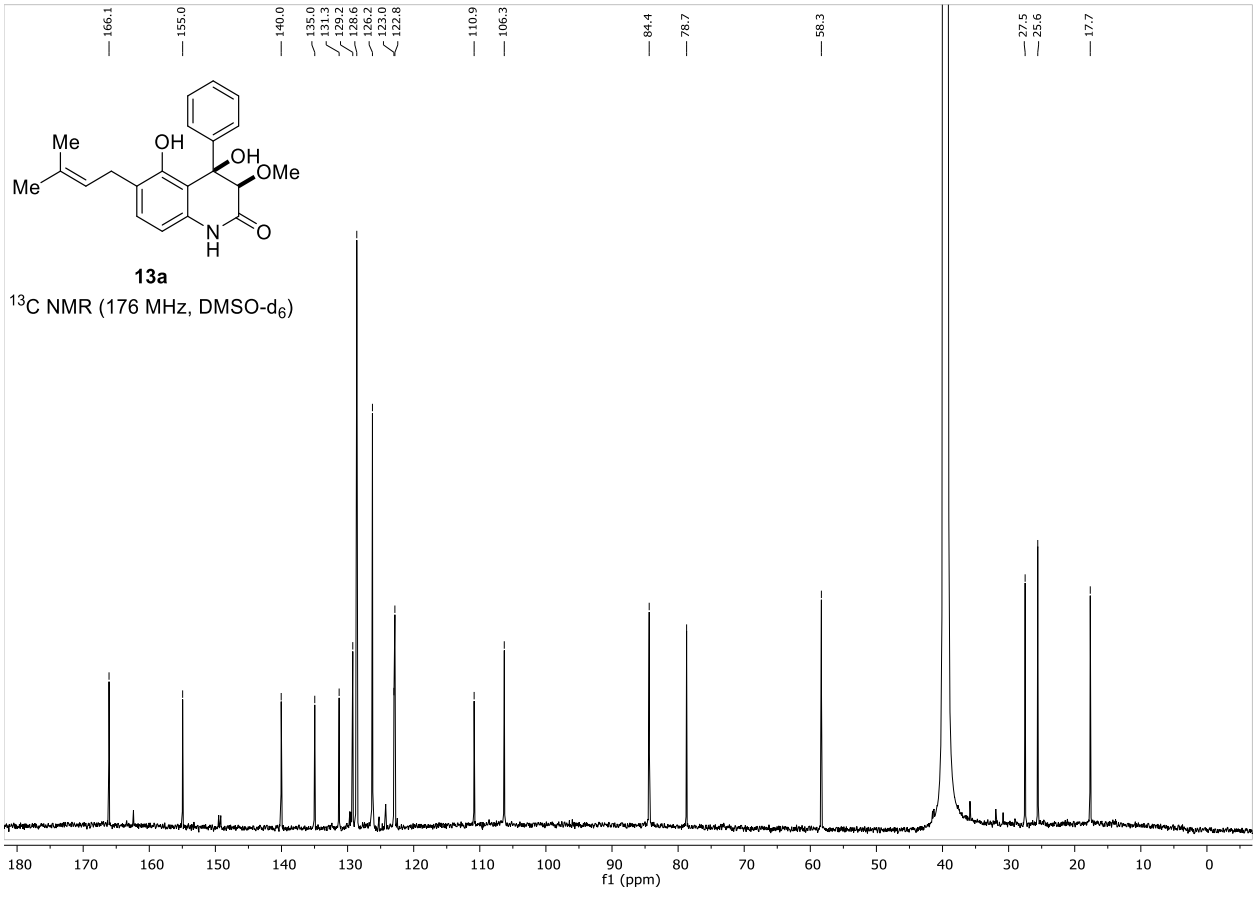

OMe
OH
OH
OMe
N
H
O
12b
1H NMR (400 MHz, acetone-d6)
f1 (ppm)


OMe
OH
OH
OMe
N
H
O
12b
13C NMR (126 MHz, acetone-d6)
f1 (ppm)



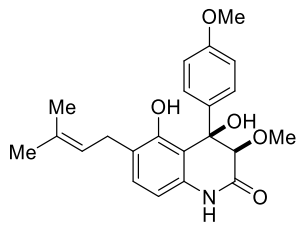
13a

^{1}H NMR (700 MHz, DMSO-d_6)



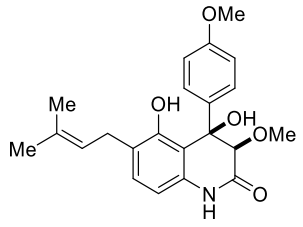
13a

^{13}C NMR (176 MHz, DMSO-d_6)



13b

^{1}H NMR (500 MHz, $CDCl_3$)



13b

^{13}C NMR (126 MHz, $CDCl_3$)