Supplementary Materials for

Photoredox Activation for the Direct β-Arylation of Ketones and Aldehydes

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Materials and Methods.

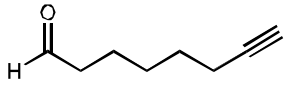
Commercial reagents were purified prior to use following the guidelines of Perrin and Armarego (*27*). All aldehydes were distilled or purified via flash chromatography prior to use. All solvents were purified by passage through columns of activated alumina. Organic solutions were concentrated under reduced pressure on a Büchi rotary evaporator using an acetone-dry ice bath for volatile compounds. Chromatographic purification of products was accomplished by flash chromatography on silica gel (Fluka, 230-400 mesh). Thin layer chromatography (TLC) was performed on Analtech Uniplate 250 μm silica gel plates. Visualization of the developed chromatogram was performed by fluorescence quenching, *p*-anisaldehyde, potassium permanganate, or ceric ammonium molybdate stain. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker 500 (500 and 125 MHz) instrument, and are internally referenced to residual protio solvent signals (note: $CDCl_3$ referenced at δ 7.27 and 77.0 ppm respectively). Data for ^{1}H NMR are reported as follows: chemical shift (δ ppm), integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constant (Hz) and assignment. Data for ^{13}C NMR are reported in terms of chemical shift and no special nomenclature is used for equivalent carbons. IR spectra were recorded on a Perkin Elmer Paragon 1000 spectrometer and are reported in terms of frequency of absorption (cm^{-1}). High resolution mass spectra were obtained at Princeton University mass spectrometry facilities. Supercritical fluid chromatography (SFC) was performed on a Berger Minigram equipped with a diode array UV detector (λ = 214–280 nm) using a chiral column (25 cm) and guard column (5 cm) as noted for each compound. Optical rotations were measured on a Jasco P-1010 polarimeter with $[\alpha]_D$ values reported in degrees; concentration (c) is in g/100 mL. All aldehydes were used from commercial suppliers or prepared using standard literature procedures. All cyano aromatics were used from commercial suppliers or prepared using standard literature procedures.

Supplementary Text

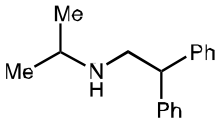
Synthesis of Starting Material Aldehydes

General Procedure - To a solution of the respective alcohol in DCM (0.5 M) was added TEMPO (0.10 equiv) and iodobenzene diacetate (1.1 equiv). The reaction mixture was stirred for 12 h and then quenched with a saturated solution of sodium thiosulfate. The layers were separated and the aqueous layer was extracted with DCM three times. The combined organic layers were then dried

with sodium sulfate and concentrated *in vacuo*. Purification of the crude product by flash chromatography on silica gel using the indicated solvent system afforded the desired aldehyde.



Oct-7-ynal. Prepared according to the general procedure using 505 mg of oct-7-yn-1-ol (4.0 mmol, 1.00 equiv), 31 mg of TEMPO (0.20 mmol, 0.05 equiv), 1.42 g of iodobenzene diacetate (4.4 mmol, 1.10 equiv), and 16 mL of DCM. After 12 h, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (silica gel: 10% to 100% ethyl acetate in hexanes) to afford the title compound as a clear oil (373 mg, 3.0 mmol, 75%). The spectral data for the title compound were identical to the previously reported data (*28*).



(2,2-Diphenylethyl)(propan-2-yl)amine. To a solution of diphenylacetaldehyde (1.05 mL, 5.84 mmol, 1.0 equiv), isopropylamine (1.00 mL, 11.7 mmol, 2.0 equiv) and acetic acid (33 μL, 0.58 mmol, 0.1 equiv) in MeOH (14.6 mL) was added 5Å MS (300 mg). After 1h of stirring at room temperature, sodium triacetoxyborohydride (3.71 g, 17.5 mmol, 3.0 equiv) was added in 3 portions over 20 h. The reaction mixture was diluted with EtOAc (50 mL) and 1M NaOH (50 mL). The layers were separated and the aqueous layer was extracted with EtOAc (50 mL). The

combined organic extracts were washed with brine, dried over Na_2SO_4 and concentrated *in vacuo*. Purification of the crude product by flash chromatography (silica gel: 0% to 3% NH_4OH/MeOH in DCM) to afford the title compound as a clear oil (640 mg, 2.69 mmol, 46%). IR (film) 3026, 2963, 1494, 1450, 1174, 740, 697 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.35–7.25 (m, 8H, Ph**H**), 7.25-7.19 (m, 2H, Ph**H**), 4.20 (t, *J* = 7.7 Hz, 1H, $CH_2C\mathbf{H}Ph_2$), 3.24 (d, *J* = 7.7 Hz, 2H, $C\mathbf{H}_2CHPh_2$), 2.83 (hept, *J* = 6.2 Hz, 1H, $(CH_3)_2C\mathbf{H}N$), 1.03 (d, *J* = 6.2 Hz, 6H, $(C\mathbf{H}_3)_2CHN$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 142.9, 128.6, 128.0, 126.5, 52.2, 51.2, 48.6, 22.9; HRMS (ESI) exact mass calculated for $[M+H]^+$ ($C_{17}H_{21}N$) requires *m/z* 240.1752, found *m/z* 240.1751.

DFT Calculations

(1). Complete reference for Ref. *25*.

Gaussian 09, Revision B.01, M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G. A. Petersson, H. Nakatsuji, M. Caricato, X. Li, H. P. Hratchian, A. F. Izmaylov, J. Bloino, G. Zheng, J. L. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, J. A. Montgomery, Jr., J. E. Peralta, F. Ogliaro, M. Bearpark, J. J. Heyd, E. Brothers, K. N. Kudin, V. N. Staroverov, T. Keith, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, N. Rega, J. M. Millam, M. Klene, J. E. Knox, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, R. L. Martin, K. Morokuma, V. G. Zakrzewski, G. A. Voth, P. Salvador, J. J. Dannenberg, S. Dapprich, A. D. Daniels, O. Farkas, J. B. Foresman, J. V. Ortiz, J. Cioslowski, and D. J. Fox, Gaussian, Inc., Wallingford CT, **2010**.

(2) Computational results with solvation corrections.

Solvation energy corrections were calculated by UB3LYP-6-311+G(d) single point calculations with the IEFPCM solvation model in DMSO for the structures reported in the main text. The solvation-corrected energy profile is summarized in Figure S1 and Table S1. In the solvation-corrected energy diagram, the maximum deviations from the gas-phase results were roughly 10 kcal/mol.

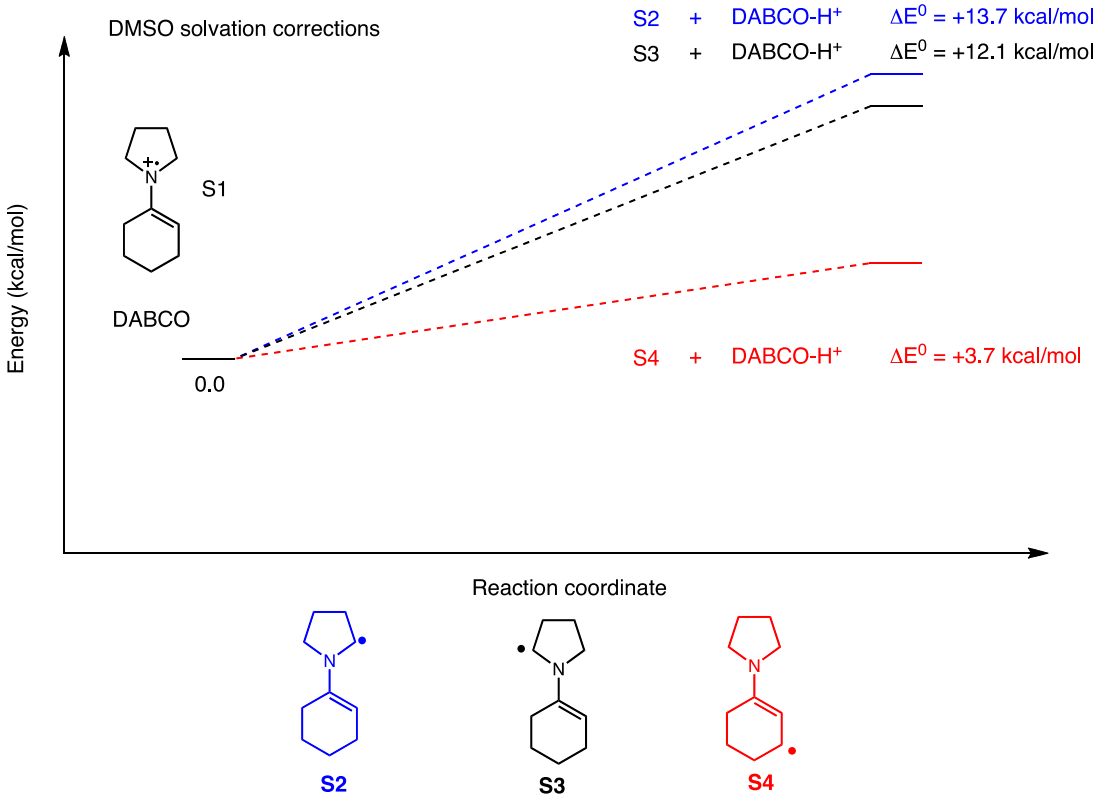


Figure S1. The energy profile in solution of C-H deprotonation of radical cation S1. All energies include solvation energy corrections computed by UB3LYP-6-311+G(d) single point calculations with the IEFPCM solvation model in DMSO.

(3). UB3LYP electronic energies (a.u.).

Geometry	E(B3LYP)
S1	-445.9683481
S2	-445.4896965
S3	-445.4920977
S4	-445.5055125
DABCO	-345.4132425
DABCOH+	-345.8701448

(4). UB3LYP geometries for all the optimized compounds.

S1

C	-1.78981	-1.20521	0.05526
C	-3.21234	-0.71277	-0.21782
C	-3.20148	0.72583	0.31166
C	-1.80924	1.23644	-0.06854
H	-1.68343	-1.62438	1.06184
H	-1.4407	-1.95183	-0.65785
H	-3.41551	-0.72853	-1.29185
H	-3.95645	-1.34298	0.26883
H	-3.98735	1.3469	-0.11793
H	-3.32369	0.74023	1.39792
H	-1.78761	1.6437	-1.08433
H	-1.42118	1.98777	0.61811
N	-0.95183	0.01812	-0.0323
C	0.38578	0.01528	-0.04079
C	1.09718	1.22103	-0.1647
C	1.1267	-1.29477	0.10673
C	2.57835	1.31089	-0.10821
H	0.55178	2.14199	-0.33775
C	2.61535	-1.19411	-0.25662
H	1.01527	-1.62619	1.14823
H	0.64722	-2.06558	-0.50112
C	3.26358	0.03252	0.3842
H	2.85599	2.18482	0.49463
H	2.92843	1.57029	-1.12237
H	3.11658	-2.11047	0.06164
H	2.72356	-1.14493	-1.34593
H	4.3294	0.0725	0.15162
H	3.18615	-0.031	1.4754

S2

C	1.82737	1.161	-0.10684
C	3.24052	0.61309	-0.36074
C	3.23032	-0.76899	0.32134
C	1.79589	-1.18084	0.18251
H	1.78801	1.76582	0.80821
H	1.47257	1.78242	-0.93211
H	3.40047	0.49297	-1.43574
H	4.01572	1.28124	0.0203
H	3.92921	-1.47028	-0.14415
H	3.53321	-0.68079	1.37858
H	1.36074	-2.04541	0.66904
N	1.0021	-0.05048	0.04312
C	-0.39343	-0.05964	-0.04925
C	-1.0831	-1.19275	-0.3081
C	-1.09255	1.25403	0.23905
C	-2.58709	-1.28572	-0.28818
H	-0.53653	-2.09394	-0.56832
C	-2.58271	1.22007	-0.12419
H	-0.97419	1.49816	1.30447
H	-0.60925	2.07221	-0.30412
C	-3.24101	-0.0678	0.37333
H	-2.89518	-2.20279	0.23003
H	-2.96893	-1.39506	-1.31503
H	-3.08072	2.10194	0.29213
H	-2.69315	1.28379	-1.21384
H	-4.31743	-0.05622	0.1726
H	-3.12454	-0.13549	1.46247

S3

C	-1.79425	-1.16134	0.09943
C	-3.22585	-0.7891	-0.13046
C	-3.24172	0.69991	0.26643
C	-1.82378	1.18853	-0.06985
H	-1.37439	-2.13285	-0.11455
H	-3.52182	-0.90764	-1.18752
H	-3.92563	-1.38896	0.45827
H	-4.01007	1.2786	-0.25027
H	-3.41856	0.79377	1.34119
H	-1.7634	1.64011	-1.06838
H	-1.45297	1.92524	0.64825
N	-0.99858	-0.02643	-0.028
C	0.3888	0.03063	-0.06511
C	1.06626	1.20203	-0.17277
C	1.10472	-1.29788	0.04611

C	2.56991	1.30353	-0.13187
H	0.52355	2.13375	-0.28965
C	2.61232	-1.19885	-0.22309
H	0.91918	-1.71832	1.0441
H	0.66532	-2.0121	-0.65894
C	3.22148	0.03893	0.43558
H	2.86152	2.17607	0.46577
H	2.96978	1.49783	-1.13962
H	3.10434	-2.11288	0.12506
H	2.78446	-1.14683	-1.30531
H	4.30545	0.06485	0.28178
H	3.05595	-0.00407	1.51947

S4

C	1.75059	-1.2065	-0.07537
C	1.77642	1.21238	0.12067
C	3.19615	0.67394	0.33009
C	3.16196	-0.68729	-0.37915
H	1.7406	-1.79104	0.85689
H	1.36975	-1.85505	-0.86972
H	1.69988	1.7967	-0.80951
H	1.4529	1.86411	0.93955
H	3.96029	1.3471	-0.06462
H	3.39316	0.53956	1.39862
H	3.28611	-0.55318	-1.4586
H	3.94102	-1.37301	-0.03843
N	0.94848	0.01188	0.0522
C	-0.4294	0.05403	-0.02434
C	-1.14404	1.25666	-0.07223
C	-1.18816	-1.25286	-0.06345
C	-2.52735	1.31833	-0.16581
H	-0.59535	2.19341	-0.04958
C	-2.62149	-1.0967	0.47033
H	-1.2237	-1.63826	-1.09427
H	-0.66859	-2.01821	0.52222
C	-3.35892	0.06843	-0.20473
H	-3.01788	2.28362	-0.23247
H	-3.17008	-2.03428	0.33181
H	-2.5766	-0.91029	1.54927
H	-4.32752	0.23035	0.28297
H	-3.59798	-0.20727	-1.24553

DABCO

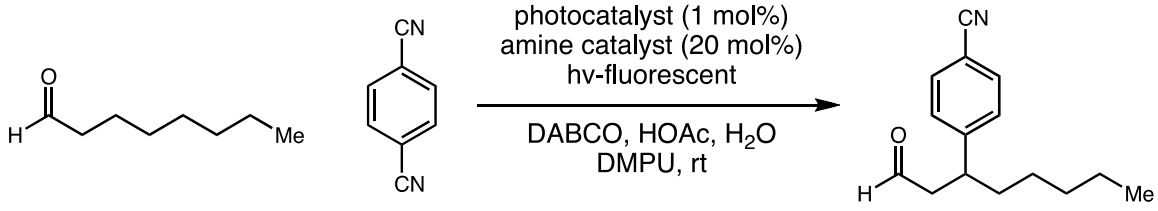
C	-0.78196	0.37252	-1.33249
C	0.78198	0.37258	-1.33247

H	-1.18521	-0.33846	-2.05996
H	-1.18515	1.35779	-1.58558
H	1.1853	-0.33821	-2.06008
H	1.1851	1.35792	-1.58532
C	-0.78207	-1.34046	0.34379
H	-1.18526	-1.61462	1.32339
H	-1.1855	-2.05225	-0.38281
C	0.78191	-1.3406	0.34363
H	1.18527	-1.61504	1.32307
H	1.18505	-2.0523	-0.38322
C	0.78211	0.96789	0.98891
H	1.18547	0.69439	1.96865
H	1.18564	1.95326	0.73671
C	-0.78196	0.9681	0.98883
H	-1.18552	0.69492	1.96858
H	-1.1852	1.95353	0.73635
N	-1.28702	0.	-0.00006
N	1.28702	-0.00016	-0.00008

DABCO-H$^+$

C	-0.7407	-0.52191	1.33913
C	0.81773	-0.50389	1.29367
H	-1.15993	0.12852	2.1072
H	-1.15951	-1.52078	1.46326
H	1.21502	0.1309	2.0863
H	1.21526	-1.50735	1.4486
C	-0.73724	1.42228	-0.21869
H	-1.15451	1.76237	-1.16678
H	-1.15601	2.03072	0.58324
C	0.82044	1.37063	-0.2094
H	1.2198	1.73886	-1.1549
H	1.21844	2.00588	0.5825
C	0.82041	-0.86825	-1.08142
H	1.21986	-0.50057	-2.02707
H	1.21775	-1.87194	-0.9272
C	-0.73789	-0.89929	-1.12291
H	-1.15504	-0.50884	-2.05143
H	-1.15687	-1.88971	-0.9434
N	-1.22713	0.00102	-0.00147
N	1.2879	-0.00064	0.00149
H	-2.24617	0.00177	-0.00268

Optimization Studies



Photocatalyst	Product %
$Ir(ppy)_3$, no light	0%
no photocatalyst	0%
$Ru(bpy)_3Cl_2$	0%
$Ir(ppy)_3$	**90%**

Using 0.20 equiv, *i*PrNHBn amine, 5 equiv DABCO, 0.20 equiv HOAc, 3 equiv H_2O, 1.4 equiv octanal, 1.0 equiv 1,4-DCB, 0.50 M, DMPU at 23 °C.

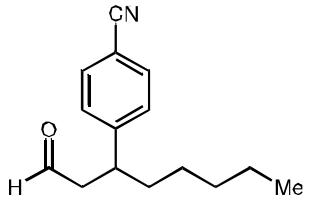
Amine catalyst	Product %
no amine catalyst	0%
pyrrolidine	31%
diethylamine	70%
MeNHBn	78%
*i*PrNHBn	**90%**

Using 0.01 equiv $Ir(ppy)_3$, 5 equiv DABCO, 0.20 equiv HOAc, 3 equiv H_2O, 1.4 equiv octanal, 1.0 equiv 1,4-DCB, 0.50 M DMPU at 23 ºC.

Table S1. Optimization Studies
* % Yields calculated by ^{1}H-NMR with methyl benzoate as an internal standard.

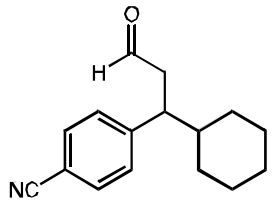
General Procedure for the β-Arylation of Aldehydes: An oven-dried 8 mL vial equipped with a Teflon septum and magnetic stir bar was charged with tris[2-phenylpyridinato-C^2,*N*]iridium(III) (10.0 μmol, 0.01 equiv), the corresponding aromatic nitrile (1.00 mmol, 1.0 equiv), the corresponding aldehyde (1.40–3.00 mmol, 1.4–3.0 equiv, if solid), and 1,4-diazabicyclo[2.2.2]octane (5.00 mmol, 5.0 equiv). The vial was purged with a stream of nitrogen and 2.0 mL of DMPU was added via syringe, followed by the corresponding aldehyde (1.40–3.00

mmol, 1.4–3.0 equiv, if liquid), acetic acid (0.20 mmol, 0.20 equiv), water (3.00 mmol, 3.00 equiv) and *N*-Isopropylbenzylamine (0.20 mmol, 0.20 equiv). The reaction mixture was then cooled to –78 ºC and degassed via vacuum evacuation (5 min), backfilled with nitrogen, and warmed to room temperature. This process was repeated three times. After the reaction was thoroughly degassed, the vial was placed approximately 2 cm from a 26 W fluorescent lamp. After the indicated time period, the reaction mixture was diluted with ethyl acetate and added to a separatory funnel containing 25 mL of a 1 M aqueous solution of NaOH. The layers were separated and the aqueous layer was extracted with EtOAc (3 × 10 mL). The combined organic extracts were dried over Na_2SO_4 and concentrated *in vacuo*. Purification of the crude product by flash chromatography on silica gel using the indicated solvent system afforded the desired β-arylated aldehyde product.

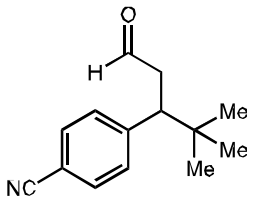


4-(1-Oxooctan-3-yl)benzonitrile. Prepared according to the general procedure using 6.6 mg of tris[2-phenylpyridinato-C^2,*N*]iridium(III) (10.0 μmol, 0.01 equiv), 128 mg of terephthalonitrile (1.00 mmol, 1.00 equiv), 561 mg of DABCO (5.00 mmol, 5.00 equiv), 219 μL of octanal (1.40 mmol, 1.4 equiv), 33 μL of *N*-isopropylbenzylamine (0.20 mmol, 0.20 equiv), 54 μL of water (3.00 mmol, 3.00 equiv), 11 μL of acetic acid (0.20 mmol, 0.20 equiv) and 2.0 mL of DMPU. After 26 h, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (silica gel: 10% to 100% ethyl acetate in hexanes) to afford the title compound as a clear oil (197 mg, 0.86 mmol, 86%). IR (film) 2928, 2228, 1717, 1466, 1417, 1374, 1242, 1045, 834, 733 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.66 (s, 1H, C**H**O), 7.58 (d, *J* = 8.1 Hz, 2H, Ar**H**), 7.31 (d, *J* = 8.1 Hz, 2H, Ar**H**), 3.30–3.19 (m, 1H, C**H**(Ph-4-CN)), 2.82-2.69 (m, 2H, C$\mathbf{H}_2$CHO), 1.75–1.50 (m, 2H, CH(Ph-4-CN)C$\mathbf{H}_2$$(CH_2)_3CH_3$), 1.36–1.12 (m, 6H, CH(Ph-4-CN)CH_2(C$\mathbf{H}_2$$)_3CH_3$), 0.87–0.70 (m, 3H, $(CH_2)_3$C$\mathbf{H}_3$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.8, 150.0, 132.4, 128.4, 118.9, 110.3, 39.8, 36.1, 31.6, 26.9, 22.4, 14.0, 12.7;

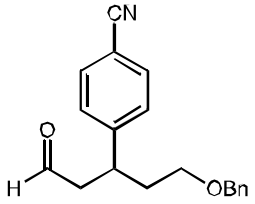
HRMS (ESI) exact mass calculated for $[M+H]^+$ ($C_{15}H_{20}NO$) requires *m/z* 230.1545, found *m/z* 230.1545.



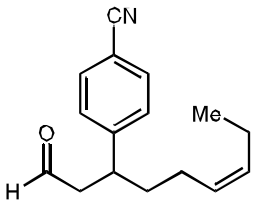
4-(1-Cyclohexyl-3-oxopropyl)benzonitrile. Prepared according to the general procedure using 6.6 mg of tris[2-phenylpyridinato-C^2,*N*]iridium(III) (10.0 μmol, 0.01 equiv), 128 mg of terephthalonitrile (1.00 mmol, 1.00 equiv), 561 mg of DABCO (5.00 mmol, 5.00 equiv), 196 mg of 3-cyclohexylpropanal (1.40 mmol, 1.4 equiv), 33 μL of *N*-isopropylbenzylamine (0.200 mmol, 0.20 equiv), 54 μL of water (3.00 mmol, 3.00 equiv), 11 μL of acetic acid (0.200 mmol, 0.20 equiv) and 2.0 mL of DMPU. After 46 h, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (silica gel: 10% to 100% ethyl acetate in hexanes) to afford the title compound as a clear oil (192 mg, 0.79 mmol, 79%). IR (film) 2924, 2852, 2227, 1722, 1607, 1449, 840 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.55 (s, 1H, C**H**O), 7.51 (d, *J* = 8.1 Hz, 2H, Ar**H**), 7.19 (d, *J* = 8.1 Hz, 2H, Ar**H**), 3.04–2.95 (m, 1H, C**H**(Ph-4-CN)), 2.85 (dd, *J* = 4.5, 17.2 Hz, 1H, C**H**$_2$CHO), 2.69 (dd, *J* = 9.1, 16.7 Hz, 1H, C**H**$_2$CHO), 1.76–1.48 (m, 4H, cyc**H**), 1.48-1.27 (m, 2H, cyc**H**), 1.20-0.92 (m, 3H, cyc**H**), 0.91-0.62 (m, 2H, cyc**H**); ^{13}C NMR (125 MHz, $CDCl_3$) δ 201.3, 148.9, 132.2, 129.2, 119.0, 110.3, 46.9, 45.9, 42.8, 31.0, 30.7, 26.3; HRMS (ESI) exact mass calculated for $[M+H]^+$ ($C_{16}H_{20}NO$) requires *m/z* 242.1545, found *m/z* 242.1548.



4-(4,4-dimethyl-1-oxopentan-3-yl)benzonitrile. Prepared according to the general procedure using 6.6 mg of tris[2-phenylpyridinato-C^2,*N*]iridium(III) (10.0 μmol, 0.01 equiv), 128 mg of terephthalonitrile (1.00 mmol, 1.00 equiv), 561 mg of DABCO (5.00 mmol, 5.00 equiv), 195 μL of 4,4-dimethylpentanal (1.40 mmol, 1.4 equiv), 64 mg of (2,2-diphenylethyl)(propan-2-yl)amine (0.25 mmol, 0.25 equiv), 54 μL of water (3.00 mmol, 3.00 equiv), 11 μL of acetic acid (0.20 mmol, 0.20 equiv) and 2.0 mL of DMPU (*29*). After 48 h, the reaction mixture was diluted with DCM (40 mL) and added to a separatory funnel containing 25 mL of a 1 M aqueous solution of NaOH. The layers were separated and the aqueous layer was extracted with DCM (2 × 10 mL). The combined organic extracts were washed with brine (40 mL), dried over Na_2SO_4, filtered, and concentrated *in vacuo* to afford the crude mixture. Purification of the crude mixture by flash chromatography (silica gel: 10% to 100% ethyl acetate in hexanes) afforded the title compound as a light yellow oil (95 mg, 0.44 mmol, 44%). IR (film) 2963, 2227, 1722, 1607, 1367, 1223, 842 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.59 (t, *J* = 1.8 Hz, 1H, C**H**O), 7.59 (d, *J* = 8.3 Hz, 2H, Ar**H**), 7.29 (d, *J* = 8.3 Hz, 2H, Ar**H**), 3.16–3.10 (m, *J* = 8.4, 1H, C**H**(Ph-4-CN)), 2.91 (dd, *J* = 8.4, 1.8 Hz, 2H, C$\mathbf{H}_2$CHO), 0.90 (s, 9H, C(C$\mathbf{H}_3$)$_3$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 201.1, 147.2, 131.7, 130.1, 118.8, 110.5, 49.9, 44.5, 33.8, 27.8; HRMS (ESI) exact mass calculated for $[M+H]^+$ ($C_{14}H_{18}NO$) requires *m/z* 216.1388, found *m/z* 216.1382.

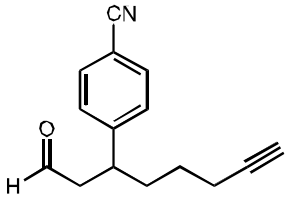


4-(1-(Benzyloxy)-5-oxopentan-3-yl)benzonitrile. Prepared according to the general procedure using 6.6 mg of tris[2-phenylpyridinato-C^2,*N*]iridium(III) (10.0 μmol, 0.01 equiv), 128 mg of terephthalonitrile (1.00 mmol, 1.00 equiv), 561 mg of DABCO (5.00 mmol, 5.00 equiv), 269 mg of 5-(benzyloxy)pentanal (1.40 mmol, 1.4 equiv), 33 μL of *N*-isopropylbenzylamine (0.20 mmol, 0.20 equiv), 54 μL of water (3.00 mmol, 3.00 equiv), 11 μL of acetic acid (0.20 mmol, 0.20 equiv) and 2.0 mL of DMPU. After 66 h, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (silica gel: 10% to 100% ethyl acetate in hexanes) to afford the title compound as a clear oil (220 mg, 0.75 mmol, 75%). IR (film) 2935, 2865, 2228, 1717, 1454, 1363, 1275, 1096, 1072, 736, 698 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.62 (s, 1H, C**H**O), 7.55 (d, *J* = 8.3 Hz, 2H, Ar**H**), 7.36–7.24 (m, 7H, Ar**H**), 4.37 (dd, *J* = 11.8, 29.1 Hz, 2H, OC$\mathbf{H}_2$Ph), 3.55–3.46 (m, 1H, C**H**(Ph-4-CN)), 3.35 (dt, *J* = 5.3, 5.3, 10.4 Hz, 1H, C$\mathbf{H}_2$OBn), 3.19 (dt, *J* = 4.9, 9.0, 9.3 Hz, 1H, C$\mathbf{H}_2$OBn), 2.86–2.69 (m, 2H, C$\mathbf{H}_2$CHO), 2.05–1.95 (m, 1H, C$\mathbf{H}_2$$CH_2$OBn), 1.86–1.75 (m, 1H, C$\mathbf{H}_2$$CH_2$OBn); ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.5, 149.3, 138.2, 132.7, 128.66, 128.65, 128.00, 127.99, 119.0, 110.7, 73.2, 67.2, 50.0, 36.7, 36.2; HRMS (ESI) exact mass calculated for $[M+H]^+$ ($C_{19}H_{20}NO_2$) requires *m/z* 294.1494, found *m/z* 294.1497.



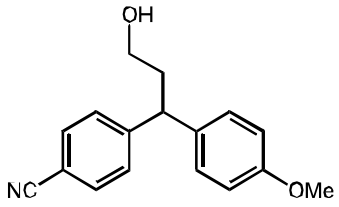
(*Z*)-4-(1-Oxonon-6-en-3-yl)benzonitrile. Prepared according to the general procedure using 6.6 mg of tris[2-phenylpyridinato-C^2,*N*]iridium(III) (10.0 μmol, 0.01 equiv), 128 mg of

terephthalonitrile (1.00 mmol, 1.00 equiv), 561 mg of DABCO (5.00 mmol, 5.00 equiv), 233 μL of (Z)-non-6-enal (1.40 mmol, 1.4 equiv), 33 μL of *N*-isopropylbenzylamine (0.20 mmol, 0.20 equiv), 54 μL of water (3.00 mmol, 3.00 equiv), 11 μL of acetic acid (0.20 mmol, 0.20 equiv) and 2.0 mL of DMPU. After 48 h, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (silica gel: 10% to 100% ethyl acetate in hexanes) to afford the title compound as a clear oil (184 mg, 0.76 mmol, 76%). IR (film) 2963, 2228, 1722, 1455, 1417, 909, 836 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.69 (s, 1H, C**H**O), 7.63 (d, *J* = 8.3 Hz, 2H, Ar**H**), 7.34 (d, *J* = 8.2 Hz, 2H, Ar**H**), 5.44–5.35 (m, 1H, $CH_2C\mathbf{H}CHCH_2$), 5.31–5.22 (m, 1H, $CH_2CHC\mathbf{H}CH_2$), 3.33–3.21 (m, 1H, C**H**(Ph-4-CN)), 2.81-2.67 (m, 2H, $C\mathbf{H}_2CHO$), 1.94-1.65 (m, 6H, $C\mathbf{H}_2C\mathbf{H}_2CHCHC\mathbf{H}_2$), 0.92 (t, *J* = 7.54 Hz, 3H, $CH_2CHCHCH_2C\mathbf{H}_3$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.6 149.6, 133.0, 132.7, 128.6, 127.6, 119.0, 110.7, 50.4, 39.4, 36.2, 24.8, 20.7, 14.4; HRMS (ESI) exact mass calculated for $[M+H]^+$ ($C_{19}H_{20}NO$) requires *m/z* 242.1545, found *m/z* 242.1540.



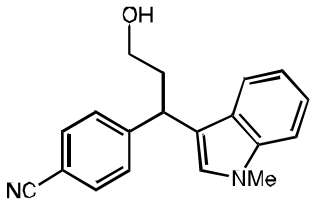
4-(1-Oxooct-7-yn-3-yl)benzonitrile. Prepared according to the general procedure using 6.6 mg of tris[2-phenylpyridinato-C^2,*N*]iridium(III) (10.0 μmol, 0.01 equiv), 128 mg of terephthalonitrile (1.00 mmol, 1.00 equiv), 561 mg of DABCO (5.00 mmol, 5.00 equiv), 106 mg of sodium carbonate (1.00 mmol, 1.00 equiv), 174 mg of oct-7-ynal (1.40 mmol, 1.4 equiv), 33 μL of *N*-isopropylbenzylamine (0.20 mmol, 0.20 equiv), 54 μL of water (3.00 mmol, 3.00 equiv), 11 μL of acetic acid (0.20 mmol, 0.20 equiv) and 2.0 mL of DMPU. After 46 h, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (silica gel: 10% to 100% ethyl acetate in hexanes) to afford the title compound as a clear oil (149 mg, 0.66 mmol, 66%). IR (film) 3302, 2942, 2228, 1720, 1417, 1276, 1261, 910, 834 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.65 (s, 1H, C**H**O), 7.58 (d, *J* = 8.2 Hz, 2H, Ar**H**),

7.29 (d, J = 8.2 Hz, 2H, Ar**H**), 3.31–3.21 (m, 1H, C**H**(Ph-4-CN)), 2.82–2.70 (m, 2H, C**H**$_2$CHO), 2.16–2.06 (m, 2H, CH(Ph-4-CN)C**H**$_2$(CH$_2$)$_2$CCH), 1.95–1.88 (m, 1H, CH(Ph-4-CN)C**H**$_2$(CH$_2$)$_2$CC**H**), 1.84–1.62 (m, 2H, CH(Ph-4-CN)C**H**$_2$(C**H**$_2$)$_2$CCH), 1.44-1.18 (m, 2H, CH(Ph-4-CN)CH$_2$(C**H**$_2$)$_2$CCH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.5, 149.4, 132.6, 128.6, 118.8, 111.0, 83.9, 69.2, 50.7, 39.5, 35.1, 26.2, 18.2; HRMS (ESI) exact mass calculated for $[M+H]^+$ ($C_{15}H_{16}NO$) requires *m/z* 226.1232, found *m/z* 226.1232.



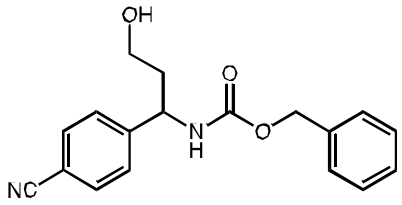
4-(3-Hydroxy-1-(4-methoxyphenyl)propyl)benzonitrile. Prepared according to the general procedure using 6.6 mg of tris[2-phenylpyridinato-C^2,*N*]iridium(III) (10.0 μmol, 0.01 equiv), 128 mg of terephthalonitrile (1.00 mmol, 1.00 equiv), 561 mg of DABCO (5.00 mmol, 5.00 equiv), 230 mg of 3-(4-methoxyphenyl)propanal (1.40 mmol, 1.4 equiv), 33 μL of *N*-isopropylbenzylamine (0.20 mmol, 0.20 equiv), 54 μL of water (3.00 mmol, 3.00 equiv), 11 μL of acetic acid (0.20 mmol, 0.20 equiv) and 2.0 mL of DMPU. After 45 h, the reaction mixture was transferred to a 25 mL round-bottom flask and diluted with 8 mL of DCM and 2 mL of MeOH. The reaction mixture was then cooled to 0 ºC and 189 mg of sodium borohydride (5.00 mmol, 5.00 equiv) was added to reduce the resulting aldehyde to the respective alcohol. The reaction mixture was stirred for 30 min and then diluted with ethyl acetate and added to a separatory funnel containing 25 mL of a saturated aqueous solution of NaCl. The layers were separated and the aqueous layer was extracted with EtOAc (3 × 10 mL). The combined organic extracts were then dried with Na_2SO_4 and concentrated *in vacuo*. Purification of the crude product by flash chromatography (silica gel: 10% to 100% ethyl acetate in hexanes) afforded the title compound as a clear oil (235 mg, 0.88 mmol, 88%). IR (film) 3418, 2935, 2227, 1608, 1510, 1246, 1178, 1030, 825, 733 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.51 (d, J = 8.3 Hz, 2H, Ph**H**-4-CN), 7.30 (d, J = 8.2 Hz, 2H, Ph**H**-4-CN), 7.10 (d, J = 8.7 Hz, 2H, Ph**H**-4-OMe), 6.80 (d, J = 8.7

Hz, 2H, Ph**H**-4-OMe), 4.15 (t, *J* = 7.9 Hz, 1H, (Ph-4-OMe)C**H**(Ph-4-CN)), 3.73 (s, 3H, (Ph-4-OC**H**$_3$), 3.54 (t, *J* = 6.32 Hz, 2H, C**H**$_2$OH), 2.31–2.15 (m, 2H, C**H**$_2$CH$_2$OH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.5, 150.8, 135.0, 132.5, 123.0, 128.7, 119.2, 114.2, 110.0, 60.5, 55.4, 46.5, 37.9; HRMS (ESI) exact mass calculated for $[M+H]^+$ ($C_{17}H_{18}NO_2$) requires *m/z* 268.1338, found *m/z* 268.1344.



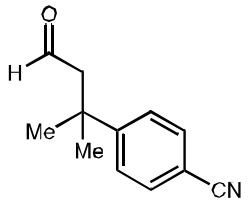
4-(3-Hydroxy-1-(1-methyl-1*H*-indol-3-yl)propyl)benzonitrile. Prepared according to the general procedure using 6.6 mg of tris[2-phenylpyridinato-C^2,*N*]iridium(III) (10.0 μmol, 0.01 equiv), 128 mg of terephthalonitrile (1.00 mmol, 1.00 equiv), 561 mg of DABCO (5.00 mmol, 5.00 equiv), 106 mg of sodium carbonate (1.00 mmol, 1.00 equiv), 262 mg of 3-(1methyl-1*H*-indol-3-yl)propanal (1.40 mmol, 1.4 equiv), 33 μL of *N*-isopropylbenzylamine (0.20 mmol, 0.20 equiv), 54 μL of water (3.00 mmol, 3.00 equiv), 11 μL of acetic acid (0.20 mmol, 0.20 equiv) and 2.0 mL of DMPU (*30*). After 57 h, the reaction mixture was transferred to a 25 mL round-bottom flask and diluted with 8 mL of DCM and 2 mL of MeOH. The reaction mixture was then cooled to 0 °C and 189 mg of sodium borohydride (5.00 mmol, 5.00 equiv) was added to reduce the resulting aldehyde to the respective alcohol. The reaction mixture was stirred for 30 min and then diluted with ethyl acetate and added to a separatory funnel containing 25 mL of a saturated aqueous solution of NaCl. The layers were separated and the aqueous layer was extracted with EtOAc (3 × 10 mL). The combined organic extracts were then dried with Na_2SO_4 and concentrated *in vacuo*. Purification of the crude product by flash chromatography (silica gel: 10% to 100% ethyl acetate in hexanes) afforded the title compound as a yellow oil (181 mg, 0.63 mmol, 63%). IR (film) 3400, 2935, 2880, 2226, 1472, 1327, 1265, 1154, 1034, 1012 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.53 (d, *J* = 8.3 Hz, 2H, Ph**H**-4-CN), 7.41 (d, *J* = 8.2 Hz, 2H, Ph**H**-4-CN), 7.34 (d, *J* = 8.0 Hz, 1H, Indole**H**), 7.27 (d, *J* = 8.2 Hz, 1H, Indole**H**), 7.19 (t, *J* = 7.7 Hz, 1H,

Indole**H**), 7.00 (t, *J* = 7.5 Hz, 1H, Indole**H**), 6.93 (s, 1H, Indole**H**), 4.47 (t, *J* = 7.7 Hz, 1H, (NMeIndole)C**H**(Ph-4-CN)), 3.76 (s, 3H, N**Me**Indole), 3.70-3.56 (m, 2H, C**H**$_2$OH), 2.44 (td, *J* = 13.7, 6.8 Hz, 1H, C**H**$_2$CH$_2$OH), 2.22 (td, *J* = 13.9, 6.2 Hz, 1H, C**H**$_2$CH$_2$OH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 150.8, 137.3, 132.3, 128.7, 127.0, 126.1, 122.0, 119.2, 119.14, 119.11, 116.4, 109.9, 109.4, 60.8, 39.0, 38.2, 32.9; HRMS (ESI) exact mass calculated for $[M+H]^+$ ($C_{19}H_{19}N_2O$) requires *m/z* 291.1497, found *m/z* 291.1478.

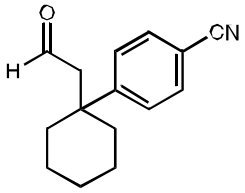


Benzyl 1-(4-cyanophenyl)-3-hydroxypropylcarbamate. Prepared according to the general procedure using 6.6 mg of tris[2-phenylpyridinato-C^2,*N*]iridium(III) (10.0 μmol, 0.01 equiv), 128 mg of terephthalonitrile (1.00 mmol, 1.00 equiv), 561 mg of DABCO (5.00 mmol, 5.00 equiv), 290 mg of benzyl (3-oxopropyl)carbamate (1.40 mmol, 1.4 equiv), 33 μL of *N*-isopropylbenzylamine (0.20 mmol, 0.20 equiv), 54 μL of water (3.00 mmol, 3.00 equiv), 11 μL of acetic acid (0.20 mmol, 0.20 equiv) and 2.0 mL of DMPU (*31*). After 53 h, the reaction mixture was transferred to a 25 mL round-bottom flask and diluted with 8 mL of DCM and 2 mL of MeOH. The reaction mixture was then cooled to 0 °C and 189 mg of sodium borohydride (5.00 mmol, 5.00 equiv) was added to reduce the resulting aldehyde to the respective alcohol. The reaction mixture was stirred for 30 min and then diluted with ethyl acetate and added to a separatory funnel containing 25 mL of a saturated aqueous solution of NaCl. The layers were separated and the aqueous layer was extracted with EtOAc (3 × 10 mL). The combined organic extracts were then dried with Na_2SO_4 and concentrated *in vacuo*. Purification of the crude product by flash chromatography (silica gel: 10% to 20% acetonitrile in DCM) afforded the title compound as a yellow oil (218 mg, 0.71 mmol, 71%). IR (film) 3327, 2952, 2229, 1693, 1518, 1253, 1049 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.58 (d, *J* = 7.7 Hz, 2H, Ph**H**-4-CN), 7.38 (d, *J* = 7.6 Hz, 2H, Ph**H**-4-CN), 7.35–7.25 (m, 5H, OCH$_2$Ph**H**), 5.98 (d, *J* = 5.8 Hz, 1H, N**H**CBz), 5.11–

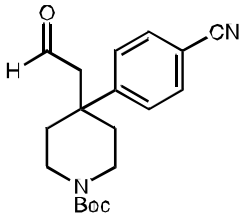
4.89 (m, 3H, OC**H**$_2$Ph & NHCBzC**H**(Ph-4-CN)), 3.70–3.53 (m, 2H, C**H**$_2$OH), 2.08–1.97 (m, 1H, C**H**$_2$CH$_2$OH), 1.89–1.77 (m, 1H, C**H**$_2$CH$_2$OH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.4, 147.8, 136.3, 132.6, 128.7, 128.4, 128.3, 127.3, 118.9, 111.2, 67.2, 59.1, 53.2, 38.1; HRMS (ESI) exact mass calculated for $[M+H]^+$ ($C_{18}H_{19}N_2O_3$) requires *m/z* 311.1396, found *m/z* 311.1393.



4-(2-Methyl-4-oxobutan-2-yl)benzonitrile. Prepared according to the general procedure using 6.6 mg of tris[2-phenylpyridinato-C^2,*N*]iridium(III) (10.0 μmol, 0.01 equiv), 128 mg of terephthalonitrile (1.00 mmol, 1.00 equiv), 561 mg of DABCO (5.00 mmol, 5.00 equiv), 147 μL of isovaleraldehyde (1.40 mmol, 1.4 equiv), 33 μL of *N*-isopropylbenzylamine (0.20 mmol, 0.20 equiv), 54 μL of water (3.00 mmol, 3.00 equiv), 11 μL of acetic acid (0.20 mmol, 0.20 equiv) and 2.0 mL of DMPU. After 48 h, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (silica gel: 10% to 100% ethyl acetate in hexanes) to afford the title compound as a clear oil (138 mg, 0.74 mmol, 74%). IR (film) 2970, 2228, 1707, 1403, 1267, 1235, 1187, 1130, 1097, 837 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.30 (t, *J* = 2.6 Hz, 1H, C**H**O), 7.40 (d, *J* = 8.5 Hz, 2H, Ar**H**), 7.27 (d, *J* = 8.5 Hz, 2H, Ar**H**), 2.52 (d, *J* = 2.6 Hz, 2H, C**H**$_2$CHO), 1.24 (s, 6H, (C**H**$_3$)C(Ph-4-CN)); ^{13}C NMR (125 MHz, $CDCl_3$) δ 201.6, 153.1, 132.1, 126.6, 119.0, 110.2, 56.1, 37.3, 29.1; HRMS (ESI) exact mass calculated for $[M+H]^+$ ($C_{12}H_{14}NO$) requires *m/z* 188.1075, found *m/z* 188.1077.

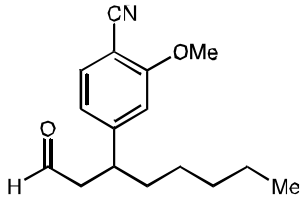


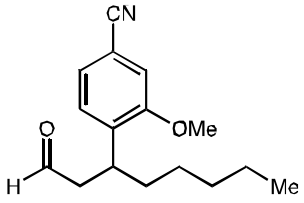
4-(1-(2-Oxoethyl)cyclohexyl)benzonitrile. Prepared according to the general procedure using 6.6 mg of tris[2-phenylpyridinato-C^2,*N*]iridium(III) (10.0 μmol, 0.01 equiv), 128 mg of terephthalonitrile (1.00 mmol, 1.00 equiv), 561 mg of DABCO (5.00 mmol, 5.00 equiv), 147 μL of isovaleraldehyde (1.40 mmol, 1.4 equiv), 33 μL of *N*-isopropylbenzylamine (0.20 mmol, 0.20 equiv), 54 μL of water (3.00 mmol, 3.00 equiv), 11 μL of acetic acid (0.20 mmol, 0.20 equiv) and 2.0 mL of DMPU. After 72 h, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (silica gel: 10% to 100% ethyl acetate in hexanes) to afford the title compound as a clear oil (160 mg, 0.70 mmol, 70%). IR (film) 2932, 2859, 2227, 1717, 1454, 1406, 1268, 1017, 834, 736 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.36 (s, 1H, C**H**O), 7.63 (d, *J* = 8.3 Hz, 2H, Ar**H**), 7.49 (d, *J* = 8.3 Hz, 2H, Ar**H**), 2.60 (d, *J* = 2.2 Hz, 2H, C$\mathbf{H}_2$CHO), 2.18–2.06 (m, 2H, cyc**H**), 1.81–1.69 (m, 2H, cyc**H**), 1.62–1.50 (m, 2H, cyc**H**), 1.48–1.31 (m, 4H, cyc**H**); ^{13}C NMR (125 MHz, $CDCl_3$) δ 201.7, 151.1, 132.5, 127.5, 118.7, 110.2, 55.2, 40.9, 36.2, 25.9, 21.9; HRMS (ESI) exact mass calculated for $[M+H]^+$ ($C_{15}H_{18}NO$) requires *m/z* 228.1388, found *m/z* 228.1389.



***tert*-Butyl 4-(4-cyanophenyl)-4-(2-oxoethyl)piperidine-1-carboxylate.** Prepared according to the general procedure using 6.6 mg of tris[2-phenylpyridinato-C^2,*N*]iridium(III) (10.0 μmol, 0.01 equiv), 128 mg of terephthalonitrile (1.00 mmol, 1.00 equiv), 561 mg of DABCO (5.00 mmol, 5.00 equiv), 318 mg of *tert*-butyl 4-(2-oxoethyl)piperidine-1-carboxylate (1.40 mmol, 1.4 equiv),

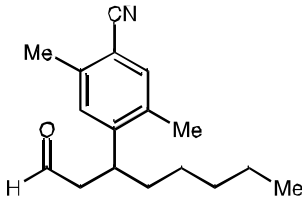
33 μL of *N*-isopropylbenzylamine (0.20 mmol, 0.20 equiv), 54 μL of water (3.00 mmol, 3.00 equiv), 11 μL of acetic acid (0.20 mmol, 0.20 equiv) and 2.0 mL of DMPU. After 47 h, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (silica gel: 5% to 40% ethyl acetate in benzene) to afford the title compound as a clear oil (232 mg, 0.71 mmol, 71%). IR (film) 2977, 2934, 2229, 1720, 1683, 1420, 1244, 1162, 733 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.39 (s, 1H, C**H**O), 7.65 (d, *J* = 8.4 Hz, 2H, Ar**H**), 7.47 (d, *J* = 8.4 Hz, 2H, Ar**H**), 3.62–3.52 (m, 2H, C**H**$_2$NBoc), 3.28–3.19 (m, 2H, C**H**$_2$NBoc), 2.71 (d, *J* = 1.4 Hz, 2H, C**H**$_2$CHO), 2.23–2.12 (m, 2H, C**H**$_2$CH$_2$NBoc), 1.94–1.84 (m, 2H, C**H**$_2$CH$_2$NBoc), 1.41 (s, 9H, C(C**H**$_3$)$_3$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.6, 154.9, 149.3, 132.9, 127.7, 118.7, 110.7, 80.1, 59.4, 54.1, 39.4, 35.1, 28.6; HRMS (ESI) exact mass calculated for $[M+H]^+$ ($C_{19}H_{25}N_2O_3$) requires *m/z* 329.1865, found *m/z* 329.1853.





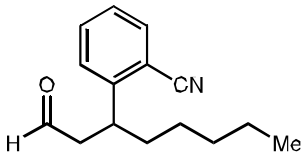
2-Methoxy-4-(1-oxooctan-3-yl)benzonitrile and 3-methoxy-4-(1-oxooctan-3-yl)benzonitrile. Prepared according to the general procedure using 6.6 mg of tris[2-phenylpyridinato-C^2,*N*]iridium(III) (10.0 μmol, 0.01 equiv), 158 mg of 2-methoxyterephthalonitrile (1.00 mmol, 1.00 equiv), 561 mg of DABCO (5.00 mmol, 5.00 equiv), 106 mg of sodium carbonate (1.00 mmol, 1.00 equiv), 219 μL of octanal (1.40 mmol, 1.4 equiv), 33 μL of *N*-isopropylbenzylamine (0.20 mmol, 0.20 equiv), 54 μL of water (3.00 mmol, 3.00 equiv), 11 μL of acetic acid (0.20 mmol, 0.20 equiv) and 2.0 mL of DMPU. After 48 h, the reaction mixture was subjected to the workup protocol outlined in the general procedure. Analysis of the crude reaction mixture by ^1H NMR in $CDCl_3$ determined that the regioisomer ratio was 3.7:1. The crude reaction mixture was purified by flash chromatography (silica gel: 10% to 100% ethyl acetate in hexanes) to afford 2-methoxy-4-(1-oxooctan-3-yl)benzonitrile (148 mg, 0.58 mmol, 58% yield) and 3-methoxy-4-(1-oxooctan-3-yl)benzonitrile (40 mg, 0.15 mmol, 15% yield) as colorless oils. *2-methoxy-4-(1-*

oxooctan-3-yl)benzonitrile; IR (film) 2928, 2857, 2226, 1723, 1606, 1464, 1420, 1267, 1030 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.66 (s, 1H, C**H**O), 7.47 (d, *J* = 7.9 Hz, 1H, Ar**H**), 6.82 (dd, *J* = 1.2, 7.9 Hz, 1H, Ar**H**), 6.76 (s, 1H, Ar**H**), 3.91 (s, 3H, OC$\mathbf{H}_3$), 3.24–3.15 (m, 1H, C**H**(Ar)), 2.78–2.68 (m, 2H, C$\mathbf{H}_2$CHO), 1.70–1.49 (m, 2H, CH(Ar)C$\mathbf{H}_2$$(CH_2)_3CH_3$), 1.28–1.12 (m, 6H, CH(Ar)$CH_2$$(C\mathbf{H}_2)_3CH_3$), 0.86–0.73 (m, 3H, CH(Ar)$CH_2$$(CH_2)_3C\mathbf{H}_3$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.9, 161.7, 152.2, 134.1, 119.7, 116.7, 111.1, 100.1, 56.2, 50.7, 40.7, 36.3, 31.8, 27.1, 22.5, 13.9; HRMS (ESI) exact mass calculated for $[M+H]^+$ ($C_{16}H_{22}NO_2$) requires *m/z* 260.1651, found *m/z* 260.1648. *3-methoxy-4-(1-oxooctan-3-yl)benzonitrile*; IR (film) 2928, 2858, 2230, 1721, 1502, 1463, 1407, 1262, 1034 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.62 (t, *J* = 1.9 Hz, 1H, C**H**O), 7.23–7.18 (m, 2H, Ar**H**), 7.05 (s, 1H, Ar**H**), 3.83 (s, 3H, OC$\mathbf{H}_3$), 3.67–3.57 (m, 1H, C**H**(Ar)), 2.74–2.60 (m, 2H, C$\mathbf{H}_2$CHO), 1.71–1.54 (m, 2H, CH(Ar)C$\mathbf{H}_2$$(CH_2)_3CH_3$), 1.32–1.12 (m, 6H, CH(Ar)$CH_2$$(C\mathbf{H}_2)_3CH_3$), 0.89–0.74 (m, 3H, CH(Ar)$CH_2$$(CH_2)_3C\mathbf{H}_3$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 201.4, 157.4, 138.3, 128.8, 125.0, 118.7, 113.5, 110.7, 55.8, 49.1, 34.5, 33.1, 31.7, 27.0, 22.6, 14.1; HRMS (ESI) exact mass calculated for $[M+H]^+$ ($C_{16}H_{22}NO_2$) requires *m/z* 260.1651, found *m/z* 260.1656.



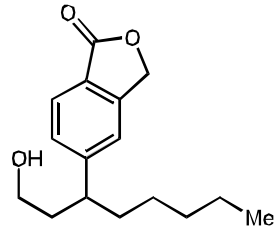
2,5-Dimethyl-4-(1-oxooctan-3-yl)benzonitrile. Prepared according to the general procedure using 6.6 mg of tris[2-phenylpyridinato-C^2,*N*]iridium(III) (10.0 μmol, 0.01 equiv), 156 mg of 2,5-dimethylterephthalonitrile (1.00 mmol, 1.00 equiv), 561 mg of DABCO (5.00 mmol, 5.00 equiv), 106 mg of sodium carbonate (1.00 mmol, 1.00 equiv), 219 μL of octanal (1.40 mmol, 1.4 equiv), 33 μL of *N*-isopropylbenzylamine (0.20 mmol, 0.20 equiv), 54 μL of water (3.00 mmol, 3.00 equiv), 11 μL of acetic acid (0.20 mmol, 0.20 equiv) and 2.0 mL of DMPU. After 36 h, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (silica gel: 10% to 100% ethyl acetate in hexanes) to afford the

title compound as a clear oil (201 mg, 0.78 mmol, 78%). IR (film) 2927, 2222, 1723, 1459, 1392, 1266, 908, 729 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.62 (s, 1H, C**H**O), 7.33 (s, 1H, Ar**H**), 7.02 (s, 1H, Ar**H**), 3.48–3.38 (m, 1H, C**H**(Ar)), 2.77–2.65 (m, 2H, C$\mathbf{H}_2$CHO), 2.44 (s, 3H, ArC$\mathbf{H}_3$), 2.32 (s, 3H, ArC$\mathbf{H}_3$), 1.66–1.42 (m, 2H, CH(Ar)C$\mathbf{H}_2$$(CH_2)_3CH_3$), 1.29–1.10 (m, 6H, CH(Ar)CH_2(C$\mathbf{H}_2$$)_3CH_3$), 0.82–0.72 (t, *J* = 6.6 Hz, 3H, CH(Ar)$CH_2$$(CH_2)_3C\mathbf{H}_3$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 201.0, 148.3, 139.9, 134.6, 134.2, 127.7, 118.5, 110.4, 50.4, 36.5, 34.5, 32.0, 27.0, 22.8, 20.4, 19.4, 14.2; HRMS (ESI) exact mass calculated for $[M+H]^+$ ($C_{17}H_{24}NO$) requires *m/z* 258.1858, found *m/z* 258.1859.



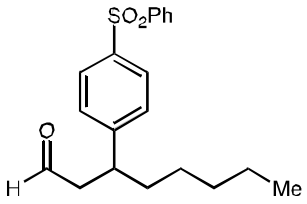
2-(1-Oxooctan-3-yl)benzonitrile. Prepared according to the general procedure using 6.6 mg of tris[2-phenylpyridinato-C^2,*N*]iridium(III) (10.0 μmol, 0.01 equiv), 128 mg of 1,2-dicyanobenzene (1.00 mmol, 1.00 equiv), 561 mg of DABCO (5.00 mmol, 5.00 equiv), 123 mg NaOAc (1.50 mmol, 1.50 equiv), 468 μL of octanal (3.00 mmol, 3.0 equiv), 47.9 μL of *N*-*tert*-butylmethylamine (0.400 mmol, 0.40 equiv), 90 μL of water (5.00 mmol, 5.00 equiv), 11 μL of acetic acid (0.20 mmol, 0.20 equiv) and 5.0 mL of DMSO. After 48 h, the reaction mixture was diluted with DCM (50 mL) and added to a separatory funnel containing 30 mL of a 1 M aqueous solution of NaOH. The layers were separated and the aqueous layer was extracted with DCM (20 mL). The combined organic extracts were washed with brine (40 mL), dried over Na_2SO_4, filtered, and concentrated *in vacuo* to afford the crude mixture. The crude material was purified by flash chromatography (silica gel: 5% to 15% ethyl acetate in hexanes) to afford the title compound as a light yellow oil (128.8 mg, 0.562 mmol, 56%). IR (film) 2929, 2224, 1722, 1485, 1448, 1165, 1109, 763 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.70 (t, *J* = 1.6 Hz, 1H, C**H**O), 7.65 (d, *J* = 8.0 Hz, 1H, Ar**H**), 7.57 (t, *J* = 7.8 Hz, 1H, Ar**H**), 7.35–7.30 (m, 2H, Ar**H**), 3.73–3.64 (m, 1H, C**H**(Ar)), 2.89–2.7 8 (m, 2H, C$\mathbf{H}_2$CHO), 1.78–1.64 (m, 2H, CH(Ar)C$\mathbf{H}_2$$(CH_2)_3CH_3$), 1.33–1.05 (m, 6H, CH(Ar)CH_2(C$\mathbf{H}_2$$)_3CH_3$), 0.89–0.77 (m, 3H, $(CH_2)_3$C$\mathbf{H}_3$); ^{13}C NMR (125 MHz,

$CDCl_3$) δ 200.4, 147.7, 133.2, 133.1, 127.3, 127.0, 118.1, 112.6, 49.7, 38.0, 36.0, 31.6, 26.8, 22.4, 14.0; HRMS (ESI) exact mass calculated for $[M+H]^+$ ($C_{15}H_{20}NO$) requires *m/z* 230.1545, found *m/z* 230.1546.



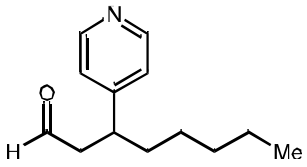
5-(1-Hydroxyoctan-3-yl)isobenzofuran-1(3*H*)-one. Prepared according to the general procedure using 6.6 mg of tris[2-phenylpyridinato-C^2,*N*]iridium(III) (10.0 μmol, 0.01 equiv), 159 mg of 5-cyanophthalide (1.00 mmol, 1.00 equiv), 561 mg of DABCO (5.00 mmol, 5.00 equiv), 82.0 mg NaOAc (1.00 mmol, 1.00 equiv), 468 μL of octanal (3.00 mmol, 3.0 equiv), 66.9 μL of *N*-isopropylbenzylamine (0.400 mmol, 0.40 equiv), 54 μL of water (3.00 mmol, 3.00 equiv), 11 μL of acetic acid (0.20 mmol, 0.20 equiv) and 4.0 mL of DMSO. After 23 h, the reaction mixture was transferred to a 20 mL scintillation vial and diluted with 4 mL of DCM and 4 mL of EtOH. The reaction mixture was then cooled to 0 ºC and 114 mg of sodium borohydride (3.00 mmol, 3.0 equiv) was added to reduce the resulting aldehyde to the respective alcohol. The reaction mixture was stirred for 15 min, warmed to room temperature for a further 30 min, and quenched with saturated aqueous NH_4Cl. The reaction mixture was then diluted with EtOAc and added to a separatory funnel containing 25 mL of water. The layers were separated and the aqueous layer was extracted with EtOAc (1 × 25 mL). The combined organic extracts were then washed with brine, dried with Na_2SO_4 and concentrated *in vacuo*. Purification of the crude product by flash chromatography (silica gel: 20% to 45% ethyl acetate in hexanes) to afford the title compound as a colorless oil (164.4 mg, 0.627 mmol, 63%). IR (film) 3415, 2928, 1745, 1455, 1346, 1042, 778, 700 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.85 (d, *J* = 7.9 Hz, 1H, Ar**H**), 7.36 (d, *J* = 7.9 Hz, 1H, Ar**H**), 7.30 (s, 1H, Ar**H**), 5.31 (s, 2H, ArC**H**$_2$O), 3.59–3.52 (m, 1H, C**H**$_2$OH), 3.47–3.39 (m, 1H, C**H**$_2$OH), 2.93–2.85 (m, 1H, C**H(**Ar)), 2.06-1.96 (m, 1H, C**H**$_2$CH$_2$OH), 1.87–1.77 (m, 1H, C**H**$_2$CH$_2$OH), 1.75–1.56 (m, 2H, CH(Ar)C**H**$_2$(CH$_2$)$_3$CH$_3$), 1.30 (br s, 1H, O**H**), 1.27–1.03 (m, 6H,

CH(Ar)CH_2($C\mathbf{H}_2$)$_3$$CH_3$), 0.86–0.79 (m, 3H, ($CH_2$)$_3$$C\mathbf{H}_3$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.1, 152.9, 147.1, 128.7, 125.8, 123.9 121.2, 69.5, 60.6, 42.7, 39.4, 36.7, 31.7, 27.2, 22.5, 14.0; HRMS (ESI) exact mass calculated for $[M+H]^+$ ($C_{16}H_{23}O_3$) requires *m/z* 263.1647, found *m/z* 263.1643.

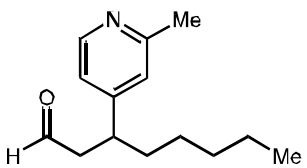


3-(4-(Phenylsulfonyl)phenyl)octanal. Prepared according to the general procedure using 6.6 mg of tris[2-phenylpyridinato-C^2,*N*]iridium(III) (10.0 μmol, 0.01 equiv), 243 mg of 4-(phenylsulfonyl)benzonitrile (1.00 mmol, 1.00 equiv), 561 mg of DABCO (5.00 mmol, 5.00 equiv), 82.0 mg NaOAc (1.00 mmol, 1.00 equiv), 468 μL of octanal (3.00 mmol, 3.0 equiv), 50.1 μL of *N*-isopropylbenzylamine (0.300 mmol, 0.30 equiv), 90 μL of water (5.00 mmol, 5.00 equiv), 11 μL of acetic acid (0.20 mmol, 0.20 equiv) and 4.0 mL of DMSO (*32*). After 20 h, the reaction mixture was diluted with DCM (50 mL) and added to a separatory funnel containing 30 mL of a 1 M aqueous solution of NaOH. The layers were separated and the aqueous layer was extracted with DCM (20 mL). The combined organic extracts were washed with brine (40 mL), dried over Na_2SO_4, filtered, and concentrated *in vacuo* to afford the crude mixture. The crude material was purified by flash chromatography (silica gel: 0% to 0.75% ethyl acetate in DCM) to afford the title compound as a colorless oil (238.4 mg, 0.691 mmol, 69%). IR (film) 2927, 1721, 1447, 1306, 1153, 1105, 833, 687 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.64 (t, *J* = 1.6 Hz, 1H, C**H**O), 7.95 (d, *J* = 7.1 Hz, 2H, Ph**H**), 7.87 (d, *J* = 8.4 Hz, 2H, SO_2Ar**H**), 7.58 (t, *J* = 7.3 Hz, 1H, Ph**H**), 7.52 (dd, *J* = 7.3, 7.1 Hz, 2H, Ph**H**), 7.33 (d, *J* = 8.4 Hz, 2H, SO_2Ar**H**), 3.29–3.21 (m, 1H, C**H**(Ar)), 2.79–2.68 (m, 2H, C$\mathbf{H}_2$CHO), 1.68–1.52 (m, 2H, CH(Ar)C$\mathbf{H}_2$(CH_2)$_3$$CH_3$), 1.28–1.02 (m, 6H, CH(Ar)CH_2($C\mathbf{H}_2$)$_3$$CH_3$), 0.85-0.77 (m, 3H, ($CH_2$)$_3$$C\mathbf{H}_3$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.7, 150.2, 141.5, 139.6, 133.1, 129.3, 128.4, 128.0, 127.6, 50.2, 39.6, 36.2, 31.5, 26.8, 22.4, 14.0; HRMS (ESI) exact mass calculated for $[M+H]^+$ ($C_{20}H_{25}O_3S$) requires *m/z* 345.1524, found

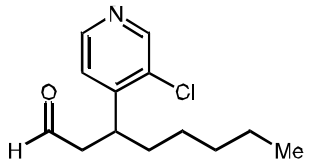
m/z 345.1520.



3-(Pyridin-4-yl)octanal. Prepared according to the general procedure using 6.6 mg of tris[2-phenylpyridinato-C^2,*N*]iridium(III) (10.0 μmol, 0.01 equiv), 104 mg of isonicotinonitrile (1.00 mmol, 1.00 equiv), 561 mg of DABCO (5.00 mmol, 5.00 equiv), 219 μL of octanal (1.40 mmol, 1.4 equiv), 33 μL of *N*-isopropylbenzylamine (0.20 mmol, 0.20 equiv), 54 μL of water (3.00 mmol, 3.00 equiv), 11 μL of acetic acid (0.20 mmol, 0.20 equiv) and 2.0 mL of DMPU. After 38 h, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (silica gel: 25% to 100% ethyl acetate in hexanes) to afford the title compound as a yellow oil (144 mg, 0.70 mmol, 70%). IR (film) 2928, 2858, 1722, 1599, 1415, 993, 820 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.61 (s, 1H, C**H**O), 8.44 (d, *J* = 4.8 Hz, 2H, Ar**H**), 7.07 (d, *J* = 5.1 Hz, 2H, Ar**H**), 3.17–3.05 (m, 1H, C**H**Ar), 2.77–2.61 (m, 2H, C$\mathbf{H}_2$CHO), 1.66–1.45 (m, 2H, CH(Ar)C$\mathbf{H}_2(CH_2)_3CH_3$), 1.22–1.07 (m, 6H, CH(Ar)$CH_2(C\mathbf{H}_2)_3CH_3$), 0.81–0.70 (m, 3H, CH(Ar)$CH_2(CH_2)_3C\mathbf{H}_3$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.7, 153.6, 150.0, 123.1, 50.0, 39.2, 35.8, 31.8, 27.0, 22.5, 14.1; HRMS (ESI) exact mass calculated for $[M+H]^+$ ($C_{13}H_{20}NO$) requires *m/z* 206.1545, found *m/z* 206.1563.

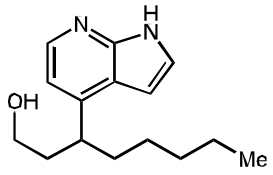


3-(2-Methylpyridin-4-yl)octanal. Prepared according to the general procedure using 5.3 mg of tris[2-phenylpyridinato-C^2,*N*]iridium(III) (8.00 μmol, 0.01 equiv), 95 mg of 2-methylisonicotinonitrile (0.80 mmol, 1.00 equiv), 449 mg of DABCO (4.00 mmol, 5.00 equiv), 175 μL of octanal (1.12 mmol, 1.4 equiv), 27 μL of *N*-isopropylbenzylamine (0.16 mmol, 0.20 equiv), 43 μL of water (2.40 mmol, 3.00 equiv), 9 μL of acetic acid (0.16 mmol, 0.20 equiv) and 1.6 mL of DMPU. After 48 h, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (silica gel: 25% to 100% ethyl acetate in hexanes) to afford the title compound as a yellow oil (119 mg, 0.54 mmol, 68%). IR (film) 2956, 2857, 2927, 1722, 1598, 1415, 1069, 993, 819 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.64 (t, *J* = 1.5 Hz, 1H, C**H**O), 8.35 (d, *J* = 5 Hz, 1H, Ar**H**), 6.95 (s, 1H, Ar**H**), 6.90 (d, *J* = 4.80 Hz, 1H, Ar**H**), 3.14–3.04 (m, 1H, C**H**Ar), 2.74–2.66 (m, 2H, C$\mathbf{H}_2$CHO), 2.50 (s, 3H, ArC$\mathbf{H}_3$), 1.67–1.47 (m, 2H, CH(Ar)C$\mathbf{H}_2$$(CH_2)_3CH_3$), 1.27–1.10 (m, 6H, CH(Ar)$CH_2$$(C\mathbf{H}_2)_3CH_3$), 0.84–0.75 (m, 3H, CH(Ar)$CH_2$$(CH_2)_3C\mathbf{H}_3$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 201.1, 158.9, 153.7, 149.2, 122.7, 120.2, 50.1, 39.1, 36.1, 31.8, 26.9, 24.5, 22.5, 14.4; HRMS (ESI) exact mass calculated for $[M+H]^+$ ($C_{14}H_{22}NO$) requires *m/z* 220.1701, found *m/z* 220.1705.



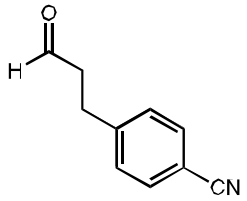
3-(3-Chloropyridin-4-yl)octanal. Prepared according to the general procedure using 6.6 mg of tris[2-phenylpyridinato-C^2,*N*]iridium(III) (10.0 μmol, 0.01 equiv), 139 mg of 3-chloroisonicotinonitrile (1.00 mmol, 1.00 equiv), 561 mg of DABCO (5.00 mmol, 5.00 equiv), 106 mg of sodium carbonate (1.00 mmol, 1.00 equiv), 219 μL of octanal (1.40 mmol, 1.4 equiv), 33 μL of *N*-isopropylbenzylamine (0.20 mmol, 0.20 equiv), 54 μL of water (3.00 mmol, 3.00 equiv), 11 μL of acetic acid (0.20 mmol, 0.20 equiv) and 2.0 mL of DMPU. After 26 h, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (silica gel: 10% to 75% ethyl acetate in hexanes) to afford the title compound as a yellow oil (130 mg, 0.54 mmol, 54%). IR (film) 2928, 2858, 1723, 1585,

1467, 1400, 1096, 1033, 833, 731 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.67 (s, 1H, C**H**O), 8.53 (s, 1H, Ar**H**), 8.39 (d, *J* = 5.0 Hz, 1H, Ar**H**), 7.11 (d, *J* = 5.0 Hz, 1H, Ar**H**), 3.80–3.65 (m, 1H, C**H**Ar), 2.83–2.64 (m, 2H, C**H**$_2$CHO), 1.68–1.58 (m, 2H, CH(Ar)C**H**$_2$(CH$_2$)$_3$CH$_3$), 1.29–1.15 (m, 6H, CH(Ar)CH$_2$(C**H**$_2$)$_3$CH$_3$), 0.87–0.74 (m, 3H, CH(Ar)CH$_2$(CH$_2$)$_3$C**H**$_3$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.4, 154.5, 150.5, 149.8, 133.9, 128.3, 49.0, 35.5, 34.8, 31.8, 26.8, 22.6, 13.9; HRMS (ESI) exact mass calculated for $[M+H]^+$ ($C_{13}H_{19}ClNO$) requires *m/z* 240.1155, found *m/z* 240.1152.



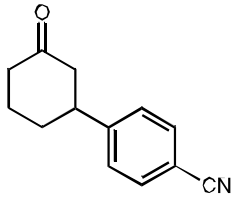
3-(1*H*-Pyrrolo[2,3-*b*]pyridin-4-yl)octan-1-ol. Prepared according to the general procedure using 6.6 mg of tris[2-phenylpyridinato-C^2,*N*]iridium(III) (10.0 μmol, 0.01 equiv), 143.1 mg of 7-azaindole-4-carbonitrile (1.00 mmol, 1.00 equiv), 561 mg of DABCO (5.00 mmol, 5.00 equiv), 123 mg NaOAc (1.50 mmol, 1.5 equiv), 468 μL of octanal (3.00 mmol, 3.0 equiv), 66.9 μL of *N*-isopropylbenzylamine (0.400 mmol, 0.40 equiv), 90 μL of water (5.00 mmol, 5.0 equiv), 11 μL of acetic acid (0.200 mmol, 0.20 equiv) and 4.0 mL of DMSO. After 48 h, the reaction mixture was transferred to a 20 mL scintillation vial and diluted with 4 mL of DCM and 4 mL of EtOH. The reaction mixture was then cooled to 0 ºC and 114 mg of sodium borohydride (3.00 mmol, 3.0 equiv) was added to reduce the resulting aldehyde to the respective alcohol. The reaction mixture was stirred for 20 min, warmed to room temperature for a further 40 min, and quenched with saturated aqueous NH_4Cl. The reaction mixture was then diluted with EtOAc and added to a separatory funnel containing 25 mL of water. The layers were separated and the aqueous layer was extracted with EtOAc (1 × 25 mL). The combined organic extracts were then washed with brine, dried with Na_2SO_4, and concentrated *in vacuo*. Purification of the crude product by flash chromatography (silica gel: 50% to 100% ethyl acetate in hexanes) to afford the title compound as a light yellow oil (130 mg, 0.53 mmol, 53%). IR (film) 3158, 2927, 1592, 1340, 1051, 726 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 10.68 (br s, 1H, N**H**), 8.24 (d, *J* = 5.0 Hz, 1H, Ar**H**), 7.32 (d, *J* =

3.5 Hz, 1H, Ar**H**), 6.92 (d, *J* = 5.0 Hz, 1H, Ar**H**), 6.58 (d, *J* = 3.5 Hz, 1H, Ar**H**), 3.57–3.50 (m, 1H, C**H**$_2$OH), 3.47–3.41 (m, 1H, C**H**$_2$OH), 3.23–3.15 (m, 1H, C**H(**Ar)), 2.13–1.96 (m, 2H, C**H**$_2$CH$_2$OH), 1.88 (br s, 1H, O**H**), 1.83–1.71 (m, 2H, CH(Ar)C**H**$_2$(CH$_2$)$_3$CH$_3$), 1.27–1.05 (m, 6H, CH(Ar)CH$_2$(C**H**$_2$)$_3$CH$_3$), 0.85–0.77 (m, 3H, (CH$_2$)$_3$C**H**$_3$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.6, 147.6, 142.8, 124.3, 120.1, 113.9, 99.3, 60.9, 39.7, 38.6, 35.9, 31.8, 27.3, 22.5, 14.0; HRMS (ESI) exact mass calculated for $[M+H]^+$ ($C_{16}H_{23}O_3$) requires *m/z* 247.1810, found *m/z* 247.1803.



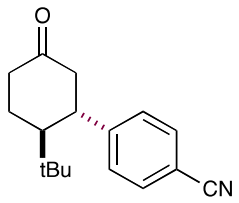
4-(3-Oxopropyl)benzonitrile. Prepared according to the general procedure using 6.6 mg of tris[2-phenylpyridinato-C^2,*N*]iridium(III) (10.0 μmol, 0.01 equiv), 128 mg of terephthalonitrile (1.00 mmol, 1.00 equiv), 561 mg of DABCO (5.00 mmol, 5.00 equiv), 220 μL of propionaldehyde (1.40 mmol, 3.0 equiv), 33 μL of *N*-isopropylbenzylamine (0.20 mmol, 0.20 equiv), 54 μL of water (3.00 mmol, 3.00 equiv), 11 μL of acetic acid (0.20 mmol, 0.20 equiv) and 2.0 mL of DMPU. After 24 h, the reaction mixture was diluted with DCM (40 mL) and added to a separatory funnel containing 25 mL of a 1 M aqueous solution of NaOH. The layers were separated and the aqueous layer was extracted with DCM (2 × 10 mL). The combined organic extracts were washed with brine (40 mL), dried over Na_2SO_4, filtered, and concentrated *in vacuo* to afford a yellow liquid containing the product as a 4:1 mixture of aldehyde and cyanohydrin, as determined by ^{1}H NMR analysis of the crude mixture. Purification of the crude product by flash chromatography (silica gel: 10% to 75% ethyl acetate in hexanes) afforded a pure mixture of the β-aryl aldehyde and cyanohydrin product. This mixture was placed under high vacuum for 8 h to afford the desired aldehyde as a colorless oil (124 mg, 0.78 mmol, 78% yield). The spectral data matched that reported in the literature (*33*).

General Procedure for the Racemic β-Arylation of Ketones: An oven-dried 8 mL vial equipped with a Teflon septum and magnetic stir bar was charged with tris[2-phenylpyridinato-C^2,*N*]iridium(III) (10.0 μmol, 0.01 equiv), the corresponding aromatic nitrile (1.00 mmol, 1.0 equiv), azepane (0.20 mmol, 0.20 equiv), and 1,4-diazabicyclo[2.2.2]octane (5.00 mmol, 5.0 equiv). The vial was purged with a stream of nitrogen and 2.0 mL of DMPU was added via syringe, followed by the corresponding ketone (5.00 mmol, 5.0 equiv), acetic acid (0.20 mmol, 0.20 equiv), and water (3.00 mmol, 3.00 equiv). The reaction mixture was then cooled to –78 ºC and degassed via vacuum evacuation (5 min), backfilled with nitrogen, and warmed to room temperature. This process was repeated three times. After the reaction was thoroughly degassed, the vial was placed approximately 2 cm from a 26 W fluorescent lamp. After the indicated time period, the reaction mixture was diluted with ethyl acetate and added to a separatory funnel containing 25 mL of a saturated solution of NaCl. The layers were separated and the aqueous layer was extracted with EtOAc (3 × 10 mL). The combined organic extracts were dried over Na_2SO_4 and concentrated *in vacuo*. Purification of the crude product by flash chromatography on silica gel using the indicated solvent system afforded the desired β-arylated ketone product.

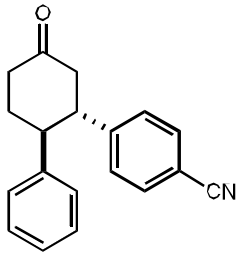


4-(3-Oxocyclohexyl)benzonitrile. Prepared according to the general procedure using 6.6 mg of tris[2-phenylpyridinato-C^2,*N*]iridium(III) (10.0 μmol, 0.01 equiv), 128 mg of terephthalonitrile (1.00 mmol, 1.00 equiv), 561 mg of DABCO (5.00 mmol, 5.00 equiv), 24.0 μL of azepane (0.20 mmol, 0.20 equiv), 1517 μL of cyclohexanone (5.00 mmol, 5.00 equiv), 360 μL of water (20.00 mmol, 20.00 equiv), 11 μL of acetic acid (0.20 mmol, 0.20 equiv) and 2.0 mL of DMPU. After 98 h, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (silica gel: 10% to 100% ethyl acetate in hexanes) to afford

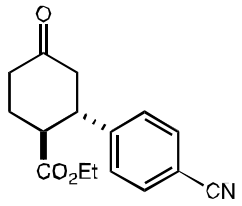
the title compound as a colorless oil (171 mg, 0.86 mmol, 86%). The spectral data for the title compound were identical to the previously reported data (*34*).



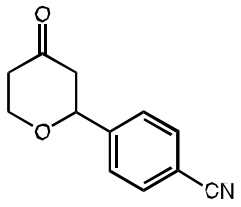
4-(2-*tert*-Butyl-5-oxocyclohexyl)benzonitrile. Prepared according to the general procedure using 6.6 mg of tris[2-phenylpyridinato-C^2,*N*]iridium(III) (10.0 μmol, 0.01 equiv), 128 mg of terephthalonitrile (1.00 mmol, 1.00 equiv), 561 mg of DABCO (5.00 mmol, 5.00 equiv), 22.5 μL of azepane (0.20 mmol, 0.20 equiv), 1.542 g of 4-*t*-butyl cyclohexanone (10.00 mmol, 10.00 equiv), 360 μL of water (5.00 mmol, 5.00 equiv), 11 μL of acetic acid (0.20 mmol, 0.20 equiv) and 2.0 mL of DMPU. After 24 h, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (silica gel: 10% to 100% ethyl acetate in hexanes) to afford the title compounds as an inseparable mixture (179 mg, 0.70 mmol, 70%, >20:1 dr determined by crude ^{1}H NMR in $CDCl_3$, colorless oil). IR (film) 2964, 2230, 1716, 1607, 1504, 1419, 1265, 840, 702 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.53 (d, *J* = 8.3 Hz, 2H, Ar**H**), 7.23 (d, *J* = 8.1 Hz, 2H, Ar**H**), 3.16 (q, *J* = 7.3 Hz, 1H, C**H**Ar), 2.55 (dd, *J* = 14.9, 6.5 Hz, 1H, $CH_2COC\mathbf{H}_2CHAr$), 2.46 (dt, *J* = 17.1, 4.2 Hz, 1H, $C\mathbf{H}_2COCH_2CHAr$), 2.37–2.27 (m, 2H, $C\mathbf{H}_2COC\mathbf{H}_2CHAr$), 2.11 (dq, *J* = 13.9, 4.6 Hz, 1H, $C\mathbf{H}_2CHt$Bu), 1.89 (ddd, *J* = 12.0, 7.9, 4.4 Hz, 1H, $CH_2C\mathbf{H}t$Bu), 1.71 (qd, *J* = 13.1, 4.4 Hz, 1H, $C\mathbf{H}_2CHt$Bu), 0.76 (s, 9H, $C\mathbf{H}_3$); ^{13}C NMR (125 MHz, $CDCl_3$) Key overlapping signals δ 211.5, 152.7, 132.7, 128.4, 118.8, 110.2, 49.4, 47.7, 43.8, 39.7, 34.6, 28.5, 24.7; HRMS (ESI) exact mass calculated for $[M+H]^+$ ($C_{17}H_{22}NO$) requires *m/z* 256.1695, found *m/z* 256.1696. The relative stereochemistry between C3 and C4 was assigned as a *trans*-configuration based on 2D NOESY spectra.



4-(5-Oxo-2-phenylcyclohexyl)benzonitrile. Prepared according to the general procedure using 6.6 mg of tris[2-phenylpyridinato-C^2,*N*]iridium(III) (10.0 μmol, 0.01 equiv), 128 mg of terephthalonitrile (1.00 mmol, 1.00 equiv), 561 mg of DABCO (5.00 mmol, 5.00 equiv), 24.0 μL of azepane (0.20 mmol, 0.20 equiv), 870 mg of 4-phenylcyclohexanone (5.00 mmol, 5.00 equiv), 90 μL of water (5.00 mmol, 5.00 equiv), 11 μL of acetic acid (0.20 mmol, 0.20 equiv) and 2.0 mL of DMPU. After 18 h, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (silica gel: 10% to 100% ethyl acetate in hexanes) to afford the title compounds as an inseparable mixture (216 mg, 0.79 mmol, 79%, >20:1 dr determined by crude ^{1}H NMR in $CDCl_3$, colorless oil). IR (film) 2937, 2863, 2228, 1710, 1607, 1495, 1452, 1087 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.46 (d, *J* = 8.2 Hz, 2H, Ar**H**), 7.20–7.13 (m, 4H, Ar**H**), 7.13–7.05 (m, 1H, Ar**H**), 7.01 (d, *J* = 7.2 Hz, 2H, Ar**H**), 3.33 (td, *J* = 12.6, 12.5, 4.1 Hz, 1H, C**H**Ar), 3.23 (td, *J* = 11.7, 11.7, 3.2 Hz, 1H, C**H**Ar), 2.83–2.59 (m, 4H, C$\mathbf{H}_2$COC$\mathbf{H}_2$), 2.39–2.29 (m, 1H, C$\mathbf{H}_2$CHAr), 2.21–2.09 (m, 1H, C$\mathbf{H}_2$CHAr); ^{13}C NMR (125 MHz, $CDCl_3$) δ 209.3, 148.04, 141.9, 132.4, 128.7, 128.2, 127.4, 126.9, 118.8, 110.5, 50.8, 49.1, 48.6, 41.5, 34.3; HRMS (ESI) exact mass calculated for $[M+H]^+$ ($C_{19}H_{18}NO$) requires *m/z* 276.1388, found *m/z* 276.1381. The relative stereochemistry between C3 and C4 was assigned as a *trans*-configuration based on 2D NOESY spectra.

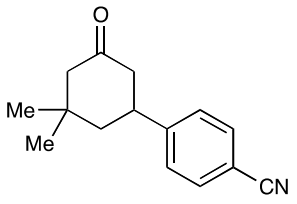


Ethyl 2-(4-cyanophenyl)-4-oxocyclohexanecarboxylate. Prepared according to the general procedure using 6.6 mg of tris[2-phenylpyridinato-C^2,*N*]iridium(III) (10.0 μmol, 0.01 equiv), 128 mg of terephthalonitrile (1.00 mmol, 1.00 equiv), 561 mg of DABCO (5.00 mmol, 5.00 equiv), 24.0 μL of azepane (0.20 mmol, 0.20 equiv), 791 μL of ethyl 4-oxocyclohexanecarboxylate (5.00 mmol, 5.00 equiv), 180 μL of water (10.0 mmol, 10.0 equiv), 11 μL of acetic acid (0.20 mmol, 0.20 equiv) and 2.0 mL of DMPU. After 42 h, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (silica gel: 10% to 100% ethyl acetate in hexanes; then 10% to 50% ethyl acetate in hexanes) to afford the title compound as a colorless oil (219 mg, 0.81 mmol, 81%, >20:1 dr determined by crude ^{1}H NMR in $CDCl_3$). IR (film) 2938, 2229, 1717, 1261, 1177, 1091, 1025, 734 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.58 (d, *J* = 8.2 Hz, 2H, Ar**H**), 7.31 (d, *J* = 8.2 Hz, 2H, Ar**H**), 3.93–3.84 (m, 2H, $CO_2C\mathbf{H}_2CH_3$), 3.32 (td, *J* = 11.5, 11.4, 5.4 Hz, 1H, C**H**Ar), 2.96 (td, *J* = 11.4, 11.3, 3.4 Hz, 1H, C**H**CO_2Et), 2.59–2.40 (m, 4H, $C\mathbf{H}_2COC\mathbf{H}_2$), 2.34–2.22 (m, 2H, $C\mathbf{H}_2CHCO_2Et$), 0.93 (t, 3H, *J* = 7.1 Hz, $CO_2CH_2C\mathbf{H}_3$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 207.7, 173.1, 147.1, 132.7, 128.2, 118.7, 111.3, 60.9, 48.1, 47.2, 46.6, 39.9, 28.7, 14.1; HRMS (ESI) exact mass calculated for $[M+H]^+$ ($C_{16}H_{18}NO_3$) requires *m/z* 272.1287, found *m/z* 272.1284. The relative stereochemistry between C3 and C4 was assigned as a *trans*-configuration based on 2D NOESY spectra.



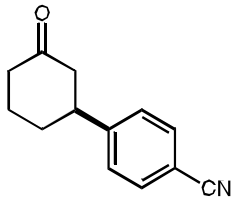
4-(4-Oxotetrahydro-2*H*-pyran-2-yl)benzonitrile. Prepared according to the general procedure using 6.6 mg of tris[2-phenylpyridinato-C^2,*N*]iridium(III) (10.0 μmol, 0.01 equiv), 128 mg of terephthalonitrile (1.00 mmol, 1.00 equiv), 561 mg of DABCO (5.00 mmol, 5.00 equiv), 20.0 μL

of piperidine (0.20 mmol, 0.20 equiv), 0.92 mL of tetrahydro-4*H*-pyran-4-one (10.0 mmol, 10.0 equiv), 54 μL of water (3.00 mmol, 3.00 equiv), 11 μL of acetic acid (0.20 mmol, 0.20 equiv) and 2.0 mL of DMPU. After 67 h, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (silica gel: 10% to 100% ethyl acetate in hexanes; then 0% to 25% ether in DCM) to afford the title compounds as a colorless oil (127 mg, 0.63 mmol, 63%). IR (film) 2972, 2862, 2228, 1715, 1247, 1235, 1152, 1088, 1026, 831 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.64 (d, *J* = 8.3 Hz, 2H, Ar**H**), 7.46 (d, *J* = 8.2 Hz, 2H, Ar**H**), 4.67 (dd, *J* = 11.5, 2.7 Hz, 1H, OC**H**Ar), 4.49–4.38 (m, 1H, C$\mathbf{H}_2$O), 3.82 (td, *J* = 12.1 12.0, 2.8 Hz, 1H, C$\mathbf{H}_2$O), 2.76–2.58 (m, 2H, C$\mathbf{H}_2$COC$\mathbf{H}_2$), 2.56–2.36 (m, 2H, C$\mathbf{H}_2$COC$\mathbf{H}_2$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 205.3, 146.0, 132.7, 126.3, 118.7, 112.0, 78.8, 66.9, 49.8, 42.1; HRMS (ESI) exact mass calculated for $[M+H]^+$ ($C_{12}H_{12}NO_2$) requires *m/z* 202.0868, found *m/z* 202.0869.



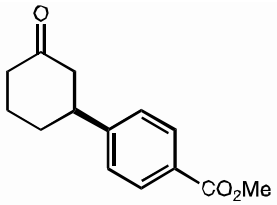
4-(3,3-Dimethyl-5-oxocyclohexyl)benzonitrile. Prepared according to the general procedure using 6.6 mg of tris[2-phenylpyridinato-C^2,*N*]iridium(III) (10.0 μmol, 0.01 equiv), 128 mg of terephthalonitrile (1.00 mmol, 1.00 equiv), 561 mg of DABCO (5.00 mmol, 5.00 equiv), 48.0 μL of azepane (0.40 mmol, 0.40 equiv), 1.39 mL of 3,3-dimethylcyclohexanone (10.0 mmol, 10.0 equiv), 54 μL of water (3.00 mmol, 3.00 equiv), 11 μL of acetic acid (0.20 mmol, 0.20 equiv) and 2.0 mL of DMPU. After 53 h, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified by flash chromatography (silica gel: 10% to 100% ethyl acetate in hexanes) to afford the title compound as a colorless oil (188 mg, 0.83 mmol, 83%). IR (film) 2958, 2227, 1708, 1608, 1271, 1230, 842, 734 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.61 (d, *J* = 8.3 Hz, 2H, Ar**H**), 7.33 (d, *J* = 8.2 Hz, 2H, Ar**H**), 3.19 (tt, *J* = 12.66, 4.31 Hz, 1H, C**H**Ar), 2.56–2.46 (m, 1H, C$\mathbf{H}_2$CO), 2.43–2.16 (m, 3H, C$\mathbf{H}_2$COC$\mathbf{H}_2$), 1.88–1.70 (m, 2H, C$\mathbf{H}_2$CHAr), 1.12

(s, 3H, C(C**H**$_3$)$_2$), 1.00 (s, 3H, C(C**H**$_3$)$_2$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 209.97, 149.71, 132.74, 127.77, 118.95, 110.91, 54.38, 47.68, 45.98, 40.63, 35.66, 32.33, 25.85; HRMS (ESI) exact mass calculated for $[M+H]^+$ ($C_{15}H_{18}NO$) requires *m/z* 228.1388, found *m/z* 228.1380.



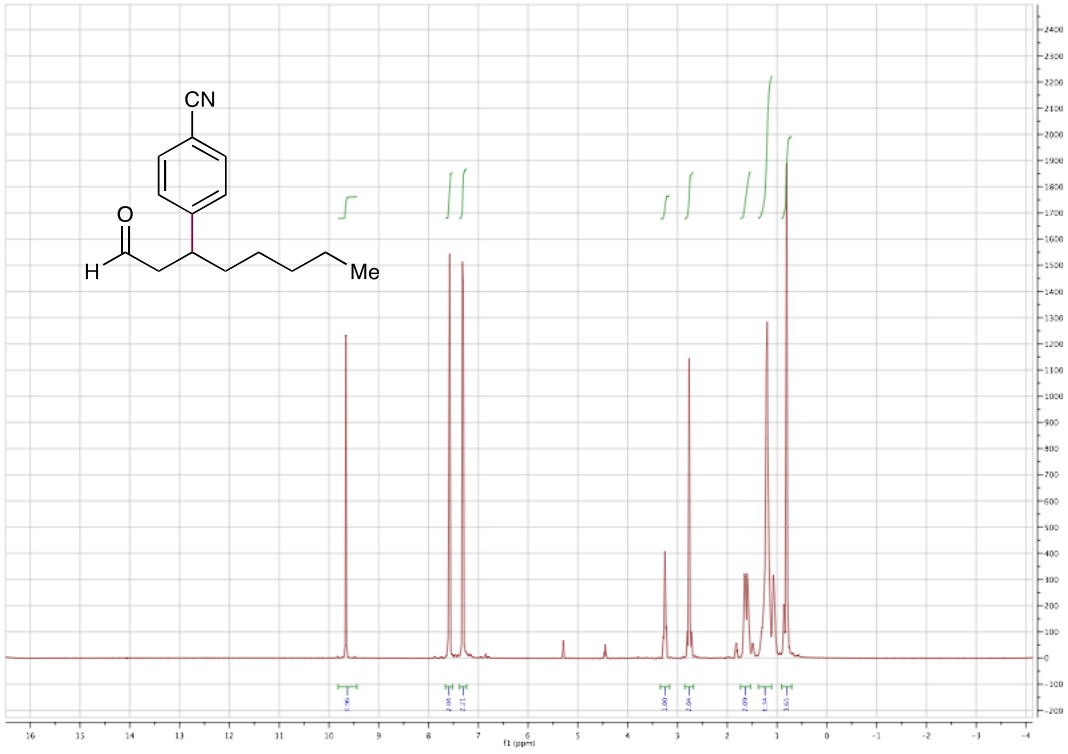
(*S*)-4-(3-Oxocyclohexyl)benzonitrile. 20 mg of (*9S*)-9-amino-9-deoxycinchonidine•3HCl (0.020 mmol, 0.20 equiv) (*35*) was converted to the free base by being placed in a separatory funnel with 10 mL of 1 M NaOH. The solution was extracted with DCM (3 × 10 mL) and concentrated *in vacuo*. The catalyst was then redissolved in DCM and transferred to a 8 mL vial and then concentrated *in vacuo*. The vial was then equipped with a Teflon septum and magnetic stir bar and charged with 1.6 mg of tris[2-phenylpyridinato-C^2,*N*]iridium(III) (2.50 μmol, 0.01 equiv), 32 mg of terephthalonitrile (0.25 mmol, 1.0 equiv), and 140 mg of 1,4-diazabicyclo[2.2.2]octane (1.25 mmol, 5.0 equiv). The vial was purged with a stream of nitrogen and 0.5 mL of DMPU was added via syringe, followed by 259 μL of cyclohexanone (2.50 mmol, 10.0 equiv), 2.86 μL of acetic acid (0.05 mmol, 0.20 equiv), and 14.0 μL of water (0.05 mmol, 3.00 equiv). The reaction mixture was then cooled to –78 ºC and degassed via vacuum evacuation (5 min), backfilled with nitrogen, and warmed to room temperature. This process was repeated three times. After the reaction was thoroughly degassed, the vial was placed approximately 2 cm from a 26 W fluorescent lamp. After the indicated time period, the reaction mixture was diluted with ethyl acetate and added to a separatory funnel containing 25 mL of a saturated solution of NaCl. The layers were separated and the aqueous layer was extracted with EtOAc (3 × 10 mL). The combined organic extracts were dried over Na_2SO_4 and concentrated *in vacuo*. Purification of the crude product by flash chromatography on silica gel (10% to 100% ethyl acetate in hexanes) afforded the desired product as a colorless oil (41 mg, 0.205 mmol, 82%). The spectral data for the title compound were identical to the previously reported data (*34*). $[\alpha]_D$ = –2.03 (c = 1.0,

$CHCl_3$, 22.0 °C); SFC analysis (IA, 5-50% MeCN/CO_2, 3.0 mL/min, 220 nm) indicates 50% ee: t_R(minor) = 5.40 minutes, t_R(major) = 6.01 minutes.



Confirmation of the absolute configuration of the major enantiomer of 4-(3-oxocyclohexyl)benzonitrile. (*S*)-methyl 4-(3-Oxocyclohexyl)benzoate. The absolute configuration of the title compound was determined by comparison of the observed optical rotation of methyl 4-(3-oxocyclohexyl)benzoate, which was synthesized as follows: To a solution of 50 mg (0.25 mmol, 1.0 equiv) of 4-(3-oxocyclohexyl)benzonitrile (56% ee) in water (1 mL) was added 127 mg of KOH (2.26 mmol, 9.0 equiv). The reaction mixture was then refluxed for six hours while under nitrogen. After six hours, the reaction mixture was cooled to 0 °C and acidified with concentrated HCl to a pH of 1. The aqueous mixture was then extracted with DCM (3 × 10 mL), dried with sodium sulfate, and concentrated *in vacuo* to provide the crude acid. This mixture was then redissolved in MeOH (1 mL) and concentrated sulfuric acid (6 μL) was added to the solution. The reaction mixture was refluxed under nitrogen for sixteen hours and then cooled to room temperature and the methanol was evaporated *in vacuo*. The residue was redissolved in water (5 mL) and DCM (10 mL) and the layers were separated. The aqueous layer was extracted with DCM (2 × 10 mL). The combined organic layers were dried with sodium sulfate and then concentrated *in vacuo*. The crude material was purified by flash chromatography on silica gel (10% to 100% ethyl acetate in hexanes) to afford the desired product as a colorless oil (11 mg, 0.047 mmol, 19%). The spectral data for the title compound were identical to the previously reported data (*36*). The absolute configuration of the title compound was determined by comparison of the observed optical rotation ($[\alpha]_D$ = –2.72 (c = 0.87, $CDCl_3$, 20.8 °C), 56% ee) to the reported optical rotation for the (*S*)-isomer ($[\alpha]_D$ = –8.6 (c = 1.22, $CDCl_3$, 20.0 °C), 87% ee) (*37*). Therefore, the absolute configuration of the title compound is (*S*).

Spectra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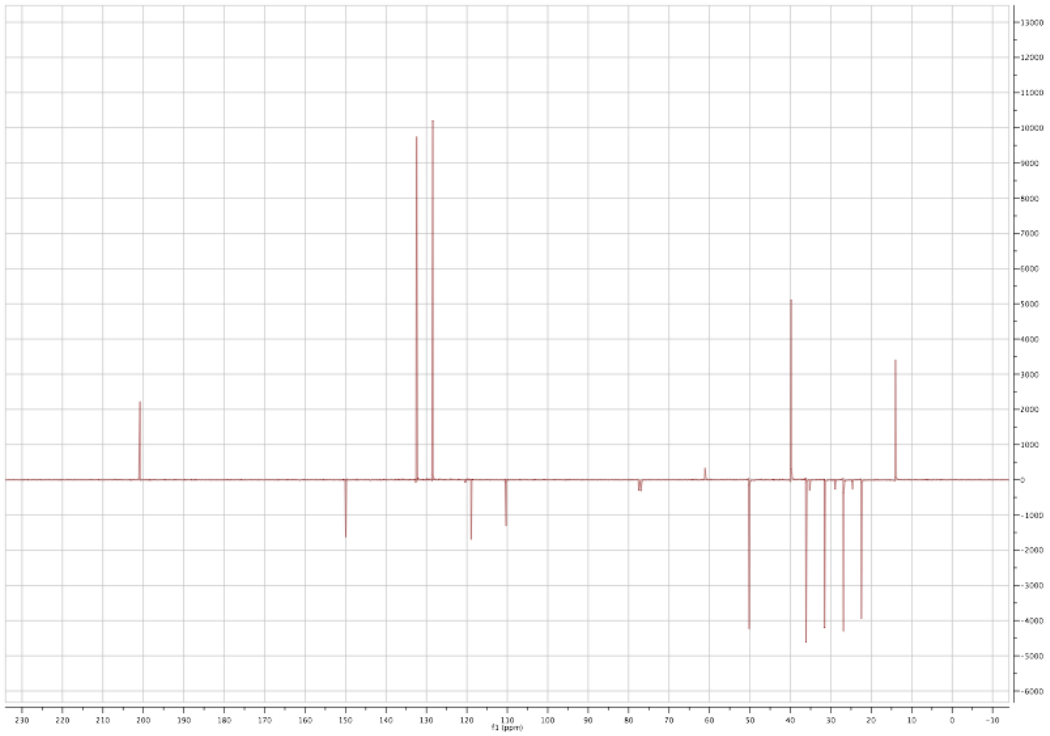

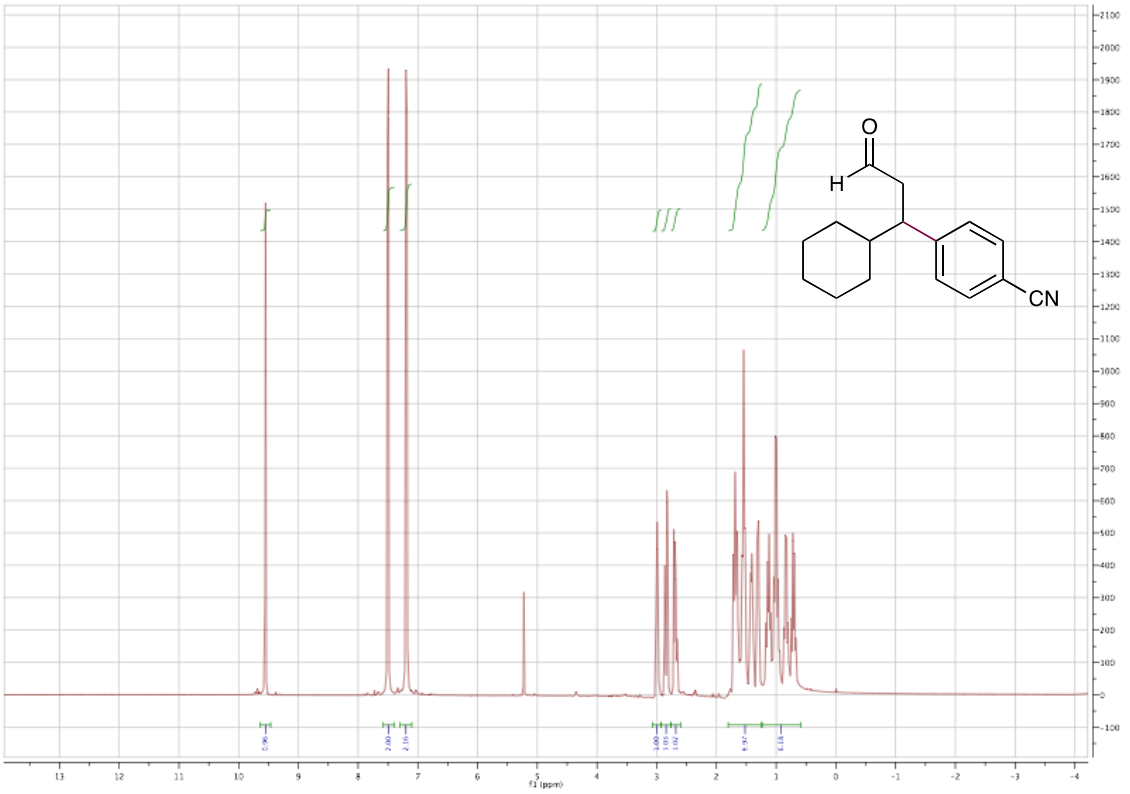
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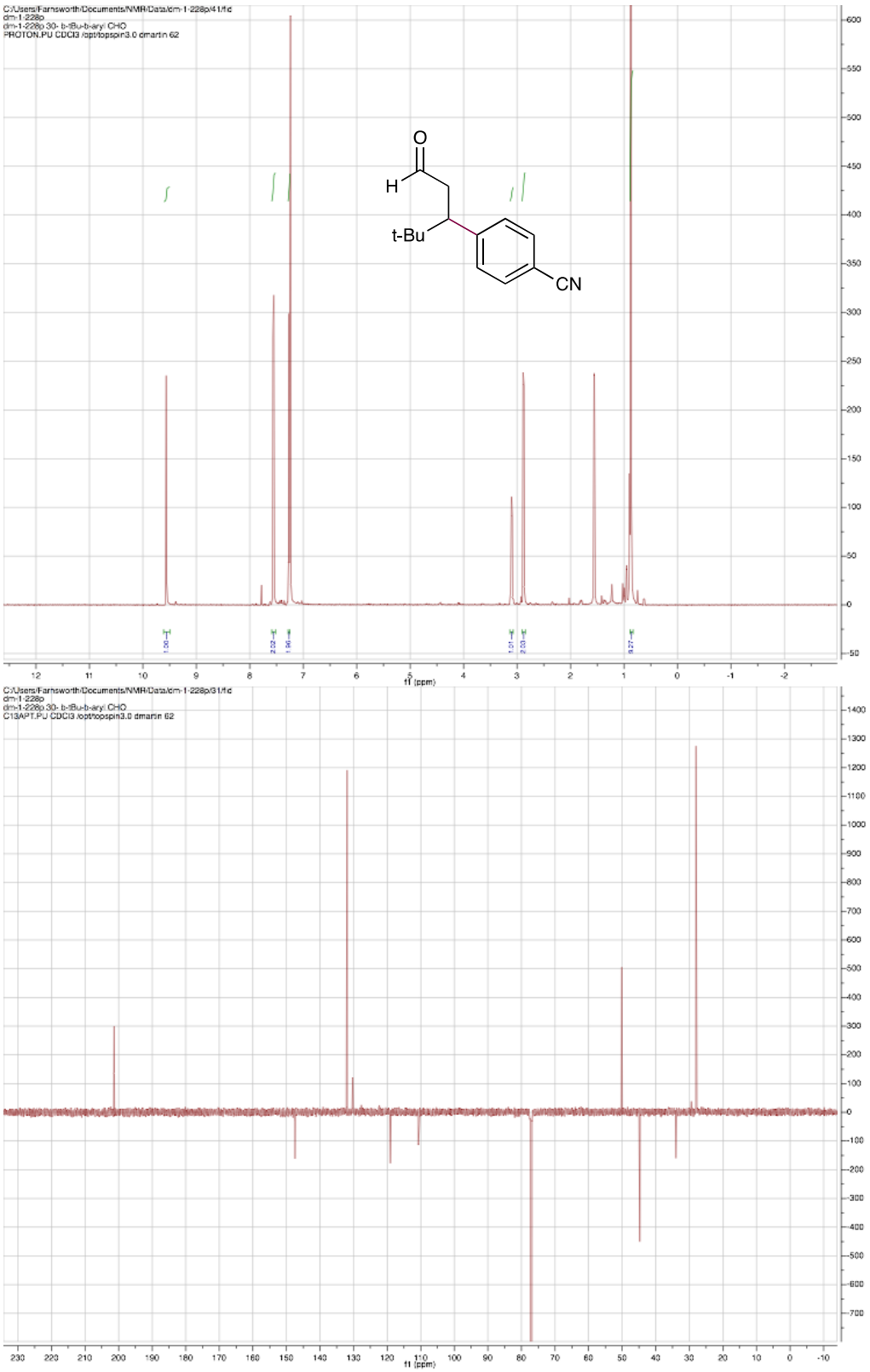
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t-Bu
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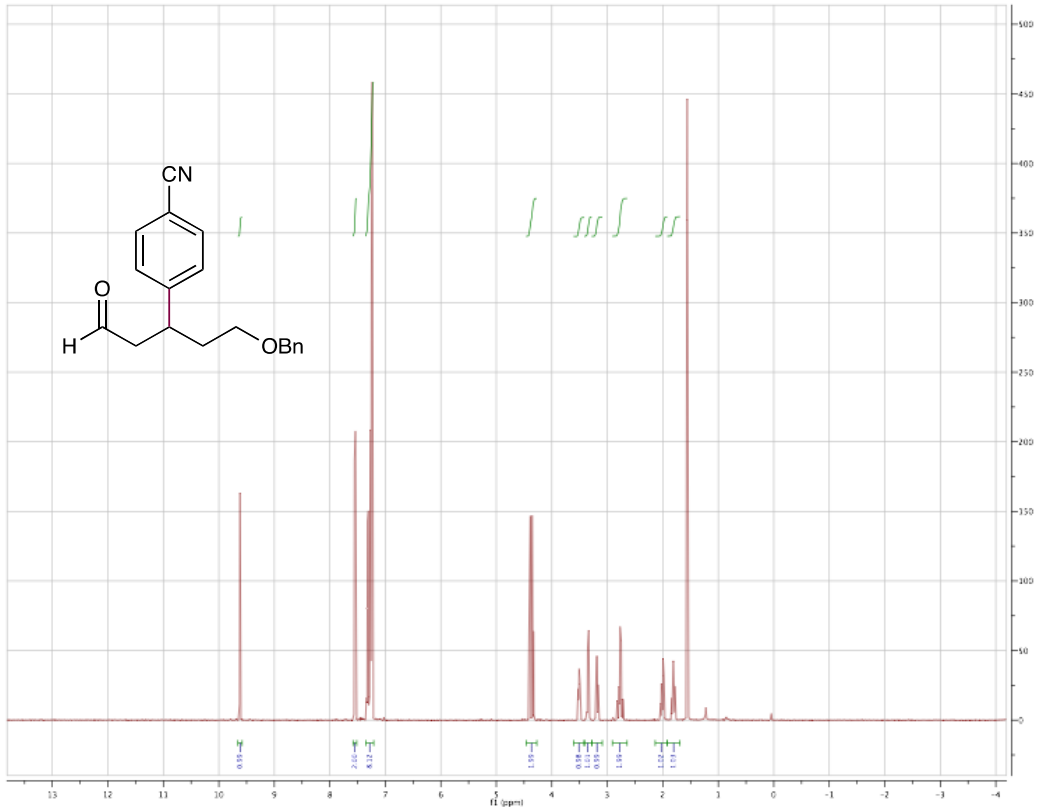
f1 (ppm)
f1 (ppm)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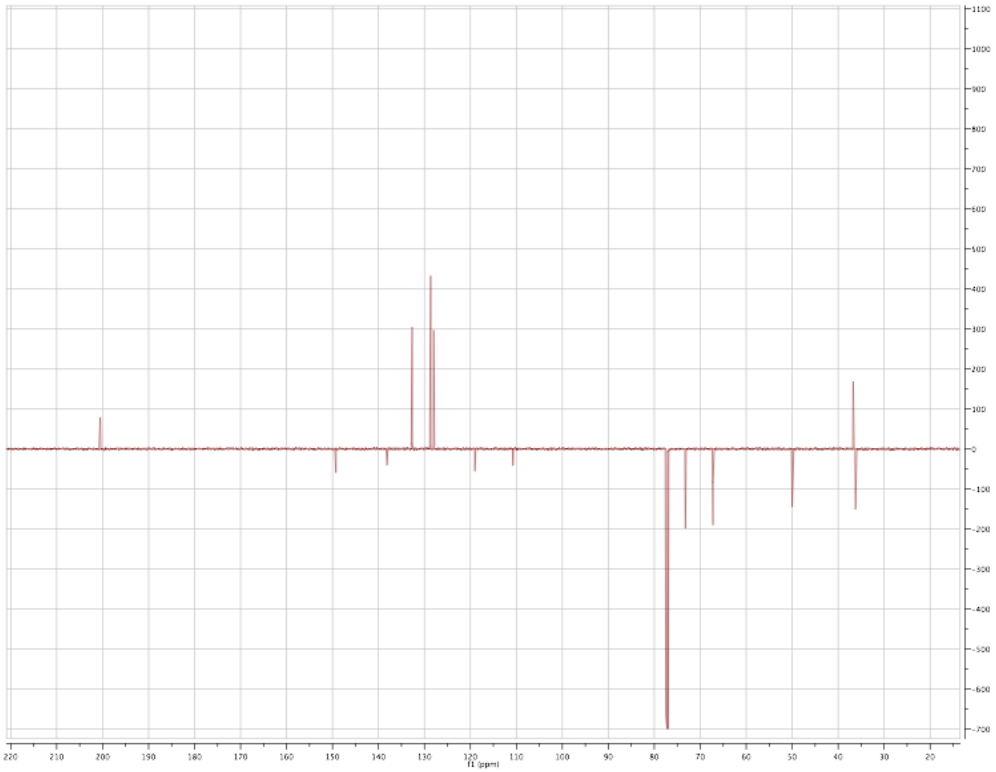

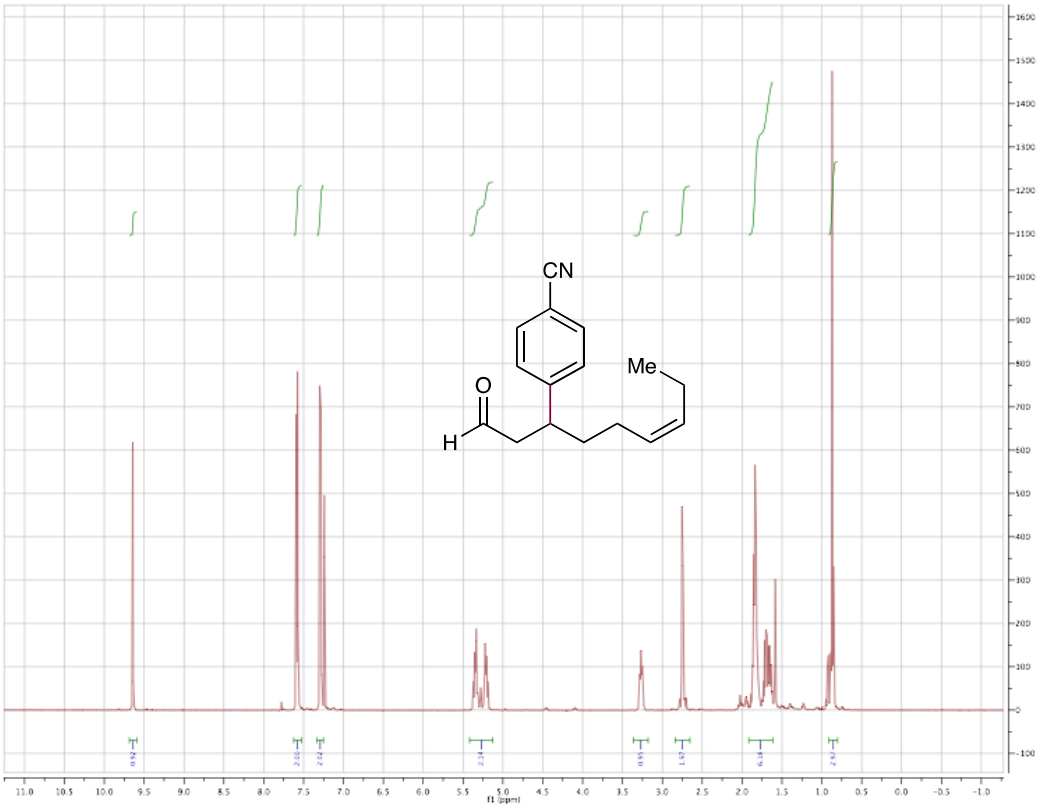
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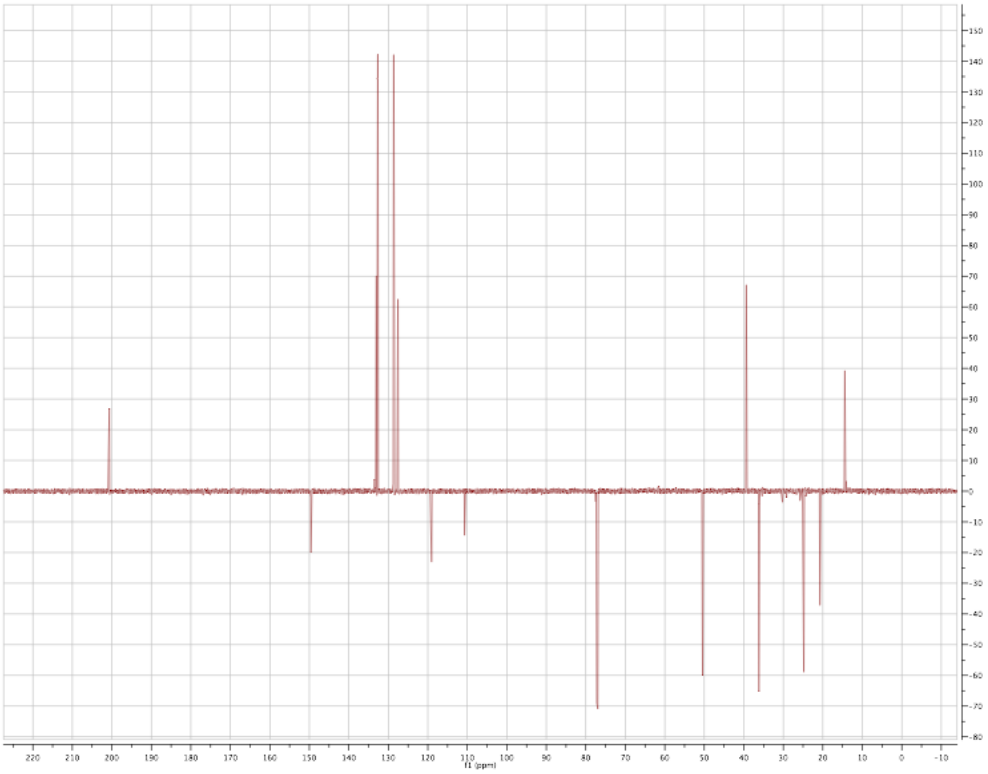

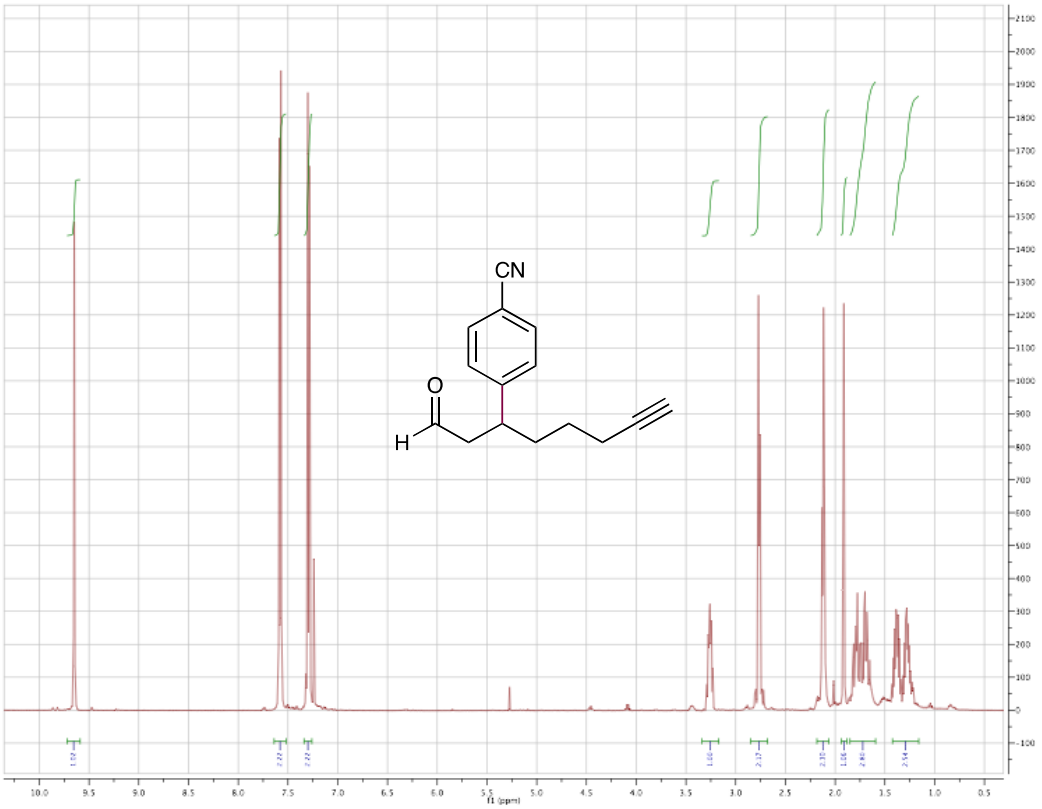
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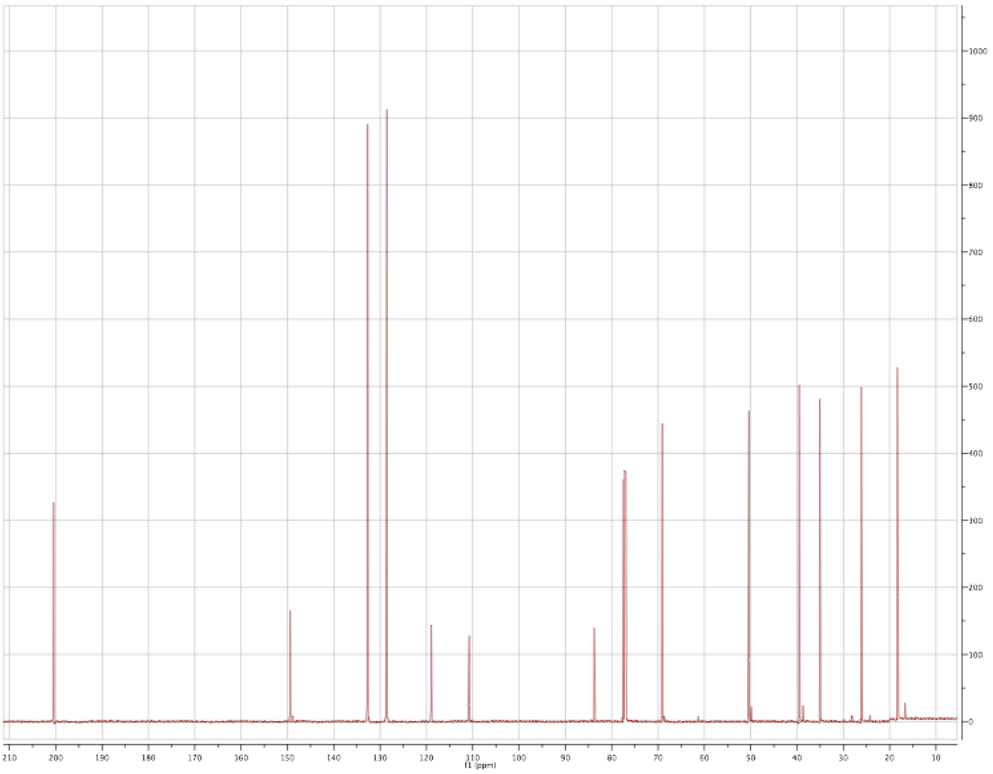

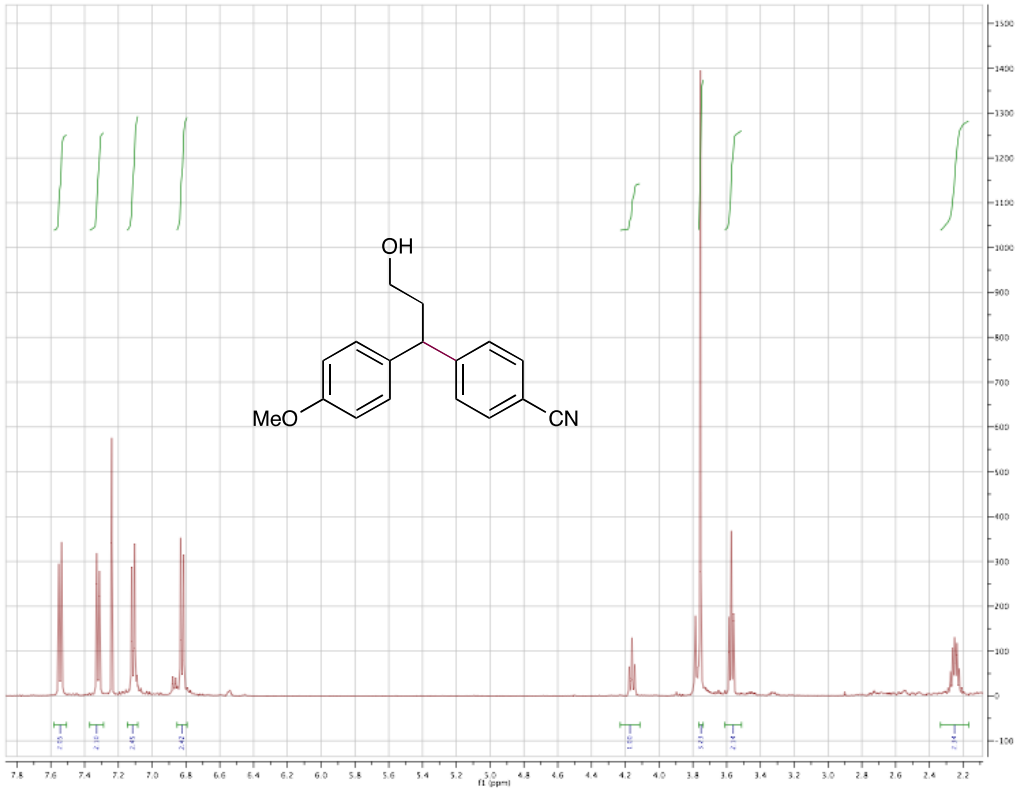
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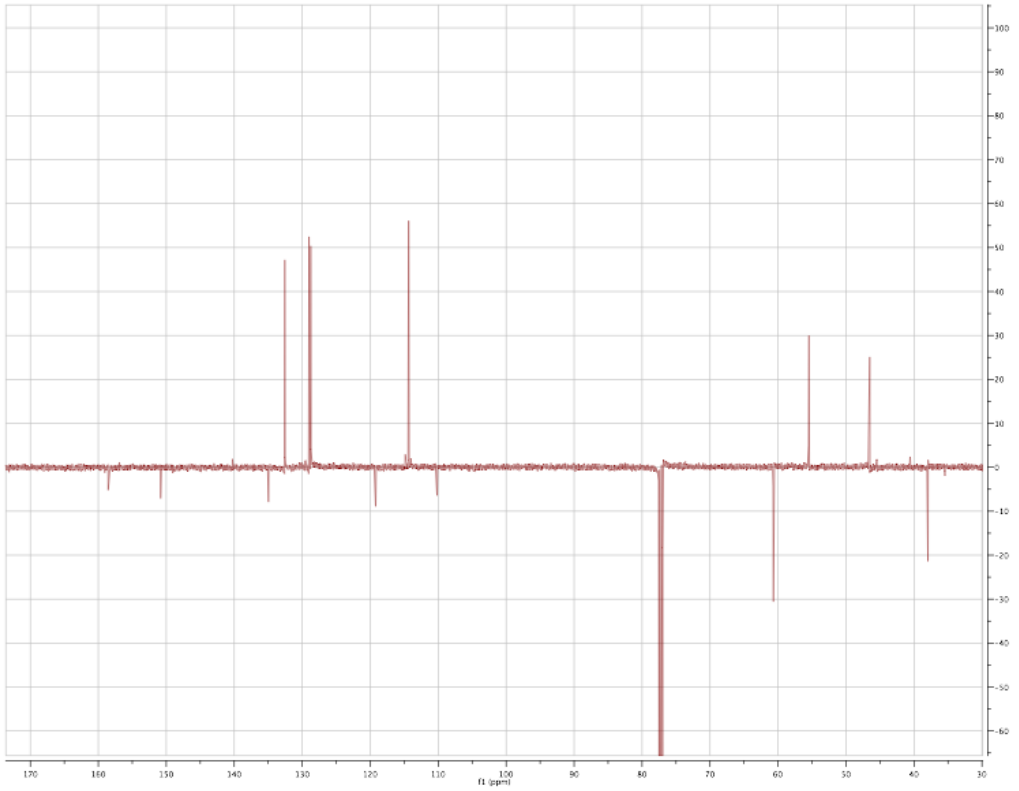

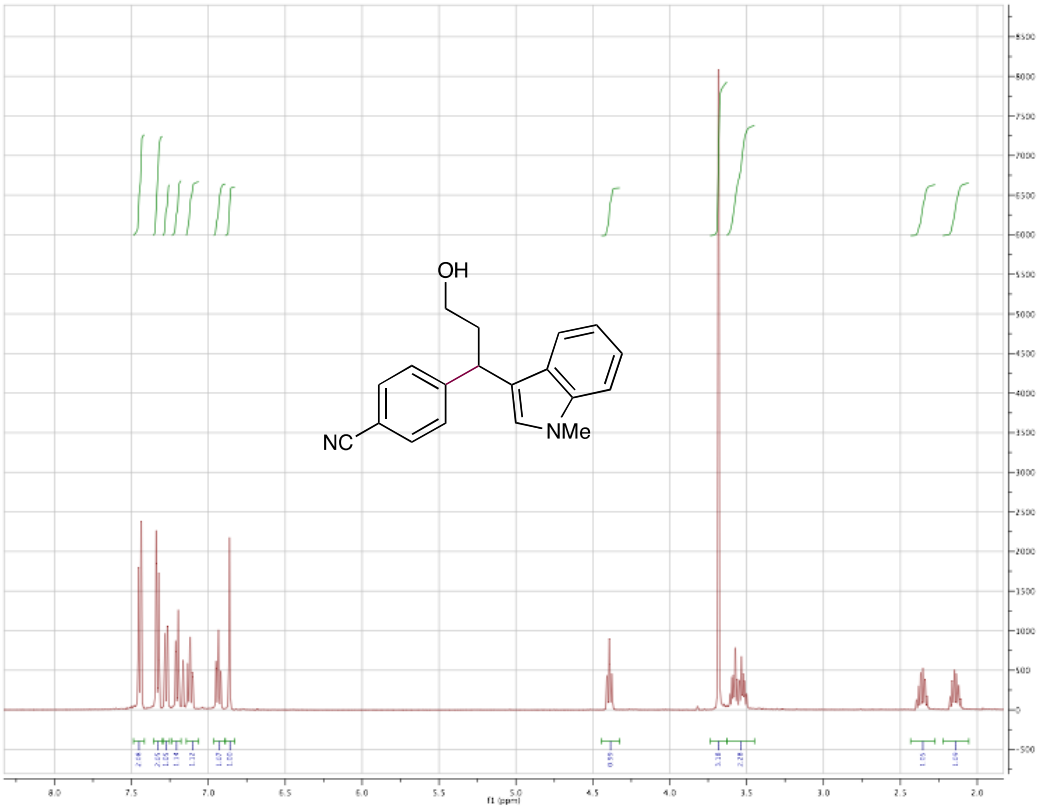
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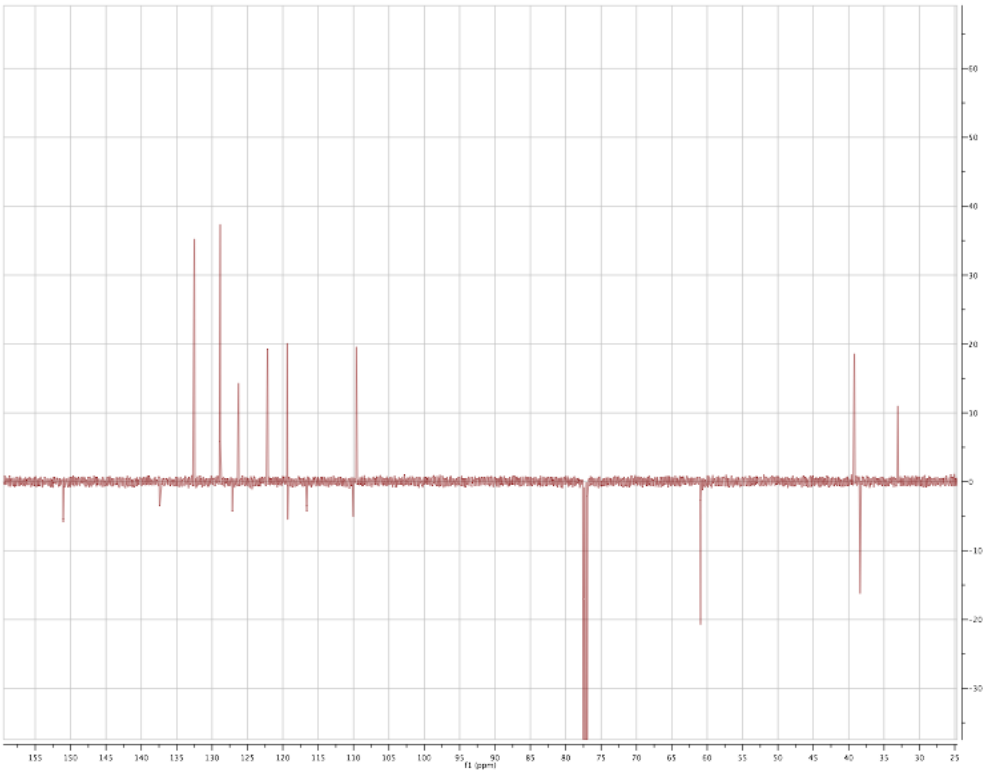

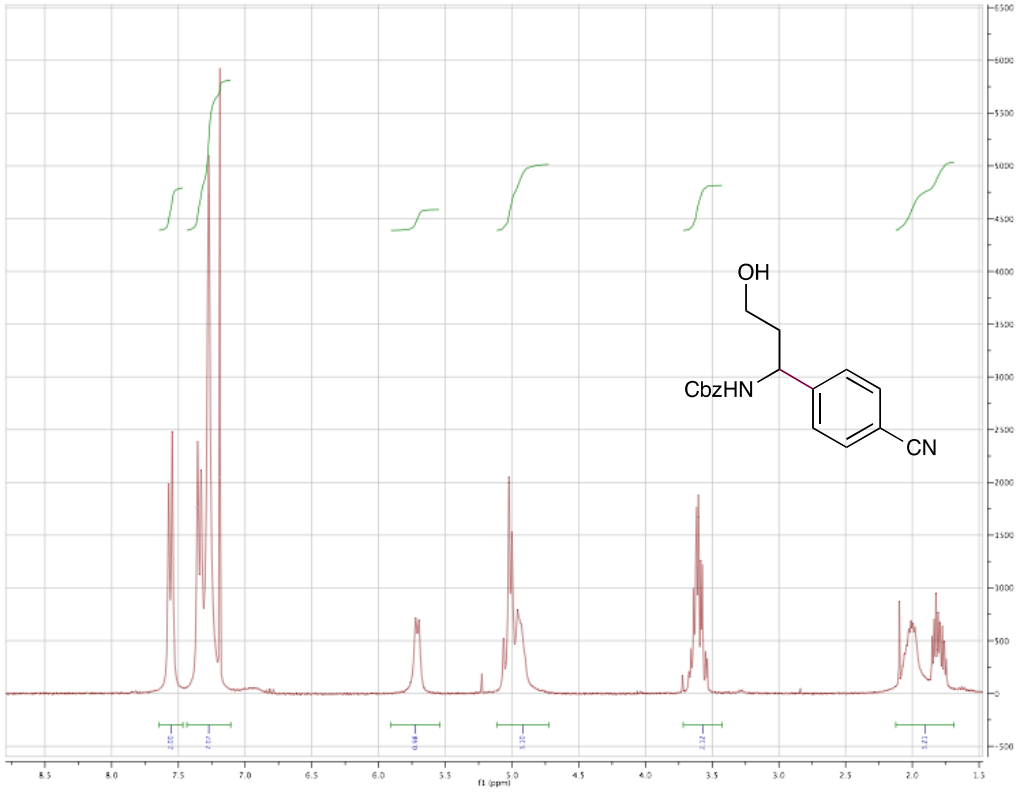
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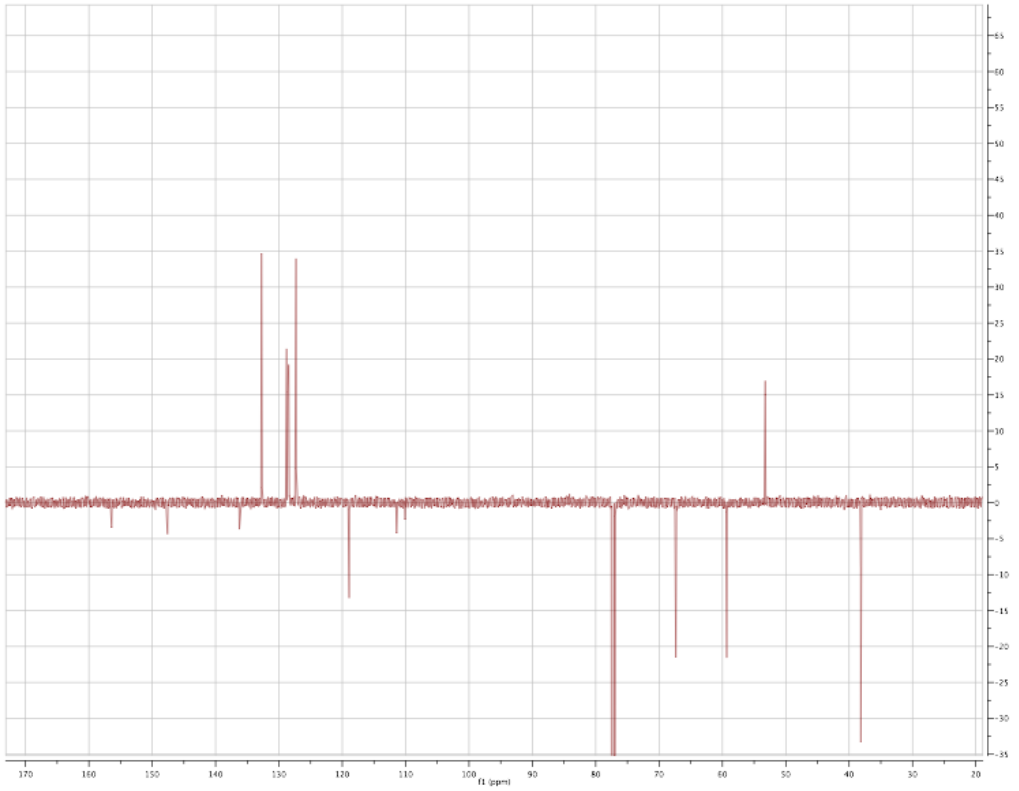

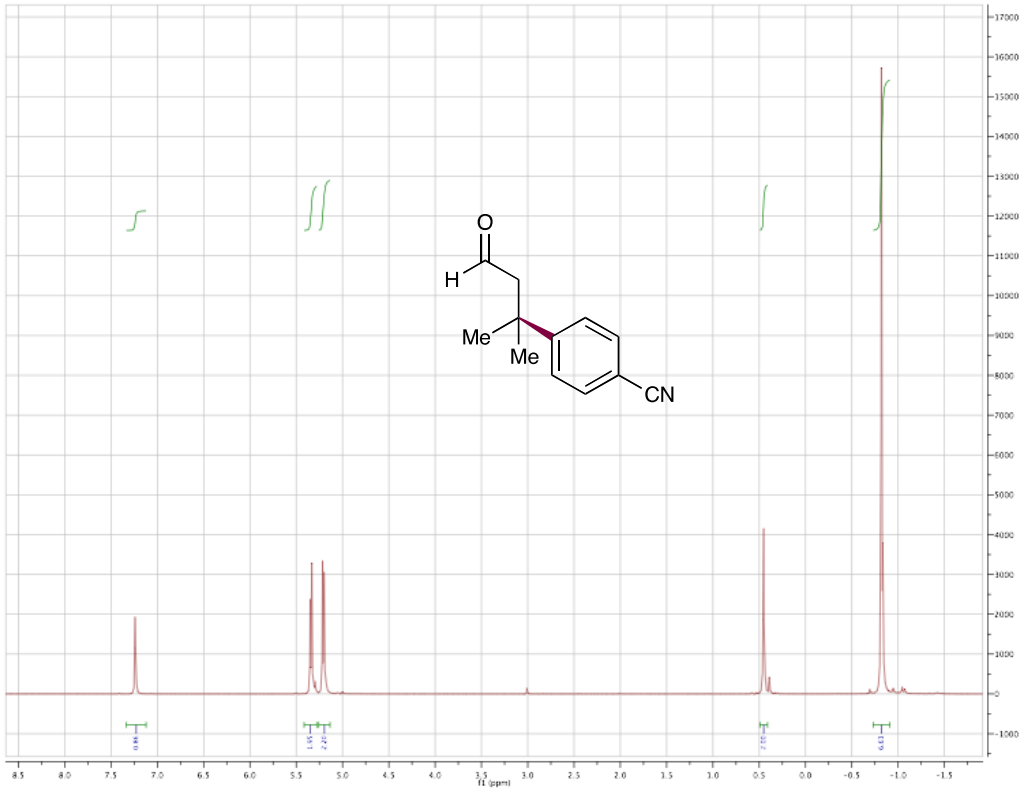
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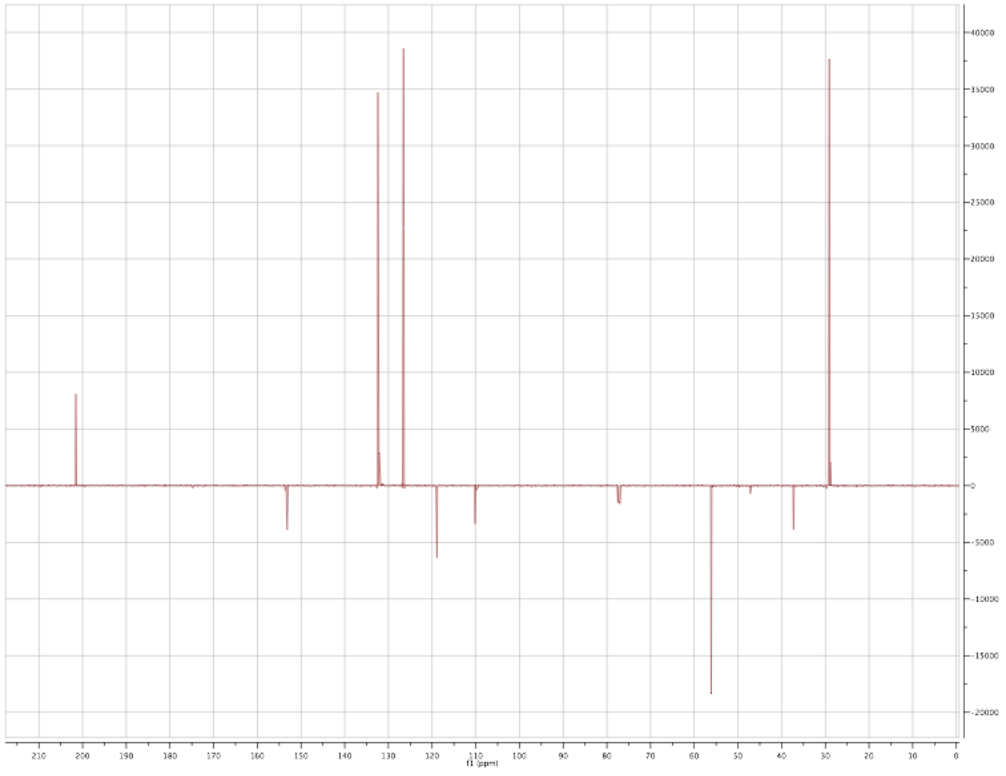

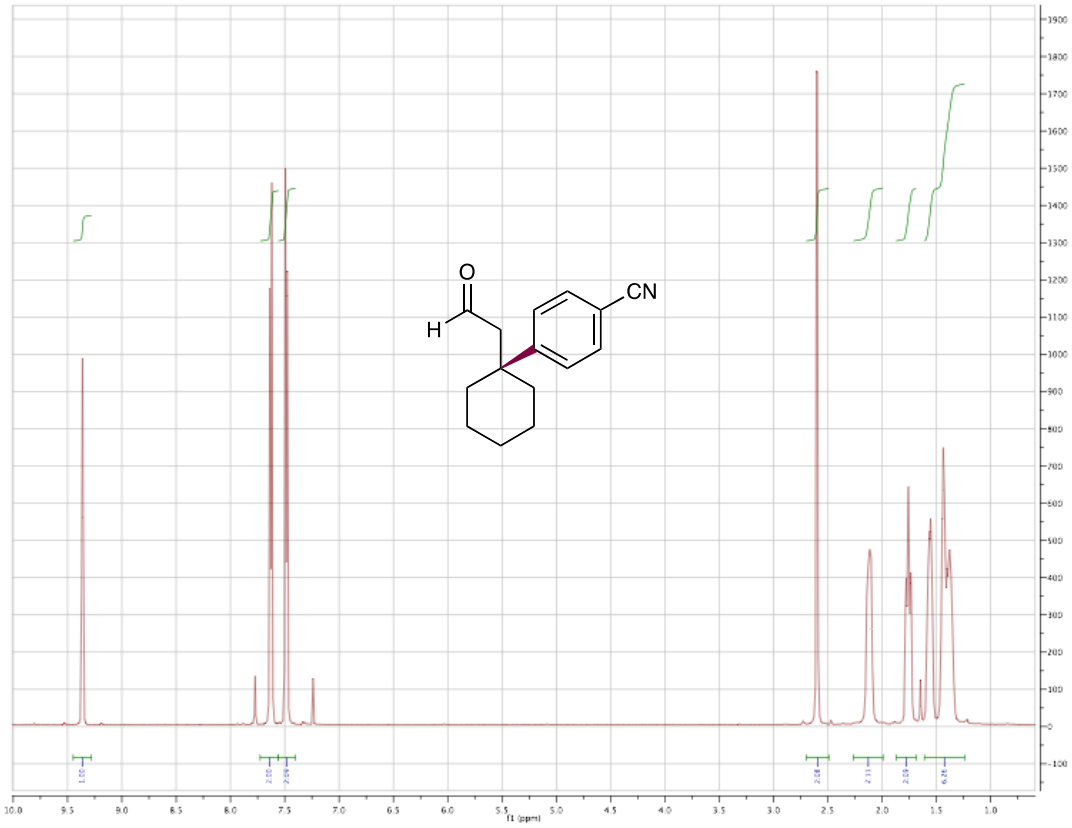
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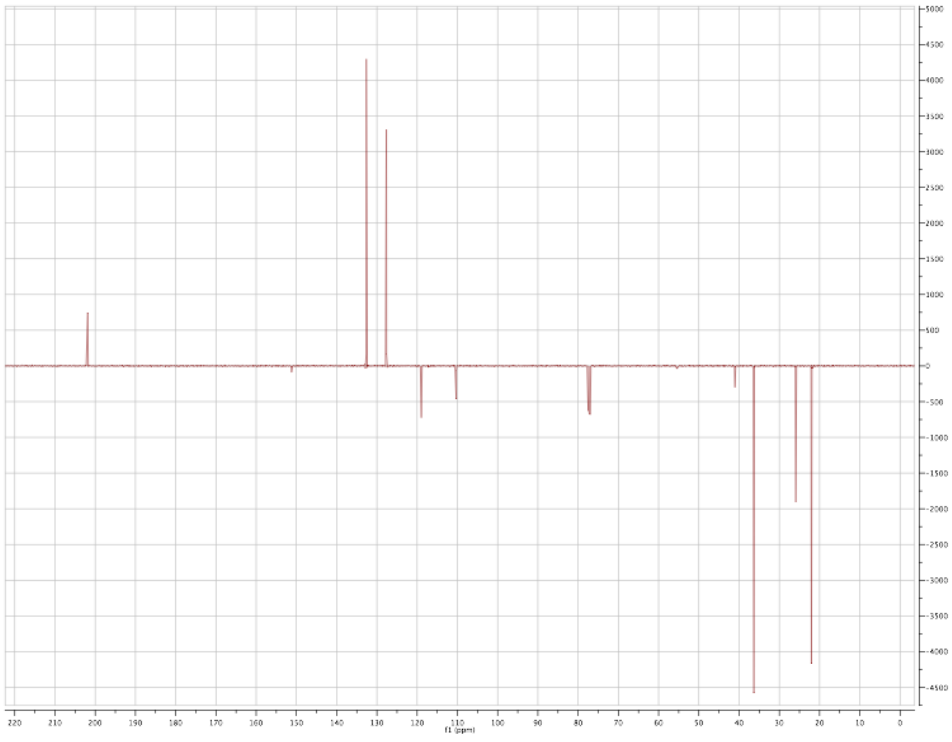

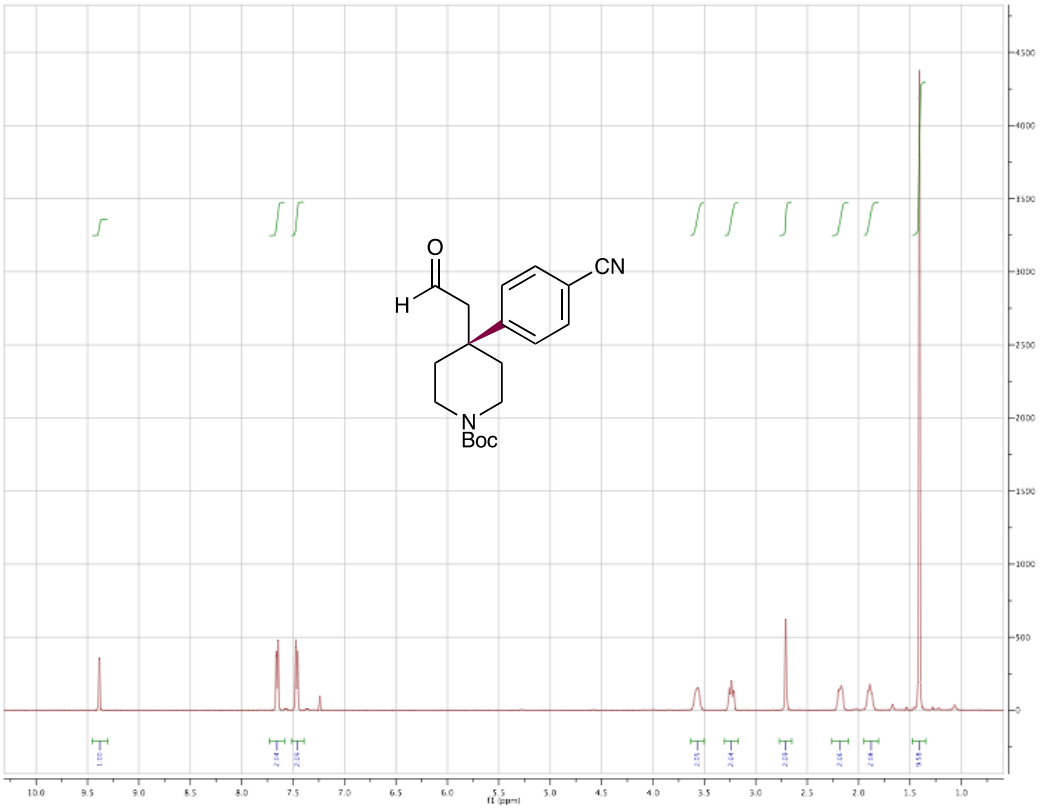
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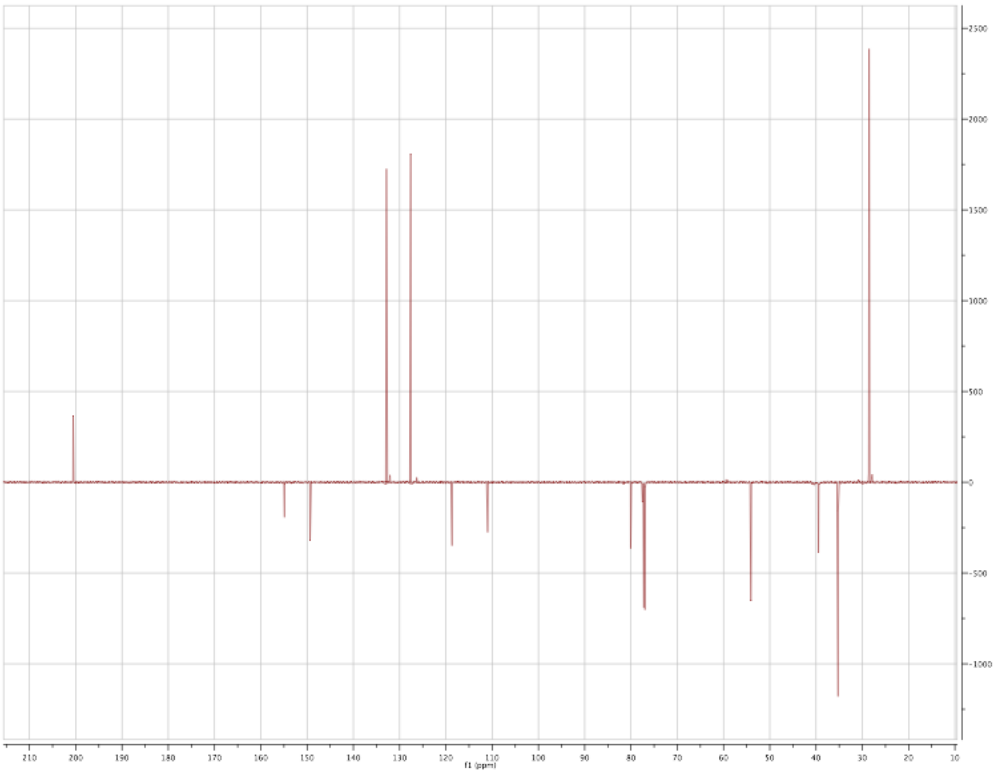

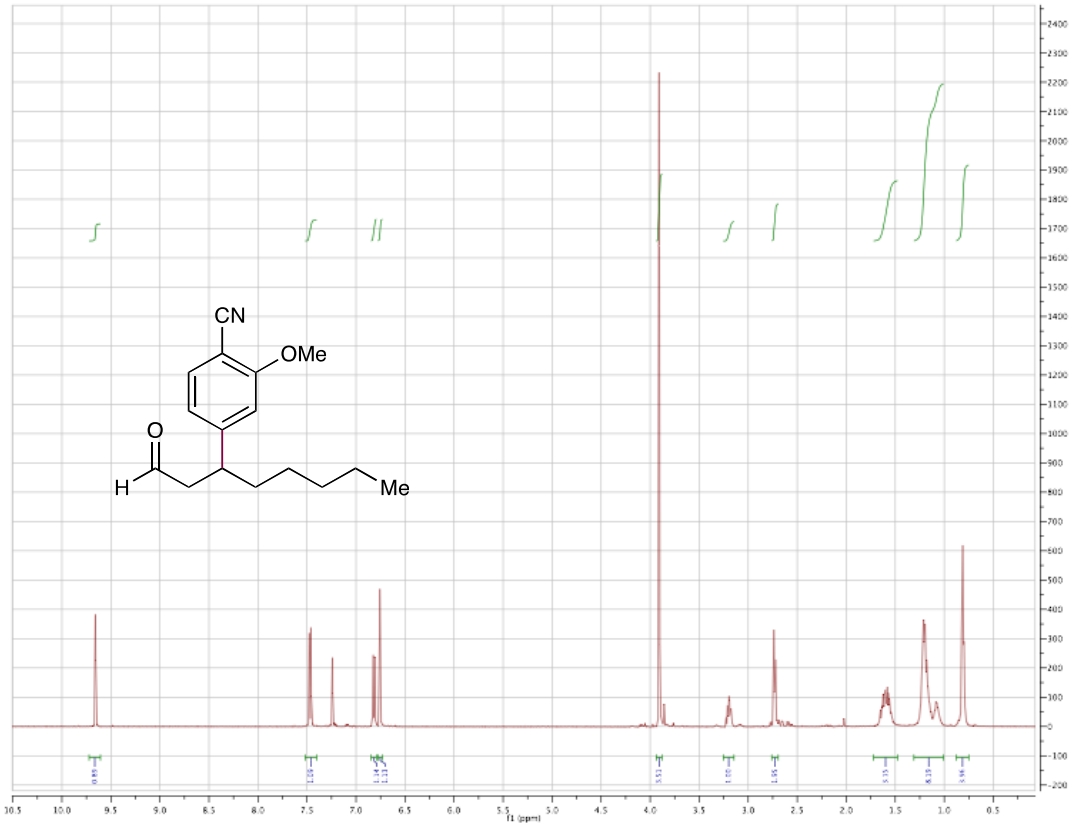
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OMe
O
H
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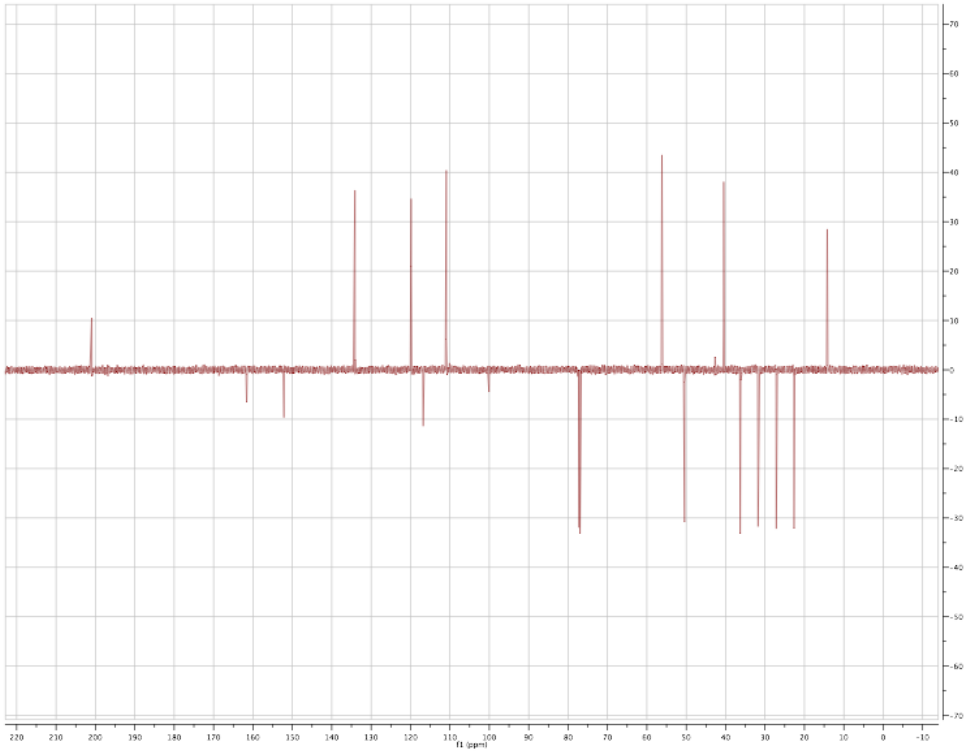

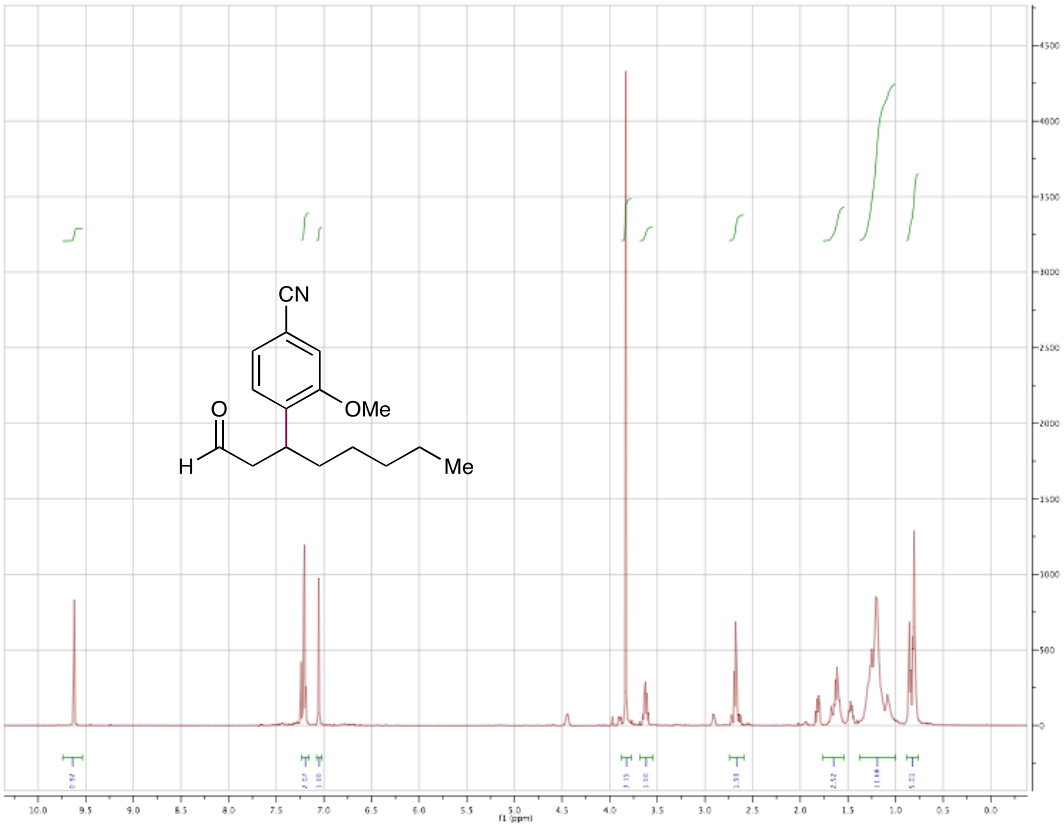
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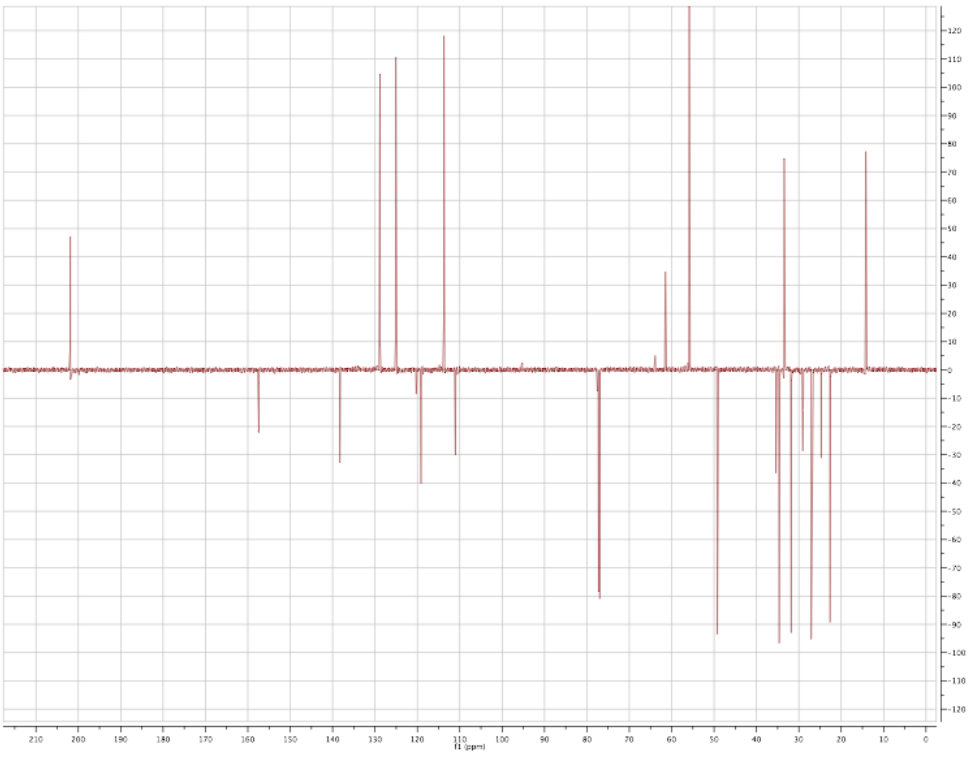

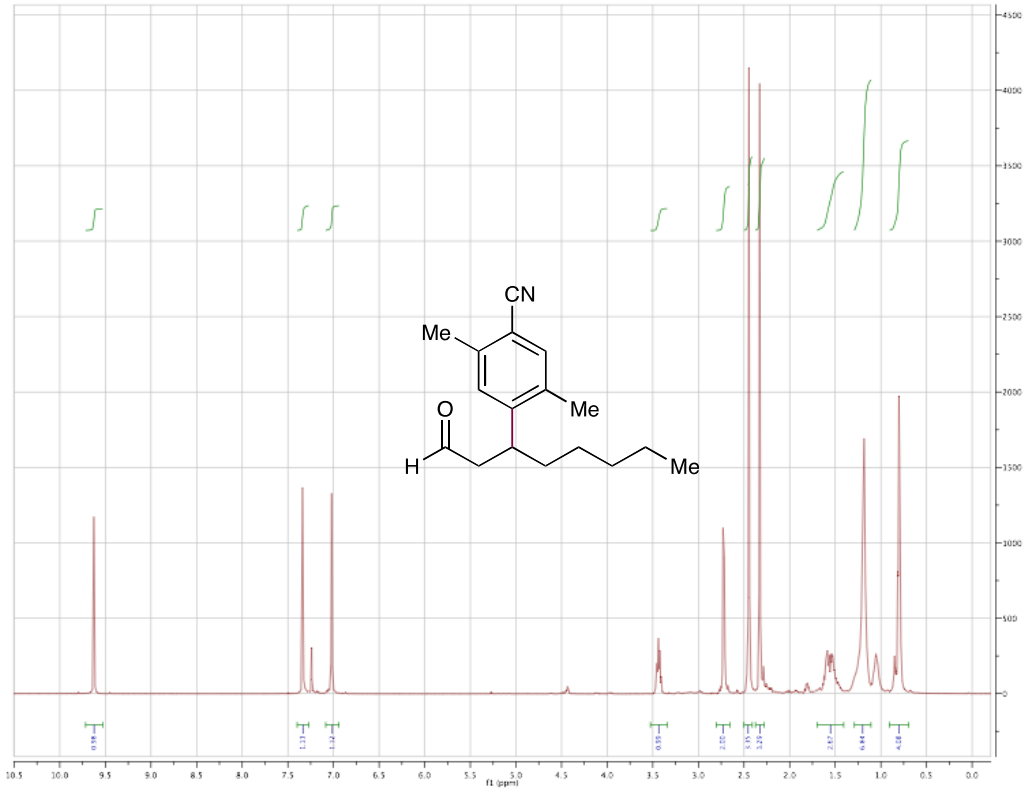
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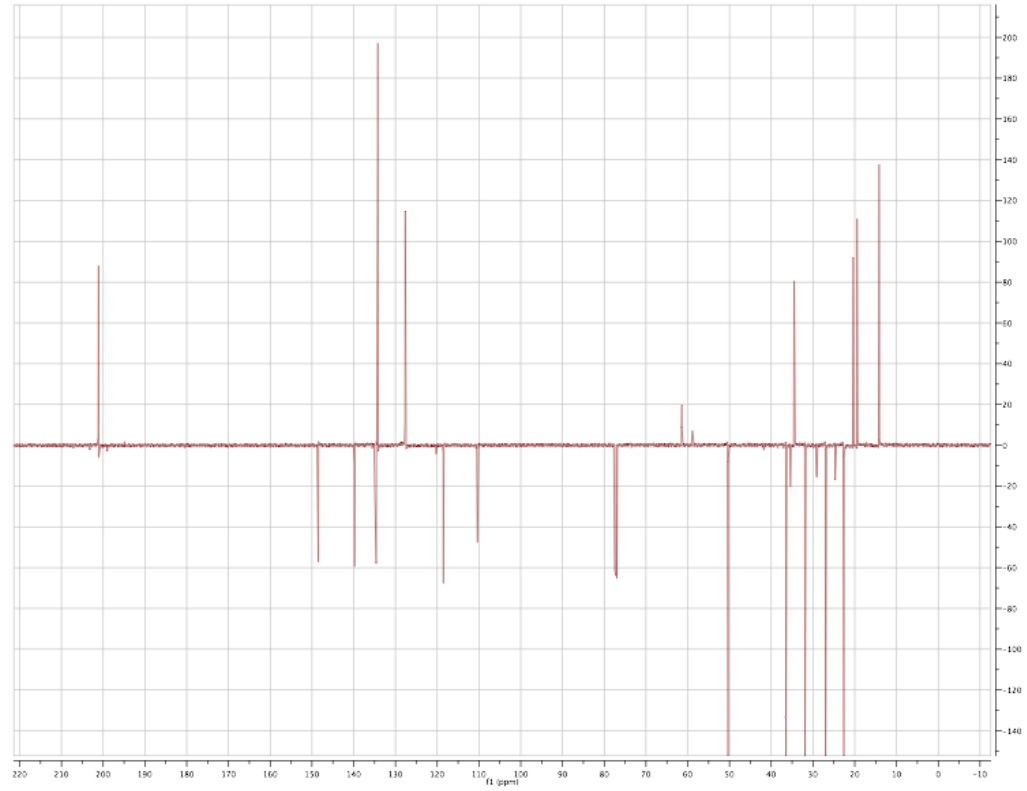

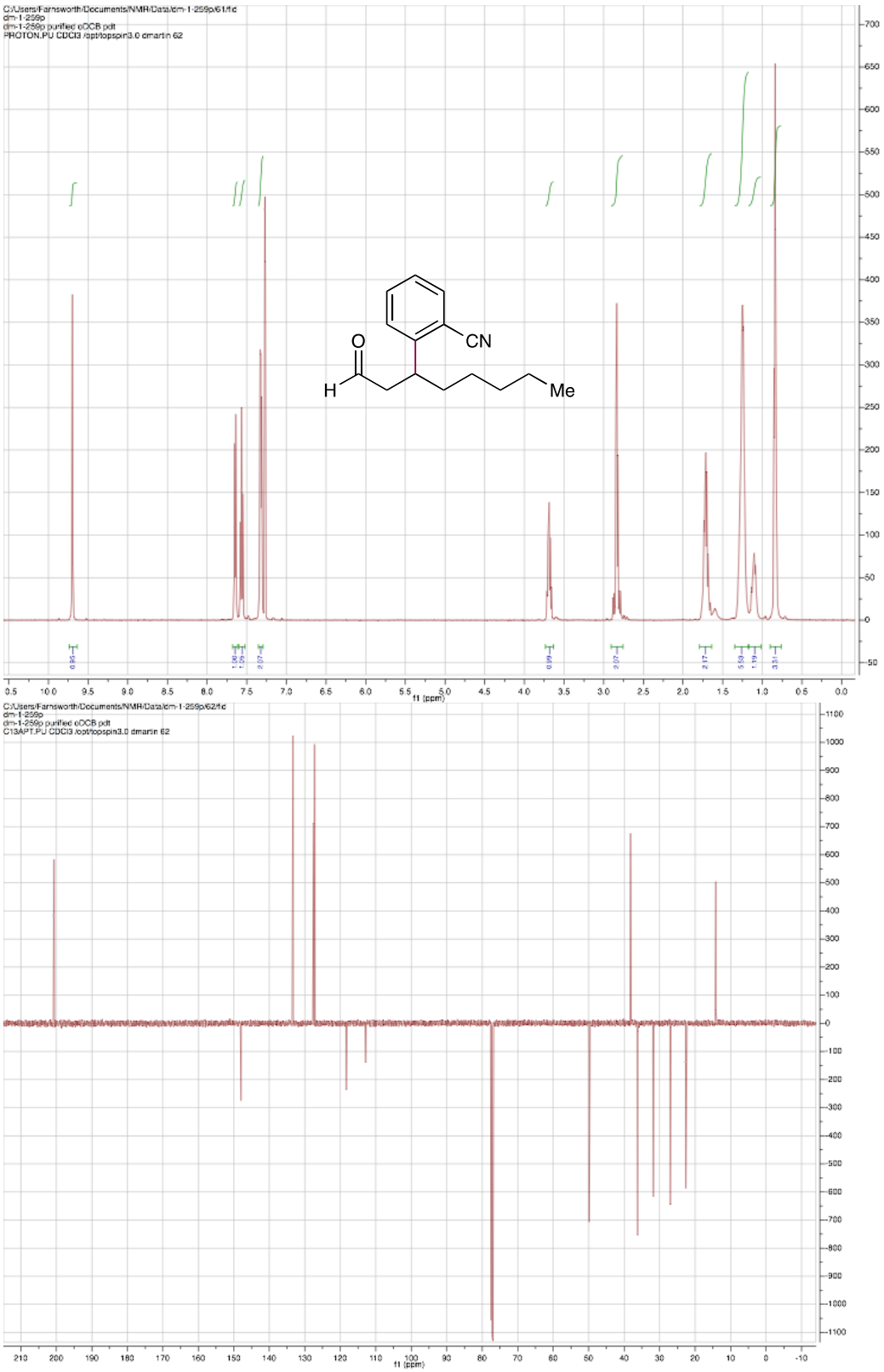
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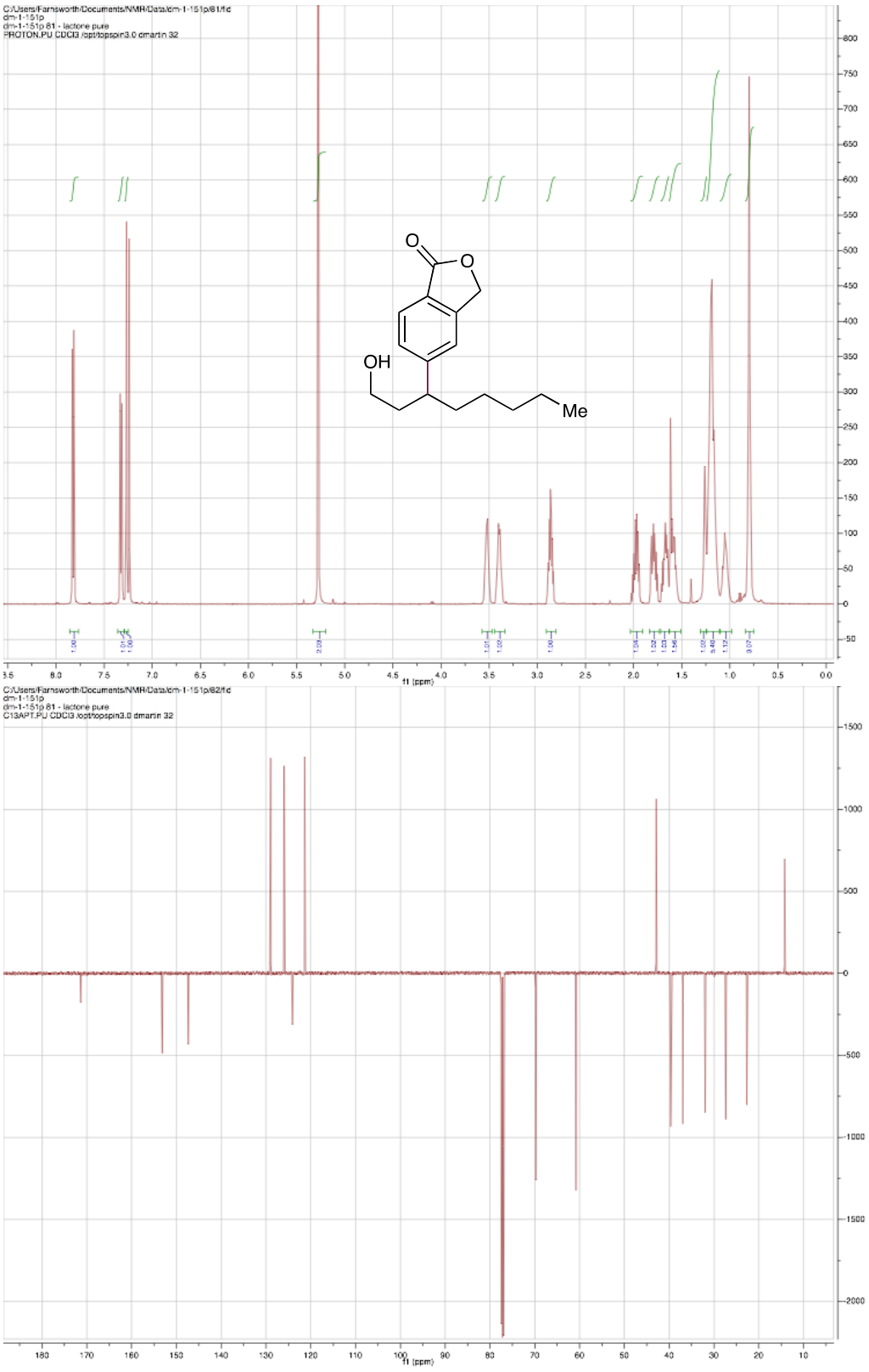
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OH
Me
f1 (ppm)
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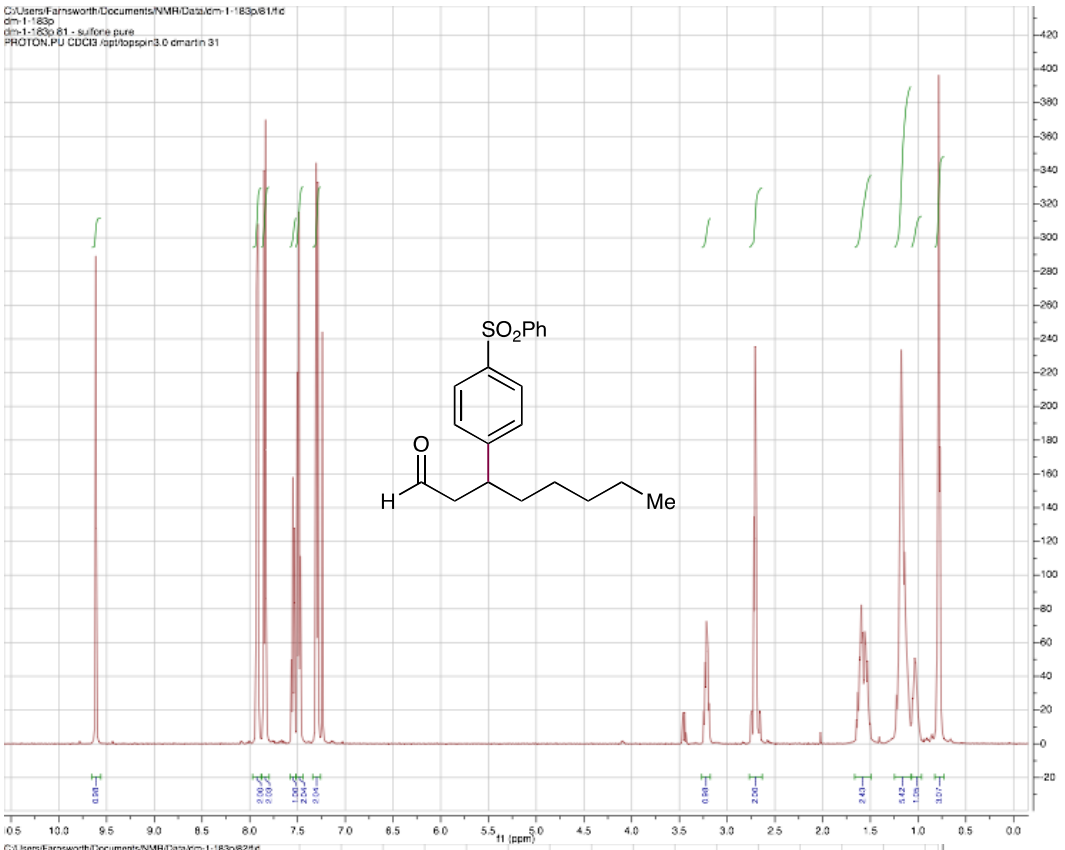
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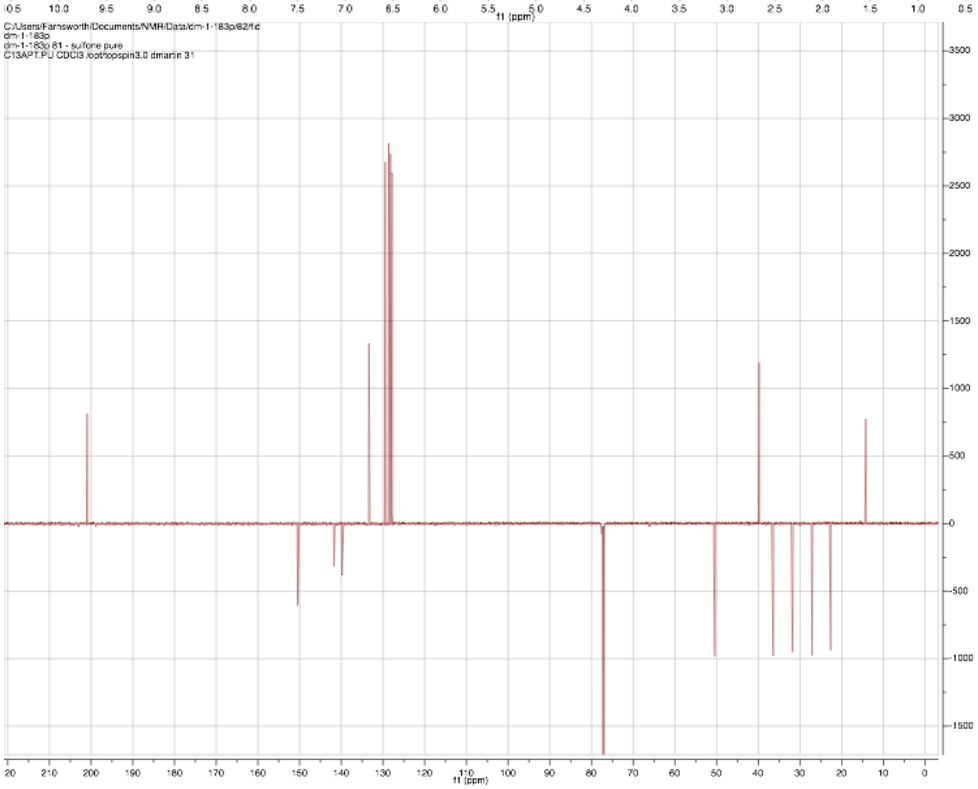
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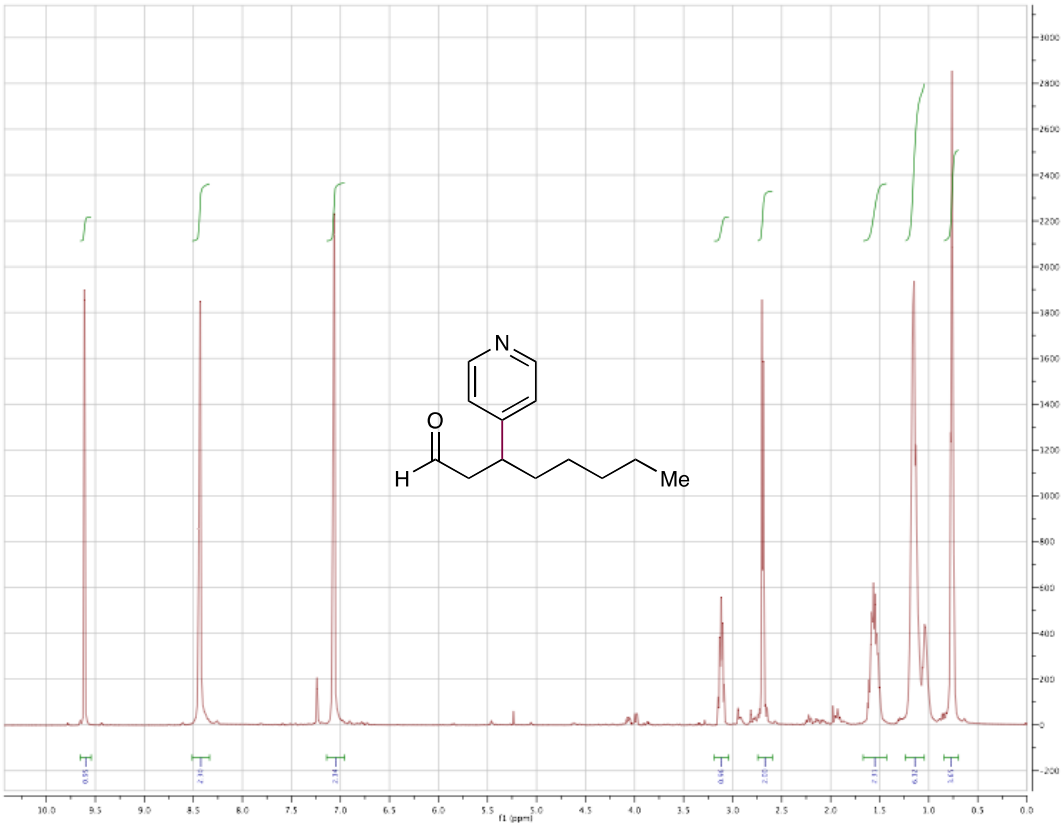
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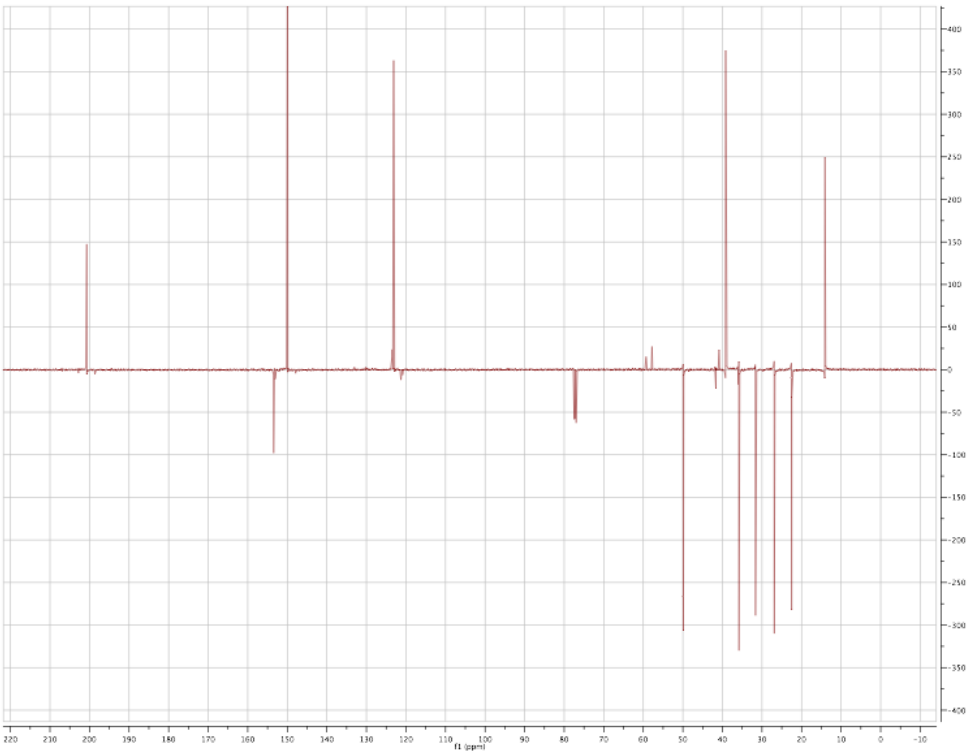

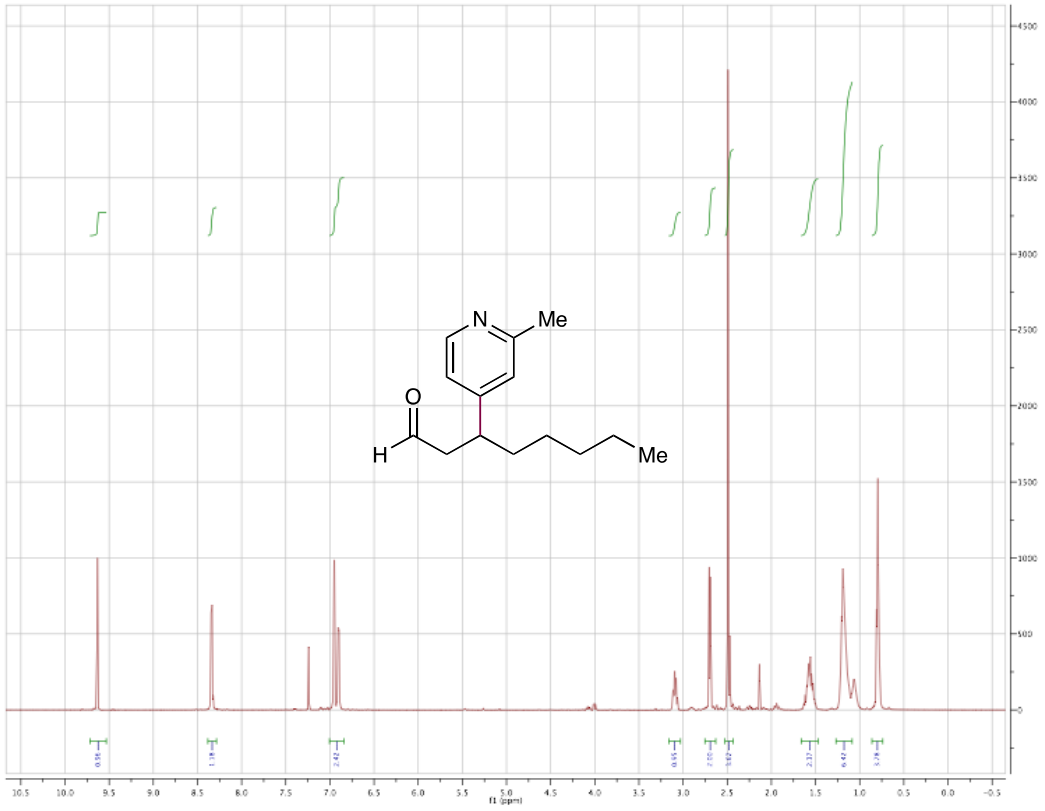
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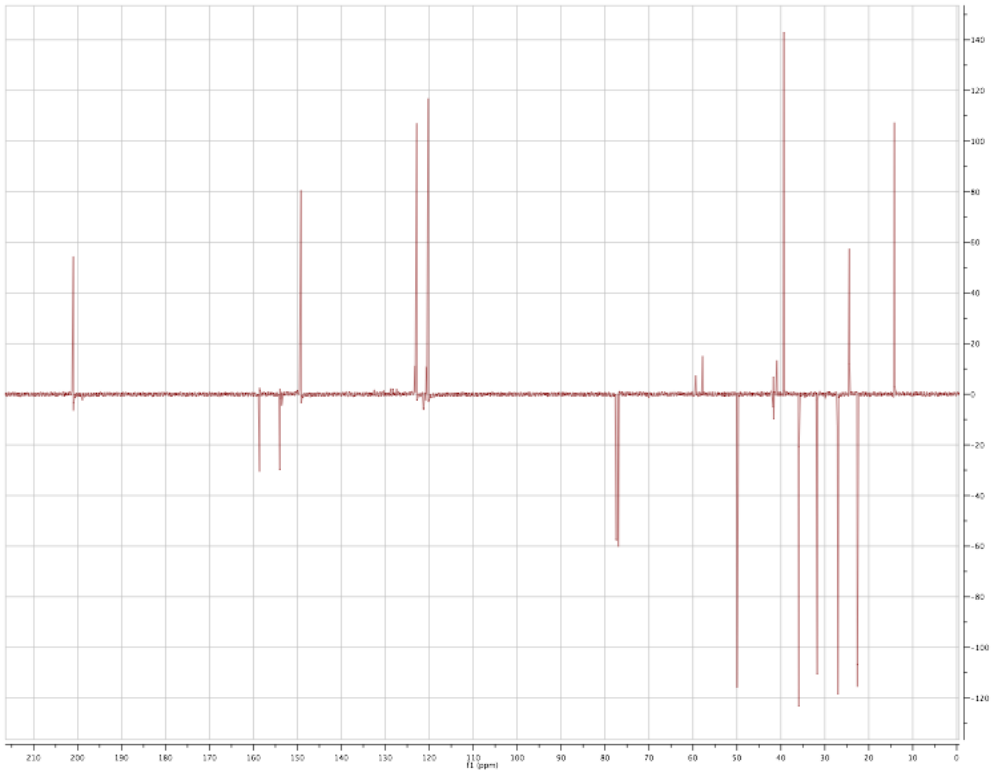

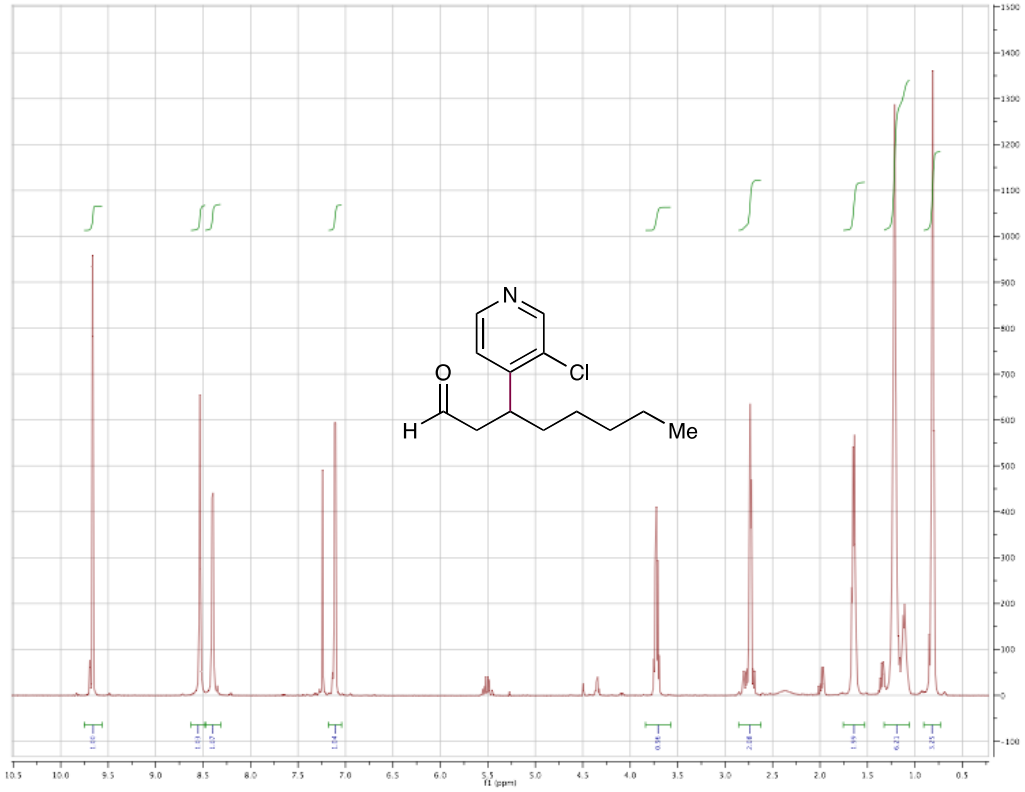
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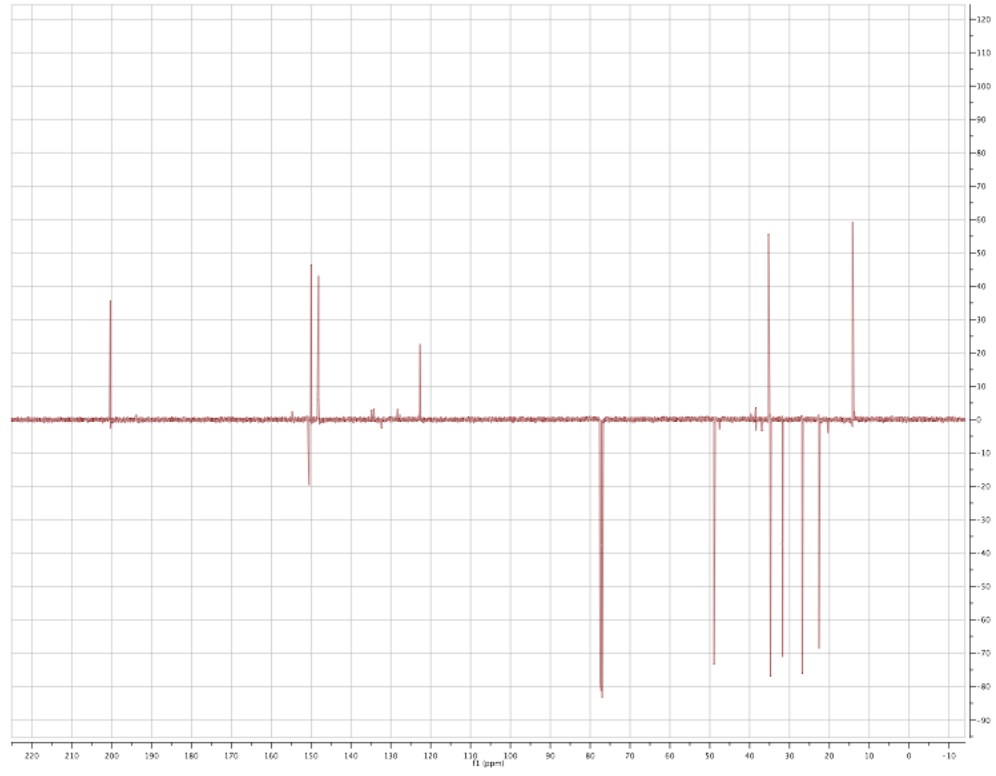

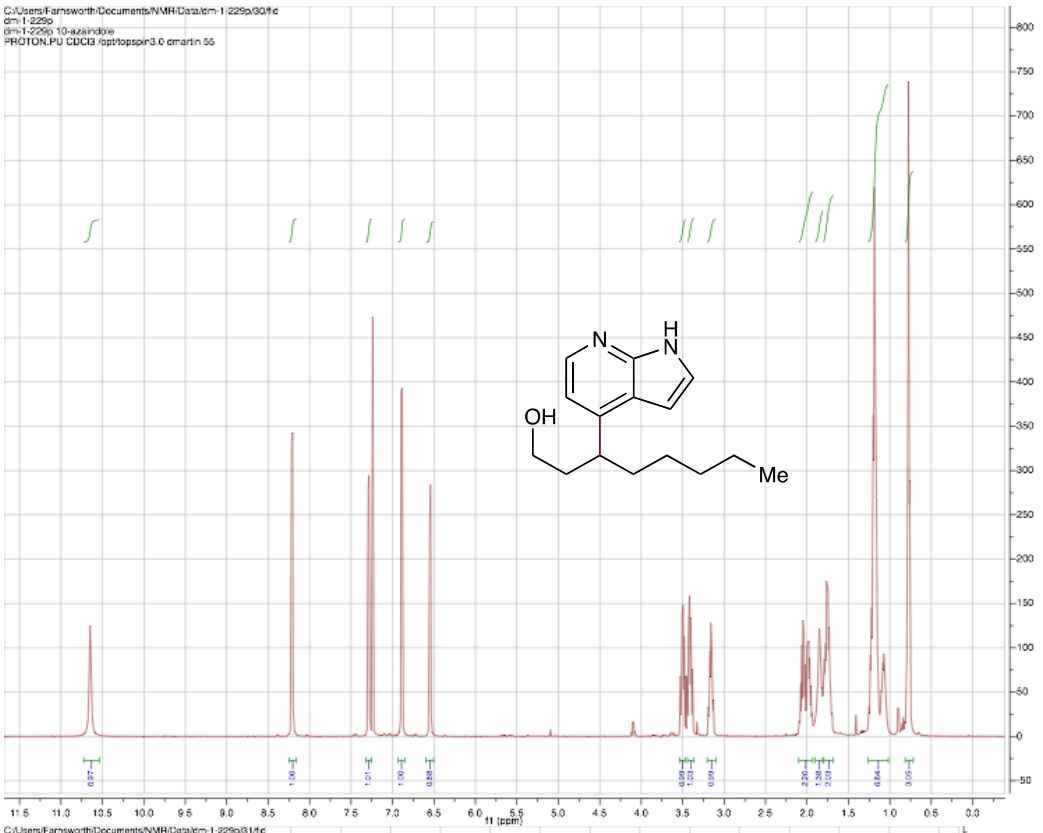
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H
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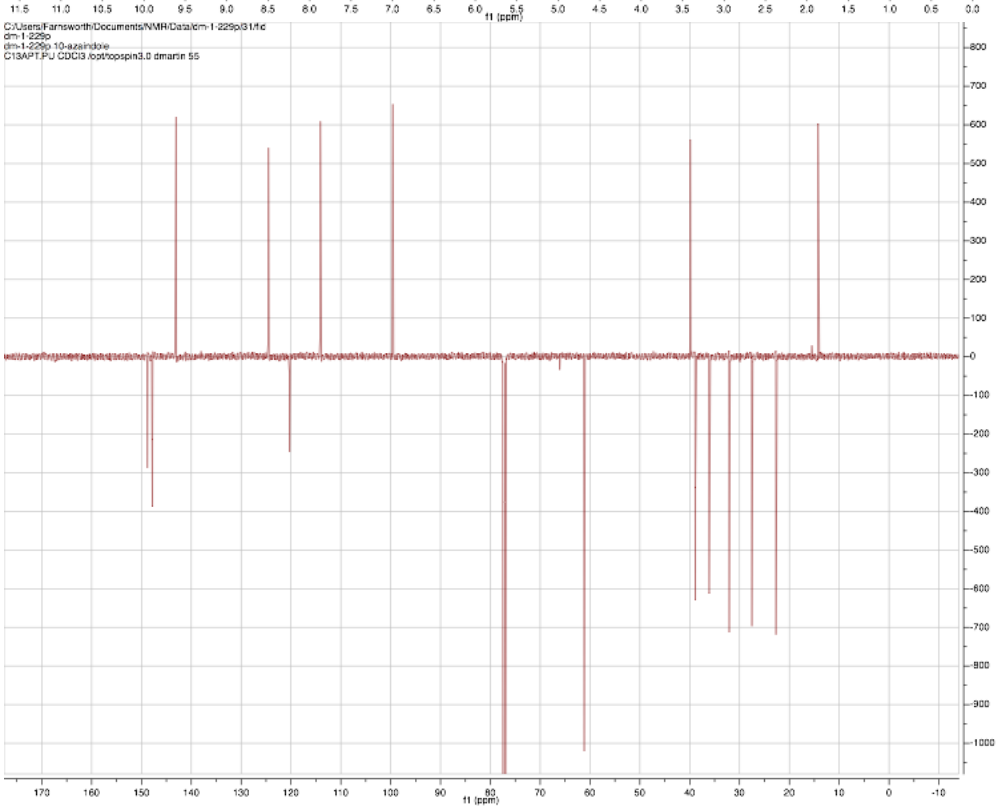

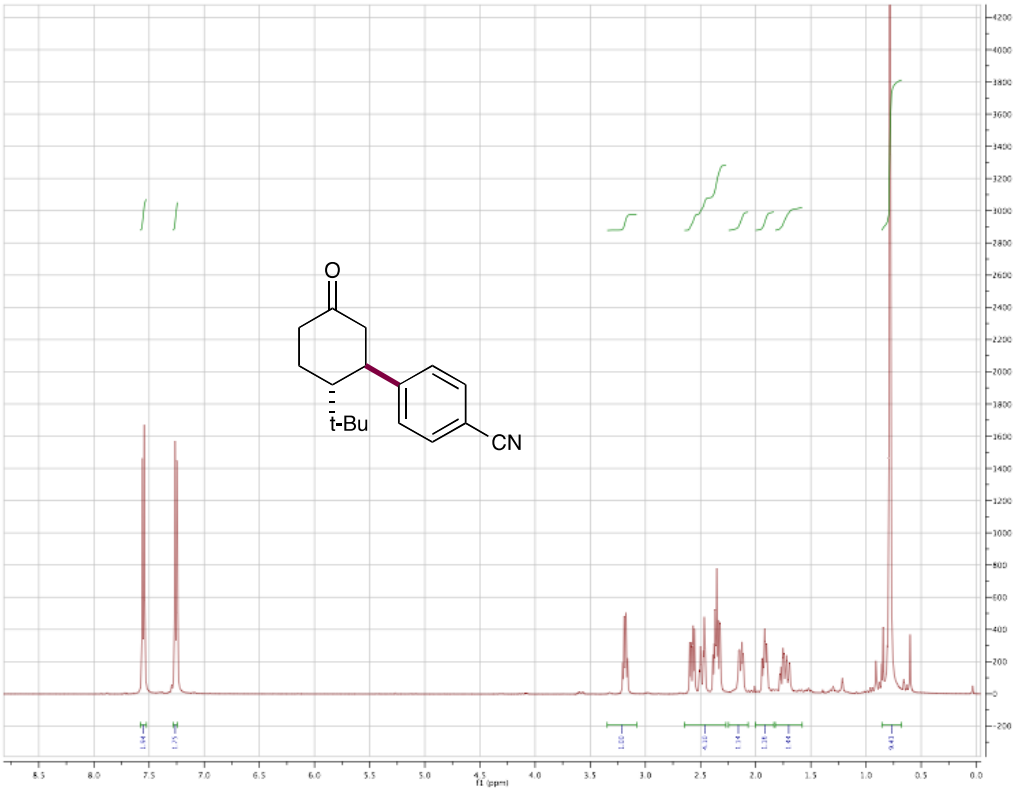
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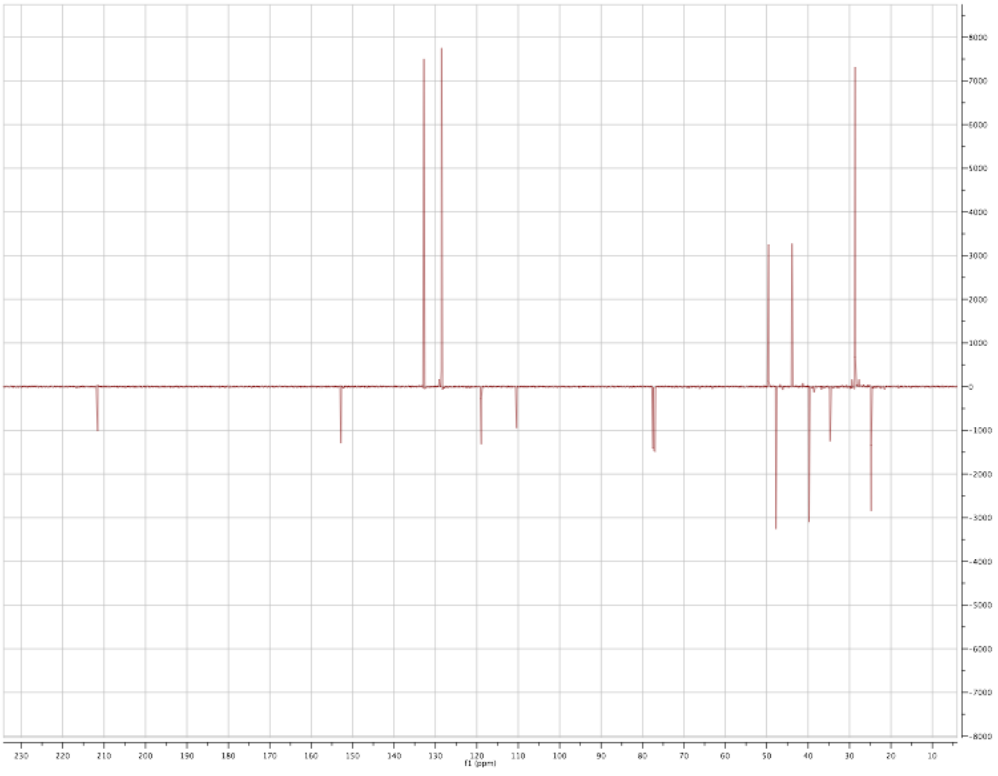

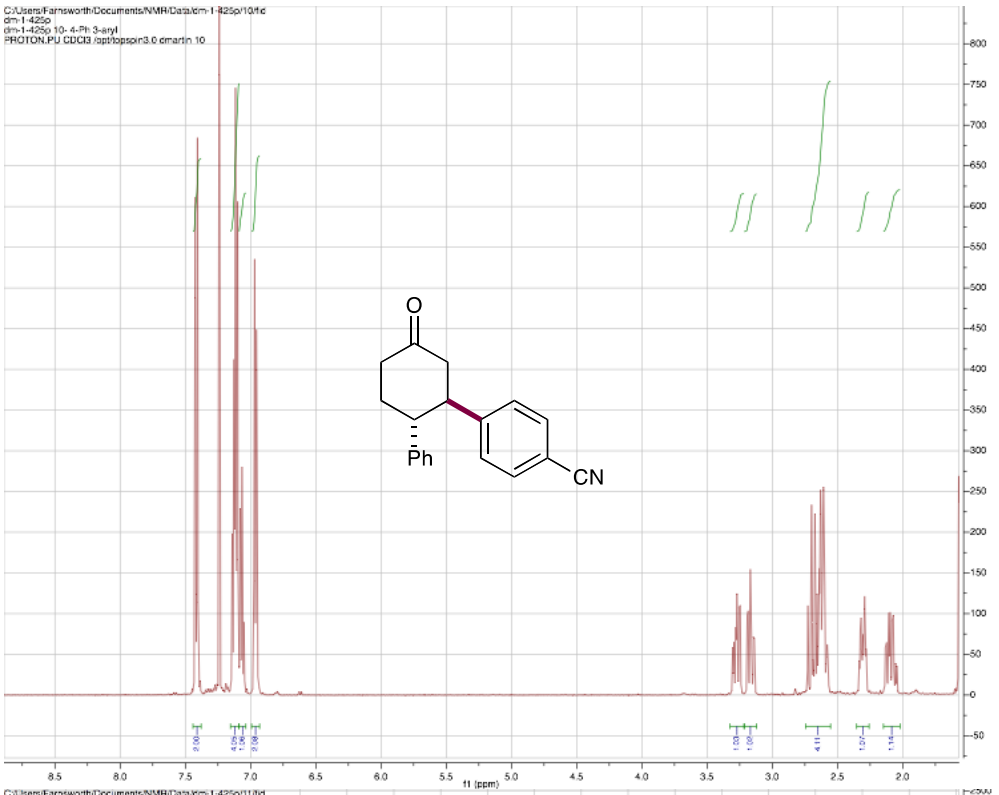
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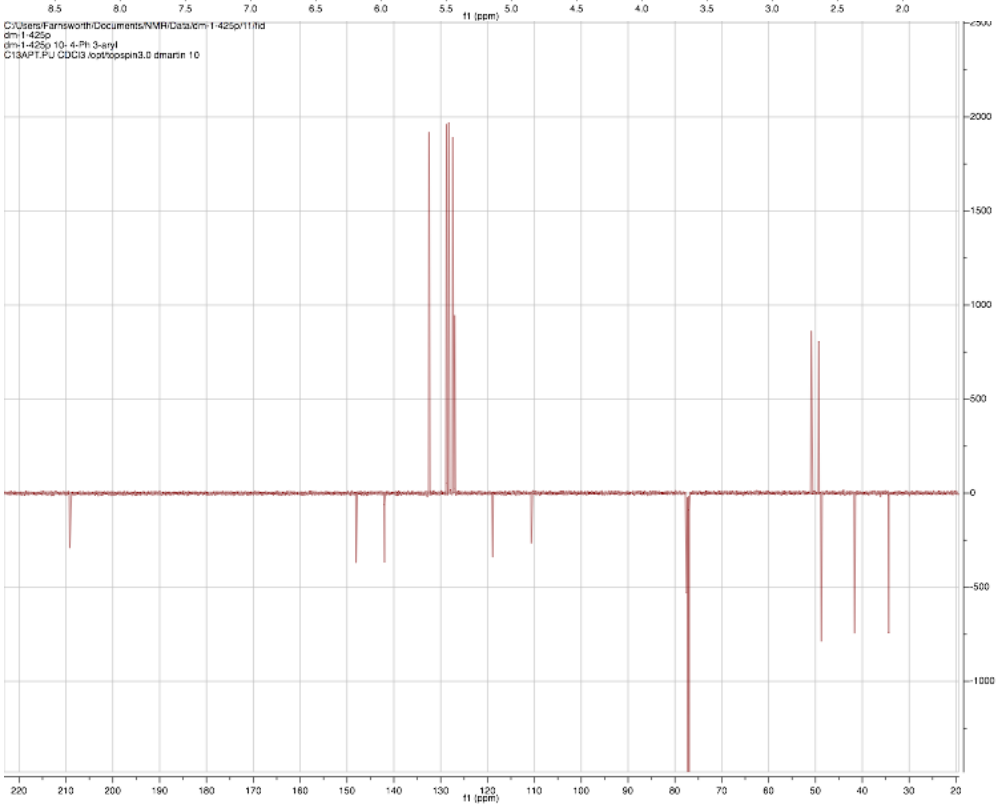
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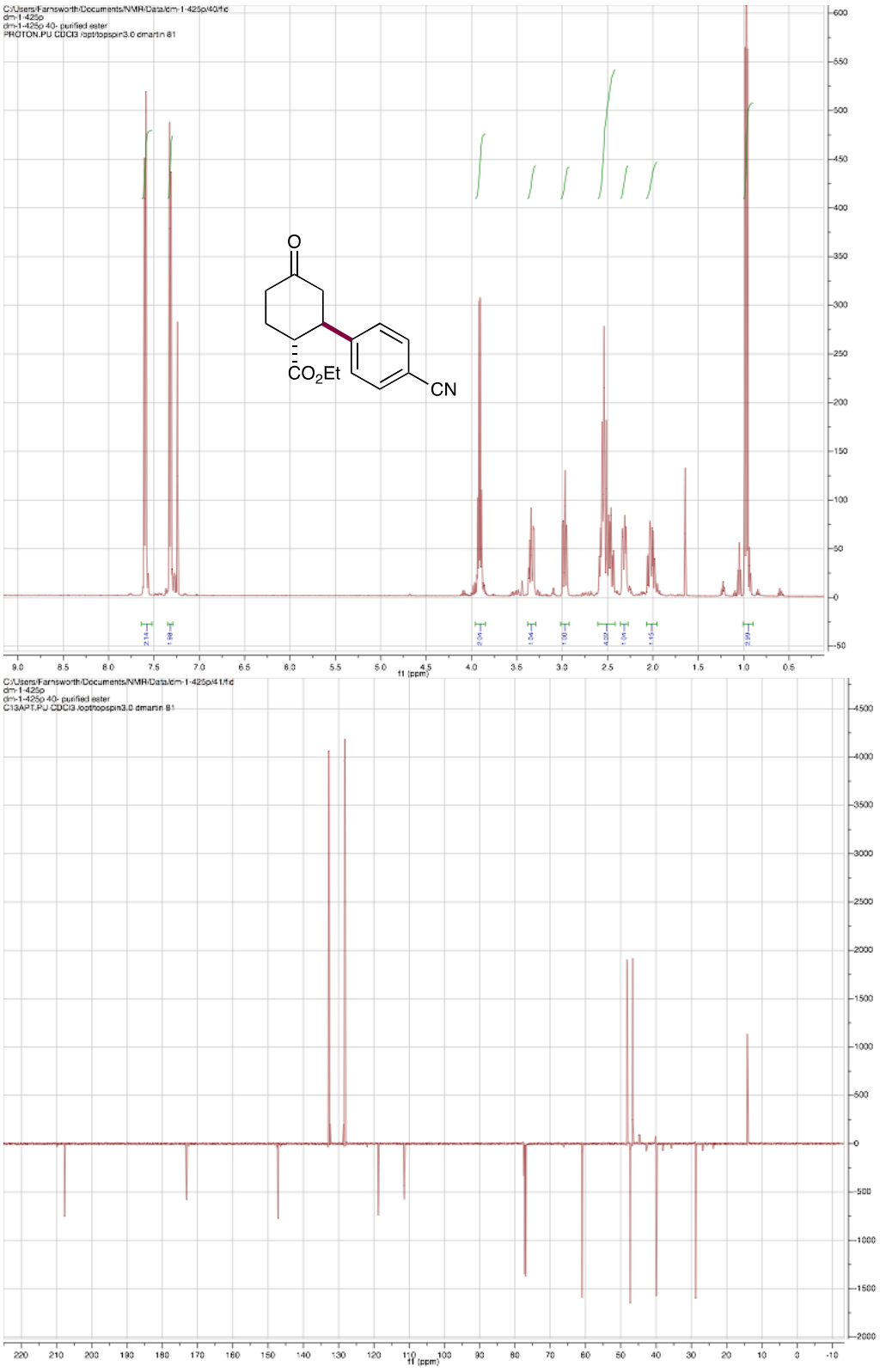
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dm-1-425p 40- purified ester
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CO2Et
CN
f1 (ppm)
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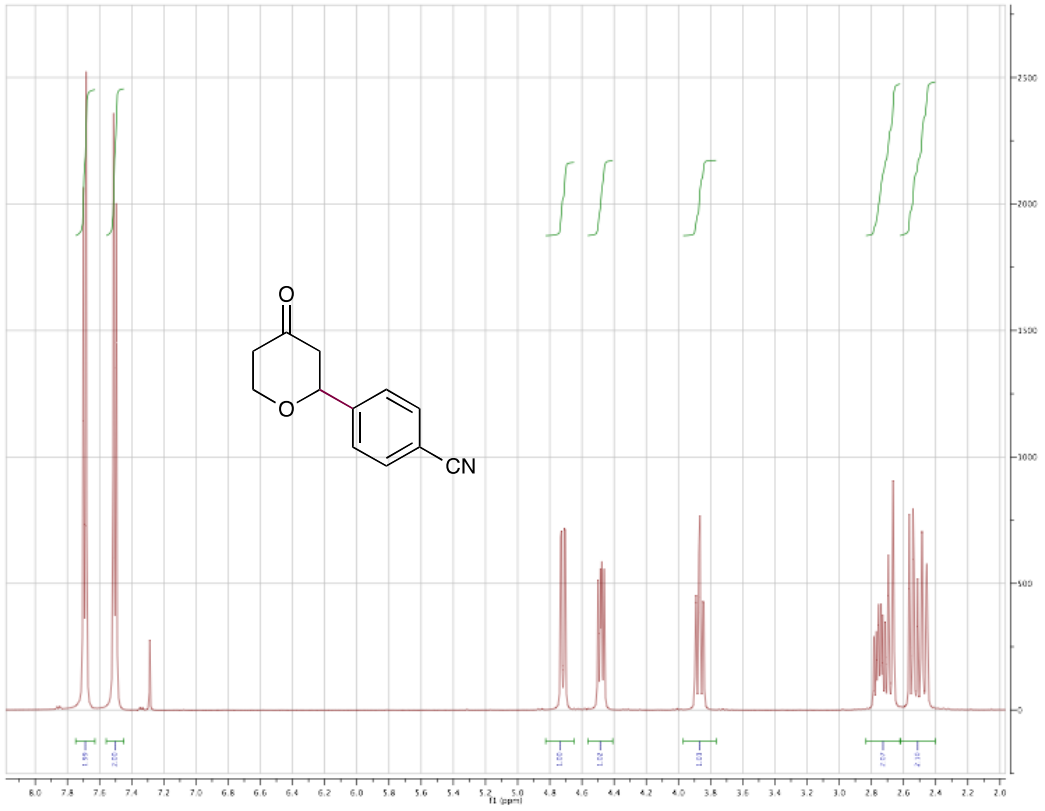
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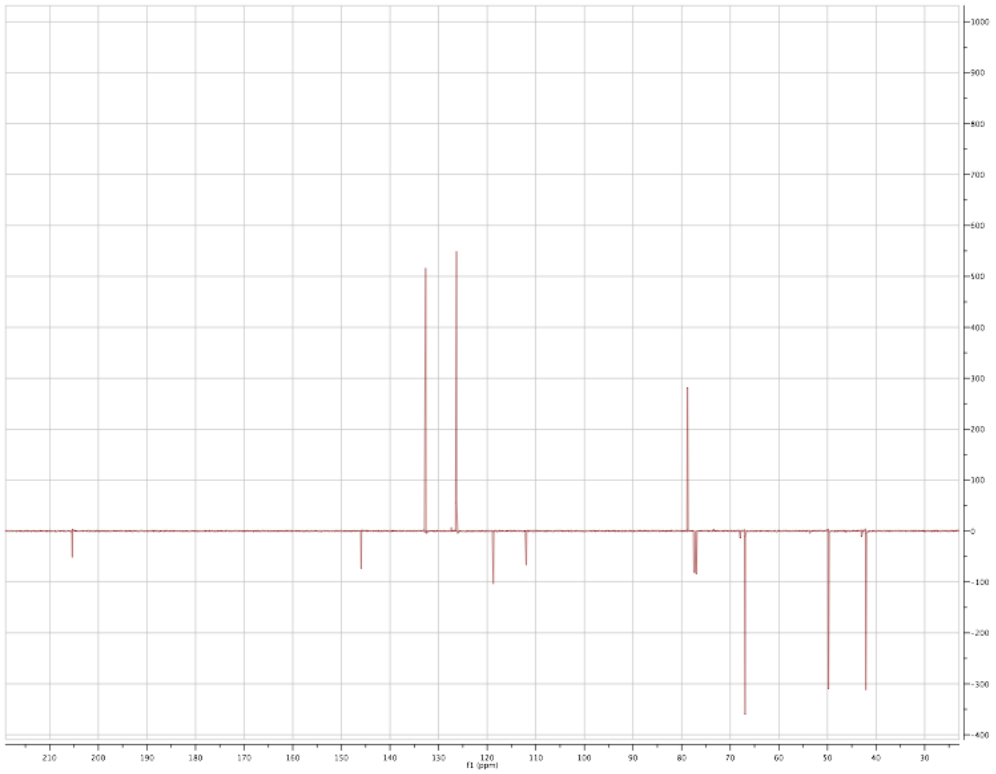

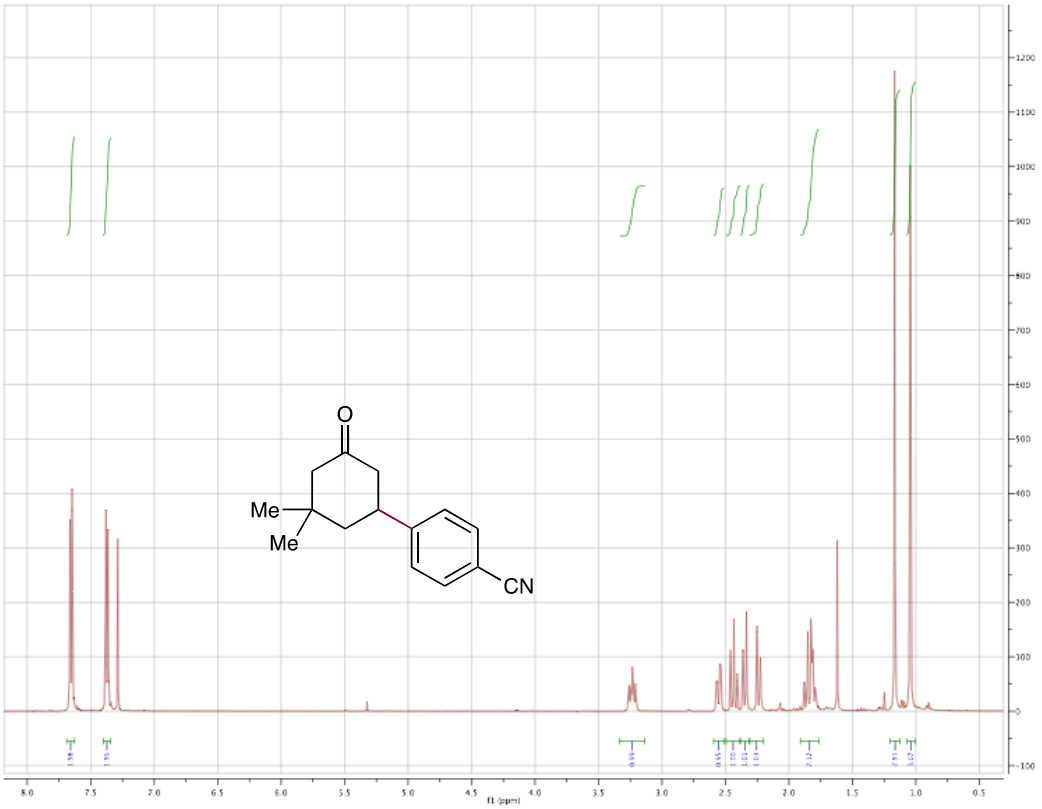
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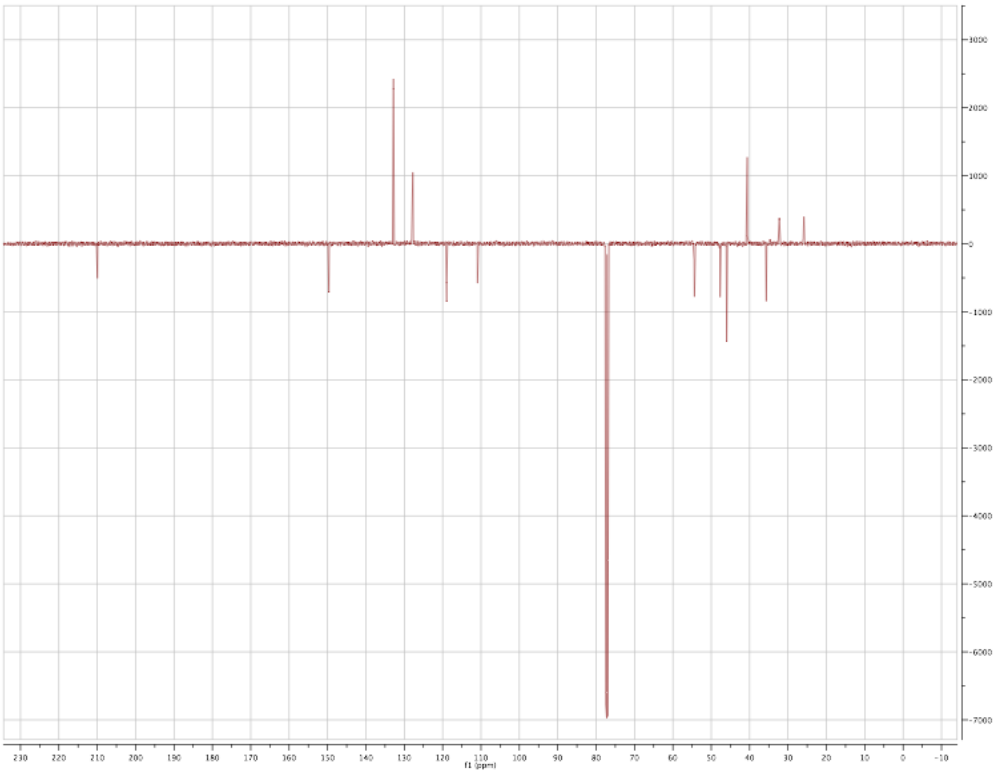

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