SUPPORTING INFORMATION

Mechanochemical One-Pot Barbier/Simmons-Smith Reaction *via* Sequential Zinc Activation

Asma A. Alharthi,[a,d] Benson M. Kariuki,[a] Louis C. Morrill,*[a,b] and Duncan L. Browne*[c]

[a]Cardiff Catalysis Institute, School of Chemistry, Cardiff University, Main Building, Park Place, Cardiff, CF10 3AT, U.K.

[b]Department of Chemistry, University of Bath, Claverton Down, Bath, BA2 7AY, U.K.

Email: lcm71@bath.ac.uk.

[c]Department of Pharmaceutical and Biological Chemistry, University College London (UCL), School of Pharmacy, 29-39 Brunswick Square, Bloomsbury, London, WC1N 1AX, U.K.

Email: duncan.browne@ucl.ac.uk.

[d]Department of Chemistry, College of Science, University of Jeddah, Jeddah 21589, Saudi Arabia.

Contents

1. General Information and Mechanochemistry Equipment

Mixer mills: Mechanochemical reactions (1.00- 5.00 mmol) were conducted using an Insolido Tech IST500 mixer mill (see www.insolidotech.org for more details) or a Retsch MM400 mixer mill (see www.retsch.com for more details).

Stainless steel jars: Mechanochemical reactions were conducted using Formtech Scientific SMARTSNAPTM stainless steel grinding jars (for further details see www.formtechscientific.com) at 15 mL (for 1.00- 5.00 mmol reactions).

Stainless steel balls: Stainless steel balls were purchased from Formtech Scientific or Retsch either 8.56 g (9 g, 12.7 mm, for 5.00 mmol reactions),or 4.18 g (4 g, 10 mm, for 1.00 mmol reactions).

Analytical equipment: **^{1}H NMR**, **^{13}C NMR** and **^{19}F NMR** spectra were obtained on a Bruker Avance 300 (300 M 1H, 75 M 13C, 282 M 19F), a Bruker Avance 400 (400 M 1H, 101 M 13C, 376 M 19F) or a Bruker Avance 500 (500 M 1H, 126 M 13C, 471 M 19F) spectrometer at rt in the solvent stated. NMR data are presented in the following format: chemical shift (multiplicity [app = apparent, br = broad, d = doublet, t = triplet, q = quartet, dd = doublet of doublets, dt = doublet of triplets, dq = doublet of quartets, ddd = doublet of doublet of doublets, m = multiplet], coupling constant [in Hz], number of equivalent nuclei by integration). Spin-spin coupling constants J are given in Hz and refer to apparent multiplicities rather than true coupling constants. Data are reported as: chemical shift, multiplicity and integration. NMR yields were obtained using 0.33 mmol of mesitylene as an internal standard.

Analytical thin layer chromatography was carried out using aluminium plates coated with silica (Kieselgel 60 F254 silica) and visualization was achieved using ultraviolet light (254 nm), followed by staining with a phosphomolybdic acid stain, unless otherwise stated. Flash column chromatography (FCC) used Kieselgel 60 silica in the solvent system stated. The petroleum ether (PE) utilised was in the 40 – 60 °C boiling.

Melting points (m.p.) were recorded on a Gallenkamp melting point apparatus and are reported corrected by linear calibration to benzophenone (47 – 49 °C) and benzoic acid (121 – 123 °C).

Infrared spectra were recorded on a Shimadzu IRAffinity-1 Fourier Transform ATIR spectrometer as thin films using a Pike MIRacle ATR accessory, with absorbance peaks quoted (vmax/cm^{-1}).

High resolution mass spectral (HRMS) data were obtained on a Waters MALDI-TOF mx in Cardiff University.

Reagents: Unless otherwise stated all reagents were purchased from commercial sources and used without further purifications.

Reactions in solution involving air- and moisture-sensitive reagents: All reactions involving air- and moisture-sensitive reagents were conducted in oven-dried glassware under inert nitrogen atmosphere.

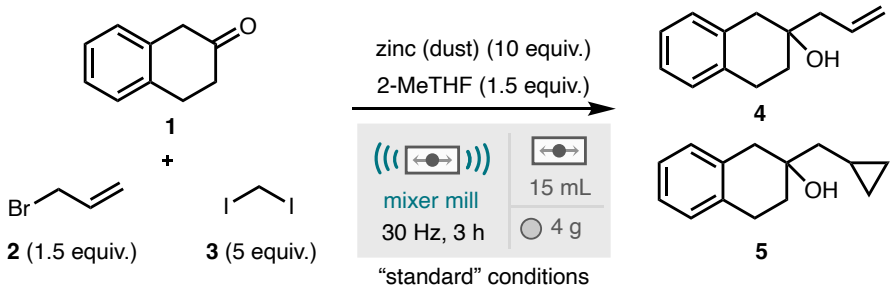
Room temperature (rt) refers to 20 – 25 °C. Ice/water baths were used to obtain temperatures of 0 °C.

All reactions involving heating were carried out using DrySyn blocks and a contact thermometer.

In vacuo refers to reduced pressure through the use of a rotary evaporator.

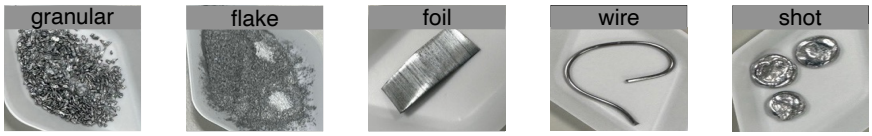
2. **Table S1**

Table S1 Reaction optimization.[a]



Entry	Variation from "standard" conditions	**4**[b] (%)	**5**[b] (%)
1	none	2	62 (54)
2	zinc (7 equiv.)	8	52
3	DMSO instead of 2-MeTHF	6	48
4	DMA instead of 2-MeTHF	3	43
5	2-MeTHF (3.5 equiv.)	4	55
6	No LAG	42	19
7	diiodomethane (3.5 or 7.5 equiv.)	10 or 5	51 or 61
8	allyl bromide (1.1 equiv.)	5	53
9	GA: Sand (3 mass equivalent)	4	58
10	GA: Na_2SO_4 (3 mass equivalent)	6	53
11	diiodomethane (5 equiv.) added after 1 h	0	68 (64)

Zinc forms

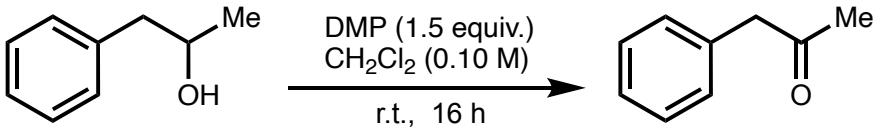


12, 51% **13,** 47% **14,** 58% **15,** 47% **16,** 52%

[a] Reactions performed using 1.00 mmol of 2-tetralone **1** using the Insolido Tech IST500 mixer mill. [b] Yield determined by ^{1}H NMR analysis of the crude reaction mixture with mesitylene as the internal standard. Isolated yield after silica gel column chromatography given in parentheses.

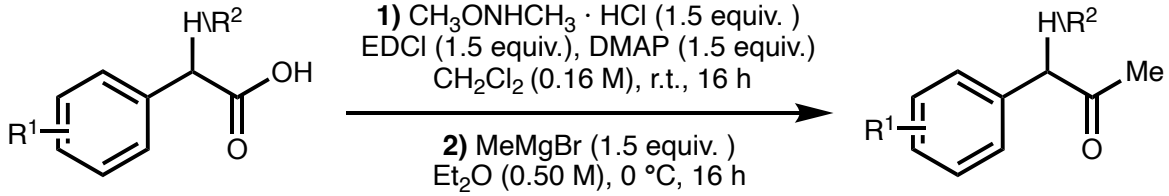
3. **Synthesis of Starting Materials**:

1- **1-phenylpropan-2-one (S1)**



To a stirred solution of 1-phenyl-2-propanol (1.4 mL, 10.0 mmol) in CH_2Cl_2 (100 mL), was added Dess-Martin Periodinane (6.36 g, 15.0 mmol, 1.5 equiv.) portion wise at 0 °C. The resulting mixture was then allowed to warm to room temperature and stirred for an overnight. After completion, the mixture was quenched with a 1:1 mixture of 10 wt% $Na_2S_2O_3$ / sat. aq. $NaHCO_3$ (80 mL), extracted with CH_2Cl_2 (2 x 80 mL). The combined organic phases were dried over $MgSO_4$, filtered and concentrated *in vacuo*. The crude residue was purified by silica gel flash chromatography (Eluent: Et_2O/Petroleum ether) yielding pure product a colorless oil (1.21 g, 93%), $\mathbf{R_f}$ = 0.22 (Eluent: EtOAc/hexane, 5%).^{1}**H NMR** (500 MHz, $CDCl_3$) δ 7.28 – 7.22 (m, 2H), 7.22 – 7.15 (m, 1H), 7.15 – 7.09 (m, 2H), 3.58 (s, 2H), 2.04 (s, 3H).^{13}**C NMR** (126 MHz, $CDCl_3$) δ 205.8, 134.1, 129.1, 128.4, 126.6, 50.5, 28.8. The NMR data is consistent with literature.[1]

General procedure A - Synthesis of non-conjugated ketones*:*



Weinreb amide synthesis:

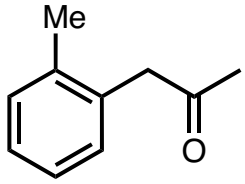
A 250 mL round-bottomed flask equipped with a magnetic stirrer bar was charged with acid (10.0 mmol), *N*,*O*-Dimethylhydroxylamine (1.46 g, 15 mmol, 1.50 equiv.) , 1-(3-Dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (2.87 g, 15 mmol, 1.50 equiv.), 4-Dimethylaminopyridine (DMAP) (1.83 g, 15 mmol, 1.50 equiv.) and CH_2Cl_2 (60 mL).

The mixture was left to react at room temperature overnight. After this period, the reaction mixture was quenched with water (80 mL). The phases were separated, and the aqueous layer was extracted with CH_2Cl_2 (2 x 50 mL). The combined organic phases were dried over $MgSO_4$. The mixture was concentrated *in vacuo* and used in the next step without further purification.

Ketone synthesis:

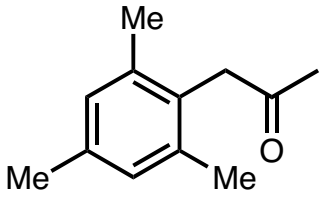
To a stirred solution of Weinreb amide product (1 equiv.) in Et_2O (0.5 M) under a nitrogen atmosphere, was added Methylmagnesium bromide (1.5 equiv.) dropwise at 0 °C. The resulting mixture was then allowed to warm to room temperature and stirred for an overnight. After completion, the mixture was quenched with saturated NH_4Cl solution, extracted with EtOAc (2x 10 mL). The combined organic phases were washed with brine and dried over $MgSO_4$, filtered and concentrated *in vacuo* yielding crude ketone product. The crude residue was purified by silica gel flash chromatography (Eluent: EtOAc/Petroleum ether) yielding pure ketone product

2- **1-(*o*-tolyl)propan-2-one (S2)**



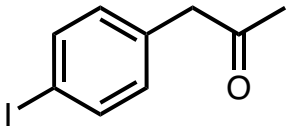
Prepared according to general procedure A**.** Purified by silica gel flash chromatography (Eluent: EtOAc/Petroleum ether, 5%) as a colorless oil in 95% yield (1.40 g). $\mathbf{R_f}$= 0.32 (Eluent: EtOAc/hexane, 10%).^{1}**H NMR** (500 MHz, $CDCl_3$) δ 7.24 – 7.05 (m, 4H), 3.72 (s, 2H), 2.27 (s, 3H), 2.14 (s, 3H).^{13}**C NMR** (126 MHz, $CDCl_3$) δ 206.0, 136.7, 133.1, 130.3, 130.2, 127.2, 126.1, 48.9, 29.0, 19.6. The NMR data is consistent with literature.[2]

3- **1-mesitylpropan-2-one (S3)**



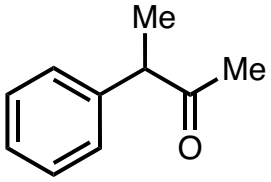
Prepared according to general procedure A**.** Purified by silica gel flash chromatography (Eluent: EtOAc/Petroleum ether, 5%) as a white crystal in 98% yield (1.73 g). $\mathbf{R_f}$= 0.25 (Eluent: EtOAc/hexane, 10%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 6.91 (s, 2H), 3.75 (s, 2H), 2.30 (s, 3H), 2.24 (s, 6H), 2.17 (s, 3H).**^{13}C NMR** (126 MHz, $CDCl_3$) δ 206.6, 136.6, 136.4, 129.1, 129.0, 44.8, 29.3, 20.9, 20.3. The NMR data is consistent with literature.[3]

4- **1-(4-iodophenyl)propan-2-one (S4)**



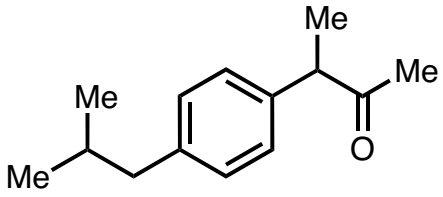
Prepared according to general procedure A**.** Purified by silica gel flash chromatography (Eluent: EtOAc/Petroleum ether, 5%) as a white solid in 93% yield (2.08 g). $\mathbf{R_f}$=0.22 (Eluent: EtOAc/hexane, 10%). **m.p.**= 51- 54 °C. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.69 – 7.63 (m, 2H), 6.96 – 6.93 (m, 2H), 3.64 (s, 2H), 2.16 (s, 3H).**^{13}C NMR** (126 MHz, $CDCl_3$) δ 205.5, 137.9, 133.8, 131.5, 92.7, 50.3, 29.5. **IR** (thin film): ν_{max}: 2916, 2893, 1709, 1483, 1402, 1354, 1319, 1161, 1098, 1057, 1005, 851, 831, 779 cm^{-1}. **HRMS** (ASAP-HESI) m/z: $[M]^+$ Calcd for C_9H_9OI 259.96926, found: 259.9694.

5- **3-phenylbutan-2-one (S5)**



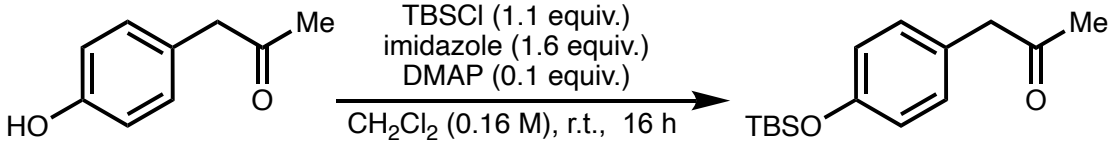
Prepared according to general procedure A**.** Purified by silica gel flash chromatography (Eluent: EtOAc/Petroleum ether, 5%) as a colorless oil in 93% yield (1.37 g). **R_f**=0.67 (Eluent: EtOAc/hexane, 10%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.35 – 7.29 (m, 2H), 7.28 – 7.21 (m, 1H), 7.22 – 7.18 (m, 2H), 3.73 (q, *J* = 7.0 Hz, 1H), 2.02 (s, 3H), 1.38 (d, *J* = 7.0 Hz, 3H).**^{13}C NMR** (126 MHz, $CDCl_3$) δ 208.6, 140.6, 128.9, 127.8, 127.1, 53.6, 28.3, 17.2. The NMR data is consistent with literature.[4]

6- **3-(4-isobutylphenyl)butan-2-one (S6)**



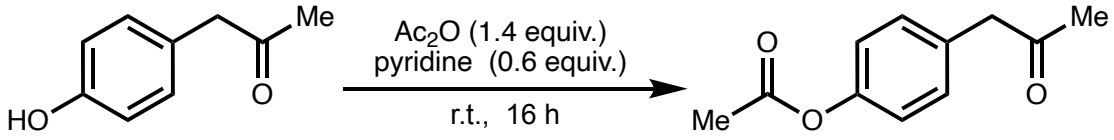
Prepared according to general procedure A**.** Purified by silica gel flash chromatography (Eluent: EtOAc/Petroleum ether, 5%) as a colorless oil in 97% yield (1.85 g). **R_f**=0.43 (Eluent: EtOAc/hexane, 10%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.11 (s, 4H), 3.71 (q, *J* = 7.0 Hz, 1H), 2.45 (d, *J* = 7.2 Hz, 2H), 2.04 (s, 3H), 1.84 (hept, *J* = 6.6 Hz, 1H), 1.37 (d, *J* = 7.0 Hz, 3H), 0.89 (d, *J* = 6.7 Hz, 6H).**^{13}C NMR** (126 MHz, $CDCl_3$) δ 208.8, 140.4, 137.7, 129.5, 127.4, 53.2, 44.9, 30.1, 28.2, 22.3, 17.1. **IR** (thin film): V_{max}: 2955, 2929, 2868, 1713, 1512, 1419, 1352, 1165, 1067, 1020, 848, 800 cm^{-1}. **HRMS** (ASAP-HESI) m/z: $[M]^+$ Calcd for $C_{14}H_{20}O$ 204.15087, found: 204.1504.

7- **1-(4-((*tert*-butyldimethylsilyl)oxy)phenyl)propan-2-one (S7)**



A 250 mL round-bottomed flask equipped with a magnetic stirrer bar was charged with 1-(4-hydroxyphenyl) propan-2-one (10.0 mmol), *tert*-butyldimethylsilyl chloride (1.65 g, 11 mmol, 1.1 equiv.), imidazole (1.09 g, 16 mmol, 1.6 equiv.), DMAP (0.122 g, 1 mmol, 0.1 equiv.), and CH_2Cl_2 (60 mL). The mixture was allowed to stir at room temperature overnight. After completion, the reaction was quenched with water and extracted with CH_2Cl_2 (2 × 30 mL). The combined organic phases were dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The crude residue was purified by silica gel flash chromatography (Eluent: EtOAc/ Petroleum ether, 2%) yielding the pure product as a colorless oil in 95% yield (2.5 g). $\mathbf{R_f}$= 1.59 (Eluent: EtOAc/hexane, 10%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.08 – 7.02 (m, 2H), 6.81 – 6.77 (m, 2H), 3.60 (s, 2H), 2.11 (s, 3H), 0.98 (s, 9H), 0.19 (s, 3H).**^{13}C NMR** (126 MHz, $CDCl_3$) δ 207.0, 154.8, 130.4, 127.0, 120.4, 50.3, 29.1, 25.7, 18.2, -4.3. The NMR data is consistent with literature.[5]

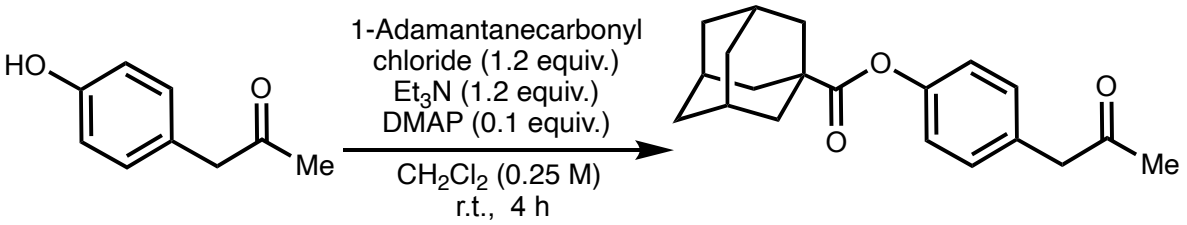
8- **4-(2-oxopropyl)phenyl acetate (S8)**



A 25 mL round-bottomed flask equipped with a magnetic stirrer bar was charged with 1-(4-hydroxyphenyl) propan-2-one (13.0 mmol), acetic anhydride (1.75 mL, 18 mmol, 1.4 equiv.), and pyridine (0.65 mL, 8 mmol, 0.6 equiv.), The mixture was allowed to stir up to room temperature overnight. After completion, the mixture was quenched with water, extracted with EtOAc (2x 10 mL). The combined organic phases were washed with brine and dried over $MgSO_4$, filtered and concentrated *in vacuo*. The crude residue was purified

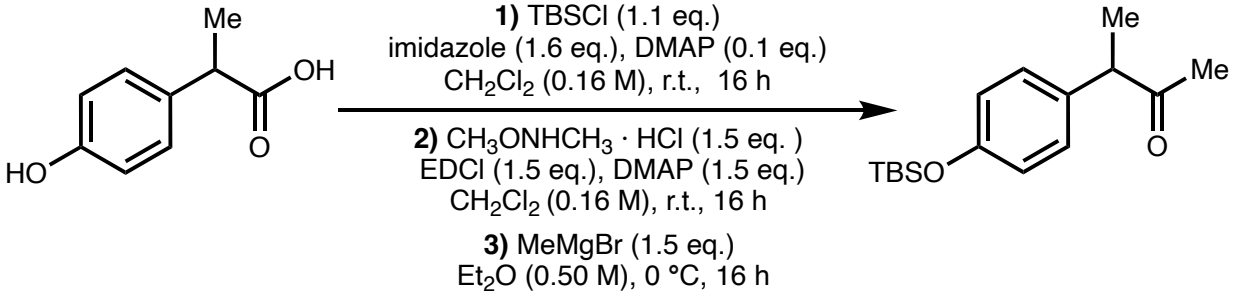
by silica gel flash chromatography (Eluent: EtOAc/ Petroleum ether, 4-8%) yielding pure product as a colorless oil in 94% yield (2.3 g). **R_f**= 0.33 (Eluent: EtOAc/hexane, 20%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.24 – 7.19 (m, 2H), 7.08 – 7.04 (m, 2H), 3.69 (s, 2H), 2.30 (s, 3H), 2.17 (s, 3H).**^{13}C NMR** (126 MHz, $CDCl_3$) δ 206.2, 169.6, 149.7, 131.8, 130.5, 121.9, 50.3, 29.5, 21.3. The NMR data is consistent with literature.[6]

9- **4-(2-oxopropyl)phenyl (3*r*,5*r*,7*r*)-adamantane-1-carboxylate (S9)**



A 25 mL round-bottomed flask equipped with a magnetic stirrer bar was charged with 1-(4-hydroxyphenyl) propan-2-one (6.65 mmol), 1-Adamantanecarbonyl chloride (1.58 g, 7.9 mmol, 1.2 equiv.), Et_3N (1.1 mL, 7.9 mmol, 1.2 equiv.), DMAP (0.8 g, 0.66 mmol, 0.1 equiv.) and CH_2Cl_2 (27 mL). The mixture was allowed to stir at room temperature overnight. After completion, the mixture was quenched with sat. aq. $NaHCO_3$ (10 mL) and extracted with CH_2Cl_2 (2 x 10 mL). The combined organic phases were washed with brine and dried over $MgSO_4$, filtered and concentrated *in vacuo*. The crude residue was purified by silica gel flash chromatography (Eluent: EtOAc/Petroleum ether, 10-15%) yielding pure product as a colorless solid in 82% yield (1.7 g). **R_f**= 0.67 (Eluent: EtOAc/hexane, 30%). **m.p.**= 71-77 °C. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.22 – 7.17 (m, 2H), 7.06 – 6.99 (m, 2H), 3.67 (s, 2H), 2.15 (s, 3H), 2.10 – 2.01 (m, 9H), 1.82 – 1.71 (m, 6H).**^{13}C NMR** (126 MHz, $CDCl_3$) δ 206.2, 176.2, 150.3, 131.5, 130.4, 121.9, 5.4, 41.1, 38.8, 36.5, 29.3, 28.0. **IR** (thin film): V_{max}: 2905, 2851, 1739, 1715, 1508, 1452, 1418, 1323,1219, 1198, 1157, 1055, 1020, 866 cm^{-1}. **HRMS** (ASAP-HESI) m/z: $[M+H]^+$ Calcd for $C_{20}H_{25}O_3$ 313.1804, found: 313.1803.

10-**3-(4-((*tert*-butyldimethylsilyl)oxy)phenyl)butan-2-one (S10)**



Protection of phenol:

A 250 mL round-bottomed flask equipped with a magnetic stirrer bar was charged with 2-(4-hydroxyphenyl) propanoic acid (10.0 mmol), *tert*-butyldimethylsilyl chloride (1.65 g, 11 mmol, 1.1 equiv.), imidazole (1.09 g, 16 mmol, 1.6 equiv.), DMAP (0.122 g, 1 mmol, 0.1 equiv.), and CH_2Cl_2 (60 mL). The mixture was allowed to stir at room temperature overnight. After completion, the reaction was quenched with water and extracted with CH_2Cl_2 (2 × 30 mL). The combined organic phases were dried over $MgSO_4$. The mixture was concentrated *in vacuo* and used in the next step without further purification.

Weinreb amide synthesis:

A 250 mL round-bottomed flask equipped with a magnetic stirrer bar was charged with acid (10.0 mmol), *N*,*O*-Dimethylhydroxylamine (1.46 g, 15 mmol, 1.50 equiv.) , 1-(3-Dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (2.87 g, 15 mmol, 1.50 equiv.), 4-Dimethylaminopyridine (DMAP) (1.83 g, 15 mmol, 1.50 equiv.) and CH_2Cl_2 (60 mL). The mixture was left to react at room temperature overnight. After this period, the reaction mixture was quenched with water (80 mL). The phases were separated, and the aqueous layer was extracted with CH_2Cl_2 (2 x 50 mL). The combined organic phases were dried over $MgSO_4$. The mixture was concentrated *in vacuo* and used in the next step without further purification.

Ketone synthesis:

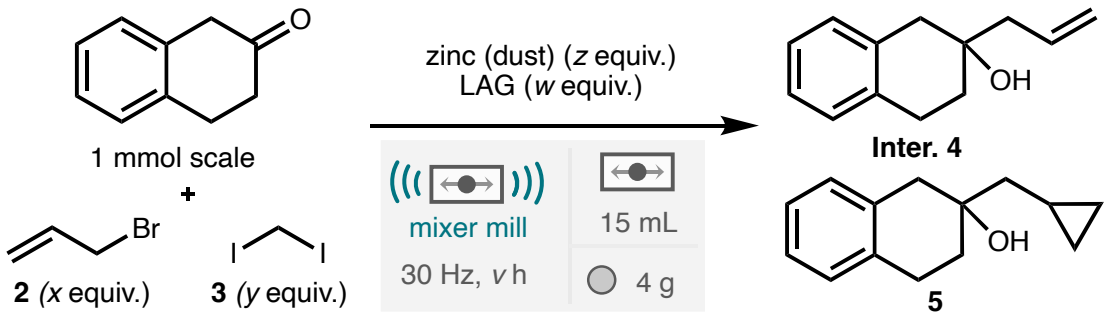
To a stirred solution of Weinreb amide product (1 equiv.) in Et_2O (0.5 M) under a nitrogen atmosphere, was added Methylmagnesium bromide (1.5 equiv.) dropwise at 0 °C. The

resulting mixture was then allowed to warm to room temperature and stirred for an overnight. After completion, the mixture was quenched with saturated NH_4Cl solution, extracted with EtOAc (2x 10 mL). The combined organic phases were washed with brine and dried over $MgSO_4$, filtered and concentrated *in vacuo* yielding crude ketone product. The crude residue was purified by silica gel flash chromatography (Eluent: EtOAc/Petroleum ether, 4-8%) yielding pure product as a colorless oil in 65% yield (1.70 g). $\mathbf{R_f}$= 0.75 (Eluent: EtOAc/hexane, 30%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.07 – 7.01 (m, 2H), 6.80 – 6.74 (m, 2H), 3.64 (q, *J* = 7.0 Hz, 1H), 1.99 (s, 3H), 1.32 (d, *J* = 7.8 Hz, 3H), 0.96 (s, 9H), 0.17 (s, 6H).**^{13}C NMR** (126 MHz, $CDCl_3$) δ 208.9, 154.7, 133.3, 128.7, 120.4, 52.9, 28.1, 25.6, 18.1, 17.2, -4.4. **IR** (thin film): V_{max}: 2956, 2929, 2858, 1714, 1604, 1508, 1471, 1462, 1354, 1251, 1170, 1066, 1006, 910, 835, 779 cm^{-1}. **HRMS** (ASAP-HESI) m/z: $[M+H]^+$ Calcd for $C_{16}H_{27}O_2Si$ 279.1780, found: 279.1773.

4. **Full Optimization Details & Control Experiments:**

I. **Optimization of the mechanochemical one pot Barbier/Simmons–Smith reaction:**

To a 15 mL stainless jar charged with one 4 g stainless steel ball, β-tetralone (1.00 mmol), allyl bromide, diiodomethane, zinc metal, and 2-MeTHF were added and milled at 30 Hz for *v* h at room temperature in a Insolido Tech mixer mill. After the milling period the jar was opened and rinsed into a conical flask using CH_2Cl_2 (20.00 mL). 1.0 M HCl (10.00 mL) was added to the flask and stirred for 10 minutes. The resulting biphasic mixture was transferred to a separating funnel where the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (2 x 15.00 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated *in vacuo* yielding the crude product.

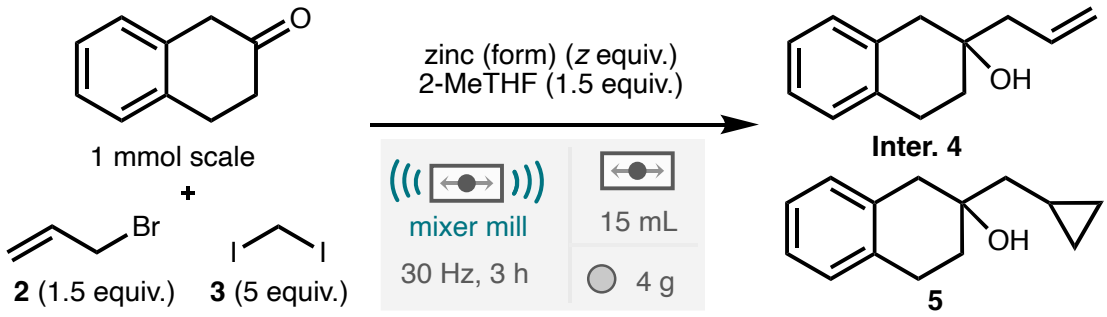


Entry	(2) eq.	(3) eq.	Zn eq.	LAG (eq.)	GA	Time (v)	SM[a] (%)	Inter. 4[a] (%)	FP[a] (%)
1	1.5	5	7	2-MeTHF (1.5)	—	3	Less than 2	8	52
2	1.5	5	7	—	—	3	16	38	17
3	1.5	2.5	7	2-MeTHF (1.5)	—	3	35	40	22
4	1.5	3.5	7	2-MeTHF (1.5)	—	3	4	19	42
5	1.5	7.5	7	2-MeTHF (1.5)	—	3	Less than 2	5	51
6	1.5	5	5	2-MeTHF (1.5)	—	3	Less than 2	14	39
7	1.5	5	10	2-MeTHF (1.5)	—	3	Less than 2	2	62 (54)
8	1.5	5	10	DMSO (1.5)	—	3	Less than 2	6	48

Entry	(2) eq.	(3) eq.	Zn eq.	LAG (eq.)	GA	Time (v)	SM[a] (%)	Inter. 4[a] (%)	FP[a] (%)
9	1.5	5	10	DMA (1.5)	—	3	Less than 2	3	43
10	1.5	5	10	2-MeTHF (3.5)	—	3	Less than 2	4	55
11	1.5	5	10	—	—	3	17	42	19
12	1.5	7.5	10	2-MeTHF (1.5)	—	3	Less than 2	5	61
13	1,5	3.5	10	2-MeTHF (1.5)	—	3	Less than 2	10	51
14	1.1	5	10	2-MeTHF (1.5)	—	3	Less than 2	5	53
15	1.5	5	10	2-MeTHF (1.5)	—	2	Less than 2	3	58 (53)
16	1.5	5	10	2-MeTHF (1.5)	—	1	Less than 2	9	53
17	1.5	5	10	2-MeTHF (1.5)	Sand (3ME)	3	Less than 2	4	58
18	1.5	5	10	2-MeTHF (1.5)	$NaSO_4$(3ME)	3	4	6	53
19	1.5	5	10	2-MeTHF (1.5)	Silica (3ME)	3	27	4	21
20	0	0	10	2-MeTHF (1.5)	—	3	88	0	0

Table S2. Reaction Optimization of the one pot Barbier/Simmons–Smith. [a]Yield determined *via* ^{1}H NMR analysis of the crude reaction mixture using mesitylene (0.33 mmol) as an internal standard.

II. **Zinc form screening:**

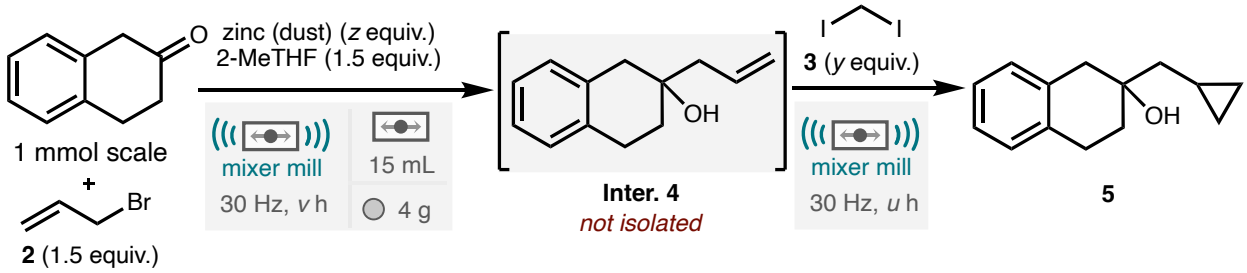


Entry	Zn eq.	Zn form	SM[a] (%)	Inter. 4[a] (%)	FP[a] (%)
1	7	Dust	Less than 2	2	62 (54)
2	7	Granular 20-30 mesh	Less than 2	4	51
3	7	Flake	Less than 2	6	47
4	7	Foil	Less than 2	4	58

Table S3. Zinc form screening. [a]Yield determined *via* ^{1}H NMR analysis of the crude reaction mixture using mesitylene (0.33 mmol) as an internal standard.

III. Optimization of the mechanochemical one pot- two step Barbier/Simmons–Smith reaction:

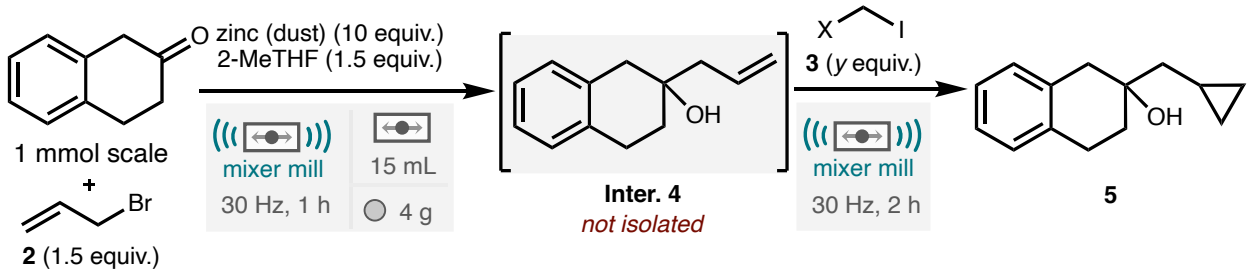
To a 15 mL stainless jar charged with one 4 g stainless steel ball, β-tetralone (1.00 mmol), allyl bromide, zinc metal, and 2-MeTHF were added and milled at 30 Hz for *v* h at room temperature in a Insolido Tech mixer mill. Then the jar was opened and diiodomethane was added and milled at 30 Hz for *u* h at room temperature. After the milling period the jar was opened and rinsed into a conical flask using CH_2Cl_2 (20.00 mL). 1.0 M HCl (10.00 mL) was added to the flask and stirred for 10 minutes. The resulting biphasic mixture was transferred to a separating funnel where the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (2 x 15.00 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated *in vacuo* yielding the crude product.



Entry	(3) eq.	Zn eq.	Cu eq.	Time (*v*+*u*)	SM[a] (%)	Inter. 4[a] (%)	FP[a] (%)
1	5	10	0	1+2	Less than 2	0	68 (64)
2	5	7	0	1+2	Less than 2	4	63
3	5	7	0.5	1+2	Less than 2	Less than 2	61
4	5	5	0	1+2	4	9	55
5	5	5	0	2+2	Less than 2	9	56
6	2.5	10	0	1+2	Less than 2	24	48

Table S4. Reaction optimization of the one pot- two steps Barbier/Simmons–Smith**.** [a]Yield determined *via* ^{1}H NMR analysis of the crude reaction mixture using mesitylene (0.33 mmol) as an internal standard.

IV. **Carbenoid precursor screening:**



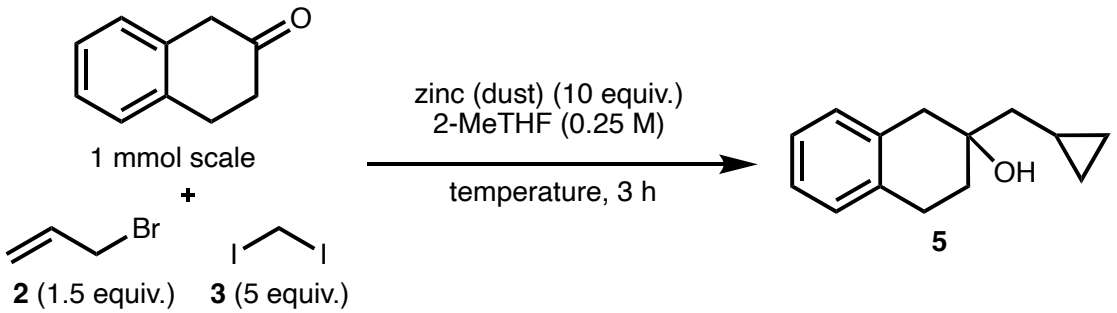
Entry	(3)	FP[a] (%)
1	diiodomethane	68 (64)
2	bromo-iodomethane	63

Table S5. Carbenoid precursor screening. [a]Yield determined *via* ^{1}H NMR analysis of the crude reaction mixture using mesitylene (0.33 mmol) as an internal standard.

V. Solution-Phase Comparisons

General procedure in round bottom flask:

β-tetralone (1.00 mmol), allyl bromide (130 µL, 1.50 mmol, 1.50 equiv.), diiodomethane (403 µL, 5.00 mmol, 5.00 equiv.), zinc metal (653 mg, 10.00 mmol, 10.00 equiv.) and 2-MeTHF (4.00 mL) were added to a 25 mL round bottom flask and refluxed for 3 h. After this time, the reaction mixture was rinsed into a conical flask using CH_2Cl_2 (20.00 mL). 1.0 M HCl (10.00 mL) was added to the flask and stirred for 10 minutes. The resulting biphasic mixture was transferred to a separating funnel where the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (2 x 10.00 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated *in vacuo*.



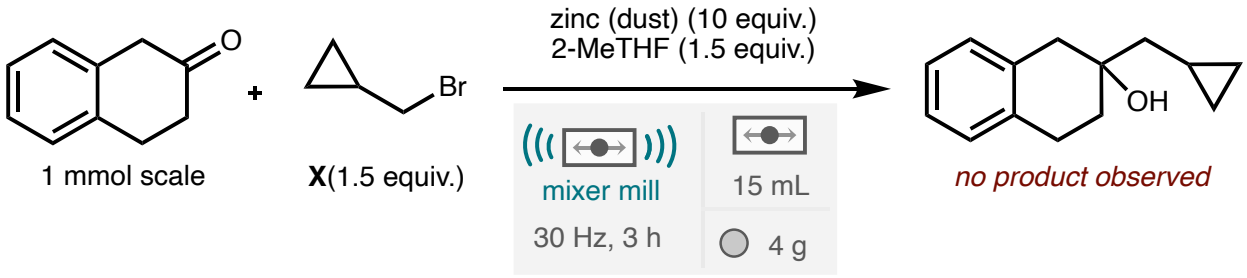
Entry	Inert atmosphere	temperature	SM[a] (%)	Inter. 4[a] (%)	FP[a] (%)
1	No	r.t	89	0	0
2	Yes	r.t	95	0	0
3	No	reflux	3	20	31
4	Yes	reflux	3	12	35

Table S6. Solution-phase comparisons. [a]Yield determined *via* ^{1}H NMR analysis of the crude reaction mixture using mesitylene (0.33 mmol) as an internal standard.

VI. Control reaction:

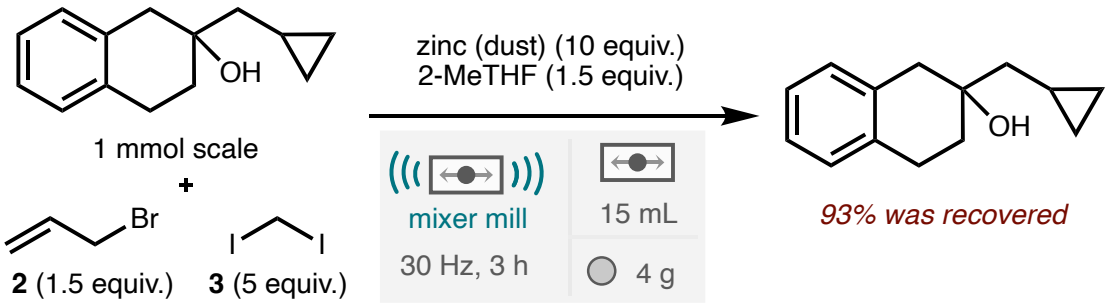
Reaction of ketone with (bromomethyl)cyclopropane:

To a 15 mL stainless jar charged with one 4 g stainless steel ball, β-tetralone (1.00 mmol), (bromomethyl)cyclopropane (145 µL, 1.50 mmol, 1.50 equiv.),zinc metal (653 mg, 10.00 mmol, 10.00 equiv.), and 2-MeTHF (151 µL, 1.50 mmol, 1.50 equiv.) were added and milled at 30 Hz for 3 h at room temperature in a Insolido Tech mixer mill. After the milling period the jar was opened and rinsed into a conical flask using CH_2Cl_2 (20.00 mL). 1.0 M HCl (10.00 mL) was added to the flask and stirred for 10 minutes. The resulting biphasic mixture was transferred to a separating funnel where the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (2 x 15.00 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated *in vacuo*.



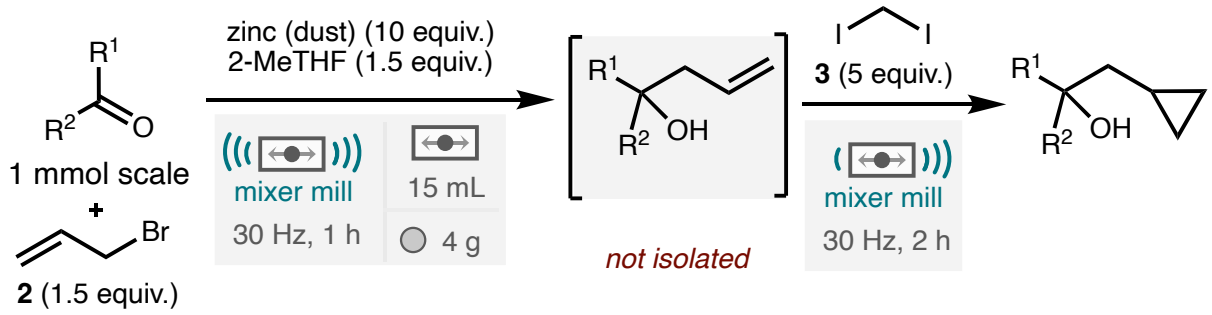
This experiment was conducted to determine whether the reaction could proceed without allyl bromide by using bromomethylcyclopropane as an alternative. However, no product was obtained. This result suggests that allyl bromide plays a crucial role in the reaction mechanism.

Stability of products:



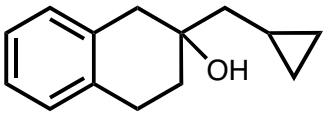
In this experiment, we investigated whether the reaction product would undergo further transformation or remain stable under the same conditions. To test this, the product was re-subjected to the standard reaction conditions. The results confirmed that the product remained unchanged, indicating that the reaction had reached completion, and the product is stable.

5. **General procedure B - Barbier/Simmons–Smith reaction:**



To a 15 mL stainless jar charged with one 4 g stainless steel ball, ketone (1.00 mmol), allyl bromide (130 µL, 1.50 mmol, 1.50 equiv.), zinc metal (653 mg, 10.00 mmol, 10.00 equiv.), and 2-MeTHF (151 µL, 1.50 mmol, 1.50 equiv.) were added and milled at 30 Hz for 1 h at room temperature in a Insolido Tech mixer mill. Then the jar was opened and diiodomethane (403 µL, 5.00 mmol, 5.00 equiv.) was added and milled at 30 Hz for 2 h at room temperature. After the milling period the jar was opened and rinsed into a conical flask using CH_2Cl_2 (20.00 mL). 1.0 M HCl (10.00 mL) was added to the flask and stirred for 10 minutes. The resulting biphasic mixture was transferred to a separating funnel where the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (2 x 15.00 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated *in vacuo* yielding the crude product that was further purified by silica gel flash column chromatography using the noted solvent system.

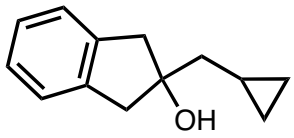
1- **2-(cyclopropylmethyl)-1,2,3,4-tetrahydronaphthalen-2-ol (5)**



Prepared according to general procedure B**.** Purified by silica gel flash chromatography (Eluent: EtOAc/Petroleum ether, 5-10%) as a yellow oil in 64% yield (130 mg). **R_f**= 0.31(Eluent: EtOAc/hexane, 10%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.19 – 6.95 (m, 4H), 3.08 – 3.00 (m, 1H), 2.97 (d, *J* = 17.6 Hz, 1H), 2.88 – 2.75 (m, 2H), 1.97 – 1.91 (m, 1H), 1.90

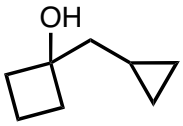
– 1.82 (m, 1H), 1.71 (s, 1H), 1.56 (dd, *J* = 14.2, 6.8 Hz, 1H), 1.49 (dd, *J* = 14.2, 7.0 Hz, 1H), 0.96 – 0.80 (m, 1H), 0.62 – 0.46 (m, 2H), 0.21 – -0.01 (m, 2H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 135.7, 134.7, 129.8, 128.8, 126.0, 125.9, 71.9, 46.1, 42.0, 34.1, 26.3, 5.6, 4.3, 4.2. **IR** (thin film): V_{max}: 3381, 3074, 2999, 2920, 2843, 1581, 1495, 1452, 1427, 1036, 1016, 957, 731 cm^{-1}. **HRMS** (ASAP-HESI) m/z: $[M-H_2O+H]^+$ Calcd for $C_{14}H_{17}$ 185.1330, found: 185.1332.

2- **2-(cyclopropylmethyl)-2,3-dihydro-1*H*-inden-2-ol (6)**



Prepared according to general procedure B**.** Purified by silica gel flash chromatography (Eluent: EtOAc/Petroleum ether, 10-15%) as a colorless oil in 58% yield (109 mg). **R_f** = 0.18 (Eluent: EtOAc/hexane, 10%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.25 – 7.14 (m, 4H), 3.14 (d, *J* = 16.8 Hz, 2H), 2.99 (d, *J* = 16.1 Hz, 2H), 2.03 (s, 1H), 1.70 (d, *J* = 6.8 Hz, 2H), 0.93 – 0.82 (m, 1H), 0.57 – 0.52 (m, 2H), 0.19 – 0.15 (m, 2H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 141.6, 126.6, 125.1, 83.3, 46.8, 45.0, 6.8, 4.3. **IR** (thin film): V_{max}: 3408, 3073, 3001, 2907, 2641, 1481, 1458, 1425, 1219, 1061, 1018, 824, 736 cm^{-1}. **HRMS** (ASAP-HESI) m/z: $[M]^+$ Calcd for $C_{13}H_{16}O$ 188.1195, found: 188.1192.

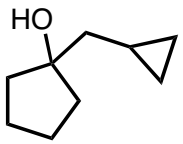
3- **1-(cyclopropylmethyl)cyclobutan-1-ol (7)**



Prepared according to general procedure B**.** Purified by silica gel flash chromatography (Eluent: EtOAc/Petroleum ether, 4-8%) as a colorless oil in 52% yield (65 mg). **R_f** = 0.18

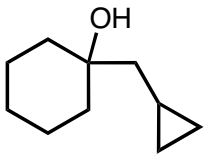
(Eluent: EtOAc/hexane, 10%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 2.22 – 1.95 (m, 5H), 1.79 – 1.68 (m, 1H), 1.57 – 1.53 (m, 2H), 1.53 – 1.46 (m, 1H), 0.81 – 0.70 (m, 1H), 0.53 – 0.45 (m, 2H), 0.15 – 0.09 (m, 2H).**^{13}C NMR** (126 MHz, $CDCl_3$) δ 76.0, 44.0, 35.7, 12.2, 5.8, 3.8. **IR** (thin film): V_{max}: 3341, 2968, 2932, 2882, 1466, 1379, 1304, 1159, 1128, 1107, 951, 816 cm^{-1}. **HRMS** (ASAP-HESI) m/z: $[M-H]^+$ Calcd for $C_8H_{13}O$ 125.09609, found:125.0961.

4- **1-(cyclopropylmethyl)cyclopentan-1-ol (8)**



Prepared according to general procedure B**.** Purified by silica gel flash chromatography (Eluent: EtOAc/Petroleum ether, 4-8%) as a colorless oil in 46% yield (65 mg). **R_f** = 0.27 (Eluent: EtOAc/hexane, 10%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 1.84 – 1.55 (m, 9H), 1.50 (d, *J* = 6.8 Hz, 2H), 0.77 (dddt, *J* = 14.7, 7.9, 6.8, 5.0 Hz, 1H), 0.54 – 0.39 (m, 2H), 0.15 – -0.00 (m, 2H).**^{13}C NMR** (126 MHz, $CDCl_3$) δ 83.3, 45.8, 39.6, 23.8, 6.8, 4.1. **IR** (thin film): V_{max}: 3360, 3076, 2967, 1456, 1379, 1302, 1209, 1159, 1128, 1105, 1016, 951, 874, 818 cm^{-1}. **HRMS** (ASAP-HESI) m/z: $[M-H]^+$ Calcd for $C_9H_{15}O$ 139.11174, found: 139.1117.

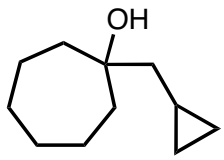
5- **(Cyclopropylmethyl)cyclohexanol (9)**



Prepared according to general procedure B**.** Purified by silica gel flash chromatography (Eluent: EtOAc/Hexane, 5%) as a colorless oil in 58% yield (89 mg). **^{1}H NMR** (500 MHz,

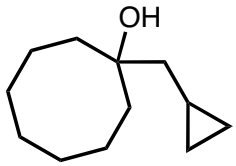
$CDCl_3$) δ 1.69 – 1.41 (m, 10H), 1.37 (d, *J* = 6.9 Hz, 2H), 1.32 – 1.19 (m, 1H), 0.83 – 0.70 (m, 1H), 0.53 – 0.41 (m, 2H), 0.21 – -0.04 (m, 2H).**^{13}C NMR** (126 MHz, $CDCl_3$) δ 72.4, 47.3, 37.6, 26.0, 22.3, 5.4, 4.2.The NMR data is consistent with literature.[7]

6- **1-(cyclopropylmethyl)cycloheptan-1-ol (10)**



Prepared according to general procedure B**.** Purified by silica gel flash chromatography (Eluent: EtOAc/Petroleum ether, 4-8 %) as a colorless oil in 44% yield (73 mg). **R_f** = 0.24 (Eluent: EtOAc/hexane, 10%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 1.71 (dd, *J* = 6.7, 4.0 Hz, 3H), 1.69 – 1.56 (m, 5H), 1.50 (dddd, *J* = 15.9, 10.6, 8.3, 3.7 Hz, 3H), 1.46 – 1.30 (m, 4H), 0.82 – 0.70 (m, 1H), 0.54 – 0.43 (m, 2H), 0.14 – 0.03 (m, 2H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 76.4, 48.2, 41.3, 30.0, 22.5, 5.7, 4.3. **IR** (thin film): V_{max}: 3345, 2970, 2928, 2886, 1464, 1379, 1306, 1159, 1128, 1107, 1030, 951, 816 cm^{-1}. **HRMS** (ASAP-HESI) m/z: $[M-H_2O]^+$ Calcd for $C_{11}H_{18}$ 150.1403 found :150.1400.

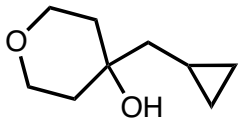
7- **(cyclopropylmethyl)cyclooctan-1-ol (11)**



Prepared according to general procedure B**.** Purified by silica gel flash chromatography (Eluent: EtOAc/Petroleum ether, 10%) as a yellow oil in 48% yield (88 mg). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 1.79 (dd, *J* = 12.5, 10.1 Hz, 2H), 1.68 – 1.53 (m, 8H), 1.52 – 1.35 (m, 7H),

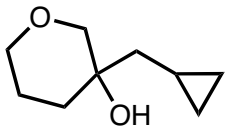
0.91 – 0.69 (m, 1H), 0.57 – 0.37 (m, 2H), 0.16 – 0.01 (m, 2H).**^{13}C NMR** (126 MHz, $CDCl_3$) δ 75.7, 46.3, 36.3, 28.4, 25.0, 22.3, 5.5, 4.2. The NMR data is consistent with literature.[8]

8- **4-(cyclopropylmethyl)tetrahydro-2*H*-pyran-4-ol (12)**



Prepared according to general procedure B**.** Purified by silica gel flash chromatography (Eluent: EtOAc/Petroleum ether, 20%) as a yellow oil in 60% yield (94 mg). **R_f** = 0.11 (Eluent: EtOAc/hexane, 20%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 3.80 (td, *J* = 11.3, 2.6 Hz, 2H), 3.75 (ddd, *J* = 11.7, 5.2, 3.4 Hz, 2H), 1.75 (ddd, *J* = 13.6, 11.2, 5.2 Hz, 2H), 1.58 – 1.53 (m, 3H), 1.42 (d, *J* = 6.9 Hz, 2H), 0.83 – 0.70 (m, 1H), 0.54 – 0.46 (m, 2H), 0.14 – 0.07 (m, 2H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 69.8, 63.9, 48.0, 37.8, 4.9, 4.1. **IR** (thin film): Vmax: 3410, 3076, 2999, 2954, 2914, 2868, 1466, 1427, 1387, 1298, 1238, 1173, 1098, 1015, 951, 906, 841 cm^{-1}. **HRMS** (ASAP-HESI) m/z: $[M-H]^+$ Calcd for $C_9H_{15}O_2$ 155.1066, found: 155.1062.

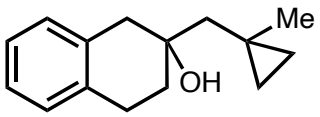
9- **3-(cyclopropylmethyl)tetrahydro-2*H*-pyran-3-ol (13)**



Prepared according to general procedure B**.** Purified by silica gel flash chromatography (Eluent: EtOAc/Petroleum ether, 10-15%) as a colorless oil in 55% yield (86 mg). **R_f** = 0.15 (Eluent: EtOAc/hexane, 20%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 3.85 (dt, *J* = 11.3, 3.5 Hz, 1H), 3.61 (dd, *J* = 11.4, 2.4 Hz, 1H), 3.45 – 3.37 (m, 2H), 2.00 – 1.84 (m, 2H), 1.78 (dtdd, *J* = 13.3, 4.1, 2.4, 1.5 Hz, 1H), 1.62 (ddd, *J* = 13.6, 11.6, 4.9 Hz, 1H), 1.58 – 1.49

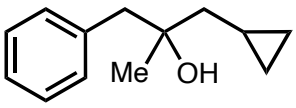
(m, 1H), 1.40 (dd, *J* = 14.3, 6.8 Hz, 1H), 1.34 (dd, *J* = 14.3, 6.9 Hz, 1H), 0.84 – 0.73 (m, 1H), 0.52 – 0.45 (m, 2H), 0.09 – 0.02 (m, 2H).**^{13}C NMR** (126 MHz, $CDCl_3$) δ 76.1, 70.1, 68.3, 43.3, 34.3, 22.4, 5.1, 4.5. **IR** (thin film): V_{max}: 3437, 3076, 3003, 2943, 2851, 1464, 1445, 1304, 1202, 1157, 1086, 1017, 905, 843, 727 cm^{-1}. **HRMS** (ASAP-HESI) m/z: $[M]^+$ Calcd for $C_9H_{16}O_2$ 156.1144, found: 156.1140.

10- **2-((1-methylcyclopropyl)methyl)-1,2,3,4-tetrahydronaphthalen-2-ol (14)**



Prepared according to general procedure B**.** Purified by silica gel flash chromatography (Eluent: EtOAc/Petroleum ether, 5-10%) as a yellow oil in 58% yield (103 mg). **R_f**= 0.32 (Eluent: EtOAc/hexane, 10%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.18 – 7.06 (m, 4H), 3.11 – 2.97 (m, 2H), 2.90 (d, *J* = 17.2 Hz, 1H), 2.81 (dt, *J* = 17.2, 5.4 Hz, 1H), 1.97 (dddd, *J* = 13.1, 6.5, 4.7, 1.9 Hz, 1H), 1.88 – 1.76 (m, 1H), 1.76 – 1.61 (m, 2H), 1.50 (d, *J* = 14.7 Hz, 1H), 1.26 (s, 3H), 0.59 – -0.09 (m, 4H).**^{13}C NMR** (126 MHz, $CDCl_3$) δ 135.6, 134.7, 129.9, 128.8, 126.0, 125.9, 72.7, 50.3, 42.5, 35.2, 26.1, 25.0, 13.9, 13.8, 12.7. **IR** (thin film): V_{max}: 3448, 3067, 2995, 2922, 1514, 1495, 1452, 1429, 1383, 1271, 1227, 1175, 1096, 1080, 1040, 1011, 964, 937, 883, 764 cm^{-1}. **HRMS** (ASAP-HESI) m/z: $[M-H_2O]^+$ Calcd for $C_{15}H_{18}$ 198.1401, found: 198.14030.

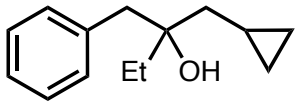
11- **1-cyclopropyl-2-methyl-3-phenylpropan-2-ol (16)**



Prepared according to general procedure B**.** Purified by silica gel flash chromatography (Eluent: EtOAc/Petroleum ether, 5%) as a colorless oil in 56% yield (106 mg). **R_f**= 0.23

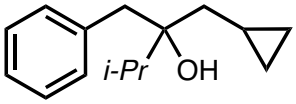
(Eluent: EtOAc/hexane, 10%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.28 – 7.20 (m, 2H), 7.20 – 7.11 (m, 3H), 2.78 (d, *J* = 13.3 Hz, 1H), 2.72 (d, *J* = 13.4 Hz, 1H), 1.61 (s, 1H), 1.39 (dd, *J* = 14.0, 6.7 Hz, 1H), 1.34 (dd, *J* = 14.0, 6.8 Hz, 1H), 1.15 (s, 3H), 0.82 – 0.69 (m, 1H), 0.51 – 0.42 (m, 2H), 0.17 – -0.04 (m, 2H).**^{13}C NMR** (126 MHz, $CDCl_3$) δ 137.7, 130.6, 128.1, 126.4, 73.4, 48.3, 46.7, 26.7, 6.2, 4.7, 4.3. **IR** (thin film): V_{max}: 3356, 3074, 3028, 2971, 2927, 2884, 2363, 1464, 1377, 1341, 1304, 1159, 1128, 1103, 1018, 951, 883, 816 cm^{-1}. **HRMS** (ASAP-HESI) m/z: $[M- H_2O]^+$ Calcd for $C_{13}H_{16}$ 172.1246, found: 172.12465.

12- **2-benzyl-1-cyclopropylbutan-2-ol (17)**



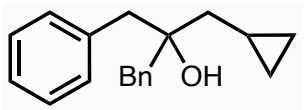
Prepared according to general procedure B**.** Purified by silica gel flash chromatography (Eluent: EtOAc/Petroleum ether, 5%) as a yellow oil in 61% yield (124 mg). **R_f**= 0.48 (Eluent: EtOAc/hexane, 10%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.31 – 7.13 (m, 5H), 2.79 (d, *J* = 13.5 Hz, 1H), 2.75 (d, *J* = 13.6 Hz, 1H), 1.56 – 1.43 (m, 2H), 1.37 (dd, *J* = 14.2, 6.7 Hz, 1H), 1.32 (dd, *J* = 14.2, 6.8 Hz, 1H), 1.20 (s, 1H), 0.89 (t, *J* = 7.5 Hz, 3H), 0.78 – 0.65 (m, 1H), 0.56 – 0.41 (m, 2H), 0.07 – 0.00 (m, 2H).**^{13}C NMR** (126 MHz, $CDCl_3$) δ 137.7, 130.7, 128.2, 126.4, 75.3, 45.4, 43.1, 31.3, 8.4, 5.8, 4.5, 4.4. **IR** (thin film): V_{max}: 3354, 2968, 2924, 2855, 2358, 1454, 1416, 1377, 1304, 1159, 1126, 1030, 951, 874 cm^{-1}. **HRMS** (ASAP-HESI) m/z: $[M- H_2O]^+$ Calcd for $C_{14}H_{18}$ 186.1430, found: 186.1402.

13- **2-benzyl-1-cyclopropyl-3-methylbutan-2-ol (18)**



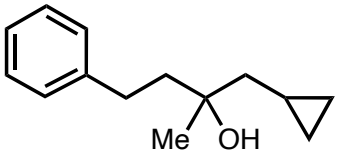
Prepared according to general procedure B**.** Purified by silica gel flash chromatography (Eluent: EtOAc/Petroleum ether, 5%) as a yellow oil in 63% yield (137 mg). $\mathbf{R_f}$= 0.53 (Eluent: EtOAc/hexane, 10%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.62 – 6.98 (m, 5H), 2.86 (d, *J* = 13.7 Hz, 1H), 2.80 (d, *J* = 13.6 Hz, 1H), 1.96 (hept, *J* = 6.9 Hz, 1H), 1.60 – 1.47 (m, 2H), 1.20 (dd, *J* = 14.5, 7.0 Hz, 1H), 1.02 (d, *J* = 6.8 Hz, 3H), 0.95 (d, *J* = 6.9 Hz, 3H), 0.81 – 0.65 (m, 1H), 0.52 – 0.41 (m, 2H), 0.11 – -0.07 (m, 2H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 138.1, 130.9, 128.2, 126.3, 41.8, 40.4, 34.6, 17.4, 17.4, 5.4, 4.7, 4.4. **IR** (thin film): V_{max}: 3586, 3075, 3028, 2959, 2933, 2363, 1495, 1454, 1366, 1082, 1032, 822 cm^{-1}. **HRMS** (ASAP-HESI) m/z: $[M- H]^+$ Calcd for $C_{15}H_{21}O$ 217.1586, found: 217.1586.

14- **2-benzyl-1-cyclopropyl-3-phenylpropan-2-ol (19)**



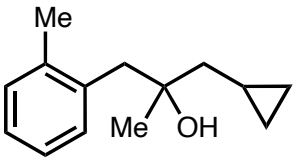
Prepared according to general procedure B**.** Purified by silica gel flash chromatography (Eluent: EtOAc/Petroleum ether, 5-10%) as a yellow oil in 58% yield (155 mg). $\mathbf{R_f}$= 0.38 (Eluent: EtOAc/hexane, 10%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.78 – 6.94 (m, 10H), 2.92 (d, *J* = 13.7 Hz, 2H), 2.85 (d, *J* = 13.7 Hz, 2H), 1.63 (s, 1H), 1.36 (d, *J* = 6.6 Hz, 2H), 0.94 – 0.78 (m, 1H), 0.65 – 0.44 (m, 2H), 0.14 – 0.02 (m, 2H).**^{13}C NMR** (126 MHz, $CDCl_3$) δ 137.7, 130.9, 128.2, 126.4, 75.1, 45.9, 43.7, 5.9, 4.8. **IR** (thin film): V_{max}: 3332, 2970, 2932, 2882, 1466, 1406, 1379, 1341, 1304, 1159, 1128, 1107, 951, 816 cm^{-1}. **HRMS** (ASAP-HESI) m/z: $[M- H_2O]^+$ Calcd for $C_{19}H_{20}$ 248.1559, found: 248.1559.

15- **1-cyclopropyl-2-methyl-4-phenylbutan-2-ol (20)**



Prepared according to general procedure B**.** Purified by silica gel flash chromatography (Eluent: EtOAc/Petroleum ether, 5-10%) as a colorless oil in 64% yield (131 mg). **R_f**= 0.28 (Eluent: EtOAc/hexane, 10%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.31 – 7.27 (m, 2H), 7.23 – 7.15 (m, 3H), 2.74 – 2.66 (m, 2H), 1.92 – 1.79 (m, 2H), 1.54 (s, 1H), 1.48 (d, *J* = 6.8 Hz, 2H), 1.31 (s, 3H), 0.84 – 0.66 (m, 1H), 0.55 – 0.41 (m, 2H), 0.17 – 0.04 (m, 2H).**^{13}C NMR** (126 MHz, $CDCl_3$) δ 142.8, 128.5, 128.4, 125.8, 73.6, 46.8, 44.0, 30.5, 27.1, 6.1, 4.4, 4.3. **IR** (thin film): V_{max}: 3385, 3075, 3024, 2970, 2913, 2359, 1495, 1454, 1373, 1016, 822, 739 cm^{-1}. **HRMS** (ASAP-HESI) m/z: $[M-H]^+$ Calcd for $C_{14}H_{19}O$ 203.14304, found: 203.1428.

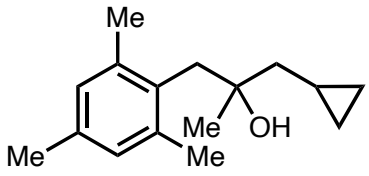
16- **1-cyclopropyl-2-methyl-3-(*o*-tolyl)propan-2-ol (21)**



Prepared according to general procedure B**.** Purified by silica gel flash chromatography (Eluent: EtOAc/Petroleum ether, 2-4%) as a colorless oil in 49% yield (99 mg). **R_f**= 0.3 (Eluent: EtOAc/hexane, 10%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.26 – 7.23 (m, 1H), 7.22 – 7.14 (m, 3H), 2.92 (d, *J* = 13.6 Hz, 1H), 2.86 (d, *J* = 13.6 Hz, 1H), 2.40 (s, 3H), 1.70 (s, 1H), 1.51 (h, *J* = 7.0 Hz, 2H), 1.26 (s, 3H), 0.96 – 0.81 (m, 1H), 0.59 – 0.52 (m, 2H), 0.15 (tdd, *J* = 4.9, 2.5, 1.2 Hz, 2H).**^{13}C NMR** (126 MHz, $CDCl_3$) δ 137.7, 136.1, 131.5, 130.6, 126.5, 125.6, 74.4, 47.3, 44.1, 26.8, 20.6, 6.2, 4.7, 4.4. **IR** (thin film): V_{max}: 3456, 3075,

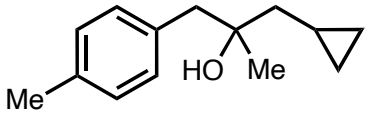
2995, 2970, 2916, 1491, 1458, 1427, 1375, 1256, 1117, 1016, 932, 881, 821 cm^{-1}. **HRMS** (ASAP-HESI) m/z: $[M- H_2O]^+$ Calcd for $C_{14}H_{18}$ 186.14030, found: 186.1401.

17- **1-cyclopropyl-3-mesityl-2-methylpropan-2-ol (22)**



Prepared according to general procedure B**.** Purified by silica gel flash chromatography (Eluent: EtOAc/Petroleum ether, 2-4%) as a colorless oil in 38% yield (88 mg). $\mathbf{R_f}$= 0.39 (Eluent: EtOAc/hexane, 10%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 6.87 (s, 2H), 2.99 (d, *J* = 14.2 Hz, 1H), 2.87 (d, *J* = 14.2 Hz, 1H), 2.35 (s, 6H), 2.26 (s, 3H), 1.53 (d, *J* = 6.7 Hz, 2H), 1.46 (s, 1H), 1.24 (s, 3H), 0.95 – 0.80 (m, 1H), 0.67 – 0.39 (m, 2H), 0.16 – 0.07 (m, 2H) **^{13}C NMR** (126 MHz, $CDCl_3$) δ 138.4, 135.5, 131.7, 129.3, 75.7, 48.2, 39.9, 27.5, 21.6, 20.9, 6.4, 4.7, 4.6. **IR** (thin film): V_{max}: 3453, 3075, 2980, 2916, 2866, 2241, 1458, 1375, 1167, 1016, 968, 907, 853, 731 cm^{-1}. **HRMS** (ASAP-HESI) m/z: $[M- H_2O]^+$ Calcd for $C_{16}H_{22}$ 214.17160, found: 214.1716.

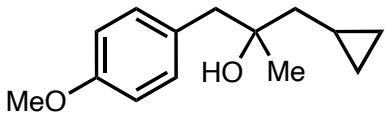
18- **1-cyclopropyl-2-methyl-3-(*p*-tolyl)propan-2-ol (23)**



Prepared according to general procedure B**.** Purified by silica gel flash chromatography (Eluent: EtOAc/Petroleum ether, 5%) as a colorless oil in 52% yield (106 mg). $\mathbf{R_f}$= 0.26 (Eluent: EtOAc/hexane, 10%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.14 (s, 4H), 2.83 (d, *J* = 13.3 Hz, 1H), 2.77 (d, *J* = 13.4 Hz, 1H), 2.36 (s, 3H), 1.68 (s, 1H), 1.47 (dd, *J* = 14.0, 6.7 Hz,

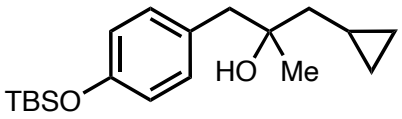
1H), 1.42 (dd, *J* = 14.0, 6.8 Hz, 1H), 1.23 (s, 3H), 0.93 – 0.76 (m, 1H), 0.61 – 0.51 (m, 2H), 0.15 – 0.10 (m, 2H).**^{13}C NMR** (126 MHz, $CDCl_3$) δ 135.8, 134.5, 130.5, 128.8, 73.4, 47.8, 46.6, 26.7, 21.0, 6.2, 4.7, 4.3. **IR** (thin film): V_{max}: 3345, 3079, 2970, 2928, 2884, 2359, 1514, 1458, 1377, 1341, 1304, 1159, 1128, 1018, 951, 816 cm^{-1}. **HRMS** (ASAP-HESI) m/z: $[M- H_2O]^+$ Calcd for $C_{14}H_{18}$ 186.1403, found: 186.1403.

19- **1-cyclopropyl-3-(4-methoxyphenyl)-2-methylpropan-2-ol (24)**



Prepared according to general procedure B**.** Purified by silica gel flash chromatography (Eluent: EtOAc/Petroleum ether, 5-10%) as a colorless oil in 53% yield (117 mg). **R_f**= 0.19 (Eluent: EtOAc/hexane, 10%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.20 – 7.11 (m, 2H), 6.87 – 6.83 (m, 2H), 3.80 (s, 3H), 2.78 (d, *J* = 13.5 Hz, 1H), 2.73 (d, *J* = 13.5 Hz, 1H), 1.57 (s, 1H), 1.46 – 1.37 (m, 2H), 1.20 (s, 3H), 0.89 – 0.73 (m, 1H), 0.55 – 0.43 (m, 2H), 0.21 – 0.02 (m, 2H).**^{13}C NMR** (126 MHz, $CDCl_3$) δ 158.4, 131.6, 129.8, 113.7, 73.5, 55.3, 47.4, 46.6, 26.7, 6.2, 4.7, 4.4. **IR** (thin film): V_{max}: 3456, 3075, 2980, 2911, 2835, 1611, 1510, 1462, 1300, 1244, 1177, 1034, 826 cm^{-1}. **HRMS** (ASAP-HESI) m/z: $[M- H_2O+H]^+$ Calcd for $C_{14}H_{19}O$ 203.1436, found: 203.1436.

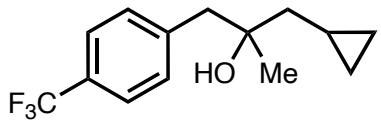
20- **1-(4-((*tert*-butyldimethylsilyl)oxy)phenyl)-3-cyclopropyl-2-methylpropan-2-ol (26)**



Prepared according to general procedure B**.** Purified by silica gel flash chromatography (Eluent: EtOAc/Petroleum ether, 2-4%) as a colorless oil in 46% yield (147 mg). **R_f** = 0.40 (Eluent: EtOAc/hexane, 10%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.11 – 7.03 (m, 2H), 6.80 –

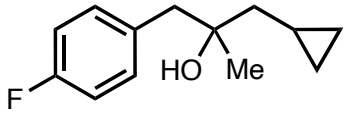
6.75 (m, 2H), 2.76 (d, *J* = 13.5 Hz, 1H), 2.71 (d, *J* = 13.5 Hz, 1H), 1.57 (s, 1H), 1.46 – 1.33 (m, 2H), 1.19 (s, 3H), 0.98 (s, 9H), 0.84 – 0.70 (m, 1H), 0.50 (dtd, *J* = 9.8, 3.3, 1.8 Hz, 2H), 0.19 (s, 6H), 0.11 – 0.05 (m, 2H).**^{13}C NMR** (126 MHz, $CDCl_3$) δ 154.3, 131.5, 130.3, 119.8, 73.5, 47.4, 46.5, 26.7, 25.8, 18.3, 6.2, 4.7, 4.4, -4.3. **IR** (thin film): V_{max}: 3433, 3075, 2929, 2857, 1713, 1609, 1508, 1472, 1462, 1389, 1362, 1252, 1169, 1101, 1016, 910, 837, 800, 779 cm^{-1}. **HRMS** (ASAP-HESI) m/z: $[M-H_2O+H]^+$ Calcd for $C_{19}H_{31}OSi$,303.2147 found: 303.2144.

21- **1-cyclopropyl-2-methyl-3-(4-(trifluoromethyl)phenyl)propan-2-ol (28)**



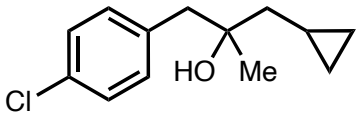
Prepared according to general procedure B**.** Purified by silica gel flash chromatography (Eluent: EtOAc/Petroleum ether, 5%) as a colorless oil in 61% yield (157 mg). **R_f**= 0.64 (Eluent: EtOAc/hexane, 20%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.54 (d, *J* = 7.8 Hz, 2H), 7.35 (d, *J* = 7.9 Hz, 2H), 2.89 (d, *J* = 13.3 Hz, 1H), 2.82 (d, *J* = 13.3 Hz, 1H), 1.69 (s, 1H), 1.42 (d, *J* = 6.8 Hz, 2H), 1.20 (s, 3H), 0.85 – 0.75 (m, 1H), 0.56 – 0.49 (m, 2H), 0.13 – 0.06 (m, 2H).**^{13}C NMR** (126 MHz, $CDCl_3$) δ 142.1, 131.0, 129.1, 128.8, 128.5, 128.3, 125.5, 124.99, 124.96, 124.93, 124.90, 123.4, 73.5, 48.0, 46.9, 26.7, 6.0, 4.5, 4.3. **^{19}F NMR** (471 MHz, $CDCl_3$) δ -62.36. **IR** (thin film): Vmax: 3352, 3080 , 2970, 2929, 2884, 2359, 1464, 1379, 1325, 1161, 1123, 1067, 1020, 949, 816 cm^{-1}. **HRMS** (ASAP-HESI) m/z: $[M-H_2O+H]^+$ Calcd for $C_{14}H_{16}F_3$ 241.1201, found: 241.1204.

22- **1-cyclopropyl-3-(4-fluorophenyl)-2-methylpropan-2-ol (29)**



Prepared according to general procedure B**.** Purified by silica gel flash chromatography (Eluent: EtOAc/Petroleum ether, 5%) as a colorless oil in 68% yield (142 mg). $\mathbf{R_f}$= 0.24 (Eluent: EtOAc/hexane, 10%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.11 – 7.06 (m, 2H), 6.92 – 6.86 (m, 2H), 2.72 (d, *J* = 13.5 Hz, 1H), 2.65 (d, *J* = 13.5 Hz, 1H), 1.42 (s, 1H), 1.31 (d, *J* = 6.8 Hz, 2H), 1.10 (s, 3H), 0.75 – 0.65 (m, 1H), 0.42 (dtt, *J* = 8.0, 3.3, 1.5 Hz, 2H), -0.00 (ddt, *J* = 4.7, 3.4, 1.6 Hz, 2H).**^{13}C NMR** (126 MHz, $CDCl_3$) 162.8, 160.9, 133.5, 133.5, 132.0, 132.0, 115.0, 114.9, 73.4, 47.4, 46.7, 26.7, 6.1, 4.6, 4.4. **^{19}F NMR** (471 MHz, $CDCl_3$) δ -117.01. **IR** (thin film): V_{max}: 3341, 2970, 2930, 2882, 1510, 1466, 1408, 1379, 1304, 1223, 1159, 1128, 951, 816 cm^{-1}. **HRMS** (ASAP-HESI) m/z: $[M- H_2O]^+$ Calcd for $C_{13}H_{15}F$ 190.1151, found: 190.1152.

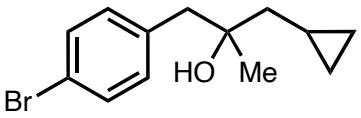
23- **1-(4-chlorophenyl)-3-cyclopropyl-2-methylpropan-2-ol (30)**



Prepared according to general procedure B**.** Purified by silica gel flash chromatography (Eluent: EtOAc/Petroleum ether, 5%) as a colorless oil in 59% yield (133 mg). $\mathbf{R_f}$= 0.30 (Eluent: EtOAc/hexane, 10%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.29 – 7.24 (m, 2H), 7.19 – 7.12 (m, 2H), 2.81 (d, *J* = 13.4 Hz, 1H), 2.74 (d, *J* = 13.4 Hz, 1H), 1.56 (s, 1H), 1.41 (d, *J* = 6.8 Hz, 2H), 1.20 (s, 3H), 0.84 – 0.74 (m, 1H), 0.56 – 0.48 (m, 2H), 0.13 – 0.06 (m, 2H).**^{13}C NMR** (126 MHz, $CDCl_3$) δ 136.3, 132.3, 131.9, 128.2, 73.4, 47.5, 46.7, 26.7, 6.1,

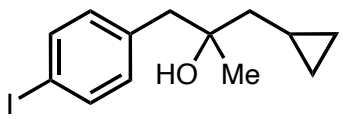
4.6, 4.3. **IR** (thin film): V_{max}: 3358, 2970, 2928, 2884, 1491, 1464, 1408, 1379, 1341, 1304, 1159, 1128, 1016, 951, 843, 816 cm^{-1}. **HRMS** (ASAP-HESI) m/z: $[M- H_2O]^+$ Calcd for $C_{13}H_{15}Cl$ 206.0854, found: 206.0856.

24- **1-(4-bromophenyl)-3-cyclopropyl-2-methylpropan-2-ol (31)**



Prepared according to general procedure B**.** Purified by silica gel flash chromatography (Eluent: EtOAc/Petroleum ether, 5%) as a colorless oil in 53% yield (143 mg). $\mathbf{R_f}$= 0.20 (Eluent: EtOAc/hexane, 10%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.47 – 7.38 (m, 2H), 7.12 – 7.07 (m, 2H), 2.79 (d, *J* = 13.4 Hz, 1H), 2.72 (d, *J* = 13.4 Hz, 1H), 1.59 (s, 1H), 1.40 (d, *J* = 6.8 Hz, 2H), 1.19 (s, 3H), 0.84 – 0.73 (m, 1H), 0.55 – 0.47 (m, 2H), 0.12 – 0.03 (m, 2H).**^{13}C NMR** (126 MHz, $CDCl_3$) δ 136.8, 132.4, 131.2, 120.4, 73.4, 47.6, 46.7, 26.8, 6.1, 4.6, 4.4. **IR** (thin film): V_{max}: 3337, 2968, 2930, 2880, 1466, 1379, 1304, 1159, 1128, 1013, 951, 816 cm^{-1}. **HRMS** (ASAP-HESI) m/z: $[M- H_2O]^+$ Calcd for $C_{13}H_{15}Br$ 250.0352, found: 250.03516.

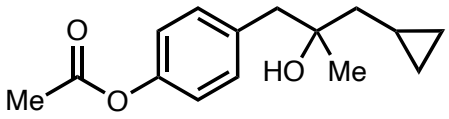
25- **1-cyclopropyl-3-(4-iodophenyl)-2-methylpropan-2-ol (32)**



Prepared according to general procedure B**.** Purified by silica gel flash chromatography (Eluent: EtOAc/Petroleum ether, 5%) as a colorless oil in 52% yield (164 mg). $\mathbf{R_f}$= 0.22 (Eluent: EtOAc/hexane, 10%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.61 – 7.58 (m, 2H), 6.99 – 6.95 (m, 2H), 2.75 (d, *J* = 13.4 Hz, 1H), 2.69 (d, *J* = 13.4 Hz, 1H), 1.71 (s, 1H), 1.38 (dd,

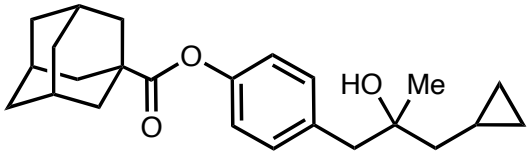
J = 6.8, 2.5 Hz, 2H), 1.17 (s, 3H), 0.82 – 0.72 (m, 1H), 0.52 – 0.47 (m, 2H), 0.12 – 0.03 (m, 2H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 137.4, 137.0, 132.6, 91.9, 73.3, 47.6, 46.6, 26.6, 6.0, 4.6, 4.3. **IR** (thin film): V_{max}: 3447, 3073, 2998, 2970, 2918, 2851, 1483, 1458, 1400, 1375, 1300, 1169, 1109, 1061, 1007, 907 cm^{-1}. **HRMS** (ASAP-HESI) m/z: $[M- H_2O]^+$ Calcd for $C_{13}H_{15}I$ 298.02130, found: 298.0214.

26- **4-(3-cyclopropyl-2-hydroxy-2-methylpropyl)phenyl acetate (33)**



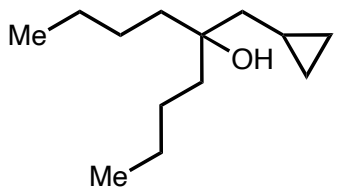
Prepared according to general procedure B**.** Purified by silica gel flash chromatography (Eluent: EtOAc/Petroleum ether, 4-8%) as a colorless oil in 40% yield (99 mg). **R_f**= 0.28 (Eluent: EtOAc/hexane, 20%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.25 – 7.19 (m, 2H), 7.05 – 6.96 (m, 2H), 2.83 (d, *J* = 13.4 Hz, 1H), 2.76 (d, *J* = 13.4 Hz, 1H), 2.29 (s, 3H), 1.59 (s, 1H), 1.42 (dd, *J* = 6.8, 2.2 Hz, 2H), 1.21 (s, 3H), 0.80 (dddd, *J* = 13.4, 8.1, 4.9, 1.8 Hz, 1H), 0.51 (dtd, *J* = 9.3, 3.1, 1.4 Hz, 2H), 0.09 (dtd, *J* = 4.7, 3.1, 1.4 Hz, 2H).**^{13}C NMR** (126 MHz, $CDCl_3$) δ 169.6, 149.4, 135.4, 131.6, 121.2, 73.5, 47.6, 46.7, 26.7, 21.2, 6.1, 4.6, 4.4. **IR** (thin film): V_{max}: 3462, 3076, 2999, 2972, 2918, 1753, 1506, 1427, 1369, 1215, 1194, 1165, 1018, 910, 729 cm^{-1}. **HRMS** (ASAP-HESI) m/z: $[M- H_2O+H]^+$ Calcd for $C_{15}H_{19}O_2$ 231.1385, found: 231.1395.

27- **4-(3-cyclopropyl-2-hydroxy-2-methylpropyl)phenyl (3*r*,5*r*,7*r*)-adamantane-1-carboxylate (34)**



Prepared according to general procedure B**.** Purified by silica gel flash chromatography (Eluent: EtOAc/Petroleum ether, 20-25%) as a colorless oil in 36% yield (133 mg). $\mathbf{R_f}$ =0.5 (Eluent: EtOAc/hexane, 30%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.24 – 7.19 (m, 2H), 7.00 – 6.96 (m, 2H), 2.83 (d, *J* = 13.4 Hz, 1H), 2.77 (d, *J* = 13.4 Hz, 1H), 2.12 – 2.01 (m, 9H), 1.82 – 1.72 (m, 7H), 1.42 (dd, *J* = 6.8, 2.4 Hz, 2H), 1.21 (s, 3H), 0.84 – 0.76 (m, 1H), 0.53 – 0.49 (m, 2H), 0.13 – 0.05 (m, 2H).**^{13}C NMR** (126 MHz, $CDCl_3$) δ 176.4, 149.8, 135.0, 131.5, 121.2, 73.5, 47.7, 46.7, 41.1, 38.9, 36.6, 28.0, 26.8, 6.2, 4.7, 4.4. **IR** (thin film): V_{max}: 3445, 2907, 2851, 1746, 1506, 1452, 1219, 1196, 1165, 1055, 1018, 905 cm^{-1}. **HRMS** (ASAP-HESI) m/z: $[M+H]^+$ Calcd for $C_{24}H_{33}O_3$ 369.2430, found: 369.2426.

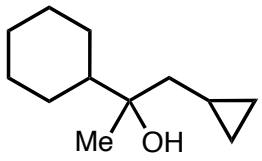
28- **5-(cyclopropylmethyl)nonan-5-ol (35)**



Prepared according to general procedure B**.** Purified by silica gel flash chromatography (Eluent: EtOAc/Petroleum ether, 10-15%) as a colorless oil in 55% yield (109 mg). $\mathbf{R_f}$= 0.42 (Eluent: EtOAc/hexane, 10%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 1.53 – 1.46 (m, 4H), 1.37 (d, *J* = 6.8 Hz, 2H), 1.37 – 1.21 (m, 9H), 0.91 (t, *J* = 7.0 Hz, 6H), 0.75 – 0.64 (m, 1H), 0.52 – 0.42 (m, 2H), 0.14 – 0.01 (m, 2H).**^{13}C NMR** (126 MHz, $CDCl_3$) δ 75.3, 44.0, 39.1,

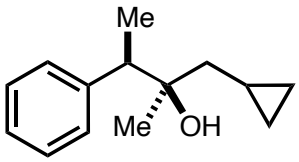
25.9, 23.5, 14.2, 5.7, 4.2. **IR** (thin film): V_{max}: 3354, 2968, 2932, 1647, 1466, 1379, 1304, 1161, 1128, 1107, 951, 816, 772 cm^{-1}. **HRMS** (ASAP-HESI) m/z: $[M-H_2O]^+$ Calcd for $C_{13}H_{24}$ 180.18725, found:180.1869

29- **2-cyclohexyl-1-cyclopropylpropan-2-ol (36)**



Prepared according to general procedure B**.** Purified by silica gel flash chromatography (Eluent: EtOAc/Petroleum ether, 10-15%) as a colorless oil in 43% yield (78 mg). $\mathbf{R_f}$= 0.37 (Eluent: EtOAc/hexane, 10%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 1.89 – 1.61 (m, 6H), 1.47 – 1.36 (m, 2H), 1.32 (dd, *J* = 14.2, 7.1 Hz, 1H), 1.26 – 1.16 (m, 2H), 1.13 (s, 3H), 1.12 – 1.03 (m, 1H), 1.00 (dd, *J* = 12.0, 3.4 Hz, 1H), 0.98 – 0.90 (m, 1H), 0.78 – 0.69 (m, 1H), 0.51 – 0.43 (m, 2H), 0.09 – 0.03 (m, 2H).**^{13}C NMR** (126 MHz, $CDCl_3$) δ 75.5, 47.7, 44.2, 27.8, 27.0, 26.9, 26.9, 26.7, 24.0, 5.6, 4.5, 4.0. **IR** (thin film): V_{max}: 3440, 3075, 2997, 2922, 2851, 2359, 1449, 1427, 1375, 1298, 1194, 1148, 1015, 970, 932, 891, 867, 824 cm^{-1}. **HRMS** (ASAP-HESI) m/z: $[M-CH_3]^+$ Calcd for $C_{11}H_{19}O$ 167.14304, found: 167.1430.

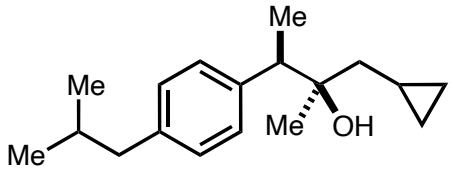
30- **(anti)-1-cyclopropyl-2-methyl-3-phenylbutan-2-ol (37)**



Prepared according to general procedure B**.** Purified by silica gel flash chromatography (Eluent: EtOAc/Petroleum ether, 5-10%) as a colorless oil in 41% yield (84 mg) as >95:<5 d.r. of inseparable diastereomers after purification. Data for major diastereomer, $\mathbf{R_f}$= 0.32

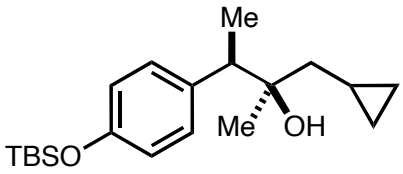
(Eluent: EtOAc/hexane, 10%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.26 – 7.15 (m, 5H), 2.82 (q, *J* = 7.2 Hz, 1H), 1.46 (s, 1H), 1.37 (dd, *J* = 14.2, 6.6 Hz, 1H), 1.33 (dd, *J* = 14.1, 7.1 Hz, 1H), 1.28 (d, *J* = 7.2 Hz, 3H), 1.11 (s, 3H), 0.74 – 0.67 (m, 1H), 0.48 – 0.36 (m, 2H), 0.08 – -0.06 (m, 2H).**^{13}C NMR** (126 MHz, $CDCl_3$) δ 143.7, 129.1, 128.1, 126.4, 75.2, 49.2, 44.2, 25.4, 15.5, 6.1, 4.8, 4.1. **IR** (thin film): V_{max}: 3460, 3076, 3026, 2974, 2916, 2849, 1493, 1452, 1373, 1246, 1072, 1016, 972, 939, 824, 700 cm^{-1}. **HRMS** (ASAP-HESI) m/z: $[M- H_2O]^+$ Calcd for $C_{14}H_{18}$ 186.14030, found: 186.1403.

31- **(anti)-1-cyclopropyl-3-(4-isobutylphenyl)-2-methylbutan-2-ol (38)**



Prepared according to general procedure B**.** Purified by silica gel flash chromatography (Eluent: EtOAc/Petroleum ether, 5%) as a colorless oil in 50% yield (130 mg) as >95:<5 d.r. of inseparable diastereomers after purification. Data for major diastereomer, **R_f**= 0.25 (Eluent: EtOAc/hexane, 10%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.15 (d, *J* = 8.0 Hz, 2H), 7.07 (d, *J* = 8.3 Hz, 2H), 2.85 (q, *J* = 7.2 Hz, 1H), 2.45 (d, *J* = 7.2 Hz, 2H), 1.85 (hept, *J* = 6.9 Hz, 1H), 1.54 (s, 1H), 1.43 (dd, *J* = 14.1, 6.5 Hz, 1H), 1.38 (dd, *J* = 14.1, 7.0 Hz, 1H), 1.32 (d, *J* = 7.2 Hz, 3H), 1.17 (s, 3H), 0.90 (d, *J* = 6.6 Hz, 6H), 0.82 – 0.70 (m, 1H), 0.58 – 0.41 (m, 2H), 0.07 (td, *J* = 4.6, 3.4 Hz, 2H) .**^{13}C NMR** (126 MHz, $CDCl_3$) δ 140.7, 139.8, 128.8, 75.2, 48.8, 45.1, 44.0, 30.3, 25.4, 22.5, 15.5, 6.1, 4.9, 4.1. **IR** (thin film): V_{max}: 3453, 2955, 2924, 2870, 2847, 1512, 1462, 1373, 1250, 1169, 1018, 972, 910, 733 cm^{-1}. **HRMS** (ASAP-HESI) m/z: $[M- H_2O]^+$ Calcd for $C_{18}H_{26}$ 242.20290, found: 242.2028.

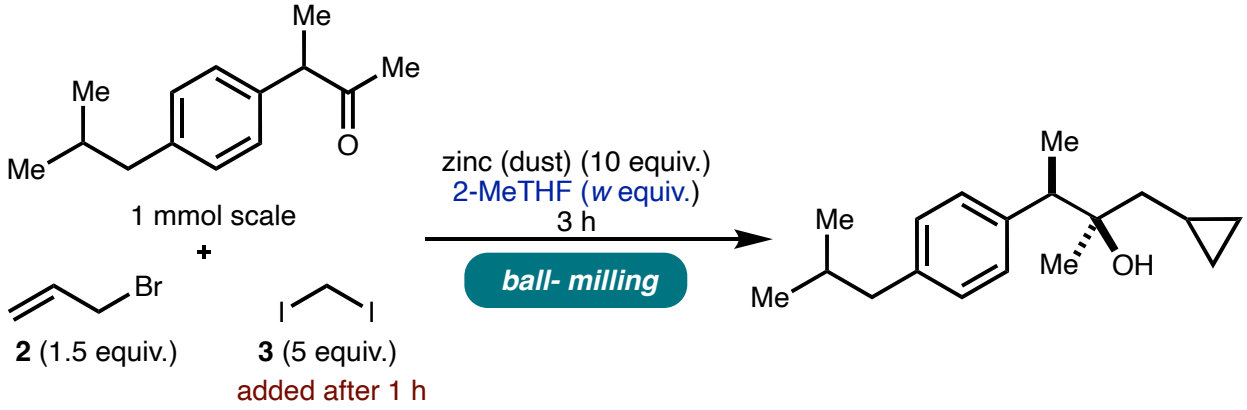
32- **(anti)-3-(4-((*tert*-butyldimethylsilyl)oxy)phenyl)-1-cyclopropyl-2-methylbutan-2-ol (39)**



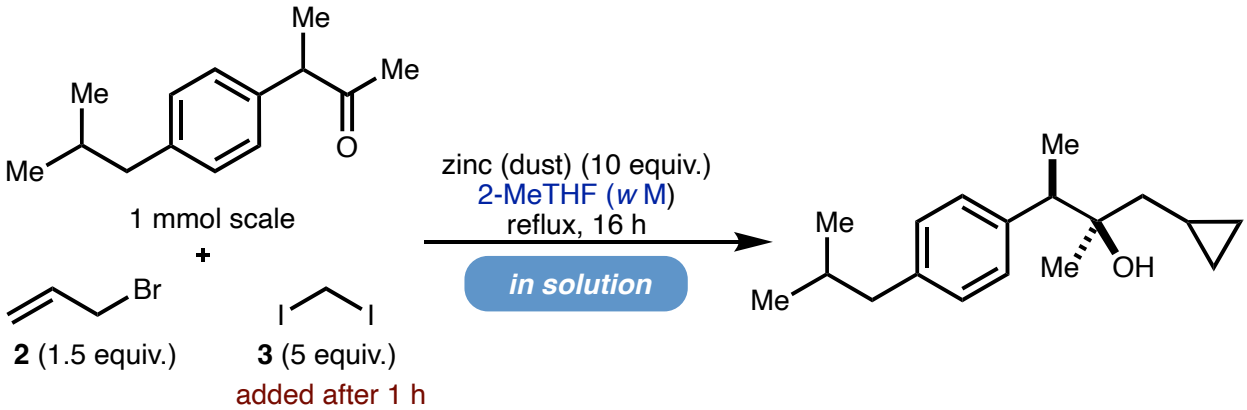
Prepared according to general procedure**.** Purified by silica gel flash chromatography (Eluent: EtOAc/Petroleum ether, 16-20%) as a colorless oil in 41% yield (137 mg) as an approximately 85:15 d.r. of inseparable diastereomers mixture after purification. $\mathbf{R_f}$= 0.70 (Eluent: EtOAc/hexane, 30%). **IR** (thin film): V_{max}: 3306, 2953, 2930, 2886, 2857, 1607, 1508, 1472, 1391, 1254, 1173, 1142, 1080, 1015, 914, 833, 810 cm^{-1}. **HRMS** (ASAP-HESI) m/z: $[M-H_2O+H]^+$ Calcd for $C_{20}H_{33}OSi$ 317.2301, found: 317.2299. Data for major diastereomer, ^{1}**H NMR** (500 MHz, $CDCl_3$) δ 6.94 – 6.86 (m, 2H), 6.61 – 6.53 (m, 2H), 2.61 (q, *J* = 7.2 Hz, 1H), 1.30 (s, 1H), 1.22 – 1.14 (m, 2H), 1.10 (d, *J* = 7.2 Hz, 3H), 0.95 (s, 3H), 0.79 (s, 9H), 0.55 (dtt, *J* = 13.4, 6.5, 1.7 Hz, 1H), 0.31 – 0.25 (m, 2H), -0.00 (s, 6H), -0.11 – -0.16 (m, 2H).^{13}**C NMR** (126 MHz, $CDCl_3$) δ 154.2, 136.3, 129.9, 119.5, 75.3, 48.5, 44.1, 25.8, 25.3, 18.3, 15.6, 6.1, 4.9, 4.1, -4.2.

6. **Diastereoselectivity**

Mechanochemical vs. solution phase processes:



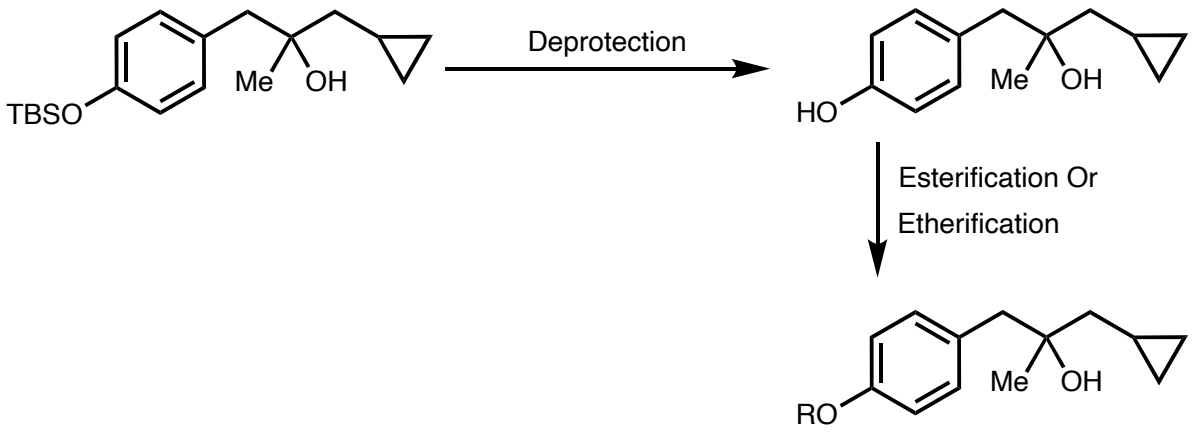
Entry	2-MeTHF	FP[a] (%)
1	1.5 equiv. "standard" condition	50 (>95:<5 d.r.)
2	No LAG	22
3	3 equiv.	51 (90:10 d.r.)
4	6 equiv.	48 (86:14 d.r.)



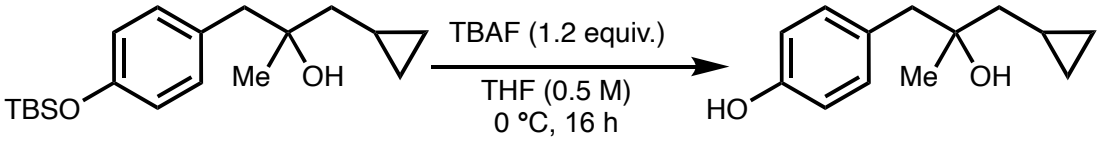
Entry	2-MeTHF	FP[a] (%)
1	0.25 M	37 (70:30 d.r.)
2	0.5 M	42 (71:29 d.r.)

- Higher diastereoselectivity observed in mechanochemical setup compared to solution phase experiments. In order to determine the major diasteroisomer, we focus on synthesizing derivatives for X-Ray analysis. Functionalization of the tertiary alcohols was unsuccessful. We focus on functionalizing the aromatic ring.

Diastereoselectivity - model system:



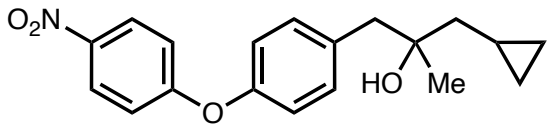
33- **4-(3-cyclopropyl-2-hydroxy-2-methylpropyl)phenol (25)**



To a stirred solution of 1-(4-((*tert*-butyldimethylsilyl)oxy)phenyl)-3-cyclopropyl-2-methylpropan-2-ol (26) (1 mmol, 1 equiv.) in THF (0.5 M) under a nitrogen atmosphere, was added *Tetra*-n-butylammonium fluoride (TBAF) (1.1 mL, 1M solution in THF, 1.2 equiv.) dropwise at 0 °C. The resulting mixture was then allowed to warm to room temperature and stirred for an overnight. After completion, the mixture was quenched with water, extracted with CH_2Cl_2 (2x 10 mL). The combined organic phases were dried over $MgSO_4$, filtered and concentrated *in vacuo* yielding crude residue. The crude residue was purified by silica gel flash chromatography (Eluent: EtOAc/Petroleum ether 18-20%) yielding pure product as a colorless oil in 79% yield (163 mg). $\mathbf{R_f}$= 28 (Eluent: EtOAc/hexane, 30%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.11 – 7.06 (m, 2H), 6.80 – 6.74 (m,

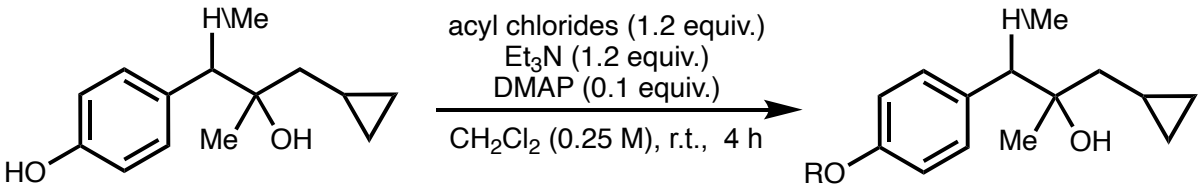
2H), 2.78 (d, *J* = 13.5 Hz, 1H), 2.72 (d, *J* = 13.6 Hz, 1H), 1.47 – 1.35 (m, 2H), 1.21 (s, 3H), 0.86 – 0.74 (m, 1H), 0.62 – 0.43 (m, 2H), 0.13 – 0.04 (m, 2H).**^{13}C NMR** (126 MHz, $CDCl_3$) δ 154.4, 131.8, 129.8, 115.1, 73.7, 47.4, 46.6, 26.7, 6.2, 4.7, 4.4. **IR** (thin film): V_{max}: 3335, 2973, 2932, 2884, 1719, 1458, 1379, 1259, 1161, 1126, 949, 901, 816, 735, 644 cm^{-1}. **HRMS** (ASAP-HESI) m/z: $[M- H_2O]^+$ Calcd for $C_{13}H_{16}O$ 188.11957, found: 188.1191.

34- **1-cyclopropyl-2-methyl-3-(4-(4-nitrophenoxy)phenyl)propan-2-ol (S11)**



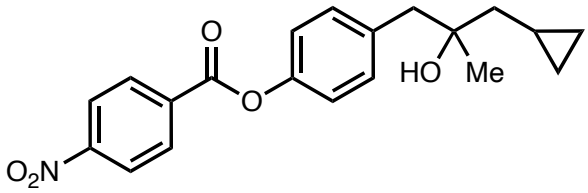
A 20 mL vial equipped with a magnetic stirrer bar was charged with 4-(3-cyclopropyl-2-hydroxy-2-methylpropyl)phenol (206 mg, 1.0 mmol), 4-fluoronitrobenzene (0.1 mL, 1.1 mmol, 1.1 equiv), KF (290 mg, 5.0 mmol, 5 equiv), and DMSO (5 mL). The vial was sealed and stirred at 115 °C overnight. After completion, the mixture was cooled to room temperature, diluted with water, and extracted with ethyl acetate (2 × 10 mL). The combined organic phases were washed with brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The crude residue was purified by silica gel flash chromatography (Eluent: EtOAc/Petroleum ether 16-20%) yielding pure product as a yellow oil in 59% yield (194 mg). **R_f**= 0.46 (Eluent: EtOAc/hexane, 30%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.20 – 8.16 (m, 2H), 7.31 – 7.27 (m, 2H), 7.05 – 6.97 (m, 4H), 2.86 (d, *J* = 13.5 Hz, 1H), 2.79 (d, *J* = 13.4 Hz, 1H), 1.65 (s, 1H), 1.45 (d, *J* = 6.8 Hz, 2H), 1.23 (s, 3H), 0.86 – 0.77 (m, 1H), 0.55 – 0.51 (m, 2H), 0.13 – 0.09 (m, 2H).**^{13}C NMR** (126 MHz, $CDCl_3$) δ 163.5, 153.3, 142.6, 135.2, 132.4, 126.0, 120.1, 117.1, 73.5, 47.5, 46.8, 26.8, 6.1, 4.6, 4.4. **IR** (thin film): V_{max}: 3570, 3076, 2962, 2889, 1606, 1587, 1989, 1342, 1248, 1165, 1111, 1018, 878, 750 cm^{-1}. **HRMS** (ASAP-HESI) m/z: $[M+ H]^+$ Calcd for $C_{19}H_{22}NO_4$ 328.1549, found: 328.1546.

General procedure of esterification C:



A 10 mL round-bottomed flask equipped with a magnetic stirrer bar was charged with phenol (1 equiv.), acyl chlorides (1.2 equiv.), Et_3N (1.2 equiv.), DMAP (0.1 equiv.) and CH_2Cl_2 (0.25 M). The mixture was allowed to stir at room temperature overnight. After completion, the mixture was quenched with sat. aq. $NaHCO_3$ (5 mL) and extracted with CH_2Cl_2 (2 x 10 mL). The combined organic phases were washed with brine and dried over $MgSO_4$, filtered and concentrated *in vacuo*.

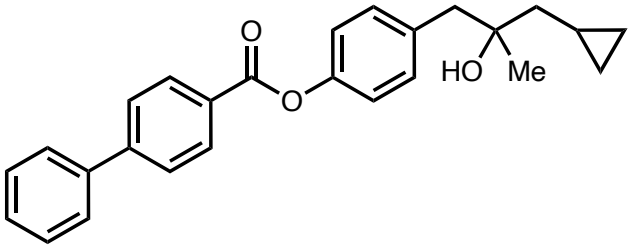
35- **4-(3-cyclopropyl-2-hydroxy-2-methylpropyl)phenyl 4-nitrobenzoate (S12)**



Prepared according to general procedure C on 0.5 mmol scale. Purified by silica gel flash chromatography (Eluent: EtOAc/Petroleum ether, 16-20%) as a white solid in 78% yield (138 mg). $\mathbf{R_f}$= 0.42 (Eluent: EtOAc/hexane, 30%). **m.p.**= 101-103 °C. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.40 – 8.34 (m, 4H), 7.34 – 7.30 (m, 2H), 7.19 – 7.15 (m, 2H), 2.88 (d, *J* = 13.4 Hz, 1H), 2.82 (d, *J* = 13.4 Hz, 1H), 1.56 (s, 1H), 1.45 (d, *J* = 6.8 Hz, 2H), 1.24 (s, 3H), 0.88 – 0.77 (m, 1H), 0.56 – 0.51 (m, 2H), 0.16 – 0.07 (m, 2H).**^{13}C NMR** (126 MHz, $CDCl_3$) δ 163.5, 151.0, 149.2, 136.2, 135.1, 131.8, 131.4, 123.8, 121.0, 73.5, 47.7, 46.8, 26.8, 6.2, 4.6, 4.4. **IR** (thin film): V_{max}: 3547, 3387, 3075, 2999, 2918, 1742, 1732, 1608, 1520,

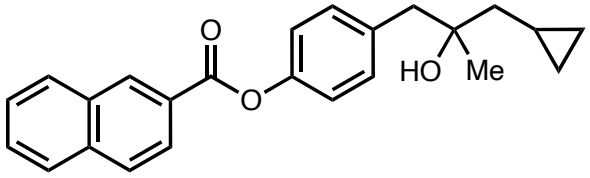
1506, 1346, 1269, 1190, 1165, 1072, 1013, 869, 714 cm^{-1}. **HRMS** (ASAP-HESI) m/z: $[M+Na]^+$ Calcd for $C_{20}H_{21}NO_5Na$ 378.1317, found: 378.1312.

36- **4-(3-cyclopropyl-2-hydroxy-2-methylpropyl)phenyl[1,1'-biphenyl]-4-carboxylate (S13)**



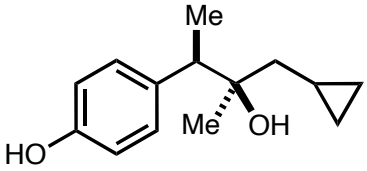
Prepared according to general procedure C on 0.5 mmol scale**.** Purified by silica gel flash chromatography (Eluent: EtOAc/Petroleum ether, 16-20%) as a white solid in 80% yield (154 mg). $\mathbf{R_f}$= 0.48 (Eluent: EtOAc/hexane, 30%). **m.p.**= 96-102 °C. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.17 – 8.13 (m, 2H), 7.64 – 7.59 (m, 2H), 7.56 – 7.52 (m, 2H), 7.41 – 7.34 (m, 2H), 7.33 – 7.27 (m, 1H), 7.21 – 7.16 (m, 2H), 7.09 – 7.04 (m, 2H), 2.76 (d, *J* = 13.4 Hz, 1H), 2.70 (d, *J* = 13.4 Hz, 1H), 1.46 (s, 1H), 1.34 (dd, *J* = 6.8, 1.6 Hz, 2H), 1.13 (s, 3H), 0.75 – 0.66 (m, 1H), 0.45 – 0.38 (m, 2H), 0.04 – -0.05 (m, 2H).**^{13}C NMR** (126 MHz, $CDCl_3$) δ165.2, 149.7, 146.4, 140.0, 135.5, 131.7, 130.8, 129.1, 128.4, 127.4, 127.3, 121.4, 73.5, 26.8, 6.1, 4.6, 4.4. **IR** (thin film): V_{max}: 3319, 2995, 2906, 1718, 1602, 1504, 1404, 1267, 1190, 1072, 1006, 935, 744 cm^{-1}. **HRMS** (ASAP-HESI) m/z: $[M+H]^+$ Calcd for $C_{26}H_{27}O_3$ 387.1960, found: 387.1946.

37- **4-(3-cyclopropyl-2-hydroxy-2-methylpropyl)phenyl 2-naphthoate (S14)**



Prepared according to general procedure C on 0.5 mmol scale. Purified by silica gel flash chromatography (Eluent: EtOAc/Petroleum ether, 16-20%) as a white solid in 73% yield (220 mg). $\mathbf{R_f}$= 0.51 (Eluent: EtOAc/hexane, 30%). **m.p.**= 97-99 °C. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.79 (d, *J* = 1.0 Hz, 1H), 8.20 (dd, *J* = 8.6, 1.7 Hz, 1H), 8.01 (dd, *J* = 8.1, 0.8 Hz, 1H), 7.95 (d, *J* = 9.2 Hz, 1H), 7.92 (d, *J* = 8.2 Hz, 1H), 7.64 (ddd, *J* = 8.2, 6.9, 1.4 Hz, 1H), 7.58 (ddd, *J* = 8.1, 6.9, 1.3 Hz, 1H), 7.34 – 7.30 (m, 2H), 7.24 – 7.19 (m, 2H), 2.89 (d, *J* = 13.3 Hz, 1H), 2.83 (d, *J* = 13.3 Hz, 1H), 1.59 (s, 1H), 1.46 (dd, *J* = 6.8, 1.6 Hz, 2H), 1.26 (s, 3H), 0.89 – 0.79 (m, 1H), 0.58 – 0.50 (m, 2H), 0.15 – 0.09 (m, 2H).**^{13}C NMR** (126 MHz, $CDCl_3$) δ 165.5, 149.8, 135.9, 135.5, 132.6, 132.0, 131.7, 129.6, 128.7, 128.5, 127.9, 126.9, 126.9, 125.6, 121.4, 73.6, 47.7, 46.7, 26.8, 6.2, 4.7, 4.4. **IR** (thin film): ν_{max}: 3510, 2059, 2974, 2914, 1728, 1709, 1630, 1595, 1506, 1462, 1279, 1263, 1192, 1165, 1076, 951, 826 cm^{-1}. **HRMS** (ASAP-HESI) m/z: $[M+H]^+$ Calcd for $C_{24}H_{25}O_3$ 361.1804, found: 361.1799.

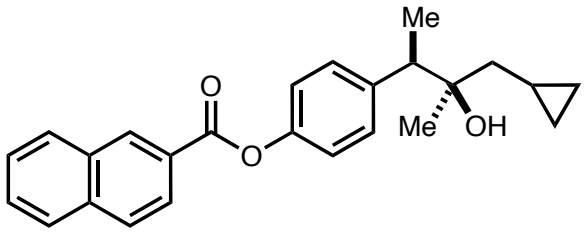
38- **4-((anti)-4-cyclopropyl-3-hydroxy-3-methylbutan-2-yl)phenol (40)**



To a stirred solution of 1-(4-((*tert*-butyldimethylsilyl)oxy)phenyl)-3-cyclopropyl-2-methylpropan-2-ol (39) (1.2 mmol, 1 equiv.) in THF (0.5 M) under a nitrogen atmosphere, was added Tetra-n-butylammonium fluoride (TBAF) (2.39 mL, 1M solution in THF, 2 equiv.) dropwise at 0 °C. The resulting mixture was then allowed to warm to room

temperature and stirred for an overnight. After completion, the mixture was quenched with water, extracted with CH_2Cl_2 (2x 10 mL). The combined organic phases were dried over $MgSO_4$, filtered and concentrated *in vacuo* yielding crude residue. The crude residue was purified by silica gel flash chromatography (Eluent: EtOAc/Petroleum ether 18-20%) yielding pure product as a colorless oil in 48% yield (125 mg) as an approximately 84:16 d.r. of inseparable diastereomers mixture after purification. **R_f**= 0.33 (Eluent: EtOAc/hexane, 30%). **IR** (thin film): V_{max}: 3391, 3107, 3073, 2980, 2924, 1707, 1612, 1595, 1514, 1450, 1373, 1333, 1306, 1261, 1227, 1175, 1117, 1078, 1015, 999, 972, 941, 914, 864, 833 cm^{-1}. **HRMS** (ASAP-HESI) m/z: $[M- H_2O]^+$ Calcd for $C_{14}H_{19}O$ 203.1435, found: 203.1436. Data for major diastereomer, **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.17 – 7.07 (m, 2H), 6.79 – 6.73 (m, 2H), 2.82 (q, *J* = 7.2 Hz, 1H), 1.61 (s, 1H), 1.44 – 1.34 (m, 2H), 1.29 (d, *J* = 7.2 Hz, 3H), 1.17 (s, 3H), 0.88 – 0.67 (m, 1H), 0.55 – 0.46 (m, 2H), 0.15 – -0.04 (m, 2H).**^{13}C NMR** (126 MHz, $CDCl_3$) δ 154.3, 135.5, 130.2, 114.9, 75.6, 48.3, 43.9, 25.3, 15.7, 6.0, 4.9, 4.1.

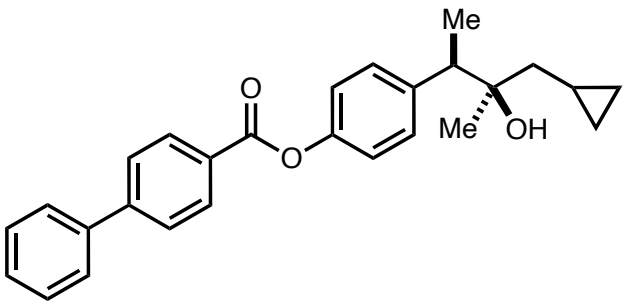
39- **4-((anti)-4-cyclopropyl-3-hydroxy-3-methylbutan-2-yl)phenyl 2-naphthoate (S15)**



Prepared according to general procedure C on 0.5 mmol scale**.** Purified by silica gel flash chromatography (Eluent: EtOAc/Petroleum ether, 16-20%) as a white solid in 58% yield (105 mg) as an approximately 84:16 d.r. of inseparable diastereomers mixture after purification. **R_f**= 0.67 (Eluent: EtOAc/hexane, 30%). **m.p.**= 76-77 °C. **IR** (thin film): V_{max}: 3549, 3059, 2972, 2928, 1730, 1630, 1599, 1506, 1464, 1371, 1354, 1279, 1221, 1188, 1167, 1126, 1061, 1016, 972, 951, 893, 864, 824, 773, 760 cm^{-1}. **HRMS** (ASAP-HESI)

m/z: [M- H_2O+H]$^+$ Calcd for $C_{25}H_{25}O_2$ 357.1855, found: 357.1852. Data for major diastereomer, **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.79 (d, *J* = 1.0 Hz, 1H), 8.20 (dd, *J* = 8.6, 1.7 Hz, 1H), 8.01 (dd, *J* = 8.1, 0.8 Hz, 1H), 7.94 (dd, *J* = 13.7, 8.3 Hz, 2H), 7.64 (ddd, *J* = 8.2, 6.9, 1.4 Hz, 1H), 7.58 (ddd, *J* = 8.1, 6.9, 1.3 Hz, 1H), 7.38 – 7.31 (m, 2H), 7.21 (dd, *J* = 8.7, 2.8 Hz, 2H), 2.93 (q, *J* = 7.2 Hz, 1H), 1.56 (s, 1H), 1.44 (dd, *J* = 6.8, 2.7 Hz, 2H), 1.35 (dd, *J* = 7.2, 5.4 Hz, 3H), 1.21 (s, 3H), 0.84 – 0.72 (m, 1H), 0.54 – 0.49 (m, 2H), 0.16 – 0.04 (m, 2H).**^{13}C NMR** (126 MHz, $CDCl_3$) δ 165.5, 149.6, 141.5, 135.9, 132.6, 132.0, 130.3, 129.6, 128.7, 128.5, 127.9, 126.9, 125.6, 121.2, 75.2, 48.7, 44.3, 25.5, 15.7, 6.1, 4.8, 4.2.

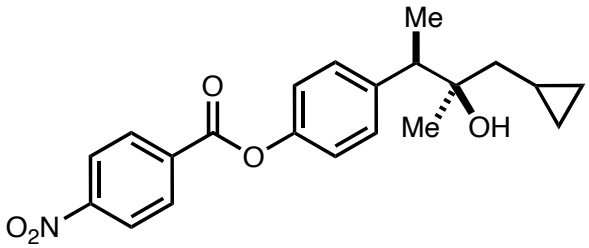
40- **4-((anti)-4-cyclopropyl-3-hydroxy-3-methylbutan-2-yl)phenyl [1,1'-biphenyl]-4-carboxylate (S16)**



Prepared according to general procedure C on 0.9 mmol scale**.** Purified by silica gel flash chromatography (Eluent: EtOAc/Petroleum ether, 16-20%) as a colorless oil in 75% yield (262 mg) as an approximately 84:16 d.r. of inseparable diastereomers mixture after purification. **R_f**= 0.57 (Eluent: EtOAc/hexane, 30%). **IR** (thin film): V_{max}: 3383, 3076, 2974, 2920, 1730, 1606, 1506, 1448, 1406, 1375, 1267, 1197, 1166, 1074, 1016, 1006, 972, 939, 918, 887, 871, 856, 815, 781, 740 cm^{-1}. **HRMS** (ASAP-HESI) m/z: [M- H_2O+H]$^+$ Calcd for $C_{27}H_{27}O_2$ 383.2011, found: 383.2011. Data for major diastereomer, **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.31 – 8.24 (m, 2H), 7.77 – 7.71 (m, 2H), 7.68 – 7.64 (m, 2H), 7.53 – 7.46 (m, 2H), 7.46 – 7.39 (m, 1H), 7.36 – 7.31 (m, 2H), 7.20 – 7.15 (m, 2H), 2.92 (q, *J*

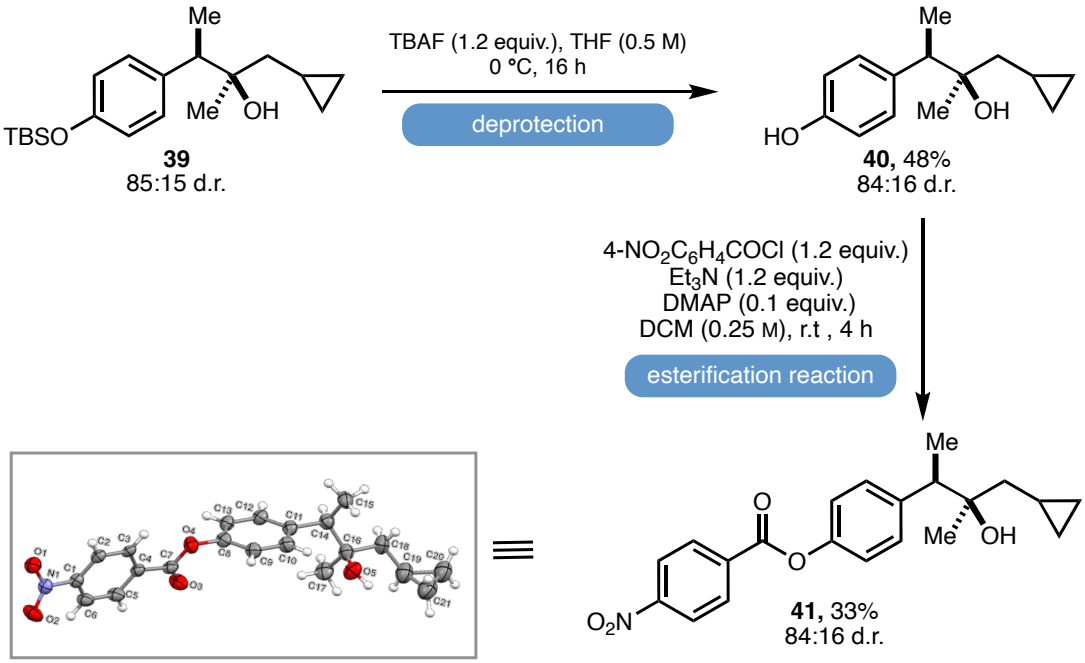
= 7.2 Hz, 1H), 1.52 (s, 1H), 1.44 (dd, *J* = 6.7, 2.4 Hz, 2H), 1.35 (d, *J* = 7.2 Hz, 3H), 1.20 (s, 3H), 0.82 – 0.72 (m, 1H), 0.54 – 0.48 (m, 2H), 0.13 – 0.04 (m, 2H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 165.2, 149.5, 146.4, 141.4, 140.0, 130.8, 130.1, 129.1, 128.4, 127.4, 127.3, 121.2, 75.2, 48.7, 44.3, 25.4, 15.7, 6.1, 4.8, 4.2.

41- **4-((anti)-4-cyclopropyl-3-hydroxy-3-methylbutan-2-yl)phenyl 4-nitrobenzoate (41)**



Prepared according to general procedure C on 0.9 mmol scale**.** Purified by silica gel flash chromatography (Eluent: EtOAc/Petroleum ether, 16-20%) as a white solid in 33% yield (106 mg). as an approximately 84:16 d.r. of inseparable diastereomers mixture after purification. **R_f**= 0.51 (Eluent: EtOAc/hexane, 30%). **IR** (thin film): V_{max}: 3603, 3072, 2935, 1741, 1605, 1524, 1504, 1371, 1348, 1321, 1267, 1199, 1168, 1130, 1076, 1014, 989, 970, 939, 875, 854, 815, 779, 754, 713 cm^{-1}. **HRMS** (ASAP-HESI) m/z: $[M- H_2O+H]^+$ Calcd for $C_{21}H_{22}NO_4$ 352.1549, found: 352.1546. Data for major diastereomer, **m.p.**= 92-94 °C. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.41 – 8.33 (m, 4H), 7.40 – 7.31 (m, 2H), 7.16 (dd, *J* = 8.9, 2.4 Hz, 2H), 2.92 (q, *J* = 7.2 Hz, 1H), 1.56 (s, 1H), 1.43 (d, *J* = 6.8 Hz, 2H), 1.34 (d, *J* = 7.2 Hz, 3H), 1.18 (s, 3H), 0.83 – 0.72 (m, 1H), 0.55 – 0.47 (m, 2H), 0.17 – -0.07 (m, 2H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 163.5, 150.9, 149.0, 142.1, 135.1, 131.4, 130.3, 123.8, 120.9, 75.2, 48.6, 44.3, 25.5, 15.7, 6.1, 4.8,4.1.

Crystal structure determination:



After deprotection of compound **(39)** and subsequent acylation of the corresponding alcohol, the reaction mixture furnished a solid derivative **(41)**. The resulting material was obtained as a diastereomeric mixture that could not be fully separated; however, the pure fractions of the major diastereoisomer (identified by ^{1}H NMR) was used for crystallization, which provided crystals suitable for X-Ray diffraction. Analysis of these crystals enabled assignment of the stereochemistry of the major diastereoisomer.

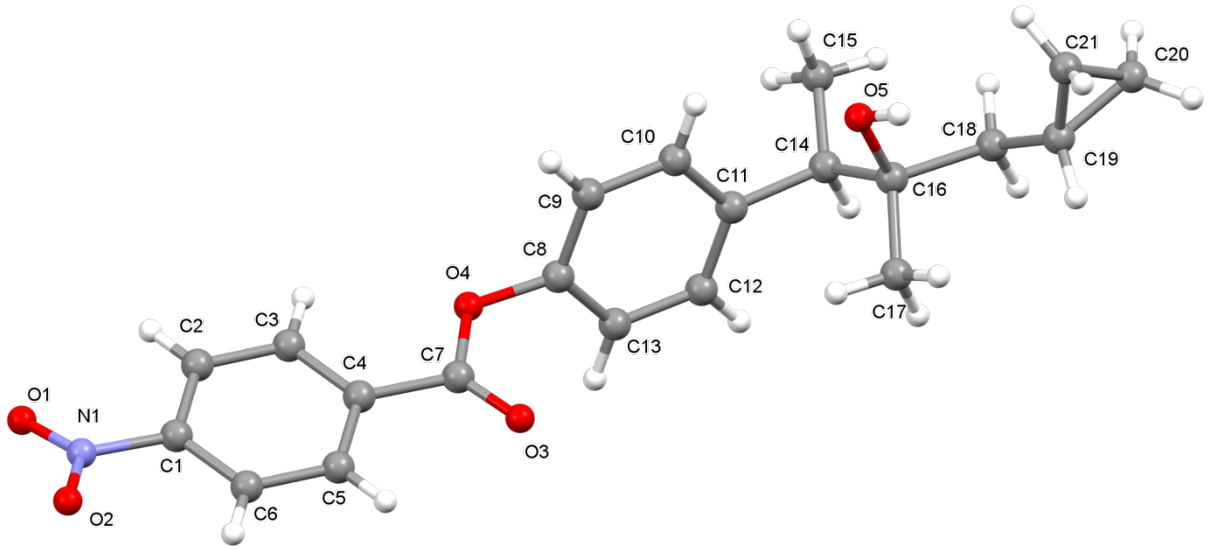
.

Crystal structure determination:

Repeated crystallization produced thin flaky crystals of poor quality. Therefore, these were used for data collection. Single-crystal X-ray diffraction data were collected on an Agilent SuperNova Dual Atlas diffractometer, equipped with a mirror monochromator and using either Cu radiation. An Oxford Cryosystems cooling apparatus was used for temperature regulation. The data were processed using CrysAlisPro[1] and the crystal structures were solved using SHELXT[2] and refined using SHELXL[3]. Non-hydrogen atoms were refined with anisotropic displacement parameters. In the final cycles of refinement, hydrogen atom geometry was idealized, and a riding model was used with U_{iso} set at 1.2 or 1.5 times the value of U_{eq} for the atom to which the hydrogen atoms are bonded. Table 1 shows crystal and structure refinement data. The structure has been deposited in the CSD under reference CCDC 2441709.

.

1. CrysAlisPro, Rigaku OD, Yarnton, England, 2022-24.
2. G. M. Sheldrick, *Acta Crystallogr., Sect. A*, 2015, 71, 3-8.
3. G. M. Sheldrick, *Acta Crystallogr., Sect. C*, 2015, 71, 3-8.



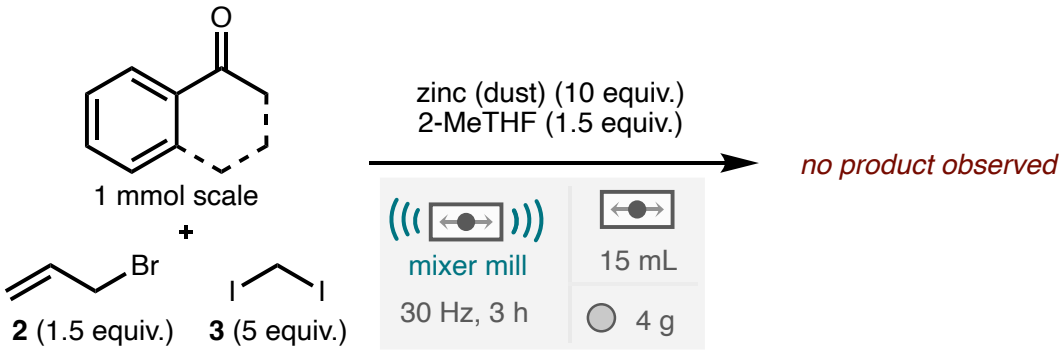
A molecule of the compound.

Table 1. Crystal and structure refinement data.

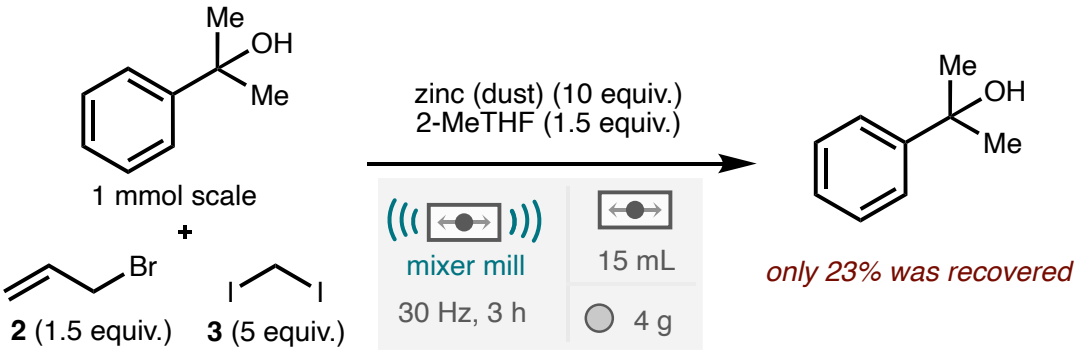
Empirical formula	$C_{21}H_{23}NO_5$	
Formula weight	369.40	
Temperature	200(2) K	
Wavelength	1.54184 Å	
Crystal system	Monoclinic	
Space group	C 2/c	
Unit cell dimensions	a = 37.481(4) Å	a= 90°.
	b = 6.5428(8) Å	b= 94.656(10)°.
	c = 15.9192(13) Å	g = 90°.
Volume	3890.9(7) $Å^3$	
Z	8	
Density (calculated)	1.261 Mg/m^3	
Absorption coefficient	0.739 mm^{-1}	
F(000)	1568	
Crystal size	0.290 x 0.120 x 0.010 mm^3	
Theta range for data collection	4.735 to 72.622°.	
Index ranges	-46<=h<=45, -5<=k<=8, -14<=l<=19	
Reflections collected	11814	
Independent reflections	3786 [R(int) = 0.1504]	
Completeness to theta = 67.684°	99.7 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	1.00000 and 0.41510	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3786 / 0 / 222	
Goodness-of-fit on F^2	1.117	
Final R indices [I>2sigma(I)]	R1 = 0.1747, wR2 = 0.4302	
R indices (all data)	R1 = 0.2989, wR2 = 0.5263	
Extinction coefficient	0.0011(4)	
Largest diff. peak and hole	0.762 and -0.309 $e.Å^{-3}$	

7. **Unsuccessful Substrates:**

- **Ketones Conjugated with Benzene ring:**



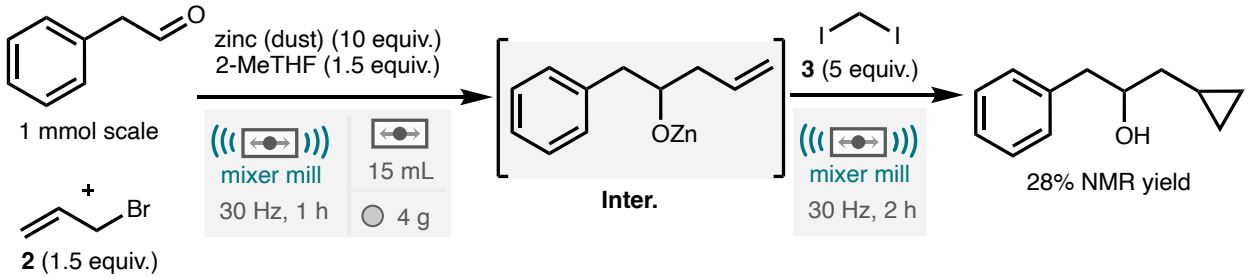
Control reaction:



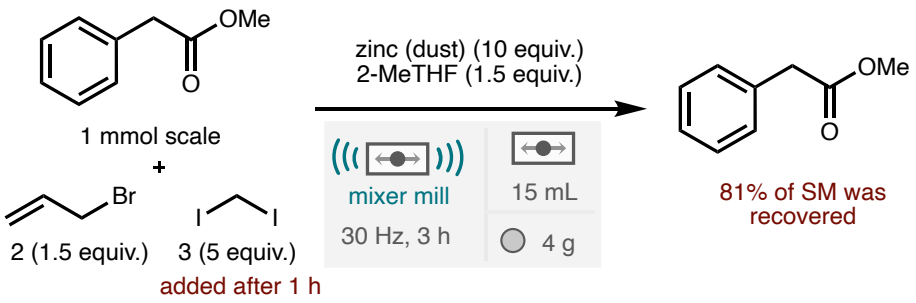
The Barbier/Simmons–Smith reaction with ketones conjugated to aromatic rings, such as α-tetralone or acetophenone, was unsuccessful, indicating that our method is only applicable to non-conjugated ketones. Additionally, a control reaction with 1-phenylethanol under standard conditions showed that the products are unstable, with only 23% of the starting material recovered.

- Reactions of other carbonyl compound and imines under the standard conditions were examined. Aldehydes afforded significantly lower yield, while ester, carboxylic acid and imines did not give the desired products. Yield determined *via* ^{1}H NMR analysis of the crude reaction mixture using mesitylene (0.33 mmol) as an internal standard.

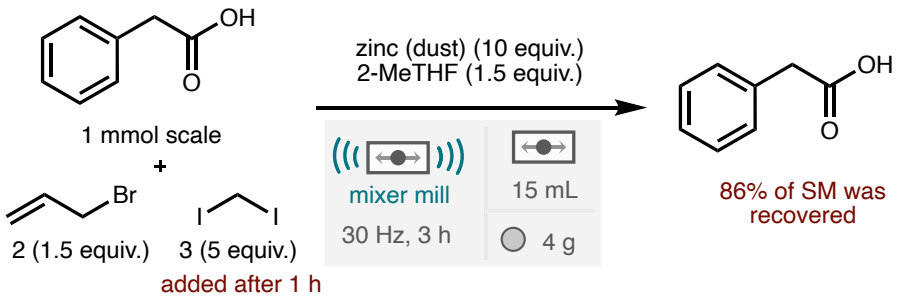
- ***Aldehyde:***



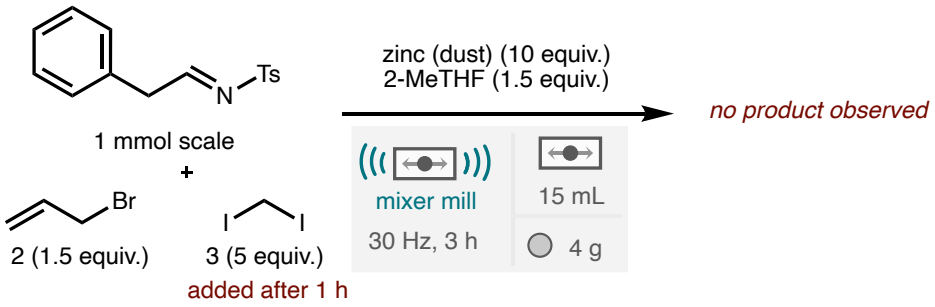
- ***Ester:***



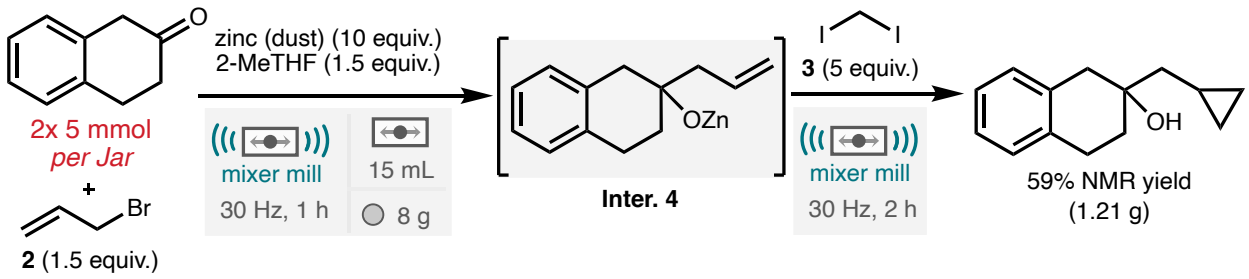
- ***Carboxylic acid:***



- ***imine:***


Ts
N
1 mmol scale
+
Br
2 (1.5 equiv.)
I
I
3 (5 equiv.)
added after 1 h
zinc (dust) (10 equiv.)
2-MeTHF (1.5 equiv.)
mixer mill
30 Hz, 3 h
15 mL
4 g
no product observed

8. **Reaction Scale-up:**



To a 15 mL stainless jar charged with one 8 g stainless steel ball, β-tetralone (0.66 mL, 5.00 mmol, 1 equiv.), allyl bromide (0.65 mL, 1.50 mmol, 1.50 equiv.),(zinc metal (3.2 g, 10.00 mmol, 10.00 equiv.), and 2-MeTHF (0.76 mL, 1.50 mmol, 1.50 equiv.) were added and milled at 30 Hz for 1 h at room temperature in a Insolido Tech mixer mill. Then the jar was opened and diiodomethane (2 mL, 5.00 mmol, 5.00 equiv.) was added and milled at 30 Hz for 2 h at room temperature. After the milling period the jar was opened and rinsed into a conical flask using CH_2Cl_2 (50.00 mL). 1.0 M HCl (25.00 mL) was added to the flask and stirred for 10 minutes. The resulting biphasic mixture was transferred to a separating funnel where the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (2 x 25.00 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated in vacuo. the crude compound was purified by silica gel flash column chromatography using (Eluent: EtOAc/Petroleum ether, 5-10%) as a yellow oil (1.21 g, 62%).

9. **Reference:**

1) K. Polidano, B. D. W. Allen, J. M. J. Williams and L. C. Morrill, *ACS Catal.,* 2018, **8,** 6440–6445.

2) P. Li, B. Lü, C. Fu and S. Ma, *Adv. Synth. Catal.*, 2013, **355**, 1255–1259.

3) L. Ackermann and V. P. Mehta, *Chem. Eur. J.*, 2012, **18**, 10230–10233.

4) D. Méndez-Sánchez, J. Mangas-Sánchez, E. Busto, V. Gotor and V. Gotor-Fernández, *Adv. Synth. Catal.*, 2016, **358**, 122–131.

5) F. Karaki, M. Kuwada, S. Tajiri, M. Kanda, M. Yanai, M. Kamimura, I. Kennosuke and H. Fujii, *Synth. Commun.*, 2019, **49**, 212–220.

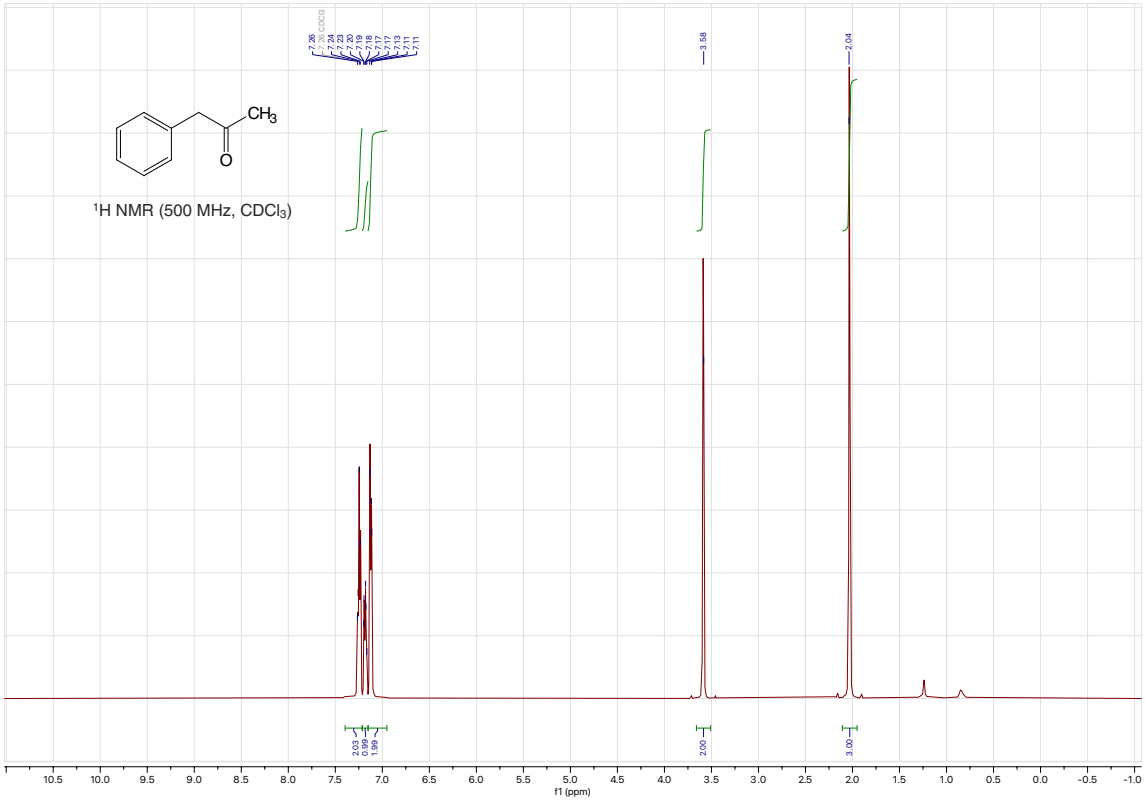
6) H. Maekawa, K. Nagakubo, M. Nishi, M. Nishimura and D. Nagahara, *Bull. Chem. Soc. Jpn.,* 2013, **86**, 1183–1189.

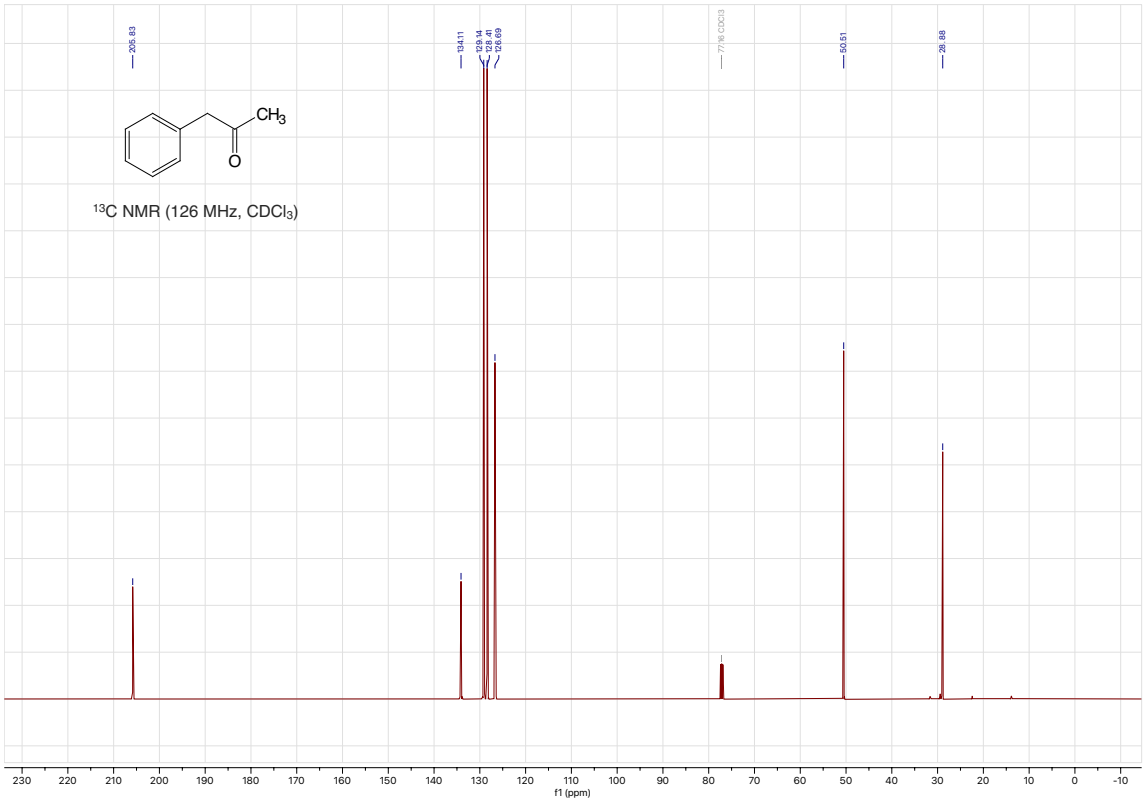
7) I. Peñafiel, I. M. Pastor and M. Yus,*Tetrahedron,* 2010, **66**, 2928–2935.

8) L. Pontini, J. Leitch and D. L. Browne, *Green Chem.,* 2023, **25**, 4319-4325

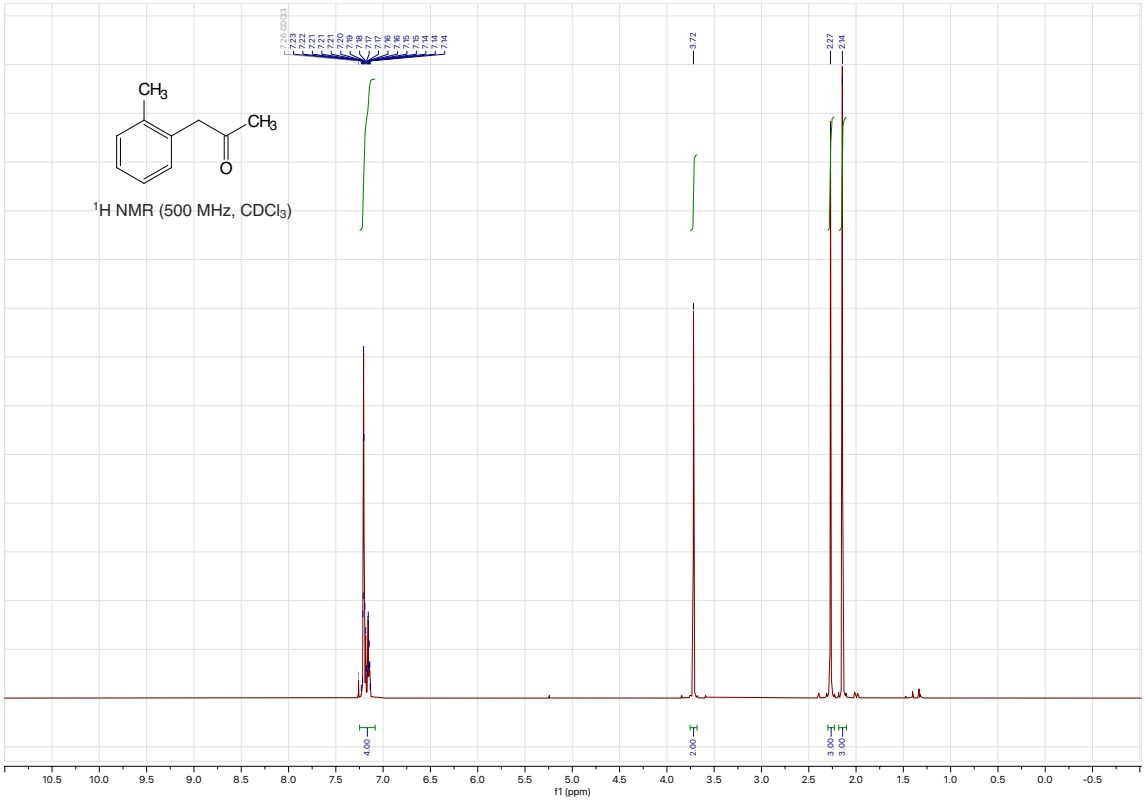
10. **NMR Spectra**

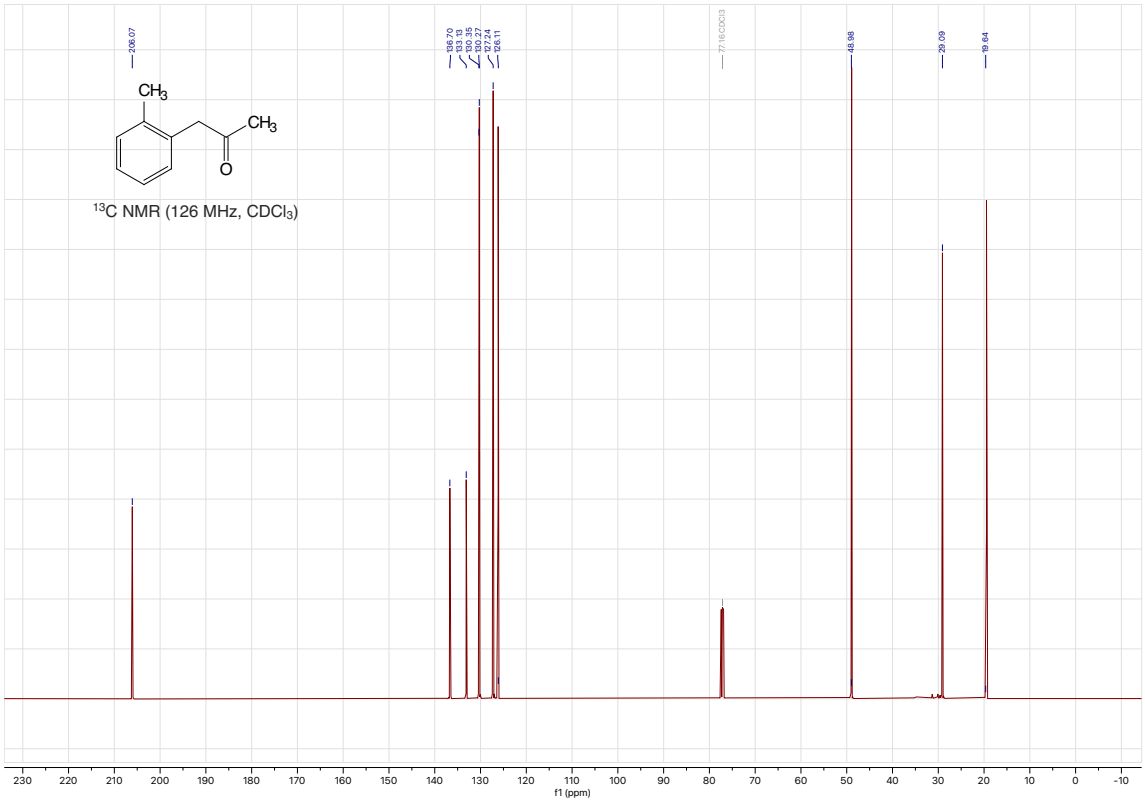
1-phenylpropan-2-one (S1)



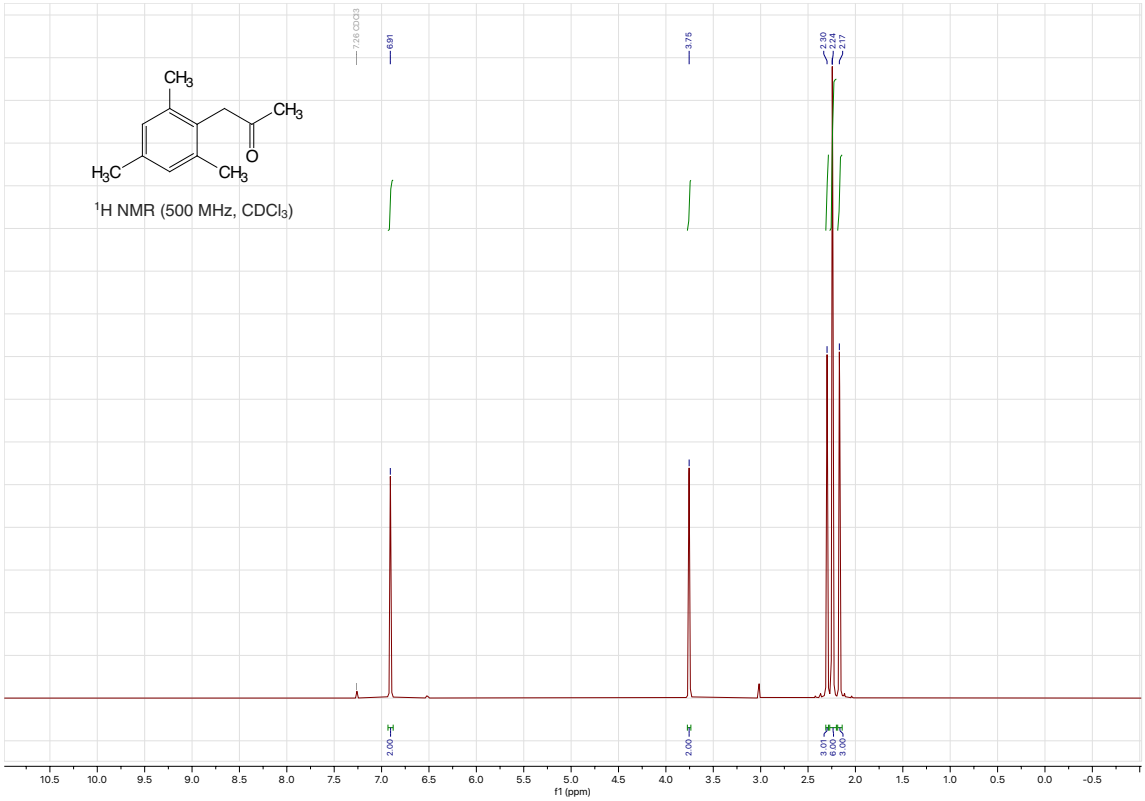


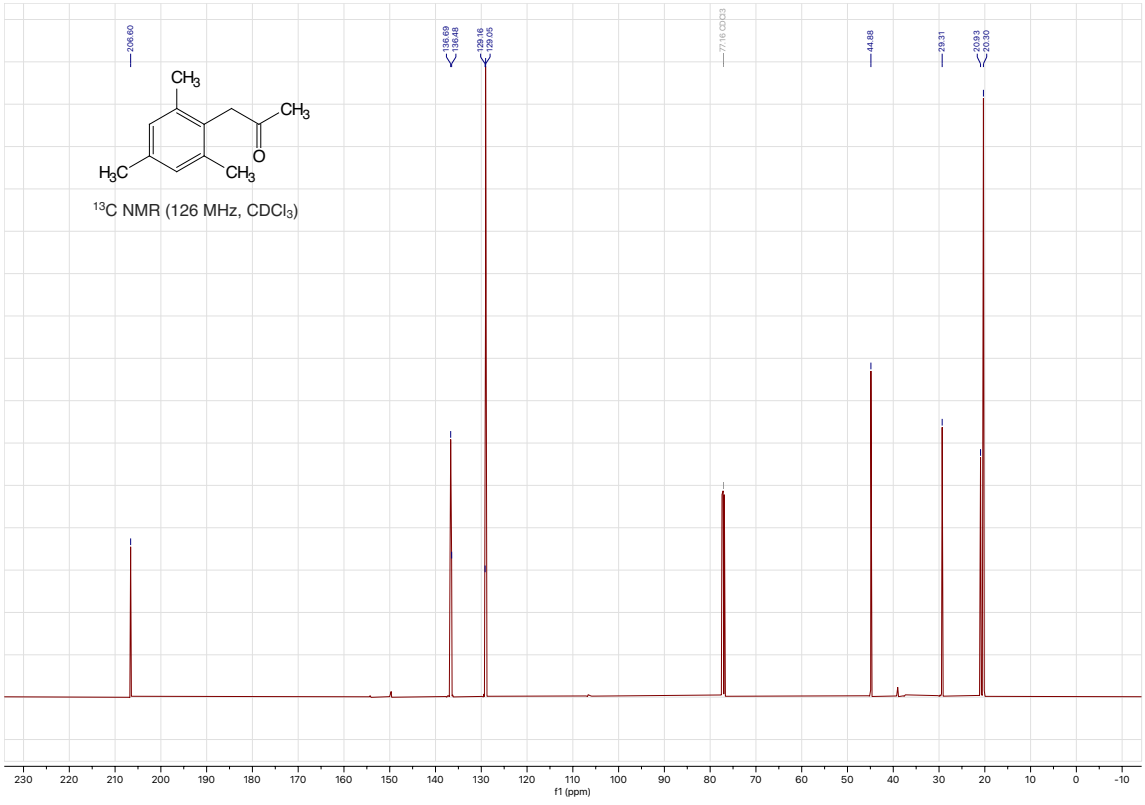
1-(*o*-tolyl)propan-2-one (S2)



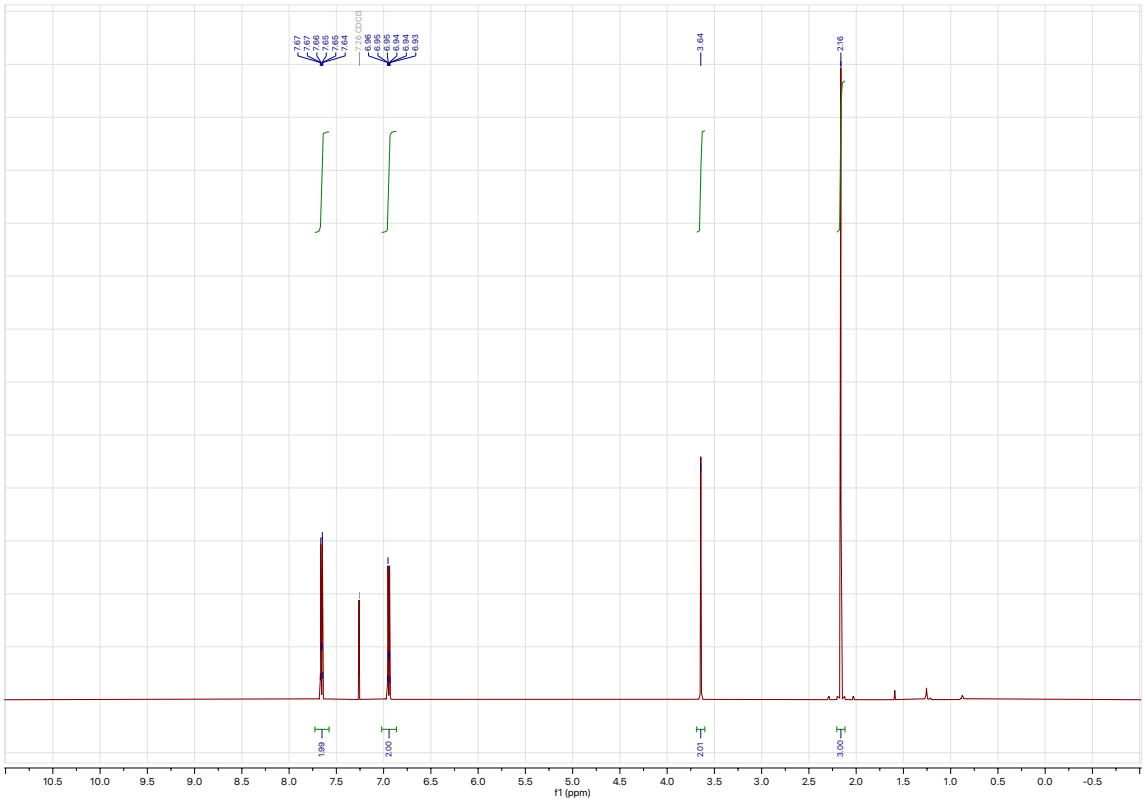


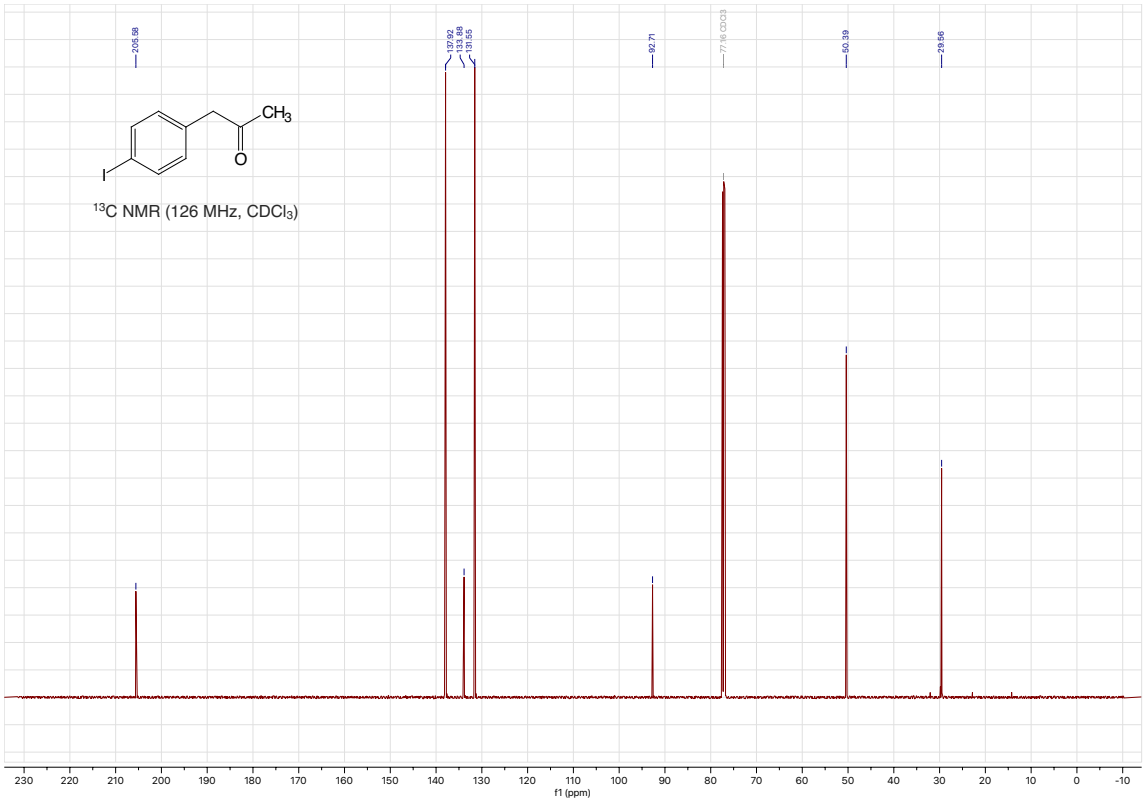
1-mesitylpropan-2-one (S3)



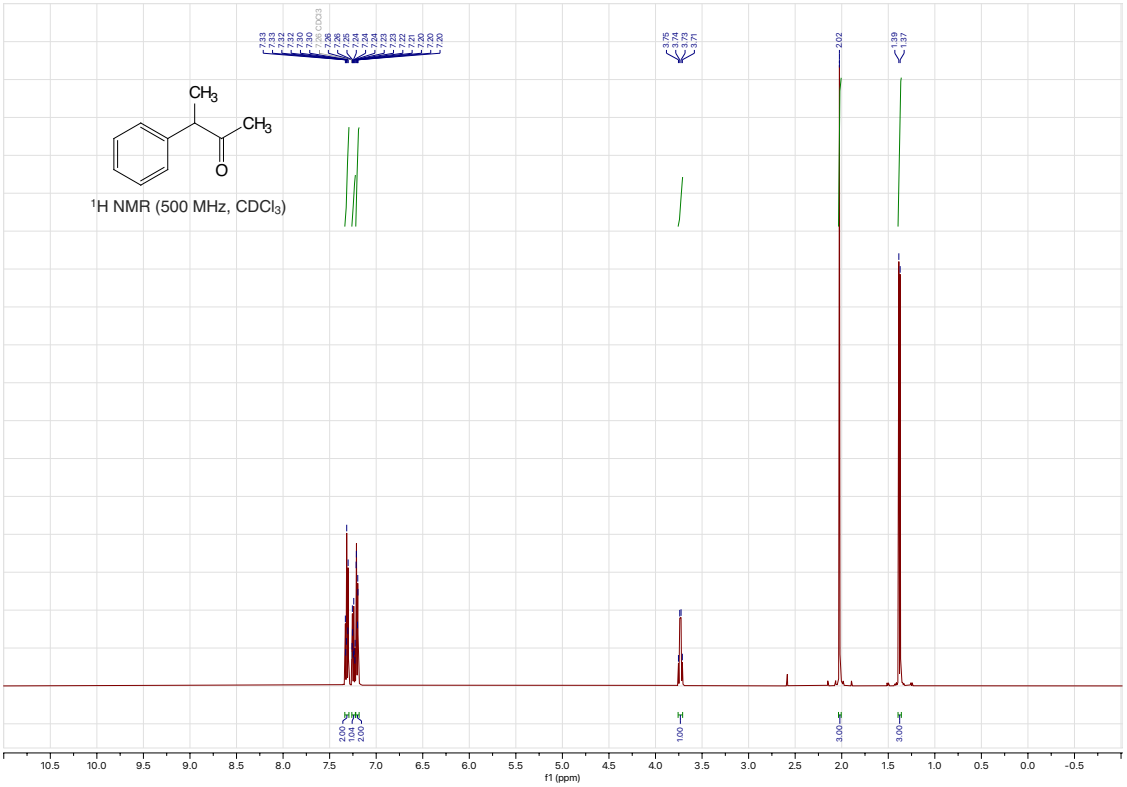


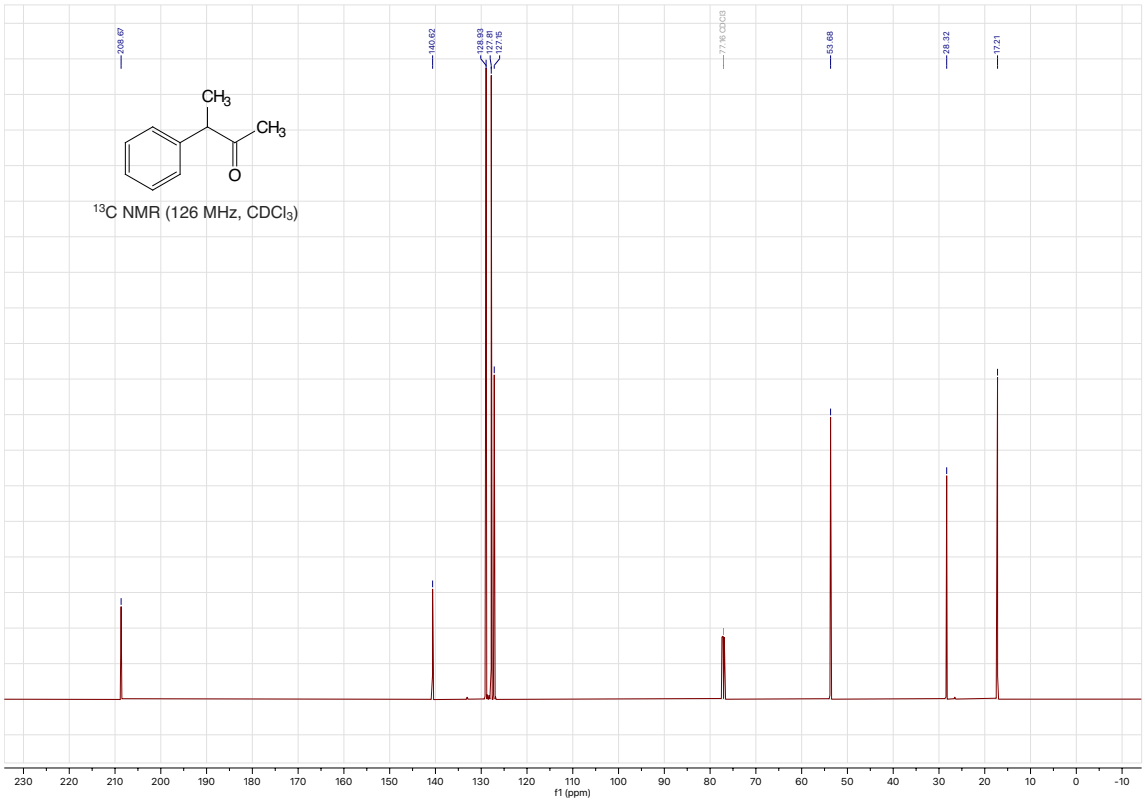
1-(4-iodophenyl)propan-2-one (S4)



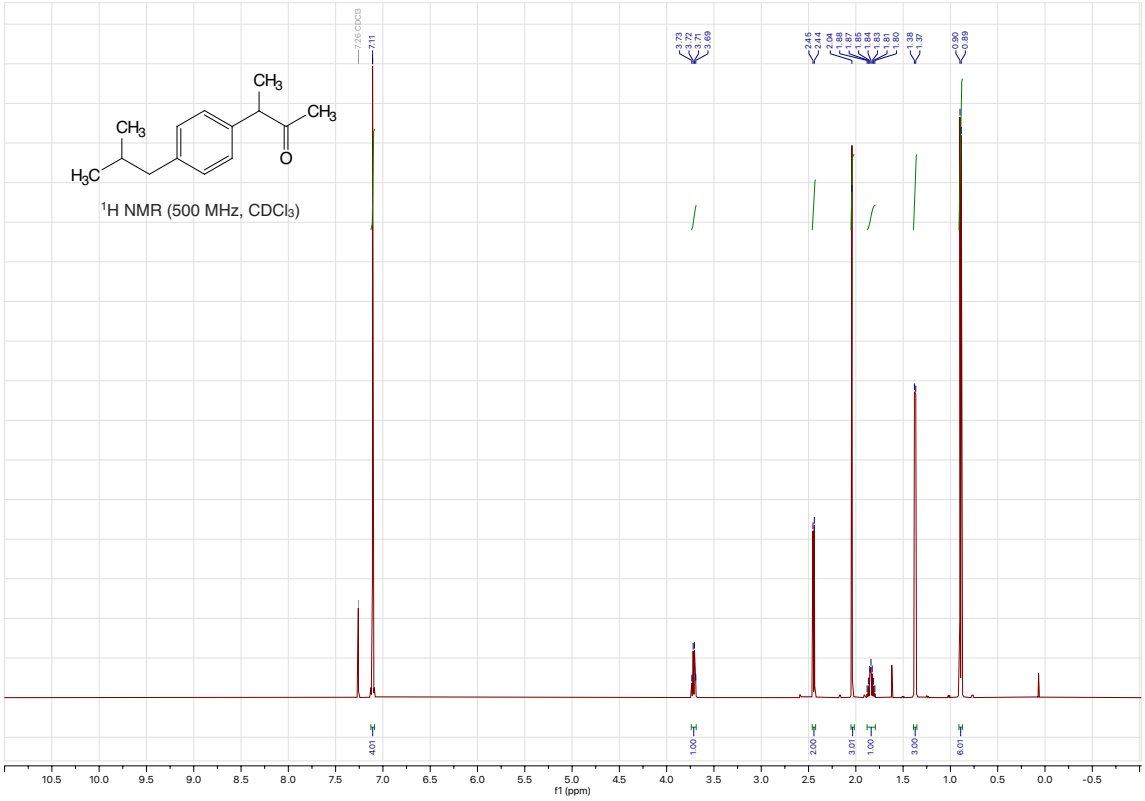


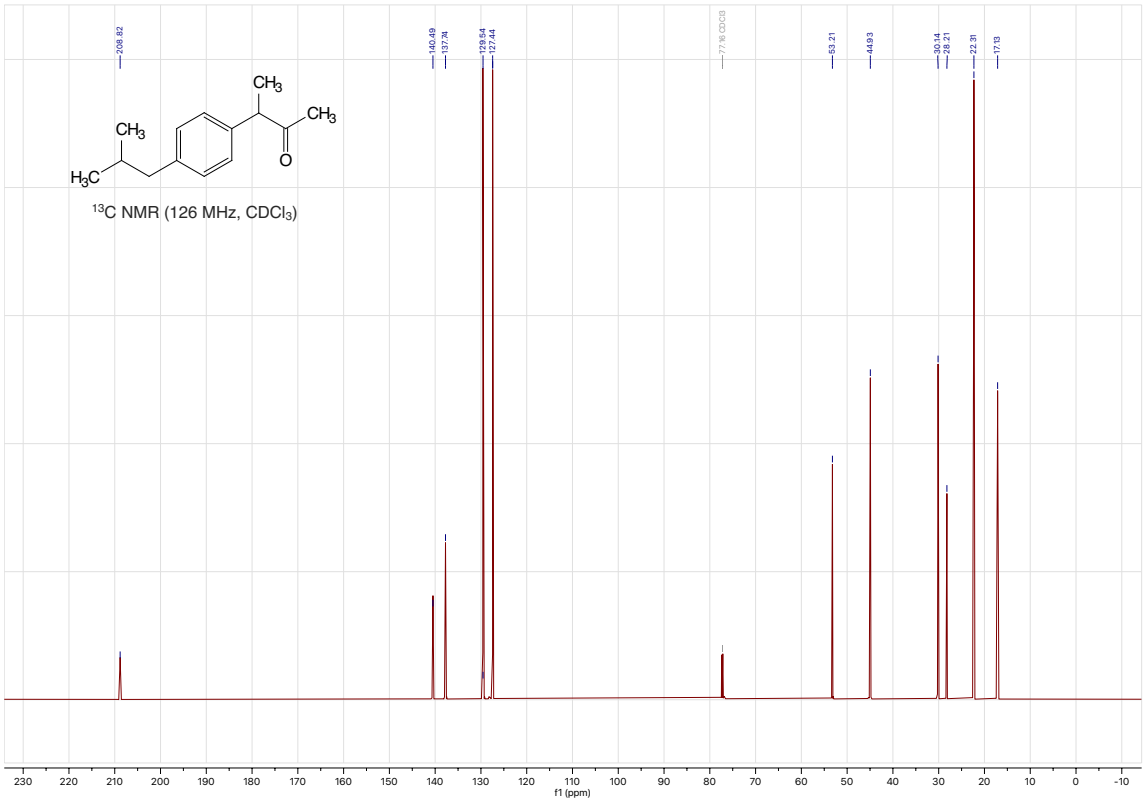
3-phenylbutan-2-one (S5)



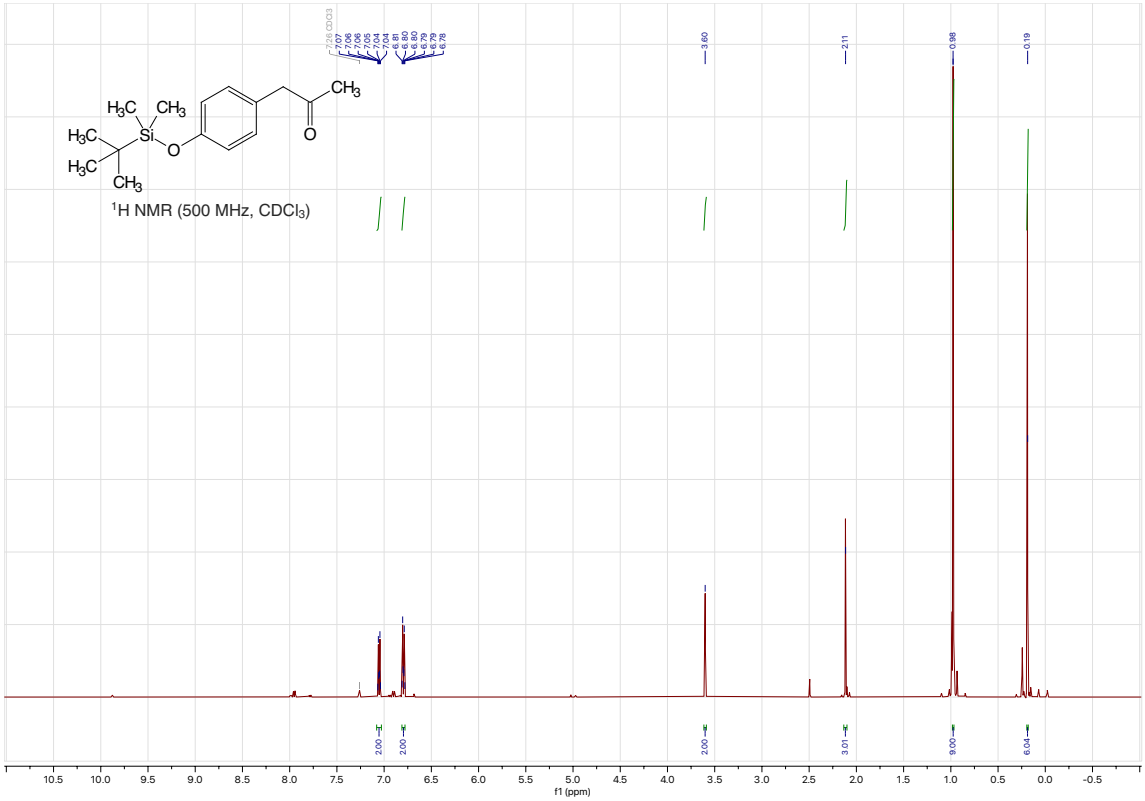


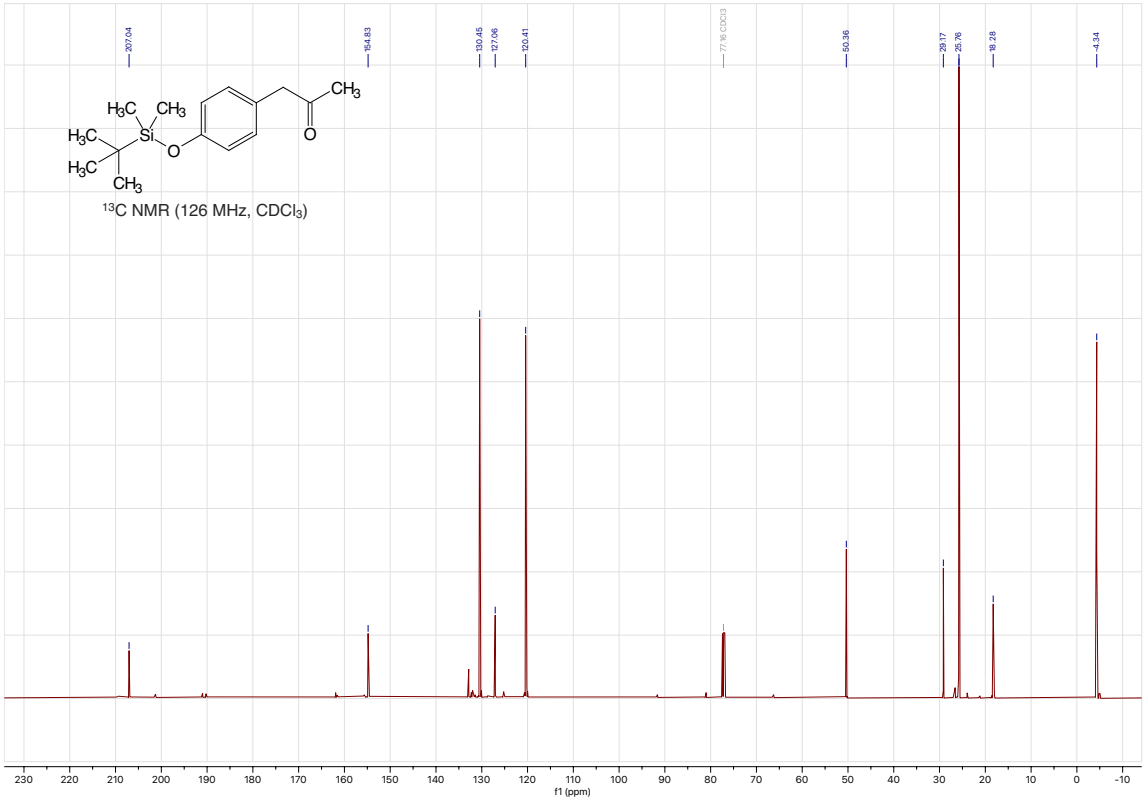
3-(4-isobutylphenyl)butan-2-one (S6)



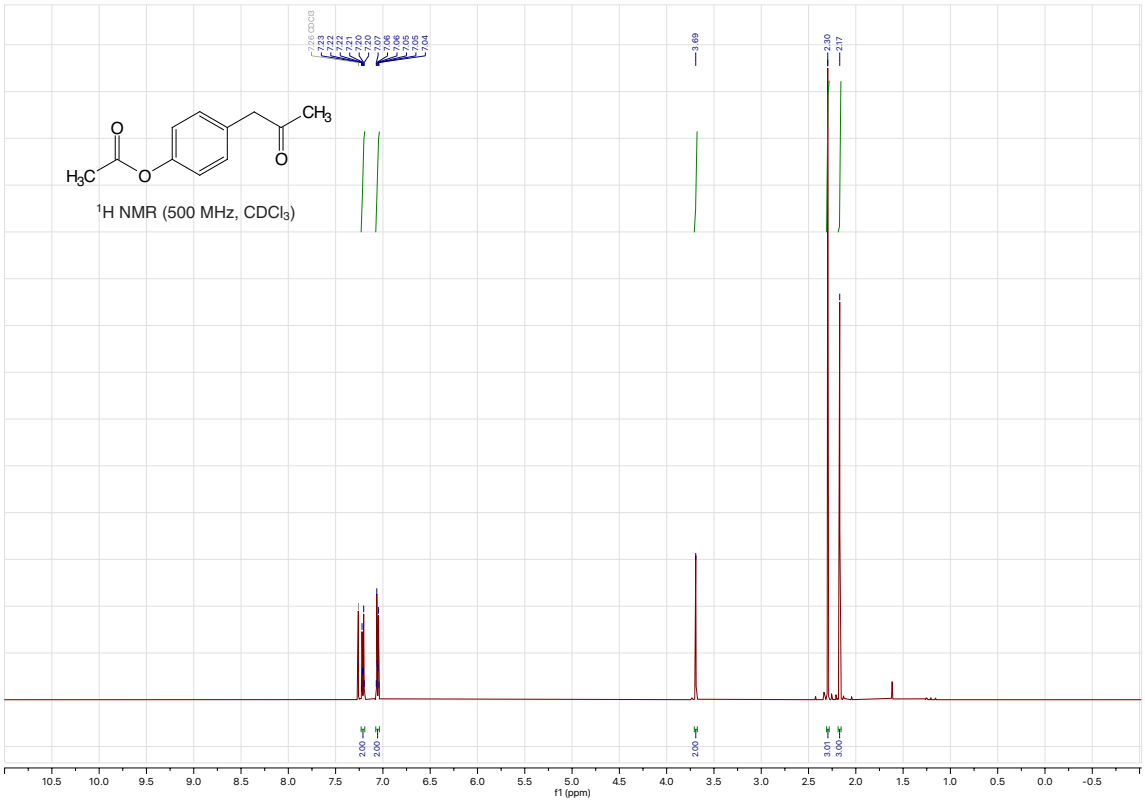


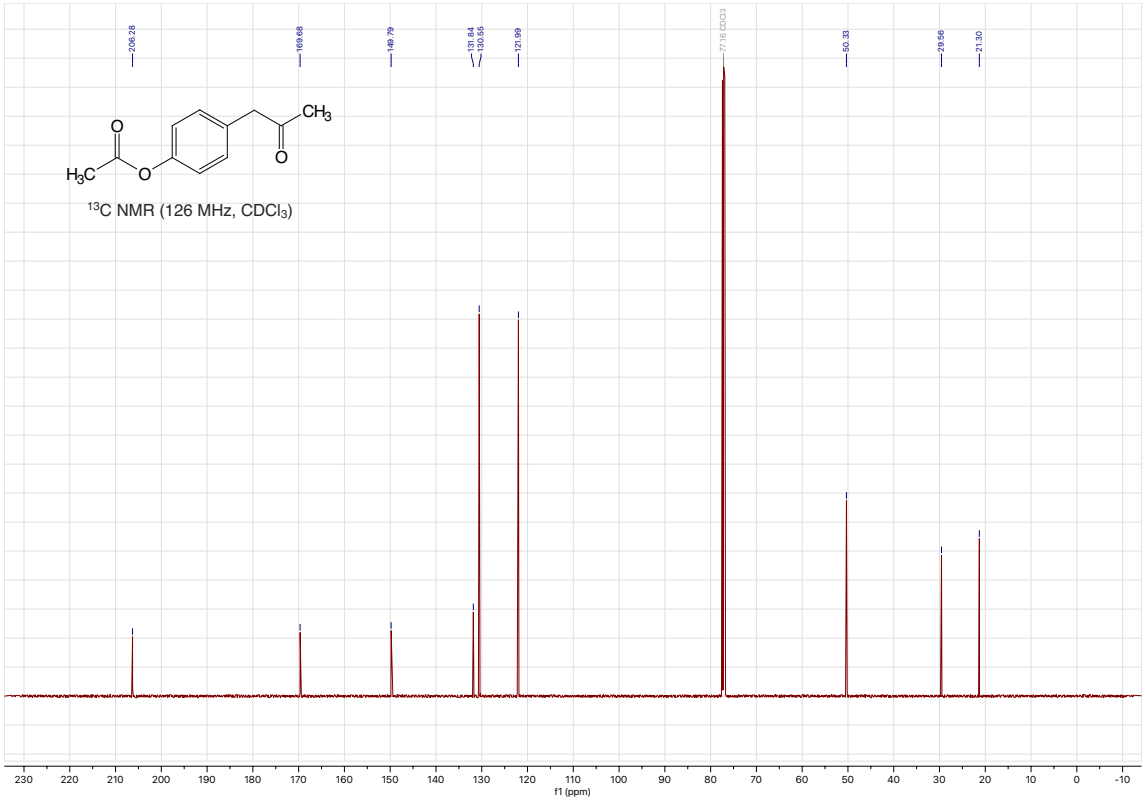
1-(4-((*tert*-butyldimethylsilyl)oxy)phenyl)propan-2-one (S7)



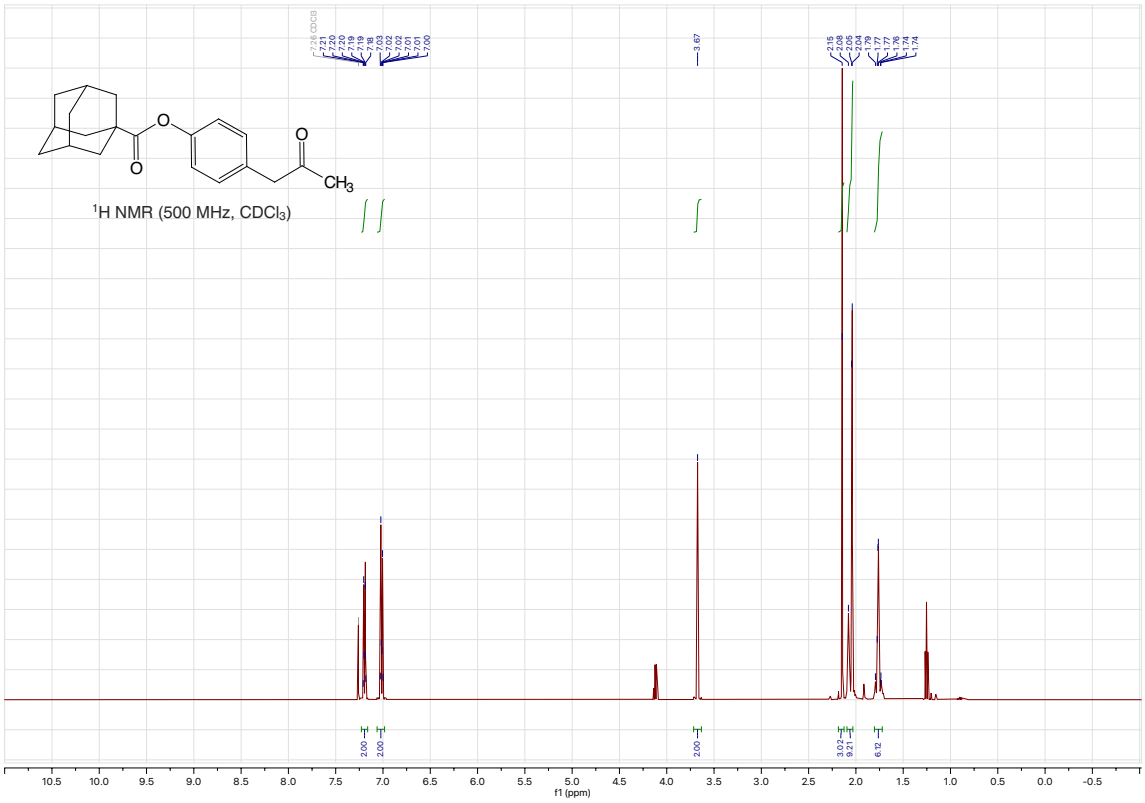


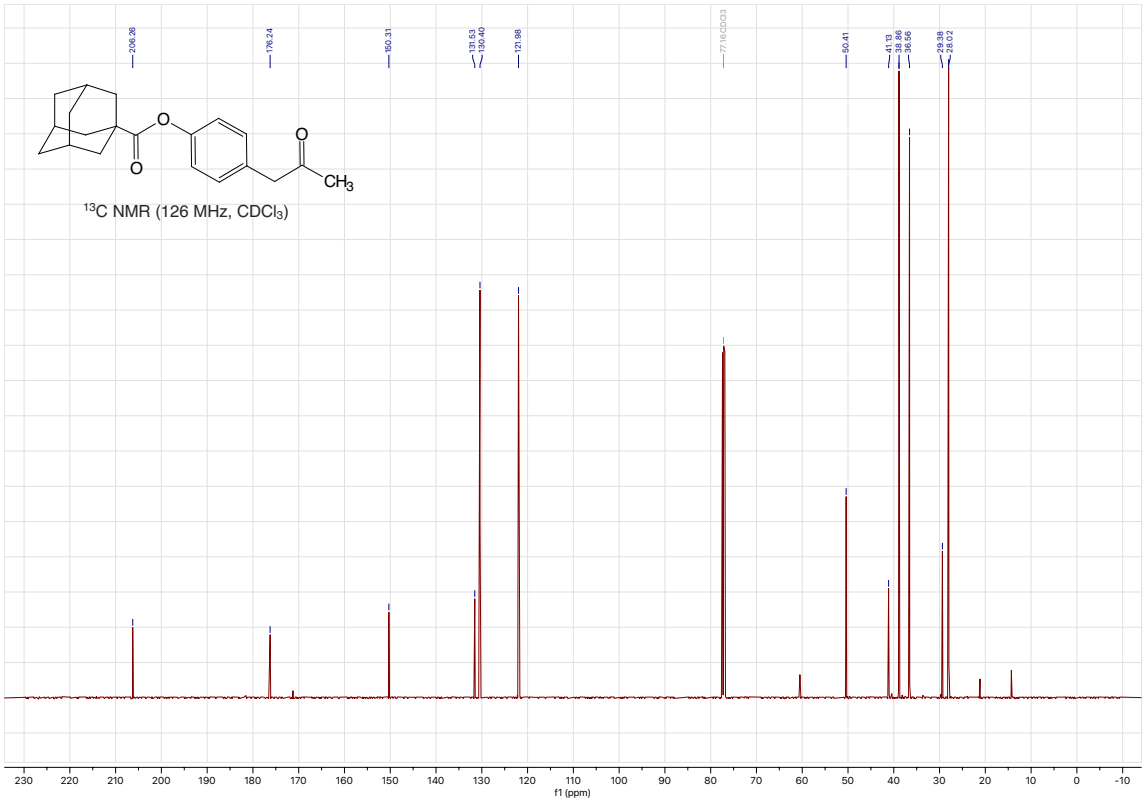
4-(2-oxopropyl)phenyl acetate (S8)



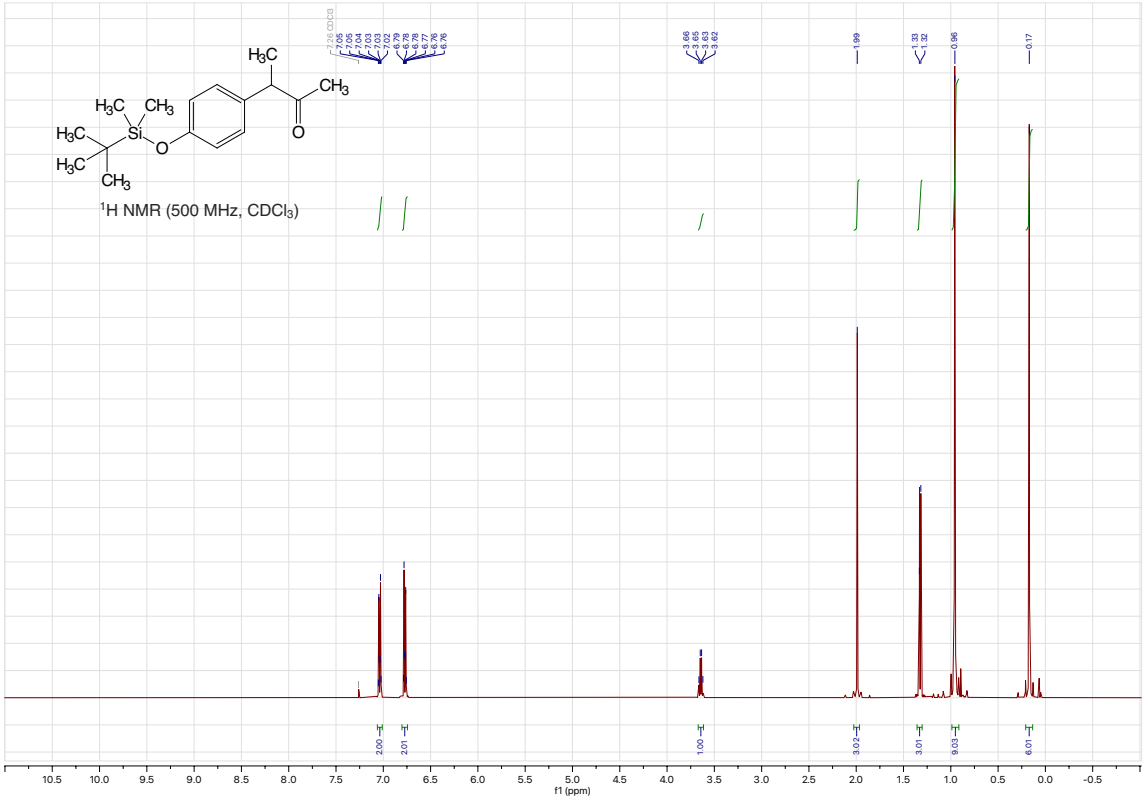


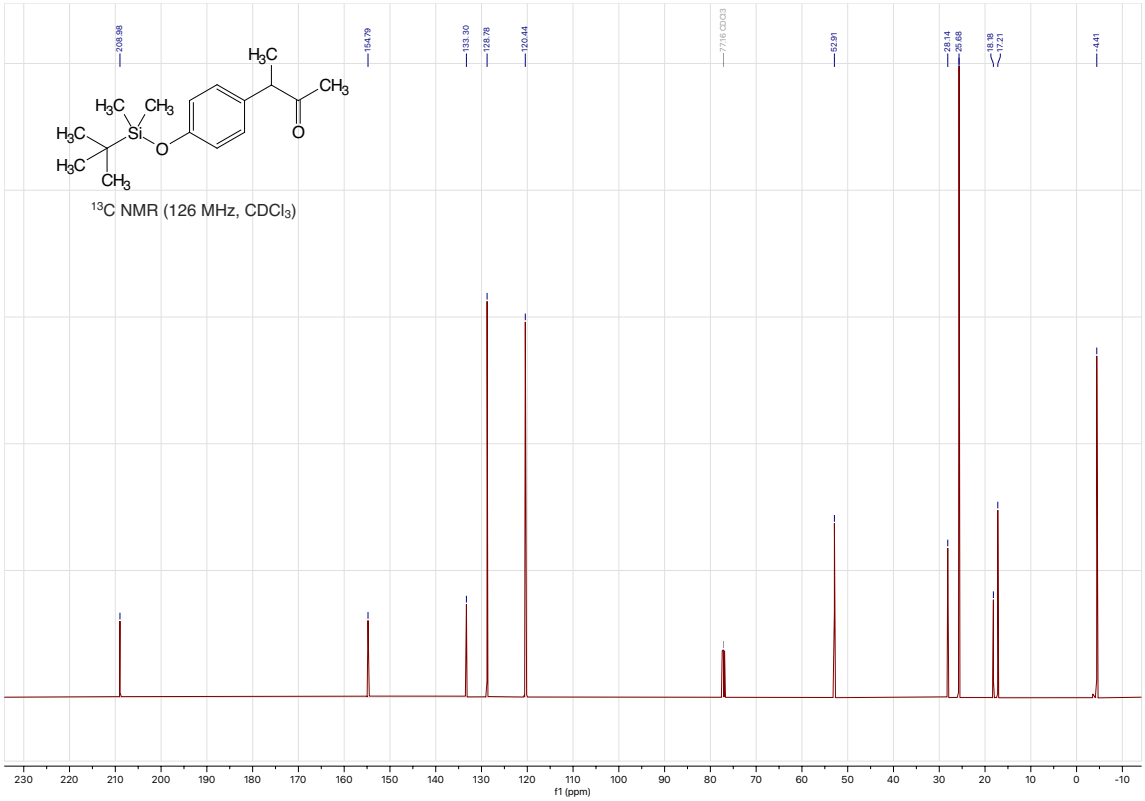
4-(2-oxopropyl)phenyl (3*r*,5*r*,7*r*)-adamantane-1-carboxylate (S9)



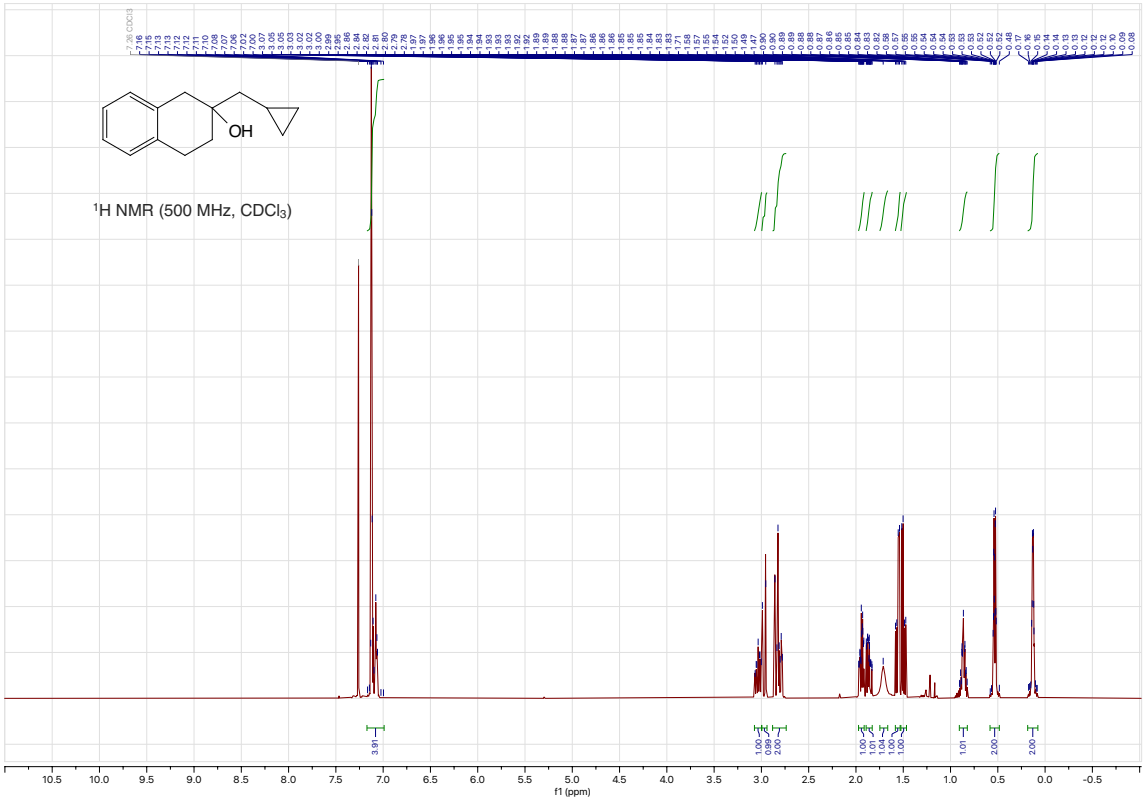


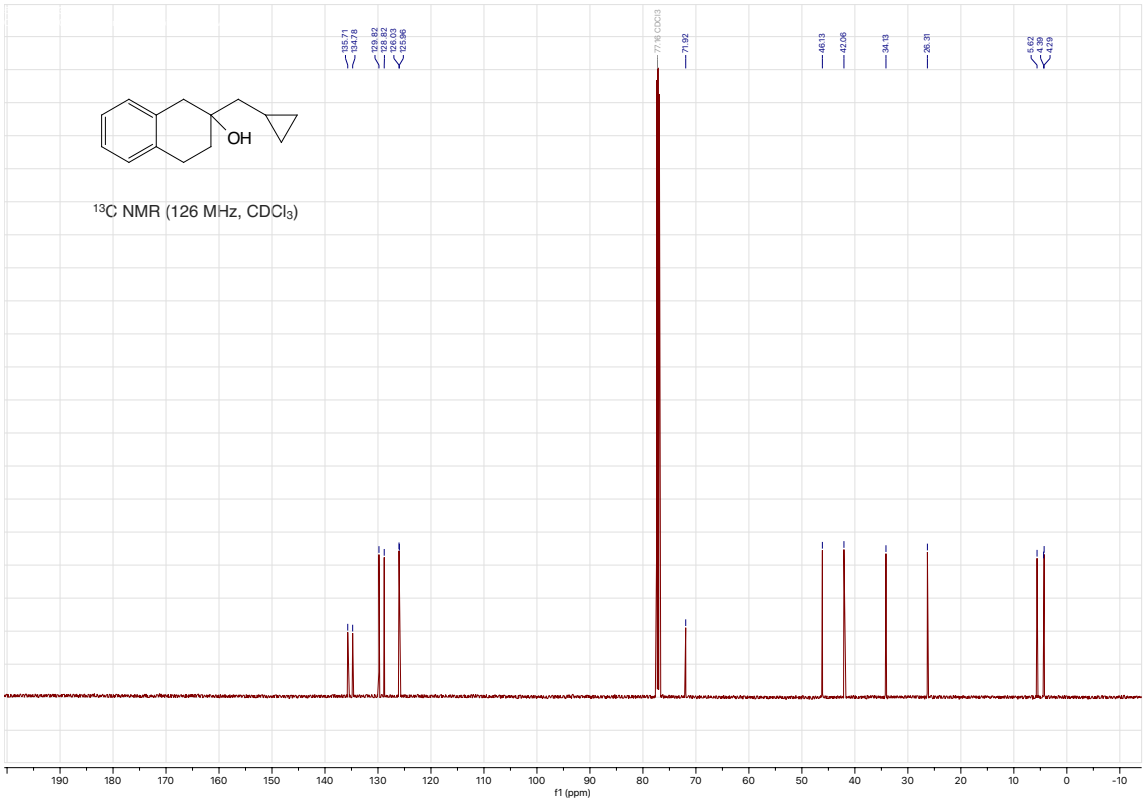
3-(4-((*tert*-butyldimethylsilyl)oxy)phenyl)butan-2-one (S10)



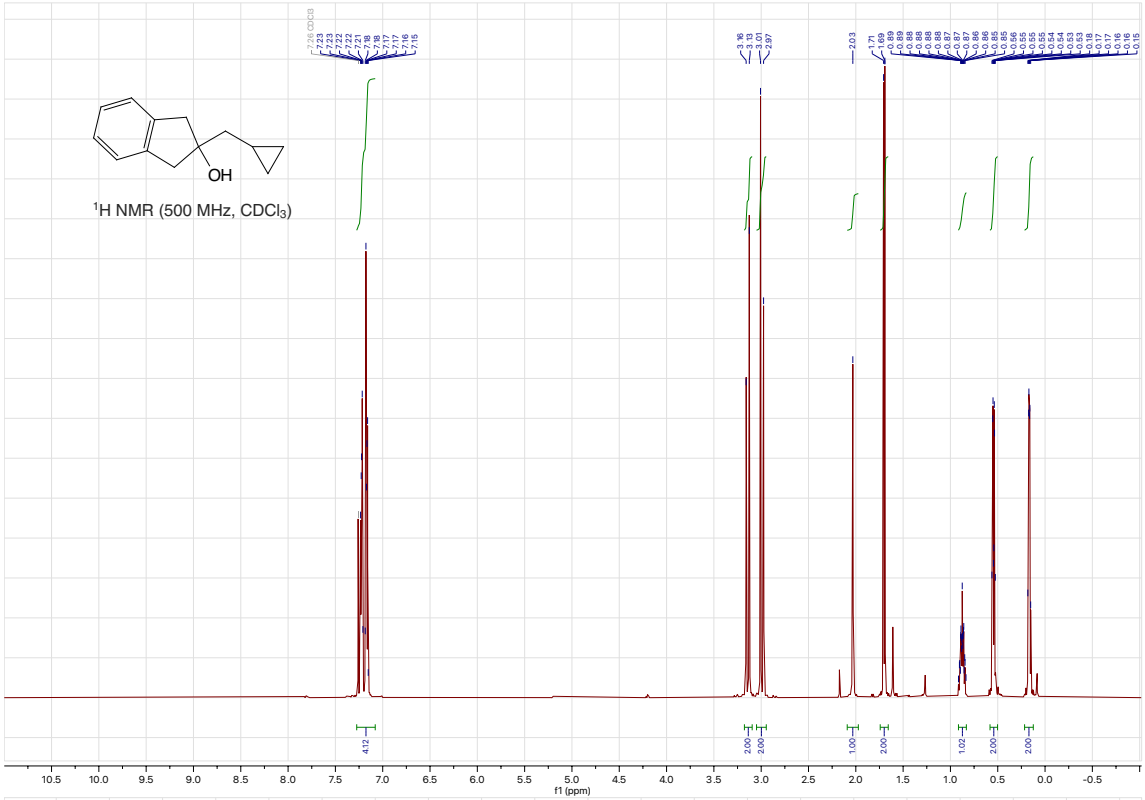


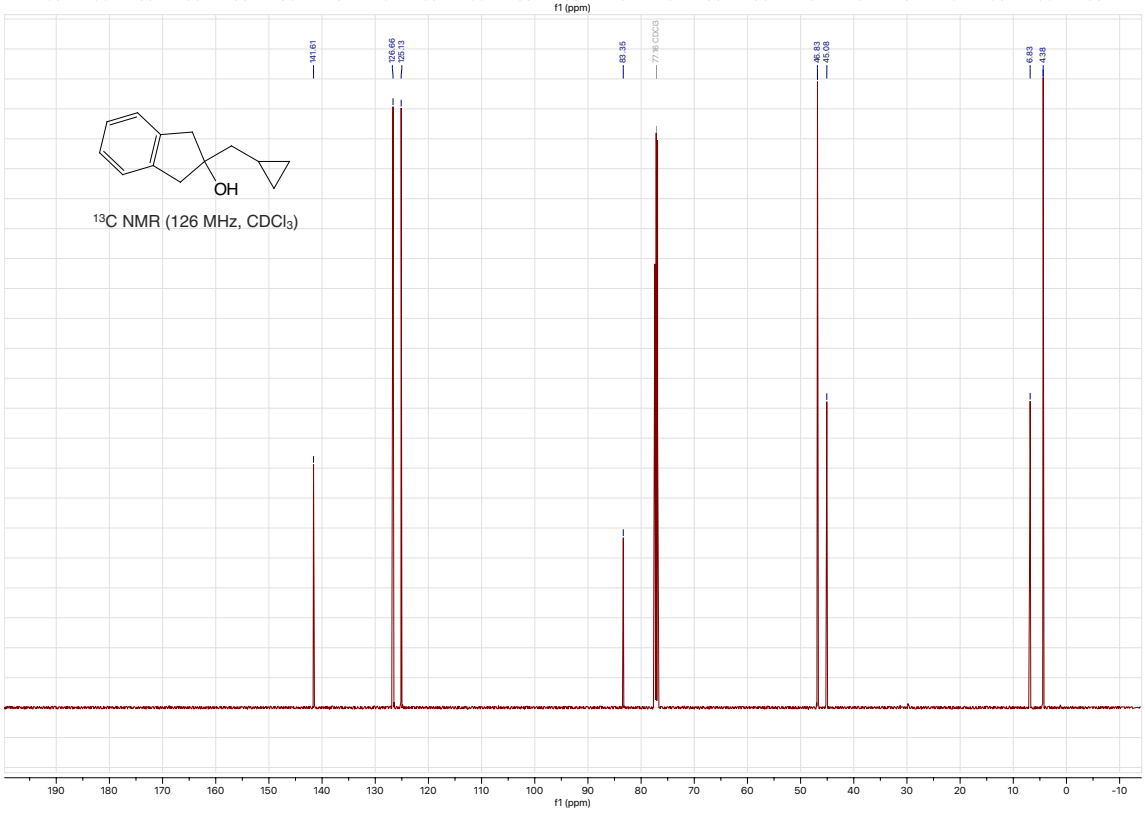
2-(cyclopropylmethyl)-1,2,3,4-tetrahydronaphthaln-2-ol (5)



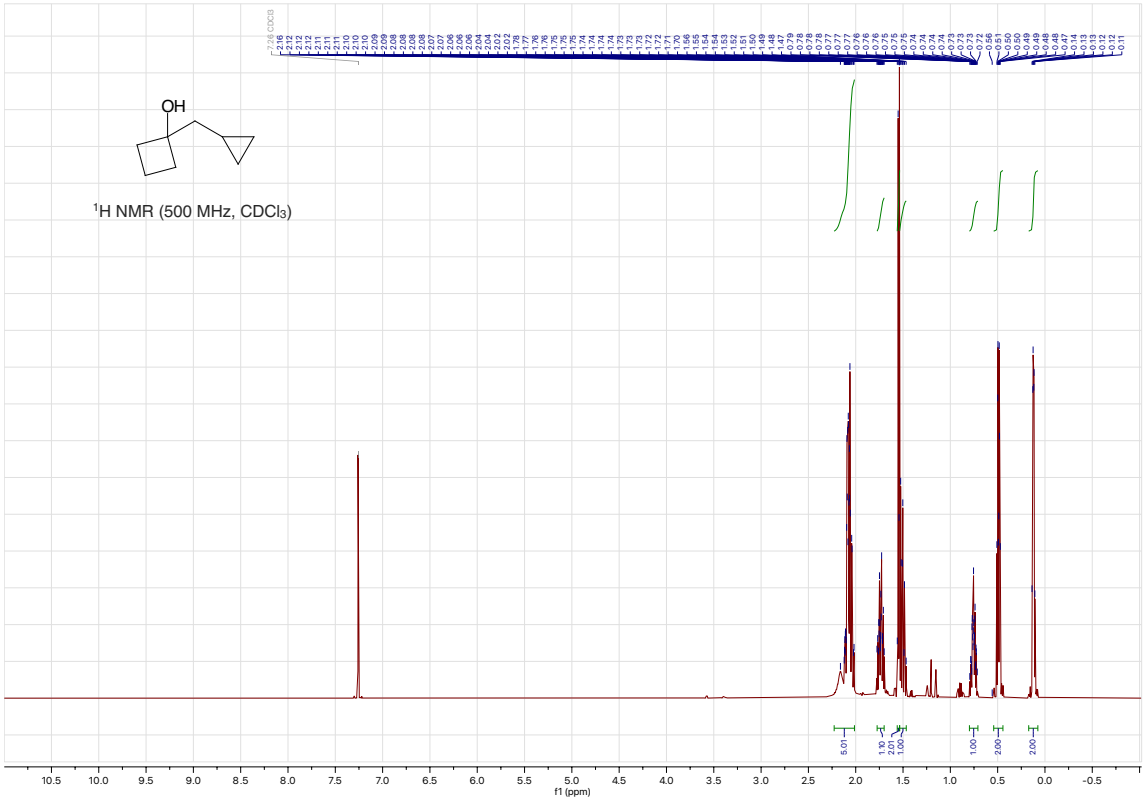


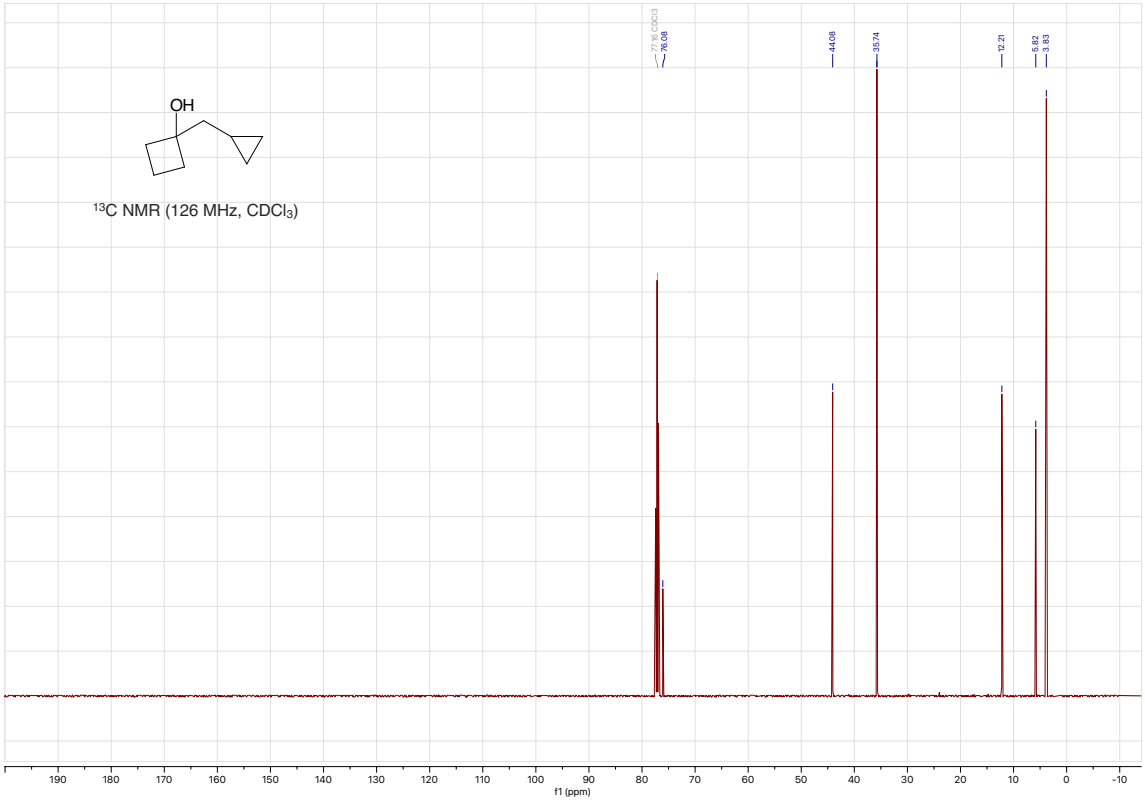
2-(cyclopropylmethyl)-2,3-dihydro-1*H*-inden-2-ol (6)



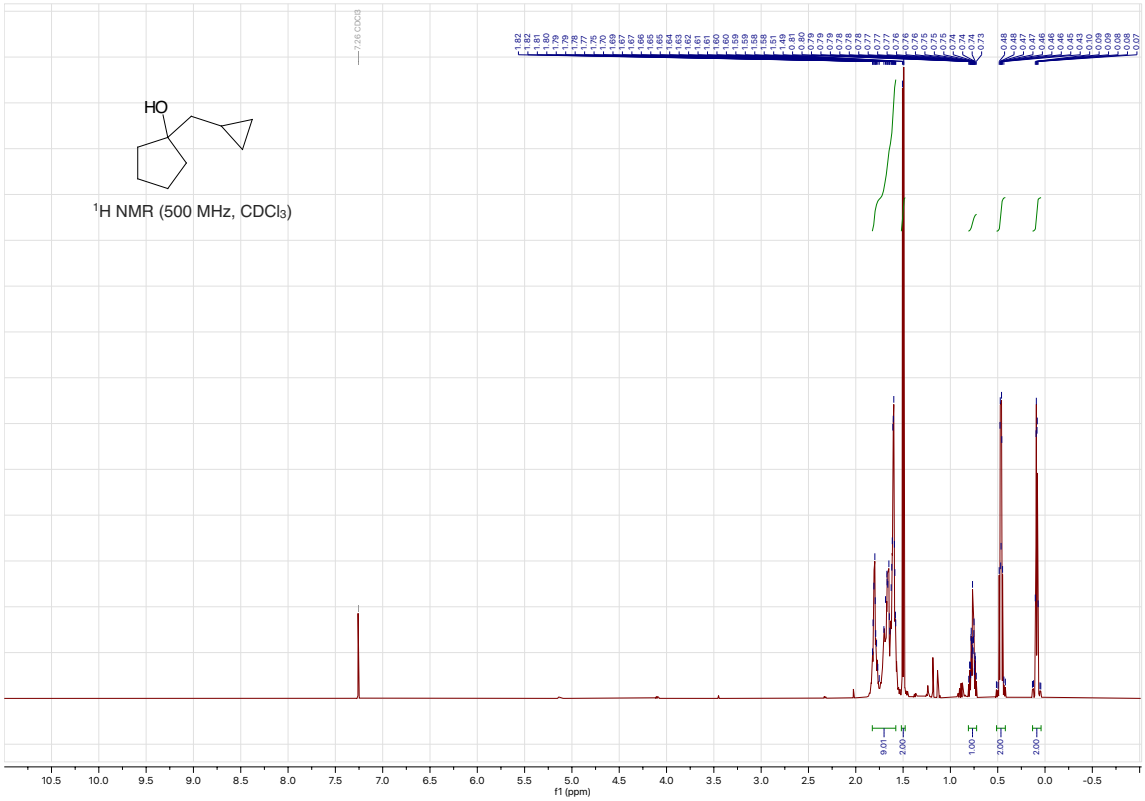


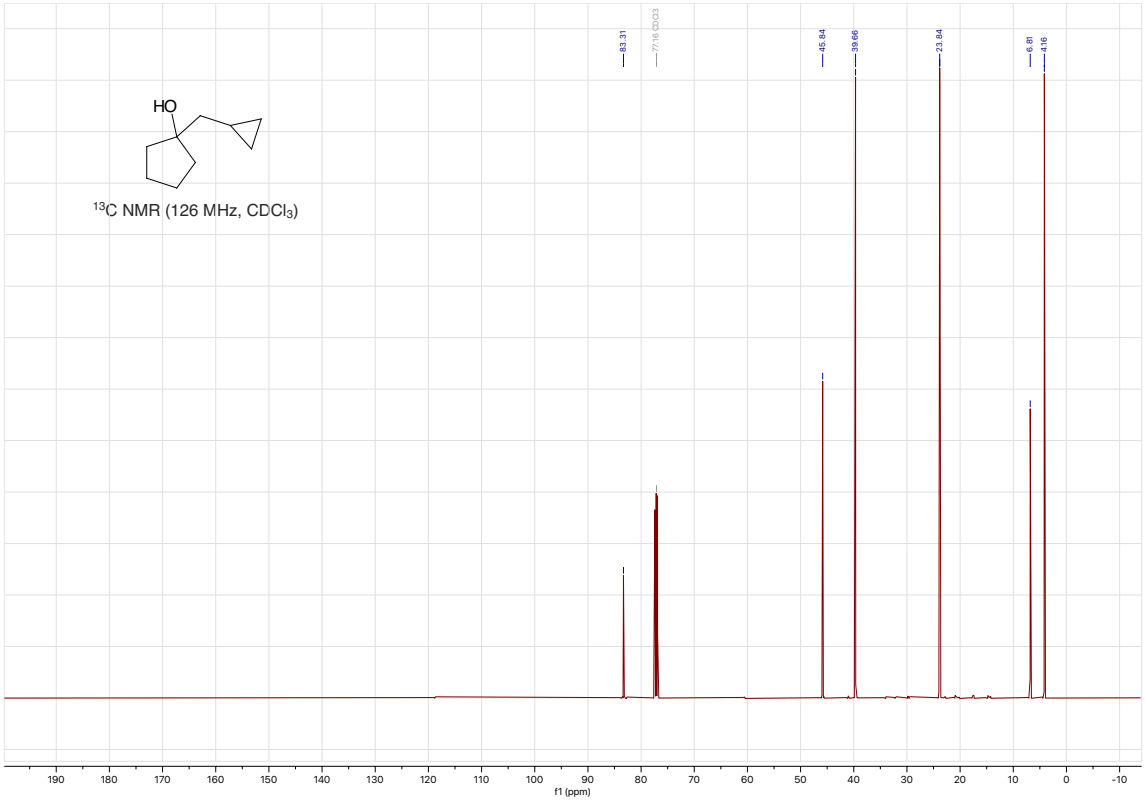
1-(cyclopropylmethyl)cyclobutan-1-ol (7)



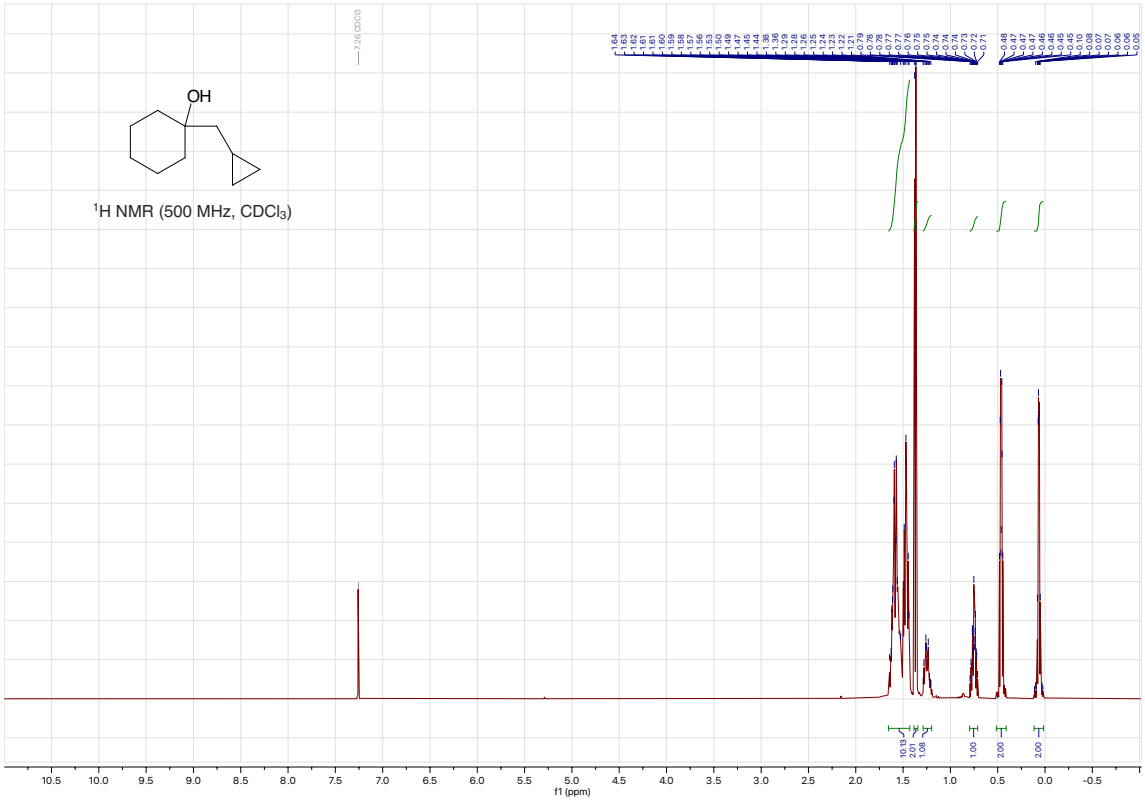


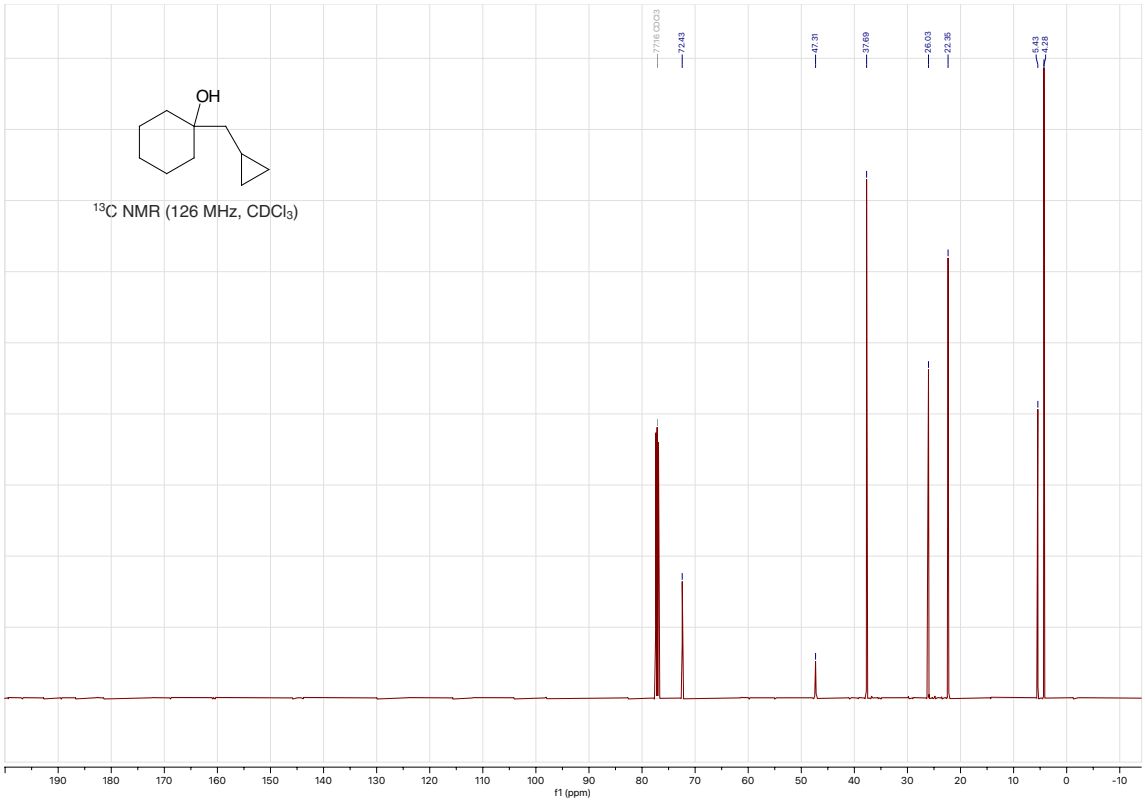
1-(cyclopropylmethyl)cyclopentan-1-ol (8)



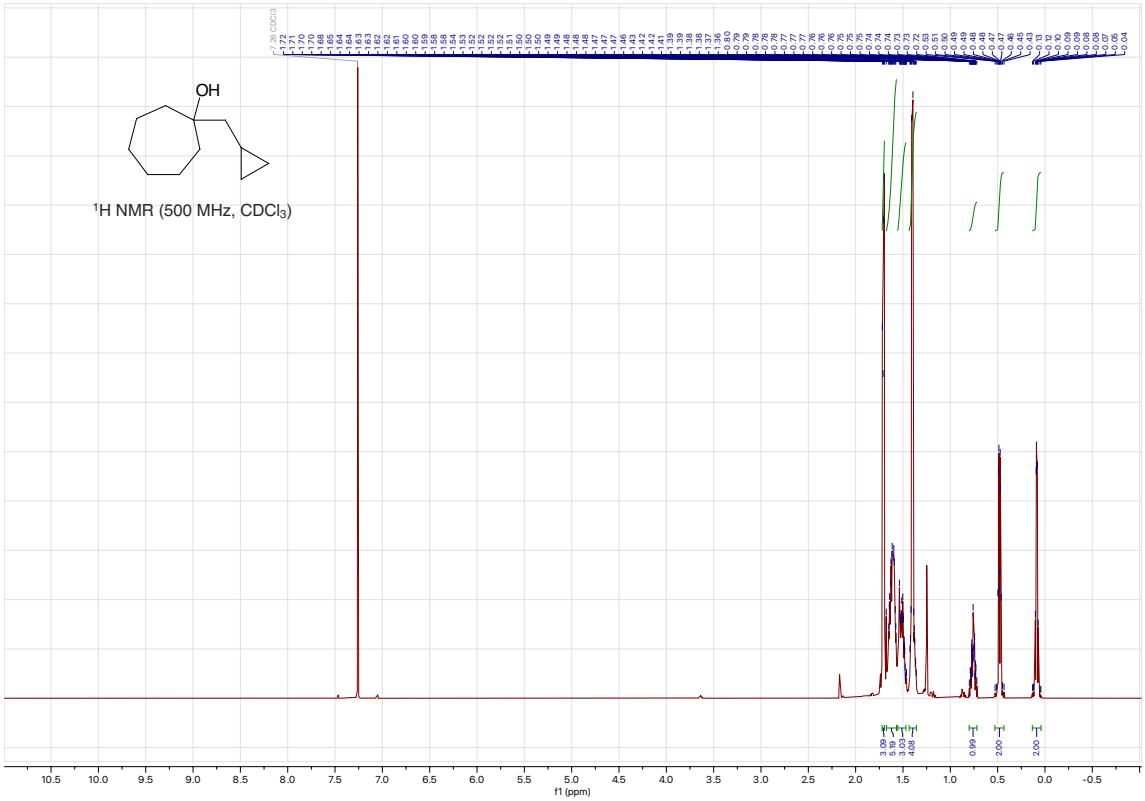


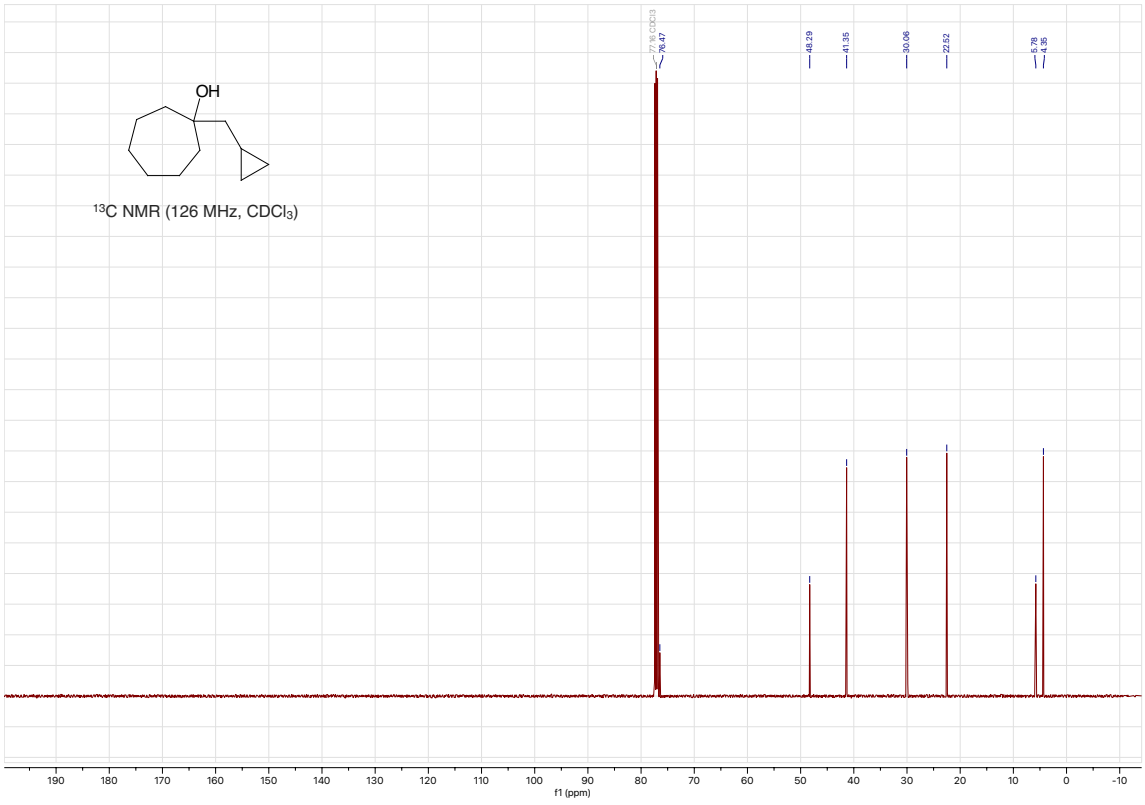
(Cyclopropylmethyl)cyclohexanol (9)



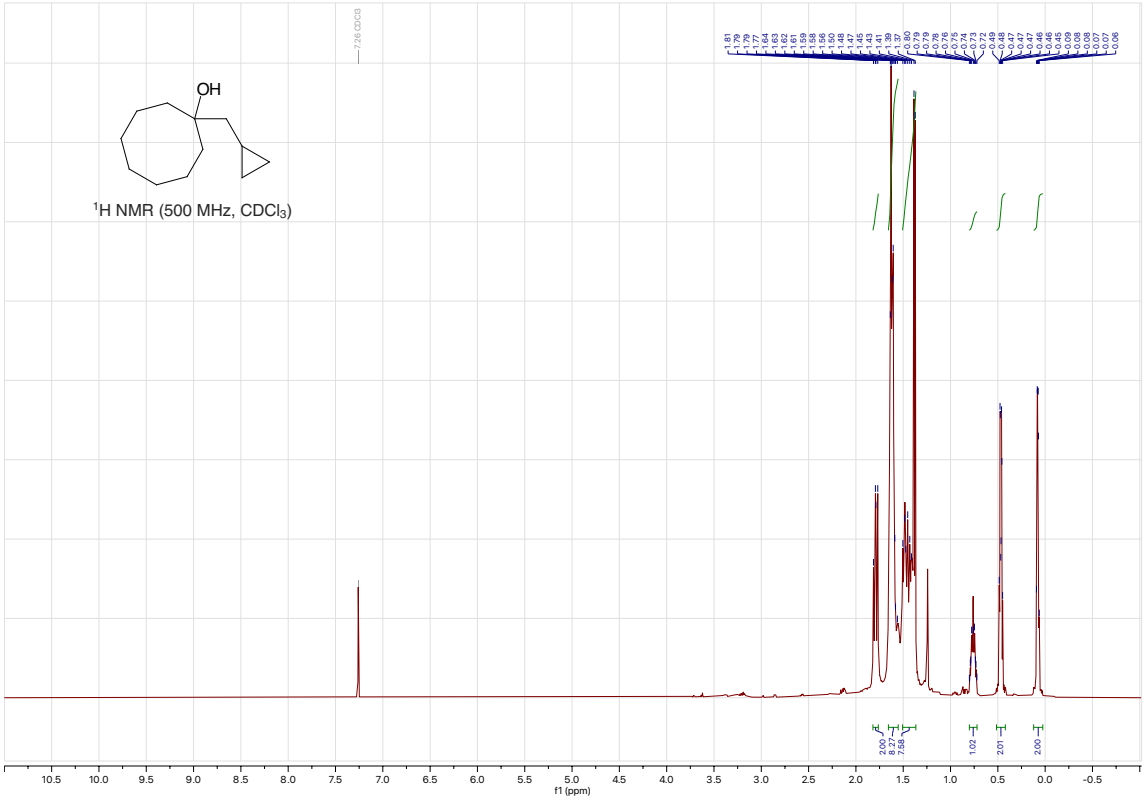


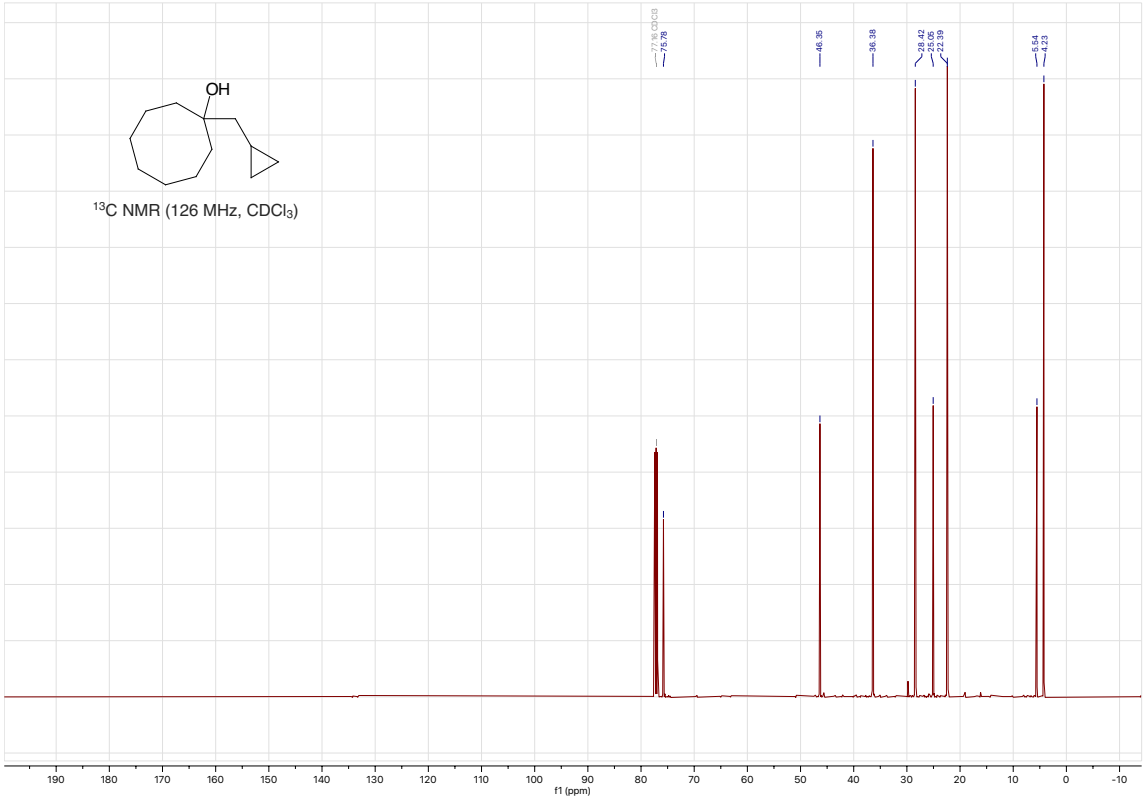
1-(cyclopropylmethyl)cycloheptan-1-ol (10)



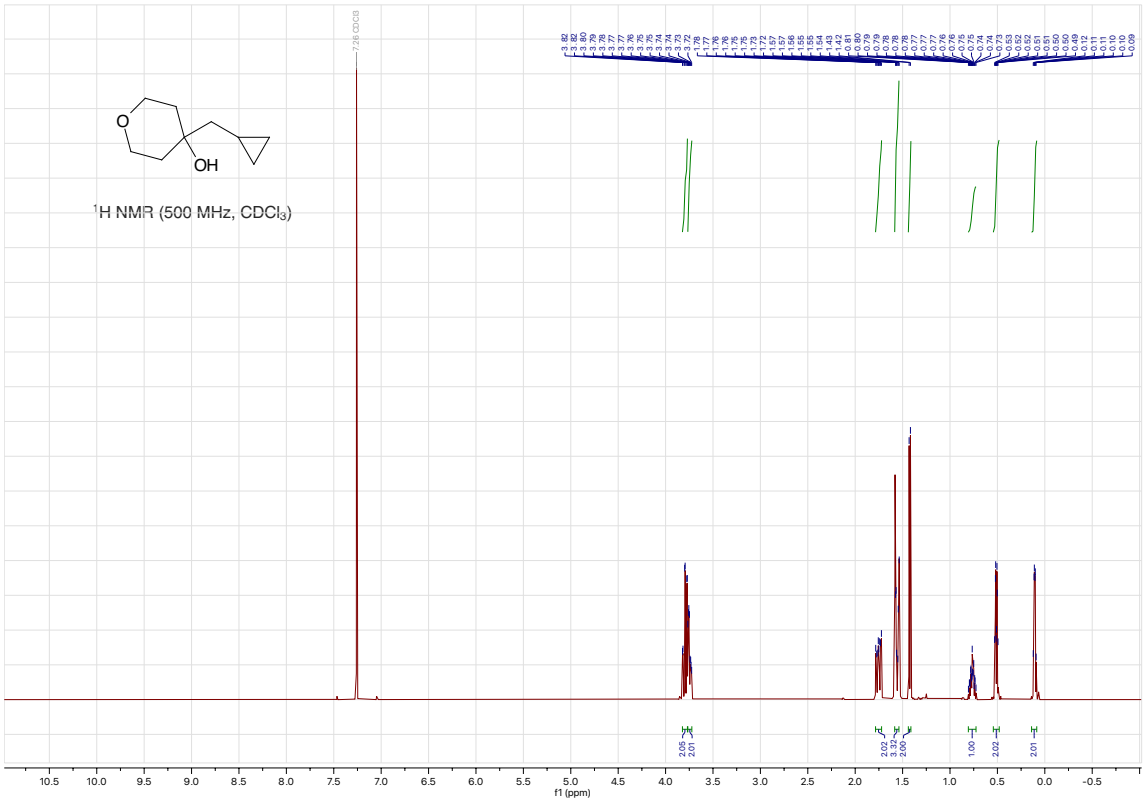


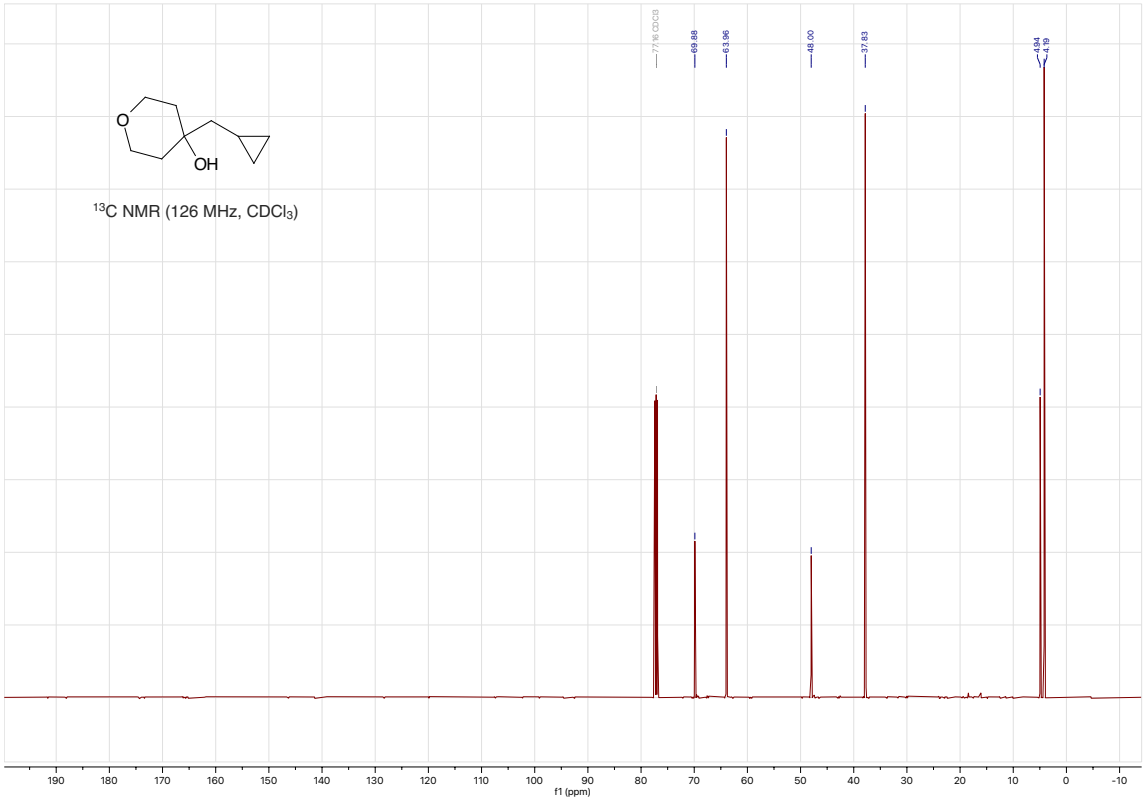
cyclopropylmethyl)cyclooctan-1-ol (11)



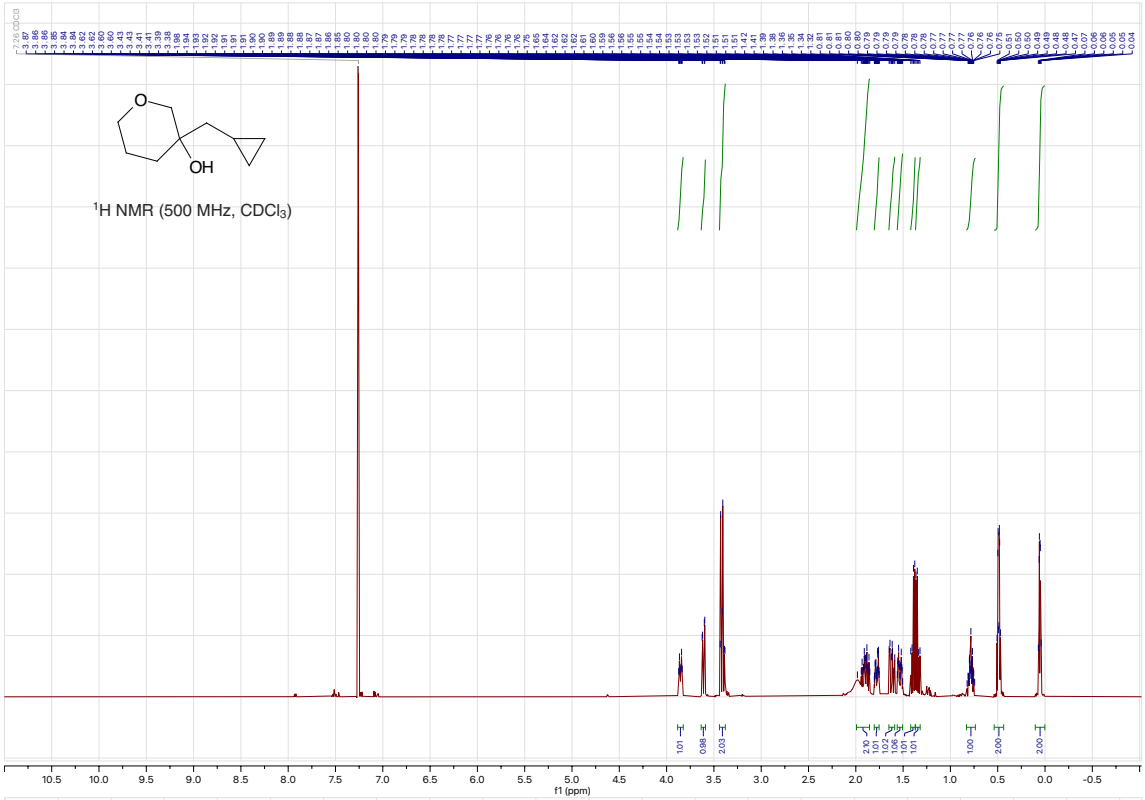


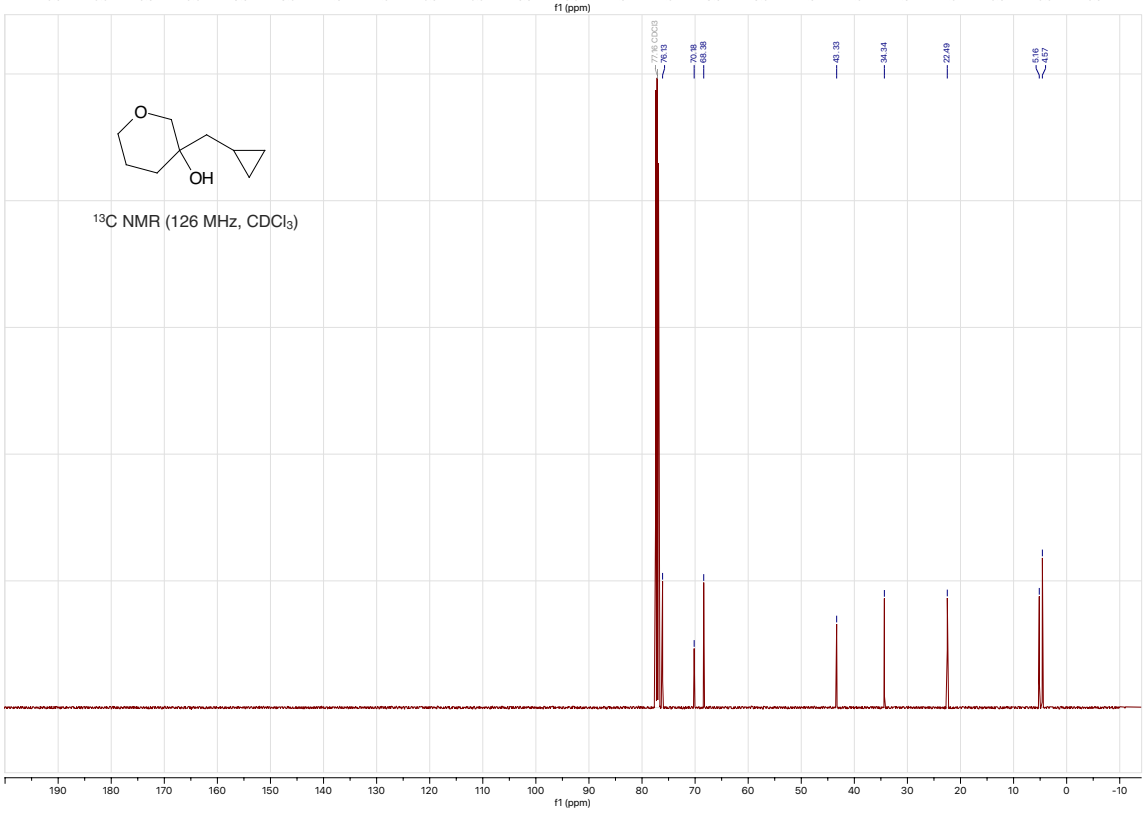
4-(cyclopropylmethyl)tetrahydro-2*H*-pyran-4-ol (12)



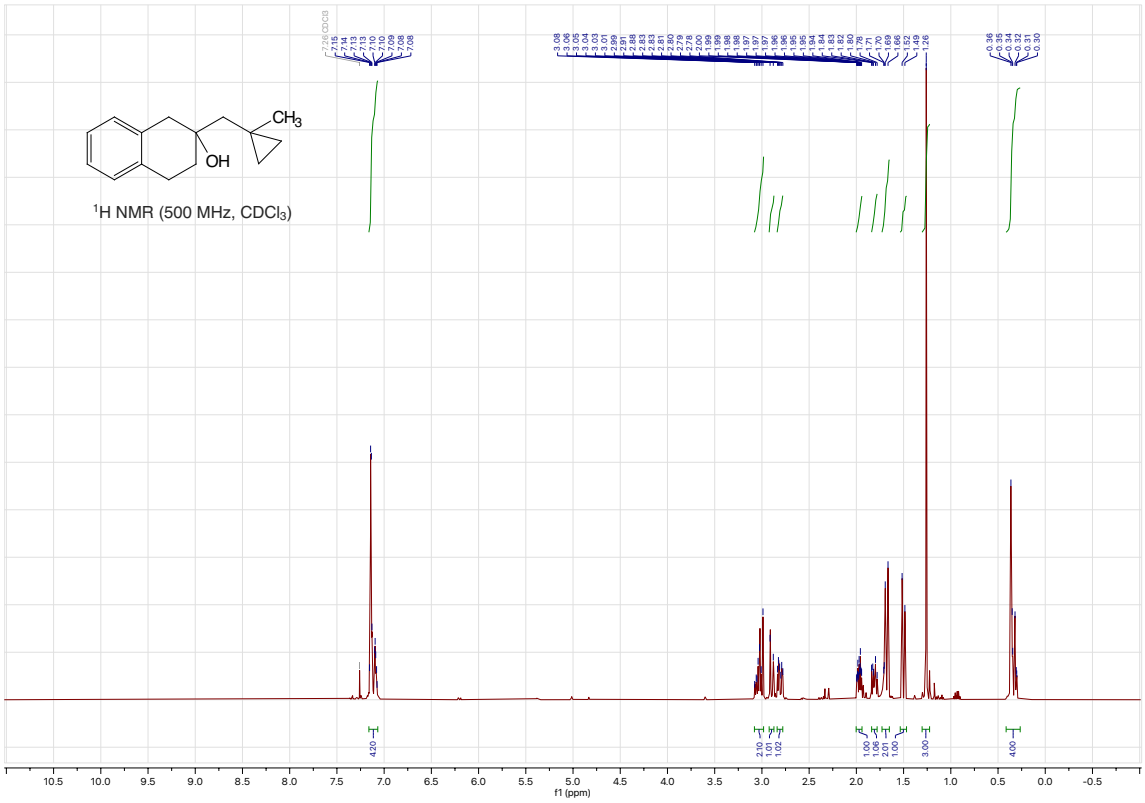


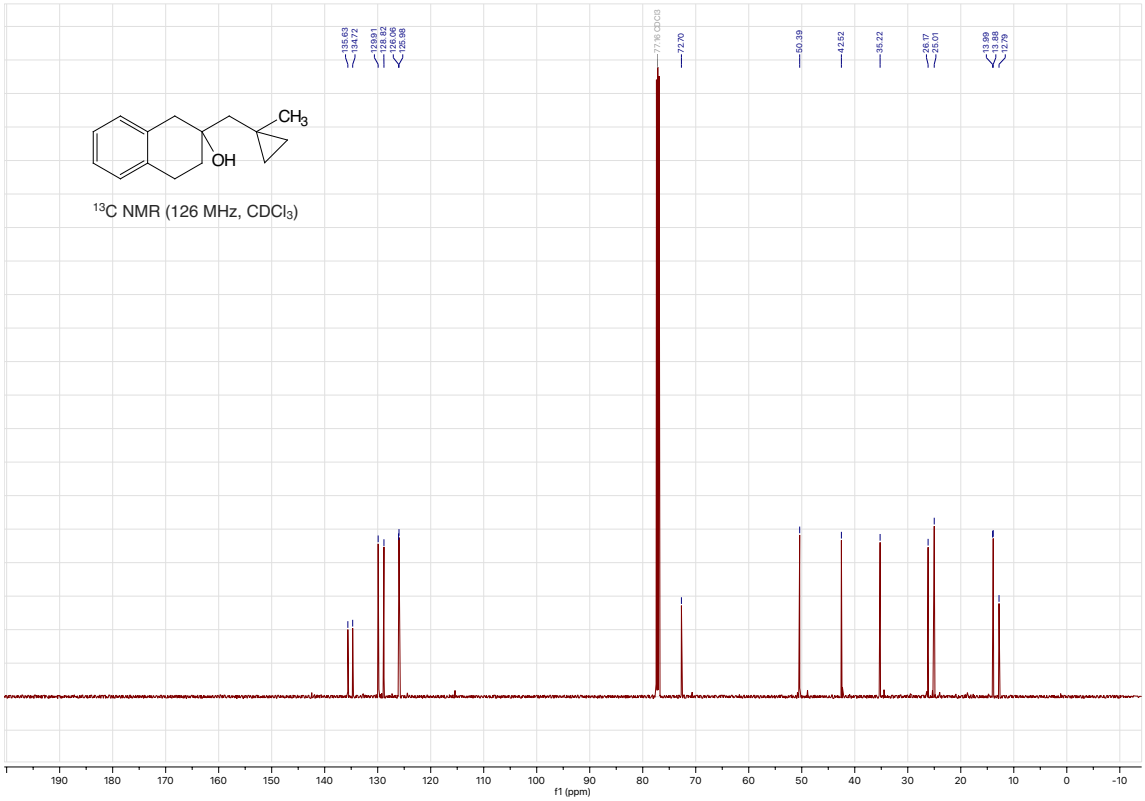
3-(cyclopropylmethyl)tetrahydro-2*H*-pyran-3-ol (13)



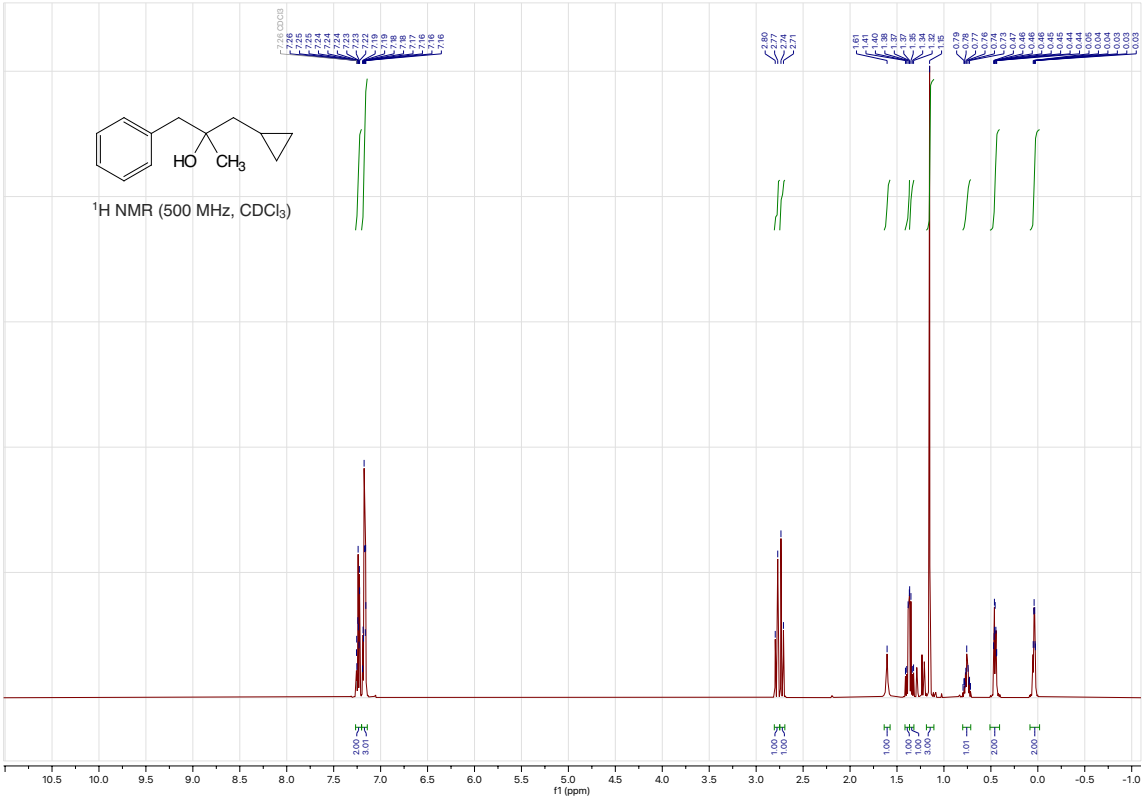


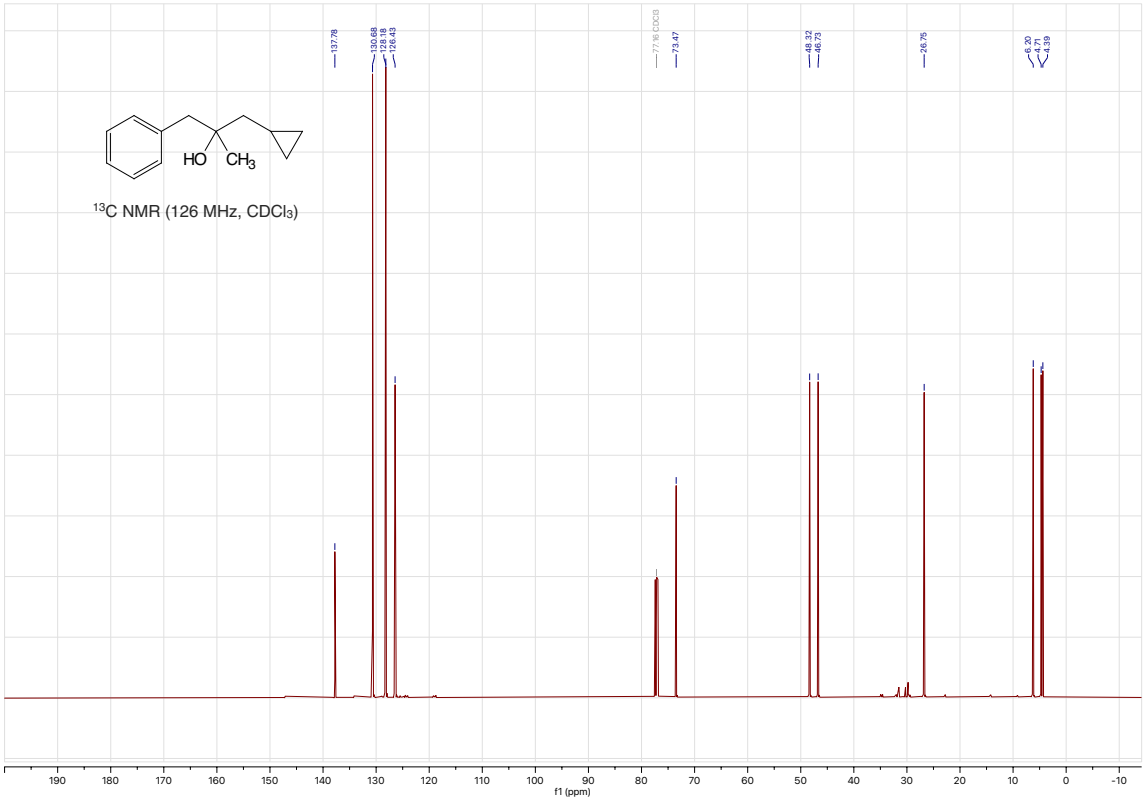
2-((1-methylcyclopropyl)methyl)-1,2,3,4-tetrahydronaphthalen-2-ol (14)



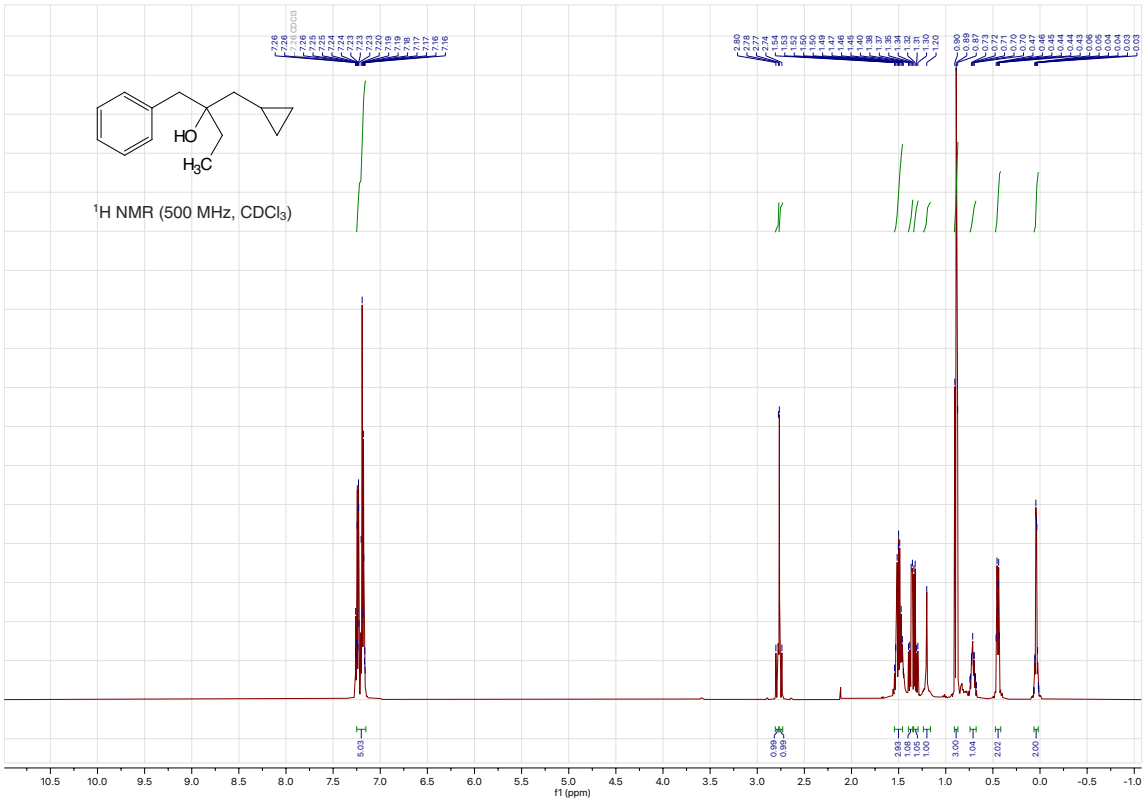


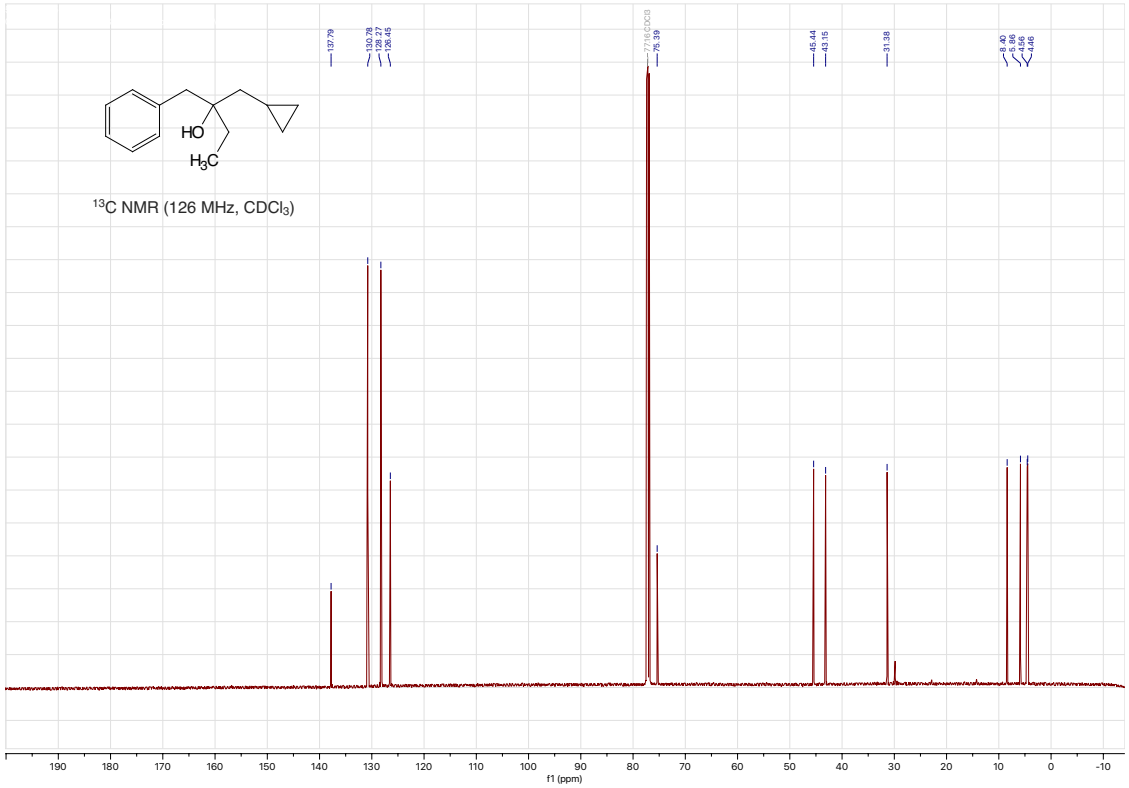
1-cyclopropyl-2-methyl-3-phenylpropan-2-ol (16)



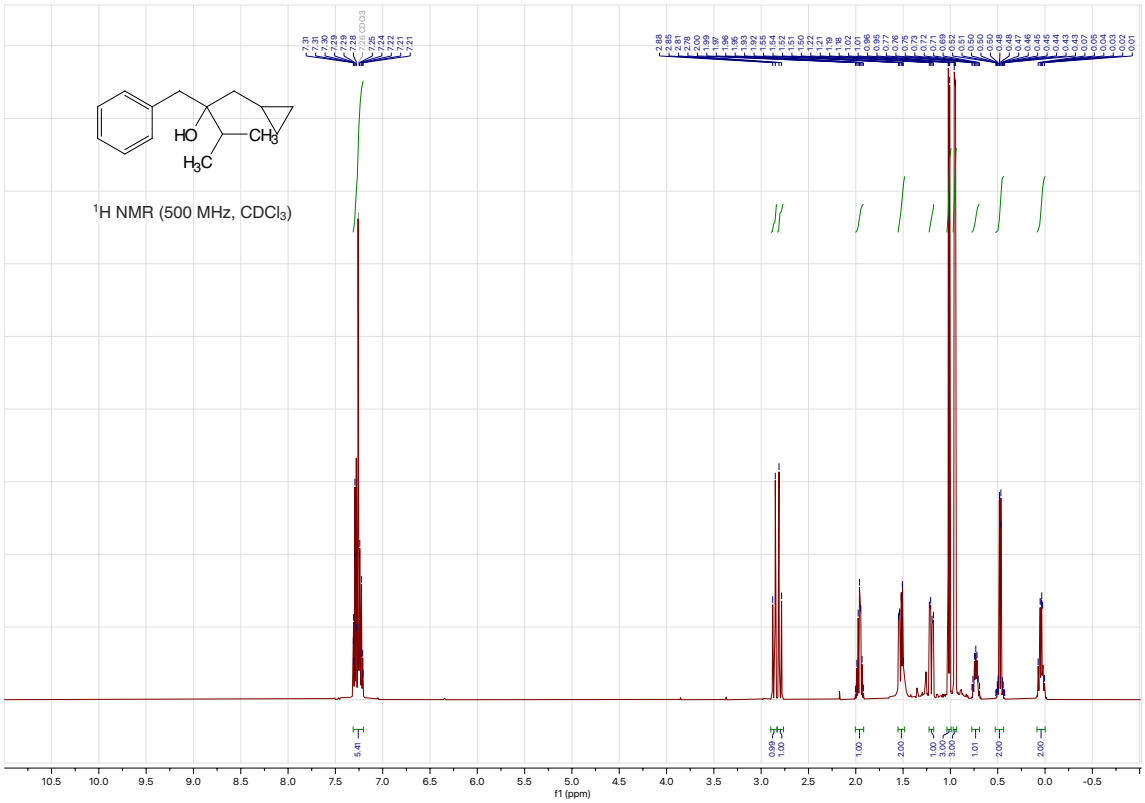


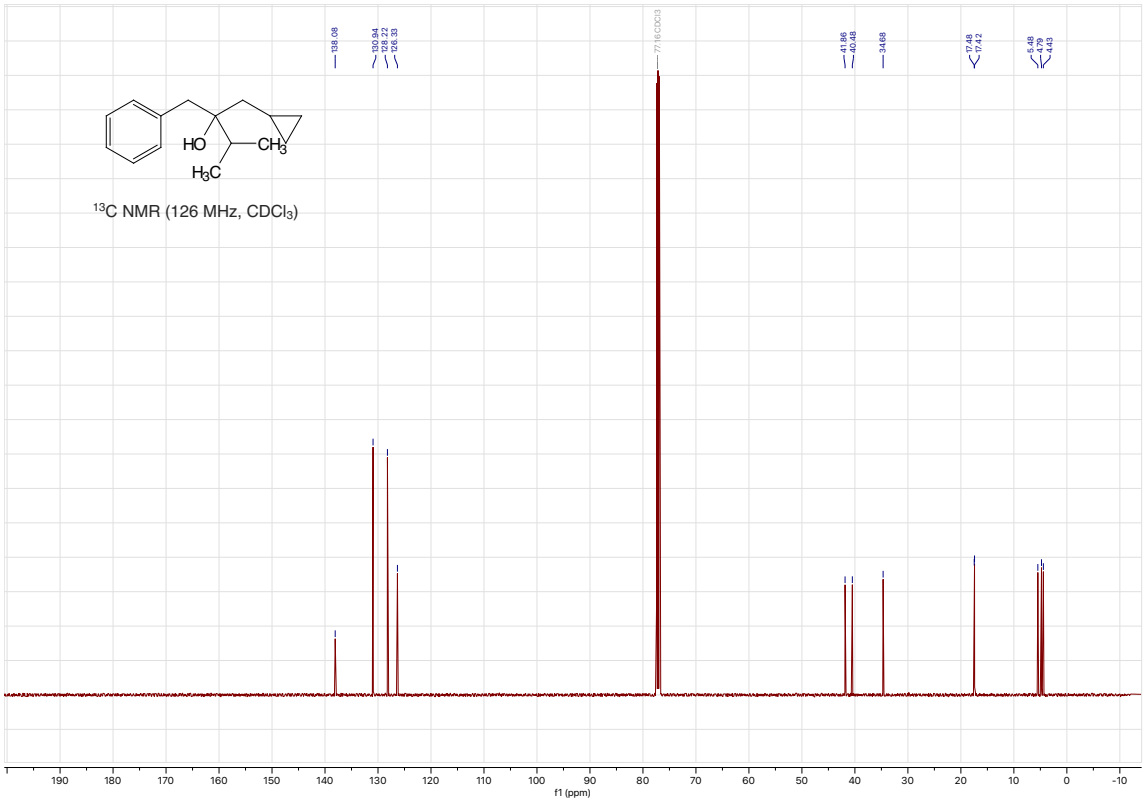
2-benzyl-1-cyclopropylbutan-2-ol (17)



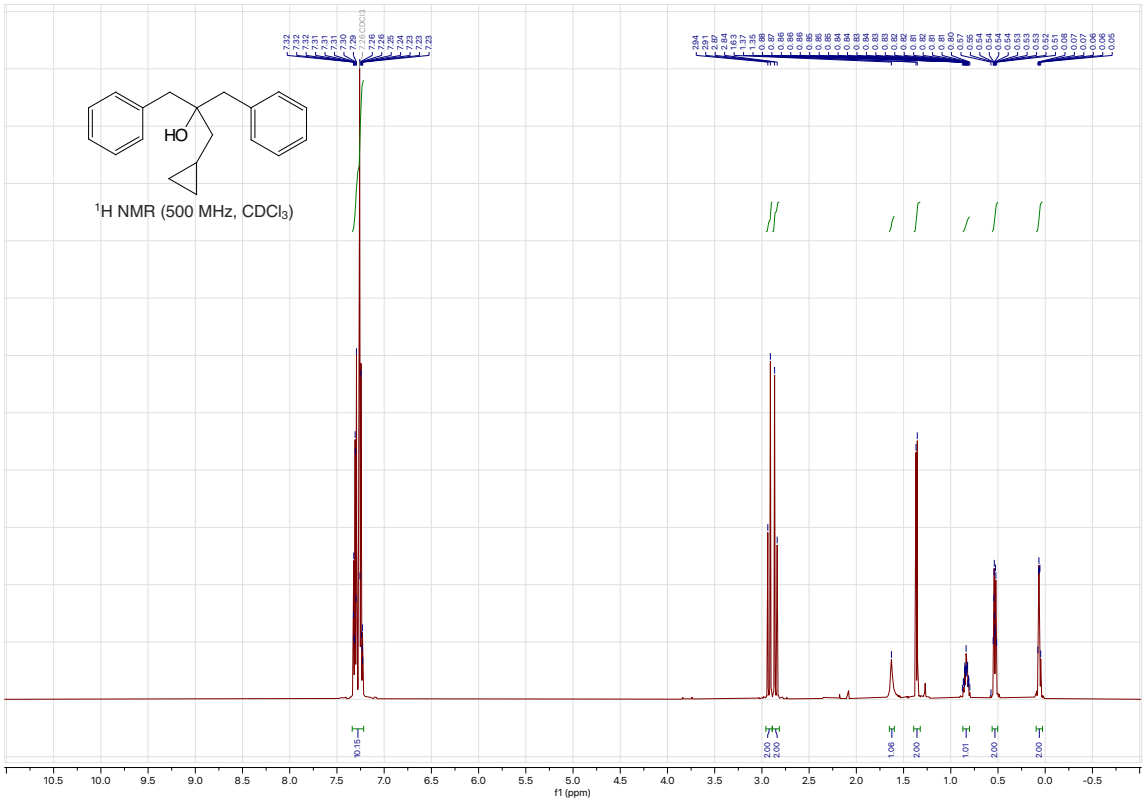


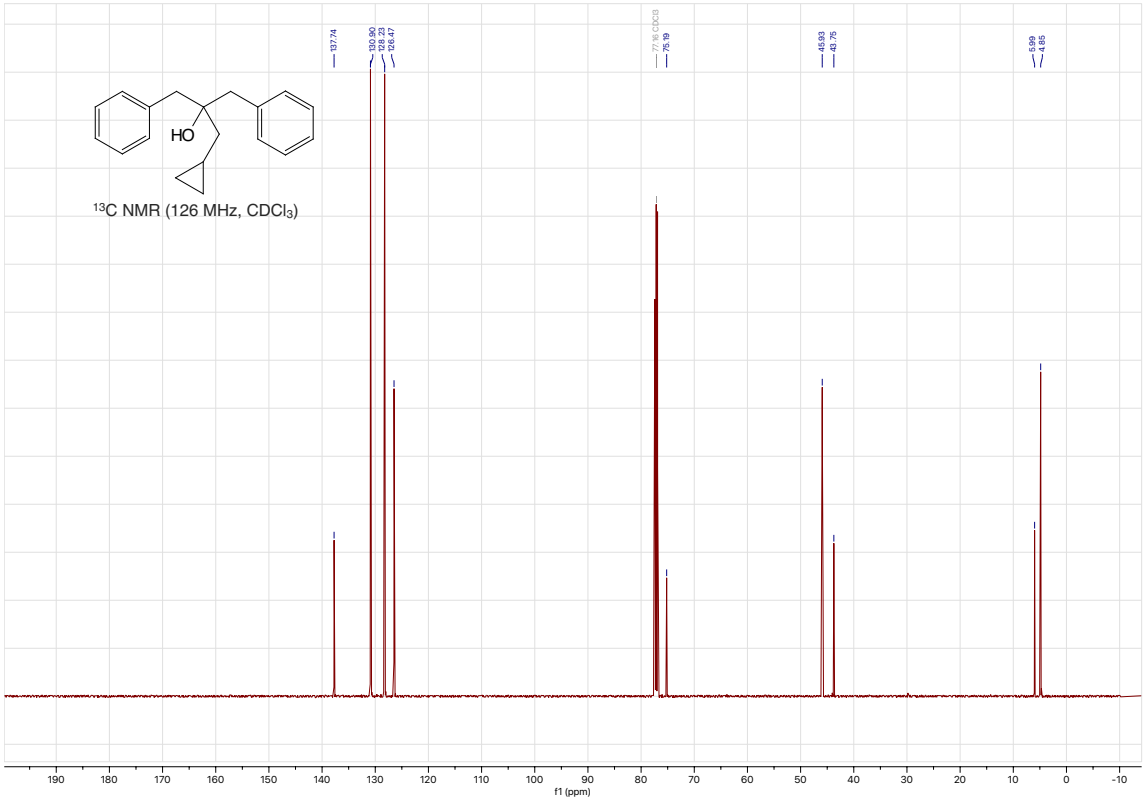
2-benzyl-1-cyclopropyl-3-methylbutan-2-ol (18)



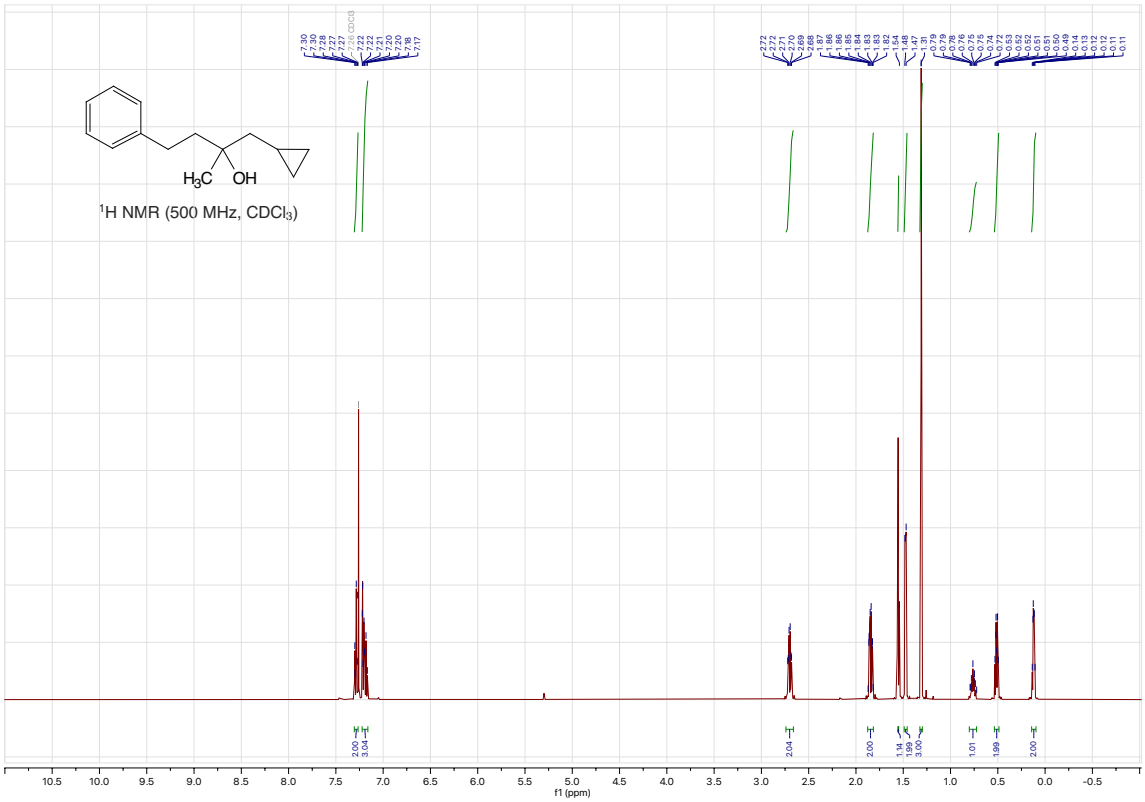


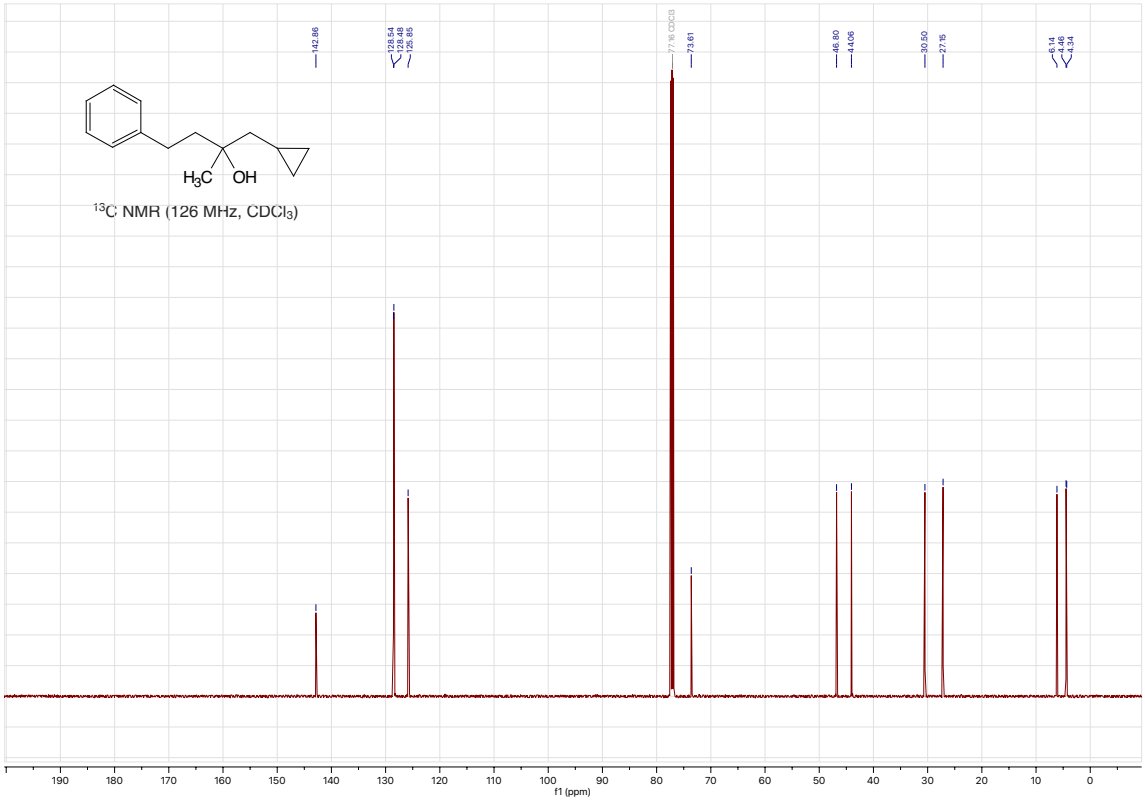
2-benzyl-1-cyclopropyl-3-phenylpropan-2-ol (19)



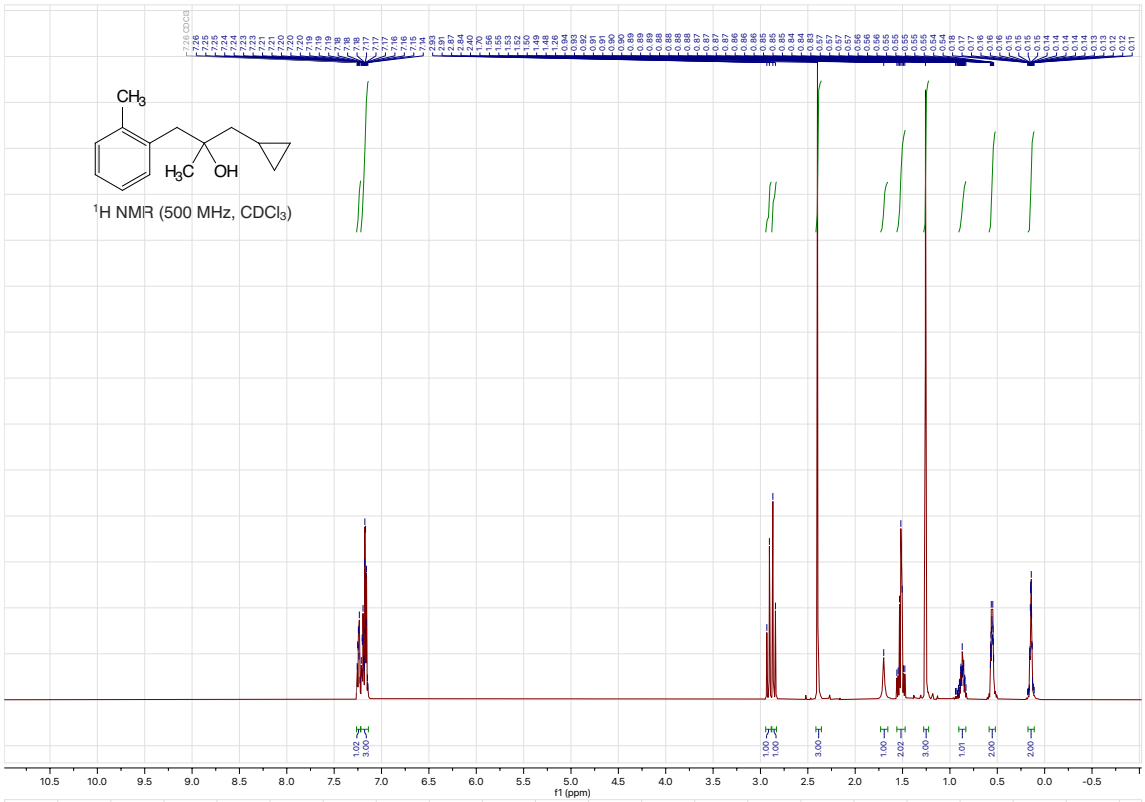


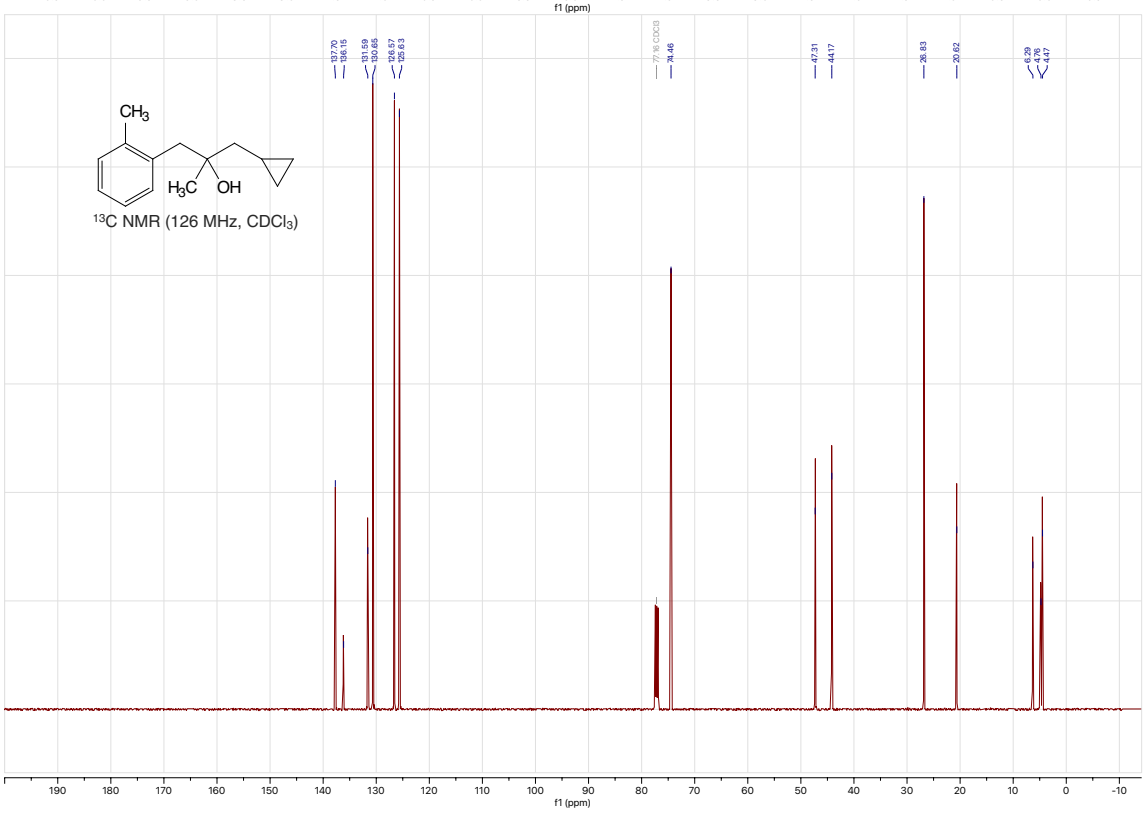
1-cyclopropyl-2-methyl-4-phenylbutan-2-ol (20)



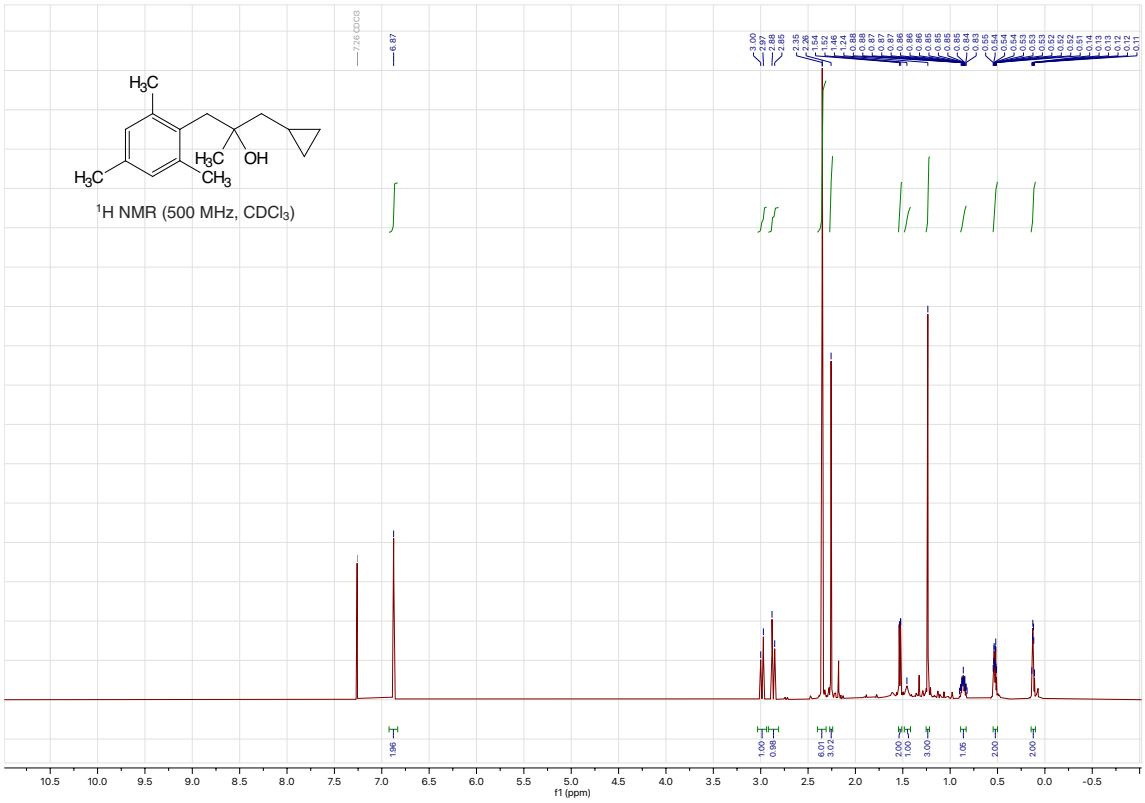


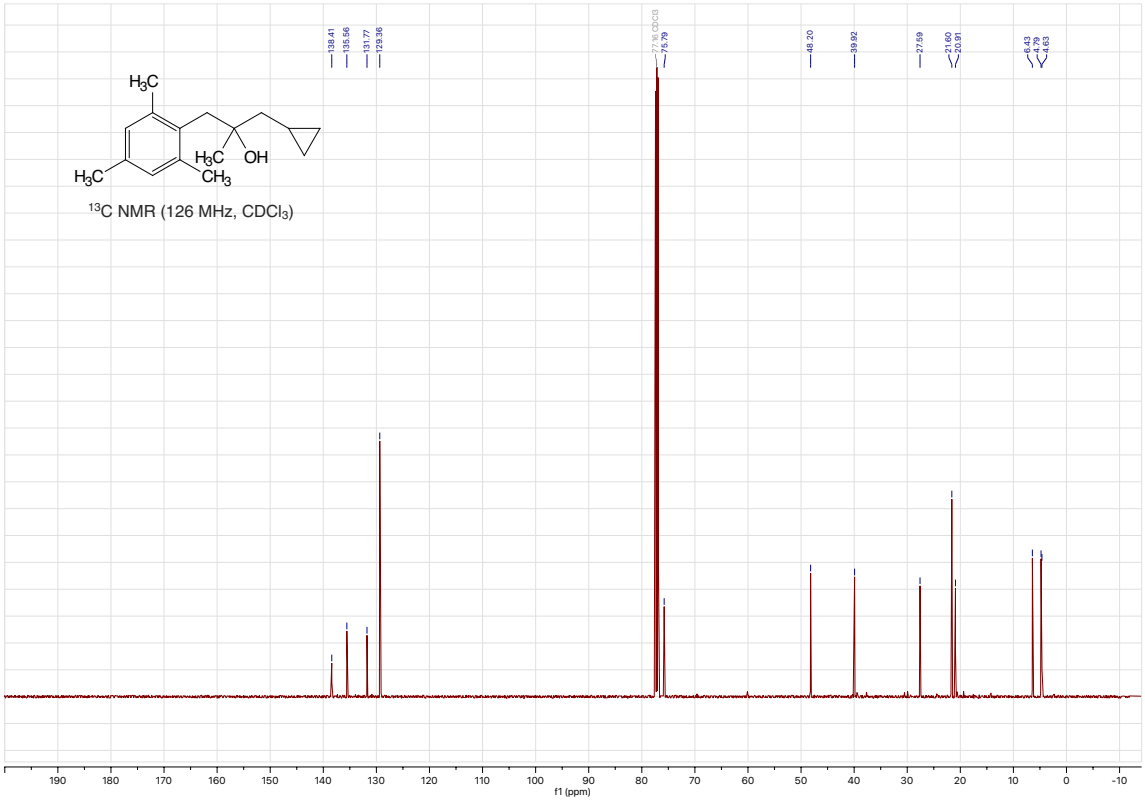
1-cyclopropyl-2-methyl-3-(*o*-tolyl)propan-2-ol (21)



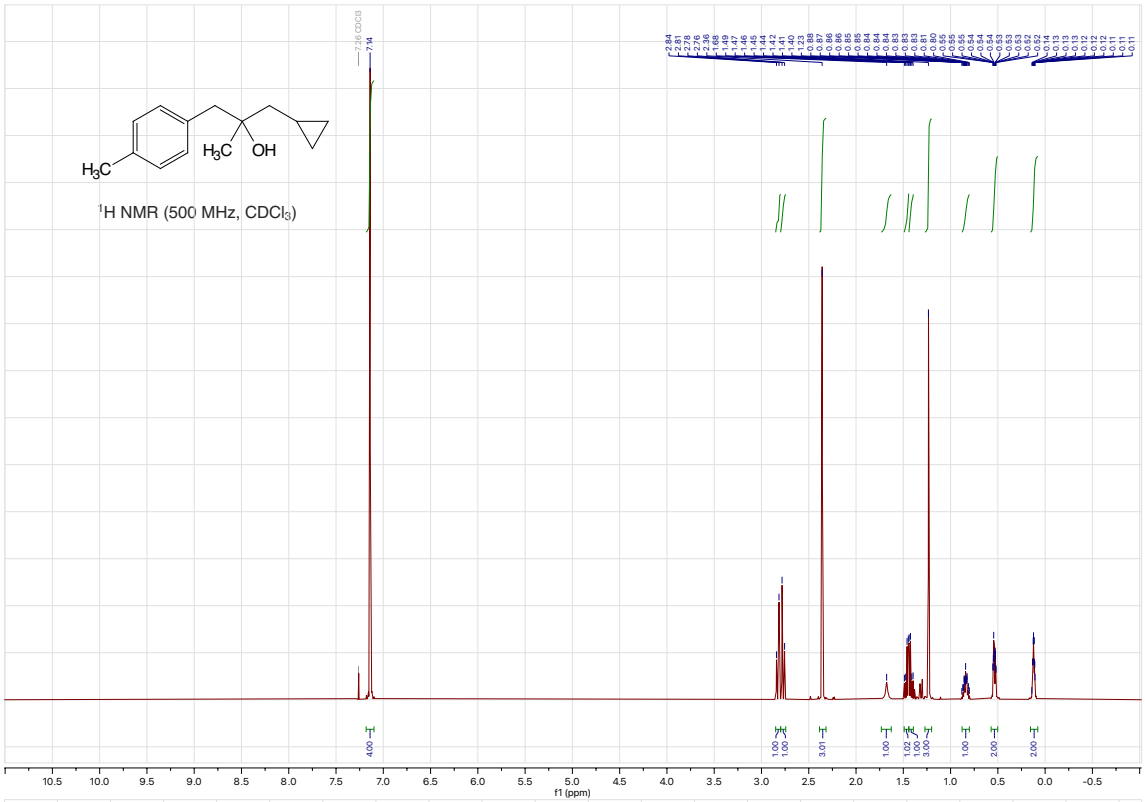


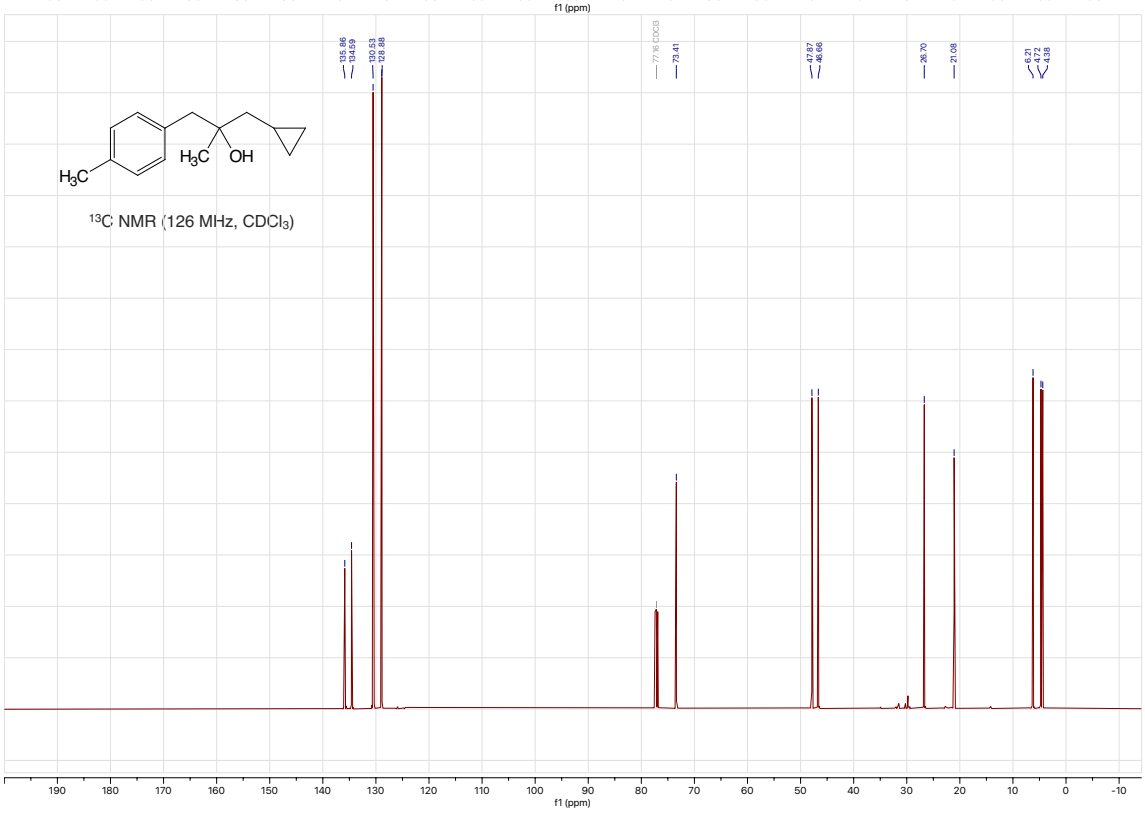
1-cyclopropyl-3-mesityl-2-methylpropan-2-ol (22)



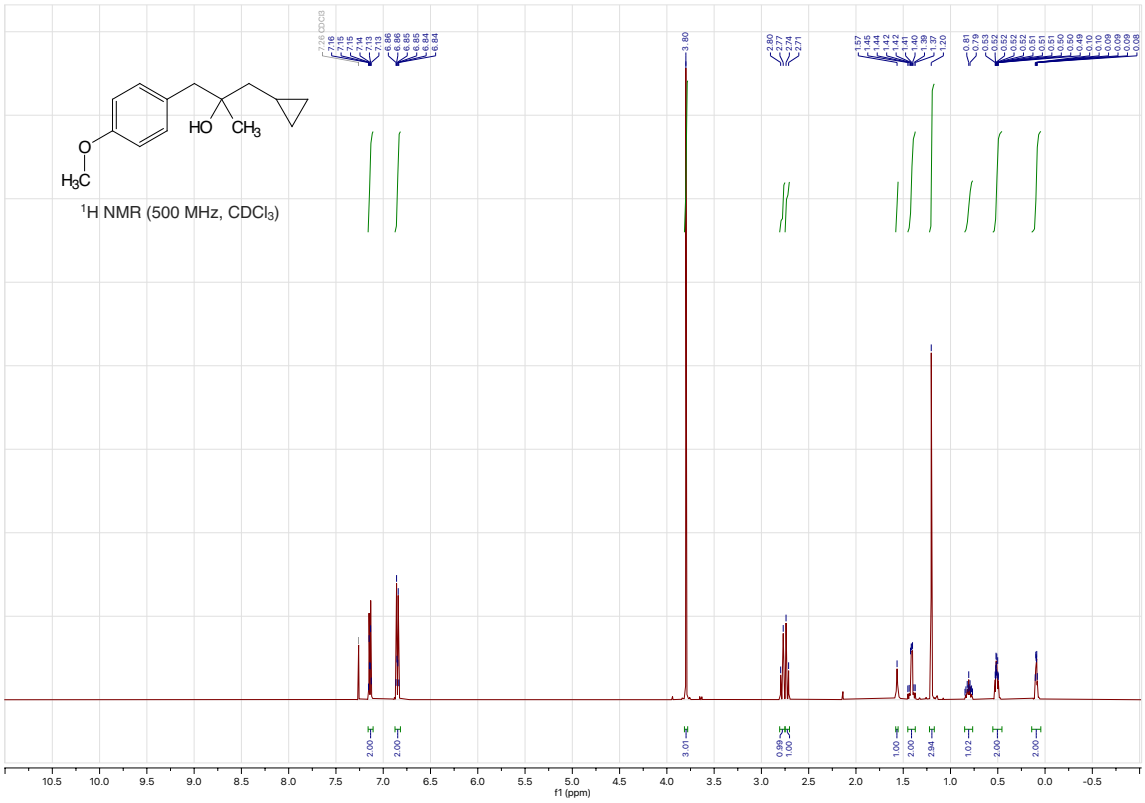


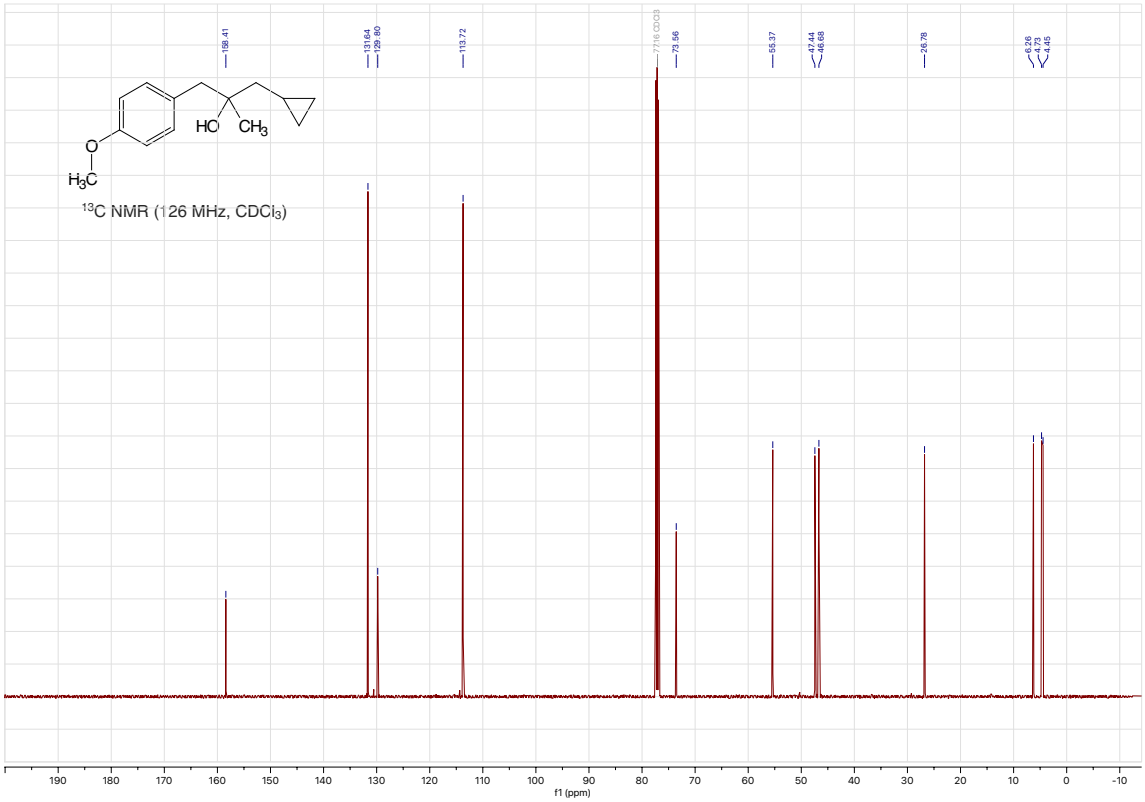
1-cyclopropyl-2-methyl-3-(*p*-tolyl)propan-2-ol (23)



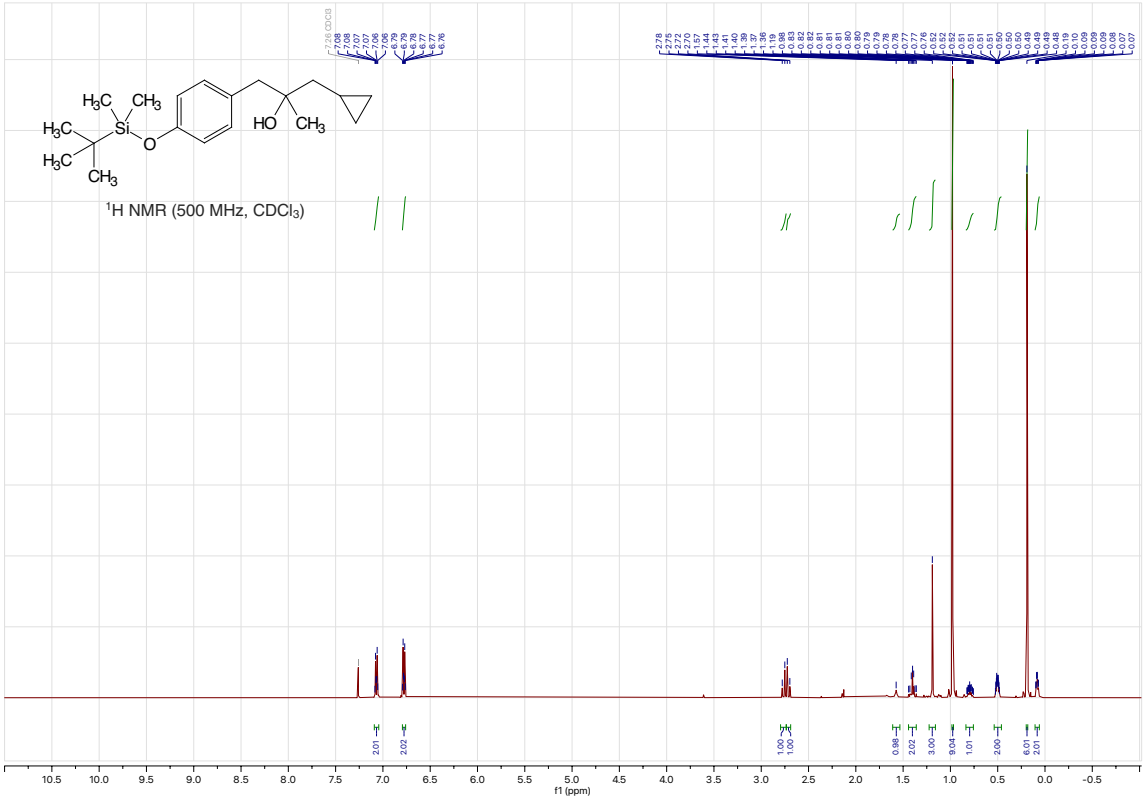


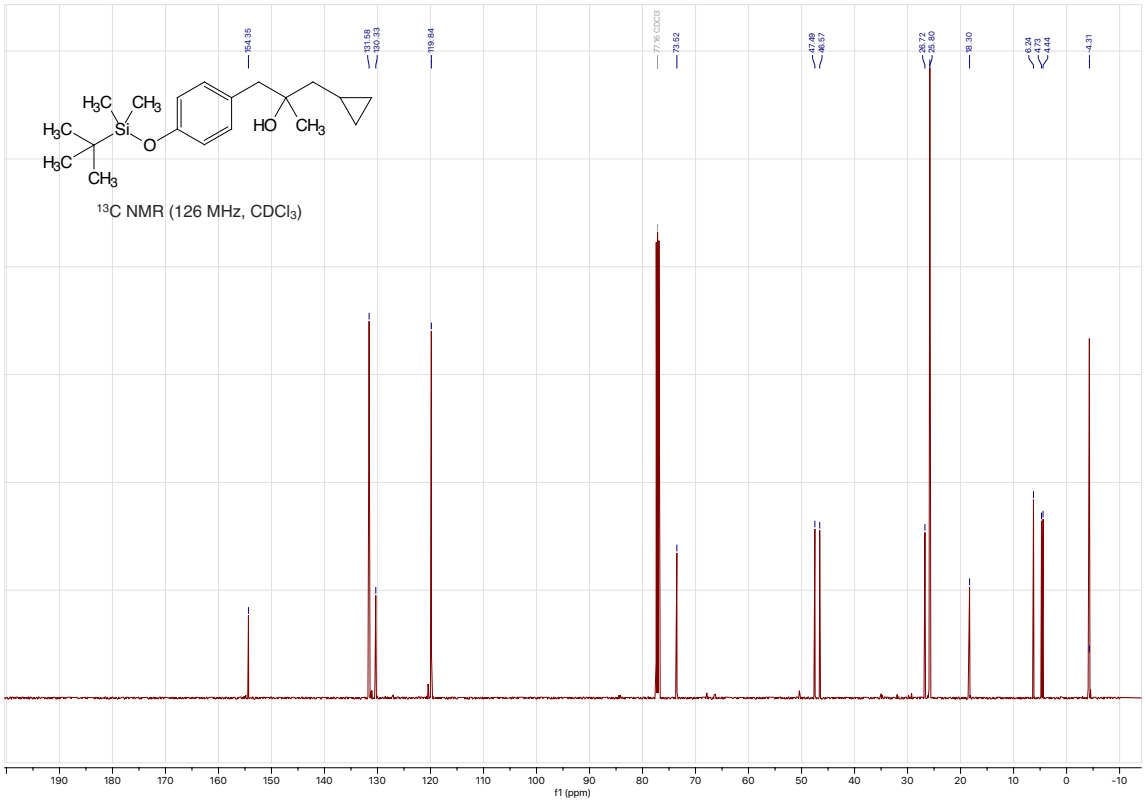
1-cyclopropyl-3-(4-methoxyphenyl)-2-methylpropan-2-ol (24)



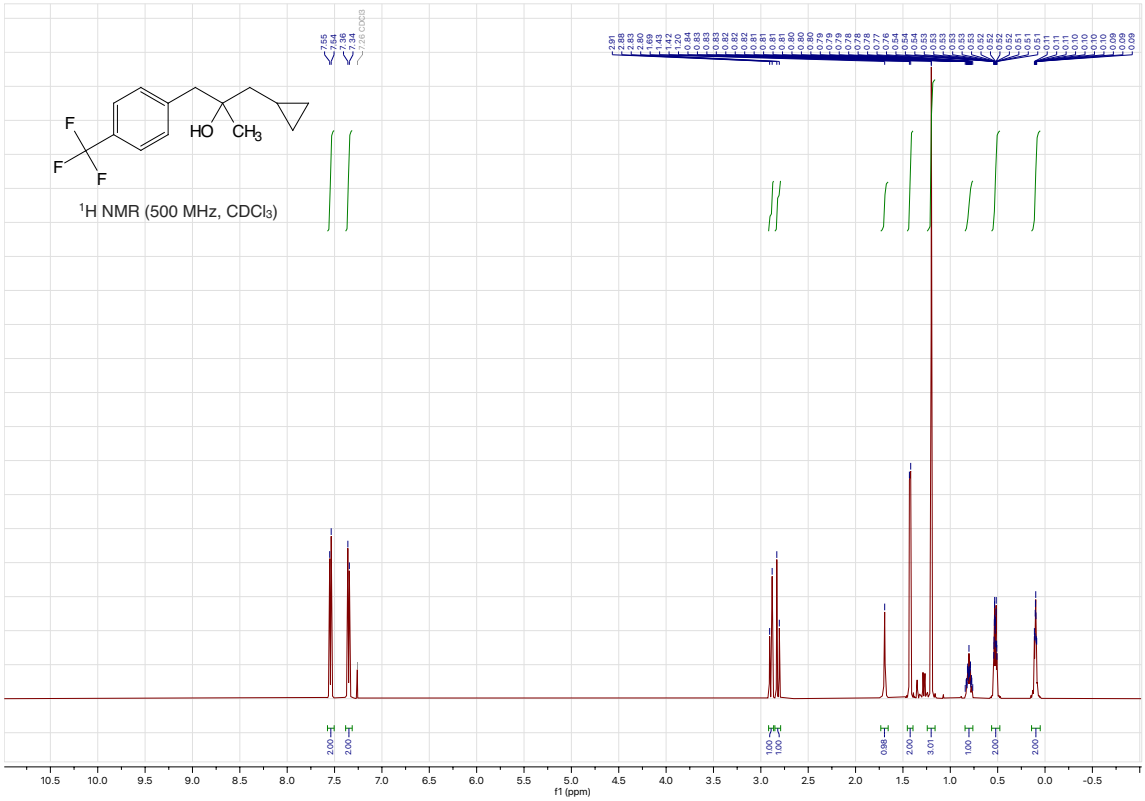


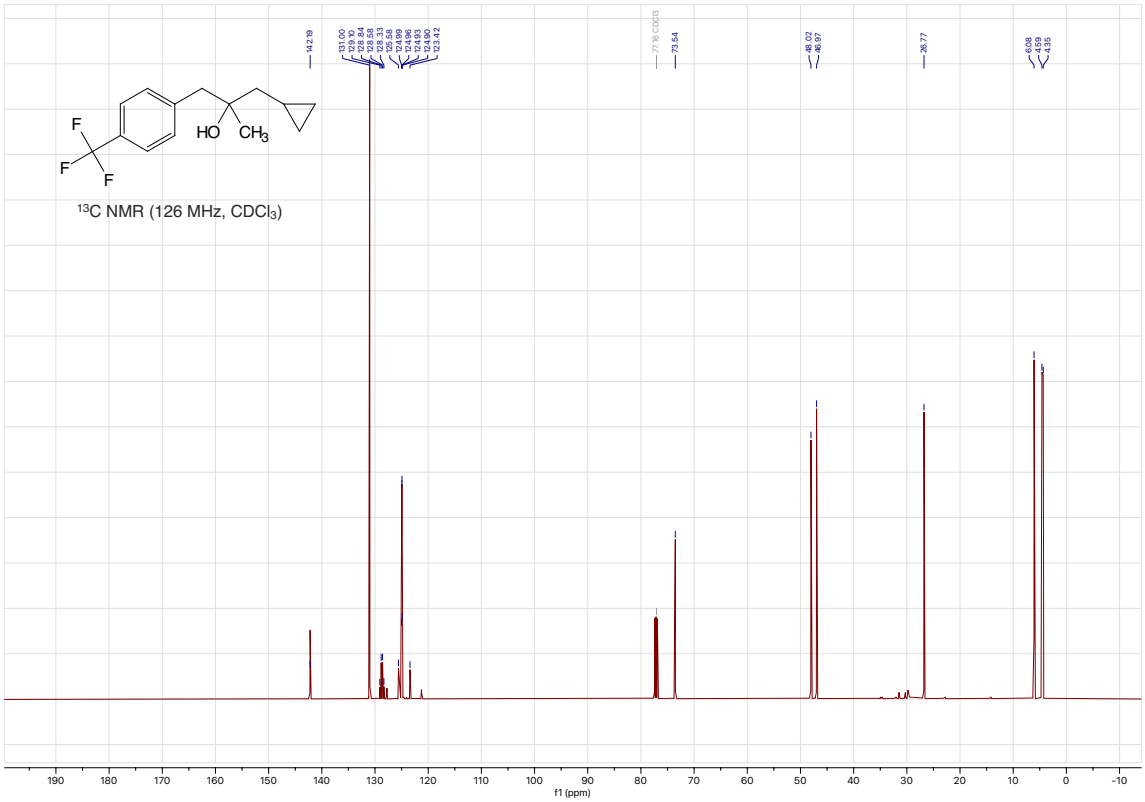
1-(4-((*tert*-butyldimethylsilyl)oxy)phenyl)-3-cyclopropyl-2-methylpropan-2-ol (26)

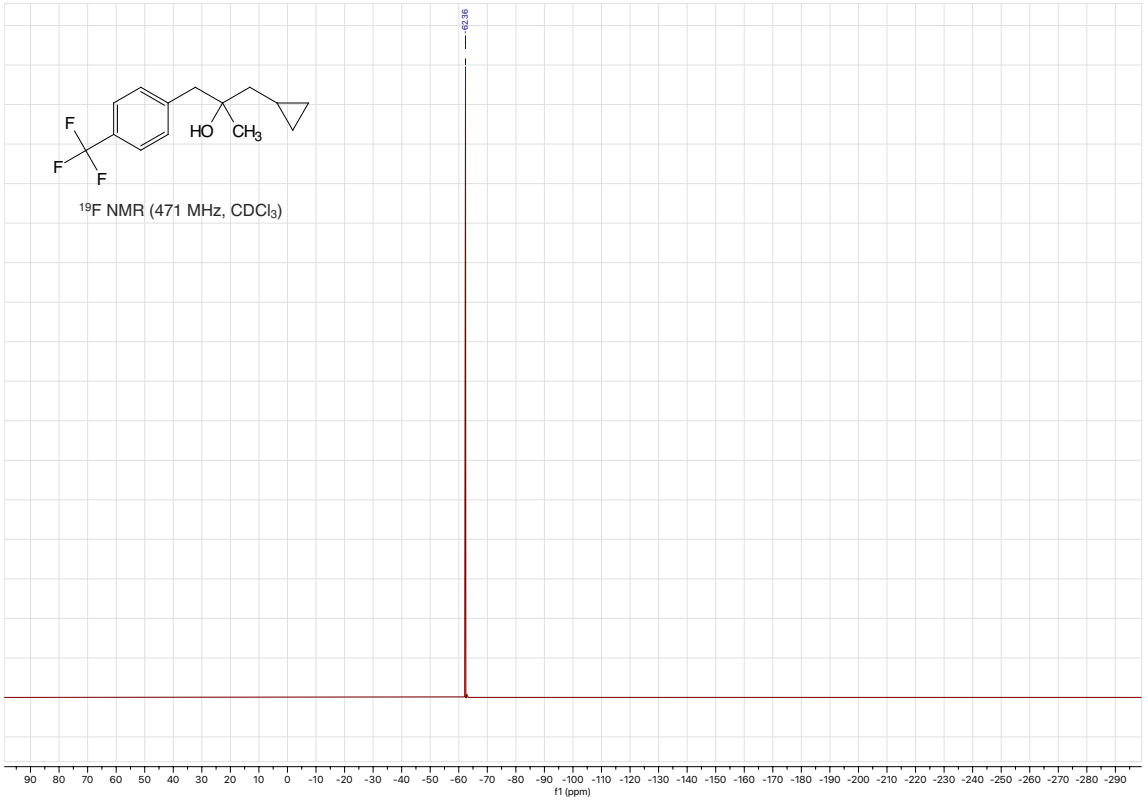




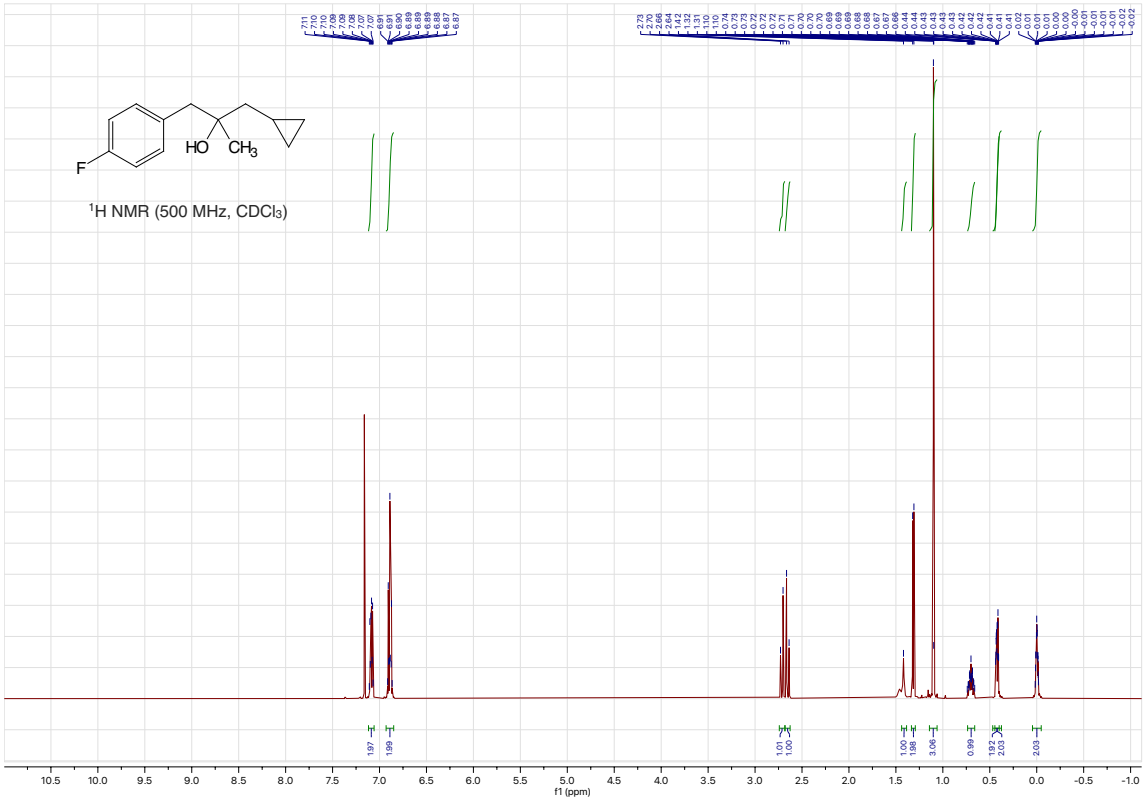
1-cyclopropyl-2-methyl-3-(4-(trifluoromethyl)phenyl)propan-2-ol (28)

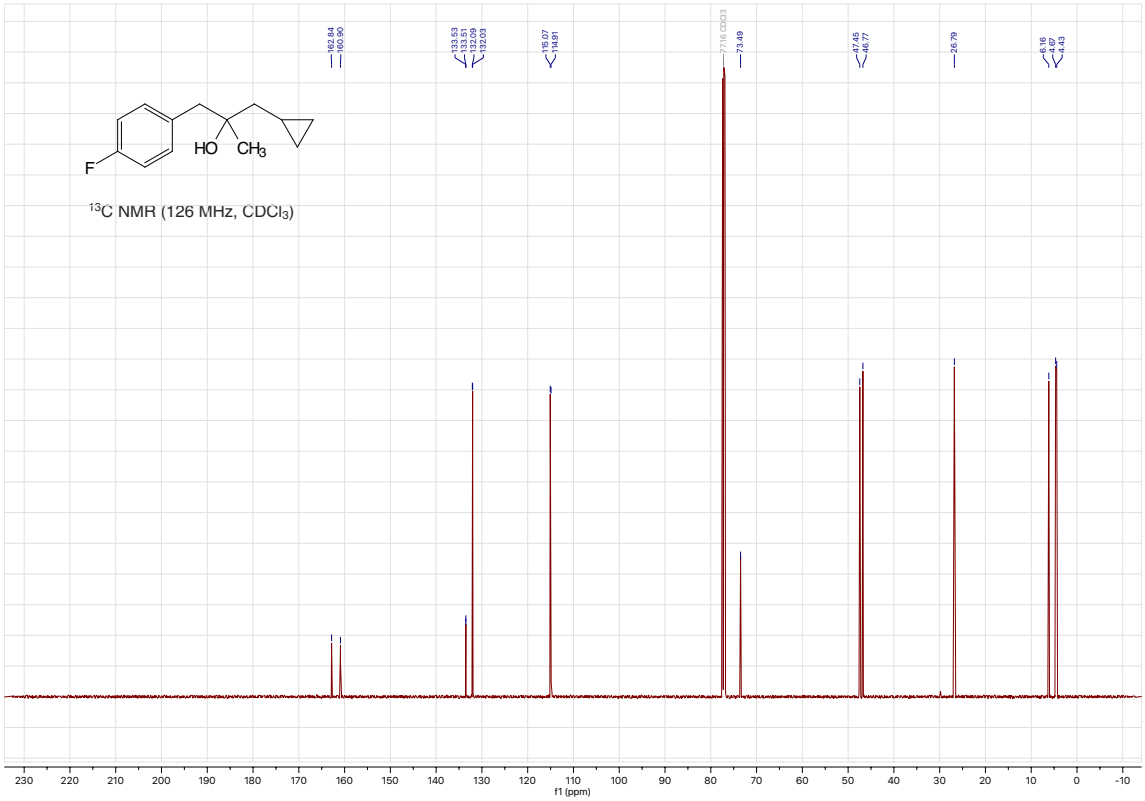


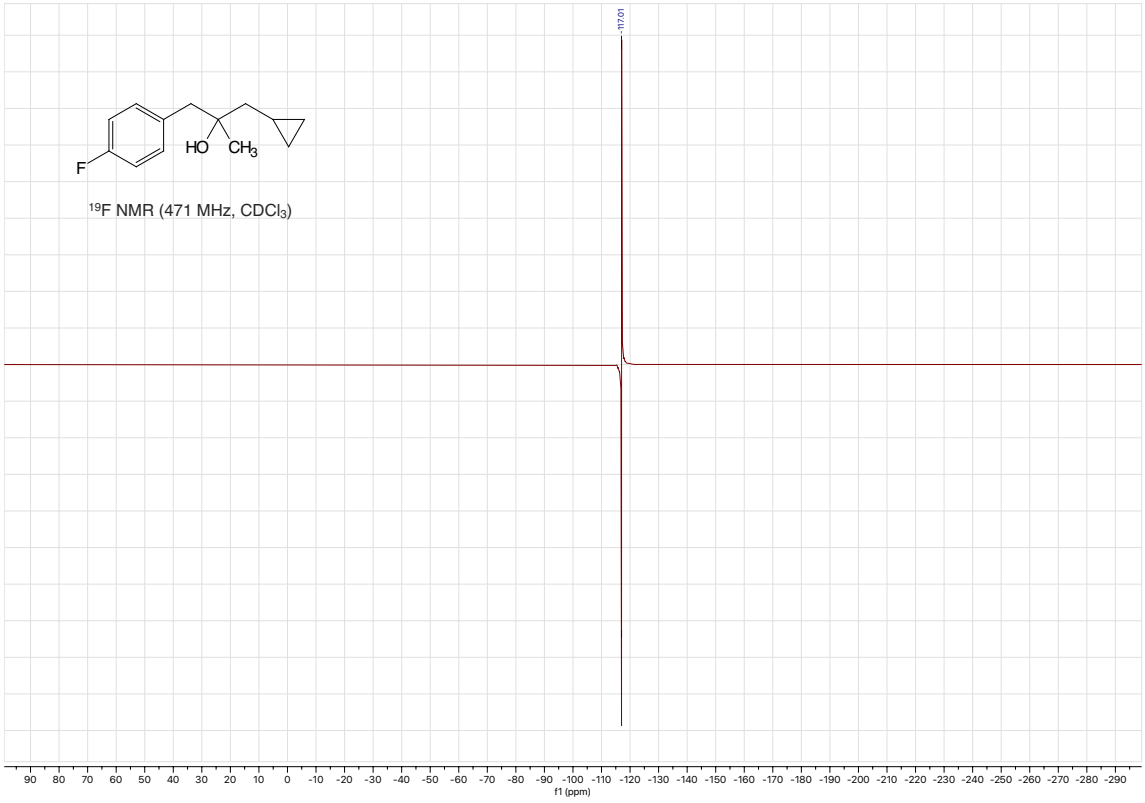



-62.36
F
F
F
HO
CH3
19F NMR (471 MHz, CDCl3)
90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220 -230 -240 -250 -260 -270 -280 -290
f1 (ppm)

1-cyclopropyl-3-(4-fluorophenyl)-2-methylpropan-2-ol (29)

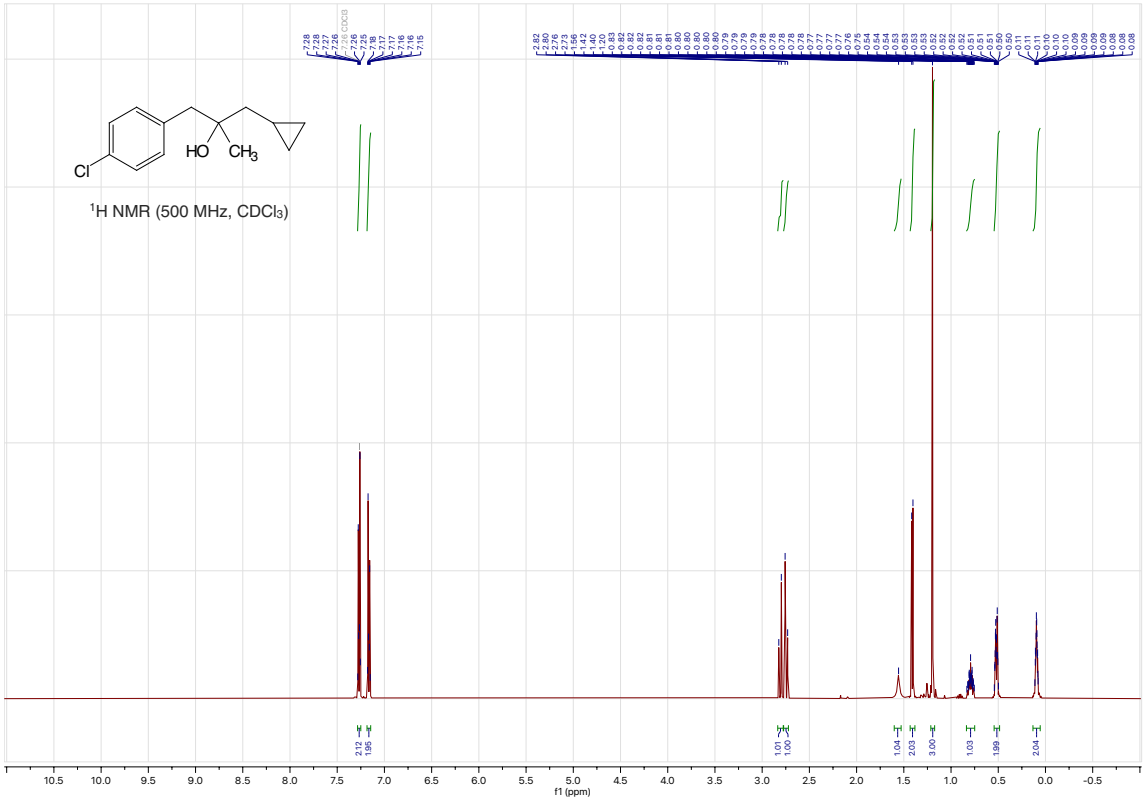


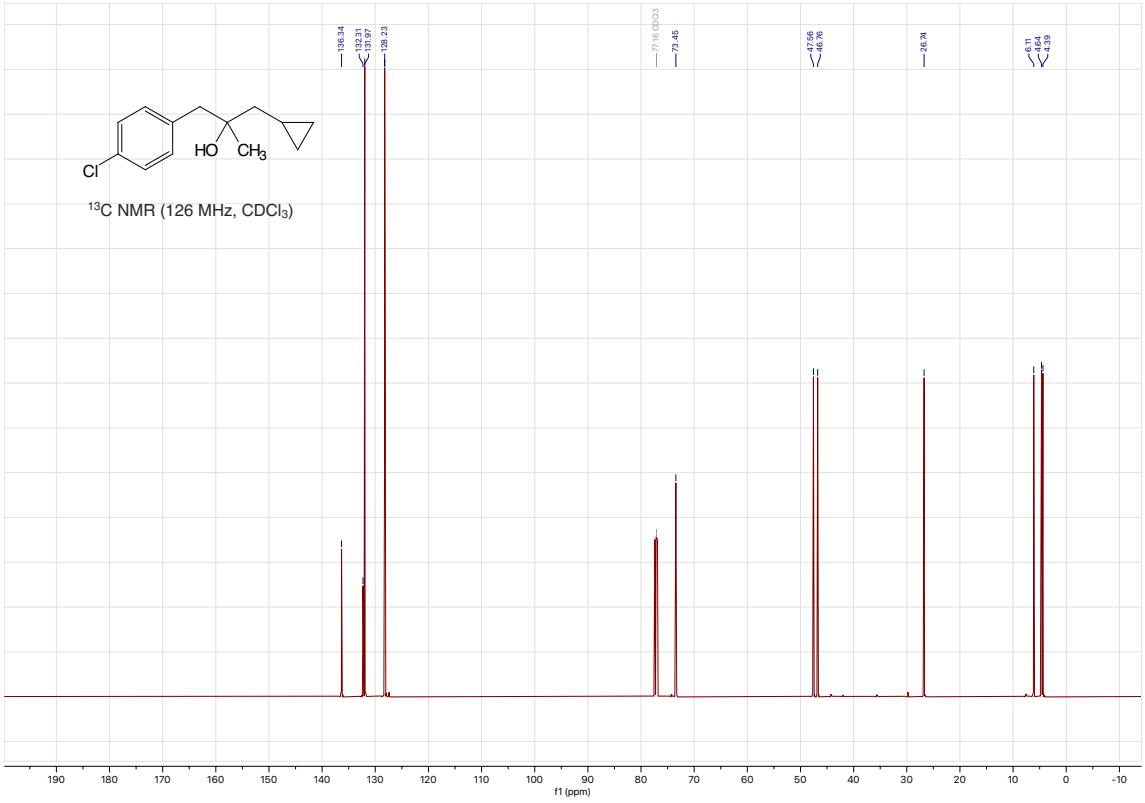




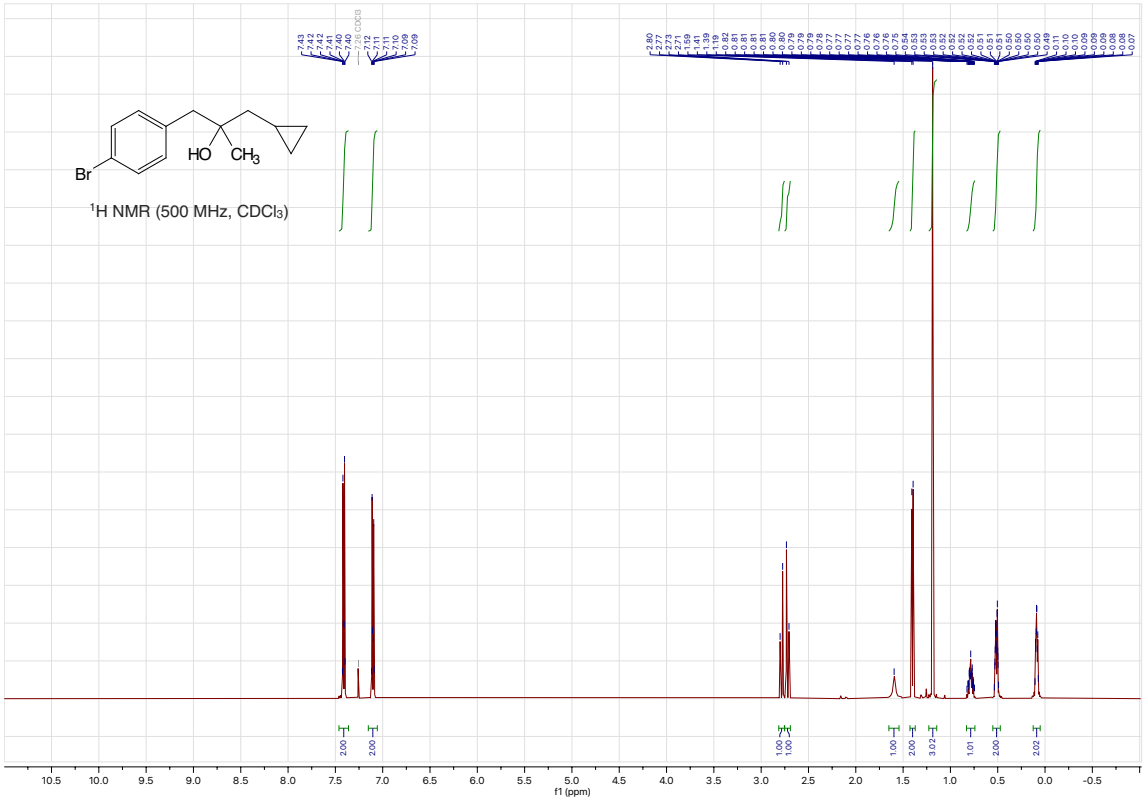
^{19}F NMR (471 MHz, $CDCl_3$)

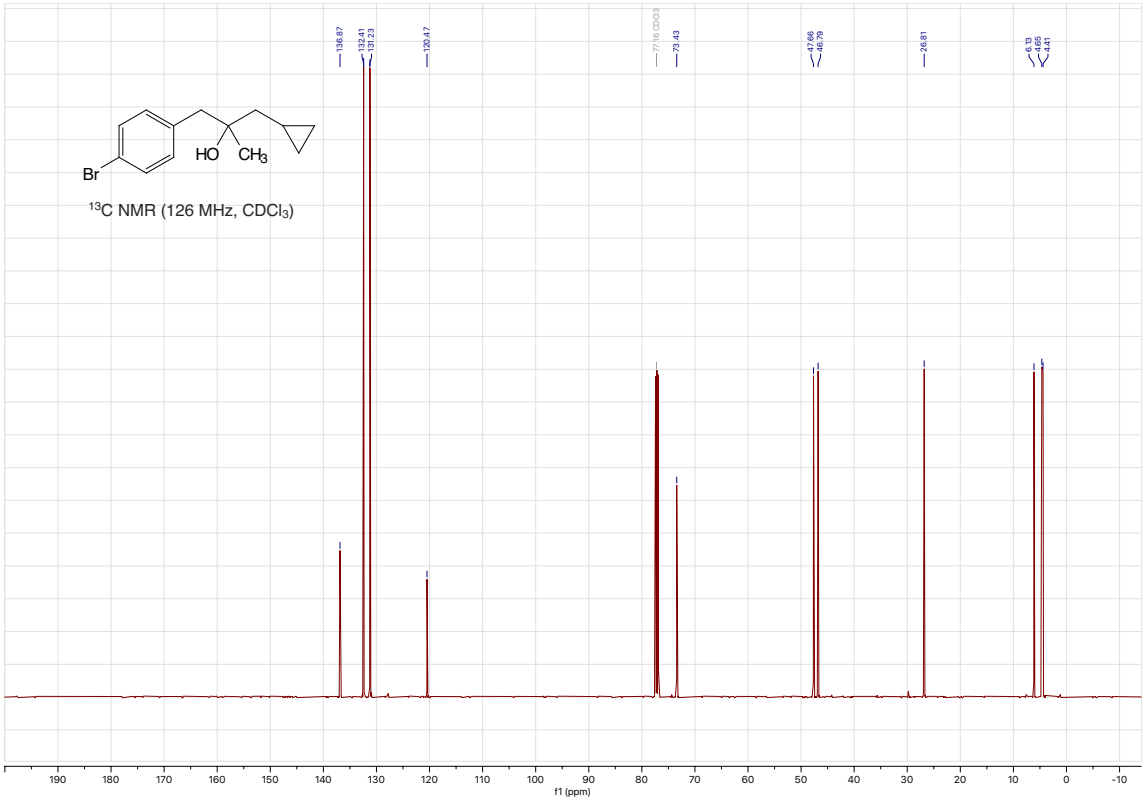
1-(4-chlorophenyl)-3-cyclopropyl-2-methylpropan-2-ol (30)



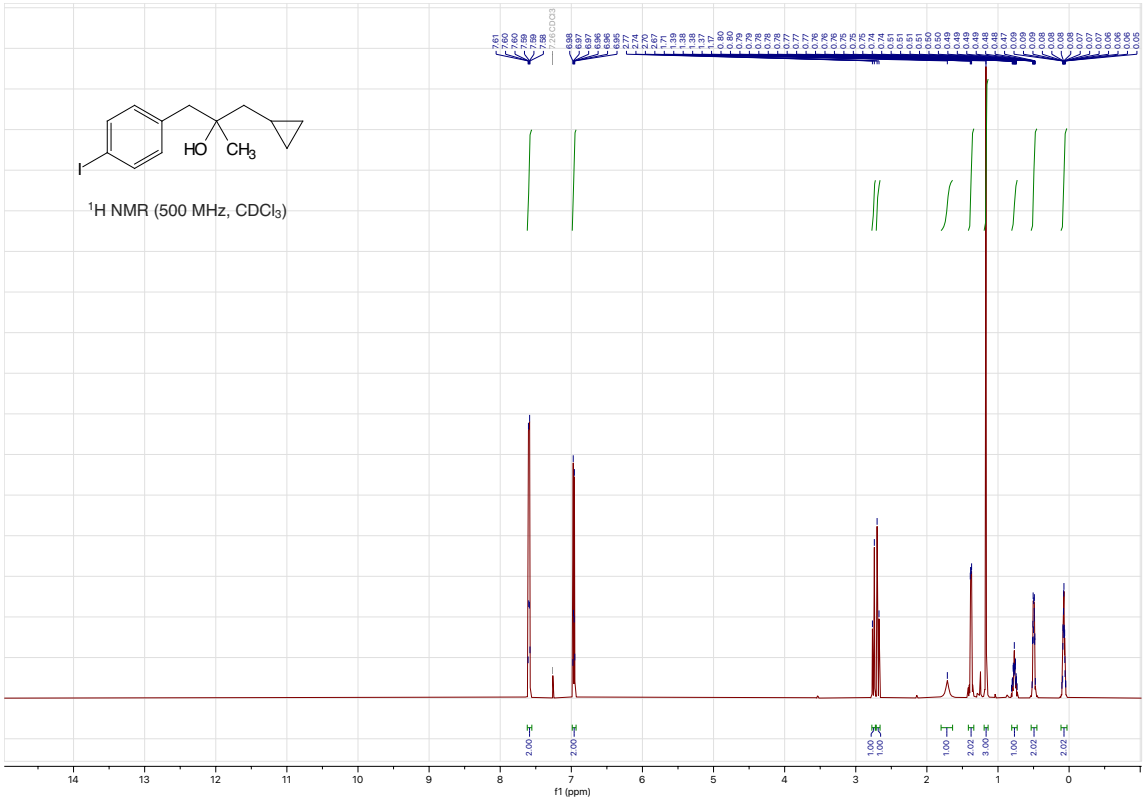


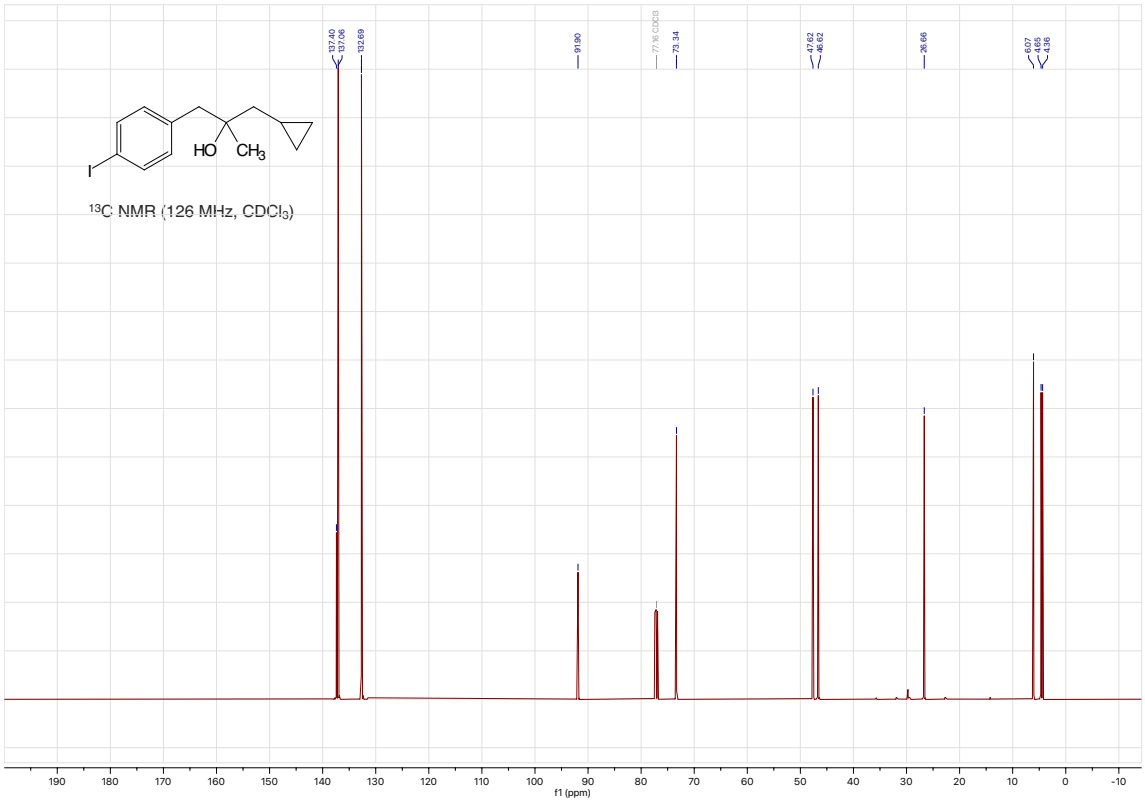
1-(4-bromophenyl)-3-cyclopropyl-2-methylpropan-2-ol (31)



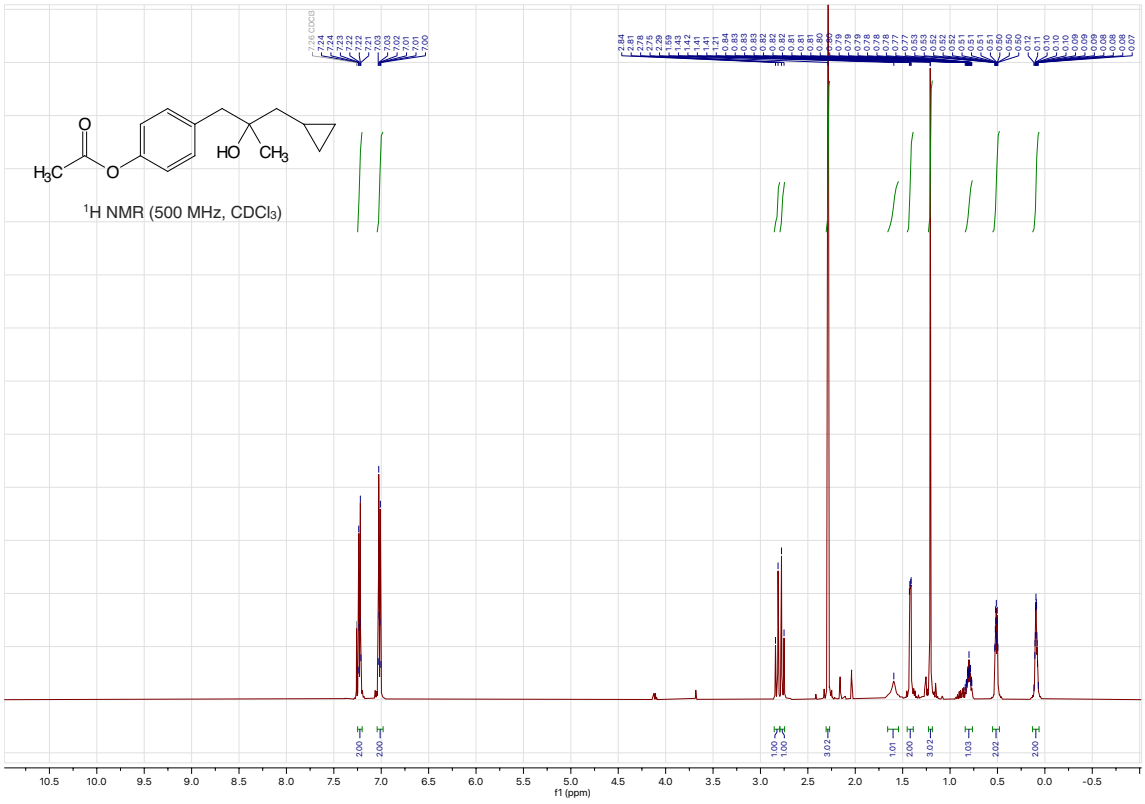


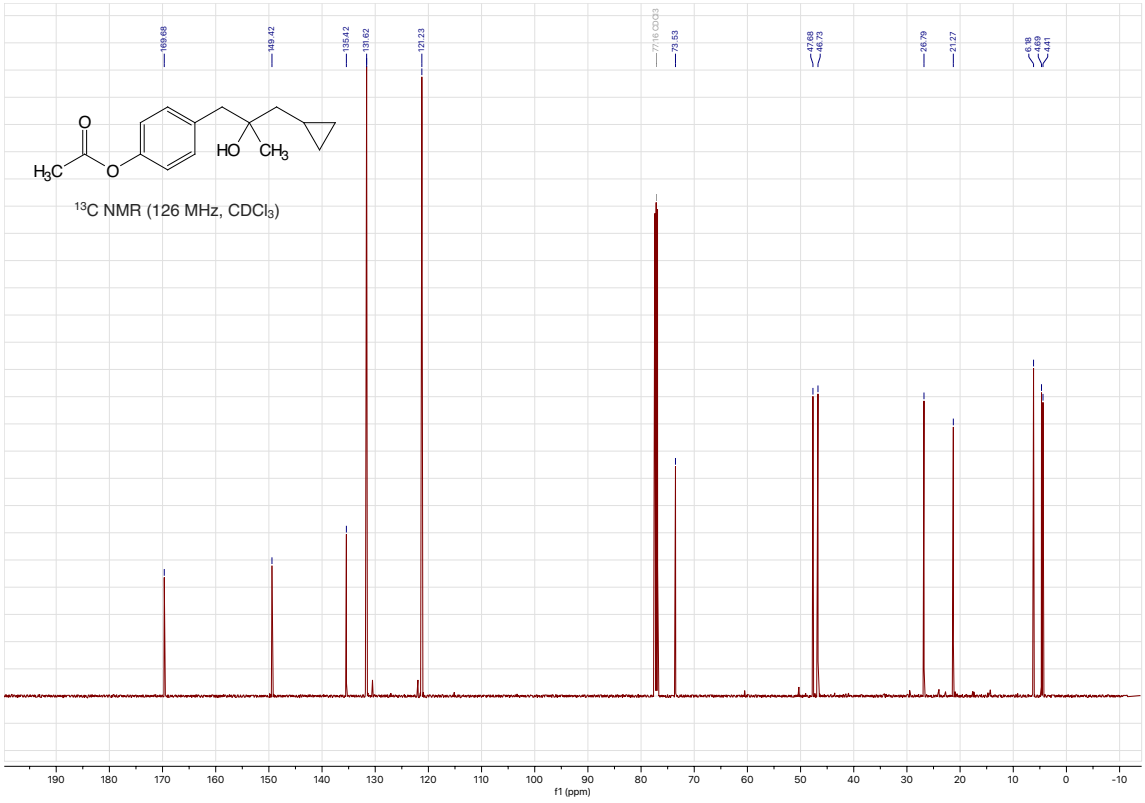
1-cyclopropyl-3-(4-iodophenyl)-2-methylpropan-2-ol (32)



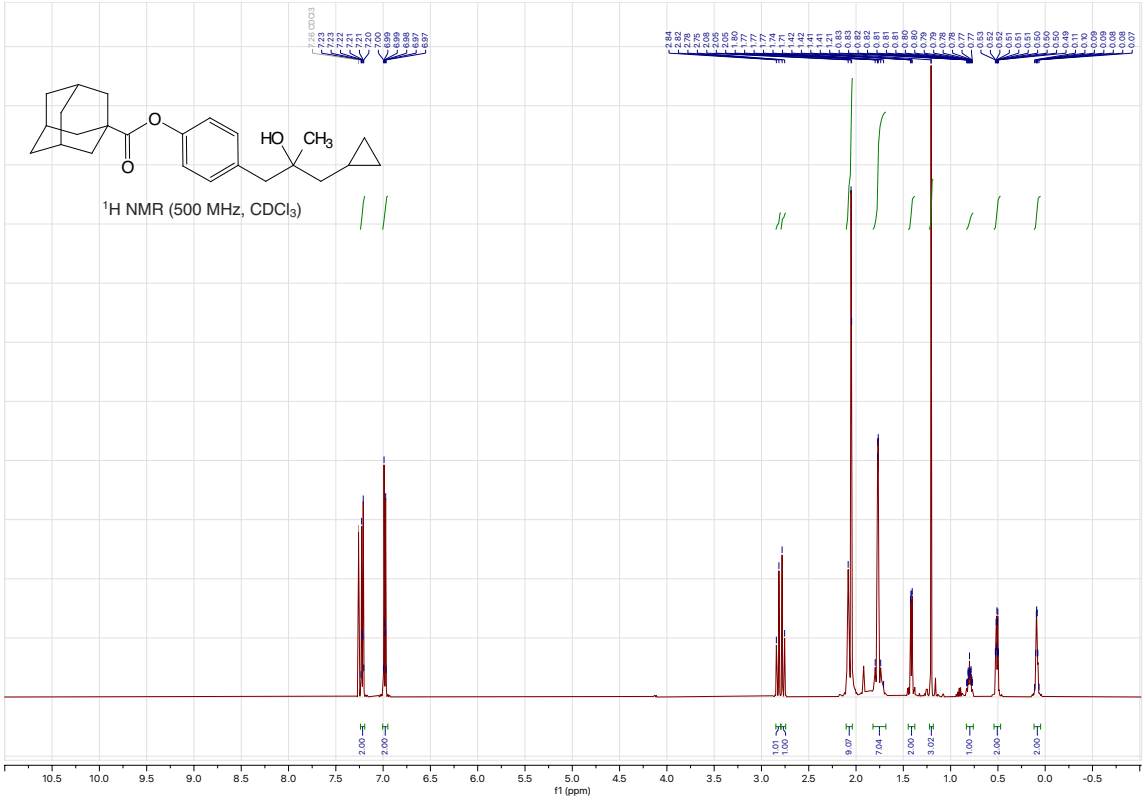


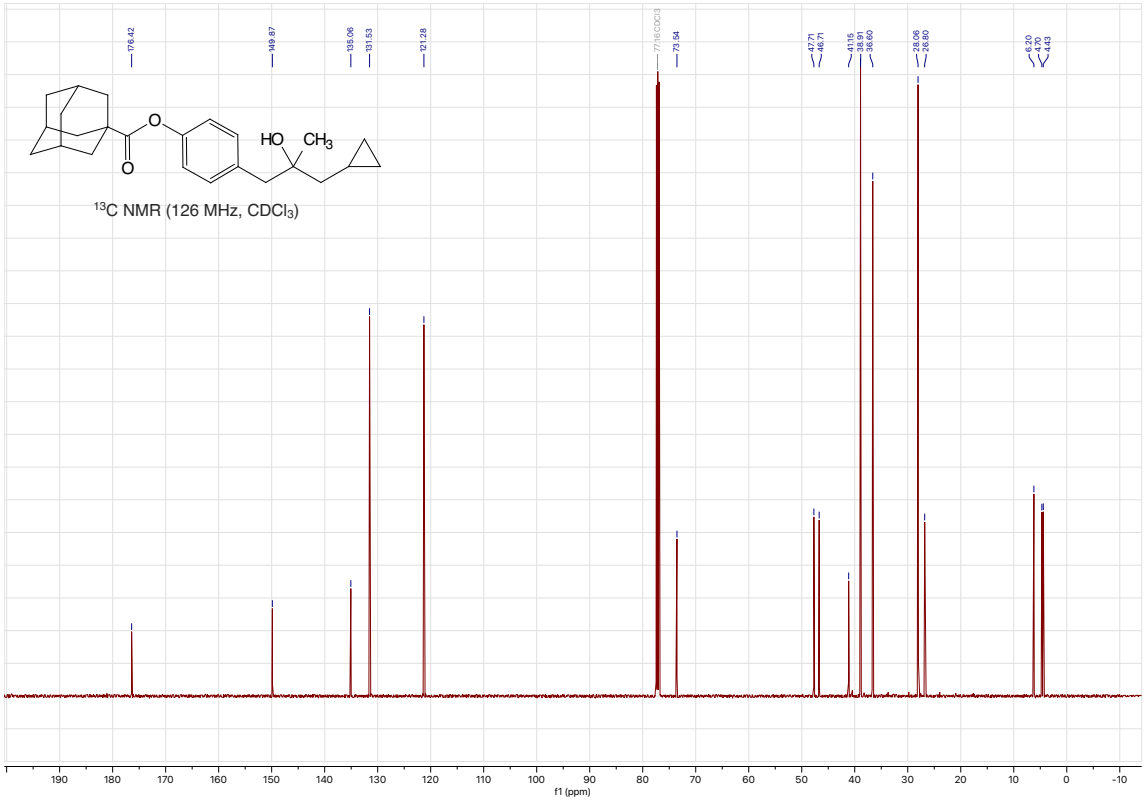
4-(3-cyclopropyl-2-hydroxy-2-methylpropyl)phenyl acetate (33)



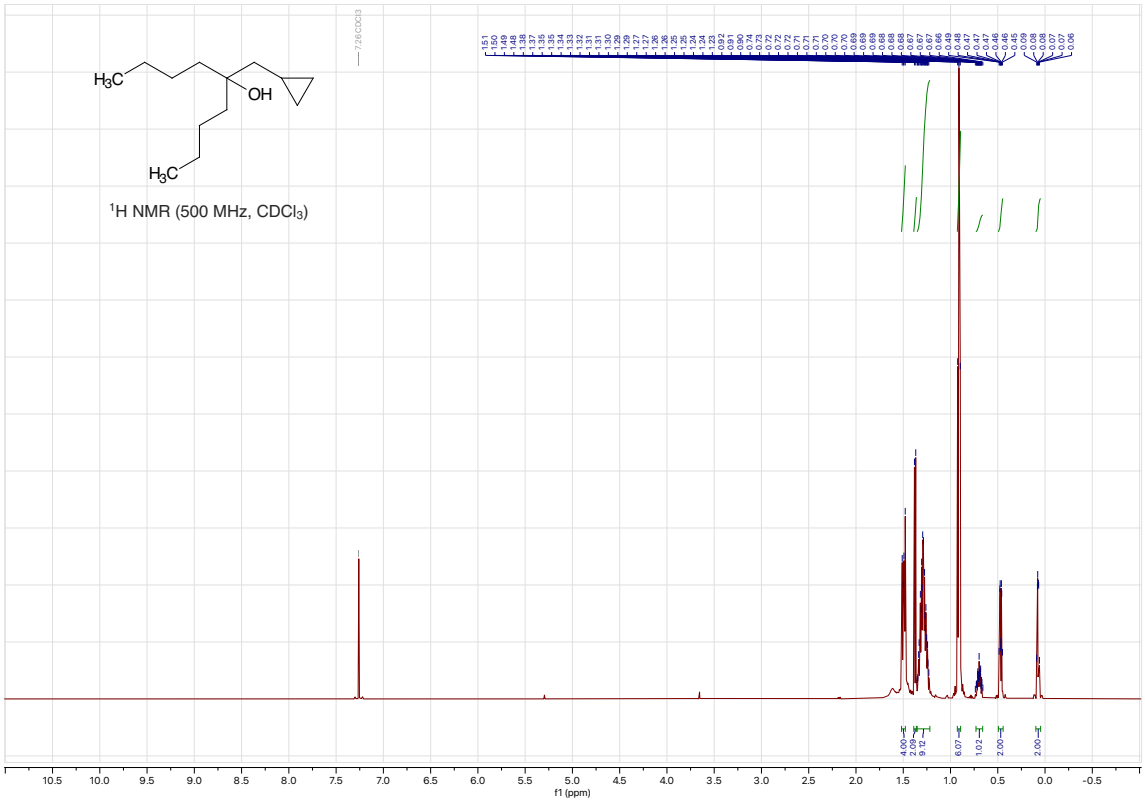


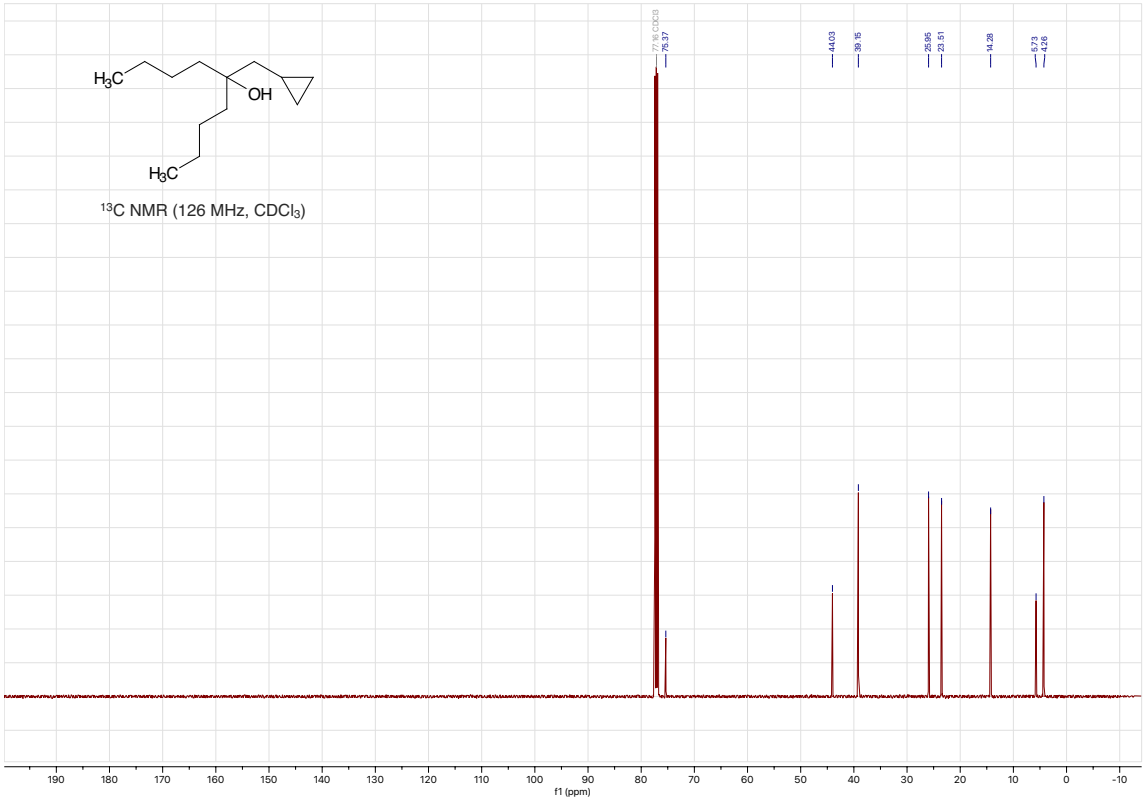
4-(3-cyclopropyl-2-hydroxy-2-methylpropyl)phenyl (3*r*,5*r*,7*r*)-adamantane-1-carboxylate (34)



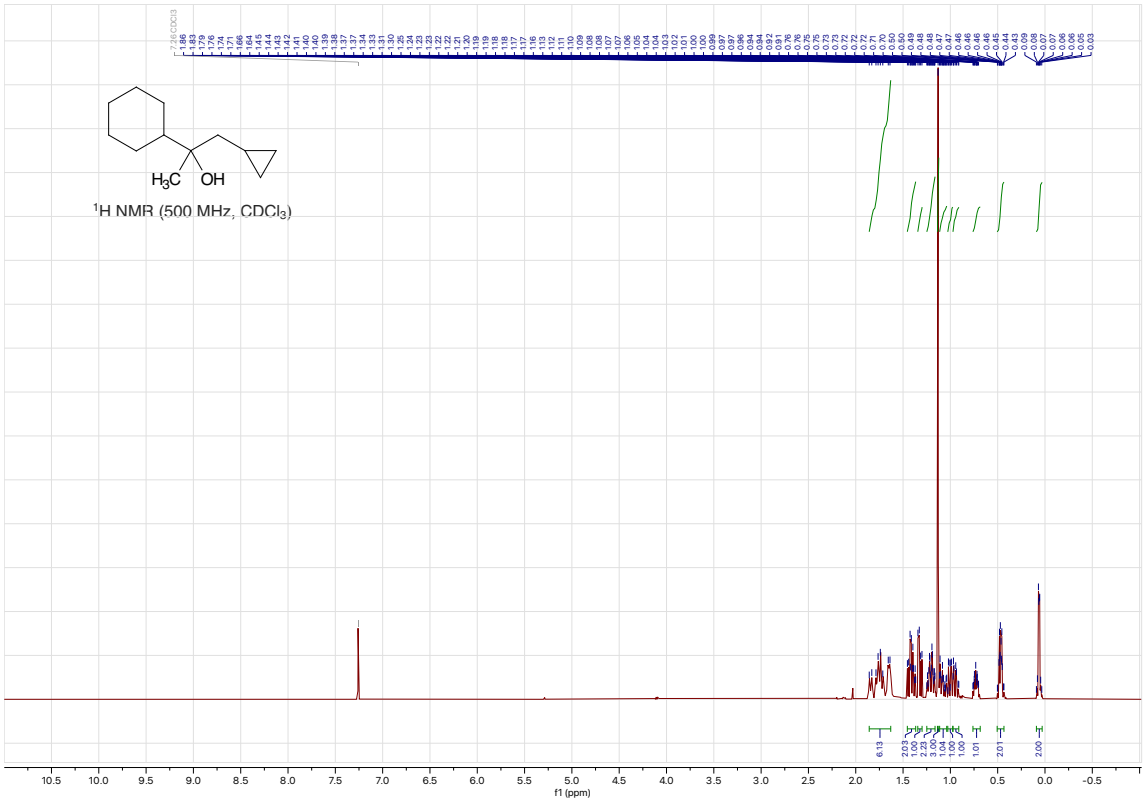


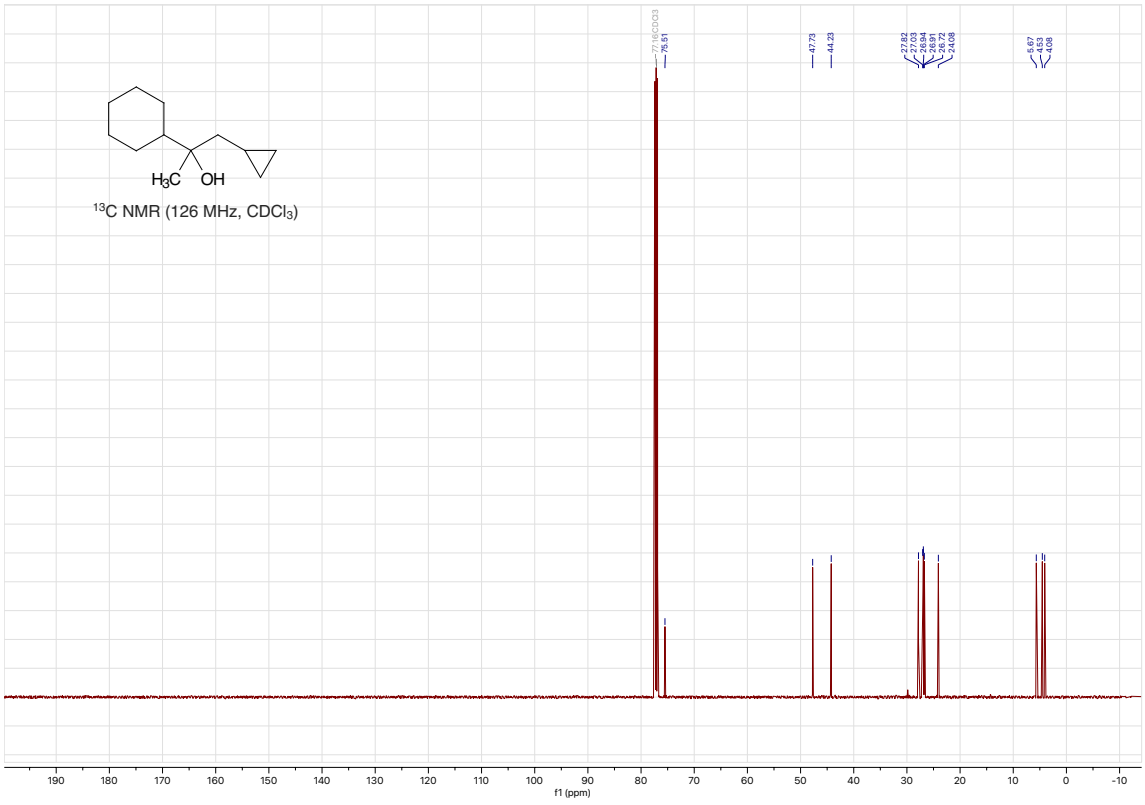
5-(cyclopropylmethyl)nonan-5-ol (35)



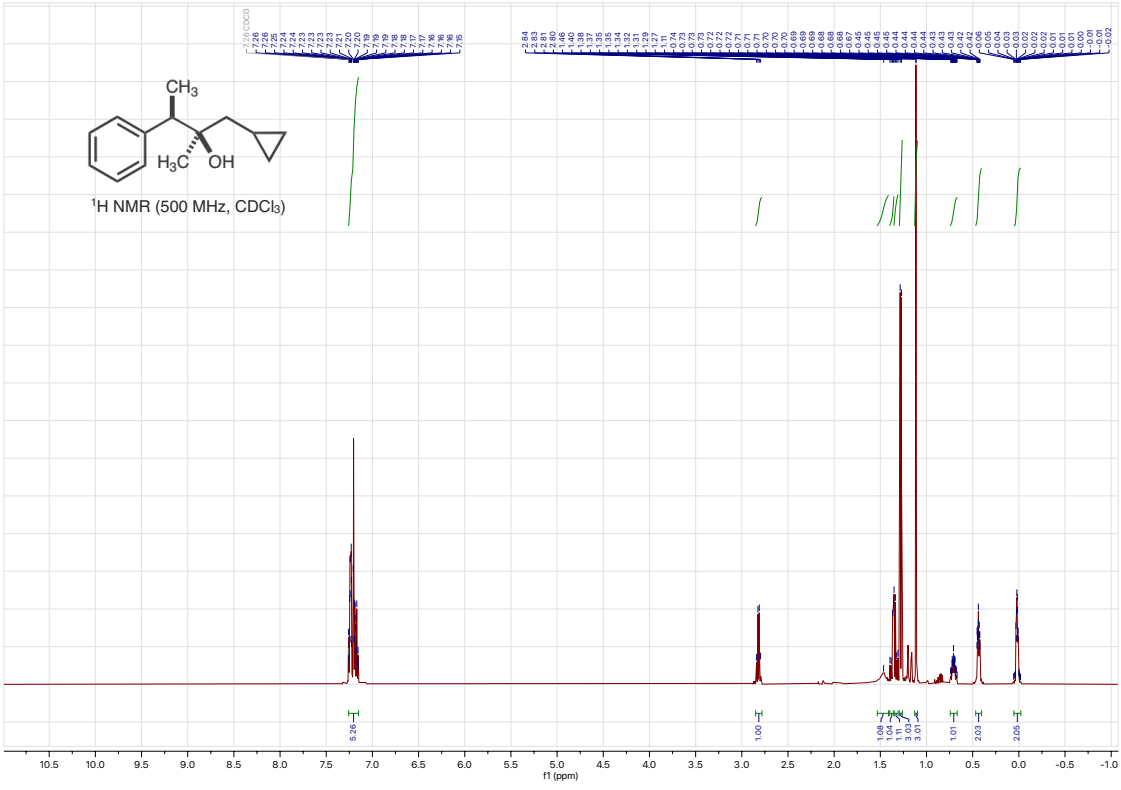


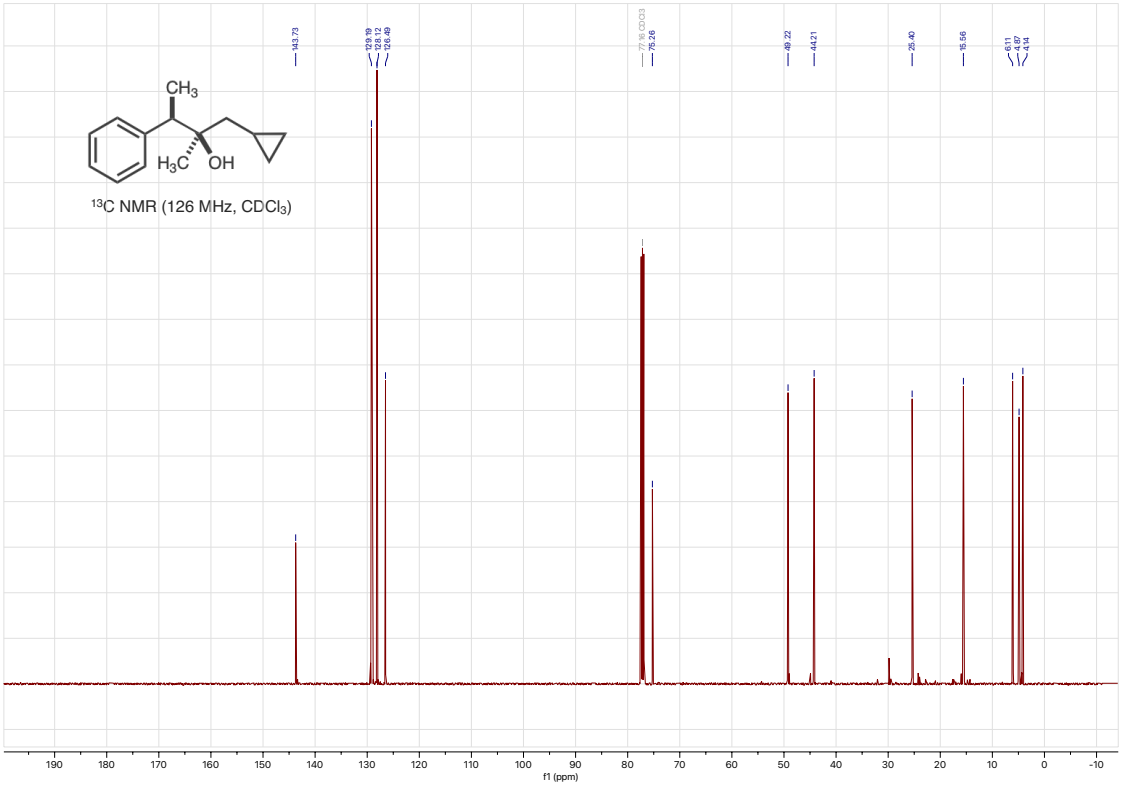
2-cyclohexyl-1-cyclopropylpropan-2-ol (36)



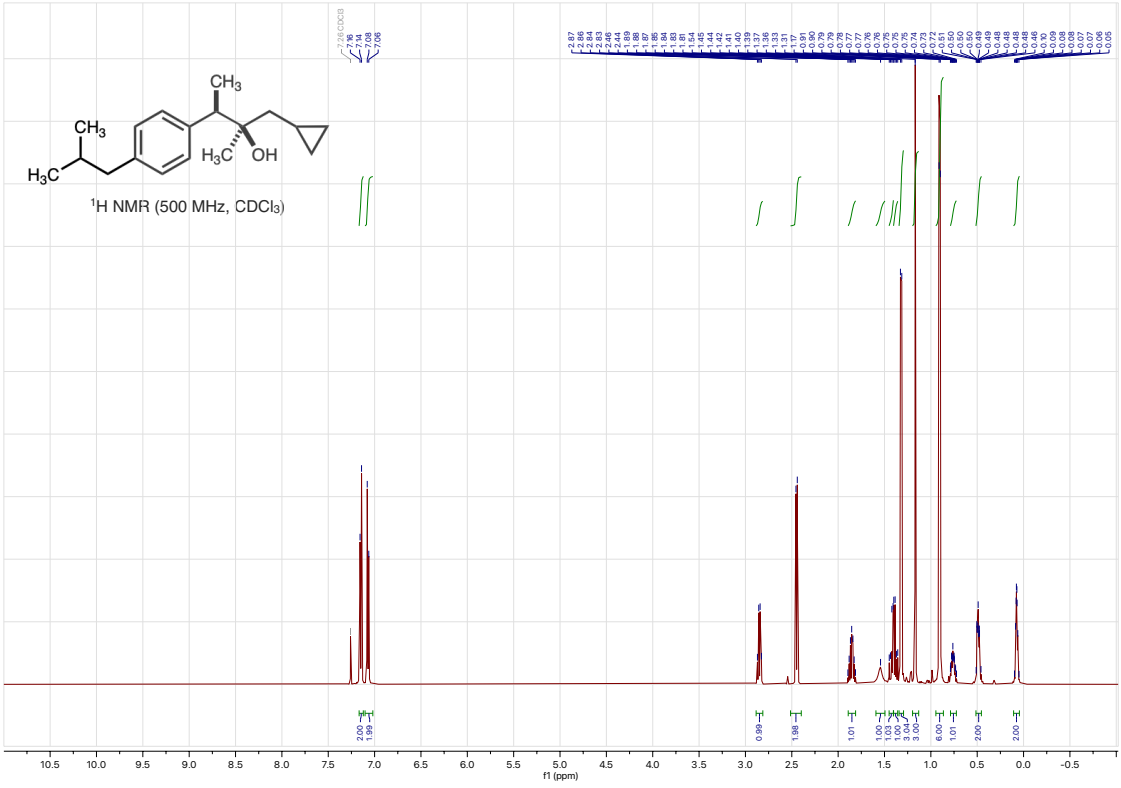


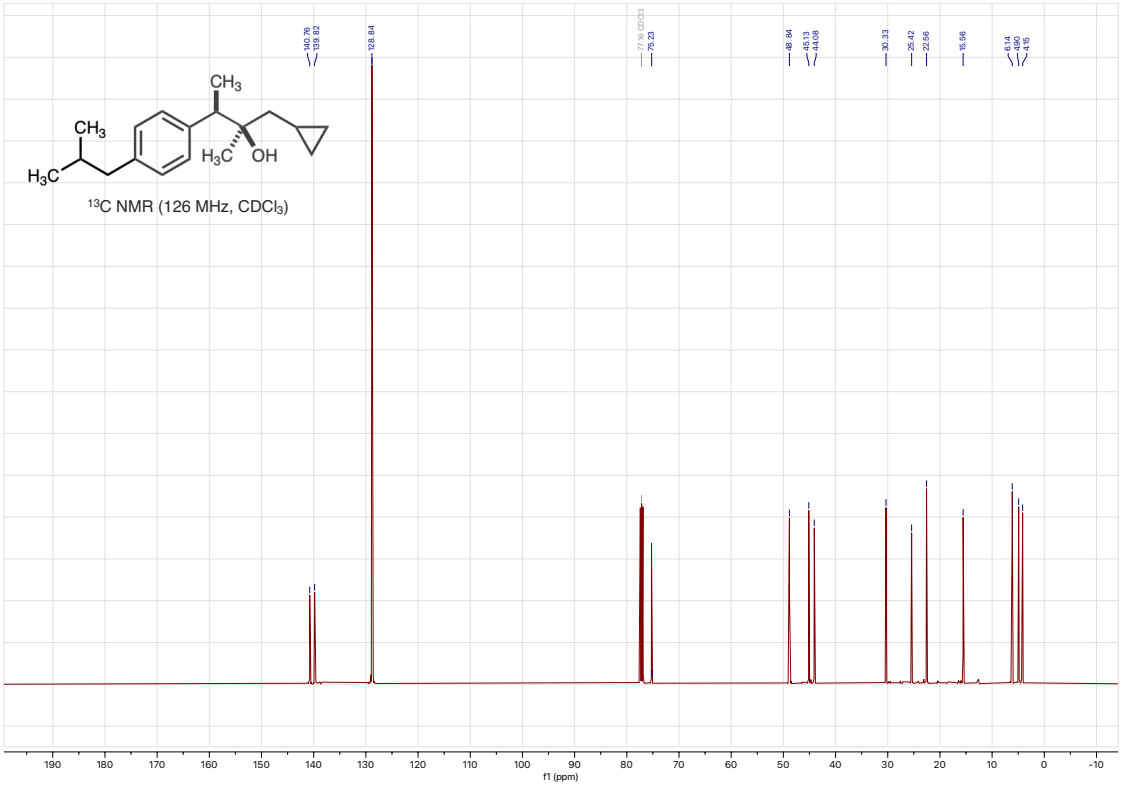
(anti)-1-cyclopropyl-2-methyl-3-phenylbutan-2-ol (37)



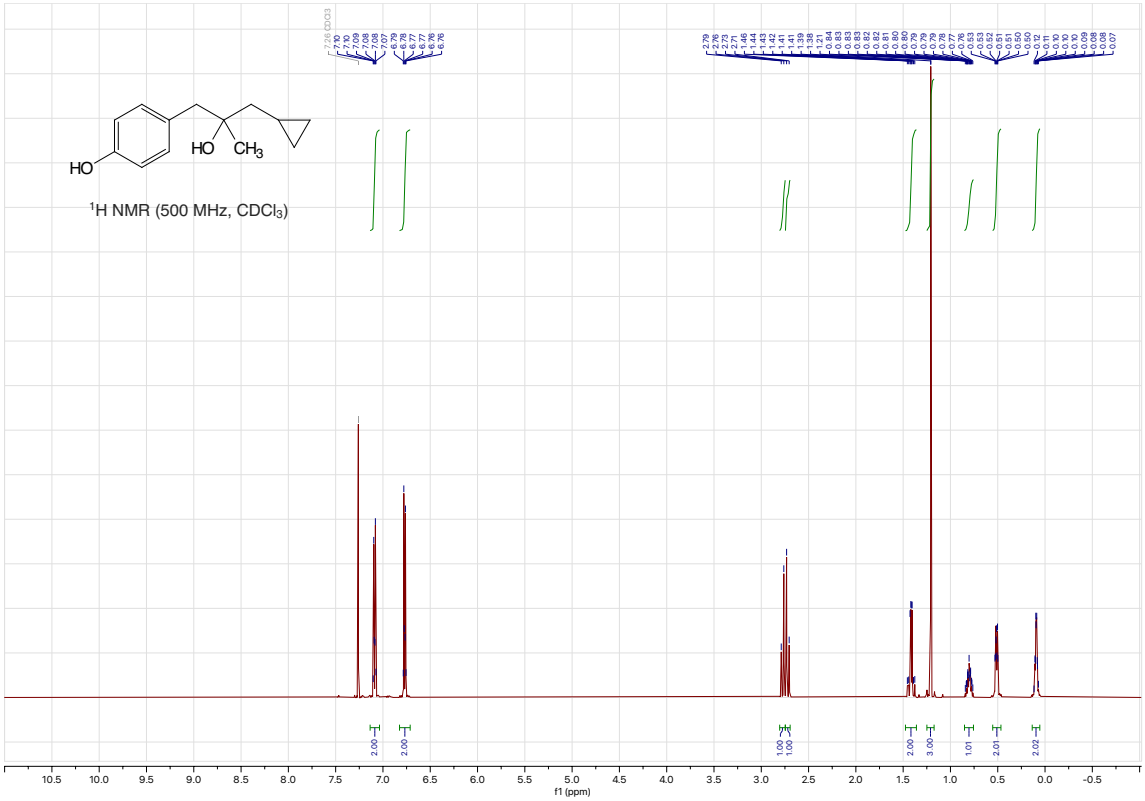


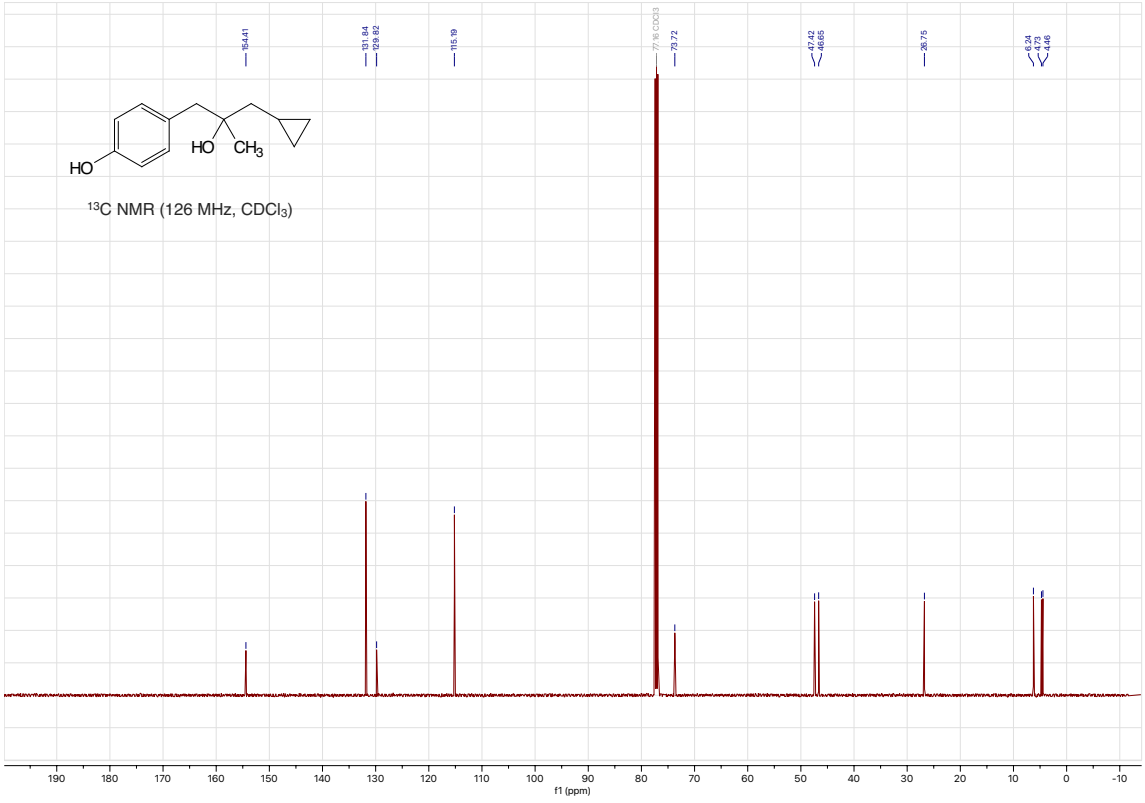
(anti)-1-cyclopropyl-3-(4-isobutylphenyl)-2-methylbutan-2-ol (38)



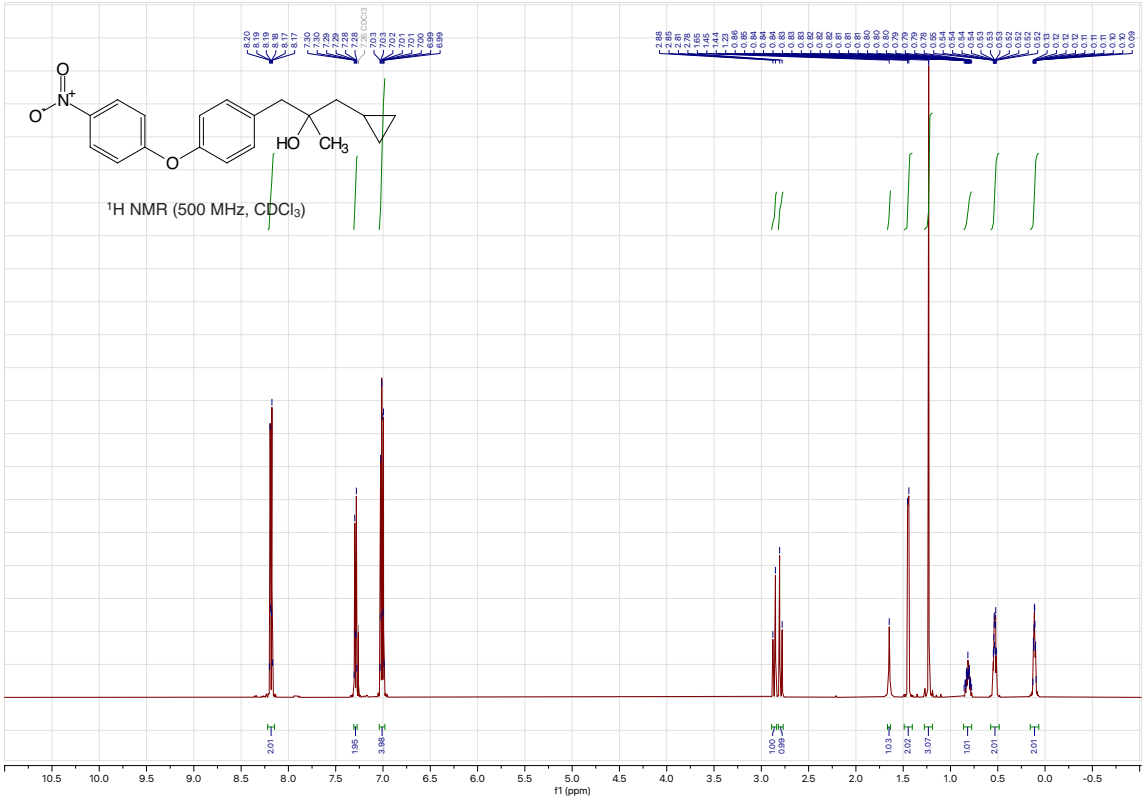


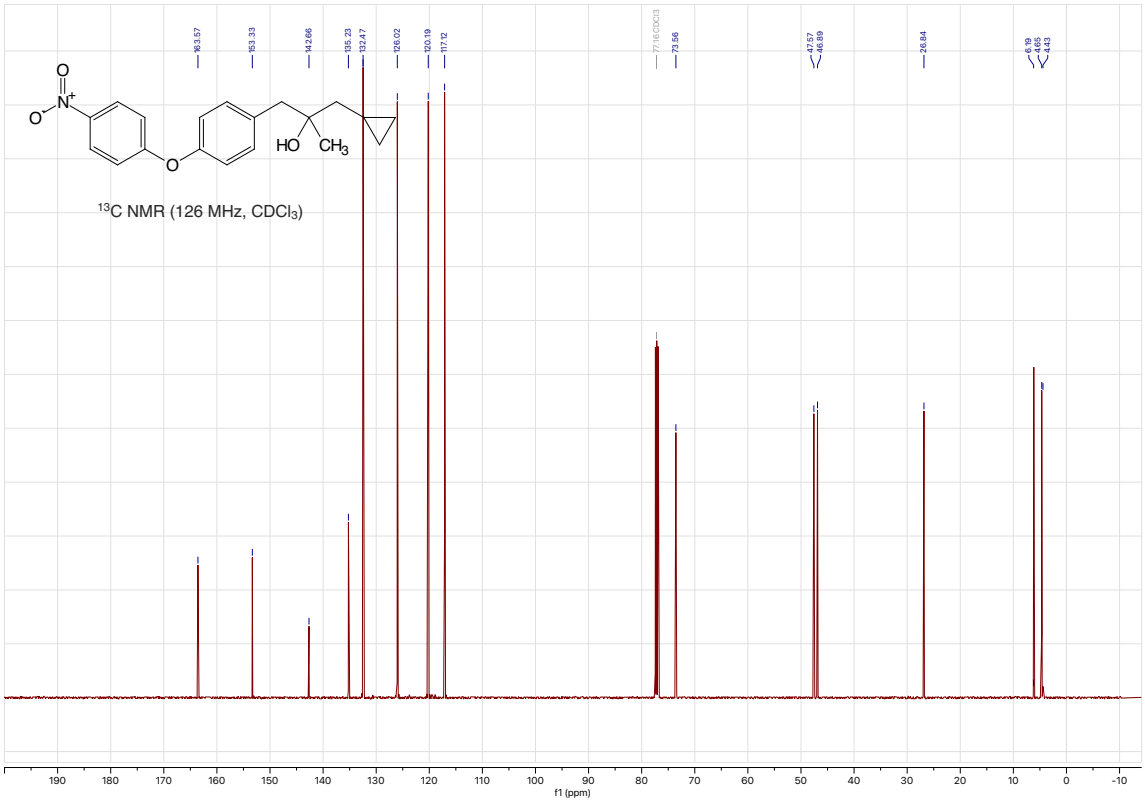
4-(3-cyclopropyl-2-hydroxy-2-methylpropyl)phenol (25)



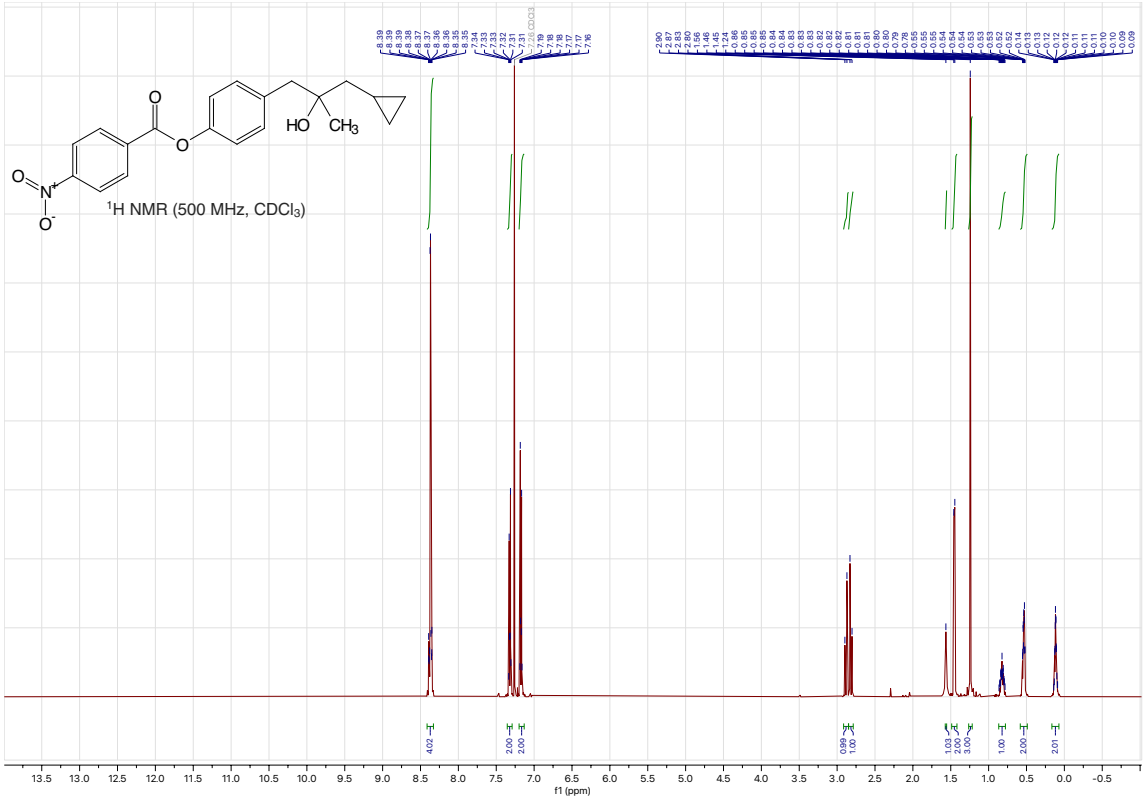


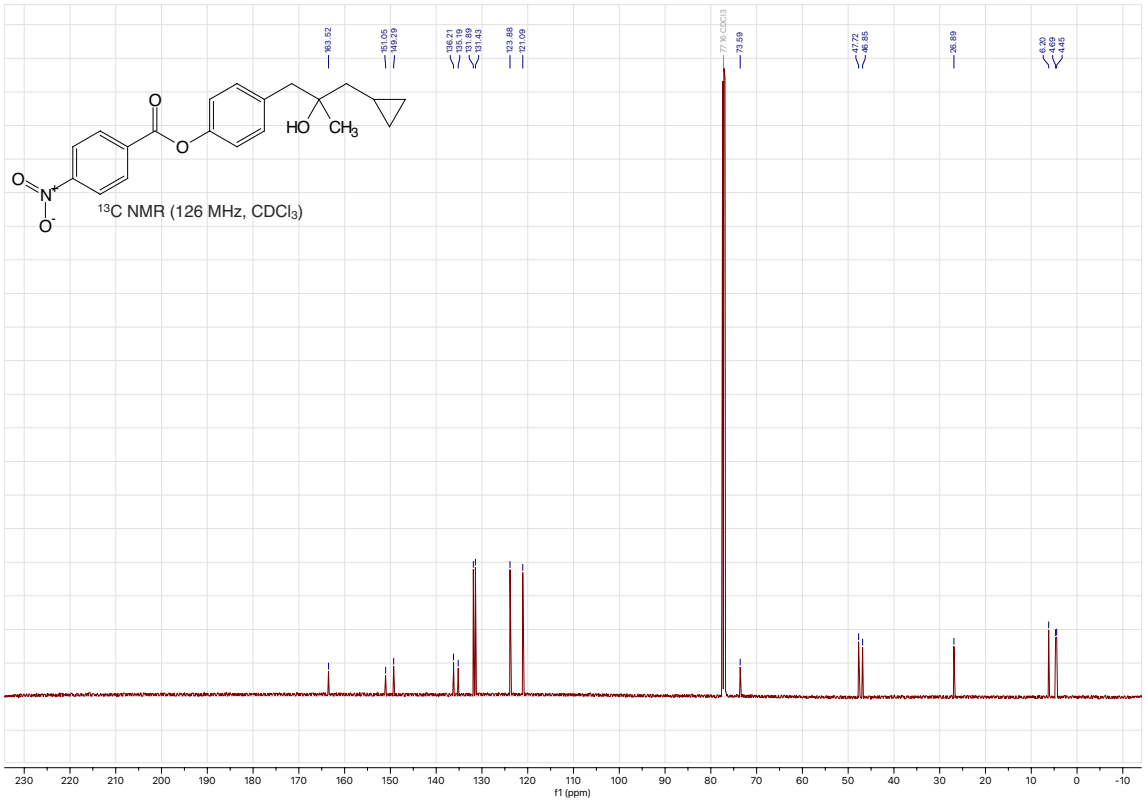
1-cyclopropyl-2-methyl-3-(4-(4-nitrophenoxy)phenyl)propan-2-ol (S11)



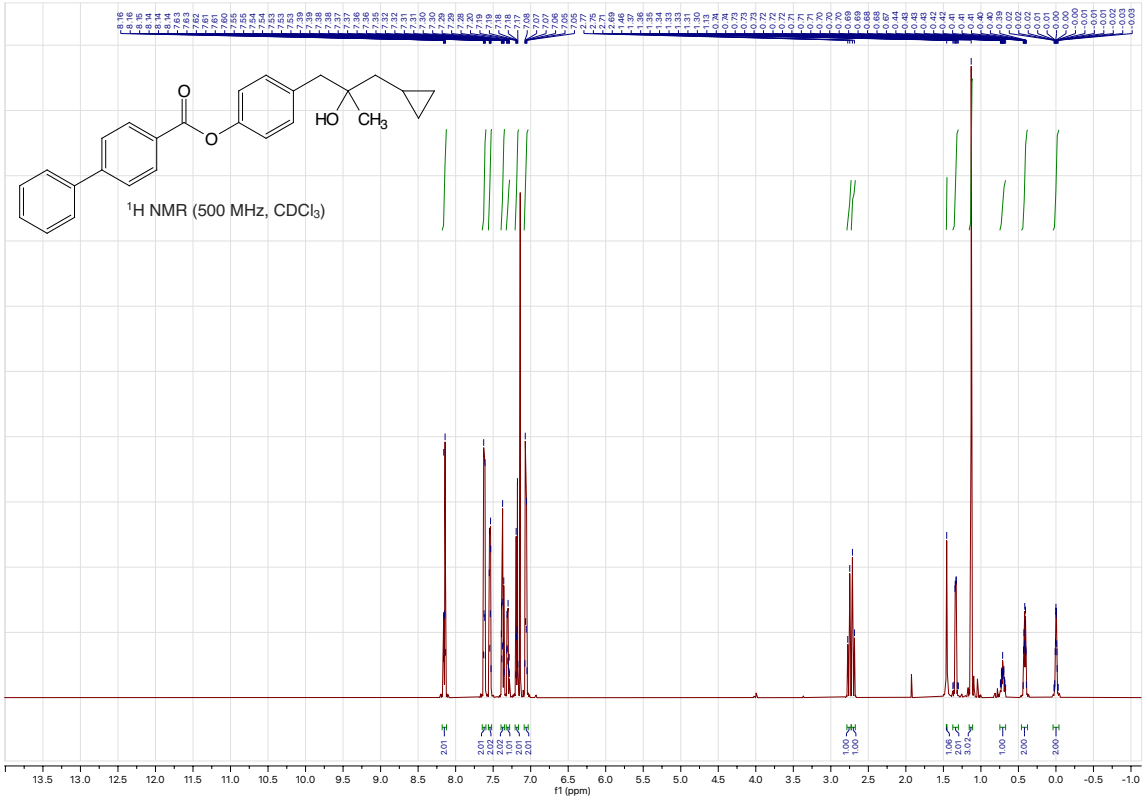


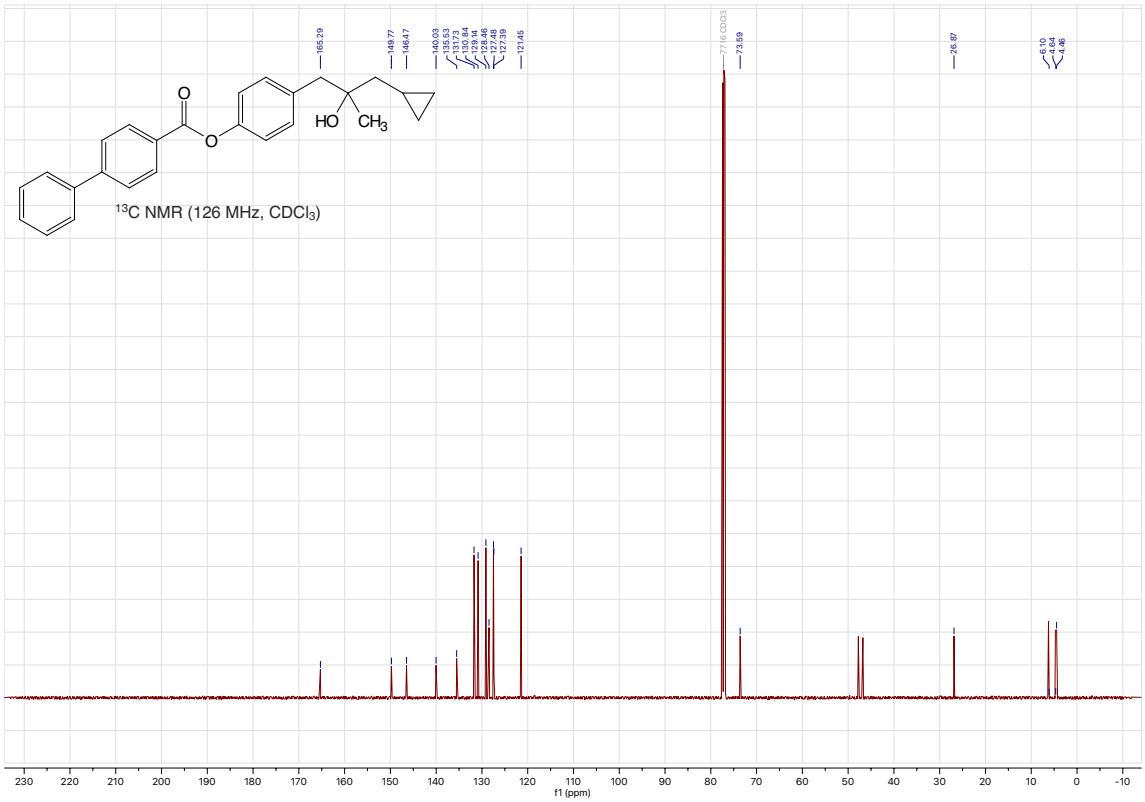
4-(3-cyclopropyl-2-hydroxy-2-methylpropyl)phenyl 4-nitrobenzoate (S12)



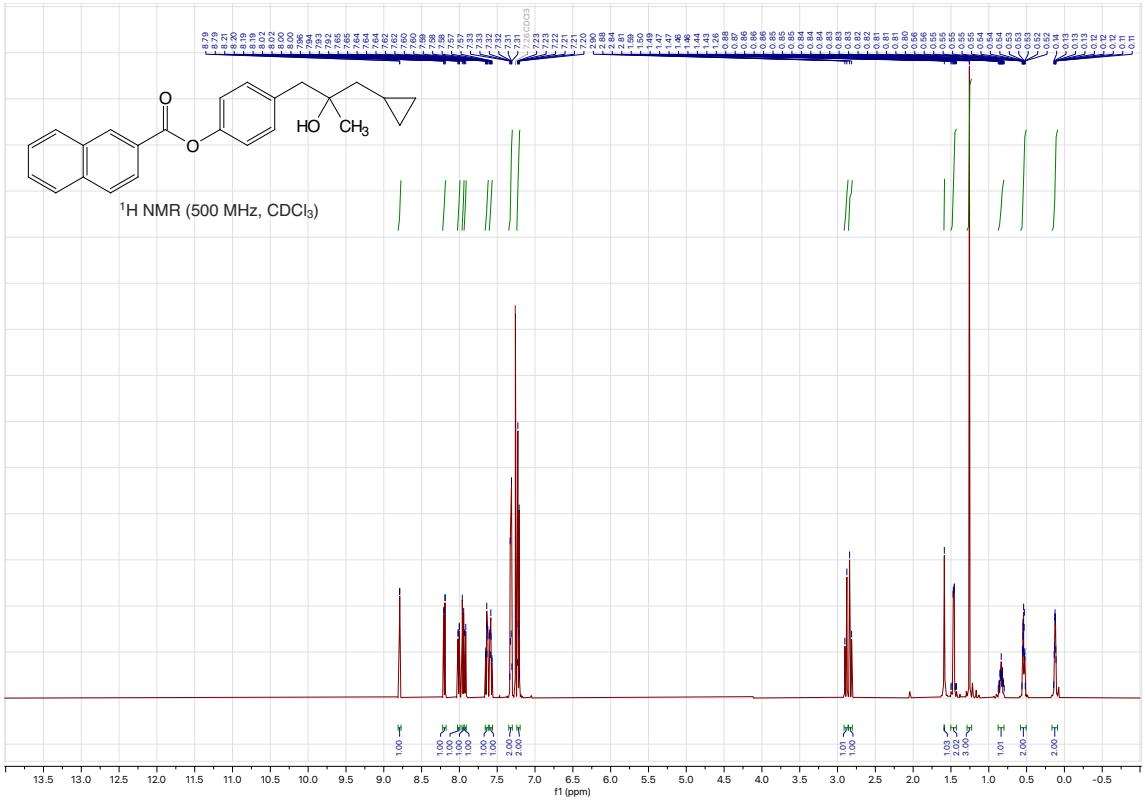


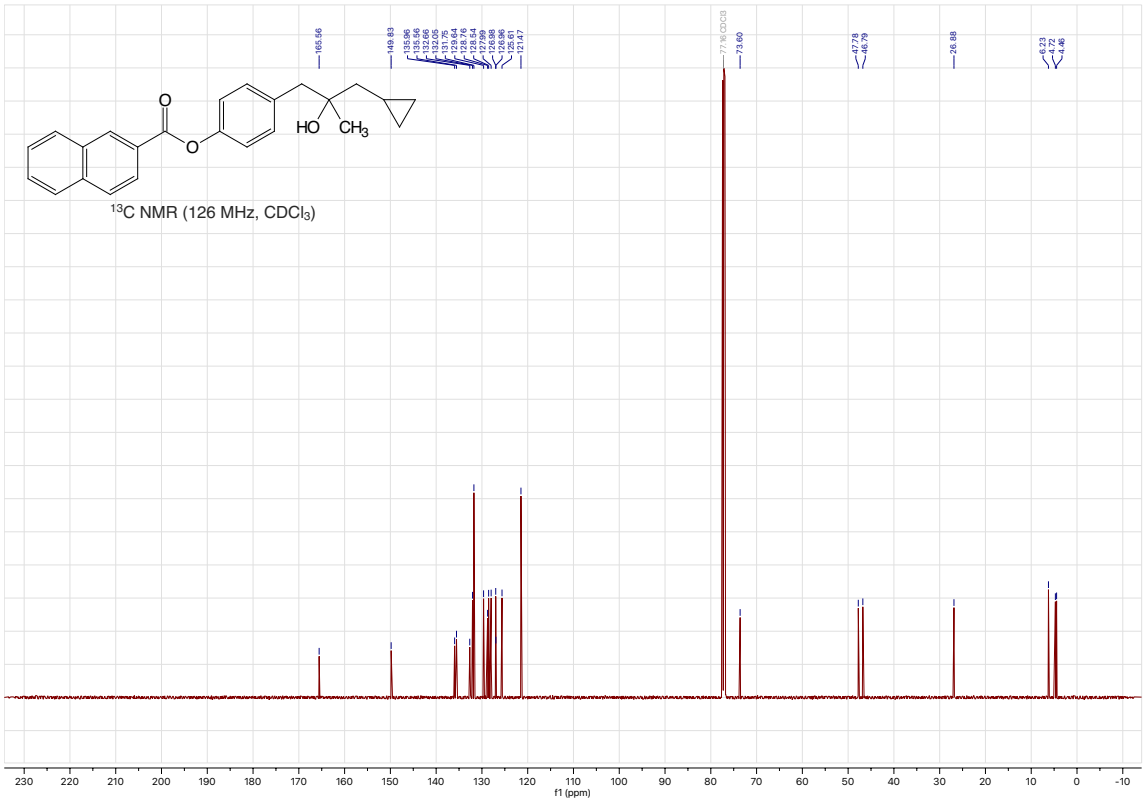
4-(3-cyclopropyl-2-hydroxy-2-methylpropyl)phenyl[1,1'-biphenyl]-4-carboxylate (S13)



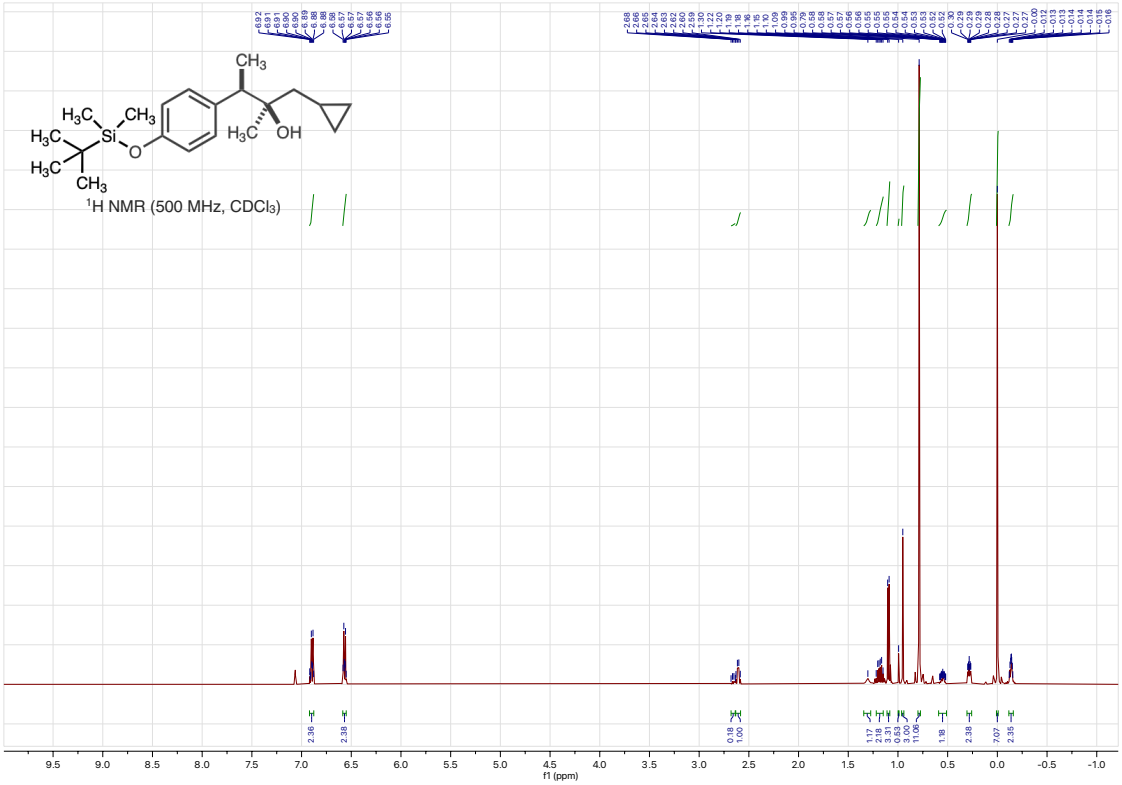


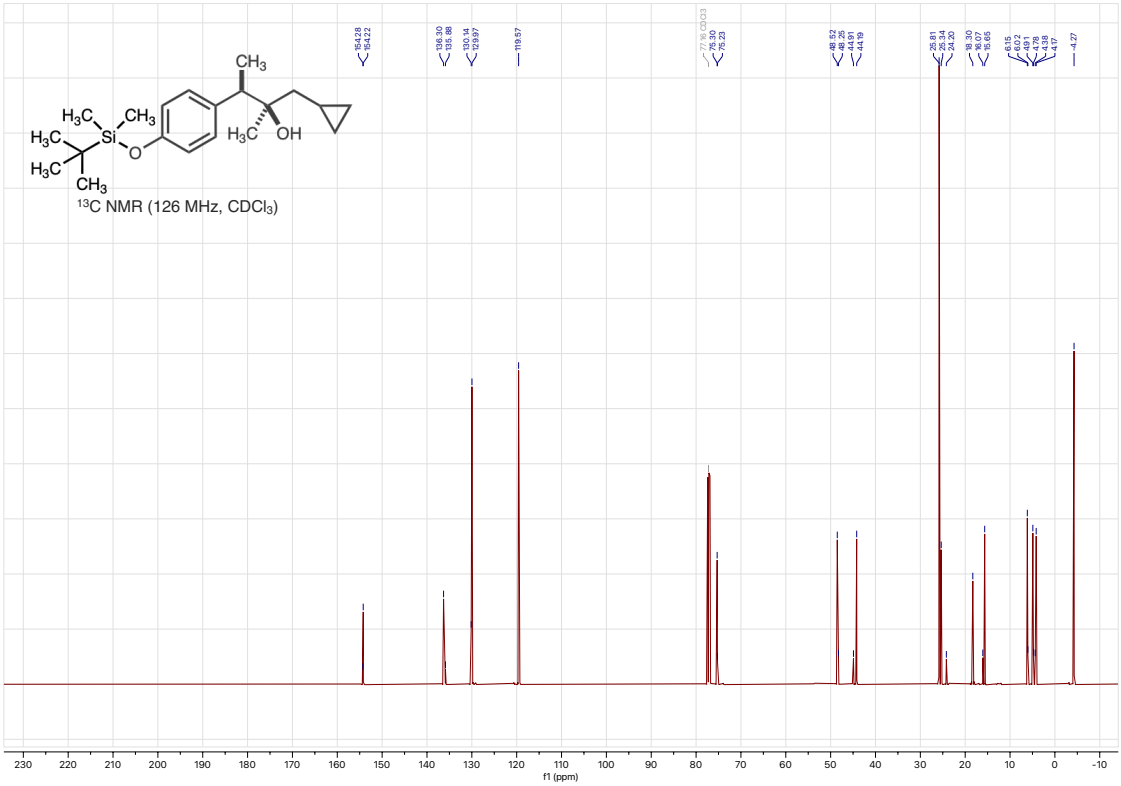
4-(3-cyclopropyl-2-hydroxy-2-methylpropyl)phenyl 2-naphthoate (S14)



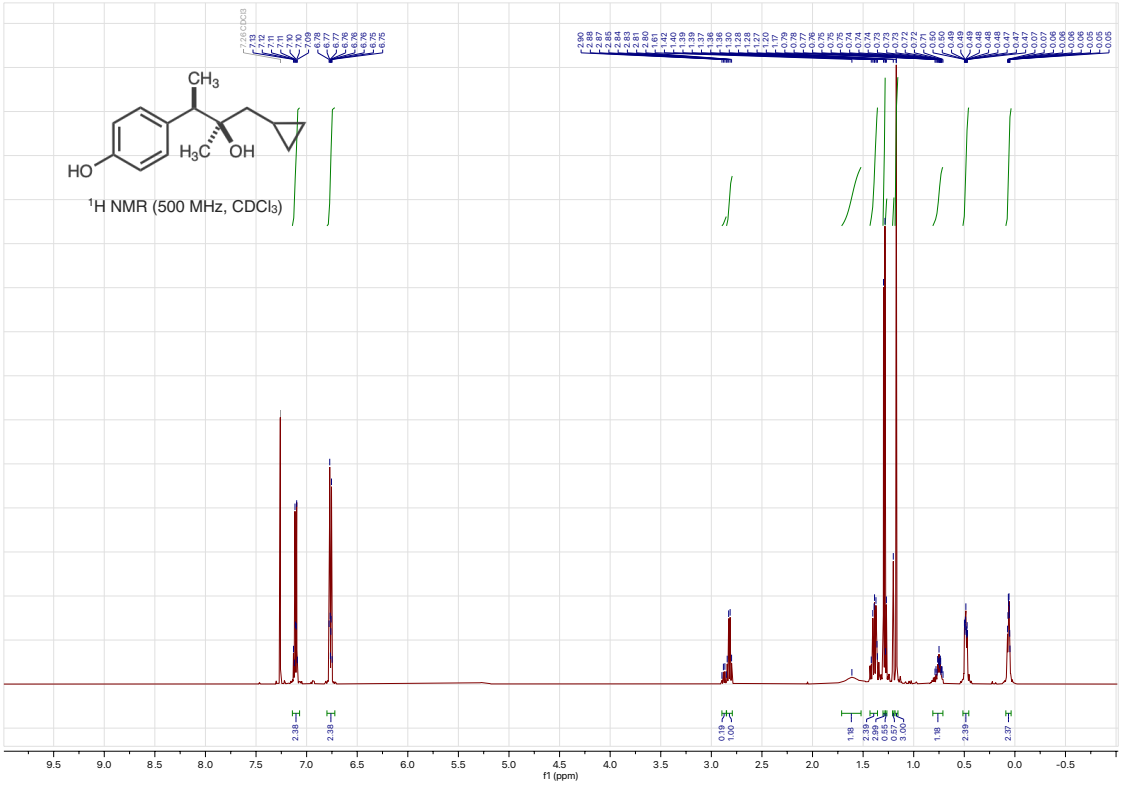


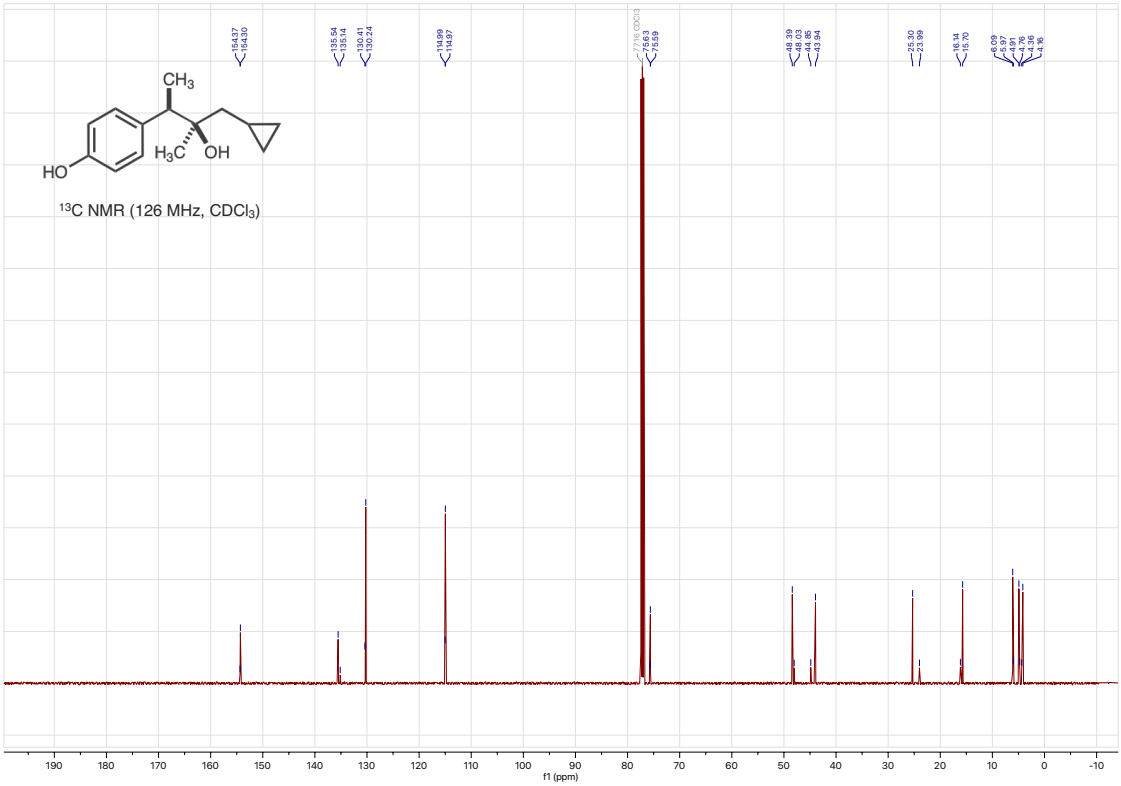
(anti)-3-(4-((*tert*-butyldimethylsilyl)oxy)phenyl)-1-cyclopropyl-2-methylbutan-2-ol (39)



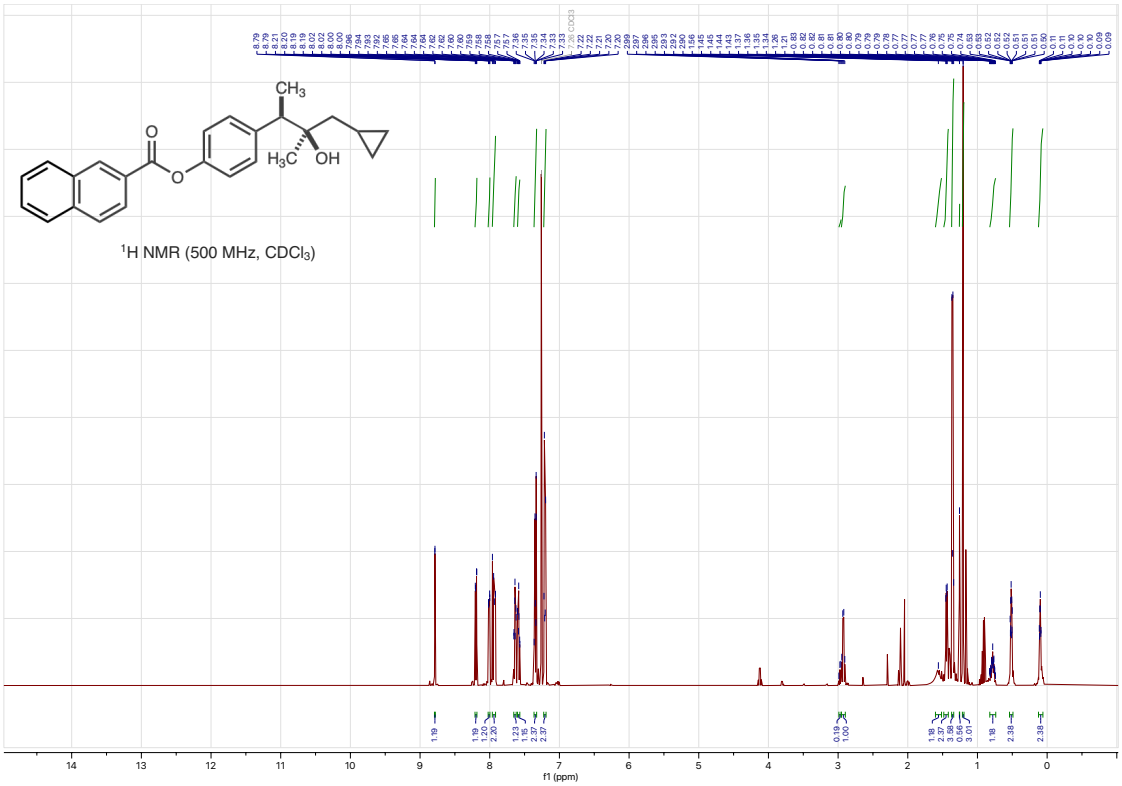


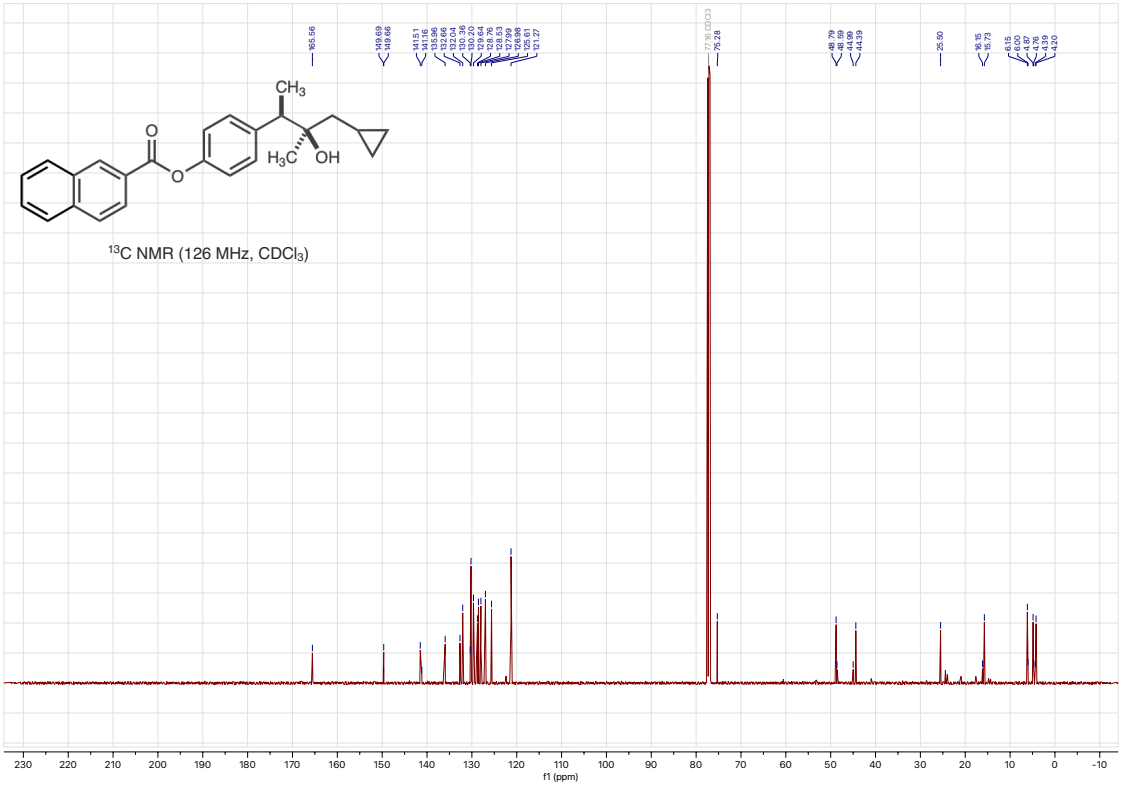
4-((anti)-4-cyclopropyl-3-hydroxy-3-methylbutan-2-yl)phenol (40)



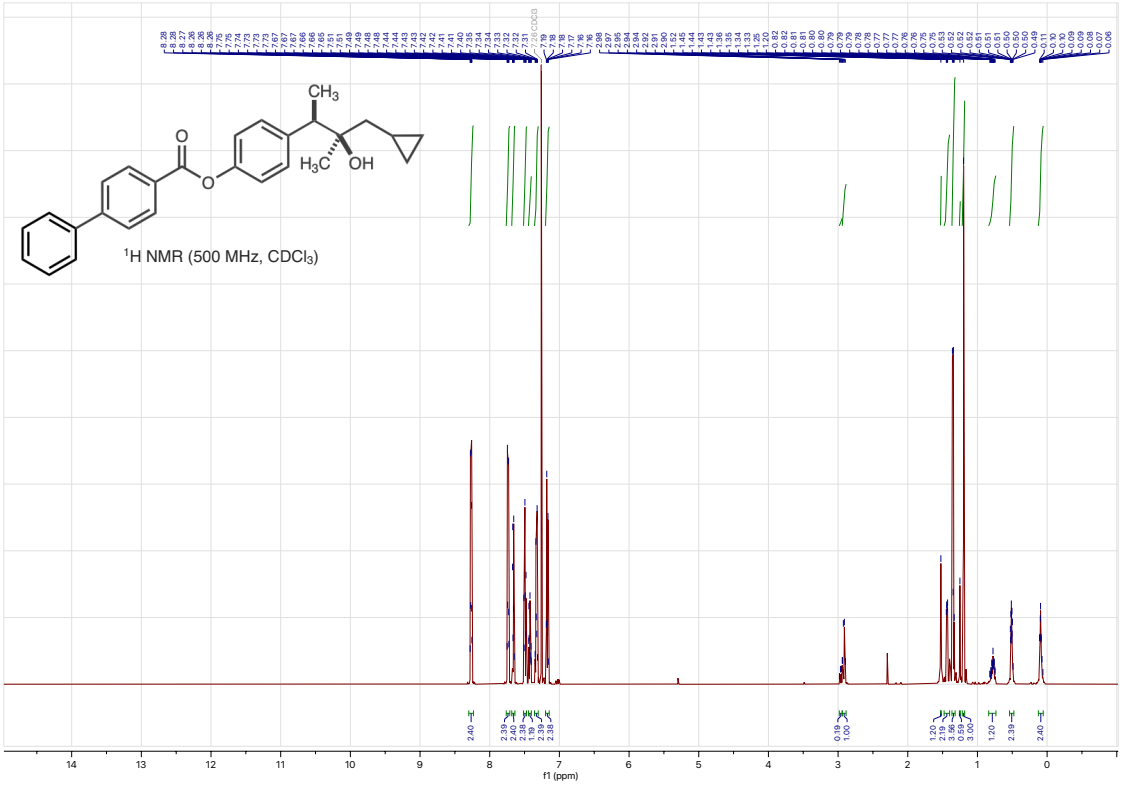


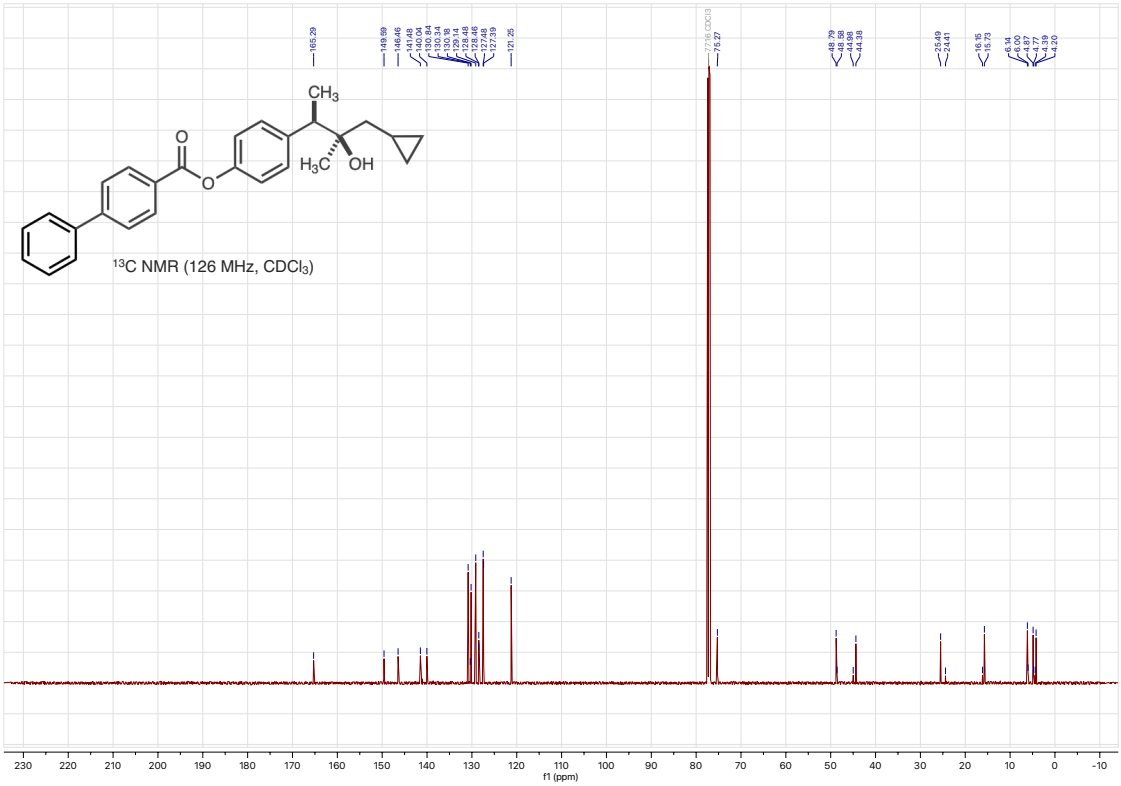
4-((anti)-4-cyclopropyl-3-hydroxy-3-methylbutan-2-yl)phenyl 2-naphthoate (S15)





4-((anti)-4-cyclopropyl-3-hydroxy-3-methylbutan-2-yl)phenyl [1,1'-biphenyl]-4-carboxylate (S16)





4-((anti)-4-cyclopropyl-3-hydroxy-3-methylbutan-2-yl)phenyl 4-nitrobenzoate (41)