

Supporting Information

Cyclization by C(sp³)-H Arylation with a Transient Directing Group for the Diastereoselective Preparation of Indanes

Philip A. Provencher,[†] Katherine L. Bay,[‡] John F. Hoskin,[†] Prof. K. N. Houk,[‡] Prof. Jin-Quan Yu^{*,‡}, Prof. Erik J. Sorensen^{*,†}

[†]Department of Chemistry, Princeton University, Princeton, New Jersey, 08544, United States

[‡]Department of Chemistry and Biochemistry, University of California, Los Angeles, California, 90095, United States

[‡]Department of Chemistry, The Scripps Research Institute, La Jolla, California, 92037, United States

* ejs@princeton.edu and yu200@scripps.edu

Table of Contents

General Information.....	2
Selected Additional Screening Tables	2
Experimental Section.....	7
Substrate Preparation	7
Procedure for Pd catalyzed C-H Arylative Ring Closure with a TDG	21
Scale-up Procedure	21
Screening Workflow	21
Formal [3+2] Cyclization by double C-H arylation.....	22
Purification and characterization data for C-H arylicative ring closure products 5, 7a-k, 2, 8a-d, 13, and 14:	22
2° C-H functionalization.....	22
1° C-H functionalization.....	26
Data for Figure 3 in Paper.....	28
Deuterium exchange experiment	29
Data for [3+2] Cyclization Reactions	30
NMR Spectra	31
2D NMR Analysis.....	89
Computational Methods.....	93
Additional Computational Discussion	93
References.....	105

General Information

Ketone substrates were prepared from 2-Alkyl-1,3-diketones by procedures detailed in the Experimental Section. 3-Alkyl-2,4-pentanediones were purchased or prepared as described herein. Reactions were performed under air unless indicated. Reactions under N₂ gas were performed by standard Schlenk techniques with a dry N₂/vacuum manifold. NMR spectra were recorded on 400, 500, or 600 MHz spectrometers, as indicated for each reported spectrum. ¹H and ¹³C NMR spectra are reported in parts per million and were referenced to residual solvent: CDCl₃ δ = 7.26 ¹H NMR, 77.00 for ¹³C NMR. The multiplicities are abbreviated as follows: s = singlet, d = doublet, dd = doublet of doublets, t = triplet, q = quartet, p = pentent, m = multiplet, and br = broad signal. Coupling constants were measured in Hz and abbreviated as *J*. All spectra were obtained at 22 °C. Mass spectra were recorded by high-resolution time-of-flight mass spectrometry with either liquid chromatography-electrospray ionization (ESI-TOF) or gas chromatography-electron impact ionization (EI-TOF). Thin layer chromatography (TLC) plates were visualized with UV light and/or potassium permanganate stain. When use of dry solvents is indicated, solvent was purified *via* passage through solvent purification columns. All other solvents and reagents were purchased and used as received.

Selected Additional Screening Tables

conditions	product	proto	SM
Ag ₃ PO ₄	43%	6%	13%
AgOBz	4%	1%	46%
Ag ₂ SO ₄	20%	10%	32%
Ag ₂ CO ₃	8%	5%	43%
Ag ₂ O	17%	7%	44%
AgF	9%	trace	33%
AgOAc	11%	5%	40%

Figure S1: Screen various silver sources. 0.1 mmol scale. Yields were determined by ¹H NMR spectroscopy using 1,3,5-trimethoxybenzene as internal standard. HFIP = hexafluoroisopropanol

phosphate additive (1 equiv.)	Product	proto	SM
no additive	43%	6%	13%
H ₃ PO ₄	8%	3%	86%
Li ₃ PO ₄	6%	1%	93%
LiH ₂ PO ₄	13%	--	86%
Na ₃ PO ₄	27%	3%	45%
Na ₂ HPO ₄	12%	--	78%
NaH ₂ PO ₄	6%	--	81%
K ₃ PO ₄	10%	--	70%
K ₂ HPO ₄	8%	--	80%
KH ₂ PO ₄	13%	--	74%
BINOLPO ₄ H	20%	--	20%
Et ₂ PO ₃ NH ₂	15%	--	75%
Cu ₃ PO ₄	10%	--	65%
phosphomolybdic acid hydrate	4%	--	74%
(NH ₄) ₂ HPO ₄	7%	--	78%
Na ₃ VO ₄	9%	5%	60%

Figure S2: Phosphate additive screen. 0.1 mmol scale. Yields were determined by ¹H NMR spectroscopy using 1,3,5-trimethoxybenzene as internal standard. TFA = trifluoroacetic acid; HFIP = hexafluoroisopropanol

additive	cyclization	proto	SM
	0%	0%	99%
	35%	13%	18%
	28%	8%	42%
	41%	17%	13%
	22%	0%	83%
<i>p</i> -TsOH	2%	36%	0%

Figure S3: Acid additive screen. 0.1 mmol scale. Yields were determined by ¹H NMR spectroscopy using 1,3,5-trimethoxybenzene as internal standard. TFA = trifluoroacetic acid; HFIP = hexafluoroisopropanol

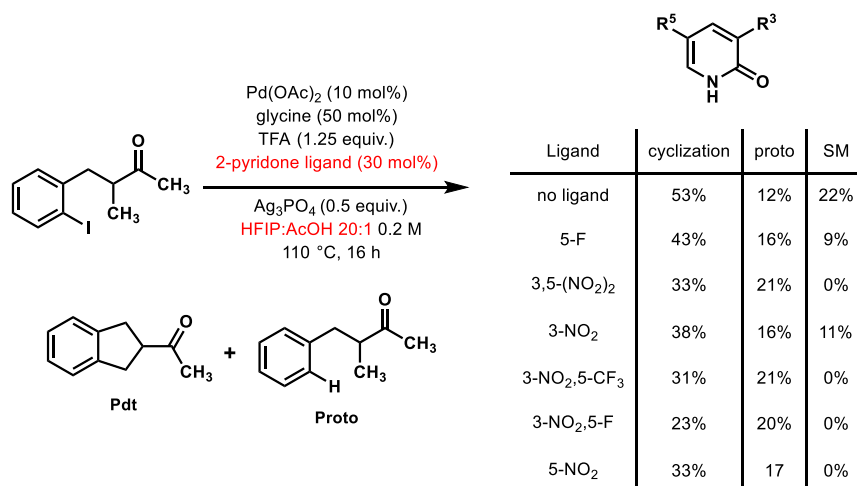


Figure S4: Pyridone ligand screen under reduced AcOH medium. 0.1 mmol scale. Yields were determined by ¹H NMR spectroscopy using 1,3,5-trimethoxybenzene as internal standard. TFA = trifluoroacetic acid; HFIP = hexafluoroisopropanol

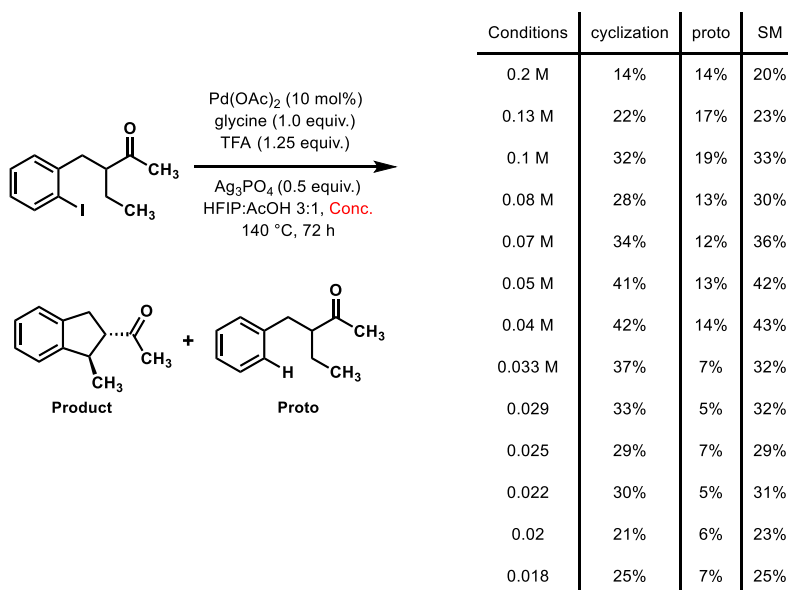
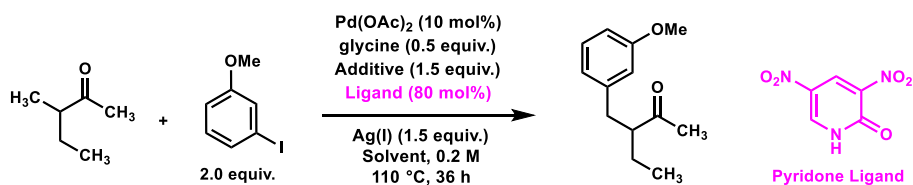
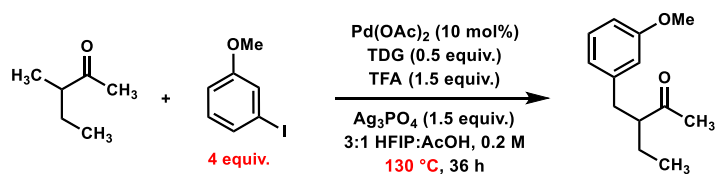


Figure S5: Concentration Screen. 0.1 mmol scale. Yields were determined by ¹H NMR spectroscopy using 1,3,5-trimethoxybenzene as internal standard. TFA = trifluoroacetic acid; HFIP = hexafluoroisopropanol



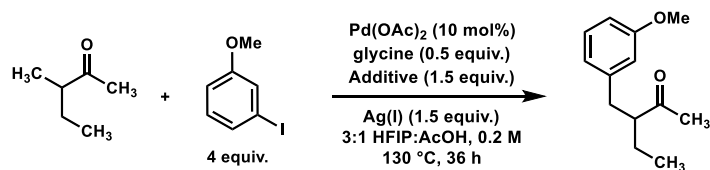
Ag(I)	solvent	additive	Ligand	Yield
AgTFA	3:1 HFIP:AcOH	--	--	16%
AgTFA	3:1 HFIP:AcOH	TFA	--	0%
AgTFA	HFIP	TFA	Pyridone	0%
Ag ₃ PO ₄	3:1 HFIP:AcOH	--	--	19%
Ag ₃ PO ₄	3:1 HFIP:AcOH	TFA	--	30%
Ag ₃ PO ₄	HFIP	TFA	Pyridone	20%

Figure S6. Comparing Ag₃PO₄ and AgTFA, Comparing Pyridone vs AcOH ligand, and TFA additive Screen. 0.1 mmol in ketone scale. Yields were determined by ¹H NMR spectroscopy using 1,3,5-timethoxybenzene as internal standard. TFA = trifluoroacetic acid; HFIP = hexafluoroisopropanol



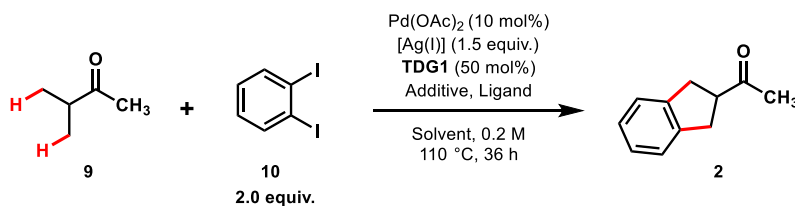
TDG	Yield	TDG	Yield
glycine (0.25)	10%	H ₂ N-CH ₂ -CH ₂ -COOH	8%
glycine (0.5)	37%	H ₂ N-CH ₂ -CH ₂ -NHTs	5%
glycine (0.75)	36%	H ₂ N-CH ₂ -CH ₂ -SO ₃ H	0%
glycine (1.5)	32%	H ₂ N-CH ₂ -CH ₂ -PO ₃ H	0%
		H ₂ N-CH ₂ -CH ₂ -PO ₃ H	2%
		H ₂ N-CH ₂ -CH ₂ -NHAc	6%

Figure S7. TDG screen. 0.1 mmol in ketone scale. Yields were determined by ¹H NMR spectroscopy using 1,3,5-timethoxybenzene as internal standard. TFA = trifluoroacetic acid; HFIP = hexafluoroisopropanol



Ag(I)	additive	Yield
Ag ₃ PO ₄	TFA	37%
Ag ₃ PO ₄ (0.33 equiv.)	TFA	25%
Ag ₃ PO ₄	--	26%
AgTFA	TFA	17%
AgTFA (1.0 equiv.)	TFA	15%
Ag ₂ CO ₃	TFA	53%
Ag ₂ O	TFA	45%
AgOAc	TFA	59%
Ag ₂ SO ₄	TFA	0%

Figure S8. Silver(I) screen. Yields were determined by ¹H NMR spectroscopy using 1,3,5-trimethoxybenzene as internal standard. TFA = trifluoroacetic acid; HFIP = hexafluoroisopropanol



Ag(I)	Solvent	Additive	Ligand	Yield
AgTFA (1.5 equiv.)	3:1 HFIP: AcOH	--	--	5%
Ag ₃ PO ₄ (0.5 equiv.)	HFIP	TFA (1.5 equiv.)	L9 (80 mol%)	0%

Figure S9: Incompatibility of inter- and intramolecular reactivity pathways of the [3+2] double C(sp³)-H arylation stymie reaction development. Comparing optimized conditions for inter- and intramolecular C-H arylation. TFA = trifluoroacetic acid; HFIP = hexafluoroisopropanol. Yields were determined by ¹H NMR spectroscopy using 1,3,5-trimethoxybenzene as an internal standard.

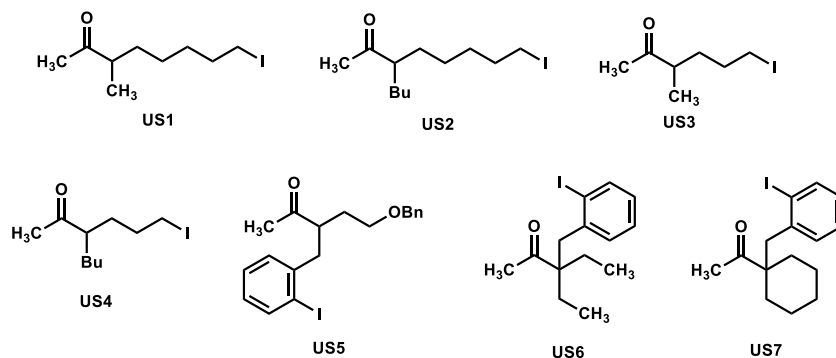
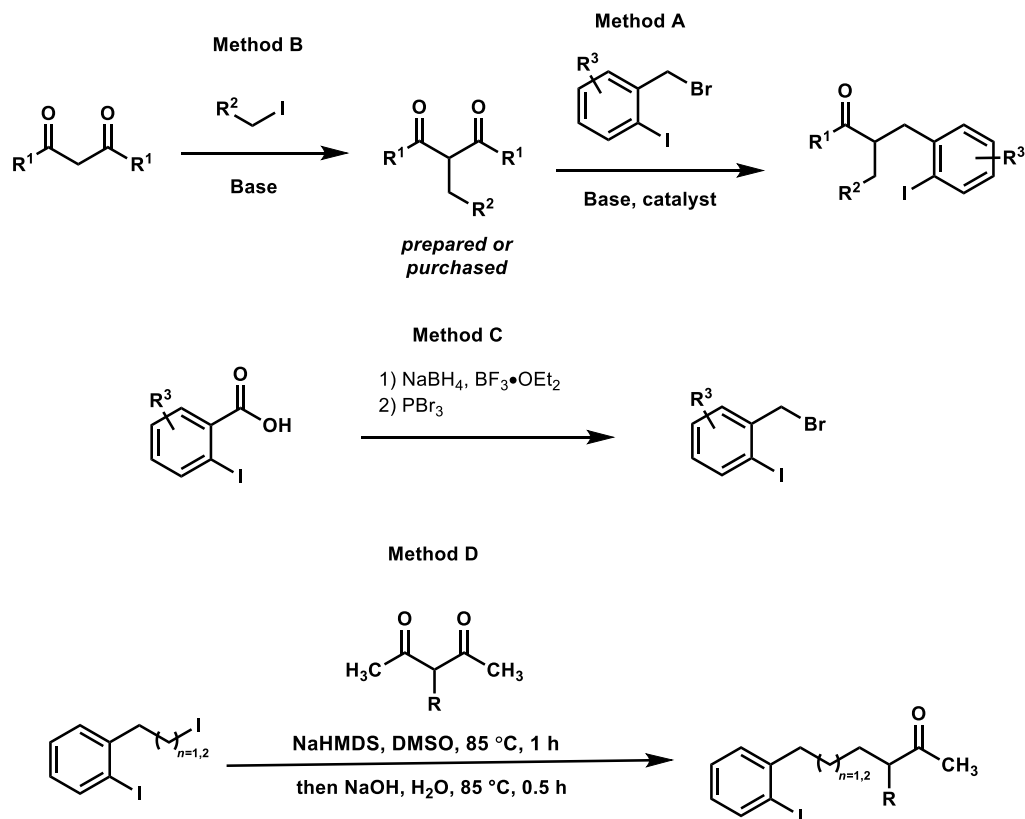


Figure S10: Unsuccessful substrates

Experimental Section

Substrate Preparation

General Scheme for Substrate Preparation



Scheme S1: General Scheme for Substrate Preparation

Method A

Under air, a round bottom flask was charged with 2-bromomethyl iodobenzene (1.0 equiv.), tetrabutylammonium bromide (0.05 equiv.), toluene (2 M), and a stir bar. NaOH (50% in H₂O) was then added (0.25 mL/[mmol 2-bromomethyl iodobenzene]). To this stirred mixture was added dropwise 1,3-diketone (1.5 equiv.) in toluene (1.3 M). The reaction mixture was then heated to 85 °C for 16 h. After cooling, the reaction was diluted with water and hexanes. The aqueous layer was extracted with hexanes

two times. The collected hexanes fractions were washed with brine and then dried with anhydrous sodium sulfate. After decanting the hexanes layer, the solvent was removed under reduced pressure. The product was then purified by column chromatography in either 9:1 or 20:1 hexanes:ethyl acetate. If closer to unity in stoichiometry is used, significant amount of overalkylated ketone is observed as impurity depending on the steric hindrance of the ketone, and this impurity is typically inseparable.

2-Alkylated 1,3-diones were prepared as follows

Method B

K_2CO_3 (1.0 equiv.) was added to a stirred solution of dione (1.0 equiv.) in anhydrous acetone (0.33 M, distilled from CaH_2 under N_2) under N_2 atmosphere at room temperature. After stirring the mixture for 15 minutes, alkyl iodide (1.2 equiv.) was added dropwise. The reaction mixture was heated to reflux for 36 h. The reaction was then cooled to room temperature, quenched with 50 mL 1M HCl, and extracted three times with 20 mL ethyl acetate. The organic fractions were collected, washed with brine, and then dried with anhydrous sodium sulfate. The solution was decanted, and the solvent was removed under reduced pressure. The alkylated dione was then isolated by purification with column chromatography in hexanes:ethyl acetate.

Most of the substituted benzyl bromides were prepared as follows

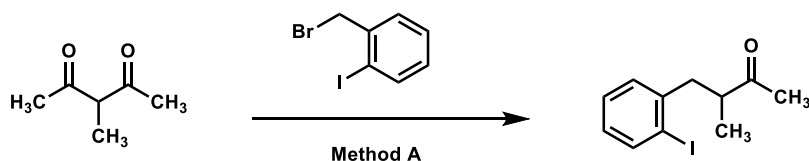
Method C

A flamed two-neck round-bottomed flask under N_2 atmosphere was charged with substituted benzoic acid (1 equiv.) and anhydrous THF (0.37 M) and then cooled to 0 °C with stirring. $NaBH_4$ (2 equiv.) was then added and the reaction mixture was stirred for 20 minutes. $BF_3 \cdot OEt_2$ (2 equiv.) was then added dropwise. The reaction mixture was then allowed to warm to room temperature and stirred for 16 hours. Chilled MeOH was added slowly (0.4 mL/mmol substrate) and the solvent was removed by distillation under reduced pressure. Ethyl acetate was added and 1 M HCl. The EtOAc layer was separated and washed with brine. After the organic layer was dried with sodium sulfate and then decanted, the solvent was removed by distillation under reduced pressure to furnish pure substituted benzyl alcohol (typically a white/beige solid).

A flamed round-bottomed flask under N_2 atmosphere was charged with this substituted benzyl alcohol and cooled to 0 °C with stirring. To this flask with neat benzyl alcohol was added PBr_3 (1.2 equiv.) dropwise. The reaction mixture was then warmed to 85 °C for 2 hours, after which it was cooled to room temperature. To the reaction mixture was added ice and then saturated sodium bicarbonate. The resulting mixture was extracted three times with methylene chloride. The combined organic extracts were washed with saturated sodium bicarbonate and then brine. The organic layer was dried with sodium sulfate and then decanted. Solvent was removed by distillation under reduced pressure to furnish pure substituted benzyl bromide.

Method D

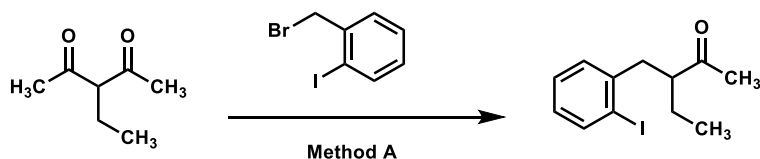
Under an atmosphere of N_2 , an oven-dried round bottom flask was charged with 1,3-diketone (1.5 equiv) followed by NaHMDS (1.5 equiv, 1M in THF) with stirring. Anhydrous DMSO (3 ml/1 mmol diketone) was then added, followed by alkyl iodide (1.0 equiv) in DMSO (1 mL/1 mmol alkyl iodide). The reaction mixture was brought to 85 °C and stirred until the alkyl iodide was consumed (monitored by TLC), typically less than an hour. NaOH (50% in H_2O) was then added by syringe and stirred until intermediate quaternary diketone was consumed (monitored by TLC), typically 10-15 minutes. At the conclusion of the reaction, water was added and the aqueous portion was extracted with diethyl ether, dried with brine and $MgSO_4$, and concentrated *in vacuo*. The residue was purified by column chromatography on silica using EtOAc/pentane as eluent.



Scheme S2: Preparation of 1

4-(2-iodophenyl)-3-methylbutan-2-one (1)

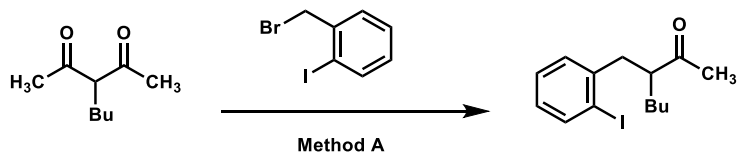
Prepared by Method A. Colorless oil. 4.3 g isolated. 89% yield. ^1H NMR (500 MHz, Chloroform-*d*) δ 7.82 (dd, $J = 7.9, 1.0$ Hz, 1H), 7.25 (dd, $J = 7.5, 1.1$ Hz, 1H), 7.17 (dd, $J = 7.6, 1.5$ Hz, 1H), 6.90 (td, $J = 7.7, 1.7$ Hz, 1H), 3.13 (dd, $J = 13.6, 6.6$ Hz, 1H), 2.98 (q, $J = 7.1$ Hz, 1H), 2.68 – 2.58 (m, 1H), 2.13 (s, 9H), 1.11 (d, $J = 7.0$ Hz, 3H). HRMS (ESI+ TOF) ^{13}C NMR (126 MHz, Chloroform-*d*) δ 211.54, 142.11, 139.56, 130.71, 128.15, 128.13, 100.60, 46.59, 43.04, 29.05, 15.94. Calcd for $\text{C}_{11}\text{H}_{13}\text{IO} + \text{H}^+$: 289.0094, found: 289.0092



Scheme S3: Preparation of 4

3-(2-iodobenzyl)pentan-2-one (4)

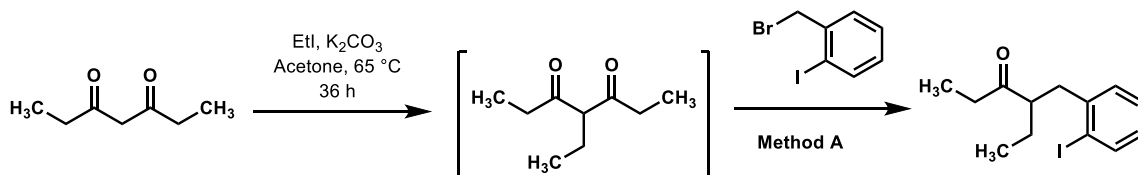
Prepared by Method A. Colorless oil. 3.5 g isolated (69% Yield). R_f : 0.5 in 9:1 hexanes:ethyl acetate. ^1H NMR (400 MHz, Chloroform-*d*) δ 7.29 (d, $J = 7.0$ Hz, 1H), 7.18 (dd, $J = 22.7, 7.3$ Hz, 3H), 3.00 (dd, $J = 13.6, 6.8$ Hz, 1H), 2.83 (h, $J = 7.0$ Hz, 1H), 2.56 (dd, $J = 13.6, 7.7$ Hz, 1H), 2.09 (d, $J = 0.4$ Hz, 3H), 1.09 (d, $J = 7.0$ Hz, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 212.05, 142.24, 139.70, 128.29, 128.21, 100.57, 53.67, 41.80, 30.73, 24.52, 11.58. HRMS (ESI+ TOF) Calcd for $\text{C}_{12}\text{H}_{15}\text{IO} + \text{H}^+$: 303.0240, found: 303.0240



Scheme S4: Preparation of S1

3-(2-iodobenzyl)heptan-2-one (S1)

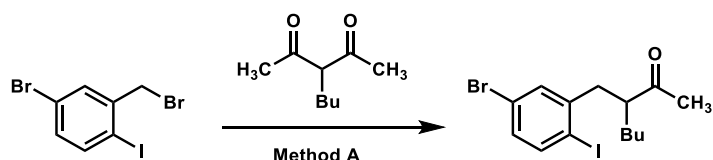
Prepared by Method A. Yellow oil. 950 mg isolated (85% yield). R_f : 0.5 in 9:1 hexanes:ethyl acetate. ^1H NMR (500 MHz, Chloroform-*d*) δ 7.82 (dd, $J = 7.9, 1.3$ Hz, 1H), 7.24 (td, $J = 7.5, 1.3$ Hz, 1H), 7.14 (dd, $J = 7.6, 1.8$ Hz, 1H), 6.89 (td, $J = 7.6, 1.7$ Hz, 1H), 3.03 – 2.92 (m, 2H), 2.75 (d, $J = 7.4$ Hz, 1H), 2.02 (s, 3H), 1.67 (ddd, $J = 12.5, 6.4, 4.3$ Hz, 1H), 1.47 (ddd, $J = 9.1, 7.6, 4.6$ Hz, 1H), 1.35 – 1.17 (m, 4H), 0.88 (t, $J = 7.0$ Hz, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 212.24, 142.17, 139.66, 130.67, 128.27, 128.18, 100.50, 52.18, 42.29, 31.34, 30.74, 29.30, 22.82, 13.88. HRMS (ESI+ TOF) Calcd for $\text{C}_{14}\text{H}_{19}\text{IO} + \text{H}^+$: 331.0553, found: 331.0556



Scheme S5: Preparation of S2

4-(2-iodobenzyl)hexan-3-one (S2)

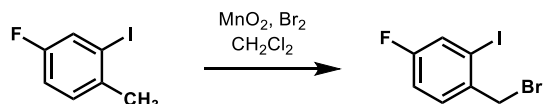
3,5-heptanedione and iodoethane were subjected to Method B to give 4-ethyl-3,5-heptanedione contaminated with 3,5-heptanedione. 788 mg (~5.1 mmol) of this oil was then subjected to Method A with 2-bromomethyliodobenzene. Purified by gradient column chromatography hexanes to 15:1 hexanes:ethyl acetate to furnish 545 mg colorless oil (50% yield). ^1H NMR (500 MHz, Chloroform-*d*) δ 7.81 (d, J = 8.9 Hz, 1H), 7.22 (t, J = 8.0 Hz, 1H), 7.11 (d, J = 7.6 Hz, 1H), 6.88 (t, J = 7.6 Hz, 1H), 3.01 – 2.88 (m, 2H), 2.76 (dd, J = 12.3, 5.0 Hz, 1H), 2.34 (dd, J = 17.9, 7.3 Hz, 1H), 2.14 (dd, J = 17.9, 7.3 Hz, 1H), 1.76 – 1.63 (m, 1H), 1.57 – 1.46 (m, 2H), 0.90 (td, J = 7.4, 1.6 Hz, 6H); ^{13}C NMR (126 MHz, Chloroform-*d*) δ 214.70, 139.64, 130.71, 128.21, 128.14, 77.00, 52.65, 42.30, 37.39, 24.89, 11.75, 7.30. HRMS (ESI+ TOF) Calcd for $\text{C}_{13}\text{H}_{17}\text{IO} + \text{H}^+$: 317.0397, found: 317.0396



Scheme S6: Preparation of S3

3-(5-bromo-2-iodobenzyl)heptan-2-one (S3)

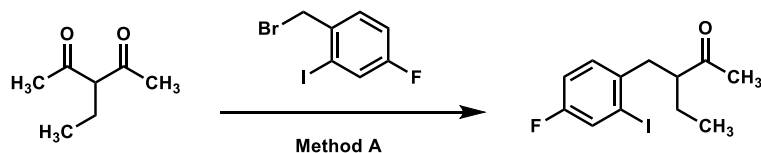
Prepared by Method A. Purified by column chromatography in 20:1 hexanes:ethyl acetate. 558 mg colorless oil isolated, 90% yield. ^1H NMR (500 MHz, Chloroform-*d*) δ 7.65 (d, J = 8.4 Hz, 1H), 7.29 (d, J = 2.4 Hz, 1H), 7.03 (dd, J = 8.4, 2.4 Hz, 1H), 3.05 – 2.87 (m, 2H), 2.69 (d, J = 7.5 Hz, 1H), 2.06 (s, 3H), 1.72 – 1.60 (m, 1H), 1.52 – 1.41 (m, 1H), 1.37 – 1.18 (m, 4H), 0.88 (t, J = 7.0 Hz, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 211.41, 144.49, 140.83, 133.36, 131.30, 122.52, 98.42, 52.02, 41.65, 31.30, 30.52, 29.15, 22.80, 13.87. HRMS (ESI+ TOF) Calcd for $\text{C}_{14}\text{H}_{18}\text{BrIO} + \text{H}^+$: 408.9664, found: 408.9667



Scheme S7: Preparation of S4

1-(bromomethyl)-4-fluoro-2-iodobenzene (S4)

Under N_2 atmosphere, iodotoluene substrate (3 g, 12.7 mmol, 1.0 equiv.) was dissolved in anhydrous CH_2Cl_2 (25 mL, 0.5 M) with stirring at ambient temperature. Br_2 (0.66 mL, 12.9 mmol, 1.02 equiv.) was added and then MnO_2 (1.1 g, 12.7 mmol, 1.0 equiv., activated by heating in the oven overnight). After stirring for 16 h, the reaction was diluted with CH_2Cl_2 and filtered through celite. After removal of solvent by distillation under reduced pressure, the desired product was purified by column chromatography in 0.75% ethyl acetate in hexanes. Spectroscopic data matched previous reports.¹

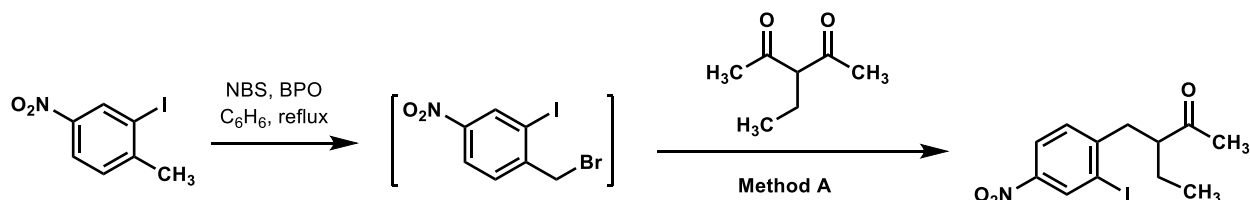


Scheme S8: Preparation of S5

3-(4-fluoro-2-iodobenzyl)pentan-2-one (S5)

Prepared by Method A. 528 mg isolated (88% yield). Yellow oil. R_f : 0.5 in 9:1 hexanes:ethyl acetate. ^1H NMR (500 MHz, Chloroform-*d*) δ 7.54 (dd, J = 8.1, 2.7 Hz, 1H), 7.11 (dd, J = 8.5, 6.0 Hz, 1H), 6.97 (td, J = 8.3, 2.7 Hz, 1H), 3.04 – 2.95 (m, 1H), 2.92 – 2.83 (m, 1H), 2.76 – 2.67 (m, 1H), 2.04 (s, 3H), 1.75 – 1.64 (m, 1H), 1.60 – 1.48 (m, 1H), 0.93 (t, J = 7.5 Hz, 3H); ^{13}C NMR (126 MHz, Chloroform-*d*) δ 211.79,

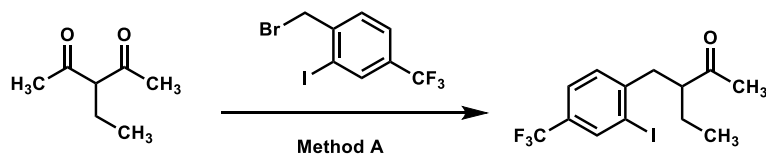
161.55, 159.56, 131.02, 126.45, 115.31, 53.73, 40.59, 30.68, 24.57, 11.49. ^{19}F NMR (282 MHz, Chloroform-*d*) δ -115.05. HRMS (ESI+ TOF) Calcd for $\text{C}_{13}\text{H}_{14}\text{FIO} + \text{H}^+$: 321.0152, found: 321.0155



Scheme S9: Preparation of S6 NBS = N-bromosuccinimide; BPO = benzoyl peroxide

3-(2-iodo-4-nitrobenzyl)pentan-2-one (S6)

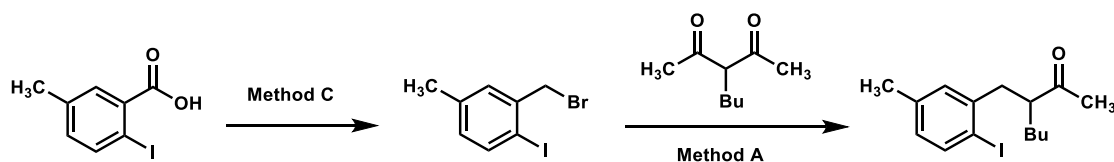
A flamed two-necked round-bottomed flask was fitted with a reflux condenser and septa. Under N_2 atmosphere with stirring, the vessel was charged with 2-iodo-4-nitrotoluene (3 g, 11.4 mmol), anhydrous benzene (11 mL), NBS (2.23 g, 12.5 mmol, 1.1 equiv.), and benzoylperoxide (0.57 g, 0.05 equiv.). The reaction mixture was heated to reflux for 16 h, after which the mixture was allowed to cool to ambient temperature. The reaction mix was diluted with ethyl acetate and filtered through celite. The filtrate was washed with sat. sodium bicarbonate and sat. sodium thiosulfate and brine. The organic layer was dried with sodium sulfate, decanted, and solvent was removed by distillation under reduced pressure. The material was purified with column chromatography in 19:1 hexanes ethyl acetate; however, significant impurity of 2-iodo-4-nitrotoluene remained (560 mg isolated). The mixture of product and starting material was carried through and subjected to Method A with 3-ethyl-2,4-pentanedione and 126 mg yellow oil was isolated after column chromatography in 9:1 hexanes:ethyl acetate (R_f 0.1). ^1H NMR (500 MHz, Chloroform-*d*) δ 8.66 (d, $J = 2.3$ Hz, 1H), 8.10 (dd, $J = 8.4, 2.4$ Hz, 1H), 7.34 (d, $J = 8.4$ Hz, 1H), 3.17 (dd, $J = 13.5, 8.6$ Hz, 1H), 2.93 (q, $J = 6.7$ Hz, 1H), 2.82 (dd, $J = 13.4, 5.6$ Hz, 1H), 2.07 (s, 3H), 1.75 (dt, $J = 14.3, 7.2$ Hz, 1H), 1.65 – 1.57 (m, 1H), 0.97 (t, $J = 7.4$ Hz, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 210.57, 150.17, 146.53, 134.42, 130.85, 123.02, 99.42, 53.17, 40.92, 30.37, 24.81, 11.26. HRMS (ESI+ TOF) Calcd for $\text{C}_{12}\text{H}_{14}\text{INO}_3 + \text{H}^+$: 348.0097, found: 348.0099



Scheme S10: Preparation of S7

3-(2-iodo-5-(trifluoromethyl)benzyl)pentan-2-one (S7)

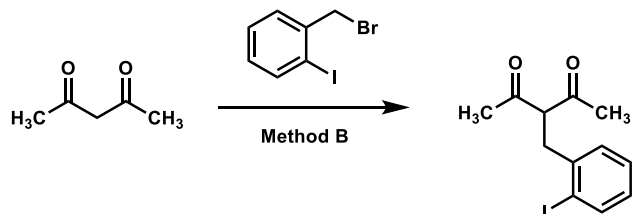
Prepared by Method A. 406 mg isolated (80% yield). Yellow oil. R_f : 0.4 in 9:1 hexanes:ethyl acetate. ^1H NMR (500 MHz, Chloroform-*d*) δ 7.95 (dd, $J = 8.3, 0.9$ Hz, 1H), 7.40 (d, $J = 2.3$ Hz, 1H), 7.14 (dd, $J = 8.3, 2.3$ Hz, 1H), 3.10 (dd, $J = 13.6, 8.0$ Hz, 1H), 2.96 – 2.86 (m, 1H), 2.78 (dd, $J = 13.7, 6.2$ Hz, 1H), 2.08 (s, 3H), 1.73 (dt, $J = 13.8, 7.4$ Hz, 1H), 1.63 – 1.51 (m, 1H), 0.94 (t, $J = 7.4$ Hz, 3H). ^{19}F NMR (282 MHz, Chloroform-*d*) δ -62.90. ^{13}C NMR (126 MHz, Chloroform-*d*) δ 210.97, 143.53, 140.24, 132.66 – 128.96 (m), 126.90 (q, $J = 3.8$ Hz), 124.63 (q, $J = 3.7$ Hz), 122.68, 104.74 (d, $J = 1.8$ Hz), 53.37, 41.22, 30.34, 24.48, 11.35. ^{19}F NMR (282 MHz, Chloroform-*d*) δ -62.90. HRMS (ESI+ TOF) Calcd for $\text{C}_{13}\text{H}_{14}\text{F}_3\text{IO} + \text{H}^+$: 372.0148, found: 372.0148



Scheme S11: Preparation of S8

3-(2-iodo-5-methylbenzyl)heptan-2-one (S8)

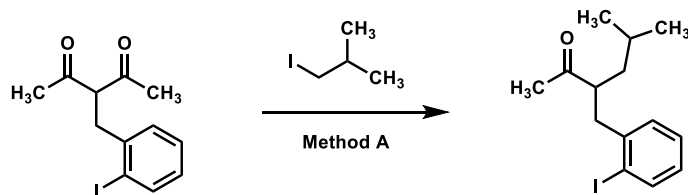
2-bromomethyl-4-methyl-iodobenzene was prepared by Method C. 93% over two steps, Spectroscopic data matches previous report.¹ This material was subjected to Method A with 3-butyl-2,4-pentanedione to furnish the desired ketone. 451 mg pale oil, 55% yield. ¹H NMR (500 MHz, Chloroform-*d*) δ 7.67 (d, J = 8.0 Hz, 1H), 6.95 (d, J = 2.2 Hz, 1H), 6.72 (dd, J = 7.9, 2.2 Hz, 1H), 3.02 – 2.89 (m, 2H), 2.75 – 2.66 (m, 1H), 2.25 (s, 3H), 2.02 (s, 3H), 1.73 – 1.61 (m, 1H), 1.46 (td, J = 9.2, 4.9 Hz, 1H), 1.36 – 1.16 (m, 4H), 0.88 (t, J = 7.0 Hz, 3H). ¹³C NMR (126 MHz, Chloroform-*d*) δ 212.31, 141.86, 139.34, 138.24, 131.55, 129.19, 96.38, 52.24, 42.17, 31.33, 30.74, 29.32, 22.83, 20.86, 13.90. HRMS (ESI+ TOF) Calcd for C₁₅H₂₁IO + H⁺: 345.0715, found: 345.0714



Scheme S12: Preparation of S9

3-(2-iodobenzyl)pentane-2,4-dione (S9)

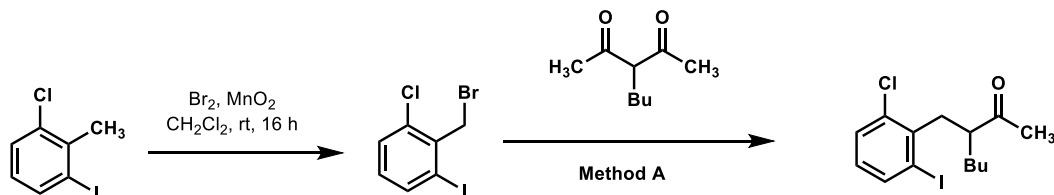
Diketone was prepared by Method B. Colorless oil. 38% Yield. Spectroscopic data matches previous report.²



Scheme S13: Preparation of S10

3-(2-iodobenzyl)-5-methylhexan-2-one (S10)

Prepared by Method A. Colorless residue. Purified by column chromatography in 9:1 and then 20:1 hexanes:ethyl acetate. 26.4 mg isolated, 9% yield. ¹H NMR (400 MHz, Chloroform-*d*) δ 7.82 (dd, J = 7.9, 1.3 Hz, 1H), 7.23 (td, J = 7.6, 1.4 Hz, 1H), 6.89 (td, J = 7.6, 1.8 Hz, 1H), 3.09 (tt, J = 8.5, 5.7 Hz, 1H), 2.95 (dd, J = 13.5, 8.8 Hz, 1H), 2.75 (dd, J = 13.5, 6.0 Hz, 1H), 1.98 (s, 3H), 1.61 (dddd, J = 19.6, 17.0, 10.7, 6.3 Hz, 3H), 1.25 (ddd, J = 13.0, 7.3, 5.3 Hz, 1H), 0.90 (dd, J = 10.9, 6.4 Hz, 7H). ¹³C NMR (126 MHz, Chloroform-*d*) δ 212.38, 141.95, 139.68, 130.66, 128.28, 128.22, 100.39, 50.12, 43.15, 41.03, 26.04, 23.26, 22.31. HRMS (ESI+ TOF) Calcd for C₁₄H₁₉IO + H⁺: 331.0559, found: 331.0555

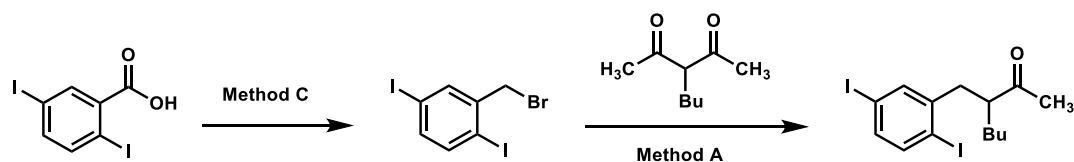


Scheme S14: Preparation of S11

3-(2-chloro-6-iodobenzyl)heptan-2-one (S11)

A flamed 2-neck flask with septa and allowed to cool under stream of N₂. The flask was charged with 1-chloro-3-iodo-2-methylbenzene (3.2 g, 12.7 mmol) and anhydrous CH₂Cl₂ (25 mL, 0.5 M). Br₂ (2.07

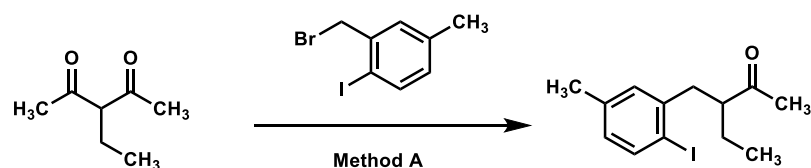
g, 12.8 mmol) was added, followed by MnO_2 (1.1 g, 12.7 mmol). The reaction mixture was stirred for 1.5 hours and then MnO_2 (5.5 g, 6.35 mmol) was added a second time. The reaction mixture was stirred for 16 hours, after which it was filtered through celite with added CH_2Cl_2 . The filtrate was collected and washed with saturated aqueous solution of sodium bicarbonate and then sodium thiosulfate and then brine. The organic layer was collected, dried with anhydrous sodium sulfate, and after decanting the solvent was removed by distillation under reduced pressure. The material was purified with column chromatography in hexanes (R_f 0.5). 240 mg (6% yield) white crystals were collected, which matched previously reported spectroscopic data.¹ The methyl ketone was prepared by subjecting this material and 3-butyl-2,4-pentanedione to Method A. 160 mg of a colorless oil (43% yield) was isolated after purification by column chromatography in 19:1 hexanes:ethyl acetate. ^1H NMR (400 MHz, Chloroform-*d*) δ 7.77 (dd, $J = 7.9, 1.2$ Hz, 1H), 7.36 (dd, $J = 8.0, 1.2$ Hz, 1H), 6.83 (t, $J = 7.9$ Hz, 1H), 3.18 (dd, $J = 13.6, 6.3$ Hz, 1H), 3.10 (dd, $J = 13.6, 8.1$ Hz, 1H), 3.00 (tdd, $J = 8.3, 6.2, 4.3$ Hz, 1H), 2.15 (s, 3H), 1.79 (dddd, $J = 13.2, 10.2, 9.1, 4.2$ Hz, 1H), 1.43 (dddd, $J = 13.4, 10.1, 5.5, 4.2$ Hz, 1H), 1.33 – 1.18 (m, 3H), 1.18 – 1.05 (m, 1H), 0.84 (t, $J = 7.1$ Hz, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 211.56, 140.01, 138.77, 134.22, 130.10, 129.08, 101.97, 51.90, 40.03, 30.50, 29.99, 29.63, 22.78, 13.87. HRMS (ESI+ TOF) Calcd for $\text{C}_{14}\text{H}_{18}\text{ClO} + \text{H}^+$: 365.0164, found: 356.0167



Scheme S15: Preparation of S12

3-(2,5-diiodobenzyl)heptan-2-one (S12)

2-bromomethyl-1,4-diiodobenzene (**S12-1**) was prepared by Method C. 67% over two steps, Spectroscopic data matches previous report for 2-hydroxymethyl-1,4-diiodobenzene.³ 2-bromomethyl-1,4-diiodobenzene is a white solid ^1H NMR (500 MHz, Chloroform-*d*) δ 7.78 (s, 1H), 7.55 (s, 1H), 7.27 (s, 1H), 4.49 (s, 2H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 142.29, 141.43, 139.01, 138.99, 99.25, 93.93, 37.32. This 2-bromomethyl-1,4-diiodobenzene material was subjected to Method A with 3-butyl-2,4-pentanedione to furnish the desired ketone. 451 mg pale oil, 55% yield. ^1H NMR (500 MHz, Chloroform-*d*) δ 7.51 (d, $J = 8.3$ Hz, 1H), 7.47 (d, $J = 2.2$ Hz, 1H), 7.20 (dd, $J = 8.2, 2.2$ Hz, 1H), 2.99 – 2.86 (m, 2H), 2.71 – 2.60 (m, 1H), 2.06 (s, 3H), 1.66 (ddtd, $J = 10.3, 7.1, 5.3, 3.3$ Hz, 1H), 1.46 (ddt, $J = 13.3, 10.3, 5.4$ Hz, 1H), 1.36 – 1.18 (m, 4H), 0.92 – 0.83 (m, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 211.37, 144.67, 141.06, 139.20, 137.22, 99.84, 93.91, 52.01, 41.49, 31.26, 30.51, 29.14, 22.80, 13.88. HRMS (ESI+ TOF) Calcd for $\text{C}_{14}\text{H}_{18}\text{I}_2\text{O} + \text{H}^+$: 456.9520, found: 456.9518

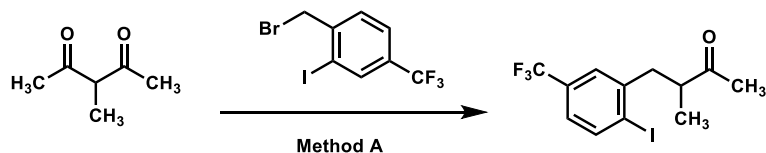


Scheme S16: Preparation of S13

3-(2-iodo-5-methylbenzyl)pentan-2-one (S13)

Prepared by Method A. Colorless oil. 263 mg isolated. 52% yield. ^1H NMR (500 MHz, Chloroform-*d*) δ 7.67 (d, $J = 8.1$ Hz, 1H), 6.96 (d, $J = 2.2$ Hz, 1H), 6.72 (dd, $J = 8.1, 2.2$ Hz, 1H), 3.00 – 2.84 (m, 2H), 2.70 (dd, $J = 12.5, 5.5$ Hz, 1H), 2.25 (s, 3H), 2.04 (s, 3H), 1.75 – 1.64 (m, 1H), 1.59 – 1.48 (m, 2H), 0.91 (t, $J = 7.5$ Hz, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 212.16, 141.87, 139.34, 138.24, 131.56,

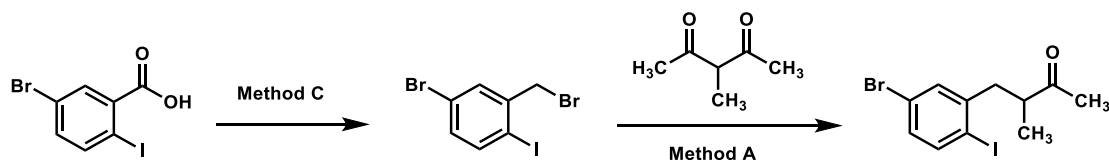
129.19, 96.42, 53.70, 41.67, 30.71, 24.46, 20.87, 11.59. HRMS (ESI+ TOF) Calcd for C₁₃H₁₇IO + H⁺: 317.0397, found: 317.0400



Scheme S17: Preparation of S14

4-(2-iodo-5-(trifluoromethyl)phenyl)-3-methylbutan-2-one (S14)

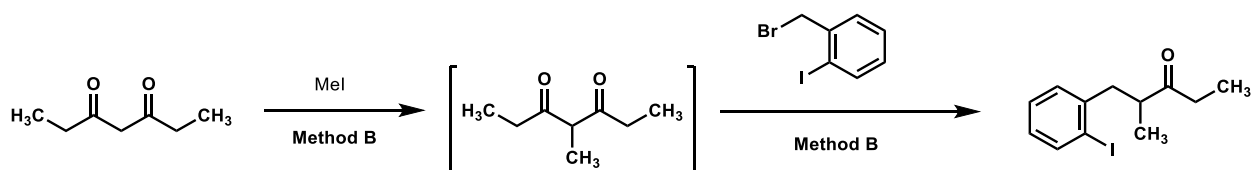
Ketone was prepared by Method A. Colorless oil, 430 mg isolated, 74% yield. ¹H NMR (600 MHz, Chloroform-*d*) δ 7.98 – 7.93 (m, 1H), 7.41 (d, *J* = 2.2 Hz, 1H), 7.15 (dd, *J* = 8.2, 2.2 Hz, 1H), 3.21 (dd, *J* = 13.8, 6.6 Hz, 1H), 2.96 (h, *J* = 7.1 Hz, 1H), 2.69 (dd, *J* = 13.8, 7.7 Hz, 1H), 2.16 (s, 3H), 1.14 (d, *J* = 7.1 Hz, 3H). ¹³C NMR (126 MHz, Chloroform-*d*) δ 210.76, 143.55, 140.67, 140.25, 130.78 (q, *J* = 32.7 Hz), 127.00 (q, *J* = 3.7 Hz), 124.68 (q, *J* = 3.7 Hz), 104.89, 46.59, 42.76, 28.90, 16.18. ¹⁹F NMR (282 MHz, Chloroform-*d*) δ -62.90. HRMS (ESI+ TOF) Calcd for C₁₂H₁₂F₃IO + H⁺: 356.9963, found: 356.9960



Scheme S18: Preparation of S15

4-(5-bromo-2-iodophenyl)-3-methylbutan-2-one (S15)

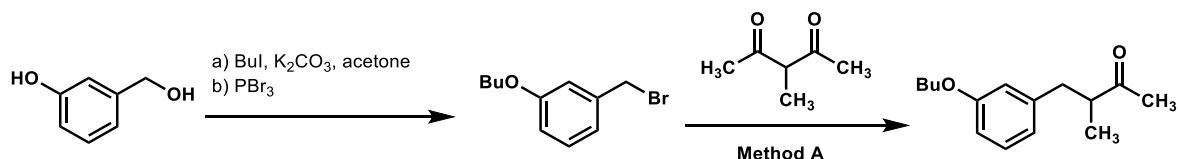
Benzyl bromide was prepared by Method C. White needles, 92% yield over two steps. Spectroscopic data matches previous report.⁴ Ketone was prepared by Method A. Purified by column chromatography in 19:1 hexanes:ethyl acetate. Colorless oil. 1.4 g, 72% yield. ¹H NMR (500 MHz, Chloroform-*d*) δ 7.66 (d, *J* = 8.4 Hz, 1H), 7.32 (d, *J* = 2.4 Hz, 1H), 7.04 (dd, *J* = 8.4, 2.4 Hz, 1H), 3.11 (dd, *J* = 13.7, 6.6 Hz, 1H), 2.93 (h, *J* = 7.0 Hz, 1H), 2.58 (dd, *J* = 13.7, 7.8 Hz, 1H), 2.16 (s, 3H), 1.13 (d, *J* = 7.1 Hz, 3H). ¹³C NMR (126 MHz, Chloroform-*d*) δ 210.95, 144.51, 140.81, 133.45, 131.30, 122.48, 98.57, 46.58, 42.60, 28.95, 16.11. HRMS (ESI+ TOF) Calcd for C₁₄H₁₉BrIO + H⁺: 366.9189, found: 366.9183



Scheme S19: Preparation of S16

1-(2-iodophenyl)-2-methylpentan-3-one (S16)

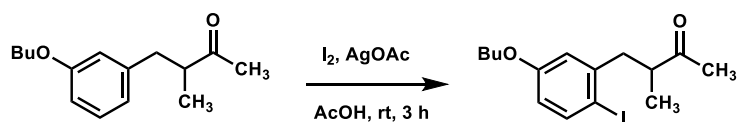
Dione prepared by Method B, and was carried through without purification, with the main contaminant being 3,5-heptanedione. 600 mg of the resulting oil was then subjected to Method A, and the ketone product with isolated by column chromatography in 9:1 hexanes:ethyl acetate. 804 mg isolated (94% yield). colorless oil. *R_f*: 0.5 in 9:1 hexanes:ethyl acetate. ¹H NMR (500 MHz, Chloroform-*d*) δ 7.82 (dd, *J* = 7.9, 1.3 Hz, 1H), 7.23 (dd, *J* = 7.4, 1.3 Hz, 1H), 7.14 (dd, *J* = 7.6, 1.8 Hz, 1H), 6.89 (td, *J* = 7.6, 1.8 Hz, 1H), 3.09 (dd, *J* = 13.3, 7.1 Hz, 1H), 3.00 (q, *J* = 7.0 Hz, 1H), 2.65 (dd, *J* = 13.4, 7.3 Hz, 1H), 2.47 (dd, *J* = 17.9, 7.2 Hz, 1H), 2.30 (dd, *J* = 17.8, 7.3 Hz, 1H), 1.56 (s, 1H), 1.10 (d, *J* = 6.9 Hz, 3H), 0.98 (t, *J* = 7.3 Hz, 3H). ¹³C NMR (126 MHz, Chloroform-*d*) δ 214.45, 142.32, 139.62, 130.79, 128.18, 128.16, 100.59, 45.56, 43.50, 35.38, 16.39, 7.60. HRMS (ESI+ TOF) Calcd for C₁₂H₁₅IO + H⁺: 303.0240, found: 303.0242



Scheme S20: Preparation of S17

4-(3-butoxyphenyl)-3-methylbutan-2-one (S17)

3-hydroxymethylphenol was subjected to conditions reported previously to furnish 3-butoxybenzyl alcohol.⁵ 5.2 g colorless oil isolated (75% yield) after purification by column chromatography in 2:1 hexanes:ethyl acetate. ¹H NMR (500 MHz, Chloroform-*d*) δ 7.32 – 7.23 (m, 1H), 6.94 (d, *J* = 1.8 Hz, 1H), 6.93 (s, 1H), 6.86 – 6.84 (m, 0H), 6.84 – 6.83 (m, 1H), 4.68 (d, *J* = 5.0 Hz, 2H), 3.99 (t, *J* = 6.5 Hz, 2H), 1.78 (dq, *J* = 8.1, 6.3, 5.9 Hz, 2H), 1.60 – 1.42 (m, 2H), 1.00 (t, *J* = 7.4 Hz, 3H). 3-butoxybenzyl alcohol was then subjected to bromination as described in Method C to furnish 3-butoxybenzyl bromide, a colorless oil (4g, 98% yield). ¹H NMR (400 MHz, Chloroform-*d*) δ 7.23 (d, *J* = 7.9 Hz, 1H), 6.96 (dt, *J* = 7.5, 1.3 Hz, 1H), 6.93 (t, *J* = 2.1 Hz, 1H), 6.83 (ddd, *J* = 8.3, 2.5, 1.0 Hz, 1H), 4.46 (s, 2H), 3.97 (t, *J* = 6.5 Hz, 2H), 1.85 – 1.70 (m, 2H), 1.61 – 1.40 (m, 2H), 0.98 (t, *J* = 7.4 Hz, 3H). 3-butoxybenzyl bromide and 3-methyl-2,4-pentanedione were then subjected to conditions from Method A to furnish ketone, which was purified by column chromatography in (9:1 hexanes:ethyl acetate). A colorless oil obtained, 2.6 g colorless oil, 90% yield. ¹H NMR (500 MHz, Chloroform-*d*) δ 7.18 (t, *J* = 7.9 Hz, 1H), 6.74 – 6.71 (m, 2H), 6.69 (t, *J* = 2.1 Hz, 1H), 3.94 (t, *J* = 6.5 Hz, 2H), 2.97 (dd, *J* = 13.5, 6.7 Hz, 1H), 2.83 (h, *J* = 7.0 Hz, 1H), 2.52 (dd, *J* = 13.6, 7.9 Hz, 1H), 2.10 (s, 3H), 1.80 – 1.70 (m, 2H), 1.53 – 1.42 (m, 2H), 1.09 (d, *J* = 7.0 Hz, 3H), 0.97 (t, *J* = 7.4 Hz, 3H). ¹³C NMR (126 MHz, Chloroform-*d*) δ 212.20, 159.19, 141.21, 129.32, 121.10, 115.27, 112.05, 67.54, 48.72, 38.93, 31.35, 28.88, 19.25, 16.25, 13.87. HRMS (ESI+ TOF) Calcd for C₁₅H₂₂O₂ + H⁺: 235.1693, found: 235.1692



Scheme S21: Preparation of S18

4-(5-butoxy-2-iodophenyl)-3-methylbutan-2-one (S18)

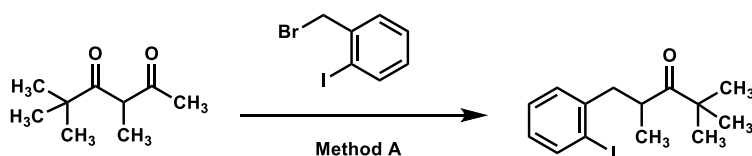
⁶Under N₂ atmosphere, AgOAc (1.07 g, 6.4 mmol, 1 equiv.) was added followed by portionwise addition of I₂ (1.62 g, 6.4 mmol, 1 equiv.) to a stirred solution of ketone (1.5 g, 6.4 mmol, 1 equiv.) at ambient temperature in AcOH (6.4 mL, 1 M). The reaction mixture was stirred for 3 h, after which AgI was filtered off by vacuum filtration through celite. The filter cake was washed with AcOH. The resultant AcOH solution was poured onto ice water, and a white precipitate was collected by vacuum filtration. The solid was dissolved in Et₂O, which was washed successively with water, 1 M NaOH, sat. Na₂S₂O₃, and then finally brine. The solvent was removed to furnish 2.3 g of a white solid, 99% yield. ¹H NMR (500 MHz, Chloroform-*d*) δ 7.65 (d, *J* = 8.7 Hz, 1H), 6.73 (d, *J* = 3.0 Hz, 1H), 6.51 (dd, *J* = 8.7, 3.0 Hz, 1H), 3.90 (t, *J* = 6.5 Hz, 2H), 3.07 (dd, *J* = 13.5, 6.6 Hz, 1H), 2.96 (h, *J* = 7.0 Hz, 1H), 2.57 (dd, *J* = 13.5, 7.8 Hz, 1H), 2.14 (s, 3H), 1.74 (dq, *J* = 8.8, 6.6 Hz, 2H), 1.53 – 1.41 (m, 2H), 1.11 (d, *J* = 7.0 Hz, 3H), 0.96 (t, *J* = 7.4 Hz, 3H); ¹³C NMR (126 MHz, Chloroform-*d*) δ 211.70, 159.33, 143.13, 139.91, 117.31, 114.76, 88.74, 67.79, 46.68, 43.16, 31.17, 29.12, 19.17, 16.02, 13.83. HRMS (ESI+ TOF) Calcd for C₁₅H₂₁IO₂ + H⁺: 361.0659, found: 361.0661



Scheme S22: Preparation of S19

3,5,5-trimethylhexane-2,4-dione (S19)

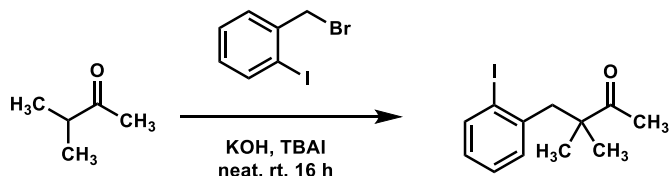
Methylated diketone was prepared by a modification of Method B. 3 equiv. iodomethane and K_2CO_3 were used in 0.7 M acetone over a reaction time of 2 days. A colorless oil was obtained after column chromatography in 9:1 hexanes:ethyl acetate. 436 mg colorless oil isolated (80% yield). 1H NMR (400 MHz, Chloroform-*d*) δ 4.07 (q, $J = 7.0$ Hz, 1H), 2.15 (s, 3H), 1.32 (d, $J = 6.9$ Hz, 3H), 1.18 (s, 9H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 212.49, 205.07, 55.34, 45.57, 27.49, 26.07, 15.20. HRMS (ESI+ TOF) Calcd for $C_9H_{16}O_2 + H^+$: 157.1223, found: 157.1226



Scheme S23: Preparation of S20

1-(2-iodophenyl)-2,4,4-trimethylpentan-3-one (S20)

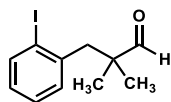
Prepared by Method A. 272 mg isolated (62% yield). A 19% yield of the methyl ketone was also isolated after chromatography. Yellow oil. R_f : 0.2 in 19:1 hexanes:ethyl acetate. 1H NMR (500 MHz, Chloroform-*d*) δ 7.78 (dd, $J = 7.9, 1.4$ Hz, 1H), 7.20 (td, $J = 7.4, 1.3$ Hz, 1H), 7.09 (dd, $J = 7.6, 1.8$ Hz, 1H), 6.86 (td, $J = 7.6, 1.8$ Hz, 1H), 3.68 – 3.27 (m, 1H), 3.02 (dd, $J = 13.2, 9.1$ Hz, 1H), 2.73 (dd, $J = 13.2, 5.7$ Hz, 1H), 1.54 (s, 1H), 1.10 (d, $J = 6.8$ Hz, 3H), 0.91 (s, 7H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 218.79, 142.52, 139.45, 131.24, 128.16, 128.12, 100.70, 44.66, 44.61, 39.50, 25.60, 18.93. HRMS (ESI+ TOF) Calcd for $C_{14}H_{19}IO + H^+$: 331.0553, found: 331.0556



Scheme S24: Preparation of S21

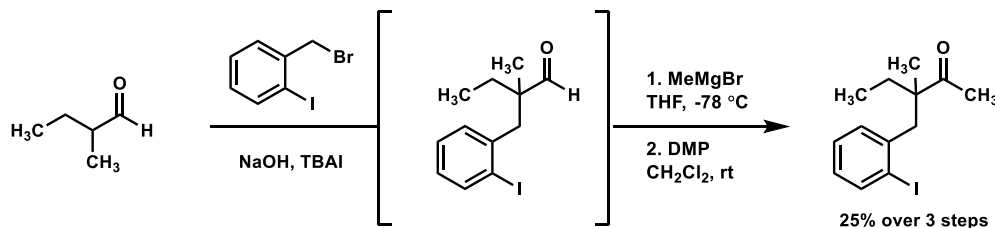
4-(2-iodophenyl)-3,3-dimethylbutan-2-one (S21)

Prepared by a similar reaction reported elsewhere.⁷ Under air, a round-bottomed flask was charged with methyl isopropyl ketone, (4 g, 45 mmol), 2-bromomethyliodobenzene (5.5 g, 18.5 mmol), tetrabutylammonium iodide (2.06 g, 5.6 mmol), and powdered potassium hydroxide (3.14 g, 56 mmol) and a stir bar. The reaction was stirred vigorously for 16 hours and then water and diethyl ether were added. The mixture was separated, and the aqueous layer was extracted twice more with diethyl ether. The organic fractions were collected, washed with brine, and then dried with anhydrous sodium sulfate. The solution was decanted, and the solvent was removed under reduced pressure. The product was then isolated by purification with column chromatography in 9:1 hexanes:ethyl acetate. R_f 0.3. 700 mg colorless oil, 41% yield. 1H NMR (500 MHz, Chloroform-*d*) δ 7.85 (d, $J = 8.9$ Hz, 1H), 7.23 (d, $J = 8.3$ Hz, 1H), 7.11 (d, $J = 7.7$ Hz, 1H), 6.89 (t, $J = 8.4$ Hz, 1H), 3.09 (s, 2H), 2.19 (s, 3H), 1.19 (s, 6H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 213.80, 141.18, 139.97, 130.44, 128.19, 128.03, 103.17, 49.55, 47.46, 26.02, 24.34. HRMS (ESI+ TOF) Calcd for $C_{12}H_{15}IO + H^+$: 303.0240, found: 303.0237



3-(2-iodophenyl)-2,2-dimethylpropanal (S22)

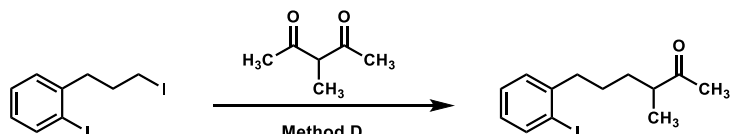
S22 was prepared as previously and matched spectroscopically.⁸



Scheme S25: Preparation of S23

3-(2-iodobenzyl)-3-methylpentan-2-one (S23)

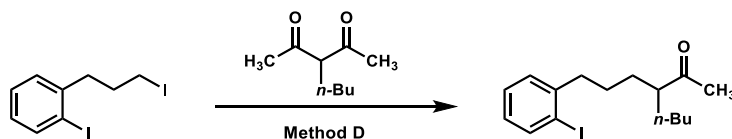
S23 was prepared as per described for **US7** (480 mg, 25% yield over three steps). ¹H NMR (500 MHz, CDCl₃) δ 7.86 (dd, *J* = 7.9, 1.3 Hz, 1H), 7.25 (td, *J* = 7.5, 1.3 Hz, 1H), 7.10 (dd, *J* = 7.8, 1.7 Hz, 1H), 6.89 (td, *J* = 7.6, 1.7 Hz, 1H), 3.24 (d, *J* = 14.2 Hz, 1H), 2.99 (d, *J* = 14.2 Hz, 1H), 2.18 (s, 3H), 1.89 (dq, *J* = 14.8, 7.5 Hz, 1H), 1.56 (dq, *J* = 13.7, 7.5 Hz, 1H), 1.14 (s, 3H), 0.87 (t, *J* = 7.5 Hz, 3H). ¹³C NMR (126 MHz, CDCl₃) δ 213.69, 141.25, 139.93, 130.19, 128.12, 128.10, 103.38, 53.49, 46.48, 31.93, 26.61, 19.70, 8.96. HRMS (ESI+ TOF) Calcd for C₁₃H₁₇IO + H⁺: 317.0402, found: 317.0399



Scheme S26: Preparation of 9a

6-(2-iodophenyl)-3-methylhexan-2-one (9a)

3-(2'-Iodophenyl)propyl iodide was prepared by Method C and NMR spectroscopy matches previous report.⁹ **9a** was then prepared by Method D. 47 mg isolated (46% yield). Colorless oil. *R_f* 0.5 in 9:1 pentane:ethyl acetate. ¹H NMR (500 MHz, Chloroform-*d*) δ 7.93 – 7.87 (m, 1H), 7.36 (t, *J* = 7.5 Hz, 1H), 7.29 (dd, *J* = 7.7, 1.8 Hz, 1H), 6.98 (td, *J* = 7.6, 1.8 Hz, 1H), 2.80 (dh, *J* = 13.7, 6.9 Hz, 2H), 2.66 (h, *J* = 6.8 Hz, 1H), 2.24 (s, 3H), 1.86 (ddt, *J* = 13.4, 9.3, 6.5 Hz, 1H), 1.75 – 1.59 (m, 2H), 1.54 (ddt, *J* = 13.0, 10.1, 6.3 Hz, 1H), 1.21 (d, *J* = 7.0 Hz, 3H). ¹³C NMR (126 MHz, CDCl₃) δ 212.63, 144.13, 139.49, 129.35, 128.36, 127.77, 100.54, 47.01, 40.78, 32.38, 28.11, 27.89, 16.31. HMRS (EI-TOF) Calcd for C₁₃H₁₇IO [M⁺]: 316.0319, found: 316.0309.

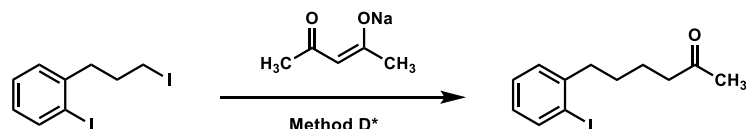


Scheme S27: Preparation of 9b

3-(3-(2-iodophenyl)propyl)heptan-2-one (9b)

2-(2'-Iodophenyl)propyl iodide was prepared by Method C and NMR spectroscopy matches previous report.⁹ **9b** was then prepared by Method D. 55 mg isolated (55% yield). Colorless oil. *R_f* 0.5 in 9:1 pentane:ethyl acetate. ¹H NMR (500 MHz, Chloroform-*d*) δ 7.81 (d, *J* = 7.9 Hz, 1H), 7.27 (t, *J* = 7.3 Hz, 1H), 7.19 (d, *J* = 8.0 Hz, 1H), 6.88 (t, *J* = 7.7 Hz, 1H), 2.71 (t, *J* = 7.0 Hz, 2H), 2.50 (dd, *J* = 8.6, 4.7 Hz,

1H), 2.14 (s, 3H), 1.71 (q, $J = 12.9, 11.8$ Hz, 1H), 1.60 (dt, $J = 19.9, 9.4$ Hz, 1H), 1.46 (q, $J = 8.4, 7.8$ Hz, 1H), 1.28 (ddq, $J = 32.7, 15.7, 8.1$ Hz, 6H), 0.90 (t, $J = 7.2$ Hz, 4H). ^{13}C NMR (126 MHz, CDCl_3) δ 212.83, 144.59, 139.48, 129.34, 128.35, 127.76, 100.55, 53.08, 40.83, 31.38, 31.13, 29.54, 28.78, 28.08, 22.82, 13.96. HRMS (EI-TOF) Calcd for $\text{C}_{16}\text{H}_{23}\text{IO}$ [M^+]: 358.0794, found: 358.0779.

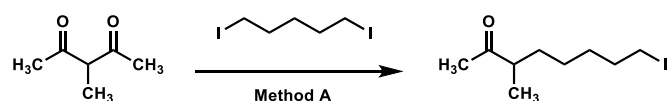


Scheme S28: Preparation of 9c

3-(2-iodophenethyl)heptan-2-one (9c)

Prepared by modified Method D. Under an atmosphere of N_2 , an oven-dried round bottom flask was charged with sodium acetylacetonate (87 mg, 0.71 mmol, 1.2 equiv, purchased and then dried overnight in vacuum oven at 100°C), alkyl iodide (220 mg, 0.59 mmol, 1.0 equiv), and 3 mL anhydrous DMSO. The reaction mixture was brought to 85°C and stirred until the alkyl iodide was consumed (monitored by TLC), typically less than an hour. KOH (100 mg, 1.8 mmol, 3.0 equiv) was then added as a solid followed by 3 mL ethanol. After 3 hours, water was added and the aqueous portion was extracted with ethyl acetate, dried with brine and MgSO_4 , and concentrated *in vacuo*. The residue was purified by column chromatography on silica using EtOAc/hexane as eluent. 51 mg isolated (29% yield). Slightly yellow oil. R_f 0.25 in 19:1 hexane:ethyl acetate. ^1H NMR (500 MHz, CDCl_3) δ 7.82 (dd, $J = 7.9, 1.3$ Hz, 1H), 7.32 – 7.25 (m, 1H), 7.22 (dd, $J = 7.6, 1.8$ Hz, 1H), 6.89 (td, $J = 7.5, 1.8$ Hz, 1H), 2.78 – 2.70 (m, 2H), 2.51 (t, $J = 7.3$ Hz, 2H), 2.17 (s, 3H), 1.78 – 1.65 (m, 2H), 1.65 – 1.55 (m, 2H). ^{13}C NMR (126 MHz, CDCl_3) δ 208.93, 144.69, 139.48, 129.38, 128.35, 127.74, 100.55, 43.51, 40.61, 29.98, 29.73, 23.43. HRMS (ESI-TOF) Calcd for $\text{C}_{12}\text{H}_{15}\text{IO} + \text{H}^+$: 303.02403, found: 303.02406.

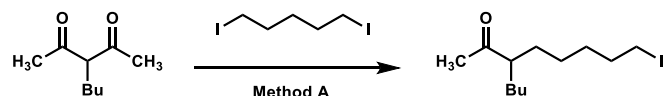
US1, US2, US3, and US4 were prepared by method A by use of 1,5-diiodopentane and 1,3-diiodopropane as electrophiles.



Scheme S29: Preparation of US1

8-iodo-3-methyloctan-2-one (US1)

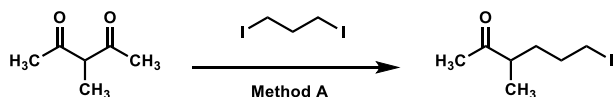
Prepared by Method A. Colorless oil. 190 mg isolated (25% yield). The low yield manifests an inefficient purification. Purified in 20:1 hexanes:ethyl acetate. ^1H NMR (500 MHz, Chloroform-*d*) δ 3.17 (t, $J = 7.0$ Hz, 2H), 2.43 (tt, $J = 8.3, 5.6$ Hz, 1H), 2.12 (s, 3H), 1.80 (p, $J = 7.1$ Hz, 2H), 1.64 – 1.56 (m, 2H), 1.46 – 1.34 (m, 4H), 1.33 – 1.15 (m, 6H), 0.88 (t, $J = 7.2$ Hz, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 212.97, 53.11, 33.20, 31.42, 31.32, 30.54, 29.55, 28.75, 26.35, 22.78, 13.91, 7.00. HRMS (ESI+ TOF) Calcd for $\text{C}_9\text{H}_{17}\text{IO} + \text{H}^+$: 269.0402, found: 269.0402



Scheme S30: Preparation of US2

3-butyl-8-iodooctan-2-one (US2)

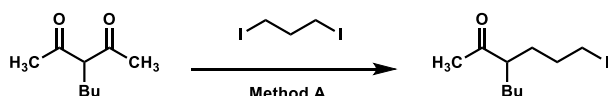
Prepared by Method A. Colorless oil. 135 mg isolated (20% yield). The low yield manifests an inefficient purification. Purified in 20:1 hexanes:ethyl acetate. ^1H NMR (300 MHz, Chloroform-*d*) δ 3.18 (t, $J = 7.0$ Hz, 2H), 2.50 (h, $J = 6.8$ Hz, 1H), 2.13 (s, 3H), 1.82 (p, $J = 7.0$ Hz, 2H), 1.68 (ddd, $J = 12.1, 8.3, 5.8$ Hz, 1H), 1.47 – 1.20 (m, 6H), 1.09 (d, $J = 7.0$ Hz, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 212.75, 47.04, 33.21, 32.55, 30.47, 28.07, 26.12, 16.27, 7.00. HRMS (ESI+ TOF) Calcd for $\text{C}_{12}\text{H}_{23}\text{IO} + \text{H}^+$: 311.0872, found: 311.0871



Scheme S31: Preparation of US3

6-iodo-3-methylhexan-2-one (US3)

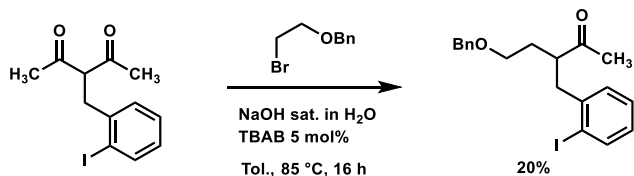
Prepared by Method A. Colorless oil. 27 mg isolated (5% yield). Purified in 20:1 hexanes:ethyl acetate. The low yield manifests an inefficient purification. ^1H NMR (300 MHz, Chloroform-*d*) δ 3.26 – 3.07 (m, 2H), 2.53 (h, $J = 6.7$ Hz, 1H), 2.15 (s, 3H), 1.87 – 1.67 (m, 3H), 1.55 – 1.38 (m, 1H), 1.11 (d, $J = 7.0$ Hz, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 212.01, 46.18, 33.39, 30.95, 28.05, 16.30, 6.32. HRMS (ESI+ TOF) Calcd for $\text{C}_7\text{H}_{13}\text{IO} + \text{H}^+$: 241.0089, found: 241.0089



Scheme S32: Preparation of US4

3-(3-iodopropyl)heptan-2-one (US4)

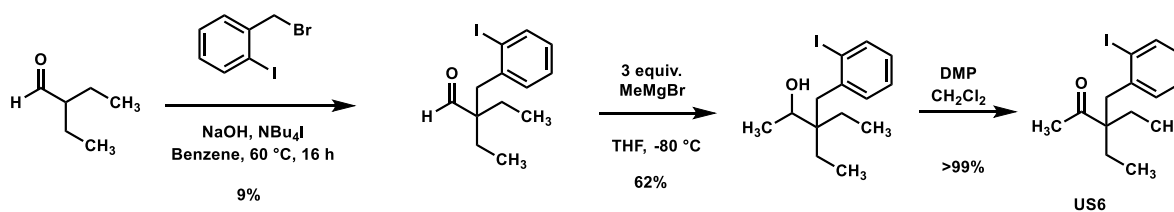
Prepared by Method A. Colorless oil. 47 mg isolated (8% yield). The low yield manifests an inefficient purification. Purified in 20:1 hexanes:ethyl acetate. ^1H NMR (300 MHz, Chloroform-*d*) δ 3.16 (t, $J = 6.6$ Hz, 2H), 2.55 – 2.38 (m, 1H), 2.13 (s, 3H), 1.86 – 1.12 (m, 12H), 0.89 (t, $J = 7.0$ Hz, 4H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 212.24, 52.16, 32.00, 31.27, 29.40, 28.66, 22.74, 13.88, 6.41. HRMS (ESI+ TOF) Calcd for $\text{C}_{10}\text{H}_{19}\text{IO} + \text{H}^+$: 283.0559, found: 283.0556



Scheme S33: Preparation of US5

5-(benzyloxy)-3-(2-iodobenzyl)pentan-2-one (US5)

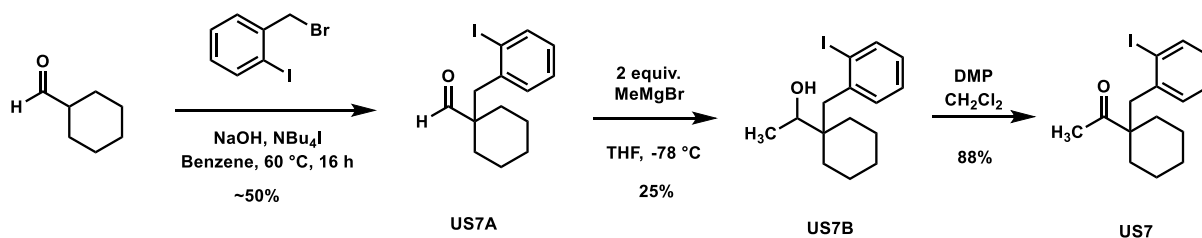
Prepared by Method A from S9. 98 mg colorless oil, 18% yield. Purified gradient 19:1 to 9:1 hexanes:ethyl acetate. ^1H NMR (500 MHz, Chloroform-*d*) δ 7.85 – 7.80 (m, 1H), 7.37 – 7.27 (m, 5H), 7.25 – 7.20 (m, 1H), 7.14 (dd, $J = 7.7, 1.7$ Hz, 1H), 6.90 (td, $J = 7.6, 1.7$ Hz, 1H), 4.43 (d, $J = 2.7$ Hz, 2H), 3.54 – 3.40 (m, 2H), 3.15 (qd, $J = 8.2, 7.8, 4.9$ Hz, 1H), 3.01 (dd, $J = 13.6, 7.9$ Hz, 1H), 2.75 (dd, $J = 13.6, 6.9$ Hz, 1H), 2.08 – 2.01 (m, 1H), 2.00 (s, 3H), 1.75 (dq, $J = 14.1, 5.5$ Hz, 1H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 211.75, 141.78, 139.73, 138.17, 130.74, 128.35, 128.31, 127.68, 127.57 (overlap in aromatic region), 100.56, 72.88, 68.04, 49.30, 42.60, 31.36, 30.79. HRMS (ESI+ TOF) Calcd for $\text{C}_{19}\text{H}_{21}\text{IO}_2 + \text{H}^+$: 409.0665, found: 409.0666.



Scheme S34: Preparation of US6

3-ethyl-3-(2-iodobenzyl)pentan-2-one (US6)

US6 was prepared in the same fashion as US7. ¹H NMR (500 MHz, Chloroform-*d*) δ 7.84 (dd, *J* = 8.0, 1.3 Hz, 1H), 7.22 (td, *J* = 7.5, 1.3 Hz, 1H), 7.05 (dd, *J* = 7.9, 1.7 Hz, 1H), 6.87 (td, *J* = 7.6, 1.7 Hz, 1H), 3.06 (s, 2H), 2.13 (s, 3H), 1.70 (ddq, *J* = 29.3, 14.7, 7.3 Hz, 4H), 0.80 (t, *J* = 7.5 Hz, 6H). ¹³C NMR (126 MHz, Chloroform-*d*) δ 213.40, 140.79, 139.99, 129.56, 128.05, 128.01, 103.06, 56.14, 44.39, 26.66, 25.83, 8.52. HRMS (ESI+ TOF) Calcd for C₁₅H₁₉IO + H⁺: 331.0559, found: 331.0560



Scheme S35: Preparation of US7

1-(1-(2-iodobenzyl)cyclohexyl)ethan-1-one (US7)

NaOH (640 mg, 16 mmol) and tetrabutylammonium iodide (60 mg, 1 mol%) were combined with 2 mL benzene and stirred at 60 °C. Cyclohexanecarbaldehyde (1.8 g, 16 mmol) and 2-bromomethyl iodobenzene was dissolved in a minimum amount of benzene, and this mixture was added slowly to the stirred mixture of NaOH and NBu₄I. The mixture was stirred for 16 hours at 60 °C. After cooling to room temperature, the reaction was diluted with water and hexanes. The aqueous layer was extracted with hexanes two times. The collected hexanes fractions were washed with brine and then dried with anhydrous sodium sulfate. After decanting the hexanes layer, the solvent was removed under reduced pressure. The product was then purified by column chromatography in 20:1 hexanes:ethyl acetate. 2.7 g beige oil (<50% yield) was isolated but significant amount of 2-bromomethyl iodobenzene contaminated the sample. The benzylated aldehyde US7A (1.0 g, ~3 mmol) was then dissolved in 15 mL dry THF under nitrogen atmosphere with stirring. The mixture was cooled to -78 °C by means of a dry ice/acetone bath. MeMgBr (1.2 mL, 3 M in Et₂O) was then added in a dropwise fashion. After 1 hour stirring at -78 °C, 1 mL MeMgBr (3 M in Et₂O) was added. After an additional 45 minutes stirring, the reaction mixture was quenched with 30 mL saturated NH₄Cl (aq). This mixture was extracted three times with ethyl acetate, the organic fractions were combined and washed with brine, and then dried with anhydrous sodium sulfate. The product was purified by column chromatography 9:1 hexanes:ethyl acetate (*R_F* 0.2). 170 mg of the secondary alcohol was isolated with some impurities (~25% yield). US7B (170 mg, ~0.5 mmol) was dissolved in dry CH₂Cl₂ (10 mL) with stirring under nitrogen atmosphere. Dess-Martin periodinane (300 mg, 0.7 mmol) was then added in one portion. After stirring for one hour, the reaction was quenched with 20 mL saturated sodium thiosulfate (aq). The layers were separated, then the aqueous layer was extracted twice with 20 mL CH₂Cl₂. The organic fractions were combined and washed with brine, and then dried with anhydrous sodium sulfate. The product was purified by column chromatography 9:1 hexanes:ethyl acetate (*R_F* 0.5). 150 mg of the ketone was isolated, a colorless oil (~88% yield). ¹H NMR (500 MHz, Chloroform-*d*) δ 7.84 (d, *J* = 7.9 Hz, 1H), 7.23 (d, *J* = 7.6 Hz, 1H), 7.05 (dd, *J* = 7.8, 1.7 Hz, 1H), 6.89 (td, *J* = 7.7, 1.7 Hz, 1H), 2.96 (s, 2H), 2.19 (s, 3H), 2.17 (d, *J* = 13.6 Hz, 2H), 1.67 – 1.56 (m, 2H), 1.37 (td, *J* = 12.6, 3.5 Hz, 2H), 1.18 (tdt, *J* = 23.5, 15.4, 5.8 Hz, 3H). ¹³C

NMR (126 MHz, Chloroform-*d*) δ 213.03, 140.12, 139.95, 130.75, 128.26, 127.84, 102.96, 54.28, 48.54, 33.10, 26.41, 25.62, 23.31. HRMS (ESI+ TOF) Calcd for C₁₅H₁₉IO + H⁺: 343.0559, found: 343.0555

Procedure for Pd catalyzed C-H Arylative Ring Closure with a TDG

Under air, a 16 x 100 mm screw thread culture tube was charged ketone starting material (0.1 mmol) by syringe. Glycine (0.05 mmol, 3.7 mg or 0.1 mmol, 7.5 mg; 0.05 mmol glycine (50 mol%) is indicated for the 1° methyl substrate C-H arylation protocol. 0.1 mmol glycine (100 mol%) is indicated for the 2° methyl substrate C-H arylation protocol), Pd(OAc)₂ (0.01 mmol, 2.2 mg), Ag₃PO₄ (21 mg, 0.05 mmol), and substituted 2-hydroxypyridine ligand **L9** or **L10** (0.08 mmol) were then added. A stir bar was then added. HFIP (2.5 mL) and then TFA (12 μ L, 0.15 mmol) were added. The tube was sealed with a teflon septum lined screw cap and placed in a heating block at 110° C or 150° C (110° C is indicated for the 1° methyl substrate C-H arylation protocol. 150° C is indicated for the 2° methyl substrate C-H arylation protocol). To obtain aryl ether products **8d** and **14**, the 2-pyridone ligand was omitted and the solvent used was 3:1 HFIP:AcOH; see purification and characterization section for more details. The reaction mixture was stirred vigorously (600 rpm) at these temperatures for 36 hours.

Isolation workup: After allowing the reaction to cool to room temperature, 1 mL CHCl₃ was added, after which the reaction mixture was filtered through celite, washing with CHCl₃. Solvent was then removed from the filtrate by distillation under reduced pressure. The residue was purified by preparatory plate chromatography (typically with 19:1 hexanes:ethyl acetate as the mobile phase).

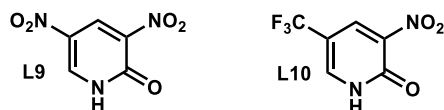


Figure S11. Structures of **L9** and **L10**

Scale-up Procedure

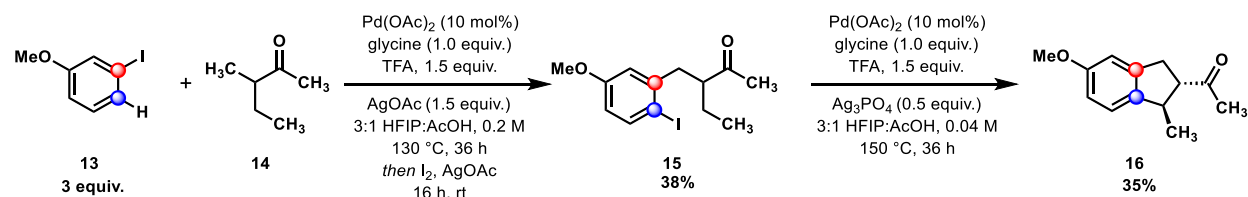
The reaction was performed as described in Procedure for Pd catalyzed C-H Arylative Ring Closure with a TDG (S.I. page 21), however, the reaction was performed on 1 mmol scale in a sealed, thick-walled glass bomb using **L9** as ligand. After filtration through celite and solvent removal by rotary evaporation, substituted indane product **7a** was purified by column chromatography in 19:1 hexanes:ethyl acetate. 173 mg beige oil isolated. 86% yield.

Screening Workflow

The screening reactions were run as indicated on 0.1 mmol scale (Procedure for Pd catalyzed C-H Arylative Ring Closure with a TDG). Workup and analysis are as follows. After allowing the reaction to cool to room temperature, 0.5 mL of 0.2 M stock solution of NMR internal standard 1,3,5-trimethoxybenzene in CHCl₃ was added to the reaction mixture. The mixture was stirred for five minutes to ensure mixing. The reaction mixture was then filtered through celite. Solvent was then removed from the filtrate by distillation under reduced pressure. The residue was dissolved in CDCl₃ and analyzed by ¹H NMR spectroscopy. The yield was determined by integrating the 1,3,5-trimethoxybenzene aromatic H signal of the standard at 6.08 ppm and comparing it with the integration of the cyclic methine H pentet signal of the analytes in the 3.42-3.47 ppm region for compound **2**. NMR spectroscopically determined yields of the protodeiodinated products were determined by matching with known literature spectra,^{10,11} and these were confirmed by resynthesis using Method A. For yield of the protodeiodinated compound **3** (see paper) the quartet at 2.54-2.59 ppm was integrated. For screening of the methylene product **5**, yield the major diastereomer was determined by NMR spectroscopy. Integration of the pentet at 3.46-3.51 ppm was used to determine the yield of **5** as the

major *trans* diastereomer. Integration of the pentet at 3.59-3.63 ppm enabled determination of the minor *cis* diastereomer of **5** as indicated by previous reports of this diastereomer.¹² Our assignments for this compound agree with ¹H NMR spectroscopic data from previous reports of diastereomeric mixtures of this compound.¹³ **5** and **7a** were characterized by 2D NMR spectroscopic techniques as reported in section 2D NMR Analysis (page 89). For all other diastereomeric mixtures, the configurations were assigned by analogy. Mixtures of diastereomers of all the reported compounds were inseparable by preparatory plate chromatography, as previously reported for **5**.¹³

Formal [3+2] Cyclization by double C-H arylation



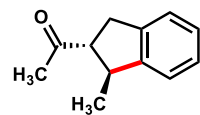
Scheme S36: Process for Annulation by Sequential C-H Arylation. TFA = trifluoroacetic acid; HFIP = hexafluoroisopropanol

One Pot telescoped process to **15**:

Under air, a 16 x 100 mm screw thread culture tube was charged 3-methyl-pentan-2-one (0.4 mmol) by syringe. Glycine (0.4 mmol, 30 mg), Pd(OAc)₂ (0.04 mmol, 8.8 mg), and AgOAc (0.6 mmol, 100 mg), and 3-iodoanisole (1.2 mmol, 281 mg) were then added. A stir bar was then added. 3:1 HFIP:AcOH (2.0 mL) and then TFA (48 μL, 0.6 mmol) were added. The tube was sealed with a teflon septum lined screw cap and placed in a heating block at 130 °C. The reaction mixture was stirred vigorously (600 rpm) at these temperatures for 36 hours. After 36 hours, the reaction vessel was removed from the heating block and allowed to cool to room temperature. While stirring at ambient temperature, AgOAc (67 mg, 0.4 mmol) and I₂ (0.4 mmol, 102 mg) were then added. The reaction mixture was then stirred for 16 hours, after which the reaction mixture was quenched with 1 mL CHCl₃, stirred briefly, and then filtered through celite, washing with CHCl₃. Solvent was then removed from the filtrate by distillation under reduced pressure. The residue was purified by preparatory plate chromatography in 19:1 hexanes:ethyl acetate to furnish **15**. See Data for [3+2] Cyclization Reactions, page 30 for purification, yield, and characterization data.

Purification and characterization data for C-H arylation ring closure products **5**, **7a-k**, **2**, **8a-d**, **13**, and **14**:

2° C-H functionalization

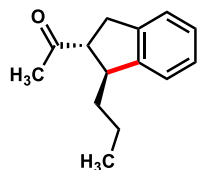


1-(1-methyl-2,3-dihydro-1H-inden-2-yl)ethan-1-one (**5**)

Preparatory TLC plate developed twice in 19:1 hexanes:ethyl acetate. Fraction 2 (of 4), *R_f* ~0.3 (after two runs). 15 mg residue isolated, 86% yield using L9 as ligand. ¹H NMR (500 MHz, Chloroform-*d*) δ 7.19 (m, 4H), 3.50 (p, *J* = 6.9 Hz, 1H), 3.21 (dd, *J* = 15.5, 8.8 Hz, 1H), 3.09 (dd, *J* = 15.5, 9.1 Hz, 1H), 3.00 (q, *J* =

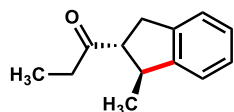
8.8 Hz, 1H), 2.27 (s, 3H), 1.38 (d, $J = 6.9$ Hz, 3H). ^{13}C NMR (126 MHz, Chloroform- d) δ 209.51, 146.45, 140.56, 126.81, 126.73, 124.23, 123.28, 61.06, 41.49, 34.86, 29.21, 19.58. HRMS (EI-TOF) Calcd for $\text{C}_{12}\text{H}_{14}\text{O}$ [M^+]: 174.1039, found: 174.1041

For assignment of the *trans* stereochemistry, see 2D NMR Analysis section. The minor *cis* isomer matches previous reports.¹² This data matches previous report with ^1H spectroscopic data for mixtures of the diastereomers.¹³



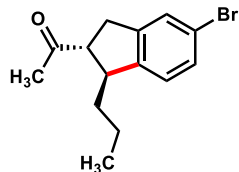
1-(1-propyl-2,3-dihydro-1H-inden-2-yl)ethan-1-one (7a)

Preparatory TLC plate developed twice in 19:1 hexanes:ethyl acetate. Fraction 1 (of 1), $R_f \sim 0.3$ (after two runs). 14 mg residue isolated, 69% yield using L9 as ligand. 14.5 mg residue isolated, 72% yield using L10 as ligand. ^1H NMR (500 MHz, Chloroform- d) δ 7.18 (m, 4H), 3.53 (s, 1H), 3.22 (s, 1H), 3.10 (s, 2H), 2.23 (s, 3H), 1.80 (s, 1H), 1.54 (s, 1H), 1.39 (s, 2H), 0.96 (d, $J = 7.3$ Hz, 3H). ^{13}C NMR (126 MHz, Chloroform- d) δ 209.78, 126.76, 126.65, 124.29, 123.91, 57.90, 46.84, 37.65, 34.89, 28.50, 20.39, 14.31. HRMS (EI-TOF) Calcd for $\text{C}_{14}\text{H}_{18}\text{O}$ [M^+]: 202.1352, found: 202.1356



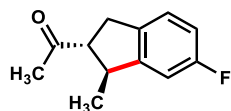
1-(1-methyl-2,3-dihydro-1H-inden-2-yl)propan-1-one (7b)

Preparatory TLC plate developed twice in 19:1 hexanes:ethyl acetate. Fraction 1 (of 2), $R_f \sim 0.5$ (after two runs). 8.5 mg residue isolated, 45% yield using L9 as ligand. 8 mg residue isolated, 42% yield using L10 as ligand. ^1H NMR (500 MHz, Chloroform- d) δ 7.24 – 7.13 (m, 5H), 3.51 (p, $J = 7.0$ Hz, 1H), 3.18 (dd, $J = 15.1, 8.5$ Hz, 1H), 3.11 – 2.97 (m, 2H), 2.64 – 2.50 (m, 2H), 1.36 (d, $J = 6.8$ Hz, 3H), 1.12 (t, $J = 7.3$ Hz, 3H). ^{13}C NMR (126 MHz, Chloroform- d) δ 212.19, 146.54, 140.75, 126.76, 126.68, 124.18, 123.22, 60.19, 41.70, 35.46, 35.21, 19.45, 7.79. HRMS (EI-TOF) Calcd for $\text{C}_{13}\text{H}_{16}\text{O}$ [M^+]: 188.1196, found: 188.1194



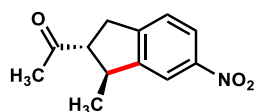
1-(5-bromo-1-propyl-2,3-dihydro-1H-inden-2-yl)ethan-1-one (7c)

Preparatory TLC plate developed twice in 19:1 hexanes:ethyl acetate. Fraction 1 (of 3), $R_f \sim 0.6$ (after two runs). 26 mg residue isolated, 93% yield using L9 as ligand. ^1H NMR (400 MHz, Chloroform- d) δ 7.26 (dd, $J = 14.0, 6.0$ Hz, 2H), 7.00 (d, $J = 8.0$ Hz, 1H), 3.46 – 3.39 (m, 1H), 3.16 (dd, $J = 14.0, 7.5$ Hz, 1H), 3.12 – 2.98 (m, 2H), 2.19 (s, 3H), 1.71 (m, 1H), 1.56 – 1.44 (m, 1H), 1.42 – 1.25 (m, 2H), 0.92 (t, $J = 7.3$ Hz, 3H). ^{13}C NMR (126 MHz, Chloroform- d) δ 209.06, 144.58, 143.26, 129.70, 127.44, 125.44, 120.38, 57.57, 46.43, 37.54, 34.41, 28.57, 20.26, 14.23. HRMS (EI-TOF) Calcd for $\text{C}_{14}\text{H}_{17}\text{BrO}$ [M^+]: 280.0457, found: 280.0457



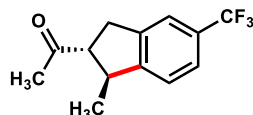
1-(6-fluoro-1-methyl-2,3-dihydro-1H-inden-2-yl)ethan-1-one (7d)

Preparatory TLC plate developed twice in 19:1 hexanes:ethyl acetate. Fraction 2 (of 3), R_f ~0.3 (after two runs). 10 mg residue isolated, 53% yield using L9 as ligand. 8.5 mg residue isolated, 53% yield using L10 as ligand. ^1H NMR (500 MHz, Chloroform-*d*) δ 7.13 – 7.07 (m, 1H), 6.85 (t, J = 8.3 Hz, 2H), 3.49 (p, J = 7.0 Hz, 1H), 3.22 – 3.11 (m, 1H), 3.08 – 2.97 (m, 2H), 2.26 (s, 3H), 1.34 (d, J = 6.9 Hz, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 208.96, 162.48 (d, J = 243.4 Hz), 148.77 (d, J = 7.5 Hz), 135.72 (d, J = 2.4 Hz), 125.12 (d, J = 8.8 Hz), 113.60 (d, J = 22.5 Hz), 110.44 (d, J = 22.2 Hz), 61.36, 41.40 (d, J = 2.1 Hz), 34.13, 29.22, 19.43. ^{19}F NMR (282 MHz, Chloroform-*d*) δ -116.55. HRMS (EI-TOF) Calcd for $\text{C}_{12}\text{H}_{13}\text{FO}$ [M^{++}]: 192.0945, found: 192.0945



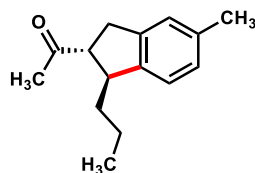
1-(1-methyl-6-nitro-2,3-dihydro-1H-inden-2-yl)ethan-1-one (7e)

Run on 0.046 mmol scale. Preparatory TLC plate developed three times in 9:1 hexanes:ethyl acetate. Fraction 1 (of 3), R_f ~0.4 (after three runs). 4 mg residue isolated, 40% yield using L9 as ligand. ^1H NMR (400 MHz, Chloroform-*d*) δ 8.06 (d, J = 8.2 Hz, 1H), 8.00 (s, 1H), 7.31 (d, J = 8.1 Hz, 1H), 3.56 (p, J = 6.8 Hz, 1H), 3.34 – 3.05 (m, 3H), 2.29 (s, 3H), 1.44 (d, J = 6.8 Hz, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 208.02, 148.43, 148.30, 147.72, 147.72, 124.77, 122.70, 118.72, 60.66, 41.40, 34.62, 29.46, 19.55. Calcd for $\text{C}_{12}\text{H}_{13}\text{NO}_3$ [M^{++}]: 219.0890, found: 219.0890



1-(1-methyl-5-(trifluoromethyl)-2,3-dihydro-1H-inden-2-yl)ethan-1-one (7f)

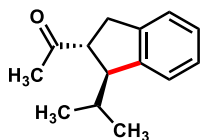
Preparatory TLC plate developed twice in 19:1 hexanes:ethyl acetate. Fraction 2 (of 3), R_f ~0.2 (after two runs). 16 mg residue isolated, 67% yield using L9 as ligand. 17 mg residue isolated, 71% yield using L10 as ligand. ^1H NMR (500 MHz, Chloroform-*d*) δ 7.49 – 7.42 (m, 2H), 7.24 (s, 1H), 3.58 – 3.49 (m, 1H), 3.25 (dd, J = 15.6, 8.7 Hz, 1H), 3.12 (dd, J = 15.7, 9.0 Hz, 1H), 3.05 (q, J = 8.7 Hz, 1H), 2.28 (s, 3H), 1.39 (d, J = 6.9 Hz, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 208.62, 150.64 – 150.47 (m), 141.34, 129.51 (d, J = 31.9 Hz), 128.99 (d, J = 33.3 Hz), 124.09 (q, J = 3.8 Hz), 123.59, 121.17 (q, J = 3.8 Hz), 60.71, 41.40, 34.50, 29.32, 19.47. ^{19}F NMR (282 MHz, Chloroform-*d*) δ -62.04. Calcd for $\text{C}_{13}\text{H}_{13}\text{F}_3\text{O}$ [M^{++}]: 242.0918, found: 242.0917



1-(5-methyl-1-propyl-2,3-dihydro-1H-inden-2-yl)ethan-1-one (7g)

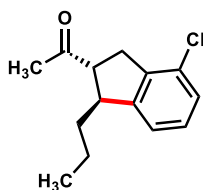
Preparatory TLC plate developed twice in 19:1 hexanes:ethyl acetate. Fraction 2 (of 2), R_f ~0.6 (after two runs). 18 mg residue isolated, 83% yield using L9 as ligand. ^1H NMR (400 MHz, Chloroform-*d*) δ 7.06 (d,

$J = 7.6$ Hz, 1H), 6.99 (d, $J = 9.1$ Hz, 2H), 3.47 (d, $J = 7.2$ Hz, 1H), 3.18 (dd, $J = 14.1, 7.6$ Hz, 1H), 3.12 – 2.97 (m, 2H), 2.31 (s, 3H), 2.21 (s, 3H), 1.77 (m, 1H), 1.62 – 1.46 (m, 1H), 1.45 – 1.29 (m, 2H), 0.95 (t, $J = 7.2$ Hz, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 209.91, 142.62, 141.04, 136.45, 127.47, 124.98, 123.66, 58.14, 46.59, 37.86, 34.71, 28.43, 21.20, 20.42, 14.31. Calcd for $\text{C}_{15}\text{H}_{20}\text{O}$ [M^+]: 216.1509, found: 216.1512



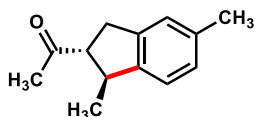
1-(1-isopropyl-2,3-dihydro-1H-inden-2-yl)ethan-1-one (7h)

Reaction performed on 0.08 mmol. Preparatory TLC plate developed twice in 19:1 hexanes:ethyl acetate. Fraction 1 (of 2), $R_f \sim 0.3$ (after two runs). 6 mg residue isolated, 38% yield using L9 as ligand. ^1H NMR (400 MHz, Chloroform-*d*) δ 7.17 (d, $J = 2.5$ Hz, 4H), 3.47 (t, $J = 4.4$ Hz, 1H), 3.25 – 2.92 (m, 3H), 2.20 (s, 3H), 2.14 (pt, $J = 6.8, 3.3$ Hz, 1H), 0.99 (d, $J = 6.9$ Hz, 3H), 0.81 (d, $J = 6.9$ Hz, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 209.86, 144.08, 141.70, 126.85, 126.46, 124.58, 124.27, 53.63, 52.87, 34.88, 32.28, 27.95, 20.67, 18.06. Calcd for $\text{C}_{14}\text{H}_{18}\text{O}$ [M^+]: 202.1352, found: 202.1351



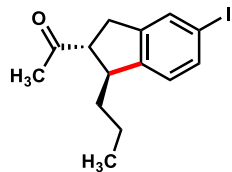
1-(4-chloro-1-propyl-2,3-dihydro-1H-inden-2-yl)ethan-1-one (7i)

Preparatory TLC plate developed twice in 19:1 hexanes:ethyl acetate. Fraction 1 (of 1), $R_f \sim 0.4$ (after two runs). 20.5 mg residue isolated, 87% yield using L9 as ligand. 21.5 mg residue isolated, 91% yield using L10 as ligand. ^1H NMR (500 MHz, Chloroform-*d*) δ 7.18 – 7.09 (m, 2H), 7.06 (dt, $J = 6.8, 1.4$ Hz, 1H), 3.60 (dt, $J = 8.1, 5.5$ Hz, 1H), 3.29 (dd, $J = 15.8, 8.6$ Hz, 1H), 3.17 – 3.00 (m, 2H), 2.25 (s, 3H), 1.77 (ddt, $J = 13.6, 10.7, 5.4$ Hz, 1H), 1.54 (dddd, $J = 13.5, 10.4, 8.2, 5.2$ Hz, 1H), 1.44 – 1.21 (m, 2H), 0.95 (t, $J = 7.3$ Hz, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 208.95, 147.74, 139.04, 128.36, 126.79, 122.20, 56.72, 47.41, 37.62, 34.16, 28.61, 20.20, 14.24. Calcd for $\text{C}_{14}\text{H}_{17}\text{ClO}$ [M^+]: 236.0962, found: 236.0968



1-(1,5-dimethyl-2,3-dihydro-1H-inden-2-yl)ethan-1-one (7j)

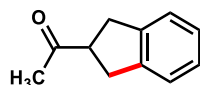
Preparatory TLC plate developed twice in 19:1 hexanes:ethyl acetate. Fraction 2 (of 2), $R_f \sim 0.4$ (after two runs). 9 mg residue isolated, 48% yield using L9 as ligand. 13 mg residue isolated, 69% yield using L10 as ligand. ^1H NMR (400 MHz, Chloroform-*d*) δ 7.02 – 6.90 (m, 3H), 3.37 (p, $J = 7.3$ Hz, 1H), 3.08 (dd, $J = 15.4, 8.9$ Hz, 1H), 2.98 (dd, $J = 15.5, 8.8$ Hz, 1H), 2.89 (q, $J = 8.7$ Hz, 1H), 2.25 (s, 3H), 2.18 (s, 3H), 1.28 (d, $J = 6.8$ Hz, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 209.60, 143.50, 140.74, 136.44, 127.57, 124.92, 123.01, 61.26, 41.19, 34.70, 29.15, 21.21, 19.77. Calcd for $\text{C}_{13}\text{H}_{16}\text{O}$ [M^+]: 188.1196, found: 188.1202



1-(5-iodo-1-propyl-2,3-dihydro-1H-inden-2-yl)ethan-1-one (7k)

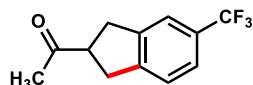
Preparatory TLC plate developed twice in 19:1 hexanes:ethyl acetate. Fraction 2 (of 3), R_f ~0.5 (after two runs). 9 mg residue isolated, 27% yield using L9 as ligand. ^1H NMR (500 MHz, Chloroform-*d*) δ 7.52 (d, $J = 1.6$ Hz, 1H), 7.49 (dd, $J = 7.9, 1.7$ Hz, 1H), 6.92 (d, $J = 8.0$ Hz, 1H), 3.48 – 3.41 (m, 1H), 3.18 (dd, $J = 14.6, 7.8$ Hz, 1H), 3.12 – 3.00 (m, 2H), 2.22 (s, 3H), 1.74 (ddt, $J = 13.5, 10.8, 5.5$ Hz, 1H), 1.58 – 1.46 (m, 2H), 1.43 – 1.23 (m, 2H), 0.94 (t, $J = 7.3$ Hz, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 209.1, 145.4, 143.6, 135.6, 133.4, 125.9, 91.8, 57.4, 46.6, 37.5, 34.3, 28.6, 20.3, 14.2. Calcd for $\text{C}_{14}\text{H}_{17}\text{IO}$ [M^+]: 328.0319, found: 328.0328

1° C-H functionalization



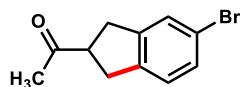
1-(2,3-dihydro-1H-inden-2-yl)ethan-1-one (2)

Preparatory TLC plate developed twice in 19:1 hexanes:ethyl acetate. Fraction 2 (of 3), R_f ~0.4 (after two runs). 11.5 mg residue isolated, 71% yield using L10 as ligand. 10 mg residue isolated, 63% yield using L9 as ligand. ^1H NMR (500 MHz, Chloroform-*d*) δ 7.18 (ddd, $J = 25.9, 5.4, 3.3$ Hz, 4H), 3.45 (p, $J = 8.6$ Hz, 1H), 3.26 – 3.12 (m, 4H), 2.25 (s, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 209.38, 141.44, 126.62, 124.41, 51.89, 34.95, 28.50. HRMS (EI-TOF) Calcd for $\text{C}_{11}\text{H}_{12}\text{O}$ [M^+]: 160.0883, found: 160.0882



1-(5-(trifluoromethyl)-2,3-dihydro-1H-inden-2-yl)ethan-1-one (8a)

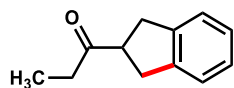
Preparatory TLC plate developed twice in 19:1 hexanes:ethyl acetate. Fraction 1 (of 4), R_f ~0.2 (after two runs). 16 mg residue isolated, 70% yield using L9 as ligand. ^1H NMR (400 MHz, Chloroform-*d*) δ 7.47 – 7.39 (m, 2H), 7.29 (d, $J = 7.9$ Hz, 1H), 3.56 – 3.43 (m, 1H), 3.32 – 3.13 (m, $J = 7.5$ Hz, 4H), 2.26 (s, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 208.54, 145.68, 142.25, 129.48 (d, $J = 31.9$ Hz), 128.97 (d, $J = 31.9$ Hz), 124.69, 123.92 (q, $J = 3.8$ Hz), 121.34 (q, $J = 3.8$ Hz), 51.66, 34.77 (d, $J = 5.2$ Hz), 28.62. ^{19}F NMR (282 MHz, Chloroform-*d*) δ -62.07. ^{19}F NMR (282 MHz, Chloroform-*d*) δ -62.07. HRMS (EI-TOF) Calcd for $\text{C}_{12}\text{H}_{11}\text{F}_3\text{O}$ [M^+]: 228.0756, found: 228.0760



1-(5-bromo-2,3-dihydro-1H-inden-2-yl)ethan-1-one (8b)

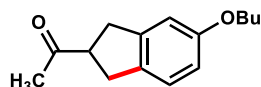
Preparatory TLC plate developed twice in 19:1 hexanes:ethyl acetate. Fraction 1 (of 3), R_f ~0.4 (after two runs). 12 mg residue isolated, 50% yield using L9 as ligand. ^1H NMR (500 MHz, Chloroform-*d*) δ 7.33 (s, 1H), 7.28 (s, 1H), 7.06 (d, $J = 8.0$ Hz, 1H), 3.45 (p, $J = 8.5$ Hz, 1H), 3.25 – 3.05 (m, 4H), 2.24 (s, 3H). ^{13}C

NMR (126 MHz, Chloroform-*d*) δ 208.71, 143.88, 140.41, 129.67, 127.55, 125.87, 120.27, 51.83, 34.70, 34.46, 28.54. HRMS (EI-TOF) Calcd for C₁₁H₁₁BrO [M⁺]: 237.9988, found: 237.9985



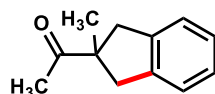
1-(2,3-dihydro-1H-inden-2-yl)propan-1-one (8c)

Preparatory TLC plate developed twice in 19:1 hexanes:ethyl acetate. Fraction 2 (of 3), R_f ~0.5 (after two runs). 12 mg residue isolated, 69% yield using L9 as ligand. 14 mg residue isolated, 80% yield using L10 as ligand. ¹H NMR (500 MHz, Chloroform-*d*) δ 7.20 (dd, J = 5.3, 3.4 Hz, 2H), 7.18 – 7.12 (m, 2H), 3.46 (p, J = 8.7 Hz, 1H), 3.18 (qd, J = 15.7, 8.8 Hz, 4H), 2.57 (q, J = 7.3 Hz, 2H), 1.11 (t, J = 7.3 Hz, 1H). ¹³C NMR (126 MHz, Chloroform-*d*) δ 212.12, 141.58, 126.58, 124.38, 50.95, 35.22, 34.54, 7.87. HRMS (EI-TOF) Calcd for C₁₂H₁₄O [M⁺]: 174.1039, found: 174.1038



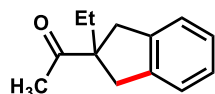
1-(5-butoxy-2,3-dihydro-1H-inden-2-yl)ethan-1-one (8d)

Cyclization reaction run in 3:1 HFIP:AcOH without 2-pyridone ligand. Preparatory TLC plate developed twice in 19:1 hexanes:ethyl acetate. Fraction 3 (of 5), R_f ~0.3 (after two runs). 14 mg residue isolated, 60% yield. ¹H NMR (500 MHz, Chloroform-*d*) δ 7.08 (d, J = 8.2 Hz, 1H), 6.75 (s, 1H), 6.71 (d, J = 8.2 Hz, 1H), 3.92 (t, J = 6.5 Hz, 2H), 3.44 (p, J = 8.5 Hz, 1H), 3.23 – 3.04 (m, 4H), 2.23 (s, 3H), 1.80 – 1.69 (m, 2H), 1.48 (h, J = 7.4 Hz, 2H), 0.97 (t, J = 7.4 Hz, 3H). ¹³C NMR (126 MHz, Chloroform-*d*) δ 209.47, 158.50, 142.97, 133.07, 124.85, 113.26, 110.45, 67.86, 52.39, 35.03, 34.28, 31.36, 28.44, 19.24, 13.85. HRMS (EI-TOF) Calcd for C₁₅H₂₀O₂ [M⁺]: 232.1458, found: 232.1454



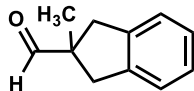
1-(2-methyl-2,3-dihydro-1H-inden-2-yl)ethan-1-one (8f)

Cyclization reaction performed using 1.0 equiv. glycine at 150 °C. Preparatory TLC plate developed five times in 19:1 hexanes:ethyl acetate. Fraction 2 (of 5), R_f ~0.2 (after a single run). 7 mg residue isolated, 40% yield using L9 as ligand. NMR spectroscopic data matches previous reports¹² and was confirmed by HRMS. HRMS (EI-TOF) Calcd for C₁₂H₁₄O [M⁺]: 174.1039, found: 174.1037



1-(2-ethyl-2,3-dihydro-1H-inden-2-yl)ethan-1-one (8g)

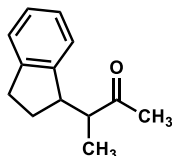
Cyclization reaction performed using 1.0 equiv. glycine at 150 °C. 10% yield was determined by analysis of the ¹H NMR spectrum of the crude mixture and comparison to the known spectral data. See NMR spectra for this spectrum. NMR spectroscopic data matches previous reports¹² and was confirmed by HRMS. HRMS (EI-TOF) Calcd for C₁₂H₁₄O [M⁺]: 174.1039, found: 174.1037



2-methyl-2,3-dihydro-1H-indene-2-carbaldehyde (8h)

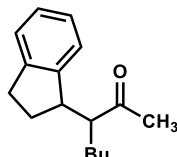
Cyclization reaction performed using 1.0 equiv. glycine at 150 °C. 30% yield was determined by analysis of the ¹H NMR spectrum of the crude mixture and comparison to the known spectral data.¹⁴ See NMR spectra for this spectrum. NMR spectroscopic data matches previous reports.

Data for Figure 3 in Paper



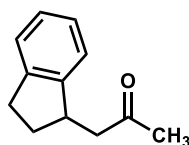
3-(2,3-dihydro-1H-inden-1-yl)butan-2-one (10a)

10a was prepared by standard cyclization method for primary C-H bonds using **L10** (0.5 equiv. glycine, 110 °C). 57% yield and 2.1:1 dr were determined by analysis of the ¹H NMR spectrum of the crude reaction mixture using dibromomethane as the internal standard. A tight separation precluded a high yielding isolation, but 2 mg were isolated by preparatory TLC plate developed twice in 19:1 hexanes:ethyl acetate in order to elucidate the structure of **10a** by 2D NMR. Generally structural assignments are consistent with similar compounds reported previously.¹⁵ ¹H NMR (500 MHz, Chloroform-*d*) δ 7.25 – 7.05 (m, 4H), 3.54 (m, 1H), 3.01 – 2.67 (m, 3H), 2.16 (m, 4H), 1.78 (m, 1H), 1.12 (d, *J* = 7.0 Hz, 1H), 0.98 (d, *J* = 7.0 Hz, 2H). ¹³C NMR (126 MHz, Chloroform-*d*) δ 212.30, 212.03, 126.81, 126.69, 126.24, 125.91, 125.10, 124.71, 124.59, 123.67, 50.51, 50.37, 47.03, 46.11, 31.52, 31.06, 30.04, 29.35, 29.11, 27.36, 14.31. HRMS (ESI-TOF) Calcd for C₁₃H₁₆O + H⁺: 189.1279, found: 189.1277.



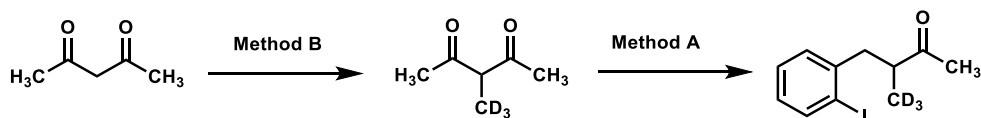
3-(2,3-dihydro-1H-inden-1-yl)heptan-2-one (10b)

10b was prepared by standard cyclization method for secondary C-H bonds using **L10** (1.0 equiv. glycine, 150 °C). 79% yield was determined by analysis of the ¹H NMR spectrum using dibromomethane as the internal standard. A tight separation precluded a high yielding isolation, but 3 mg were isolated by preparatory TLC plate developed twice in 19:1 hexanes:ethyl acetate in order to elucidate the structure of **10b** by 2D NMR. ¹H NMR (500 MHz, Chloroform-*d*) δ 7.29 – 7.06 (m, 4H), 3.54 – 3.30 (m, 1H), 2.99 – 2.64 (m, 3H), totaling 5H{2.23 – 2.04 (m, 3H), 2.01 (s, 1H), 1.96 – 1.83 (m, 1H), 1.82 – 1.65 (m, 1H),} 1.35 – 1.04 (m, 6H), 0.93 – 0.79 (m, 3H). ¹³C NMR (126 MHz, Chloroform-*d*) δ 212.40, 144.70, 144.60, 144.30, 144.20, 126.85, 126.74, 126.22, 125.92, 124.90, 124.79, 124.63, 123.81, 56.25, 56.18, 46.90, 46.38, 31.27, 31.01, 30.91, 30.78, 30.07, 30.01, 29.88, 29.69, 29.18, 28.39, 27.69, 22.86, 22.82, 13.94, 13.90. HRMS (ESI-TOF) Calcd for C₁₆H₂₂O + H⁺: 231.1749, found: 231.1746.



1-(2,3-dihydro-1H-inden-1-yl)propan-2-one (10c)

10c was observed in the ^1H NMR spectrum of the crude reaction mixture generated by exposing **9c** to standard cyclization method for secondary C-H bonds using **L10** (1.0 equiv. glycine, 150 °C) on 0.06 mmol scale. 19% yield was determined by analysis of the ^1H NMR spectrum using dibromomethane (0.1 mmol added) as the internal standard in CDCl_3 . Analysis of the spectrum included the integration of the multiplet at 3.62 ppm corresponding to the benzylic methine. As determined by HSQC NMR spectroscopy, this signal corresponds to a ^{13}C NMR signal at 40.2 ppm, and these data agree with previous characterization of this compound.^{16,17} Isolation was complicated by the low yield. These spectra appear in the NMR spectra section.

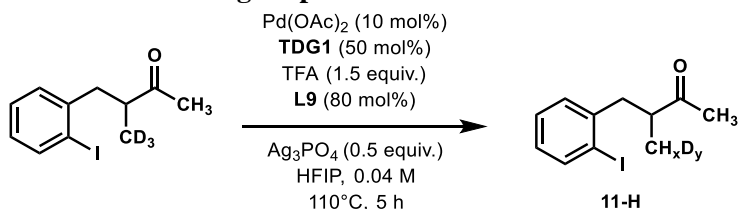


Scheme S37: Preparation of **11**

3-(2-iodobenzyl)butan-2-one-4,4,4-d₃ (**11**)

11 was prepared by Method B and then Method A in sequence. Preparation of 3-methyl-2,4-pentanedione-d₃ has been reported elsewhere and matched spectroscopically.¹⁸ 2.04 g of **11** was isolated in 65% yield, a colorless oil. ^1H NMR (400 MHz, Chloroform-*d*) δ 7.82 (dd, $J = 7.9, 1.2$ Hz, 1H), 7.25 (td, $J = 7.4, 1.3$ Hz, 1H), 7.16 (dd, $J = 7.6, 1.8$ Hz, 1H), 6.90 (td, $J = 7.6, 1.8$ Hz, 1H), 3.13 (dd, $J = 13.6, 6.6$ Hz, 1H), 2.96 (t, $J = 7.2$ Hz, 1H), 2.63 (dd, $J = 13.6, 7.8$ Hz, 1H), 2.13 (s, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 211.69, 142.19, 139.62, 128.20, 128.17, 100.62, 46.46, 43.03, 29.09, 15.23 (apparent dq, $J = 39.0, 19.7$ Hz). HRMS (ESI-TOF) Calcd for $\text{C}_{11}\text{H}_{10}\text{D}_3\text{IO} + \text{H}^+$: 292.0278, found: 292.0277.

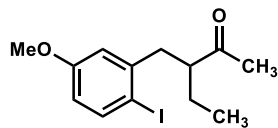
Deuterium exchange experiment



Scheme S38: Deuterium Exchange Experiment

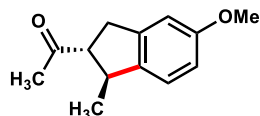
Deuterium exchange experiment. After treating **11** (0.1 mmol scale) with standard conditions for cyclization of primary C-H bonds for 5 hours as indicated by the above scheme (see Screening Workflow on page 21 of S.I.), the reaction was worked up as usual by diluting with stock solution of NMR standard 1,3,5-trimethoxybenzene (0.1 mmol standard added) in chloroform. Hydrogen incorporation was approximated by analysis of the ^1H NMR spectrum of the crude mixture integrating the complex signal arising at 1.07-1.12 ppm, which is the position at which the methyl C-H appears in the ^1H NMR spectrum of H-analog **1**. Purification by preparative plate chromatography yielded a sample of **11-H** contaminated with grease. Analysis of the HSQC NMR spectrum of this sample indicated a complex ^{13}C signal at 15.55-16.13 ppm corresponding to the complex signal at 1.07-1.12 in the ^1H NMR spectrum. These spectra appear in the NMR spectra section of this document. By HRMS (ESI-TOF) we detected both the dihydrogen and trihydrogen incorporated form of **11-H** ($x = 2$ and $x = 3$). For $x=2$ HRMS (ESI-TOF) Calcd for $\text{C}_{11}\text{H}_{12}\text{DIO} + \text{H}^+$: 290.0152, found: 290.0152. For $x=3$ HRMS (ESI-TOF) Calcd for $\text{C}_{11}\text{H}_{13}\text{IO} + \text{H}^+$: 289.0089, found: 289.0087.

Data for [3+2] Cyclization Reactions



3-(2-iodo-5-methoxybenzyl)pentan-2-one (15)

Reaction performed on 0.4 mmol scale (from 3-methyl-pentan-2-one. Preparatory TLC plate developed twice in 19:1 hexanes:ethyl acetate. Fraction 2 (of 5) $R_f \sim 0.2$ (after two runs). 50 mg residue isolated, 38% yield. $^1\text{H NMR}$ (400 MHz, Chloroform-*d*) δ 7.67 (d, $J = 8.7$ Hz, 1H), 6.73 (d, $J = 3.0$ Hz, 1H), 6.51 (dd, $J = 8.7, 3.0$ Hz, 1H), 3.76 (s, 3H), 3.03 – 2.84 (m, 2H), 2.71 (dd, $J = 12.5, 5.4$ Hz, 1H), 2.05 (s, 3H), 1.79 – 1.63 (m, 1H), 1.62 – 1.45 (m, 1H), 0.92 (t, $J = 7.4$ Hz, 3H). $^{13}\text{C NMR}$ (126 MHz, Chloroform-*d*) δ 212.00, 159.79, 143.23, 139.99, 116.57, 114.26, 77.00, 55.33, 53.59, 30.69, 24.49, 11.54. HRMS (ESI+ TOF) Calcd for $\text{C}_{13}\text{H}_{17}\text{IO}_2 + \text{H}^+$: 333.0346, found: 333.0346



1-(5-methoxy-1-methyl-2,3-dihydro-1H-inden-2-yl)ethan-1-one (16)

Reaction performed on 0.07 mmol scale in 3:1 HFIP:AcOH without 2-pyridone ligand. Preparatory TLC plate developed twice in 19:1 hexanes:ethyl acetate. Fraction 2 (of 3), $R_f \sim 0.2$ (after two runs). 5 mg residue isolated, 35% yield using conditions deviating from standard conditions: 3:1 HFIP:AcOH solvent, omitting TFA. $^1\text{H NMR}$ (500 MHz, Chloroform-*d*) δ 7.1 – 7.0 (m, 1H), 6.8 – 6.6 (m, 2H), 3.8 (d, $J = 2.6$ Hz, 4H), 3.4 (p, $J = 7.1$ Hz, 1H), 3.1 (qd, $J = 15.7, 8.9$ Hz, 2H), 3.0 (q, $J = 8.7$ Hz, 1H), 2.3 (s, 3H), 1.3 (d, $J = 6.8$ Hz, 3H). $^{13}\text{C NMR}$ (126 MHz, Chloroform-*d*) δ 209.5, 159.0, 142.1, 138.5, 123.8, 112.7, 109.7, 61.4, 55.4, 40.9, 34.8, 29.2, 20.1. Calcd for $\text{C}_{13}\text{H}_{16}\text{O}_2 [\text{M}^+]$: 204.1145, found: 204.1143

NMR Spectra

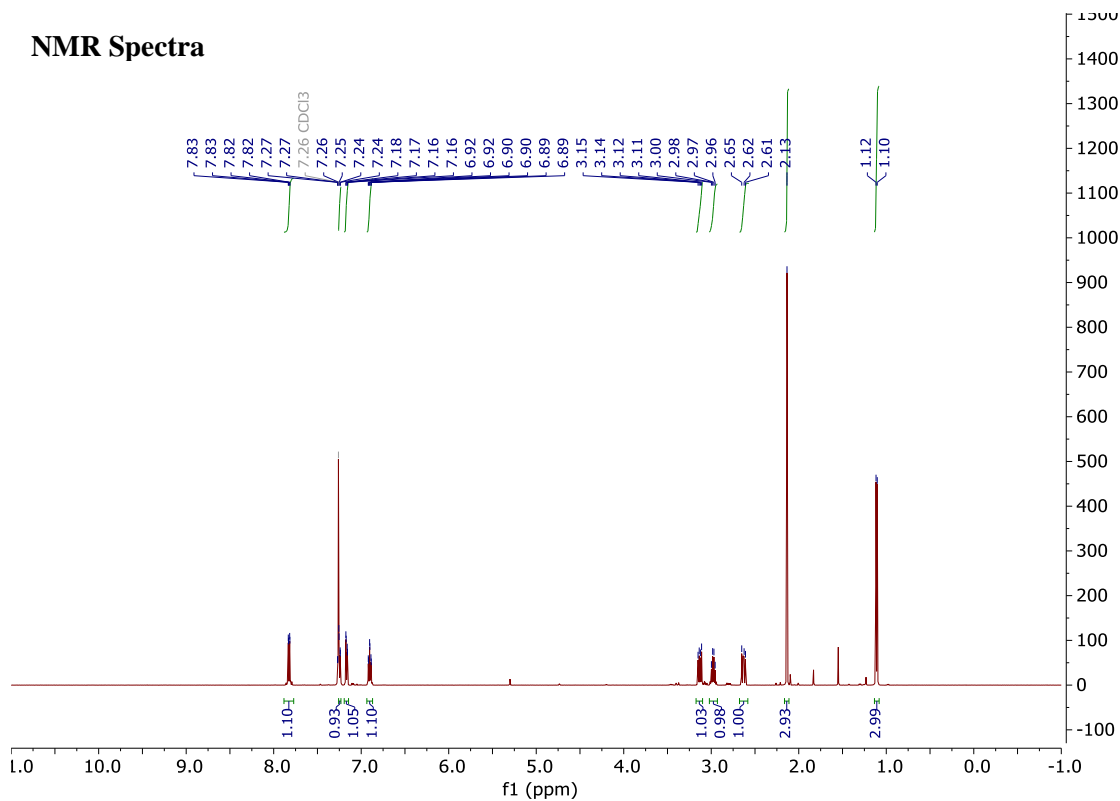


Figure S12: ¹H NMR spectrum of **1** in CDCl₃. Spectrometer Frequency 500.40 MHz. 22 °C

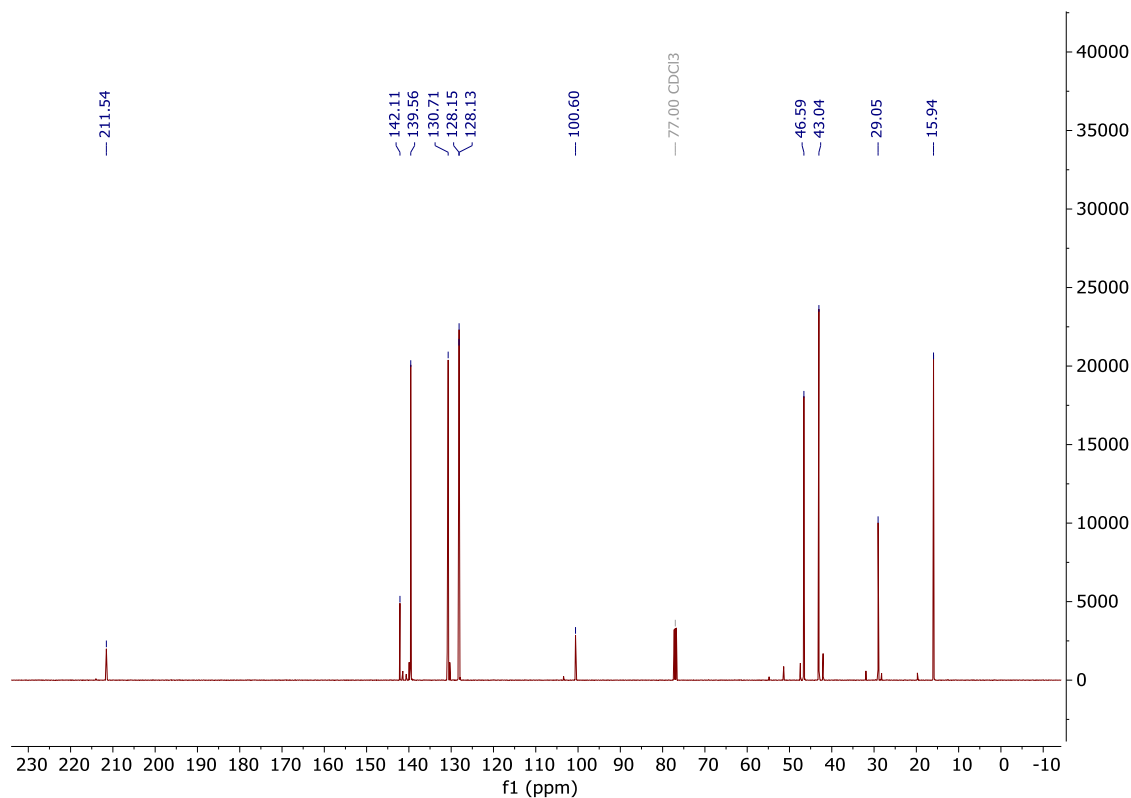


Figure S13: ¹³C NMR spectrum of **1** in CDCl₃. Spectrometer Frequency 125.85 MHz. 22 °C

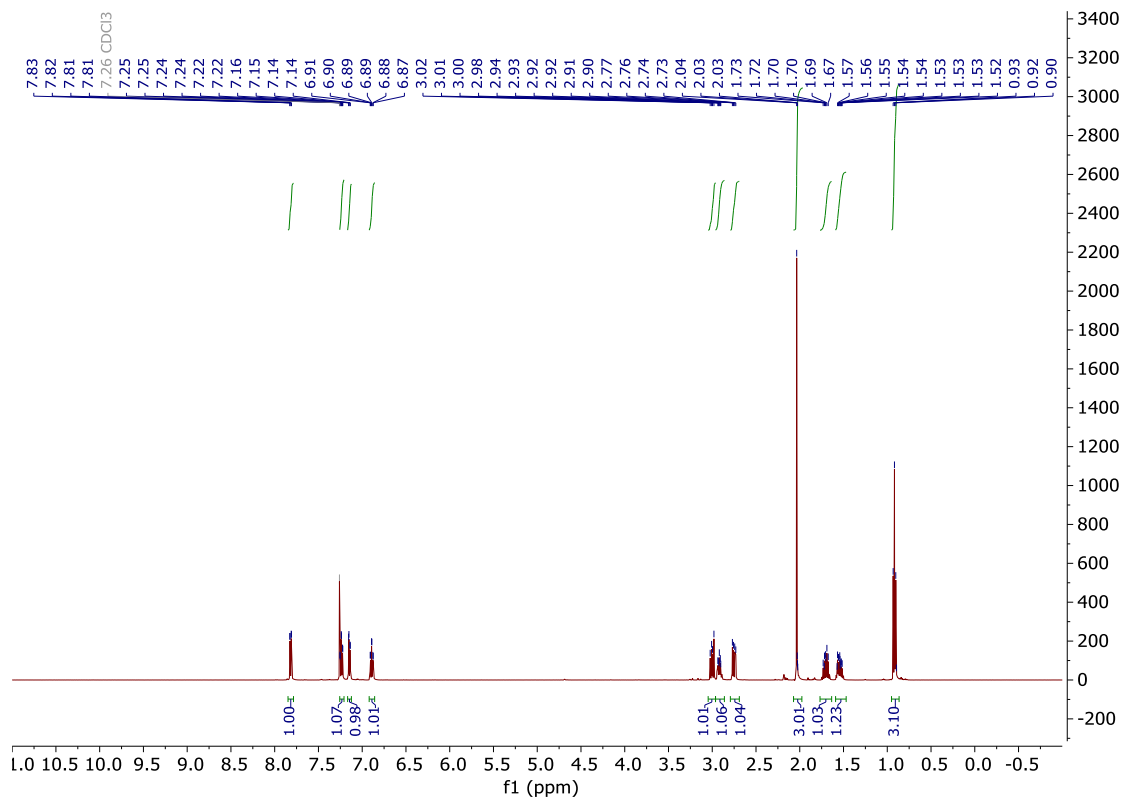


Figure S14: ¹H NMR spectrum of **4** in CDCl₃. Spectrometer Frequency 500.46 MHz. 22 °C

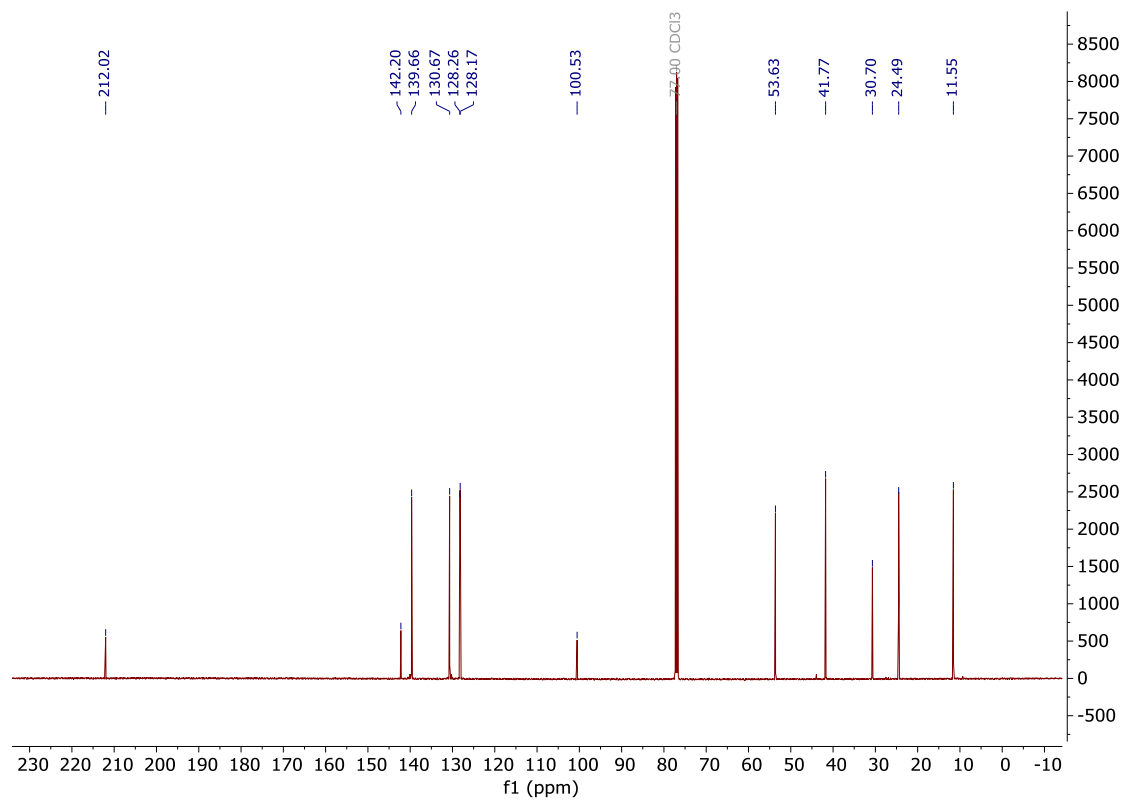


Figure S15: ¹³C NMR spectrum of **4** in CDCl₃. Spectrometer Frequency 125.85 MHz. 22 °C

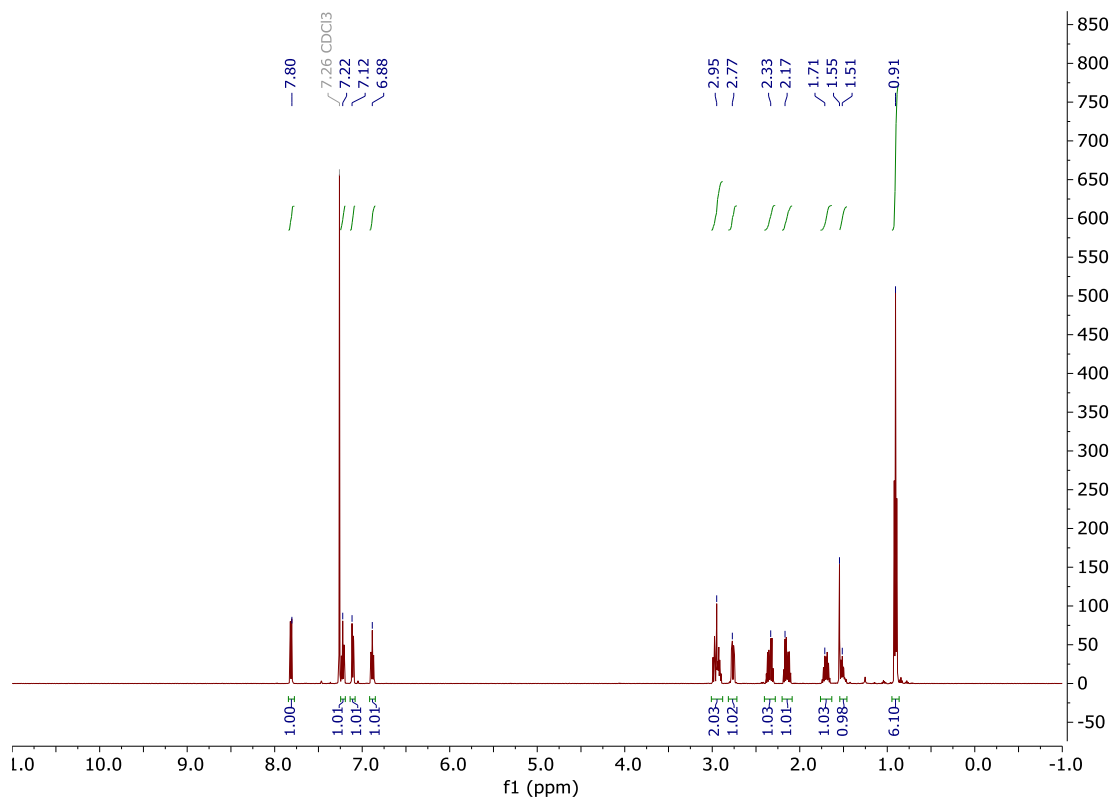


Figure S18: ^1H NMR spectrum of **S2** in CDCl_3 . Spectrometer Frequency 500.40 MHz. 22 °C

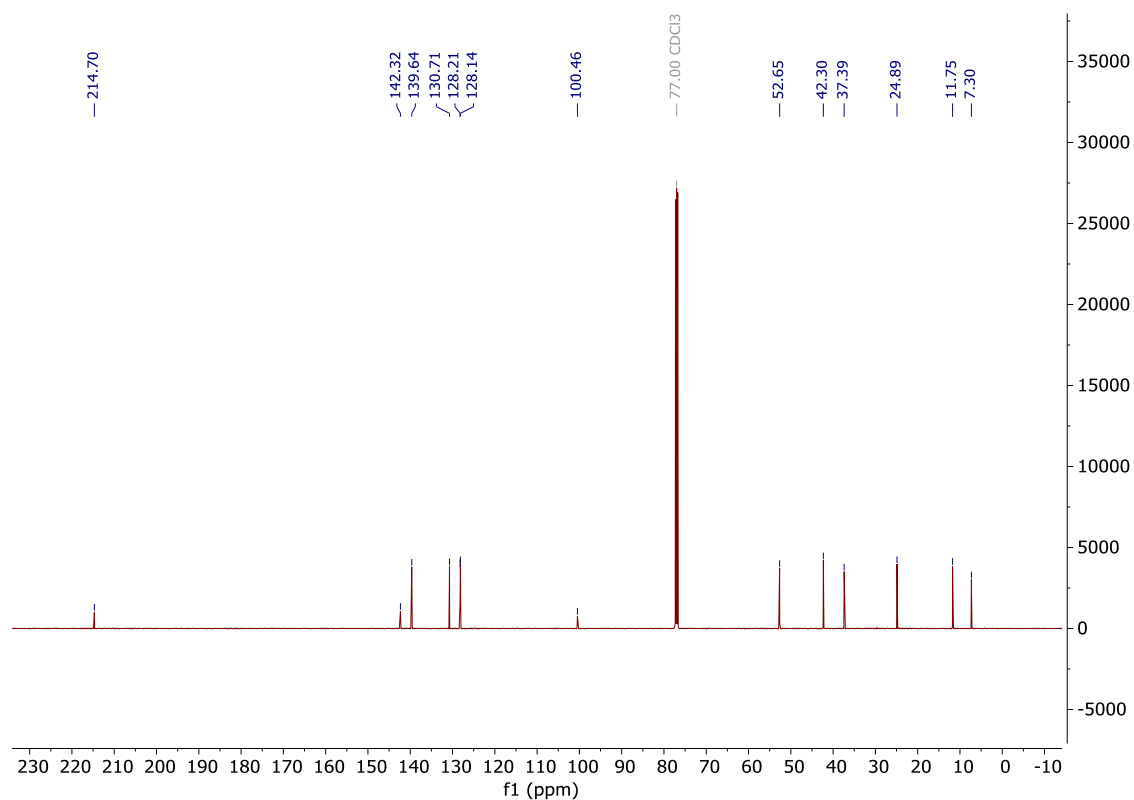


Figure S19: ^{13}C NMR spectrum of **S2** in CDCl_3 . Spectrometer Frequency 125.85 MHz. 22 °C

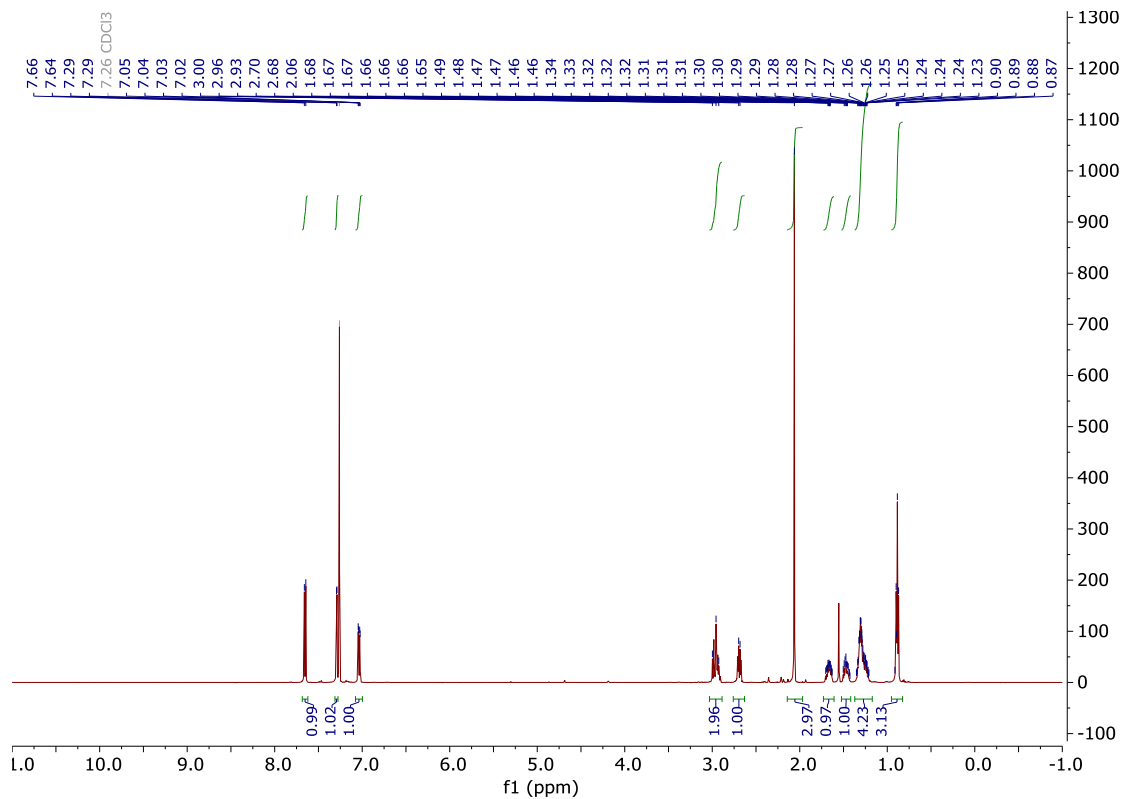


Figure S20: ^1H NMR spectrum of **S3** in CDCl_3 . Spectrometer Frequency 500.15 MHz. 22 $^\circ\text{C}$

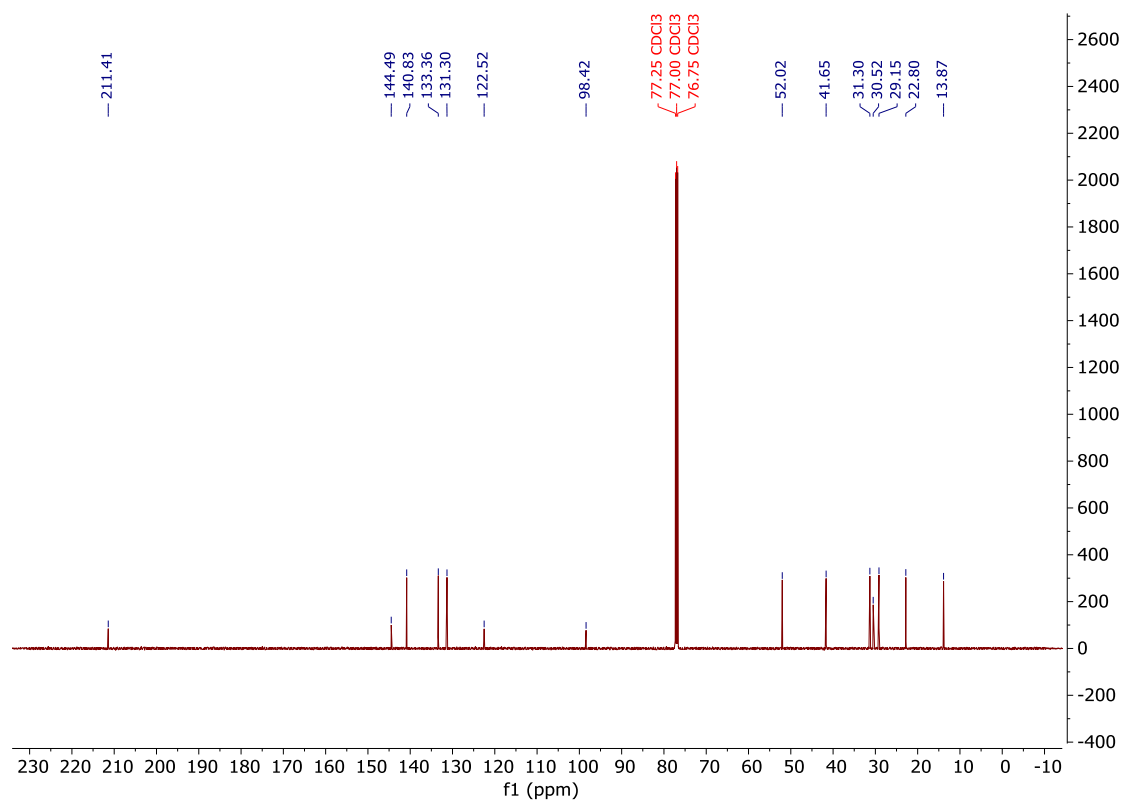


Figure S21: ^{13}C NMR spectrum of **S3** in CDCl_3 . Spectrometer Frequency 125.85 MHz. 22 $^\circ\text{C}$

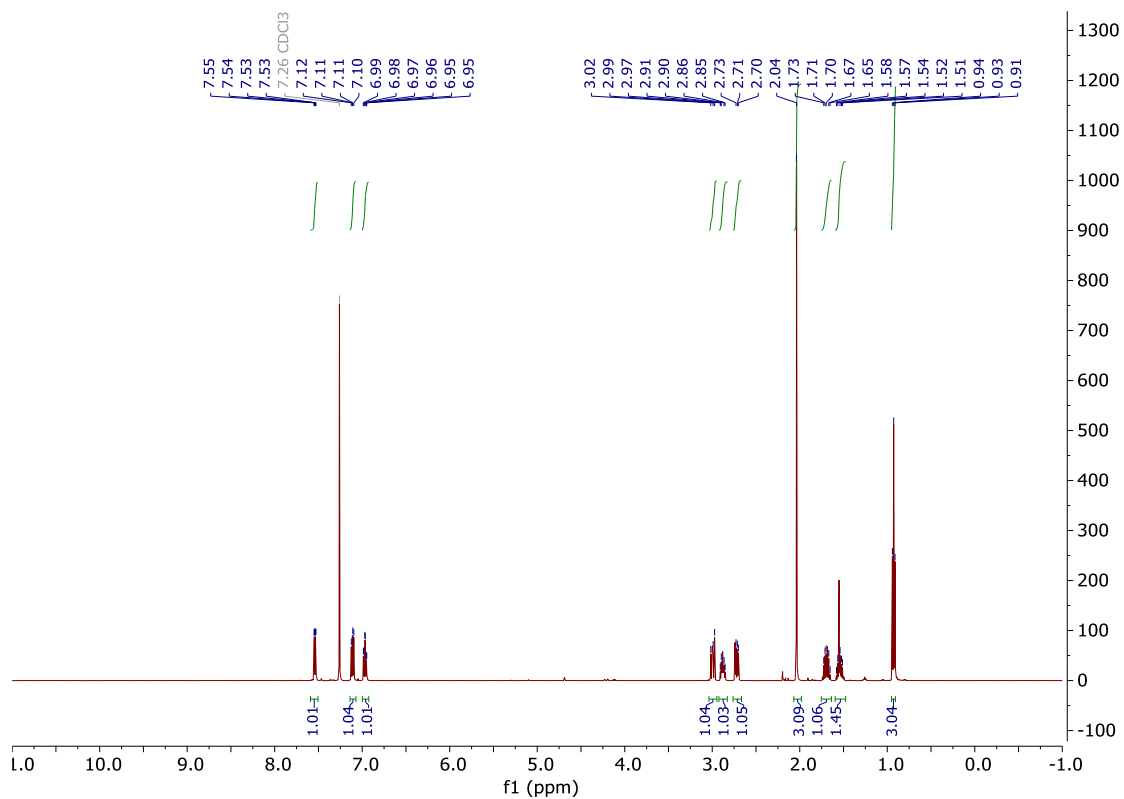


Figure S22: ¹H NMR spectrum of **S5** in CDCl₃. Spectrometer Frequency 500.46 MHz. 22 °C

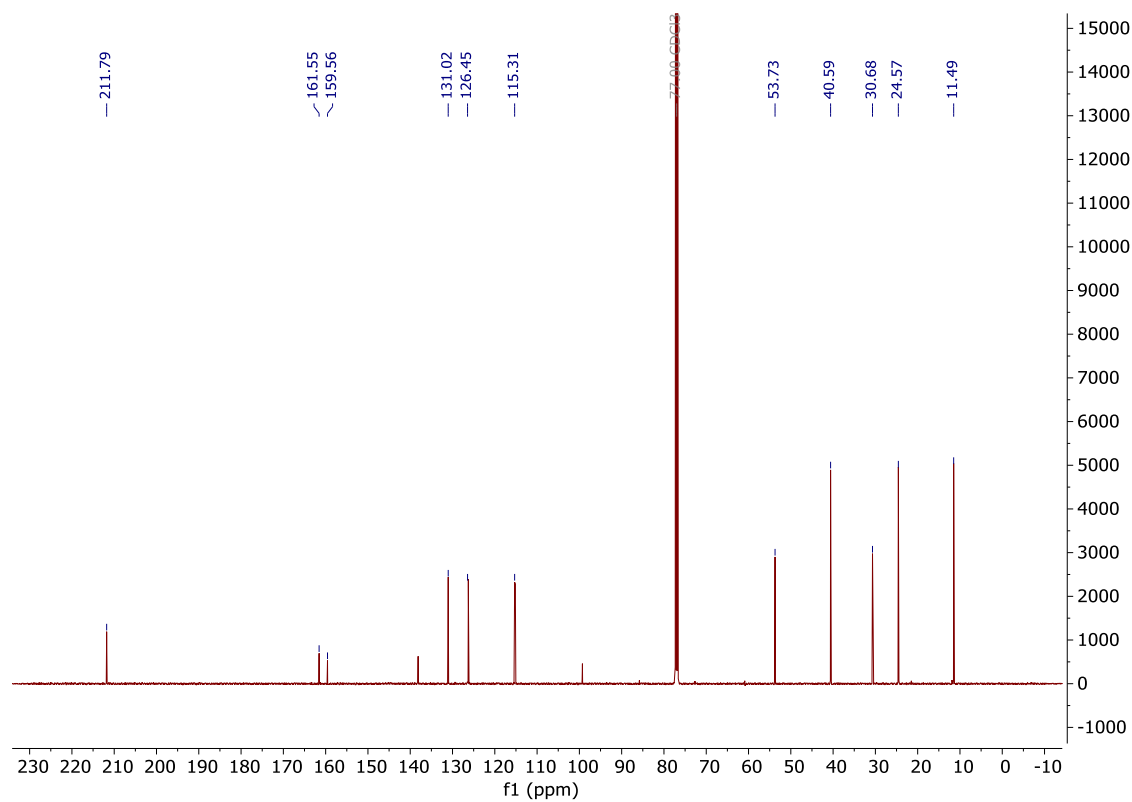


Figure S23: ¹³C NMR spectrum of **S5** in CDCl₃. Spectrometer Frequency 125.85 MHz. 22 °C

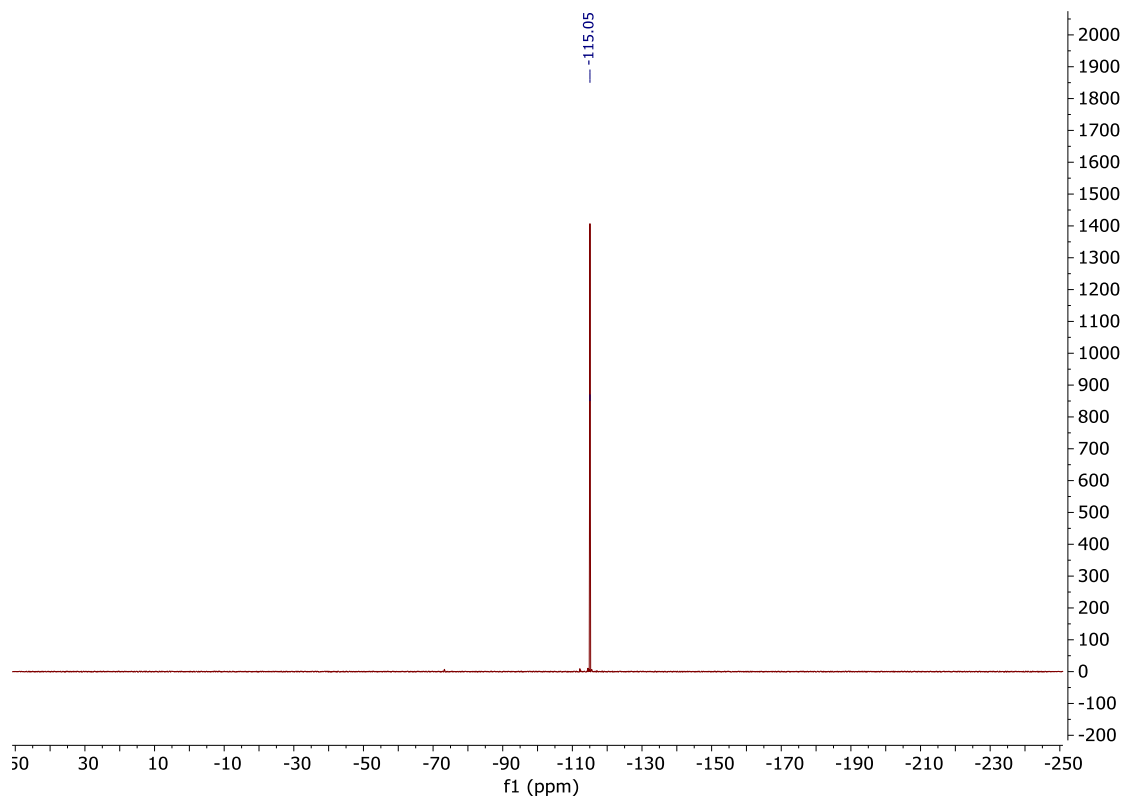


Figure S24: ^{19}F NMR spectrum of **S5** in CDCl_3 . Spectrometer Frequency 282.38 MHz. 22 °C

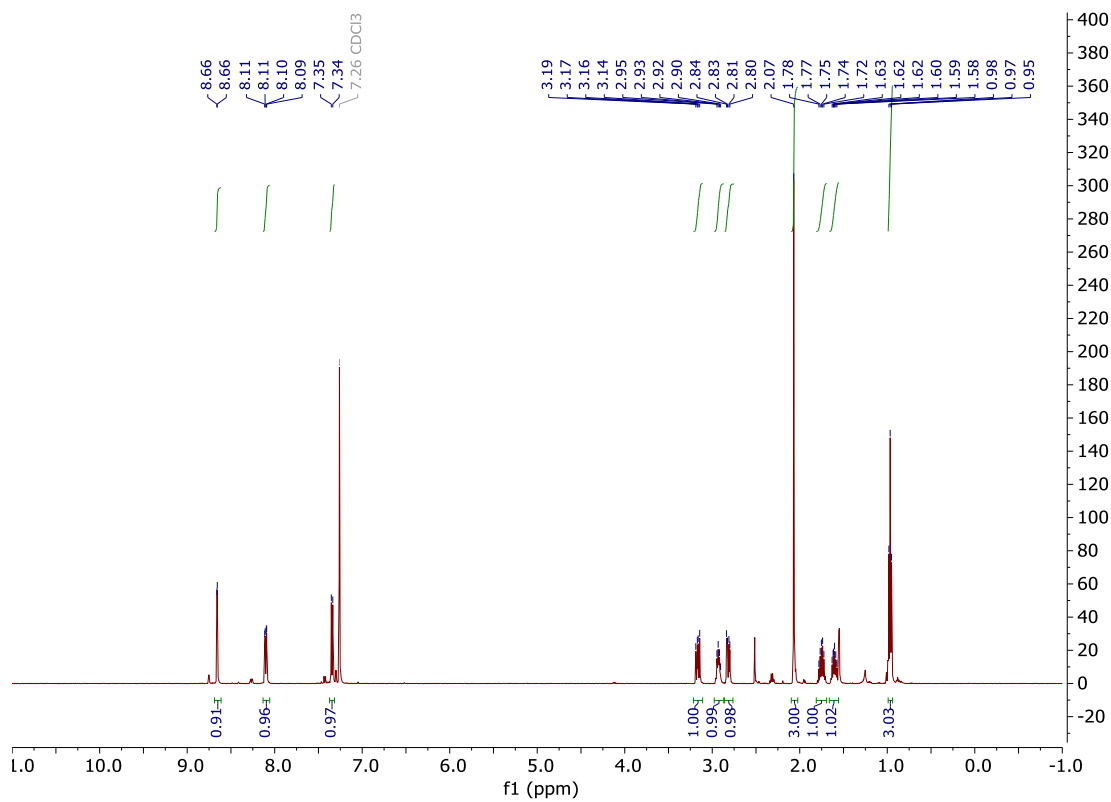


Figure S25: ^1H NMR spectrum of **S6** in CDCl_3 . Spectrometer Frequency 500.46 MHz. 22 °C

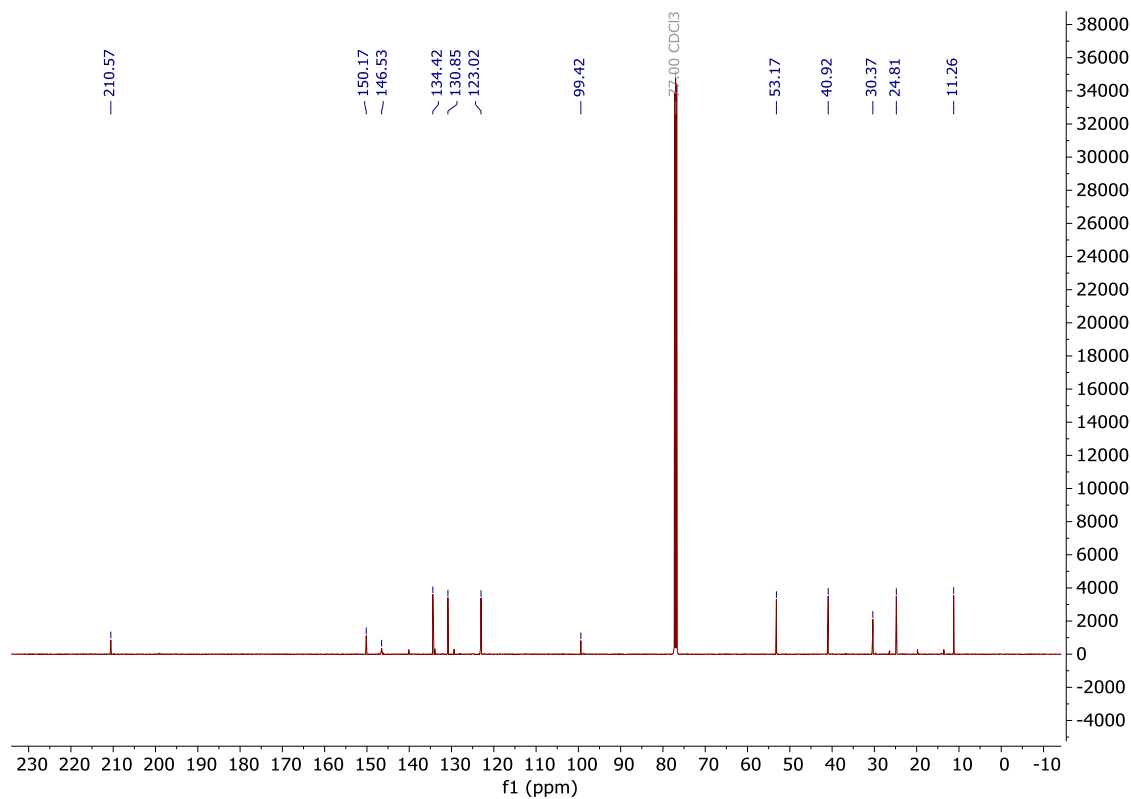


Figure S26: ¹³C NMR spectrum of **S6** in CDCl₃. Spectrometer Frequency 125.85 MHz. 22 °C

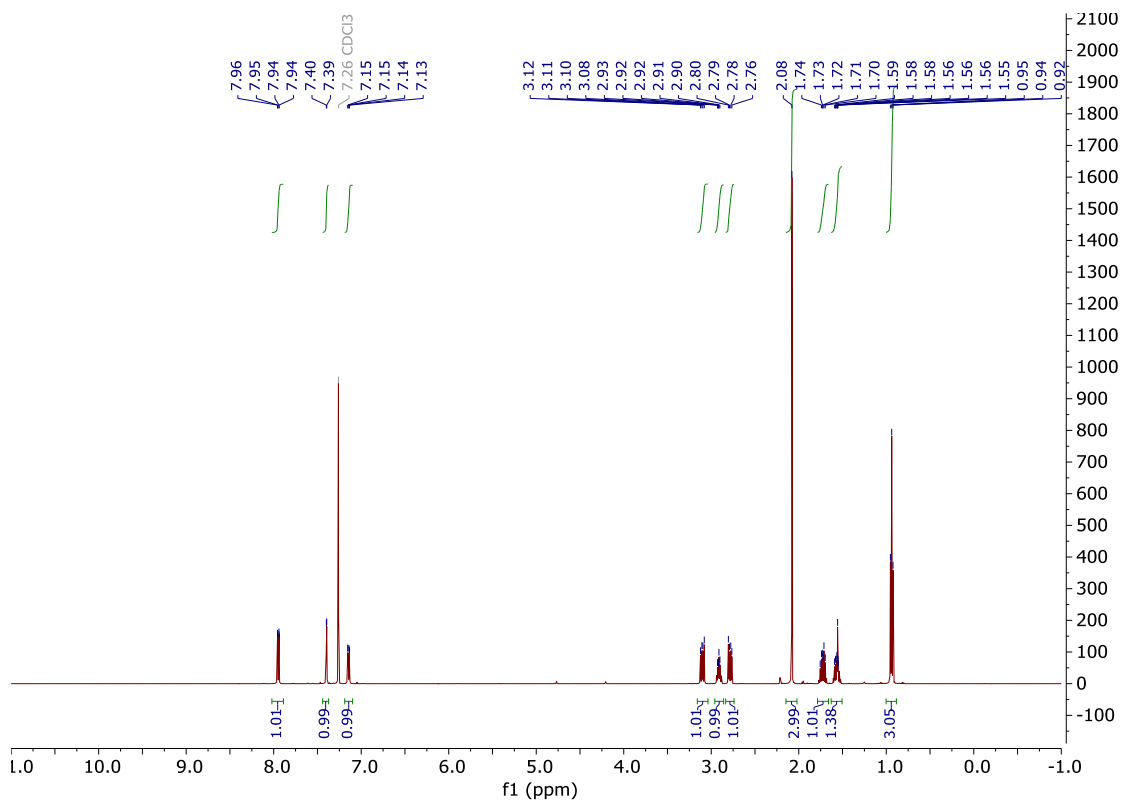


Figure S27: ¹H NMR spectrum of **S7** in CDCl₃. Spectrometer Frequency 500.15 MHz. 22 °C

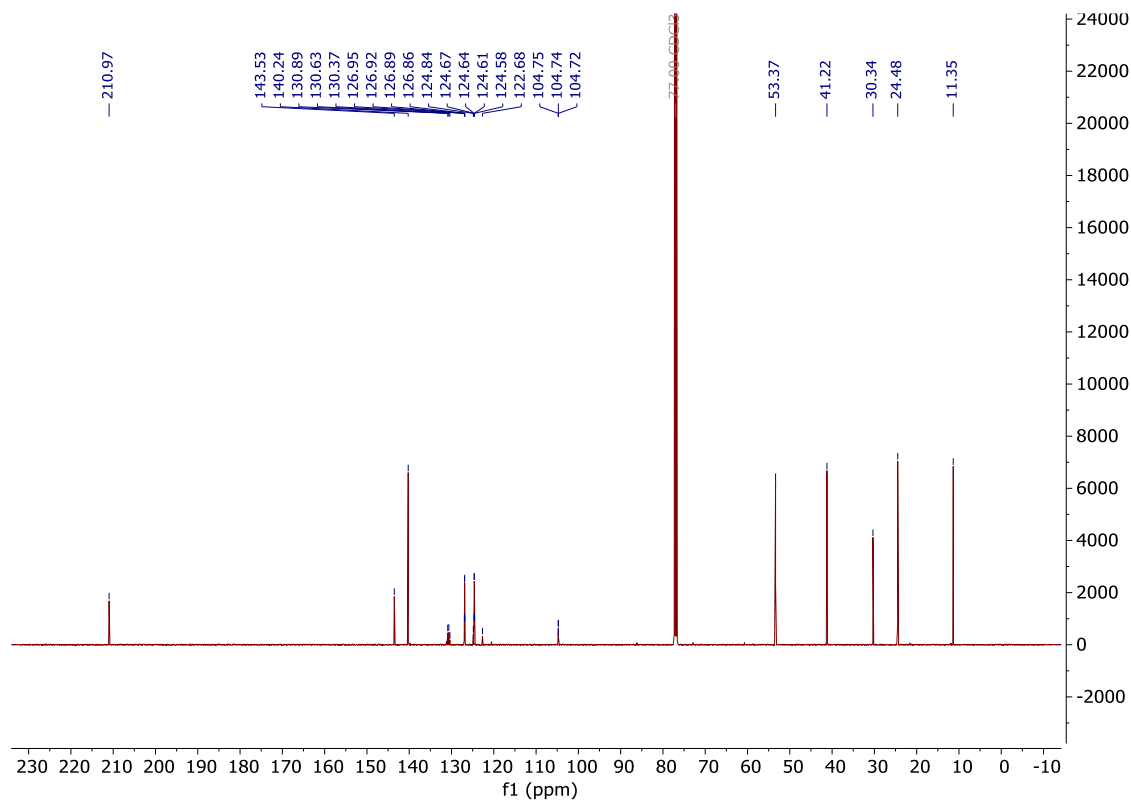


Figure S28: ¹³C NMR spectrum of **S7** in CDCl₃. Spectrometer Frequency 125.85 MHz. 22 °C

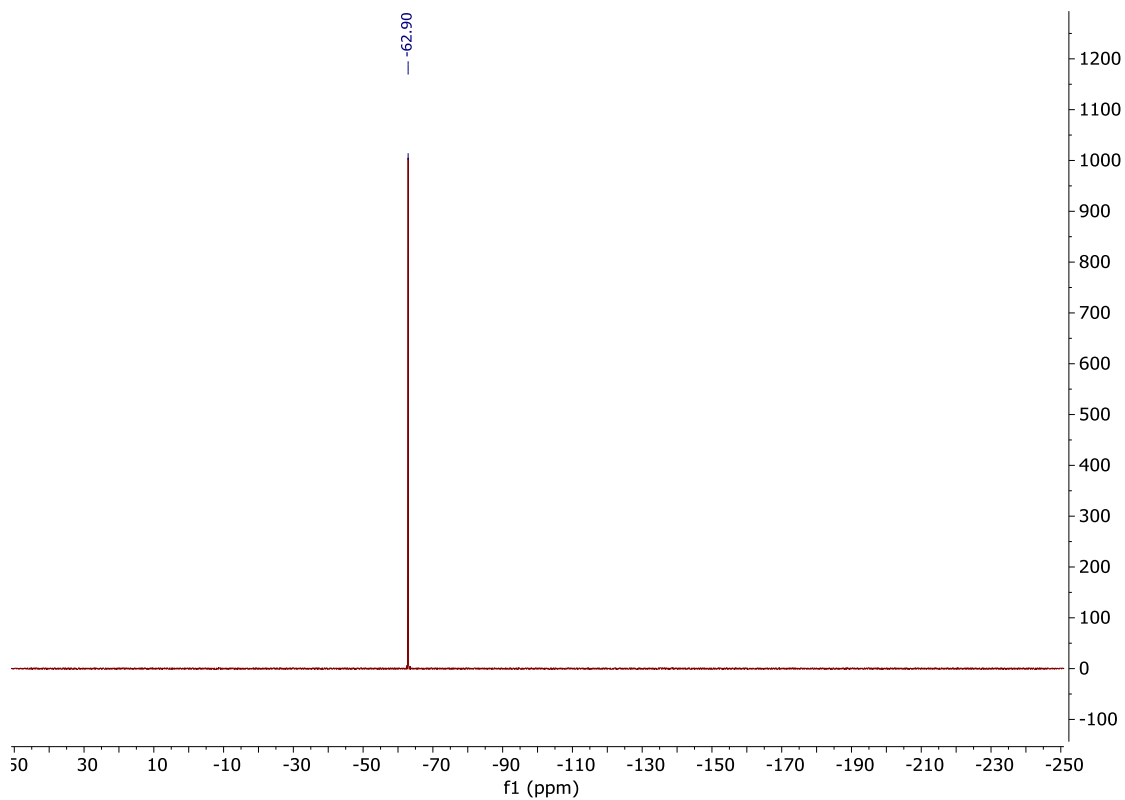


Figure S29: ¹⁹F NMR spectrum of **S7** in CDCl₃. Spectrometer Frequency 282.38 MHz. 22 °C

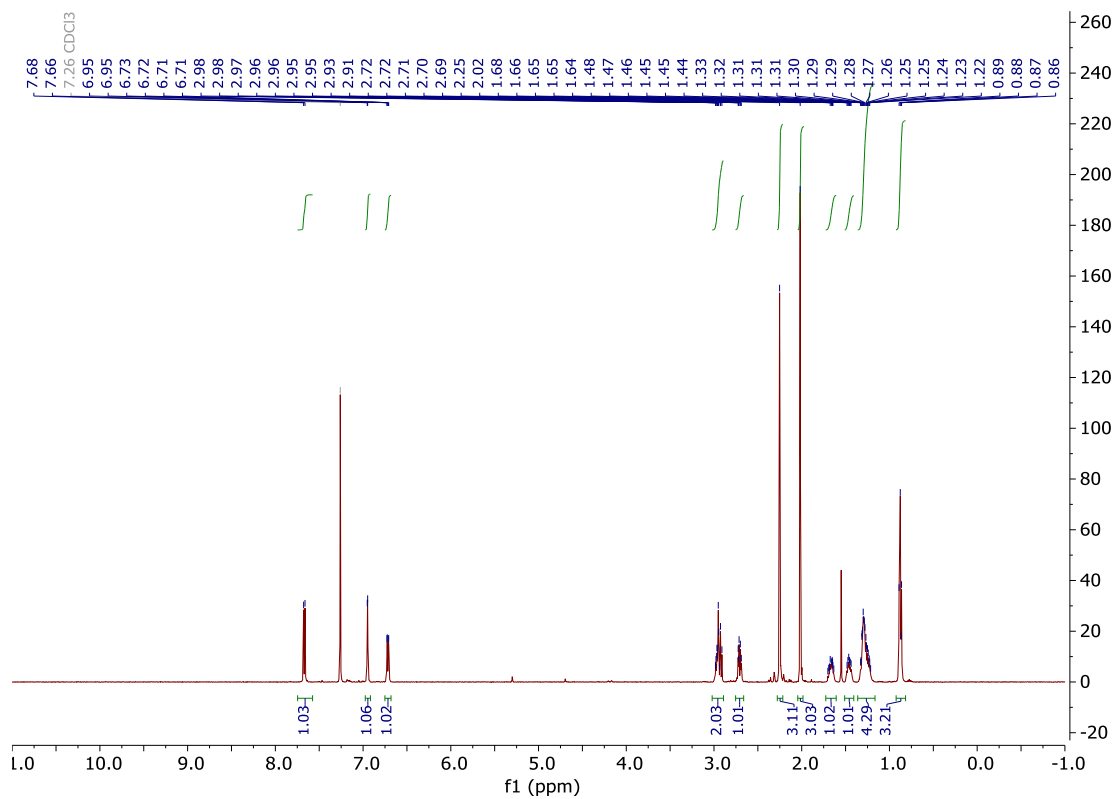


Figure S30: ^1H NMR spectrum of **S8** in CDCl_3 . Spectrometer Frequency 500.46 MHz. 22 °C

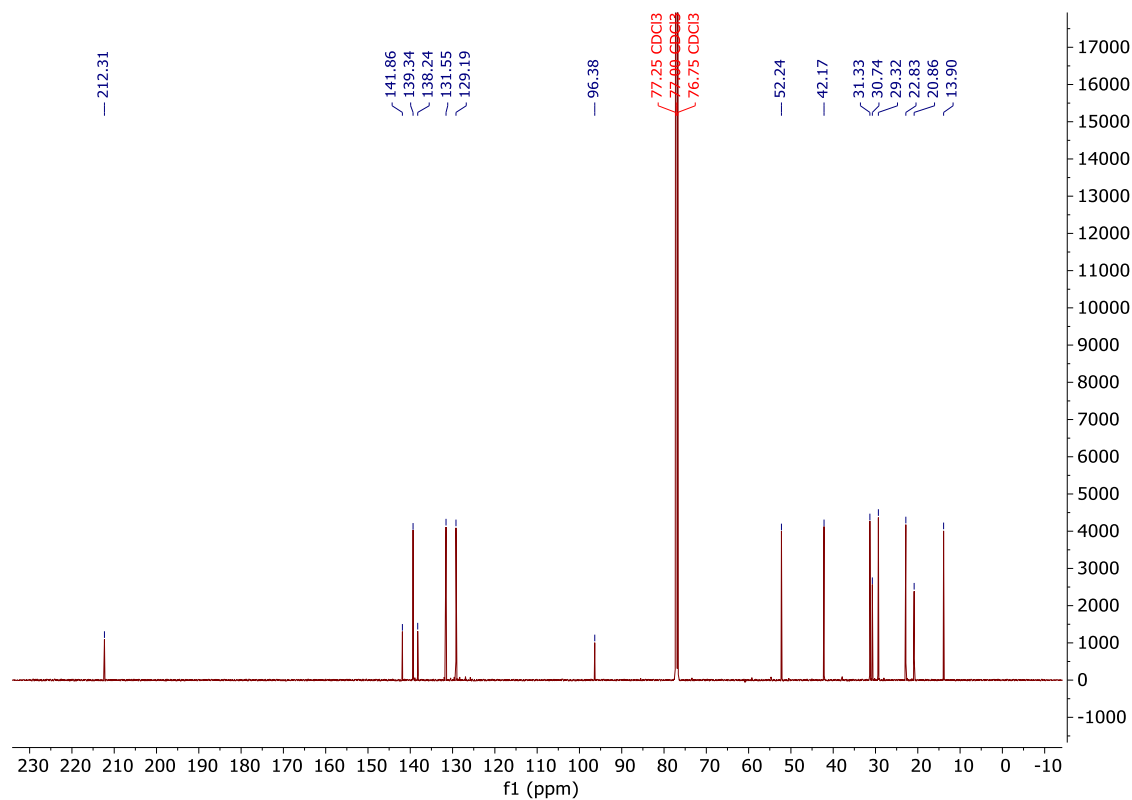


Figure S31: ^{13}C NMR spectrum of **S8** in CDCl_3 . Spectrometer Frequency 125.85 MHz. 22 °C

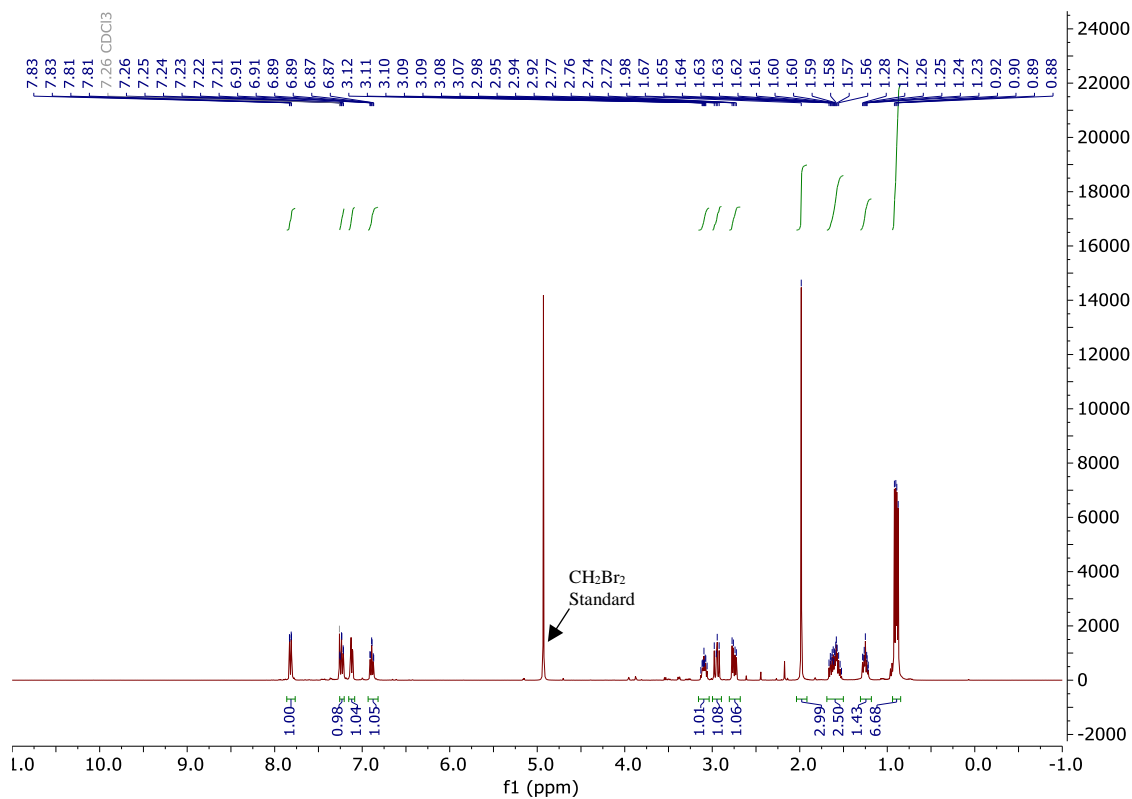


Figure S32: ¹H NMR spectrum of **S10** in CDCl₃. Spectrometer Frequency 399.80 MHz. 22 °C

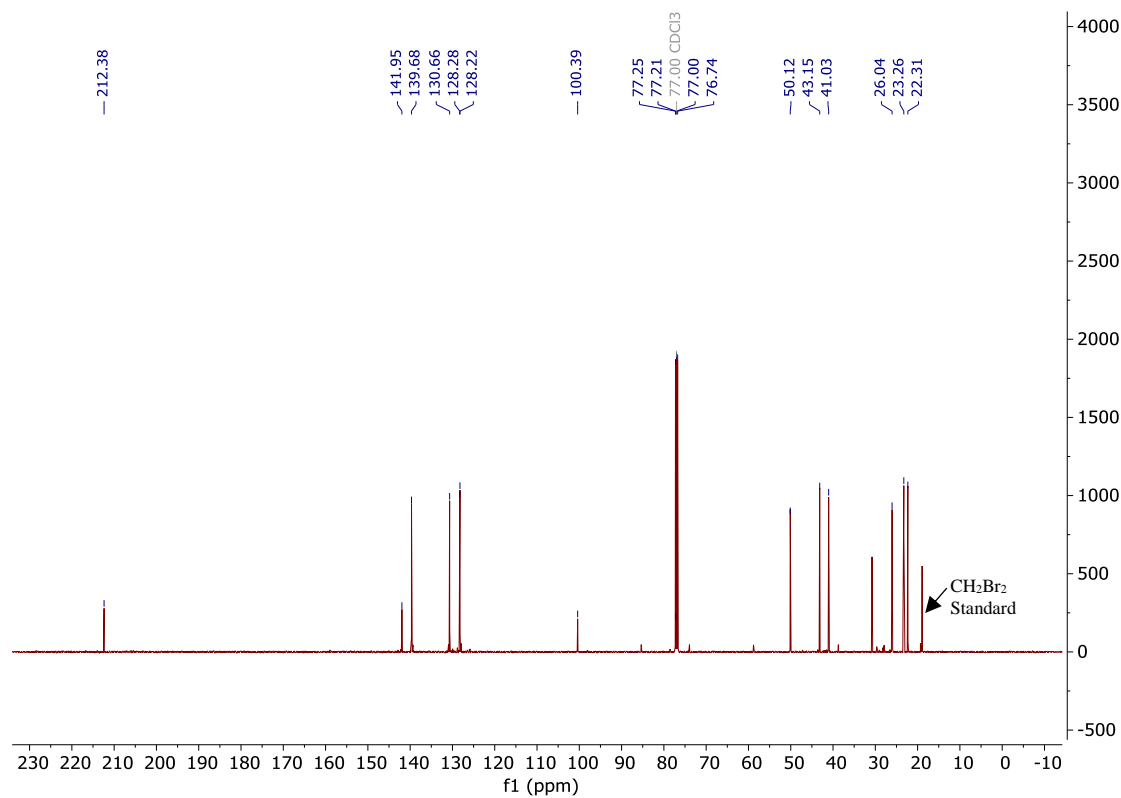


Figure S33: ¹³C NMR spectrum of **S10** in CDCl₃. Spectrometer Frequency 125.85 MHz. 22 °C

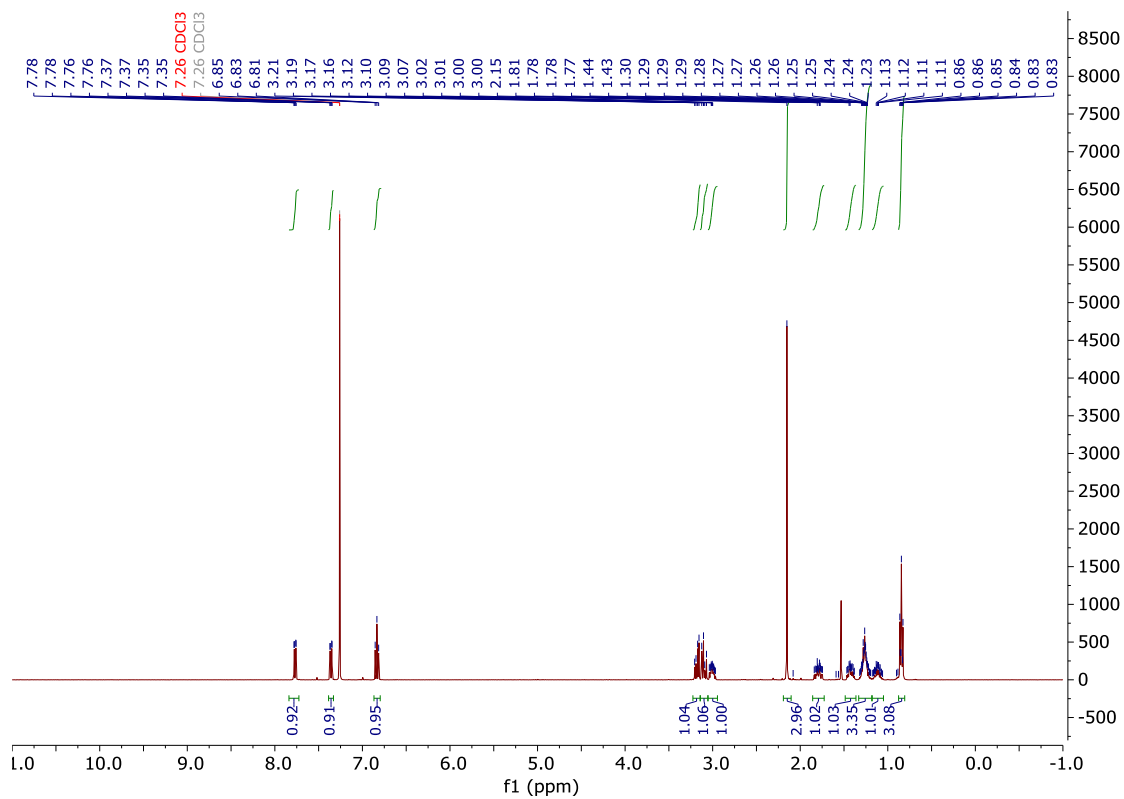


Figure S34: ^1H NMR spectrum of **S11** in CDCl_3 . Spectrometer Frequency 399.80 MHz. 22 °C

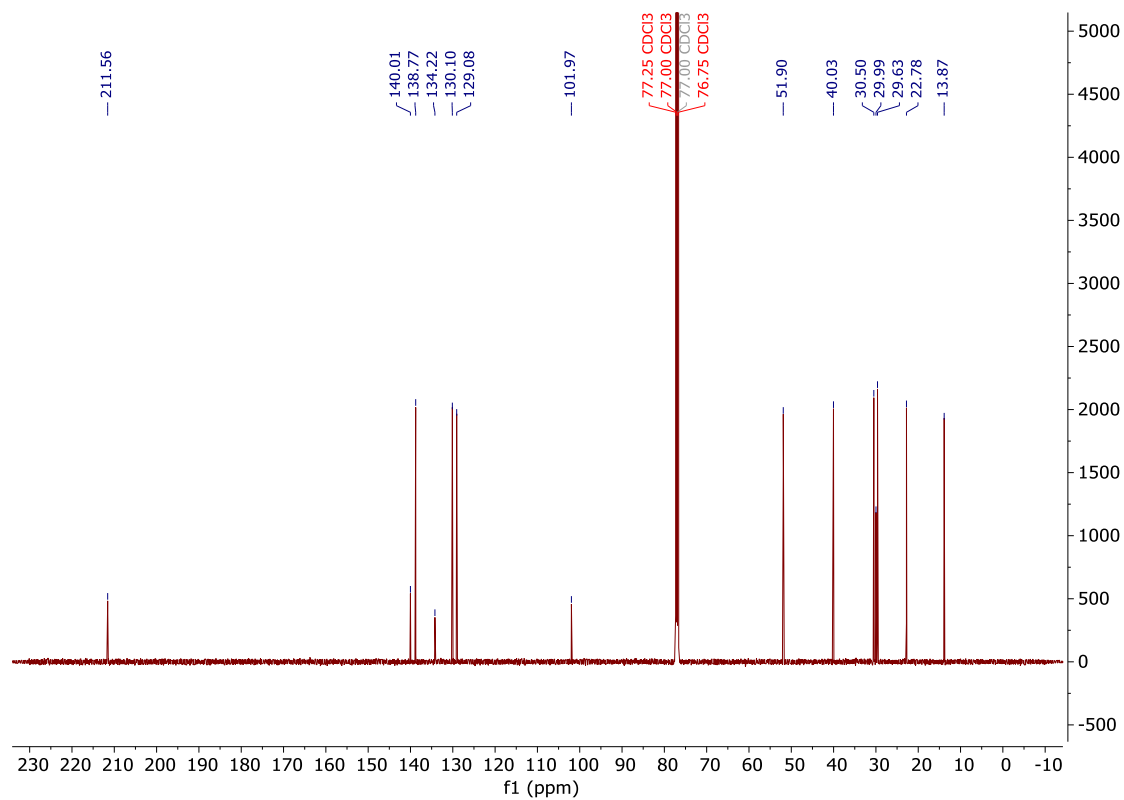


Figure S35: ^{13}C NMR spectrum of **S11** in CDCl_3 . Spectrometer Frequency 125.85 MHz. 22 °C

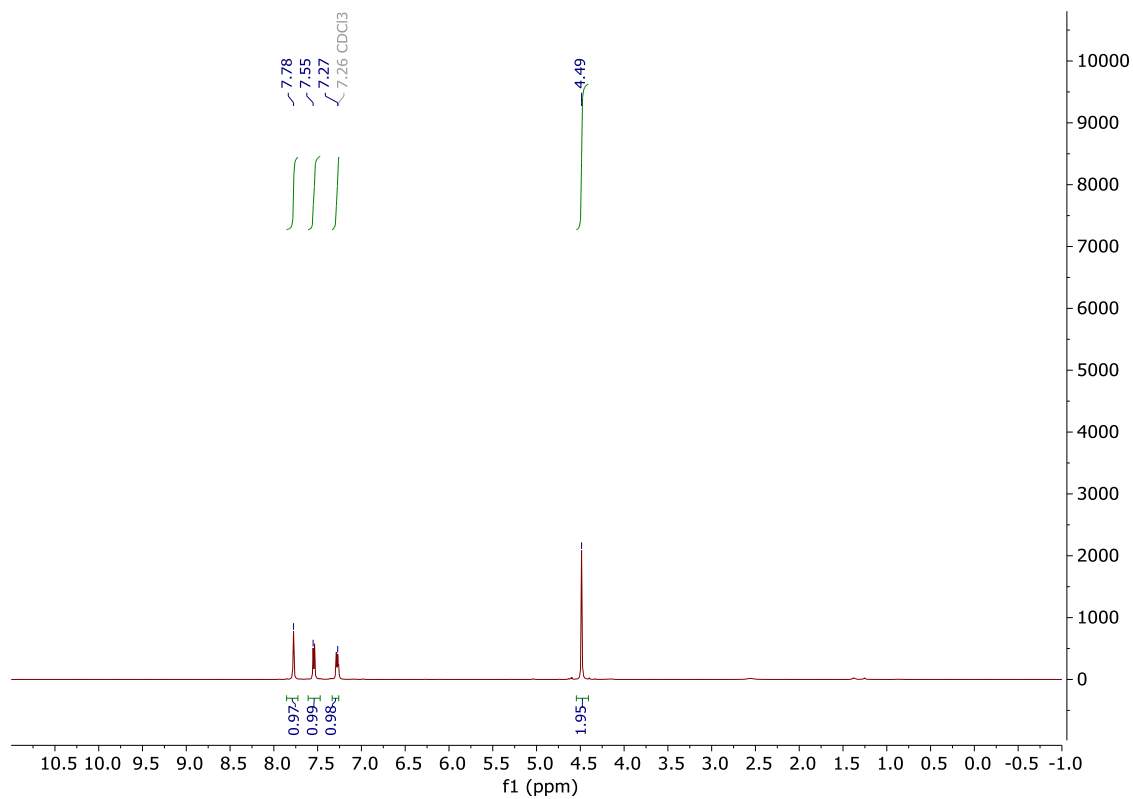


Figure S36: ^1H NMR spectrum of **S12-1** in CDCl_3 . Spectrometer Frequency 500.46 MHz. 22 °C

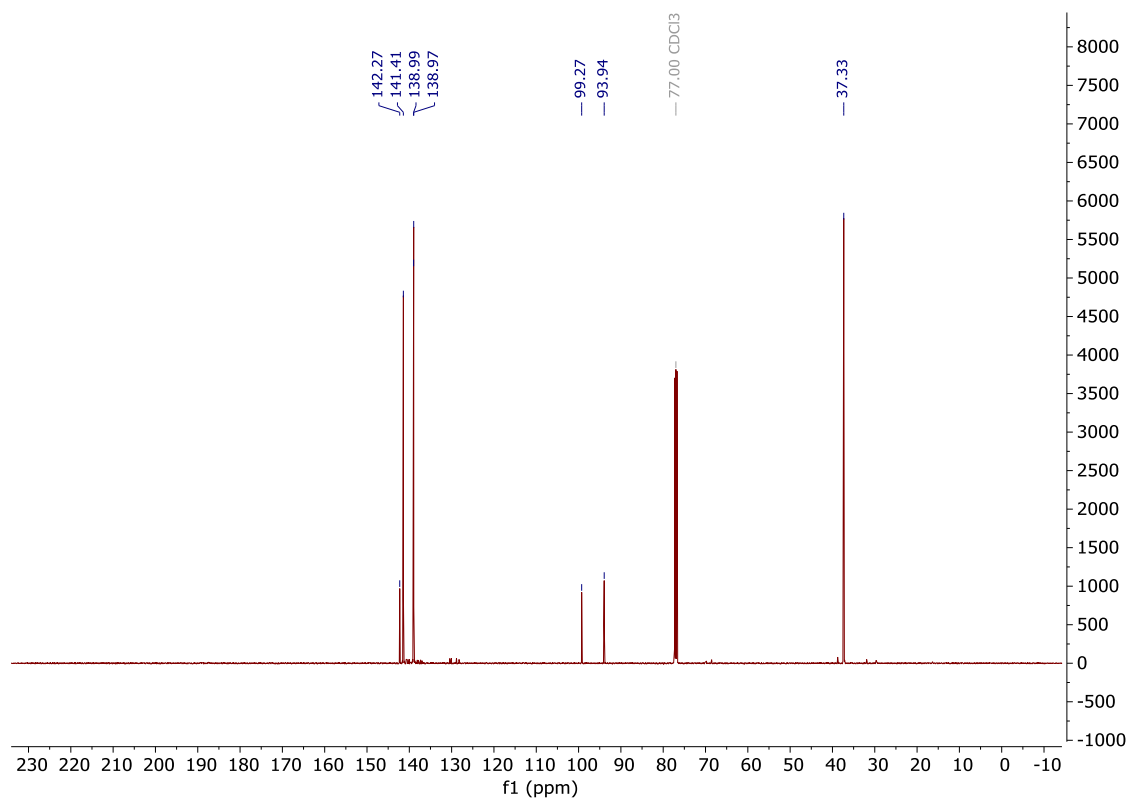


Figure S37: ^{13}C NMR spectrum of **S12-1** in CDCl_3 . Spectrometer Frequency 125.85 MHz. 22 °C

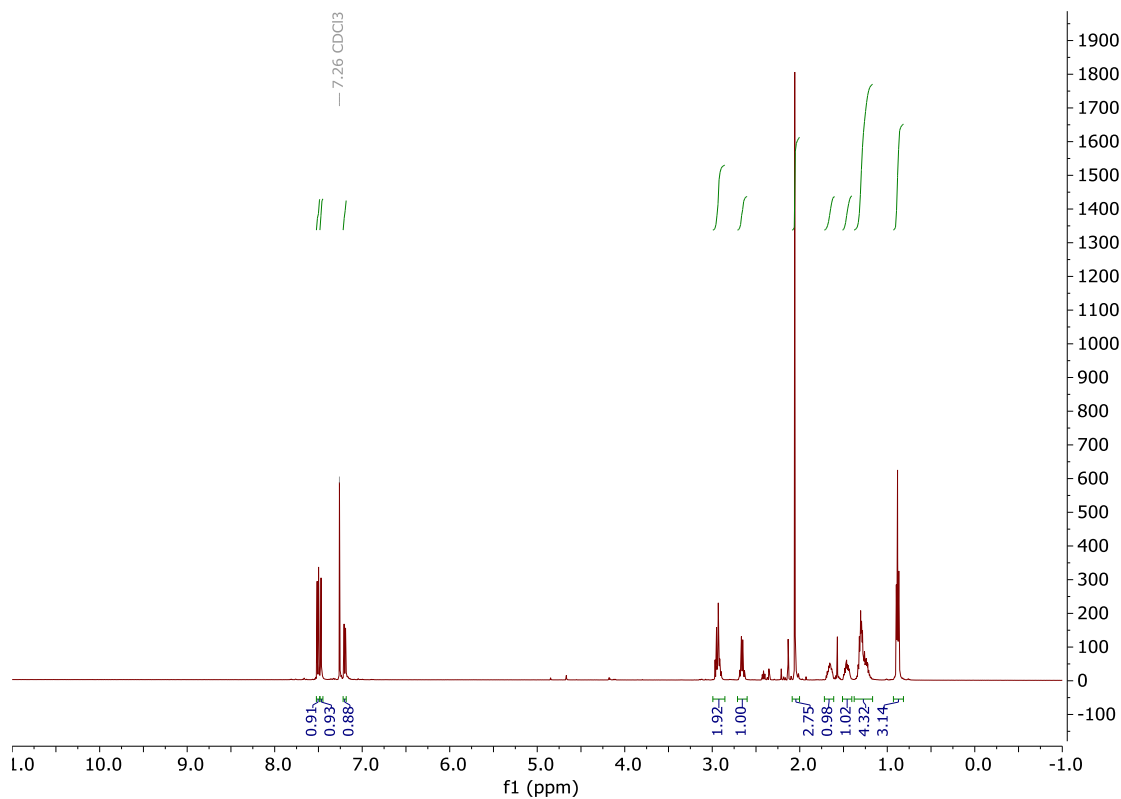


Figure S38: ^1H NMR spectrum of **S12** in CDCl_3 . Spectrometer Frequency 500.46 MHz. 22 $^\circ\text{C}$

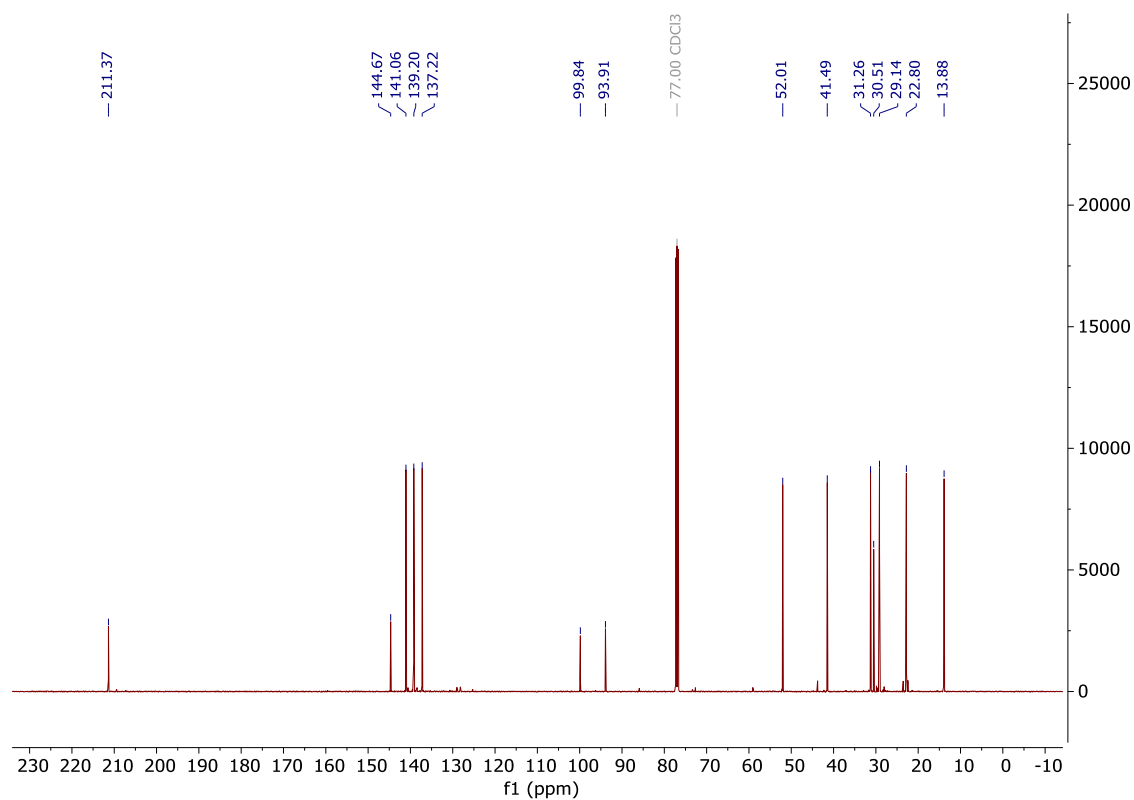


Figure S39: ^{13}C NMR spectrum of **S12** in CDCl_3 . Spectrometer Frequency 125.85 MHz. 22 $^\circ\text{C}$

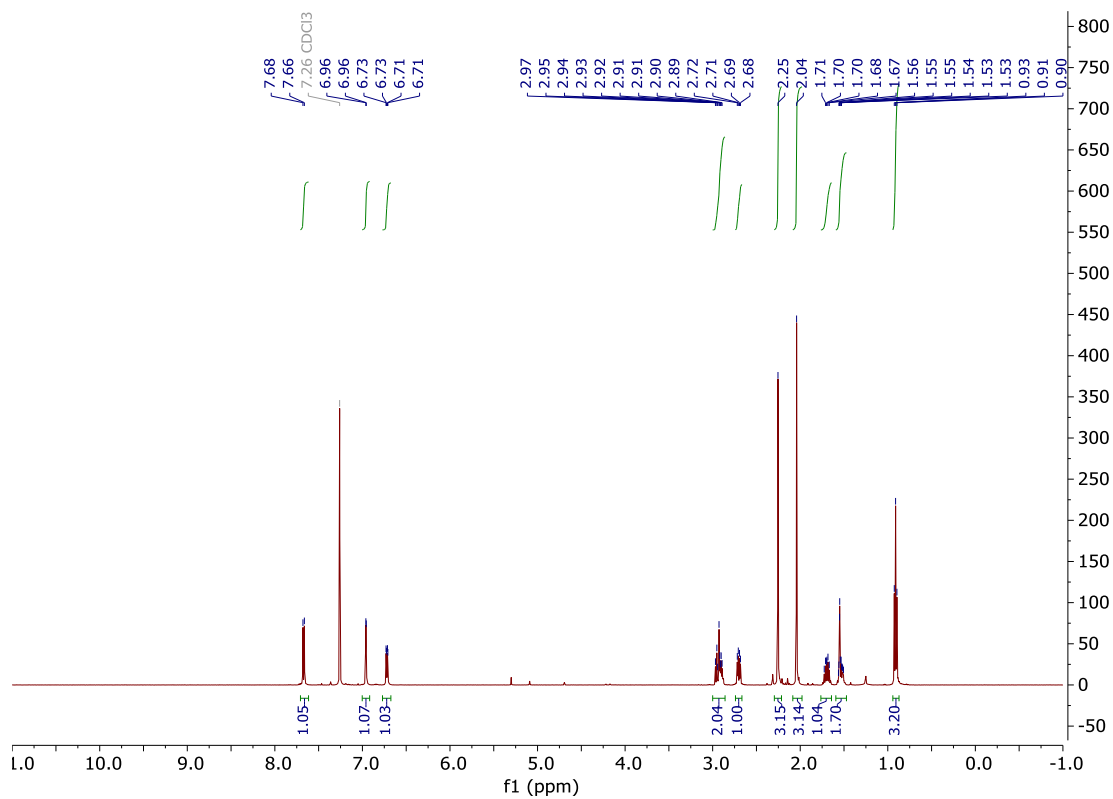


Figure S40: ¹H NMR spectrum of **S13** in CDCl₃. Spectrometer Frequency 500.15 MHz. 22 °C

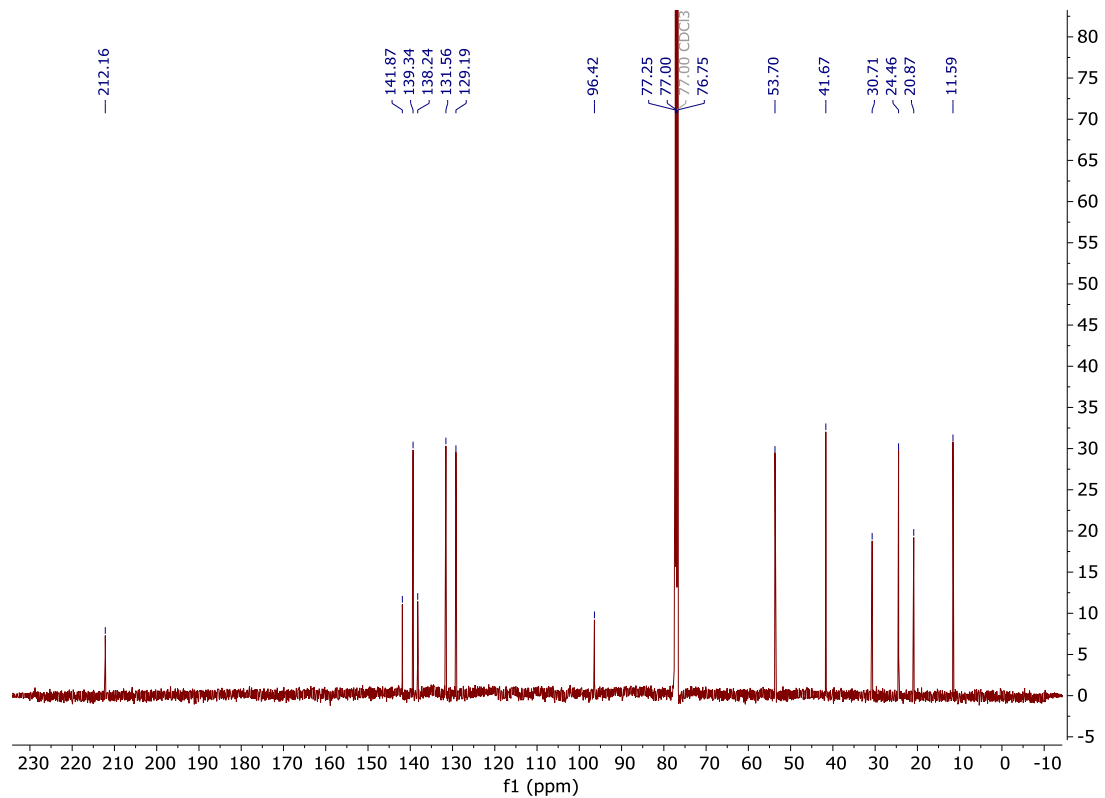


Figure S41: ¹³C NMR spectrum of **S13** in CDCl₃. Spectrometer Frequency 125.85 MHz. 22 °C

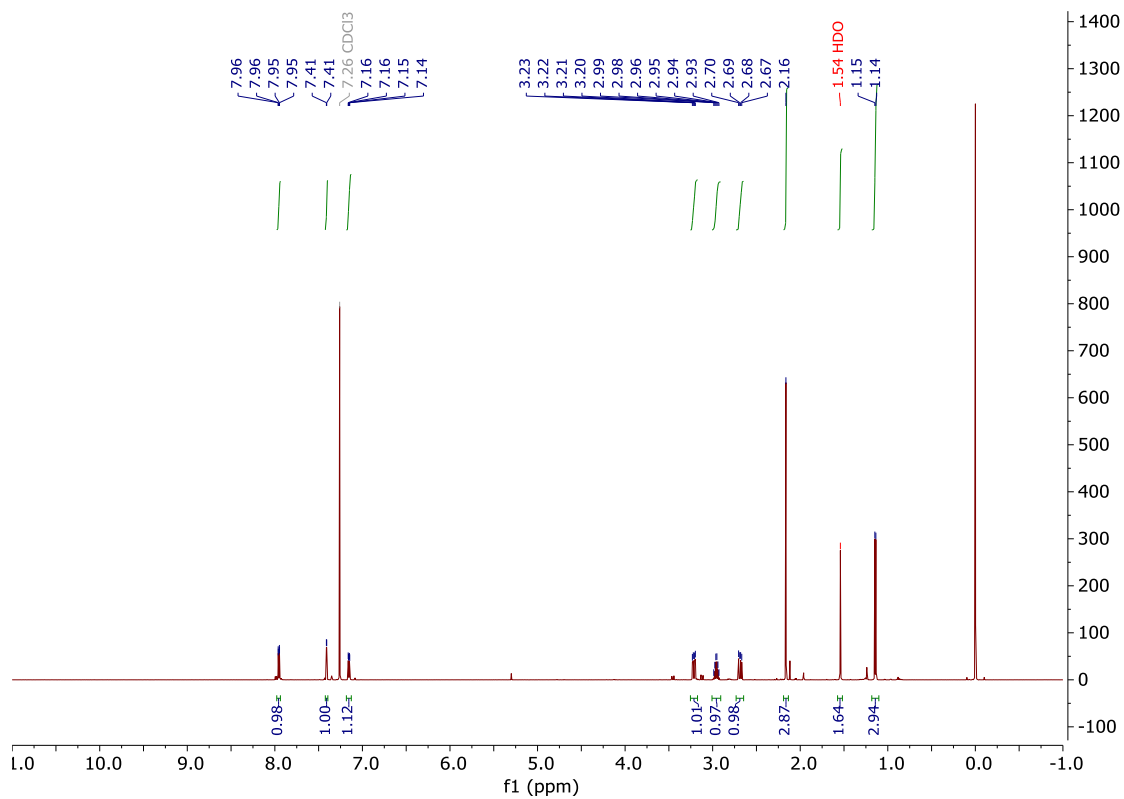


Figure S42: ^1H NMR spectrum of **S14** in CDCl_3 . Spectrometer Frequency 500.15 MHz. 22 °C

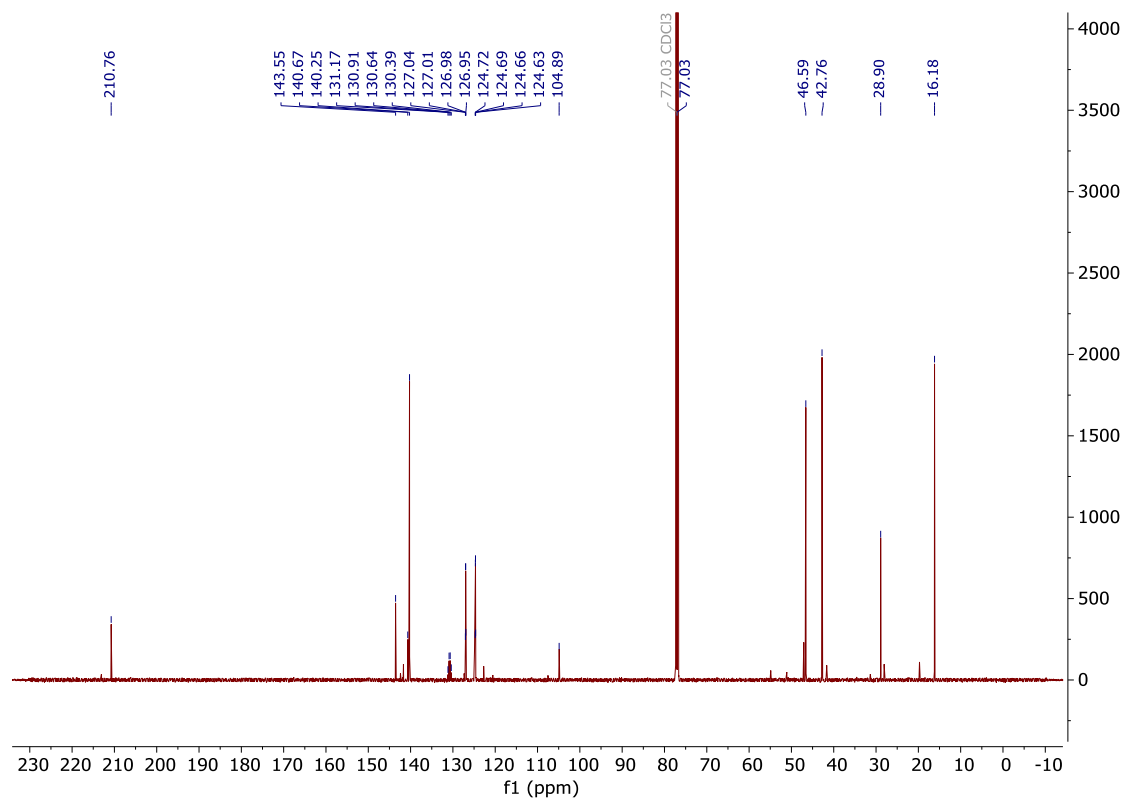


Figure S43: ^{13}C NMR spectrum of **S14** in CDCl_3 . Spectrometer Frequency 125.85 MHz. 22 °C

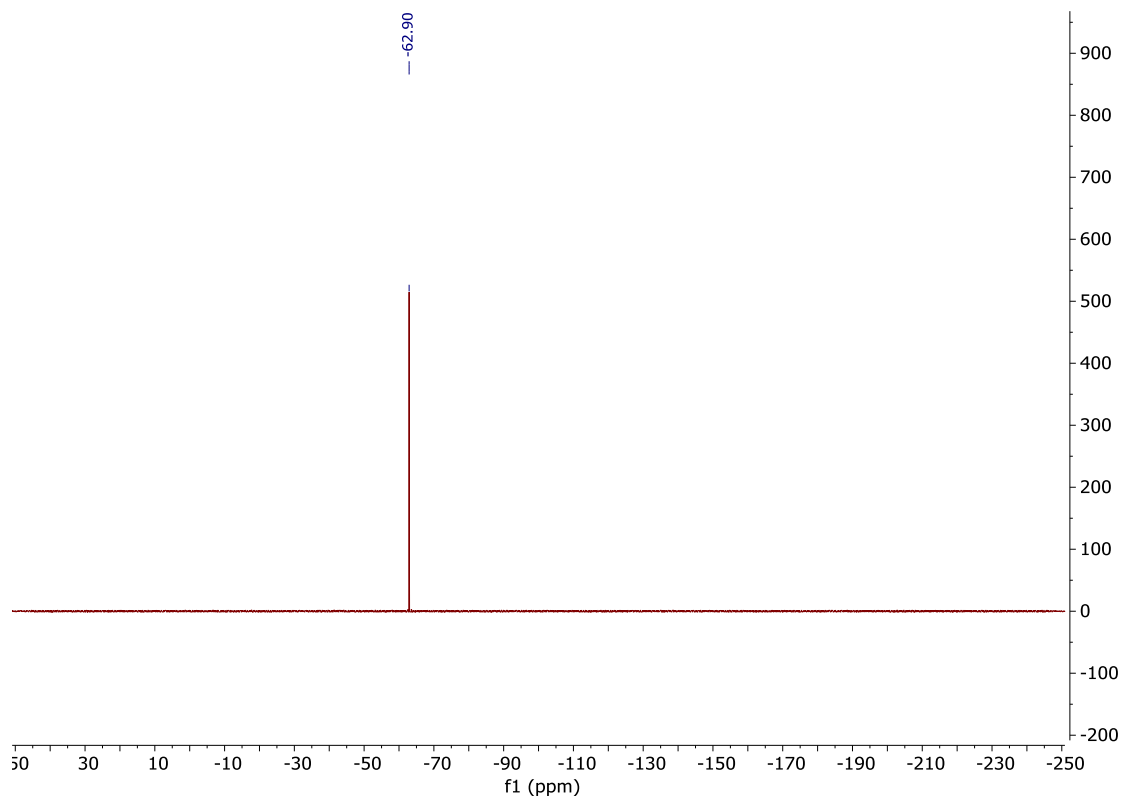


Figure S44: ^{19}F NMR spectrum of **S14** in CDCl_3 . Spectrometer Frequency 125.85 MHz. 22 °C

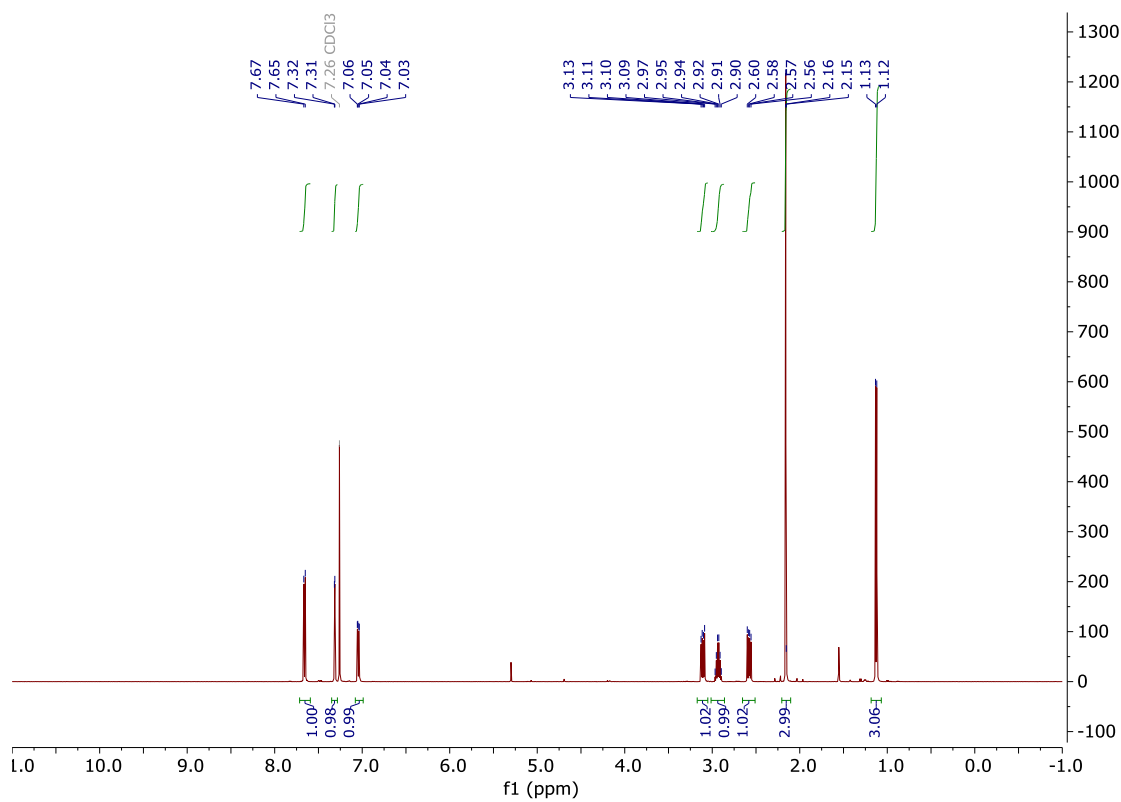


Figure S45: ^1H NMR spectrum of **S15** in CDCl_3 . Spectrometer Frequency 500.46 MHz. 22 °C

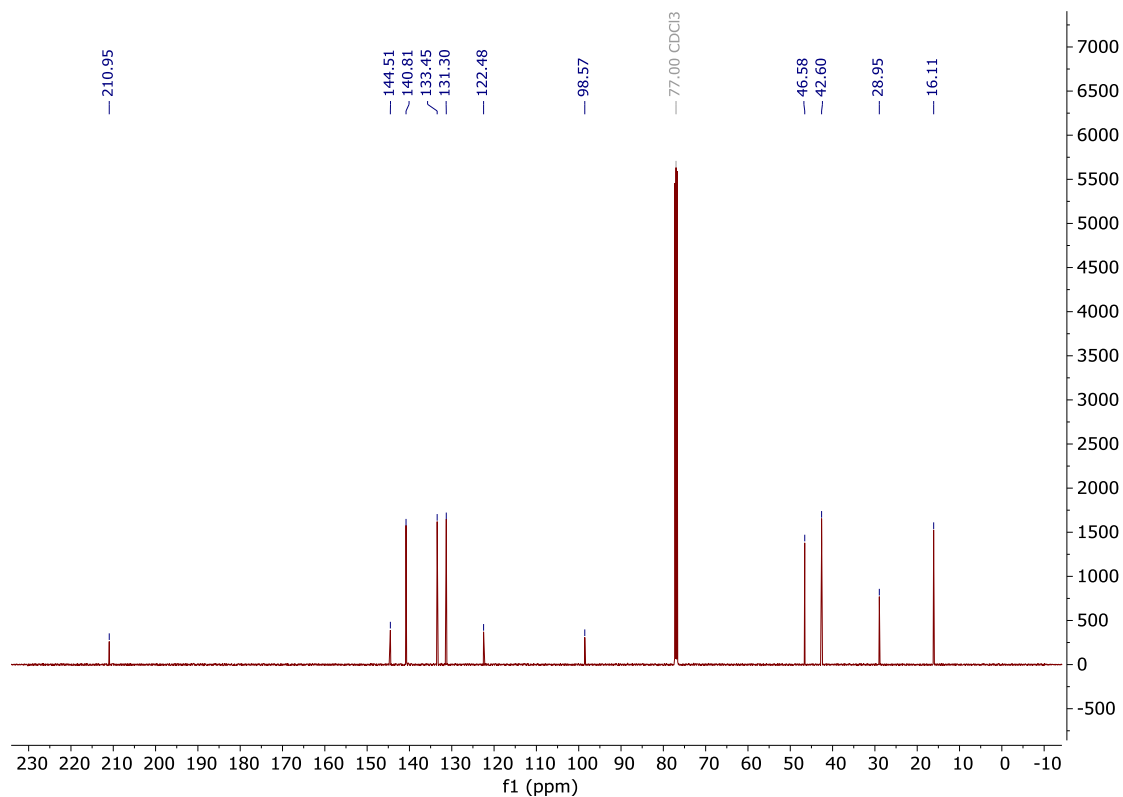


Figure S46: ^{13}C NMR spectrum of **S15** in CDCl_3 . Spectrometer Frequency 125.85 MHz. 22 °C

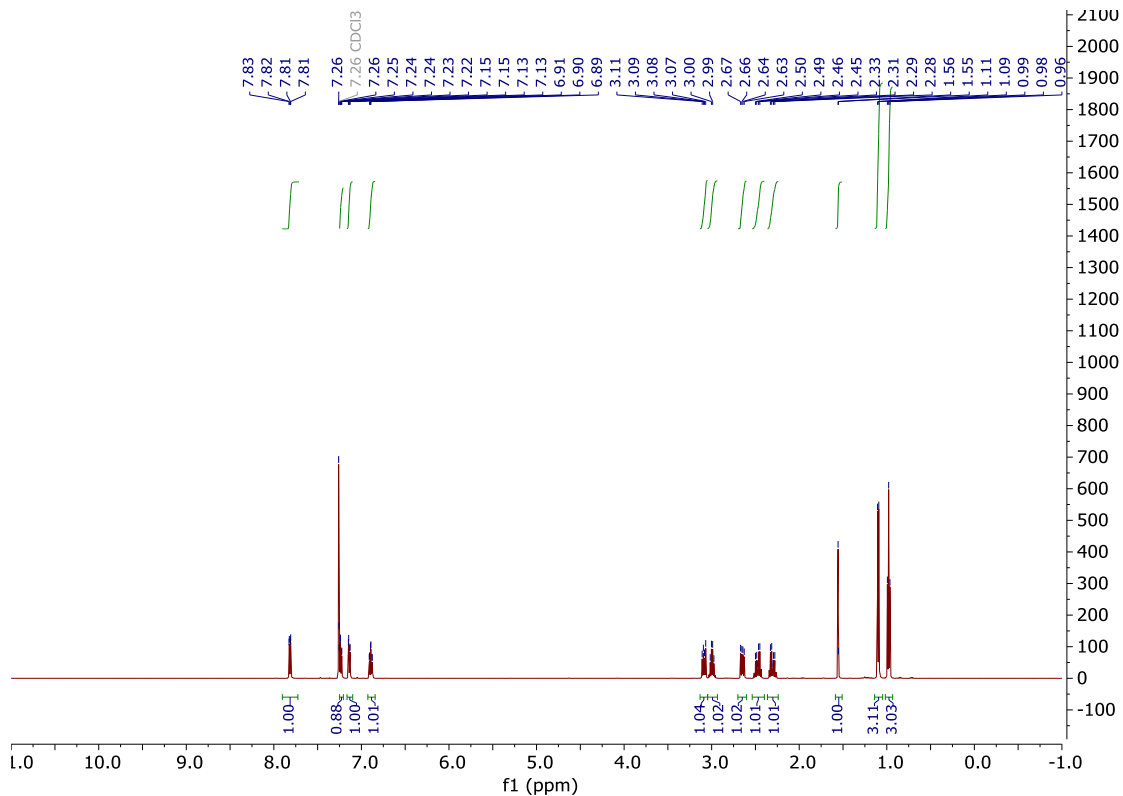


Figure S47: ^1H NMR spectrum of **S16** in CDCl_3 . Spectrometer Frequency 500.46 MHz. 22 °C

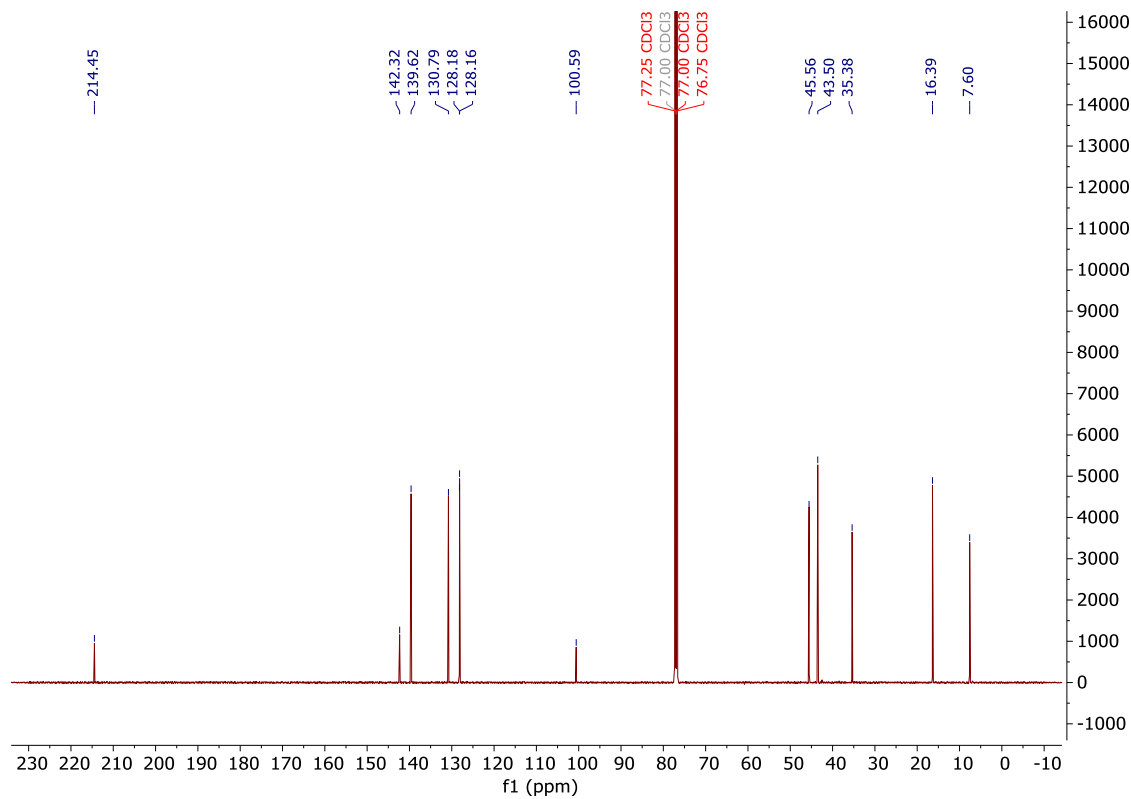


Figure S48: ^{13}C NMR spectrum of **S16** in CDCl_3 . Spectrometer Frequency 125.85 MHz. 22 $^\circ\text{C}$

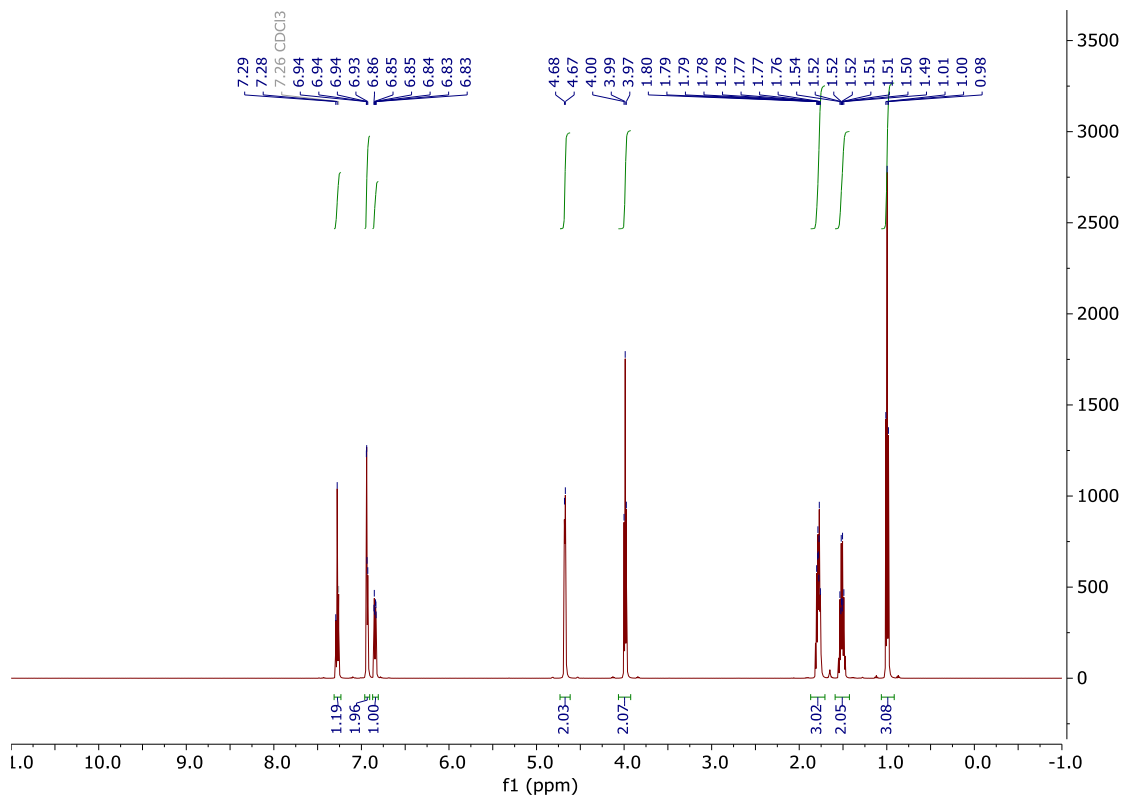


Figure S49: ^1H NMR spectrum of **S17-1** in CDCl_3 . Spectrometer Frequency 500.46 MHz. 22 $^\circ\text{C}$

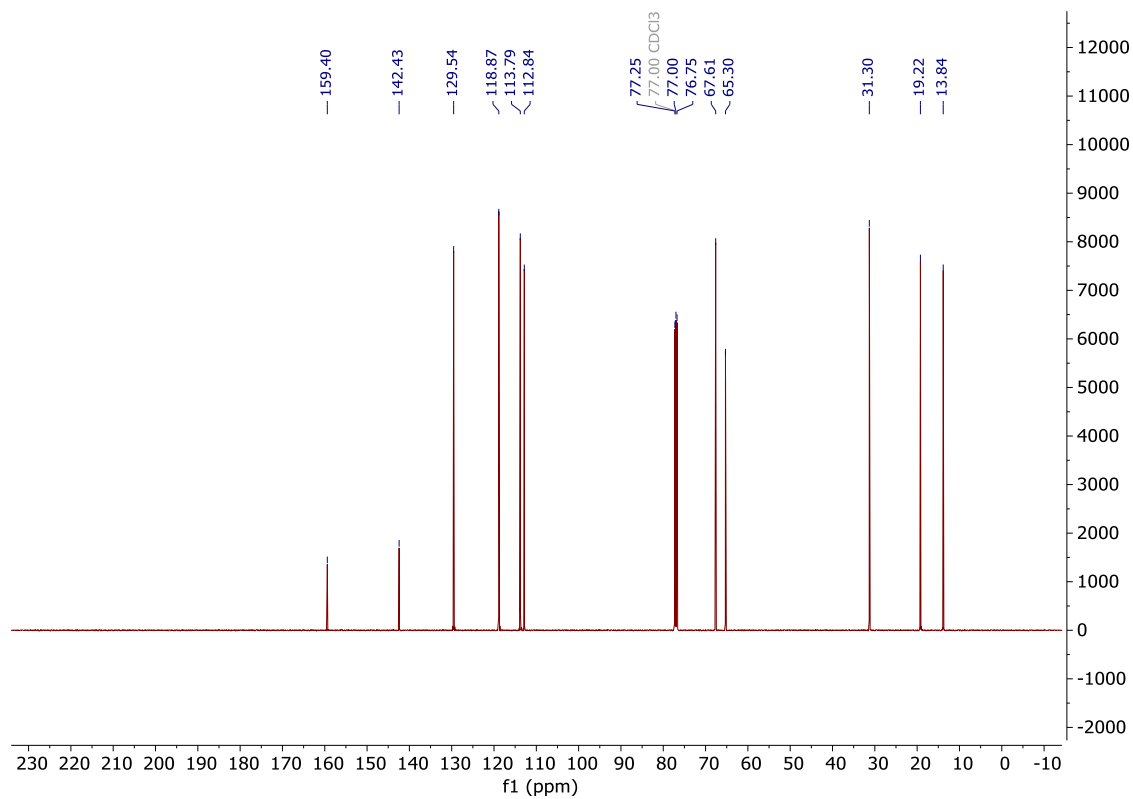


Figure S50: ^{13}C NMR spectrum of **S17-1** in CDCl_3 . Spectrometer Frequency 125.85 MHz. 22 °C

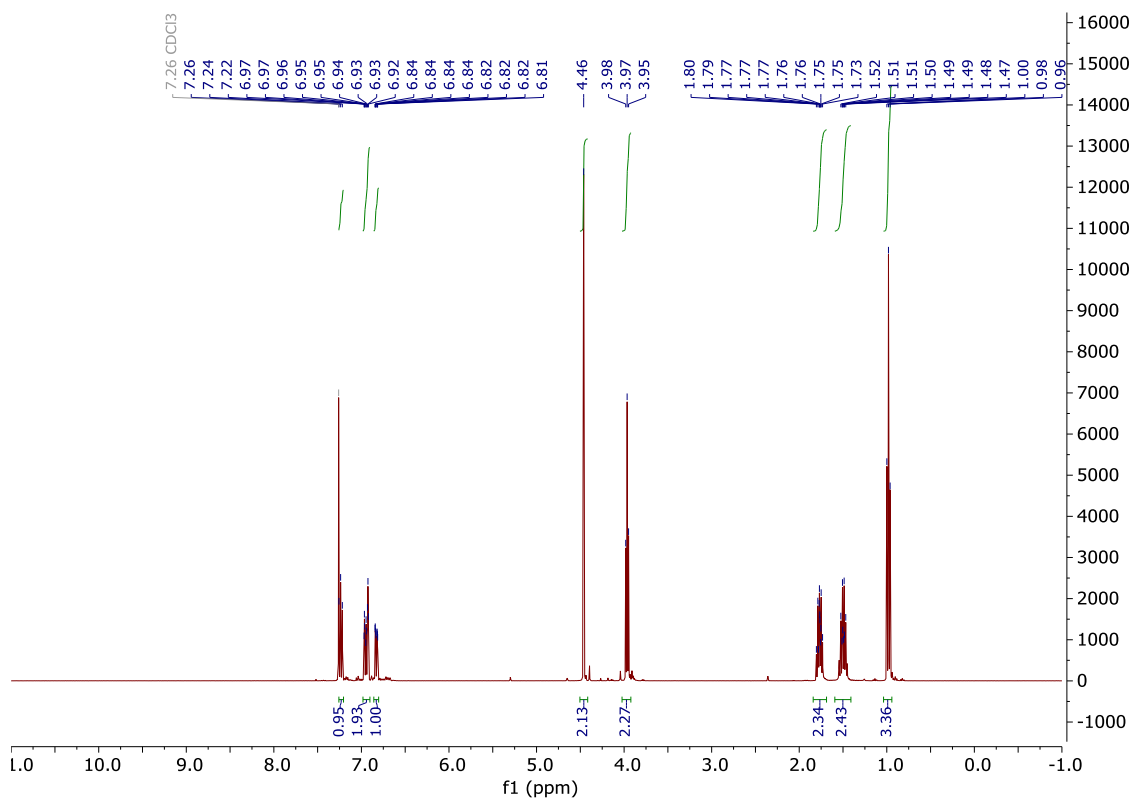


Figure S51: ^1H NMR spectrum of **S17-2** in CDCl_3 . Spectrometer Frequency 399.80 MHz. 22 °C

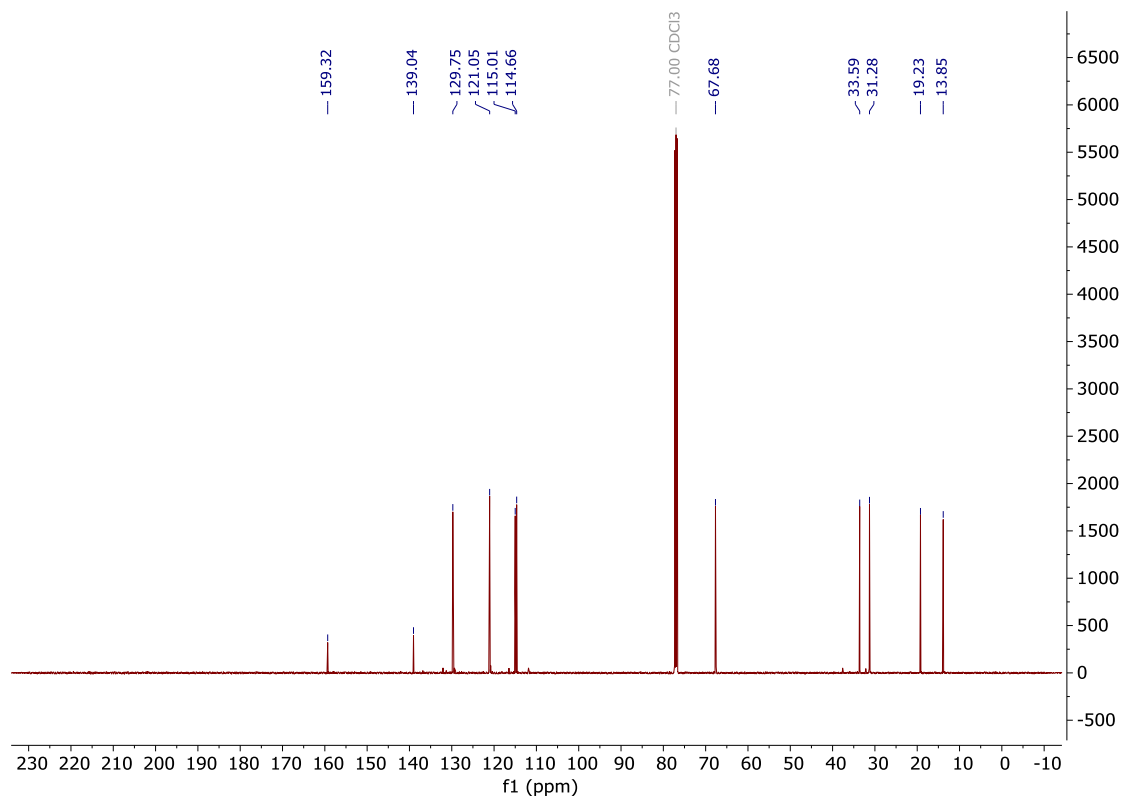


Figure S52: ^{13}C NMR spectrum of **S17-2** in CDCl_3 . Spectrometer Frequency 125.85 MHz. 22 $^\circ\text{C}$

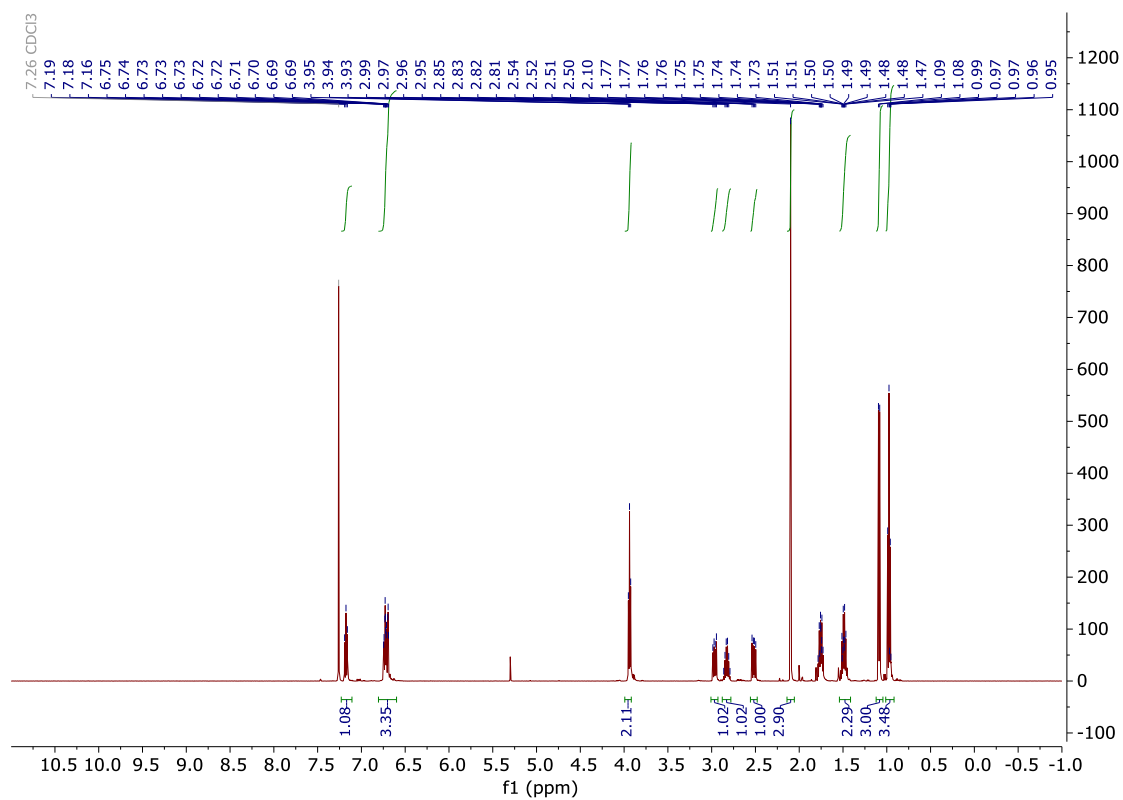


Figure S53: ^1H NMR spectrum of **S17** in CDCl_3 . Spectrometer Frequency 500.46 MHz. 22 $^\circ\text{C}$

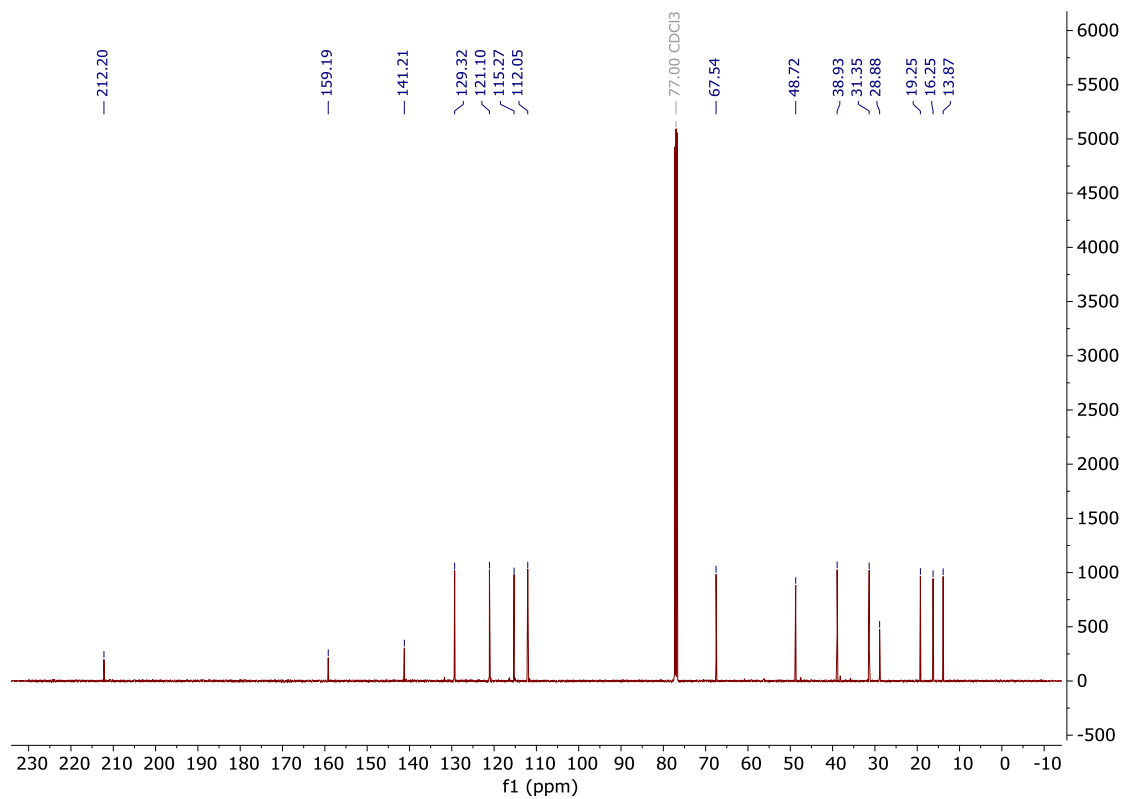


Figure S54: ^{13}C NMR spectrum of **S17** in CDCl_3 . Spectrometer Frequency 125.85 MHz. 22 $^\circ\text{C}$

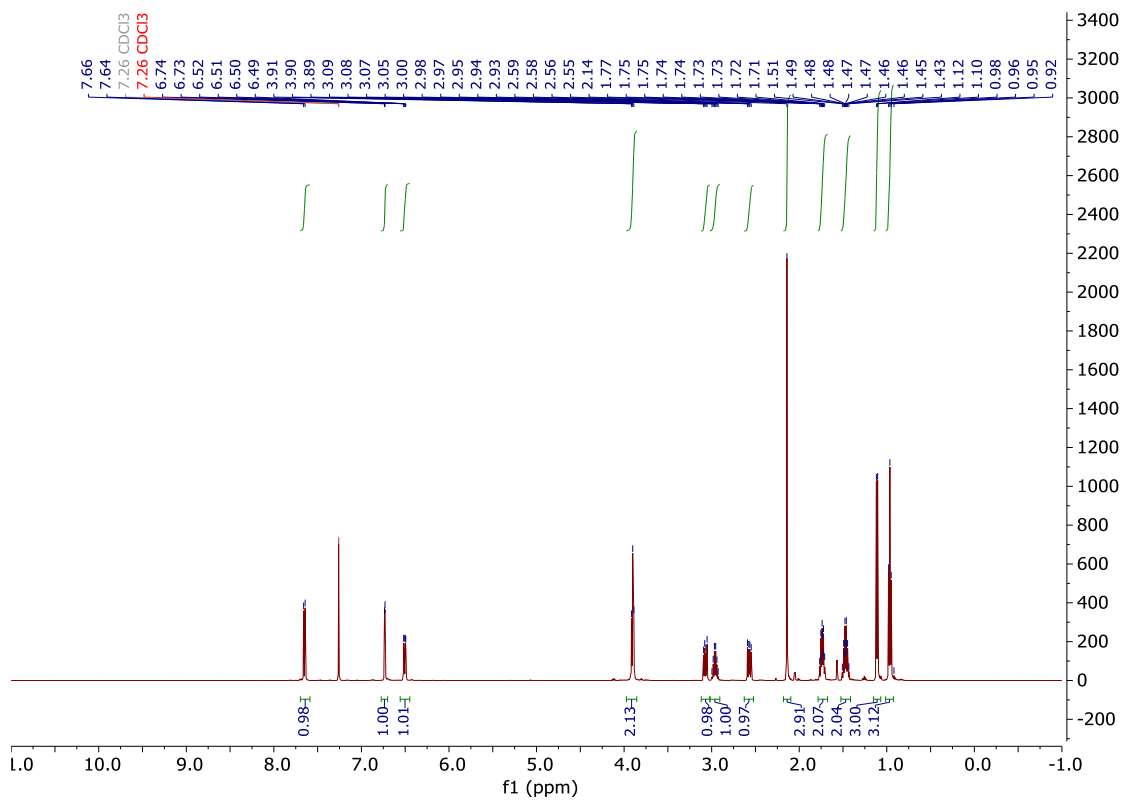


Figure S55: ^1H NMR spectrum of **S18** in CDCl_3 . Spectrometer Frequency 500.46 MHz. 22 $^\circ\text{C}$

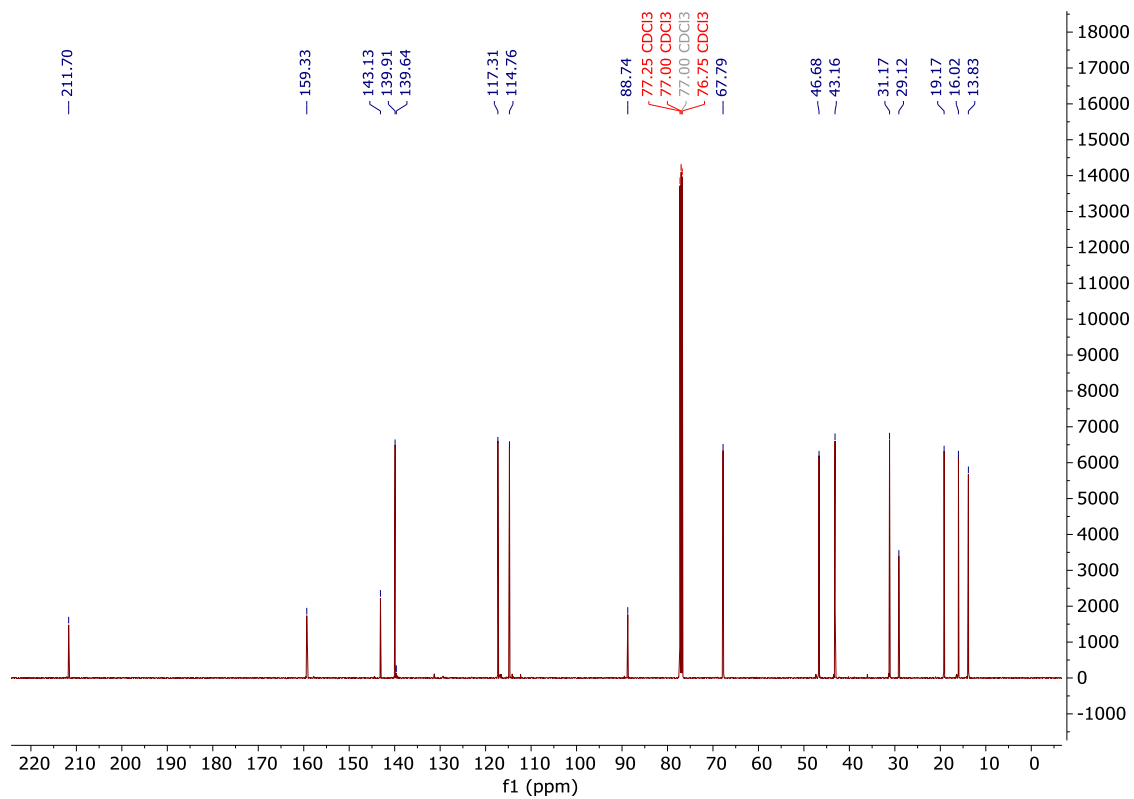


Figure S56: ^{13}C NMR spectrum of **S18** in CDCl_3 . Spectrometer Frequency 125.85 MHz. 22 $^\circ\text{C}$

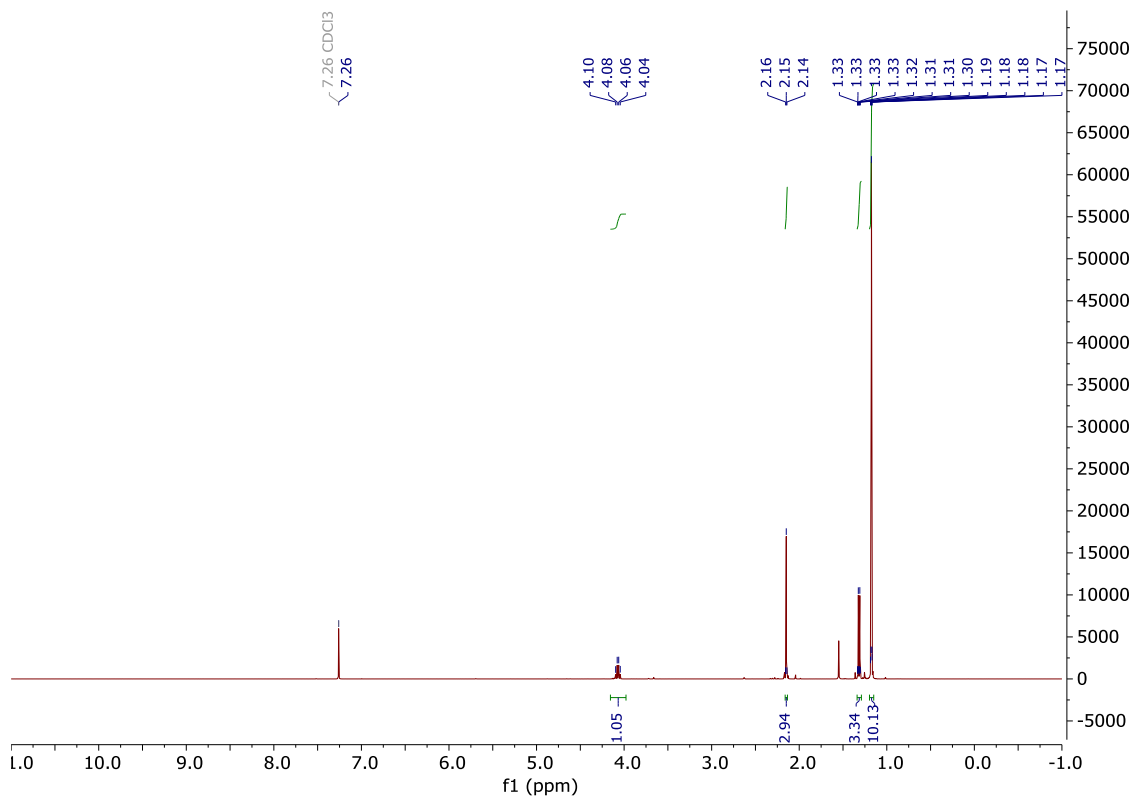


Figure S57: ^1H NMR spectrum of **S19** in CDCl_3 . Spectrometer Frequency 399.80 MHz. 22 $^\circ\text{C}$

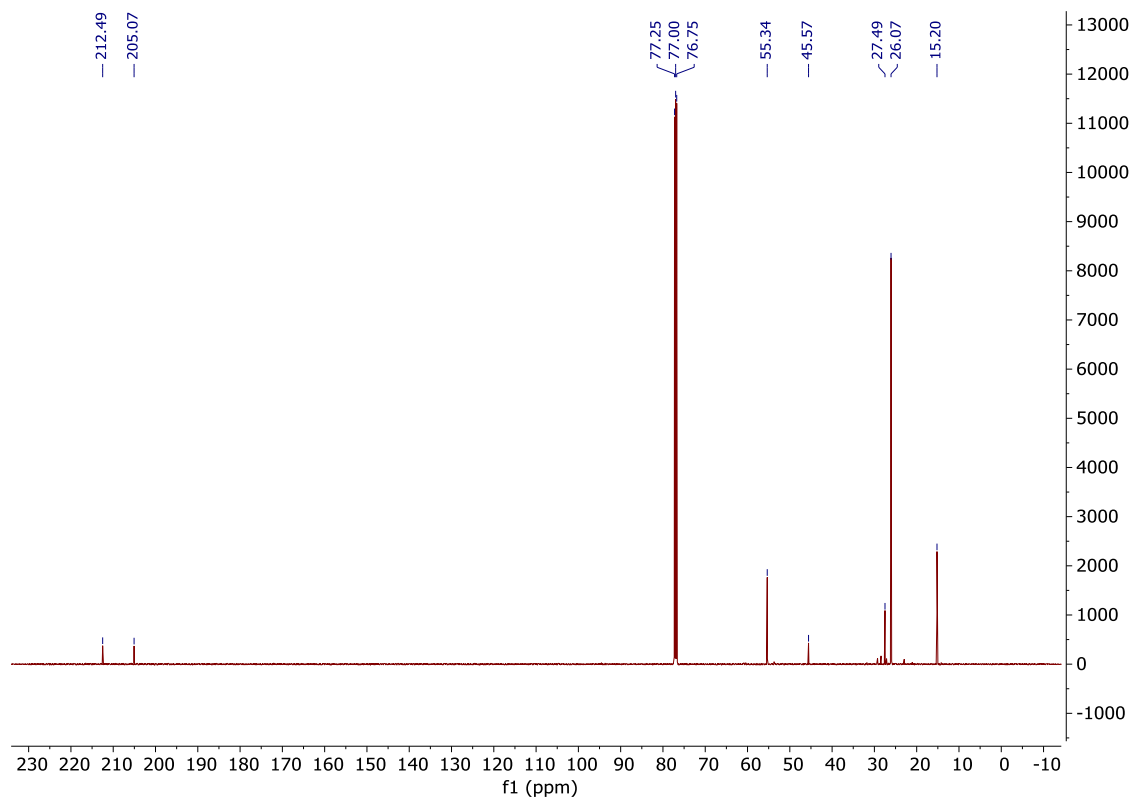


Figure S58: ^{13}C NMR spectrum of **S19** in CDCl_3 . Spectrometer Frequency 125.85 MHz. 22 $^\circ\text{C}$

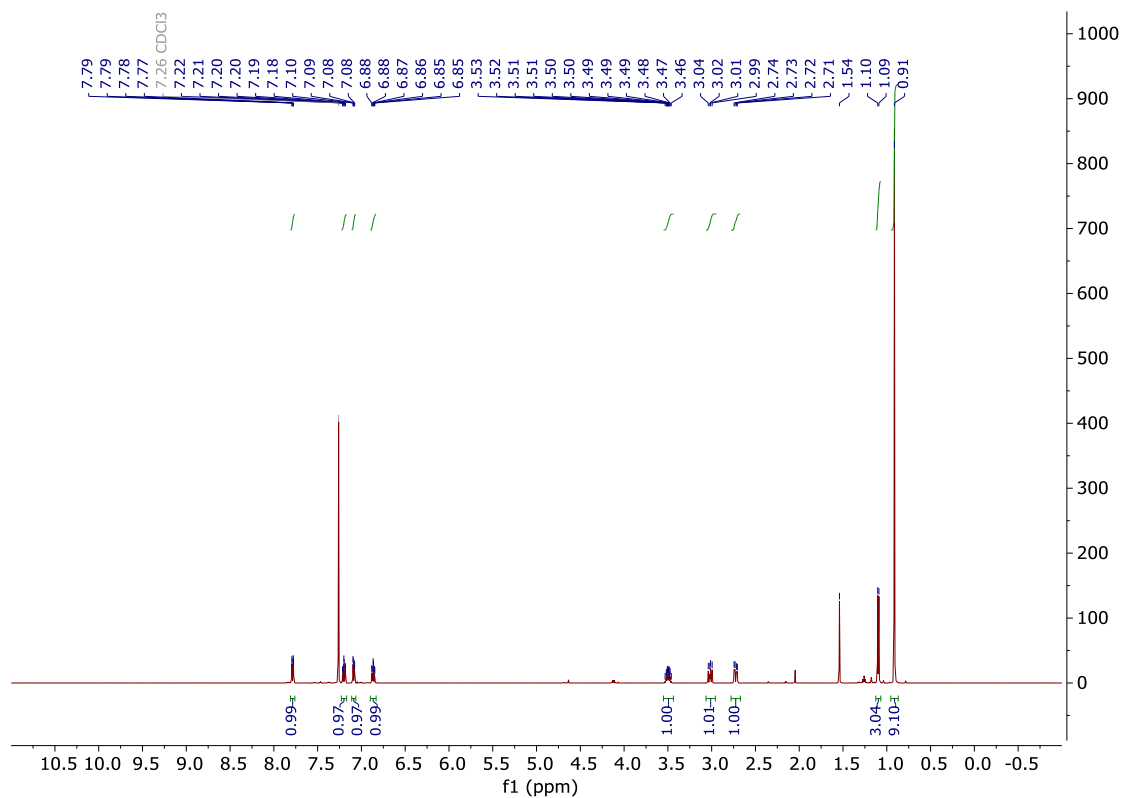


Figure S59: ^1H NMR spectrum of **S20** in CDCl_3 . Spectrometer Frequency 500.40 MHz. 22 $^\circ\text{C}$

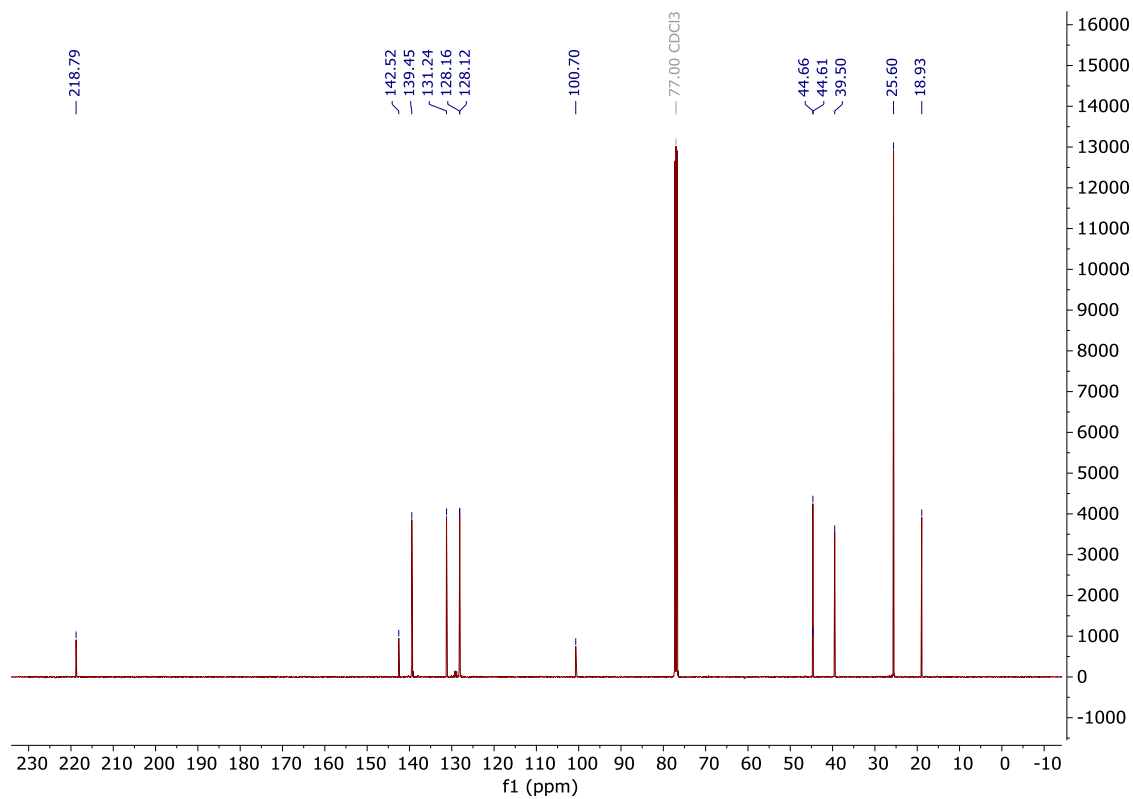


Figure S60: ^{13}C NMR spectrum of **S20** in CDCl_3 . Spectrometer Frequency 125.85 MHz. 22 $^\circ\text{C}$

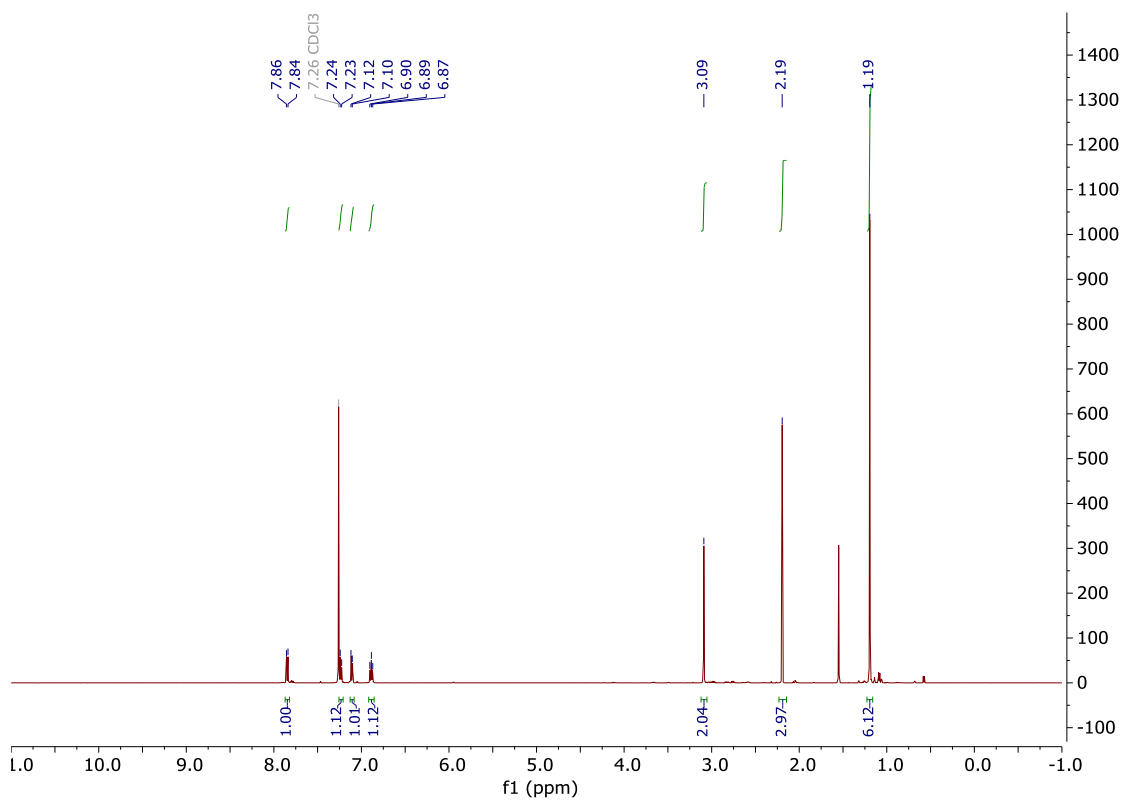


Figure S61: ^1H NMR spectrum of **S21** in CDCl_3 . Spectrometer Frequency 500.40 MHz. 22 $^\circ\text{C}$

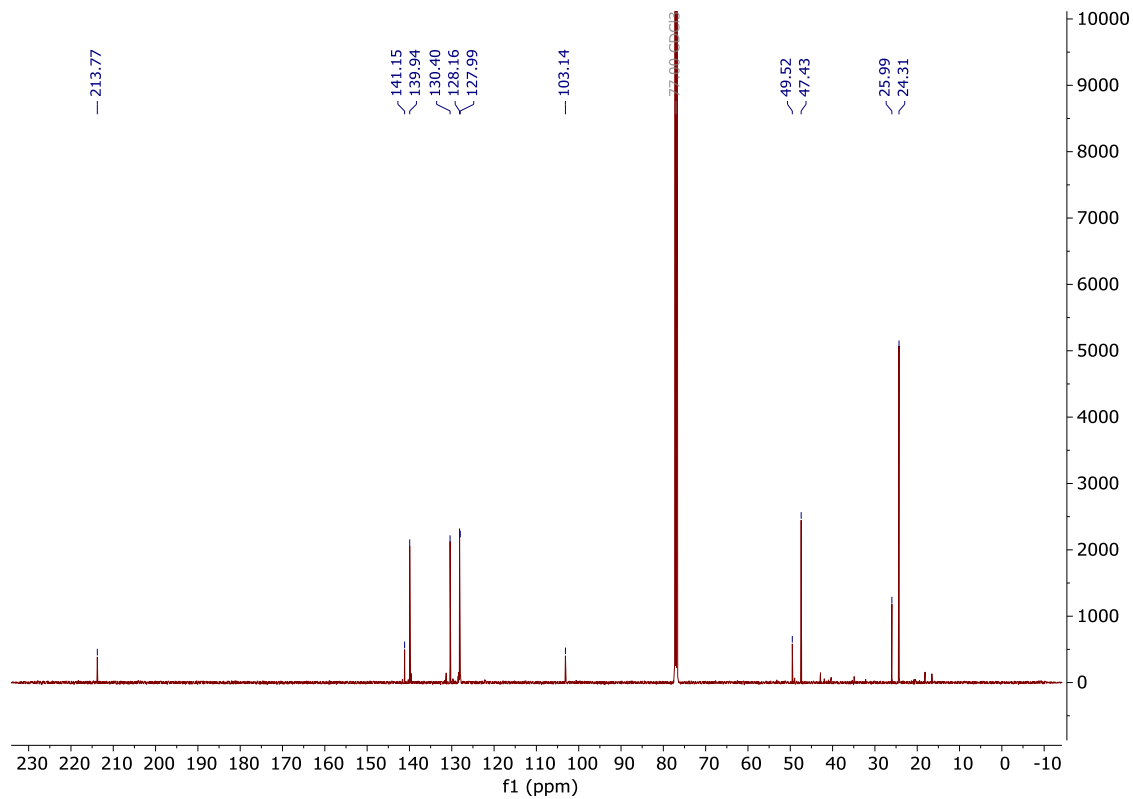


Figure S62: ^{13}C NMR spectrum of **S21** in CDCl_3 . Spectrometer Frequency 125.85 MHz. 22 $^\circ\text{C}$

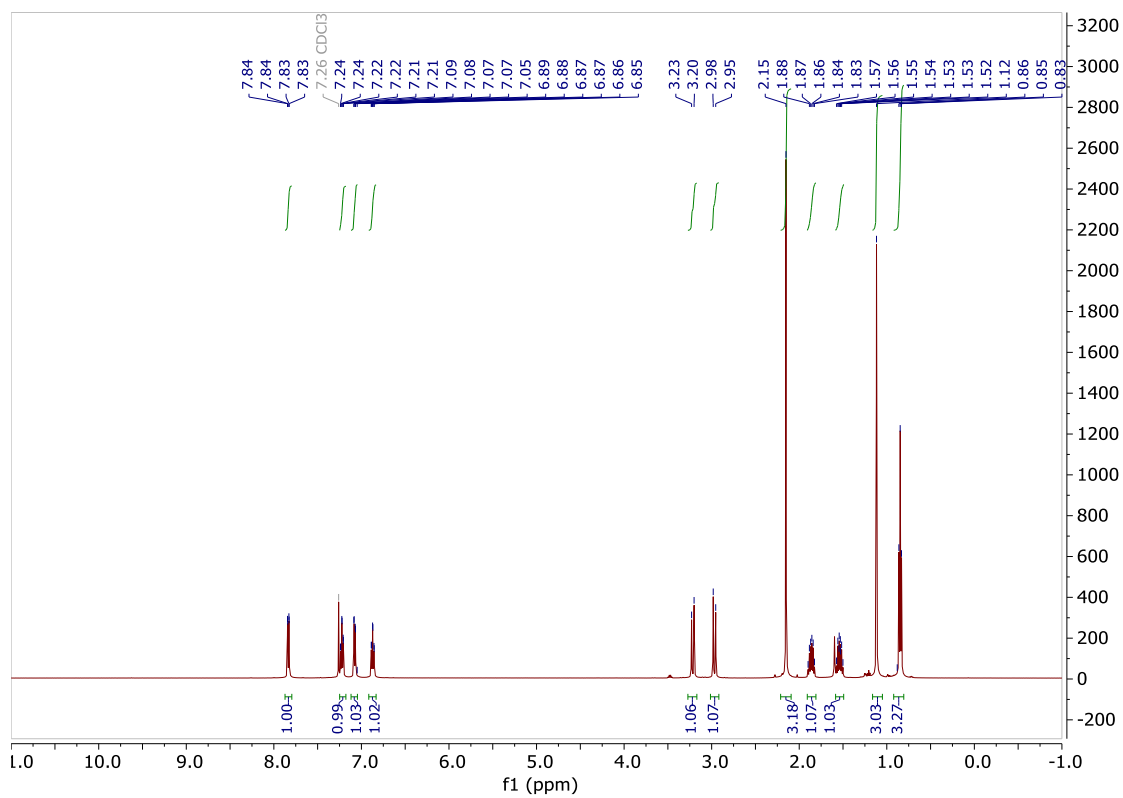


Figure S63: ^1H NMR spectrum of **S23** in CDCl_3 . Spectrometer Frequency 500.15 MHz. 22 $^\circ\text{C}$

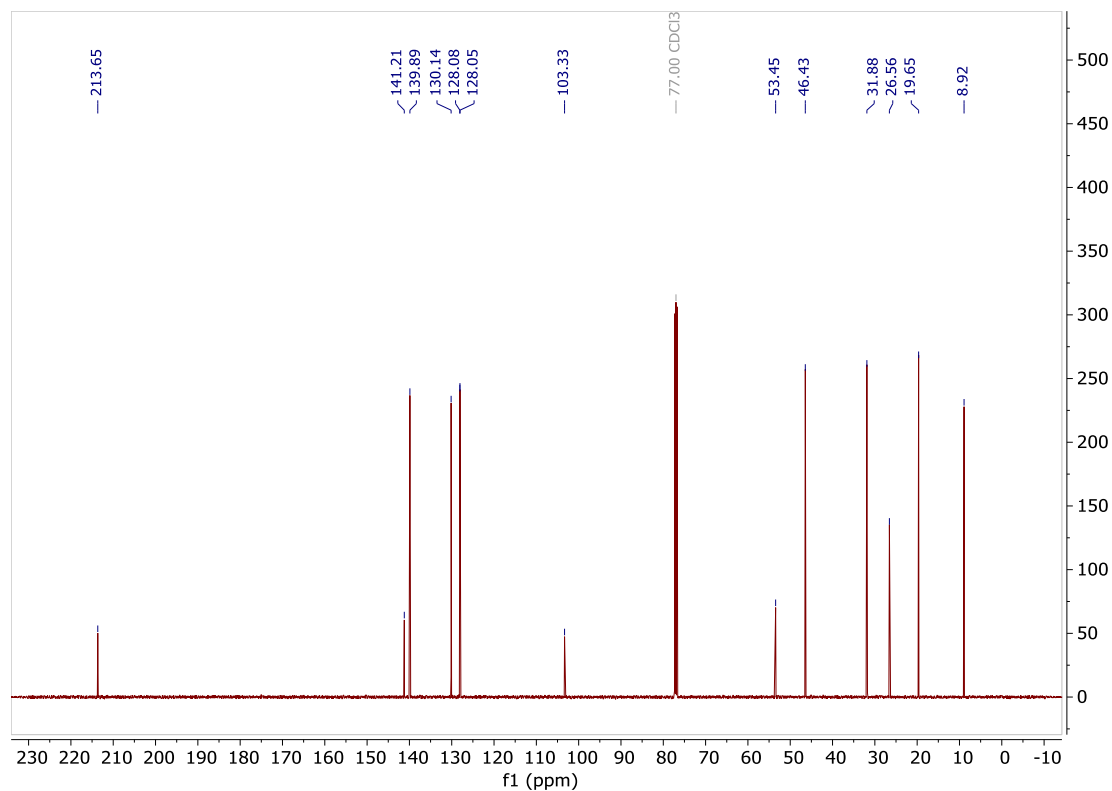


Figure S64: ^{13}C NMR spectrum of **S23** in CDCl_3 . Spectrometer Frequency 125.85 MHz. 22 $^\circ\text{C}$

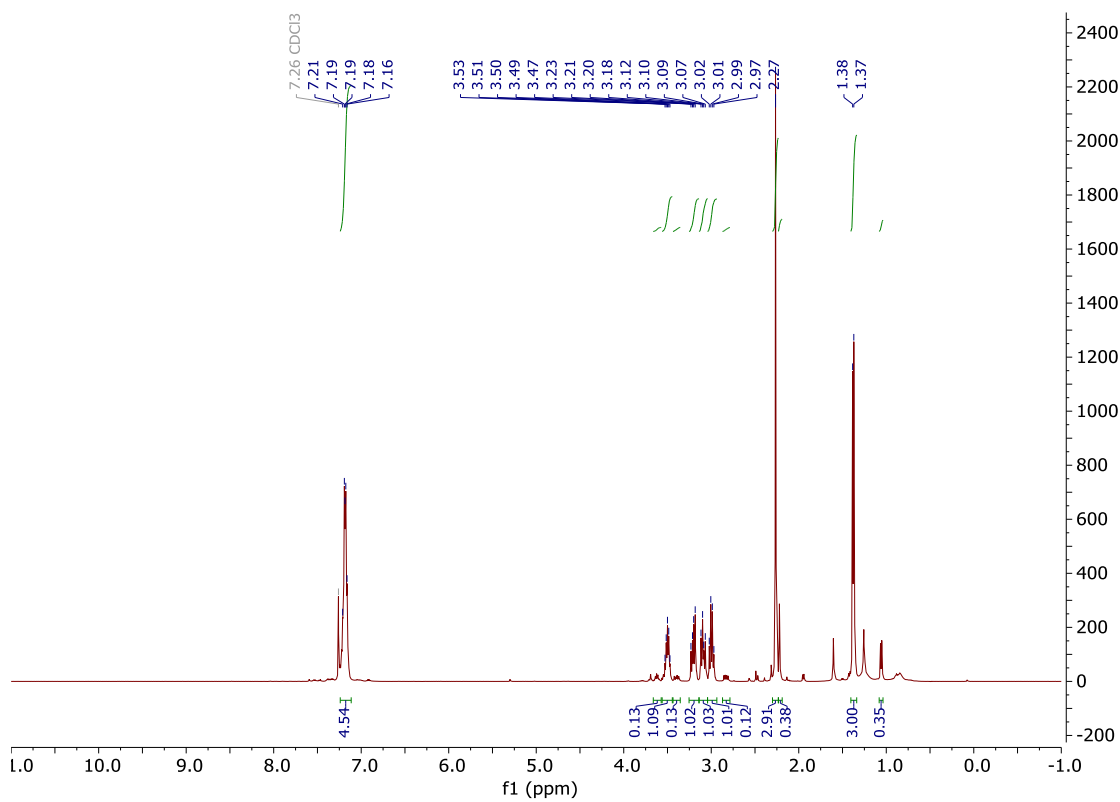


Figure S65: ^1H NMR spectrum of **5** in CDCl_3 . Spectrometer Frequency 500.15 MHz. 22 $^\circ\text{C}$

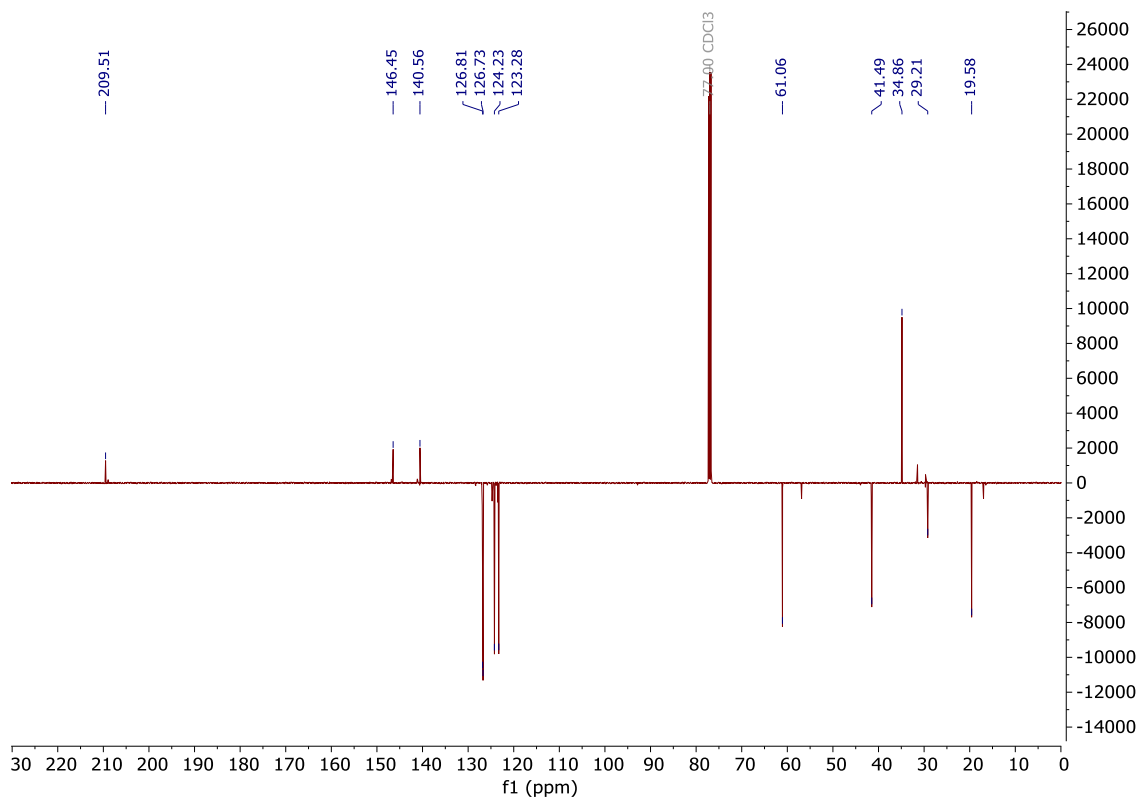


Figure S66: ^{13}C APT NMR spectrum of **5** in CDCl_3 . Spectrometer Frequency 125.85 MHz. 22 $^\circ\text{C}$

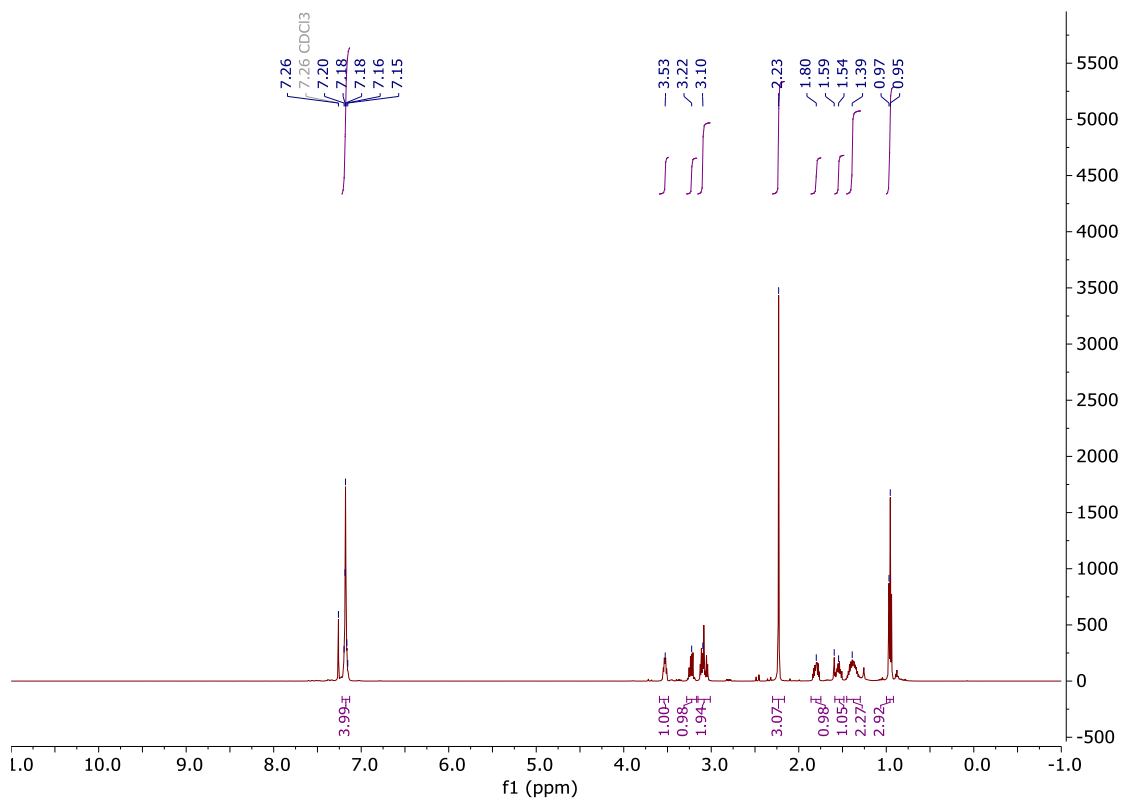


Figure S67: ^1H NMR spectrum of **7a** in CDCl_3 . Spectrometer Frequency 500.15 MHz. 22 $^\circ\text{C}$

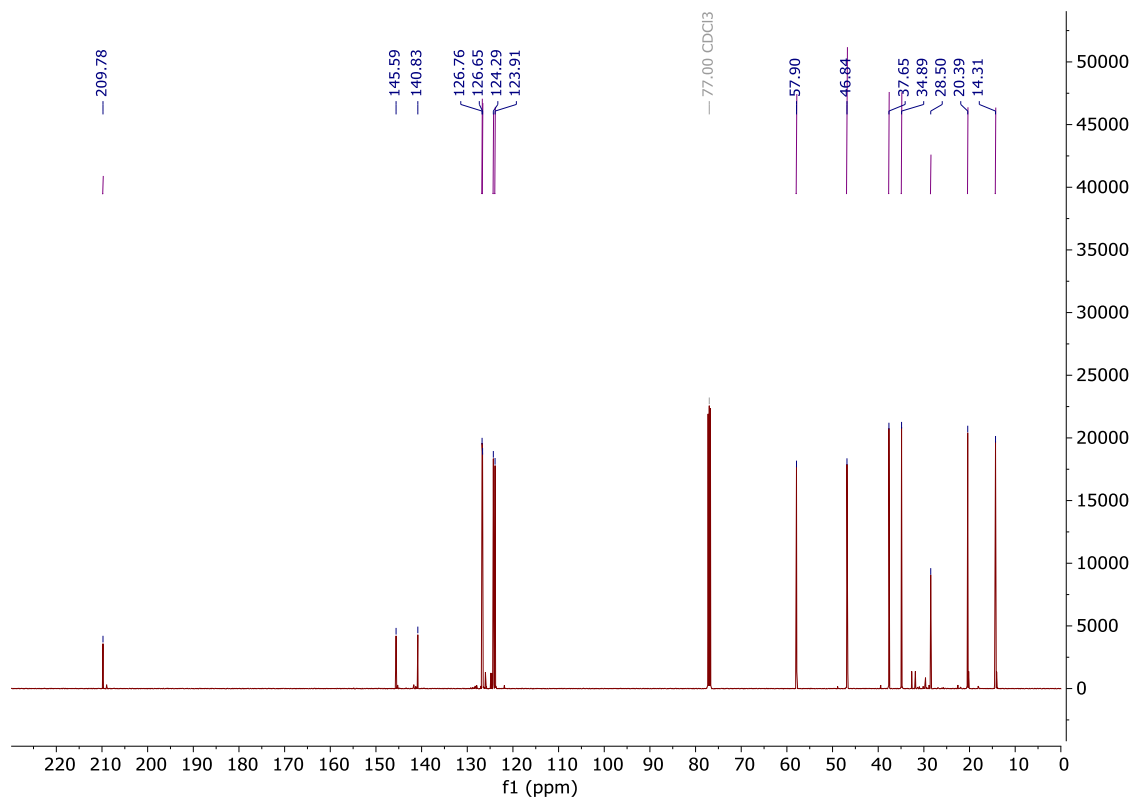


Figure S68: ^{13}C NMR spectrum of **7a** in CDCl_3 . Spectrometer Frequency 125.85 MHz. 22 $^\circ\text{C}$

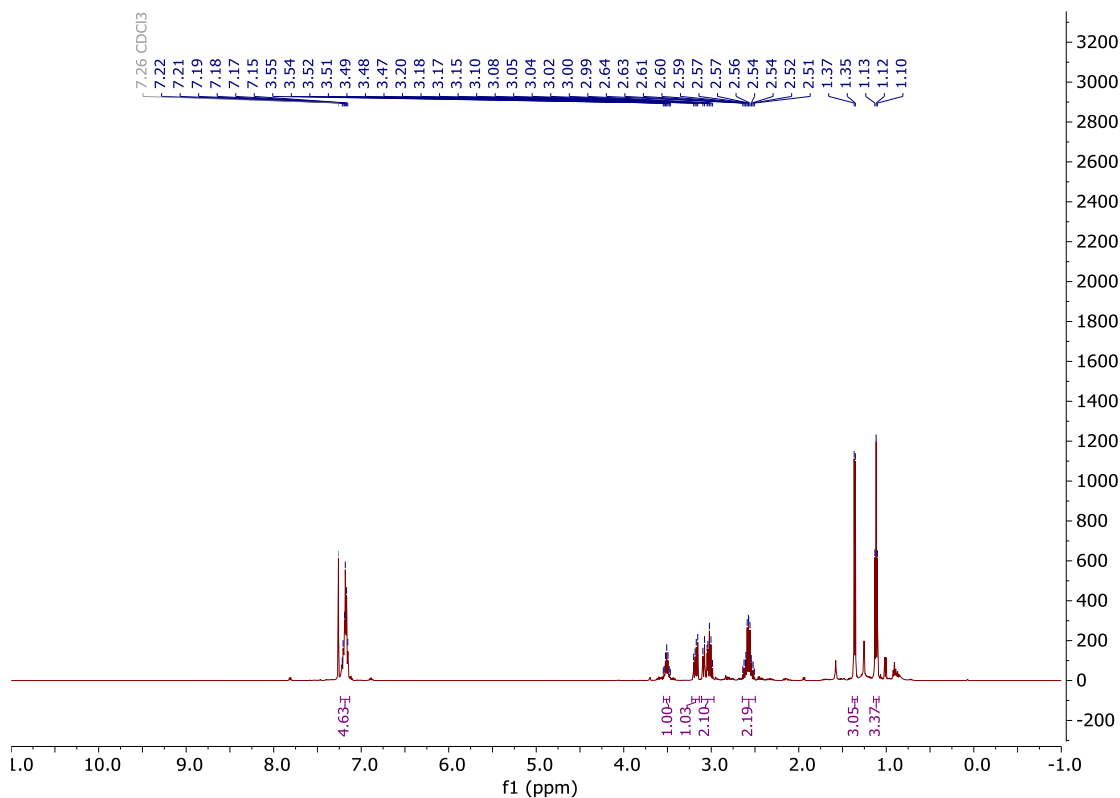


Figure S69: ^1H NMR spectrum of **7b** in CDCl_3 . Spectrometer Frequency 399.80 MHz. 22 $^\circ\text{C}$

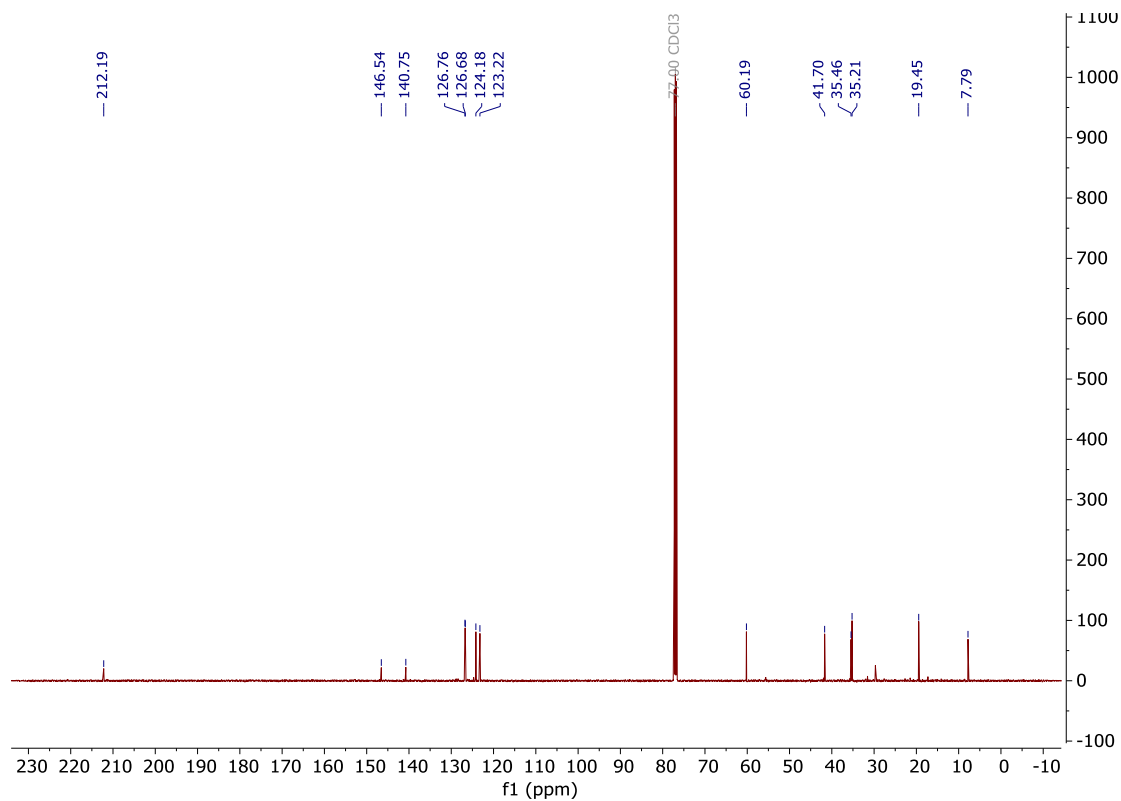


Figure S70: ¹³C NMR spectrum of **7b** in CDCl₃. Spectrometer Frequency 125.85 MHz. 22 °C

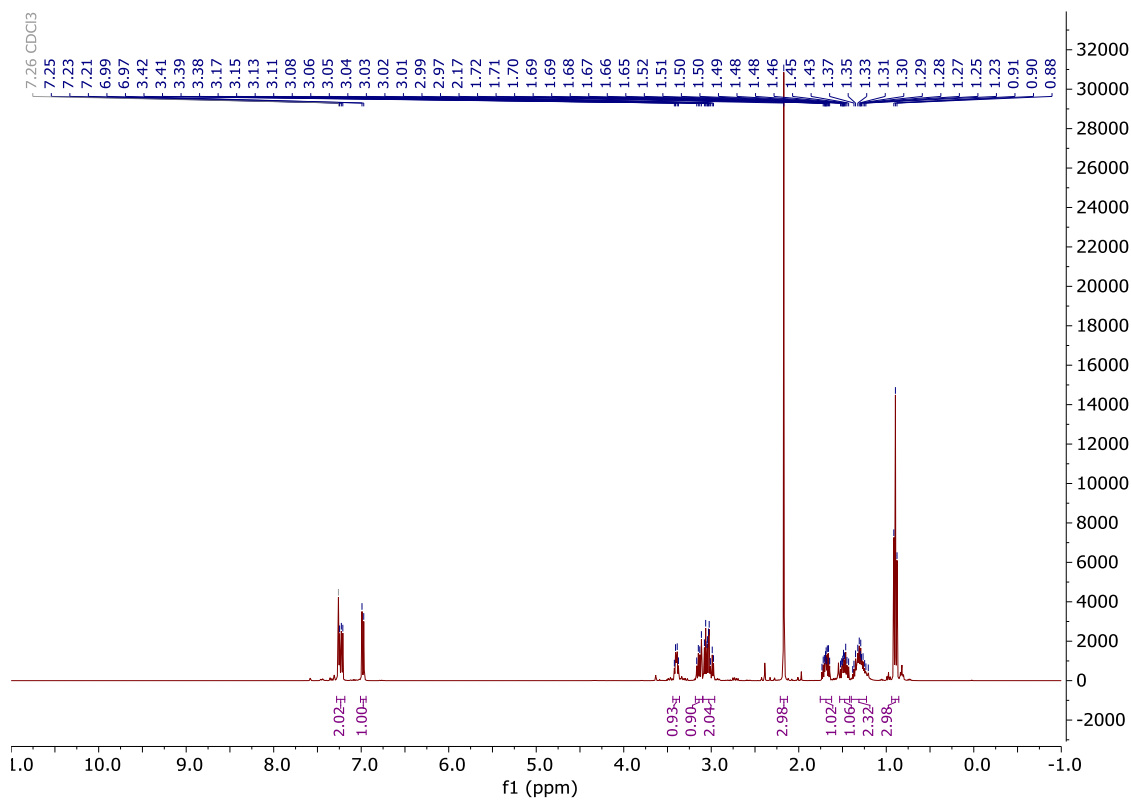


Figure S71: ¹H NMR spectrum of **7c** in CDCl₃. Spectrometer Frequency 399.80 MHz. 22 °C

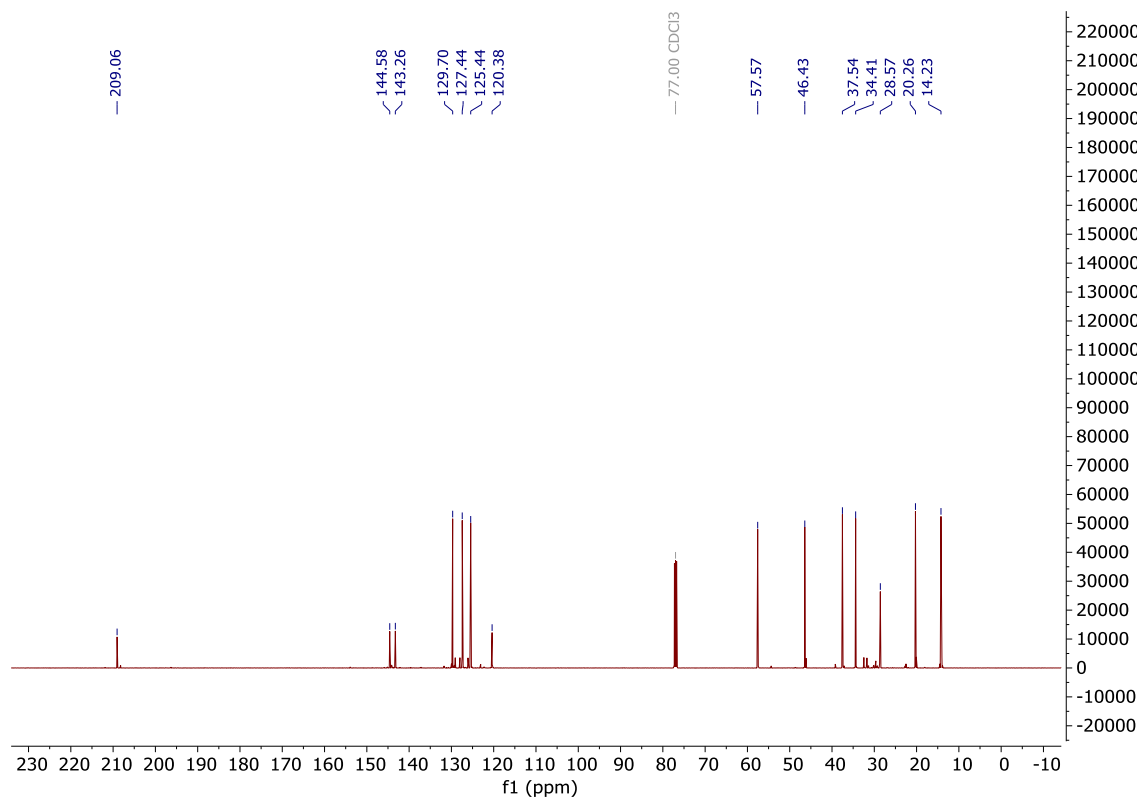


Figure S72: ^{13}C NMR spectrum of **7c** in CDCl_3 . Spectrometer Frequency 125.85 MHz. 22 $^\circ\text{C}$

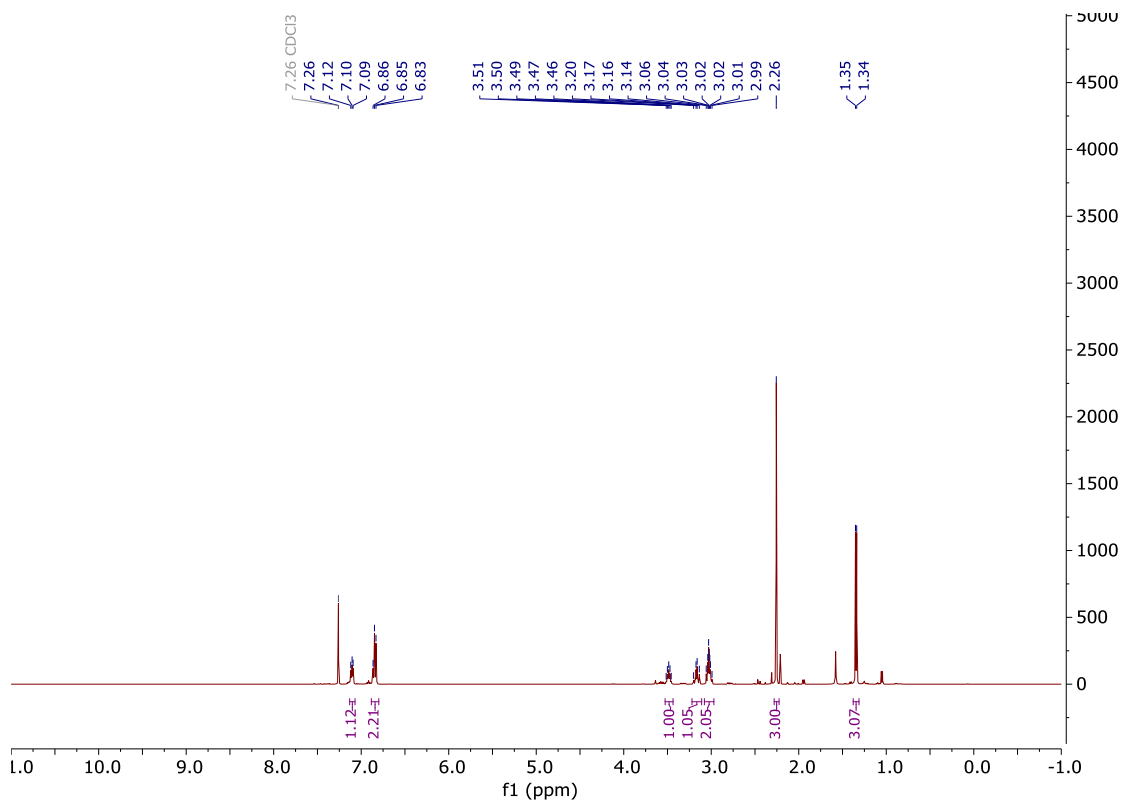


Figure S73: ^1H NMR spectrum of **7d** in CDCl_3 . Spectrometer Frequency 500.15 MHz. 22 $^\circ\text{C}$

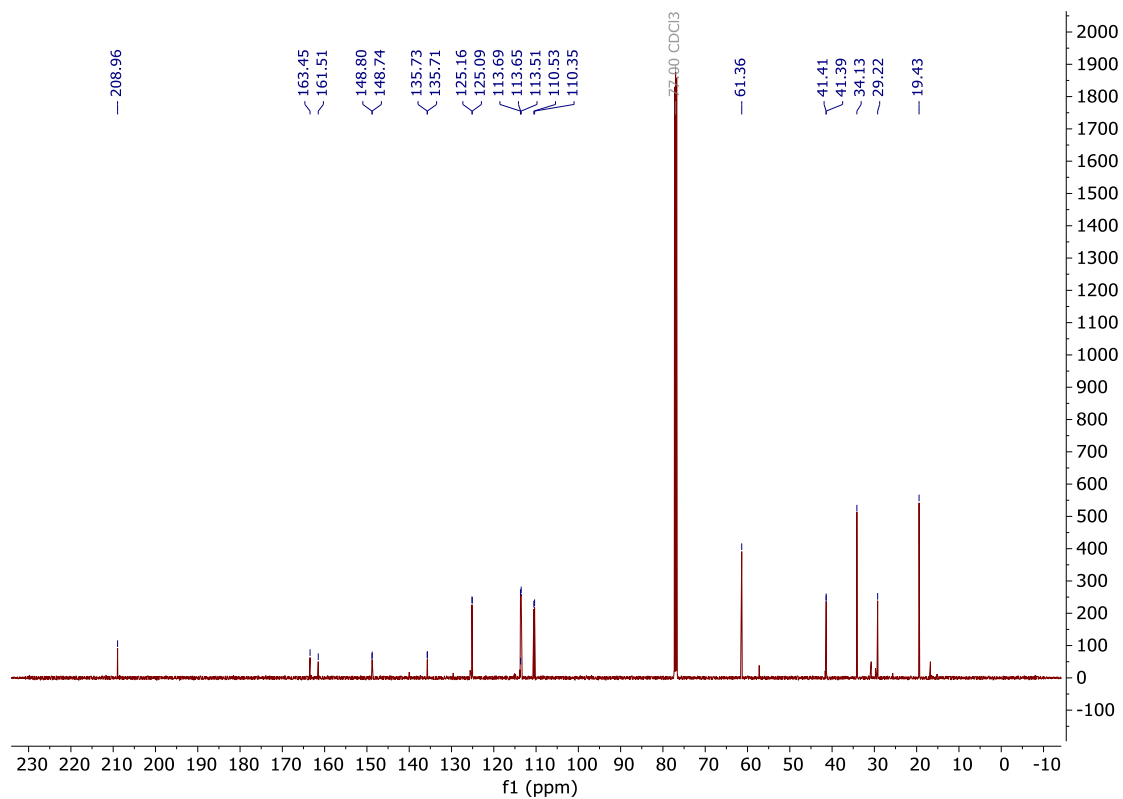


Figure S74: ^{13}C NMR spectrum of **7d** in CDCl_3 . Spectrometer Frequency 125.85 MHz. 22 °C

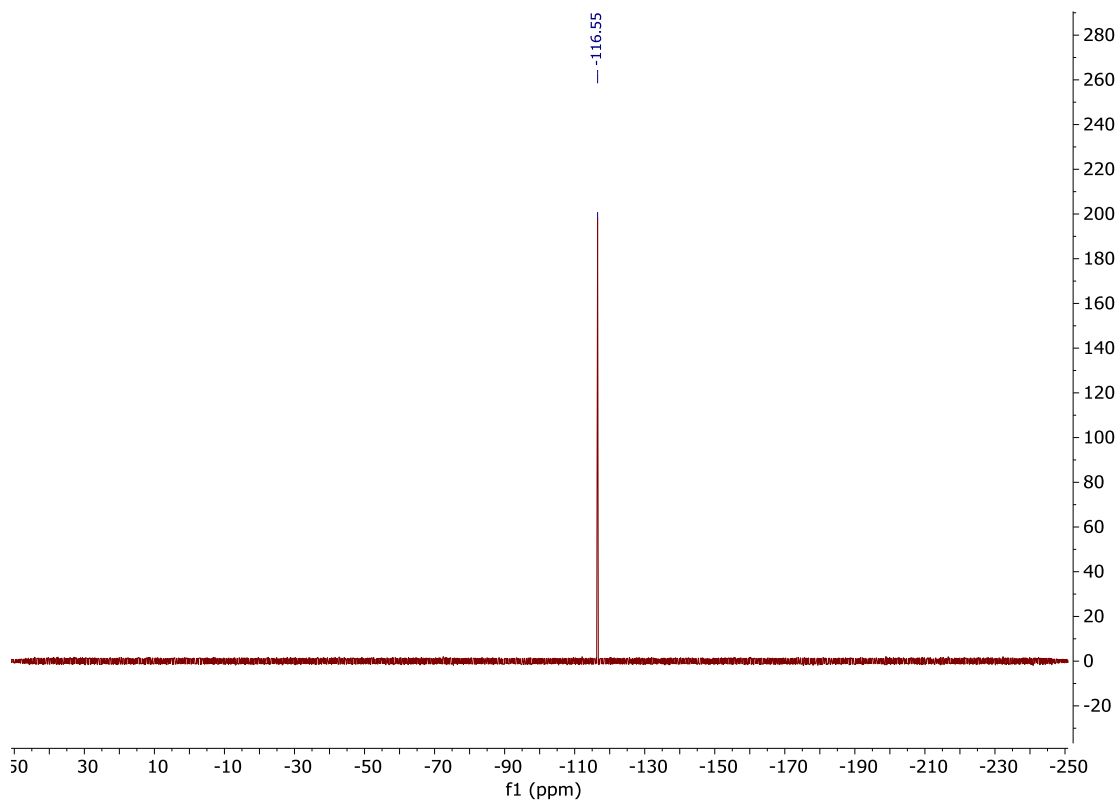


Figure S75: ^{19}F NMR spectrum of **7d** in CDCl_3 . Spectrometer Frequency 282.38 MHz. 22 °C

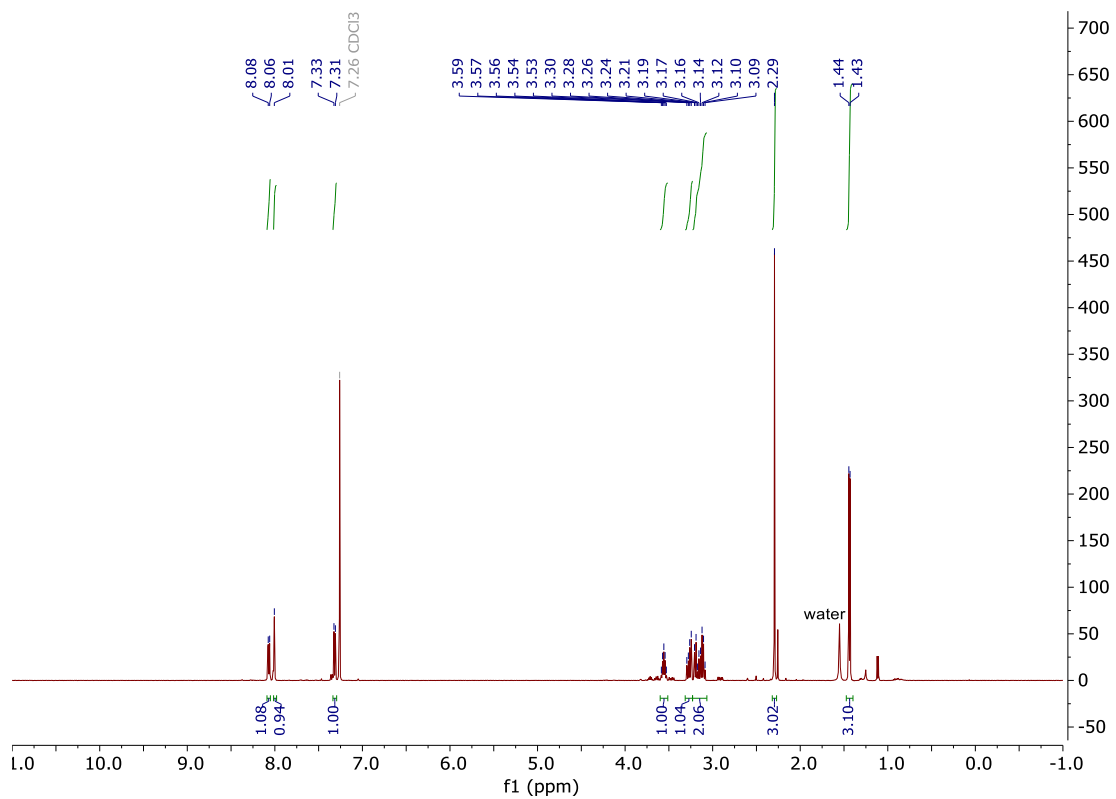


Figure S76: ^1H NMR spectrum of **7e** in CDCl_3 . Spectrometer Frequency 399.80 MHz. 22 $^\circ\text{C}$

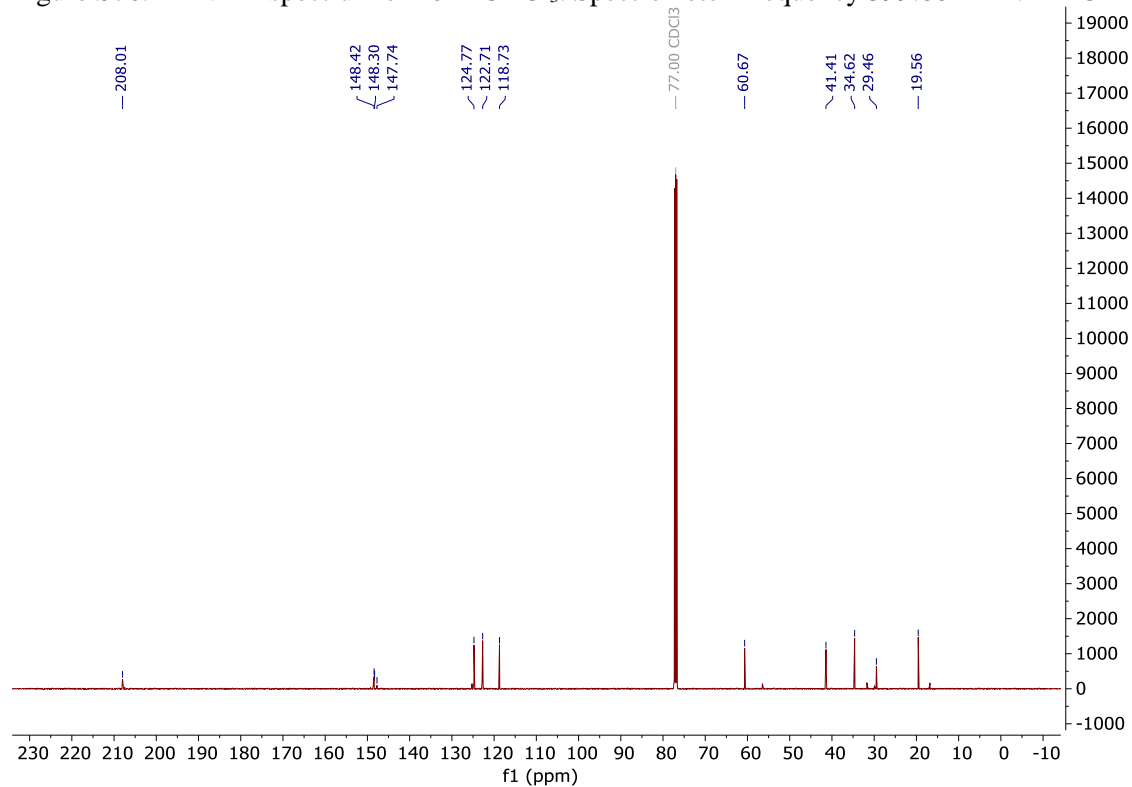


Figure S77: ^{13}C NMR spectrum of **7e** in CDCl_3 . Spectrometer Frequency 125.85 MHz. 22 $^\circ\text{C}$

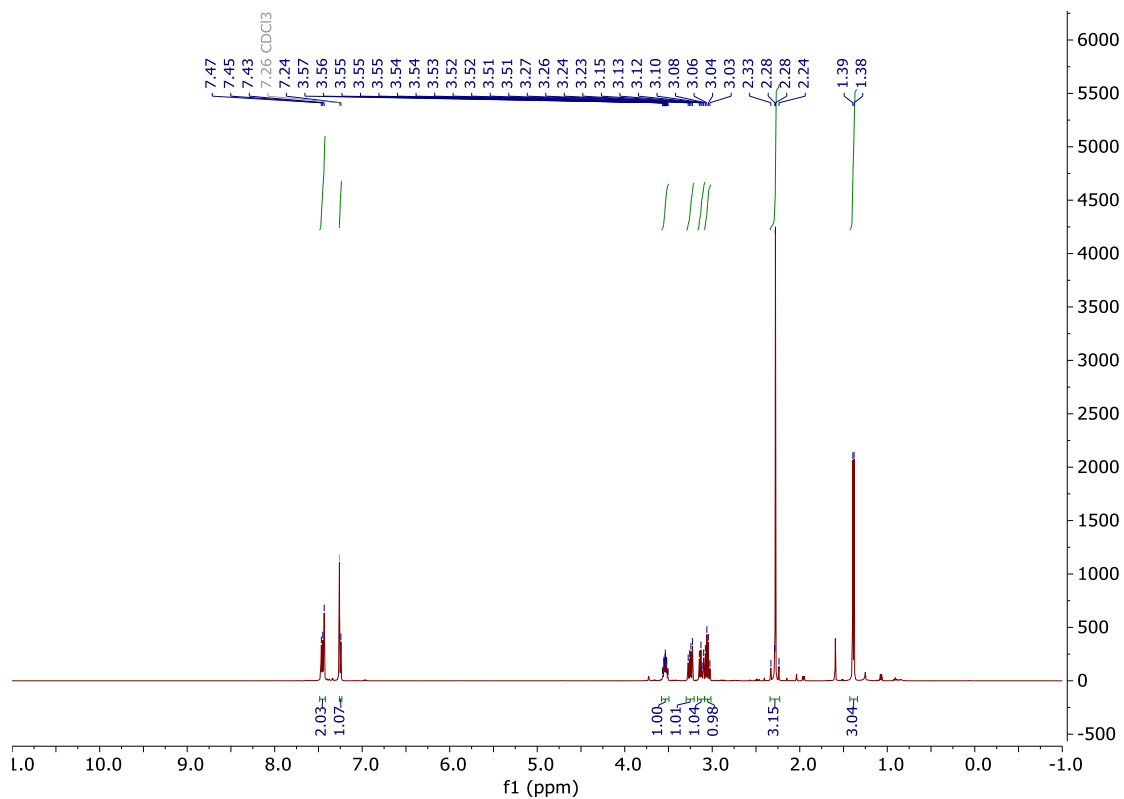


Figure S78: ¹H NMR spectrum of **7f** in CDCl₃. Spectrometer Frequency 500.15 MHz. 22 °C

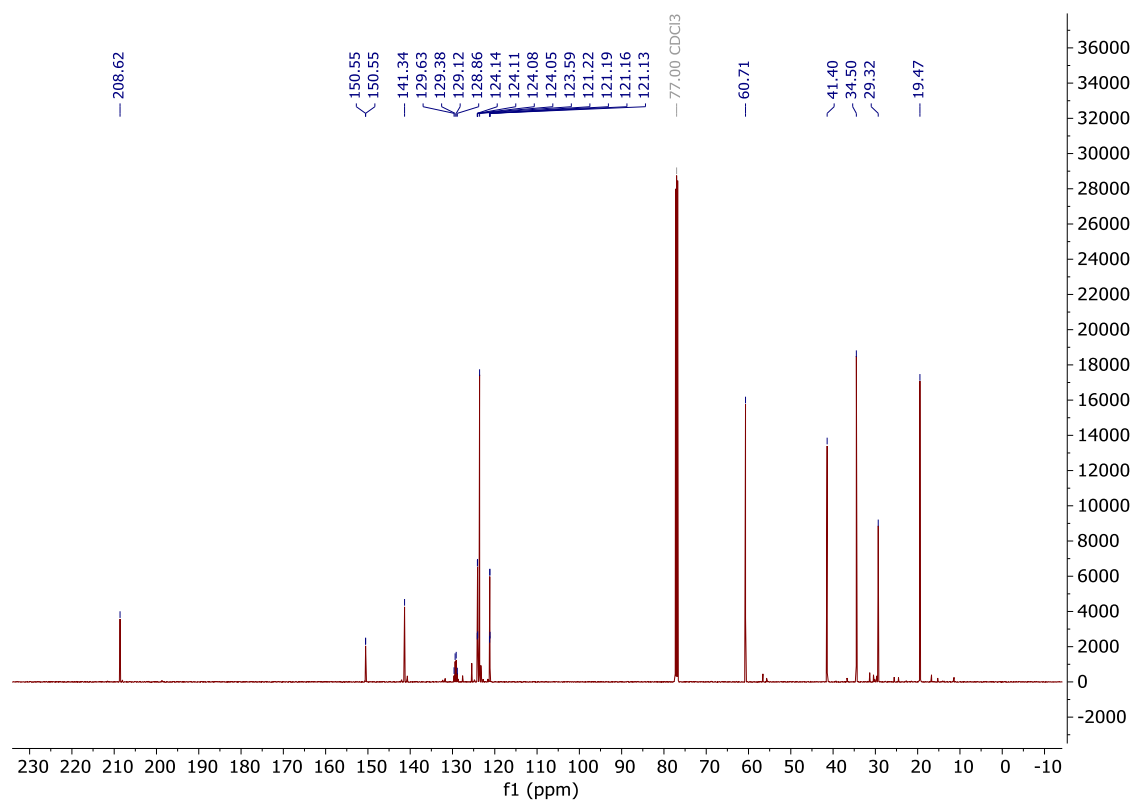


Figure S79: ¹³C NMR spectrum of **7f** in CDCl₃. Spectrometer Frequency 125.85 MHz. 22 °C

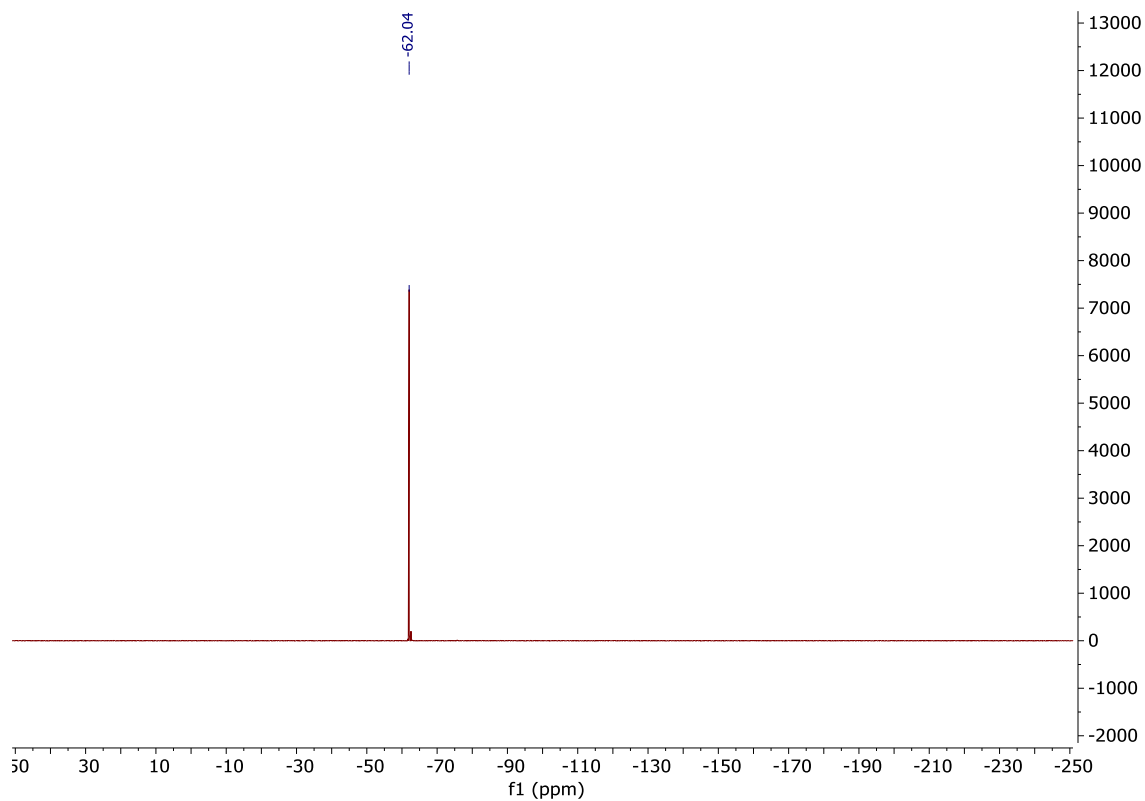


Figure S80: ^{19}F NMR spectrum of **7f** in CDCl_3 . Spectrometer Frequency 282.38 MHz. 22 $^\circ\text{C}$

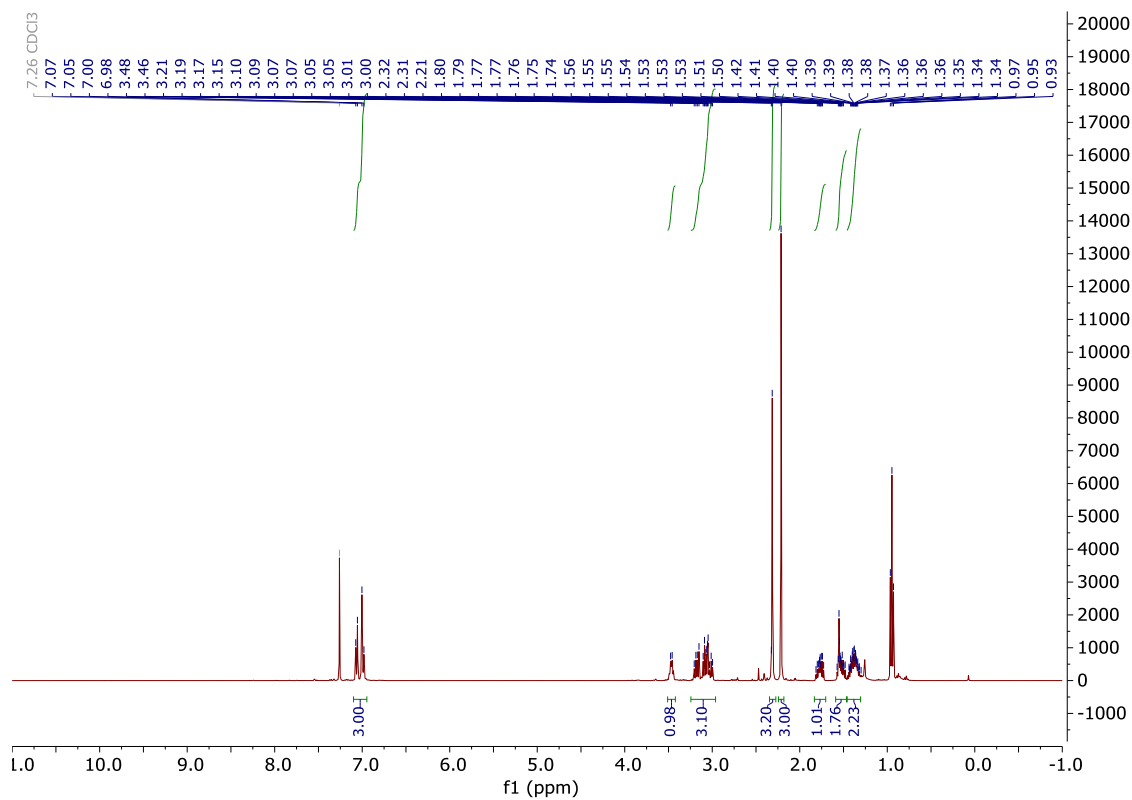


Figure S81: ^1H NMR spectrum of **7g** in CDCl_3 . Spectrometer Frequency 399.80 MHz. 22 $^\circ\text{C}$

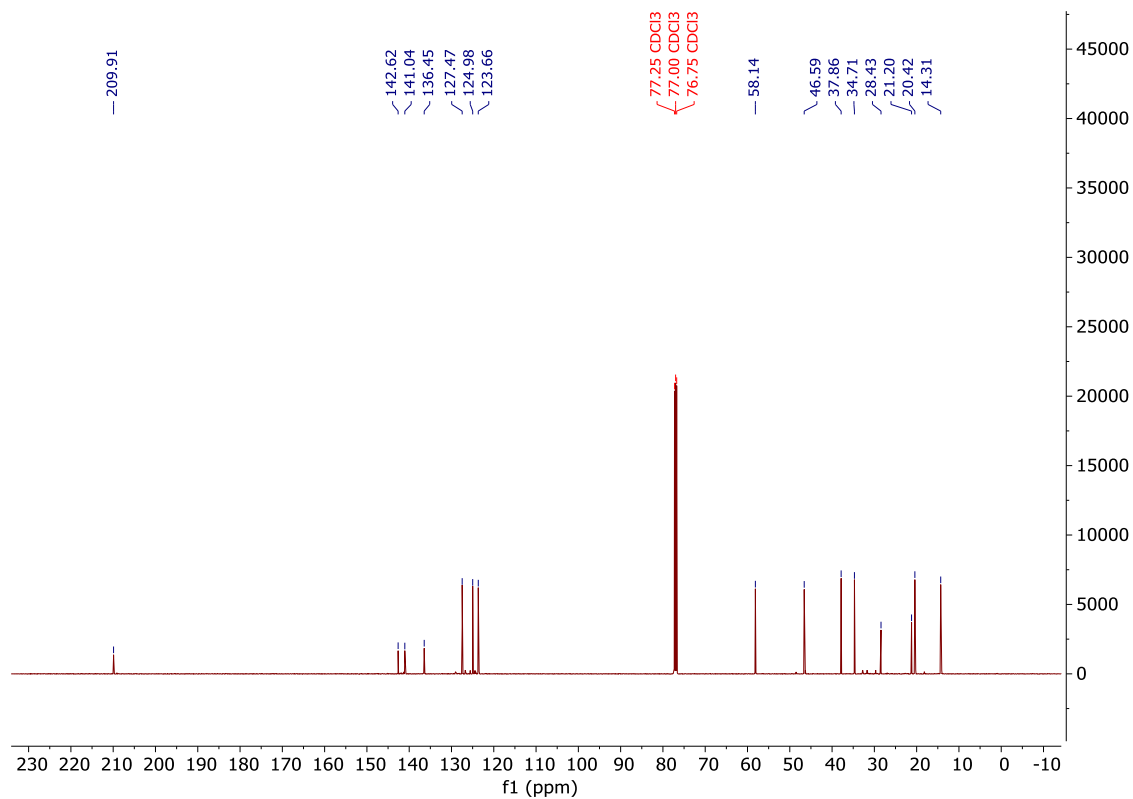


Figure S82: ^{13}C NMR spectrum of **7g** in CDCl_3 . Spectrometer Frequency 125.85 MHz. 22 $^\circ\text{C}$

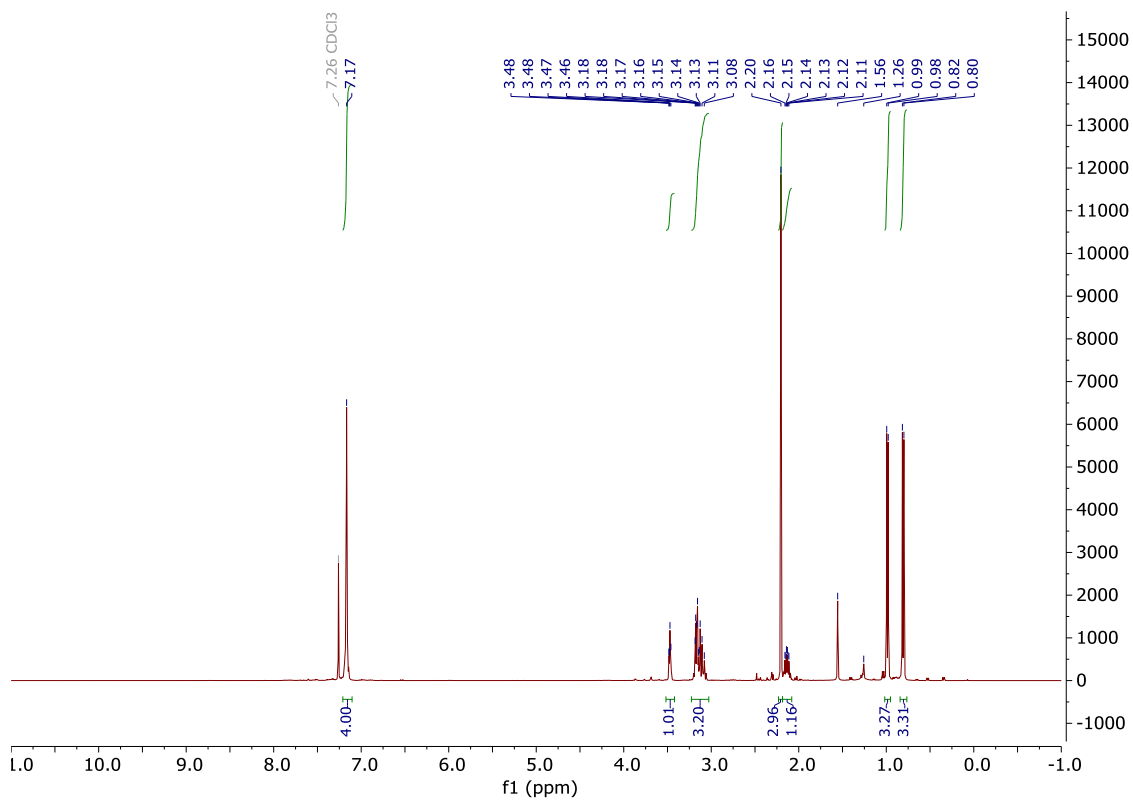


Figure S83: ^1H NMR spectrum of **7h** in CDCl_3 . Spectrometer Frequency 399.80 MHz. 22 $^\circ\text{C}$

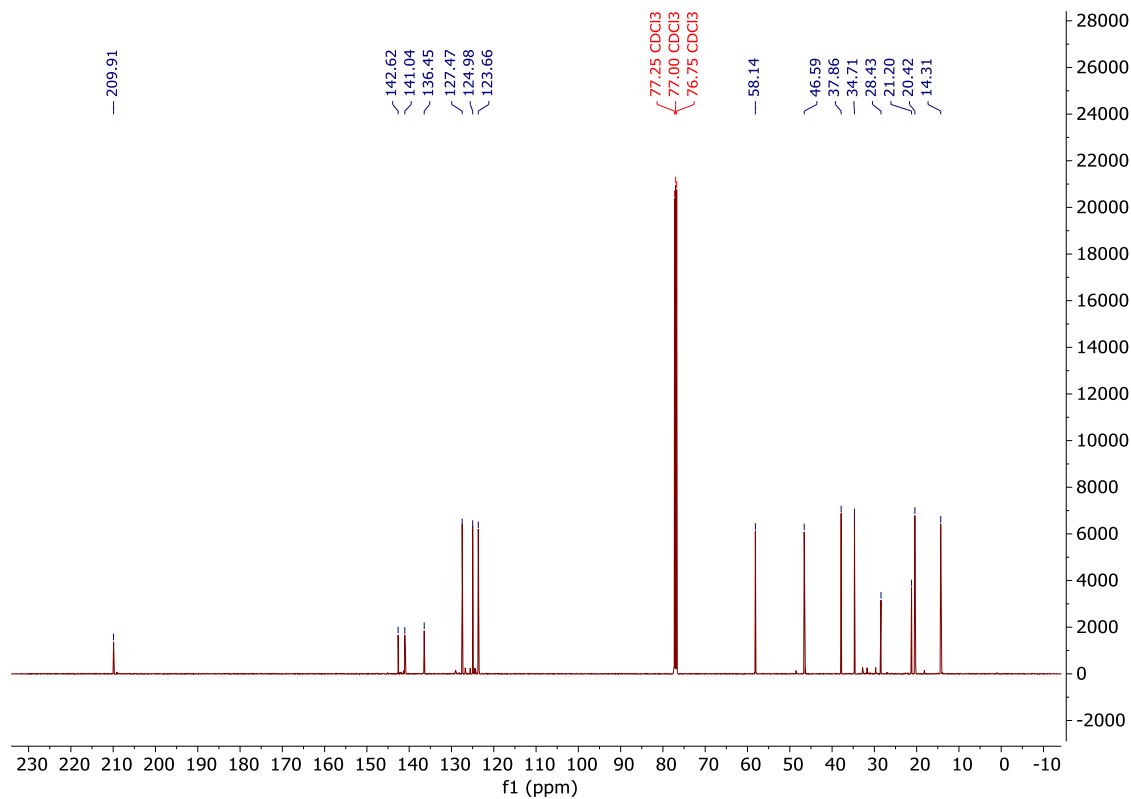


Figure S84: ^{13}C NMR spectrum of **7h** in CDCl_3 . Spectrometer Frequency 125.85 MHz. 22 $^\circ\text{C}$

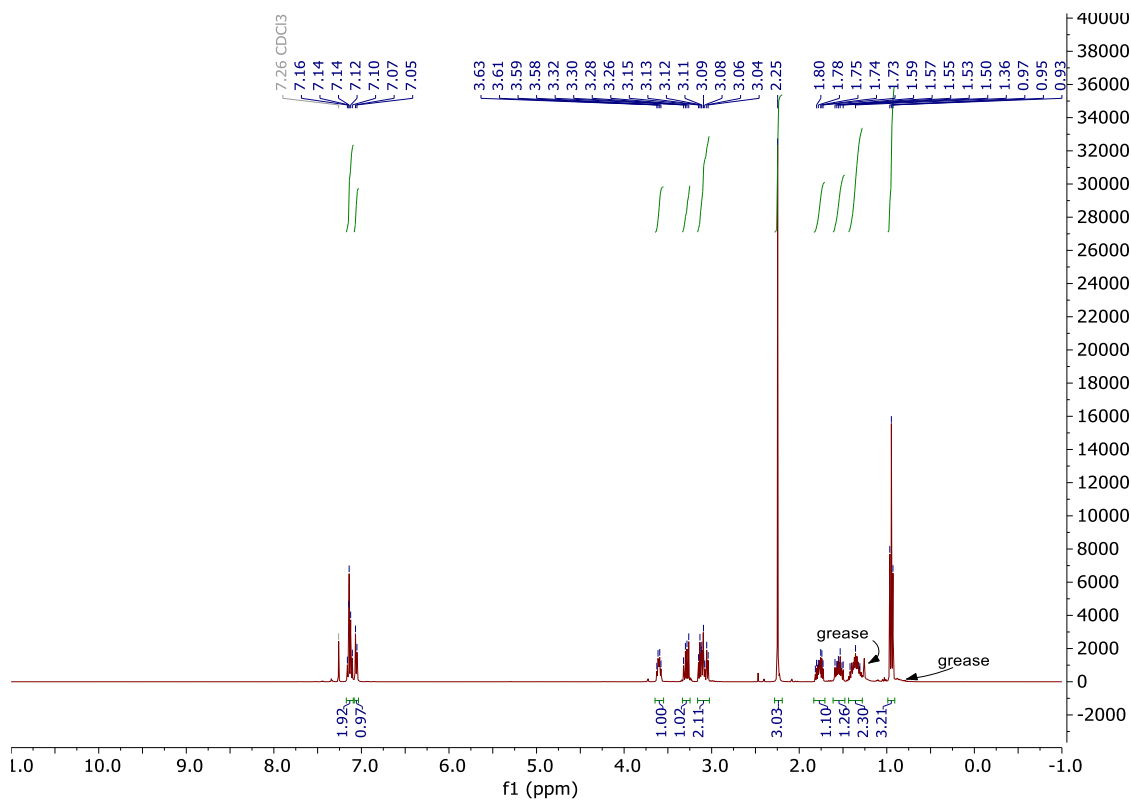


Figure S85: ^1H NMR spectrum of **7i** in CDCl_3 . Spectrometer Frequency 500.40 MHz. 22 $^\circ\text{C}$

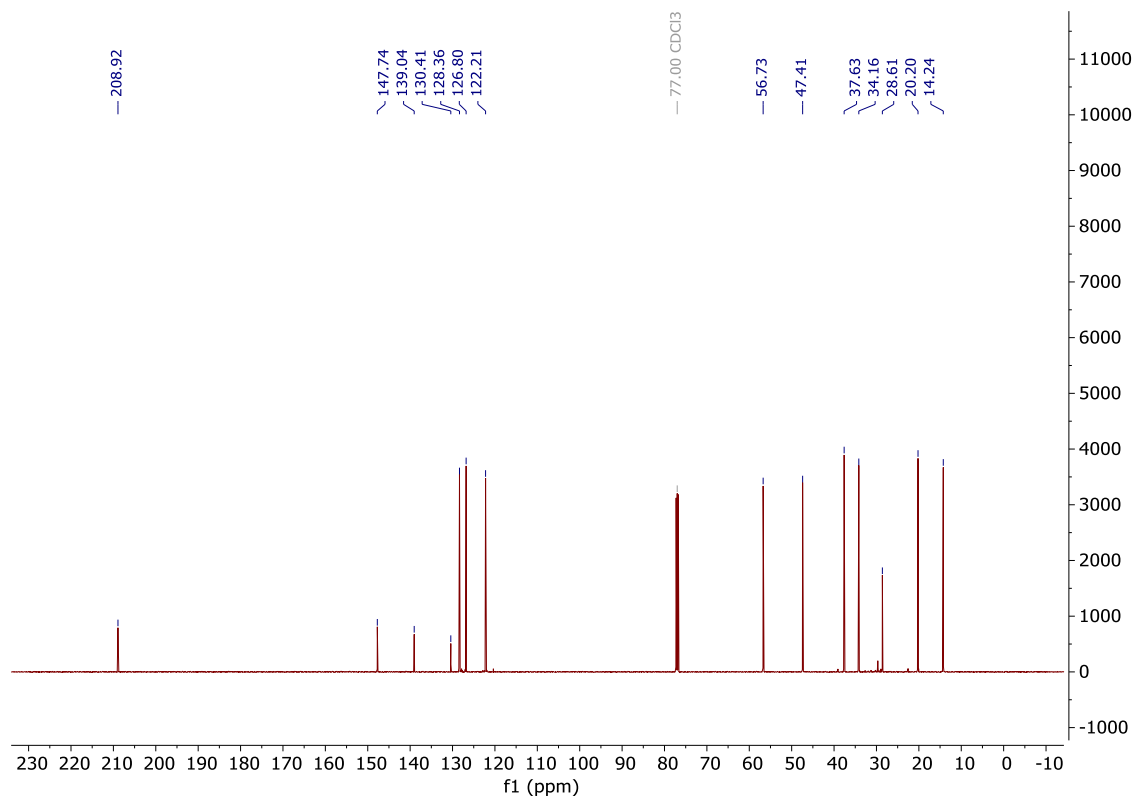


Figure S86: ^{13}C NMR spectrum of **7i** in CDCl_3 . Spectrometer Frequency 125.85 MHz. 22 °C

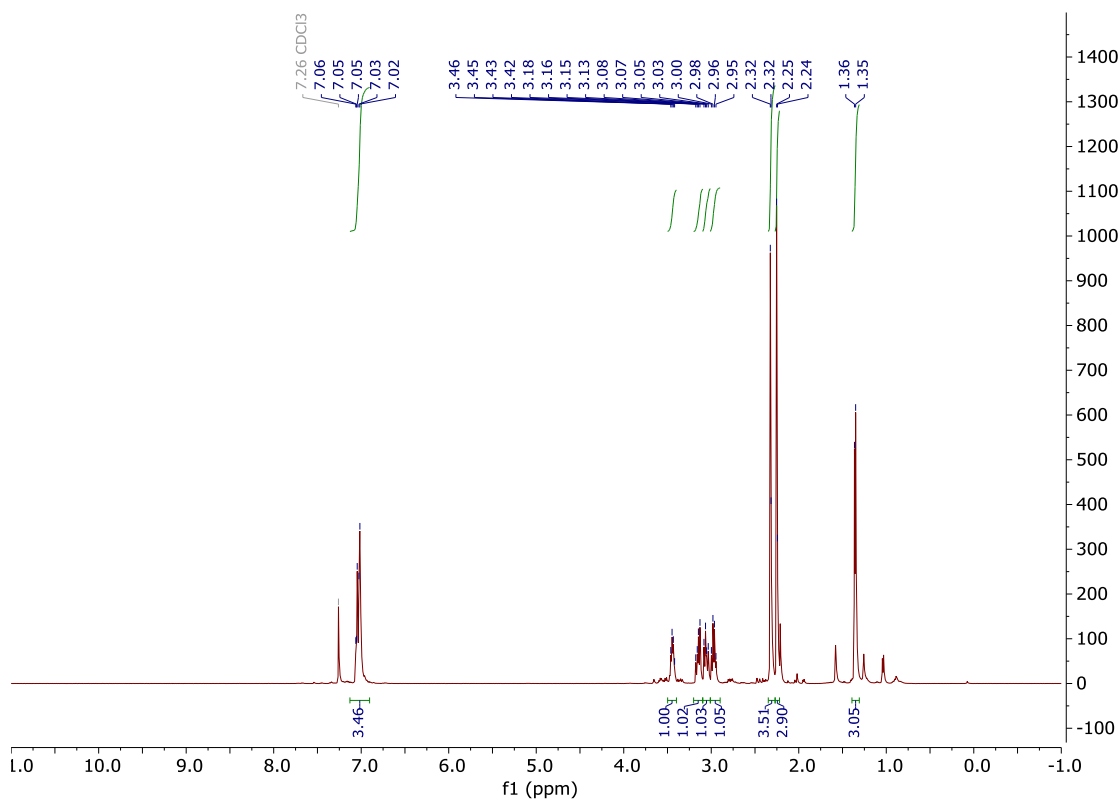


Figure S87: ^1H NMR spectrum of **7j** in CDCl_3 . Spectrometer Frequency 500.40 MHz. 22 °C

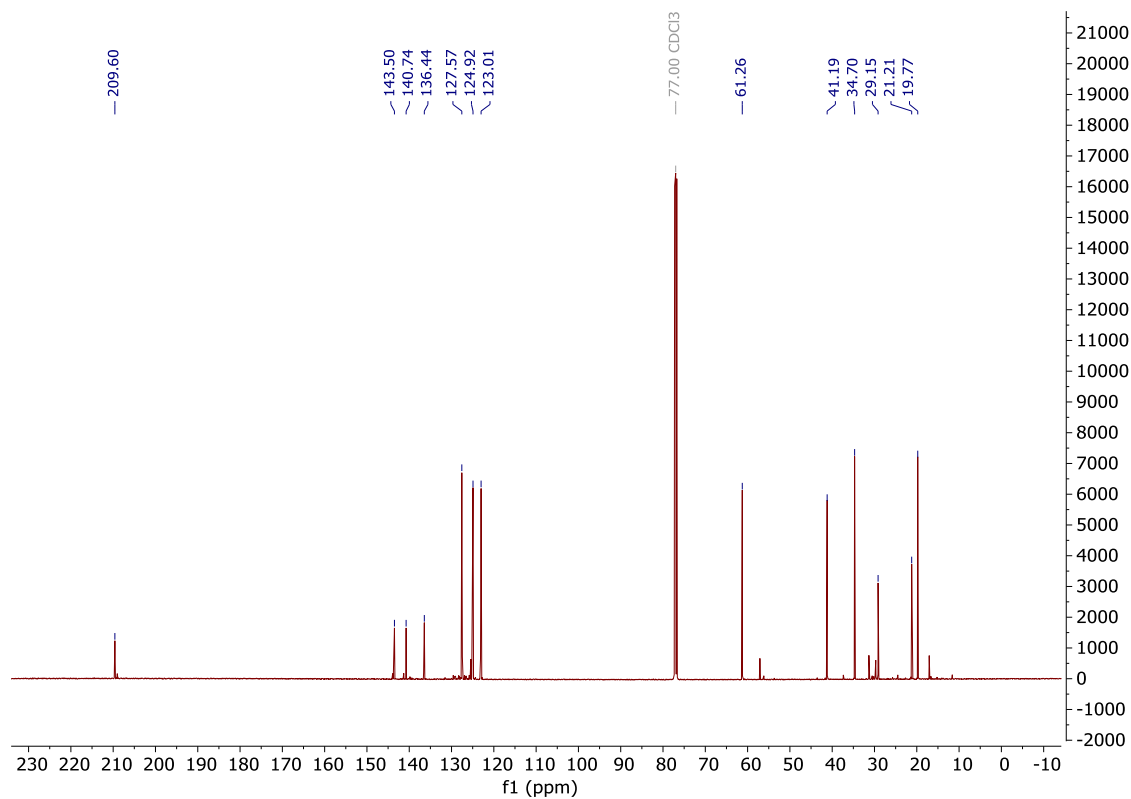


Figure S88: ^{13}C NMR spectrum of **7j** in CDCl_3 . Spectrometer Frequency 125.85 MHz. 22 $^\circ\text{C}$

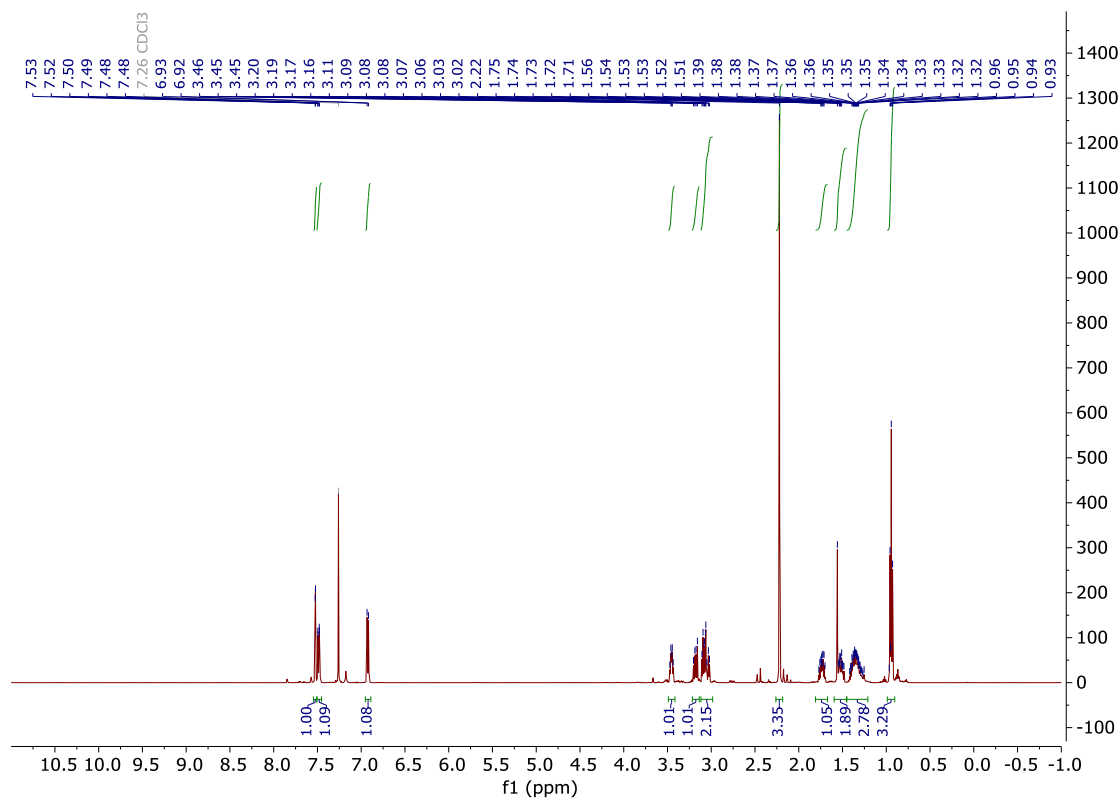


Figure S89: ^1H NMR spectrum of **7k** in CDCl_3 . Spectrometer Frequency 500.40 MHz. 22 $^\circ\text{C}$

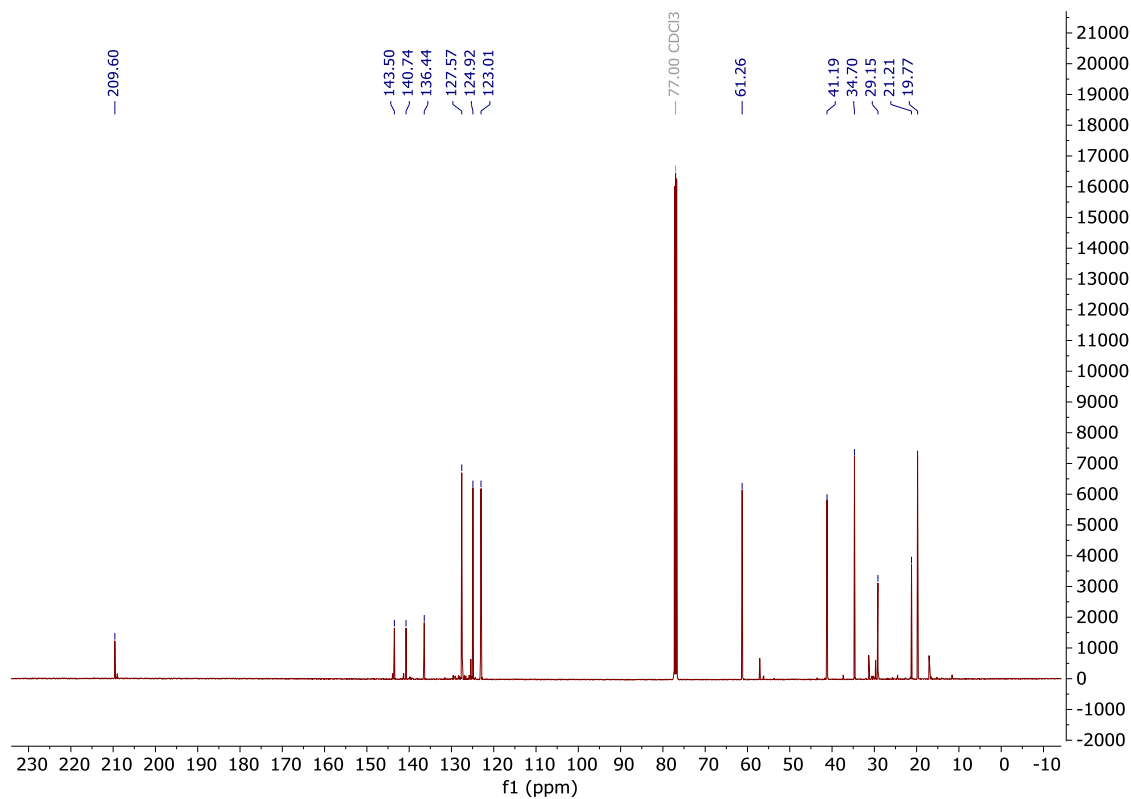


Figure S90: ^{13}C NMR spectrum of **7k** in CDCl_3 . Spectrometer Frequency 125.85 MHz. 22 $^\circ\text{C}$

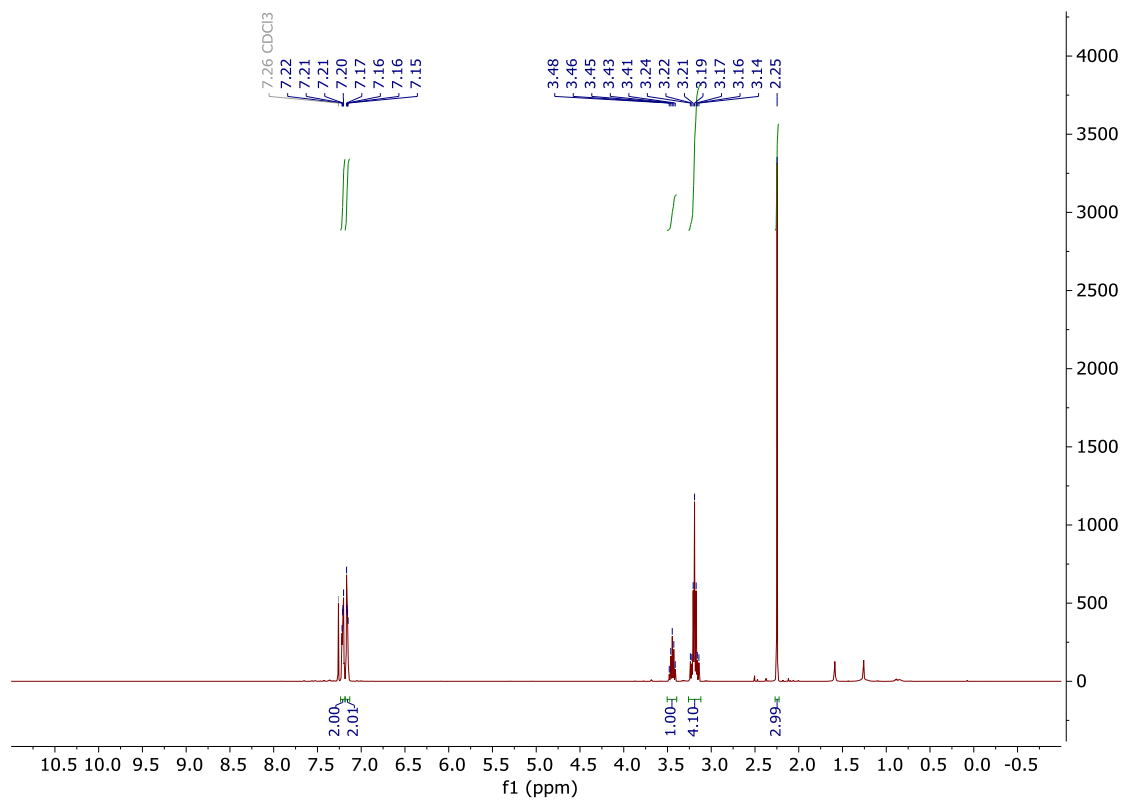


Figure S91: ^1H NMR spectrum of **2** in CDCl_3 . Spectrometer Frequency 500.40 MHz. 22 $^\circ\text{C}$

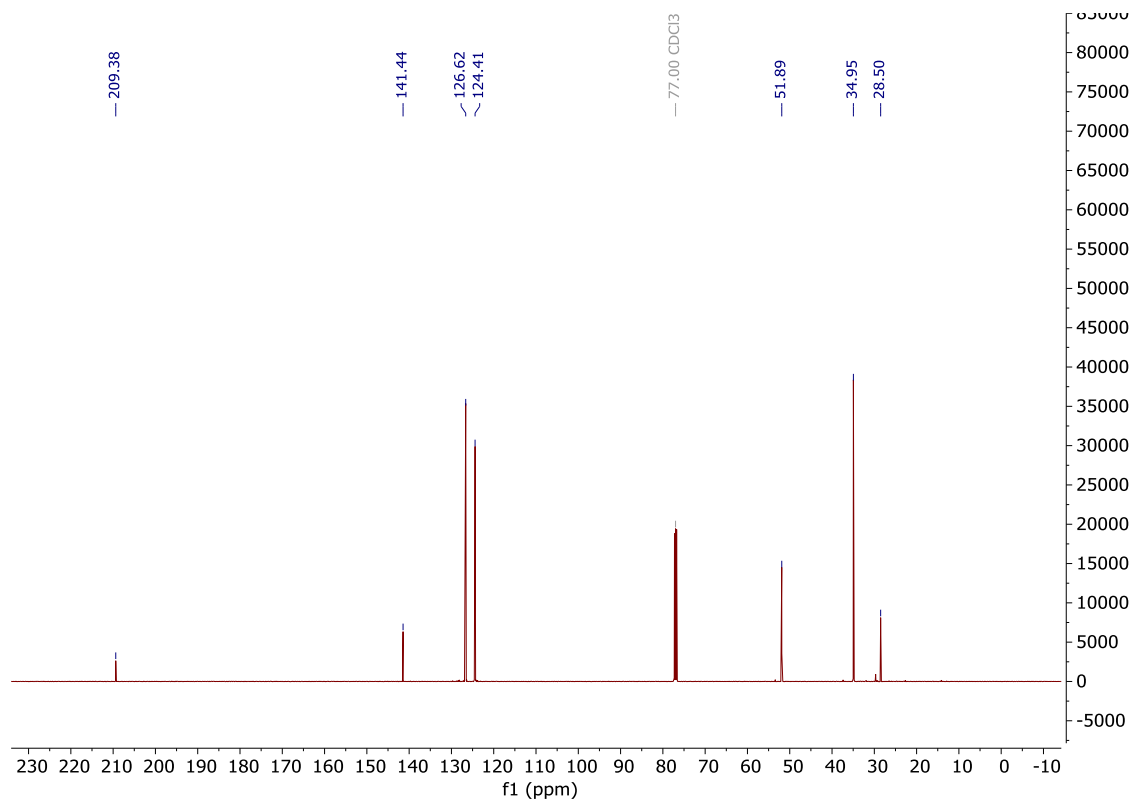


Figure S92: ^{13}C NMR spectrum of **2** in CDCl_3 . Spectrometer Frequency 125.85 MHz. 22 $^\circ\text{C}$

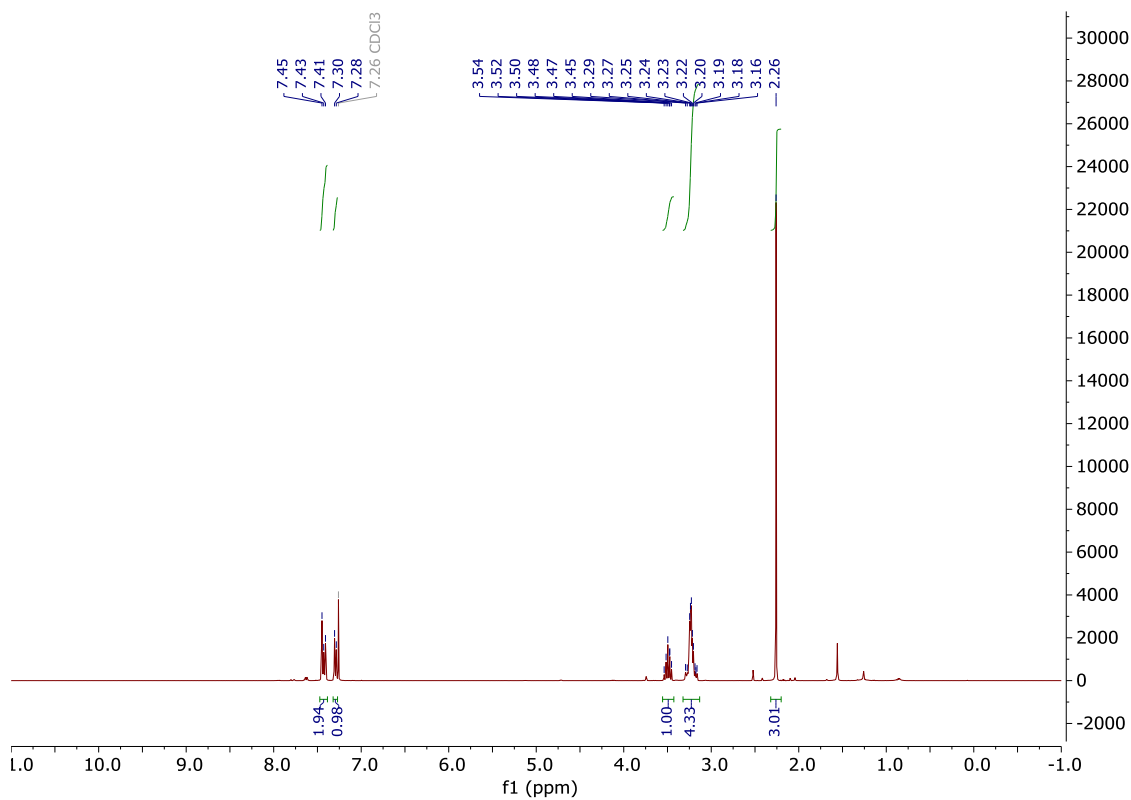


Figure S93: ^1H NMR spectrum of **8a** in CDCl_3 . Spectrometer Frequency 399.80 MHz. 22 $^\circ\text{C}$

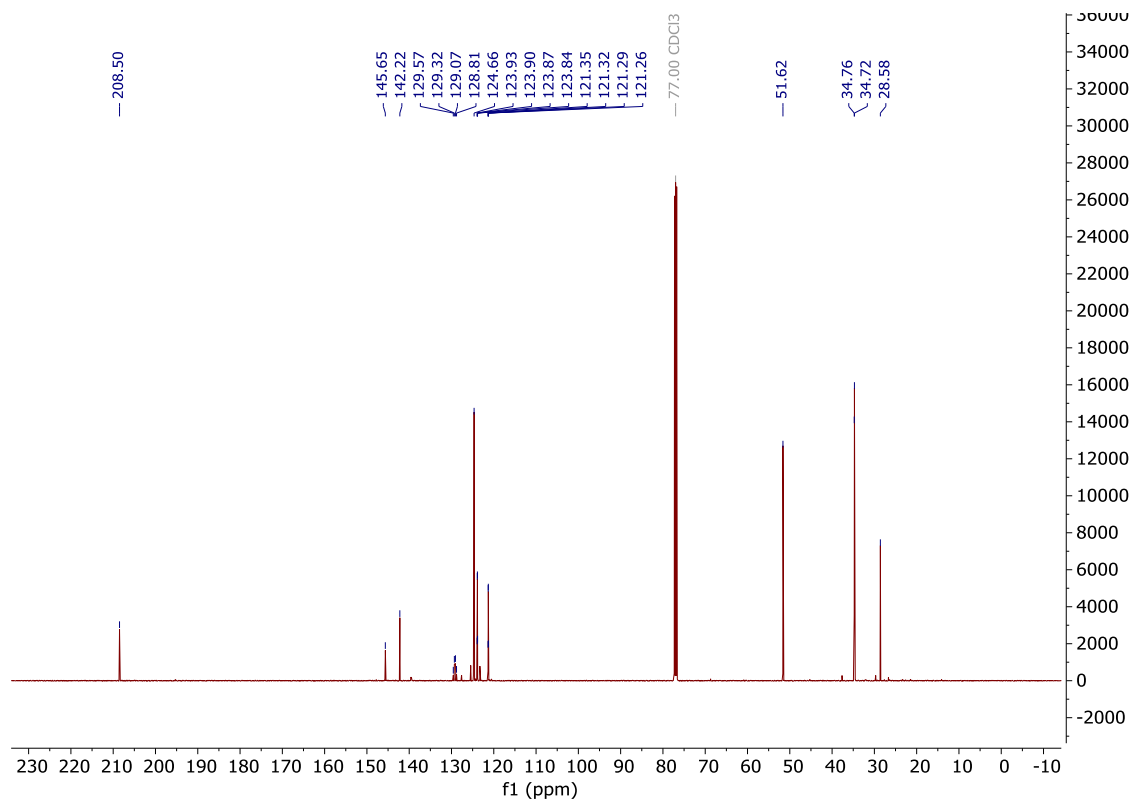


Figure S94: ¹³C NMR spectrum of **8a** in CDCl₃. Spectrometer Frequency 125.85 MHz. 22 °C

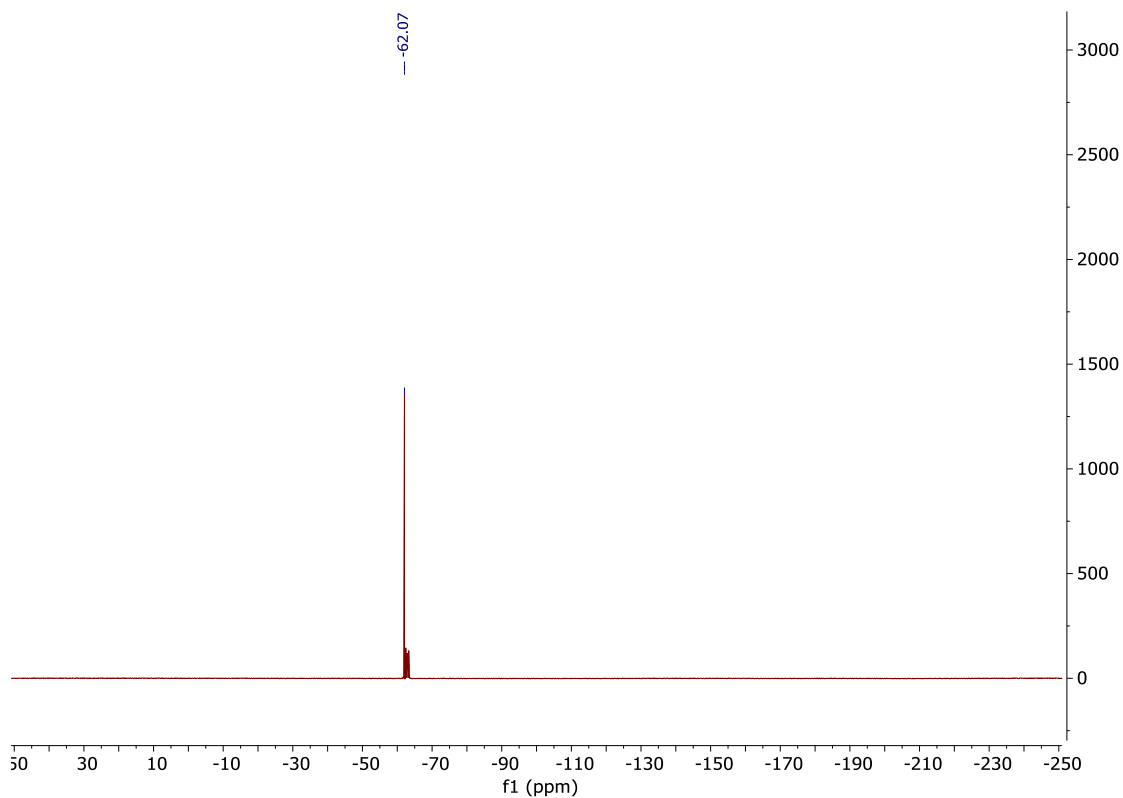


Figure S95: ¹⁹F NMR spectrum of **8a** in CDCl₃. Spectrometer Frequency 282.38 MHz. 22 °C

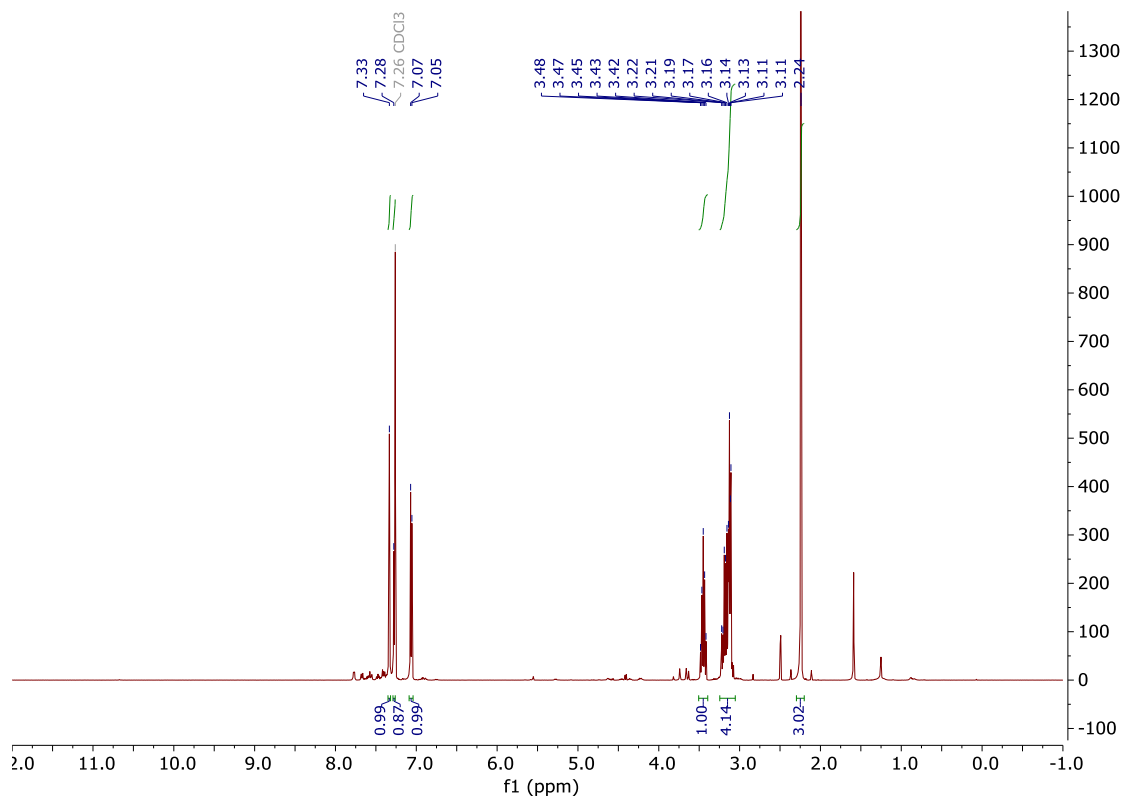


Figure S96: ^1H NMR spectrum of **8b** in CDCl_3 . Spectrometer Frequency 500.15 MHz. 22 $^\circ\text{C}$

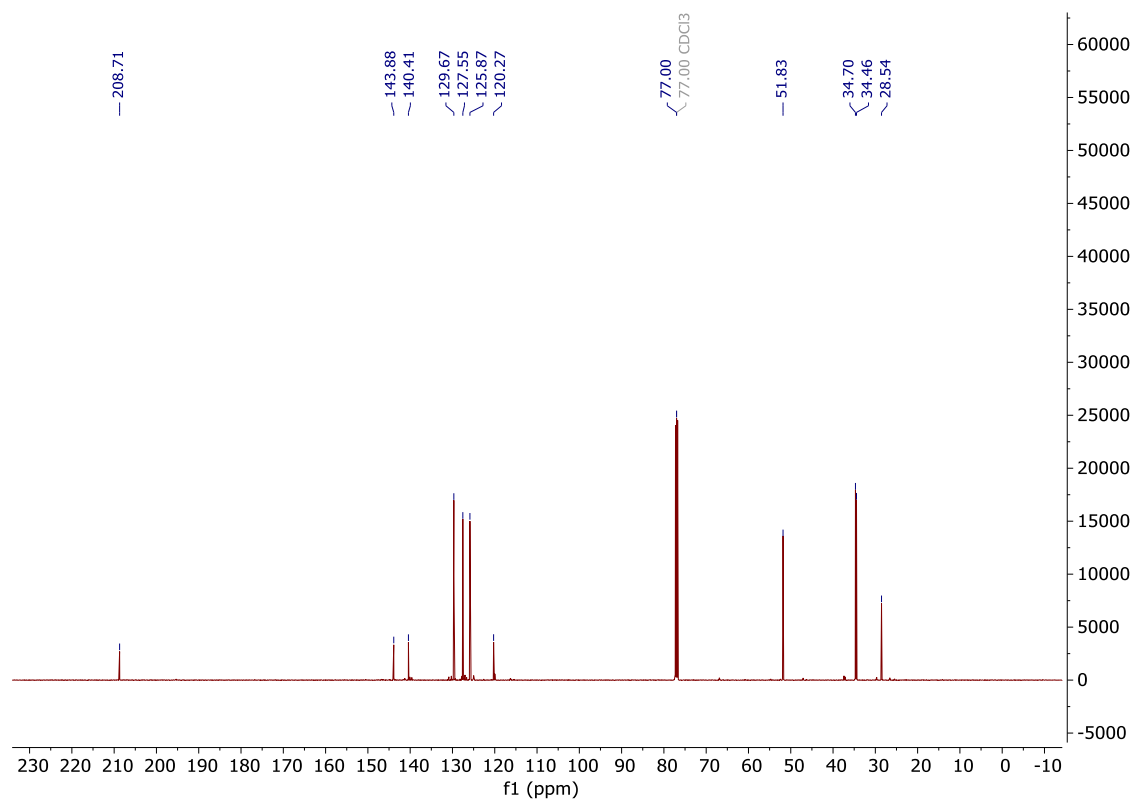


Figure S97: ^{13}C NMR spectrum of **8b** in CDCl_3 . Spectrometer Frequency 125.85 MHz. 22 $^\circ\text{C}$

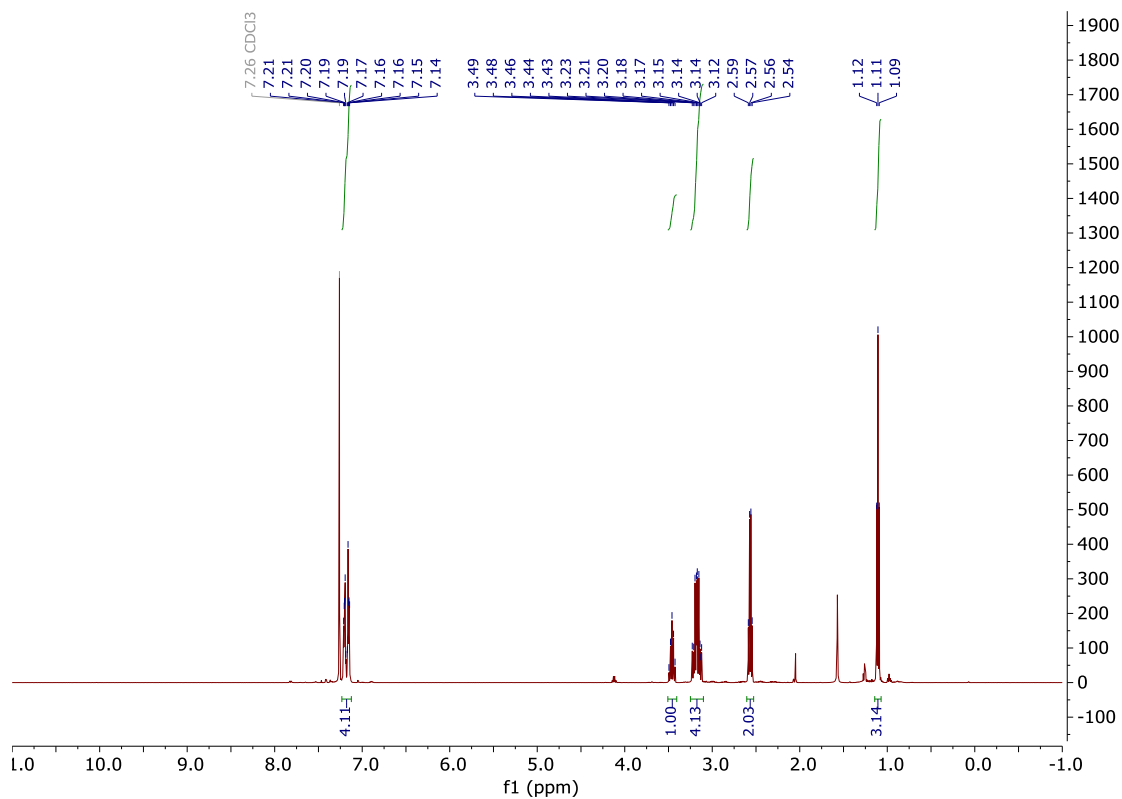


Figure S98: ¹H NMR spectrum of **8c** in CDCl₃. Spectrometer Frequency 500.15 MHz. 22 °C

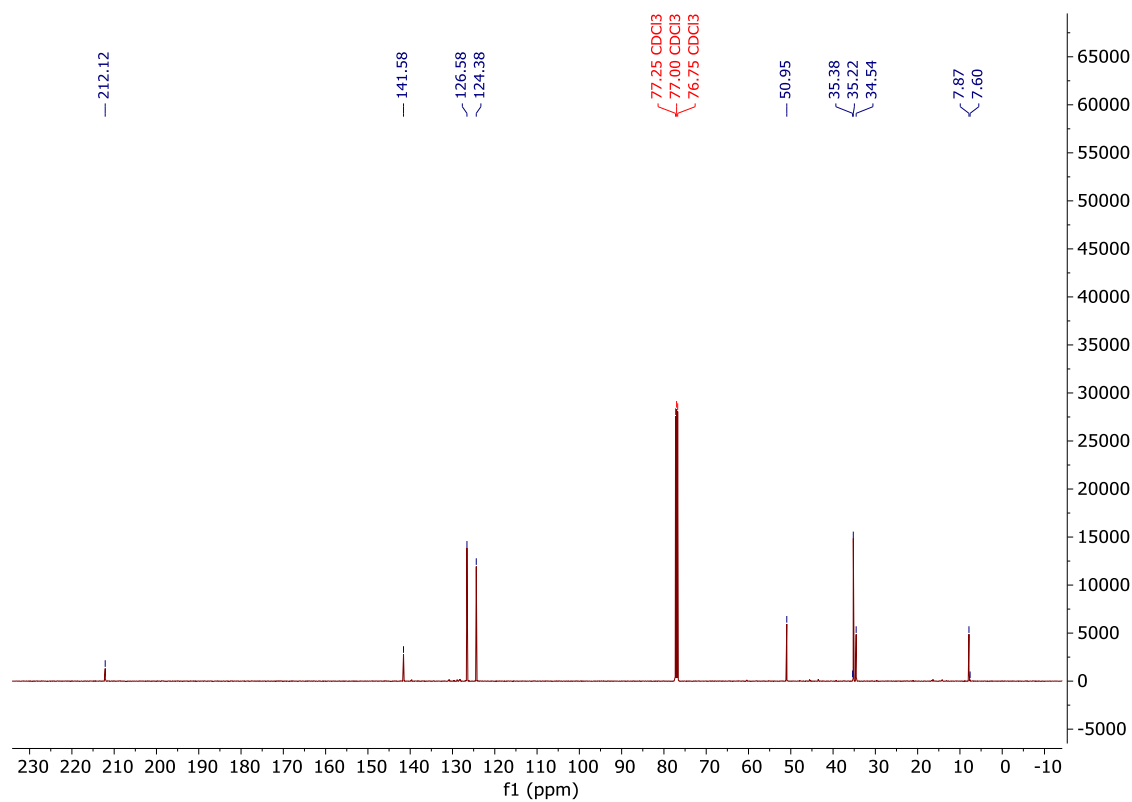


Figure S99: ¹³C NMR spectrum of **8c** in CDCl₃. Spectrometer Frequency 125.85 MHz. 22 °C

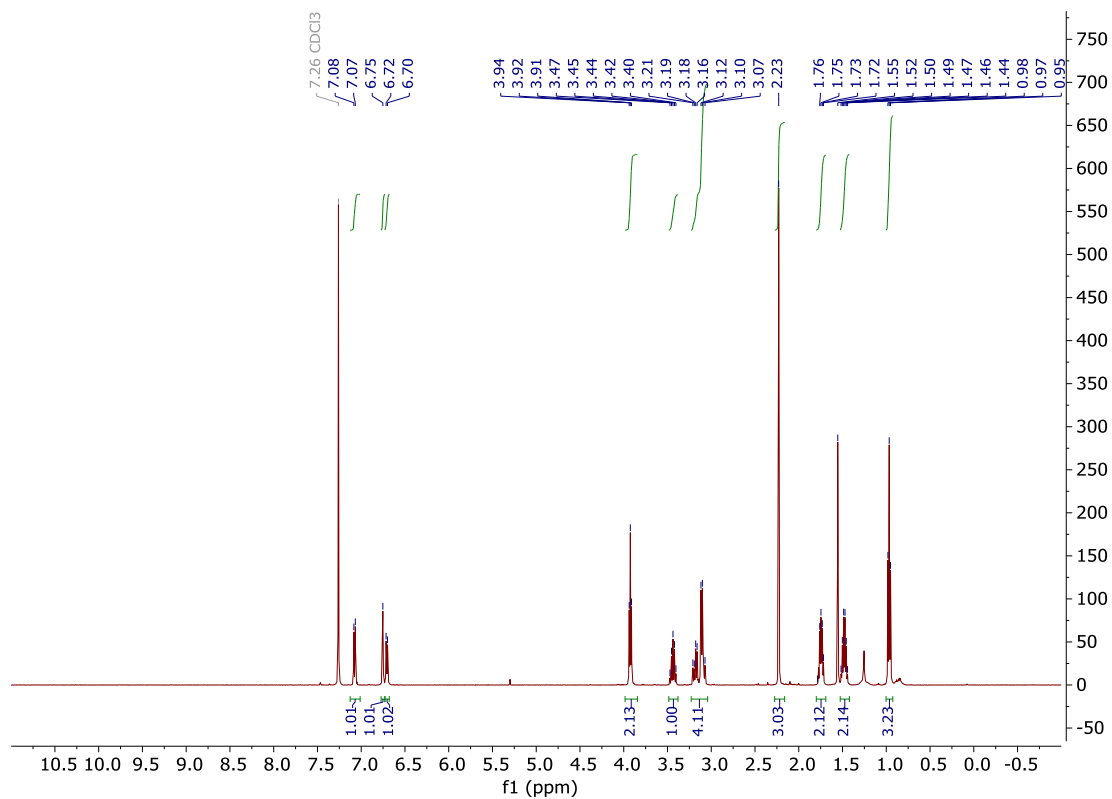


Figure S100: ^1H NMR spectrum of **8d** in CDCl_3 . Spectrometer Frequency 500.40 MHz. 22 $^\circ\text{C}$

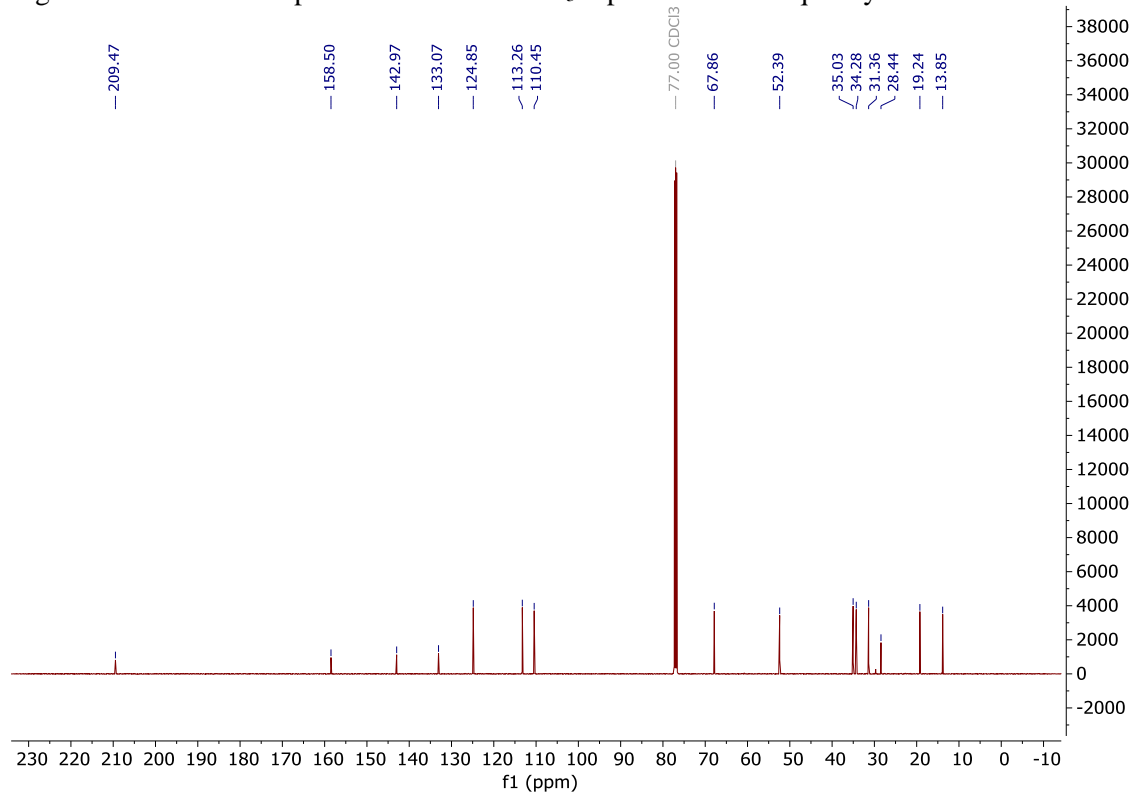
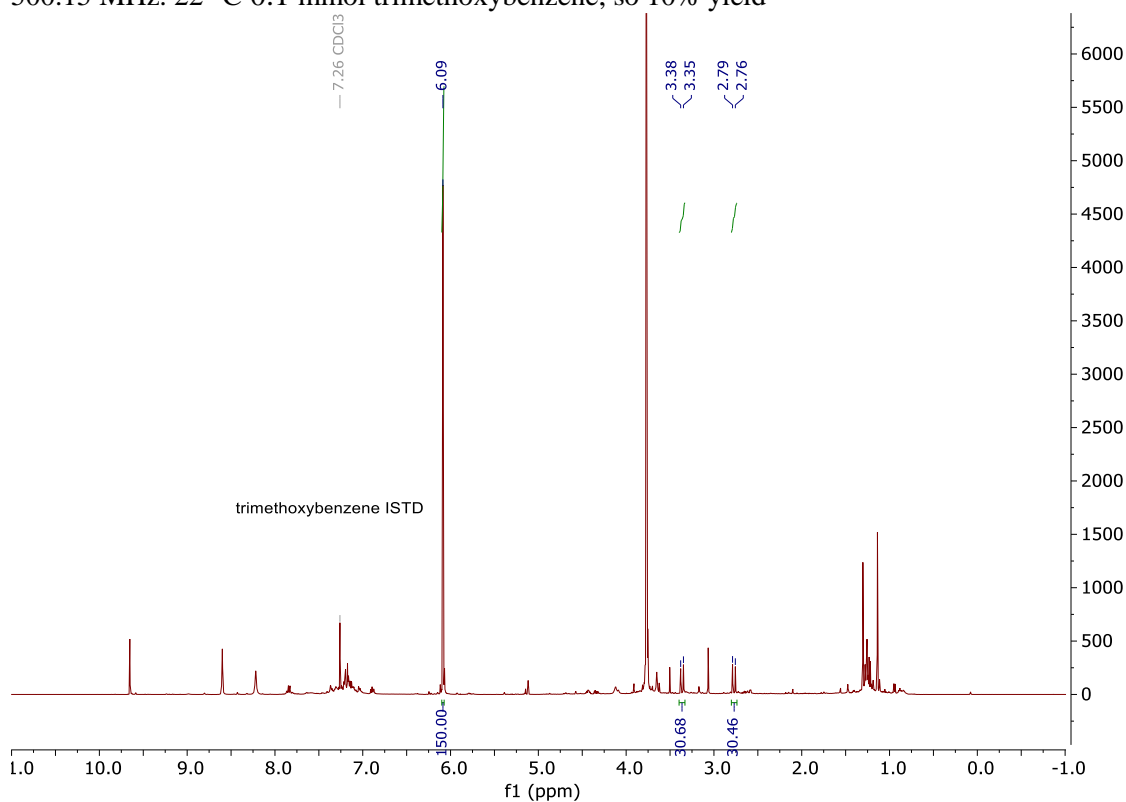
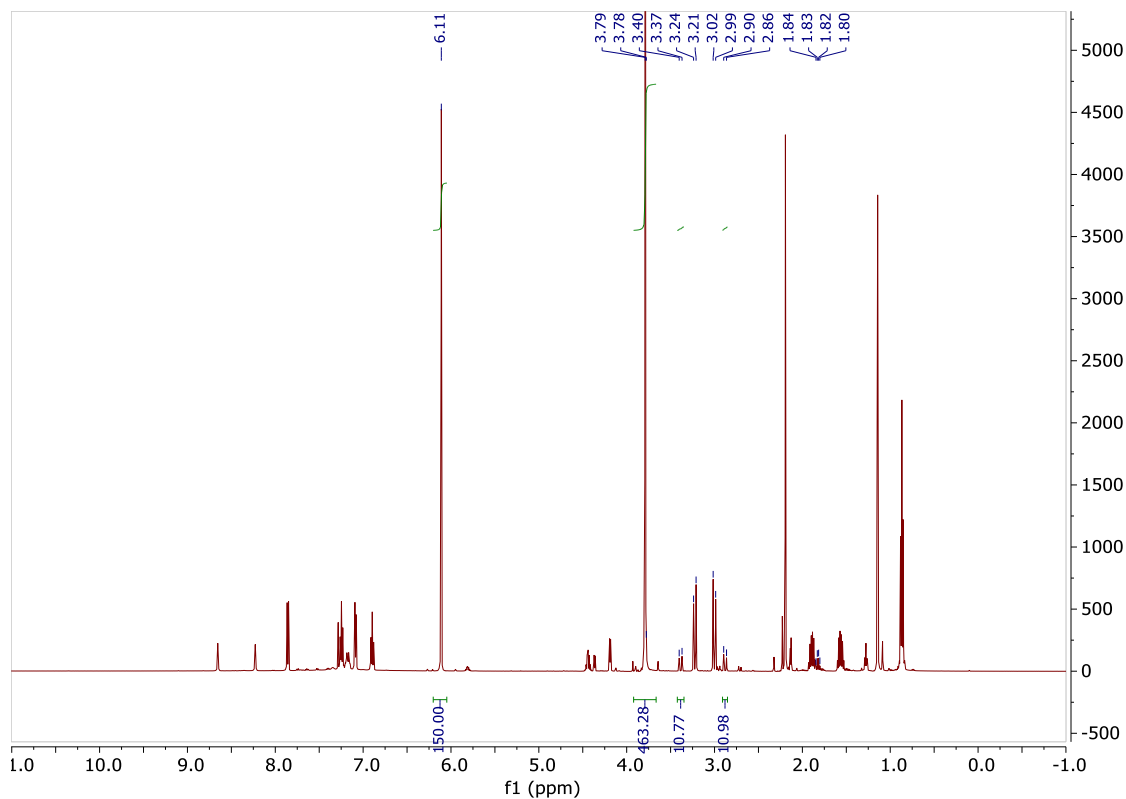


Figure S101: ^{13}C NMR spectrum of **8d** in CDCl_3 . Spectrometer Frequency 125.85 MHz. 22 $^\circ\text{C}$



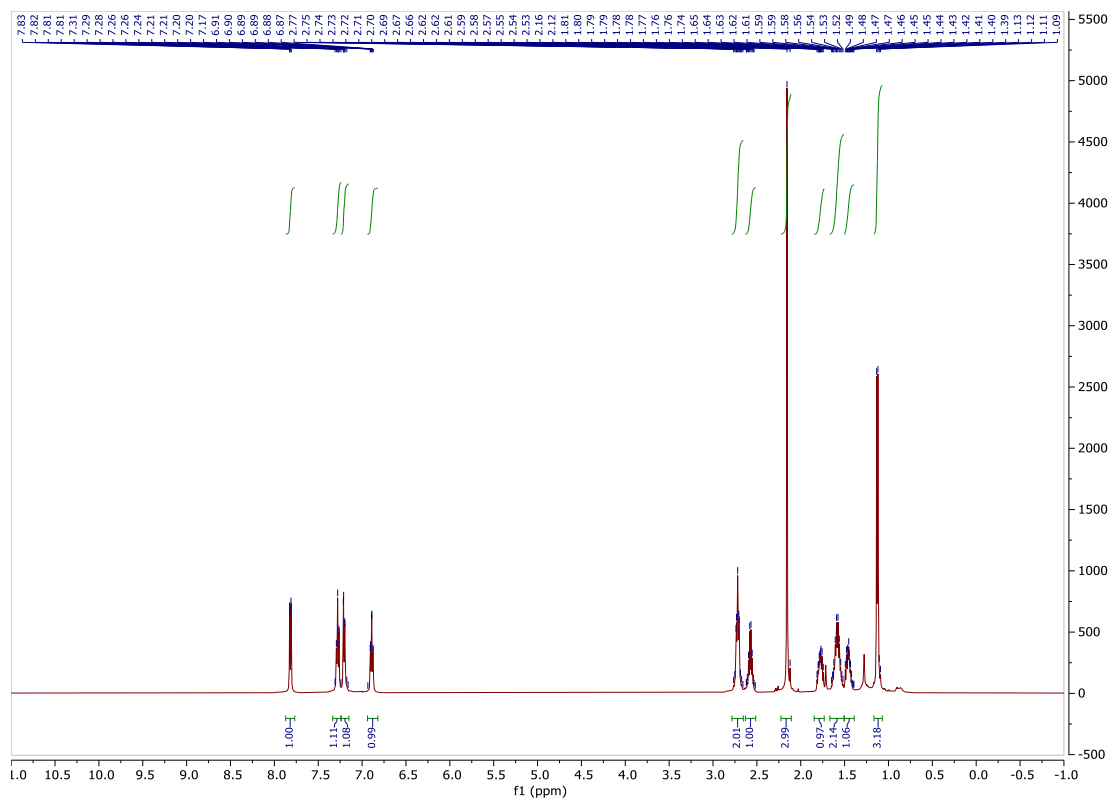


Figure S104: ^1H NMR spectrum of **9a** in CDCl_3 . Spectrometer Frequency 500.15 MHz. 22 $^\circ\text{C}$

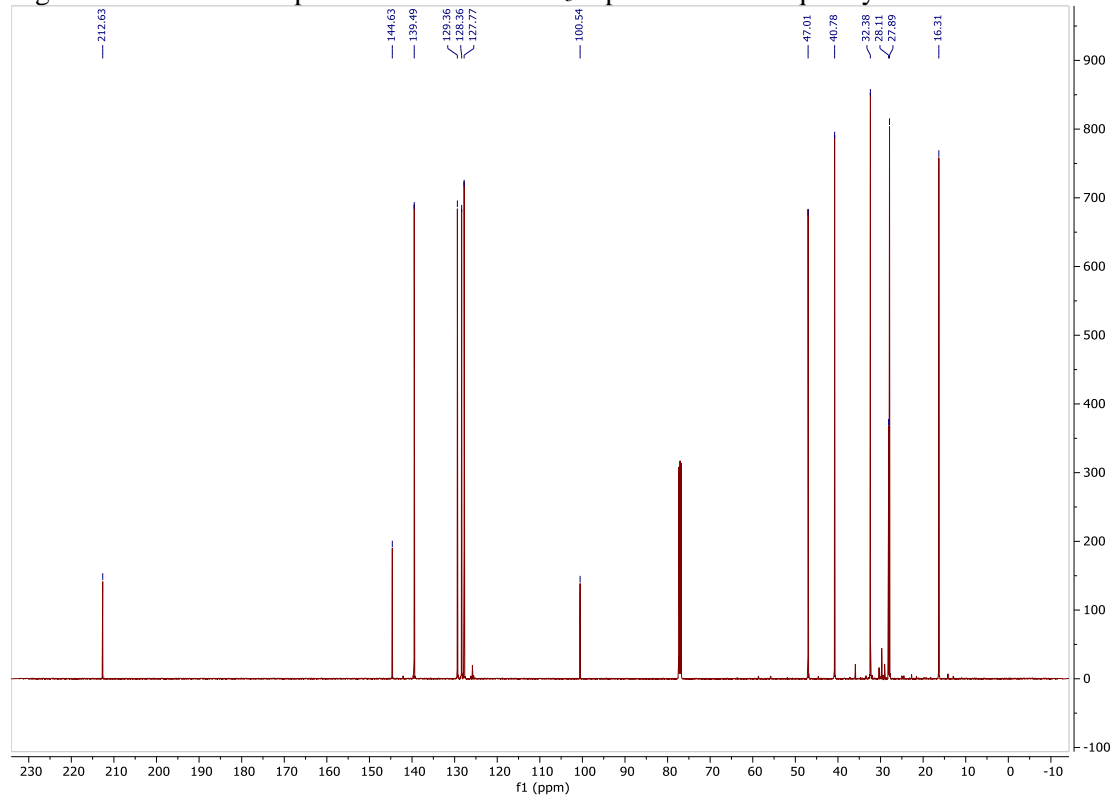


Figure S105: ^{13}C NMR spectrum of **9a** in CDCl_3 . Spectrometer Frequency 125.85 MHz. 22 $^\circ\text{C}$

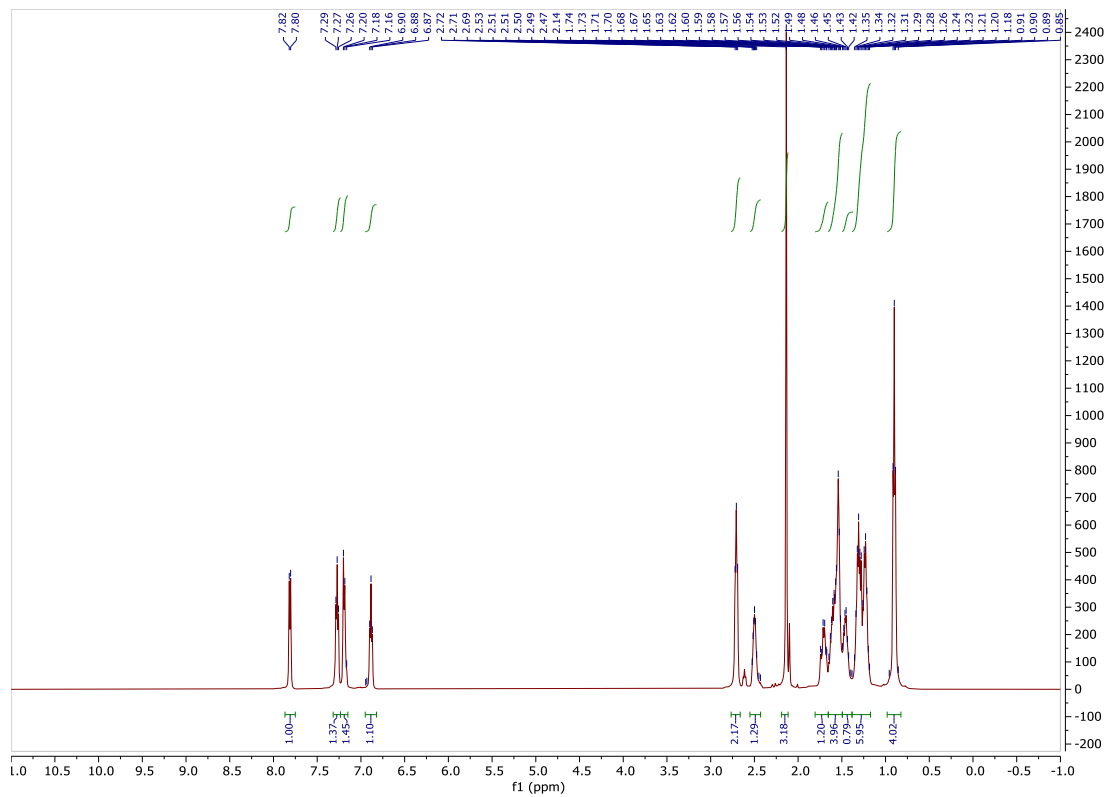


Figure S106: ^1H NMR spectrum of **9b** in CDCl_3 . Spectrometer Frequency 500.15 MHz. 22 $^\circ\text{C}$

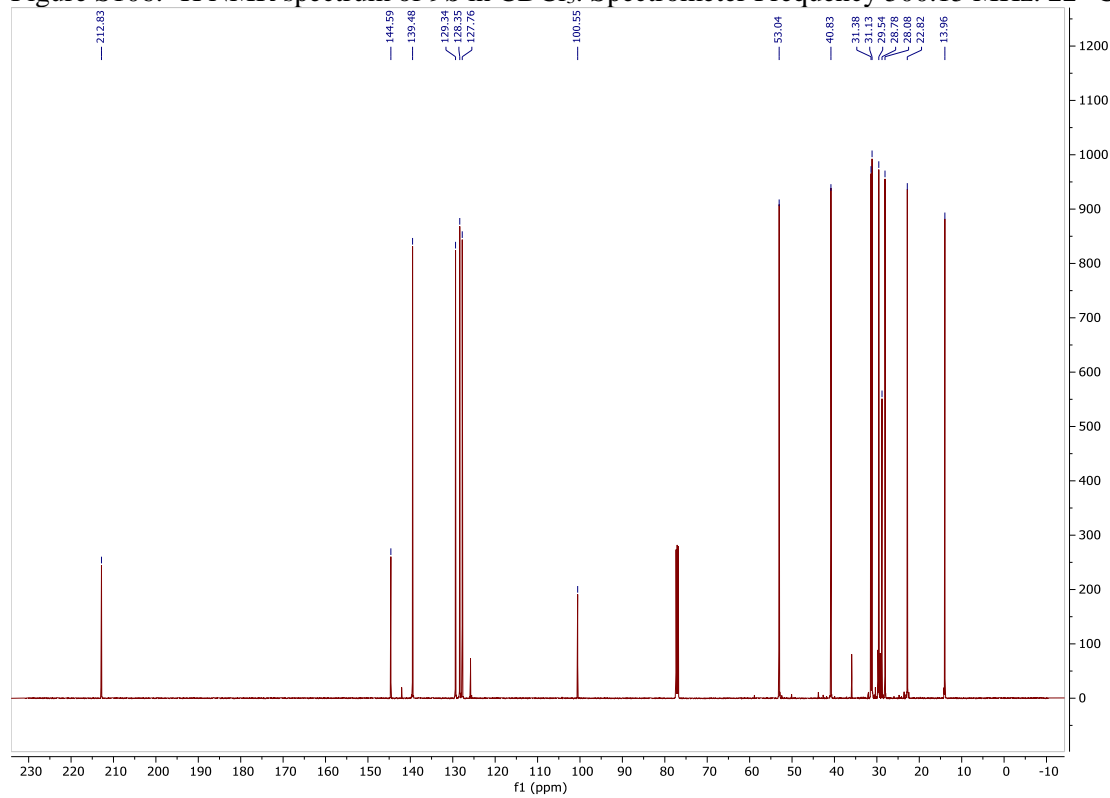


Figure S107: ^{13}C NMR spectrum of **9b** in CDCl_3 . Spectrometer Frequency 125.85 MHz. 22 $^\circ\text{C}$

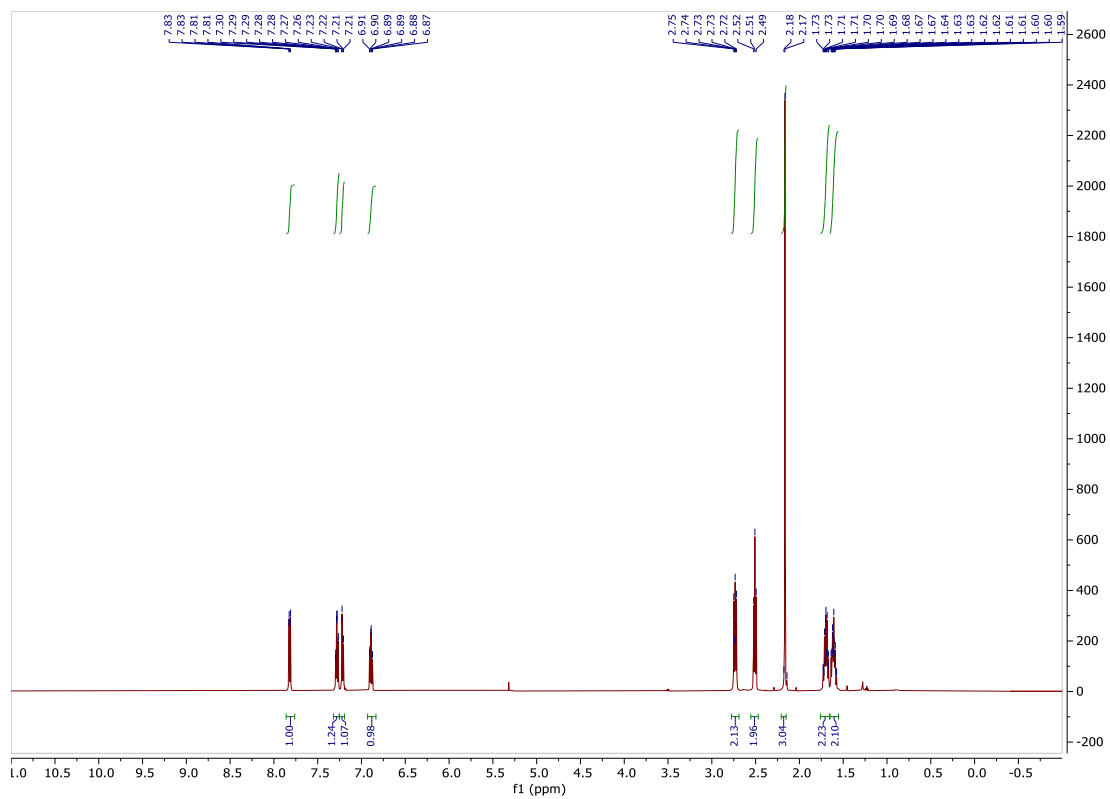


Figure S108: ^1H NMR spectrum of **9c** in CDCl_3 . Spectrometer Frequency 500.15 MHz. 22 $^\circ\text{C}$

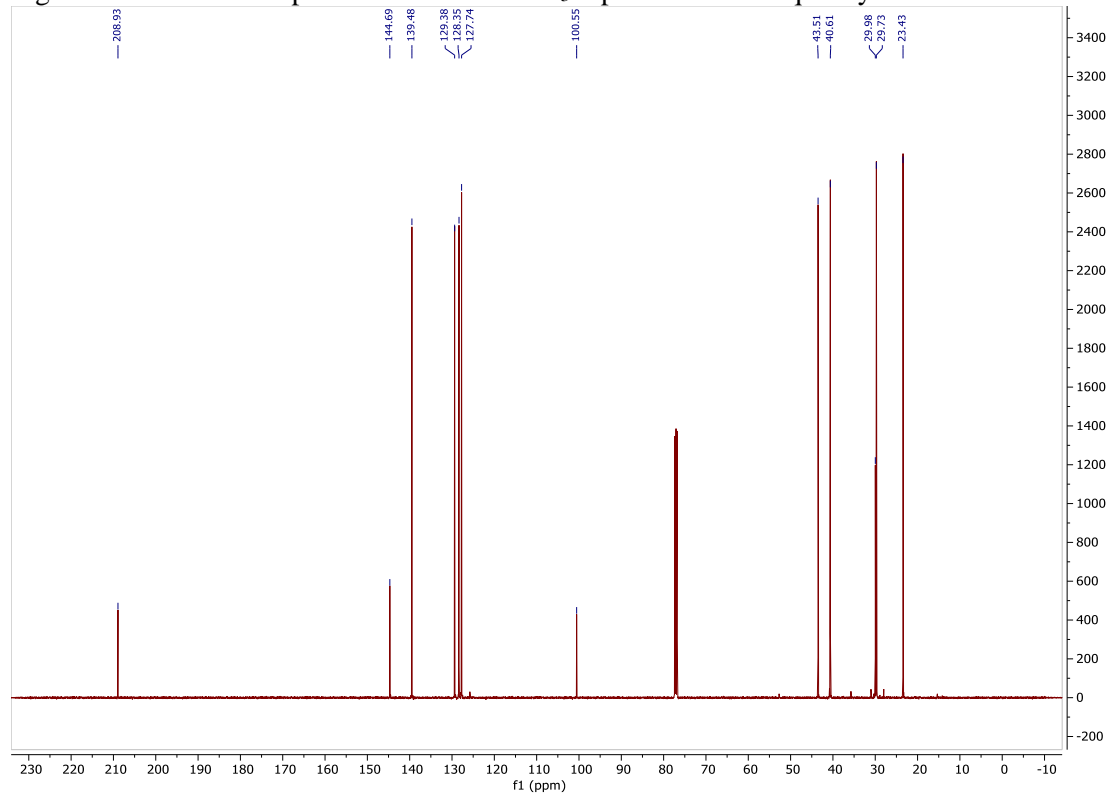
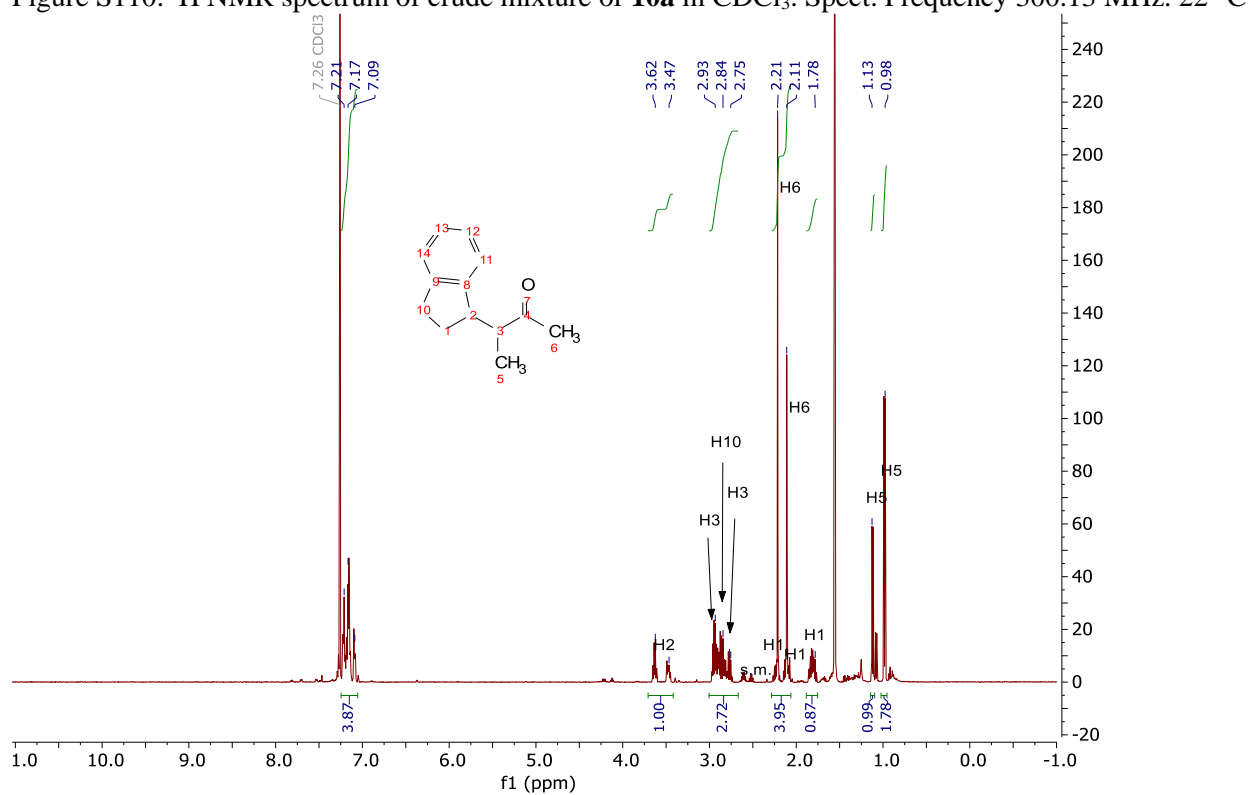
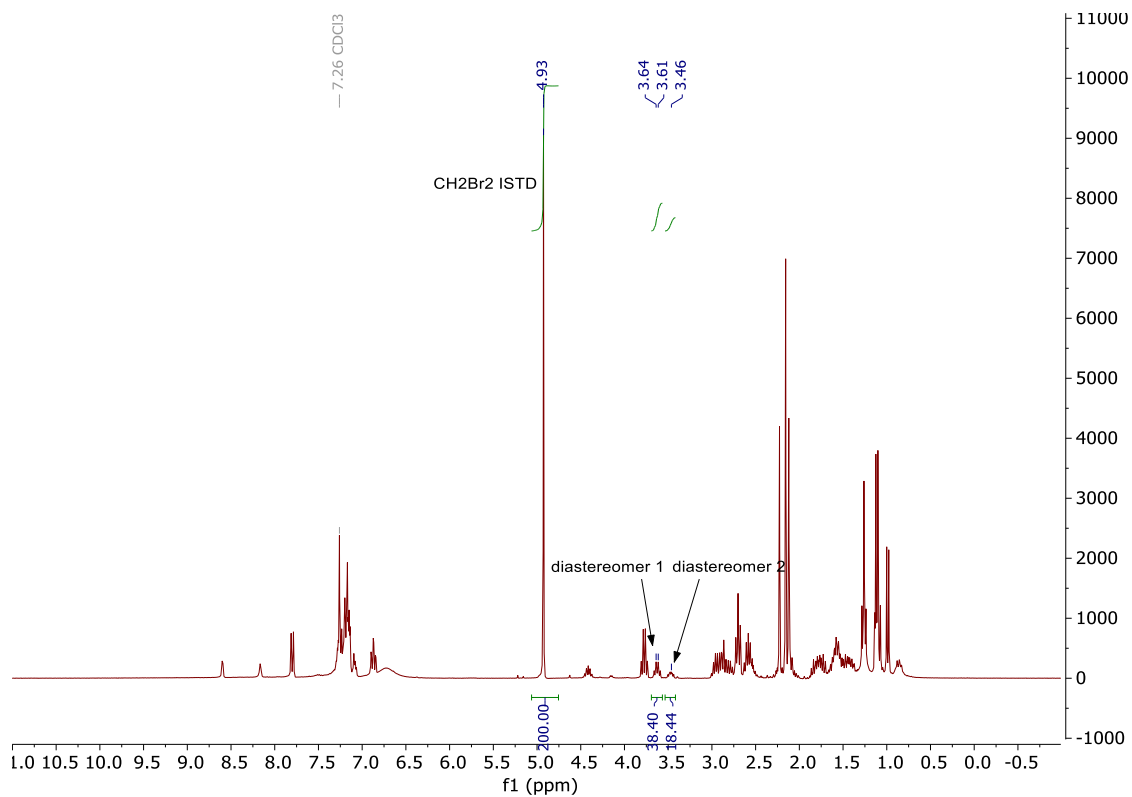


Figure S109: ^{13}C NMR spectrum of **9c** in CDCl_3 . Spectrometer Frequency 125.85 MHz. 22 $^\circ\text{C}$



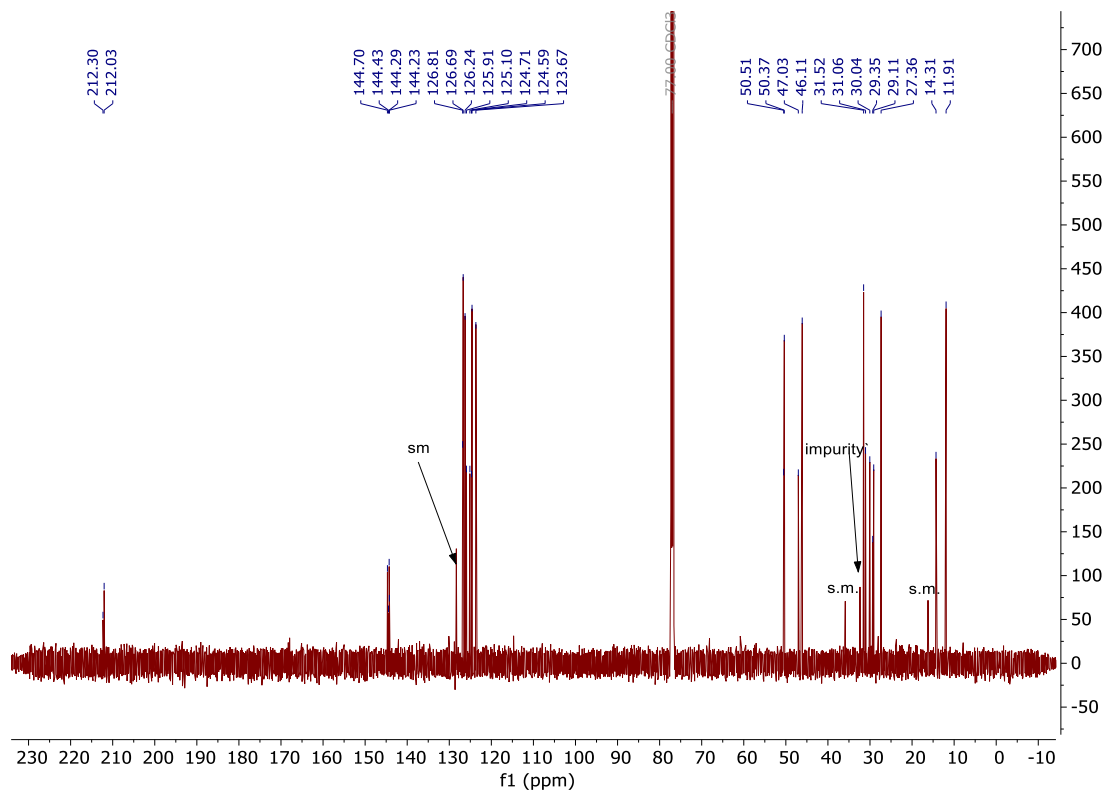


Figure S112: ^{13}C NMR spectrum purified mixture of diastereomers of **10a** in CDCl_3 . Spectrometer Frequency 125.85 MHz. 22 °C

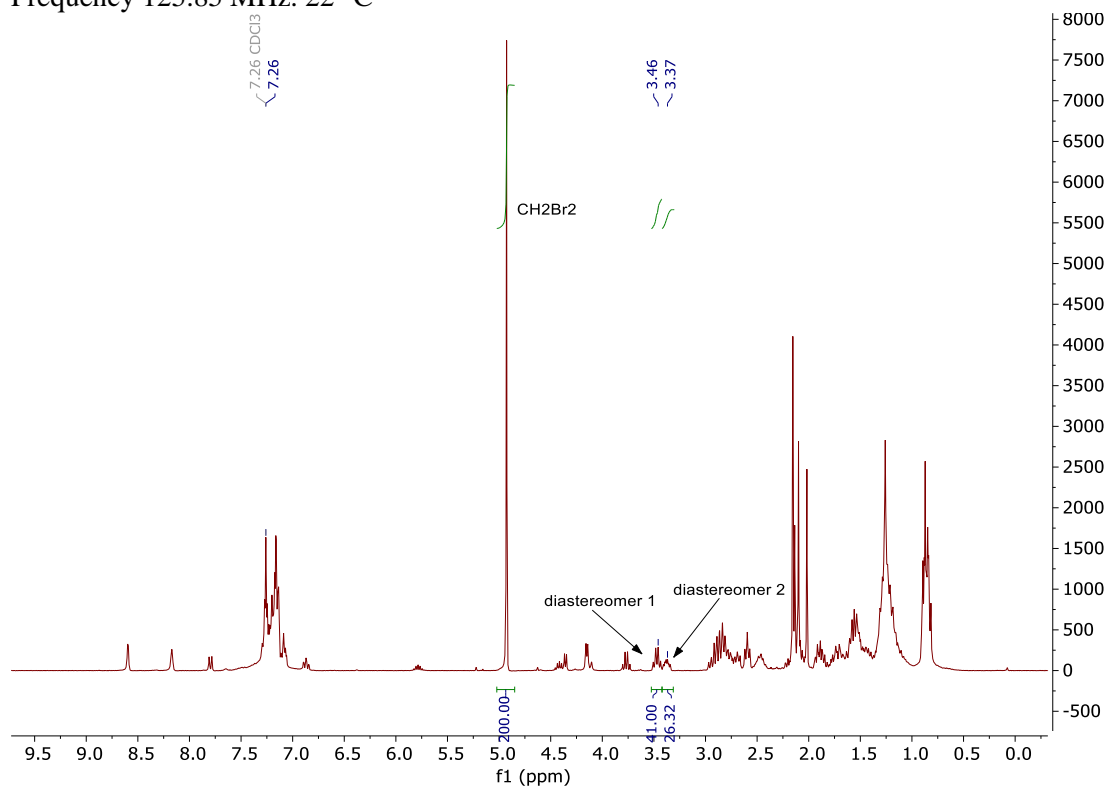


Figure S113: ^1H NMR spectrum of crude mixture of **10b** in CDCl_3 . Spectrometer Frequency 300.13 MHz. 22 °C. 0.1 mmol CH_2Br_2 standard added to 0.085 mmol scale reaction.

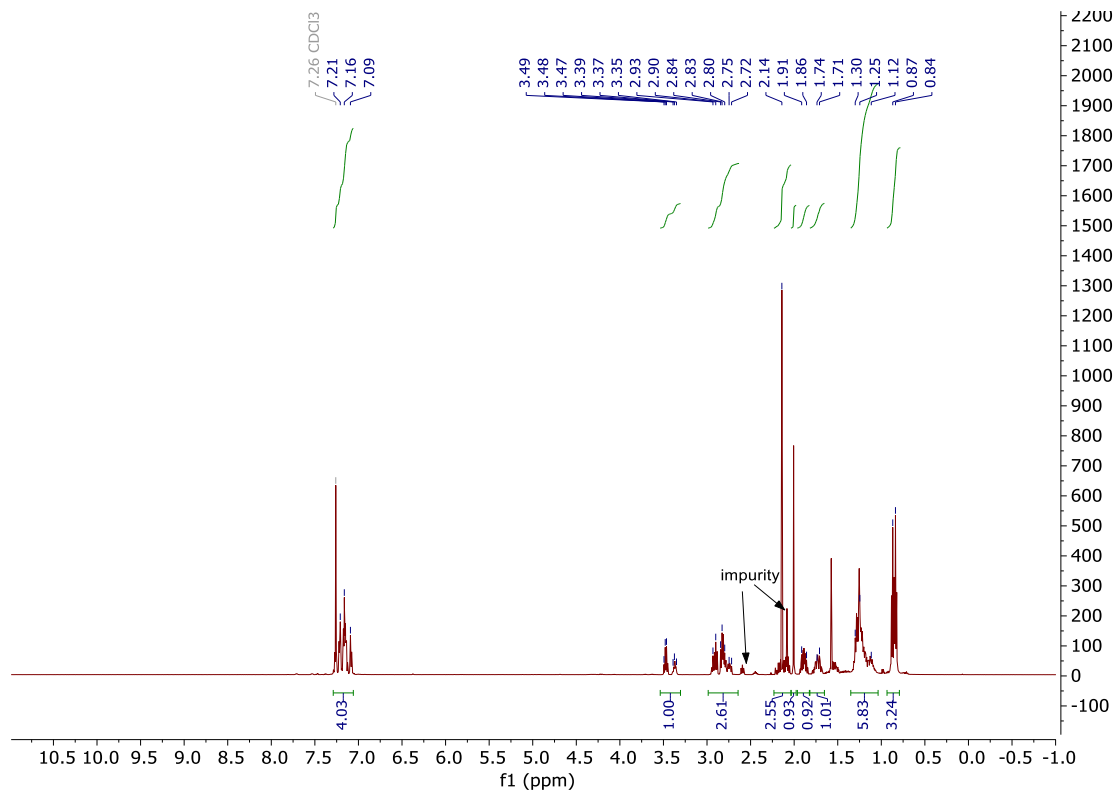


Figure S114: ¹H NMR spectrum of purified mixture of diastereomers of **10a** in CDCl₃. Spectrometer Frequency 500.15 MHz. 22 °C

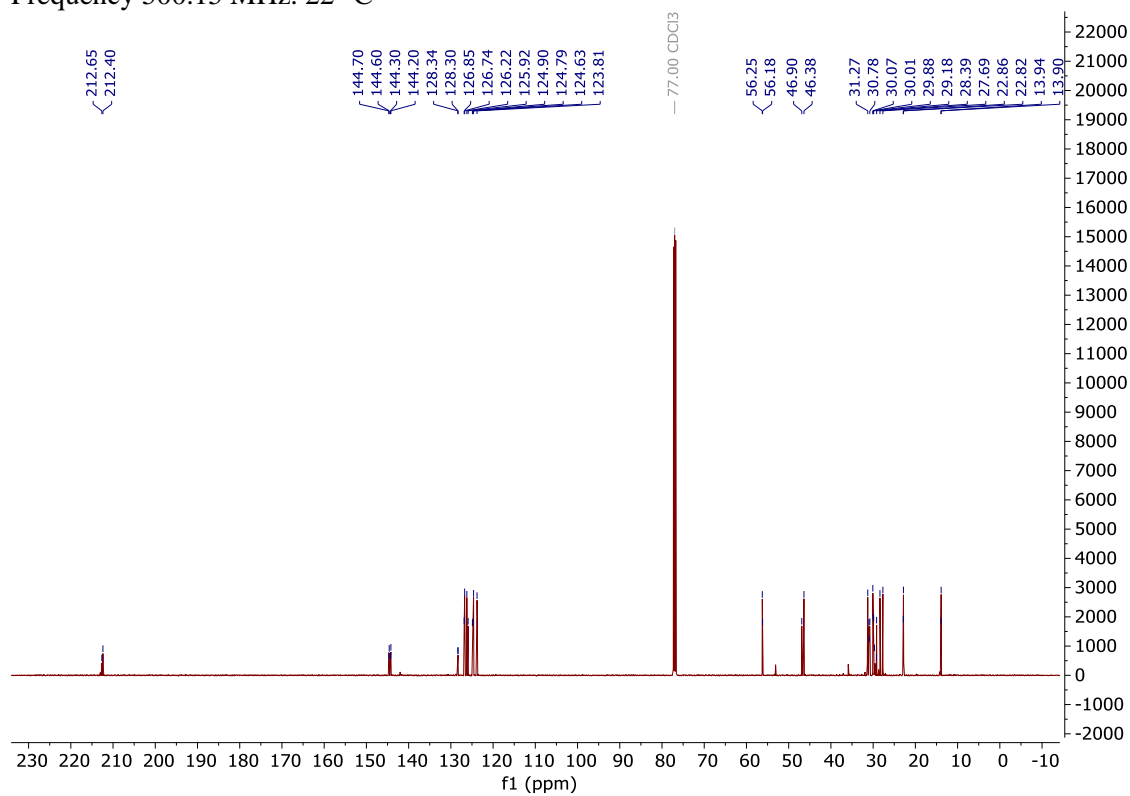


Figure S115: ¹³C NMR spectrum purified mixture of diastereomers of **10b** in CDCl₃. Spectrometer Frequency 125.85 MHz. 22 °C

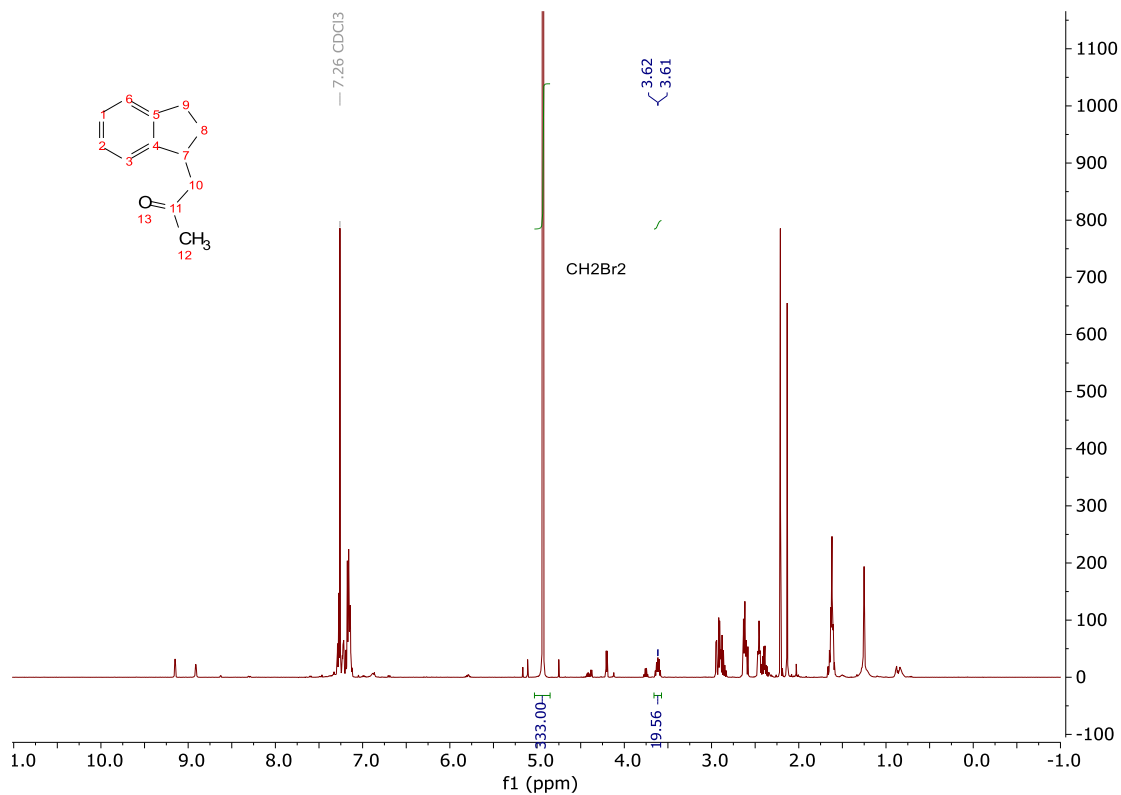


Figure S116: ^1H NMR spectrum of crude reaction mixture of **10c** in CDCl_3 . Spectrometer Frequency 399.80 MHz. 22 °C. 0.1 mmol CH_2Br_2 standard added to 0.06 mmol scale reaction.

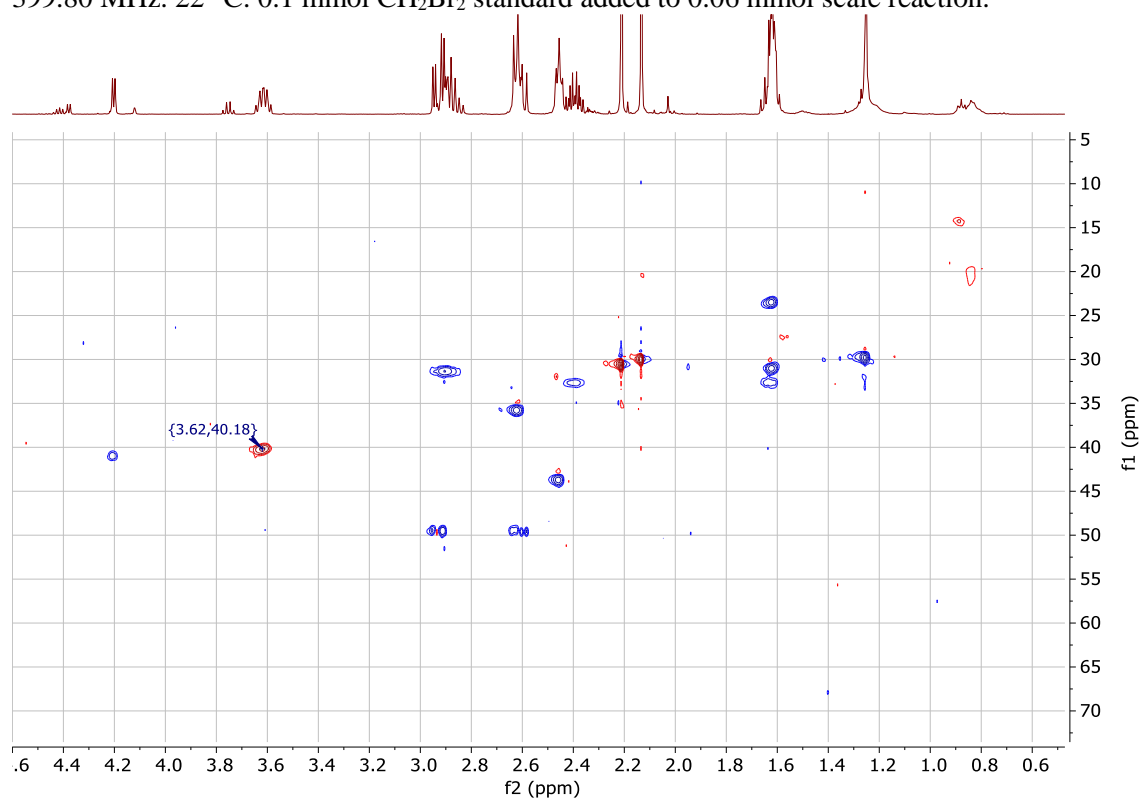


Figure S117: HSQC NMR spectrum of crude reaction mixture of **10c** in CDCl_3 . Spectrometer Frequency 500.15, 125.77 MHz. 22 °C. 0.1 mmol.

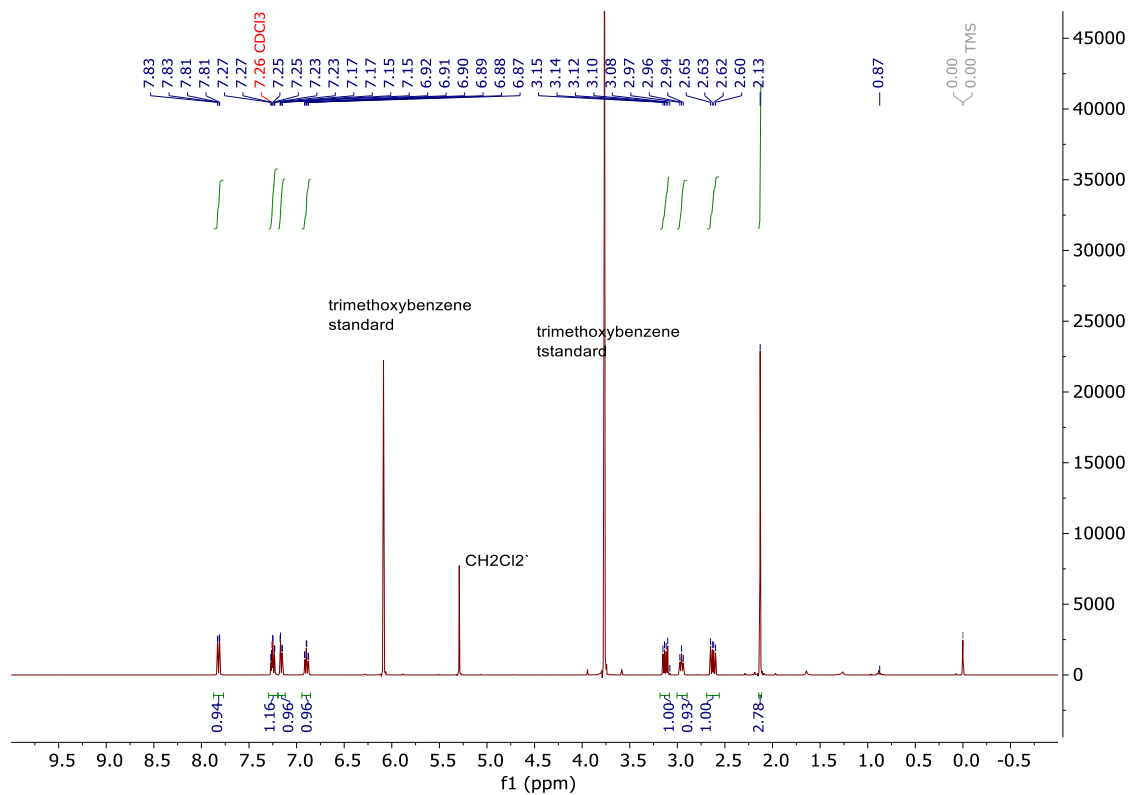


Figure S118: ¹H NMR spectrum of **11** in CDCl₃. Spectrometer Frequency 400.13 MHz. 22 °C

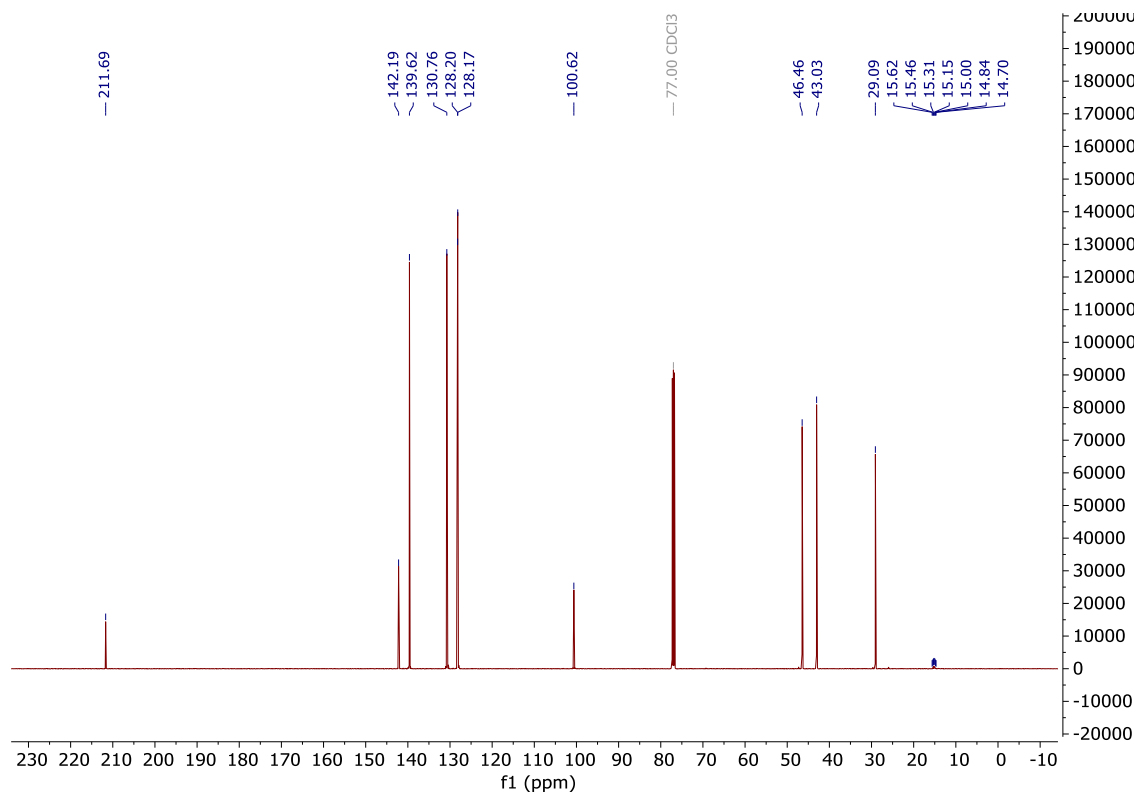


Figure S119: ¹³C NMR spectrum of **11** in CDCl₃. Spectrometer Frequency 125.85 MHz. 22 °C

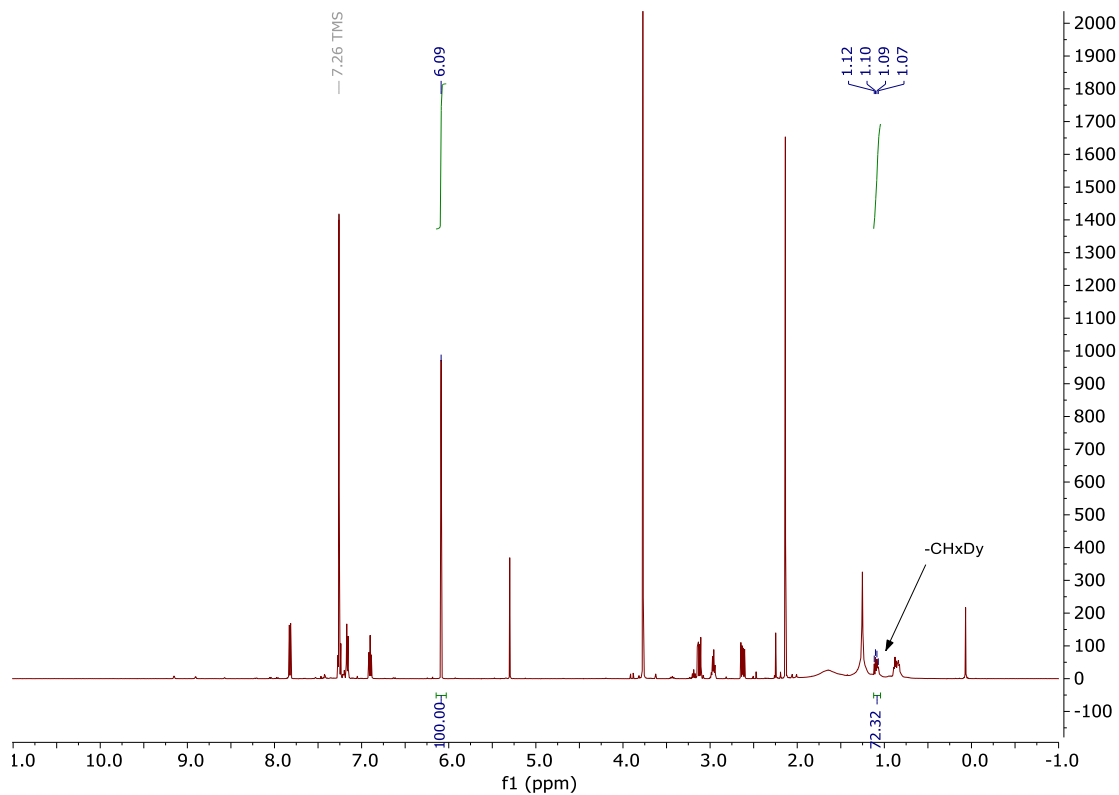


Figure S120: ^1H NMR spectrum of crude **11-H** in CDCl_3 . Spectrometer Frequency 500.15 MHz. 22 °C

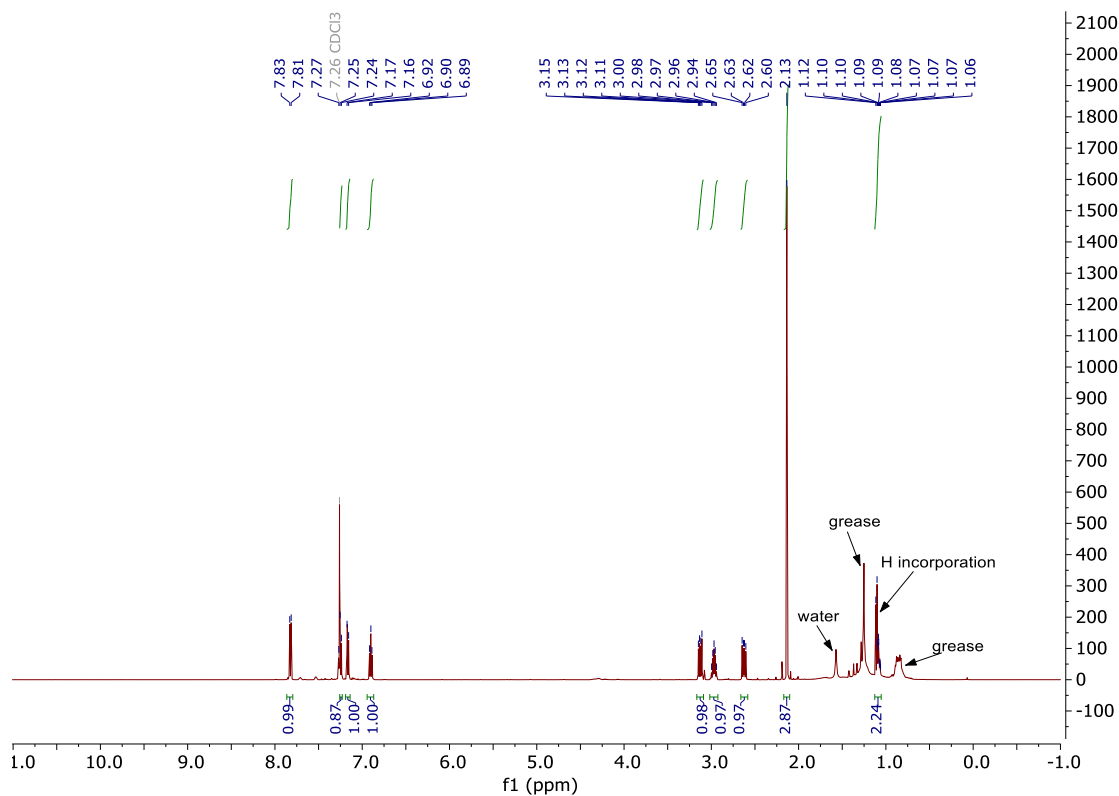


Figure S121: ^1H NMR spectrum of purified **11-H** in CDCl_3 . Spectrometer Frequency 500.15 MHz. 22 °C

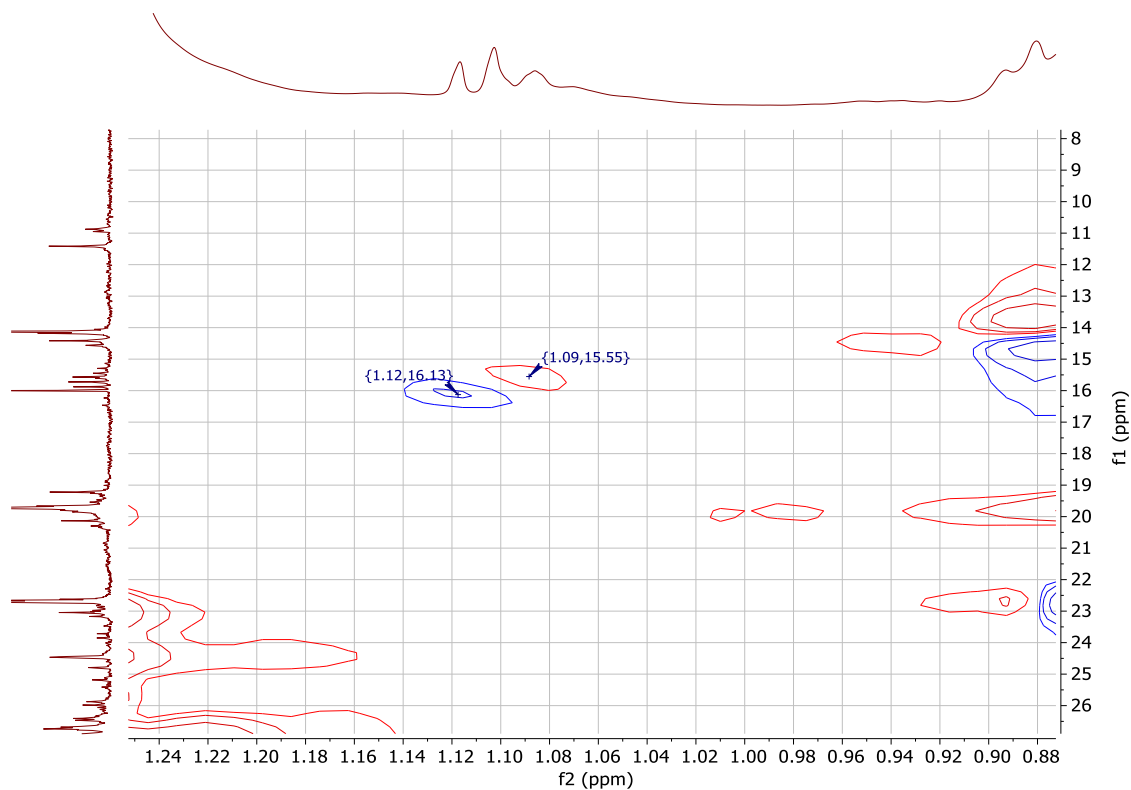


Figure S122: HSQC NMR spectrum of crude **11-H** in CDCl_3 . Spectrometer Frequency 500.15 MHz. 22 °C

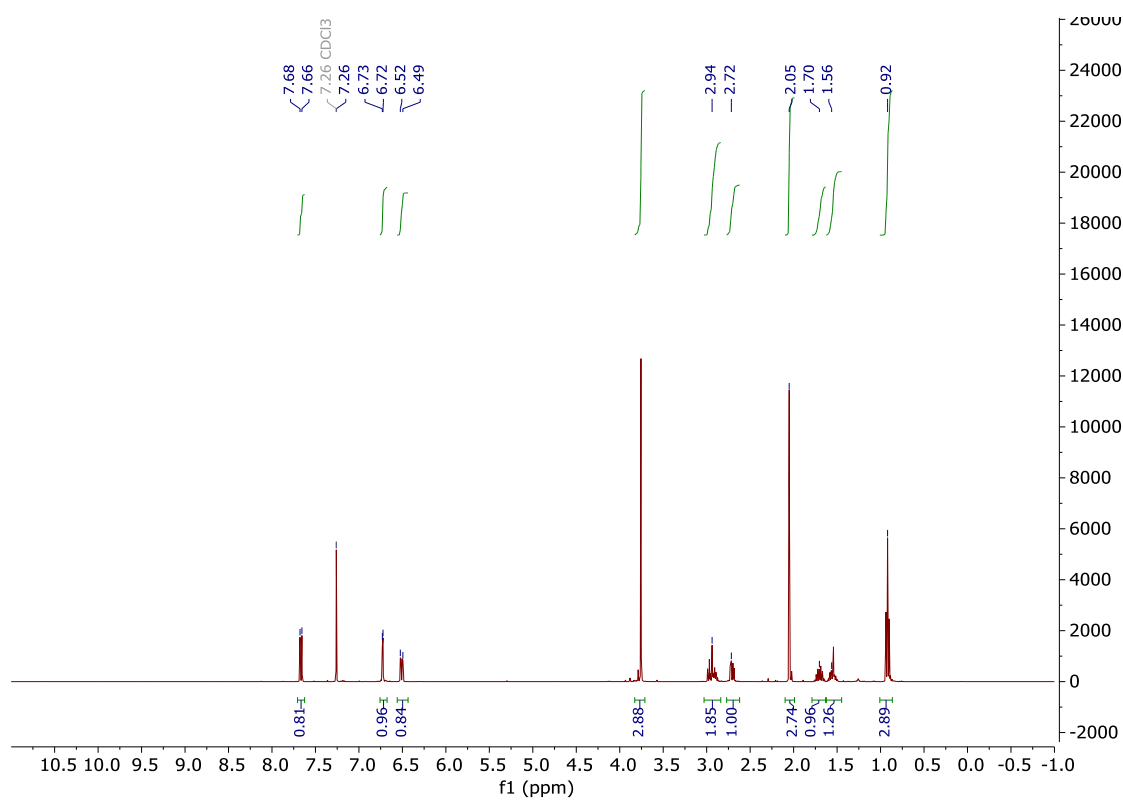


Figure S123: ^1H NMR spectrum of **15** in CDCl_3 . Spectrometer Frequency 399.80 MHz. 22 °C

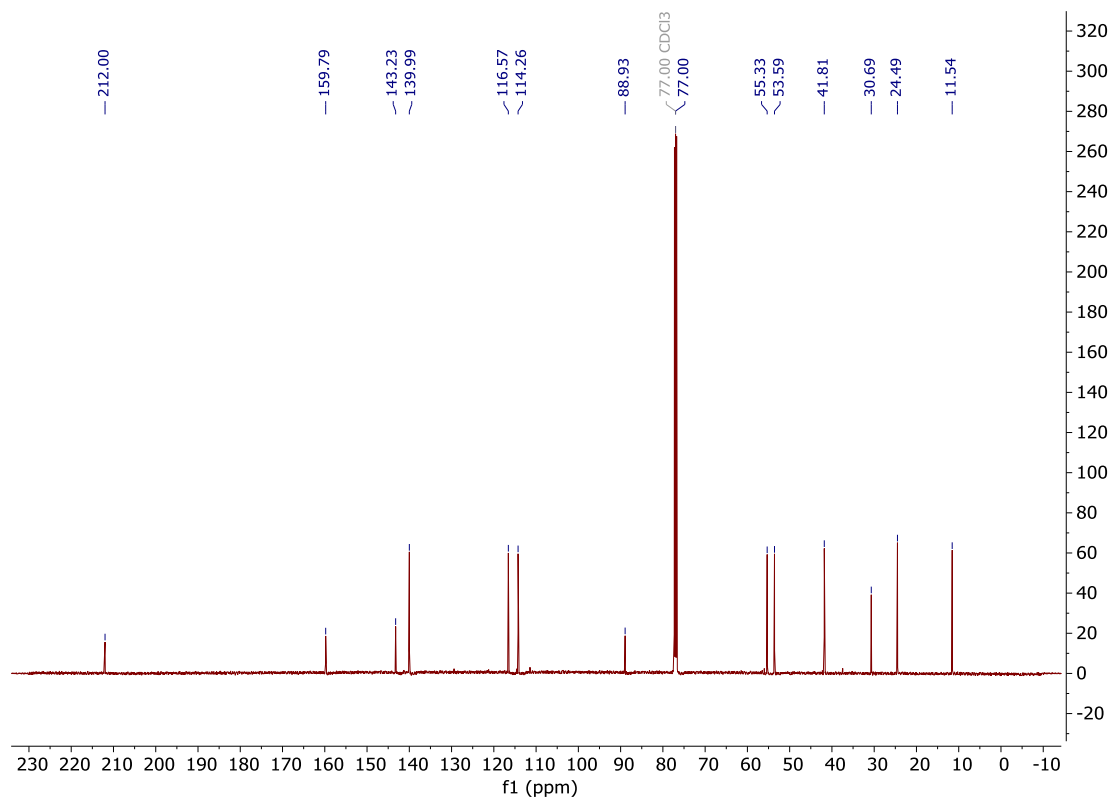


Figure S124: ¹³C NMR spectrum of **15** in CDCl₃. Spectrometer Frequency 125.85 MHz. 22 °C

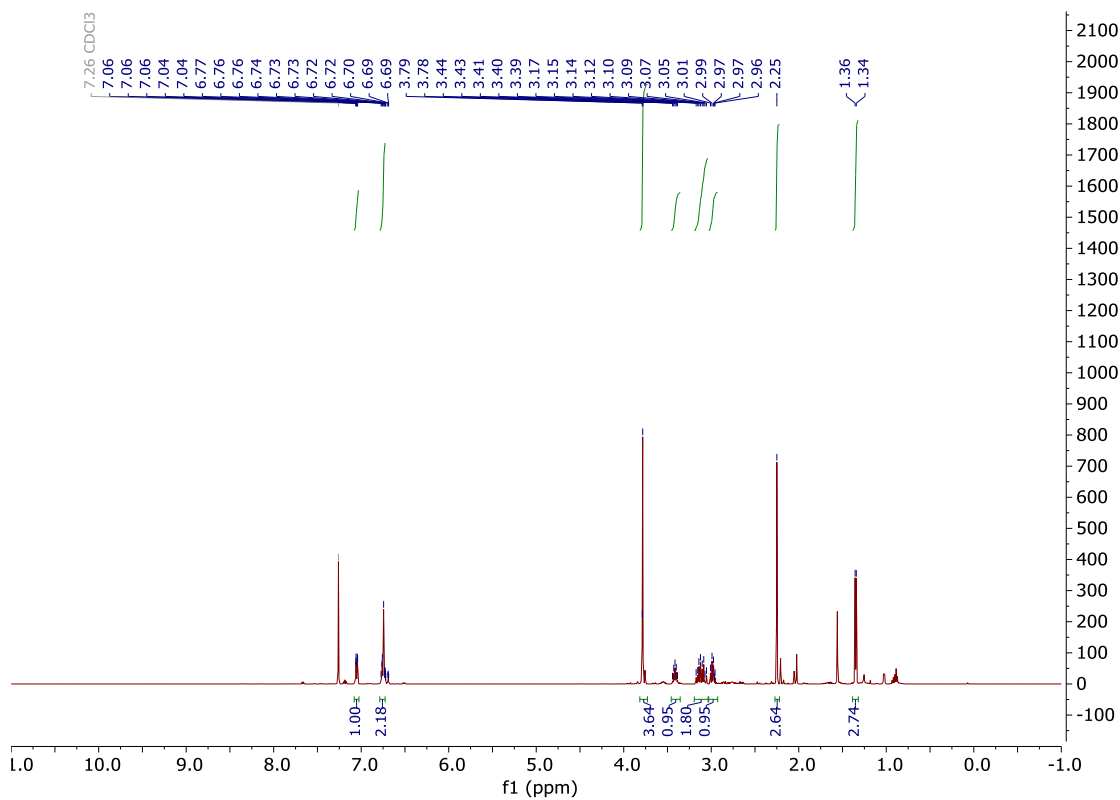


Figure S125: ¹H NMR spectrum of **16** in CDCl₃. Spectrometer Frequency 500.40 MHz. 22 °C

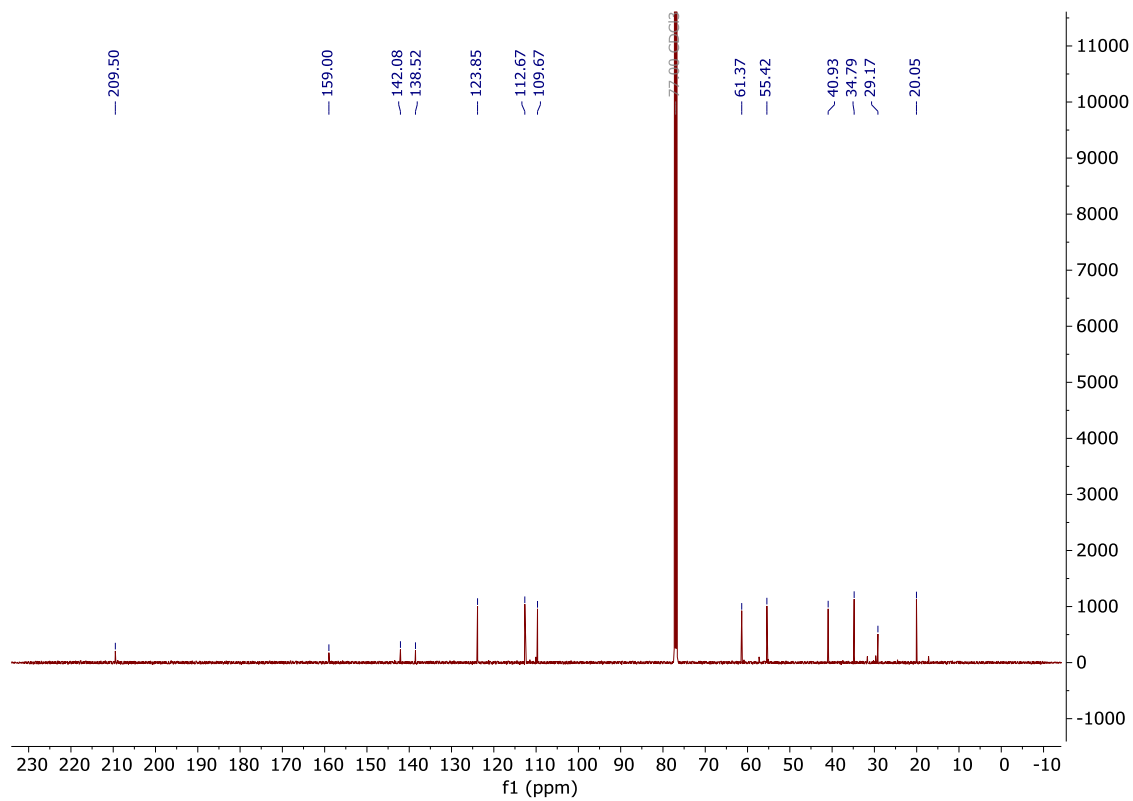


Figure S126: ^{13}C NMR spectrum of **16** in CDCl_3 . Spectrometer Frequency 125.85 MHz. 22 °C

2D NMR Analysis

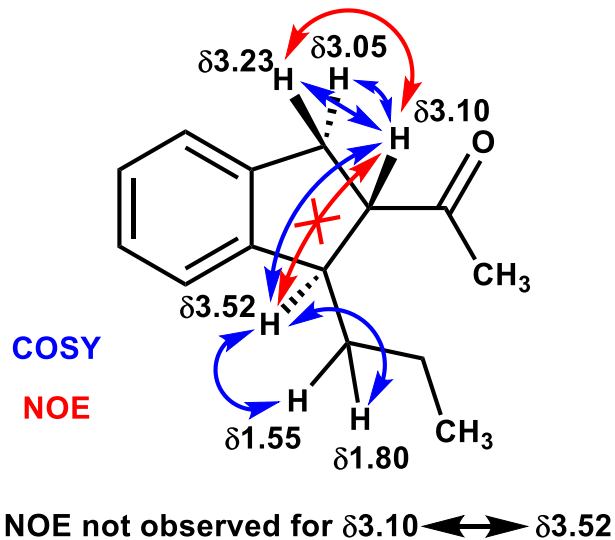


Figure S127: 2D NMR spectroscopy diagram for **7a** establishing ^1H NMR signal assignments and *trans* stereochemistry. COSY contacts indicated in blue, and NOESY contacts indicated in red.

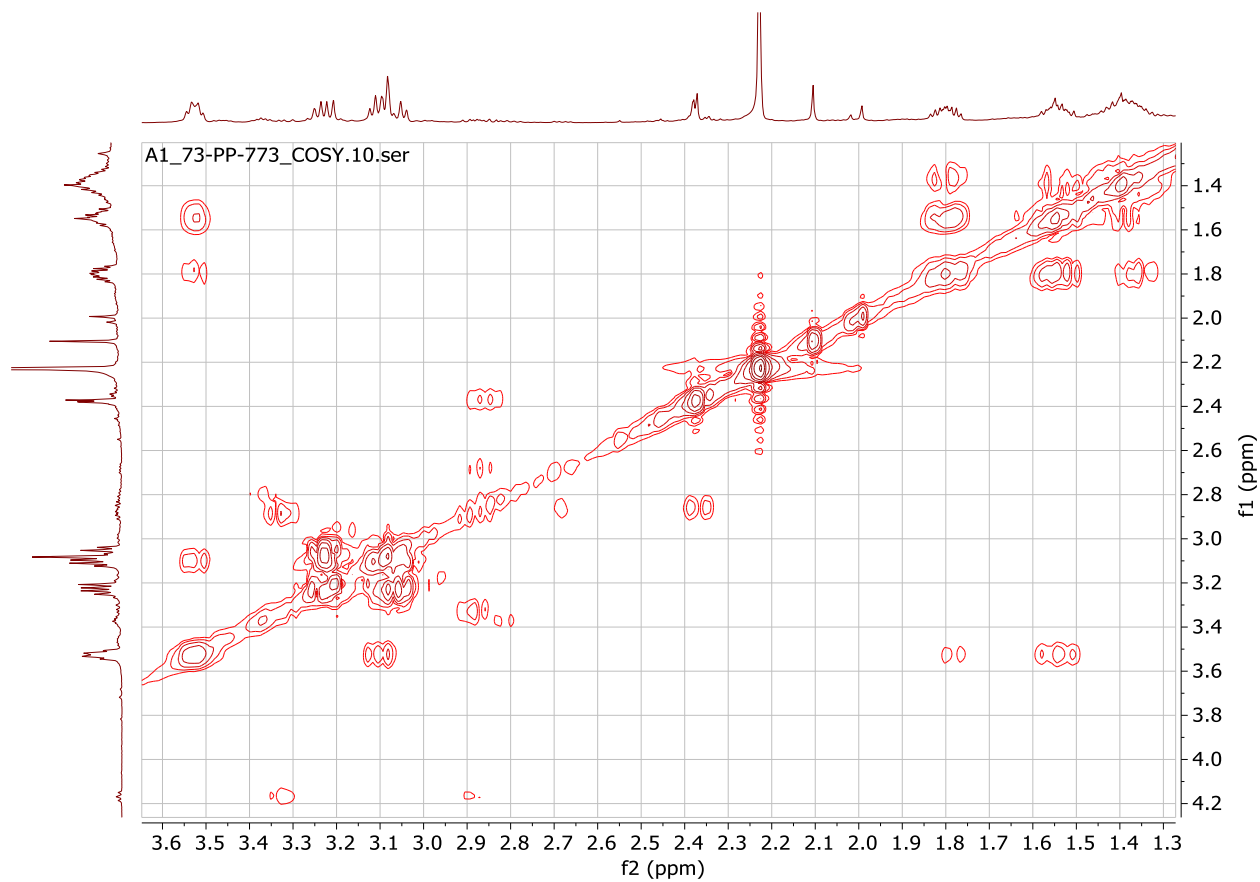


Figure S128: COSY NMR Spectrum of **7a** in CDCl_3 . Spectrometer frequency 500.15 Hz, 500.15 Hz, 22 $^\circ\text{C}$

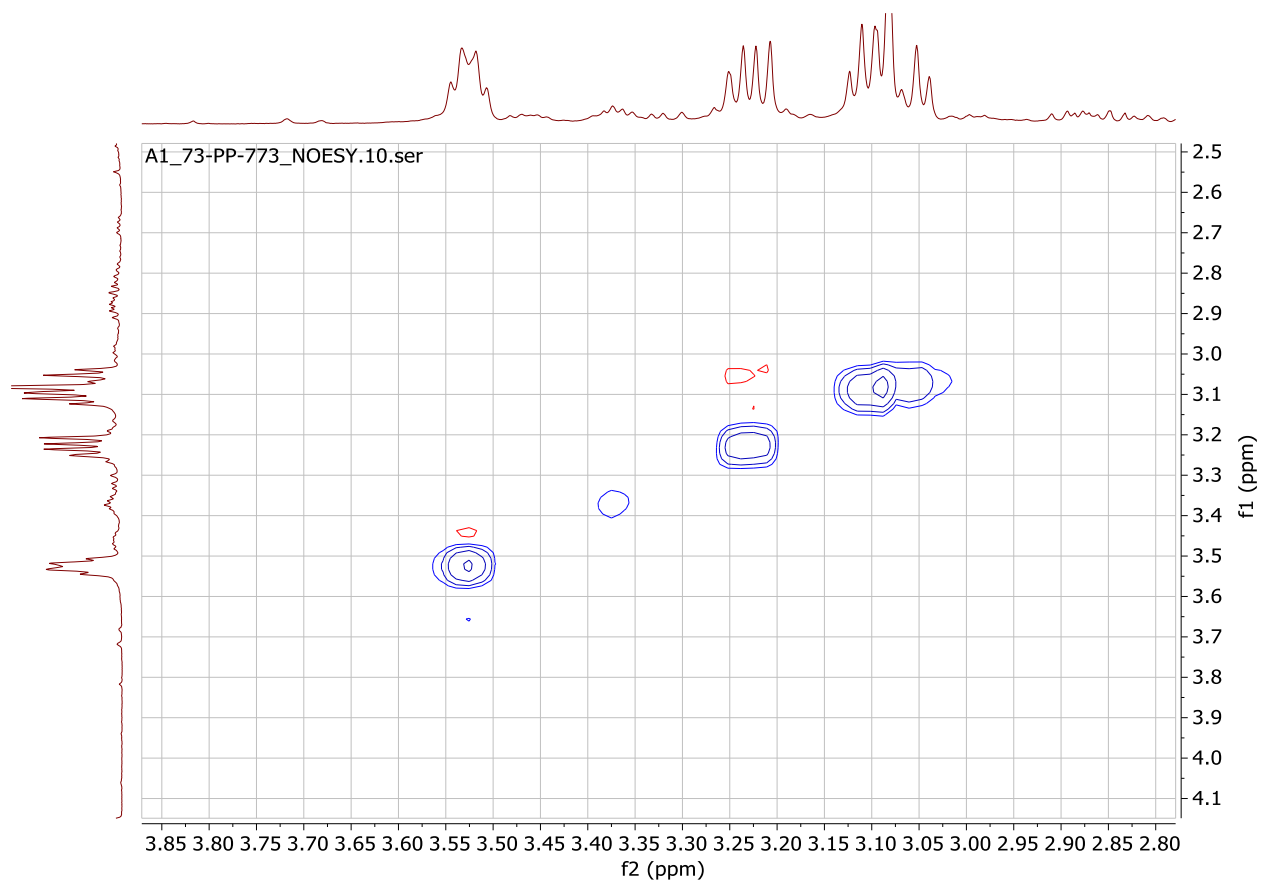
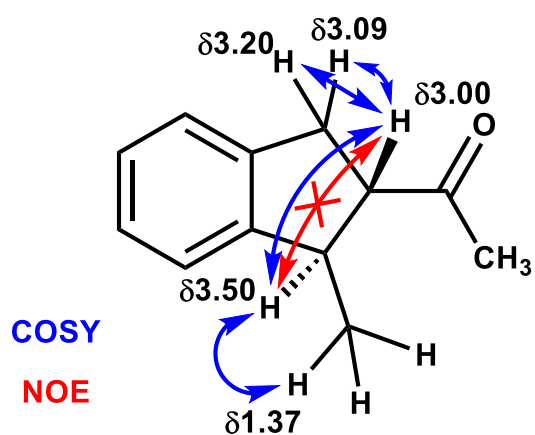


Figure S129: NOESY NMR Spectrum of **7a** in CDCl₃. Spect. frequency 500.15 Hz, 500.15 Hz, 22 °C



NOE not observed for $\delta 3.00 \longleftrightarrow \delta 3.50$

Figure S130: 2D NMR spectroscopy diagram for **5** establishing ¹H NMR signal assignments and *trans* stereochemistry. COSY contacts indicated in blue, and NOESY contacts indicated in red. This data is consistent with previously reported spectroscopic data of this compound.^{12,13}

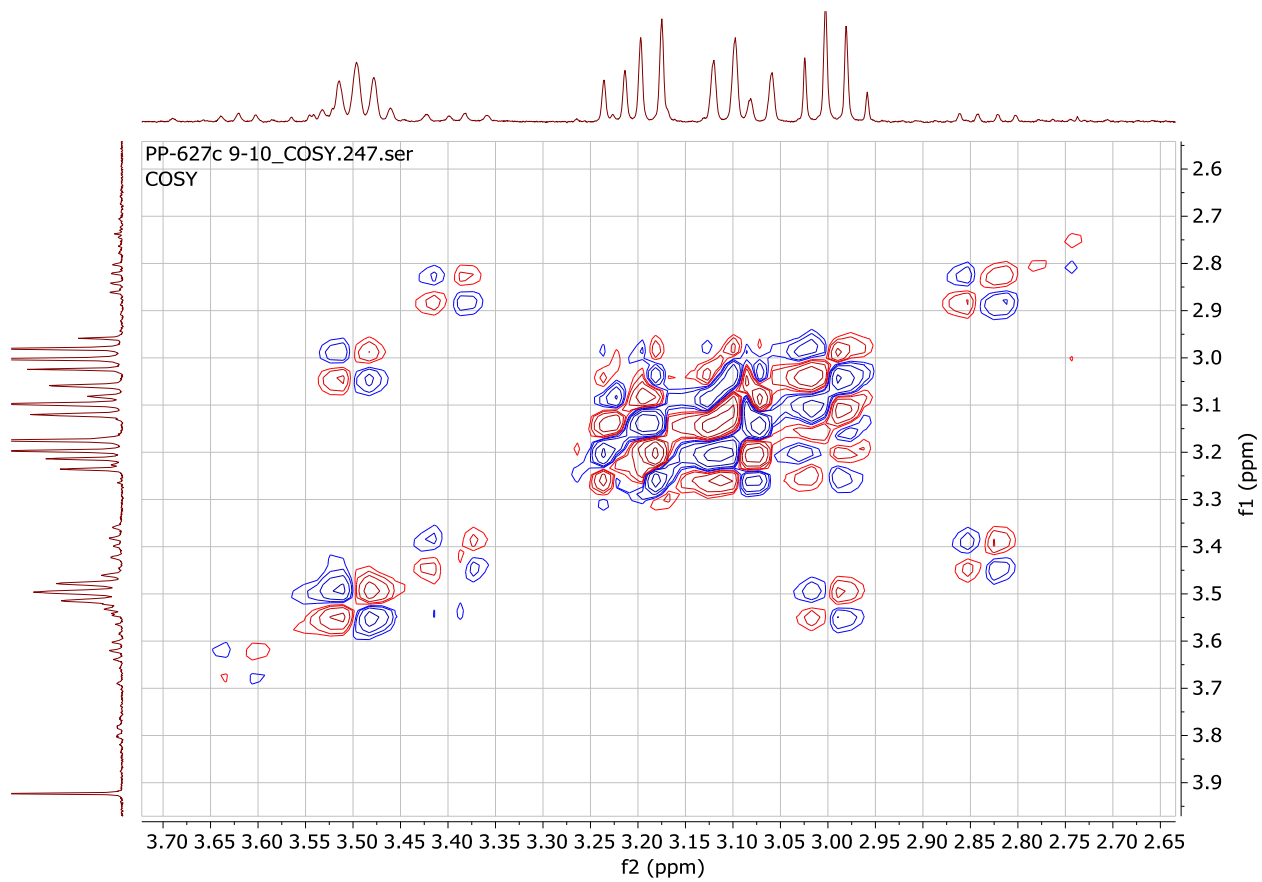


Figure S131: COSY NMR Spectrum of **5** in CDCl_3 . Spectrometer frequency 600.13 Hz, 600.13 Hz, 22 °C

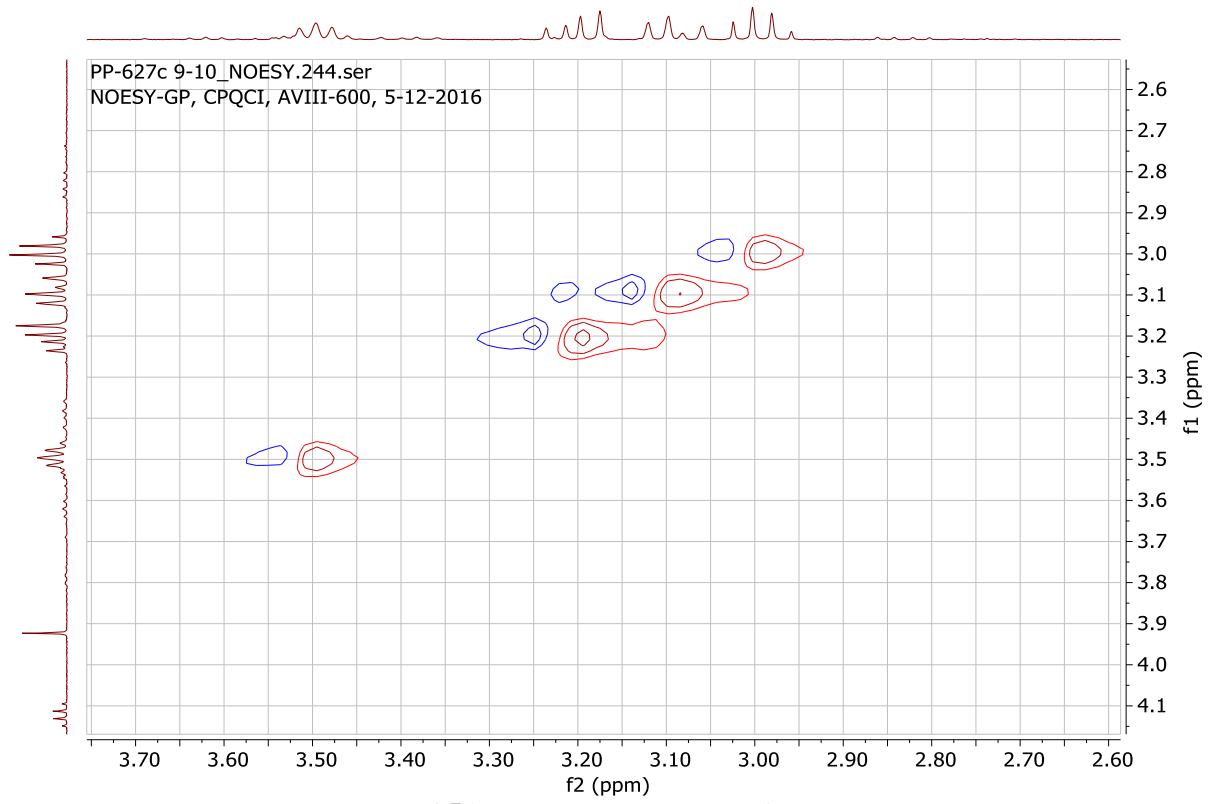


Figure S132: NOESY NMR Spectrum of **5** in CDCl₃. Spectrometer frequency 600.13 Hz, 600.13 Hz, 22 °C

Computational Methods

Quantum mechanical calculations were performed with Gaussian 09.¹⁹ Ground state and transition state geometries were optimized in the gas phase using the B3LYP^{20–23} functional with the 6-31G(d)^{24,25} basis set for all nonmetal atoms and the LANL2DZ^{26,27} basis set with effective core potential (ECP) for Pd. Single-point corrections were calculated using Truhlar's M06²⁸ functional with the 6-311++G(d,p)²⁹ basis set for all nonmetal atoms and the SDD^{30,31} effective core potential for Pd. Single-point solvation energies were calculated by using SMD solvation model (solvent = generic, eps = 16.7, epsinf = 1.625625) to model HFIP. Vibrational frequencies were computed to determine if the optimized structures are minima or saddle points on the potential energy surface corresponding to minima and transition state geometries, respectively. The reported free energies include zero-point energies and thermal corrections calculated at 298.15 K and 1 atm. Molecular structures were illustrated with CYLview.³²

Additional Computational Discussion

First, we studied the first C(sp³)-H functionalization starting with glycine and **A** to form imine **B**. The proposed catalytic cycle shown in Figure S133 undergoes concerted metallation deprotonation (CMD) using acetate as a base from **Int C** to **Int D** through **CMD TS A** followed by oxidative addition with diiodobenzene from **Int E** to **Int F** through **OA TS B** and reductive elimination from **Int G** to **Int H** through **RE TS C** to form the arylated product. The unique, stabilizing role of AgTFA is seen in Int E to Int H – the coordination of AgTFA to the carboxylate moiety of each respective palladacycle was energetically favorable. This would then undergo a second C-H functionalization to form the final product. The free energy diagram is shown in Figure S134 and the CMD, OA, and RE transition state (TS) structures are shown in Figure S135. Interestingly, the CMD step is rate-determining with the activation free energy barrier at 19.0 kcal/mol.

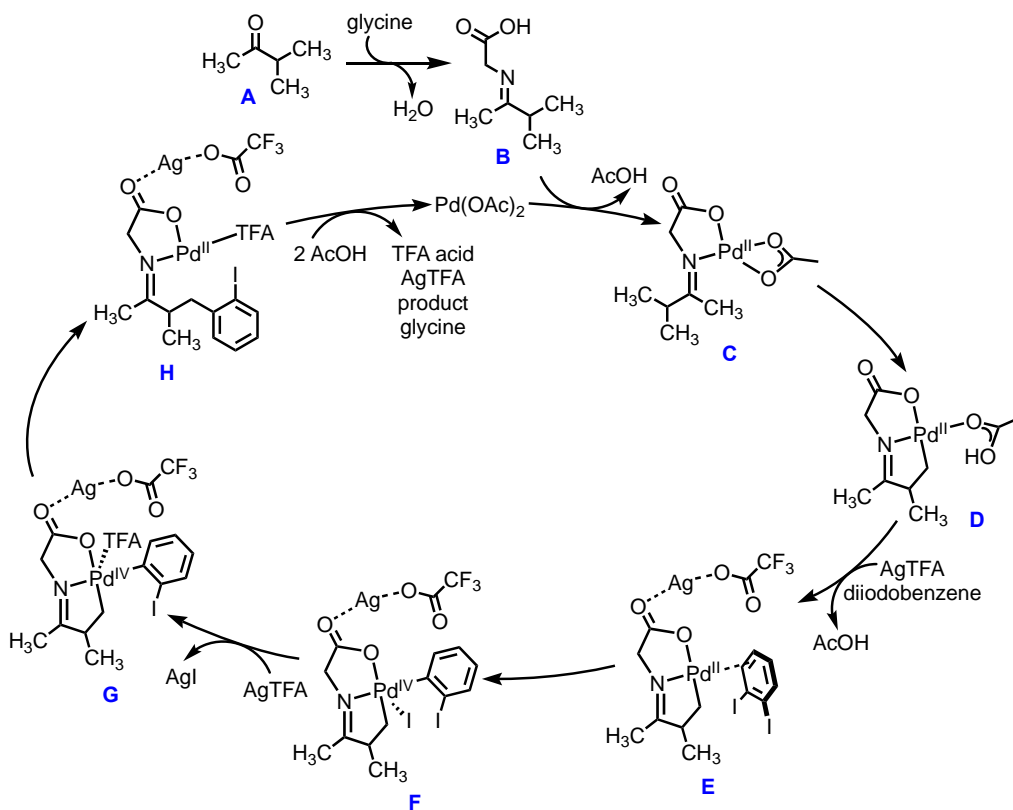
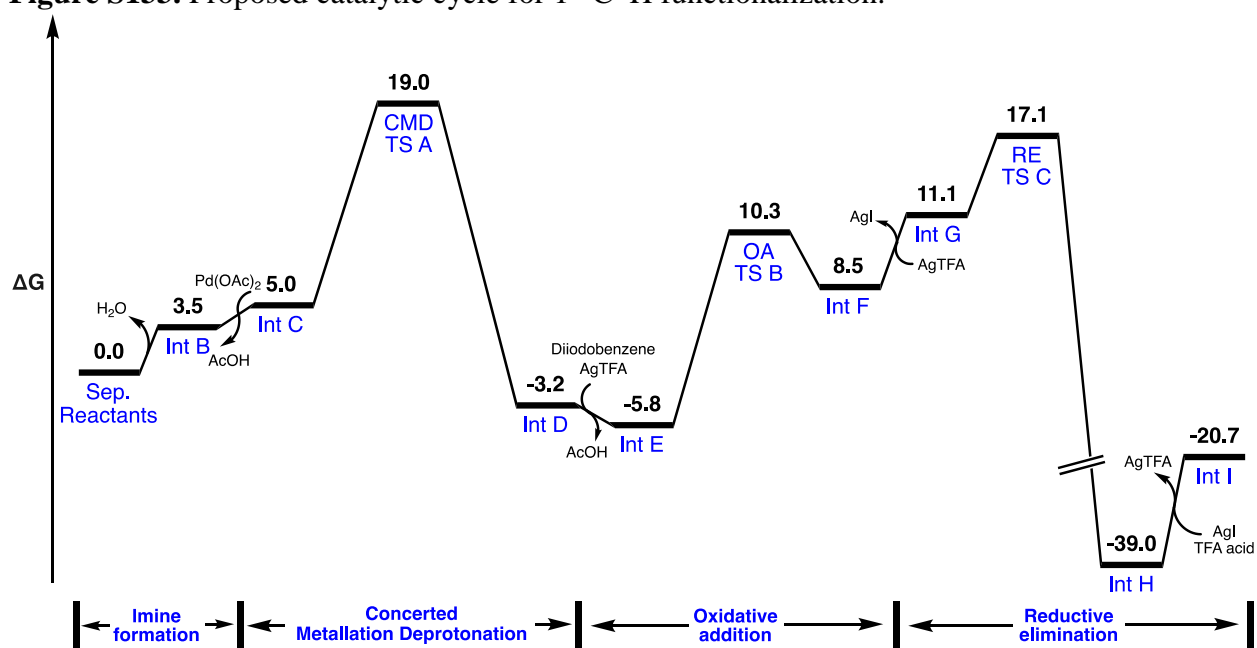


Figure S133. Proposed catalytic cycle for 1st C–H functionalization.



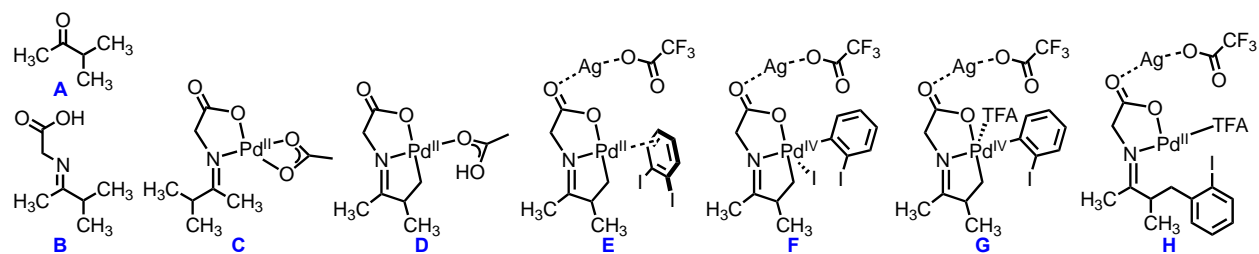


Figure S134. Free energy diagram for 1st C–H functionalization.

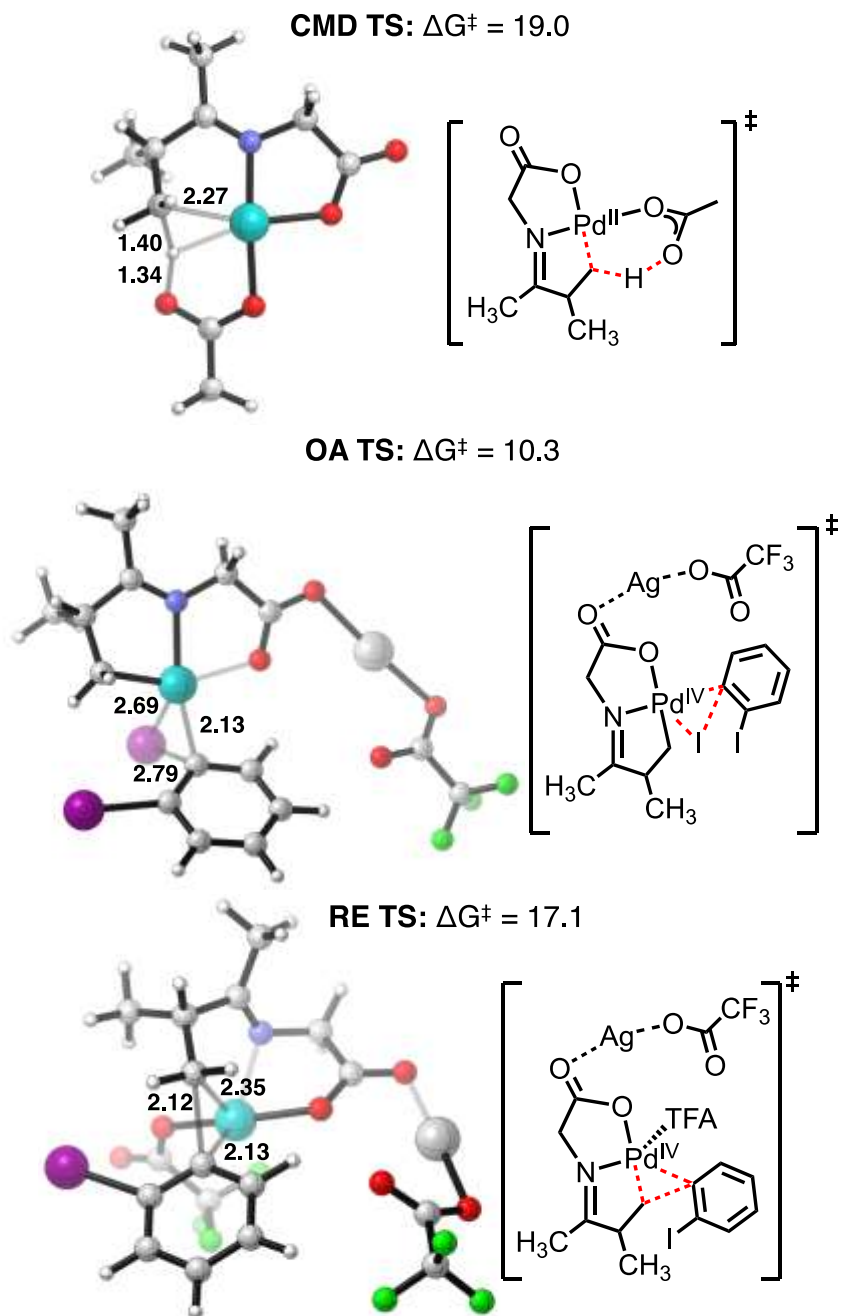


Figure S135. Transition state structures of the CMD, OA, and RE steps of the 1st C–H functionalization.

Table S1. Energies, and vibrational frequencies

Filename	E(sol)	ZPVE	TCE	TCH	TCG	Neg. Freq.
AcOH	-229.04165	0.062024	0.066603	0.067547	0.034691	--
AgI	-158.45942	0.000427	0.003368	0.004312	-0.025826	--
AgTFA	-673.18929	0.027549	0.035538	0.036482	-0.008843	--
glycine	-284.37958	0.080737	0.08599	0.086934	0.052326	--
water	-76.425996	0.02114	0.023974	0.024919	0.003474	--
Pd3OAc6	-1754.4706	0.315923	0.350637	0.351582	0.244065	--
product	-501.40455	0.202219	0.212744	0.213688	0.165011	--
ArI	-242.91352	0.090288	0.096182	0.097126	0.058515	--
diiodobenzene	-253.69779	0.079598	0.087105	0.08805	0.043924	--
TFA acid	-526.75982	0.039119	0.045364	0.046308	0.007577	--
A – substrate	-271.67517	0.141716	0.149521	0.150465	0.109859	--
Int B – imine	-479.62405	0.197854	0.209509	0.210453	0.159604	--
Int C	-835.39091	0.240469	0.258279	0.259223	0.19361	--
CMD TS A	-835.36306	0.234648	0.251741	0.252686	0.188107	-1354.009
Int D	-835.40206	0.239317	0.256856	0.2578	0.191639	--
Int E	-1533.2714	0.285336	0.316583	0.317527	0.211919	--
OA TS B	-1533.2472	0.284452	0.315343	0.316287	0.213249	-55.8
Int F	-1533.2495	0.284775	0.31621	0.317154	0.212734	--
Int G	-2047.9696	0.313867	0.349836	0.35078	0.236911	--
RE TS C	-2047.9262	0.31311	0.348613	0.349557	0.237741	-341.275
Int H	-2048.0176	0.317133	0.352711	0.353655	0.239915	--
Int I – Ar imine / Int 1	-721.33761	0.268411	0.286363	0.287307	0.217463	--
Int 2	-1077.1132	0.311905	0.335741	0.336685	0.254723	--
CMD TS 1	-1077.0851	0.305827	0.328984	0.329929	0.248438	-1376.365
Int 3	-1077.1238	0.310668	0.334143	0.335088	0.252683	--
Int 4	-848.04355	0.246501	0.264284	0.265228	0.19871	--
OA TS 2	-848.02346	0.246198	0.263137	0.264081	0.20046	-50.489
Int 5	-848.06155	0.247102	0.264801	0.265745	0.199406	--
Int 6	-1362.7987	0.275325	0.297885	0.298829	0.221392	--
RE TS 3	-1362.7913	0.274928	0.297105	0.298049	0.220759	-265.077
Int 7	-1362.8593	0.277057	0.299755	0.300699	0.22277	--

E(sol)= Single-point solvation energies; ZPVE = zero-point vibrational energy; TCE = thermal correction to energy; TCH = thermal correction to enthalpy; TCG = thermal correction to Gibbs free energy.

Cartesian Coordinates

AcOH

C	-0.09252100	0.12556800	-0.00012700
O	-0.64608200	1.20175800	-0.00011100
O	-0.77845000	-1.04681400	0.00014000
H	-1.72336900	-0.80245200	0.00017600
C	1.39764000	-0.10952700	0.00002600
H	1.91743400	0.84878900	-0.00006000
H	1.68580300	-0.69118300	-0.88192900
H	1.68567300	-0.69094500	0.88218100

AgI

Ag	0.00000000	0.00000000	-1.40890500
I	0.00000000	0.00000000	1.24940700

AgTFA

C	-0.67200500	0.03825500	-0.00037000
O	-0.10786200	1.16065000	-0.00037700
O	-0.10856300	-1.08938500	-0.00041200
C	-2.21990500	0.00281600	-0.00001800
F	-2.66568100	-0.65205400	-1.08848000
F	-2.75661200	1.22982300	-0.00303300
F	-2.66490400	-0.64640700	1.09222000
Ag	1.95463100	-0.00423000	0.00004800

Glycine

C	-0.69340500	-0.03861100	0.00517700
O	-1.75761100	-0.60087300	-0.09103400
O	-0.55605700	1.29505600	0.05856300
C	0.64329800	-0.79484000	0.11319600
H	0.61281600	-1.64056500	-0.58360300
H	0.68784300	-1.21539100	1.12384500
N	1.77540600	0.12341600	-0.07931400
H	2.57346800	-0.13320400	0.49443500
H	2.08713500	0.12483700	-1.04760900
H	0.42087500	1.44765700	0.11765700

Water

O	0.00000000	0.00000000	0.11942600
H	0.00000000	0.76261700	-0.47770500
H	0.00000000	-0.76261700	-0.47770500

Pd₃OAc₆

Pd	-0.02814500	-1.85326200	-0.00113000
C	2.27638200	-1.29365300	-1.87956300
O	1.53863800	-2.14088500	-1.29557800
O	2.36963900	-0.05170600	-1.64243100
C	0.09040700	2.60997400	1.88311100
O	-1.01193400	2.44466800	1.28343000
O	1.19120100	2.02385100	1.65442900
C	0.10435400	3.65535900	2.98178500
H	0.91370900	3.45606500	3.68637600
H	0.27659000	4.63705700	2.52469100
H	-0.86059900	3.68086200	3.49203500
C	3.17915300	-1.83465300	-2.97165100
H	2.68709800	-2.65591900	-3.49674500
H	3.45472100	-1.03869700	-3.66588200
H	4.09346700	-2.22224200	-2.50718700
Pd	-1.59888300	0.95295500	-0.00005900
C	-0.01307800	2.61022000	-1.88284400
O	1.08396800	2.41416200	-1.28260300
O	-1.13026700	2.05607900	-1.65402100
C	2.23881100	-1.38626400	1.86453300
O	1.17962800	-2.04447300	1.63582700
O	2.64506000	-0.34316600	1.27263800
C	3.14080800	-1.93294500	2.95446900

H	3.68076100	-1.11961100	3.44314200
H	2.55551200	-2.50194700	3.67939700
H	3.87249100	-2.60846600	2.49594600
C	0.00349500	3.65484200	-2.98225100
H	0.96546500	3.64460200	-3.49875400
H	-0.81712300	3.48484100	-3.68137500
H	-0.12879600	4.64260100	-2.52493100
Pd	1.62733300	0.90632900	0.00150300
C	-2.31360000	-1.22624800	1.87978400
O	-1.60299800	-2.09457200	1.29300900
O	-2.36908000	0.01828100	1.64450600
C	-3.22898800	-1.74324600	2.97303100
H	-2.72415300	-2.52310500	3.54768300
H	-3.54675300	-0.92637800	3.62307700
H	-4.11584400	-2.18612500	2.50514200
C	-2.28018700	-1.31732500	-1.86553400
O	-1.24077700	-2.00686500	-1.63849200
O	-2.65503100	-0.26396600	-1.27114200
C	-3.19867600	-1.83378900	-2.95638500
H	-3.97004100	-2.46167600	-2.49526500
H	-3.69087200	-1.00065200	-3.46215600
H	-2.63736200	-2.44315000	-3.66716000

Product

C	2.68985100	-0.15898200	0.10816600
C	3.74629200	0.75938800	-0.48306300
H	3.38811300	1.79503000	-0.53181500
H	4.66073300	0.70930700	0.11156100
H	3.96817800	0.45164200	-1.51356200
C	1.28559600	-0.05036000	-0.48132100
H	1.36945800	0.12467300	-1.56201600
C	0.49705600	1.15845300	0.12858800
H	0.80423500	1.33338000	1.17032600
H	0.67280100	2.09125800	-0.41902800
C	0.38667600	-1.28310300	-0.22334300
H	0.48482900	-2.03819900	-1.01176400
H	0.68835800	-1.76038200	0.71798600
C	-3.34560300	0.79118800	0.14866200
C	-3.40897300	-0.59098900	-0.05295900
C	-2.23703900	-1.34244700	-0.18900200
C	-1.00380000	-0.69573000	-0.12558500
C	-0.94216200	0.68998900	0.07438300
C	-2.10819100	1.43991400	0.21647100
H	-4.26275400	1.36584300	0.24782300
H	-4.37576200	-1.08453800	-0.10881800
H	-2.29127500	-2.41708600	-0.34717700
H	-2.06172600	2.51563900	0.37051200
O	2.94957400	-0.92381300	1.01874900

ArI

C	3.36204600	0.00000900	-0.00000100
C	2.66145500	1.20714000	0.00000200
C	1.26392800	1.21562700	-0.00000100
C	0.58101800	-0.00002300	0.00000400
C	1.26394200	-1.21563800	0.00000300
C	2.66149500	-1.20711700	-0.00000300
H	4.44830800	0.00004200	0.00000000
H	3.19855200	2.15190400	-0.00000300
H	0.72249900	2.15536500	0.00000100
H	0.72256900	-2.15540800	0.00000700
H	3.19857800	-2.15188800	-0.00000700
I	-1.56705300	0.00000000	0.00000000

Diiodobenzene

C	0.69710900	3.35606300	0.00004100
---	------------	------------	------------

C	-0.69711500	3.35606100	0.00000400
C	-1.39209100	2.14825000	-0.00001300
C	-0.69947400	0.93173500	-0.00009900
C	0.69947300	0.93174000	-0.00010400
C	1.39209000	2.14825400	0.00000700
H	1.24976700	4.29102600	0.00012400
H	-1.24977700	4.29102100	0.00003500
H	-2.47665000	2.14715600	0.00002100
H	2.47664900	2.14716200	0.00008100
I	1.88789300	-0.85008400	0.00000400
I	-1.88789200	-0.85008600	0.00001000

A – substrate

C	3.05944900	-0.33740500	0.37123200
O	3.70071600	0.38615700	-0.37008000
C	3.45741800	-0.54418400	1.82063400
H	2.73171900	-0.03121200	2.46616900
H	3.43257900	-1.60495600	2.09652500
H	4.45192600	-0.13106200	2.00192700
C	1.82759500	-1.10587400	-0.12484200
H	1.17432600	-1.31205800	0.73212500
C	2.30509000	-2.45665200	-0.70196200
H	2.87757900	-3.03428200	0.03285800
H	1.44492500	-3.06178900	-1.00764300
H	2.94372900	-2.29487600	-1.57742800
C	1.04561400	-0.30436000	-1.18969600
H	1.75696700	0.01071700	-1.95937900
H	0.32314400	-0.97522800	-1.66543700
C	0.33306600	0.91588000	-0.64493000
C	0.97151000	2.16881500	-0.70625800
C	-0.94101200	0.89016400	-0.05944100
C	0.37465700	3.32662400	-0.21336900
H	1.96349500	2.21303700	-1.14545900
C	-1.55807800	2.03849700	0.43846600
C	-0.89484800	3.26334900	0.36058400
H	0.89969600	4.27533200	-0.28113500
H	-2.54703800	1.98053500	0.87935900
H	-1.37532800	4.15866100	0.74547800
I	-2.06728700	-0.95115500	0.10453200

Int B – imine

C	2.61553500	-1.45694100	0.38063700
O	-1.75019900	0.92748800	1.03578000
C	-2.21286100	0.04677000	0.35857300
O	-3.54843800	-0.21012300	0.38573200
C	-1.40950300	-0.81761100	-0.62688000
H	-1.82634400	-1.83397600	-0.63339800
H	-1.60107300	-0.39216400	-1.62841300
N	-0.01003300	-0.90487200	-0.27898800
C	0.79136100	0.04087500	-0.59335900
C	0.42414100	1.29289700	-1.37260500
H	-0.14810200	1.04544200	-2.27551700
H	-0.19889900	1.95061200	-0.75788600
H	1.31403200	1.84695900	-1.68295200
C	2.24123000	-0.06559700	-0.13718500
H	2.86578900	0.16381500	-1.01546700
C	2.52822200	1.01808400	0.92670600
H	3.58223000	0.98614200	1.22479100
H	1.91378900	0.84801300	1.81791700
H	2.31468300	2.02750800	0.55877000
H	2.42691900	-2.22696600	-0.37378800
H	3.67836200	-1.48450600	0.64828400
H	2.02662300	-1.71615100	1.26533400
H	-3.75743300	-0.97040400	-0.18218300

Int C

Pd	0.50512600	-0.58702300	-0.04535200
----	------------	-------------	-------------

C	-0.23061500	2.26771700	-1.67420600
O	2.51043300	-1.20140800	-0.13077700
C	2.90315300	-0.03406300	0.19832500
O	2.00866000	0.86283600	0.38940500
H	0.67355600	1.70909300	-1.42588300
C	4.36057400	0.27062500	0.38333200
O	-0.48679200	-2.26065800	-0.44783300
C	-1.73851100	-2.28399500	-0.05178800
H	4.63966600	0.06949500	1.42447400
H	4.96368000	-0.37142500	-0.26294200
H	4.55667800	1.32446500	0.17193700
O	-2.47684500	-3.24543200	-0.14031100
C	-2.24455900	-0.97946900	0.59454400
H	-3.28954000	-0.83945600	0.31222700
H	-2.19384400	-1.10337500	1.68448200
N	-1.39846100	0.16235800	0.19819500
C	-1.88340900	1.35135500	0.09636200
C	-3.30515200	1.66379000	0.51878200
H	-3.99593000	1.49244500	-0.31823600
H	-3.64253100	1.06005000	1.36384900
H	-3.38407000	2.71961700	0.79166300
C	-1.10299900	2.54564000	-0.43947100
H	-1.87931300	3.25584000	-0.75492800
C	-0.30978900	3.22467600	0.70121500
H	0.11387000	4.16747400	0.33810000
H	0.51188600	2.58748800	1.03658000
H	-0.95236400	3.45535900	1.55931900
H	-0.78456200	1.71415000	-2.44009500
H	0.08043100	3.22496700	-2.10815500

CMD TS A

Pd	0.29633800	-0.36043000	-0.20444900
C	0.40825300	1.81416800	-0.85108400
O	2.27143800	-0.96925000	-0.17928700
C	3.09991900	-0.04835800	0.10134600
O	2.77518500	1.17326900	0.24215500
H	1.50037700	1.29121700	-0.14499100
C	4.55061200	-0.43104600	0.27963700
O	-0.39148500	-2.22142700	0.17345800
C	-1.69623700	-2.33702100	0.23522000
H	4.85216000	-0.21769000	1.31063100
H	4.70220200	-1.48908500	0.06403300
H	5.17359900	0.18364700	-0.37729900
O	-2.29734200	-3.37301000	0.44921100
C	-2.51743600	-1.04333000	-0.00572600
H	-3.09048800	-1.17198900	-0.93175000
H	-3.23065000	-0.92176300	0.81648400
N	-1.63837000	0.12286900	-0.12105400
C	-1.98599900	1.35994000	-0.13797600
C	-3.41609500	1.82416400	-0.09451700
H	-3.77291500	1.99711400	-1.11908400
H	-4.08167300	1.09460700	0.37251500
H	-3.49719100	2.77468600	0.44072200
C	-0.87186100	2.38370600	-0.20164100
H	-1.23618500	3.22678100	-0.80997100
C	-0.59604100	2.93172000	1.21848200
H	0.17021600	3.71234900	1.16920900
H	-0.22813600	2.13523600	1.87353600
H	-1.49242200	3.36943000	1.67186600
H	0.22941400	1.49241200	-1.88388600
H	1.12568400	2.64243500	-0.94672800

Int D

Pd	0.21234400	0.33865900	-0.09759400
C	-0.89411600	1.98338500	-0.56370600
O	2.14790000	1.21448400	-0.09020100
C	3.20412800	0.56395800	0.01568700

O	3.29960500	-0.73152500	0.16488100
H	2.40537100	-1.21922500	0.20863800
C	4.53552200	1.26766600	-0.02023800
O	0.90389100	-1.65690900	0.28600100
C	-0.02744800	-2.56538600	0.15740300
H	5.15171300	0.84592500	-0.82075000
H	4.39345300	2.33680900	-0.17795100
H	5.06475600	1.09488000	0.92278300
O	0.11858200	-3.77298300	0.20218800
C	-1.47539700	-2.02624000	-0.07347900
H	-1.83544700	-2.45138100	-1.01737700
H	-2.10922700	-2.41809200	0.73018300
N	-1.54920300	-0.56021900	-0.11868600
C	-2.60662400	0.17071900	-0.22103300
C	-3.99756500	-0.38280600	-0.35999700
H	-4.29321600	-0.36495800	-1.41803000
H	-4.07762800	-1.41337400	-0.00600800
H	-4.71697400	0.23694900	0.18395600
C	-2.36530100	1.66510800	-0.17589600
H	-3.06709000	2.14990500	-0.87423100
C	-2.69920100	2.18292400	1.24248900
H	-2.59651500	3.27269200	1.26823500
H	-2.00353700	1.75676500	1.97366900
H	-3.72199200	1.93540100	1.54988800
H	-0.78974900	2.11265800	-1.64825100
H	-0.53113000	2.88776600	-0.06494700

Int E

C	-2.46666900	2.59694800	0.40381000
C	-1.63399000	3.81744100	-0.04488400
N	-0.28649200	3.40148000	-0.44917200
Pd	0.07705500	1.41424400	-0.34784400
H	-1.58278200	4.52744300	0.79041300
O	-1.86627700	1.50158500	0.65148500
O	-3.70526200	2.76050700	0.48997800
H	-2.15710800	4.30947800	-0.87132800
C	0.64906300	4.16206300	-0.90605100
C	0.49805700	5.64103600	-1.12663000
H	1.44191400	6.15883800	-0.93274100
H	0.23724300	5.82748800	-2.17755200
H	-0.28369400	6.08194800	-0.50318000
C	1.95725400	3.46276900	-1.19598400
H	2.41170600	3.92387600	-2.08789800
C	1.70597800	1.95441500	-1.44793500
H	1.39963700	1.77009700	-2.48411600
H	2.58398400	1.34789200	-1.21421400
I	3.11512200	-0.72699200	2.28315500
C	1.86501200	-1.61324100	-1.89327800
C	0.50151000	-1.38482800	-1.86476700
C	-0.12504100	-0.96398200	-0.67107100
C	0.66561500	-0.76365000	0.48049400
C	2.06386800	-1.00528400	0.44618500
C	2.65559200	-1.42732300	-0.73674300
H	2.33874500	-1.95361800	-2.80738500
H	-1.21280400	-0.95394000	-0.60300100
H	0.18221900	-0.58622700	1.43574800
C	2.92708400	3.69533200	-0.01375000
H	2.53874800	3.22823700	0.89749400
H	3.89675100	3.24180100	-0.24230300
H	3.09290200	4.76051300	0.18327000
Ag	-4.44967000	0.62365100	0.56851500
C	-4.27050500	-2.03581200	-0.29342400
O	-3.26804500	-1.56563800	-0.84879900
O	-5.12803100	-1.44280500	0.43763300
C	-4.58149100	-3.54291200	-0.48561600
F	-4.68124100	-4.17198700	0.70403000
F	-3.62714800	-4.17006000	-1.19677200

F	-5.75165200	-3.70928400	-1.13801100
I	4.74568700	-1.82810500	-0.94876200
H	-0.10168800	-1.56590100	-2.74889100

OA TS B

C	-1.03610300	2.65575400	-0.44933000
C	0.14440900	3.55637200	-0.85069700
N	1.41187900	2.85182600	-0.68929100
Pd	1.34710500	0.79605800	-0.18770300
H	0.11684000	4.46419100	-0.23565300
O	-0.80324700	1.46595700	-0.08514900
O	-2.17084300	3.18612600	-0.53039300
H	0.00115500	3.86728600	-1.89356600
C	2.57176100	3.38785600	-0.84378600
C	2.77901700	4.82308300	-1.24788700
H	3.82949700	5.11211400	-1.17554200
H	2.45270000	4.97258000	-2.28544900
H	2.18435000	5.50071000	-0.62471000
C	3.73864600	2.48698400	-0.53479500
H	4.53902300	2.67832000	-1.26907200
C	3.33882800	1.00460400	-0.65254000
H	3.31239000	0.65772900	-1.69210800
H	3.97280000	0.35715000	-0.05386700
I	1.79839500	-0.36377500	2.19694800
C	1.10387800	-3.40242600	-1.43502800
C	-0.28629200	-3.49303200	-1.49030500
C	-1.07882600	-2.51236900	-0.89658600
C	-0.47005400	-1.42633100	-0.26805900
C	0.92837100	-1.28583000	-0.28461200
C	1.72629400	-2.32486700	-0.78991400
H	1.71509000	-4.18543500	-1.87030400
H	-2.16398000	-2.55551800	-0.89383900
H	-1.10108200	-0.67527600	0.18779900
C	4.30295800	2.84350200	0.86090800
H	3.56122800	2.64469900	1.64047100
H	5.18748000	2.23256500	1.06676600
H	4.60037300	3.89622100	0.91978000
Ag	-3.75833500	1.71164200	-0.11176400
C	-4.94107000	-0.80506400	-0.01871600
O	3.79815500	-1.09197500	-0.39855400
O	-5.41524200	0.34629700	0.24872900
C	-5.97125500	-1.94995600	0.14977600
F	-6.53518500	-1.92687900	1.37400700
F	-5.40899100	-3.16145500	-0.01627000
F	-6.96139300	-1.83212500	-0.76141600
I	3.85958800	-2.50340600	-0.64730300
H	-0.74262700	-4.35213400	-1.97413600

Int F

C	-1.07943900	2.67099200	-0.02370000
C	0.11113200	3.54693200	-0.45413400
N	1.25792700	2.71646700	-0.80239900
Pd	1.14260900	0.61677200	-0.39138400
H	0.37039500	4.20777000	0.38372100
O	-0.88676900	1.43678100	0.19464100
O	-2.18151800	3.26231300	0.08148300
H	-0.20331200	4.18562900	-1.28763800
C	2.30715200	3.13163100	-1.41616900
C	2.49774000	4.55599600	-1.87018800
H	3.46452900	4.69838500	-2.35723600
H	1.70951000	4.83938900	-2.57877500
H	2.42986000	5.24696000	-1.02148500
C	3.39779300	2.10684800	-1.63682200
H	3.74483500	2.21513100	-2.67891900
C	2.88248200	0.66312300	-1.48915000
H	2.43997100	0.27456100	-2.41617100
H	3.62883700	-0.02437000	-1.10174700

I	2.28814000	0.44885100	1.98414200
C	0.91168900	-3.76550500	-0.72860100
C	-0.46939600	-3.84228700	-0.92606800
C	-1.25798500	-2.70298100	-0.80824100
C	-0.65392600	-1.48369300	-0.48735300
C	0.74337500	-1.38076900	-0.34607700
C	1.52152700	-2.54724900	-0.41045400
H	1.51858300	-4.65982300	-0.81722700
H	-2.33659500	-2.72185600	-0.92810900
H	-1.29968000	-0.62200600	-0.35773100
C	4.60778600	2.41068600	-0.72433600
H	4.33775800	2.29682300	0.32918700
H	5.42207600	1.71450500	-0.94825500
H	4.98376300	3.42722300	-0.88187600
Ag	-3.77549700	1.74755200	0.36541000
C	-4.80491500	-0.78151400	-0.16256200
O	-3.77846600	-0.79839600	-0.85614200
O	-5.26563000	0.17093200	0.54488000
C	-5.68929100	-2.05481300	-0.16449200
F	-6.28008700	-2.27444800	1.02282000
F	-4.96773200	-3.15686700	-0.46642300
F	-6.66233200	-1.94207300	-1.09521300
I	3.65012800	-2.69737900	-0.11092000
H	-0.91975800	-4.80502400	-1.15178400

Int G

C	0.85969400	-2.67589700	0.00453100
C	-0.34581600	-3.50824000	0.50707300
N	-1.51276700	-2.86778200	-0.05981300
Pd	-1.25332200	-0.67208000	-0.00225000
H	-0.37208700	-3.44799200	1.60095600
O	0.63521700	-1.50377700	-0.48408600
O	1.98971500	-3.18543100	0.09859900
H	-0.19931500	-4.55340800	0.21937300
C	-2.22144600	-3.31878000	-1.02888100
C	-2.26518400	-4.74444100	-1.50707200
H	-3.29051000	-5.00636900	-1.78938700
H	-1.64646900	-4.85740000	-2.40755900
H	-1.91796400	-5.45671900	-0.75620800
C	-2.99590900	-2.25877500	-1.79171900
H	-3.05845500	-2.60209800	-2.83951900
C	-2.14790700	-0.98263900	-1.84554100
H	-1.26181200	-1.07075200	-2.47619100
H	-2.70926700	-0.06760000	-2.02274300
C	-0.70888300	3.66908200	-0.55597300
C	0.63017700	3.76794000	-0.18148400
C	1.33730400	2.62710700	0.18563000
C	0.69206800	1.38743300	0.17715300
C	-0.65560700	1.27651800	-0.19045800
C	-1.35841500	2.42756200	-0.55911600
H	-1.25632900	4.55840900	-0.84875400
H	2.38613100	2.66058600	0.46212400
H	1.27752400	0.51702800	0.44734100
C	-4.44194900	-2.07930500	-1.28605000
H	-4.45939300	-1.68683600	-0.26874800
H	-4.97384000	-1.37478600	-1.93317900
H	-4.97884300	-3.03396200	-1.31628100
Ag	3.65957400	-1.77243900	-0.29621100
C	-3.27254400	-0.05660400	2.02503200
O	-4.37607900	-0.07151100	2.52560000
O	-3.04853800	-0.12935600	0.73579600
C	-2.04623900	0.12565100	2.96259500
F	-0.95008300	-0.59576700	2.51414600
F	-2.30501100	-0.30500700	4.19238400
F	-1.66734500	1.40713300	3.01265300
I	-3.41870200	2.53020000	-1.19495500
H	1.11435800	4.74052600	-0.18578400

C	4.84530100	0.66746100	0.03615700
O	3.85203400	0.71464900	0.77841100
O	5.24415200	-0.31263300	-0.67116500
C	5.74620200	1.92556400	-0.02992800
F	6.69426600	1.86456500	0.92923300
F	5.02916900	3.05104500	0.17697500
F	6.36596100	2.05382700	-1.21490300

RE TS C

C	1.45329700	-2.14370300	-1.91219300
C	0.39492900	-3.12619900	-1.33360200
N	-0.31597000	-2.42471800	-0.28493400
Pd	-0.40916700	-0.28902000	-0.76542600
H	0.90826000	-4.03924000	-1.01870600
O	1.31901400	-0.86705100	-1.58463600
O	2.34616300	-2.55385100	-2.62394500
H	-0.30526500	-3.38466900	-2.13501100
C	-0.13105000	-2.55136000	0.97971400
C	0.58354000	-3.70644200	1.63129600
H	1.50201600	-3.35284300	2.11654300
H	-0.04214100	-4.14260700	2.41676200
H	0.84772200	-4.49420100	0.92556700
C	-0.65200600	-1.39035800	1.83852400
H	-1.71415700	-1.26961000	1.61253900
C	0.04293600	-0.02414400	1.54694000
H	-0.50152700	0.74117900	2.08892700
H	1.10031100	-0.05144800	1.79713700
C	-0.16938400	3.83981400	-0.15439300
C	1.18103600	4.17333900	-0.24599600
C	2.15286400	3.17909100	-0.12721000
C	1.78273500	1.84296400	0.04808300
C	0.42128900	1.47514900	0.08690000
C	-0.53846700	2.51058400	0.02778300
H	-0.93587600	4.60662900	-0.21745300
H	1.48826600	5.20603600	-0.38504000
H	3.20317300	3.44741700	-0.15994300
H	-1.58623100	2.26466000	0.12722200
C	-0.53884500	-1.60781800	3.36270600
H	0.49997600	-1.69293900	3.70003500
H	-1.00011300	-0.76632100	3.88704800
H	-1.07664600	-2.51228200	3.66730800
C	-3.22625600	0.40399100	0.32621400
O	-2.41249400	0.11636200	-0.63152700
C	-4.68478800	0.48418400	-0.20712300
F	-4.79199500	1.44559200	-1.14647100
F	-5.05103500	-0.68664300	-0.76581100
F	-5.54839500	0.76429600	0.77645600
O	-2.99788200	0.61293500	1.51054900
I	3.44715400	0.51655200	0.38555100

Int H

C	-1.39399200	3.60311400	0.96310200
C	-0.15271500	3.15309900	0.18552600
N	-0.31554300	1.81902500	-0.41852900
Pd	-2.12468800	1.01276800	0.10385600
H	0.69946000	3.15105600	0.87565700
O	-2.38600800	2.73712100	1.01222500
O	-1.42491400	4.69630000	1.48937700
H	0.05436800	3.90341400	-0.58571900
C	0.61597500	1.32247000	-1.16304800
C	1.87785400	2.10677100	-1.43276200
H	2.55331300	1.56363600	-2.09305100
H	1.64526400	3.07371200	-1.89456900
H	2.41296600	2.31391600	-0.49892800
C	0.45878100	-0.03795100	-1.80882100
H	-0.48946000	-0.45811500	-1.47861400
C	1.59365400	-1.02297700	-1.40667600

H	1.35976500	-1.97552800	-1.90028000
H	2.54335000	-0.69075400	-1.83270400
C	0.67715900	-1.96634400	2.17840900
C	1.86760000	-1.75440500	2.87417200
C	2.99806300	-1.31592400	2.18767900
C	2.92578800	-1.07918600	0.81227000
C	1.74068500	-1.26332700	0.08501400
C	0.62361500	-1.72614900	0.80859000
H	-0.20784800	-2.32161800	2.69824000
H	3.93072100	-1.16287700	2.71849600
H	-0.30805200	-1.90067900	0.27762600
C	0.38767600	0.10595600	-3.34442400
H	1.31448000	0.50846400	-3.76839900
H	0.21569900	-0.87776400	-3.79362700
H	-0.43984200	0.75902200	-3.64088800
C	-3.55687900	-0.99741100	-0.10673700
O	-2.42074800	-1.00128400	-0.67287100
C	-4.43421400	-2.25420400	-0.21728300
F	-4.66117700	-2.53994500	-1.51037800
F	-3.79327100	-3.29870800	0.33957500
F	-5.60512500	-2.08871700	0.40059800
O	-3.95720200	0.00663300	0.54169700
H	1.92533700	-1.93542300	3.94365700
I	4.78127900	-0.46558500	-0.12445700

Int I – Ar imine / Int 1

C	-1.38779900	2.78170200	-1.76471600
O	-4.96726100	0.23195600	-0.52912400
C	-4.40806700	-0.30026000	0.39757300
O	-5.01170100	-1.23010700	1.18792000
C	-2.99010500	-0.04920800	0.89054900
H	-3.07537800	0.35621300	1.91211500
H	-2.49803500	-1.02707800	1.00044300
N	-2.25658100	0.78918000	-0.02647500
C	-1.21760300	1.41337100	0.37114800
C	-0.67338200	1.38303200	1.79063700
H	-1.40630300	1.80818300	2.49001300
H	-0.47491600	0.35555600	2.11695800
H	0.25257700	1.95364400	1.88456200
C	-0.46222700	2.25000900	-0.66222300
H	-0.01682400	3.10458300	-0.13281500
C	0.70377600	1.43574600	-1.30563400
H	1.10810800	2.04717100	-2.12248300
H	0.27990700	0.53856400	-1.76371000
C	1.85015300	1.08168100	-0.38001100
C	2.15596500	-0.20346900	0.08935000
C	2.70068100	2.12115500	0.04577700
C	3.23674000	-0.44549000	0.94261500
C	3.77882800	1.90275900	0.89721100
H	2.49998300	3.12737800	-0.31598300
C	4.04846000	0.61078500	1.35106400
H	3.44498700	-1.45349600	1.28353100
H	4.40958700	2.73440400	1.19856800
H	4.88810400	0.41896500	2.01322700
I	0.99990000	-1.93990200	-0.47829100
H	-2.19519200	3.38466800	-1.33744300
H	-0.82436600	3.40552800	-2.46873500
H	-1.85469900	1.95897500	-2.31174000
H	-5.91701600	-1.32835700	0.83783500

Int 2

Pd	-2.88571100	0.26302400	-0.03293100
C	-0.10185500	0.25180500	1.91064100
O	-3.88406200	2.09164600	-0.24427000
C	-2.78715800	2.70794800	-0.44098900
O	-1.70620500	2.01960200	-0.42432900
H	-0.86858300	0.94893400	1.56807200

C	-2.75727700	4.19211500	-0.66032000
O	-4.39193000	-0.98723000	0.26720100
C	-4.13541200	-2.25902100	0.06028600
H	-2.05915900	4.43677200	-1.46597200
H	-3.75730100	4.56018800	-0.89733900
H	-2.40313200	4.68507300	0.25262600
O	-4.95868300	-3.14958800	0.13567600
C	-2.68332500	-2.58009300	-0.33265600
H	-2.40215200	-3.52153600	0.14278700
H	-2.65451100	-2.72237100	-1.42118600
N	-1.77310200	-1.47814000	0.03553900
C	-0.53047600	-1.70743000	0.29177800
C	0.07636600	-3.08304600	0.10751600
H	-0.04496600	-3.67256500	1.02701200
H	-0.37464400	-3.64367500	-0.71389200
H	1.14961100	-2.98988600	-0.07737400
C	0.43891000	-0.64011200	0.78222900
H	1.28614400	-1.19749400	1.19868800
C	0.98798700	0.14462200	-0.45428700
H	0.16370600	0.70379600	-0.90186600
H	-0.52511000	-0.35993800	2.71481500
H	0.72012500	0.83903600	2.33100800
H	1.33784100	-0.57808400	-1.20088700
C	2.10577600	1.10763800	-0.11652600
C	1.78972000	2.46482700	0.08249400
C	3.45483200	0.75017800	0.01498900
C	2.76288900	3.40828500	0.40278500
C	4.44517700	1.68005800	0.33358100
C	4.09509100	3.01603100	0.53069900
H	2.48125400	4.44753900	0.54734500
H	5.47999500	1.36876500	0.42214700
H	4.86595400	3.74093600	0.77675600
H	0.75071800	2.76424100	-0.02515800
I	4.12392900	-1.28453100	-0.30111400

CMD TS 1

Pd	-2.61326300	0.03252600	0.24285200
C	-0.60857600	0.52934900	1.18738600
O	-3.63096000	1.83553600	0.25315100
C	-2.88786500	2.85542000	0.14325000
O	-1.61347300	2.80072400	0.15371000
H	-1.27514300	1.56278100	0.48322600
C	-3.54361300	4.20724800	-0.00774900
O	-4.22285500	-0.98642100	-0.43066000
C	-4.04694300	-2.27755600	-0.58104400
H	-3.25284000	4.64133100	-0.97016600
H	-4.62911600	4.11865600	0.04360900
H	-3.18080600	4.87837200	0.77701600
O	-4.89711200	-3.05900200	-0.96418900
C	-2.64313100	-2.82964100	-0.22158300
H	-2.74856900	-3.50437100	0.63666100
H	-2.26999300	-3.42015400	-1.06560300
N	-1.71964700	-1.74218500	0.10791500
C	-0.45055200	-1.83813200	0.29052300
C	0.28855500	-3.14760400	0.23531600
H	0.19957300	-3.65714100	1.20466300
H	-0.11948900	-3.81914200	-0.52570400
H	1.35211700	-2.98866900	0.04312300
C	0.30053900	-0.55392100	0.56754000
H	1.10877500	-0.79116900	1.27492700
C	0.98628800	-0.08890000	-0.76136300
H	0.19850700	0.24952500	-1.44322400
H	-1.00332300	0.20274700	2.15658400
H	0.02469100	1.39352500	1.43304200
H	1.47378400	-0.94743700	-1.23592100
C	1.99655000	1.02273000	-0.57100300
C	1.59066800	2.35726000	-0.75794500

C	3.33795600	0.81810100	-0.21441300
C	2.46895500	3.42545500	-0.59022600
C	4.23333500	1.87412800	-0.04466900
C	3.79450800	3.18507500	-0.23249300
H	2.11495400	4.44098500	-0.74141600
H	5.26423200	1.67822500	0.22734500
H	4.49225800	4.00736800	-0.10151800
H	0.55744400	2.55439800	-1.02818900
I	4.15010800	-1.16719800	0.07848500

Int 3

Pd	-2.25151700	0.06983000	0.21221900
C	-0.44034600	0.51836200	1.03128000
O	-3.23892800	1.92959300	0.48991800
C	-4.46349300	2.08926200	0.32796000
O	-5.31108700	1.18139100	-0.07884600
H	-4.89243500	0.27469100	-0.29233000
C	-5.09760800	3.42654500	0.60866500
O	-3.96501200	-0.94398600	-0.59991300
C	-3.81901100	-2.24365800	-0.63977800
H	-5.86903400	3.31034100	1.37700200
H	-4.34354100	4.14013000	0.94087700
H	-5.59279500	3.79438900	-0.29584000
O	-4.68348500	-3.06835800	-0.87146100
C	-2.37294900	-2.77308700	-0.37783600
H	-2.43362400	-3.51157800	0.42940400
H	-2.04044800	-3.29712900	-1.28174400
N	-1.42288100	-1.71085900	-0.02566200
C	-0.16055700	-1.83299500	0.20984800
C	0.57172700	-3.14546900	0.19249800
H	0.61544100	-3.55052700	1.21301500
H	0.08175800	-3.88900700	-0.44153100
H	1.60422700	-3.01009700	-0.14221200
C	0.56388700	-0.53321800	0.49237500
H	1.36538700	-0.72455000	1.22123300
C	1.25230200	-0.08611900	-0.84048500
H	0.45855400	0.16505600	-1.55271400
H	-0.57865100	0.39900100	2.11321600
H	-0.11353700	1.54269100	0.83559000
H	1.81083600	-0.92876100	-1.26380700
C	2.17512200	1.10281300	-0.69047900
C	1.69731400	2.38525300	-1.01717400
C	3.50324300	1.02419000	-0.24689100
C	2.48953500	3.52446800	-0.89683200
C	4.31467700	2.15189300	-0.11978900
C	3.80291400	3.40867300	-0.44388300
H	2.08215800	4.49632600	-1.16012300
H	5.33841900	2.05258400	0.22304500
H	4.43570800	4.28632600	-0.34655000
H	0.67578200	2.47577000	-1.37743800
I	4.42289200	-0.87080100	0.24837800

Int 4

C	2.26321300	-0.71082500	-2.04141700
C	2.99878900	-0.32437900	-0.70129600
N	2.08000400	-0.33207400	0.43030100
Pd	0.40342900	-1.40093400	0.08481700
H	3.49531500	0.64220500	-0.82829700
O	1.11491100	-1.29674400	-1.92889600
O	2.87249200	-0.45463300	-3.07079400
H	3.76859500	-1.08749600	-0.53188000
C	2.05216000	0.40310700	1.48827000
C	3.12300200	1.38129900	1.88306700
H	2.67847800	2.32767500	2.20975300
H	3.68377100	0.98118200	2.73850000
H	3.82987300	1.58315900	1.07598000
C	0.82413700	0.20087700	2.36386500

H	1.11178300	0.32532800	3.42124800
C	0.29114000	-1.22254900	2.11058000
H	0.98745300	-1.97903500	2.49482800
H	-0.69267200	-1.37717000	2.56389800
C	-0.28678300	1.30022800	2.12357700
H	-1.21926500	0.88027600	2.51772100
H	-0.04776000	2.15847900	2.76068000
C	-0.80470800	3.08247600	-1.82468800
C	-0.02258500	3.68353600	-0.84132300
C	0.10989400	3.07218600	0.40248900
C	-0.50870800	1.84783500	0.72288400
C	-1.30092800	1.28678800	-0.29338900
C	-1.44937600	1.87745700	-1.54804800
H	-0.91651000	3.53777100	-2.80408900
H	0.48049500	4.62592300	-1.03728800
H	0.70728600	3.55880500	1.16992200
H	-2.05139000	1.39770200	-2.31077600
I	-2.35033800	-0.60499100	-0.06460000

OA TS 2

C	-3.09128800	-1.47222900	0.96887200
C	-3.08405100	0.12326600	0.95092200
N	-2.05630100	0.56267600	0.04498000
Pd	-0.32892700	-0.68664400	0.08365600
H	-2.84666200	0.45530400	1.96836600
O	-2.02950300	-2.04898100	0.52379700
O	-4.10138600	-1.97804800	1.43495700
H	-4.08315700	0.47854100	0.68346400
C	-2.08715800	1.38250800	-0.94261700
C	-3.18219500	2.37268600	-1.22400100
H	-2.74657700	3.35706300	-1.43478100
H	-3.74806300	2.07569500	-2.11674100
H	-3.87613500	2.47014100	-0.38705500
C	-0.93501000	1.19629000	-1.92353100
H	-1.27605200	1.47059500	-2.93608400
C	-0.61301400	-0.28600200	-1.91314200
H	-1.45556800	-0.94987400	-2.11343500
H	0.27370000	-0.56556900	-2.47899100
I	2.21603100	-1.28149800	-0.36410800
C	0.34694200	2.04460000	-1.66159700
H	1.09016100	1.70158900	-2.39669100
H	0.13893900	3.09233500	-1.90379200
C	1.76209900	2.02653600	2.42933900
C	1.68095100	3.21607000	1.70673200
C	1.24580100	3.17673500	0.38405200
C	0.91532400	1.97311400	-0.25819300
C	1.07464400	0.76736000	0.45801100
C	1.45871500	0.81283900	1.81331500
H	2.07715600	2.02959900	3.46924000
H	1.93301400	4.16487300	2.17099900
H	1.12725800	4.10733900	-0.16760900
H	1.56366500	-0.10775900	2.37880400

Int 5

C	-1.05990700	-2.90781600	1.19181000
C	-2.25637200	-1.88444800	1.11379000
N	-1.93222000	-0.84990800	0.15064400
Pd	0.09658600	-0.45637600	0.04717400
H	-2.36121800	-1.42940300	2.10595700
O	0.07588600	-2.49109400	0.71504200
O	-1.29038400	-3.98128400	1.71839400
H	-3.17813800	-2.41880500	0.87109000
C	-2.63562100	-0.37970600	-0.81477300
C	-4.09455500	-0.66081900	-1.03945200
H	-4.60730400	0.25675900	-1.34877400
H	-4.21330000	-1.38521400	-1.85624100
H	-4.58882900	-1.05673100	-0.15078900

C	-1.87467200	0.50076400	-1.79036100
H	-2.33974900	0.40572100	-2.78428800
C	-0.42934400	0.02476900	-1.88323700
H	-0.30349300	-0.96177300	-2.33516600
H	0.25574900	0.75046800	-2.31727300
I	2.71729700	-0.29314800	-0.45457000
C	-1.93481200	1.99286100	-1.40324000
H	-1.57091600	2.56553500	-2.26791400
H	-2.97752900	2.30318100	-1.25706900
C	0.37731100	3.23662200	2.04550400
C	-0.59439900	4.06879100	1.48855900
C	-1.32603200	3.63034800	0.38967300
C	-1.11183700	2.36241700	-0.18070800
C	-0.13871700	1.54101800	0.39572500
C	0.61097600	1.97433700	1.49561400
H	0.96254200	3.56337700	2.90058100
H	-0.78013100	5.05398900	1.90693100
H	-2.08556500	4.27710600	-0.04603400
H	1.37762600	1.33950500	1.92580100

Int 6

C	0.83513500	-1.93464600	-2.15806200
C	1.67366800	-2.40198600	-0.91511800
N	1.48670400	-1.51902300	0.23783900
Pd	-0.06646400	-0.27250100	0.07145800
H	2.72869400	-2.44977000	-1.19934400
O	-0.05132200	-1.01244600	-1.94653500
O	1.07718400	-2.50499400	-3.20825900
H	1.33798200	-3.41197200	-0.65300800
C	2.17394100	-1.41868000	1.32086700
C	3.33430200	-2.30285800	1.66761100
H	4.17053500	-1.70261500	2.04278500
H	3.03941400	-2.98234400	2.47827300
H	3.67450000	-2.90264300	0.82175600
C	1.75004400	-0.29256600	2.24482400
H	1.98873200	-0.56596700	3.28300100
C	0.24849300	-0.02105000	2.07965600
H	-0.38679700	-0.79988500	2.51101000
H	-0.05691200	0.96649600	2.42890700
C	2.56461200	0.98047900	1.91115100
H	2.33890400	1.71708400	2.69432500
H	3.64007600	0.77568400	1.99556600
C	1.80710900	2.91213000	-1.90768600
C	2.85197500	3.32537300	-1.07872700
C	3.07855300	2.67468900	0.12993700
C	2.27319800	1.59974900	0.55293600
C	1.24073700	1.22169400	-0.30276000
C	0.99269800	1.84495800	-1.52272000
H	1.62512600	3.40595600	-2.85790300
H	3.49235600	4.15097600	-1.37592300
H	3.89148400	3.00092900	0.77605700
H	0.19442600	1.49547900	-2.16734400
C	-2.62510900	-0.03944300	0.23134300
O	-1.78598600	0.89687300	-0.02914600
C	-4.10892800	0.37913000	0.23329200
F	-4.38729300	1.01728200	1.39058300
F	-4.38150800	1.21354000	-0.78063600
F	-4.91139500	-0.68630300	0.13864100
O	-2.29598800	-1.20339800	0.51060900

RE TS 3

C	0.87599600	-2.96029900	-1.34225500
C	2.22139300	-2.40818000	-0.79068100
N	1.98387600	-1.24740700	0.06571600
Pd	0.15754800	-0.43706300	-0.20208700
H	2.82538500	-2.09478800	-1.65107500
O	-0.17369400	-2.19243500	-1.17295900

O	0.87968500	-4.03427200	-1.90932900
H	2.75157200	-3.20733800	-0.26664900
C	2.66791400	-0.87481000	1.08570500
C	3.92622300	-1.54954000	1.55902300
H	4.62065900	-0.81221000	1.97337200
H	3.68107500	-2.25223500	2.36702100
H	4.43264700	-2.10339900	0.76630900
C	2.17890100	0.36199800	1.81208200
H	2.44615400	0.27924100	2.87448400
C	0.67016600	0.56665800	1.68643700
H	0.03893500	-0.22382500	2.10614100
H	0.32518500	1.51848800	2.08567700
C	2.89205000	1.59697600	1.20626200
H	2.97890500	2.36792200	1.98364500
H	3.91722700	1.36763000	0.88827400
C	0.28354700	3.46792400	-1.65048300
C	1.58604000	3.94378300	-1.49326100
C	2.45475000	3.29452800	-0.61896500
C	2.05059000	2.14631300	0.07470700
C	0.77191300	1.62873000	-0.16774800
C	-0.13944000	2.31849800	-0.97781300
H	-0.41499500	3.98273600	-2.30415300
H	1.91301700	4.83403800	-2.02278500
H	3.44882700	3.69822300	-0.43811400
H	-1.14937800	1.94997800	-1.10717300
C	-2.55414500	-0.24697700	0.62940700
O	-1.81874600	0.06940100	-0.38941500
C	-4.04020100	0.11164000	0.36501900
F	-4.15826600	1.43219400	0.09597400
F	-4.52267000	-0.56905400	-0.68941000
F	-4.80576600	-0.16220300	1.42819600
O	-2.21767300	-0.73764300	1.69714900

Int 7

C	1.52484200	-2.95698500	-0.31239400
C	2.74878400	-2.09821500	0.05509500
N	2.43856600	-0.65844000	0.09152100
Pd	0.42731400	-0.33740700	-0.19977600
H	3.53677300	-2.30389100	-0.67665400
O	0.38504100	-2.32540600	-0.45479000
O	1.66814300	-4.15729600	-0.44500000
H	3.10535800	-2.42939300	1.03700400
C	3.32603400	0.23809200	0.32505500
C	4.77838500	-0.05304600	0.59493100
H	5.05953700	0.37881300	1.56389000
H	5.02277500	-1.11496000	0.60165800
H	5.39750700	0.44658100	-0.16137100
C	2.91069600	1.69664100	0.34191500
H	3.80365500	2.29444200	0.54057600
C	1.81854200	1.97584900	1.42598700
H	1.83534900	1.24964700	2.24466400
H	1.98607100	2.96684700	1.86847400
C	2.25715000	2.12997300	-1.00945700
H	2.54515300	3.16430800	-1.24038800
H	2.57590400	1.51083000	-1.85415100
C	-1.78632000	2.59270500	0.26810400
C	-1.53712200	2.66849800	-1.11828900
C	-0.27410300	2.41974000	-1.63118800
C	0.76591500	2.08097500	-0.74140800
C	0.51471600	1.98959700	0.65015600
C	-0.77774400	2.25379400	1.15542500
H	-2.78942900	2.77750800	0.63778300
H	-2.35157300	2.92153400	-1.79020900
H	-0.08056700	2.49919400	-2.69714900
H	-0.97274600	2.19046900	2.22119800
C	-2.28050900	-0.61011500	0.49416700
O	-1.56819800	-0.31638200	-0.54670500

C	-3.78988100	-0.66773200	0.13896700
F	-4.25818100	0.59534300	-0.05095600
F	-4.02566900	-1.35932800	-0.98765400
F	-4.50484600	-1.21856300	1.12723600
O	-1.92226300	-0.76814200	1.65070400

References

- (1) Yi, D.; Zhu, F.; Walczak, M. A. Stereoretentive Intramolecular Glycosyl Cross-Coupling: Development, Scope, and Kinetic Isotope Effect Study. *Org. Lett.* **2018**, *20* (15), 4627–4631. <https://doi.org/10.1021/acs.orglett.8b01927>.
- (2) Gutman, E. S.; Arredondo, V.; Van Vranken, D. L. Cyclization of H³-Benzylpalladium Intermediates Derived from Carbene Insertion. *Org. Lett.* **2014**, *16* (20), 5498–5501. <https://doi.org/10.1021/ol502813u>.
- (3) Chahdoura, F.; Mallet-Ladeira, S.; Gómez, M. Palladium Nanoparticles in Glycerol: A Clear-Cut Catalyst for One-Pot Multi-Step Processes Applied in the Synthesis of Heterocyclic Compounds. *Org. Chem. Front.* **2015**, *2* (4), 312–318. <https://doi.org/10.1039/C4QO00338A>.
- (4) Amijs, C. H. M.; van Klink, G. P. M.; van Koten, G. Carbon Tetrachloride Free Benzylic Brominations of Methyl Aryl Halides. *Green Chem.* **2003**, *5* (4), 470. <https://doi.org/10.1039/b304673g>.
- (5) An, H.; Lee, S.; Lee, J. M.; Jo, D. H.; Kim, J.; Jeong, Y. S.; Heo, M. J.; Cho, C. S.; Choi, H.; Seo, J. H.; Hwang, S.; Lim, J.; Kim, T.; Jun, H. O.; Sim, J.; Lim, C.; Hur, J.; Ahn, J.; Kim, H. S.; Seo, S. Y.; Na, Y.; Kim, S. H.; Lee, J.; Lee, J.; Chung, S. J.; Kim, Y. M.; Kim, K. W.; Kim, S. G.; Kim, J. H.; Suh, Y. G. Novel Hypoxia-Inducible Factor 1 α (HIF-1 α) Inhibitors for Angiogenesis-Related Ocular Diseases: Discovery of a Novel Scaffold via Ring-Truncation Strategy. *J. Med. Chem.* **2018**, *61* (20), 9266–9286. <https://doi.org/10.1021/acs.jmedchem.8b00971>.
- (6) Carson, J. R.; Almond, H. R.; Brannan, M. D.; Carmosin, R. J.; Flaim, S. F.; Gill, A.; Gleason, M. M.; Keely, S. L.; Ludovici, D. W.; Pitis, P. M.; Rebarchak, M. C.; Villani, F. J. 2-Ethynylbenzenealkanamines. A New Class of Calcium Entry Blockers. *J. Med. Chem.* **1988**, *31* (3), 630–636. <https://doi.org/10.1021/jm00398a023>.
- (7) Hoffmann, S.; Helmke, H.; Peris, G.; Nising, F. C.; Tsuchiya, T.; Sudau, A.; Benting, J.; Bernier, D. Novel Heterocyclic Alkanol-Derivatives. 20140274952A1, 2014.
- (8) Milde, B.; Leibel, M.; Pawliczek, M.; Grunenberg, J. J.; Jones, P. G.; Werz, D. B. π -Helicenes Truncated to a Minimum: Access Through a Domino Approach Involving Multiple Carbopalladations and a Stille Coupling. *Angew. Chem. Int. Ed.* **2015**, *54* (4), 1331–1335. <https://doi.org/10.1002/anie.201408637>.
- (9) Ripa, L.; Hallberg, A. Controlled Double-Bond Migration in Palladium-Catalyzed Intramolecular Arylation of Enamidines. *J. Org. Chem.* **1996**, *61* (20), 7147–7155. <https://doi.org/10.1021/jo960970y>.
- (10) Li, Y.; Xue, D.; Lu, W.; Wang, C.; Liu, Z.-T.; Xiao, J. DMF as Carbon Source: Rh-Catalyzed α -Methylation of Ketones. *Org. Lett.* **2014**, *16* (1), 66–69. <https://doi.org/10.1021/ol403040g>.
- (11) Cheng, Y.; Zheng, J.; Tian, C.; He, Y.; Zhang, C.; Tan, Q.; An, G.; Li, G. Palladium-Catalyzed C–H Arylation of Aliphatic and Aromatic Ketones Using Dipeptide Transient Directing Groups. *Asian J. Org. Chem.* **2019**, *8* (4), 526–531. <https://doi.org/10.1002/ajoc.201900037>.
- (12) Karjalainen, A. J.; Virtanen, R. E.; Karjalainen, A. L.; Kurkela, K. O. A. Substituted Imidazole Derivatives and Their Preparation and Use. EP0183492 (A1), 1985.
- (13) Collonges, F.; Descotes, G. Ketols. Cyclization Reactions. IX. Synthesis and Thermolysis of 1,5-Dihydro-2-Benzoxepins. *Bull. la Soc. Chim. Fr.* **1975**, No. 3–4, 789–792.

- (14) St John-Campbell, S.; Bull, J. A. Intramolecular Palladium(Ii)/(Iv) Catalysed C(Sp³)–H Arylation of Tertiary Aldehydes Using a Transient Imine Directing Group. *Chem. Commun.* **2019**, 55 (62), 9172–9175. <https://doi.org/10.1039/C9CC03644J>.
- (15) Feng, Y.; Wang, Y.; Landgraf, B.; Liu, S.; Chen, G. Facile Benzo-Ring Construction via Palladium-Catalyzed Functionalization of Unactivated Sp³ C–H Bonds under Mild Reaction Conditions. *Org. Lett.* **2010**, 12 (15), 3414–3417. <https://doi.org/10.1021/ol101220x>.
- (16) Reetz, M. T.; Sauerwald, M. Stereoselective α -Alkylation of Carbonyl Compounds Using Tricarbonylchromium-Complexed Benzyl Acetates. *J. Organomet. Chem.* **1990**, 382 (1–2), 121–128. [https://doi.org/10.1016/0022-328X\(90\)85221-J](https://doi.org/10.1016/0022-328X(90)85221-J).
- (17) Lorentzen, R. J.; Brewster, J. H.; Smith, H. E. Application of the Benzene Sector and the Benzene Chirality Rules to Perhydrobenzocycloalkenes and Related Compounds. *J. Am. Chem. Soc.* **1992**, 114 (6), 2181–2187. <https://doi.org/10.1021/ja00032a037>.
- (18) Kenny, M.; Christensen, J.; Coles, S. J.; Franckevičius, V. Regioswitchable Palladium-Catalyzed Decarboxylative Coupling of 1,3-Dicarbonyl Compounds. *Org. Lett.* **2015**, 17 (15), 3926–3929. <https://doi.org/10.1021/acs.orglett.5b01979>.
- (19) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Mennucci, B.; Petersson, G. A.; Nakatsuji, H.; Caricato, M.; Li, X.; Hratchian, H. P.; Izmaylov, A. F.; Bloino, J.; Zheng, G.; Sonnenberg, J. L.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Montgomery, J. A.; Peralta, J. E.; Ogliaro, F.; Bearpark, M.; Heyd, J. J.; Brothers, E.; Kudin, K. N.; Staroverov, V. N.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Rega, N.; Millam, J. M.; Klene, M.; Knox, J. E.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Zakrzewski, V. G.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Dapprich, S.; Daniels, A. D.; Farkas; Foresman, J. B.; Ortiz, J. V.; Cioslowski, J.; Fox, D. J. Gaussian 09. Gaussian 09; Gaussian Inc.: Wallingford, CT 2009.
- (20) Becke, A. D. Density-functional Thermochemistry. III. The Role of Exact Exchange. *J. Chem. Phys.* **1993**, 98 (7), 5648–5652. <https://doi.org/10.1063/1.464913>.
- (21) Lee, C.; Yang, W.; Parr, R. G. Development of the Colle-Salvetti Correlation-Energy Formula into a Functional of the Electron Density. *Phys. Rev. B* **1988**, 37 (2), 785–789. <https://doi.org/10.1103/PhysRevB.37.785>.
- (22) Becke, A. D. A New Mixing of Hartree–Fock and Local Density-functional Theories. *J. Chem. Phys.* **1993**, 98 (2), 1372–1377. <https://doi.org/10.1063/1.464304>.
- (23) Stephens, P. J.; Devlin, F. J.; Chabalowski, C. F.; Frisch, M. J. Ab Initio Calculation of Vibrational Absorption and Circular Dichroism Spectra Using Density Functional Force Fields. *J. Phys. Chem.* **1994**, 98 (45), 11623–11627. <https://doi.org/10.1021/j100096a001>.
- (24) Ditchfield, R.; Hehre, W. J.; Pople, J. A. Self-Consistent Molecular-Orbital Methods. IX. An Extended Gaussian-Type Basis for Molecular-Orbital Studies of Organic Molecules. *J. Chem. Phys.* **1971**, 54 (2), 724–728. <https://doi.org/10.1063/1.1674902>.
- (25) Hehre, W. J.; Ditchfield, R.; Pople, J. A. Self—Consistent Molecular Orbital Methods. XII. Further Extensions of Gaussian—Type Basis Sets for Use in Molecular Orbital Studies of Organic Molecules. *J. Chem. Phys.* **1972**, 56 (5), 2257–2261. <https://doi.org/10.1063/1.1677527>.

- (26) Hay, P. J.; Wadt, W. R. Ab Initio Effective Core Potentials for Molecular Calculations. Potentials for K to Au Including the Outermost Core Orbitals. *J. Chem. Phys.* **1985**, *82* (1), 299–310. <https://doi.org/10.1063/1.448975>.
- (27) Roy, L. E.; Hay, P. J.; Martin, R. L. Revised Basis Sets for the LANL Effective Core Potentials. *J. Chem. Theory Comput.* **2008**, *4* (7), 1029–1031. <https://doi.org/10.1021/ct8000409>.
- (28) Zhao, Y.; Truhlar, D. G. The M06 Suite of Density Functionals for Main Group Thermochemistry, Thermochemical Kinetics, Noncovalent Interactions, Excited States, and Transition Elements: Two New Functionals and Systematic Testing of Four M06-Class Functionals and 12 Other Function. *Theor. Chem. Acc.* **2008**, *120*, 215–241. <https://doi.org/10.1007/s00214-007-0310-x>.
- (29) Marenich, A. V.; Cramer, C. J.; Truhlar, D. G. Universal Solvation Model Based on Solute Electron Density and on a Continuum Model of the Solvent Defined by the Bulk Dielectric Constant and Atomic Surface Tensions. *J. Phys. Chem. B* **2009**, *113* (18), 6378–6396. <https://doi.org/10.1021/jp810292n>.
- (30) Dolg, M.; Wedig, U.; Stoll, H.; Preuss, H. Energy-adjusted Ab Initio Pseudopotentials for the First Row Transition Elements. *J. Chem. Phys.* **1987**, *86* (2), 866–872. <https://doi.org/10.1063/1.452288>.
- (31) Andrae, D.; Haussermann, U.; Dolg, M.; Stoll, H.; Preuss, H. Energy-Adjusted Ab Initio Pseudopotentials for the Second and Third Row Transition Elements. *Theor. Chim. Acta* **1990**, *77* (2), 123–141. <https://doi.org/10.1007/BF01114537>.
- (32) Legault, C. Y. CYLview. CYLview 1.0b; Université de Sherbrooke; <http://www.cylview.org>; 2009.