Electronic Supplementary Material (ESI) for Chemical Communications.

Reductive Cyclodimerization of Chalcones: Exploring the "Self-adaptability" of Galvanostatic Electrosynthesis

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1. General Methods

^{1}H-NMR spectra were recorded on Varian 400 (400 MHz) . Chemical shifts are reported in ppm from TMS with the solvent resonance as the internal standard ($CHCl_3$: 7.26 ppm). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, dd= double doublet, t = triplet, td = triple doublet, dt = double triplet, q = quartet, b = broad, m = multiplet), coupling constants (Hz).

^{13}C-NMR spectra were recorded on a Varian 400 (400 MHz) with complete proton decoupling. Chemical shifts are reported in ppm from TMS with the solvent as the internal standard ($CHCl_3$: 77.0 ppm).

HRMS spectra were obtained with a G2XS QTof mass spectrometer using either ESI or APCI ionization techniques, as specified case by case.

Chromatographic purification was done with 240-400 mesh silica gel.

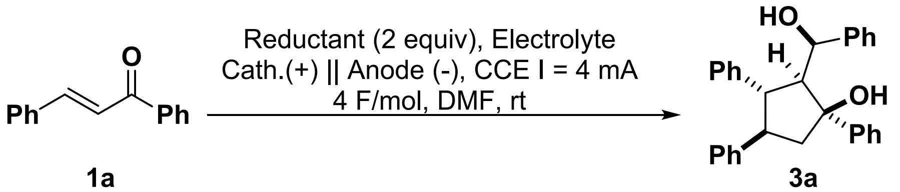
Anhydrous solvents, including DMF for the electrochemical processes, were supplied by Merck in Sureseal® bottles and used without any further purification.

All other commercially available starting materials and (non-anhydrous) solvents were purchased from Merck, TCI chemicals, Fluorochem or Alfa Aesar and were used as such without further purification.

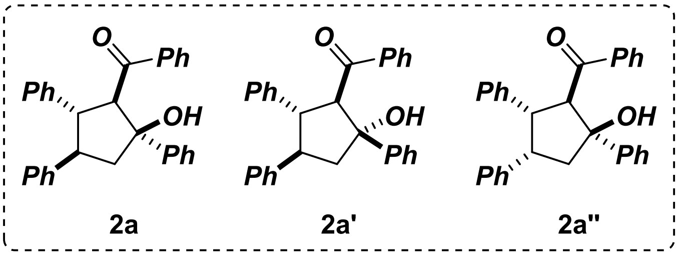
Chalcones **1b-1y** are known compounds and were synthesized according to literature procedures.[1]

2. Additional Optimization Tables

2.1. **Table S1**: Additional Reaction Optimization Results.[a]



1a **3a**



Entry	Anode	Cathode	Electrolyte (mol%)	**Reductant**	Yield of **3a** (%)	**2a/2a'/2a''**
1	SS	Ag	TEABF$_4$ (20)	TEOA	31	-
2[c]	Mg[b]	Ag	TEABF$_4$ (20)	TEOA	-	-
3	C$_{graph.}$	SS	TEABF$_4$ (20)	TEOA	33	7/-/-
4	C$_{graph.}$	Pt	TEABF$_4$ (20)	TEOA	26	9/-/-
5	C$_{graph.}$	GC	TEABF$_4$ (20)	TEOA	39	9/-/7
6	C$_{graph.}$	Ni foam	TEABF$_4$ (20)	TEOA	-	13/2/5
7[c]	C$_{graph.}$	Al	TEABF$_4$ (20)	TEOA	-	-
8	C$_{graph.}$	Ag	TEABF$_4$ (20)	TEOA	84	-
9	C$_{graph.}$	Ag	TEABF$_4$ (100)	TEOA	82	-
10	C$_{graph.}$	Ag	LiBF$_4$ (100)	TEOA	79	-
11	C$_{graph.}$	Ag	LiBF$_4$ (20)	TEOA	44	-
12	C$_{graph.}$	Ag	TBAClO$_4$ (20)	TEOA	-	11/-/-
13	C$_{graph.}$	Ag	TBAPF$_6$ (20)	TEOA	80	-
14	C$_{graph.}$	Ag	Zn(OTf)$_2$ (20)	TEOA	-	18/-/9
15	C$_{graph.}$	Ag	NaI (20)	TEOA	-	15/-/-
16	C$_{graph.}$	Ag	TEABF$_4$ (20)	DIPEA	-	-

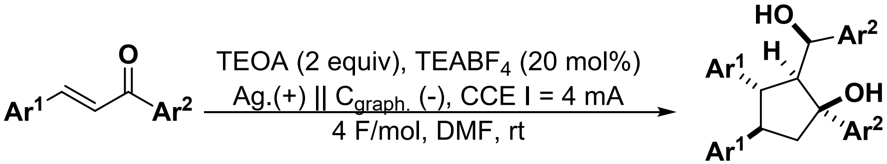
[a] Reaction conditions: **1a** (0.15 mmol), TEOA (0.30 mmol), Electrolyte (0.030 or 0.15 mmol), DMF (3.0 mL), CCE **I** = 4 mA, 4 F/mol$_{1a}$, rt. Isolate yields of **3a** after FC are provided. Yields of **2a**,

2a' and **2a''** are given by ^{1}H NMR analysis on the reaction crude using mesitylene as internal standard. [b] Reaction run in the absence of TEOA, using Mg as a potentially sacrificial electrode. [c] Complex reaction mixture showing substantial decomposition.

A metal non-sacrificial anode such as Stainless Steel (SS, entry 1) performed worse than optimal $C_{graph.}$, while Mg as a potential sacrificial electrode (entry 2) led to a complex reaction mixture, highlighting the importance of an organic terminal reductant. Cathodes different from Ag led either to unselective formation of **3a** (various amounts of aldols **2** detected, along with reduced chalcone, entries 3-5, GC stands for Glassy Carbon) or to complex mixtures showing decomposition (entry 7) or to the chemoselective (but poorly diastereoselective) formation of **2**. Entries 8-11 show how only in the presence of $TEABF_4$ the supporting electrolyte amount can be lowered to a substoichiometric amount without loss of efficiency, this might be explained considering the limited electrodic stability of Li-based electrolytes. While $TBAClO_4$, $Zn(OTf)_2$ and NaI (entries 12, 14 and 15) did not favor the formation of **3a**, $TBAPF_6$ (entry 13) behaved very similarly to optimal $TEABF_4$. A non-protic, more basic amine reductant such as DIPEA (entry 15) led to a complex reaction mixture showing extensive decomposition.

3. Electroreductive Cyclodimerization of Chalcones 1

3.1 General procedures for the electroreductive cyclodimerization of chalcones **1**.



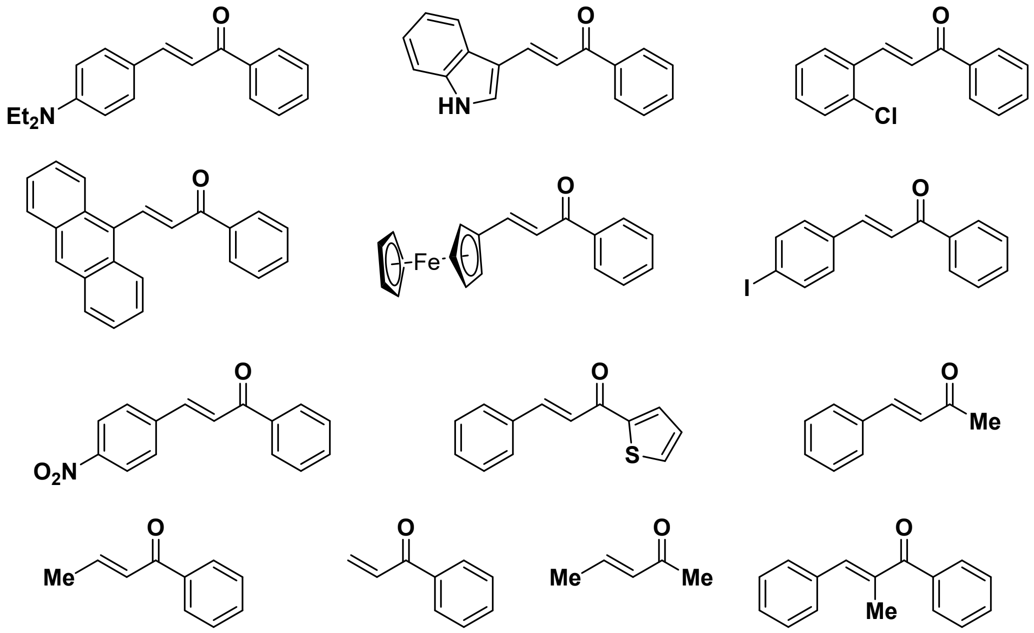
1 **3**

The ElectraSyn vial (5 mL), equipped with a stir bar, was charged with chalcone **1** (0.15 mmol), TEOA (0.30 mmol, 44.7 mg), and $TEABF_4$ (0.030 mmol, 6.5 mg). The ElectraSyn vial cap, equipped with anode ($C_{graph.}$) and cathode (Ag), was inserted into the mixture and closed with a rubber septum. The vessel was evacuated and backfilled with N_2 three times, then dry DMF (3.0 mL) was added, and the mixture stirred until complete dissolution of the solids occurred, while bubbling with N_2 (balloon,1 min). The reaction mixture was electrolyzed (under N_2, balloon) at a constant current of 4.0 mA, until a total charge of 0.60 mF (4.0 F/mol$_{\mathbf{1}}$) was reached. The ElectraSyn vial cap was removed, and the electrodes and vial were rinsed with EtOAc (10 mL) and $NH_4Cl_{(aq)}$ (saturated, 5 mL) and water (5 mL), which were combined with the crude mixture in a separatory funnel. Then, the organic layer was separated, and the aqueous layer was extracted with EtOAc (2 x 10 mL). The combined organic layers were washed with $NH_4Cl_{(aq)}$ (0.1 M, 3 x 10 mL), dried over Na_2SO_4 and concentrated *in vacuo*. The crude product was finally purified by FC to afford pure products **3**.

Additional notes:

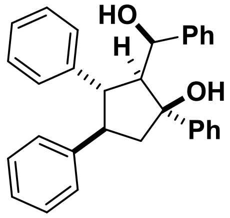
1. The reaction was found to be extremely sensitive to even small contaminations of trace metals with potential Lewis acidity, such as zinc. Therefore, to ensure that no such metals were present, all the reaction equipment (electrodes, vial, stirrer, and cap) were thoroughly washed with HCl (2 M) prior to use (rinsing with water and acetone).
2. In some cases, the formation of a precipitate leading to a cloudy mixture was observed during the electrolysis, disappearing near the end of the process. This is putatively attributed to the presence of compounds **2’**, which were found to be scarcely soluble in most organic solvents.

3.2. Unsuccessful substrates



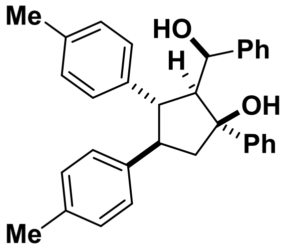
Under the optimized conditions the depicted substrates did not lead to any desired product **3** formation. In most cases substantial hydrogenation of the double bond or decomposition was observed.

3.3 Characterization data of compounds **3**.



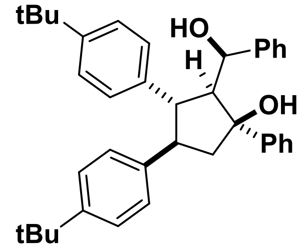
3a. White solid (m.p. = 142 – 144 °C). FC eluent: DCM/Et_2O: from 100:0 to 20:1. Yield = 84%, (0.063 mmol, 26.2 mg). *dr* = 20:1. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 7.75 – 7.69 (m, 2H), 7.51 – 7.44 (m, 2H), 7.37 – 7.31 (m, 1H), 7.21 – 7.18 (m, 4H), 7.16 – 7.10 (m, 1H), 6.88 – 6.75 (m, 6H), 6.71 – 6.59 (m, 4H), 4.94 (s, 1H), 3.93 (s, 1H), 3.85 (dd, *J* = 12.0, 10.2 Hz, 1H), 3.26 (td, *J* = 10.4, 7.0 Hz, 1H), 2.99 – 2.83 (m, 3H), 2.33 (dd, *J* = 14.7, 7.0 Hz, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 146.4, 144.2, 142.0, 141.5, 128.5 (2C), 128.2 (2C), 127.8 (2C), 127.7 (2C), 127.5 (2C), 127.2 (2C), 127.0, 126.1, 126.0, 125.5, 125.2 (2C), 124.8 (2C), 85.1, 71.2, 63.4, 53.8, 52.6, 51.1; **HRMS (ESI)** m/z: $[M + Na]^+$ calcd. for $C_{30}H_{28}O_2Na$ 443.1982; found 443.1987.

Preparation of **3a** on 1.0 mmol scale. The ElectraSyn vial (10 mL), equipped with a stir bar, was charged with chalcone **1a** (1.0 mmol, 208 mg), TEOA (2.0 mmol, 298 mg), and $TEABF_4$ (0.20 mmol, 43.3 mg). The ElectraSyn vial cap, equipped with anode ($C_{graph.}$) and cathode (Ag), was inserted into the mixture and closed with a rubber septum. The vessel was evacuated and backfilled with N_2 three times, then dry DMF (8.0 mL) was added, and the mixture stirred until complete dissolution of the solids occurred, while bubbling with N_2 (balloon,2 min). The reaction mixture was electrolyzed (under N_2, balloon) at a constant current of 4.0 mA, until a total charge of 4.0 mF (4.0 F/mol$_{\mathbf{1a}}$) was reached. The ElectraSyn vial cap was removed, and the electrodes and vial were rinsed with EtOAc (20 mL) and $NH_4Cl_{(aq)}$ (saturated, 10 mL) and water (10 mL), which were combined with the crude mixture in a separatory funnel. Then, the organic layer was separated, and the aqueous layer was extracted with EtOAc (2 x 20 mL). The combined organic layers were washed with $NH_4Cl_{(aq)}$ (0.1 M, 3 x 30 mL), dried over Na_2SO_4 and concentrated *in vacuo*. The crude product was finally purified by FC (DCM/Et_2O: from 100:0 to 20:1) to afford pure product **3a** in 79% yield (0.395 mmol, 166 mg). *dr* = 20:1.

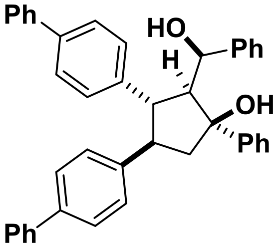


3b. White solid (m.p. = 152 – 154 °C). FC eluent: DCM/Et_2O: from 100:0 to 20:1. Yield = 80%, (0.395 mmol, 27.8 mg). *dr* > 20:1. **^{1}H NMR** (600 MHz, $CDCl_3$) δ =7.72 – 7.68 (m, 2H), 7.50 – 7.44 (m, 2H), 7.37 – 7.30 (m, 1H), 7.12 – 7.08 (m, 2H), 7.03 – 6.99 (m, 2H), 6.84 – 6.76 (m, 3H), 6.64 – 6.58 (m, 3H), 6.58 – 6.54 (m, 2H), 4.92 (s, 1H), 3.81

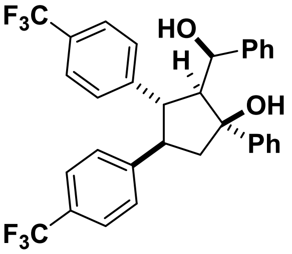
(s, 1H), 3.78 (dd, 1H), 3.23 (td, *J* = 10.5, 7.1 Hz, 1H), 2.94 – 2.83 (m, 3H), 2.28 (dd, *J* = 14.3, 7.0 Hz, 1H) partially overlapped with 2.26 (s, 3H), 2.11 (s, 3H); ^{13}**C NMR** (100 MHz, $CDCl_3$) δ = 146.6, 142.2, 141.2, 138.4, 135.4, 134.7, 128.9 (2C), 128.5 (2C), 128.2 (2C), 127.6 (2C + 2C overlapped), 127.2 (2C), 126.9, 125.7, 125.2 (2C), 124.8 (2C), 85.0, 71.3, 63.8, 53.1, 52.1, 51.4, 21.0, 20.8; **HRMS (ESI)** m/z: $[M + Na]^+$ calcd. for $C_{32}H_{32}O_2Na$ 471.2295; found 471.2302.



3c. White solid (m.p. = 102 – 105 °C). FC eluent: DCM/Et_2O: from 100:0 to 20:1. Yield = 43%, (0.032 mmol, 17,0 mg). *dr* > 20:1. ^{1}**H NMR** (400 MHz, $CDCl_3$) δ = 7.75 – 7.68 (m, 2H), 7.50 – 7.44 (m, 2H), 7.36 – 7.32 (m, 2H), 7.24 – 7.20 (m, 2H), 7.19 – 7.15 (m, 2H), 6.85 – 6.78 (m, 2H), 6.78 – 6.74 (m, 2H), 6.68 – 6.63 (m, 2H), 6.62 – 6.57 (m, 2H), 4.90 (s, 1H), 3.87 (dd, *J* = 12.1, 9.8 Hz, 1H), 3.74 (s, 1H), 3.33 (td, *J* = 10.4, 6.4 Hz, 1H), 2.94 – 2.83 (m, 3H), 2.28 (dd, *J* = 14.7, 6.5 Hz, 1H), 1.27 (s, 9H), 1.17 (s, 9H).; ^{13}**C NMR** (100 MHz, $CDCl_3$) δ = 148.5, 147.8, 146.4, 142.1, 141.5, 138.6, 128.5 (2C), 127.5 (2C), 127.3 (2C), 127.2 (2C), 126.9, 125.8, 125.2 (2C), 125.0 (2C), 124.7 (2C), 124.4 (2C), 85.2, 71.1, 63.9, 52.3, 51.4, 51.1, 34.3, 34.1, 31.4 (3C), 31.3 (3C); **HRMS (ESI)** m/z: $[M + Na]^+$ calcd. for $C_{38}H_{44}O_2Na$ 555.3234; found 555.3228.

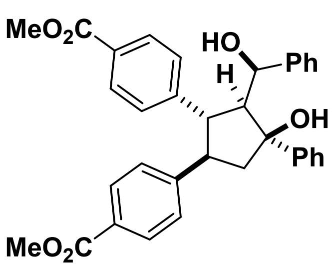


3d. White solid (m.p. = 177 – 180 °C). FC eluent: DCM/Et_2O: from 100:0 to 20:1. Yield = 66%, (0.050 mmol, 28,7 mg). *dr* > 20:1. ^{1}**H NMR** (400 MHz, $CDCl_3$) δ = 7.77 – 7.71 (m, 2H), 7.50 – 7.37 (m, 10H), 7.28 – 7.18 (m, 5H), 7.14 – 7.05 (m, 5H), 6.79 – 6.74 (m, 2H), 6.73 – 6.65 (m, 4H), 4.81 (s, 1H), 4.10 (dd, *J* = 12.1, 10.1 Hz, 1H), 4.04 (s, 1H), 3.32 (td, *J* = 10.6, 6.6 Hz, 1H), 2.92 (d, *J* = 12.1 Hz, 1H), 2.78 (dd, *J* = 14.5, 11.0 Hz, 1H), 2.44 (dd, *J* = 14.6, 6.6 Hz, 1H), 2.27 (s, 1H); ^{13}**C NMR** (100 MHz, $CDCl_3$) δ = 146.8, 143.8, 142.4, 141.5, 141.2, 141.0, 139.2, 138.4, 128.6 (2C), 128.5 (2C), 128.4 (2C), 128.3 (2C), 128.2, 127.5 (partially overlapped with the solvent signal), 127.1 (2C), 127.0 (2C), 126.9 (2C), 126.8 (2C), 126.8 (2C), 126.7, 126.4 (2C), 125.6, 125.5 (2C), 124.8 (2C), 84.8, 71.1, 63.5, 53.4, 52.5, 50.7; **HRMS (ESI)** m/z: $[M + Na]^+$ calcd. for $C_{42}H_{36}O_2Na$ 595.2608; found 595.2599.

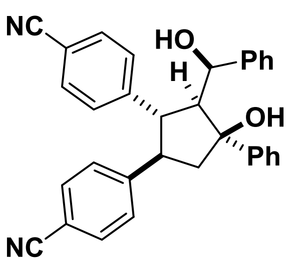


3e. White solid (m.p. = 178 – 181 °C). FC eluent: DCM/Et_2O: from 100:0 to 20:1. Yield = 65%, (0.049 mmol, 27.1 mg). *dr* > 20:1. ^{1}**H**

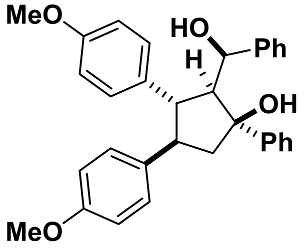
NMR (400 MHz, CDCl$_3$) δ = 7.76 – 7.69 (m, 2H), 7.53 – 7.47 (m, 2H), 7.47 – 7.43 (m, 2H), 7.40 – 7.34 (m, 1H), 7.34 – 7.28 (m, 2H), 7.08 – 7.02 (m, 2H), 6.87 – 6.80 (m, 1H), 6.79 – 6.74 (m, 2H), 6.74 – 6.69 (m, 2H), 6.61 – 6.55 (m, 2H), 4.91 (s, 1H), 4.32 (s, 1H), 3.90 (dd, *J* = 12.1, 10.0 Hz, 1H), 3.28 (td, *J* = 10.6, 6.2 Hz, 1H), 2.96 – 2.83 (m, 3H), 2.31 (dd, *J* = 14.7, 6.2 Hz, 1H); **^{13}C NMR** (100 MHz, CDCl$_3$) δ = 148.1 (q, *J* = 1.5 Hz), 145.5, 145.4 (q, *J* = 1.5 Hz), 141.5, 128.7 (2C), 128.6 (q, *J* = 32.3 Hz), 128.1 (2C), 127.9 (2C), 127.9 (q, *J* = 30.1 Hz), 127.4 (2C), 127.3, 126.5, 125.3 (q, *J* = 3.9 Hz, 2C), 125.1 (2C), 124.6 (q, *J* = 3.8 Hz, 2C), 124.5 (2C), 124.3 (q, *J* = 271.1 Hz), 124.1 (q, *J* = 271.7 Hz), 85.1, 70.9, 63.1, 53.4, 52.5, 50.4; **^{19}F NMR** (377 MHz, CDCl$_3$) δ = -62.34 (s, 3F), -62.65 (s, 3F); **HRMS (ESI)** m/z: [M + Na]$^+$ calcd. for C$_{32}$H$_{26}$F$_6$O$_2$Na 579.1729; found 579.1727.



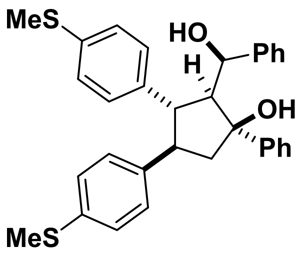
3f. White solid (m.p. = 183 – 186 °C). FC eluent: DCM/Et$_2$O: from 100:0 to 20:1. Yield = 65%, (0.063 mmol, 26,9 mg). *dr* > 20:1. **^{1}H NMR** (600 MHz, CDCl$_3$) δ = 7.87 – 7.81 (m, 2H), 7.77 – 7.70 (m, 2H), 7.50 – 7.42 (m, 4H), 7.26 – 7.19 (m, 3H), 6.84 – 6.71 (m, 4H), 6.66 – 6.60 (m, 3H), 4.93 (s, 1H), 4.45 (s, 1H), 3.96 – 3.86 (m, 1H), 3.85 (s, 3H), 3.82 (s, 3H), 3.33 – 3.19 (m, 2H), 3.00 – 2.78 (m, 2H), 2.34 (dd, *J* = 14.6, 6.6 Hz, 1H); **^{13}C NMR** (100 MHz, CDCl$_3$) δ = 167.1, 167.1, 149.5, 147.1, 145.8, 141.6, 129.6 (2C), 129.0 (2C), 128.6 (2C), 128.2, 127.9 (2C), 127.6 (2C), 127.4, 127.3 (2C), 127.2, 126.4, 125.2, 124.7, 85.2, 70.9, 63.0, 54.0, 52.8, 52.0, 51.9, 50.4.; **HRMS (ESI)** m/z: [M + Na]$^+$ calcd. for C$_{34}$H$_{32}$O$_6$Na 559.2091; found 559.2097.



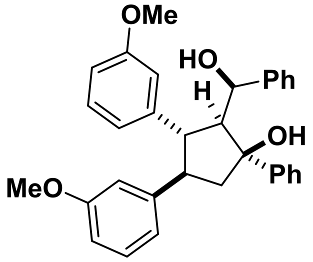
3g. White solid (m.p. = 221 – 223 °C). FC eluent: DCM/Et$_2$O: from 100:0 to 20:1. Yield = 71%, (0.053 mmol, 25.0 mg). *dr* > 20:1. **^{1}H NMR** (400 MHz, CDCl$_3$) δ = 7.74 – 7.67 (m, 2H), 7.53 – 7.45 (m, 4H), 7.39 – 7.34 (m, 1H), 7.31 – 7.27 (m, 2H), 7.12 – 7.03 (m, 2H), 6.90 – 6.84 (m, 1H), 6.83 – 6.76 (m, 2H), 6.70 – 6.66 (m, 2H), 6.62 – 6.58 (m, 2H), 4.91 (s, 1H), 4.49 (s, 1H), 3.86 (dd, *J* = 12.1, 9.9 Hz, 1H), 3.20 (td, *J* = 10.5, 5.9 Hz, 1H), 2.96 (s, 1H), 2.92 (d, *J* = 12.1 Hz, 1H), 2.85 (dd, *J* = 14.8, 11.1 Hz, 1H), 2.28 (dd, *J* = 14.7, 5.9 Hz, 1H); **^{13}C NMR** (100 MHz, CDCl$_3$) δ = 149.5, 147.0, 145.1, 141.4, 132.2 (2C), 131.5 (2C), 128.8 (2C), 128.6 (2C), 128.3 (2C), 127.5 (2C), 127.4, 126.7, 125.1 (2C), 124.6 (2C), 118.9, 118.9, 110.3, 109.4, 85.1, 70.7, 62.8, 53.9, 52.9, 50.0; **HRMS (ESI)** m/z: [M + Na]$^+$ calcd. for C$_{32}$H$_{26}$N$_2$O$_2$Na 493.1886; found 493.1994.



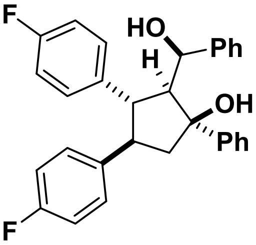
3h. White solid (m.p. = 217 – 219 °C). FC eluent: DCM/Et$_2$O: from 100:0 to 20:1. Yield = 53%, (0.040 mmol, 19.1 mg). *dr* = 8:1. **^{1}H NMR** (600 MHz, CDCl$_3$) δ = 7.73 – 7.66 (m, 2H), 7.49 – 7.44 (m, 2H), 7.36 – 7.29 (m, 2H), 7.13 – 7.08 (m, 2H), 6.85 – 6.77 (m, 3H), 6.76 – 6.71 (m, 2H), 6.67 – 6.60 (m, 2H), 6.58 – 6.53 (m, 2H), 6.39 – 6.33 (m, 2H), 4.92 (s, 1H), 3.84 – 3.53 (m, 8H), 3.16 (td, *J* = 10.4, 7.0 Hz, 1H), 2.91 – 2.79 (m, 3H), 2.26 (dd, *J* = 14.7, 7.2 Hz, 1H).; **^{13}C NMR** (100 MHz, CDCl$_3$) δ = 157.8, 157.4, 146.6, 142.2, 136.4, 133.7, 128.7 (2C), 128.6 (2C), 128.5 (2C), 127.2 (2C), 126.9, 125.9, 125.2 (2C), 124.8 (2C), 113.5 (2C), 113.1 (2C), 84.9, 71.2, 63.5, 55.1, 55.1, 52.8, 51.9, 51.2.; **HRMS (ESI)** m/z: [M + Na]$^+$ calcd. for $C_{32}H_{32}O_4Na$ 503.2193; found 503.2200.



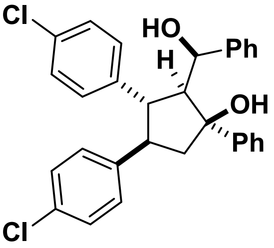
3i. White solid (m.p. = 172 – 176 °C). FC eluent: DCM/Et$_2$O: from 100:0 to 20:1. Yield = 80%, (0.060 mmol, 30,7 mg). *dr* > 20:1. **^{1}H NMR** (400 MHz, CDCl$_3$) δ = 7.72 – 7.67 (m, 2H), 7.51 – 7.43 (m, 2H), 7.37 – 7.31 (m, 1H), 7.13 – 7.05 (m, 4H), 6.85 – 6.77 (m, 3H), 6.74 – 6.70 (m, 2H), 6.64 – 6.58 (m, 2H), 6.57 – 6.52 (m, 2H), 4.90 (s, 1H), 4.00 (s, 1H), 3.76 (dd, *J* = 12.1, 10.2 Hz, 1H), 3.17 (td, *J* = 10.5, 6.9 Hz, 1H), 2.92 (d, *J* = 2.3 Hz, 1H), 2.89 – 2.79 (m, 2H), 2.41 (s, 3H), 2.34 (s, 3H), 2.26 (dd, *J* = 14.7, 6.9 Hz, 1H); **^{13}C NMR** (100 MHz, CDCl$_3$) δ = 146.2, 142.0, 141.3, 138.9, 135.6, 134.6, 128.6 (2C), 128.3 (2C), 128.2 (2C), 127.3 (2C), 127.0, 126.9 (2C), 126.8 (2C), 126.0, 125.1 (2C), 124.7 (2C), 85.0, 71.1, 63.4, 53.1, 52.1, 51.0, 16.5, 16.1; **HRMS (ESI)** m/z: [M + Na]$^+$ calcd. for $C_{32}H_{32}O_2S_2Na$ 535.1736; found 535.1744.



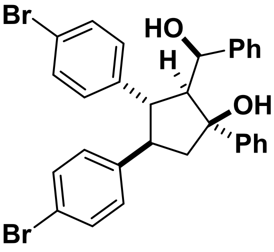
3j. Colourless sticky solid. FC eluent: DCM/Et$_2$O: from 100:0 to 20:1. Yield = 86%, (0.064 mmol, 30.9 mg). *dr* > 20:1. **^{1}H NMR** (400 MHz, CDCl$_3$) δ = 7.72 – 7.69 (m, 2H), 7.50 – 7.44 (m, 2H), 7.37 – 7.31 (m, 1H), 7.14 – 7.09 (m, 1H), 6.85 – 6.78 (m, 5H), 6.77 – 6.72 (m, 1H), 6.70 – 6.64 (m, 3H), 6.41 – 6.37 (m, 1H), 6.33 – 6.28 (m, 1H), 6.21 – 6.16 (m, 1H), 4.93 (s, 1H), 3.88 (s, 1H), 3.86 – 3.78 (m, 1H), 3.71 (s, 3H), 3.53 (s, 3H), 3.24 (td, *J* = 10.4, 6.9 Hz, 1H), 2.96 (d, *J* = 2.4 Hz, 1H), 2.90 – 2.83 (m, 2H), 2.31 (dd, *J* = 14.7, 6.9 Hz, 1H); **^{13}C NMR** (100 MHz, CDCl$_3$) δ = 159.4, 158.9, 146.3, 146.0, 143.3, 142.1, 129.1, 128.5 (2C), 128.5, 127.2 (2C), 127.0, 126.0, 125.2 (2C), 124.8 (2C), 120.7, 120.2, 113.6, 113.2, 111.4, 111.2, 85.1, 71.1, 63.4, 55.1, 54.9, 53.5, 52.4, 50.9; **HRMS (ESI)** m/z: [M + Na]$^+$ calcd. for $C_{32}H_{32}O_4Na$ 503.2193; found 503.2198.



3k. White solid (m.p. = 176 – 179 °C). FC eluent: DCM/Et$_2$O: from 100:0 to 20:1. Yield = 70%, (0.053 mmol, 24.2 mg). *dr* > 20:1. **^{1}H NMR** (400 MHz, CDCl$_3$) δ = 7.73 – 7.66 (m, 2H), 7.53 – 7.44 (m, 2H), 7.40 – 7.31 (m, 1H), 7.17 – 7.07 (m, 2H), 6.93 – 6.78 (m, 5H), 6.64 – 6.44 (m, 6H), 4.91 (s, 1H), 4.12 (s, 1H), 3.75 (dd, *J* = 12.1, 10.2 Hz, 1H), 3.14 (td, *J* = 10.5, 6.8 Hz, 1H), 2.96 (d, *J* = 2.4 Hz, 1H), 2.84 (dd, *J* = 13.8, 10.6 Hz, 2H), 2.26 (dd, *J* = 14.6, 6.8 Hz, 1H); **^{13}C NMR** (100 MHz, CDCl$_3$) δ = 161.4 (d, *J* = 244 Hz), 160.9 (d, *J* = 244 Hz), 146.1, 141.9, 139.7 (d, *J* = 3.1 Hz), 137.0 (d, *J* = 3.1 Hz), 129.2 (d, *J* = 7.9 Hz, 2C), 129.0 (d, *J* = 7.9 Hz, 2C), 128.6 (2C), 127.3 (2C), 127.1, 126.2, 125.1 (2C), 124.7 (2C), 115.0 (d, *J* = 21.2 Hz, 2C), 114.3 (d, *J* = 21.2 Hz, 2C), 85.0, 71.0, 63.2, 53.2, 52.1, 50.8.; **^{19}F NMR** (377 MHz, CDCl$_3$) δ = 117.27 – 117.32 (m, 1F), -117.95 – 118.06 (m, 1F); **HRMS (ESI)** m/z: [M + Na]$^+$ calcd. for $C_{30}H_{26}F_2O_2Na$ 479.1793; found 479.1787.

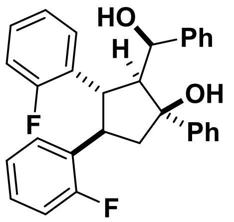


3l. White solid (m.p. = 176 – 178 °C). FC eluent: DCM/Et$_2$O: from 100:0 to 20:1. Yield = 84%, (0.063 mmol, 30.8 mg). *dr* > 20:1. **^{1}H NMR** (400 MHz, CDCl$_3$) δ = 7.72 – 7.66 (m, 2H), 7.52 – 7.44 (m, 2H), 7.39 – 7.27 (m, 1H), 7.19 – 7.13 (m, 2H), 7.12 – 7.08 (m, 2H), 6.93 – 6.86 (m, 1H), 6.86 – 6.80 (m, 2H), 6.79 – 6.75 (m, 2H), 6.63 – 6.58 (m, 2H), 6.55 – 6.50 (m, 2H), 4.91 (s, 1H), 4.12 (s, 1H), 3.75 (t, *J* = 11.1 Hz, 1H), 3.13 (td, *J* = 10.5, 6.7 Hz, 1H), 2.89 – 2.78 (m, 3H), 2.25 (dd, *J* = 14.7, 6.7 Hz, 1H); **^{13}C NMR** (100 MHz, CDCl$_3$) δ = 145.9, 142.5, 141.7, 139.8, 131.9, 131.2, 129.1 (2C), 128.9 (2C), 128.6 (2C), 128.4 (2C), 127.7 (2C), 127.4 (2C), 127.2, 126.3, 125.1 (2C), 124.7 (2C), 85.0, 71.0, 63.2, 53.2, 52.2, 50.6.; **HRMS (ESI)** m/z: [M + Na]$^+$ calcd. for $C_{30}H_{26}{}^{35}Cl_2O_2Na$ 511.1202; found 511.1195.

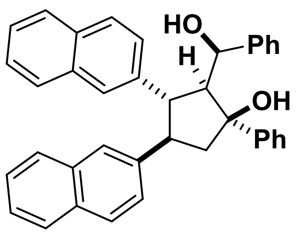


3m. White solid (m.p. = 199 – 202 °C). FC eluent: DCM/Et$_2$O: from 100:0 to 20:1. Yield = 64%, (0.048 mmol, 27.6 mg). *dr* > 20:1. **^{1}H NMR** (400 MHz, CDCl$_3$) δ = 7.72 – 7.68 (m, 2H), 7.51 – 7.45 (m, 2H), 7.39 – 7.29 (m, 3H), 7.08 – 7.03 (m, 2H), 6.94 – 6.87 (m, 3H), 6.85 – 6.80 (m, 2H), 6.63 – 6.57 (m, 2H), 6.49 – 6.45 (m, 2H), 4.91 (s, 1H), 4.11 (s, 1H), 3.74 (dd, *J* = 12.2, 10.1 Hz, 1H), 3.12 (td, *J* = 10.6, 6.6 Hz, 1H), 2.88 – 2.76 (m, 3H), 2.25 (dd, *J* = 14.7, 6.6 Hz, 1H); **^{13}C NMR** (100 MHz, CDCl$_3$) δ = 145.8, 143.1, 141.7, 140.3, 131.3 (2C), 130.6 (2C), 129.6 (2C), 129.3 (2C), 128.6 (2C), 127.4 (2C), 127.2, 126.3, 125.1

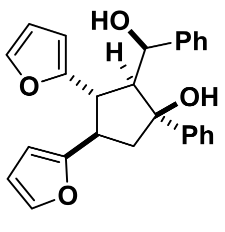
(2C), 124.6 (2C), 120.0, 119.3, 85.0, 71.0, 63.2, 53.2, 52.2, 50.6; **HRMS (ESI)** m/z: [M + Na]$^+$ calcd. for $C_{30}H_{26}{}^{79}Br_2O_2Na$ 599.0192; found 599.0208.



3n. White solid (m.p. = 181 – 184 °C). FC eluent: DCM/Et$_2$O: from 100:0 to 20:1. Yield = 59%, (0.044 mmol, 20.2 mg). *dr* > 20:1. **^{1}H NMR** (600 MHz, CDCl$_3$) δ = 7.74 – 7.70 (m, 2H), 7.66 – 7.60 (m, 1H), 7.50 – 7.44 (m, 2H), 7.36 – 7.31 (m, 1H), 7.12 – 7.05 (m, 2H), 6.88 – 6.74 (m, 6H), 6.73 – 6.68 (m, 2H), 6.64 – 6.58 (m, 1H), 6.54 – 6.47 (m, 1H), 4.92 (s, 1H), 4.19 (t, *J* = 11.3 Hz, 1H), 3.93 (s, 1H), 3.87 (td, *J* = 10.7, 6.8 Hz, 1H), 3.16 (d, *J* = 2.5 Hz, 1H), 3.11 (d, *J* = 12.1 Hz, 1H), 2.95 (dd, *J* = 14.7, 10.9 Hz, 1H), 2.21 (dd, *J* = 14.7, 6.8 Hz, 1H); **^{13}C NMR** (100 MHz, CDCl$_3$) δ = 160.9 (d, *J* = 244.5 Hz), 160.8 (d, *J* = 244.6 Hz), 146.0, 141.6, 130.8 (d, *J* = 14.0 Hz), 130.0 (b), 129.0 (d, *J* = 4.5 Hz), 128.5 (2C), 127.9 (d, *J* = 12.6 Hz), 127.5 (d, *J* = 8.4 Hz), 127.4 (d, *J* = 8.8 Hz), 127.2 (2C), 127.0, 126.0, 125.2 (2C), 124.4 (2C), 124.3 (d, *J* = 3.5 Hz), 123.4 (d, *J* = 3.3 Hz), 114.9 (d, *J* = 22.9 Hz,), 114.9 (d, *J* = 22.9 Hz,) 85.1, 70.7, 61.7, 50.5, 42.9, 21.9.; **^{19}F NMR** (376 MHz, CDCl$_3$) δ = -121.93 – -122.39 (m, 1F), -124.42 – -124.56 (m, 1F); **HRMS (ESI)** m/z: [M + Na]$^+$ calcd. for $C_{30}H_{26}F_2O_2Na$ 479.1793; found 479.1800.

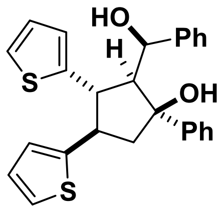


3o. White solid (m.p. = 211 – 214 °C). FC eluent: DCM/Et$_2$O: from 100:0 to 20:1. Yield = 95%, (0.071 mmol, 32.8 mg). *dr* > 20:1. **^{1}H NMR** (400 MHz, DMSO-*d$_6$*) δ = 7.88 – 7.83 (m, 2H), 7.80 – 7.73 (m, 2H), 7.67 – 7.63 (m, 1H), 7.60 (d, *J* = 1.7 Hz, 1H), 7.59 – 7.54 (m, 1H), 7.53 – 7.50 (m, 1H), 7.49 – 7.43 (m, 3H), 7.37 – 7.31 (m, 2H), 7.31 – 7.27 (m, 1H), 7.25 – 7.21 (m, 3H), 7.07 (dd, *J* = 8.6, 1.7 Hz, 1H), 6.56 – 6.41 (m, 6H), 6.07 (s, 1H), 5.41 (d, *J* = 2.6 Hz, 1H), 4.71 (s, 1H), 4.11 (t, *J* = 11.0 Hz, 1H), 3.66 (td, *J* = 10.5, 6.7 Hz, 1H), 3.05 – 2.99 (m, 1H), 2.92 (dd, *J* = 14.2, 10.9 Hz, 1H), 2.28 (dd, *J* = 14.2, 6.7 Hz, 1H); **^{13}C NMR** (100 MHz, DMSO-*d$_6$*) δ = 147.8, 143.8, 143.0, 140.3, 133.3, 133.0, 132.1, 131.9, 128.5 (2C), 128.3, 127.8, 127.7, 127.5, 127.4, 127.3, 127.1, 126.9 (C + C overlapped), 126.8 (2C), 126.5, 126.2, 126.2, 126.1 (2C), 125.6, 125.5, 125.4, 125.1 (2C), 125.0, 84.6, 70.0, 64.0, 53.0, 52.9, 51.4; **HRMS (ESI)** m/z: [M + Na]$^+$ calcd. for $C_{38}H_{32}O_2Na$ 543.2295; found 543.2303.

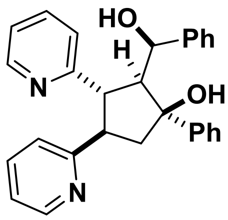


3p. Colourless sticky solid. FC eluent: DCM/Et$_2$O: from 100:0 to 20:1. Yield = 35%, (0.026 mmol, 10.4 mg). *dr* = 11:1. **^{1}H NMR** (400 MHz, CDCl$_3$) δ =

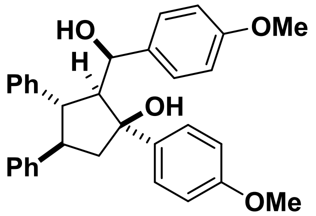
7.70 – 7.66 (m, 2H), 7.48 – 7.41 (m, 2H), 7.35 – 7.29 (m, 2H), 7.02 – 6.97 (m, 2H), 6.96 – 6.92 (m, 1H), 6.90 – 6.86 (m, 2H), 6.85 – 6.83 (m, 1H), 6.26 (dd, *J* = 3.2, 1.9 Hz, 1H), 6.03 – 6.00 (m, 1H), 5.88 (dd, *J* = 3.2, 1.9 Hz, 1H), 5.62 – 5.60 (m, 1H), 4.89 (s, 1H), 4.05 (dd, *J* = 11.6, 8.5 Hz, 1H), 3.60 (s, 1H), 3.56 – 3.45 (m, 2H), 2.99 (dd, *J* = 11.5, 1.5 Hz, 1H), 2.79 (dd, *J* = 14.6, 10.9 Hz, 1H), 2.28 (dd, *J* = 14.6, 4.8 Hz, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 157.2, 154.4, 144.6, 142.0, 141.3, 140.6, 128.5 (2C), 127.4 (2C), 127.1, 126.0, 125.2 (2C), 124.6 (2C), 110.3, 109.8, 106.4, 105.0, 85.4, 70.3, 60.8, 47.5, 42.1, 41.8; **HRMS (ESI)** m/z: $[M + Na]^+$ calcd. for $C_{26}H_{24}O_4Na$ 423.1567; found 423.1573.



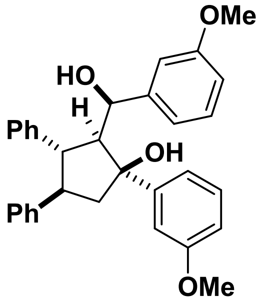
3q. White solid (m.p. = 161 – 163 °C). FC eluent: DCM/Et_2O: from 100:0 to 20:1. Yield = 70%, (0.053 mmol, 23.0 mg). *dr* > 20:1. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 7.69 – 7.65 (m, 2H), 7.50 – 7.44 (m, 2H), 7.37 – 7.31 (m, 1H), 7.10 (dd, *J* = 5.0, 1.2 Hz, 1H), 6.95 – 6.91 (m, 3H), 6.86 (dd, *J* = 5.1, 3.5 Hz, 1H), 6.83 – 6.77 (m, 3H), 6.75 (dd, *J* = 3.5, 1.1 Hz, 1H), 6.54 (dd, *J* = 5.1, 3.4 Hz, 1H), 6.41 (dd, *J* = 3.5, 1.3 Hz, 1H), 4.97 (s, 1H), 4.21 (dd, *J* = 11.5, 9.5 Hz, 1H), 3.68 – 3.53 (m, 2H), 3.00 (s, 1H), 2.95 (dd, *J* = 14.5, 10.3 Hz, 1H), 2.81 (d, *J* = 11.5 Hz, 1H), 2.37 (dd, *J* = 14.5, 6.8 Hz, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) = 147.9, 146.2, 145.6, 142.0, 128.6 (2C), 127.4 (2C), 127.2, 126.6, 126.2, 125.9, 125.1 (2C), 125.1, 124.8 (2C), 124.0, 123.3, 123.3, 84.8, 70.9, 64.8, 51.4, 49.3, 48.1 **HRMS (ESI)** m/z: $[M + Na]^+$ calcd. for $C_{26}H_{24}S_2O_2Na$ 455.1110; found 455.1113.



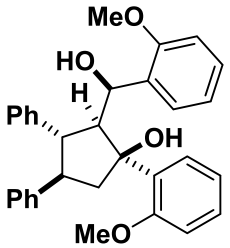
3r. White solid (m.p. = 189 – 191 °C). FC eluent: DCM/Et_2O: 10:1. Yield = 64%, (0.048 mmol, 20.3 mg). *dr* > 20:1. **^{1}H NMR** (600 MHz, $CDCl_3$) δ = 8.87 (bs, 1H), 8.57 (d, *J* = 4.5 Hz, 1H), 8.22 (d, *J* = 5.4 Hz, 1H), 7.85 – 7.80 (m, 2H), 7.48 (td, *J* = 7.6, 1.8 Hz, 1H), 7.43 – 7.36 (m, 2H), 7.28 – 7.21 (m, 1H), 7.13 (ddd, *J* = 7.6, 5.0, 1.2 Hz, 1H), 6.99 (td, *J* = 7.6, 1.8 Hz, 1H), 6.83 – 6.78 (m, 2H), 6.78 – 6.75 (m, 1H), 6.75 – 6.71 (m, 2H), 6.71 – 6.65 (m, 2H), 6.35 (dt, *J* = 7.7, 1.1 Hz, 1H), 5.61 (bs, 1H), 4.84 (s, 1H), 3.72 (dd, *J* = 10.9, 5.9 Hz, 1H), 3.62 (ddd, *J* = 10.7, 5.9, 1.4 Hz, 1H), 3.35 (dd, *J* = 11.0, 1.8 Hz, 1H), 2.96 (dd, *J* = 14.4, 10.7 Hz, 1H), 2.28 (dd, *J* = 14.4, 1.4 Hz, 1H); **^{13}C NMR** (150 MHz, $CDCl_3$) = 164.0, 161.6, 148.3, 148.0, 142.7, 141.3, 136.4, 134.2, 127.3 (2C), 126.0 (2C), 125.8, 124.8 (2C), 124.5, 124.0 (2C), 123.2, 121.6, 120.7, 119.6, 85.2, 69.0, 62.3, 52.5, 51.4, 46.9; **HRMS (ESI)** m/z: $[M + H]^+$ calcd. for $C_{28}H_{27}N_2O_2$ 423.2067; found 423.2059.



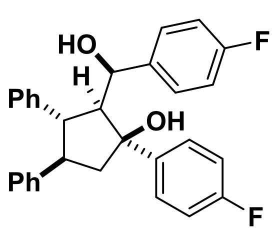
3s. White solid (m.p. = 200 – 202 °C). FC eluent: DCM/Et$_2$O: from 100:0 to 20:1. Yield = 62%, (0.047 mmol, 22.3 mg). *dr* > 20:1. **^{1}H NMR** (400 MHz, CDCl$_3$) δ = 7.64 – 7.58 (m, 2H), 7.16 – 7.07 (m, 1H), 7.02 – 6.96 (m, 2H), 6.90 – 6.81 (m, 3H), 6.67 – 6.61 (m, 2H), 6.58 – 6.52 (m, 2H), 6.36 – 6.30 (m, 2H), 4.92 (s, 1H), 3.85 (s, 3H) partially overlapped with 3.84 (bs, 1H), 3.83 – 3.76 (m, 1H), 3.60 (s, 3H), 3.20 (td, *J* = 10.4, 6.9 Hz, 1H), 2.88 – 2.77 (m, 3H), 2.29 (dd, *J* = 14.6, 6.9 Hz, 1H); **^{13}C NMR** (100 MHz, CDCl$_3$) δ = 158.5, 157.8, 144.3, 141.9, 138.5, 134.3, 128.1 (2C), 127.8 (2C), 127.7 (2C), 127.6 (2C), 126.3 (2C), 126.0, 125.9 (2C), 125.4, 113.8 (2C), 112.8 (2C), 84.8, 71.0, 63.2, 55.3, 55.2, 53.7, 52.7, 51.0; **HRMS (ESI)** m/z: [M + Na]$^+$ calcd. for $C_{32}H_{32}O_4Na$ 503.2193; found 503.2187.



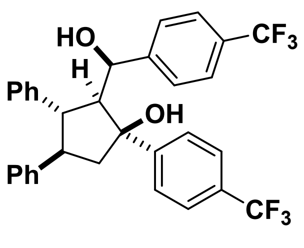
3t. White solid (m.p. = 135 -137 °C). FC eluent: DCM/Et$_2$O: from 100:0 to 20:1. Yield = 63%, (0.048 mmol, 22.9 mg). *dr* > 20:1. **^{1}H NMR** (400 MHz, CDCl$_3$) δ = 7.40 (t, *J* = 7.9 Hz, 1H), 7.32 (t, *J* = 2.1 Hz, 1H), 7.27 – 7.23 (m, 1H), 7.22 – 7.16 (m, 4H), 7.15 – 7.10 (m, 1H), 6.87 (ddd, *J* = 8.4, 2.6, 0.9 Hz, 1H), 6.85 – 6.81 (m, 3H), 6.78 (t, *J* = 8.0 Hz, 1H), 6.69 – 6.64 (m, 2H), 6.37 (dd, *J* = 7.8, 3.1 Hz, 1H), 6.27 – 6.20 (m, 2H), 4.93 (s, 1H), 3.95 (s, 1H), 3.88 (s, 3H), 3.82 (dd, *J* = 12.2, 10.3 Hz, 1H), 3.48 (s, 3H), 3.23 (td, *J* = 10.5, 6.9 Hz, 1H), 2.92 (dd, *J* = 12.1, 1.5 Hz, 1H), 2.90 – 2.82 (m, 2H), 2.30 (dd, *J* = 14.7, 6.9 Hz, 1H); **^{13}C NMR** (100 MHz, CDCl$_3$) δ = 159.9, 158.8, 148.3, 144.2, 143.9, 141.6, 129.6, 128.3, 128.2 (2C), 127.8 (2C), 127.7 (2C), 127.5 (2C), 126.1, 125.4, 117.5, 117.2, 112.0, 111.8, 111.7, 110.4, 85.1, 71.1, 63.0, 55.3, 54.8, 53.9, 52.7, 51.1; **HRMS (ESI)** m/z: [M + Na]$^+$ calcd. for $C_{32}H_{32}O_4Na$ 503.2193; found 503.2201.



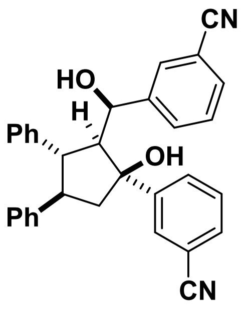
3u. Colourless sticky solid. FC eluent: DCM/Et$_2$O: from 100:0 to 20:1. Yield = 56%, (0.042 mmol, 20.0 mg). *dr* = 4.4:1. **^{1}H NMR** (600 MHz, CDCl$_3$) δ = 7.76 (dd, *J* = 7.7, 1.7 Hz, 1H), 7.28 (ddd, *J* = 8.2, 7.4, 1.7 Hz, 1H), 7.22 – 7.19 (m, 1H), 7.16 – 7.07 (m, 4H), 7.07 – 7.04 (m, 1H), 7.02 (td, *J* = 7.5, 1.1 Hz, 1H), 6.99 (d, *J* = 6.8 Hz, 1H), 6.97 (dd, *J* = 8.2, 1.1 Hz, 1H), 6.77 (td, *J* = 7.8, 1.8 Hz, 1H), 6.72 – 6.66 (m, 2H), 6.48 – 6.40 (m, 3H), 6.32 (d, *J* = 8.2 Hz, 1H), 5.37 (s, 1H), 4.83 (s, 1H), 4.20 (s, 1H), 3.94 (s, 3H), 3.62 (t, *J* = 10.7 Hz, 1H), 3.47 (s, 3H), 3.44 (dd, *J* = 11.0, 2.2 Hz, 1H), 3.08 (q, *J* = 9.5 Hz, 1H), 2.84 (dd, *J* = 14.1, 9.2 Hz, 1H); **^{13}C NMR** (100 MHz, CDCl$_3$) δ = 155.9, 153.9, 143.1, 142.3, 132.8, 129.1, 127.4, 127.1 (2C), 126.8 (2C), 126.5 (2C), 126.3 (2C), 126.1, 125.9, 125.3, 124.9, 124.0, 119.9, 119.1, 110.2, 108.1, 83.7, 67.2, 54.8, 54.4, 53.8, 52.2, 51.9, 47.8; **HRMS (ESI)** m/z: [M + Na]$^+$ calcd. for $C_{32}H_{32}O_4Na$ 503.2193; found 503.2190.



3v. White solid (m.p. = 164 – 166 °C). FC eluent: DCM/Et_2O: from 100:0 to 20:1. Yield = 67%, (0.050 mmol, 22.9 mg). *dr* > 20:1. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 7.70 – 7.61 (m, 2H), 7.22 – 7.09 (m, 7H), 6.90 – 6.79 (m, 3H), 6.67 – 6.62 (m, 2H), 6.60 – 6.53 (m, 2H), 6.49 – 6.43 (m, 2H), 4.89 (s, 1H), 3.85 – 3.78 (m, 2H), 3.24 (td, *J* = 10.5, 7.0 Hz, 1H), 2.95 (d, *J* = 2.3 Hz, 1H), 2.85 (dd, *J* = 14.7, 10.8 Hz, 1H), 2.78 (dd, *J* = 12.0, 1.5 Hz, 1H), 2.31 (dd, *J* = 14.7, 7.0 Hz, 1H).; **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 161.9 (d, *J* = 245.7 Hz), 161.1 (d, *J* = 243.9 Hz), 143.8, 142.0 (d, *J* = 2.9 Hz), 141.3, 137.6 (d, *J* = 3.0 Hz), 128.2 (2C), 127.7 (2C + 2C + 2C overlapped), 126.8 (d, *J* = 8.0 Hz, 2C), 126.3 (d, *J* = 8.1 Hz, 2C), 126.2, 125.7, 115.4 (d, *J* = 21.3 Hz, 2C), 114.0 (d, *J* = 21.6 Hz, 2C), 84.8, 70.6, 63.6, 53.6, 52.5, 51.2; **^{19}F NMR** (376 MHz, $CDCl_3$) δ = -116.00 – -116.17 (m, 1F), -116.99 – -117.13 (m, 1F); **HRMS (ESI)** m/z: [M + Na]$^+$ calcd. for $C_{30}H_{26}F_2O_2Na$ 479.1793; found 479.1786.

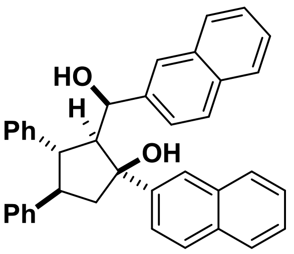


3w. White solid (m.p. = 219 – 222 °C). FC eluent: DCM/Et_2O: from 100:0 to 20:1. Yield = 90%, (0.068 mmol, 37.5 mg). *dr* > 20:1. **^{1}H NMR** (400 MHz, Acetone-d_6) δ = 8.18 – 8.11 (m, 2H), 7.84 – 7.77 (m, 2H), 7.28 – 7.22 (m, 2H), 7.18 (dd, *J* = 8.5, 6.7 Hz, 2H), 7.14 – 7.03 (m, 3H), 6.92 – 6.86 (m, 2H), 6.84 – 6.73 (m, 5H), 5.01 (d, *J* = 2.3 Hz, 1H), 4.93 (s, 1H), 3.97 (dd, *J* = 12.1, 10.4 Hz, 1H), 3.50 (td, *J* = 10.7, 6.9 Hz, 1H), 3.13 (dd, *J* = 12.1, 1.6 Hz, 1H), 2.99 (dd, *J* = 14.5, 11.0 Hz, 1H), 2.84 (s, 1H), 2.35 (dd, *J* = 14.5, 6.9 Hz, 1H); **^{13}C NMR** (100 MHz, Acetone-d_6) δ = 152.0 (q, *J* = 1.5 Hz), 147.4 (q, *J* = 1.5 Hz), 144.6, 141.6, 128.3 (q, *J* = 31.7 Hz), 128.2 (2C), 128.0 (2C), 127.8 (2C), 127.3 (2C), 127.1 (q, *J* = 31.7 Hz), 126.5 (2C), 125.9, 125.6 (2C), 125.4, 125.1 (q, *J* = 3.8 Hz, 2C), 124.7 (q, *J* = 271.0 Hz), 124.4 (q, *J* = 271.1 Hz), 123.7 (q, *J* = 3.9 Hz, 2C), 84.6, 70.0, 63.4, 53.4, 52.8, 51.2; **^{19}F NMR** (377 MHz, $CDCl_3$) δ = -62.72 (s, 3F), -63.14 (s, 3F); **HRMS (ESI)** m/z: [M + Na]$^+$ calcd. for $C_{32}H_{26}F_6O_2Na$ 579.1729; found 579.1736.



3x. White solid (m.p. = 143 – 146 °C). FC eluent: DCM/Et_2O: from 100:0 to 20:1. Yield = 75%, (0.056 mmol, 26.4 mg). *dr* > 20:1. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.05 (t, *J* = 1.7 Hz, 1H), 7.91 (dt, *J* = 7.4, 1.8 Hz, 1H), 7.66 – 7.56 (m, 2H), 7.22 – 7.10 (m, 5H), 7.09 – 7.04 (m, 1H), 6.96 – 6.77

(m, 6H), 6.72 – 6.63 (m, 2H), 4.82 (s, 1H), 4.22 (s, 1H), 3.86 (dd, *J* = 12.1, 10.4 Hz, 1H), 3.53 (d, *J* = 2.2 Hz, 1H), 3.32 (td, *J* = 10.6, 7.1 Hz, 1H), 2.87 (dd, *J* = 14.9, 10.8 Hz, 1H), 2.70 (dd, *J* = 12.1, 1.5 Hz, 1H), 2.34 (dd, *J* = 14.9, 7.2 Hz, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 148.0, 143.1, 143.1, 140.3, 130.9, 129.9, 129.6, 129.6, 129.2 (2C), 129.1, 128.4 (2C), 128.0 (C + C + C overlapped), 127.7 (2C), 127.6 (2C), 126.4, 126.3, 118.9, 118.6, 112.7, 111.3, 84.5, 70.1, 63.7, 53.4, 52.4, 51.3 **HRMS (ESI)** m/z: $[M + Na]^+$ calcd. for $C_{32}H_{26}N_2O_2Na$ 493.1886; found 493.1990.

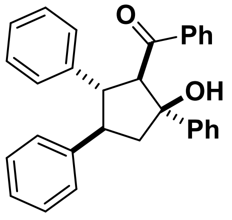


3y. White solid (m.p. = 202 - 204 °C). FC eluent: DCM/Et_2O: from 100:0 to 20:1. Yield = 82%, (0.061 mmol, 25.0 mg). *dr* > 20:1. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 8.26 (s, 1H), 7.99 (d, *J* = 8.6 Hz, 1H), 7.94 – 7.89 (m, 2H), 7.75 (dt, *J* = 8.6, 1.6 Hz, 1H), 7.57 – 7.50 (m, 3H), 7.37 – 7.32 (m, 1H), 7.31 – 7.17 (m, 7H), 7.16 – 7.11 (m, 1H), 7.07 (s, 1H), 6.69 – 6.61 (m, 3H), 6.60 – 6.54 (m, 2H), 6.52 – 6.44 (m, 1H), 5.07 (s, 1H), 4.17 (s, 1H), 3.94 (dd, *J* = 12.0, 10.2 Hz, 1H), 3.32 (td, *J* = 10.5, 7.0 Hz, 1H). 3.16 (s, 1H), 3.07 (d, *J* = 1.6 Hz, 1H), 3.00 (dd, *J* = 14.7, 10.8 Hz, 1H), 2.39 (dd, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 144.2, 143.6, 141.4, 139.2, 133.3, 132.6, 132.5, 132.0, 128.5, 128.3, 128.2 (2C), 127.8 (2C), 127.8, 127.6 (2C + C overlapped), 127.3 (2C), 127.1, 126.9, 126.4, 126.1, 126.0, 125.4, 125.3, 125.1, 124.2, 124.0, 123.5, 123.2, 85.3, 71.4, 62.7, 53.8, 52.8, 50.9; **HRMS (ESI)** m/z: $[M + Na]^+$ calcd. for $C_{38}H_{32}O_2Na$ 543.2295; found 543.2290.

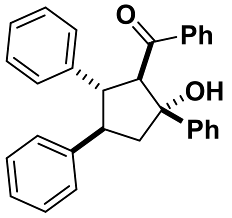
4. Further Experiments

4.1 Preparation, isolation and characterization of compounds **2a** and **2a'**.

The ElectraSyn vial (5 mL), equipped with a stir bar, was charged with chalcone **1** (0.15 mmol), and $TEABF_4$ (0.030 mmol, 6.5 mg). The ElectraSyn vial cap, equipped with anode ($C_{graph.}$) and cathode (Ag), was inserted into the mixture and closed with a rubber septum. The vessel was evacuated and backfilled with N_2 three times, then dry DMF (3.0 mL) was added and the mixture stirred until complete dissolution of the solids occurred, while bubbling with N_2 (balloon,1 min). The reaction mixture was electrolyzed (under N_2, balloon) at a constant current of 4.0 mA, **until a total charge of 0.15 mF (1.0 F/mol$_{1a}$) was reached**. The ElectraSyn vial cap was removed, and the electrodes and vial were rinsed with EtOAc (20 mL) and $NH_4Cl_{(aq)}$ (saturated, 5 mL) and water (5 mL), which were combined with the crude mixture, appearing as a cloudy suspension, in a separatory funnel. Additional EtOAc (10-20 mL) was usually found to be necessary to dissolve most of the precipitate formed. Then, the organic layer was separated, and the aqueous layer was extracted with EtOAc (2 x 10 mL). The combined organic layers (remaining slightly cloudy, due to the presence of scarcely soluble **2a'**) were washed with $NH_4Cl_{(aq)}$ (0.1 M, 3 x 10 mL), dried over Na_2SO_4 (decantation) and concentrated *in vacuo*. The crude product (**2a**:**2a'** = 1.9:1 by ^{1}H NMR analysis) was finally purified by FC (*n*-hexane/EtOAc = 12:1) to afford products **2a** and **2a'**.



2a (first eluting fraction of the FC). White solid. Yield = 36%, (0.027 mmol, 11.3 mg). *dr* > 20:1 (after FC). **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 7.62 – 7.56 (m, 2H), 7.47 – 7.39 (m, 4H), 7.38 – 7.24 (m, 5H), 7.22 – 7.09 (m, 8H), 7.07 – 7.02 (m, 1H), 5.25 (s, 1H), 4.55 (d, *J* = 12.0 Hz, 1H), 4.12 (dd, *J* = 12.0, 10.1 Hz, 1H), 3.80 (td, *J* = 10.7, 6.0 Hz, 1H), 3.01 (dd, *J* = 14.6, 11.3 Hz, 1H), 2.60 (dd, *J* = 14.6, 6.0 Hz, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ = 205.0, 145.2, 144.0, 139.8, 137.5, 133.3, 128.4, 128.4 (2C), 128.3 (2C), 128.1 (2C), 128.1 (2C), 127.9 (2C), 127.6 (2C), 127.0, 126.9, 126.3, 124.8 (2C), 84.3, 63.5, 59.6, 51.3, 22.6. **2a** is a known compound and the given data match with the ones reported in the literature (ref. 6h, 6i and 6j of the main text).



2a' (second eluting fraction of the FC). White solid (m.p. = 150 – 154 °C). Yield = 32%, (0.024 mmol, 10.1 mg). *dr* > 20:1 (after FC). **^{1}H NMR** (400

MHz, DMSO-d_6) δ = 7.62 – 7.59 (m, 2H), 7.47 – 7.43 (m, 1H), 7.41 – 7.37 (m, 4H), 7.36 – 7.33 (m, 2H), 7.33 – 7.28 (m, 4H), 7.25 – 7.21 (m, 2H), 7.22 – 7.18 (m, 1H), 7.15 – 7.11 (m, 1H), 7.11 – 7.07 (m, 2H), 7.03 – 7.00 (m, 1H), 5.79 (s, 1H), 4.43 (d, *J* = 8.7 Hz, 1H), 4.05 (dd, *J* = 11.4, 8.7 Hz, 1H), 3.97 (td, *J* = 11.9, 5.8 Hz, 1H), 2.77 (t, *J* = 12.7 Hz, 1H), 2.45 (dd, *J* = 12.9, 5.8 Hz, 1H); **^{13}C NMR** (100 MHz, DMSO-d_6) δ = 200.1, 144.7, 143.0, 142.6, 137.8, 133.1, 128.8 (2C), 128.8 (2C), 128.5 (2C), 128.5 (2C), 128.3 (2C), 128.0 (2C), 127.5 (2C), 126.8, 126.7 (2C + 1 C overlapped), 83.0, 55.9, 55.4, 51.8, 50.5. **HRMS (ESI)** m/z: [M + Na]$^+$ calcd. for $C_{30}H_{26}O_2Na$ 441.1825; found 441.1828.

4.3 Monitoring of reaction profile.

To gain better understanding of the reaction mechanism, the amount of compounds **1a**, **2a**, **2a’** and **3a** during the reaction course was investigated. Four identical reactions (see section 3 for details) were set and then stopped after 1, 2, 3 or 4 F/mol$_{\mathbf{1a}}$. The amount of the species present in the reaction crude were then analyzed by ^{1}H NMR spectroscopy using mesitylene as an internal standard and the data are collected below in **Figure S1**.

As a matter of fact, after 1 F/mol$_{\mathbf{1a}}$, starting chalcone **1a** was almost absent and product **3a** was detectable only in trace amounts (**Table S2**, entry 2). This clearly demonstrates the self-adaptability principle: indeed, the potential increases only when the mixture specifically requires it, leading to the beginning of the second step of the cascade only when the most easily reducible species (**1a**) is completely consumed. Interestingly, although after 1 F/mol$_{\mathbf{1a}}$ the relative amount of **2a** and **2a’** is comparable, in entries 3 and 4 the amount of **2a’** is higher than the one of **2a**. In accordance with the hypothesized dynamic kinetic resolution mechanism, as product **3a** forms directly from **2a**, **2a’** is accumulated in solution, indicating plausibly a slow epimerization. At the end of the process (entry 5) product **3a** is present almost exclusively.

Table S2. Monitoring formation/consumption of **1a**, **2a**, **2a’** and **3a** during the reaction course.[a]

Entry	F/mol$_{\mathbf{1a}}$	**1a** [%][b]	**2a** [%][b]	**2a'** [%][b]	**3a** [%][b]
1	0	100	0	0	0
2	1	5	45	48	2
3	2	0	25	35	31
4	3	0	7	19	64
5	4	0	0	2	84

[a] Reaction conditions: **1a** (0.15 mmol), TEOA (0.30 mmol), TEABF$_4$ (0.030 mmol), DMF (3.0 mL), CCE **I** = 4 mA, rt. [b] Yields were determined by ^{1}H-NMR analysis on the reaction crude using mesitylene as the internal standard.

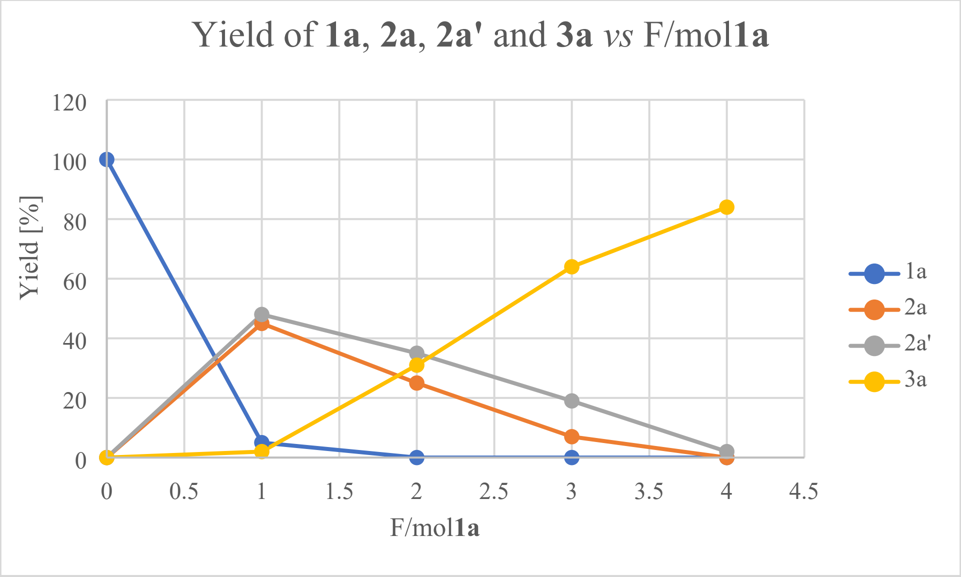


Figure S1. Amount of **1a** (blue line), **2a** (orange line), **2a’** (grey line) and **3a** (yellow line) during the reaction course.

5. Crystallographic data for compounds 2a' and 3a

The X-ray intensity data were measured on a Bruker Apex II CCD diffractometer. Cell dimensions and the orientation matrix were initially determined from a least-squares refinement on reflections measured in three sets of 20 exposures, collected in three different ω regions, and eventually refined against all data. A full sphere of reciprocal space was scanned by 0.5° ω steps. The software SMART[3] was used for collecting frames of data, indexing reflections and determination of lattice parameters. The collected frames were then processed for integration by the SAINT program,[2] and an empirical absorption correction was applied using SADABS.[3] The structures were solved by direct methods (SIR 2014)[4] and subsequent Fourier syntheses and refined by full-matrix least-squares on F^2 (SHELXTL)[5] using anisotropic thermal parameters for all non-hydrogen atoms. The aromatic, methylene, methine and hydroxy hydrogen atoms were placed in calculated positions, refined with isotropic thermal parameters $U(H) = 1.2\ Ueq(\mathrm{C})$ and allowed to ride on their carrier carbons. In the asymmetric unit of **3a** one acetone solvent molecule is present. The PLATON "TWINrotMAT" routine showed the presence of twinning in **2a'** with a refined minor twin fraction of 0.40 (BASF parameter in SHELXL) and both twin domains were reindexed by TWINrotMAT and used for the final refinement.

Crystal data and experimental details of the data collection for **2a'** and **3a** are reported in **Table S3**. Molecular drawings were generated using Mercury.[6]

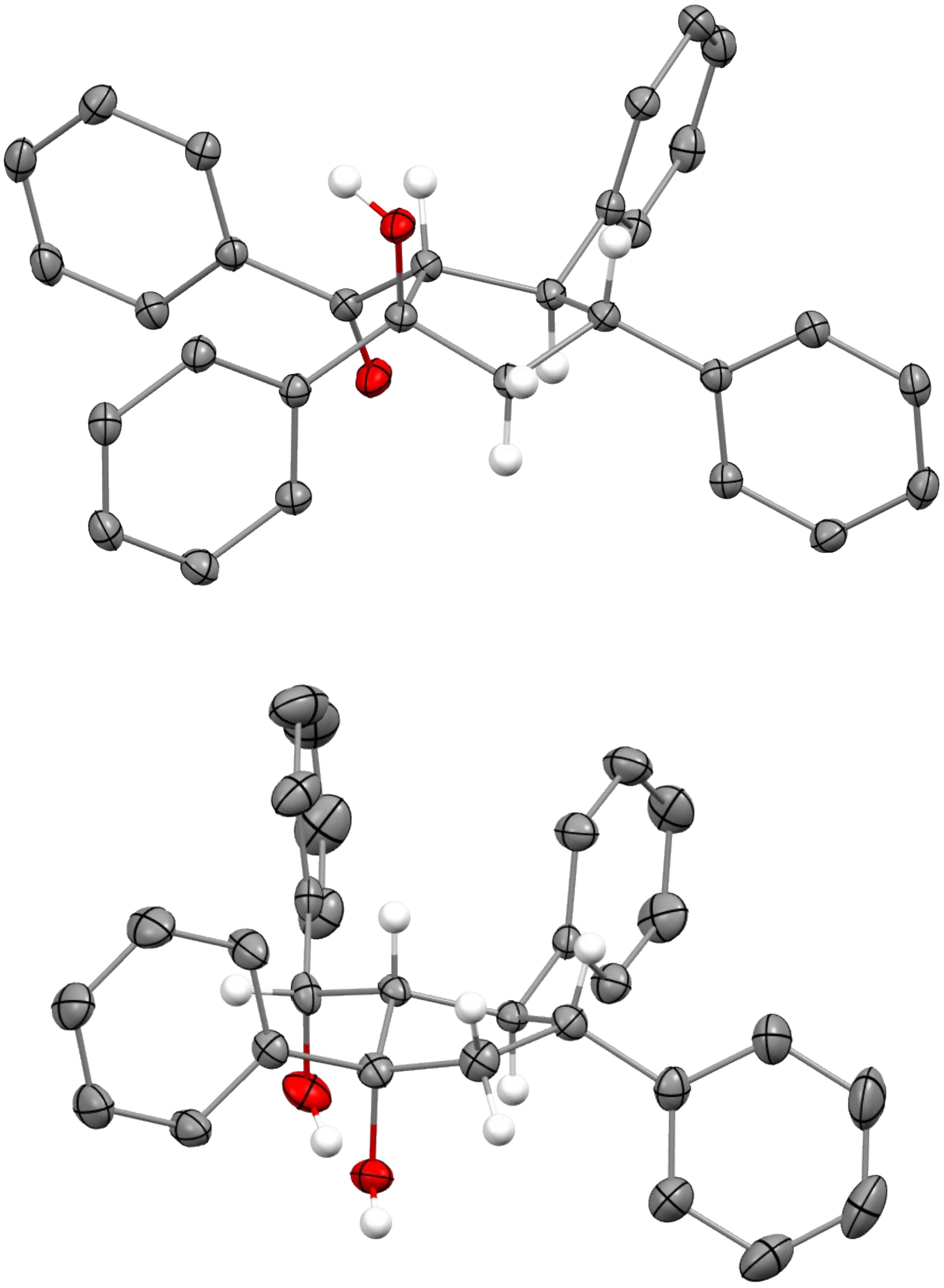
Crystallographic data have been deposited with the Cambridge Crystallographic Data Centre (CCDC) as supplementary publication number CCDC 2290358 (**2a'**) and CCDC 2290359 (**3a**). Copies of the data can be obtained free of charge via www.ccdc.cam.ac.uk/getstructures.

Table S3. Crystal data and experimental details for **2a’** and **3a**.

Compound	**2a'**	**3a**
Formula	$C_{30}H_{26}O_2$	$C_{30}H_{28}O_2 \cdot C_3H_6O$
Fw	418.51	478.60
T, K	150(2)	296(2)
λ, Å	1.54178	0.71073
Crystal symmetry	Triclinic	Monoclinic
Space group	P-1	$P2_1/n$
***a*, Å**	6.0915(3)	20.754(2)
***b*, Å**	10.7543(4)	5.9450(5)
***c*, Å**	17.1562(8)	24.108(2)
α	100.087(3)	90
β	92.581(3)	112.709(2)
γ	102.264(2)	90
Cell volume, Å^3	1077.32(8)	2744.0(4)
Z	2	4
D_c, Mg m^{-3}	1.290	1.159
μ(Mo-K_α), mm^{-1}	0.617	0.073
F(000)	444	1024
Crystal size/ mm	0.10 x 0.08 x 0.06	0.61 x 0.12 x 0.04
θ limits, °	2.625 to 66.575	2.534 to 24.999
Reflections collected	3803	31699
Unique obs. Reflections [$F_o > 4\sigma(F_o)$]	3803	4793[R(int)= 0.0631]
Goodness-of-fit-on F^2	1.258	1.139
R_1 (F)^a, wR_2 (F^2) [$I > 2\sigma(I)$]^b	R1 = 0.0540, wR2 = 0.1550	R1 = 0.0982, wR2 = 0.2160
Largest diff. peak and hole, e. Å^{-3}	0.287 and -0.266	0.360 and -0.262

$^{a)}R_1 = \Sigma||F_o|-|F_c||/\Sigma|F_o|$. ^{b} $wR_2 = [\Sigma w(F_o^2-F_c^2)^2/\Sigma w(F_o^2)^2]^{1/2}$ where $w = 1/[\sigma^2(F_o^2) + (aP)^2+ bP]$ where $P = (F_o^2 + F_c^2)/3$.

Figure S2. ORTEP drawing of **2a'** (top) and **3a** (bottom)**.** Thermal ellipsoids are drawn at 30% of the probability level. Aromatic hydrogens and solvated acetone (**3a**) are removed for clarity.



6. Cyclic Voltammetry Experiments

Electrochemical or analytical grade tetraethylammonium tetrafluoborate ($TEABF_4$) from Sigma-Aldrich was used as received as supporting electrolytes. *N,N*-Dimethylformamide (DMF, anhydrous, ≥ 99.8%, Merck) was purified and dried over molecular sieves 4Å, under argon, in order to remove water, proton donors and oxygen as previously reported,[7] stored in a specially designed Schlenk flask and protected from light.

The solvent was distilled via a closed system into a custom designed electrochemical cell containing the supporting electrolyte and the species under examination, immediately before performing the experiment. Electrochemical experiments were carried out in an airtight single-compartment cell using platinum as working and counter electrodes and a silver spiral as a quasi-reference electrode. The drift of the quasi-reference electrode was negligible during the time required for an experiment. All the $E_{½}$ potentials have been directly obtained from cyclic voltametric curves as averages of the cathodic and anodic peak potentials and by digital simulation in the case of not Nernstian or overlapping processes. The $E_{½}$ values have been determined by adding ferrocene (Fc), at the end of each experiment, as an internal standard and measuring them with respect to the ferrocinium/ferrocene couple ($Fc^{+/0}$) standard potential (which is +0.42 V vs SCE, i.e., the aqueous Saturated Calomel Electrode).[8]

The cell containing the supporting electrolyte was dried under vacuum at 100 °C for at least 5 hours before each experiment. Afterward, the electroactive compound was inserted in the cell and the system evacuated for a further hour, at room temperature. The pressure measured in the electrochemical cell prior to performing the trap-to-trap distillation of the solvent was typically about $4\text{-}5\times10^{-5}$ mbar. Cyclic voltammetric curves were recorded with a custom made fast potentiostat[9] controlled by an AMEL Mod. 568 programmable function generator. The potentiostat was interfaced to a Nicolet Mod. 3091 digital oscilloscope and the data transferred to a personal computer by the program Antigona.[10] Minimization of the uncompensated resistance effect in the voltammetric measurements was achieved by the positive-feedback circuit of the potentiostat. Digital simulations of the cyclic voltammetric curves were carried out either by Antigona or DigiSim 3.0, utilizing a best fitting procedure of the experimental curves recorded at different scan rates spanning over, at least, two orders of magnitude.

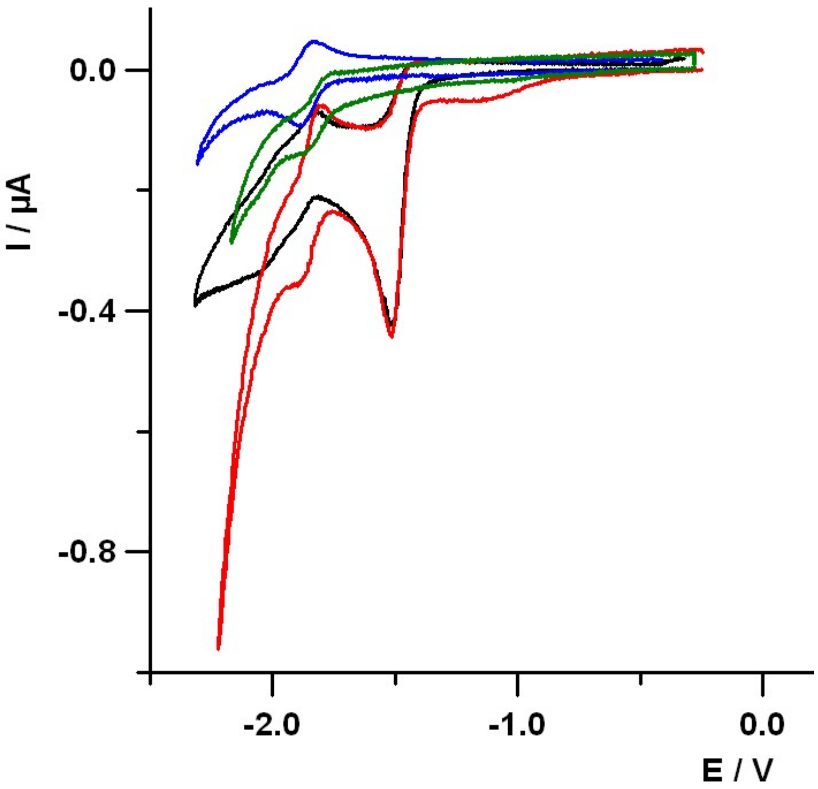
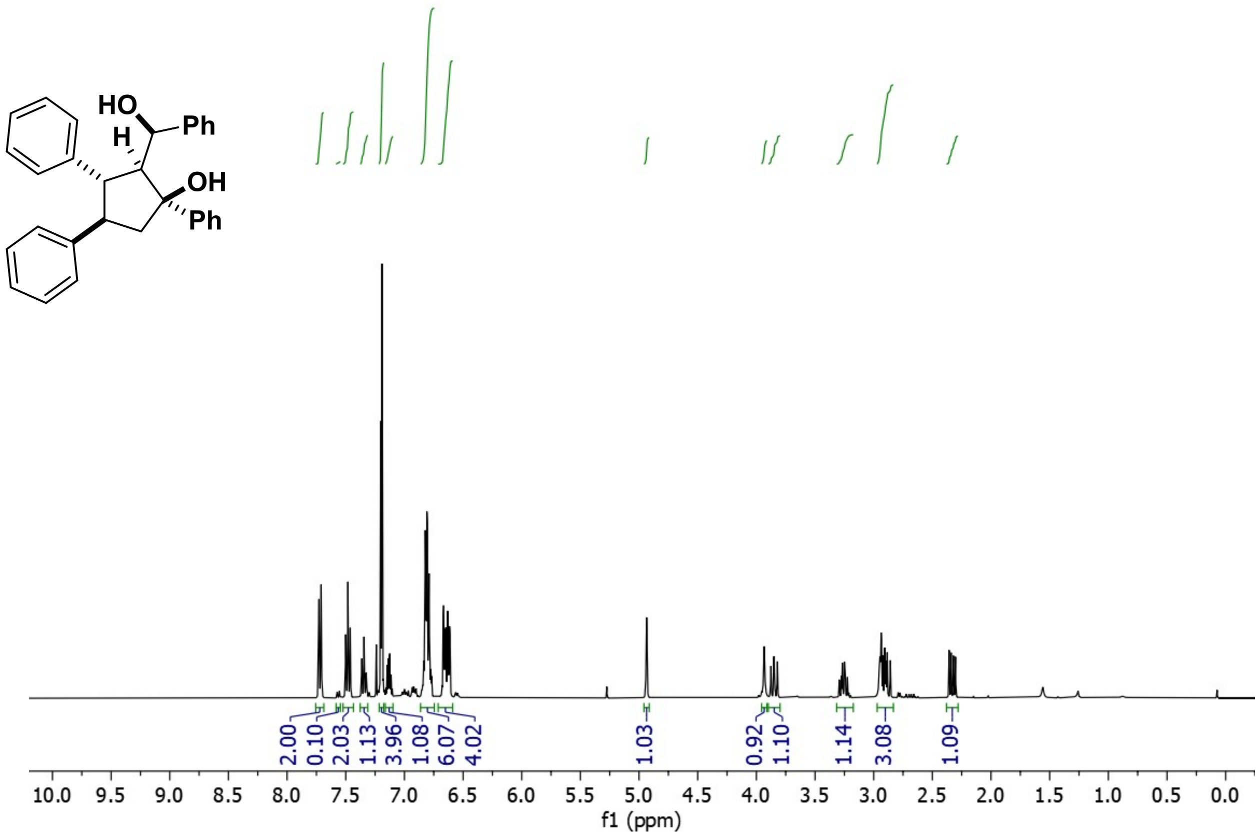


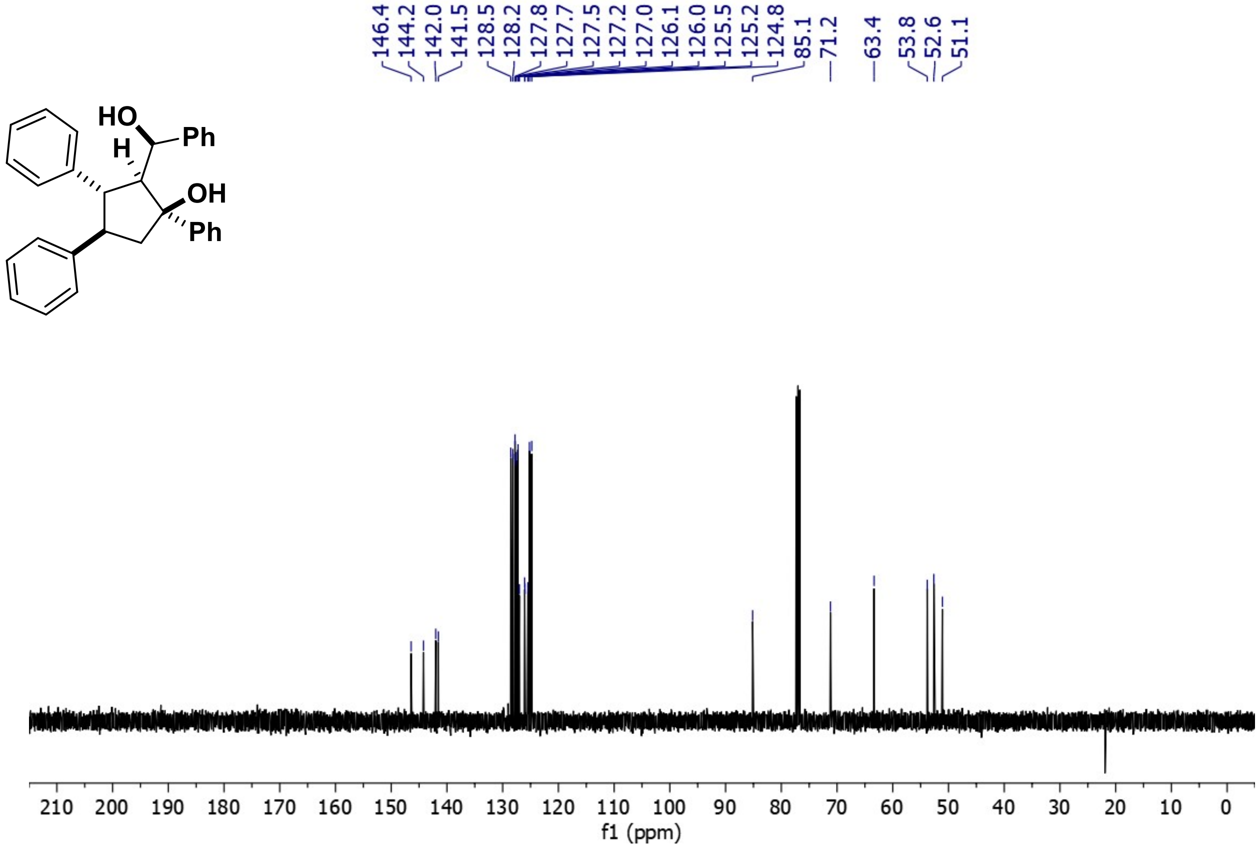
Figure S3. Cyclic voltammetry curves of: (black line) chalcone **1a** 4.0 mM in TBABF$_4$/DMF electrolyte solution; (red line) chalcone as above with 0.2 mM H_2O added; (blue line) intermediate **2a** 1.2 mM in TBABF$_4$/DMF solution; (green line) intermediate **2a'** 1.1 mM in TBABF$_4$/DMF electrolyte solution.

7. ^{1}H-, ^{19}F-, ^{13}C-NMR Spectra of New Compounds

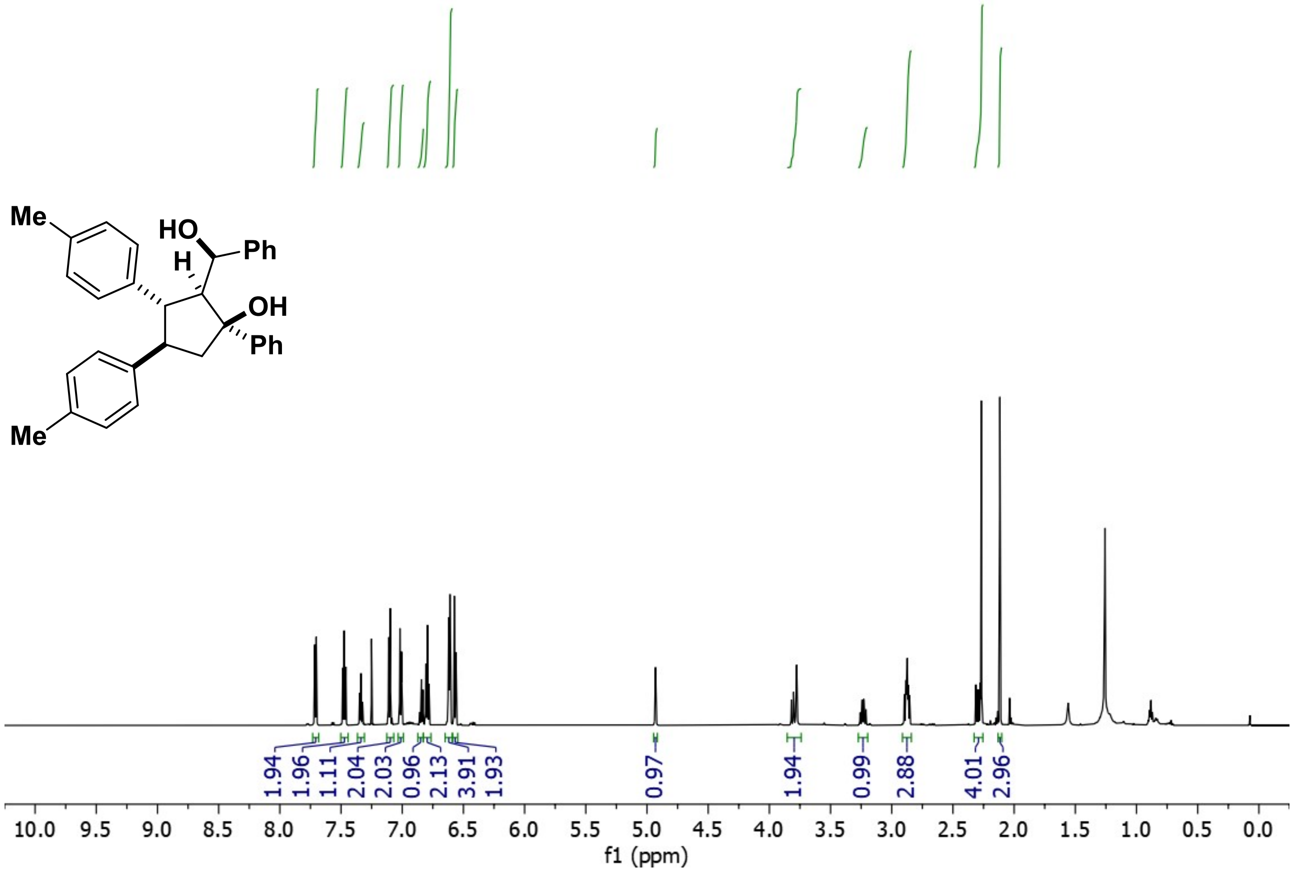
3a ^{1}H NMR (400 MHz, $CDCl_3$)



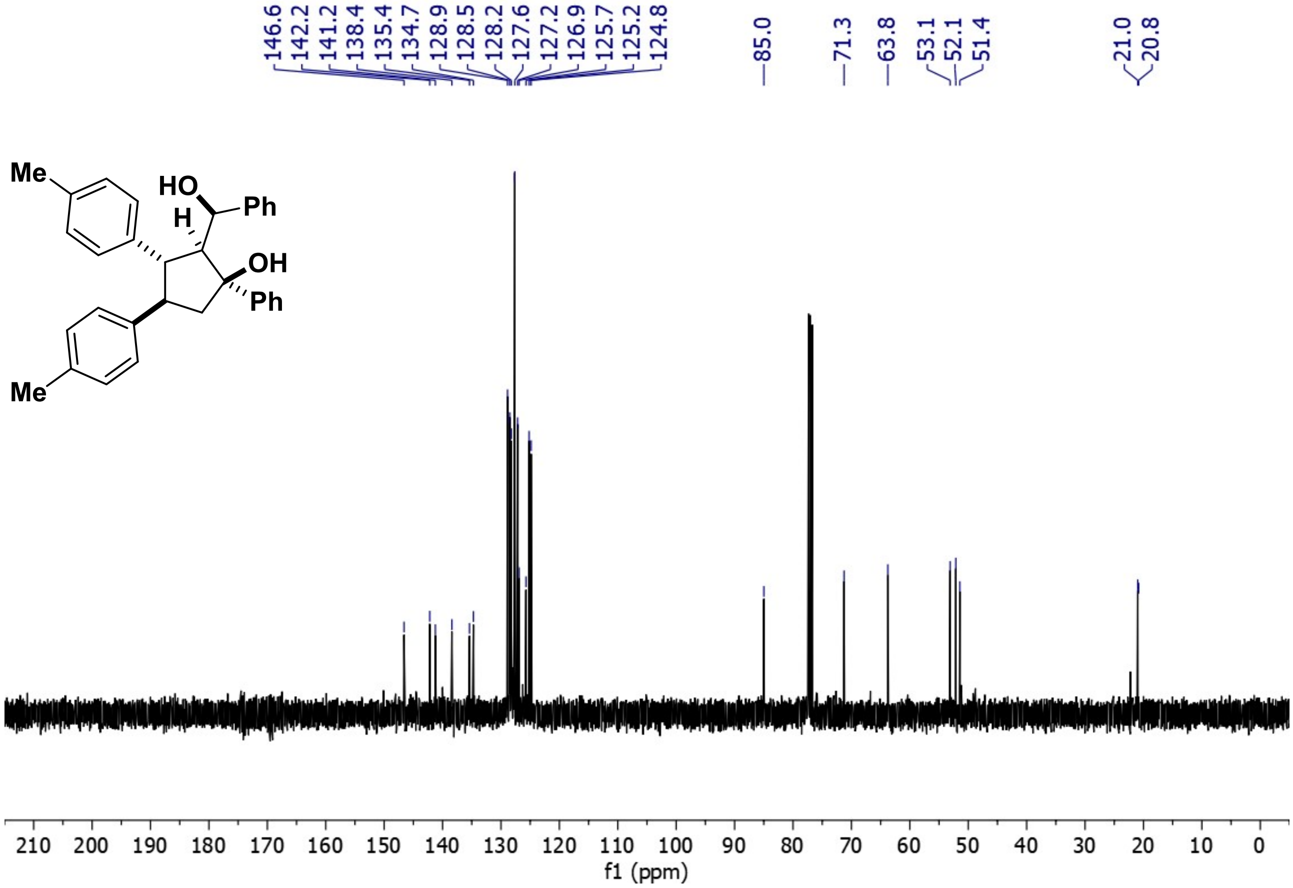
3a ^{13}C NMR (100 MHz, $CDCl_3$)



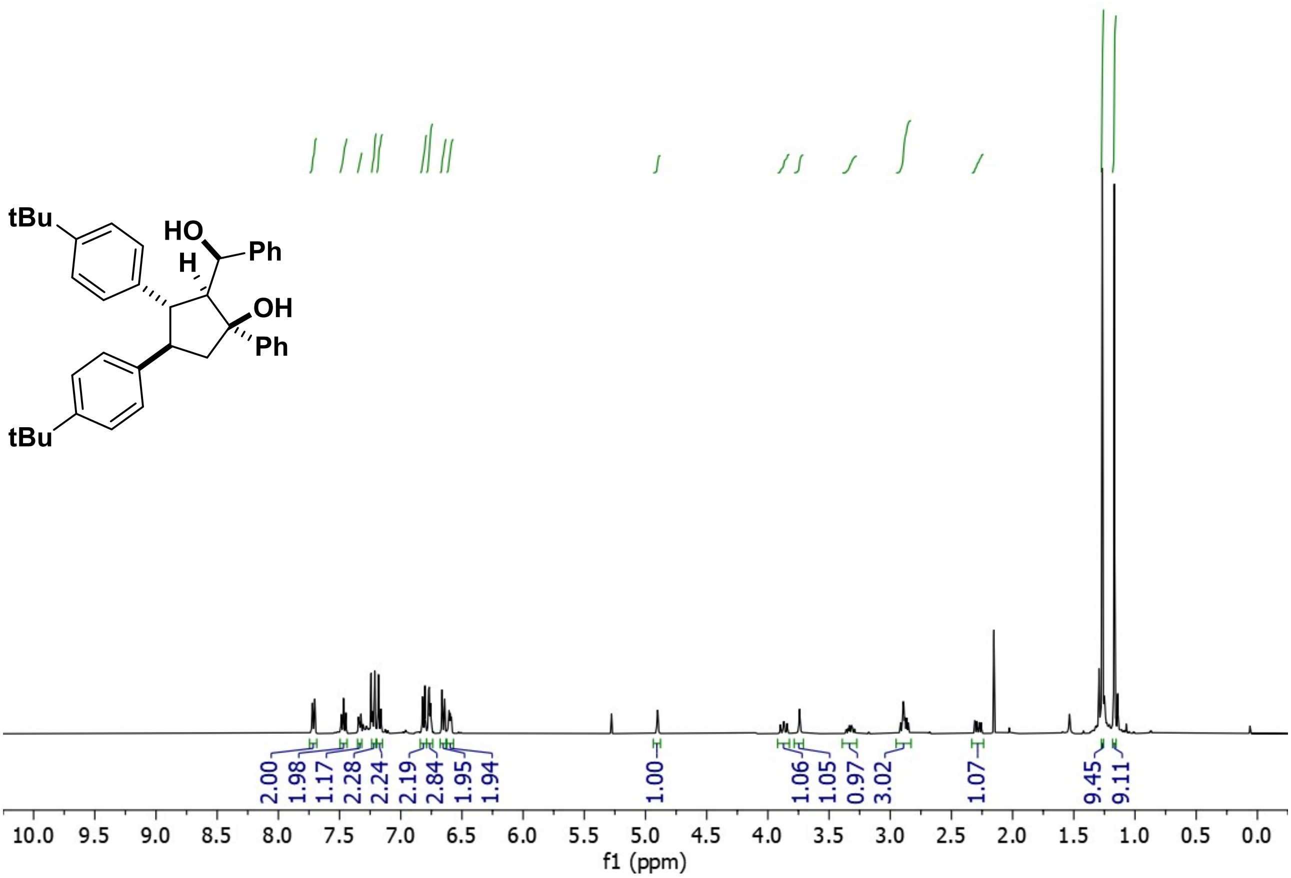
3b ^1H NMR (600 MHz, $CDCl_3$)



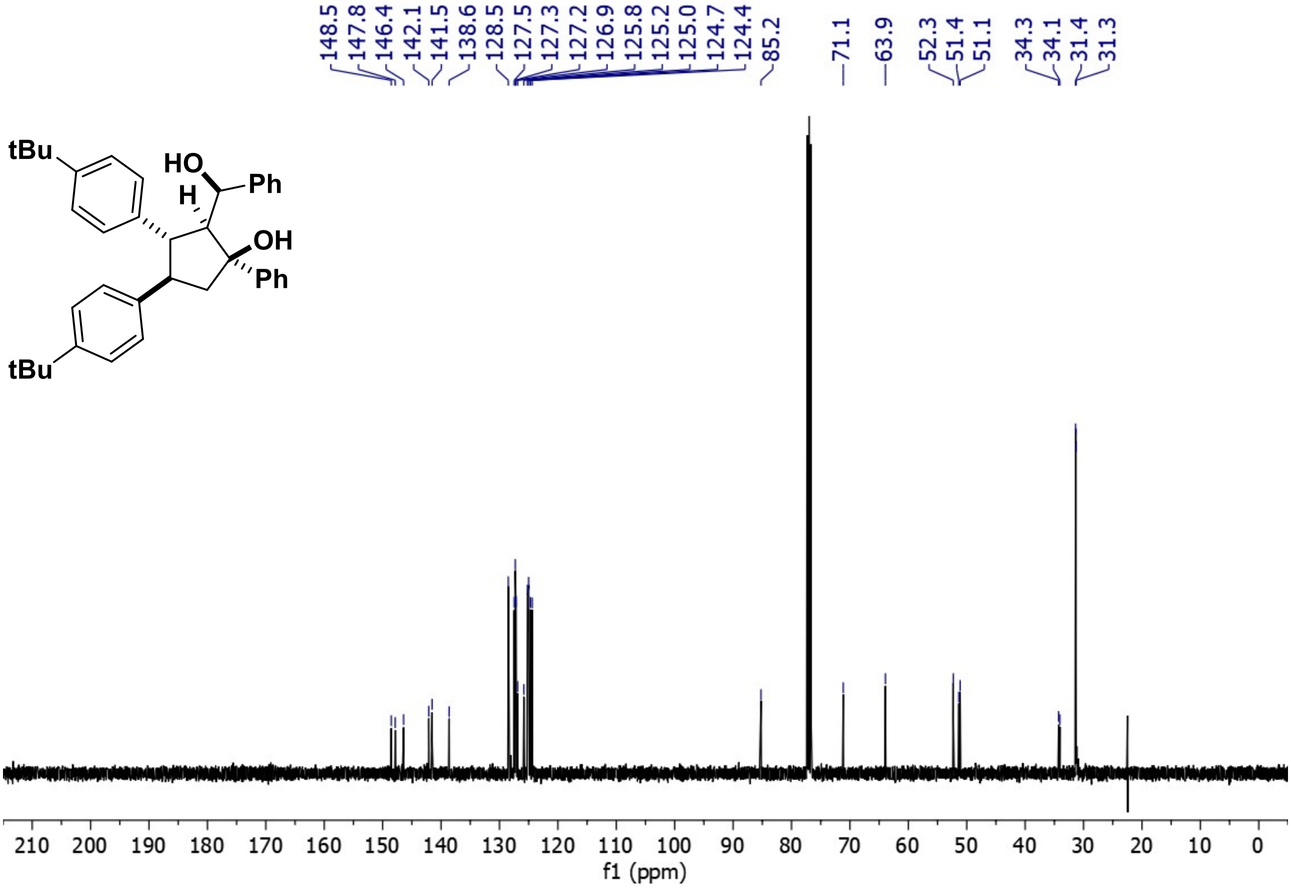
3b ^{13}C NMR (100 MHz, $CDCl_3$)



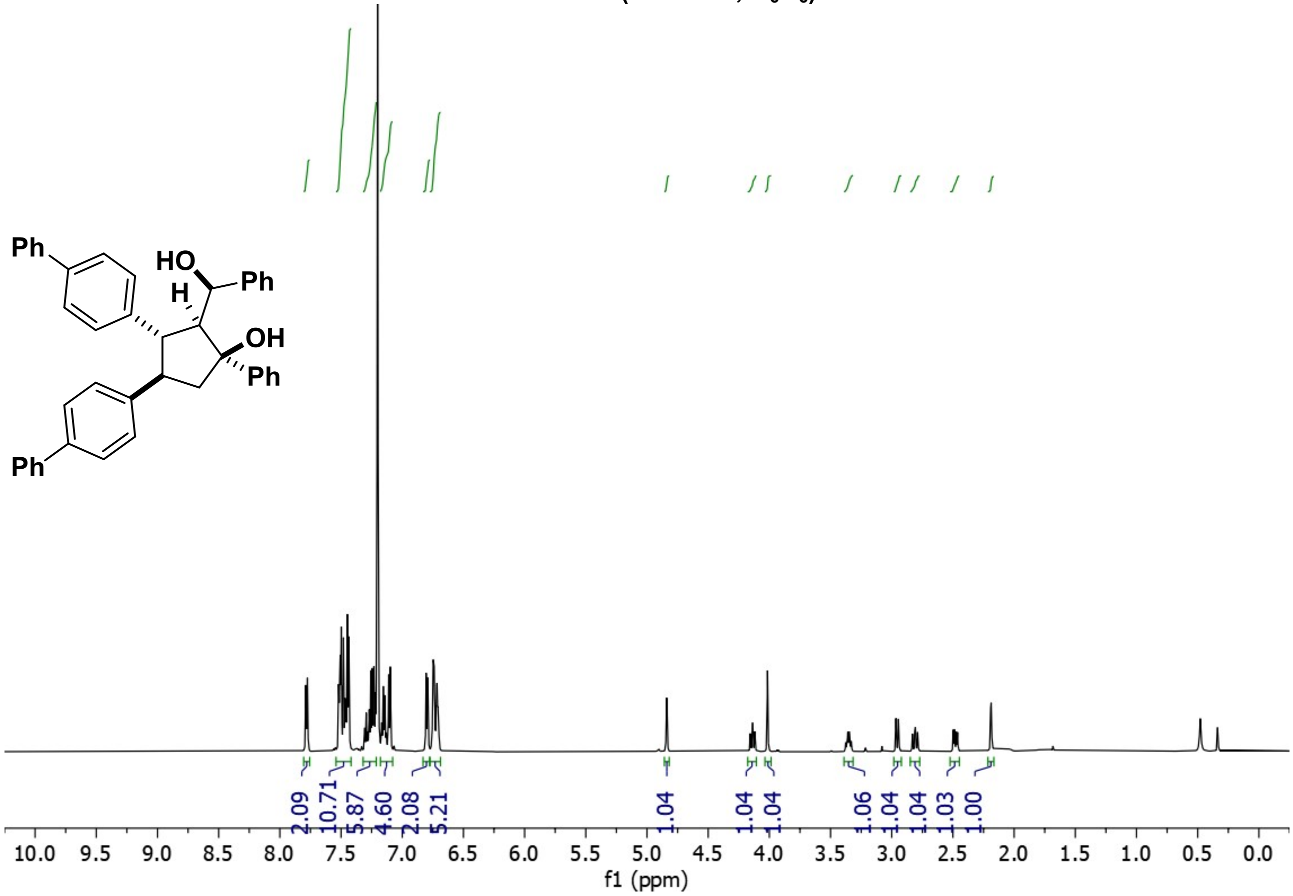
3c ^{1}H NMR (400 MHz, CDCl$_3$)



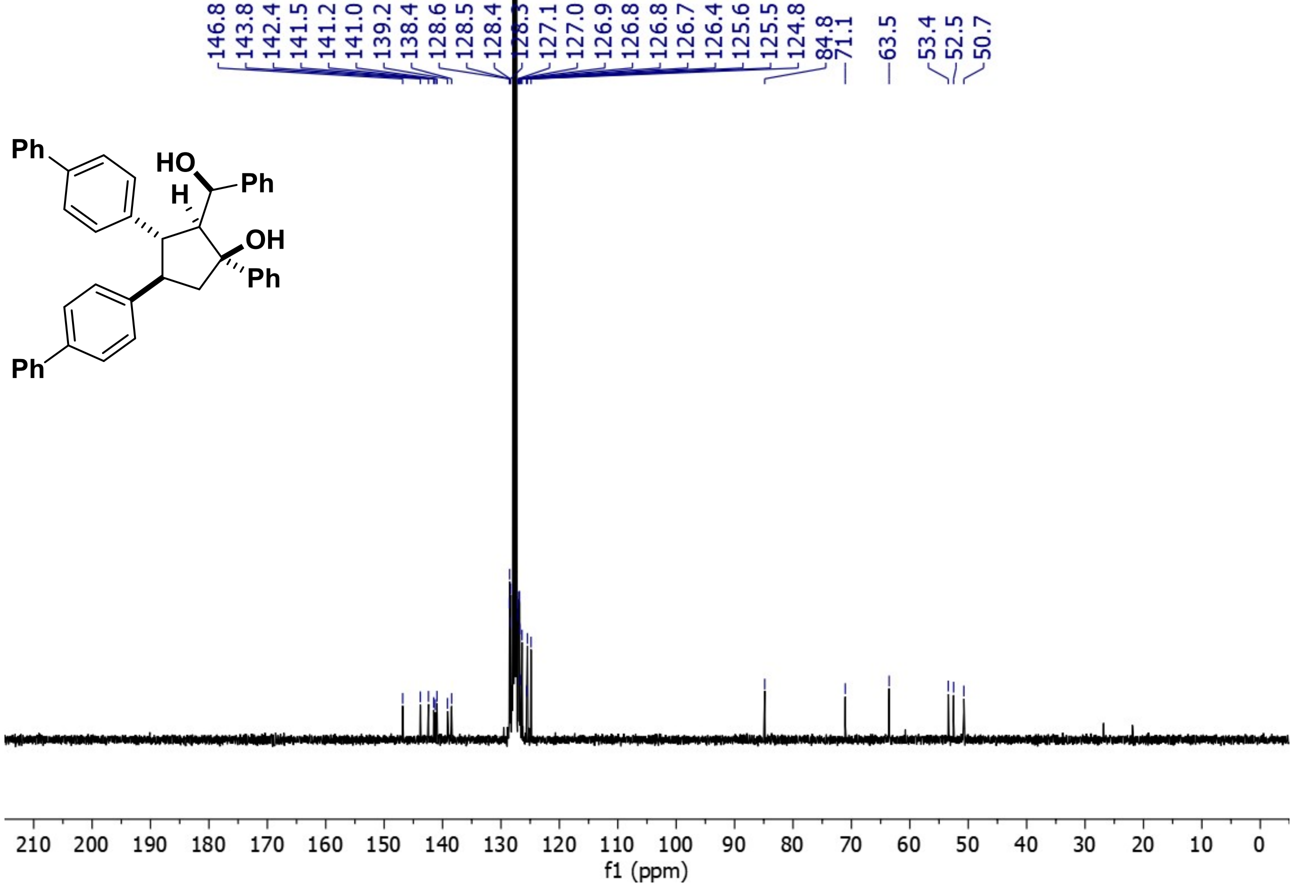
3c ^{13}C NMR (100 MHz, CDCl$_3$)



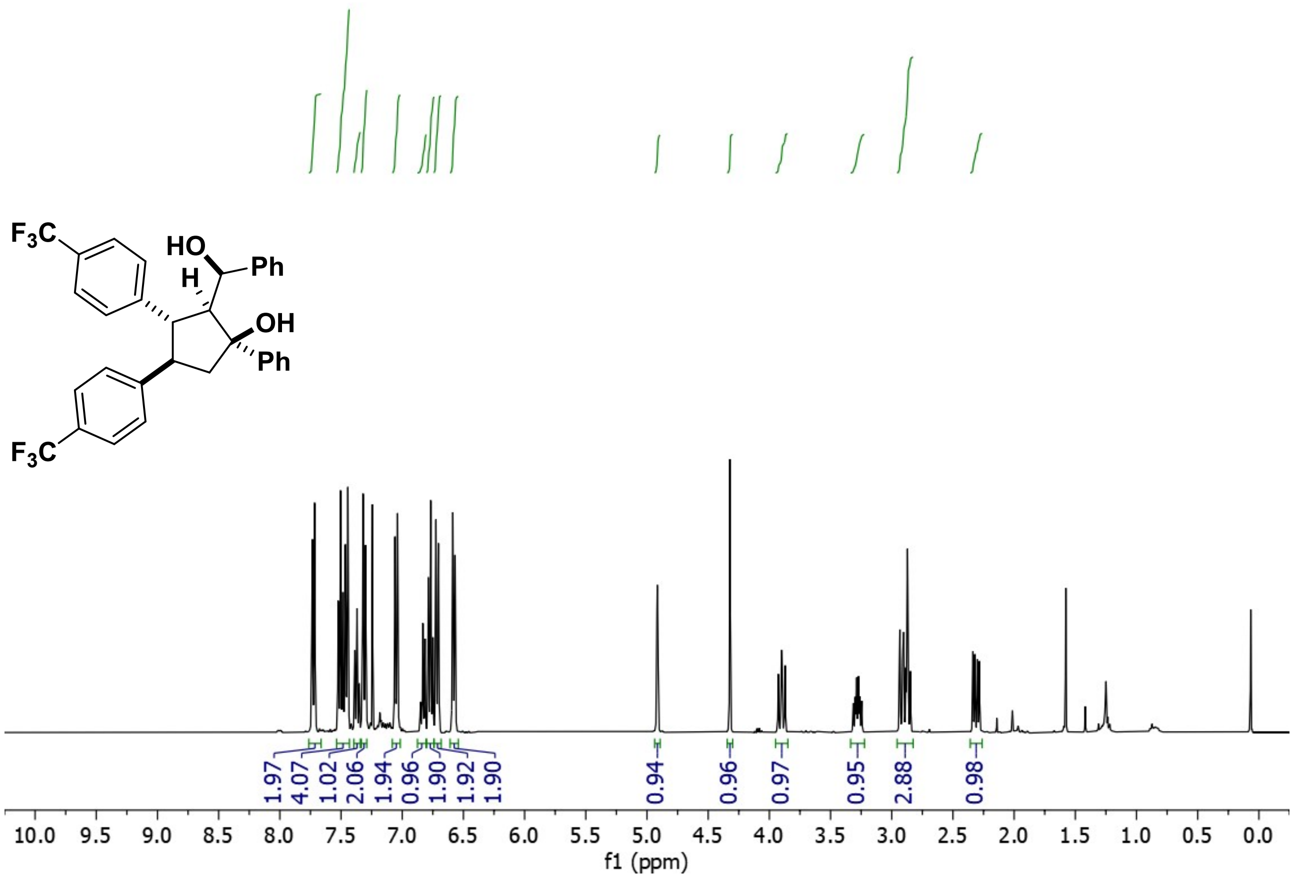
3d ^{1}H NMR (600 MHz, C_6D_6)



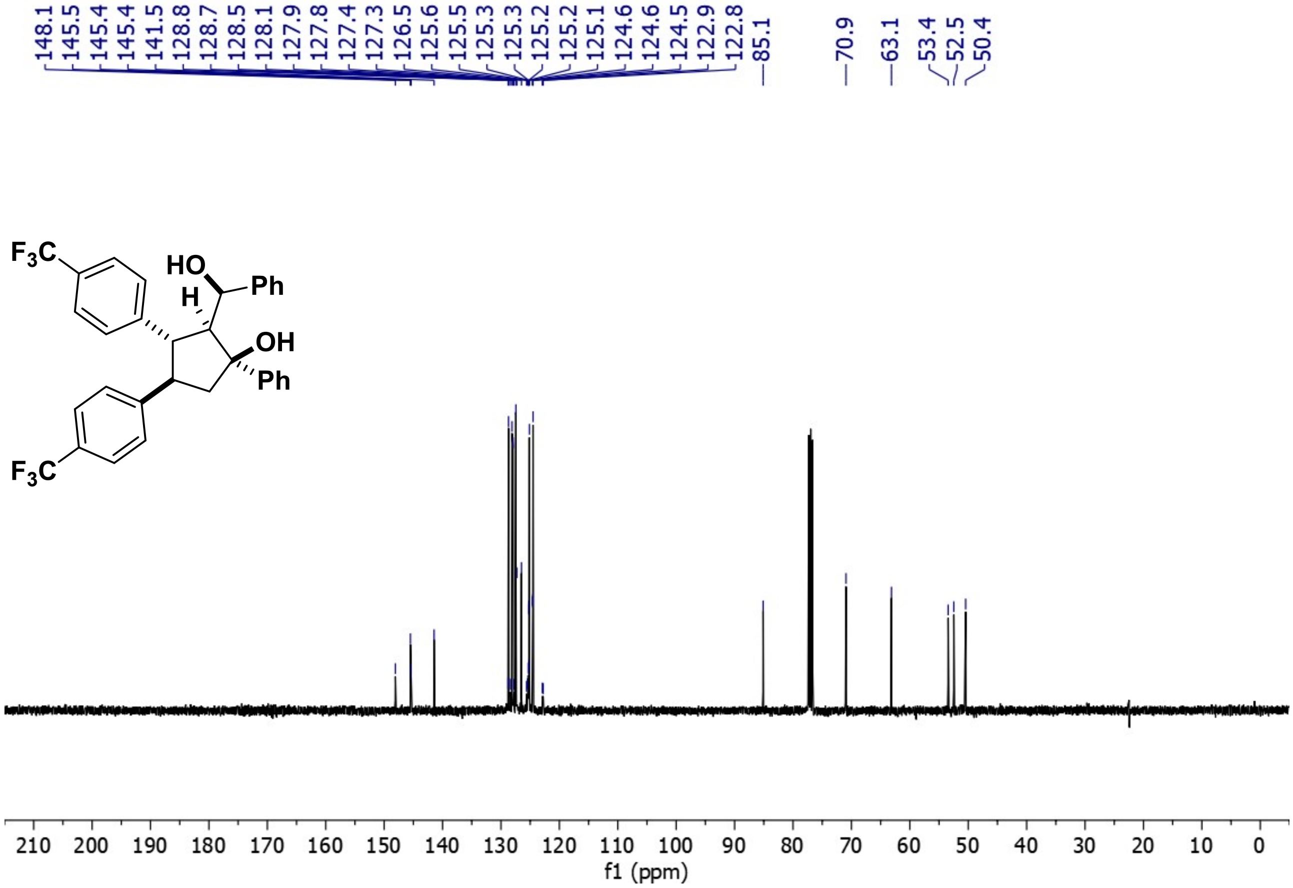
3d ^{13}C NMR (100 MHz, C_6D_6)



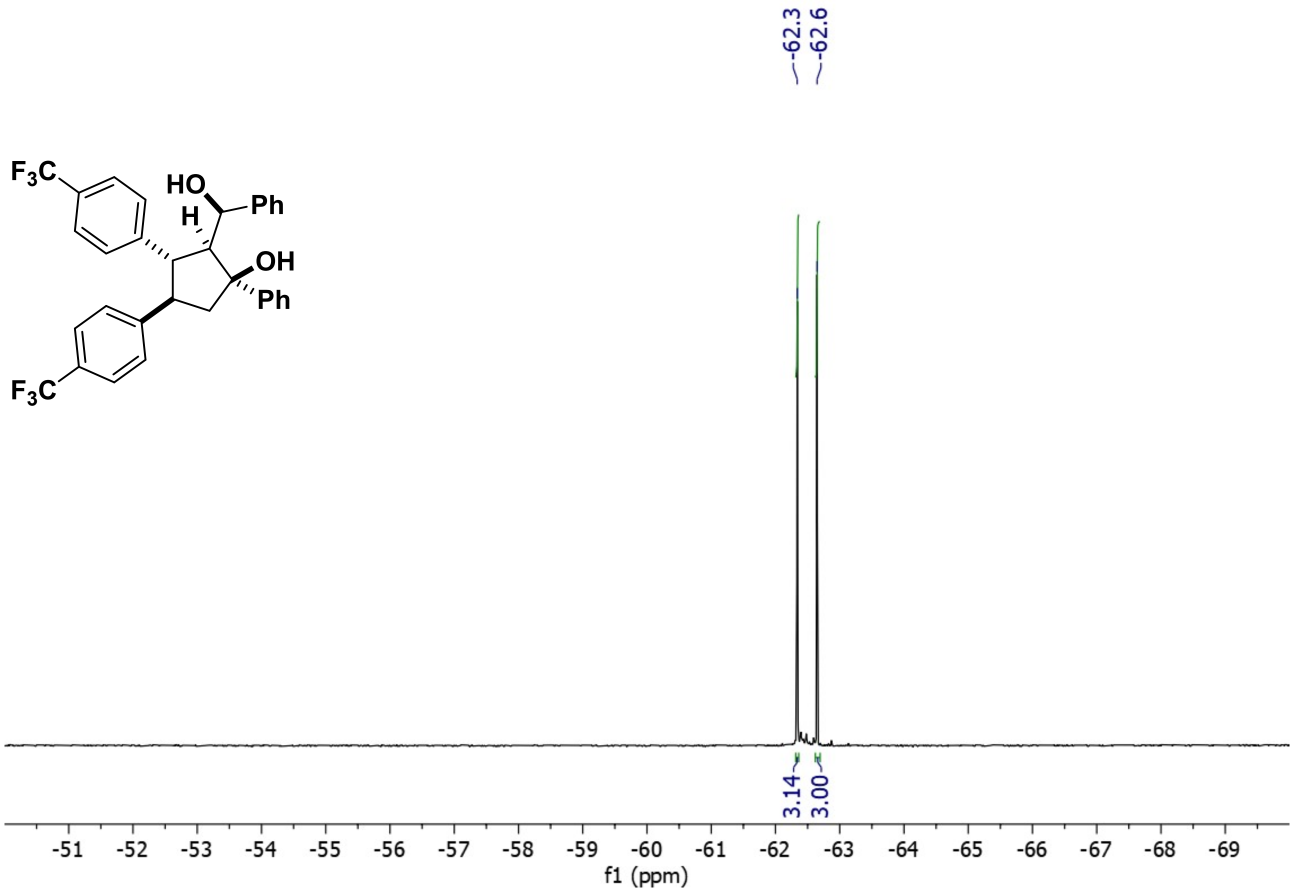
3e ^{1}H NMR (400 MHz, $CDCl_3$)



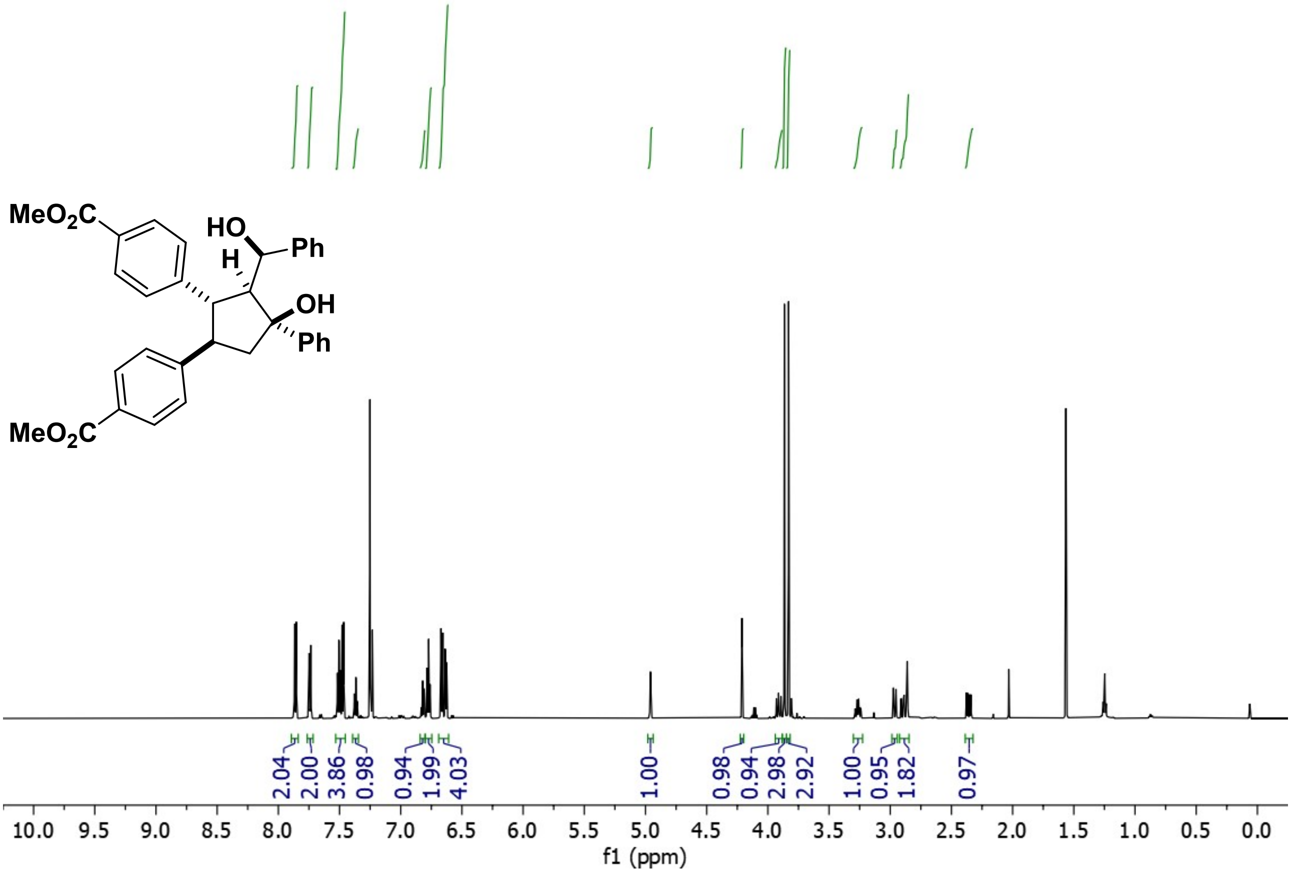
3e ^{13}C NMR (100 MHz, $CDCl_3$)



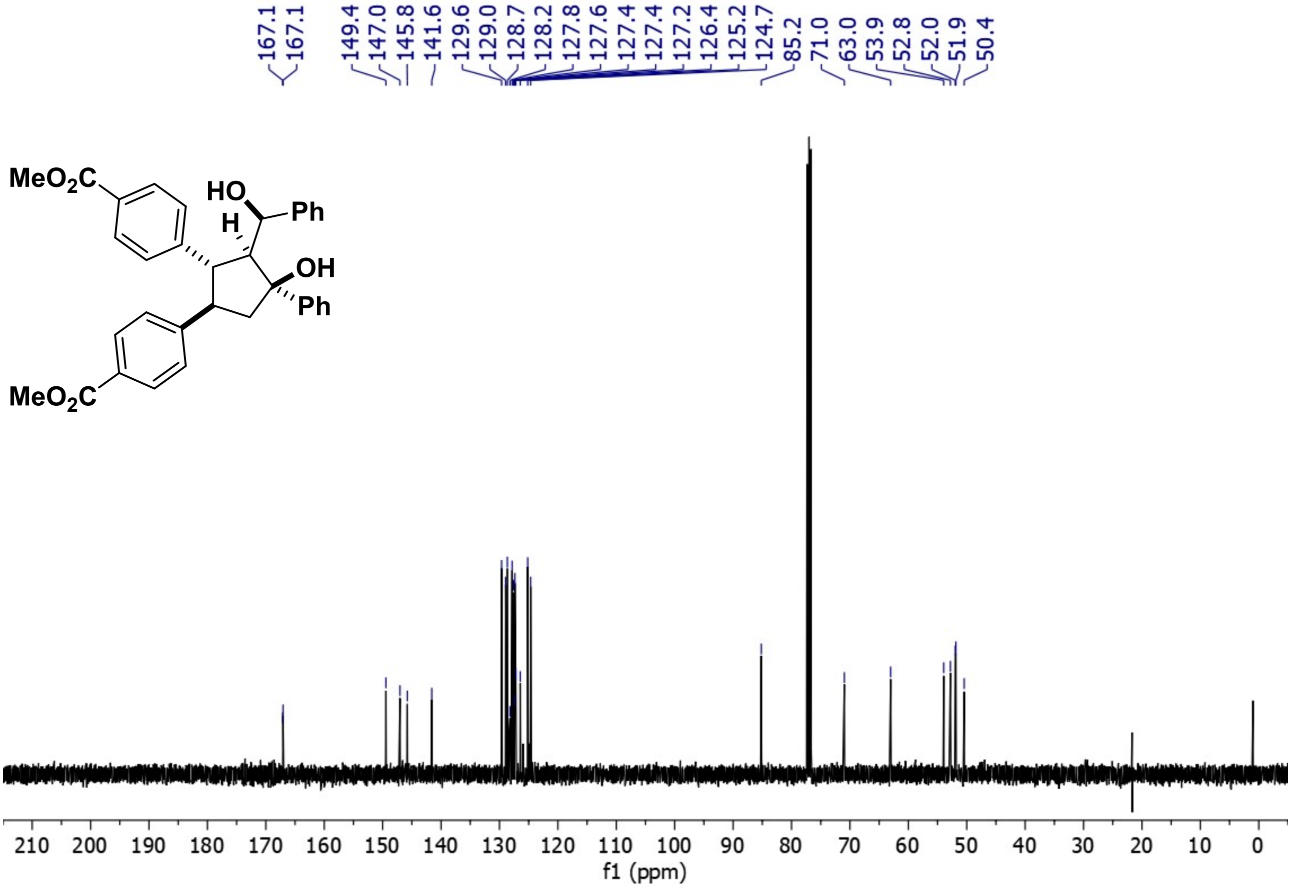
3e ^{19}F NMR (376 MHz, CDCl$_3$)



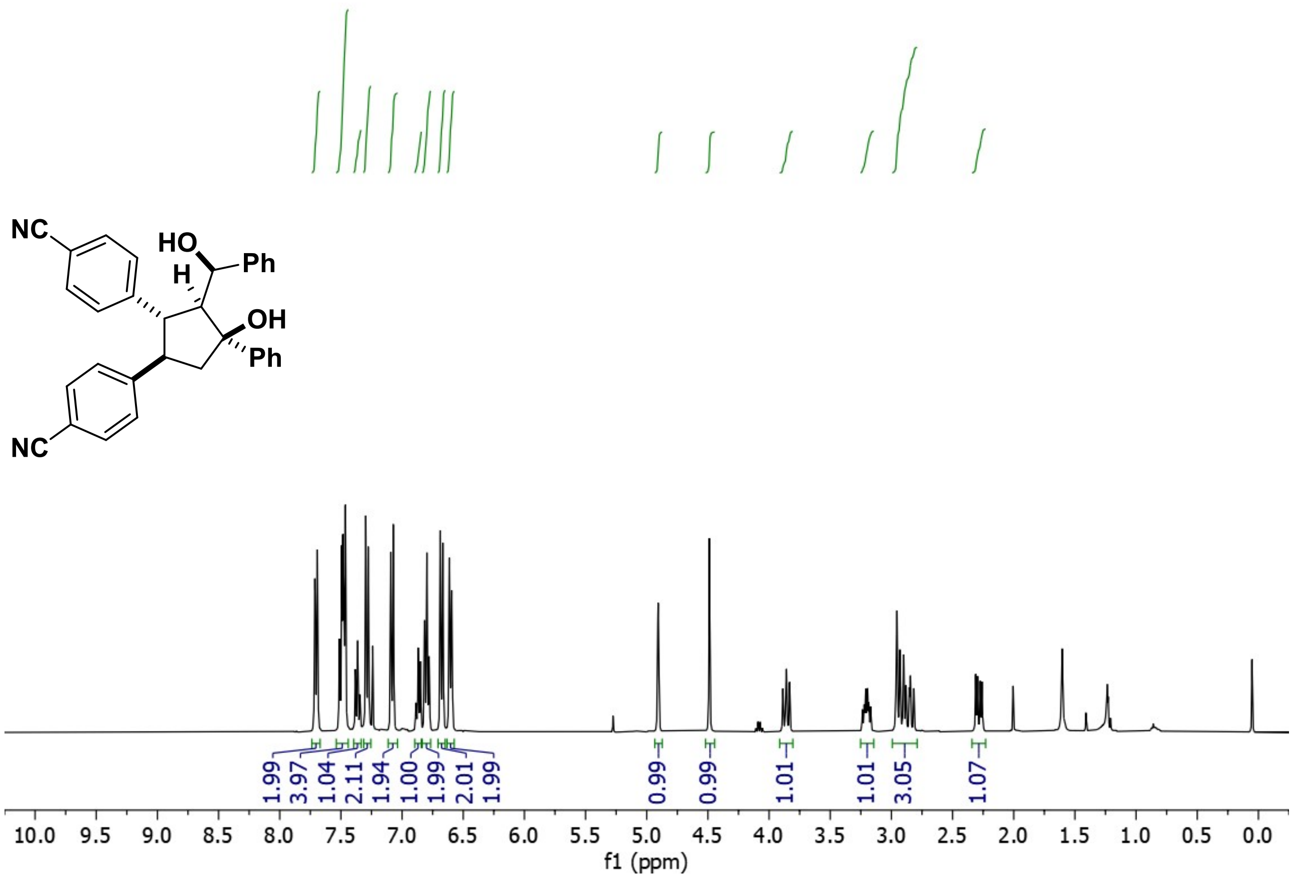
3f ^{1}H NMR (600 MHz, CDCl$_3$)



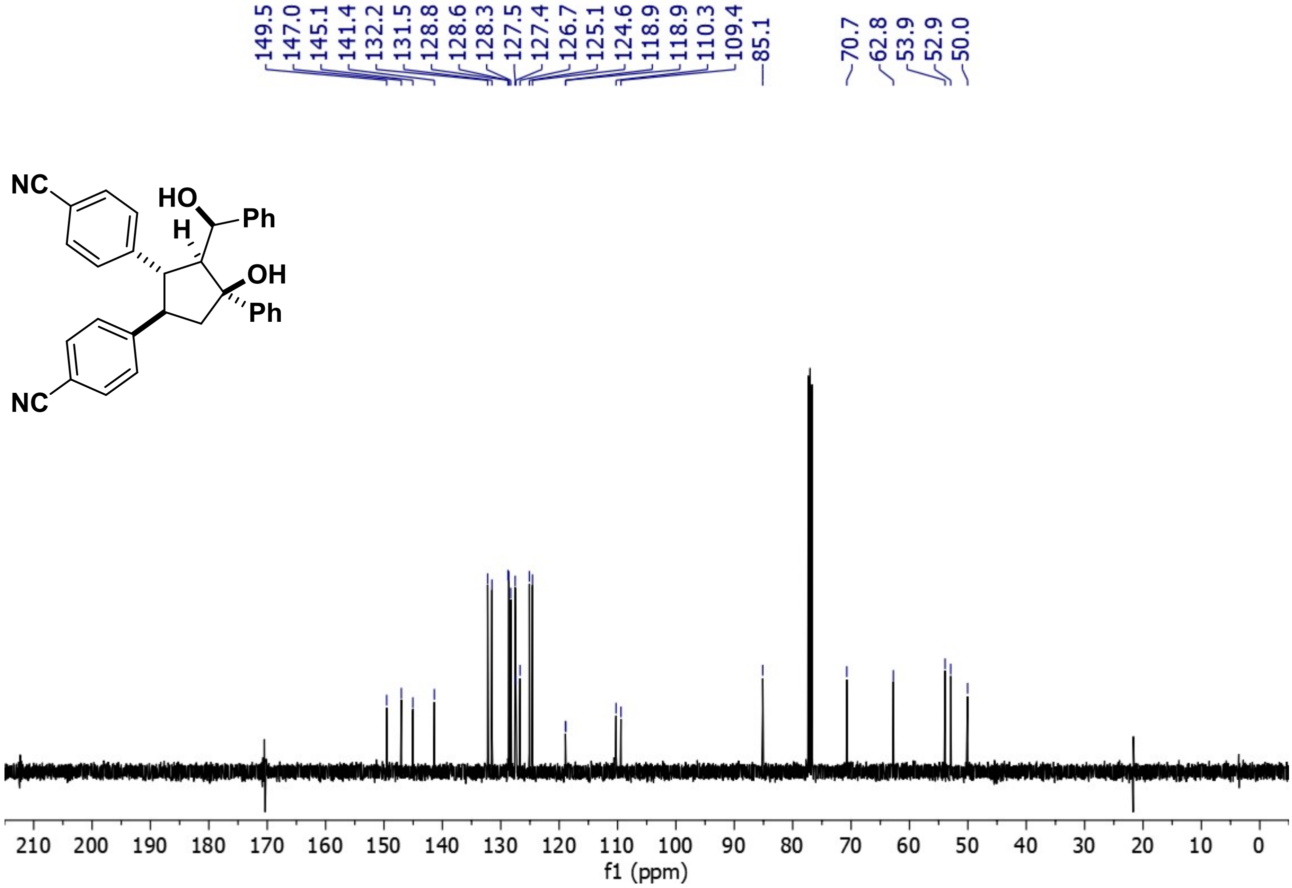
3f ^{13}C NMR (100 MHz, CDCl$_3$)



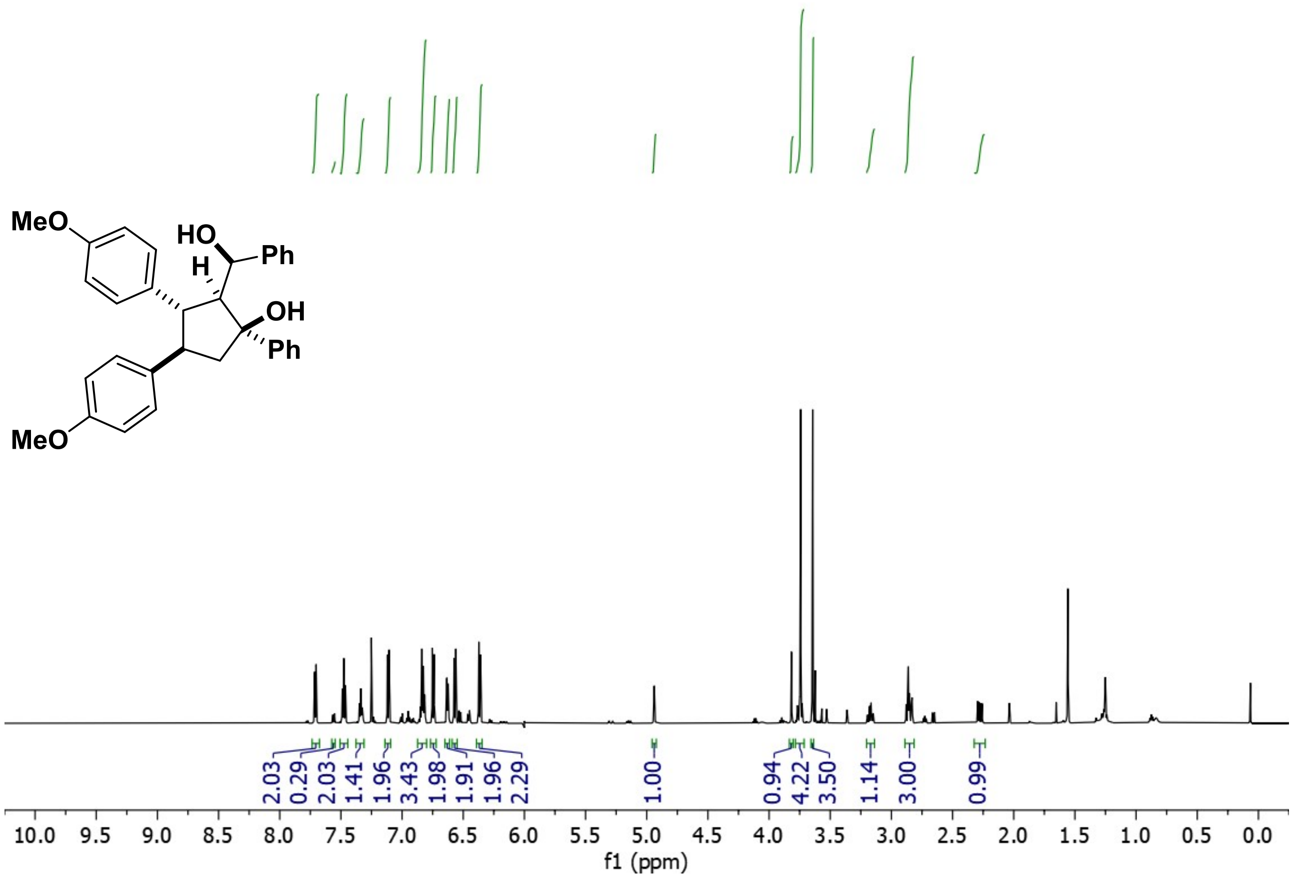
3g ^{1}H NMR (400 MHz, $CDCl_3$)



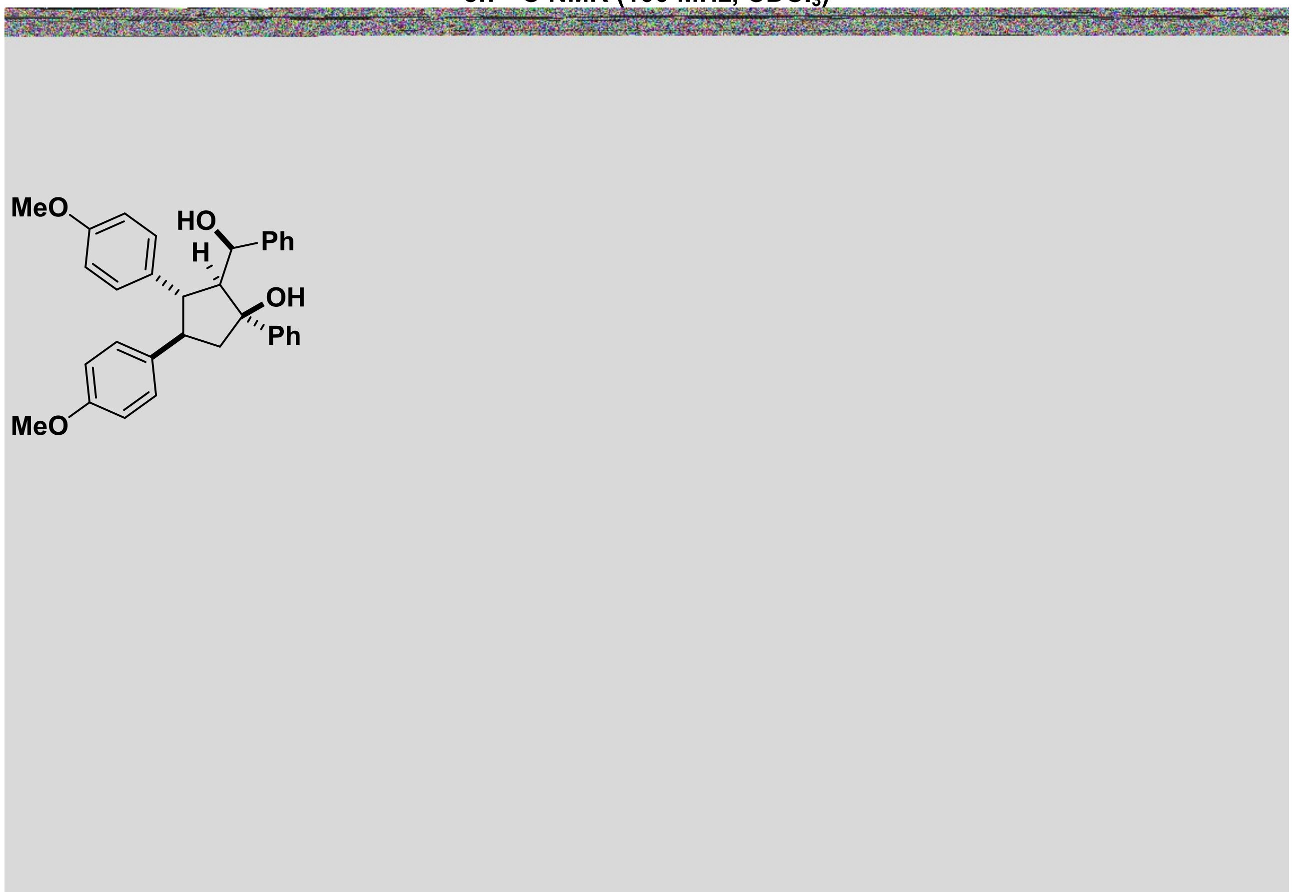
3g ^{13}C NMR (100 MHz, $CDCl_3$)



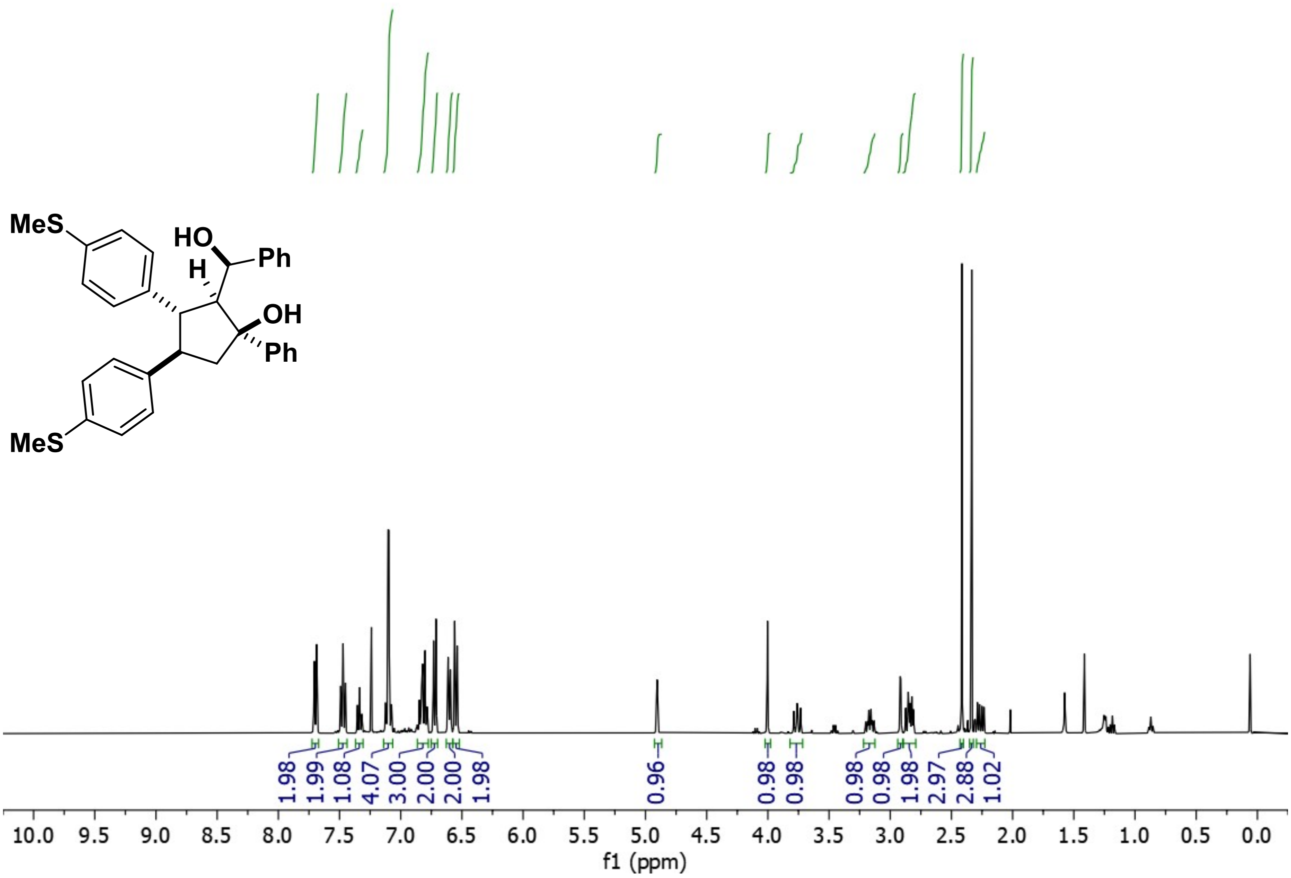
3h ^{1}H NMR (600 MHz, $CDCl_3$)



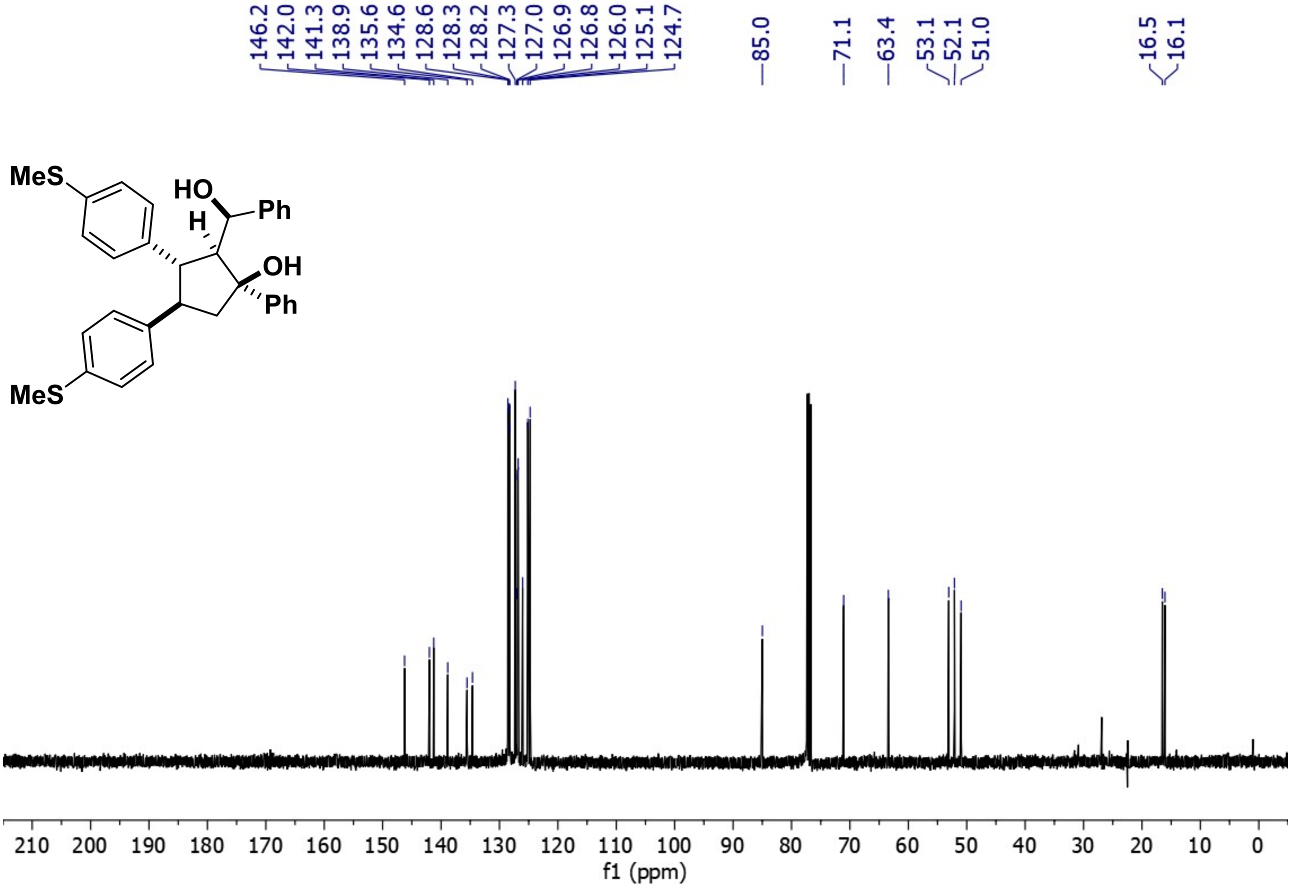
3h ^{13}C NMR (100 MHz, $CDCl_3$)



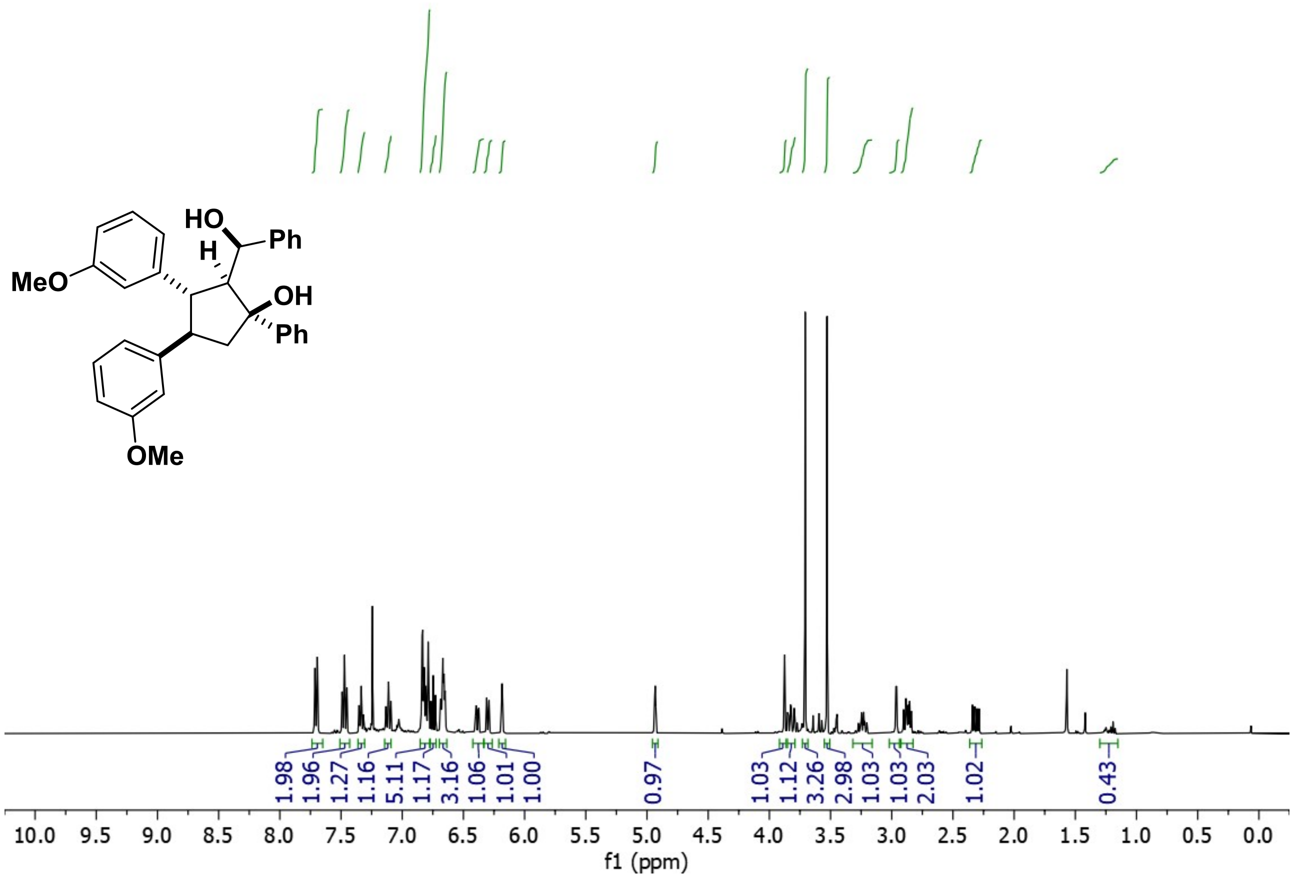
3i ^{1}H NMR (400 MHz, $CDCl_3$)



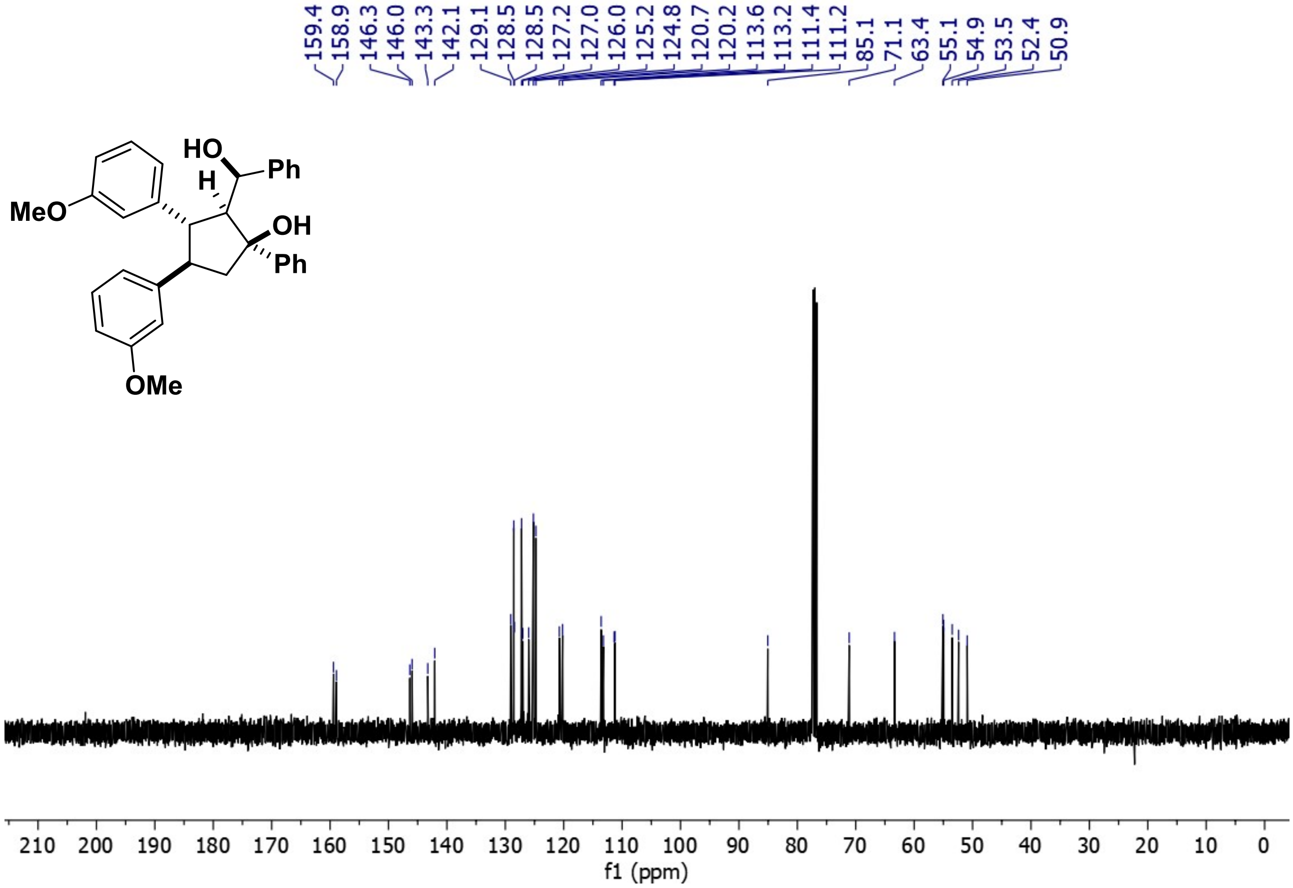
3i ^{13}C NMR (100 MHz, $CDCl_3$)



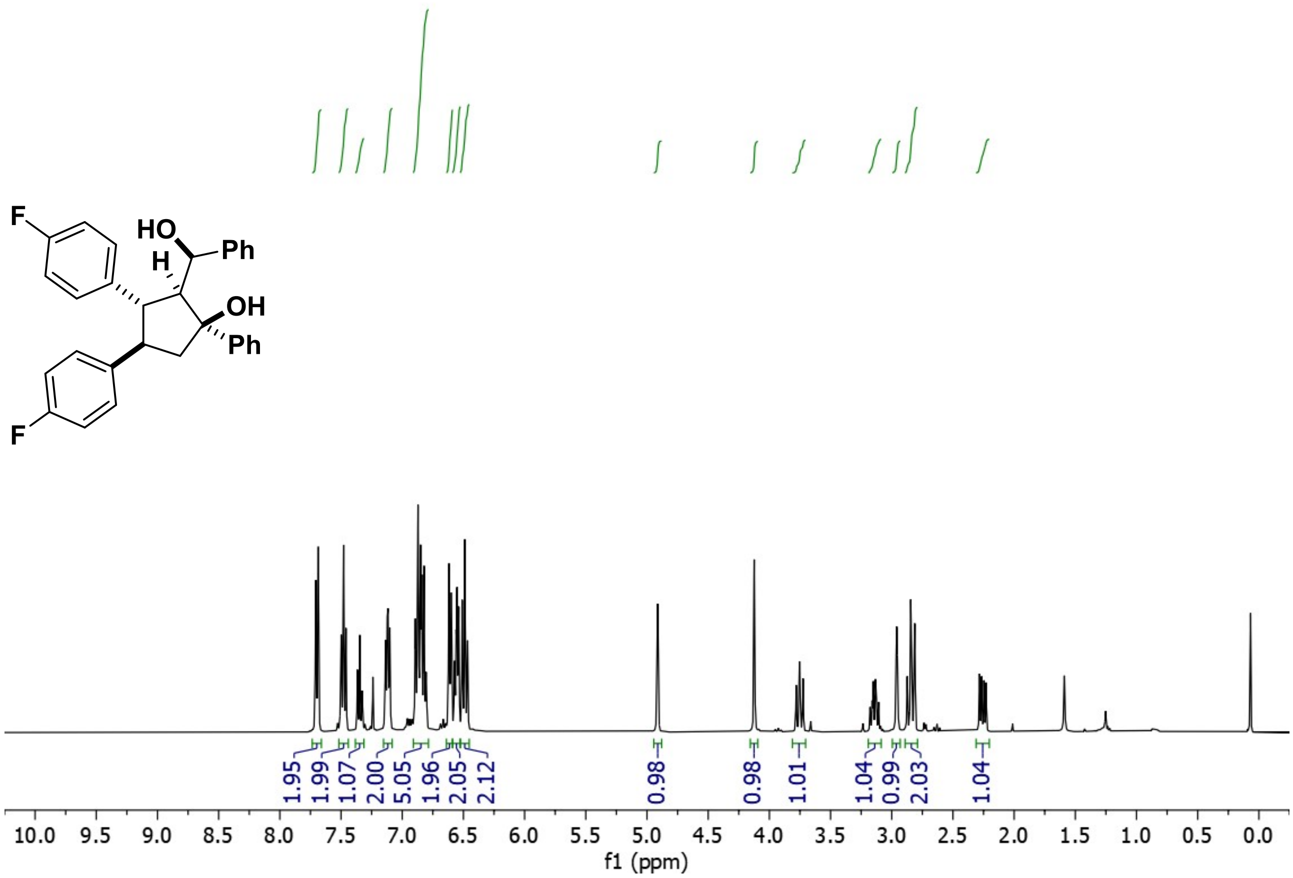
3j ^{1}H NMR (400 MHz, $CDCl_3$)



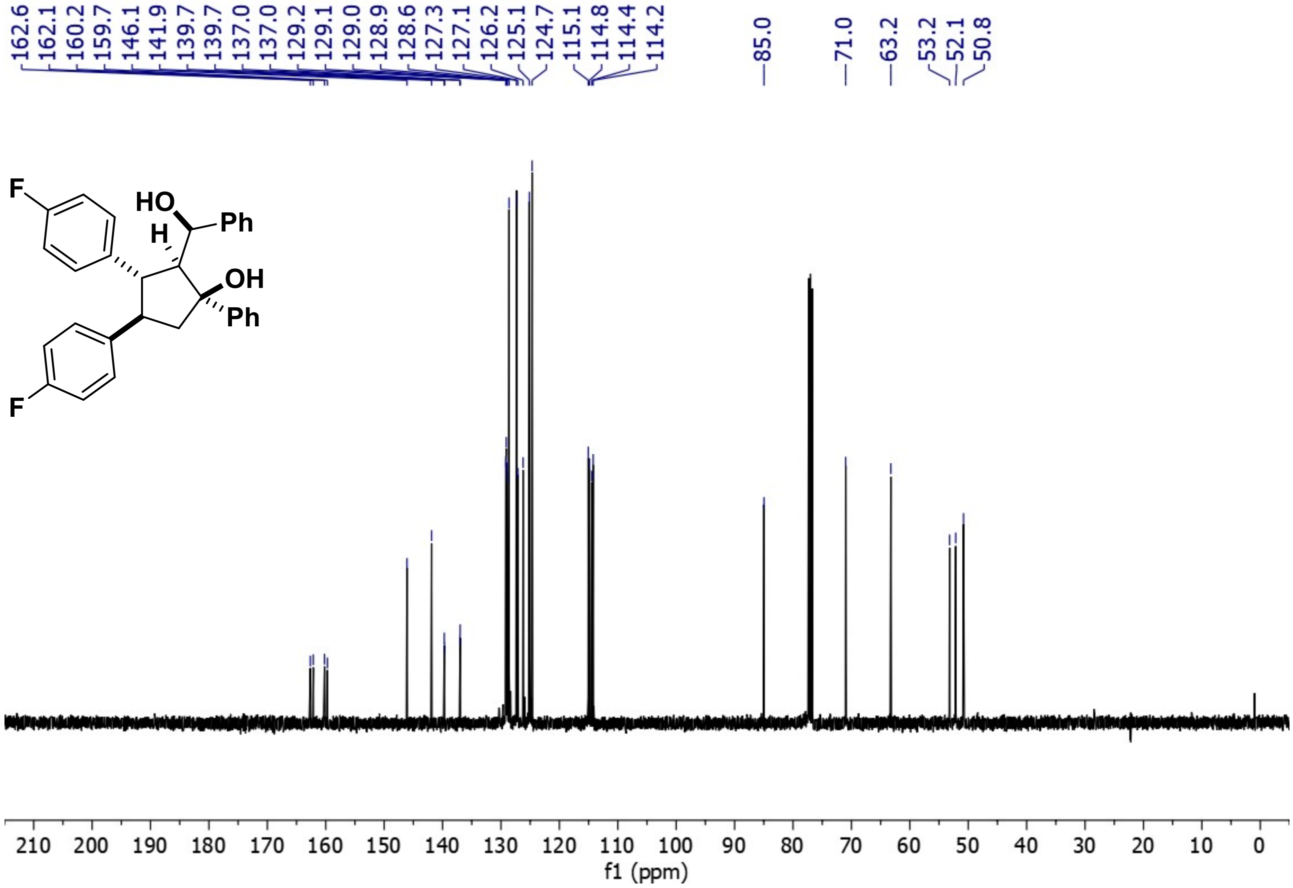
3j ^{13}C NMR (100 MHz, $CDCl_3$)



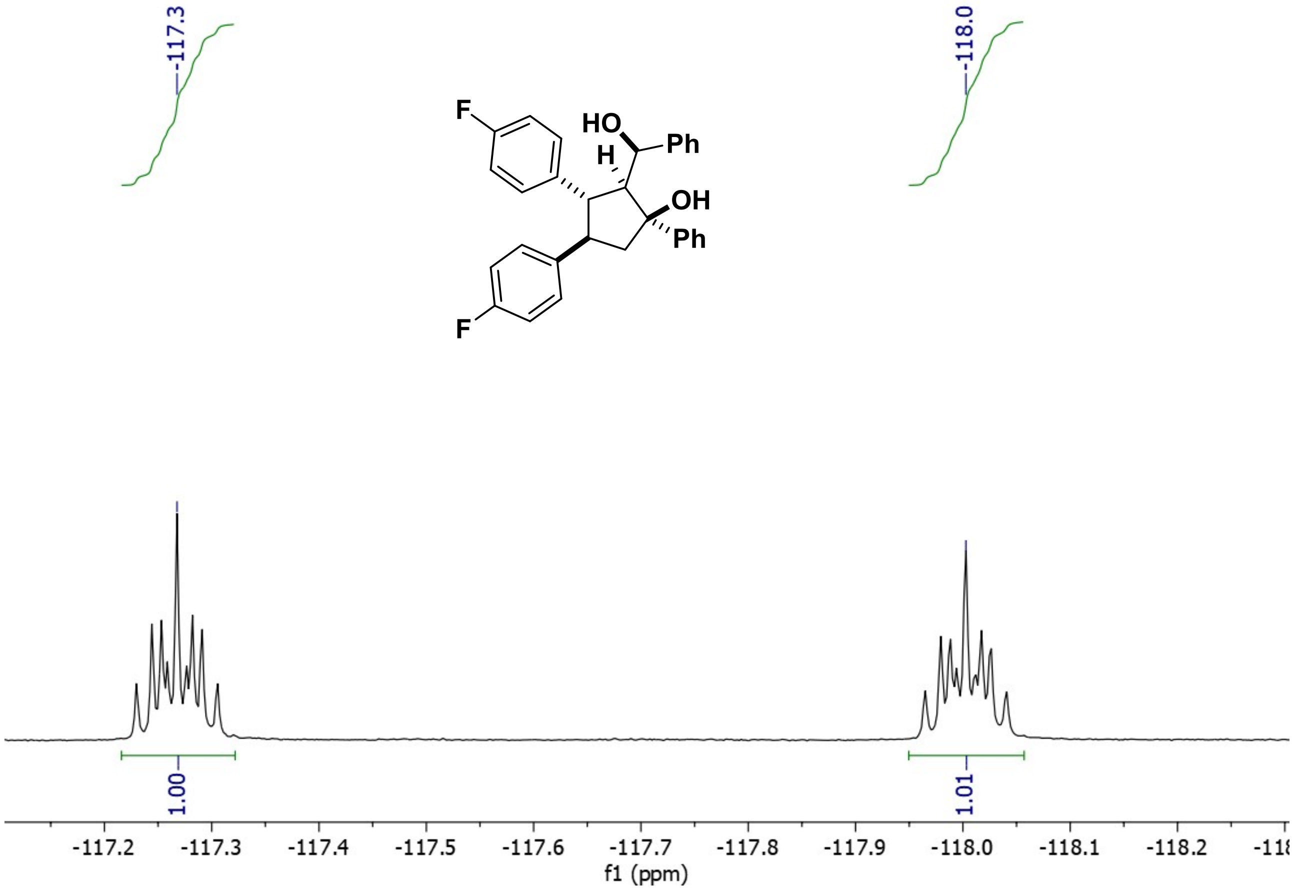
3k ^{1}H NMR (400 MHz, CDCl$_3$)



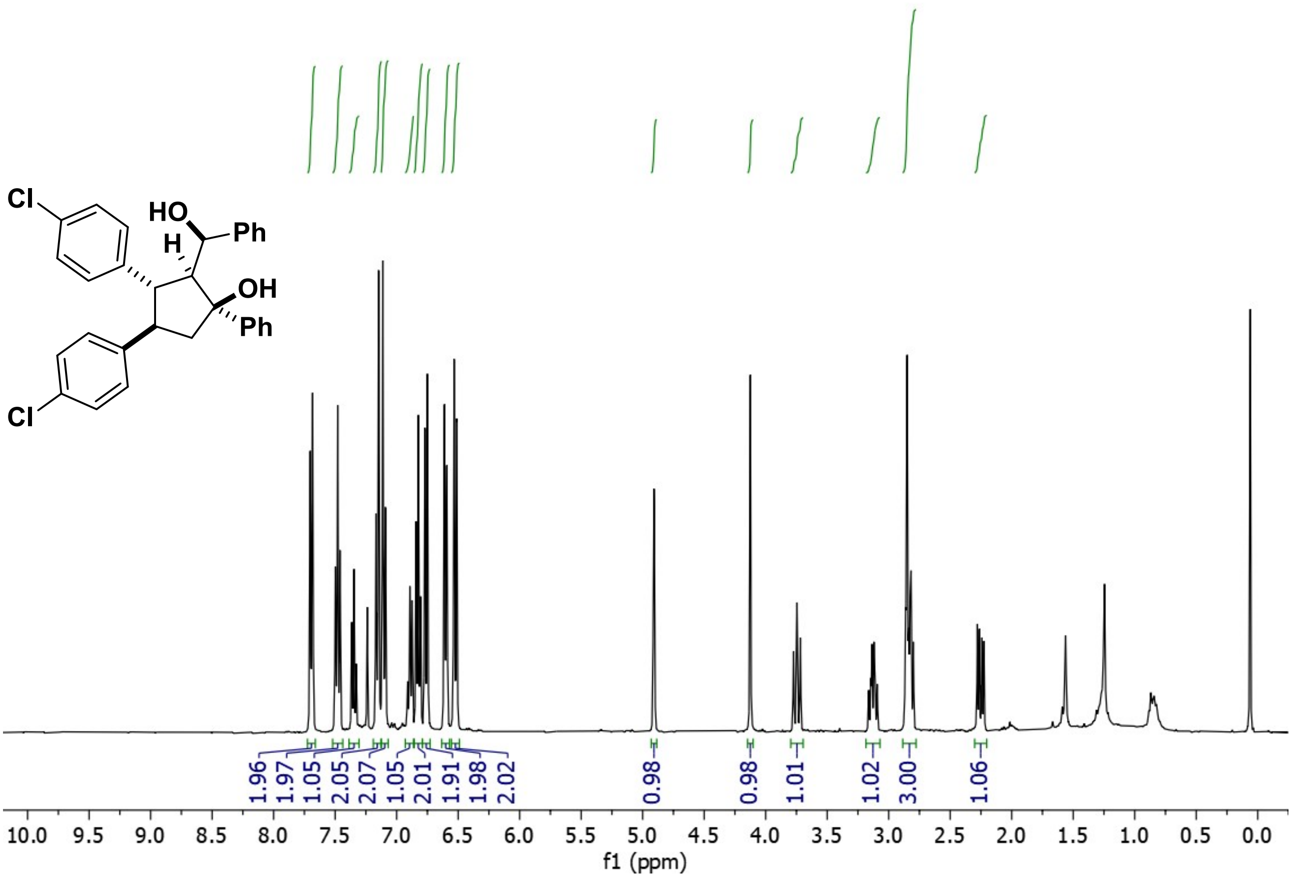
3k ^{13}C NMR (100 MHz, CDCl$_3$)



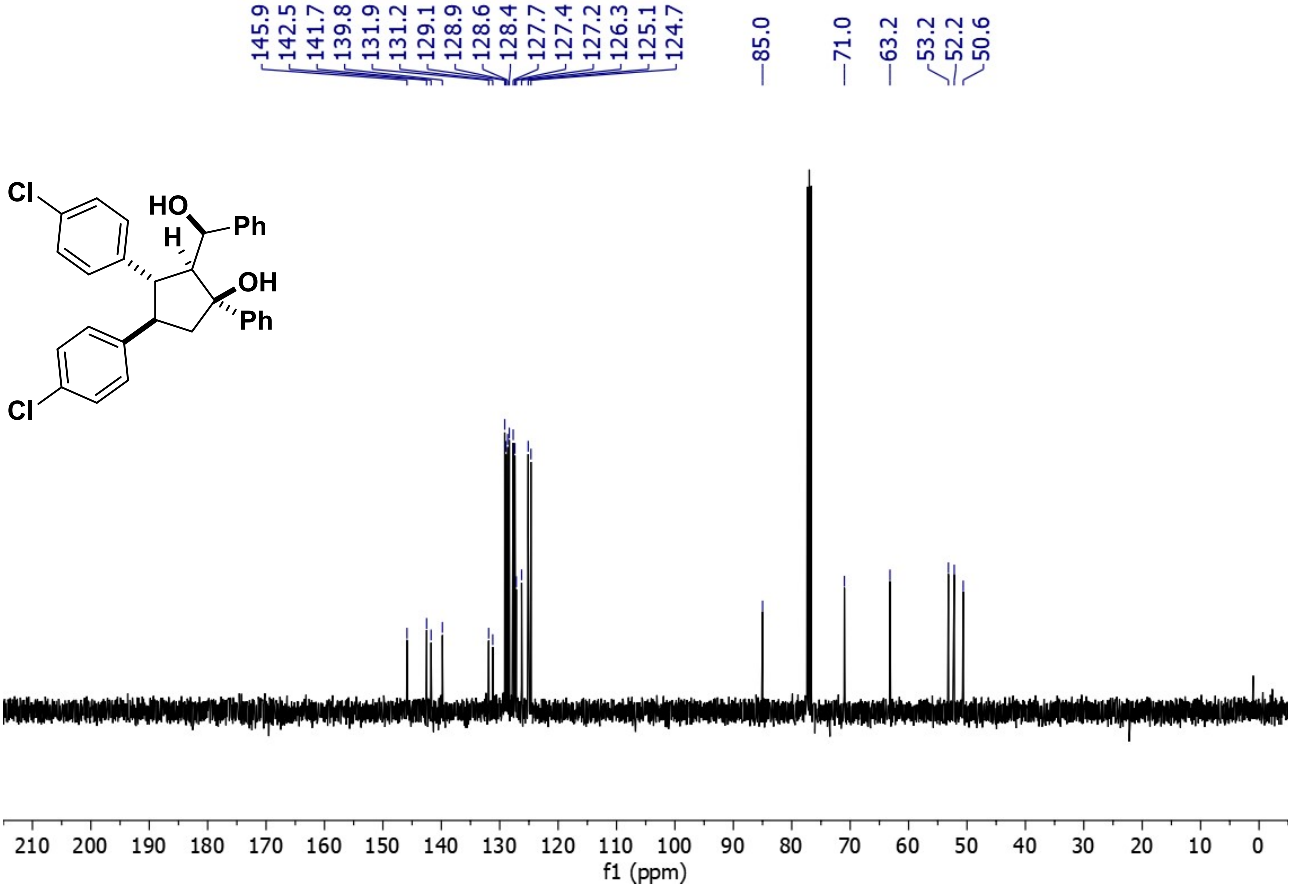
3k ^{19}F NMR (376 MHz, CDCl$_3$)



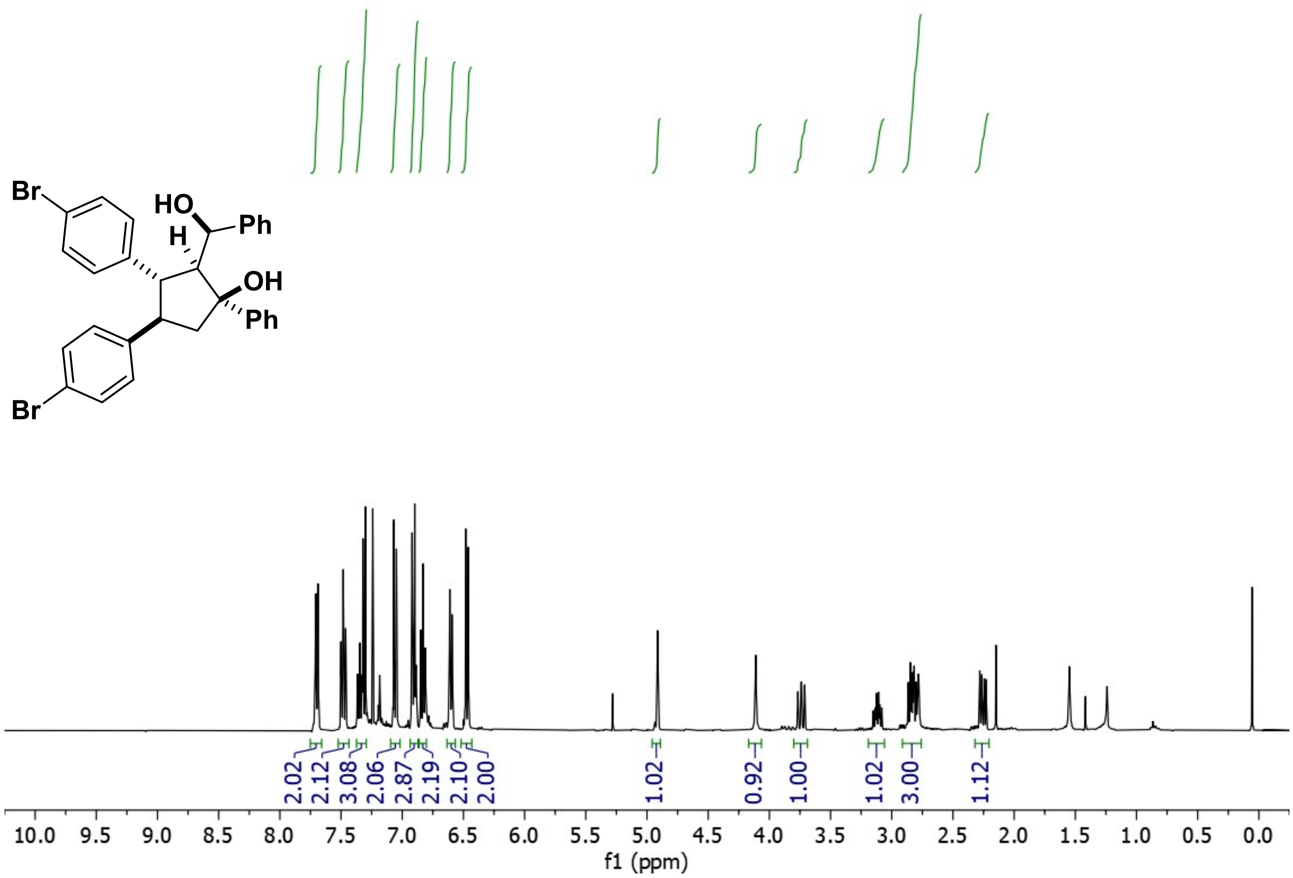
3l ^{1}H NMR (400 MHz, CDCl$_3$)



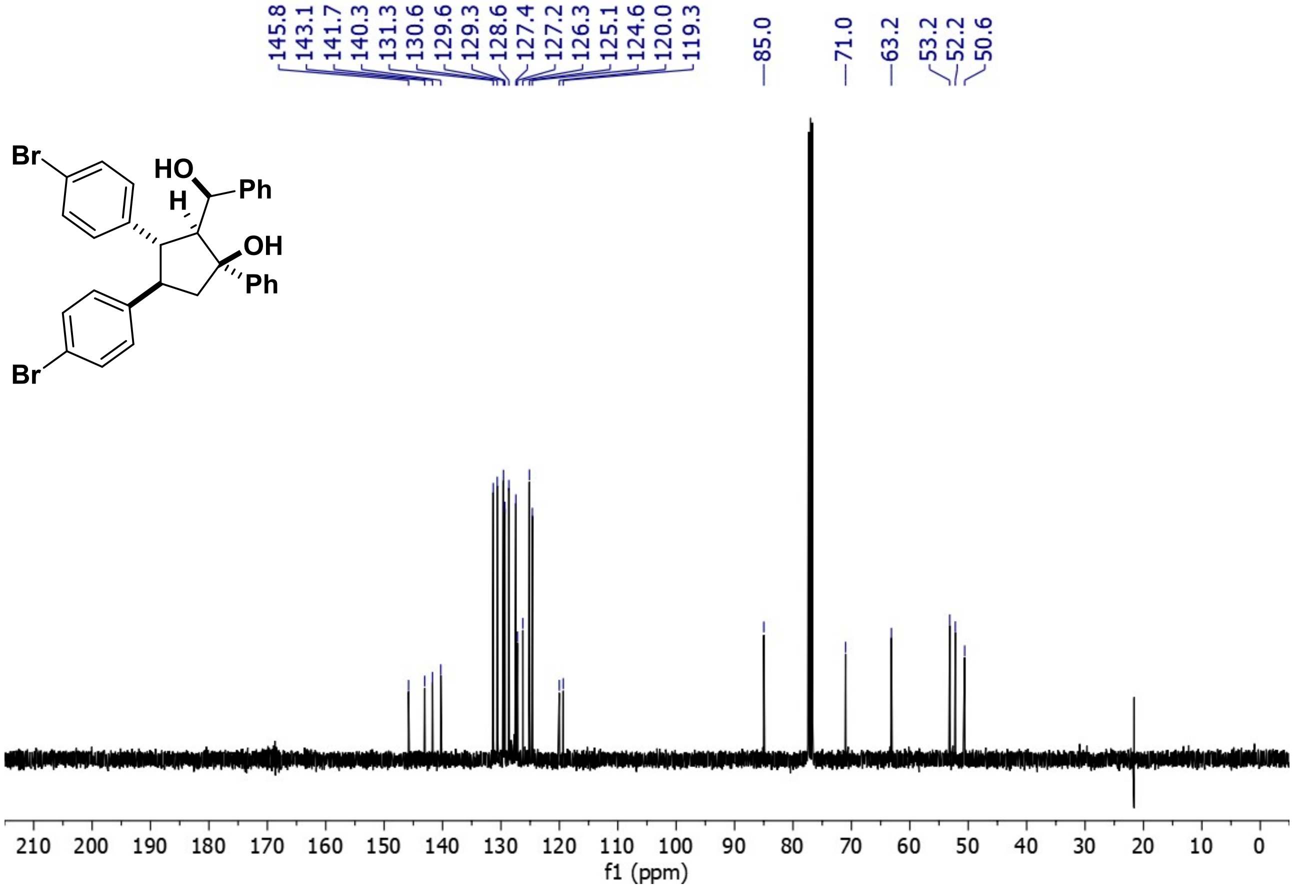
3l ^{13}C NMR (100 MHz, CDCl$_3$)



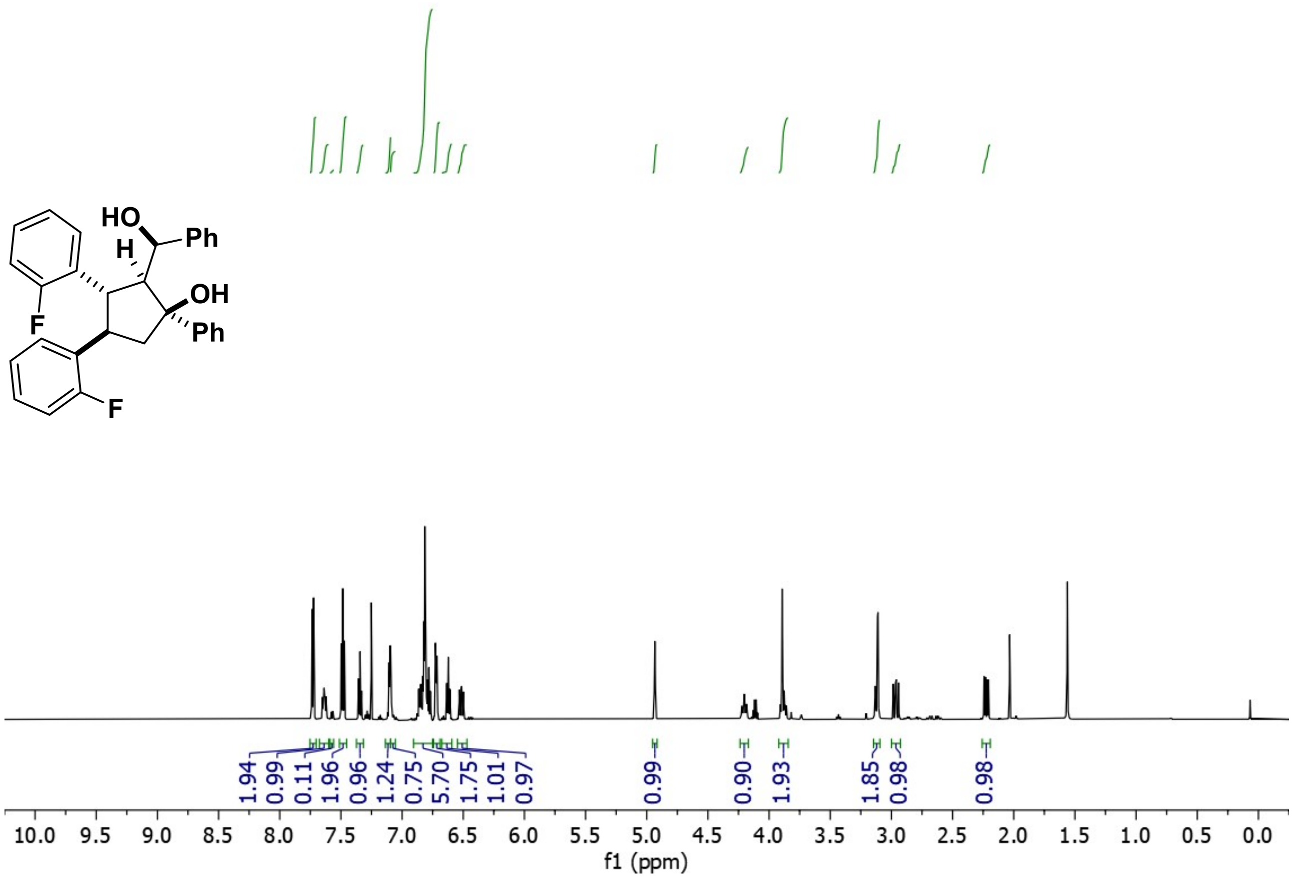
3m ^{1}H NMR (400 MHz, $CDCl_3$)



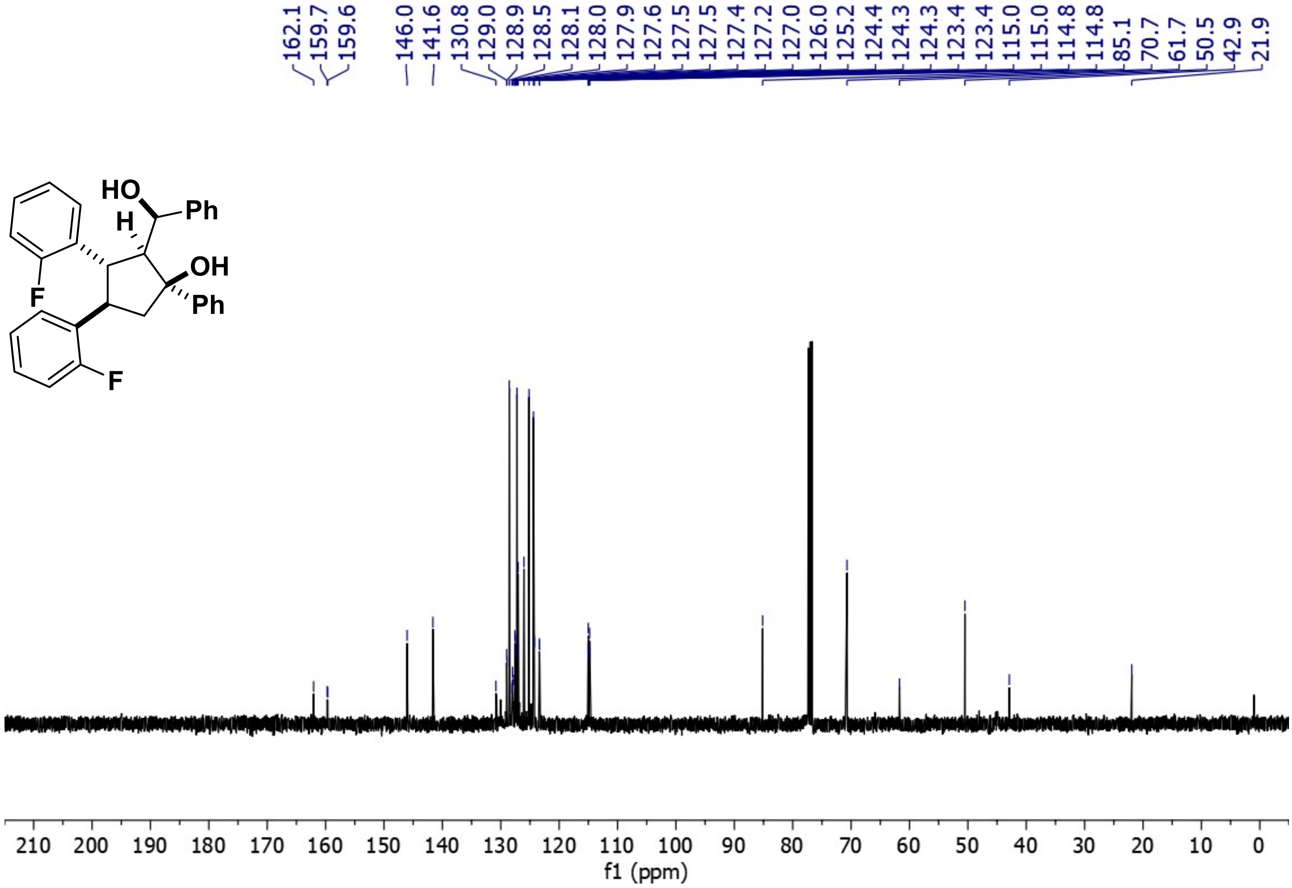
3m ^{13}C NMR (100 MHz, $CDCl_3$)



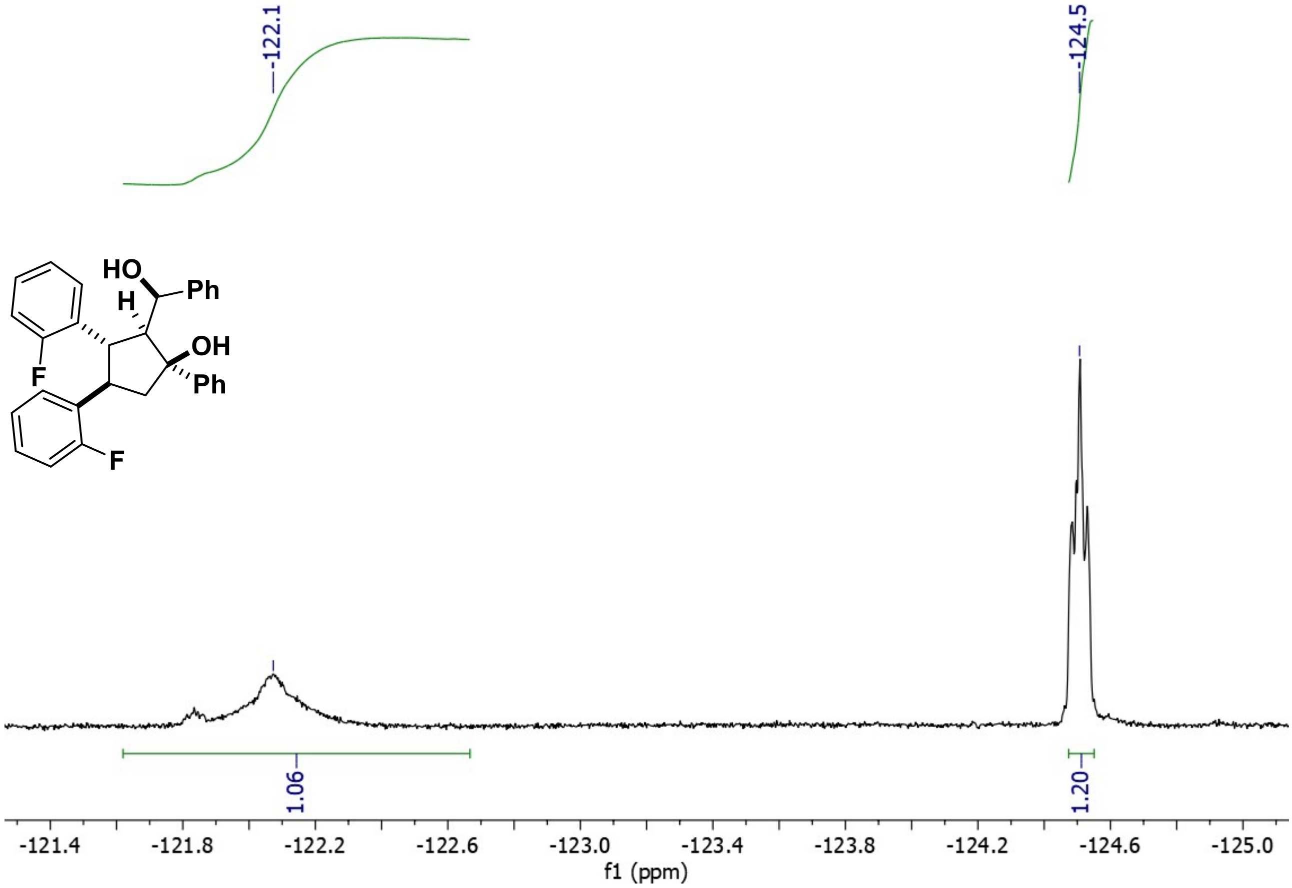
3n ^{1}H NMR (600 MHz, CDCl$_3$)



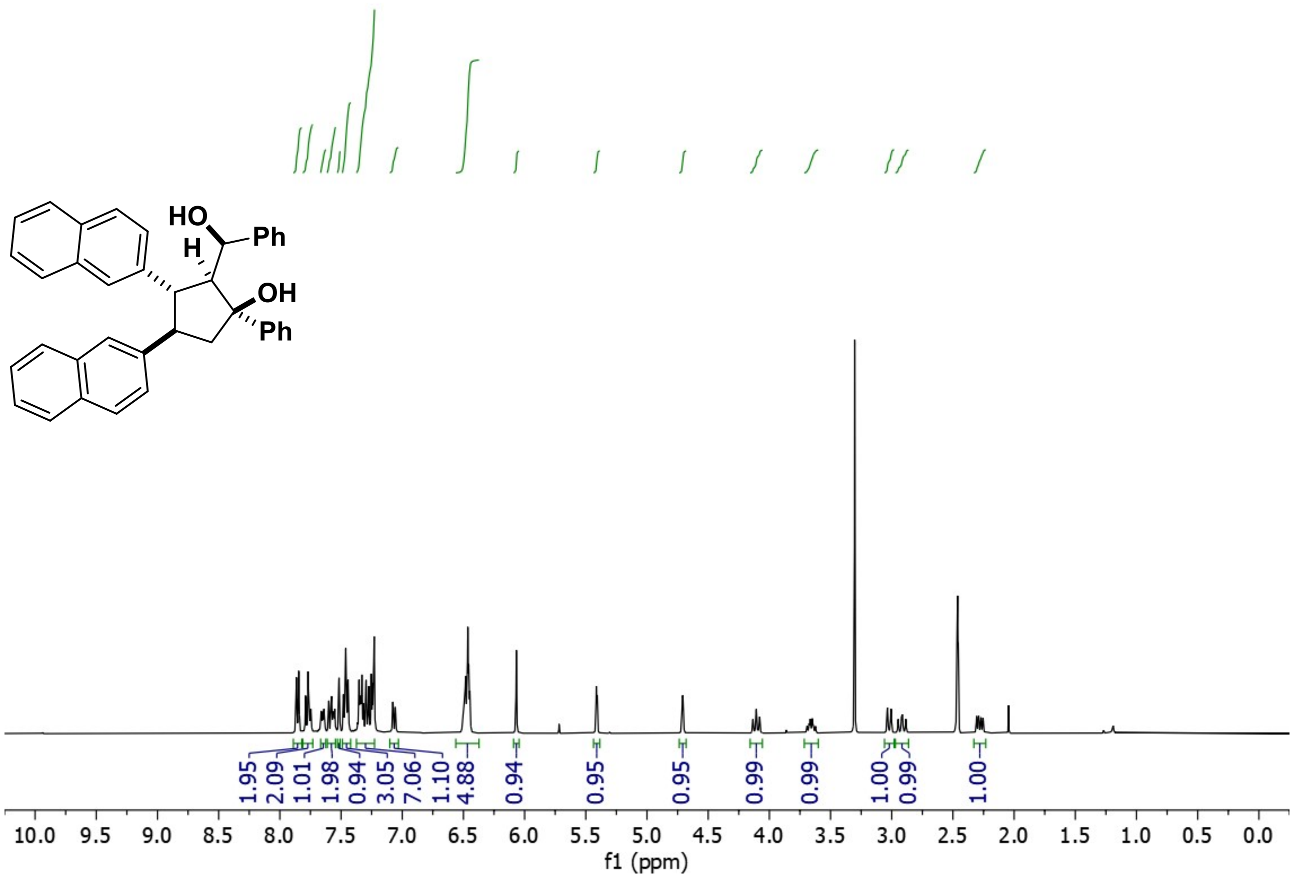
3n ^{13}C NMR (100 MHz, CDCl$_3$)



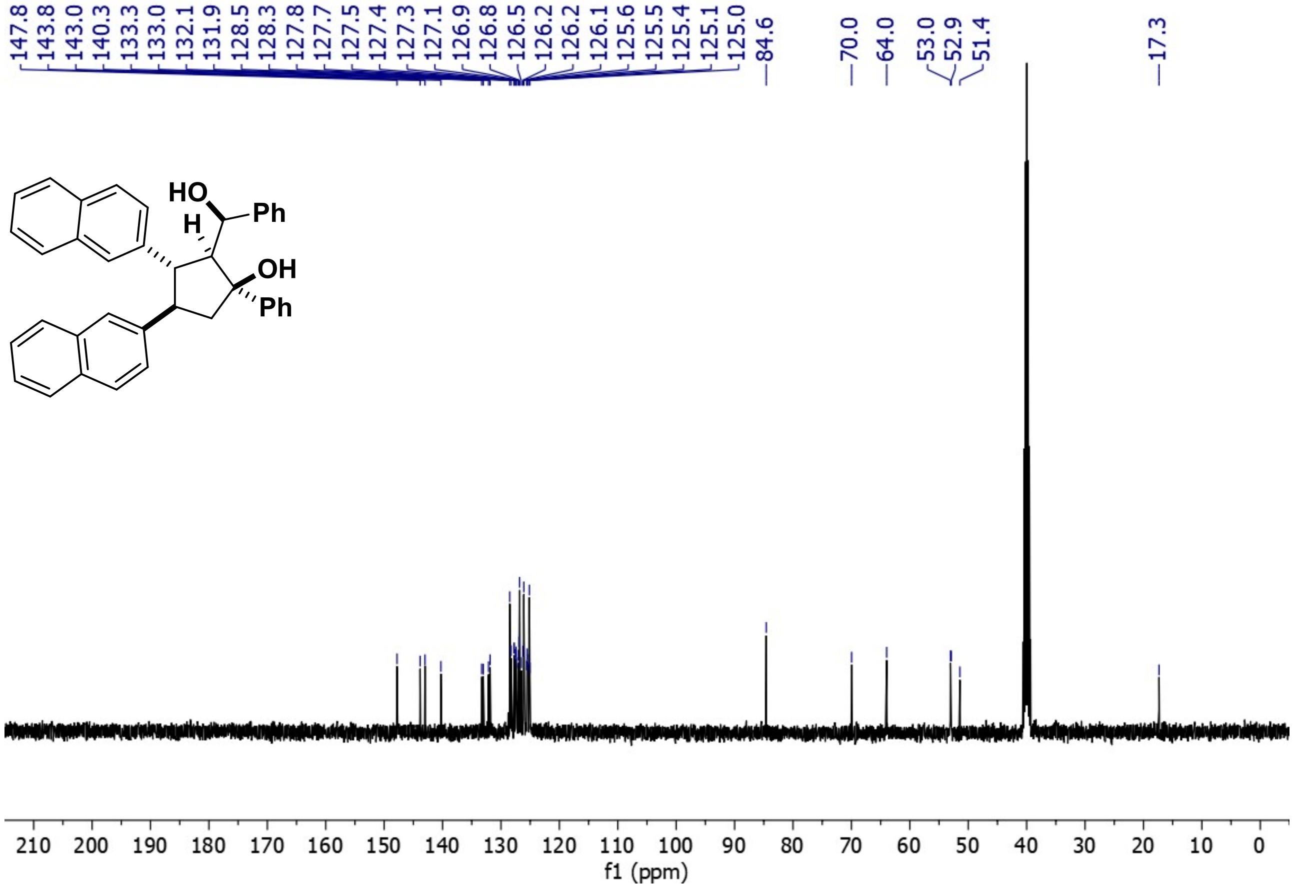
3n ^{19}F NMR (376 MHz, CDCl$_3$)



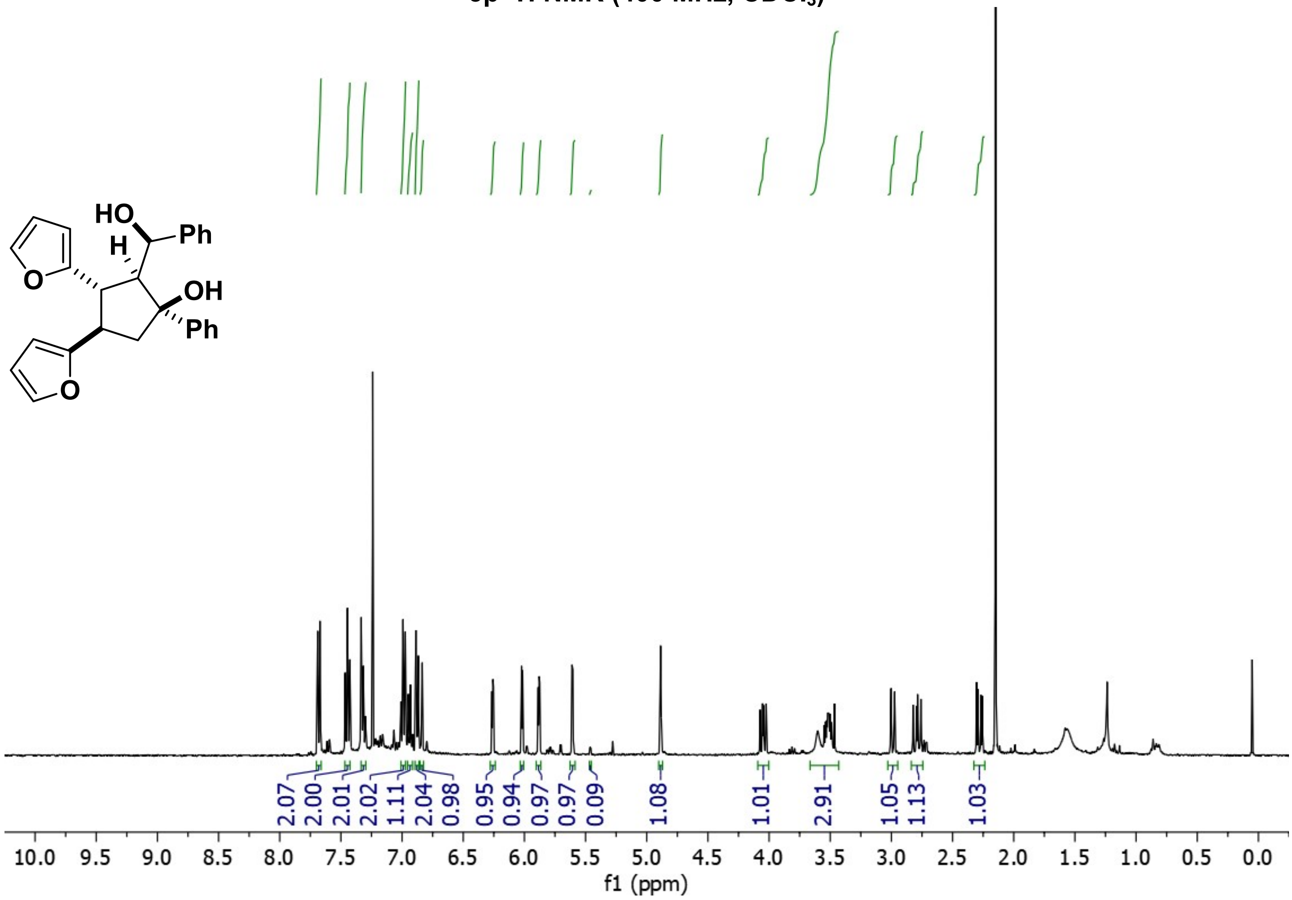
3o ^{1}H NMR (400 MHz, DMSO-d_6)



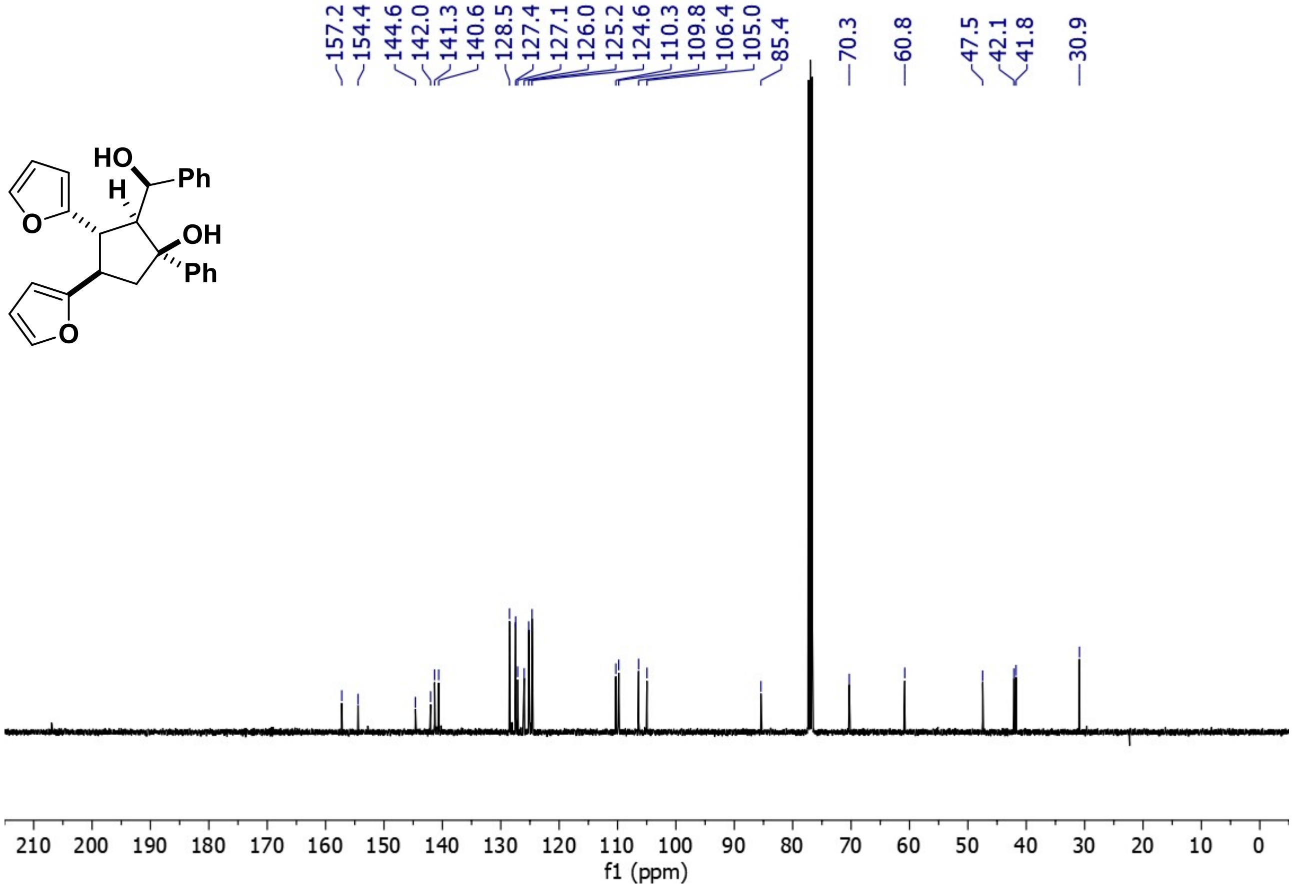
3o ^{13}C NMR (100 MHz, DMSO-d_6)



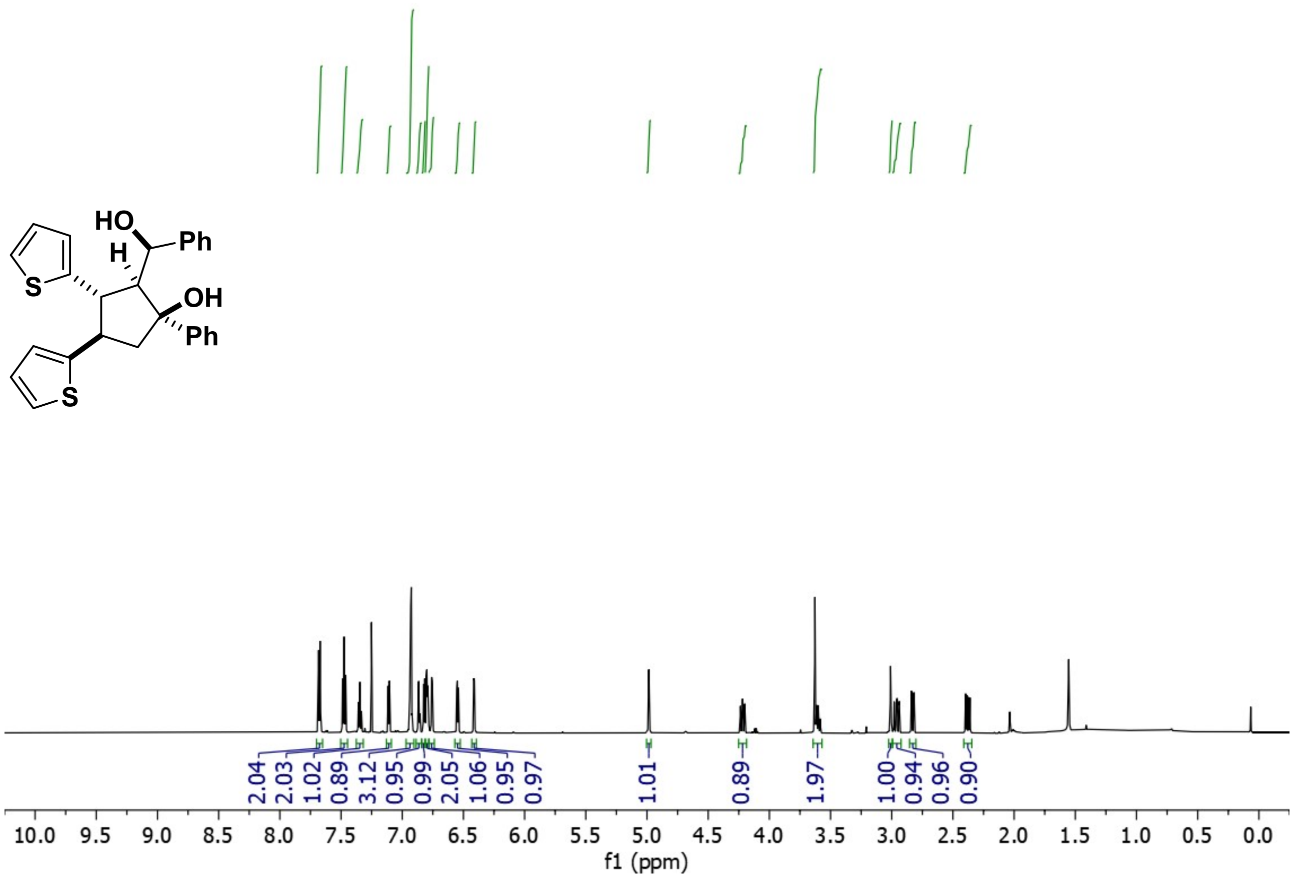
3p ^{1}H NMR (400 MHz, CDCl$_3$)



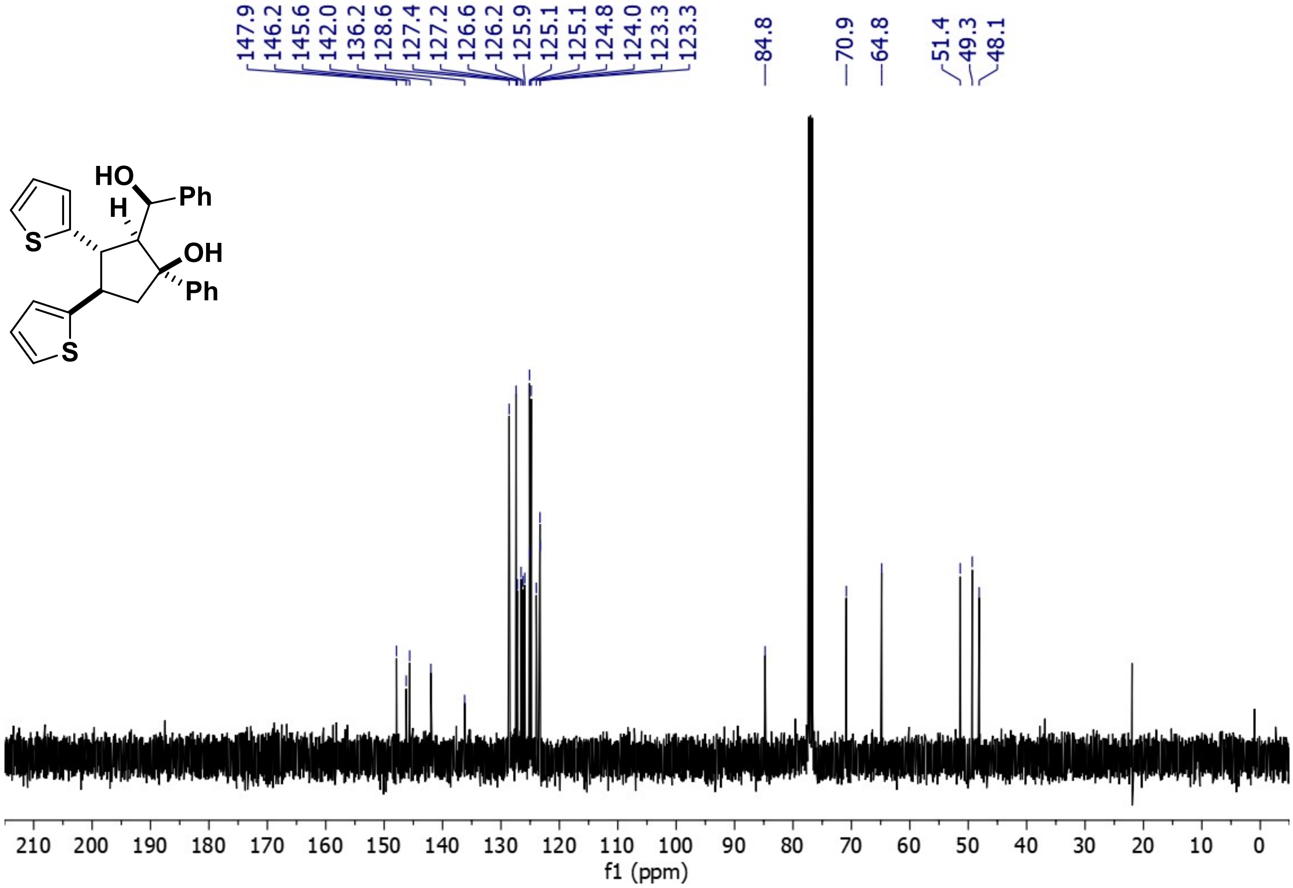
3p ^{13}C NMR (100 MHz, CDCl$_3$)



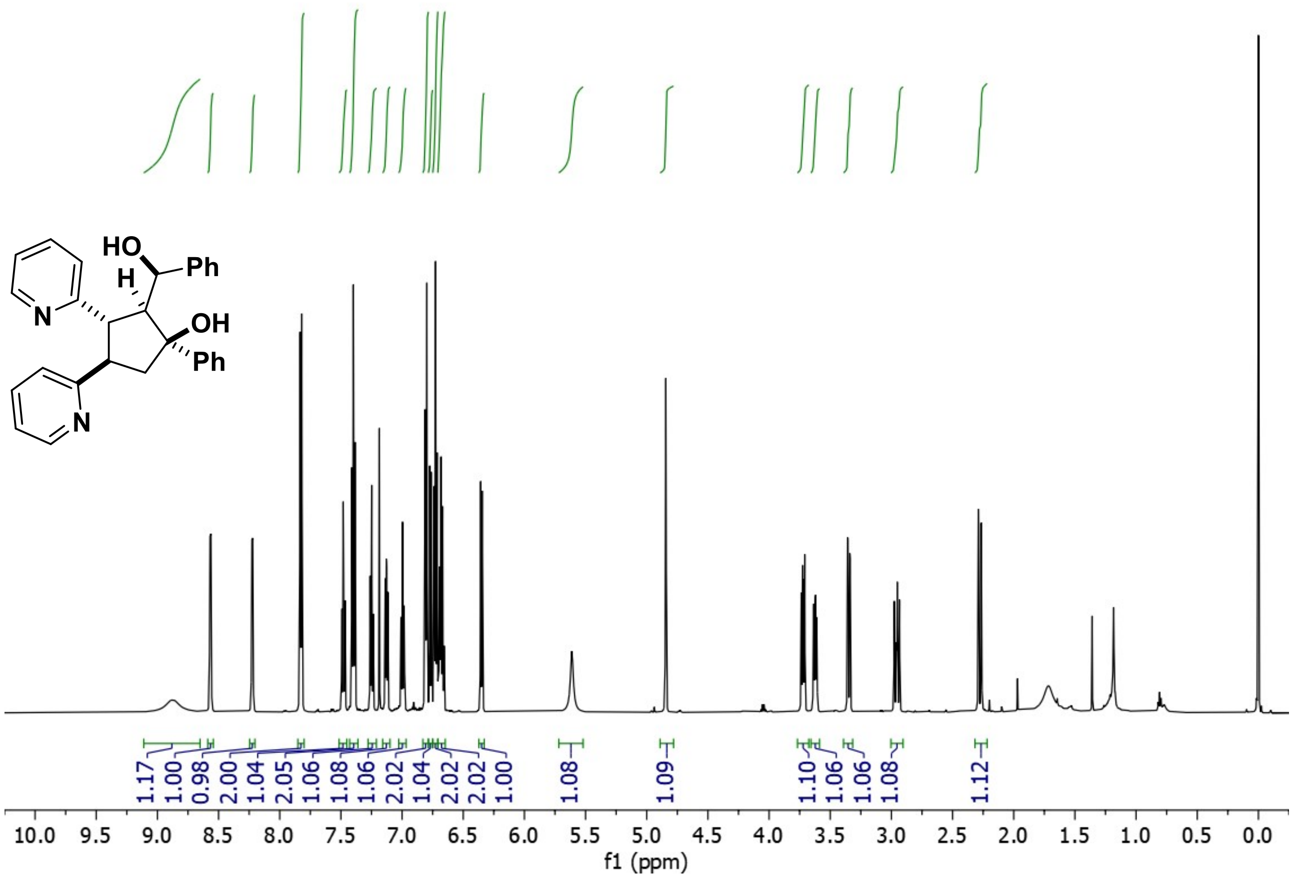
3q ^{1}H NMR (600 MHz, CDCl$_3$)



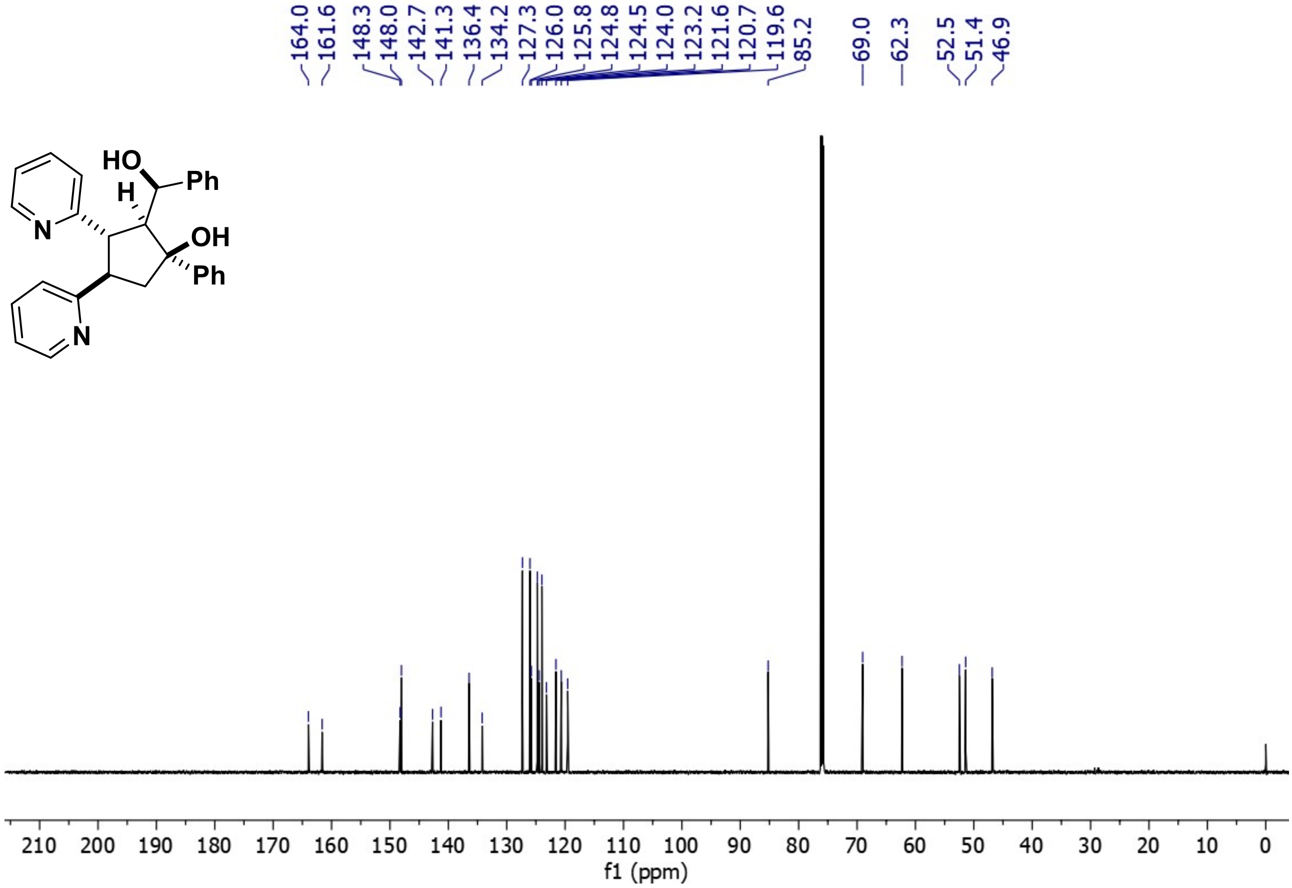
3q ^{13}C NMR (100 MHz, CDCl$_3$)



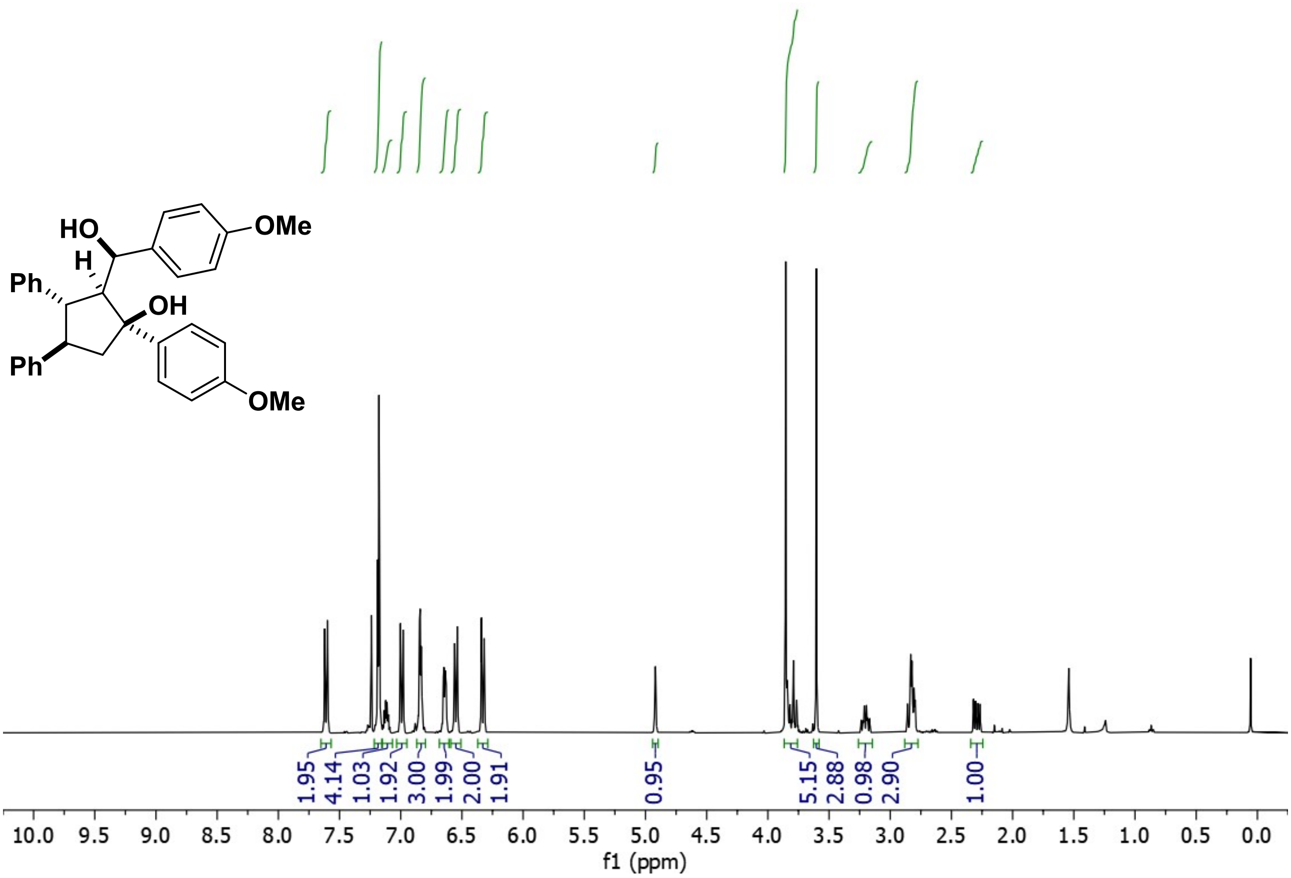
3r ^1H NMR (400 MHz, $CDCl_3$)



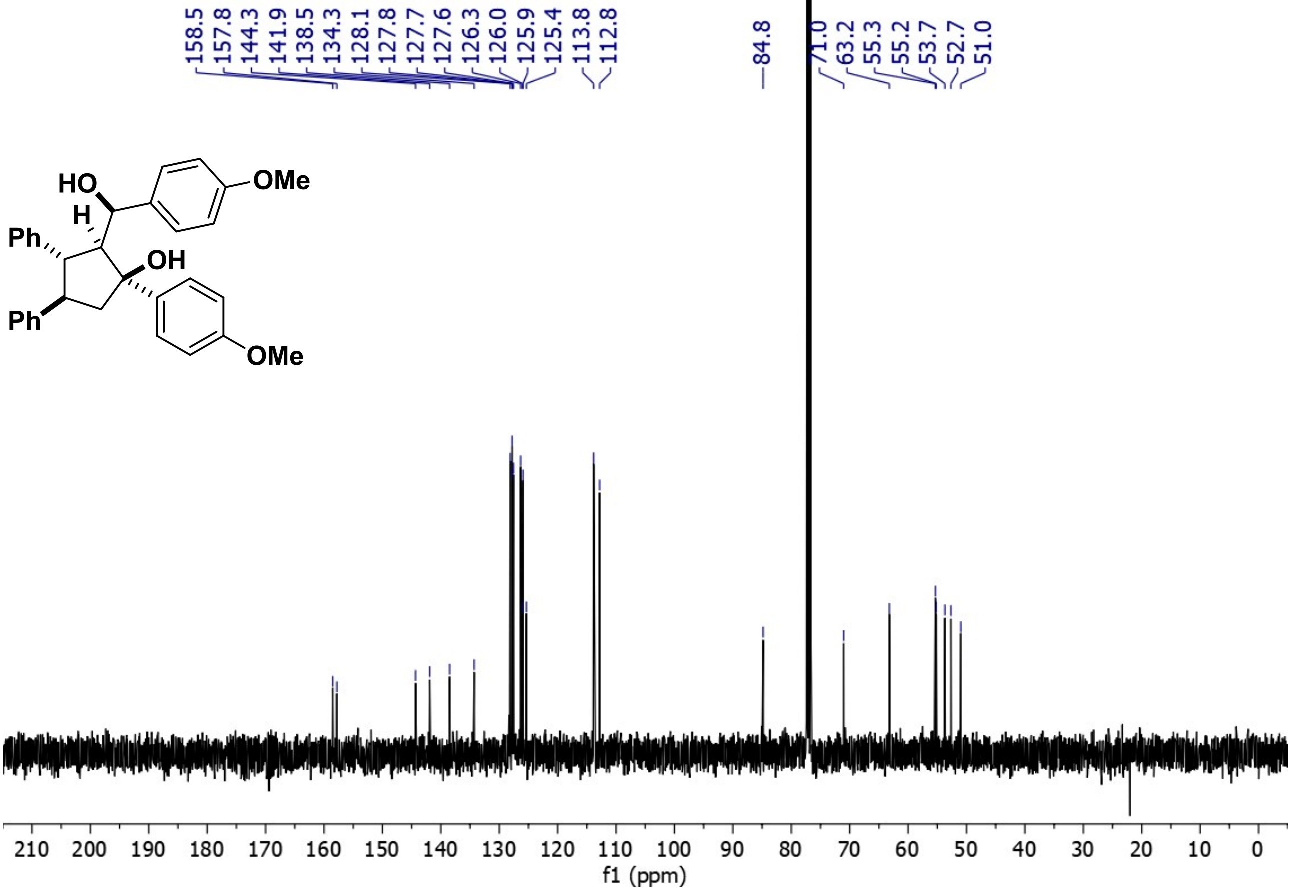
3r ^{13}C NMR (100 MHz, $CDCl_3$)



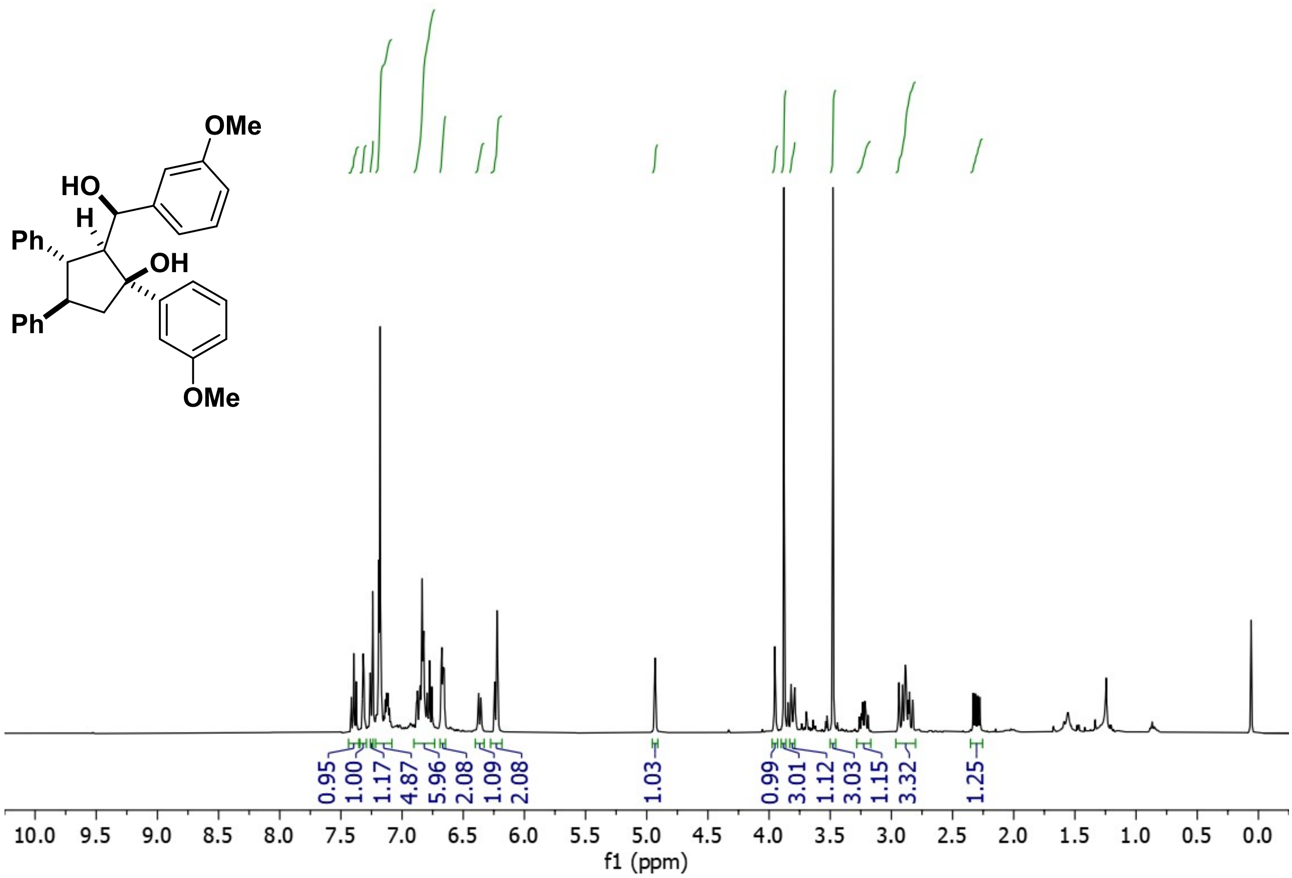
3s ^{1}H NMR (400 MHz, $CDCl_3$)



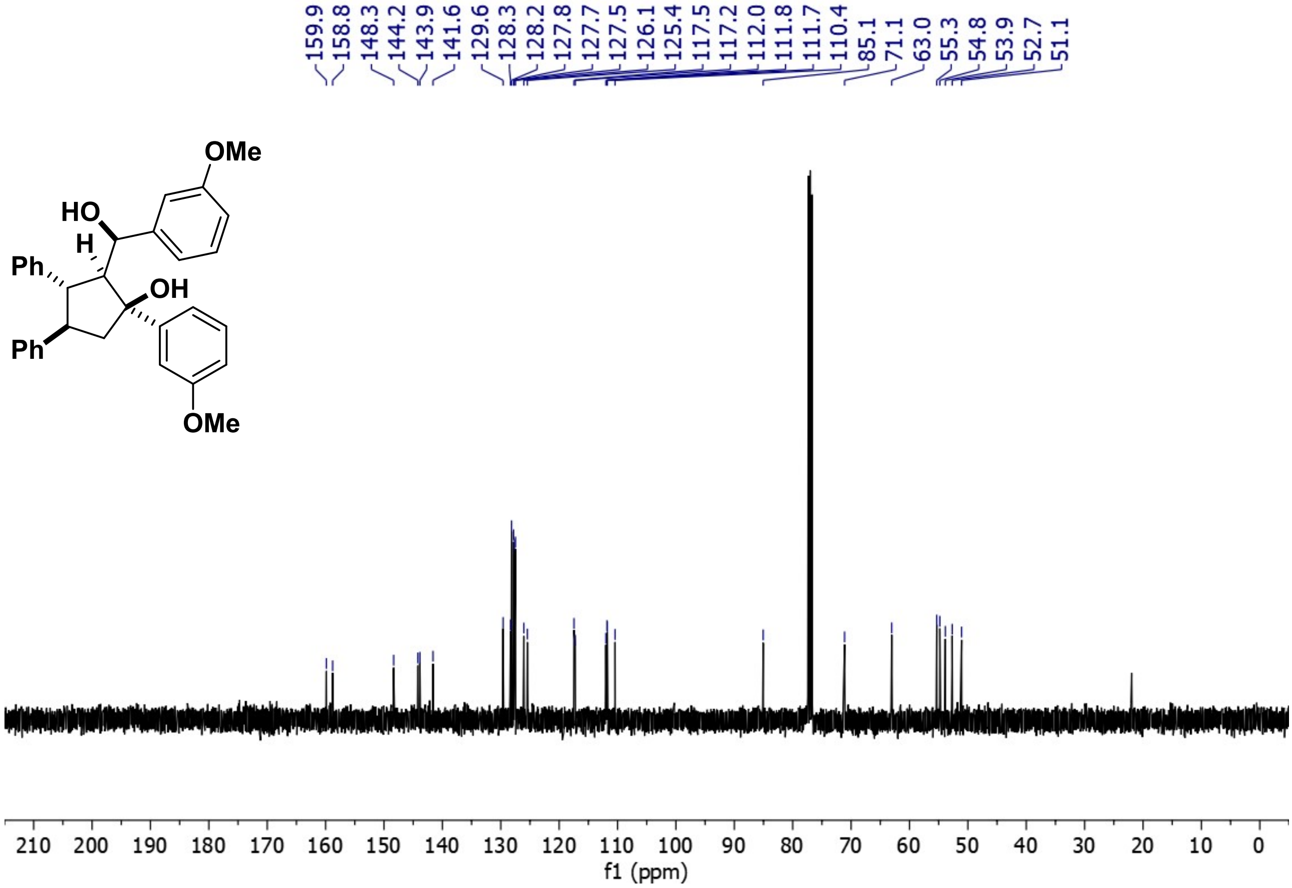
3s ^{13}C NMR (100 MHz, $CDCl_3$)



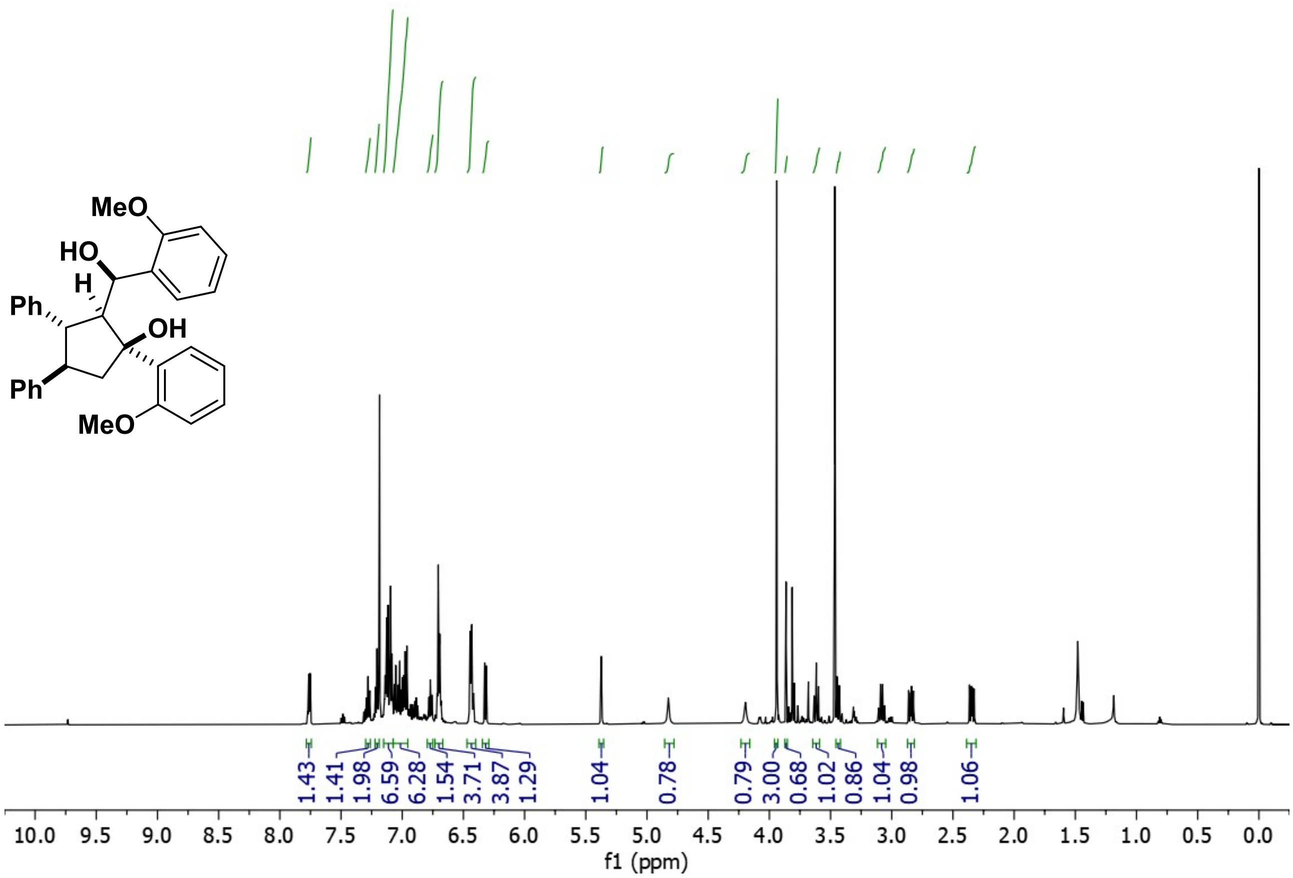
3t ^{1}H NMR (400 MHz, CDCl$_3$)



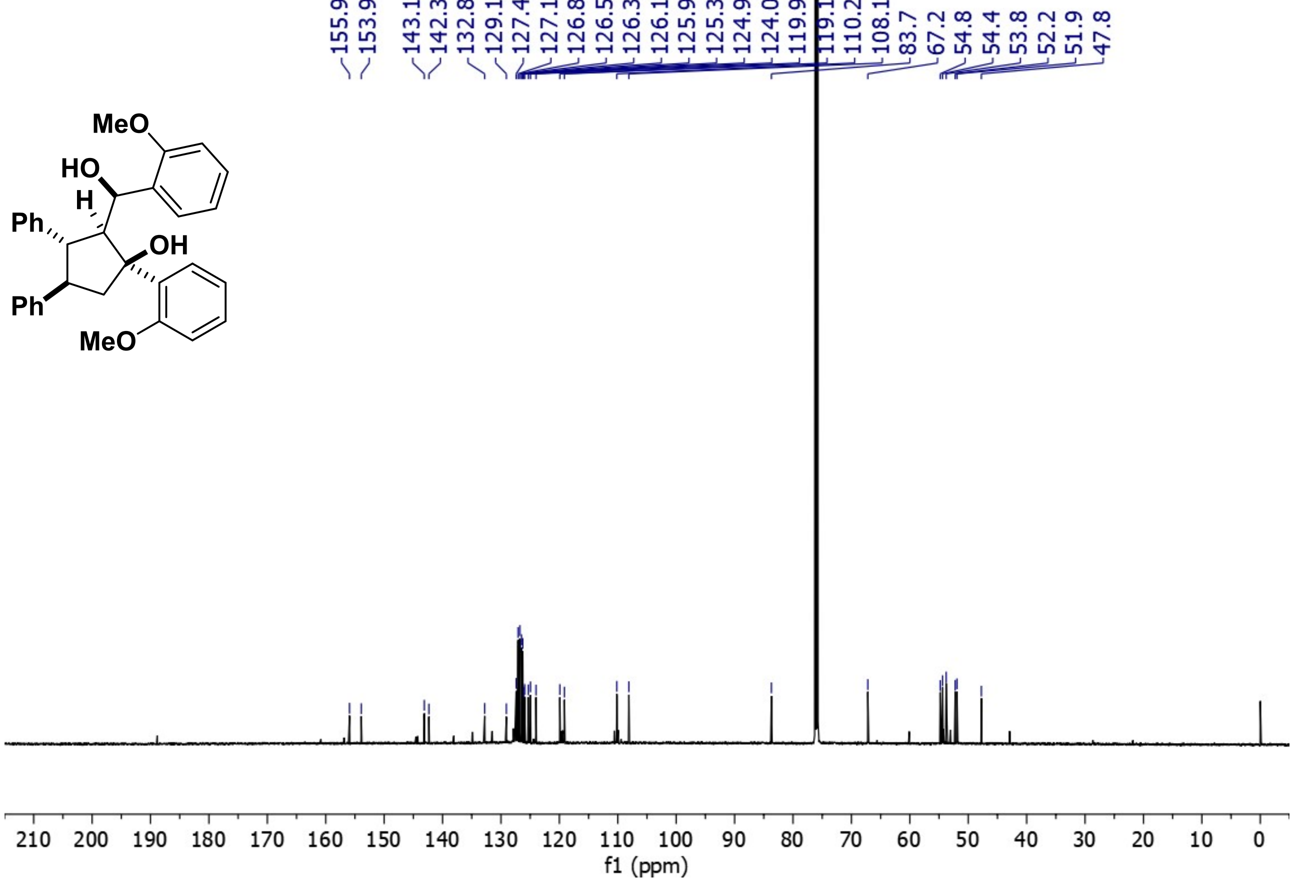
3t ^{13}C NMR (100 MHz, CDCl$_3$)



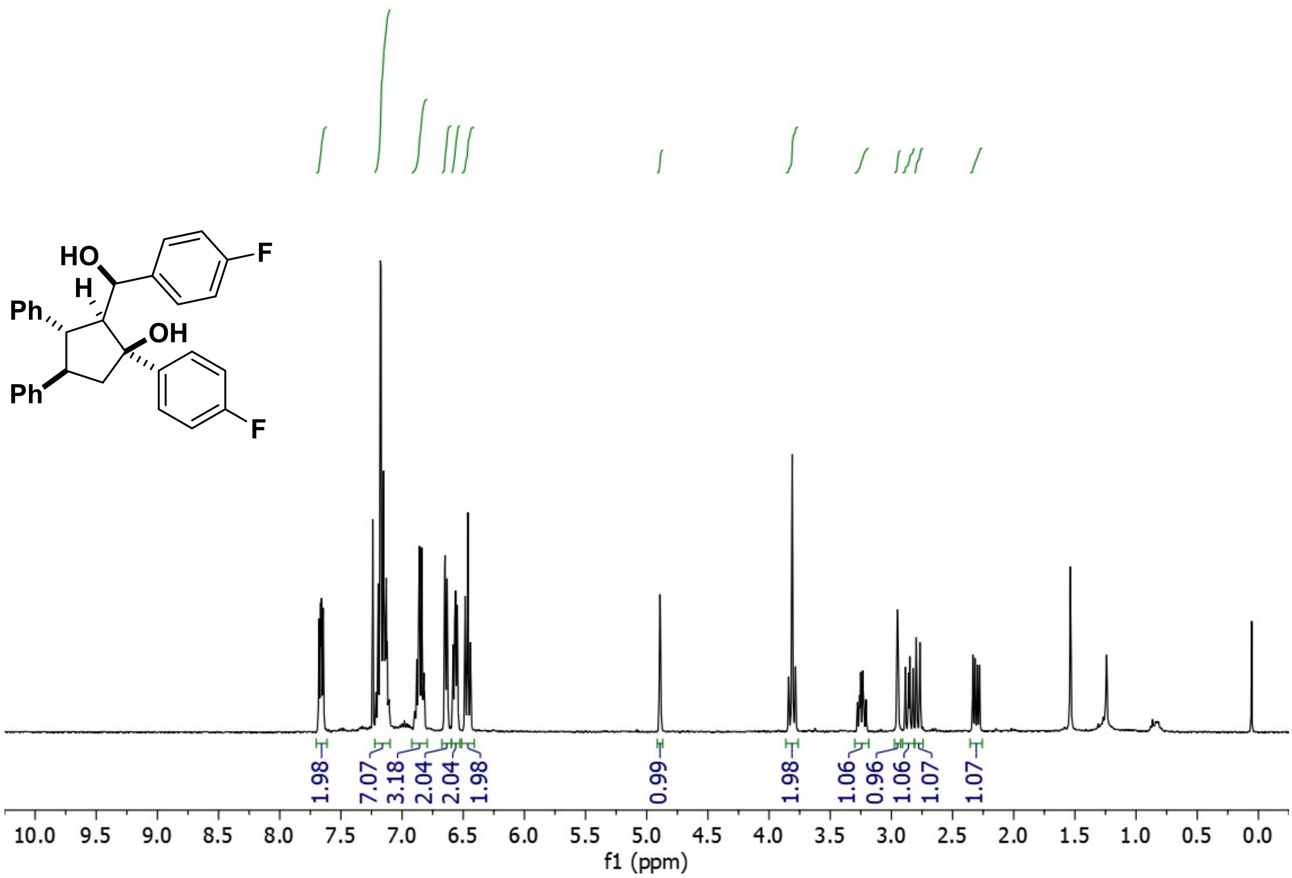
3u ^{1}H NMR (400 MHz, $CDCl_3$)



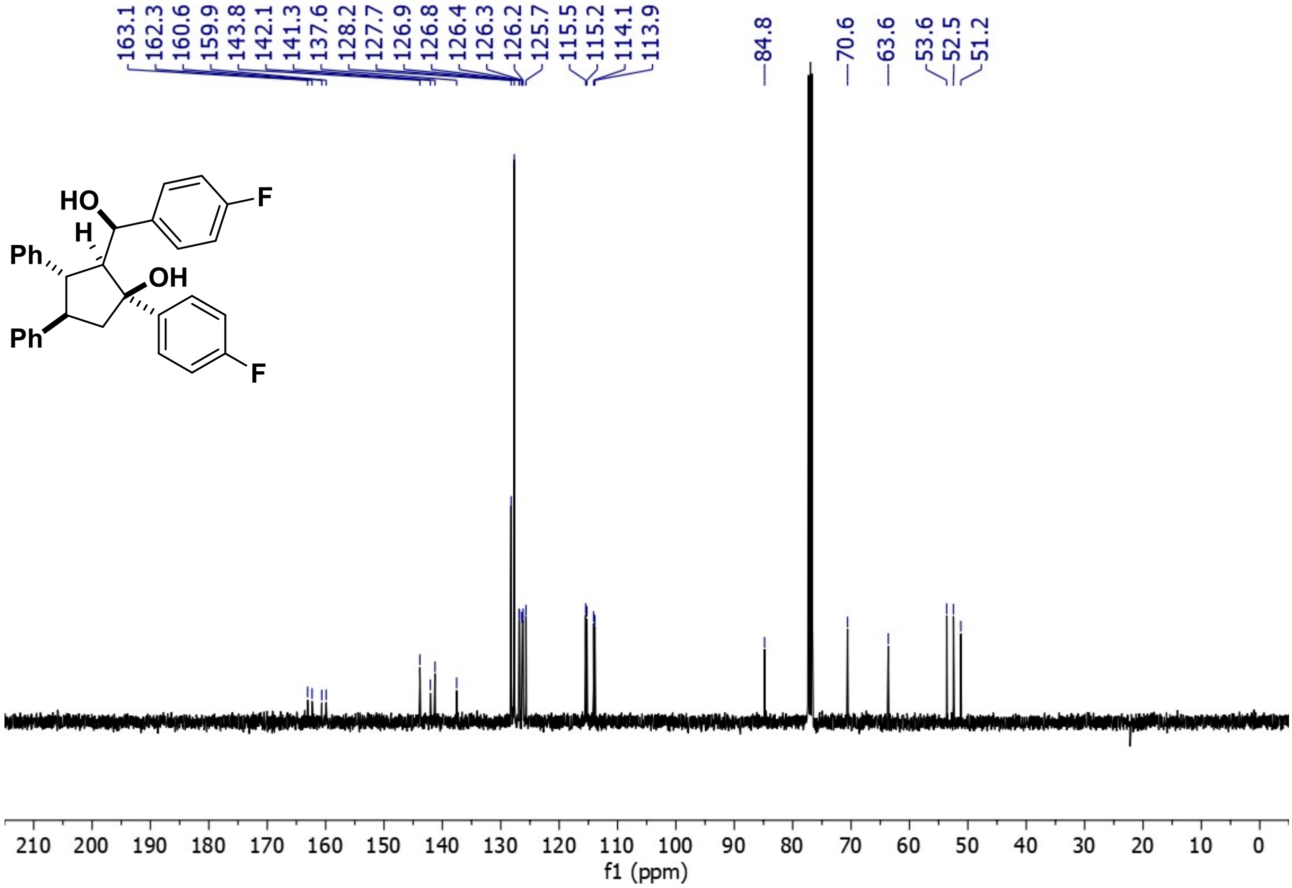
3u ^{13}C NMR (100 MHz, $CDCl_3$)



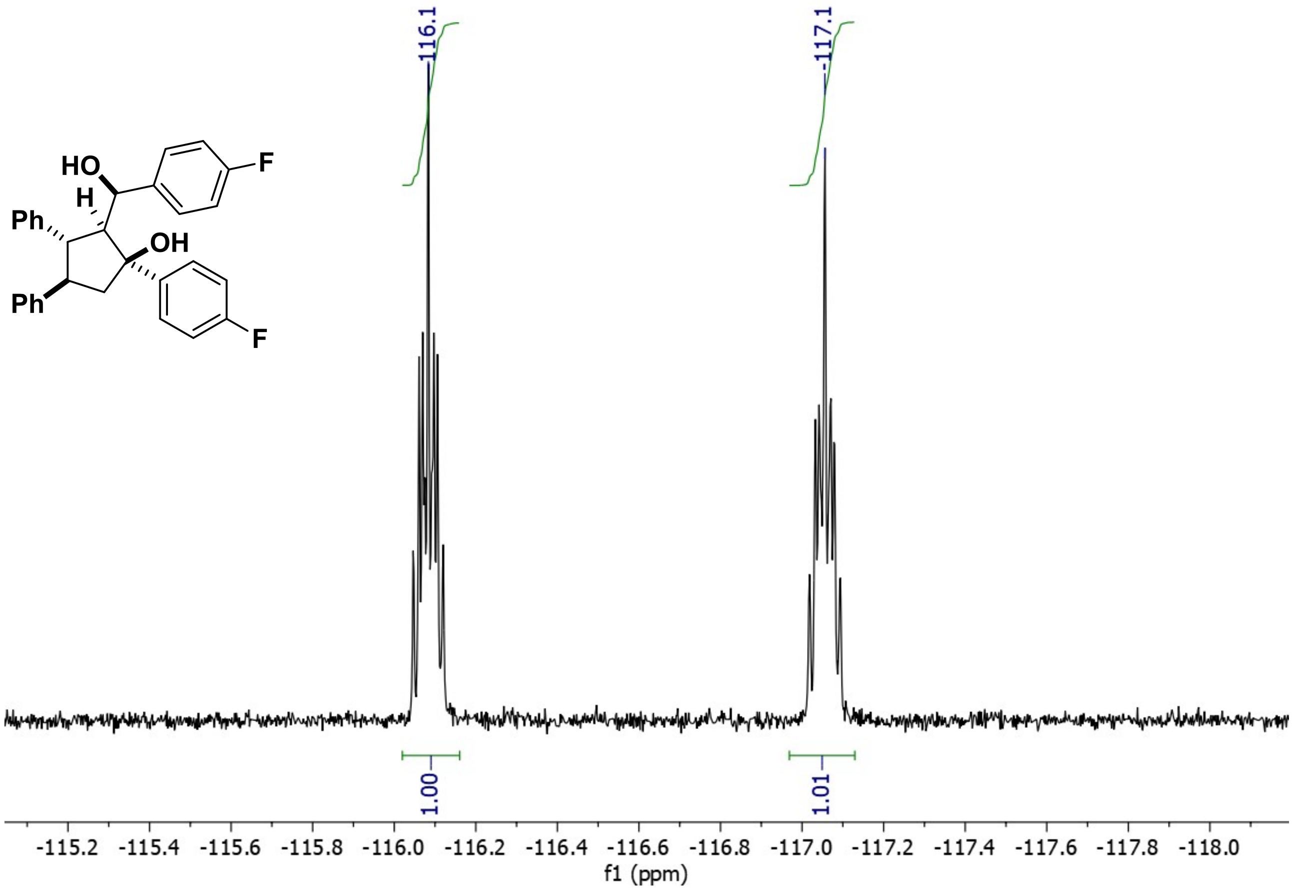
3v ^{1}H NMR (400 MHz, CDCl$_3$)



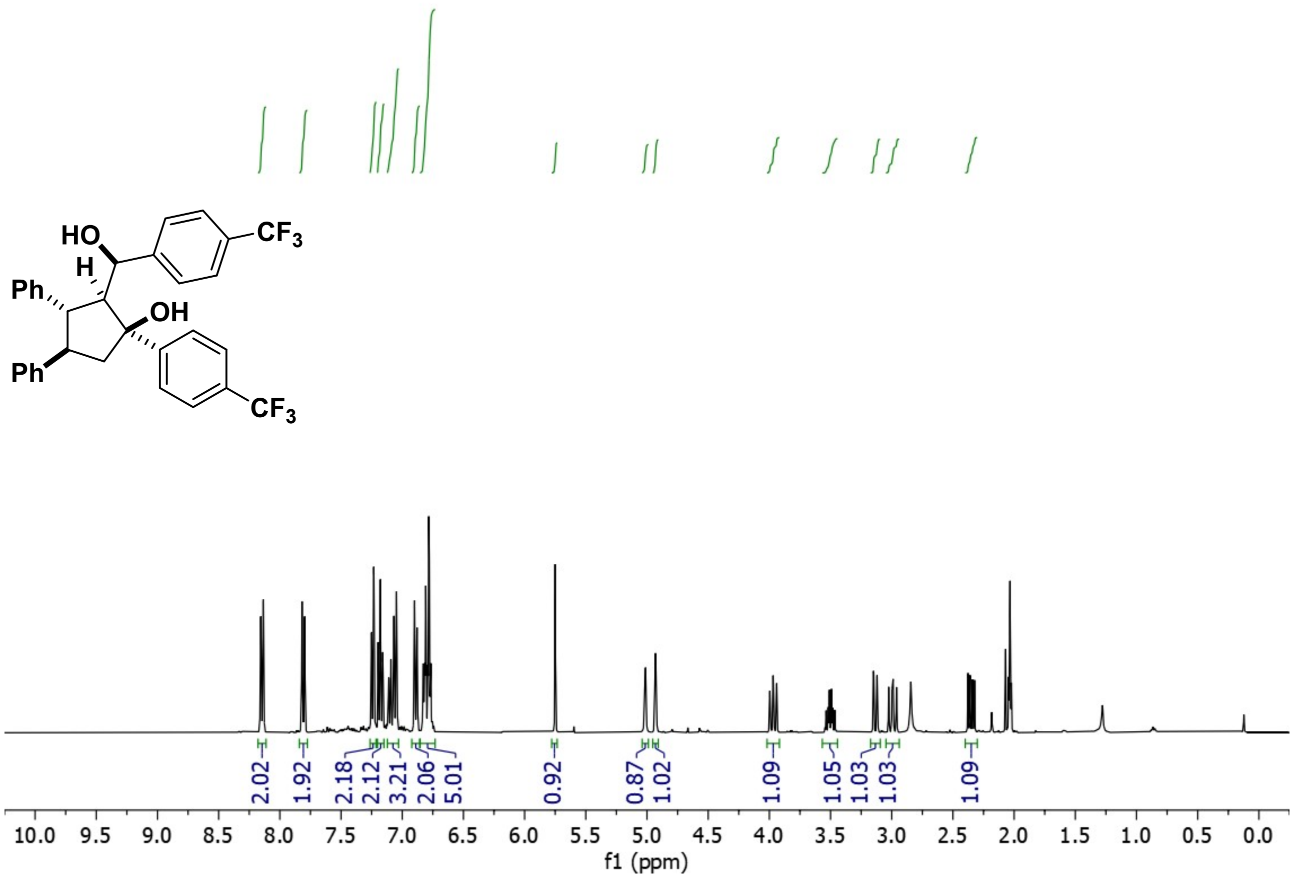
3v ^{13}C NMR (100 MHz, CDCl$_3$)



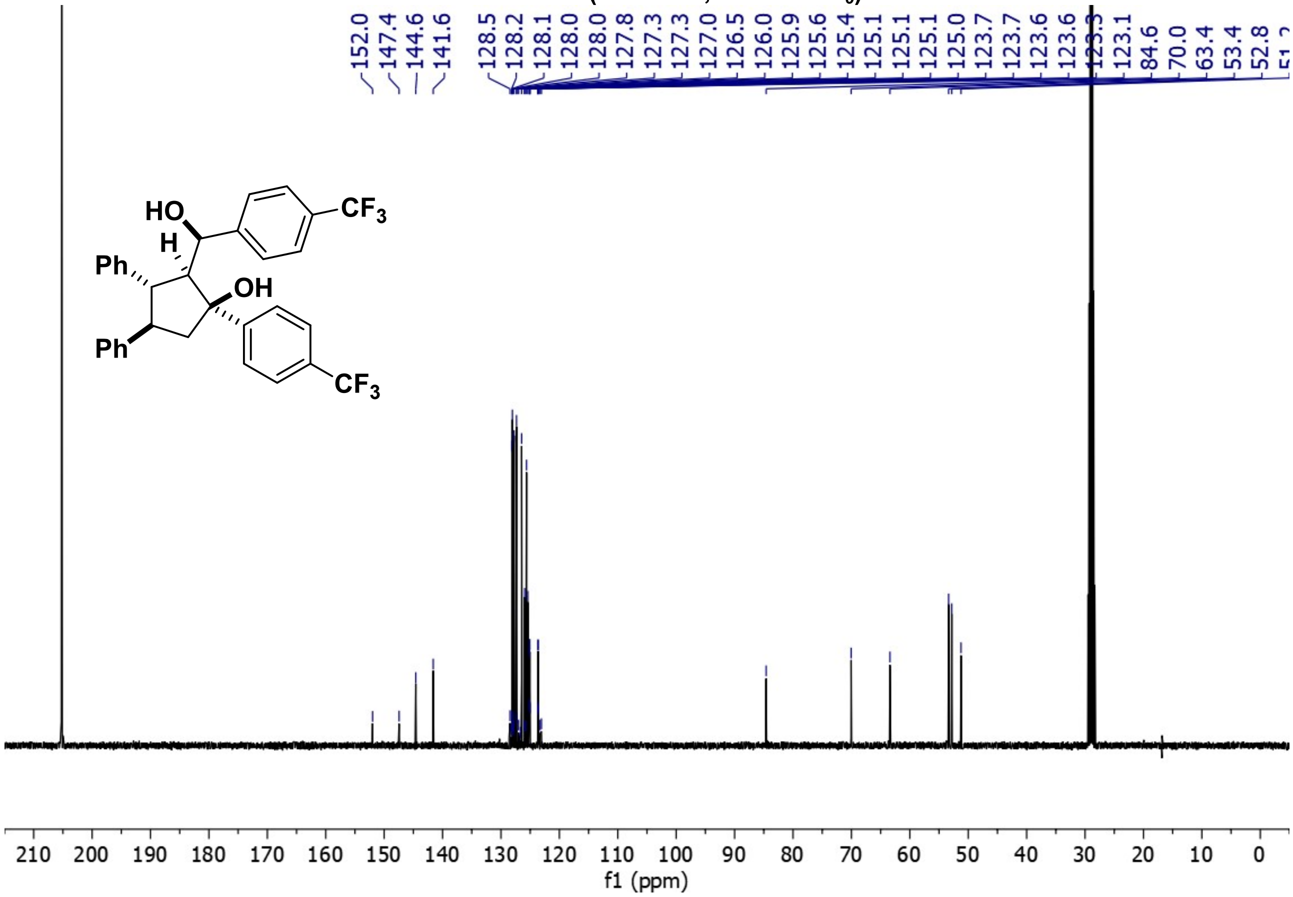
3v ^{19}F NMR (376 MHz, $CDCl_3$)



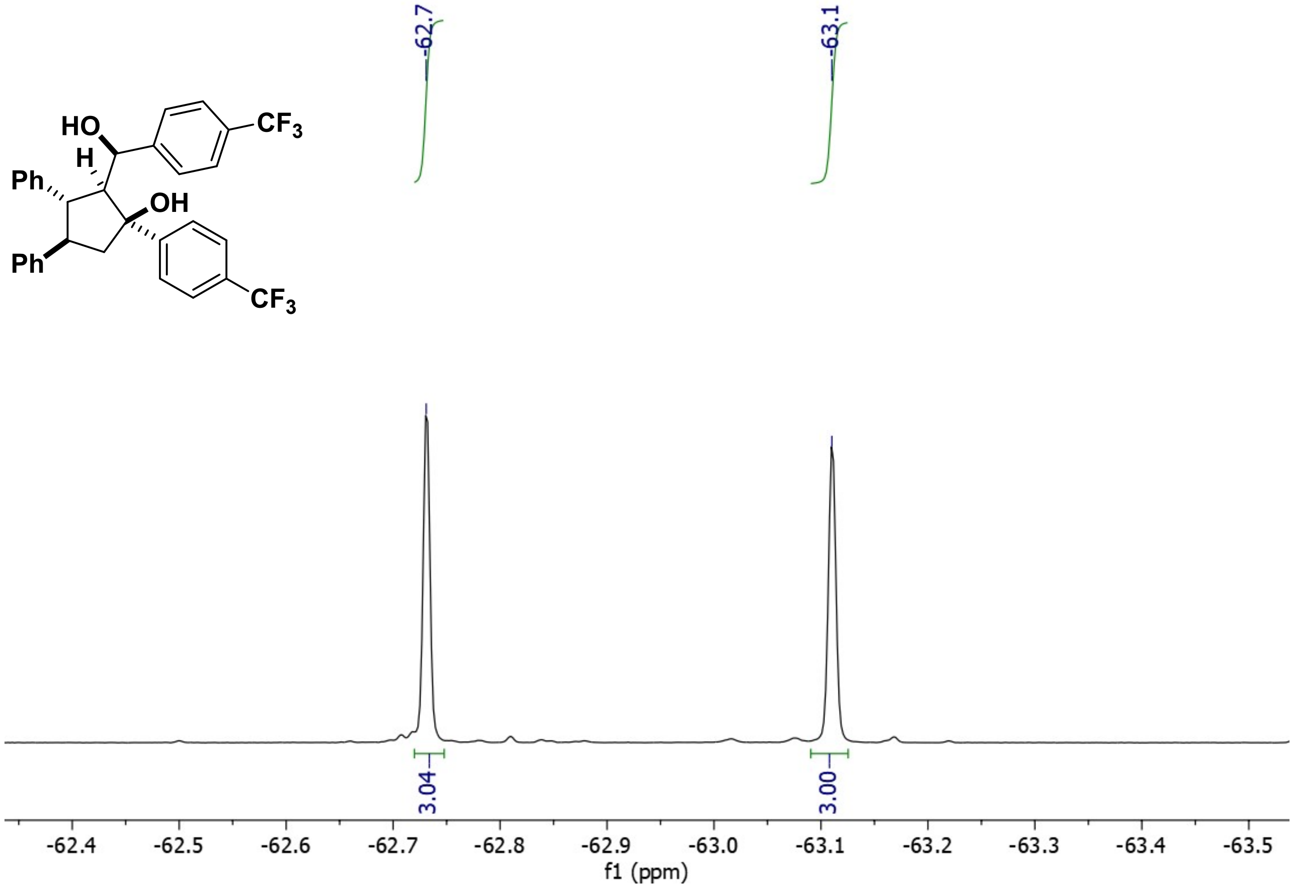
3w ^{1}H NMR (400 MHz, acetone-d_6)



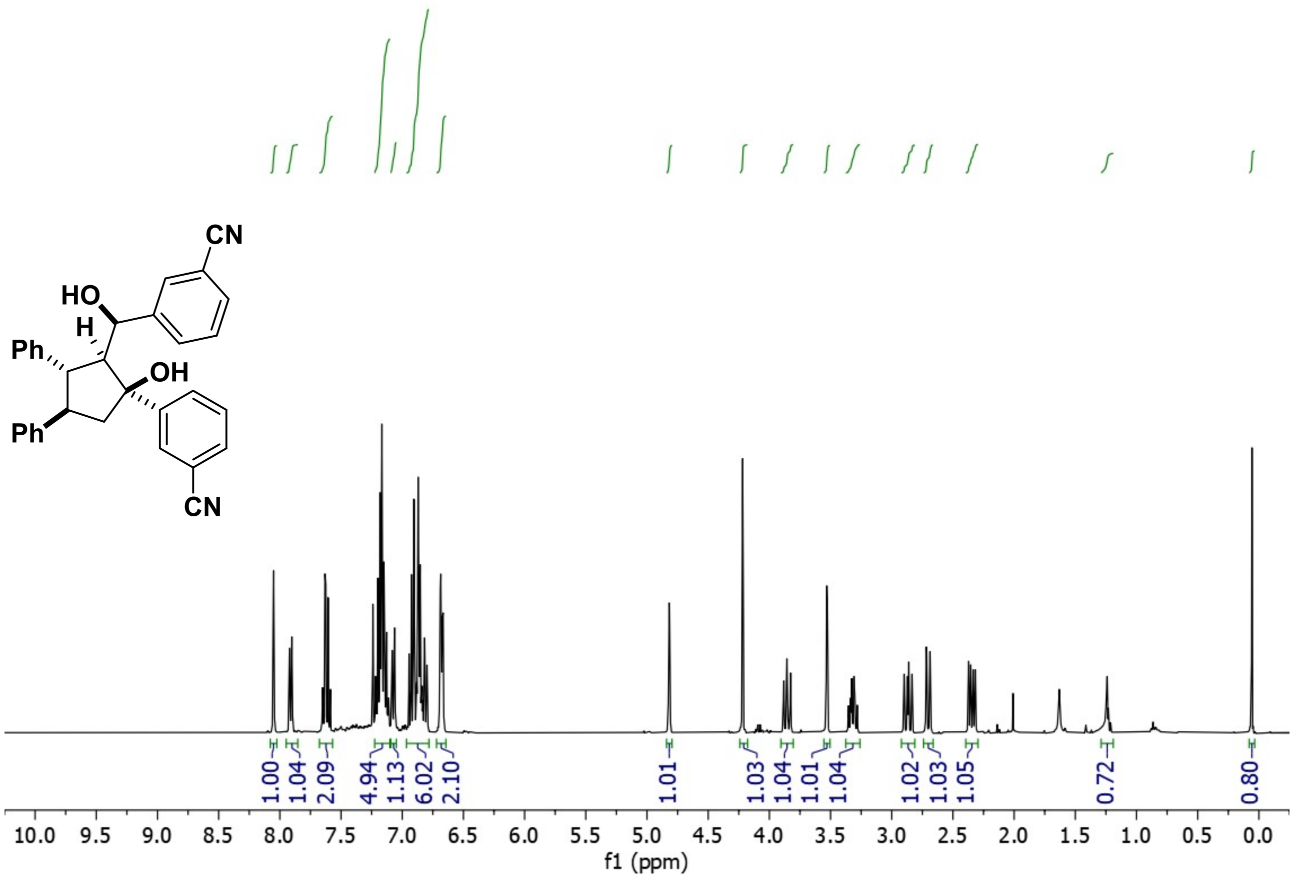
3w ^{13}C NMR (100 MHz, acetone-d_6)



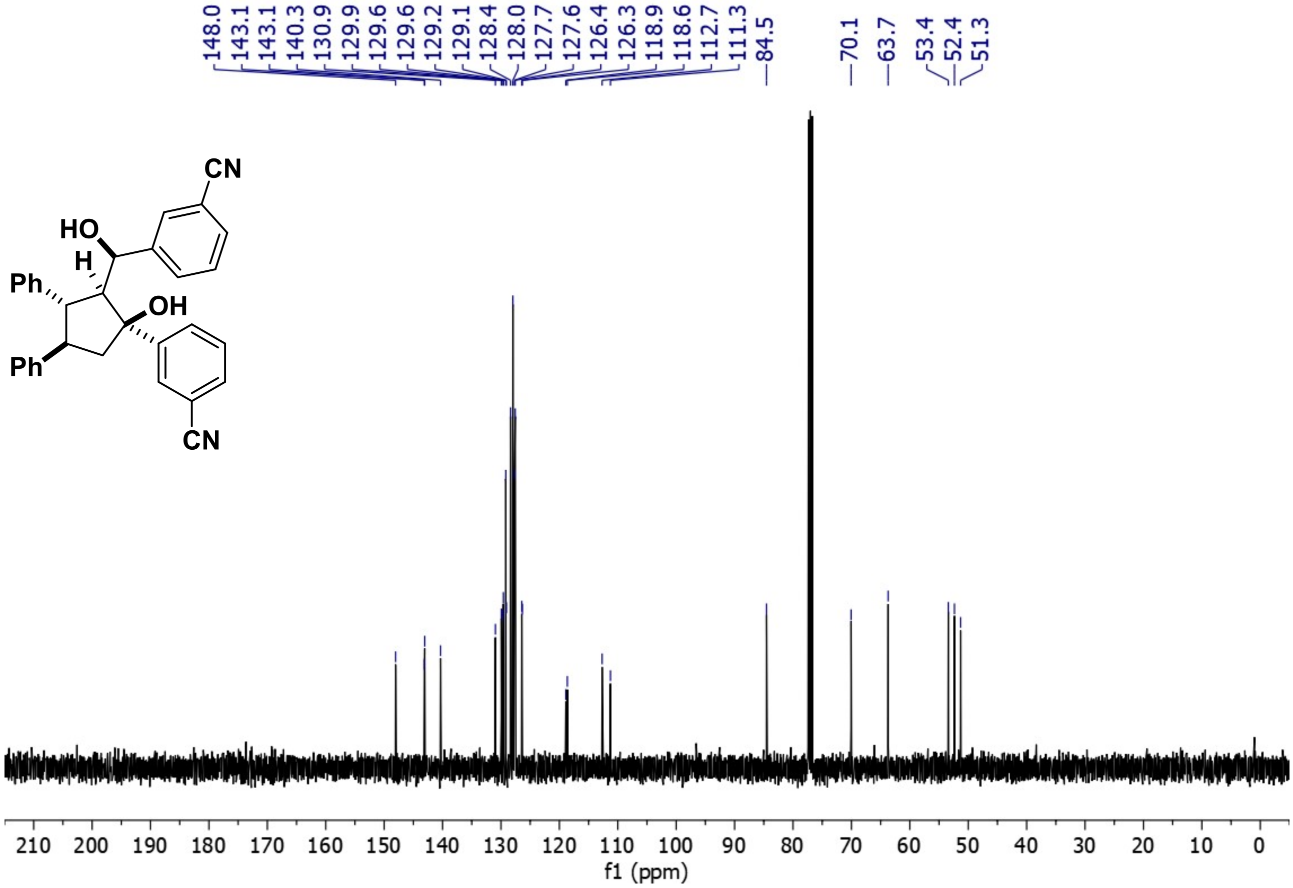
3w ^{19}F NMR (376 MHz, acetone-d_6)



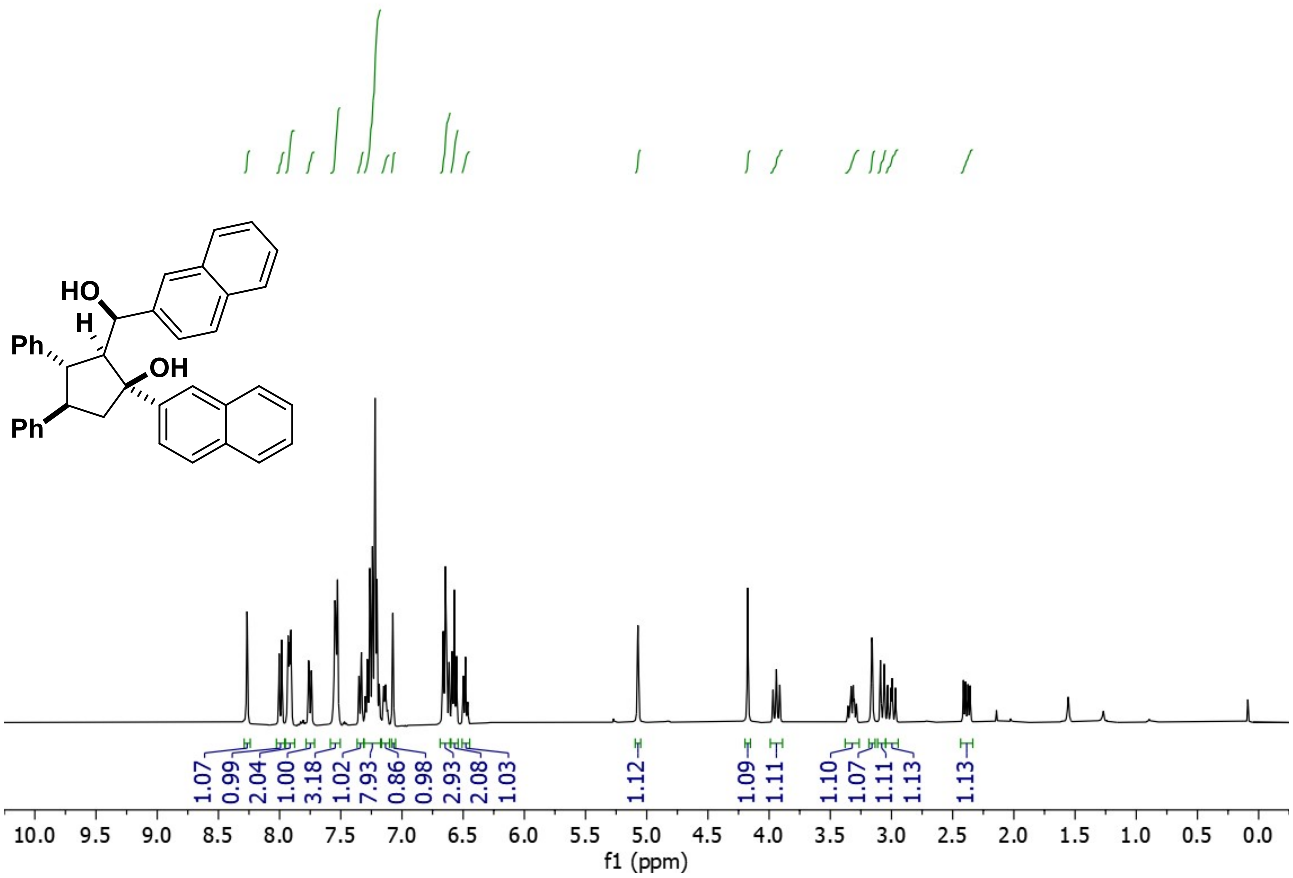
3x ^1H NMR (400 MHz, $CDCl_3$)



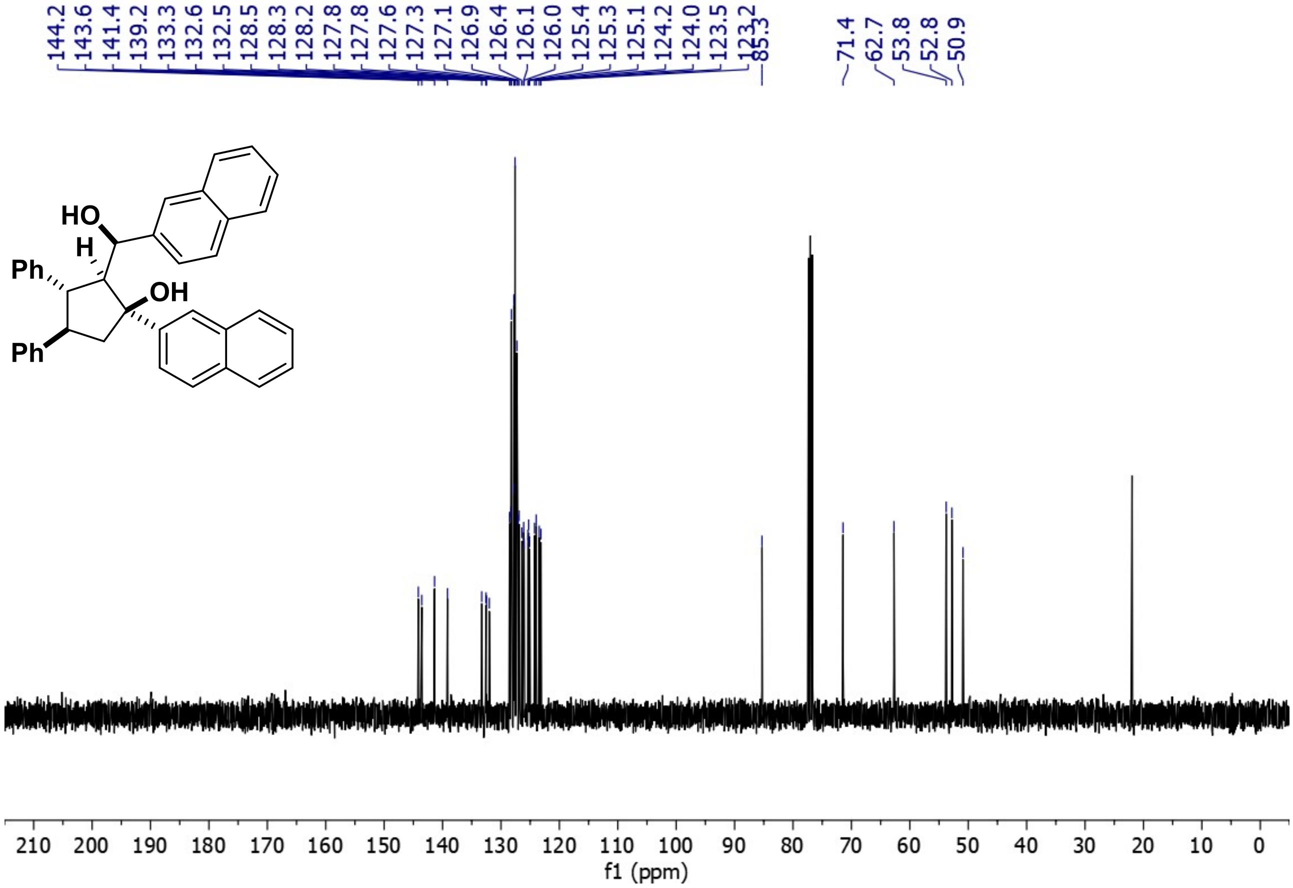
3x ^{13}C NMR (100 MHz, $CDCl_3$)



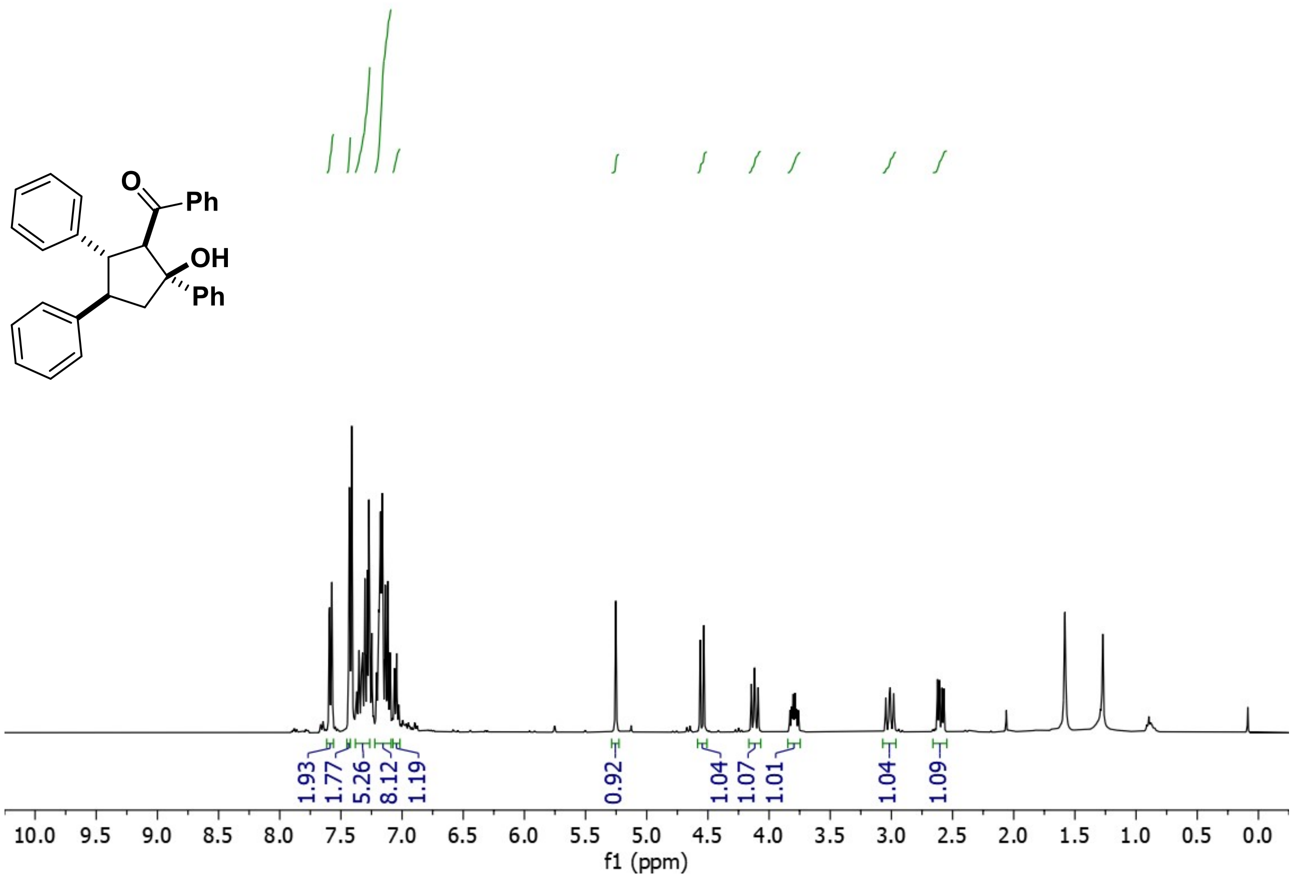
3y ^{1}H NMR (400 MHz, $CDCl_3$)



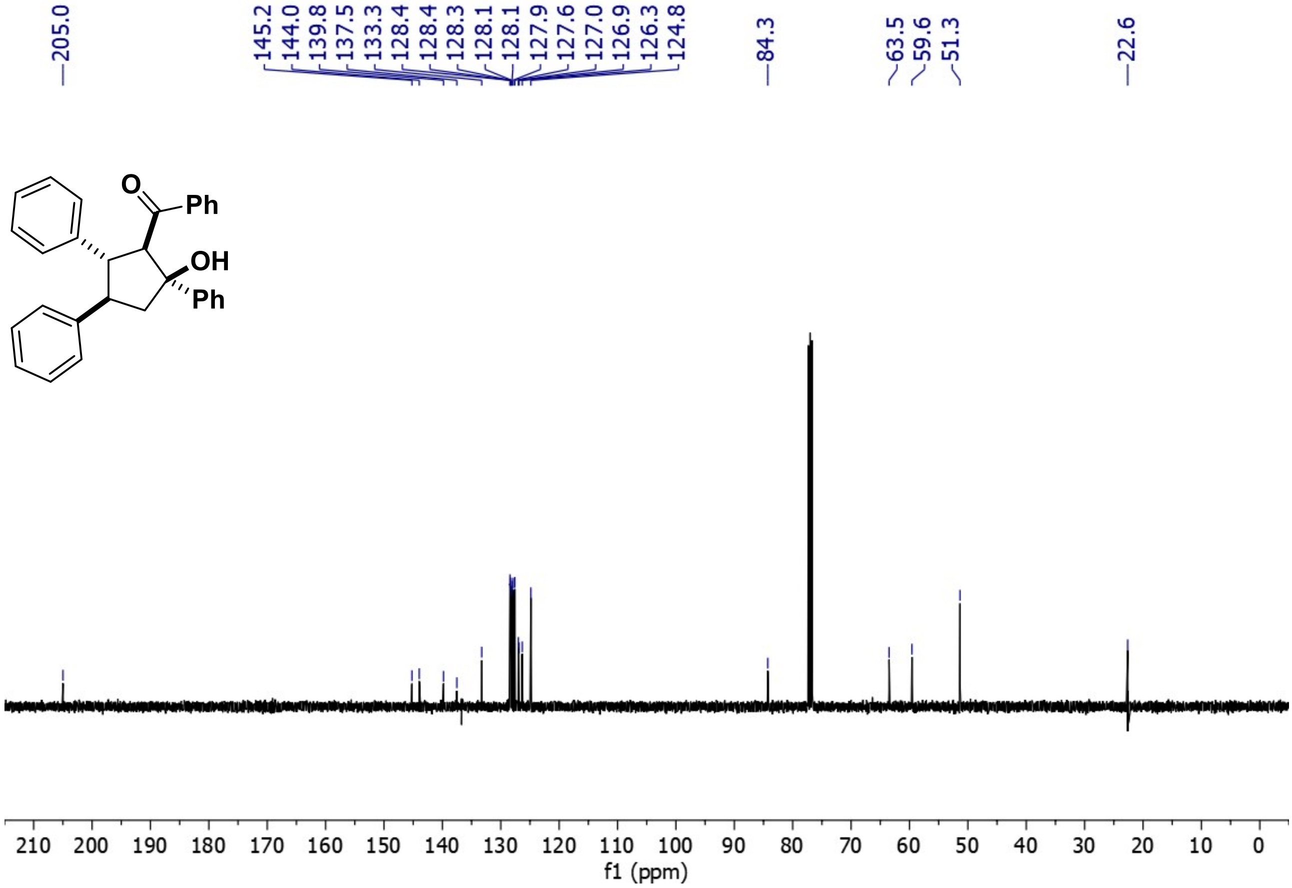
3y ^{13}C NMR (100 MHz, $CDCl_3$)



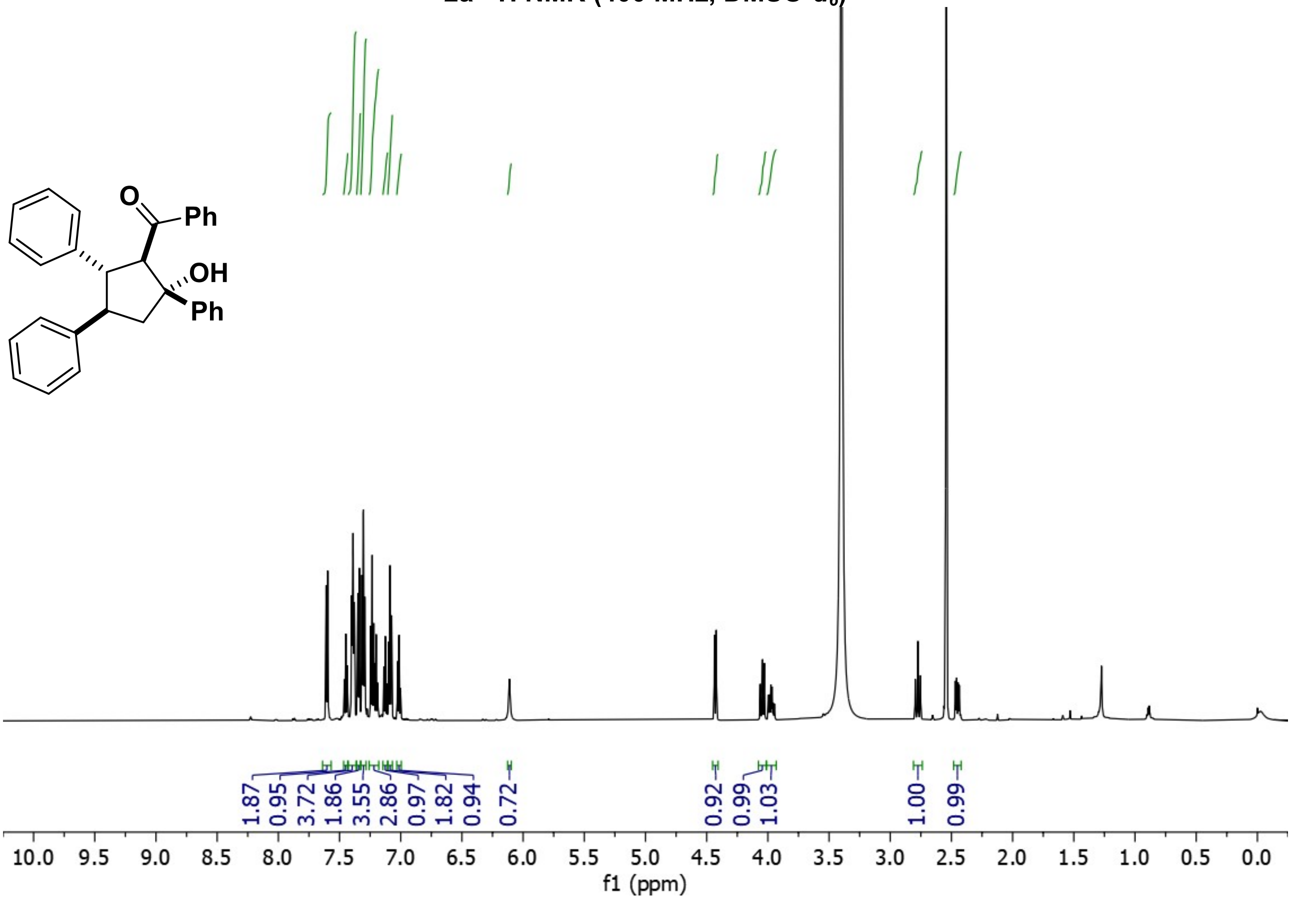
2a ^{1}H NMR (400 MHz, CDCl$_3$)



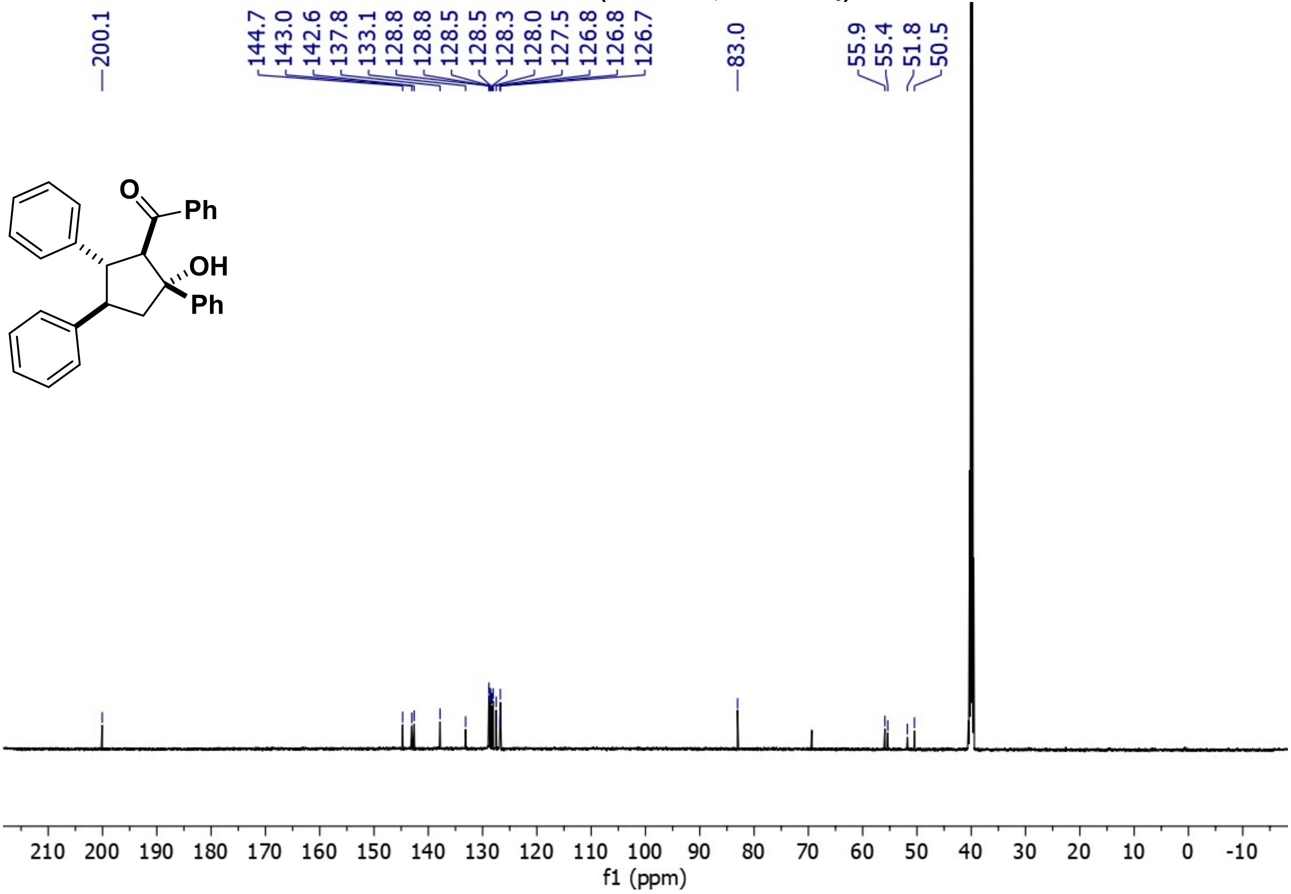
2a ^{13}C NMR (100 MHz, CDCl$_3$)



2a' ^{1}H NMR (400 MHz, DMSO-d_6)



2a' ^{13}C NMR (100 MHz, DMSO-d_6)



7. References

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