

Supporting Information for
“Chemo- and Regioselective Synthesis of Acyl-Cyclohexenes by a
Tandem Acceptorless Dehydrogenation-[1,5]-Hydride Shift Cascade”

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1. General Information

Procedures using oxygen and/or moisture-sensitive materials were performed with anhydrous solvents (*vide infra*) under an atmosphere of anhydrous argon/nitrogen in flame-dried flasks, using standard Schlenk techniques. Analytical thin-layer chromatography was performed on Merck Kieselgel 60 F254 0.25 mm pre-coated aluminium plates and visualised using a combination of UV light (254 nm) and aqueous ceric ammonium molybdate (CAM), aqueous basic potassium permanganate stains or vanillin solution. The removal of solvents *in vacuo* was achieved using a Büchi rotary evaporator with an oil pump (0.1 mmHg) or diaphragm pump (15 mmHg) at bath temperatures up to 50 °C.

Flash column chromatography (FCC) was carried out using Apollo Scientific silica gel 60 (0.040 –0.063 nm) and Merck 60 Å silica gel (0.015-0.040). Pressure was applied at the column head via a flow of nitrogen with the solvent system used in parentheses.

Reactions at 0 °C were performed using an ice-water bath, which was covered with cotton and foil if overnight stirring was required. Other temperatures were obtained using a Julabo FT902 immersion cooler or the heating plate of the stirrer with an oil bath. Unless stated otherwise, solution NMR spectra were recorded at room temperature; ¹H and ¹³C NMR experiments were carried out using Bruker NMR spectrometers (400, 500 or 700 MHz) in the deuterated solvent stated, using the residual non-deuterated solvent signal as an internal reference. Chemical shifts (δ) are given in ppm and coupling constants (J) are quoted to the nearest 0.5 hertz (Hz). ²H NMR experiments were carried out using Bruker AVIII HD 500 (77 or 92 MHz) in protonated solvent with a single drop of the corresponding deuterated solvent as an internal reference. Resonances are described as s (singlet), d (doublet), t (triplet), q (quartet), p (pentet), h (hextet), hept (heptet) and m (multiplet). ¹H and ¹³C NMR peaks for diastereomers were assigned major or minor. If major or minor diastereomers cannot be distinguished, the peaks were assigned with a ‘’ (e.g H₁ and H₁’, C₁ and C₁’). ¹H and ¹³C NMR peaks for diastereotopic environments were assigned with a subscript ‘a’ and ‘b’ (e.g H_a and H_b), or subscript ‘ax.’ (axial) and ‘eq.’ (equatorial) where applicable. Assignments were made with the assistance of gCOSY, gHSQC, gHMBC or NOESY NMR spectra.

Chiral HPLC separations were achieved using an Agilent 1260 Infinity series normal phase HPLC unit and HP Chemstation software. Chiralpak® columns (250 × 4.6 mm), fitted with matching Chiralpak® Guard Cartridges (10 × 4 mm), were used as specified in the text. Solvents used were of HPLC grade (Fisher Scientific, Sigma Aldrich or Rathburn); all eluent systems were isocratic.

Reverse phase HPLC separations were achieved using an Dionex Ultimate 3000 HPLC unit and Chromeleon software. Agilent Poroshell 120 EC-C18 4µm column (150 × 4.6 mm), fitted with matching Agilent Guard Cartridges (10 × 4 mm), were used as specified in the text. Solvents used were of HPLC grade (Fisher Scientific, Sigma Aldrich or Rathburn); all eluent systems were isocratic.

Low-resolution mass spectra were recorded using a Walters LCT premier XE. High-resolution mass spectra (EI and ESI) were recorded using a Bruker MicroTOF spectrometer by the internal service at the University of Oxford.

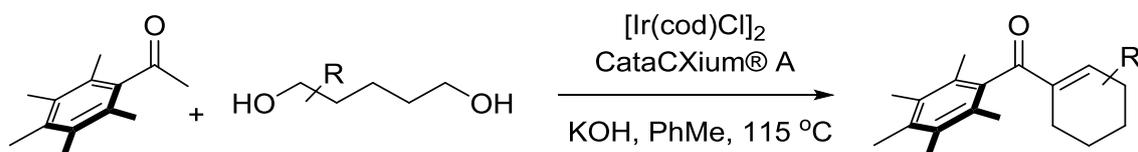
Infrared measurements (neat, thin film) were carried out using a Bruker Tensor 27 FT-IR with internal calibration in the range 600-4000 cm⁻¹.

Optical rotations were recorded on a Perkin-Elmer 241 polarimeter at 25°C in a 10 cm cell in the stated solvent; $[\alpha]_D$ values are given in 10⁻¹deg.cm²g⁻¹ (concentration c given as g/100mL).

Melting points were obtained using a Leica Galen III heated-stage microscope and are uncorrected.

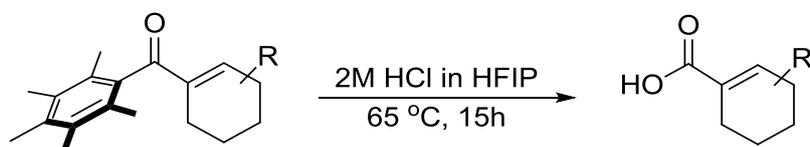
2. General Procedures

General Procedure 1: Synthesis of acyl cyclohexenes by iridium mediated annulation



A 2–5 mL Biotage[®] microwave vial was charged with CataCXium[®] A (4.3 mg, 0.012 mmol, 2 mol%), diol (1.2 mmol, 2 eq.), 1-(2,3,4,5,6-pentamethylphenyl)ethan-1-one (114 mg, 0.60 mmol, 1 eq.), [Ir(cod)Cl]₂ (2 mg, 0.003 mmol, 0.5 mol% dimer), KOH (134 mg, 2.40 mmol, 4 eq.) and toluene (2.4 mL, 0.25 M). The reaction vessel was sealed with a microwave vial cap (containing a Reseal[™] septum) and the vial was heated at 115 °C for 24 hours. After cooling to RT, the reaction mixture was diluted with aq. HCl (3M, 5 mL) and extracted with CH₂Cl₂ (4 x 10 mL). The combined organic phases were dried over MgSO₄, filtered and concentrated *in vacuo*. For details of purification, see experimental procedures.

General Procedure 2: Synthesis of carboxylic acids by retro-Friedel–Crafts acylation

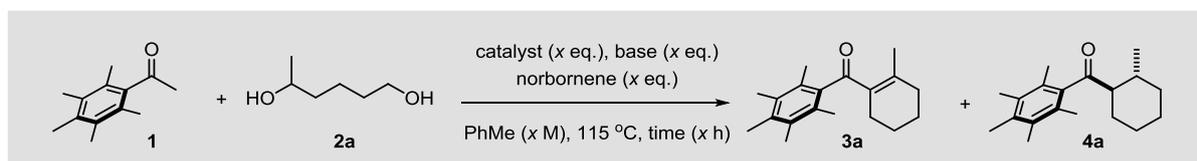


A 2–5 mL Biotage[®] microwave vial was charged with enone (0.1 mmol, 1 eq.), hexafluoroisopropanol (0.88 mL) and 37% aq. HCl (12 M, 0.13 mL). The reaction vessel was sealed with a microwave vial cap (containing a Reseal[™] septum) and heated at 65 °C for 15 h. The reaction was then cooled to RT, diluted with water (5 ml) and extracted with CH₂Cl₂ (3 x 10 mL), dried over MgSO₄, filtered and concentrated *in vacuo*. For details of purification, see experimental procedures.

3. Optimization

3.1. Optimization of Iridium Catalyzed Synthesis of Acyl Cyclohexenes

Under an air atmosphere, a 2–5 mL Biotage[®] microwave vial equipped with a stirrer bar, was sequentially charged with diol **2a**, pentamethylacetophenone **1** (114 mg, 0.60 mmol), ligand, metal precatalyst [N.B. mol% refers to stoichiometry of monomeric metal after dissociation of multimeric precursors], solvent and base. The reaction vessel was sealed with a microwave vial cap (containing a Reseal[™] septum) and the vial was heated to the indicated temperature in a preheated oil bath for 24 h. After cooling to RT, the reaction mixture was diluted with aq. HCl (3M, 5 mL) and extracted with CH₂Cl₂ (4 x 10 mL). The combined organic phases were dried over MgSO₄, filtered and concentrated *in vacuo*. The residue was dissolved in MeCN (100 mL) and durene (80 mg, 0.60 mmol) was added as an internal standard. The yields of **1**, **3a** and **4a** were determined by calibrated reverse phase HPLC analysis (Agilent InfinityLab Poroshell 120 EC-C18 column with guard, 75% MeCN, 25% H₂O, 1.0 mL/min, 25 °C, λ = 254 nm, 5 μL injection). Yields in parentheses refer to isolated material after column chromatography.



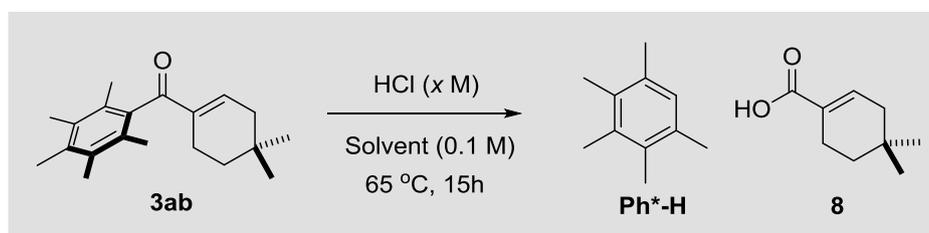
entry	2a /eq.	catalyst (mol%)	base (eq.)	norbornene/ eq.	[1]/M	time/ h	% yield of 1a	% yield of 3a	% yield of 4a
1	2	[Ir(Cp*)Cl] ₂ (4)	KOH (4)	2	4	24	5	51	25
2	1.5	[Ir(Cp*)Cl] ₂ (1)	KOH (4)	0.36	4	18	<1	29	53
3	1.5	[Ir(Cp*)Cl] ₂ (1)	KOH (4)	0.71	4	18	<1	33	39
4	1.5	[Ir(Cp*)Cl] ₂ (1)	KOH (4)	1.11	4	18	<1	(56)	20
5	1.5	[Ir(Cp*)Cl] ₂ (1)	KOH (4)	1.36	4	18	2	65	18
6	1.1	[Ir(Cp*)Cl] ₂ (1)	KOH (4)	0.55	4	18	2	40	44
7	1.1	[Ir(Cp*)Cl] ₂ (1)	KOH (4)	1.11	4	18	25	46	11
8	1.5	[Ir(Cp*)Cl] ₂ (1)	KOH (4)	1.25	4	0.5	74	12	>1

9	1.5	[Ir(Cp*)Cl] ₂ (1)	KOH (4)	1.25	4	1	74	13	>1
10	1.5	[Ir(Cp*)Cl] ₂ (1)	KOH (4)	1.25	4	2	63	23	1
11	1.5	[Ir(Cp*)Cl] ₂ (1)	KOH (4)	1.25	4	4	53	29	2
12	1.5	[Ir(Cp*)Cl] ₂ (1)	KOH (4)	1.25	4	8	44	34	5
13	1.5	[Ir(Cp*)Cl] ₂ (1)	KOH (4)	1.25	2	18	6	73	2
14	1.5	[Ir(Cp*)Cl] ₂ (1)	KOH (4)	1.25	1	18	13	71	7
15	1.5	[Ir(Cp*)Cl] ₂ (1)	KOH (4)	1.25	0.5	18	13	76	4
16	1.5	[Ir(Cp*)Cl] ₂ (1)	KOH (4)	1.25	2	24	<1	72	15
17	1.5	[Ir(Cp*)Cl] ₂ (1)	KOH (4)	1.25	0.5	24	1	(76)	6
18	2	[Ir(Cp*)Cl] ₂ (4)	KOH (4)	0	4	24	6	7	71
19	2	[Ir(Cp*)Cl] ₂ (4)	KOH (4)	0	2	24	7	16	61
20	2	[Ir(Cp*)Cl] ₂ (4)	KOH (4)	0	1	24	9	36	40
21	2	[Ir(Cp*)Cl] ₂ (4)	KOH (4)	0	0.25	24	20	54	7
22	2	[Ir(Cp*)Cl] ₂ (4)	KOH (4)	0	0.1	24	46	35	2
23	2	[Ir(Cp*)Cl] ₂ (1)	KOH (4)	0	0.25	24	21	60	4
24	2	[Ir(Cp*)Cl] ₂ (1.5)	KOH (4)	0	0.25	24	27	70	2
25	2	[Ir(Cp*)Cl] ₂ (1.5)	KOH (4)	0	0.25	24	26	62	3
26	2	[Ir(Cp*)Cl] ₂ (1.5)	KOH (4)	0	0.25	24	37	49	4
27	1.5	[Ir(Cp*)Cl] ₂ (1.5)	KOH (4)	0	0.25	24	27	70	2
28	1.75	[Ir(Cp*)Cl] ₂ (1.5)	KOH (4)	0	0.25	24	20	67	3
39	2.0	[Ir(Cp*)Cl] ₂ (1.5)	KOH (4)	0	0.25	24	16	74	3
30	2.25	[Ir(Cp*)Cl] ₂ (1.5)	KOH (4)	0	0.25	24	16	72	3
31	2	[Ir(Cp*)Cl] ₂ (1.5)	KOH (2)	0	0.25	24	37	51	3
32	4	[Ir(Cp*)Cl] ₂ (1.5)	KOH (4)	0	0.25	24	27	70	2
33	6	[Ir(Cp*)Cl] ₂ (1.5)	KOH (6)	0	0.25	24	19	62	9
34	8	[Ir(Cp*)Cl] ₂ (1.5)	KOH (8)	0	0.25	24	22	37	32
35	10	[Ir(Cp*)Cl] ₂ (1.5)	KOH (10)	0	0.25	24	13	17	62
36	2	[Ir(Cp*)Cl] ₂ (1.5)	NaOH (4)	0	0.25	24	42	46	<1

37	2	[Ir(Cp*)Cl] ₂ (1.5)	CsOH.H ₂ O (4)	0	0.25	24	19	59	8
38	2	[Ir(Cp*)Cl] ₂ (1.5)	KO ^t Bu (4)	0	0.25	24	12	5	79
39	2	[Ir(Cp*)Cl] ₂ (1.5)	NaO ^t Bu(4)	0	0.25	24	69	19	<1
40	2	[Ir(Cp*)Cl] ₂ (1.5)	BEMP (4)	0	0.25	24	98	<1	<1
41	2	[Ir(Cp*)Cl] ₂ (1.5)	Cs ₂ CO ₃ (4)	0	0.25	24	88	2	<1
42	2	[Ir(Cp*)Cl] ₂ (1.5)	K ₂ CO ₃ (4)	0	0.25	24	98	<1	<1
43	2	[Ir(COD)Cl] ₂ (1.5) PPh ₃ (3)	KOH(4)	0	0.25	24	24	(71)	2
44	2	[Ru(<i>p</i> - cymene)Cl ₂] ₂ (1.5)	KOH (4)	0	0.25	24	42	(53)	1
45	2	[Rh(Cp*)Cl ₂] ₂ (1.5)	KOH (4)	0	0.25	24	40	(52)	2
46	2	Knölker Complex (1.5)	KOH (4)	0	0.25	24	90	9	0
47	2	Knölker Complex (4)	KOH (4)	0	0.25	24	72	14	0
48	2	[RhCp*Cl ₂] ₂ (4)	KOH (4)	0	0.25	24	22	(52)	2
49	2	[Ru(Cp*)Cl ₂] _n (4)	KOH (4)	0	0.25	24	75	18	1
50	2	[IrCODCl] ₂ (4) PPh ₃ (8)	KOH (4)	0	0.25	24	16	65	2
51	2	[IrCODCl] ₂ (1) PPh ₃ (2)	KOH (4)	0	0.25	24	(10)	(67)	0
52	2	[IrCODCl] ₂ (1) PAd ₂ ⁿ Bu(2)	KOH (4)	0	0.25	24	(5)	(79)	0
53	2	-	KOH (4)	0	0.25	24	80	<5	<5

3.2. Optimization of Acid Mediated Ph* Cleavage

Under an air atmosphere, a 2–5 mL Biotage[®] microwave vial was charged with enone **3ab** (28.4 mg, 0.1 mmol, 1 eq.), solvent (1 mL) and 37% aq. HCl [N.B. molarity refers to final concentration after addition of the stated solvent]. The reaction vessel was sealed with a microwave vial cap (containing a Reseal[™] septum) and the vial was heated at 65 °C for 15 h. The reaction was then cooled to RT, diluted with water (5 ml) and extracted with CH₂Cl₂ (3 x 10 mL), dried over MgSO₄, filtered and concentrated *in vacuo*. The resulting oil was dissolved in CDCl₃ and 1,1,2,2-tetrachloroethane (10.5 μL, 0.1 mmol) was added. The yield was determined by quantitative ¹H NMR ran on a Bruker AVIIIHD 400. Yields in parentheses refer to isolated material after column chromatography.

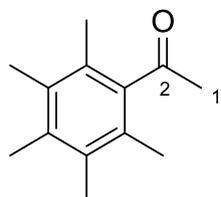


entry	final [HCl] / M	solvent	% yield of Ph*-H	% yield of 8
1	4	MeCN	0	0
2	4	MeOH	0	0
3	4	DMF	0	0
4	4	DMSO	0	0
5	4	acetone	0	0
6	4	EtOH	0	0
7	4	1,4-dioxane	0	0
8	4	H ₂ O	0	0
9	4	hexafluoroisopropanol	(99)	(99)
10	2	hexafluoroisopropanol	(100)	(100)

4. Experimental Procedures

4.1. Synthesis of Starting Materials

1-(2,3,4,5,6-Pentamethylphenyl)ethan-1-one, **1**



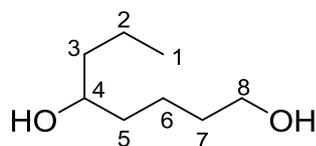
To a solution of pentamethylbenzene (10.0 g, 67.4 mmol, 1.0 eq.) and acetyl chloride (5.30 mL, 74.2 mmol, 1.1 eq) in dry CH_2Cl_2 (300 mL, 0.225 M) at 0 °C was added AlCl_3 (11.2 g, 84.3 mmol, 1.3 eq.) in several portions over 30 minutes. The reaction was warmed to RT and stirred for 2 h and then poured over crushed ice. Once the ice had melted, the layers were separated and the aqueous phase was extracted with CH_2Cl_2 (3 x 200 mL). The combined organic phases were dried over MgSO_4 , filtered and concentrated *in vacuo*. The title compound was afforded after purification by FCC (5% \rightarrow 10% Et_2O :pentane) followed by recrystallization (heptane) as a white solid (11.1 g, 58.2 mmol, 86% yield).

^1H NMR (400 MHz, CDCl_3) δ 2.46 (s, 3H, 3 x H_1), 2.24 (s, 3H, ArCH_3), 2.19 (s, 6H, 2 x ArCH_3), 2.14 (s, 6H, 2 x ArCH_3).

^{13}C NMR (101 MHz, CDCl_3) δ 210.2, 141.1, 135.5, 133.2, 127.1, 33.2, 17.2, 16.8, 16.1.

The spectroscopic data matched that previously reported in the literature.¹

Octane-1,5-diol, **2b**



A stirred solution of delta-octanolactone (1.50 g, 10.5 mmol, 1.00 eq.) in dry THF (150 ml) was cooled to 0 °C and LiAlH_4 (1.20 g, 31.5 mmol, 3 eq.) was added portion-wise. The reaction mixture was allowed to warm to RT and then stirred for 1 hour. The reaction was then cooled to 0 °C, diluted with Et_2O (150 mL) and quenched by sequential addition of water (1.2 mL), aq. NaOH (15% w/v, 1.2 mL), and water (3.6 mL), and stirred vigorously for 15 minutes. MgSO_4 was then added, stirred for 15 minutes, filtered and concentrated *in*

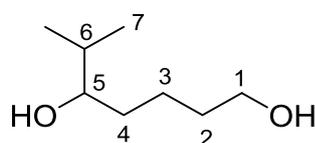
vacuo. The title compound was afforded after purification by FCC (2% MeOH/CH₂Cl₂) as a colourless oil (1.11 g, 72%).

¹H NMR (400 MHz, CDCl₃): δ 3.67 – 3.56 (m, 3H, H₄, 2 x H₈), 2.08 (br s, 1H, OH), 1.90 (br s, 1H, OH), 1.68 – 1.21 (m, 10H, 2 x H₂, 2 x H₃, 2 x H₅, 2 x H₆, 2 x H₇), 0.91 (t, *J* = 7.0 Hz, 3H, 3 x H₁).

¹³C NMR (101 MHz, CDCl₃) δ 71.6, 62.7, 39.8, 37.1, 32.7, 21.9, 19.0, 14.2.

The spectroscopic data matched that previously reported in the literature.²

6-Methylheptane-1,5-diol, 2e



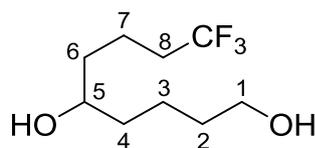
A flame-dried flask under N₂ was charged with isopropylmagnesium chloride solution (2.0 M in THF, 16.5 mL, 32.9 mmol, 3.0 eq.) and cooled to 0 °C and a solution of tetrahydro-2H-pyran-2-ol (1.12 g, 11.0 mmol, 1 eq.) in dry THF (8 mL) was added dropwise. The flask was then warmed to RT and stirred for 2 hours. The reaction was quenched with the addition of sat. aq. NH₄Cl (15 mL). The aqueous phase was extracted with EtOAc (3 x 30 mL). The combined organic phases were dried over MgSO₄, filtered and concentrated *in vacuo*. The title compound was afforded after purification by FCC (3% MeOH/CH₂Cl₂) as a colourless oil (1.12 g, 7.66 mmol, 70% yield).

¹H NMR (400 MHz, CDCl₃) δ 3.62 (t, *J* = 6.0 Hz, 2H, 2 x H₁), 3.34 (br s, 1H, H₅), 2.53 (br s, 1H, OH), 2.15 (br s, 1H, OH), 1.70 – 1.32 (m, 7H, 2 x H₂, 2 x H₃, 2 x H₄, H₆), 0.89 (d, *J* = 7.0 Hz, 3H, 3 x H₇), 0.89 (d, *J* = 7.0 Hz, 3H, 3 x H₇).

¹³C NMR (101 MHz, CDCl₃) δ 76.7, 62.6, 33.7, 33.6, 32.6, 22.3, 18.9, 17.4.

The spectroscopic data matched that previously reported in the literature.³

9,9,9-Trifluorononane-1,5-diol, 2j



A suspension of magnesium turnings (1.06 g, 43.6 mmol, 5 eq.) in THF (30 mL) was stirred at RT and a single crystal of iodine was added followed by addition of commercially available

4-bromo-1,1,1-trifluorobutane (5.00 g, 26.2 mmol, 3 eq.) at such a rate as to maintain gentle reflux. After the addition was complete the resulting suspension was heated to reflux for a further 10 min and then cooled to RT and decanted away from the excess magnesium turnings by cannulation washing with THF (2 x 2 mL). The resulting Grignard solution was cooled to 0 °C and tetrahydro-2H-pyran-2-ol (890 mg, 8.72 mmol) was added dropwise. The reaction mixture was then warmed to RT and stirred for 16 hours and then quenched with the addition of sat. aq. NH₄Cl (15 mL). The aqueous phase was extracted with Et₂O (3 x 30 mL). The combined organic phases were dried over MgSO₄, filtered and concentrated *in vacuo*. The title compound was afforded after purification by FCC (5% MeOH/CH₂Cl₂) as a white solid (1.36 g, 6.34 mmol, 73% yield).

¹H NMR (400 MHz, CDCl₃) δ = 3.73 – 3.54 (m, 3H, 2 x H₁ and H₅), 2.17 – 2.03 (m, 2H, 2 x H₈), 2.00 (s, 1H, OH), 1.92 (s, 1H, OH), 1.80 – 1.37 (m, 10H, 2 x H₂, 2 x H₃, 2 x H₄, 2 x H₆, 2 x H₇).

¹³C NMR (101 MHz, CDCl₃) δ = 127.3 (q, J = 276.5 Hz), 71.3, 62.7, 37.2, 36.4, 33.8 (q, J = 28.5 Hz), 32.5, 21.9, 18.5 (q, J = 3.0 Hz).

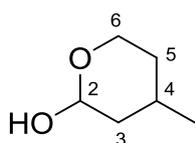
¹⁹F NMR (377 MHz, CDCl₃) δ –66.4.

HRMS (ESI+): Found [M+Na]⁺ = 237.1075; C₉H₁₇O₂F₃Na requires 237.1073, Δ 0.76 ppm.

IR (film) ν_{max}/cm⁻¹ 3327, 2939, 1391, 1255, 1211, 1138, 1054.

m.p.: 34-35 °C.

4-Methyltetrahydro-2H-pyran-2-ol, 19



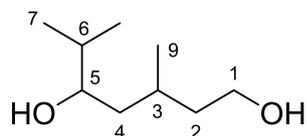
A flame dried 3-neck flask under N₂ was charged with 4-methyltetrahydro-2H-pyran-2-one⁴ (1.40 g, 13.1 mmol, 1 eq.), dry CH₂Cl₂ (25 mL), and cooled to -78 °C. DIBAL-H in hexanes (1M, 17.2 mL, 17.2 mmol, 1.37 eq.) was added dropwise and stirred at -78 °C for 2 hours. Sat. aq. Rochelle salt (20 mL) was added, warmed to RT and stirred vigorously. The aqueous phase was then extracted with CH₂Cl₂ (3 x 20 mL). The combined organic phases were then dried over MgSO₄, filtered and concentrated *in vacuo*. The title compound was afforded after purification by FCC (Et₂O) as a colourless oil (1.46 g, 12.8 mmol, 97% yield, 55:45 mixture of anomers).

^1H NMR (400 MHz, CDCl_3) δ 5.29-5.25 (m, 1H, minor H_2), 4.65 (ddd, $J = 9.5, 6.0, 2.0$ Hz, 1H, major H_2), 4.08 – 3.91 (m, 2H, major H_{6a} and minor H_{6a}), 3.62 (ddd, $J = 11.0, 5.0, 2.0$ Hz, 1H, minor H_{6b}), 3.55 – 3.29 (m, 2H, major H_{6b} and OH), 2.96 – 2.72 (m, 1H, OH), 2.07-1.93 m (m, 1H, minor H_4), 1.89 (ddt, $J = 13.0, 4.0, 2.0$ Hz, 1H, major H_{3a}), 1.84 – 1.61 (m, 2H, major H_4 and minor H_{3a}), 1.61 – 1.53 (m, 1H, minor H_{5a}), 1.52 – 1.44 (m, 1H, major H_{5a}), 1.37 – 1.10 (m, 3H, minor H_{3b} , major H_{5b} and minor H_{5b}), 1.07 – 0.99 (m, 1H, major H_{3b}), 0.97 (d, $J = 6.5$ Hz, 3H major CH_3), 0.91 (d, $J = 6.5$ Hz, 3H, minor CH_3).

^{13}C NMR (101 MHz, CDCl_3) δ 96.3, 91.9, 65.8, 59.9, 41.8, 38.8, 34.2, 33.7, 29.5, 23.7, 22.2, 21.9.

The spectroscopic data matched that previously reported in the literature.⁵

3,6-Dimethylheptane-1,5-diol, **2o**



A flame-dried flask under N_2 was charged with 4-methyltetrahydro-2H-pyran-2-ol **19** (1.0 g, 8.6 mmol, 1 eq.) and dry THF (17 mL) and cooled to 0°C and a solution of isopropyl magnesium bromide in THF (2 M, 13.0 mL, 25.8 mmol, 3 eq.) was added dropwise. The flask was then warmed to RT and stirred for 15 hours. The reaction was quenched with the addition of sat. aq. NH_4Cl (15 mL). The aqueous phase was extracted with CH_2Cl_2 (3 x 30 mL). The combined organic phases were dried over MgSO_4 , filtered and concentrated *in vacuo*. The title compound was afforded after purification by FCC (6% $\text{MeOH}/\text{CH}_2\text{Cl}_2$) as an inseparable mixture of diastereomers as a colourless oil (1.36 g, 8.49 mmol, 99% yield, 60:40 d.r. by ^1H NMR).

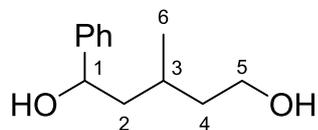
^1H NMR (400 MHz, CDCl_3) δ 3.88 – 3.57 (m, 4H, major $\text{H}_1 \times 2$ and minor $\text{H}_1 \times 2$), 3.57 – 3.39 (m, 2H, major H_5 and minor H_5), 2.28 – 1.67 (m, 7H, major H_3 and minor H_3 , minor H_{2a} , minor OH $\times 2$ and major OH $\times 2$), 1.68 – 1.58 (m, 2H, major H_6 and minor H_6), 1.59 – 1.25 (m, 6H, major H_{2a} , minor H_{2b} , major $\text{H}_4 \times 2$, minor $\text{H}_4 \times 2$), 1.25 – 1.13 (m, 1H major H_{2b}), 1.00 – 0.89 (m, 18H, major $\text{CH}_3 \times 3$ and minor $\text{CH}_3 \times 3$).

^{13}C NMR (101 MHz, CDCl_3) δ 74.7, 74.2, 61.2, 60.7, 41.7, 40.8, 40.7, 38.7, 34.4, 33.9, 26.5, 26.3, 21.2, 20.0, 19.0, 18.8, 17.5, 17.2.

HRMS (ESI⁺): Found $[\text{M}+\text{Na}]^+ = 183.1358$; $\text{C}_9\text{H}_{20}\text{O}_2\text{Na}$ requires 183.1356, Δ 1.54 ppm.

IR (film) $\nu_{\max}/\text{cm}^{-1}$ 3332, 2957, 2931, 1465, 1382, 1056, 991.

3-Methyl-1-phenylpentane-1,5-diol, 2p



A flame-dried flask under N_2 was charged with 4-methyltetrahydro-2H-pyran-2-ol **19** (1.0 g, 8.6 mmol, 1 eq.) and dry THF (17 mL) and cooled to 0°C and a solution of phenyl magnesium bromide in THF (1 M, 26.0 mL, 25.8 mmol, 3 eq.) was added dropwise. The flask was then warmed to RT and stirred for 15 hours. The reaction was quenched with the addition of sat. aq. NH_4Cl (15 mL). The aqueous phase was extracted with CH_2Cl_2 (3 x 30 mL). The combined organic phases were dried over MgSO_4 , filtered and concentrated *in vacuo*. The title compound was afforded after purification by FCC (2 \rightarrow 5% MeOH/ CH_2Cl_2) as an inseparable mixture of diastereomers as a colourless oil (1.63 g, 8.39 mmol, 98% yield, 78:22 d.r. by ^1H NMR).

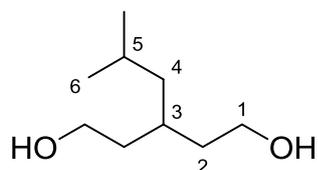
^1H NMR (400 MHz, CDCl_3) δ 7.33 – 7.11 (m, 10H, major ArCH x 5, minor ArCH x 5), 4.85 – 4.52 (m, 2H, major H_1 , minor H_1), 3.76 – 3.42 (m, 4H, major H_5 x 2, minor H_5 x 2), 2.77 (s, 1H major OH), 2.44 (s, 1H minor OH), 2.12 (s, 1H major OH), 1.97 (s, 1H minor OH), 1.89 – 1.71 (m, 2H, minor H_3 and minor H_{2a}), 1.71 – 1.50 (m, 4H, major H_2 x 2, major H_3 , major H_{4a}), 1.45 (q, $J = 6.5$ Hz, 2H, minor H_4 x 2), 1.38 – 1.23 (m, 2H, major H_{4b} and minor H_{2b}), 0.93 (d, $J = 6.5$ Hz, 3H, minor H_6 x 3), 0.88 (d, $J = 6.0$ Hz, 3H, major H_6 x 3).

^{13}C NMR (101 MHz, CDCl_3) δ 145.6, 145.1, 128.6, 128.6, 127.6, 127.5, 126.0, 125.8, 72.6, 72.3, 60.9, 60.5, 46.6, 46.4, 40.3, 39.0, 26.4, 26.4, 20.7, 20.0.

HRMS (ESI+): Found $[\text{M}+\text{Na}]^+ = 217.1200$; $\text{C}_{12}\text{H}_{18}\text{O}_2\text{Na}$ requires 217.1199, Δ 0.64 ppm.

IR (film) $\nu_{\max}/\text{cm}^{-1}$ 3330, 2980, 2929, 1494, 1380, 1056, 700.

3-Isobutylpentane-1,5-diol, 2v



A suspension of LiAlH_4 (6.00 g, 159 mmol, 3 eq.) in dry THF (130 mL) was cooled to 0 °C, followed by the dropwise addition of a solution of 3-isobutylglutaric acid (10.0 g, 53.1 mmol, 1 eq.) in THF (20 mL). The reaction was then fitted with an air condenser and heated at reflux for 15 hours. The reaction was then cooled to 0 °C, diluted with Et_2O (150 mL) and quenched by sequential addition of water (6.0 mL), aq. NaOH (15% w/v, 6.0 mL), and water (18.0 mL), and stirred vigorously for 15 minutes. MgSO_4 was then added, stirred for 15 minutes, filtered and concentrated *in vacuo*. The title compound was afforded after purification by FCC (5% MeOH/ CH_2Cl_2) as a colourless oil (7.00 g, 43.5 mmol, 82% yield).

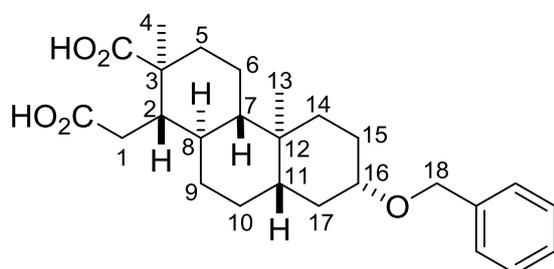
^1H NMR (400 MHz, CDCl_3) δ 3.72 (dt, $J = 10.5, 6.5$ Hz, 2H, $\text{H}_{1a} \times 2$), 3.67 (dt, $J = 10.5, 6.5$ Hz, 2H, $\text{H}_{1b} \times 2$), 2.02 (s, 2H, OH $\times 2$), 1.74 – 1.44 (m, 6H, $\text{H}_2 \times 4$, H_3 and H_5), 1.13 (t, $J = 7.0$ Hz, 2H, $\text{H}_4 \times 2$), 0.87 (d, $J = 6.5$ Hz, 6H, $\text{H}_6 \times 6$).

^{13}C NMR (101 MHz, CDCl_3) δ 61.0, 44.8, 37.1, 29.2, 25.4, 23.0.

HRMS (ESI⁺): Found $[\text{M}+\text{H}]^+ = 161.1537$; $\text{C}_9\text{H}_{21}\text{O}_2$ requires 161.1536, Δ 0.40 ppm.

IR (film) $\nu_{\text{max}}/\text{cm}^{-1}$ 3313, 2953, 2926, 2869, 2467, 1367, 1055, 1009.

(1S,2S,4aS,4bS,7S,8aS,10aR)-7-(Benzyloxy)-1-(carboxymethyl)-2,4b-dimethyltetradecahydrophenanthrene-2-carboxylic acid, S1



According to a modified literature procedure,⁶ a solution of *O*-benzyl-epiandrosterone⁷ (500 mg, 1.31 mmol, 1 eq.) in MeOH (37 mL) was stirred at room temperature. A solution of I_2 (864 mg, 3.40 mmol, 2.6 eq.) in MeOH (12 mL) and a solution of KOH (1.62 g, 28.8 mmol, 22 eq.) in 3:1 MeOH/ H_2O (12 mL) were added simultaneously over 1.5 h by syringe pump.

After addition was complete, the reaction mixture was partially evaporated to remove most of the methanol and then a solution of KOH (588 mg, 10.5 mmol, 8 eq.) was added and the resulting mixture was heated to reflux for 1 hour. The resulting mixture was then cooled to RT and carefully acidified by dropwise addition of 37% aq. HCl (until c.a. pH 1) and then extracted with Et₂O (3 x 100 mL). The combined organic phases were dried over MgSO₄, filtered and concentrated *in vacuo*. The title compound was afforded after purification by FCC (10% MeOH/CH₂Cl₂) as a white solid (263 mg, 0.61 mmol, 47% yield).

¹H NMR (400 MHz, CDCl₃) δ 13.09 – 10.02 (br s, 2H, CO₂H), 7.41 – 7.25 (m, 5H, ArCH x 5), 4.62 – 4.55 (m, 2H, H_{18a} and H_{18b}), 3.38 (tt, *J* = 10.5, 4.5 Hz, 1H, H₁₆), 2.45 – 2.36 (m, 1H, H_{1a}), 2.28 (dt, *J* = 11.0, 6.0 Hz, 1H, H₂), 2.16 (dd, *J* = 16.0, 6.0 Hz, 1H, H_{1b}), 2.01 – 1.61 (m, 7H, 7 x H_{aliph}), 1.55 – 0.76 (m, 16H, 10 x H_{aliph} and 2 x Me).

¹³C NMR (101 MHz, CDCl₃) δ 185.3, 180.6, 139.1, 128.5, 127.7, 127.5, 77.9, 70.0, 53.1, 46.5, 44.1, 43.8, 36.9, 36.8, 36.4, 36.0, 35.6, 34.7, 31.2, 28.7, 28.2, 20.0, 15.0, 12.3.

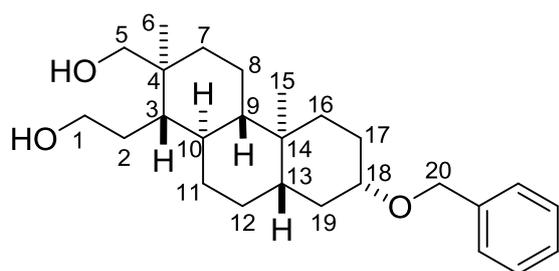
HRMS (ESI⁺): Found [M+Na]⁺ = 451.2446; C₂₆H₃₆O₅Na requires 451.2455, Δ –2.06 ppm.

IR (film) ν_{max}/cm⁻¹ 2930, 1703, 1496, 1453, 1414, 1387, 1281, 1153, 1095, 1071, 908.

m.p.: 180-184 °C.

[α]_D²⁵ = –8.8 (c=1.0, CHCl₃).

2-((1S,2S,4aS,4bS,7S,8aS,10aR)-7-(Benzyloxy)-2-(hydroxymethyl)-2,4b-dimethyltetradecahydrophenanthren-1-yl)ethan-1-ol, 2ah



A stirred solution of diacid **S1** (263 mg, 0.61 mmol, 1.00 eq.) in dry THF (4 ml) was cooled to 0 °C and LiAlH₄ (70 mg, 1.84 mmol, 3 eq.) was added. The reaction was then fitted with an air condenser and heated at reflux for 15 hours. The reaction was then cooled to 0 °C, diluted with Et₂O (5 mL) and quenched by sequential addition of water (0.07 mL), aq. NaOH (15% w/v, 0.07 mL), and water (0.21 mL), and stirred vigorously for 15 minutes. MgSO₄ was then added, stirred for 15 minutes, filtered and concentrated *in vacuo*. The title compound

was afforded after purification by FCC (5% MeOH/CH₂Cl₂) as a white solid (158 mg, 0.39 mmol, 64% yield).

¹H NMR (400 MHz, CDCl₃) δ 7.33 – 7.16 (m, 5H, ArCH x 5), 4.52 – 4.44 (m, 2H, H_{20a} and H_{20b}), 3.85 (br s, 1H, OH), 3.71 (d, *J* = 9.5 Hz, 1H, H_{1a}), 3.51 (d, *J* = 11.5 Hz, 1H, H_{5a}), 3.40 (t, *J* = 10.5 Hz, 1H, H_{1b}), 3.28 (tt, *J* = 11.0, 4.5 Hz, 1H, H₁₈), 3.09 (br s, 1H, OH), 2.91 (d, *J* = 11.5 Hz, 1H, H_{5b}), 1.91 – 1.46 (m, 7H, 7 x H_{aliph}), 1.43 – 1.10 (m, 9H, 9 x H_{aliph}), 1.04 – 0.80 (m, 3H, 3 x H_{aliph}), 0.72 (s, 3H, Me), 0.68 – 0.53 (m, 4H, Me and H_{aliph}).

¹³C NMR (101 MHz, CDCl₃) δ 139.2, 128.4, 127.7, 127.5, 78.1, 70.3, 69.9, 64.1, 53.7, 44.7, 41.8, 38.6, 38.4, 36.9, 36.1, 35.4, 34.8, 32.3, 30.5, 29.2, 28.3, 20.6, 16.1, 12.4.

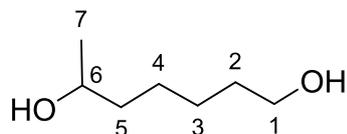
HRMS (ESI+): Found [M+Na]⁺ = 423.2870; C₂₆H₄₀O₃Na requires 423.2870, Δ 0.05 ppm.

IR (film) ν_{max}/cm⁻¹ 3326, 2930, 2855, 1453, 1361, 1327, 1097, 1076, 1038, 852, 732.

m.p.: 137-139 °C.

[α]_D²⁵ = -1.3 (c=1.0, CHCl₃).

Heptane-1,6-diol, 2aj



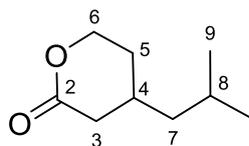
A suspension of LiAlH₄ (3.90 g, 105 mmol, 3 eq.) in dry THF (90 mL) was cooled to 0 °C, followed by the dropwise addition of a solution of 6-oxoheptanoic acid (5.0 g, 35 mmol, 1 eq.) in THF (25 mL) and the resulting suspension was stirred at RT for 24 h. The reaction was then cooled to 0 °C, diluted with Et₂O (115 mL) and quenched by sequential addition of water (3.9 mL), aq. NaOH (15% w/v, 3.9 mL), and water (11.7 mL), and stirred vigorously for 15 minutes. MgSO₄ was then added, stirred for 15 minutes, filtered and concentrated *in vacuo*. The title compound was afforded after purification by FCC (4% MeOH/CH₂Cl₂) as a colourless oil (1.60 g, 12.1 mmol, 35% yield).

¹H NMR (400 MHz, CDCl₃) δ 3.85 – 3.73 (m, 1H, H₆), 3.64 (t, *J* = 6.5 Hz, 2H, H₁ x 2), 3.47 (s, 1H, OH), 1.73 (s, 1H, OH), 1.64 – 1.27 (m, 8H, H₂ x 2, H₃ x 2, H₄ x 2, H₅ x 2), 1.18 (d, *J* = 6.0 Hz, 3H, H₇ x 3).

¹³C NMR (101 MHz, CDCl₃) δ 68.0, 62.8, 39.3, 32.7, 25.8, 25.6, 23.6.

The spectroscopic data matched that previously reported in the literature.⁸

4-Isobutyltetrahydro-2H-pyran-2-one, **S2**



A flame dried 3-neck flask fitted with a reflux condenser was charged with 3-isobutylpentane-1,5-diol **2v** (3.00 g, 18.7 mmol, 1 eq.) and copper chromite (117 mg, 0.374 mmol, 0.02 eq.). The reaction was heated to 200 °C for 41 hours and then cooled to RT. The title compound was afforded after purification by FCC (20% EtOAc/pentane) as a colourless oil (2.70 g, 17.3 mmol, 92% yield).

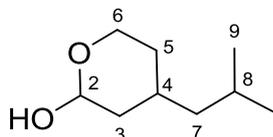
^1H NMR (400 MHz, CDCl_3) δ 4.40 (ddd, $J = 11.5, 5.0, 4.0$ Hz, 1H, H_{6a}), 4.25 (ddd, $J = 11.5, 10.5, 4.0$ Hz, 1H, H_{6b}), 2.72 – 2.62 (m, 1H, H_{3a}), 2.15 – 1.97 (m, 2H, H_4 and H_{3b}), 1.97 – 1.87 (m, 1H, H_{5a}), 1.72 – 1.58 (m, 1H, H_8), 1.56 – 1.43 (m, 1H, H_{5b}), 1.29 – 1.14 (m, 2H, $\text{H}_7 \times 2$), 0.89 (d, $J = 6.5$ Hz, 3H, $\text{H}_{9a} \times 3$), 0.89 (d, $J = 6.5$, 3H, $\text{H}_{9b} \times 3$).

^{13}C NMR (101 MHz, CDCl_3) δ 171.6, 68.7, 45.7, 36.9, 29.3, 29.3, 24.8, 22.7, 22.7.

HRMS (ESI+): Found $[\text{M}+\text{H}]^+ = 157.1223$; $\text{C}_9\text{H}_{17}\text{O}_2$ requires 157.1223, $\Delta -0.24$ ppm.

IR (film) $\nu_{\text{max}}/\text{cm}^{-1}$ 2967, 2911, 1732, 1386, 1254, 1167, 1070, 972.

4-Isobutyltetrahydro-2H-pyran-2-ol, **23**



A flame dried 3-neck flask under N_2 was charged with 4-Isobutyltetrahydro-2H-pyran-2-one **S2** (1.0 g, 6.4 mmol, 1 eq.), dry CH_2Cl_2 (13 mL), and cooled to -78 °C. DIBAL-H in hexanes (9 mL, 1M, 1.4 eq.) was added dropwise and stirred at -78 °C for 2 hours. Sat. aq. Rochelle salt (20 mL) was added, warmed to RT and stirred vigorously. The aqueous phase was then extracted with CH_2Cl_2 (3 x 20 mL). The combined organic phases were then dried over MgSO_4 , filtered and concentrated *in vacuo*. The title compound was afforded after purification by FCC (Et_2O) as a colourless oil (1.01 g, 16.4 mmol, 100% yield, 52:48 anomeric mixture by ^1H NMR).

^1H NMR (400 MHz, CDCl_3) δ 5.34 – 5.20 (m, 1H, major H_2), 4.66 (ddd, $J = 9.5, 6.5, 2.0$ Hz, 1H, minor H_2), 4.06 – 3.92 (m, 2H, major H_{6a} and minor H_{6a}), 3.68 – 3.57 (m, 2H, major H_{6b} , and minor OH), 3.48 (td, $J = 12.0, 2.5$ Hz, 1H minor H_{6b}), 3.04 (dd, $J = 3.0, 2.0$ Hz, 1H, major OH),

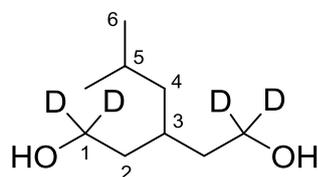
2.04 – 1.93 (m, 1H, major H₄), 1.90 (ddt, *J* = 12.5, 4.0, 2.0 Hz, 1H, minor H_{3a}), 1.79 – 1.55 (m, 5H, major H_{3a}, major H_{5a} and major H₈, minor H₄ and, minor H₈), 1.50 (ddq, *J* = 13.5, 4.0, 2.0 Hz, 1H, minor H_{5a}), 1.31 – 0.93 (m, 8H, major H_{3b}, major H_{5b} and major H₇ x 2, minor H_{3b}, minor H_{5b} and minor H₇ x 2), 0.90 – 0.83 (m, 12H major H₉ x 6 and minor H₉ x 6).

¹³C NMR (101 MHz, CDCl₃) δ 96.4, 91.9, 65.8, 59.9, 46.4, 46.1, 40.2, 37.3, 32.5, 32.1, 32.1, 26.1, 24.5, 24.4, 23.1, 22.9, 22.8, 22.8.

HRMS (ESI+): Found [M+Na]⁺ = 181.1201 ; C₉H₁₈O₂Na requires 181.1199, Δ 1.10 ppm.

IR (film) ν_{max}/cm⁻¹ 3380, 2953, 2870, 1467, 1370, 1070, 898.

3-Isobutylpentane-1,1,5,5-*d*₄-1,5-diol, *d*₄-2v



Iodine (12.1 g, 47.8 mmol 1.2 eq) in dry THF (200 mL) was added dropwise *via* dropping funnel to a 1 litre three necked flask at 0 °C under argon atmosphere charged with 3-isobutylglutaric acid (7.49 g, 39.8 mmol, 1 eq.), NaBD₄ (5.00 g, 120 mmol, 3 eq.) and dry THF (200 mL). The reaction mixture was then warmed to RT and stirred for 48 hours. The reaction was quenched with MeOH (30 mL) at 0 °C, and then concentrated *in vacuo*. The resulting residue was diluted with water (100 mL), extracted with EtOAc (3x 200 mL), dried over MgSO₄, filtered and concentrated *in vacuo*. The title compound was afforded after three purifications by FCC (5% MeOH/CH₂Cl₂, then 3% MeOH/CH₂Cl₂, and 3% MeOH/CH₂Cl₂) as a colourless oil (3.9 g, 23.9 mmol, 60% yield, >95% D incorporation by quantitative ¹H NMR and ¹³C NMR).

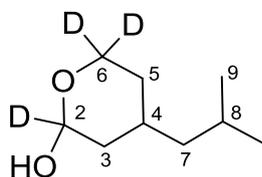
¹H NMR (400 MHz, CDCl₃) δ 2.24 (s, 2H, OH x 2), 1.77 – 1.61 (m, 2H, H₃, H₅), 1.60 – 1.47 (m, 4H, H₂ x 4), 1.15 (t, *J* = 7.0 Hz, 2H, H₄ x 2), 0.90 (d, *J* = 6.5 Hz, 6H, H₆ x 6). [N.B. in the absence of any deuteration, the peak for H₁ (δ = 3.74-3.64 ppm) would be 4.00, the measured integral by quantitative ¹H NMR was 0.14 thus indicating that overall 3.86 D was incorporated across the four symmetrical positions, i.e. >95% D at each position].

¹³C NMR (101 MHz, CDCl₃) δ 60.2 (1:2:3:2:1 quintet, *J* = 21.5 Hz), 44.8, 36.8, 29.1, 25.4, 23.0.

²H NMR (77 MHz, CHCl₃) δ 3.7 (s, ²H₁ x 4).

Apart from deuterium incorporation at C₁, the spectral data of **d₄-2v** was consistent with that of **2v** (see data above for **2v** and also spectra).

4-Isobutyltetrahydro-2H-pyran-2,6,6-d₃-2-ol, **d₃-23**



A 25 mL RBF under argon atmosphere was charged with IBX (30% wt. with stabilizer, 2.68 g, 2.88 mmol, 1.2 eq.), dry DMSO (2.8 mL) and acetone (10 mL), and stirred for 40 min at RT. 3-isobutylpentane-1,1,5,5-d₄-1,5-diol **d₄-2v** (400 mg, 2.40 mmol, 1 eq.) was added, stirring for 5 hours at RT. The reaction was then diluted with water (10 mL) and filtered. The resulting aqueous solution was extracted with Et₂O (4 x 20 mL). The organic phase was then washed with sat. aq. Na₂CO₃ (20 mL), brine (20 mL), dried over MgSO₄ and concentrated *in vacuo*. The title compound was afforded after purification by FCC (20 → 30% Et₂O/pentane) as a colourless oil (232 mg, 1.44 mmol, 60% yield, 51:49 mixture of anomers ¹H NMR, >95% D incorporation by quantitative ¹H NMR and ¹³C NMR).

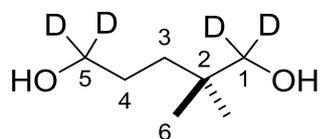
¹H NMR (400 MHz, CDCl₃) δ 3.50 (s, 1H, minor OH), 2.91 (d, *J* = 2.0 Hz, 1H, major OH), 2.04 – 1.93 (m, 1H, major H₄) 1.90 (ddd, *J* = 12.5, 4.0, 2.0 Hz, 1H, minor H_{3a}), 1.78 – 1.54 (m, 5H, major H_{3a}, major H_{5a} and major H₈, minor H₄ and minor H₈), 1.49 (ddd, *J* = 13.5, 4.0, 2.0 Hz, 1H, minor H_{5a}), 1.31 – 0.93 (m, 8H, major H_{3b}, major H_{5b} and major H₇ x 2, minor H_{3b}, minor H_{5b} and minor H₇ x 2), 0.91 – 0.83 (m, 12H, major H₉ x 6 and minor anomer H₉ x 6). [N.B. in the absence of any deuteration, the peaks for H₂, H_{6a} and H_{6b} (see spectra) should each integrate to 1.00. Integration of the quantitative ¹H NMR spectrum showed an integral for each of these peaks of 0.02 thus indicating 0.98 D incorporation at each position, i.e. >95% D at each position].

¹³C NMR (101 MHz, CDCl₃) δ 95.9 (1:1:1 t, *J* = 32 Hz), 91.5 (1:1:1 t *J* = 33 Hz), 46.5, 46.1, 40.1, 37.2, 32.3, 32.1, 31.8, 26.1, 24.5, 24.4, 23.1, 22.9, 22.8, 22.8. n.b C₆ for major and minor anomer not observed.

²H NMR (77 MHz, CHCl₃) δ 5.3 (major anomer ²H₂), 4.7 (minor anomer ²H₂), 4.0 (major anomer ²H_{6a} and minor anomer ²H_{6a}), 3.6 (major anomer ²H_{6b}), 3.5 (minor anomer ²H_{6b}).

The spectral data of **d₃-23** was consistent with that of **23** (see above) with >95% incorporation of deuterium at C2 and C6 (see spectra).

2,2-Dimethylpentane-1,1,5,5-d₄-1,5-diol, **d₄-2af**



Iodine (12.1 g, 47.8 mmol 1.2 eq) in dry THF (200 mL) was added dropwise *via* dropping funnel to a 1 litre three necked flask at 0 °C under argon atmosphere charged with 2,2-dimethylglutaric acid (6.37 g, 39.8 mmol, 1 eq.), NaBD₄ (5.00 g, 120 mmol, 3 eq.) and dry THF (200 mL). The reaction mixture was then warmed to RT and stirred for 24 hours. The reaction was quenched with MeOH (30 mL) at 0 °C, and then concentrated *in vacuo*. The resulting residue was diluted with water (100 mL), extracted with EtOAc (3 x 200 mL), dried over MgSO₄, filtered and concentrated *in vacuo*. The title compound was afforded after two purifications by FCC (3→5% MeOH/CH₂Cl₂, then 100% EtOAc) as a colourless oil (1.04 g, 7.63 mmol, 19% yield, >95% D incorporation by quantitative ¹H NMR and ¹³C NMR).

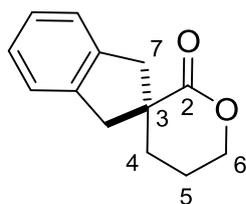
¹H NMR (400 MHz, CDCl₃) δ 2.23 (s, 2H, OH x 2), 1.62 – 1.40 (m, 2H, H₄ x 2), 1.37 – 1.22 (m, 2H, H₃ x 2), 0.86 (s, 6H, H₆ x 6). [N.B. in the absence of any deuteration, the peak for H₅ (δ = 3.63 ppm) would be 2.00, and the peak for H₁ (δ = 3.32 ppm) would be 2.00. The measured integral by quantitative ¹H NMR was for H₅ was 0.07 and for H₁ was 0.09, thus indicating 1.93 D at H₅ and 1.91 D at H₁, i.e. >95% D at each position].

¹³C NMR (101 MHz, CDCl₃) δ 70.5 (1:2:3:2:1 quintet, J = 21.5 Hz), 62.9 (1:2:3:2:1 quintet, J = 21.5 Hz), 34.8, 34.3, 26.9, 24.2.

²H NMR (92 MHz, CHCl₃) δ 3.60 (s, ²H₁ x 2), 3.29 (s, ²H₅ x 2).

Apart from deuterium incorporation at C₁ and C₅, the spectral data of **d₄-2af** was consistent with that of **2af**.⁴

1,3,5,6'-Tetrahydro-2'H,4'H-spiro[indene-2,3'-pyran]-2'-one, S3



A flame-dried 100 mL three-necked flask was charged with hexamethyldisilazane (4.33 mL, 22 mmol, 2.2 eq.), dry THF (40 mL) and cooled to $-78\text{ }^{\circ}\text{C}$ under Argon. *n*-BuLi in hexanes (8.8 mL, 2.5 M, 22 mmol, 2.2 eq.) was added dropwise, and the resulting solution was stirred for 10 minutes at $-78\text{ }^{\circ}\text{C}$. A solution of δ -valerolactone (1.00 g, 9.98 mmol, 1 eq.) in dry THF (5 mL) was added dropwise, and stirred for 30 minutes at $-78\text{ }^{\circ}\text{C}$. A solution of α,α' -dibromo-*o*-xylene (2.90 g, 11.0 mmol, 1.1 eq.) in dry THF (5 mL) was added dropwise, and the resulting solution was stirred for 10 minutes at $-78\text{ }^{\circ}\text{C}$. The reaction mixture was then warmed to $0\text{ }^{\circ}\text{C}$ and stirred for 3 hours. The reaction was quenched by the dropwise addition of sat. aq. NH_4Cl (10 mL) and extracted with CH_2Cl_2 (3 x 30 mL). The combined organic extracts were dried over MgSO_4 and concentrated *in vacuo*. The title compound was afforded after purification by FCC (20-40% Et_2O /pentane) as a white solid (820 mg, 4.06 mmol, 41% yield).

^1H NMR (400 MHz, CDCl_3) δ 7.21 – 7.14 (m, 4H, ArCH x 4), 4.44 (t, $J = 6.0$ Hz, 2H, H_6 x 2), 3.64 (d, $J = 15.5$ Hz, 2H, H_7 x 2), 2.97 (d, $J = 15.5$ Hz, 2H, H_7' x 2), 2.04 – 1.87 (m, 4H, H_4 x 2 and H_5 x 2).

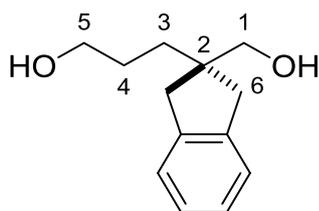
^{13}C NMR (101 MHz, CDCl_3) δ 176.5, 140.5, 127.0, 124.7, 70.2, 49.7, 45.8, 33.1, 21.1.

HRMS (ESI⁺): Found $[\text{M}+\text{H}]^+ = 203.1069$; $\text{C}_{13}\text{H}_{15}\text{O}_2$ requires 203.1067, Δ 0.99 ppm.

IR (film) $\nu_{\text{max}}/\text{cm}^{-1}$ 2932, 2854, 1717, 1441, 1411, 1292, 1170, 975, 727.

m.p.: 99-100 $^{\circ}\text{C}$.

3-(2-(Hydroxymethyl)-2,3-dihydro-1H-inden-2-yl)propan-1-ol, 2as



A suspension of LiAlH_4 (580 mg, 12 mmol, 3 eq.) in dry THF (20 mL) was cooled to $0\text{ }^{\circ}\text{C}$, followed by the portionwise addition of 1,3,5,6'-tetrahydro-2'H,4'H-spiro[indene-2,3'-

pyran]-2'-one **S3** (800 mg, 4 mmol, 1 eq.). The reaction was then heated at reflux for 15 hours and then cooled to 0 °C, diluted with Et₂O (20 mL) and quenched by sequential dropwise addition of water (0.4 mL), aq. NaOH (15% w/v, 0.4 mL), and water (1.2 mL), and stirred vigorously for 15 minutes. MgSO₄ was then added, stirred for 15 minutes, filtered and concentrated *in vacuo*. The title compound was afforded after purification by FCC (5% MeOH/CH₂Cl₂) as a colourless solid (633 mg, 3.07 mmol, 77% yield).

¹H NMR (400 MHz, CDCl₃) δ 7.20 – 7.08 (m, 4H, ArCH x 4), 3.66 (t, J = 6.0 Hz, 2H, H₅ x 2), 3.60 – 3.46 (m, 2H, H₁ x 2), 2.86 (d, J = 16.0 Hz, 2H, H₆ x 2), 2.75 (d, J = 16.0 Hz, 2H, H_{6'} x 2), 2.05 (s, 1H, OH), 1.72 (s, 1H, OH), 1.69 – 1.54 (m, 4H, H₃ x 2, H₄ x 2).

¹³C NMR (101 MHz, CDCl₃) δ 142.5, 126.4, 124.9, 67.9, 63.6, 47.8, 41.5, 32.8, 27.8.

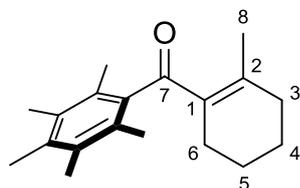
HRMS (ESI⁺): Found [M+Na]⁺ = 229.1200; C₁₃H₁₉O₂Na requires 229.1199, Δ 0.61 ppm.

IR (film) ν_{max}/cm⁻¹ 3334, 2940, 2845, 1485, 1051, 740.

m.p.: 96-97 °C.

4.2 Synthesis of Acyl Cyclohexenes

(2-Methylcyclohex-1-en-1-yl)(2,3,4,5,6-pentamethylphenyl)methanone, 3a



Commercially available 1,5-hexanediol (142 mg, 1.20 mmol, 2 eq.) was subjected to **General Procedure 1**. The title compound was afforded after purification by FCC (5% Et₂O/pentane) as a white solid (128 mg, 0.473 mmol, 79% yield).

¹H NMR (400 MHz, CDCl₃) δ 2.21 – 2.02 (m, 13H, ArCH₃ x 3, H₃ x 2 and H₆ x 2), 1.98 (s, 6H, ArCH₃ x 2), 1.79 (s, 3H, H₈ x 3), 1.58 – 1.44 (m, 4H, H₄ x 2 and H₅ x 2).

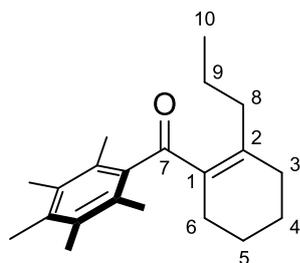
¹³C NMR (101 MHz, CDCl₃) δ 204.1, 148.9, 141.3, 135.0, 133.4, 133.0, 128.3, 35.1, 26.7, 22.8, 22.5, 22.2, 17.1, 16.8, 16.1.

HRMS (ESI⁺): C₁₉H₂₇O requires 271.2056, found [M+H]⁺=271.2056, Δ -0.17 ppm.

IR (film) ν_{max}/cm⁻¹ 2923, 1666, 1600, 1422, 1305, 1172, 906, 709.

m.p.: 116-118 °C.

(2,3,4,5,6-Pentamethylphenyl)(2-propylcyclohex-1-en-1-yl)methanone, 3b



Octane-1,5-diol **2b** (175 mg, 1.20 mmol, 2 eq.) was subjected to **General Procedure 1**. The title compound was afforded after purification by FCC (3% Et₂O/pentane) as a colourless oil (170 mg, 0.570 mmol, 95% yield).

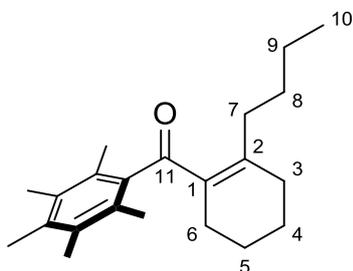
¹H NMR (400 MHz, CDCl₃) δ 2.20 (t, *J* = 7.5 Hz, 2H, H₈ x 2), 2.16 – 1.94 (m, 19H, ArCH₃ x 5, H₃ x 2 and H₆ x 2), 1.56 – 1.44 (m, 4H, H₄ x 2 and H₅ x 2), 1.35 (h, *J* = 7.5 Hz, 2H, H₉ x 2), 0.74 (t, *J* = 7.5 Hz, 3H, H₁₀ x 3).

¹³C NMR (101 MHz, CDCl₃) δ 203.8, 153.0, 141.1, 134.7, 132.7, 132.7, 128.2, 37.5, 32.4, 27.0, 22.8, 22.3, 21.9, 17.1, 16.7, 16.0, 14.4.

HRMS (ESI+): Found $[M+H]^+ = 299.2369$; $C_{21}H_{31}O$ requires 299.2369, $\Delta -0.32$ ppm.

IR (film) $\nu_{\max}/\text{cm}^{-1}$ 2927, 2858, 1667, 1598, 1450, 1305, 1264, 1166, 913.

(2-Butylcyclohex-1-en-1-yl)(2,3,4,5,6-pentamethylphenyl)methanone, 3c



Nonane-1,5-diol⁹ (192.3mg, 1.20 mmol, 2 eq.) was subjected to **General Procedure 1**. The title compound was afforded after purification by FCC (3% Et₂O/pentane) as a colourless oil (185 mg, 0.594 mmol, 99% yield).

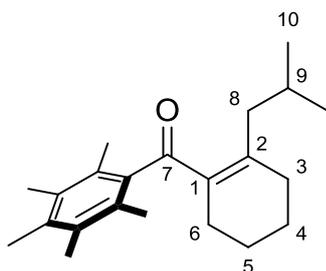
¹H NMR (400 MHz, CDCl₃) δ 2.32 – 2.09 (m, 15H, ArCH₃ x 3, H₃ x 2, H₆ x 2, H₇ x 2), 2.06 (s, 6H, ArCH₃ x 2), 1.68 – 1.50 (m, 4H, H₄ x 2, H₅ x 2), 1.33 (p, $J = 8.5$ Hz, 2H, H₈ x 2), 1.25 – 1.10 (m, 2H, H₉ x 2), 0.82 (t, $J = 7.5$ Hz, 3H, H₁₀ x 3).

¹³C NMR (101 MHz, CDCl₃) δ 204.0, 153.3, 141.3, 134.9, 132.9, 132.8, 128.4, 35.5, 32.6, 30.9, 27.0, 23.3, 22.9, 22.4, 17.3, 16.8, 16.1, 14.0.

HRMS (ESI+): Found $[M+H]^+ = 313.2521$; $C_{22}H_{33}O$ requires 313.2526, $\Delta -1.55$ ppm.

IR (film) $\nu_{\max}/\text{cm}^{-1}$ 2929, 2865, 1666, 1596, 1450, 1381, 1305, 1164, 904.

(2-Isobutylylcyclohex-1-en-1-yl)(2,3,4,5,6-pentamethylphenyl)methanone, 3d



7-Methyloctane-1,5-diol⁹ (192 mg, 1.20 mmol, 2 eq.) was subjected to **General Procedure 1**. The title compound was afforded after purification by FCC (4% Et₂O/pentane) as a colourless oil (186 mg, 0.594 mmol, 99% yield).

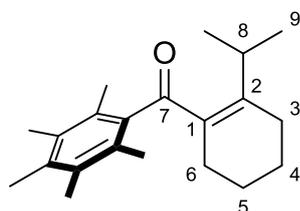
^1H NMR (400 MHz, CDCl_3) δ 2.33 – 2.22 (m, 2H, $\text{H}_8 \times 2$), 2.19 – 1.94 (m, 19H, $\text{ArCH}_3 \times 5$, $\text{H}_6 \times 2$ and $\text{H}_3 \times 2$), 1.94 – 1.81 (m, 1H, H_9), 1.55 – 1.42 (m, 4H, $\text{H}_4 \times 2$ and $\text{H}_5 \times 2$), 0.79 (d, $J = 6.5$ Hz, 6H, $\text{H}_{10} \times 6$).

^{13}C NMR (101 MHz, CDCl_3) δ 203.9, 152.4, 141.0, 134.7, 133.4, 132.7, 128.2, 43.6, 33.0, 27.6, 27.5, 22.8, 22.7, 22.2, 17.1, 16.7, 16.0.

HRMS (ESI⁺): Found $[\text{M}+\text{H}]^+ = 313.2524$; $\text{C}_{22}\text{H}_{33}\text{O}$ requires 313.2526, $\Delta -0.77$ ppm.

IR (film) $\nu_{\text{max}}/\text{cm}^{-1}$ 2928, 2866, 1666, 1591, 1449, 1304, 1164, 909, 711.

(2-Isopropylcyclohex-1-en-1-yl)(2,3,4,5,6-pentamethylphenyl)methanone, **3e**



6-Methylheptane-1,5-diol **2e** (175 mg, 1.20 mmol, 2 eq.) was subjected to **General Procedure 1**. The title compound was afforded after purification by FCC (3% Et_2O /pentane) as a white solid (114 mg, 0.382 mmol, 64% yield).

^1H NMR (400 MHz, CDCl_3) δ 3.66 – 3.48 (m, 1H, H_8), 2.26 – 2.03 (m, 19H, $\text{ArCH}_3 \times 5$, $\text{H}_6 \times 2$ and $\text{H}_3 \times 2$), 1.63 – 1.49 (m, 4H, $\text{H}_4 \times 2$ and $\text{H}_5 \times 2$), 0.98 (d, $J = 6.8$ Hz, 6H, $\text{H}_9 \times 6$).

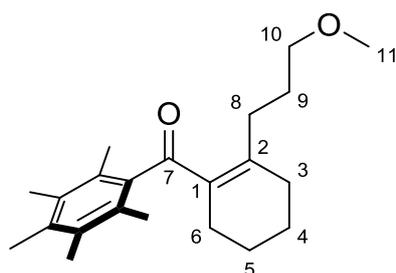
^{13}C NMR (101 MHz, CDCl_3) δ 204.5, 156.4, 141.2, 134.9, 132.9, 132.3, 128.4, 30.3, 27.2, 24.7, 22.9, 22.3, 20.8, 17.2, 16.9, 16.1.

HRMS (ESI⁺): Found $[\text{M}+\text{H}]^+ = 299.2368$; $\text{C}_{21}\text{H}_{31}\text{O}$ requires 299.2369, $\Delta -0.52$ ppm.

IR (film) $\nu_{\text{max}}/\text{cm}^{-1}$ 2930, 2870, 1664, 1604, 1450, 1303, 1262, 1165, 1010, 707.

m.p.: 90-92 °C.

(2-(3-Methoxypropyl)cyclohex-1-en-1-yl)(2,3,4,5,6-pentamethylphenyl)methanone, 3f



8-Methoxyoctane-1,5-diol⁹ (212 mg, 1.20 mmol, 2 eq.) was subjected to **General Procedure**

1. The title compound was afforded after purification by FCC (3% Et₂O/pentane) as a white solid (153 mg, 0.466 mmol, 78% yield).

¹H NMR (400 MHz, CDCl₃) δ 3.38 – 3.21 (m, 5H, H₁₀ x 2 and H₁₁ x 3), 2.43 – 2.30 (m, 2H, H₈ x 2), 2.28 – 1.99 (m, 19H, H₃ x 2, H₆ x 2 and ArCH₃ x 5), 1.76 – 1.64 (m, 2H, H₉ x 2), 1.64 – 1.51 (m, 4H, H₄ x 2 and H₅ x 2).

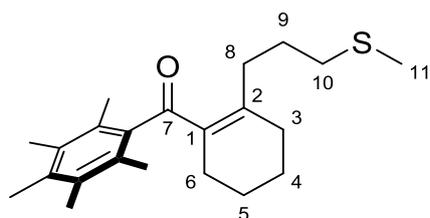
¹³C NMR (101 MHz, CDCl₃) δ 203.9, 152.6, 141.0, 134.9, 133.0, 132.9, 128.3, 73.0, 58.6, 32.6, 32.3, 28.6, 27.2, 22.8, 22.4, 17.2, 16.8, 16.1.

HRMS (ESI⁺): Found [M+H]⁺ = 329.2478; C₂₂H₃₃O₂ requires 329.2475, Δ 0.92 ppm.

IR (film) ν_{max}/cm⁻¹ 1926, 1860, 1666, 1597, 1449, 1305, 1174, 1117, 707.

m.p.: 60-62 °C.

(2-(3-(Methylthio)propyl)cyclohex-1-en-1-yl)(2,3,4,5,6-pentamethylphenyl)methanone, 3g



8-(Methylthio)octane-1,5-diol⁹ (231 mg, 1.20 mmol, 2 eq.) was subjected to **General Procedure 1.** The title compound was afforded after purification by FCC (2→5% Et₂O/pentane) as a colourless oil (205 mg, 0.594 mmol, 99% yield).

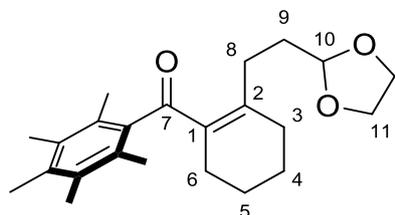
¹H NMR (400 MHz, CDCl₃) δ 2.45 – 2.31 (m, 4H, H₈ x 2, H₁₀ x 2), 2.25 – 2.20 (m, 5H, ArCH₃, H₃ x 2), 2.17 (s, 6H, ArCH₃ x 2), 2.15 – 2.04 (m, 11H, ArCH₃ x 2, H₆ x 2, H₁₁ x 3), 1.70 (p, *J* = 8.0 Hz, 2H, H₉ x 2), 1.63 – 1.51 (m, 4H, H₄ x 2, H₅ x 2).

¹³C NMR (101 MHz, CDCl₃) δ 203.9, 151.9, 141.1, 135.0, 133.3, 132.9, 128.3, 35.1, 34.6, 32.7, 28.4, 27.1, 22.8, 22.4, 17.3, 16.8, 16.1, 15.6.

HRMS (ESI+): Found $[M+H]^+ = 345.2244$; $C_{22}H_{33}OS$ requires 345.2247, $\Delta -0.77$ ppm.

IR (film) ν_{max}/cm^{-1} 2927, 2859, 1665, 1598, 1449, 1305, 1170.

(2-(2-(1,3-Dioxolan-2-yl)ethyl)cyclohex-1-en-1-yl)(2,3,4,5,6-pentamethylphenyl)methanone, 3h



A 2–5 mL Biotage[®] microwave vial was charged with CataCXium[®] A (2.2 mg, 0.0060 mmol, 2 mol%), 7-(1,3-dioxolan-2-yl)heptane-1,5-diol⁹ (126 mg, 0.600 mmol, 2 eq.), 1-(2,3,4,5,6-pentamethylphenyl)ethan-1-one **1** (57 mg, 0.30 mmol, 1 eq.), $[Ir(cod)Cl]_2$ (1.0 mg, 0.0015 mmol, 0.5 mol% dimer), KOH (67 mg, 1.2 mmol, 4 eq.) and toluene (1.2 mL, 0.25 M). The vial was then sealed with a microwave vial cap (containing a Reseal[™] septum) and heated at 115 °C for 24 hours. After cooling to RT, the reaction mixture was diluted with aq. HCl (3 M, 5 mL), extracted with CH_2Cl_2 (4 x 10 mL), dried with $MgSO_4$, filtered and concentrated *in vacuo*. The title compound was afforded after purification by FCC (25% pentane: Et_2O) as a white solid (91.0 mg, 0.255 mmol, 85% yield).

1H NMR (400 MHz, $CDCl_3$) δ 4.77 (t, $J = 5.0$ Hz, 1H, H_{10}), 3.98 – 3.77 (m, 4H, $H_{11} \times 4$), 2.46 (t, $J = 8.5$ Hz, 2H, $H_8 \times 2$), 2.28 – 2.18 (m, 5H, $ArCH_3$ and $H_3 \times 2$), 2.16 (s, 6H, $ArCH_3 \times 2$), 2.13–1.98 (m, 8H, $ArCH_3 \times 2$, $H_6 \times 2$), 1.82 – 1.74 (m, 2H, $H_9 \times 2$), 1.61 – 1.52 (m, 4H, $H_4 \times 2$ and $H_5 \times 2$).

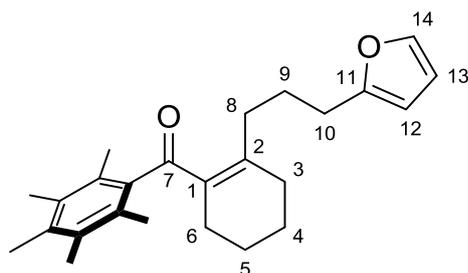
^{13}C NMR (101 MHz, $CDCl_3$) δ 203.8, 151.9, 140.9, 134.9, 133.2, 132.9, 128.3, 104.7, 64.9, 32.8, 32.6, 30.3, 27.2, 22.8, 22.4, 17.3, 16.9, 16.1.

HRMS (ESI+): Found $[M+H]^+ = 357.2428$; $C_{23}H_{33}O_3$ requires 357.2424, $\Delta 1.05$ ppm.

IR (film) ν_{max}/cm^{-1} 2928, 1665, 1598, 1449, 1305, 1130, 1032, 878, 707.

m.p.: 78–80 °C.

(2-(3-(Furan-2-yl)propyl)cyclohex-1-en-1-yl)(2,3,4,5,6-pentamethylphenyl)methanone, 3i



8-(Furan-2-yl)octane-1,5-diol⁹ (255 mg, 1.20 mmol, 2 eq.) was subjected to **General Procedure 1**. The title compound was afforded after purification by FCC (3→5% Et₂O/pentane) as a colourless oil (190 mg, 0.521 mmol, 87% yield).

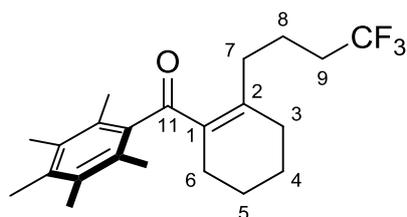
¹H NMR (400 MHz, CDCl₃) δ 7.28 (dd, *J* = 2.0, 1.0 Hz, 1H, H₁₄), 6.26 (dd, *J* = 3.0, 2.0 Hz, 1H, H₁₃), 5.96 (d, *J* = 3.0 Hz, 1H, H₁₂), 2.55 – 2.41 (m, 2H, H₁₀ x 2), 2.40 – 2.27 (m, 2H, H₈ x 2), 2.24 – 2.19 (m, 5H, ArCH₃, H₃ x 2), 2.17 (s, 6H, ArCH₃ x 2), 2.15 – 2.09 (m, 2H, H₆ x 2), 2.06 (s, 6H, ArCH₃ x 2), 1.73 (p, *J* = 8.0 Hz, 2H, H₉ x 2), 1.63 – 1.46 (m, 4H, H₄ x 2, H₅ x 2).

¹³C NMR (101 MHz, CDCl₃) δ 203.9, 156.3, 152.3, 141.2, 140.8, 135.0, 133.3, 132.9, 128.4, 110.2, 104.8, 35.3, 32.5, 28.4, 27.1, 27.1, 22.8, 22.4, 17.3, 16.9, 16.1.

HRMS (ESI⁺): Found [M+H]⁺ = 365.2467 ; C₂₅H₃₃O₂ requires 365.2475, Δ -2.11 ppm.

IR (film) ν_{max}/cm⁻¹ 2929, 2860, 1665, 1597, 1449, 1171, 726.

(2,3,4,5,6-Pentamethylphenyl)(2-(4,4,4-trifluorobutyl)cyclohex-1-en-1-yl)methanone, 3j



9,9,9-Trifluorononane-1,5-diol **2j** (257 mg, 1.20 mmol, 2 eq.) was subjected to **General Procedure 1**. The title compound was afforded after purification by FCC (2% Et₂O/pentane) as a white solid (193 mg, 0.527 mmol, 88% yield).

¹H NMR (400 MHz, CDCl₃) δ 2.34 – 2.21 (m, 2H, H₇ x 2), 2.19 – 2.08 (m, 11H, H₃ x 2, ArCH₃ x 3), 2.07 – 2.02 (m, 2H, H₆ x 2), 1.98 (s, 6H, ArCH₃ x 2), 1.93 – 1.74 (m, 2H, H₉ x 2), 1.66 – 1.44 (m, 6H, H₄ x 2, H₅ x 2, H₈ x 2).

^{13}C NMR (101 MHz, CDCl_3) δ 203.7, 150.5, 140.8, 135.1, 133.9, 132.9, 128.2, 127.1 (q, J = 276.5 Hz), 34.3, 33.7 (q, J = 28.5 Hz), 32.2, 26.9, 22.6, 22.2, 20.9 (q, J = 3.0 Hz), 17.1, 16.7, 15.9.

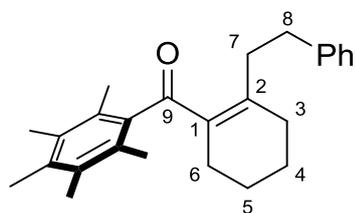
^{19}F NMR (376 MHz, CDCl_3) δ -66.4.

HRMS (ESI+): Found $[\text{M}+\text{H}]^+ = 367.2242$; $\text{C}_{22}\text{H}_{30}\text{OF}_3$ requires 367.2443, Δ -0.39 ppm.

IR (film) $\nu_{\text{max}}/\text{cm}^{-1}$ 2931, 1666, 1599, 1461, 1384, 1250, 1195, 1128, 1011.

m.p.: 60-62 $^\circ\text{C}$.

(2,3,4,5,6-Pentamethylphenyl)(2-phenethylcyclohex-1-en-1-yl)methanone, 3k



7-Phenylheptane-1,5-diol⁹ (250 mg, 1.20 mmol, 2 eq.) was subjected to **General Procedure 1**. The title compound was afforded after purification by FCC (3% Et_2O /pentane) as a white solid (187mg, 0.519 mmol, 86% yield).

^1H NMR (400 MHz, CDCl_3) δ 7.27 – 7.06 (m, 5H, ArCH x 5), 2.78 – 2.50 (m, 4H, H_7 x 2, H_8 x 2), 2.29 – 2.21 (m, 5H, ArCH₃, H_3 x 2), 2.17 (s, 8H, ArCH₃ x 2, H_6 x 2), 2.08 (s, 6H, ArCH₃ x 2), 1.65 – 1.55 (m, 4H, H_4 x 2, H_5 x 2).

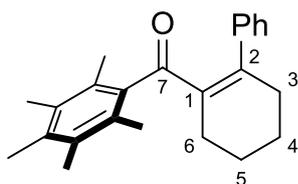
^{13}C NMR (101 MHz, CDCl_3) δ 203.8, 152.1, 142.3, 141.1, 135.0, 133.3, 132.9, 128.4, 128.3, 128.2, 125.7, 38.4, 34.8, 32.8, 27.0, 22.7, 22.3, 17.2, 16.7, 16.0.

HRMS (ESI+): Found $[\text{M}+\text{H}]^+ = 361.2523$; $\text{C}_{26}\text{H}_{33}\text{O}$ requires 361.2526, Δ -0.76 ppm.

IR (film) $\nu_{\text{max}}/\text{cm}^{-1}$ 2927, 2859, 1665, 1602, 1452, 1306, 1173, 1068, 903, 700.

m.p.: 100-102 $^\circ\text{C}$.

(2,3,4,5,6-Pentamethylphenyl)(3,4,5,6-tetrahydro-[1,1'-biphenyl]-2-yl)methanone, 3l



1-Phenylpentane-1,5-diol⁴ (216 mg, 1.20 mmol, 2 eq.) was subjected to **General Procedure 1**. The title compound was afforded after purification by FCC (3% → 5% Et₂O/pentane) as a white solid (119 mg, 0.36 mmol, 60% yield).

¹H NMR (400 MHz, CDCl₃) δ 6.98 – 6.77 (m, 3H, ArCH x 3), 6.76 – 6.59 (m, 2H, ArCH x 2), 2.64 – 2.51 (m, 2H, H₆ x 2), 2.35 – 2.23 (m, 2H, H₃ x 2), 2.00 (s, 3H, ArCH₃), 1.92 (s, 6H, ArCH₃ x 2), 1.91 (s, 6H, ArCH₃ x 2), 1.81 – 1.68 (m, 4H, H₄ x 2, H₅ x 2).

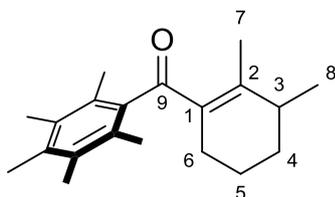
¹³C NMR (101 MHz, CDCl₃) δ 203.7, 151.7, 143.0, 140.9, 136.5, 134.7, 132.2, 128.6, 126.6, 126.1, 125.7, 36.5, 25.9, 22.9, 22.5, 18.2, 16.5, 15.7.

HRMS (ESI+): Found [M+H]⁺ = 333.2213; C₂₄H₂₉O requires 333.2213, Δ 0.05 ppm.

IR (film) ν_{max}/cm⁻¹ 2922, 2859, 1636, 1618, 1443, 1304, 1194, 757, 700.

m.p.: 78-80 °C.

(2,3-Dimethylcyclohex-1-en-1-yl)(2,3,4,5,6-pentamethylphenyl)methanone, 3m



4-Methylhexane-1,5-diol⁴ (159 mg, 1.2 mmol, 2 eq.) was subjected to **General Procedure 1**. The title compound was afforded after purification by FCC (4% Et₂O/pentane) as a white solid (148 mg, 0.522 mmol, 87% yield).

¹H NMR (400 MHz, CDCl₃) δ 2.15 (s, 4H, ArCH₃, H₃), 2.10 (s, 6H, ArCH₃ x 2), 2.09 – 1.98 (m, 2H, H₆ x 2), 1.98 (s, 6H, ArCH₃ x 2), 1.84 (s, 3H, H₇ x 3), 1.66 – 1.40 (m, 3H, H₅ x 2, H_{4a}), 1.38 – 1.27 (m, 1H, H_{4b}), 1.05 (d, J = 7.0 Hz, 3H, H₈ x 3).

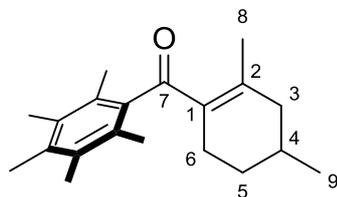
¹³C NMR (101 MHz, CDCl₃) δ 204.8, 152.2, 141.2, 135.0, 133.1, 132.9, 128.2, 37.5, 30.4, 27.3, 20.9, 19.7, 19.3, 17.1, 16.8, 16.1.

HRMS (ESI+): Found [M+H]⁺ = 285.2208; C₂₀H₂₉O requires 285.2213, Δ -1.85 ppm.

IR (film) ν_{max}/cm⁻¹ 2930, 2870, 1666, 1610, 1454, 1305, 1159, 968.

m.p.: 80-82 °C.

(2,4-Dimethylcyclohex-1-en-1-yl)(2,3,4,5,6-pentamethylphenyl)methanone, 3n



3-Methylhexane-1,5-diol⁴ (159 mg, 1.20 mmol, 2 eq.) was subjected to **General Procedure 1**. The title compound was afforded after purification by FCC (2% → 4% Et₂O/pentane) as a white solid (160 mg, 0.564 mmol, 94% yield).

¹H NMR (400 MHz, CDCl₃) δ 2.35 – 2.24 (m, 2H, H_{3a} and H_{6a}), 2.22 (s, 3H, ArCH₃), 2.17 (s, 6H, ArCH₃ x 2), 2.15 – 2.08 (m, 1H, H_{6b}), 2.05 (s, 6H, ArCH₃ x 2), 1.94 – 1.78 (m, 4H, H₈ x 3 and H_{3b}), 1.76 – 1.60 (m, 2H, H₄ and H_{5a}), 1.15 (dtd, *J* = 12.5, 10.5, 5.5 Hz, 1H, H_{5b}), 0.96 (d, *J* = 6.5 Hz, 3H, H₉ x 3).

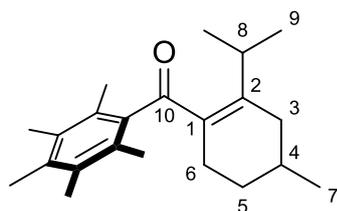
¹³C NMR (101 MHz, CDCl₃) δ 204.0, 148.6, 141.4, 135.0, 133.0, 132.9, 128.2, 43.7, 30.9, 28.4, 26.7, 22.1, 21.5, 17.1, 16.8, 16.1.

HRMS (ESI⁺): Found [M+H]⁺ = 285.2209; C₂₀H₂₉O requires 285.2213, Δ –1.32 ppm.

IR (film) ν_{max}/cm⁻¹ 2942, 1666, 1602, 1172, 715.

m.p.: 126-127 °C.

(2-Isopropyl-4-methylcyclohex-1-en-1-yl)(2,3,4,5,6-pentamethylphenyl)methanone, 3o



3,6-Dimethylheptane-1,5-diol **2o** (192 mg, 1.20 mmol, 2 eq.) was subjected to **General Procedure 1**. The title compound was afforded after purification by FCC (3% Et₂O/pentane) as a white solid (131 mg, 0.420 mmol, 70% yield).

¹H NMR (400 MHz, CDCl₃) δ 3.57 (hept, *J* = 6.0 Hz, 1H, H₈), 2.37 – 2.25 (m, 1H, H_{3a}), 2.25 – 2.13 (m, 10H, ArCH₃ x 3, H_{6a}), 2.07 (s, 7H, ArCH₃ x 2, H_{6b}), 1.80 – 1.52 (m, 3H, H_{3a}, H₄, H_{5a}), 1.11 (dtd, *J* = 12.5, 10.5, 6.0 Hz, 1H, H_{5b}), 1.00 – 0.93 (m, 9H, H₉ x 6, H₇ x 3).

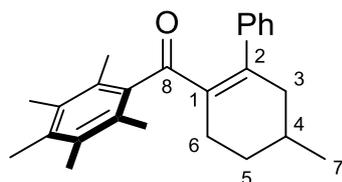
^{13}C NMR (101 MHz, CDCl_3) δ 204.5, 155.8, 141.3, 135.0, 132.9, 131.8, 128.4, 33.3, 30.9, 30.1, 28.1, 27.3, 21.7, 21.0, 20.5, 17.3, 16.9, 16.1.

HRMS (ESI+): Found $[\text{M}+\text{H}]^+ = 313.2524$; $\text{C}_{22}\text{H}_{33}\text{O}$ requires 313.2526 Δ -0.47 ppm.

IR (film) $\nu_{\text{max}}/\text{cm}^{-1}$ 2953, 2925, 1663, 1604, 1456, 1381, 1166, 863, 716.

m.p.: 96-98 $^\circ\text{C}$.

(5-Methyl-3,4,5,6-tetrahydro-[1,1'-biphenyl]-2-yl)(2,3,4,5,6-pentamethylphenyl)methanone, 3p



3-Methyl-1-phenylpentane-1,5-diol **2p** (233 mg, 1.20 mmol, 2 eq.) was subjected to **General Procedure 1**. The title compound was afforded after purification by FCC (3 \rightarrow 4% Et_2O /pentane) as a white solid (146 mg, 0.420 mmol, 70% yield, 5% inseparable impurity of $\text{Ph}^*\text{C}(\text{O})\text{Me}$).

^1H NMR (400 MHz, CDCl_3) δ 6.92 – 6.82 (m, 3H, ArCH x 3), 6.71 – 6.63 (m, 2H, ArCH x 2), 2.89 – 2.74 (m, 1H, H_{6a}), 2.52 – 2.28 (m, 2H, H_{6b} , H_{3a}), 2.02 – 1.85 (m, 17H, ArCH₃ x 5, H_{3b} , H_{5a}), 1.88 – 1.72 (m, 1H, H_4), 1.41 – 1.22 (m, 1H, H_{5b}), 1.01 (d, $J = 6.5$ Hz, 3H, H_7 x 3).

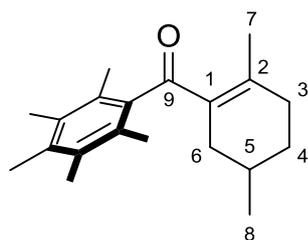
^{13}C NMR (101 MHz, CDCl_3) δ 203.6, 151.4, 142.8, 140.8, 136.0, 134.7, 132.1, 128.6, 126.6, 126.0, 125.7, 44.9, 30.6, 28.8, 25.9, 21.4, 18.2, 16.5, 15.7.

HRMS (ESI+): Found $[\text{M}+\text{H}]^+ = 347.2367$; $\text{C}_{25}\text{H}_{31}\text{O}$ requires 347.2369, Δ -0.79 ppm.

IR (film) $\nu_{\text{max}}/\text{cm}^{-1}$ 2922, 1642, 1595, 1418, 1314, 1268, 1195, 811, 755, 699.

m.p.: 60-62 $^\circ\text{C}$.

(2,5-Dimethylcyclohex-1-en-1-yl)(2,3,4,5,6-pentamethylphenyl)methanone, 3q



2-Methylhexane-1,5-diol⁴ (159 mg, 1.20 mmol, 2 eq.) was subjected to **General Procedure 1**. The title compound was afforded after purification by FCC (4% Et₂O/pentane) as a white solid (137 mg, 0.480 mmol, 80% yield).

¹H NMR (400 MHz, CDCl₃) δ 2.42 – 2.30 (m, 1H, H_{6a}), 2.26 – 2.19 (m, 4H, ArCH₃, H_{3a}) 2.19 – 2.13 (m, 7H, ArCH₃ x 2, H_{3b}), 2.05 (s, 6H, ArCH₃ x 2), 1.81 (s, 3H, H₇ x 3), 1.76 – 1.53 (m, 3H, H_{4a}, H₅, H_{6b}), 1.25 – 1.13 (m, 1H, H_{4b}), 0.94 (d, *J* = 6.5 Hz, 3H, H₈ x 3).

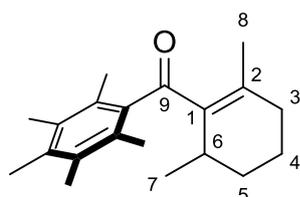
¹³C NMR (101 MHz, CDCl₃) δ 204.1, 148.6, 141.4, 135.0, 133.0, 133.0, 128.2, 35.2, 34.7, 30.6, 28.7, 21.8, 21.6, 17.1, 16.9, 16.1.

HRMS (ESI⁺): Found [M+H]⁺ = 285.2213; C₂₀H₂₉O requires 285.2213, Δ -0.14 ppm.

IR (film) ν_{max}/cm⁻¹ 2921, 1667, 1621, 1454, 1306, 1266, 1176, 891, 709.

m.p.: 84-86 °C.

(2,6-Dimethylcyclohex-1-en-1-yl)(2,3,4,5,6-pentamethylphenyl)methanone, 3r



Heptane-2,6-diol⁴ (159 mg, 1.20 mmol, 2 eq.) was subjected to **General Procedure 1**. The title compound was afforded after purification by FCC (3% → 5% Et₂O/pentane) as a white solid (111 mg, 0.39 mmol, 65% yield).

¹H NMR (400 MHz, CDCl₃) δ 2.88 – 2.77 (m, 1H, H₆), 2.23 (s, 3H, ArCH₃), 2.21 – 2.13 (m, 8H, ArCH₃ x 2, H₃ x 2), 1.78 – 1.63 (m, 6H, ArCH₃ x 2), 1.63 – 1.52 (m, 7H, H₄ x 2, H₅ x 2, H₈ x 3), 1.01 (d, *J* = 7.0 Hz, 3H, H₇ x 3).

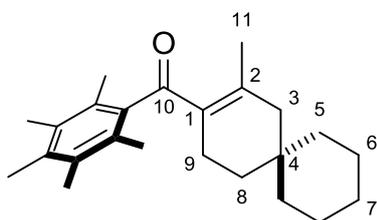
¹³C NMR (101 MHz, CDCl₃) δ 203.1, 149.2, 141.5, 139.4, 135.1, 133.1, 128.8, 35.4, 30.2, 29.0, 22.2, 20.8, 17.7, 17.3, 16.9, 16.2.

HRMS (ESI⁺): Found [M+H]⁺ = 285.2213; C₂₀H₂₉O requires 285.2213, Δ -0.03 ppm.

IR (film) $\nu_{\max}/\text{cm}^{-1}$ 2912, 2866, 1630, 1610, 1448, 1271, 1219, 1152, 893, 704.

m.p.: 100-102 °C.

(2-Methylspiro[5.5]undec-2-en-3-yl)(2,3,4,5,6-pentamethylphenyl)methanone, 3s



1-(1-(2-Hydroxyethyl)cyclohexyl)propan-2-ol⁹ (224 mg, 1.20 mmol, 2 eq.) was subjected to

General Procedure 1. The title compound was afforded after purification by FCC (3 → 5% Et₂O/pentane) as a white solid (142 mg, 0.420 mmol, 70% yield).

¹H NMR (400 MHz, CDCl₃) δ 2.15 (s, 3H, ArCH₃), 2.09 (s, 8H, ArCH₃ x 2 and H₉ x 2), 2.00 – 1.91 (m, 8H, ArCH₃ x 2 and H₃ x 2), 1.80 (s, 3H, H₁₁ x 3), 1.42 – 1.27 (m, 8H, H₆ x 4, H₇ x 2, H₈ x 2), 1.18 (t, J = 5.5 Hz, 4H, H₅ x 4).

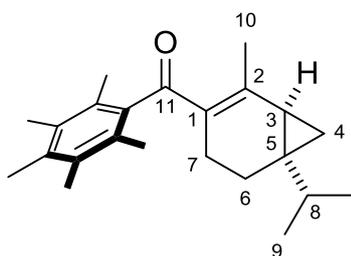
¹³C NMR (101 MHz, CDCl₃) δ 203.8, 148.2, 141.4, 134.9, 132.9, 132.0, 128.2, 47.4, 36.6, 32.4, 31.4, 26.7, 23.5, 22.5, 21.9, 17.1, 16.8, 16.1.

HRMS (ESI+): Found $[M+H]^+$ = 339.2679; C₂₄H₃₅O requires 339.2682, Δ -0.97 ppm.

IR (film) $\nu_{\max}/\text{cm}^{-1}$ 2921, 1667, 1620, 1445, 1305, 1266, 1159, 851.

m.p.: 94-96 °C.

((1S,6R)-6-Isopropyl-2-methylbicyclo[4.1.0]hept-2-en-3-yl)(2,3,4,5,6-pentamethylphenyl)methanone, 3t



2-((1S,2S)-2-(1-Hydroxyethyl)-1-isopropylcyclopropyl)ethan-1-ol⁴ (208 mg, 1.20 mmol, 2 eq., 85:15 d.r.) was subjected to **General Procedure 1.** The title compound was afforded after purification by FCC (4% → 10% Et₂O/pentane) as a white solid (157 mg, 0.480 mmol, 80% yield, 5% inseparable impurity of Ph*C(O)Me).

^1H NMR (400 MHz, CDCl_3) δ 2.68 – 2.30 (m, 1H, H_{7a}), 2.22 (s, 3H, ArCH_3), 2.17 (s, 6H, $\text{ArCH}_3 \times 2$), 2.10 – 1.97 (m, 9H, $\text{ArCH}_3 \times 2$, $\text{H}_{10} \times 3$), 1.88 – 1.71 (m, 2H, H_{7b} , H_{6a}), 1.48 – 1.34 (m, 1H, H_{6b}), 1.24 – 1.04 (m, 3H, H_3 , H_{4a} , H_8), 0.98 (d, $J = 7.0$, 3H, $\text{H}_{9a} \times 3$), 0.96 (d, $J = 7.0$, 3H, $\text{H}_{9b} \times 3$), 0.77 (ddd, $J = 8.5$, 4.0, 1.0 Hz, 1H, H_{4b}).

^{13}C NMR (101 MHz, CDCl_3) δ 201.1 (Br), 154.3, 141.6 (Br), 134.8, 133.2 (Br), 132.9, 128.2, 36.6, 32.6, 28.0, 23.2 (Br), 22.6 (Br), 19.4, 19.3, 19.1, 18.2, 17.1, 16.8, 16.1.

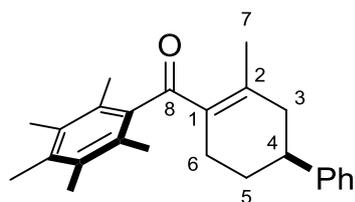
HRMS (ESI+): Found $[\text{M}+\text{H}]^+ = 325.2524$; $\text{C}_{23}\text{H}_{33}\text{O}$ requires 325.2526, $\Delta -0.46$ ppm.

IR (film) $\nu_{\text{max}}/\text{cm}^{-1}$ 2957, 2925, 1659, 1603, 1463, 1307, 1269, 1170, 884, 713.

m.p.: 78-80 $^\circ\text{C}$.

$[\alpha]_{\text{D}}^{25} = 139.1$ ($c=1.0$, CHCl_3).

(S)-(5-Methyl-1,2,3,6-tetrahydro-[1,1'-biphenyl]-4-yl)(2,3,4,5,6-pentamethylphenyl)methanone, 3u



A 2–5 mL Biotage[®] microwave vial was charged with CataCXium[®] A (2.2 mg, 0.0060 mmol, 2 mol%), (3S)-3-phenylhexane-1,5-diol⁴ (117 mg, 0.60 mmol, 2 eq. >99:1 e.r., 60:40 d.r.), 1-(2,3,4,5,6-pentamethylphenyl)ethan-1-one **1** (57 mg, 0.30 mmol, 1 eq.), $[\text{Ir}(\text{cod})\text{Cl}]_2$ (1.0 mg, 0.0015 mmol, 0.5 mol% dimer), KOH (67 mg, 1.2 mmol, 4 eq.) and toluene (1.2 mL, 0.25 M). The vial was then sealed with a microwave vial cap (containing a Reseal[™] septum) and heated at 115 $^\circ\text{C}$ for 24 hours. After cooling to RT, the reaction mixture was diluted with aq. HCl (3 M, 5 mL) and extracted with CH_2Cl_2 (4 x 10 mL). The title compound was afforded after purification by FCC (4.5 \rightarrow 6% pentane: Et_2O) as a white solid (70.0 mg, 0.201 mmol, 67% yield, >99:1 e.r.). Racemic cyclohexane *rac*-**3u** was synthesised *via* an identical procedure starting from the corresponding racemic diol *rac*-**2u**.⁴

^1H NMR (400 MHz, CDCl_3) δ 7.35 – 7.28 (m, 2H, $\text{ArCH} \times 2$), 7.25 – 7.17 (m, 3H, $\text{ArCH} \times 3$), 2.87 – 2.76 (m, 1H, H_4), 2.53 – 2.32 (m, 3H, $\text{H}_3 \times 2$, H_{6a}), 2.29 – 2.14 (m, 10H, $\text{ArCH}_3 \times 3$, H_{6b}), 2.09 (s, 6H, $\text{ArCH}_3 \times 2$), 2.02 – 1.86 (m, 4H, $\text{H}_7 \times 3$, H_{5a}), 1.70 (dtd, $J = 12.5$, 11.0, 5.0 Hz, 1H, H_{5b}).

^{13}C NMR (101 MHz, CDCl_3) δ 203.8, 148.3, 146.1, 141.2, 135.1, 133.0, 133.0, 128.6, 128.2, 126.9, 126.4, 43.0, 39.9, 29.8, 27.2, 22.0, 17.2, 16.9, 16.1.

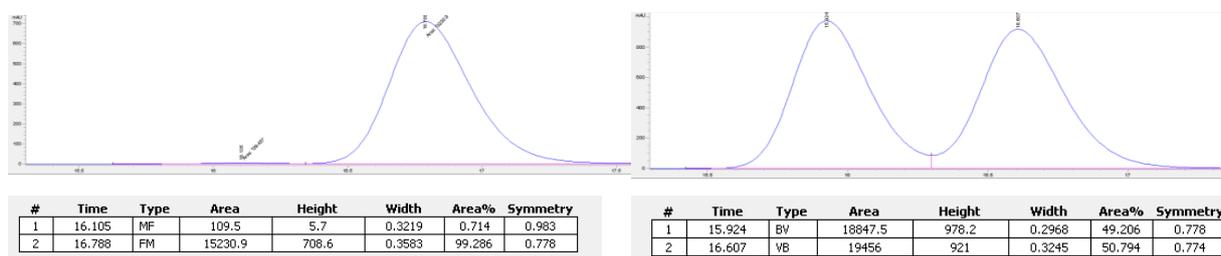
HRMS (ESI+): Found $[\text{M}+\text{H}]^+ = 347.2369$; $\text{C}_{25}\text{H}_{31}\text{O}$ requires 347.2369, Δ -0.10 ppm.

m.p.: 126-128 $^\circ\text{C}$.

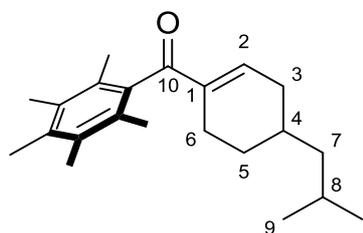
IR (film) $\nu_{\text{max}}/\text{cm}^{-1}$ 2927, 1668, 1619, 1453, 1379, 1265, 1168, 896, 757, 700.

$[\alpha]_{\text{D}}^{25} = -93.2$ ($c=1.0$, CHCl_3).

Chiral HPLC: Chiralpak IG with guard, 1.7 % IPA, 98.3 % hexane, 0.5 mL/min, 25 $^\circ\text{C}$, $\lambda = 254$ nm, 10 μL injection:



(4-Isobutylcyclohex-1-en-1-yl)(2,3,4,5,6-pentamethylphenyl)methanone, 3v



3-Isobutylpentane-1,5-diol **2v** (192 mg, 1.20 mmol, 2 eq.) was subjected to **General Procedure 1**. The title compound was afforded after purification by FCC (3 \rightarrow 5% Et_2O /pentane) as a white solid (140 mg, 0.448 mmol, 75% yield).

^1H NMR (400 MHz, CDCl_3) δ 6.46 (ddt, $J = 5.0, 3.0, 2.0$ Hz, 1H, H_2), 2.69 – 2.59 (m, 1H, H_{6a}), 2.34 – 2.21 (m, 5H, ArCH_3 , H_{3a} and H_{6b}), 2.18 (s, 6H, $\text{ArCH}_3 \times 2$), 2.03 (s, 3H, ArCH_3), 2.01 (s, 3H, ArCH_3), 1.89 (dddd, $J = 13.5, 6.0, 5.0, 3.0$ Hz, 1H, H_{5a}), 1.82 – 1.57 (m, 3H, H_{3b} , H_4 and H_8), 1.29 – 1.09 (m, 3H, H_{5b} and $\text{H}_7 \times 2$), 0.89 (d, $J = 6.5$, 3H, $\text{H}_{9a} \times 3$), 0.89 (d, $J = 6.5$, 3H, $\text{H}_{9b} \times 3$).

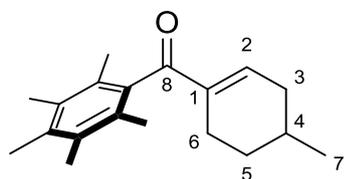
^{13}C NMR (101 MHz, CDCl_3) δ 203.5, 145.2, 140.8, 138.4, 135.0, 132.7, 132.6, 129.3, 129.2, 45.8, 33.3, 30.6, 28.6, 25.1, 23.1, 22.9, 22.5, 17.6, 17.6, 16.8, 16.1. N.B. additional peaks for C_6Me_5 were observed due to restricted rotation about the Ar-C(O) axis.

HRMS (ESI+): Found $[\text{M}+\text{H}]^+ = 313.2525$; $\text{C}_{22}\text{H}_{33}\text{O}$ requires 313.2527, Δ -0.29 ppm.

IR (film) $\nu_{\max}/\text{cm}^{-1}$ 3014, 2956, 1651, 1638, 1467, 1188, 861.

m.p.: 100-102 °C.

(4-Methylcyclohex-1-en-1-yl)(2,3,4,5,6-pentamethylphenyl)methanone, 3w



Commercially available 3-methylpentane-1,5-diol (142 mg, 1.20 mmol, 2 eq.) was subjected to **General Procedure 1** The title compound was afforded after purification by FCC (5% Et₂O/pentane) as a white solid (136 mg, 0.50 mmol, 84% yield).

¹H NMR (400 MHz, CDCl₃) δ 6.49 – 6.43 (m, 1H, H₂), 2.70 – 2.58 (m, 1H, H_{6a}), 2.35 – 2.11 (m, 11H, H_{3a}, H_{6b} and ArCH₃ x 3), 2.01 (s, 6H, ArCH₃ x 2), 1.90 – 1.63 (m, 3H, H_{3b}, H₄ and H_{5a}), 1.27 (dtd, $J = 13.0, 10.5, 5.5$ Hz, 1H, H_{5b}), 0.99 (d, $J = 6.5$ Hz, 3H, H₇).

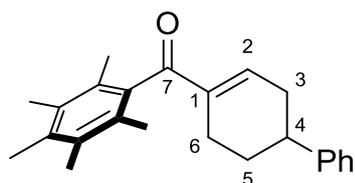
¹³C NMR (101 MHz, CDCl₃) δ 203.5, 145.2, 140.5, 138.4, 135.0, 132.7, 129.2, 34.8, 30.4, 28.0, 22.5, 21.5, 17.6, 16.8, 16.1.

HRMS (ESI⁺): Found $[M+H]^+ = 271.2055$; C₁₉H₂₇O requires 271.2056, $\Delta -0.39$ ppm.

IR (film) $\nu_{\max}/\text{cm}^{-1}$ 2931, 1652, 1633, 1192, 1168, 700.

m.p.: 143-144 °C.

(2,3,4,5,6-Pentamethylphenyl)(1,2,3,6-tetrahydro-[1,1'-biphenyl]-4-yl)methanone, 3x



3-Phenylpentane-1,5-diol⁴ (216 mg, 1.20 mmol, 2 eq.) was subjected to **General Procedure 1**. The title compound was afforded after purification by FCC (5% Et₂O/pentane) as a white solid (140 mg, 0.47 mmol, 70% yield).

¹H NMR (400 MHz, CDCl₃) δ 7.35 – 7.28 (m, 2H, ArCH x 2), 7.25 – 7.18 (m, 3H, ArCH x 3), 6.62 – 6.54 (m, 1H, H₂), 2.91 – 2.80 (m, 1H, H₄), 2.80 – 2.69 (m, 1H, H_{6a}), 2.54 – 2.36 (m, 2H, H_{6b}, H_{3a}), 2.37 – 2.26 (m, 1H, H_{3b}), 2.25 (s, 3H, ArCH₃), 2.20 (s, 6H, ArCH₃ x 2), 2.12 (dddt, $J = 11.5, 5.5, 2.5, 1.5$ Hz, 1H, H_{5a}), 2.08-2.03 (m, 6H, ArCH₃ x 2), 1.86 – 1.72 (m, 1H, H_{5b}).

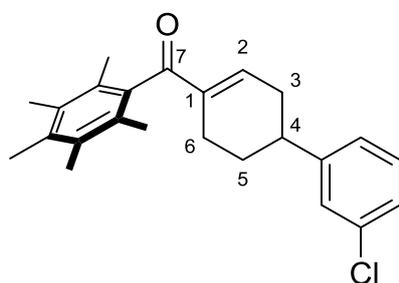
^{13}C NMR (101 MHz, CDCl_3) δ 203.3, 146.1, 144.6, 140.6, 138.3, 135.2, 132.8, 129.3, 129.2, 128.7, 127.0, 126.5, 39.6, 34.4, 29.5, 23.2, 17.6, 16.8, 16.1. N.B. additional peaks for C_6Me_5 were observed due to restricted rotation about the Ar-C(O) axis.

HRMS (ESI+): Found $[\text{M}+\text{H}]^+ = 333.2214$; $\text{C}_{24}\text{H}_{29}\text{O}$ requires 333.2213, Δ 0.30 ppm.

IR (film) $\nu_{\text{max}}/\text{cm}^{-1}$ 2931, 1650, 1635, 1451, 1428, 1379, 1311, 1265, 1181, 852, 756, 699.

m.p.: 160-162 $^\circ\text{C}$.

(3'-Chloro-1,2,3,6-tetrahydro-[1,1'-biphenyl]-4-yl)(2,3,4,5,6-pentamethylphenyl)methanone, 3y



3-(3-Chlorophenyl)pentane-1,5-diol⁴ (258 mg, 1.20 mmol, 2 eq.) was subjected to **General Procedure 1**. The title compound was afforded after purification by FCC (5 \rightarrow 10% Et_2O /pentane) as a white solid (192 mg, 0.522 mmol, 87% yield).

^1H NMR (400 MHz, CDCl_3) δ 7.18 – 7.10 (m, 3H, ArCH x 3), 7.03 (dt, $J = 7.5, 1.5$ Hz, 1H, ArCH), 6.53 – 6.43 (m, 1H, H_2), 2.84 – 2.71 (m, 1H, H_4), 2.71 – 2.59 (m, 1H, H_{6a}), 2.47 – 2.29 (m, 2H, H_{3a} and H_{6b}), 2.26 – 1.93 (m, 17H, H_{3b} , H_{5a} and Ar CH_3 x 5), 1.78 – 1.65 (m, 1H, H_{5b}).

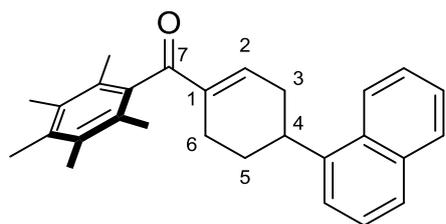
^{13}C NMR (101 MHz, CDCl_3) δ 203.2, 148.0, 144.1, 140.6, 138.1, 135.3, 134.4, 132.8, 129.9, 129.3, 129.2, 127.1, 126.7, 125.3, 39.2, 34.0, 29.2, 22.9, 17.7, 16.8, 16.1. N.B. additional peaks for C_6Me_5 were observed due to restricted rotation about the Ar-C(O) axis.

HRMS (ESI+): Found $[\text{M}+\text{H}]^+ = 367.1823$; $\text{C}_{24}\text{H}_{28}\text{O}^{35}\text{Cl}$ requires 367.1823, Δ -0.19 ppm.

IR (film) $\nu_{\text{max}}/\text{cm}^{-1}$ 2927, 1856, 1691, 1686, 1596, 1448, 830, 656.

m.p.: 98-100 $^\circ\text{C}$.

4-(Naphthalen-1-yl)cyclohex-1-en-1-yl)(2,3,4,5,6-pentamethylphenyl)methanone, 3z



3-(Naphthalen-1-yl)pentane-1,5-diol⁴ (276 mg, 1.20 mmol, 2 eq.) was subjected to **General Procedure 1**. The title compound was afforded after purification by FCC (50 → 70% CH₂Cl₂/pentane) as a white solid (117 mg, 0.306 mmol, 51% yield).

¹H NMR (400 MHz, CDCl₃) δ 8.02 (d, *J* = 8.5 Hz, 1H, ArCH), 7.80 (dd, *J* = 8.0, 1.5 Hz, 1H, ArCH), 7.66 (d, *J* = 8.0 Hz, 1H, ArCH), 7.50 – 7.25 (m, 4H, ArCH x 4), 6.57 (qd, *J* = 3.0, 1.0 Hz, 1H, H₂), 3.62 (tdd, *J* = 10.5, 5.0, 2.5 Hz, 1H, H₄), 2.71 (dtdd, *J* = 18.0, 4.5, 2.5, 1.0 Hz, 1H, H_{6a}), 2.60 (dtt, *J* = 19.0, 5.5, 2.0 Hz, 1H, H_{3a}), 2.49 (ddddt, *J* = 14.5, 11.0, 5.5, 3.0, 2.0 Hz, 1H, H_{6b}), 2.39 – 2.26 (m, 1H, H_{3b}), 2.24 – 2.09 (m, 10H, ArCH₃ x 3, H_{5a}), 2.09 – 1.85 (m, 7H, ArCH₃ x 2, H_{5b}).

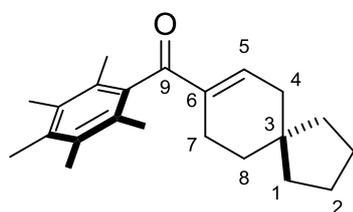
¹³C NMR (101 MHz, CDCl₃) δ 203.2, 144.7, 141.6, 140.6, 138.1, 135.1, 134.0, 132.7, 132.7, 131.4, 129.2, 129.1, 126.9, 126.0, 125.6, 125.5, 123.0, 122.4, 34.2, 34.0, 28.9, 23.3, 17.6, 17.6, 16.7, 16.0. N.B. additional peaks for C₆Me₅ were observed due to restricted rotation about the Ar-C(O) axis.

HRMS (ESI⁺): Found [M+H]⁺ = 383.2368; C₂₈H₃₁O₂ requires 383.2369, Δ -0.33 ppm.

IR (film) ν_{max}/cm⁻¹ 2927, 1652, 1636, 1379, 1267, 1183, 856, 797, 778.

m.p.: 156-158 °C.

(2,3,4,5,6-Pentamethylphenyl)(spiro[4.5]dec-7-en-8-yl)methanone, 3aa



2,2'-(Cyclopentane-1,1-diyl)bis(ethan-1-ol)⁴ (190 mg, 1.20 mmol, 2 eq.) was subjected to **General Procedure 1**. The title compound was afforded after purification by FCC (4 → 5% Et₂O/pentane) as a white solid (175 mg, 0.560 mmol, 94% yield).

¹H NMR (400 MHz, CDCl₃) δ 6.37 (tt, *J* = 4.0, 1.5 Hz, 1H, H₅), 2.41 (tq, *J* = 6.5, 2.0 Hz, 2H, H₇ x 2), 2.16 (s, 3H, ArCH₃), 2.11 (s, 6H, ArCH₃ x 2), 1.97 (dt, *J* = 4.5, 2.5 Hz, 2H, H₄ x 2), 1.94 (s, 6H,

ArCH₃ x 2), 1.61 – 1.53 (m, 4H, H₁ x 4), 1.52 (t, *J* = 6.5 Hz, 2H, H₈ x 2) 1.42 – 1.23 (m, 4H, H₂ x 4).

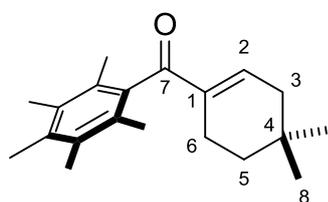
¹³C NMR (101 MHz, CDCl₃) δ 203.6, 145.4, 140.4, 138.4, 135.1, 132.7, 129.2, 40.7, 39.1, 38.3, 33.4, 24.5, 21.1, 17.6, 16.8, 16.1.

HRMS (ESI+): Found [M+H]⁺ = 311.2366; C₂₂H₃₁O requires 311.2369, Δ –1.09 ppm.

IR (film) ν_{max}/cm⁻¹ 2924, 2860, 1654, 1636, 1449, 138, 1268, 1192, 857.

m.p.: 90-92 °C.

(4,4-Dimethylcyclohex-1-en-1-yl)(2,3,4,5,6-pentamethylphenyl)methanone, **3ab**



Small scale reaction: 3,3-Dimethylpentane-1,5-diol⁴ (158.6 mg, 1.20 mmol, 2 eq.) was subjected to **General Procedure 1**. The title compound was afforded after purification by FCC (4% Et₂O/pentane) as a white solid (160 mg, 0.576 mmol, 96% yield).

Gram scale reaction: A 100 mL pressure tube was charged with 3,3-dimethylpentane-1,5-diol⁴ (1.59 g, 12.0 mmol, 2 eq.), 1-(2,3,4,5,6-pentamethylphenyl)ethan-1-one **1** (1.14 g, 6.00 mmol, 1 eq.), CataCXium® A (43 mg, 0.12 mmol, 2 mol%), [Ir(cod)Cl]₂ (20 mg, 0.030 mmol, 0.5 mol% dimer), KOH (1.43 g, 24.0 mmol, 4 eq.) and toluene (24 mL, 0.25 M). The reaction was heated at 115 °C for 24 hours. After cooling to RT, the reaction mixture was diluted with 3M aq. HCl (30 mL) and extracted with CH₂Cl₂ (4 x 50 mL). The combined organic phase was dried over MgSO₄, filtered and concentrated in vacuo. The title compound was afforded after purification by FCC (4% Et₂O/pentane) as a white solid (1.60 g, 5.64 mmol, 94% yield).

¹H NMR (400 MHz, CDCl₃) δ 6.43 (tt, *J* = 4.0, 1.5 Hz, 1H, H₂), 2.46 (tq, *J* = 6.5, 2.5 Hz, 2H, H₆ x 2), 2.23 (s, 3H, ArCH₃), 2.18 (s, 6H, ArCH₃ x 2), 2.01 (s, 6H, ArCH₃ x 2), 1.94 (dt, *J* = 4.5, 2.5 Hz, 2H, H₃ x 2), 1.48 (t, *J* = 6.5 Hz, 2H, H₅ x 2), 0.93 (s, 6H, H₈ x 6).

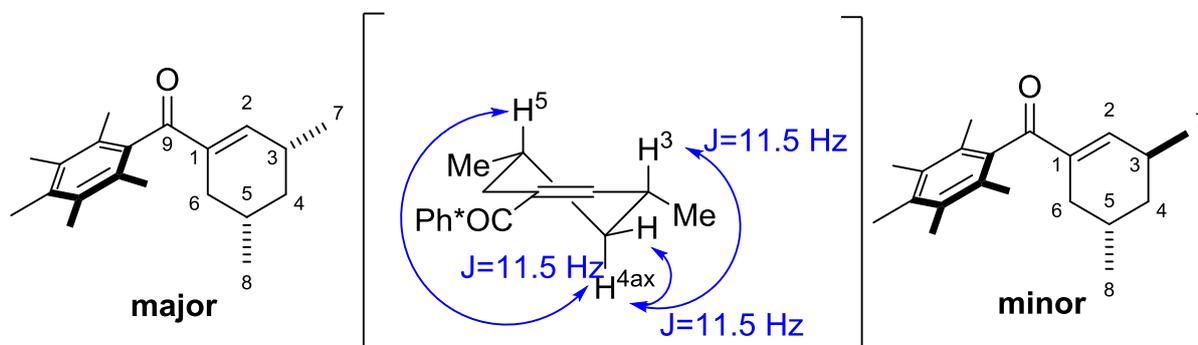
¹³C NMR (101 MHz, CDCl₃) δ 203.5, 145.0, 139.6, 138.4, 135.1, 132.7, 129.2, 40.3, 35.0, 28.9, 28.2, 20.4, 17.6, 16.8, 16.1.

HRMS (ESI+): Found [M+H]⁺ = 285.2213; C₂₀H₂₉O requires 285.2213, Δ –0.24 ppm.

IR (film) $\nu_{\max}/\text{cm}^{-1}$ 2961, 2922, 2866, 1651, 1636, 1424, 1170, 1129, 810.

m.p.: 110-112 °C.

(3,5-Dimethylcyclohex-1-en-1-yl)(2,3,4,5,6-pentamethylphenyl)methanone, 3ac



rac-(2*R*,4*S*)-2,4-Dimethylpentane-1,5-diol⁴ (192 mg, 1.20 mmol, 2 eq.) was subjected to **General Procedure 1**. The title compound was afforded after purification by FCC (2% Et₂O/pentane) as a white solid (104 mg, 0.366 mmol, 61% yield, inseparable diastereomeric mixture with 66:34 d.r). The relative stereochemistry was assigned by *J*-coupling constant analysis.

Major diastereomer: ¹H NMR (400 MHz, CDCl₃) δ 6.28 (td, *J* = 2.0, 1.0 Hz, 1H, H₂), 2.72 – 2.63 (m, 1H, H_{6a}), 2.47 – 2.31 (m, 1H, H₃), 2.24 (s, 3H, ArCH₃), 2.18 (s, 6H, ArCH₃ x 2), 2.01 (s, 6H, ArCH₃ x 2), 1.80 (ddd, *J* = 11.5, 4.0, 2.5 Hz, 1H, H_{4eq}), 1.78 – 1.66 (m, 2H, H₅, H_{6b}), 1.06 (d, *J* = 6.5 Hz, 3H, H₈ x 3), 0.96 (d, *J* = 7.0 Hz, 3H, H₇ x 3), 0.85 (q, *J* = 11.5 Hz, 1H, H_{4ax}).

¹³C NMR (101 MHz, CDCl₃) δ 204.0, 150.6, 139.8, 138.4, 135.0, 132.7, 129.3, 129.1, 40.1, 32.8, 31.2, 29.0, 22.2, 20.8, 17.7, 17.6, 16.8, 16.1. N.B. additional peaks for C₆Me₅ were observed due to restricted rotation about the Ar-C(O) axis.

Minor diastereomer: ¹H NMR (400 MHz, CDCl₃) δ 6.38 (td, *J* = 4.0, 2.0 Hz, 1H, H₂), 2.66 – 2.55 (m, 1H, H_{6a}), 2.47 – 2.38 (m, 1H, H₃), 2.24 (s, 3H, ArCH₃), 2.18 (s, 6H, ArCH₃ x 2), 2.01 (s, 6H, ArCH₃ x 2), 1.96 – 1.83 (m, 2H, H₅, H_{6b}), 1.49 – 1.39 (m, 2H, H₄ x 2), 1.03 (d, *J* = 6.5 Hz, 3H, H₈ x 3), 0.99 (d, *J* = 7.0 Hz, 3H, H₇ x 3).

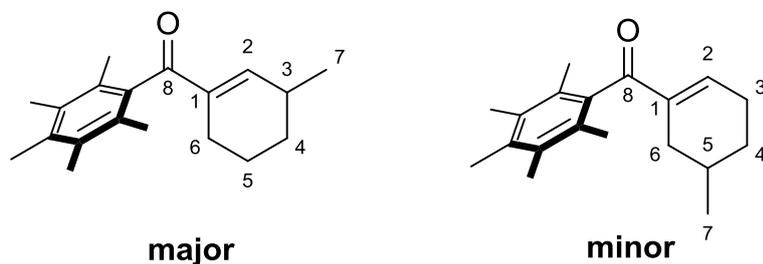
¹³C NMR (101 MHz, CDCl₃) δ 204.1, 150.1, 139.0, 138.4, 135.0, 132.7, 129.3, 129.2, 37.2, 30.6, 29.7, 24.4, 21.2, 20.4, 17.6, 17.6, 16.8, 16.1. N.B. additional peaks for C₆Me₅ were observed due to restricted rotation about the Ar-C(O) axis.

HRMS (ESI⁺): Found [M+H]⁺ = 285.2210; C₂₀H₂₉O requires 285.2213, Δ –0.99 ppm.

IR (film) $\nu_{\max}/\text{cm}^{-1}$ 2953, 2925, 1652, 1630, 1455, 1380, 1308, 1268, 1182, 1026, 699.

m.p.: 103-105 °C.

(3-Methylcyclohex-1-en-1-yl) (2,3,4,5,6-pentamethylphenyl)methanone, 3ad



2-Methylpentane-1,5-diol⁴ (142 mg, 1.20 mmol, 2 eq.) was subjected to **General Procedure 1**. The title compound was afforded after purification by FCC (4% Et₂O/pentane) as a white solid (143 mg, 0.528 mmol, 88% yield, inseparable regioisomeric mixture 78:22 of **A:B**).

Major regioisomer 3ad: ¹H NMR (400 MHz, CDCl₃) δ 6.37 – 6.29 (m, 1H, H₂), 2.53 – 2.40 (m, 1H, H_{6a}), 2.38 – 2.15 (m, 11H, H₃, H_{6b}, ArCH₃ x 3), 2.01 (s, 6H, ArCH₃ x 2), 1.92 – 1.77 (m, 2H, H_{4a}, H_{5a}), 1.67 – 1.49 (m, 1H, H_{4b}), 1.32 – 1.15 (m, 1H, H_{5b}), 0.97 (d, *J* = 7.0 Hz, 3H, H₇ x 3).

¹³C NMR (101 MHz, CDCl₃) δ 204.1, 150.7, 139.8, 138.3, 135.0, 132.7, 129.3, 129.2, 31.3, 30.5, 22.6, 20.9, 20.6, 17.6, 17.6, 16.8, 16.1. N.B. additional peaks for C₆Me₅ were observed due to restricted rotation about the Ar-C(O) axis.

Diagnostic peaks for minor regioisomer 3ad-minor: ¹H NMR (400 MHz, CDCl₃) δ 6.50 – 6.45 (m, 1H, H₂), 2.74 – 2.62 (m, 1H, H_{6a}), 1.77 – 1.66 (m, 1H, H_{5a} or H_{4a}), 1.06 (d, *J* = 6.4 Hz, 3H, H₇ x 3).

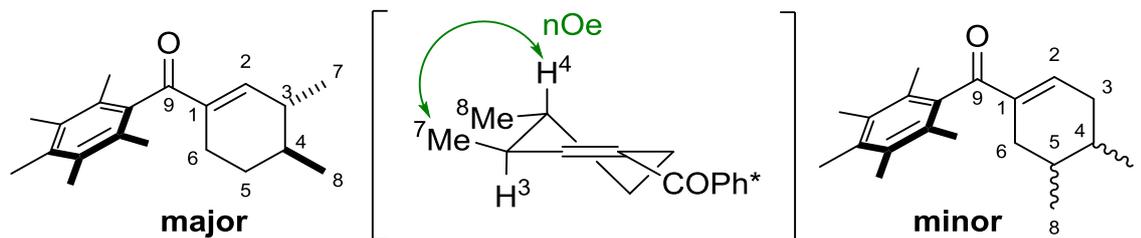
¹³C NMR (101 MHz, CDCl₃) δ 145.2, 140.3, 21.6.

HRMS (ESI⁺): Found [M+H]⁺ = 271.2054; C₁₉H₂₇O requires 271.2056, Δ –0.95 ppm.

IR (film) ν_{max}/cm⁻¹ 2926, 2856, 1654, 1634, 1455, 1308, 1268, 1192.

m.p.: 96-98 °C.

(3,4-dimethylcyclohex-1-en-1-yl)(2,3,4,5,6-pentamethylphenyl)methanone, 3ae



2,3-Dimethylpentane-1,5-diol⁴ (159 mg, 1.20 mmol, 2 eq.) was subjected to **General Procedure 1**. The title compound was afforded after purification by FCC (3 → 4% Et₂O/pentane) as a white solid (154 mg, 0.540 mmol, 90% yield, 64:36 inseparable mixture of regioisomers **A:B**; major regioisomer **A** >95:5 d.r., minor regioisomer **B** 52:48 d.r.). The relative stereochemistry of the major regioisomer was assigned by nOe analysis.

Major regioisomer 3ae-major: ¹H NMR (400 MHz, CDCl₃) δ 6.27 (dt, *J* = 3.0, 1.0 Hz, 1H, H₂), 2.63 – 2.52 (m, 1H, H_{6a}), 2.38 – 2.26 (m, 1H, H_{6b}), 2.24 (s, 3H, ArCH₃), 2.19 (s, 6H, ArCH₃ x 2), 2.02 (s, 6H, ArCH₃ x 2), 1.95 – 1.77 (m, 2H, H₃, H_{5a}), 1.37 – 1.22 (m, 2H, H₄, H_{5b}), 1.01 (d, *J* = 6.0 Hz, 3H, H₈ x 3), 0.99 (d, *J* = 7.0 Hz, 3H, H₇ x 3).

¹³C NMR (101 MHz, CDCl₃) δ 203.9, 150.6, 139.5, 138.4, 135.0, 132.6, 129.2, 129.1, 38.7, 35.3, 30.0, 22.4, 20.1, 19.0, 17.6, 17.5, 16.8, 16.1. N.B. additional peaks for C₆Me₅ were observed due to restricted rotation about the Ar-C(O) axis.

Diagnostic peaks for minor regioisomer 3ae-minor: ¹H NMR (400 MHz, CDCl₃) δ 6.45 – 6.41 (m, 1H, H₂), 6.39 – 6.36 (m, 1H, H_{2'}), 2.74 – 2.65 (m, 1H, H₆ or H_{6'}), 1.04 (d, *J* = 6.0 Hz, 3H, CH₃ or CH_{3'}), 0.92 – 0.84 (m, 6H, CH₃ x 2 or CH_{3'} x 2).

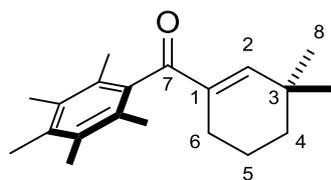
¹³C NMR (101 MHz, CDCl₃) δ 204.0, 203.6, 150.7, 145.0, 35.1, 31.0, 19.5, 19.3, 16.5, 14.7.

IR (film) ν_{max} /cm⁻¹ 2954, 2925, 2872, 1653, 1636, 1455, 1383, 1306, 1266, 1192, 854.

HRMS (ESI⁺): Found [M+H]⁺ = 285.2209; C₂₀H₂₉O requires 285.2213, Δ -1.32 ppm.

m.p.: 98-100 °C.

(3,3-Dimethylcyclohex-1-en-1-yl)(2,3,4,5,6-pentamethylphenyl)methanone, 3af



2,2-Dimethylpentane-1,5-diol⁴ (158 mg, 1.20 mmol, 2 eq.) was subjected to **General Procedure 1**. The title compound was afforded after purification by FCC (2% → 3% Et₂O/pentane) as a white solid (128 mg, 0.450 mmol, 75% yield).

¹H NMR (400 MHz, CDCl₃) δ 6.19 (t, *J* = 2.0 Hz, 1H, H₂), 2.36 (td, *J* = 6.5, 2.0 Hz, 2H, H₆ x 2), 2.25 (s, 3H, ArCH₃), 2.18 (s, 6H, ArCH₃ x 2), 2.00 (s, 6H, ArCH₃ x 2), 1.76 – 1.66 (m, 2H, H₅ x 2), 1.52 – 1.44 (m, 2H, H₄ x 2), 0.97 (s, 6H, H₈ x 6).

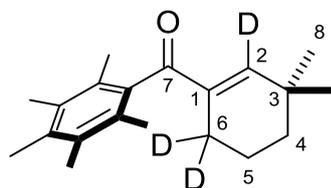
¹³C NMR (101 MHz, CDCl₃) δ 204.2, 154.2, 138.4, 138.2, 135.0, 132.7, 129.3, 36.8, 33.0, 28.9, 22.8, 19.3, 17.5, 16.8, 16.1.

HRMS (ESI⁺): Found [M+H]⁺ = 285.2211; C₂₀H₂₉O requires 285.2213, Δ –0.61 ppm.

IR (film) ν_{max}/cm⁻¹ 2954, 1651, 1631, 1456, 699.

m.p.: 129-130 °C.

(3,3-Dimethylcyclohex-1-en-1-yl-2,6,6-d₃)(2,3,4,5,6-pentamethylphenyl)methanone, d₃-3af



2,2-Dimethylpentane-1,1,5,5-d₄-1,5-diol **d₄-2af** (164 mg, 1.20 mmol, 2 eq.) was subjected to **General Procedure 1**. The title compound was afforded after purification by FCC (2% → 3% Et₂O/pentane) as a white solid (130 mg, 0.450 mmol, 75% yield).

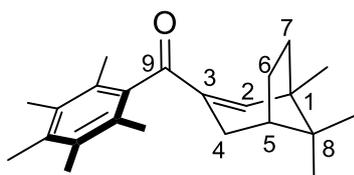
¹H NMR (700 MHz, CDCl₃) δ 2.24 (s, 3H, ArCH₃), 2.18 (s, 6H, ArCH₃ x 2), 2.00 (s, 6H, ArCH₃ x 2), 1.78 – 1.62 (m, 2H, H₅ x 2), 1.54 – 1.38 (m, 2H, H₄ x 2), 0.96 (s, 6H, H₈ x 6). [N.B. in the absence of any deuteration, the integral for H₂ (δ = 6.19 ppm) would be 1.00, and the integral for H₆ (δ = 2.36 ppm) would be 2.00. The measured integral by quantitative ¹H NMR was for H₂ was 0.03 and for H₆ was <0.10 (n.b. peak overlaps with ¹³C satellite peak for ArCH₃ peak), thus indicating 0.97 D at H₂ and >1.90 D at H₆, i.e. >95% D at each position].

^{13}C NMR (101 MHz, CDCl_3) δ 203.9, 154.0 (1:1:1 triplet, 23.5 Hz), 138.4, 138.0, 135.1, 132.7, 129.3, 36.7, 32.9, 28.9, 22.2 (1:2:3:2:1 quintet, $J=22.0$ Hz), 19.1, 17.5, 16.8, 16.1.

^2H NMR (92 MHz, CHCl_3) δ 6.19, (s, $^2\text{H}_2$), 2.32 (s, $^2\text{H}_6 \times 2$).

Apart from deuterium incorporation at C2 and C6, the spectral data of **d₃-2af** was consistent with that of **2af** (see data above for **2af** and also spectra).

(2,3,4,5,6-Pentamethylphenyl)((1S,5S)-1,8,8-trimethylbicyclo[3.2.1]oct-2-en-3-yl)methanone, 3ag



((1*R*,3*S*)-1,2,2-Trimethylcyclopentane-1,3-diyl)dimethanol⁴ (207 mg, 1.20 mmol, 2 eq.) was subjected to **General Procedure 1**, heating for 48 h instead of 24 h. The title compound was afforded after purification by FCC (3→5% Et_2O /pentane) as a white solid (145 mg, 0.282 mmol, 47% yield, 1:1 inseparable mixture with Ph*COMe **1**).

^1H NMR (CDCl_3 , 400 MHz) δ = 6.28 (1H, s, H_2), 2.67-2.58 (1H, m, H_{4a}), 2.38-2.30 (1H, m, H_{4b}), 2.24 (3H, s, ArCH_3), 2.20 (3H, s, ArCH_3), 2.18 (3H, s, ArCH_3), 2.06–1.92 (8H, m, $\text{ArCH}_3 \times 2$, H_{6a} and H_5), 1.82 – 1.67 (2H, m, $\text{H}_7 \times 2$), 1.34 (1H, ddd, $J = 13.0, 9.0, 6.0$ Hz, H_{6b}), 0.94 (3H, s, CH_3), 0.92 (3H, s, CH_3), 0.90 (3H, s, CH_3).

^{13}C NMR (CDCl_3 , 101 MHz) δ = 203.9, 156.9, 138.2, 137.4, 135.0, 132.7, 132.6, 129.2, 129.0, 46.0, 43.7, 42.5, 40.8, 32.3, 29.0, 23.4, 19.3, 17.9, 17.5, 17.5, 16.8, 16.1. N.B. additional peaks for C_6Me_5 were observed due to restricted rotation about the Ar-C(O) axis.

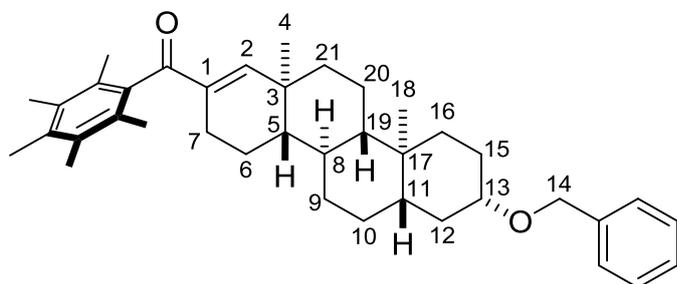
HRMS (ESI⁺): Found $[\text{M}+\text{H}]^+ = 325.2522$; $\text{C}_{23}\text{H}_{33}\text{O}$ requires 325.2526, Δ -1.31 ppm.

IR (film) $\nu_{\text{max}}/\text{cm}^{-1}$ 2947, 1865, 1650, 1628, 1445, 1389, 1307, 1272, 1166, 865.

m.p.: 58–60 °C.

$[\alpha]_{\text{D}}^{25} = -45.6$ ($c=1.0$, CHCl_3).

((4a*S*,4b*S*,6a*S*,8*S*,10a*S*,10b*S*,12a*S*)-8-(Benzyloxy)-10a,12a-dimethyl-3,4,4a,4b,5,6,6a,7,8,9,10,10a,10b,11,12,12a-hexadecahydrochrysen-2-yl)(2,3,4,5,6-pentamethylphenyl)methanone, **3ah**



A 1 dram vial was charged with CataCXium® A (0.7 mg, 0.002 mmol, 2 mol%), diol **2ah** (80 mg, 0.20 mmol, 2 eq.), 1-(2,3,4,5,6-pentamethylphenyl)ethan-1-one **1** (19 mg, 0.10 mmol, 1 eq.), [Ir(COD)Cl]₂ (0.3 mg, 0.0005 mmol, 0.5 mol% dimer), KOH (22 mg, 0.40 mmol, 4 eq.) and toluene (0.4 mL, 0.25 M). The vial was then sealed and heated at 115 °C for 24 hours. After cooling to RT, the reaction mixture was diluted with aq. HCl (3 M, 5 mL) and extracted with CH₂Cl₂ (4 x 10 mL). The title compound was afforded after purification by FCC (7→10% Et₂O/pentane) as a white solid (28 mg, 0.051 mmol, 51% yield).

¹H NMR (CDCl₃, 400 MHz) δ 7.38 – 7.24 (m, 5H, 5 x ArCH), 6.18 (t, *J* = 1.6 Hz, 1H, H₂), 4.60 – 4.51 (m, 2H, H_{14a} and H_{14b}), 3.34 (tt, *J* = 11.1, 4.6 Hz, 1H, H₁₃), 2.62 (dd, *J* = 18.2, 6.4 Hz, 1H, H_{7a}), 2.34 – 2.11 (m, 10H, 3 x ArCH₃ and H_{7b}), 2.04 – 1.88 (m, 9H, 2 x ArCH₃ and 3 x H_{aliph}), 1.78 – 1.67 (m, 2H, 2 x H_{aliph}), 1.59 – 1.14 (m, 10H, 10 x H_{aliph}), 1.10 – 0.76 (m, 10H, 2 x Me and 4 x H_{aliph}), 0.70 (ddd, *J*=12.1, 10.5, 4.0, 1H, H_{aliph}).

¹³C NMR (CDCl₃, 101 MHz) δ 204.5, 155.8, 139.3, 138.4, 137.2, 135.0, 132.6, 132.6, 129.3, 129.2, 128.5, 127.7, 127.5, 78.0, 69.9, 54.5, 48.0, 44.6, 38.2, 36.9, 36.2, 35.8, 34.8, 34.8, 31.1, 28.9, 28.4, 23.8, 20.5, 20.0, 18.8, 17.7, 17.6, 16.8, 16.1, 12.4. N.B. additional peaks for C₆Me₅ were observed due to restricted rotation about the Ar-C(O) axis.

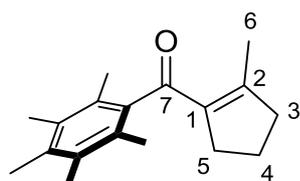
HRMS (ESI⁺): Found [M+H]⁺ = 553.4038; C₃₉H₅₃O₂ requires 553.4040, Δ -0.36 ppm.

IR (film) ν_{max}/cm⁻¹ 2934, 1649, 1634, 1453, 1383, 1365, 1186, 1101, 1071, 911, 731.

m.p.: 77-80 °C.

[α]_D²⁵ = +68.9 (c=1.0, CHCl₃).

(2-Methylcyclopent-1-en-1-yl)(2,3,4,5,6-pentamethylphenyl)methanone, 3ai



Commercially available 1,4-pentandiol (125 mg, 1.2 mmol, 2 eq.) was subjected to **General Procedure 1**. The title compound was afforded after purification by FCC (5% Et₂O/pentane) as a white solid (58 mg, 0.088 mmol, 15% yield, 32:68 inseparable mixture with Ph*COMe **1**).

¹H NMR (400 MHz, CDCl₃) δ 2.61 (ddq, *J* = 9.5, 6.0, 2.0 Hz, 2H, H₅ x 2), 2.52 – 2.43 (m, 2H, H₃ x 2), 2.17 – 1.99 (m, 9H, ArCH₃ x 3), 1.97 (s, 6H, ArCH₃ x 2), 1.74 (p, *J* = 8.0 Hz, 2H, H₄ x 2), 1.53 – 1.42 (m, 3H, H₆ x 3).

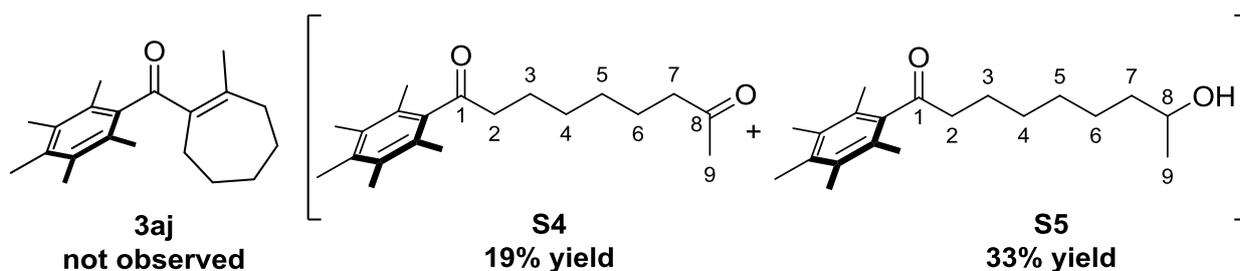
¹³C NMR (101 MHz, CDCl₃) δ 200.6, 156.9, 140.8, 137.6, 135.0, 133.0, 128.0, 42.3, 33.5, 21.1, 17.1, 16.8, 16.1, 16.0.

HRMS (ESI⁺): Found [M+H]⁺ = 257.1900; C₁₈H₂₅O requires 257.1900, Δ -0.15 ppm.

IR (film) ν_{max}/cm⁻¹ 2982, 2860, 1696, 1614, 1416, 1350, 1167, 949.

m.p.: 72-74 °C.

(2-Methylcyclohept-1-en-1-yl)(2,3,4,5,6-pentamethylphenyl)methanone, 3aj



Heptane-1,6-diol **2aj** (79 mg, 0.6 mmol, 2 eq.) was subjected to **General Procedure 1**. The title compound was not observed. Purification by FCC (5 → 40% Et₂O/pentane) afforded 1-(2,3,4,5,6-pentamethylphenyl)nonane-1,8-dione **S4** as a colourless oil (17 mg, 0.056 mmol, 19% yield), 8-hydroxy-1-(2,3,4,5,6-pentamethylphenyl)nonan-1-one **S5** as a colourless oil (32 mg, 0.10 mmol, 33% yield) and 1-(2,3,4,5,6-pentamethylphenyl)ethan-1-one **1** as a white solid (18 mg, 0.094 mmol, 32% yield).

Data for 1-(2,3,4,5,6-pentamethylphenyl)nonane-1,8-dione, S4:

^1H NMR (400 MHz, CDCl_3) δ 2.66 (t, $J = 7.5$ Hz, 2H, $\text{H}_2 \times 2$), 2.43 (t, $J = 7.5$ Hz, 2H, $\text{H}_7 \times 2$), 2.23 (s, 3H, $\text{H}_9 \times 3$), 2.18 (s, 6H, $\text{ArCH}_3 \times 2$), 2.13 (s, 3H, ArCH_3), 2.09 (s, 6H, $\text{ArCH}_3 \times 2$), 1.71 (p, $J = 7.5$ Hz, 2H, $\text{H}_3 \times 2$), 1.59 (p, $J = 7.5$ Hz, 2H, $\text{H}_6 \times 2$), 1.42 – 1.26 (m, 4H, $\text{H}_4 \times 2$, $\text{H}_5 \times 2$).

^{13}C NMR (101 MHz, CDCl_3) δ 212.6, 209.3, 140.9, 135.5, 133.2, 127.4, 45.7, 43.8, 29.8, 29.2, 29.1, 23.8, 23.2, 17.3, 16.8, 16.1.

HRMS (ESI+): Found $[\text{M}+\text{Na}]^+ = 325.2138$; $\text{C}_{20}\text{H}_{30}\text{O}_2\text{Na}$ requires 325.2138, Δ 0.01 ppm.

IR (film) $\nu_{\text{max}}/\text{cm}^{-1}$ 2923, 2851, 1701, 1463, 1407, 1260, 1166, 1120.

Data for 8-hydroxy-1-(2,3,4,5,6-pentamethylphenyl)nonan-1-one, S5:

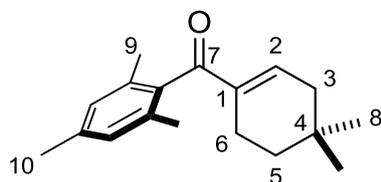
^1H NMR (400 MHz, CDCl_3) δ 3.87 – 3.69 (m, 1H, H_8), 2.67 (t, $J = 7.5$ Hz, 2H, $\text{H}_2 \times 2$), 2.23 (s, 3H, ArCH_3), 2.18 (s, 6H, $\text{ArCH}_3 \times 2$), 2.09 (s, 6H, $\text{ArCH}_3 \times 2$), 1.78 – 1.65 (m, 2H, $\text{H}_3 \times 2$), 1.65 – 1.23 (m, 9H, OH, $\text{H}_4 \times 2$, $\text{H}_5 \times 2$, $\text{H}_6 \times 2$ and $\text{H}_7 \times 2$), 1.19 (d, $J = 6.0$ Hz, 3H, $\text{H}_9 \times 3$).

^{13}C NMR (101 MHz, CDCl_3) δ 212.3, 141.0, 135.4, 133.2, 127.4, 67.6, 45.7, 39.4, 29.7, 29.3, 25.8, 23.6, 23.3, 17.3, 16.8, 16.1.

HRMS (ESI+): Found $[\text{M}+\text{H}]^+ = 305.2477$; $\text{C}_{20}\text{H}_{33}\text{O}_2$ requires 305.2475, Δ 0.57 ppm.

IR (film) $\nu_{\text{max}}/\text{cm}^{-1}$ 3425, 2941, 2860, 1693, 1456, 1377, 1303, 1127, 939.

(4,4-Dimethylcyclohex-1-en-1-yl)(mesityl)methanone, 3ak



A 2–5 mL Biotage[®] microwave vial was charged with CataCXium[®] A (2.2 mg, 0.006 mmol, 2 mol%), 3,3-dimethylpentane-1,5-diol (79 mg, 0.6 mmol, 2 eq.), 2-acetylmesitylene (49 mg, 0.3 mmol, 1 eq.), $[\text{Ir}(\text{cod})\text{Cl}]_2$ (1 mg, 0.0015 mmol, 0.5 mol% dimer), KOH (67 mg, 1.2 mmol, 4 eq.) toluene (1.2 mL, 0.25 M). The reaction vessel was sealed with a microwave vial cap (containing a Reseal[™] septum) and the vial was heated at 115 °C for 24 hours. After cooling to RT, the reaction mixture was filtered through a silica plug, eluting with diethyl ether, and concentrated in vacuo. The title compound was afforded after purification by FCC (3% Et_2O /pentane) as a colourless oil (66 mg, 0.257 mmol, 86% yield).

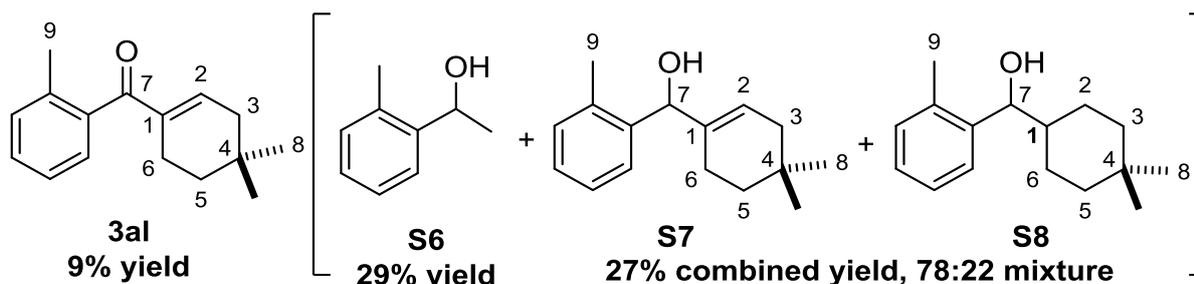
^1H NMR (400 MHz, CDCl_3) δ 6.82 (s, 2H, $\text{ArCH} \times 2$), 6.43 (tt, $J = 4.0, 1.5$ Hz, 1H, H_2), 2.44 (tq, $J = 6.0, 2.0$ Hz, 2H, $\text{H}_6 \times 2$), 2.28 (s, 3H, $\text{H}_{10} \times 3$), 2.10 (s, 6H, $\text{H}_9 \times 6$), 1.95 (dt, $J = 4.5, 2.5$ Hz, 2H, $\text{H}_3 \times 2$), 1.48 (t, $J = 6.5$ Hz, 2H, $\text{H}_5 \times 2$), 0.93 (s, 6H, $\text{H}_8 \times 6$).

^{13}C NMR (101 MHz, CDCl_3) δ 202.1, 144.6, 139.3, 137.9, 137.7, 134.2, 128.1, 40.3, 34.9, 28.8, 28.2, 21.2, 20.4, 19.3.

HRMS (ESI⁺): Found $[\text{M}+\text{H}]^+ = 257.1901$; $\text{C}_{18}\text{H}_{25}\text{O}$ requires 257.1900, Δ 0.28 ppm.

IR (film) $\nu_{\text{max}}/\text{cm}^{-1}$ 2950, 2921, 2864, 1651, 1635, 1611, 1433, 1259, 1165, 1101, 848.

(4,4-Dimethylcyclohex-1-en-1-yl)(*o*-tolyl)methanone, **3al**



A 2–5 mL Biotage[®] microwave vial was charged with CataCXium[®] A (2.2 mg, 0.006 mmol, 2 mol%), 3,3-dimethylpentane-1,5-diol⁴ (79 mg, 0.6 mmol, 2 eq.), *o*-methylacetophenone (40 mg, 0.3 mmol, 1 eq.), $[\text{Ir}(\text{cod})\text{Cl}]_2$ (1 mg, 0.0015 mmol, 0.5 mol% dimer), KOH (67 mg, 1.2 mmol, 4 eq.) toluene (1.2 mL, 0.25 M). The reaction vessel was sealed with a microwave vial cap (containing a Reseal[™] septum) and the vial was heated at 115 °C for 24 hours. After cooling to RT, the reaction mixture was filtered through a silica plug, eluting with diethyl ether, and concentrated in vacuo. Purification by FCC (3-15% Et_2O /pentane) afforded (4,4-dimethylcyclohex-1-en-1-yl)(*o*-tolyl)methanone **3al** as a colourless oil (6 mg, 0.026 mmol, 9% yield), 1-(*o*-tolyl)ethan-1-ol **S6** as a colourless oil (12 mg, 0.088 mmol, 29% yield), and an inseparable mixture of (4,4-dimethylcyclohex-1-en-1-yl)(*o*-tolyl)methanol **S7** and (4,4-dimethylcyclohexyl)(*o*-tolyl)methanol **S8** as a colourless oil (19 mg, 0.081 mmol, 27% yield, 78:22 **S7**:**S8**). The spectral data for **S6** matched that reported in the literature.¹⁰

Data for (4,4-dimethylcyclohex-1-en-1-yl)(*o*-tolyl)methanone, **3al**:

^1H NMR (400 MHz, CDCl_3) δ 7.32 – 7.27 (m, 1H, ArCH), 7.22 – 7.13 (m, 3H, ArCH x 3), 6.41 (tt, $J = 4.0, 1.5$ Hz, 1H, H_2), 2.45 (ttd, $J = 6.5, 2.5, 1.5$ Hz, 2H, H_6 x 2), 2.26 (s, 3H, H_9 x 3), 1.99 (dt, $J = 5.0, 2.5$ Hz, 2H, H_3 x 2), 1.48 (t, $J = 6.5$ Hz, 2H, H_5 x 2), 0.95 (s, 6H, H_8 x 6).

^{13}C NMR (101 MHz, CDCl_3) δ 200.3, 145.7, 140.0, 139.0, 135.7, 130.6, 129.3, 127.6, 125.1, 40.4, 35.0, 28.8, 28.3, 20.9, 19.7.

HRMS (ESI⁺): Found $[\text{M}+\text{H}]^+ = 229.1589$; $\text{C}_{16}\text{H}_{21}\text{O}$ requires 229.1587, Δ 0.73 ppm.

IR (film) $\nu_{\text{max}}/\text{cm}^{-1}$ 2952, 2924, 1651, 1634, 1455, 1380, 1260, 1098, 759, 732.

Data for (4,4-dimethylcyclohex-1-en-1-yl)(*o*-tolyl)methanol, S7:

^1H NMR (400 MHz, CDCl_3) δ 7.47 (dd, $J = 7.5, 1.5$ Hz, 1H, ArCH), 7.25 – 7.10 (m, 3H, ArCH x 3), 5.75 – 5.66 (m, 1H, H_2), 5.28 (s, 1H, H_7), 2.30 (s, 3H, H_9 x 3), 2.01 – 1.71 (m, 4H, H_3 x 2, H_6 x 2), 1.35 (t, $J = 6.5$ Hz, 2H, H_5 x 2), 0.90 (s, 3H, H_{8a} x 3), 0.85 (s, 3H, H_{8b} x 3).

^{13}C NMR (101 MHz, CDCl_3) δ 140.5, 137.3, 135.6, 130.4, 127.3, 126.0, 126.0, 123.4, 74.8, 39.2, 35.5, 28.9, 28.6, 28.1, 22.8, 19.3.

HRMS (ESI+): Found $[\text{M}+\text{H}]^+ = 231.1745$; $\text{C}_{16}\text{H}_{23}\text{O}$ requires 231.1743, Δ 0.83 ppm.

IR (film) $\nu_{\text{max}}/\text{cm}^{-1}$ 3346, 2948, 2908, 1459, 1383, 1054, 1008, 988, 782, 735.

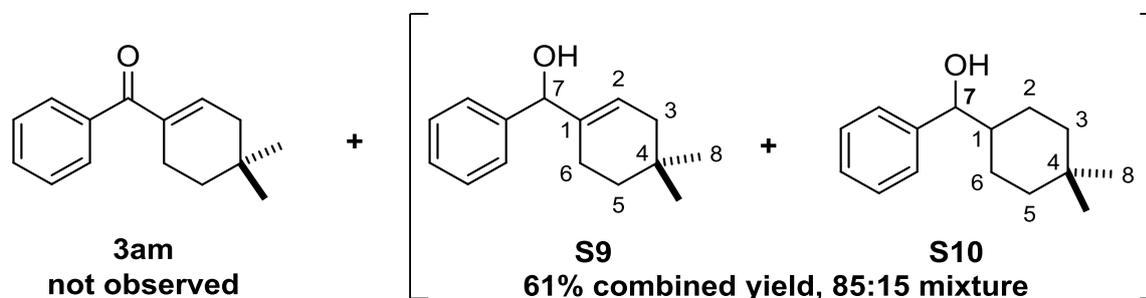
Data for (4,4-dimethylcyclohexyl)(*o*-tolyl)methanol, S8:

^1H NMR (400 MHz, CDCl_3) δ 7.41 (dd, $J = 7.5, 1.5$ Hz, 1H, ArCH), 7.25 – 7.07 (m, 3H, ArCH x 3), 4.69 (d, $J = 7.0$ Hz, 1H, H_7), 2.35 (s, 3H, H_9 x 3), 1.63 – 1.50 (m, 1H, H_1) 1.48 – 1.04 (m, 8H, H_2 x 2, H_3 x 2, H_5 x 2, H_6 x 2), 0.89 (s, 3H, H_{8a} x 3), 0.88 (s, 3H, H_{8b} x 3).

^{13}C NMR (101 MHz, CDCl_3) δ 142.2, 135.2, 130.4, 127.2, 126.4, 126.2, 75.1, 44.7, 39.2, 39.0, 33.1, 30.1, 25.5, 24.4, 24.4, 19.6.

HRMS (ESI+): Found $[\text{M}+\text{H}]^+ = 233.1901$; $\text{C}_{16}\text{H}_{25}\text{O}$ requires 233.1900, Δ 0.61 ppm.

(4,4-Dimethylcyclohex-1-en-1-yl)(phenyl)methanone, 3am



A 2–5 mL Biotage[®] microwave vial was charged with CataCXium[®] A (2.2 mg, 0.006 mmol, 2 mol%), 3,3-dimethylpentane-1,5-diol (79 mg, 0.6 mmol, 2 eq.), acetophenone (36 mg, 0.3 mmol, 1 eq.), $[\text{Ir}(\text{cod})\text{Cl}]_2$ (1 mg, 0.0015 mmol, 0.5 mol% dimer), KOH (67 mg, 1.2 mmol, 4 eq.) toluene (1.2 mL, 0.25 M). The reaction vessel was sealed with a microwave vial cap (containing a Reseal[™] septum) and the vial was heated at 115 °C for 24 hours. After cooling to RT, the reaction mixture was filtered through a silica plug, eluting with diethyl ether, and concentrated in vacuo. Purification by FCC (3-15% Et_2O /pentane) afforded an inseparable mixture of (4,4-dimethylcyclohex-1-en-1-yl)(phenyl)methanol **S9** and (4,4-

dimethylcyclohexyl)(phenyl)methanol **S10** as a colourless oil (85:15 mixture **S9:S10**, 40 mg, 0.183 mmol, 61% yield).

Data for (4,4-dimethylcyclohex-1-en-1-yl)(phenyl)methanol, S9:

^1H NMR (400 MHz, CDCl_3) δ 7.39 – 7.20 (m, 5H, ArCH x 5), 5.92 – 5.75 (m, 1H, H_2), 5.16 – 5.06 (m, 1H, H_7), 1.96 – 1.69 (m, 4H, H_3 x 2, H_6 x 2), 1.32 (t, $J = 6.5$ Hz, 2H, H_5 x 2) 0.89 (s, 3H, CH_3 , H_{8a} x 3), 0.85 (s, 3H, CH_3 , H_{8b} x 3).

^{13}C NMR (101 MHz, CDCl_3) δ 142.8, 138.3, 128.4, 127.4, 126.4, 122.6, 78.1, 39.2, 35.4, 28.9, 28.6, 28.1, 22.0.

HRMS (ESI+): Found $[\text{M}+\text{H}]^+ = 217.1587$; $\text{C}_{15}\text{H}_{21}\text{O}$ requires 217.1587, Δ 0.17 ppm.

IR (film) $\nu_{\text{max}}/\text{cm}^{-1}$ 3356, 2948, 2908, 1451, 1052, 1007, 760, 700.

Data for (4,4-dimethylcyclohexyl)(phenyl)methanol, S10:

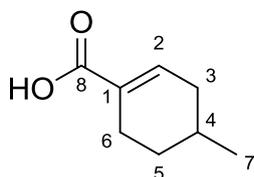
^1H NMR (400 MHz, CDCl_3) δ 7.39 – 7.20 (m, 5H, ArCH x 5), 4.39 (dd, $J = 7.5, 2.0$ Hz, 1H, H_7), 1.57 – 1.47 (m, 1H, H_1), 1.46 – 1.01 (m, 8H, H_2 x 2, H_3 x 2, H_5 x 2, H_6 x 2), 0.96 (s, 3H, CH_3 , H_{8a} x 3), 0.88 (s, 3H, CH_3 , H_{8b} x 3).

^{13}C NMR (101 MHz, CDCl_3) δ 143.9, 128.4, 127.6, 126.7, 79.4, 45.1, 39.0, 38.9, 33.0, 30.1, 25.3, 24.7, 24.4.

HRMS (ESI+): Found $[\text{M}+\text{H}]^+ = 219.1744$; $\text{C}_{15}\text{H}_{23}\text{O}$ requires 219.1743, Δ 0.24 ppm.

4.3 Derivatization of Acyl Cyclohexenes

4-Methylcyclohex-1-ene-1-carboxylic acid, **6**



(4-Methylcyclohex-1-en-1-yl)(2,3,4,5,6-pentamethylphenyl)methanone **3w** (27.4 mg, 0.100 mmol, 1 eq.) was subjected to **General Procedure 2**. The title compound was afforded after purification by FCC (2 → 5% MeOH/CH₂Cl₂) as a white solid (14.2 mg, 0.100 mmol, 100% yield).

¹H NMR (400 MHz, CDCl₃) δ 10.35 (s, 1H, OH), 7.09 (dtd, *J* = 5.0, 2.5, 1.0 Hz, 1H, H₂), 2.47 – 2.26 (m, 2H, H_{6a}, H_{3a}), 2.26 – 2.11 (m, 1H, H_{6b}), 1.88 – 1.74 (m, 2H, H_{3b}, H_{5a}), 1.73 – 1.59 (m, 1H, H₄), 1.31 – 1.16 (m, 1H, H_{5b}), 0.98 (d, *J* = 6.5 Hz, 3H, H₇ x 3).

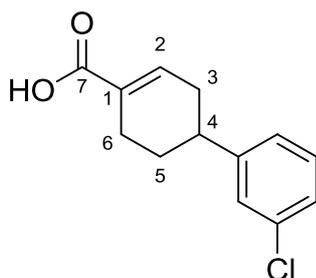
¹³C NMR (101 MHz, CDCl₃) δ 173.1, 142.2, 129.6, 34.5, 30.4, 27.6, 23.9, 21.5.

HRMS (ESI⁻): Found [M-H]⁻ = 139.0764 ; C₈H₁₁O₂ requires 139.0765, Δ -0.72 ppm.

IR (film) ν_{max}/cm⁻¹ 2922, 2860, 1674, 1638, 1421, 1227, 738, 705.

m.p.: 104-106 °C.

3'-Chloro-1,2,3,6-tetrahydro-[1,1'-biphenyl]-4-carboxylic acid, **7**



(3'-Chloro-1,2,3,6-tetrahydro-[1,1'-biphenyl]-4-yl)(2,3,4,5,6-pentamethylphenyl)methanone **3y** (37 mg, 0.10 mmol, 1 eq.) was subjected to **General Procedure 2**. The title compound was afforded after purification by FCC (1% MeOH/CH₂Cl₂) as a white solid (20 mg, 0.084 mmol, 84% yield).

¹H NMR (400 MHz, CDCl₃) δ, 10.5 (s, 1H, OH), 7.21 – 7.10 (m, 4H, ArCH x 3, H₂), 7.03 (dt, *J* = 7.5, 1.5 Hz, 1H, ArCH), 2.81 – 2.63 (m, 1H, H₄), 2.56 – 2.38 (m, 2H, H_{3a}, H_{6a}), 2.36 – 2.16 (m, 2H, H_{3b}, H_{6b}), 2.03 – 1.89 (m, 1H, H_{5a}), 1.79 – 1.59 (m, 1H, H_{5b}).

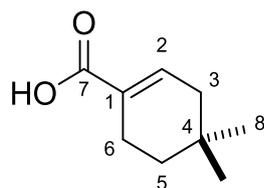
^{13}C NMR (101 MHz, CDCl_3) δ 172.3, 148.0, 141.4, 134.5, 130.0, 129.8, 127.2, 126.7, 125.2, 39.0, 33.8, 29.3, 24.5.

HRMS (ESI⁻): Found $[\text{M}-\text{H}]^- = 235.0531$; $\text{C}_{13}\text{H}_{12}\text{O}_2\text{Cl}$ requires 235.0531, Δ -0.04 ppm.

IR (film) $\nu_{\text{max}}/\text{cm}^{-1}$ 2920, 1669, 1638, 1429, 1283, 783.

m.p.: 158-160 °C.

4,4-Dimethylcyclohex-1-ene-1-carboxylic acid, **8**



(4,4-Dimethylcyclohex-1-en-1-yl)(2,3,4,5,6-pentamethylphenyl)methanone **3ab** (28.4 mg, 0.100 mmol, 1 eq.) was subjected to **General Procedure 2**. The title compound was afforded after purification by FCC (2 \rightarrow 4% MeOH/ CH_2Cl_2) as a white solid (15.4 mg, 0.100 mmol, 100% yield). 1,2,3,4,5-Pentamethylbenzene **Ph^{*}-H** was also isolated as a white solid (14.8 mg, 0.100 mmol, 100% yield).

Data for 4,4-Dimethylcyclohex-1-ene-1-carboxylic acid, **8**:

^1H NMR (400 MHz, CDCl_3) δ 11.29 (s, 1H, OH), 7.07 (tt, $J = 4.0, 2.0$ Hz, 1H, H_2), 2.29 (tq, $J = 6.5, 2.5$ Hz, 2H, $\text{H}_6 \times 2$), 2.00 (dt, $J = 5.0, 2.0$ Hz, 2H, $\text{H}_3 \times 2$), 1.42 (t, $J = 6.5$ Hz, 2H, $\text{H}_5 \times 2$), 0.92 (s, 6H, $\text{H}_8 \times 6$).

^{13}C NMR (101 MHz, CDCl_3) δ 173.1, 141.9, 128.7, 40.0, 35.0, 28.4, 28.2, 21.8.

HRMS (ESI⁺): Found $[\text{M}-\text{H}]^- = 153.0922$; $\text{C}_9\text{H}_{13}\text{O}_2$ requires 153.0921, Δ 0.89 ppm.

IR (film) $\nu_{\text{max}}/\text{cm}^{-1}$ 2981, 2888, 1663, 1640, 1383, 1295, 1155, 1086, 955.

m.p.: 107-109 °C.

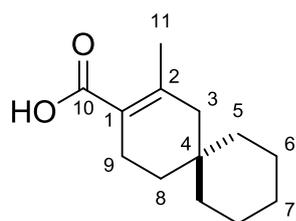
Data for 1,2,3,4,5-pentamethylbenzene, **Ph^{*}-H**:

^1H NMR (400 MHz, CDCl_3) δ 7.00 (s, 1H, ArCH), 2.41 (s, 3H, CH_3), 2.38 (s, 6H $\text{CH}_3 \times 2$), 2.34 (s, 6H $\text{CH}_3 \times 2$).

^{13}C NMR (101 MHz, CDCl_3) δ 135.0, 133.3, 132.4, 129.1, 20.6, 16.4, 16.0.

The spectroscopic data matched that previously reported in the literature.¹¹

2-Methylspiro[5.5]undec-2-ene-3-carboxylic acid, **9**



(2-Methylspiro[5.5]undec-2-en-3-yl)(2,3,4,5,6-pentamethylphenyl)methanone **3s** (33.8 mg, 0.100 mmol, 1 eq.) was subjected to **General Procedure 2**. The title compound was afforded after purification by FCC (2% MeOH/CH₂Cl₂) as a white solid (15 mg, 0.072 mmol, 72% yield).

¹H NMR (400 MHz, CDCl₃) δ 11.1 (s, 1H, OH), 2.24 (tq, *J* = 6.5, 2.0 Hz, 2H, H₉ x 2), 2.00 (s, 3H, H₁₁ x 3), 1.95 – 1.89 (m, 2H, H₃ x 2), 1.48 – 1.28 (m, 8H, H₆ x 4, H₇ x 2, H₈ x 2), 1.28 – 1.11 (m, 4H, H₅ x 4).

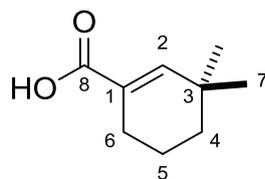
¹³C NMR (101 MHz, CDCl₃) δ 173.6, 149.7, 122.2, 46.7, 36.5, 32.2, 31.5, 26.8, 23.2, 22.9, 21.9.

HRMS (ESI+): Found [M-H]⁻ = 207.1388; C₁₃H₁₉O₂ requires 207.1380, Δ 4.07 ppm.

IR (film) ν_{max}/cm⁻¹ 2930, 2847, 1679, 1619, 1441, 1284, 959.

m.p.: 133-135 °C.

3,3-Dimethylcyclohex-1-ene-1-carboxylic acid, **10**



(3,3-Dimethylcyclohex-1-en-1-yl)(2,3,4,5,6-pentamethylphenyl)methanone **3af** (28.4 mg, 0.100 mmol, 1 eq.) was subjected to **General Procedure 2**. The title compound was afforded after purification by FCC (2→4% MeOH/CH₂Cl₂) as a white solid (15.4 mg, 0.100 mmol, 100% yield).

¹H NMR (400 MHz, CDCl₃) δ 10.03 (s, 1H, OH), 6.82 (t, *J* = 2.0 Hz, 1H, H₂), 2.20 (td, *J* = 6.0, 2.0 Hz, 2H, H₆ x 2), 1.72 – 1.62 (m, 2H, H₄ x 2), 1.47 – 1.41 (m, 2H, H₅ x 2), 1.05 (s, 6H, H₇ x 6).

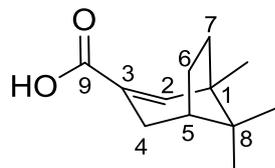
¹³C NMR (101 MHz, CDCl₃) δ 173.2, 151.2, 127.6, 36.3, 32.8, 29.1, 24.1, 19.3.

HRMS (ESI-): Found [M-H]⁻ = 153.0919; C₉H₁₃O₂ requires 153.0921, Δ -1.06 ppm.

IR (film) ν_{max}/cm⁻¹ 2935, 2853, 1687, 1641, 1423, 1286.

m.p.: 76-78 °C.

(1S,5S)-1,8,8-Trimethylbicyclo[3.2.1]oct-2-ene-3-carboxylic acid, **11**



(2,3,4,5,6-Pentamethylphenyl)((1S,5S)-1,8,8-trimethylbicyclo[3.2.1]oct-2-en-3-yl)methanone **3ag** (52 mg, 0.10 mmol, 1 eq., 1:1 mixture with pentamethylacetophenone **1**) was subjected to **General Procedure 2**. The title compound was afforded after purification by FCC (2 → 4% MeOH/CH₂Cl₂) as a white solid (19.0 mg, 0.098 mmol, 98% yield)

¹H NMR (400 MHz, CDCl₃) δ 10.10 (s, 1H, OH), 6.91 (dd, *J* = 2.0, 1.0 Hz, 1H, H₂), 2.50 (ddq, *J* = 18.0, 4.0, 2.0 Hz, 1H, H_{4a}), 2.18 – 2.09 (m, 1H, H_{4b}), 2.02 – 1.90 (m, 1H, H_{6a}), 1.89 – 1.79 (m, 2H, H₅, H_{7a}), 1.78 – 1.67 (m, 1H, H_{7b}), 1.32 (ddd, *J* = 13.5, 9.5, 6.0 Hz, 1H, H_{6b}), 1.02 (s, 3H, CH₃), 0.93 (s, 3H, CH₃), 0.90 (s, 3H, CH₃).

¹³C NMR (101 MHz, CDCl₃) δ 173.1, 154.1, 126.5, 45.8, 43.8, 42.2, 41.0, 33.5, 28.9, 23.3, 19.2, 17.9.

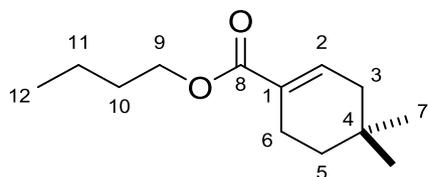
HRMS (ESI⁻): Found [M-H]⁻ = 193.1232 ; C₁₂H₁₇O₂ requires 193.1234, Δ -1.16 ppm.

IR (film) ν_{max}/cm⁻¹ 2950, 2872, 1683, 1637, 1422, 1286.

m.p.: 106-108 °C.

[α]_D²⁵ = -122.8 (c=1.0, CHCl₃).

Butyl 4,4-dimethylcyclohex-1-ene-1-carboxylate, **12**



A 2–5 mL Biotage[®] microwave vial was charged with (4,4-dimethylcyclohex-1-en-1-yl)(2,3,4,5,6-pentamethylphenyl) methanone **3ab** (50.0 mg, 0.175 mmol, 1 eq.) and H₂SO₄ (98% wt., 0.3 mL). The vial was then sealed with a microwave vial cap (containing a Reseal[™] septum) and heated at 65 °C. After 30 minutes, *n*-butanol (1 mL) was added and heated at 65 °C for 24 hours. The reaction mixture was then cooled to RT, diluted with water (5 mL), extracted with CH₂Cl₂ (3 x 10 mL), dried over MgSO₄, filtered and concentrated in *vacuo*. The

title compound was afforded after purification by FCC (2% Et₂O/pentane) as a colourless oil (37 mg, 0.175 mmol, 100% yield).

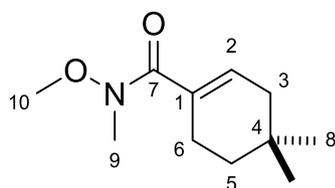
¹H NMR (400 MHz, CDCl₃) δ 6.91 (tt, *J* = 4.0, 2.0 Hz, 1H, H₂), 4.12 (t, *J* = 6.5 Hz, 2H, H₉ x 2), 2.31 – 2.26 (m, 2H, H₆ x 2), 1.97 (dt, *J* = 5.0, 2.5 Hz, 2H, H₃ x 2), 1.72 – 1.56 (m, 2H, H₁₀ x 2), 1.49 – 1.32 (m, 4H, H₅ x 2, H₁₁ x 2), 0.94 (t, *J* = 7.4 Hz, 3H, H₁₂ x 3), 0.91 (s, 6H, H₇ x 6).

¹³C NMR (101 MHz, CDCl₃) δ 167.8, 138.8, 129.4, 64.2, 39.8, 35.1, 30.9, 28.5, 28.3, 22.2, 19.4, 13.9.

HRMS (ESI+): Found [M+H]⁺ = 211.1695; C₁₃H₂₃O₂ requires 211.1693, Δ 1.20 ppm.

IR (film) ν_{max}/cm⁻¹ 2956, 1711, 1650, 1249, 1180, 1084, 715.

***N*-methoxy-*N*,4,4-trimethylcyclohex-1-ene-1-carboxamide, 13**



A 2–5 mL Biotage[®] microwave vial was charged with (4,4-dimethylcyclohex-1-en-1-yl)(2,3,4,5,6-pentamethylphenyl)methanone **3ab** (50.0 mg, 0.175 mmol, 1 eq.) and 2M HCl in hexafluoroisopropanol (1.75 mL). The vial was then sealed with a microwave vial cap (containing a Reseal™ septum) and heated at 65 °C for 15 h. The reaction was then cooled to RT, and concentrated *in vacuo*, azeotroping with toluene. EDCI (50 mg, 0.26 mmol, 1.5 eq), DIPEA (0.15 mL, 0.88 mmol, 5 eq), HOBT (36 mg, 0.26 mmol, 1.5 eq), DMF (1 mL, 0.175 M) and *N,O*-(dimethyl)hydroxylamine hydrochloride (26 mg, 0.26 mmol, 1.5 eq.) were added, stirring at RT for 15 h. The reaction mixture was diluted with sat. aq. Na₂CO₃ (5 mL), extracted with CH₂Cl₂ (3 x 5 mL), dried over MgSO₄, filtered and concentrated *in vacuo*. The title compound was afforded after purification by FCC (30% Et₂O/pentane) as a colourless oil (26 mg, 0.13 mmol, 75% yield).

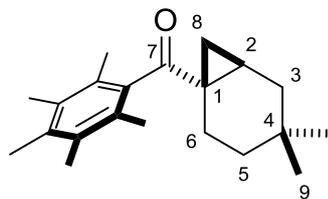
¹H NMR (400 MHz, CDCl₃) δ 6.07 (tt, *J* = 4.0, 2.0 Hz, 1H, H₂), 3.63 (s, 3H, H₁₀ x 3), 3.21 (s, 3H, H₉ x 3), 2.28 (ttd, *J* = 6.5, 2.5, 2.0 Hz, 2H, H₆ x 2), 1.90 (dt, *J* = 4.0, 2.5 Hz, 2H, H₃ x 2), 1.41 (t, *J* = 6.5 Hz, 2H, H₅), 0.93 (s, 6H, H₈ x 6).

¹³C NMR (101 MHz, CDCl₃) δ 172.1, 132.7, 130.1, 61.2, 39.1, 35.1, 33.8, 28.4, 28.3, 23.5.

HRMS (ESI+): Found [M+H]⁺ = 198.1490 ; C₁₁H₂₀O₂N requires 198.1489, Δ 0.51 ppm.

IR (film) ν_{max}/cm⁻¹ 2926, 2868, 1660, 1631, 1457, 1377, 974.

(4,4-dimethylbicyclo[4.1.0]heptan-1-yl)(2,3,4,5,6-pentamethylphenyl)methanone, 14



A 5 mL RBF was charged with trimethylsulfoxonium iodide (58.0 mg, 0.264 mmol, 1.5 eq.) (4,4-dimethylcyclohex-1-en-1-yl)(2,3,4,5,6-pentamethylphenyl)methanone **3ab** (50.0 mg, 0.175 mmol, 1 eq.), NaH (60% wt, 11.0 mg, 0.275 mmol, 1.6 eq.) and DMSO (0.5 mL). The reaction was heated at 50 °C under an Argon atmosphere for 48 hours. The reaction mixture was then cooled to RT, diluted with 3M HCl (3 mL), extracted with CH₂Cl₂ (3 x 5 mL), dried over MgSO₄, filtered and concentrated *in vacuo*. The title compound was afforded after purification by FCC (65% CH₂Cl₂/pentane) as a white solid (37.0 mg, 1.23 mmol, 70% yield).

¹H NMR (400 MHz, CDCl₃) δ 2.34 – 2.05 (m, 16H, H_{6a} and ArCH₃ x 5), 1.85 – 1.72 (m, 2H, H_{3a} and H_{6b}), 1.68 – 1.56 (m, 1H, H₂), 1.40 (dd, *J* = 9.5, 3.5 Hz, 1H, H_{8a}), 1.33 – 1.24 (m, 1H, H_{3b}), 1.24 – 1.16 (m, 1H, H_{5a}), 0.99 (td, *J* = 13.5, 5.5 Hz, 1H, H_{5b}), 0.86 (s, 3H, H_{9a} x 3), 0.83 (s, 3H, H_{9b} x 3), 0.75 (dd, *J* = 6.5, 3.5 Hz, 1H, H_{8b}).

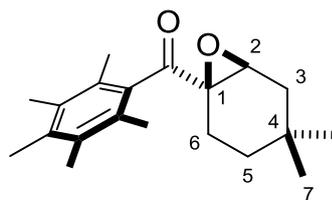
¹³C NMR (101 MHz, CDCl₃) δ 214.4, 138.5, 135.0, 133.0, 132.9, 128.1, 127.9, 38.1, 33.1, 32.0, 31.9, 27.8, 25.7, 23.7, 23.1, 20.4, 18.1, 17.8, 16.8, 16.1, 16.1. N.B. additional peaks for C₆Me₅ were observed due to restricted rotation about the Ar-C(O) axis.

HRMS (ESI+): Found [M+H]⁺ = 299.2370; C₂₁H₃₁O requires 299.2369, Δ 0.09 ppm.

IR (film) ν_{max}/cm⁻¹ 2949, 2806, 1669, 1457, 1384, 1127, 878, 809.

m.p.: 80-82 °C.

(4,4-Dimethyl-7-oxabicyclo[4.1.0]heptan-1-yl)(2,3,4,5,6-pentamethylphenyl)methanone, 15



To a stirred room temperature solution of (4,4-dimethylcyclohex-1-en-1-yl)(2,3,4,5,6-pentamethylphenyl)methanone **3ab** (28 mg, 0.10 mmol, 1 eq.) in *t*-BuOH (1 mL) was

successively NaOH (20 mg, 0.50 mmol, 5 eq.) and *t*-BuOOH (~5.5 M in decane, 91 μ L, 0.50 mmol, 5 eq.) and the resulting suspension was heated to 85 °C and stirred for 1 h. The reaction mixture was then cooled to RT, diluted with sat. aq. NH₄Cl (10 mL), extracted with Et₂O (3 x 10 mL), dried over MgSO₄, filtered and concentrated *in vacuo*. The title compound was afforded after purification by FCC (5% Et₂O/pentane) as a white solid (26 mg, 0.087 mmol, 87% yield).

¹H NMR (400 MHz, CDCl₃) δ 3.05 (dt, *J* = 5.0, 1.0 Hz, 1H, H₂), 2.70 (ddd, *J* = 15.5, 11.5, 6.0 Hz, 1H, H_{6ax}), 2.21 (s, 3H, ArCH₃), 2.17 (s, 6H, ArCH₃), 2.11 (br s, 3H, ArCH₃), 2.06 (br s, 3H, ArCH₃), 2.02 (dddd, *J* = 15.5, 5.5, 3.5, 1.0 Hz, 1H, H_{6eq}), 1.69 (ddd, *J* = 15.0, 5.0, 2.0 Hz, 1H, H_{3eq}), 1.60 (d, *J* = 14.0 Hz, 1H, H_{3ax}), 1.35 (ddd, *J* = 13.5, 11.5, 5.5 Hz, 1H, H_{5ax}), 1.24 (dddd, *J* = 13.5, 5.5, 3.5, 2.0 Hz, 1H, H_{5eq}), 0.90 (s, 6H, H₇).

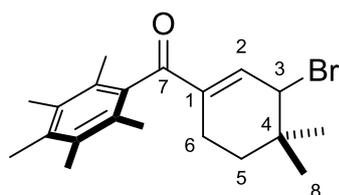
¹³C NMR (101 MHz, CDCl₃) δ 210.9, 136.2, 135.2, 132.9, 132.7, 130.3, 128.6, 63.3, 57.4, 38.0, 31.6, 30.8, 27.8, 26.8, 19.6, 18.0, 17.6, 16.9, 16.1, 15.9. N.B. additional peaks for C₆Me₅ were observed due to restricted rotation about the Ar-C(O) axis.

HRMS (ESI⁺): Found [M+Na]⁺ = 323.1982; C₂₀H₂₈O₂Na requires 323.1982, Δ 0.09 ppm.

IR (film) ν_{max} /cm⁻¹ 2952, 1688, 1453, 1385, 1309, 1273, 1143, 1113, 864, 813.

m.p.: 82-83 °C.

(3-Bromo-4,4-dimethylcyclohex-1-en-1-yl)(2,3,4,5,6-pentamethylphenyl)methanone, 16



Bromine in CHCl₃ (1.9 mL, 0.10 M, 1.2 eq) was added dropwise at -17 °C to a 2–5 mL Biotage[®] microwave vial charged with (4,4-dimethylcyclohex-1-en-1-yl)(2,3,4,5,6-pentamethylphenyl)methanone **3ab** (50.0 mg, 0.175 mmol, 1 eq.) in CHCl₃ (1 mL). The reaction mixture was then warmed to room temperature, stirred for 3 hours and then concentrated *in vacuo*. The title compound was afforded after purification by FCC (2% Et₂O/pentane) as a white solid (58 mg, 0.16 mmol, 91% yield).

¹H NMR (400 MHz, CDCl₃) δ 6.47 (dt, *J* = 4.5, 1.8 Hz, 1H, H₂), 4.46 (dq, *J* = 4.5, 1.5 Hz, 1H, H₃), 2.67 (dddt, *J* = 19.0, 6.0, 4.5, 1.5 Hz, 1H, H_{6a}), 2.48 (dddt, *J* = 19.0, 8.5, 6.5, 2.0 Hz, 1H, H_{6b}), 2.24 (s, 3H, ArCH₃), 2.18 (s, 6H, ArCH₃ x 2), 2.03 (s, 3H, ArCH₃), 1.99 (s, 3H, ArCH₃), 1.89 (ddd,

$J = 13.5, 9.0, 6.0$ Hz, 1H, H_{5a}), 1.52 (dddd, $J = 13.5, 6.0, 4.5, 1.5$ Hz, 1H, H_{5b}), 1.13 (s, 3H, H_{8a} x 3), 1.06 (s, 3H, H_{8b} x 3).

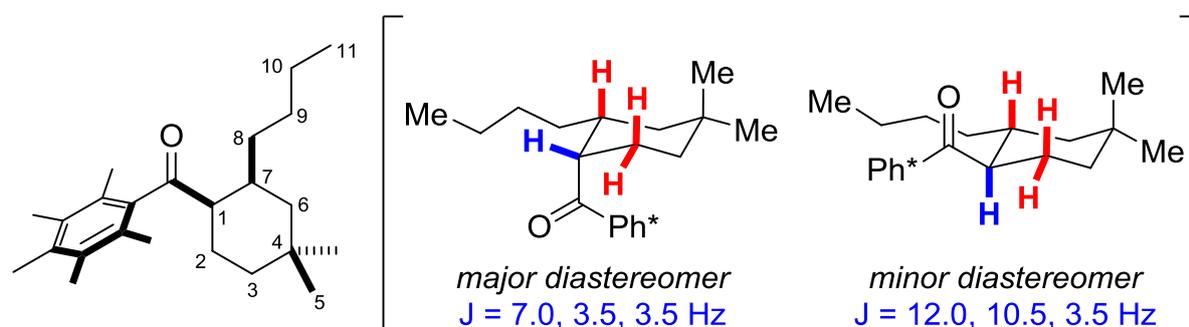
¹³C NMR (101 MHz, CDCl₃) δ 203.5, 142.6, 139.3, 137.4, 135.6, 132.9, 129.4, 129.1, 59.6, 33.8, 31.0, 28.1, 25.3, 20.3, 17.5, 16.9, 16.1. N.B. additional peaks for C₆Me₅ were observed due to restricted rotation about the Ar-C(O) axis.

HRMS (ESI⁺): Found $[M+H]^+ = 363.1319$; C₂₀H₂₈O⁷⁹Br requires 363.1318, Δ 0.25 ppm.

IR (film) $\nu_{\max}/\text{cm}^{-1}$ 2926, 2854, 1657, 1633, 1453, 1267, 1199, 1166, 891.

m.p.: 98-100 °C.

***rac*-((1*R*,2*S*)-2-Butyl-4,4-dimethylcyclohexyl)(2,3,4,5,6-pentamethylphenyl)methanone, 17**



A Schlenk tube was charged with (4,4-dimethylcyclohex-1-en-1-yl)(2,3,4,5,6-pentamethylphenyl)methanone **3ab** (40 mg, 0.14 mmol, 1 eq.) and pentane (3 mL) and the resulting solution was stirred at RT. A solution of *n*-BuLi (1.6 M in hexanes, 0.18 mmol, 0.28 mmol, 2 eq.) was added dropwise. The resulting solution was stirred at RT for 5 minutes and then cooled to -78 °C and quenched by dropwise addition of a solution of 2,6-di-*tert*-butylphenol (116 mg, 0.56 mmol, 4.0 eq.) in pentane (1 mL). The quenched reaction mixture was then warmed to RT and diluted with sat. aq. NH₄Cl (10 mL) and then extracted with Et₂O (3 x 10 mL), dried over MgSO₄, filtered and concentrated in vacuo. The title compound was afforded after purification by FCC (2:98% Et₂O/pentane) as a white solid (42 mg, 0.12 mmol, 87% yield, 80:20 d.r.). The relative stereochemistry was assigned by *J*-coupling constant analysis.

¹H NMR (400 MHz, CDCl₃) δ 3.02 (dt, $J = 7.0, 3.5$ Hz, 1H, H₁), 2.24 (s, 3H, Ar-CH₃), 2.20-2.13 (m, 12H, 4 x ArCH₃), 1.89 – 1.14 (m, 13H, H₂ x 2, H₃ x 2, H₆ x 2, H₇, H₈ x 2, H₉ x 2 and H₁₀ x 2), 0.98 (s, 3H, H_{5a} x 3), 0.94 – 0.86 (m, 6H, H_{5b} x 3 and H₁₁). The minor diastereoisomer displays a characteristic signal at $\delta = 2.45$ (ddd, $J = 12.0, 10.5, 3.5$ Hz, 1H, H₁).

^{13}C NMR (101 MHz, CDCl_3) δ 213.7, 140.6, 135.4, 133.2, 133.1, 52.6, 40.8, 36.5, 36.3, 32.9, 32.7, 30.7, 30.5, 25.8, 24.0, 23.0, 18.1, 16.9, 16.2, 14.3.

HRMS (ESI+): Found $[\text{M}+\text{H}]^+ = 343.2995$; $\text{C}_{24}\text{H}_{39}\text{O}$ requires 343.3006, $\Delta -3.15$ ppm.

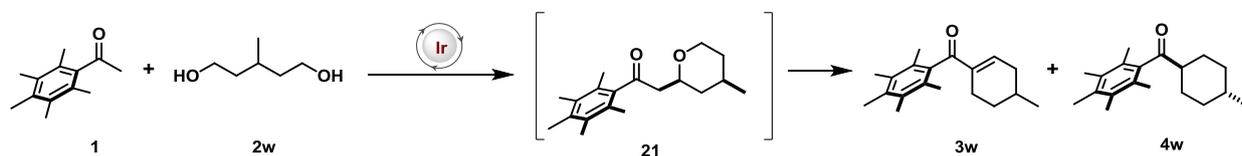
IR (film) $\nu_{\text{max}}/\text{cm}^{-1}$ 2928, 1690, 1456, 1384, 1297, 1094, 903.

m.p.: 51-52 $^{\circ}\text{C}$.

5. Mechanistic Experiments

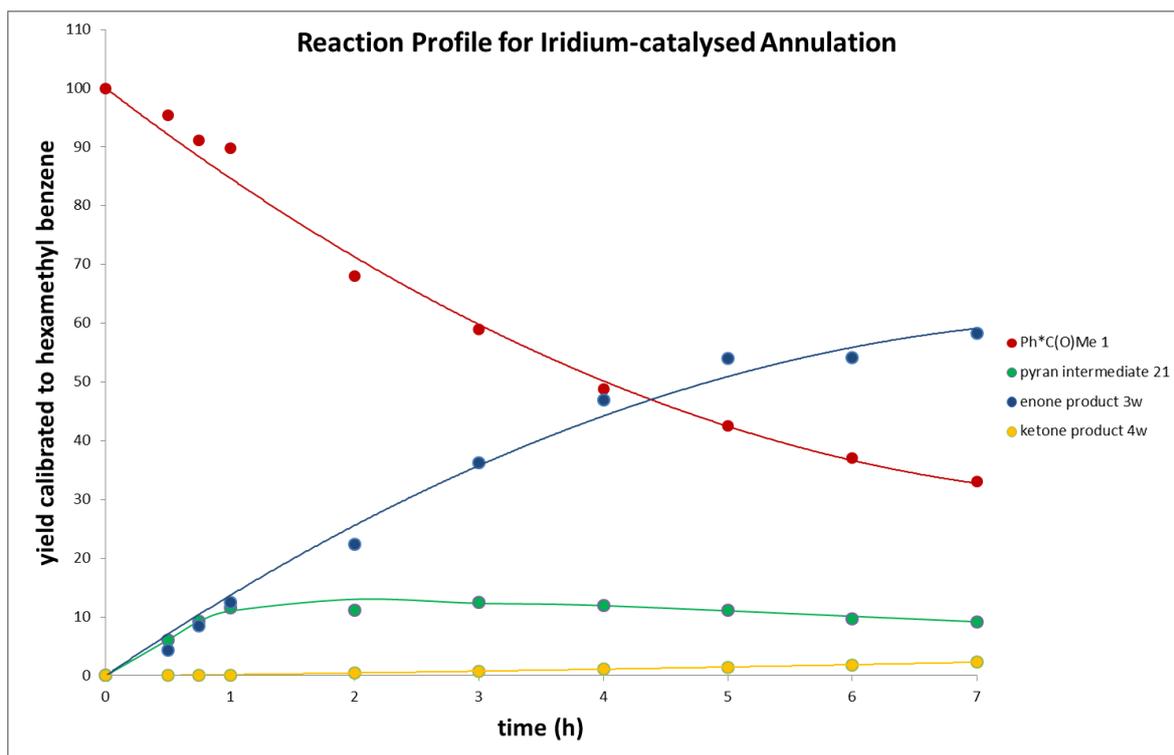
5.1 Time Course Experiments

Reaction Profile of Iridium Catalysed Reaction

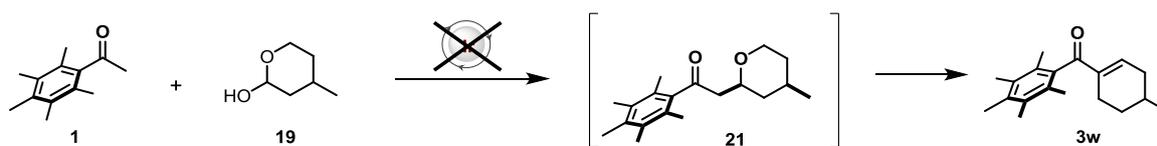


A 20 mL Biotage[®] microwave vial was charged with CataCXium[®] A (17 mg, 0.048 mmol, 2 mol%), 3-methylpentane-1,5-diol **2w** (567 mg, 4.80 mmol, 2 eq.), 1-(2,3,4,5,6-pentamethylphenyl)ethan-1-one **1** (456 mg, 2.40 mmol, 1 eq.), [Ir(cod)Cl]₂ (8.0 mg, 0.012 mmol, 0.5 mol% dimer), KOH (538 mg, 9.60 mmol, 4 eq.), hexamethylbenzene (389.5 mg, 2.40 mmol, 1 eq.) and toluene (9.6 mL, 0.25 M). The vial was then sealed with a microwave vial cap (containing a Reseal[™] septum) and heated at 115 °C for 24 hours, taking 0.1 mL aliquots at the times listed below. The aliquot was filtered through silica, washing with Et₂O and the solvent was removed *in vacuo*. The sample was diluted with 5 mL of MeCN and analysed by reverse phase HPLC analysis (Agilent InfinityLab Poroshell 120 EC-C18 column with guard, 75% MeCN, 25% H₂O, 1.0 mL/min, 25 °C, λ = 220 nm, 5 μL injection). The mmol of **1**, **21**, **3w** and **4w** were determined by relative peak area to a calibrated absorption of the internal standard hexamethylbenzene at 220 nm.

Time (h)	mmol of 1	mmol of 21	mmol of 3w	mmol of 4w
0.5	2.4	0	0	0
0.75	2.29	0.15	0.11	0
1	2.19	0.22	0.20	0
2	2.15	0.28	0.30	0
3	1.63	0.27	0.54	0.01
4	1.41	0.30	0.87	0.02
5	1.17	0.29	1.12	0.03
6	1.02	0.27	1.29	0.03
7	0.89	0.23	1.30	0.04

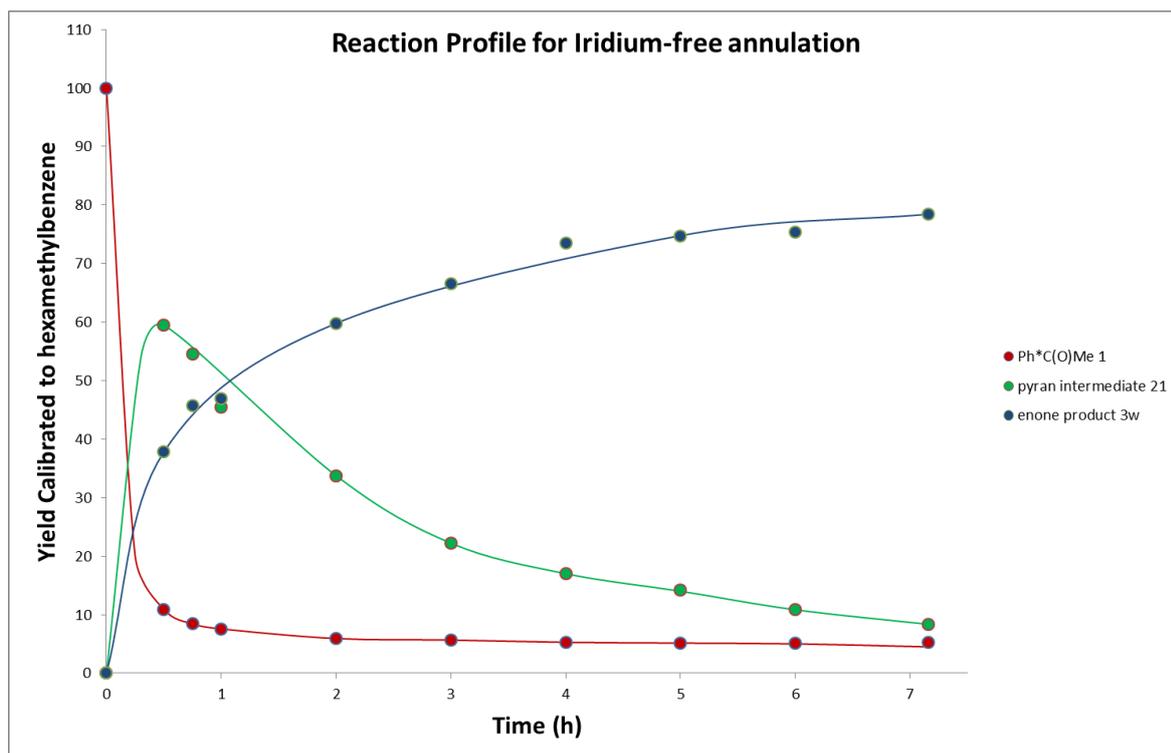


2.8.2 Reaction Profile of Iridium-Free Reaction



A 20 mL Biotage[®] microwave vial was charged with 4-methyltetrahydro-2H-pyran-2-ol **19** (558 mg, 4.80 mmol, 1 eq.), 1-(2,3,4,5,6-pentamethylphenyl)ethan-1-one **1** (456 mg, 2.40 mmol, 1 eq.), KOH (538 mg, 9.60 mmol, 4 eq.), hexamethylbenzene (390 mg, 2.40 mmol, 1 eq.) and toluene (9.6 mL, 0.25 M). The vial was then sealed with a microwave vial cap (containing a Reseal[™] septum) and heated at 115 °C for 24 hours, taking 0.1 mL aliquots at the times listed below. The aliquot was filtered through silica, washing with Et₂O and the solvent was removed *in vacuo*. The sample was diluted with 5 mL of MeCN and analysed by reverse phase HPLC analysis (Agilent InfinityLab Poroshell 120 EC-C18 column with guard, 75% MeCN, 25% H₂O, 1.0 mL/min, 25 °C, λ = 220 nm, 5 μL injection). The mmol of **1**, **21**, **3w** and **4w** were determined by relative peak area to a calibrated absorption of the internal standard hexamethylbenzene at 220 nm.

Time (h)	mmol of 1	mmol of 21	mmol of 3w	mmol of 4w
0.5	2.4	0	0	0
0.75	0.26	1.42	0.91	0
1	0.20	1.31	1.10	0
2	0.18	1.09	1.13	0
3	0.14	0.81	1.43	0
4	0.14	0.53	1.60	0
5	0.13	0.41	1.76	0
6	0.12	0.34	1.79	0
7.16	0.12	0.26	1.81	0

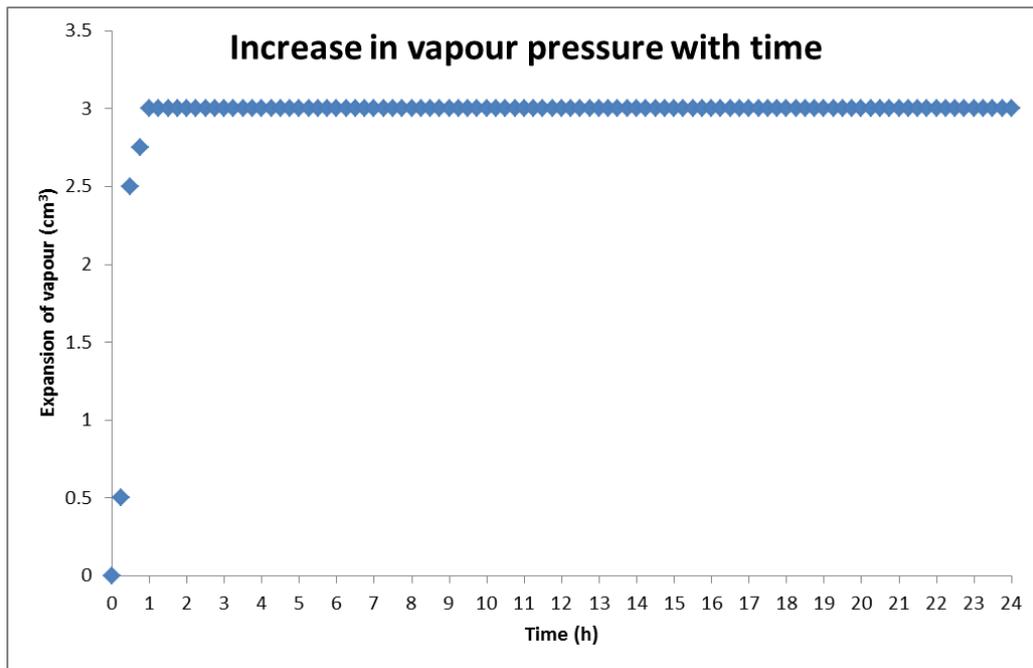


Method for Measuring Hydrogen Evolution

Apparatus: A 50 mL measuring cylinder filled with toluene was inverted and submerged in a bath of toluene and a cannula was inserted into the cylinder. The other end of the cannula was then placed into the neck of the Biotage[®] microwave vial by piercing the septum. A Canon EOS 30D camera fitted with Canon TC-80N3 Timer Remote Control was set up to take photos of the measuring cylinder and a clock at 15 minute intervals for 24 hours. See photographs below:



N.B. Heating 2.4 mL of toluene in a Biotage[®] microwave vial at 115 °C caused an increase in the vapour pressure within the reaction vessel. To account for this in our measurements, toluene (2.4 mL) was heated at 115 °C for 24 hours in a sealed 2-5 mL Biotage[®] microwave vial using the apparatus described above to measure the increase in volume. The observed expansion of the headspace amounted to approximately 3 mL and was deducted from all subsequent hydrogen evolution experiments – the data for this control experiment is plotted overleaf for reference.



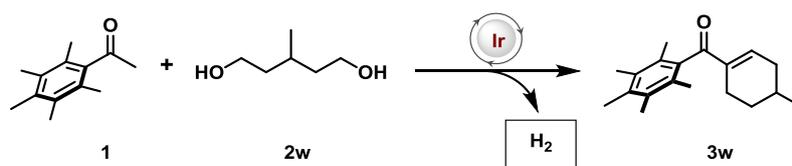
Data for vapour pressure increase of toluene at 115 °C

time	volume (cm ³)
0	0
0.25	0.5
0.5	2.5
0.75	2.75
1	3
1.25	3
1.5	3
1.75	3
2	3
2.25	3
2.5	3
2.75	3
3	3
3.25	3
3.5	3
3.75	3
4	3
4.25	3
4.5	3
4.75	3
5	3
5.25	3
5.5	3
5.75	3
6	3

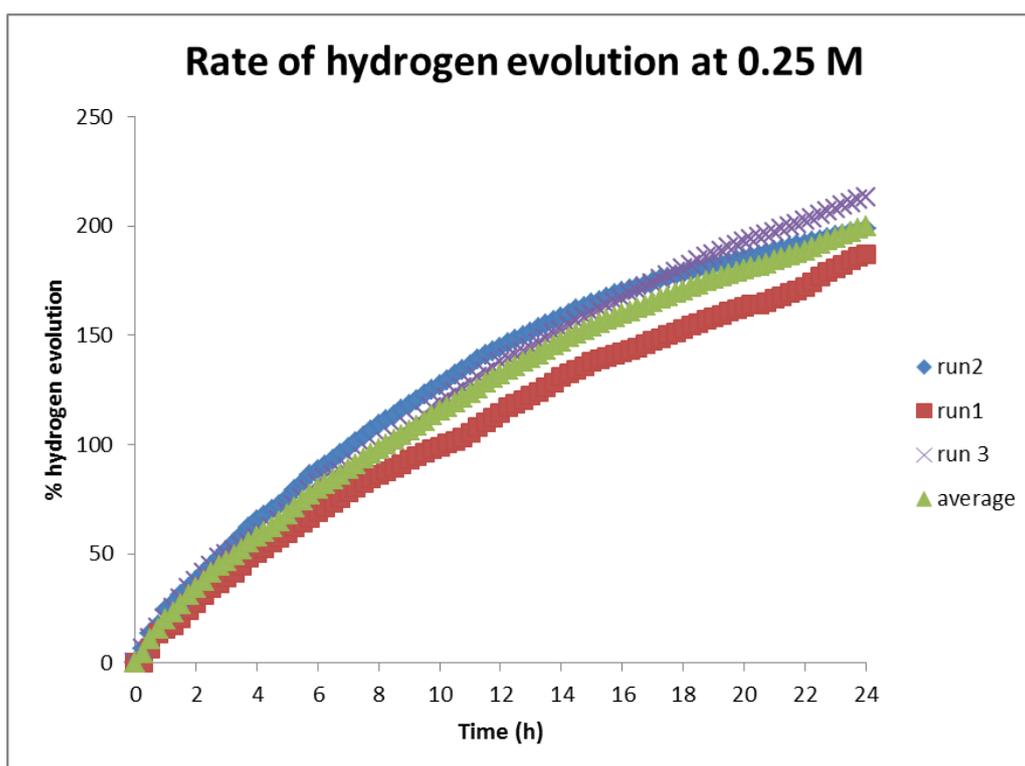
6.25	3
6.5	3
6.75	3
7	3
7.25	3
7.5	3
7.75	3
8	3
8.25	3
8.5	3
8.75	3
9	3
9.25	3
9.5	3
9.75	3
10	3
10.25	3
10.5	3
10.75	3
11	3
11.25	3
11.5	3
11.75	3
12	3
12.25	3
12.5	3
12.75	3
13	3
13.25	3
13.5	3
13.75	3
14	3
14.25	3
14.5	3
14.75	3
15	3
15.25	3
15.5	3
15.75	3
16	3
16.25	3
16.5	3
16.75	3
17	3
17.25	3
17.5	3

17.75	3
18	3
18.25	3
18.5	3
18.75	3
19	3
19.25	3
19.5	3
19.75	3
20	3
20.25	3
20.5	3
20.75	3
21	3
21.25	3
21.5	3
21.75	3
22	3
22.25	3
22.5	3
22.75	3
23	3
23.25	3
23.5	3
23.75	3
24	3

Measurement of Hydrogen Evolution in Iridium Catalyzed Annulation



A 2-5mL Biotage[®] microwave vial was charged with CataCXium[®] A (4.3 mg, 0.012 mmol, 2 mol%), 3-methylpentane-1,5-diol **2w** (143 mg, 1.20 mmol, 2 eq.), 1-(2,3,4,5,6-pentamethylphenyl)ethan-1-one **1** (114 mg, 0.600 mmol, 1 eq.), [Ir(cod)Cl]₂ (2 mg, 0.003 mmol, 0.5 mol% dimer), KOH (134 mg, 2.40 mmol, 4 eq.) and toluene (2.4 mL, 0.25 M). The vial was then sealed with a microwave vial cap (containing a Reseal[™] septum) and connected to the cannula from the hydrogen collection apparatus. The reaction was heated at 115 °C for 24 hours, with a photograph taken of the cylinder at 15 minute intervals.



Time (h)	mmol run 1	mmol run 2	mmol run 3	mmol average
0	0	0	0	0
0.25	0	0.04	0.04	0.03
0.5	0.04	0.08	0.07	0.06
0.75	0.08	0.1	0.1	0.09
1	0.09	0.14	0.12	0.12

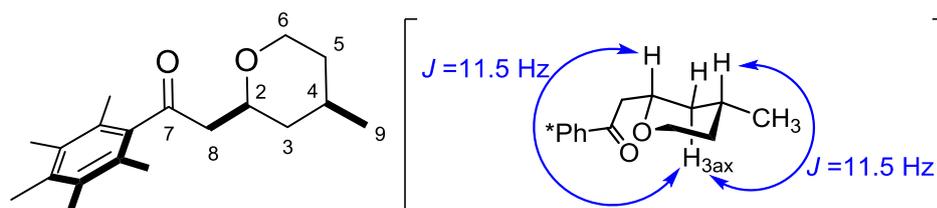
1.25	0.1	0.17	0.15	0.14
1.5	0.12	0.19	0.18	0.16
1.75	0.14	0.21	0.21	0.19
2	0.17	0.23	0.23	0.21
2.25	0.19	0.25	0.25	0.23
2.5	0.21	0.27	0.27	0.25
2.75	0.22	0.29	0.29	0.27
3	0.23	0.31	0.3	0.28
3.25	0.25	0.33	0.31	0.3
3.5	0.27	0.35	0.32	0.31
3.75	0.29	0.37	0.33	0.33
4	0.3	0.39	0.34	0.35
4.25	0.32	0.41	0.36	0.36
4.5	0.33	0.42	0.37	0.37
4.75	0.34	0.43	0.39	0.39
5	0.36	0.45	0.41	0.41
5.25	0.37	0.48	0.43	0.43
5.5	0.39	0.5	0.45	0.45
5.75	0.4	0.52	0.48	0.46
6	0.41	0.53	0.5	0.48
6.25	0.43	0.54	0.51	0.49
6.5	0.44	0.56	0.52	0.5
6.75	0.45	0.57	0.53	0.52
7	0.47	0.59	0.54	0.53
7.25	0.48	0.61	0.55	0.55
7.5	0.5	0.62	0.56	0.56
7.75	0.51	0.64	0.58	0.58
8	0.52	0.65	0.59	0.59
8.25	0.53	0.67	0.61	0.6
8.5	0.54	0.68	0.62	0.61
8.75	0.55	0.7	0.63	0.63
9	0.56	0.71	0.65	0.64
9.25	0.57	0.72	0.66	0.65
9.5	0.58	0.74	0.68	0.67
9.75	0.59	0.75	0.7	0.68
10	0.6	0.76	0.72	0.69
10.25	0.6	0.78	0.73	0.7
10.5	0.61	0.79	0.74	0.72
10.75	0.62	0.81	0.76	0.73
11	0.63	0.82	0.77	0.74
11.25	0.65	0.83	0.79	0.76
11.5	0.66	0.85	0.8	0.77
11.75	0.67	0.86	0.81	0.78
12	0.69	0.87	0.83	0.79
12.25	0.7	0.88	0.84	0.81
12.5	0.71	0.89	0.85	0.82

12.75	0.72	0.9	0.86	0.83
13	0.73	0.91	0.87	0.84
13.25	0.74	0.92	0.88	0.85
13.5	0.76	0.93	0.89	0.86
13.75	0.77	0.94	0.9	0.87
14	0.79	0.95	0.92	0.88
14.25	0.8	0.96	0.93	0.89
14.5	0.81	0.97	0.94	0.91
14.75	0.82	0.98	0.95	0.92
15	0.83	0.99	0.96	0.92
15.25	0.83	1	0.97	0.93
15.5	0.84	1	0.98	0.94
15.75	0.85	1.01	0.99	0.95
16	0.85	1.02	1	0.96
16.25	0.86	1.03	1.01	0.97
16.5	0.87	1.03	1.02	0.97
16.75	0.88	1.04	1.03	0.98
17	0.88	1.05	1.04	0.99
17.25	0.89	1.05	1.05	1
17.5	0.9	1.06	1.06	1.01
17.75	0.91	1.06	1.07	1.02
18	0.92	1.07	1.08	1.02
18.25	0.93	1.07	1.1	1.03
18.5	0.93	1.08	1.11	1.04
18.75	0.94	1.08	1.12	1.05
19	0.95	1.09	1.12	1.05
19.25	0.96	1.1	1.13	1.06
19.5	0.96	1.1	1.14	1.07
19.75	0.97	1.11	1.15	1.08
20	0.98	1.11	1.16	1.08
20.25	0.98	1.12	1.16	1.09
20.5	0.98	1.12	1.17	1.09
20.75	0.99	1.13	1.18	1.1
21	1	1.13	1.18	1.11
21.25	1.01	1.14	1.19	1.11
21.5	1.02	1.14	1.2	1.12
21.75	1.02	1.15	1.21	1.13
22	1.03	1.15	1.21	1.13
22.25	1.05	1.16	1.22	1.14
22.5	1.06	1.16	1.23	1.15
22.75	1.07	1.17	1.24	1.16
23	1.08	1.17	1.25	1.17
23.25	1.1	1.18	1.26	1.18
23.5	1.11	1.18	1.26	1.18
23.75	1.12	1.19	1.27	1.19
24	1.12	1.19	1.28	1.2

5.2 Resubjection Experiments

Pyran **21** was observed to form as an intermediate in the chemistry. To isolate and fully characterize this compound, we carried out the reaction between pentamethylacetophenone **1** and lactol **19** on a large scale and stopped the reaction after 30 minutes. Experimental details and spectral data are provided below:

rac-2-((2*R*,4*S*)-4-Methyltetrahydro-2*H*-pyran-2-yl)-1-(2,3,4,5,6-pentamethylphenyl)ethan-1-one **21**



A 20mL Biotage[®] microwave vial was charged with 4-methyltetrahydro-2*H*-pyran-2-ol **19** (278 mg, 2.40 mmol, 2 eq.), 1-(2,3,4,5,6-pentamethylphenyl)ethan-1-one **1** (234 mg, 1.20 mmol, 1 eq.), KOH (269 mg, 4.80 mmol, 4 eq.) and toluene (4.8 mL, 0.25 M). The vial was then sealed with a microwave vial cap (containing a Reseal[™] septum) and heated at 115 °C for 30 minutes. After cooling to RT, the reaction mixture was filtered through a silica plug, washing with Et₂O and concentrated in vacuo. The title compound was afforded after purification by FCC (5 → 10% Et₂O/pentane) as a white solid (83 mg, 0.29 mmol, 23% yield, >95:5 d.r.). The relative stereochemistry was determined by *J*-coupling constant analysis.

¹H NMR (400 MHz, CDCl₃) δ 4.04 – 3.93 (m, 2H, H_{2ax} and H_{6eq}), 3.52 (ddd, *J* = 12.5, 11.5, 2.0 Hz, 1H, H_{6ax}), 3.01 (dd, *J* = 18.0, 7.0 Hz, 1H, H_{8a}), 2.73 (dd, *J* = 18.0, 5.5 Hz, 1H, H_{8b}), 2.26 (s, 3H, ArCH₃), 2.21 (s, 6H, ArCH₃ × 2), 2.16 (s, 6H, ArCH₃ × 2), 1.82 (ddt, *J* = 13.0, 4.0, 2.0 Hz, 1H, H_{3eq}), 1.79 – 1.66 (m, 1H, H_{4ax}), 1.58 (ddq, *J* = 13.5, 4.0, 2.0 Hz, 1H, H_{5eq}), 1.25 (qd, *J* = 12.5, 4.5 Hz, 1H, H_{5ax}), 0.99 (q, *J* = 11.5 Hz, 1H, H_{3ax}), 0.98 (d, *J* = 6.5 Hz, 3H, H₉ × 3).

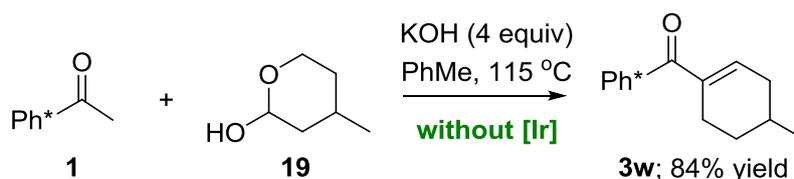
¹³C NMR (101 MHz, CDCl₃) δ 209.7, 140.5, 135.5, 133.2, 127.6, 72.9, 68.2, 52.3, 40.6, 34.5, 30.3, 22.4, 17.1, 16.8, 16.0.

HRMS (ESI⁺): Found [M+H]⁺ = 289.2163; C₁₉H₂₉O₂ requires 289.2162, Δ 0.35 ppm

IR (film) ν_{max}/cm⁻¹ 2924, 1690, 1655, 1455, 1382, 1306, 1195, 1093, 915, 732

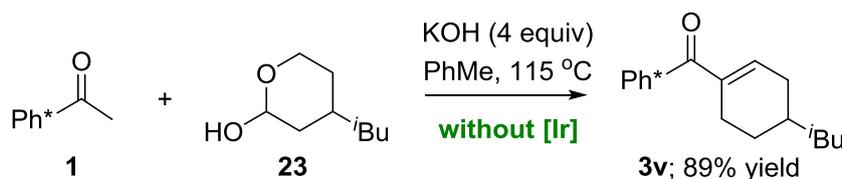
m.p.: 246-248 °C

Resubjection of lactol **19**:



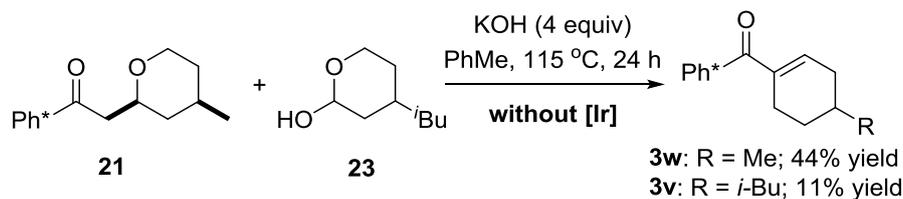
A 2-5mL Biotage[®] microwave vial was charged with 4-methyltetrahydro-2H-pyran-2-ol **19** (143 mg, 1.2 mmol, 2 eq), 1-(2,3,4,5,6-pentamethylphenyl)ethan-1-one **1** (114 mg, 0.600 mmol, 1 eq.), KOH (134 mg, 2.40 mmol, 4 eq.) and toluene (2.4 mL, 0.25 M). The vial was then sealed with a microwave vial cap (containing a Reseal[™] septum) and heated at 115 °C for 24 hours. After cooling to RT, the reaction mixture was diluted with 3M aq. HCl (6 mL) and extracted with CH₂Cl₂ (4 x 10 mL). The combined organic phase was dried over MgSO₄, filtered and concentrated *in vacuo*. **3w** was afforded after purification by FCC (5% pentane: Et₂O) as a white solid (136 mg, 0.5 mmol, 84% yield). The spectral data was identical to that described above.

Resubjection of lactol **23:** This experiment was carried out to confirm that isobutyl and methyl substituted lactols both react similarly with pentamethylacetophenone and are therefore suitable substrates for the deuterium label crossover experiment.



A 2-5mL Biotage[®] microwave vial was charged with 4-isobutyltetrahydro-2H-pyran-2-ol **23** (143 mg, 1.20 mmol, 2 eq), 1-(2,3,4,5,6-pentamethylphenyl)ethan-1-one **1** (114 mg, 0.600 mmol, 1 eq.), KOH (134 mg, 2.40 mmol, 4 eq.) and toluene (2.4 mL, 0.25 M). The vial was then sealed with a microwave vial cap (containing a Reseal[™] septum) and heated at 115 °C for 24 hours. After cooling to RT, the reaction mixture was diluted with 3M aq. HCl (6 mL) and extracted with CH₂Cl₂ (4 x 10 mL). The combined organic phase was dried over MgSO₄, filtered and concentrated *in vacuo*. **3v** was afforded after purification by FCC (5% Et₂O/pentane) as a white solid (167 mg, 0.534 mmol, 89% yield). The spectral data was identical to that described above.

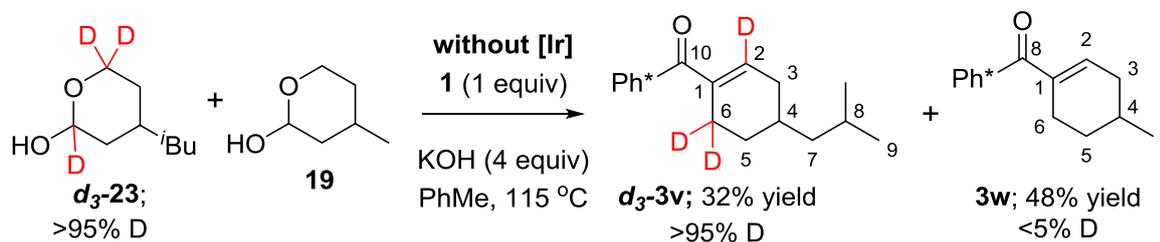
Pyran resubjection experiment



A 2-5mL Biotage[®] microwave vial was charged with 4-isobutyltetrahydro-2*H*-pyran-2-ol **23** (16 mg, 0.10 mmol, 1 eq.), 2-((*cis*)-4-methyltetrahydro-2*H*-pyran-2-yl)-1-(2,3,4,5,6-pentamethylphenyl)ethan-1-one **21** (30 mg, 0.10 mmol, 1 eq.), KOH (22 mg, 0.40 mmol, 4 eq.) and toluene (0.4 mL, 0.25 M). The vial was then sealed with a microwave vial cap (containing a Reseal[™] septum) and heated at 115 °C for 24 hours. After cooling to RT, the reaction mixture was diluted with 3M aq. HCl (6 mL) and extracted with CH₂Cl₂ (4 x 10 mL). The combined organic phase was dried over MgSO₄, filtered and concentrated in vacuo. Purification by FCC (3% Et₂O/pentane) afforded a mixture of (4-isobutylcyclohex-1-en-1-yl)(2,3,4,5,6-pentamethylphenyl)methanone **3v** and (4-methylcyclohex-1-en-1-yl)(2,3,4,5,6-pentamethylphenyl)methanone **3w** as a white solid (16 mg, 0.055 mmol, 55% yield, 79:21 **3w**:**3v** ratio by quantitative ¹H NMR). The spectral data for both **3w** and **3v** were identical to that described above.

5.3 Deuterium labelling Experiments

Lactol crossover experiment



A 2-5mL Biotage[®] microwave vial was charged with 4-isobutyltetrahydro-2H-pyran-2,6,6- d_3 -2-ol d_3 -**23** (97 mg, 0.60 mmol, 1 eq.), 4-methyltetrahydro-2H-pyran-2-ol **19** (70 mg, 0.60 mmol, 1 eq.), 1-(2,3,4,5,6-pentamethylphenyl)ethan-1-one **1** (114 mg, 0.600 mmol, 1 eq.), KOH (134 mg, 2.40 mmol, 4 eq.) and toluene (2.4 mL, 0.25 M). The vial was then sealed with a microwave vial cap (containing a Reseal[™] septum) and heated at 115 °C for 24 hours. After cooling to RT, the reaction mixture was diluted with 3M aq. HCl (6 mL) and extracted with CH₂Cl₂ (4 x 10 mL). The combined organic phases were dried over MgSO₄, filtered and concentrated in vacuo. Purification by FCC (3% Et₂O/pentane) afforded a mixture of d_3 -**3v** ($>95\%$ D incorporation by quantitative ¹H NMR, ²H and ¹³C NMR) and **3w** ($<5\%$ D incorporation by quantitative ¹H NMR and ¹³C NMR) as a white solid (140 mg, 0.480 mmol, 80% yield, 60:40 ratio **3w**: d_3 -**3v** by quantitative ¹H NMR). An analytical sample of each compound was obtained by preparative TLC (10% EtOAc/Pentane).

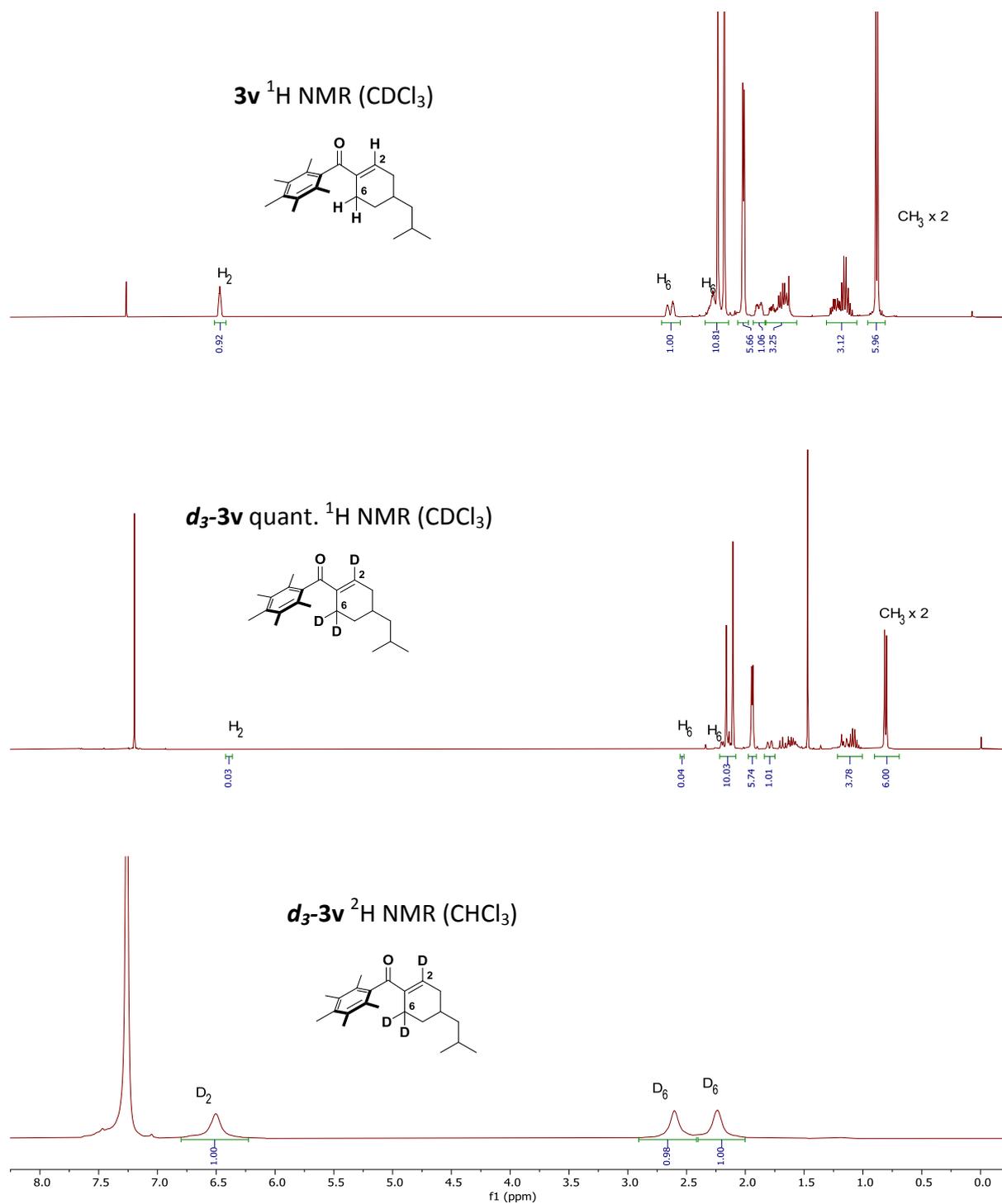
Data for d_3 -**3v** from lactol crossover experiment:

¹H NMR (400 MHz, CDCl₃) δ 2.32 – 2.12 (m, 10H, ArCH₃ x 3, H_{3a}), 2.02 (s, 3H, ArCH₃), 2.01 (s, 3H, ArCH₃), 1.91 – 1.81 (m, 1H, H_{5a}), 1.81 – 1.56 (m, 3H, H_{3b}, H₄ and H₈), 1.34 – 1.06 (m, 3H, H_{5b}, H₇ x 2), 0.88 (d, J = 6.5 Hz, 6H, H₉ x 6). Peaks at 6.46 ppm (H₂) and 2.61 ppm (H₆) integrate to $<5\%$ implying $>95\%$ D incorporation at each position.

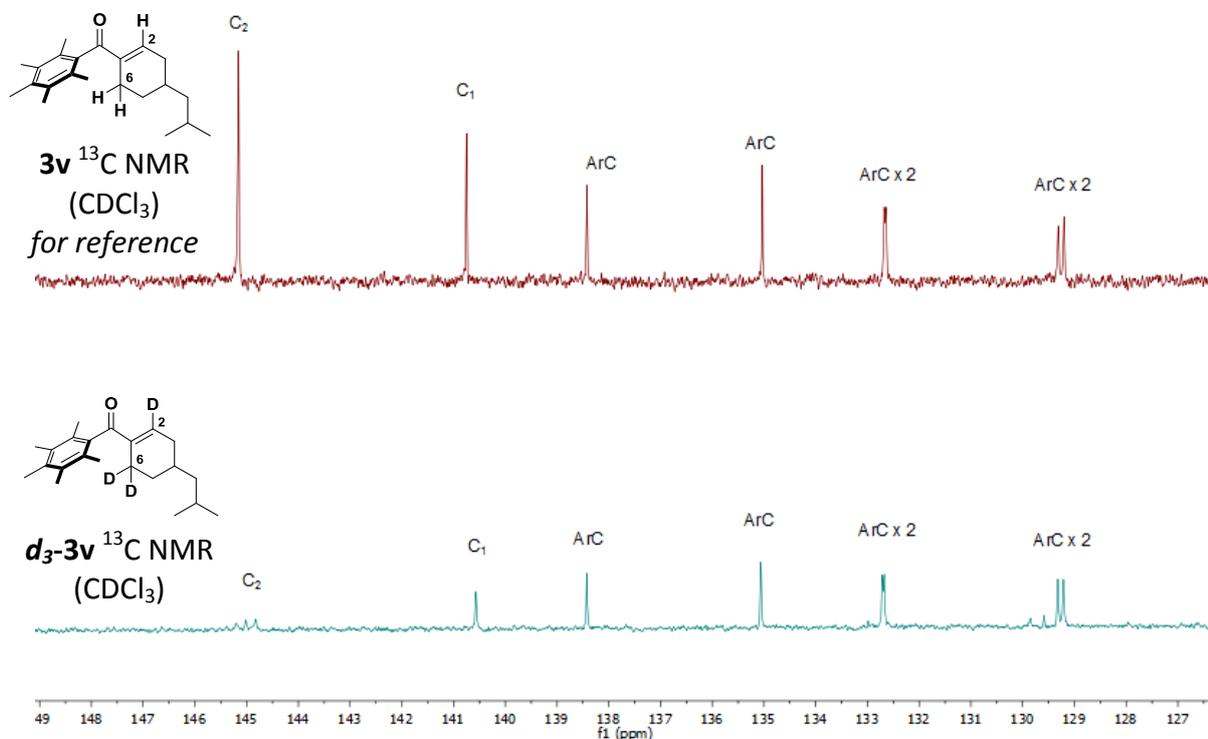
¹³C NMR (126 MHz, CDCl₃) δ 203.6 (C₁₀), 145 (1:1:1 triplet, J = 24 Hz, C₂), 140.6 (C₁), 138.4 (ArC), 135.1 (ArC), 132.7 (ArC), 132.7 (ArC), 129.3 (ArC), 129.2 (ArC), 45.8 (C₇), 33.2 (C₃), 30.5 (C₄), 28.4 (C₅), 25.1 (C₈), 23.1 (C_{9a}), 22.9 (C_{9b}), 21.8 (1:2:3:2:1 pentet, J = 20 Hz, C₆), 17.6 (ArCH₃), 17.6 (ArCH₃), 16.8 (ArCH₃), 16.1 (ArCH₃ x 2). Reduced intensity ¹³C peak corresponding to C₆ and C₂ due to ²J_{CD} coupling.

²H NMR (77 MHz, CHCl₃) δ 6.51 (s, 1 x ²H, ²H₂), 2.61 (s, 1 x ²H, ²H_{6eq}), 2.24 (s, 1 x ²H, ²H_{6ax}).

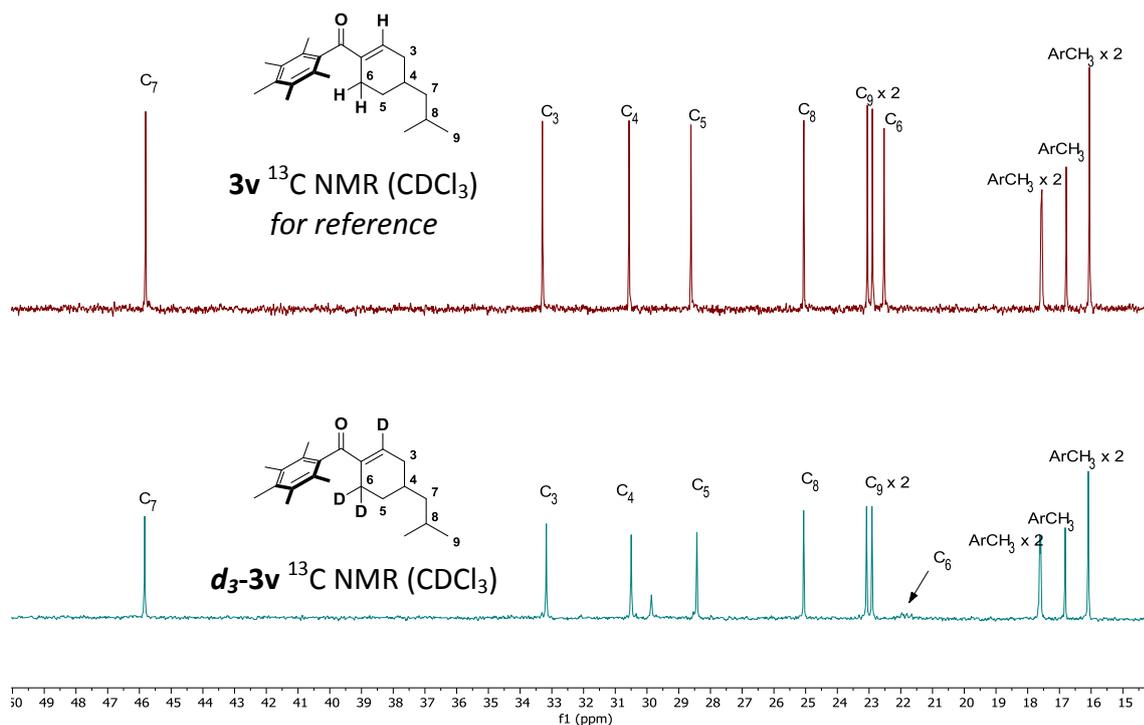
Stack plot showing reference ^1H NMR spectrum of **3v** along with quantitative ^1H NMR and ^2H NMR spectra of ***d*₃-3v** from lactol cross over experiment:



Stack plot showing reference ^{13}C NMR spectrum of **3v** (149–127 ppm) along with ^{13}C NMR spectrum of **d₃-3v** from lactol cross over experiment. Illustrates 1:1:1 triplet at C₂ from $^2J_{\text{CD}}$ coupling (CD):



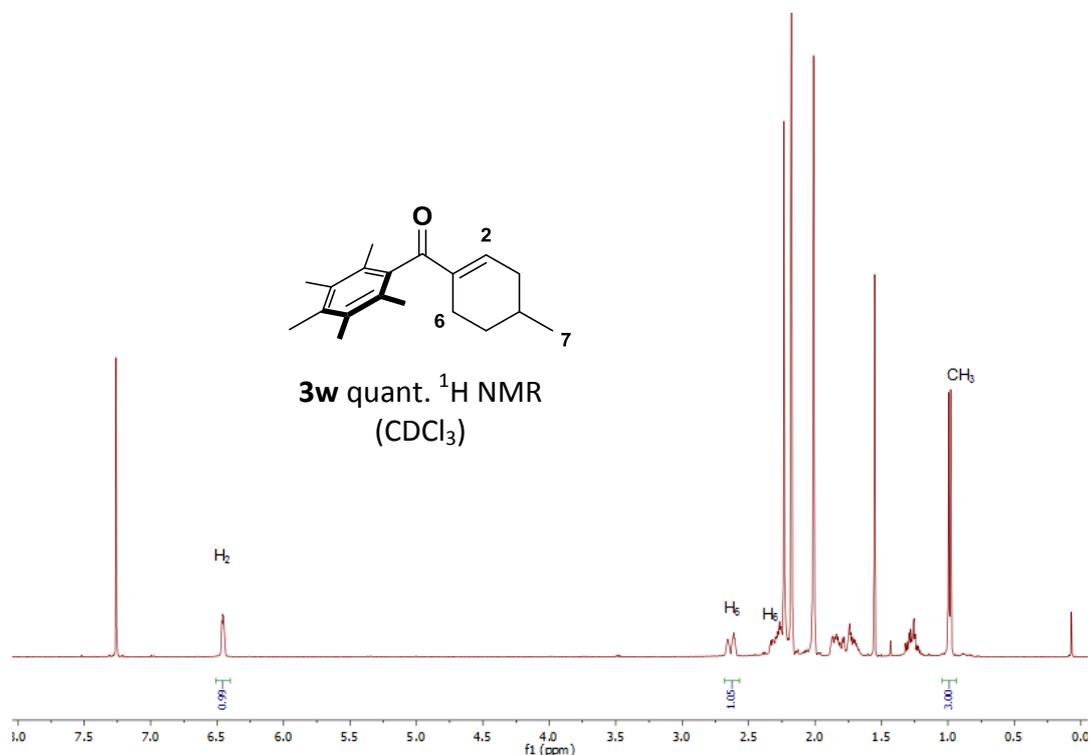
Stack plot showing reference ^{13}C NMR spectrum of **3v** (50–14 ppm) along with ^{13}C NMR spectrum of **d₃-3v** from lactol cross over experiment. Illustrates 1:2:3:2:1 pentet at C₆ from $^2J_{\text{CD}}$ coupling (CD₂):



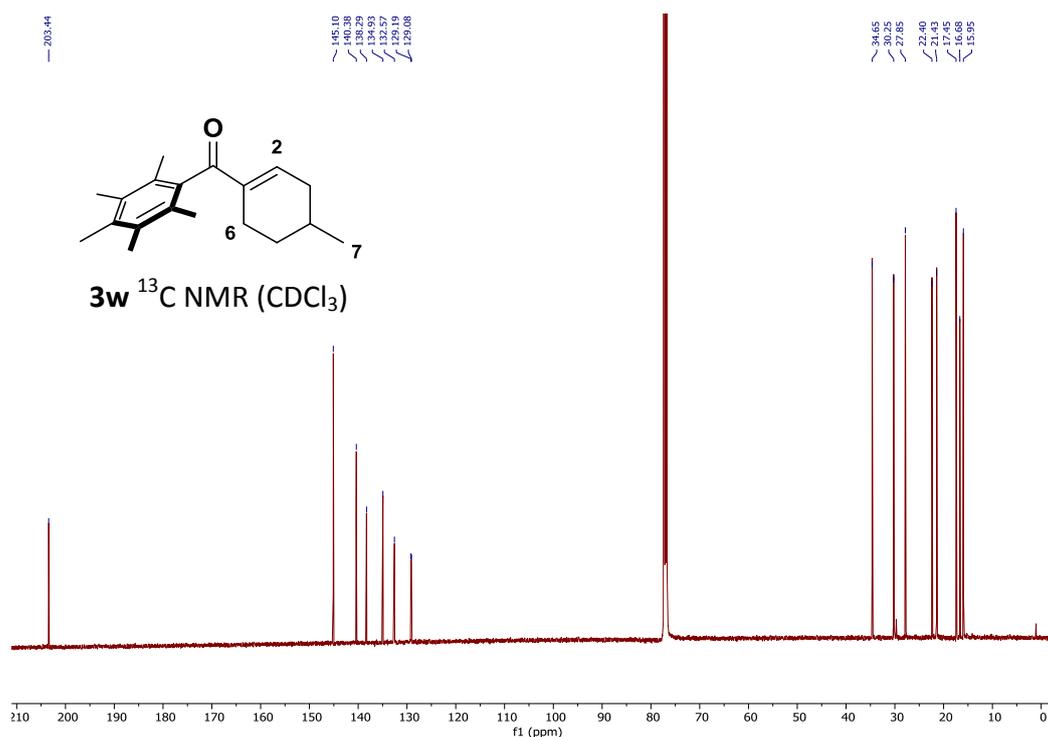
Data for **3w** from lactol crossover experiment:

<5% D incorporation at the 2- and 6-positions by quantitative ^1H NMR and ^{13}C NMR.

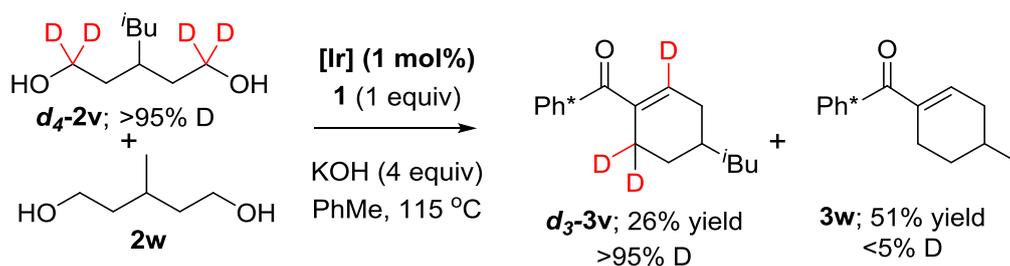
The ^1H NMR data was identical to that described previously for non-deuterated **3w** and the peaks corresponding to H₂ and H₆ integrated to >95% implying <5% D incorporation at these positions:



The ^{13}C NMR data was identical to that described previously and showed no CD coupling:



Diol Crossover Experiment

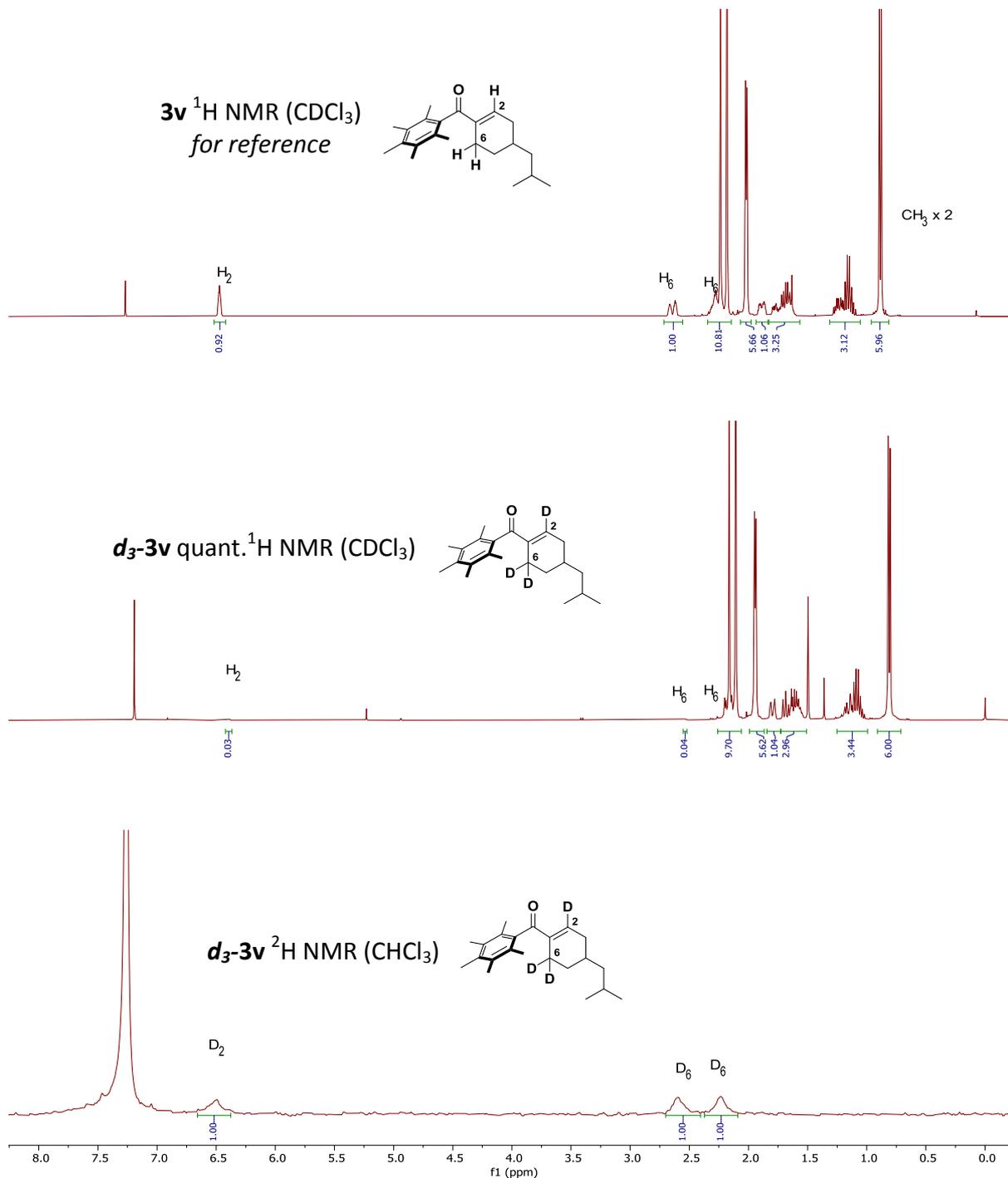


A 2-5mL Biotage[®] microwave vial was charged with CataCXium[®] A (4.3 mg, 0.012 mmol, 2 mol%), 3-isobutylpentane-1,1,5,5-*d*₄-1,5-diol **d₄-2v** (99 mg, 0.60 mmol, 1 eq.), 3-methylpentane-1,5-diol **2w** (71 mg, 0.60 mmol, 1 eq.), 1-(2,3,4,5,6-pentamethylphenyl)ethan-1-one **1** (114 mg, 0.600 mmol, 1 eq.), [Ir(cod)Cl]₂ (2 mg, 0.003 mmol, 0.5 mol% dimer), KOH (134 mg, 2.40 mmol, 4 eq.) and toluene (2.4 mL, 0.25 M). The vial was then sealed with a microwave vial cap (containing a Reseal[™] septum) and heated at 115 °C for 24 hours. After cooling to RT, the reaction mixture was diluted with aq. HCl (3 M, 5 mL) and extracted with CH₂Cl₂ (4 x 10 mL). The combined organic phases were dried over MgSO₄, filtered and concentrated *in vacuo*. Purification by FCC (3% Et₂O/pentane) afforded a mixture of **d₃-3v** (>95% D incorporation by quantitative ¹H NMR, ²H and ¹³C NMR) and **3w** (<5% D incorporation by quantitative ¹H NMR and ¹³C NMR) as a white solid (135 mg, 0.462 mmol, 77% yield, 64:34 ratio **3w**:**d₃-3v** by quantitative ¹H NMR). An analytical sample of each compound was obtained by preparative TLC (10% EtOAc/Pentane).

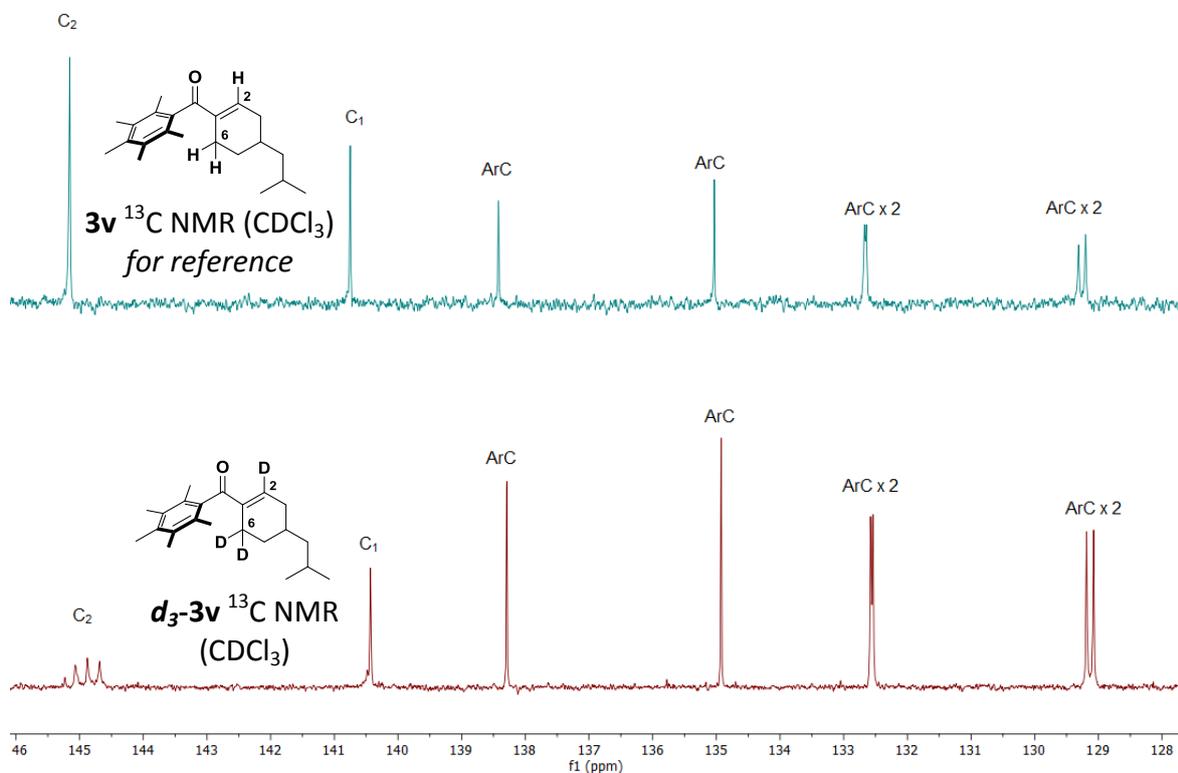
The spectral data for both **d₃-3v** and **3w** were identical to that described in the lactol crossover experiment. Copies of the spectral data are shown overleaf.

Data for d_3 -**3v** from diol crossover experiment:

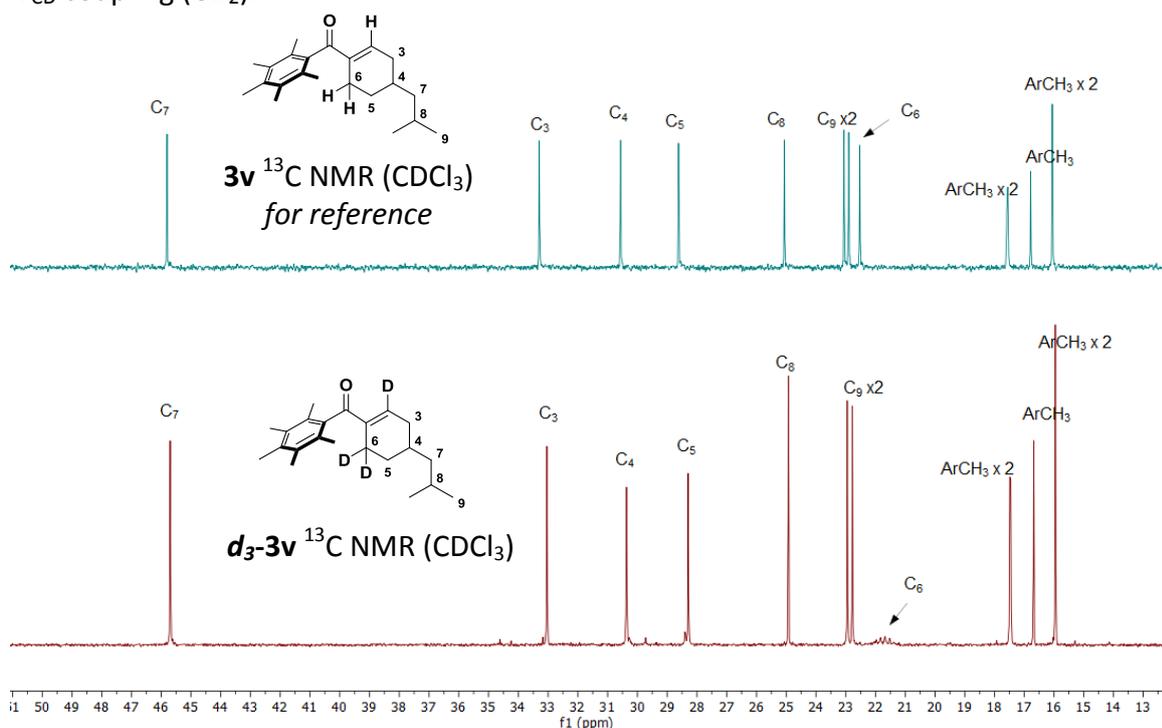
Stack plot showing reference ^1H NMR spectrum of **3v** along with quantitative ^1H NMR and ^2H NMR spectra of d_3 -**3v** from diol cross over experiment:



Stack plot showing reference ^{13}C NMR spectrum of **3v** (146–128 ppm) along with ^{13}C NMR spectrum of **d₃-3v** from diol cross over experiment. Illustrates 1:1:1 triplet at C₂ from $^2J_{\text{CD}}$ coupling (CD):



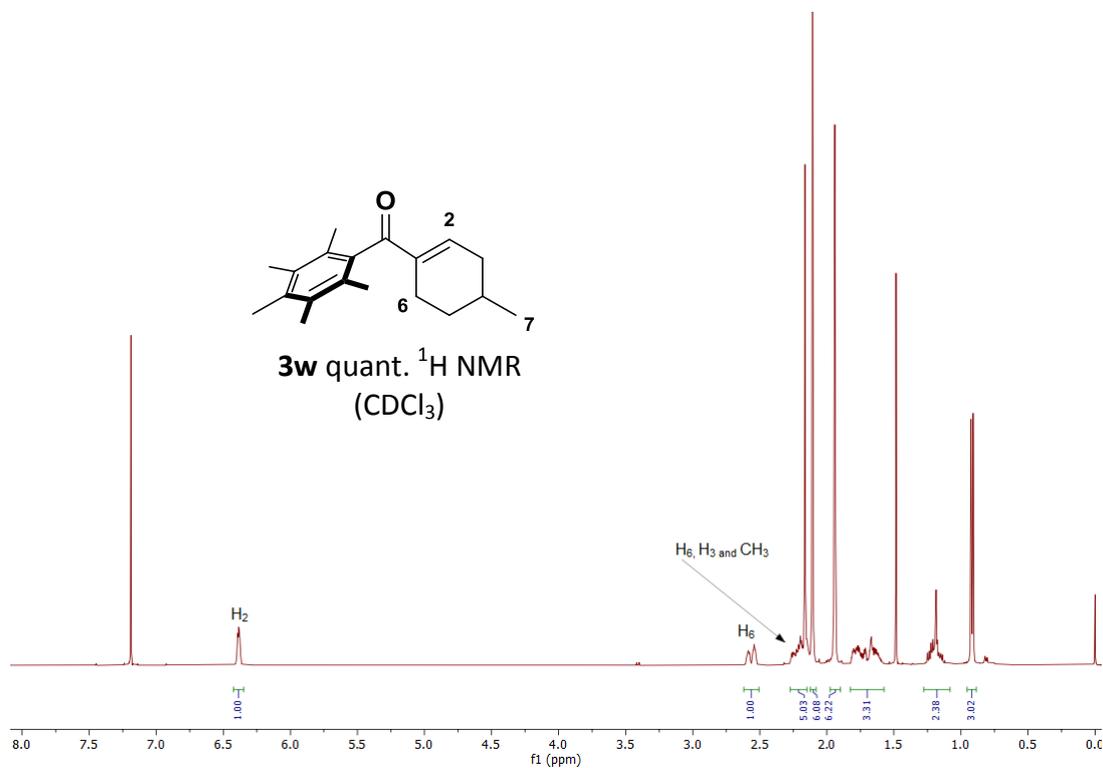
Stack plot showing reference ^{13}C NMR spectrum of **3v** (51–13 ppm) along with ^{13}C NMR spectrum of **d₃-3v** from diol cross over experiment. Illustrates 1:2:3:2:1 pentet at C₆ from $^2J_{\text{CD}}$ coupling (CD_2):



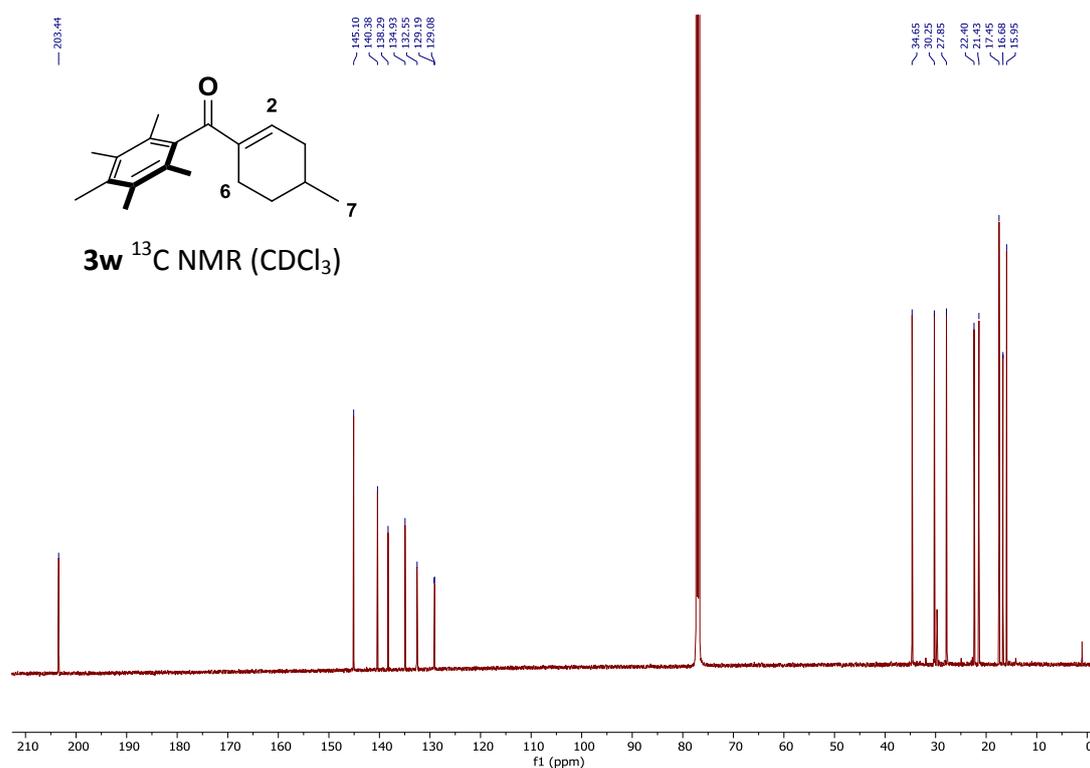
Data for **3w** from diol crossover experiment:

<5% D incorporation at the 2- and 6-positions by quantitative ^1H NMR and ^{13}C NMR

The ^1H NMR data was identical to that described previously for non-deuterated **3w** and the peaks corresponding to H_2 and H_6 integrated to >95% implying <5% deuterium incorporation at these positions:



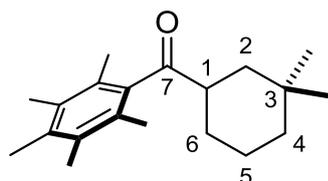
The ^{13}C NMR data was identical to that described previously and showed no CD coupling:



5.4 Cyclohexane Crossover Experiments

In advance of this experiment, we independently synthesized and characterized fully protonated cyclohexanes **26** and **27**. Experimental details and characterization data are provided below.

(3,3-Dimethylcyclohexyl)(2,3,4,5,6-pentamethylphenyl)methanone, **26**

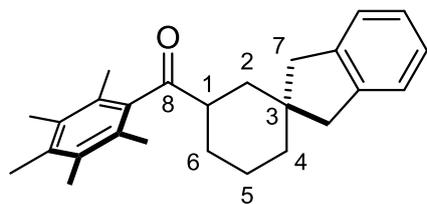


We have previously reported the synthesis of cyclohexane **26** from pentamethylacetophenone and diol **2af**.⁴ We previously reported NMR data for this compound in CDCl₃, but several of the ¹H NMR signals overlapped. Much better signal separation was observed in CD₂Cl₂ – assigned NMR data are provided below. All other data was identical to that described previously.⁴

¹H NMR (700 MHz, CD₂Cl₂) δ 2.78 (tt, J = 12.5, 3.5 Hz, 1H, H₁), 2.24 (s, 3H, ArCH₃), 2.18 (s, 6H, ArCH₃ x 2), 2.05 (s, 6H, ArCH₃ x 2), 1.90 – 1.82 (m, 1H, H_{6eq}), 1.64 – 1.59 (m, 1H, H_{5eq}), 1.57 – 1.52 (m, 1H, H_{2eq}), 1.43 (qt, J = 13.5, 3.5 Hz, 1H, H_{5ax}), 1.39 – 1.34 (m, 1H, H_{4eq}), 1.30 (t, J = 13.0 Hz, 1H, H_{2ax}), 1.23 (qd, J = 13.0, 4.0 Hz, 1H, H_{6ax}), 1.14 (td, J = 13.5, 3.5 Hz, 1H, H_{4ax}), 0.95 (s, 3H, CH₃), 0.86 (s, 3H, CH₃).

¹³C NMR (126 MHz, CD₂Cl₂) δ 215.1 (C₇), 140.7 (ArC), 135.6 (ArC), 133.3 (ArC x 2), 128.4 (ArC x 2), 49.5 (C₁), 40.9 (C₂), 39.0 (C₄), 33.4 (CH₃), 30.9 (C₃), 28.7 (C₆), 24.4 (CH₃), 22.3 (C₅), 18.1 (ArCH₃ x 2), 16.8 (ArCH₃), 16.1 (ArCH₃ x 2).

(1',3'-Dihydrospiro[cyclohexane-1,2'-inden]-3-yl)(2,3,4,5,6-pentamethylphenyl)methanone, 27



A 2–5 mL Biotage[®] microwave vial was charged with 3-(2-(hydroxymethyl)-2,3-dihydro-1*H*-inden-2-yl)propan-1-ol (123 mg, 0.6 mmol, 2 eq.), 1-(2,3,4,5,6-pentamethylphenyl)ethan-1-one (57 mg, 0.3 mmol, 1 eq.), [Cp*IrCl₂]₂ (4.8 mg, 0.006 mmol, 2 mol% dimer), KOH (67 mg, 1.2 mmol, 4 eq.) toluene (0.075 mL, 4 M). The reaction vessel was sealed with a microwave vial cap (containing a Reseal[™] septum), fitted with an Ar balloon, and the vial was heated at 115 °C for 24 hours. After cooling to RT, the reaction mixture was diluted with HCl (3M, 5 mL), extracted with CH₂Cl₂ (3 x 5 mL), dried over MgSO₄ and concentrated *in vacuo*. The title compound was afforded after purification by FCC (5% Et₂O/pentane) as a white solid (108 mg, 0.3 mmol, 100% yield).

¹H NMR (700 MHz, CD₂Cl₂) δ 7.20 – 7.02 (m, 4H, ArCH x 4), 2.88 – 2.66 (m, 5H, H₁, H₇ x 4), 2.23 (s, 3H, ArCH₃), 2.18 (s, 6H, ArCH₃ x 2), 2.06 (s, 6H, ArCH₃ x 2), 1.93 (dtq, J = 10.5, 3.5, 2.0 Hz, 1H, H_{6eq}), 1.87 (dq, J = 13.0, 2.5 Hz, 1H, H_{2eq}), 1.75 – 1.69 (m, 1H, H_{5eq}), 1.67 – 1.62 (m, 1H, H_{4eq}), 1.60 (t, J = 13.0 Hz, 1H, H_{2ax}), 1.47 (qt, J = 13.5, 3.5 Hz, 1H, H_{5ax}), 1.38 – 1.29 (m, 2H, H_{4ax}, H_{6ax}).

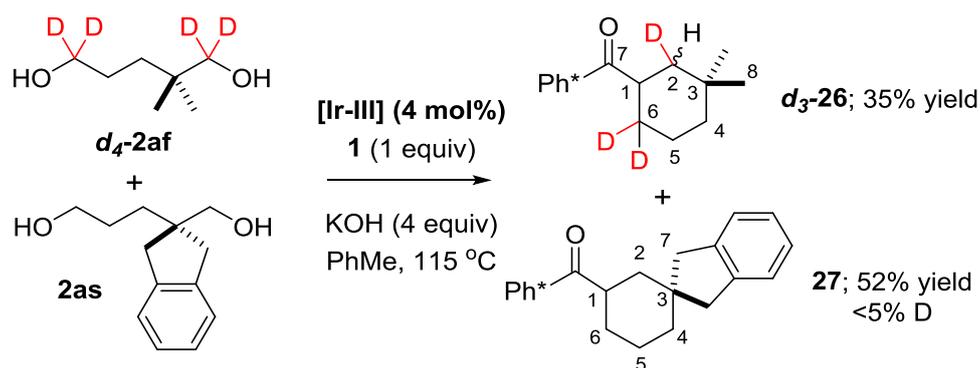
¹³C NMR (101 MHz, CD₂Cl₂) δ 214.8 (C₈), 143.1 (ArC), 143.0 (ArC), 140.7 (ArC), 135.9 (ArC), 133.6 (ArC x 2), 128.5 (ArC x 2), 126.7 (ArC), 126.6 (ArC), 125.3 (ArC), 125.2 (ArC), 50.8 (C₁), 49.4 (C_{7a}), 44.2 (C₃), 42.4 (C_{7b}), 39.5 (C₂), 37.4 (C₄), 28.8 (C₆), 23.4 (C₅), 18.3 (ArCH₃ x 2), 17.0 (ArCH₃), 16.3 (ArCH₃ x 2).

HRMS (ESI⁺): Found [M+Na]⁺ = 383.2348; C₂₆H₃₂ONa requires 383.2345, Δ 0.69 ppm.

IR (film) ν_{max}/cm⁻¹ 2925, 1689, 1448, 1382, 1306, 911, 733.

m.p.: 157-158 °C.

Reductive crossover experiment:



A 2-5 mL Biotage[®] microwave vial was charged with 2,2-dimethylpentane-1,1,5,5-*d*₄-1,5-diol ***d*₄-2af** (82 mg, 0.60 mmol, 1 eq.), 3-(2-(hydroxymethyl)-2,3-dihydro-1*H*-inden-2-yl)propan-1-ol **2as** (124 mg, 0.60 mmol, 1 eq.), 1-(2,3,4,5,6-pentamethylphenyl)ethan-1-one **1** (114 mg, 0.60 mmol, 1 eq.), [IrCp*Cl₂]₂ (9.6 mg, 0.012 mmol, 2 mol% dimer), KOH (134 mg, 2.40 mmol, 4 eq.) and toluene (0.15 mL, 4 M). The vial was then sealed with a microwave vial cap (containing a Reseal™ septum) and fitted with an argon balloon and heated at 115 °C for 24 hours. After cooling to RT, the reaction mixture was diluted with aq. HCl (3 M, 5 mL) and extracted with CH₂Cl₂ (4 x 10 mL). The combined organic phases were dried over MgSO₄, filtered and concentrated *in vacuo*. Purification by FCC (3-4% Et₂O/pentane) afforded ***d*₃-26** as a white solid (see spectra for details of deuterium incorporation, 61 mg, 0.21 mmol, 35% yield, ~1:1 d.r.) and **27** as a white solid (<5% D incorporation by quantitative ¹H NMR and ¹³C NMR, 112 mg, 0.31 mmol, 52% yield).

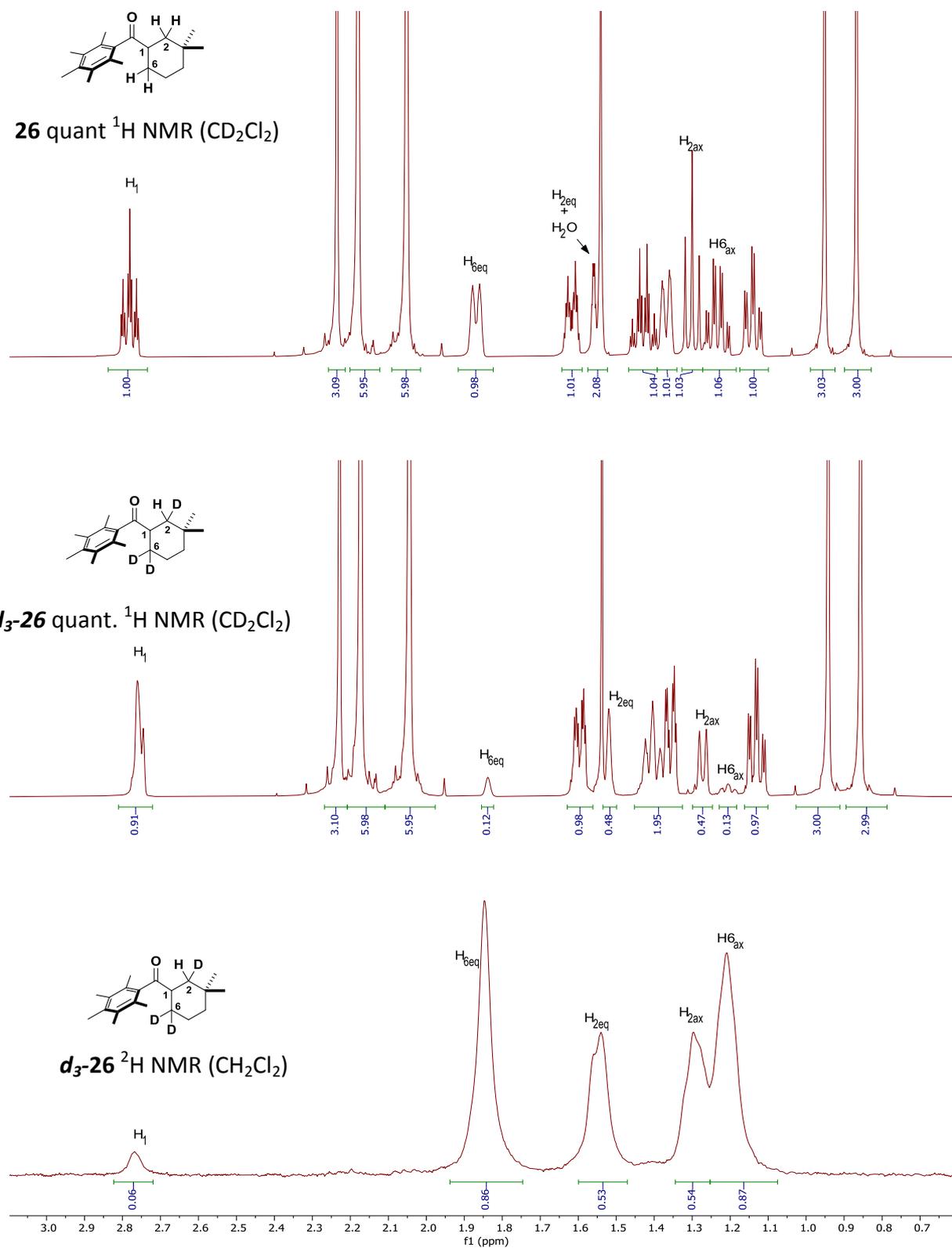
Data for *d*₃-26 from reductive crossover experiment:

¹H NMR (700 MHz, CD₂Cl₂) δ 2.79 – 2.74 (1H, m, 0.91 H, H₁), 2.23 (3H, s, ArCH₃), 2.18 (6H, s, ArCH₃), 2.05 (6H, s, ArCH₃), 1.84 (0.12H, br s, H_{6eq}), 1.63 – 1.57 (1H, m, 1H, H_{5eq}), 1.52 (0.48H, s, H_{2eq}), 1.45 – 1.38 (1H, m, H_{5ax}), 1.38 – 1.34 (1H, m, H_{4eq}), 1.28 (0.47H, br d, *J* = 12.5 Hz, H_{2ax}), 1.24 – 1.18 (0.13H, m, H_{6ax}), 1.13 (1H, td, *J* = 13.4, 4.2 Hz, H_{4ax}), 0.95 (3H, s, 3 x H_{8a}), 0.86 (3H, s, 3 x H_{8b}).

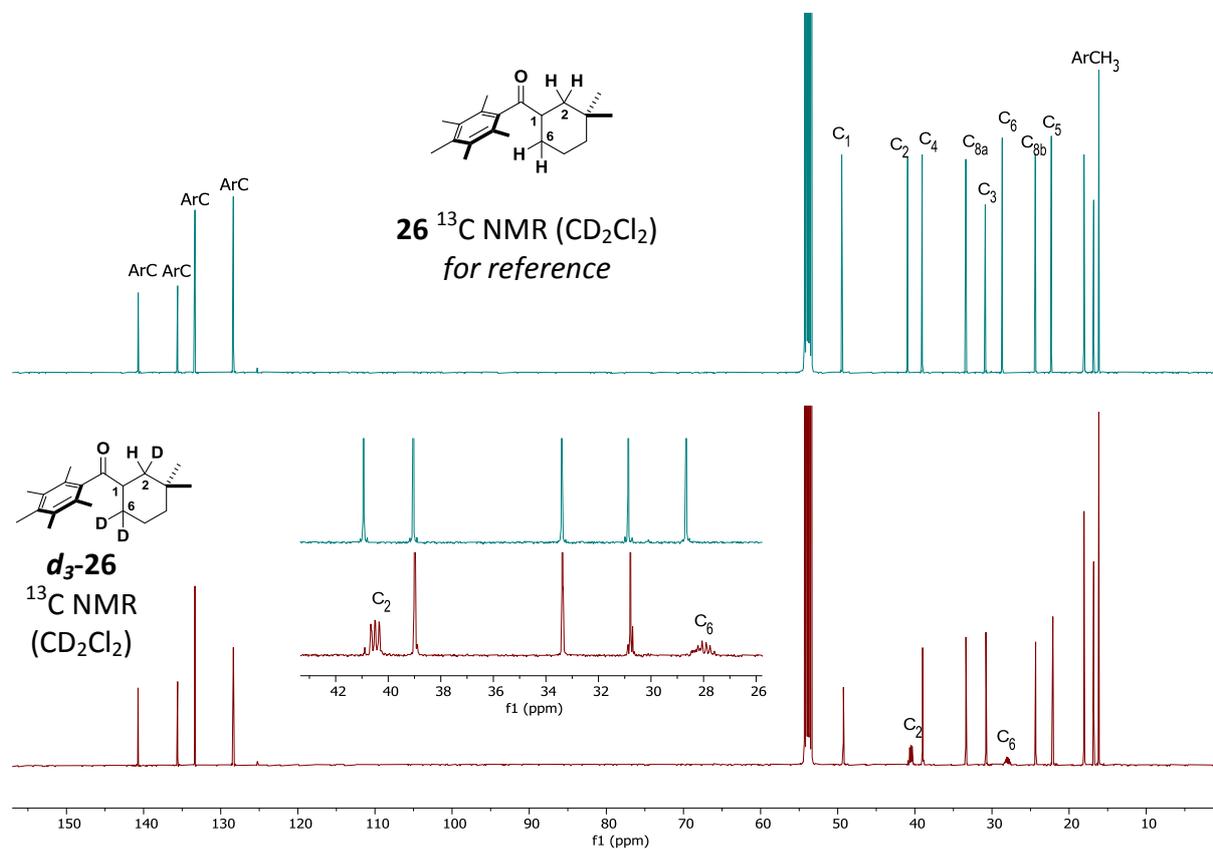
¹³C NMR (126 MHz, CD₂Cl₂) δ 215.2 (C₇), 140.7 (ArC), 135.6 (ArC), 133.3 (ArC x 2), 128.4 (ArC x 2), 49.3 (C₁), 49.2 (C_{1'}), 40.5 (1:1:1 triplet, *J* = 19.5 Hz, C₂), 40.5 (1:1:1 triplet, *J* = 19.5 Hz, C_{2'}), 39.0 (C₄), 33.4 (C_{8a}), 33.4 (C_{8a'}), 30.8 (C₃), 28.5 – 27.5 (m, C₆), 24.4 (C_{8b}), 24.3 (C_{8b'}), 22.1 (C₅), 18.1 (ArCH₃ x 2), 16.8 (ArCH₃), 16.1 (ArCH₃ x 2).

^2H NMR (92 MHz, CH_2Cl_2) δ 2.77 (s, $^2\text{H}_1$), 1.85 (s, $^2\text{H}_{6\text{eq}}$), 1.54 (s, $^2\text{H}_{2\text{eq}}$), 1.29 (s, $^2\text{H}_{2\text{ax}}$), 1.21 (s, $^2\text{H}_{6\text{ax}}$). The integrals were consistent with the integrals observed in the ^1H NMR spectrum (see below).

Stack plot showing reference ^1H NMR spectrum of **26** along with quantitative ^1H NMR and ^2H NMR spectra of d_3 -**26** from reductive cross over experiment:



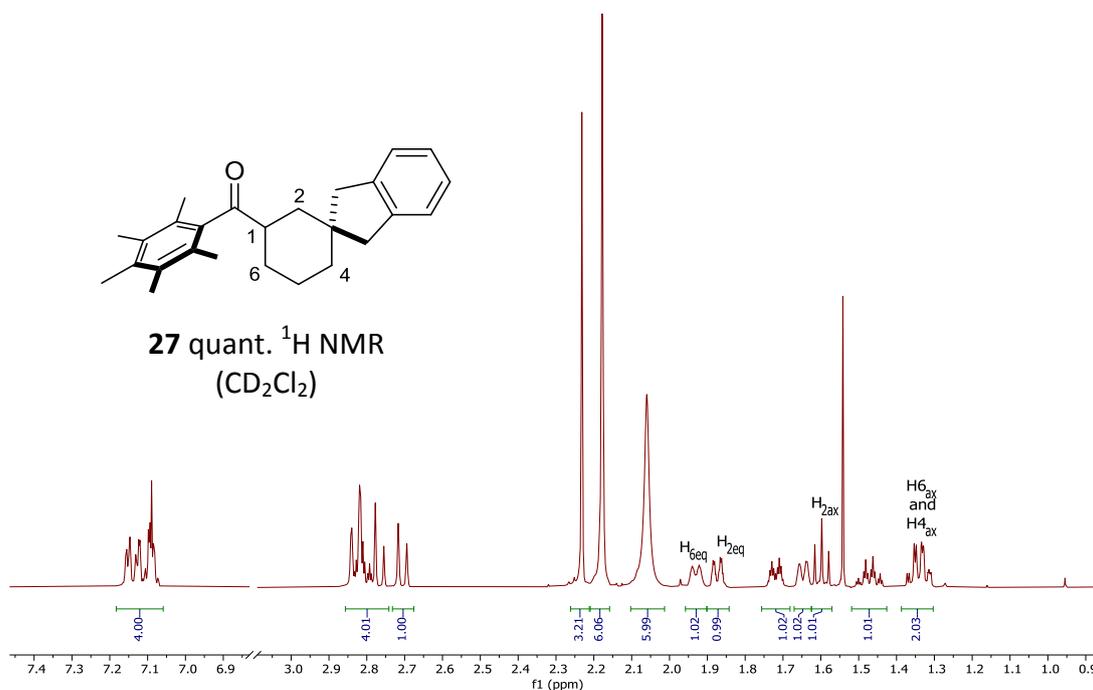
^{13}C NMR spectrum of ***d*₃-26** from reductive cross over experiment stacked with reference ^{13}C NMR spectrum of **26** (n.b. carbonyl peak omitted for clarity). Expansion illustrates 1:1:1 triplet at C_2 from $^2J_{\text{CD}}$ coupling (CHD) and multiplet for C_6 from $^2J_{\text{CD}}$ coupling (CD_2):



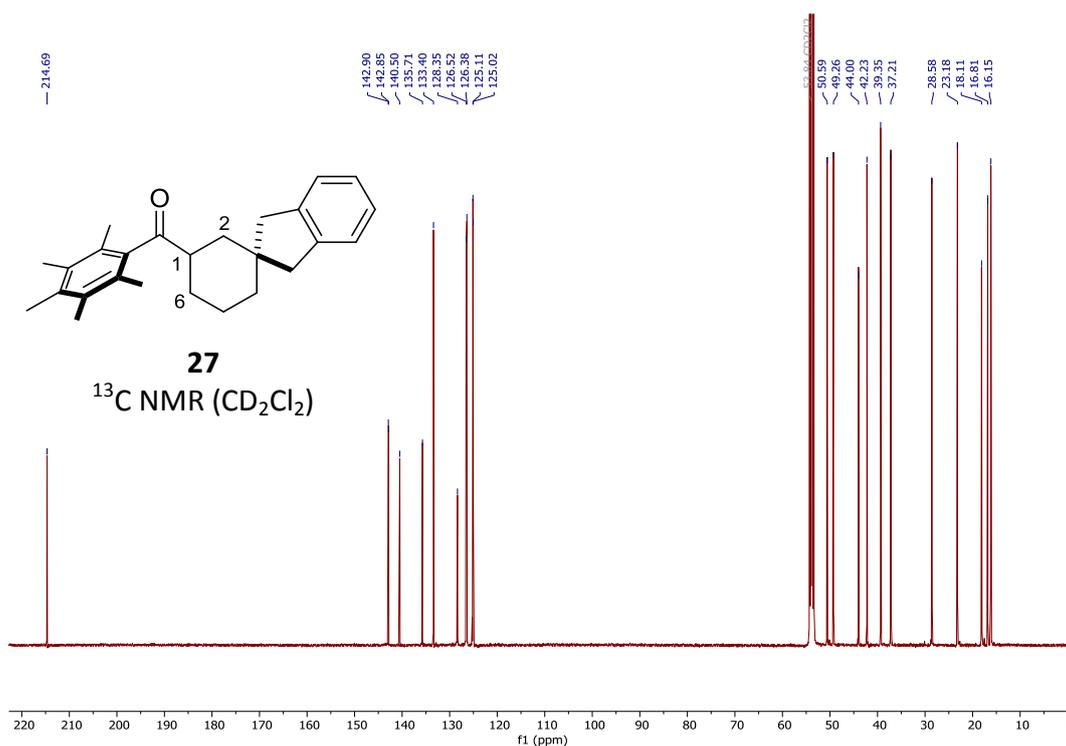
Data for **27** from reductive crossover experiment:

<5% D incorporation at the 2- and 6-positions by quantitative ^1H NMR and ^{13}C NMR.

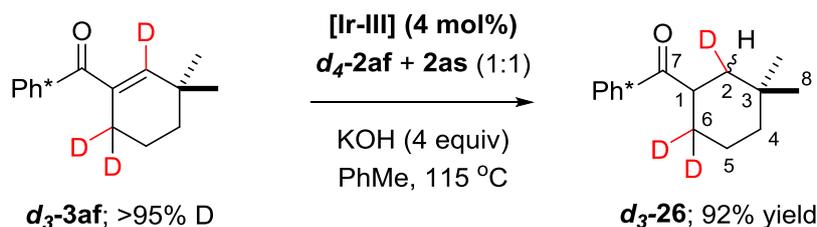
The ^1H NMR data was identical to that described previously for non-deuterated **27** and the peaks corresponding to H₂ and H₆ integrated to >95% implying <5% D incorporation at these positions:



The ^{13}C NMR data was identical to that described previously and showed no CD coupling:



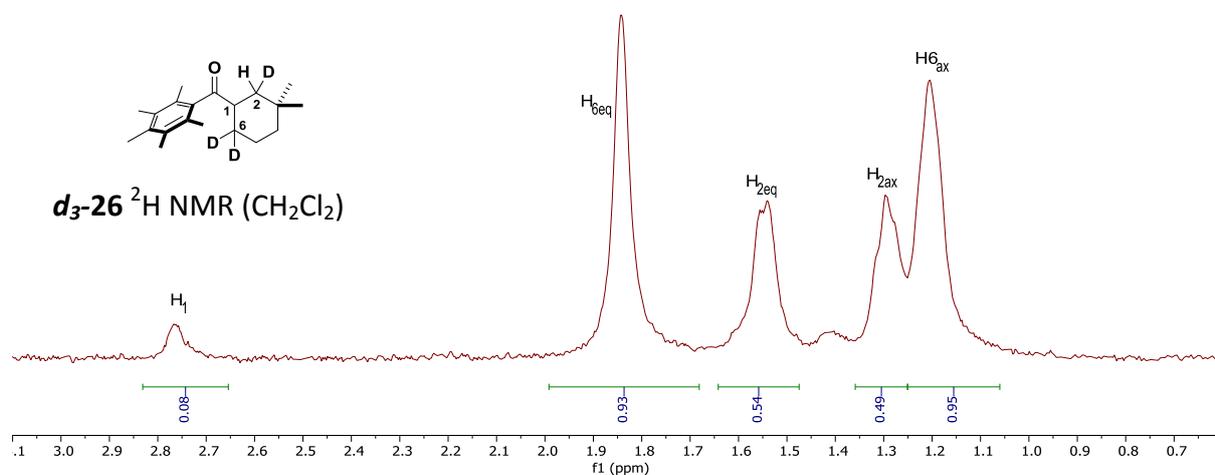
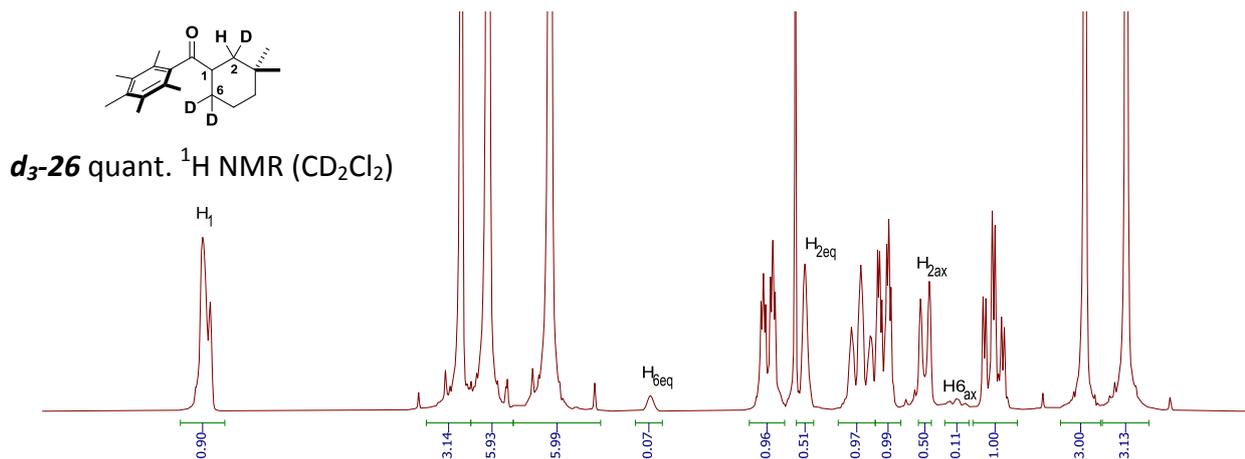
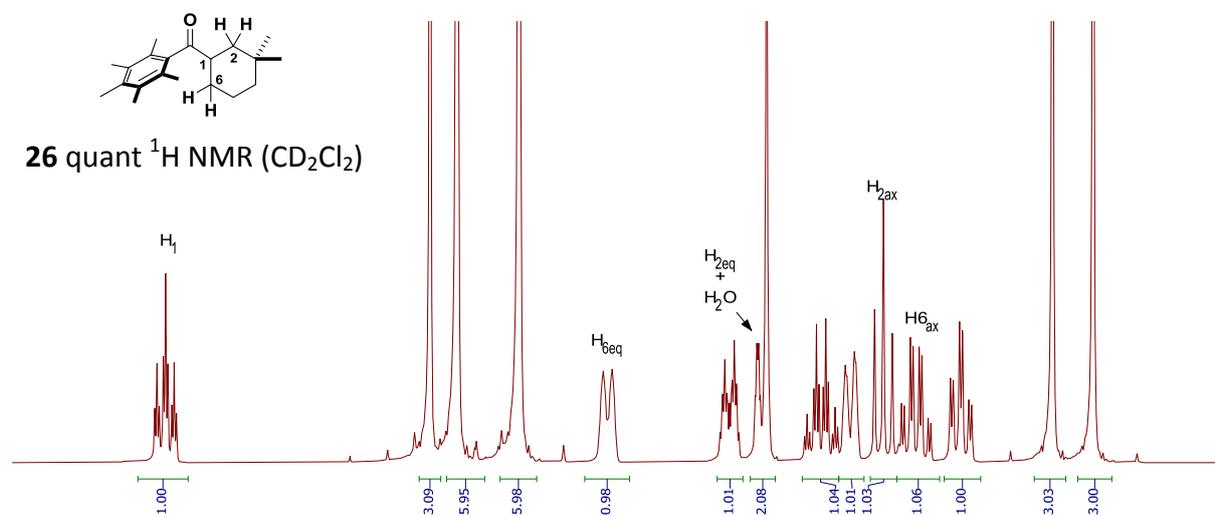
Transfer hydrogenation of deuterated enone



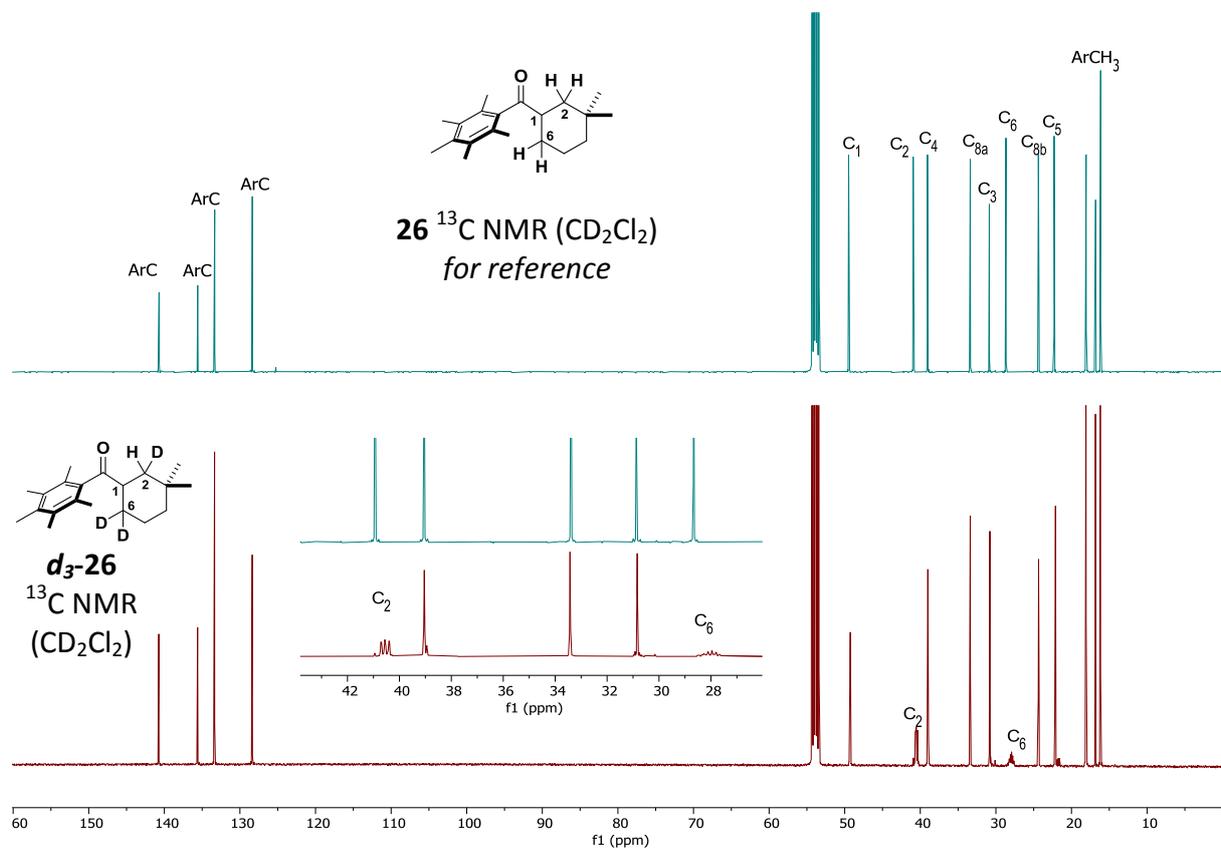
A 2-5mL Biotage[®] microwave vial was charged with 2,2-dimethylpentane-1,1,5,5-*d*₄-1,5-diol ***d*₄-2af** (16 mg, 0.12 mmol, 1 eq.), 3-(2-(hydroxymethyl)-2,3-dihydro-1*H*-inden-2-yl)propan-1-ol **2as** (25 mg, 0.12 mmol, 1 eq.), (3,3-dimethylcyclohex-1-en-1-yl-2,6,6-*d*₃)(2,3,4,5,6-pentamethylphenyl)methanone ***d*₃-3af** (35 mg, 0.12 mmol, 1 eq.), [IrCp*Cl₂]₂ (1.9 mg, 0.0026 mmol, 2 mol% dimer), KOH (27 mg, 0.48 mmol, 4 eq.) and toluene (0.03 mL, 4 M). The vial was then sealed with a microwave vial cap (containing a Reseal™ septum) and fitted with an argon balloon and heated at 115 °C for 24 hours. After cooling to RT, the reaction mixture was diluted with aq. HCl (3 M, 5 mL) and extracted with CH₂Cl₂ (4 x 10 mL). The combined organic phases were dried over MgSO₄, filtered and concentrated *in vacuo*. Purification by FCC (3% Et₂O/pentane) afforded ***d*₃-26** as a white solid (see spectra for details of deuterium incorporation, 32 mg, 0.11 mmol, 92% yield, ~1:1 d.r.).

The spectral data for ***d*₃-26** was very similar to that described in the reductive cross over experiment. Copies of the spectral data are shown overleaf.

Stack plot showing reference ^1H NMR spectrum of **26** along with quantitative ^1H NMR and ^2H NMR spectra of d_3 -**26** from transfer hydrogenation:



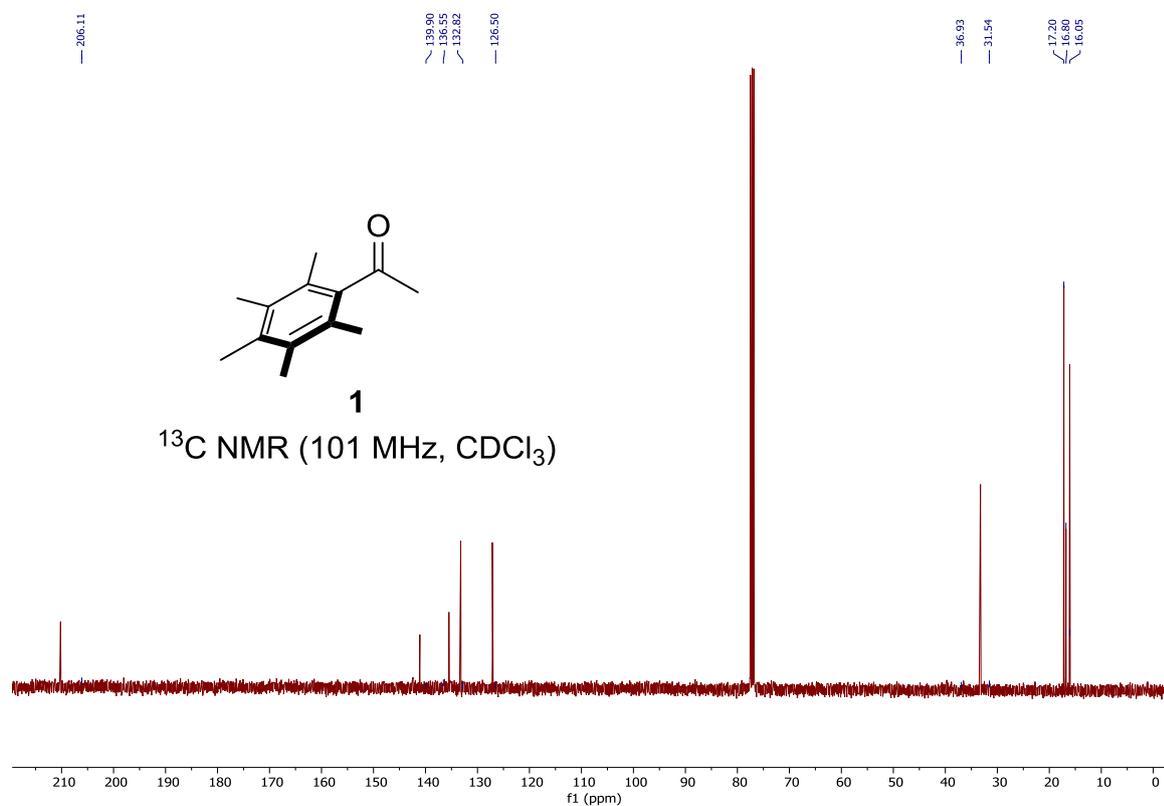
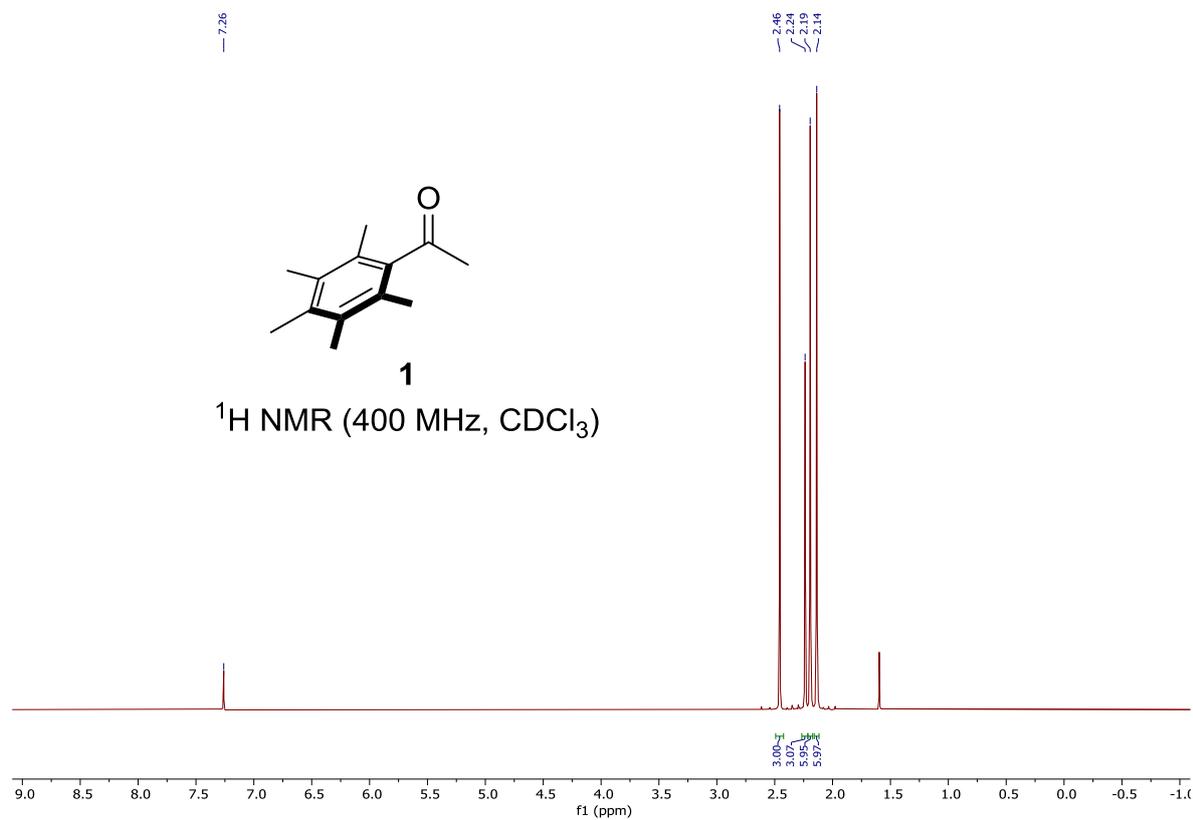
^{13}C NMR spectrum of ***d*₃-26** from transfer hydrogenation stacked with reference ^{13}C NMR spectrum of **26** (n.b. carbonyl peak omitted for clarity). Expansion illustrates 1:1:1 triplet at C₂ from $^2J_{\text{CD}}$ coupling (CHD) and multiplet for C₆ from $^2J_{\text{CD}}$ coupling (CD₂):

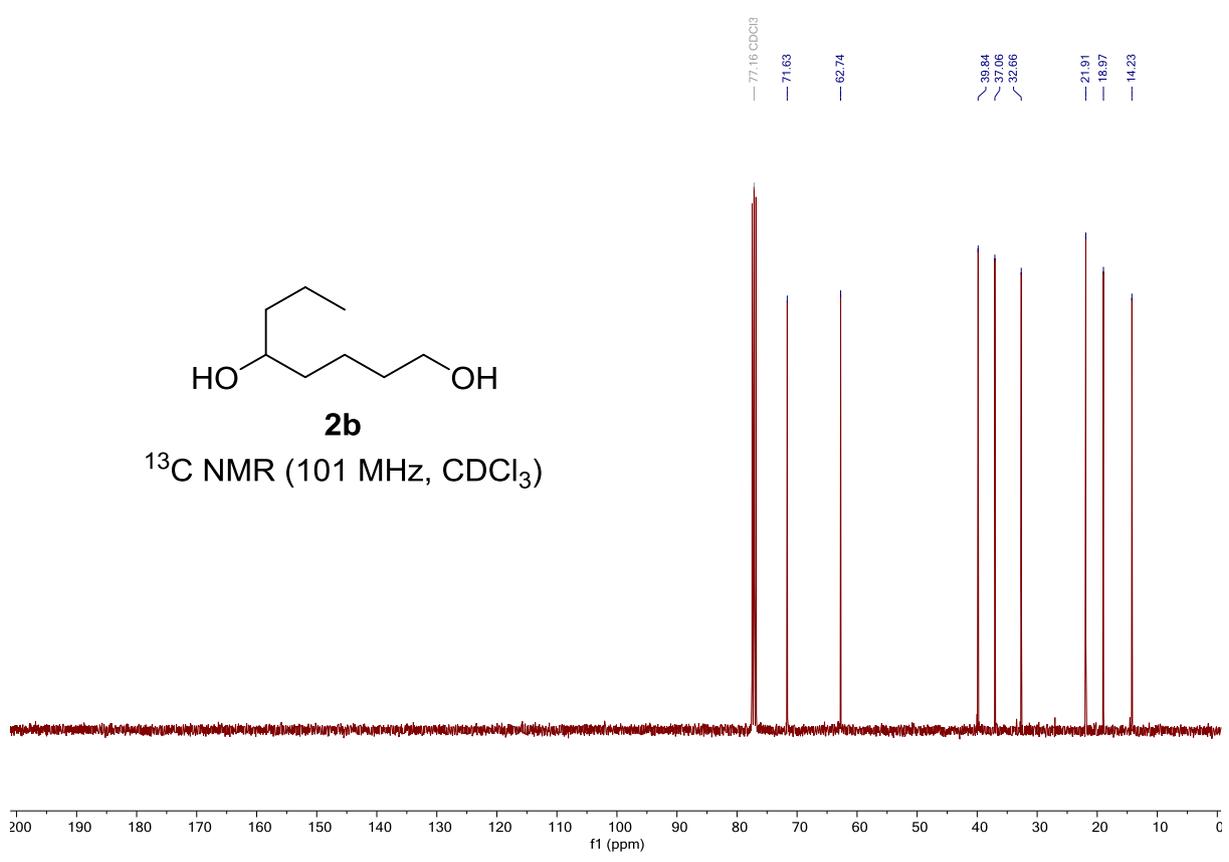
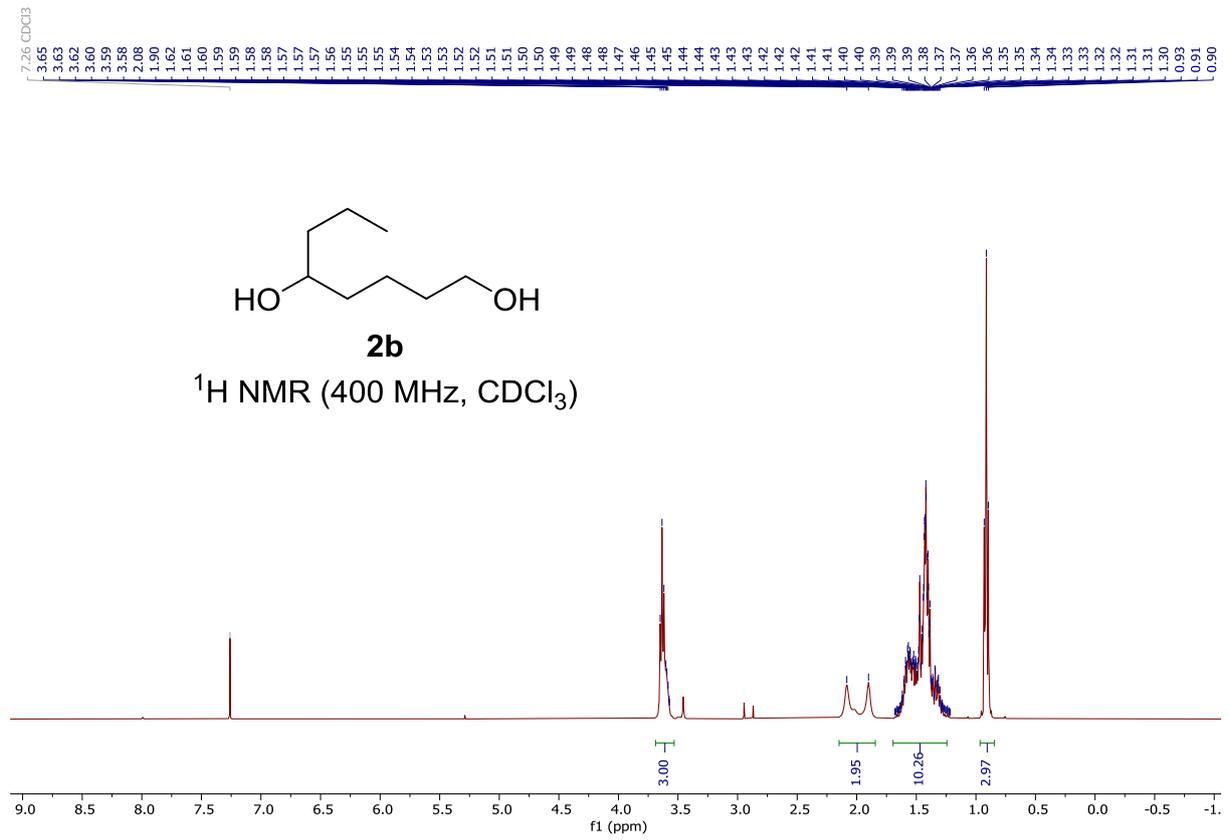


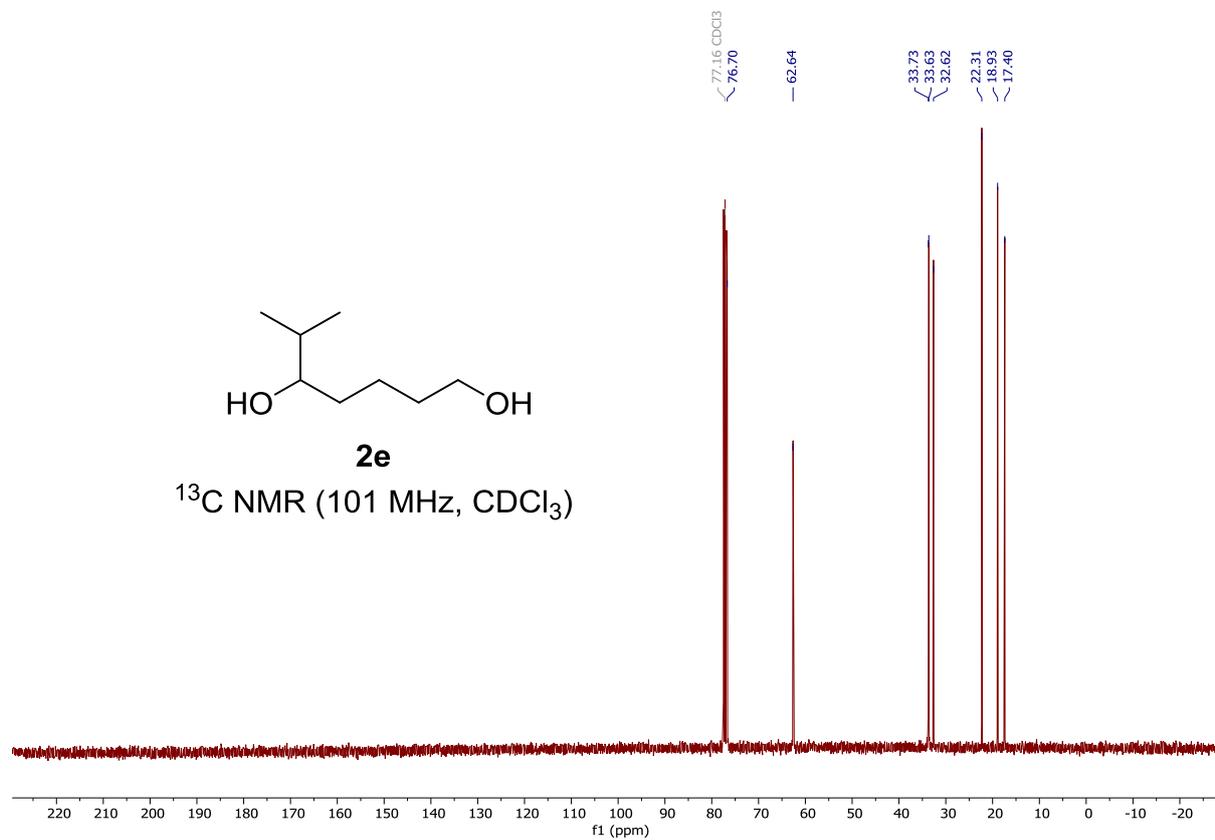
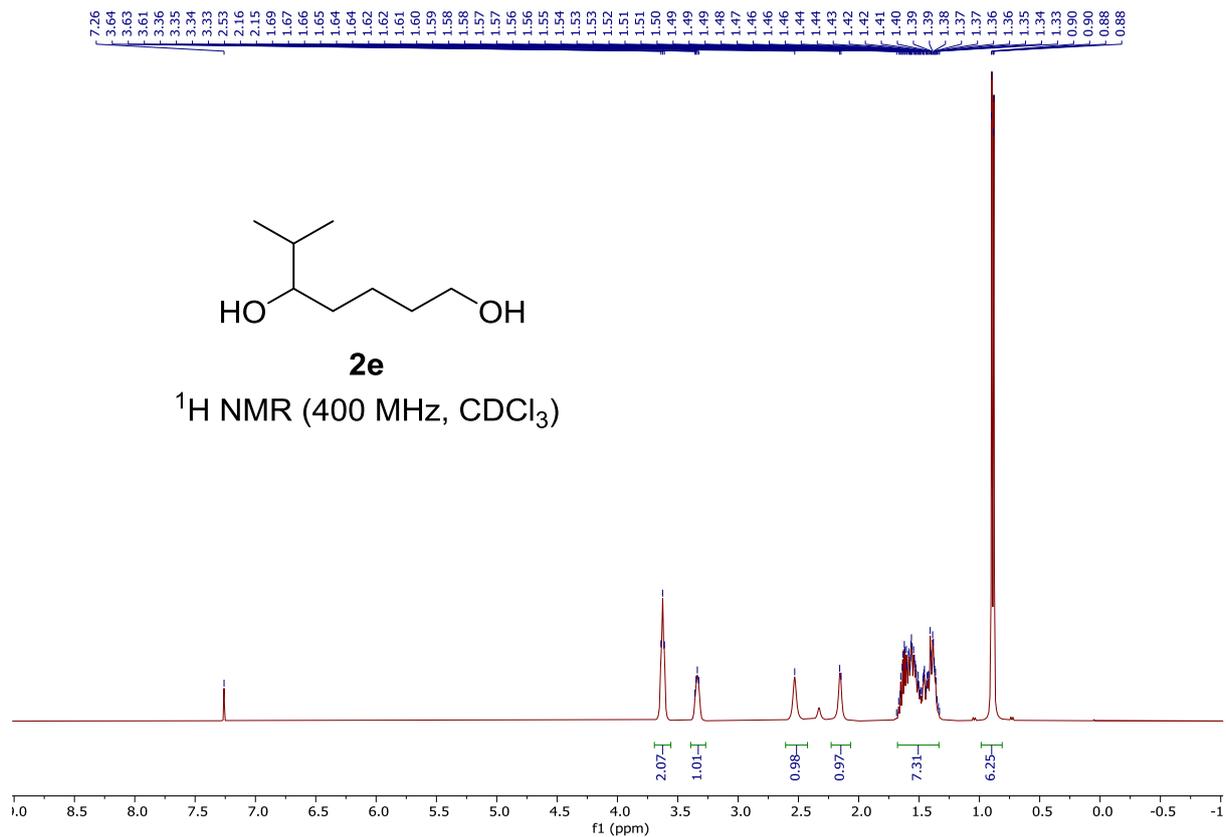
6. References

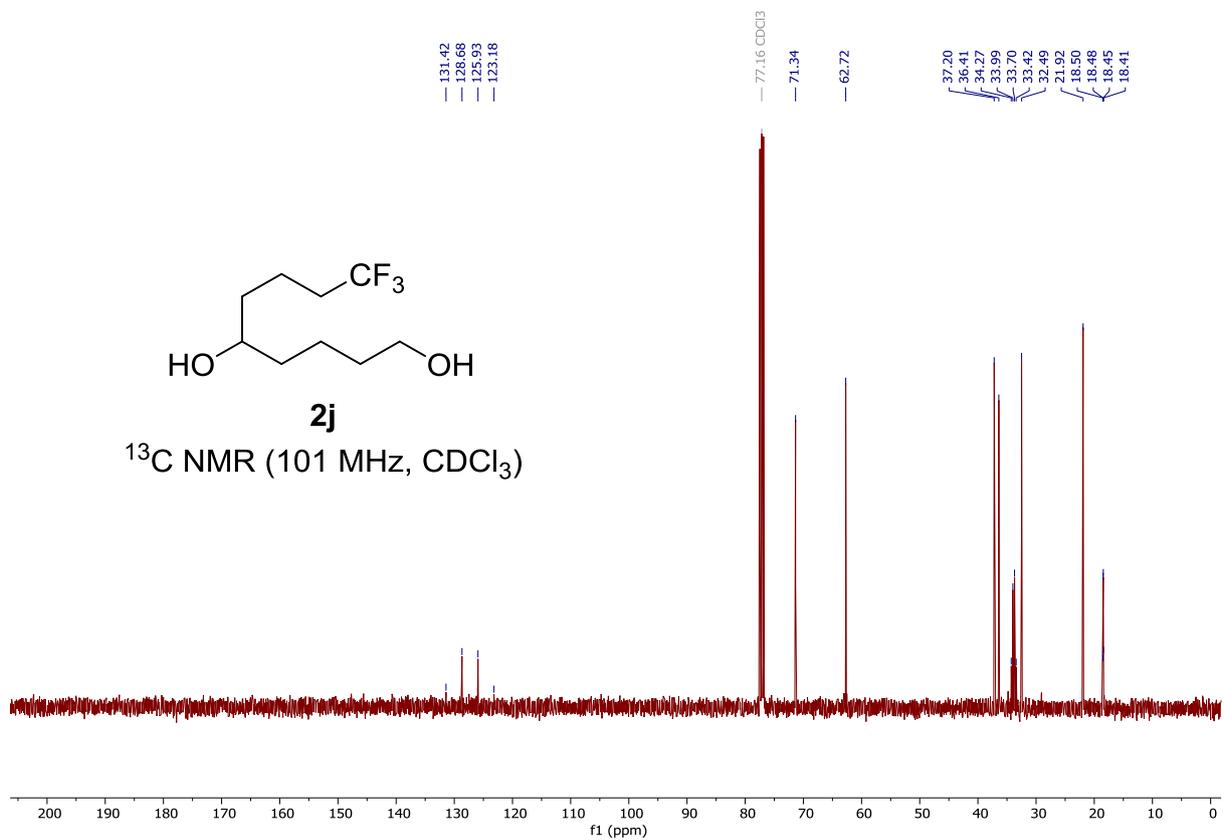
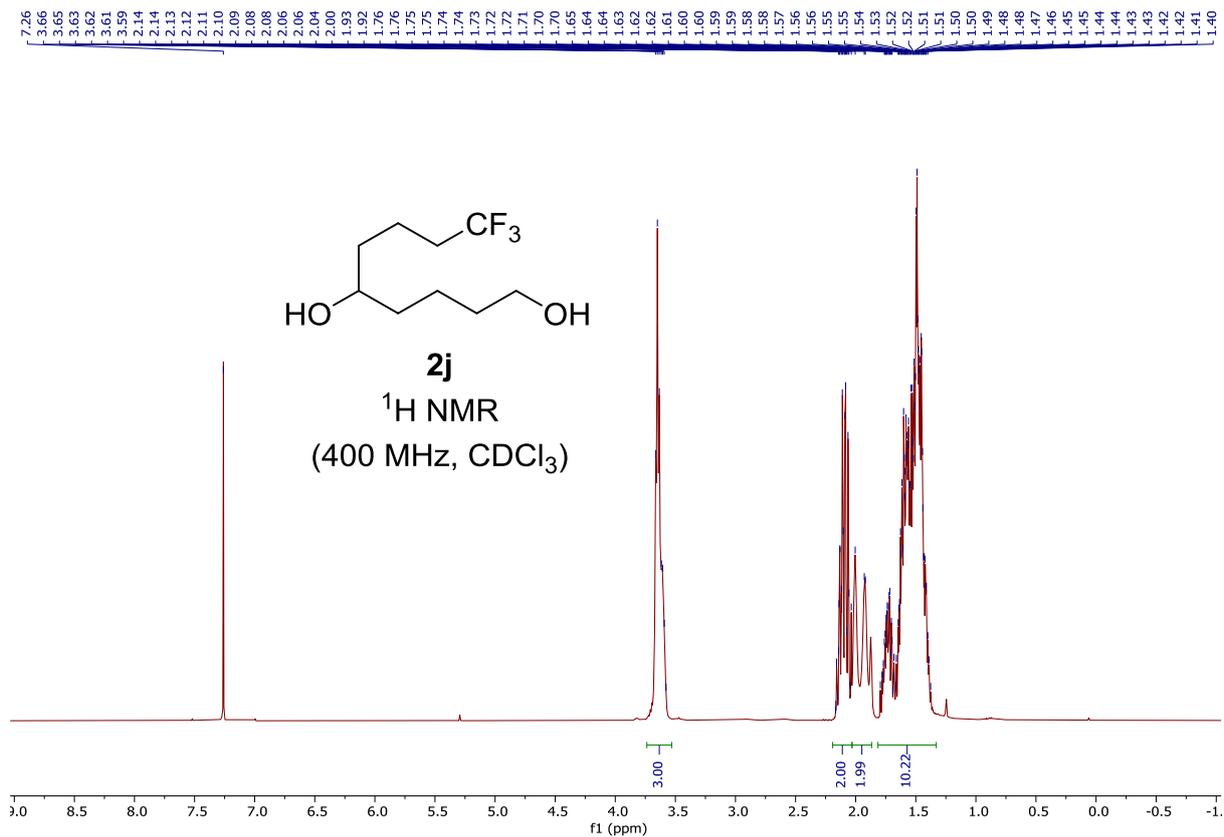
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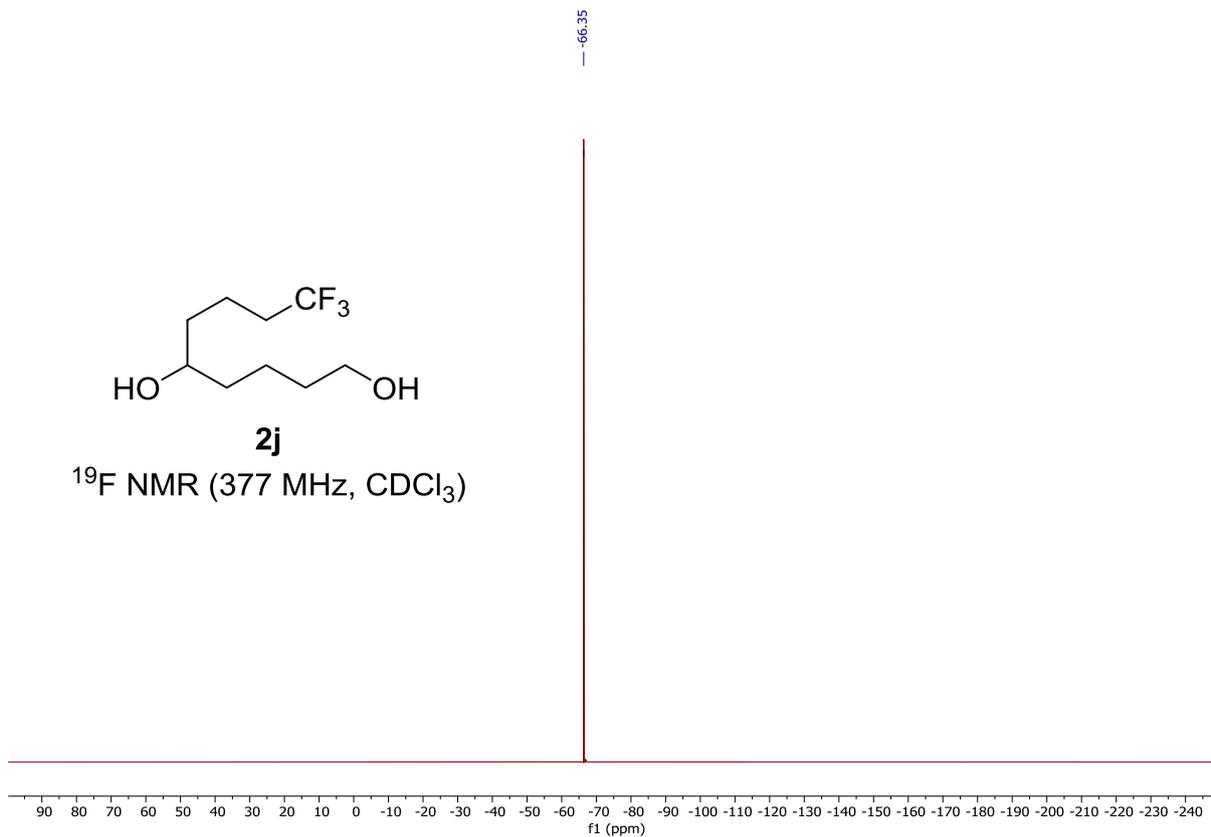
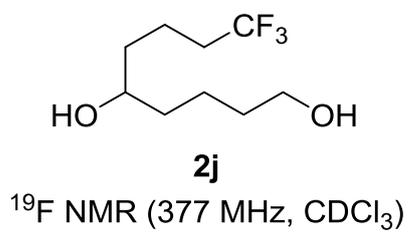
7. NMR Spectra

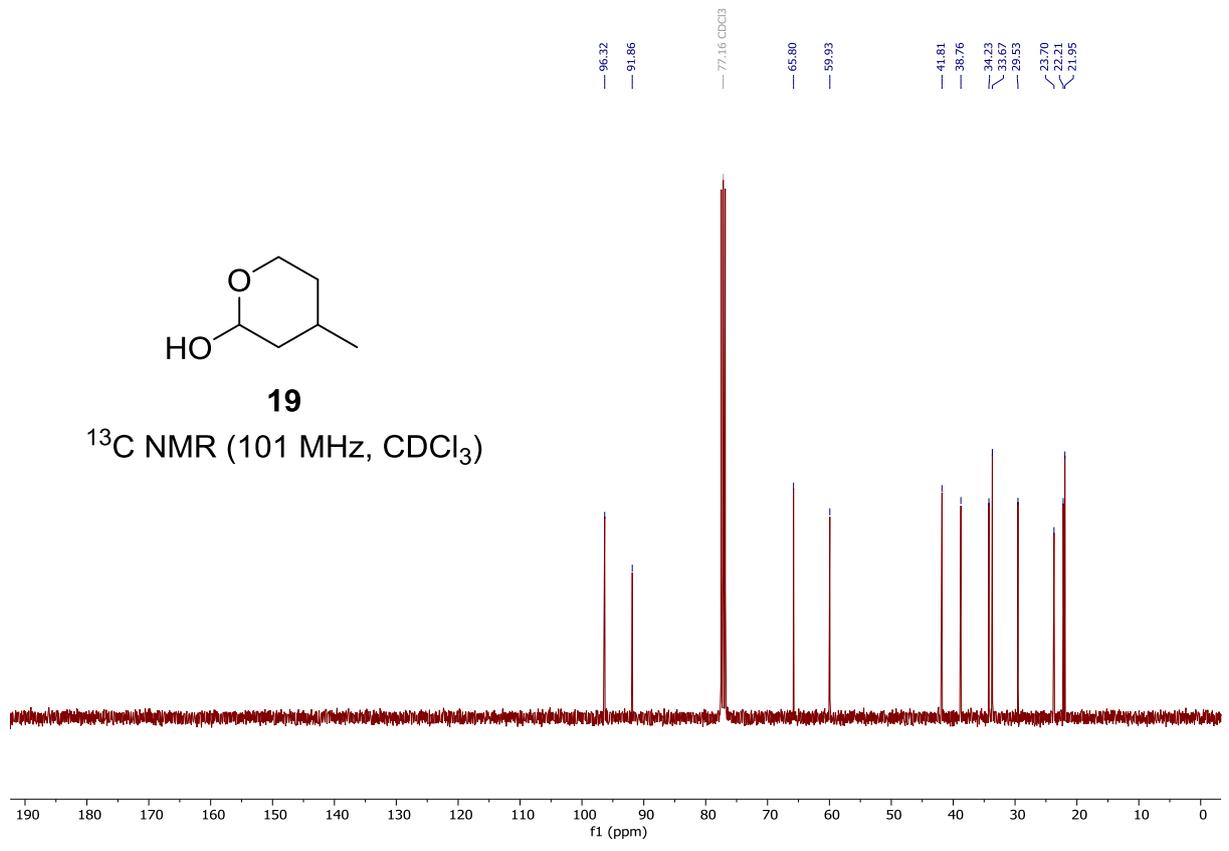
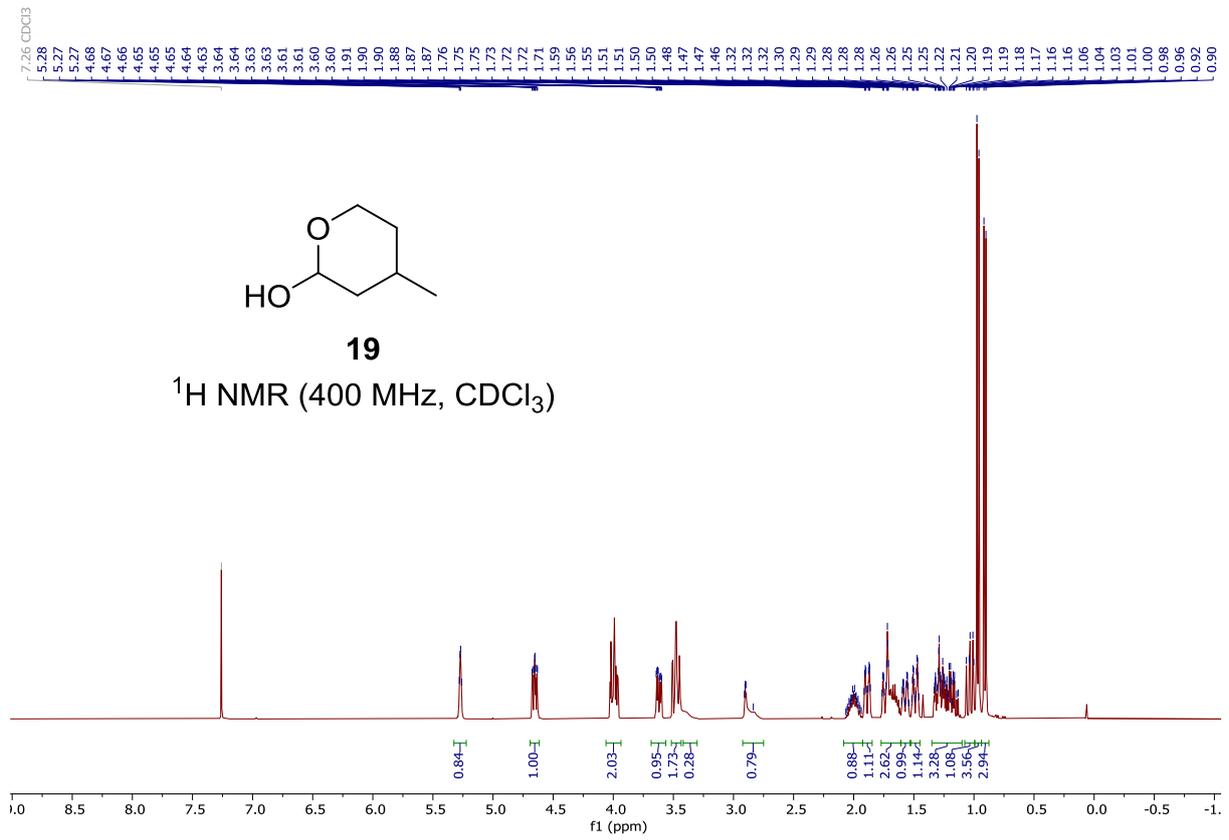


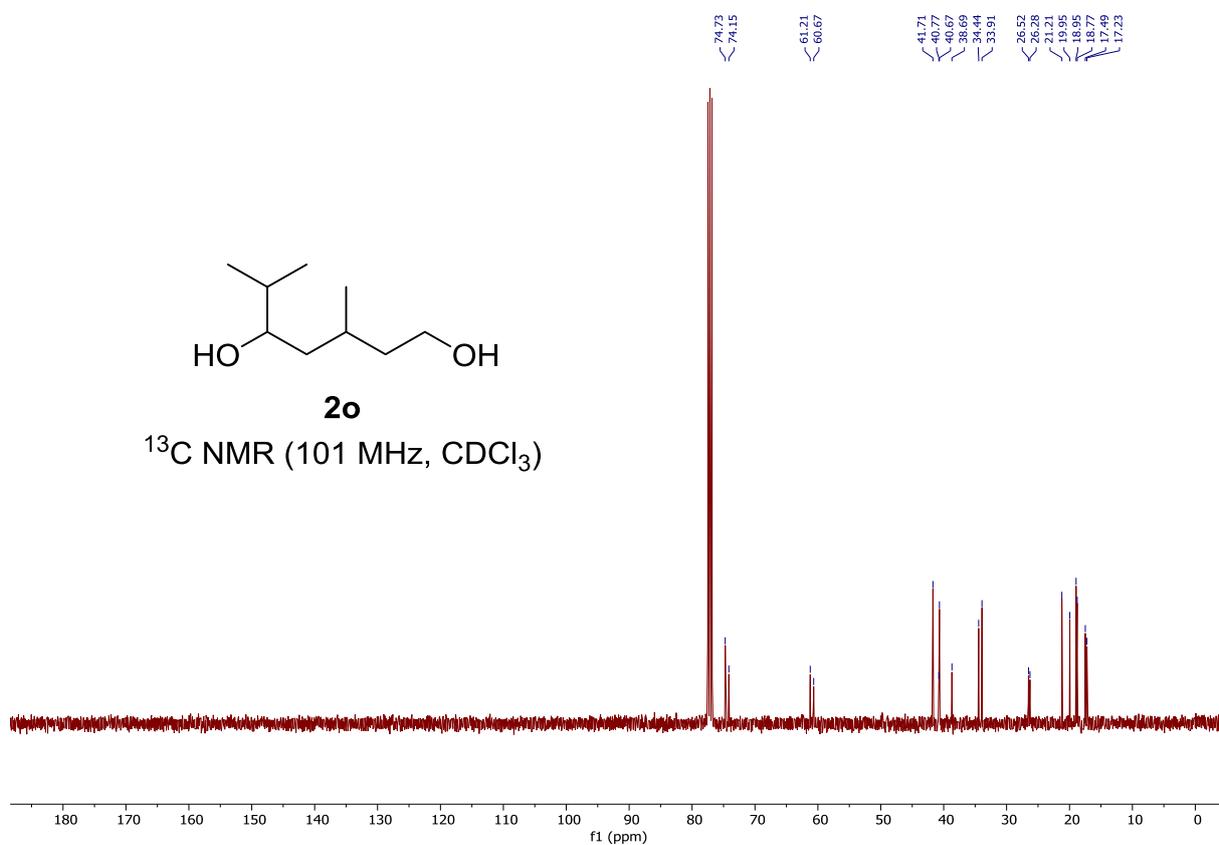
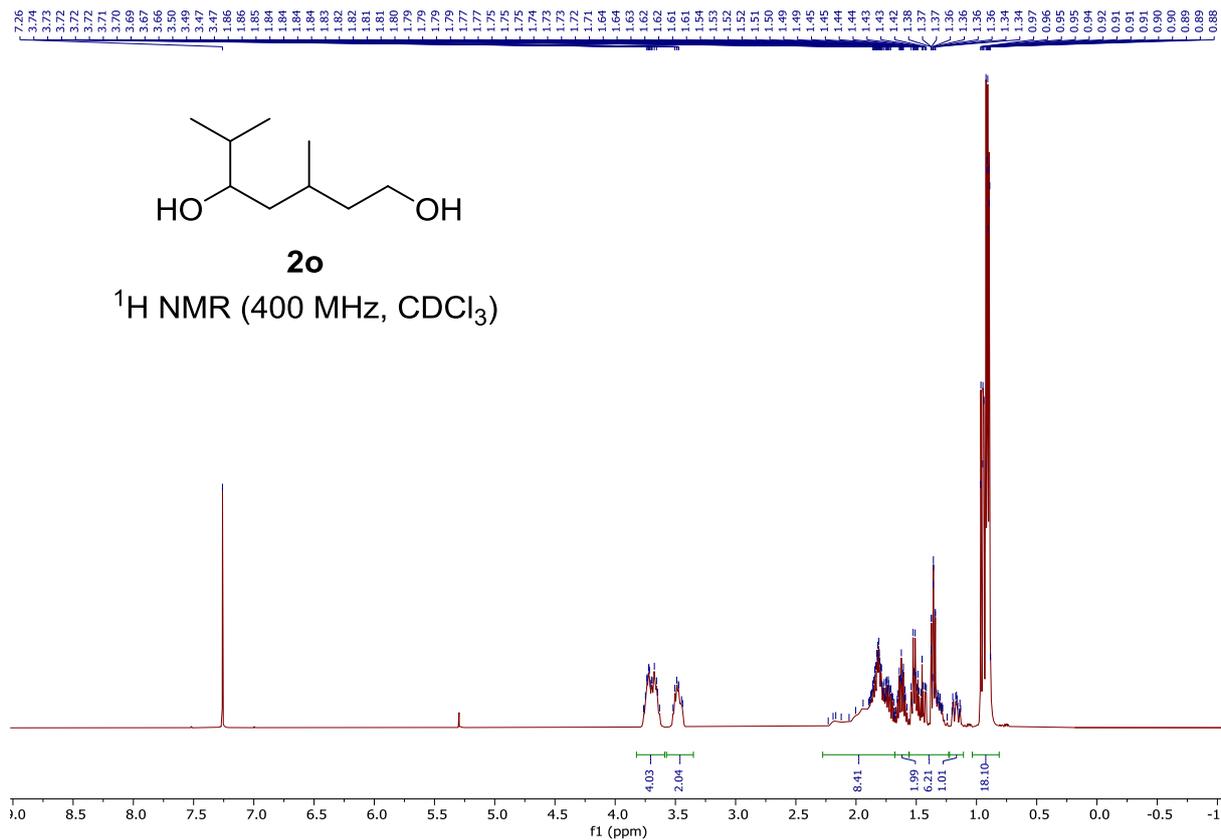


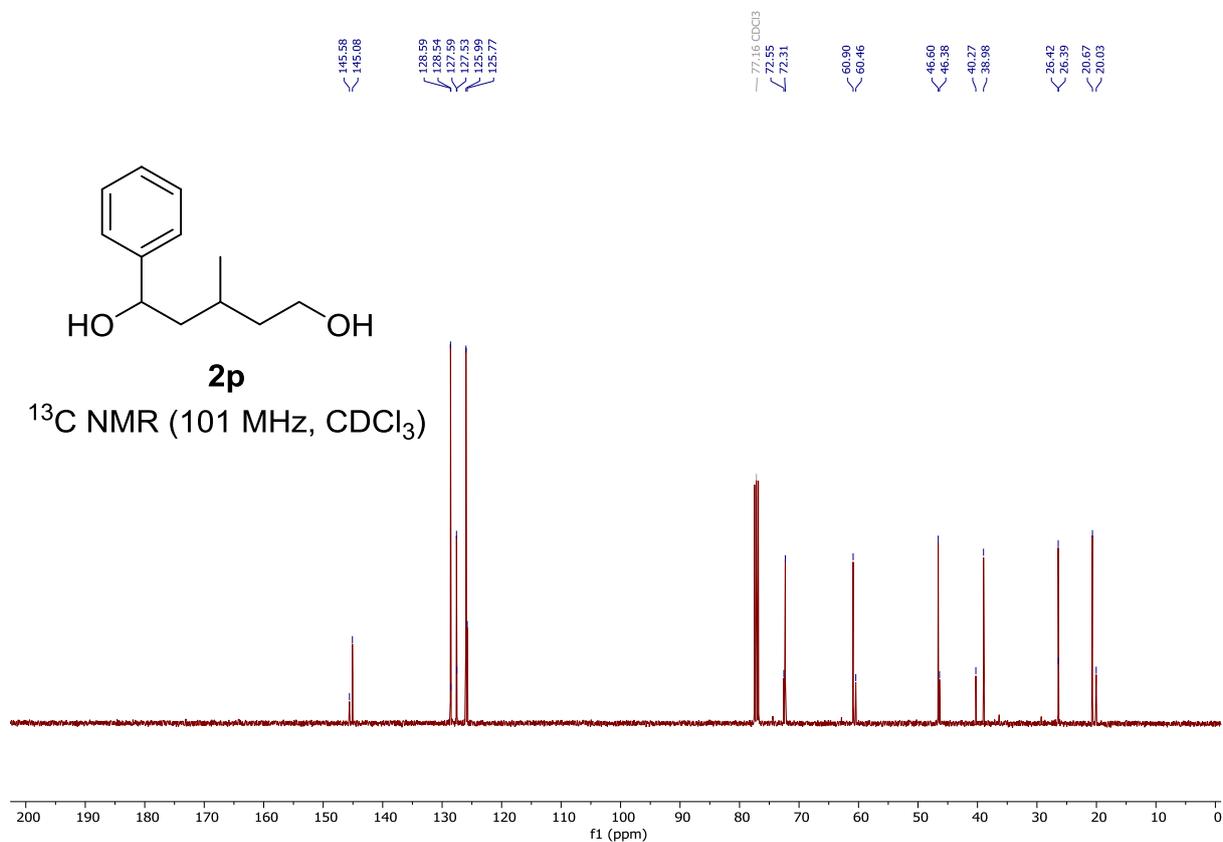
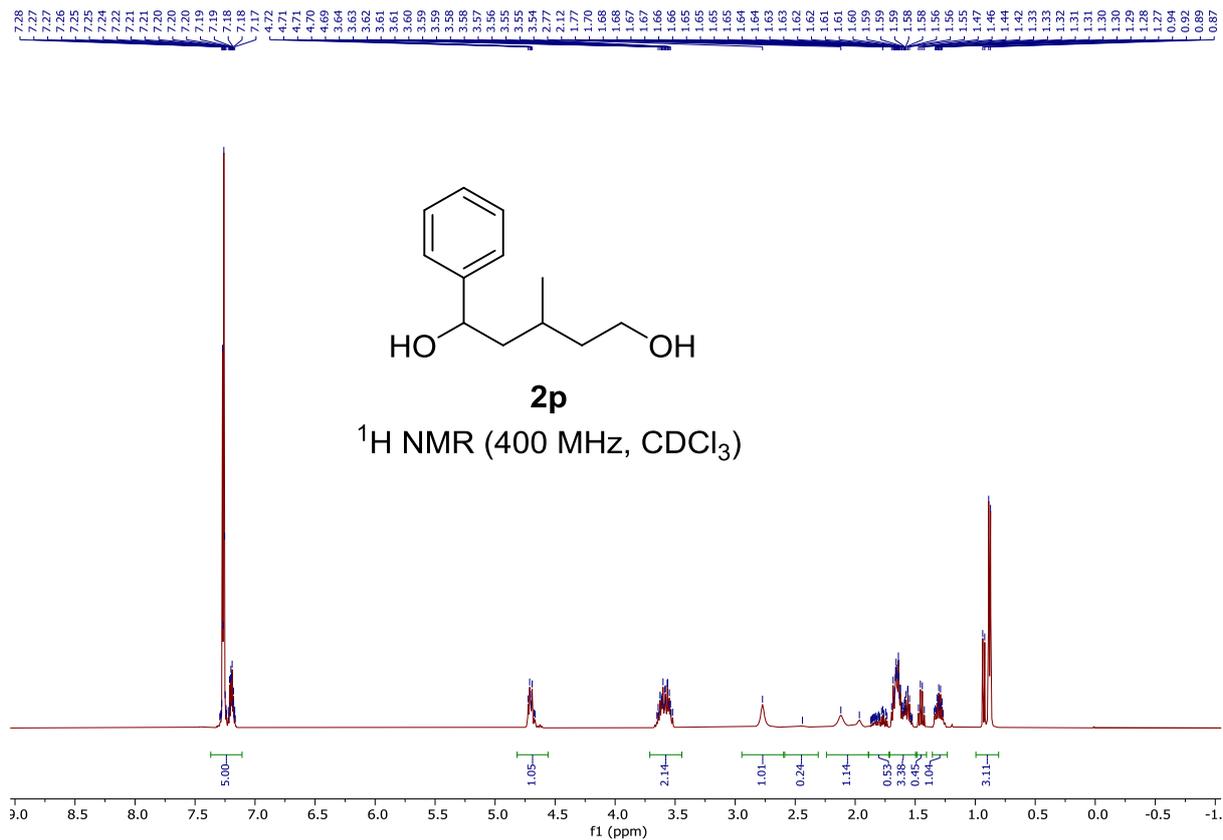


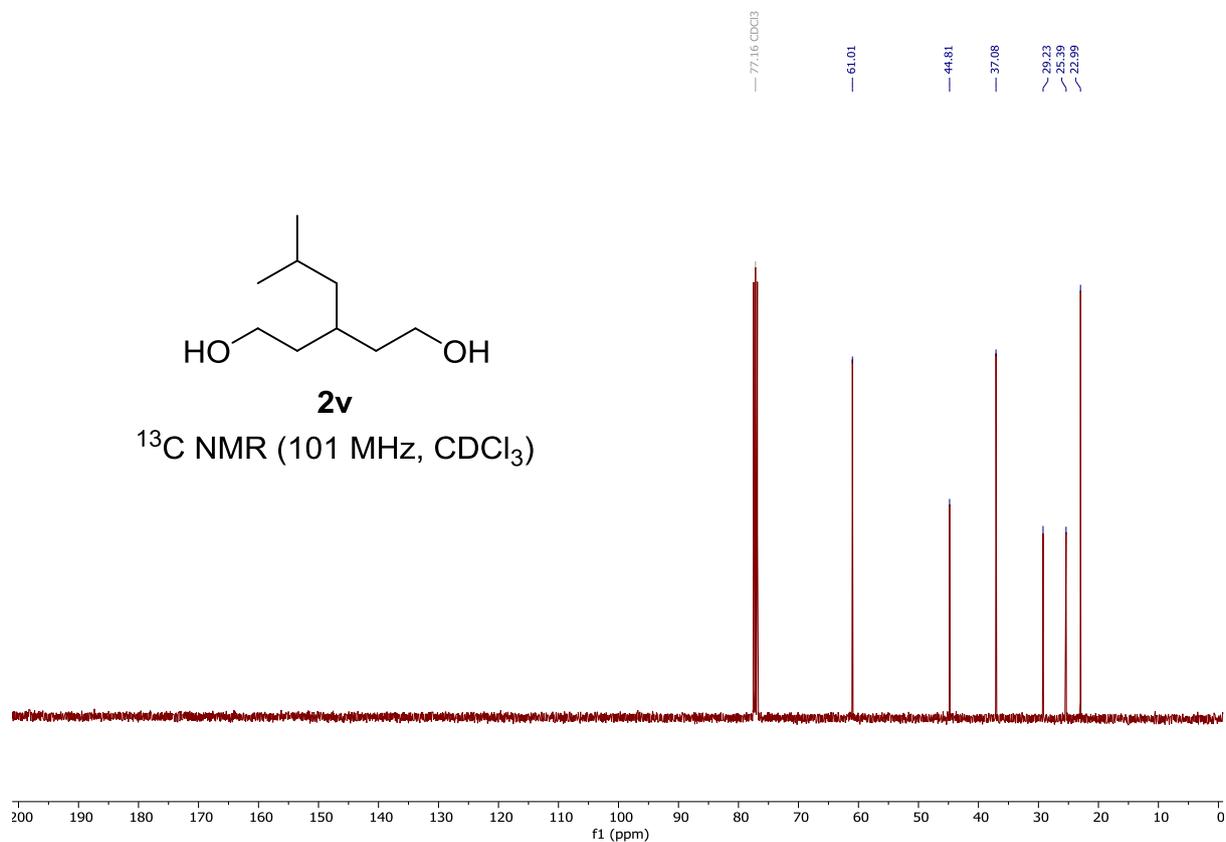
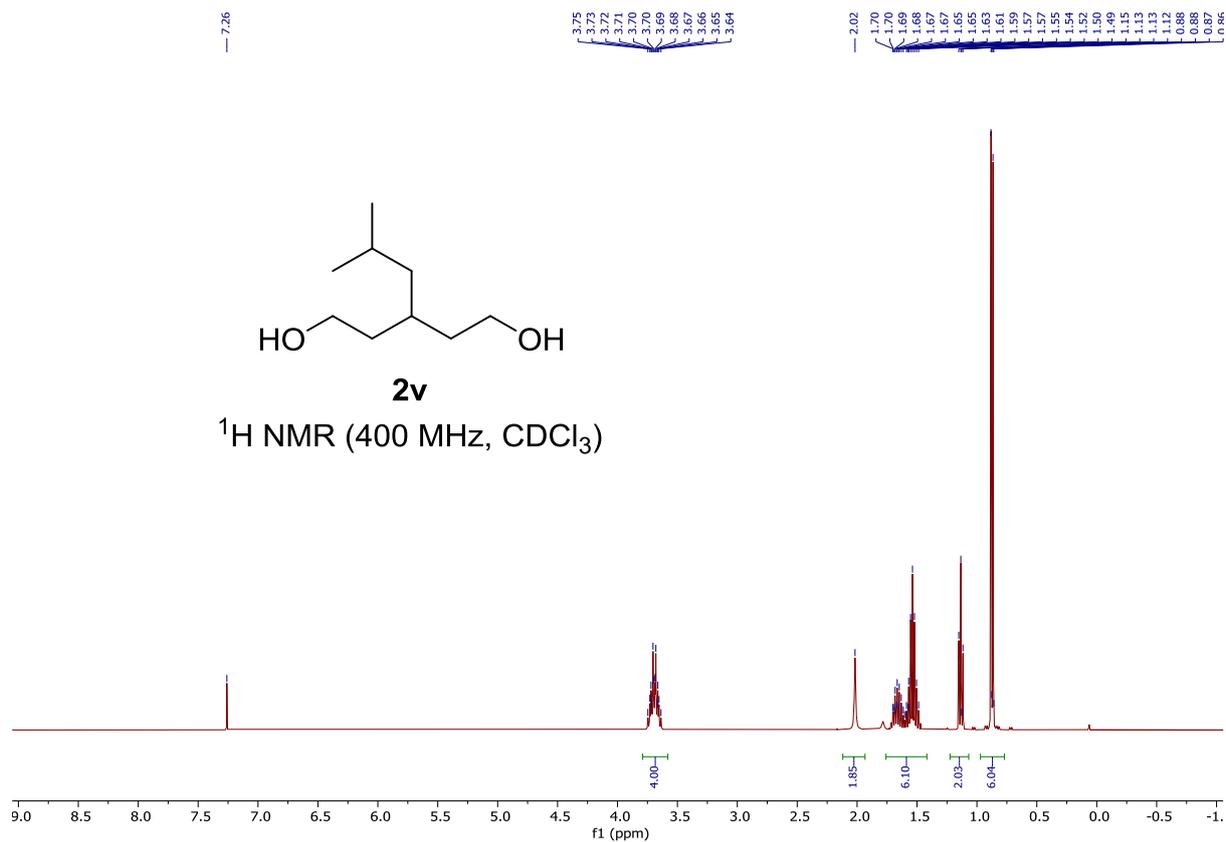


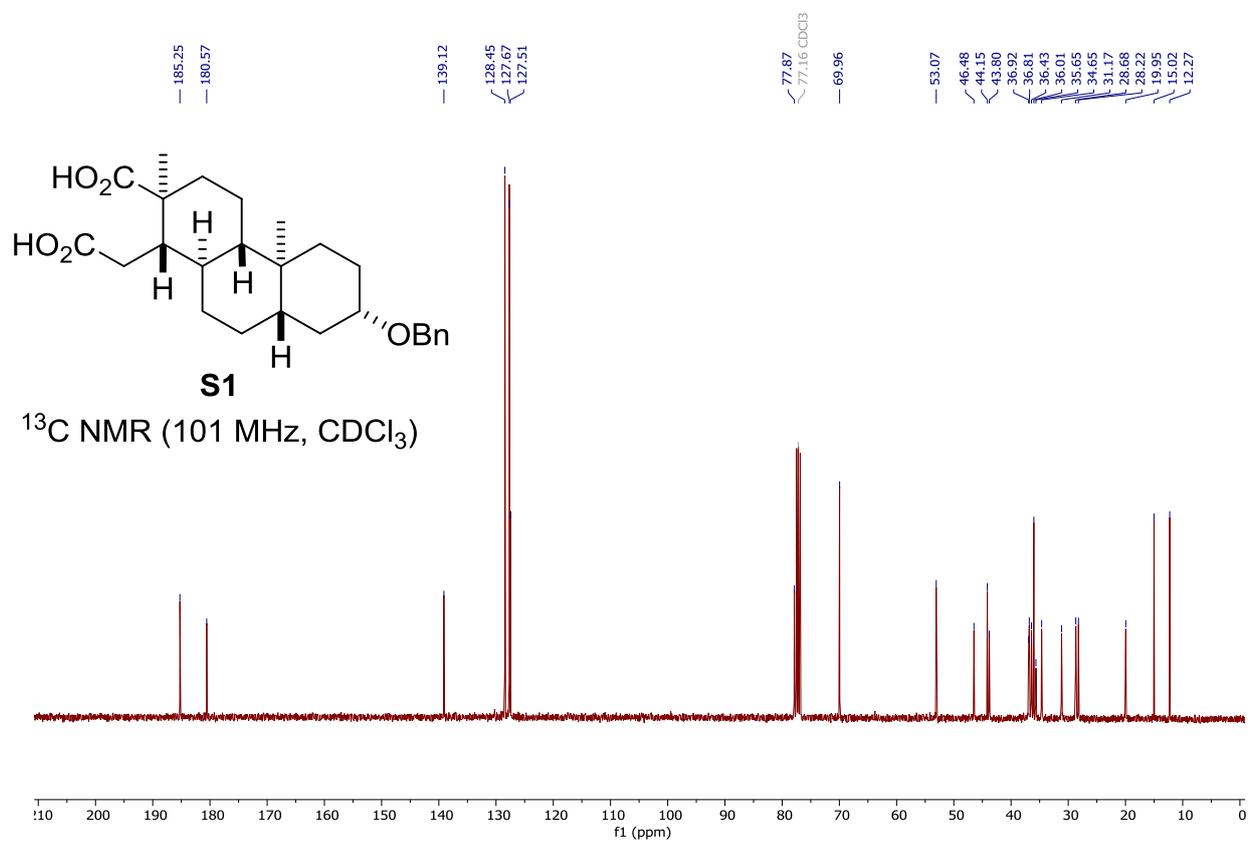
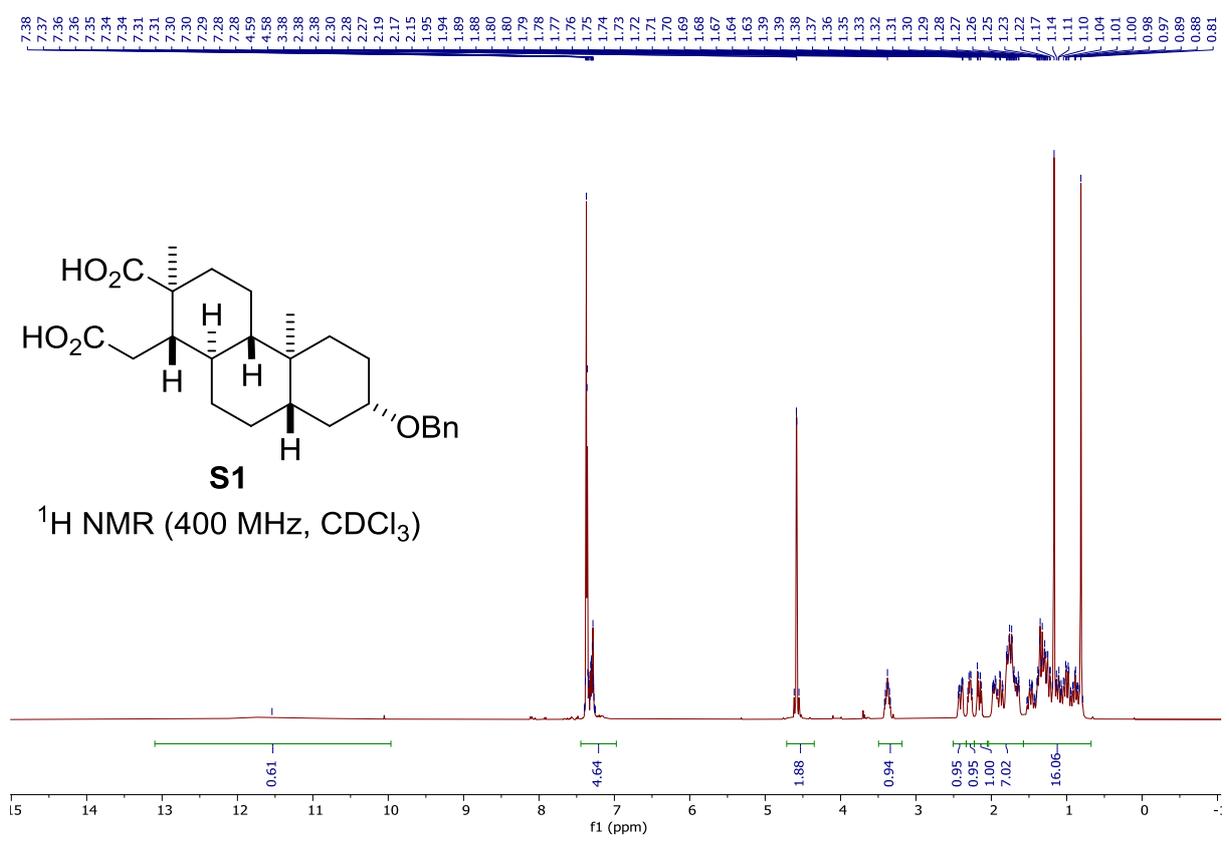


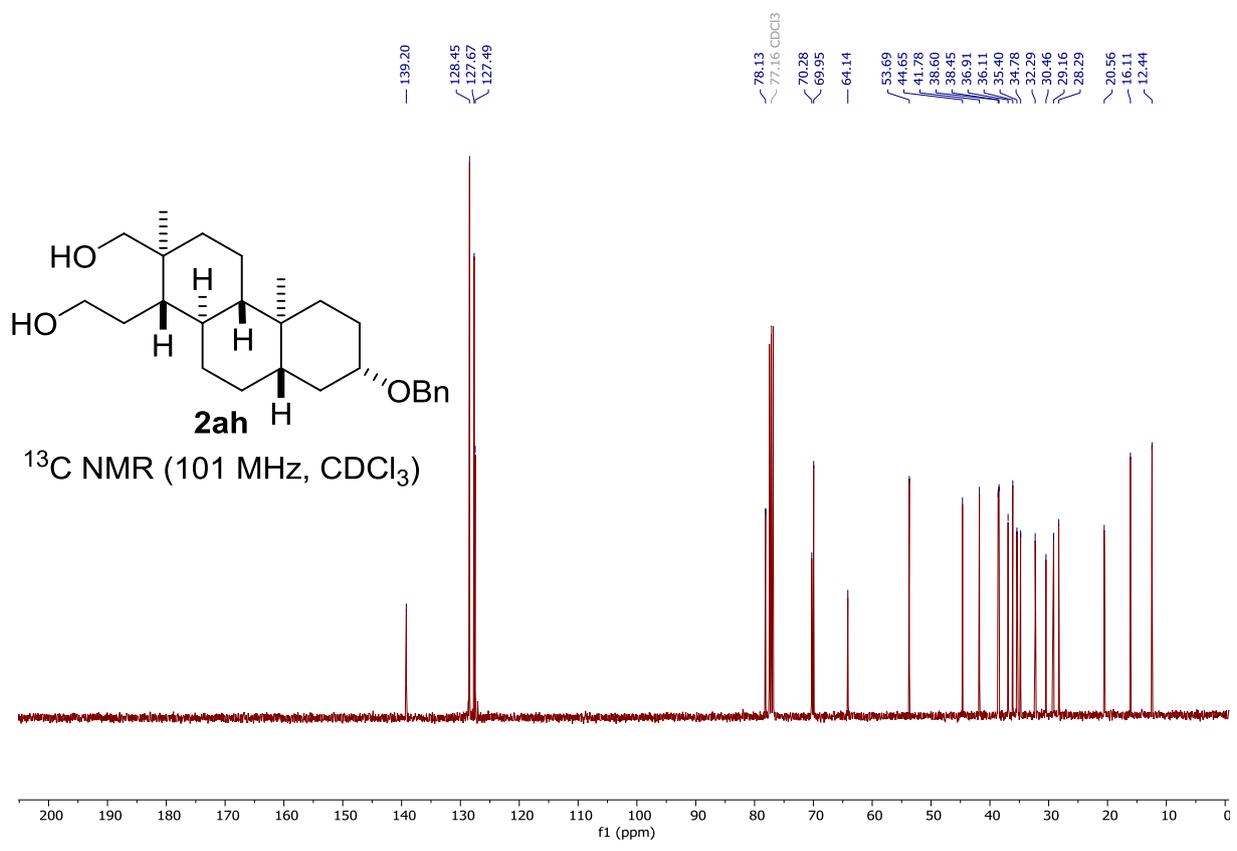
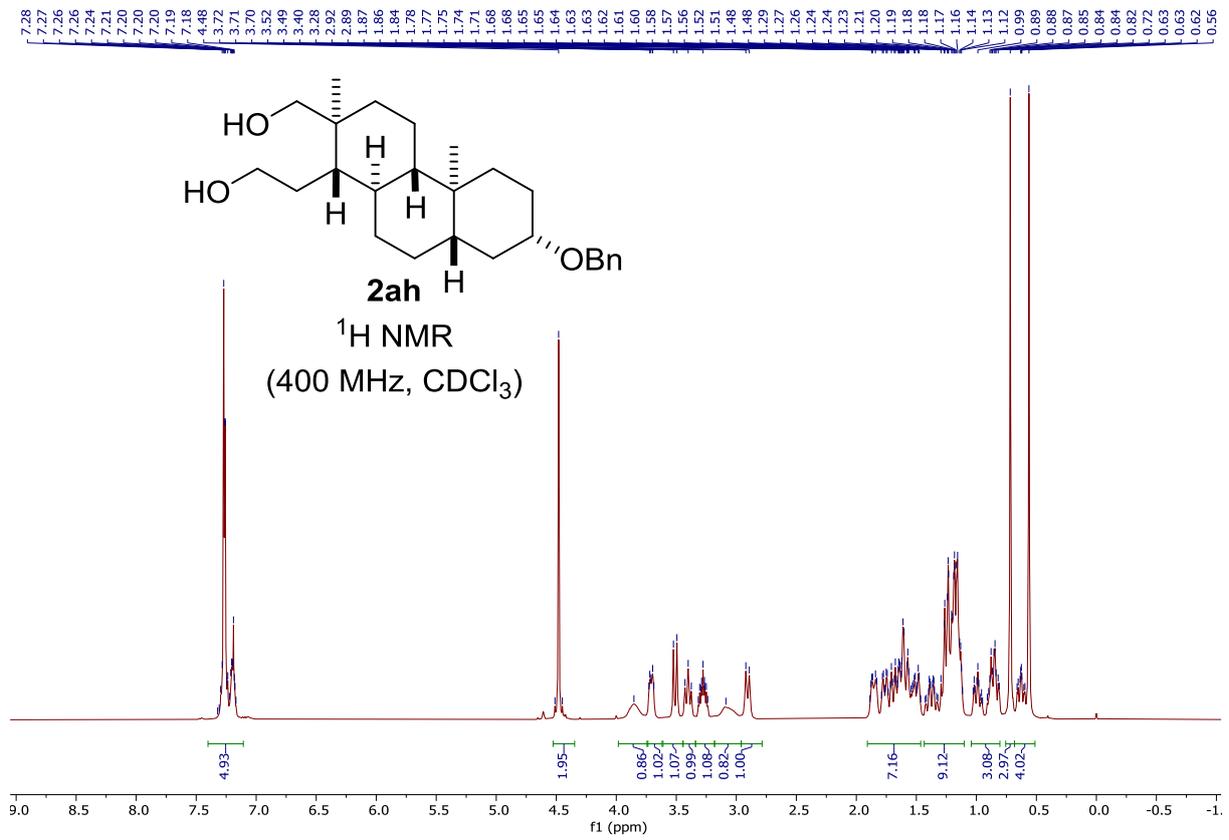


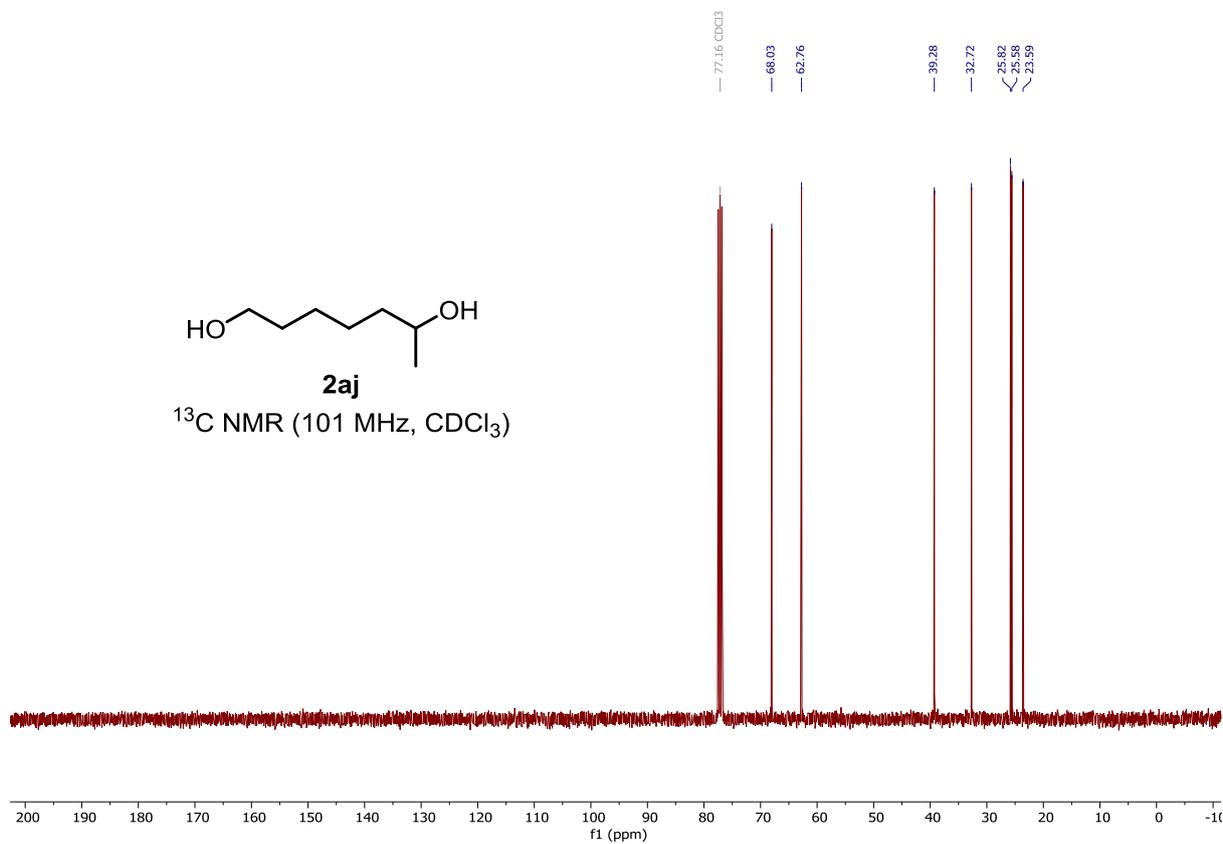
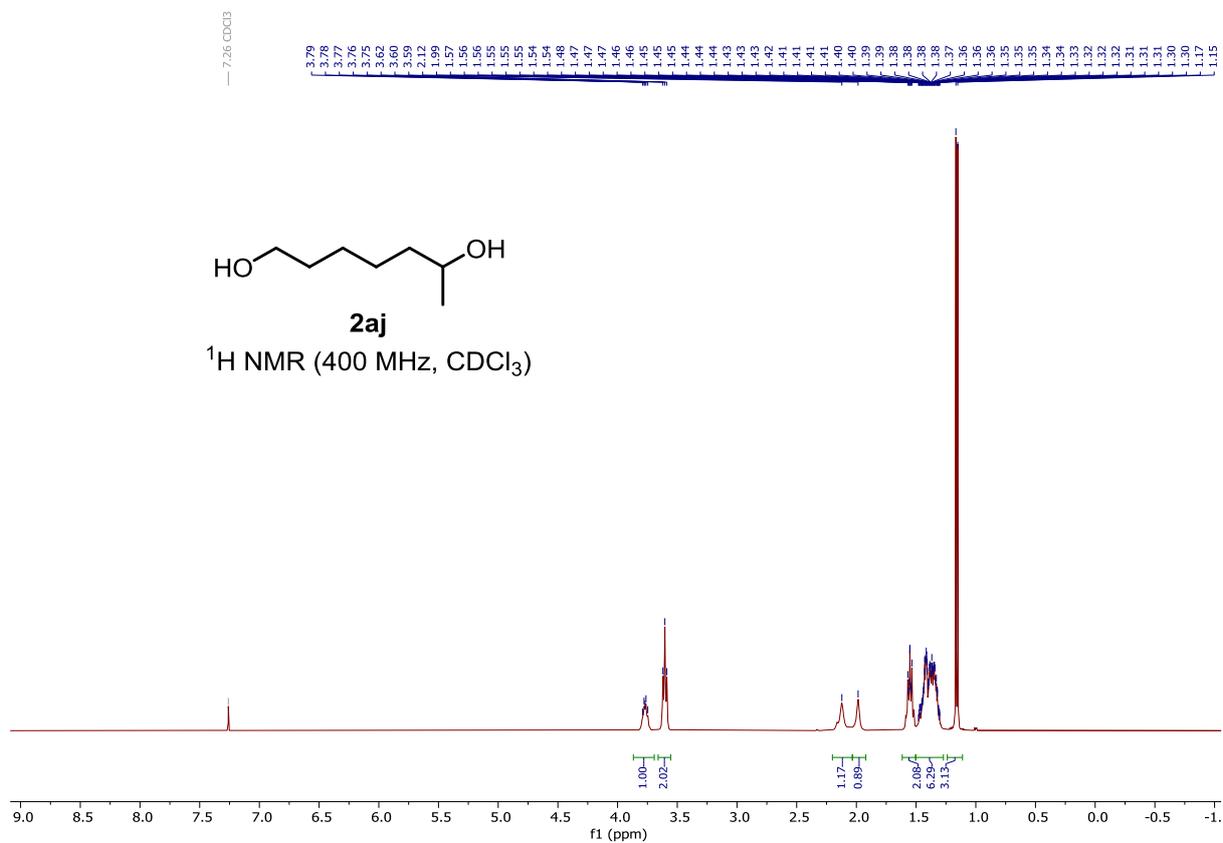




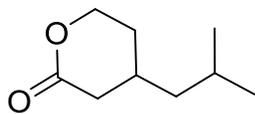






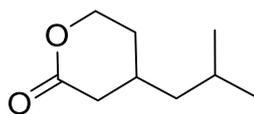
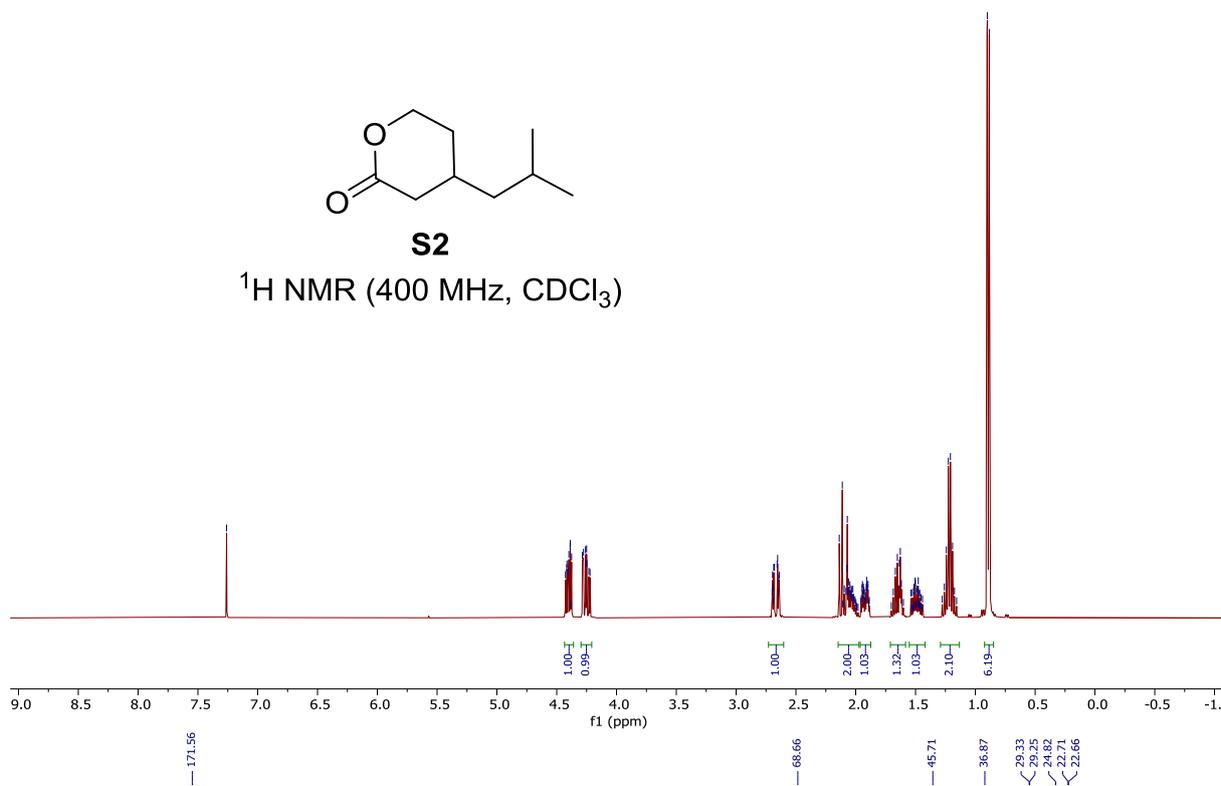


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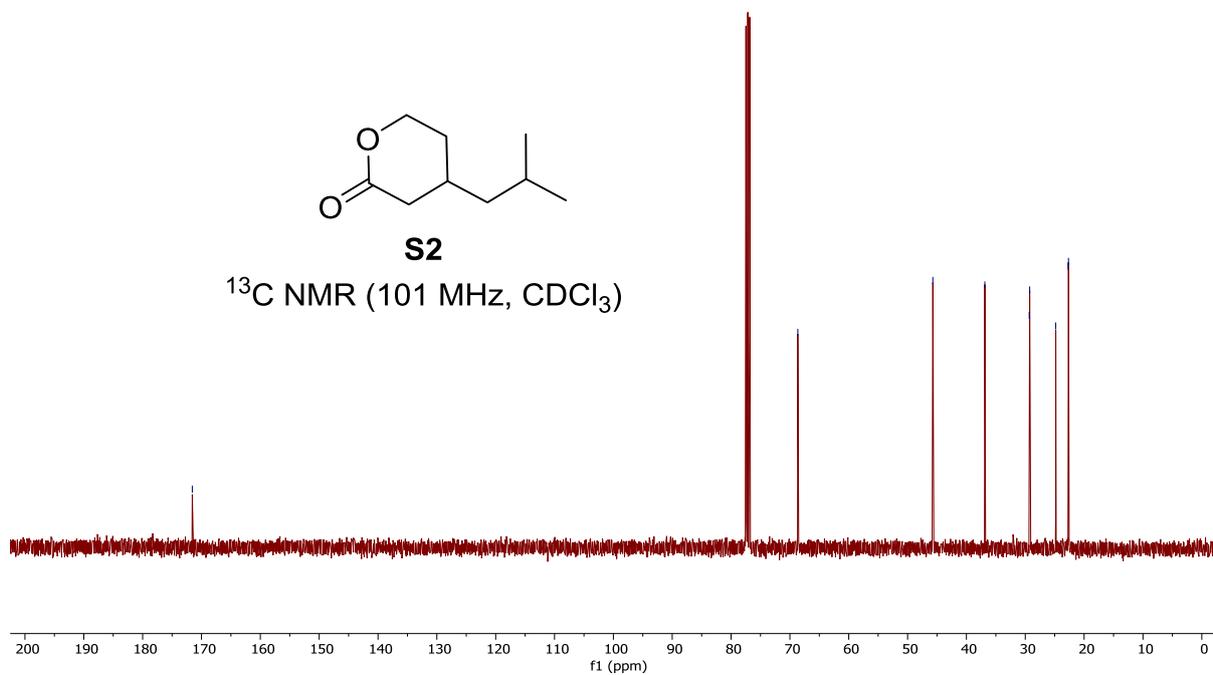
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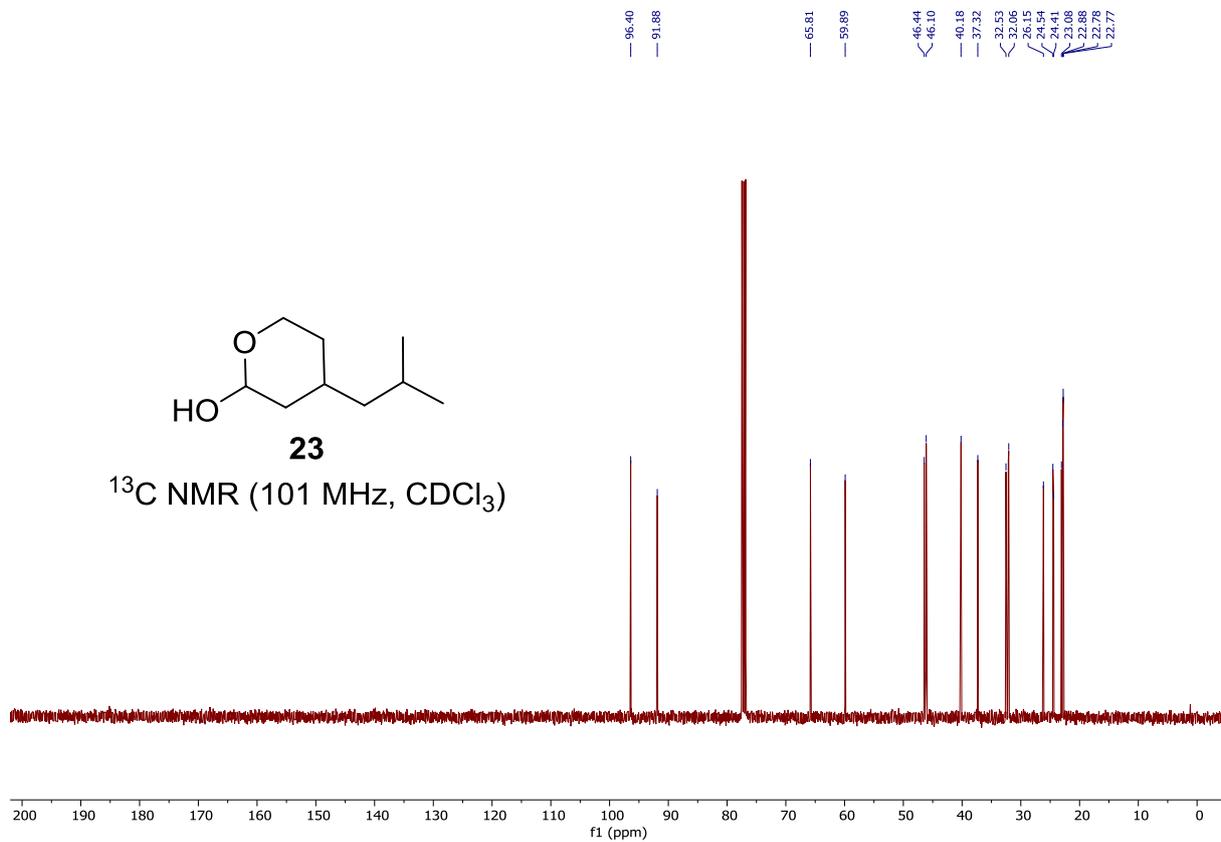
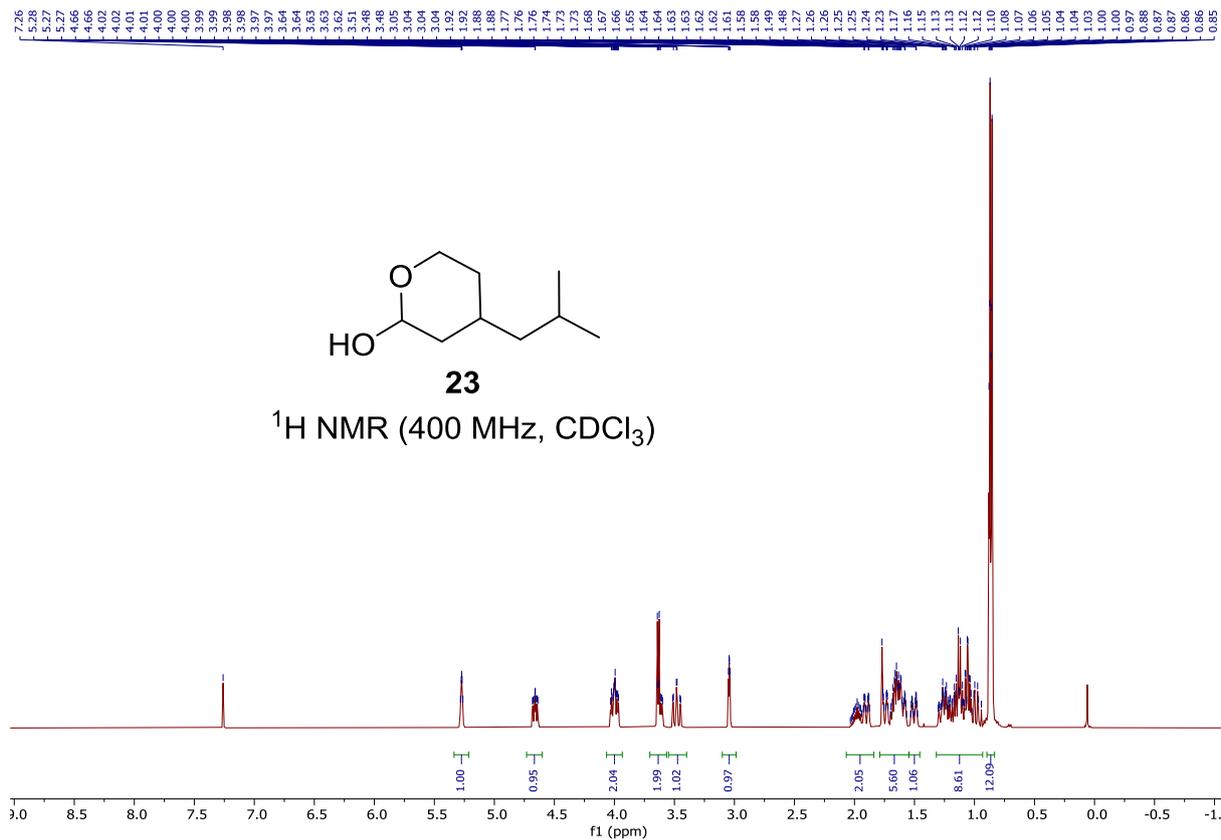
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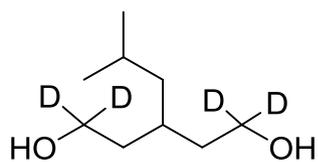
S2

^{13}C NMR (101 MHz, CDCl_3)



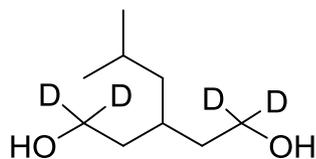
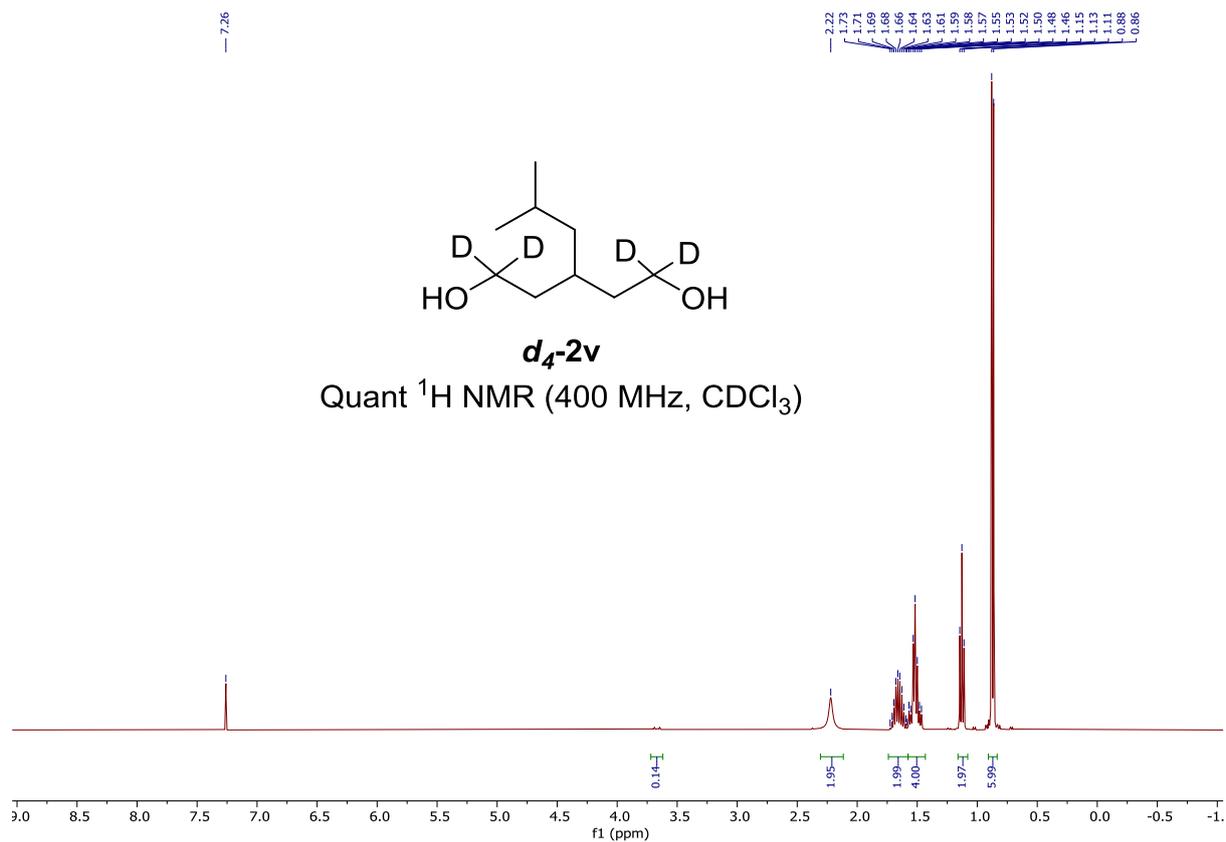


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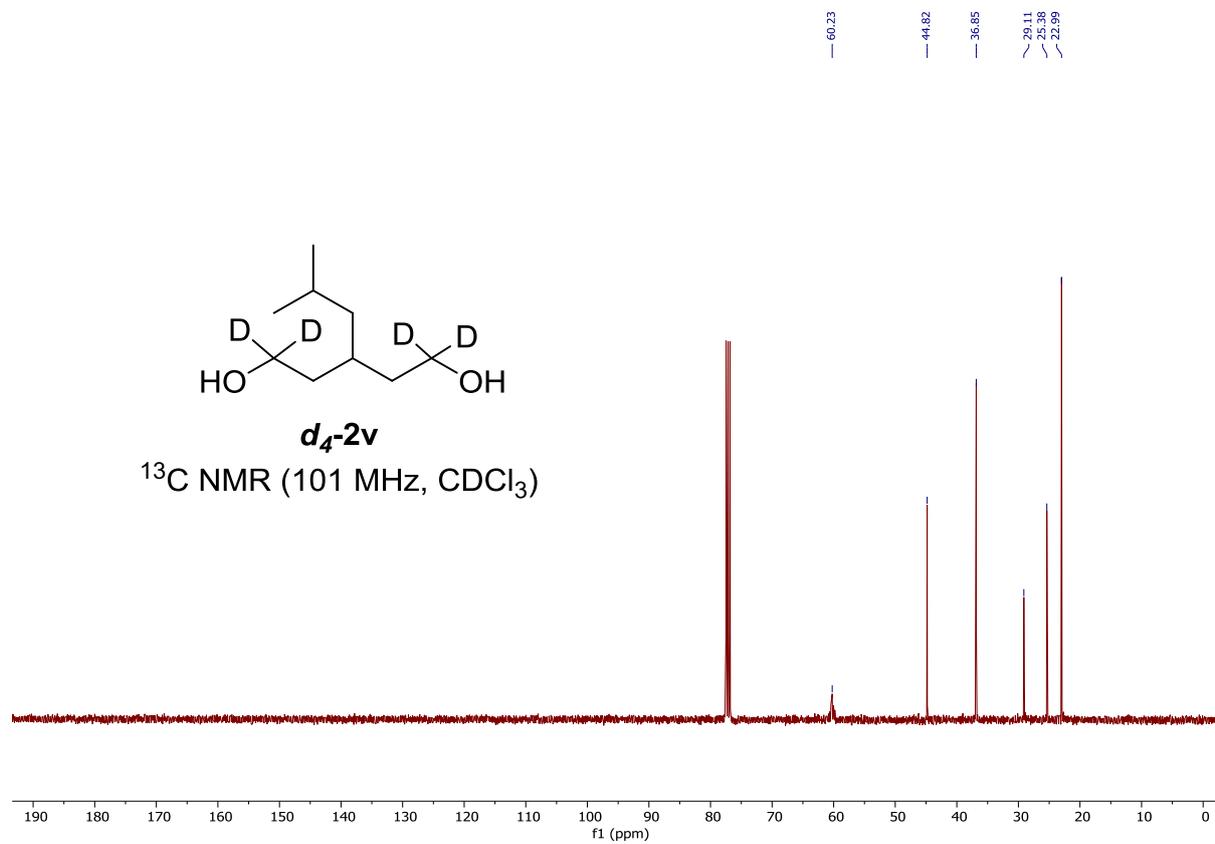
*d*₄-2v

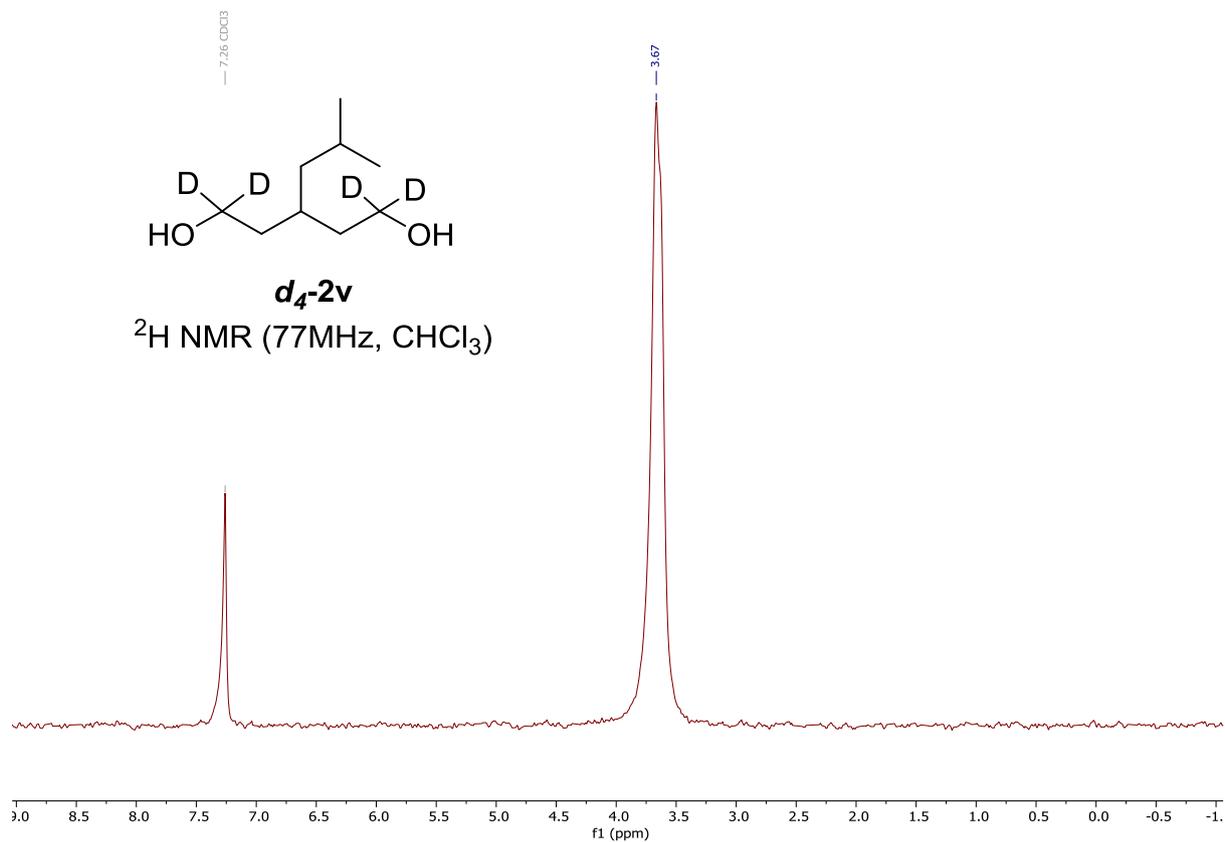
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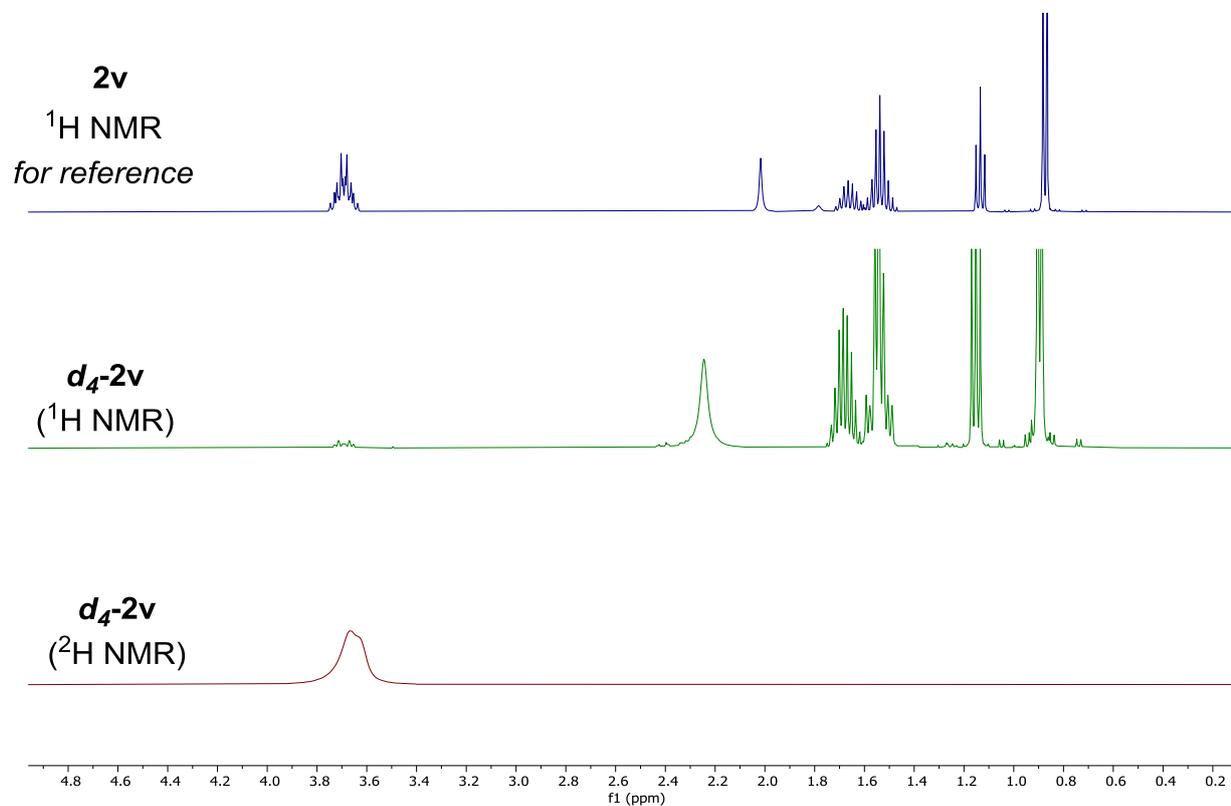
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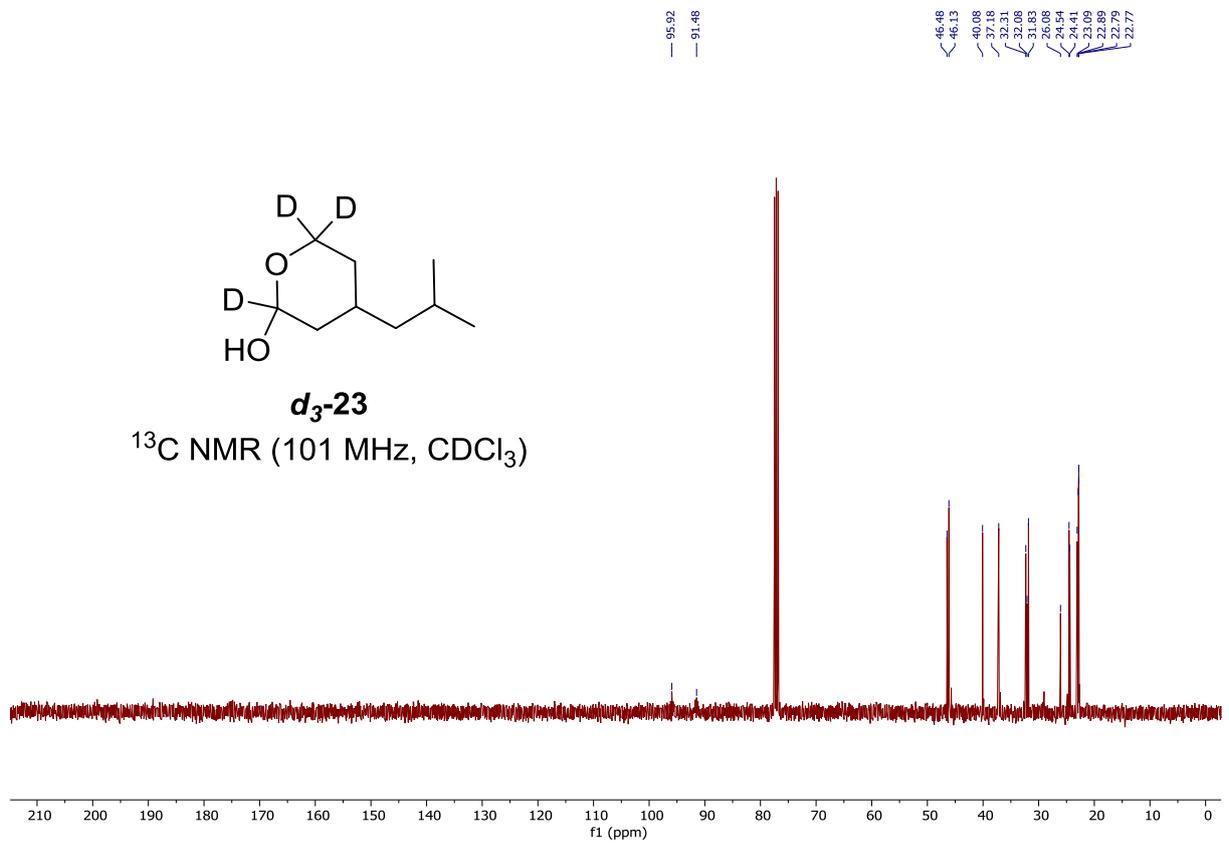
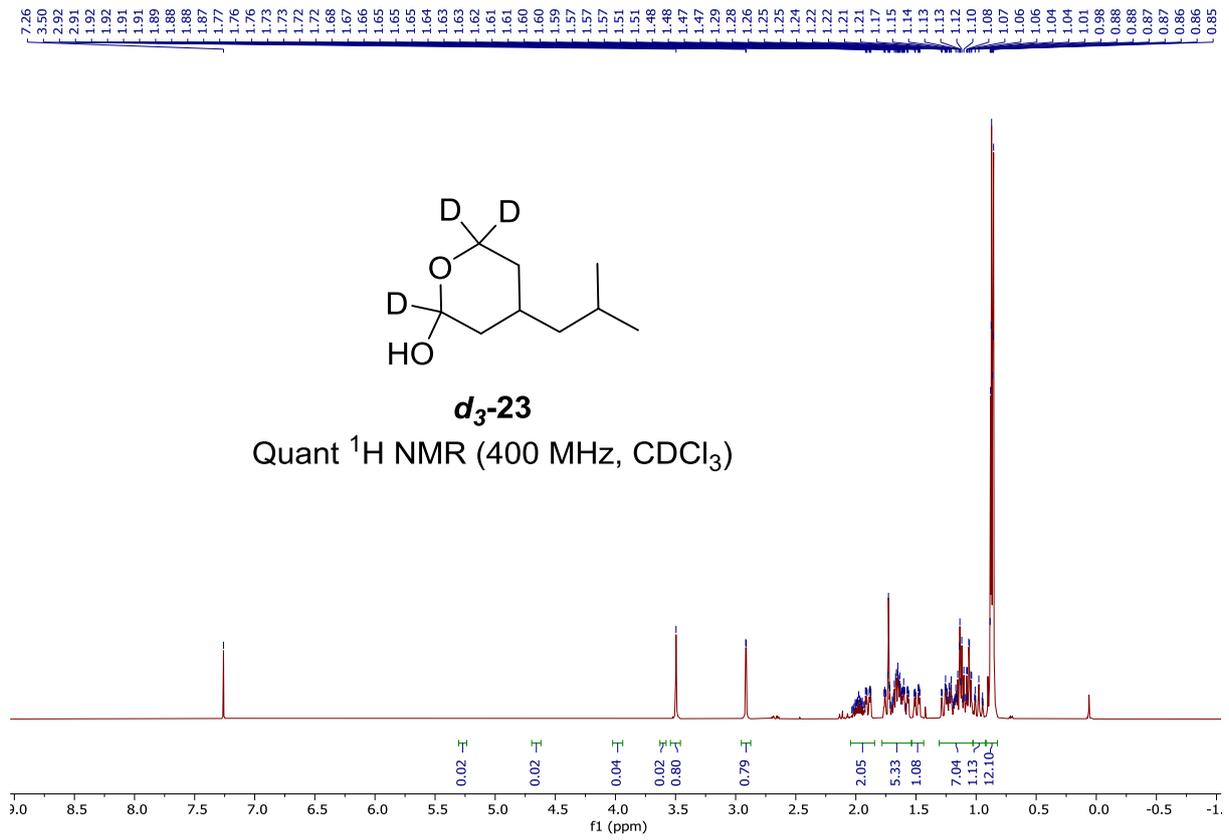
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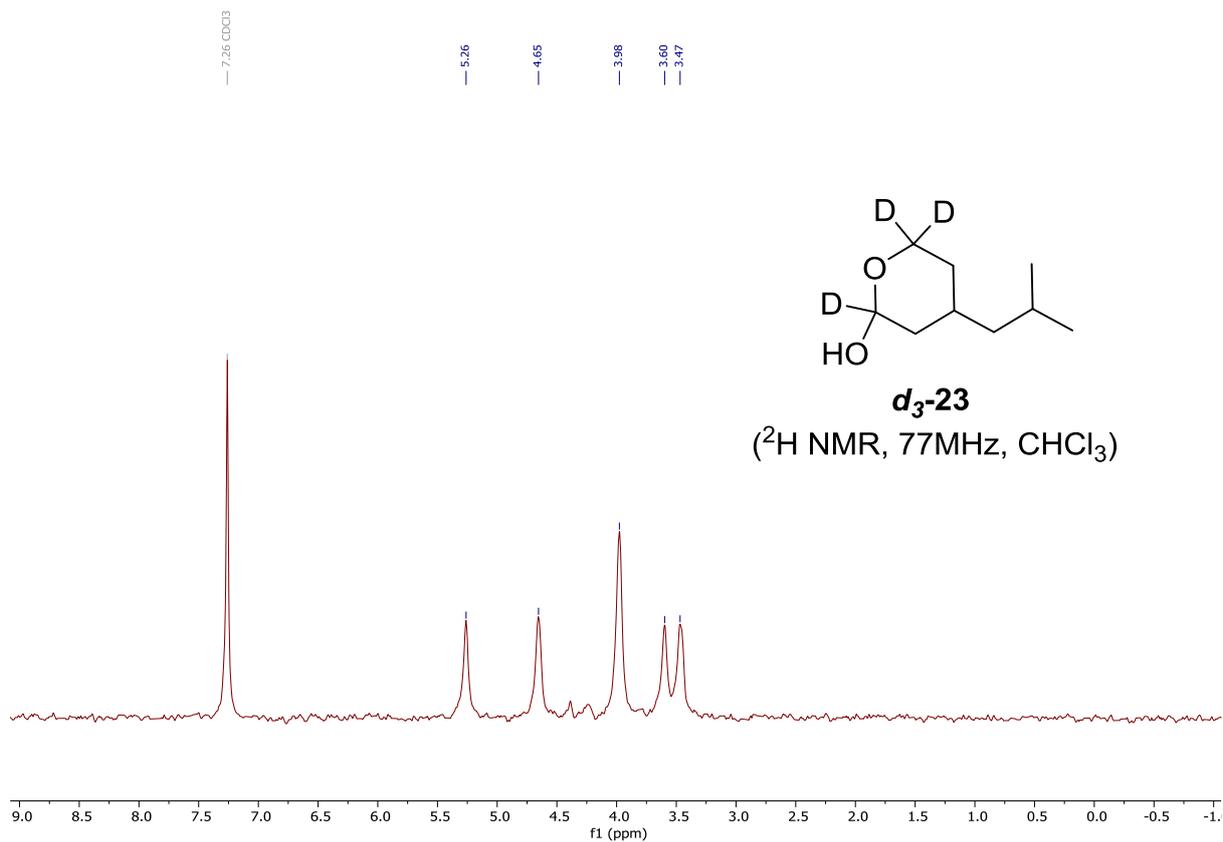




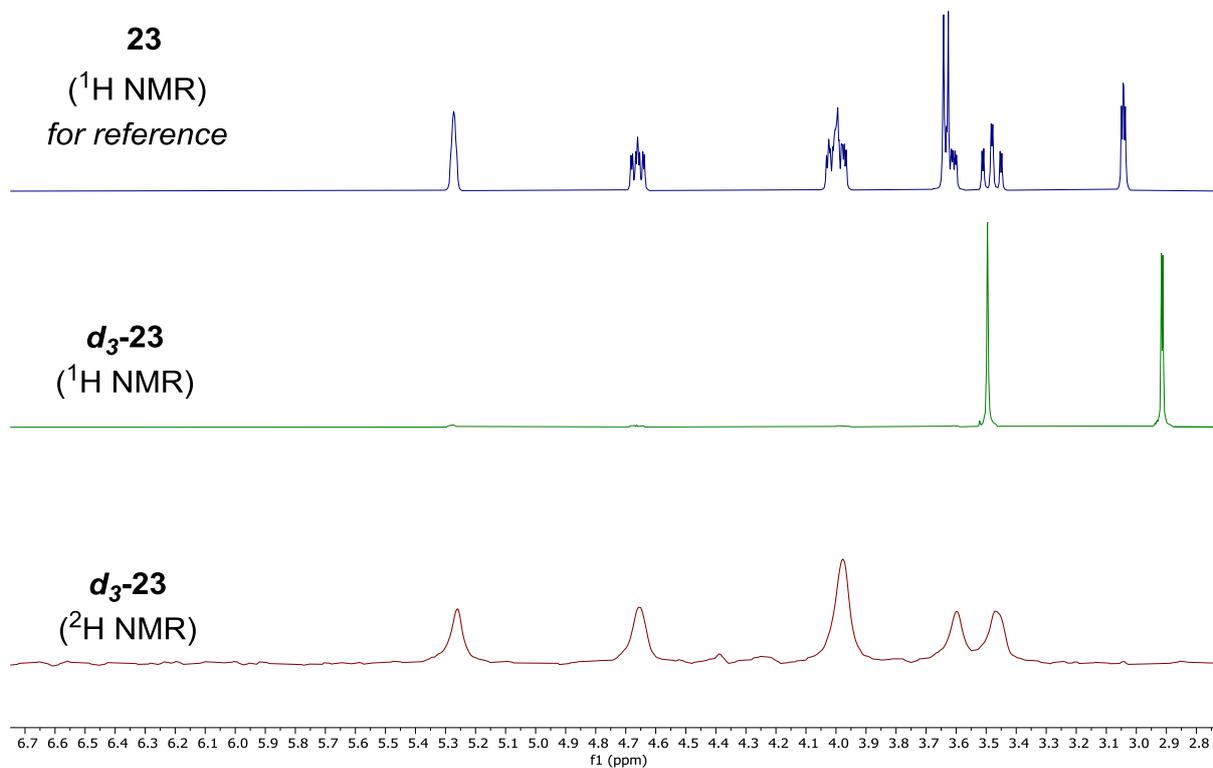
Stacked $^1\text{H NMR}$ and $^2\text{H NMR}$ Spectra for $d_4\text{-2v}$:

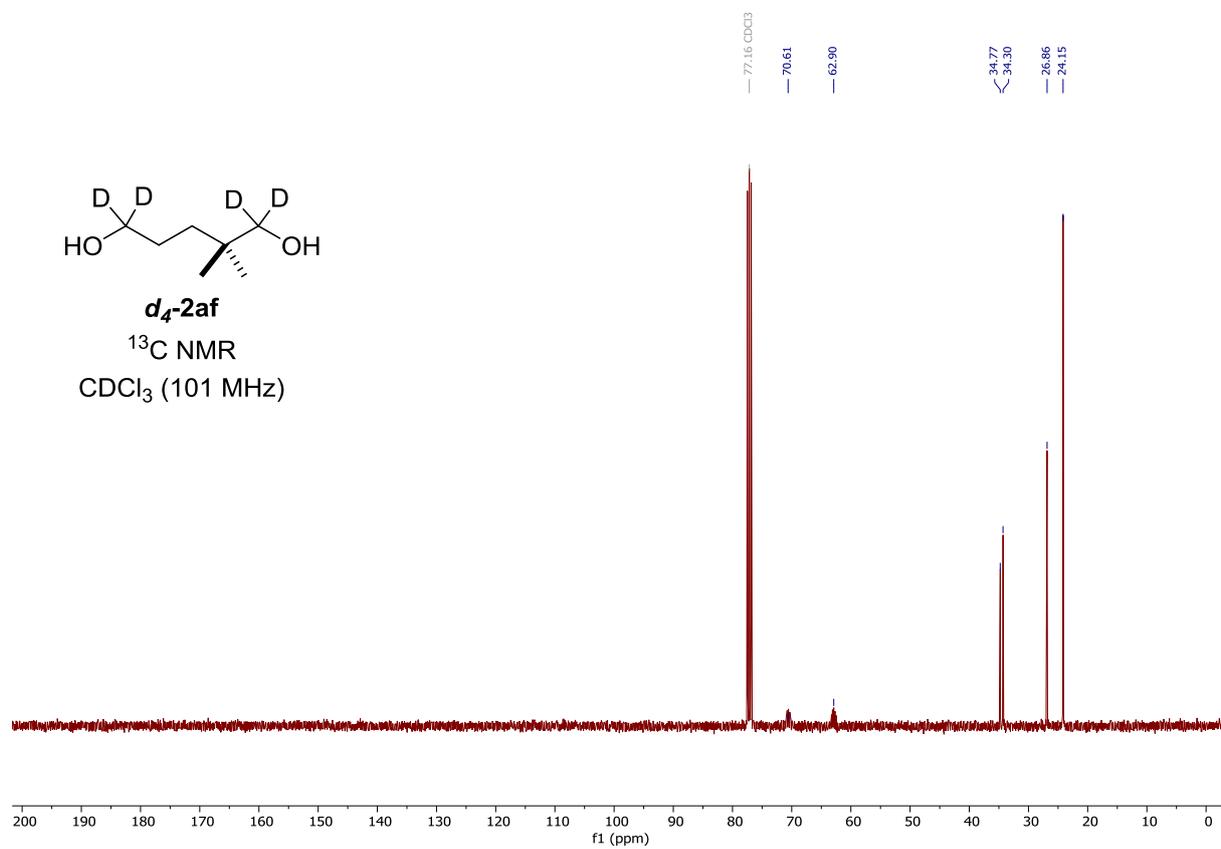
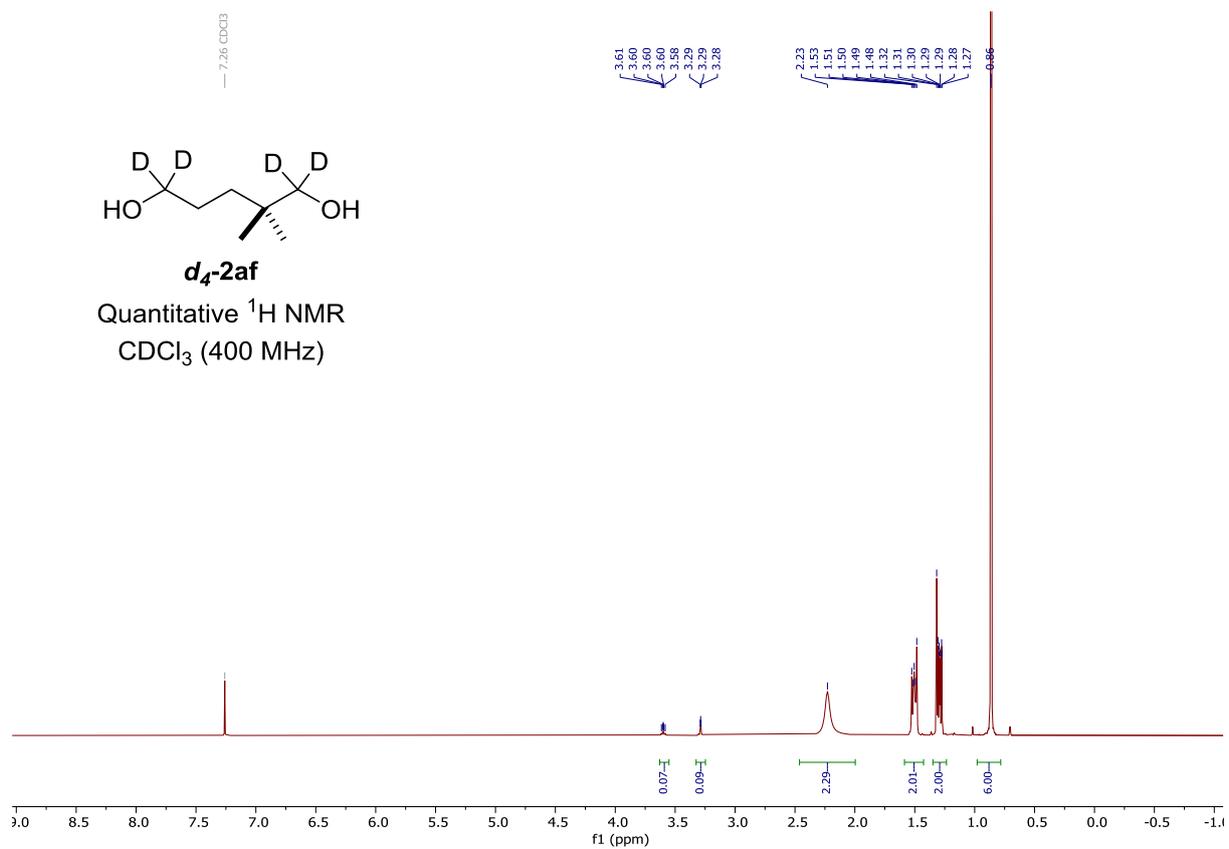


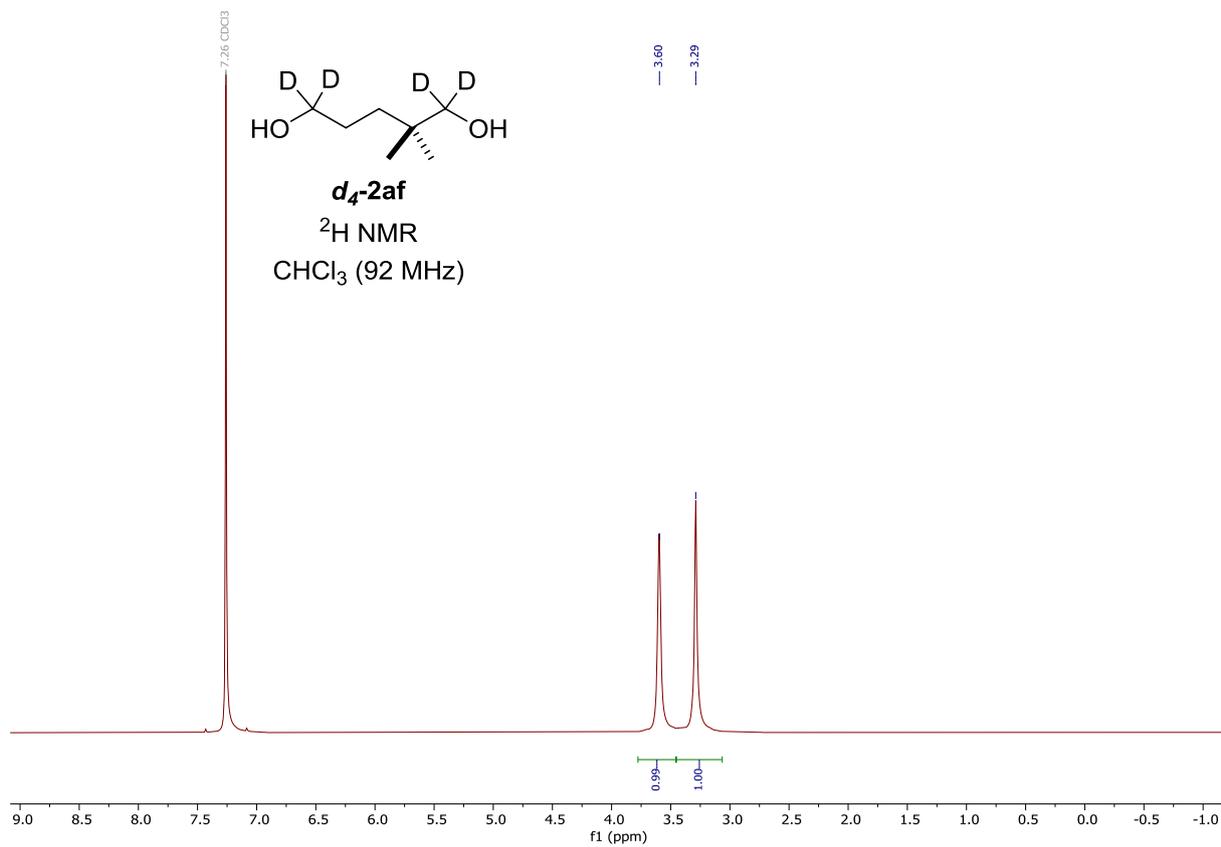




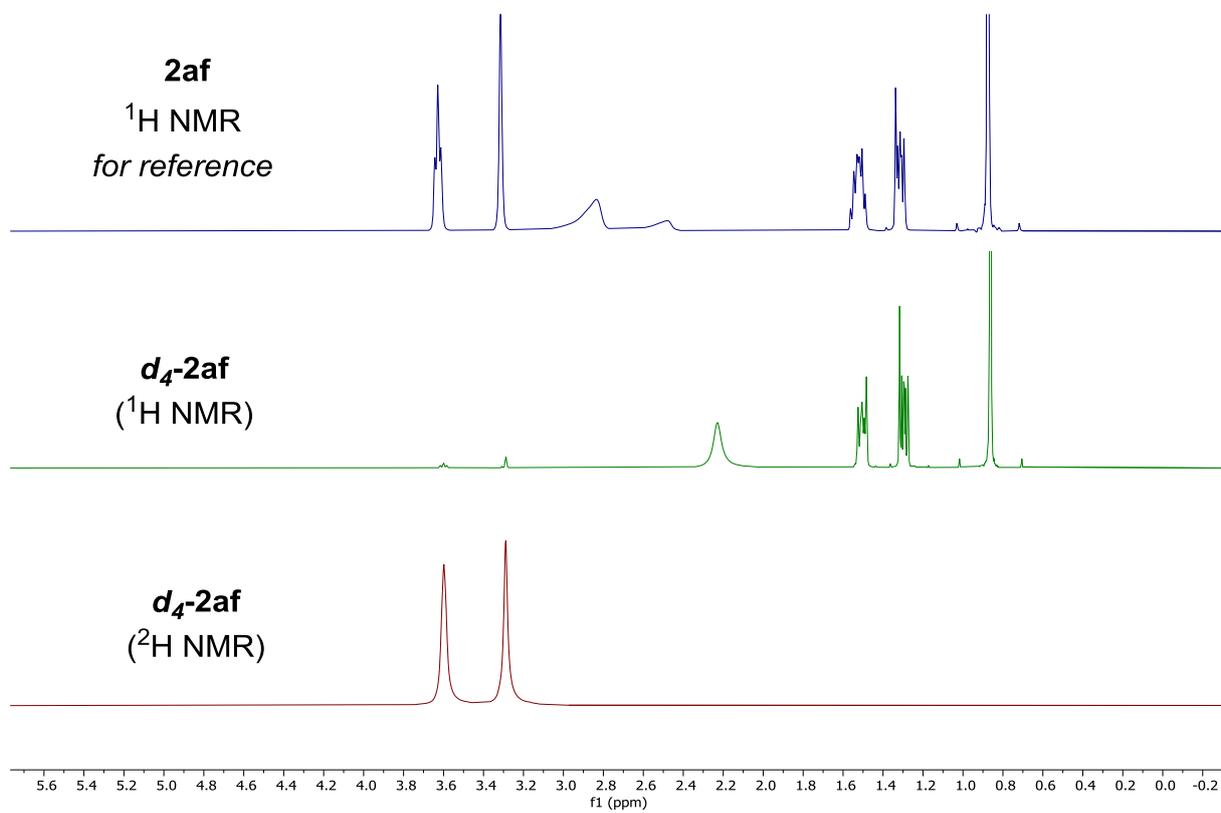
Stacked ¹H NMR and ²H NMR Spectra for d₃-23:

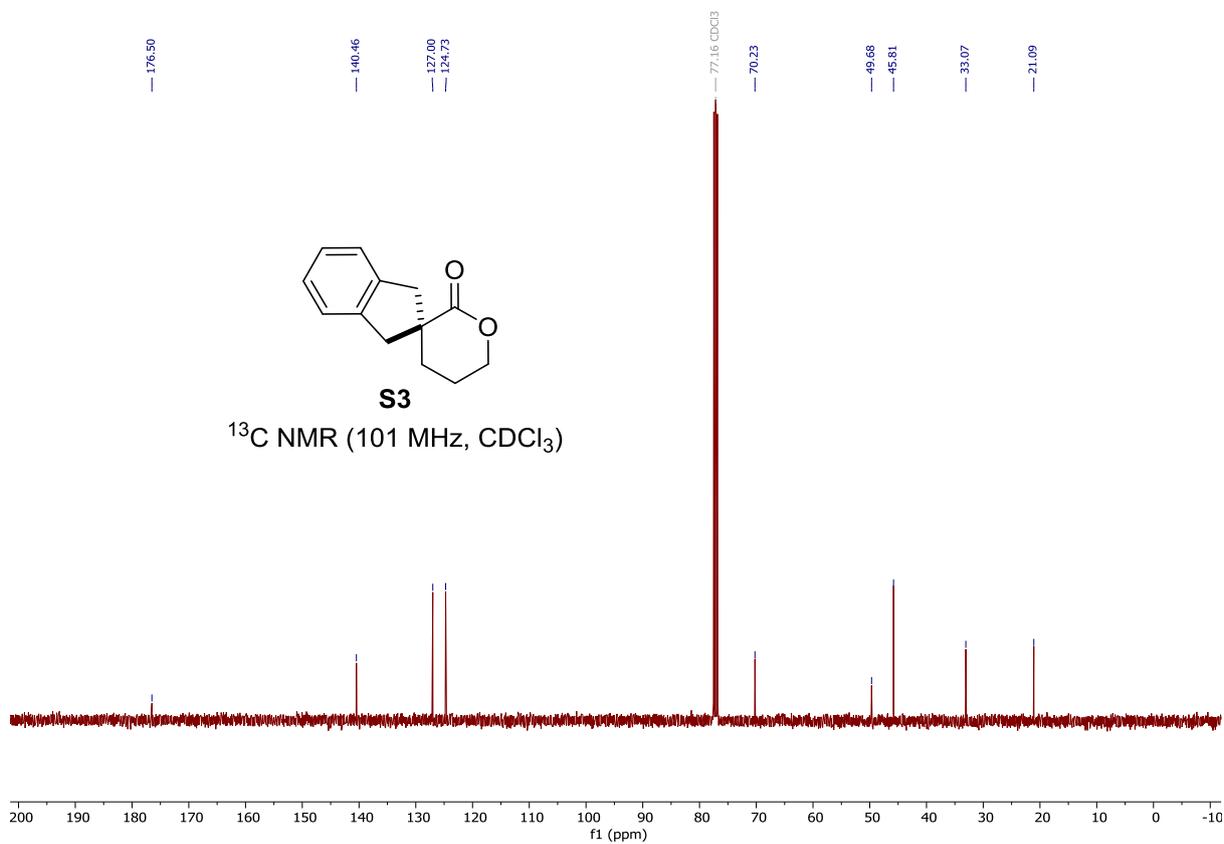
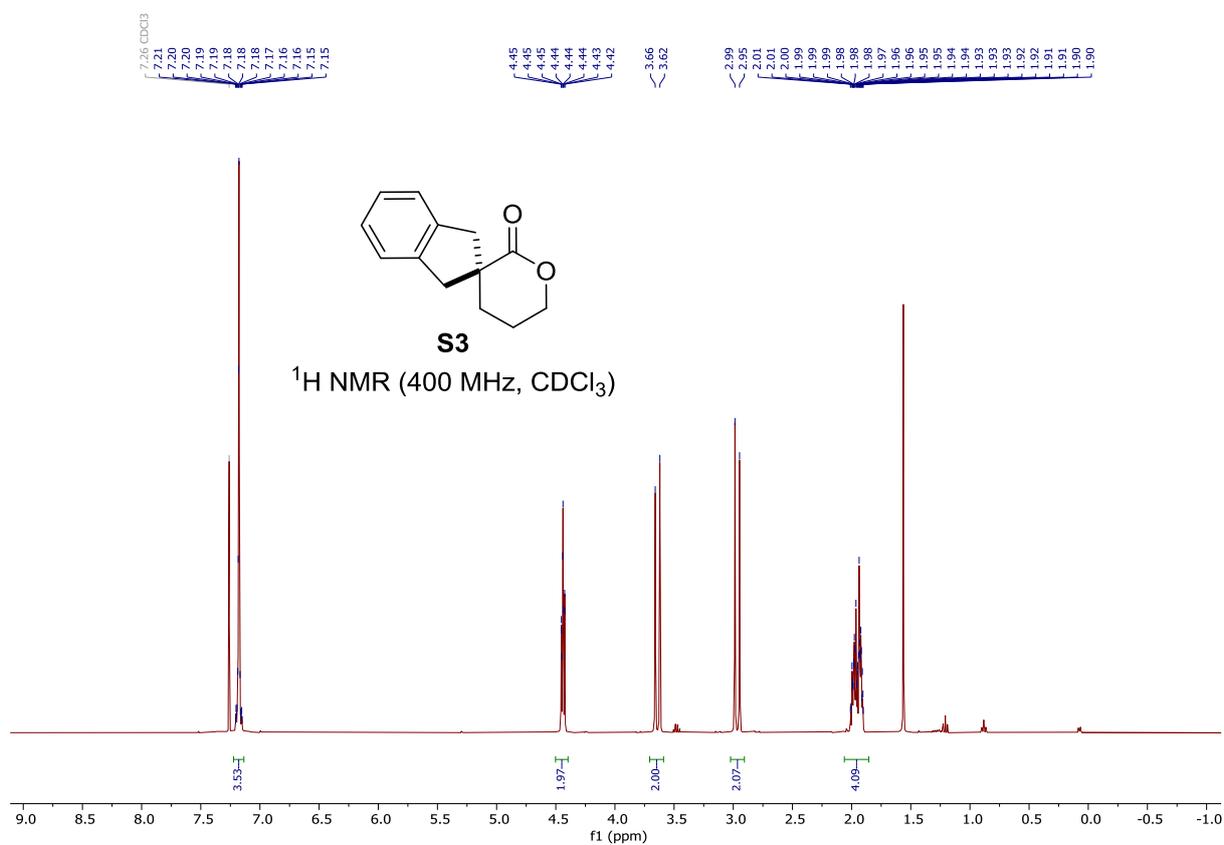


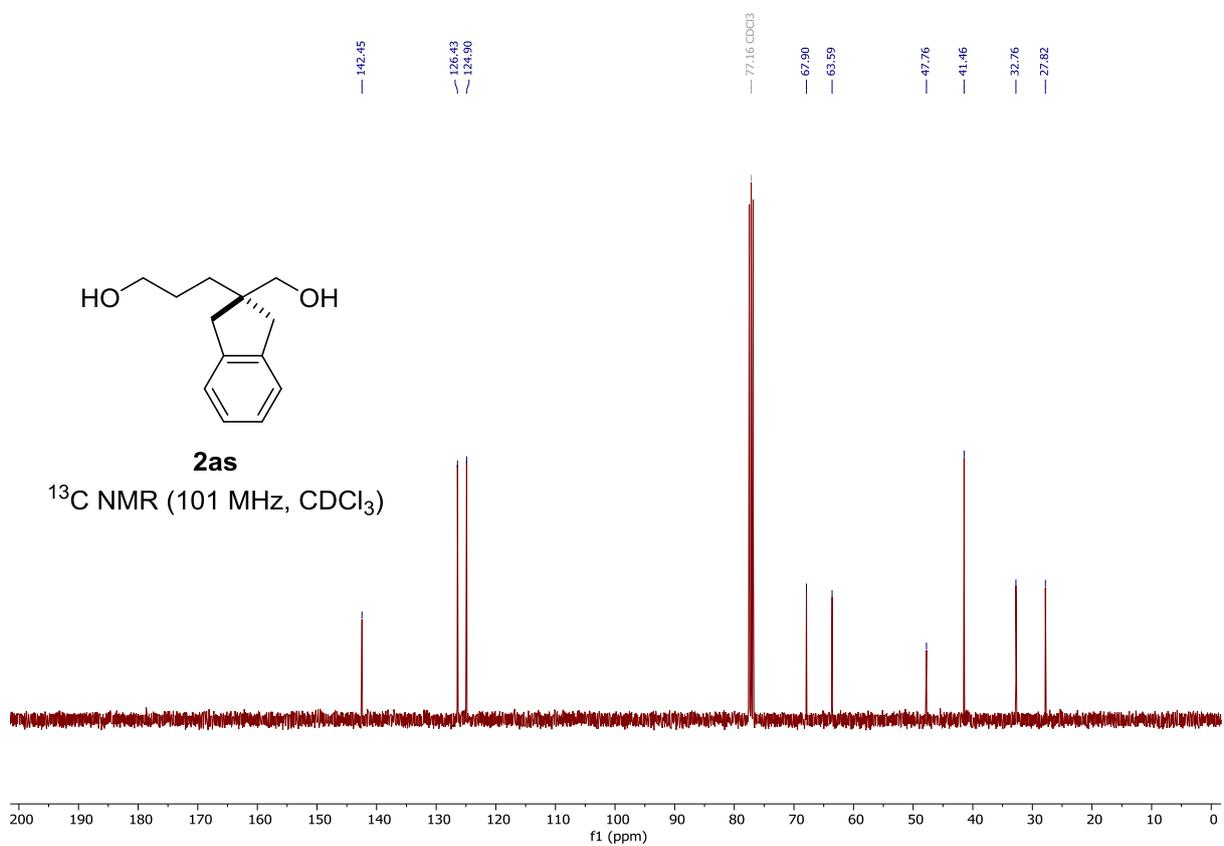
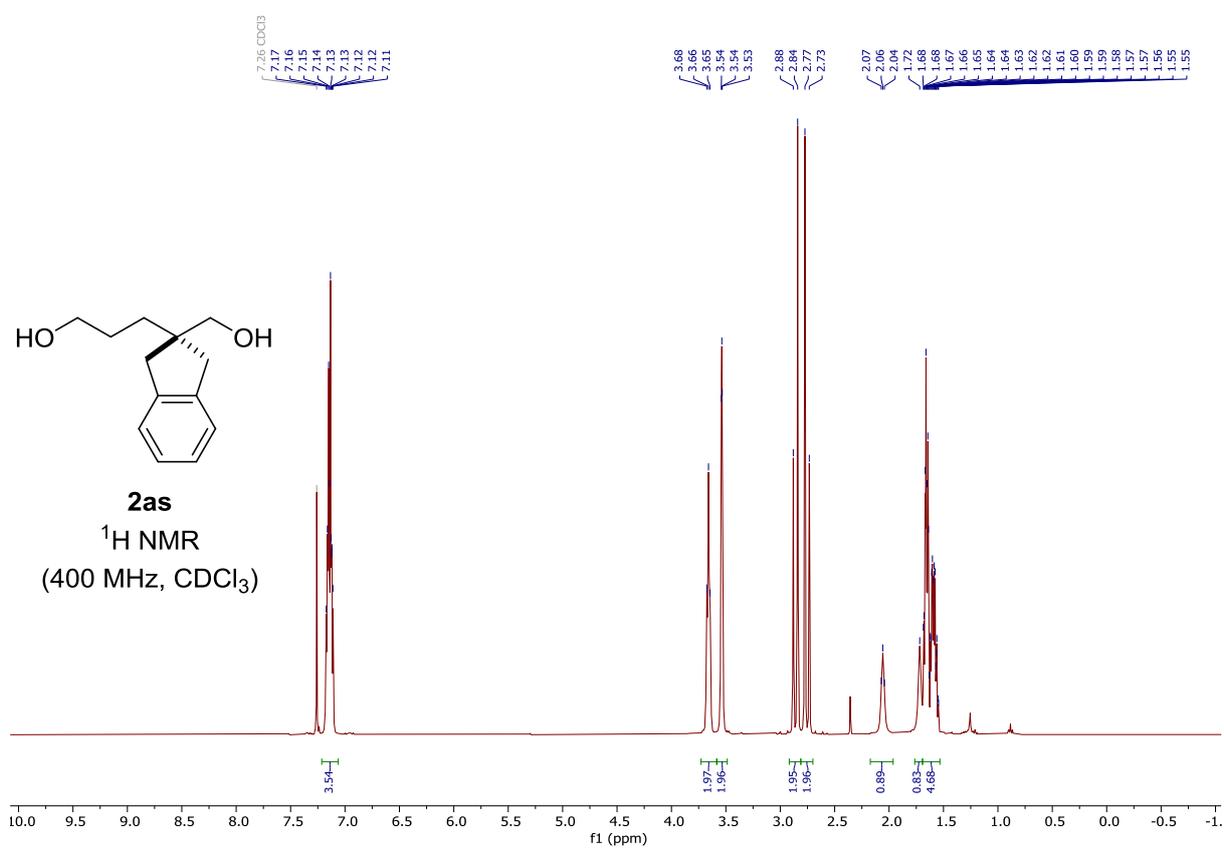


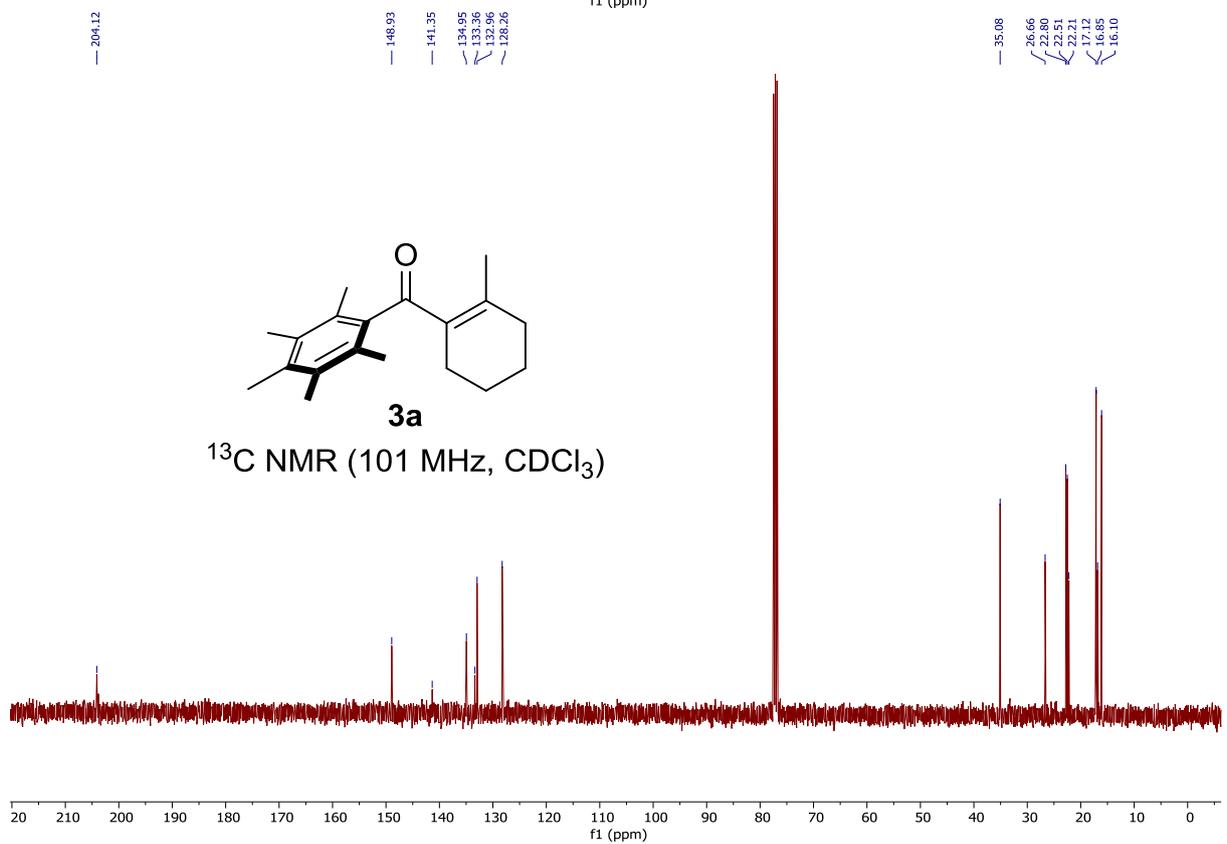
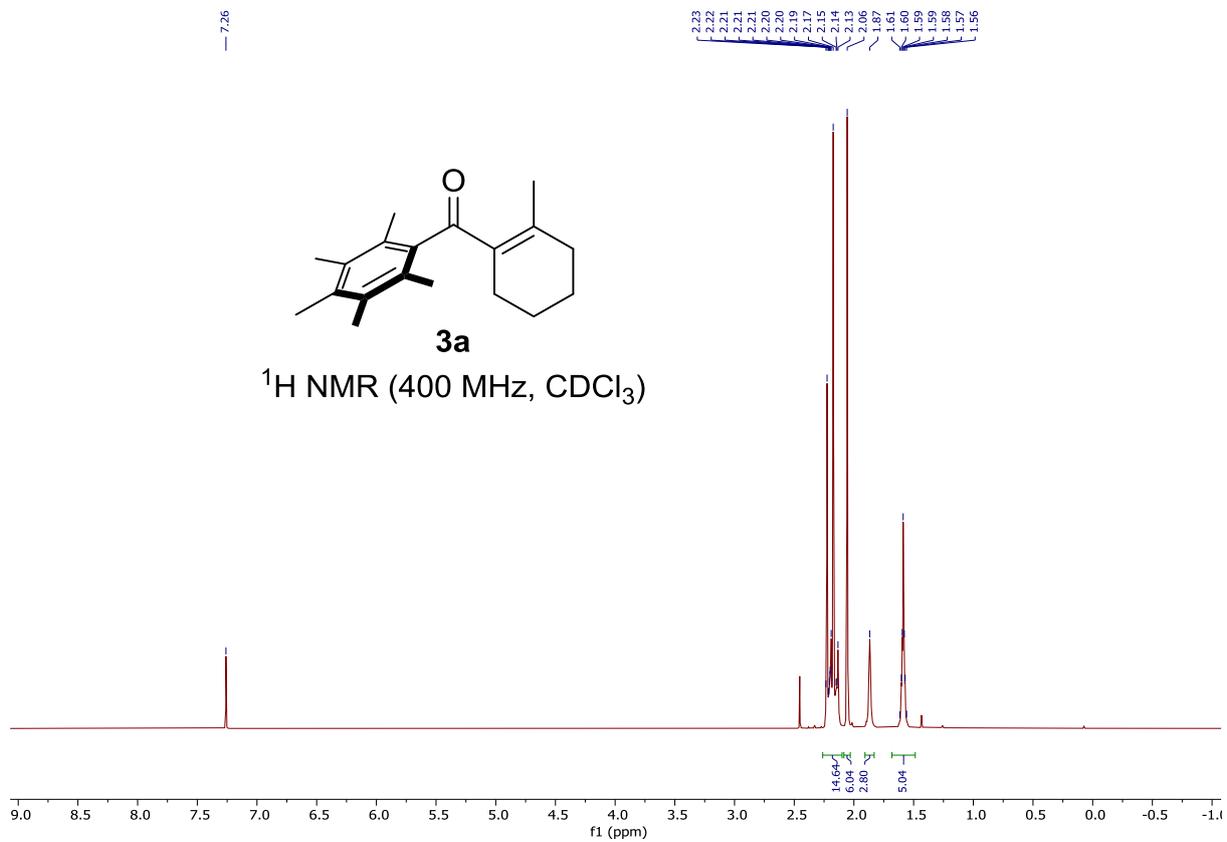


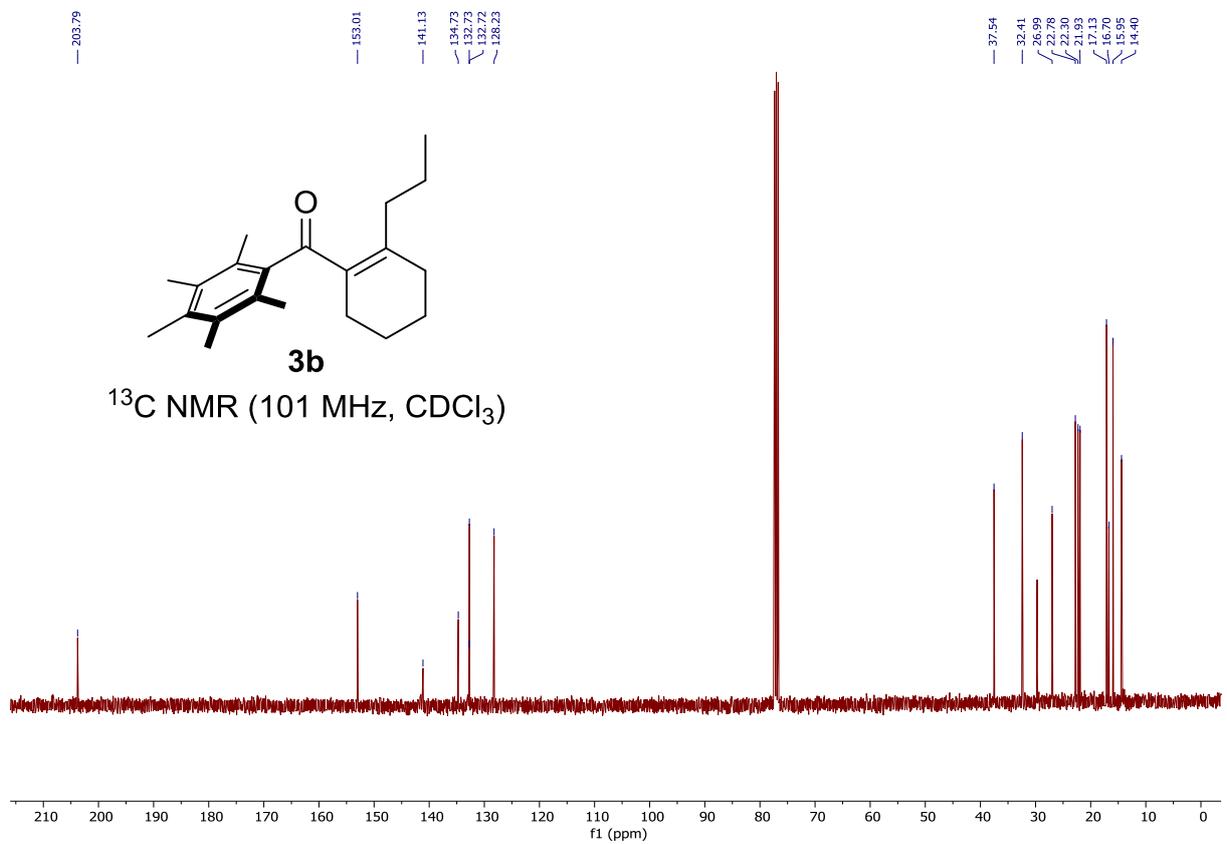
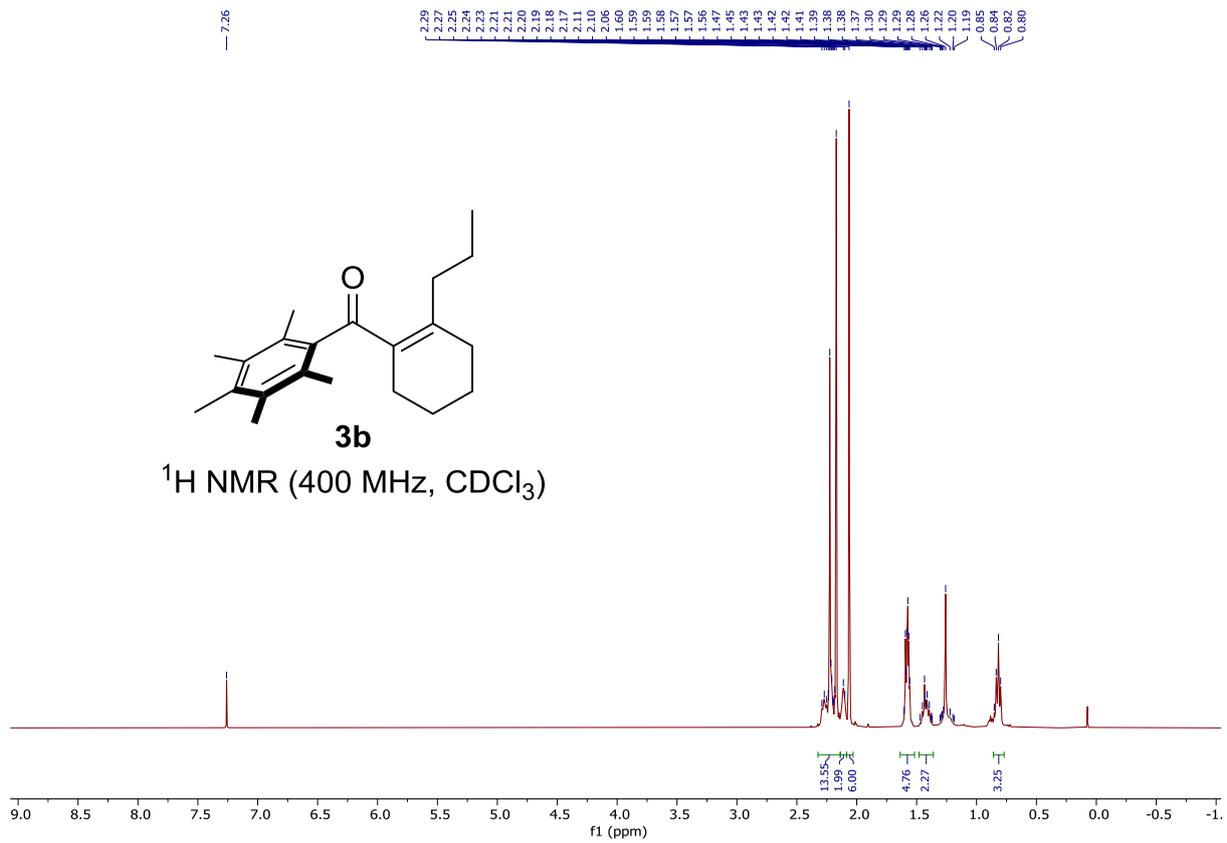
Stacked ¹H NMR and ²H NMR Spectra for d_4 -2af:

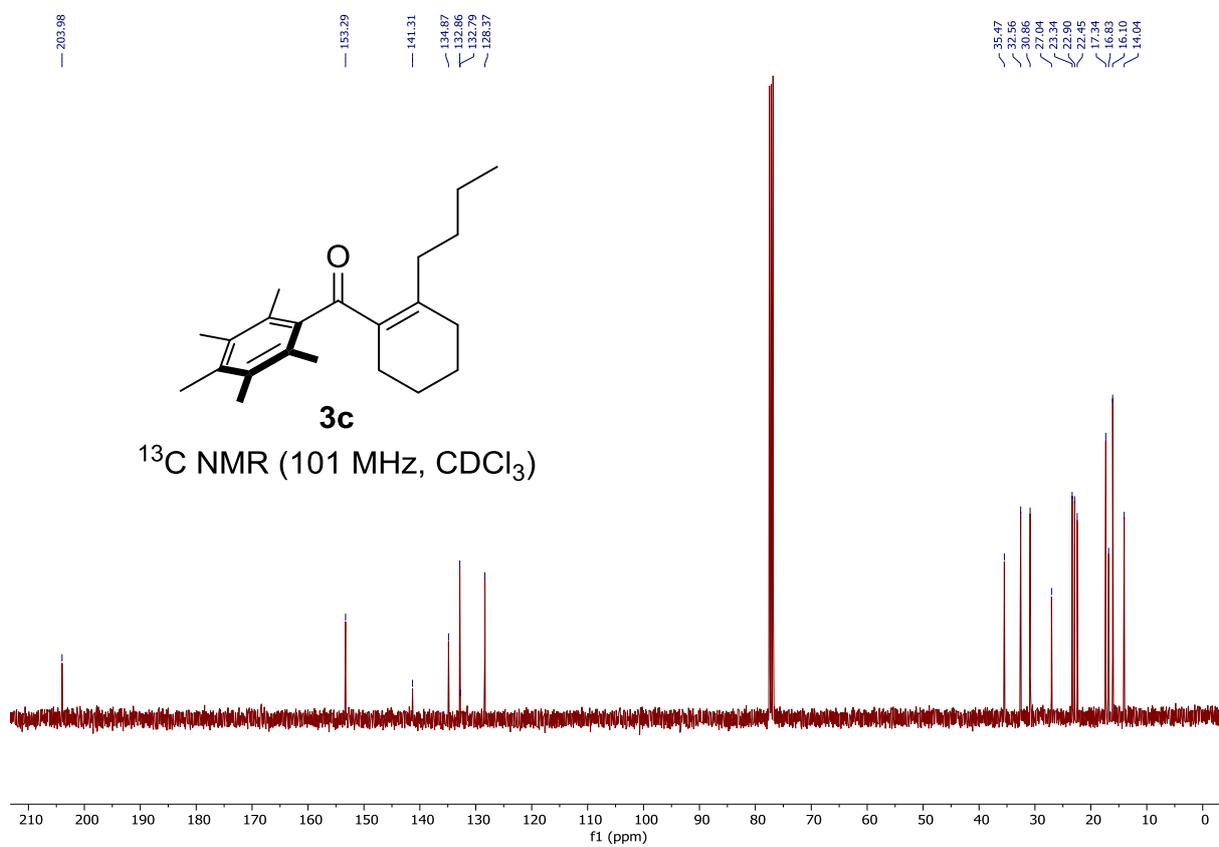
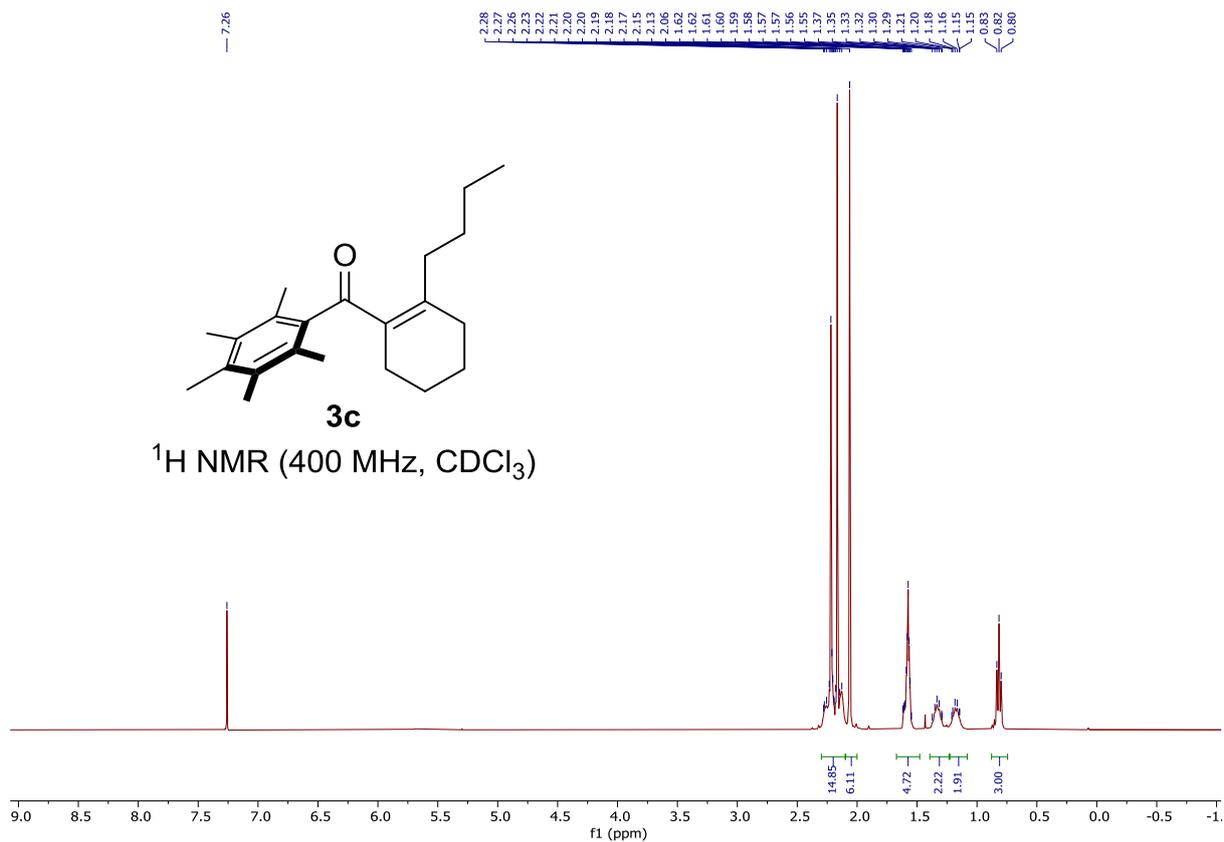


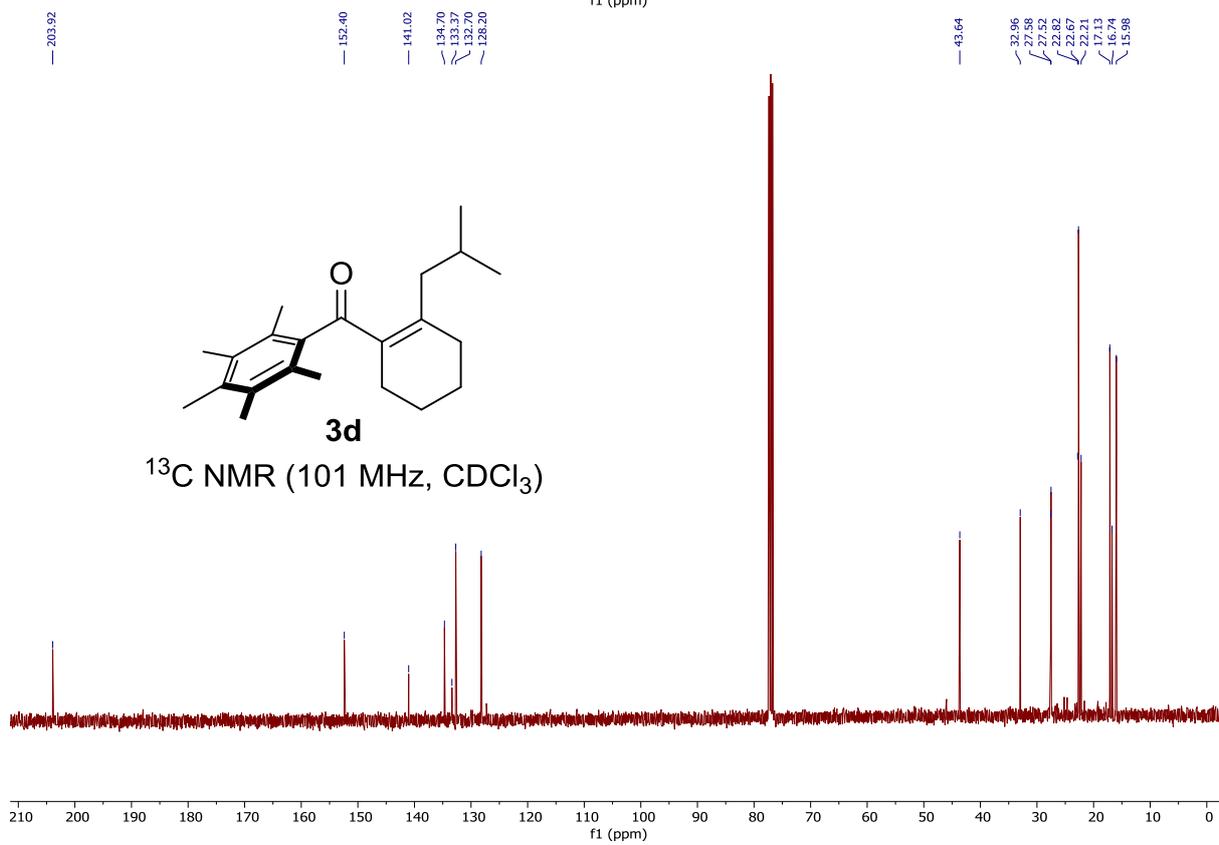
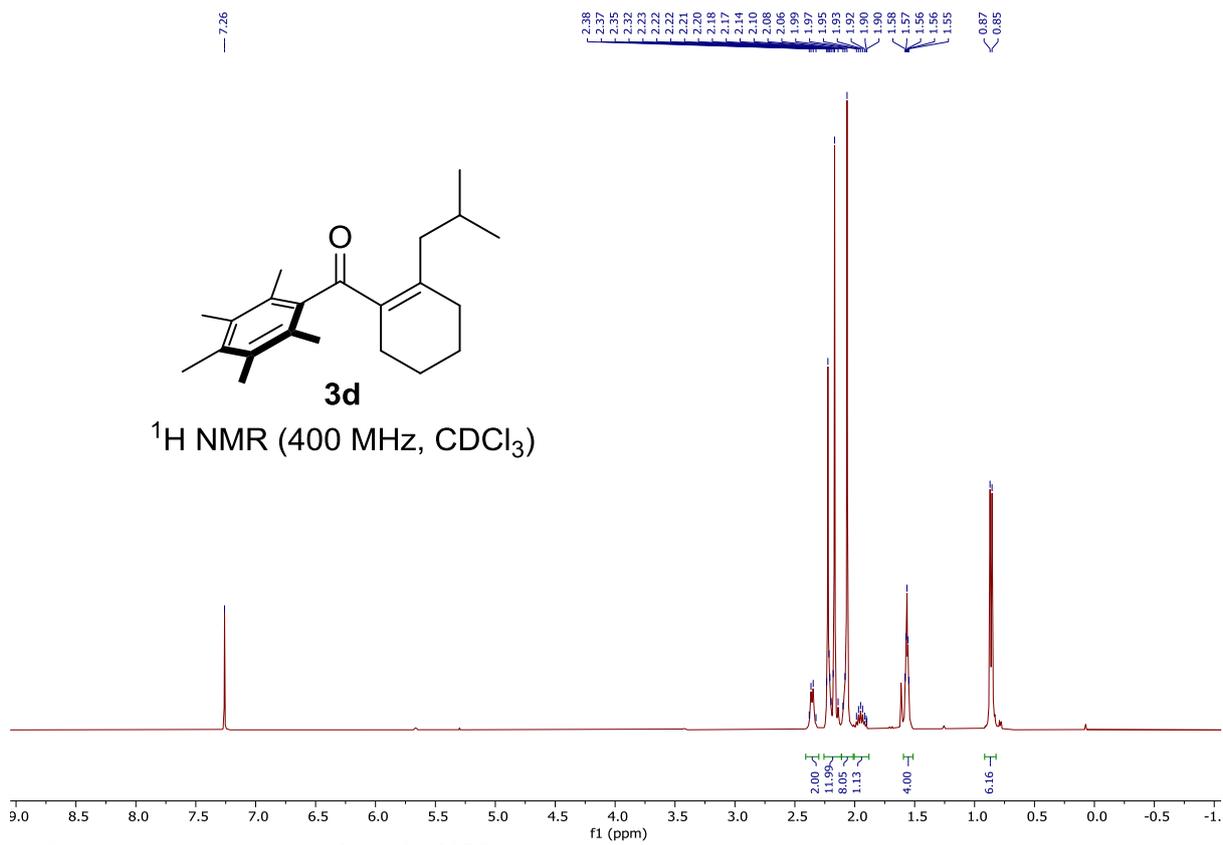


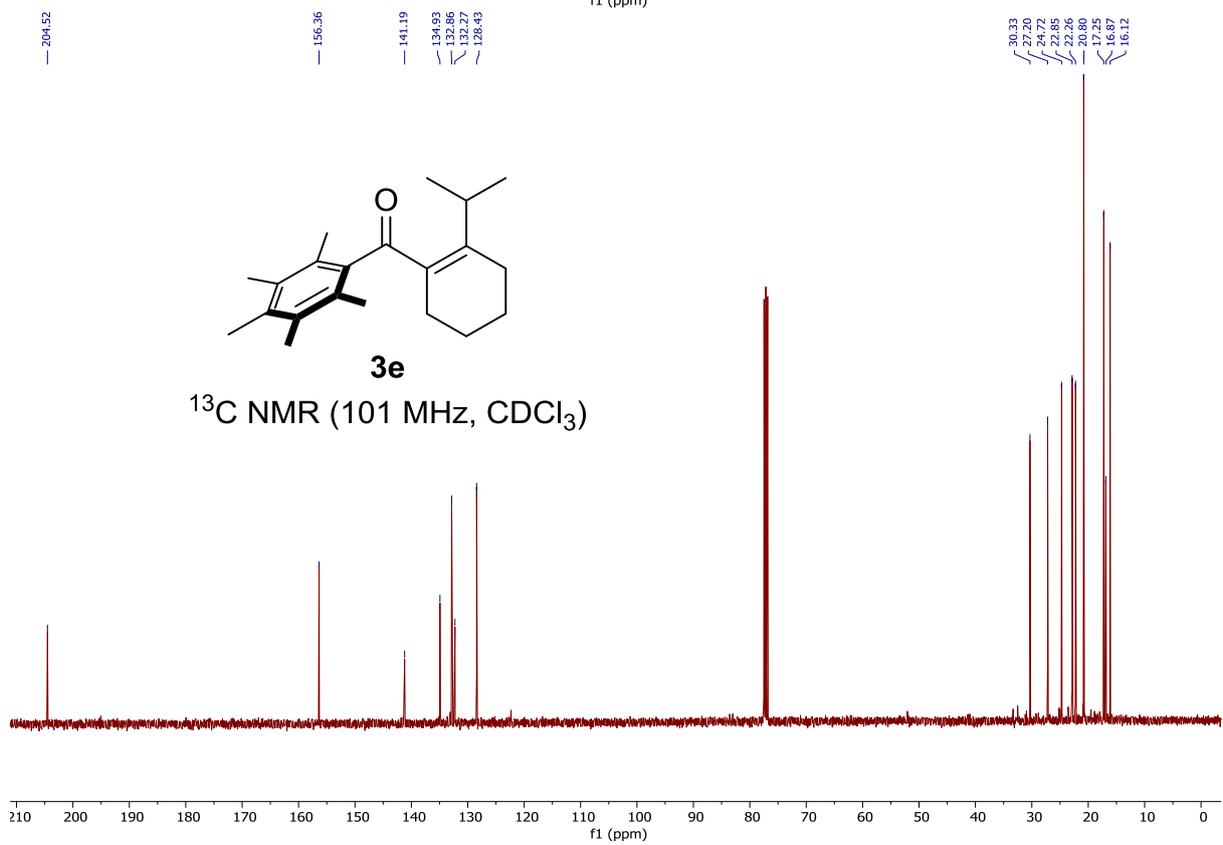
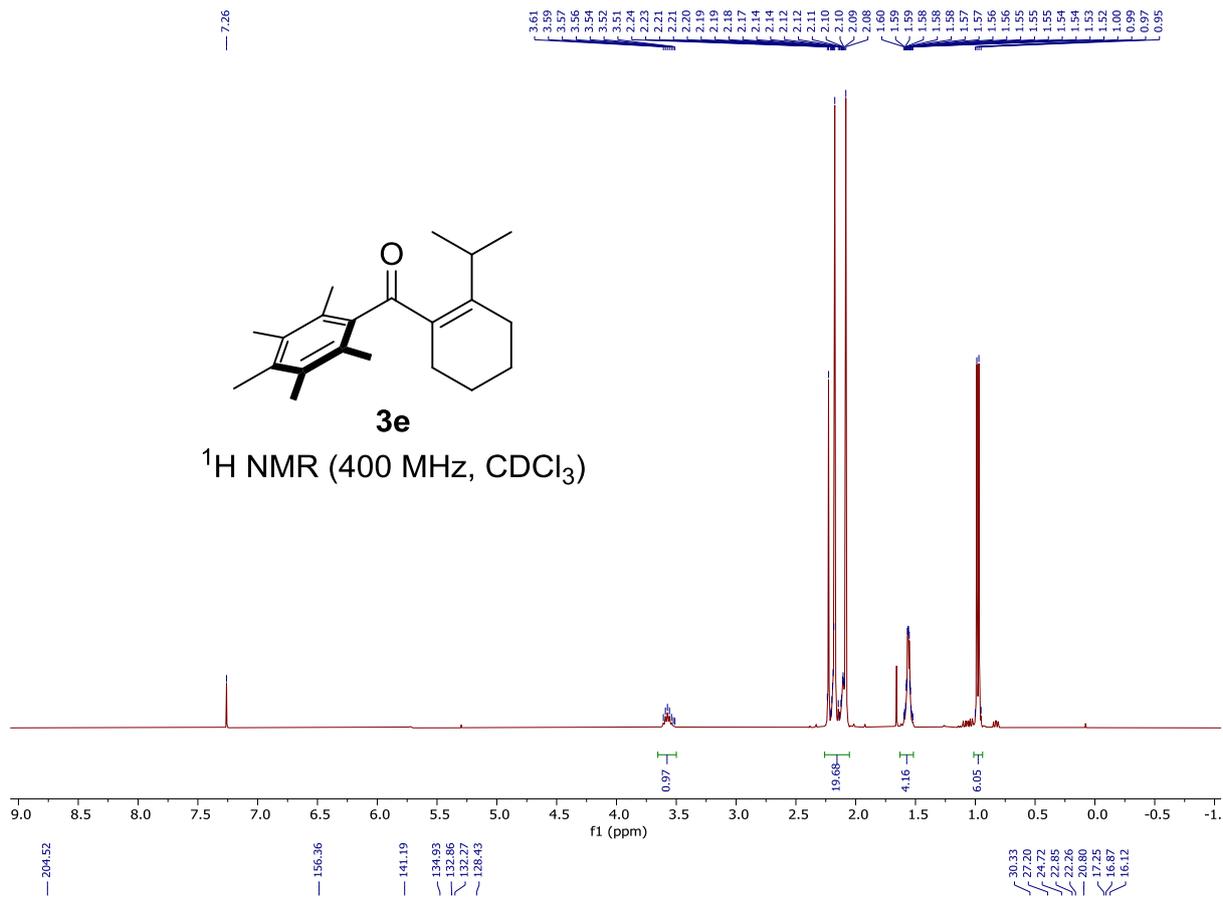


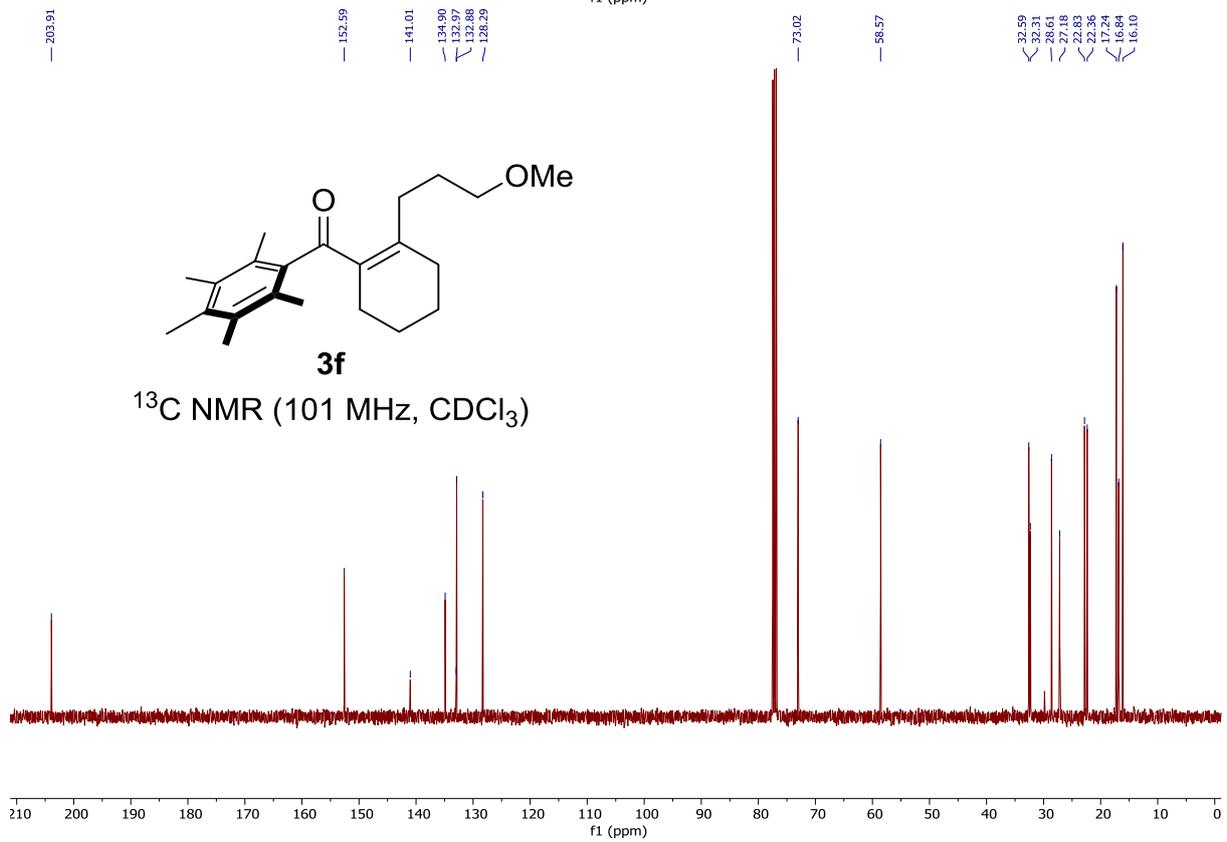
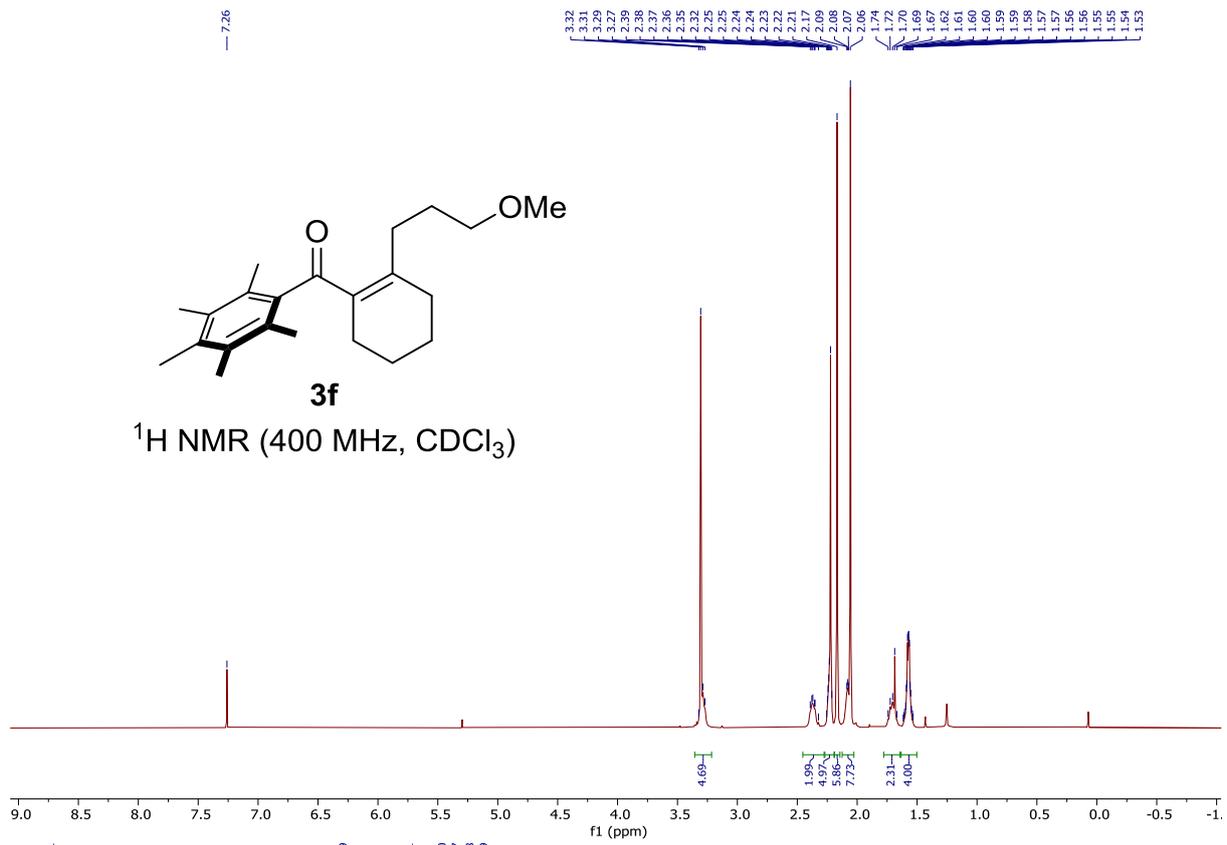


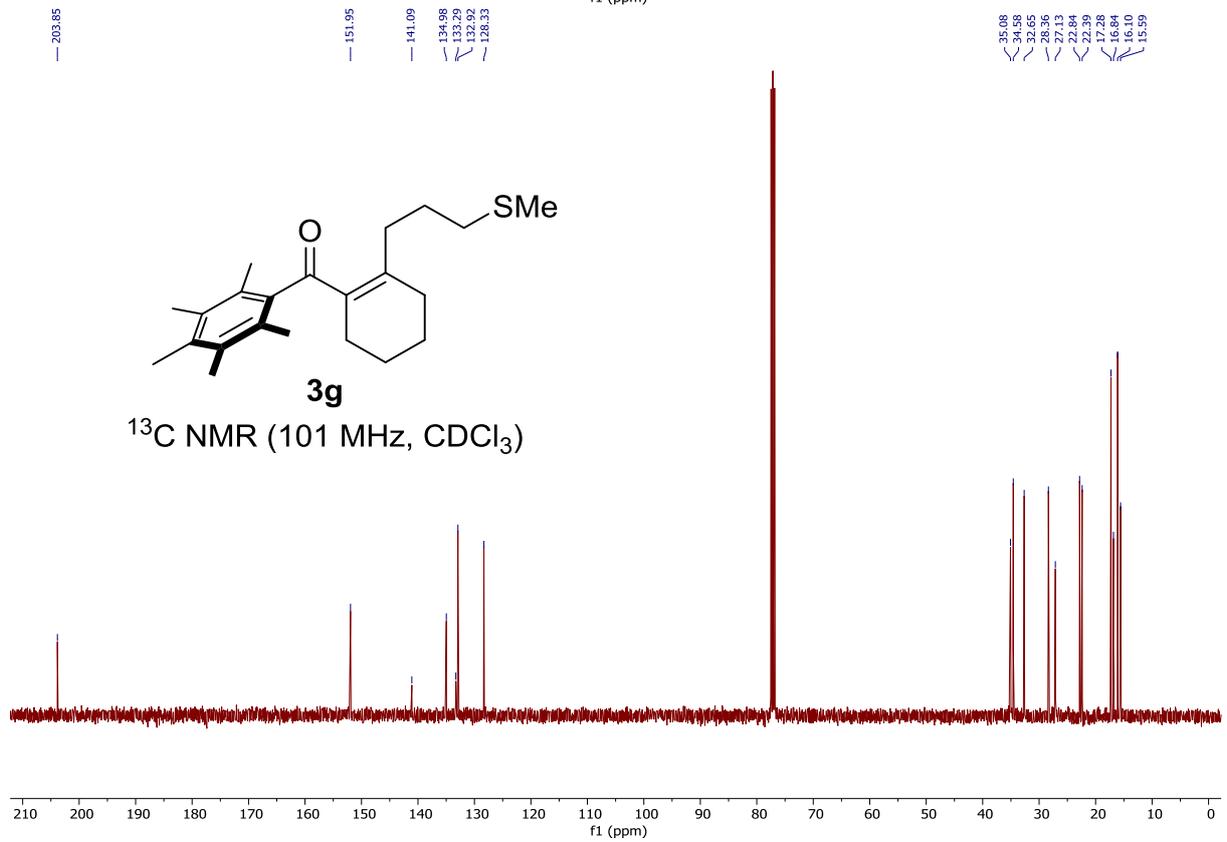
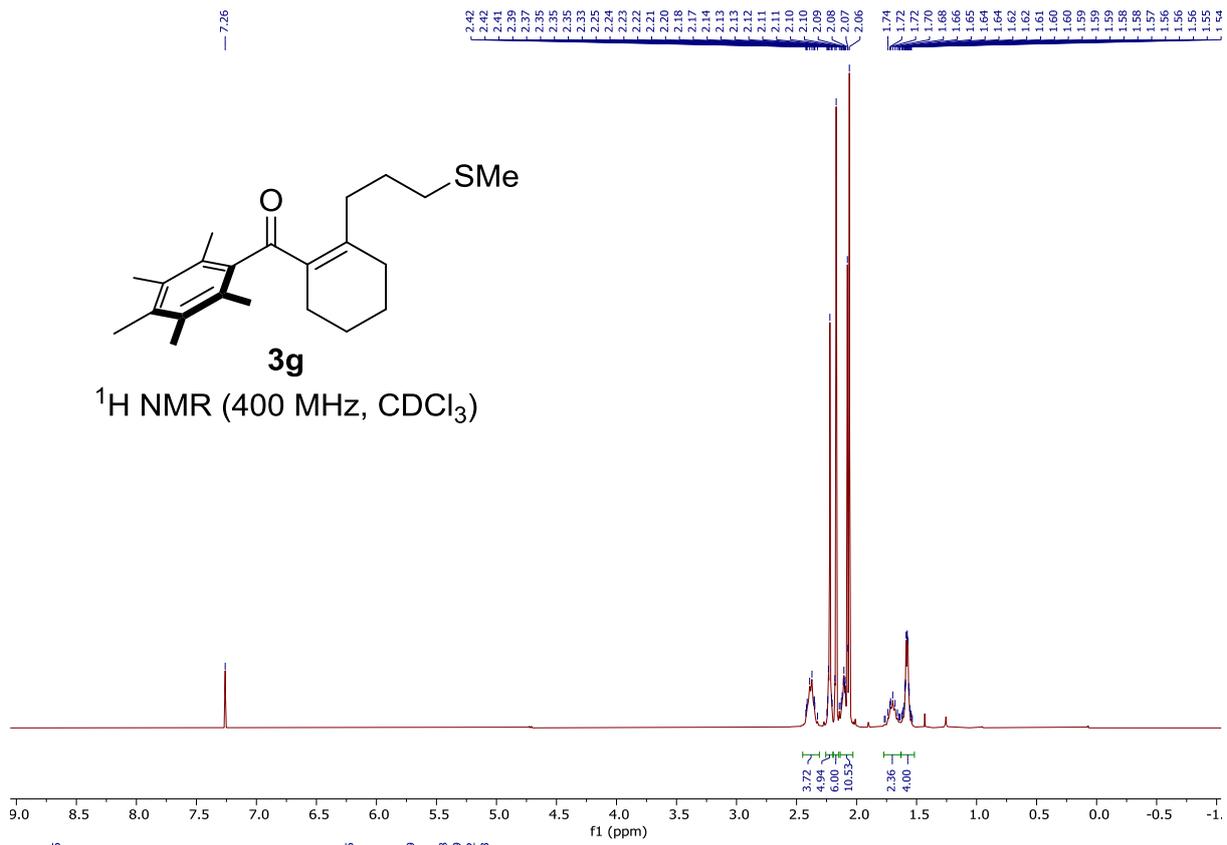


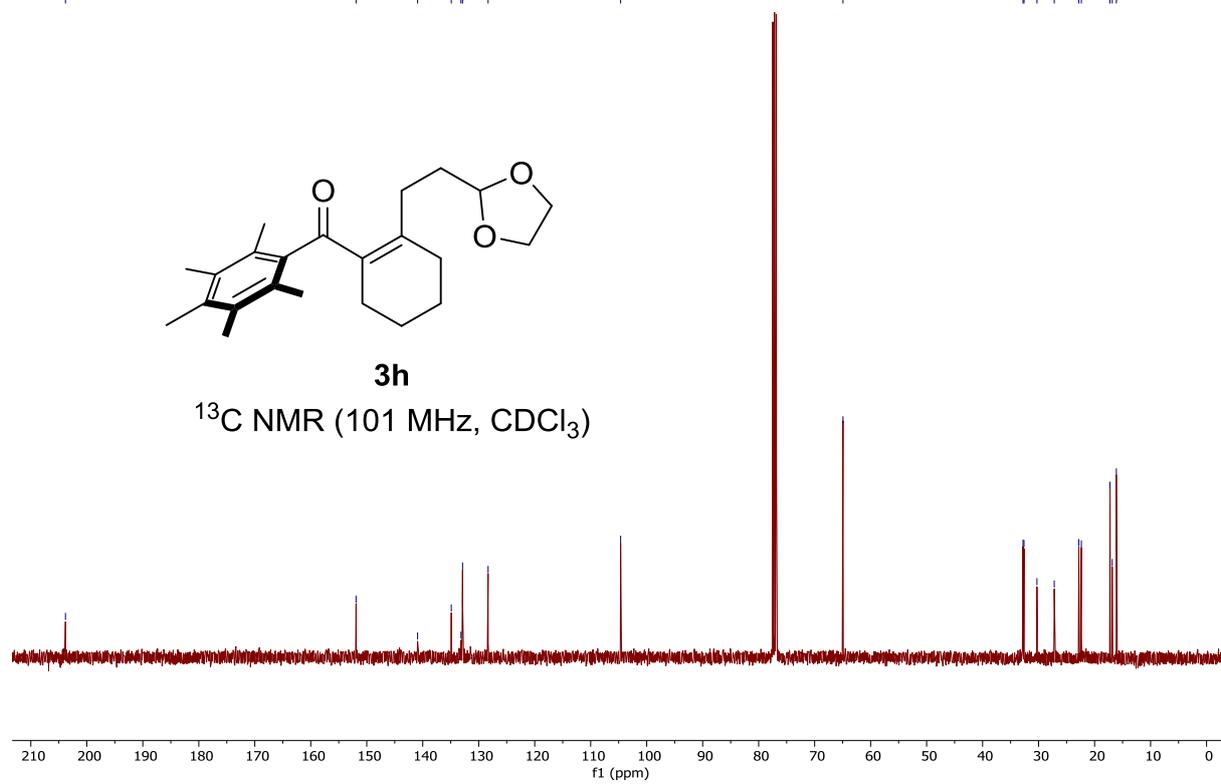
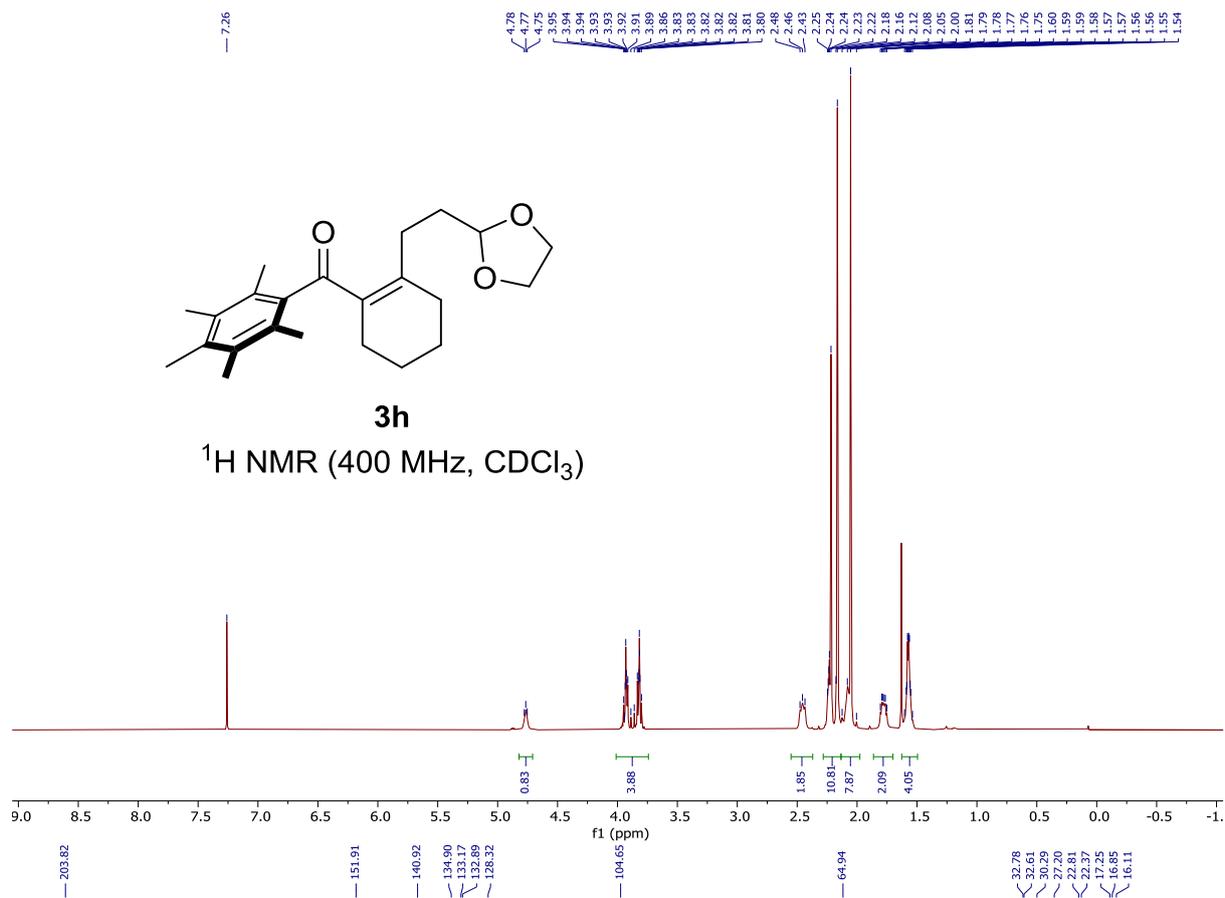


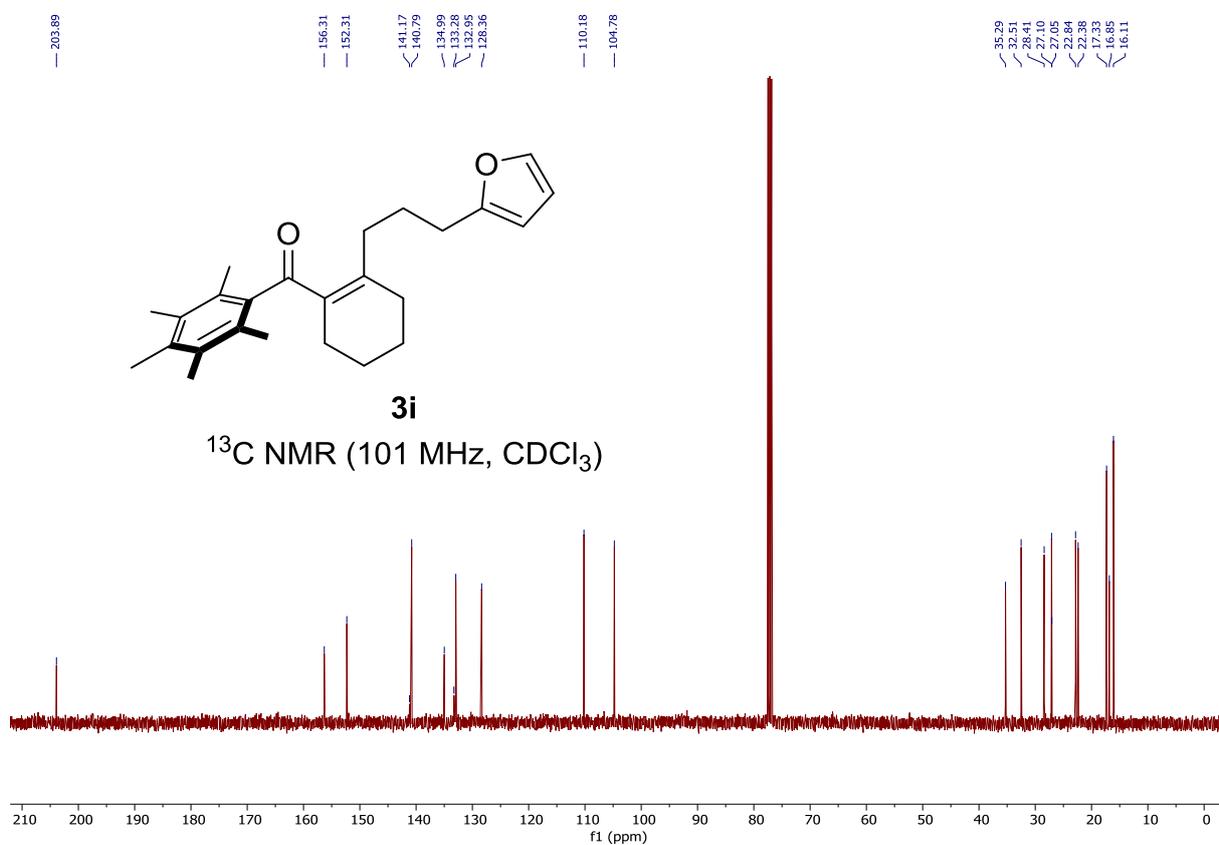
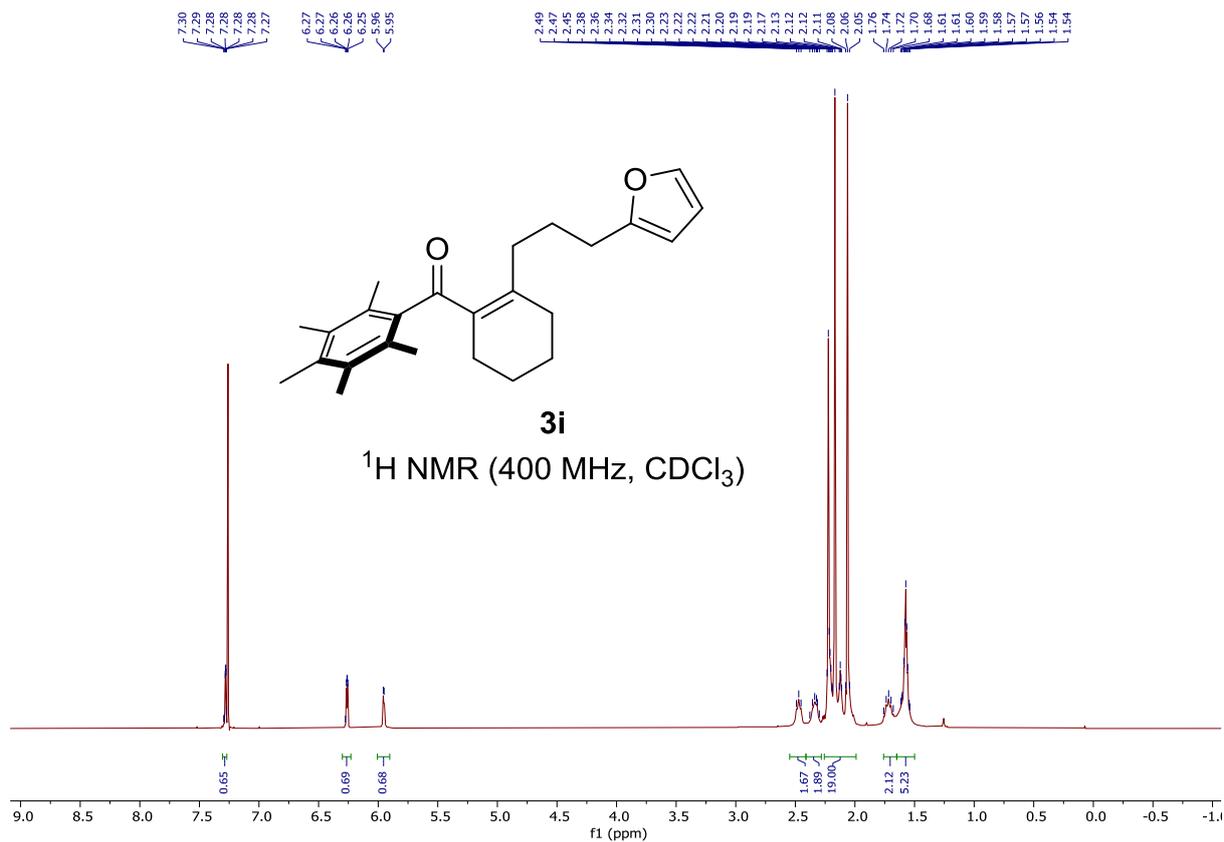


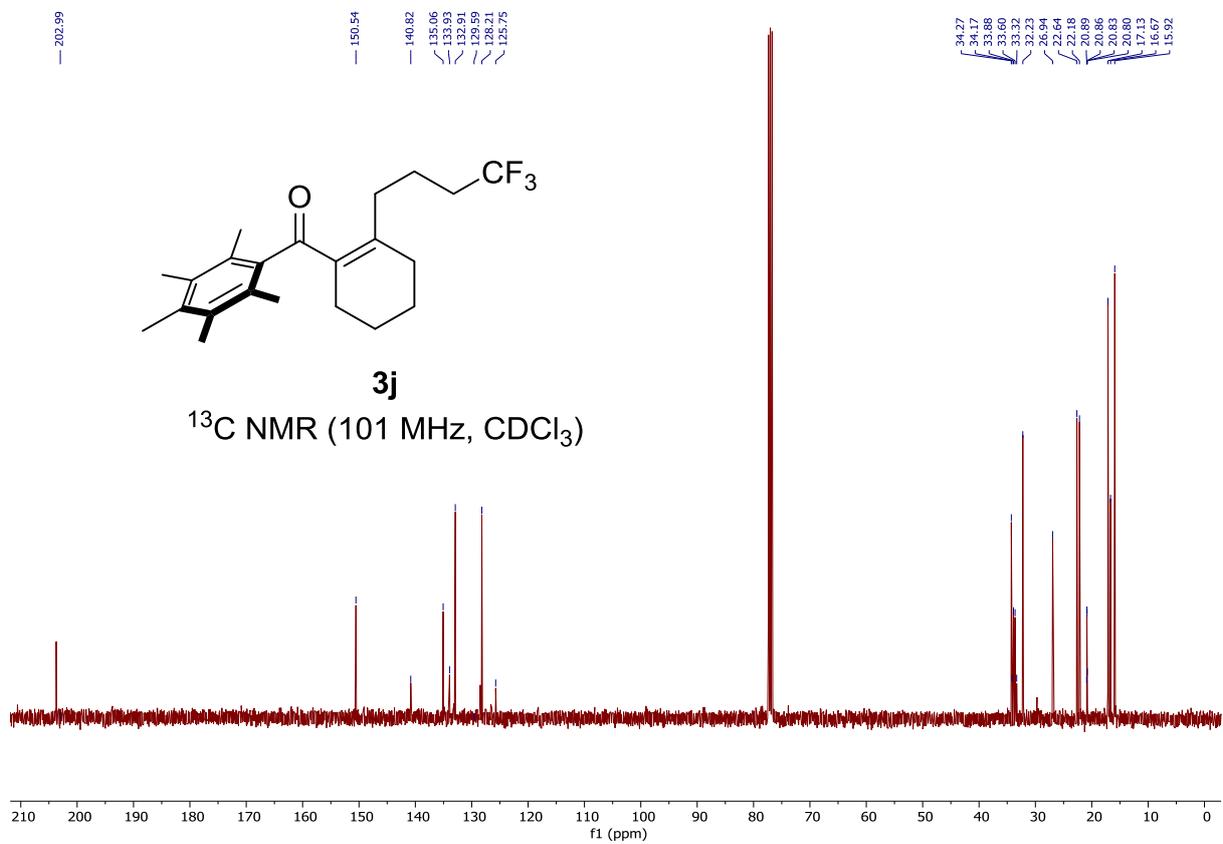
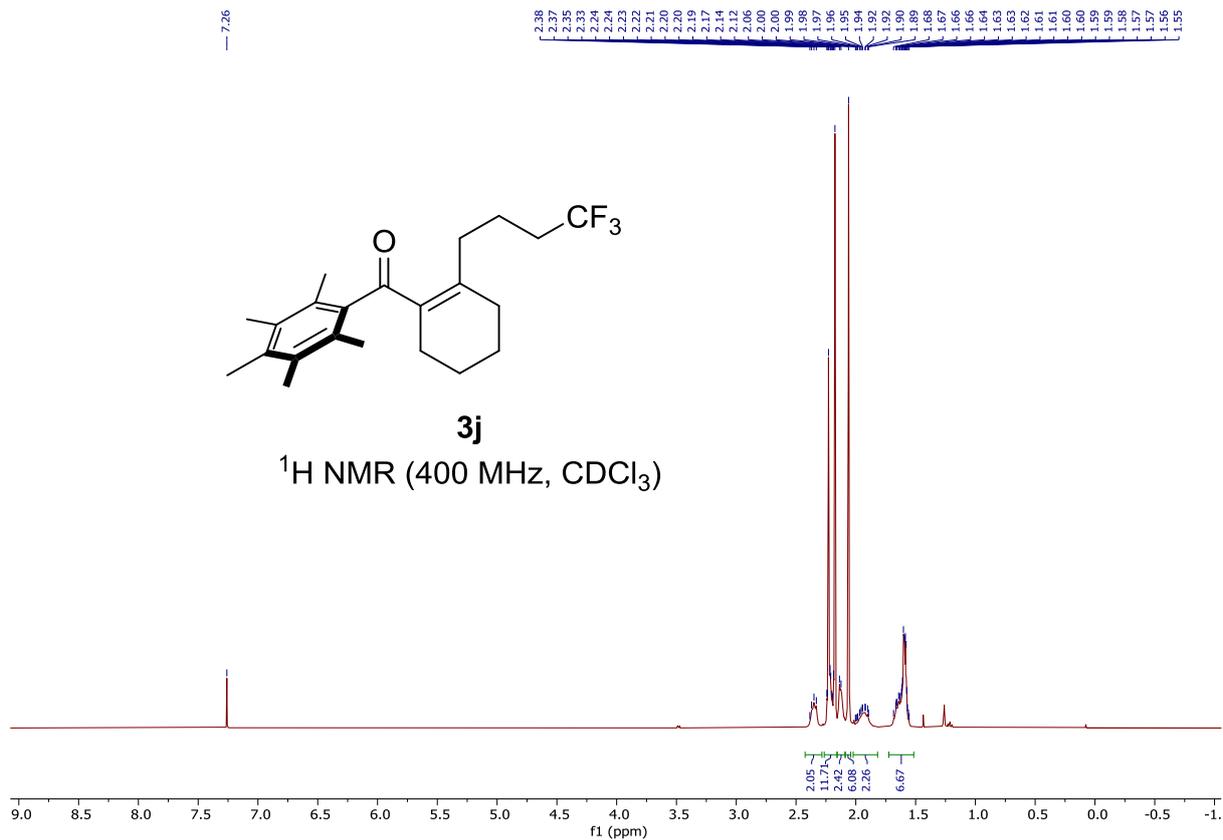


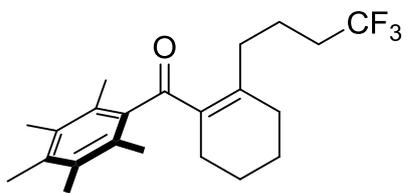






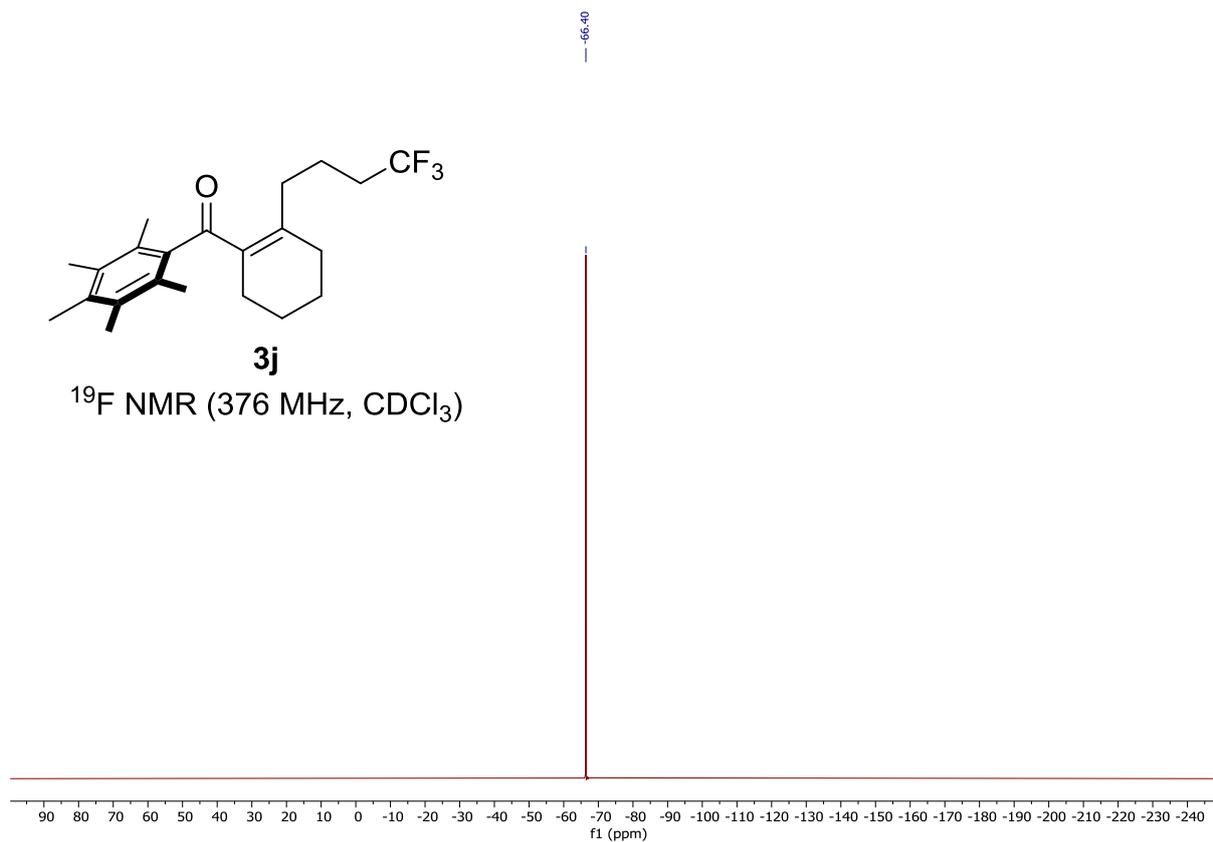


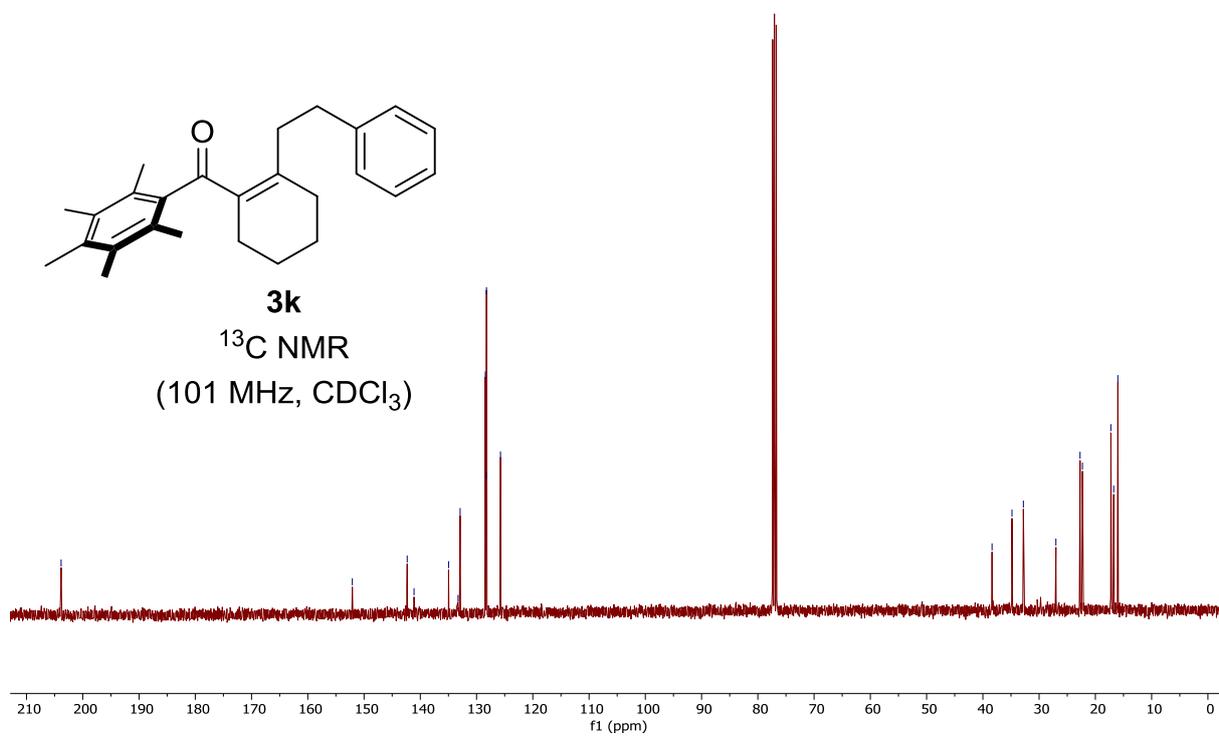
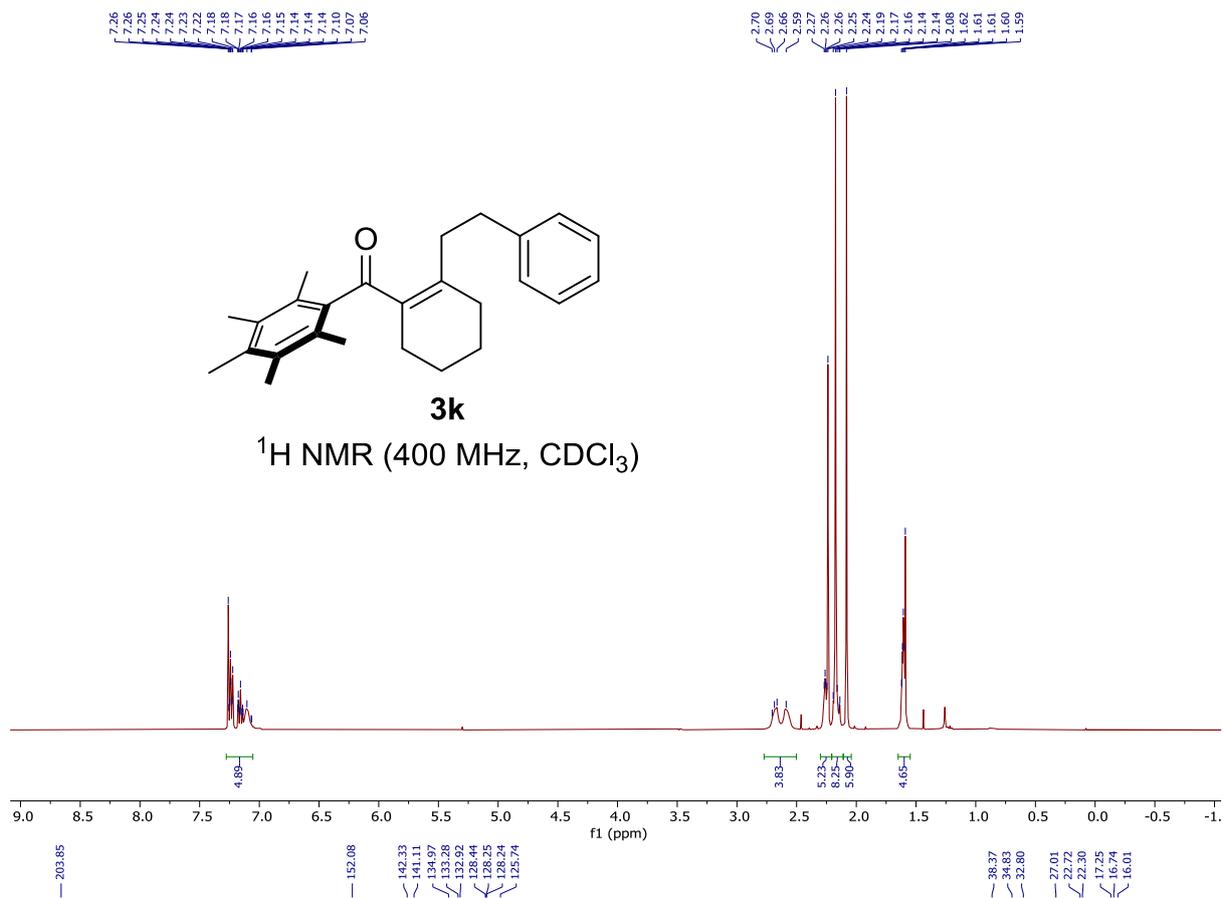


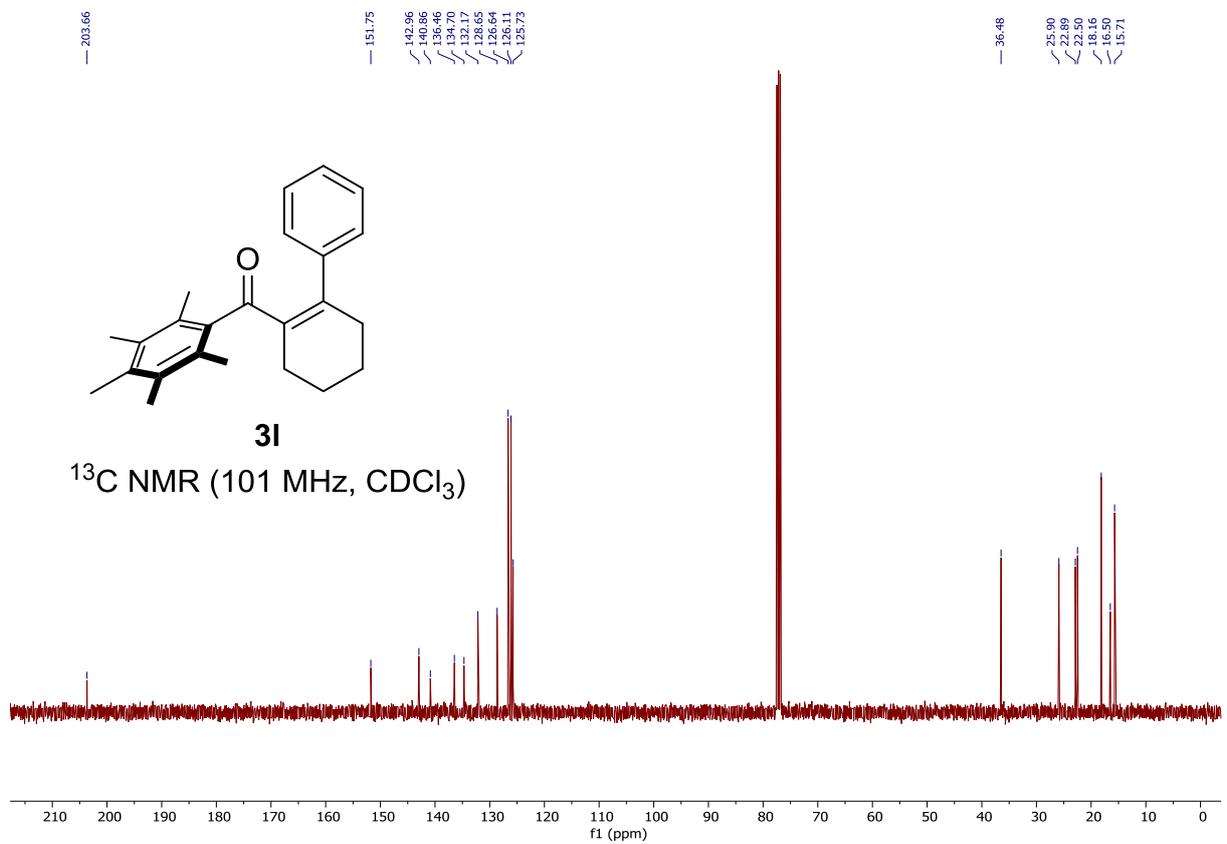
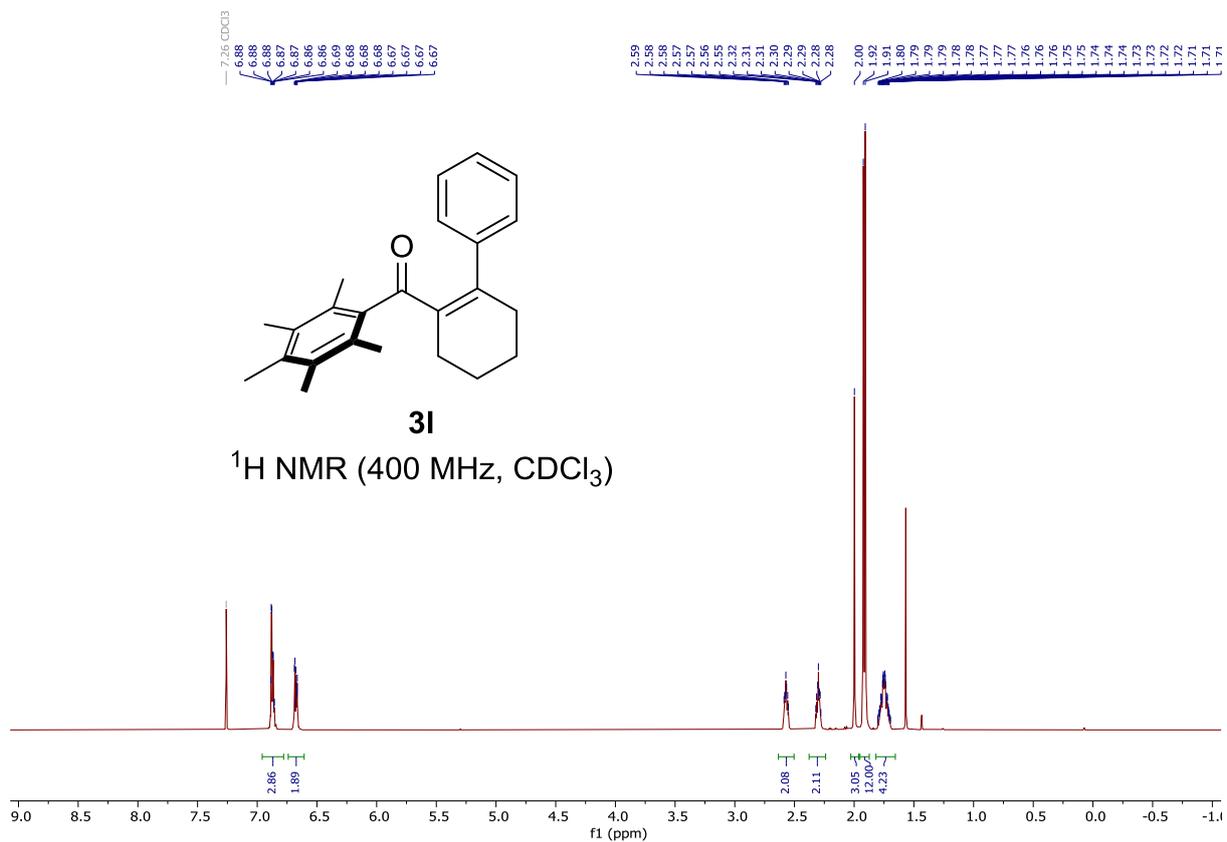


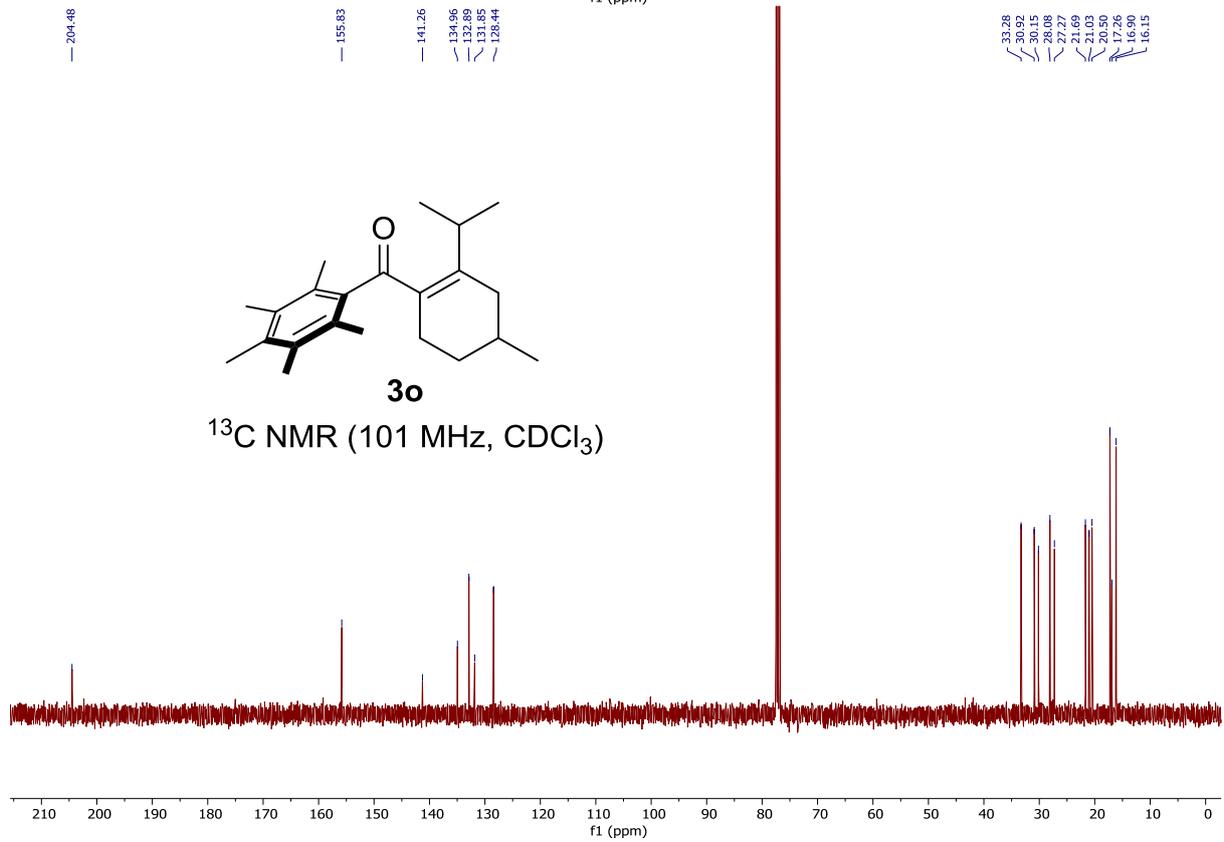
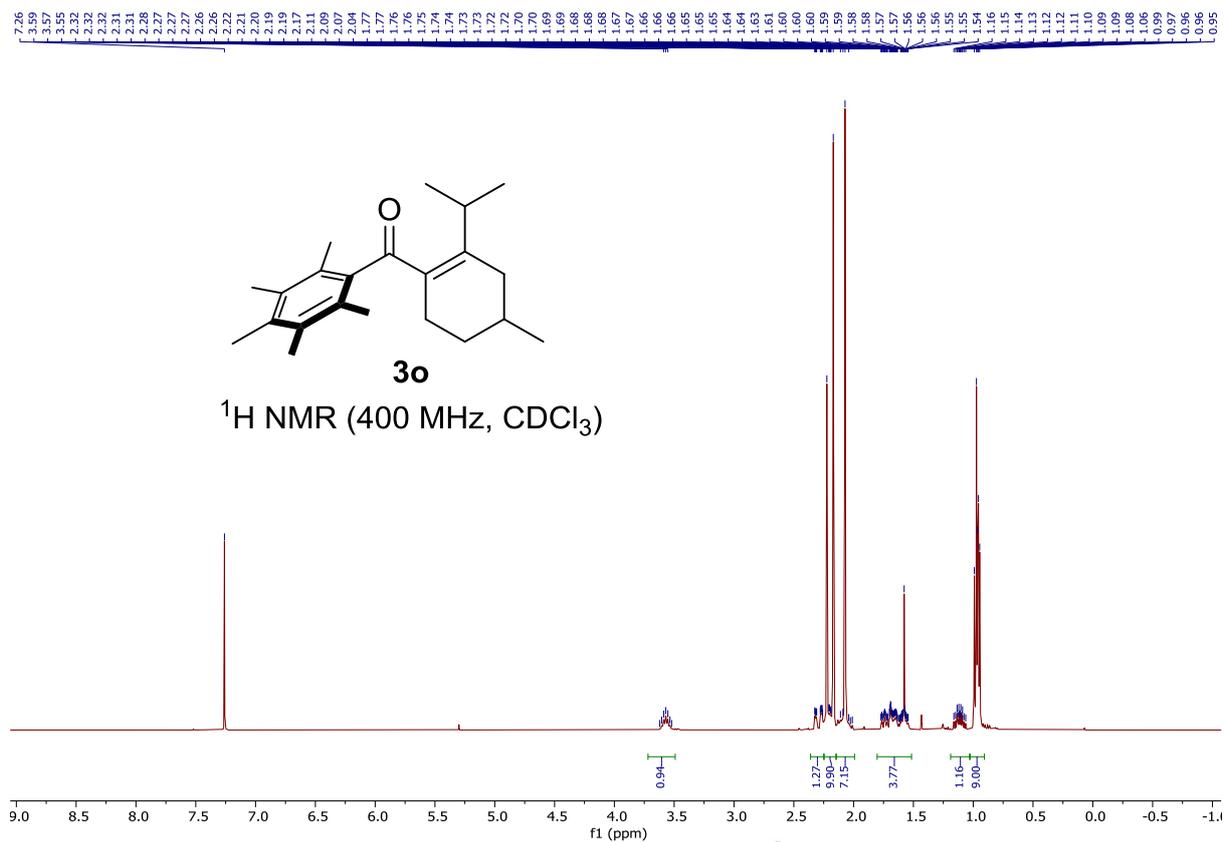
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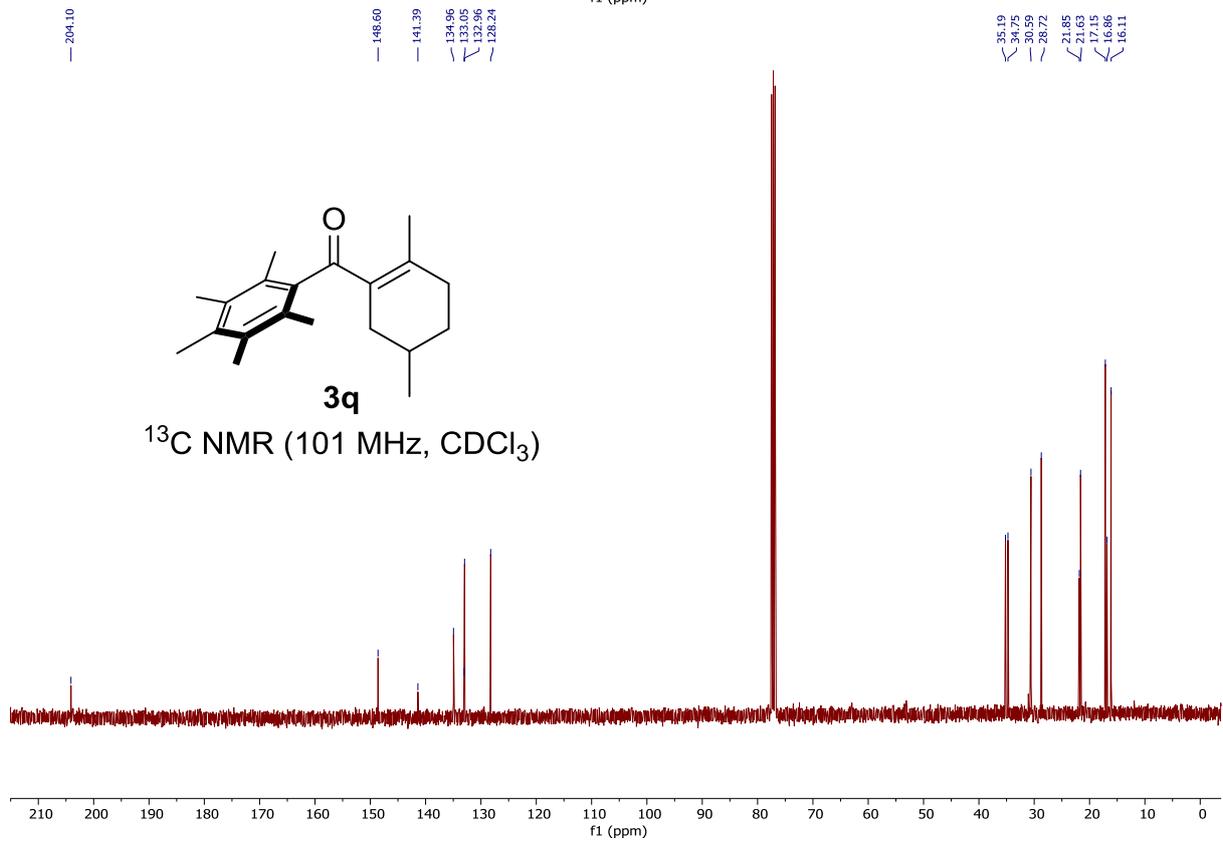
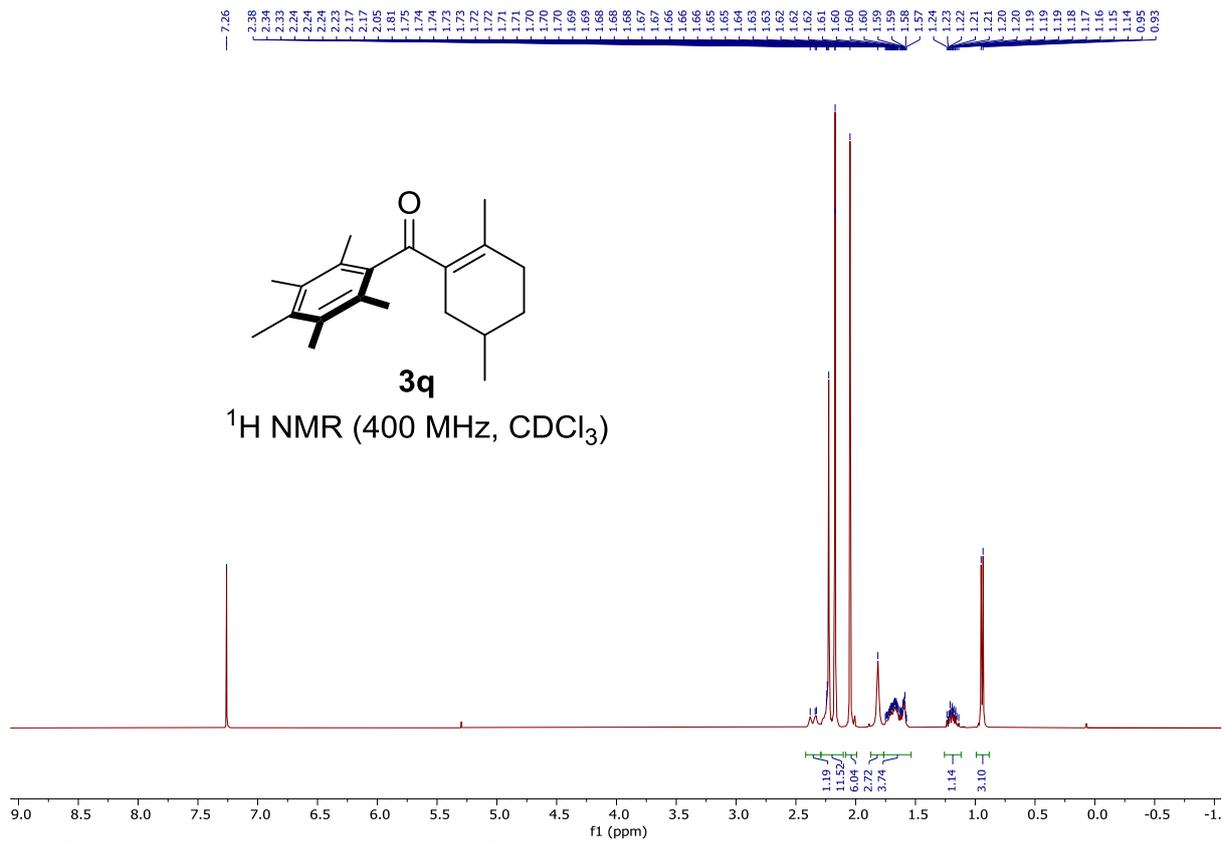
¹⁹F NMR (376 MHz, CDCl₃)

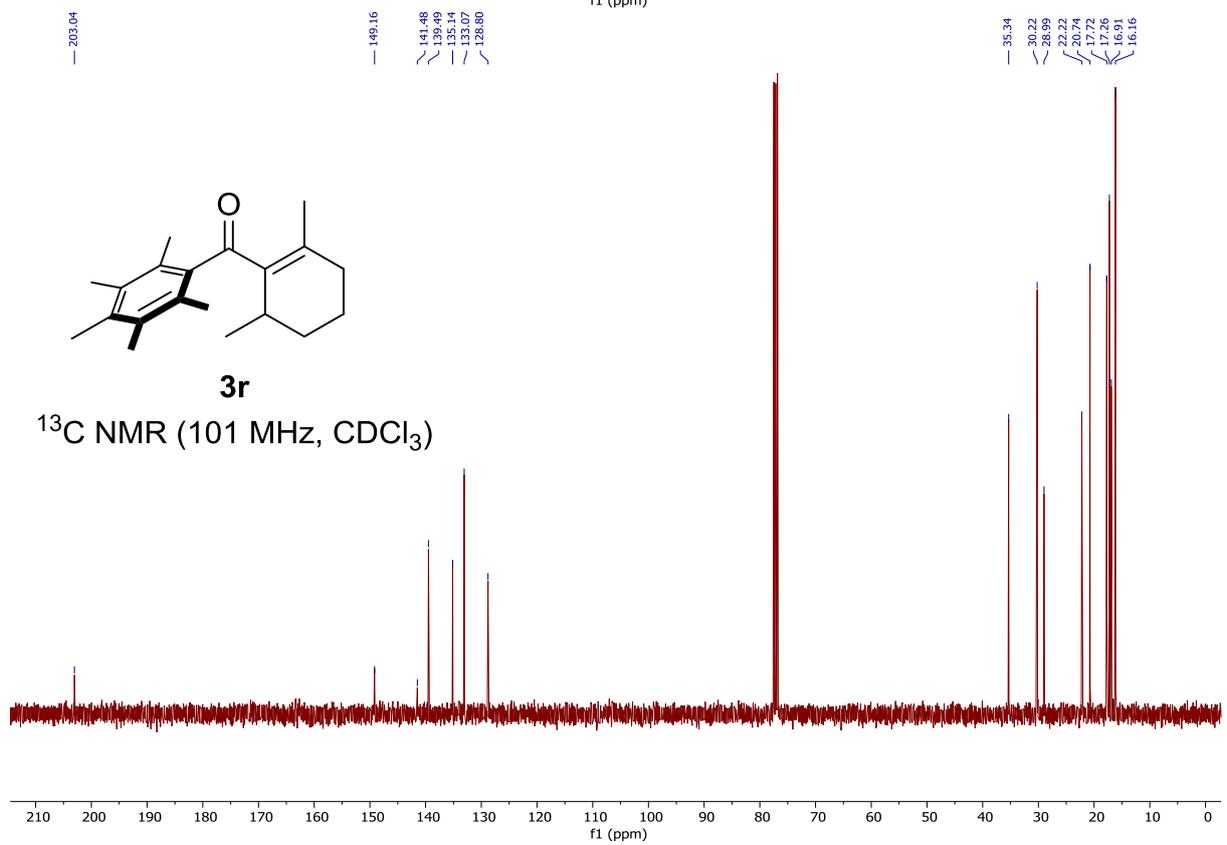
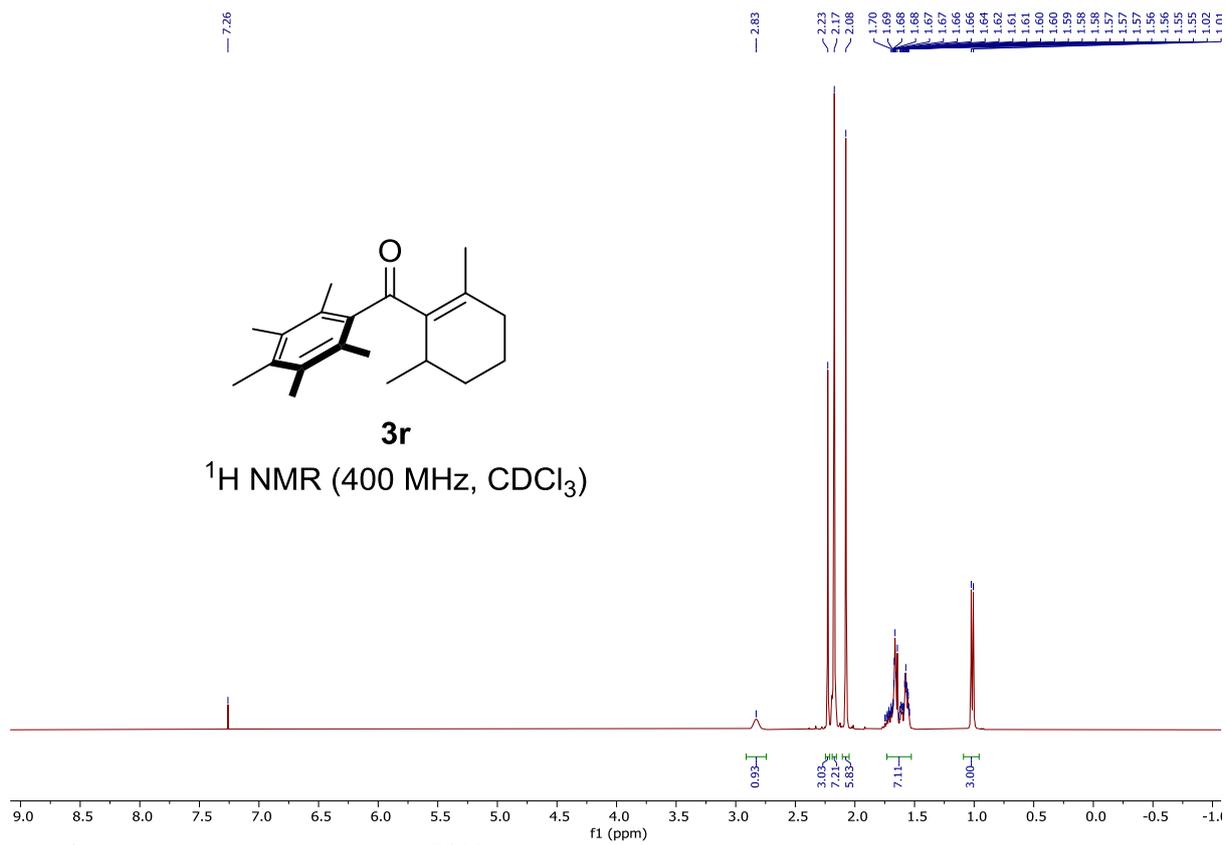


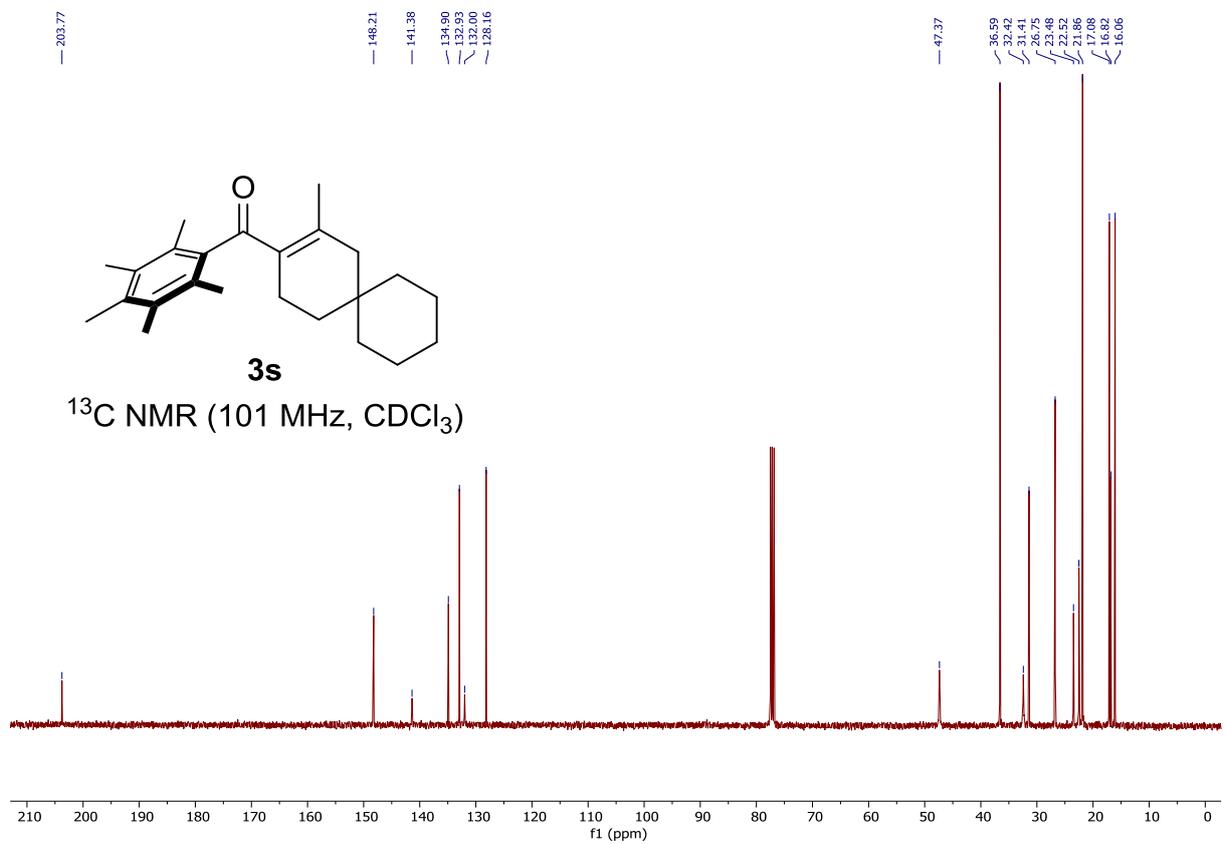
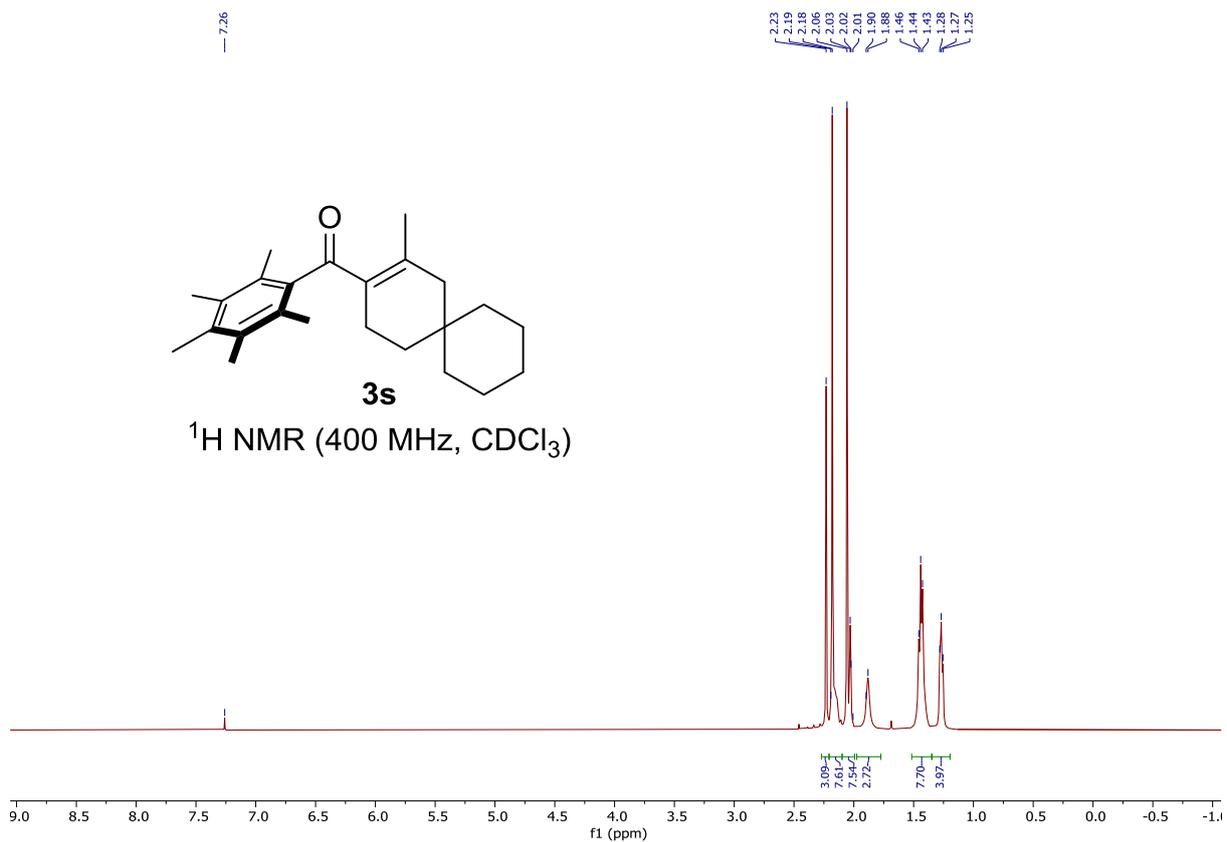


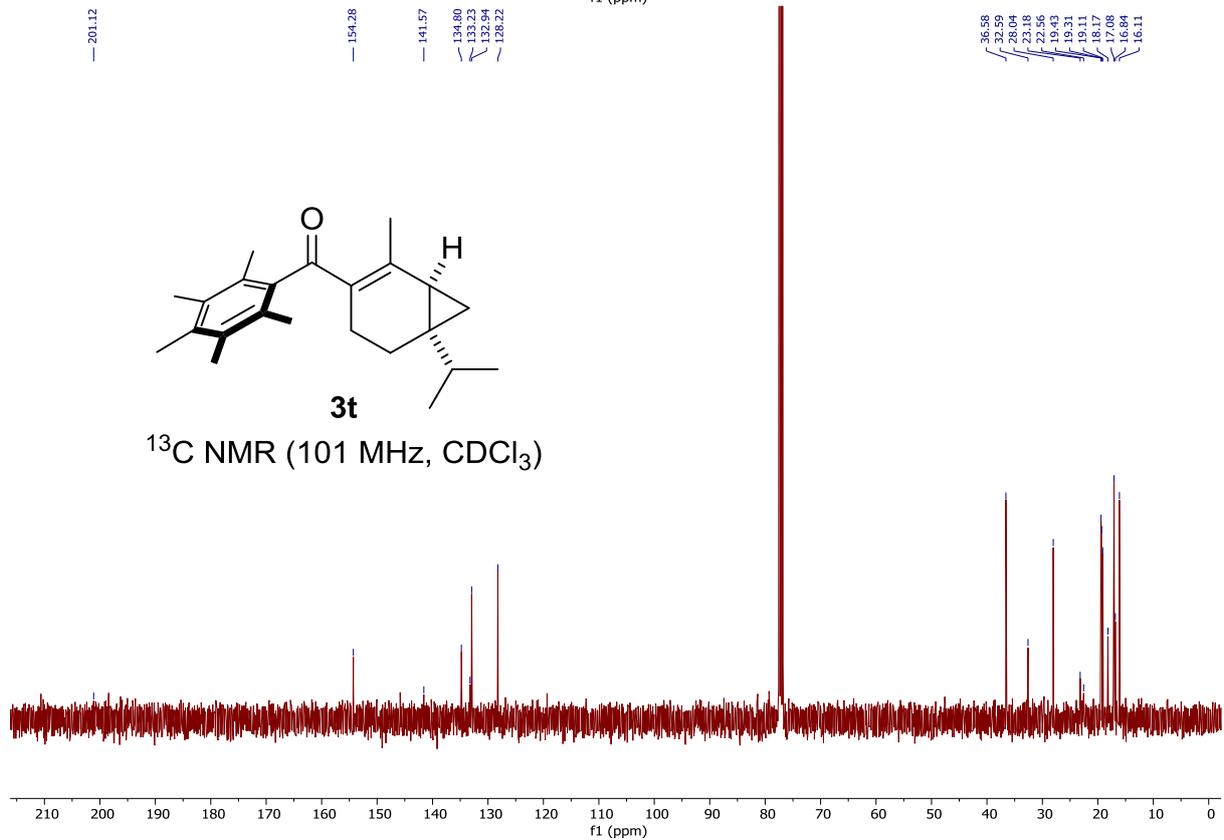
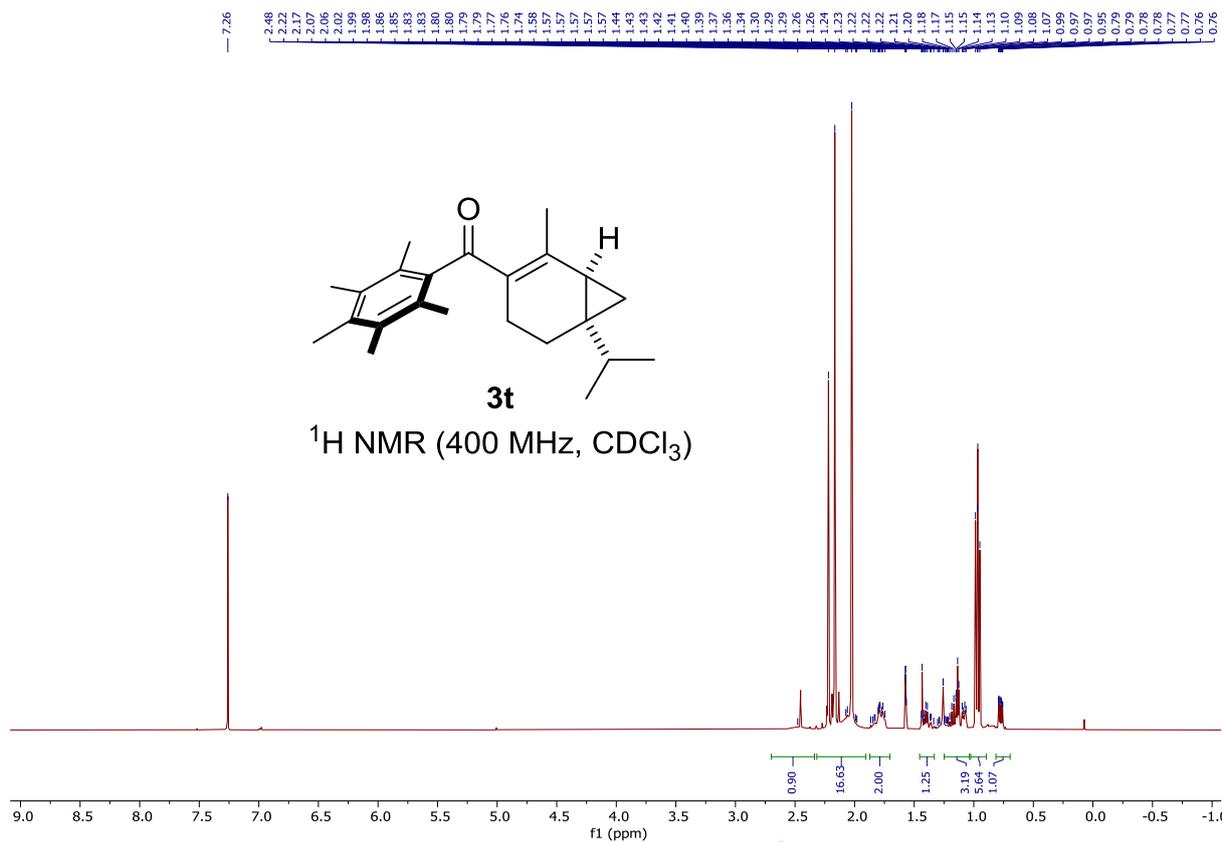


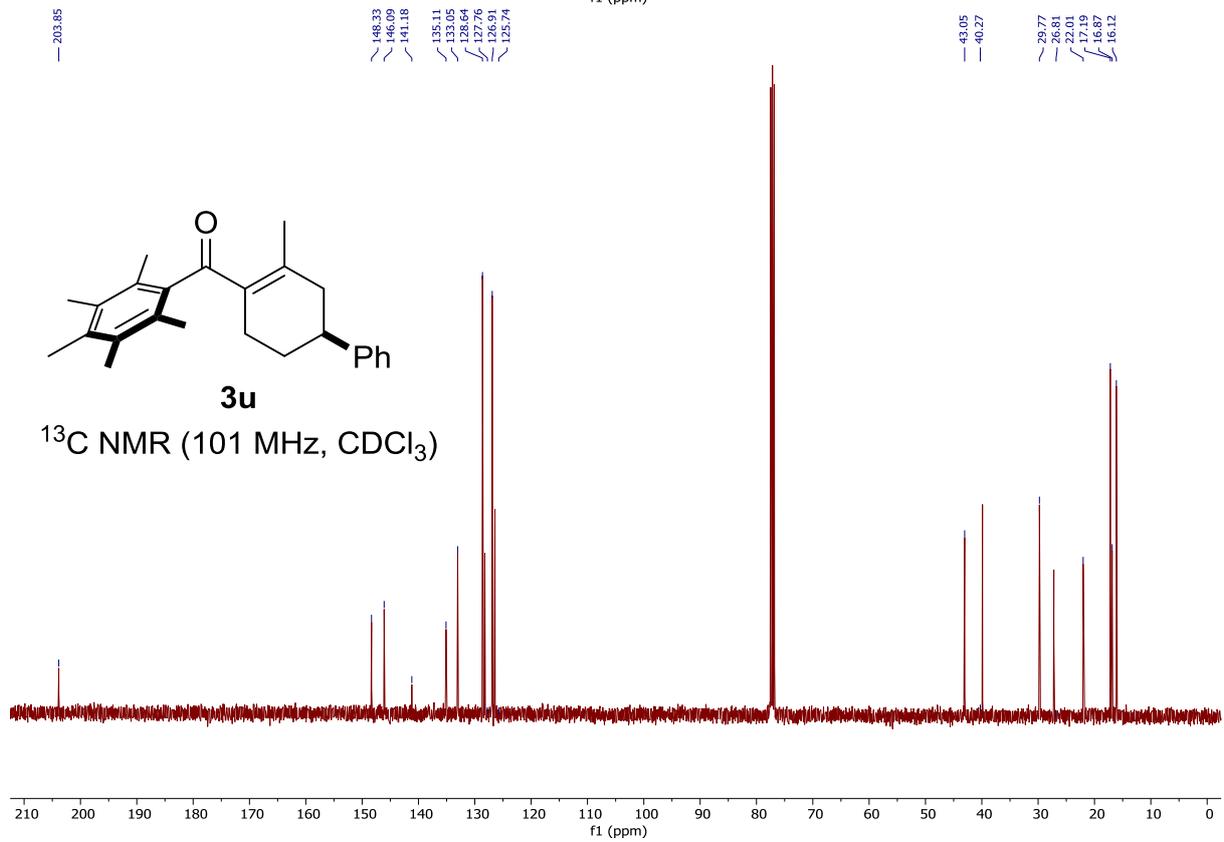
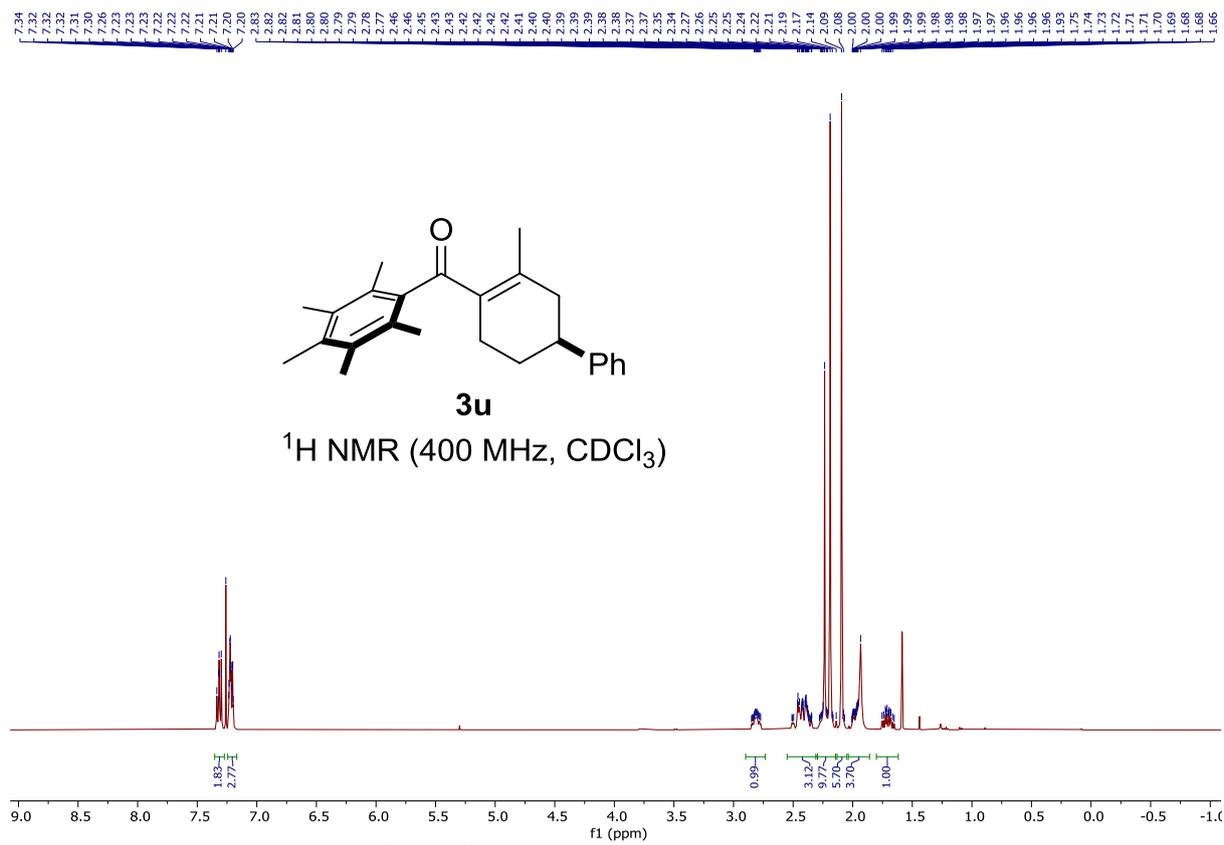


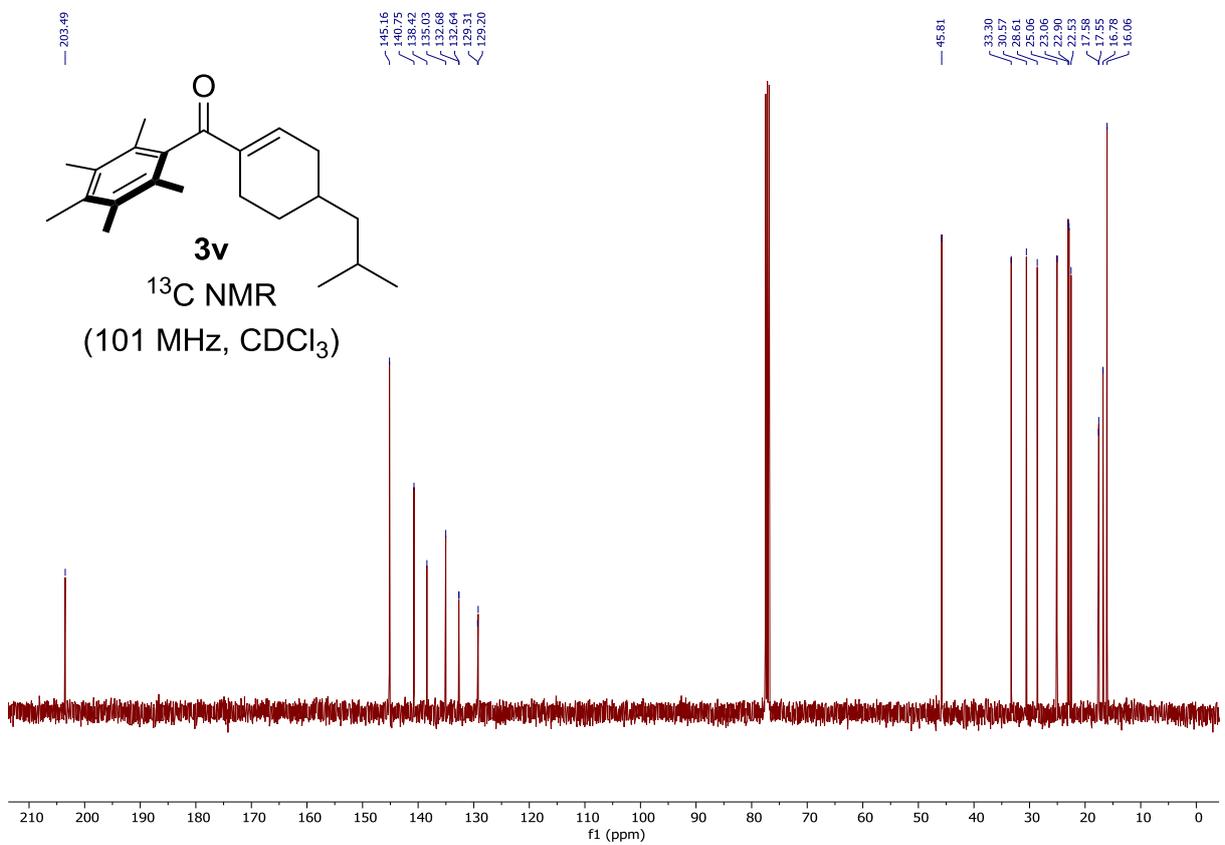
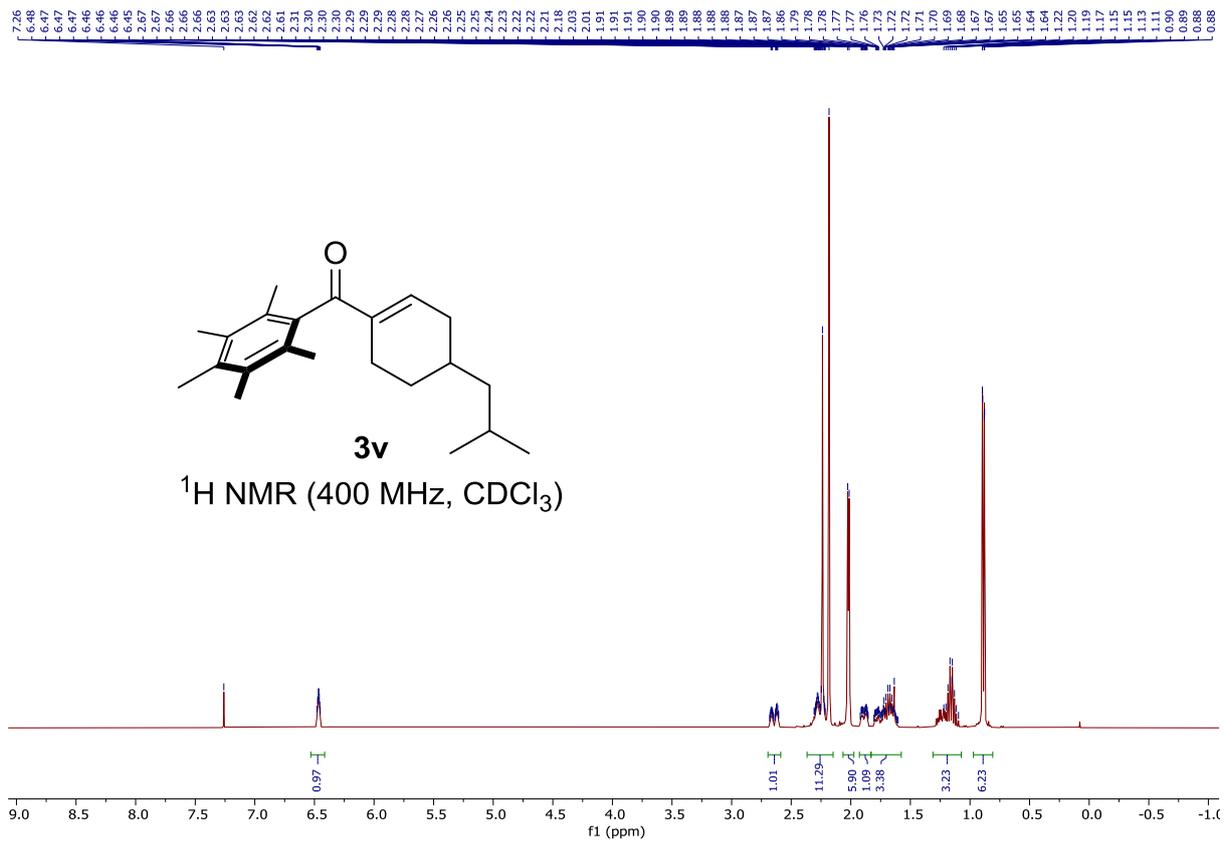


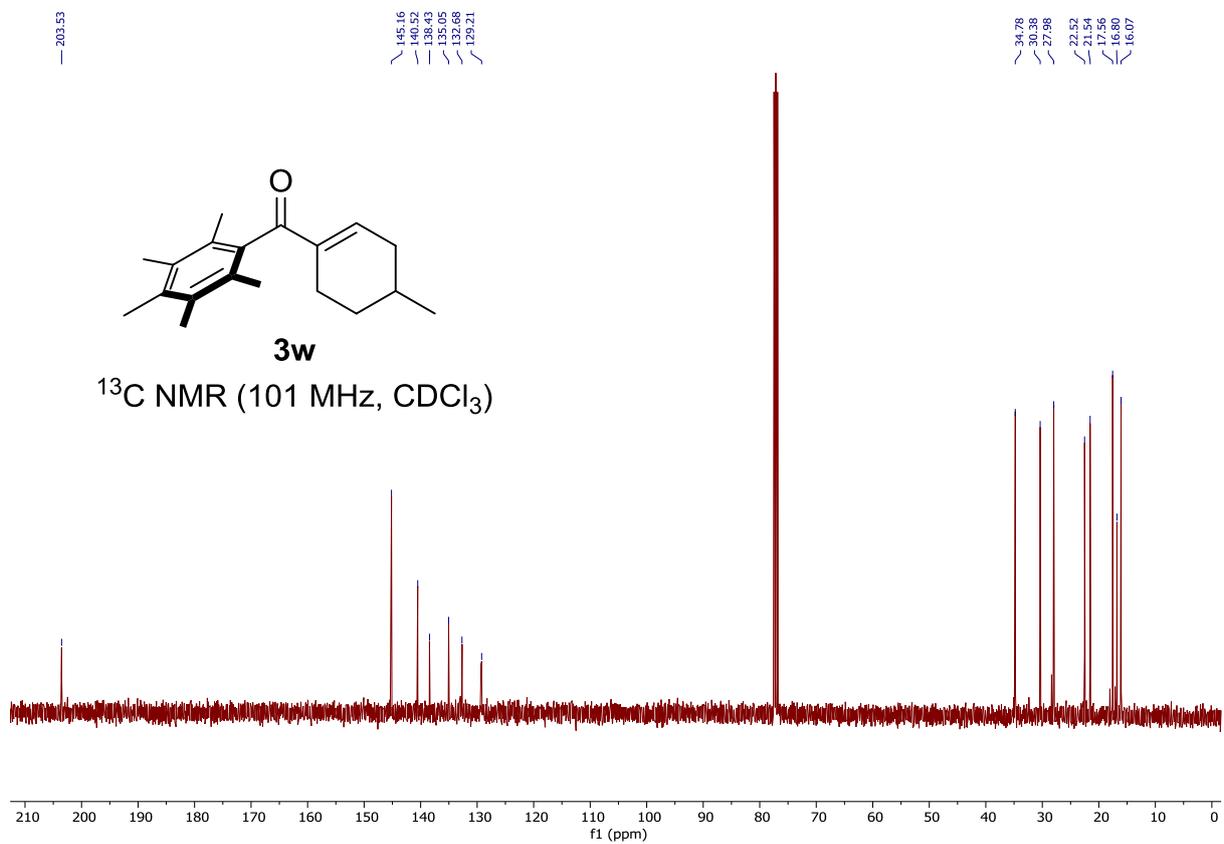
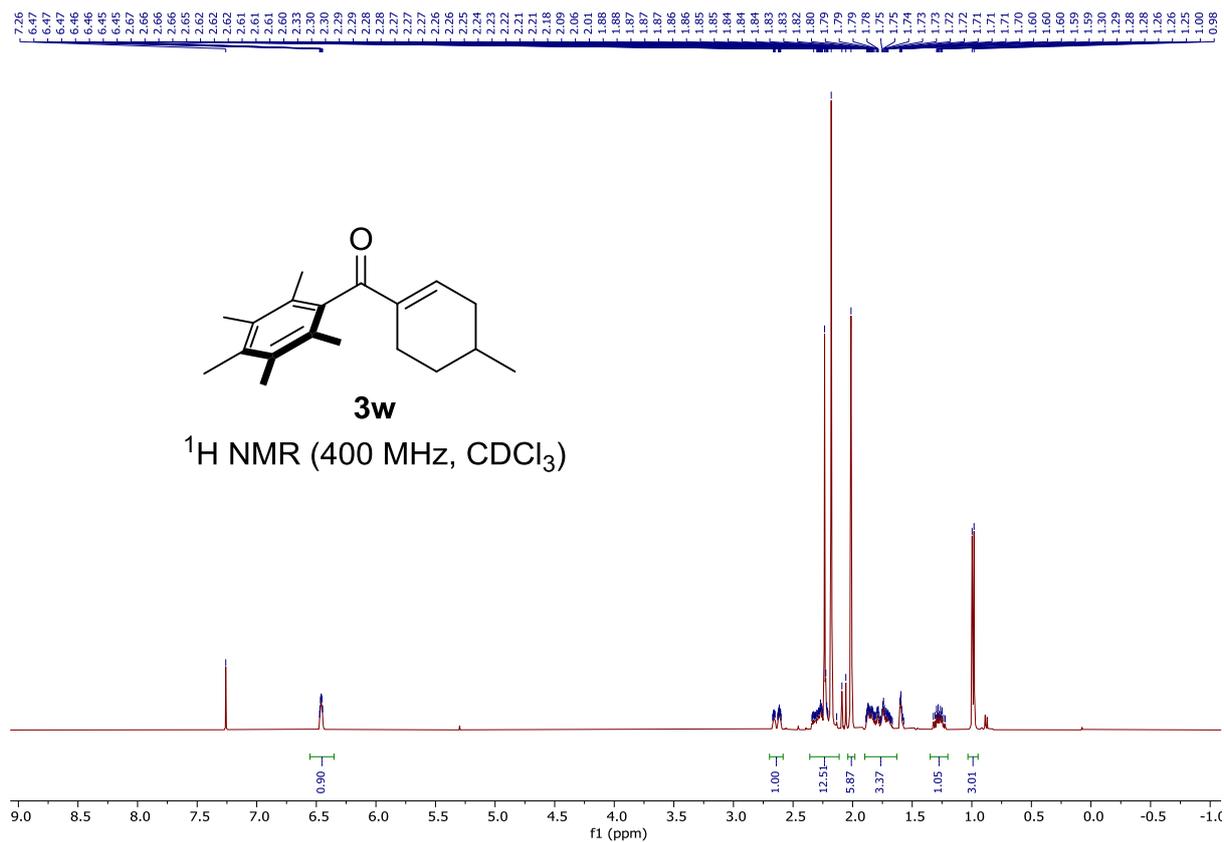


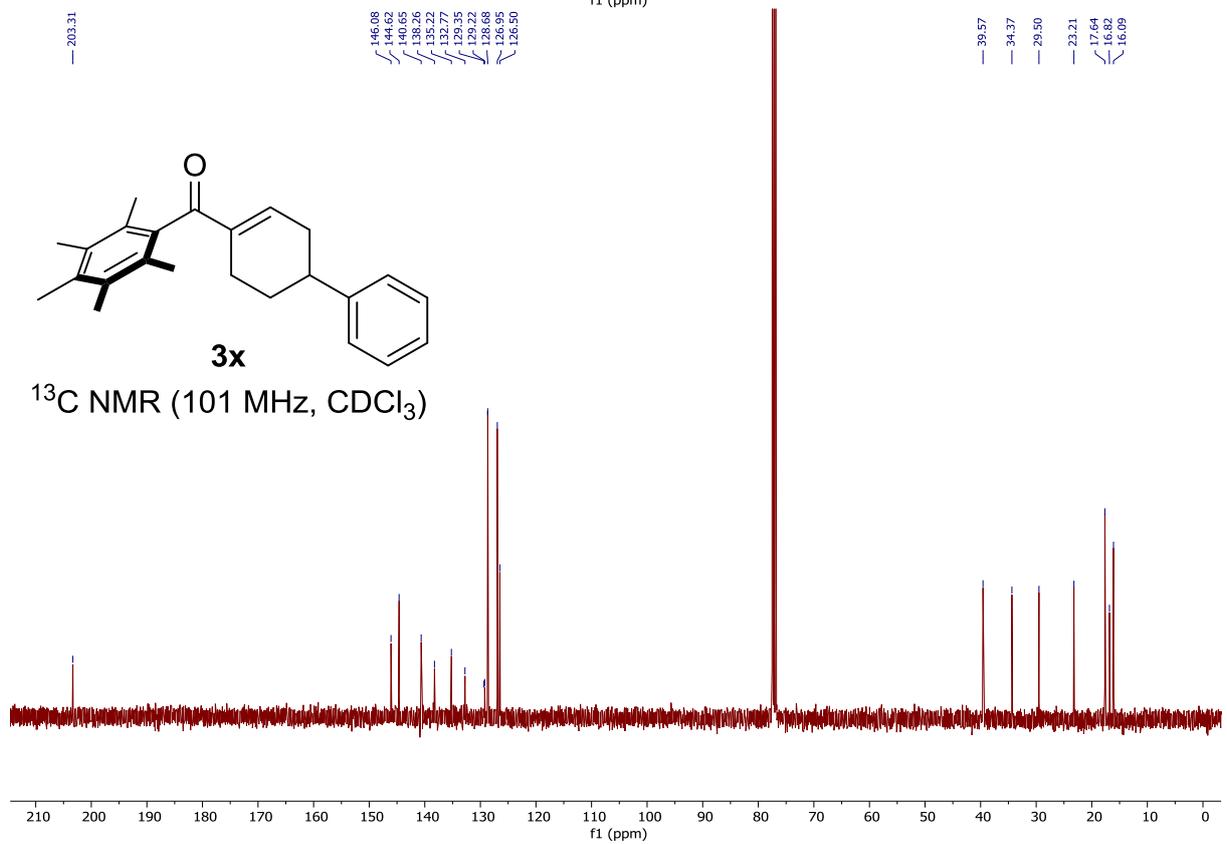
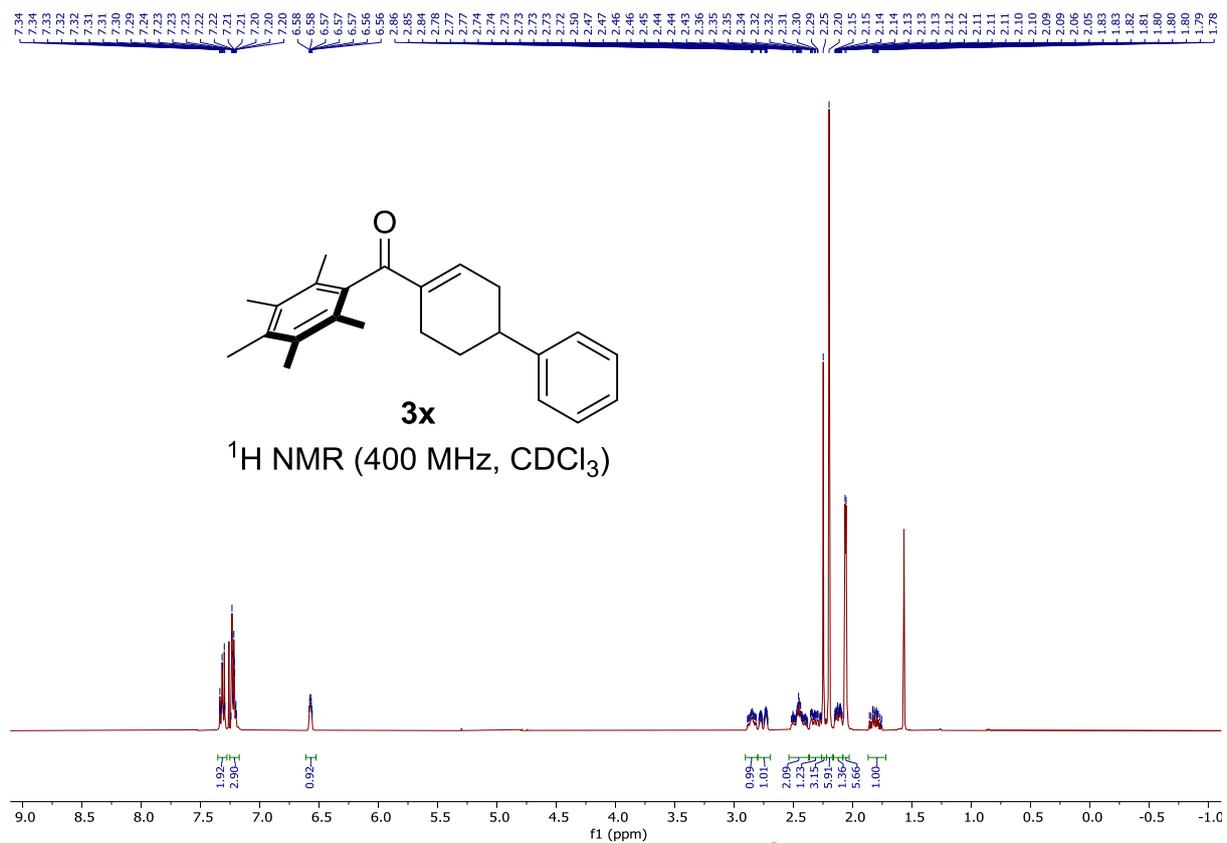


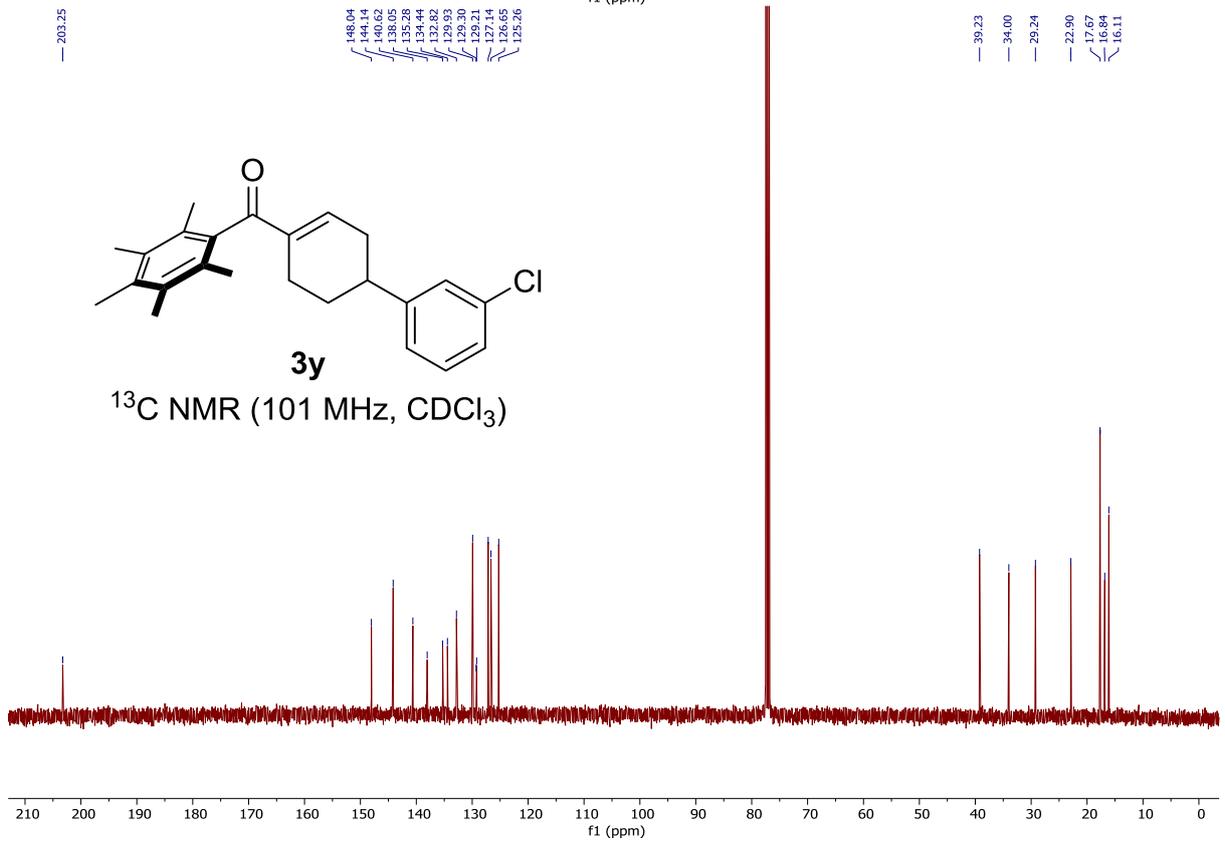
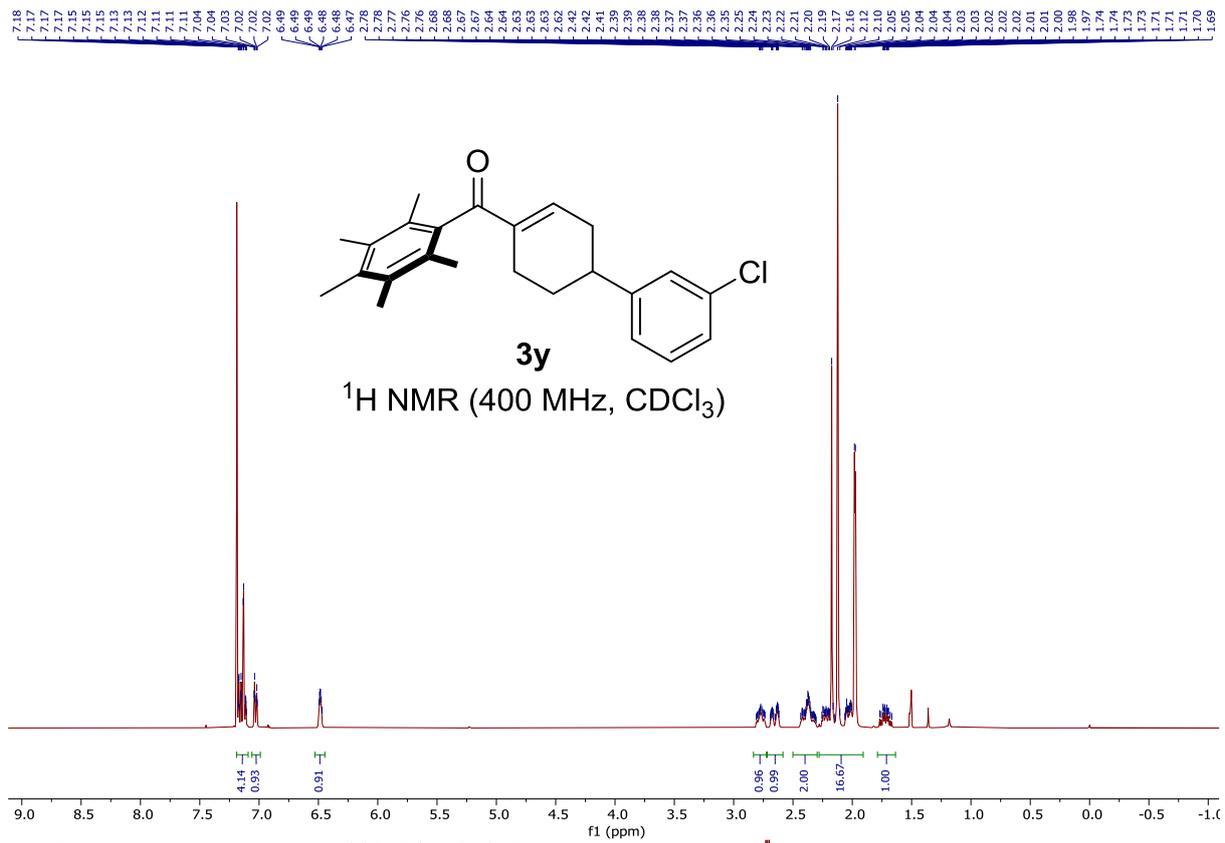


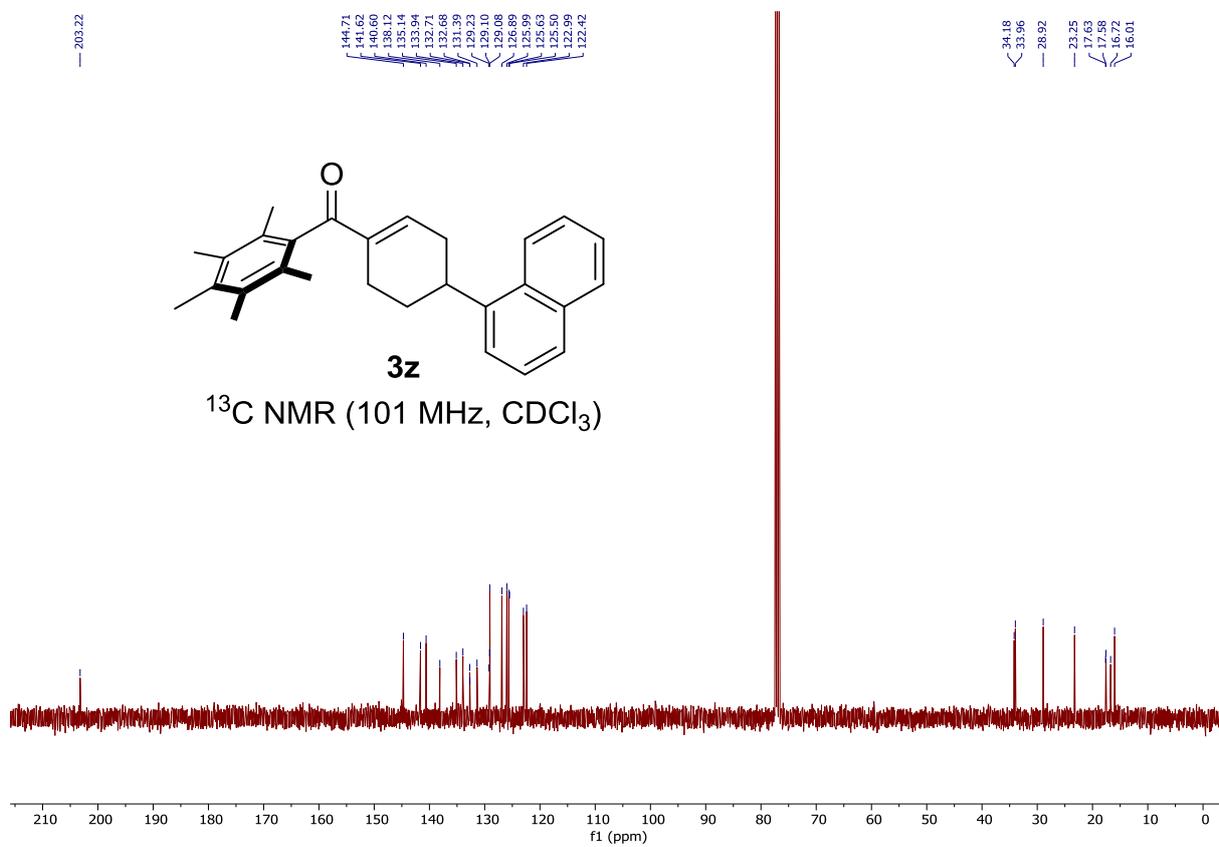
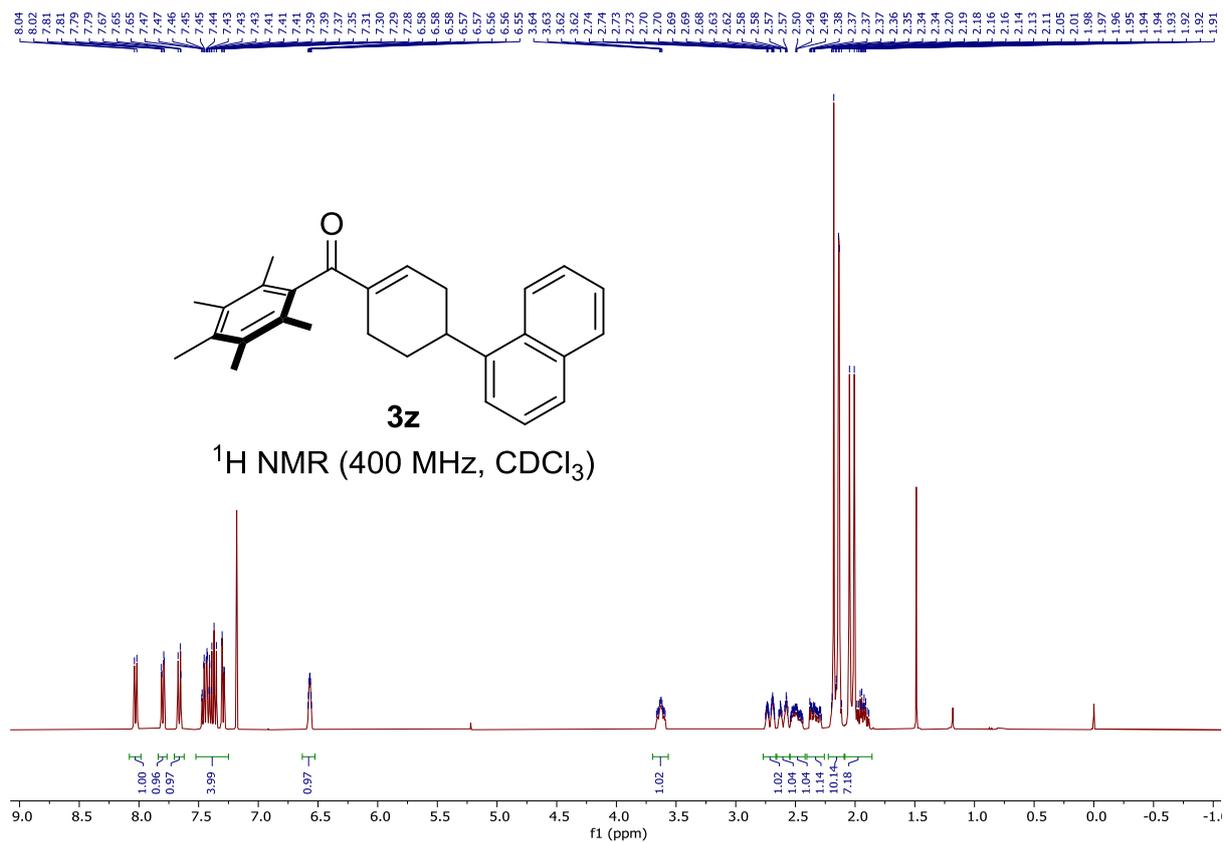


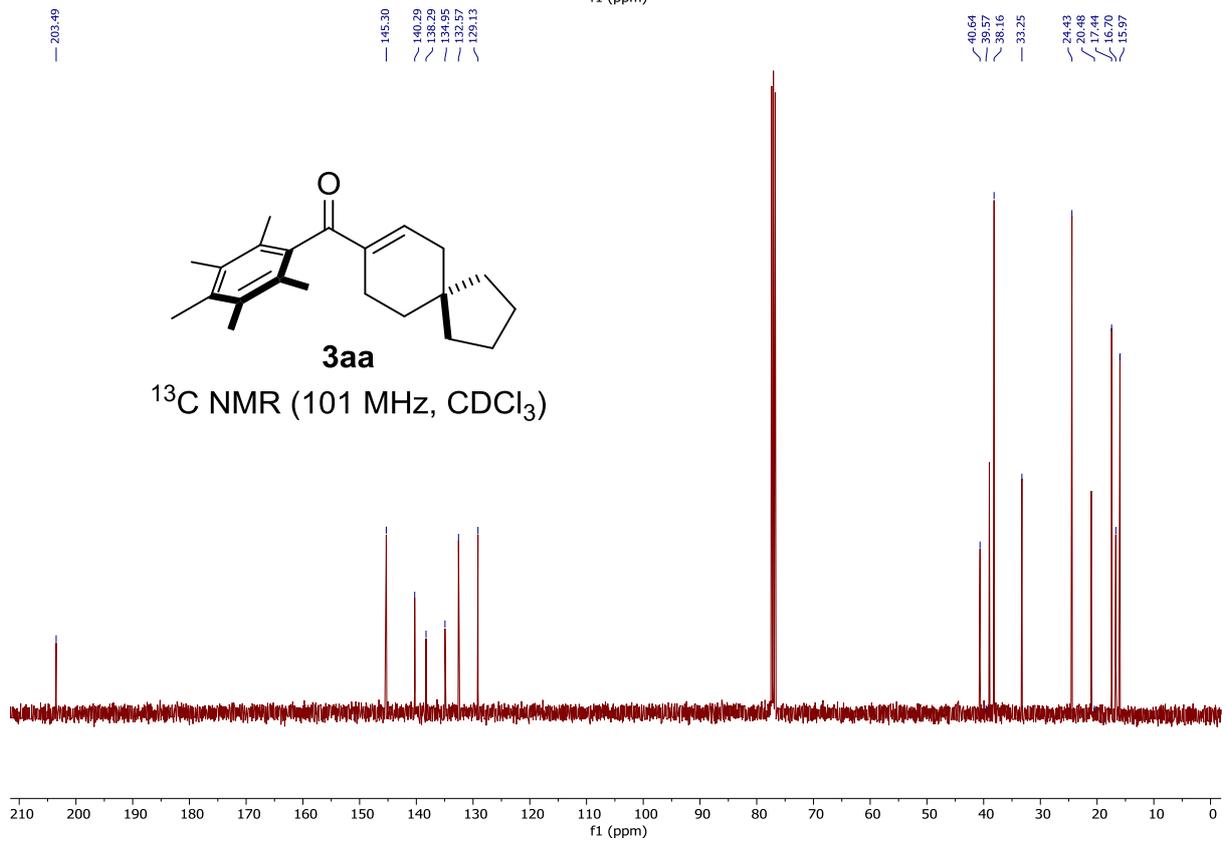
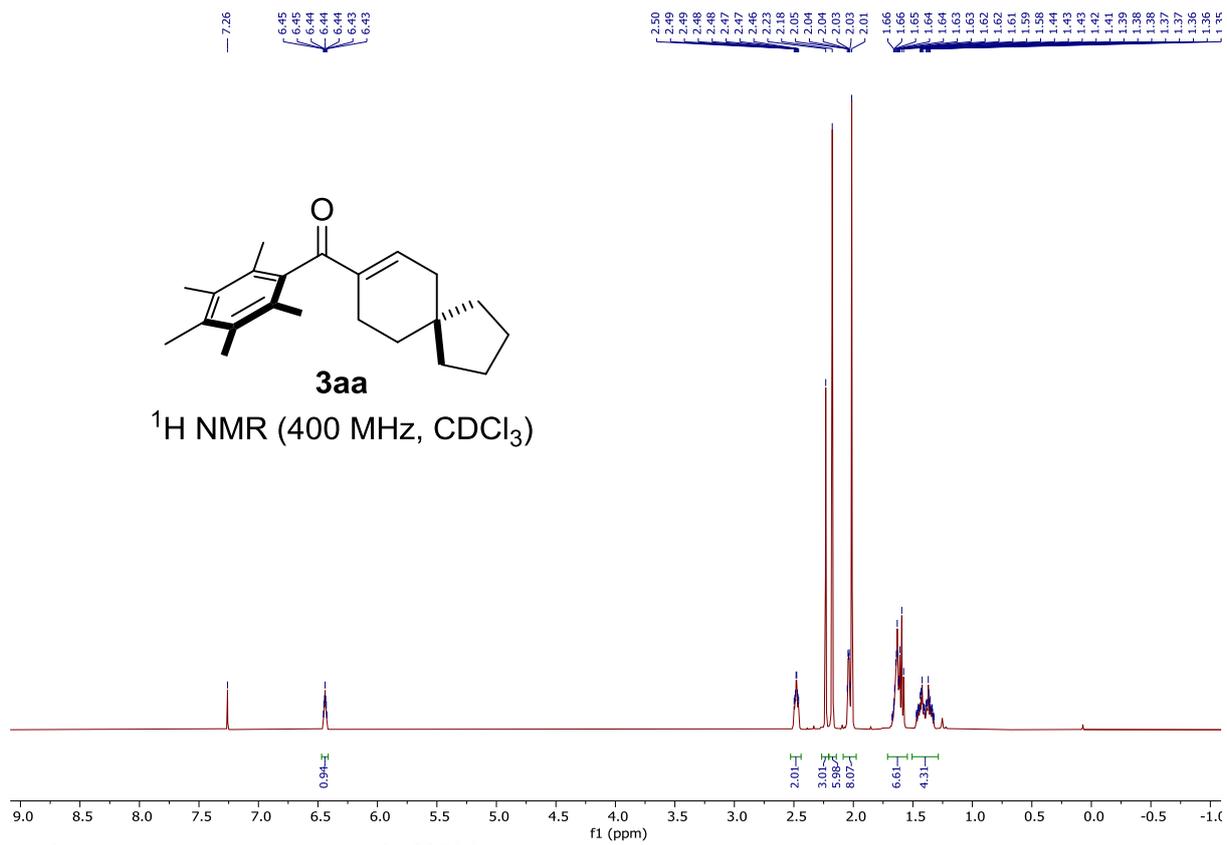


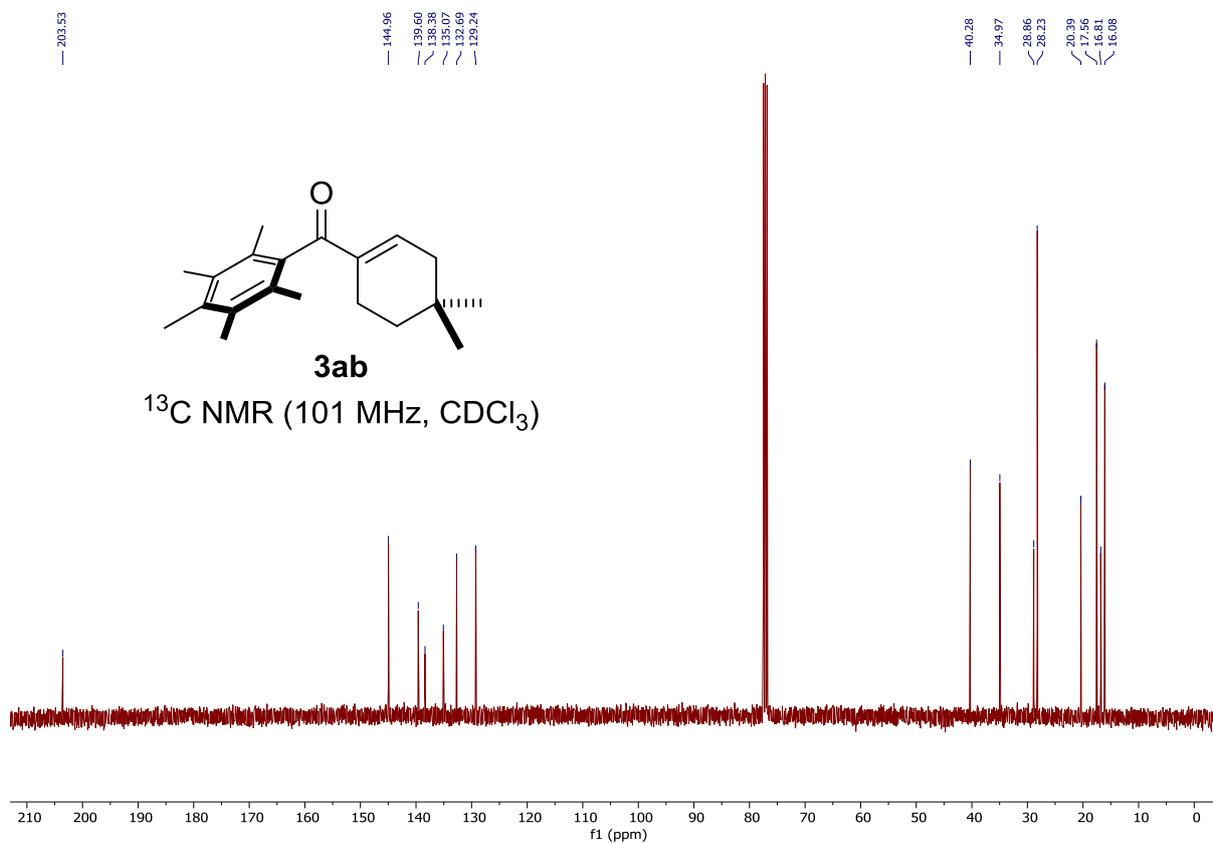
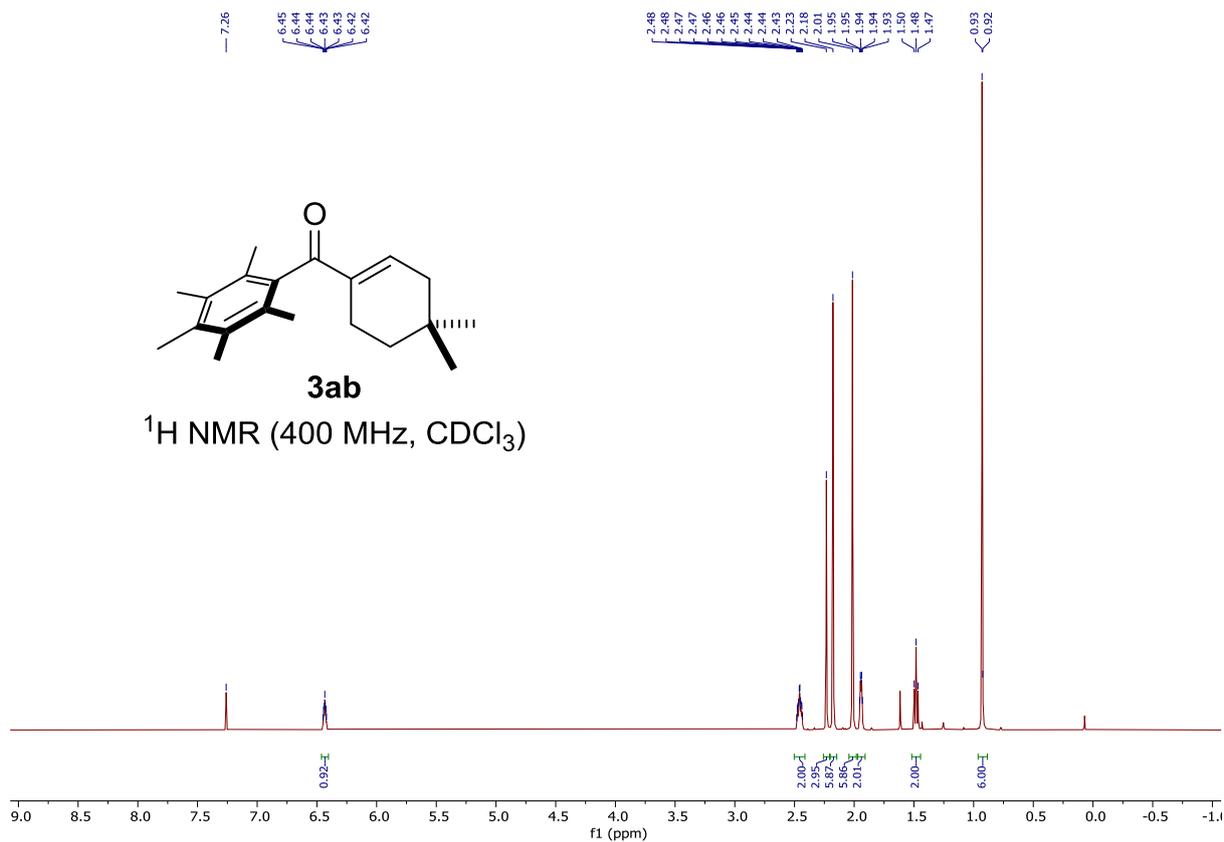


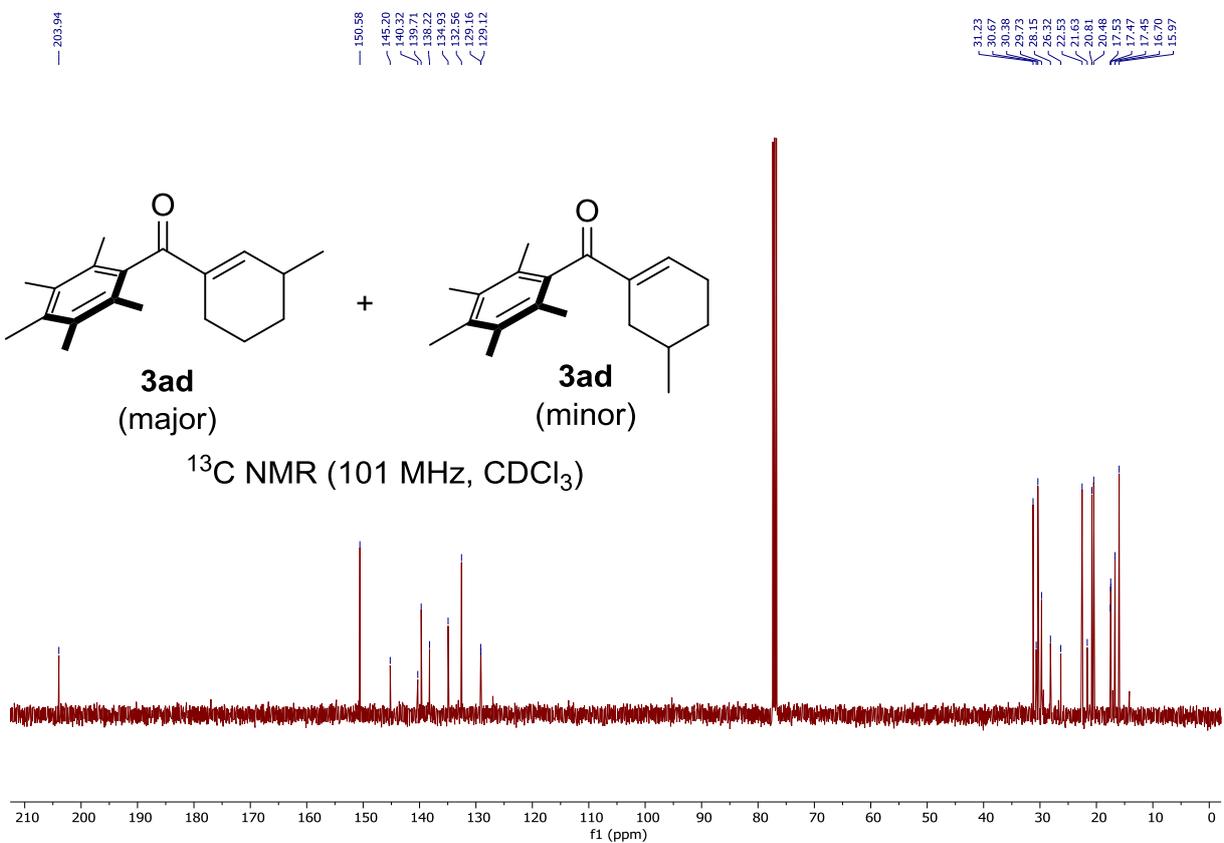
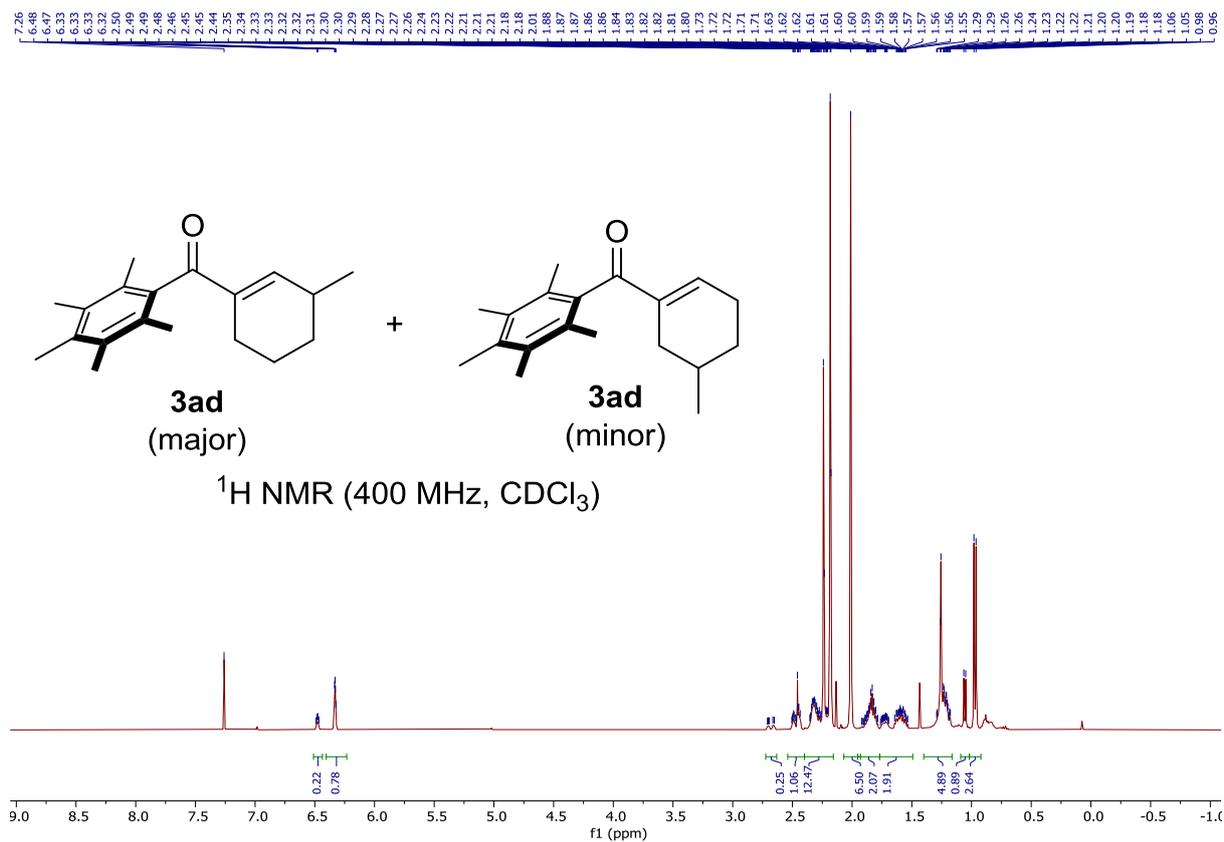




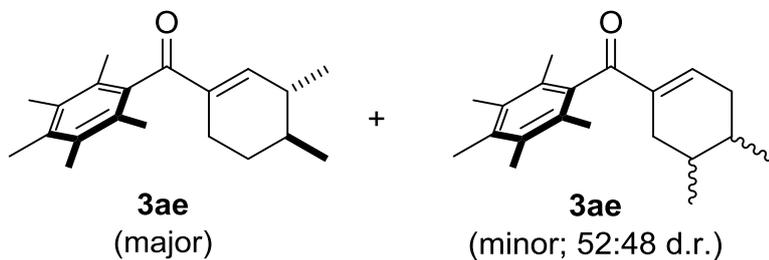




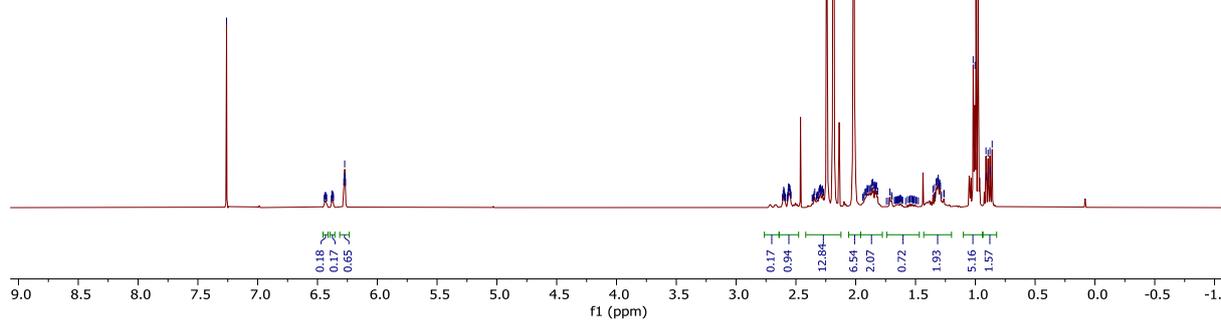




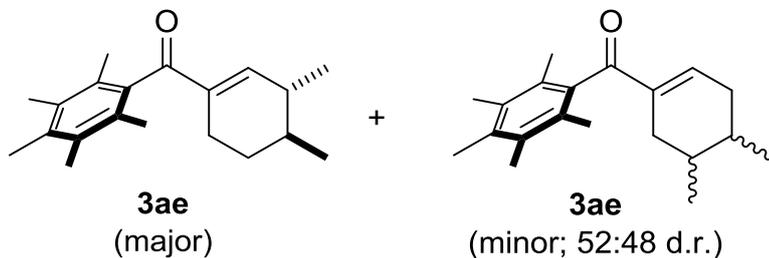
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1.31
1.31
1.30
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0.98
0.91
0.89
0.88
0.86



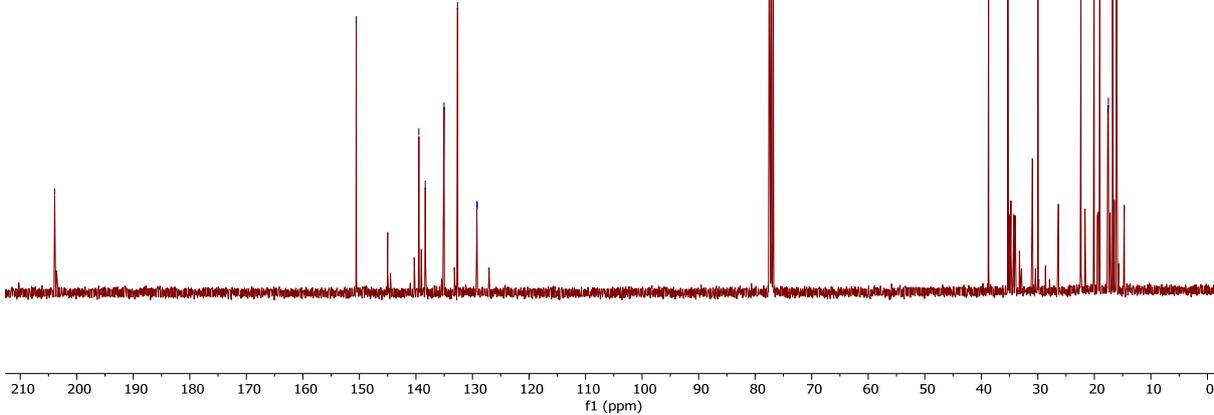
$^1\text{H NMR}$ (400 MHz, CDCl_3)

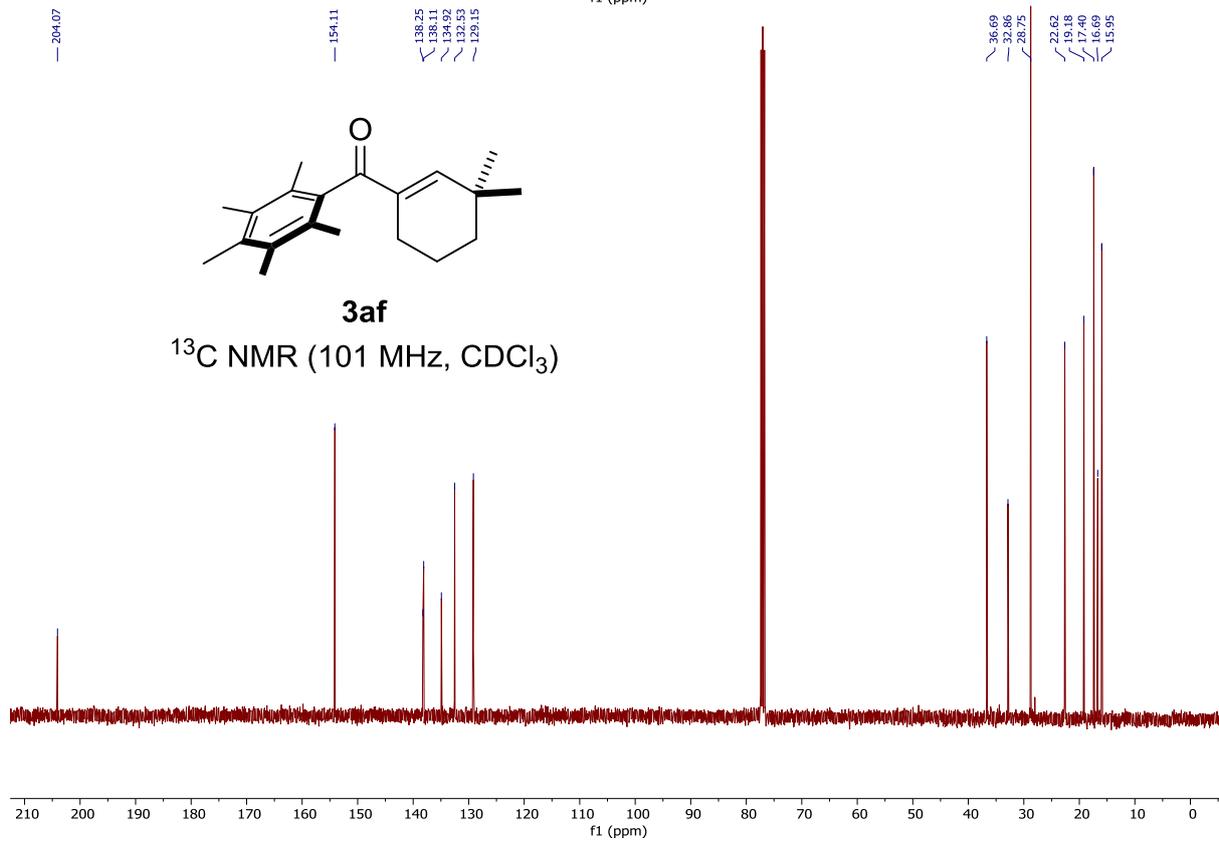
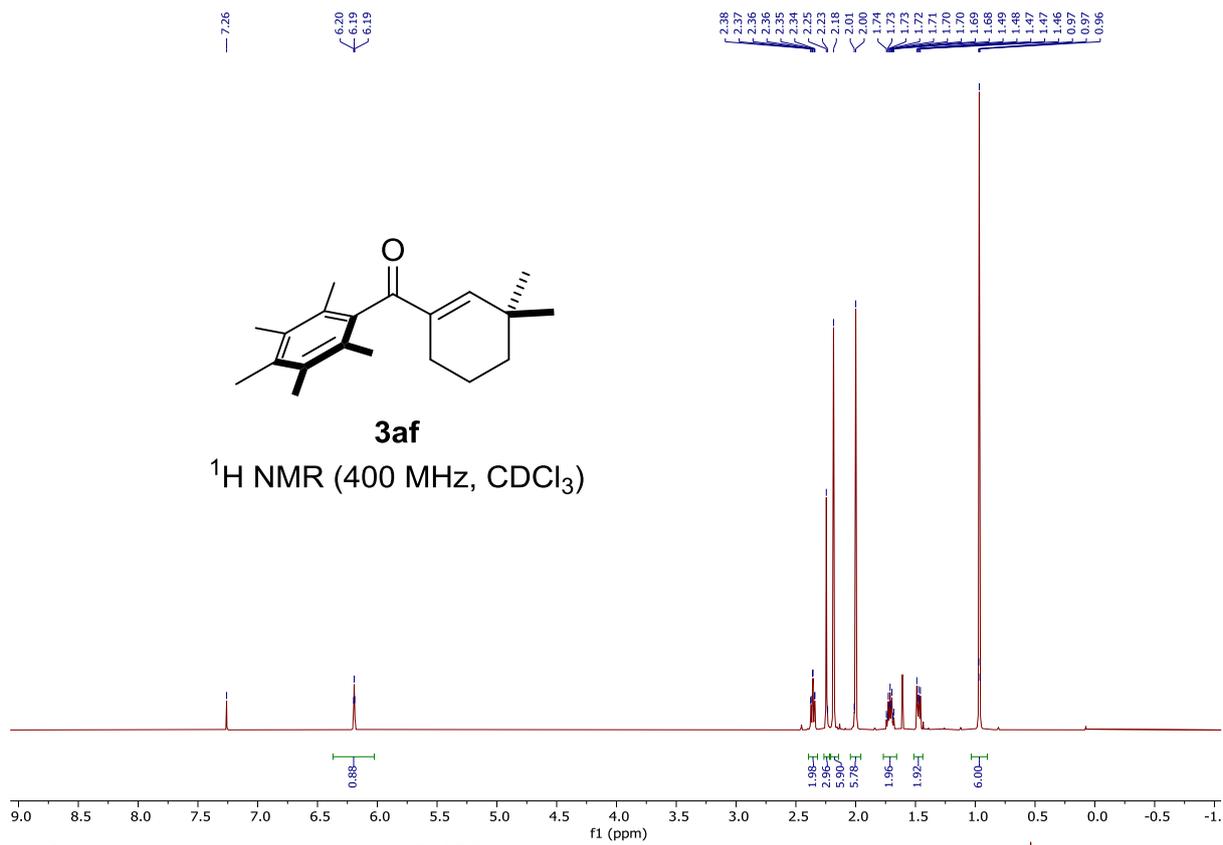


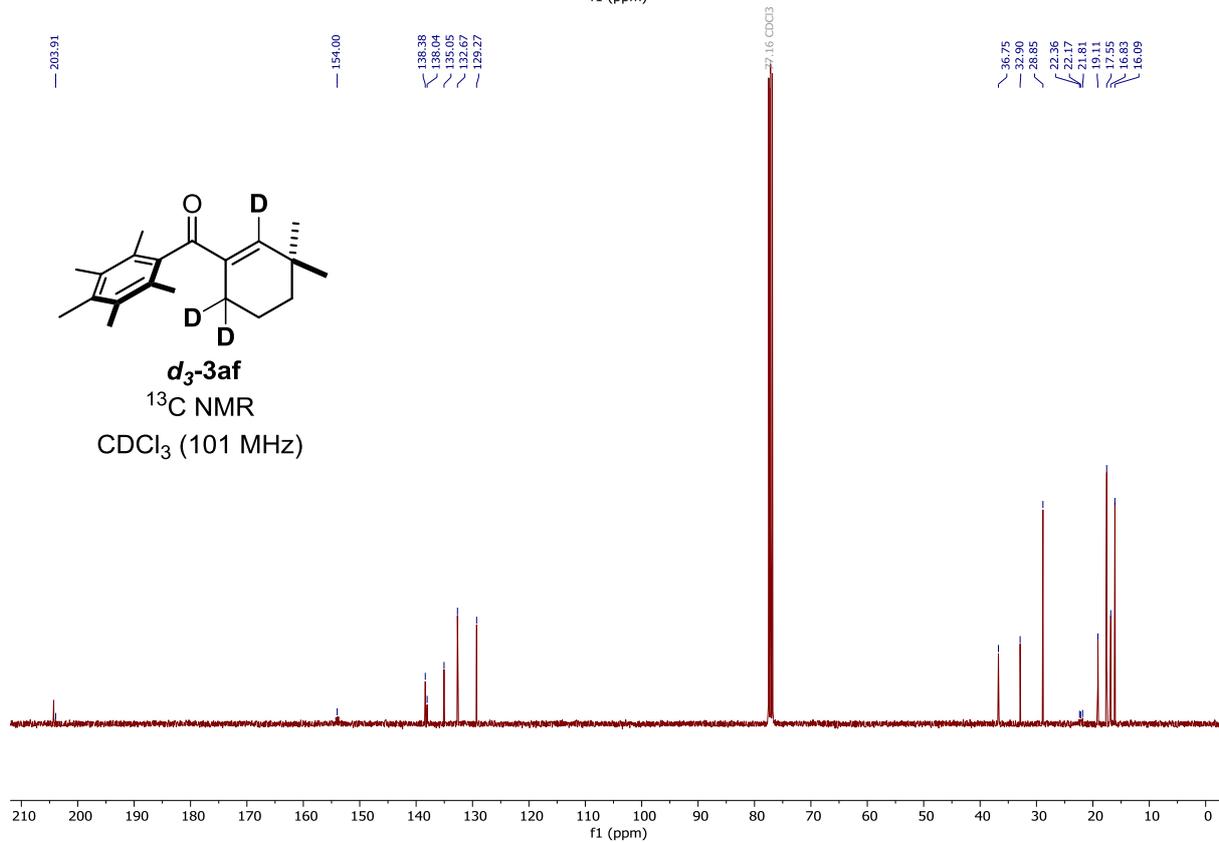
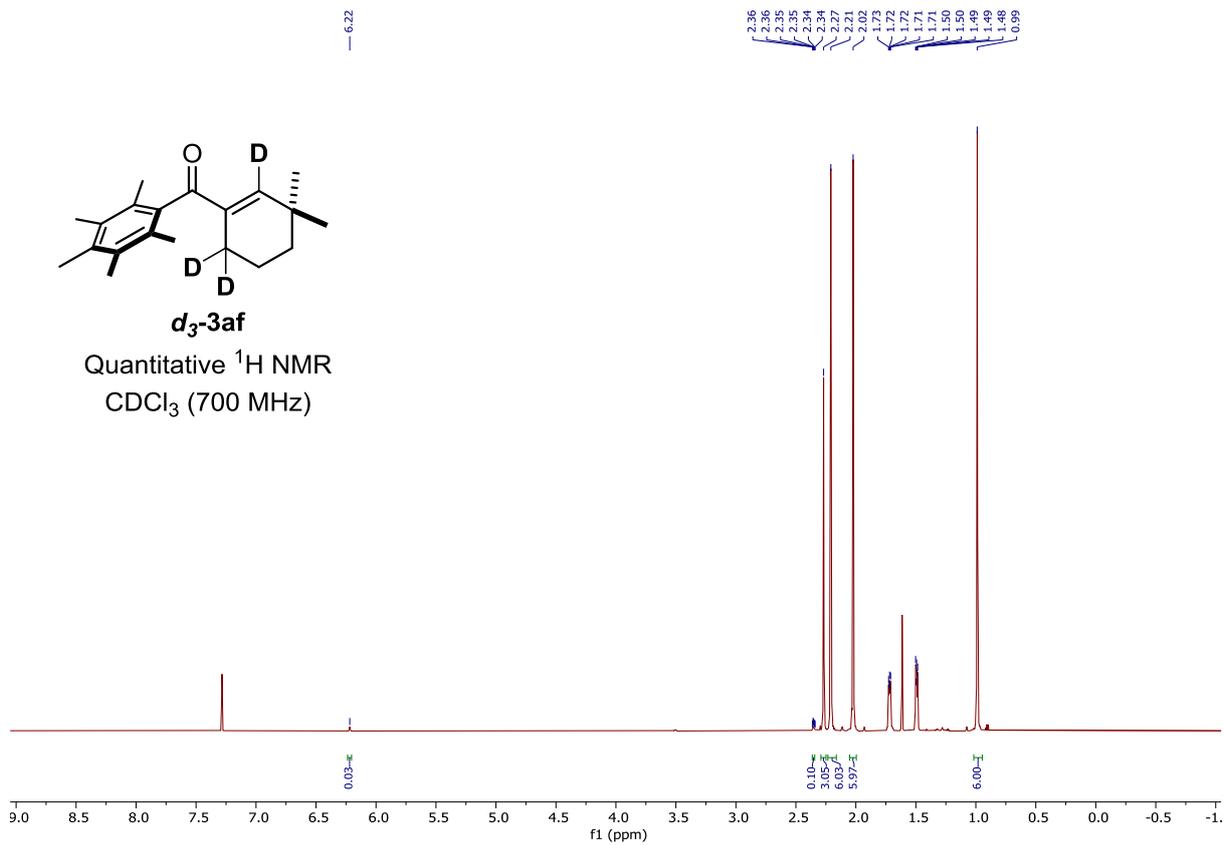
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150.55
139.48
138.35
135.02
132.65
129.74
123.15
38.72
35.30
29.98
22.38
20.06
19.04
17.63
17.52
16.79
16.06

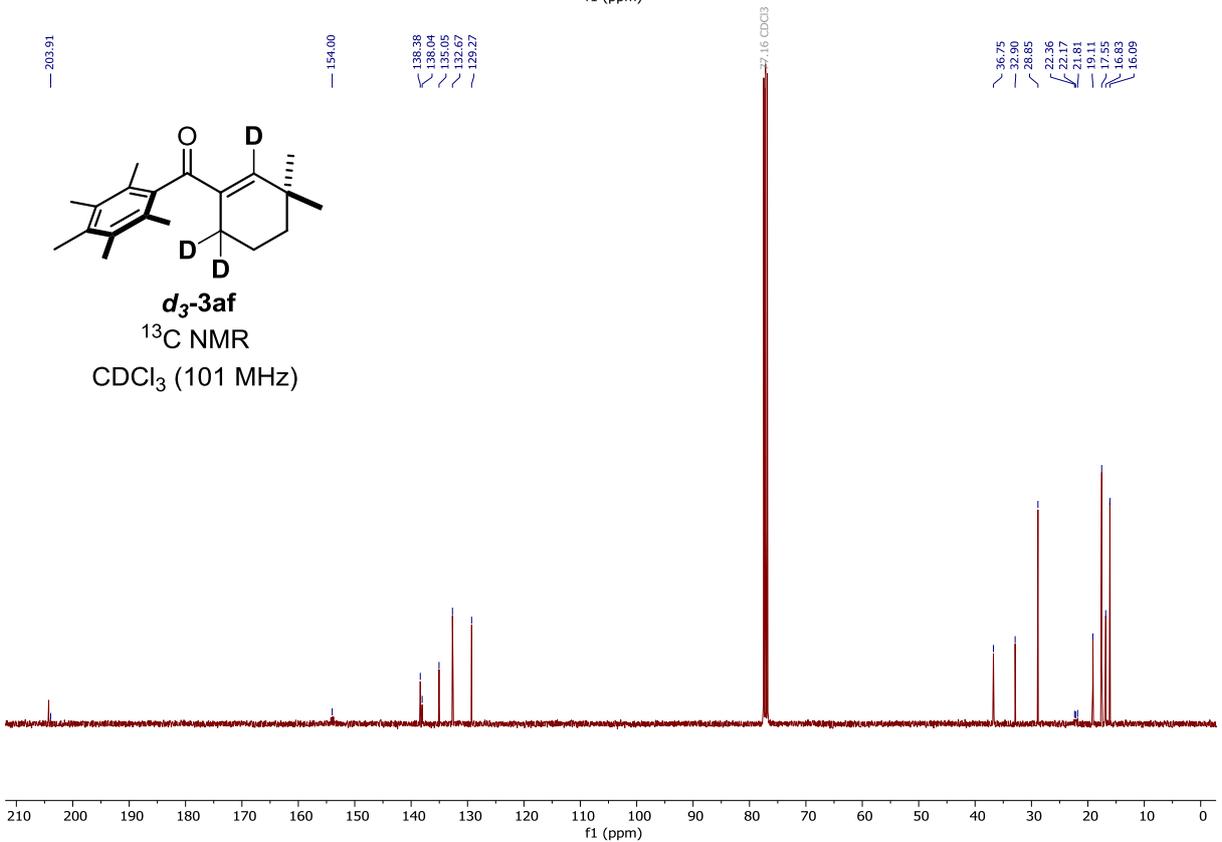
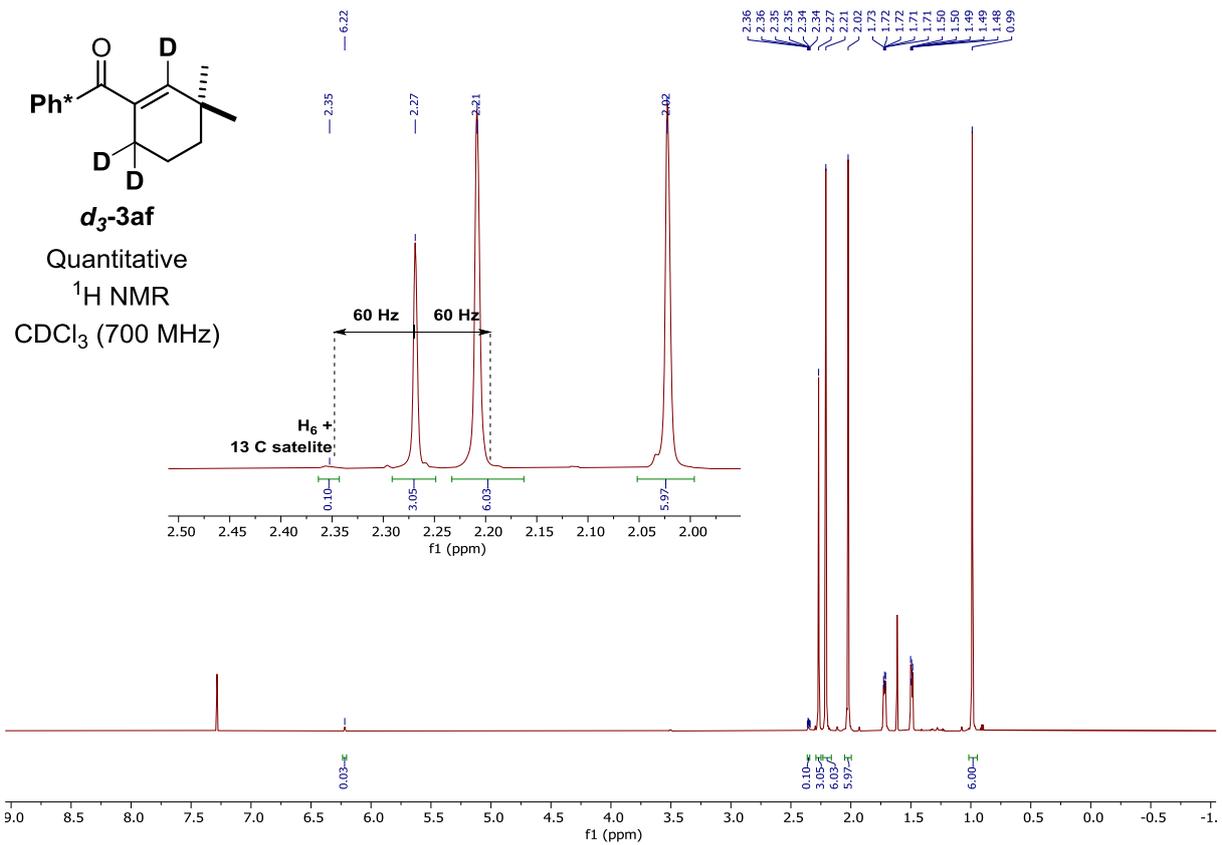


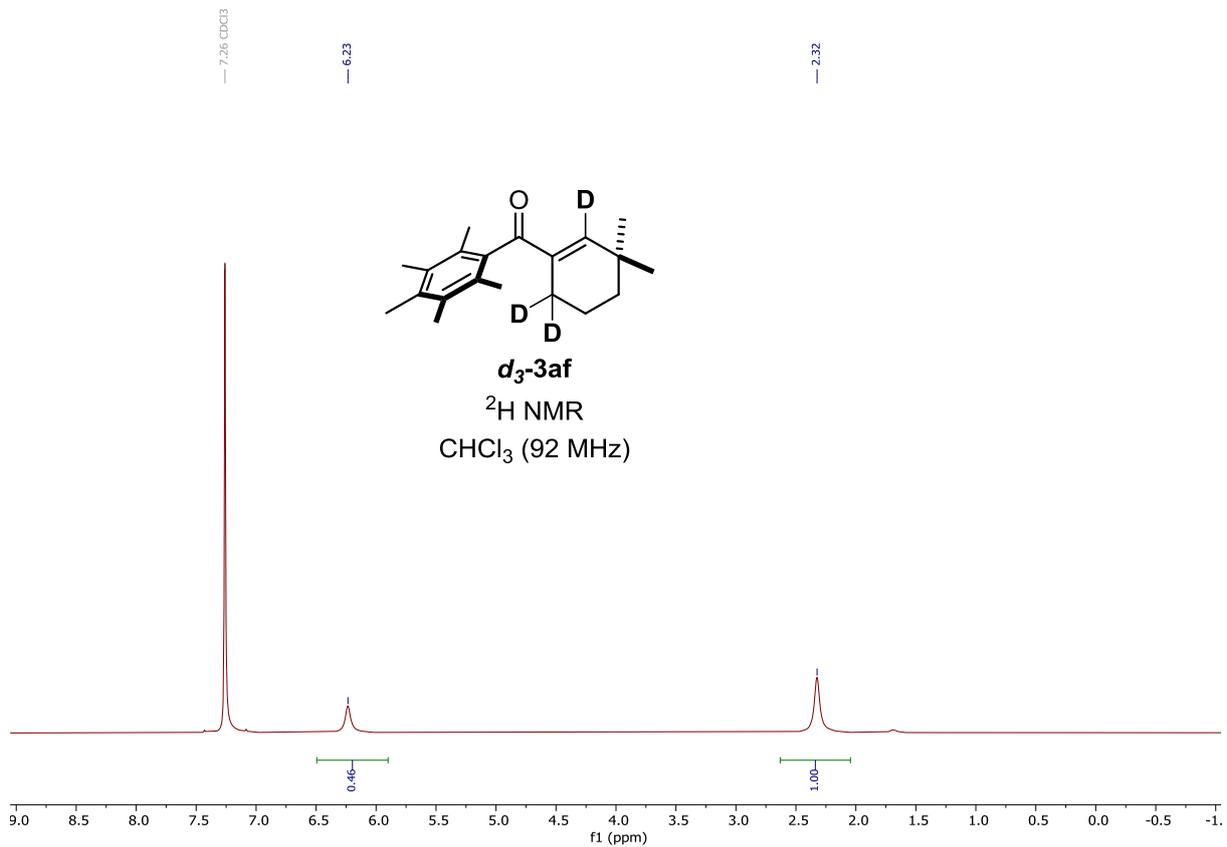
$^{13}\text{C NMR}$ (101 MHz, CDCl_3)



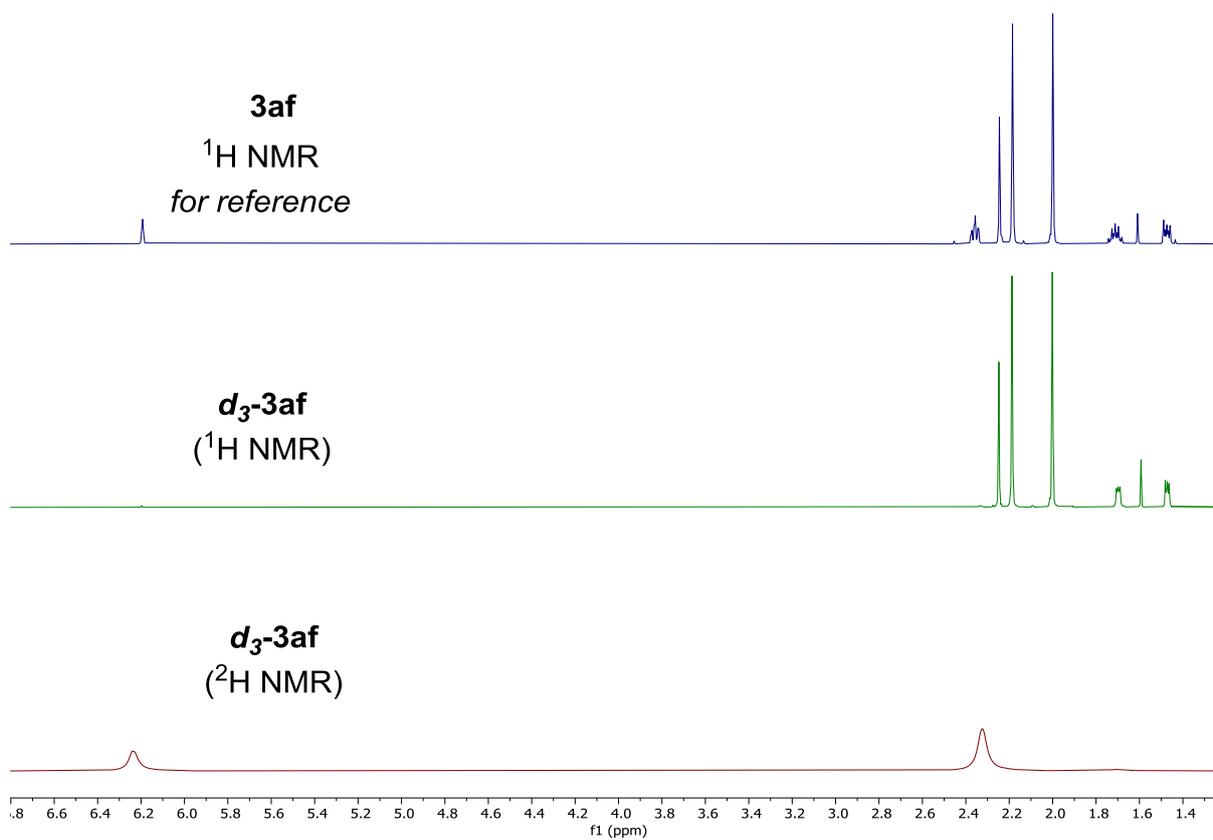


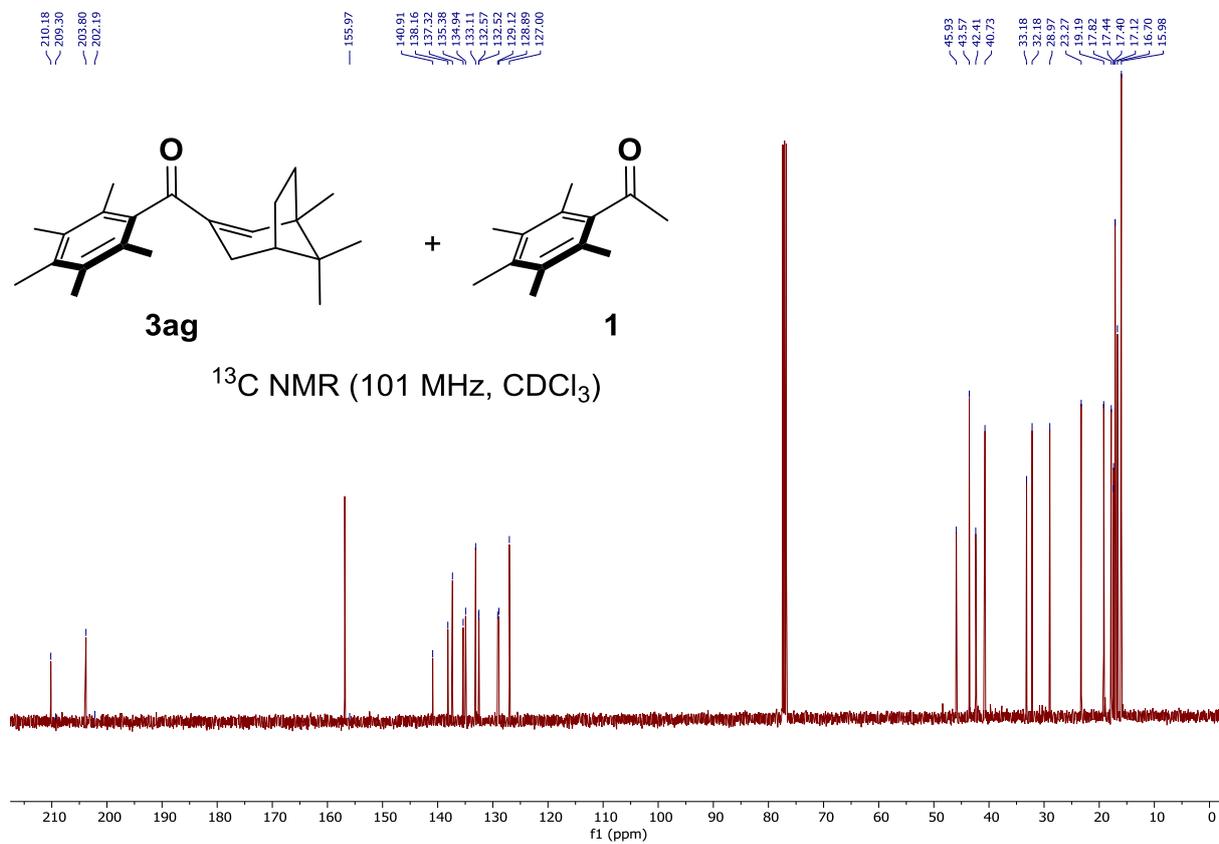
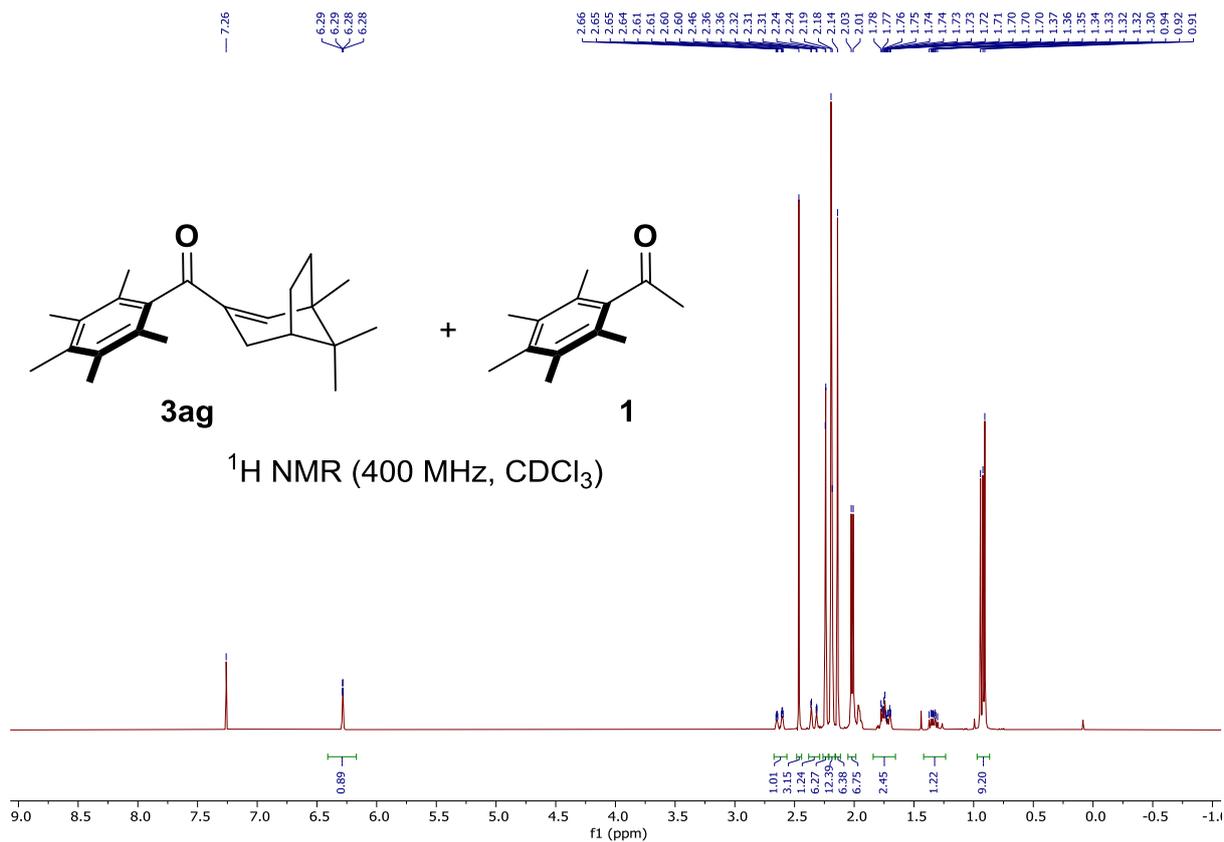


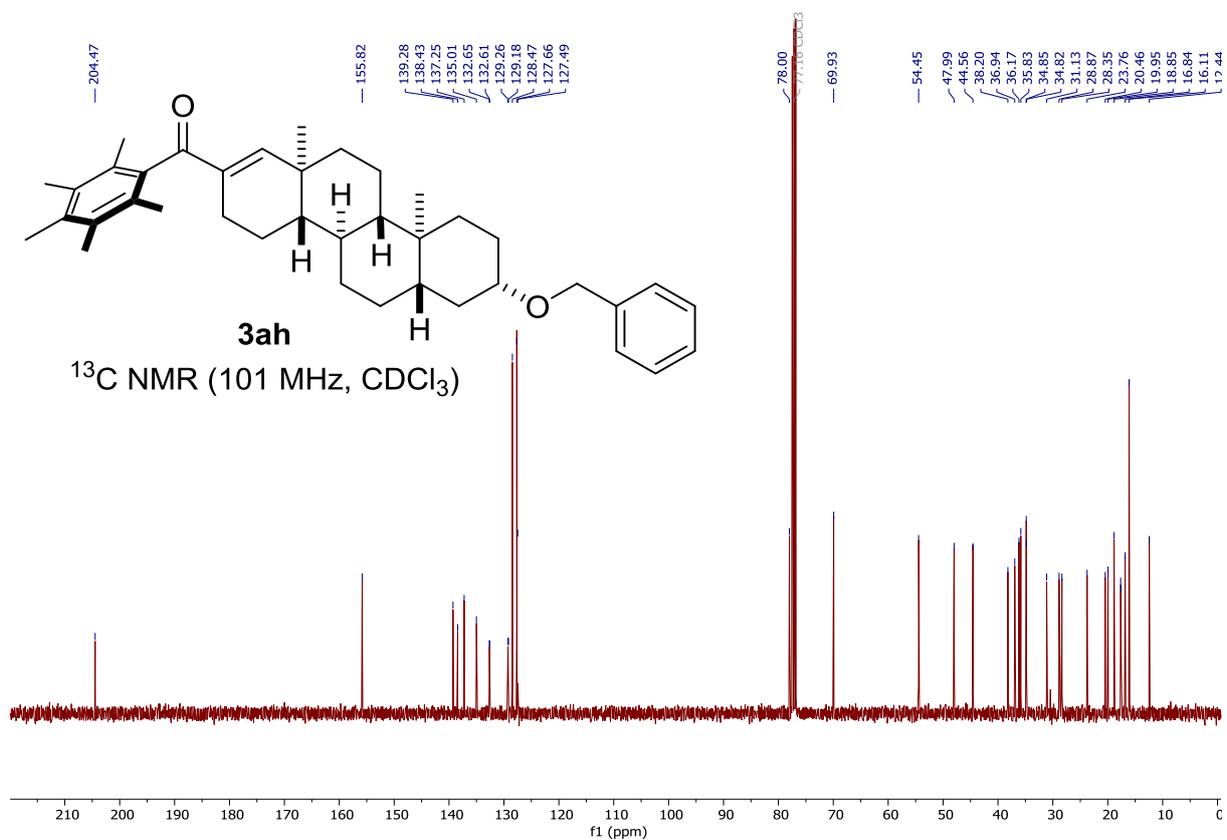
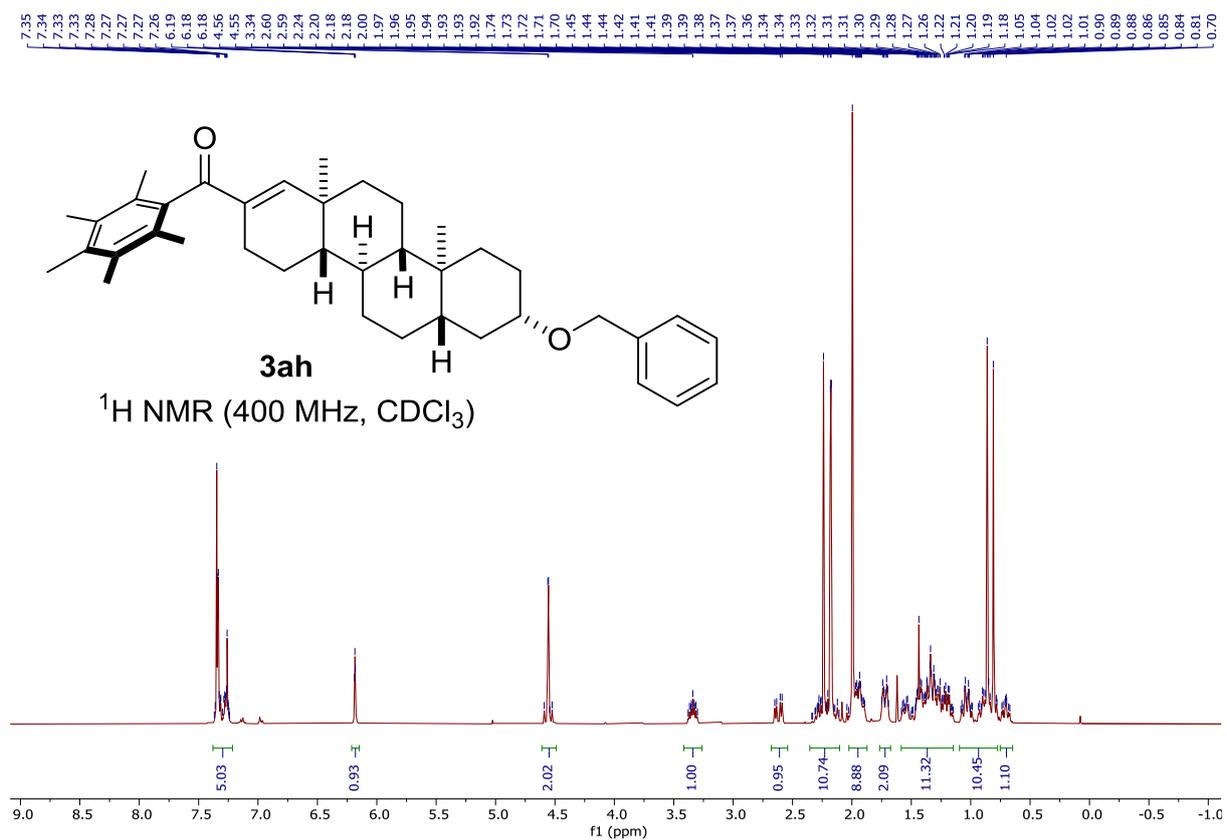


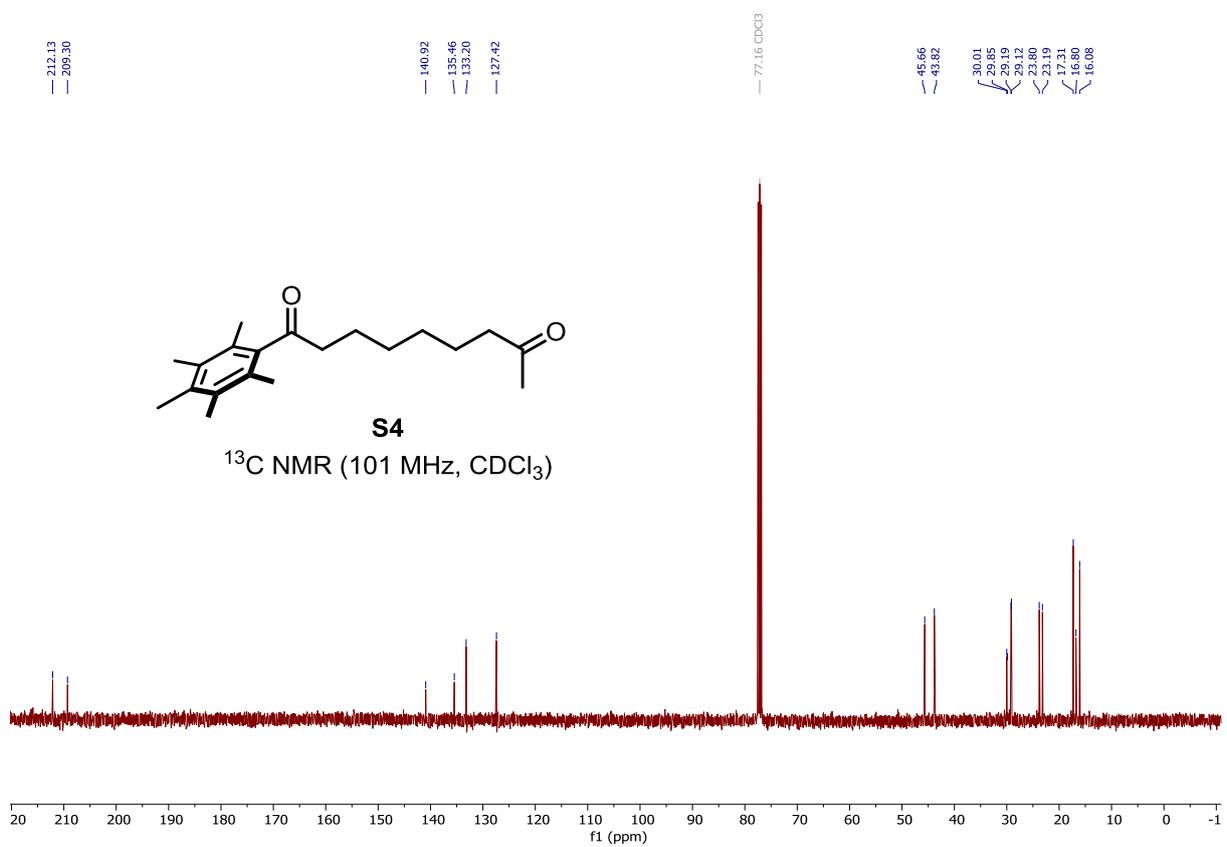
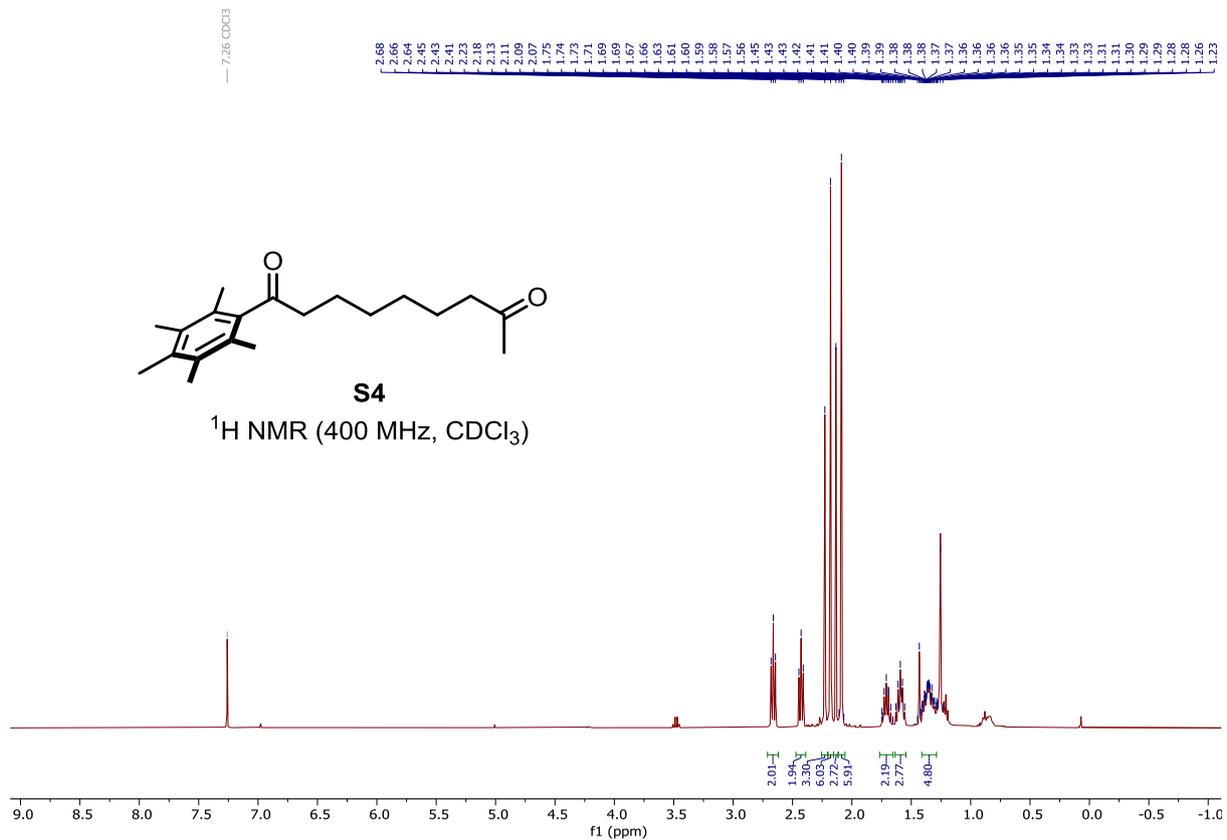


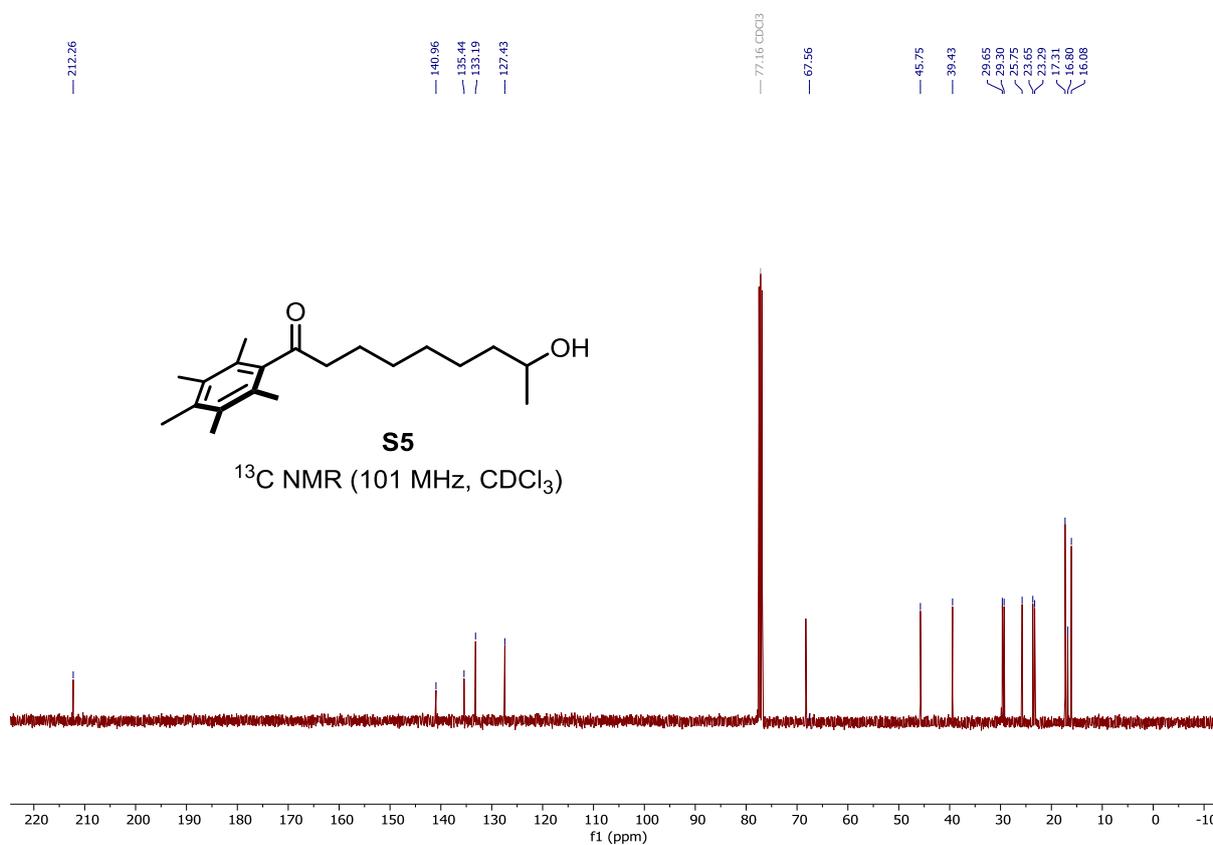
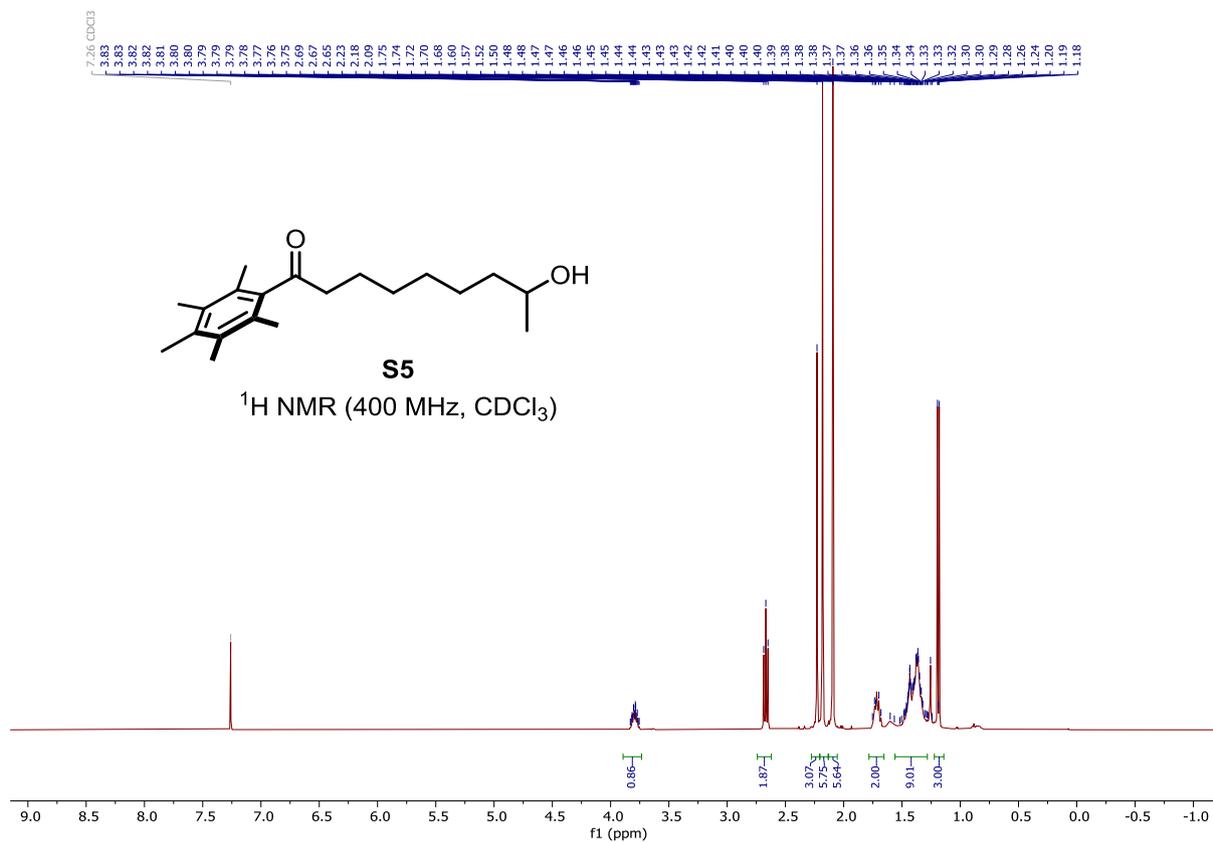
Stacked $^1\text{H NMR}$ and $^2\text{H NMR}$ Spectra for $d_3\text{-3af}$:

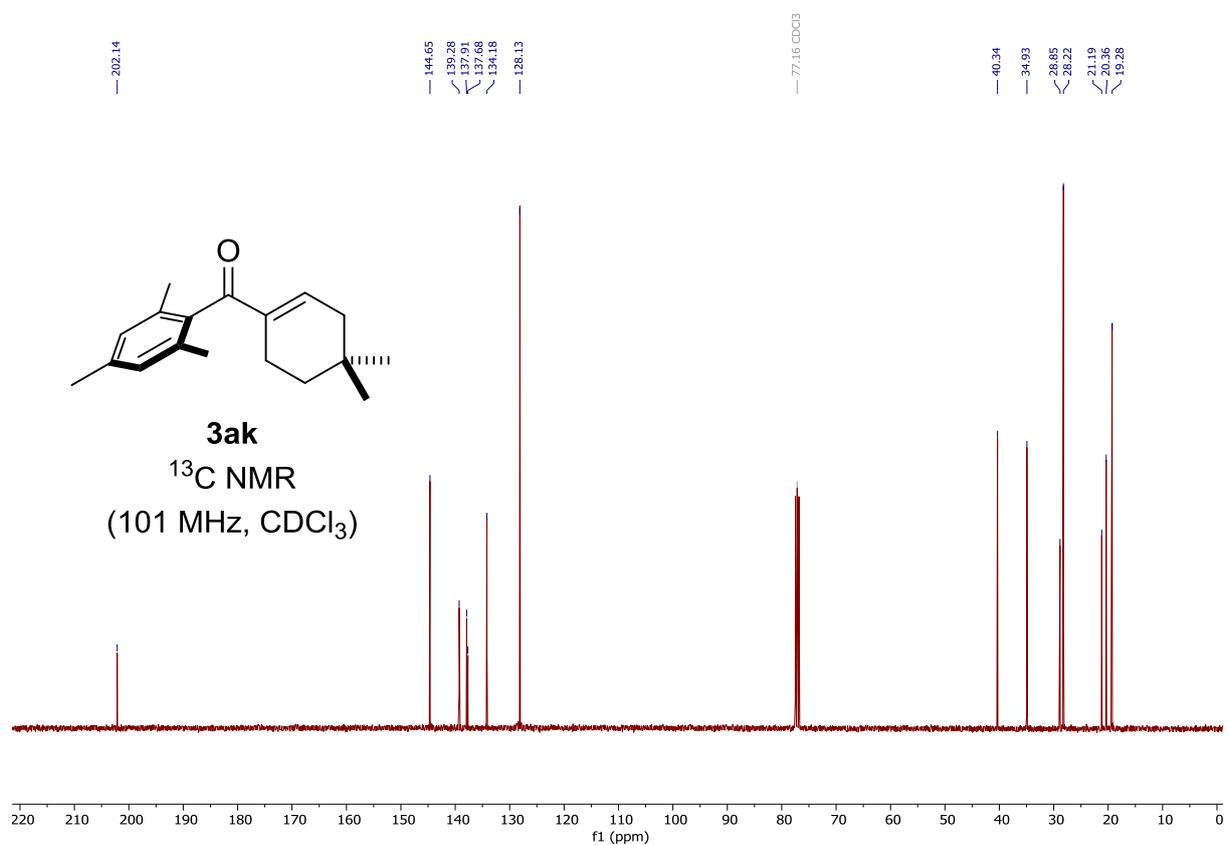
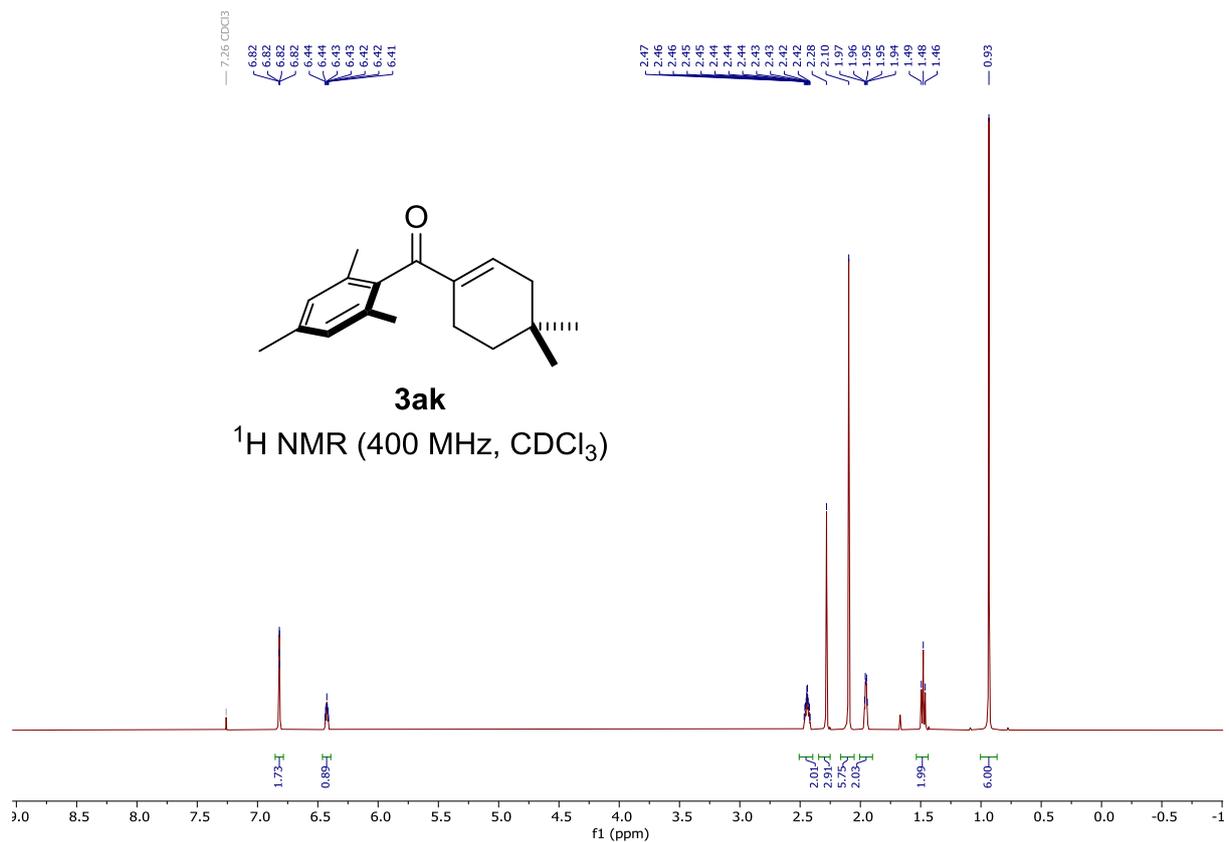


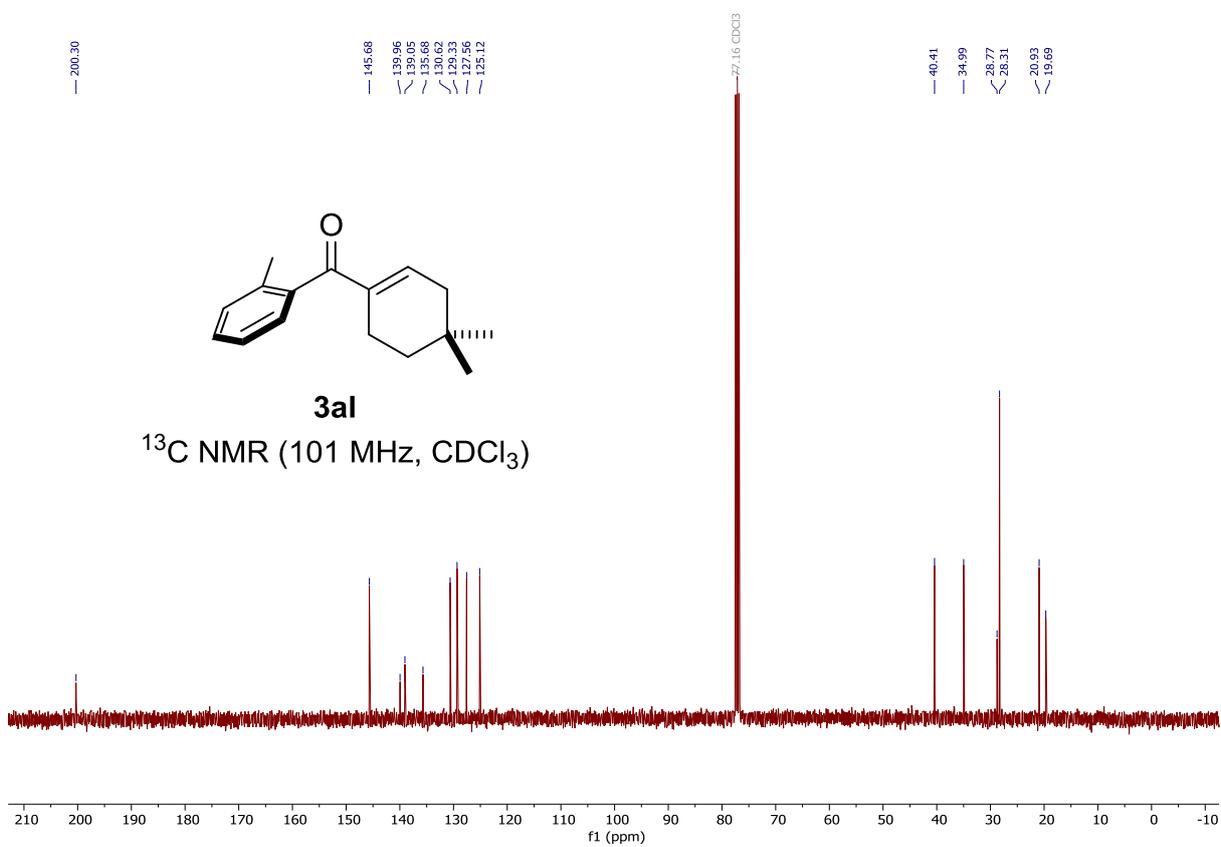
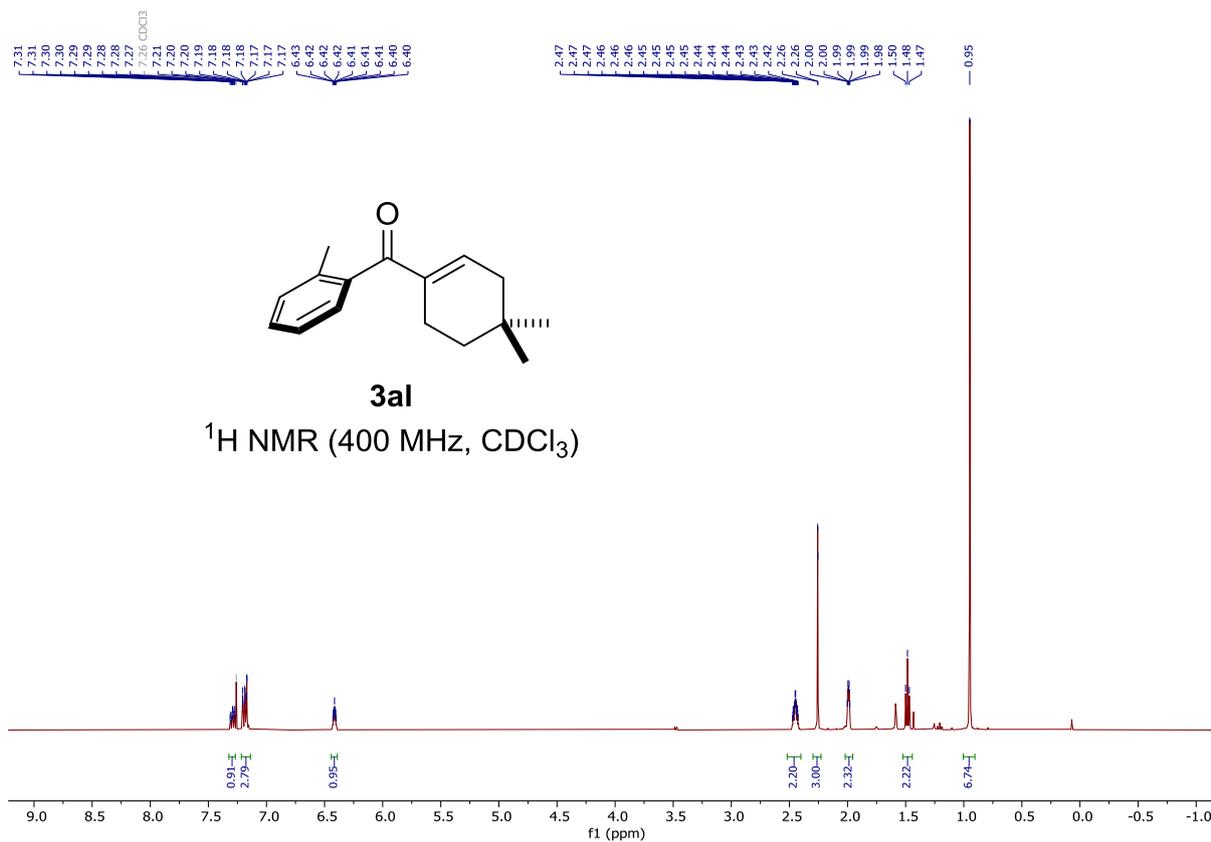


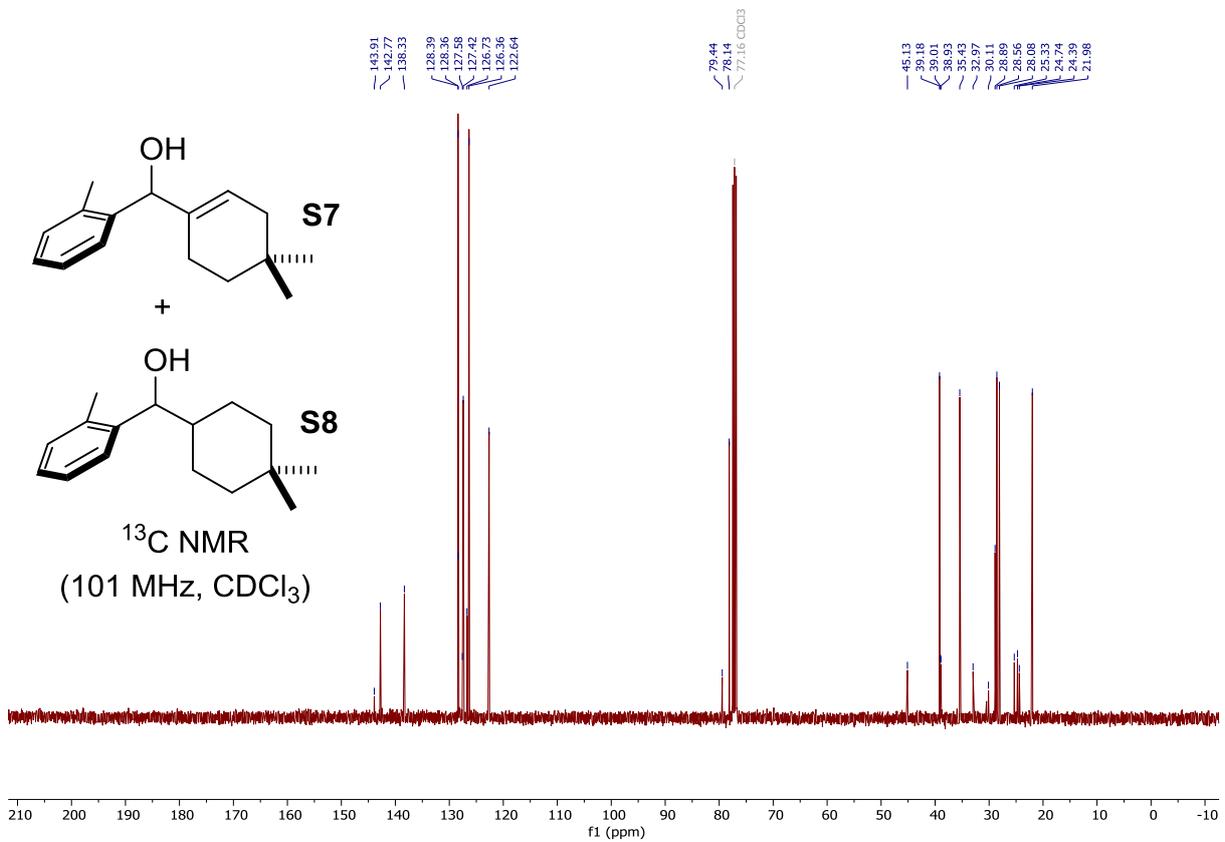
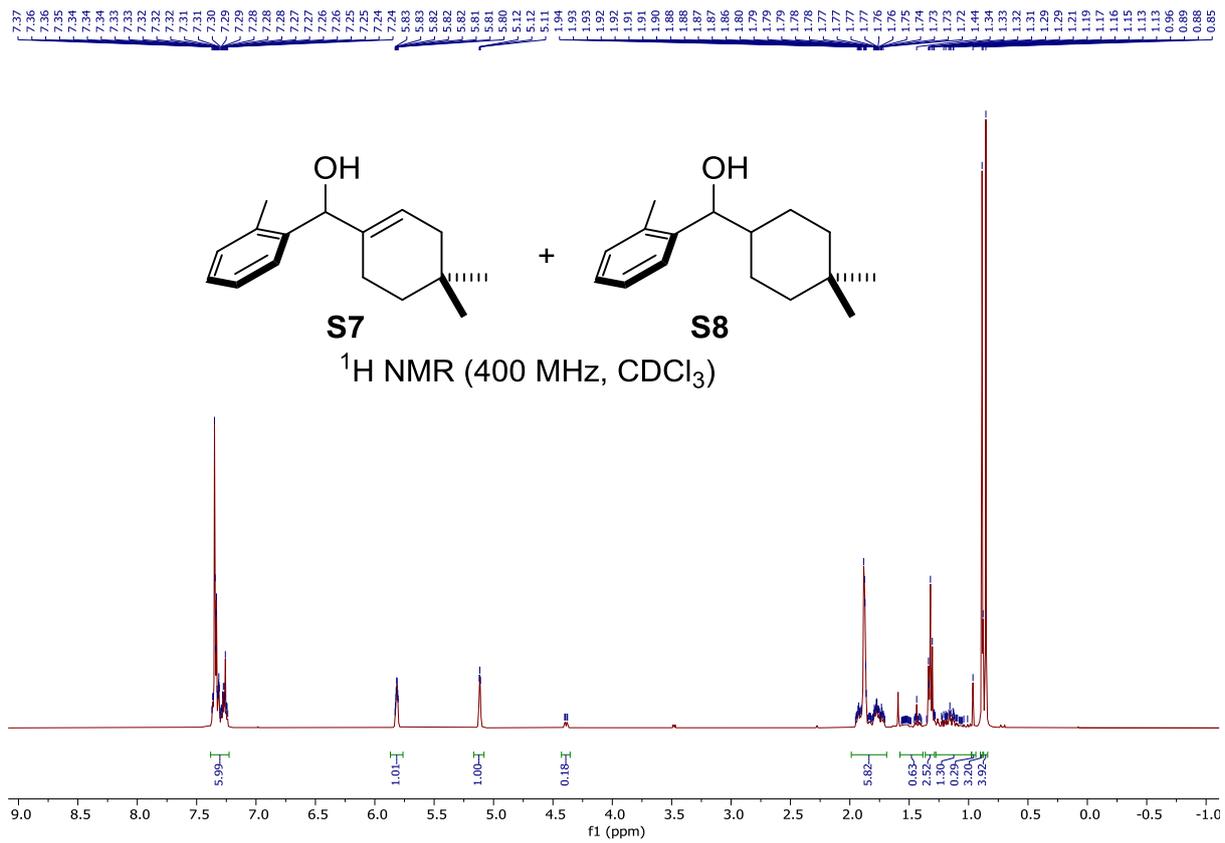


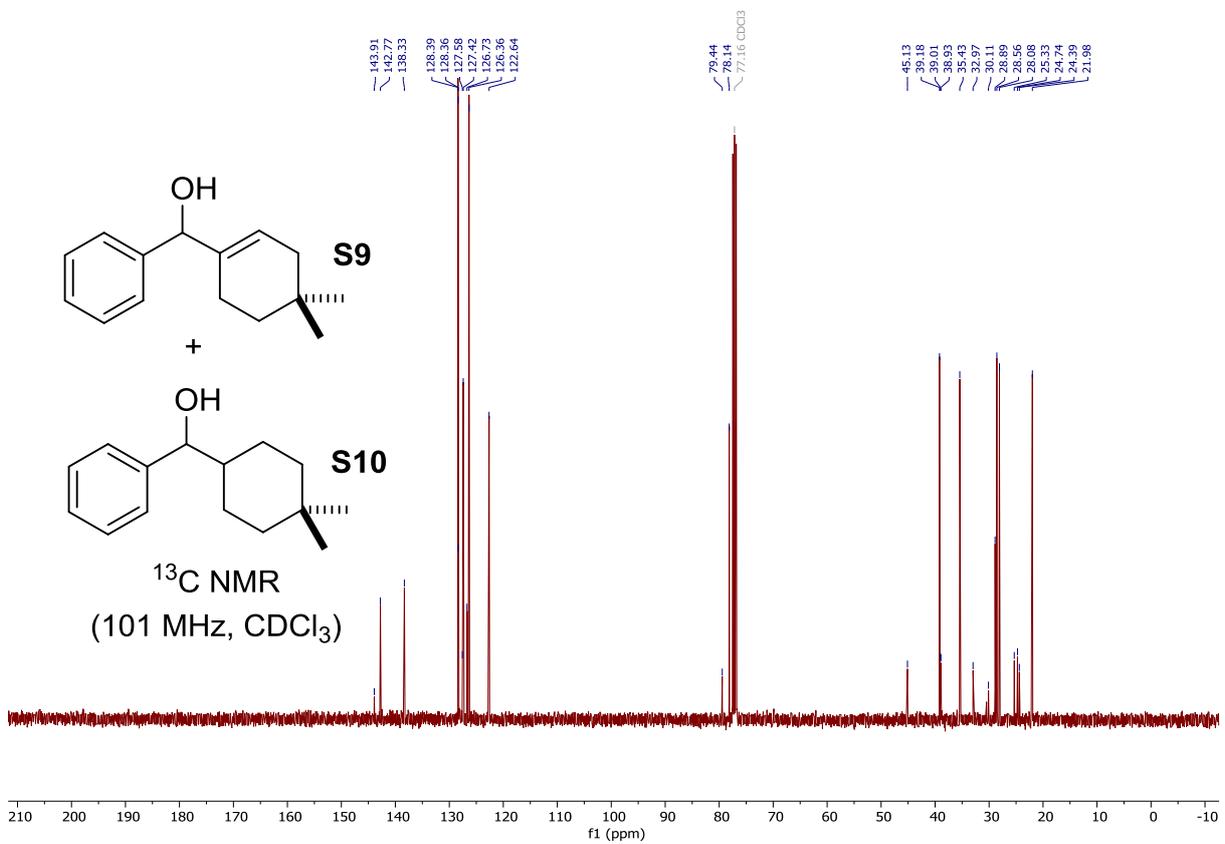
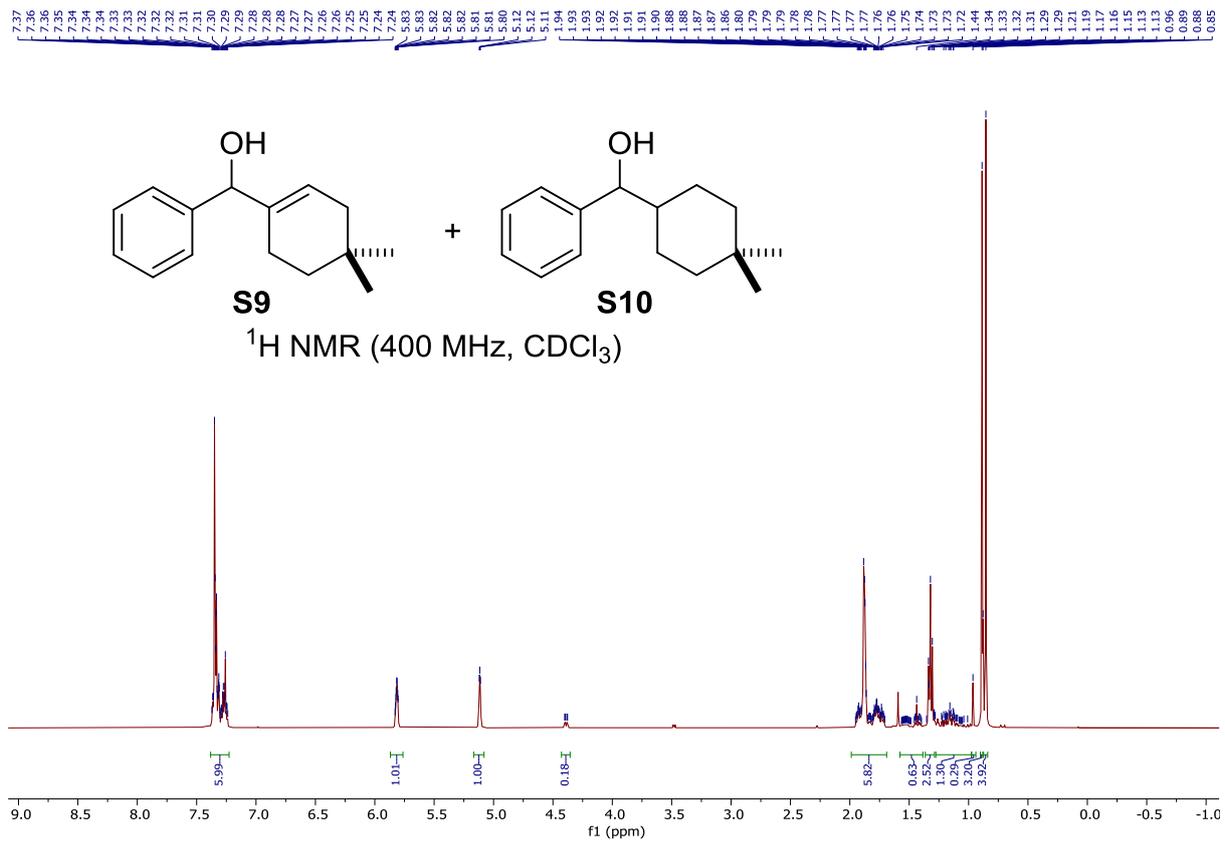




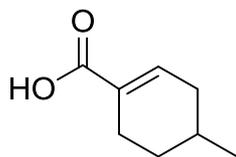






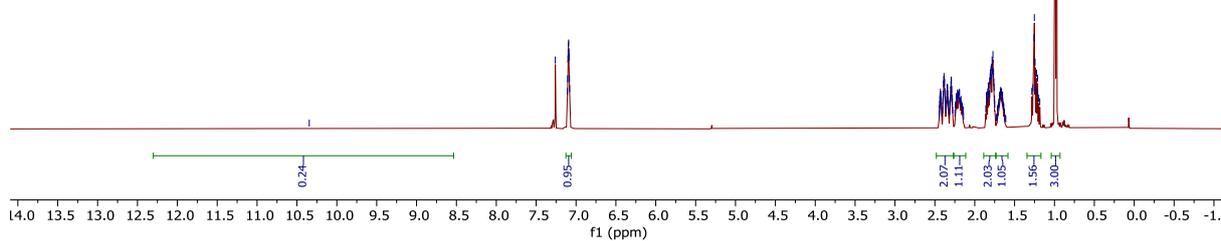


7.26
7.11
7.11
7.10
7.10
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7.09
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7.08
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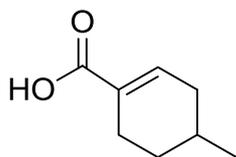


6

¹H NMR (400 MHz, CDCl₃)



173.09
142.21
129.62
34.48
30.36
27.60
23.89
21.52



6

¹³C NMR (101 MHz, CDCl₃)

