Gold(I)-Catalyzed Enantioselective Carboalkoxylation of Alkynes

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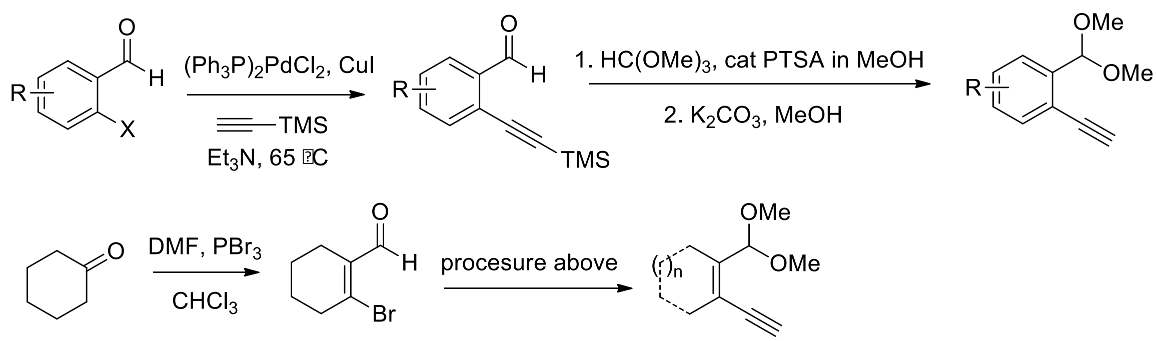
Supporting Information

1. General Information. Unless otherwise noted, reagents were obtained from commercial sources and used without further purification. All reactions were carried out under air unless otherwise stated. Dry THF, dichloromethane, diethyl ether, toluene, triethylamine, and dimethylformamide were obtained by passage through activated alumina columns under argon. All other dried solvents were obtained by storage over 3Å or 4Å molecular sieves overnight. TLC analysis of reaction mixtures was performed on Merck silica gel 60 F254 TLC plates and visualized by UV, I_2/silica, and/or ceric ammonium molybdate stain. Flash chromatography was carried out with ICN Sili Tech 32-63 D 60 Å silica gel. ^{1}H and ^{13}C NMR spectra were recorded with Bruker AV-300, AVQ-400, AVB-400 spectrometers and were referenced to residual ^{1}H and ^{13}C signals of the deuterated solvents respectively (δ H 7.26, δ C 77.00 for chloroform). Mass spectral data were obtained via the Micro-Mass/Analytical Facility operated by the College of Chemistry, University of California, Berkeley. X-Ray crystallographic analysis was carried out by X-Ray Crystallographic Facility (CHEXRAY, University of California, Berkeley).

2. Preparation of Substrates.



2.1 General Procedure for Preparation of Phenyl Acetylenes.[1]

A mixture of 2-bromobenzaldehyde (1.0 equiv), $(Ph_3P)_2PdCl_2$ (0.02 equiv) and CuI (0.01 equiv) in a flask was degassed, then Et_3N (0.2 M for substrate) was added under argon atmosphere. To this solution ethynyl trimethylsilane (5 equiv) was added by syringe. The mixture was warmed to 65 ºC for 12 hours and TLC showed the starting aldehyde was completely consumed. After cooling to room temperature, the reaction mixture was filtrated through celite. The filtrate was concentrated and purified by chromatography.

The product from the first step was dissolved in MeOH (0.2 M for substrate) and $HC(OMe)_3$ (5 equiv) was added, followed by PTSA·H_2O (0.1 equiv). The solution was stirred at room temperature for 4 hours and TLC showed the starting aldehyde was completely consumed. The solvent was removed under reduced pressure and the residue was made basic by addition of

[1] Park, J. H.; Bhilare, S. V.; Youn, S. W. *Org. Lett.* **2011**, 13, 2228

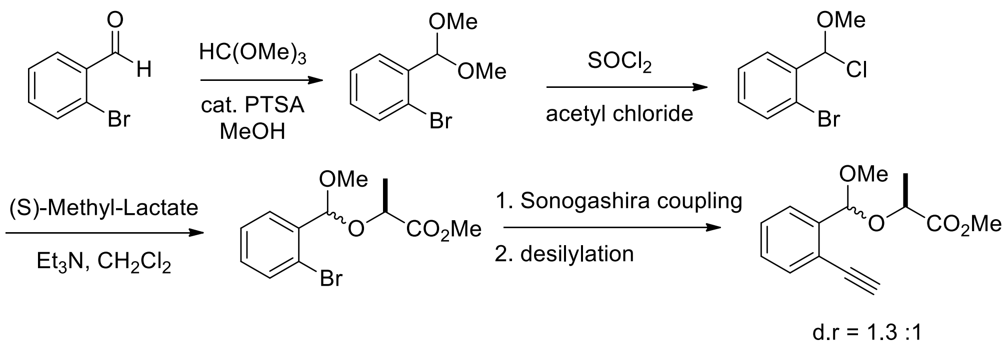
saturated $NaHCO_3$ solution, extracted with EtOAc (3 times) and the organic layer concentrated. The crude acetal was dissolved in MeOH (0.2 M for substrate) and K_2CO_3 (0.1 equiv) was added. Desilylation was conducted at room temperature for 2 hours and concentrated. The final product was purified by chromatography.

2.2 General Procedure for Preparation of Vinyl Acetylenes.[2]

To a solution of PBr_3 (2.5 equiv) in $CHCl_3$ (0.25 M for substrate), DMF (3 equiv) was added slowly at 0 ºC. The mixture was stirred for 1 hour at room temperature and ketone (1 equiv) was added slowly. After addition was complete, the solution was stirred overnight and then poured into pre-cooled saturated $NaHCO_3$ solution very carefully. The mixture was extracted with CH_2Cl_2 and the combined organic layers were dried over Na_2SO_4, concentrated under reduced pressure and the crude aldehyde purified by chromatography.

The next three steps (Sonogashira coupling, protection of aldehyde and desilylaiton) were conducted using the procedure described above.

2.3 Preparation of Mixed Acetal.[3]



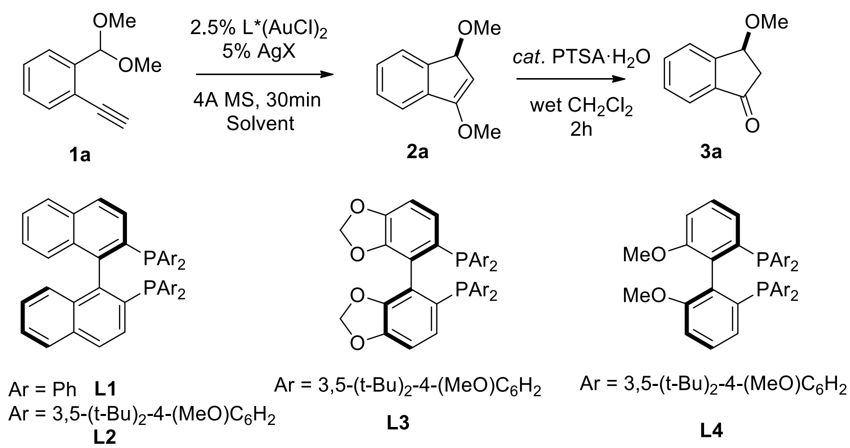
The mixed acetal for mechanistic study was prepared as follows. To a solution of 2-bromobenzaldehyde (4.6 g, 25 mmol) in MeOH (50 mL) was added $HC(OMe)_3$ (6.8 mL, 62.5 mmol), followed by $PTSA\cdot H_2O$ (475 mg, 2.5 mmol). The solution was stirred at room temperature for 4 hours and TLC showed the starting aldehyde was completely consumed. The solvent was removed under reduced pressure and the residue was made basic by addition of saturated $NaHCO_3$ solution, extracted with EtOAc (3 times) and then the organic layers. Were concentrated. The residue was dissolved in acetyl chloride (15 mL) and $SOCl_2$ (0.2 mL) was added. The mixture was stirred overnight, the solvent was removed under reduced pressure to give the benzyl chloride which was used directly for the next step without further purification.

To a solution of freshly prepared benzyl chloride (2.4 g, 10 mmol) in CH_2Cl_2 (50 mL) was added (S)-methyl lactate (1.0 g, 10 mmol) followed by Et_3N (4.1 mL, 30 mmol). The mixture was stirred at room temperature overnight then filtrated through celite. The filtrate was concentrated under reduced pressure and purified by chromatography to give mixed acetal as a colorless oil

[2] Lin, M.-Y.; Das, A.; Liu, R.-S. *J. Am. Chem. Soc.* **2006**, 128, 9340.
[3] Midtkandal, R. R.; Macdonald, S. J. F.; Migaud, M. E. *Chem. Commun.* **2010**, 46, 4538.

(1.5 g, 49% yield). The next two steps (Sonogashira coupling, desilylation) were conducted using the procedure described above.

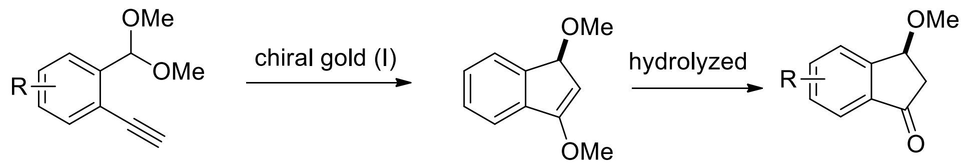
3. Optimization of Reaction Conditions



entry[a]	L	AgX	solvent	yield (%)[b]	ee (%)[c]
1	L1	$AgSbF_6$	CH_2Cl_2	75	8
2	L2	$AgSbF_6$	CH_2Cl_2	77	2
3	L3	$AgSbF_6$	CH_2Cl_2	71	5
4	L4	$AgSbF_6$	CH_2Cl_2	74	24
5	L4	$AgSbF_6$	CCl_4	74	94
6	L4	$AgSbF_6$	benzene	80	89
7	L4	$AgSbF_6$	toluene	88	94
8	L4	$AgSbF_6$	o-xylene	88	92
9	L4	$AgSbF_6$	m-xylene	81	94
10	L4	$AgBF_4$	toluene	n.r.	n.d.
11	L4	NaBARF	toluene	63	-35
12[d]	**L4**	**$AgSbF_6$**	**toluene**	**92**	**95**

[a] Reaction conditions: 1) 2.5 mol % gold catalyst, 5 mol % $AgSbF_2$, 0.05 mmol 1a, 10 mg 4Å molecular sieve, 1 mL solvent. 2) 2.5 mol % PTSA • H_2O, 1 mL CH_2Cl_2, 0.1 mL H_2O. [b]Isolated yields. [c] Determined by chiral HPLC. [d] 2.5 mmol % $AgSbF_6$ was used.

4. General Procedure for Gold(I) Catalyzed Carboalkoxylation of Alkynes



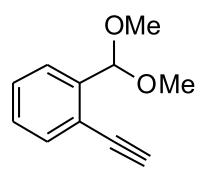
1 2 3

Step 1: (R)-DTBM-MeO-Biphep$(AuCl)_2$ (8.0 mg, 0.025 equiv) was dissolved in toluene (2 mL). $AgSbF_6$ (1.7 mg, 0.025 equiv) was added and the solution was stirred at room temperature for 10 min before adding 4 Å molecular sieve (50 mg). Substrate **1** (0.2 mmol) was added to the above solution and mixture was stirred at room temperature. The reaction was monitored by TLC, and once the reaction was done the solution was transferred to a short pad of silica gel, eluted with EtOAc and concentrated under reduced pressure to give crude **2**.

Step 2: The crude **2** was dissolve in CH_2Cl_2 (2 mL) and H_2O (0.2 mL) was added followed by PTSA·H_2O (1 mg, 0.025 equiv). The mixture was stirred at room temperature for 2-8 hours (monitored by TLC) and then saturated $NaHCO_3$ solution was added and extracted with EtOAc. The combined organic layers was concentrated under reduced pressure. The desired 3-methoxyl indanone **3** was purified by chromatography.

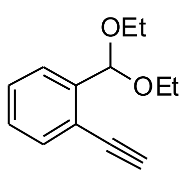
A racemic sample was obtained by using Ph_3PAuCl or racemic Binap$(AuCl)_2$ instead of (R)-DTBM-MeO-Biphep$(AuCl)_2$ under the same procedure as above.

5. Spectral Data of Substrates



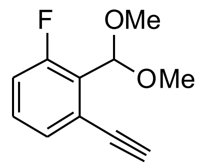
1a

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (d, J = 7.6 Hz, 1H), 7.52 (dd, J = 7.6, 1.2 Hz, 1H), 7.39 (td, J = 7.6, 1.2 Hz, 1H), 7.30 (td, J = 7.6, 1.2 Hz, 1H), 5.37 (s, 1H), 3.39 (s, 6H), 3.34 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.10, 132.99, 128.71, 128.34, 126.19, 120.91, 101.92, 81.76, 81.10, 53.81



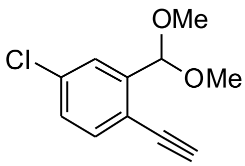
1b

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, J = 8.0 Hz, 1H), 7.50 (dd, J = 7.6, 1.2 Hz, 1H), 7.38 (td, J = 7.6, 1.2 Hz, 1H), 7.28 (td, J = 7.6, 1.6 Hz, 1H), 5.83 (s, 1H), 3.73-3.66 (m, 2H), 3.63-3.54 (m, 2H), 3.32 (s, 1H), 1.25 (t, J = 7.2 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.25, 132.87, 128.88, 128.15, 126.13, 120.82, 100.24, 81.62, 81.23, 62.39, 15.17; HRMS (ESI) calcd. for $C_{13}H_{16}O_2Na$ $(M + Na)^+$: 227.1043, Found: 227.1044.



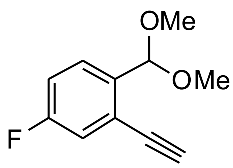
1c

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32-7.27 (m, 1H), 7.15-7.10 (m, 1H), 5.80 (s, 1H), 3.53 (s, 6H), 3.39 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.76 (d, *J* = 249.9 Hz), 129.93 (d, *J* = 9.7 Hz), 129.29 (d, J =3.6 Hz), 127.35 (d, *J* = 13.3 Hz), 123.01 (d, *J* = 7.2 Hz), 117.50 (*J* = 23.3 Hz), 103.22, 82.42, 80.50 (d, *J* = 3.3 Hz), 55.45; HRMS (ESI) calcd. for $C_{11}H_{11}O_2FNa$ $(M + Na)^+$: 217.0635, Found: 217.0637.



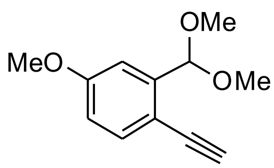
1d

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (d, *J* = 2.4 Hz, 1H), 7.45 (d, *J* = 8.4 Hz, 1H), 7.28 (dd, *J* = 8.4, 2.0 Hz, 1H), 5.67 (s, 1H), 3.39 (s, 6H), 3.37 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.95, 135.01, 134.15, 128.61, 126.79, 119.33, 101.17, 82.66, 80.14, 53.77; HRMS (EI) calcd. for $C_{11}H_{11}O_2Cl$ $(M)^+$: 210.0448, Found: 210.0450.



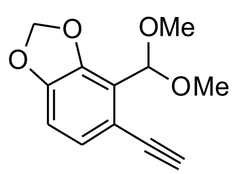
1e

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (dd, *J* = 8.8, 6.0 Hz, 1H), 7.24 (dd, *J* = 8.8, 2.8 Hz, 1H), 7.12 (td, *J* = 8.4, 2.8 Hz, 1H), 5.71 (s, 1H), 3.42 (s, 6H), 3.41 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.05 (d, *J* = 246.9 Hz), 136.42 (d, *J* = 29 Hz), 128.35 (d, *J* = 87.0 Hz), 119.53 (d, *J* = 224 Hz), 116.13 (d, *J* = 210 Hz), 82.76, 79.98 (d, *J* = 28 Hz), 53.82; HRMS (EI) calcd. for $C_{11}H_{11}OF$ $(M)^+$: 197.0743, Found: 197.0742.



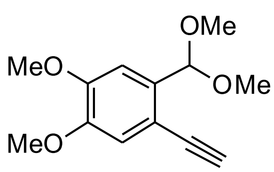
1f

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 (d, *J* = 8.4 Hz, 1H), 7.13 (d, *J* = 2.8 Hz, 1H), 6.83 (dd, *J* = 8.8, 2.8 Hz, 1H), 5.67 (s, 1H), 5.68 (s, 1H), 3.84 (s, 3H), 3.41 (s, 6H), 3.25 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.95, 141.99, 134.34, 114.72, 112.99, 111.11, 101.95, 81.19, 80.26, 55.38, 54.03; HRMS (EI) calcd. for $C_{12}H_{14}O_3$ $(M\ )^+$: 206.0943, Found: 206.0944.



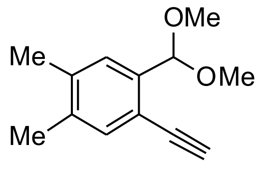
1g

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.10 (d, *J* = 8.0 Hz, 1H), 6.79 (d, *J* = 8.0 Hz, 1H), 6.09 (s, 2H), 5.75 (s, 1H), 3.52 (s, 6H), 3.24 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.02, 145.28, 127.77, 121.86, 114.43, 108.66, 103.17, 101.93, 81.2, 79.88, 55.11; HRMS (EI) calcd. for $C_{12}H_{12}O_4$ $(M)^+$: 220.0736, Found: 220.0736.



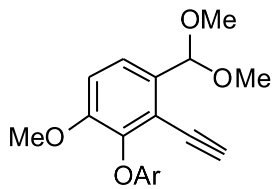
1h

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.08 (s, 1H), 6.96 (s, 1H), 5.64 (s, 1H), 3.91 (s, 3H), 3.86 (s, 3H), 3.38 (s, 6H), 3.25 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.74, 148.56, 134.01, 114.71, 112.88, 108.70, 102.16, 81.19, 80.29, 55.93, 54.10; HRMS (EI) calcd. for $C_{13}H_{16}O_4$ $(M)^+$: 236.1049, Found: 236.1053.



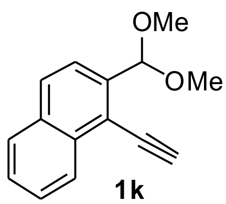
1i

[1]H NMR (400 MHz, $CDCl_3$) δ 7.36 (s, 1H), 7.30 (s, 1H), 5.67 (s, 1H), 3.39 (s, 6H), 3.26 (s, 1H), 2.28 (s, 3H), 3.24 (s, 3H); [13]C NMR (100 MHz, $CDCl_3$) δ 137.85, 137.53, 136.93, 133.84, 127.25, 118.05, 102.09, 81.42, 80.63, 53.86, 19.88, 19.26; HRMS (EI) calcd. for $C_{13}H_{16}O_2$ $(M)^+$: 204.1150, Found: 204.1155.



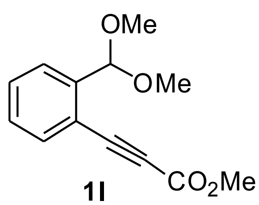
Ar = 4-Bromobenzen sulfonyl **1j**

[1]H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, *J* = 8.8 Hz, 2H), 7.69 (d, *J* = 9.2 Hz, 1H), 7.47 (d, *J* = 8.8 Hz, 1H), 6.95 (d, *J* = 8.4 Hz, 1H), 5.57 (s, 1H), 3.66 (s, 3H), 3.36 (s, 6H), 3.29 (s, 3H); [13]C NMR (100 MHz, $CDCl_3$) δ 152.16, 140.20, 136.89, 133.53, 132.03, 129.97, 128.94, 125.69, 117.69, 112.72 101.38, 87.34, 75.37, 55.86, 53.84; HRMS (ESI) calcd. for $C_{18}H_{17}O_6BrSK$ $(M + K)^+$: 475.9561, Found: 475.9564.



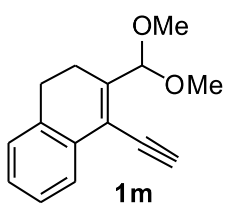
1k

[1]H NMR (400 MHz, $CDCl_3$) δ 8.43 (d, *J* = 8.4 Hz, 1H), 7.90-7.85 (m, 2H), 7.74 (d, *J* = 8.8 Hz, 1H), 7.64-7.54 (m, 2H), 5.98 (s, 1H), 3.79 (s, 1H), 3.46 (s, 6H); [13]C NMR (100 MHz, $CDCl_3$) δ 139.54, 133.41, 133.06, 129.11, 128.20, 127.18, 126.84, 126.41, 123.32, 118.43, 102.88, 87.45, 79.00, 54.31; HRMS (EI) calcd. for $C_{15}H_{14}O_2$ $(M)^+$: 226.0994, Found: 226.0993.



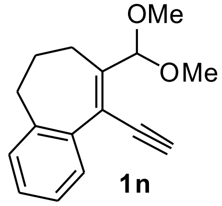
1l

[1]H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, *J* = 7.6 Hz, 1H), 7.64 (d, *J* = 7.2 Hz, 1H), 7.51 (t, *J* = 7.6 Hz, 1H), 7.64 (d, *J* = 7.2 Hz, 1H), 7.51 (t, *J* = 7.6 Hz, 1H), 7.38 (t, *J* = 7.6 Hz, 1H), 5.68 (s, 1H), 3.88 (s, 3H), 3.45 (s, 6H); [13]C NMR (100 MHz, $CDCl_3$) δ 154.41, 141.78, 133.82, 130.67, 128.59, 126.44, 118.44, 102.12, 84.61, 83.97, 54.37, 52.84; HRMS (ESI) calcd. for $C_{13}H_{14}O_4K$ $(M + K)^+$: 273.0524, Found: 273.0524.



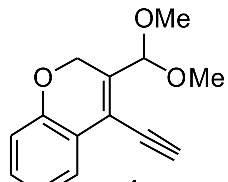
1m

[1]H NMR (400 MHz, $CDCl_3$) δ 8.43 (d, *J* = 8.4 Hz, 1H), 7.90-7.85 (m, 2H), 7.74 (d, *J* = 8.8 Hz, 1H), 7.64-7.54 (m, 2H), 5.98 (s, 1H), 3.79 (s, 1H), 3.46 (s, 6H); [13]C NMR (100 MHz, $CDCl_3$) δ 144.75, 135.49, 132.22, 128.13, 127.30, 126.63, 125.74, 119.18, 104.67, 83.98, 78.77, 55.05, 27.16, 21.33; HRMS (EI) calcd. for $C_{15}H_{16}O_2$ $(M)^+$: 228.1150, Found: 228.1154.



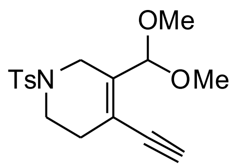
1n

[1]H NMR (400 MHz, $CDCl_3$) δ 7.53 (d, *J* = 7.6 Hz, 1H), 7.32-7.19 (m, 3H), 5.50 (s, 1H), 3.49 (s, 6H), 3.24 (s, 1H), 2.62 (t, *J* = 6.8 Hz, 2H), 2.22-2.17 (m, 2H), 2.05 (t, *J* = 6.8 Hz, 2H); [13]C NMR (100 MHz, $CDCl_3$) δ 147.86, 140.47, 138.03, 128.79, 128.15, 127.80, 126.16, 121.77, 105.38, 81.46, 81.33, 55.16, 35.33, 31.98, 23.64; HRMS (EI) calcd. for $C_{16}H_{18}O_2$ $(M)^+$: 232.1307, Found: 242.1304.



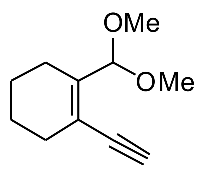
1o

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.20 (td, *J* = 8.0, 1.6 Hz, 1H), 6.97 (td, *J* = 7.6, 0.8 Hz, 1H), 6.84 (d, *J* = 8.0 Hz, 1H), 5.34 (s, 1H), 4.83 (s, 2H), 3.45 (s, 6H), 3.42 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.79, 136.71, 130.20, 126.07, 121.56, 120.94, 116.56, 115.89, 103.22, 85.00, 76.48, 63.84, 54.91; HRMS (EI) calcd. for $C_{14}H_{14}O_3$ $(M)^+$: 230.0943, Found: 230.0948.



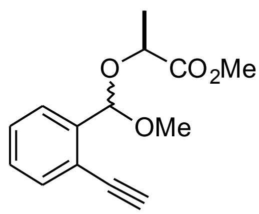
1p

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, *J* = 8.0 Hz, 2H), 7.31 (d, *J* = 8.0, 2H), 5.22 (s, 1H), 3.70 (s, 2H), 3.37 (s, 6H), 3.19-3.14 (m, 3H), 2.43 (s, 3H), 2.42- 2.39 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.64, 139.03, 133.03, 129.70, 127.73, 116.92, 103.66, 82.65, 80.35, 55.26, 42.74, 42.37, 29.80, 21.50; HRMS (ESI) calcd. for $C_{17}H_{21}N_1O_4NaS$ $(M + Na)^+$: 358.1084, Found: 358.1090.



1q

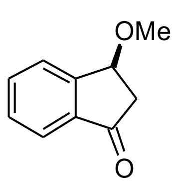
^{1}H NMR (400 MHz, $CDCl_3$) δ 5.24 (s, 1H), 3.39 (s, 6H), 3.11 (s, 1H), 2.26-2.19 (m, 2H), 2.18-2.09 (m, 2H), 1.68-1.57 (m, 24); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.40, 118.85, 105.07, 82.58, 80.80, 55.13, 30.16, 22.18, 22.07, 21.56; HRMS (EI) calcd. for $C_{11}H_{16}O_2$ $(M)^+$: 180.1150, Found: 180.1149.



4 (d.r. = 1.3:1)

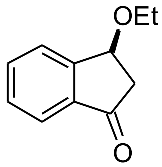
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (d, *J* = 6.4 Hz, 1H), 7.53-7.48 (m, 1H), 7.39 (t, *J* = 6.8 Hz, 1H), 7.30 (t, *J* = 7.6 Hz, 1H), 5.93 and 5.86 (s, 1H in a ratio of 1:1.3), 3.69 (s, 3H), 3.44 and 3.33 (s, 3H in a ratio of 1.3:1), 3.32 (s, 1H), 1.43 and 1.42 (d, *J* = 6.8 Hz, 3H in a ratio of 1.3:1); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.44, 173.29, 139.70, 139.63, 132.94, 132.78, 128.99, 128.73, 126.61, 128.46, 126.74, 126.36, 121.14, 120.81, 100.96, 100.26, 81.93, 81.91, 89.81, 79.89, 70.15, 54.68, 53.47, 51.88, 51.81, 18.69, 18.58; HRMS (ESI) calcd. for $C_{14}H_{16}O_4K$ $(M + K)^+$: 287.0680, Found: 287.0680.

6. Spectral Data of Products



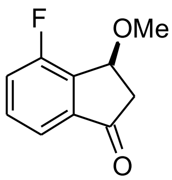
3a

Colorless oil, 92% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, *J* = 7.6 Hz, 1H), 7.70-7.63 (m, 2H), 7.50-7.45 (m, 1H), 5.62 (dd, *J* = 6.4, 2.8 Hz, 1H), 3.49 (s, 3H), 2.98 (dd, *J* = 14.4, 6.4 Hz, 1H), 2.64 (dd, *J* = 14.4, 2.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.98, 153.12, 136.76, 134.96, 129.52, 126.45, 123.22, 76.67, 57.14, 43.38; HRMS (ESI) calcd. for $C_{10}H_{11}O_2$ $(M + H)^+$: 163.0754, Found: 163.0754. HPLC (Chiralpak IC column, 90:10 hexanes/isopropanol, 1 ml/min), tr = 12.0 min (minor), 12.6 min (major); ee = 95%.



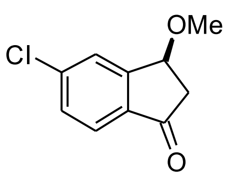
3b

Colorless oil, 90% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, J = 8.0 Hz, 1H), 7.71-7.63 (m, 2H), 7.47 (t, J = 7.2 Hz, 1H), 5.10 (dd, J = 6.4, 2.8 Hz, 1H), 3.73-3.65 (m, 2H), 3.01 (dd, J = 18.4, 6.4 Hz, 1H), 2.65 (dd, J = 18.8, 2.8 Hz, 1H), 1.28 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.20, 153.55, 136.71, 134.98, 129.38, 126.47, 123.17, 75.16, 65.29, 44.14, 15.43; HRMS (ESI) calcd. for $C_{11}H_{13}O_2$ $(M + H)^+$: 177.0910, Found: 177.0911. HPLC (Chiralpak IC column, 90:10 hexanes/isopropanol, 1 ml/min), tr = 9.5 min (minor), 10.6 min (major); ee = 90%.



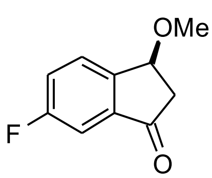
3c

White solid, 96% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (d, J = 7.6 Hz, 1H), 7.52 (td, J = 7.6, 4.4 Hz, 1H), 7.37 (t, J = 7.6 Hz, 1H), 5.24 (dd, J = 6.4, 2.0 Hz, 1H), 3.54 (d, J = 1.2 Hz, 1H), 3.02 (dd, J = 19.2, 6.8 Hz, 1H), 2.75 (dd, J = 19.2, 2.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.16 (d, J = 15 Hz), 160.43 (d, J = 252.9 Hz), 138.20 (d, J = 33 Hz), 138.55 (d, J = 17.9 Hz), 131.88 (d, J = 6.4 Hz), 121.69 (d, J = 20 Hz), 119.30 (d, J = 48 Hz), 74.17, 57.52 (d, J = 2.0 Hz), 43.59; HRMS (ESI) calcd. for $C_{10}H_{10}O_5F$ $(M + H)^+$: 181.0659, Found: 181.0661. HPLC (Chiralpak IC column, 95:05 hexanes/isopropanol, 1 ml/min), tr = 12.8 min (minor), 13.5 min (major); ee = 94%.



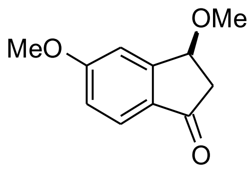
3d

White solid, 90% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72-7.69 (m, 2H), 7.48 (dd, J = 8.0, 1.6 Hz, 1H), 5.01 (dd, J = 6.4, 2.8 Hz, 1H), 3.53 (s, 3H), 3.03 (dd, J = 18.8, 6.4 Hz, 1H), 2.69 (dd, J = 18.8, 3.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.33, 154.65, 141.55, 135.18, 130.30, 126.79, 124.47, 76.25, 57.37, 43.54; HRMS (ESI) calcd. for $C_{10}H_{10}O_2Cl$ $(M + H)^+$: 197.0364, Found: 197.0365. HPLC (Chiralpak IC column, 90:10 hexanes/isopropanol, 1 ml/min), tr = 9.1 min (major), 9.9 min (minor); ee = 89%.



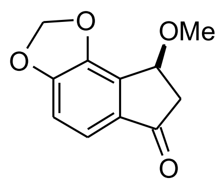
3e

Light color solid, 94% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69-7.64 (m, 1H), 7.39-7.30 (m, 2H), 4.98 (dd, J = 6.4, 2.0 Hz, 1H), 3.48 (s, 3H), 3.02 (dd, J = 18.8, 6.4 Hz, 1H), 2.68 (dd, J = 18.8, 2.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.73 (d, J = 3.8 Hz), 163.60 (d, J = 249.1 Hz), 148.77 (d, J = 1.8 Hz), 138.75 (d, J = 7.4 Hz), 128.19 (d, J = 8.6 Hz), 122.61 (d, J = 23.1 Hz), 109.14 (d, J = 22.1 Hz), 76.12, 57.17, 43.96; HRMS (ESI) calcd. for $C_{10}H_{10}O_2F$ $(M + H)^+$: 181.0659, Found: 181.0660. HPLC (Chiralpak IC column, 95:05 hexanes/isopropanol, 1 ml/min), tr = 10.7 min (minor), 11.3 min (major); ee = 83%



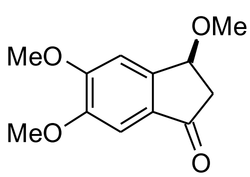
3f

Yellow powder, 95% yield. [1]H NMR (400 MHz, $CDCl_3$) δ 7.66 (d, *J* = 8.4 Hz, 1H), 7.09 (s, 1H), 6.98 (dd, *J* = 8.4, 2.0 Hz, 1H), 4.95 (dd, *J* = 6.4, 2.8 Hz, 1H), 3.89 (s, 3H), 3.47 (s, 3H), 2.95 (dd, *J* = 18.4, 6.4 Hz, 1H), 2.62 (dd, *J* = 18.4, 2.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.05, 165.52, 156.12, 130.01, 124.88, 117.76, 109.06, 76.48, 57.00, 55.71, 43.43; HRMS (ESI) calcd. for $C_{11}H_{13}O_3$ $(M + H)^+$: 193.0859, Found: 193.0859. HPLC (Chiralpak IC column, 80:20 hexanes/isopropanol, 1 ml/min), tr = 13.3 min (major), 15.4 min (minor); ee = 85%



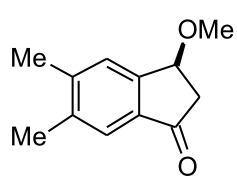
3g

Yellow powder, 80% yield. [1]H NMR (400 MHz, $CDCl_3$) δ 7.36 (d, *J* = 8.0 Hz, 1H), 6.94 (d, *J* = 8.4 Hz, 1H), 6.16 (d, *J* = 0.8 Hz, 1H), 6.10 (d, *J* = 0.8 Hz, 1H), 5.08 (dd, *J* = 6.8, 2.4 Hz, 1H), 3.51 (s, 3H), 2.96 (dd, *J* = 18.8, 6.8 Hz, 1H), 2.65 (dd, *J* = 18.8, 2.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.81, 153.26, 144.37, 132.35, 132.33, 118.81, 110.38, 102.52, 74.08, 57.41, 43.79; HRMS (ESI) calcd. for $C_{11}H_{11}O_4$ $(M + H)^+$: 207.0652, Found: 207.0652. HPLC (Chiralpak IC column, 80:20 hexanes/isopropanol, 1 ml/min), tr = 16.8 min (major), 26.6 min (minor); ee = 91%.



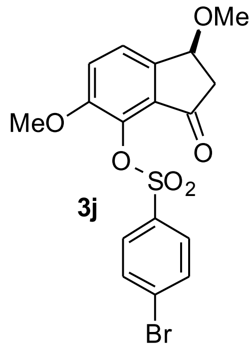
3h

Yellow powder, 92% yield. [1]H NMR (400 MHz, $CDCl_3$) δ 7.15 (s, 1H), 7.08 (s, 1H), 4.99 (dd, *J* = 6.4, 2.4 Hz, 1H), 3.99 (s, 3H), 3.91 (s, 3H), 3.46 (s, 3H), 2.95 (dd, *J* = 18.4, 6.4 Hz, 1H), 2.61 (dd, *J* = 18.4, 2.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.50, 155.69, 151.03, 148.35, 130.00, 107.06, 103.58, 76.52, 56.95, 56.36, 56.20, 43.30; HRMS (ESI) calcd. for $C_{12}H_{15}O_4$ $(M + H)^+$: 223.0965, Found: 223.0965. HPLC (Chiralpak IC column, 80:20 hexanes/isopropanol, 1 ml/min), tr = 20.5 min (major), 21.9 min (minor); ee = 98%.



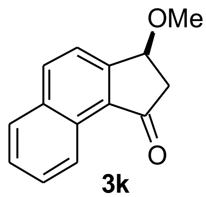
3i

Yellow solid, 97% yield. [1]H NMR (400 MHz, $CDCl_3$) δ 7.50 (s, 1H), 7.44 (s, 1H), 4.96 (dd, *J* = 6.0, 2.4 Hz, 1H), 3.47 (s, 3H), 2.94 (dd, *J* = 18.4, 6.4 Hz, 1H), 2.60 (dd, *J* = 18.4, 2.8 Hz, 1H), 2.36 (s, 3H), 2.31 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.81, 151.33, 145.28, 138.67, 134.98, 127.04, 123.55, 76.3, 57.00, 43.53, 20.74, 19.90; HRMS (ESI) calcd. for $C_{12}H_{15}O_2$ $(M + H)^+$: 191.1067, Found: 191.1068. HPLC (Chiralpak IA column, 98:02 hexanes/isopropanol, 1 ml/min), tr = 12.5 min (major), 13.9 min (minor); ee = 99%



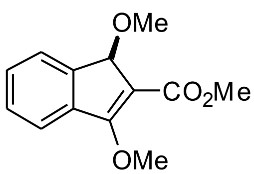
3j

Yellow powder, 85% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, *J* = 8.8 Hz, 2H), 7.69 (d, *J* = 8.8 Hz, 2H), 7.55 (d, *J* = 8.4 Hz, 1H), 7.25 (d, *J* = 8.4 Hz, 1H), 4.91 (dd, *J* = 6.4, 2.8 Hz, 1H), 3.67 (s, 3H), 3.45 (s, 3H), 2.95 (dd, *J* = 18.4, 6.4 Hz, 1H), 2.62 (dd, *J* = 18.4, 2.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.45, 153.00, 145.65, 136.12, 132.68, 132.00, 130.80, 130.03, 129.12, 125.92, 119.82, 75.43, 57.10, 56.52, 44.48; HRMS (ESI) calcd. for $C_{17}H_{15}O_6BrKS$ $(M + H)^+$: 464.9404, Found: 464.9405. HPLC (Chiralpak IA column, 90:10 hexanes/isopropanol, 1 ml/min), tr = 18.5 min (minor), 23.0 min (major); ee = 97%



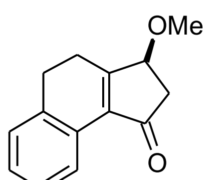
3k

White solid, 94% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.13 (d, *J* = 8.4 Hz, 1H), 8.10 (d, *J* = 8.4 Hz, 1H), 7.90 (d, *J* = 8.0 Hz, 1H), 7.71 (d, *J* = 8.4 Hz, 1H), 7.68 (d, *J* = 8.0 Hz, 1H), 7.59 (t, *J* = 8.0 Hz, 1H), 5.09 (dd, *J* = 6.4, 2.4 Hz, 1H), 3.53 (s, 3H), 3.10 (dd, *J* = 18.4, 6.4 Hz, 1H), 2.78 (dd, *J* = 18.4, 2.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.26, 155.60, 136.13, 133.65, 131.17, 129.09, 128.66, 128.16, 127.28, 124.66, 122.87, 76.31, 57.14, 43.82; HRMS (ESI) calcd. for $C_{14}H_{13}O_2$ $(M + H)^+$: 213.0910, Found: 213.0911. HPLC (Chiralpak IC column, 85:15 hexanes/isopropanol, 1 ml/min), tr = 10.1 min (minor), 15.1 min (major); ee = 99%



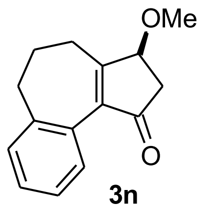
3l

Colorless oil, 97% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55-7.49 (m, 2H), 7.45-7.38 (m, 2H), 5.48 (s, 1H), 4.30 (s, 3H), 3.87 (s, 3H), 3.14 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.05, 164.98, 141.51, 138.45, 129.46, 128.80, 124.05, 120.79, 106.91, 81.21, 61.37, 52.25, 51.58; HRMS (ESI) calcd. for $C_{13}H_{15}O_4$ $(M + H)^+$: 235.0965, Found: 235.0967. HPLC (Chiralpak IA column, 98:02 hexanes/isopropanol, 1 ml/min), tr = 10.1 min (major), 15.1 min (minor); ee = 60%



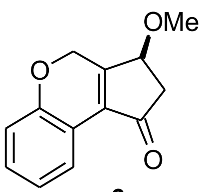
3m

Yellow powder, 83% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26-8.20 (m, 1H), 7.26-7.18 (m, 3H), 4.55 (d, *J* = 6.0 Hz, 1H), 3.45 (s, 3H), 3.00-2.94 (m, 2H), 2.91-2.81 (m, 2H), 2.69-2.49 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.99, 170.51, 136.43, 135.18, 128.57, 128.27, 127.66, 126.74, 124.85, 77.67, 57.13, 42.44, 27.46, 23.60; HRMS (ESI) calcd. for $C_{14}H_{15}O_2$ $(M + H)^+$: 215.1067, Found: 215.1068. HPLC (Chiralpak IC column, 80:10 hexanes/isopropanol, 1 ml/min), tr = 13.8 min (minor), 16.1 min (major); ee = 98%



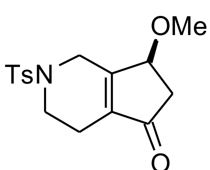
3n

Yellow powder, 79% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.28 (td, *J* = 7.2, 1.6 Hz, 1H), 7.23 (td, *J* = 7.2, 1.6 Hz, 1H), 7.18 (dd, *J* = 7.2, 1.6 Hz, 1H), 4.48 (dd, *J* = 6.0, 2.0 Hz, 1H), 3.45 (s, 3H), 2.87-2.76 (m, 2H), 2.71-2.60 (m, 2H), 2.60-2.49 (m, 2H), 2.21-2.12 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.21, 172.59, 142.55, 139.22, 129.90, 129.32, 128.86, 128.20, 125.99, 79.18, 57.14, 41.40, 33.70, 29.75, 29.30; HRMS (ESI) calcd. for $C_{15}H_{17}O_2$ $(M + H)^+$: 229.1223, Found: 229.1224. HPLC (Chiralpak IA column, 90:10 hexanes/isopropanol, 1 ml/min), tr = 6.7 min (minor), 7.1 min (major); ee = 94%



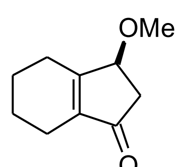
3o

Yellow powder, 58% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (dd, *J* = 8.0, 2.0 Hz, 1H), 7.24 (td, *J* = 8.0, 1.6 Hz, 1H), 6.97 (td, *J* = 7.2, 1.2 Hz, 1H), 6.98 (dd, *J* = 8.0, 1.2 Hz, 1H), 5.32 (d, *J* = 16.8 Hz, 1H), 4.61 (dd, *J* = 5.6, 1.6 Hz, 1H), 3.40 (s, 3H), 2.88 (dd, *J* = 18.0, 6.0 Hz, 1H), 2.56 (dd, *J* = 18.0, 2.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.20, 160.70, 152.98, 132.96, 130.75, 125.03, 121.66, 116.33, 115.91, 76.38, 65.90, 57.28, 42.42; HRMS (EI) calcd. for $C_{13}H_{12}O_3$ $(M)^+$: 216.0786, Found: 216.0785. HPLC (Chiralpak IC column, 80:10 hexanes/isopropanol, 1 ml/min), tr = 13.2 min (minor), 14.5 min (major); ee = 98%



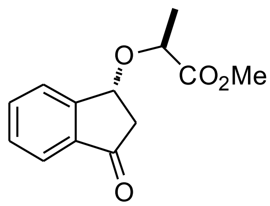
3p

Yellow powder, 80% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, *J* = 8.0 Hz, 1H), 7.34 (d, *J* = 8.0 Hz, 1H), 4.44 (d, *J* = 5.2 Hz, 1H), 4.09 (d, *J* = 17.6 Hz, 1H), 3.92 (d, *J* = 18.0 Hz, 1H), 3.38 (s, 3H), 3.34-3.26 (m, 1H), 3.25-3.15 (m, 1H), 2.70 (dd, *J* = 18.4, 6.0 Hz, 1H), 2.44 (s, 3H), 2.36-2.29 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.12, 163.92, 144.04, 138.99, 133.35, 129.91, 127.58, 77.47, 57.51, 45.18, 42.37, 41.44, 21.53, 20.45; HRMS (ESI) calcd. for $C_{16}H_{20}O_4N_1NS_1$ $(M + H)^+$: 322.1108, Found: 322.1111. HPLC (Chiralpak IA column, 94:06 hexanes/isopropanol, 1 ml/min), tr = 42.2 min (major), 45.1 min (minor); ee = 84%



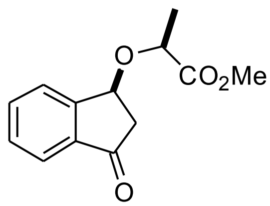
3q

Colorless oil, 71% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.41-4.36 (m, 1H), 3.38 (s, 3H), 2.67 (dd, *J* = 18.0, 5.6 Hz, 1H), 2.64-2.55 (m, 1H), 2.33 (dd, *J* = 18.0, 2.0 Hz, 1H), 2.30-2.10 (m, 3H), 1.82-1.57 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 204.59, 170.34, 141.13, 79.14, 57.19, 41.21, 25.29, 21.93, 21.46, 19.79; HRMS (ESI) calcd. for $C_{10}H_{15}O_2$ $(M + H)^+$: 167.1067, Found: 167.1068. HPLC (Chiralpak IC column, 80:10 hexanes/isopropanol, 1 ml/min), tr = 14.3 min (major), 15.0 min (minor); ee = 90%



5a

Colorless oil, d.r. = 5.0:1. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, *J* = 8.0 Hz, 1H), 7.82-7.68 (m, 2H), 7.53 (t, *J* = 7.2 Hz, 1H), 5.20 (dd, *J* = 6.0, 2.4 Hz, 1H), 4.28 (q, *J* = 6.8 Hz, 1H), 3.86 (s, 3H), 3.06 (dd, *J* = 18.4, 6.4 Hz, 1H), 2.65 (dd, *J* = 18.4, 2.8 Hz, 1H), 1.50 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.64, 173.61, 153.09, 136.68, 134.27, 129.69, 127.15, 123.09, 74.77, 73.85, 52.15, 44.11, 19.20; HRMS (ESI) calcd. for $C_{13}H_{15}O_4$ $(M + H)^+$: 235.0965, Found: 235.0967.

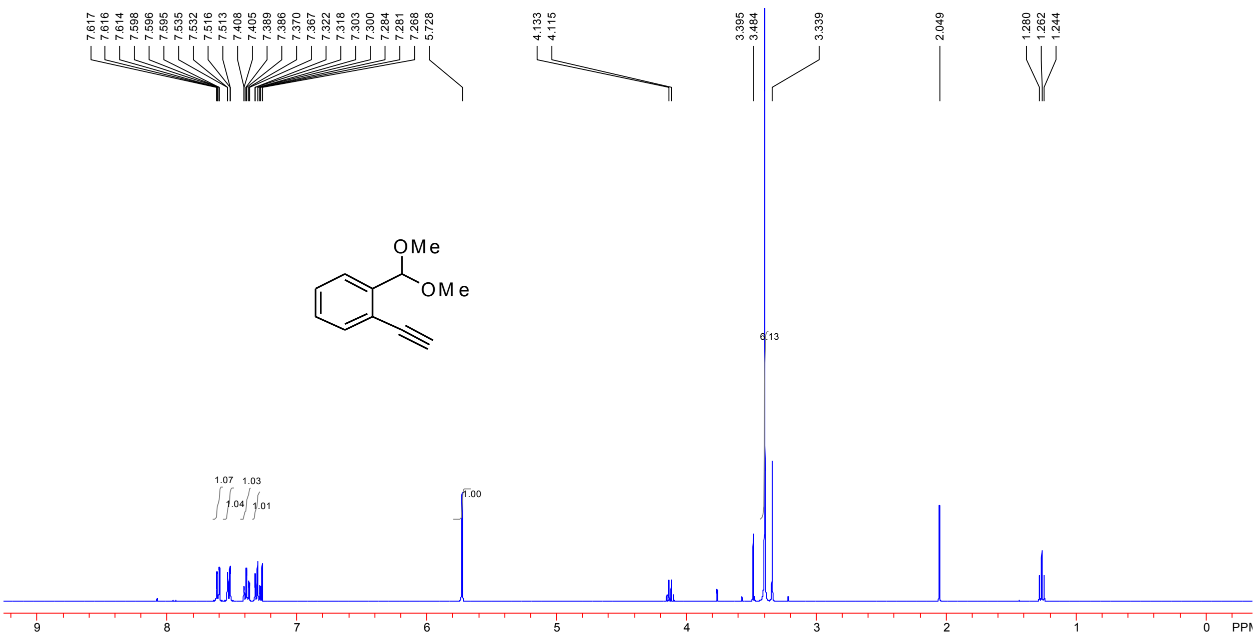


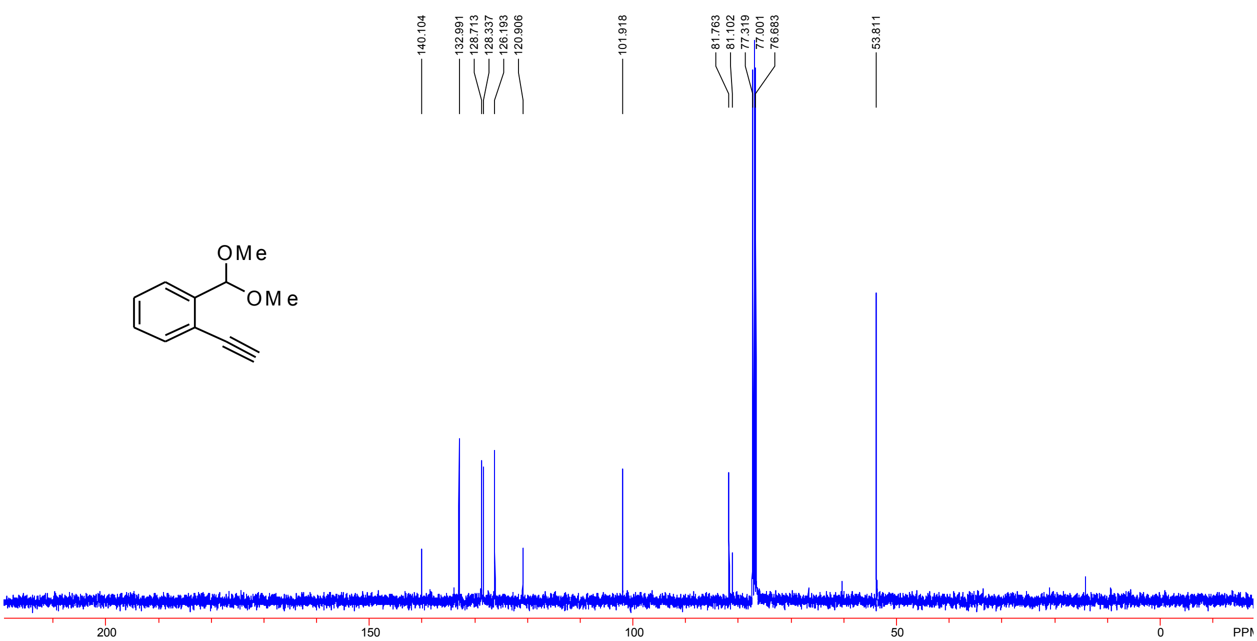
5b

Colorless oil, d.r. = 6.6:1. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, *J* = 7.6 Hz, 1H), 7.70-7.64 (m, 2H), 7.52-7.47 (m, 1H), 5.18 (dd, *J* = 6.4, 2.8 Hz, 1H), 4.36 (q, *J* = 6.8 Hz, 1H), 3.78 (s, 3H), 3.02 (dd, *J* = 18.4, 6.4 Hz, 1H), 2.79 (dd, *J* = 18.8, 2.8 Hz, 1H), 1.51 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.76, 173.35, 152.83, 136.72, 134.93, 129.64, 126.43, 123.29, 75.54, 74.92, 52.16, 44.88, 18.76; HRMS (ESI) calcd. for $C_{13}H_{15}O_4$ $(M + H)^+$: 239.0905, Found: 235.0966.

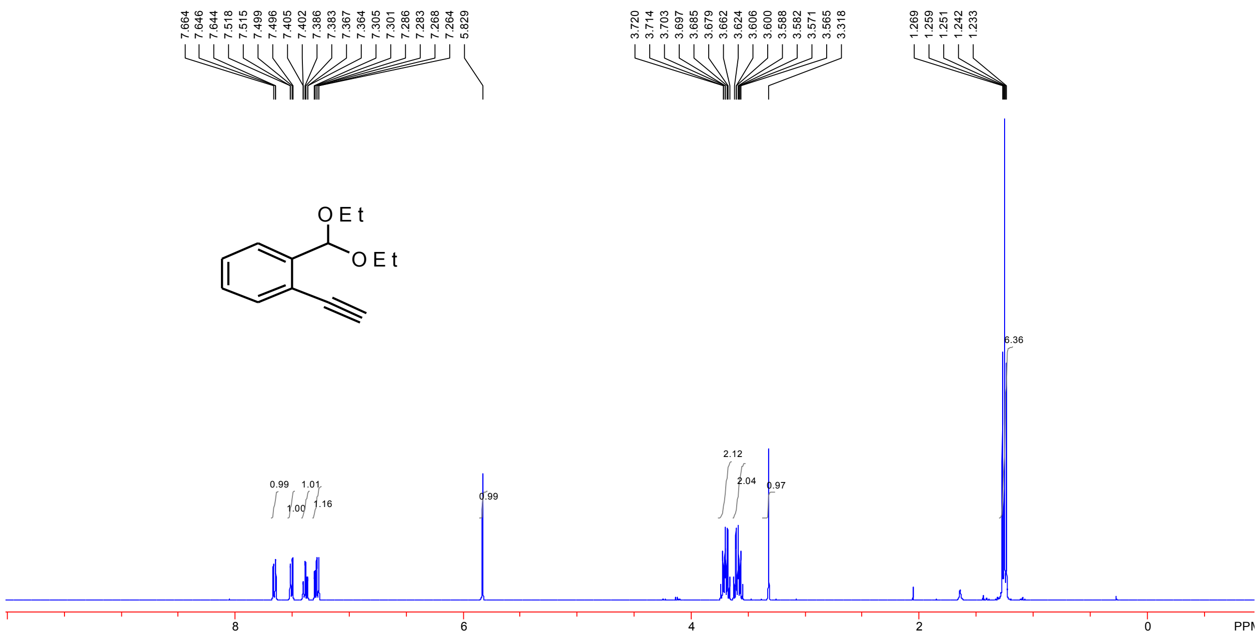
7. Spectral Data

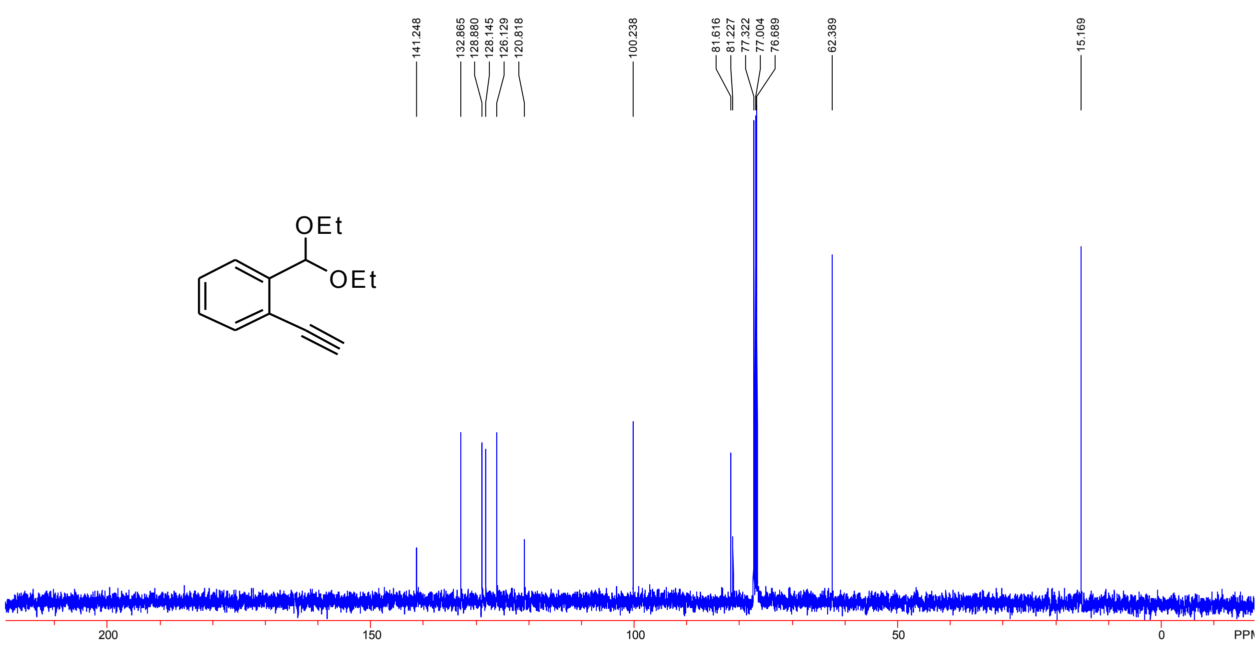
^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) of **1a**



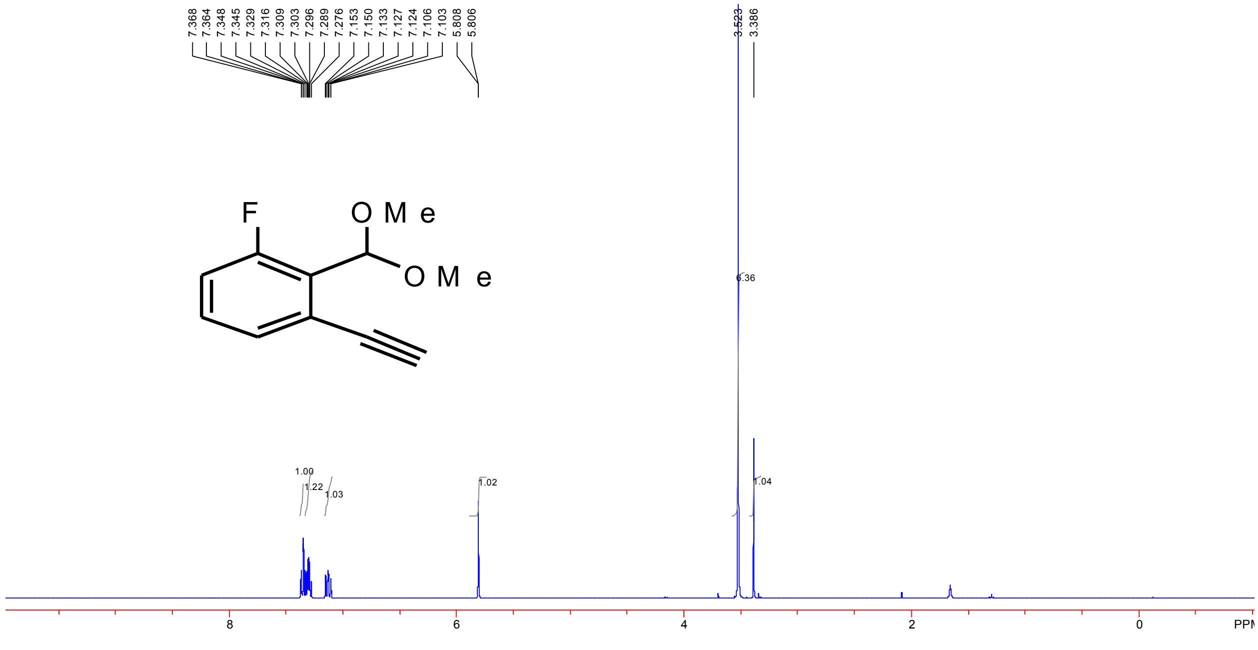


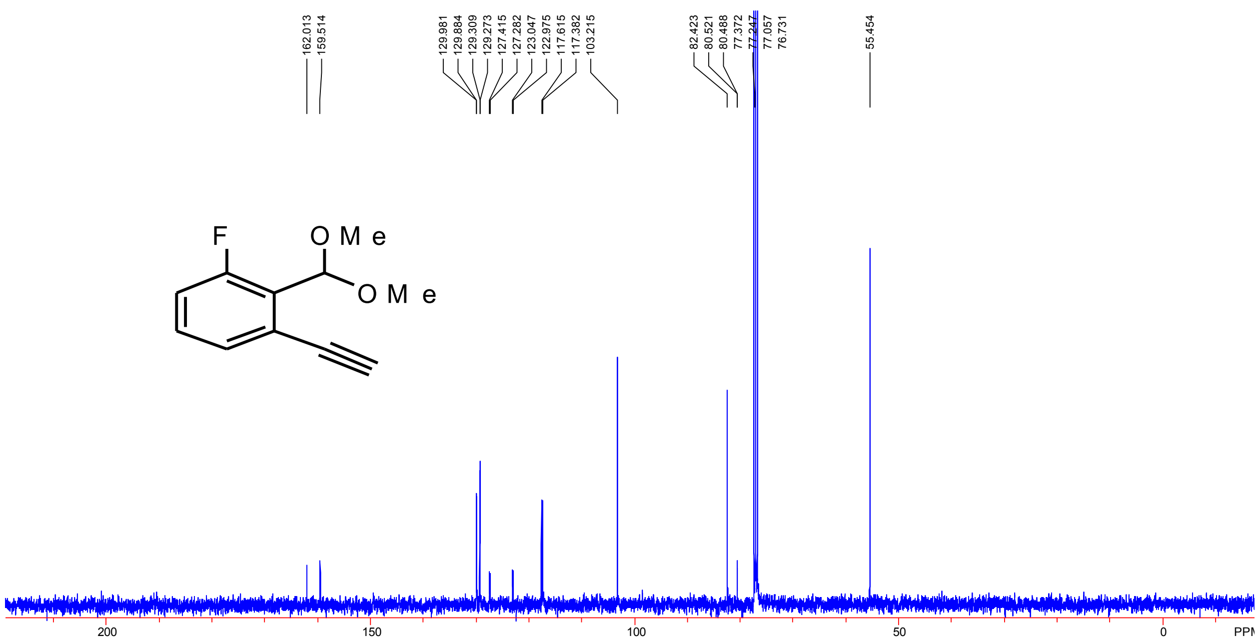
^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) of **1b**



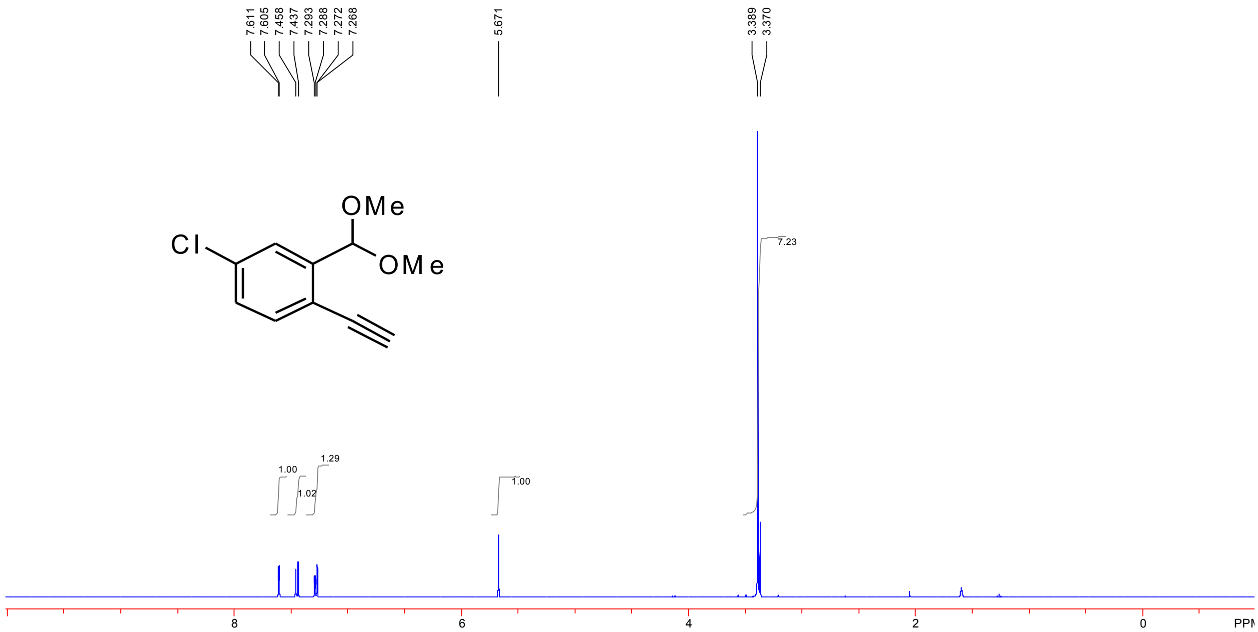


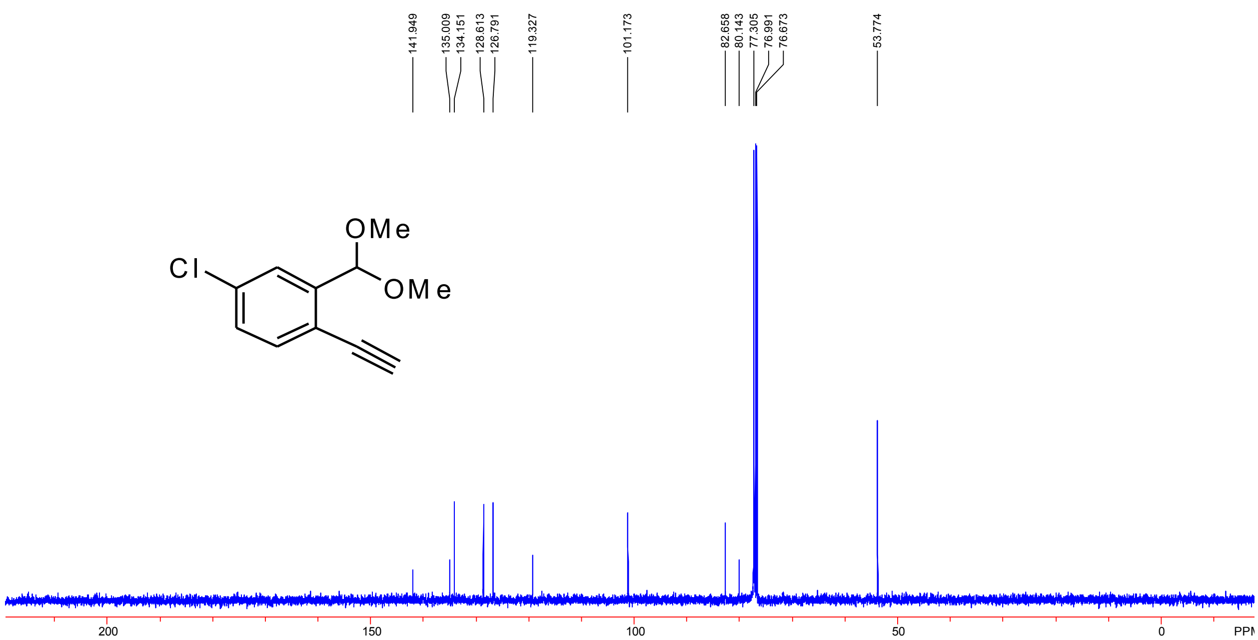
^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) of **1c**



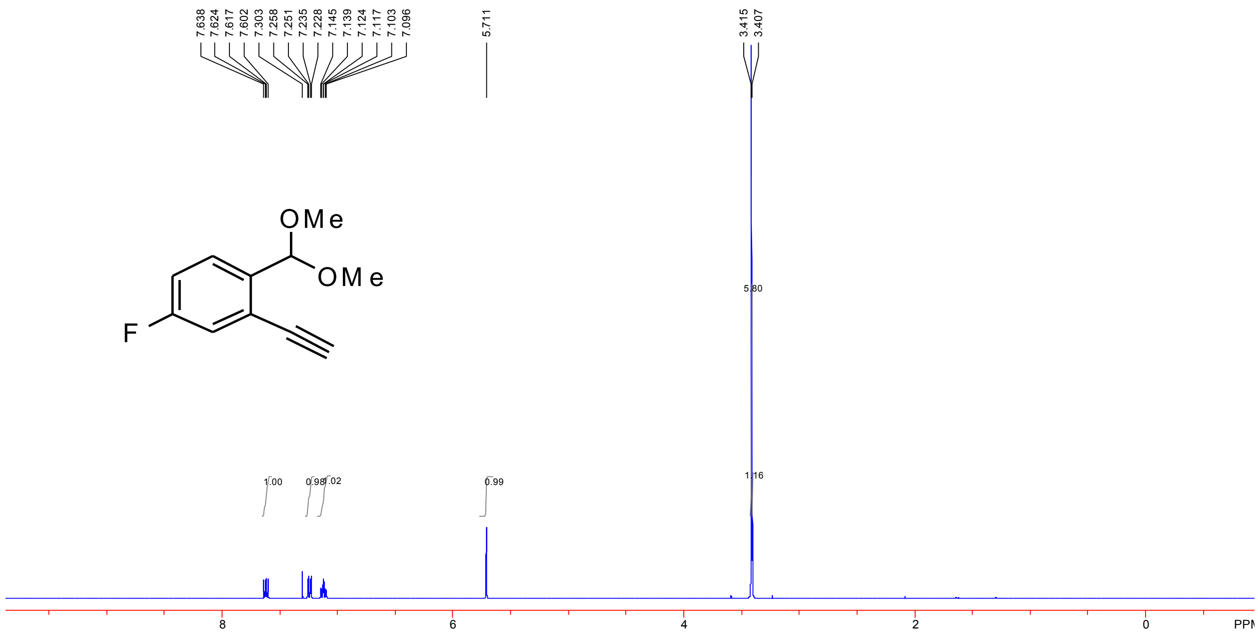


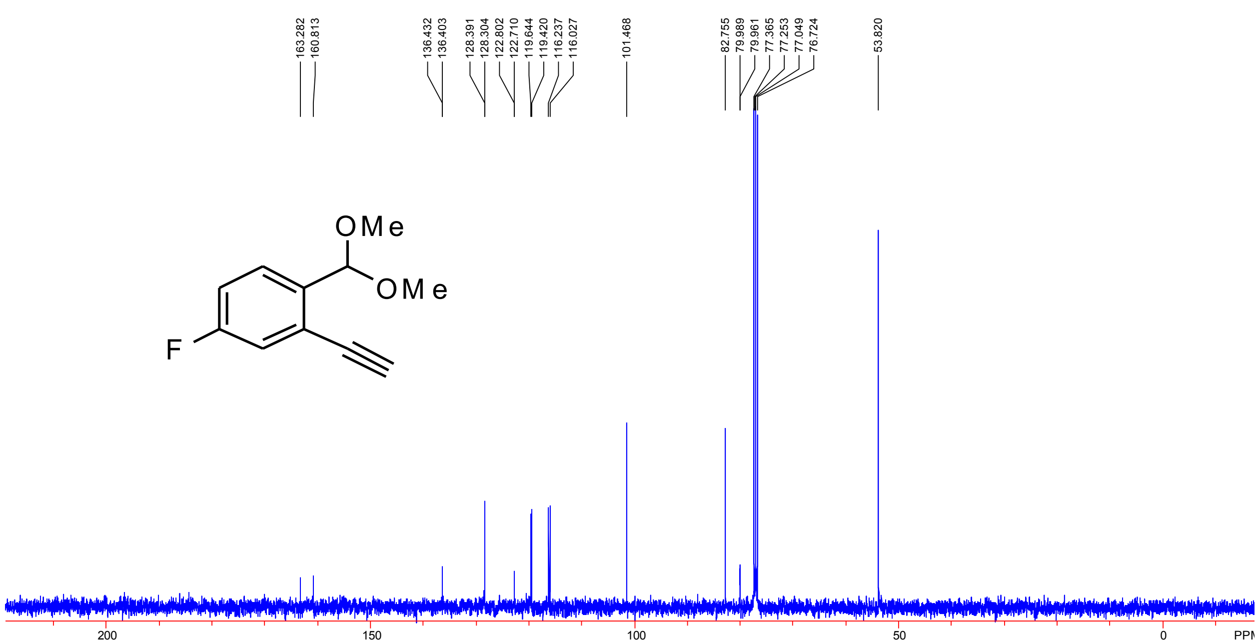
^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) of **1d**



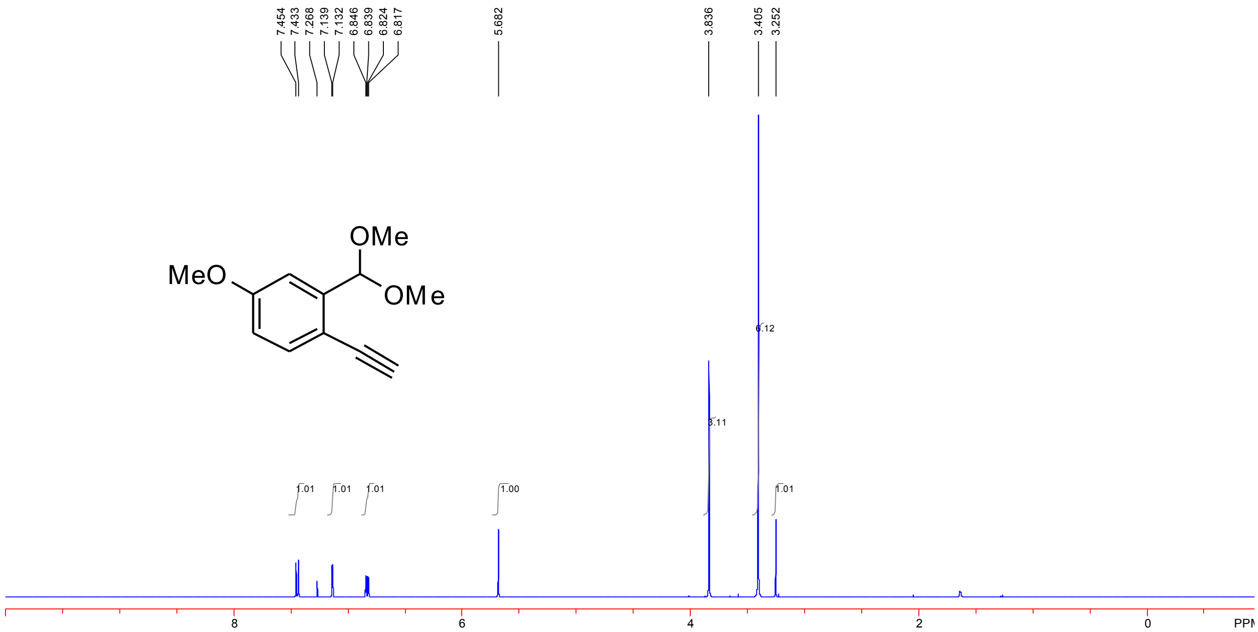


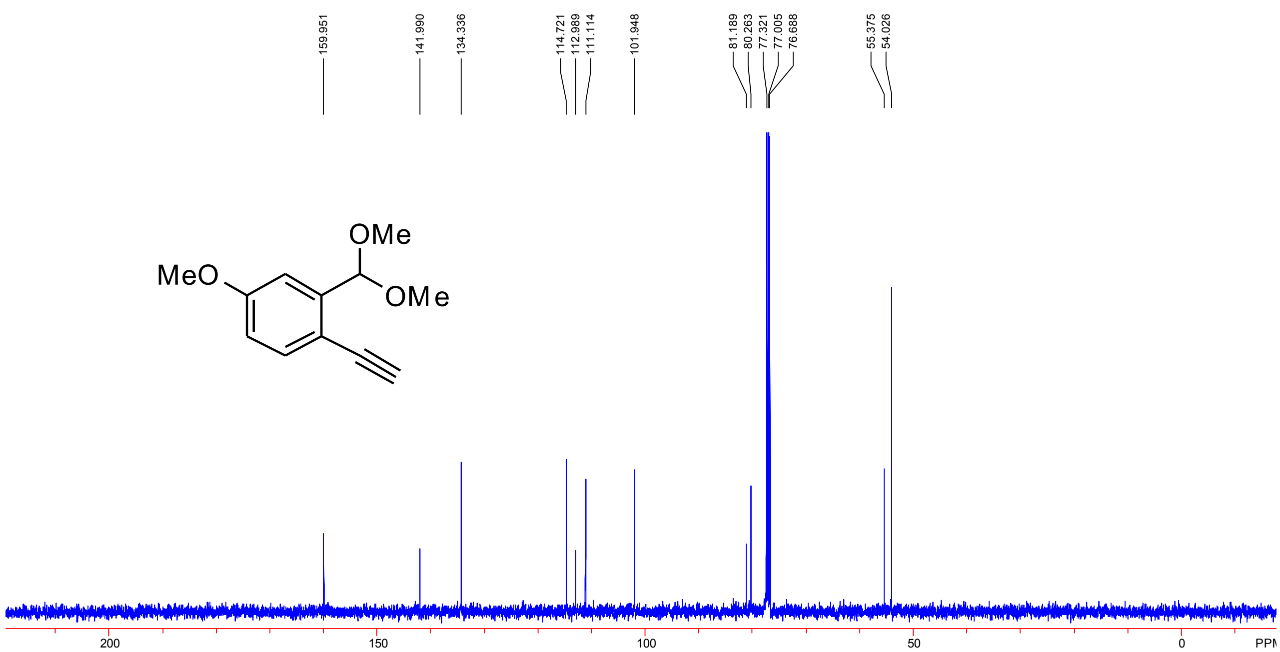
^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) of **1e**



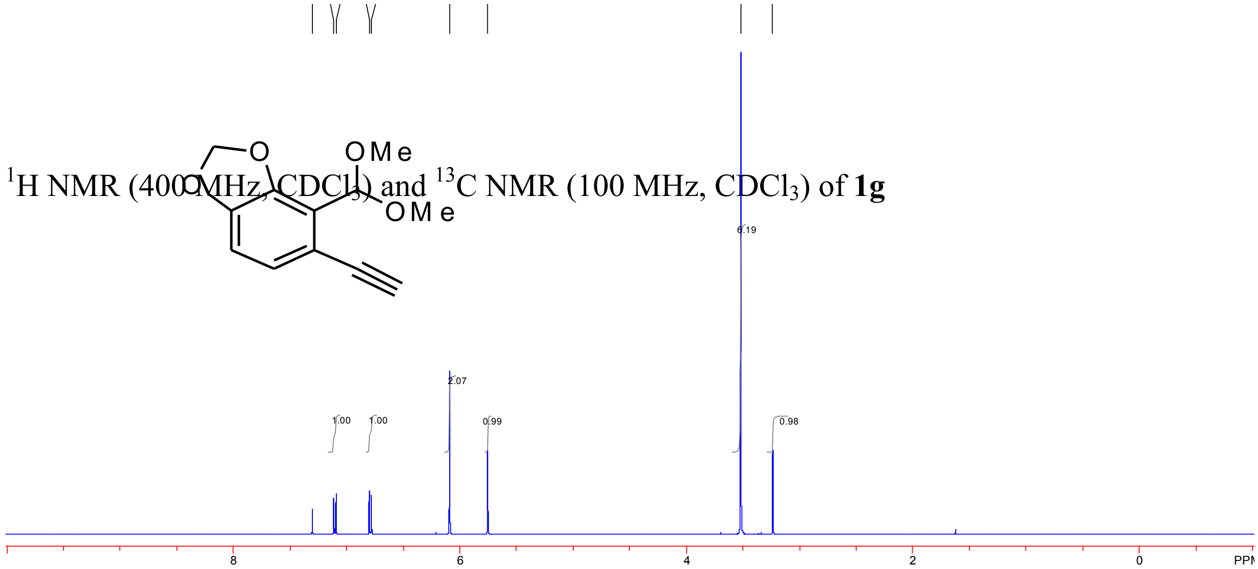


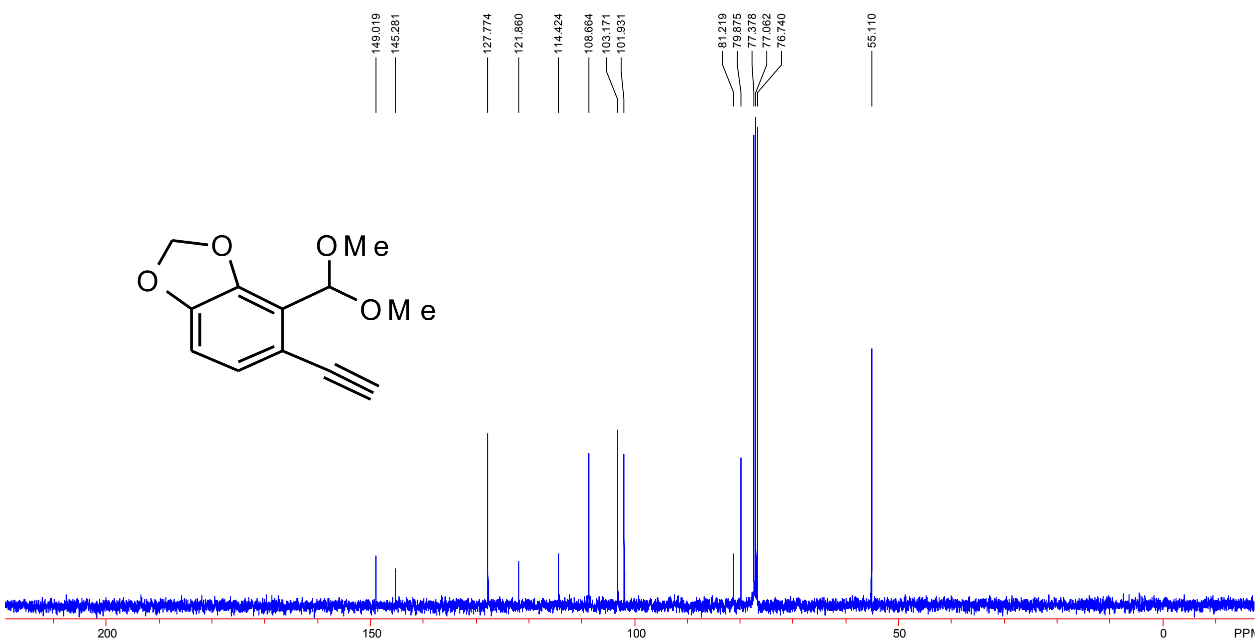
^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) of **1f**



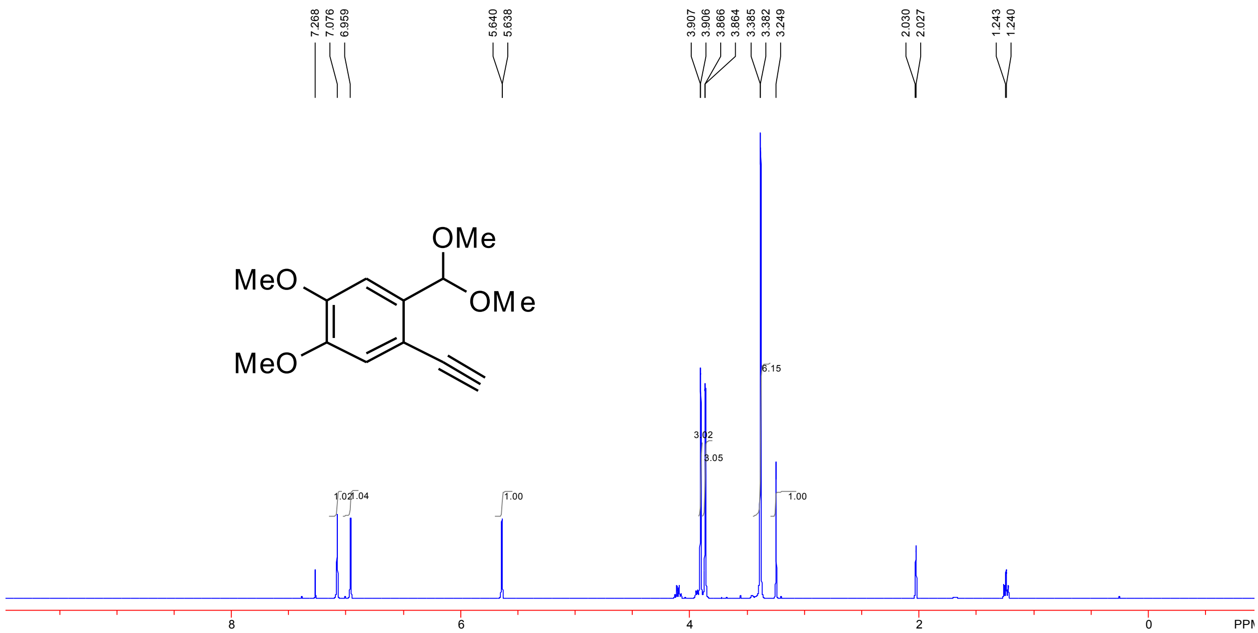


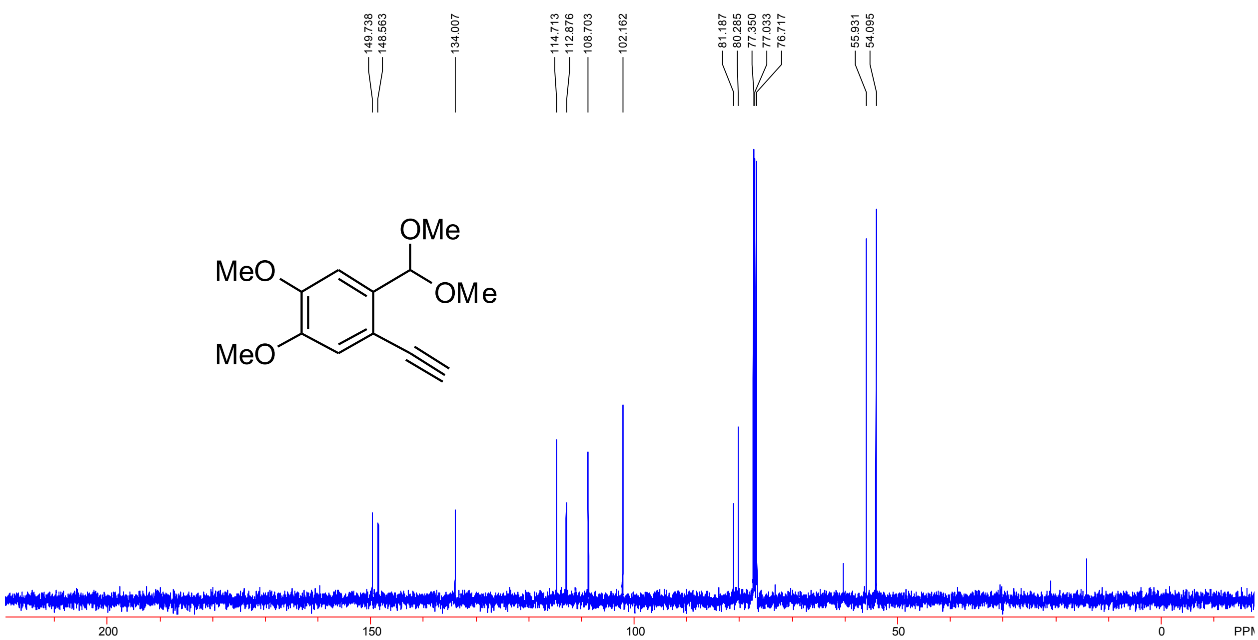
^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) of **1g**



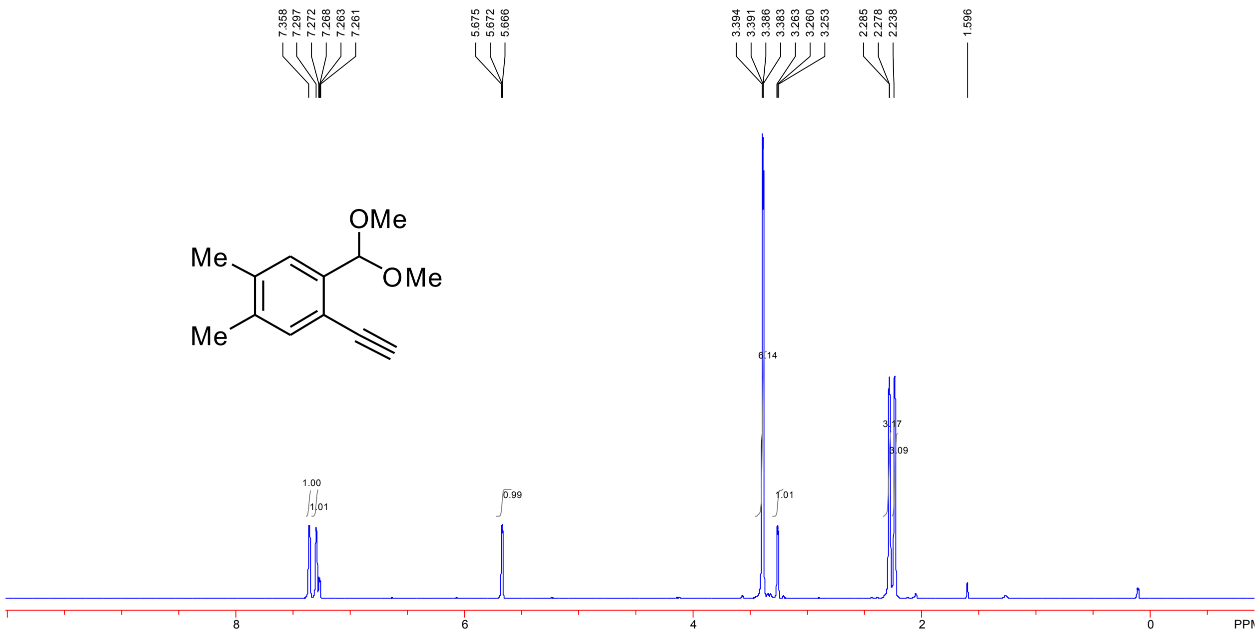


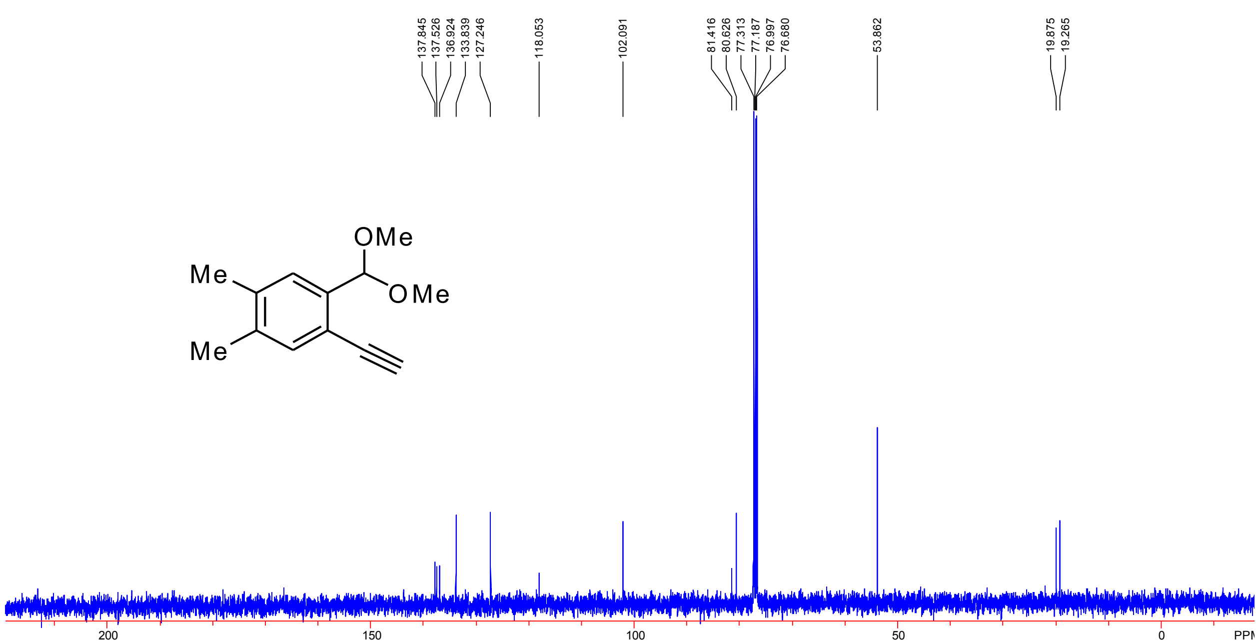
^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) of **1h**



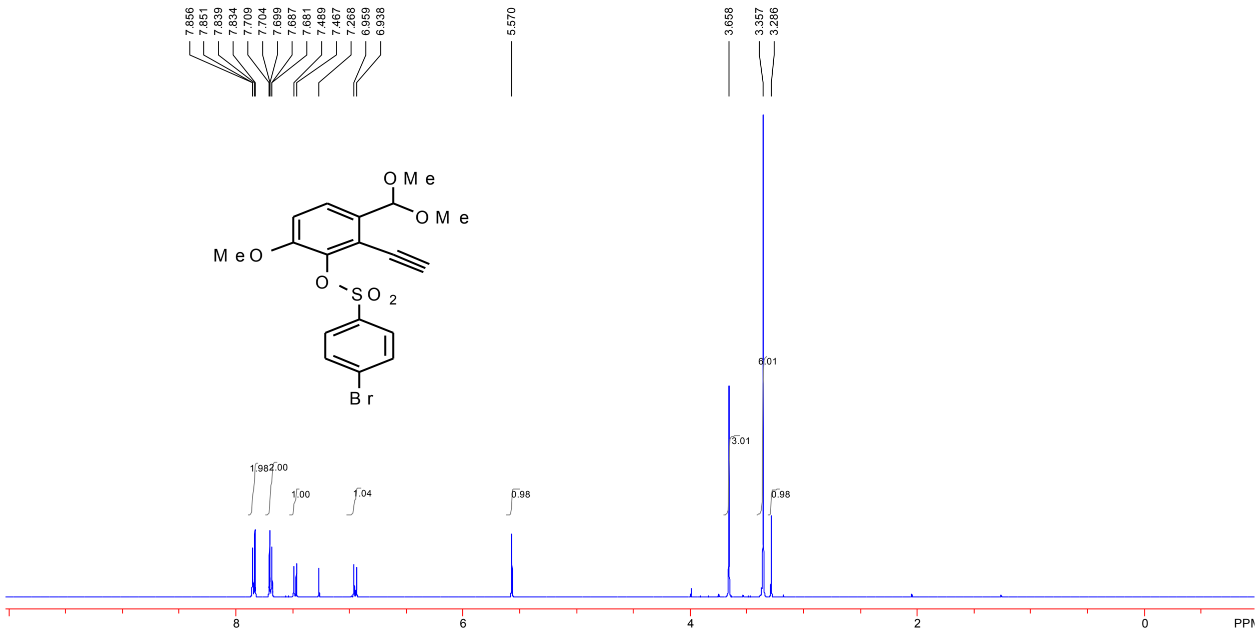


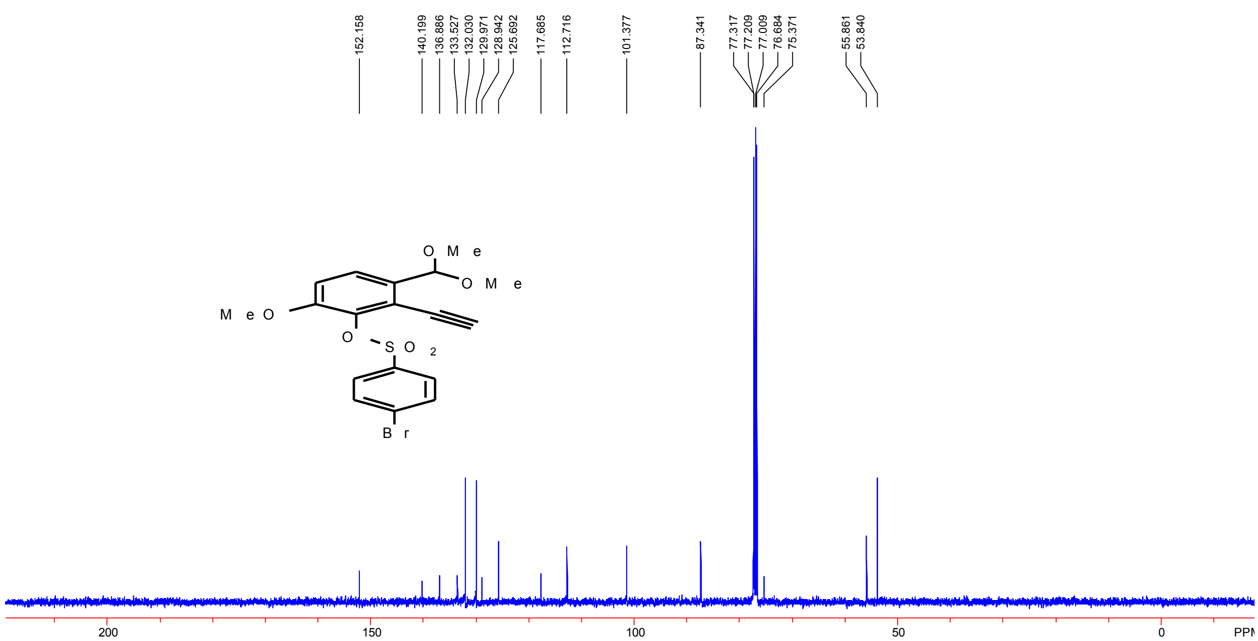
^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) of **1i**



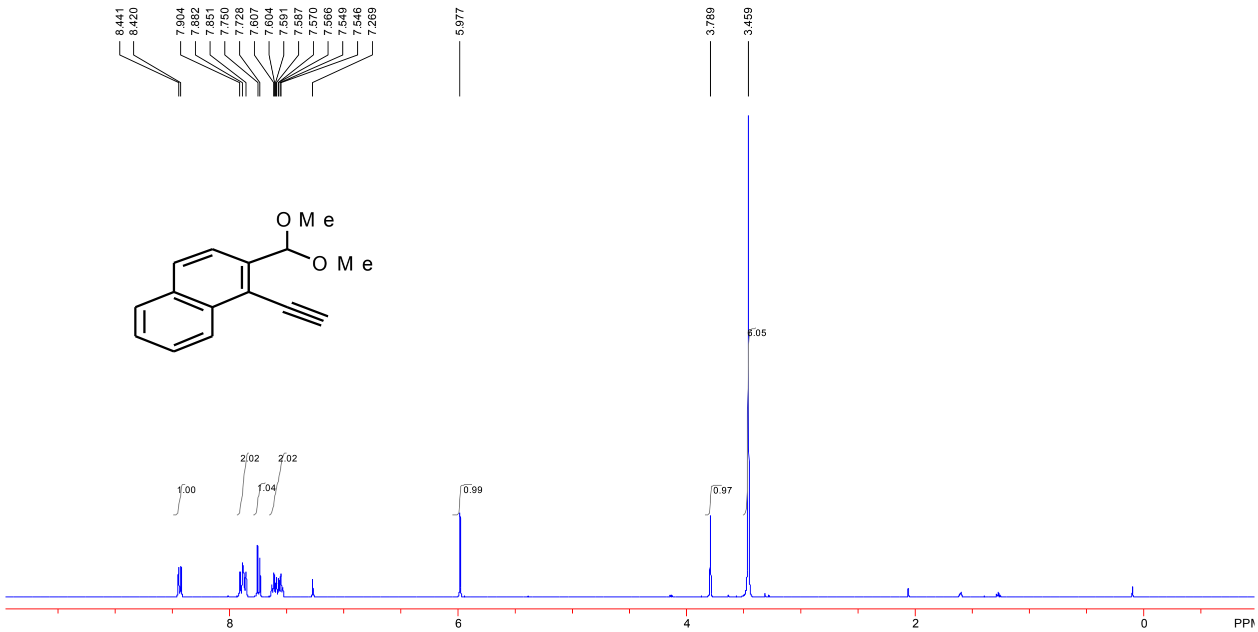


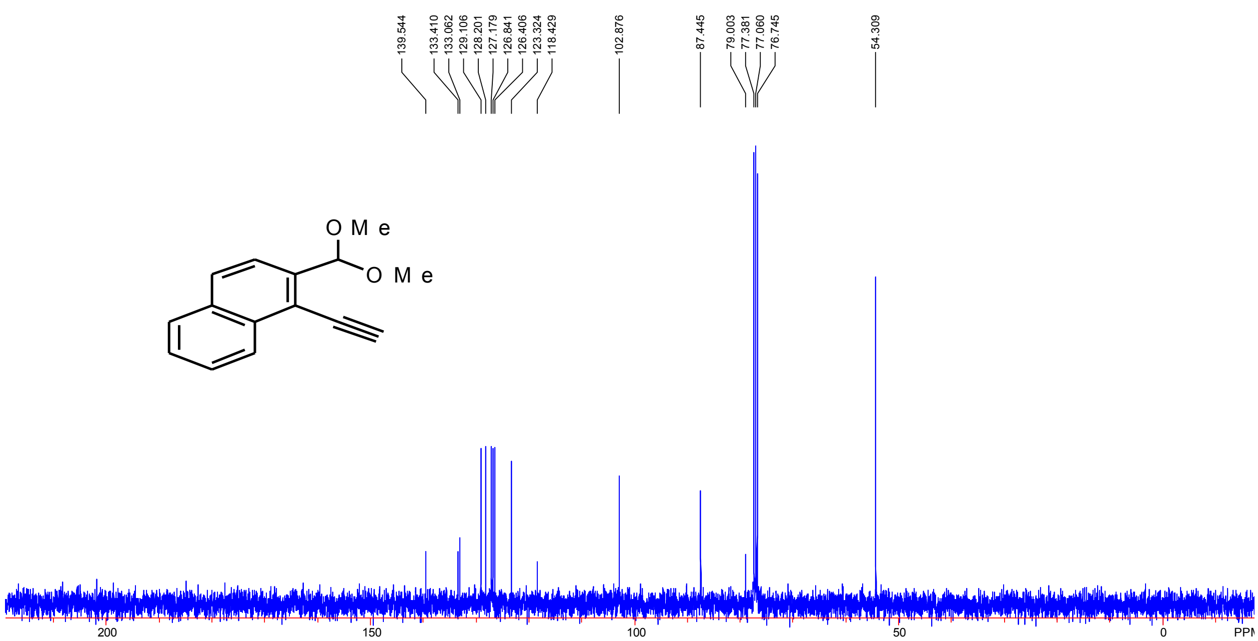
^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) of **1j**



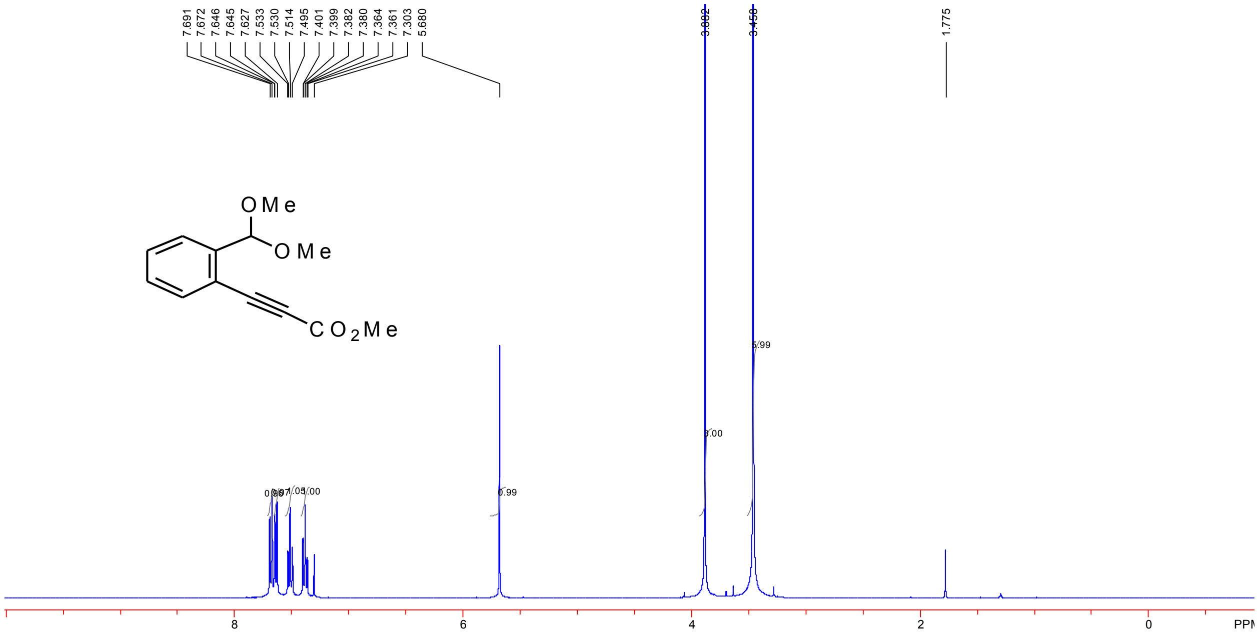


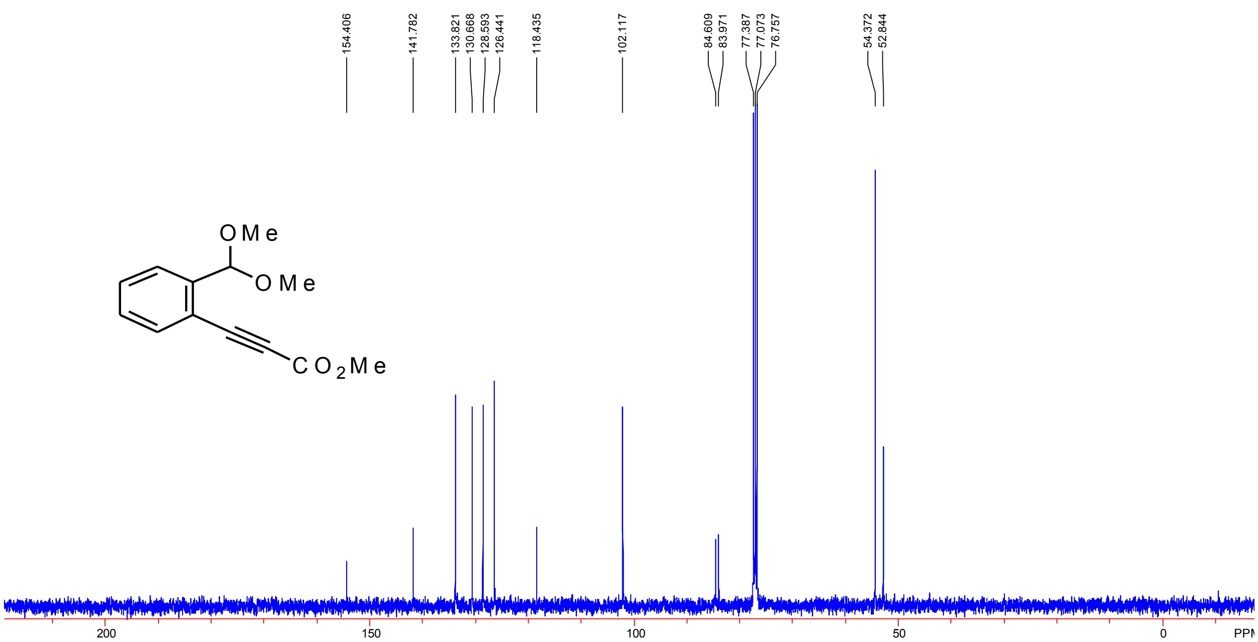
[1]H NMR (400 MHz, $CDCl_3$) and [13]C NMR (100 MHz, $CDCl_3$) of **1k**



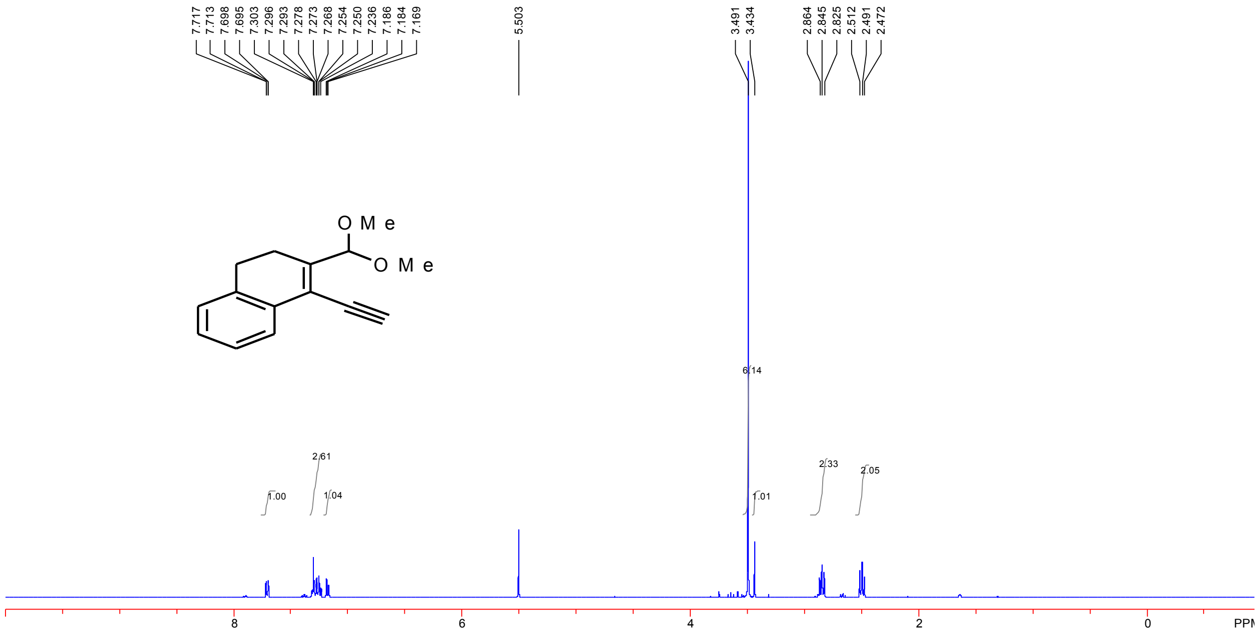


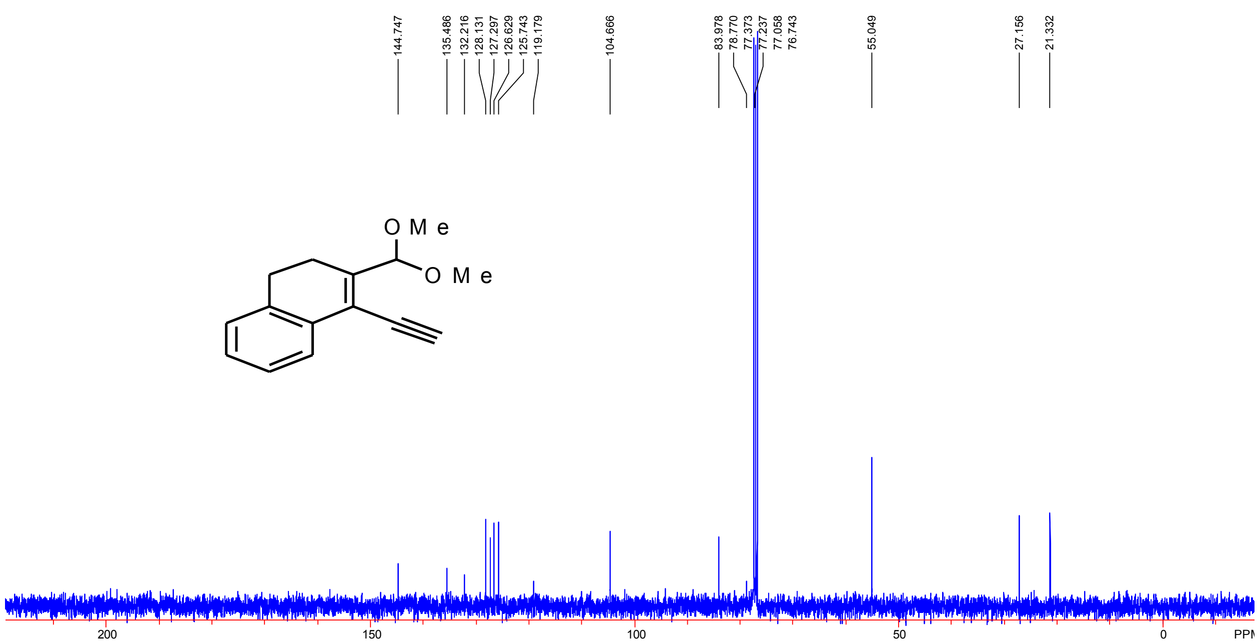
^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) of **1l**



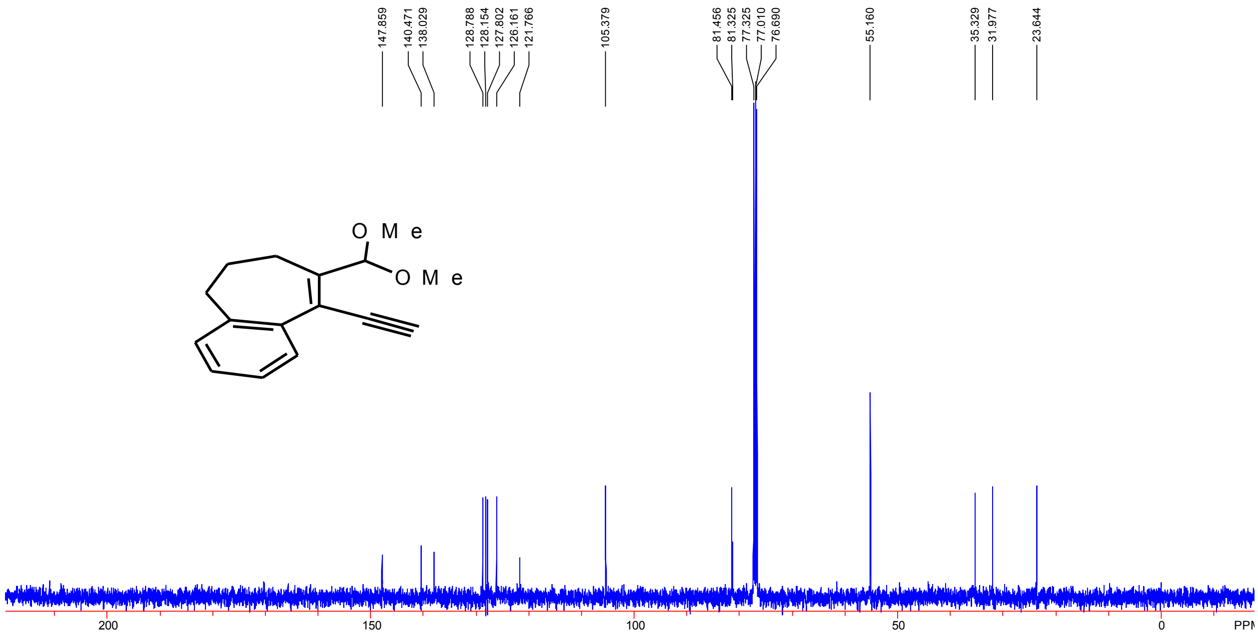


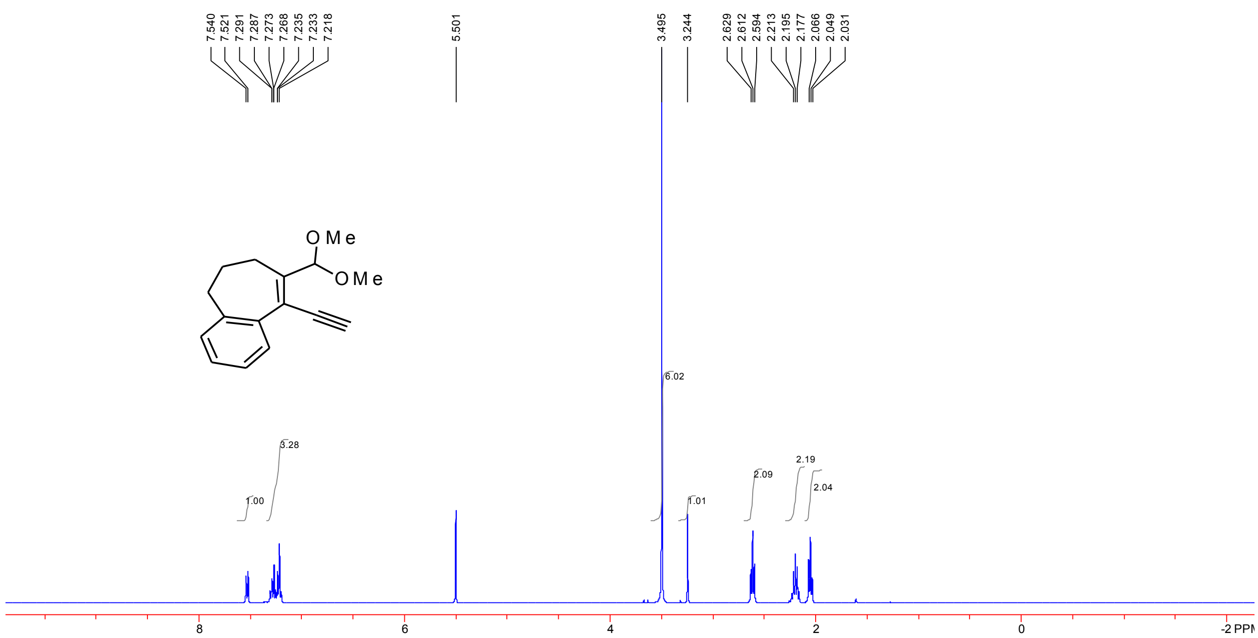
^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) of **1m**



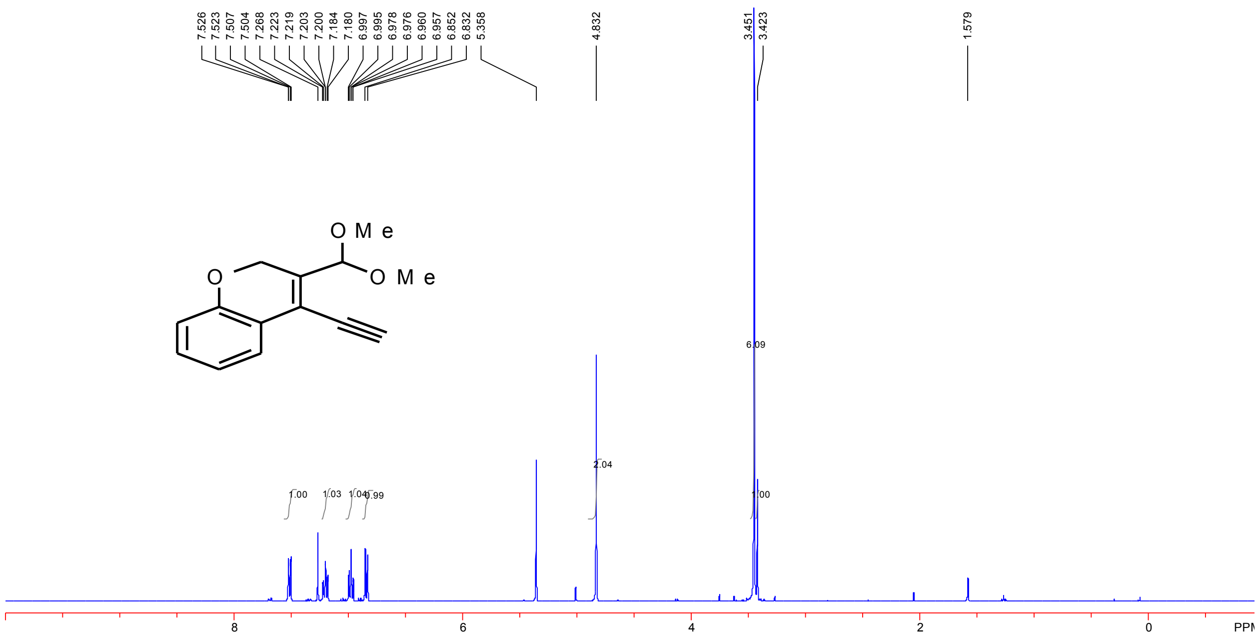


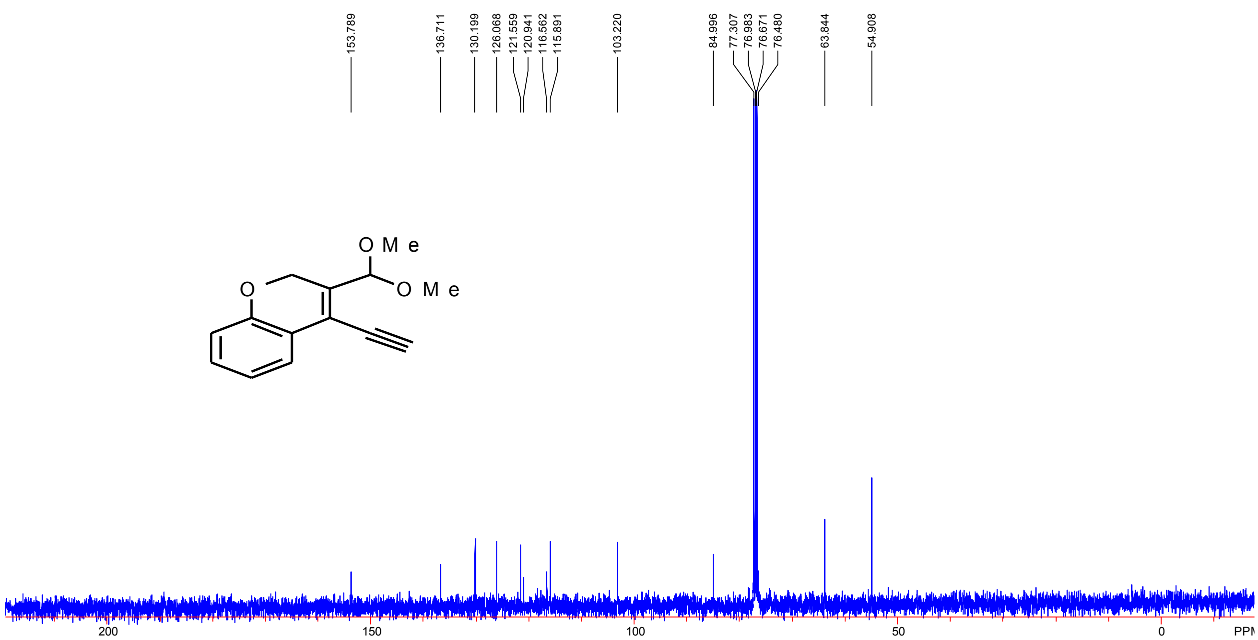
^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) of **1n**



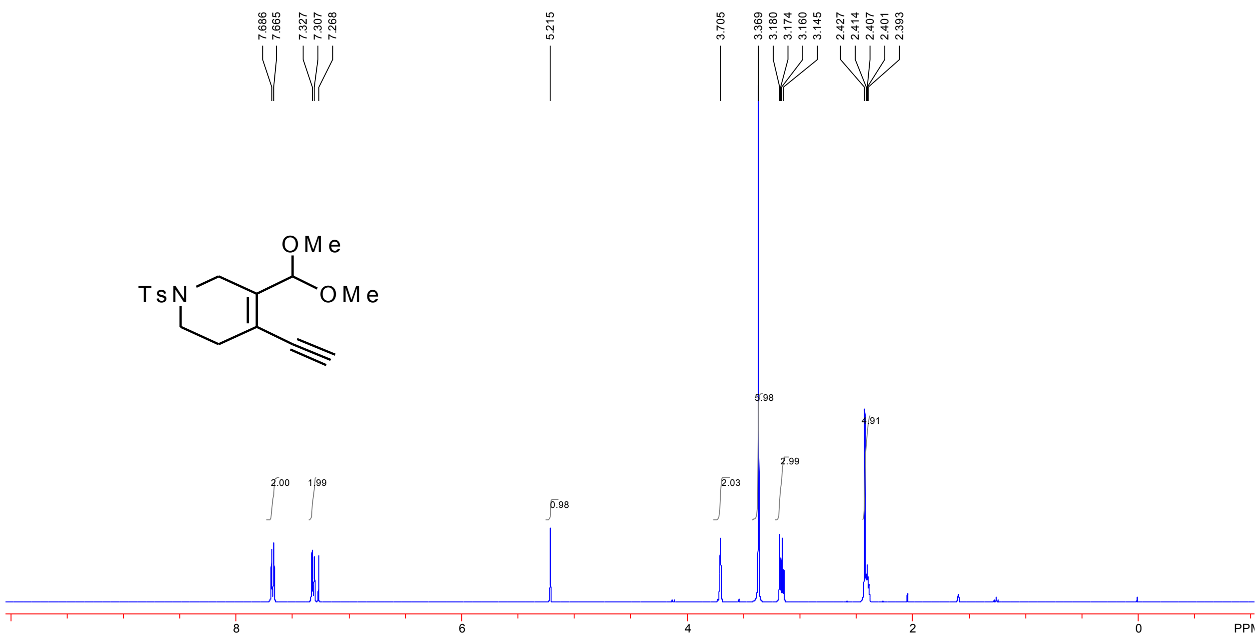


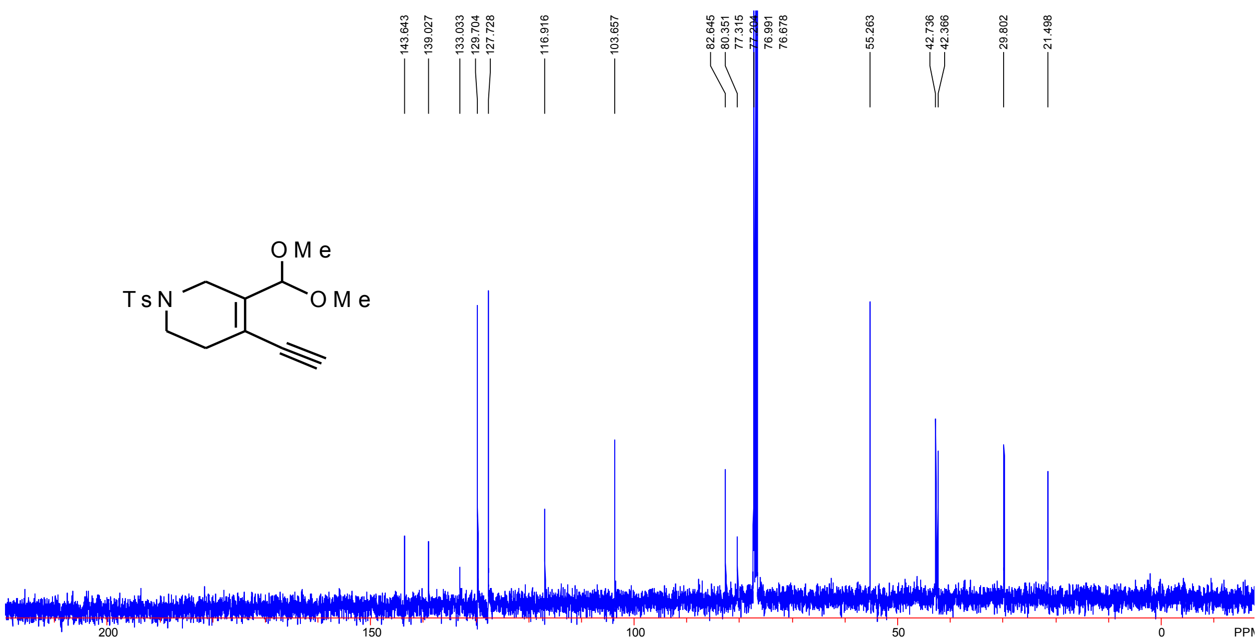
[1]H NMR (400 MHz, $CDCl_3$) and [13]C NMR (100 MHz, $CDCl_3$) of **1o**



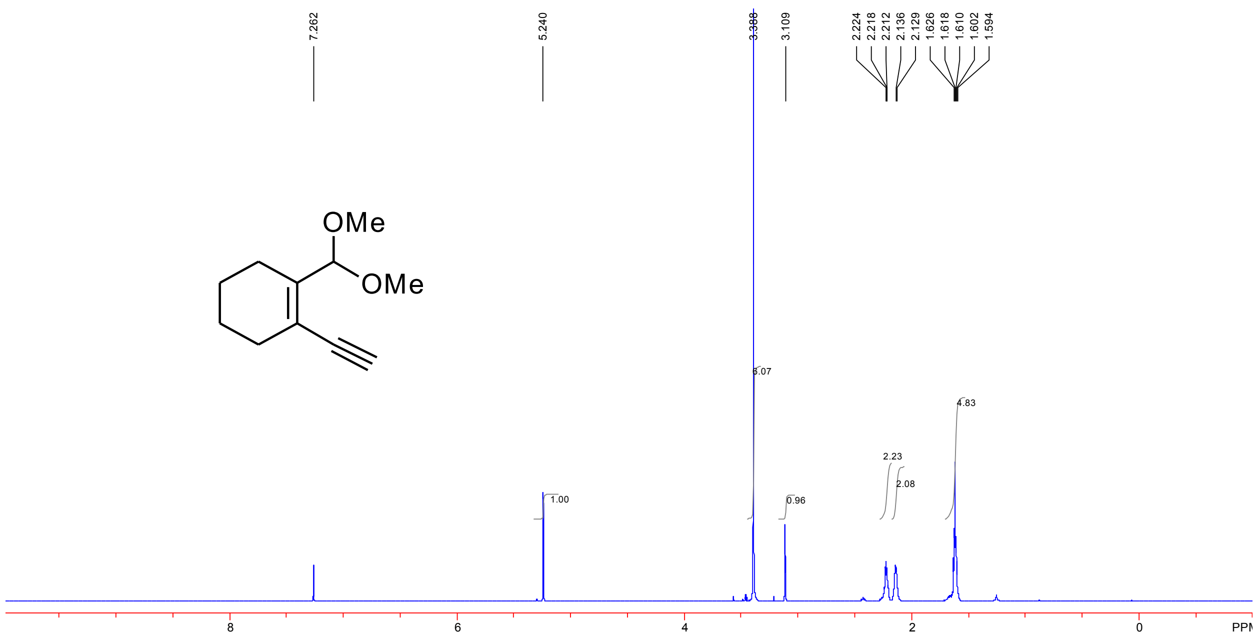


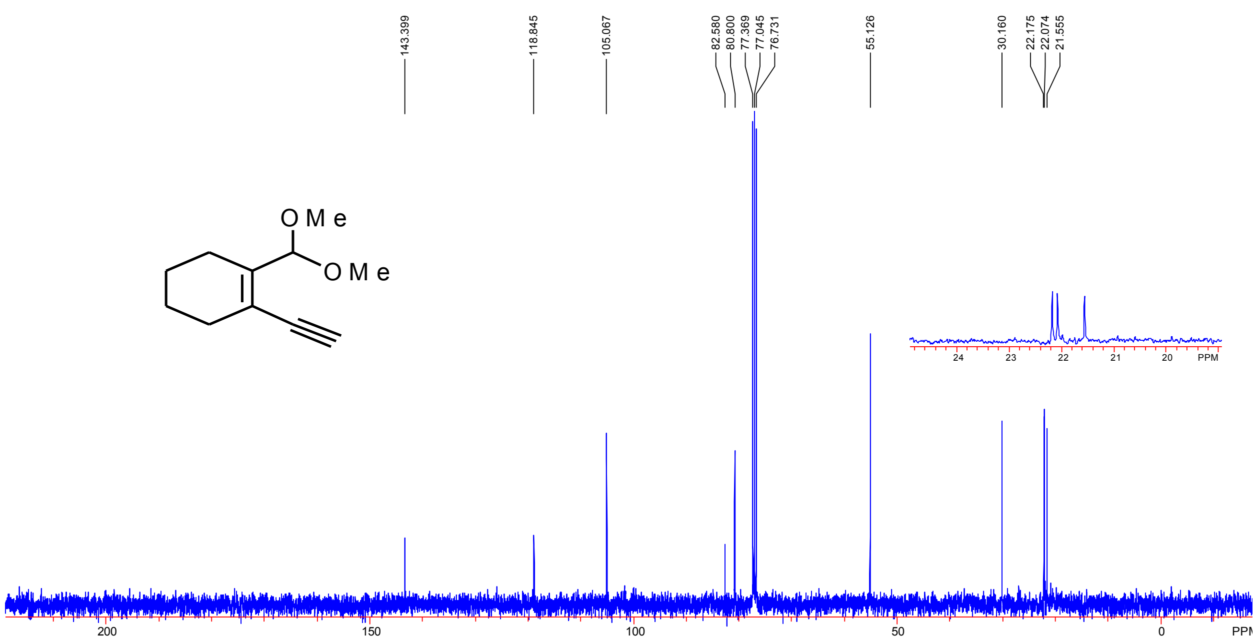
[1]H NMR (400 MHz, $CDCl_3$) and [13]C NMR (100 MHz, $CDCl_3$) of **1p**



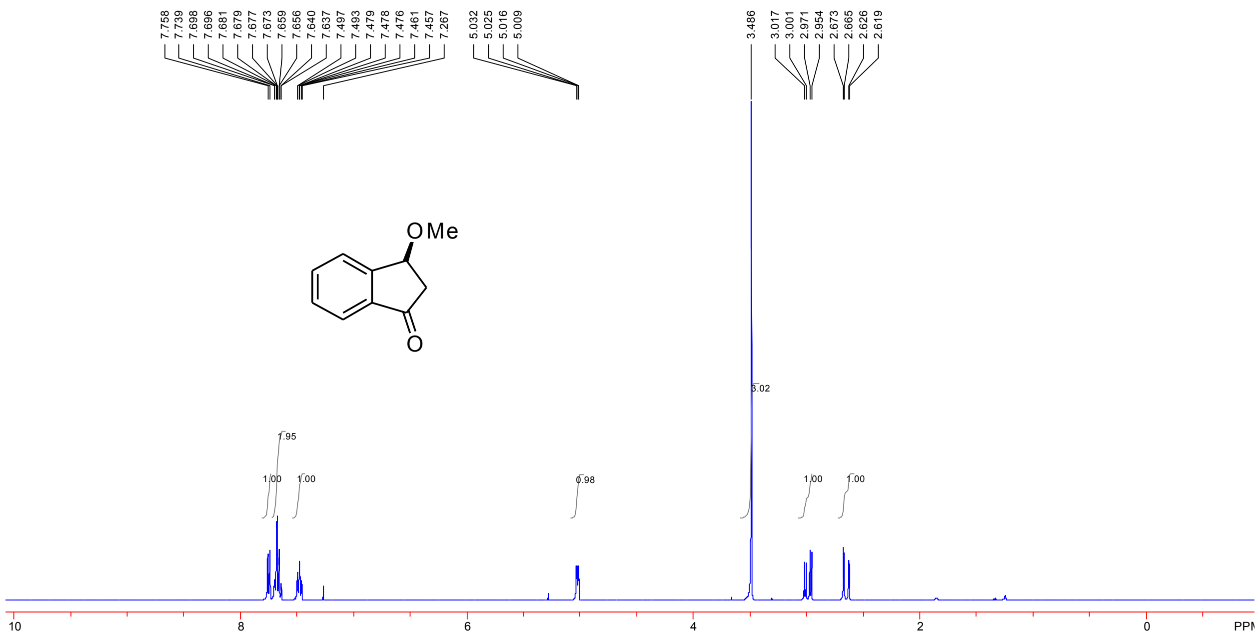


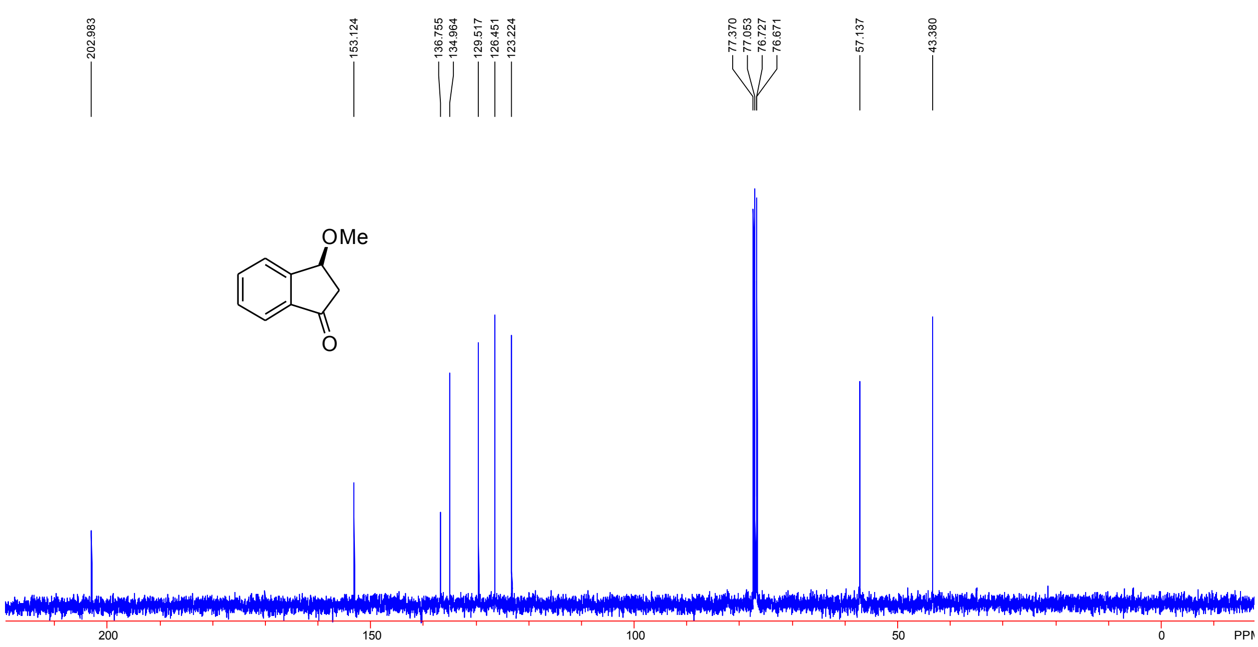
^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) of **1q**



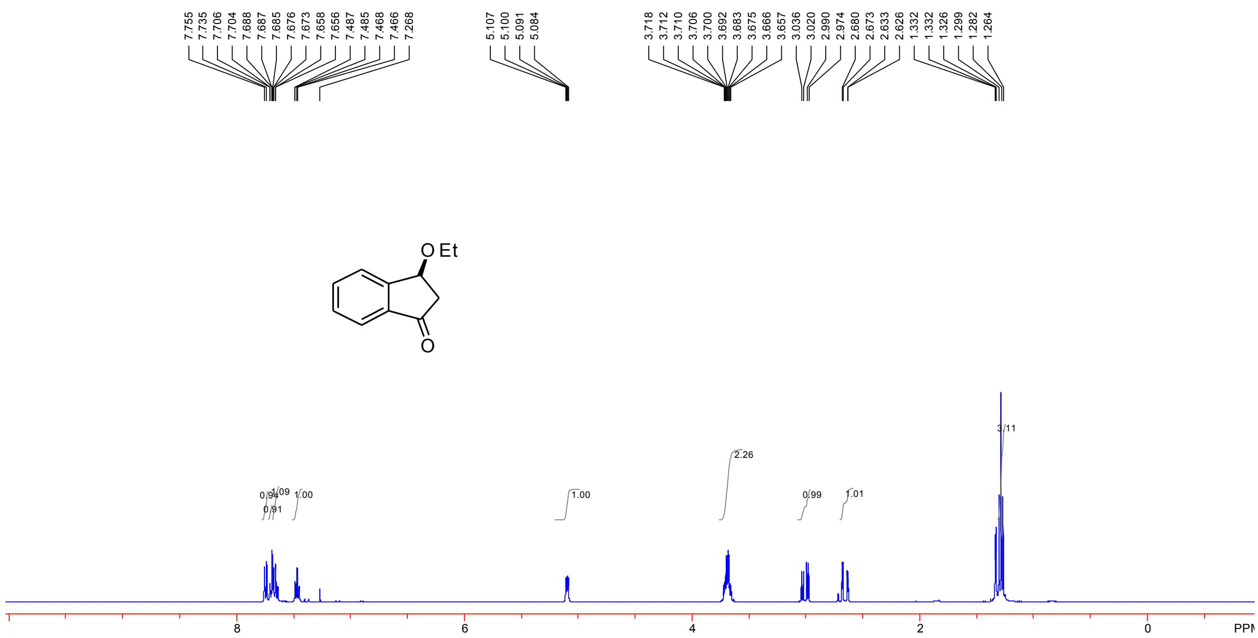


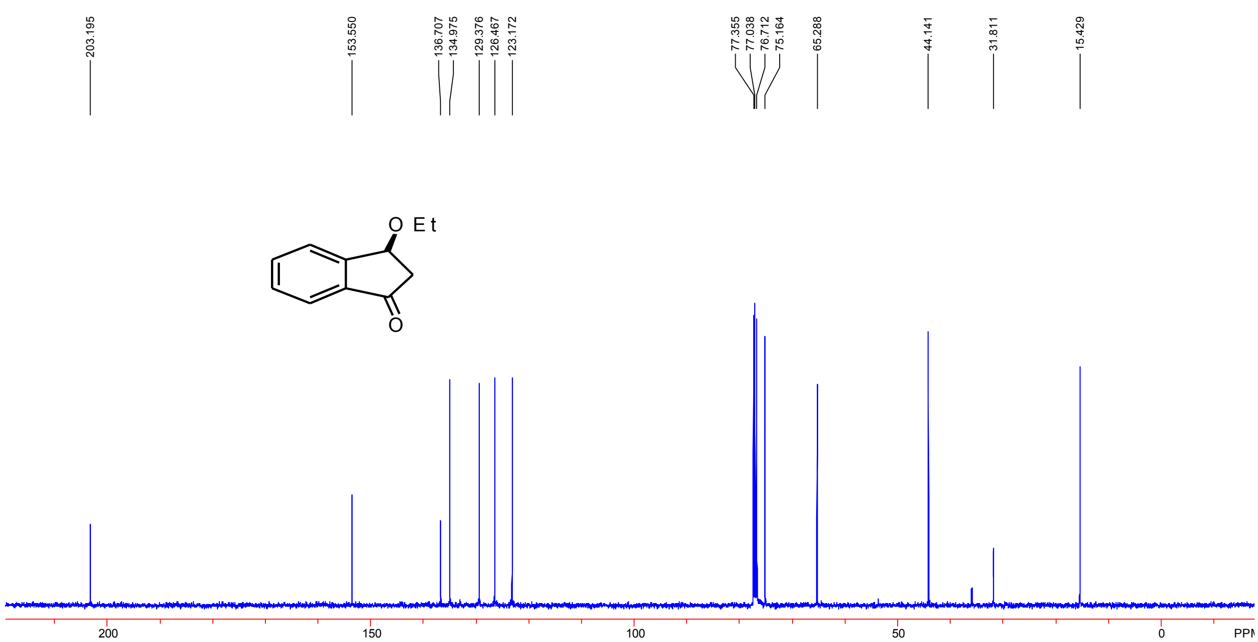
[1]H NMR (400 MHz, $CDCl_3$) and [13]C NMR (100 MHz, $CDCl_3$) of **3a**



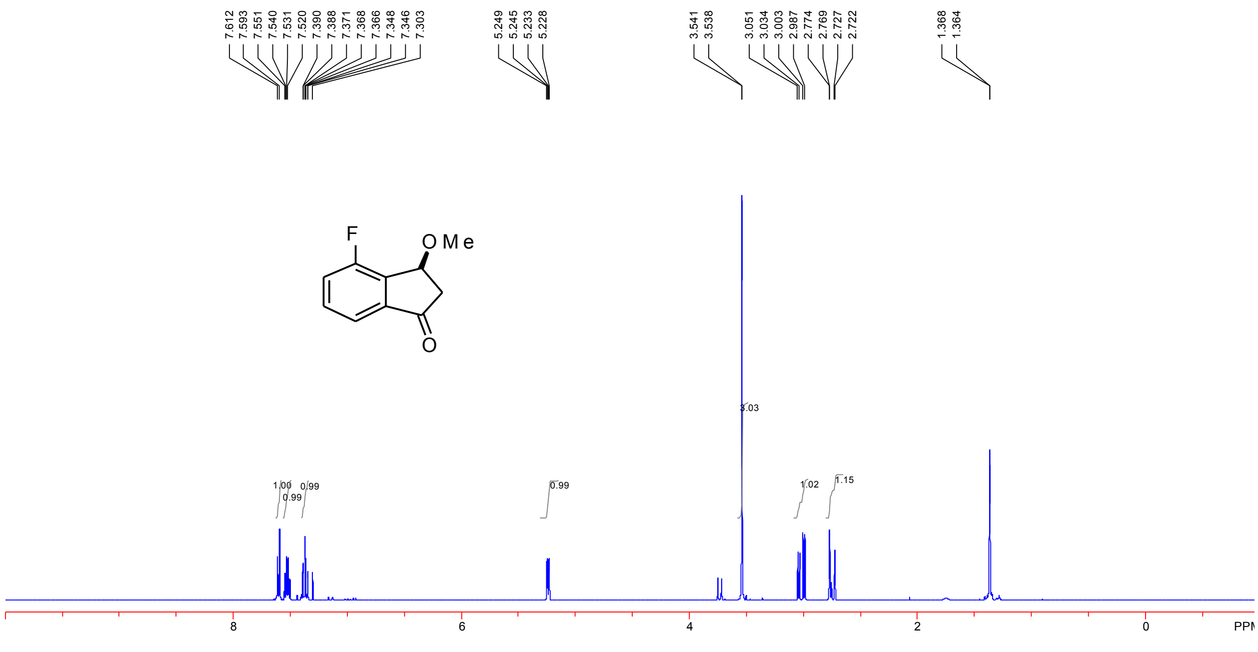


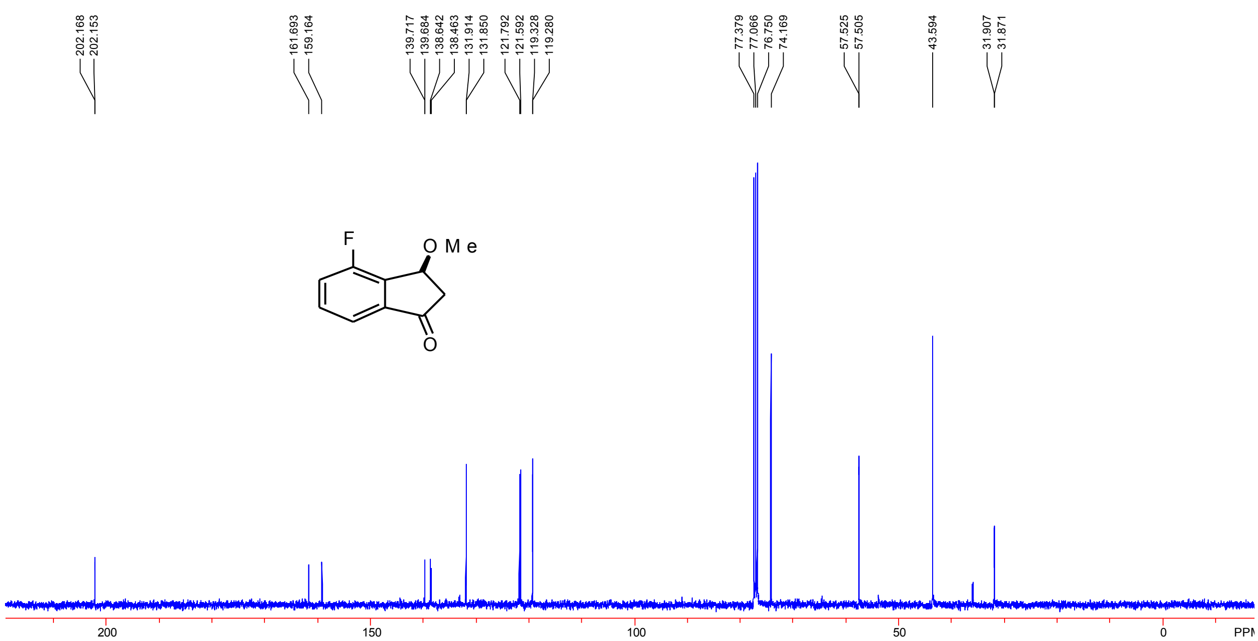
^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) of **3b**



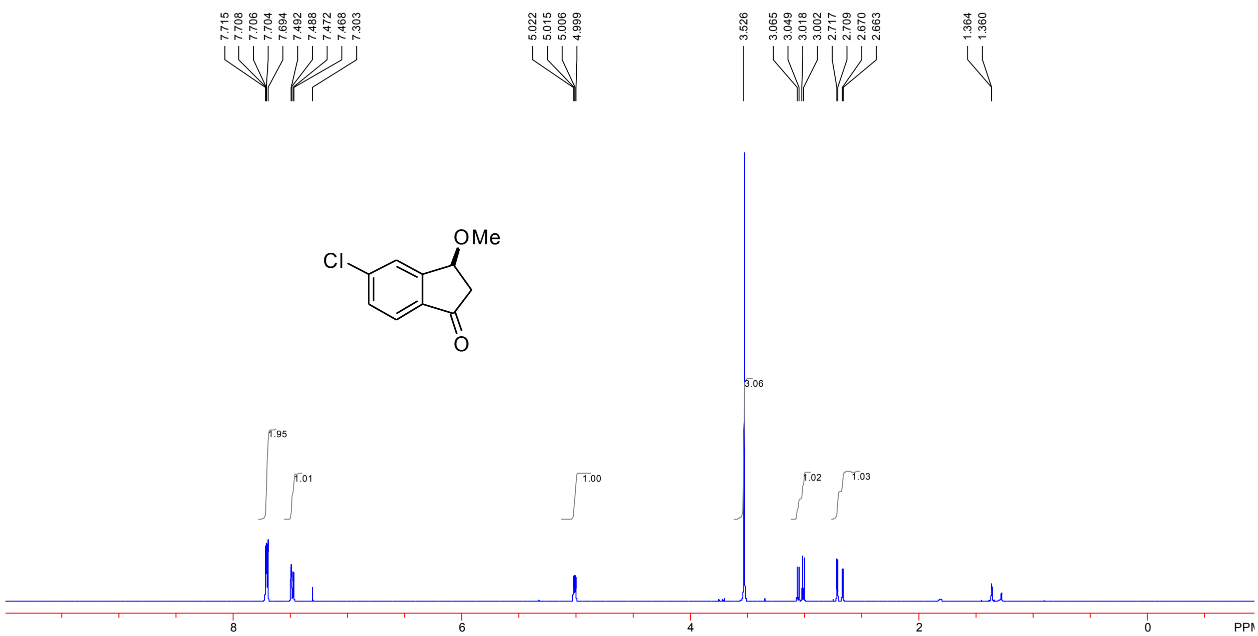


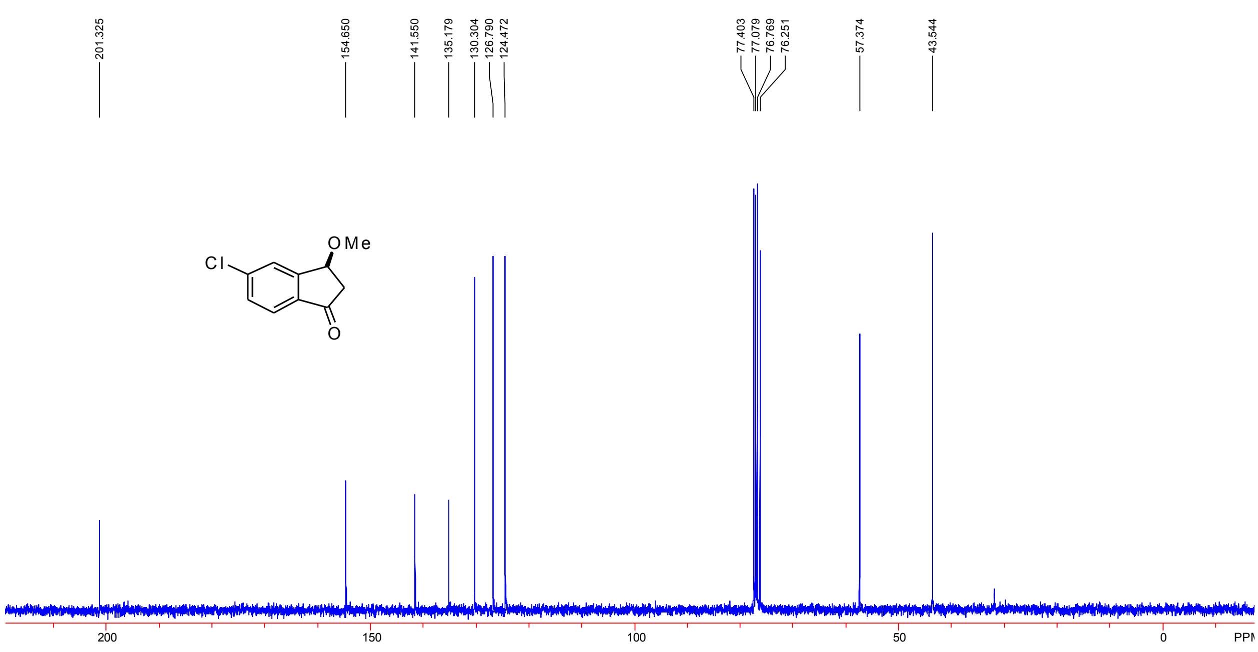
^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) of **3c**



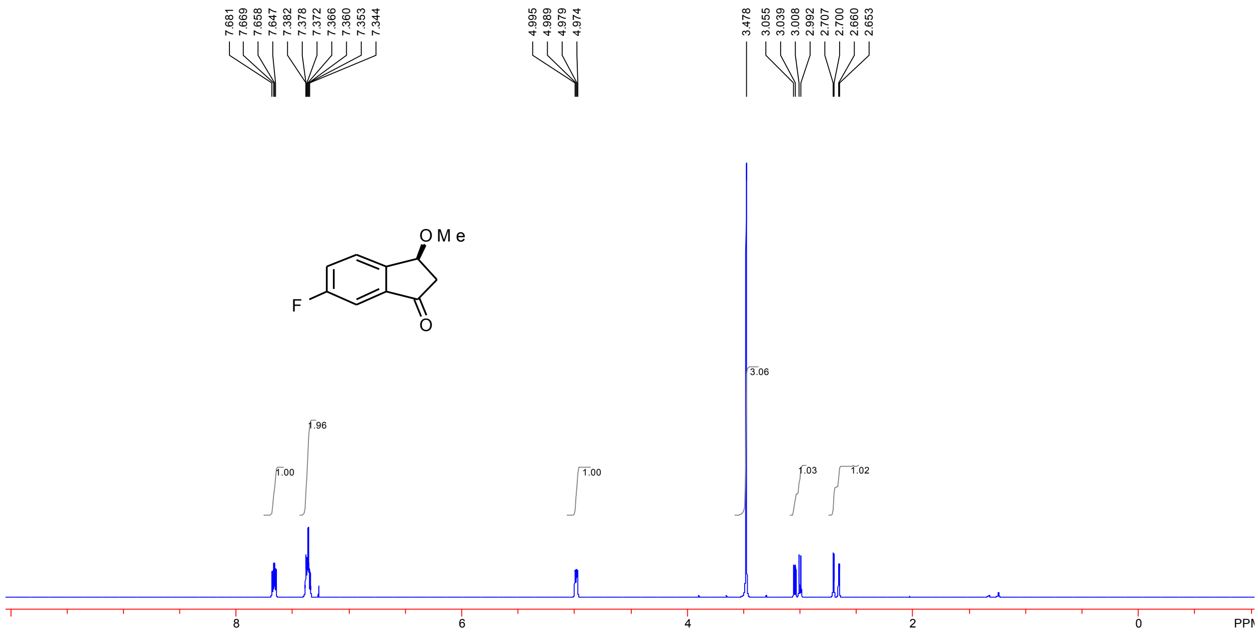


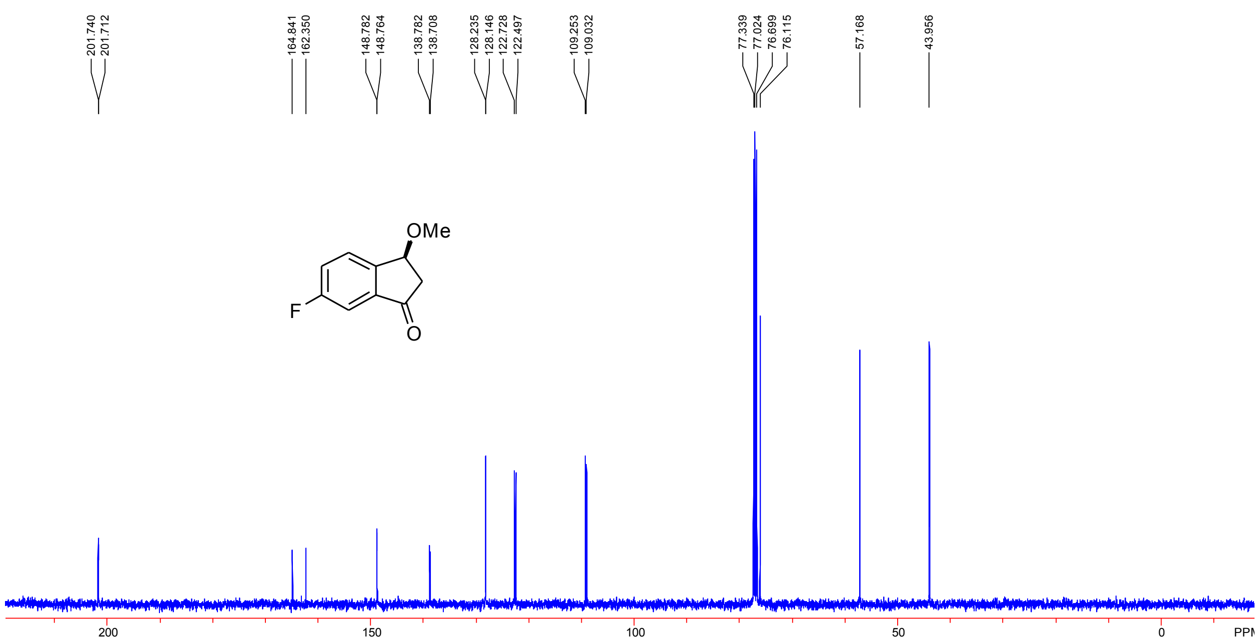
[1]H NMR (400 MHz, $CDCl_3$) and [13]C NMR (100 MHz, $CDCl_3$) of **3d**



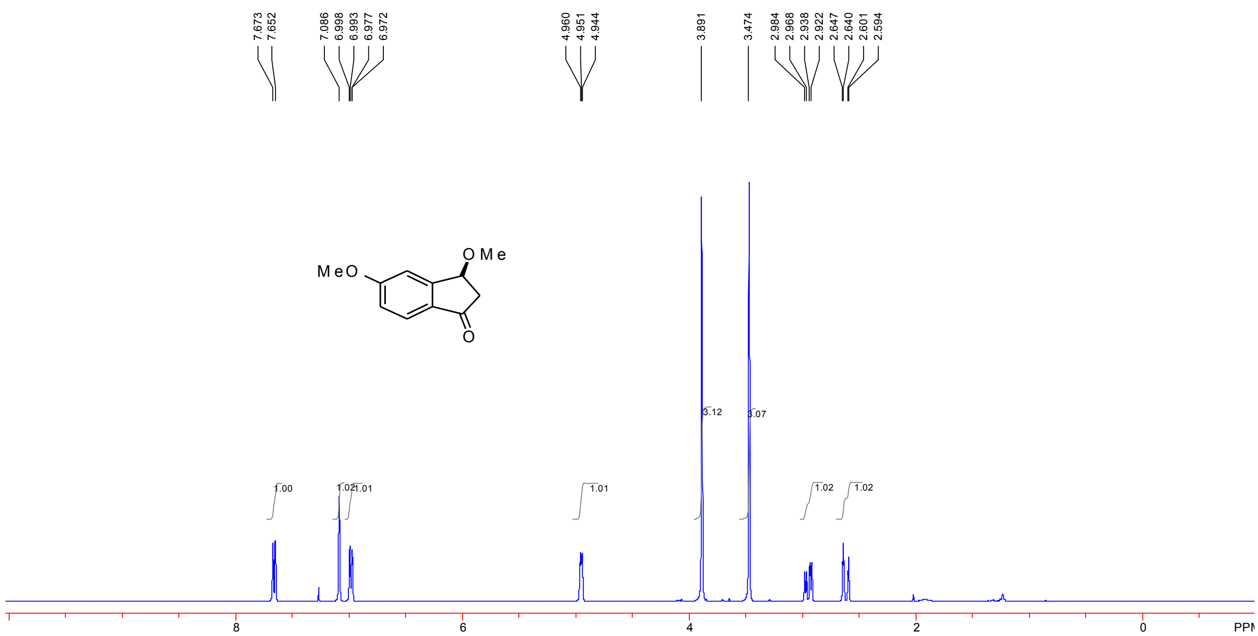


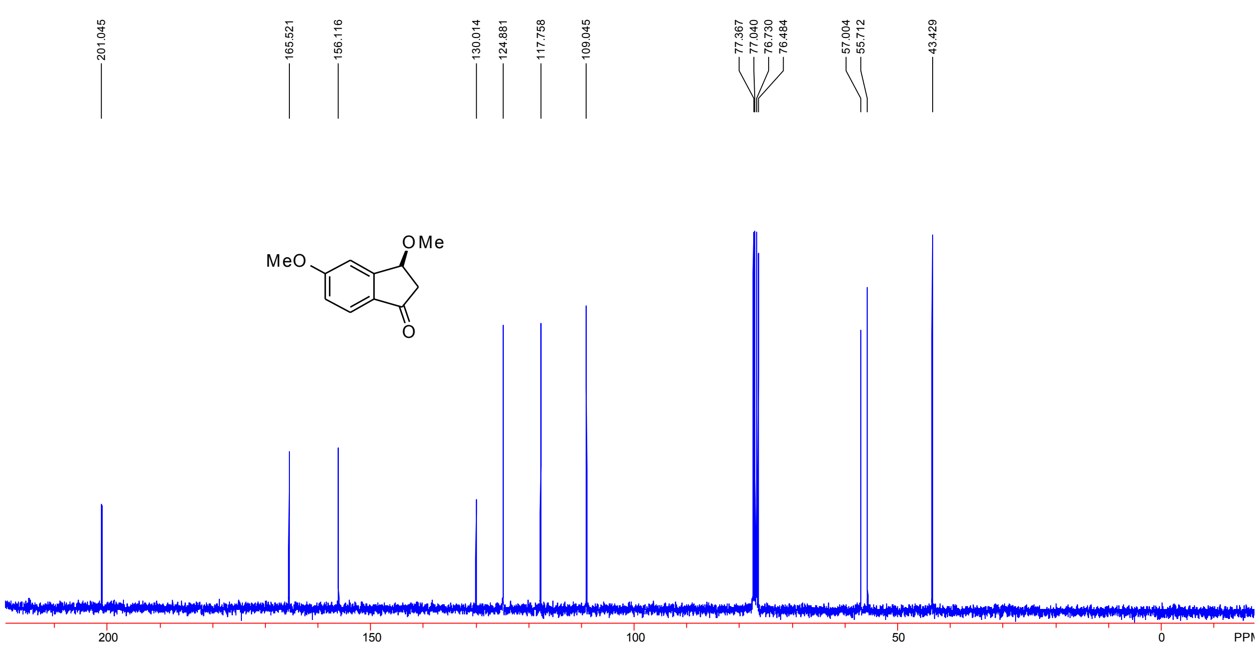
^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) of **3e**



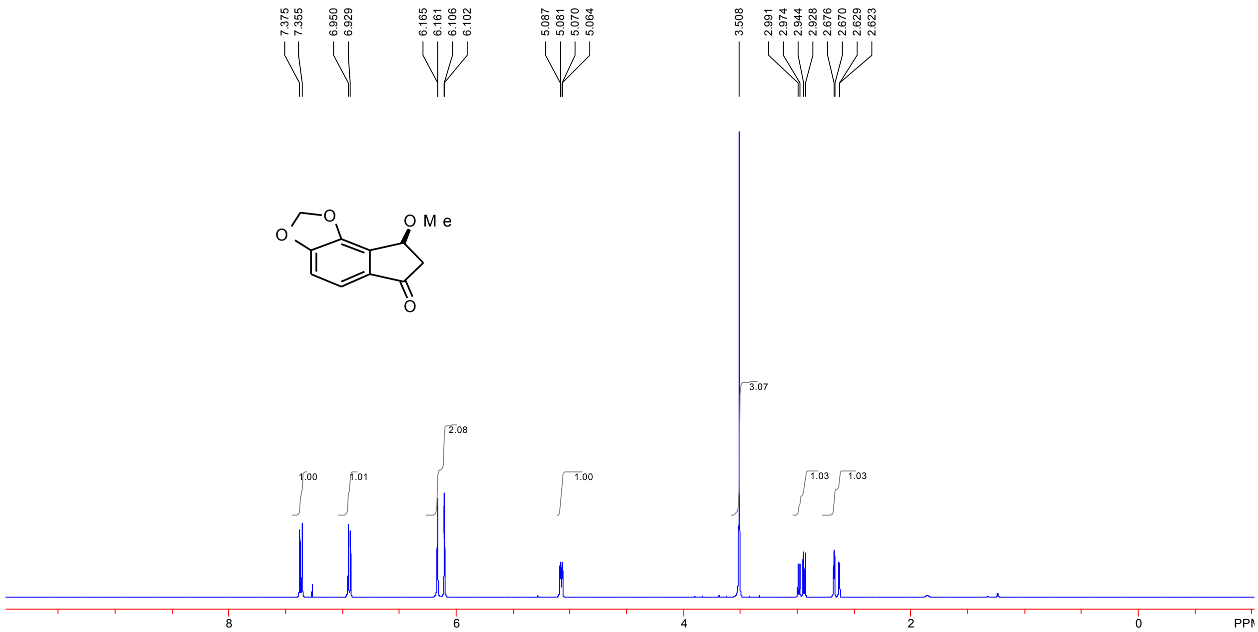


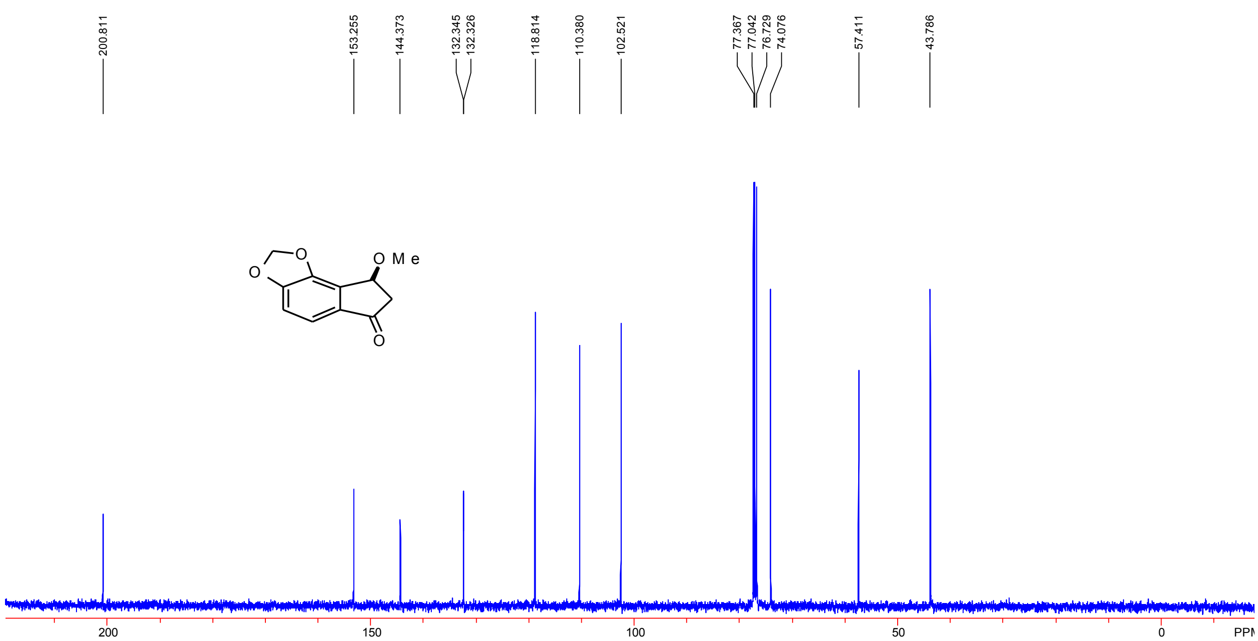
[1]H NMR (400 MHz, $CDCl_3$) and [13]C NMR (100 MHz, $CDCl_3$) of **3f**



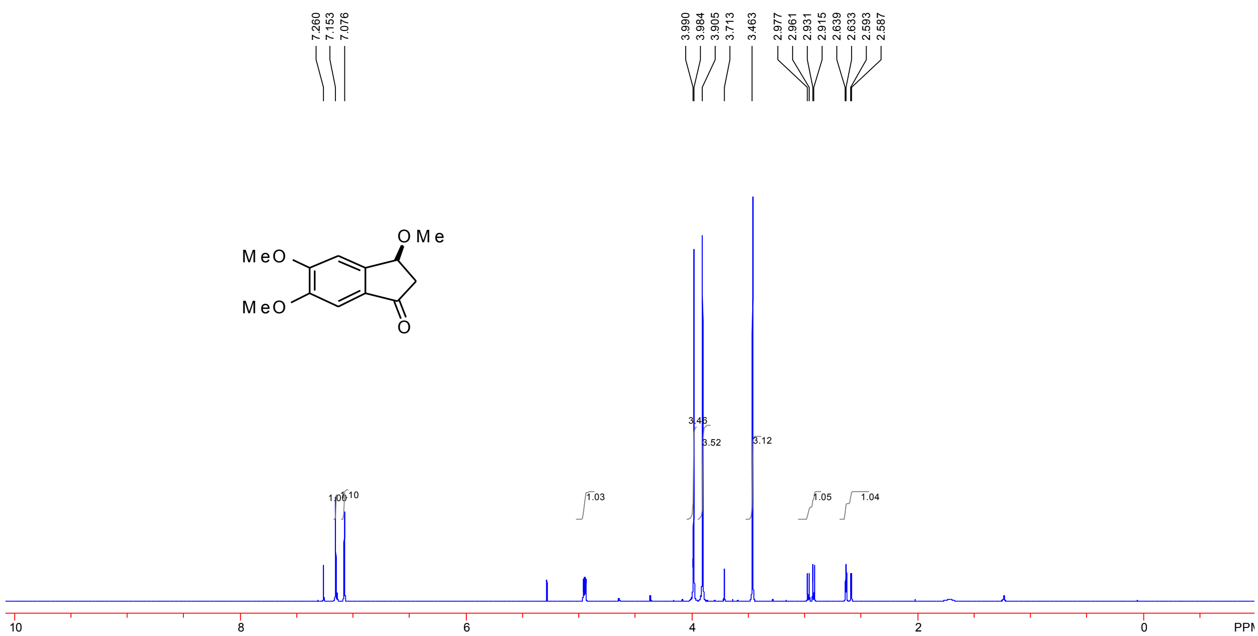


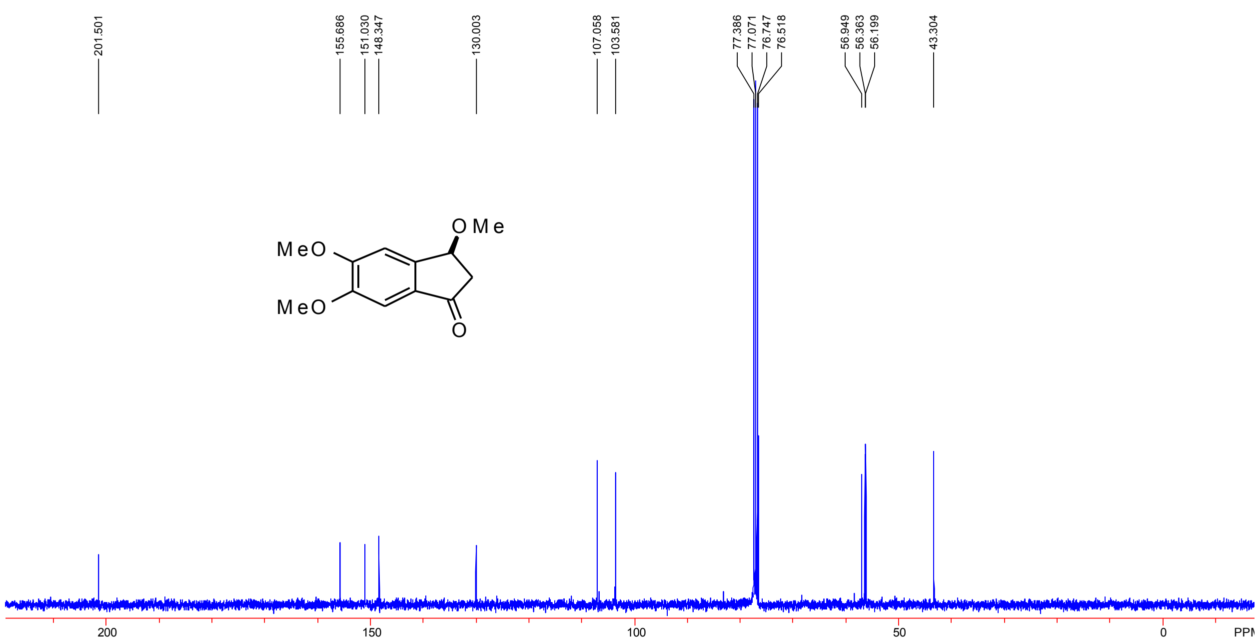
[1]H NMR (400 MHz, $CDCl_3$) and [13]C NMR (100 MHz, $CDCl_3$) of **3g**



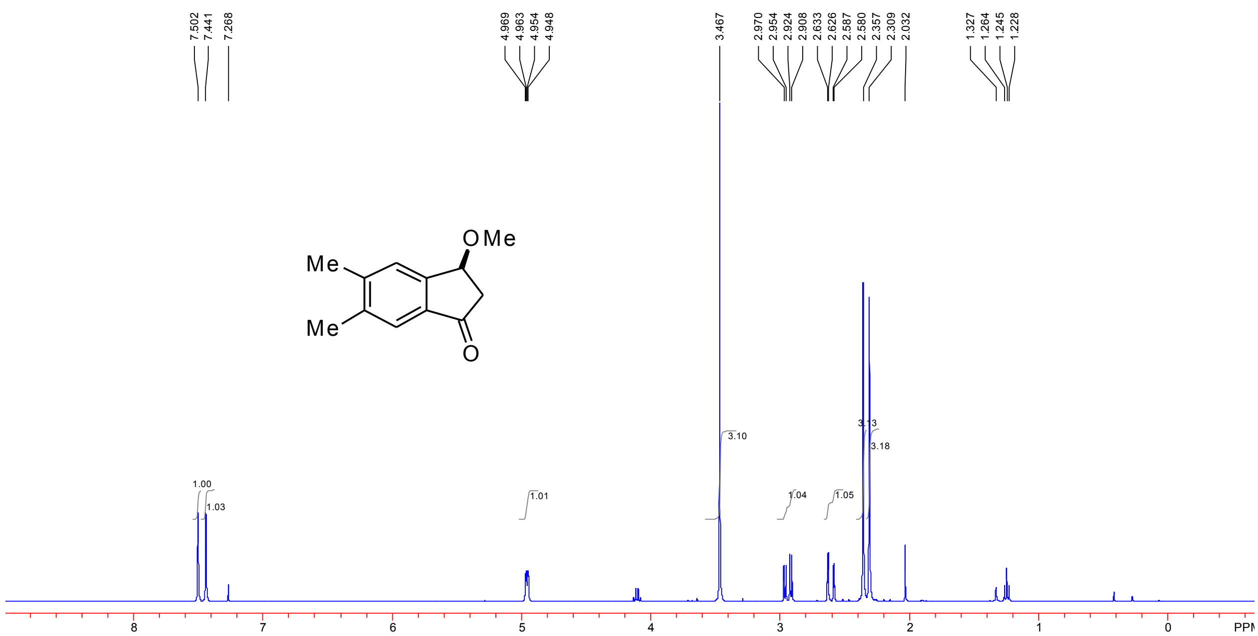


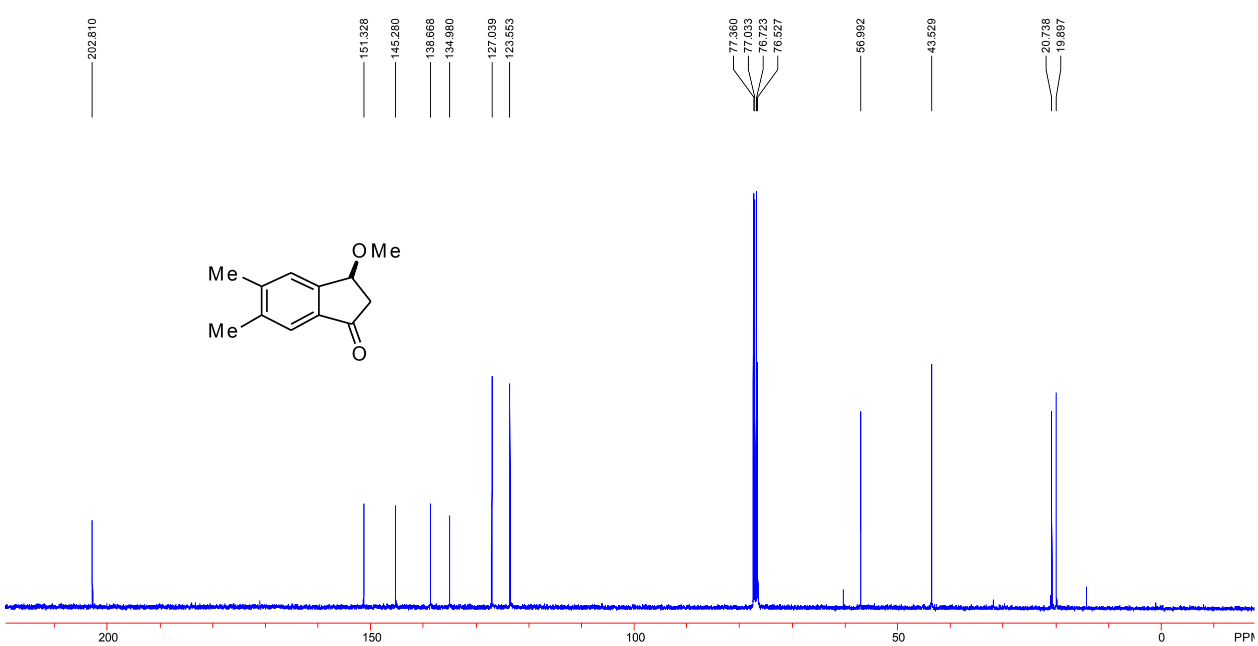
^1H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) of **3h**



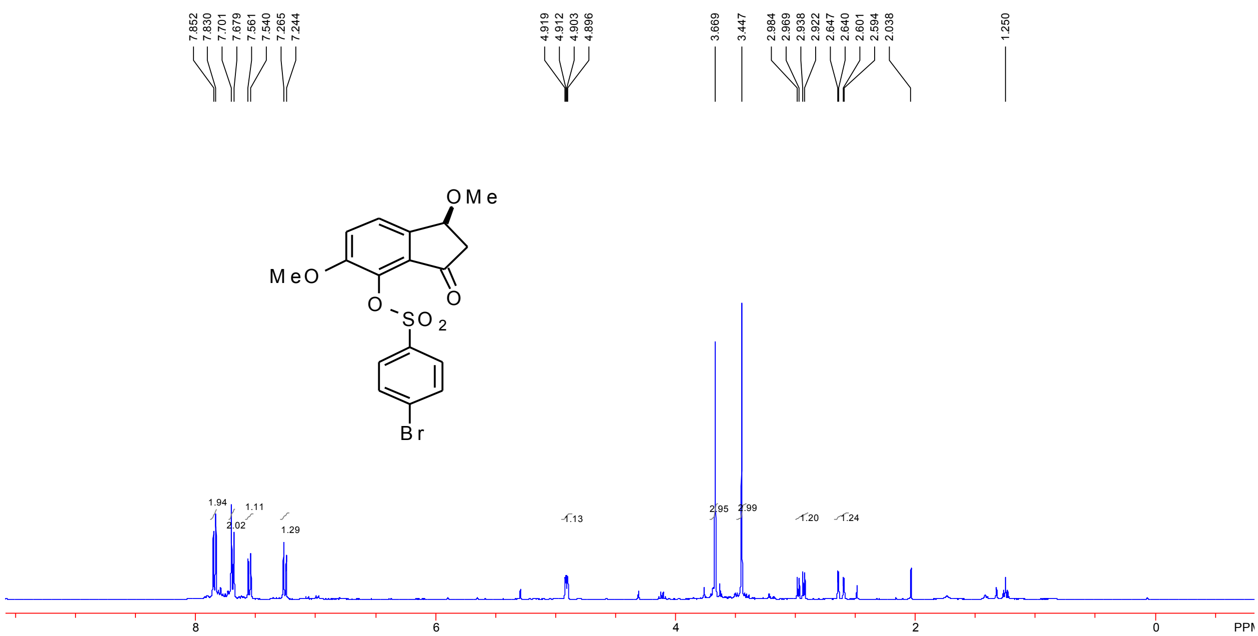


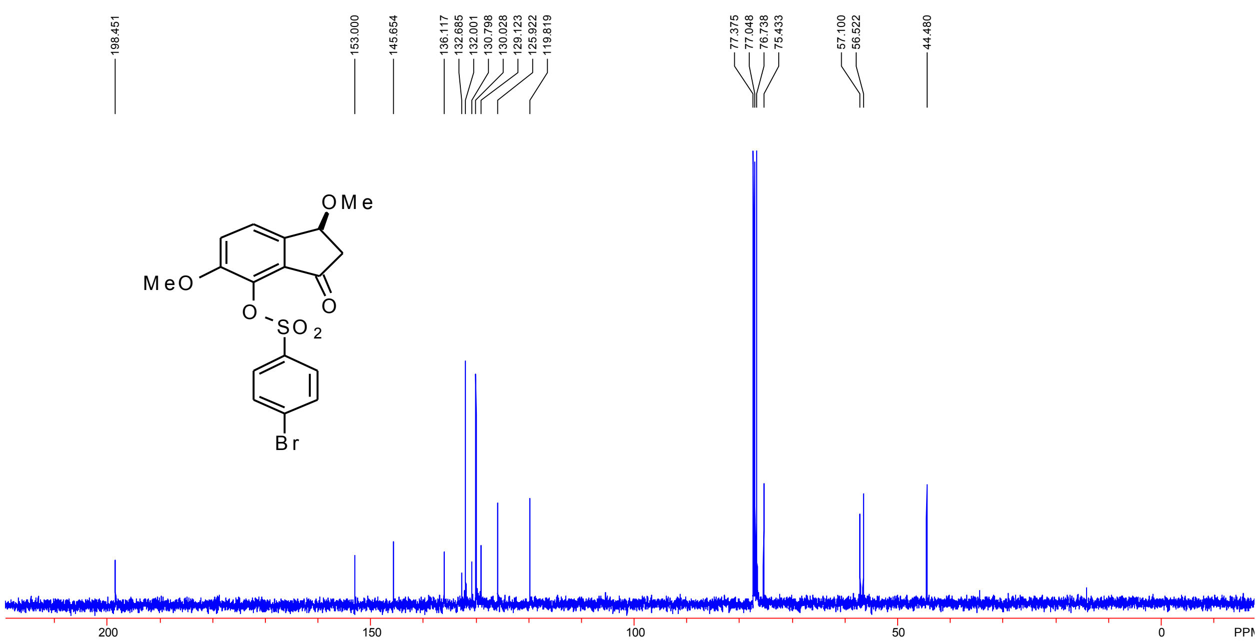
^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) of **3i**



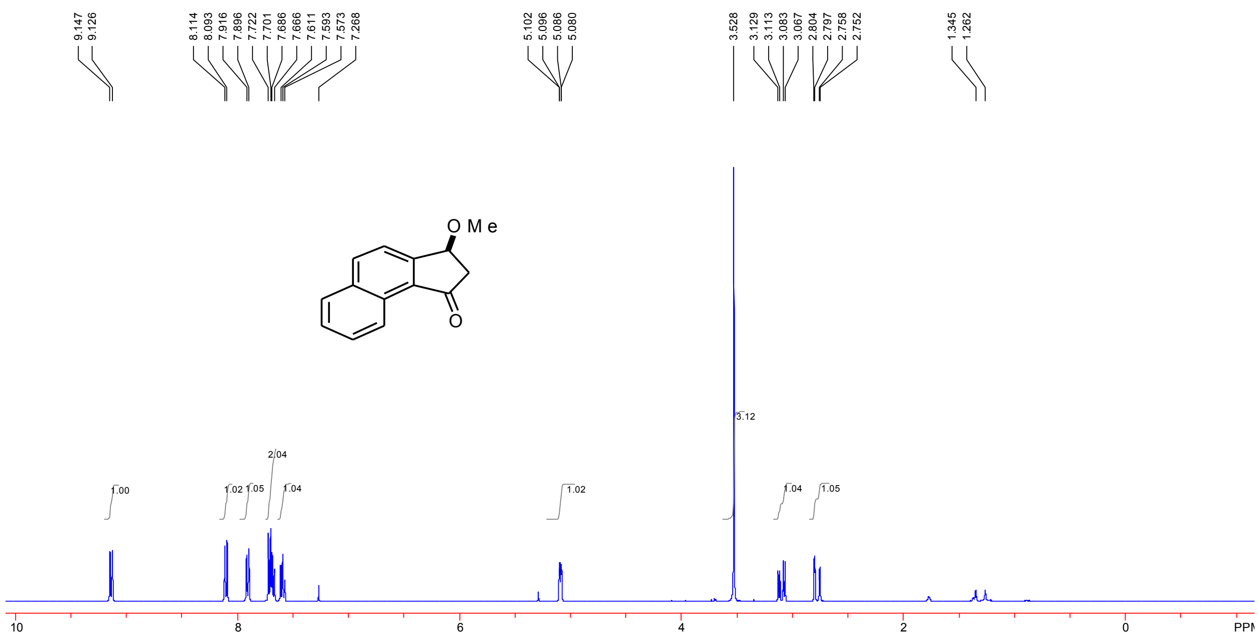


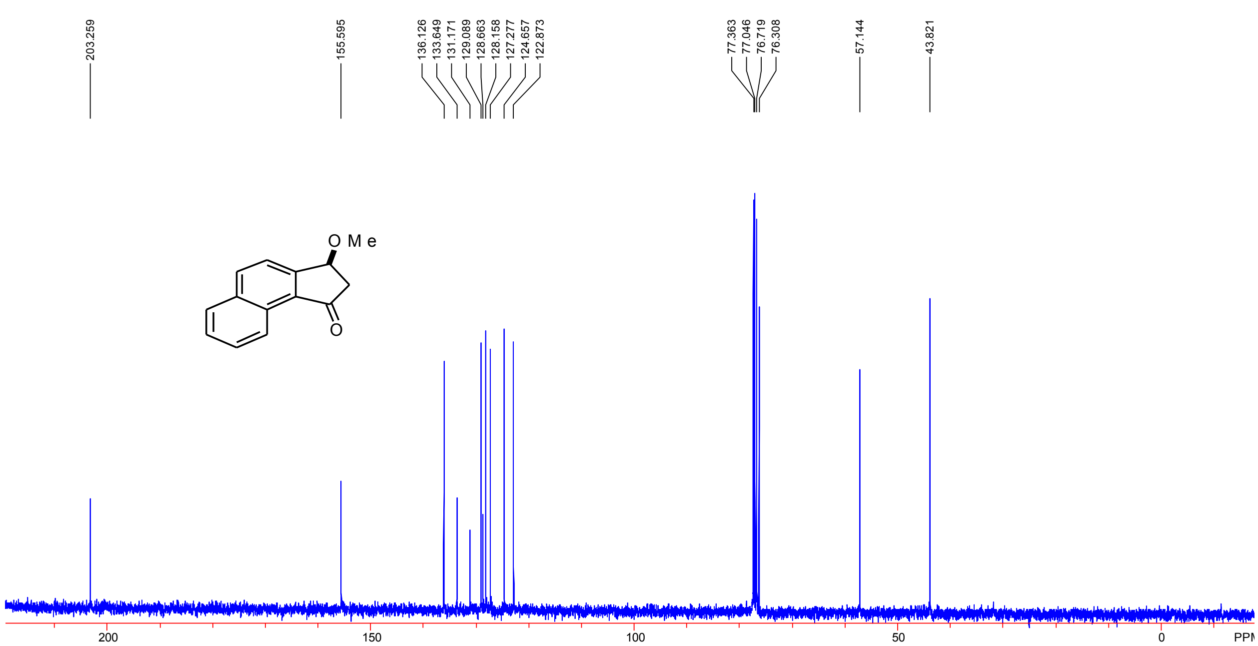
^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) of **3j**



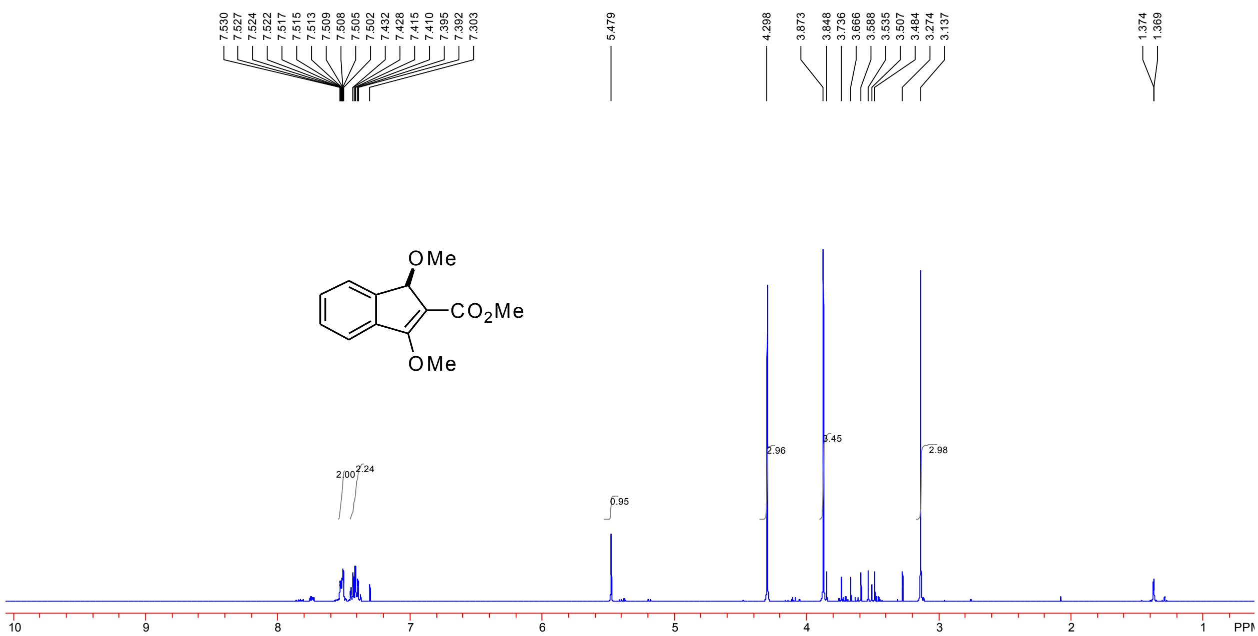


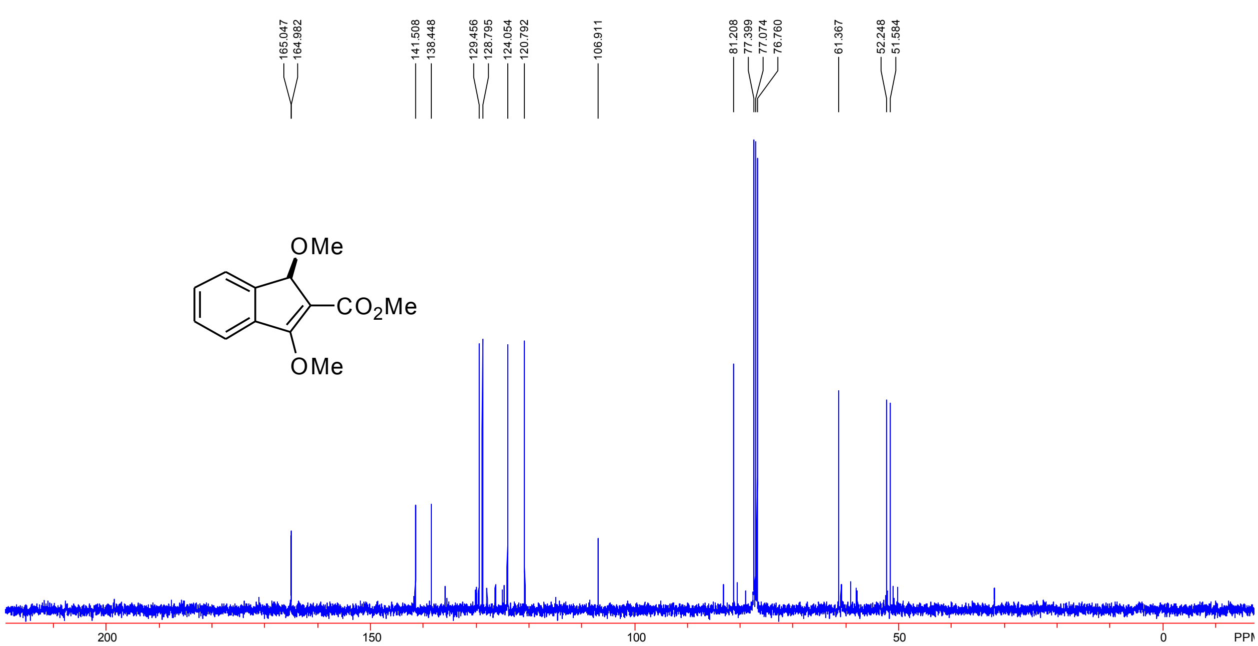
^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) of **3k**



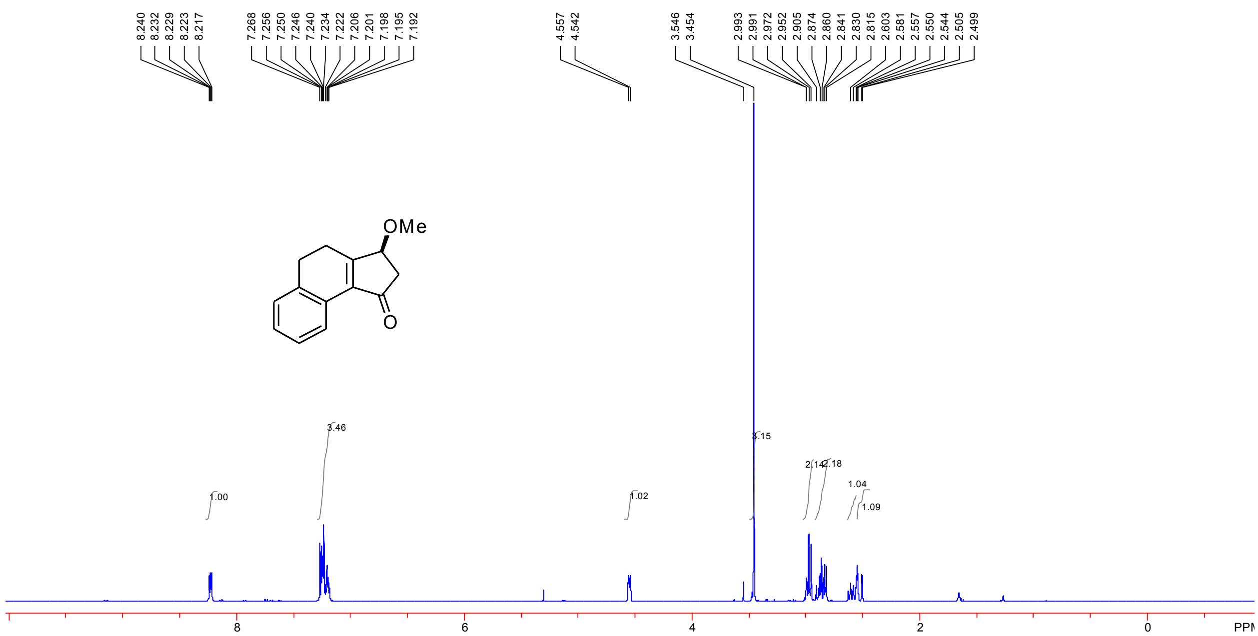


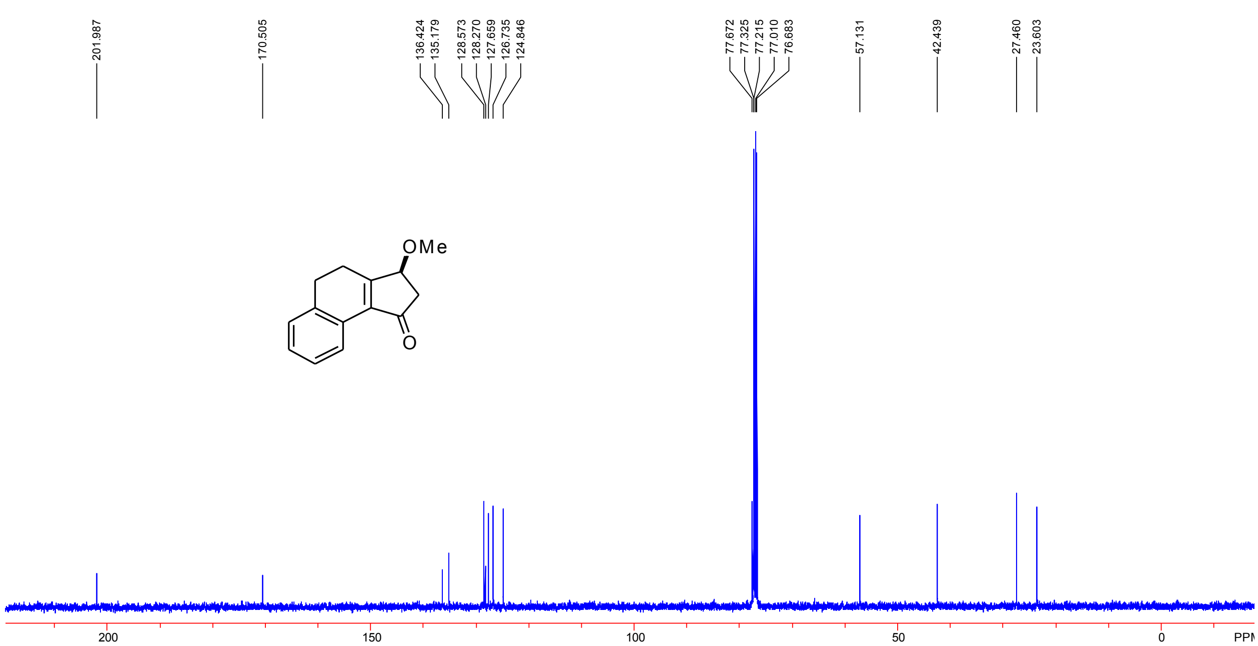
^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) of **3l**



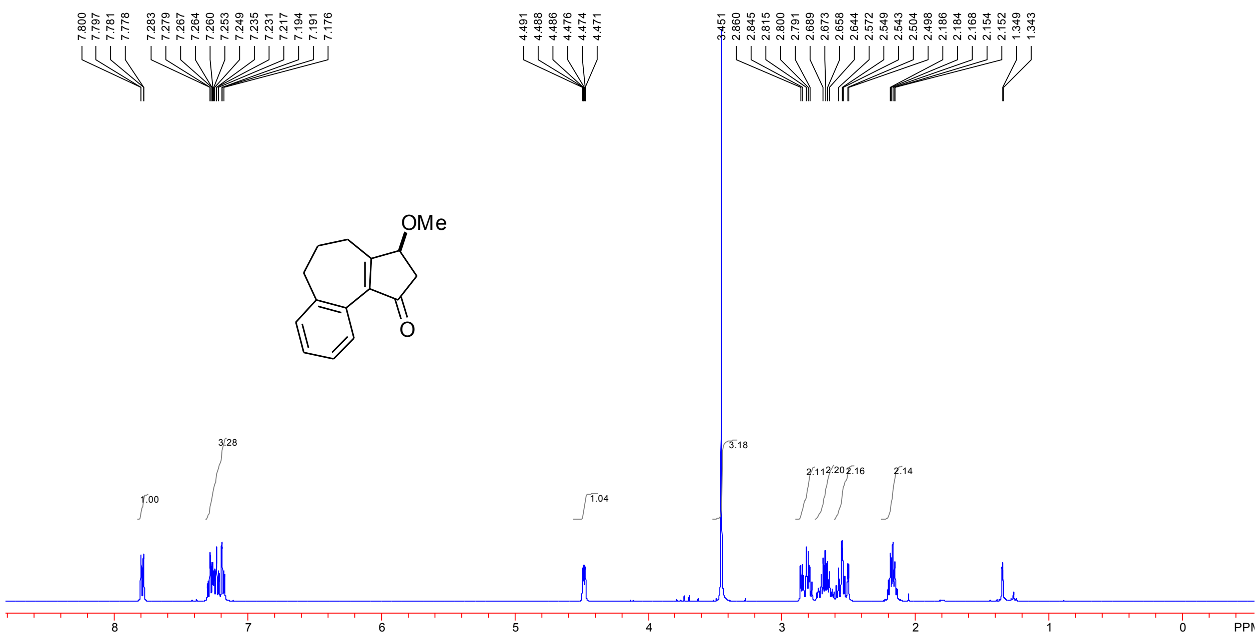


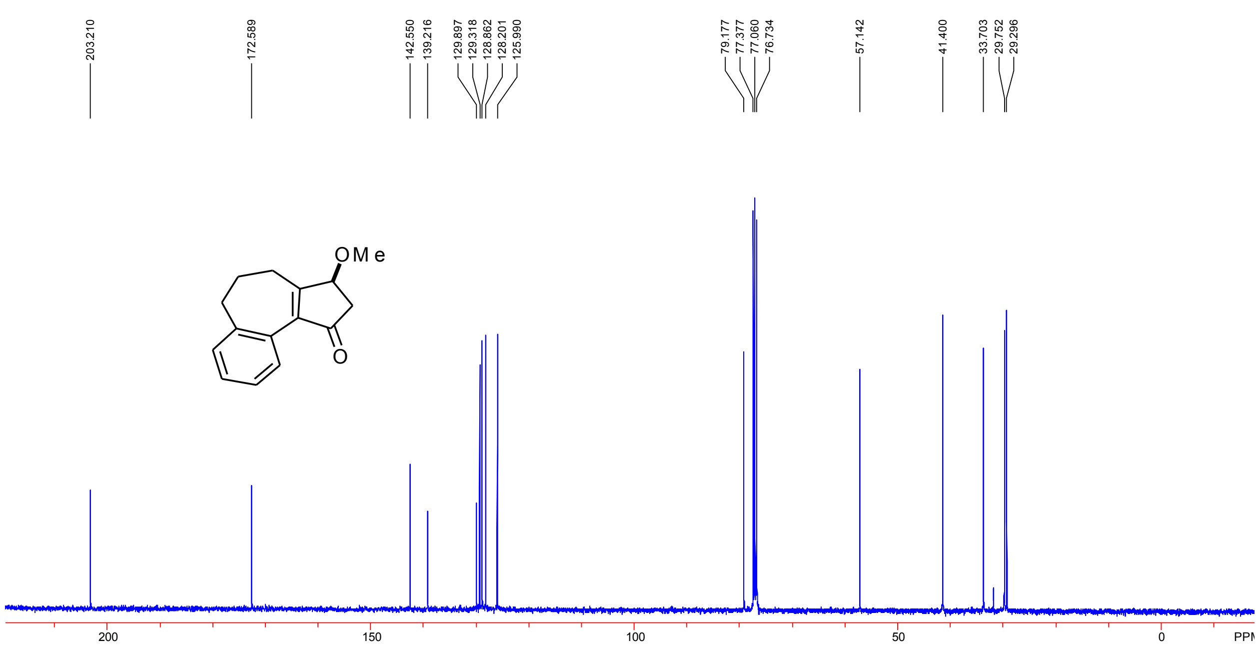
[1]H NMR (400 MHz, $CDCl_3$) and [13]C NMR (100 MHz, $CDCl_3$) of **3m**



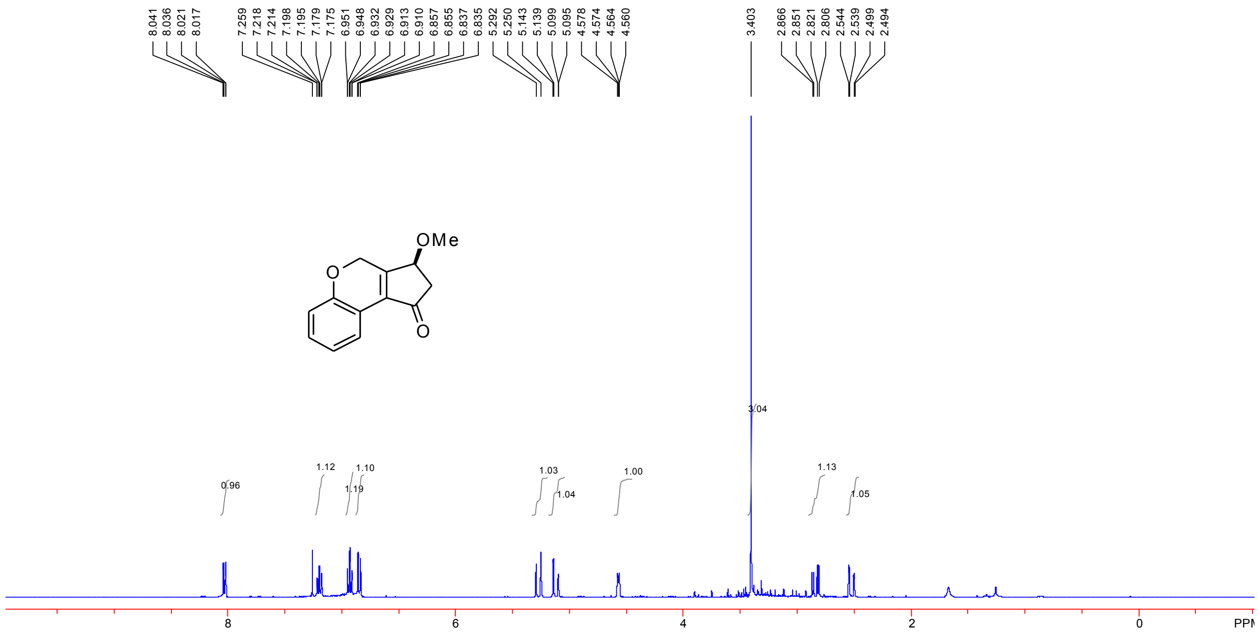


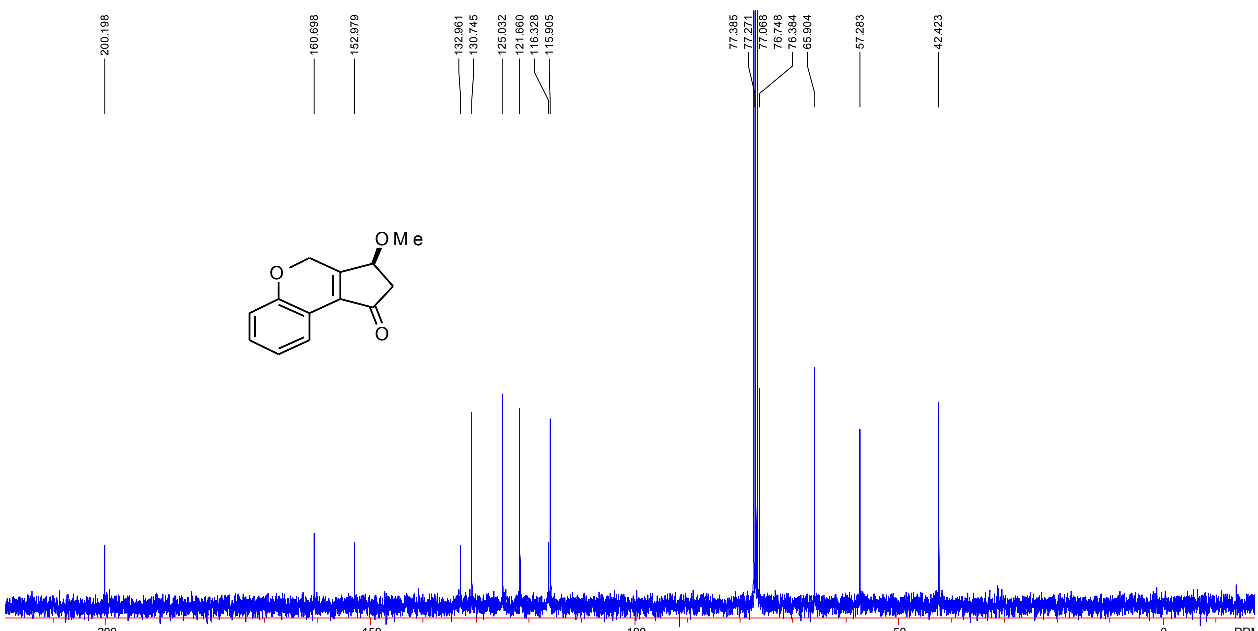
^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) of **3n**



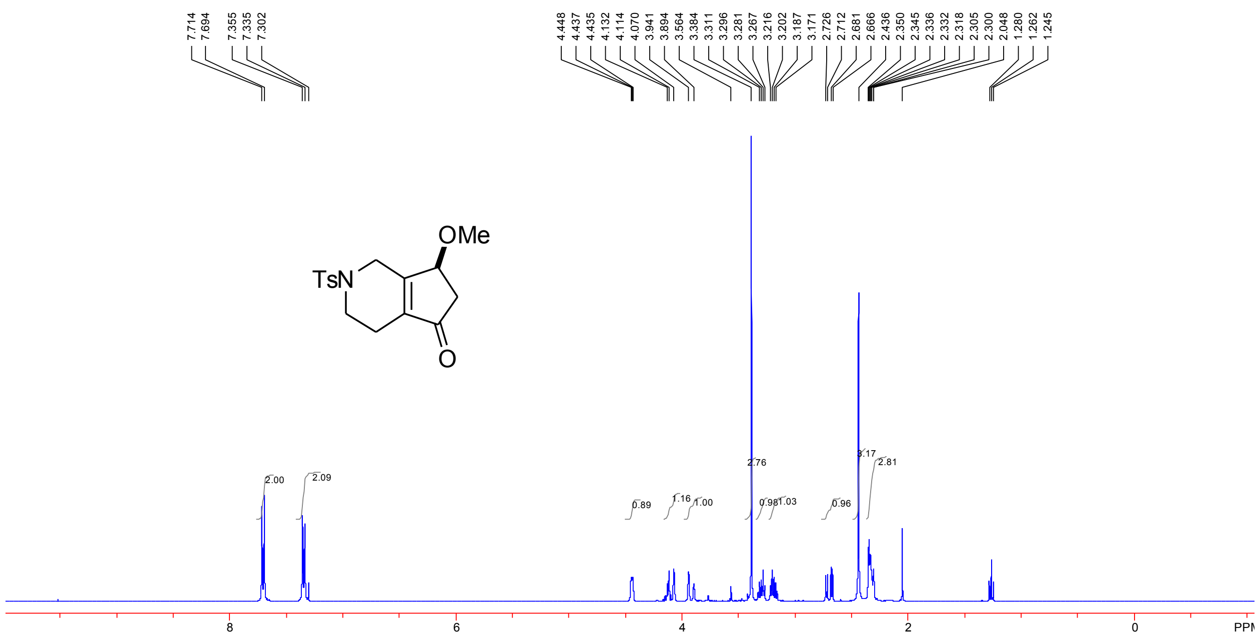


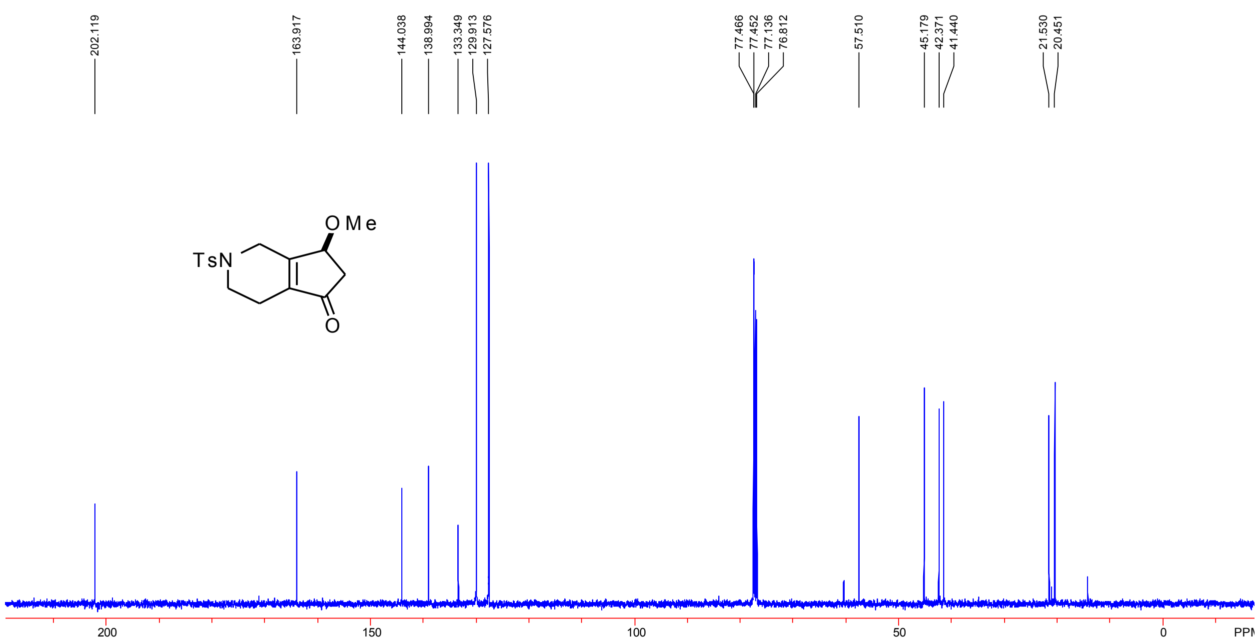
^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) of **3o**



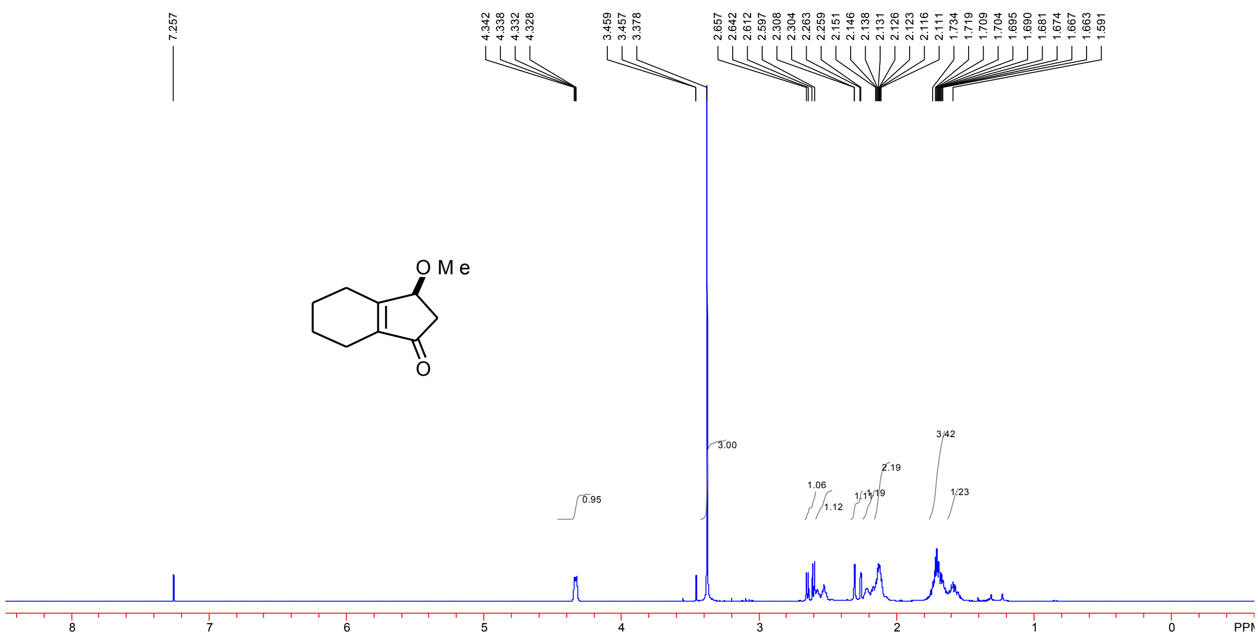


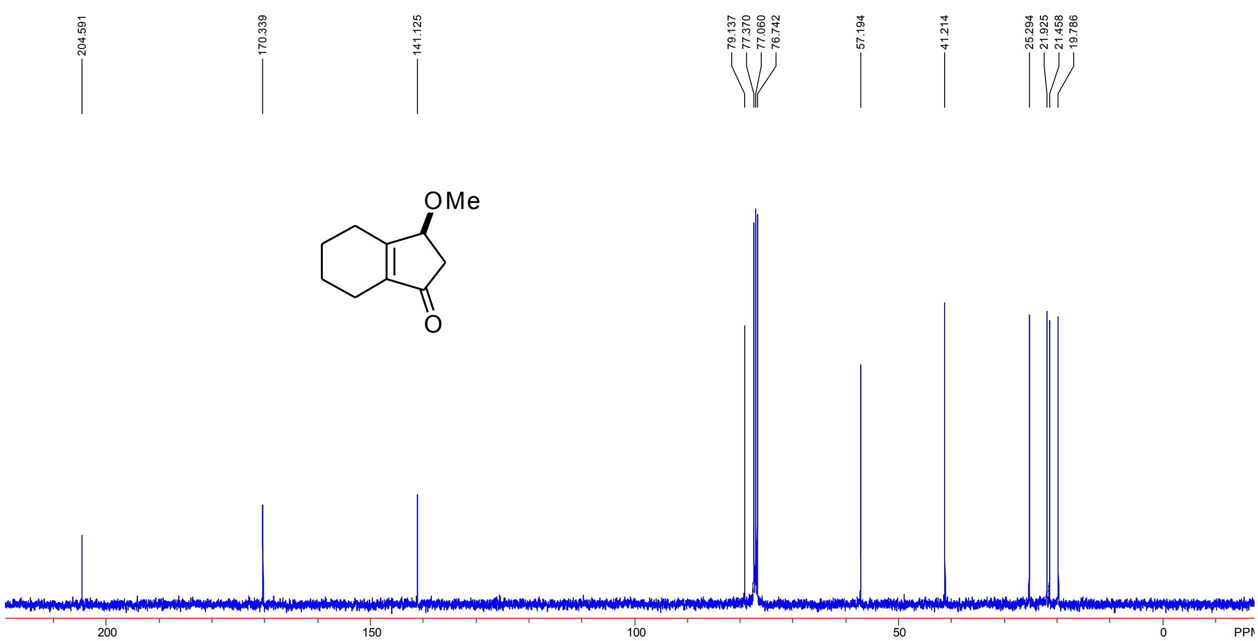
^{1}H NMR (400 MHz, CDCl$_3$) and ^{13}C NMR (100 MHz, CDCl$_3$) of **3p**



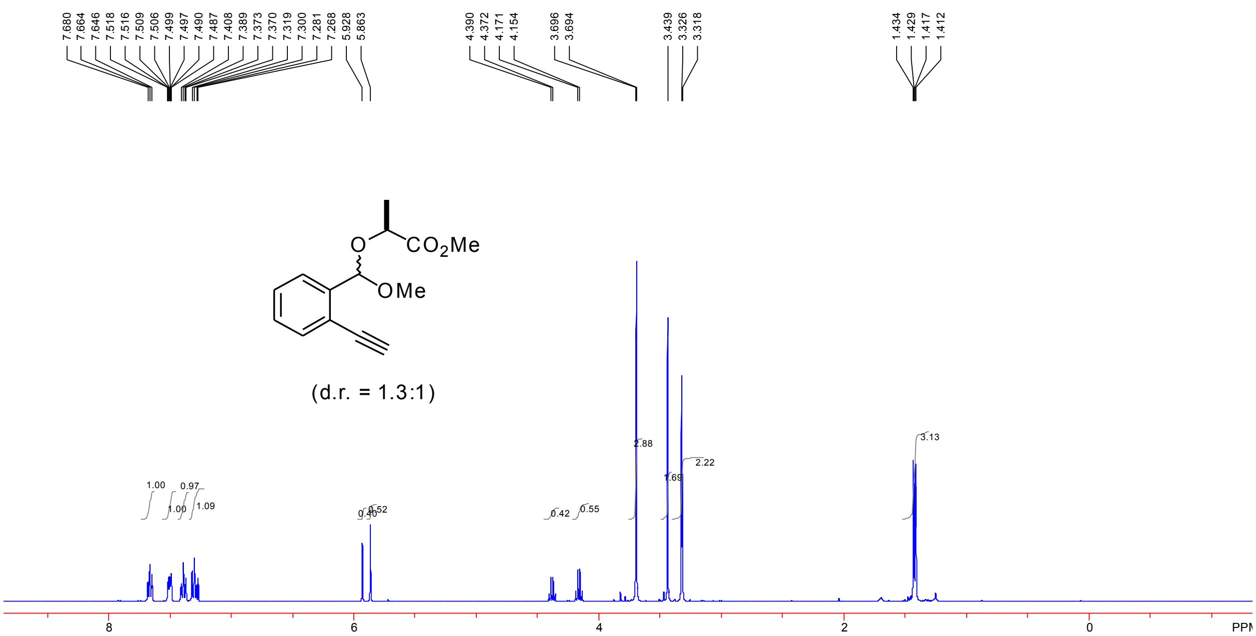


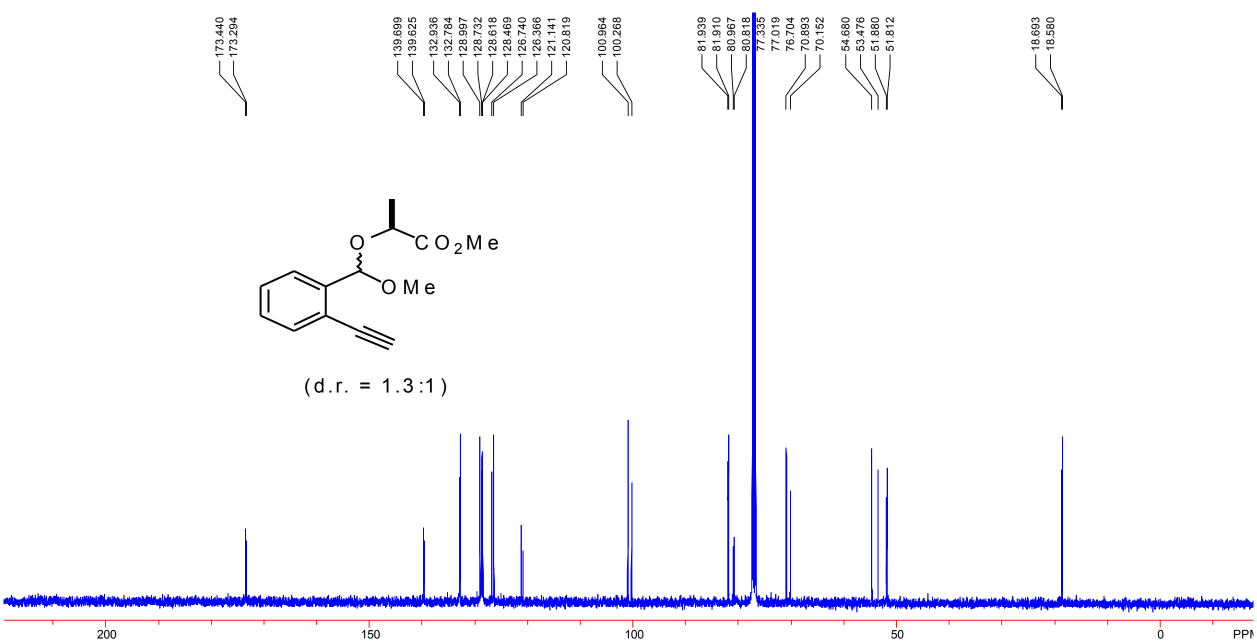
[1]H NMR (400 MHz, $CDCl_3$) and [13]C NMR (100 MHz, $CDCl_3$) of **3q**



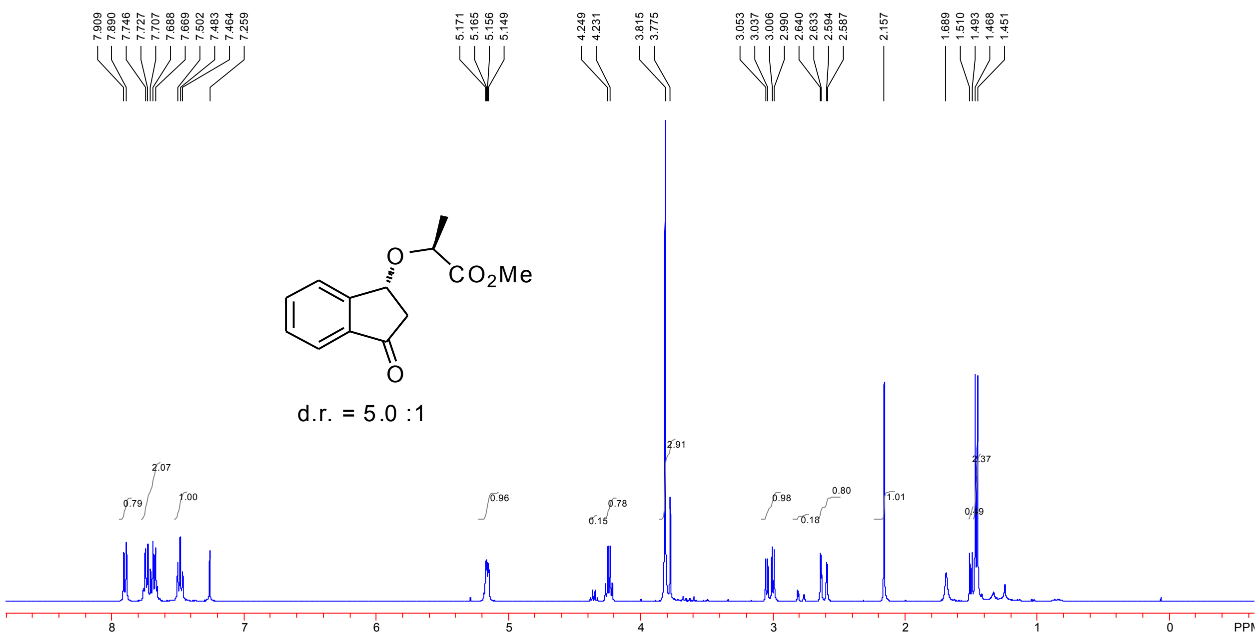


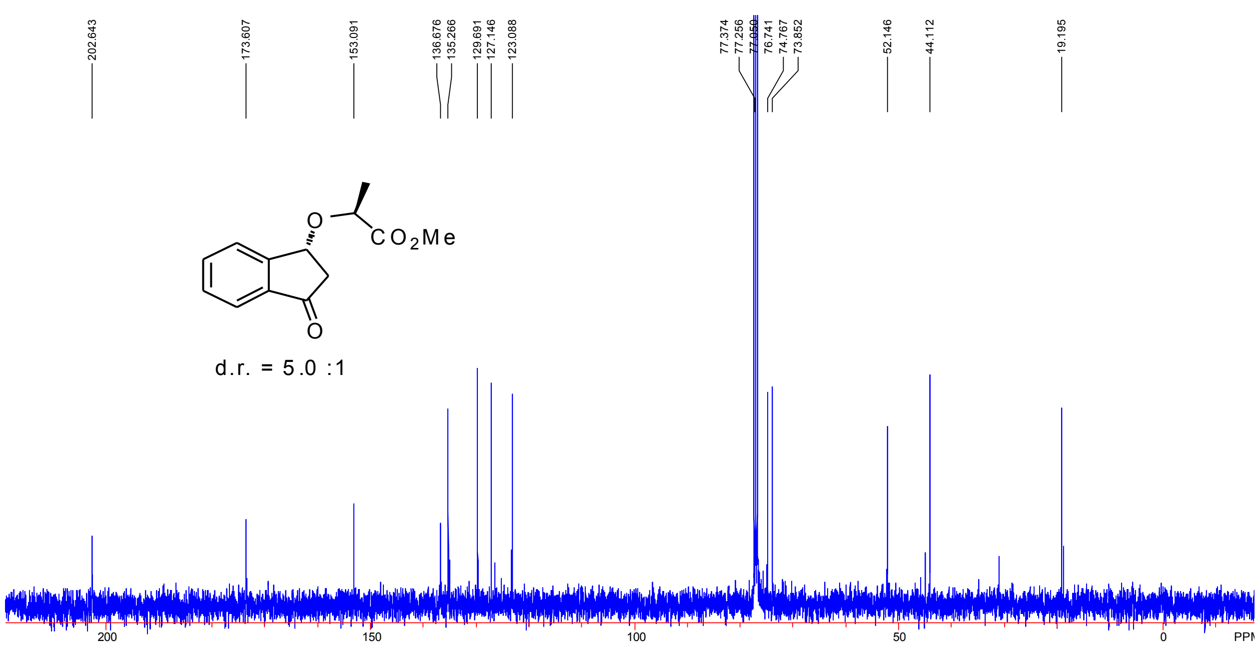
^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) of **4**



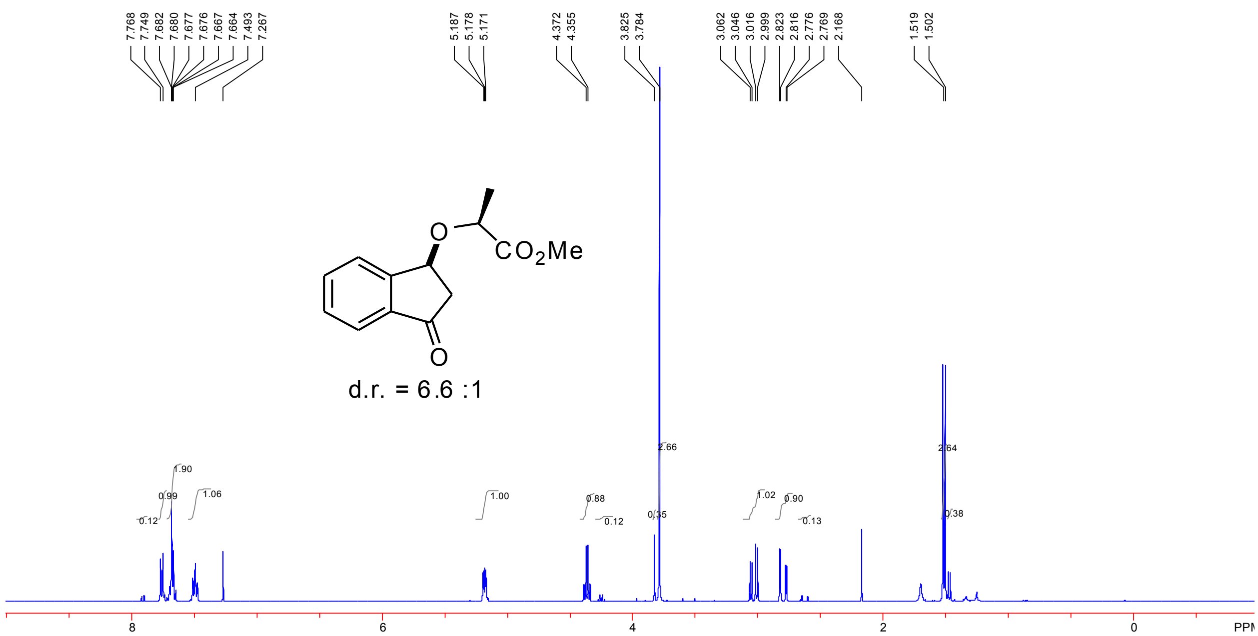


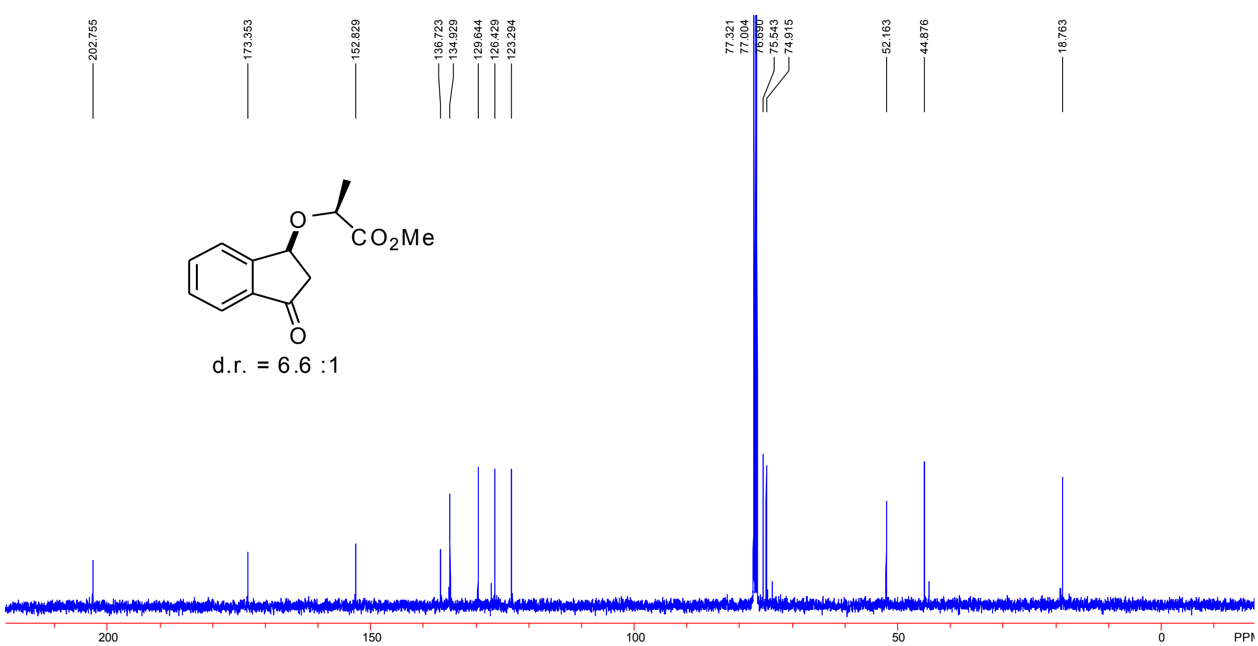
^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) of **5a**



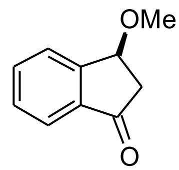


^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) of **5b**

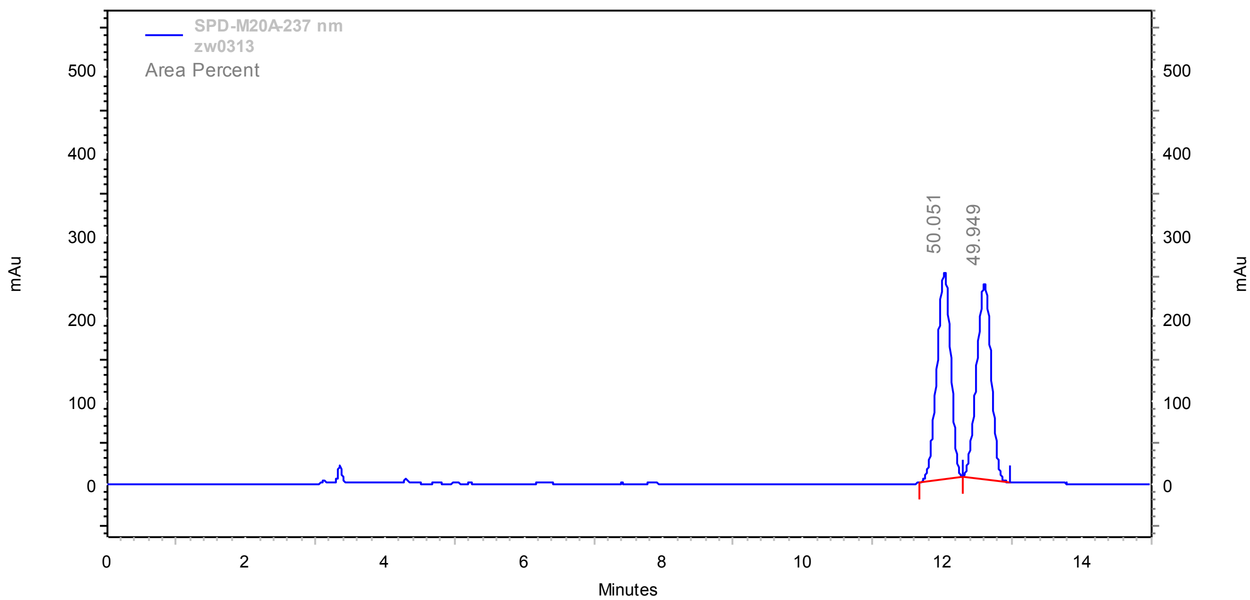


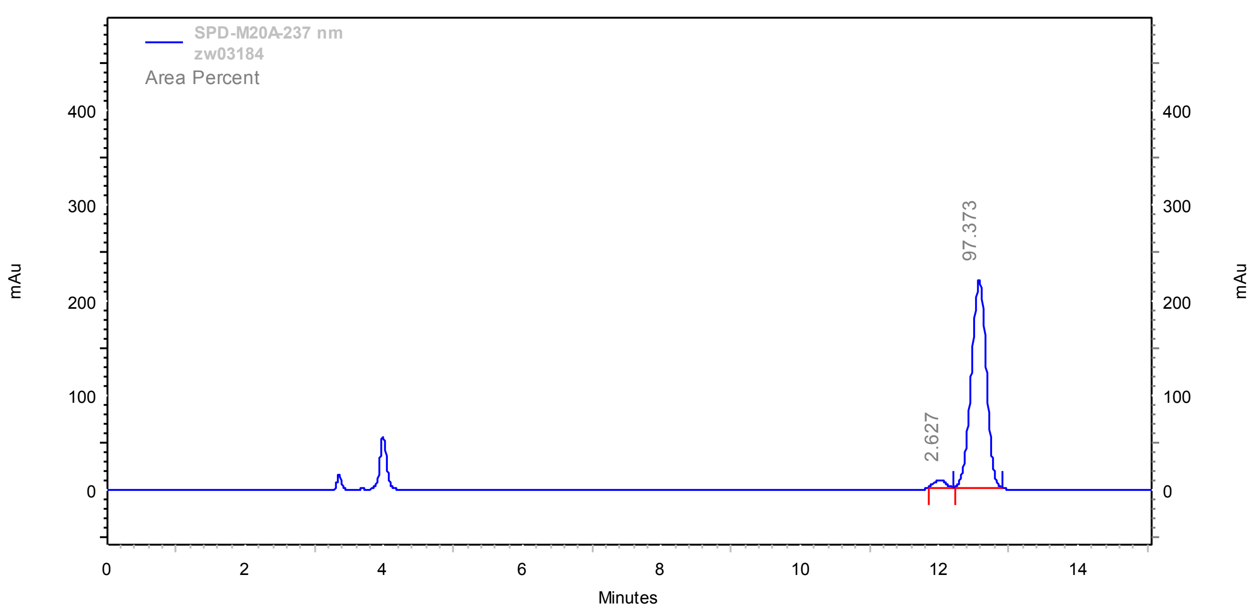


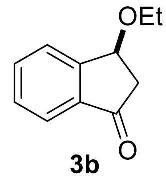
8. Copies of Chiral HPLC Analysis



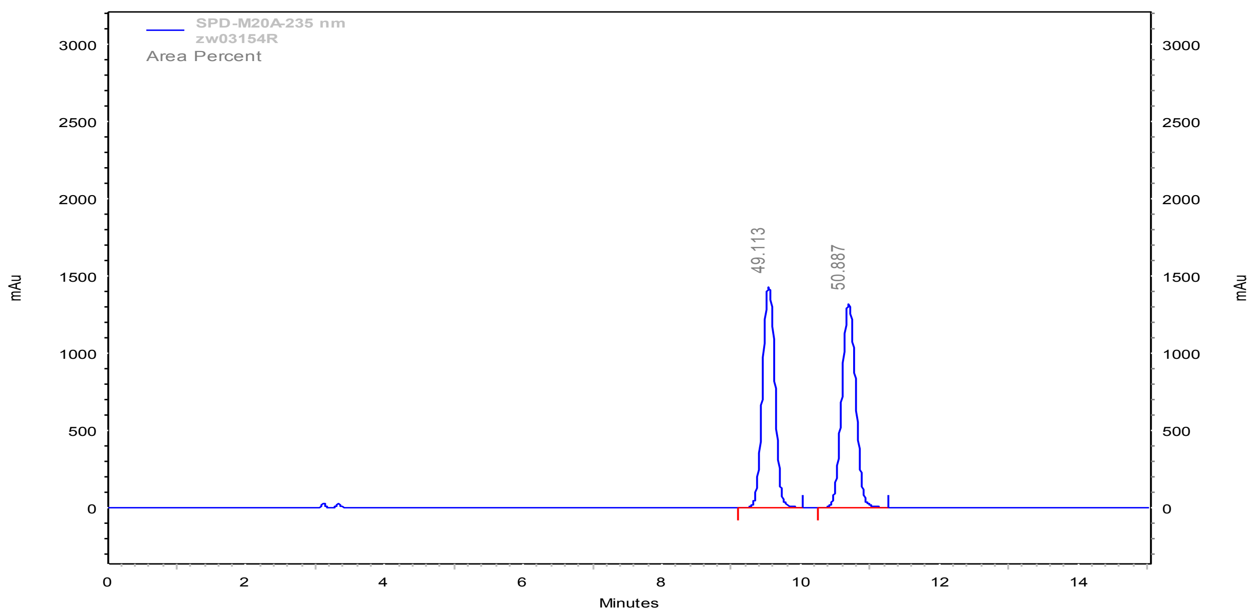
3a

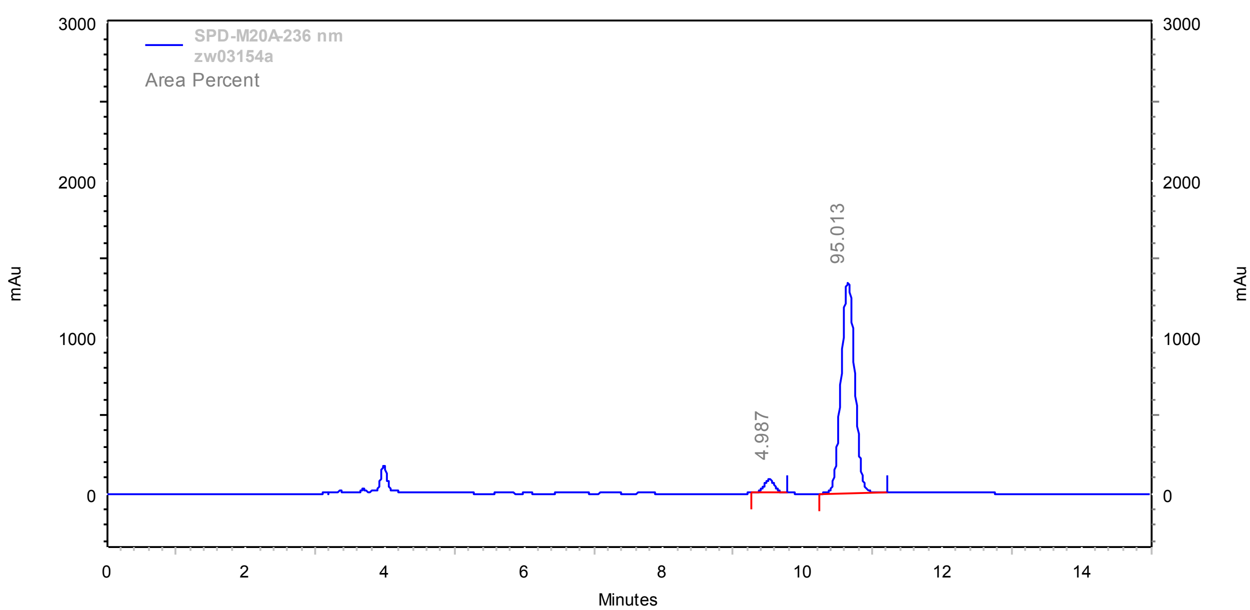


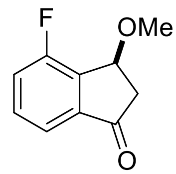



OEt
O

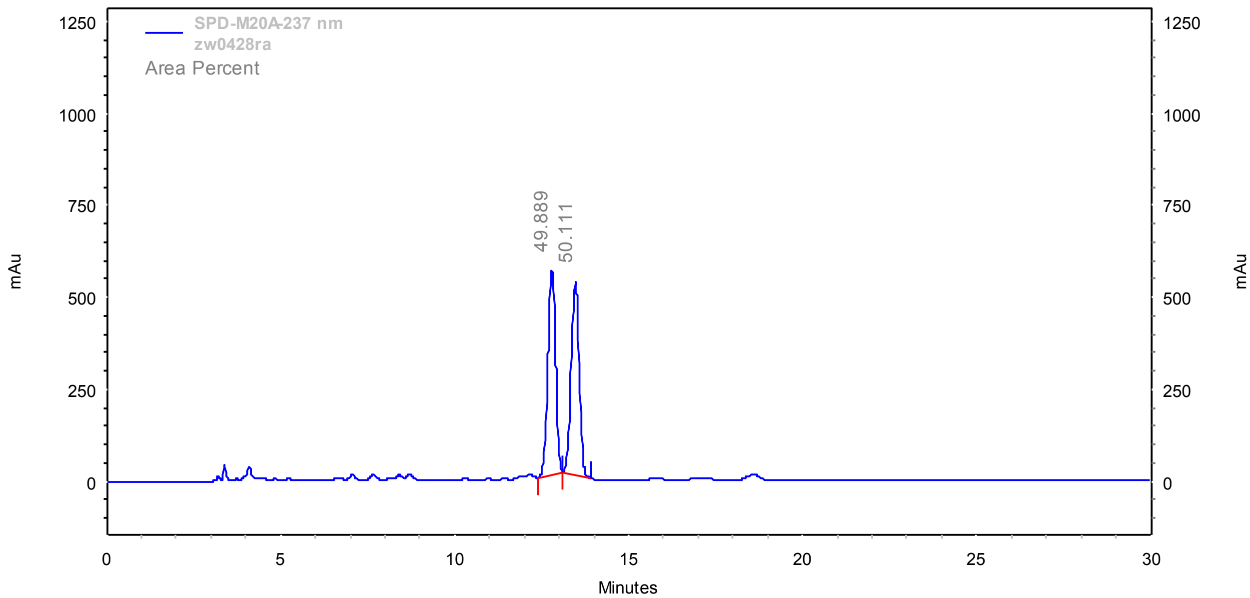
3b

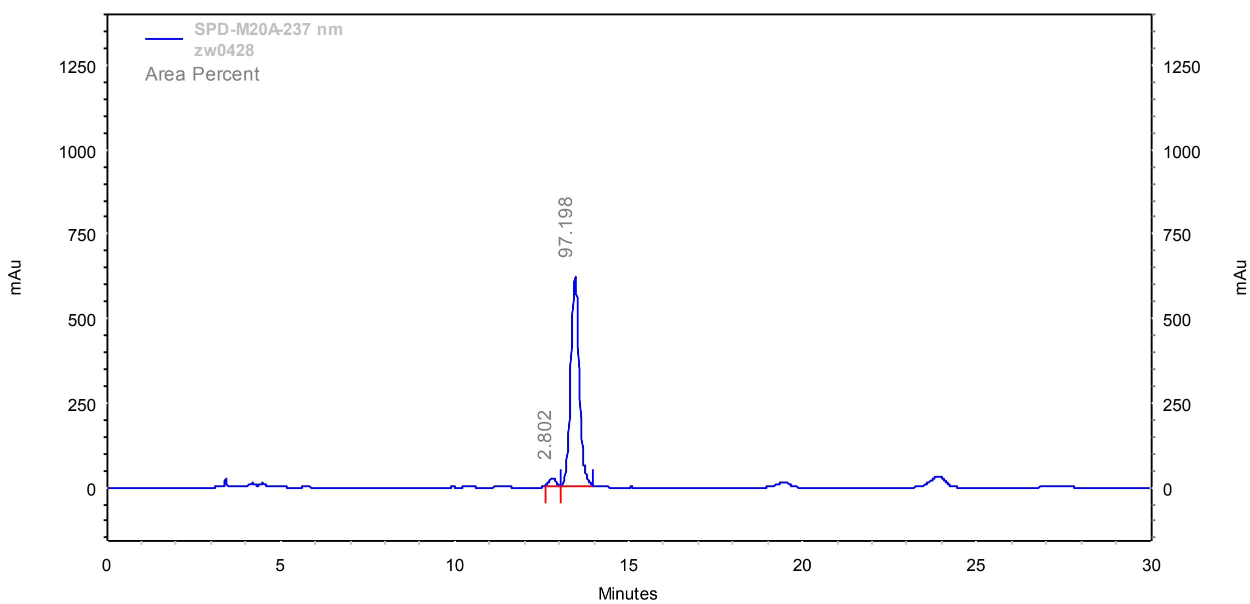

SPD-M20A-235 nm
zw03154R
Area Percent
49.113
50.887
mAu
Minutes

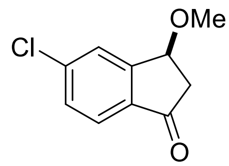

SPD-M20A-236 nm
zw03154a
Area Percent
4.987
95.013
mAu
Minutes


F
OMe
O

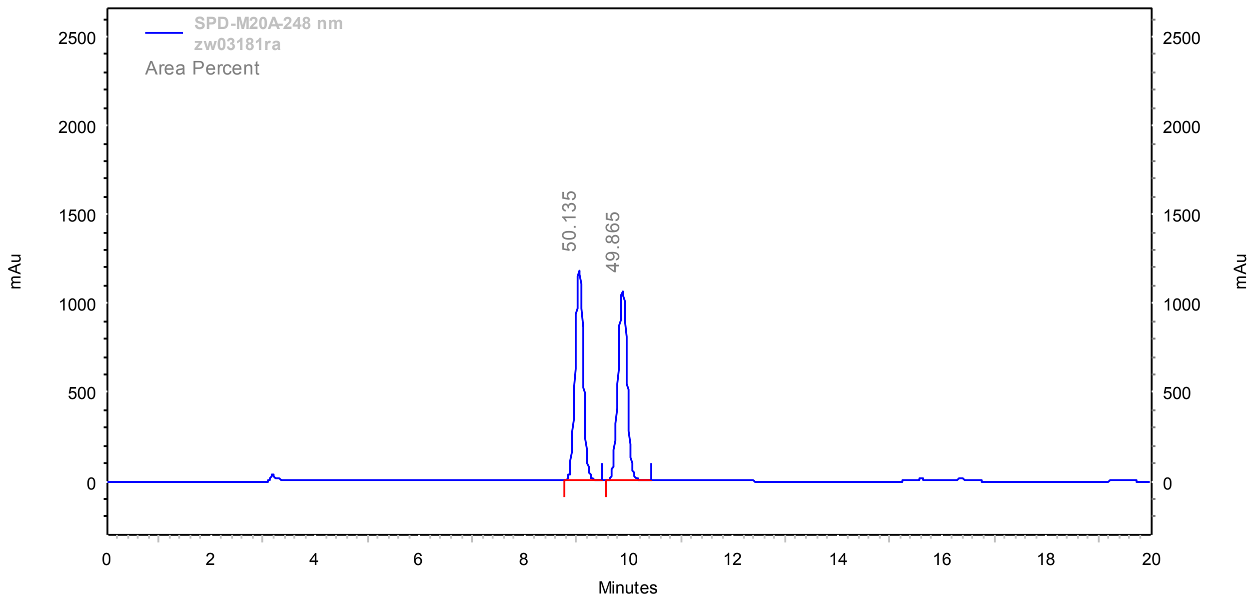
3c

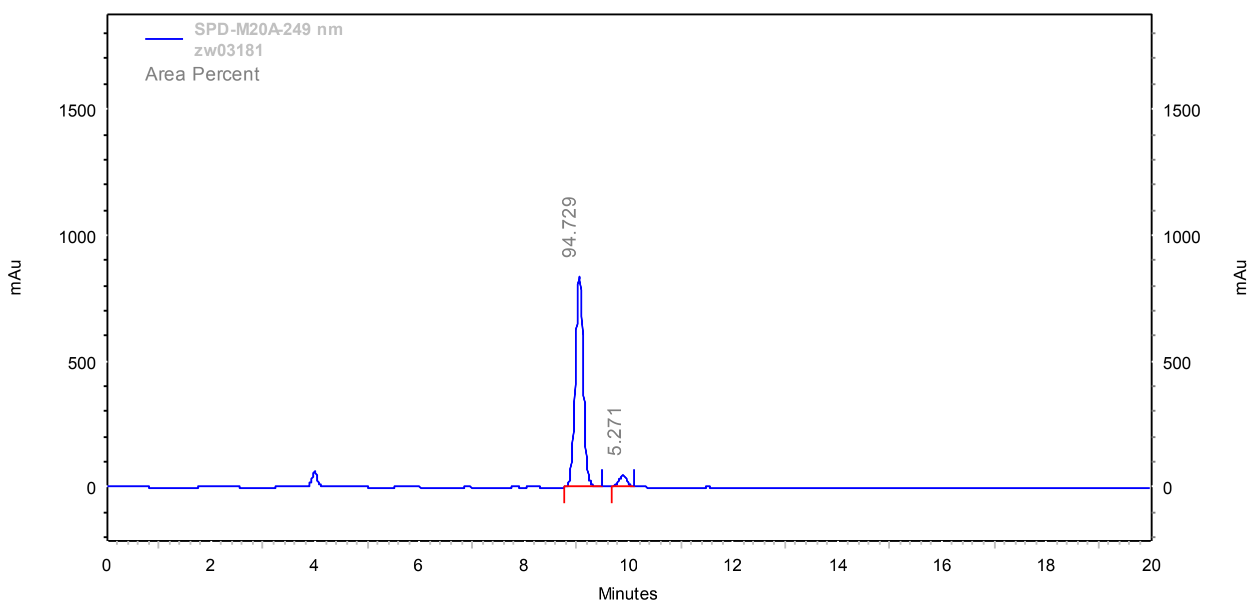

SPD-M20A-237 nm
zw0428ra
Area Percent
49.889
50.111
mAu
Minutes

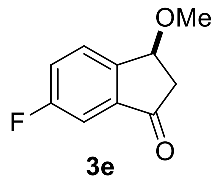

SPD-M20A-237 nm
zw0428
Area Percent
97.198
2.802
mAu
Minutes


OMe
Cl
O

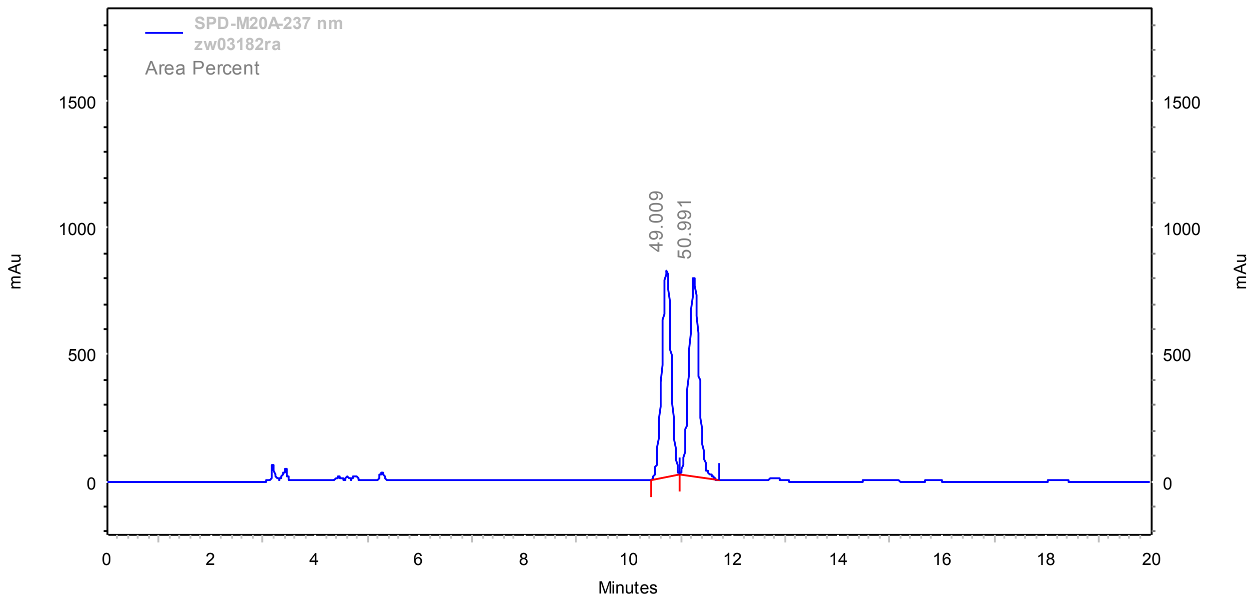
3d

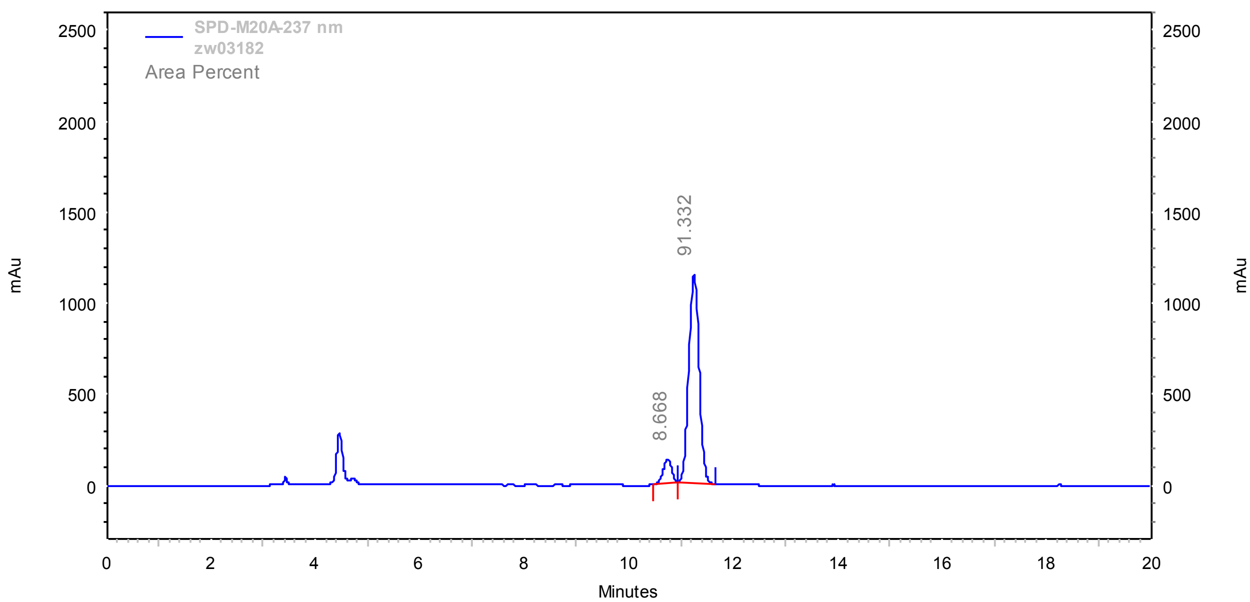

SPD-M20A-248 nm
zw03181ra
Area Percent
50.135
49.865
mAu
Minutes


SPD-M20A-249 nm
zw03181
Area Percent
94.729
5.271
mAu
Minutes


OMe
F
O

3e


SPD-M20A-237 nm
zw03182ra
Area Percent
49.009
50.991
mAu
Minutes
0
2
4
6
8
10
12
14
16
18
20
500
1000
1500


SPD-M20A-237 nm
zw03182
Area Percent
8.668
91.332
mAu
Minutes
0
2
4
6
8
10
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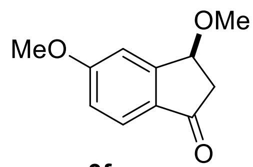
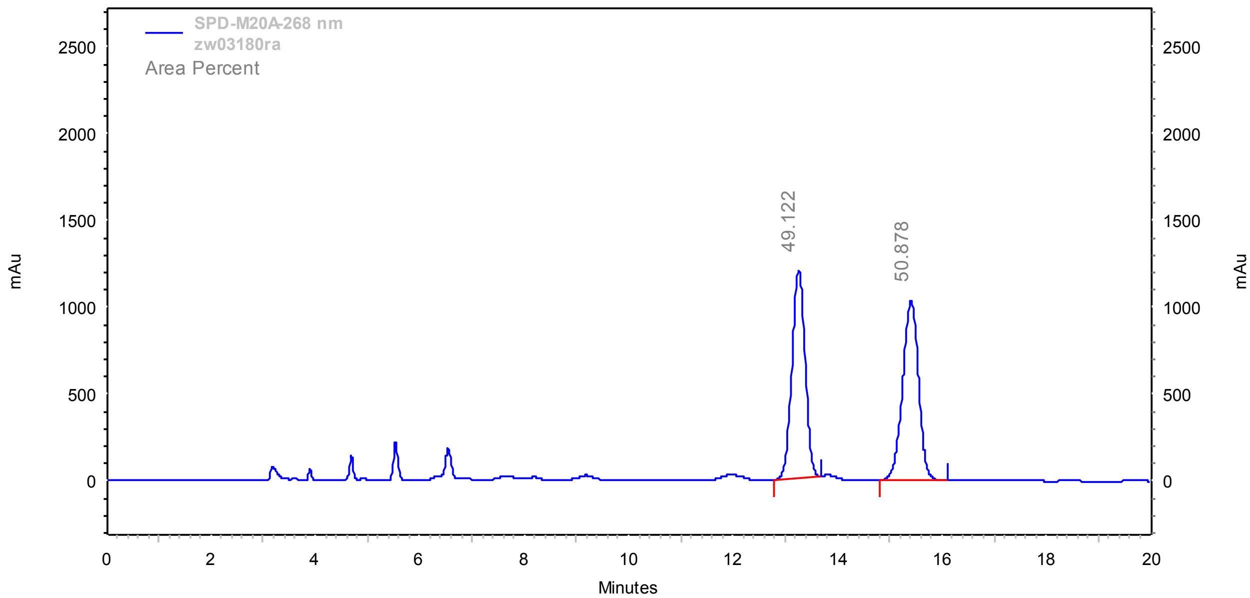
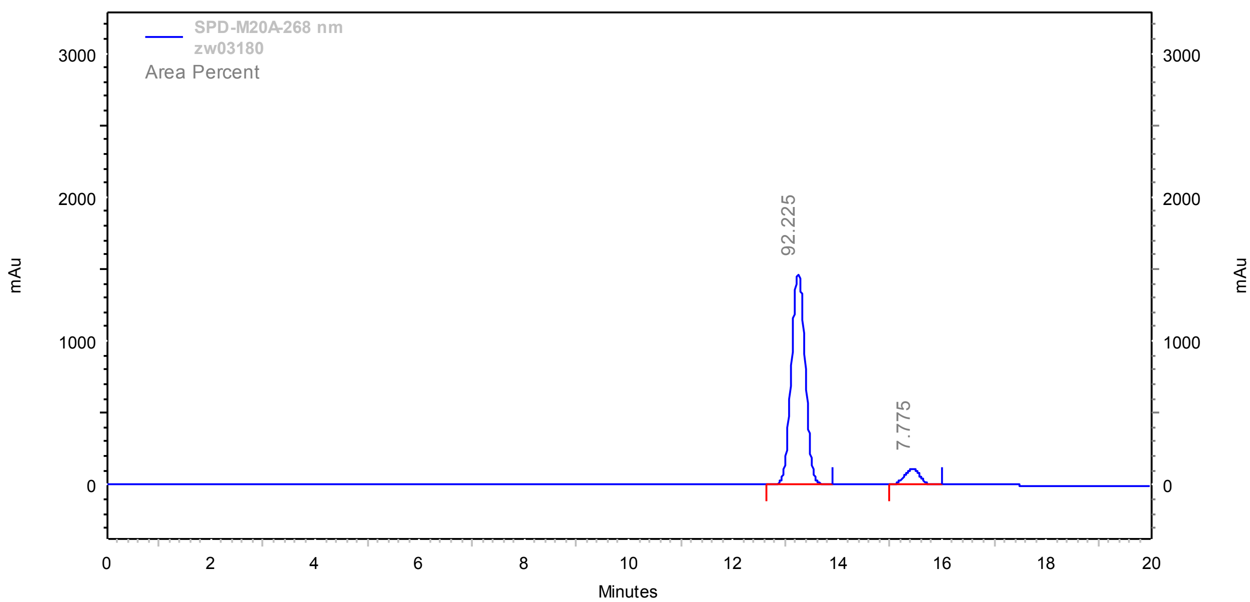
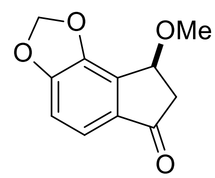
16
18
20
500
1000
1500
2000
2500


OMe
MeO
O

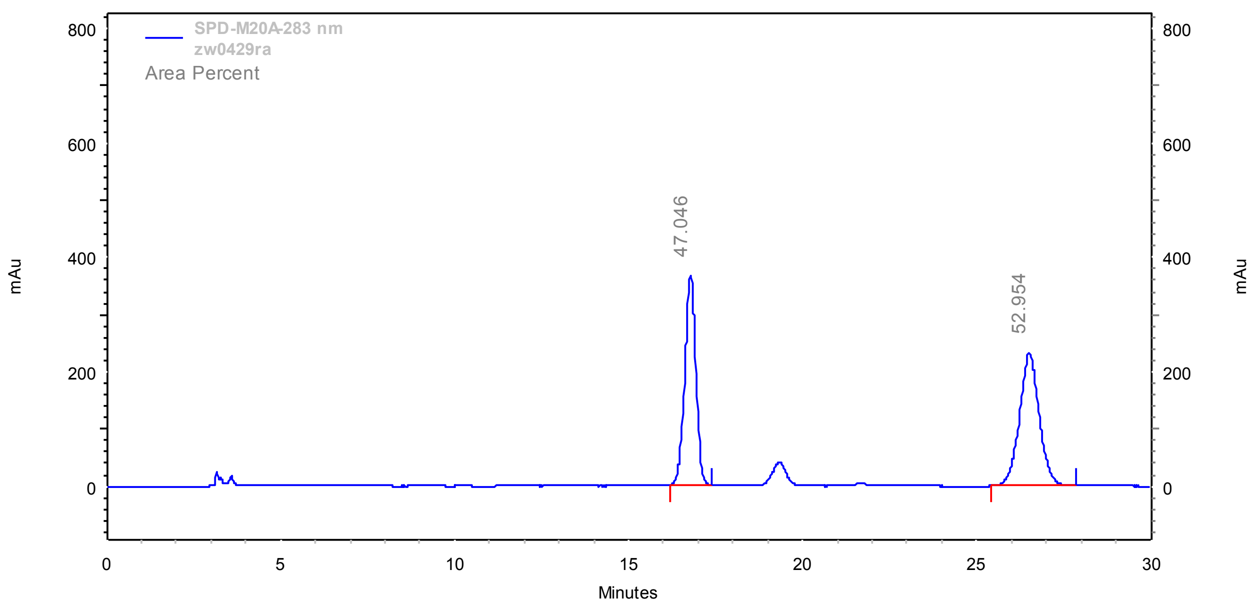
3f

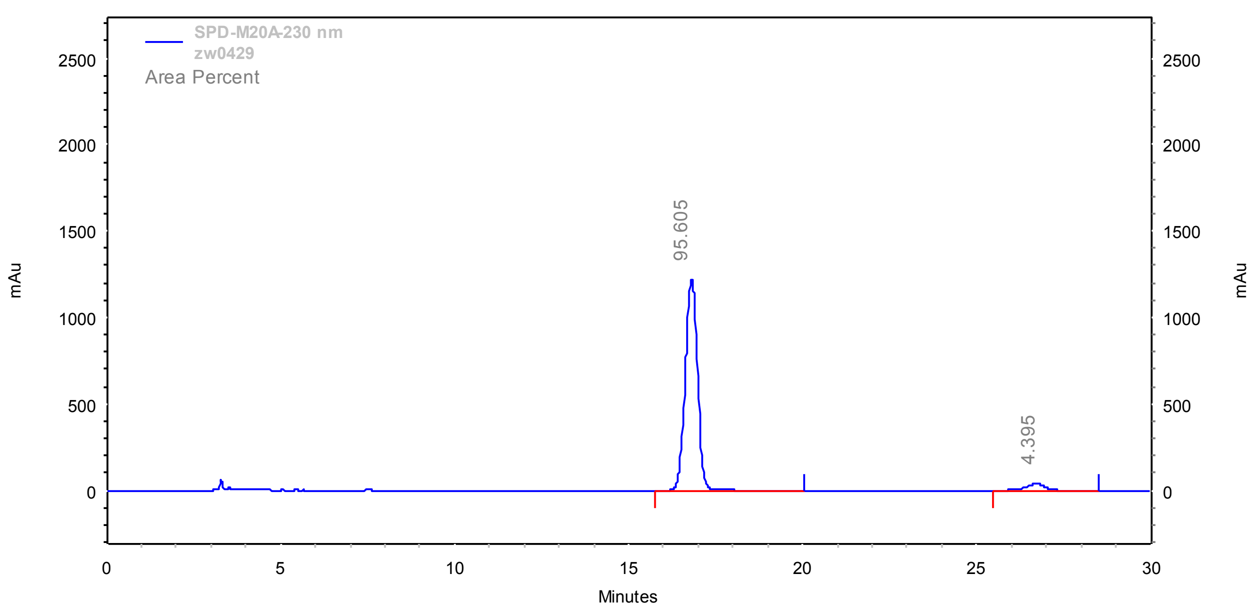

SPD-M20A-268 nm
zw03180ra
Area Percent
49.122
50.878
mAu
Minutes

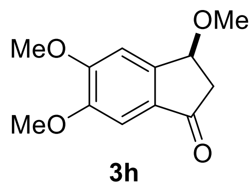

SPD-M20A-268 nm
zw03180
Area Percent
92.225
7.775
mAu
Minutes


O
O
OMe
O

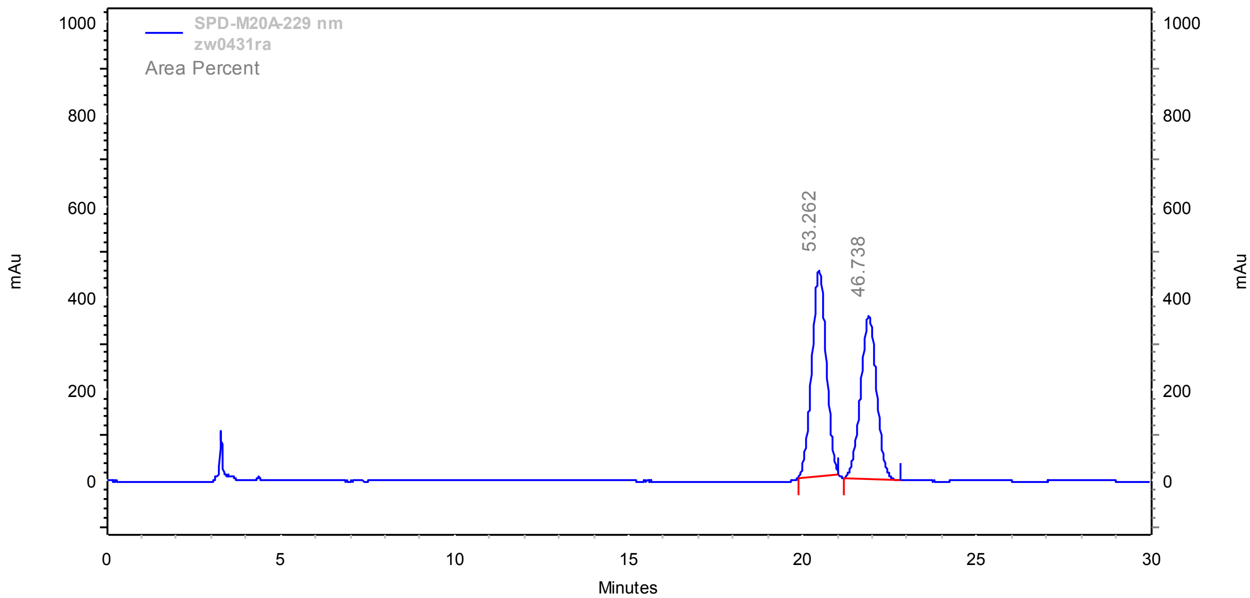
3g

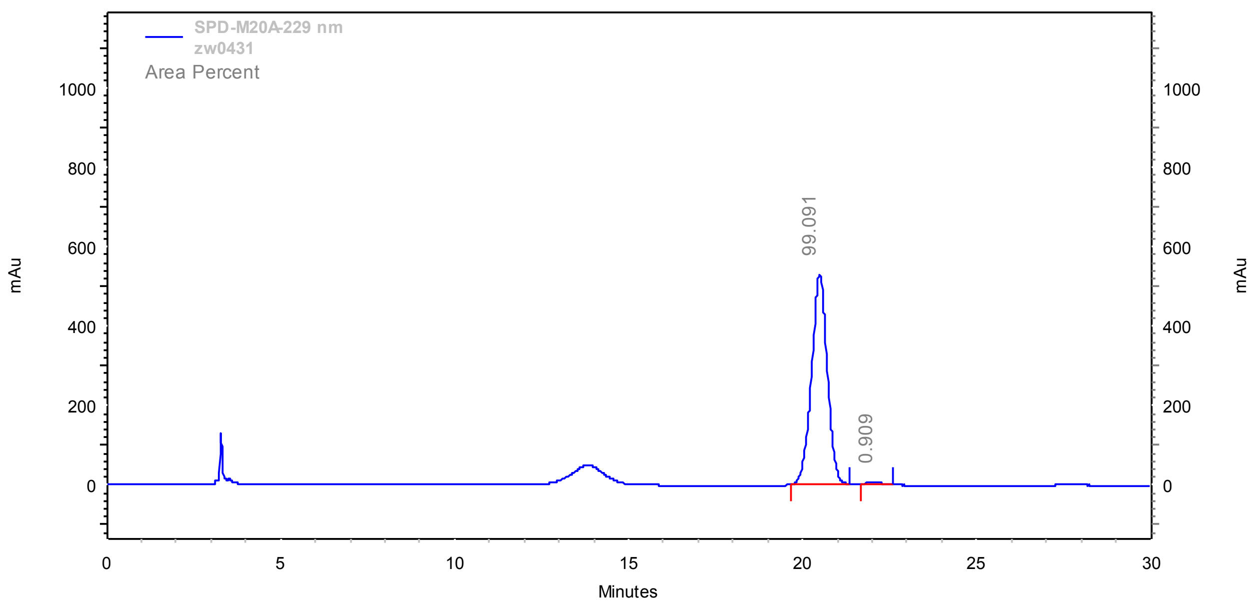

SPD-M20A-283 nm
zw0429ra
Area Percent
47.046
52.954
mAu
Minutes
0
5
10
15
20
25
30
800
600
400
200
0

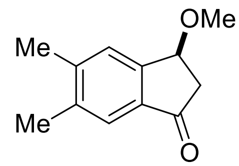

SPD-M20A-230 nm
zw0429
Area Percent
95.605
4.395
mAu
Minutes
0
5
10
15
20
25
30
2500
2000
1500
1000
500
0


OMe
MeO
MeO
O

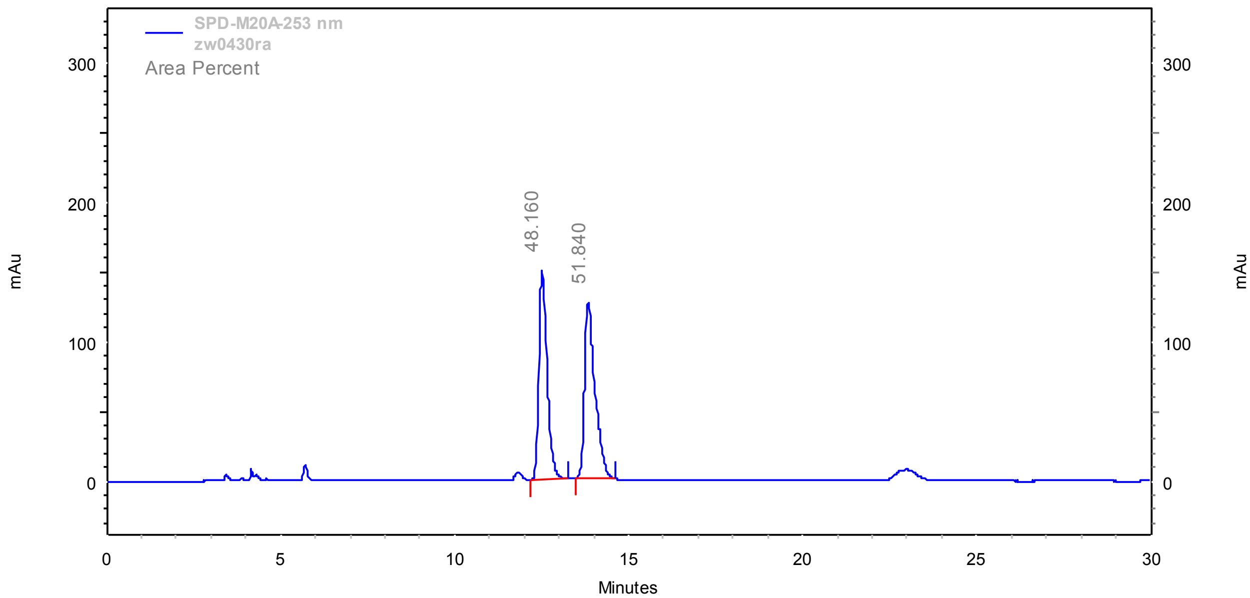
3h

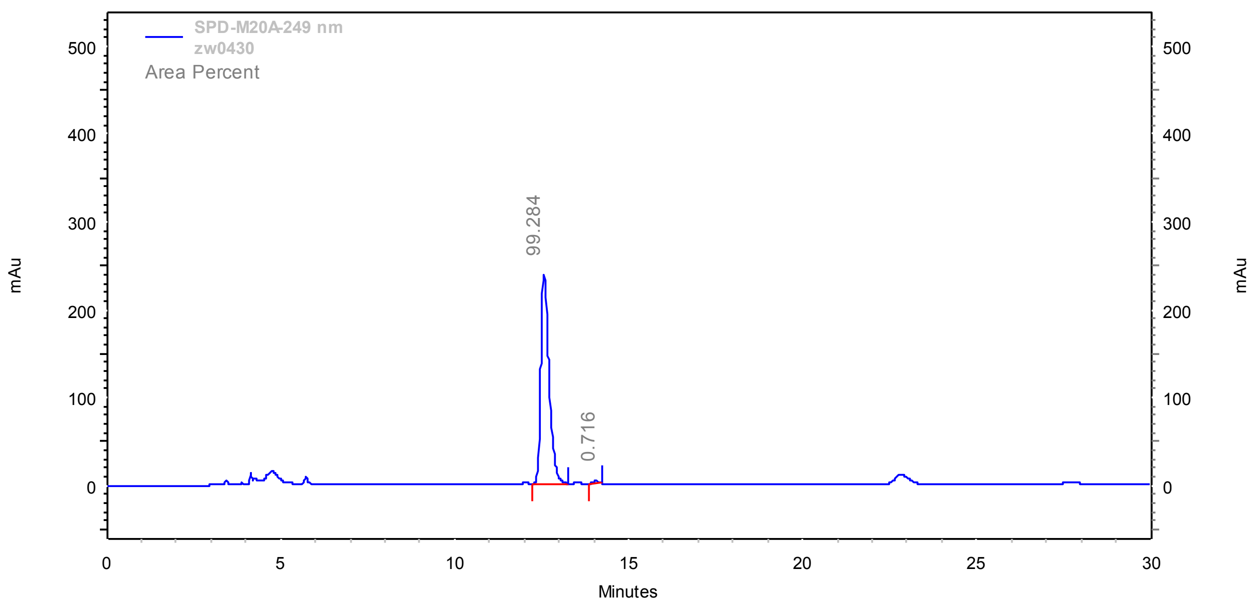

SPD-M20A-229 nm
zw0431ra
Area Percent
53.262
46.738
mAu
Minutes

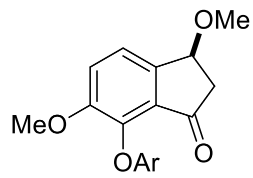

SPD-M20A-229 nm
zw0431
Area Percent
99.091
0.909
mAu
Minutes


OMe
Me
Me
O

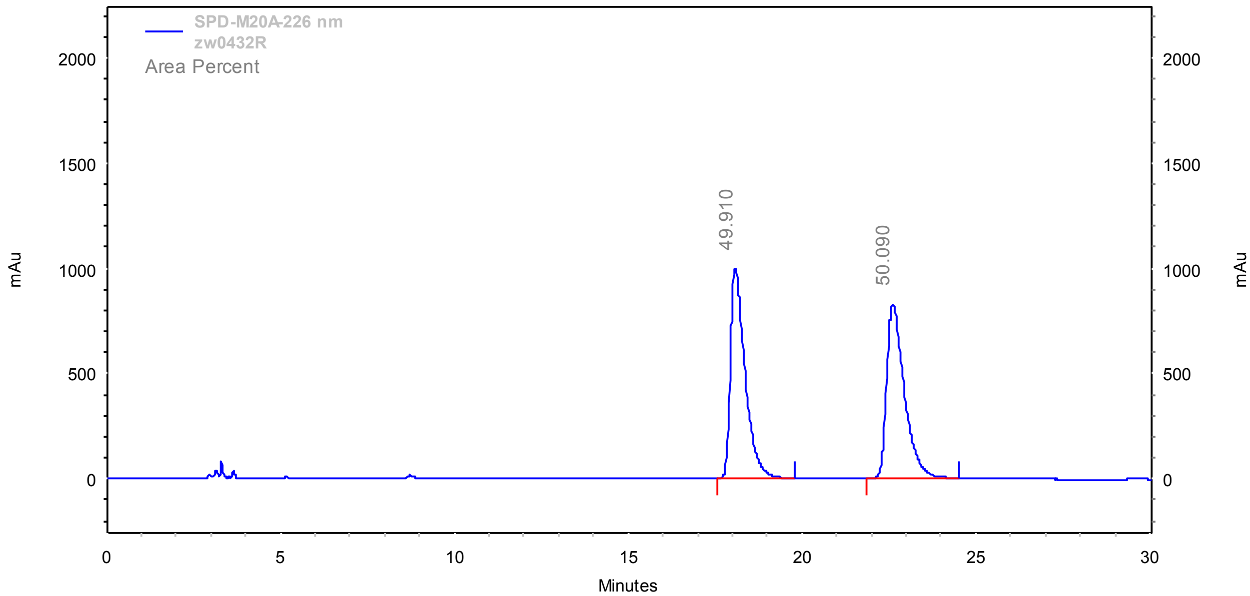
3i

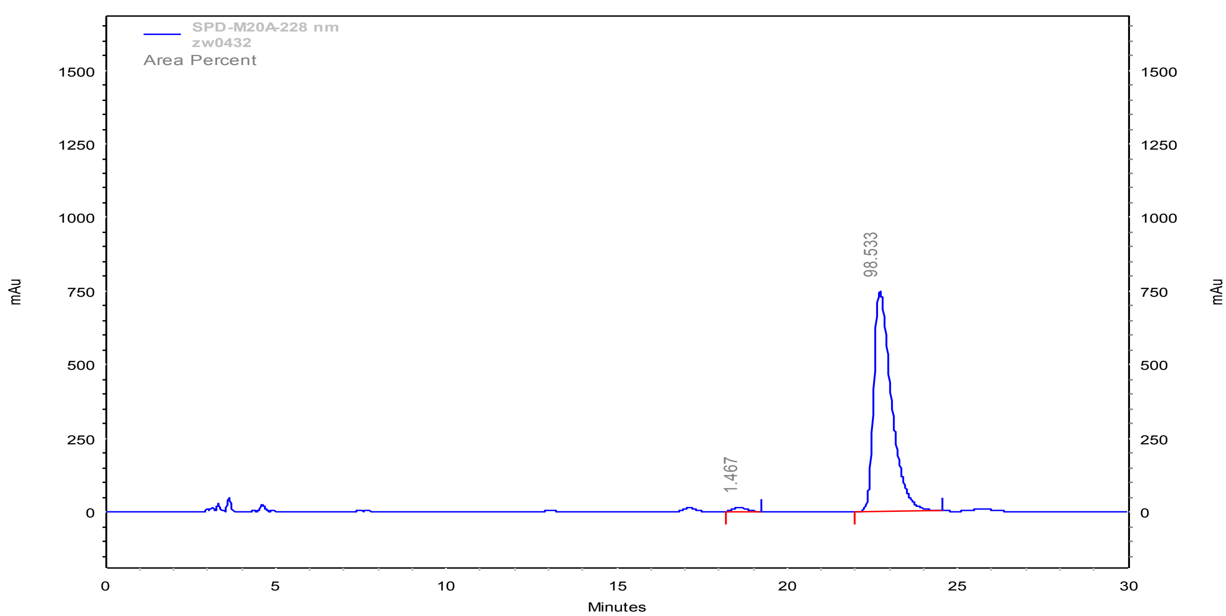

SPD-M20A-253 nm
zw0430ra
Area Percent
48.160
51.840
mAu
Minutes
0
5
10
15
20
25
30
300
200
100
0

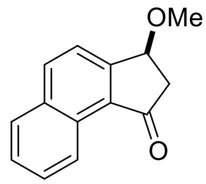

SPD-M20A-249 nm
zw0430
Area Percent
99.284
0.716
mAu
Minutes
0
5
10
15
20
25
30
500
400
300
200
100
0


OMe
MeO
OAr
O

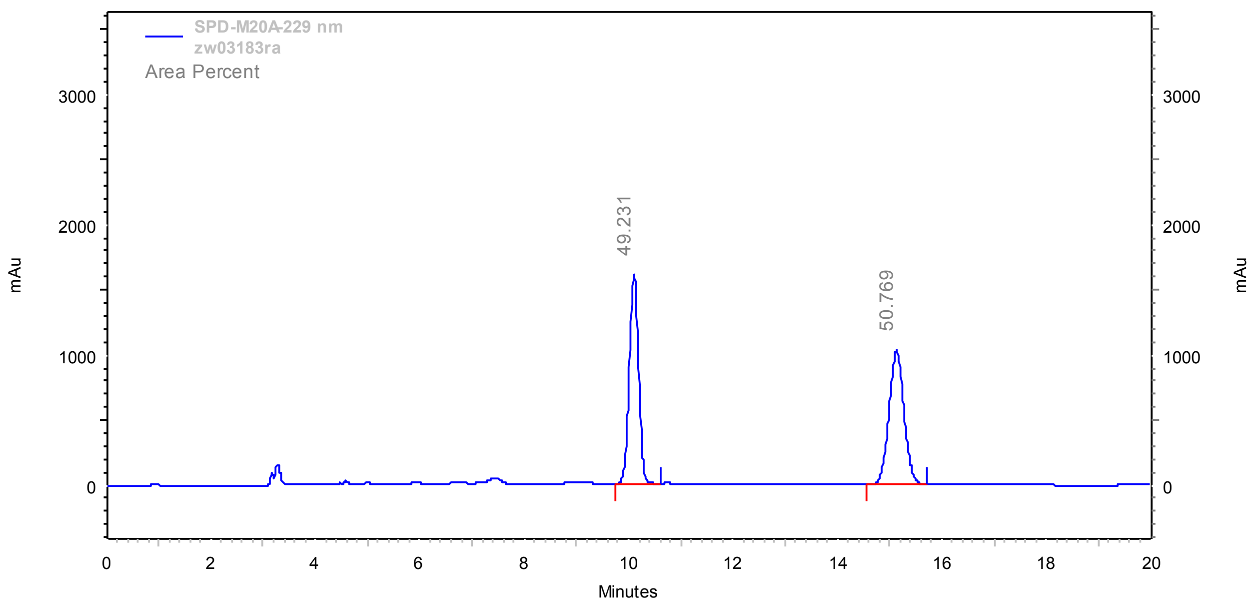
3j

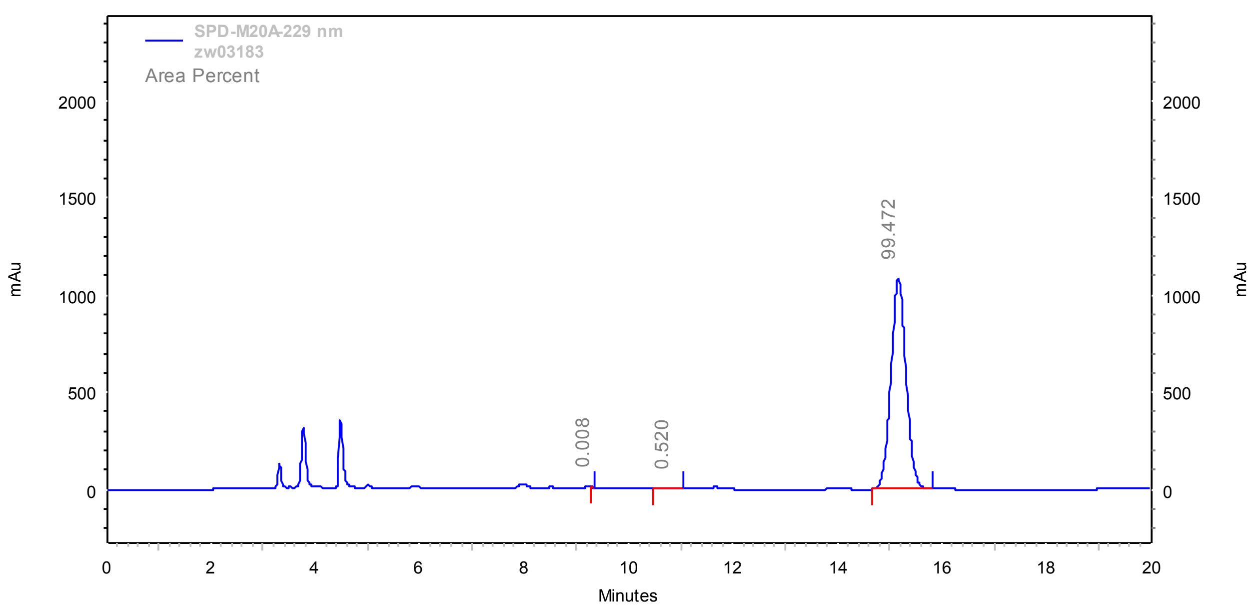

SPD-M20A-226 nm
zw0432R
Area Percent
49.910
50.090
mAu
Minutes

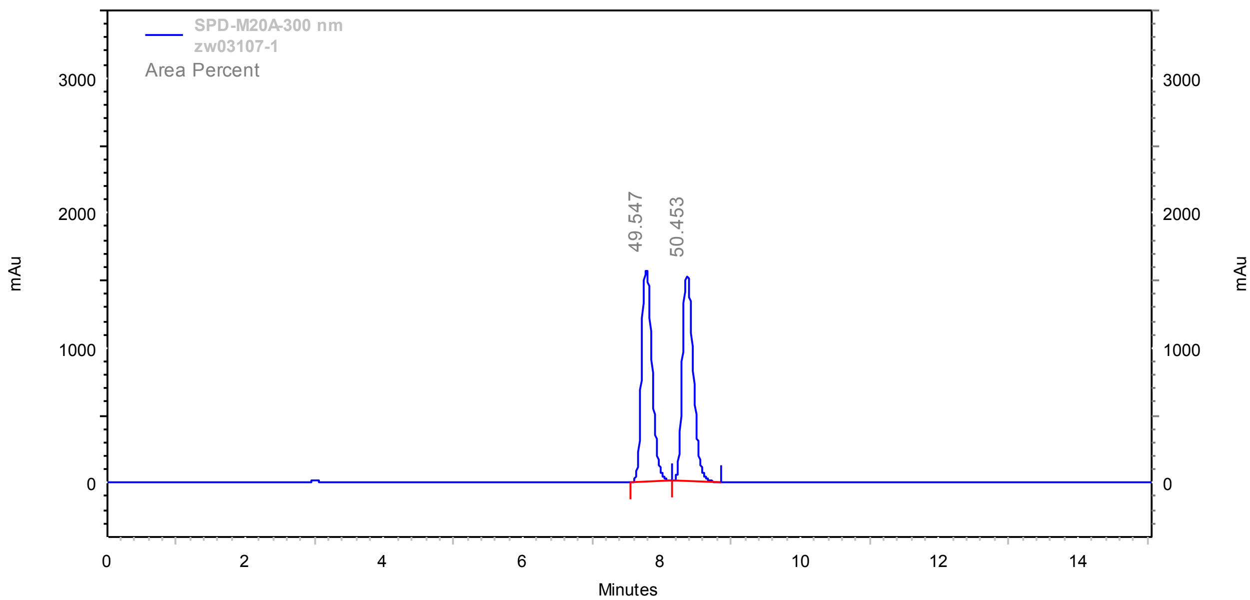

SPD-M20A-228 nm
zw0432
Area Percent
1.467
98.533
mAu
Minutes

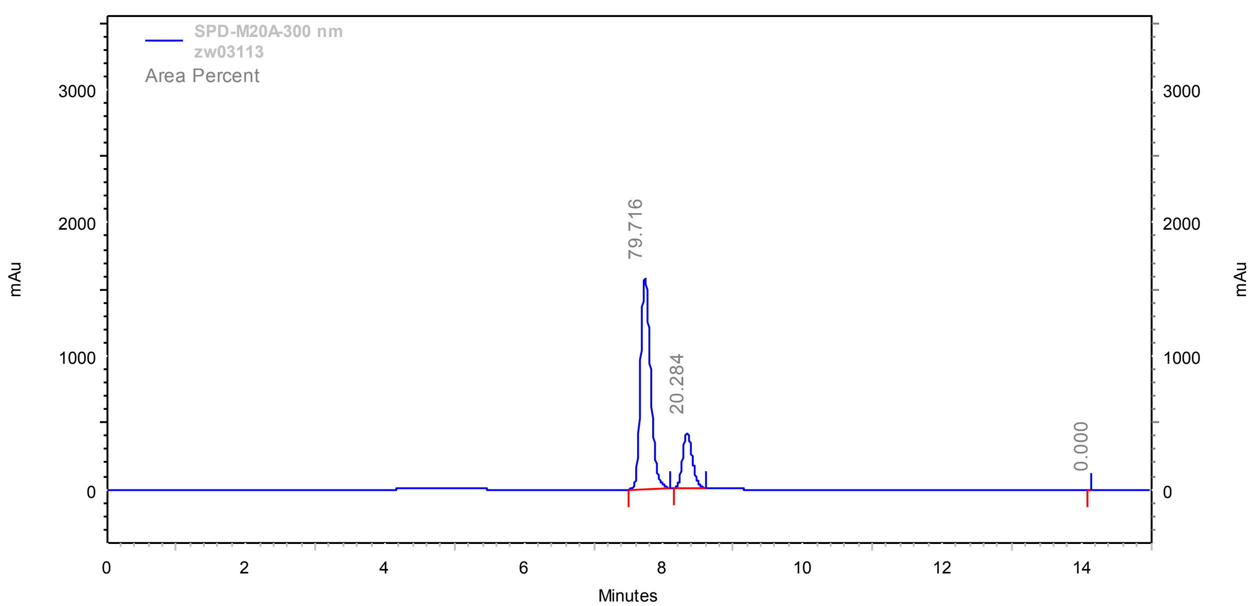

OMe
O

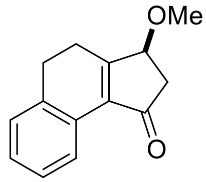
3k


SPD-M20A-229 nm
zw03183ra
Area Percent
49.231
50.769
mAu
Minutes

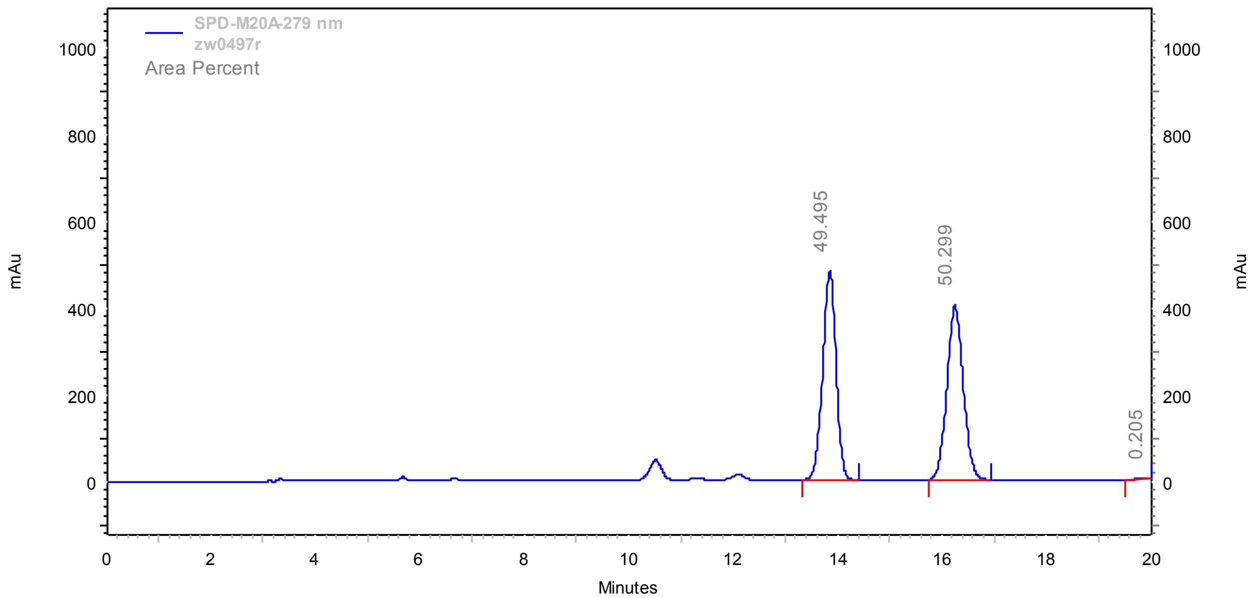

SPD-M20A-229 nm
zw03183
Area Percent
0.008
0.520
99.472
mAu
Minutes

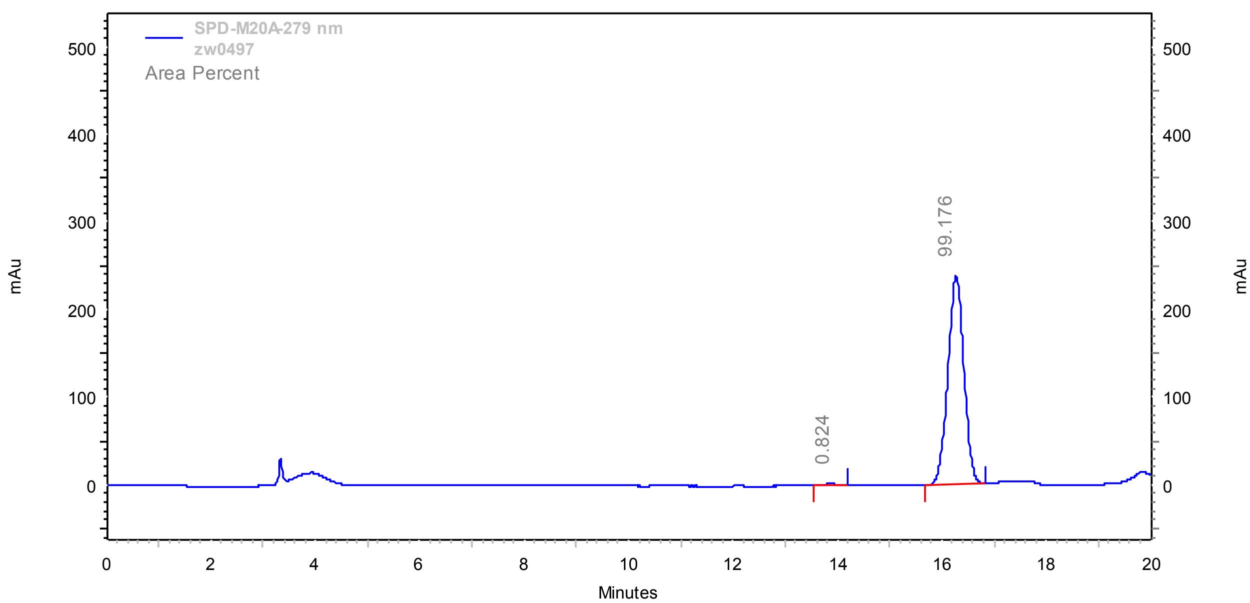

SPD-M20A-300 nm
zw03107-1
Area Percent
49.547
50.453
mAu
Minutes

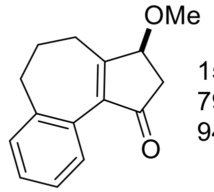

SPD-M20A-300 nm
zw03113
Area Percent
79.716
20.284
0.000
mAu
Minutes


OMe
O

3m

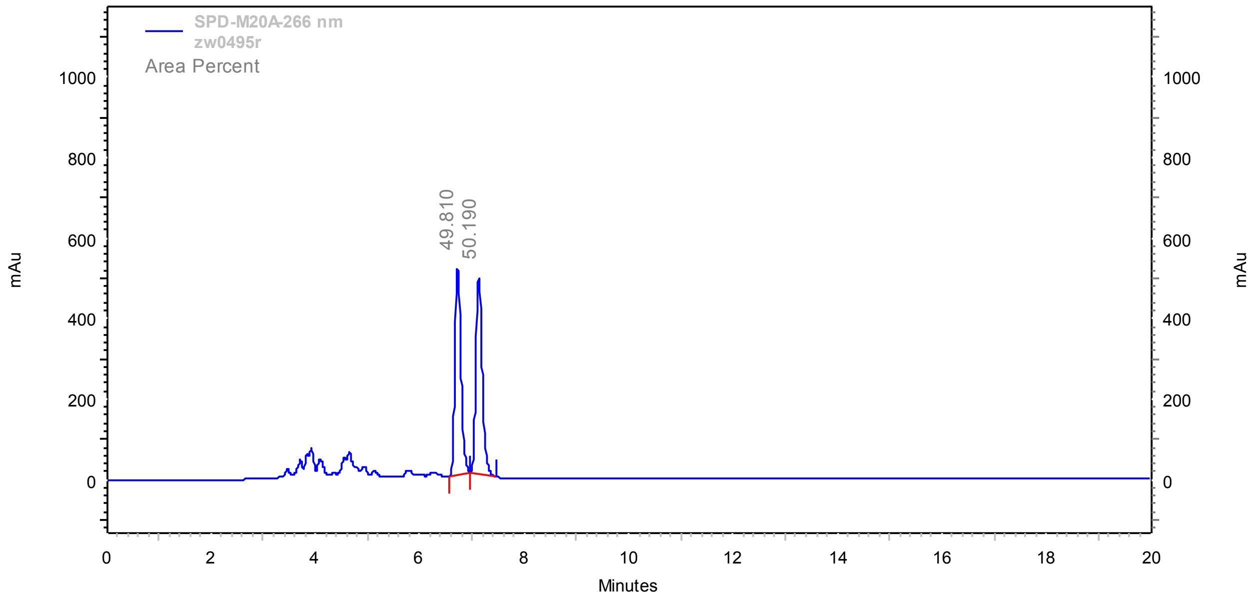

SPD-M20A-279 nm
zw0497r
Area Percent
49.495
50.299
0.205
mAu
Minutes

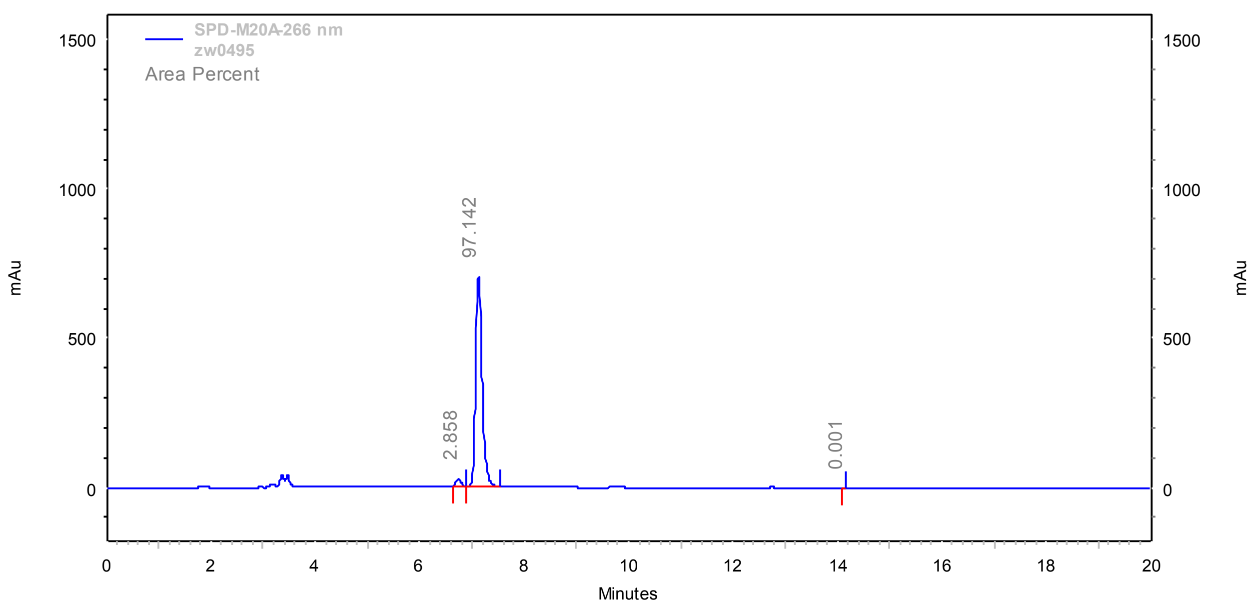

SPD-M20A-279 nm
zw0497
Area Percent
0.824
99.176
mAu
Minutes

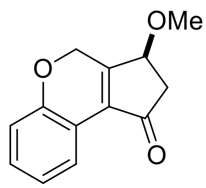


15 min
79% yield
94% ee

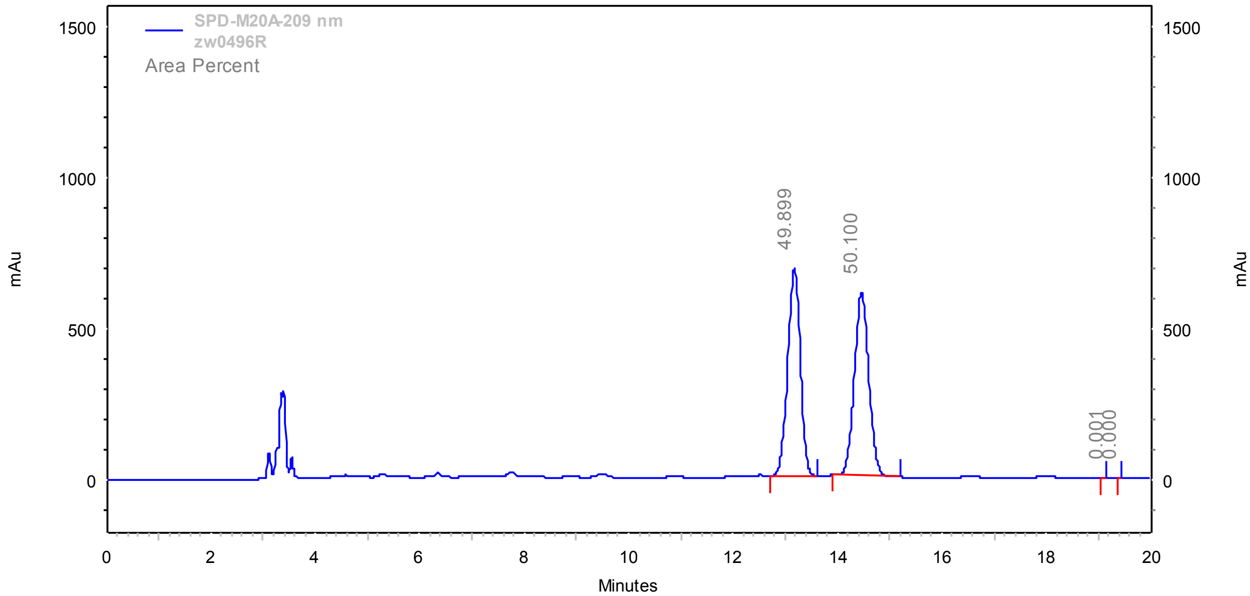
3n

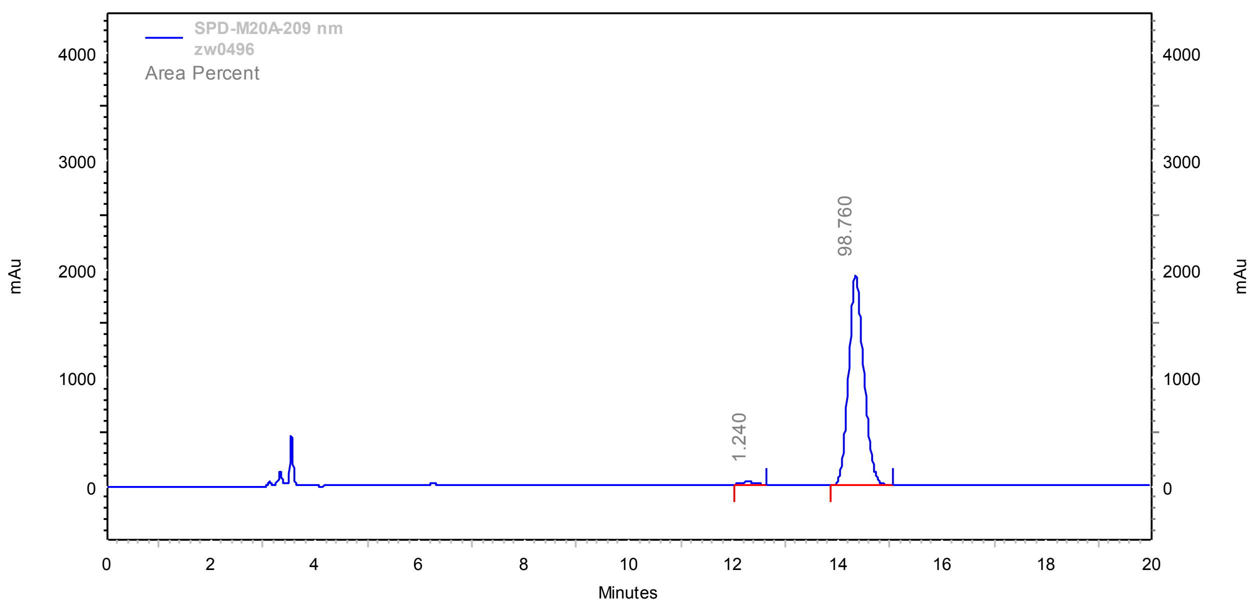


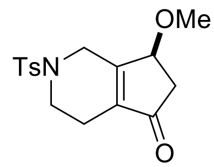



OMe
O
O

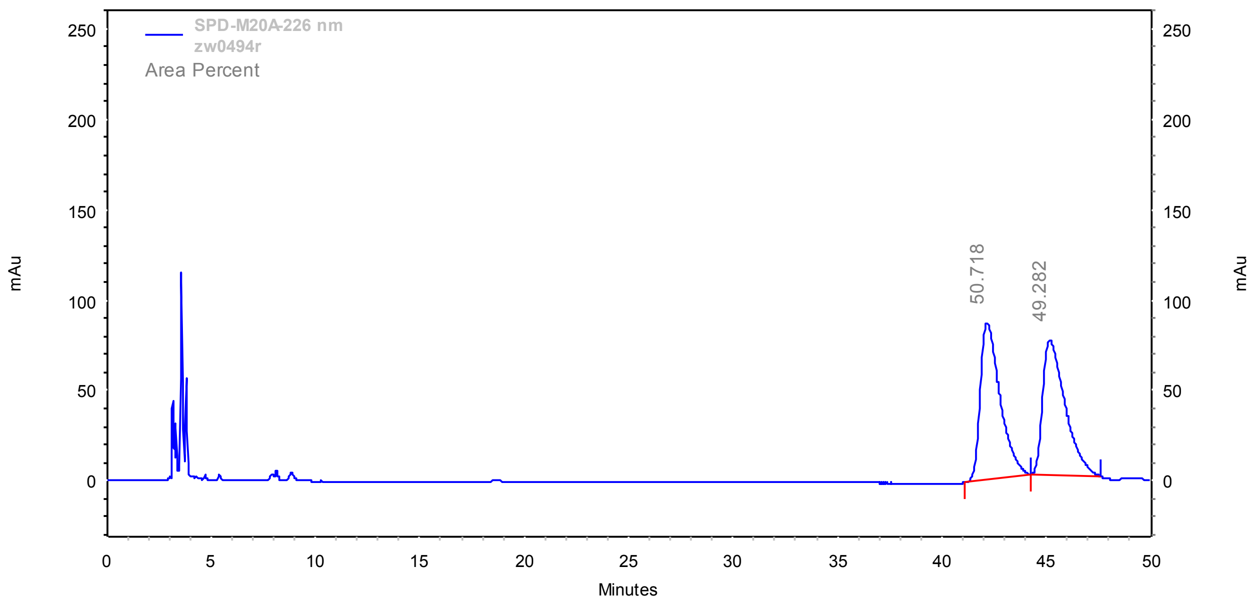
3o

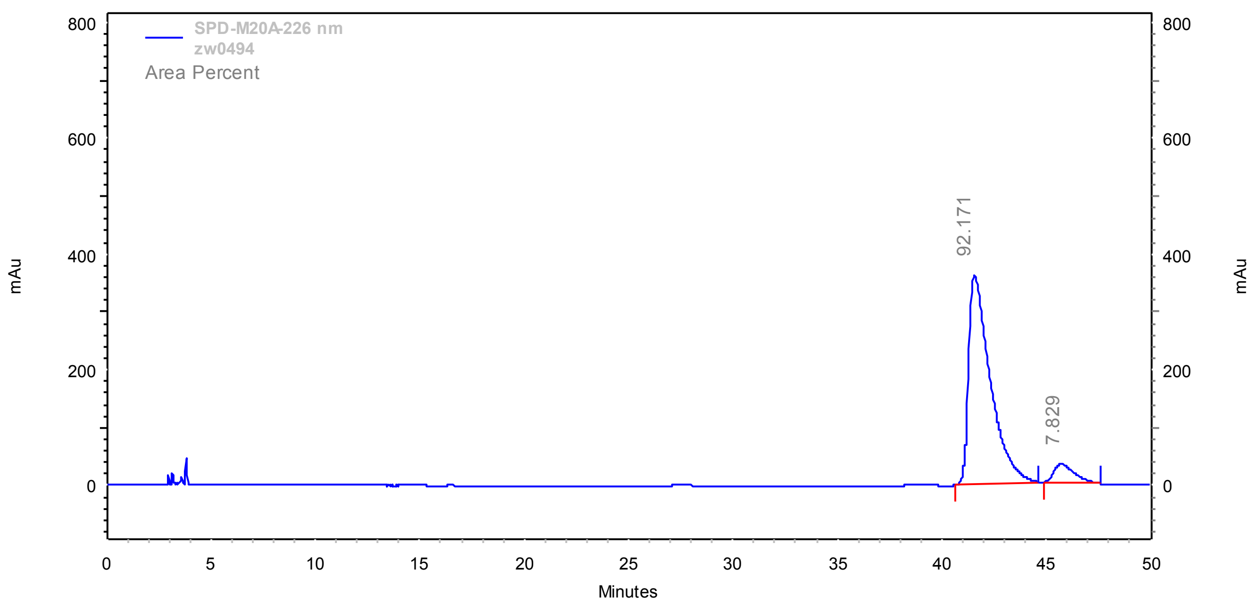

SPD-M20A-209 nm
zw0496R
Area Percent
49.899
50.100
0.001
0.000
mAu
Minutes

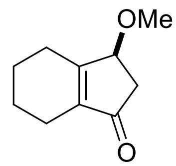

SPD-M20A-209 nm
zw0496
Area Percent
1.240
98.760
mAu
Minutes



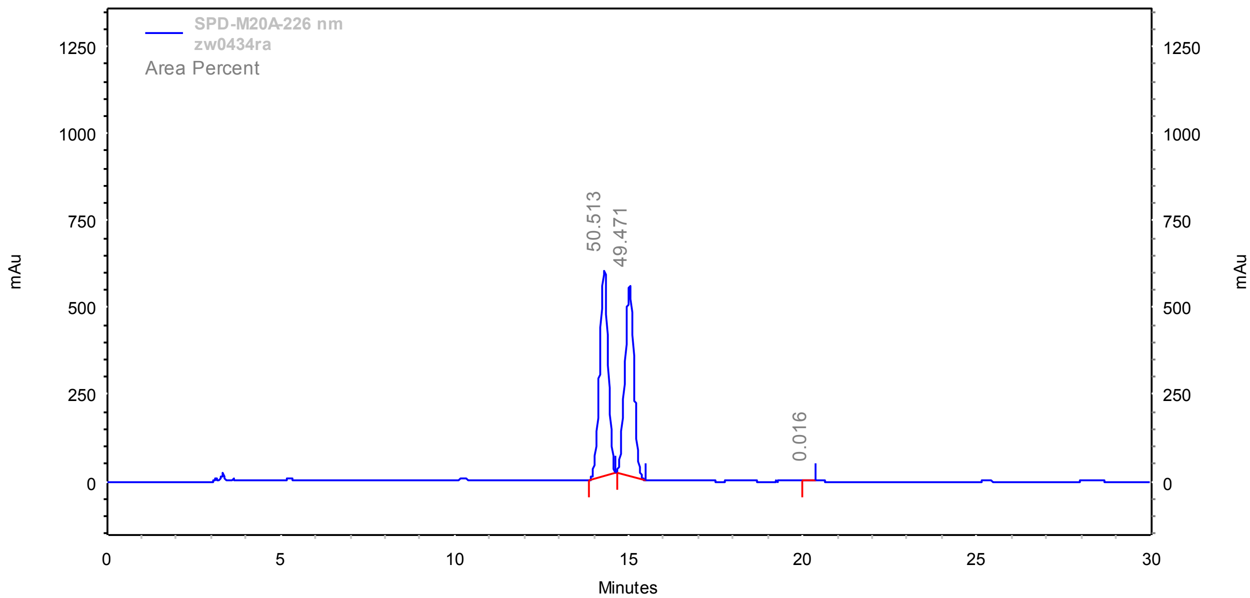
3p

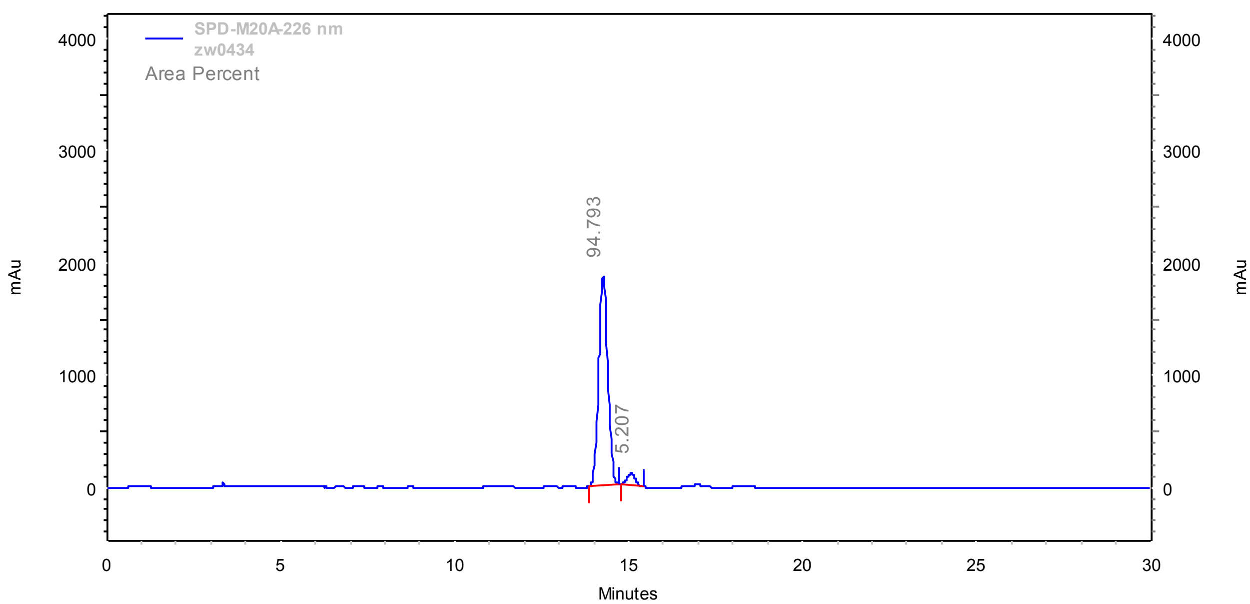

SPD-M20A-226 nm
zw0494r
Area Percent
50.718
49.282
mAu
Minutes


SPD-M20A-226 nm
zw0494
Area Percent
92.171
7.829
mAu
Minutes


OMe
O

3q


SPD-M20A-226 nm
zw0434ra
Area Percent
50.513
49.471
0.016
mAu
Minutes
1250
1000
750
500
250
0
0
5
10
15
20
25
30


SPD-M20A-226 nm
zw0434
Area Percent
94.793
5.207
mAu
Minutes
4000
3000
2000
1000
0
0
5
10
15
20
25
30

9. Single Crystal X-ray Analysis of 3k

A yellow prism 0.060 x 0.050 x 0.020 mm in size was mounted on a Cryoloop with Paratone oil. Data were collected in a nitrogen gas stream at 100(2) K using phi and omega scans. Crystal-to-detector distance was 60 mm and exposure time was 5 seconds per frame using a scan width of 1.0°. Data collection was 99.7% complete to 67.000° in θ. A total of 15454 reflections were collected covering the indices, $-10<=h<=10$, $-12<=k<=10$, $-13<=l<=13$. 1885 reflections were found to be symmetry independent, with an R_{int} of 0.0270. Indexing and unit cell refinement indicated a primitive, orthorhombic lattice. The space group was found to be P 21 21 21 (No. 19). The data were integrated using the Bruker SAINT software program and scaled using the SADABS software program. Solution by iterative methods (SHELXT) produced a complete heavy-atom phasing model consistent with the proposed structure. All non-hydrogen atoms were refined anisotropically by full-matrix least-squares (SHELXL-2013). All hydrogen atoms were placed using a riding model. Their positions were constrained relative to their parent atom using the appropriate HFIX command in SHELXL-2013. Absolute stereochemistry was unambiguously determined to be *S* at C1.

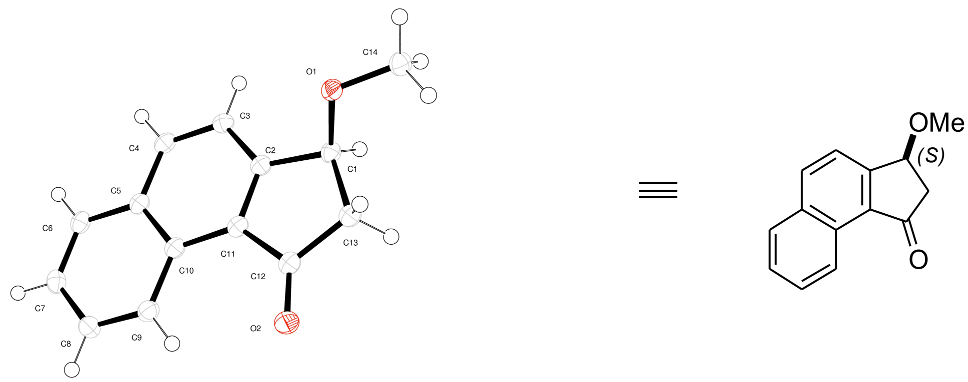


Table 1. Crystal data and structure refinement for toste79.

X-ray ID	toste79	
Sample/notebook ID	ZW03183	
Empirical formula	C14 H12 O2	
Formula weight	212.24	
Temperature	100(2) K	
Wavelength	1.54178 Å	
Crystal system	Orthorhombic	
Space group	P 21 21 21	
Unit cell dimensions	a = 8.3759(11) Å	α= 90°.
	b = 10.6746(14) Å	β= 90°.
	c = 11.5652(15) Å	γ = 90°.
Volume	1034.0(2) $Å^3$	
Z	4	
Density (calculated)	1.363 Mg/m^3	
Absorption coefficient	0.725 mm^{-1}	
F(000)	448	
Crystal size	0.060 x 0.050 x 0.020 mm^3	
Crystal color/habit	yellow prism	
Theta range for data collection	5.640 to 68.311°.	
Index ranges	-10<=h<=10, -12<=k<=10, -13<=l<=13	
Reflections collected	15454	
Independent reflections	1885 [R(int) = 0.0270]	
Completeness to theta = 67.000°	99.7 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.929 and 0.881	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	1885 / 0 / 146	
Goodness-of-fit on F^2	1.072	
Final R indices [I>2sigma(I)]	R1 = 0.0245, wR2 = 0.0656	
R indices (all data)	R1 = 0.0247, wR2 = 0.0658	
Absolute structure parameter	-0.04(4)	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.111 and -0.179 e.$Å^{-3}$	

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for toste79. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
C(1)	9046(2)	8720(1)	3829(1)	18(1)
C(2)	10240(2)	9571(2)	4416(1)	18(1)
C(3)	11892(2)	9636(2)	4177(1)	19(1)
C(4)	12797(2)	10480(2)	4775(1)	20(1)
C(5)	12122(2)	11288(1)	5628(1)	18(1)
C(6)	13070(2)	12162(2)	6238(1)	20(1)
C(7)	12404(2)	12951(2)	7040(1)	22(1)
C(8)	10756(2)	12883(2)	7278(1)	23(1)
C(9)	9801(2)	12035(2)	6714(1)	21(1)
C(10)	10455(2)	11220(1)	5876(1)	18(1)
C(11)	9544(2)	10325(1)	5238(1)	18(1)
C(12)	7814(2)	10044(2)	5304(1)	19(1)
C(13)	7469(2)	8988(2)	4461(1)	22(1)
C(14)	8767(2)	6625(2)	3210(1)	21(1)
O(1)	9602(1)	7467(1)	3944(1)	20(1)
O(2)	6824(1)	10553(1)	5919(1)	25(1)

Table 3. Bond lengths [Å] and angles [°] for toste79.

C(1)-O(1)	1.4222(18)	C(7)-H(7)	0.9500
C(1)-C(2)	1.512(2)	C(8)-C(9)	1.373(2)
C(1)-C(13)	1.537(2)	C(8)-H(8)	0.9500
C(1)-H(1)	1.0000	C(9)-C(10)	1.413(2)
C(2)-C(11)	1.376(2)	C(9)-H(9)	0.9500
C(2)-C(3)	1.413(2)	C(10)-C(11)	1.428(2)
C(3)-C(4)	1.365(2)	C(11)-C(12)	1.482(2)
C(3)-H(3)	0.9500	C(12)-O(2)	1.2206(19)
C(4)-C(5)	1.427(2)	C(12)-C(13)	1.518(2)
C(4)-H(4)	0.9500	C(13)-H(13A)	0.9900
C(5)-C(6)	1.414(2)	C(13)-H(13B)	0.9900
C(5)-C(10)	1.427(2)	C(14)-O(1)	1.4206(18)
C(6)-C(7)	1.371(2)	C(14)-H(14A)	0.9800
C(6)-H(6)	0.9500	C(14)-H(14B)	0.9800
C(7)-C(8)	1.410(2)	C(14)-H(14C)	0.9800

O(1)-C(1)-C(2)	107.86(12)
O(1)-C(1)-C(13)	114.34(13)
C(2)-C(1)-C(13)	104.10(12)
O(1)-C(1)-H(1)	110.1
C(2)-C(1)-H(1)	110.1
C(13)-C(1)-H(1)	110.1
C(11)-C(2)-C(3)	121.42(15)
C(11)-C(2)-C(1)	112.43(13)
C(3)-C(2)-C(1)	126.15(14)
C(4)-C(3)-C(2)	118.49(14)
C(4)-C(3)-H(3)	120.8
C(2)-C(3)-H(3)	120.8
C(3)-C(4)-C(5)	121.95(13)
C(3)-C(4)-H(4)	119.0
C(5)-C(4)-H(4)	119.0
C(6)-C(5)-C(4)	121.42(13)
C(6)-C(5)-C(10)	118.86(14)
C(4)-C(5)-C(10)	119.72(14)
C(7)-C(6)-C(5)	120.93(14)
C(7)-C(6)-H(6)	119.5
C(5)-C(6)-H(6)	119.5
C(6)-C(7)-C(8)	119.97(15)
C(6)-C(7)-H(7)	120.0
C(8)-C(7)-H(7)	120.0
C(9)-C(8)-C(7)	120.73(15)
C(9)-C(8)-H(8)	119.6
C(7)-C(8)-H(8)	119.6
C(8)-C(9)-C(10)	120.44(14)
C(8)-C(9)-H(9)	119.8
C(10)-C(9)-H(9)	119.8
C(9)-C(10)-C(5)	119.06(14)
C(9)-C(10)-C(11)	124.01(13)
C(5)-C(10)-C(11)	116.92(14)
C(2)-C(11)-C(10)	121.49(14)
C(2)-C(11)-C(12)	109.35(14)
C(10)-C(11)-C(12)	129.15(14)

O(2)-C(12)-C(11)	127.18(15)
O(2)-C(12)-C(13)	125.14(14)
C(11)-C(12)-C(13)	107.69(13)
C(12)-C(13)-C(1)	106.24(12)
C(12)-C(13)-H(13A)	110.5
C(1)-C(13)-H(13A)	110.5
C(12)-C(13)-H(13B)	110.5
C(1)-C(13)-H(13B)	110.5
H(13A)-C(13)-H(13B)	108.7
O(1)-C(14)-H(14A)	109.5
O(1)-C(14)-H(14B)	109.5
H(14A)-C(14)-H(14B)	109.5
O(1)-C(14)-H(14C)	109.5
H(14A)-C(14)-H(14C)	109.5
H(14B)-C(14)-H(14C)	109.5
C(14)-O(1)-C(1)	112.22(11)

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($Å^2$x 10^3) for toste79. The anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2 a^{*2}U^{11} + ... + 2 h k a^* b^* U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
C(1)	18(1)	18(1)	18(1)	2(1)	-1(1)	0(1)
C(2)	19(1)	16(1)	17(1)	4(1)	-1(1)	1(1)
C(3)	19(1)	20(1)	19(1)	2(1)	2(1)	2(1)
C(4)	15(1)	22(1)	22(1)	4(1)	2(1)	0(1)
C(5)	19(1)	18(1)	18(1)	5(1)	-2(1)	1(1)
C(6)	19(1)	21(1)	21(1)	5(1)	-2(1)	-1(1)
C(7)	25(1)	19(1)	21(1)	2(1)	-5(1)	-2(1)
C(8)	26(1)	23(1)	22(1)	-3(1)	-1(1)	2(1)
C(9)	19(1)	24(1)	21(1)	1(1)	0(1)	1(1)
C(10)	19(1)	17(1)	18(1)	4(1)	-1(1)	1(1)
C(11)	18(1)	20(1)	17(1)	4(1)	0(1)	1(1)
C(12)	19(1)	21(1)	18(1)	4(1)	0(1)	0(1)
C(13)	17(1)	24(1)	25(1)	-2(1)	1(1)	-1(1)
C(14)	20(1)	20(1)	25(1)	1(1)	0(1)	-3(1)
O(1)	19(1)	18(1)	23(1)	0(1)	-3(1)	1(1)
O(2)	18(1)	30(1)	26(1)	-4(1)	4(1)	-1(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for toste79.

	x	y	z	U(eq)
H(1)	8948	8946	2993	22
H(3)	12363	9105	3613	23
H(4)	13908	10531	4618	24
H(6)	14185	12204	6091	24
H(7)	13053	13542	7434	26
H(8)	10300	13430	7836	28
H(9)	8694	11996	6888	25
H(13A)	6632	9242	3904	27
H(13B)	7099	8233	4880	27
H(14A)	7641	6595	3438	32
H(14B)	9234	5787	3277	32
H(14C)	8849	6913	2407	32