Supporting Information

Spin-Center Shift-Enabled Direct Enantioselective α-Benzylation of Aldehydes with Alcohols

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I. General Information

Commercial aldehydes and 2,6-lutidine were distilled at reduced pressure before use. Methanol, acetonitrile, dimethylformamide, 1,4-dioxane, 1,2-dimethoxyethane, CH_2Cl_2, tetrahydrofuran, ether, and dimethylsulfoxide were dried using a J. C. Meyer solvent purification system. All other commercial reagents and solvents were used as received. Organic solutions were concentrated under reduced pressure on a Büchi rotary evaporator. Chromatographic purification of products was accomplished by flash chromatography on Silicycle F60 silica gel. Thin-layer chromatography was performed on Analtech 250 micron silica gel F-254 plates and preparative thin-layer chromatography was performed on analogous 1000 micron silica gel plates. ^{1}H NMR spectra were recorded on a Bruker Ultrashield Plus Avance III 500 MHz spectrometer, and are internally referenced to residual protic solvent signals of $CDCl_3$ (7.26 ppm), DMSO-d_6 (2.50 ppm), or CD_2Cl_2 (5.32 ppm). 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, br = broad, app = apparent), and coupling constant (Hz). ^{13}C NMR spectra are internally referenced to $CDCl_3$ (77.16 ppm), DMSO-d_6 (39.52 ppm), or CD_2Cl_2 (53.84 ppm). Data for ^{13}C NMR are reported in terms of chemical shift and, if coupled to fluorine, multiplicity and coupling constant (Hz). High-resolution mass spectra were obtained at the Princeton University Mass Spectrometry Facilities. IR spectra were recorded on a Perkin Elmer Paragon 1000 spectrometer and peaks are reported in terms of frequency of absorption (cm^{-1}). HPLC was performed on an Agilent 1260 Infinity instrument using chiral columns as noted for each compound. Optical rotations were measured on a Jasco P-1010 polarimeter with $[\alpha]_D$ values reported in degrees and concentration (c) in g/100 mL. UV-Vis spectra were recorded on an Agilent 8453 UV-Vis spectrometer. Fluorescence emission spectra were recorded on an Agilent Cary Eclipse fluorescence spectrometer. CV experiments were performed using a CH Instruments electrochemical analyzer.

II. Apparatus for Controlled Cooling Under Blue LED Irradiation

A large crystallizing dish filled with isopropanol was placed on a stir plate. Four 34 W blue Kessil LED lamps were held next to the dish using a system of metal bars and clamps. 8 mL vials (up to two vials per LED lamp) were suspended at the edge of the dish and immersed in the isopropanol bath using copper wire. Both the isopropanol bath and the reaction vials were stirred using Teflon-coated stir bars at 200–300 rpm. Cooling was achieved by using the clamp system to hold the coils of a Neslab CC 100 Immersion Cooler in the isopropanol bath. To achieve temperatures of 0 °C, the system was cooled to ~ –10 °C over ~ 1 hour, the desired number of LED lamps were switched on, and the cooling system was iteratively adjusted so the bath temperature was held at (0 ± 2) °C as judged by a thermometer positioned in the bath directly in front of a working LED lamp (the LED lamps produce a substantial amount of heat) before exposing the reactions to light. Although ice collects on the sides of the dish, the heat from the lamps tends to prevent ice or water from obstructing the incident light, ensuring reliable photon penetration into the reaction medium.

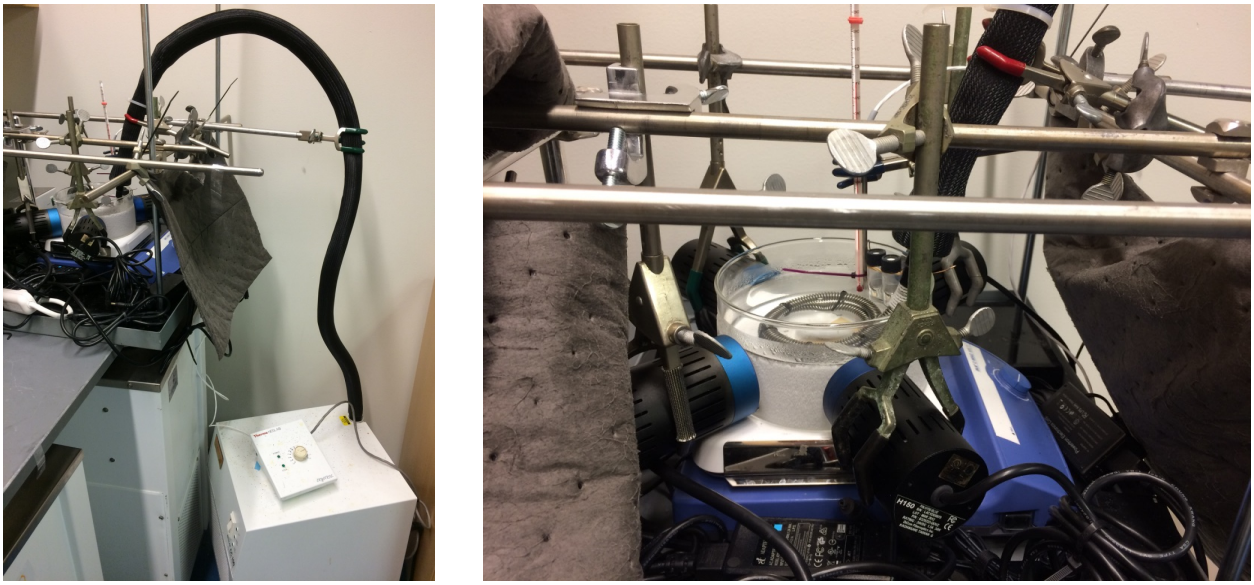


Figure S1. Photographs of the irradiation setup with controlled cooling.

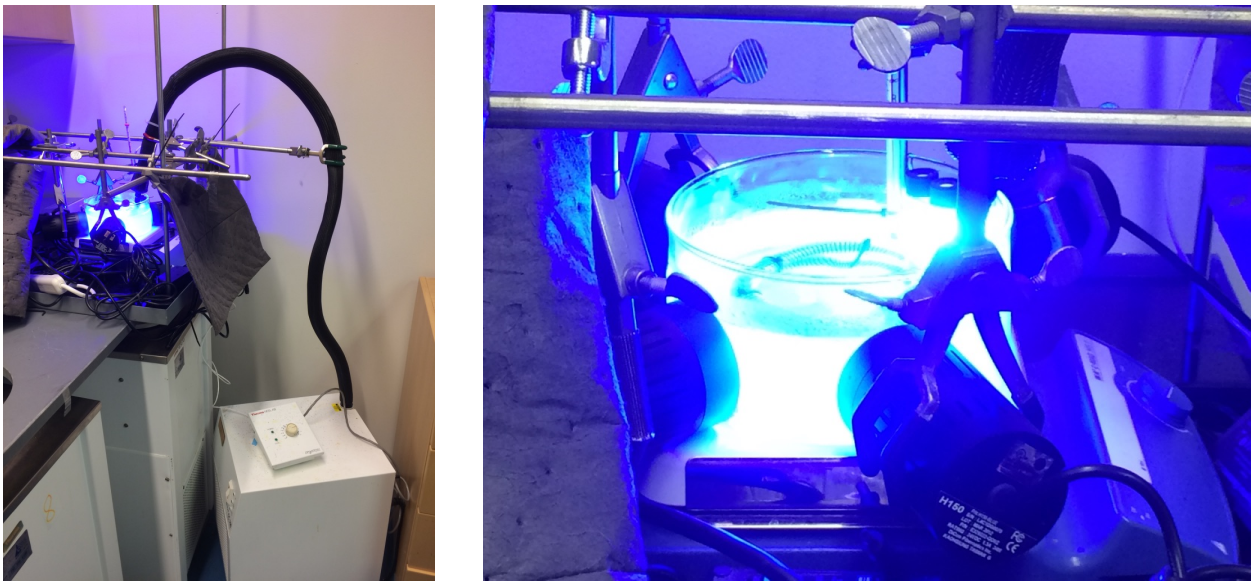


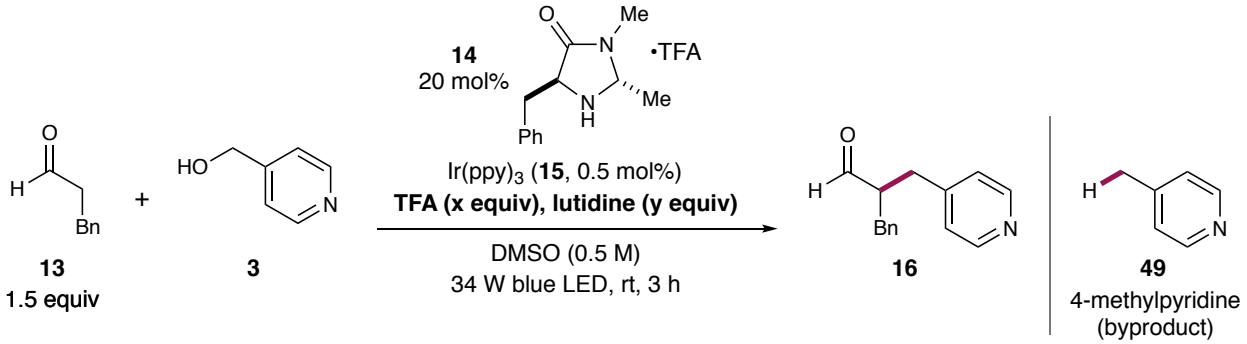
Figure S2. Photographs of the irradiation setup (lights switched on) with controlled cooling.

III. Optimization Studies (Table 1)

A stock solution of 4-(hydroxymethyl)pyridine (**3**), photocatalyst, organocatalyst, and any other materials such as hydrocinnamaldehyde (**13**), 2,6-lutidine, water, and acids used in constant amounts throughout each experiment in the indicated solvent was prepared and transferred to 8 mL vials such that 0.1 mmol of 4-(hydroxymethyl)pyridine was added. Any materials used in varying quantities throughout an experiment were then added to each reaction vial. The solutions were sparged with nitrogen for 15 minutes while stirring at 150 rpm, and the vials were sealed with parafilm and stirred next to a 34 W blue LED lamp in an ice water bath or cooled by a fan. After the indicated time, an aliquot of the reaction (~ 25 μL) was dissolved in ~ 5:1 $CDCl_3$/DMSO-d_6 (0.6 mL) in an NMR tube and the yield of the desired aldehyde, the 4-methylpyridine byproduct, and consumption of 4-(hydroxymethyl)pyridine was determined relative to an internal standard (typically the 2,6-lutidine present in the reaction, which is not consumed). The remaining mixture was diluted with saturated $NaHCO_3$ (5 mL) and extracted with ether (3 × 5 mL). The combined organic extracts were dried over Na_2SO_4 and concentrated. The crude material was dissolved in CH_2Cl_2 (1 mL) and methanol (0.2 mL) and treated with sodium borohydride (39 mg, 1.0 mmol, 10 equiv). After 1 hour, the reaction was quenched with water (5 mL), the mixture was extracted with CH_2Cl_2 (3 × 5 mL), and the combined organic extracts were dried over Na_2SO_4 and concentrated. The residue was purified by chromatography on silica gel (0 → 1% methanol/CH_2Cl_2 + 0.5% triethylamine), and the enantiopurity of the alcohol was determined by chiral HPLC.

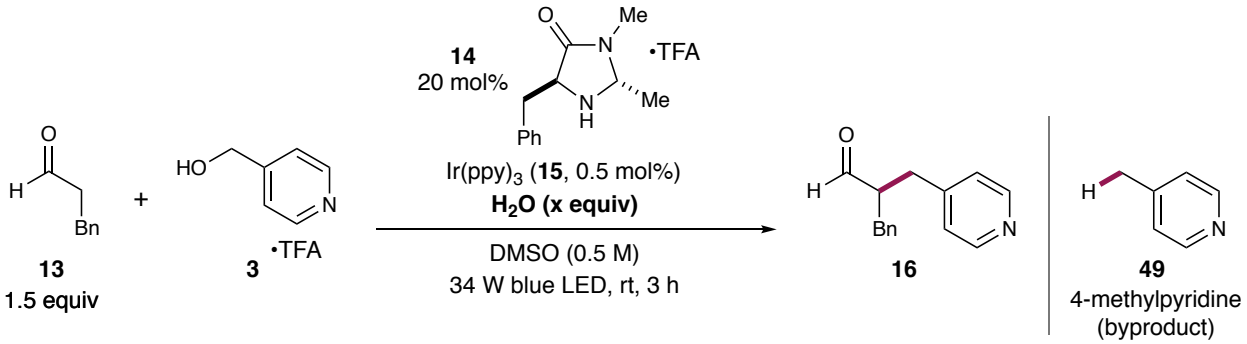
Chiral HPLC: AD-H column, 10% ethanol/hexanes, 1.0 mL/min. t_R = 15.0 min (major (*R*)-enantiomer), 18.6 min (minor (*S*)-enantiomer).

Table S1. Initial discovery of enantioselective α-alkylation of aldehydes with alcohols and its dependence of trifluoroacetic acid (TFA) and 2,6-lutidine stoichiometry.



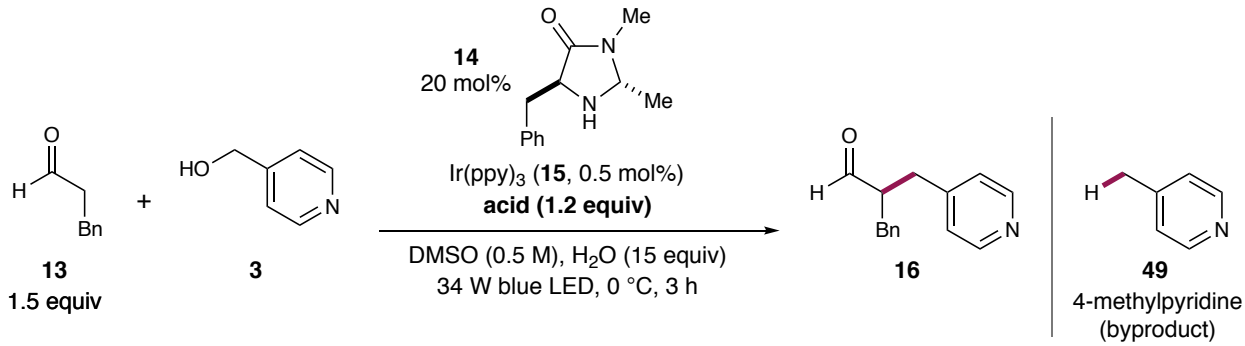
equiv TFA	equiv lutidine	conversion (%)	4-methylpyridine (%)	yield (%)	ee (%)
0	**0**	42	0	**0**	**nd**
0.5	**0**	58	18	**24**	**66**
1.0	**0**	77	25	**37**	**62**
1.5	**0**	84	22	**44**	**60**
2.0	**0**	92	21	**55**	**57**
1.0	**3.0**	51	0	**0**	**nd**
0	**2.0**	39	0	**0**	**nd**

Table S2. Effect of water content on the enantioselective α-alkylation of aldehydes with alcohols.



equiv H_2O	conversion (%)	4-methylpyridine (%)	yield (%)	ee (%)
0	60	22	**34**	**66**
1	60	23	**32**	**73**
2	59	21	**35**	**76**
3	61	23	**37**	**78**
5	65	26	**38**	**80**
10	71	23	**38**	**82**
15	75	23	**36**	**86**
25	nd	nd	**27**	**90**
50	nd	nd	**24**	**90**
100	nd	nd	**4**	**nd**

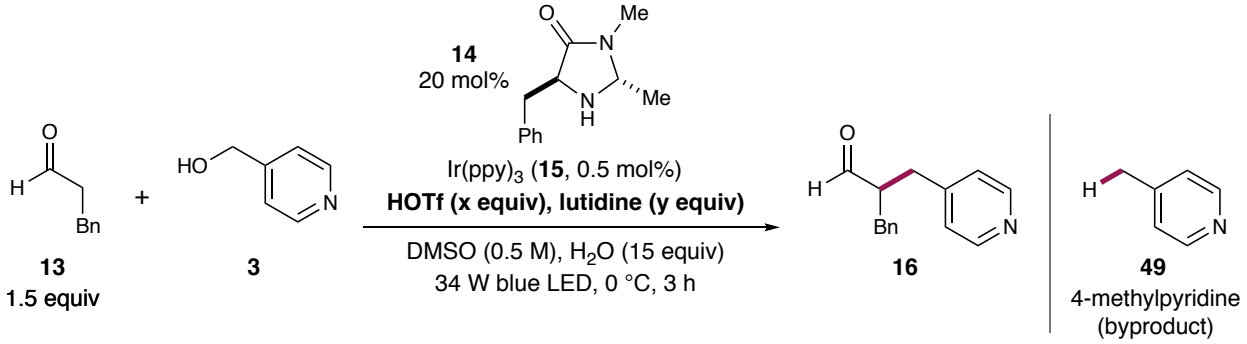
Table S3. Effect of acid additive on the enantioselective α-alkylation of aldehydes with alcohols.



acid	conversion (%)	4-methylpyridine (%)	yield (%)	ee (%)
AcOH	37	8	**13**	**nd**
ClH_2CCO_2H	72	18	**32**	**75**
Cl_2HCCO_2H	70	10	**28**	**86**
TFA	71	8	**22**	**92**
HBr	81	6	**17**	**90**
HBF_4	82	6	**15**	**94**
TsOH	79	11	**18**	**93**
HOTf	84	6	**21**	**92**
lutidine•HOTf*	91	17	**47**	**88**

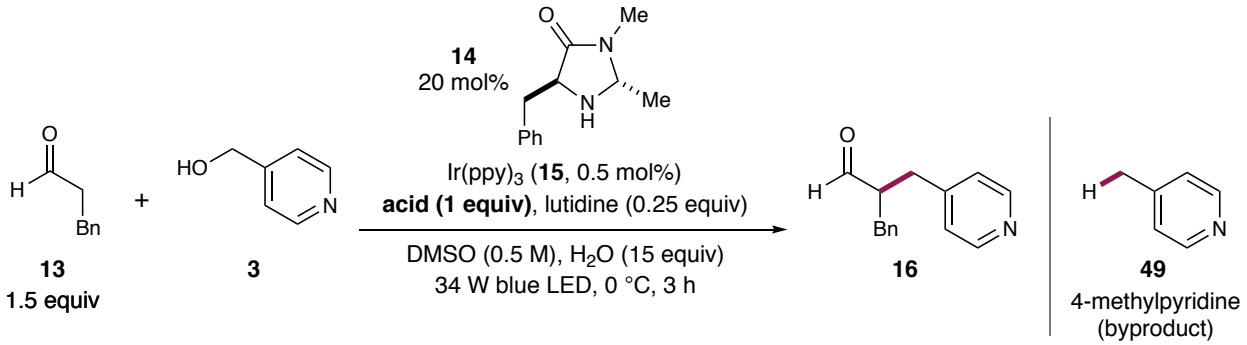
*Prepared by addition of trifluoromethanesulfonic acid (1 equiv) to a solution of 2,6-lutidine (1 equiv) in ether (1 M) at 0 °C. The precipitate was collected and recrystallized from 5:1 ether/acetone.

Table S4. Effect of HOTf and 2,6-lutidine stoichiometry on the enantioselective α-alkylation of aldehydes with alcohols.



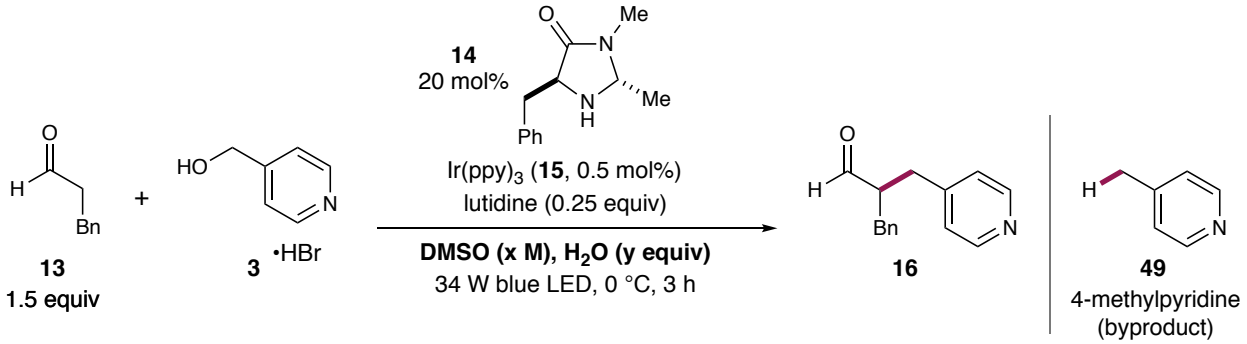
equiv HOTf	equiv lutidine	conversion (%)	4-methylpyridine (%)	yield (%)	ee (%)
0.25	**0.25**	86	23	**46**	**87**
0.50	**0.50**	88	23	**50**	**88**
1.00	**1.00**	88	18	**51**	**89**
1.20	**1.20**	nd	17	**47**	**88**
1.50	**1.50**	87	15	**48**	**89**
0.50	**1.00**	69	22	**40**	**89**
1.00	**0.50**	91	17	**56**	**90**
1.00	**0.25**	93	14	**65**	**90**
1.00	**0.00**	nd	4	**27**	**92**

Table S5. Effect of acid additive on enantioselective α-alkylation of aldehydes with alcohols with 2,6-lutidine present.



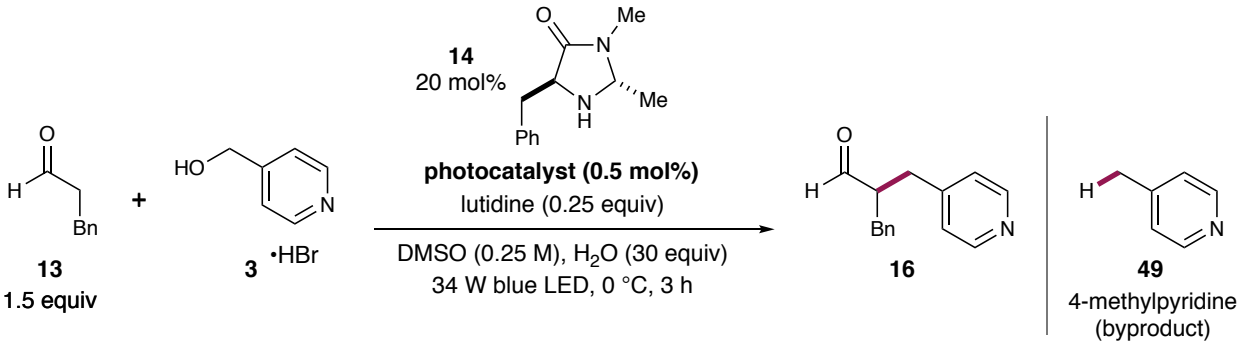
acid	conversion (%)	4-methylpyridine (%)	yield (%)	ee (%)
TFA	78	20	**48**	**88**
TsOH	87	13	**59**	**89**
$HClO_4$	84	15	**60**	**89**
HBF_4	89	15	**61**	**90**
HOTf	93	14	**65**	**90**
HBr	91	14	**66**	**90**

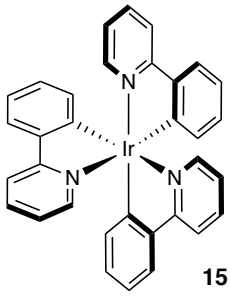
Table S6. Effect of concentration and water content on enantioselective α-alkylation of aldehydes with alcohols.



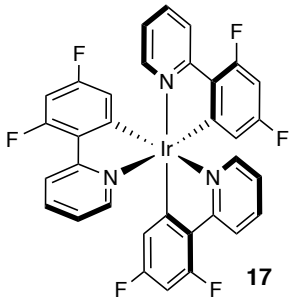
concentration (M)	equiv. H_2O	conversion (%)	4-methylpyridine (%)	yield (%)	ee (%)
0.05	**15**	45	24	**11**	**nd**
0.10	**15**	47	27	**14**	**93**
0.25	**15**	72	24	**39**	**90**
0.50	**15**	80	15	**51**	**87**
0.25	**30**	84	18	**48**	**90**
0.25	**50**	88	12	**53**	**89**
0.25	**75**	60	5	**41**	**88**
0.25	**100**	36	6	**24**	**88**

Table S7. Effect of photocatalyst on enantioselective α-alkylation of aldehydes with alcohols.

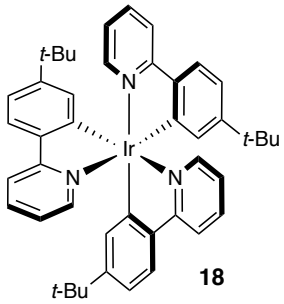




84% conversion, 18% **49**
48% yield, 90% ee

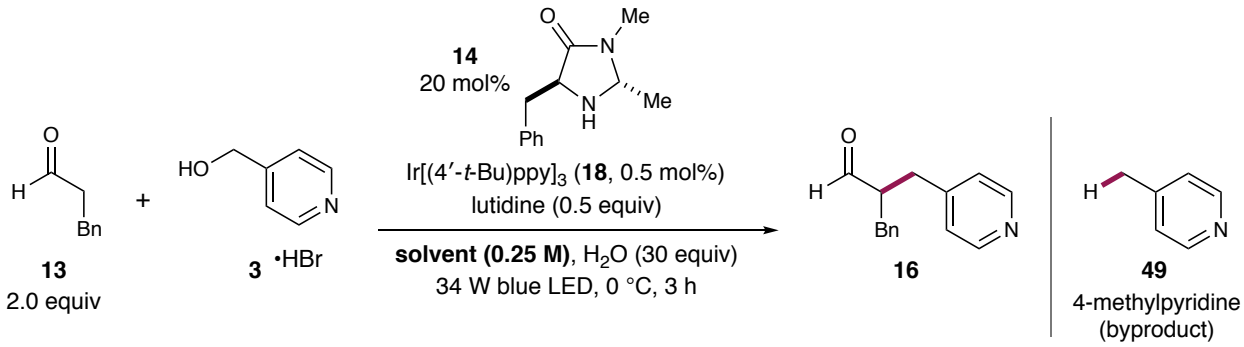


61% conversion, 34% **49**
18% yield, ee nd



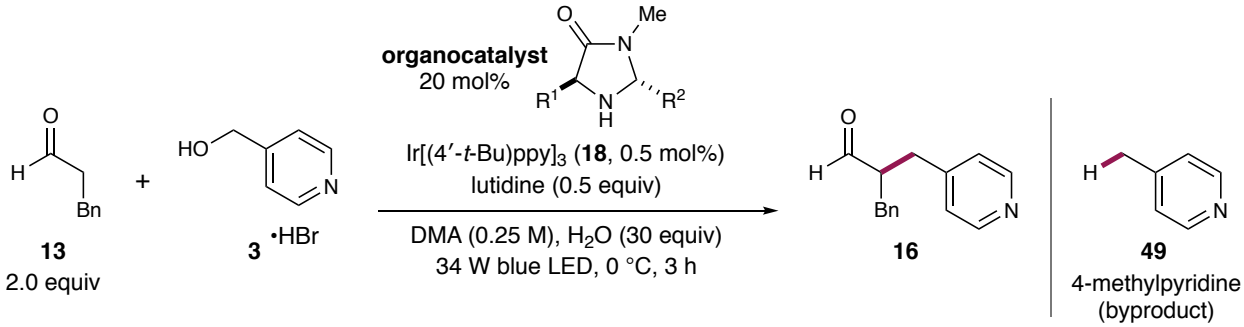
92% conversion, 10% **49**
78% yield, 92% ee

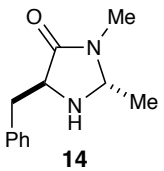
Table S8. Effect of solvent on enantioselective α-alkylation of aldehydes with alcohols.



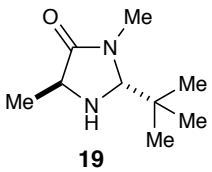
solvent	conversion (%)	4-methylpyridine (%)	yield (%)	ee (%)
dioxane	82	9	**62**	**93**
DME	89	12	**71**	**95**
MeOH	34	7	**4**	**nd**
NMP	100	10	**78**	**92**
DMPU	94	19	**66**	**90**
DMF	98	8	**72**	**93**
MeCN	44	7	**36**	**nd**
DMA	100	8	**90**	**92**
DMSO	100	6	**84**	**89**

Table S9. Effect of organocatalyst on enantioselective α-alkylation of aldehydes with alcohols.

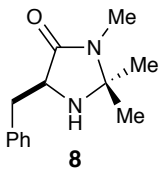




14
100% conversion, 9% **49**
89% yield, 93% ee



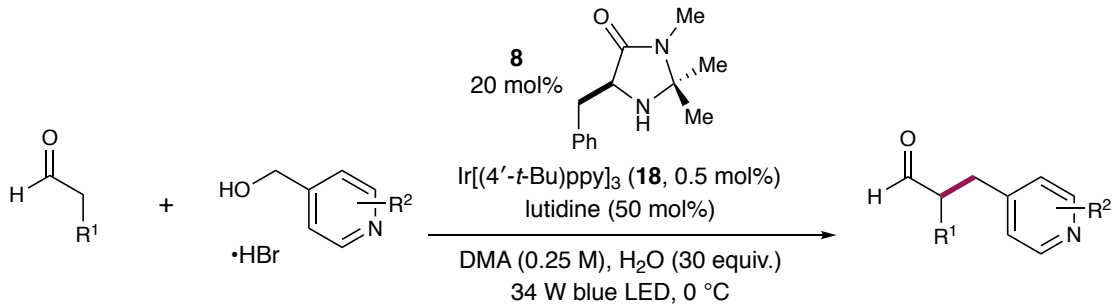
19
22% conversion, 12% **49**
6% yield, ee nd



8
100% conversion, 11% **49**
88% yield, 98% ee (6 h)

IV. General Procedures

General Procedure A. Enantioselective α-Benzylation of Aldehydes with 4-(Hydroxymethyl) -substituted Pyridines and Quinolines (Tables 2 & 4, Figure 3).



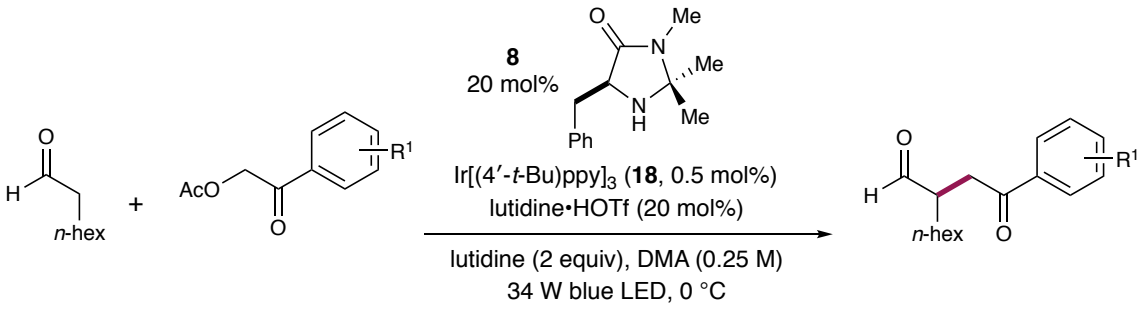
Photocatalyst **18** (2.1 mg, 2.6 μmol, 0.5 mol%), organocatalyst **8** (22 mg, 0.10 mmol, 20 mol%), and starting alcohol (0.50 mmol, 1.0 equiv) were added to an 8 mL vial, followed by dimethylacetamide (2.0 mL), 2,6-lutidine (29 μL, 0.25 mmol, 0.50 equiv), water (0.27 mL, 15 mmol, 30 equiv), and aldehyde (1.0 mmol, 2.0 equiv). The mixture was sparged with nitrogen for 15 minutes while stirring at 250 rpm, and the vial was sealed with parafilm and stirred in an isopropanol bath maintained at 0 °C with an immersion cooler next to a 34 W blue LED lamp. Once the alcohol was consumed, the mixture was diluted with saturated $NaHCO_3$ (10 mL) and extracted with ether (3 × 10 mL). The combined organic extracts were dried over Na_2SO_4 and concentrated. The residue was purified by flash chromatography on silica gel. The aldehyde product, itself, was characterized, except for optical rotation and chiral HPLC analysis, since these aldehydes are prone to racemization. Products which could not be isolated cleanly were characterized as the corresponding alcohols.

To assess the enantiopurity of the products, a duplicate experiment was performed, except the crude material was dissolved in CH_2Cl_2 (5 mL) and methanol (1 mL) and treated with sodium borohydride (190 mg, 5.0 mmol, 10 equiv). After 1 hour, the reaction was quenched with water (10 mL), the mixture was extracted with CH_2Cl_2 (3 × 10 mL), and the combined organic extracts were dried over Na_2SO_4 and concentrated. The residue was purified by flash chromatography on silica gel, and often purified further by preparative thin layer chromatography. The optical rotation

was measured and the enantiopurity was determined by chiral HPLC. Racemic alcohols to develop chiral HPLC assays were obtained by conducting the reaction with racemic organocatalyst.

Reactions in Table 4 were performed on 0.25 mmol scale and yields were determined by ^{1}H NMR. The crude residue was then reduced with $NaBH_4$ and assessed for product enantiopurity, as for optimization experiments. Reactions in Figure 3 were also performed on 0.25 mmol scale, employed racemic organocatalyst, and yields were determined by ^{1}H NMR, as for optimization experiments.

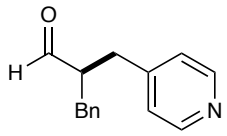
General Procedure B. Enantioselective α-Alkylation of Aldehydes with α-acetoxy-substituted Acetophenones (Table 3).



Photocatalyst **18** (2.1 mg, 2.6 μmol, 0.5 mol%), organocatalyst **8** (22 mg, 0.10 mmol, 20 mol%), 2,6-lutidine•HOTf (26 mg, 0.10 mmol, 20 mol%) and starting acetate (0.50 mmol, 1.0 equiv) were added to an 8 mL vial, followed by dimethylacetamide (2.0 mL), 2,6-lutidine (117 μL, 1.00 mmol, 2.00 equiv), and octanal (**45**) (156 μL,1.0 mmol, 2.0 equiv). The mixture was sparged with nitrogen for 15 minutes while stirring at 250 rpm, and the vial was sealed with parafilm and stirred in an isopropanol bath maintained at 0 °C with an immersion cooler next to a 34 W blue LED lamp. Once the acetate was consumed, the mixture was diluted with saturated $NaHCO_3$ (10 mL) and extracted with ether (3 × 10 mL). The combined organic extracts were dried over Na_2SO_4 and concentrated. The residue was purified by flash chromatography on silica gel. Racemic products to develop chiral HPLC assays were obtained by conducting the reaction with racemic organocatalyst.

V. Data for Enantioenriched α-Alkylated Aldehydes (Tables 2 & 3)

(*R*)-2-benzyl-3-(4-pyridinyl)propionaldehyde (16)



Prepared according to General Procedure A, irradiating for 5 hours. The aldehyde was purified by flash chromatography using an ethyl acetate/hexanes eluent (10 → 25%) containing 1% triethylamine to afford a clear, colorless oil (95 mg, 84% yield). The corresponding alcohol was purified by flash chromatography using a methanol/CH_2Cl_2 eluent (0 → 1%) containing 0.5% triethylamine followed by preparative thin layer chromatography (50% ethyl acetate/hexanes + 1% triethylamine) to afford a pale yellow oil.

^{1}H NMR (500 MHz, $CDCl_3$): δ 9.71 (s, 1H), 8.47 (d, *J* = 5.3 Hz, 2H), 7.28 (app t, 2H), 7.22 (app t, 1H), 7.13 (d, *J* = 7.6 Hz, 2H), 7.04 (d, *J* = 5.2 Hz, 2H), 3.10 – 2.92 (m, 3H), 2.79 – 2.62 (m, 2H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 202.8, 149.9, 148.0, 137.8, 129.0, 128.8, 126.8, 124.4, 53.9, 35.0, 33.7.

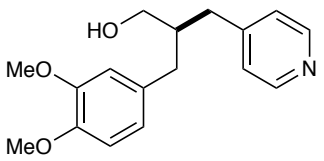
IR (film): ν 3065, 3028, 2925, 2845, 2726, 1722, 1601, 1558, 1497, 1454, 1416, 1394, 1221, 1070, 1030, 993, 916, 880, 835, 789, 749, 701 cm^{-1}.

HRMS (ESI-TOF): m/z calculated for $C_{15}H_{16}NO$ $[M+H]^+$ 226.1226, found 226.1227.

Chiral HPLC (alcohol): AD-H column, 10% ethanol/hexanes, 1.0 mL/min, 98% ee. t_R = 15.0 min (major (*R*)-enantiomer), 18.6 min (minor (*S*)-enantiomer).

$[\alpha]_D^{20}$ (alcohol): –3.0 (c = 1.0, CH_2Cl_2), –3.1 (c = 1.0, $CHCl_3$), lit[1] $[\alpha]_D^{23}$ –3.42 (c = 1.0, $CHCl_3$).

(*S*)-2-(3,4-dimethoxybenzyl)-3-(pyridin-4-yl)propan-1-ol (alcohol of aldehyde 20)



Prepared according to General Procedure A, irradiating for 5 hours. Following workup, the crude aldehyde was reduced without purification, and the resulting alcohol was purified by flash chromatography using a methanol/CH_2Cl_2 eluent (0 → 0.5%) containing 0.5% triethylamine to afford a clear, colorless oil (123 mg, 86% yield).

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.44 (d, *J* = 5.1 Hz, 2H), 7.10 (d, *J* = 5.2 Hz, 2H), 3.49 (m, 2H), 2.82 (dd, *J* = 13.4, 6.0 Hz, 2H), 2.38 (dd, *J* = 13.4, 8.5 Hz, 1H), 1.96 (dq, *J* = 12.9, 6.6 Hz, 1H), 0.88 (d, *J* = 6.9 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 150.3, 149.5, 124.8, 67.0, 39.0, 37.2, 16.4.

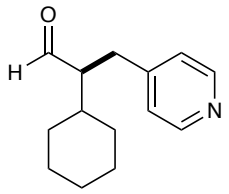
IR (film): ν 3252, 3000, 2927, 2835, 1603, 1558, 1514, 1464, 1451, 1417, 1333, 1260, 1235, 1192, 1155, 1139, 1090, 1070, 1027, 1004, 956, 945, 912, 859, 841, 807, 791, 765, 727 cm^{-1}.

HRMS (ESI-TOF): m/z calculated for $C_{17}H_{21}NO_3$ $[M+H]^+$ 288.1594, found 288.1592.

Chiral HPLC: OD-H column, 15% isopropanol/hexanes, 1.0 mL/min, 98% ee. t_R = 29.6 min (minor (*R*)-enantiomer), 32.9 min (major (*S*)-enantiomer).

$[\alpha]_D^{20}$: –4.6 (c = 1.0, CH_2Cl_2).

(*S*)-2-cyclohexyl-3-(pyridin-4-yl)propanal (21)



Prepared according to General Procedure A, irradiating for 12 hours, and using 5 equiv of cyclohexylacetaldehyde. The aldehyde was purified by flash chromatography using an ethyl acetate/toluene eluent (20%) to afford a clear, colorless oil (93 mg, 86% yield). The corresponding alcohol was purified by flash chromatography using an ethyl acetate/hexanes eluent (60%) containing 1% triethylamine followed by preparative thin layer chromatography (70% ethyl acetate/hexanes + 1% triethylamine) to afford a pale yellow oil.

^{1}H NMR (500 MHz, $CDCl_3$): δ 9.68 (d, *J* = 2.3 Hz, 1H), 8.46 (m, 2H), 7.07 (m, 2H), 3.00 (dd, *J* = 14.1, 9.2 Hz, 1H), 2.69 (dd, *J* = 14.2, 4.6 Hz, 1H), 2.55 (dtd, *J* = 9.3, 4.7, 2.3 Hz, 1H), 1.87 – 1.60 (m, 6H), 1.35 – 1.07 (m, 5H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 203.9, 150.0, 149.3, 124.4, 58.6, 38.6, 31.1, 30.6, 30.3, 26.5, 26.5, 26.3

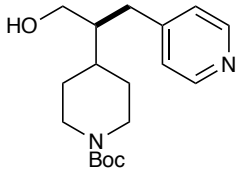
IR (film): ν 3068, 3026, 2924, 2853, 2716, 1721, 1600, 1559, 1496, 1448, 1416, 1396, 1371, 1351, 1264, 1220, 1172, 1070, 1047, 993, 913, 890, 878, 855, 837, 799, 731, 668 cm^{-1}.

HRMS (ESI-TOF): m/z calculated for $C_{14}H_{19}NO$ $[M+H]^+$ 218.1539, found 218.1541.

Chiral HPLC (alcohol): AS-H column, 5% isopropanol/hexanes, 1.0 mL/min, 96% ee. t_R = 20.7 min (major (*R*)-enantiomer), 27.1 min (minor (*S*)-enantiomer).

$[\alpha]_D^{20}$ (alcohol): –13.0 (c = 1.0, CH_2Cl_2).

***tert*-butyl (*S*)-4-(1-hydroxy-3-(pyridin-4-yl)propan-2-yl)piperidine-1-carboxylate (alcohol of aldehyde 22)**



Prepared according to General Procedure A, irradiating for 12 hours, and using 5 equiv of *tert*-butyl 4-(2-oxoethyl)-1-carboxylate. Following workup, the crude aldehyde was reduced without purification, and the resulting alcohol was purified by flash chromatography using a methanol/CH_2Cl_2 eluent (2.5 → 5%) to afford a clear, colorless oil (127 mg, 80% yield).

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.47 (m, 2H), 7.11 (m, 2H), 4.15 (br s, 2H), 3.53 (m, 2H), 2.78 – 2.50 (m, 4H), 1.67 (m, 4H), 1.45 (s, 9H), 1.28 (m, 2H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 154.9, 150.65, 150.58, 149.79, 149.75, 124.71, 124.69, 79.5, 61.51, 61.46, 46.8, 44.20, 44.10, 36.8, 33.9, 29.4, 28.6.

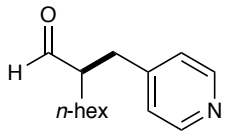
IR (film): ν 3382, 2978, 2930, 2860, 2241, 1647, 1603, 1559, 1476, 1467, 1421, 1393, 1365, 1297, 1280, 1264, 1240, 1164, 1143, 1070, 1039, 1003, 980, 913, 865, 829, 809, 770, 728 cm^{-1}.

HRMS (ESI-TOF): m/z calculated for $C_{18}H_{28}N_2O_3$ $[M+H]^+$ 321.2173, found 321.2173.

Chiral HPLC: AD-H column, 10% isopropanol/hexanes, 1.0 mL/min, 94% ee. t_R = 13.5 min (major (*S*)-enantiomer), 19.8 min (minor (*R*)-enantiomer).

$[\alpha]_D^{20}$: +7.7 (c = 1.0, CH_2Cl_2).

(*R*)-2-(pyridin-4-ylmethyl)octanal (23)[1]



Prepared according to General Procedure A, irradiating for 5 hours. The aldehyde was purified by flash chromatography using an ethyl acetate/hexanes eluent (40%) to afford a clear, colorless oil (99 mg, 90% yield). The corresponding alcohol was purified by flash chromatography using an ethyl acetate/hexanes eluent (65%) containing 1% triethylamine followed by preparative thin layer chromatography (75% ethyl acetate/hexanes + 1% triethylamine) to afford a clear, colorless oil.

^{1}H NMR (500 MHz, $CDCl_3$): δ 9.64 (t, *J* = 1.7 Hz, 1H), 8.48 (dt, *J* = 4.4, 1.5 Hz, 2H), 7.08 (d, *J* = 5.5 Hz, 2H), 2.98 (m, 1H), 2.66 (m, 2H), 1.65 (m, 1H), 1.46 (m, 1H), 1.40 – 1.16 (m, 8H), 0.85 (t, *J* = 6.9 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 203.6, 150.0, 148.3, 124.4, 52.6, 34.0, 31.6, 29.3, 28.7, 26.9, 22.6, 14.1.

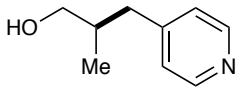
IR (film): ν 3068, 3028, 2927, 2857, 2716, 1724, 1601, 1559, 1497, 1461, 1415, 1391, 1378, 1220, 1123, 1090, 1071, 1047, 993, 961, 850, 833, 792, 724 cm^{-1}.

HRMS (ESI-TOF): m/z calculated for $C_{14}H_{21}NO$ $[M+H]^+$ 220.1696, found 220.1695.

Chiral HPLC (alcohol): OD-H column, 5% isopropanol/hexanes, 1.0 mL/min, 96% ee. t_R = 16.2 min (minor (*S*)-enantiomer), 18.8 min (major (*R*)-enantiomer).

$[\alpha]_D^{20}$ (alcohol): +7.4 (c = 1.0, CH_2Cl_2).

(*R*)-2-methyl-3-(pyridin-4-yl)propan-1-ol (alcohol of aldehyde 24)



Prepared according to General Procedure A, irradiating for 5 hours. ^{1}H NMR analysis of an aliquot of the reaction showed 93% yield of the aldehyde vs. 2,6-lutidine. Following workup, the crude aldehyde was reduced without purification, and the resulting alcohol was purified by flash chromatography using a ethyl acetate/hexanes eluent (65%) containing 1% triethylamine followed by preparative thin layer chromatography (ethyl acetate + 1% triethylamine) to afford a pale yellow oil. The alcohol remained contaminated with ~ 10% of the organocatalyst which proved inseparable, so this material was fully characterized. NMR signals attributable to the organocatalyst are not listed.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.44 (d, *J* = 5.1 Hz, 2H), 7.10 (d, *J* = 5.2 Hz, 2H), 3.49 (m, 2H), 2.82 (dd, *J* = 13.4, 6.0 Hz, 2H), 2.38 (dd, *J* = 13.4, 8.5 Hz, 1H), 1.96 (dq, *J* = 12.9, 6.6 Hz, 1H), 0.88 (d, *J* = 6.9 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 150.3, 149.5, 124.8, 67.0, 39.0, 37.2, 16.4.

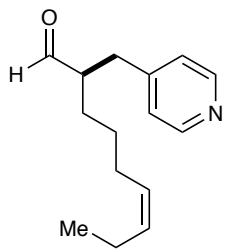
IR (film): ν 3276, 3063, 3028, 2958, 2925, 2872, 1679, 1603, 1558, 1497, 1455, 1417, 1382, 1262, 1221, 1186, 1134, 1094, 1041, 1002, 991, 916, 887, 848, 837, 827, 787, 730, 701 cm^{-1}.

HRMS (ESI-TOF): m/z calculated for $C_9H_{13}NO$ $[M+H]^+$ 152.1070, found 152.1071.

Chiral HPLC: AS-H column, 10% isopropanol/hexanes, 1.0 mL/min, 96% ee. t_R = 13.7 min (minor (*S*)-enantiomer), 16.4 min (major (*R*)-enantiomer).

$[\alpha]_D^{21}$: +12.1 (c = 0.5, CH_2Cl_2).

(*R*,*Z*)-2-(pyridin-4-ylmethyl)non-6-enal (25)



Prepared according to General Procedure A, irradiating for 5 hours. The aldehyde was purified by flash chromatography using an ethyl acetate/hexanes eluent (40%) to afford a clear, colorless oil (98 mg, 85% yield). Quantitative ^{13}C NMR analysis of the aldehyde showed a 4.5:1 *Z*/*E* mixture of alkene isomers. The corresponding alcohol was purified by flash chromatography using an ethyl acetate/hexanes eluent (70%) containing 1% triethylamine followed by preparative thin layer chromatography (75% ethyl acetate/hexanes + 1% triethylamine) to afford a pale yellow oil. The 4 stereoisomers could not be separated by HPLC, so the alkenyl alcohol (50 mg) was dissolved in methanol (1 mL), palladium (10 wt% on carbon, 5 mg) was added, and the mixture was stirred under hydrogen (balloon, 1 atm). After 12 hours, the mixture was filtered thourgh Celite®, washed with methanol (20 mL), and concentrated. The resulting (*R*)-2-(pyridin-4-ylmethyl)nonan-1-ol was sufficiently pure for determination of optical properties.

^{1}H NMR (500 MHz, $CDCl_3$): δ 9.65 (s, 1H), 8.49 (d, *J* = 6.0 Hz, 2H), 7.08 (d, *J* = 6.0 Hz, 2H), 5.48 – 5.16 (m, 2H), 2.98 (m, 1H), 2.67 (m, 2H), 1.99 (m, 4H), 1.65 (m, 1H), 1.56 – 1.29 (m, 3H), 0.93 (t, *J* = 7.6 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): 4.5:1 mixture of isomers; *Z* isomer δ 203.37, 149.99, 148.20, 132.63, 127.95, 124.38, 52.45, 33.98, 28.23, 26.97, 26.90, 20.6, 14.40; *E* isomer δ 203.43, 149.97, 148.25, 133.08, 128.03, 124.38, 52.41, 33.93, 32.38, 28.04, 26.72, 25.62, 13.98.

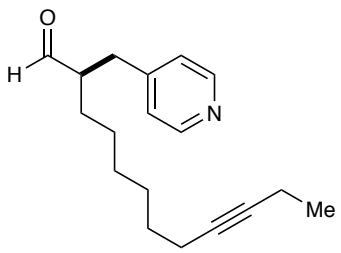
IR (film): ν 3004, 2962, 2932, 2859, 2716, 1724, 1601, 1559, 1497, 1458, 1415, 1372, 1304, 1220, 1070, 993, 968, 912, 855, 828, 792, 731 cm^{-1}.

HRMS (ESI-TOF): m/z calculated for $C_{15}H_{21}NO$ $[M+H]^+$ 232.1696, found 232.1698.

Chiral HPLC (alcohol, alkene reduced): OD-H column, 3% isopropanol/hexanes, 1.0 mL/min, 95% ee. t_R = 29.3 min (minor (*S*)-enantiomer), 33.6 min (major (*R*)-enantiomer).

$[\alpha]_D^{21}$ (alcohol, alkene reduced): –5.2 (c = 1.0, CH_2Cl_2).

(*R*)-2-(pyridin-4-ylmethyl)dodec-9-ynal (26)



Prepared according to General Procedure A, irradiating for 5 hours. The aldehyde was purified by flash chromatography using an ethyl acetate/hexanes eluent (40%) to afford a clear, colorless oil (121 mg, 89% yield). The corresponding alcohol was purified by flash chromatography using an ethyl acetate/hexanes eluent (50%) containing 1% triethylamine followed by preparative thin layer chromatography (60% ethyl acetate/hexanes + 1% triethylamine) to afford a pale yellow oil.

^{1}H NMR (500 MHz, $CDCl_3$): δ 9.64 (s, 1H), 8.48 (d, *J* = 5.0 Hz, 2H), 7.08 (d, *J* = 5.1 Hz, 2H), 2.98 (m, 1H), 2.65 (m, 2H), 2.12 (m, 4H), 1.65 (m, 1H), 1.54 – 1.38 (m, 3H), 1.38 – 1.19 (m, 6H), 1.08 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 203.5, 150.0, 148.3, 124.4, 81.9, 79.4, 52.5, 34.0, 29.2, 29.0, 28.7, 28.6, 26.8, 18.7, 14.5, 12.5.

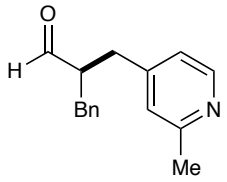
IR (film): ν 2975, 2931, 2857, 2715, 1724, 1601, 1559, 1497, 1461, 1416, 1320, 1220, 1070, 993, 912, 847, 832, 791, 730 cm^{-1}.

HRMS (ESI-TOF): m/z calculated for $C_{18}H_{25}NO$ $[M+H]^+$ 272.2009, found 272.2009.

Chiral HPLC (alcohol): OD-H column, 5% isopropanol/hexanes, 1.0 mL/min, 96% ee. t_R = 21.1 min (minor (*S*)-enantiomer), 26.0 min (major (*R*)-enantiomer).

$[\alpha]_D^{22}$ (alcohol): –1.7 (c = 0.5, CH_2Cl_2).

(*R*)-2-benzyl-3-(2-methylpyridin-4-yl)propionaldehyde (27)



Prepared according to General Procedure A, irradiating for 5 hours. The aldehyde was purified by flash chromatography using an ethyl acetate/hexanes eluent (25 → 40%) containing 1% triethylamine to afford a clear, colorless oil (98 mg, 82% yield). The corresponding alcohol was purified by flash chromatography using an ethyl acetate/hexanes eluent (35 → 75%) containing 1% triethylamine followed by preparative thin layer chromatography (60% ethyl acetate/hexanes + 1% triethylamine) to afford a pale yellow oil.

^{1}H NMR (500 MHz, $CDCl_3$): δ 9.71 (d, *J* = 1.4 Hz, 1H), 8.37 (d, *J* = 5.1 Hz, 1H), 7.29 (app t, 2H), 7.23 (m, 1H), 7.14 (m, 2H), 6.91 (s, 1H), 6.86 (d, *J* = 4.4 Hz, 1H), 3.01 (m, 2H), 2.94 (dd, *J* = 13.8, 7.3 Hz, 1H), 2.75 (m, 1H), 2.65 (dd, *J* = 14.0, 5.3 Hz, 1H), 2.50 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 203.0, 158.7, 149.4, 148.23, 138.0, 129.1, 128.8, 126.9, 124.0, 121.5, 54.02, 35.2, 33.9, 24.5.

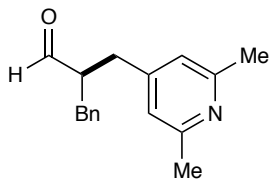
IR (film): ν 3062, 3027, 2923, 2854, 2725, 1723, 1603, 1561, 1496, 1454, 1406, 1295, 1195, 1168, 1076, 1031, 997, 911, 845, 822, 745, 731, 700 cm^{-1}.

HRMS (ESI-TOF): m/z calculated for $C_{16}H_{17}NO$ $[M+H]^+$ 239.1383, found 239.1381.

Chiral HPLC (alcohol): AD-H column, 5% ethanol/hexanes, 1.0 mL/min, 98% ee. t_R = 25.4 min (minor (*S*)-enantiomer), 27.4 min (major (*R*)-enantiomer).

$[\alpha]_D^{20}$ (alcohol): +0.29 (c = 1.0, CH_2Cl_2).

(*R*)-2-benzyl-3-(2,6-dimethylpyridin-4-yl)propionaldehyde (28)



Prepared according to General Procedure A, irradiating for 5 hours. The aldehyde was purified by flash chromatography using an ethyl acetate/hexanes eluent (25%) containing 1% triethylamine to afford a clear, colorless oil (92 mg, 73% yield). The corresponding alcohol was purified by flash chromatography using an ethyl acetate/hexanes eluent (30 → 50%) containing 1% triethylamine followed by preparative thin layer chromatography (50% ethyl acetate/hexanes + 1% triethylamine) to afford a pale yellow oil.

^{1}H NMR (500 MHz, $CDCl_3$): δ 9.70 (d, *J* = 1.5 Hz, 1H), 7.29 (m, 2H), 7.22 (m, 1H), 7.14 (m, 2H), 6.72 (s, 2H), 3.04 – 2.95 (m, 2H), 2.89 (m, 1H), 2.78 – 2.69 (m, 1H), 2.65 – 2.58 (m, 1H), 2.47 (s, 6H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 203.2, 158.0, 148.4, 138.1, 129.1, 128.8, 126.8, 120.9, 54.0, 35.2, 33.9, 24.5.

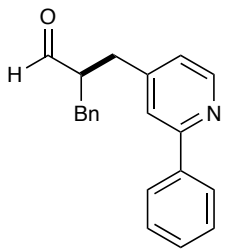
IR (film): ν 3029, 2925, 2853, 2727, 2253, 2204, 1725, 1608, 1568, 1497, 1449, 1382, 1223, 1077, 1030, 996, 908, 867, 727, 700 cm^{-1}.

HRMS (ESI-TOF): m/z calculated for $C_{17}H_{19}NO$ $[M+H]^+$ 254.1539, found 254.1540.

Chiral HPLC (alcohol): AS-H column, 5% isopropanol/hexanes, 1.0 mL/min, 98% ee. t_R = 11.0 min (major (*R*)-enantiomer), 17.8 min (minor (*S*)-enantiomer).

$[\alpha]_D^{20}$ (alcohol): –8.3 (c = 1.0, CH_2Cl_2).

(*R*)-2-benzyl-3-(2-phenylpyridin-4-yl)propionaldehyde (29)



Prepared according to General Procedure A, irradiating for 24 hours. The aldehyde was purified by flash chromatography using an ethyl acetate/hexanes eluent (10 → 20%) containing 1% triethylamine to afford a clear, colorless oil (112 mg, 74% yield). The corresponding alcohol was purified by flash chromatography using an ethyl acetate/hexanes eluent (50 → 100%) containing 1% triethylamine followed by preparative thin layer chromatography (ethyl acetate + 1% triethylamine) to afford a pale yellow oil.

^{1}H NMR (500 MHz, $CDCl_3$): δ 9.71 (s, 1H), 8.54 (d, *J* = 5.0 Hz, 1H), 7.92 (d, *J* = 7.5 Hz, 2H), 7.44 (m, 3H), 7.38 (t, *J* = 7.3 Hz, 1H), 7.27 (t, *J* = 7.5 Hz, 2H), 7.20 (t, *J* = 7.5 Hz, 1H), 7.12 (d, *J* = 7.5 Hz, 2H), 6.96 (d, *J* = 4.3 Hz, 1H), 3.13 – 2.97 (overlapping signals, 3H), 2.74 (m, 2H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 202.9, 157.7, 149.8, 148.8, 139.2, 137.9, 129.1, 129.1, 128.8, 128.8, 127.0, 126.9, 122.8, 121.3, 54.0, 35.1, 33.9.

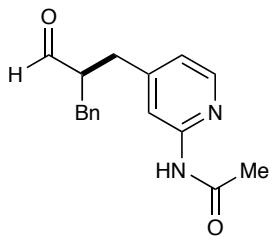
IR (film): ν 3061, 3029, 2924, 2833, 2723, 1723, 1599, 1581, 1556, 1496, 1475, 1446, 1405, 1074, 1029, 991, 906, 847, 776, 735, 696 cm^{-1}.

HRMS (ESI-TOF): m/z calculated for $C_{21}H_{19}NO$ $[M+H]^+$ 302.1539, found 302.1538.

Chiral HPLC (alcohol): AD-H column, 8% ethanol/hexanes, 1.0 mL/min, 97% ee. t_R = 13.0 min (minor (*S*)-enantiomer), 15.0 min (major (*R*)-enantiomer).

$[\alpha]_D^{20}$ (alcohol): +2.2 (c = 1.0, CH_2Cl_2).

(*R*)-*N*-(4-(2-benzyl-3-oxopropyl)pyridin-2-yl)acetamide (30)



Prepared according to General Procedure A, irradiating for 24 hours. The aldehyde was purified by flash chromatography using an ethyl acetate/hexanes eluent (25 → 60%) containing 1% triethylamine to afford a white semisolid (102 mg, 72% yield). The corresponding alcohol was purified by flash chromatography using an ethyl acetate/hexanes eluent (15 → 35%) containing 1% triethylamine followed by preparative thin layer chromatography (ethyl acetate + 1% triethylamine) to afford a pale yellow oil.

^{1}H NMR (500 MHz, $CDCl_3$): δ 9.71 (s, 1H), 8.88 (s, 1H), 8.12 (m, 2H), 7.35 – 7.19 (m, 3H), 7.15 (d, *J* = 5.0 Hz, 2H), 6.83 (s, 1H), 3.13 – 2.93 (m, 3H), 2.85 – 2.65 (m, 2H), 2.18 (d, *J* = 2.9 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 203.1, 169.0, 152.0, 151.0, 147.7, 137.9, 129.1, 128.8, 126.9, 120.7, 114.4, 53.8, 35.2, 34.3, 24.9.

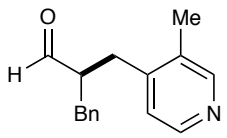
IR (film): ν 3211, 3030, 2929, 1725, 1696, 1611, 1567, 1533, 1497, 1422, 1368, 1296, 1264, 1239, 1163, 1025, 966, 909, 844, 736, 701 cm^{-1}.

HRMS (ESI-TOF): m/z calculated for $C_{17}H_{18}N_2O_2$ $[M+H]^+$ 282.1441, found 282.1442.

Chiral HPLC (alcohol): AS-H column, 5% ethanol/hexanes, 1.0 mL/min, 98% ee. t_R = 10.8 min (major (*R*)-enantiomer), 24.2 min (minor (*S*)-enantiomer).

$[\alpha]_D^{20}$ (alcohol): –1.8 (c = 1.0, CH_2Cl_2).

(*R*)-2-benzyl-3-(3-methylpyridin-4-yl)propionaldehyde (31)



Prepared according to General Procedure A, irradiating for 5 hours. The aldehyde was purified by flash chromatography using an ethyl acetate/hexanes eluent (20 → 40%) containing 1% triethylamine to afford a clear, colorless oil (90 mg, 75% yield). The corresponding alcohol was purified by flash chromatography using a methanol/CH_2Cl_2 eluent (0 → 0.5%) containing 0.5% triethylamine to afford a pale yellow oil.

^{1}H NMR (500 MHz, $CDCl_3$): δ 9.71 (s, 1H), 8.32 (overlapping signals, 2H), 7.28 (app t, 2H), 7.22 (t, *J* = 7.5 Hz, 1H), 7.14 (d, *J* = 7.5 Hz, 2H), 6.99 (d, *J* = 5.1 Hz, 1H), 3.06 (dd, *J* = 13.7, 6.5 Hz, 1H), 3.01 – 2.91 (m, 2H), 2.73 (dd, *J* = 13.8, 6.3 Hz, 1H), 2.64 (q, *J* = 9.3 Hz, 1H), 2.12 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 202.8, 151.1, 147.6, 146.2, 137.9, 131.9, 129.1, 128.8, 126.9, 124.0, 53.1, 35.4, 30.9, 16.2.

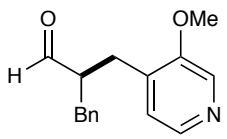
IR (film): ν 3062, 3027, 2925, 2855, 2727, 1723, 1594, 1561, 1495, 1454, 1404, 1309, 1195, 1076, 1064, 1031, 1000, 913, 880, 845, 819, 747, 732, 700 cm^{-1}.

HRMS (ESI-TOF): m/z calculated for $C_{16}H_{17}NO$ $[M+H]^+$ 239.1383, found 239.1382.

Chiral HPLC (alcohol): AD-H column, 10% ethanol/hexanes, 1.0 mL/min, 98% ee. t_R = 11.6 min (minor (*S*)-enantiomer), 13.8 min (major (*R*)-enantiomer).

$[\alpha]_D^{21}$ (alcohol): –8.3 (c = 0.33, CH_2Cl_2).

(*R*)-2-benzyl-3-(3-methoxypyridin-4-yl)propionaldehyde (32)



Prepared according to General Procedure A, irradiating for 24 hours. The aldehyde was purified by flash chromatography using an ethyl acetate/hexanes eluent (30 → 50%) containing 1% triethylamine to afford a pale orange oil (90 mg, 71% yield). The corresponding alcohol was purified by flash chromatography using an ethyl acetate/hexanes eluent (40 → 70%) containing 1% triethylamine followed by preparative thin layer chromatography (80% ethyl acetate/hexanes + 1% triethylamine) to afford a pale orange oil.

^{1}H NMR (500 MHz, $CDCl_3$): δ 9.68 (d, *J* = 1.6 Hz, 1H), 8.19 (s, 1H), 8.15 (d, *J* = 4.7 Hz, 1H), 7.29 (t, *J* = 7.3 Hz, 2H), 7.21 (t, *J* = 7.3 Hz, 1H), 7.14 (d, *J* = 6.8 Hz, 2H), 7.00 (d, *J* = 4.6 Hz, 1H), 3.86 (s, 3H), 3.09 – 2.92 (m, 3H), 2.78 – 2.67 (m, 2H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 203.3, 153.9, 142.7, 138.3, 135.9, 133.0, 129.1, 128.7, 126.7, 125.4, 55.9, 52.6, 35.2, 29.1.

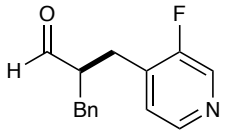
IR (film): ν 3027, 2931, 2841, 2719, 1725, 1595, 1567, 1498, 1455, 1417, 1269, 1212, 1182, 1073, 1025, 910, 840, 824, 731, 701 cm^{-1}.

HRMS (ESI-TOF): m/z calculated for $C_{16}H_{17}NO_2$ $[M+H]^+$ 256.1332, found 256.1332.

Chiral HPLC (alcohol): AS-H column, 5% ethanol/hexanes, 1.0 mL/min, 98% ee. t_R = 15.9 min (major (*R*)-enantiomer), 18.9 min (minor (*S*)-enantiomer).

$[\alpha]_D^{21}$ (alcohol): +1.1 (c = 1.0, CH_2Cl_2).

(*R*)-2-benzyl-3-(3-fluoropyridin-4-yl)propionaldehyde (33)



Prepared according to General Procedure A, irradiating for 36 hours, and using 5 equiv of hydrocinnamaldehyde. The aldehyde was purified by flash chromatography using an ethyl acetate/hexanes eluent (10 → 25%) containing 1% triethylamine, followed by preparative thin layer chromatography (50% ethyl acetate/hexanes + 1% triethylamine) to afford a pale yellow oil (95 mg, 78% yield). The corresponding alcohol was purified by flash chromatography using an ethyl acetate/hexanes eluent (25 → 40%) containing 1% triethylamine followed by preparative thin layer chromatography (60% ethyl acetate/hexanes + 1% triethylamine) to afford an oil.

^{1}H NMR (500 MHz, $CDCl_3$): δ 9.70 (s, 1H), 8.36 (d, *J* = 1.7 Hz, 1H), 8.28 (d, *J* = 4.9 Hz, 1H), 7.29 (t, *J* = 7.5 Hz, 2H), 7.23 (m, 1H), 7.15 (d, *J* = 7.2 Hz, 2H), 7.09 (m, 1H), 3.13 – 2.97 (m, 3H), 2.77 (m, 2H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 202.4, 158.4 (d, *J* = 254.9 Hz), 145.8 (d, *J* = 5.1 Hz), 138.1 (d, *J* = 24.6 Hz), 137.6, 134.8 (d, *J* = 13.1 Hz), 128.9 (d, *J* = 21.7 Hz), 127.0, 125.8 (d, *J* = 1.9 Hz), 52.8, 35.4, 27.4 (d, *J* = 2.0 Hz).

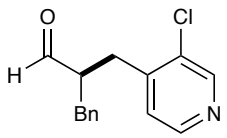
IR (film): ν 3058, 3029, 2925, 2832, 2727, 1724, 1606, 1562, 1494, 1455, 1415, 1246, 1237, 1196, 1142, 1076, 1057, 1030, 913, 881, 841, 778, 747, 699 cm^{-1}.

HRMS (ESI-TOF): m/z calculated for $C_{15}H_{14}FNO$ $[M+H]^+$ 244.1132, found 244.1128.

Chiral HPLC (alcohol): AS-H column, 10% isopropanol/hexanes, 1.0 mL/min, 96% ee. t_R = 9.6 min (major (*R*)-enantiomer), 13.2 min (minor (*S*)-enantiomer).

$[\alpha]_D^{21}$ (alcohol): –0.13 (c = 1.0, CH_2Cl_2).

(*R*)-2-benzyl-3-(3-chloropyridin-4-yl)propionaldehyde (34)



Prepared according to General Procedure A, irradiating for 36 hours, and using 5 equiv of hydrocinnamaldehyde. The aldehyde was purified by flash chromatography using an ethyl acetate/hexanes eluent (10 → 20%) containing 1% triethylamine, followed by preparative thin layer chromatography (50% ethyl acetate/hexanes + 1% triethylamine) to afford a clear, colorless oil (89 mg, 69% yield). The corresponding alcohol was purified by flash chromatography using an ethyl acetate/hexanes eluent (20 → 35%) containing 1% triethylamine followed by preparative thin layer chromatography (50% ethyl acetate/hexanes + 1% triethylamine) to afford a pale yellow oil.

^{1}H NMR (500 MHz, $CDCl_3$): δ 9.71 (s, 1H), 8.51 (s, 1H), 8.35 (d, *J* = 5.0 Hz, 1H), 7.30 (t, *J* = 7.4 Hz, 2H), 7.24 (t, *J* = 7.3 Hz, 1H), 7.17 (d, *J* = 7.5 Hz, 2H), 7.12 (d, *J* = 5.0 Hz, 1H), 3.18 – 3.01 (m, 3H), 2.86 – 2.74 (m, 2H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 202.5, 149.7, 147.8, 145.8, 137.6, 132.2, 129.1, 128.9, 127.0, 126.0, 52.5, 35.6, 31.7.

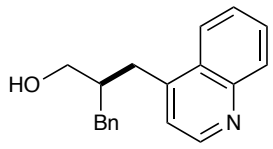
IR (ATR): ν 3059, 3028, 2926, 2834, 2728, 1724, 1601, 1585, 1497, 1479, 1455, 1399, 1294, 1221, 1176, 1095, 1077, 1035, 915, 881, 842, 818, 751, 735, 700 cm^{-1}.

HRMS (ESI-TOF): m/z calculated for $C_{15}H_{14}ClNO$ $[M+H]^+$ 260.0837, found 260.0835.

Chiral HPLC (alcohol): AS-H column, 10% isopropanol/hexanes, 1.0 mL/min, 94% ee. t_R = 8.6 min (major (*R*)-enantiomer), 10.5 min (minor (*S*)-enantiomer).

$[\alpha]_D^{20}$ (alcohol): –14.0 (c = 1.0, CH_2Cl_2).

(*R*)-2-benzyl-3-(4-quinolinyl)propan-1-ol (alcohol of aldehyde 35)



Prepared according to General Procedure A, irradiating for 24 hours. Following workup, the crude aldehyde was reduced without purification, and the resulting alcohol was purified by flash chromatography using a methanol/CH_2Cl_2 eluent (0 → 0.5%) containing 0.5% triethylamine to afford a pale yellow syrup (114 mg, 83% yield).

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.65 (d, *J* = 4.5 Hz, 1H), 8.05 (d, *J* = 8.5 Hz, 1H), 7.76 (d, *J* = 8.5 Hz, 1H), 7.63 (t, *J* = 7.3 Hz, 1H), 7.41 (t, *J* = 7.7 Hz, 1H), 7.29 (t, *J* = 7.4 Hz, 2H), 7.24 – 7.13 (m, 4H), 3.54 (d, *J* = 4.9 Hz, 2H), 3.29 (br s, 1H), 3.17 (dd, *J* = 13.8, 8.4 Hz, 1H), 3.04 (dd, *J* = 13.7, 5.8 Hz, 1H), 2.90 (dd, *J* = 13.6, 7.3 Hz, 1H), 2.68 (dd, *J* = 13.6, 7.3 Hz, 1H), 2.25 (tdd, *J* = 12.7, 7.3, 4.9 Hz, 1H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 149.7, 148.2, 147.5, 140.2, 129.8, 129.3, 129.2, 128.5, 127.8, 126.4, 126.3, 123.9, 122.2, 63.6, 44.0, 38.1, 33.4.

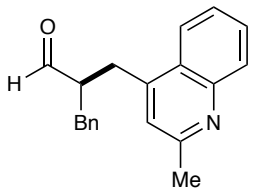
IR (film): ν 3237, 3062, 3027, 2921, 2861, 1590, 1573, 1509, 1495, 1453, 1424, 1393, 1359, 1308, 1242, 1151, 1089, 1044, 1028, 1012, 952, 907, 854, 825, 813, 762, 728, 699 cm^{-1}.

HRMS (ESI-TOF): m/z calculated for $C_{19}H_{19}NO$ $[M+H]^+$ 278.1539, found 278.1537.

Chiral HPLC: AS-H column, 10% isopropanol/hexanes, 1.0 mL/min, 96% ee. t_R = 10.3 min (major (*R*)-enantiomer), 15.1 min (minor (*S*)-enantiomer).

$[\alpha]_D^{20}$: +8.2 (c = 1.0, CH_2Cl_2).

(*R*)-2-benzyl-3-(2-methylquinolin-4-yl)propionaldehyde (36)



Prepared according to General Procedure A, irradiating for 24 hours. The aldehyde was purified by flash chromatography using an ethyl acetate/hexanes eluent (10 → 25%) containing 1% triethylamine to afford a clear, colorless syrup (109 mg, 75% yield). The corresponding alcohol was purified by flash chromatography using an ethyl acetate/hexanes eluent (50%) containing 1% triethylamine to afford a white solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ 9.75 (s, 1H), 8.01 (d, *J* = 8.4 Hz, 1H), 7.64 (t, *J* = 7.6 Hz, 1H), 7.57 (d, *J* = 8.4 Hz, 1H), 7.40 (m, 1H), 7.33 (t, *J* = 7.4 Hz, 2H), 7.27 (m, 1H), 7.18 (d, *J* = 7.1 Hz, 2H), 7.09 (s, 1H), 3.39 (dd, *J* = 13.4, 6.7 Hz, 1H), 3.19 – 3.05 (m, 3H), 2.79 (m, 1H), 2.68 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 202.9, 158.6, 148.3, 144.8, 138.0, 129.7, 129.3, 129.3, 128.9, 127.0, 125.9, 125.5, 123.0, 53.6, 35.8, 30.6, 25.4.

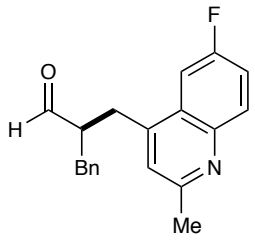
IR (film): ν 3062, 3028, 2921, 2839, 2725, 1723, 1601, 1562, 1510, 1497, 1454, 1414, 1377, 1338, 1192, 1156, 1126, 1079, 1028, 960, 876, 833, 762, 744, 701 cm^{-1}.

HRMS (ESI-TOF): m/z calculated for $C_{20}H_{19}NO$ $[M+H]^+$ 290.1539, found 290.1544.

Chiral HPLC (alcohol): AS-H column, 5% isopropanol/hexanes, 1.0 mL/min, 98% ee. t_R = 14.3 min (major (*R*)-enantiomer), 21.4 min (minor (*S*)-enantiomer).

$[\alpha]_D^{21}$ (alcohol): +9.2 (c = 1.0, CH_2Cl_2).

(*R*)-2-benzyl-3-(6-fluoro-2-methylquinolin-4-yl)propionaldehyde (37)



Prepared according to General Procedure A, irradiating for 24 hours. The aldehyde was purified by flash chromatography using an ethyl acetate/hexanes eluent (10 → 25%) containing 1% triethylamine to afford a white solid (97 mg, 63% yield). The corresponding alcohol was purified by flash chromatography using an ethyl acetate/hexanes eluent (50%) containing 1% triethylamine to afford a colorless semisolid.

^{1}H NMR (500 MHz, $CDCl_3$): δ 9.76 (d, *J* = 1.6 Hz, 1H), 7.99 (dd, *J* = 9.2, 5.6 Hz, 1H), 7.40 (ddd, *J* = 9.2, 8.0, 2.8 Hz, 1H), 7.35 (m, 2H), 7.31 – 7.27 (m, 1H), 7.21 (m, 2H), 7.11 (overlapping signals, 2H), 3.33 (dd, *J* = 14.3, 8.3 Hz, 1H), 3.16 (dd, *J* = 13.6, 6.5 Hz, 1H), 3.13 – 3.06 (m, 1H), 3.01 (dd, *J* = 14.3, 5.0 Hz, 1H), 2.77 (dd, *J* = 13.6, 7.7 Hz, 1H), 2.66 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 202.6, 161.2, 159.2, 157.9, 145.4, 144.4 (d, *J* = 5.5 Hz), 137.8, 132.1 (d, *J* = 9.1 Hz), 129.1 (d, *J* = 25.9 Hz), 127.2, 126.2 (d, *J* = 9.2 Hz), 123.6, 119.3 (d, *J* = 25.3 Hz), 106.7 (d, *J* = 22.5 Hz), 53.5, 35.8, 30.4, 25.3.

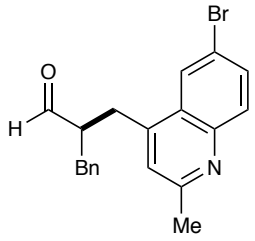
IR (film): ν 3064, 3028, 2923, 2853, 2728, 1723, 1625, 1605, 1564, 1511, 1498, 1471, 1454, 1392, 1379, 1342, 1232, 1199, 1177, 1114, 1079, 1030, 1002, 967, 930, 869, 833, 773, 747, 701, 678 cm^{-1}.

HRMS (ESI-TOF): m/z calculated for $C_{20}H_{18}FNO$ $[M+H]^+$ 308.1445, found 308.1446.

Chiral HPLC (alcohol): AS-H column, 10% isopropanol/hexanes, 1.0 mL/min, 97% ee. t_R = 6.5 min (major (*R*)-enantiomer), 9.6 min (minor (*S*)-enantiomer).

$[\alpha]_D^{21}$ (alcohol): +11.7 (c = 1.0, CH_2Cl_2).

(*R*)-2-benzyl-3-(6-bromo-2-methylquinolin-4-yl)propionaldehyde (38)



Prepared according to General Procedure A, irradiating for 24 hours. The aldehyde was purified by flash chromatography using an ethyl acetate/hexanes eluent (15 → 30%) containing 1% triethylamine to afford an off-white solid (111 mg, 60% yield). The corresponding alcohol was purified by flash chromatography using an ethyl acetate/hexanes eluent (30 → 60%) containing 1% triethylamine followed by preparative thin layer chromatography (65% ethyl acetate/hexanes + 1% triethylamine) to afford an off-white solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ 9.75 (d, *J* = 1.5 Hz, 1H), 7.84 (d, *J* = 8.9 Hz, 1H), 7.68 (dd, *J* = 8.9, 2.2 Hz, 1H), 7.65 (d, *J* = 2.1 Hz, 1H), 7.36 (m, 2H), 7.29 (m, 1H), 7.21 (m, 2H), 7.09 (s, 1H), 3.29 (dd, *J* = 14.2, 8.6 Hz, 1H), 3.16 (dd, *J* = 13.5, 6.2 Hz, 1H), 3.10 (dddd, *J* = 14.8, 8.3, 6.2, 1.6 Hz, 1H), 3.02 (dd, *J* = 14.2, 4.8 Hz, 1H), 2.73 (dd, *J* = 13.5, 8.0 Hz, 1H), 2.64 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 202.3, 159.1, 146.9, 144.0, 137.7, 132.7, 131.4, 129.1, 129.1, 127.2, 126.8, 125.4, 123.7, 119.9, 53.566 35.7, 30.1, 25.4.

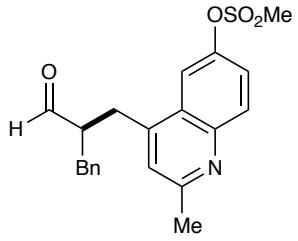
IR (film): ν 3063, 3027, 2922, 2852, 2727, 1723, 1600, 1557, 1495, 1471, 1454, 1379, 1339, 1316, 1256, 1221, 1191, 1153, 1074, 1030, 997, 966, 877, 829, 785, 746, 701, 685, 655 cm^{-1}.

HRMS (ESI-TOF): m/z calculated for $C_{20}H_{18}BrNO$ $[M+H]^+$ 368.0645, found 368.0639.

Chiral HPLC (alcohol): OD-H column, 10% isopropanol/hexanes, 1.0 mL/min, 99% ee. t_R = 14.3 min (minor (*S*)-enantiomer), 20.5 min (major (*R*)-enantiomer).

$[\alpha]_D^{22}$ (alcohol): +14.2 (c = 1.0, CH_2Cl_2).

(*R*)-2-benzyl-3-(6-mesyloxy-2-methylquinolin-4-yl)propionaldehyde (39)



Prepared according to General Procedure A, irradiating for 24 hours. The aldehyde was purified by flash chromatography using an ethyl acetate/hexanes eluent (40 → 60%) containing 1% triethylamine to afford a pale yellow oil (134 mg, 70% yield). The corresponding alcohol was purified by flash chromatography using an ethyl acetate/hexanes eluent (40 → 65 → 80%) containing 1% triethylamine followed by preparative thin layer chromatography (80% ethyl acetate/hexanes + 1% triethylamine) to afford a white solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ 9.73 (d, *J* = 1.5 Hz, 1H), 8.04 (d, *J* = 9.1 Hz, 1H), 7.55 (dd, *J* = 9.1, 2.6 Hz, 1H), 7.49 (d, *J* = 2.6 Hz, 1H), 7.35 (t, *J* = 7.5 Hz, 2H), 7.29 (t, *J* = 7.0 Hz, 1H), 7.22 (d, *J* = 6.9 Hz, 2H), 7.13 (s, 1H), 3.35 (dd, *J* = 14.2, 8.4 Hz, 1H), 3.21 – 3.10 (overlapping signals, 5H), 3.04 (dd, *J* = 14.2, 4.3 Hz, 1H), 2.76 (dd, *J* = 12.9, 7.3 Hz, 1H), 2.67 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): ^{13}C NMR (126 MHz, $CDCl_3$) δ 202.5, 159.5, 146.7, 146.4, 145.2, 137.67, 131.9, 129.3, 129.0, 127.2, 126.0, 124.0, 115.7, 53.6, 37.6, 35.8, 30.4, 25.3.

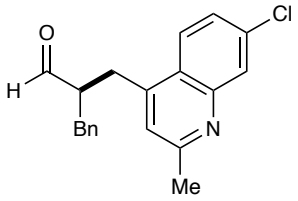
IR (film): ν 3029, 2939, 2836, 2731, 1723, 1605, 1562, 1504, 1464, 1454, 1416, 1366, 1281, 1225, 1184, 1143, 1100, 1030, 968, 929, 909, 886, 855, 839, 798, 728, 701, 667 cm^{-1}.

HRMS (ESI-TOF): m/z calculated for $C_{21}H_{21}NO_4S$ $[M+H]^+$ 384.1264, found 384.1261.

Chiral HPLC (alcohol): OD-H column, 20% isopropanol/hexanes, 1.0 mL/min, 98% ee. t_R = 15.6 min (minor (*S*)-enantiomer), 18.3 min (major (*R*)-enantiomer).

$[\alpha]_D^{20}$ (alcohol): +3.7 (c = 1.0, CH_2Cl_2).

(*R*)-2-benzyl-3-(7-chloro-2-methylquinolin-4-yl)propionaldehyde (40)



Prepared according to General Procedure A, irradiating for 24 hours. The aldehyde was purified by flash chromatography using an ethyl acetate/hexanes eluent (8 → 15%) containing 1% triethylamine to afford a pale yellow oil (122 mg, 76% yield). The corresponding alcohol was purified by flash chromatography using an ethyl acetate/hexanes eluent (25 → 50%) containing 1% triethylamine followed by preparative thin layer chromatography (60% ethyl acetate/hexanes + 1% triethylamine) to afford an off-white solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ 9.74 (d, *J* = 1.5 Hz, 1H), 7.98 (d, *J* = 2.1 Hz, 1H), 7.41 (d, *J* = 8.9 Hz, 1H), 7.36 – 7.32 (m, 2H), 7.32 – 7.30 (m, 1H), 7.29 – 7.26 (m, 1H), 7.19 (m, 2H), 7.06 (s, 1H), 3.40 – 3.33 (m, 1H), 3.14 (dd, *J* = 13.7, 6.2 Hz, 1H), 3.09 – 3.01 (m, 2H), 2.78 – 2.72 (m, 1H), 2.65 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 202.5, 160.0, 148.8, 145.0, 137.8, 135.1, 129.3, 129.0, 128.7, 127.1, 126.7, 124.4, 123.9, 123.1, 53.8, 35.7, 30.2, 25.4.

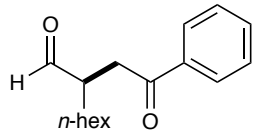
IR (film): ν 3064, 3028, 2927, 2857, 2728, 1724, 1602, 1561, 1498, 1454, 1435, 1407, 1377, 1338, 1319, 1257, 1185, 1154, 1116, 1074, 1043, 1002, 970, 900, 883, 839, 815, 774, 747, 700 cm^{-1}.

HRMS (ESI-TOF): m/z calculated for $C_{20}H_{18}ClNO$ $[M+H]^+$ 324.1150, found 324.1153.

Chiral HPLC (alcohol): AS-H column, 10% isopropanol/hexanes, 1.0 mL/min, 99% ee. t_R = 5.9 min (major (*R*)-enantiomer), 7.2 min (minor (*S*)-enantiomer).

$[\alpha]_D^{20}$ (alcohol): +26.1 (c = 0.50, MeOH).

(*R*)-2-(2-oxo-2-phenylethyl)octanal (46)[2]



Prepared according to General Procedure B, irradiating for 16 hours. The aldehyde was purified by flash chromatography using an ethyl acetate/hexanes eluent (4%) to afford a clear, colorless oil (96 mg, 78% yield).

^{1}H NMR (500 MHz, $CDCl_3$): δ 9.82 (s, 1H), 7.97 (d, *J* = 7.7 Hz, 2H), 7.57 (t, *J* = 7.4 Hz, 1H), 7.47 (t, *J* = 7.6 Hz, 2H), 3.48 (dd, *J* = 17.8, 7.8 Hz, 1H), 3.11 (dt, *J* = 14.1, 6.5 Hz, 1H), 3.02 (dd, *J* = 17.8, 4.8 Hz, 1H), 1.79 (m, 1H), 1.54 (m, 1H), 1.43 – 1.22 (m, 8H), 0.88 (t, *J* = 6.7 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 203.8, 198.2, 136.7, 133.4, 128.8, 128.2, 46.9, 37.8, 31.7, 29.5, 29.0, 27.2, 22.7, 14.2.

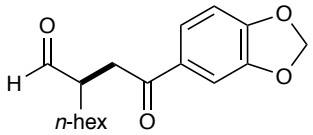
IR (film): ν 2955, 2927, 2857, 2719, 1724, 1683, 1598, 1581, 1464, 1449, 1405, 1391, 1359, 1279, 1247, 1219, 1181, 1075, 1002, 969, 903, 887, 850, 754, 725, 690, 655 cm^{-1}.

HRMS (ESI-TOF): m/z calculated for $C_{16}H_{22}O_2$ $[M+H]^+$ 247.1693, found 247.1692.

Chiral HPLC (alcohol): OD-H column, 5% isopropanol/hexanes, 1.0 mL/min, 93% ee. t_R = 8.9 min (major (*R*)-enantiomer), 10.2 min (minor (*S*)-enantiomer).

$[\alpha]_D^{21}$ (alcohol): +68.4 (c = 1.0, CH_2Cl_2), +65.2 (c = 1.0, $CHCl_3$), lit[2] $[\alpha]_D^{23}$ +66.9 (c = 1.30, $CHCl_3$).

(*R*)-2-(2-(benzo[*d*][1,3]dioxol-5-yl)-2-oxoethyl)octanal (47)



Prepared according to General Procedure B, irradiating for 48 hours. The aldehyde was purified by flash chromatography using an ethyl acetate/hexanes eluent (4%) to afford a clear, colorless oil (106 mg, 73% yield).

^{1}H NMR (500 MHz, $CDCl_3$): δ 9.80 (d, *J* = 1.1 Hz, 1H), 7.57 (dd, *J* = 8.1, 1.8 Hz, 1H), 7.42 (d, *J* = 1.8 Hz, 1H), 6.84 (d, *J* = 8.2 Hz, 1H), 6.03 (s, 2H), 3.38 (dd, *J* = 17.6, 7.9 Hz, 1H), 3.06 (m, 1H), 2.94 (dd, *J* = 17.6, 4.7 Hz, 1H), 1.76 (m, 1H), 1.51 (m, 1H), 1.41 – 1.20 (m, 8H), 0.86 (t, *J* = 6.8 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 203.9, 196.1, 152.0, 148.3, 131.5, 124.5, 108.0, 108.0, 102.0, 47.0, 37.6, 31.7, 29.5, 29.0, 27.2, 22.7, 14.2.

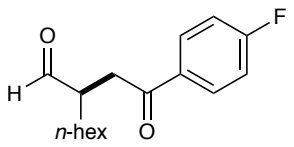
IR (film): ν 2952, 2926, 2857, 2719, 1724, 1675, 1604, 1505, 1488, 1443, 1361, 1250, 1140, 1107, 1096, 1037, 1004, 934, 893, 878, 810, 722 cm^{-1}.

HRMS (ESI-TOF): m/z calculated for $C_{17}H_{22}O_4$ $[M+H]^+$ 291.1591, found 291.1591.

Chiral HPLC (alcohol): OD-H column, 5% isopropanol/hexanes, 1.0 mL/min, 92% ee. t_R = 14.3 min (major (*R*)-enantiomer), 17.6 min (minor (*S*)-enantiomer).

$[\alpha]_D^{21}$: +54.7 (c = 1.0, CH_2Cl_2).

(*R*)-2-(2-(4-fluorophenyl)-2-oxoethyl)octanal (48)



Prepared according to General Procedure B, irradiating for 16 hours. The aldehyde was purified by flash chromatography using an ethyl acetate/hexanes eluent (4%) to afford a white solid (106 mg, 80% yield).

^{1}H NMR (500 MHz, $CDCl_3$): δ 9.79 (s, 1H), 7.98 (dd, *J* = 8.6, 5.5 Hz, 2H), 7.11 (t, *J* = 8.5 Hz, 2H), 3.43 (dd, *J* = 17.8, 8.1 Hz, 1H), 3.08 (dt, *J* = 12.0, 6.0 Hz, 1H), 2.95 (dd, *J* = 17.8, 4.6 Hz, 1H), 1.77 (dq, *J* = 13.6, 6.9 Hz, 1H), 1.52 (dq, *J* = 14.5, 7.2 Hz, 1H), 1.42 – 1.19 (m, 8H), 0.86 (t, *J* = 6.8 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 203.6, 196.5, 165.9 (d, *J* = 255.0 Hz), 133.1 (d, *J* = 3.0 Hz), 130.8 (d, *J* = 9.3 Hz), 115.8 (d, *J* = 21.9 Hz), 46.8, 37.6, 31.7, 29.4, 28.9, 27.1, 22.6, 14.1.

IR (film): ν 3076, 2956, 2928, 2858, 2719, 1724, 1683, 1597, 1507, 1464, 1409, 1359, 1299, 1282, 1228, 1156, 1100, 999, 969, 834, 724 cm^{-1}.

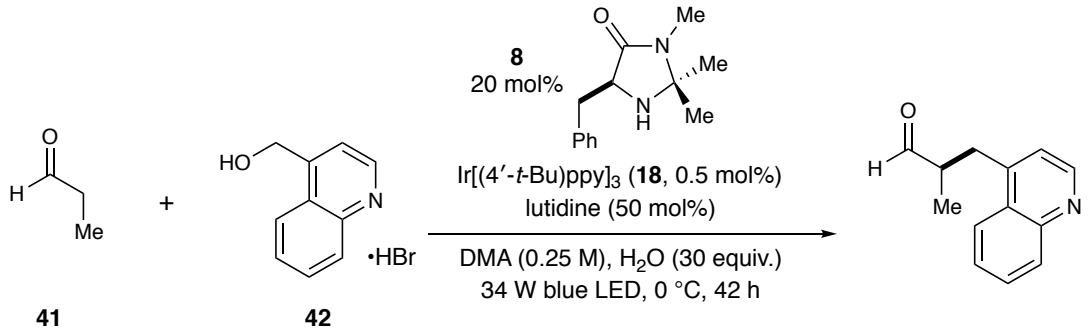
HRMS (ESI-TOF): m/z calculated for $C_{16}H_{21}FO_2$ $[M+H]^+$ 265.1598, found 265.1599.

Chiral HPLC (alcohol): OD-H column, 0.5% isopropanol/hexanes, 1.0 mL/min, 87% ee. t_R = 17.5 min (minor (*S*)-enantiomer), 19.2 min (major (*R*)-enantiomer).

$[\alpha]_D^{20}$: +59.0 (c = 1.0, CH_2Cl_2).

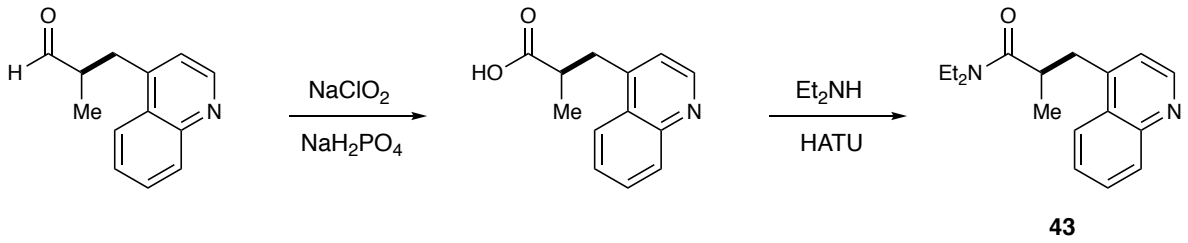
VI. Enantioselective Synthesis of PK–14067 (44) (Figure 2)

Step 1: (*R*)-2-methyl-3-(quinolin-4-yl)propionaldehyde



4-(Hydroxymethyl)quinoline (**42**)•HBr (480 mg, 2.00 mmol, 1.00 equiv) and propionaldehyde (**41**) (0.72 mL, 10 mmol, 5.0 equiv) were subjected to General Procedure A, with the reaction volume split evenly between two 8 mL vials, irradiating for 42 hours. ^{1}H NMR analysis of the reaction mixture indicated that no starting alcohol remained, with 84% yield of the desired aldehyde. Following workup, the crude material was used in the next step without further purification.

Steps 2 & 3: *N*,*N*-diethyl-(*R*)-2-methyl-3-(quinolin-4-yl)propionamide (43)



Sodium chlorite (80 wt%, 1.13 g, 10.0 mmol, 5.00 equiv vs. starting alcohol **42**) was added in one portion to a mixture of the crude aldehyde from step 1 (1.00 equiv), sodium dihydrogen phosphate monohydrate (2.76 g, 20.00 mmol, 10.0 equiv) and 2-methyl-2-butene (90 wt%, 4.70 mL, 40.0 mmol, 20.0 equiv) in 2:1 *tert*-butanol/water (20 mL) at 0 °C, and the mixture was allowed to warm to room temperature. After 2 hours, water (75 mL) was added, the mixture was extracted with 4:1

CH_2Cl_2/isopropanol (50, 2 × 25 mL), and the combined organic extracts were dried over Na_2SO_4 and concentrated. The residue was used immediately without further purification.

Diethylamine (0.62 mL, 6.0 mmol, 3.0 equiv vs. starting alcohol **42**) was added to a mixture of the crude acid from step 1 (1.00 equiv) and HATU (1.14 g, 3.00 mmol, 1.50 equiv) in dimethylformamide (10 mL) at 0 °C, and the mixture was allowed to warm to room temperature. After 2 hours, saturated $NaHCO_3$ (50 mL) and saturated Na_2CO_3 (50 mL) were added, the mixture was extracted with ethyl acetate (3 × 50 mL), and the combined organic extracts were dried over Na_2SO_4 and concentrated. The residue was purified by flash chromatography on silica gel (1 → 3% methanol/CH_2Cl_2) to afford a brown oil (426 mg, 79% yield over 3 steps).

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.76 (d, *J* = 4.3 Hz, 1H), 8.09 (d, *J* = 9.0 Hz, 1H), 8.04 (d, *J* = 9.0 Hz, 1H), 7.68 (ddd, *J* = 8.3, 6.8, 1.4 Hz, 1H), 7.56 (ddd, *J* = 8.3, 6.9, 1.3 Hz, 1H), 7.24 (d, *J* = 4.4 Hz, 1H), 3.43 (dd, *J* = 13.5, 8.9 Hz, 1H), 3.30 (dq, *J* = 14.1, 7.1 Hz, 1H), 3.22 – 3.12 (m, 2H), 3.07 (m, 1H), 2.87 (ddt, *J* = 19.2, 15.0, 7.5 Hz, 2H), 1.26 (d, *J* = 6.7 Hz, 3H), 0.92 (t, *J* = 7.1 Hz, 3H), 0.76 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 174.4, 150.2, 148.4, 146.2, 130.4, 129.2, 127.6, 126.6, 123.5, 122.3, 41.8, 40.6, 36.8, 36.7, 19.0, 14.6, 13.0.

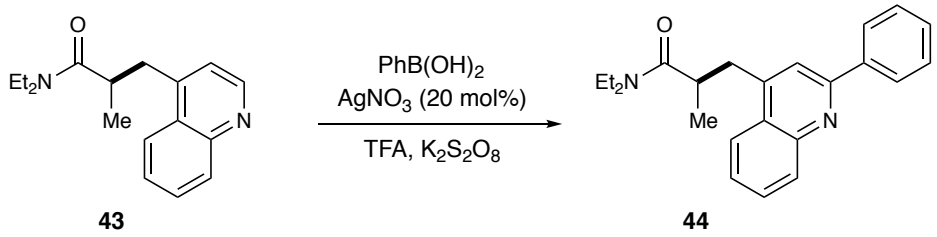
IR (film): ν 3467, 2972, 2933, 2872, 1630, 1591, 1568, 1509, 1482, 1463, 1446, 1431, 1380, 1362, 1345, 1308, 1257, 1219, 1160, 1138, 1096, 1072, 1024, 945, 907, 879, 841, 814, 764, 753 cm^{-1}.

HRMS (ESI-TOF): m/z calculated for $C_{17}H_{22}N_2O$ $[M+H]^+$ 271.1805, found 271.1807.

Chiral HPLC (alcohol): AS-H column, 5% isopropanol/hexanes, 1.0 mL/min, 95% ee. t_R = 11.7 min (minor (*S*)-enantiomer), 14.0 min (major (*R*)-enantiomer).

$[\alpha]_D^{21}$: –109 (c = 1.0, CH_2Cl_2).

Step 4: *N*,*N*-diethyl-(*R*)-2-methyl-3-(2-phenylquinolin-4-yl)propionamide (PK–14067, 44)[3,4]



43 **44**

Based on the method of Baran,[5] trifluoroacetic acid (76 μL, 0.99 mmol, 2.0 equiv) was added to a solution of *N*,*N*-diethyl-(*R*)-2-methyl-3-(2-phenylquinolin-4-yl)propionamide (**43**) (135 mg, 0.499 mmol, 1.00 equiv) in CH_2Cl_2 (2.5 mL), followed by phenylboronic acid (91 mg, 0.75 mmol, 1.5 equiv), water (2.5 mL), silver(I) nitrate (17 mg, 0.10 mmol, 0.20 equiv), and potassium persulfate (405 mg, 1.50 mmol, 3.00 equiv) under air. After stirring vigorously for 12 hours, sat. $NaHCO_3$ (15 mL) was added, the mixture was extracted with CH_2Cl_2 (3 × 10 mL), and the combined organic extracts were dried over Na_2SO_4 and concentrated. The residue was purified by flash chromatography on silica gel (20 → 30% ethyl acetate/hexanes) to afford a pale yellow oil (90 mg, 52% yield).

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.17 (d, *J* = 8.4 Hz, 1H), 8.14 (d, *J* = 7.0 Hz, 2H), 8.05 (d, *J* = 8.3 Hz, 1H), 7.75 (s, 1H), 7.70 (t, *J* = 7.6 Hz, 1H), 7.55 (d, *J* = 8.0 Hz, 1H), 7.50 (app t, 2H), 7.44 (t, *J* = 7.2 Hz, 1H), 3.51 (dd, *J* = 13.5, 9.0 Hz, 1H), 3.28 (m, 2H), 3.14 (m, 2H), 2.88 (m, 2H), 1.31 (d, *J* = 6.7 Hz, 3H), 0.88 (t, *J* = 7.1 Hz, 3H), 0.76 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 174.5, 157.0, 148.6, 146.7, 139.7, 130.778 129.4, 129.4, 128.9, 127.6, 126.6, 126.3, 123.3, 120.1, 41.8, 40.7, 37.2, 36.8, 19.1, 14.6, 13.1.

HRMS (ESI-TOF): m/z calculated for $C_{23}H_{26}N_2O$ $[M+H]^+$ 347.2118, found 347.2116.

Chiral HPLC (alcohol): AD-H column, 1% isopropanol/hexanes, 1.0 mL/min, 95% ee. t_R = 15.5 min (minor (*S*)-enantiomer), 19.6 min (major (*R*)-enantiomer).

$[\alpha]_D^{21}$: –88 (c = 1.0, EtOH), lit[3b] $[\alpha]_D^{18}$ –90 (c = 2.86, EtOH, 99% ee).

VII. Synthesis of Aldehyde Substrates

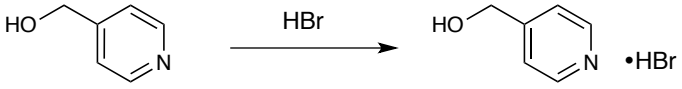
Hydrocinnamaldehyde (**13**), octanal (**45**), propionaldehyde (**41**), and *cis*-non-6-enal were commercially available and distilled before use.

All of the remaining aldehydes were obtained by PCC oxidation of the corresponding alcohols. Pyridinium chlorochromate (6.48 g, 30.0 mmol, 1.50 equiv) was added in one portion to a solution of alcohol (20.0 mmol) in CH_2Cl_2 (100 mL) at 0 °C. The bath was removed after 15 minutes, and after a total of 3 hours, silica gel (7.5 g) and ether (150 mL) were added. After stirring for 1 hour further, the mixture was concentrated and the solid residue was loaded directly onto a silica gel column and eluted with ethyl acetate/hexanes. The purified material was distilled before use.

These alcohols were all commercially available, except 3-(3′,4′-dimethoxyphenyl)propan-1-ol, which was prepared by the method of Doyle.[6]

VIII. Synthesis of Benzylic Electrophile Substrates

4-(hydroxymethyl)pyridine (3)•HBr



Hydrobromic acid (48% aqueous solution, 5.70 mL, 50.0 mmol, 1.00 equiv) was added dropwise to a solution of 4-(hydroxymethyl)pyridine (5.46 g, 50.0 mmol, 1.00 equiv) in warm acetone (125 mL) and a minimum of ethanol (5–10 mL). After storage at –20 °C for 1 hour, the solid was collected by filtration and recrystallized from > 10:1 ethanol/water to provide the salt as a white solid (6.86 g, 72% yield).

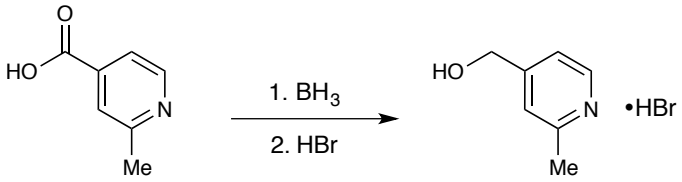
^{1}H NMR (500 MHz, DMSO-d_6): δ 15.22 (br s, 1H), 8.90 (d, J = 6.8 Hz, 2H), 8.00 (d, J = 6.1 Hz, 2H), 5.91 (br s, 1H), 4.81 (s, 2H).

^{13}C NMR (126 MHz, DMSO-d_6): δ 163.8, 141.3, 123.6, 61.3.

IR (ATR): ν 3299, 3210, 3120, 3103, 3079, 3043, 2981, 2929, 2894, 2810, 2776, 2011, 1990, 1923, 1906, 1849, 1796, 1712, 1639, 1605, 1515, 1508, 1456, 1435, 1370, 1332, 1268, 1247, 1210, 1185, 1095, 1052, 1007, 987, 922, 872, 789, 698 cm^{-1}.

HRMS (ESI-TOF): m/z calculated for C_6H_7NO $[M+H]^+$ 110.0600, found 110.0601.

4-(hydroxymethyl)-2-methylpyridine•HBr



Based on the method of Birch *et al.*,[7] borane-THF adduct (1.0 M solution in tetrahydrofuran, 21.0

mL, 21.0 mmol, 2.10 equiv) was added dropwise to a solution of 2-methylisonicotinic acid (1.37 g, 9.99 mmol, 1.00 equiv) in tetrahydrofuran (10 mL) at 0 °C, and the mixture was warmed to ambient temperature. After 16 hours, the solution was re-cooled to 0 °C and excess borane was quenched with methanol (40 mL) and 1 M HCl (60 mL). The resulting mixture was basified with saturated $NaHCO_3$ (75 mL), saturated with solid NaCl, and extracted with CH_2Cl_2 (4 × 25 mL) and EtOAc (6 × 25 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated. The residue was purified by flash chromatography on silica gel (5% methanol/CH_2Cl_2) to afford a white solid (1.18 g, 96% yield).

Hydrobromic acid (48% aqueous solution, 1.09 mL, 9.58 mmol, 1.00 equiv) was added dropwise to a solution of 4-(hydroxymethyl)-2-methylpyridine (1.18 g, 9.58 mmol, 1.00 equiv) in ether (5 mL) and acetone (25 mL), immediately forming a white precipitate. The mixture was stored overnight at –20 °C, and the precipitate was collected by filtration and recrystallized from 2:1 ethanol/ether to provide the salt as a white solid (1.48 g, 76% yield).

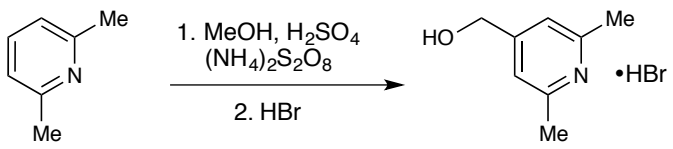
^{1}H NMR (500 MHz, DMSO-d_6): δ 15.49 (br s, 1H), 8.75 (d, J = 6.2 Hz, 1H), 7.86 (s, 1H), 7.79 (d, J = 5.9 Hz, 1H), 5.82 (br s, 1H), 4.75 (s, 2H), 2.72 (s, 3H).

^{13}C NMR (126 MHz, DMSO-d_6): δ 163.2, 152.8, 140.3, 123.9, 121.1, 61.2, 19.2.

IR (ATR): ν 3314, 3244, 3079, 3057, 3028, 2988, 2897, 2801, 1942, 1874, 1851, 1741, 1638, 1622, 1519, 1490, 1421, 1407, 1389, 1363, 1302, 1271, 1230, 1216, 1156, 1118, 1064, 1009, 982, 938, 927, 824, 749, 668 cm^{-1}.

HRMS (ESI-TOF): m/z calculated for C_7H_9NO $[M+H]^+$ 124.0757, found 124.0758.

4-(hydroxymethyl)-2,6-dimethylpyridine•HBr



Based on the method of Minisci,[8] sulfuric acid (2.3 mL, 43 mmol, 1.0 equiv), methanol (60 mL), and 2,6-lutidine (5.0 mL, 43 mmol, 1.0 equiv) were successively added to a solution of ammonium persulfate (19.3 g, 85 mmol, 2.0 equiv) in water (30 mL), and the mixture was heated to 100 °C. After 24 hours, the methanol was evaporated, the aqueous solution was basified with 1 M NaOH (200 mL) and extracted with CH_2Cl_2 (4 × 75 mL), and the combined organic extracts were dried over $MgSO_4$ and concentrated. The residue was purified by flash chromatography on silica gel (50% ethyl acetate/hexanes + 1% triethylamine) to afford a white solid (590 mg, 10% yield).

Hydrobromic acid (48% aqueous solution, 0.50 mL, 4.4 mmol, 1.0 equiv) was added dropwise to a solution of 4-(hydroxymethyl)-2,6-dimethylpyridine (590 mg, 4.3 mmol, 1.0 equiv) in acetone (10 mL), immediately forming a light yellow precipitate. Ether was diffused into the solution for 3 hours and the mixture was stored at –20 °C for 3 hours further. The precipitate was collected by filtration and recrystallized from ethanol, diffusing ether into the mixture to provide the salt as an off-white solid (722 mg, 77% yield).

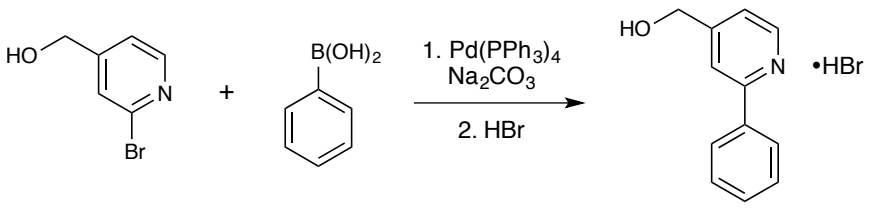
^{1}H NMR (500 MHz, DMSO-d_6): δ 15.10 (br s, 1H), 7.64 (s, 2H), 5.78 (br s, 1H), 4.70 (s, 2H), 2.69 (s, 6H).

^{13}C NMR (126 MHz, DMSO-d_6): δ 162.8, 152.2, 121.1, 61.2, 19.0.

IR (ATR): ν 3297, 3070, 3030, 2986, 2850, 2762, 2734, 2701, 2587, 1997, 1882, 1630, 1439, 1399, 1374, 1355, 1325, 1267, 1228, 1216, 1156, 1081, 1044, 991, 950, 920, 869, 713 cm^{-1}.

HRMS (ESI-TOF): m/z calculated for $C_8H_{11}NO$ $[M+H]^+$ 138.0913, found 138.0914.

4-(hydroxymethyl)-2-phenylpyridine•HBr



Based on the method of Sadler,[9] a mixture of 2-bromo-4-(hydroxymethyl)pyridine (1.88 g, 10.0 mmol, 1.00 equiv), phenylboronic acid (1.71 g, 14.0 mmol, 1.40 equiv), and sodium carbonate (3.97 g, 37.5 mmol, 3.75 equiv) in water (75 mL) and tetrahydrofuran (38 mL) was sparged with nitrogen for 15 minutes, then $Pd(PPh_3)_4$ (231 mg, 0.20 mmol, 2 mol%) was added and the mixture was heated to 100 °C. After 38 hours, the mixture was extracted with CH_2Cl_2 (3 × 75 mL), and the combined organic extracts were dried over $MgSO_4$ and concentrated. The residue was purified by flash chromatography on silica gel (40% ethyl acetate/hexanes) to afford a pale yellow oil (810 mg, 44% yield).

Hydrobromic acid (48% aqueous solution, 0.50 mL, 4.4 mmol, 1.0 equiv) was added dropwise to a solution of 4-(hydroxymethyl)-2-phenylpyridine (810 mg, 4.4 mmol, 1.0 equiv) in 3:1 acetone/ether (20 mL), immediately forming a white precipitate. The mixture was stored at –20 °C overnight, and the precipitate was collected by filtration and recrystallized from 10:1 ethanol/water provide the salt as a white solid (1.11 g, 95% yield).

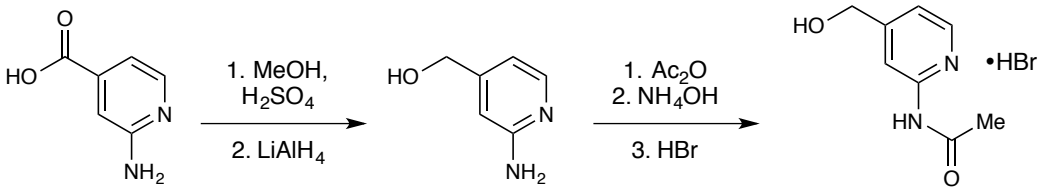
^{1}H NMR (500 MHz, DMSO-d_6): δ 8.83 (d, J = 6.0 Hz, 1H), 8.24 (s, 1H), 8.02 (m, 2H), 7.86 (d, J = 6.1 Hz, 1H), 7.66 (m, 3H), 4.83 (s, 2H).

^{13}C NMR (126 MHz, DMSO-d_6): δ 163.2, 150.9, 142.4, 131.9, 131.5, 129.5, 128.2, 122.0, 121.7, 61.5.

IR (ATR): ν 3315, 3215, 3082, 2995, 2880, 2843, 1983, 1911, 1832, 1800, 1633, 1606, 1582, 1521, 1491, 1475, 1426, 1402, 1378, 1338, 1314, 1263, 1230, 1168, 1159, 1109, 1061, 1054, 1035, 998, 986, 920, 812, 772, 731, 715, 683 cm^{-1}.

HRMS (ESI-TOF): m/z calculated for $C_{12}H_{11}NO$ $[M+H]^+$ 186.0913, found 186.0915.

***N*-(4-(hydroxymethyl)pyridin-2-yl)acetamide•HBr**



Based on the method of Lüning,[10] sulfuric acid (20.0 mL, 375 mmol, 10.4 equiv) was added to a suspension of 2-aminoisonicotinic acid (5.00 g, 36.2 mmol, 1.00 equiv) in methanol (200 mL) and the mixture was heated to 80 °C. After 3 days, the solution was diluted with water (200 mL), basified with $NaHCO_3$ (52 g), extracted with ethyl acetate (6 × 120 mL), and the combined organic extracts were dried over $MgSO_4$ and concentrated to provide the methyl ester a pale yellow solid (4.89 g, 89% yield).

Based on the method of Bilodeau *et al.*,[11] lithium aluminum hydride (1.0 M solution in tetrahydrofuran, 35.0 mL, 35.0 mmol, 1.09 equiv) was added over 15 minutes at –78 °C to a solution of methyl 2-aminoisonicotinate (4.89 g, 32.1 mmol, 1.00 equiv) in tetrahydrofuran (55 mL). After 30 minutes, the mixture was warmed to ambient temperature, and after 3 hours further, cooled to 0 °C and quenched with methanol (50 mL). The suspension was filtered through Celite, washed with methanol (50 mL), and the filtrate was concentrated. The crude material (~ 10 g) was used without further purification.

Based on the method of Honda *et al.*,[12] acetic anhydride (10.0 mL, 106 mmol, ≥ 3.30 equiv) was added to a suspension of the crude 2-amino-4-(hydroxymethyl)pyridine (≤ 32.1 mmol, 1.00 equiv) in pyridine (36.0 mL, 445 mmol, 13.9 equiv). After 4 hours, the mixture was diluted with ethyl acetate (300 mL), washed with saturated $NaHCO_3$ (300 mL), water (100 mL) and brine (50 mL), dried over Na_2SO_4, and concentrated to provide the bis(acetylated) compound as a yellow oil (4.30 g, 64% yield over 2 steps).

Based on the method of Guo *et al.*,[13] ammonium hydroxide (28% ammonia, 14.5 M solution in water, 10 mL, 145 mmol, 7.0 equiv) was added to a solution of the *N*-(4-(acetoxymethyl)pyridin-2-yl)acetamide (4.30 g, 20.7 mmol, 1.0 equiv) in methanol (50 mL). After 24 hours, the mixture was concentrated, and the residue was purified by flash chromatography on silica gel (ethyl acetate) to afford a white solid (1.45 g, 42% yield).

Hydrobromic acid (48% aqueous solution, 0.99 mL, 8.7 mmol, 1.0 equiv) was added dropwise to a solution of *N*-(4-(hydroxymethyl)pyridin-2-yl)acetamide (1.45 g, 8.7 mmol, 1.0 equiv) in 1:1 acetone/ethanol (20 mL), forming an off-white precipitate. The mixture was stored at –20 °C overnight, and the precipitate was collected by filtration and recrystallized from ethanol to provide the salt as an off-white solid (1.27 g, 48% yield).

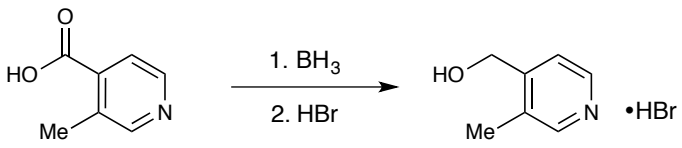
^{1}H NMR (500 MHz, DMSO-d_6): δ 12.16 (s, 1H), 8.33 (d, J = 6.3 Hz, 1H), 7.62 (s, 1H), 7.44 (d, J = 6.4 Hz, 1H), 4.69 (s, 2H), 2.26 (s, 3H).

^{13}C NMR (126 MHz, DMSO-d_6): δ 172.3, 163.3, 147.6, 138.3, 117.5, 111.2, 61.3, 24.2.

IR (ATR): ν 3308, 3084, 3023, 2909, 2810, 1687, 1647, 1607, 1559, 1555, 1507, 1437, 1413, 1372, 1352, 1322, 1309, 1270, 1227, 1208, 1162, 1107, 1070, 1035, 1020, 997, 982, 917, 823, 796, 782, 681 cm^{-1}.

HRMS (ESI-TOF): m/z calculated for $C_8H_{10}N_2O_2$ $[M+H]^+$ 167.0815, found 167.0817.

4-(hydroxymethyl)-3-methylpyridine•HBr



Based on the method of Birch *et al.*,[7] borane-THF adduct (1.0 M solution in tetrahydrofuran, 15.5

mL, 15.5 mmol, 2.13 equiv) was added dropwise to a solution of 3-methylisonicotinic acid (1.00 g, 7.26 mmol, 1.00 equiv) in tetrahydrofuran (8 mL) at 0 °C, and the mixture was warmed to ambient temperature. After 16 hours, the solution was re-cooled to 0 °C and excess borane was quenched with 1 M HCl (20 mL), and the solution was basified with 1 M NaOH (40 mL). The resulting mixture was extracted with CH_2Cl_2 (8 × 25 mL), and the combined organic extracts were dried over $MgSO_4$ and concentrated. The residue was purified by flash chromatography on silica gel (10% methanol/CH_2Cl_2) to afford a white solid (900 mg, 100% yield).

Hydrobromic acid (48% aqueous solution, 0.83 mL, 7.3 mmol, 1.0 equiv) was added dropwise to a solution of 4-(hydroxymethyl)-3-methylpyridine (900 mg, 7.3 mmol, 1.0 equiv) in acetone (15 mL), immediately forming a white precipitate. The mixture was stored for 2 days at –20 °C, and the precipitate was collected by filtration and recrystallized from ethanol to provide the salt as a white solid (1.05 g, 71% yield).

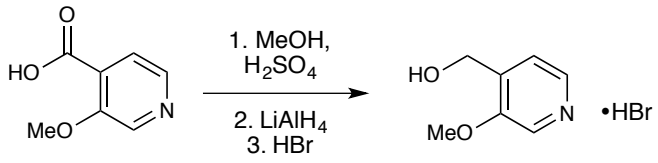
^{1}H NMR (500 MHz, DMSO-d_6): δ 15.39 (sbr , 1H), 8.79 (d, J = 5.9 Hz, 1H), 8.73 (s, 1H), 8.03 (s, 1H), 5.84 (br s, 1H), 4.75 (s, 2H), 2.34 (s, 3H).

^{13}C NMR (126 MHz, DMSO-d_6): δ 162.1, 139.7, 139.3, 134.3, 122.3, 59.8, 14.8.

IR (ATR): ν 3303, 3180, 3109, 3057, 3009, 2897, 1633, 1591, 1508, 1478, 1452, 1423, 1403, 1366, 1326, 1278, 1235, 1219, 1177, 1145, 1069, 1049, 1017, 993, 950, 905, 830, 772, 699 cm^{-1}.

HRMS (ESI-TOF): m/z calculated for C_7H_9NO $[M+H]^+$ 124.0757, found 124.0758.

4-(hydroxymethyl)-3-methoxypyridine•HBr



Sulfuric acid (1.4 mL, 26 mmol, 2.0 equiv) was added to a suspension of 3-methoxyisonicotinic acid (1.99 g, 13.0 mmol, 1.0 equiv) in methanol (40 mL) and the mixture was heated to 85 °C. After 12 hours, the solution was basified with saturated $NaHCO_3$ (100 mL), extracted with CH_2Cl_2 (3 × 75 mL), and the combined organic extracts were dried over $MgSO_4$ and concentrated to provide the methyl ester as a white solid (1.55 g, 71% yield).

Based on the method of Martell,[14] lithium aluminum hydride (1.0 M solution in tetrahydrofuran, 15.0 mL, 15.0 mmol, 1.62 equiv) was added dropwise at 0 °C to a solution of methyl 3-methoxyisonicotinate (1.55 g, 9.27 mmol, 1.00 equiv) in tetrahydrofuran (15 mL). After 2 hours, saturated potassium sodium tartrate (15 mL) was added and the mixture was stirred at 1000 rpm. After 30 minutes, the tetrahydrofuran was evaporated, the mixture was basified with 1 M NaOH (25 mL) and extracted with CH_2Cl_2 (7 × 50 mL), and the combined organic extracts were dried over Na_2SO_4 and concentrated. The residue was purified by flash chromatography on silica gel (2.5 → 5% methanol/CH_2Cl_2) to afford a pale yellow solid (277 mg, 22% yield).

Hydrobromic acid (48% aqueous solution, 0.22 mL, 1.9 mmol, 0.95 equiv) was added dropwise to a solution of 4-(hydroxymethyl)-3-methoxypyridine (277 mg, 2.0 mmol, 1.0 equiv) in hot ethanol (2 mL), forming a white precipitate. Ether was diffused into the mixture for 1 day, the suspension was stored overnight at –20 °C, and the precipitate was collected by filtration and recrystallized from ethanol to provide the salt as a light brown solid (261 mg, 59% yield).

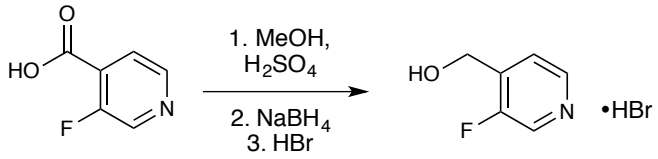
^{1}H NMR (500 MHz, DMSO-d_6): δ 8.60 (overlapping signals, 2H), 7.98 (d, J = 5.3 Hz, 1H), 5.76 (br s, 1H), 4.68 (s, 2H), 4.01 (s, 3H).

^{13}C NMR (126 MHz, DMSO-d_6): δ 153.9, 150.8, 135.2, 124.1, 123.0, 57.6, 57.4.

IR (ATR): ν 3322, 3205, 3123, 3059, 2981, 2949, 2904, 2796, 2012, 1947, 1884, 1626, 1604, 1521, 1492, 1463, 1441, 1411, 1385, 1370, 1340, 1297, 1247, 1202, 1177, 1069, 1055, 1002, 979, 944, 884, 822, 778, 700 cm^{-1}.

HRMS (ESI-TOF): m/z calculated for $C_7H_9NO_2$ $[M+H]^+$ 140.0706, found 140.0707.

3-fluoro-4-(hydroxymethyl)pyridine•HBr



Sulfuric acid (4.5 mL, 84 mmol, 3.3 equiv) was added to a suspension of 3-fluoroisonicotinic acid (3.56 g, 25.2 mmol, 1.0 equiv) in methanol (55 mL) and the mixture was heated to 85 °C. After 40 hours, the solution was concentrated, basified with saturated $NaHCO_3$ (100 mL), and extracted with CH_2Cl_2 (3 × 75 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated to provide the methyl ester as a yellow oil (2.70 g, 69% yield).

Sodium borohydride (2.02 g, 53.4 mmol, 3.13 equiv) was added in one portion to a solution of methyl 3-fluoroisonicotinate (2.65 g, 17.1 mmol, 1.00 equiv) in methanol (60 mL). After 1 hour, the reaction was quenched with saturated $NaHCO_3$ (100 mL) and extracted with CH_2Cl_2 (16 × 50 mL), and the combined organic extracts were dried over $MgSO_4$ and concentrated. The residue was purified by flash chromatography on silica gel (3% methanol/CH_2Cl_2) to afford a white solid (1.96 g, 90% yield).

Hydrobromic acid (48% aqueous solution, 1.7 mL, 15 mmol, 1.0 equiv) was added dropwise to a solution of 3-fluoro-4-(hydroxymethyl)pyridine (1.96 g, 15.4 mmol, 1.0 equiv) in warm acetone (15 mL), forming a yellow solution. Ether was diffused into the mixture for 1 hour, the suspension was stored at –20 °C for 4 hours, and the precipitate was collected by filtration and recrystallized

from ethanol to provide the salt as a white solid (1.89 g, 59% yield).

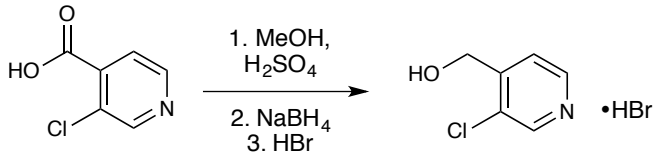
^{1}H NMR (500 MHz, DMSO-d_6): δ 9.00 (d, J = 3.1 Hz, 1H), 8.75 (d, J = 5.5 Hz, 1H), 8.71 (br s, 2H), 7.98 (t, J = 6.1 Hz, 1H), 4.77 (s, 2H).

^{13}C NMR (126 MHz, DMSO-d_6): δ 156.7 (d, J = 251.4 Hz), 148.0 (d, J = 12.3 Hz), 140.7 (d, J = 4.4 Hz), 131.7 (d, J = 32.7 Hz), 124.9 (d, J = 4.4 Hz), 56.2 (d, J = 3.3 Hz).

IR (ATR): ν 3283, 3062, 2987, 2896, 2787, 1643, 1602, 1514, 1482, 1422, 1368, 1336, 1276, 1223, 1178, 1140, 1074, 1043, 1015, 985, 953, 895, 878, 849, 830, 781, 688, 668 cm^{-1}.

HRMS (ESI-TOF): m/z calculated for C_6H_6FNO $[M+H]^+$ 128.0506, found 128.0506.

3-chloro-4-(hydroxymethyl)pyridine•HBr



Sulfuric acid (4.5 mL, 84 mmol, 3.2 equiv) was added to a suspension of 3-chloroisonicotinic acid (4.14 g, 26.3 mmol, 1.0 equiv) in methanol (55 mL) and the mixture was heated to 85 °C. After 40 hours, the solution was concentrated, basified with saturated $NaHCO_3$ (100 mL), and extracted with CH_2Cl_2 (3 × 50 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated to provide the methyl ester as a yellow oil (3.15 g, 70% yield).

Sodium borohydride (1.91 g, 50.5 mmol, 3.03 equiv) was added in one portion to a solution of methyl 3-chloroisonicotinate (2.86 g, 16.7 mmol, 1.00 equiv) in methanol (60 mL). After 1.5 hours, the reaction was quenched with saturated $NaHCO_3$ (100 mL) and extracted with CH_2Cl_2 (6 × 50 mL), and the combined organic extracts were dried over Na_2SO_4 and concentrated. The residue was purified by flash chromatography on silica gel (3% methanol/CH_2Cl_2) to afford a white

solid (2.31 g, 96% yield).

Hydrobromic acid (48% aqueous solution, 1.8 mL, 16 mmol, 1.0 equiv) was added dropwise to a solution of 3-chloro-4-(hydroxymethyl)pyridine (2.31 g, 16.1 mmol, 1.0 equiv) in warm acetone (20 mL), forming a white precipitate. The suspension was stored at –20 °C for 4 hours, and the precipitate was collected by filtration and recrystallized from ethanol to provide the salt as a white solid (3.09 g, 85% yield).

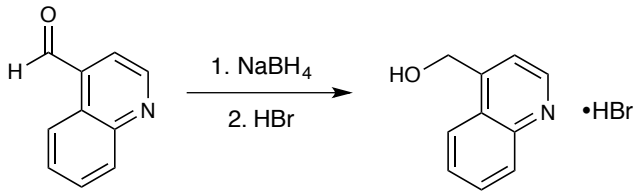
^{1}H NMR (500 MHz, DMSO-d_6): δ 10.29 (br s, 2H), 9.03 (s, 1H), 8.84 (d, J = 5.7 Hz, 1H), 7.97 (d, J = 5.7 Hz, 1H), 4.70 (s, 2H).

^{13}C NMR (126 MHz, DMSO-d_6): δ 157.6, 142.8, 142.6, 130.1, 123.8, 59.8.

IR (ATR): ν 3312, 3046, 2713, 1621, 1582, 1491, 1466, 1414, 1368, 1321, 1260, 1234, 1197, 1145, 1120, 1095, 1075, 1042, 1025, 962, 891, 837, 812, 723, 689, 668 cm^{-1}.

HRMS (ESI-TOF): m/z calculated for C_6H_6ClNO $[M+H]^+$ 144.0211, found 144.0209.

4-(hydroxymethyl)quinoline (42)•HBr



Sodium borohydride (420 mg, 11.1 mmol, 1.11 equiv) was added in small portions to a solution of quinoline-4-carboxaldehyde (1.57 g, 9.99 mmol, 1.00 equiv) in methanol (40 mL). After 12 hours, the reaction was quenched with saturated NH_4Cl (100 mL) and extracted with ethyl acetate (3 × 25 mL), and the combined organic extracts were dried over Na_2SO_4 and concentrated. The residue was purified by flash chromatography on silica gel (40 → 100% ethyl acetate/hexanes) to afford a white solid (1.26 g, 79% yield).

Hydrobromic acid (48% aqueous solution, 0.90 mL, 8.0 mmol, 1.0 equiv) was added dropwise to a solution of 4-(hydroxymethyl)quinoline (1.26 g, 7.91 mmol, 1.0 equiv) in acetone (25 mL), forming a white precipitate. The suspension was stored at –20 °C for 3 days, and the precipitate was collected by filtration and recrystallized from 4:1 ethanol/water to provide the salt as light yellow needles (1.66 g, 87% yield).

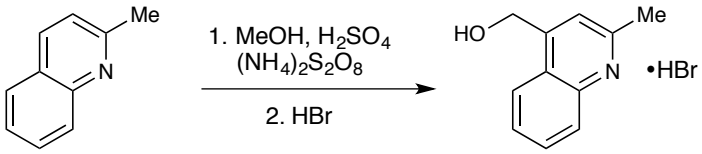
^{1}H NMR (500 MHz, DMSO-d_6): δ 9.36 (d, J = 5.6 Hz, 1H), 8.35 (d, J = 8.6 Hz, 1H), 8.31 (d, J = 8.6 Hz, 1H), 8.20 – 8.07 (m, 2H), 7.94 (t, J = 7.7 Hz, 1H), 5.30 (s, 2H).

^{13}C NMR (126 MHz, DMSO-d_6): δ 160.9, 145.0, 136.7, 134.2, 129.5, 125.2, 124.7, 121.3, 118.0, 59.9.

IR (ATR): ν 3278, 3102, 3037, 2890, 2807, 2576, 2678, 2021, 1933, 1847, 1761, 1632, 1600, 1543, 1493, 1456, 1408, 1388, 1378, 1348, 1283, 1257, 1216, 1186, 1166, 1140, 1090, 1004, 996, 973, 931, 877, 853, 830, 807, 771 cm^{-1}.

HRMS (ESI-TOF): m/z calculated for $C_{10}H_9NO$ $[M+H]^+$ 160.0757, found 160.0756.

4-(hydroxymethyl)-2-methylquinoline•HBr



Based on the method of Minisci,[8] sulfuric acid (2.3 mL, 43 mmol, 1.0 equiv), methanol (60 mL), and 2-methylquinoline (5.8 mL, 43 mmol, 1.0 equiv) were successively added to a solution of ammonium persulfate (19.3 g, 85.0 mmol, 2.0 equiv) in water (30 mL), and the mixture was heated to 100 °C. After 38 hours, the methanol was evaporated, the aqueous solution was basified with 25% saturated K_2CO_3 (800 mL) and extracted with CH_2Cl_2 (4 × 75 mL), and the combined organic

extracts were dried over $MgSO_4$ and concentrated. The residue was purified by flash chromatography on silica gel (2 → 5% methanol/CH_2Cl_2) to afford a brown solid (2.71 g, 36% yield).

Hydrobromic acid (48% aqueous solution, 1.75 mL, 15.4 mmol, 0.99 equiv) was added dropwise to a solution of 4-(hydroxymethyl)-2-methylquinoline (2.71 g, 15.6 mmol, 1.00 equiv) in hot ethanol (25 mL), immediately forming a beige precipitate, and the mixture was stored at –20 °C for 5 hours further. The precipitate was collected by filtration and recrystallized twice from ethanol and a small amount of water, diffusing ether into the suspensions, to provide the salt as a brown solid (3.03 g, 76% yield).

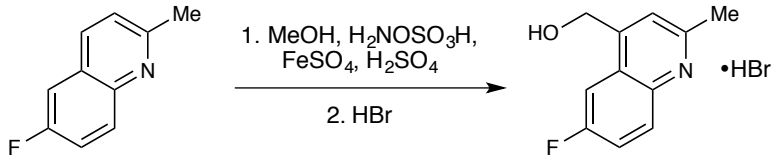
^{1}H NMR (500 MHz, DMSO-d_6): δ 8.27 (t, J = 9.7 Hz, 2H), 8.10 (t, J = 7.8 Hz, 1H), 7.99 (s, 1H), 7.88 (t, J = 7.7 Hz, 1H), 5.93 (br s, 1H), 5.25 (s, 2H), 2.98 (s, 3H).

^{13}C NMR (126 MHz, DMSO-d_6): δ 159.5, 157.5, 136.7, 133.9, 128.8, 124.5, 123.6, 120.5, 119.6, 59.7, 20.8.

IR (ATR): ν 3283, 2967, 2828, 2778, 2746, 2719, 2582, 1833, 1793, 1641, 1607, 1533, 1495, 1466, 1433, 1413, 1403, 1393, 1364, 1341, 1324, 1244, 1234, 1184, 1137, 1091, 1031, 1000, 980, 965, 917, 879, 864, 763 cm^{-1}.

HRMS (ESI-TOF): m/z calculated for $C_{11}H_{11}NO$ $[M+H]^+$ 174.0913, found 174.0913.

6-fluoro-4-(hydroxymethyl)-2-methylquinoline•HBr



Based on the method of Minisci,[15] iron(II) sulfate heptahydrate (2.41 g, 8.67 mmol, 30 mol%) and hydroxylamine *O*-sulfonic acid (9.78 g, 86.5 mmol, 3.00 equiv) were added to a solution of 6-

fluoro-2-methylquinoline (4.65 g, 28.9 mmol, 1.00 equiv) and sulfuric acid (1.55 mL, 29.1 mmol, 1.01 equiv) in methanol (60 mL) and water (30 mL), stirred in a water bath to minimize temperature rise from the exothermic process. After 3 hours, the methanol was evaporated, the aqueous solution was basified with 75% saturated $NaHCO_3$ (400 mL) containing sodium citrate dihydrate (6 g) and extracted with 4:1 CH_2Cl_2/isopropanol (150, 5 × 75 mL), and the combined organic extracts were dried over Na_2SO_4 and concentrated. The residue was purified by flash chromatography on silica gel (1 → 2.5% methanol/CH_2Cl_2) to afford an off-white solid (2.89 g, 52% yield).

Hydrobromic acid (48% aqueous solution, 1.7 mL, 15 mmol, 1.0 equiv) was added dropwise to a solution of 6-fluoro-4-(hydroxymethyl)-2-methylquinoline (4.63 g, 15.1 mmol, 1.0 equiv) in hot acetone (50 mL), forming a white precipitate, and the mixture was stored at –20 °C for 4 hours. The precipitate was collected by filtration and recrystallized from > 20:1 ethanol/water to provide the salt as a golden powder (3.56 g, 87% yield).

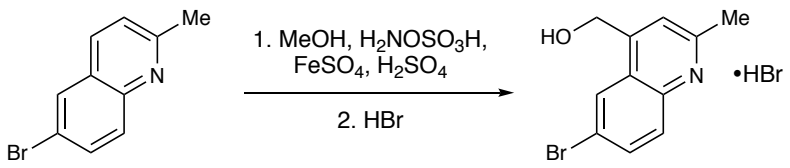
^{1}H NMR (500 MHz, DMSO-d_6): δ 8.36 (dd, J = 9.4, 5.0 Hz, 1H), 8.09 (dd, J = 9.7, 2.8 Hz, 1H), 8.02 (m, 1H), 7.99 (s, 1H), 5.94 (br s, 1H), 5.16 (s, 2H), 2.98 (s, 3H).

^{13}C NMR (126 MHz, DMSO-d_6): δ 160.4 (d, J = 249.1 Hz), 158.9 (d, J = 5.2 Hz), 157.1 (d, J = 2.1 Hz), 134.0, 124.9 (d, J = 10.3 Hz), 123.6, 123.4 (d, J = 16.1 Hz), 120.4, 109.1 (d, J = 23.7 Hz), 59.8, 20.6.

IR (ATR): ν 3269, 3067, 2721, 2603, 1950, 1888, 1834, 1643, 1615, 1526, 1496, 1465, 1420, 1392, 1369, 1321, 1243, 1203, 1170, 1136, 1127, 1087, 1033, 1011, 973, 953, 925, 883, 841, 734 cm^{-1}.

HRMS (ESI-TOF): m/z calculated for $C_{11}H_{10}FNO$ $[M+H]^+$ 192.0819, found 192.0820.

6-bromo-4-(hydroxymethyl)-2-methylquinoline•HBr



Based on the method of Minisci,[15] iron(II) sulfate heptahydrate (1.91 g, 6.87 mmol, 30 mol%) and hydroxylamine *O*-sulfonic acid (7.77 g, 68.7 mmol, 3.00 equiv) were added to a solution of 6-bromo-2-methylquinoline (5.08 g, 22.9 mmol, 1.00 equiv) and sulfuric acid (1.25 mL, 23.5 mmol, 1.03 equiv) in methanol (50 mL) and water (25 mL), stirred in a water bath to minimize temperature rise from the exothermic process. After 8 hours, the methanol was evaporated, the aqueous solution was basified with 75% saturated $NaHCO_3$ (400 mL) containing sodium citrate dihydrate (6 g) and extracted with 4:1 CH_2Cl_2/isopropanol (150, 5 × 75 mL), and the combined organic extracts were dried over Na_2SO_4 and concentrated. The residue was purified by flash chromatography on silica gel (1 → 3% methanol/CH_2Cl_2) to afford an off-white solid (1.80 g, 31% yield).

Hydrobromic acid (48% aqueous solution, 0.81 mL, 7.1 mmol, 1.0 equiv) was added dropwise to a solution of 6-bromo-4-(hydroxymethyl)-2-methylquinoline (1.80 g, 7.14 mmol, 1.0 equiv) in hot acetone (50 mL), forming an off-white precipitate, and the mixture was stored at –20 °C for 30 minutes. The precipitate was collected by filtration and recrystallized from 10:1 ethanol/water to provide the salt as a light golden solid (2.00 g, 84% yield).

^{1}H NMR (500 MHz, DMSO-d_6): δ 8.50 (d, J = 2.0 Hz, 1H), 8.24 – 8.14 (m, 2H), 7.99 (s, 1H), 6.04 (s, 2H), 5.20 (s, 2H), 2.95 (s, 3H).

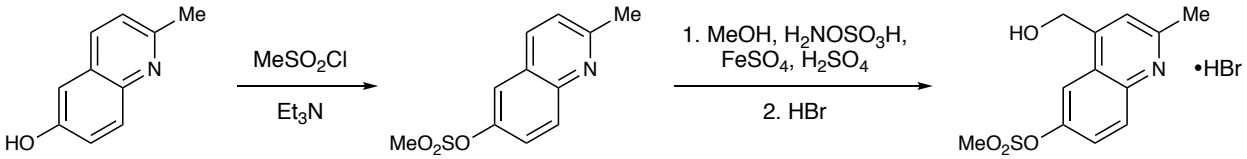
^{13}C NMR (126 MHz, DMSO-d_6): δ 158.2, 158.1, 136.4, 136.2, 126.8, 125.0, 123.1, 121.9, 120.6, 59.7, 21.1.

IR (ATR): ν 3312, 3052, 2965, 2901, 2698, 1966, 1851, 1741, 1643, 1599, 1521, 1479, 1453,

1429, 1397. 1381, 1365, 1320, 1226, 1141, 1100, 1072, 1031, 1002, 988, 934, 886, 868, 839, 810, 675 cm^{-1}.

HRMS (ESI-TOF): m/z calculated for $C_{11}H_{10}BrNO$ $[M+H]^+$ 252.0019, found 252.0014.

6-mesyloxy-4-(hydroxymethyl)-2-methylquinoline•HBr



Methanesulfonyl chloride (0.93 mL, 12 mmol, 1.2 equiv) was added to a solution of 6-hydroxy-2-methylquinoline (1.59 g, 9.99 mmol, 1.00 equiv) and triethylamine (2.1 mL, 15 mmol, 1.5 equiv) in ethyl acetate (50 mL) at 0 °C. After 1 hour, water (50 mL) was added, the layers were separated, the aqueous layer was extracted with ethyl acetate (50 mL), and the combined organic layers were dried over Na_2SO_4 and concentrated. The solid residue (2.25 g, 95% yield) was used directly in the next step.

Based on the method of Minisci,[15] iron(II) sulfate heptahydrate (791 mg, 2.85 mmol, 30 mol%) and hydroxylamine *O*-sulfonic acid (3.22 g, 28.5 mmol, 3.00 equiv) were added to a solution of crude 6-mesyloxy-2-methylquinoline (2.25 g, 9.48 mmol, 1.00 equiv) and sulfuric acid (0.51 mL, 9.6 mmol, 1.0 equiv) in methanol (23 mL) and water (11.5 mL), stirred in a water bath to minimize temperature rise from the exothermic process. After 12 hours, the methanol was evaporated, the aqueous solution was basified with 75% saturated $NaHCO_3$ (200 mL) containing sodium citrate dihydrate (3 g) and extracted with 4:1 CH_2Cl_2/isopropanol (75, 5 × 40 mL), and the combined organic extracts were dried over Na_2SO_4 and concentrated. The residue was purified by flash chromatography on silica gel (4 → 8% methanol/CH_2Cl_2) to afford an off-white solid (1.88 g, 74% yield).

Hydrobromic acid (48% aqueous solution, 0.80 mL, 7.0 mmol, 1.0 equiv) was added dropwise to a solution of 6-mesyloxy-4-(hydroxymethyl)-2-methylquinoline (1.88 g, 7.03 mmol, 1.0 equiv) in

hot acetone (125 mL) and a minimum of ethanol (< 5 mL), ether (50 mL) was added so that the solution remained cloudy. The resulting mixture was stored at –20 °C overnight. The precipitate was collected by filtration and recrystallized from ethanol and a few drops of water to provide the salt as a white solid (1.49 g, 61% yield).

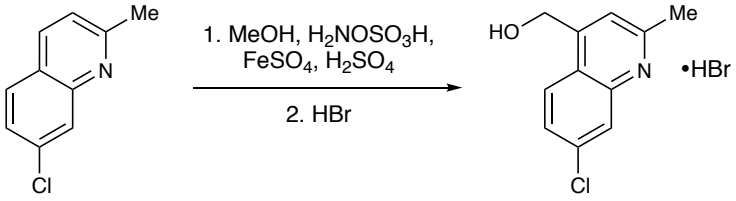
^{1}H NMR (500 MHz, DMSO-d_6): δ 8.34 (d, J = 9.2 Hz, 1H), 8.24 (d, J = 2.5 Hz, 1H), 8.05 (dd, J = 9.2, 2.5 Hz, 1H), 8.02 (s, 1H), 5.27 (br s overlapping with the following signal, 2H), 5.22 (d, J = 1.3 Hz, 2H), 3.56 (s, 3H), 2.97 (s, 3H).

^{13}C NMR (126 MHz, DMSO-d_6): δ 158.6, 158.4, 147.7, 136.2, 128.7, 124.5, 123.7, 120.4, 117.2, 59.8, 21.2.

IR (ATR): ν 3358, 3028, 3000, 2704, 1837, 1798, 1649, 1613, 1529, 1500, 1469, 1446, 1427, 1399, 1371, 1342, 1285, 1238, 1198, 1178, 1157, 1137, 1088, 1028, 982, 930, 898, 877, 861, 835, 800, 762, 705, 665 cm^{-1}.

HRMS (ESI-TOF): m/z calculated for $C_{12}H_{13}NO_4S$ $[M+H]^+$ 268.0638, found 268.0637.

7-chloro-4-(hydroxymethyl)-2-methylquinoline•HBr



Based on the method of Minisci,[15] iron(II) sulfate heptahydrate (2.09 g, 7.52 mmol, 30 mol%) and hydroxylamine *O*-sulfonic acid (8.49 g, 75.1 mmol, 3.00 equiv) were added to a solution of 7-chloro-2-methylquinoline (4.44 g, 25.0 mmol, 1.00 equiv) and sulfuric acid (1.35 mL, 25.3 mmol, 1.01 equiv) in methanol (50 mL) and water (25 mL), stirred in a water bath to minimize temperature rise from the exothermic process. After 3 hours, the methanol was evaporated, the aqueous solution was basified with 75% saturated $NaHCO_3$ (400 mL) containing sodium citrate

dihydrate (6 g) and extracted with 4:1 CH_2Cl_2/isopropanol (150, 5 × 75 mL), and the combined organic extracts were dried over Na_2SO_4 and concentrated. The residue was purified by flash chromatography on silica gel (0.5 → 3% methanol/CH_2Cl_2) to afford an off-white solid (4.02 g, 78% yield).

Hydrobromic acid (48% aqueous solution, 2.2 mL, 19 mmol, 1.0 equiv) was added dropwise to a solution of 7-chloro-4-(hydroxymethyl)-2-methylquinoline (1.80 g, 19.4 mmol, 1.0 equiv) in hot ethanol (75 mL), forming a yellow precipitate, and the mixture was stored at –20 °C for 30 minutes. The precipitate was collected by filtration and recrystallized from > 15:1 ethanol/water to provide the salt a cream solid (2.00 g, 84% yield).

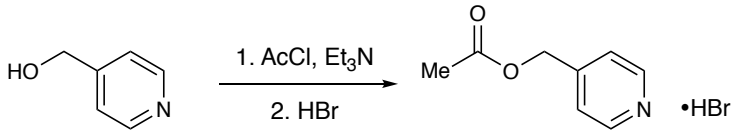
^{1}H NMR (500 MHz, DMSO-d_6): δ 14.89 (br s, 1H), 8.30 (d, J = 9.0 Hz, 1H), 8.28 (d, J = 2.0 Hz, 1H), 7.97 (s, 1H), 7.90 (dd, J = 9.0, 2.1 Hz, 1H), 6.48 (br s, 1H), 5.21 (s, 2H), 2.97 (s, 3H).

^{13}C NMR (126 MHz, DMSO-d_6): δ 159.0, 158.8, 137.9, 137.8, 129.1, 126.8, 122.40, 120.0, 119.8, 59.7, 21.0.

IR (ATR): ν 3265, 3064, 3032, 2965, 2900, 2851, 2815, 2748, 2696, 2638, 1953, 1847, 1796, 1643, 1603, 1528, 1486, 1434, 1407, 1370, 1334, 1321, 1255, 1213, 1191, 1164, 1095, 1082, 1034, 1001, 989, 969, 929, 913, 893, 857, 819, 781, 760, 688, 662 cm^{-1}.

HRMS (ESI-TOF): m/z calculated for $C_{11}H_{10}ClNO$ $[M+H]^+$ 208.0524, found 208.0526.

4-(acetoxymethyl)pyridine•HBr



Acetyl chloride (0.78 mL, 11 mmol, 1.1 equiv) was added dropwise to a solution of 4-(hydroxymethyl)pyridine (1.09 g, 9.99 mmol, 1.00 equiv) and triethylamine (1.70 mL, 12.2 mmol,

1.22 equiv) in CH_2Cl_2 (50 mL) at 0 °C. The mixture was then allowed to warm slowly to room temperature. After 20 hours, sat. $NaHCO_3$ (75 mL) was added, the layers were separated, the aqueous layer was extracted with CH_2Cl_2 (2 × 30 mL), and the combined organic extracts were dried over Na_2SO_4 and concentrated. The residue was purified by flash chromatography on silica gel (40% ethyl acetate/hexanes + 1% triethylamine) to afford a yellow oil (577 mg, 38% yield).

Hydrobromic acid (48% aqueous solution, 0.43 mL, 3.8 mmol, 1.0 equiv) was added dropwise to a solution of 4-(acetoxymethyl)pyridine (577 mg, 3.81 mmol, 1.0 equiv) in 1:1 ether/acetone (20 mL), forming a white precipitate, and the mixture was stored at –20 °C overnight. The precipitate was collected by filtration and recrystallized from 1:1 ether/acetone to provide the salt as a beige solid (580 mg, 66% yield).

^{1}H NMR (500 MHz, DMSO-d_6): δ 14.81 (br s, 1H), 9.00 (d, J = 6.9 Hz, 2H), 8.07 (d, J = 7.0 Hz, 2H), 5.41 (s, 2H), 2.16 (s, 3H).

^{13}C NMR (126 MHz, DMSO-d_6): δ 170.1, 156.9, 141.8, 124.3, 63.3, 20.7.

IR (ATR): ν 3055, 2574, 2073, 1976, 1888, 1736, 1635, 1596, 1512, 1433, 1388, 1369, 1332, 1308, 1238, 1208, 1192, 1046, 1003, 947, 926, 825, 798, 707, 656 cm^{-1}.

HRMS (ESI-TOF): m/z calculated for $C_8H_9NO_2$ $[M+H]^+$ 152.0706, found 152.0703.

***N*-(pyridin-4-ylmethyl)-*N*,*N*,*N*-trimethylammonium bromide•HBr**

4-Bromomethylpyridine hydrobromide (1.02 g, 4.03 mmol, 1.00 equiv) was added to sat. $NaHCO_3$ (40 mL), and the resulting free base was extracted with ether (2 × 25 mL). The combined organic extracts were quickly dried over Na_2SO_4 and concentrated to a volume of ~ 20 mL. Trimethylamine (1 M solution in tetrahydrofuran, 20 mL, 20 mmol, 5.0 equiv) was added to the

ethereal solution, forming a white precipitate. After 18 hours, the mixture was filtered, and the resulting off-white solid was washed with acetone to provide trimethylammonium salt (852 mg, 91% yield).

Hydrobromic acid (48% aqueous solution, 0.42 mL, 3.7 mmol, 1.0 equiv) was added dropwise to a solution of *N*-(pyridin-4-ylmethyl)-*N*,*N*,*N*-trimethylammonium bromide (582 mg, 3.67 mmol, 1.00 equiv) in ethanol (30 mL), forming a white precipitate within ~ 5 minutes, and the mixture was stored at –20 °C for 4 hours. The precipitate was collected by filtration and recrystallized from ethanol and a few drops of water to provide the dicationic salt as white prisms (858 mg, 75% yield).

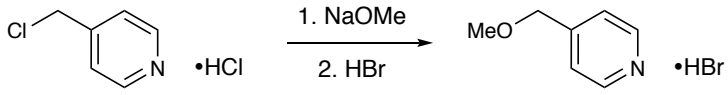
^{1}H NMR (500 MHz, DMSO-d_6): δ 11.89 (br s, 1H), 9.09 (d, J = 6.5 Hz, 2H), 8.22 (d, J = 6.6 Hz, 2H), 5.00 (s, 2H), 3.19 (s, 9H).

^{13}C NMR (126 MHz, DMSO-d_6): δ 145.1, 143.9, 130.5, 64.6, 52.3.

IR (ATR): ν 3002, 2957, 2599, 2045, 1967, 1834, 1639, 1603, 1515, 1493, 1483, 1474, 1420, 1404, 1363, 1337, 1309, 1247, 1228, 1199, 1189, 1138, 1092, 1066, 1026, 1006, 972, 931, 910, 866, 850, 807, 758, 714 cm^{-1}.

HRMS (ESI-TOF): m/z calculated for $C_9H_{15}N_2^+$ $[M]^+$ 151.1230, found 151.1230.

4-(methoxymethyl)pyridine•HBr



Based on the method of Walsh,[16] methanol (8 mL) was added to freshly cut sodium (1.00 g, 43.5 mmol, 2.50 equiv) at 0 °C. The mixture was allowed to warm slowly to room temperature and stirred for 11 hours, at which point the solid had completely dissolved. 4-(Chloromethyl)pyridine hydrochloride (2.85 g, 17.4 mmol, 1.00 equiv) was added in one portion and the suspension was

heater to 90 °C. After 12 hours, sat. $NaHCO_3$ (75 mL) was added, the mixture was extracted with CH_2Cl_2 (3 × 40 mL), and the combined organic extracts were dried over Na_2SO_4 and concentrated. The residue was purified by flash chromatography on silica gel (70% ether/hexanes + 1% triethylamine) to afford a pale yellow oil (2.13 g, 100% yield).

Hydrobromic acid (48% aqueous solution, 1.90 mL, 16.7 mmol, 0.97 equiv) was added dropwise to a solution of 4-(methoxymethyl)pyridine (2.13 g, 17.3 mmol, 1.00 equiv) in 1:1 ether/acetone (50 mL), forming a white precipitate, and the mixture was stored at –20 °C for 6 hours. The precipitate was collected by filtration and recrystallized from ethanol to provide the salt as a white solid (2.42 g, 68% yield).

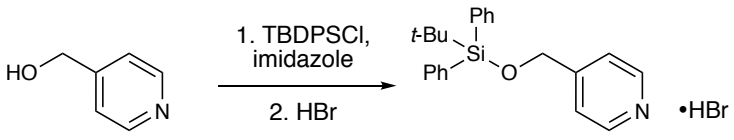
^{1}H NMR (500 MHz, DMSO-d_6): δ 14.57 (s, 1H), 8.95 (d, J = 6.8 Hz, 2H), 7.99 (d, J = 6.9 Hz, 2H), 4.76 (s, 2H), 3.41 (s, 3H).

^{13}C NMR (126 MHz, DMSO-d_6): δ 159.4, 141.6, 124.1, 71.3, 58.5.

IR (ATR): ν 3075, 2742, 2035, 1938, 1854, 1719, 1639, 1603, 1511, 1469, 1456, 1443, 1384, 1364, 1344, 1322, 1303, 1248, 1215, 1189, 1153, 1107, 1086, 1054, 1020, 1005, 988, 973, 933, 832, 785, 704 cm^{-1}.

HRMS (ESI-TOF): m/z calculated for C_7H_9NO $[M+H]^+$ 124.0757, found 124.0759.

4-(*tert*-butyldiphenylsiloxymethyl)pyridine•HBr



Based on a published procedure,[17] *tert*-butylchlorodiphenylsilane (2.60 mL, 9.99 mmol, 1.00 equiv) was added dropwise to a mixture of 4-(hydroxymethyl)pyridine (1.09 g, 9.99 mmol, 1.00 equiv) and imidazole (1.02 g, 15.0 mmol, 1.50 equiv) in CH_2Cl_2 (50 mL) at 0 °C. After 2 hours,

water (75 mL) was added, the layers were separated, the aqueous layer was extracted with CH_2Cl_2 (2 × 40 mL), and the combined organic extracts were dried over Na_2SO_4 and concentrated. The residue was purified by flash chromatography on silica gel (40% ethyl acetate/hexanes) to afford a white solid (2.28 g, 66% yield).

Hydrobromic acid (48% aqueous solution, 0.75 mL, 6.6 mmol, 1.0 equiv) was added dropwise to a solution of 4-(*tert*-butyldiphenylsiloxymethyl)pyridine (2.28 g, 6.56 mmol, 1.00 equiv) in 3:1 ether/acetone (40 mL), forming a white precipitate, and the mixture was stored at –20 °C overnight. The precipitate was collected by filtration and recrystallized from 1:1 ether/acetone to provide the salt as a colorless solid (1.16 g, 41% yield).

^{1}H NMR (500 MHz, DMSO-d_6): δ 14.63 (br s, 1H), 8.95 (d, J = 6.7 Hz, 2H), 8.05 (d, J = 6.2 Hz, 2H), 7.64 (m, 4H), 7.48 (m, 2H), 7.44 (m, 4H), 5.08 (s, 2H), 1.07 (s, 9H).

^{13}C NMR (126 MHz, DMSO-d_6): δ 160.879 141.8, 135.0, 132.0, 130.3, 128.2, 123.2, 63.7, 26.6, 18.9.

IR (ATR): ν 3053, 2930, 2890, 2856, 2471, 2073, 1975, 1739, 1636, 1605, 1589, 1520, 1471, 1426, 1388, 1367, 1326, 1306,1253, 1235, 1214, 1189, 1157, 1108, 1083, 1006, 997, 938, 850, 838, 823, 806, 778, 742, 701, 691 cm^{-1}.

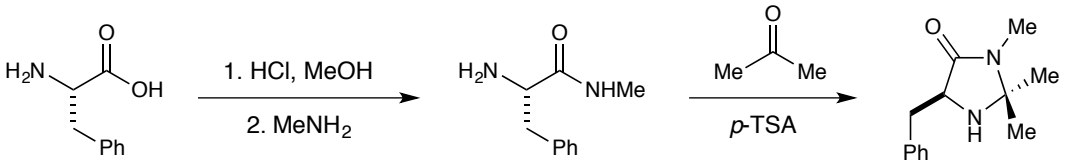
HRMS (ESI-TOF): m/z calculated for $C_{22}H_{25}NOSi$ $[M+H]^+$ 348.1778, found 348.1776.

IX. Synthesis of α-Acetoxyacetophenone Electrophile Substrates

α-Acetoxyacetophenone was prepared according to the method of Mioskowski,[18] and the resulting white solid was recrystallized from ether/hexanes. α-Acetoxy-4-fluoroacetophenone[19] was prepared according to the method of Hou,[20] and the white solid obtained was recrystallized from ethyl acetate/hexanes. α-Acetoxy-3,4-(methylenedioxy)acetophenone[21] was prepared over 2 steps according to the method of Zhang,[22] using the crude intermediate material without purification, and the white solid was recrystallized from ethyl acetate/hexanes.

X. Synthesis of Catalysts

Organocatalyst 8



A modification to our original procedure[23] was made to avoid recrystallization of the catalyst as the HCl salt, which can promote hydrolysis due to adventitious water in isopropanol.

Acetyl chloride (31 mL, 440 mmol, 1.7 equiv) was added to methanol (325 mL) at 0 °C. After 10 minutes, *L*-phenylalanine (41.2 g, 249 mmol, 1.0 equiv) was added and the mixture was heated to 75 °C. After 3 hours, the solution was concentrated, and the residue basified with saturated $NaHCO_3$ (500 mL) and extracted with CH_2Cl_2 (200, 3 × 100 mL). The combined organic extracts were dried over Na_2SO_4 and concentrated to afford a yellow oil (39.5 g, 88% yield).

The crude methyl ester (39.5 g, 220 mmol, 1.0 equiv) was treated with methylamine (33% solution in ethanol, 55 mL, 440 mmol, 2.0 equiv) at 0 °C and allowed to warm to room temperature. After 14 hours, the solution was concentrated, and the residue dissolved in saturated $NaHCO_3$ (150 mL) and extracted with CH_2Cl_2 (200, 3 × 100 mL). The combined organic extracts were dried over Na_2SO_4 and concentrated. The resulting off-white solid was recrystallized from 2:1 ethyl acetate/hexanes (400 mL) to afford the pure amide as a fluffy, off-white solid (23.7 g, 60% yield). This purification simplifies the isolation of the catalyst in the following step.

A mixture of the amide (23.7 g, 133 mmol, 1.0 equiv), acetone (50 mL, 680 mmol, 5.1 equiv) and *para*-toluenesulfonic acid monohydrate (260 mg, 1.37 mmol, 1 mol%) in methanol (400 mL) was heated to 85 °C. After 36 hours, the solution was concentrated, and the residue was dissolved in 50% saturated K_2CO_3 (200 mL) and extracted with CH_2Cl_2 (200, 2 × 75 mL). The combined organic extracts were dried over K_2CO_3 and concentrated to afford an orange oil. This material was purified by flash chromatography on silica gel (700 mL SiO_2), eluting with 75% ethyl

acetate/hexanes (discarding 1 L and collecting the next 4 L), providing a clear, nearly colorless oil. This imidazolidinone free base (20.6 g, 94 mmol, 1.0 equiv) was dissolved in ether (500 mL) and treated with trifluoroacetic acid (7.2 mL, 94 mmol, 1.0 equiv), forming a white precipitate. After standing at –20 °C for 6 hours, the solid was collected by filtration and air-dried overnight to afford the imidazolidinone as the trifluoroacetate salt (32.4 g, 73% yield from the amino amide).

This salt was stored under nitrogen at –20 °C and periodically liberated in batches (1 – 2 g) to afford the free base which was used in these studies. The trifluoroacetate salt was dissolved in 50% saturated K_2CO_3 (50 mL/g) and extracted with CH_2Cl_2 (3 × 50 mL/g). The combined organic extracts were dried over K_2CO_3 and concentrated to afford a low-melting white solid in quantitative yields. The free base was stored under nitrogen at –20 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.22 (m, 2H), 7.15 (m, 3H), 3.71 (t, *J* = 5.6 Hz, 1H), 3.07 (dd, *J* = 14.2, 4.5 Hz, 1H), 2.93 (dd, *J* = 14.2, 6.9 Hz, 1H), 2.68 (s, 3H), 1.59 (s, 1H), 1.18 (s, 3H), 1.08 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 173.4, 137.2, 129.5, 128.6, 126.8, 75.6, 59.3, 37.3, 27.3, 25.4, 25.3.

IR (ATR): ν 3062, 3028, 2974, 2927, 1681, 1496, 1476, 1453, 1425, 1397, 1367, 1320, 1263, 1204, 1182, 1147, 1090, 1072, 1030, 922, 800, 744, 700 cm^{-1}.

HRMS (ESI-TOF): m/z calculated for $C_{13}H_{18}N_2O$ $[M+H]^+$ 219.1492, found 219.1491.

$[\alpha]_D^{20}$: –81.3 (c = 1.0, CH_2Cl_2).

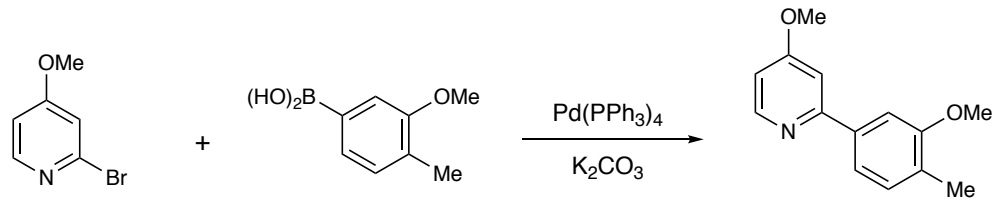
The 3-step sequence was also performed starting from *D*-phenylalanine to provide the amino amide (24.1 g, 54% yield over 2 steps) and ultimately the trifluoroacetate salt of the imidazolidinone (41.5 g, 92% yield).

Racemic quantities of the imidazolidinone free base were obtained by liberating 1:1 mixtures of

(*R*)- and (*S*)-enantiomers of the trifluoroacetate salt with K_2CO_3 as described for the (*S*)-organocatalyst. Attempts to prepare the racemic catalyst starting from *DL*-phenylalanine were complicated by the lower crystallinity of the intermediate amino amide, which impeded its recrystallization.

Photocatalyst Ligand Synthesis

4-methoxy-2-(3′-methoxy-4′-methylphenyl)pyridine



A mixture of 3-methoxy-4-*tert*-butylbenzeneboronic acid (4.54 g, 27.4 mmol, 1.18 equiv), 2-bromo-4-methoxypyridine (4.35 g, 23.1 mmol, 1.00 equiv), K_2CO_3 (12.8 g, 92.6 mmol, 4.00 equiv), and $Pd(PPh_3)_4$ (0.53 g, 0.46 mmol, 2.0 mol%) in ethanol (25 mL), water (50 mL), and toluene (100 mL) was sparged with nitrogen for 10 minutes, then heated to 70 °C. After 16 hours, the layers were separated, the upper, organic layer was washed with brine (25 mL), the original lower, aqueous layer was extracted with ether (2 × 25 mL), both ethereal extracts were also each washed with brine (25 mL), and the organic solutions were combined, dried over $MgSO_4$, and concentrated. The residue was purified by flash chromatography on silica gel (400 mL SiO_2, 10 → 15 → 25% ethyl acetate/hexanes) and recrystallized from hexanes (25 mL), to afford a white solid (2.61 g, 49% yield).

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.51 (d, *J* = 5.7 Hz, 1H), 7.55 (s, 1H), 7.39 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.21 (m, 2H), 6.76 (dd, *J* = 5.7, 2.4 Hz, 1H), 3.94 (s, 3H), 3.90 (s, 3H), 2.27 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 166.5, 159.4, 158.2, 150.9, 138.5, 130.8, 127.9, 118.8, 108.7, 108.0, 106.8, 55.6, 55.3, 16.3.

IR (ATR): ν 3088, 3018, 2973, 2947, 2918, 2834, 1591, 1565, 1507, 1477, 1441, 1421, 1390, 1375, 1328, 1312, 1298, 1265, 1236, 1209, 1185, 1163, 1140, 1060, 1041, 1032, 997, 990, 917, 881, 860, 821, 803, 769, 742, 714, 666 cm^{-1}.

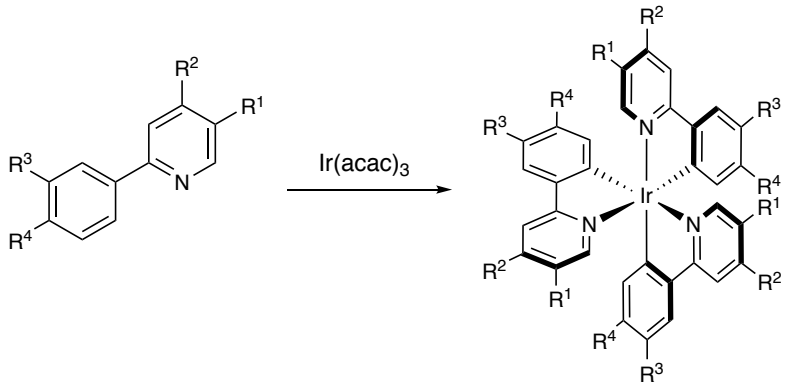
HRMS (ESI-TOF): m/z calculated for $C_{14}H_{15}NO_2$ $[M+H]^+$ 230.1176, found 230.1176.

All other substituted phenylpyridine ligands used in this study were prepared analogously, and have been previously described. Following chromatography, 5-*tert*-butyl-2-phenylpyridine,[24] 4-*tert*-butyl-2-phenylpyridine,[5] 2-(3′-*tert*-butylphenyl)pyridine,[25] 2-(4′-*tert*-butylphenyl)pyridine,[26] 2-(3′-methoxyphenyl)pyridine,[27] and 2-(4′-methoxyphenyl)pyridine[26] were liquid compounds that were distilled under reduced pressure (~ 100 mTorr), while 4-methoxy-2-phenylpyridine[28] was a low-melting solid which was used without further purification.

Iridium(III) acetylacetonate

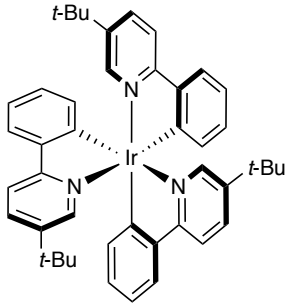
Prepared according to the method of Stoessel *et al.*,[29] using acetylacetone (16 equiv) and $NaHCO_3$ (10 equiv) as described in Example 7 of the patent, to provide 30–40% yields of the desired complex on 10–30 mmol scales.

Photocatalyst Synthesis: Method A[30]



A mixture of iridium(III) acetylacetonate (1.0 equiv) and phenylpyridine ligand (6.0 equiv) in glycerol (0.02 M iridium) was sparged with nitrogen for 10 minutes and heated between 210 °C and 240 °C for 12 to 18 hours. After cooling to room temperature, the mixture was diluted with 1 M HCl (3 volumes with respect to glycerol), filtered, and the filtrate was discarded. The solid was filtered in a minimum of warm CH_2Cl_2 and the filtrate was purified by flash chromatography on silica gel (CH_2Cl_2/hexanes eluent). The resulting yellow solids were dissolved in a minimum of hot CH_2Cl_2, methanol (1-2 volumes) was added, causing a solid to precipitate, and the solvent was boiled down to a minimum workable volume such that no CH_2Cl_2 remained. After standing for several hours at –20 °C, the solid was collected and washed with methanol.

Tris(5-*tert*-butyl-2-phenylpyridinato)iridium(III) (Figure 3, R^1 = *t*-Bu)



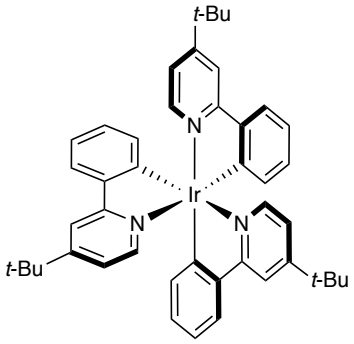
Prepared from iridium(III) acetylacetonate (2.7 mmol), heating at 210 °C for 18 hours. Chromatography was performed using a 30 → 50% CH_2Cl_2/hexanes eluent, but instead of subsequent precipitation with methanol, further chromatography was performed using an 0 → 30% CH_2Cl_2/hexanes eluent. The title compound was obtained as a yellow solid (220 mg, 55% yield).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.78 (d, *J* = 8.6 Hz, 3H), 7.61 (m, 6H), 7.44 (d, *J* = 2.3 Hz, 3H), 7.00 (m, 3H), 6.90 (m, 6H), 1.09 (s, 27H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 164.5, 160.7, 144.3, 144.2, 143.6, 137.3, 133.6, 129.6, 123.7, 119.6, 118.3, 33.4, 30.9.

HRMS (ESI-TOF): m/z calculated for $C_{45}H_{48}IrN_3$ $[M+Na]^+$ 844.3346, found 844.3355.

Tris(4-*tert*-butyl-2-phenylpyridinato)iridium(III) (Figure 3, R^2 = *t*-Bu)



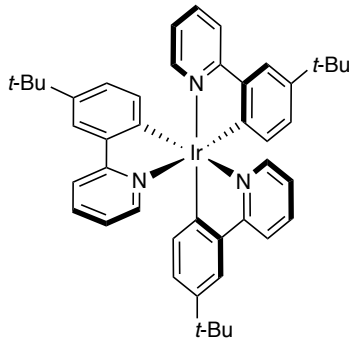
Prepared from iridium(III) acetylacetonate (0.34 mmol), heating at 230 °C for 12 hours. Chromatography was performed using a 50% CH_2Cl_2/hexanes eluent. The title compound was obtained as a yellow solid (121 mg, 44% yield).

^{1}H NMR (500 MHz, CD_2Cl_2): δ 7.91 (d, *J* = 2.0 Hz, 3H), 7.70 (d, *J* = 7.7 Hz, 3H), 7.43 (d, *J* = 5.9 Hz, 3H), 6.96 (dd, *J* = 5.9, 2.0 Hz, 3H), 6.86 (td, *J* = 7.4, 1.4 Hz, 3H), 6.79 (td, *J* = 7.3, 1.4 Hz, 3H), 6.71 (d, *J* = 7.5 Hz, 3H), 1.35 (s, 27H).

^{13}C NMR (126 MHz, CD_2Cl_2): δ 166.2, 161.5, 160.7, 147.0, 144.9, 137.4, 129.6, 123.9, 120.2, 120.1, 116.0, 35.3, 30.6.

HRMS (ESI-TOF): m/z calculated for $C_{45}H_{48}IrN_3$ $[M+Na]^+$ 844.3346, found 844.3345.

Tris(2-(5′-*tert*-butylphenyl)pyridinato)iridium(III) (Figure 3, R^3 = *t*-Bu)[31]



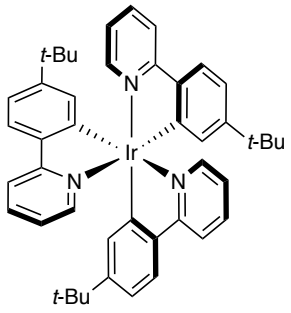
Prepared from iridium(III) acetylacetonate (0.15 mmol), heating at 240 °C for 12 hours. Chromatography was performed using a 50% CH_2Cl_2/hexanes eluent. The title compound was obtained as a yellow solid (17 mg, 13% yield).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.89 (d, *J* = 8.1 Hz, 3H), 7.63 (d, *J* = 2.1 Hz, 3H), 7.56 (m, 6H), 6.92 (dd, *J* = 8.0, 2.1 Hz, 3H), 6.84 (td, *J* = 5.6, 2.7 Hz, 3H), 6.68 (d, *J* = 8.0 Hz, 3H), 1.29 (s, 27H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 167.4, 157.7, 147.3, 143.0, 141.9, 136.3, 135.6, 128.0, 121.6, 120.5, 118.8, 34.2, 31.6.

HRMS (ESI-TOF): m/z calculated for $C_{45}H_{48}IrN_3$ $[M+Na]^+$ 844.3346, found 844.3348.

Tris(2-(4′-*tert*-butylphenyl)pyridinato)iridium(III) (Figure 3, R^4 = *t*-Bu)[30]



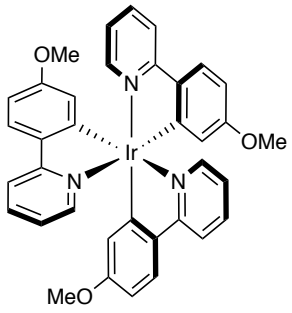
Prepared from iridium(III) acetylacetonate (3.9 mmol), heating at 210 °C for 17 hours. Chromatography was performed using a 50% CH_2Cl_2/hexanes eluent. The title compound was obtained as a yellow solid (1.77 g, 55% yield).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.79 (d, *J* = 8.1 Hz, 3H), 7.55 (m, 9H), 6.85 (d, *J* = 8.1 Hz, 3H), 6.81 (t, *J* = 6.5 Hz, 3H), 6.73 (s, 3H), 1.09 (s, 27H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 167.0, 160.3, 151.6, 147.3, 141.9, 135.7, 135.0, 122.8, 121.6, 118.5, 117.7, 34.5, 31.4.

HRMS (ESI-TOF): m/z calculated for $C_{45}H_{48}IrN_3$ $[M+Na]^+$ 844.3346, found 844.3341.

Tris(2-(4′-methoxyphenyl)pyridinato)iridium(III) (Figure 3, R^4 = MeO)[30]



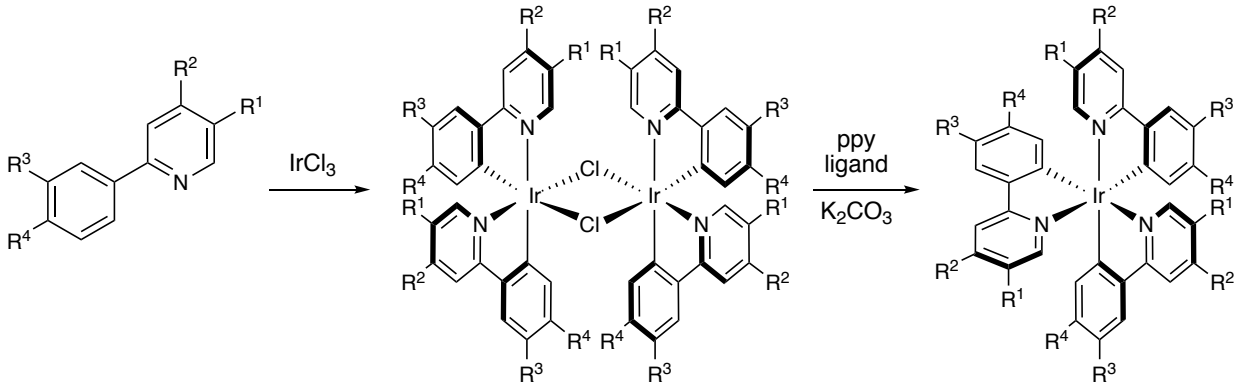
Prepared from iridium(III) acetylacetonate (1.8 mmol), heating at 210 °C for 12 hours. Chromatography was performed using a CH_2Cl_2 eluent, but instead of subsequent precipitation with methanol, the solid was triturated with ethyl acetate and hexanes. The title compound was obtained as a yellow solid (645 mg, 48% yield).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.73 (d, *J* = 8.4 Hz, 3H), 7.55 (m, 3H), 7.51 (ddd, *J* = 8.4, 7.4, 1.7 Hz, 3H), 7.46 (ddd, *J* = 5.5, 1.6, 0.8 Hz, 3H), 6.77 (ddd, *J* = 7.0, 5.5, 1.3 Hz, 3H), 6.45 (m, 6H), 3.55 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 166.5, 164.0, 160.8, 147.1, 137.1, 135.8, 125.3, 120.8, 120.7, 118.2, 106.7, 54.8.

HRMS (ESI-TOF): m/z calculated for $C_{36}H_{30}IrN_3O_3$ $[M+Na]^+$ 766.1785, found 766.1779.

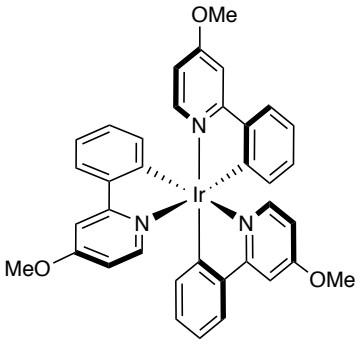
Photocatalyst Synthesis: Method B[32]



A mixture of iridium(III) chloride monohydrate (1.0 equiv) and phenylpyridine ligand (3.0 equiv) in 3:1 2-ethoxyethanol/water (0.05 M iridium) was sparged with nitrogen for 10 minutes and heated at 130 °C for 8 to 13 hours. After cooling to –20 °C, the mixture was filtered, the solid was washed with cold methanol and ether, and the filtrate was discarded. The solid chloro-bridged dimer was in the next step without further purification.

A mixture of the iridium(III) chloro-bridged dimer (0.50 equiv), phenylpyridine ligand (2.0 equiv), and K_2CO_3 (5.0 equiv) in glycerol (0.05 M iridium dimer) was sparged with nitrogen for 10 minutes and heated between 200 °C and 300 °C for 12 to 24 hours. After cooling to room temperature, the mixture was diluted with 1 M HCl (3 volumes with respect to glycerol), filtered, and the filtrate was discarded. The solid was filtered in a minimum of warm CH_2Cl_2 and the filtrate was purified by flash chromatography on silica gel (CH_2Cl_2/hexanes eluent). The resulting yellow or orange solids were dissolved in a minimum of hot CH_2Cl_2, methanol (1-2 volumes) was added, causing a solid to precipitate, and the solvent was boiled down to a minimum workable volume such that no CH_2Cl_2 remained. After standing for several hours at –20 °C, the solid was collected and washed with methanol.

Tris(4-methoxy-2-phenylpyridinato)iridium(III) (Figure 3, R^2 = MeO)



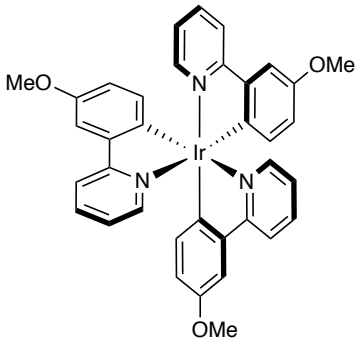
The dimer was prepared from iridium(III) chloride monohydrate (0.41 mmol), heating for 8 hours, and obtained as a yellow solid (180 mg, 74% yield). The photocatalyst was prepared from this dimer (0.075 mmol), heating at 230 °C for 12 hours. Chromatography was performed using a 50% CH_2Cl_2/hexanes eluent, and the title compound was obtained as a yellow solid (18 mg, 16% yield).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.59 (m, 3H), 7.37 (dd, *J* = 6.3, 1.0 Hz, 3H), 7.34 (d, *J* = 2.6 Hz, 3H), 6.85 (m, 9H), 6.46 (dd, *J* = 6.4, 2.6 Hz, 3H), 3.87 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 168.3, 166.980 162.1, 148.1, 144.2, 137.4, 129.8, 123.7, 119.6, 109.2, 103.7, 55.5.

HRMS (ESI-TOF): m/z calculated for $C_{36}H_{30}IrN_3O_3$ $[M+Na]^+$ 766.1785, found 766.1783.

Tris(2-(5′-methoxyphenyl)pyridinato)iridium(III) (Figure 3, R^3 = MeO)[30]



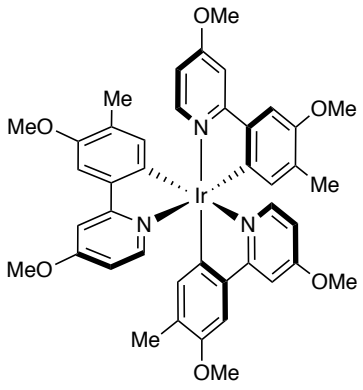
The dimer was prepared from iridium(III) chloride monohydrate (1.5 mmol), heating for 12 hours, and obtained as an orange solid (625 mg, 69% yield). The photocatalyst was prepared from this dimer (0.10 mmol), heating at 300 °C for 14 hours. Chromatography was performed using an 80 → 95% CH_2Cl_2/hexanes eluent, and the title compound was obtained as an orange solid (18 mg, 12% yield).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.81 (d, *J* = 8.2 Hz, 3H), 7.57 (td, *J* = 7.8, 1.7 Hz, 3H), 7.54 (d, *J* = 5.7 Hz, 3H), 7.24 (d, *J* = 2.7 Hz, 3H), 6.85 (ddd, *J* = 7.1, 5.5, 1.3 Hz, 3H), 6.71 (d, *J* = 8.3 Hz, 3H), 6.58 (dd, *J* = 8.4, 2.7 Hz, 3H), 3.77 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 166.7, 154.4, 150.7, 147.3, 144.0, 137.3, 135.9, 122.2, 119.0, 116.9, 109.7, 55.4.

HRMS (ESI-TOF): m/z calculated for $C_{36}H_{30}IrN_3O_3$ $[M+Na]^+$ 766.1785, found 766.1772.

Tris(4-methoxy-2-(3′-methoxy-4′-methylphenyl)pyridinato)iridium(III) (Figure 3, R^2, R^3 = MeO, R^4 = Me)



The dimer was prepared from iridium(III) chloride monohydrate (2.0 mmol), heating for 13 hours, and obtained as an orange solid (1.04 g, 75% yield). The photocatalyst was prepared from this dimer (0.10 mmol), heating at 200 °C for 24 hours. Chromatography was performed using an 80 → 95% CH_2Cl_2/hexanes eluent, and the title compound was obtained as an orange solid (23 mg, 13% yield).

^{1}H NMR (500 MHz, CD_2Cl_2): δ 7.29 (m, 6H), 7.10 (s, 3H), 6.43 (m, 6H), 3.90 (s, 9H), 3.85 (s, 9H), 1.97 (s, 9H).

^{13}C NMR (126 MHz, CD_2Cl_2): δ 168.2, 166.3, 154.0, 151.8, 148.4, 142.7, 139.3, 129.0, 108.72, 105.9, 103.8, 16.8.

HRMS (ESI-TOF): m/z calculated for $C_{42}H_{42}IrN_3O_6$ $[M]^{+\bullet}$ 877.2697, found 877.2712.

Note on Photocatalyst Selection

While photocatalysts Ir[(4,5′-$(MeO)_2$-4′-Me)ppy]$_3$ (R^2, R^3 = MeO, R^4 = Me), Ir[(5′-MeO)ppy]$_3$ (R^3 = MeO), and Ir[(5′-*t*-Bu)ppy]$_3$ (R^3 = *t*-Bu) are the three most chemoselective (see Figure 3 of the manuscript), we favored photocatalyst Ir[(4′-*t*-Bu)ppy]$_3$ (R^4 = *t*-Bu), despite its slightly lower selectivity, because (1) it was the only photocatalyst that consistently consumed the starting alcohols completely, and (2) it could be prepared in useful yields (> 50%), whereas we were unable to obtain any of the three of the more selective photocatalysts even in 15% yields, despite efforts to improve reaction conditions or increase the scale in their synthesis.

XI. Photophysical Properties of Photocatalysts (Figure 3)

Photocatalyst (~ 3 μmol) was dissolved in acetonitrile or CH_2Cl_2 (10 mL) to prepare a ~ 0.3 mM solution. This solution (0.10 mL) was then diluted 100-fold by adding further solvent (9.9 mL). The resulting ~ 3 μM solution (4 mL) was added to a screw-top 1.0 cm quartz cuvette and sparged with nitrogen for 10 minutes before obtaining UV-Vis absorption and fluorescence emission spectra, the latter obtained by irradiation at 400 nm. Wavelengths of the near-UV and visible maxima are noted, as are the high-energy wavelengths in the emission spectra corresponding to 10% of the intensity at the maximum to approximate E^{0-0}.

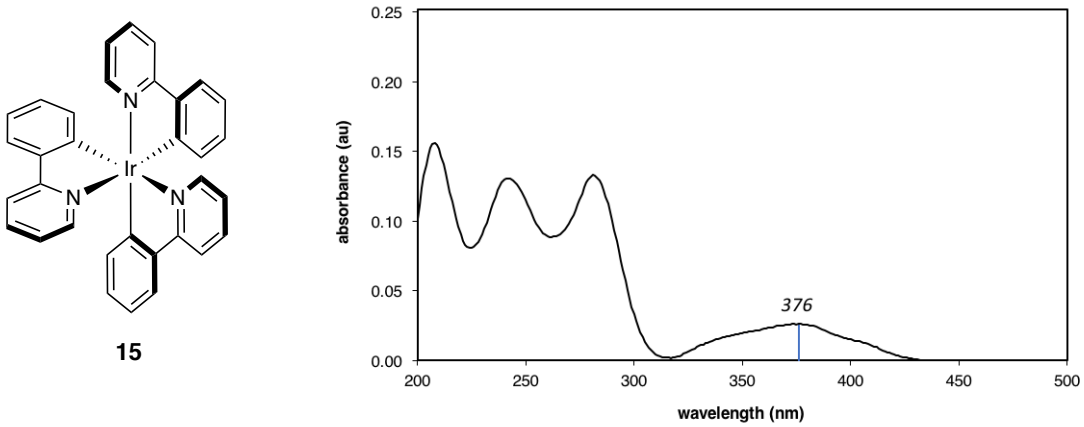


Figure S3. UV-Vis absorption spectrum of $Ir(ppy)_3$ (**15**) in acetonitrile.

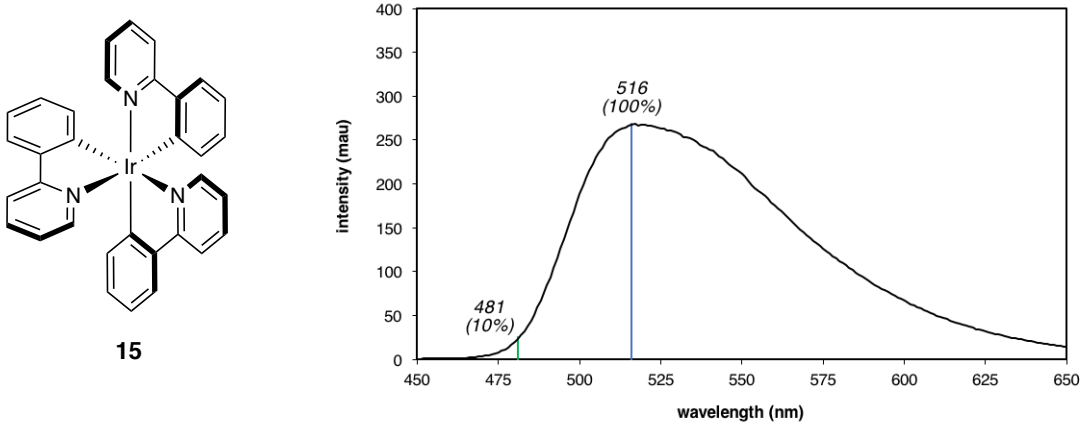


Figure S4. Fluorescence emission spectrum of $Ir(ppy)_3$ (**15**) in acetonitrile.

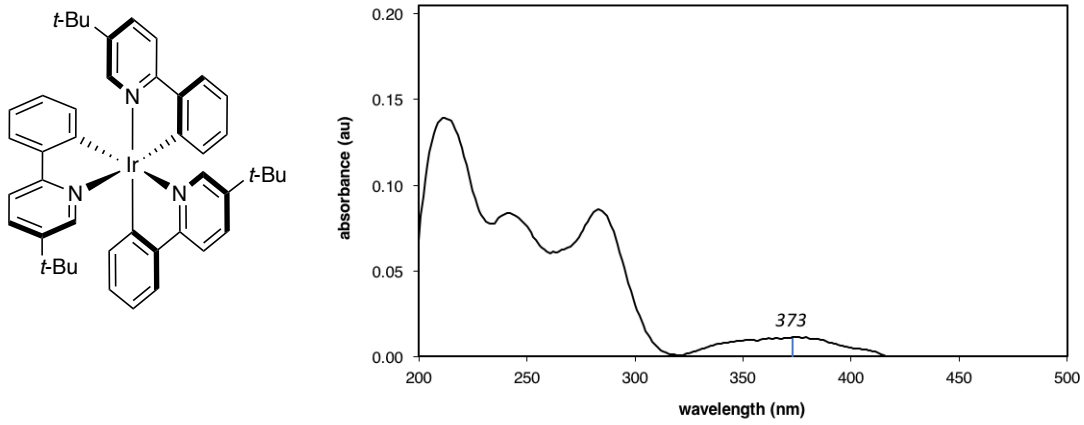


Figure S5. UV-Vis absorption spectrum of Ir[(5-*t*-Bu)ppy]$_3$ (R^1 = *t*-Bu) in acetonitrile.

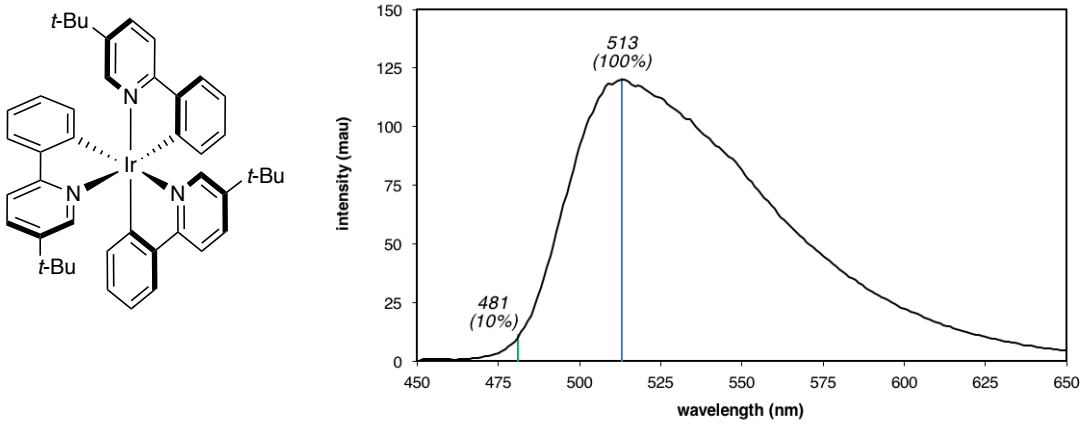


Figure S6. Fluorescence emission spectrum of Ir[(5-*t*-Bu)ppy]$_3$ (R^1 = *t*-Bu) in acetonitrile.

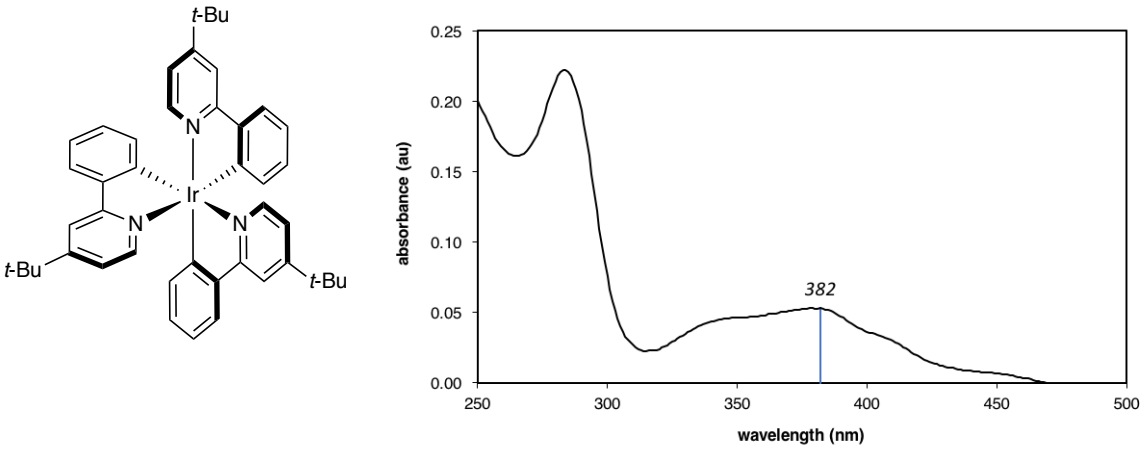


Figure S7. UV-Vis absorption spectrum of Ir[(4-*t*-Bu)ppy]$_3$ (R^2 = *t*-Bu) in CH_2Cl_2.

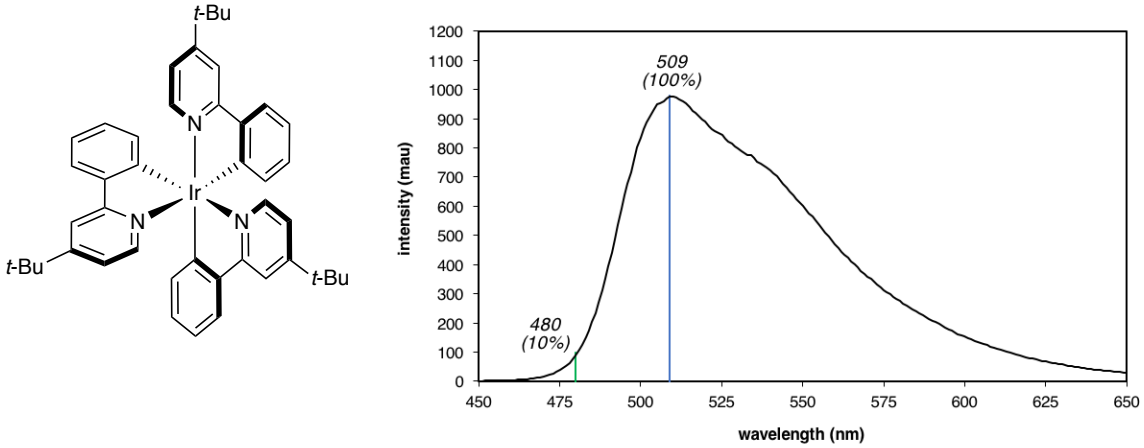


Figure S8. Fluorescence emission spectrum of Ir[(4-*t*-Bu)ppy]$_3$ (R^2 = *t*-Bu) in CH_2Cl_2.

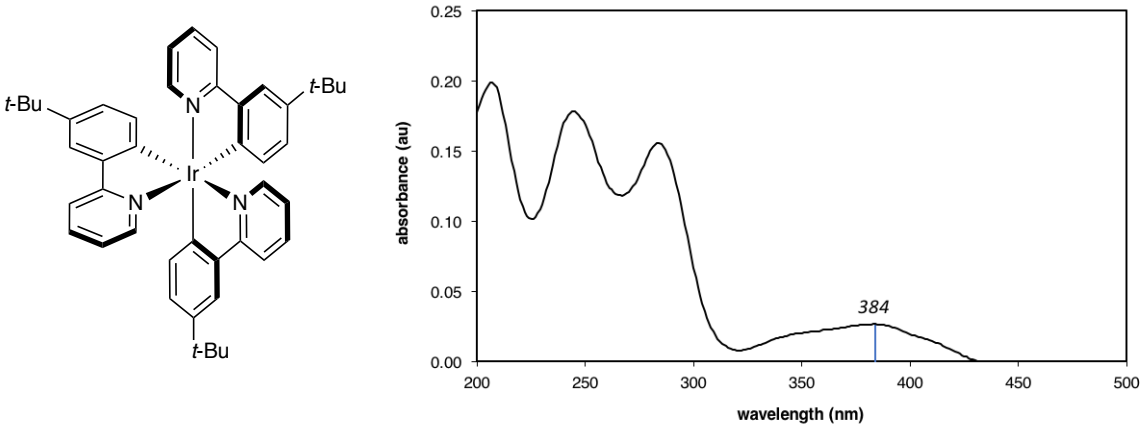


Figure S9. UV-Vis absorption spectrum of Ir[(5′-*t*-Bu)ppy]$_3$ (R^3 = *t*-Bu) in acetonitrile.

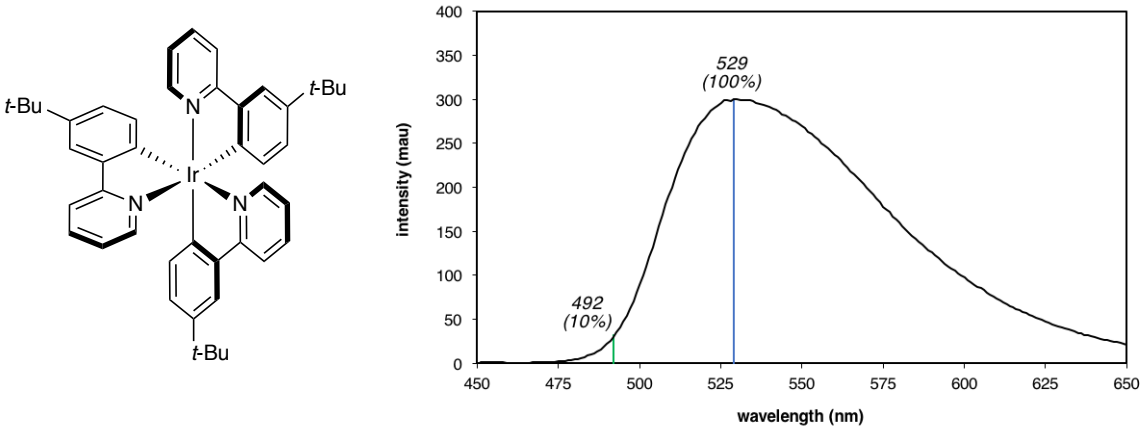


Figure S10. Fluorescence emission spectrum of Ir[(5′-*t*-Bu)ppy]$_3$ (R^3 = *t*-Bu) in acetonitrile.

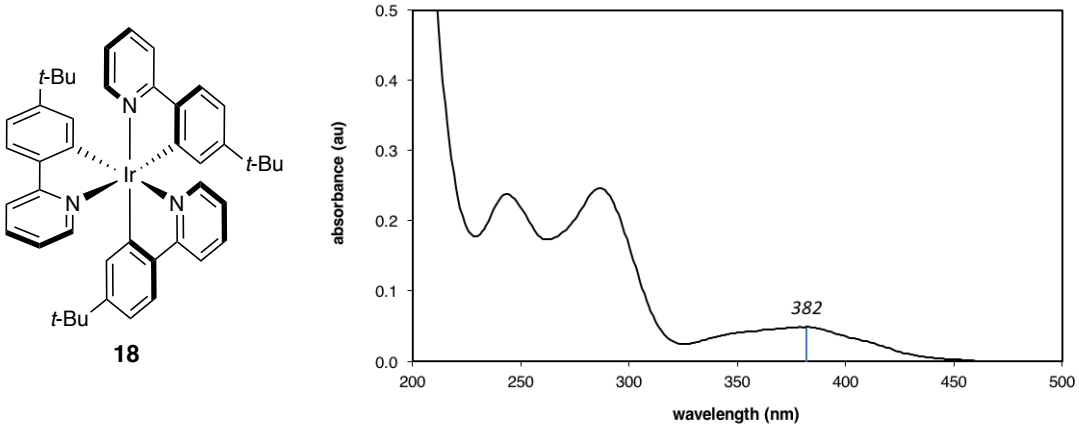


Figure S11. UV-Vis absorption spectrum of Ir[(4′-*t*-Bu)ppy]$_3$ (**18**, R^4 = *t*-Bu) in acetonitrile.

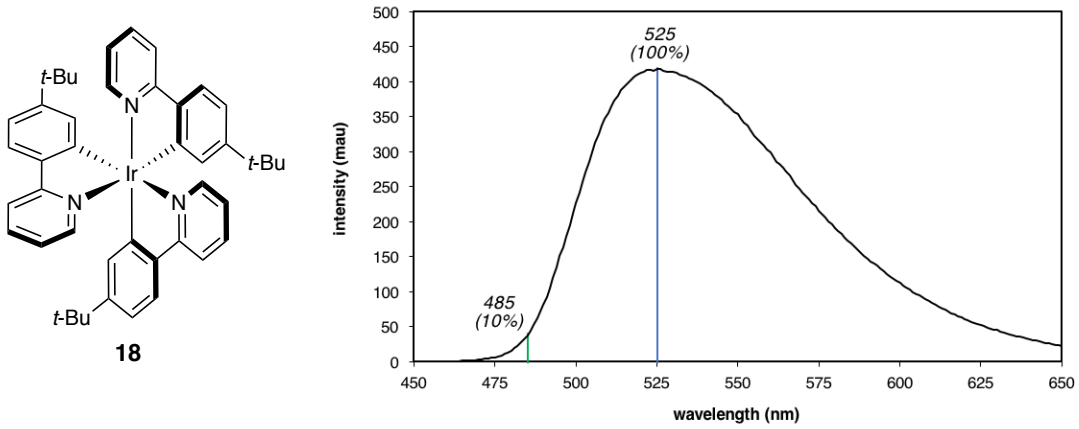


Figure S12. Fluorescence emission spectrum of Ir[(4′-*t*-Bu)ppy]$_3$ (**18**, R^4 = *t*-Bu) in acetonitrile.

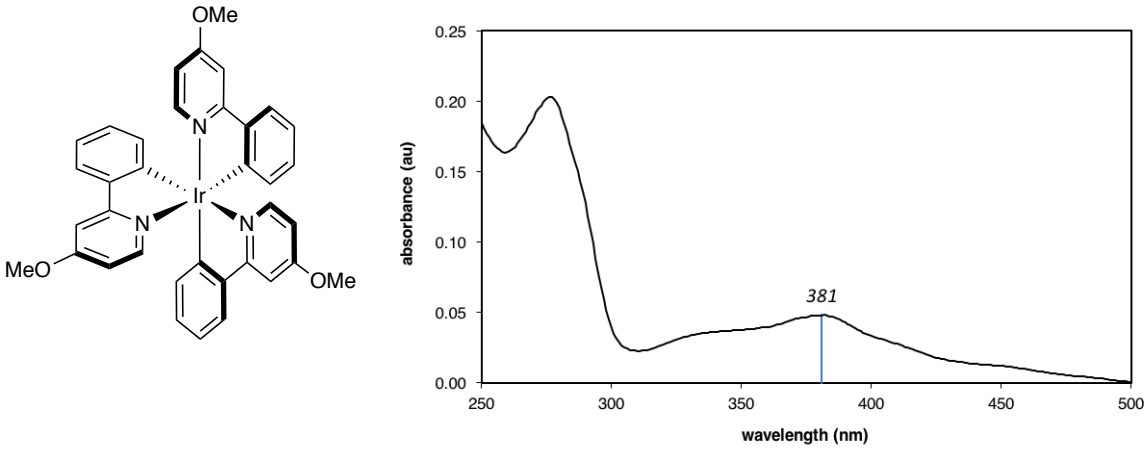


Figure S13. UV-Vis absorption spectrum of Ir[(4-MeO)ppy]$_3$ (R^2 = MeO) in CH_2Cl_2.

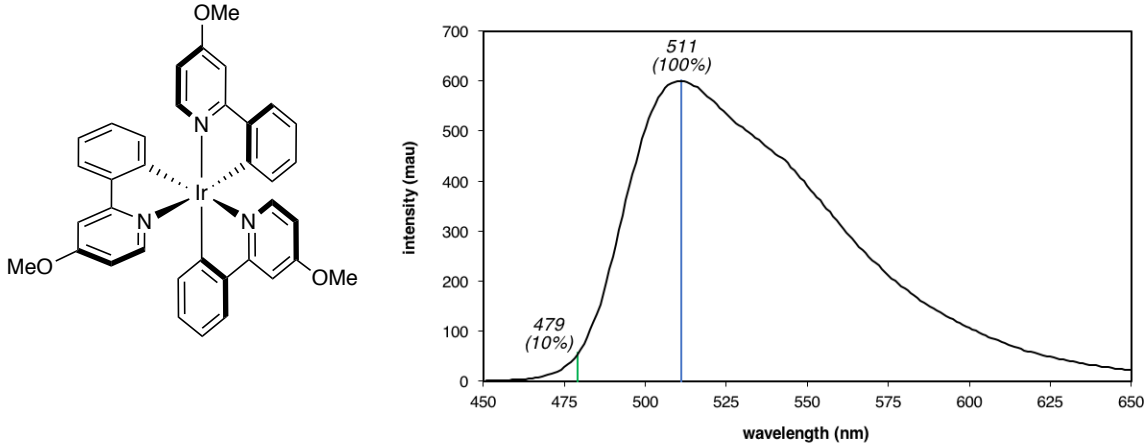


Figure S14. Fluorescence emission spectrum of Ir[(4-MeO)ppy]$_3$ (R^2 = MeO) in CH_2Cl_2.

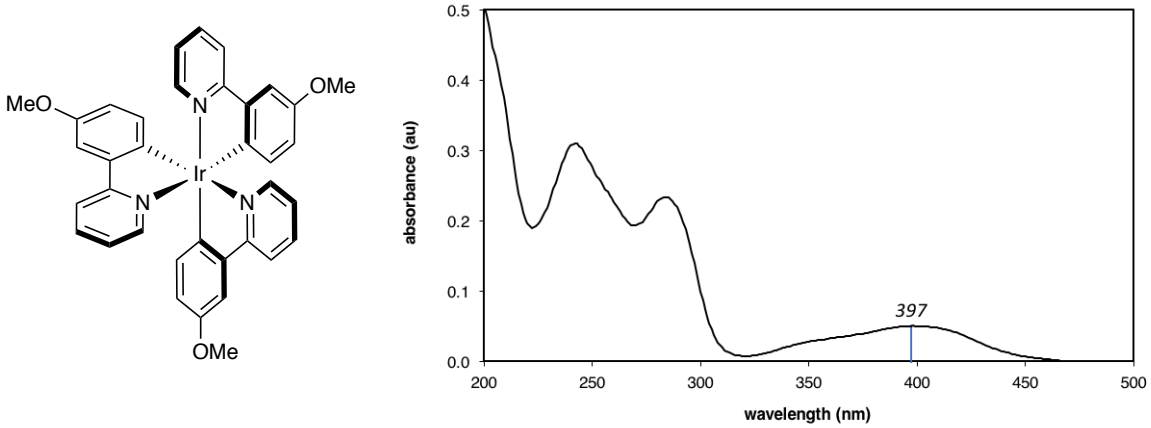


Figure S15. UV-Vis absorption spectrum of Ir[(5′-MeO)ppy]$_3$ (R^3 = MeO) in acetonitrile.

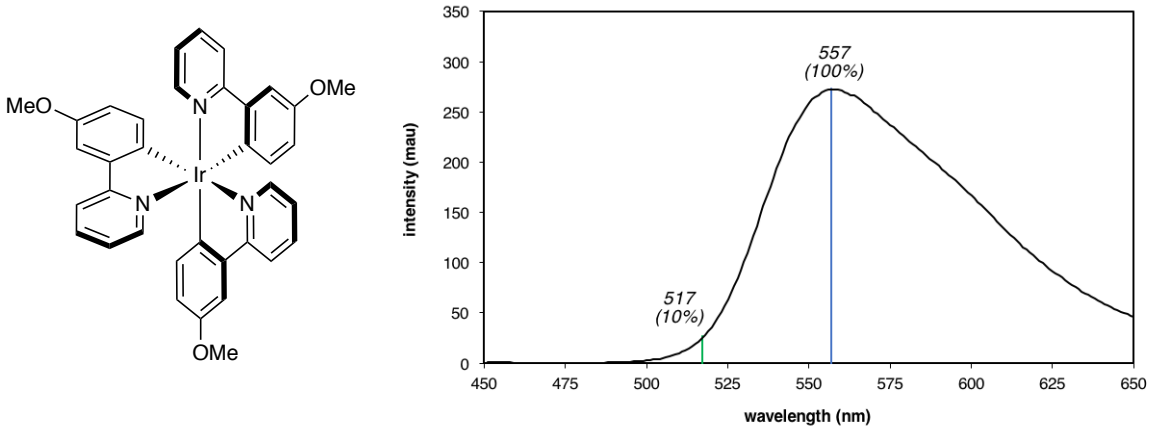


Figure S16. Fluorescence emission spectrum of Ir[(5′-MeO)ppy]$_3$ (R^3 = MeO) in acetonitrile.

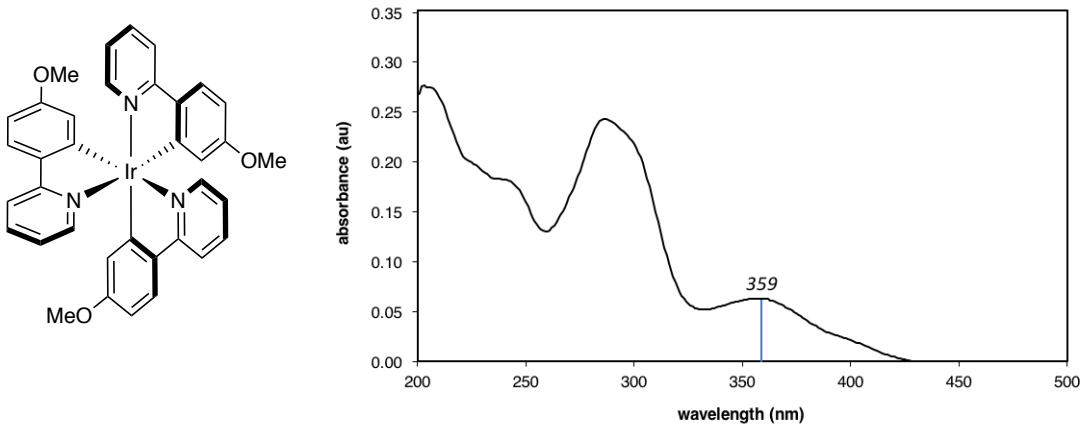


Figure S17. UV-Vis absorption spectrum of Ir[(4′-MeO)ppy]$_3$ (R^4 = MeO) in acetonitrile.

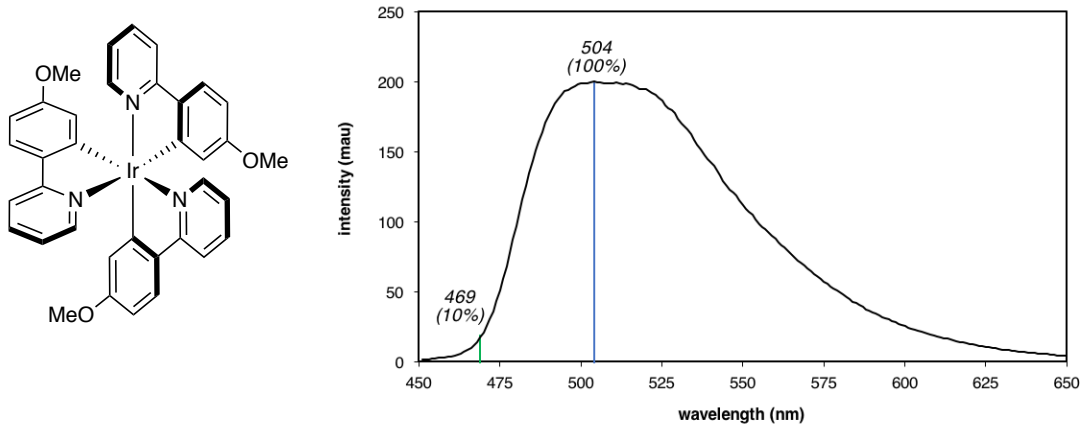


Figure S18. Fluorescence emission spectrum of Ir[(4′-MeO)ppy]$_3$ (R^4 = MeO) in acetonitrile.

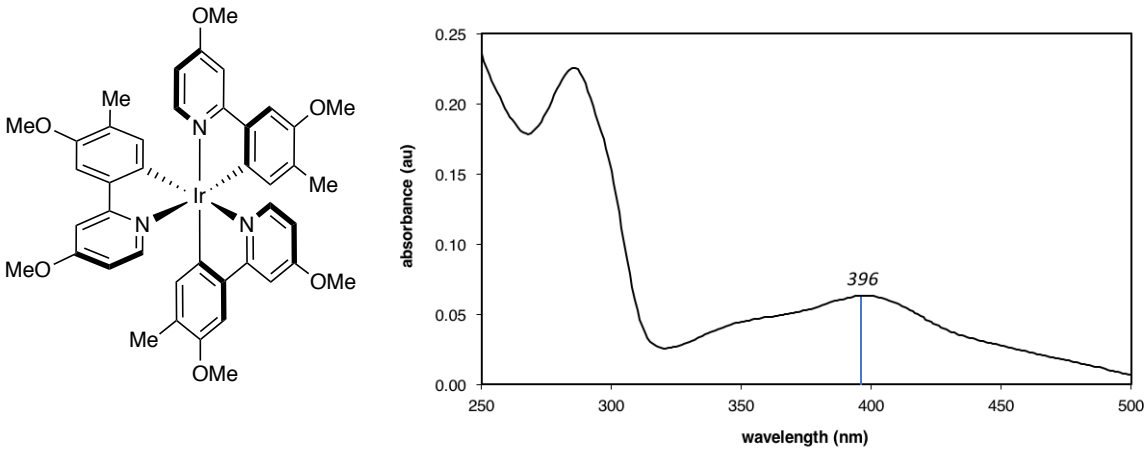


Figure S19. UV-Vis absorption spectrum of Ir[(4,5′-(MeO)$_2$-4′-Me)ppy]$_3$ (R^2, R^3 = MeO, R^4 = Me) in CH_2Cl_2.

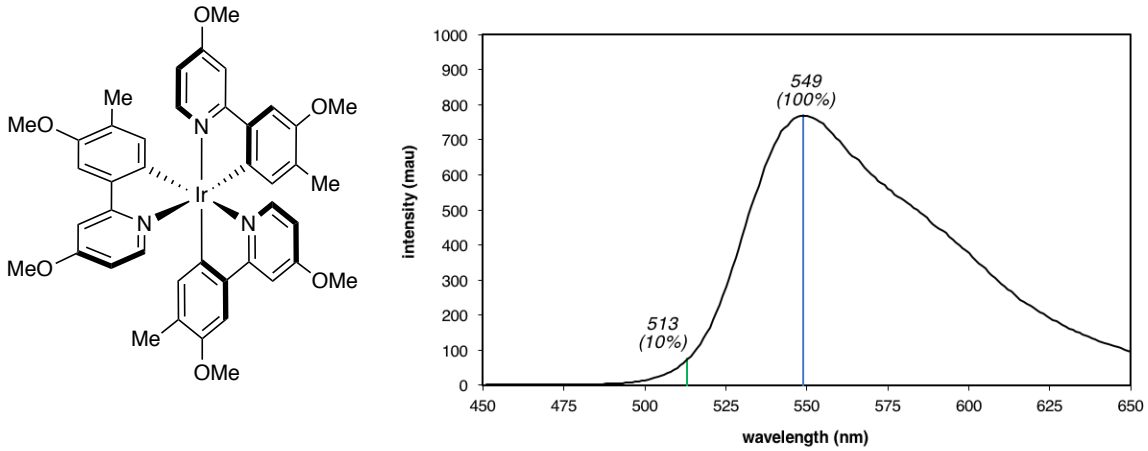
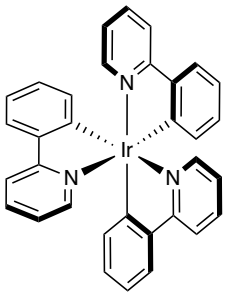


Figure S20. Fluorescence emission spectrum of Ir[(4,5′-(MeO)$_2$-4′-Me)ppy]$_3$ (R^2, R^3 = MeO, R^4 = Me) in CH_2Cl_2.

XII. Electrochemical Properties of Photocatalysts (Figure 3)

Photocatalyst (0.020 mmol) and tetrabutylammonium hexafluorophosphate (775 mg, 2.0 mmol) were dissolved in acetonitrile or CH_2Cl_2 (20 mL) in a 25 mL 3-neck flask (as little as 1/5 of this scale was used for photocatalysts obtained in small quantities). The solution was sparged with nitrogen for 10 minutes and analyzed by cyclic voltammetry.



15

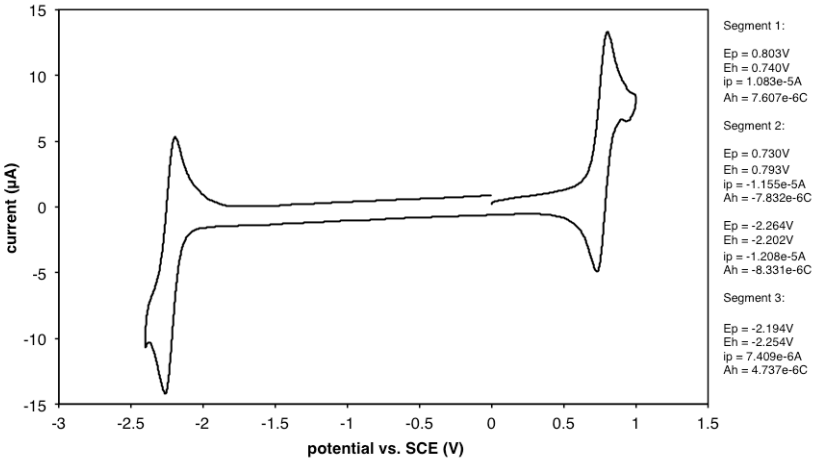
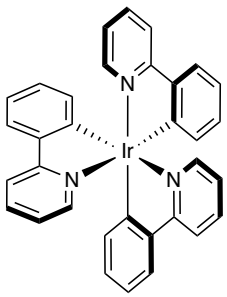


Figure S21. Cyclic voltammogram of $Ir(ppy)_3$ (**15**) in acetonitrile. Scanned from 0 V to +1 V to –2.5 V to 0 V at 0.1 V/s.



15

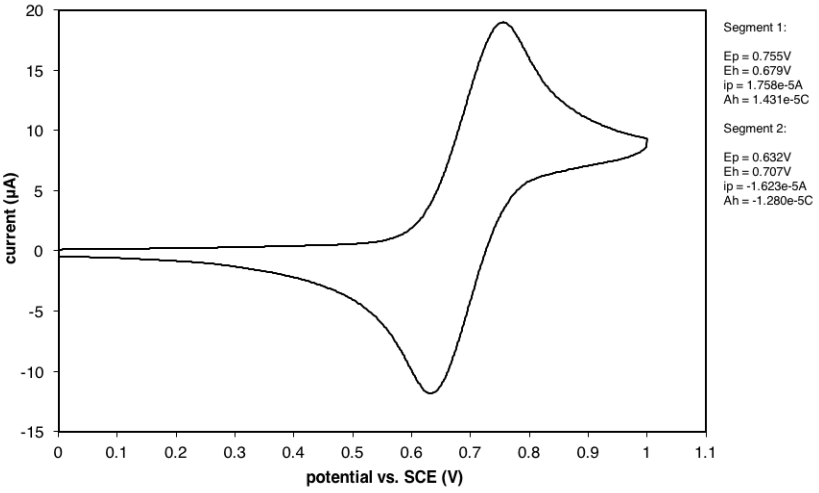


Figure S22. Cyclic voltammogram of $Ir(ppy)_3$ (**15**) in CH_2Cl_2. Scanned from 0 V to +1 V to 0 V at 0.1 V/s.

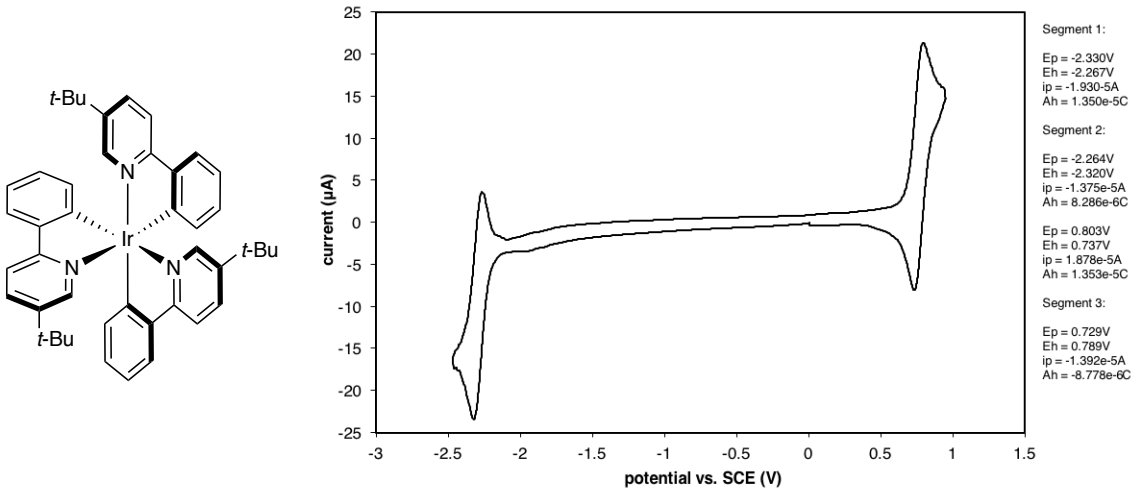


Figure S23. Cyclic voltammogram of Ir[(5-*t*-Bu)ppy]$_3$ (R^1 = *t*-Bu) in acetonitrile. Scanned from 0 V to –2.47 V to +0.95 V to 0 V at 0.1 V/s.

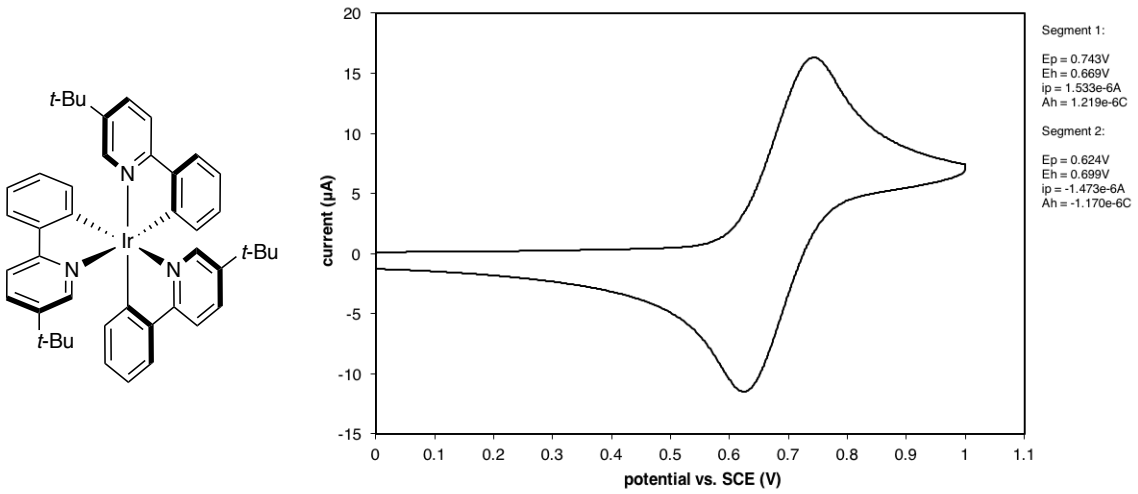


Figure S24. Cyclic voltammogram of Ir[(5-*t*-Bu)ppy]$_3$ (R^1 = *t*-Bu) in CH_2Cl_2. Scanned from 0 V to +1 V to 0 V at 0.1 V/s.

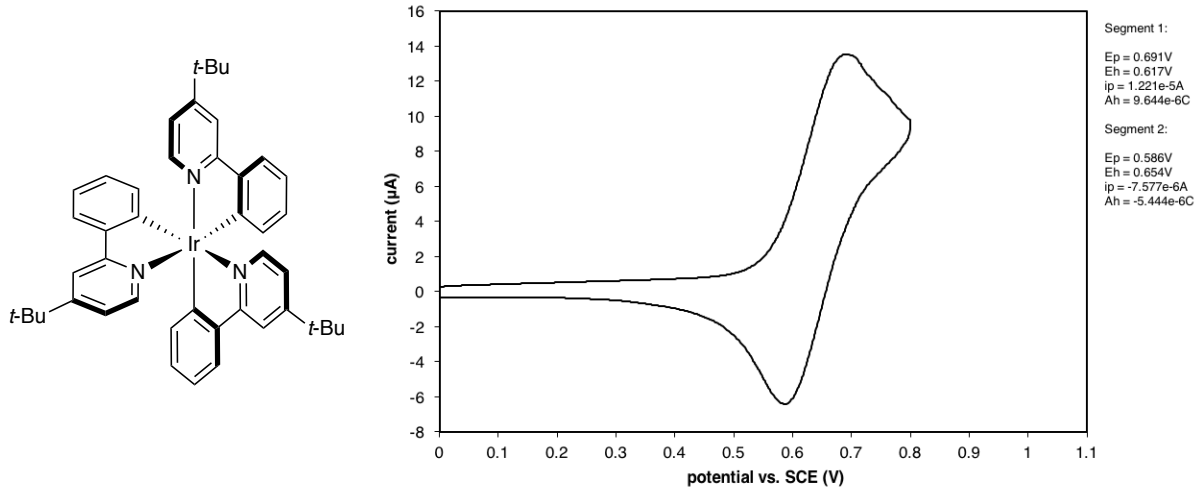


Figure S25. Cyclic voltammogram of Ir[(4-*t*-Bu)ppy]$_3$ (R^2 = *t*-Bu) in CH_2Cl_2. Scanned from 0 V to +0.8 V to 0 V at 0.1 V/s.

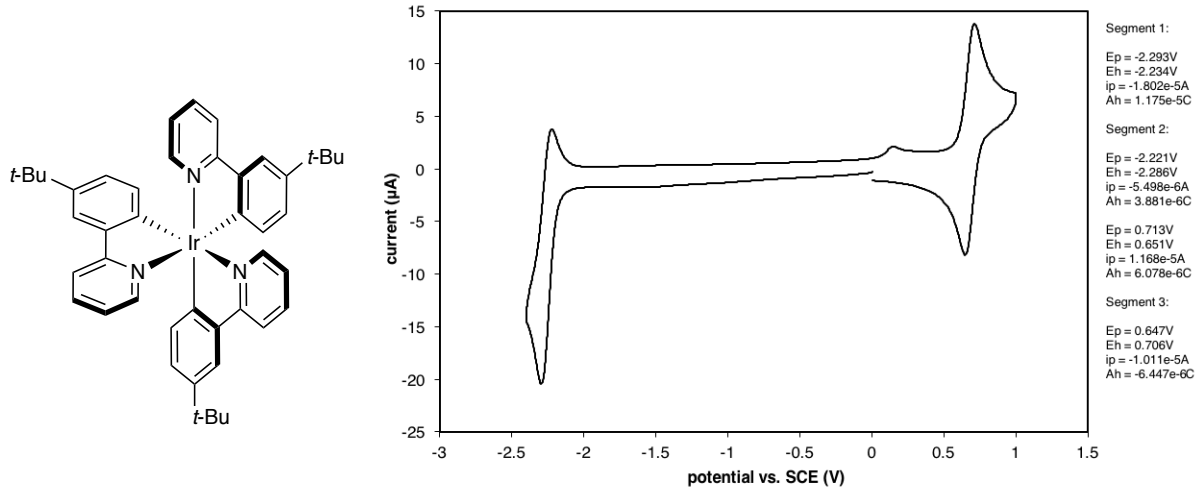


Figure S26. Cyclic voltammogram of Ir[(5′-*t*-Bu)ppy]$_3$ (R^3 = *t*-Bu) in acetonitrile. Scanned from 0 V to –2.4 V to +1 V to 0 V at 0.1 V/s.

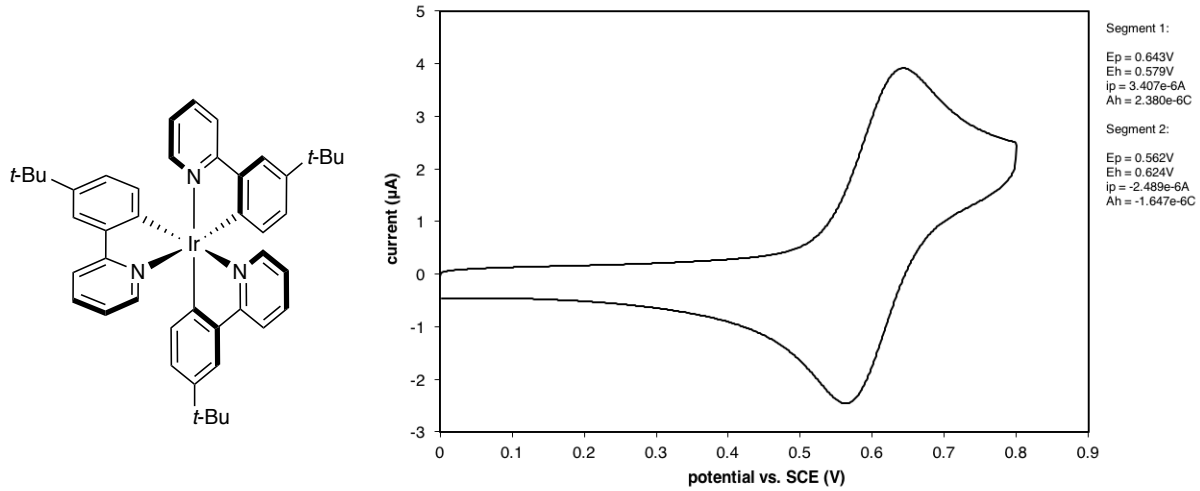
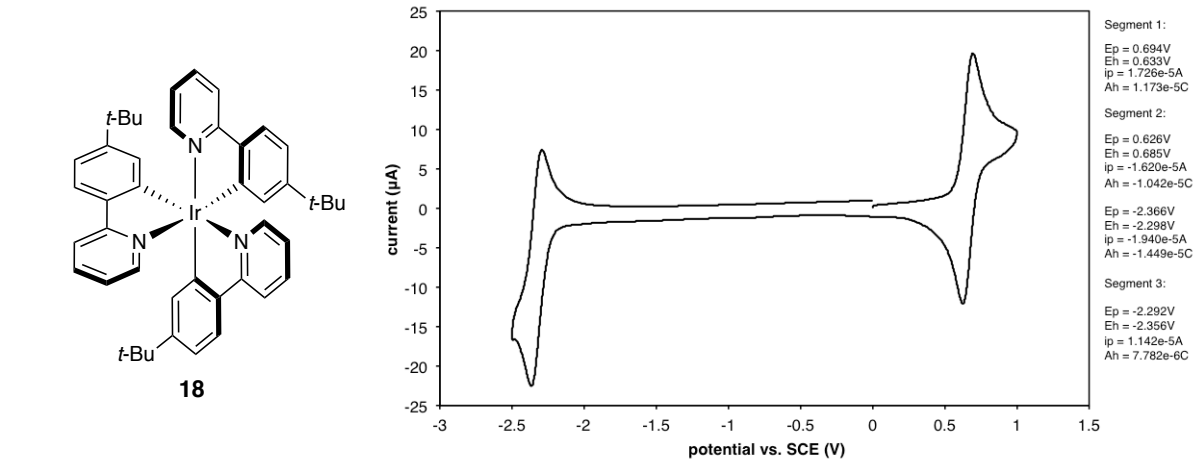


Figure S27. Cyclic voltammogram of Ir[(5′-*t*-Bu)ppy]$_3$ (R^3 = *t*-Bu) in CH_2Cl_2. Scanned from 0 V to +0.8 V to 0 V at 0.1 V/s.



18

Figure S28. Cyclic voltammogram of Ir[(4′-*t*-Bu)ppy]$_3$ (R^4 = *t*-Bu) in acetonitrile. Scanned from 0 V to +1 V to –2.5 V to 0 V at 0.1 V/s.

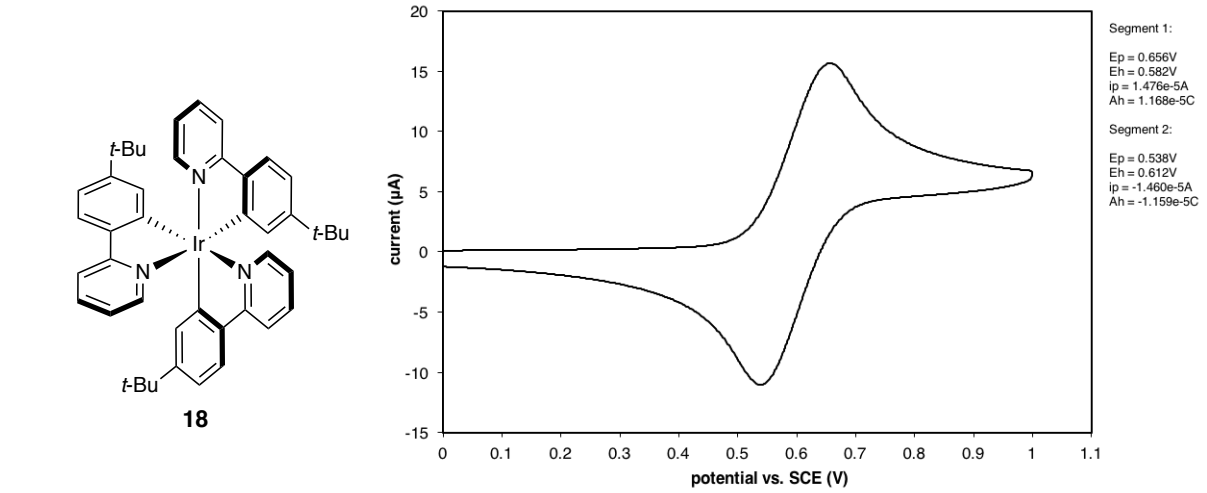


Figure S29. Cyclic voltammogram of Ir[(4′-*t*-Bu)ppy]$_3$ (R^4 = *t*-Bu) in CH_2Cl_2. Scanned from 0 V to +1 V to 0 V at 0.1 V/s.

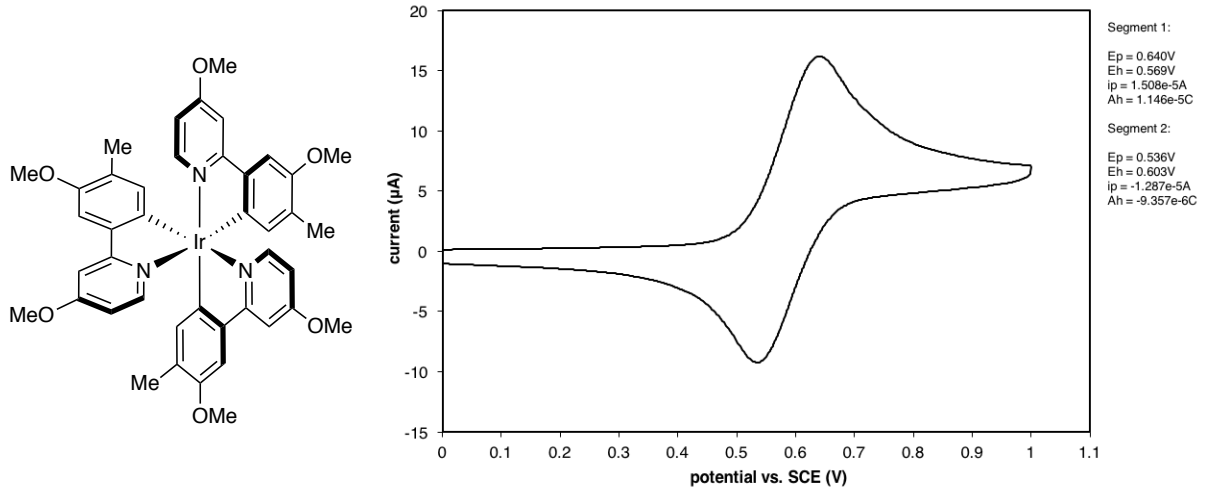


Figure S30. Cyclic voltammogram of Ir[(4-MeO)ppy]$_3$ (R^2 = MeO) in CH_2Cl_2. Scanned from 0 V to +1 V to 0 V at 0.1 V/s.

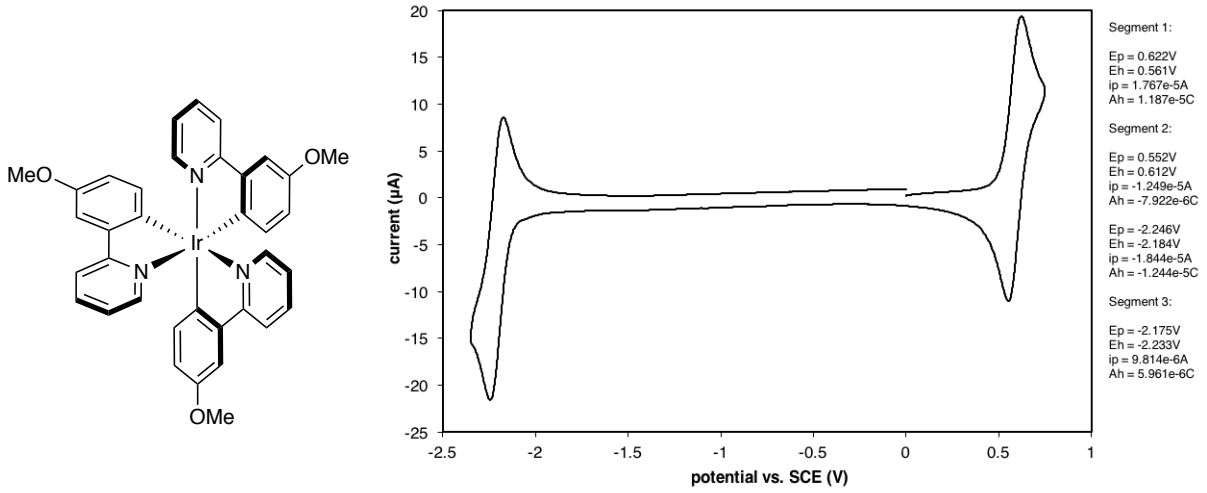


Figure S31. Cyclic voltammogram of Ir[(5′-MeO)ppy]$_3$ (R^3 = MeO) in acetonitrile. Scanned from 0 V to +0.75 V to –2.35 V to 0 V at 0.1 V/s.

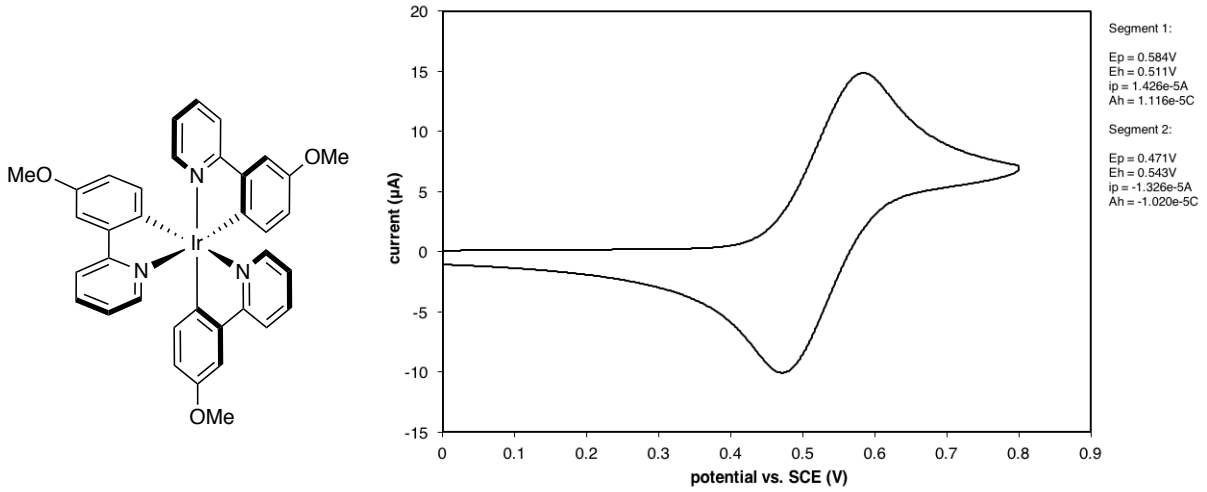


Figure S32. Cyclic voltammogram of Ir[(5′-MeO)ppy]$_3$ (R^3 = MeO) in CH_2Cl_2. Scanned from 0 V to +0.8 V to 0 V at 0.1 V/s.

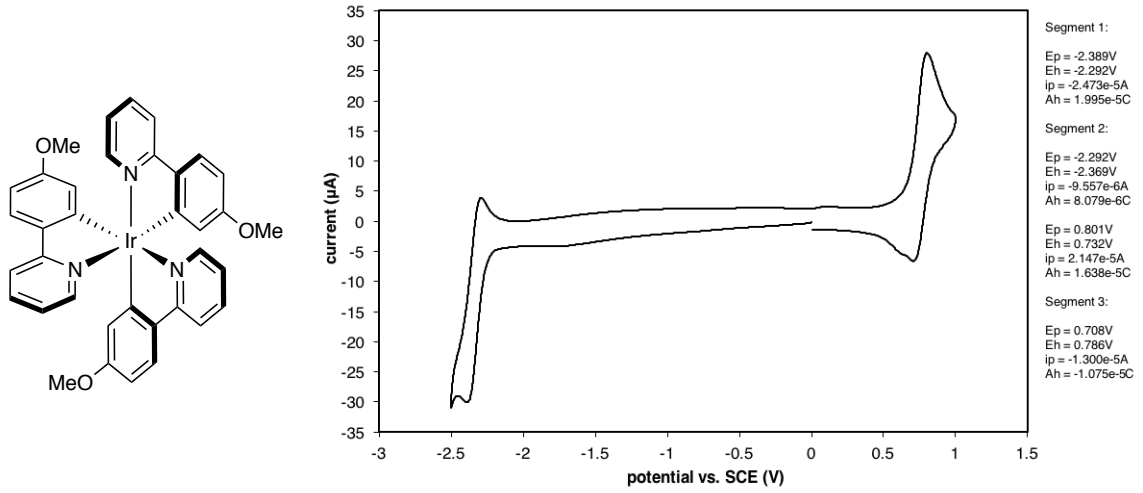


Figure S33. Cyclic voltammogram of Ir[(4′-MeO)ppy]$_3$ (R^4 = MeO) in acetonitrile. Scanned from 0 V to –2.45 V to +1 V to 0 V at 0.1 V/s.

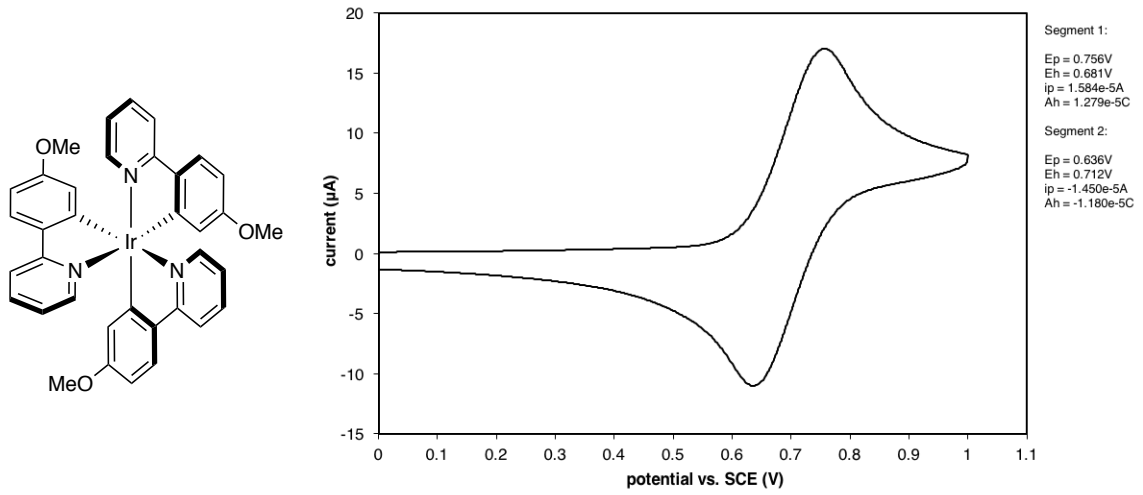


Figure S34. Cyclic voltammogram of Ir[(4′-MeO)ppy]$_3$ (R^4 = MeO) in CH_2Cl_2. Scanned from 0 V to +1 V to 0 V at 0.1 V/s.

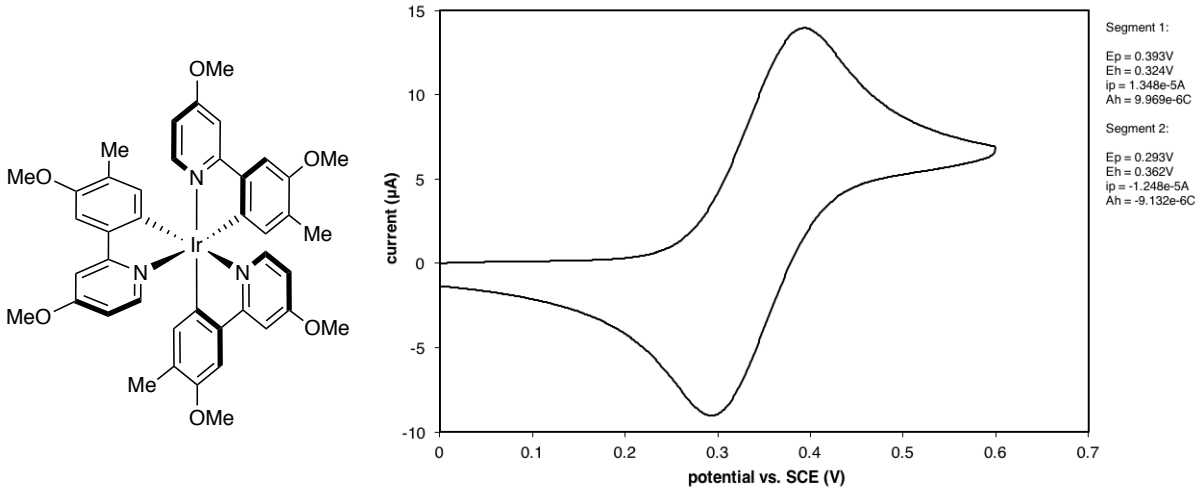
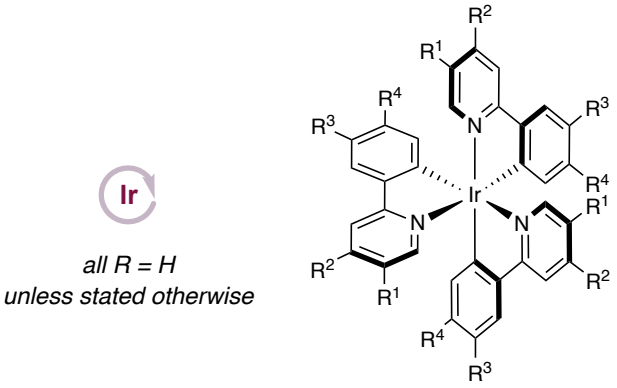


Figure S35. Cyclic voltammogram of Ir[(4,5′-$(MeO)_2$-4′-Me)ppy]$_3$ (R^2, R^3 = MeO, R^4 = Me) in CH_2Cl_2. Scanned from 0 V to +0.6 V to 0 V at 0.1 V/s.

XIII. Comprehensive Summary of Photocatalyst Properties (Figure 3)

Table S10. Complete list of properties of all photocatalysts used in this investigation.



Ir	$E_{1/2}^{red}$ vs. SCE in CH_2Cl_2 (V)		$E_{1/2}^{red}$ vs. SCE in CH_3CN (V)				absorbance & emission (nm)			E^{0-0}
	$Ir^{IV/III}$	$Ir^{IV/*III}$	$Ir^{IV/III}$	$Ir^{IV/*III}$	$Ir^{III/II}$	$Ir^{*III/II}$	λ_{max}^{abs}	λ_{onset}^{em}	λ_{max}^{em}	(eV)
$Ir(ppy)_3$	+0.69	–1.88	+0.77	–1.81	–2.23	+0.35	376	481	516	2.58
R^1 = *t*-Bu	+0.68	–1.89	+0.77	–1.81	–2.30	+0.28	373	481	513	2.58
R^2 = *t*-Bu	+0.64	–1.94	*insoluble*				382	480	509	2.58
R^3 = *t*-Bu	+0.60	–1.92	+0.68	–1.84	–2.26	+0.26	384	492	529	2.52
R^4 = *t*-Bu	+0.60	–1.96	+0.66	–1.90	–2.33	+0.23	382	485	525	2.56
R^2 = MeO	+0.59	–2.00	*insoluble*				381	479	511	2.59
R^3 = MeO	+0.53	–1.87	+0.59	–1.81	–2.21	+0.19	397	517	557	2.40
R^4 = MeO	+0.70	–1.95	+0.76	–1.89	–2.34	+0.26	359	469	504	2.64
R^2, R^3 = MeO, R^4 = Me	+0.34	–2.07	*insoluble*				396	513	549	2.42

To be consistent with much of the electrochemical literature, we attempted to acquire all the data in CH_3CN whenever possible. Three photocatalysts were insoluble in all solvents we evaluated except for CH_2Cl_2, however, necessitating their study in this solvent. Thus, in our attempt to correlate the photocatalysts' performance in the enantioselective α-benzylation reaction with their electrochemical potentials, we also obtained all $Ir^{IV/III}$ data (and estimated the associated excited state potential for $Ir^{IV/*III}$) in this medium to be consistent throughout our analysis, so these data are presented in Figure 3. Solvent reduction occurred in CH_2Cl_2 before an $Ir^{III/II}$ signal was observed, so for these values (and the associated excited state potential for $Ir^{*III/II}$), data in CH_3CN are provided in Figure 3, with no measurements available for the three insoluble photocatalysts.

The $Ir^{IV/III}$ and $Ir^{IV/*III}$ potentials in CH_3CN, obtained where possible but not listed in Figure 3, are also provided in Table S10 for completeness.

The excited state potentials were estimated using the Rehm-Weller equations,[33]

$$E_{ox}^{\circ *} = E_{ox}^{\circ\prime} - E^{0-0}, \text{ and}$$

$$E_{red}^{\circ *} = E_{red}^{\circ\prime} + E^{0-0},$$

where $E^{\circ *}$ is the excited state potential, $E^{\circ\prime}$ is the ground state potential, and E^{0-0} is the energy gap between the zero-level vibrational levels of the ground and excited states. E^{ox} is to the $Ir^{IV/III}$ reduction potential and E^{red} is the $Ir^{III/II}$ potential. E^{0-0} is approximated as the high-energy onset of phosphorescence where the emission intensity is 10% of that observed at the maximum emission wavelength.[34]

XIV. Electrochemical Properties of Substrates (Table 4)

Substrate (0.020 mmol) and tetrabutylammonium hexafluorophosphate (775 mg, 2.0 mmol) were dissolved in acetonitrile (20 mL) in a 25 mL 3-neck flask. The solution was sparged with nitrogen for 10 minutes and studied by cyclic voltammetry.

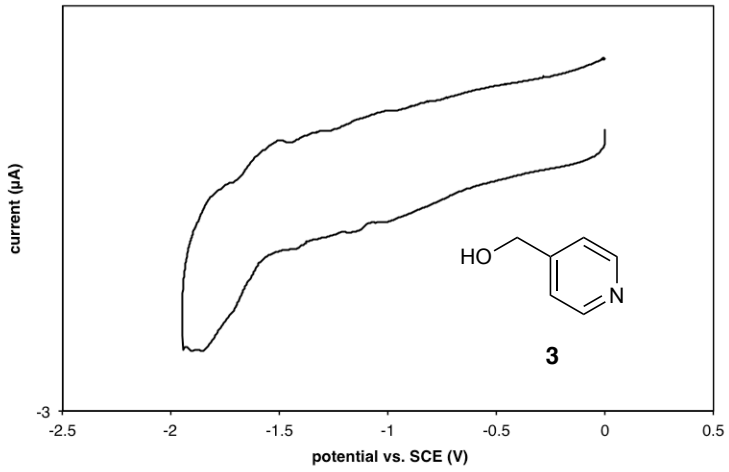


Figure S36. Cyclic voltammogram of 4-(hydroxymethyl)pyridine (**3**). Scanned from 0 V to –2.0 V to 0 V at 0.1 V/s.

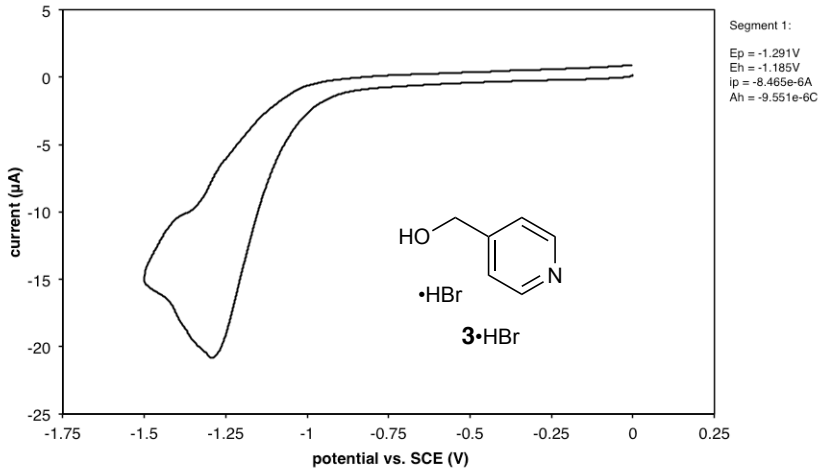


Figure S37. Cyclic voltammogram of 4-(hydroxymethyl)pyridine (**3**)•HBr. Scanned from 0 V to –1.5 V to 0 V at 0.1 V/s.

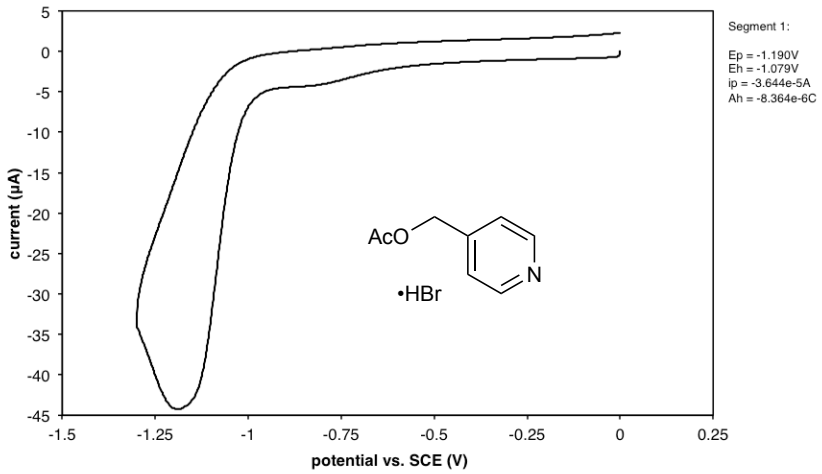


Figure S38. Cyclic voltammogram of 4-(acetoxymethyl)pyridine•HBr. Scanned from 0 V to –1.25 V to 0 V at 0.1 V/s.

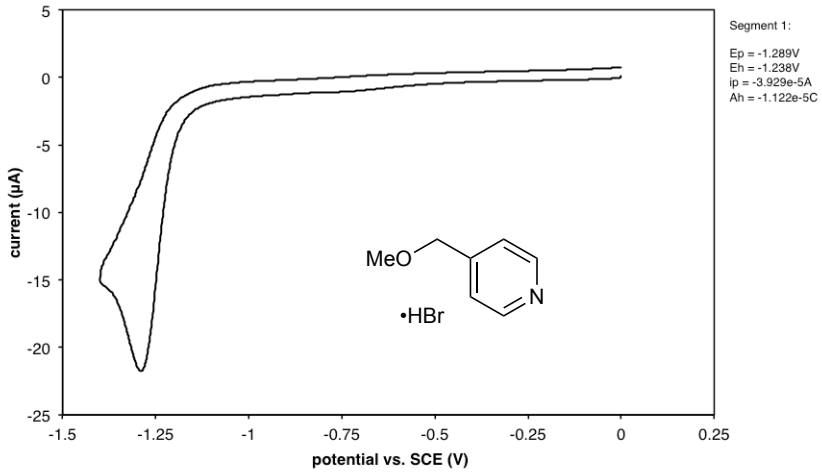


Figure S39. Cyclic voltammogram of 4-(methoxymethyl)pyridine•HBr. Scanned from 0 V to –1.4 V to 0 V at 0.1 V/s.

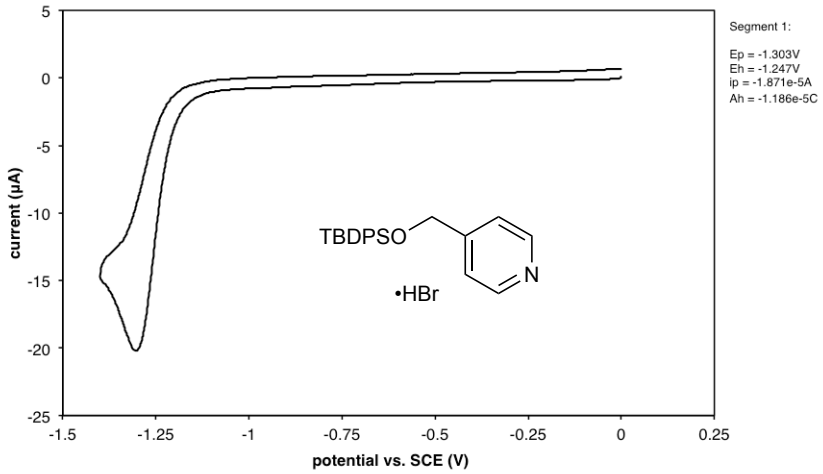


Figure S40. Cyclic voltammogram of 4-(*tert*-butyldimethylsiloxymethyl)pyridine•HBr. Scanned from 0 V to –1.4 V to 0 V at 0.1 V/s.

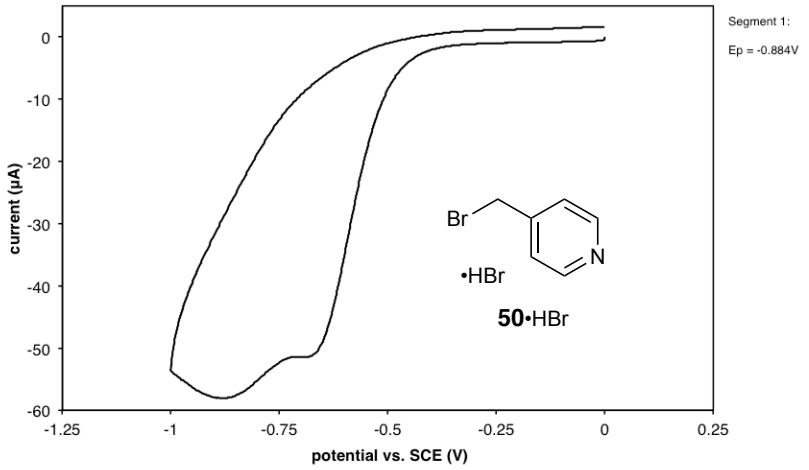


Figure S41. Cyclic voltammogram of 4-(bromomethyl)pyridine (**50**)•HBr. Scanned from 0 V to –1.0 V to 0 V at 0.1 V/s.

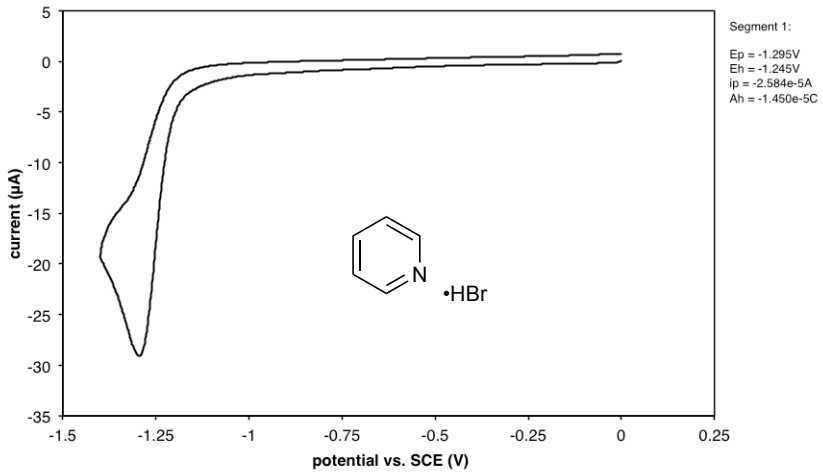


Figure S42. Cyclic voltammogram of pyridine•HBr. Scanned from 0 V to –1.4 V to 0 V at 0.1 V/s.

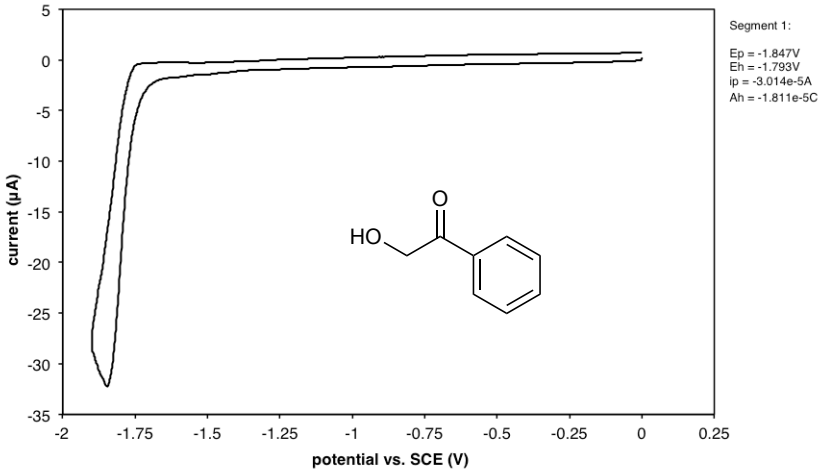


Figure S43. Cyclic voltammogram of α-hydroxyacetophenone. Scanned from 0 V to –1.9 V to 0 V at 0.1 V/s.

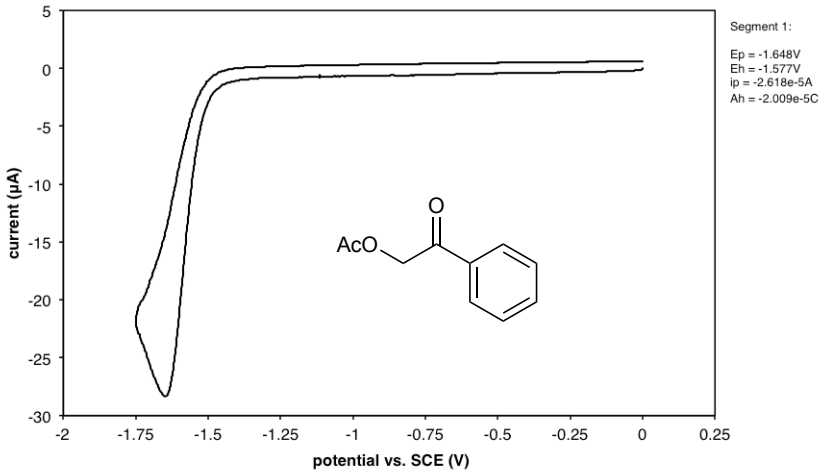


Figure S44. Cyclic voltammogram of α-acetoxyacetophenone. Scanned from 0 V to –1.75 V to 0 V at 0.1 V/s.

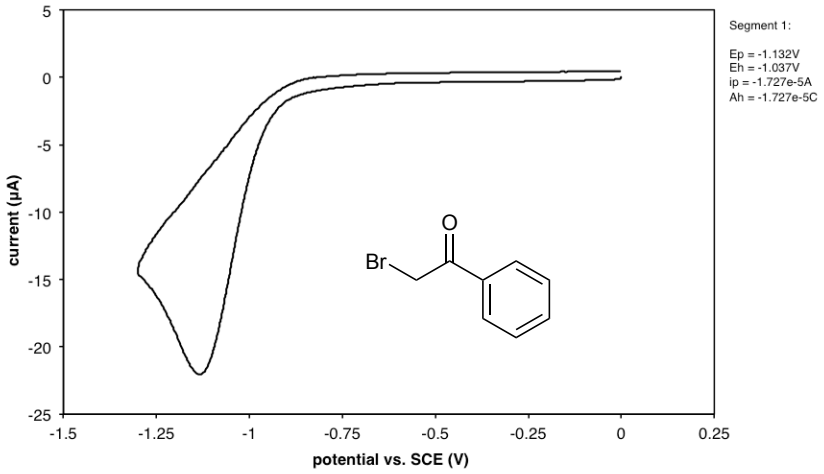


Figure S45. Cyclic voltammogram of α-bromoacetophenone. Scanned from 0 V to –1.3 V to 0 V at 0.1 V/s.

XV. Electrochemical Properties of Catalytically-Generated Enamine (Scheme 2)

Solutions of either octanal (**45**) (31 μL, 0.20 mmol), organocatalyst **8** (22 mg, 0.10 mmol), or of a 2:1 mixture of both octanal (**45**) (31 μL, 0.20 mmol) and organocatalyst **8** (22 mg, 0.10 mmol), each with tetrabutylammonium hexafluorophosphate (775 mg, 2.0 mmol), were prepared in acetonitrile (20 mL) in a 25 mL 3-neck flask under air. The solutions were studied by cyclic voltammetry. Since no signals beyond those corresponding to the oxidation of octanal or the organocatalyst were observed in the mixture, 2,6-lutidine•HOTf (13 mg, 0.10 mmol) was added to each of the three solutions, and they were each analyzed again by cyclic voltammetry. A new signal below +1 V was now observed in the mixture, and was assigned to enamine oxidation.

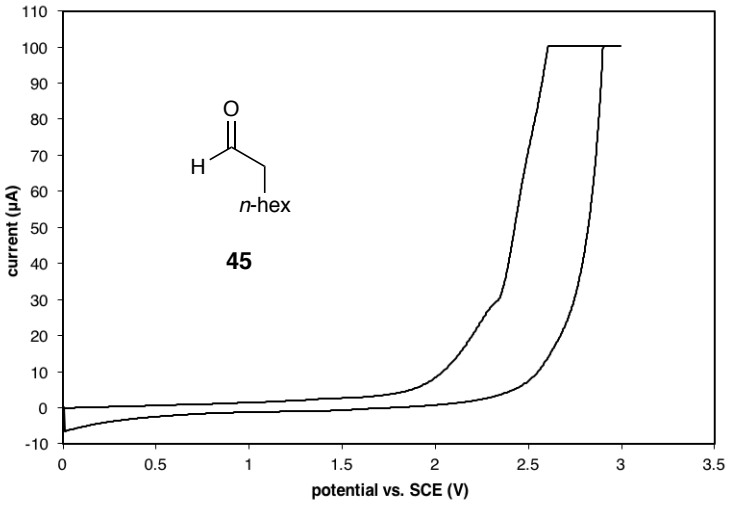


Figure S46. Cyclic voltammogram of octanal (**45**). Scanned from 0 V to +3.0 V to 0 V at 0.1 V/s.

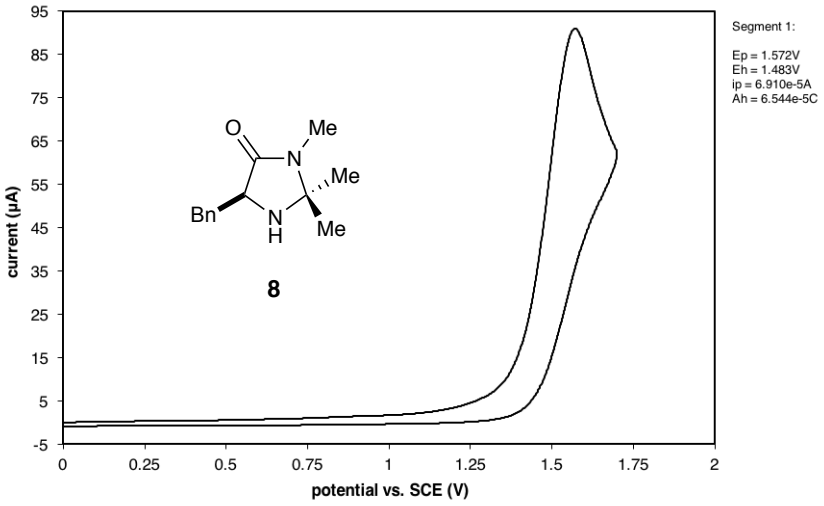


Figure S47. Cyclic voltammogram of organocatalyst **8**. Scanned from 0 V to +1.7 V to 0 V at 0.1 V/s.

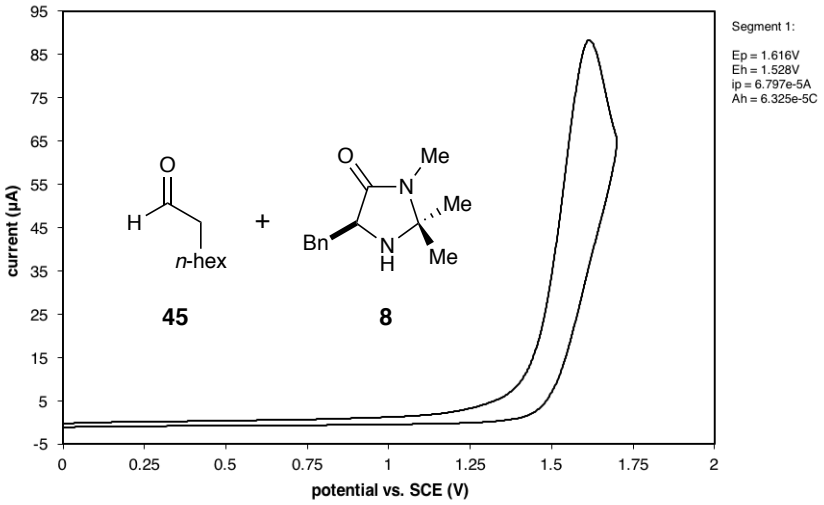


Figure S48. Cyclic voltammogram of a 2:1 mixture of octanal (**45**) and organocatalyst **8**. Scanned from 0 V to +1.7 V to 0 V at 0.1 V/s.

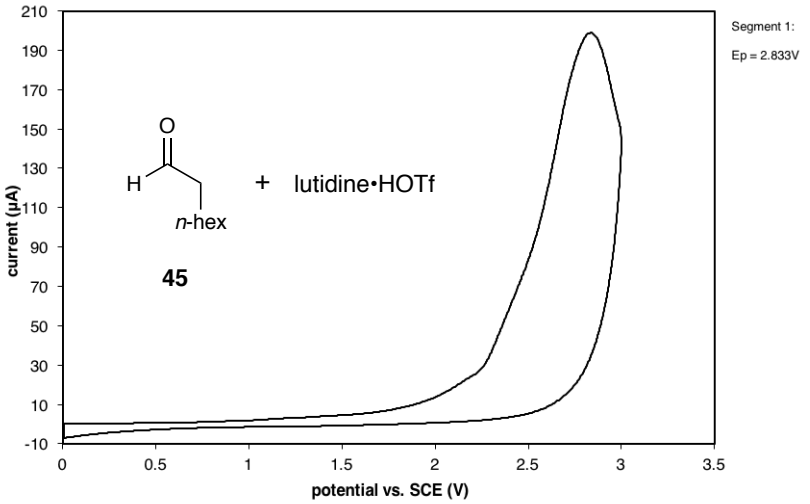


Figure S49. Cyclic voltammogram of a 2:1 mixture of octanal (**45**) and 2,6-lutidine•HOTf. Scanned from 0 V to +3.0 V to 0 V at 0.1 V/s.

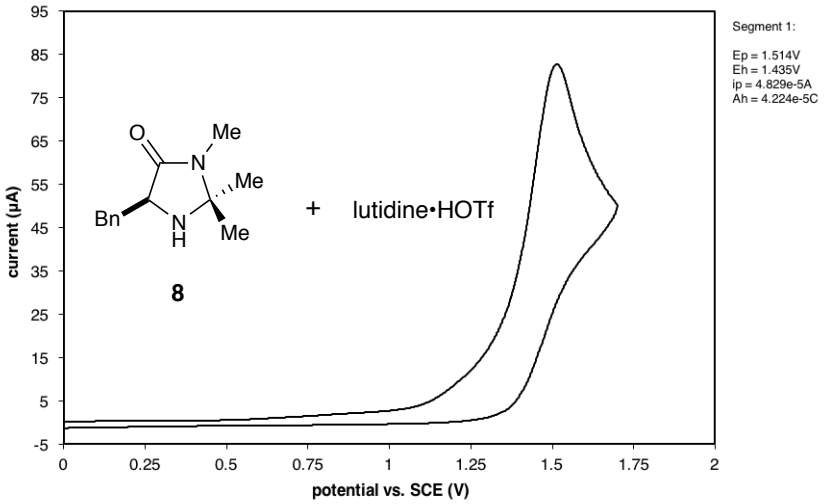


Figure S50. Cyclic voltammogram of a 1:1 mixture of organocatalyst **8** and 2,6-lutidine•HOTf. Scanned from 0 V to +1.7 V to 0 V at 0.1 V/s.

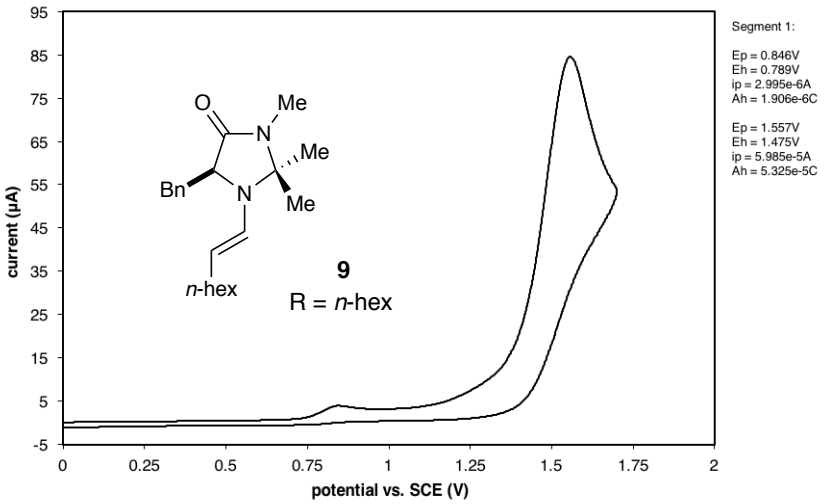


Figure S51. Cyclic voltammogram of a 2:1:1 mixture of octanal (**45**), organocatalyst **8**, and 2,6-lutidine•HOTf, forming enamine **9** (R = *n*-hex) . Scanned from 0 V to +1.7 V to 0 V at 0.1 V/s.

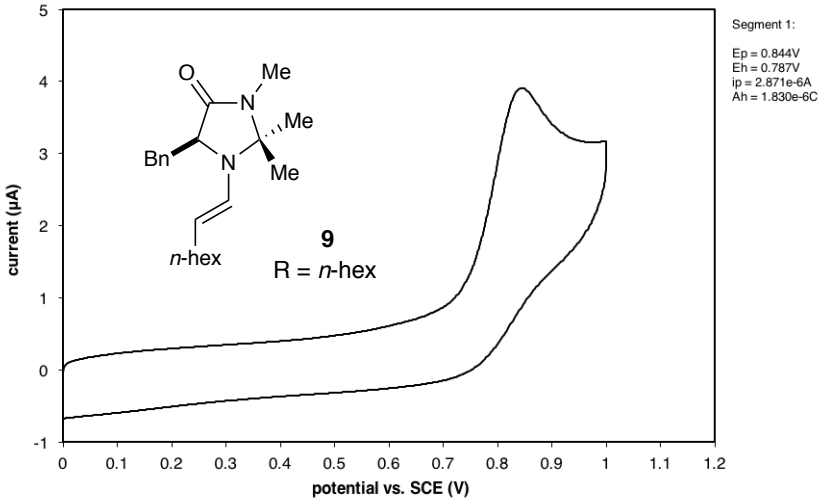


Figure S52. Cyclic voltammogram of a 2:1:1 mixture of octanal (**45**), organocatalyst **8**, and 2,6-lutidine•HOTf, forming enamine **9** (R = *n*-hex) . Scanned from 0 V to +1.0 V to 0 V at 0.1 V/s.

XVI. Stern-Volmer Fluorescence Quenching Studies (Table 4)

Photocatalyst (1.2 μmol) was dissolved in 7.4:1 dimethylacetamide/water (5.0 mL) to prepare a 0.24 mM solution. This solution (0.95 mL) was then diluted to a volume of 46 mL by adding further 7.4:1 dimethylacetamide/water. The resulting 5.0 μM solution (1.6 mL) was added to each of a set of 4 screw-top 1.0 cm quartz cuvettes. A stock solution of quencher (0.25 mmol) in 7.4:1 dimethylacetamide/water (5.0 mL, 50 mM in quencher) was added in increasing amounts (0, 0.40, 0.80, and 1.2 mL) to the cuvettes containing the photocatalyst solution, and the volume for each vessel was adjusted to 3.2 mL by adding the necessary amount of 7.4:1 dimethylacetamide/water (1.6, 1.2, 0.80, and 0.40 mL). The resulting mixtures were sparged with nitrogen for 15 minutes, then irradiated at 380 nm. The fluorescence emission spectra (5 trials per sample) were recorded. The ratio of the maximum fluorescence emission intensities maximum between samples without and with quencher were plotted against the quencher concentration to generate the Stern-Volmer plots below.

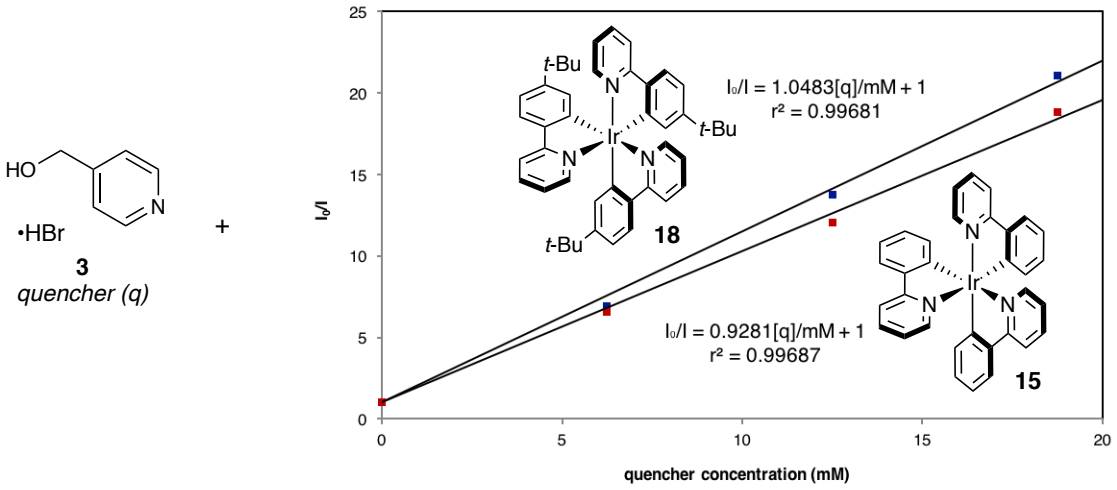


Figure S53. Fluorescence quenching experiments of $Ir(ppy)_3$ (**15**) and $Ir[(4'\text{-}t\text{-}Bu)ppy]_3$ (**18**) in the presence of 4-(hydroxymethyl)pyridine•HBr (**3**).

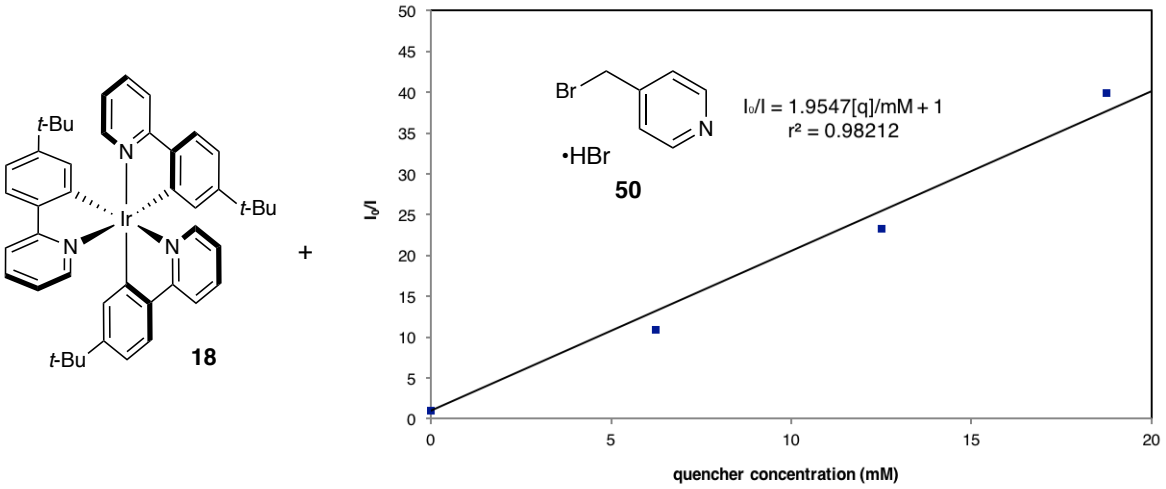


Figure S54. Fluorescence quenching experiments of Ir[(4′-*t*-Bu)ppy]$_3$ (**18**) in the presence of 4-(bromomethyl)pyridine•HBr (**50**).

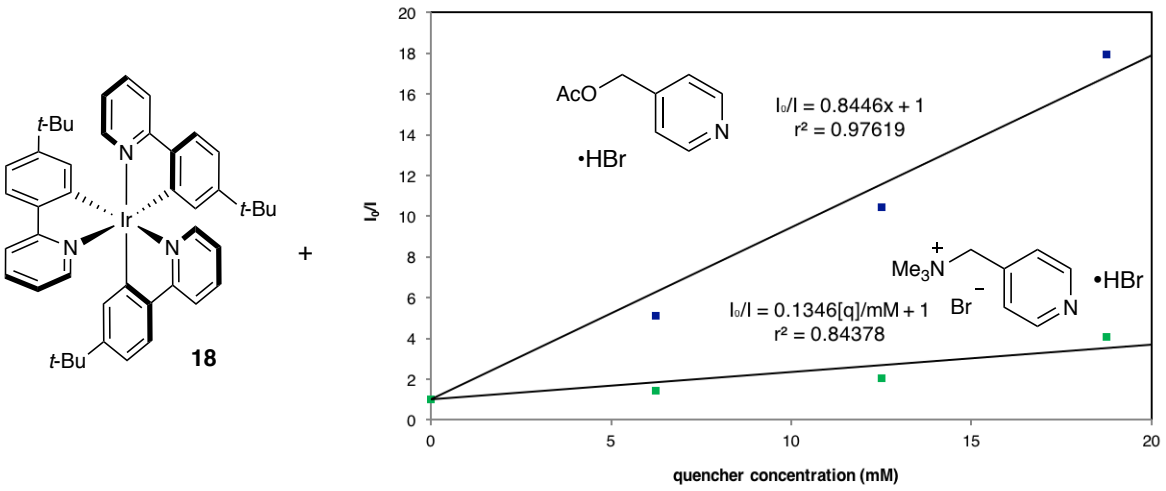


Figure S55. Fluorescence quenching experiments of Ir[(4′-*t*-Bu)ppy]$_3$ (**18**) in the presence of 4-(acetoxymethyl)pyridine•HBr and *N*-(pyridin-4-ylmethyl)-*N*,*N*,*N*-trimethylammonium bromide•HBr.

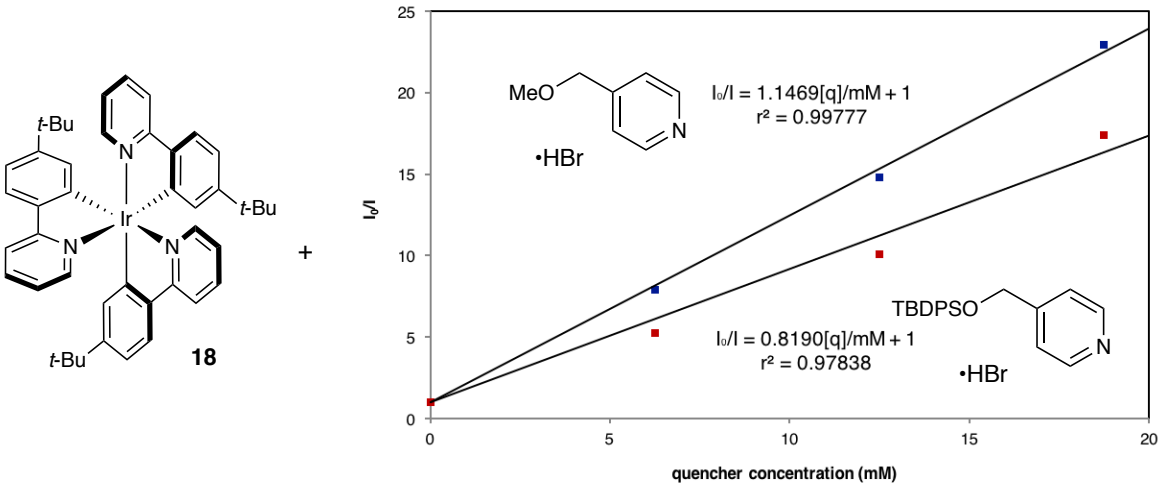


Figure S56. Fluorescence quenching experiments of Ir[(4′-*t*-Bu)ppy]$_3$ (**18**) in the presence of 4-(methoxymethyl)pyridine•HBr and 4-(*tert*-butyldiphenylsiloxymethyl)pyridine•HBr.

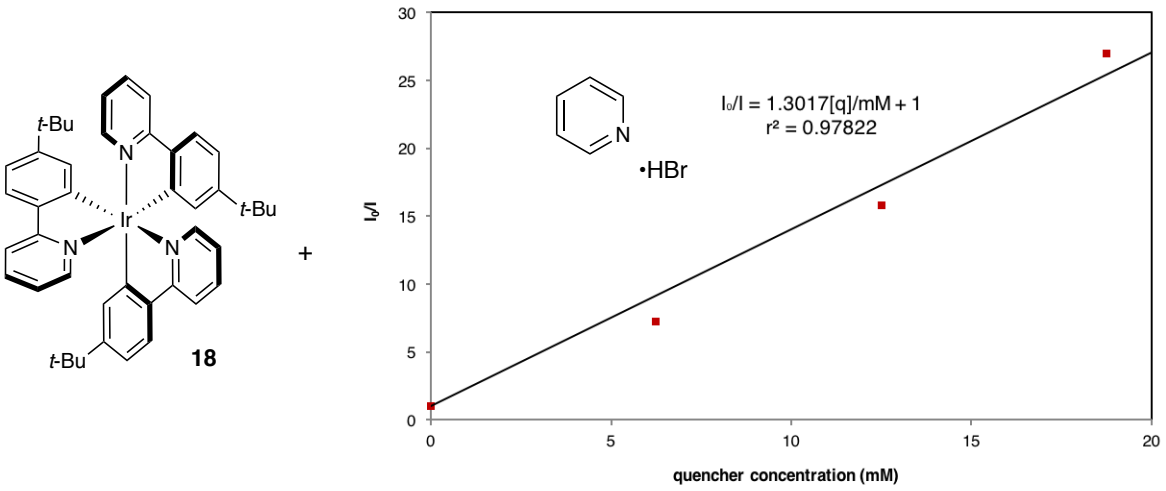


Figure S57. Fluorescence quenching experiments of Ir[(4′-*t*-Bu)ppy]$_3$ (**18**) in the presence of pyridine•HBr.

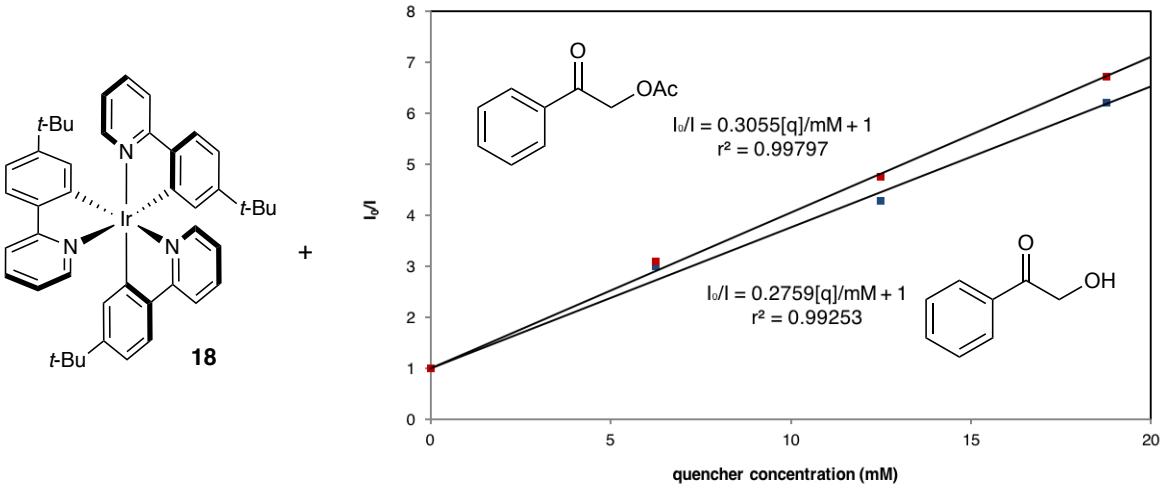


Figure S58. Fluorescence quenching experiments of Ir[(4′-*t*-Bu)ppy]$_3$ (**18**) in the presence of α-hydroxyacetophenone and α-acetoxyacetophenone.

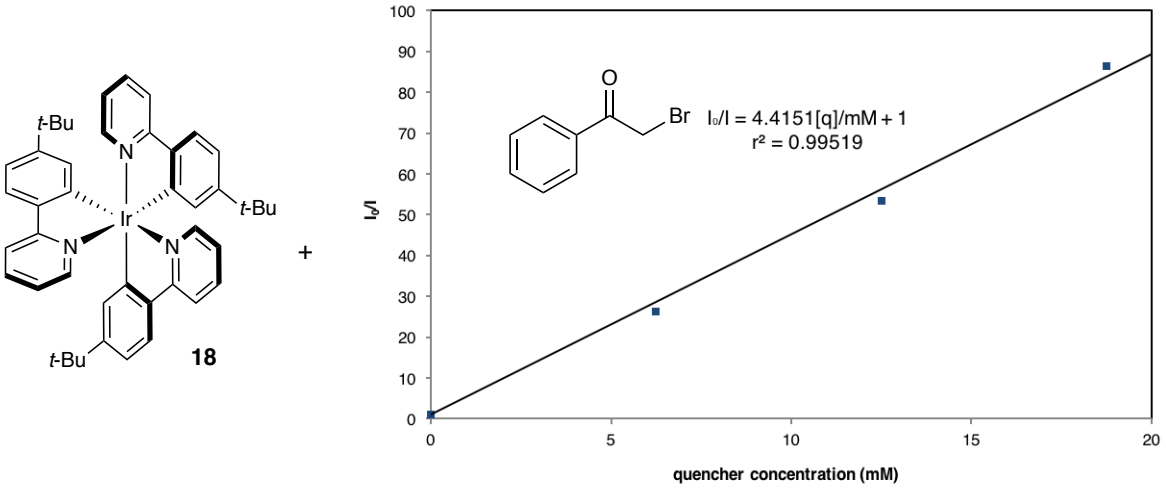


Figure S59. Fluorescence quenching experiments of Ir[(4′-*t*-Bu)ppy]$_3$ (**18**) in the presence of α-bromoacetophenone.

XVII. Quantum Yield Determination (Figure 4)

The procedure recently described by the Knowles group[35] (Princeton University) based on standard chemical actinometry[36] was first followed to determine the photon flux of the apparatus used in these experiments. The actinometry data we obtained is presented below. For the full details of this procedure, the Knowles group's publication which describes a quantum yield measurement should be consulted.[35] The only minor changes we made to their procedure are listed below:

1. While the Knowles group lent us the purple LED apparatus (with an emission band tightly centered around 402 nm) used for their publication, we used a more central position in the beaker to lower the light intensity and conducted all reactions at room temperature (22 °C) by placing a fan above the beaker.
2. Potassium ferrioxalate trihydrate was purchased from Alfa Aesar and used immediately.
3. The phenanthroline developer solution was prepared on 100 mL scale, and for each actinometry experiment, a portion of this solution (3 mL) was added into four 1 cm × 1 cm quartz cuvettes wrapped in aluminum foil under nitrogen, ready for direct injection of aliquots from the irradiated ferrioxalate solution.
4. We conducted four actinometry experiments using the same reaction volume (3 mL), but removed aliquots (10 μL) before irradiation, and then at 3.0 minutes, 6.0 minutes, and 9.0 minutes. These aliquots were each added directly into a cuvette containing the developer solution, and after standing for 30 minutes, the resulting solutions were analyzed by UV-Vis absorption spectrophotometry. The absorbance of the solution at 510 nm was recorded, and the data reported are an average of two measurements, each pair of which differed by no more than 8 mau.

A typical set of UV-Vis absorbance spectra is shown below:

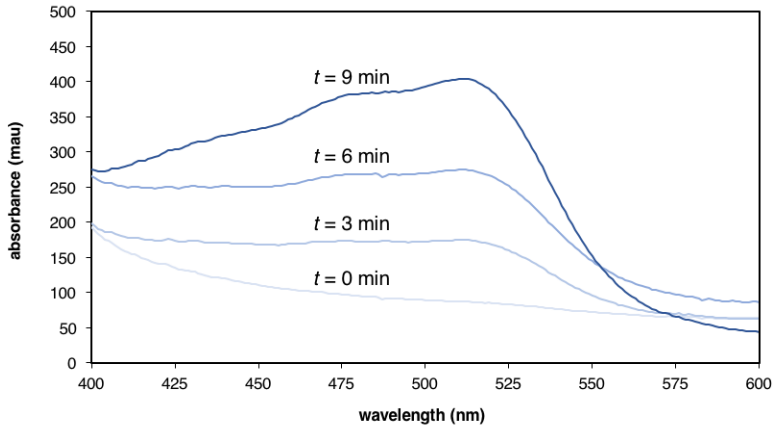


Figure S60. Typical UV-Vis absorption spectra for photon flux determination.

The data obtained in the actinometry experiments to determine photon flux are compiled below:

Table S11. UV-Vis absorbance data for determination of photon flux in quantum yield measurement.

Trial	Value	0 min	3 min	6 min	9 min
1	$A_{510\,nm}$ (au)	0.102141	0.211165	0.314650	0.404435
2	$A_{510\,nm}$ (au)	0.110730	0.203300	0.312480	0.420615
3	$A_{510\,nm}$ (au)	0.0745355	0.172780	0.288780	0.392955
4	$A_{510\,nm}$ (au)	0.0802845	0.161400	0.279550	0.385965
1	ΔA (au)	–	0.109024	0.212509	0.302294
2	ΔA (au)	–	0.092570	0.201750	0.309885
3	ΔA (au)	–	0.0982445	0.2142445	0.3184195
4	ΔA (au)	–	0.0811155	0.1992655	0.3056805
Mean	ΔA (au)	–	0.095	0.207	0.309
St. Dev.	ΔA (au)	–	0.012	0.008	0.007

The linearity of the absorbance data over time is confirmed in the plot below:

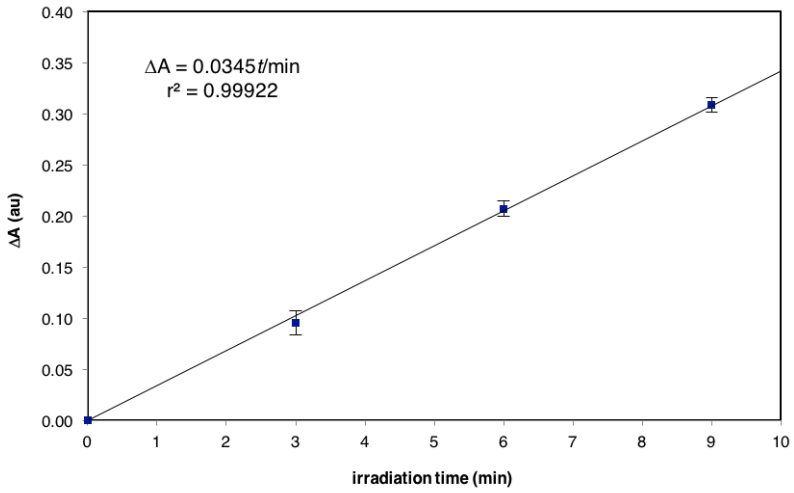


Figure S61. Summary of absorbance data used for photon flux determination.

The photon flux is estimated at each of the three irradiation time points from each of the four actinometry experiments to obtain twelve estimates of the photon flux according to the equation

$$\text{photon flux} = \frac{\Delta A_{510\ \text{nm}} \cdot V_1 \cdot V_3}{\varepsilon_{510\ \text{nm}} \cdot l \cdot \phi_{510\ \text{nm}} \cdot t \cdot F \cdot V_2}$$

where

$\Delta A_{510\ nm}$ = change in absorbance at 510 nm between samples irradiated for t and 0 s

$\varepsilon_{510\ nm}$ = extinction coefficient of the $Fe(phen)_3$ complex at 510 nm (11100 $M^{-1} \cdot cm^{-1}$)

l = path length of the cuvette (1 cm)

$\phi_{405\ nm}$ = quantum yield for ferrioxalate decomposition at 405 nm (1.14)[36]

t = irradiation time

F = fraction of light absorbed by the ferrioxalate solution at 405 nm ($\cong$ 1)[36]

V_1 = volume of the irradiated ferrioxalate solution (3 mL)

V_2 = volume of the aliquot taken from the irradiated solution (10 μL)

V_3 = volume of the developer solution into which the aliquot is injected (3 mL)

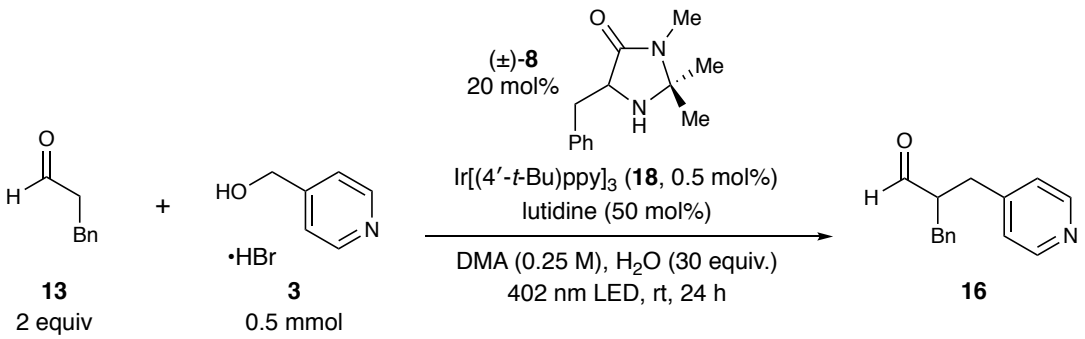
For the twelve measurements, the photon flux at the central position in the LED setup for 3 mL of

solution in a 1 cm × 1 cm cuvette is thus estimated as

$$\text{photon flux} = (4.0 \pm 0.3) \times 10^{-8}\ \text{einstein}\cdot\text{s}^{-1}$$

where the uncertainty is the standard deviation among the twelve individual estimates.

We then performed the model reaction for this study in the 402 nm LED setup using racemic catalyst at room temperature.



After 24 hours, an aliquot of the reaction was analyzed by ^{1}H NMR to determine the yield of the desired aldehyde (much shorter reaction times gave correspondingly lower yields which could not be quantified with desirable precision). This procedure was conducted three times, and yields of 40.9%, 38.6%, and 38.4% were obtained. We measured the absorbance of Ir[(4′-*t*-Bu)ppy]$_3$ (**18**) in 7.4:1 dimethylacetamide/water (1.25 mM) at 402 nm as $A_{402\ nm} = 2.30$, meaning that the photocatalyst in the reaction medium absorbs $F = 1 - 10^{-A} = 99.5\%$ of the incident light. We then estimate the quantum yield of the reaction as

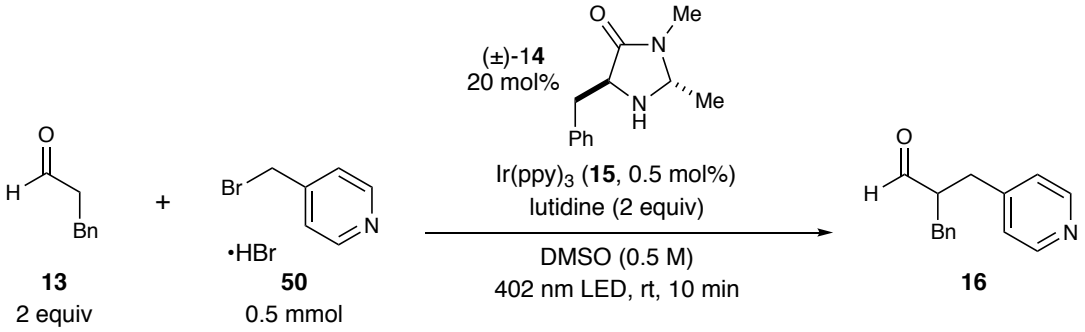
$$\phi = \frac{\text{reaction yield}}{\text{photon flux} \cdot t \cdot \text{F}}$$

Using the three 24 hour yields above, and scaling the photon flux by the ratio of the volumes (and thus surface areas exposed to incident light) of this reaction to that of the actinometry experiments (2.43 mL ÷ 3.00 mL), we estimate that

$$\phi = 7.1 \pm 0.6\ \%$$

where the uncertainty is the quadratic sum of independent contributions of uncertainty from the standard deviation among reaction yields (± 1.4% in reaction yield, which propagates to ± 0.25% in quantum yield) and photon flux (± 0.3 × 10^{-8} einstein·s^{-1}in photon flux, which propagates to ± 0.53% in quantum yield).

Finally, we also performed the corresponding reaction with the benzylic bromide electrophile **50** as described in our group's 2010 publication, again using racemic catalyst at room temperature.



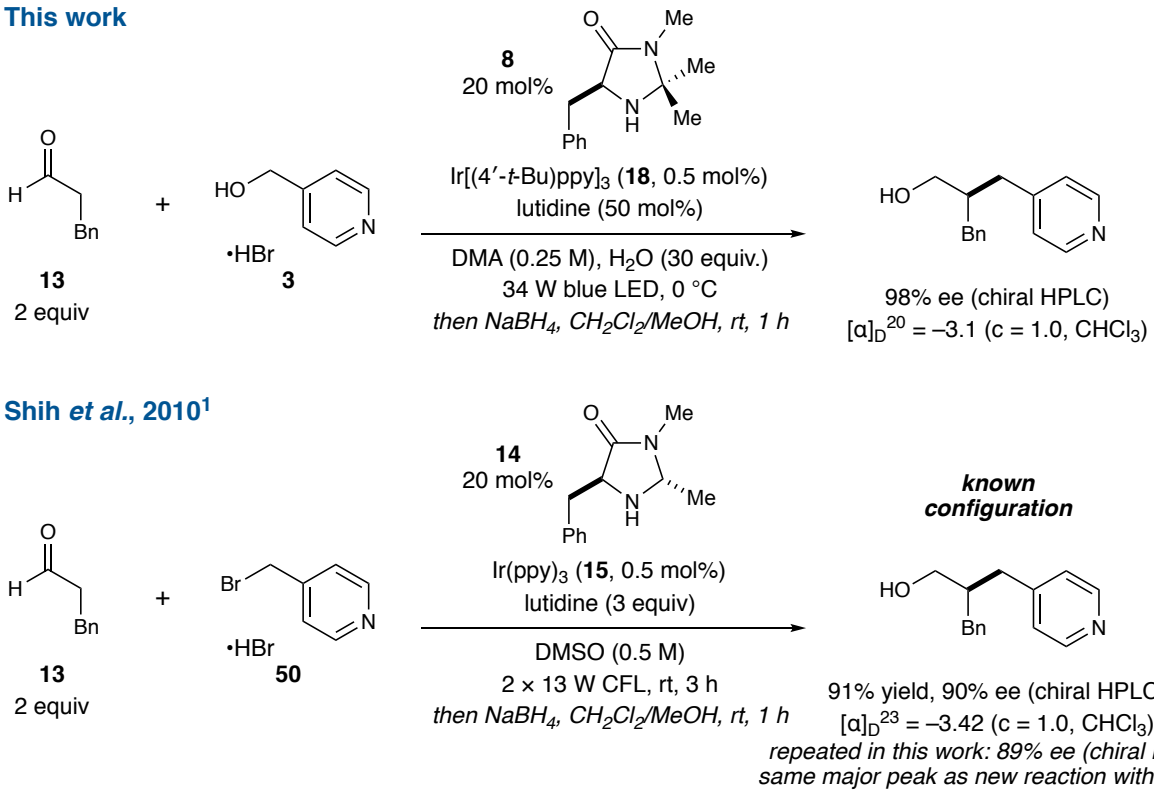
After 10 minutes, an aliquot of the reaction was analyzed by ^{1}H NMR to determine the yield of the desired aldehyde. This procedure was conducted three times, and yields of 24.8%, 27.4%, and 26.6% were obtained. We measured the absorbance of Ir(ppy)$_3$ (**15**) in dimethylsulfoxide (2.5 mM) at 402 nm as $A_{402\ nm}$ = 2.59, meaning that the photocatalyst in the reaction medium absorbs F = 1 – 10^{-A} = 99.7% of the incident light. Again, scaling the photon flux by the ratio of the volumes (and thus surface areas exposed to incident light) of this reaction to that of the actinometry experiments (1.31 mL ÷ 3.00 mL), we estimate the quantum yield of the reaction as

$$\phi = 1260 \pm 110\ \%$$

where the uncertainty is the quadratic sum of independent contributions of uncertainty from the standard deviation among reaction yields (± 1.3% in reaction yield, which propagates to ± 64% in quantum yield) and photon flux (± 0.3 × 10^{-8} einstein·s^{-1}in photon flux, which propagates to ± 95% in quantum yield).

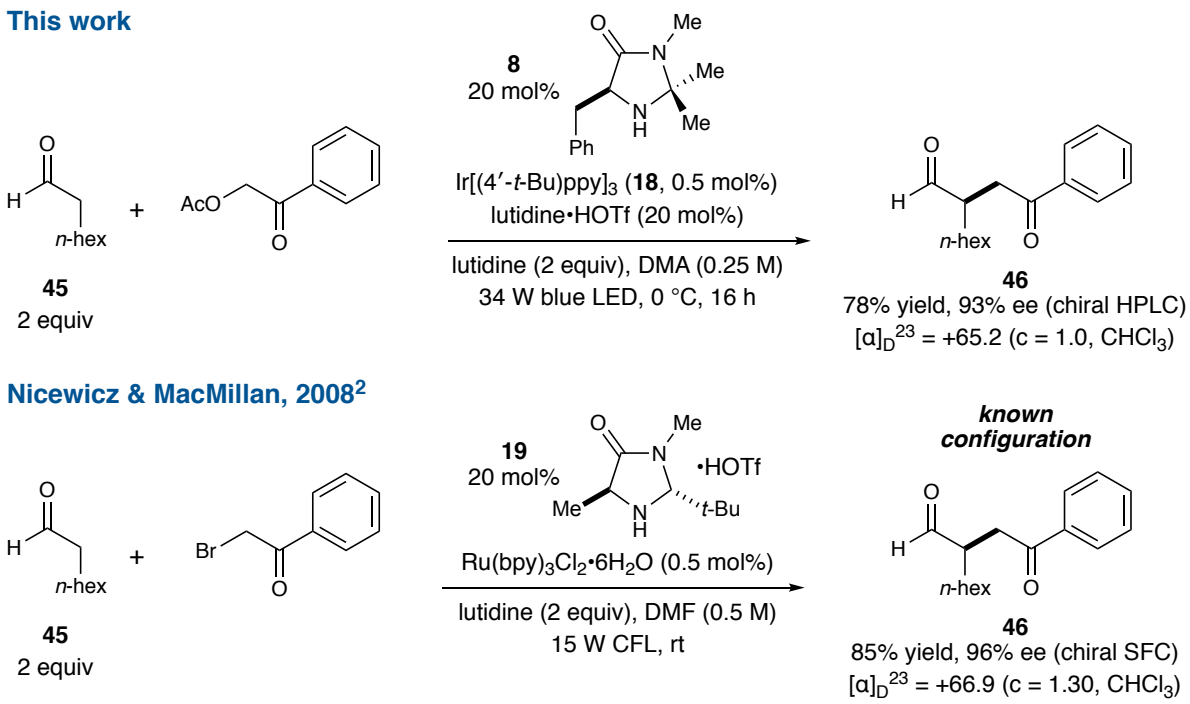
XVIII. Determination of Stereochemical Outcome

A. Benzylation with Alcohol Electrophiles



As described earlier, optimized reaction conditions for the enantioselective α-benzylation of aldehyde **13** with alcohol **3**, followed by reduction of the crude aldehyde, gave the corresponding alcohol in 98% ee as determined by chiral HPLC. The magnitude and direction of its optical rotation were consistent with data for the same compound as reported by our group in 2010,[1] but given its small absolute value, we could not definitively rule out errors in producing this result. Therefore, we repeated the optimized procedure for α-benzylation with benzylic bromides using electrophile **50** as shown.[1] Following reduction, we obtained the alcohol in 89% ee as determined by the same chiral HPLC assay as for the previous experiment. The major and minor enantiomers eluted in the same order in both the new reaction, using alcohol **3**, and the previously developed reaction, using bromide **50**,[1] demonstrating that both procedures preferentially give the same enantiomer. Other benzylation products were assigned by analogy.

B. Alkylation with Acetate Electrophiles

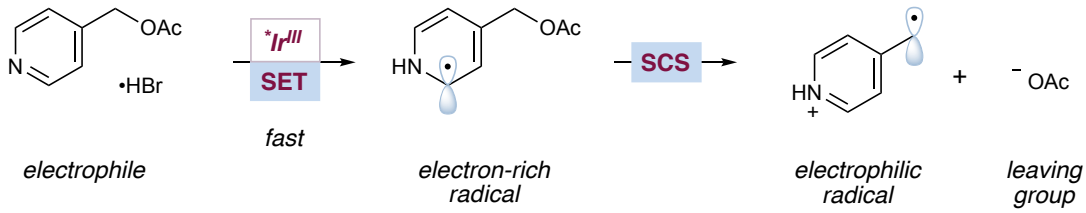


As described earlier, optimized reaction conditions for the enantioselective α-alkylation of aldehyde **45** with α-acetoxyacetophenone gave the alkylated aldehyde in 93% ee as determined by chiral HPLC. The magnitude and direction of its optical rotation were consistent with data for the same compound as reported by our group in 2008,[2] and given its appreciable absolute value, we concluded that both procedures preferentially give the same enantiomer. Other alkylation products were assigned by analogy.

XIX. Further Discussion of Table 4

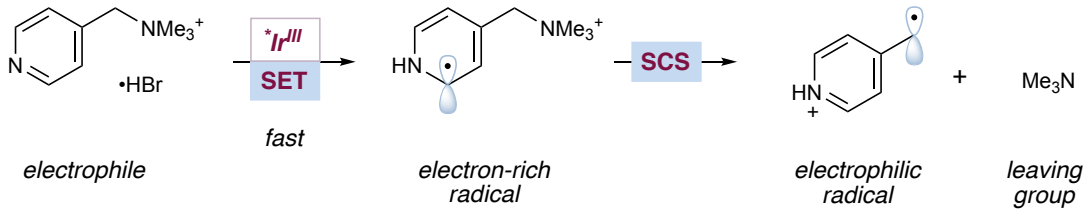
A. Weakly Basic Leaving Groups

Relevant elementary steps for entry 1 (X = OAc)

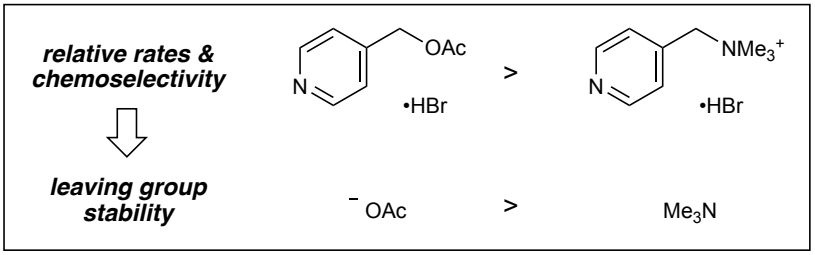


feasible: pK_a (AcOH) = 4.76

Relevant elementary steps for entry 2 (X = $NMe_3^+Br^-$)

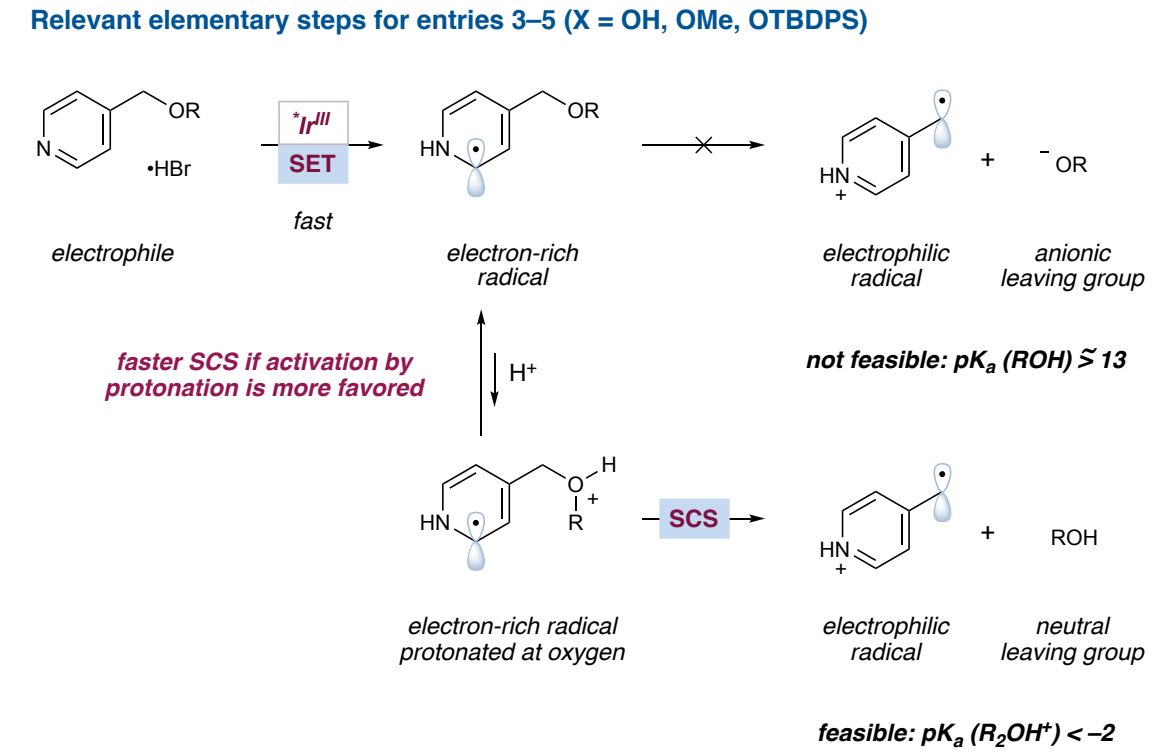


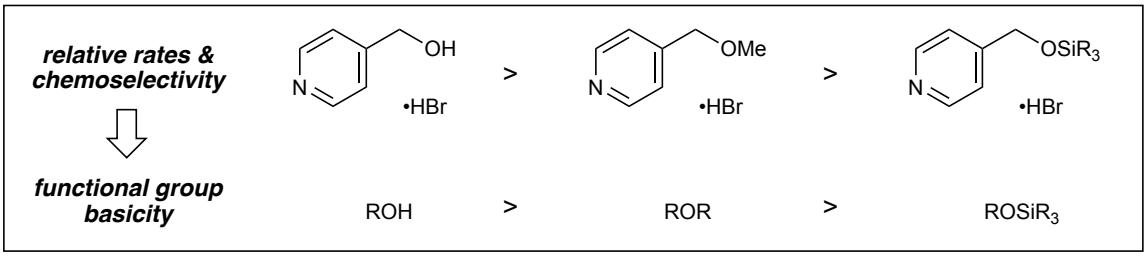
feasible: pK_a (Me_3NH^+) = 9.80



As discussed in the manuscript, the electrophiles in Table 4 with weakly basic leaving groups (entries 1–2, X = OAc, NMe_3^+) react fastest and with the highest chemoselectivities. After reduction of the pyridinium ring by the excited state $^*Ir^{III}$ photocatalyst, SCS can occur directly, with C–**X** bond scission expelling either an AcO^- anion of a neutral Me_3N molecule that are stable in the pyridine/pyridinium-type buffer of the reaction. Within this first class, the acetate substrate reacts more rapidly than the ammonium substrate because the acidities of the parent acids of the respective leaving groups (AcOH, pK_a = 4.76;[37] Me_3NH^+, pK_a = 9.80[38] in H_2O) dictate that the acetate leaving group is more stable as its conjugate base than Me_3N.

B. Strongly Basic Leaving Groups





example parent acid	$MeOH_2^+$	Me_2OH^+	$Me_3SiO(Et)H^+$ or $Ph_3SiO(Et)H^+$
pK_a	–2.5	–3.8	nd but less than Et_2OH^+

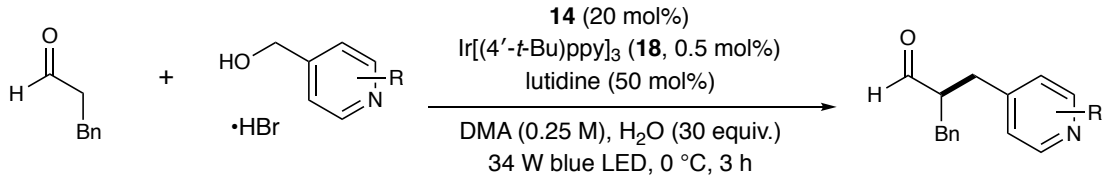
For the slower and less chemoselective electrophiles (entries 3–5, X = OH, OMe, OTBDPS), the leaving group cannot be expelled by SCS directly following reduction of the pyridinium ring because the anions are too basic to exist in the reaction medium (for the parent acids, H_2O, pK_a = 15.7;[39] MeOH, pK_a = 15.2;[39] data not available for Ph_2t-BuSiOH but for Et_3SiOH, pK_a = 13.6[40] in H_2O). We propose, therefore, that the leaving groups must become protonated to some extent prior to SCS. Within this class, reactivity (X = OH > X = OMe > X = OTBDPS) trends with the basicity of the functional group which must be protonated prior to SCS (treating the (4-pyridyl)methyl

radical fragment as an alkyl group, the basicity trend of the relevant neutral entities is ROH > ROR′ > ROSiR′$_3$, as acidity data for representative parent acids follows the order $MeOH_2^+$, pK_a = –2.5[41] > Me_2OH^+, pK_a = –3.8[41] > protonated silyl alkyl ether in H_2O, the latter relationship generalized from the observation that Me_3SiOEt and Ph_3SiOEt both weaken the O–H bond in phenol to a lesser extent than does Et_2O[42]). This correlation between reactivity and basicity suggests that in these cases, a greater degree of activation immediately preceding SCS accelerates the overall reaction. It also explains why in contrast to the weakly basic leaving groups (which are increasingly reactive as the leaving group becomes less basic), the opposite is true for this class of strongly basic leaving groups. Here, greater basicity improves reactivity, and although this basicity relates to the parent acids of the *alkylated* leaving group (i.e., prior to SCS) instead of the parent acid of the leaving group itself, pK_a values often follow the same trend for analogues of these two groups (meaning that as R varies, the basicities of RO–alkyl, represented by the pK_a values of H(R)O–alkyl$^+$, often follow the same order as the basicities of RO^-, represented by the pK_a values of ROH, since greater stabilization of oxonium cations and increasing basicity in the former case usually involves similar stereoelectronic effects as the destabilization of alkoxide anions and increasing basicity in the latter case, even though these chemical properties are distinct).

To illustrate this generalization, the methyl ether substrate reacts more rapidly than the TBDPS ether substrate. Although MeO^- is more basic than $TBDPSO^-$ (which, in the first class of leaving groups, would be expected to lead to lower reactivity for the methyl ether), the (4-pyridyl)methyl methyl ether that must become protonated to enable the SCS event and ultimately expel MeOH is more basic, and thus more activated towards the desired reaction, than the corresponding (4-pyridyl)methyl TBDPS ether that must become protonated before expelling TBDPSOH. Furthermore, while the relevant comparison in this case is that the neutral molecule ROMe (R = (4-pyridyl)methyl) is more basic than ROTBDPS, similar stereoelectronic effects also explain why MeO^- is more basic than $TBDPSO^-$. Table 4 only presents acidity data relating to the anions to simplify comparisons among all electrophiles examined, but for completeness in discussing the strongly basic leaving groups, this section provides data for the relevant neutral intermediates and their cationic parent acids.

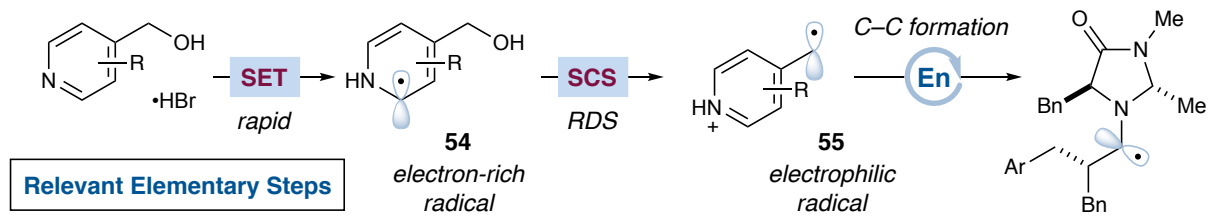
XX. Effect of Alcohol Electrophile Aromatic Structure on Reactivity

Table S12. Impact of substitution of the 4-(hydroxymethyl)pyridine electrophile on reactivity.



Structural Change	Product Structure	Effects on Intermediates
parent 4-pyridyl motif	84% NMR yield (100% conversion of alcohol)	–
2- or 3-methyl	79% NMR yield (100% conversion of alcohol); 80% NMR yield (100% conversion of alcohol)	**54**: slightly more electron-rich **55**: more hindered (for 3-Me) and slightly less electrophilic
3-methoxy	55% NMR yield (92% conversion of alcohol)	**54**: slightly more conjugated but more π-electron density **55**: slightly less electrophilic and more hindered
(4-quinolyl) or 2-phenyl	49% NMR yield (78% conversion of alcohol); 46% NMR yield (64% conversion of alcohol)	**54**: stabilized by extended conjugation **55**: minimal (slighly more hindered for quinoline)
3-halo (F or Cl)	31% NMR yield (50% conversion of alcohol); 34% NMR yield (53% conversion of alcohol)	**54**: less electron-rich **55**: more electrophilic

Decreasing Reactivity



As described in the manuscript, the elementary steps shown in Scheme 1 constitute a plausible mechanism. Consistent with the data in Table 4, single-electron reduction of the electrophile by the excited state $^{*}Ir^{III}$ photocatalyst is rapid. Considering the simplified linear reaction between the resulting electron-rich radical (e.g., **4** or **54**) and enamine **9**, either SCS or C–C bond formation then likely represent the rate-determining step (RDS). The kinetics of the organocatalytic cycle can clearly also impact the rate of the overall dual catalytic process. Since this section does not vary the structure or loading of either organocatalyst or the aldehyde, it does not effectively evaluate the impact of the organocatalytic cycle (this portion of the mechanism is considered in the following section). Nonetheless, we find it instructive to evaluate whether SCS or C–C bond formation is slower both in explaining the results obtained in this manuscript and potentially in the design of new reactions based on SCS.

Further discussion of Table 4 within the manuscript and the preceding section of the SI describe the precise impact of the leaving group structure in a series of (4-pyridyl)methyl electrophiles on reactivity. While this relationship is consistent with SCS as the RDS of the simplified linear reaction between the electrophile and enamine, it does not address the possibility that C–C bond formation is the RDS since all of these electrophiles would involve the same transition state in this elementary step.

To deconvolute the potential impacts of SCS and C–C bond formation on the overall rate of reaction, a preliminary set of data showing the impact of substituents about the heteroaromatic core of the 4-(hydroxymethyl)pyridine electrophile on reactivity is shown in Table S12. The only deviation from optimal reaction conditions (General Procedure A) are the use of organocatalyst **14** instead of **8** (the primary difference is that **14** is less stereoselective and slightly faster, though product enantiopurity was not obtained for these experiments) and that conversion data was recorded after 3 hours on 0.1 mmol scale in order to obtain a concise set of data that reflect the relative reactivities of these electrophiles.

First, the model reaction between hydrocinnamaldehyde and 4-(hydroxymethyl)pyridine was complete within 3 hours and provided the corresponding α-benzyl aldehyde in 84% yield (determined by ^{1}H NMR). A series of 7 further electrophiles featuring 4 general types of structural

changes from the parent compound are then sorted by decreasing reactivity. The expected effects of these structural variations on intermediates **54** and **55** (Table S12, bottom) are also summarized.

Overall, the parent 4-(hydroxymethyl)pyridine electrophile reacts at a comparable rate to its 2- and 3-methyl analogues. The 3-methoxy derivative is slightly slower and somewhat lower-yielding, followed by the 4-(hydroxymethyl)quinoline and 2-phenyl variants, and finally the 3-halogenated structures.

If SCS were the RDS, we would expect the stability of **54** to dictate overall reaction rate, with destabilization leading to rate acceleration and vice versa. The minimal impact of alkyl substitution at the 2- or the 3-positions on reactivity is consistent with this scenario. We would expect these structural changes to make **54** only slightly more electron-rich, as alkyl groups are primarily electron-donating by inductive effects, whereas the reactive unpaired electron involved in the SCS event is located in the π-system. The 3-methoxy substituent extends the conjugation of the electron-rich π-system, although we would expect the electron-donating character of this group to destabilize **54**, meaning this less reactive electrophile is not perfectly consistent with SCS as the RDS. The expansion of the electrophile's aromatic system to a quinoline motif or by 2-phenyl substitution, however, provides more convincing evidence that SCS is rate-limiting, since these changes should significantly stabilize **54** by extending π-conjugation. Indeed, these reactions are unambiguously slower compared to the parent electrophile. Finally, the 3-fluoro and 3-chloro substituents do not offer much additional π-conjugation to **54**, but they are expected to significantly stabilize the lone pair of electrons formally located on the pyridine nitrogen atom. This effect should slow SCS, and, consistent with this event as the RDS, also slow the reaction. We assume throughout these cases that the potential impact of these substituents on the basicity of the alcohol following single-electron reduction but prior to SCS (which could also affect reactivity, as shown in the preceding section of the SI) is minimized by the saturated methylene unit between the aromatic system and the alcoholic oxygen atom.

If C–C bond formation were the RDS, the effects of structural changes to **55** should dictate changes in reactivity. Alkyl substitution should not greatly affect the electrophilicity of **55** from an electronic standpoint since methyl groups should not significantly impact the electron-deficient

benzylic radical conjugated to the π-system. The 3-methyl analogue, however, is the most hindered electrophile in Table S12. If steric interactions were important for the reaction rate, a scenario only likely if C–C bond formation is rate-determining, this derivative would be the most impacted by such an effect. No diminution in rate is observed, however. We also would expect a slight decrease in the electrophilicity of **55** when a 3-methoxy substituent is incorporated both on electronic and steric grounds, and a modest decrease in reactivity is observed. As for the discussion of **54**, however, the quinoline-derived electrophile and the 2-phenyl, 3-fluoro, and 3-chloro derivatives provide the most definitive evidence. While all of these substituents (except for 2-phenyl) should modestly increase the steric demand of **55**, we know from the minimal impact of the 3-methyl group that steric effects do not significantly affect the overall reaction rate. Their electronic effects should be more greatly pronounced. Simple extensions of π-conjugation are typically approximated as electron-withdrawing, although they could also assist in stabilizing highly electron-deficient benzylic radicals. The 3-halogen substituted derivatives are the most notable cases, however, since we would expect these versions of **55** to be the most electrophilic from an electronic standpoint. Since they represent the most sluggish examples, it is unlikely that C–C bond formation is the RDS.

On balance, these data are more consistent with SCS being slower than C–C bond formation. Most importantly, (1) the extended conjugated π-systems in the 2-phenyl substituted and quinoline-based electrophiles lead to slower reactions, which is best explained by their stabilization of **54**, which should slow SCS (but would likely impact electrophilicity of **55** more modestly), and (2) the 3-fluoro and 3-chloro electrophiles react much more slowly, which is best explained by electronic stabilization of **54** and a correspondingly slower SCS, whereas the expected effect on C–C bond formation would be acceleration due to increased electrophilicity of **55**.

XXI. Preliminary Kinetic Studies to Evaluate Organocatalytic Cycle

A series of model reactions was performed in a manner analogous to the optimization experiments described in Section III (preparing a stock solution for materials needed in all experiments, then adding the variable component to each vial as needed). They were conducted on 0.25 mmol scale of limiting reagent (**3•HBr**) under optimized conditions (see Section IV), except for the indicated changes. Reaction progress was monitored by removing aliquots at the indicated times and analyzed by ^{1}H NMR.

As discussed in the manuscript, the data shown in Figure 4 and the alcohol structure-activity relationship described in the preceding section of the SI suggest that in the linear reaction between the electrophile and enamine (i.e., neglecting the organocatalytic cycle, which is essentially unchanged across these above-mentioned experiments), spin-center shift is the rate-determining step. Kinetic experiments in this section are consistent with this hypothesis, as initial rates (Figure S62) are independent of the concentrations of enamine components (aldehyde and organocatalyst). Beyond this short initial window (5–10% conversion), however, reaction rate increases with higher aldehyde and enamine concentrations. This dependence does not appear in the initial rates since an equilibrium amount (~ 5 mol%, see Figure S65) of enamine **9** is pre-formed under our procedure before irradiation (Figure S64 demonstrates this effect), and a photoredox-mediated, SCS-limited reaction between the electrophile and this initially available quantity of enamine is observed. After this period, the kinetics of the organocatalytic cycle become observable, as the enamine must be replenished from its aldehyde and imidazolidinone components and, ultimately, the organocatalyst must be turned over by hydrolysis of the product iminium ion. Experiments in this section also suggest that hydrolysis of the product iminium ion is turnover-limiting (Figures S63 and S65). Each of these experiments is discussed in further detail below.

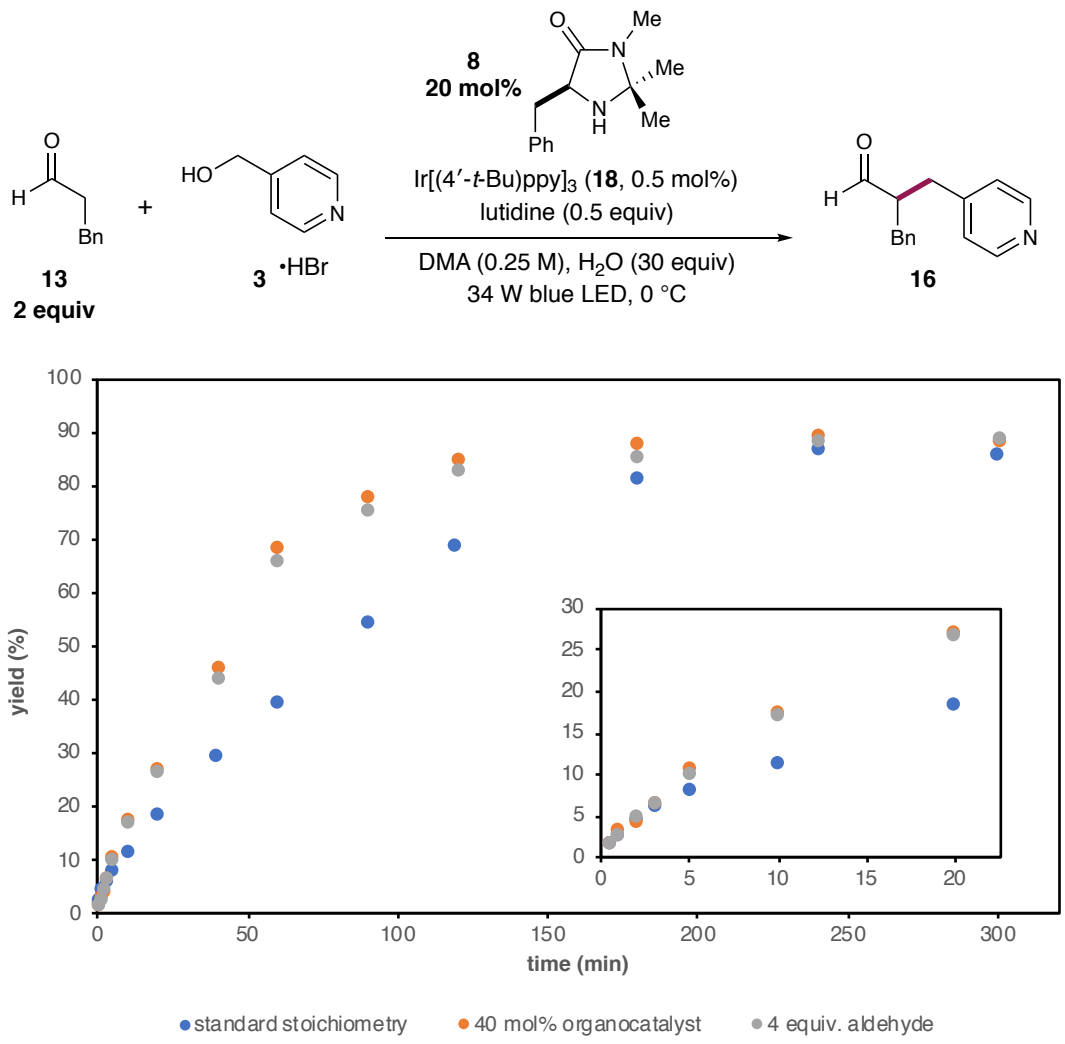


Figure S62. Effect of aldehyde and organocatalyst stoichiometry on reaction profile.

Figure S62 demonstrates that (a) initial rates are independent of enamine concentration (see inset), and (b) after this initial regime, a positive relationship exists between rate and the concentrations of enamine components. It seems notable that this initial period ends approximately when the equilibrium amount of enamine **9** that should be in solution prior to irradiation under standard reactions conditions (see Figure S65, 30 equiv water) would be consumed. Thereafter, the kinetics of enamine formation from the aldehyde and organocatalyst, as well as the turnover of the organocatalyst, become important. Descriptions of SCS representing the RDS in the direct reaction between the electrophile and enamine (i.e., in the manuscript and prior sections of the SI) also become less meaningful. We believe nonetheless that the demonstration that SCS is slower than other events such as C–C bond formation in the linear process (neglecting the organocatalytic

cycle) is helpful in understanding this reaction and could be important for future reaction development.

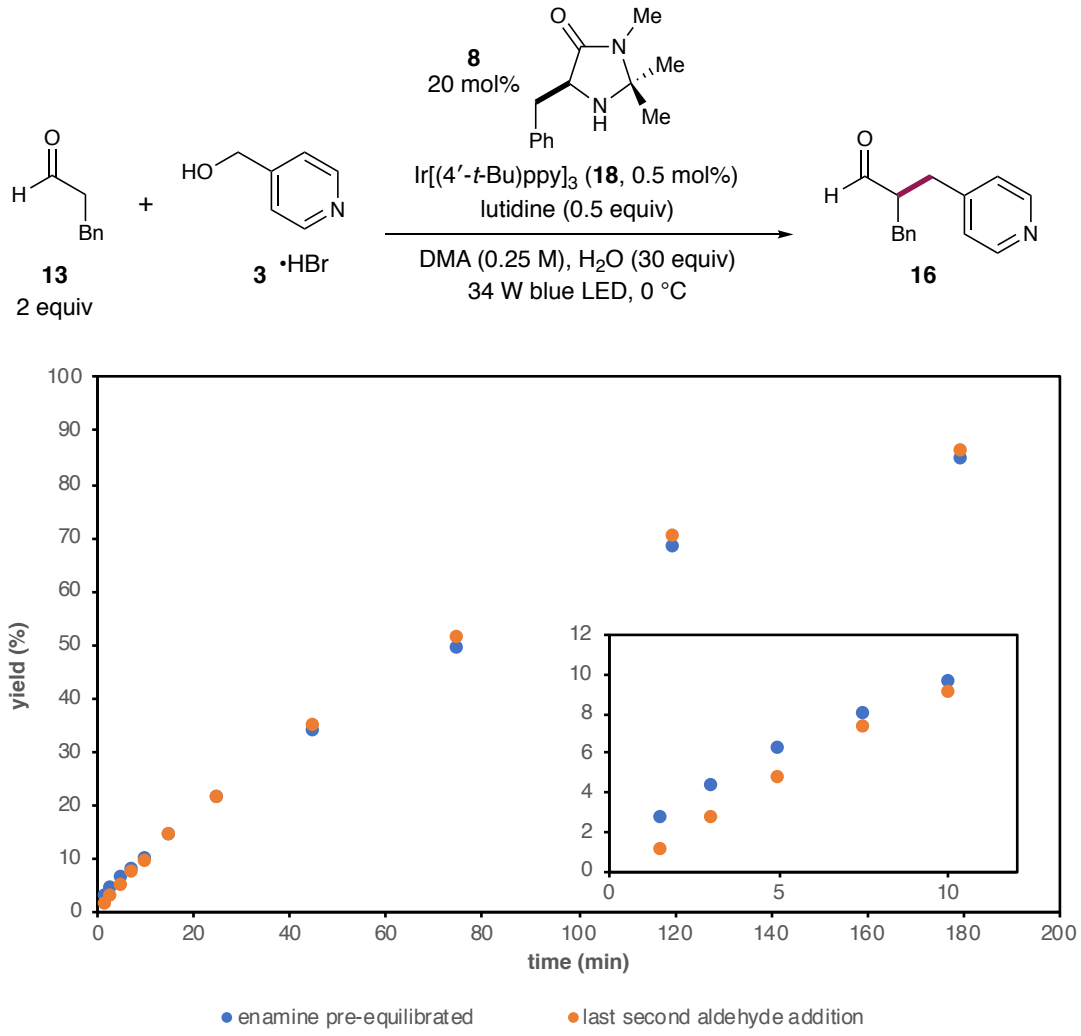


Figure S63. Effect of enamine pre-equilibration before irradiation on reaction profile.

Figure S63 examines whether the standard procedure, which involves sparging the reaction mixture prior to irradiation and thus allows for an appreciable equilibrium amount of enamine to be available at the outset, causes an initial increase in rate compared to the remainder of the process. Indeed, when the standard procedure (blue circles) was modified such that independently degassed aldehyde was added to a sparged solution of the other components immediately before irradiation (orange circles), the initial rate of the modified reaction was measurably lower. This difference in initial rates is consistent with a pre-formed concentration of enamine under standard

conditions enabling the rapid initial kinetic regime described earlier in this section, whereas under modified conditions, the kinetics of the organocatalytic cycle cannot be neglected for any portion of the process. Importantly, this discrepancy becomes negligible at later time points, as small differences in initial concentrations between equilibrating species become unimportant.

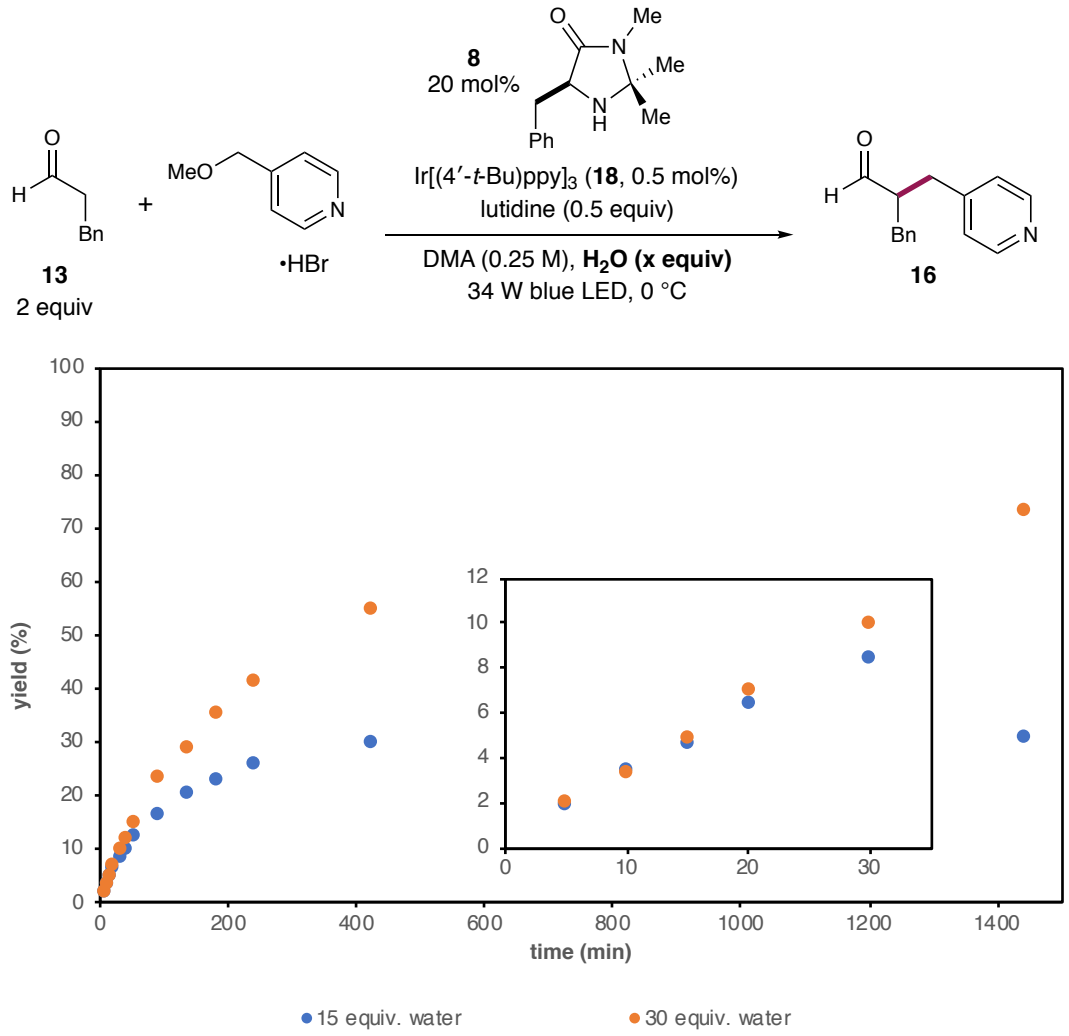


Figure S64. Effect of water content on reaction profile.

Figure S64 demonstrates a positive relationship between the water content of the reaction medium and the rate of reaction. The methyl ether analogue of the standard alcohol electrophile was employed to minimize the potential impact of water on hydrogen-bonding that could affect the ejection of the leaving group by spin-center shift. Higher amounts of water were not used since the photocatalyst is not completely soluble under such conditions. Consistent with earlier

experiments described in this section, this effect is not detected initially, as similar quantities of enamine are available as irradiation begins and organocatalyst turnover is unimportant. After this initial period, the kinetics of the organocatalytic cycle affect the rate of reaction (see also the discussion of Figure S62), which suggests that water is involved in the turnover-limiting step of the organocatalytic cycle. The most likely scenario is that hydrolysis of the product iminium ion is turnover-limiting, although the following experiment was also performed to rule out the possibility that this kinetic dependence on water is associated with enamine formation.

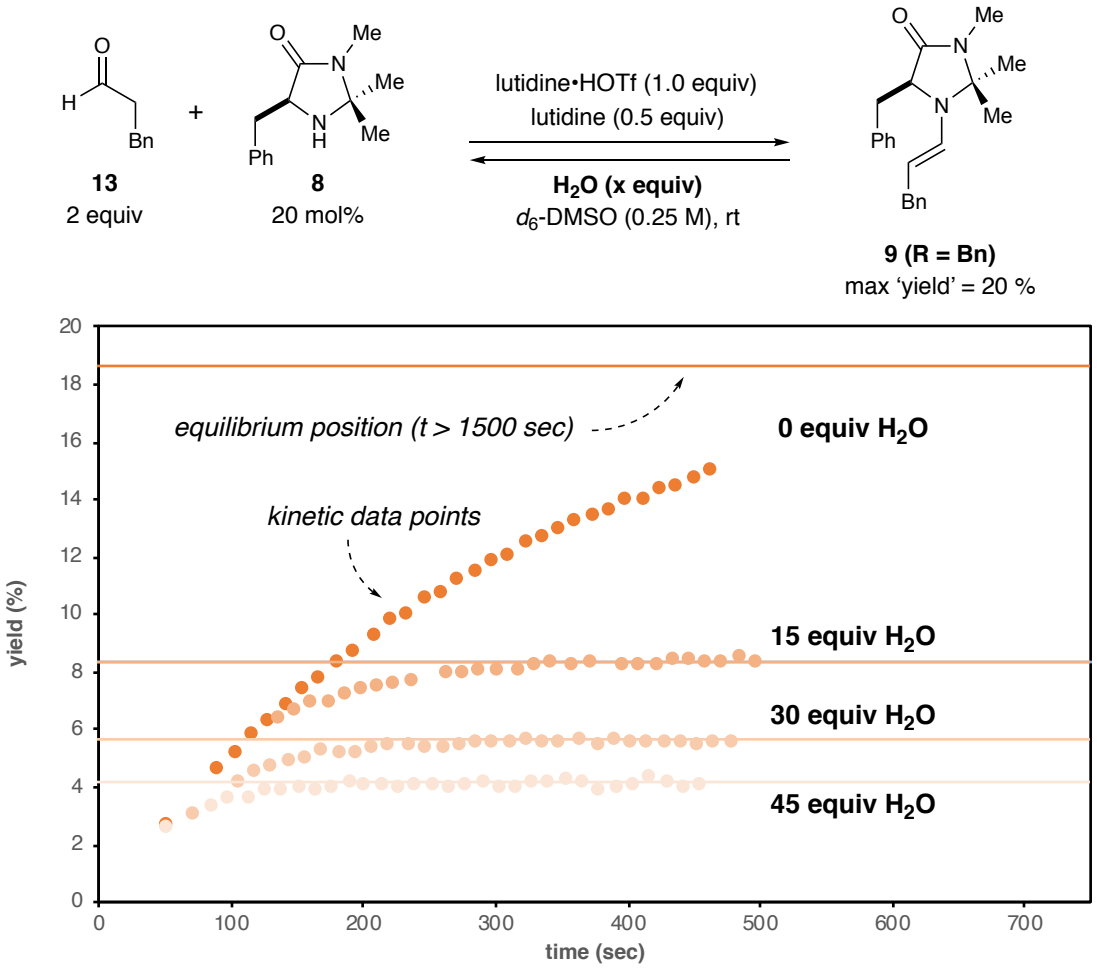


Figure S65. Effect of water content on enamine formation.

Data for Figure S65 were generated by adding an equal volume of a solution of aldehyde **13** (1 M) in d_6-DMSO to a solution of organocatalyst **8** (0.1 M), 2,6-lutidine (0.25 M), lutidinium triflate

(0.5 M), and the indicated amount of water in an NMR tube. This procedure gives final concentrations of all components representative of the standard reaction conditions, except that photocatalyst was omitted and the lutidinium salt was used instead of the electrophile to simplify the NMR spectrum without significantly altering the acid-base character of the solution. The resulting mixture was monitored by ^{1}H NMR using single-scan experiments at 12 second intervals for ~ 7 minutes following complete mixing of the solutions, as well as ~ 30 and 60 minutes thereafter to determine the equilibrium composition of the mixture. For convenience, these experiments were performed at ambient temperature in DMSO, which also depart from the optimized reaction conditions (0 ºC in DMA). Nonetheless, we expect the results to be a fair approximation of reaction conditions, since DMSO is nearly as effective as DMA and does not cause obvious changes in kinetic behavior, with the caveat that the approach to equilibrium should be slower in all cases.

Due to the stoichiometries employed (large excesses of aldehyde and water), this system can be approximated as a pseudo first-order approach to equilibrium between organocatalyst **8** and enamine **9**, where the apparent pseudo first-order rate constant for the difference between actual and equilibrium concentrations of either species is

$$k_{obs} = k_1 + k_{-1},$$

and where k_1 and k_{-1} are the pseudo first-order rate constants for the formation and hydrolysis of enamine **9**, respectively. We did not analyze the case without added water since H_2O concentration must also be considered here (complicating analysis), and since the enantioselective benzylation reaction performs very poorly without this cosolvent. Good exponential fits were obtained for early time points in the three approaches to equilibrium considered, allowing for estimates of k_{obs}. The individual pseudo first-order rate constants were obtained by solving the system of equations represented by the above expression for k_{obs} and

$$\mathrm{K_{eq}} = \frac{k_1 \cdot [\mathrm{H_2O}]}{k_{-1} \cdot [\mathbf{8}]},$$

already having obtained values for K_{eq} by NMR. The values for k_1 obtained in this manner were 0.0042 s^{-1} (15 equiv H_2O), 0.0044 s^{-1} (30 equiv H_2O), and 0.0041 s^{-1} (45 equiv H_2O), which clearly does not explain the difference in reaction rates with different quantities of water (see Figure S64), suggesting that hydrolysis of the product iminium ion is turnover-limiting.

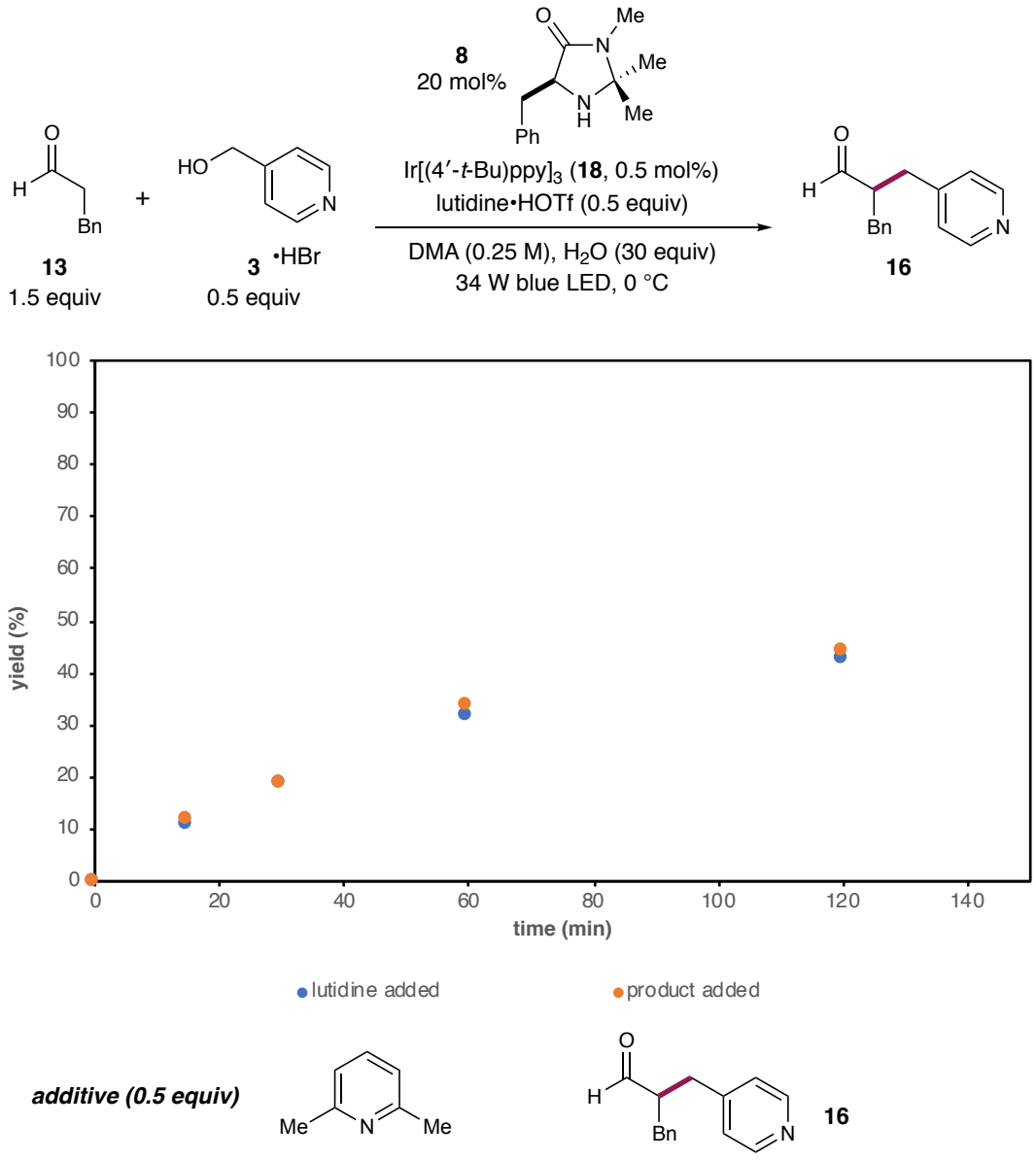


Figure S66. Product inhibition experiment.

Finally, Figure S66 illustrates the results of a modification of the standard protocol where 50 mol% less starting aldehyde was employed and 50% of the starting electrophile was replaced with lutidinium triflate (i.e., the leaving group of a representative electrophile is omitted but the

conjugate acid of a basic heteroarene is still included) for two experiments. In one experiment, 2,6-lutidine was employed as the base cocatalyst, and in the other, product **16** was employed as the base cocatalyst. These conditions are designed to simulate a reaction at 50% completion without changing the total amounts of acids and bases, but in one instance, the product aldehyde is replaced with lutidine in order to isolate the effect of removing the product aldehyde functionality from the system. Clearly, no significant difference is observed between the two experiments, suggesting that product inhibition does not occur in this process.

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XXIII. Chiral HPLC Chromatograms

Data File C:\CHEM32\2\DATA\EDN\DEF_LC 2017-07-11 08-28-13\EDN-1-345.D
Sample Name: EDN-1-345

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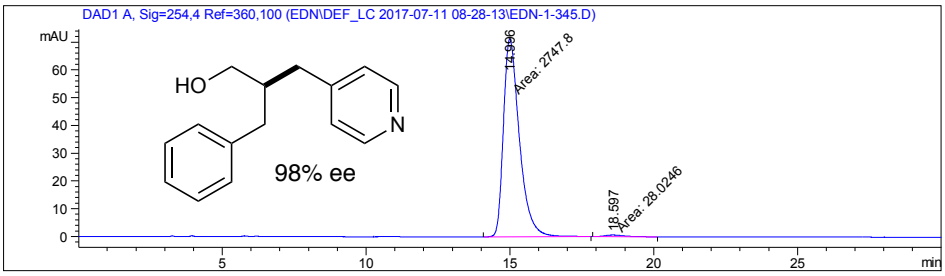
    ======================================================================
    Acq. Operator   : SYSTEM                        Seq. Line :   5
    Acq. Instrument : Biggie                         Location : Vial 52
    Injection Date  : 7/11/2017 10:14:29 AM               Inj :   1
                                                   Inj Volume : 5.000 µl
    Acq. Method     : C:\CHEM32\2\DATA\EDN\DEF_LC 2017-07-11 08-28-13\10ETOH30-AD.M
    Last changed    : 7/11/2017 8:28:13 AM by SYSTEM
    Analysis Method : C:\CHEM32\2\DATA\EDN\DEF_LC 2017-07-11 08-28-13\10ETOH30-AD.M (Sequence
                      Method)
    Last changed    : 7/12/2017 8:58:28 AM by SYSTEM
                      (modified after loading)
    Method Info     : 10% EtOH in hexanes, 30 min, AD-H, 1.0 mL/min

    Additional Info : Peak(s) manually integrated
```




```
    ======================================================================
                           Area Percent Report
    ======================================================================

    Sorted By             :      Signal
    Multiplier            :      1.0000
    Dilution              :      1.0000
    Do not use Multiplier & Dilution Factor with ISTDs


    Signal 1: DAD1 A, Sig=254,4 Ref=360,100

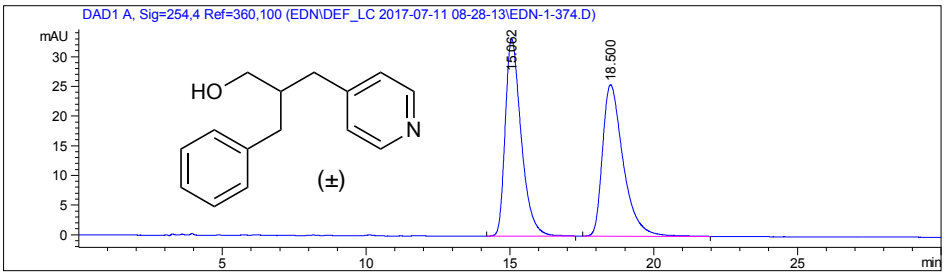
    Peak RetTime Type  Width     Area      Height     Area
      #   [min]        [min]   [mAU*s]     [mAU]       %
    ----|-------|----|-------|----------|----------|--------|
       1  14.996 MM    0.6432 2747.80420   71.20477  98.9904
       2  18.597 MM    0.7815   28.02461 5.97682e-1   1.0096

    Totals :                  2775.82881   71.80245

    ======================================================================
                              *** End of Report ***
```

Data File C:\CHEM32\2\DATA\EDN\DEF_LC 2017-07-11 08-28-13\EDN-1-374.D
Sample Name: EDN-1-374

```
==========================================================================
Acq. Operator   : SYSTEM                        Seq. Line :   4
Acq. Instrument : Biggie                         Location : Vial 51
Injection Date  : 7/11/2017 9:43:02 AM                Inj :   1
                                                Inj Volume : 5.000 µl
Acq. Method     : C:\CHEM32\2\DATA\EDN\DEF_LC 2017-07-11 08-28-13\10ETOH30-AD.M
Last changed    : 7/11/2017 8:28:13 AM by SYSTEM
Analysis Method : C:\CHEM32\2\DATA\EDN\DEF_LC 2017-07-11 08-28-13\10ETOH30-AD.M (Sequence
                  Method)
Last changed    : 7/12/2017 8:58:28 AM by SYSTEM
                  (modified after loading)
Method Info     : 10% EtOH in hexanes, 30 min, AD-H, 1.0 mL/min
```




```
==========================================================================
                        Area Percent Report
==========================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Do not use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  15.062 BB    0.5881 1280.98230   33.20050  50.1756
   2  18.500 BB    0.7494 1272.01611   25.52609  49.8244

Totals :                  2552.99841   58.72659

==========================================================================
                          *** End of Report ***
```

Data File C:\CHEM32\2\DATA\KN\DEF_LC 2017-06-29 09-01-55\EDN-1-487-15IPA45ODB.D
Sample Name: EDN-1-487-15IPA45ODb

```
    ======================================================================
    Acq. Operator   : SYSTEM                        Seq. Line :  40
    Acq. Instrument : Biggie                         Location : Vial 49
    Injection Date  : 6/29/2017 9:53:37 PM                Inj :   1
                                                  Inj Volume : 5.000 µl
    Acq. Method     : C:\CHEM32\2\DATA\KN\DEF_LC 2017-06-29 09-01-55\15IPA45-OD.M
    Last changed    : 6/29/2017 12:08:18 PM by SYSTEM
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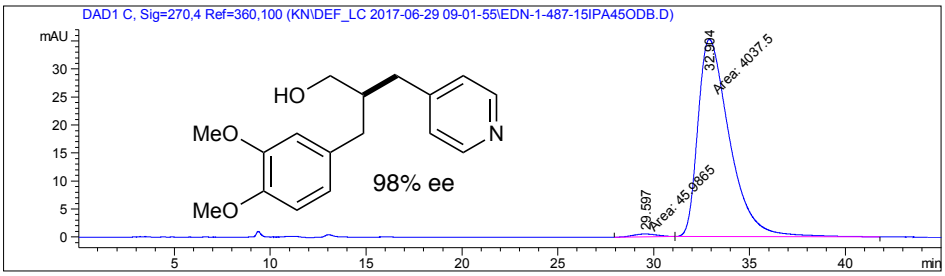
                      Method)
    Last changed    : 7/12/2017 11:16:08 AM by SYSTEM
                      (modified after loading)
    Method Info     : 15% IPA in hexanes, 45 min, OD-H, 1.0 mL/min

    Additional Info : Peak(s) manually integrated
```

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                               Area Percent Report
    ======================================================================

    Sorted By             :      Signal
    Multiplier            :      1.0000
    Dilution              :      1.0000
    Do not use Multiplier & Dilution Factor with ISTDs


    Signal 1: DAD1 C, Sig=270,4 Ref=360,100

    Peak RetTime Type  Width     Area      Height     Area
      #   [min]        [min]   [mAU*s]     [mAU]       %
    ----|-------|----|-------|----------|----------|--------|
       1  29.597 MM    1.4568   45.98654 5.26130e-1   1.1262
       2  32.904 MM    1.9103 4037.49756   35.22487  98.8738

    Totals :                  4083.48410   35.75100


    ======================================================================
                               *** End of Report ***
```

Data File C:\CHEM32\2\DATA\EDN\DEF_LC 2017-04-28 18-04-15\EDN-1-486-15IPA45OD.D
Sample Name: EDN-1-486-15IPA45OD

```
    ======================================================================
    Acq. Operator   : SYSTEM                        Seq. Line :  13
    Acq. Instrument : Biggie                         Location : Vial 21
    Injection Date  : 4/28/2017 9:46:42 PM               Inj :   1
                                                   Inj Volume : 5.000 µl
    Acq. Method     : C:\CHEM32\2\DATA\EDN\DEF_LC 2017-04-28 18-04-15\15IPA45-OD.M
    Last changed    : 4/28/2017 9:27:15 PM by SYSTEM
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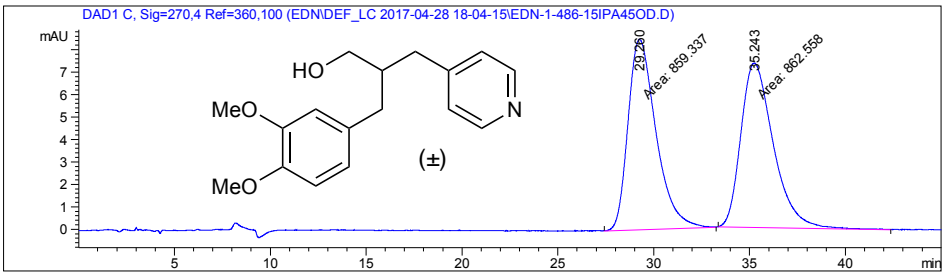
                      Method)
    Last changed    : 7/12/2017 11:18:03 AM by SYSTEM
                      (modified after loading)
    Method Info     : 15% IPA in hexanes, 45 min, OD-H, 1.0 mL/min

    Additional Info : Peak(s) manually integrated
```




```
    ======================================================================
                               Area Percent Report
    ======================================================================

    Sorted By             :      Signal
    Multiplier            :      1.0000
    Dilution              :      1.0000
    Do not use Multiplier & Dilution Factor with ISTDs


    Signal 1: DAD1 C, Sig=270,4 Ref=360,100

    Peak RetTime Type  Width     Area      Height     Area
      #   [min]        [min]   [mAU*s]     [mAU]       %
    ----|-------|----|-------|----------|----------|--------|
       1  29.260 MM    1.6897  859.33679    8.47634  49.9065
       2  35.243 MM    1.9633  862.55768    7.32240  50.0935

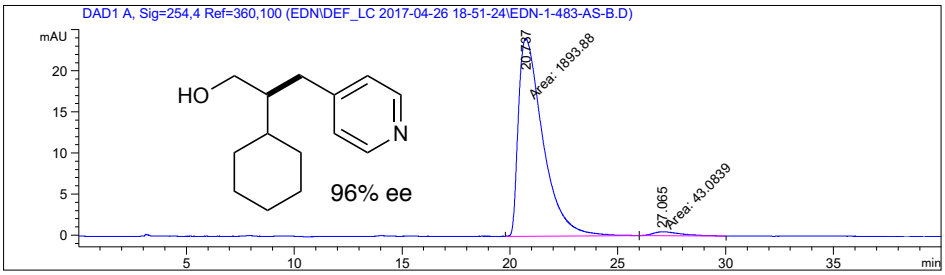
    Totals :                  1721.89447   15.79873


    ======================================================================
                               *** End of Report ***
```

Data File C:\CHEM32\2\DATA\EDN\DEF_LC 2017-04-26 18-51-24\EDN-1-483-AS-B.D
Sample Name: EDN-1-483-AS-b

```
    ======================================================================
    Acq. Operator   : SYSTEM                        Seq. Line :   4
    Acq. Instrument : Biggie                         Location : Vial 23
    Injection Date  : 4/26/2017 8:28:12 PM               Inj :   1
                                                   Inj Volume : 5.000 µl
    Acq. Method     : C:\CHEM32\2\DATA\EDN\DEF_LC 2017-04-26 18-51-24\5IPA40-AS.M
    Last changed    : 4/26/2017 6:51:24 PM by SYSTEM
    Analysis Method : C:\CHEM32\2\DATA\EDN\DEF_LC 2017-04-26 18-51-24\5IPA40-AS.M (Sequence
                      Method)
    Last changed    : 7/12/2017 11:06:17 AM by SYSTEM
                      (modified after loading)
    Method Info     : 5% IPA in hexanes, 40 min, AS-H, 1.0 mL/min

    Additional Info : Peak(s) manually integrated
```

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    ======================================================================
                               Area Percent Report
    ======================================================================

    Sorted By             :      Signal
    Multiplier            :      1.0000
    Dilution              :      1.0000
    Do not use Multiplier & Dilution Factor with ISTDs


    Signal 1: DAD1 A, Sig=254,4 Ref=360,100

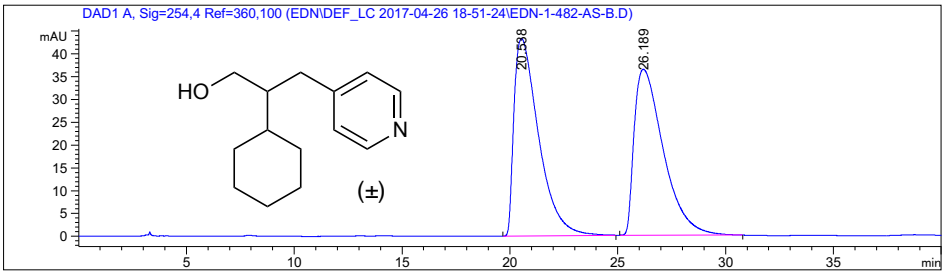
    Peak RetTime Type  Width     Area      Height     Area
      #   [min]        [min]   [mAU*s]     [mAU]       %
    ----|-------|----|-------|----------|----------|--------|
       1  20.737 MM    1.3137 1893.88306   24.02710  97.7757
       2  27.065 MM    1.4940   43.08393 4.80623e-1   2.2243

    Totals :                  1936.96699   24.50772


    ======================================================================
                               *** End of Report ***
```

Data File C:\CHEM32\2\DATA\EDN\DEF_LC 2017-04-26 18-51-24\EDN-1-482-AS-B.D
Sample Name: EDN-1-482-AS-b

```
    ======================================================================
    Acq. Operator   : SYSTEM                        Seq. Line :   5
    Acq. Instrument : Biggie                         Location : Vial 21
    Injection Date  : 4/26/2017 9:09:36 PM               Inj :   1
                                                   Inj Volume : 5.000 µl
    Acq. Method     : C:\CHEM32\2\DATA\EDN\DEF_LC 2017-04-26 18-51-24\5IPA40-AS.M
    Last changed    : 4/26/2017 6:51:24 PM by SYSTEM
    Analysis Method : C:\CHEM32\2\DATA\EDN\DEF_LC 2017-04-26 18-51-24\5IPA40-AS.M (Sequence
                      Method)
    Last changed    : 7/12/2017 11:06:17 AM by SYSTEM
                      (modified after loading)
    Method Info     : 5% IPA in hexanes, 40 min, AS-H, 1.0 mL/min
```

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    ======================================================================
                            Area Percent Report
    ======================================================================

    Sorted By             :      Signal
    Multiplier            :      1.0000
    Dilution              :      1.0000
    Do not use Multiplier & Dilution Factor with ISTDs


    Signal 1: DAD1 A, Sig=254,4 Ref=360,100

    Peak RetTime Type  Width     Area      Height     Area
      #   [min]        [min]   [mAU*s]     [mAU]       %
    ----|-------|----|-------|----------|----------|--------|
       1  20.538 BB    1.2045 3438.06519   43.29244  50.1119
       2  26.189 BB    1.3997 3422.70752   36.37831  49.8881

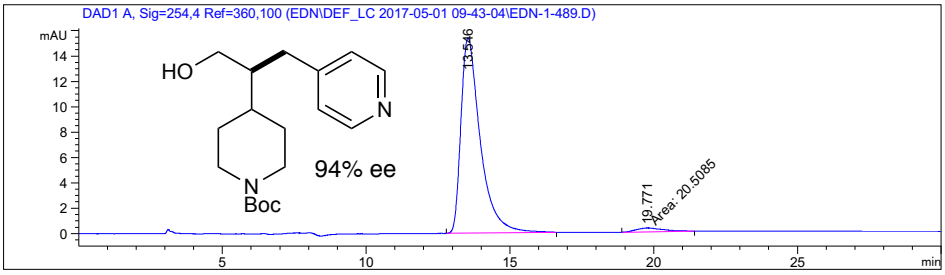
    Totals :                  6860.77271   79.67075


    ======================================================================
                              *** End of Report ***
```

Data File C:\CHEM32\2\DATA\EDN\DEF_LC 2017-05-01 09-43-04\EDN-1-489.D
Sample Name: EDN-1-489

```
    ======================================================================
    Acq. Operator   : SYSTEM                        Seq. Line :   3
    Acq. Instrument : Biggie                         Location : Vial 24
    Injection Date  : 5/1/2017 10:27:31 AM               Inj :   1
                                                   Inj Volume : 5.000 µl
    Different Inj Volume from Sample Entry!  Actual Inj Volume : 3.000 µl
    Acq. Method     : C:\CHEM32\2\DATA\EDN\DEF_LC 2017-05-01 09-43-04\10IPA30-AD.M
    Last changed    : 5/1/2017 9:43:04 AM by SYSTEM
    Analysis Method : C:\CHEM32\2\DATA\EDN\DEF_LC 2017-05-01 09-43-04\10IPA30-AD.M (Sequence
                      Method)
    Last changed    : 7/12/2017 11:08:26 AM by SYSTEM
                      (modified after loading)
    Method Info     : 10% IPA in hexanes, 30 min, AD-H, 1.0 mL/min

    Additional Info : Peak(s) manually integrated
```

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    ======================================================================
                            Area Percent Report
    ======================================================================

    Sorted By             :      Signal
    Multiplier            :      1.0000
    Dilution              :      1.0000
    Do not use Multiplier & Dilution Factor with ISTDs


    Signal 1: DAD1 A, Sig=254,4 Ref=360,100

    Peak RetTime Type  Width     Area      Height     Area
      #   [min]        [min]    [mAU*s]     [mAU]       %
    ----|-------|----|-------|----------|----------|--------|
       1  13.546 BB    0.7006  720.93195   15.38874  97.2340
       2  19.771 MM    1.1010   20.50846 3.10454e-1   2.7660

    Totals :                   741.44040   15.69920


    ======================================================================
                            *** End of Report ***
```

Data File C:\CHEM32\2\DATA\EDN\DEF_LC 2017-05-01 09-43-04\EDN-1-488-B.D
Sample Name: EDN-1-488-b

```
    ======================================================================
    Acq. Operator   : SYSTEM                        Seq. Line :   4
    Acq. Instrument : Biggie                         Location : Vial 23
    Injection Date  : 5/1/2017 10:59:04 AM                Inj :   1
                                                   Inj Volume : 5.000 µl
    Different Inj Volume from Sample Entry!  Actual Inj Volume : 3.000 µl
    Acq. Method     : C:\CHEM32\2\DATA\EDN\DEF_LC 2017-05-01 09-43-04\10IPA30-AD.M
    Last changed    : 5/1/2017 9:43:04 AM by SYSTEM
    Analysis Method : C:\CHEM32\2\DATA\EDN\DEF_LC 2017-05-01 09-43-04\10IPA30-AD.M (Sequence
                      Method)
    Last changed    : 7/12/2017 11:08:26 AM by SYSTEM
                      (modified after loading)
    Method Info     : 10% IPA in hexanes, 30 min, AD-H, 1.0 mL/min
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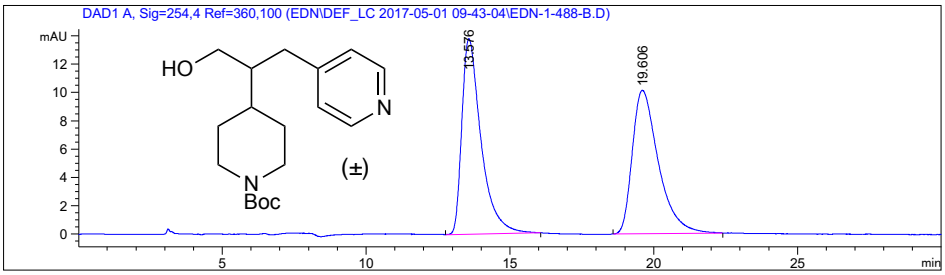


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                               Area Percent Report
    ======================================================================

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    Multiplier            :      1.0000
    Dilution              :      1.0000
    Do not use Multiplier & Dilution Factor with ISTDs


    Signal 1: DAD1 A, Sig=254,4 Ref=360,100

    Peak RetTime Type  Width     Area      Height     Area
      #   [min]        [min]   [mAU*s]     [mAU]       %
    ----|-------|----|-------|----------|----------|--------|
       1  13.576 BB    0.6856  640.49304   13.79796  50.0659
       2  19.606 BB    0.9416  638.80804   10.13159  49.9341

    Totals :                  1279.30109   23.92955


    ======================================================================
                               *** End of Report ***
```

Data File C:\CHEM32\2\DATA\EDN\DEF_LC 2017-04-14 13-49-21\EDN-1-471-B.D
Sample Name: EDN-1-471-b

```
    ======================================================================
    Acq. Operator   : SYSTEM                        Seq. Line :   3
    Acq. Instrument : Biggie                         Location : Vial 22
    Injection Date  : 4/14/2017 2:33:06 PM               Inj :   1
                                                   Inj Volume : 5.000 µl
    Acq. Method     : C:\CHEM32\2\DATA\EDN\DEF_LC 2017-04-14 13-49-21\5IPA30-OD.M
    Last changed    : 4/14/2017 1:49:22 PM by SYSTEM
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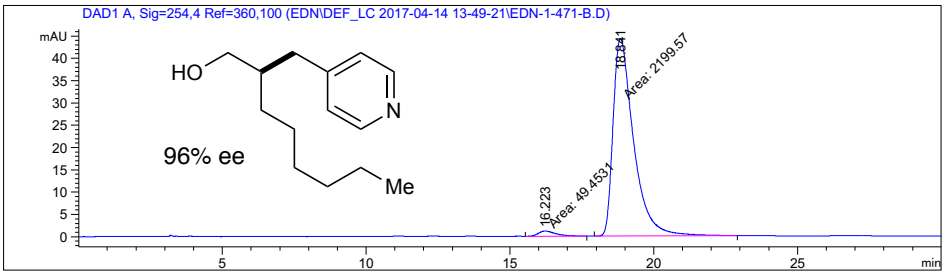
                      Method)
    Last changed    : 7/12/2017 10:57:47 AM by SYSTEM
                      (modified after loading)
    Method Info     : 5% IPA in hexanes, 30 min, OD-H, 1.0 mL/min

    Additional Info : Peak(s) manually integrated
```




```
    ======================================================================
                               Area Percent Report
    ======================================================================

    Sorted By             :      Signal
    Multiplier            :      1.0000
    Dilution              :      1.0000
    Do not use Multiplier & Dilution Factor with ISTDs


    Signal 1: DAD1 A, Sig=254,4 Ref=360,100

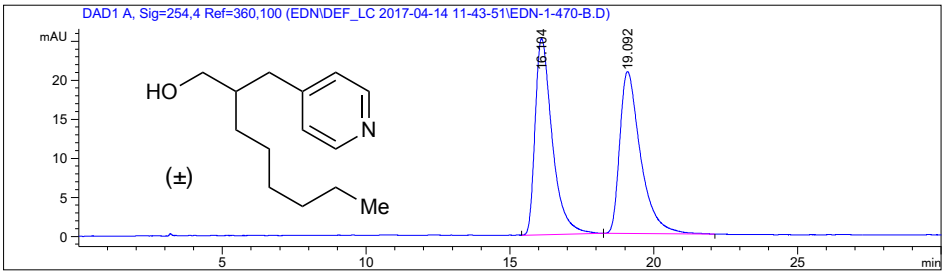
    Peak RetTime Type  Width     Area      Height     Area
      #   [min]        [min]   [mAU*s]     [mAU]       %
    ----|-------|----|-------|----------|----------|--------|
       1  16.223 MM    0.7061   49.45309    1.16727   2.1989
       2  18.841 MM    0.8293 2199.56763   44.20516  97.8011

    Totals :                  2249.02072   45.37243


    ======================================================================
                               *** End of Report ***
```

Data File C:\CHEM32\2\DATA\EDN\DEF_LC 2017-04-14 11-43-51\EDN-1-470-B.D
Sample Name: EDN-1-470-b

```
    ======================================================================
    Acq. Operator   : SYSTEM                        Seq. Line :   3
    Acq. Instrument : Biggie                         Location : Vial 21
    Injection Date  : 4/14/2017 12:27:24 PM               Inj :   1
                                                  Inj Volume : 5.000 µl
    Acq. Method     : C:\CHEM32\2\DATA\EDN\DEF_LC 2017-04-14 11-43-51\5IPA30-OD.M
    Last changed    : 4/14/2017 11:43:52 AM by SYSTEM
    Analysis Method : C:\CHEM32\2\DATA\EDN\DEF_LC 2017-04-14 11-43-51\5IPA30-OD.M (Sequence
                      Method)
    Last changed    : 7/12/2017 10:56:43 AM by SYSTEM
                      (modified after loading)
    Method Info     : 5% IPA in hexanes, 30 min, OD-H, 1.0 mL/min
```




```
    ======================================================================
                              Area Percent Report
    ======================================================================

    Sorted By             :      Signal
    Multiplier            :      1.0000
    Dilution              :      1.0000
    Do not use Multiplier & Dilution Factor with ISTDs


    Signal 1: DAD1 A, Sig=254,4 Ref=360,100

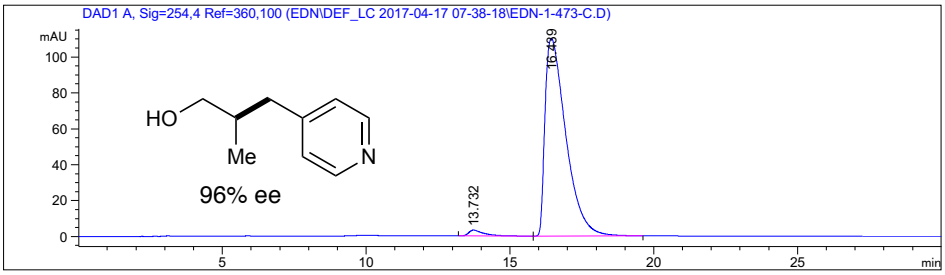
    Peak RetTime Type  Width     Area      Height     Area
      #   [min]        [min]   [mAU*s]     [mAU]       %
    ----|-------|----|-------|----------|----------|--------|
       1  16.104 BB    0.6196 1037.39380   25.12906  49.7971
       2  19.092 BB    0.7576 1045.84961   20.76440  50.2029

    Totals :                  2083.24341   45.89346


    ======================================================================
                              *** End of Report ***
```

Data File C:\CHEM32\2\DATA\EDN\DEF_LC 2017-04-17 07-38-18\EDN-1-473-C.D
Sample Name: EDN-1-473-c

```
    ======================================================================
    Acq. Operator   : SYSTEM                        Seq. Line :   4
    Acq. Instrument : Biggie                         Location : Vial 24
    Injection Date  : 4/17/2017 8:54:01 AM                Inj :   1
                                                  Inj Volume : 5.000 µl
    Acq. Method     : C:\CHEM32\2\DATA\EDN\DEF_LC 2017-04-17 07-38-18\10IPA30-AS.M
    Last changed    : 4/17/2017 7:38:19 AM by SYSTEM
    Analysis Method : C:\CHEM32\2\DATA\EDN\DEF_LC 2017-04-17 07-38-18\10IPA30-AS.M (Sequence
                      Method)
    Last changed    : 7/12/2017 10:59:51 AM by SYSTEM
                      (modified after loading)
    Method Info     : 10% IPA in hexanes, 30 min, AS-H, 1.0 mL/min
```




```
    ======================================================================
                            Area Percent Report
    ======================================================================

    Sorted By             :      Signal
    Multiplier            :      1.0000
    Dilution              :      1.0000
    Do not use Multiplier & Dilution Factor with ISTDs


    Signal 1: DAD1 A, Sig=254,4 Ref=360,100

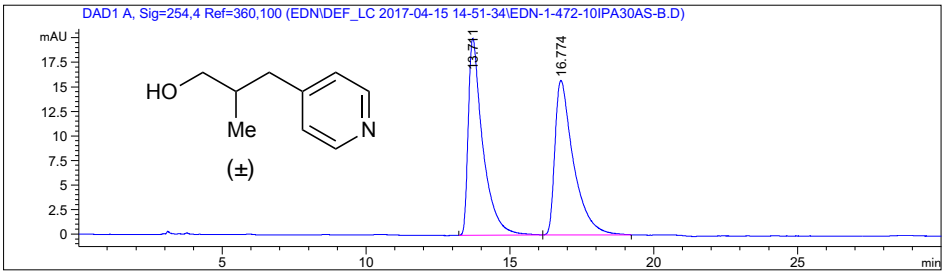
    Peak RetTime Type  Width     Area      Height     Area
      #   [min]        [min]   [mAU*s]     [mAU]       %
    ----|-------|----|-------|----------|----------|--------|
       1  13.732 BB    0.5167  118.00967    3.25697   2.0873
       2  16.439 BB    0.7771 5535.66895  110.00955  97.9127

    Totals :                  5653.67861  113.26652


    ======================================================================
                            *** End of Report ***
```

Data File C:\CHEM32\2\DATA\EDN\DEF_LC 2017-04-15 14-51-34\EDN-1-472-10IPA30AS-B.D
Sample Name: EDN-1-472-10IPA30AS-b

```
======================================================================
Acq. Operator   : SYSTEM                       Seq. Line :  12
Acq. Instrument : Biggie                        Location : Vial 23
Injection Date  : 4/15/2017 5:46:23 PM               Inj :   1
                                               Inj Volume : 5.000 µl
Acq. Method     : C:\CHEM32\2\DATA\EDN\DEF_LC 2017-04-15 14-51-34\10IPA30-AS.M
Last changed    : 4/15/2017 3:18:53 PM by SYSTEM
Analysis Method : C:\CHEM32\2\DATA\EDN\DEF_LC 2017-04-15 14-51-34\10IPA30-AS.M (Sequence
                  Method)
Last changed    : 7/12/2017 10:58:49 AM by SYSTEM
                  (modified after loading)
Method Info     : 10% IPA in hexanes, 30 min, AS-H, 1.0 mL/min
```




```
======================================================================
                        Area Percent Report
======================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Do not use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  13.711 BB    0.5023  701.84137   20.05322  49.9755
   2  16.774 BB    0.6546  702.53088   15.74252  50.0245

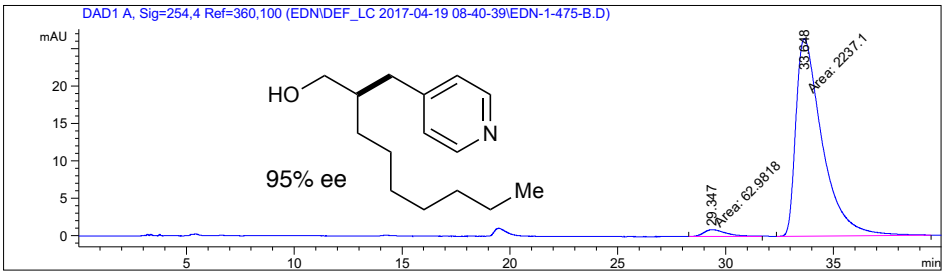
Totals :                  1404.37225   35.79574


======================================================================
                          *** End of Report ***
```

Data File C:\CHEM32\2\DATA\EDN\DEF_LC 2017-04-19 08-40-39\EDN-1-475-B.D
Sample Name: EDN-1-475-b

```
    ======================================================================
    Acq. Operator   : SYSTEM                        Seq. Line :   5
    Acq. Instrument : Biggie                         Location : Vial 27
    Injection Date  : 4/19/2017 10:58:17 AM               Inj :   1
                                                  Inj Volume : 5.000 µl
    Acq. Method     : C:\CHEM32\2\DATA\EDN\DEF_LC 2017-04-19 08-40-39\3IPA40-OD.M
    Last changed    : 4/19/2017 9:27:06 AM by SYSTEM
    Analysis Method : C:\CHEM32\2\DATA\EDN\DEF_LC 2017-04-19 08-40-39\3IPA40-OD.M (Sequence
                      Method)
    Last changed    : 7/12/2017 11:01:20 AM by SYSTEM
                      (modified after loading)
    Method Info     : 3% IPA in hexanes, 40 min, OD-H, 1.0 mL/min

    Additional Info : Peak(s) manually integrated
```




```
    ======================================================================
                               Area Percent Report
    ======================================================================

    Sorted By             :      Signal
    Multiplier            :      1.0000
    Dilution              :      1.0000
    Do not use Multiplier & Dilution Factor with ISTDs


    Signal 1: DAD1 A, Sig=254,4 Ref=360,100

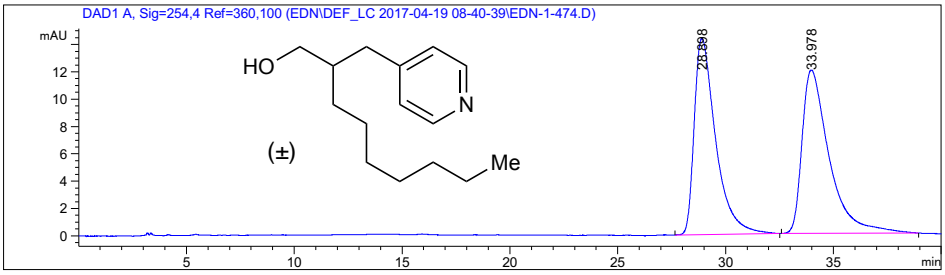
    Peak RetTime Type  Width     Area      Height     Area
      #   [min]        [min]   [mAU*s]     [mAU]       %
    ----|-------|----|-------|----------|----------|--------|
       1  29.347 MM    1.1670   62.98179 8.99461e-1   2.7382
       2  33.648 MM    1.4141 2237.09985   26.36742  97.2618

    Totals :                  2300.08165   27.26688


    ======================================================================
                               *** End of Report ***
```

Data File C:\CHEM32\2\DATA\EDN\DEF_LC 2017-04-19 08-40-39\EDN-1-474.D
Sample Name: EDN-1-474

```
    ======================================================================
    Acq. Operator   : SYSTEM                        Seq. Line :   6
    Acq. Instrument : Biggie                         Location : Vial 26
    Injection Date  : 4/19/2017 11:39:49 AM               Inj :   1
                                                  Inj Volume : 5.000 µl
    Acq. Method     : C:\CHEM32\2\DATA\EDN\DEF_LC 2017-04-19 08-40-39\3IPA40-OD.M
    Last changed    : 4/19/2017 9:27:06 AM by SYSTEM
    Analysis Method : C:\CHEM32\2\DATA\EDN\DEF_LC 2017-04-19 08-40-39\3IPA40-OD.M (Sequence
                      Method)
    Last changed    : 7/12/2017 11:02:40 AM by SYSTEM
    Method Info     : 3% IPA in hexanes, 40 min, OD-H, 1.0 mL/min
```




```
    ======================================================================
                            Area Percent Report
    ======================================================================

    Sorted By             :      Signal
    Multiplier            :      1.0000
    Dilution              :      1.0000
    Do not use Multiplier & Dilution Factor with ISTDs


    Signal 1: DAD1 A, Sig=254,4 Ref=360,100

    Peak RetTime Type  Width     Area      Height     Area
      #   [min]        [min]   [mAU*s]     [mAU]       %
    ----|-------|----|-------|----------|----------|--------|
       1  28.898 BB    1.0103  992.85840   14.36623  48.6150
       2  33.978 BB    1.2373 1049.42810   11.96429  51.3850

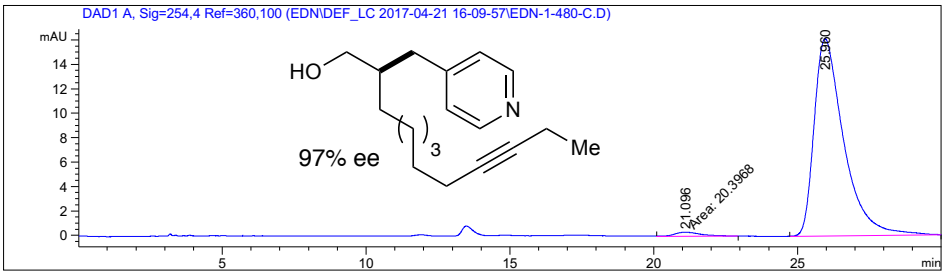
    Totals :                  2042.28650   26.33052

    ======================================================================
                              *** End of Report ***
```

Data File C:\CHEM32\2\DATA\EDN\DEF_LC 2017-04-21 16-09-57\EDN-1-480-C.D
Sample Name: EDN-1-480-c

```
    ======================================================================
    Acq. Operator    : SYSTEM                        Seq. Line :   7
    Acq. Instrument : Biggie                          Location : Vial 22
    Injection Date  : 4/21/2017 7:00:05 PM                Inj :   1
                                                    Inj Volume : 5.000 µl
    Acq. Method     : C:\CHEM32\2\DATA\EDN\DEF_LC 2017-04-21 16-09-57\5IPA30-OD.M
    Last changed    : 4/21/2017 4:09:58 PM by SYSTEM
    Analysis Method : C:\CHEM32\2\DATA\EDN\DEF_LC 2017-04-21 16-09-57\5IPA30-OD.M (Sequence
                      Method)
    Last changed    : 7/12/2017 11:03:25 AM by SYSTEM
                      (modified after loading)
    Method Info     : 5% IPA in hexanes, 30 min, OD-H, 1.0 mL/min

    Additional Info : Peak(s) manually integrated
```




```
    ======================================================================
                               Area Percent Report
    ======================================================================

    Sorted By             :      Signal
    Multiplier            :      1.0000
    Dilution              :      1.0000
    Do not use Multiplier & Dilution Factor with ISTDs


    Signal 1: DAD1 A, Sig=254,4 Ref=360,100

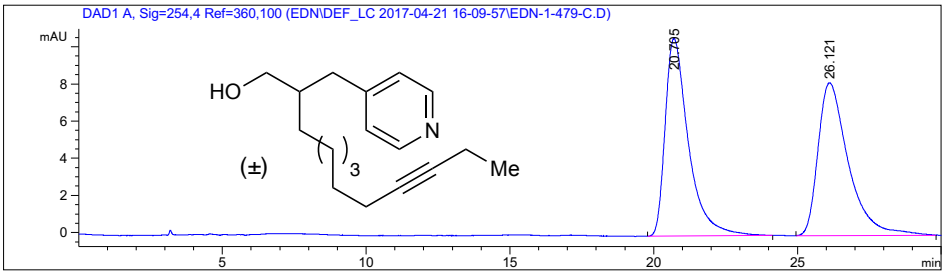
    Peak RetTime Type  Width     Area      Height     Area
      #   [min]        [min]   [mAU*s]     [mAU]       %
    ----|-------|----|-------|----------|----------|--------|
       1  21.096 MM    1.0145   20.39678 3.35085e-1   1.7331
       2  25.960 BBA   1.0402 1156.47009   16.13444  98.2669

    Totals :                  1176.86687   16.46952

    ======================================================================
                               *** End of Report ***
```

Data File C:\CHEM32\2\DATA\EDN\DEF_LC 2017-04-21 16-09-57\EDN-1-479-C.D
Sample Name: EDN-1-479-c

```
    ======================================================================
    Acq. Operator    : SYSTEM                          Seq. Line :   6
    Acq. Instrument : Biggie                           Location : Vial 21
    Injection Date  : 4/21/2017 6:28:33 PM                 Inj :   1
                                                     Inj Volume : 5.000 µl
    Acq. Method     : C:\CHEM32\2\DATA\EDN\DEF_LC 2017-04-21 16-09-57\5IPA30-OD.M
    Last changed    : 4/21/2017 4:09:58 PM by SYSTEM
    Analysis Method : C:\CHEM32\2\DATA\EDN\DEF_LC 2017-04-21 16-09-57\5IPA30-OD.M (Sequence
                      Method)
    Last changed    : 7/12/2017 11:03:25 AM by SYSTEM
                      (modified after loading)
    Method Info     : 5% IPA in hexanes, 30 min, OD-H, 1.0 mL/min
```




```
    ======================================================================
                              Area Percent Report
    ======================================================================

    Sorted By             :      Signal
    Multiplier            :      1.0000
    Dilution              :      1.0000
    Do not use Multiplier & Dilution Factor with ISTDs


    Signal 1: DAD1 A, Sig=254,4 Ref=360,100

    Peak RetTime Type  Width     Area      Height     Area
      #   [min]        [min]   [mAU*s]     [mAU]       %
    ----|-------|----|-------|----------|----------|--------|
       1  20.705 BB    0.8463  600.09369   10.63472  49.8838
       2  26.121 BB    1.0415  602.89056    8.22219  50.1162

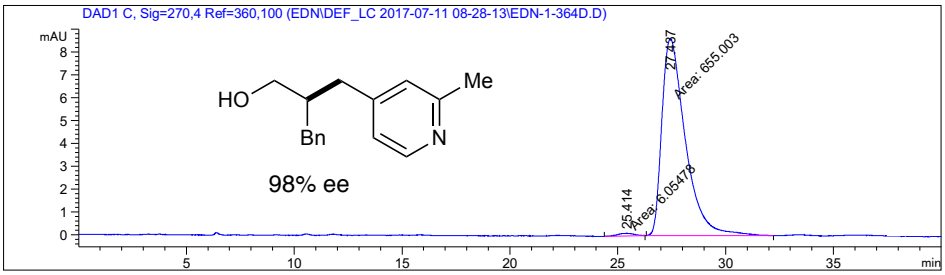
    Totals :                  1202.98425   18.85691


    ======================================================================
                              *** End of Report ***
```

Data File C:\CHEM32\2\DATA\EDN\DEF_LC 2017-07-11 08-28-13\EDN-1-364D.D
Sample Name: EDN-1-364d

```
    ======================================================================
    Acq. Operator   : SYSTEM                        Seq. Line :  30
    Acq. Instrument : Biggie                         Location : Vial 60
    Injection Date  : 7/11/2017 10:07:49 PM               Inj :   1
                                                   Inj Volume : 5.000 µl
    Different Inj Volume from Sample Entry!  Actual Inj Volume : 2.000 µl
    Acq. Method     : C:\CHEM32\2\DATA\EDN\DEF_LC 2017-07-11 08-28-13\5ETOH40-AD.M
    Last changed    : 7/11/2017 4:40:14 PM by SYSTEM
    Analysis Method : C:\CHEM32\2\DATA\EDN\DEF_LC 2017-07-11 08-28-13\5ETOH40-AD.M (Sequence
                      Method)
    Last changed    : 7/12/2017 9:22:34 AM by SYSTEM
    Method Info     : 5% EtOH in hexanes, 40 min, AD-H, 1.0 mL/min

    Additional Info : Peak(s) manually integrated
```




```
    ======================================================================
                               Area Percent Report
    ======================================================================

    Sorted By             :      Signal
    Multiplier            :      1.0000
    Dilution              :      1.0000
    Do not use Multiplier & Dilution Factor with ISTDs


    Signal 1: DAD1 C, Sig=270,4 Ref=360,100

    Peak RetTime Type  Width     Area      Height     Area
      #   [min]        [min]   [mAU*s]     [mAU]       %
    ----|-------|----|-------|----------|----------|--------|
       1  25.414 MM    0.8691    6.05478 1.16108e-1   0.9159
       2  27.437 MM    1.2663  655.00348    8.62085  99.0841

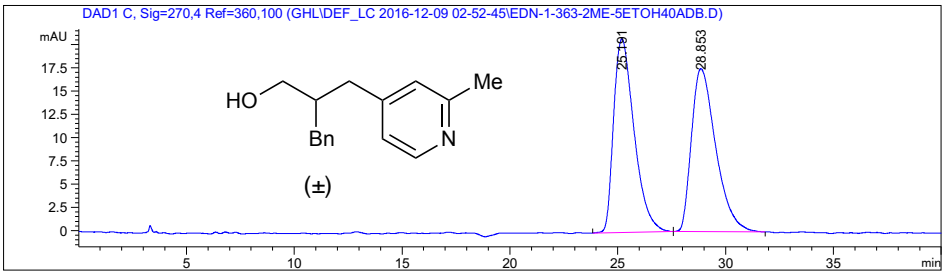
    Totals :                   661.05826    8.73696


    ======================================================================
                              *** End of Report ***
```

Data File C:\CHEM32\2\DATA\GHL\DEF_LC 2016-12-09 02-52-45\EDN-1-363-2ME-5ETOH40ADB.D
Sample Name: EDN-1-363-2Me-5EtOH40ADb

```
    ======================================================================
    Acq. Operator   : SYSTEM                        Seq. Line :  51
    Acq. Instrument : Biggie                         Location : Vial 87
    Injection Date  : 12/9/2016 5:19:16 PM                Inj :   1
                                                  Inj Volume : 5.000 µl
    Acq. Method     : C:\CHEM32\2\DATA\GHL\DEF_LC 2016-12-09 02-52-45\5ETOH40-AD.M
    Last changed    : 12/9/2016 12:14:14 PM by SYSTEM
    Analysis Method : C:\CHEM32\2\DATA\GHL\DEF_LC 2016-12-09 02-52-45\5ETOH40-AD.M (Sequence
                      Method)
    Last changed    : 7/12/2017 9:25:06 AM by SYSTEM
                      (modified after loading)
    Method Info     : 5% EtOH in hexanes, 40 min, AD-H, 1.0 mL/min

    Additional Info : Peak(s) manually integrated
```




```
    ======================================================================
                              Area Percent Report
    ======================================================================

    Sorted By             :      Signal
    Multiplier            :      1.0000
    Dilution              :      1.0000
    Do not use Multiplier & Dilution Factor with ISTDs


    Signal 1: DAD1 C, Sig=270,4 Ref=360,100

    Peak RetTime Type  Width     Area      Height     Area
      #   [min]        [min]   [mAU*s]     [mAU]       %
    ----|-------|----|-------|----------|----------|--------|
       1  25.191 BB    1.0060 1378.08496   20.82678  50.0940
       2  28.853 BB    1.1818 1372.91260   17.52743  49.9060

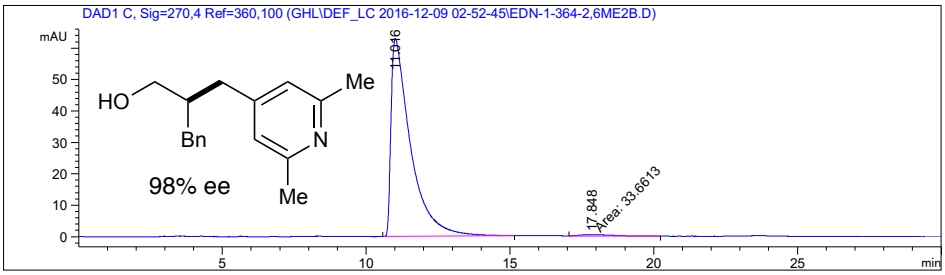
    Totals :                  2750.99756   38.35420


    ======================================================================
                              *** End of Report ***
```

Data File C:\CHEM32\2\DATA\GHL\DEF_LC 2016-12-09 02-52-45\EDN-1-364-2,6ME2B.D
Sample Name: EDN-1-364-2,6Me2b

```
    ======================================================================
    Acq. Operator   : SYSTEM                        Seq. Line :  13
    Acq. Instrument : Biggie                         Location : Vial 90
    Injection Date  : 12/9/2016 7:27:26 AM                Inj :   1
                                                   Inj Volume : 5.000 µl
    Acq. Method     : C:\CHEM32\2\DATA\GHL\DEF_LC 2016-12-09 02-52-45\5IPA30-AS.M
    Last changed    : 12/9/2016 2:52:45 AM by SYSTEM
    Analysis Method : C:\CHEM32\2\DATA\GHL\DEF_LC 2016-12-09 02-52-45\5IPA30-AS.M (Sequence
                      Method)
    Last changed    : 7/12/2017 9:57:31 AM by SYSTEM
                      (modified after loading)
    Method Info     : 5% IPA in hexanes, 30 min, AS-H, 1.0 mL/min

    Additional Info : Peak(s) manually integrated
```




```
    ======================================================================
                               Area Percent Report
    ======================================================================

    Sorted By             :      Signal
    Multiplier            :      1.0000
    Dilution              :      1.0000
    Do not use Multiplier & Dilution Factor with ISTDs


    Signal 1: DAD1 C, Sig=270,4 Ref=360,100

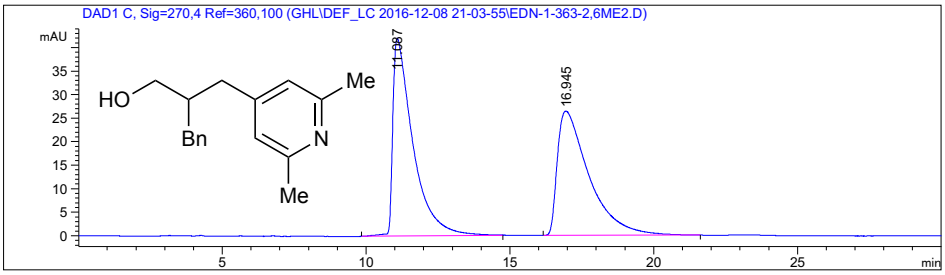
    Peak RetTime Type  Width     Area      Height     Area
      #   [min]        [min]   [mAU*s]     [mAU]       %
    ----|-------|----|-------|----------|----------|--------|
       1  11.016 BB    0.6868 2970.12012   62.90646  98.8794
       2  17.848 MM    1.2885   33.66129 4.35401e-1   1.1206

    Totals :                  3003.78140   63.34186


    ======================================================================
                               *** End of Report ***
```

Data File C:\CHEM32\2\DATA\GHL\DEF_LC 2016-12-08 21-03-55\EDN-1-363-2,6ME2.D
Sample Name: EDN-1-363-2,6Me2

```
    ======================================================================
    Acq. Operator    : SYSTEM                          Seq. Line :  14
    Acq. Instrument : Biggie                           Location : Vial 87
    Injection Date  : 12/9/2016 12:23:18 AM                 Inj :   1
                                                     Inj Volume : 5.000 µl
    Acq. Method     : C:\CHEM32\2\DATA\GHL\DEF_LC 2016-12-08 21-03-55\5IPA30-AS.M
    Last changed    : 12/8/2016 10:17:18 PM by SYSTEM
    Analysis Method : C:\CHEM32\2\DATA\GHL\DEF_LC 2016-12-08 21-03-55\5IPA30-AS.M (Sequence
                      Method)
    Last changed    : 7/12/2017 9:57:52 AM by SYSTEM
                      (modified after loading)
    Method Info     : 5% IPA in hexanes, 30 min, AS-H, 1.0 mL/min
```




```
    ======================================================================
                              Area Percent Report
    ======================================================================

    Sorted By             :      Signal
    Multiplier            :      1.0000
    Dilution              :      1.0000
    Do not use Multiplier & Dilution Factor with ISTDs


    Signal 1: DAD1 C, Sig=270,4 Ref=360,100

    Peak RetTime Type  Width     Area      Height     Area
      #   [min]        [min]   [mAU*s]     [mAU]       %
    ----|-------|----|-------|----------|----------|--------|
       1  11.087 BB    0.7178 2043.13818   41.97878  50.1474
       2  16.945 BB    1.0885 2031.12744   26.43368  49.8526

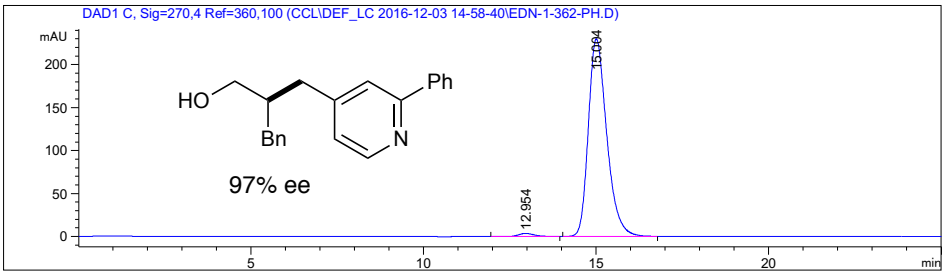
    Totals :                  4074.26563   68.41246


    ======================================================================
                              *** End of Report ***
```

Data File C:\CHEM32\2\DATA\CCL\DEF_LC 2016-12-03 14-58-40\EDN-1-362-PH.D
Sample Name: EDN-1-362-Ph

```
    ======================================================================
    Acq. Operator   : SYSTEM                        Seq. Line :  26
    Acq. Instrument : Biggie                         Location : Vial 86
    Injection Date  : 12/3/2016 10:28:15 PM               Inj :   1
                                                  Inj Volume : 5.000 µl
    Acq. Method     : C:\CHEM32\2\DATA\CCL\DEF_LC 2016-12-03 14-58-40\8ETOH25-AD.M
    Last changed    : 12/3/2016 9:11:17 PM by SYSTEM
    Analysis Method : C:\CHEM32\2\DATA\CCL\DEF_LC 2016-12-03 14-58-40\8ETOH25-AD.M (Sequence
                      Method)
    Last changed    : 7/12/2017 9:53:41 AM by SYSTEM
                      (modified after loading)
    Method Info     : 8% EtOH in hexanes, 25 min, AD-H, 1.0 mL/min

    Additional Info : Peak(s) manually integrated
```




```
    ======================================================================
                               Area Percent Report
    ======================================================================

    Sorted By             :      Signal
    Multiplier            :      1.0000
    Dilution              :      1.0000
    Do not use Multiplier & Dilution Factor with ISTDs


    Signal 1: DAD1 C, Sig=270,4 Ref=360,100

    Peak RetTime Type  Width     Area      Height     Area
      #   [min]        [min]   [mAU*s]     [mAU]       %
    ----|-------|----|-------|----------|----------|--------|
       1  12.954 BB    0.4866  114.90949    3.61692   1.3306
       2  15.004 BB    0.5683 8520.85449  229.93300  98.6694

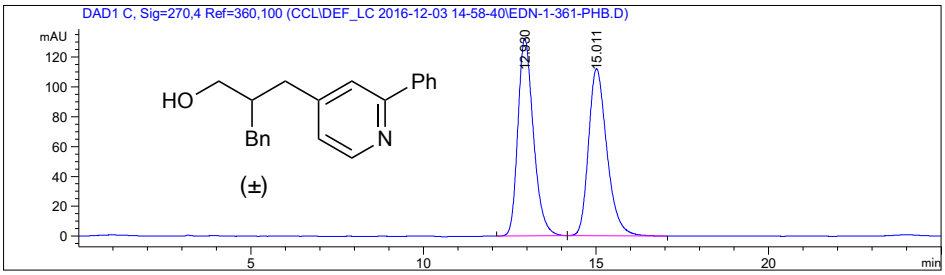
    Totals :                  8635.76398  233.54992


    ======================================================================
                               *** End of Report ***
```

Data File C:\CHEM32\2\DATA\CCL\DEF_LC 2016-12-03 14-58-40\EDN-1-361-PHB.D
Sample Name: EDN-1-361-Phb

```
    ======================================================================
    Acq. Operator   : SYSTEM                        Seq. Line :  25
    Acq. Instrument : Biggie                         Location : Vial 84
    Injection Date  : 12/3/2016 10:01:45 PM               Inj :   1
                                                  Inj Volume : 5.000 µl
    Acq. Method     : C:\CHEM32\2\DATA\CCL\DEF_LC 2016-12-03 14-58-40\8ETOH25-AD.M
    Last changed    : 12/3/2016 9:11:17 PM by SYSTEM
    Analysis Method : C:\CHEM32\2\DATA\CCL\DEF_LC 2016-12-03 14-58-40\8ETOH25-AD.M (Sequence
                      Method)
    Last changed    : 7/12/2017 9:53:41 AM by SYSTEM
                      (modified after loading)
    Method Info     : 8% EtOH in hexanes, 25 min, AD-H, 1.0 mL/min

    Additional Info : Peak(s) manually integrated
```




```
    ======================================================================
                               Area Percent Report
    ======================================================================

    Sorted By             :      Signal
    Multiplier            :      1.0000
    Dilution              :      1.0000
    Do not use Multiplier & Dilution Factor with ISTDs


    Signal 1: DAD1 C, Sig=270,4 Ref=360,100

    Peak RetTime Type  Width     Area      Height     Area
      #   [min]        [min]   [mAU*s]     [mAU]       %
    ----|-------|----|-------|----------|----------|--------|
       1  12.930 BB    0.4816 4134.17578  131.90829  49.9506
       2  15.011 BB    0.5665 4142.35010  111.74736  50.0494

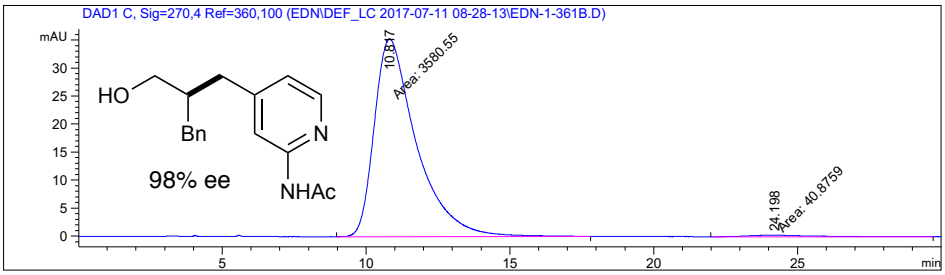
    Totals :                  8276.52588  243.65565


    ======================================================================
                               *** End of Report ***
```

Data File C:\CHEM32\2\DATA\EDN\DEF_LC 2017-07-11 08-28-13\EDN-1-361B.D
Sample Name: EDN-1-361b

```
    ======================================================================
    Acq. Operator   : SYSTEM                        Seq. Line :  23
    Acq. Instrument : Biggie                         Location : Vial 57
    Injection Date  : 7/11/2017 6:39:10 PM                Inj :   1
                                                   Inj Volume : 5.000 µl
    Acq. Method     : C:\CHEM32\2\DATA\EDN\DEF_LC 2017-07-11 08-28-13\5ETOH30-AS.M
    Last changed    : 7/11/2017 8:28:14 AM by SYSTEM
    Analysis Method : C:\CHEM32\2\DATA\EDN\DEF_LC 2017-07-11 08-28-13\5ETOH30-AS.M (Sequence
                      Method)
    Last changed    : 7/12/2017 9:01:00 AM by SYSTEM
                      (modified after loading)
    Method Info     : 5% EtOH in hexanes, 30 min, AS-H, 1.0 mL/min

    Additional Info : Peak(s) manually integrated
```




```
    ======================================================================
                               Area Percent Report
    ======================================================================

    Sorted By             :      Signal
    Multiplier            :      1.0000
    Dilution              :      1.0000
    Do not use Multiplier & Dilution Factor with ISTDs


    Signal 1: DAD1 C, Sig=270,4 Ref=360,100

    Peak RetTime Type  Width     Area      Height     Area
      #   [min]        [min]   [mAU*s]     [mAU]       %
    ----|-------|----|-------|----------|----------|--------|
       1  10.817 MM    1.6911 3580.54932   35.28786  98.8713
       2  24.198 MM    2.5231   40.87590 2.70012e-1   1.1287

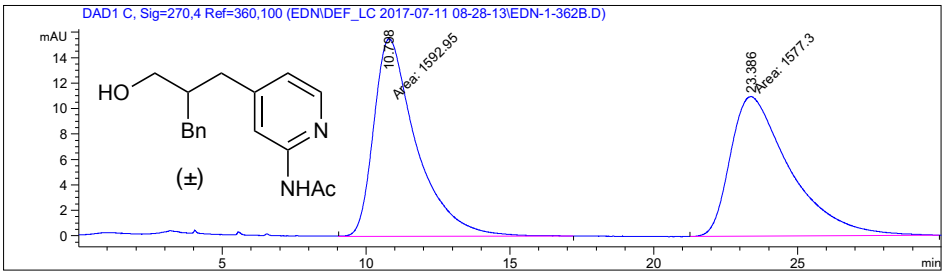
    Totals :                  3621.42522   35.55788


    ======================================================================
                               *** End of Report ***
```

Data File C:\CHEM32\2\DATA\EDN\DEF_LC 2017-07-11 08-28-13\EDN-1-362B.D
Sample Name: EDN-1-362b

```
    ======================================================================
    Acq. Operator   : SYSTEM                        Seq. Line :  24
    Acq. Instrument : Biggie                         Location : Vial 58
    Injection Date  : 7/11/2017 7:10:46 PM                Inj :   1
                                                  Inj Volume : 5.000 µl
    Acq. Method     : C:\CHEM32\2\DATA\EDN\DEF_LC 2017-07-11 08-28-13\5ETOH30-AS.M
    Last changed    : 7/11/2017 8:28:14 AM by SYSTEM
    Analysis Method : C:\CHEM32\2\DATA\EDN\DEF_LC 2017-07-11 08-28-13\5ETOH30-AS.M (Sequence
                      Method)
    Last changed    : 7/12/2017 9:01:00 AM by SYSTEM
                      (modified after loading)
    Method Info     : 5% EtOH in hexanes, 30 min, AS-H, 1.0 mL/min

    Additional Info : Peak(s) manually integrated
```




```
    ======================================================================
                               Area Percent Report
    ======================================================================

    Sorted By             :      Signal
    Multiplier            :      1.0000
    Dilution              :      1.0000
    Do not use Multiplier & Dilution Factor with ISTDs


    Signal 1: DAD1 C, Sig=270,4 Ref=360,100

    Peak RetTime Type  Width     Area      Height     Area
      #   [min]        [min]   [mAU*s]     [mAU]       %
    ----|-------|----|-------|----------|----------|--------|
       1  10.798 MM    1.7108 1592.95020   15.51888  50.2468
       2  23.386 MM    2.3951 1577.30286   10.97604  49.7532

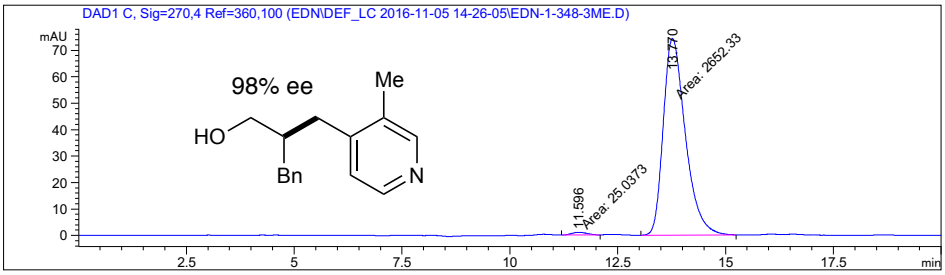
    Totals :                  3170.25305   26.49492


    ======================================================================
                               *** End of Report ***
```

Data File C:\CHEM32\2\DATA\EDN\DEF_LC 2016-11-05 14-26-05\EDN-1-348-3ME.D
Sample Name: edn-1-348-3Me

```
    ======================================================================
    Acq. Operator   : SYSTEM                        Seq. Line :   7
    Acq. Instrument : Biggie                         Location : Vial 12
    Injection Date  : 11/5/2016 4:53:52 PM                Inj :   1
                                                  Inj Volume : 5.000 µl
    Acq. Method     : C:\CHEM32\2\DATA\EDN\DEF_LC 2016-11-05 14-26-05\10ETOH20-AD.M
    Last changed    : 11/5/2016 4:41:28 PM by SYSTEM
    Analysis Method : C:\CHEM32\2\DATA\EDN\DEF_LC 2016-11-05 14-26-05\10ETOH20-AD.M (Sequence
                      Method)
    Last changed    : 7/12/2017 8:47:48 AM by SYSTEM
    Method Info     : 10% EtOH in hexanes, 20 min, AD-H, 1.0 mL/min

    Additional Info : Peak(s) manually integrated
```




```
    ======================================================================
                              Area Percent Report
    ======================================================================

    Sorted By             :      Signal
    Multiplier            :      1.0000
    Dilution              :      1.0000
    Do not use Multiplier & Dilution Factor with ISTDs


    Signal 1: DAD1 C, Sig=270,4 Ref=360,100

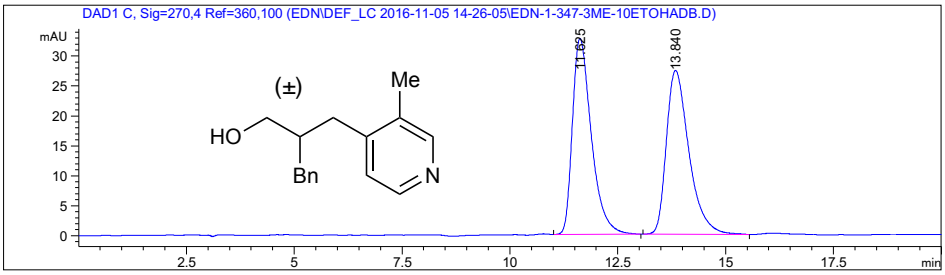
    Peak RetTime Type  Width     Area      Height     Area
      #   [min]        [min]   [mAU*s]     [mAU]       %
    ----|-------|----|-------|----------|----------|--------|
       1  11.596 MM    0.4103   25.03733    1.01697   0.9351
       2  13.770 MM    0.5945 2652.33374   74.35678  99.0649

    Totals :                  2677.37107   75.37375


    ======================================================================
                              *** End of Report ***
```

Data File C:\CHEM32\2\DATA\EDN\DEF_LC 2016-11-05 14-26-05\EDN-1-347-3ME-10ETOHADB.D
Sample Name: edn-1-347-3Me-10EtOHADb

```
    ======================================================================
    Acq. Operator   : SYSTEM                        Seq. Line :   6
    Acq. Instrument : Biggie                         Location : Vial 11
    Injection Date  : 11/5/2016 4:22:24 PM                Inj :   1
                                                  Inj Volume : 5.000 µl
    Acq. Method     : C:\CHEM32\2\DATA\EDN\DEF_LC 2016-11-05 14-26-05\10ETOH30-AD.M
    Last changed    : 11/5/2016 2:26:06 PM by SYSTEM
    Analysis Method : C:\CHEM32\2\DATA\EDN\DEF_LC 2016-11-05 14-26-05\10ETOH30-AD.M (Sequence
                      Method)
    Last changed    : 7/12/2017 9:31:21 AM by SYSTEM
                      (modified after loading)
    Method Info     : 10% EtOH in hexanes, 30 min, AD-H, 1.0 mL/min
```




```
    ======================================================================
                              Area Percent Report
    ======================================================================

    Sorted By             :      Signal
    Multiplier            :      1.0000
    Dilution              :      1.0000
    Do not use Multiplier & Dilution Factor with ISTDs


    Signal 1: DAD1 C, Sig=270,4 Ref=360,100

    Peak RetTime Type  Width     Area      Height     Area
      #   [min]        [min]   [mAU*s]     [mAU]       %
    ----|-------|----|-------|----------|----------|--------|
       1  11.625 BB    0.4679  997.85852   32.70863  50.0478
       2  13.840 BB    0.5588  995.95441   27.35552  49.9522

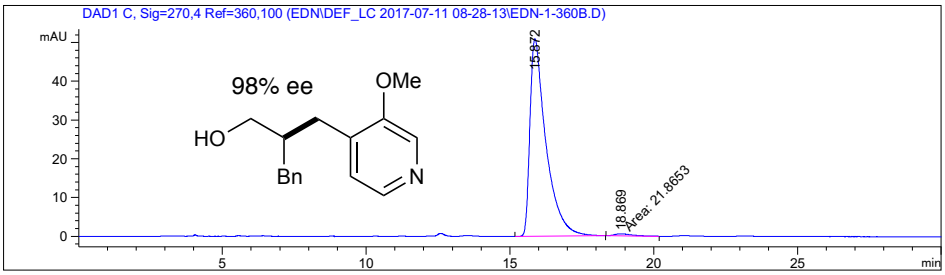
    Totals :                  1993.81293   60.06415


    ======================================================================
                              *** End of Report ***
```

Data File C:\CHEM32\2\DATA\EDN\DEF_LC 2017-07-11 08-28-13\EDN-1-360B.D
Sample Name: EDN-1-360b

```
    ======================================================================
    Acq. Operator   : SYSTEM                        Seq. Line :  20
    Acq. Instrument : Biggie                         Location : Vial 56
    Injection Date  : 7/11/2017 5:04:29 PM                Inj :   1
                                                  Inj Volume : 5.000 µl
    Acq. Method     : C:\CHEM32\2\DATA\EDN\DEF_LC 2017-07-11 08-28-13\5ETOH30-AS.M
    Last changed    : 7/11/2017 8:28:14 AM by SYSTEM
    Analysis Method : C:\CHEM32\2\DATA\EDN\DEF_LC 2017-07-11 08-28-13\5ETOH30-AS.M (Sequence
                      Method)
    Last changed    : 7/12/2017 9:01:00 AM by SYSTEM
                      (modified after loading)
    Method Info     : 5% EtOH in hexanes, 30 min, AS-H, 1.0 mL/min

    Additional Info : Peak(s) manually integrated
```




```
    ======================================================================
                               Area Percent Report
    ======================================================================

    Sorted By             :      Signal
    Multiplier            :      1.0000
    Dilution              :      1.0000
    Do not use Multiplier & Dilution Factor with ISTDs


    Signal 1: DAD1 C, Sig=270,4 Ref=360,100

    Peak RetTime Type  Width     Area      Height     Area
      #   [min]        [min]   [mAU*s]     [mAU]       %
    ----|-------|----|-------|----------|----------|--------|
       1  15.872 BB    0.5603 1975.66357   50.95513  98.9054
       2  18.869 MM    0.6788   21.86530 5.36884e-1   1.0946

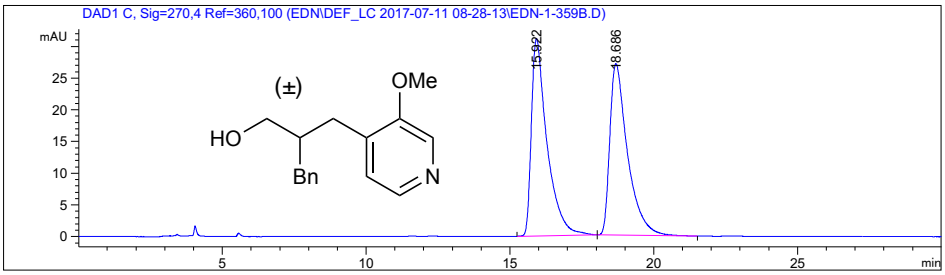
    Totals :                  1997.52887   51.49201


    ======================================================================
                               *** End of Report ***
```

Data File C:\CHEM32\2\DATA\EDN\DEF_LC 2017-07-11 08-28-13\EDN-1-359B.D
Sample Name: EDN-1-359b

```
    ======================================================================
    Acq. Operator   : SYSTEM                        Seq. Line :  19
    Acq. Instrument : Biggie                         Location : Vial 55
    Injection Date  : 7/11/2017 4:32:56 PM                Inj :   1
                                                   Inj Volume : 5.000 µl
    Acq. Method     : C:\CHEM32\2\DATA\EDN\DEF_LC 2017-07-11 08-28-13\5ETOH30-AS.M
    Last changed    : 7/11/2017 8:28:14 AM by SYSTEM
    Analysis Method : C:\CHEM32\2\DATA\EDN\DEF_LC 2017-07-11 08-28-13\5ETOH30-AS.M (Sequence
                      Method)
    Last changed    : 7/12/2017 9:01:00 AM by SYSTEM
                      (modified after loading)
    Method Info     : 5% EtOH in hexanes, 30 min, AS-H, 1.0 mL/min

    Additional Info : Peak(s) manually integrated
```




```
    ======================================================================
                               Area Percent Report
    ======================================================================

    Sorted By             :      Signal
    Multiplier            :      1.0000
    Dilution              :      1.0000
    Do not use Multiplier & Dilution Factor with ISTDs


    Signal 1: DAD1 C, Sig=270,4 Ref=360,100

    Peak RetTime Type  Width     Area      Height     Area
      #   [min]        [min]   [mAU*s]     [mAU]       %
    ----|-------|----|-------|----------|----------|--------|
       1  15.922 BB    0.5479 1177.77258   31.09594  50.3679
       2  18.686 BB    0.6285 1160.56653   27.05550  49.6321

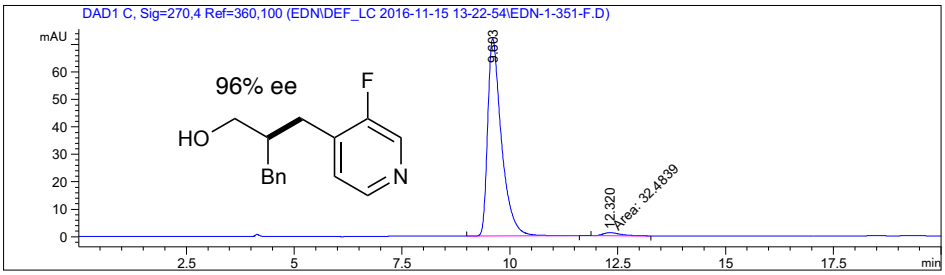
    Totals :                  2338.33911   58.15144


    ======================================================================
                               *** End of Report ***
```

Data File C:\CHEM32\2\DATA\EDN\DEF_LC 2016-11-15 13-22-54\EDN-1-351-F.D
Sample Name: EDN-1-351-F

```
    ======================================================================
    Acq. Operator   : SYSTEM                        Seq. Line :   3
    Acq. Instrument : Biggie                         Location : Vial 63
    Injection Date  : 11/15/2016 1:56:21 PM               Inj :   1
                                                   Inj Volume : 5.000 µl
    Acq. Method     : C:\CHEM32\2\DATA\EDN\DEF_LC 2016-11-15 13-22-54\10IPA20-AS.M
    Last changed    : 11/15/2016 1:22:55 PM by SYSTEM
    Analysis Method : C:\CHEM32\2\DATA\EDN\DEF_LC 2016-11-15 13-22-54\10IPA20-AS.M (Sequence
                      Method)
    Last changed    : 7/12/2017 9:35:59 AM by SYSTEM
                      (modified after loading)
    Method Info     : 10% IPA in hexanes, 20 min, AS-H, 1.0 mL/min

    Additional Info : Peak(s) manually integrated
```




```
    ======================================================================
                               Area Percent Report
    ======================================================================

    Sorted By             :      Signal
    Multiplier            :      1.0000
    Dilution              :      1.0000
    Do not use Multiplier & Dilution Factor with ISTDs


    Signal 1: DAD1 C, Sig=270,4 Ref=360,100

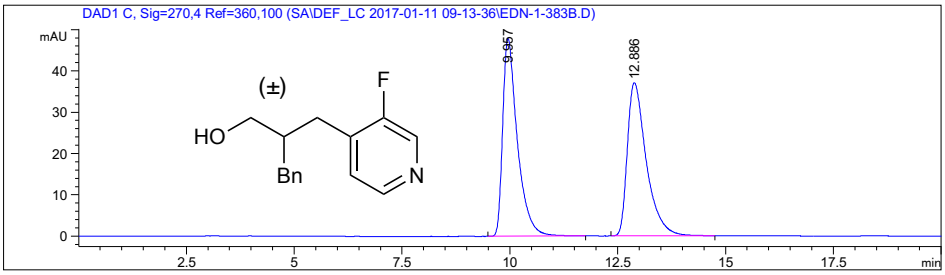
    Peak RetTime Type  Width     Area      Height     Area
      #   [min]        [min]   [mAU*s]     [mAU]       %
    ----|-------|----|-------|----------|----------|--------|
       1   9.603 BB    0.3297 1599.65784   71.85580  98.0097
       2  12.320 MM    0.4599   32.48386    1.17729   1.9903

    Totals :                  1632.14169   73.03308


    ======================================================================
                               *** End of Report ***
```

Data File C:\CHEM32\2\DATA\SA\DEF_LC 2017-01-11 09-13-36\EDN-1-383B.D
Sample Name: EDN-1-383b

```
==================================================================
Acq. Operator   : SYSTEM                       Seq. Line :   9
Acq. Instrument : Biggie                        Location : Vial 14
Injection Date  : 1/11/2017 11:53:05 AM              Inj :   1
                                               Inj Volume : 5.000 µl
Acq. Method     : C:\CHEM32\2\DATA\SA\DEF_LC 2017-01-11 09-13-36\10IPA20-AS.M
Last changed    : 1/11/2017 9:30:27 AM by SYSTEM
Analysis Method : C:\CHEM32\2\DATA\SA\DEF_LC 2017-01-11 09-13-36\10IPA20-AS.M (Sequence
                  Method)
Last changed    : 7/12/2017 10:19:57 AM by SYSTEM
                  (modified after loading)
Method Info     : 10% IPA in hexanes, 20 min, AS-H, 1.0 mL/min
```




```
==================================================================
                        Area Percent Report
==================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Do not use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 C, Sig=270,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   9.957 BB    0.3498 1131.47546   47.87123  49.9472
   2  12.886 BB    0.4648 1133.86938   37.07629  50.0528

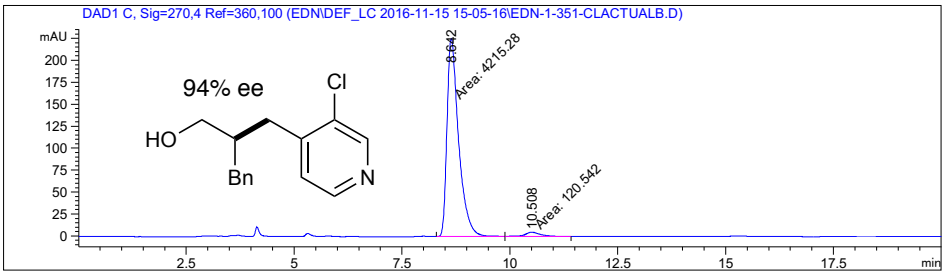
Totals :                  2265.34485   84.94752


==================================================================
                        *** End of Report ***
```

Data File C:\CHEM32\2\DATA\EDN\DEF_LC 2016-11-15 15-05-16\EDN-1-351-CLACTUALB.D
Sample Name: EDN-1-351-Clactualb

```
    ======================================================================
    Acq. Operator    : SYSTEM                          Seq. Line :   3
    Acq. Instrument  : Biggie                           Location : Vial 64
    Injection Date   : 11/15/2016 3:38:45 PM                 Inj :   1
                                                      Inj Volume : 5.000 µl
    Acq. Method      : C:\CHEM32\2\DATA\EDN\DEF_LC 2016-11-15 15-05-16\10IPA20-AS.M
    Last changed     : 11/15/2016 3:05:16 PM by SYSTEM
    Analysis Method  : C:\CHEM32\2\DATA\EDN\DEF_LC 2016-11-15 15-05-16\10IPA20-AS.M (Sequence
                       Method)
    Last changed     : 7/12/2017 9:42:17 AM by SYSTEM
                       (modified after loading)
    Method Info      : 10% IPA in hexanes, 20 min, AS-H, 1.0 mL/min

    Additional Info : Peak(s) manually integrated
```




```
    ======================================================================
                              Area Percent Report
    ======================================================================

    Sorted By             :      Signal
    Multiplier            :      1.0000
    Dilution              :      1.0000
    Do not use Multiplier & Dilution Factor with ISTDs


    Signal 1: DAD1 C, Sig=270,4 Ref=360,100

    Peak RetTime Type  Width     Area      Height     Area
      #   [min]        [min]   [mAU*s]     [mAU]       %
    ----|-------|----|-------|----------|----------|--------|
       1   8.642 MM    0.3120 4215.27881  225.15773  97.2199
       2  10.508 MM    0.4165  120.54182    4.82378   2.7801

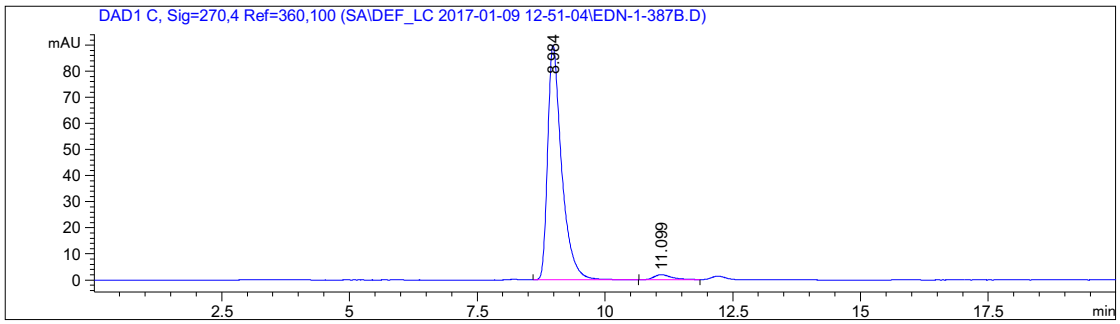
    Totals :                  4335.82063  229.98151


    ======================================================================
                              *** End of Report ***
```

Data File C:\CHEM32\2\DATA\SA\DEF_LC 2017-01-09 12-51-04\EDN-1-387B.D
Sample Name: EDN-1-387b

```
==========================================================================
Acq. Operator   : SYSTEM                          Seq. Line :  27
Acq. Instrument : Biggie                          Location : Vial 13
Injection Date  : 1/10/2017 12:13:03 AM                Inj :   1
                                                  Inj Volume : 5.000 µl
Acq. Method     : C:\CHEM32\2\DATA\SA\DEF_LC 2017-01-09 12-51-04\10IPA20-AS.M
Last changed    : 1/9/2017 9:30:07 PM by SYSTEM
Analysis Method : C:\CHEM32\2\DATA\SA\DEF_LC 2017-01-09 12-51-04\10IPA20-AS.M (Sequence
                  Method)
Last changed    : 7/12/2017 10:21:34 AM by SYSTEM
                  (modified after loading)
Method Info     : 10% IPA in hexanes, 20 min, AS-H, 1.0 mL/min

Additional Info : Peak(s) manually integrated
```




```
==========================================================================
                          Area Percent Report
==========================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Do not use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 C, Sig=270,4 Ref=360,100

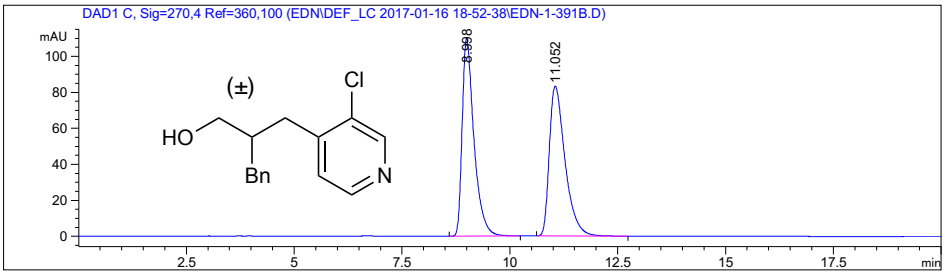
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   8.984 BB    0.2821 1709.11560   89.76730  97.3467
   2  11.099 BB    0.3589   46.58413    1.93502   2.6533

Totals :                  1755.69973   91.70231

==========================================================================
                          *** End of Report ***
```

Data File C:\CHEM32\2\DATA\EDN\DEF_LC 2017-01-16 18-52-38\EDN-1-391B.D
Sample Name: EDN-1-391b

```
    ======================================================================
    Acq. Operator   : SYSTEM                        Seq. Line :   3
    Acq. Instrument : Biggie                         Location : Vial 20
    Injection Date  : 1/16/2017 7:26:23 PM                Inj :   1
                                                  Inj Volume : 5.000 µl
    Acq. Method     : C:\CHEM32\2\DATA\EDN\DEF_LC 2017-01-16 18-52-38\10IPA20-AS.M
    Last changed    : 1/16/2017 6:52:38 PM by SYSTEM
    Analysis Method : C:\CHEM32\2\DATA\EDN\DEF_LC 2017-01-16 18-52-38\10IPA20-AS.M (Sequence
                      Method)
    Last changed    : 7/12/2017 10:25:45 AM by SYSTEM
                      (modified after loading)
    Method Info     : 10% IPA in hexanes, 20 min, AS-H, 1.0 mL/min
```




```
    ======================================================================
                            Area Percent Report
    ======================================================================

    Sorted By             :      Signal
    Multiplier            :      1.0000
    Dilution              :      1.0000
    Do not use Multiplier & Dilution Factor with ISTDs


    Signal 1: DAD1 C, Sig=270,4 Ref=360,100

    Peak RetTime Type  Width     Area      Height     Area
      #   [min]        [min]   [mAU*s]     [mAU]       %
    ----|-------|----|-------|----------|----------|--------|
       1   8.998 BB    0.2842 2091.03931  109.80045  49.8511
       2  11.052 BB    0.3849 2103.53320   83.23116  50.1489

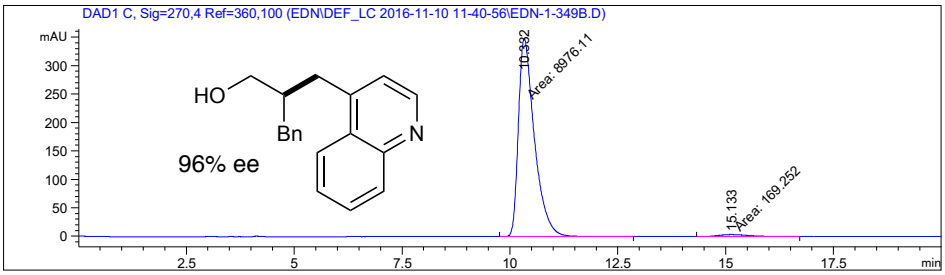
    Totals :                  4194.57251  193.03160


    ======================================================================
                            *** End of Report ***
```

Data File C:\CHEM32\2\DATA\EDN\DEF_LC 2016-11-10 11-40-56\EDN-1-349B.D
Sample Name: EDN-1-349b

```
    ======================================================================
    Acq. Operator   : SYSTEM                        Seq. Line :   3
    Acq. Instrument : Biggie                         Location : Vial 91
    Injection Date  : 11/10/2016 12:14:13 PM              Inj :   1
                                                   Inj Volume : 5.000 µl
    Acq. Method     : C:\CHEM32\2\DATA\EDN\DEF_LC 2016-11-10 11-40-56\10IPA20-AS.M
    Last changed    : 11/10/2016 11:40:56 AM by SYSTEM
    Analysis Method : C:\CHEM32\2\DATA\EDN\DEF_LC 2016-11-10 11-40-56\10IPA20-AS.M (Sequence
                      Method)
    Last changed    : 7/12/2017 10:01:25 AM by SYSTEM
                      (modified after loading)
    Method Info     : 10% IPA in hexanes, 20 min, AS-H, 1.0 mL/min

    Additional Info : Peak(s) manually integrated
```




```
    ======================================================================
                               Area Percent Report
    ======================================================================

    Sorted By             :      Signal
    Multiplier            :      1.0000
    Dilution              :      1.0000
    Do not use Multiplier & Dilution Factor with ISTDs


    Signal 1: DAD1 C, Sig=270,4 Ref=360,100

    Peak RetTime Type  Width     Area      Height     Area
      #   [min]        [min]   [mAU*s]     [mAU]       %
    ----|-------|----|-------|----------|----------|--------|
       1  10.332 MM    0.4303 8976.10938  347.65024  98.1493
       2  15.133 MM    0.7986  169.25209    3.53217   1.8507

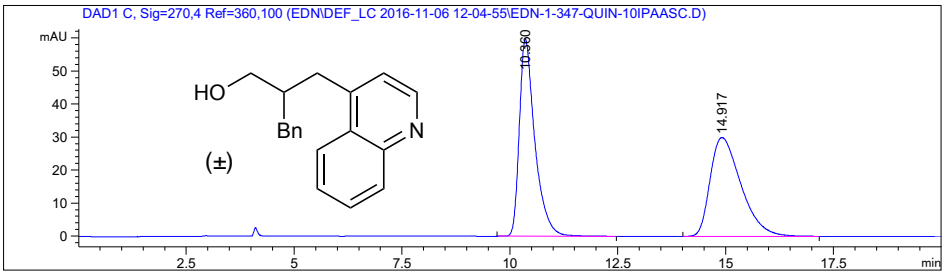
    Totals :                  9145.36147  351.18241


    ======================================================================
                               *** End of Report ***
```

Data File C:\CHEM32\2\DATA\EDN\DEF_LC 2016-11-06 12-04-55\EDN-1-347-QUIN-10IPAASC.D
Sample Name: edn-1-347-quin-10IPAASc

```
    ======================================================================
    Acq. Operator   : SYSTEM                        Seq. Line :   4
    Acq. Instrument : Biggie                         Location : Vial 13
    Injection Date  : 11/6/2016 12:59:53 PM               Inj :   1
                                                   Inj Volume : 5.000 µl
    Acq. Method     : C:\CHEM32\2\DATA\EDN\DEF_LC 2016-11-06 12-04-55\10IPA20-AS.M
    Last changed    : 11/6/2016 12:06:57 PM by SYSTEM
    Analysis Method : C:\CHEM32\2\DATA\EDN\DEF_LC 2016-11-06 12-04-55\10IPA20-AS.M (Sequence
                      Method)
    Last changed    : 7/12/2017 10:00:15 AM by SYSTEM
                      (modified after loading)
    Method Info     : 10% IPA in hexanes, 20 min, AS-H, 1.0 mL/min

    Additional Info : Peak(s) manually integrated
```




```
    ======================================================================
                               Area Percent Report
    ======================================================================

    Sorted By             :      Signal
    Multiplier            :      1.0000
    Dilution              :      1.0000
    Do not use Multiplier & Dilution Factor with ISTDs


    Signal 1: DAD1 C, Sig=270,4 Ref=360,100

    Peak RetTime Type  Width     Area      Height     Area
      #   [min]        [min]   [mAU*s]     [mAU]       %
    ----|-------|----|-------|----------|----------|--------|
       1  10.360 BB    0.3694 1493.40332   59.79351  50.1351
       2  14.917 BB    0.7653 1485.35425   29.91398  49.8649

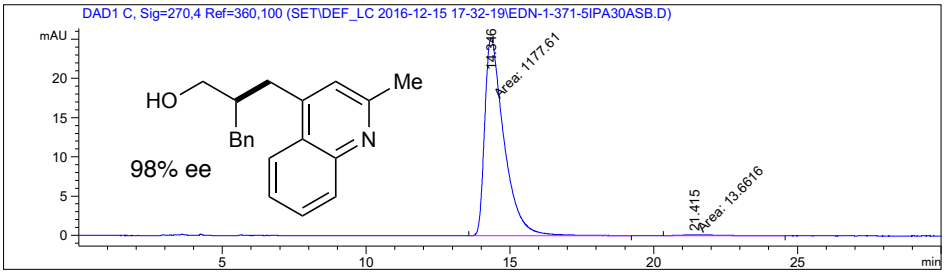
    Totals :                  2978.75757   89.70749


    ======================================================================
                               *** End of Report ***
```

Data File C:\CHEM32\2\DATA\SET\DEF_LC 2016-12-15 17-32-19\EDN-1-371-5IPA30ASB.D
Sample Name: EDN-1-371-5IPA30ASb

```
    ======================================================================
    Acq. Operator   : SYSTEM                        Seq. Line :  16
    Acq. Instrument : Biggie                         Location : Vial 84
    Injection Date  : 12/15/2016 10:34:41 PM              Inj :   1
                                                   Inj Volume : 5.000 µl
    Different Inj Volume from Sample Entry!  Actual Inj Volume : 2.000 µl
    Acq. Method     : C:\CHEM32\2\DATA\SET\DEF_LC 2016-12-15 17-32-19\5IPA30-AS.M
    Last changed    : 12/15/2016 8:21:34 PM by SYSTEM
    Analysis Method : C:\CHEM32\2\DATA\SET\DEF_LC 2016-12-15 17-32-19\5IPA30-AS.M (Sequence
                      Method)
    Last changed    : 7/12/2017 10:02:52 AM by SYSTEM
                      (modified after loading)
    Method Info     : 5% IPA in hexanes, 30 min, AS-H, 1.0 mL/min

    Additional Info : Peak(s) manually integrated
```




```
    ======================================================================
                            Area Percent Report
    ======================================================================

    Sorted By             :      Signal
    Multiplier            :      1.0000
    Dilution              :      1.0000
    Do not use Multiplier & Dilution Factor with ISTDs


    Signal 1: DAD1 C, Sig=270,4 Ref=360,100

    Peak RetTime Type  Width     Area      Height     Area
      #   [min]        [min]   [mAU*s]     [mAU]       %
    ----|-------|----|-------|----------|----------|--------|
       1  14.346 MM    0.7783 1177.60693   25.21682  98.8532
       2  21.415 MM    1.6567   13.66158 1.37440e-1   1.1468

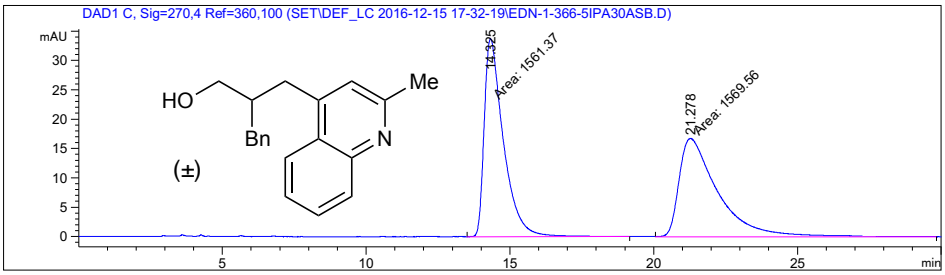
    Totals :                  1191.26851   25.35426


    ======================================================================
                            *** End of Report ***
```

Data File C:\CHEM32\2\DATA\SET\DEF_LC 2016-12-15 17-32-19\EDN-1-366-5IPA30ASB.D
Sample Name: EDN-1-366-5IPA30ASb

```
    ======================================================================
    Acq. Operator   : SYSTEM                        Seq. Line :  15
    Acq. Instrument : Biggie                         Location : Vial 83
    Injection Date  : 12/15/2016 10:03:16 PM              Inj :   1
                                                   Inj Volume : 5.000 µl
    Acq. Method     : C:\CHEM32\2\DATA\SET\DEF_LC 2016-12-15 17-32-19\5IPA30-AS.M
    Last changed    : 12/15/2016 8:21:34 PM by SYSTEM
    Analysis Method : C:\CHEM32\2\DATA\SET\DEF_LC 2016-12-15 17-32-19\5IPA30-AS.M (Sequence
                      Method)
    Last changed    : 7/12/2017 10:02:52 AM by SYSTEM
                      (modified after loading)
    Method Info     : 5% IPA in hexanes, 30 min, AS-H, 1.0 mL/min

    Additional Info : Peak(s) manually integrated
```




```
    ======================================================================
                               Area Percent Report
    ======================================================================

    Sorted By             :      Signal
    Multiplier            :      1.0000
    Dilution              :      1.0000
    Do not use Multiplier & Dilution Factor with ISTDs


    Signal 1: DAD1 C, Sig=270,4 Ref=360,100

    Peak RetTime Type  Width     Area      Height     Area
      #   [min]        [min]   [mAU*s]     [mAU]       %
    ----|-------|----|-------|----------|----------|--------|
       1  14.325 MM    0.7723 1561.36719   33.69340  49.8691
       2  21.278 MM    1.5640 1569.56226   16.72633  50.1309

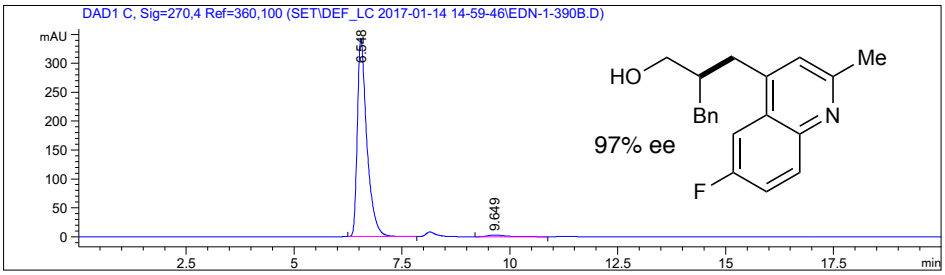
    Totals :                  3130.92944   50.41973


    ======================================================================
                               *** End of Report ***
```

Data File C:\CHEM32\2\DATA\SET\DEF_LC 2017-01-14 14-59-46\EDN-1-390B.D
Sample Name: EDN-1-390b

```
    ======================================================================
    Acq. Operator   : SYSTEM                        Seq. Line :   6
    Acq. Instrument : Biggie                         Location : Vial 19
    Injection Date  : 1/14/2017 4:59:05 PM                Inj :   1
                                                  Inj Volume : 5.000 µl
    Acq. Method     : C:\CHEM32\2\DATA\SET\DEF_LC 2017-01-14 14-59-46\10IPA20-AS.M
    Last changed    : 1/14/2017 3:13:07 PM by SYSTEM
    Analysis Method : C:\CHEM32\2\DATA\SET\DEF_LC 2017-01-14 14-59-46\10IPA20-AS.M (Sequence
                      Method)
    Last changed    : 7/12/2017 10:15:51 AM by SYSTEM
                      (modified after loading)
    Method Info     : 10% IPA in hexanes, 20 min, AS-H, 1.0 mL/min

    Additional Info : Peak(s) manually integrated
```




```
    ======================================================================
                               Area Percent Report
    ======================================================================

    Sorted By             :      Signal
    Multiplier            :      1.0000
    Dilution              :      1.0000
    Do not use Multiplier & Dilution Factor with ISTDs


    Signal 1: DAD1 C, Sig=270,4 Ref=360,100

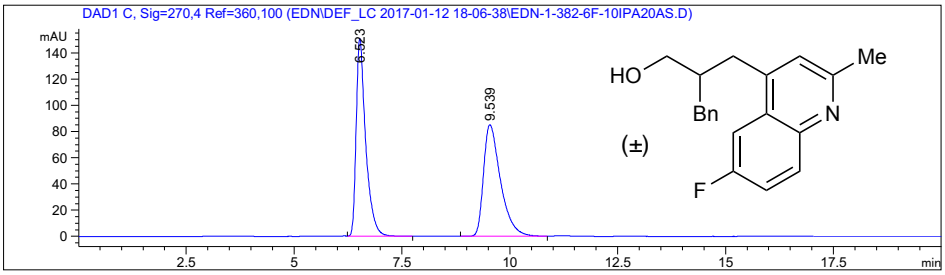
    Peak RetTime Type  Width     Area      Height     Area
      #   [min]        [min]   [mAU*s]     [mAU]       %
    ----|-------|----|-------|----------|----------|--------|
       1   6.548 BB    0.2256 5271.37012  342.45544  98.4375
       2   9.649 BB    0.4158   83.67407    2.92436   1.5625

    Totals :                   5355.04419  345.37981

    ======================================================================
                               *** End of Report ***
```

Data File C:\CHEM32\2\DATA\EDN\DEF_LC 2017-01-12 18-06-38\EDN-1-382-6F-10IPA20AS.D
Sample Name: EDN-1-382-6F-10IPA20AS

```
    ======================================================================
    Acq. Operator   : SYSTEM                        Seq. Line :   4
    Acq. Instrument : Biggie                         Location : Vial 17
    Injection Date  : 1/12/2017 7:02:23 PM               Inj :   1
                                                   Inj Volume : 5.000 µl
    Acq. Method     : C:\CHEM32\2\DATA\EDN\DEF_LC 2017-01-12 18-06-38\10IPA20-AS.M
    Last changed    : 1/12/2017 6:06:59 PM by SYSTEM
    Analysis Method : C:\CHEM32\2\DATA\EDN\DEF_LC 2017-01-12 18-06-38\10IPA20-AS.M (Sequence
                      Method)
    Last changed    : 7/12/2017 10:08:02 AM by SYSTEM
                      (modified after loading)
    Method Info     : 10% IPA in hexanes, 20 min, AS-H, 1.0 mL/min
```




```
    ======================================================================
                              Area Percent Report
    ======================================================================

    Sorted By             :      Signal
    Multiplier            :      1.0000
    Dilution              :      1.0000
    Do not use Multiplier & Dilution Factor with ISTDs


    Signal 1: DAD1 C, Sig=270,4 Ref=360,100

    Peak RetTime Type  Width     Area      Height     Area
      #   [min]        [min]   [mAU*s]     [mAU]       %
    ----|-------|----|-------|----------|----------|--------|
       1   6.523 BB    0.2244 2305.33447  150.79849  49.8527
       2   9.539 BB    0.4099 2318.96045   85.10048  50.1473

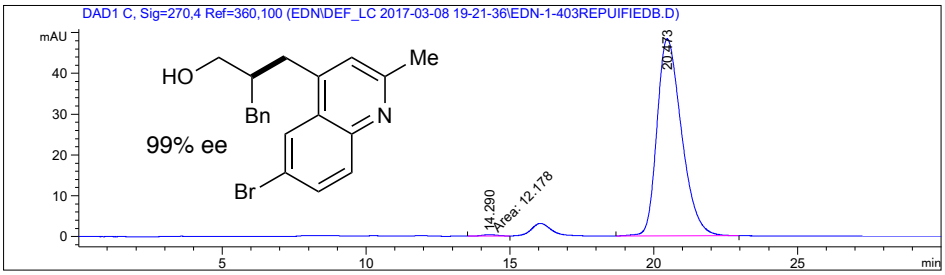
    Totals :                   4624.29492  235.89897

    ======================================================================
                              *** End of Report ***
```

Data File C:\CHEM32\2\DATA\EDN\DEF_LC 2017-03-08 19-21-36\EDN-1-403REPUIFIEDB.D
Sample Name: EDN-1-403repuifiedb

```
    ======================================================================
    Acq. Operator   : SYSTEM                        Seq. Line :   3
    Acq. Instrument : Biggie                         Location : Vial 35
    Injection Date  : 3/8/2017 8:05:14 PM                 Inj :   1
                                                  Inj Volume : 5.000 µl
    Acq. Method     : C:\CHEM32\2\DATA\EDN\DEF_LC 2017-03-08 19-21-36\10IPA30-OD.M
    Last changed    : 3/8/2017 7:21:36 PM by SYSTEM
    Analysis Method : C:\CHEM32\2\DATA\EDN\DEF_LC 2017-03-08 19-21-36\10IPA30-OD.M (Sequence
                      Method)
    Last changed    : 7/12/2017 10:39:13 AM by SYSTEM
                      (modified after loading)
    Method Info     : 10% IPA in hexanes, 30 min, OD-H, 1.0 mL/min

    Additional Info : Peak(s) manually integrated
```




```
    ======================================================================
                               Area Percent Report
    ======================================================================

    Sorted By             :      Signal
    Multiplier            :      1.0000
    Dilution              :      1.0000
    Do not use Multiplier & Dilution Factor with ISTDs


    Signal 1: DAD1 C, Sig=270,4 Ref=360,100

    Peak RetTime Type  Width     Area      Height     Area
      #   [min]        [min]   [mAU*s]     [mAU]       %
    ----|-------|----|-------|----------|----------|--------|
       1  14.290 MM    0.6088   12.17799 3.33379e-1   0.4233
       2  20.473 BB    0.9061 2864.51660   48.28809  99.5767

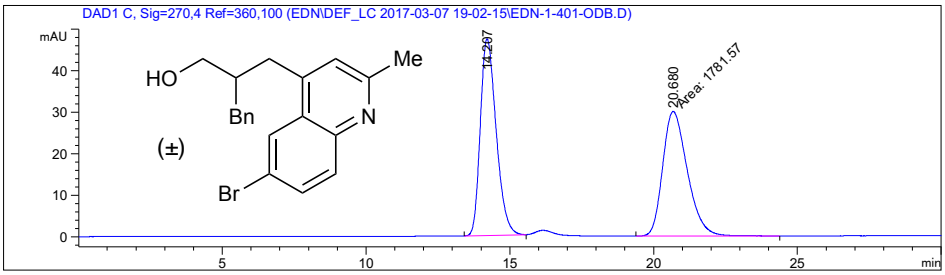
    Totals :                  2876.69459   48.62147


    ======================================================================
                               *** End of Report ***
```

Data File C:\CHEM32\2\DATA\EDN\DEF_LC 2017-03-07 19-02-15\EDN-1-401-ODB.D
Sample Name: EDN-1-401-ODb

```
    ======================================================================
    Acq. Operator   : SYSTEM                        Seq. Line :   3
    Acq. Instrument : Biggie                         Location : Vial 34
    Injection Date  : 3/7/2017 7:46:00 PM                 Inj :   1
                                                  Inj Volume : 5.000 µl
    Acq. Method     : C:\CHEM32\2\DATA\EDN\DEF_LC 2017-03-07 19-02-15\10IPA30-OD.M
    Last changed    : 3/7/2017 7:02:15 PM by SYSTEM
    Analysis Method : C:\CHEM32\2\DATA\EDN\DEF_LC 2017-03-07 19-02-15\10IPA30-OD.M (Sequence
                      Method)
    Last changed    : 7/12/2017 10:38:06 AM by SYSTEM
                      (modified after loading)
    Method Info     : 10% IPA in hexanes, 30 min, OD-H, 1.0 mL/min

    Additional Info : Peak(s) manually integrated
```




```
    ======================================================================
                               Area Percent Report
    ======================================================================

    Sorted By             :      Signal
    Multiplier            :      1.0000
    Dilution              :      1.0000
    Do not use Multiplier & Dilution Factor with ISTDs


    Signal 1: DAD1 C, Sig=270,4 Ref=360,100

    Peak RetTime Type  Width     Area      Height     Area
      #   [min]        [min]   [mAU*s]     [mAU]       %
    ----|-------|----|-------|----------|----------|--------|
       1  14.207 BB    0.5932 1814.00049   47.32883  50.4510
       2  20.680 MM    0.9900 1781.56921   29.99210  49.5490

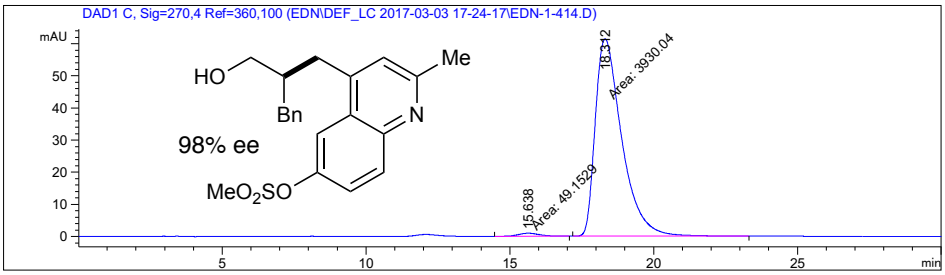
    Totals :                  3595.56970   77.32092


    ======================================================================
                               *** End of Report ***
```

Data File C:\CHEM32\2\DATA\EDN\DEF_LC 2017-03-03 17-24-17\EDN-1-414.D
Sample Name: EDN-1-414

```
    ======================================================================
    Acq. Operator    : SYSTEM                          Seq. Line :   4
    Acq. Instrument : Biggie                           Location : Vial 22
    Injection Date  : 3/3/2017 6:39:55 PM                  Inj :   1
                                                      Inj Volume : 5.000 µl
    Acq. Method     : C:\CHEM32\2\DATA\EDN\DEF_LC 2017-03-03 17-24-17\20IPA30-OD.M
    Last changed    : 3/3/2017 5:24:17 PM by SYSTEM
    Analysis Method : C:\CHEM32\2\DATA\EDN\DEF_LC 2017-03-03 17-24-17\20IPA30-OD.M (Sequence
                      Method)
    Last changed    : 7/12/2017 10:41:17 AM by SYSTEM
                      (modified after loading)
    Method Info     : 20% IPA in hexanes, 30 min, OD-H, 1.0 mL/min

    Additional Info : Peak(s) manually integrated
```




```
    ======================================================================
                               Area Percent Report
    ======================================================================

    Sorted By             :      Signal
    Multiplier            :      1.0000
    Dilution              :      1.0000
    Do not use Multiplier & Dilution Factor with ISTDs


    Signal 1: DAD1 C, Sig=270,4 Ref=360,100

    Peak RetTime Type  Width     Area      Height     Area
      #   [min]        [min]   [mAU*s]     [mAU]       %
    ----|-------|----|-------|----------|----------|--------|
       1  15.638 MM    0.8563   49.15291 9.56688e-1   1.2352
       2  18.312 MM    1.0666 3930.04346   61.41174  98.7648

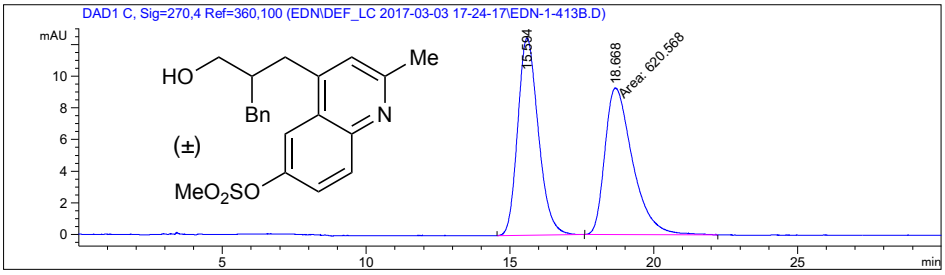
    Totals :                  3979.19637   62.36843


    ======================================================================
                               *** End of Report ***
```

Data File C:\CHEM32\2\DATA\EDN\DEF_LC 2017-03-03 17-24-17\EDN-1-413B.D
Sample Name: EDN-1-413b

```
    ======================================================================
    Acq. Operator   : SYSTEM                        Seq. Line :   3
    Acq. Instrument : Biggie                         Location : Vial 21
    Injection Date  : 3/3/2017 6:08:24 PM                Inj :   1
                                                   Inj Volume : 5.000 µl
    Different Inj Volume from Sample Entry!  Actual Inj Volume : 2.000 µl
    Acq. Method     : C:\CHEM32\2\DATA\EDN\DEF_LC 2017-03-03 17-24-17\20IPA30-OD.M
    Last changed    : 3/3/2017 5:24:17 PM by SYSTEM
    Analysis Method : C:\CHEM32\2\DATA\EDN\DEF_LC 2017-03-03 17-24-17\20IPA30-OD.M (Sequence
                      Method)
    Last changed    : 7/12/2017 10:41:17 AM by SYSTEM
                      (modified after loading)
    Method Info     : 20% IPA in hexanes, 30 min, OD-H, 1.0 mL/min

    Additional Info : Peak(s) manually integrated
```




```
    ======================================================================
                            Area Percent Report
    ======================================================================

    Sorted By             :      Signal
    Multiplier            :      1.0000
    Dilution              :      1.0000
    Do not use Multiplier & Dilution Factor with ISTDs


    Signal 1: DAD1 C, Sig=270,4 Ref=360,100

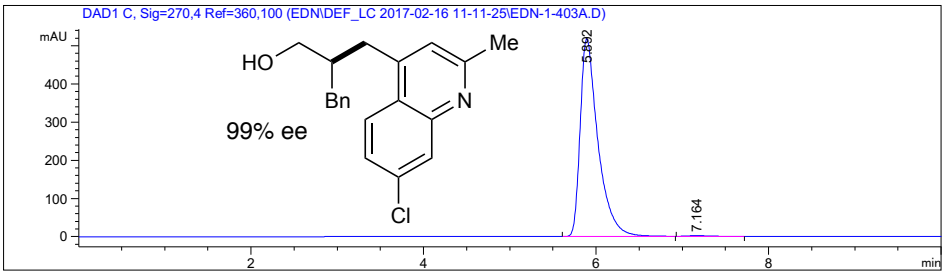
    Peak RetTime Type  Width     Area      Height     Area
      #   [min]        [min]   [mAU*s]     [mAU]       %
    ----|-------|----|-------|----------|----------|--------|
       1  15.594 BB    0.7562  619.96552   12.46588  49.9757
       2  18.668 MM    1.1153  620.56769    9.27387  50.0243

    Totals :                  1240.53320   21.73976


    ======================================================================
                            *** End of Report ***
```

Data File C:\CHEM32\2\DATA\EDN\DEF_LC 2017-02-16 11-11-25\EDN-1-403A.D
Sample Name: edn-1-402A

```
    ======================================================================
    Acq. Operator   : SYSTEM                        Seq. Line :   2
    Acq. Instrument : Biggie                         Location : Vial 58
    Injection Date  : 2/16/2017 11:23:44 AM               Inj :   1
                                                   Inj Volume : 5.000 µl
    Different Inj Volume from Sample Entry!  Actual Inj Volume : 10.000 µl
    Acq. Method     : C:\CHEM32\2\DATA\EDN\DEF_LC 2017-02-16 11-11-25\10IPA10-AS.M
    Last changed    : 2/16/2017 11:11:25 AM by SYSTEM
    Analysis Method : C:\CHEM32\2\DATA\EDN\DEF_LC 2017-02-16 11-11-25\10IPA10-AS.M (Sequence
                      Method)
    Last changed    : 7/12/2017 10:35:29 AM by SYSTEM
                      (modified after loading)
    Method Info     : 10% IPA in hexanes, 10 min, AS-H, 1.0 mL/min
```




```
    ======================================================================
                               Area Percent Report
    ======================================================================

    Sorted By             :      Signal
    Multiplier            :      1.0000
    Dilution              :      1.0000
    Do not use Multiplier & Dilution Factor with ISTDs


    Signal 1: DAD1 C, Sig=270,4 Ref=360,100

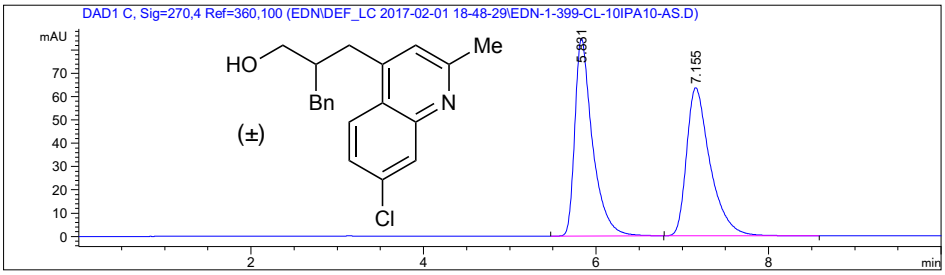
    Peak RetTime Type  Width     Area      Height     Area
      #   [min]        [min]   [mAU*s]     [mAU]       %
    ----|-------|----|-------|----------|----------|--------|
       1   5.892 BB    0.2110 7416.41064  518.11096  99.5796
       2   7.164 BB    0.2725   31.31009    1.78599   0.4204

    Totals :                  7447.72074  519.89695


    ======================================================================
                               *** End of Report ***
```

Data File C:\CHEM32\2\DATA\EDN\DEF_LC 2017-02-01 18-48-29\EDN-1-399-CL-10IPA10-AS.D
Sample Name: EDN-1-399-Cl-10IPA10-AS

```
    ======================================================================
    Acq. Operator    : SYSTEM                        Seq. Line :   3
    Acq. Instrument : Biggie                          Location : Vial 55
    Injection Date  : 2/1/2017 7:22:48 PM                 Inj :   1
                                                    Inj Volume : 5.000 µl
    Acq. Method     : C:\CHEM32\2\DATA\EDN\DEF_LC 2017-02-01 18-48-29\10IPA10-AS.M
    Last changed    : 2/1/2017 7:10:34 PM by SYSTEM
    Analysis Method : C:\CHEM32\2\DATA\EDN\DEF_LC 2017-02-01 18-48-29\10IPA10-AS.M (Sequence
                      Method)
    Last changed    : 7/12/2017 10:33:13 AM by SYSTEM
                      (modified after loading)
    Method Info     : 10% IPA in hexanes, 10 min, AS-H, 1.0 mL/min
```




```
    ======================================================================
                              Area Percent Report
    ======================================================================

    Sorted By             :      Signal
    Multiplier            :      1.0000
    Dilution              :      1.0000
    Do not use Multiplier & Dilution Factor with ISTDs


    Signal 1: DAD1 C, Sig=270,4 Ref=360,100

    Peak RetTime Type  Width     Area      Height     Area
      #   [min]        [min]   [mAU*s]     [mAU]       %
    ----|-------|----|-------|----------|----------|--------|
       1   5.831 BB    0.2078 1205.45764   84.82709  49.9844
       2   7.155 BB    0.2815 1206.21167   63.52610  50.0156

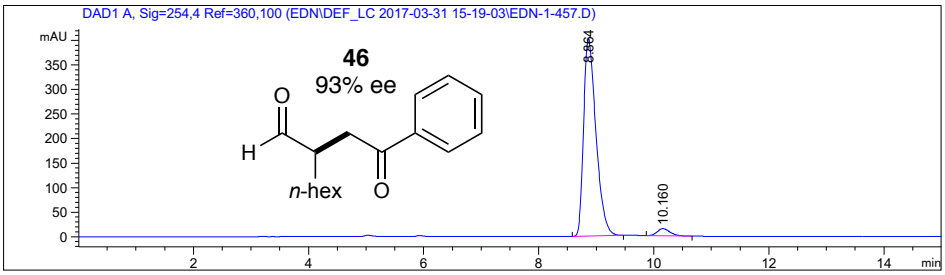
    Totals :                   2411.66931  148.35319


    ======================================================================
                              *** End of Report ***
```

Data File C:\CHEM32\2\DATA\EDN\DEF_LC 2017-03-31 15-19-03\EDN-1-457.D
Sample Name: EDN-1-457

```
    ======================================================================
    Acq. Operator   : SYSTEM                        Seq. Line :   3
    Acq. Instrument : Biggie                         Location : Vial 22
    Injection Date  : 3/31/2017 4:02:18 PM               Inj :   1
                                                   Inj Volume : 5.000 µl
    Acq. Method     : C:\CHEM32\2\DATA\EDN\DEF_LC 2017-03-31 15-19-03\5IPA15-OD.M
    Last changed    : 3/31/2017 3:19:03 PM by SYSTEM
    Analysis Method : C:\CHEM32\2\DATA\EDN\DEF_LC 2017-03-31 15-19-03\5IPA15-OD.M (Sequence
                      Method)
    Last changed    : 7/12/2017 10:55:19 AM by SYSTEM
                      (modified after loading)
    Method Info     : 5% IPA in hexanes, 15 min, OD-H, 1.0 mL/min

    Additional Info : Peak(s) manually integrated
```




```
    ======================================================================
                               Area Percent Report
    ======================================================================

    Sorted By             :      Signal
    Multiplier            :      1.0000
    Dilution              :      1.0000
    Do not use Multiplier & Dilution Factor with ISTDs


    Signal 1: DAD1 A, Sig=254,4 Ref=360,100

    Peak RetTime Type  Width     Area      Height     Area
      #   [min]        [min]   [mAU*s]     [mAU]       %
    ----|-------|----|-------|----------|----------|--------|
       1   8.864 BB    0.2302 6006.71191  402.20395  96.3978
       2  10.160 BB    0.2356  224.46104   14.58199   3.6022

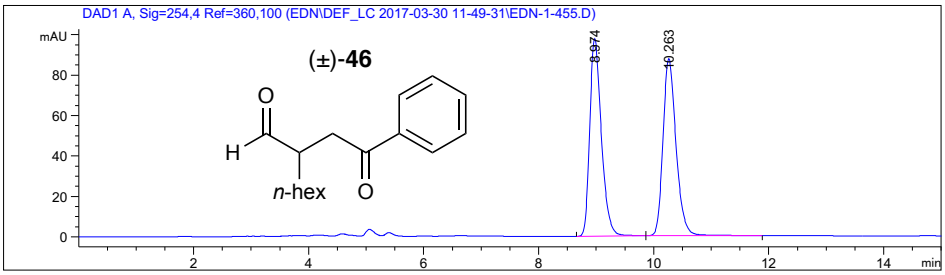
    Totals :                  6231.17296  416.78594


    ======================================================================
                               *** End of Report ***
```

Data File C:\CHEM32\2\DATA\EDN\DEF_LC 2017-03-30 11-49-31\EDN-1-455.D
Sample Name: EDN-1-455

```
    ======================================================================
    Acq. Operator    : SYSTEM                          Seq. Line :  15
    Acq. Instrument : Biggie                           Location : Vial 21
    Injection Date  : 3/30/2017 4:02:58 PM                 Inj :   1
                                                     Inj Volume : 5.000 µl
    Acq. Method     : C:\CHEM32\2\DATA\EDN\DEF_LC 2017-03-30 11-49-31\5IPA15-OD.M
    Last changed    : 3/30/2017 2:17:44 PM by SYSTEM
    Analysis Method : C:\CHEM32\2\DATA\EDN\DEF_LC 2017-03-30 11-49-31\5IPA15-OD.M (Sequence
                      Method)
    Last changed    : 7/12/2017 10:44:01 AM by SYSTEM
                      (modified after loading)
    Method Info     : 5% IPA in hexanes, 15 min, OD-H, 1.0 mL/min

    Additional Info : Peak(s) manually integrated
```




```
    ======================================================================
                               Area Percent Report
    ======================================================================

    Sorted By             :      Signal
    Multiplier            :      1.0000
    Dilution              :      1.0000
    Do not use Multiplier & Dilution Factor with ISTDs


    Signal 1: DAD1 A, Sig=254,4 Ref=360,100

    Peak RetTime Type  Width     Area      Height     Area
      #   [min]        [min]   [mAU*s]     [mAU]       %
    ----|-------|----|-------|----------|----------|--------|
       1   8.974 BB    0.2136 1368.74939   97.58306  49.8327
       2  10.263 BB    0.2418 1377.93872   87.46998  50.1673

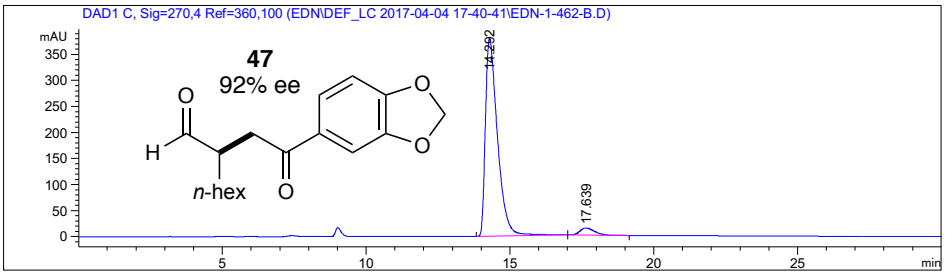
    Totals :                  2746.68811  185.05304


    ======================================================================
                               *** End of Report ***
```

Data File C:\CHEM32\2\DATA\EDN\DEF_LC 2017-04-04 17-40-41\EDN-1-462-B.D
Sample Name: EDN-1-462-b

```
    ======================================================================
    Acq. Operator    : SYSTEM                          Seq. Line :   3
    Acq. Instrument : Biggie                           Location : Vial 24
    Injection Date  : 4/4/2017 6:24:16 PM                  Inj :   1
                                                     Inj Volume : 5.000 µl
    Acq. Method     : C:\CHEM32\2\DATA\EDN\DEF_LC 2017-04-04 17-40-41\5IPA30-OD.M
    Last changed    : 4/4/2017 5:40:42 PM by SYSTEM
    Analysis Method : C:\CHEM32\2\DATA\EDN\DEF_LC 2017-04-04 17-40-41\5IPA30-OD.M (Sequence
                      Method)
    Last changed    : 7/12/2017 10:49:27 AM by SYSTEM
                      (modified after loading)
    Method Info     : 5% IPA in hexanes, 30 min, OD-H, 1.0 mL/min

    Additional Info : Peak(s) manually integrated
```




```
    ======================================================================
                               Area Percent Report
    ======================================================================

    Sorted By             :      Signal
    Multiplier            :      1.0000
    Dilution              :      1.0000
    Do not use Multiplier & Dilution Factor with ISTDs


    Signal 1: DAD1 C, Sig=270,4 Ref=360,100

    Peak RetTime Type  Width     Area      Height     Area
      #   [min]        [min]   [mAU*s]     [mAU]       %
    ----|-------|----|-------|----------|----------|--------|
       1  14.292 BB    0.4418 1.11128e4   379.36121  95.8847
       2  17.639 BB    0.5346  476.95032   13.68663   4.1153

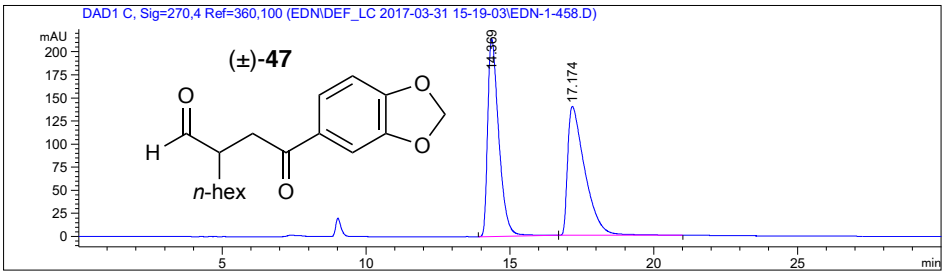
    Totals :                  1.15898e4   393.04783


    ======================================================================
                               *** End of Report ***
```

Data File C:\CHEM32\2\DATA\EDN\DEF_LC 2017-03-31 15-19-03\EDN-1-458.D
Sample Name: EDN-1-458

```
    ======================================================================
    Acq. Operator    : SYSTEM                          Seq. Line :   6
    Acq. Instrument : Biggie                           Location : Vial 23
    Injection Date  : 3/31/2017 5:06:57 PM                 Inj :   1
                                                     Inj Volume : 5.000 µl
    Acq. Method     : C:\CHEM32\2\DATA\EDN\DEF_LC 2017-03-31 15-19-03\5IPA30-OD.M
    Last changed    : 3/31/2017 3:19:03 PM by SYSTEM
    Analysis Method : C:\CHEM32\2\DATA\EDN\DEF_LC 2017-03-31 15-19-03\5IPA30-OD.M (Sequence
                      Method)
    Last changed    : 7/12/2017 10:47:09 AM by SYSTEM
                      (modified after loading)
    Method Info     : 5% IPA in hexanes, 30 min, OD-H, 1.0 mL/min

    Additional Info : Peak(s) manually integrated
```




```
    ======================================================================
                               Area Percent Report
    ======================================================================

    Sorted By             :      Signal
    Multiplier            :      1.0000
    Dilution              :      1.0000
    Do not use Multiplier & Dilution Factor with ISTDs


    Signal 1: DAD1 C, Sig=270,4 Ref=360,100

    Peak RetTime Type  Width     Area      Height     Area
      #   [min]        [min]   [mAU*s]     [mAU]       %
    ----|-------|----|-------|----------|----------|--------|
       1  14.369 BB    0.4074 5750.84766  214.08357  49.7459
       2  17.174 BB    0.6111 5809.59863  139.72382  50.2541

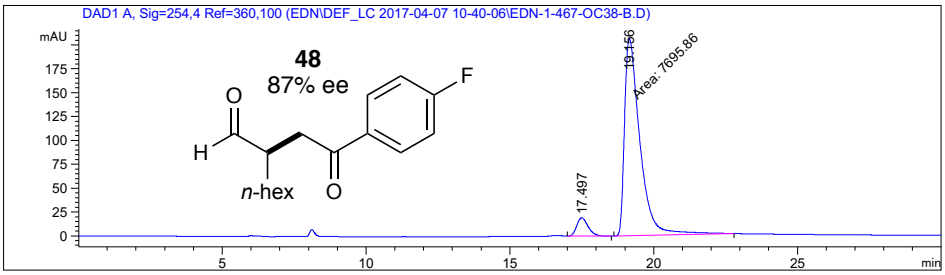
    Totals :                  1.15604e4   353.80739


    ======================================================================
                               *** End of Report ***
```

Data File C:\CHEM32\2\DATA\EDN\DEF_LC 2017-04-07 10-40-06\EDN-1-467-OC38-B.D
Sample Name: EDN-1-467-OC38-b

```
    ======================================================================
    Acq. Operator   : SYSTEM                        Seq. Line :   4
    Acq. Instrument : Biggie                         Location : Vial 23
    Injection Date  : 4/7/2017 12:05:24 PM                Inj :   1
                                                  Inj Volume : 5.000 µl
    Acq. Method     : C:\CHEM32\2\DATA\EDN\DEF_LC 2017-04-07 10-40-06\0.5IPA30-OD.M
    Last changed    : 4/7/2017 10:40:07 AM by SYSTEM
    Analysis Method : C:\CHEM32\2\DATA\EDN\DEF_LC 2017-04-07 10-40-06\0.5IPA30-OD.M (Sequence
                      Method)
    Last changed    : 7/12/2017 10:53:48 AM by SYSTEM
                      (modified after loading)
    Method Info     : 0.5% IPA in hexanes, 30 min, OD-H, 1.0 mL/min

    Additional Info : Peak(s) manually integrated
```




```
    ======================================================================
                               Area Percent Report
    ======================================================================

    Sorted By             :      Signal
    Multiplier            :      1.0000
    Dilution              :      1.0000
    Do not use Multiplier & Dilution Factor with ISTDs


    Signal 1: DAD1 A, Sig=254,4 Ref=360,100

    Peak RetTime Type  Width     Area      Height     Area
      #   [min]        [min]   [mAU*s]     [mAU]       %
    ----|-------|----|-------|----------|----------|--------|
       1  17.497 BB    0.4236  526.23383   19.21211   6.4002
       2  19.156 MM    0.6214 7695.86182  206.39928  93.5998

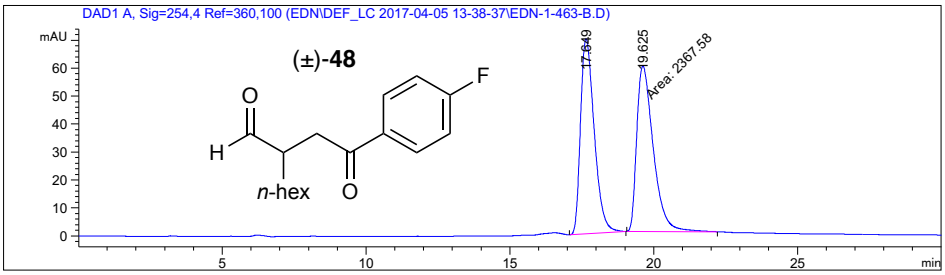
    Totals :                  8222.09564  225.61139


    ======================================================================
                               *** End of Report ***
```

Data File C:\CHEM32\2\DATA\EDN\DEF_LC 2017-04-05 13-38-37\EDN-1-463-B.D
Sample Name: EDN-1-463-b

```
    ======================================================================
    Acq. Operator   : SYSTEM                        Seq. Line :  14
    Acq. Instrument : Biggie                         Location : Vial 21
    Injection Date  : 4/5/2017 6:51:32 PM                 Inj :   1
                                                  Inj Volume : 5.000 µl
    Acq. Method     : C:\CHEM32\2\DATA\EDN\DEF_LC 2017-04-05 13-38-37\0.5IPA30-OD.M
    Last changed    : 4/5/2017 4:20:06 PM by SYSTEM
    Analysis Method : C:\CHEM32\2\DATA\EDN\DEF_LC 2017-04-05 13-38-37\0.5IPA30-OD.M (Sequence
                      Method)
    Last changed    : 7/12/2017 10:51:23 AM by SYSTEM
                      (modified after loading)
    Method Info     : 0.5% IPA in hexanes, 30 min, OD-H, 1.0 mL/min

    Additional Info : Peak(s) manually integrated
```




```
    ======================================================================
                               Area Percent Report
    ======================================================================

    Sorted By             :      Signal
    Multiplier            :      1.0000
    Dilution              :      1.0000
    Do not use Multiplier & Dilution Factor with ISTDs


    Signal 1: DAD1 A, Sig=254,4 Ref=360,100

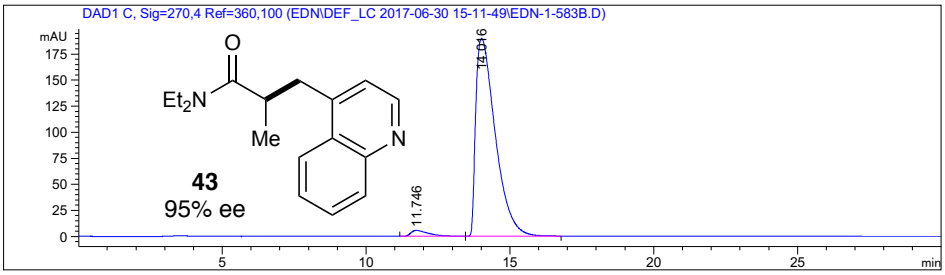
    Peak RetTime Type  Width     Area      Height     Area
      #   [min]        [min]   [mAU*s]     [mAU]       %
    ----|-------|----|-------|----------|----------|--------|
       1  17.649 BB    0.5130 2314.18018   69.76556  49.4297
       2  19.625 MM    0.6664 2367.58252   59.21370  50.5703

    Totals :                  4681.76270  128.97926


    ======================================================================
                               *** End of Report ***
```

Data File C:\CHEM32\2\DATA\EDN\DEF_LC 2017-06-30 15-11-49\EDN-1-583B.D
Sample Name: EDN-1-583b

```
    ======================================================================
    Acq. Operator    : SYSTEM                          Seq. Line :   3
    Acq. Instrument : Biggie                           Location : Vial 41
    Injection Date  : 6/30/2017 3:55:07 PM                 Inj :   1
                                                     Inj Volume : 5.000 µl
    Acq. Method     : C:\CHEM32\2\DATA\EDN\DEF_LC 2017-06-30 15-11-49\5IPA30-AS.M
    Last changed    : 6/30/2017 3:11:49 PM by SYSTEM
    Analysis Method : C:\CHEM32\2\DATA\EDN\DEF_LC 2017-06-30 15-11-49\5IPA30-AS.M (Sequence
                      Method)
    Last changed    : 7/12/2017 8:52:31 AM by SYSTEM
                      (modified after loading)
    Method Info     : 5% IPA in hexanes, 30 min, AS-H, 1.0 mL/min
```




```
    ======================================================================
                              Area Percent Report
    ======================================================================

    Sorted By             :      Signal
    Multiplier            :      1.0000
    Dilution              :      1.0000
    Do not use Multiplier & Dilution Factor with ISTDs


    Signal 1: DAD1 C, Sig=270,4 Ref=360,100

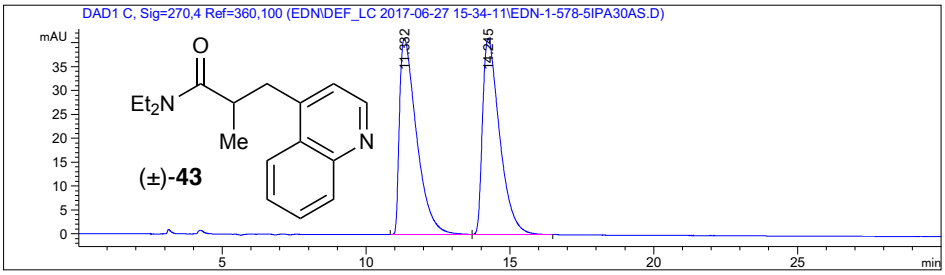
    Peak RetTime Type  Width     Area      Height     Area
      #   [min]        [min]   [mAU*s]     [mAU]       %
    ----|-------|----|-------|----------|----------|--------|
       1  11.746 BB    0.5897  231.77420    5.61322   2.5279
       2  14.016 BB    0.7237 8936.82520  189.68474  97.4721

    Totals :                  9168.59940  195.29796

    ======================================================================
                              *** End of Report ***
```

Data File C:\CHEM32\2\DATA\EDN\DEF_LC 2017-06-27 15-34-11\EDN-1-578-5IPA30AS.D
Sample Name: EDN-1-578-5IPA30AS

```
    ======================================================================
    Acq. Operator   : SYSTEM                        Seq. Line :   7
    Acq. Instrument : Biggie                         Location : Vial 41
    Injection Date  : 6/27/2017 4:53:31 PM                Inj :   1
                                                  Inj Volume : 5.000 µl
    Acq. Method     : C:\CHEM32\2\DATA\EDN\DEF_LC 2017-06-27 15-34-11\5IPA30-AS.M
    Last changed    : 6/27/2017 4:40:55 PM by SYSTEM
    Analysis Method : C:\CHEM32\2\DATA\EDN\DEF_LC 2017-06-27 15-34-11\5IPA30-AS.M (Sequence
                      Method)
    Last changed    : 7/12/2017 8:51:44 AM by SYSTEM
                      (modified after loading)
    Method Info     : 5% IPA in hexanes, 30 min, AS-H, 1.0 mL/min
```




```
    ======================================================================
                            Area Percent Report
    ======================================================================

    Sorted By             :      Signal
    Multiplier            :      1.0000
    Dilution              :      1.0000
    Do not use Multiplier & Dilution Factor with ISTDs


    Signal 1: DAD1 C, Sig=270,4 Ref=360,100

    Peak RetTime Type  Width     Area      Height     Area
      #   [min]        [min]   [mAU*s]     [mAU]       %
    ----|-------|----|-------|----------|----------|--------|
       1  11.332 BB    0.6205 1690.04517   41.03645  49.9927
       2  14.245 BB    0.6270 1690.53748   41.00703  50.0073

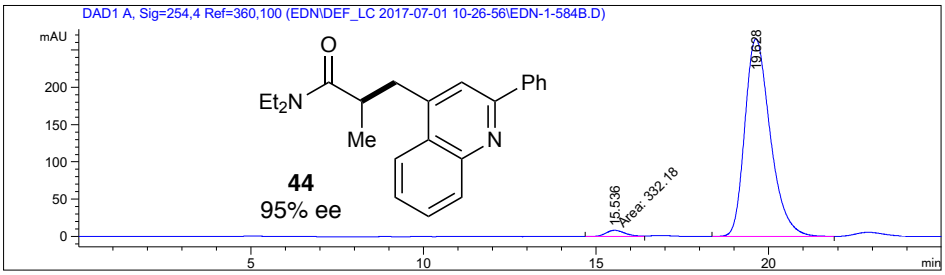
    Totals :                  3380.58264   82.04348


    ======================================================================
                              *** End of Report ***
```

Data File C:\CHEM32\2\DATA\EDN\DEF_LC 2017-07-01 10-26-56\EDN-1-584B.D
Sample Name: EDN-1-584b

```
    ======================================================================
    Acq. Operator   : SYSTEM                        Seq. Line :   3
    Acq. Instrument : Biggie                         Location : Vial 41
    Injection Date  : 7/1/2017 11:05:22 AM               Inj :   1
                                                   Inj Volume : 5.000 µl
    Acq. Method     : C:\CHEM32\2\DATA\EDN\DEF_LC 2017-07-01 10-26-56\1IPA25-AD.M
    Last changed    : 7/1/2017 10:26:56 AM by SYSTEM
    Analysis Method : C:\CHEM32\2\DATA\EDN\DEF_LC 2017-07-01 10-26-56\1IPA25-AD.M (Sequence
                      Method)
    Last changed    : 7/12/2017 8:54:58 AM by SYSTEM
                      (modified after loading)
    Method Info     : 1% IPA in hexanes, 25 min, AD-H, 1.0 mL/min

    Additional Info : Peak(s) manually integrated
```




```
    ======================================================================
                               Area Percent Report
    ======================================================================

    Sorted By             :      Signal
    Multiplier            :      1.0000
    Dilution              :      1.0000
    Do not use Multiplier & Dilution Factor with ISTDs


    Signal 1: DAD1 A, Sig=254,4 Ref=360,100

    Peak RetTime Type  Width     Area      Height     Area
      #   [min]        [min]   [mAU*s]     [mAU]       %
    ----|-------|----|-------|----------|----------|--------|
       1  15.536 MM    0.6560  332.17975    8.43964   2.3911
       2  19.628 BB    0.7874 1.35603e4   264.80692  97.6089

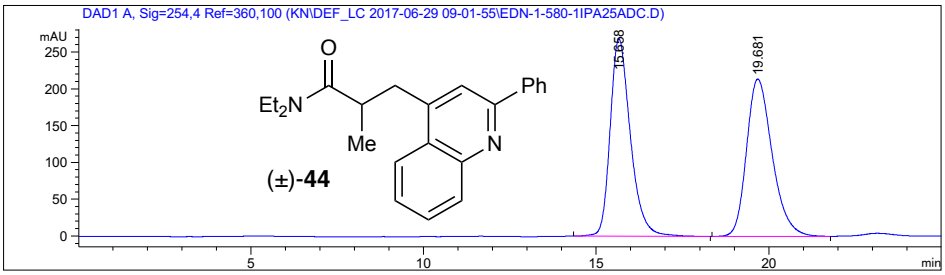
    Totals :                  1.38925e4   273.24655


    ======================================================================
                               *** End of Report ***
```

Data File C:\CHEM32\2\DATA\KN\DEF_LC 2017-06-29 09-01-55\EDN-1-580-1IPA25ADC.D
Sample Name: EDN-1-580-1IPA25ADc

```
    ======================================================================
    Acq. Operator   : SYSTEM                       Seq. Line :  20
    Acq. Instrument : Biggie                       Location : Vial 41
    Injection Date  : 6/29/2017 2:39:43 PM             Inj :   1
                                                   Inj Volume : 5.000 µl
    Acq. Method     : C:\CHEM32\2\DATA\KN\DEF_LC 2017-06-29 09-01-55\1IPA25-AD.M
    Last changed    : 6/29/2017 1:03:49 PM by SYSTEM
    Analysis Method : C:\CHEM32\2\DATA\KN\DEF_LC 2017-06-29 09-01-55\1IPA25-AD.M (Sequence Method
                      )
    Last changed    : 7/12/2017 8:56:29 AM by SYSTEM
                      (modified after loading)
    Method Info     : 1% IPA in hexanes, 25 min, AD-H, 1.0 mL/min

    Additional Info : Peak(s) manually integrated
```




```
    ======================================================================
                               Area Percent Report
    ======================================================================

    Sorted By             :      Signal
    Multiplier            :      1.0000
    Dilution              :      1.0000
    Do not use Multiplier & Dilution Factor with ISTDs

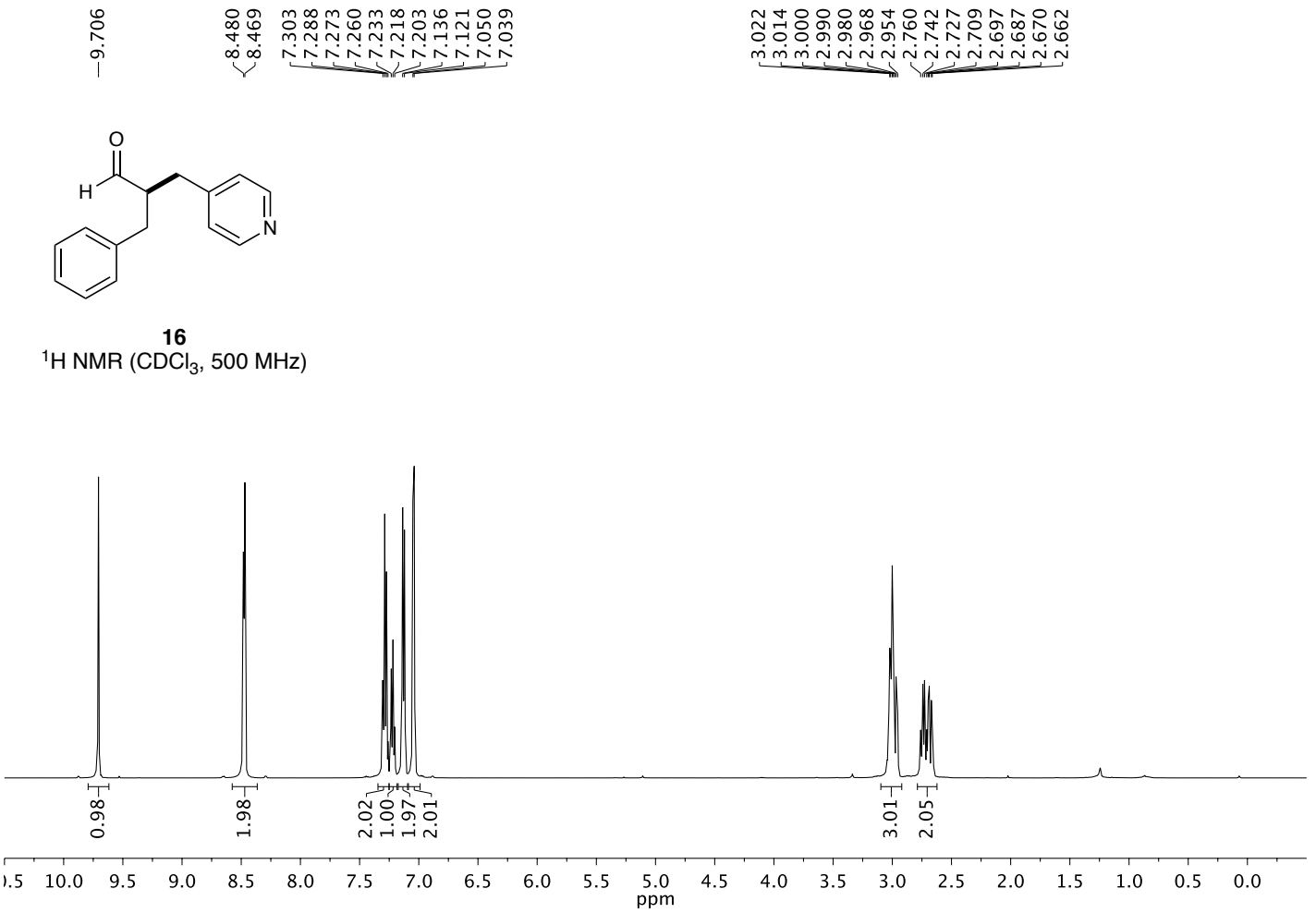

    Signal 1: DAD1 A, Sig=254,4 Ref=360,100

    Peak RetTime Type  Width     Area      Height     Area
      #   [min]        [min]   [mAU*s]     [mAU]       %
    ----|-------|----|-------|----------|----------|--------|
       1  15.658 BB    0.6216 1.09343e4   268.20300  49.7272
       2  19.681 BB    0.7934 1.10543e4   213.72421  50.2728

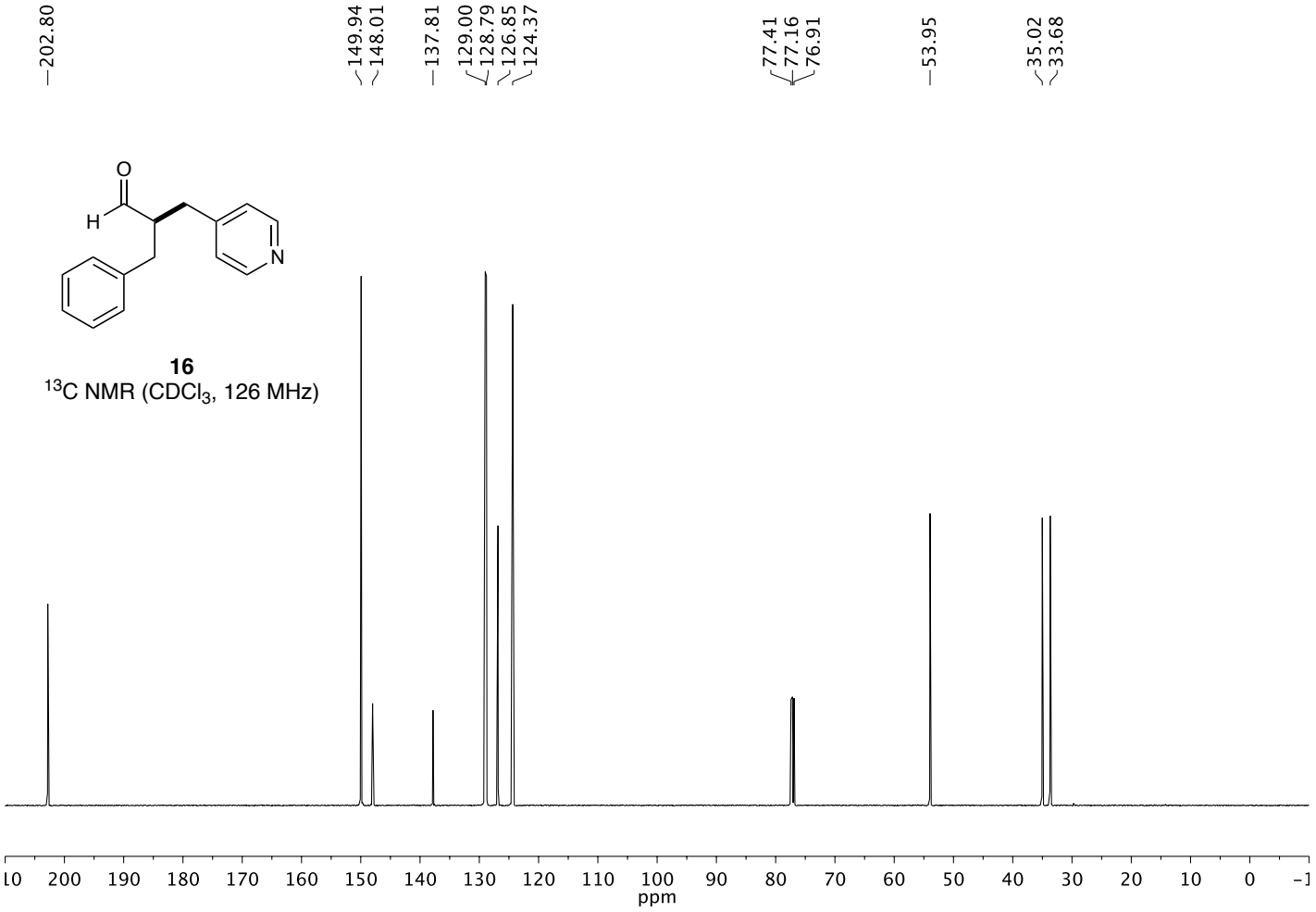
    Totals :                  2.19886e4   481.92722

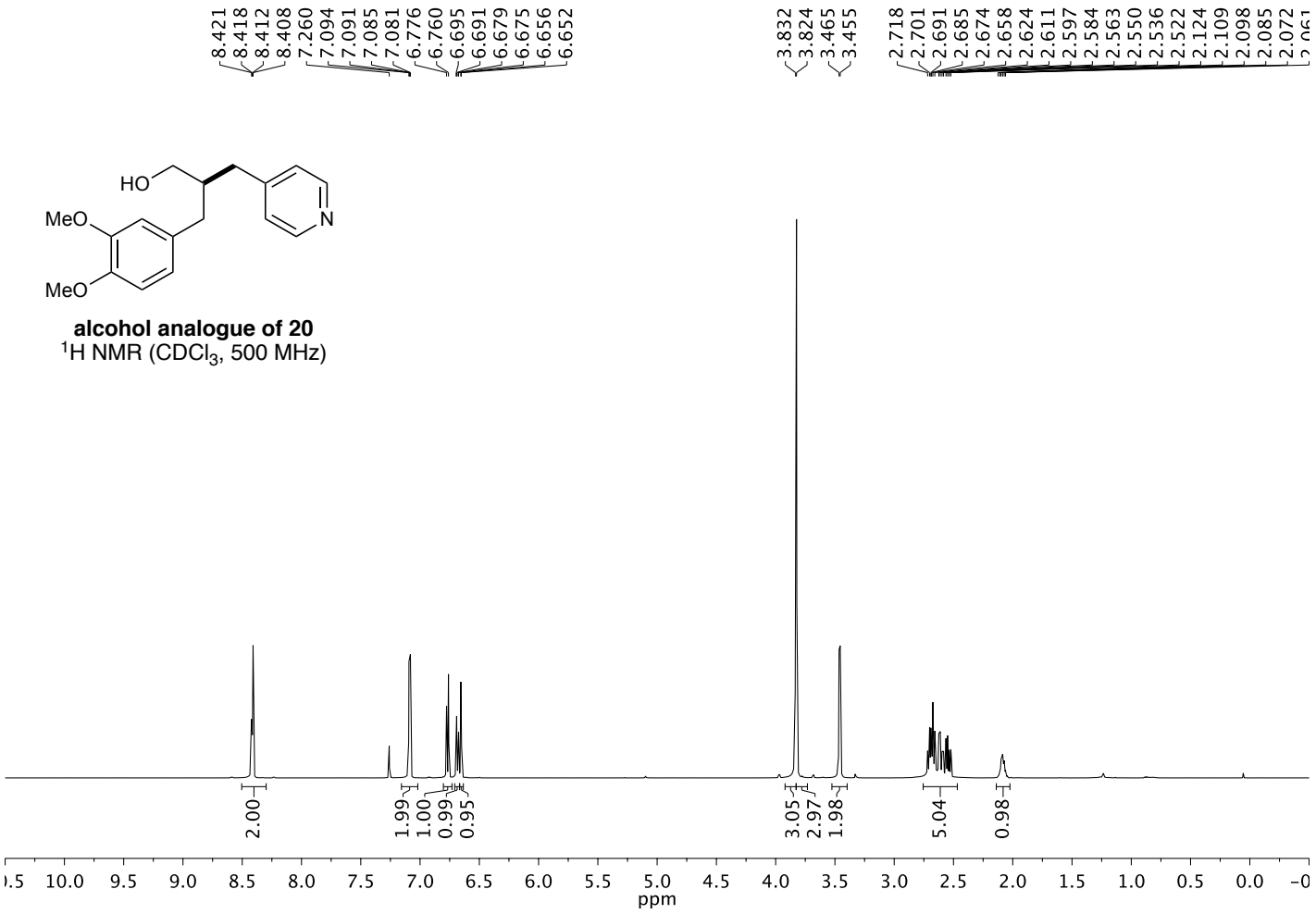

    ======================================================================
                               *** End of Report ***
```

XXIV. NMR Spectra

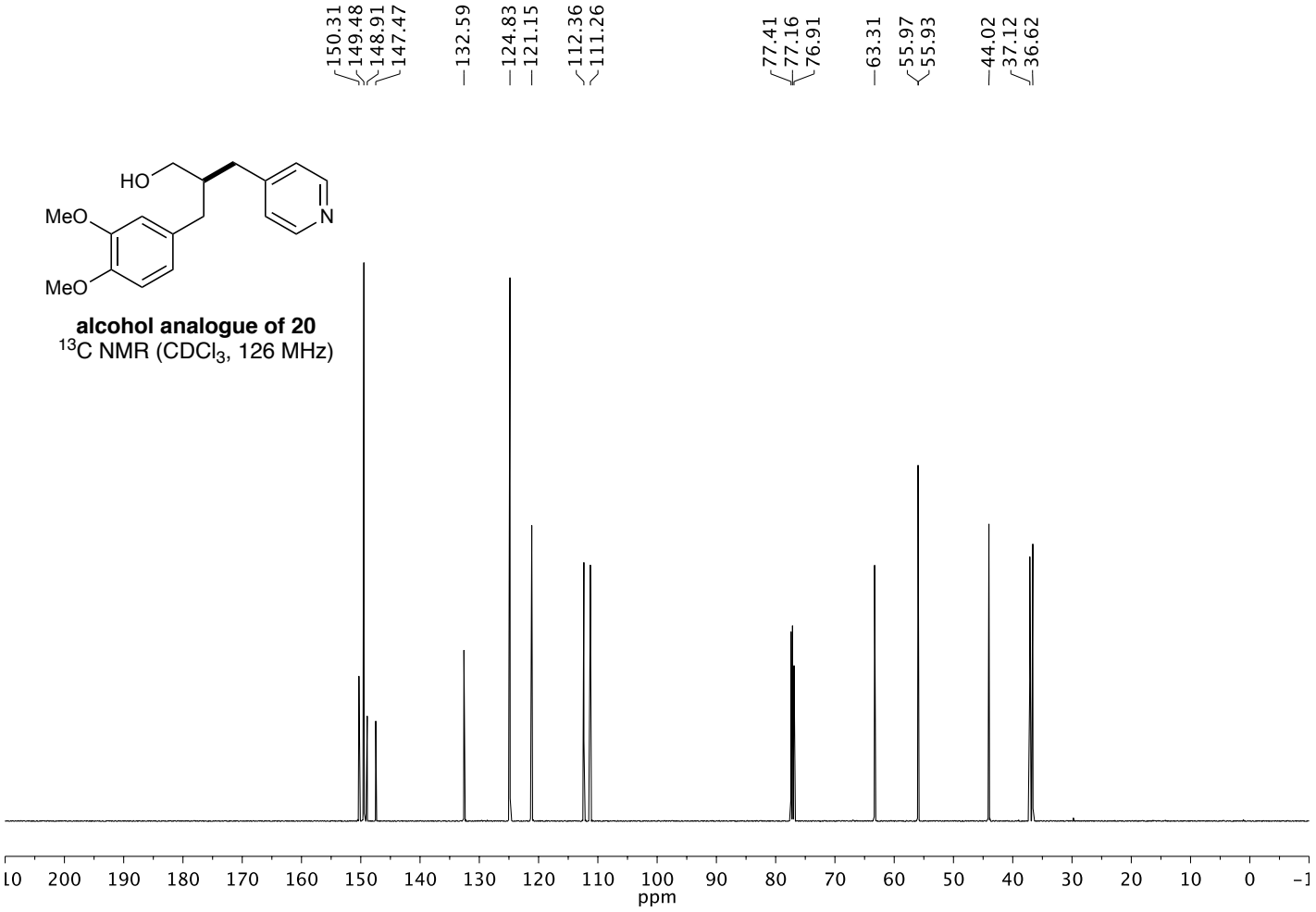


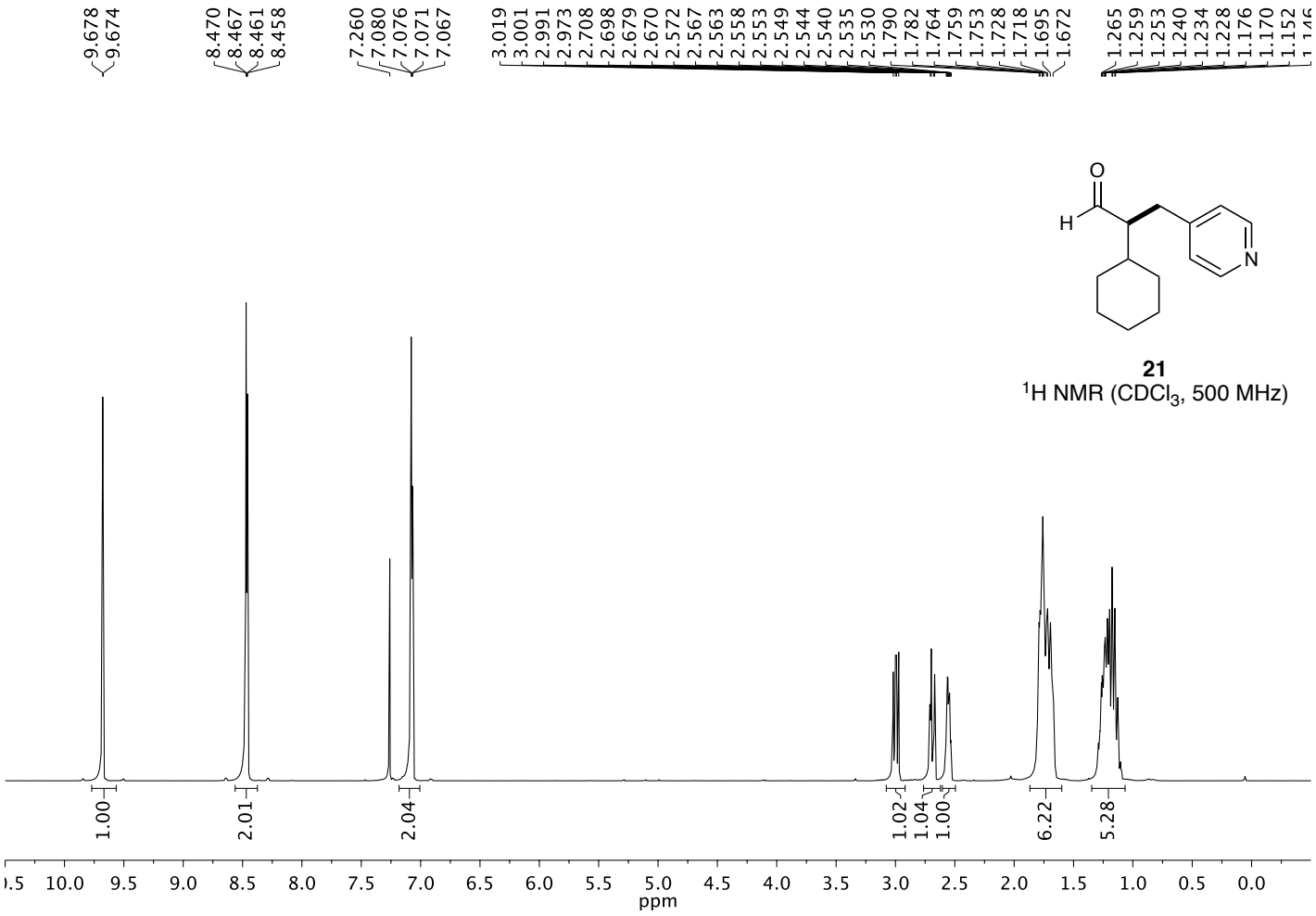
16
^{1}H NMR ($CDCl_3$, 500 MHz)


202.80
149.94
148.01
137.81
129.00
128.79
126.85
124.37
77.41
77.16
76.91
53.95
35.02
33.68
O
H
N
16
13C NMR (CDCl3, 126 MHz)
ppm

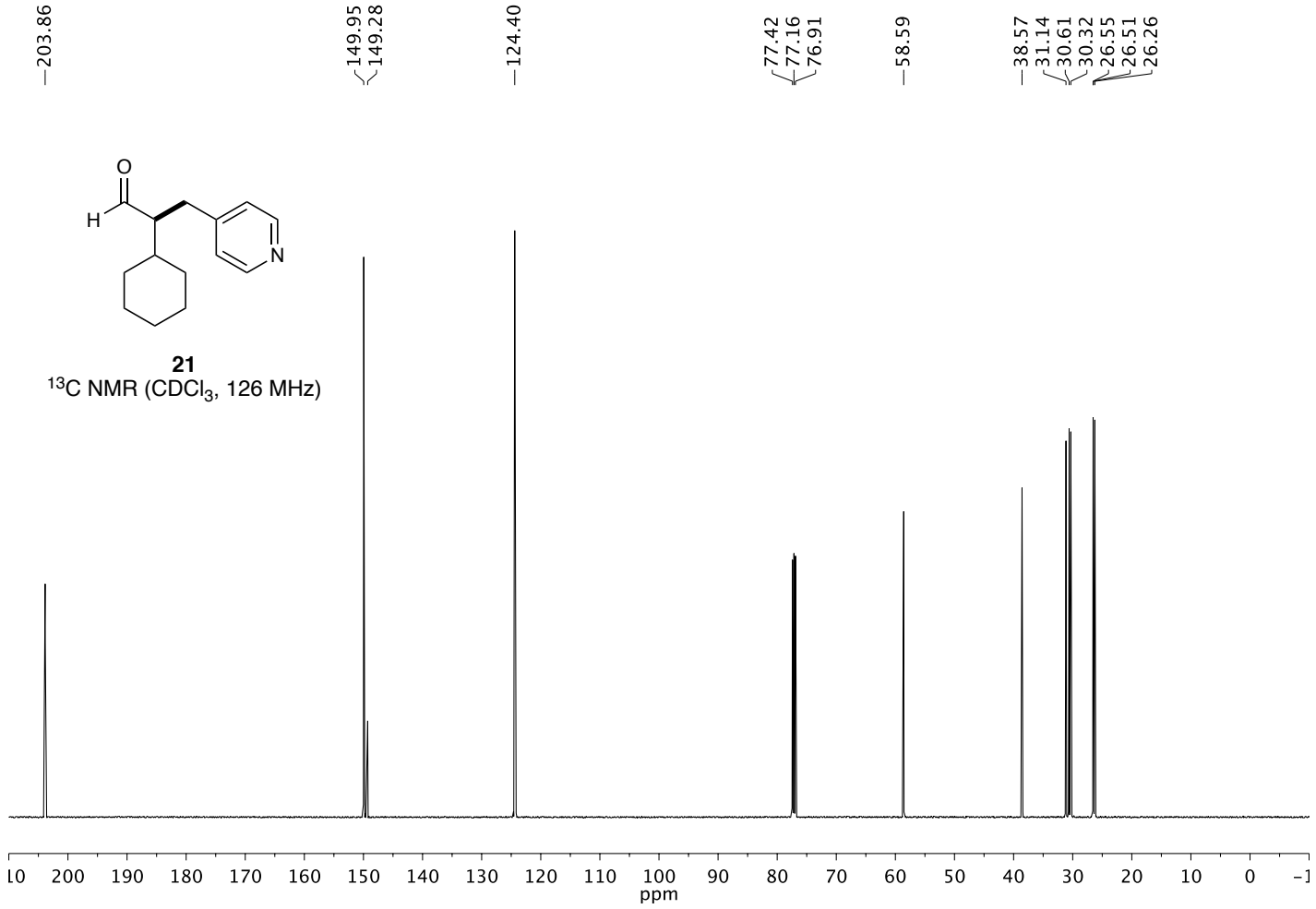


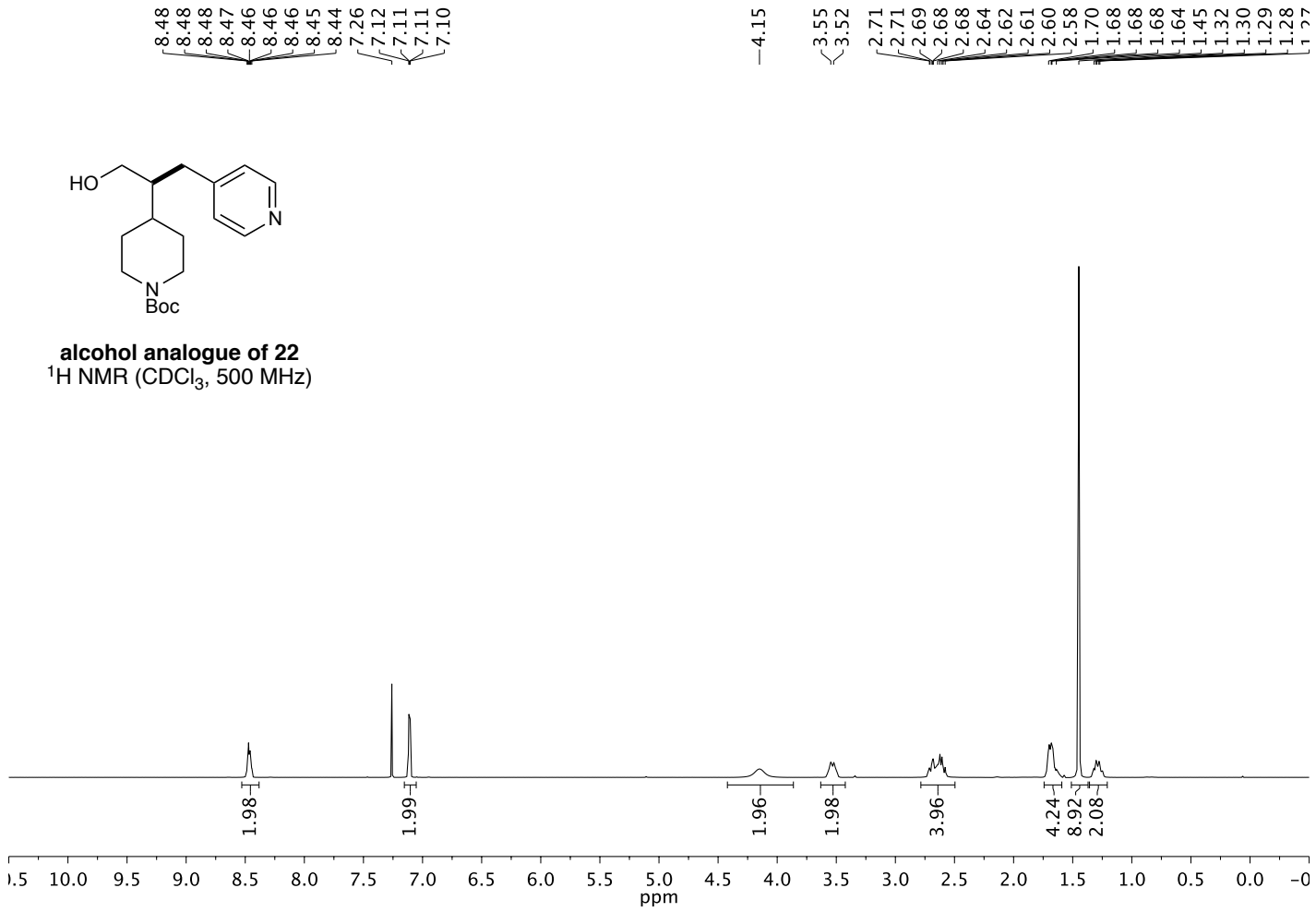
alcohol analogue of 20
^{1}H NMR ($CDCl_3$, 500 MHz)


150.31
149.48
148.91
147.47
132.59
124.83
121.15
112.36
111.26
77.41
77.16
76.91
63.31
55.97
55.93
44.02
37.12
36.62
HO
MeO
MeO
N
alcohol analogue of 20
13C NMR (CDCl3, 126 MHz)
ppm

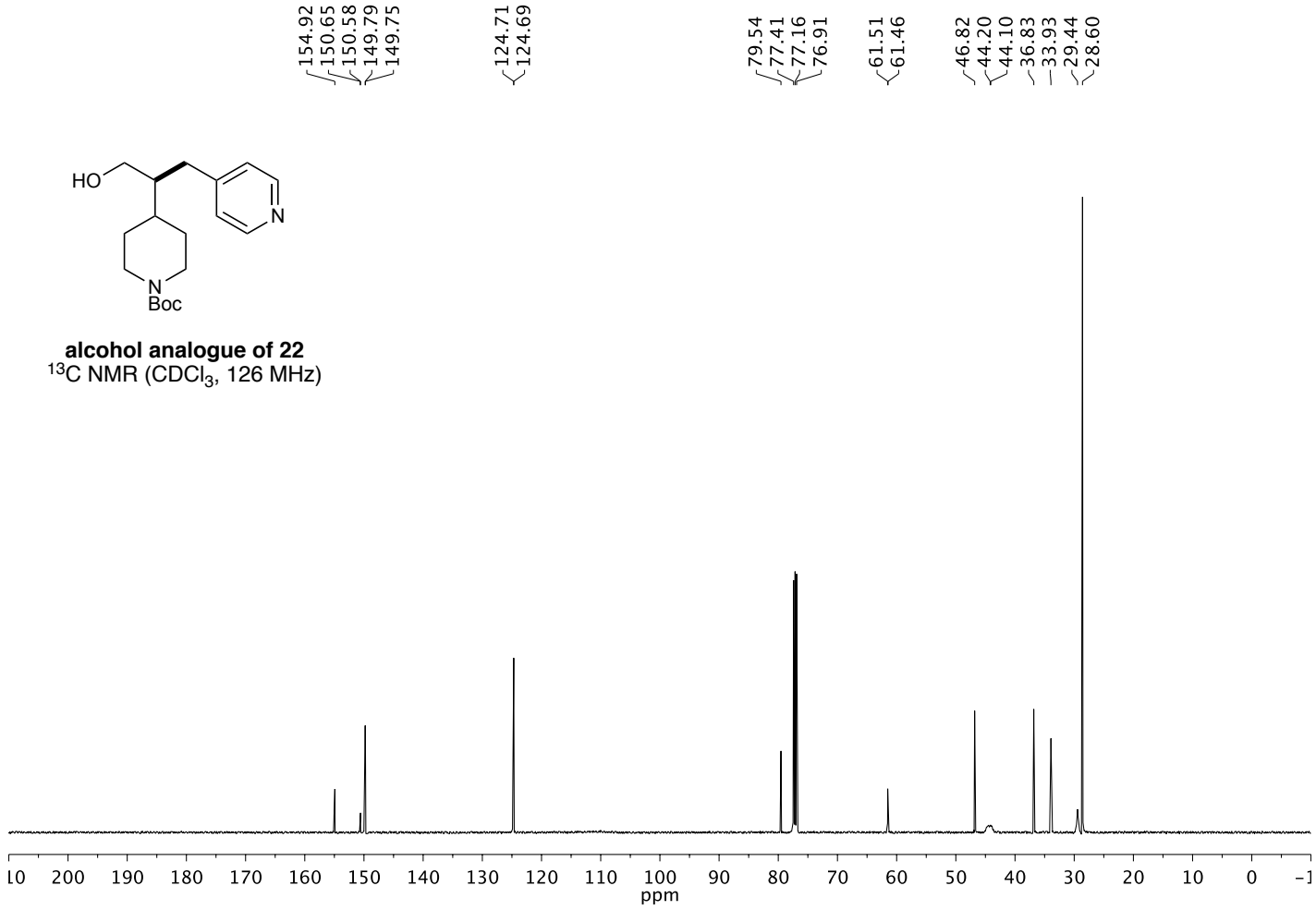


21
^{1}H NMR ($CDCl_3$, 500 MHz)

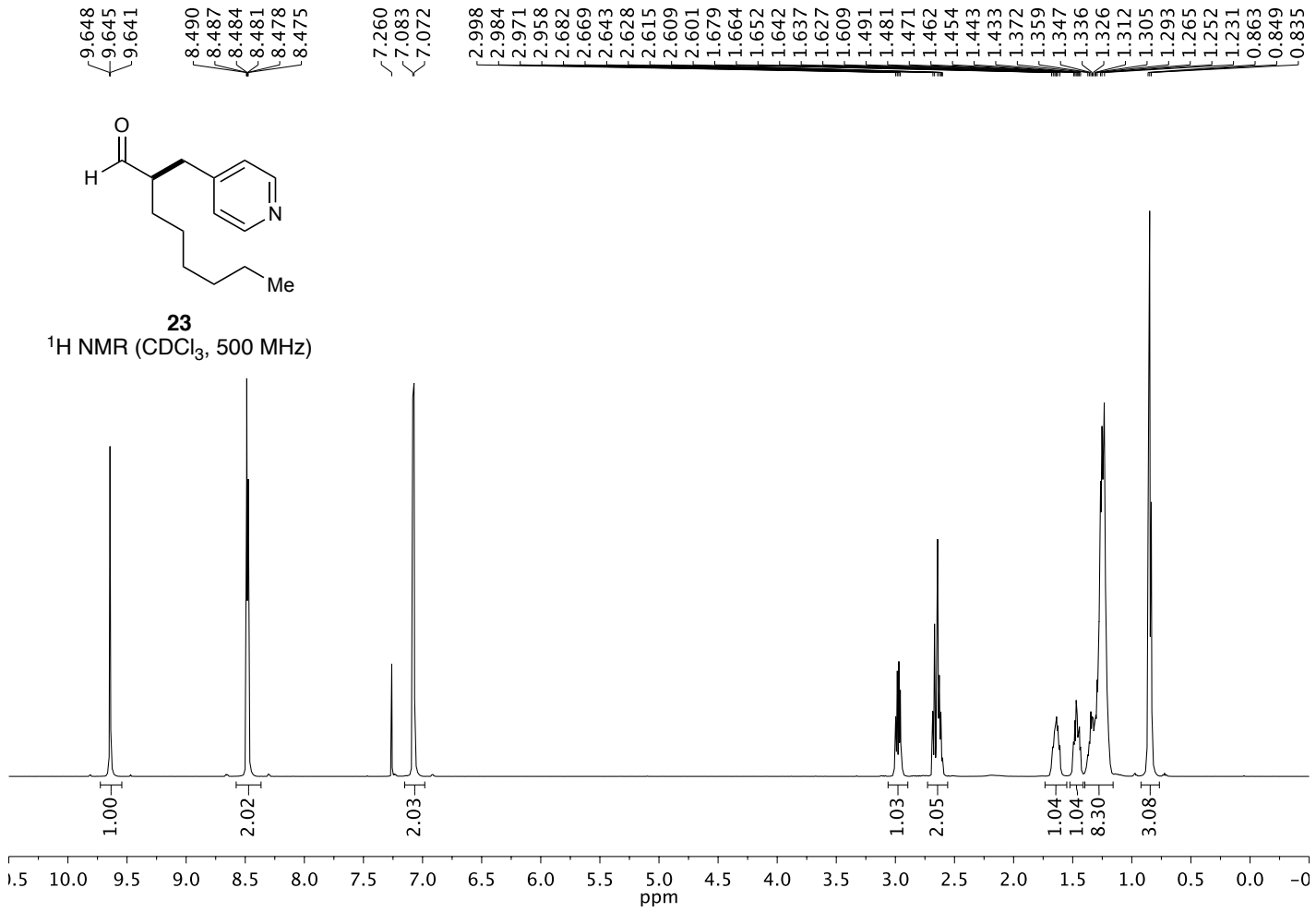

203.86
149.95
149.28
124.40
77.42
77.16
76.91
58.59
38.57
31.14
30.61
30.32
26.55
26.51
26.26
O
H
N
21
13C NMR (CDCl3, 126 MHz)
ppm



alcohol analogue of 22
^{1}H NMR ($CDCl_3$, 500 MHz)

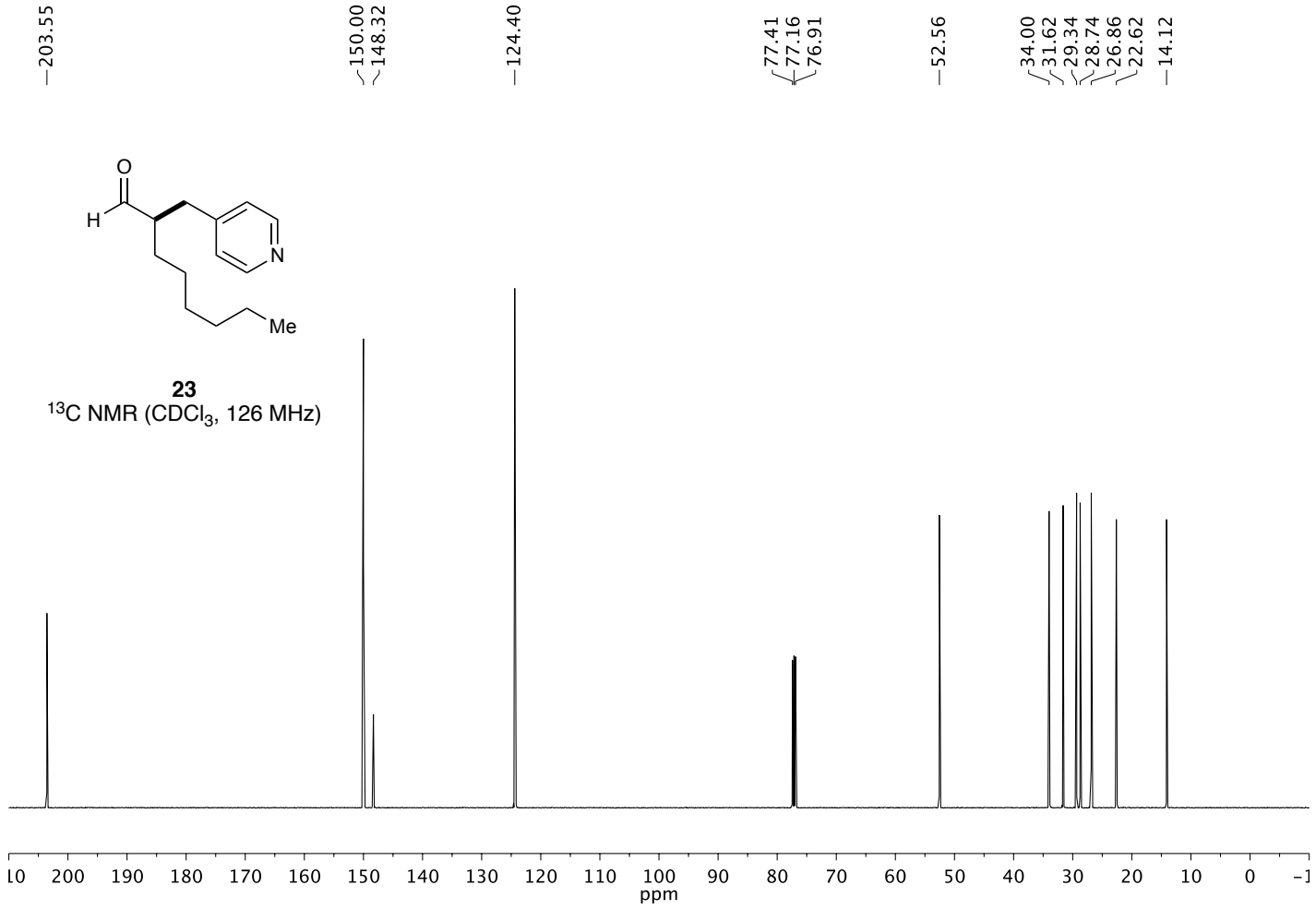


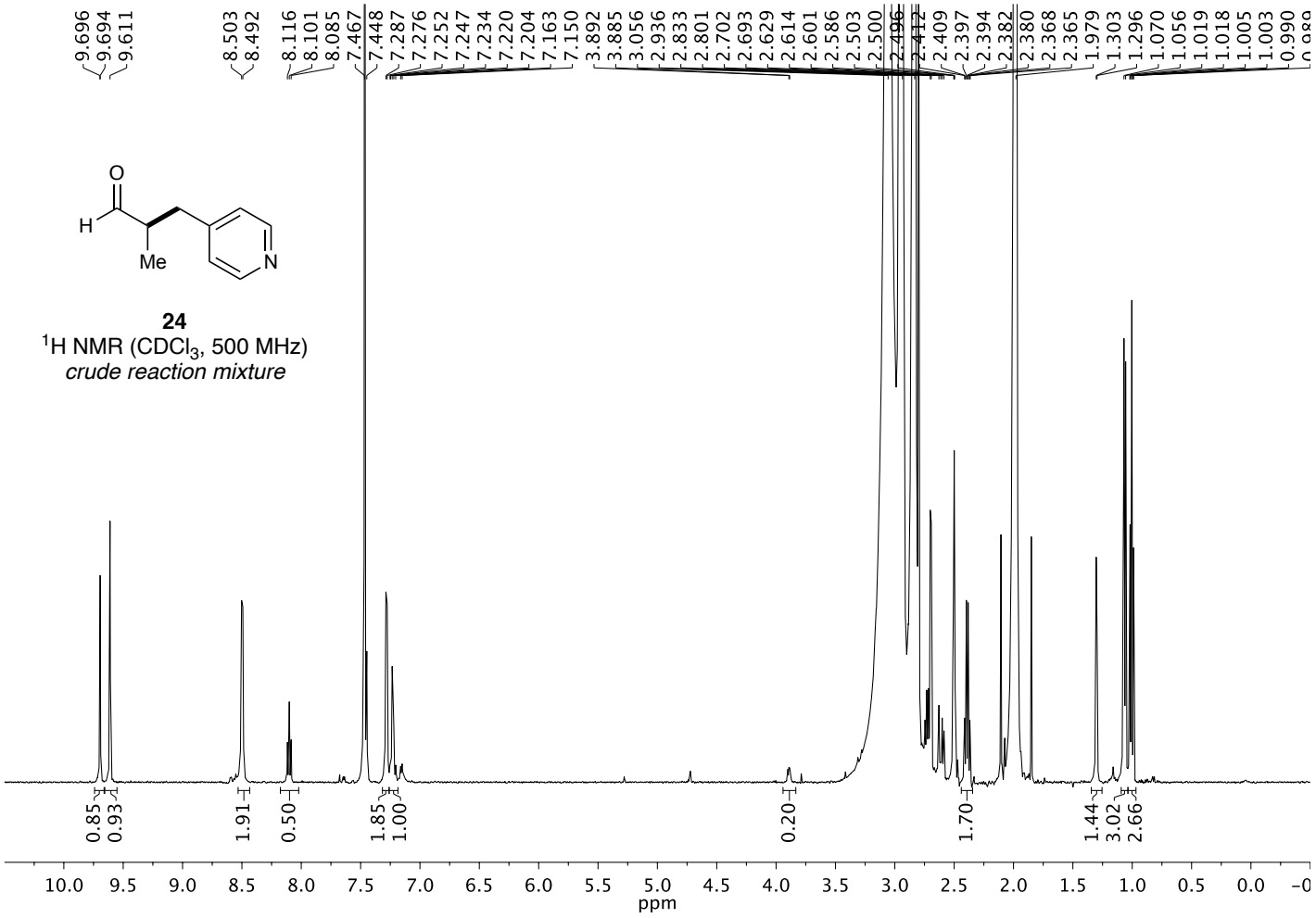
alcohol analogue of 22
^{13}C NMR ($CDCl_3$, 126 MHz)

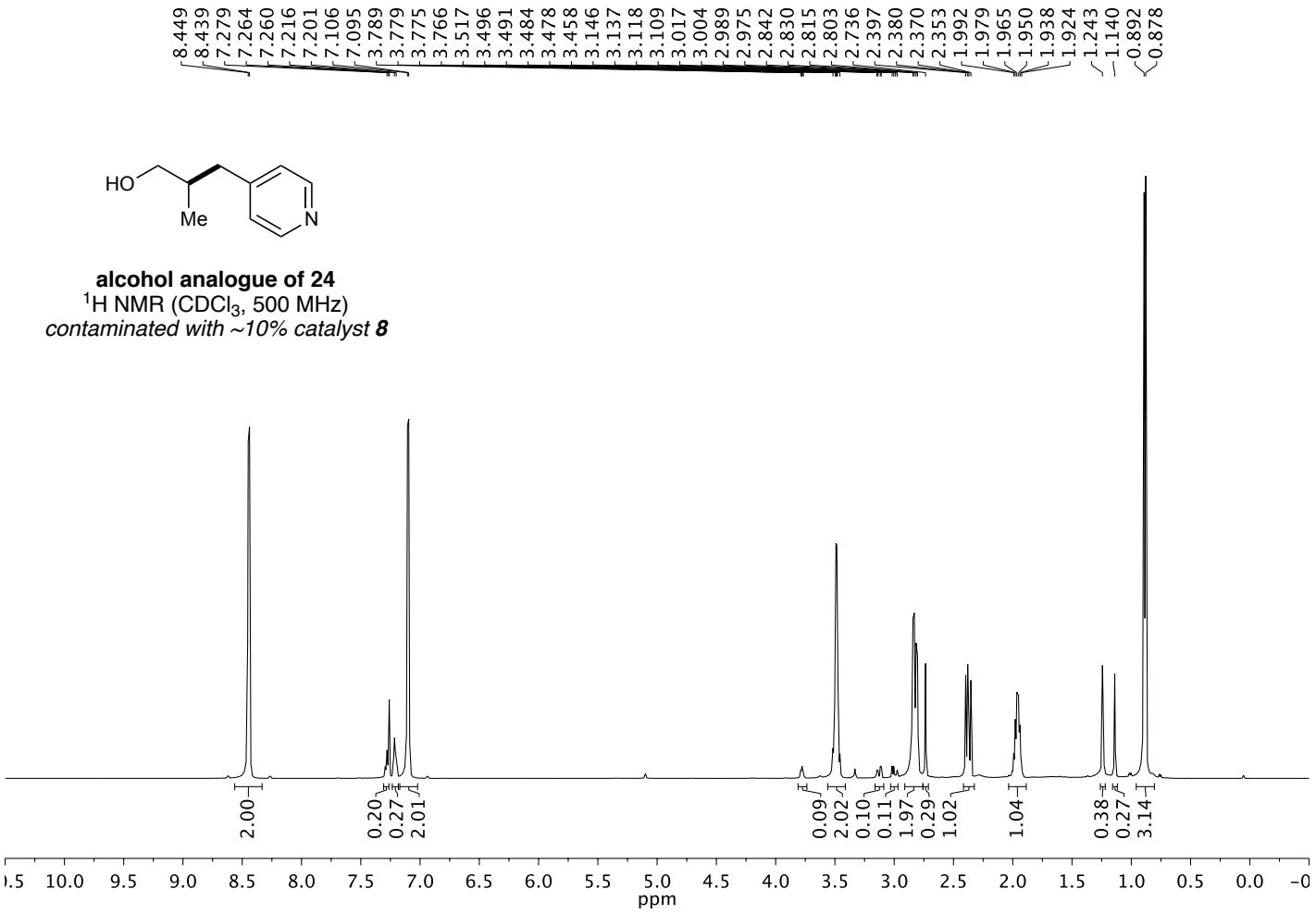


23

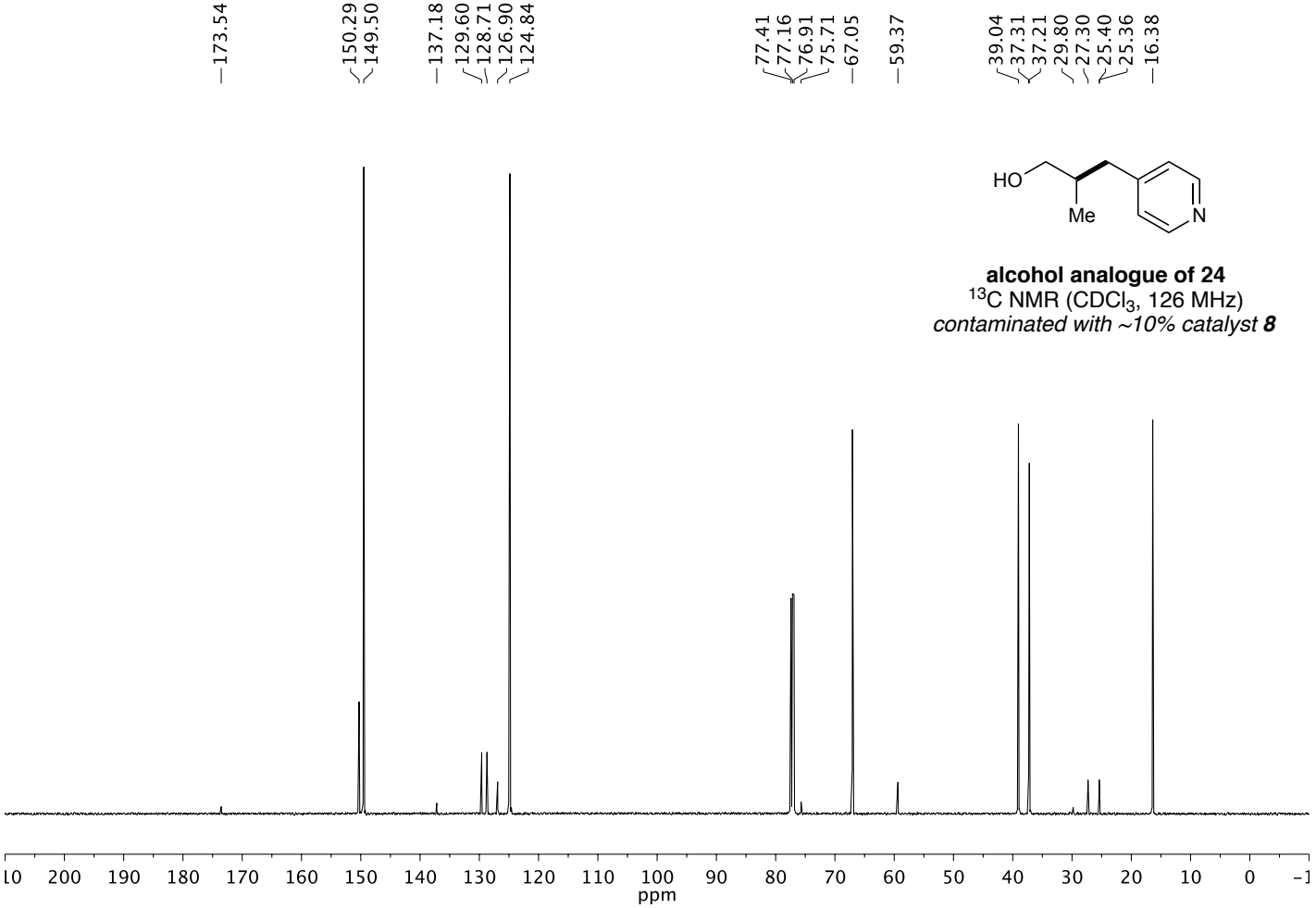
^{1}H NMR ($CDCl_3$, 500 MHz)


203.55
150.00
148.32
124.40
77.41
77.16
76.91
52.56
34.00
31.62
29.34
28.74
26.86
22.62
14.12
O
H
N
Me
23
13C NMR (CDCl3, 126 MHz)
ppm

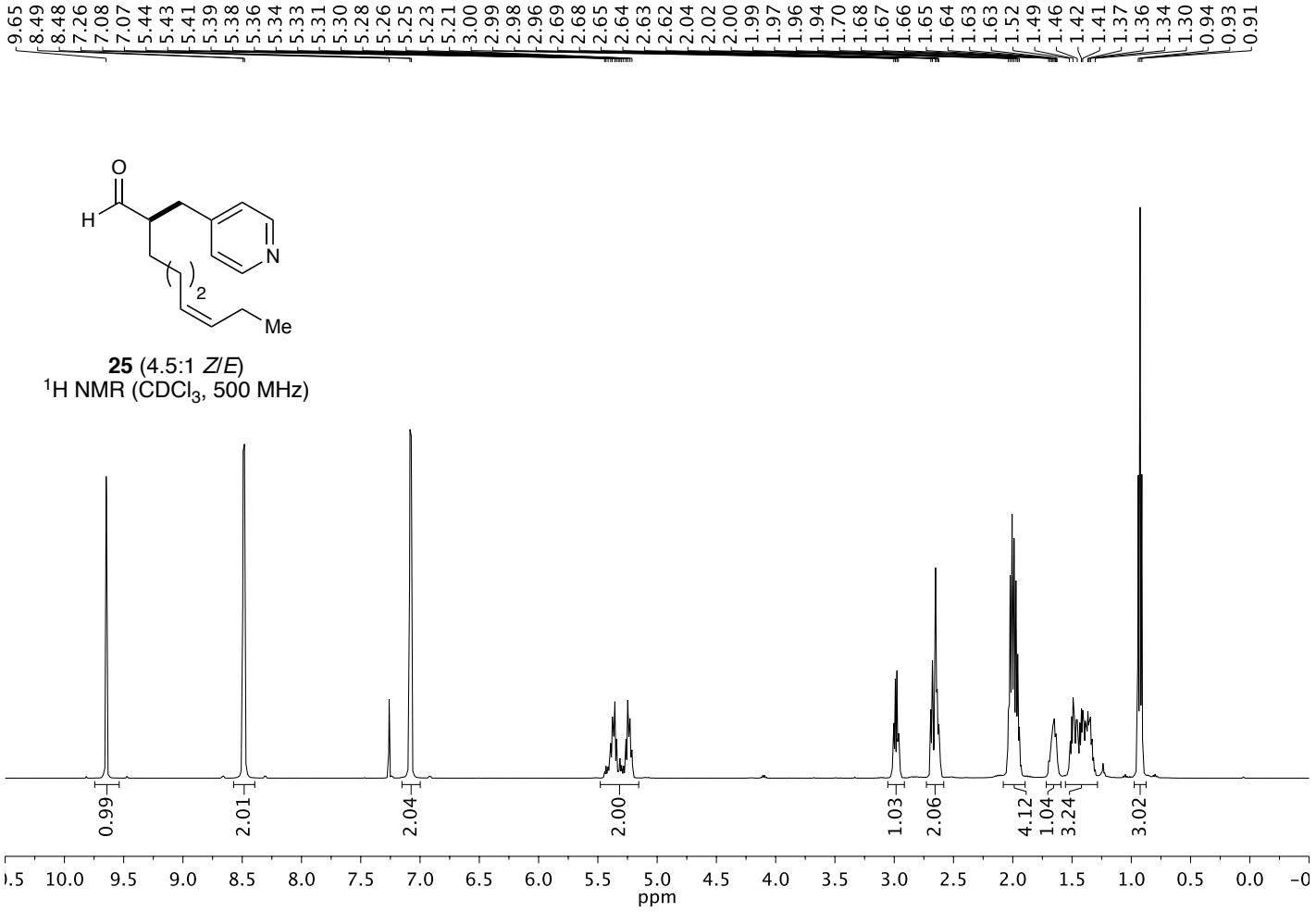

9.696
9.694
9.611
8.503
8.492
8.116
8.101
8.085
7.467
7.448
7.287
7.276
7.252
7.247
7.234
7.220
7.204
7.163
7.150
3.892
3.885
3.056
2.936
2.833
2.801
2.702
2.693
2.629
2.614
2.601
2.586
2.503
2.500
2.496
2.412
2.409
2.397
2.394
2.382
2.380
2.368
2.365
1.979
1.303
1.296
1.070
1.056
1.019
1.018
1.005
1.003
0.990
O
H
Me
N
24
1H NMR (CDCl3, 500 MHz)
crude reaction mixture
0.85
0.93
1.91
0.50
1.85
1.00
0.20
1.70
1.44
3.02
2.66
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm

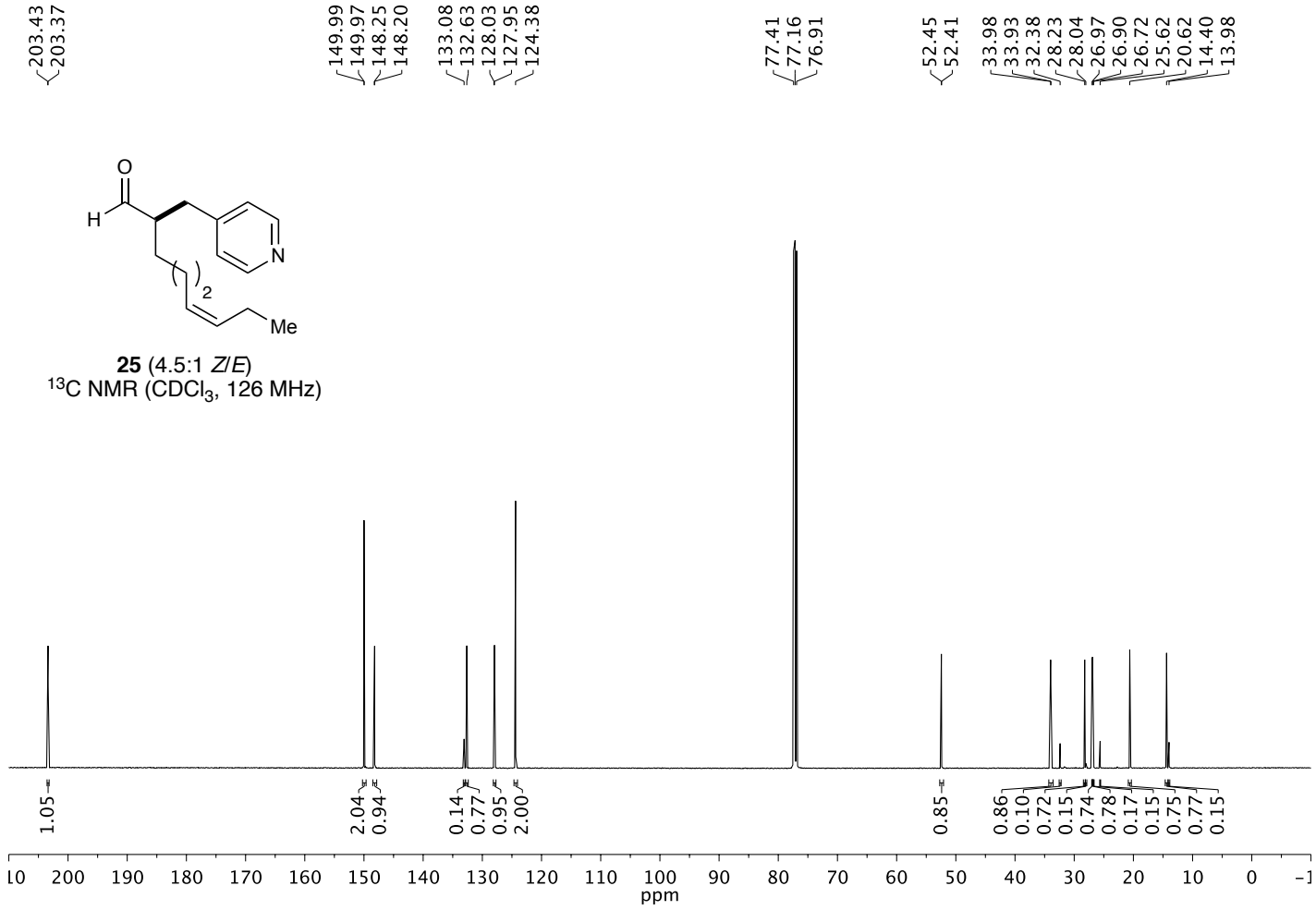


alcohol analogue of 24
^{1}H NMR ($CDCl_3$, 500 MHz)
*contaminated with ~10% catalyst **8***

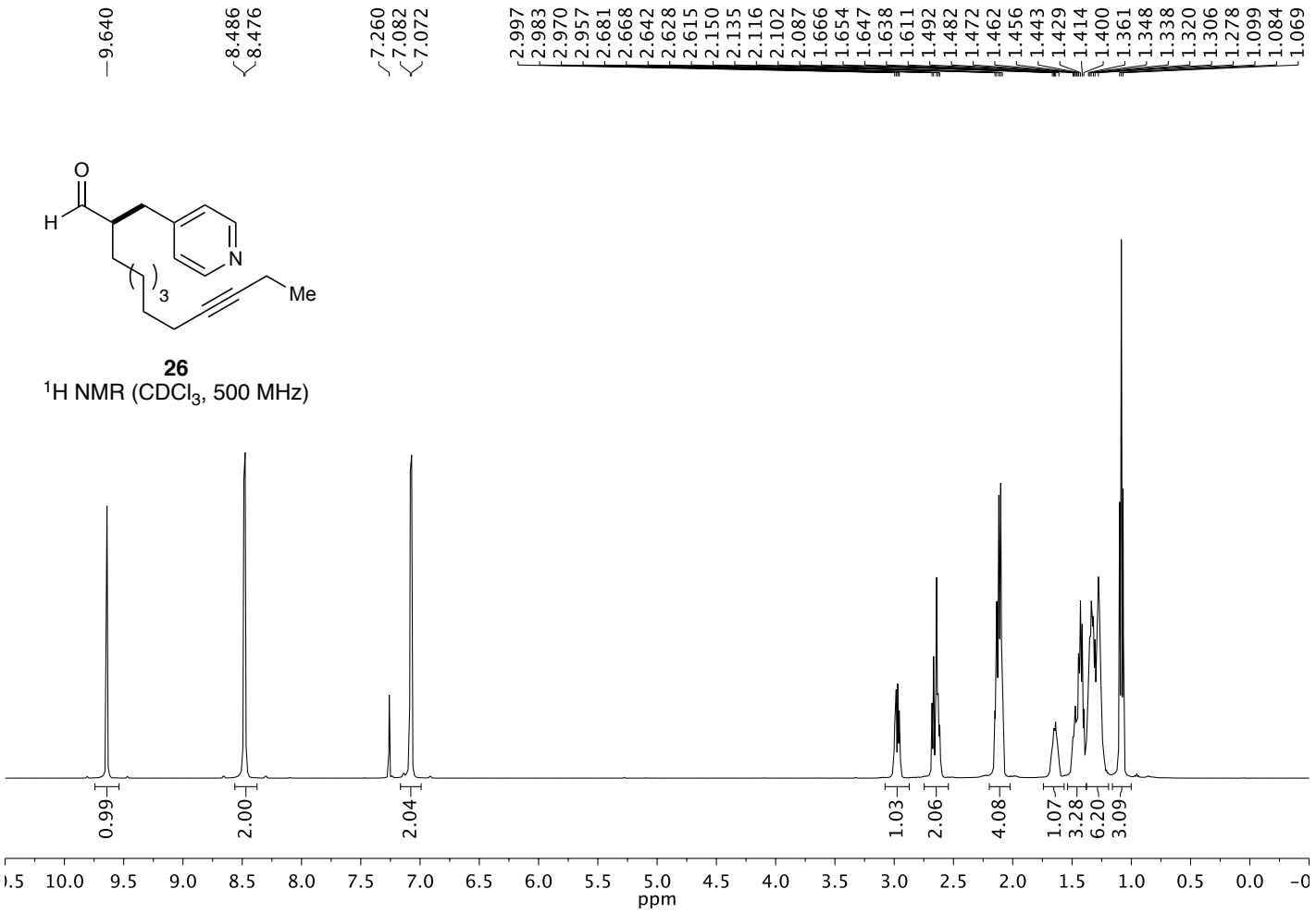


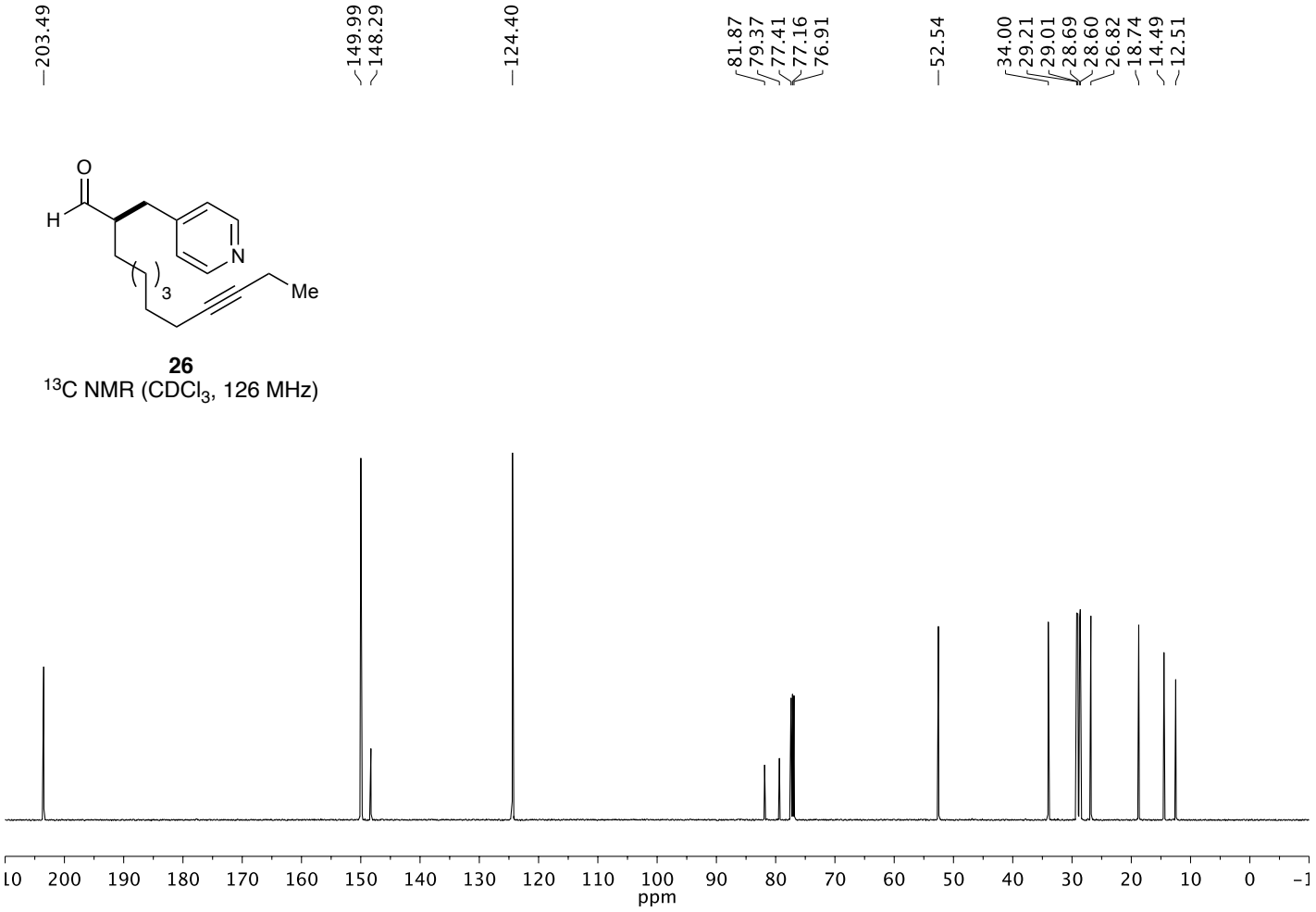
alcohol analogue of 24
^{13}C NMR ($CDCl_3$, 126 MHz)
*contaminated with ~10% catalyst **8***


9.65 8.49 8.48 7.26 7.08 7.07 5.44 5.43 5.41 5.39 5.38 5.36 5.34 5.33 5.31 5.30 5.28 5.26 5.25 5.23 5.21 3.00 2.99 2.98 2.96 2.69 2.68 2.65 2.64 2.63 2.62 2.04 2.02 2.00 1.99 1.97 1.96 1.94 1.70 1.68 1.67 1.66 1.65 1.64 1.63 1.63 1.52 1.49 1.46 1.42 1.41 1.37 1.36 1.34 1.30 0.94 0.93 0.91
O
H
N
2
Me
25 (4.5:1 Z/E)
1H NMR (CDCl3, 500 MHz)
0.99
2.01
2.04
2.00
1.03
2.06
4.12
1.04
3.24
3.02
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
ppm



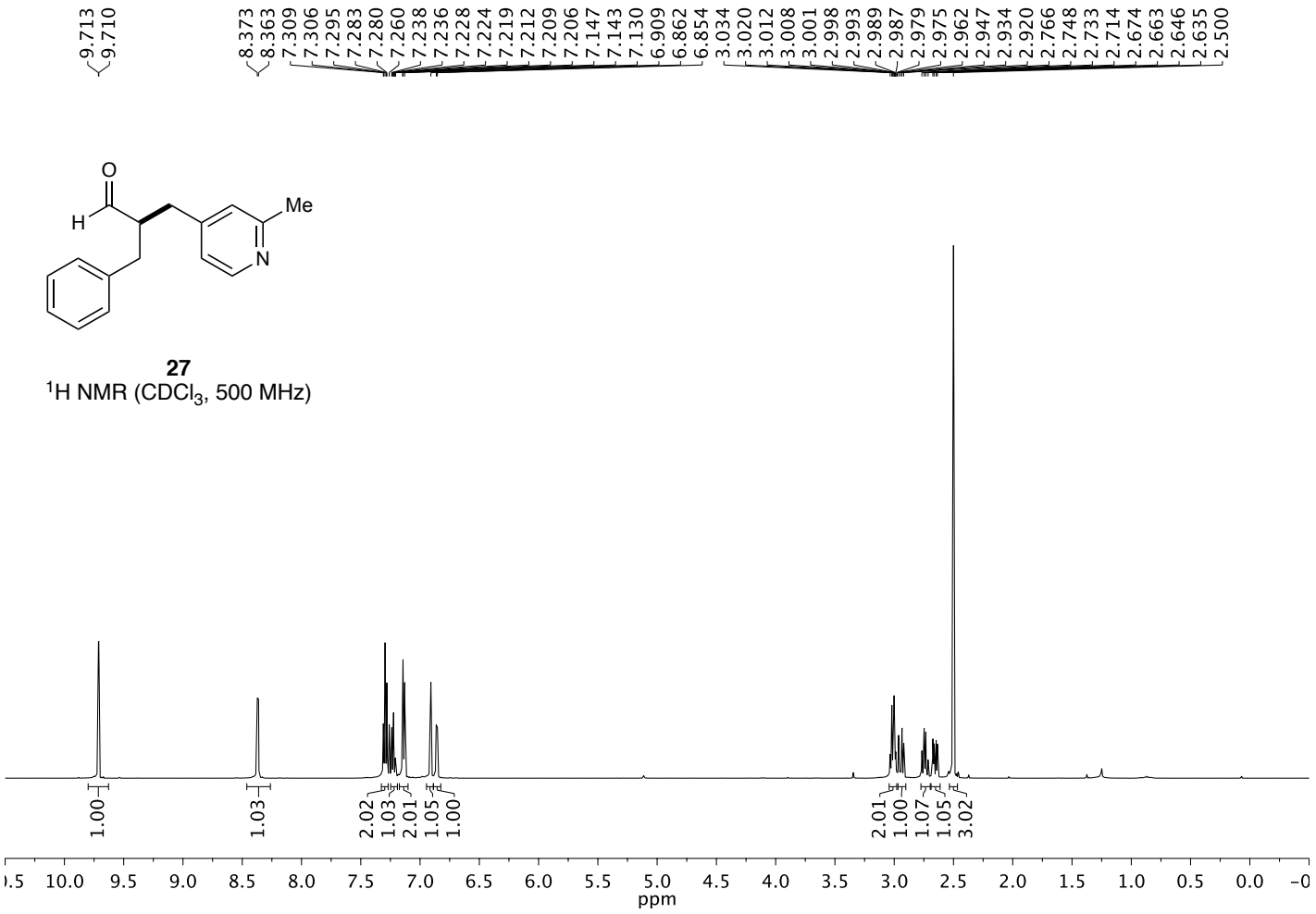
25 (4.5:1 *Z*/*E*)
^{13}C NMR ($CDCl_3$, 126 MHz)


9.640
8.486
8.476
7.260
7.082
7.072
2.997
2.983
2.970
2.957
2.681
2.668
2.642
2.628
2.615
2.150
2.135
2.116
2.102
2.087
1.666
1.654
1.647
1.638
1.611
1.492
1.482
1.472
1.462
1.456
1.443
1.429
1.414
1.400
1.361
1.348
1.338
1.320
1.306
1.278
1.099
1.084
1.069
O
H
N
3
Me
26
1H NMR (CDCl3, 500 MHz)
0.99
2.00
2.04
1.03
2.06
4.08
1.07
3.28
6.20
3.09
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm

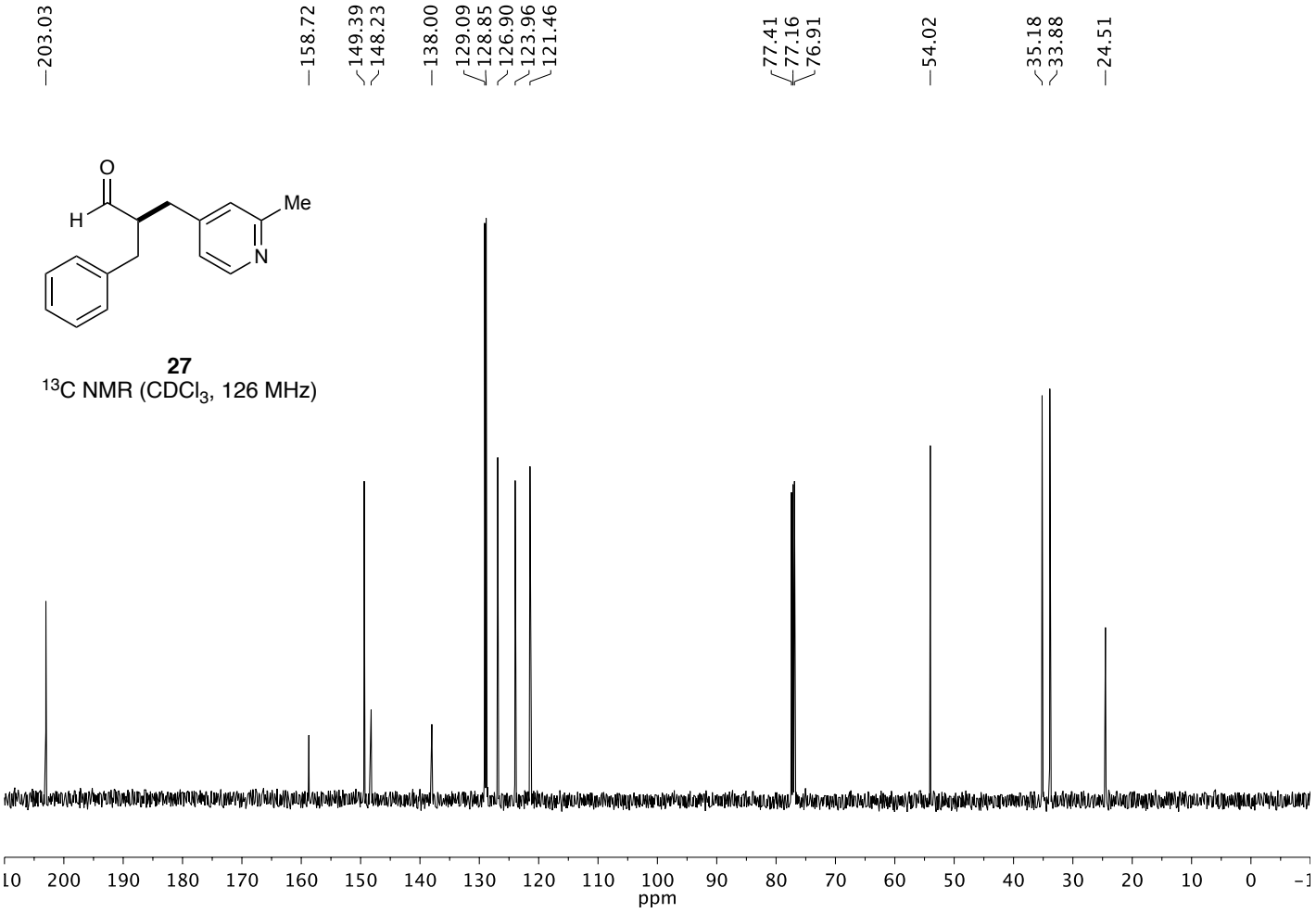


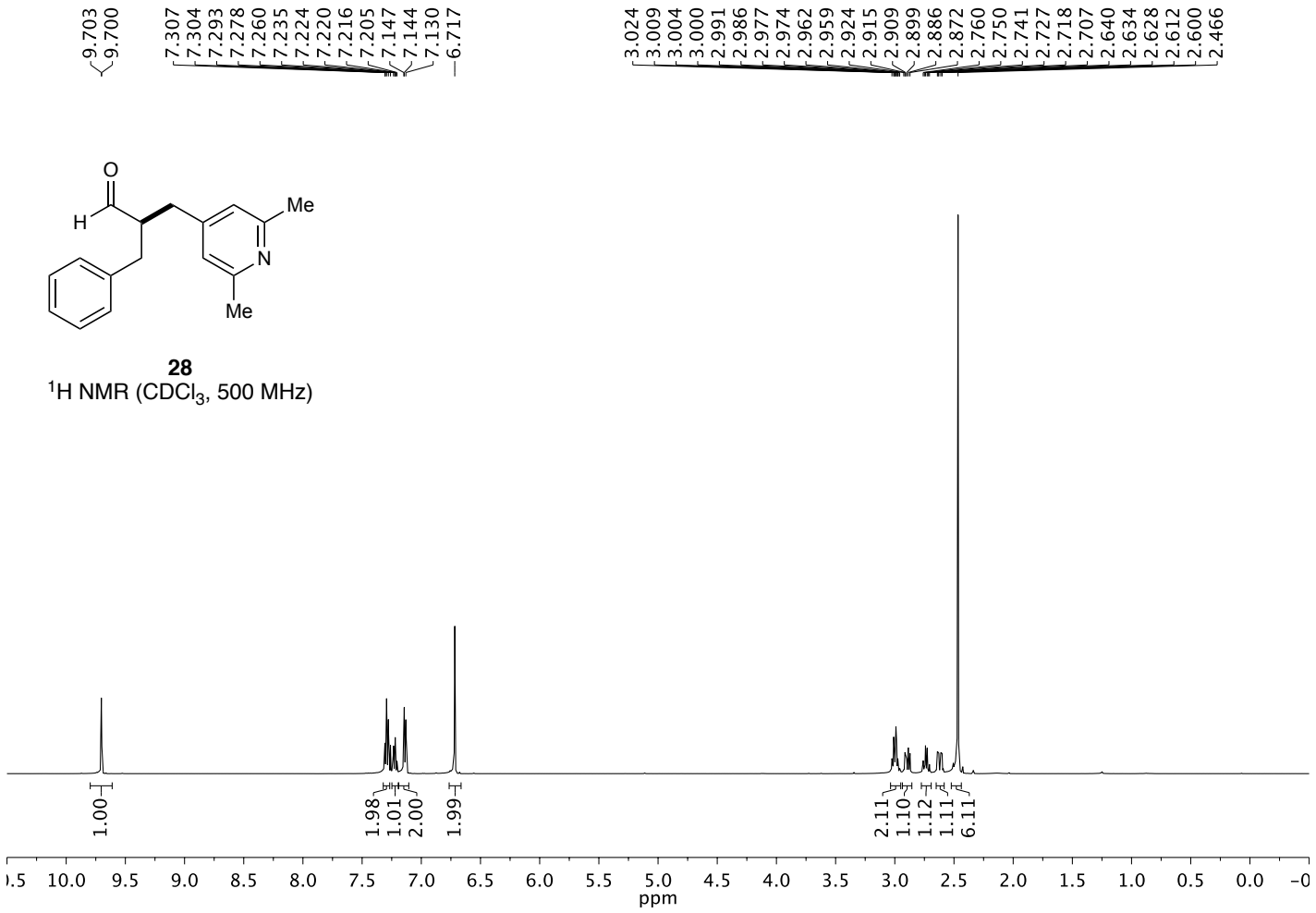
26

^{13}C NMR ($CDCl_3$, 126 MHz)



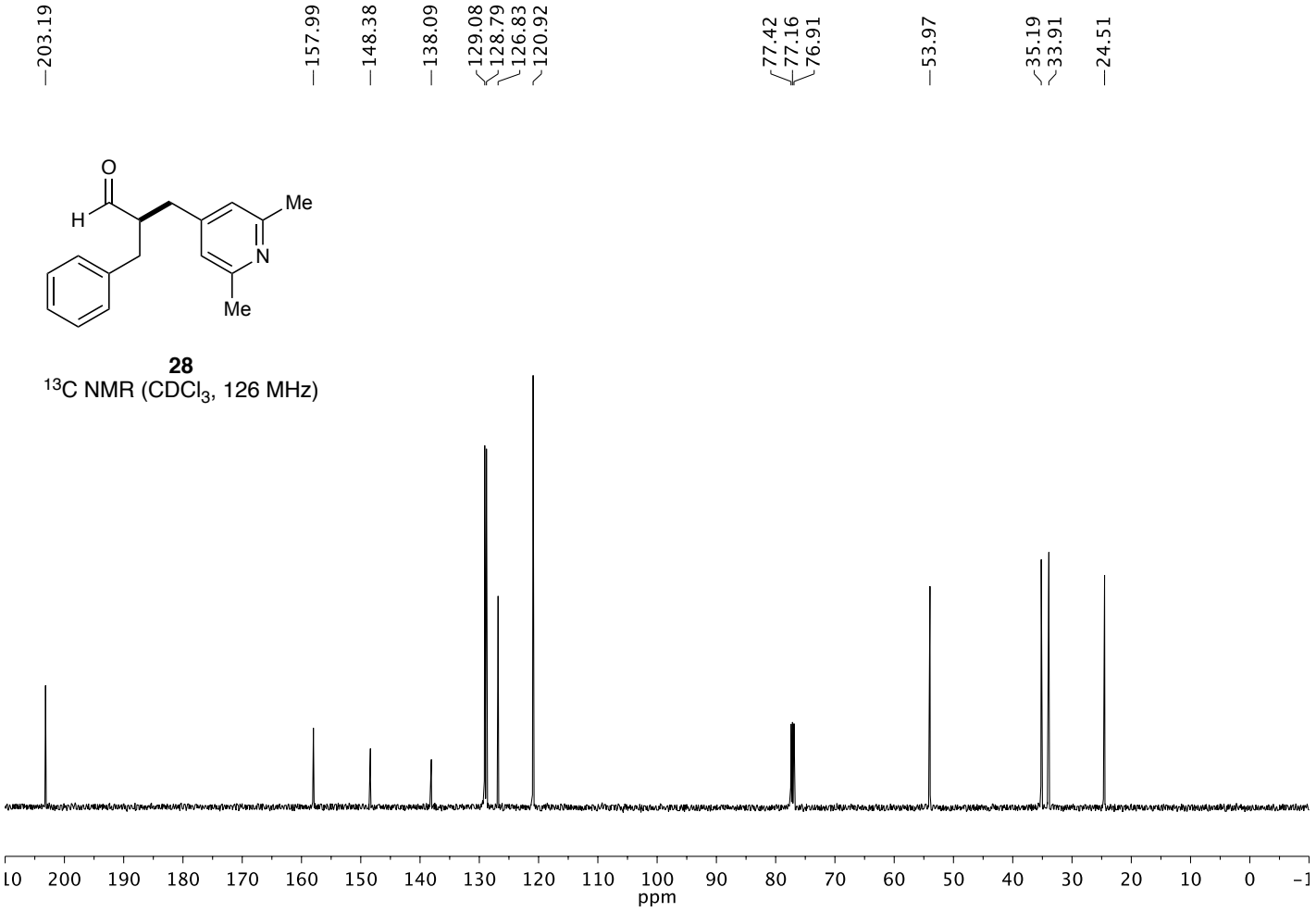
27
^{1}H NMR ($CDCl_3$, 500 MHz)

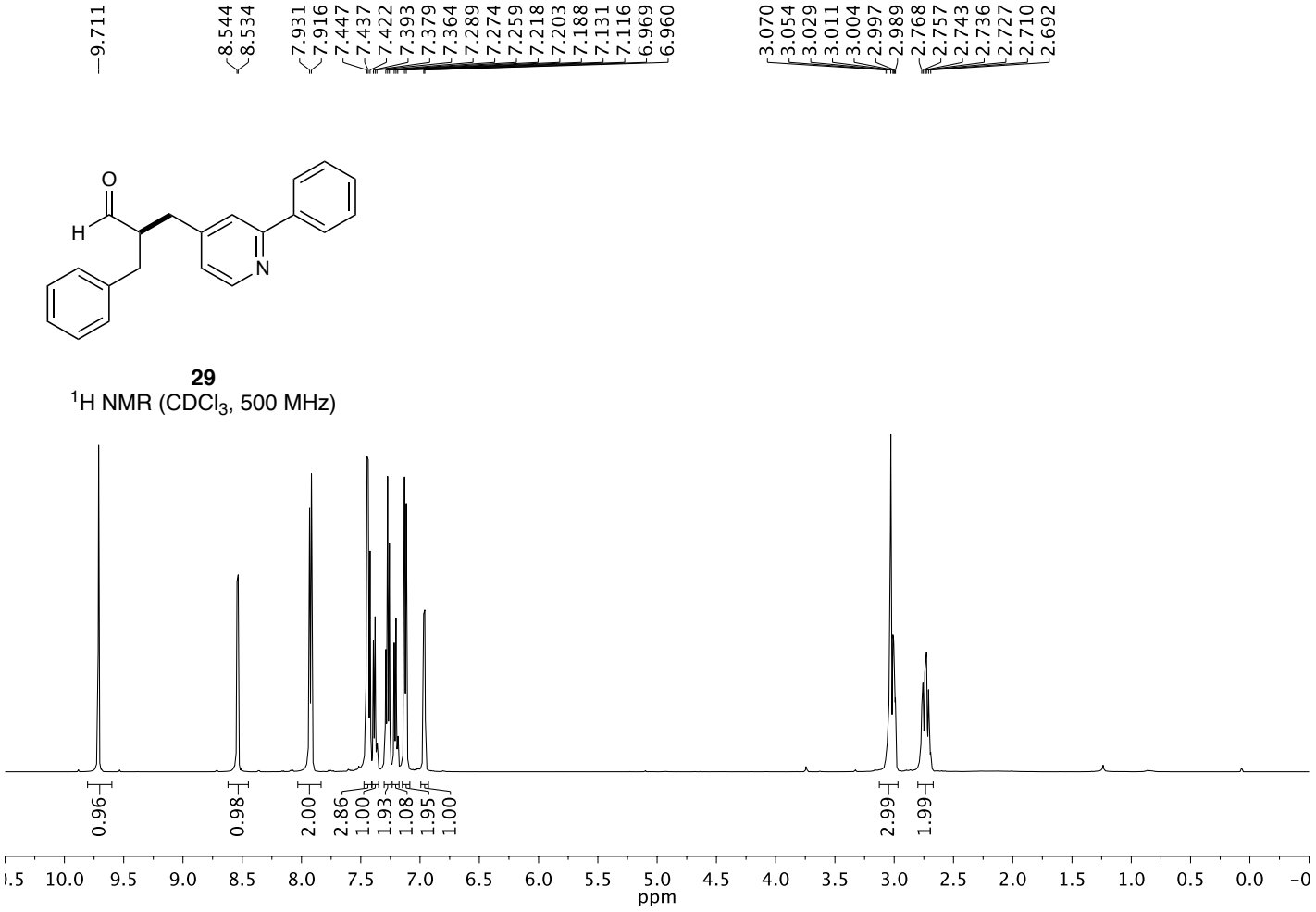

203.03
158.72
149.39
148.23
138.00
129.09
128.85
126.90
123.96
121.46
77.41
77.16
76.91
54.02
35.18
33.88
24.51
O
H
Me
N
27
13C NMR (CDCl3, 126 MHz)
ppm

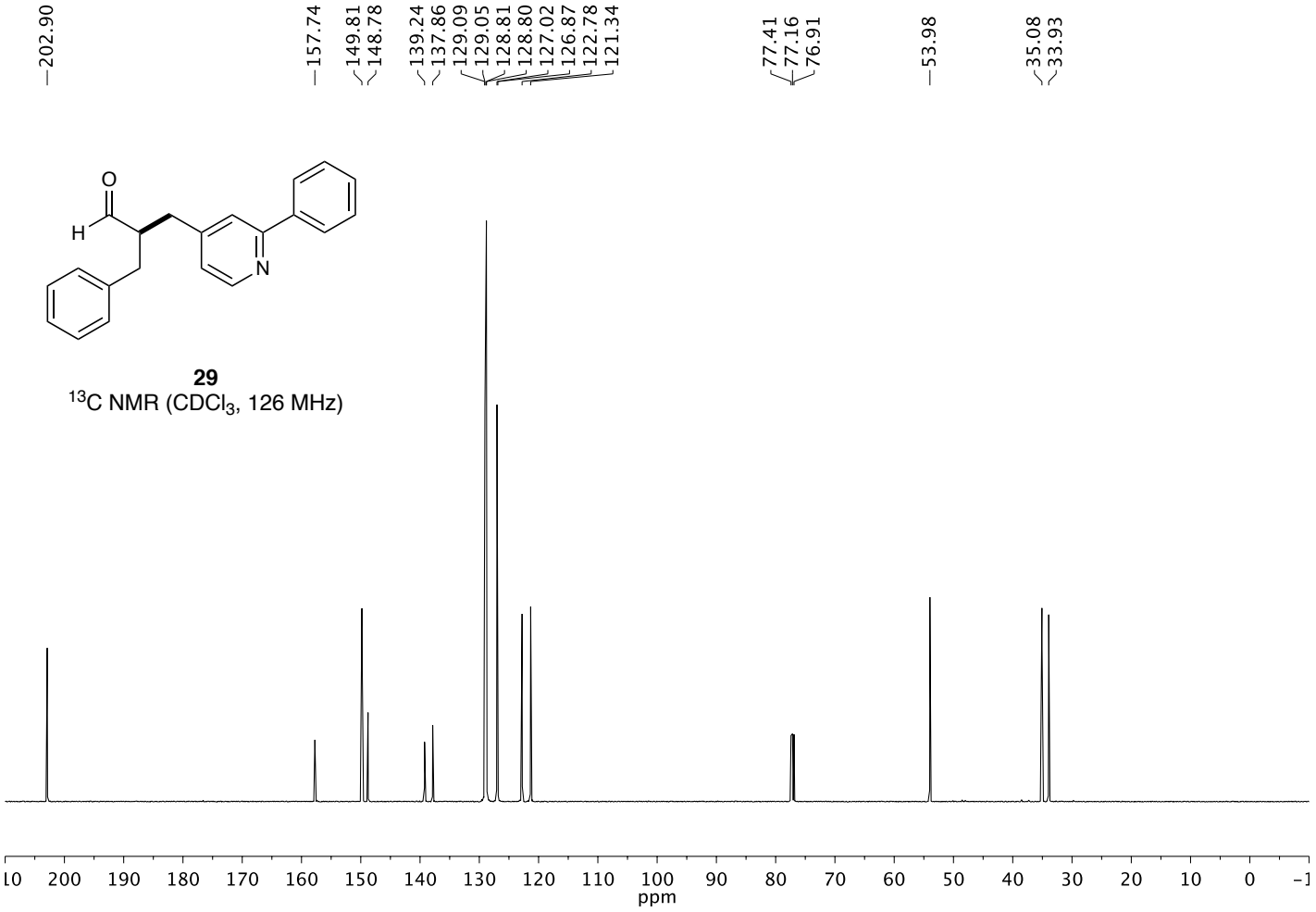


28

^{1}H NMR ($CDCl_3$, 500 MHz)

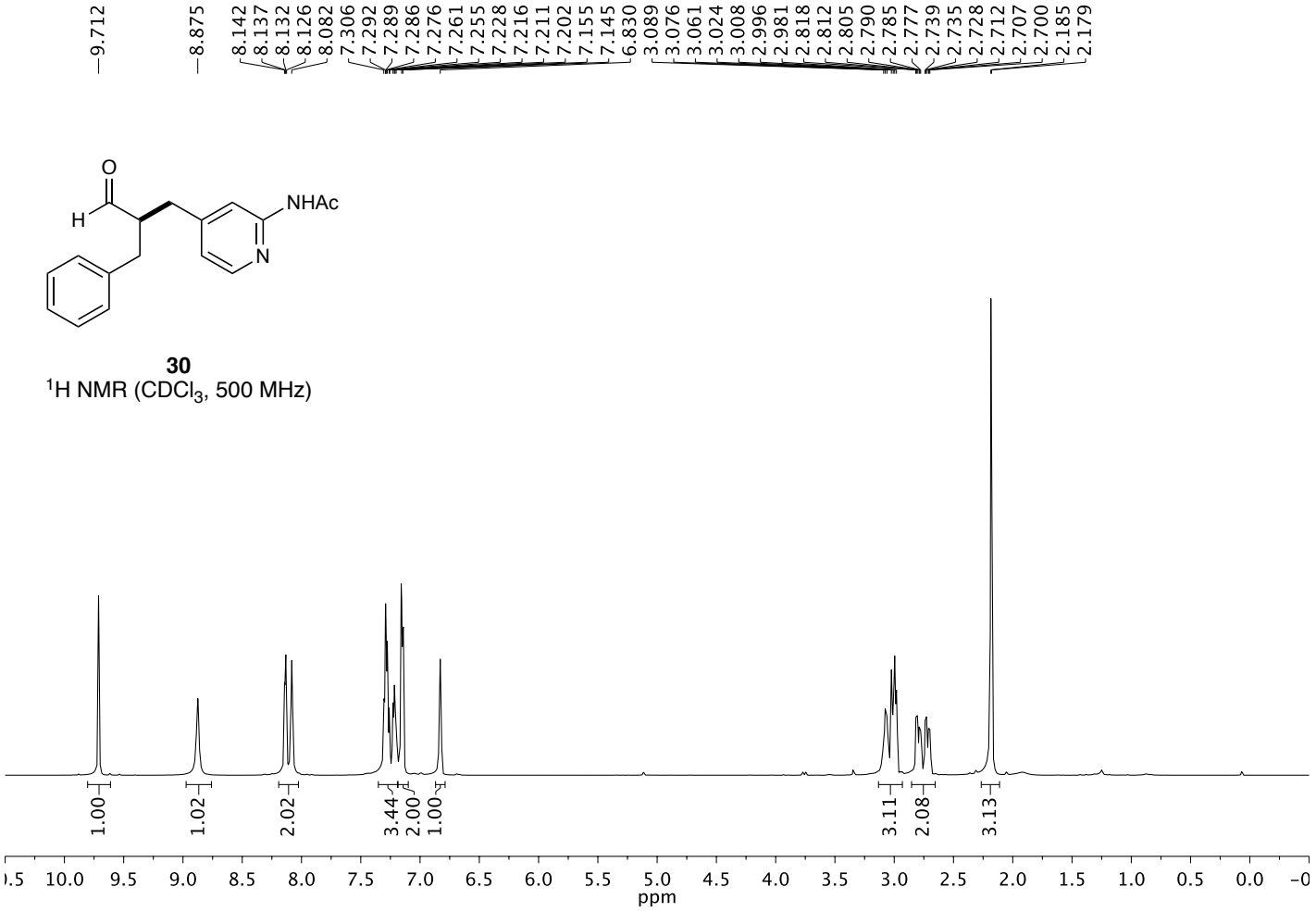

203.19
157.99
148.38
138.09
129.08
128.79
126.83
120.92
77.42
77.16
76.91
53.97
35.19
33.91
24.51
O
H
Me
N
Me
28
13C NMR (CDCl3, 126 MHz)
ppm


9.711
8.544
8.534
7.931
7.916
7.447
7.437
7.422
7.393
7.379
7.364
7.289
7.274
7.259
7.218
7.203
7.188
7.131
7.116
6.969
6.960
3.070
3.054
3.029
3.011
3.004
2.997
2.989
2.768
2.757
2.743
2.736
2.727
2.710
2.692
O
H
N
29
1H NMR (CDCl3, 500 MHz)
0.96
0.98
2.00
2.86
1.00
1.93
1.08
1.95
1.00
2.99
1.99
ppm



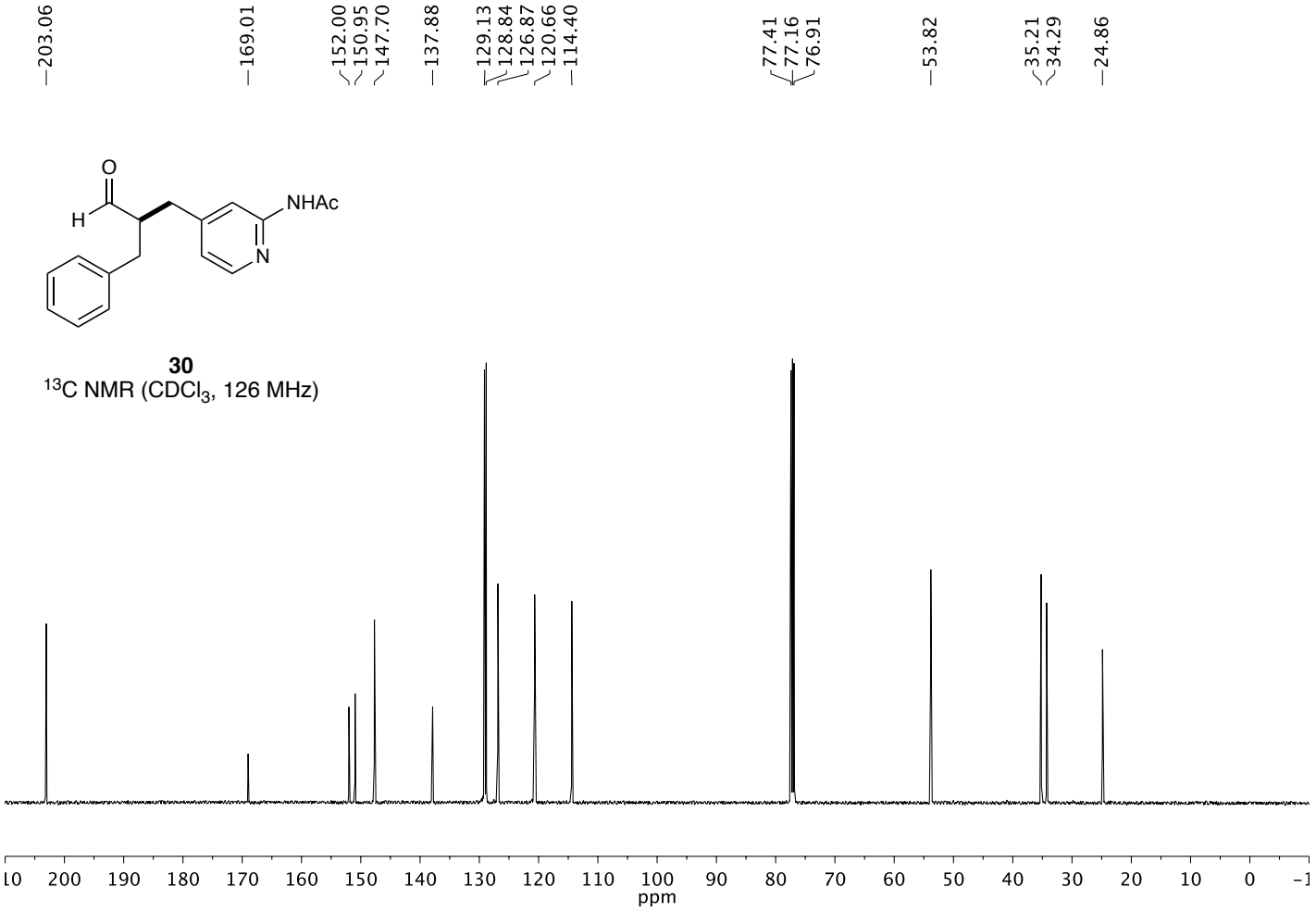
29

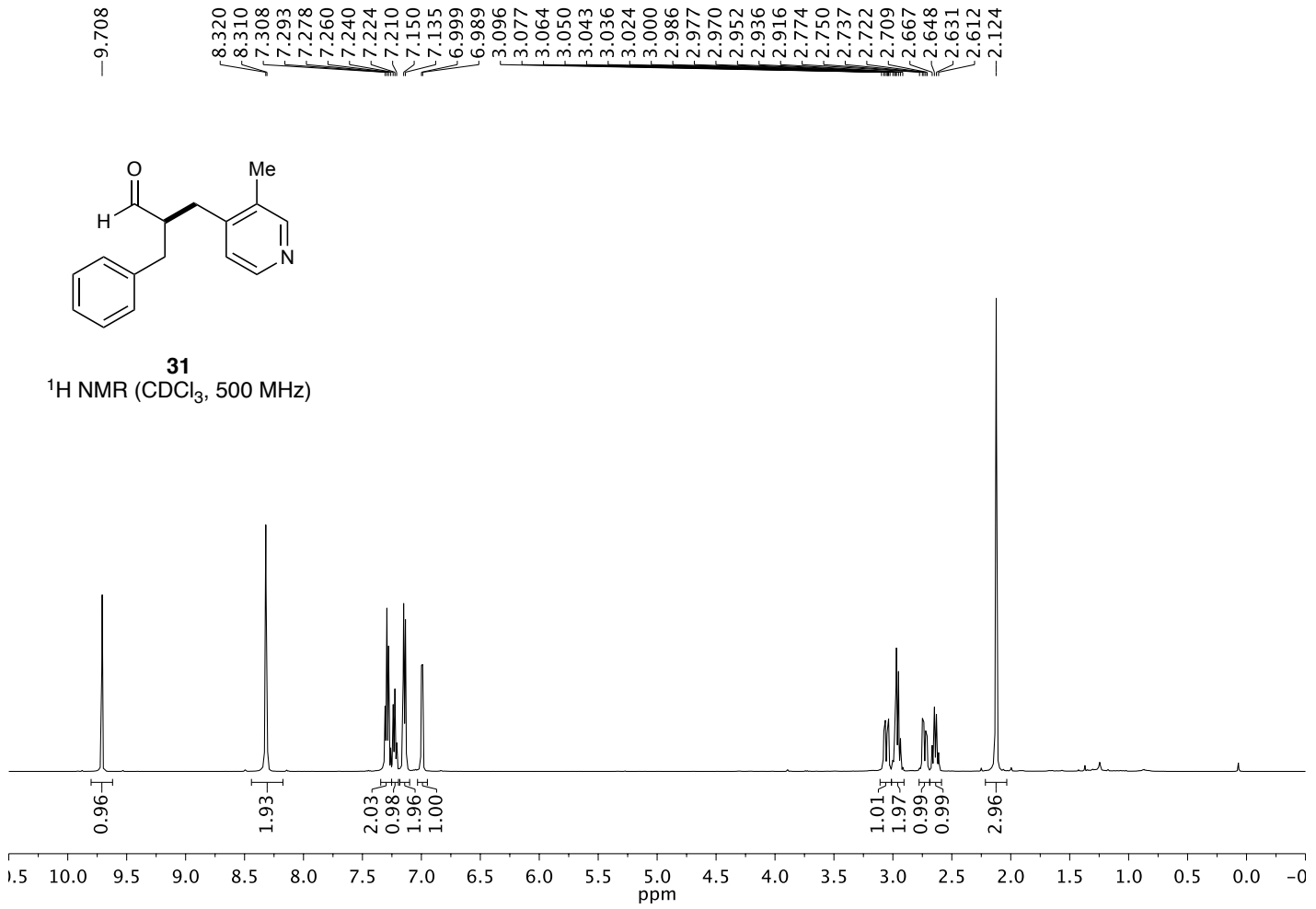
^{13}C NMR ($CDCl_3$, 126 MHz)



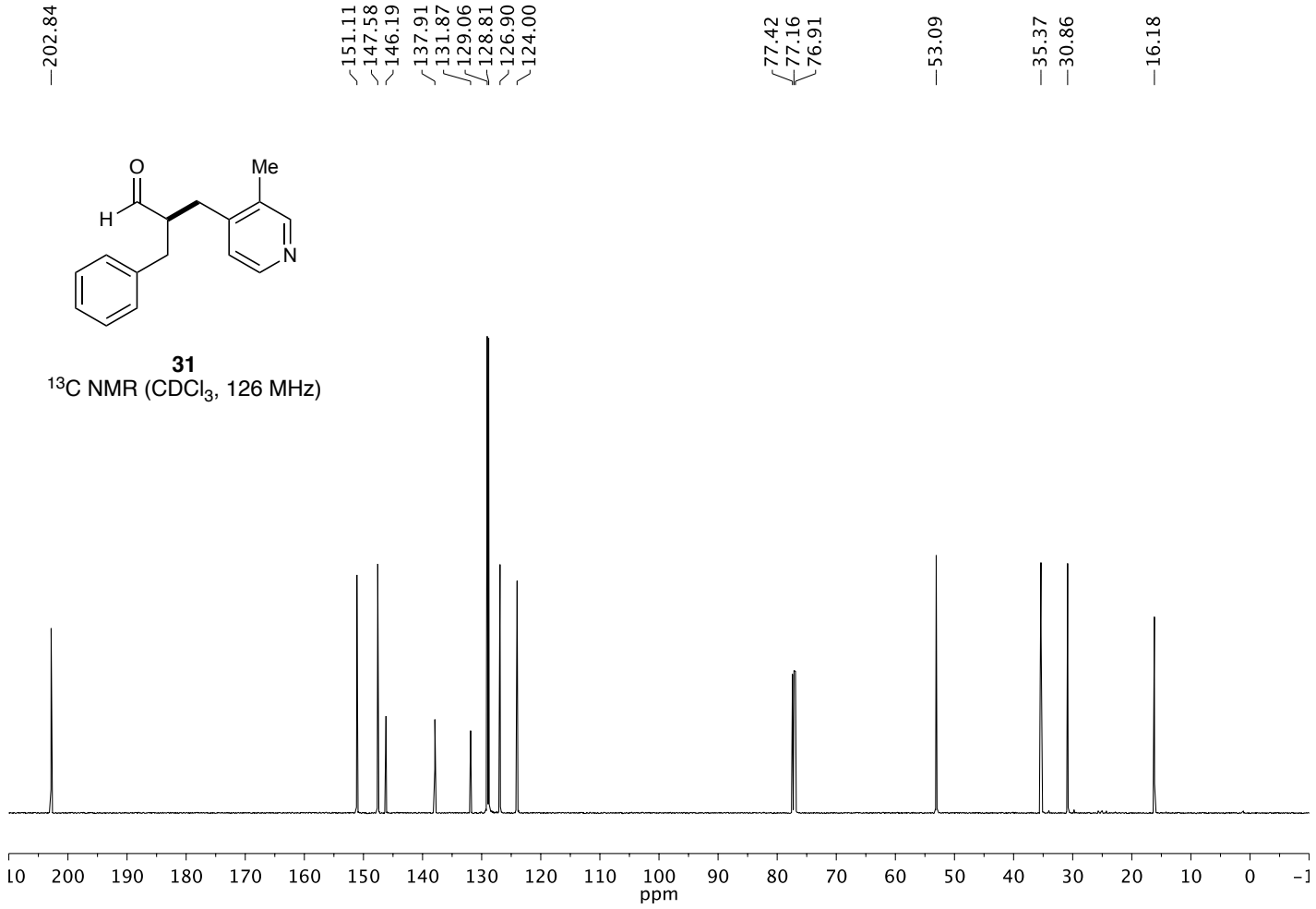
30

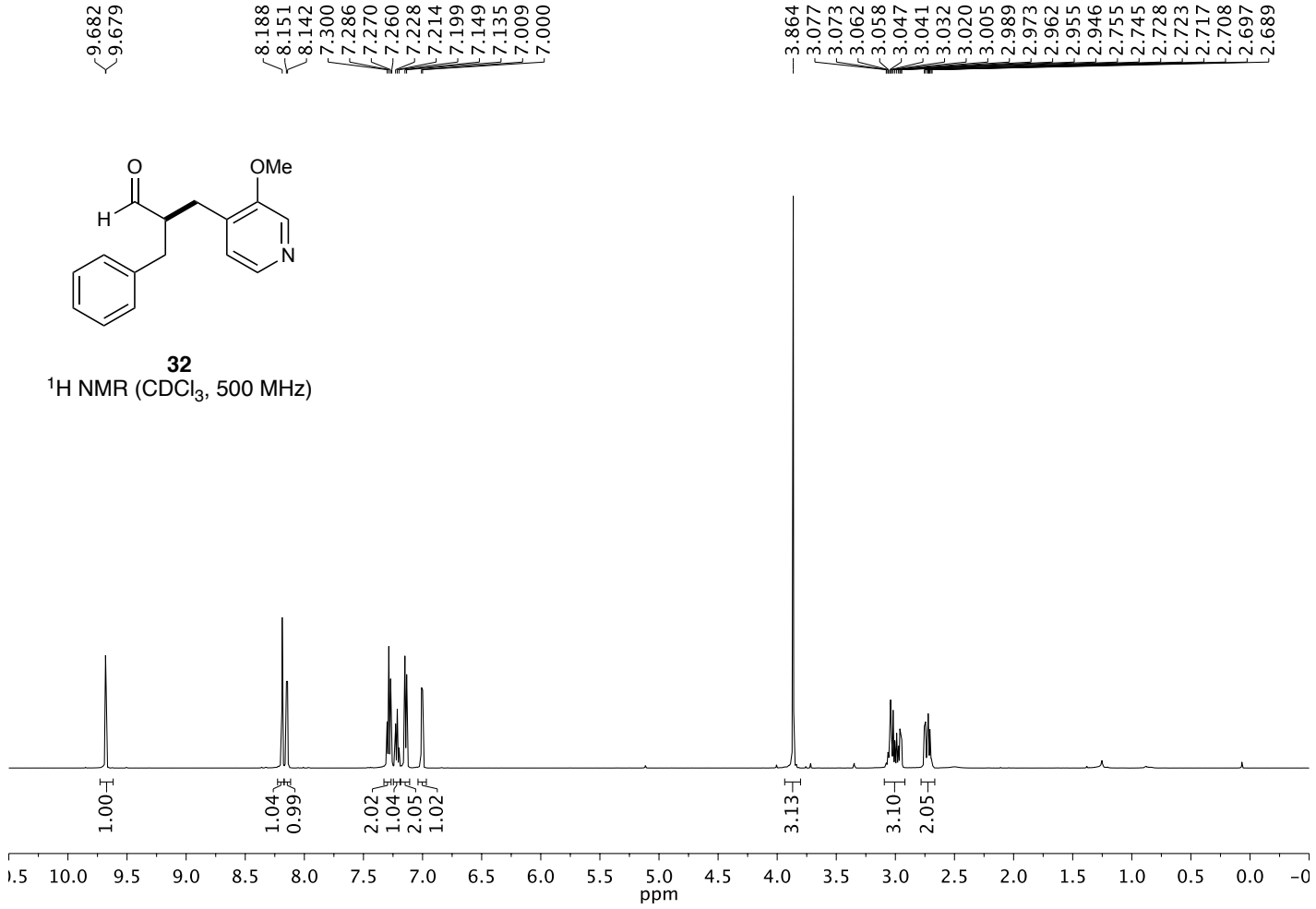
^{1}H NMR ($CDCl_3$, 500 MHz)


203.06
169.01
152.00
150.95
147.70
137.88
129.13
128.84
126.87
120.66
114.40
77.41
77.16
76.91
53.82
35.21
34.29
24.86
O
H
NHAc
N
30
13C NMR (CDCl3, 126 MHz)
ppm

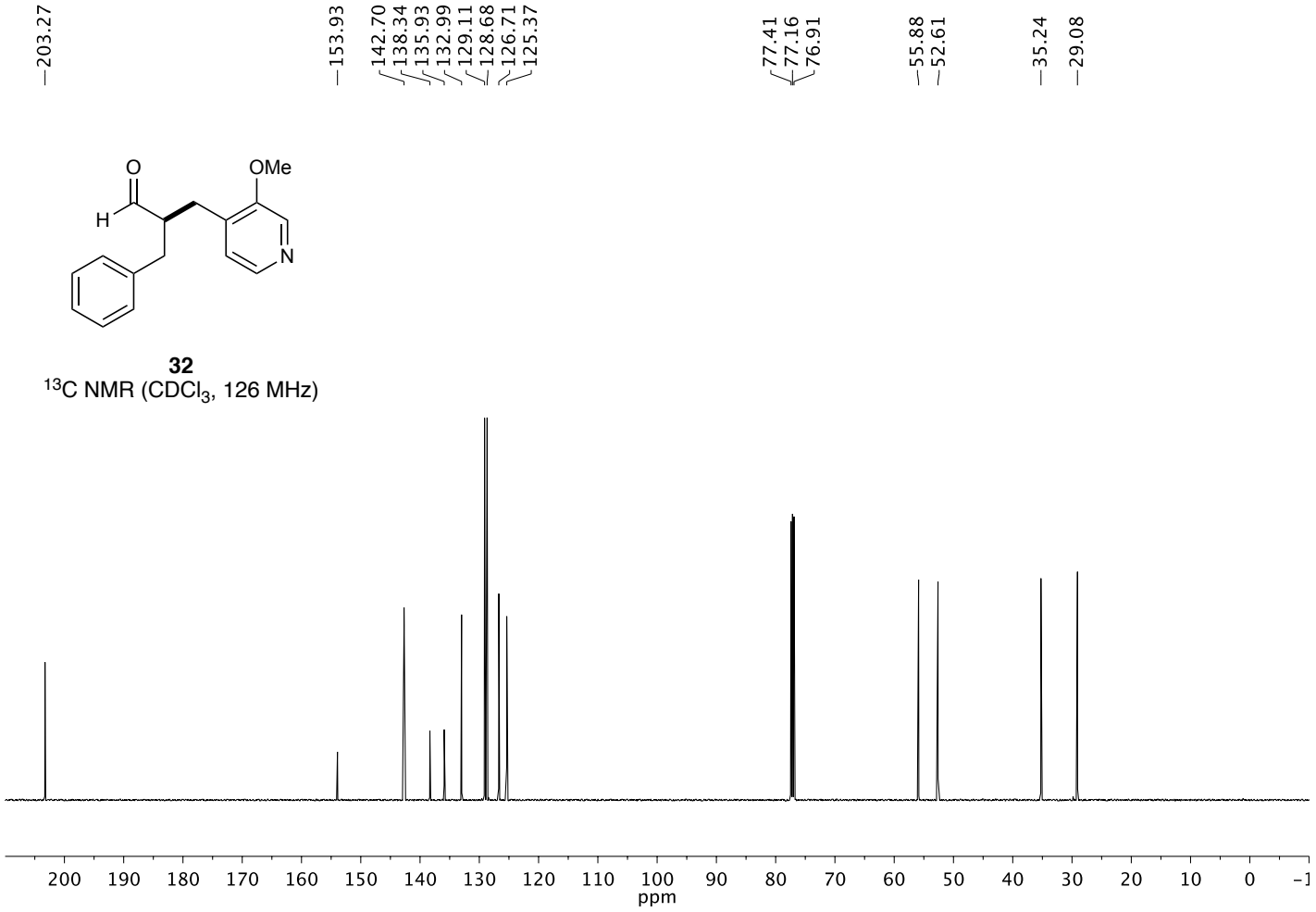


31
^{1}H NMR ($CDCl_3$, 500 MHz)


202.84
151.11
147.58
146.19
137.91
131.87
129.06
128.81
126.90
124.00
77.42
77.16
76.91
53.09
35.37
30.86
16.18
O
H
Me
N
31
13C NMR (CDCl3, 126 MHz)
ppm

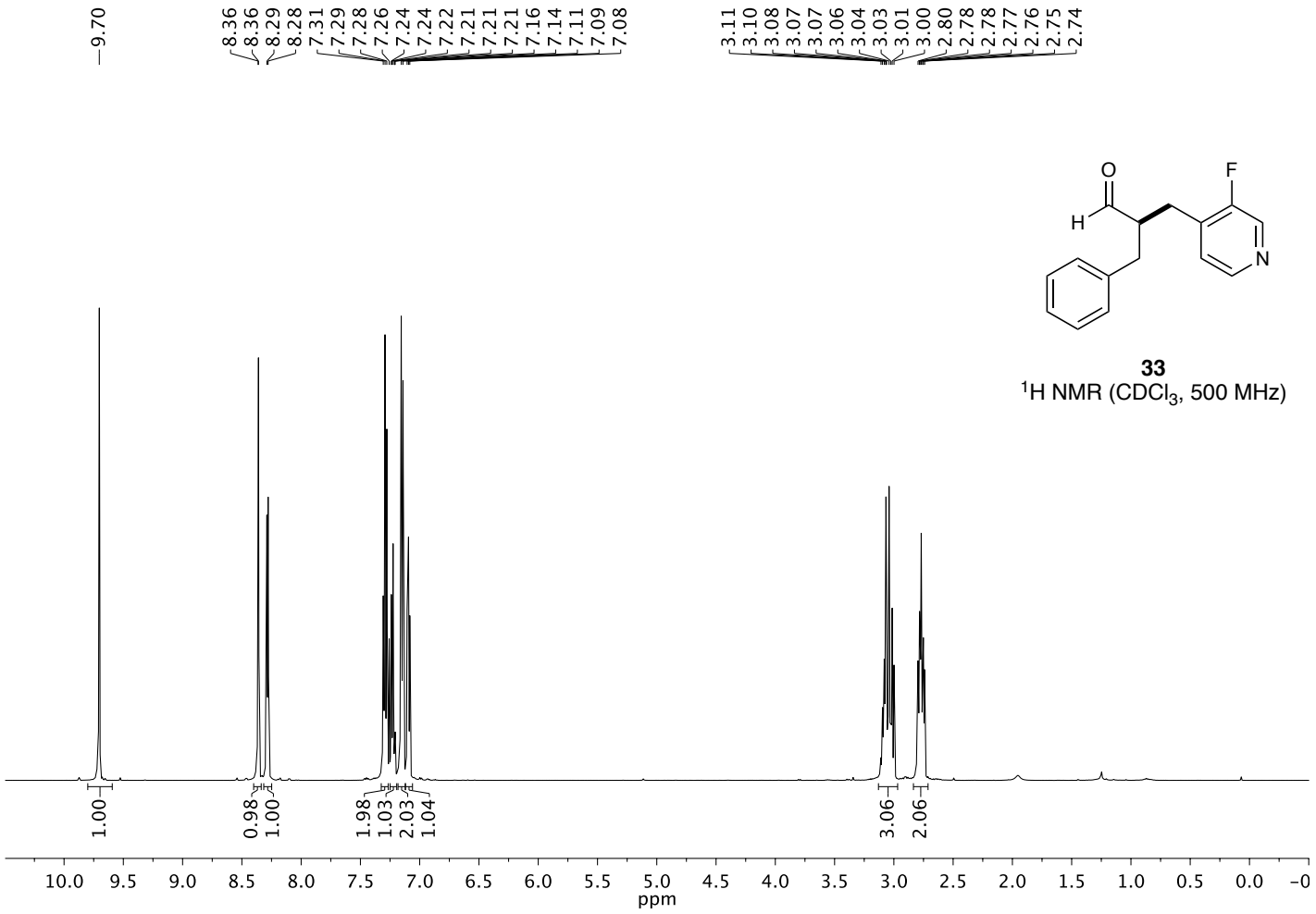


32
^{1}H NMR ($CDCl_3$, 500 MHz)



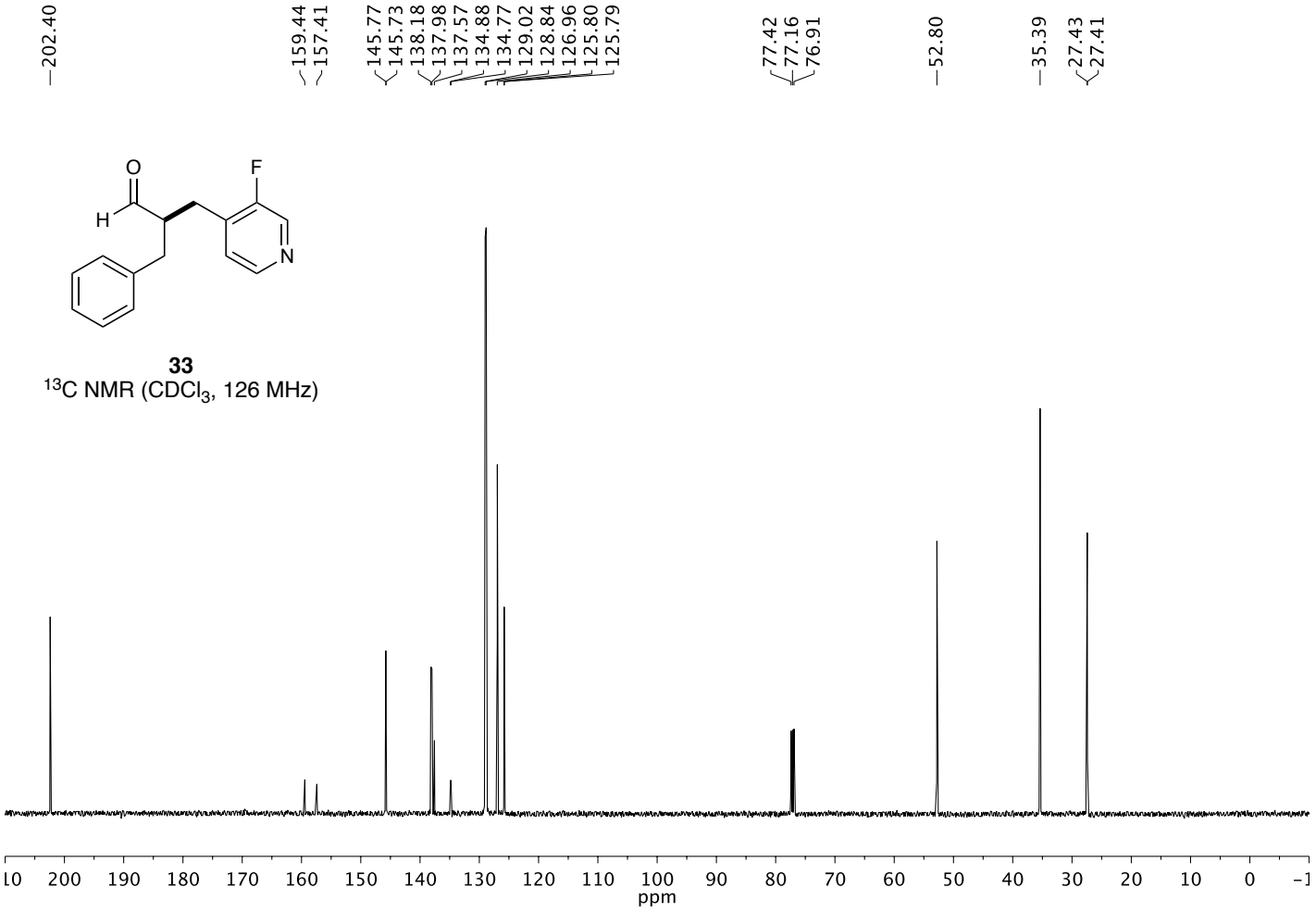
32

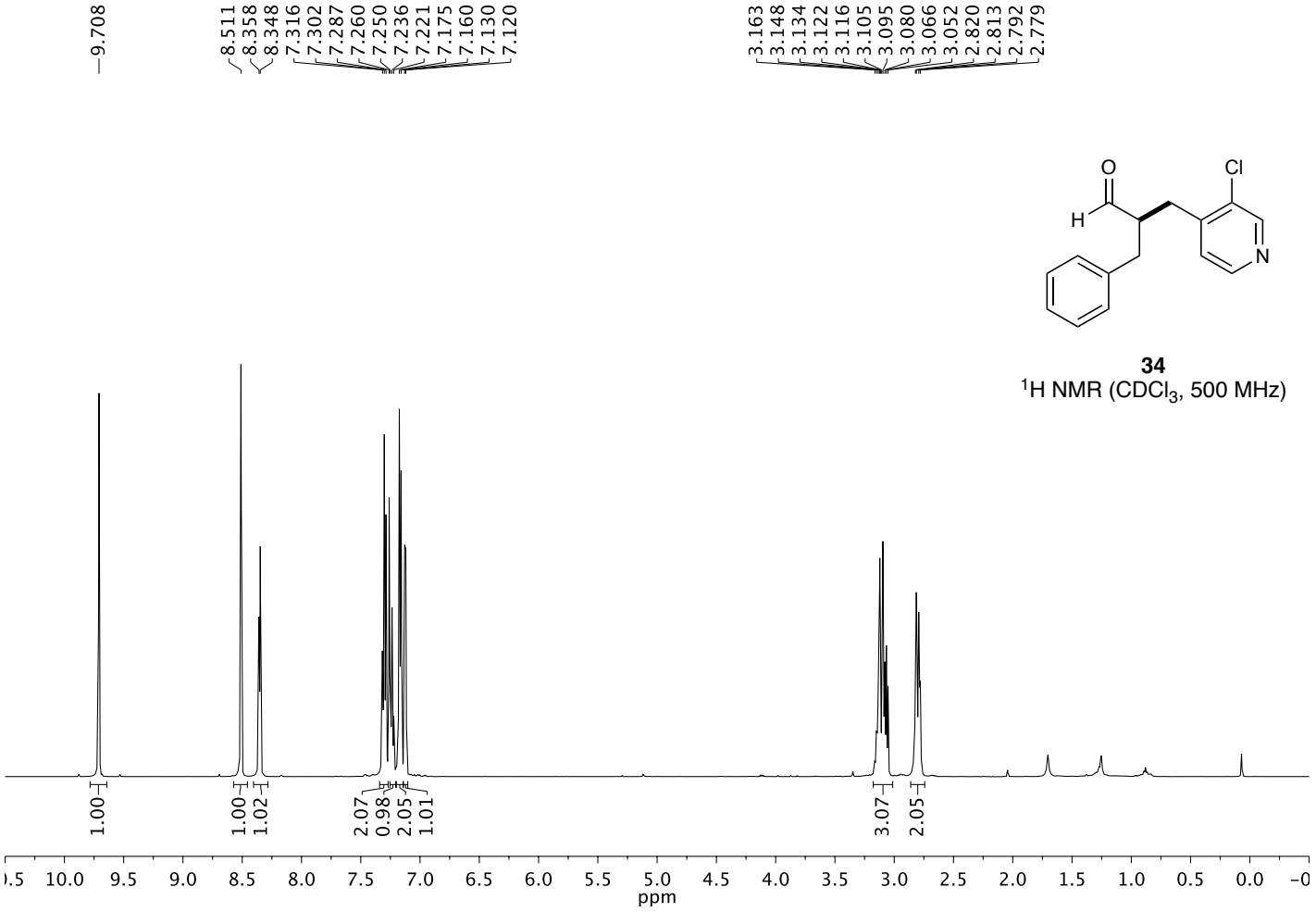
^{13}C NMR ($CDCl_3$, 126 MHz)



33

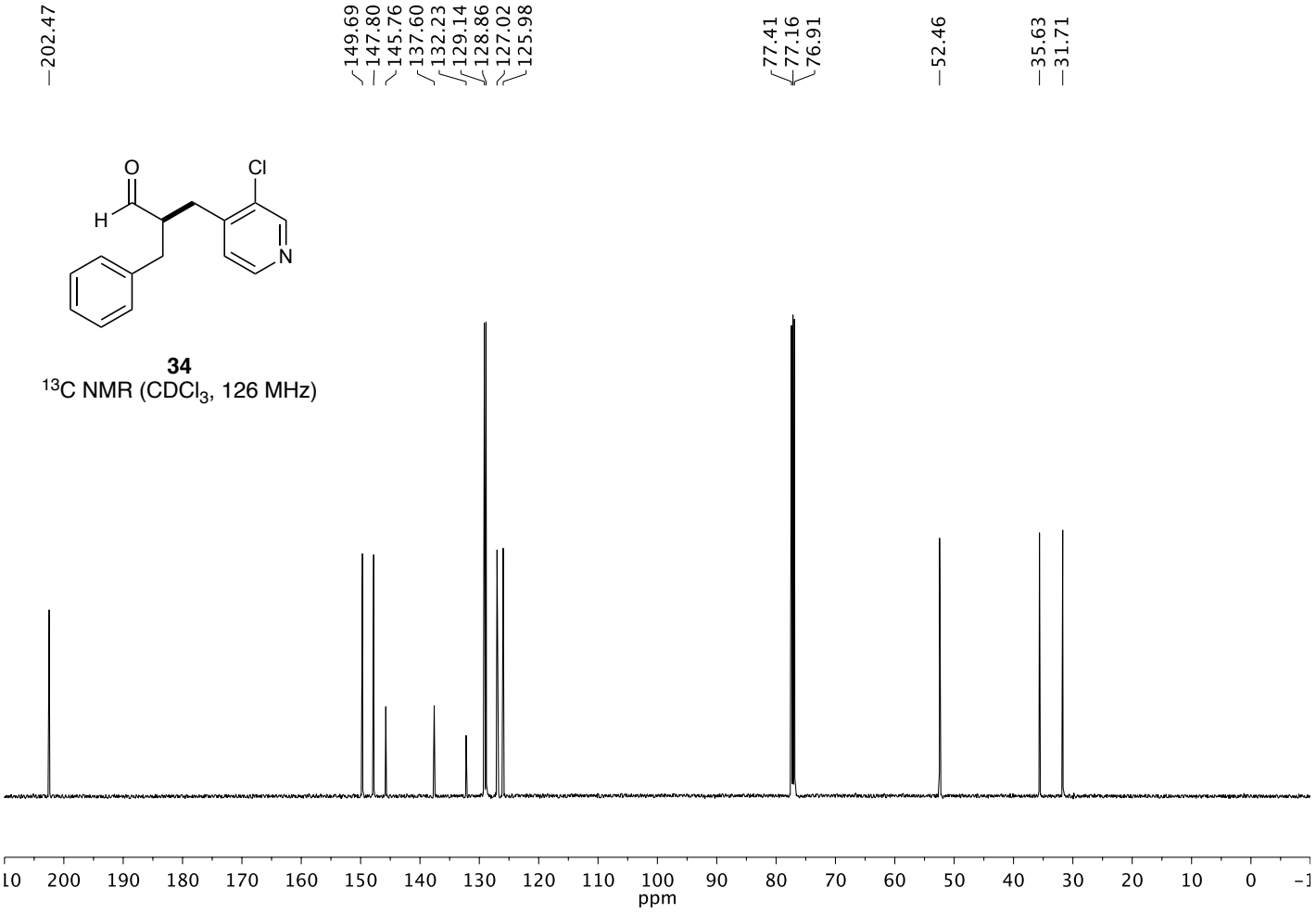
^{1}H NMR ($CDCl_3$, 500 MHz)

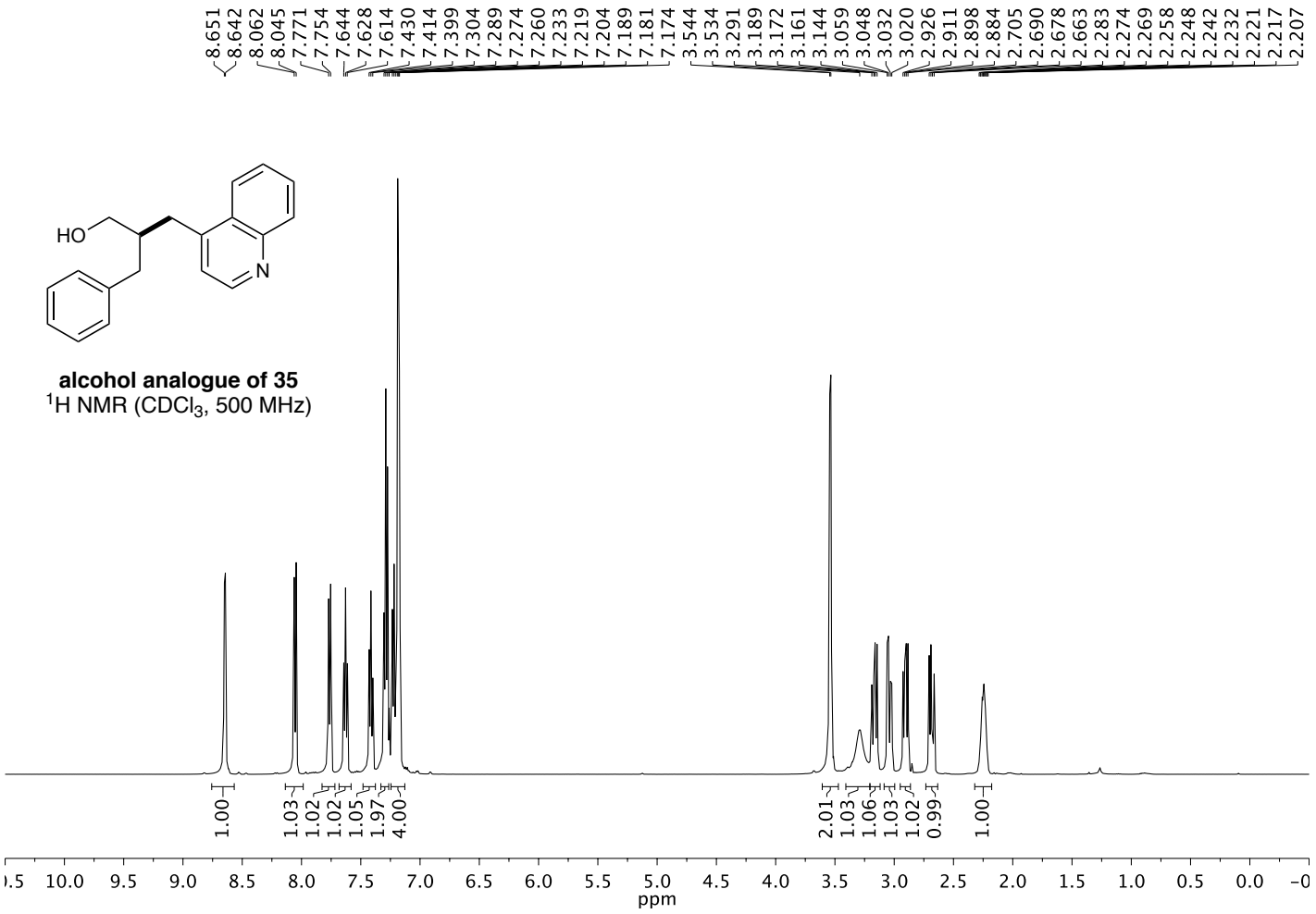

202.40
159.44
157.41
145.77
145.73
138.18
137.98
137.57
134.88
134.77
129.02
128.84
126.96
125.80
125.79
77.42
77.16
76.91
52.80
35.39
27.43
27.41
O
H
F
N
33
13C NMR (CDCl3, 126 MHz)
ppm

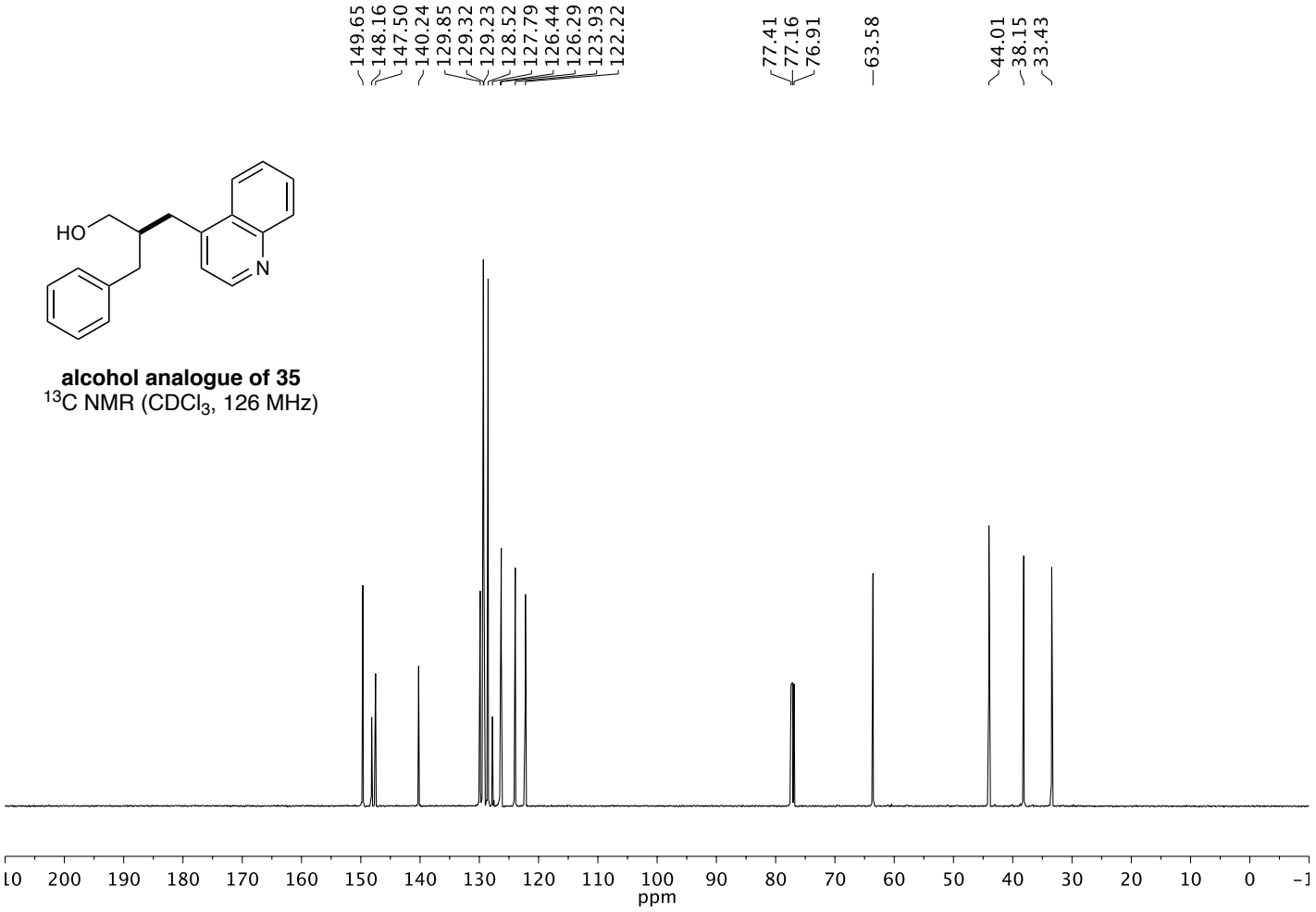


34

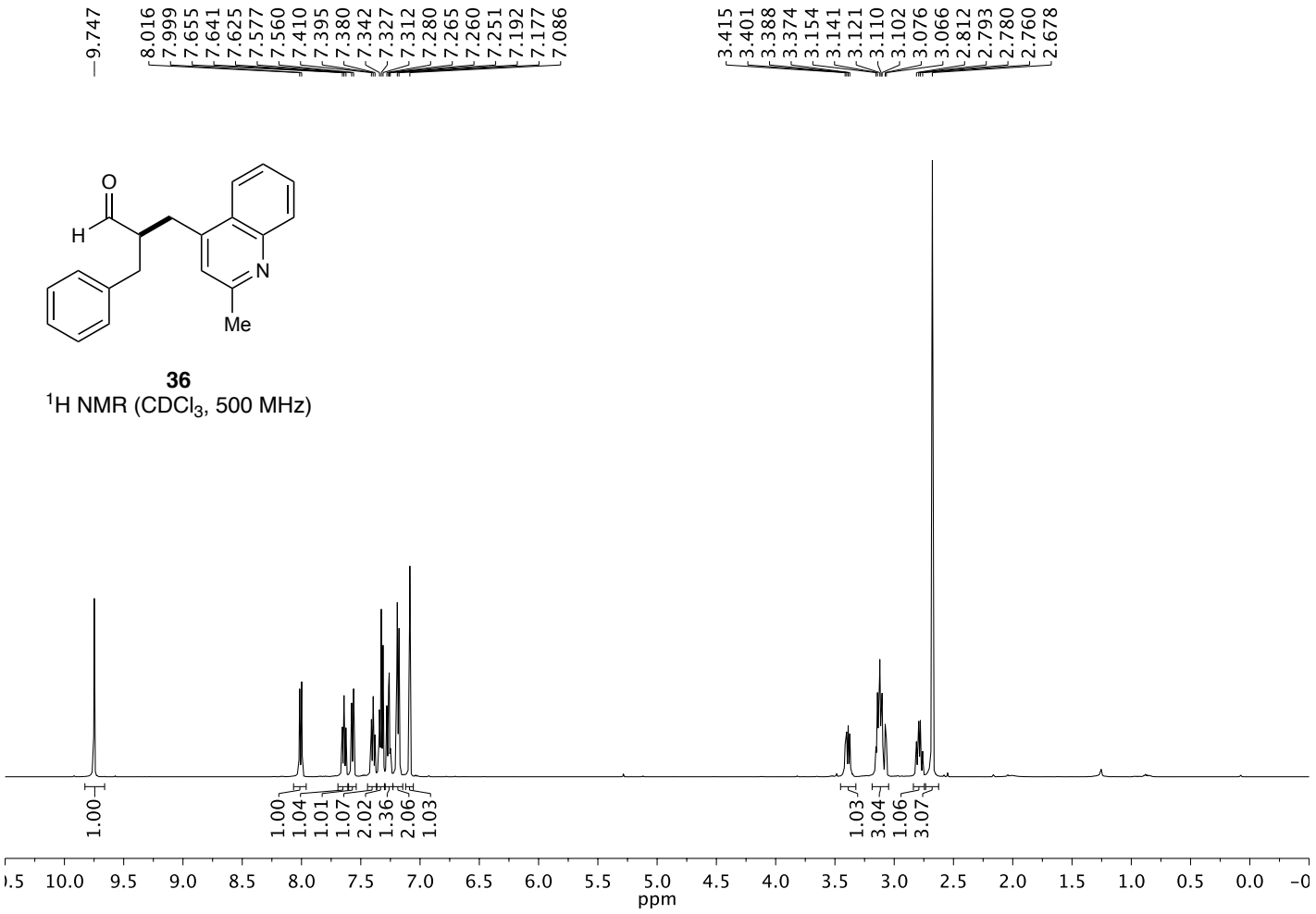
^{1}H NMR ($CDCl_3$, 500 MHz)


202.47
149.69
147.80
145.76
137.60
132.23
129.14
128.86
127.02
125.98
77.41
77.16
76.91
52.46
35.63
31.71
O
H
Cl
N
34
13C NMR (CDCl3, 126 MHz)
ppm


8.651
8.642
8.062
8.045
7.771
7.754
7.644
7.628
7.614
7.430
7.414
7.399
7.304
7.289
7.274
7.260
7.233
7.219
7.204
7.189
7.181
7.174
3.544
3.534
3.291
3.189
3.172
3.161
3.144
3.059
3.048
3.032
3.020
2.926
2.911
2.898
2.884
2.705
2.690
2.678
2.663
2.283
2.274
2.269
2.258
2.248
2.242
2.232
2.221
2.217
2.207
HO
N
alcohol analogue of 35
1H NMR (CDCl3, 500 MHz)
1.00
1.03
1.02
1.02
1.05
1.97
4.00
2.01
1.03
1.06
1.03
1.02
0.99
1.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm

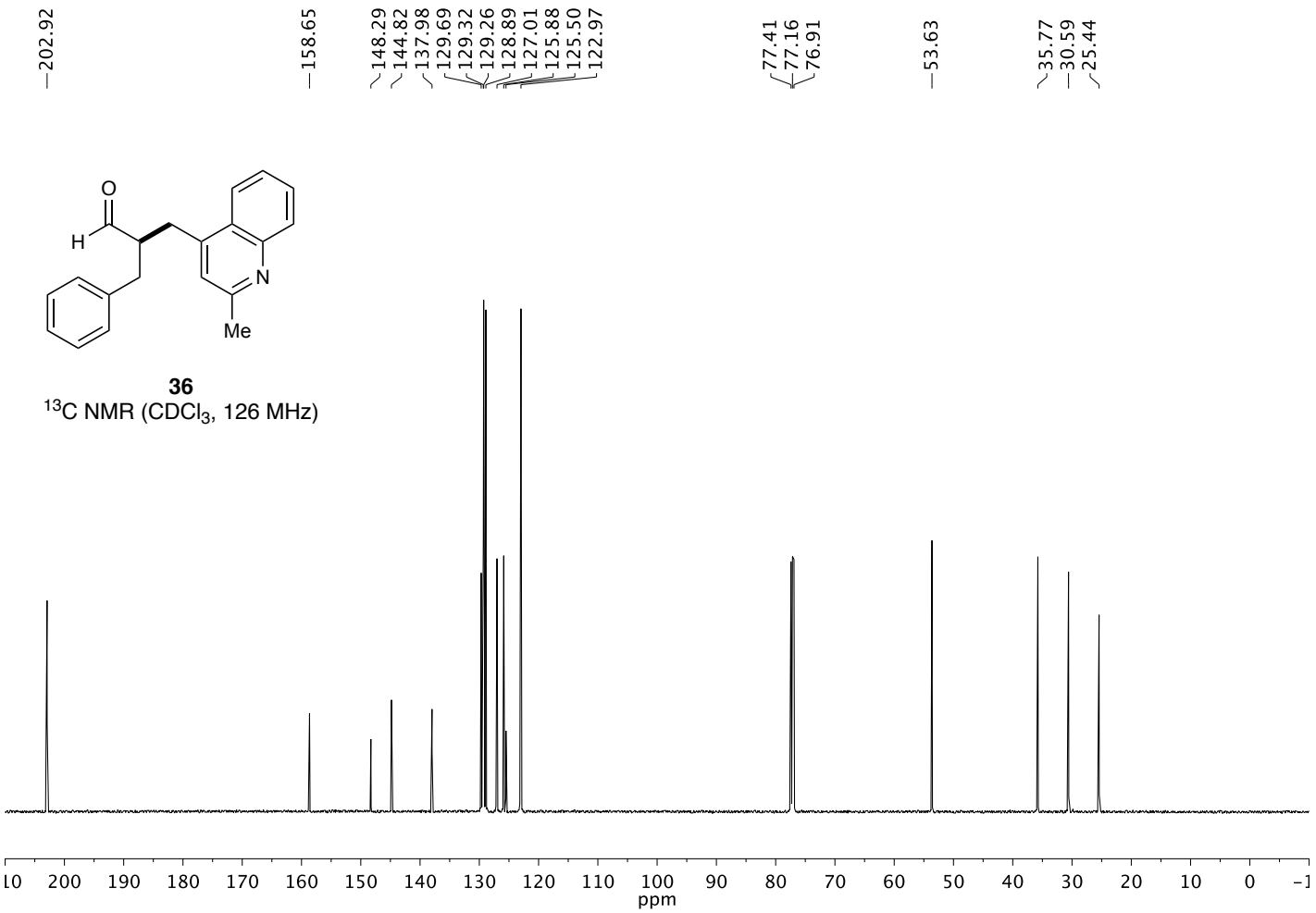


alcohol analogue of 35
^{13}C NMR ($CDCl_3$, 126 MHz)



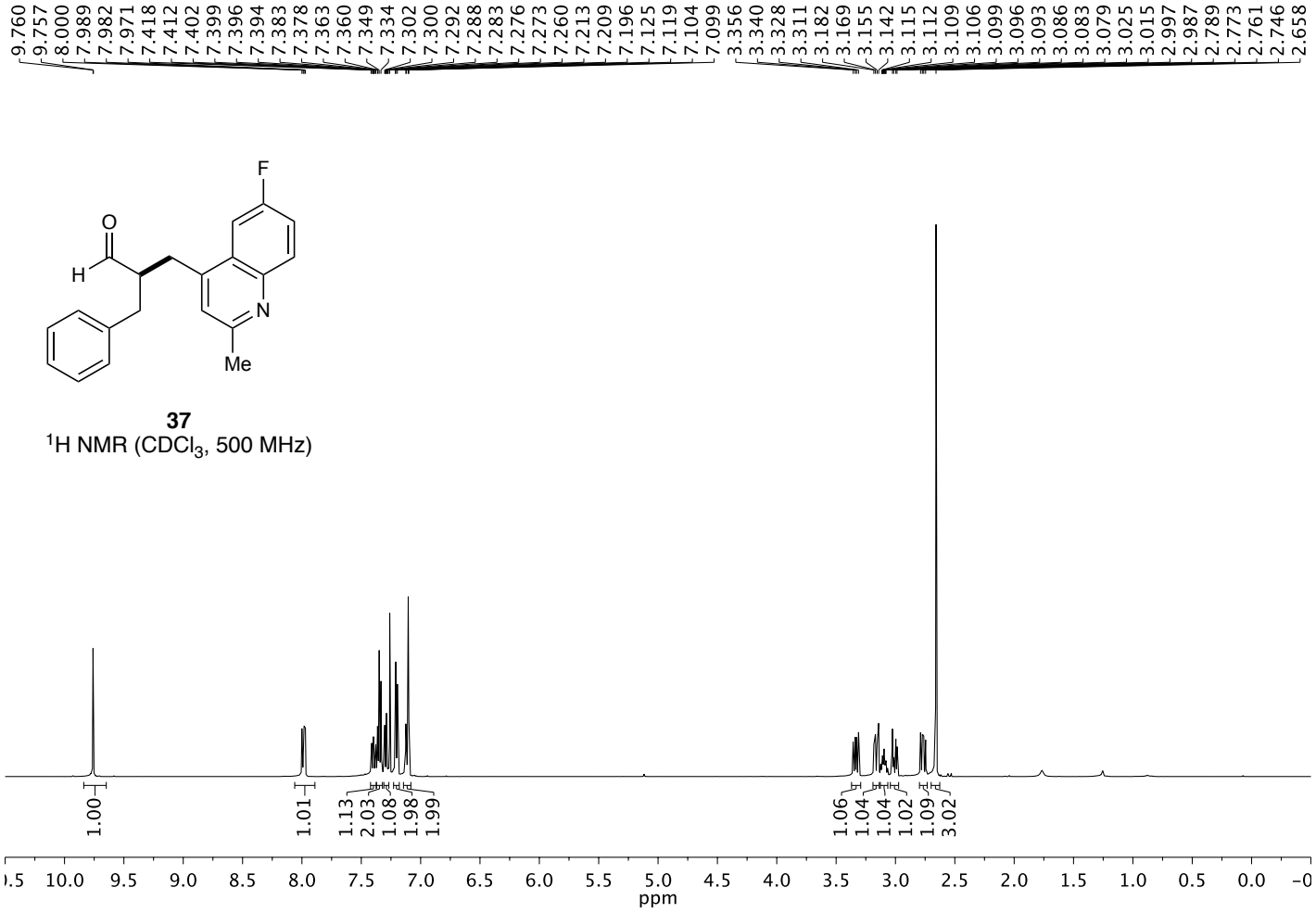
36

^{1}H NMR ($CDCl_3$, 500 MHz)



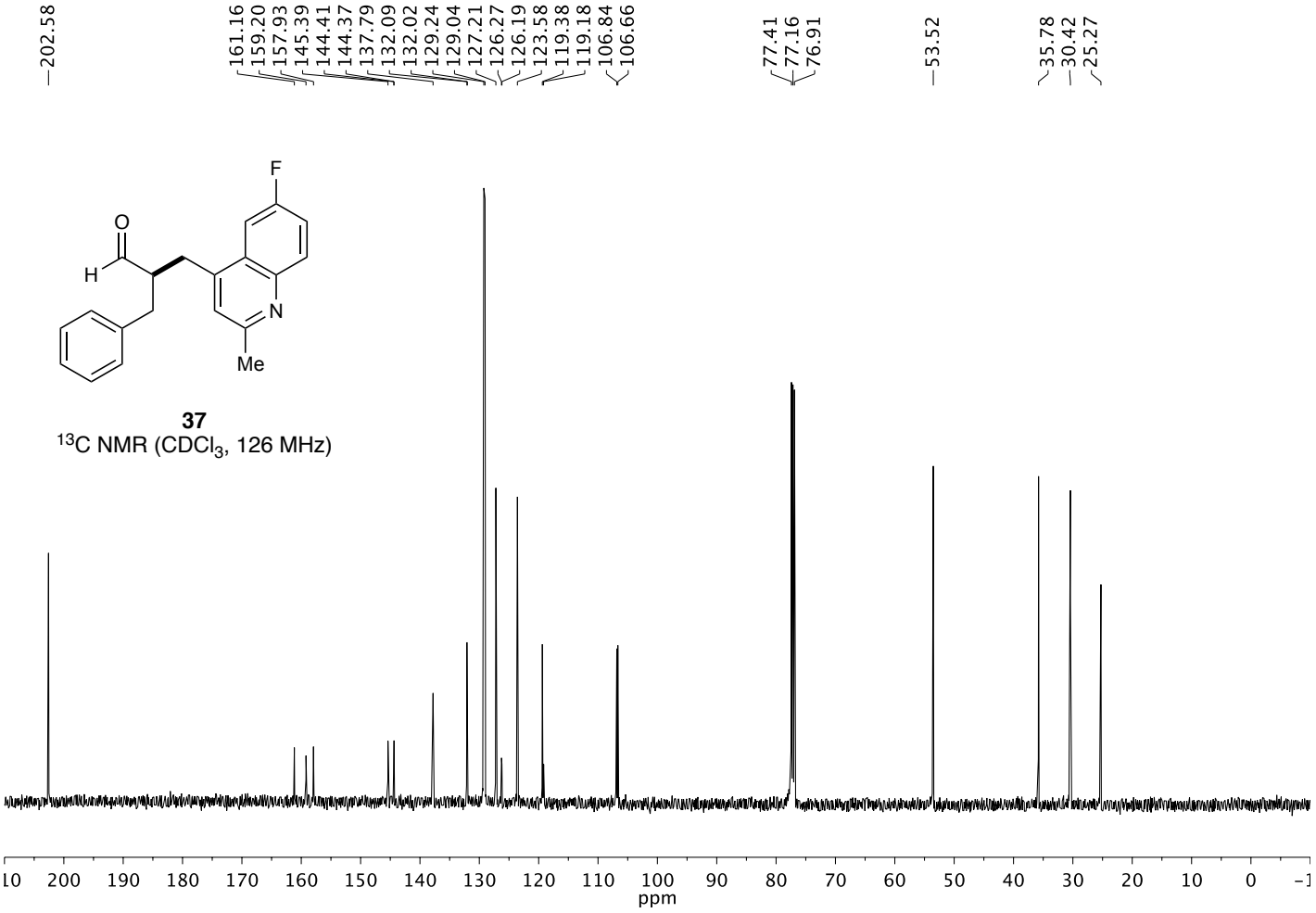
36

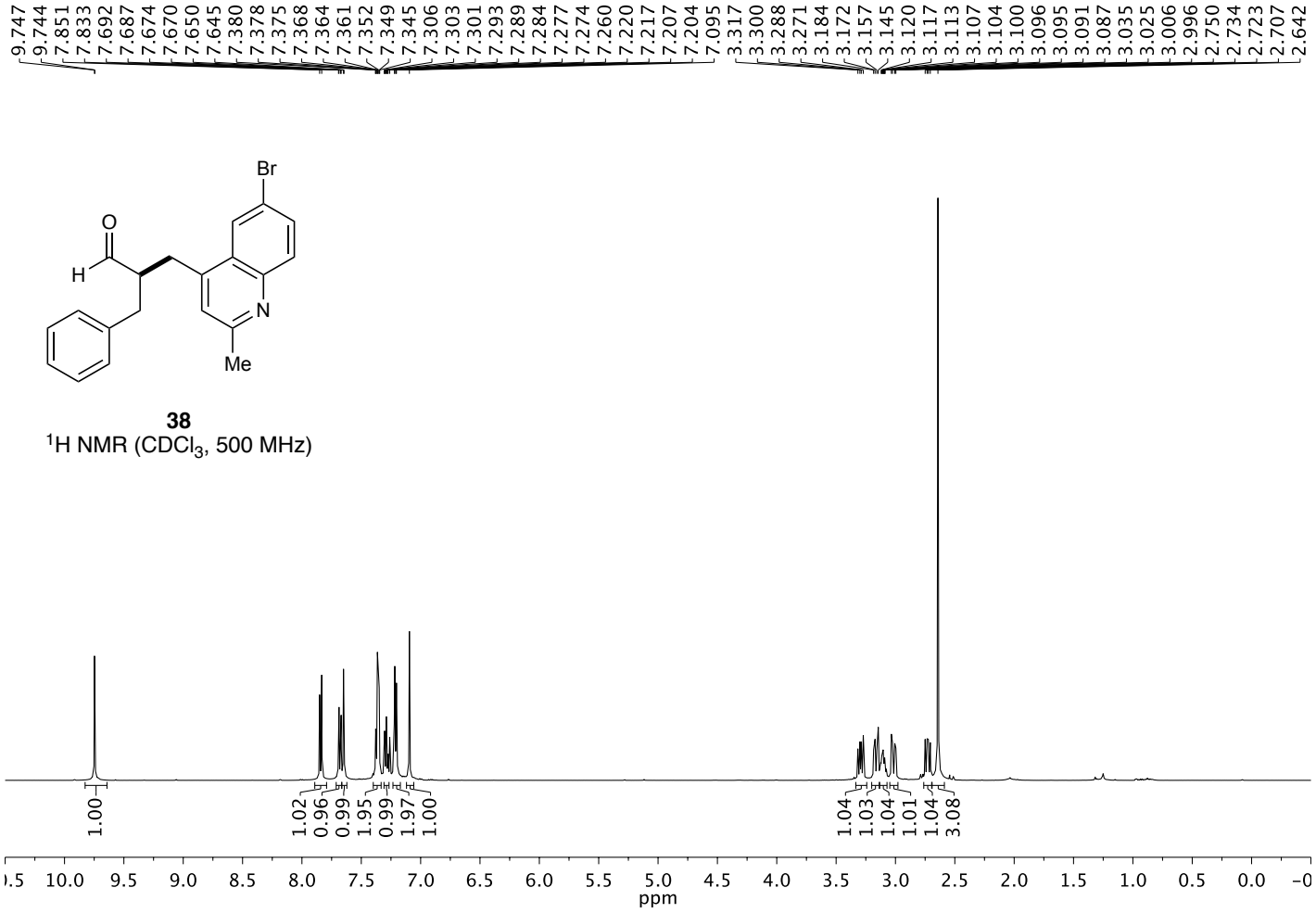
^{13}C NMR ($CDCl_3$, 126 MHz)

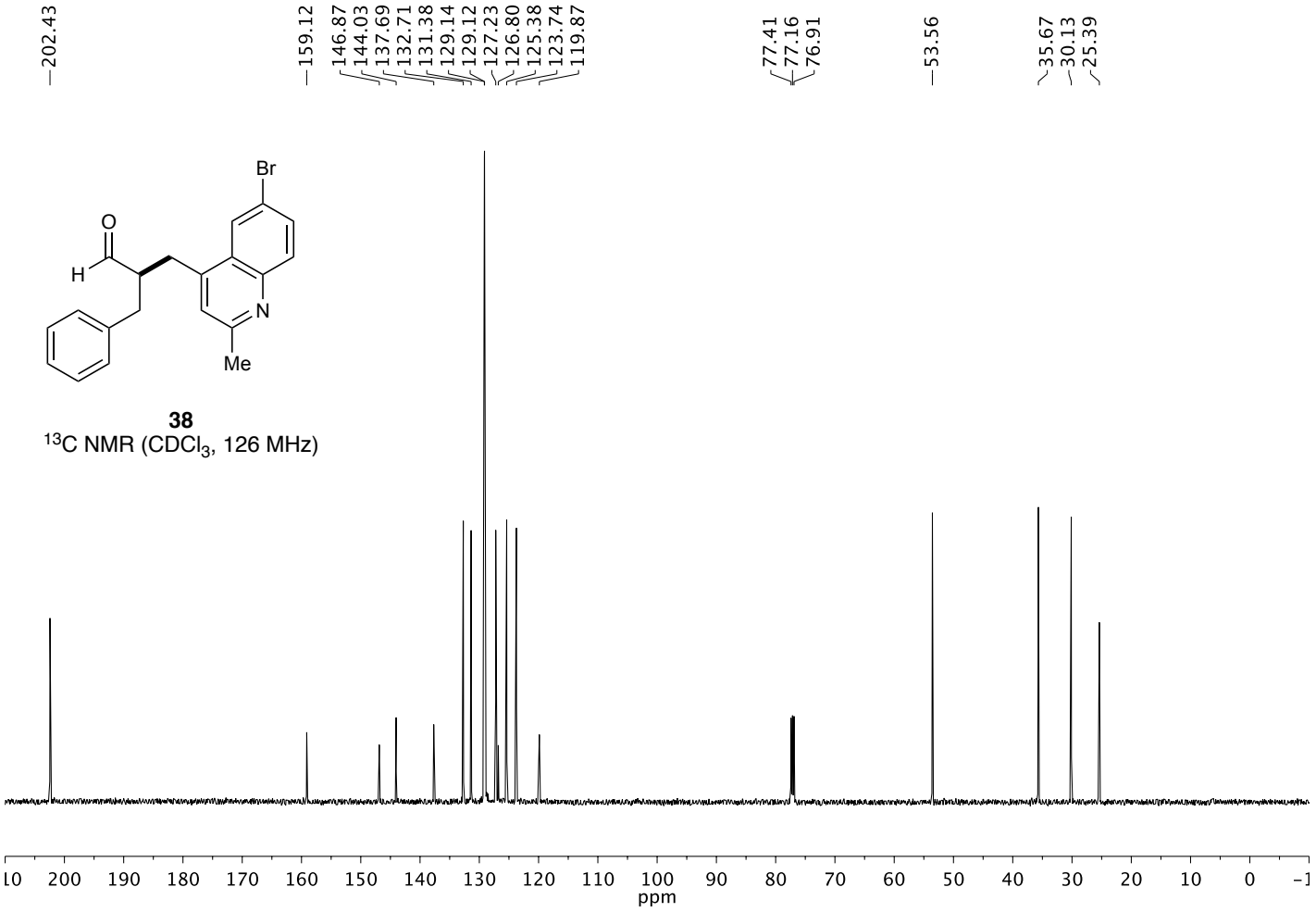


37

^{1}H NMR ($CDCl_3$, 500 MHz)

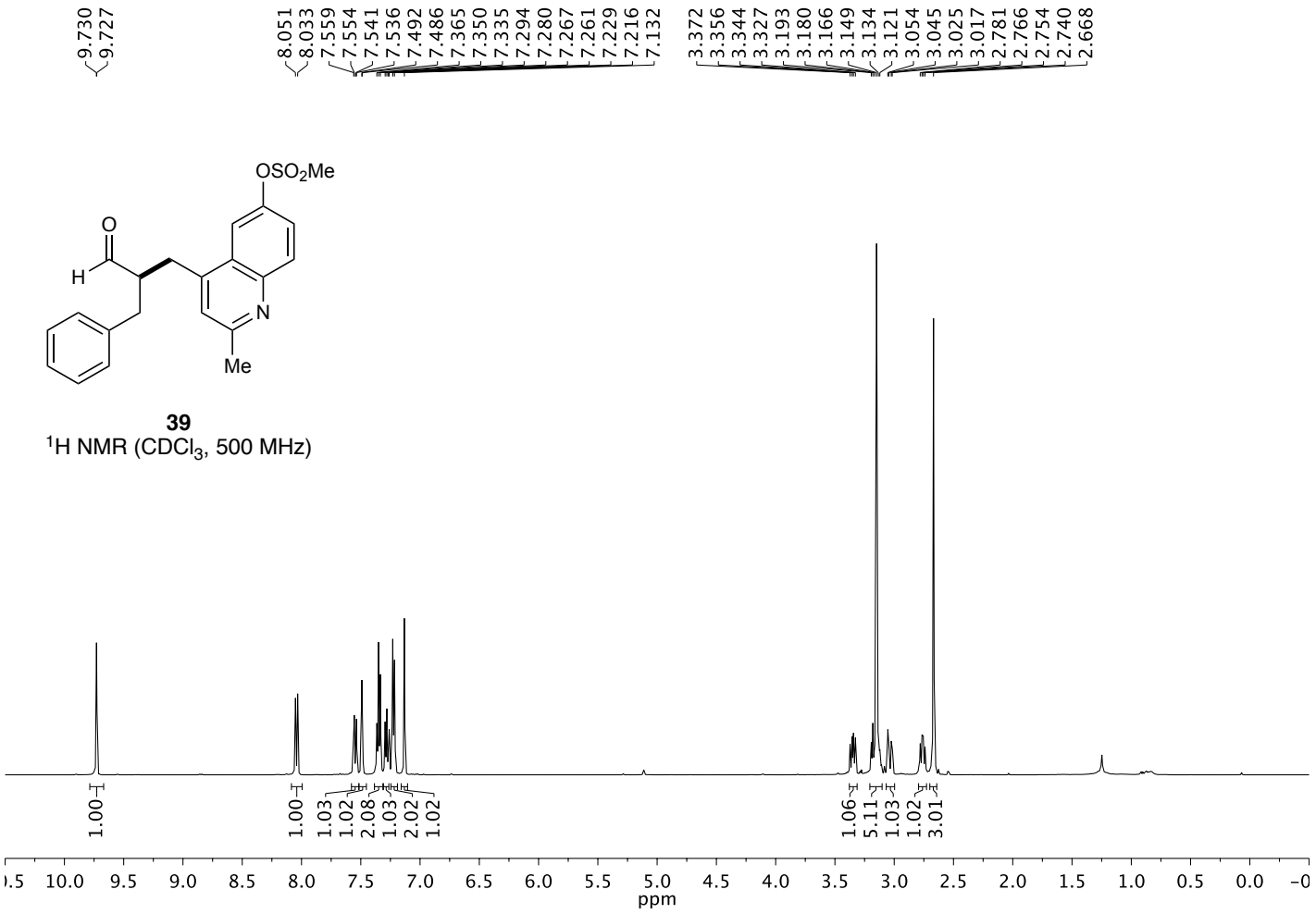

202.58
161.16
159.20
157.93
145.39
144.41
144.37
137.79
132.09
132.02
129.24
129.04
127.21
126.27
126.19
123.58
119.38
119.18
106.84
106.66
77.41
77.16
76.91
53.52
35.78
30.42
25.27
F
O
H
N
Me
37
13C NMR (CDCl3, 126 MHz)
ppm


9.747
9.744
7.851
7.833
7.692
7.687
7.674
7.670
7.650
7.645
7.380
7.378
7.375
7.368
7.364
7.361
7.352
7.349
7.345
7.306
7.303
7.301
7.293
7.289
7.284
7.277
7.274
7.260
7.220
7.217
7.207
7.204
7.095
3.317
3.300
3.288
3.271
3.184
3.172
3.157
3.145
3.120
3.117
3.113
3.107
3.104
3.100
3.096
3.095
3.091
3.087
3.035
3.025
3.006
2.996
2.750
2.734
2.723
2.707
2.642
Br
O
H
N
Me
38
1H NMR (CDCl3, 500 MHz)
1.00
1.02
0.96
0.99
1.95
0.99
1.97
1.00
1.04
1.03
1.04
1.01
1.04
3.08
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm



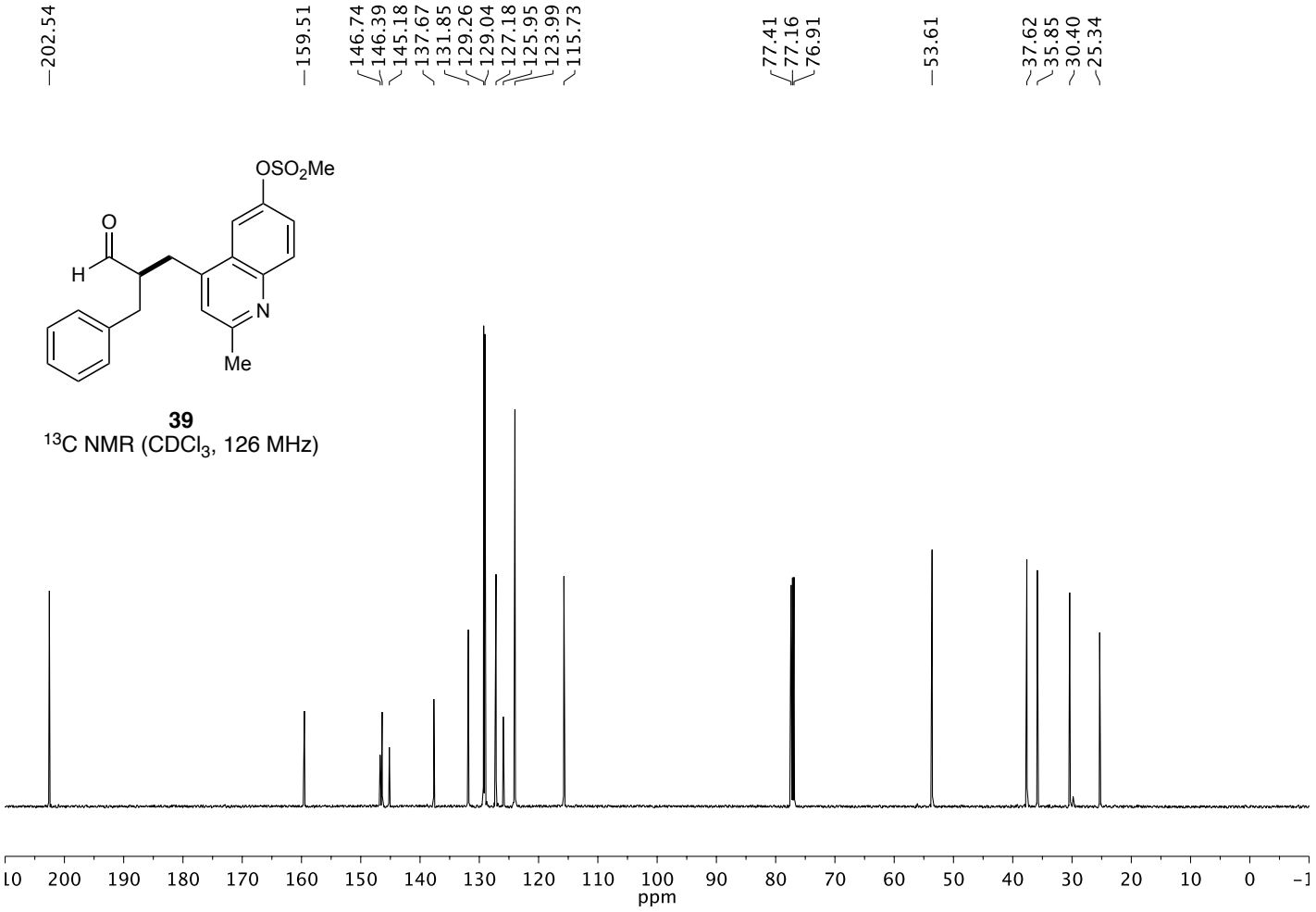
38

^{13}C NMR ($CDCl_3$, 126 MHz)



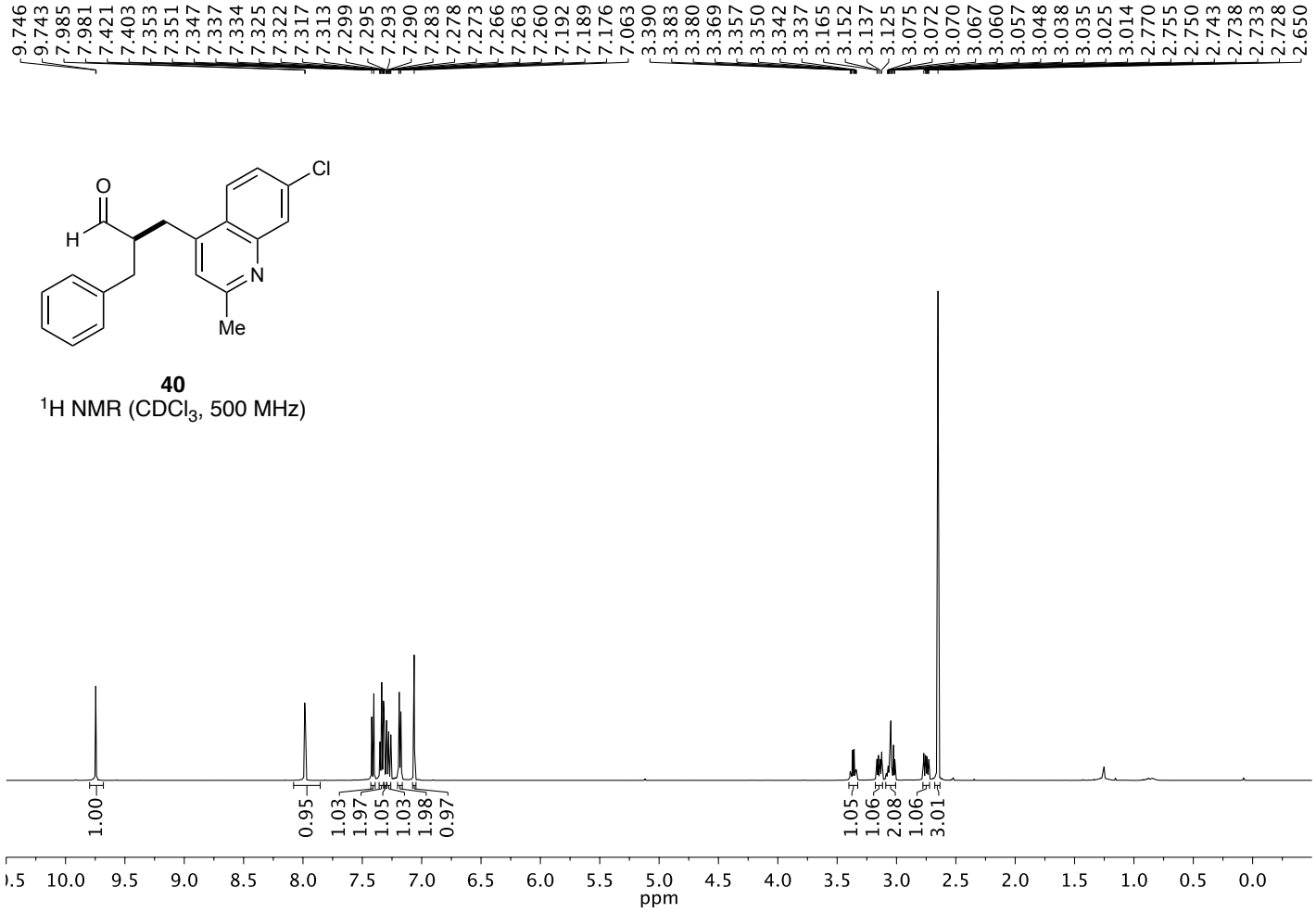
39

^{1}H NMR ($CDCl_3$, 500 MHz)



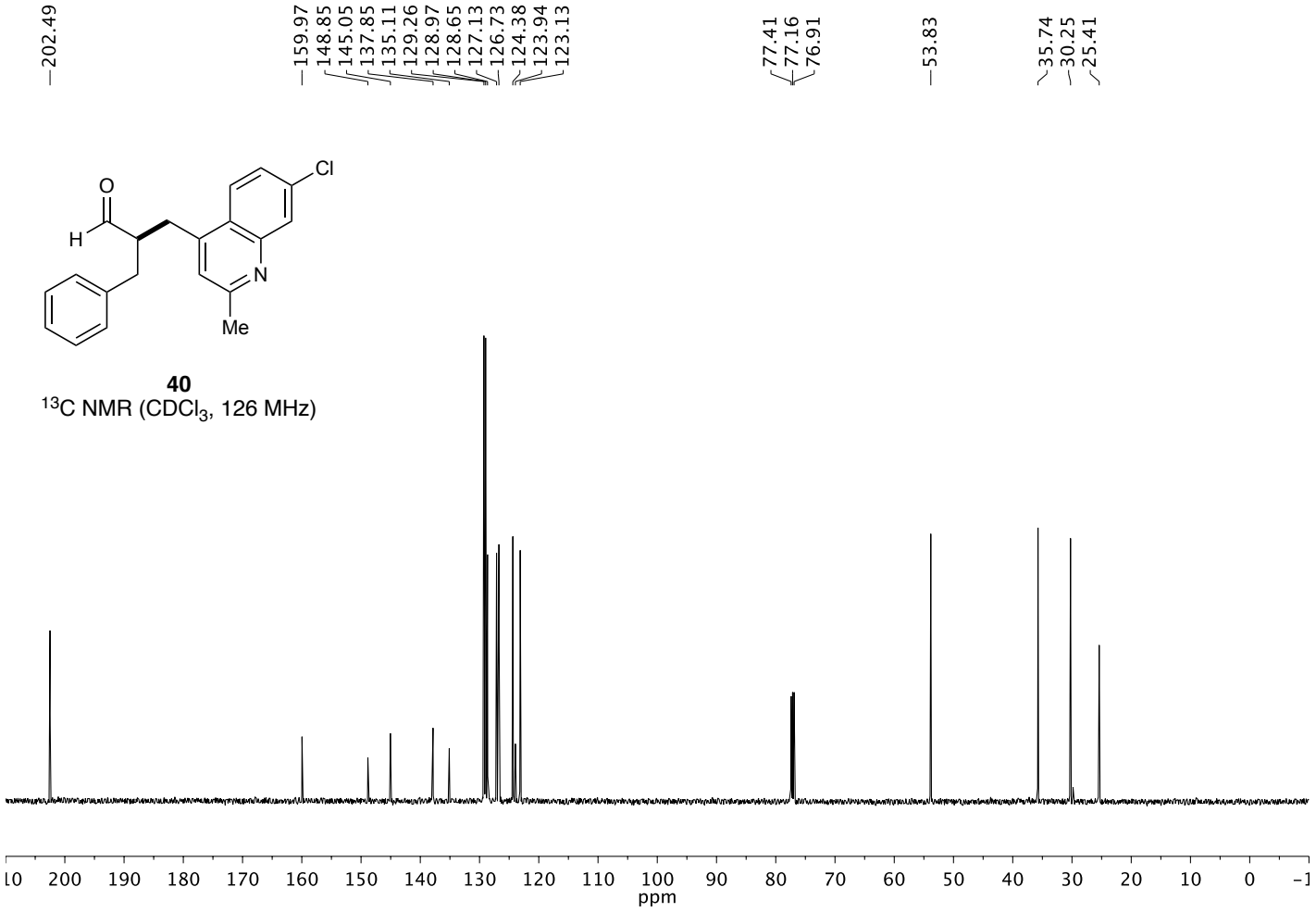
39

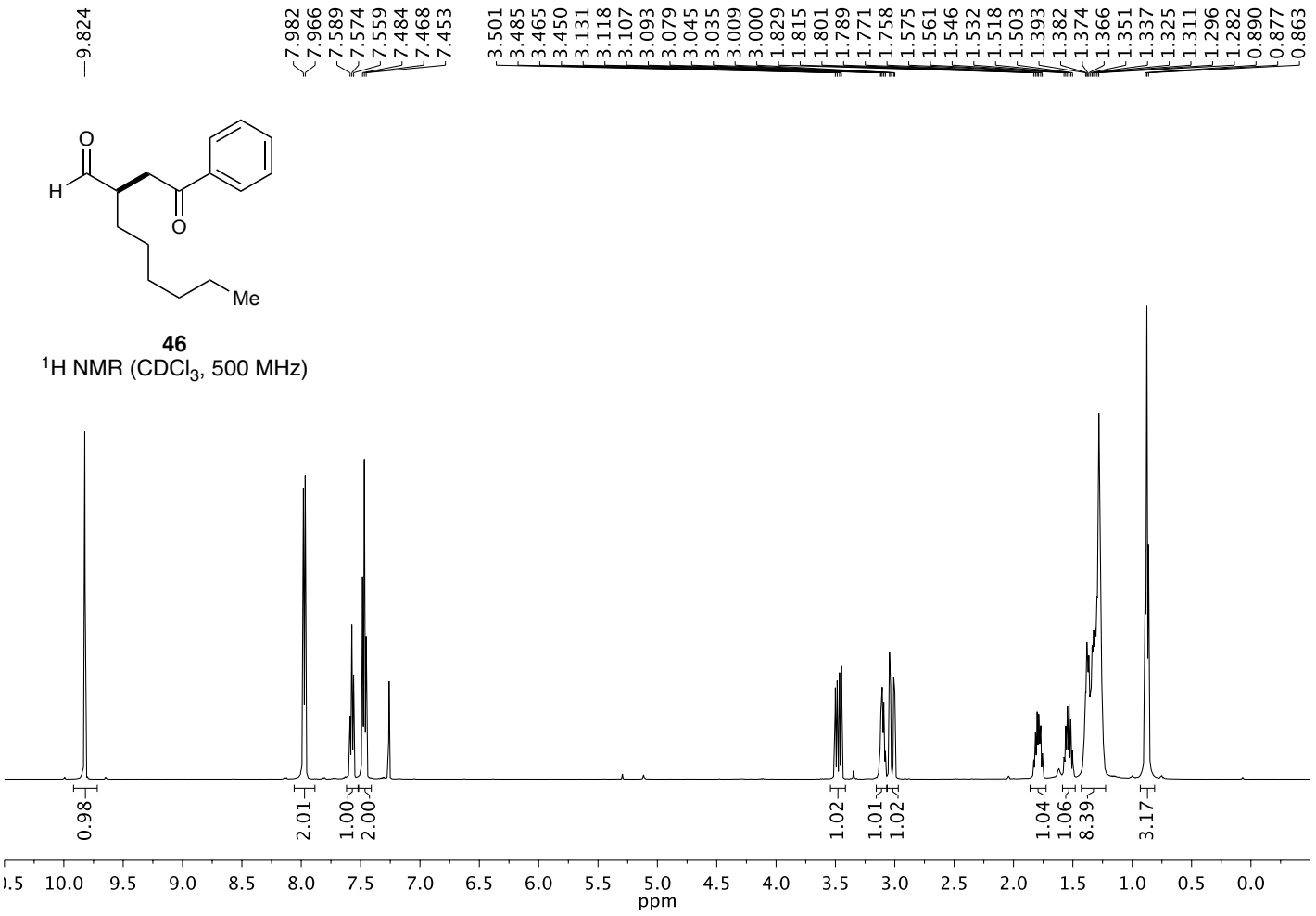
^{13}C NMR ($CDCl_3$, 126 MHz)

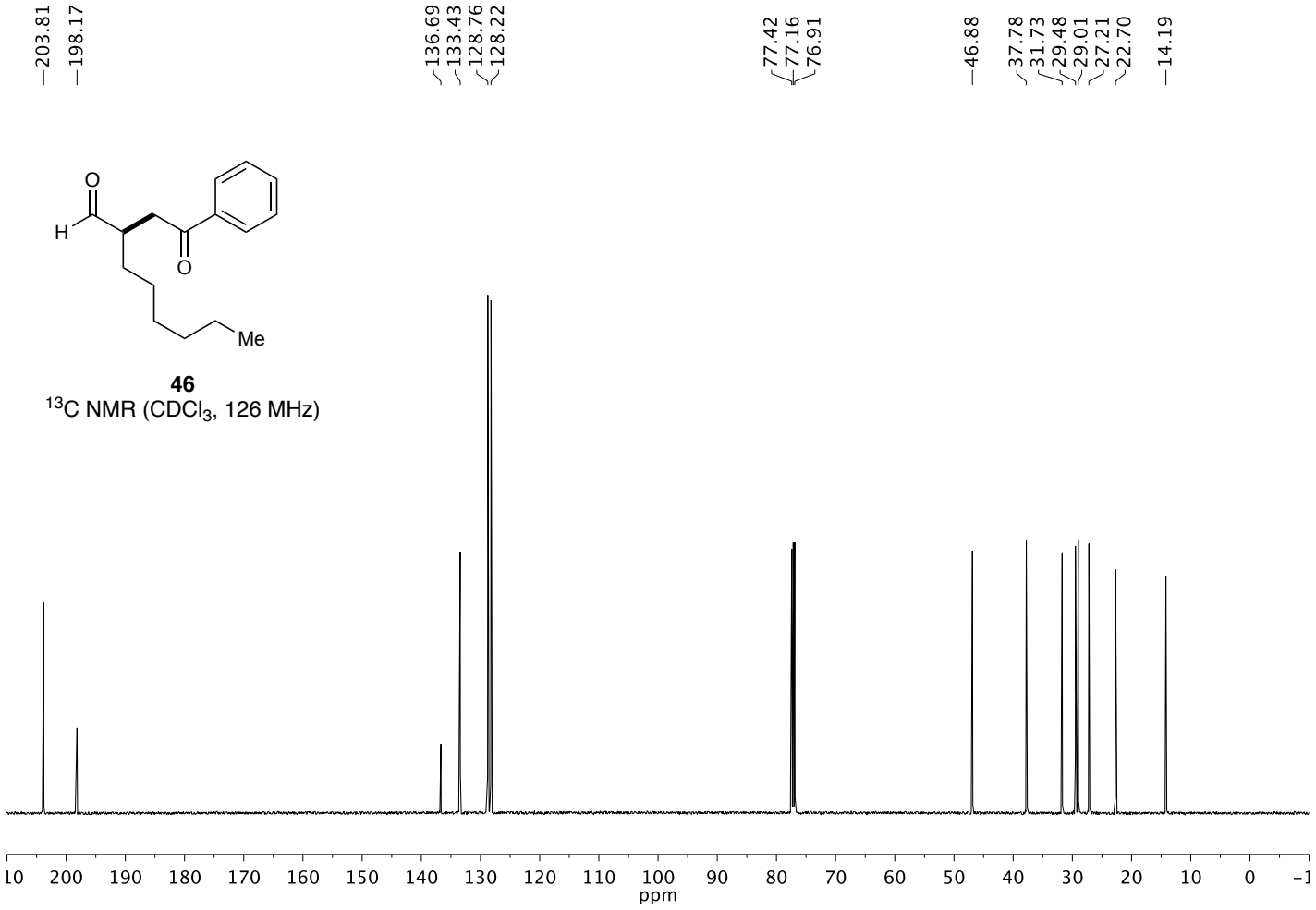


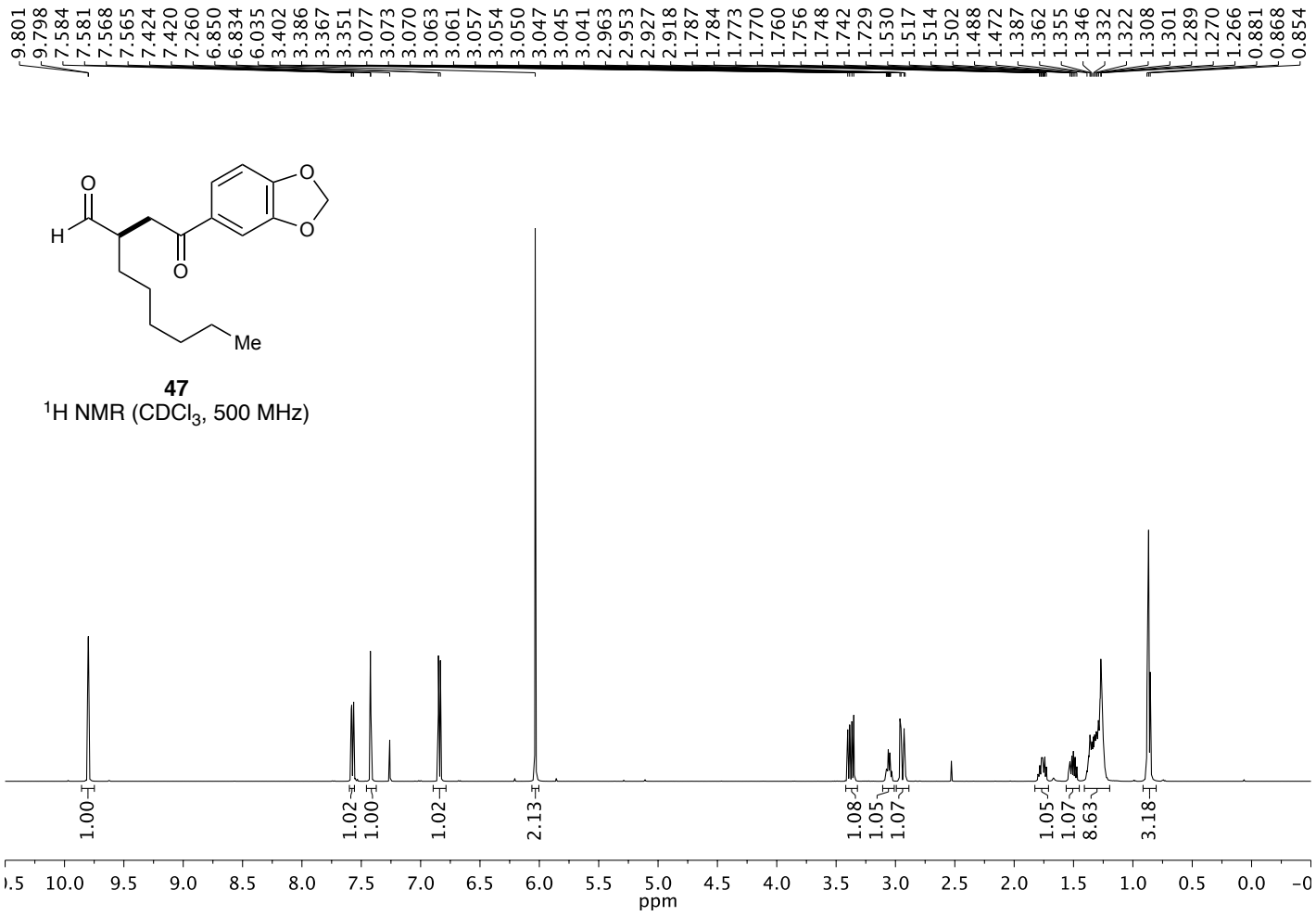
40

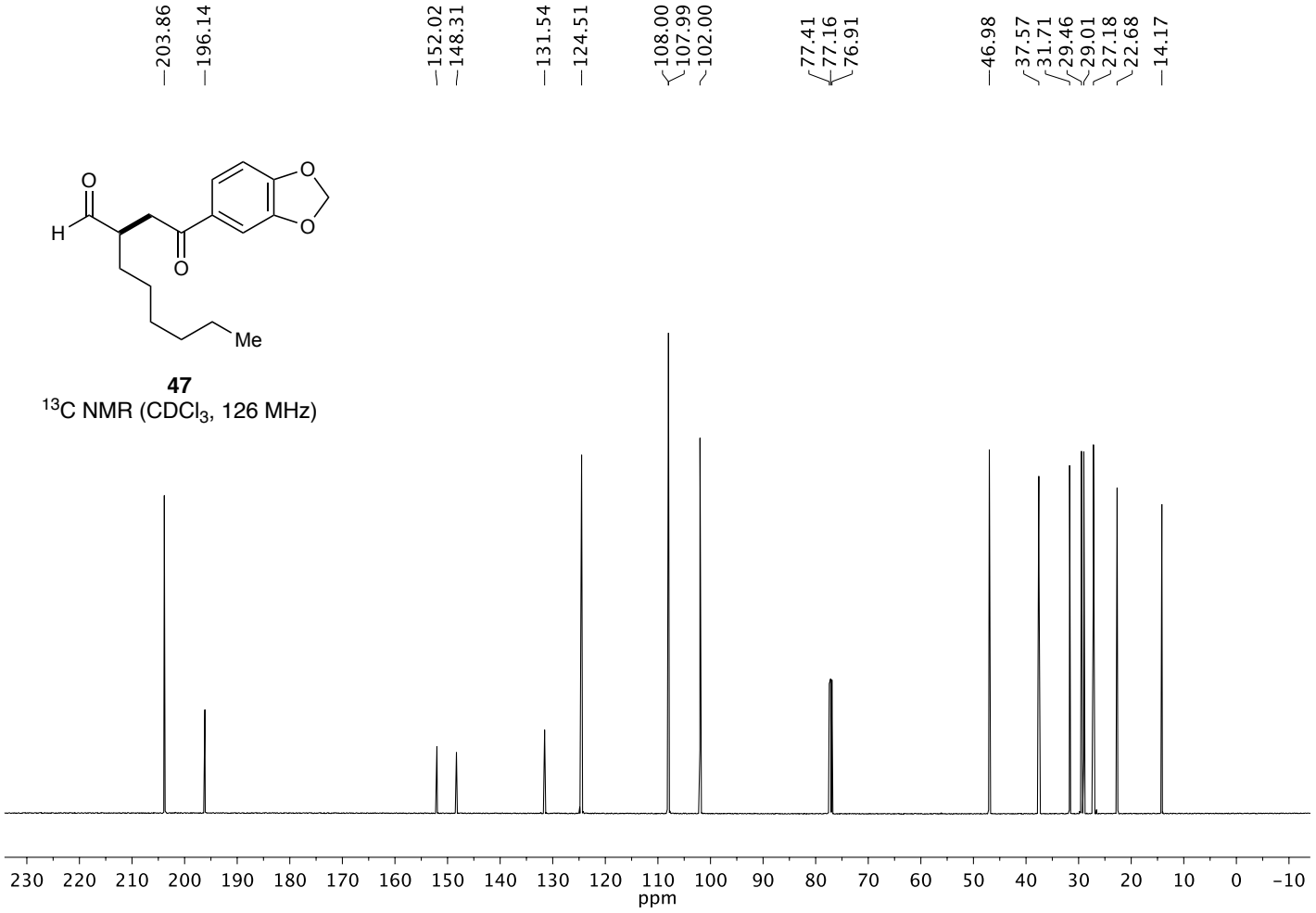
^{1}H NMR ($CDCl_3$, 500 MHz)


202.49
159.97
148.85
145.05
137.85
135.11
129.26
128.97
128.65
127.13
126.73
124.38
123.94
123.13
77.41
77.16
76.91
53.83
35.74
30.25
25.41
O
H
Cl
N
Me
40
13C NMR (CDCl3, 126 MHz)
ppm


9.824
7.982
7.966
7.589
7.574
7.559
7.484
7.468
7.453
3.501
3.485
3.465
3.450
3.131
3.118
3.107
3.093
3.079
3.045
3.035
3.009
3.000
1.829
1.815
1.801
1.789
1.771
1.758
1.575
1.561
1.546
1.532
1.518
1.503
1.393
1.382
1.374
1.366
1.351
1.337
1.325
1.311
1.296
1.282
0.890
0.877
0.863
O
H
O
Me
46
1H NMR (CDCl3, 500 MHz)
0.98
2.01
1.00
2.00
1.02
1.01
1.02
1.04
1.06
8.39
3.17
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm

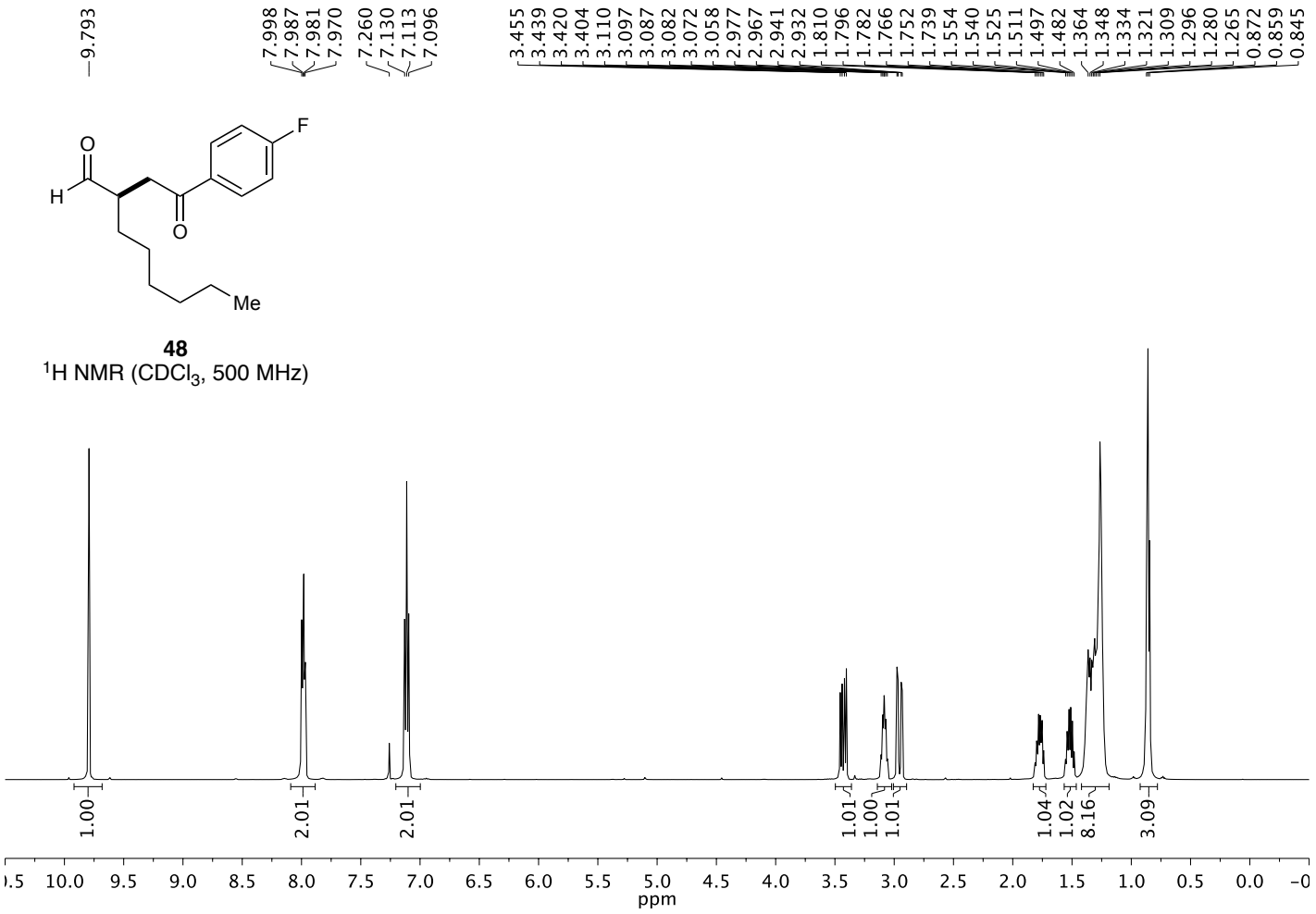

203.81
198.17
136.69
133.43
128.76
128.22
77.42
77.16
76.91
46.88
37.78
31.73
29.48
29.01
27.21
22.70
14.19
O
H
O
Me
46
13C NMR (CDCl3, 126 MHz)
ppm


9.801
9.798
7.584
7.581
7.568
7.565
7.424
7.420
7.260
6.850
6.834
6.035
3.402
3.386
3.367
3.351
3.077
3.073
3.070
3.063
3.061
3.057
3.054
3.050
3.047
3.045
3.041
2.963
2.953
2.927
2.918
1.787
1.784
1.773
1.770
1.760
1.756
1.748
1.742
1.729
1.530
1.517
1.514
1.502
1.488
1.472
1.387
1.362
1.355
1.346
1.332
1.322
1.308
1.301
1.289
1.270
1.266
0.881
0.868
0.854
O
H
O
O
O
Me
47
1H NMR (CDCl3, 500 MHz)
1.00
1.02
1.00
1.02
2.13
1.08
1.05
1.07
1.05
1.07
8.63
3.18
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm



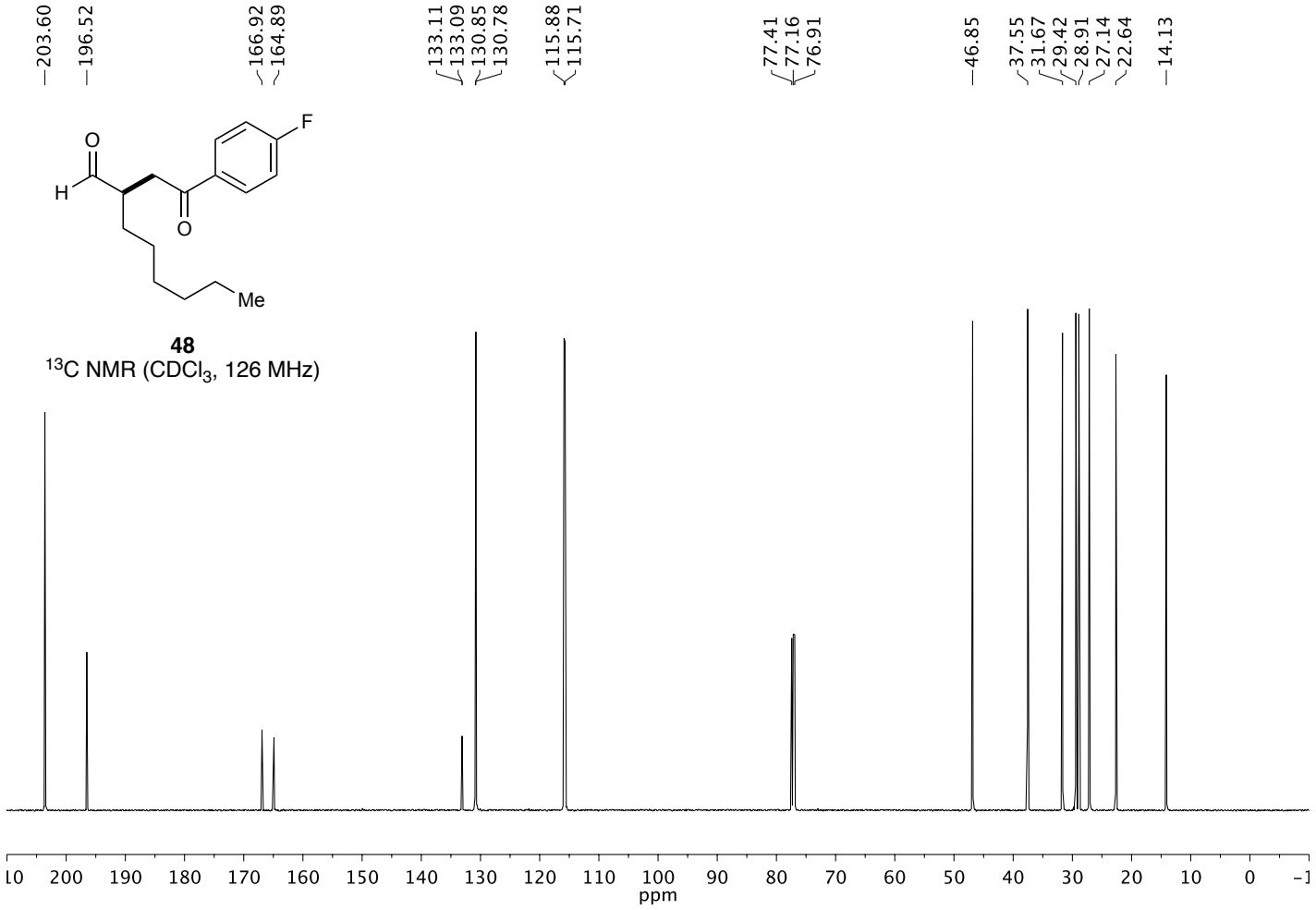
47

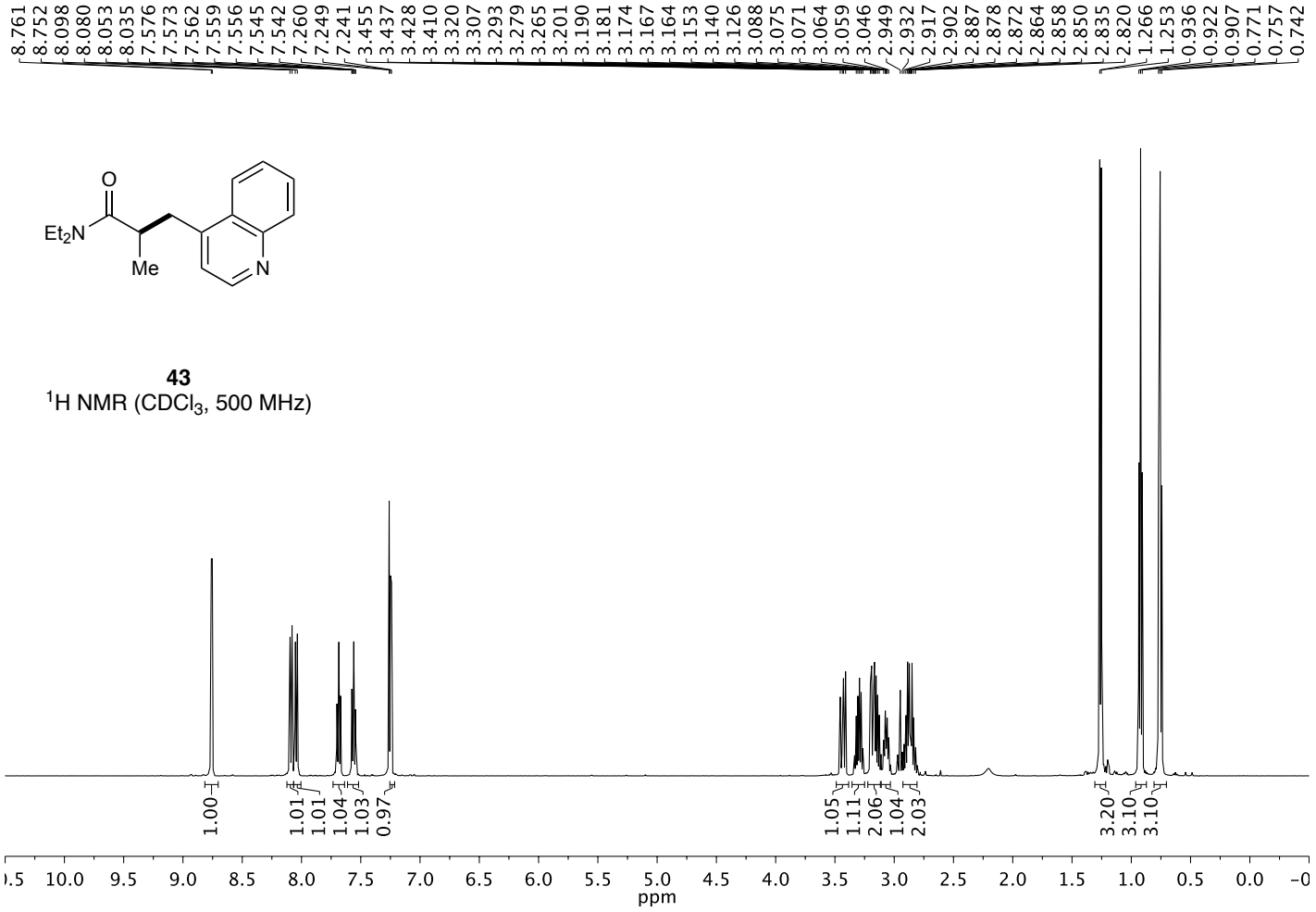
^{13}C NMR ($CDCl_3$, 126 MHz)



48

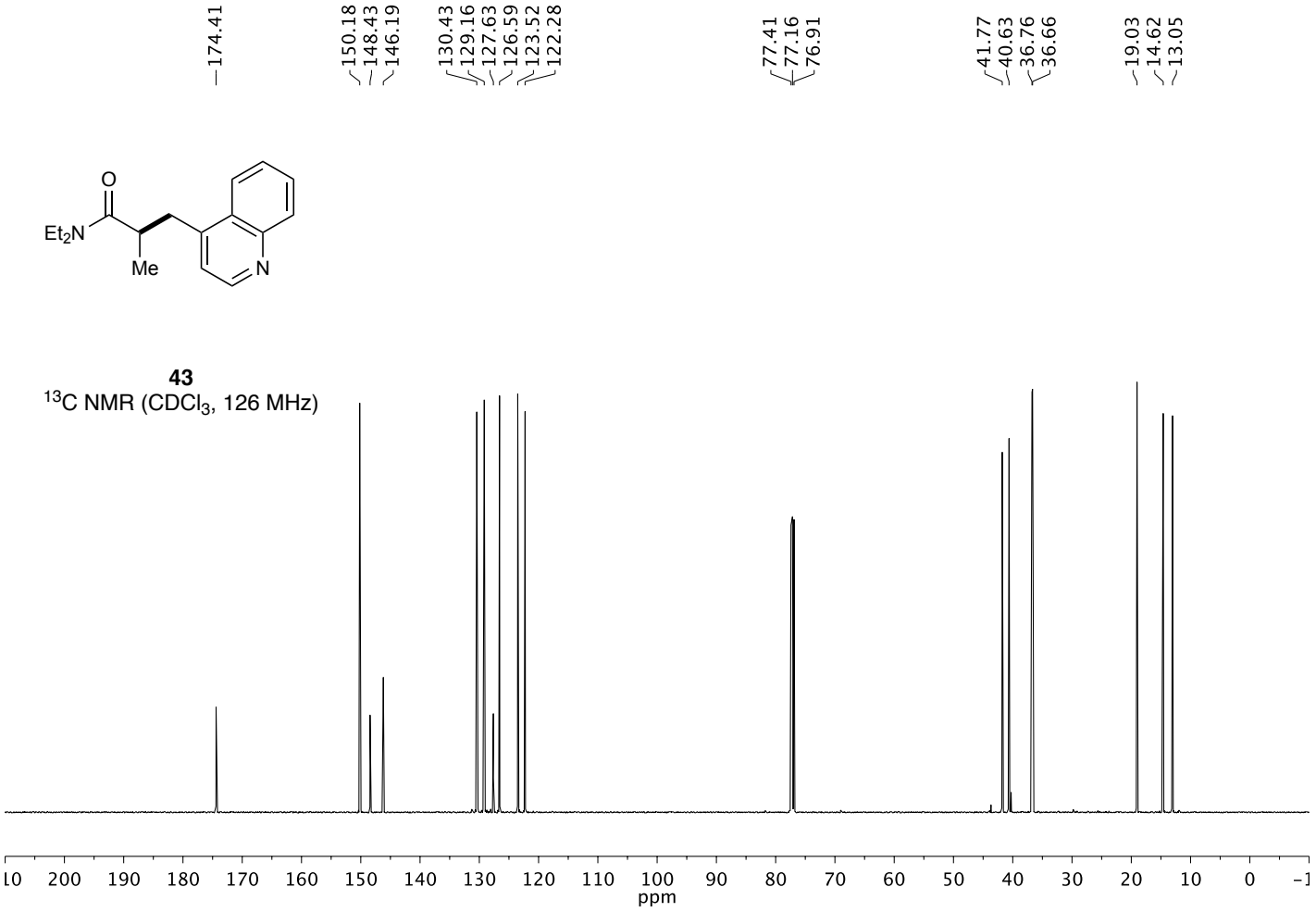
^{1}H NMR ($CDCl_3$, 500 MHz)

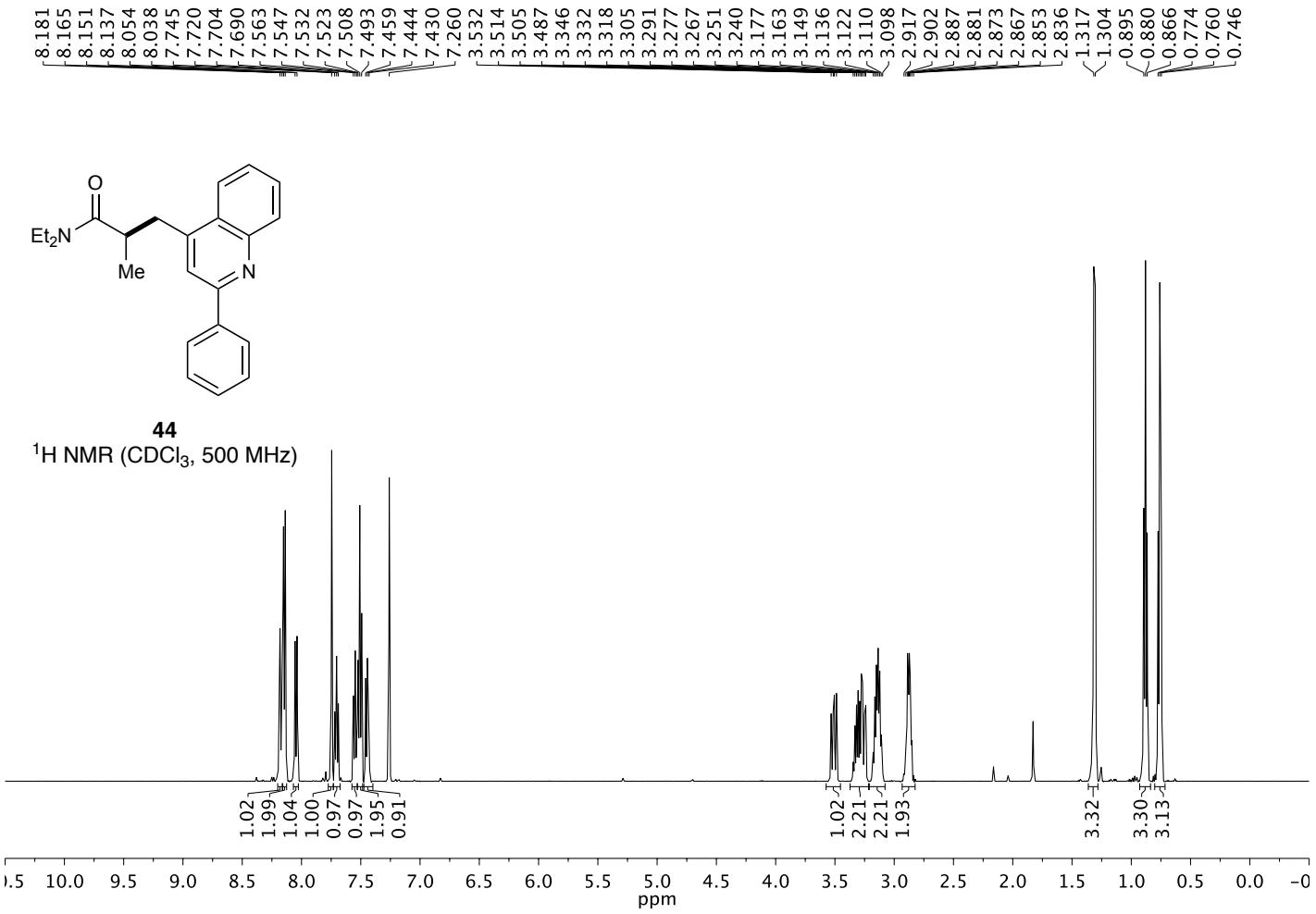

203.60
196.52
166.92
164.89
133.11
133.09
130.85
130.78
115.88
115.71
77.41
77.16
76.91
46.85
37.55
31.67
29.42
28.91
27.14
22.64
14.13
O
H
O
F
Me
48
13C NMR (CDCl3, 126 MHz)
ppm

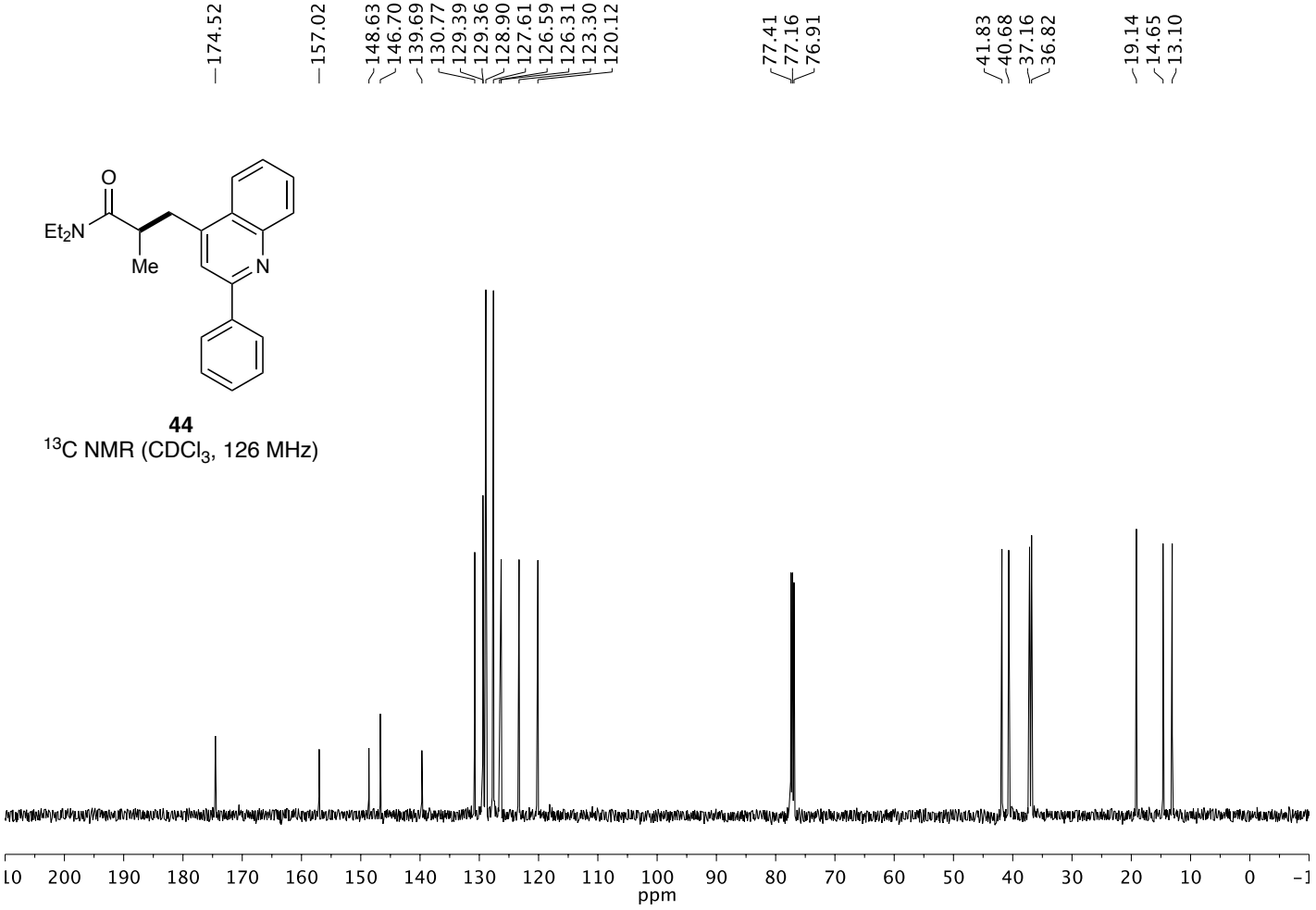


43

^{1}H NMR ($CDCl_3$, 500 MHz)

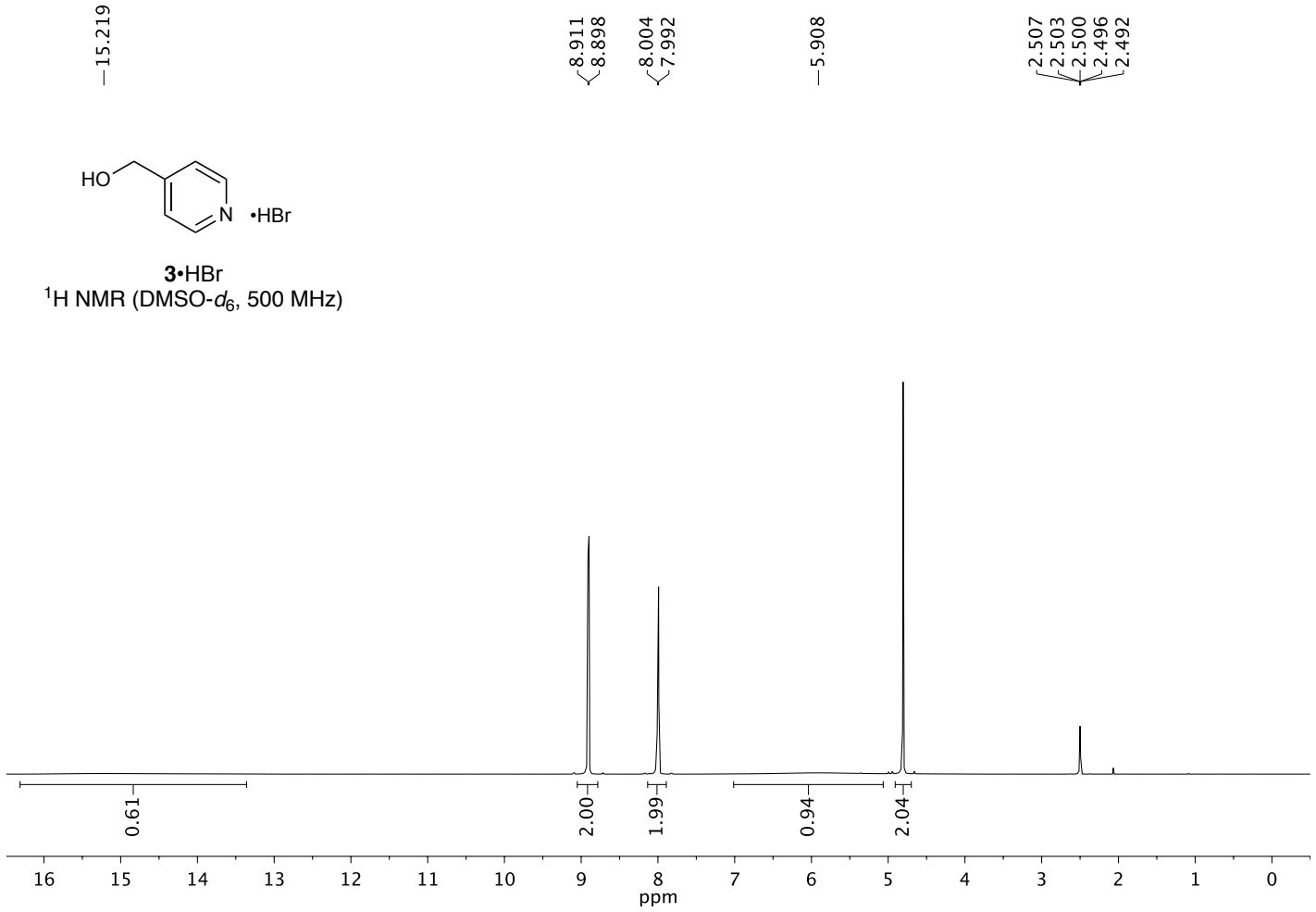

174.41
150.18
148.43
146.19
130.43
129.16
127.63
126.59
123.52
122.28
77.41
77.16
76.91
41.77
40.63
36.76
36.66
19.03
14.62
13.05
O
Et2N
Me
N
43
13C NMR (CDCl3, 126 MHz)
ppm


8.181
8.165
8.151
8.137
8.054
8.038
7.745
7.720
7.704
7.690
7.563
7.547
7.532
7.523
7.508
7.493
7.459
7.444
7.430
7.260
3.532
3.514
3.505
3.487
3.346
3.332
3.318
3.305
3.291
3.277
3.267
3.251
3.240
3.177
3.163
3.149
3.136
3.122
3.110
3.098
2.917
2.902
2.887
2.881
2.873
2.867
2.853
2.836
1.317
1.304
0.895
0.880
0.866
0.774
0.760
0.746
O
Et2N
Me
N
44
1H NMR (CDCl3, 500 MHz)
1.02
1.99
1.04
1.00
0.97
0.97
1.95
0.91
1.02
2.21
2.21
1.93
3.32
3.30
3.13
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm

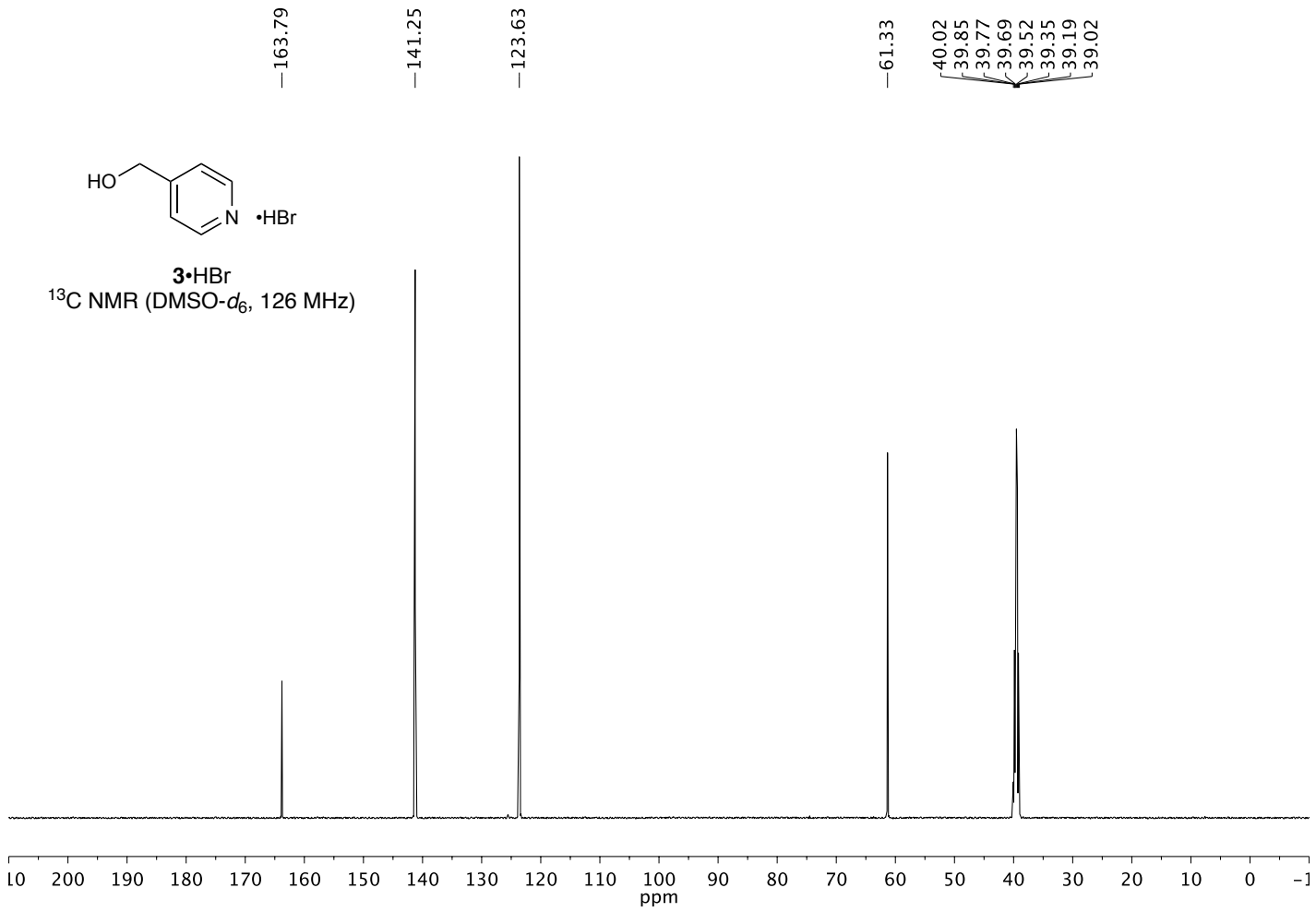


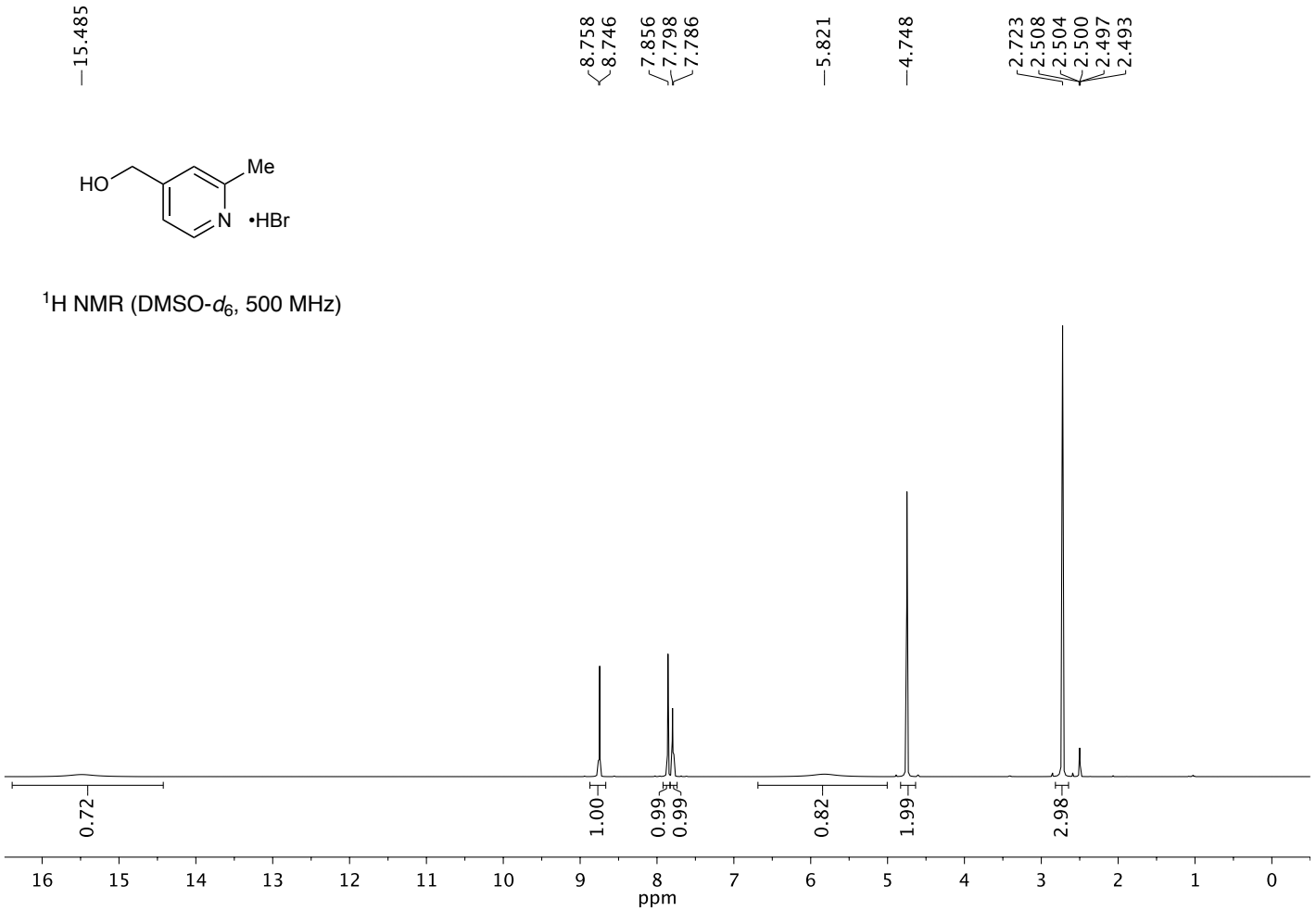
44

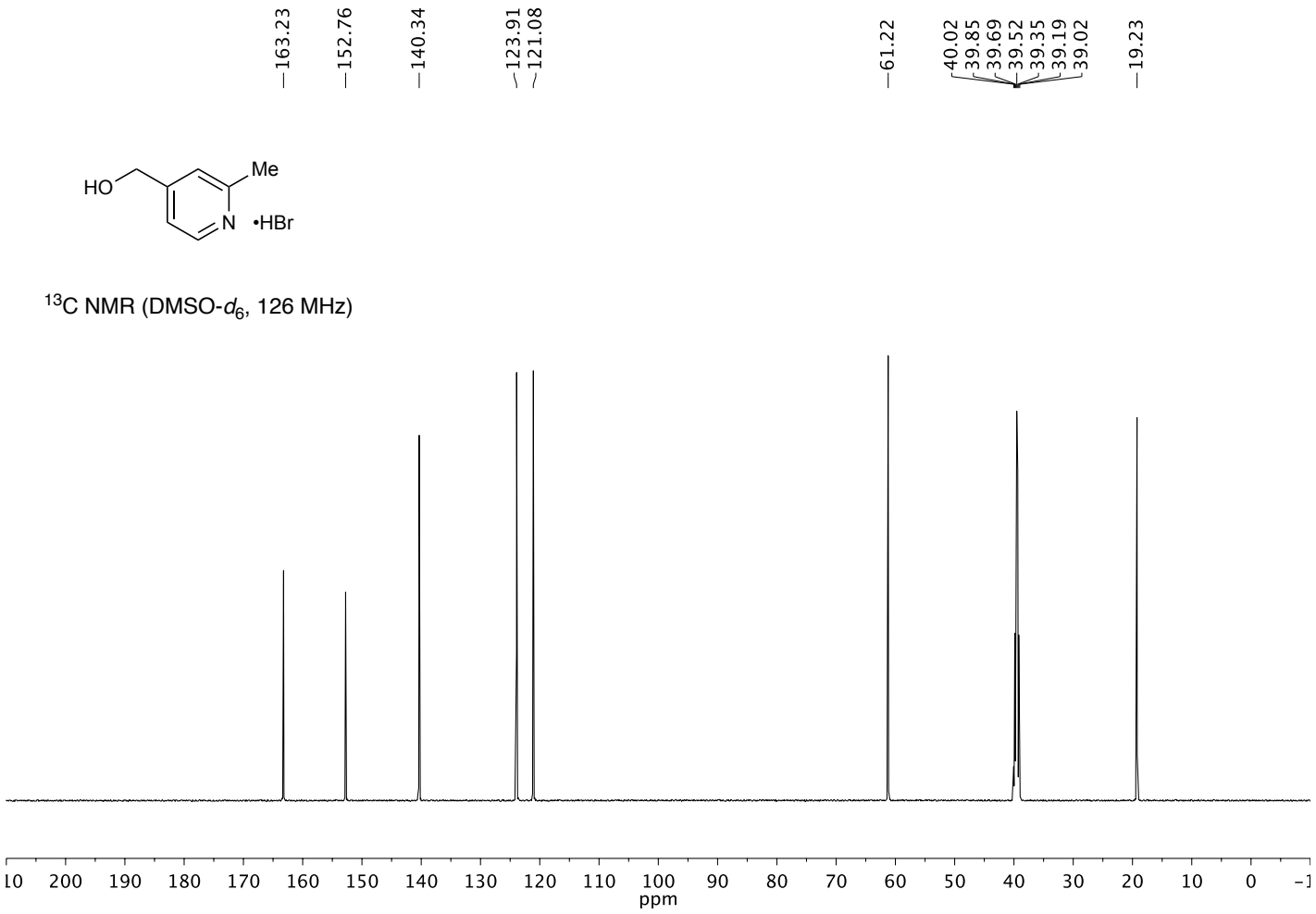
^{13}C NMR ($CDCl_3$, 126 MHz)

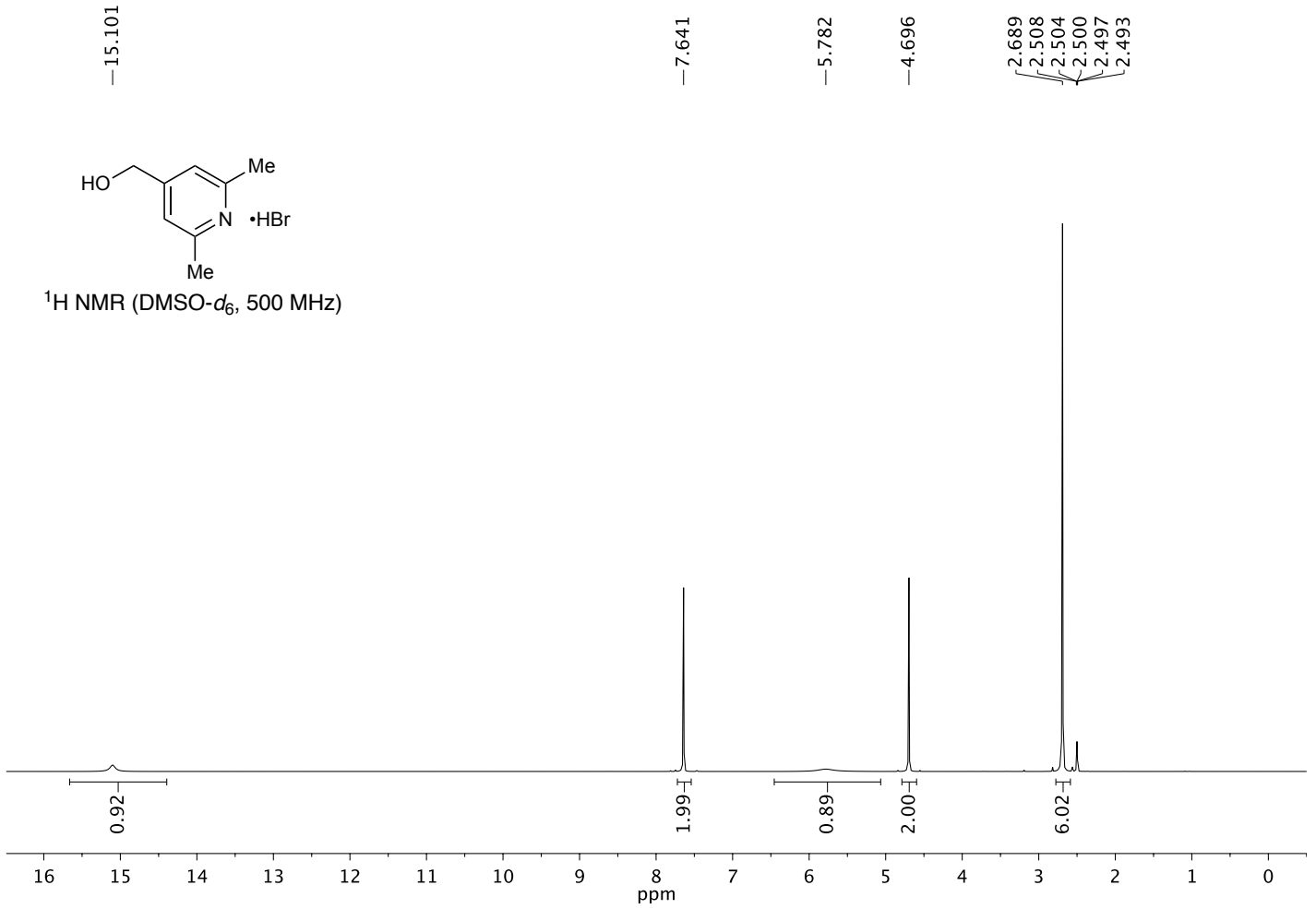


3•HBr
^{1}H NMR (DMSO-d_6, 500 MHz)

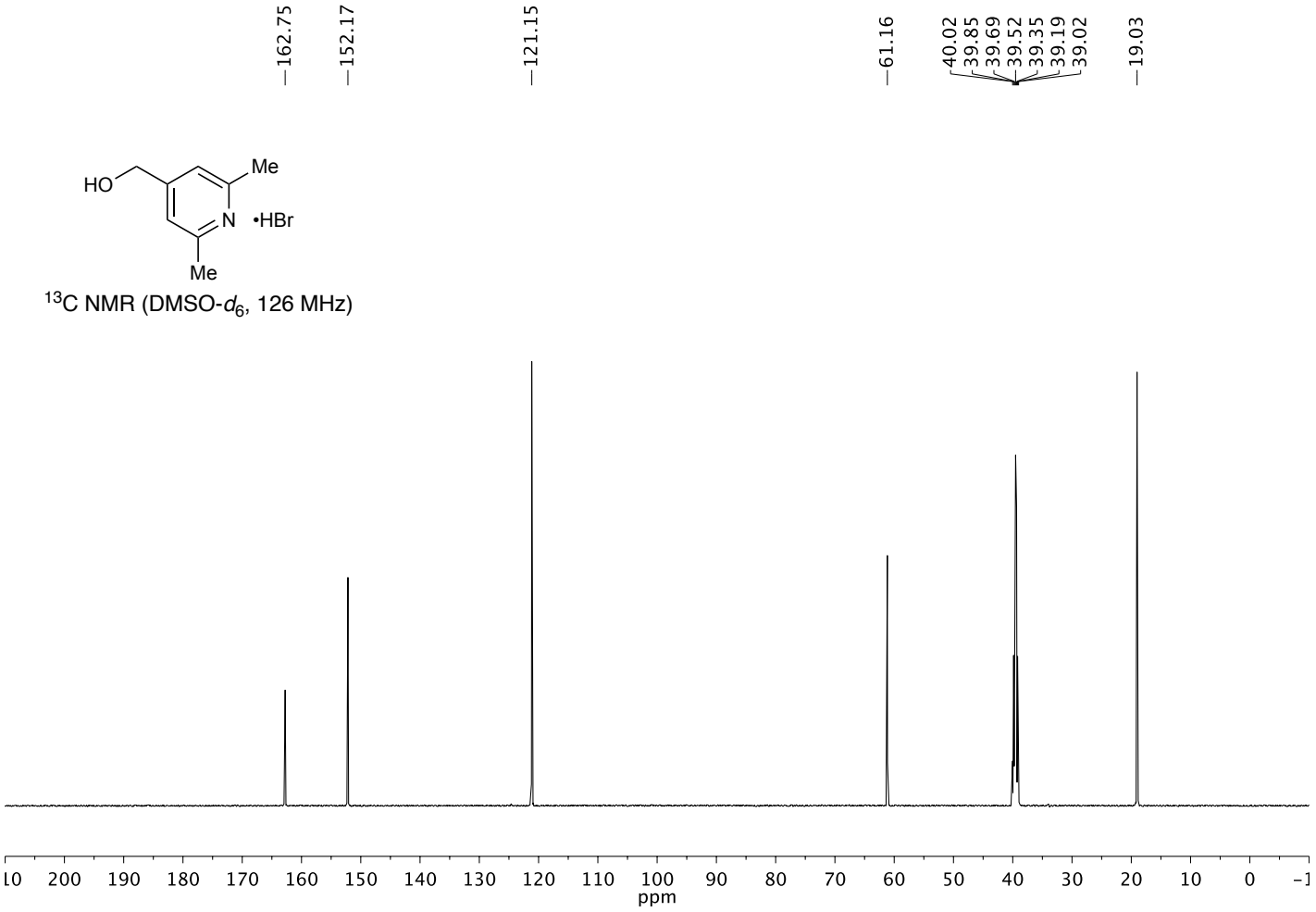

163.79
141.25
123.63
61.33
40.02
39.85
39.77
39.69
39.52
39.35
39.19
39.02
HO
N •HBr
3•HBr
13C NMR (DMSO-d6, 126 MHz)
ppm


15.485
8.758
8.746
7.856
7.798
7.786
5.821
4.748
2.723
2.508
2.504
2.500
2.497
2.493
HO
Me
N
•HBr
1H NMR (DMSO-d6, 500 MHz)
0.72
1.00
0.99
0.99
0.82
1.99
2.98
16
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
ppm

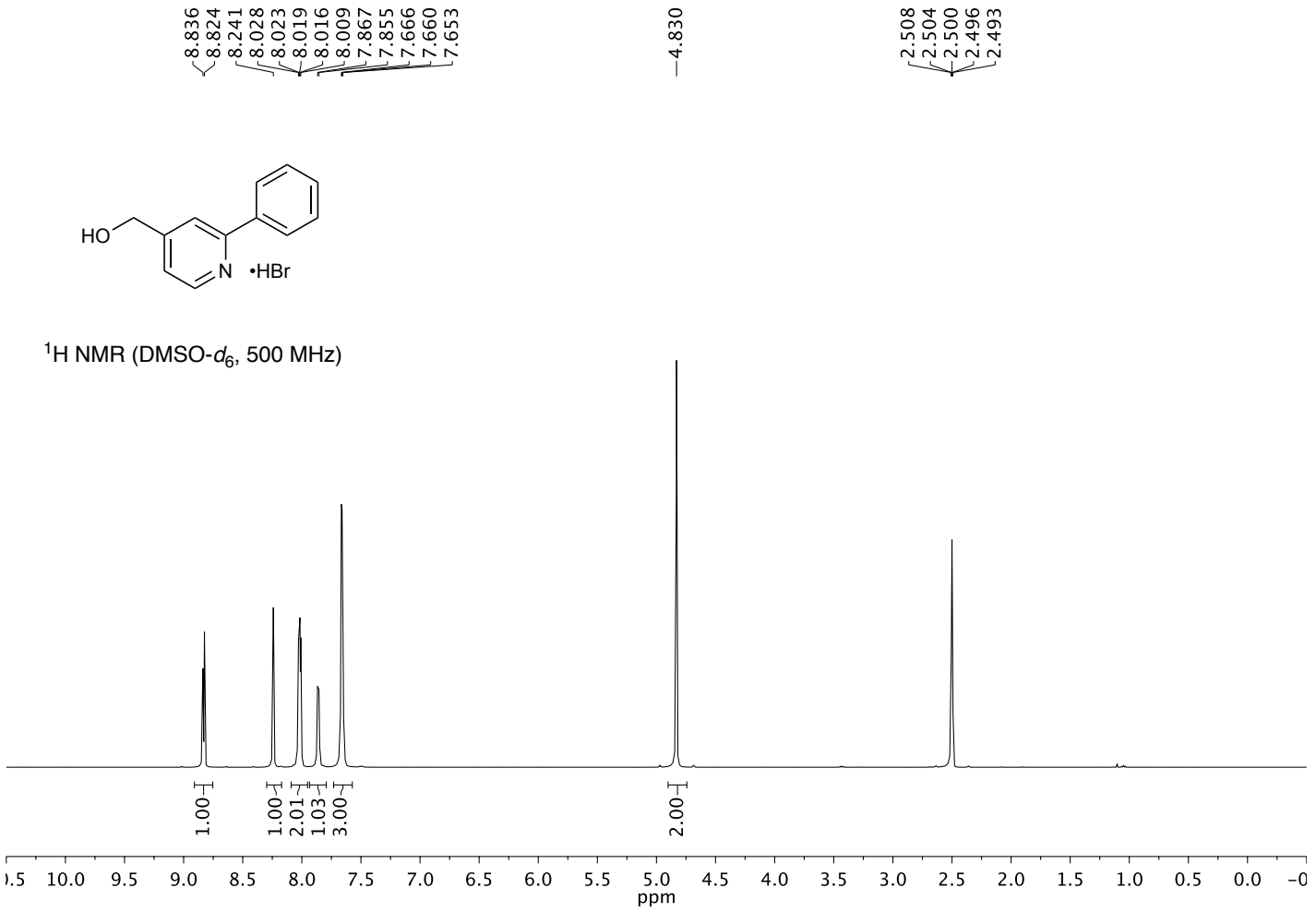

163.23
152.76
140.34
123.91
121.08
61.22
40.02
39.85
39.69
39.52
39.35
39.19
39.02
19.23
HO
Me
N
•HBr
^{13}C NMR (DMSO-d_6, 126 MHz)
ppm

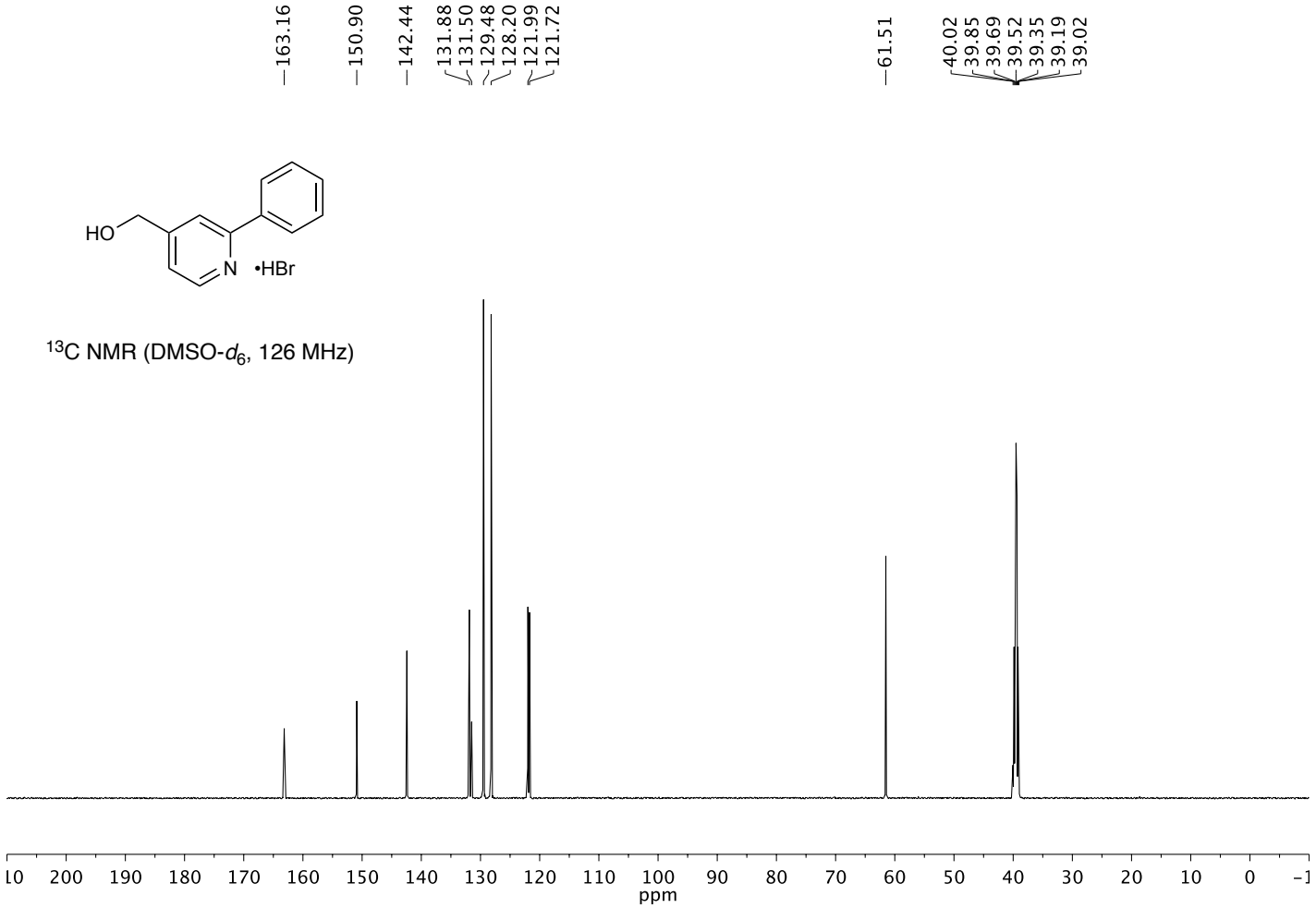


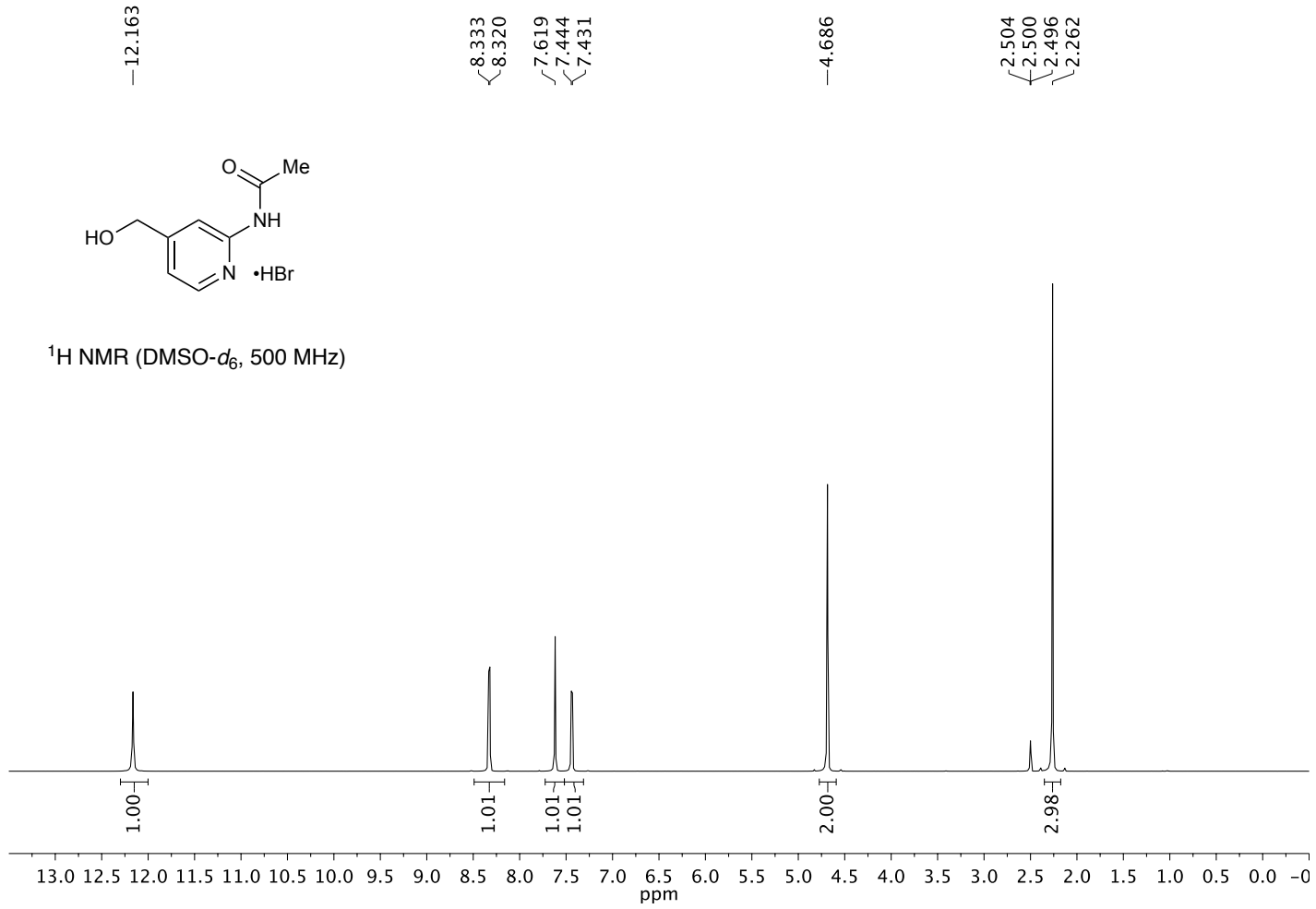
^{1}H NMR (DMSO-d_6, 500 MHz)

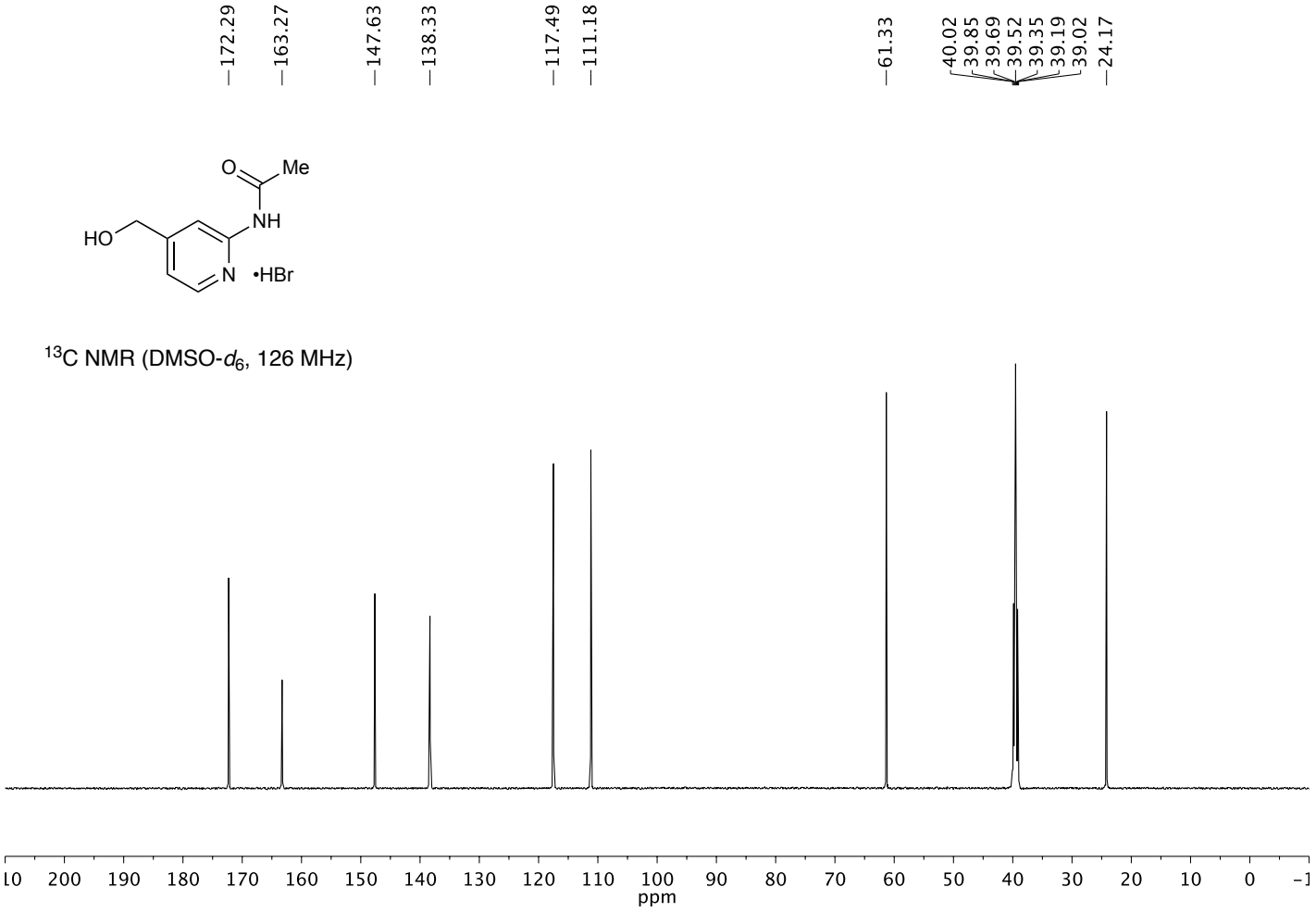


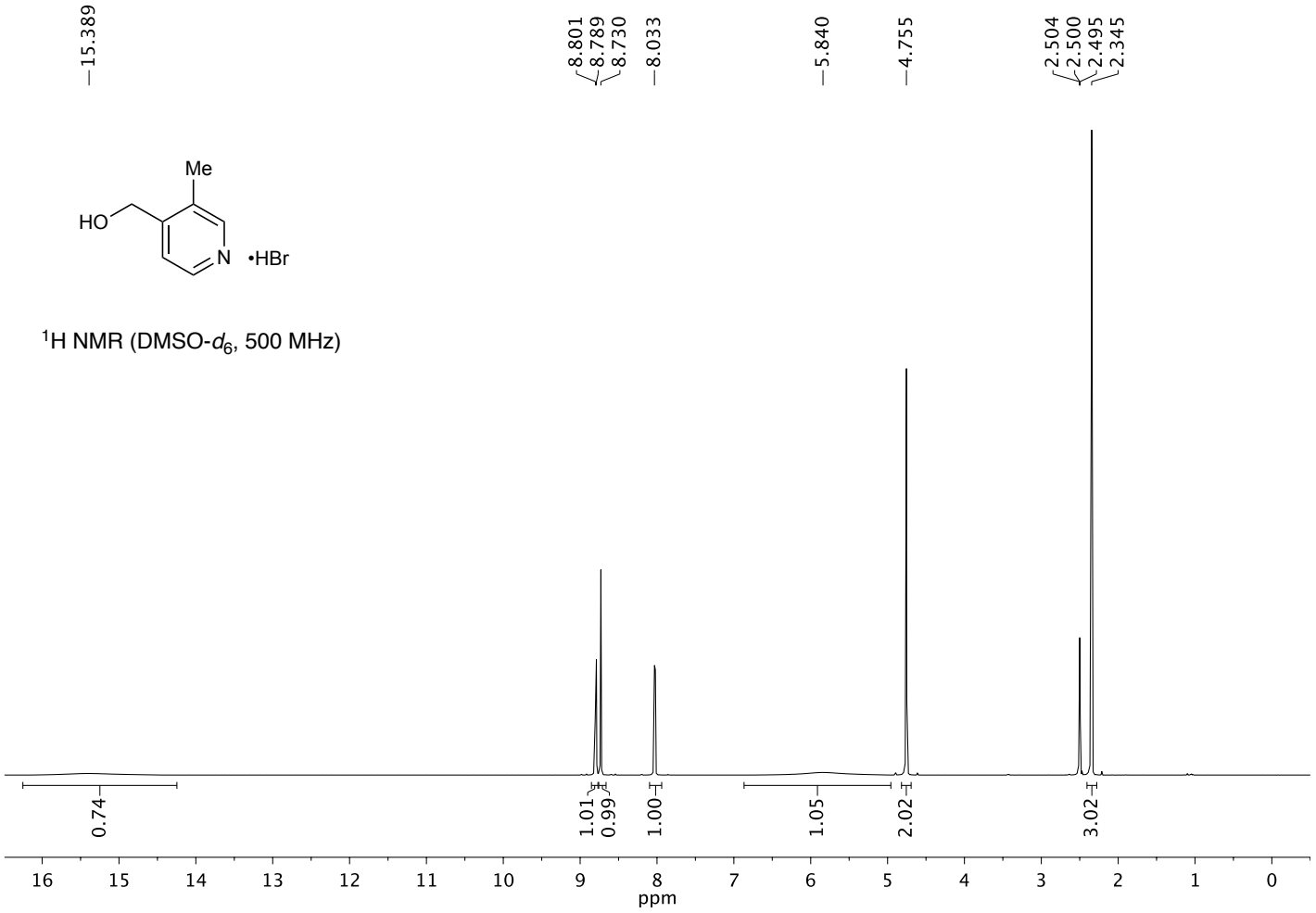
^{13}C NMR (DMSO-d_6, 126 MHz)

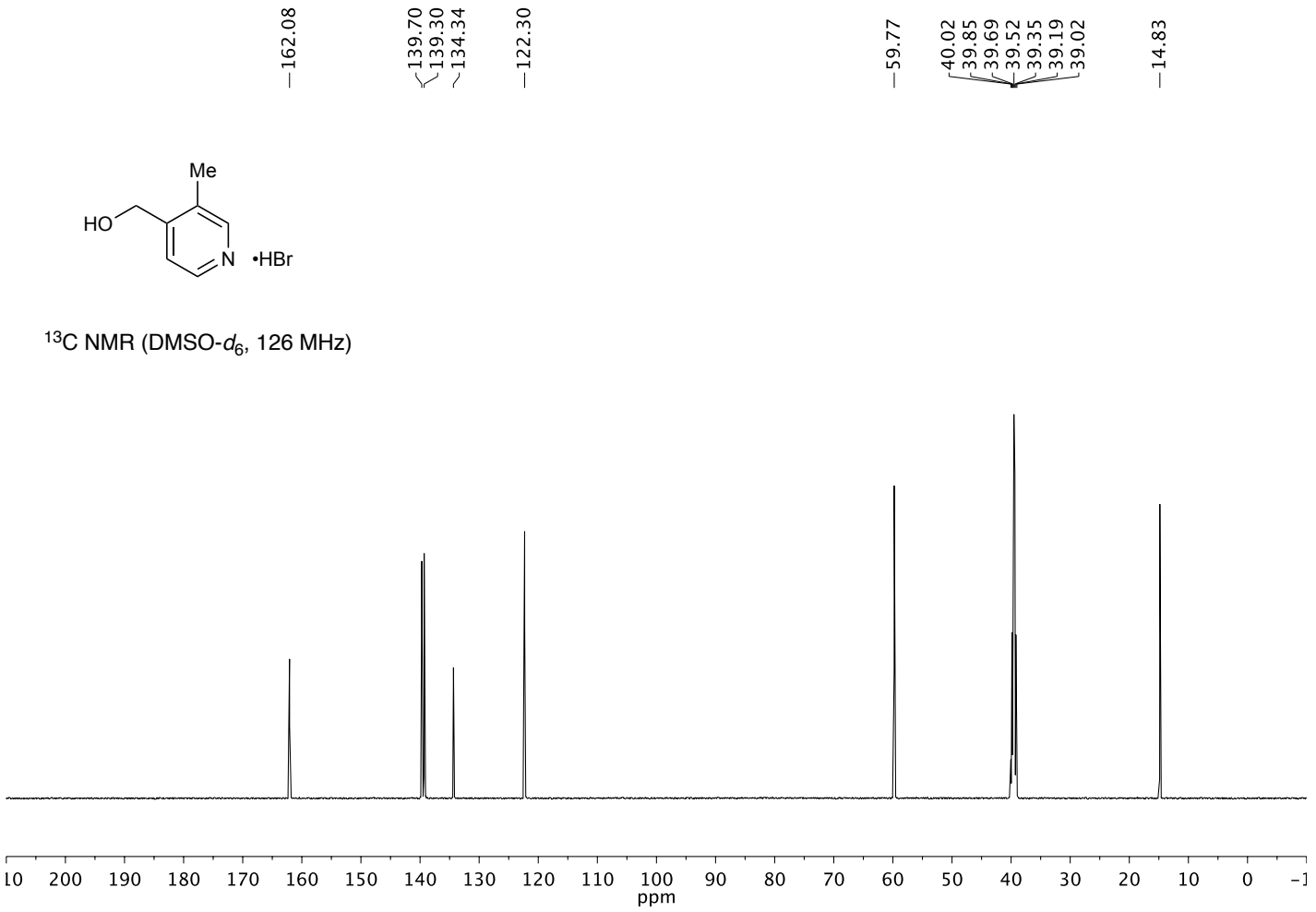

8.836
8.824
8.241
8.028
8.023
8.019
8.016
8.009
7.867
7.855
7.666
7.660
7.653
4.830
2.508
2.504
2.500
2.496
2.493
HO
N
•HBr
1H NMR (DMSO-d6, 500 MHz)
1.00
1.00
2.01
1.03
3.00
2.00
ppm

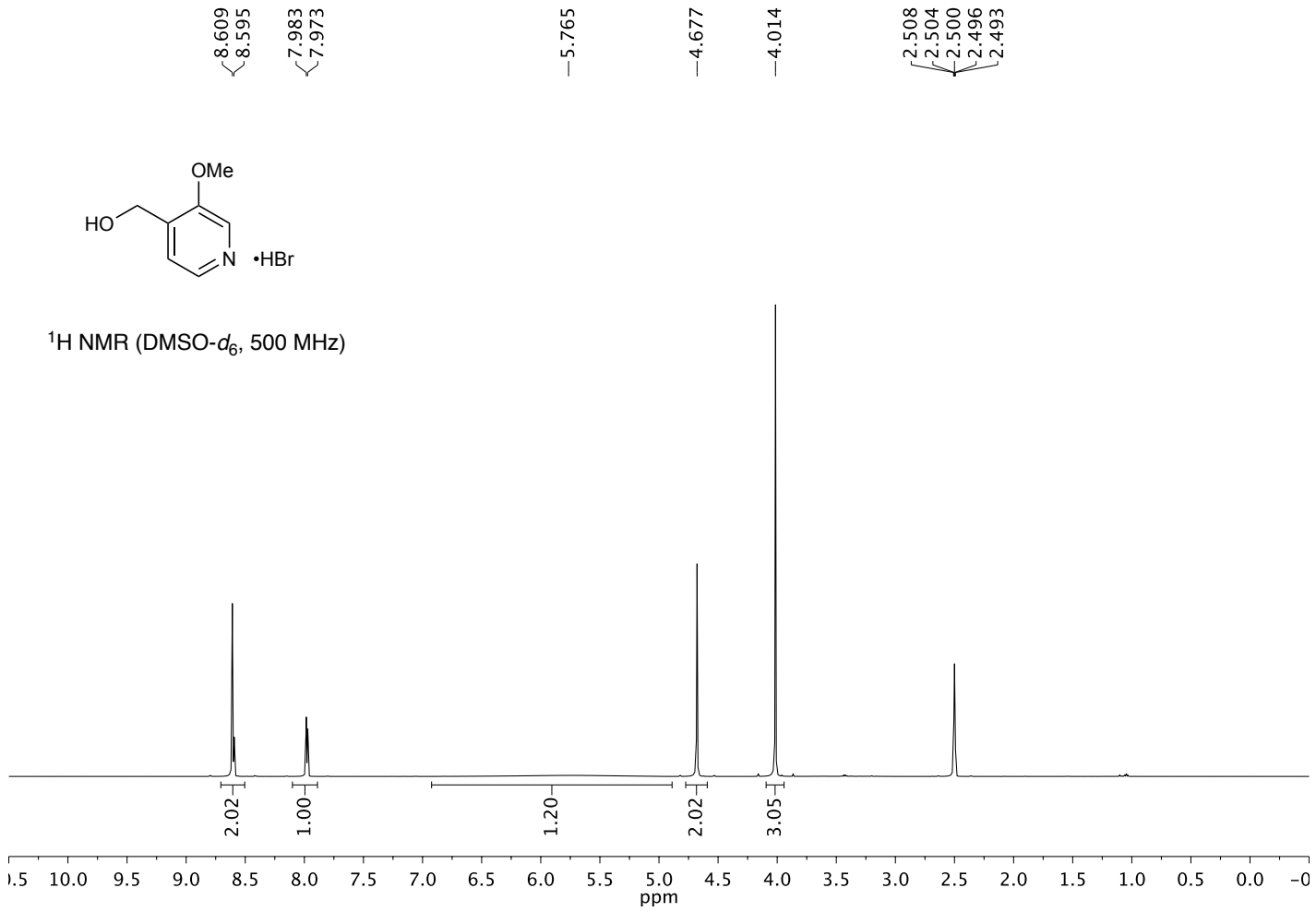

163.16
150.90
142.44
131.88
131.50
129.48
128.20
121.99
121.72
61.51
40.02
39.85
39.69
39.52
39.35
39.19
39.02
HO
N •HBr
13C NMR (DMSO-d6, 126 MHz)
ppm

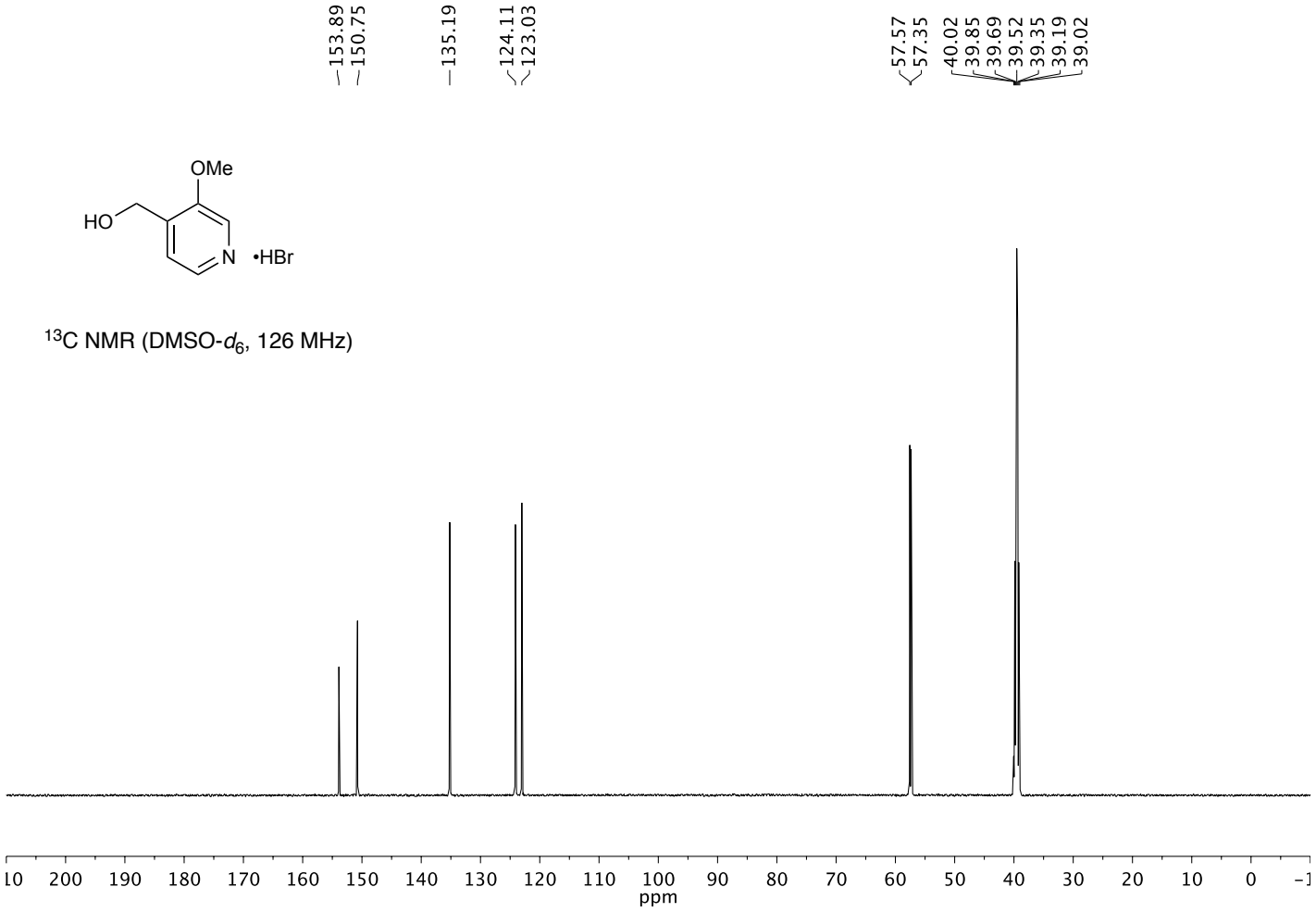

12.163
8.333
8.320
7.619
7.444
7.431
4.686
2.504
2.500
2.496
2.262
O
Me
NH
HO
N
•HBr
1H NMR (DMSO-d6, 500 MHz)
1.00
1.01
1.01
1.01
2.00
2.98
13.0 12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0
ppm

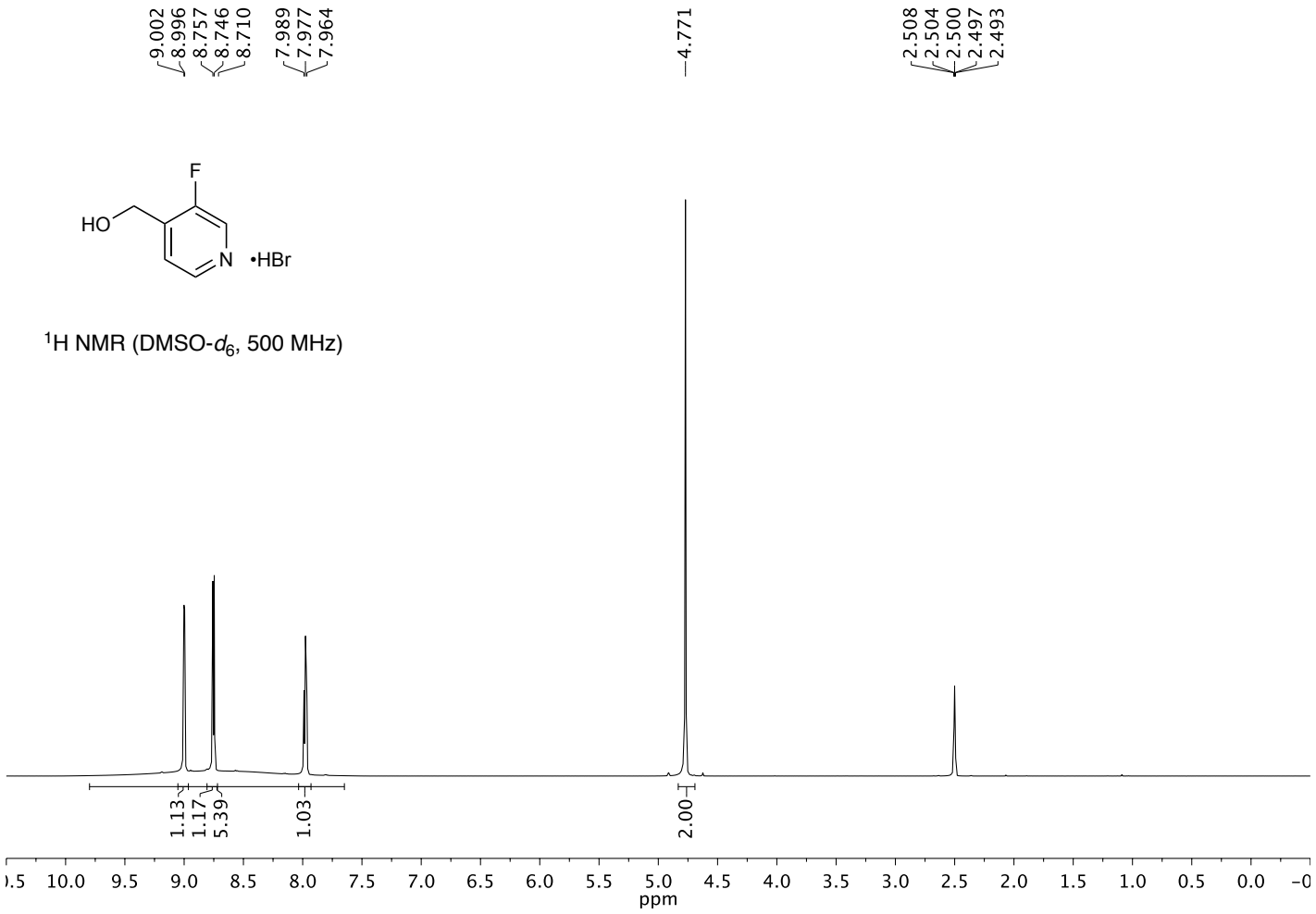

172.29
163.27
147.63
138.33
117.49
111.18
61.33
40.02
39.85
39.69
39.52
39.35
39.19
39.02
24.17
O
Me
NH
HO
N •HBr
13C NMR (DMSO-d6, 126 MHz)
ppm

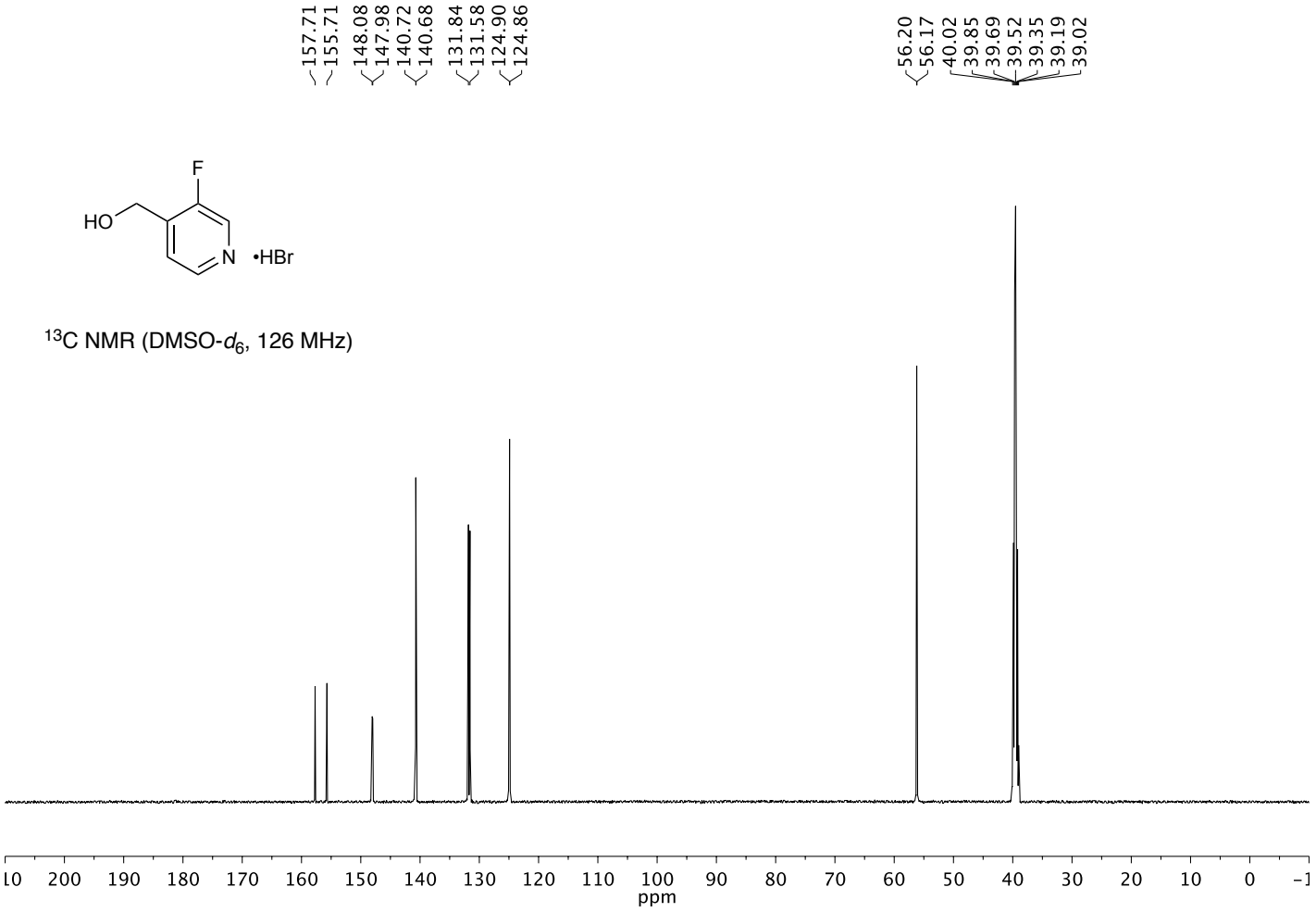

15.389
8.801
8.789
8.730
8.033
5.840
4.755
2.504
2.500
2.495
2.345
Me
HO
N
•HBr
1H NMR (DMSO-d6, 500 MHz)
0.74
1.01
0.99
1.00
1.05
2.02
3.02
16
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
ppm

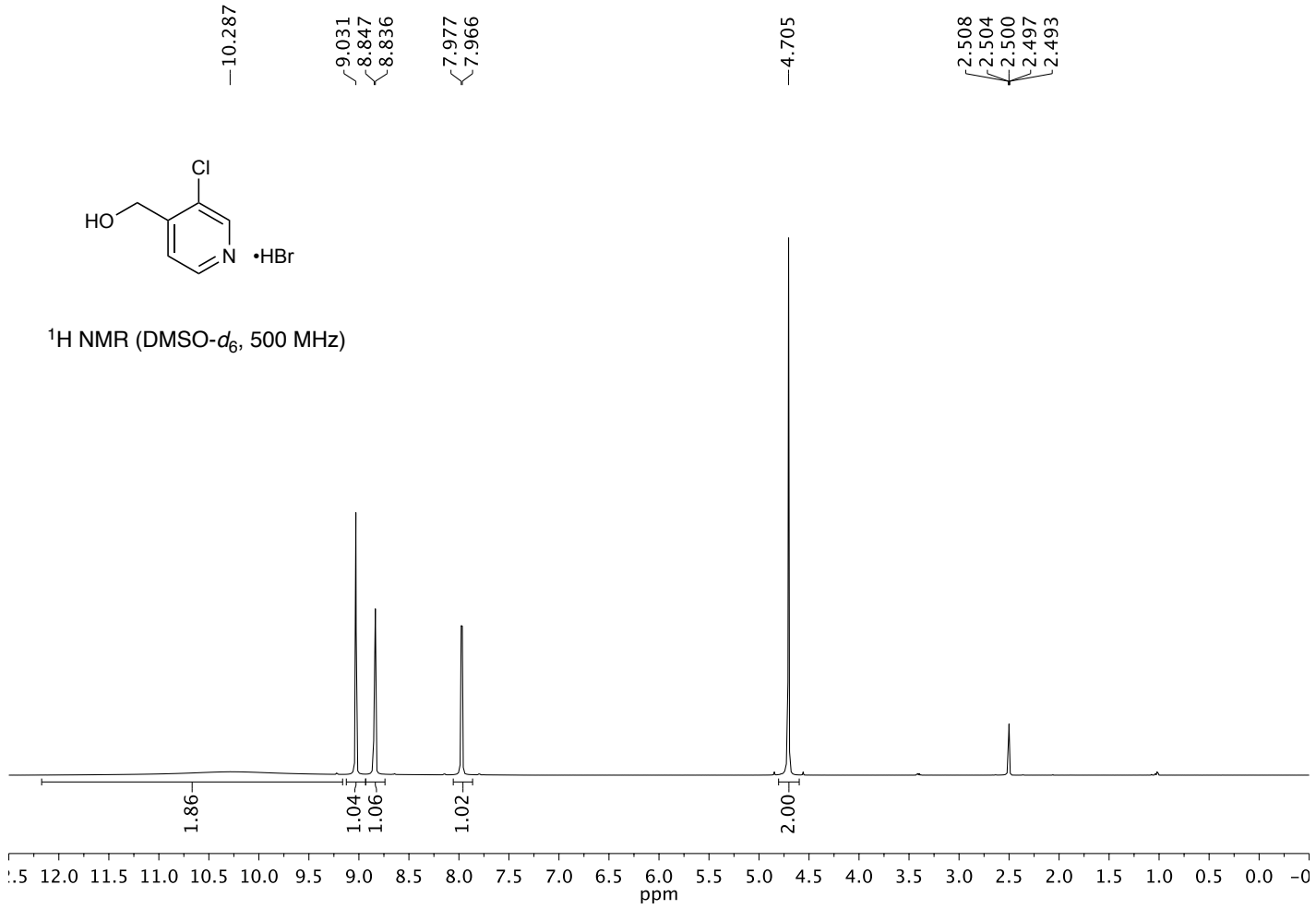

162.08
139.70
139.30
134.34
122.30
59.77
40.02
39.85
39.69
39.52
39.35
39.19
39.02
14.83
Me
HO
N
•HBr
^{13}C NMR (DMSO-d_6, 126 MHz)
ppm

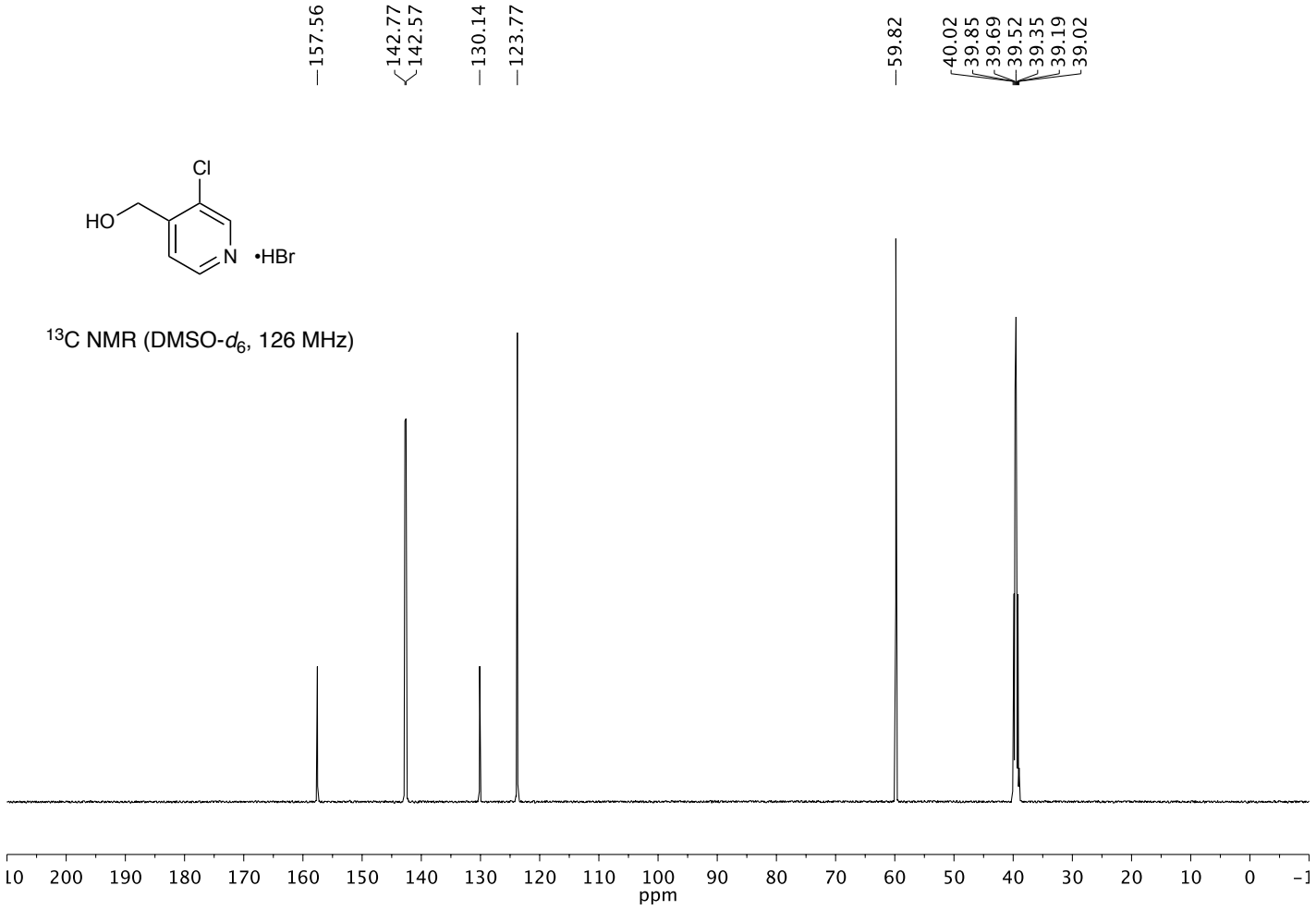

8.609
8.595
7.983
7.973
5.765
4.677
4.014
2.508
2.504
2.500
2.496
2.493
OMe
HO
N
•HBr
1H NMR (DMSO-d6, 500 MHz)
2.02
1.00
1.20
2.02
3.05
ppm

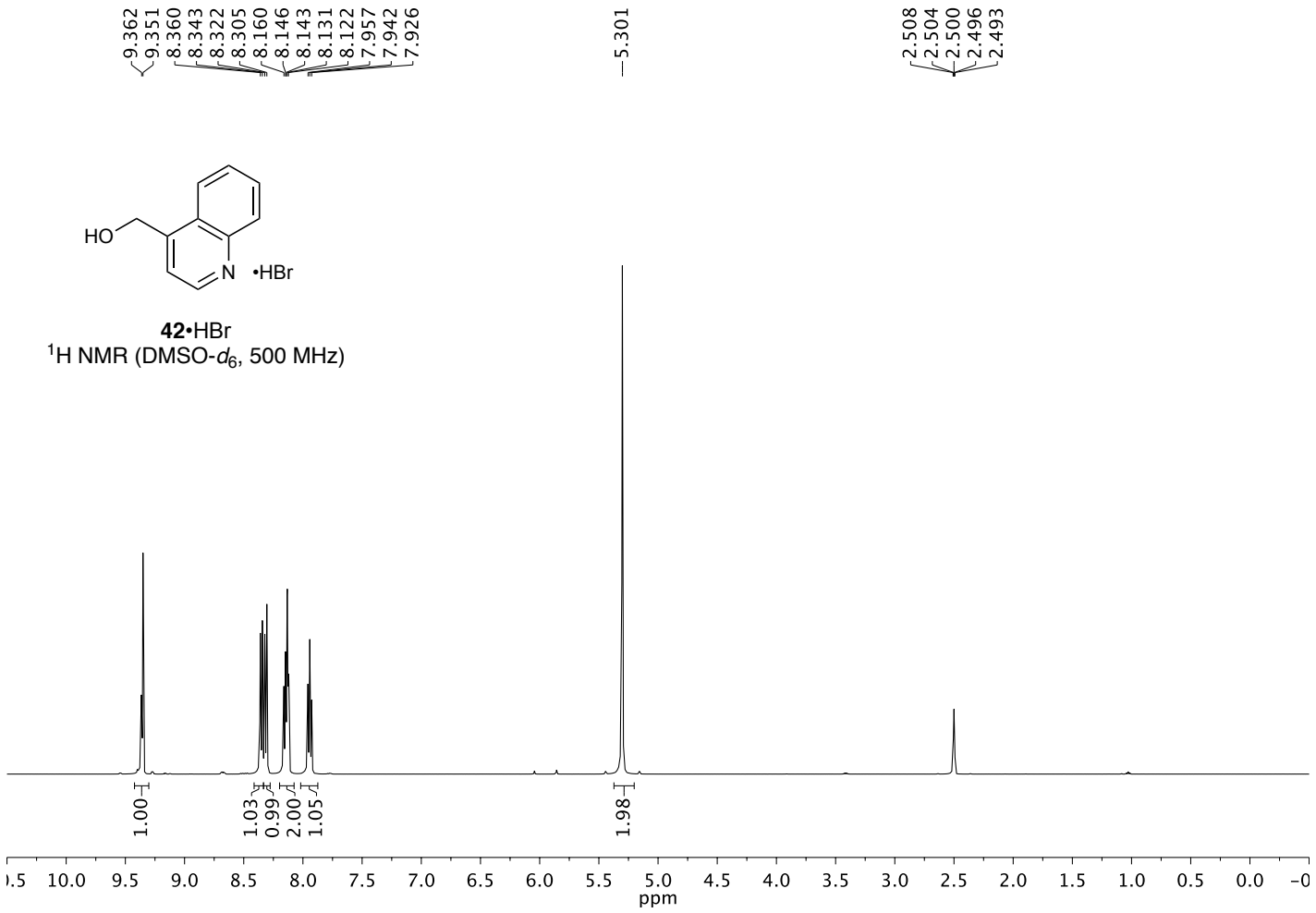

153.89
150.75
135.19
124.11
123.03
57.57
57.35
40.02
39.85
39.69
39.52
39.35
39.19
39.02
OMe
HO
N
•HBr
^{13}C NMR (DMSO-d_6, 126 MHz)
ppm


9.002
8.996
8.757
8.746
8.710
7.989
7.977
7.964
4.771
2.508
2.504
2.500
2.497
2.493
F
HO
N
•HBr
1H NMR (DMSO-d6, 500 MHz)
1.13
1.17
5.39
1.03
2.00
ppm

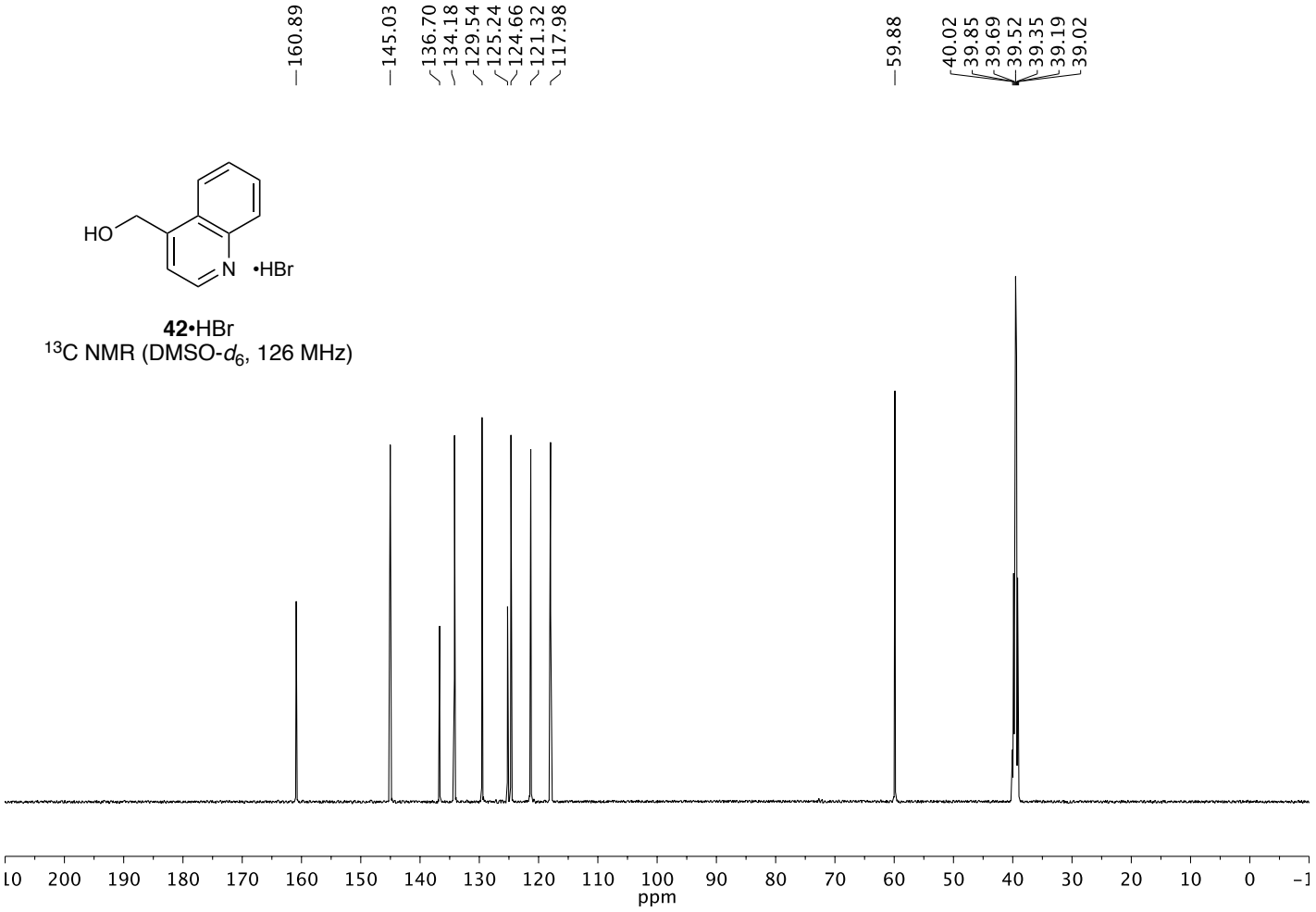

157.71
155.71
148.08
147.98
140.72
140.68
131.84
131.58
124.90
124.86
56.20
56.17
40.02
39.85
39.69
39.52
39.35
39.19
39.02
F
HO
N
•HBr
^{13}C NMR (DMSO-d_6, 126 MHz)
ppm

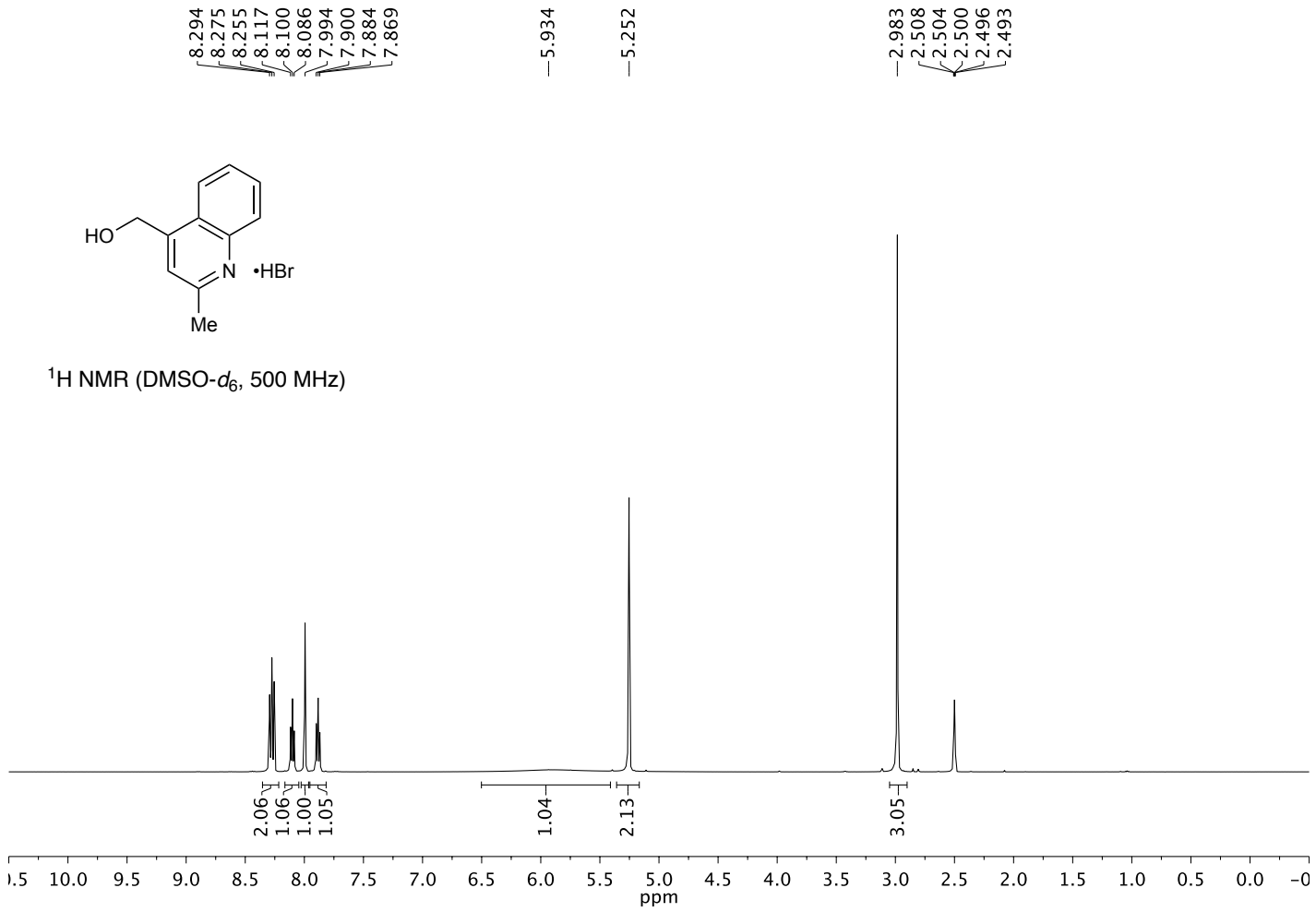

10.287
9.031
8.847
8.836
7.977
7.966
4.705
2.508
2.504
2.500
2.497
2.493
Cl
HO
N
•HBr
1H NMR (DMSO-d6, 500 MHz)
1.86
1.04
1.06
1.02
2.00
ppm


157.56
142.77
142.57
130.14
123.77
59.82
40.02
39.85
39.69
39.52
39.35
39.19
39.02
Cl
HO
N
•HBr
13C NMR (DMSO-d6, 126 MHz)
ppm

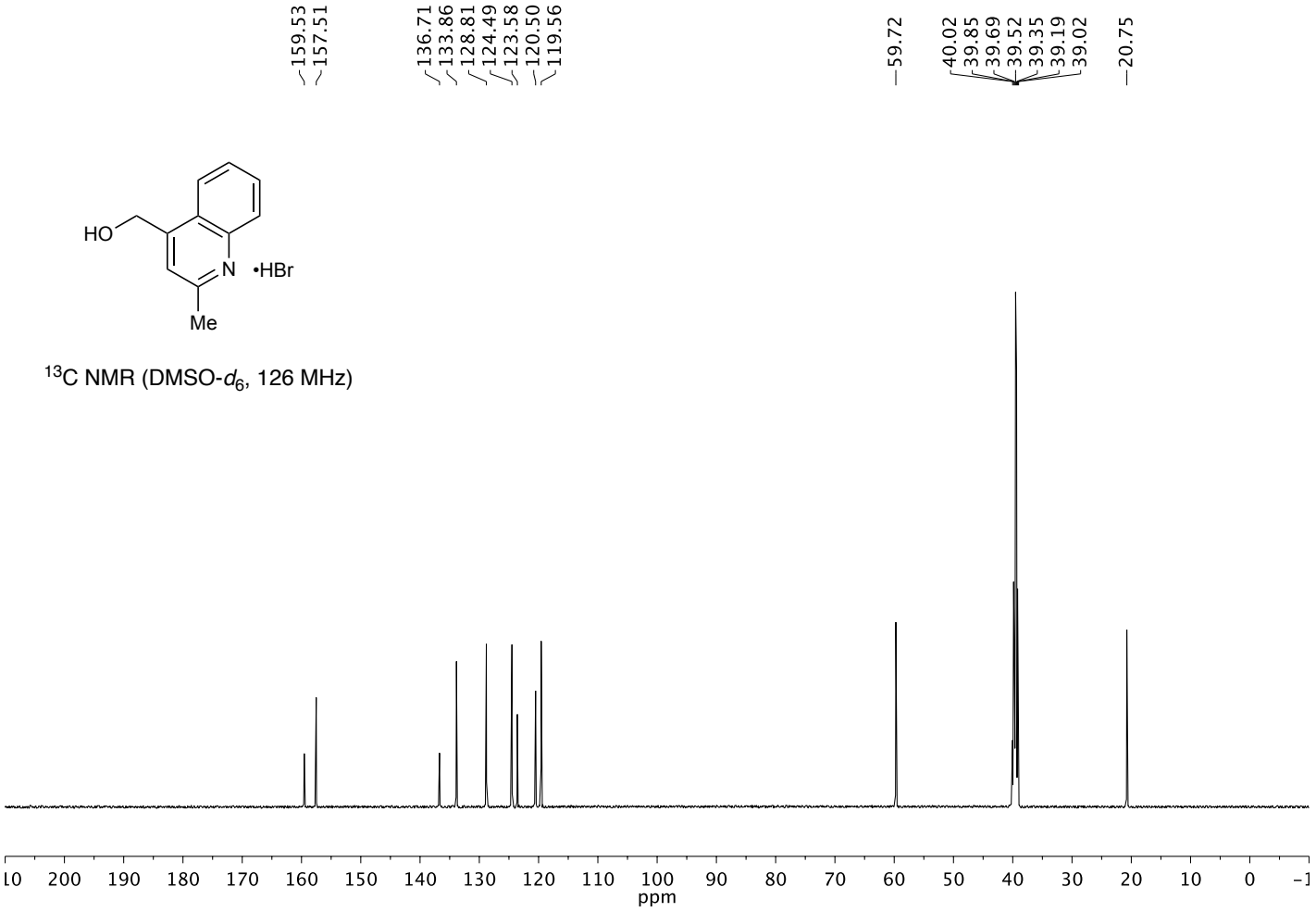


42•HBr
^{1}H NMR (DMSO-d_6, 500 MHz)

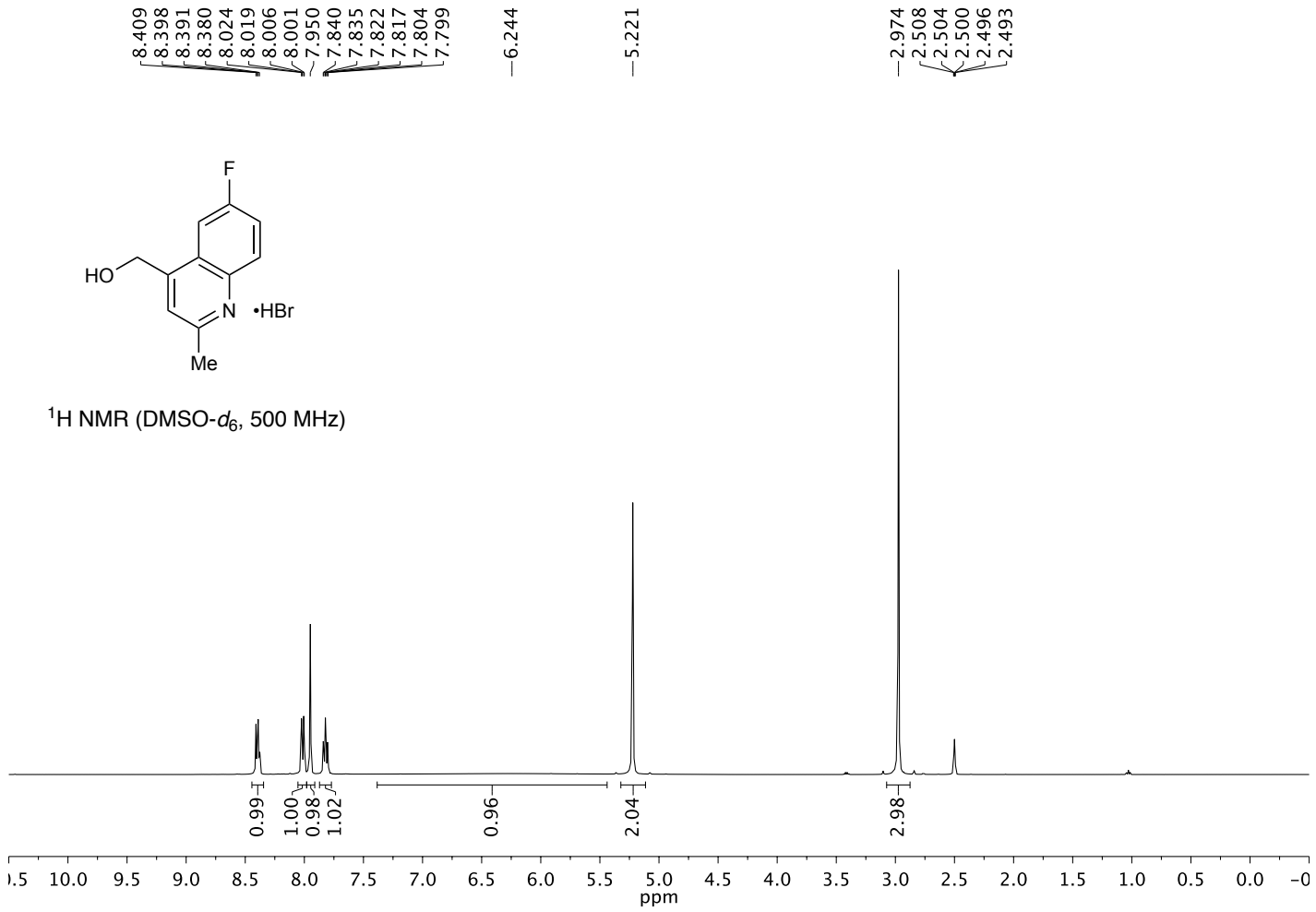

160.89
145.03
136.70
134.18
129.54
125.24
124.66
121.32
117.98
59.88
40.02
39.85
39.69
39.52
39.35
39.19
39.02
HO
N •HBr
42•HBr
13C NMR (DMSO-d6, 126 MHz)
ppm



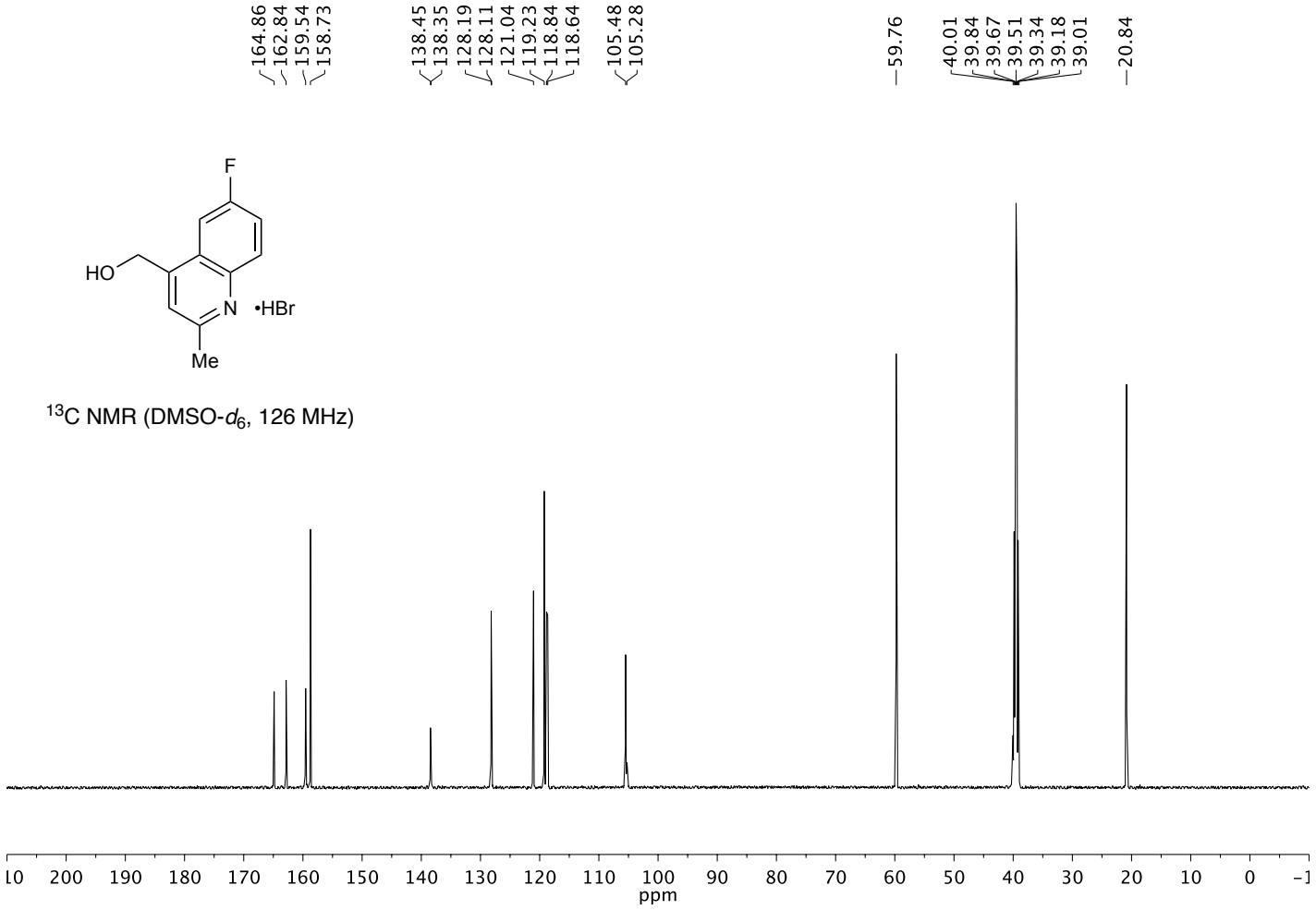
^{1}H NMR (DMSO-d_6, 500 MHz)



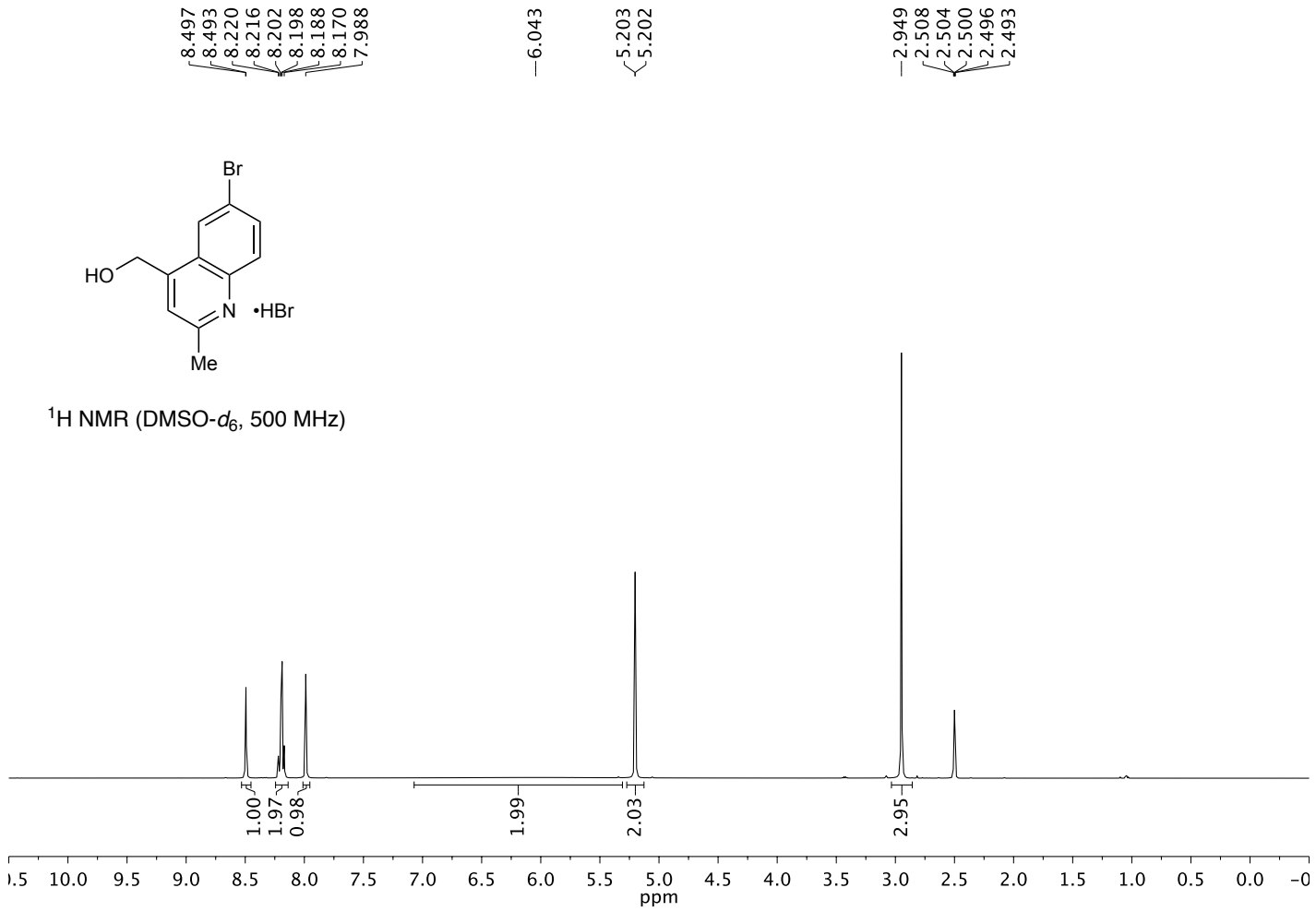
^{13}C NMR (DMSO-d_6, 126 MHz)

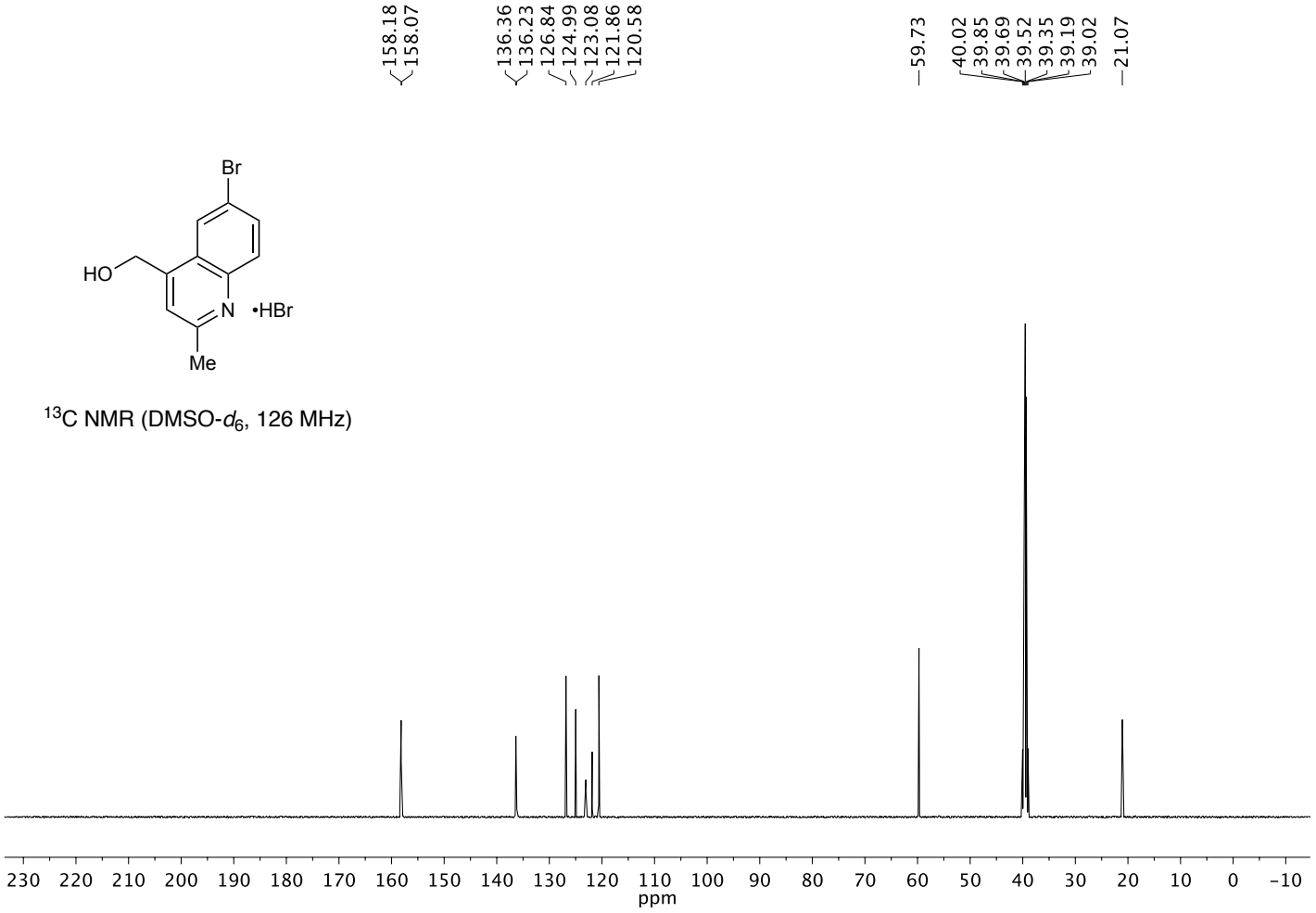


^{1}H NMR (DMSO-d_6, 500 MHz)

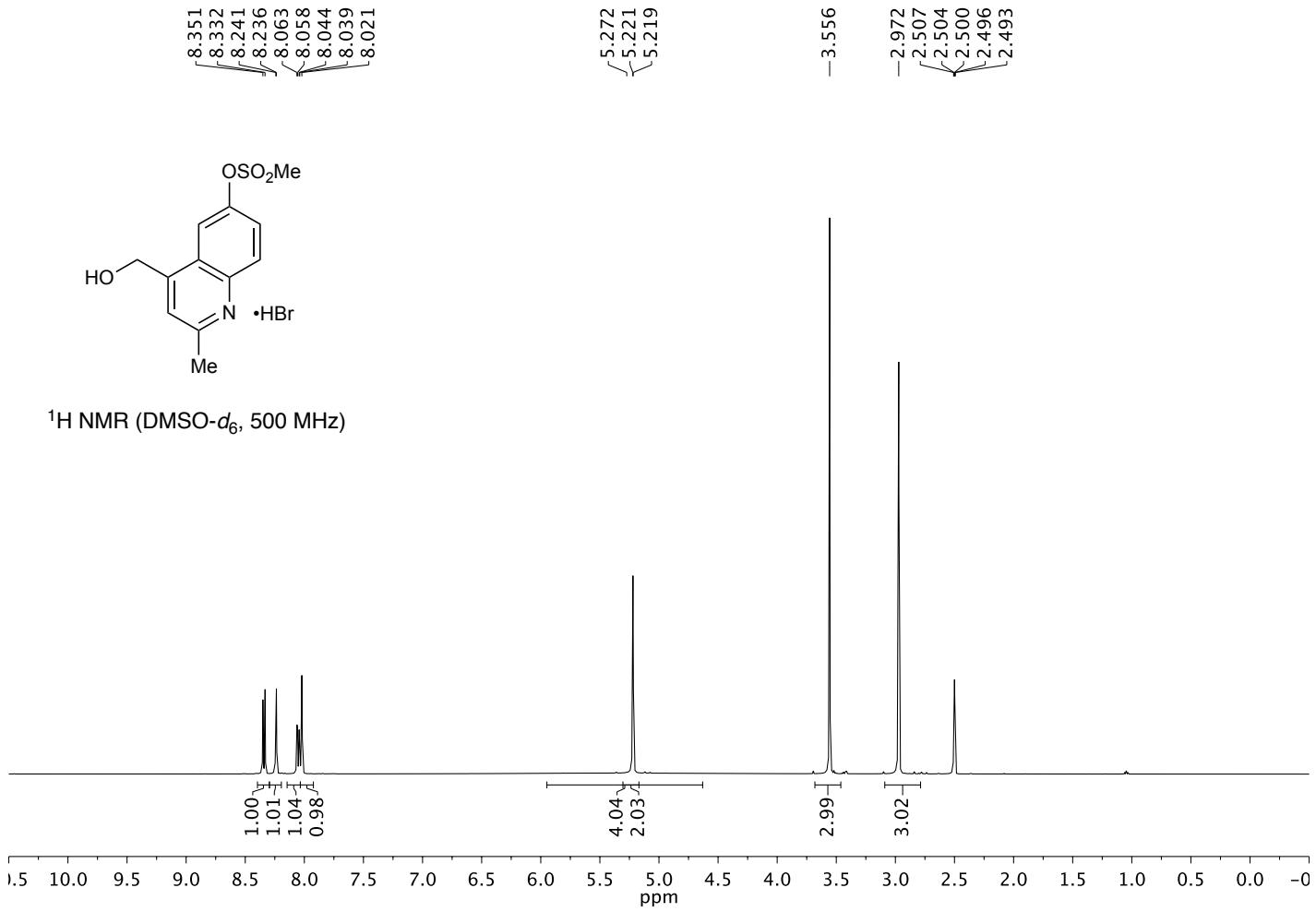


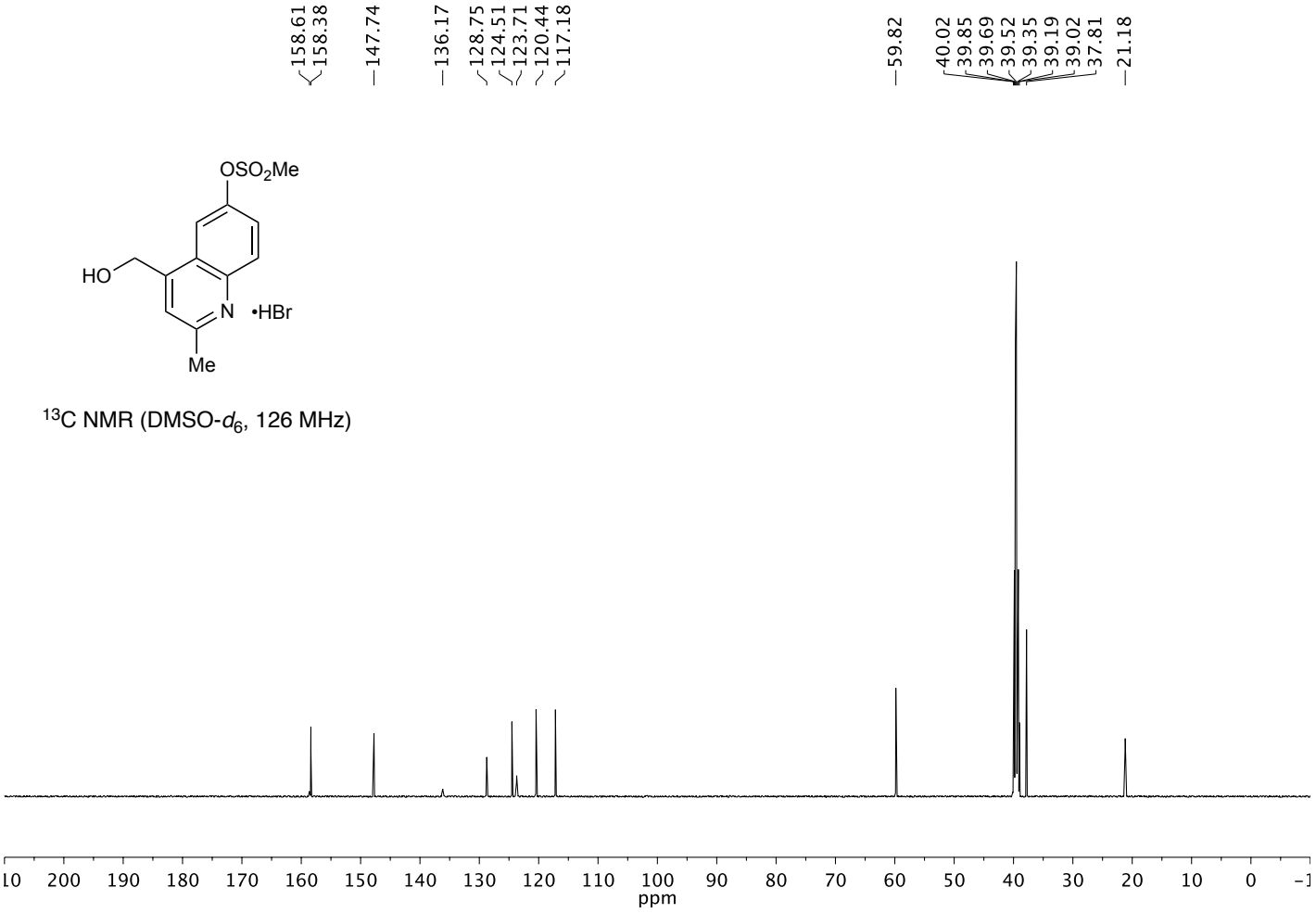
^{13}C NMR (DMSO-d_6, 126 MHz)


8.497
8.493
8.220
8.216
8.202
8.198
8.188
8.170
7.988
6.043
5.203
5.202
2.949
2.508
2.504
2.500
2.496
2.493
Br
HO
N
•HBr
Me
1H NMR (DMSO-d6, 500 MHz)
1.00
1.97
0.98
1.99
2.03
2.95
ppm

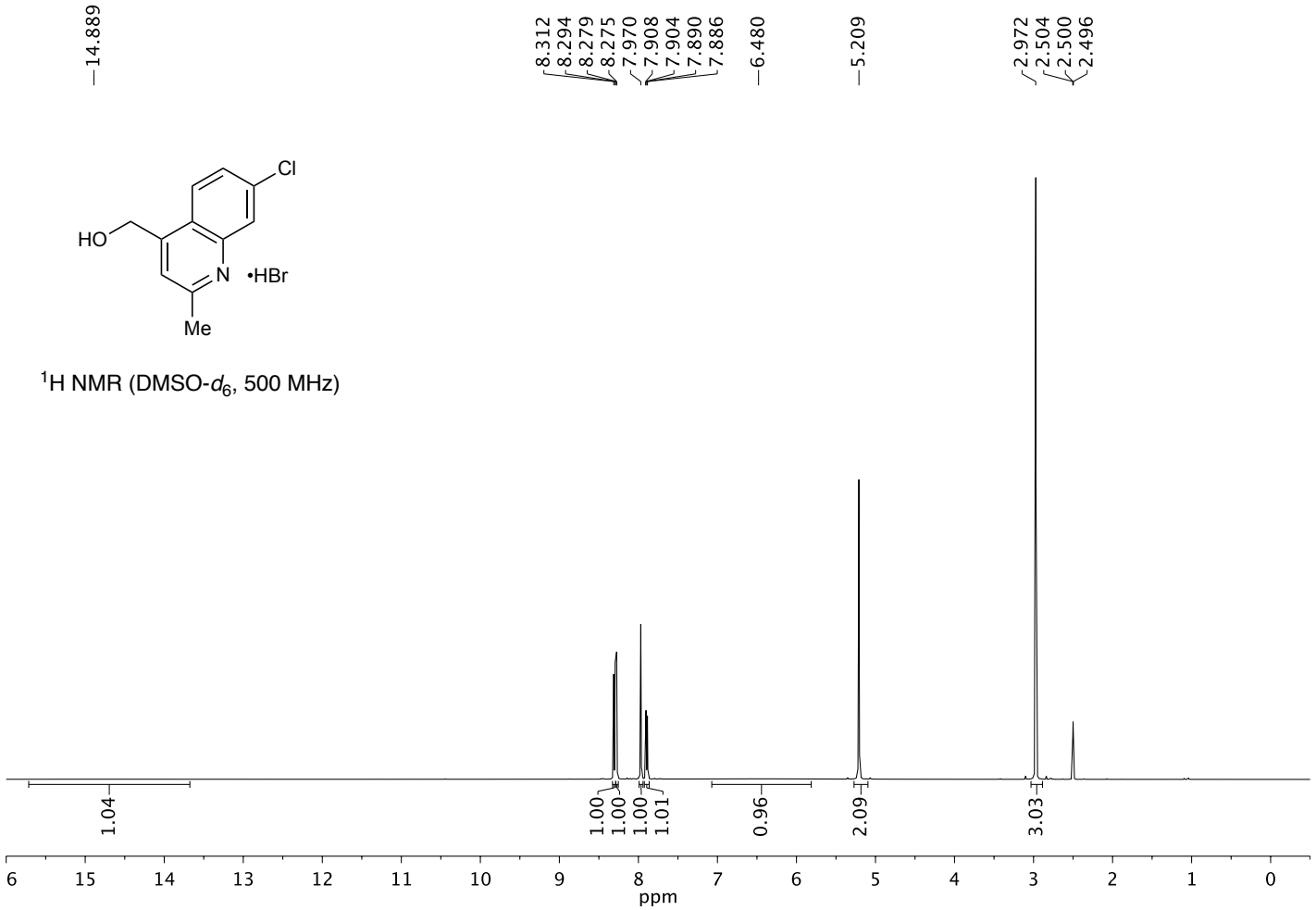


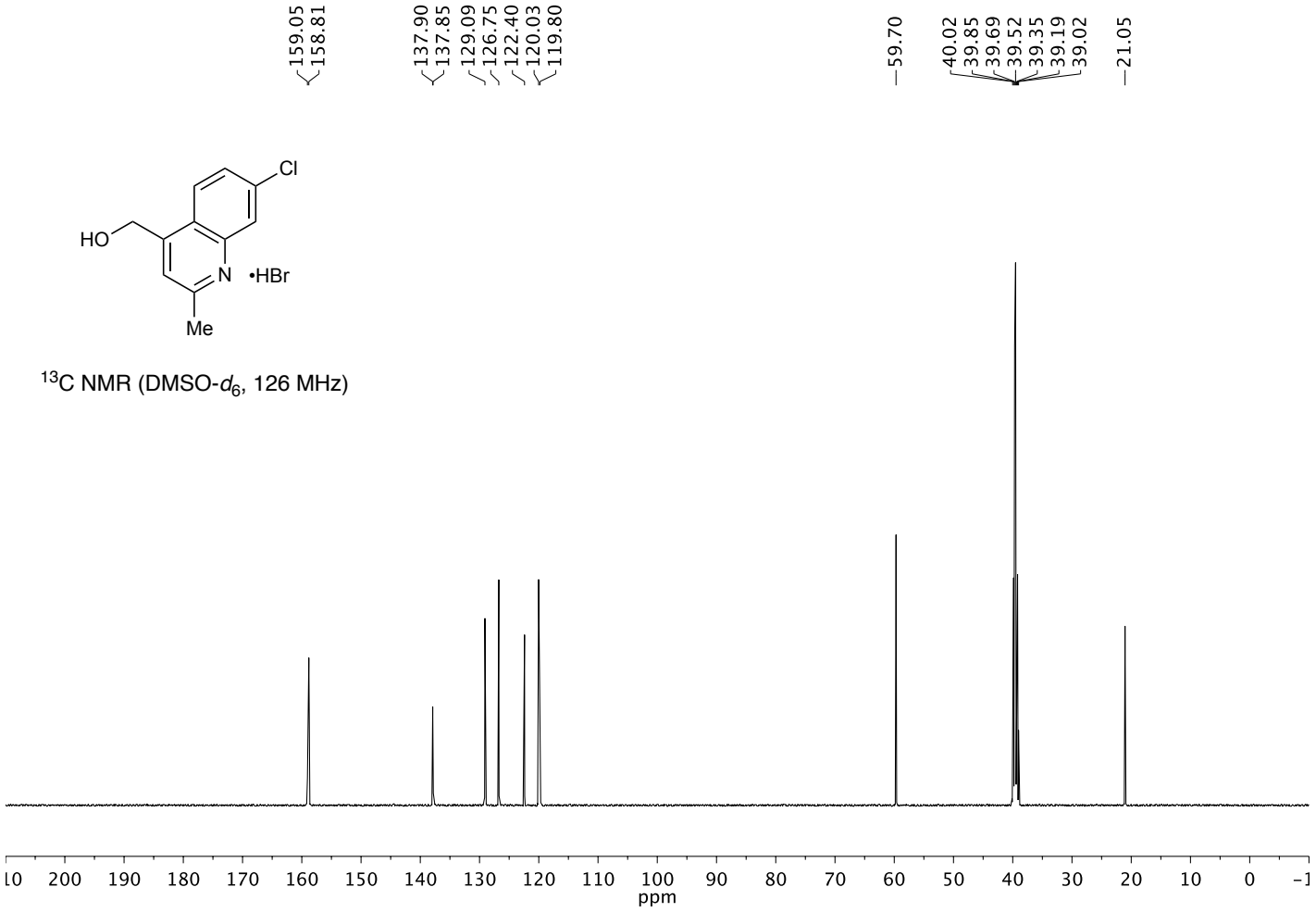
^{13}C NMR (DMSO-d_6, 126 MHz)


8.351
8.332
8.241
8.236
8.063
8.058
8.044
8.039
8.021
5.272
5.221
5.219
3.556
2.972
2.507
2.504
2.500
2.496
2.493
OSO2Me
HO
N
•HBr
Me
1H NMR (DMSO-d6, 500 MHz)
1.00
1.01
1.04
0.98
4.04
2.03
2.99
3.02
ppm

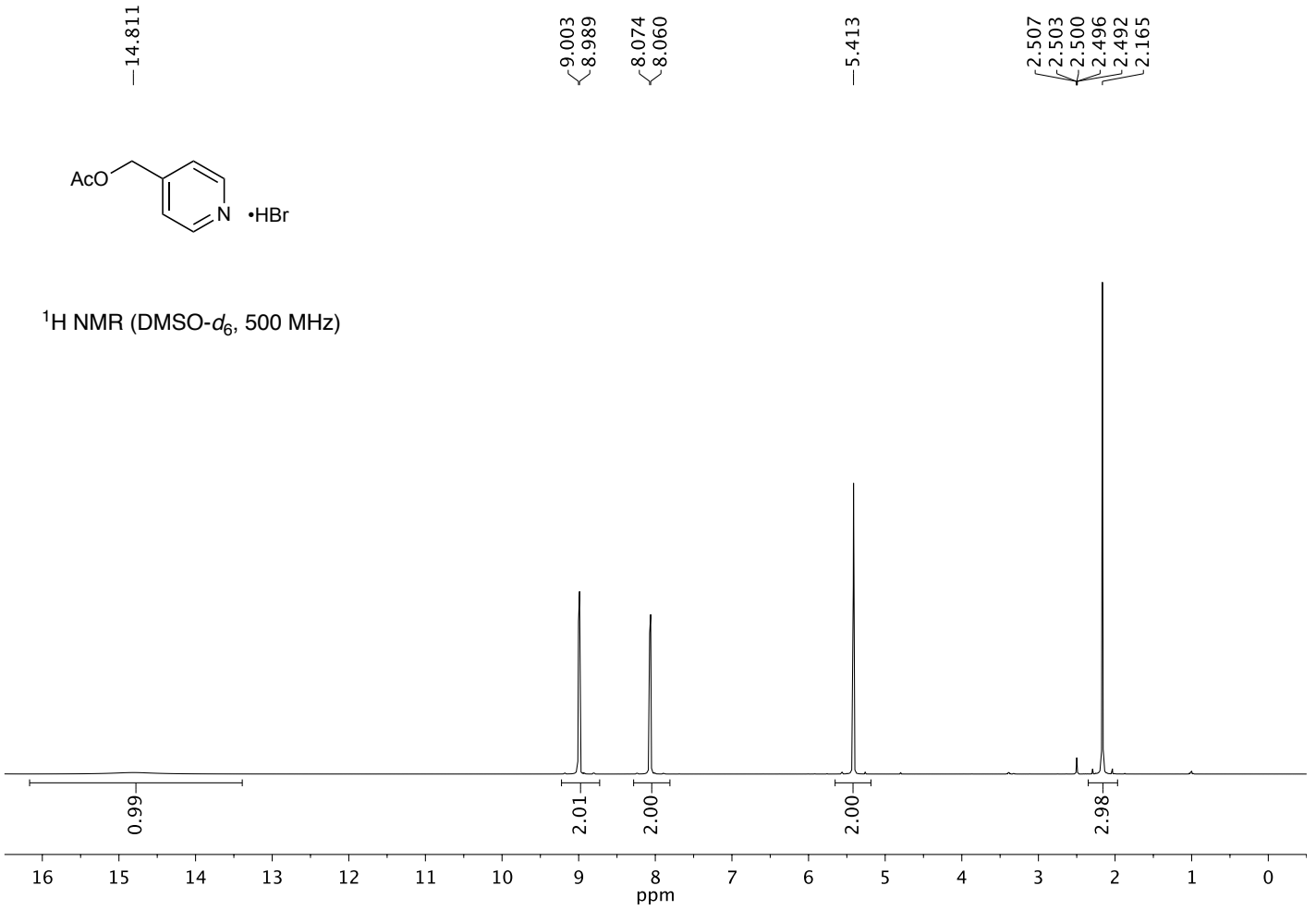


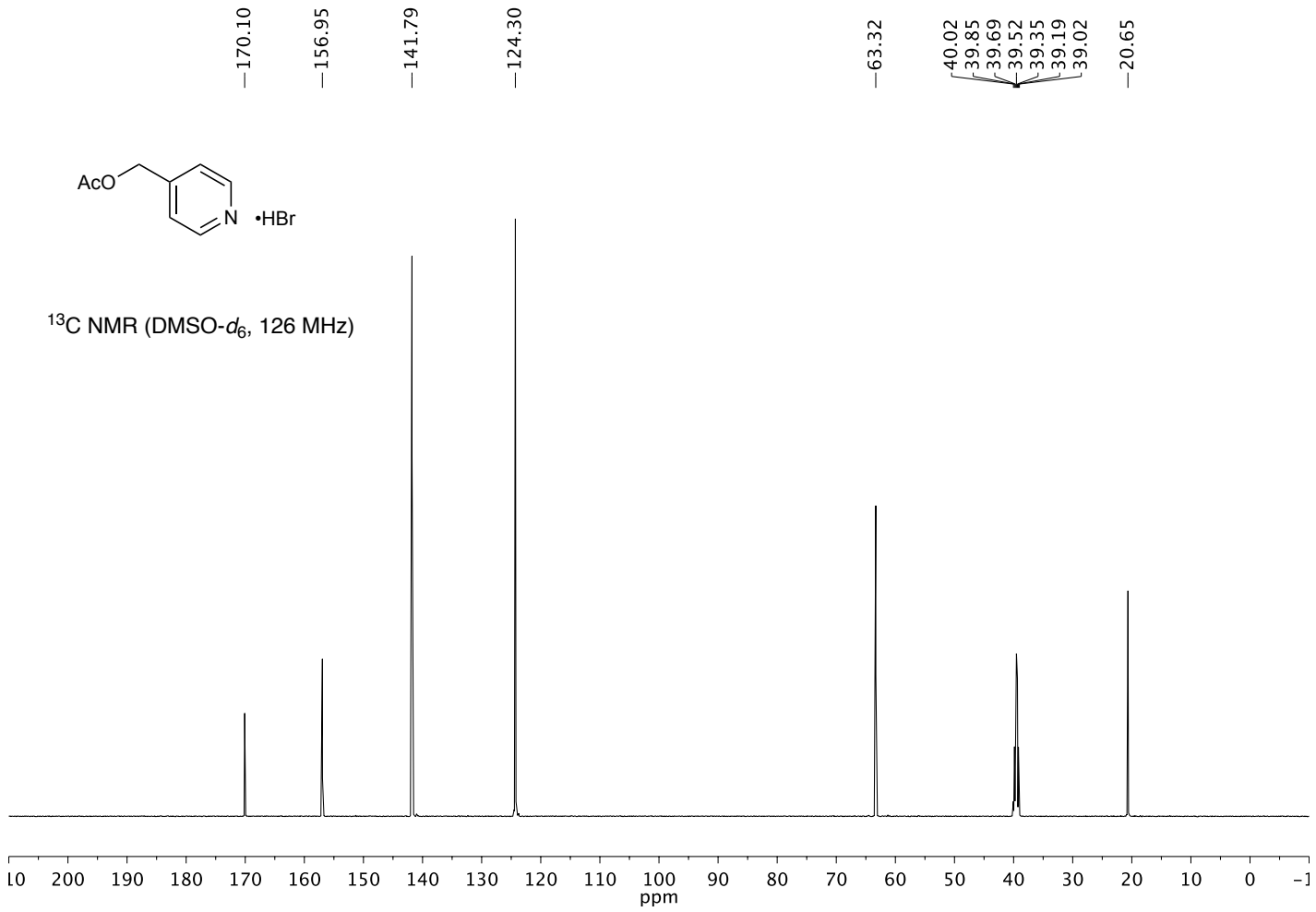
^{13}C NMR (DMSO-d_6, 126 MHz)

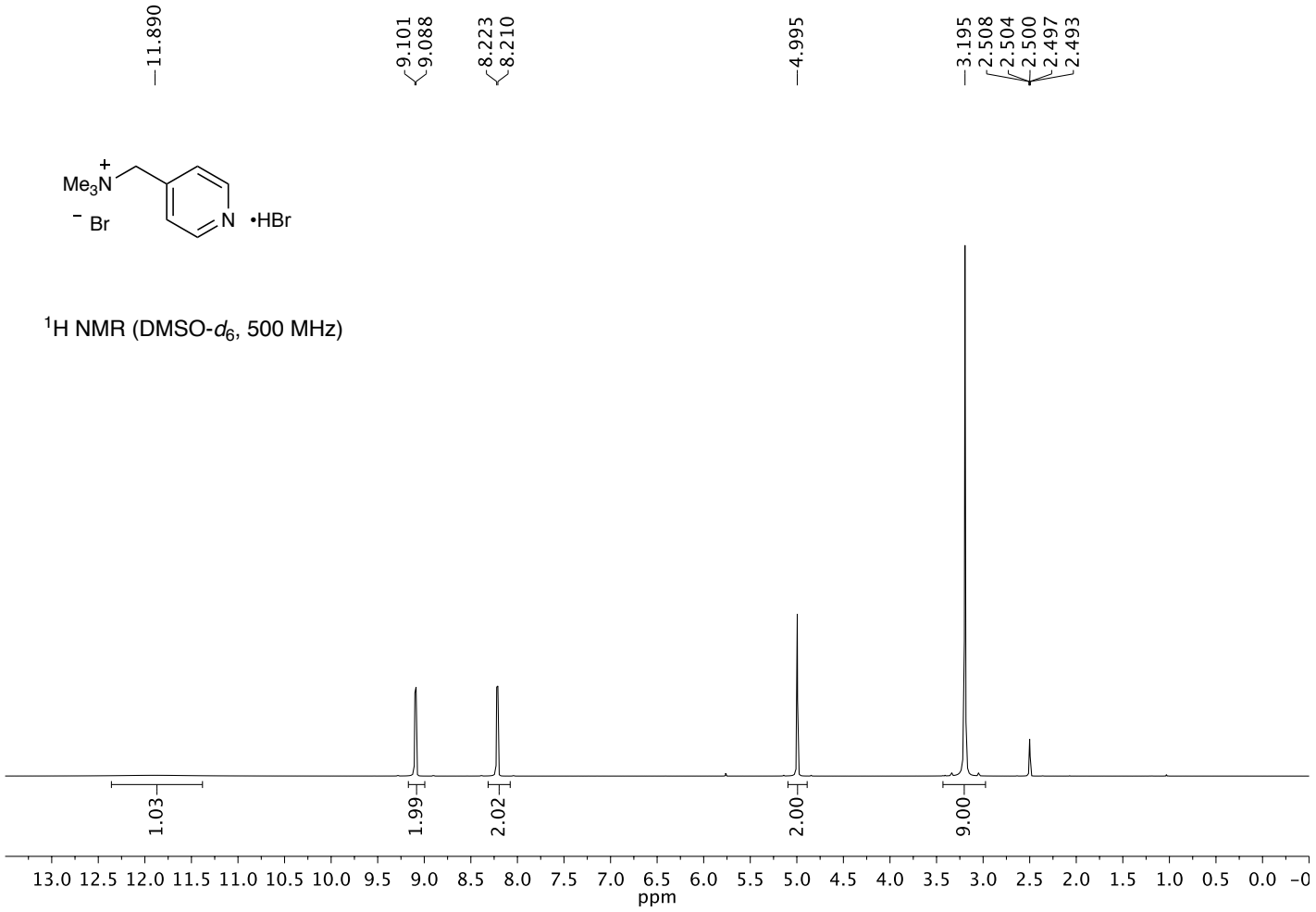

14.889
8.312
8.294
8.279
8.275
7.970
7.908
7.904
7.890
7.886
6.480
5.209
2.972
2.504
2.500
2.496
Cl
HO
N
•HBr
Me
1H NMR (DMSO-d6, 500 MHz)
1.04
1.00
1.00
1.01
0.96
2.09
3.03
6
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
ppm

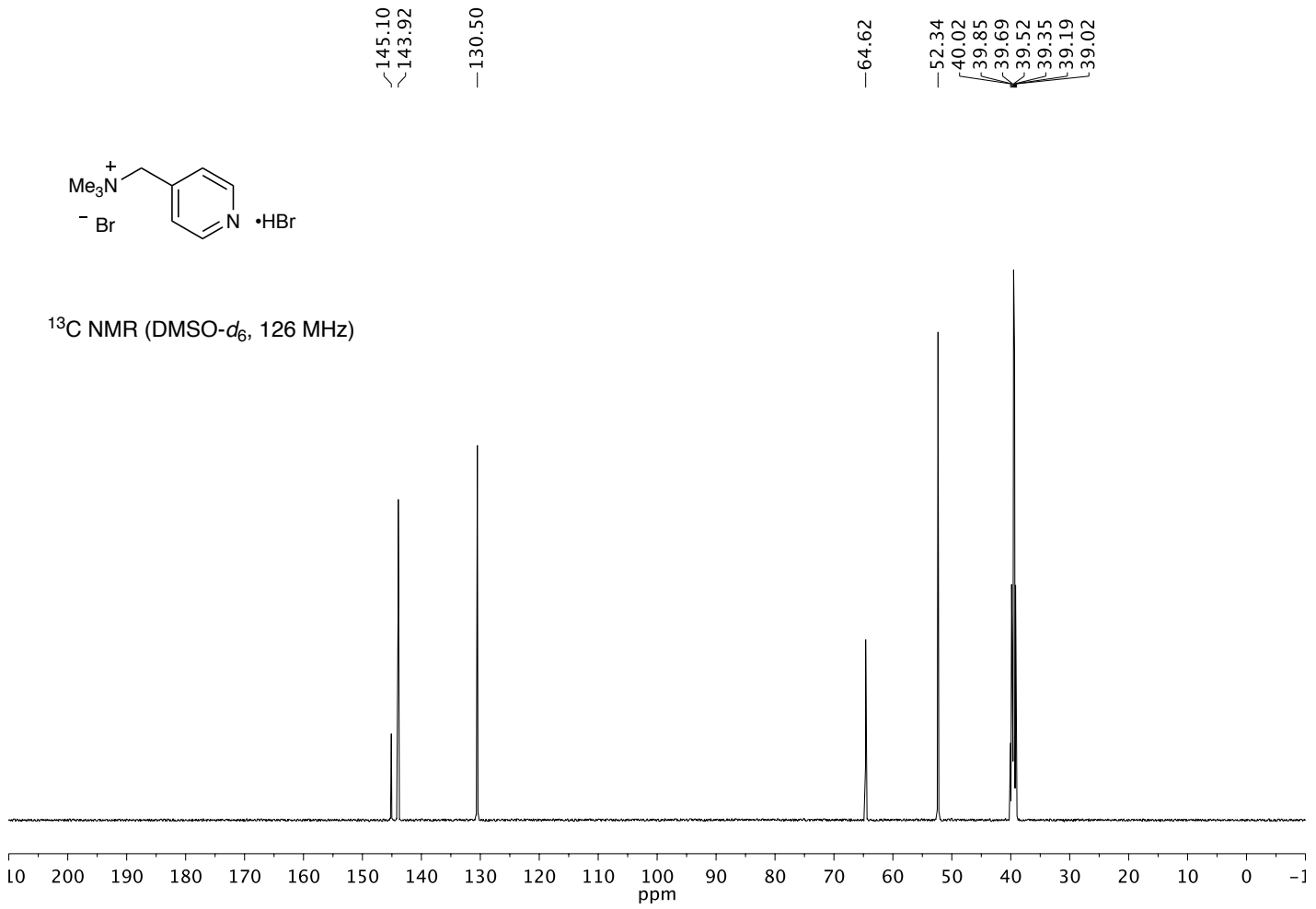


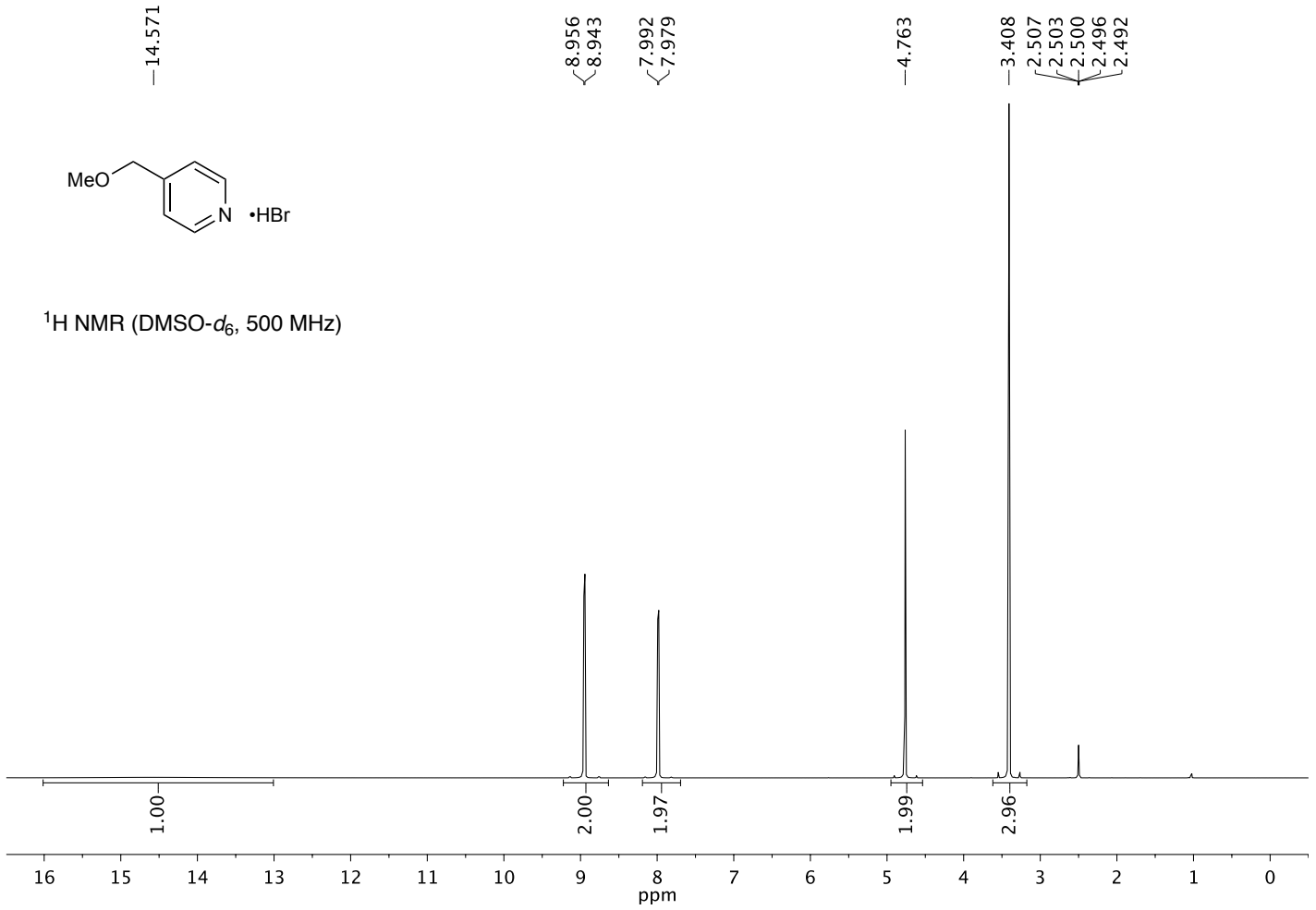
^{13}C NMR (DMSO-d_6, 126 MHz)

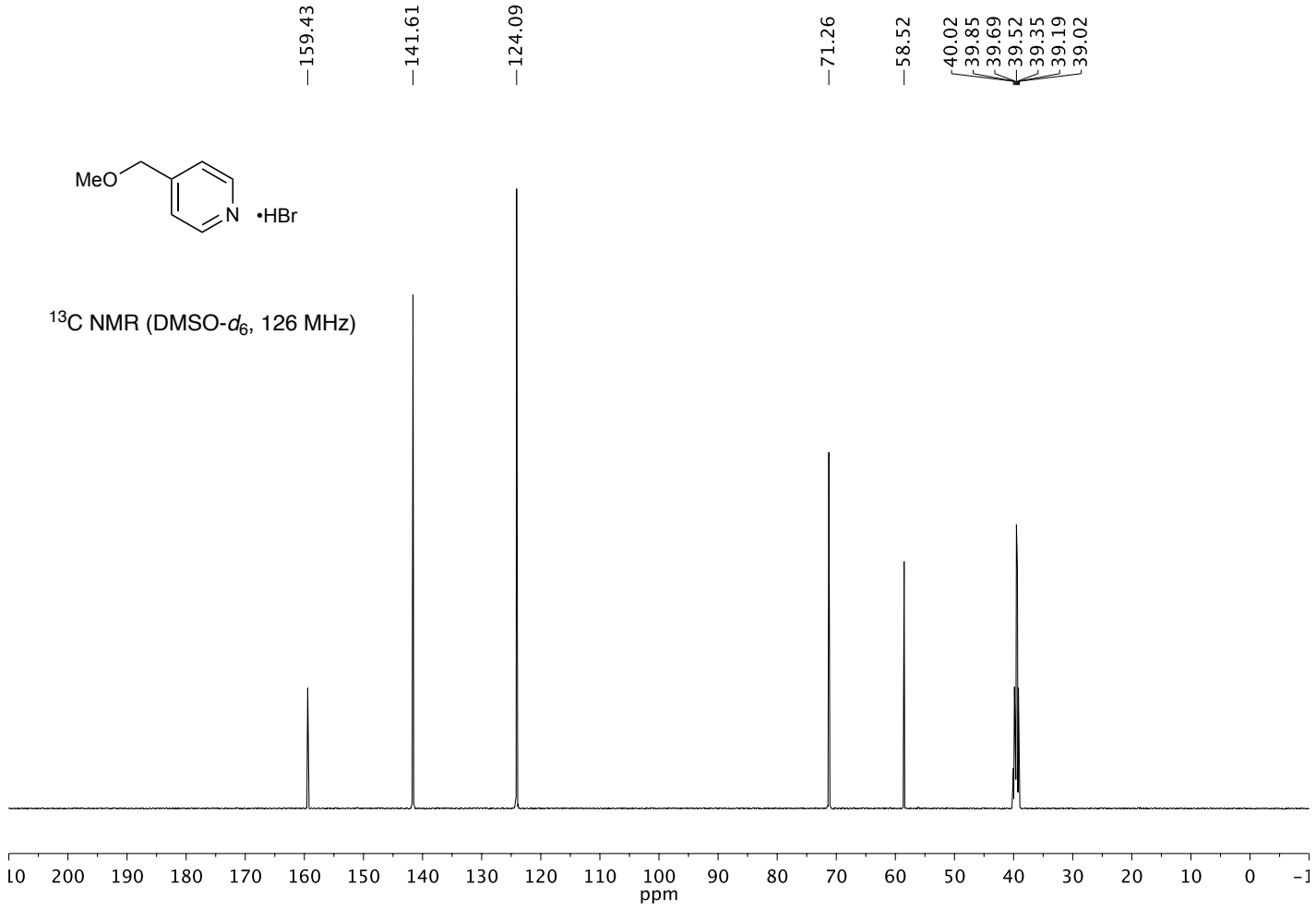

14.811
9.003
8.989
8.074
8.060
5.413
2.507
2.503
2.500
2.496
2.492
2.165
AcO
N
•HBr
1H NMR (DMSO-d6, 500 MHz)
0.99
2.01
2.00
2.00
2.98
16
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
ppm

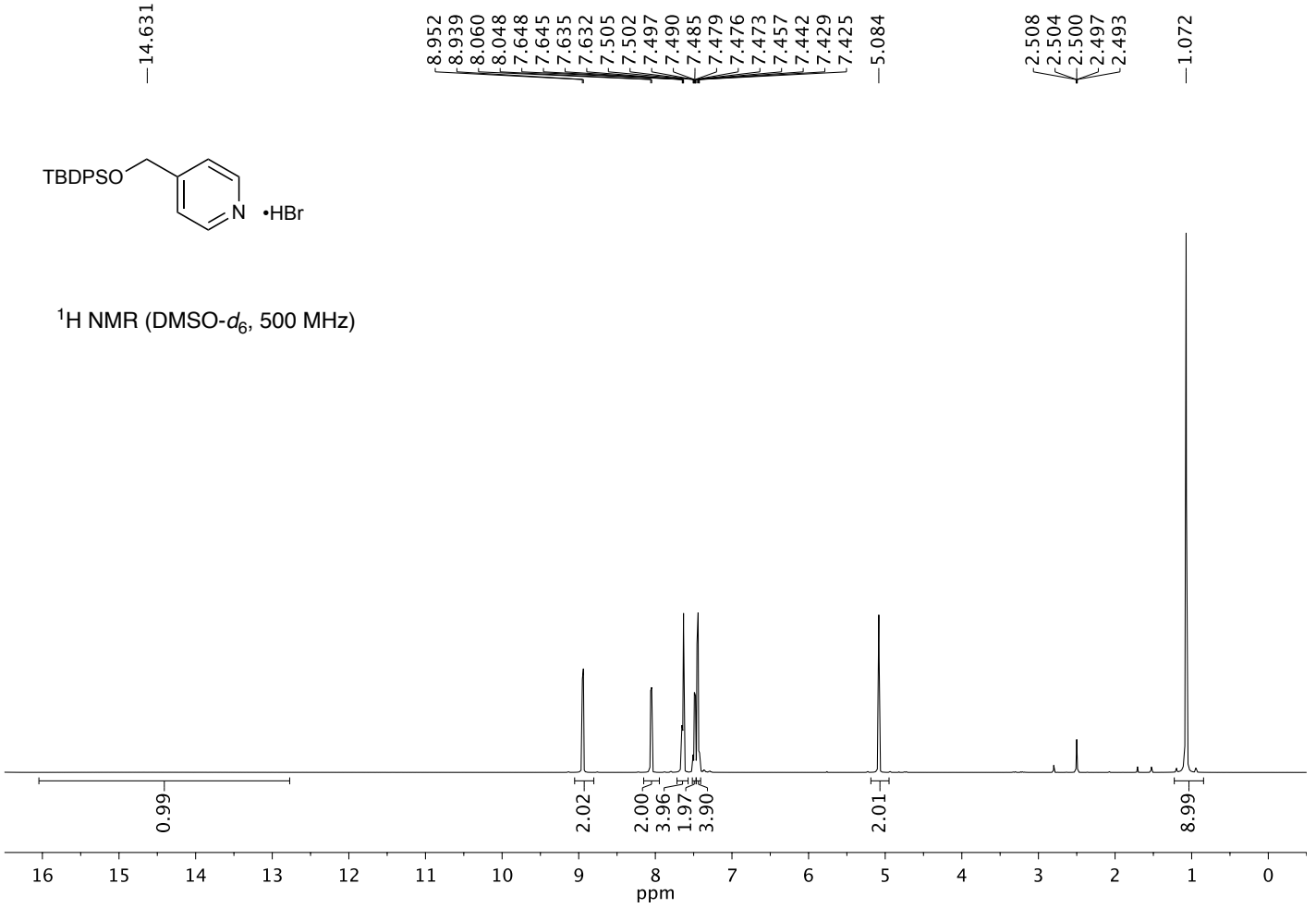

170.10
156.95
141.79
124.30
63.32
40.02
39.85
39.69
39.52
39.35
39.19
39.02
20.65
AcO
N •HBr
13C NMR (DMSO-d6, 126 MHz)
ppm

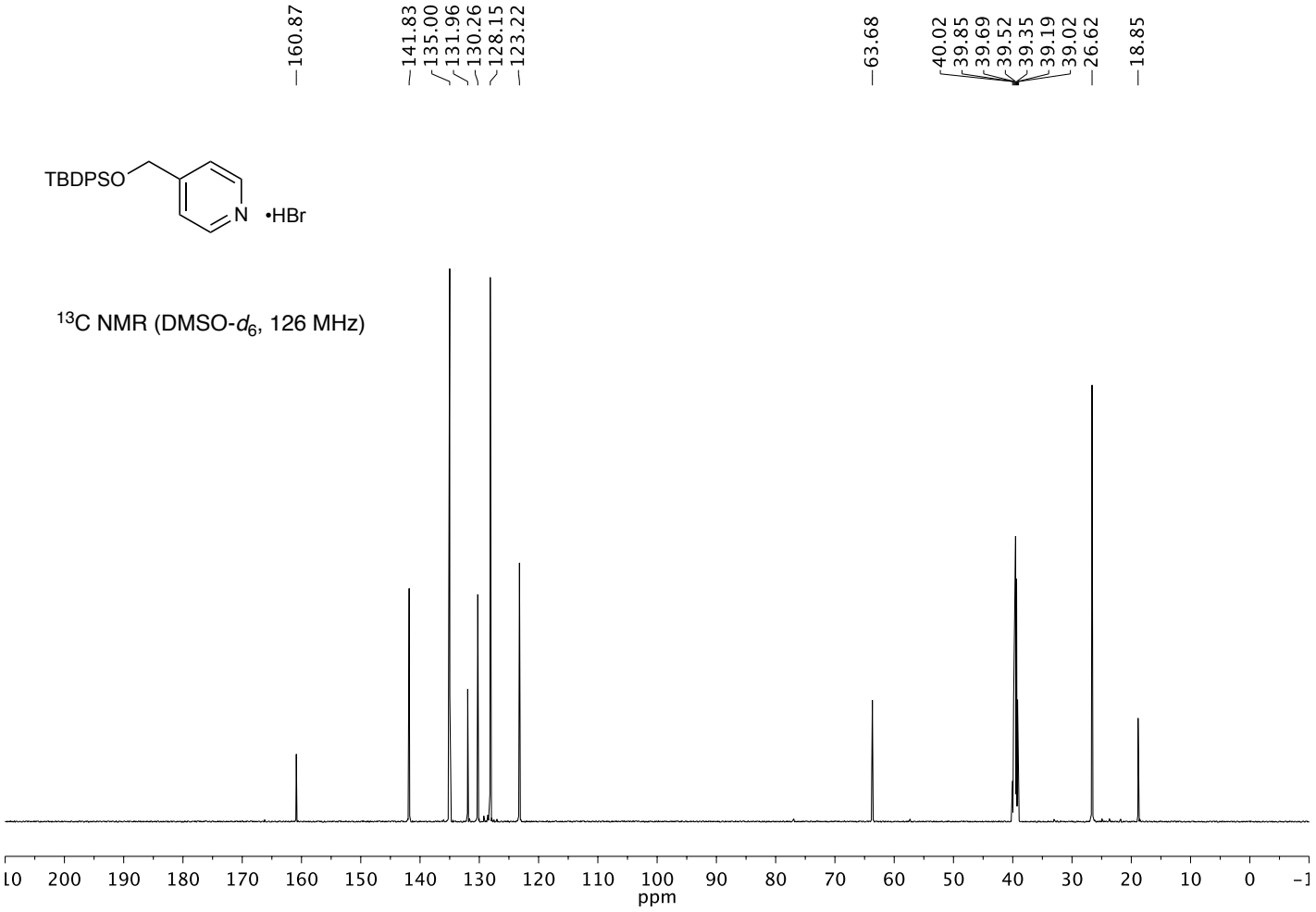

11.890
9.101
9.088
8.223
8.210
4.995
3.195
2.508
2.504
2.500
2.497
2.493
Me3N+
Br−
N •HBr
1H NMR (DMSO-d6, 500 MHz)
1.03
1.99
2.02
2.00
9.00
13.0 12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 −0
ppm

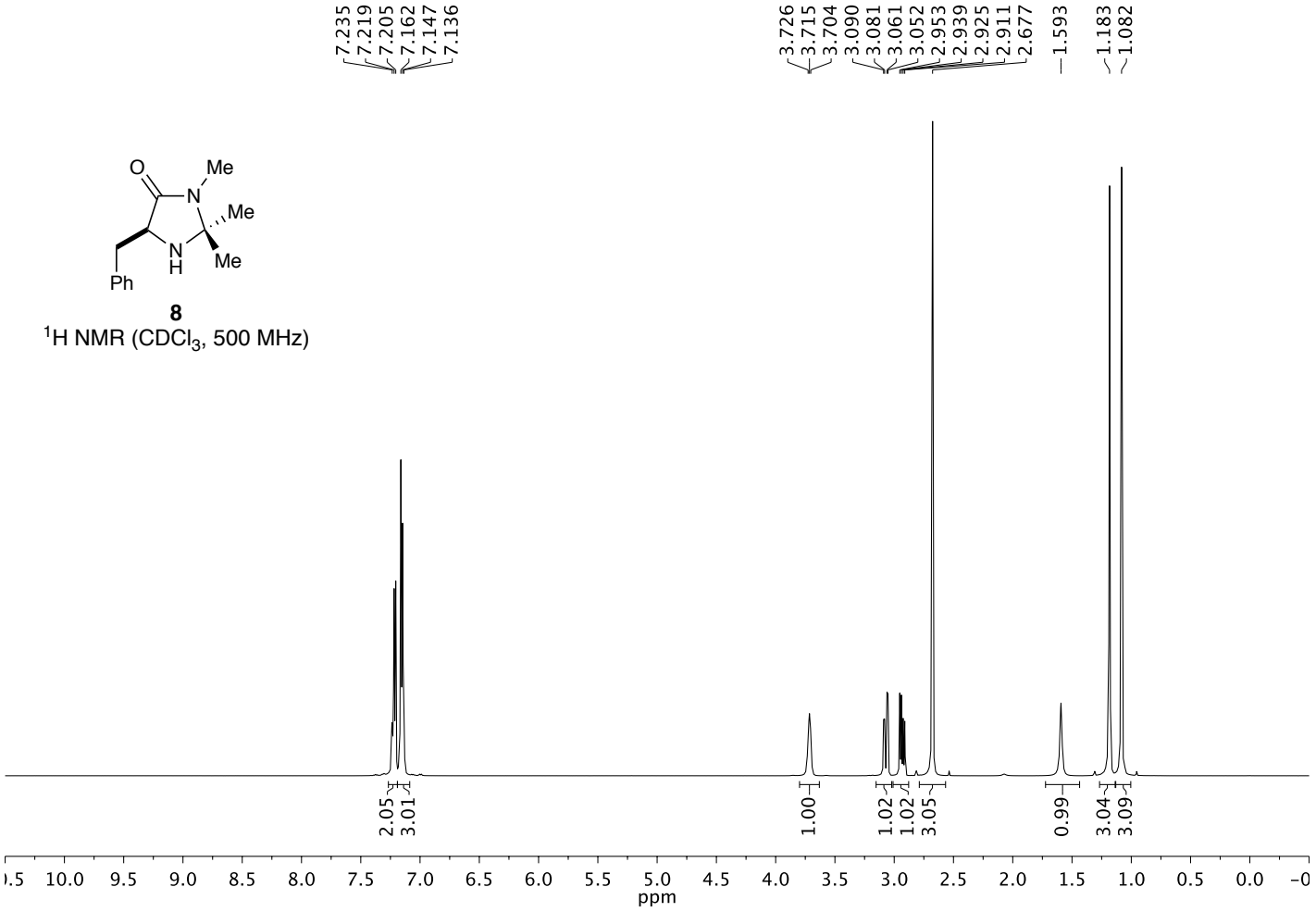

145.10
143.92
130.50
64.62
52.34
40.02
39.85
39.69
39.52
39.35
39.19
39.02
Me3N
Br
N •HBr
13C NMR (DMSO-d6, 126 MHz)
ppm


14.571
8.956
8.943
7.992
7.979
4.763
3.408
2.507
2.503
2.500
2.496
2.492
MeO
N
•HBr
1H NMR (DMSO-d6, 500 MHz)
1.00
2.00
1.97
1.99
2.96
16
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
ppm


159.43
141.61
124.09
71.26
58.52
40.02
39.85
39.69
39.52
39.35
39.19
39.02
MeO
N
•HBr
^{13}C NMR (DMSO-d_6, 126 MHz)
ppm

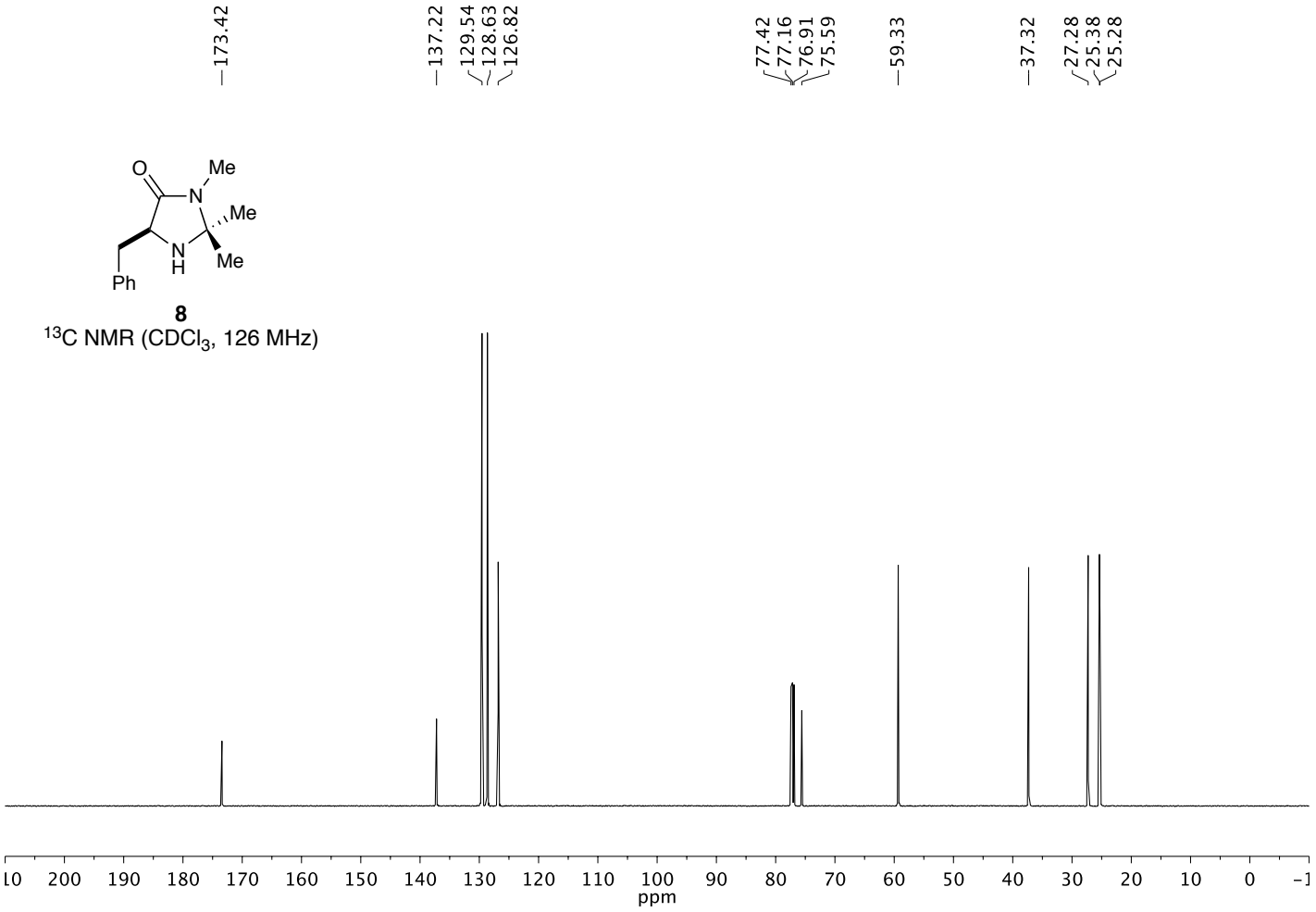

14.631
8.952
8.939
8.060
8.048
7.648
7.645
7.635
7.632
7.505
7.502
7.497
7.490
7.485
7.479
7.476
7.473
7.457
7.442
7.429
7.425
5.084
2.508
2.504
2.500
2.497
2.493
1.072
TBDPSO
N
•HBr
1H NMR (DMSO-d6, 500 MHz)
0.99
2.02
2.00
3.96
1.97
3.90
2.01
8.99
16
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
ppm


160.87
141.83
135.00
131.96
130.26
128.15
123.22
63.68
40.02
39.85
39.69
39.52
39.35
39.19
39.02
26.62
18.85
TBDPSO
N
•HBr
13C NMR (DMSO-d6, 126 MHz)
ppm



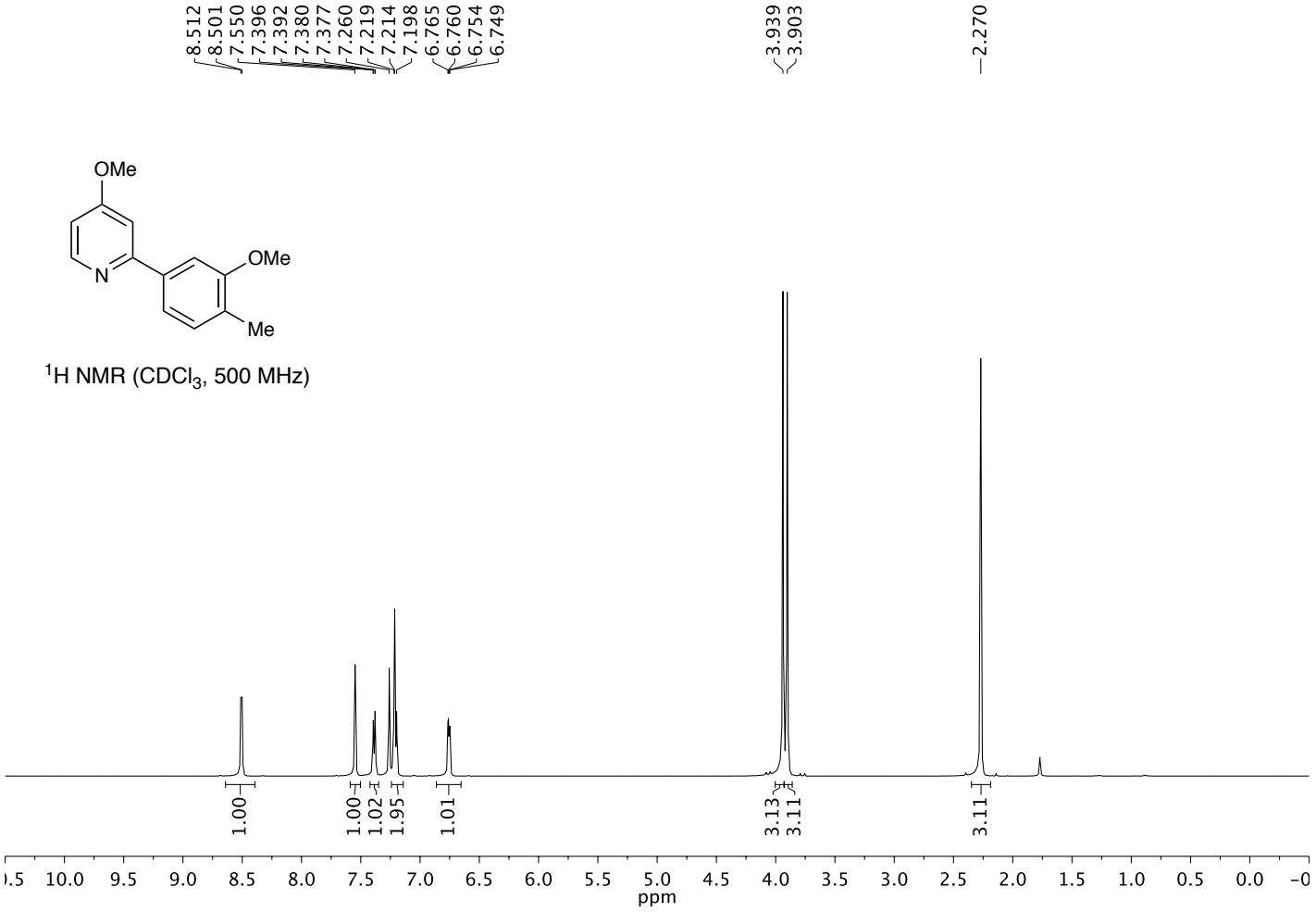
8

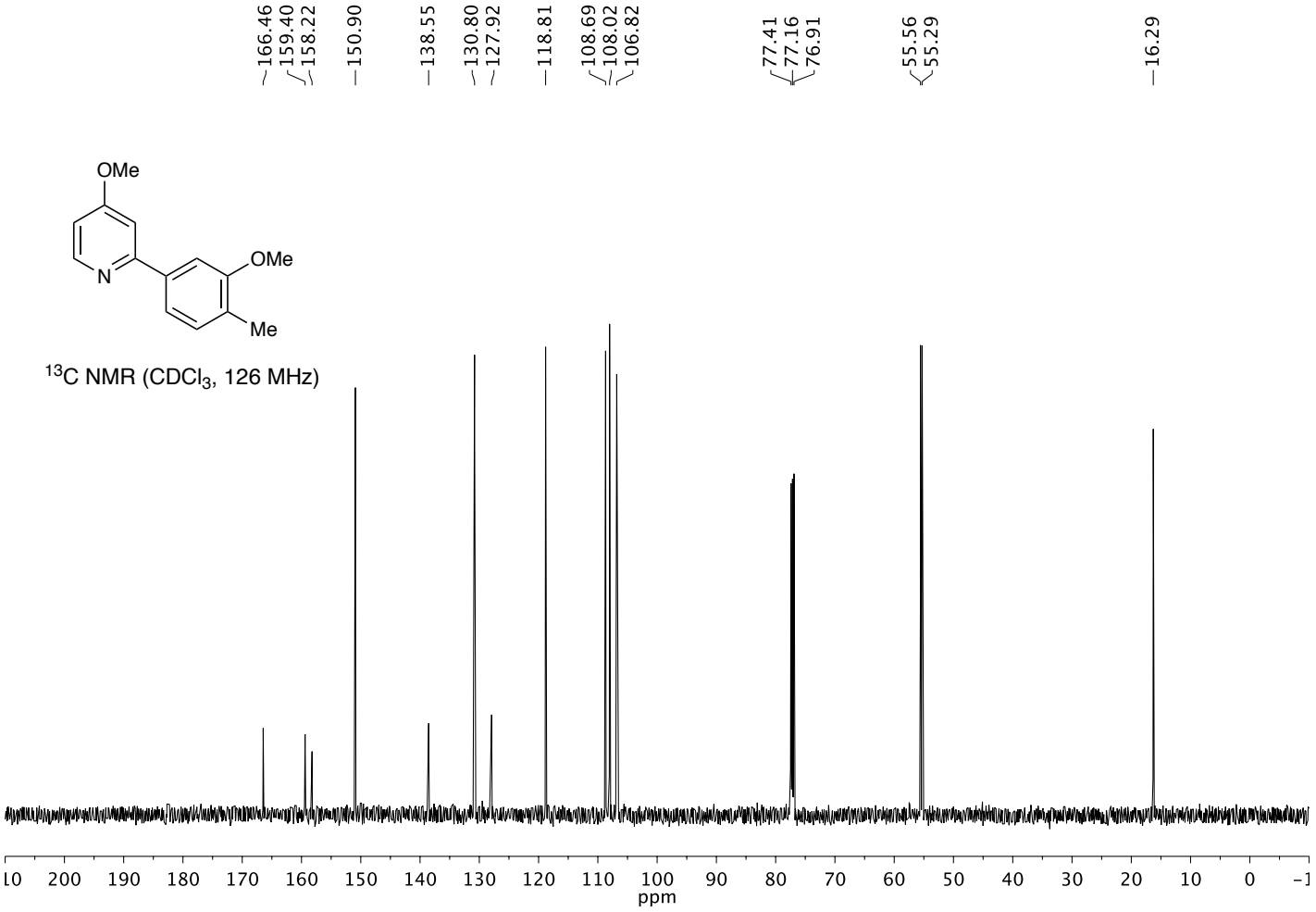
^{1}H NMR ($CDCl_3$, 500 MHz)

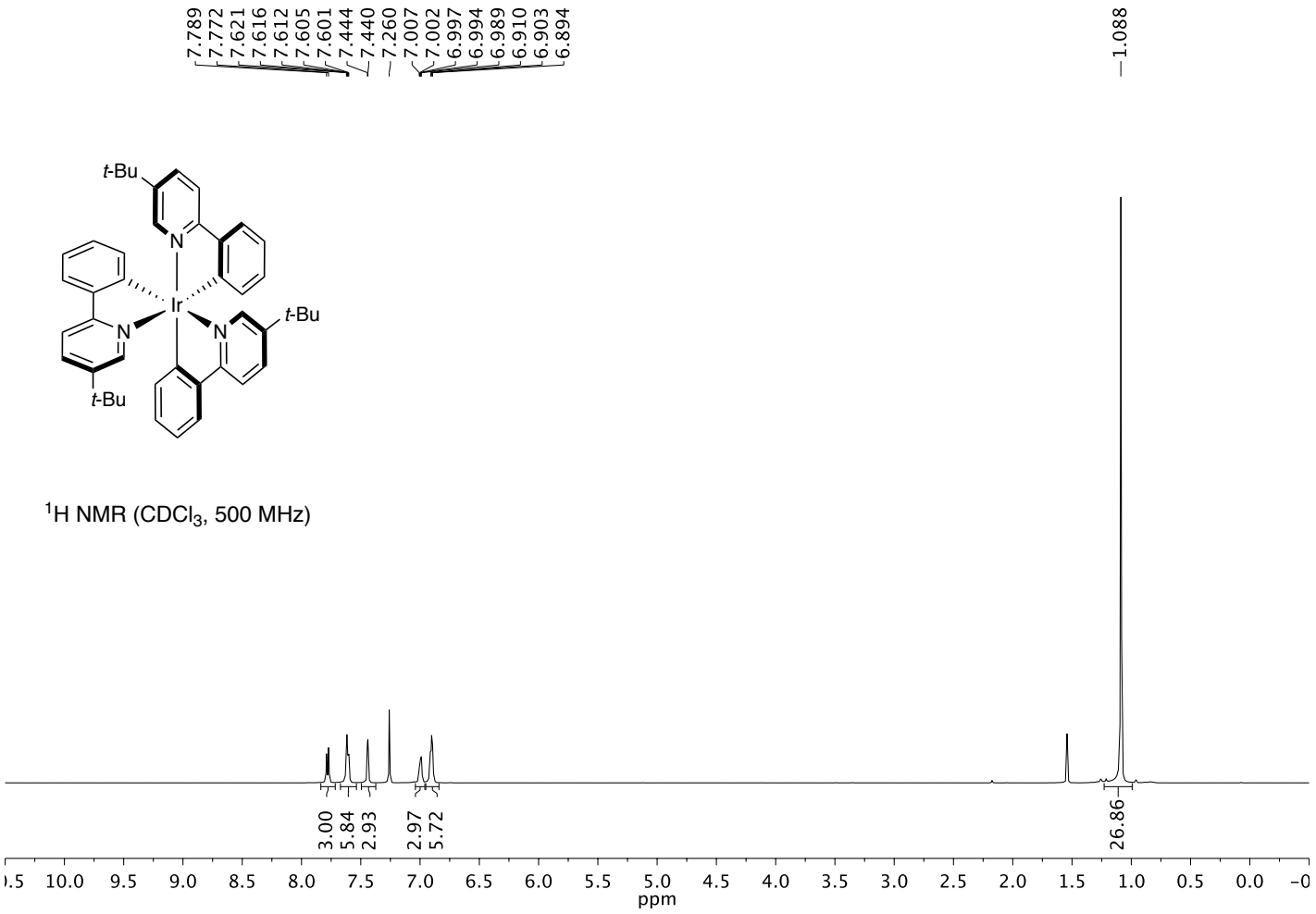


8

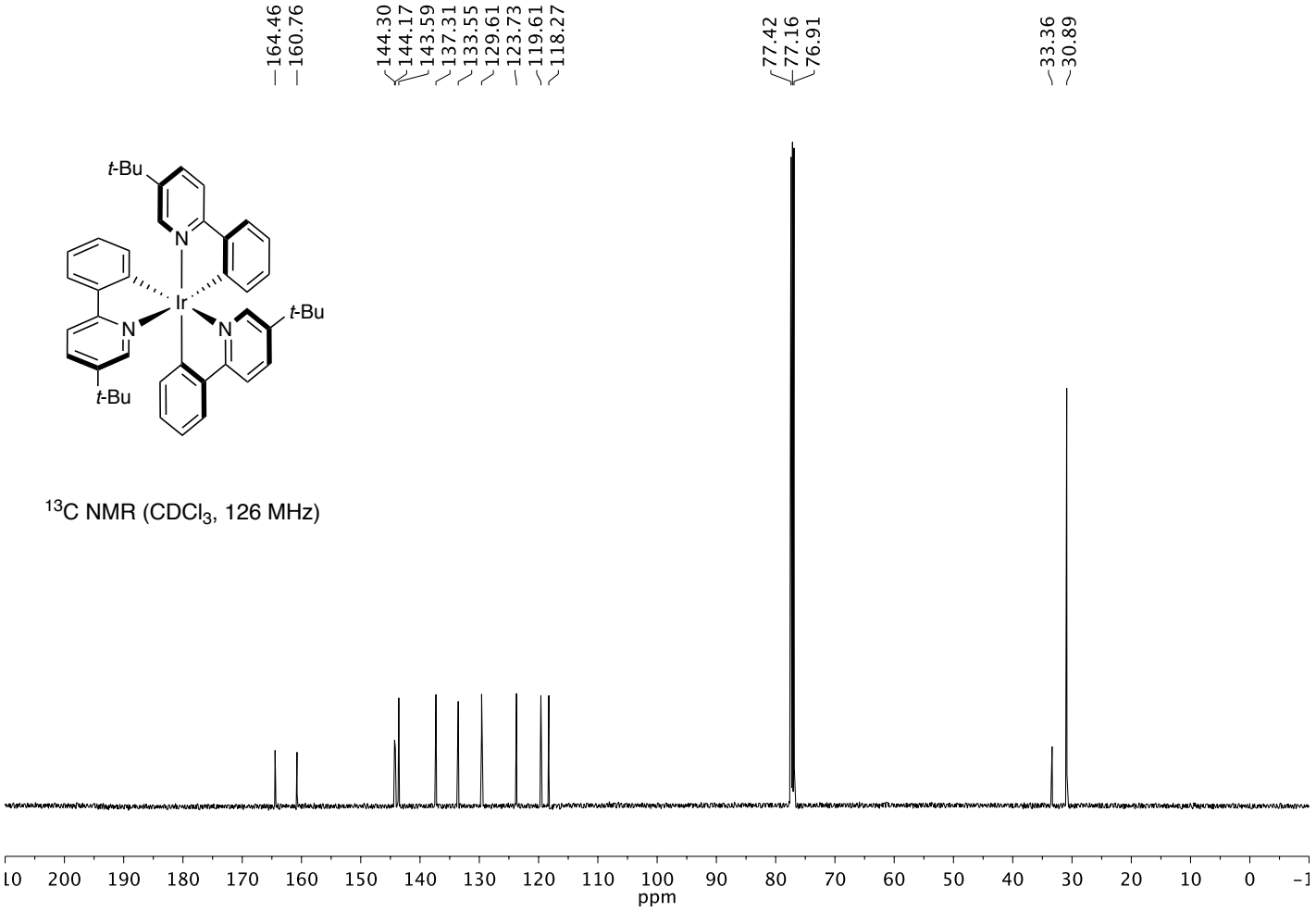
^{13}C NMR ($CDCl_3$, 126 MHz)


8.512
8.501
7.550
7.396
7.392
7.380
7.377
7.260
7.219
7.214
7.198
6.765
6.760
6.754
6.749
3.939
3.903
2.270
OMe
N
OMe
Me
1H NMR (CDCl3, 500 MHz)
1.00
1.00
1.02
1.95
1.01
3.13
3.11
3.11
ppm

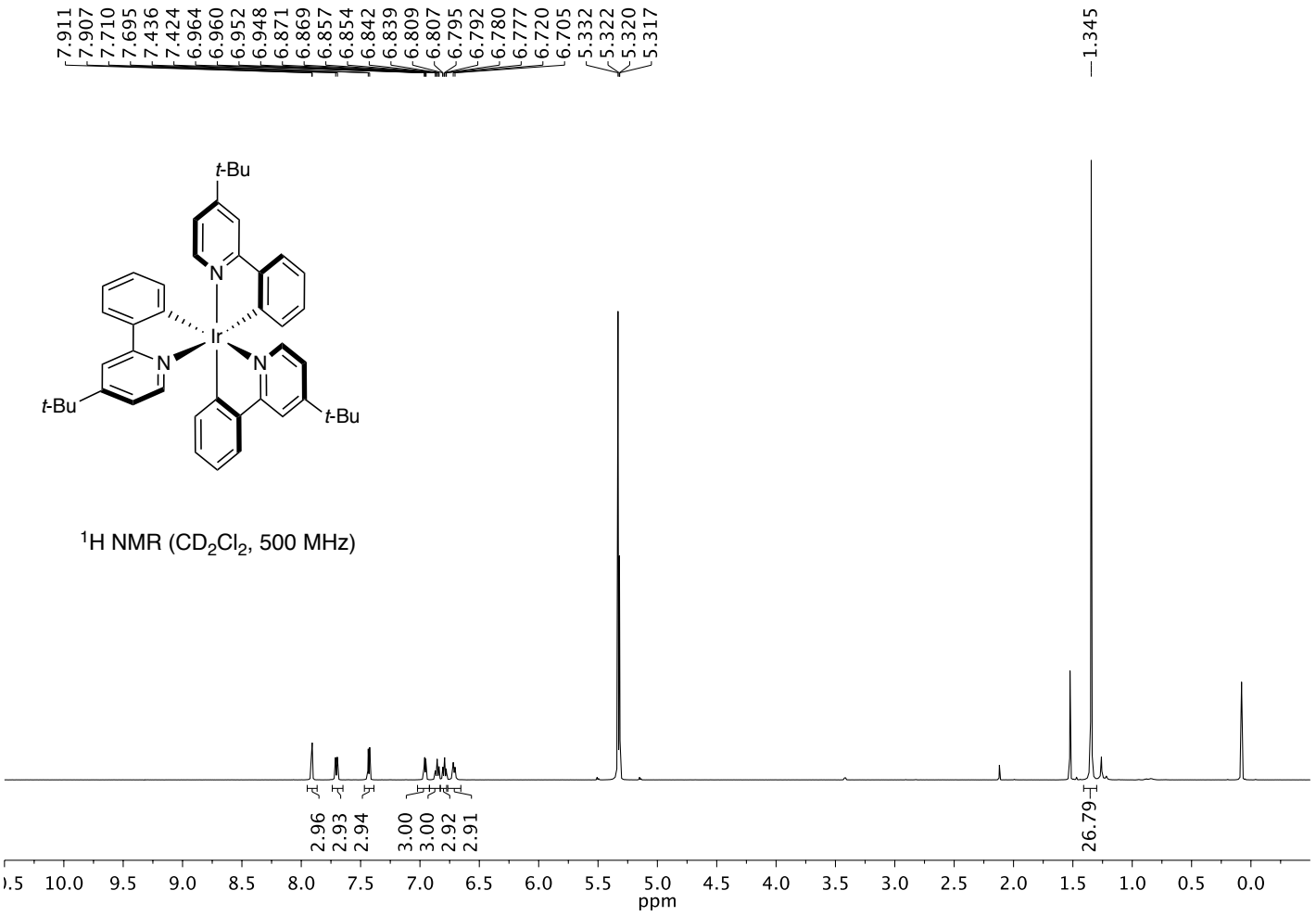

166.46
159.40
158.22
150.90
138.55
130.80
127.92
118.81
108.69
108.02
106.82
77.41
77.16
76.91
55.56
55.29
16.29
OMe
OMe
N
Me
13C NMR (CDCl3, 126 MHz)
ppm

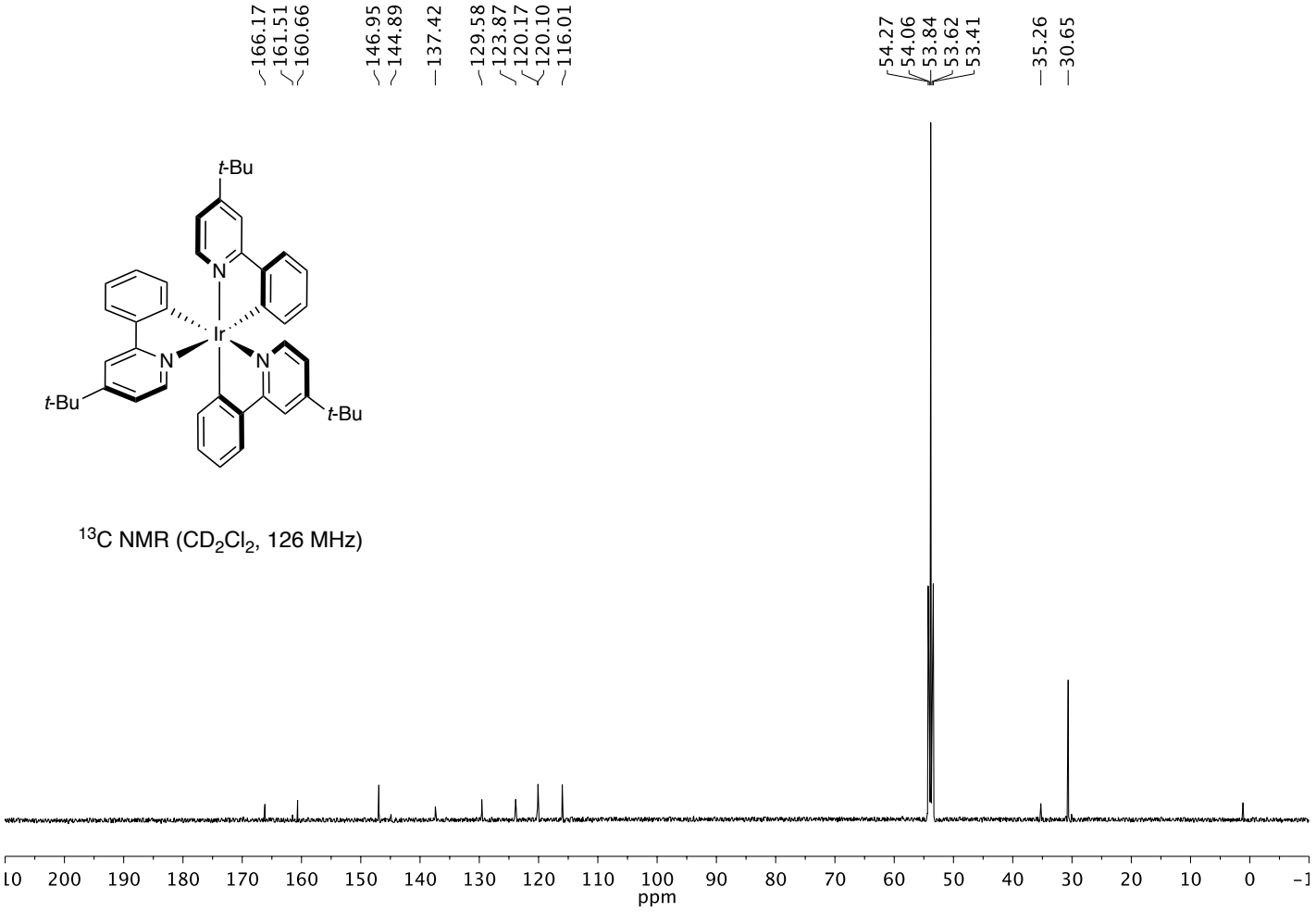


^{1}H NMR ($CDCl_3$, 500 MHz)

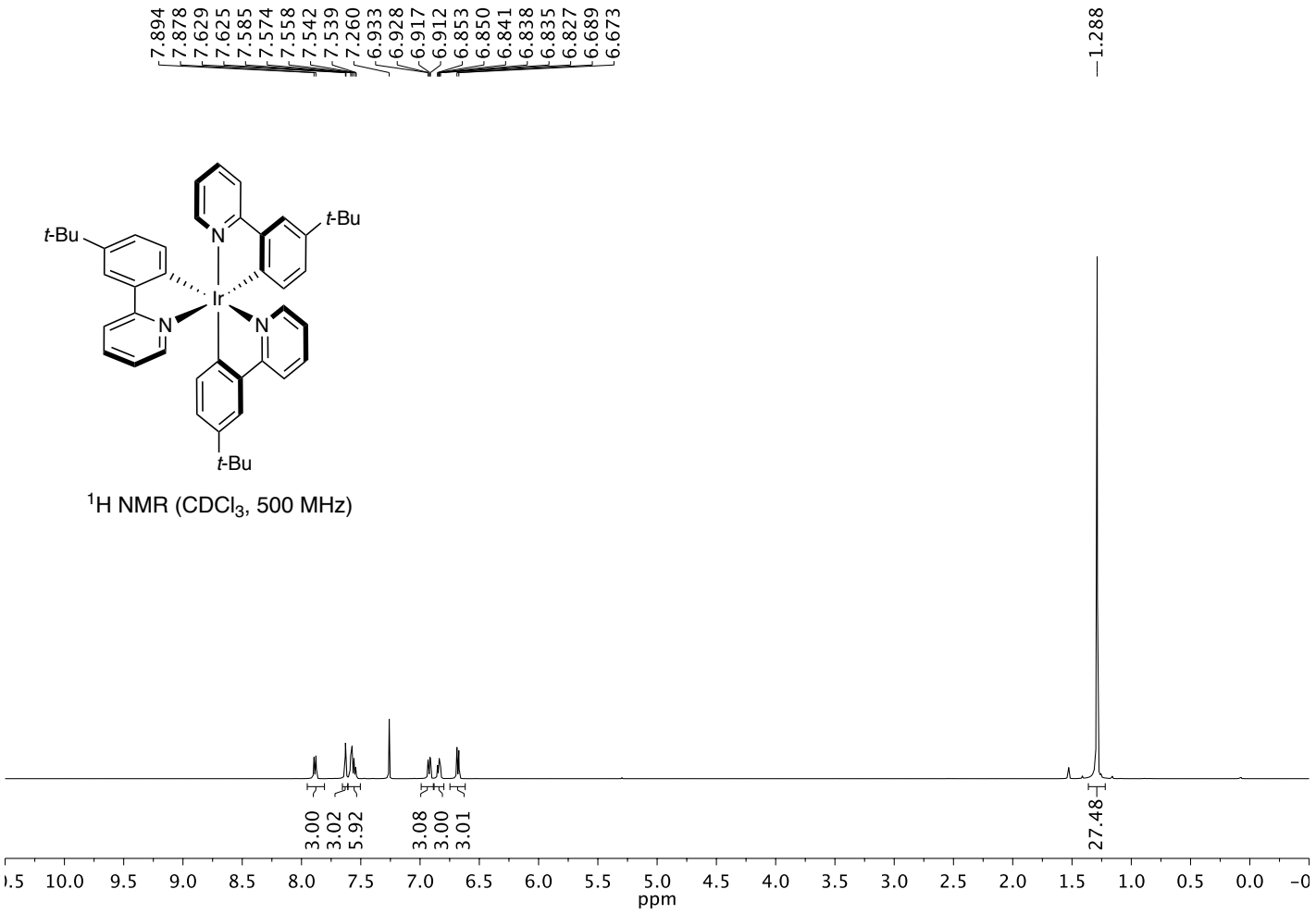


^{13}C NMR ($CDCl_3$, 126 MHz)

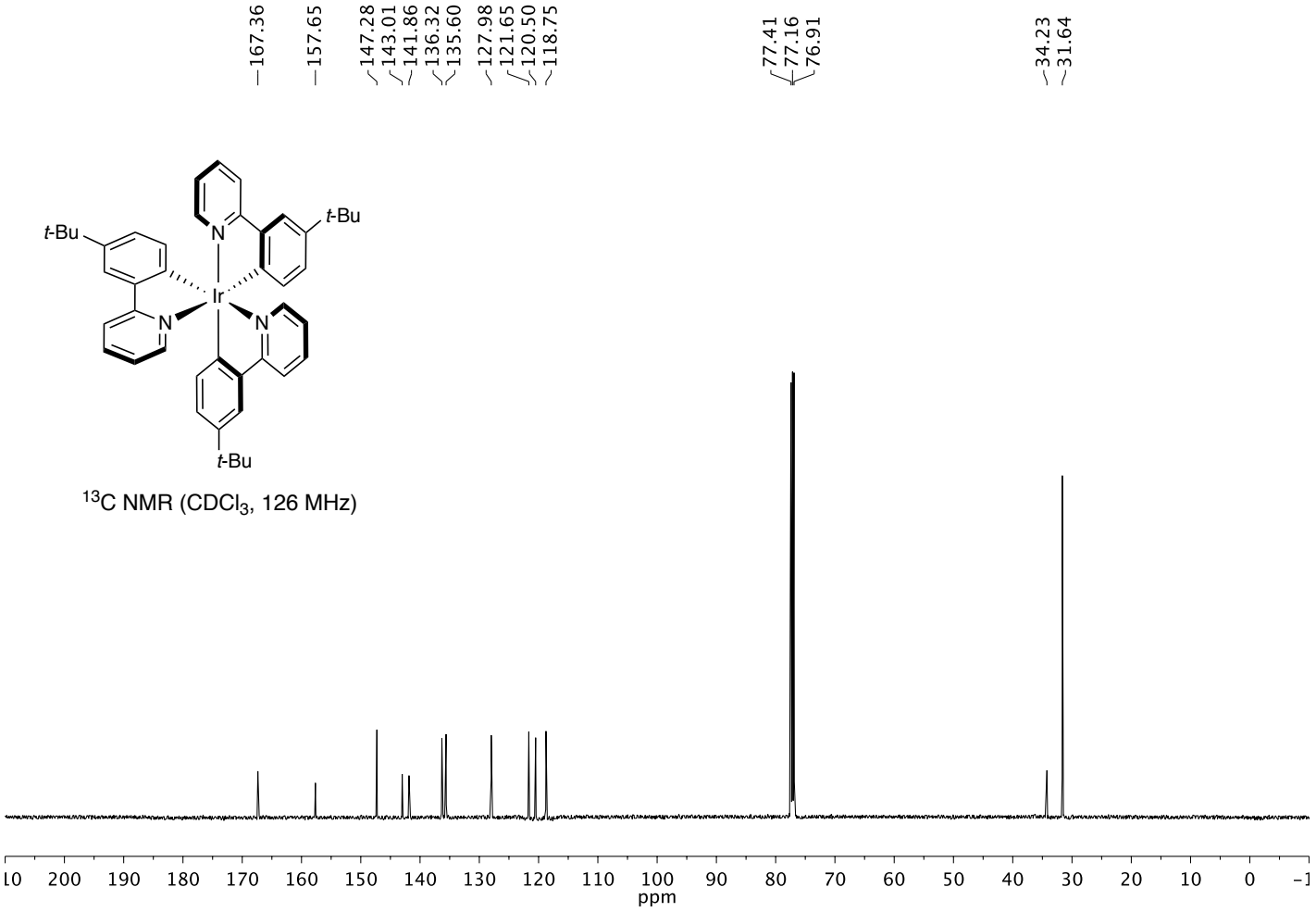

7.911
7.907
7.710
7.695
7.436
7.424
6.964
6.960
6.952
6.948
6.871
6.869
6.857
6.854
6.842
6.839
6.809
6.807
6.795
6.792
6.780
6.777
6.720
6.705
5.332
5.322
5.320
5.317
1.345
t-Bu
t-Bu
t-Bu
N
N
N
Ir
1H NMR (CD2Cl2, 500 MHz)
2.96
2.93
2.94
3.00
3.00
2.92
2.91
26.79
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm



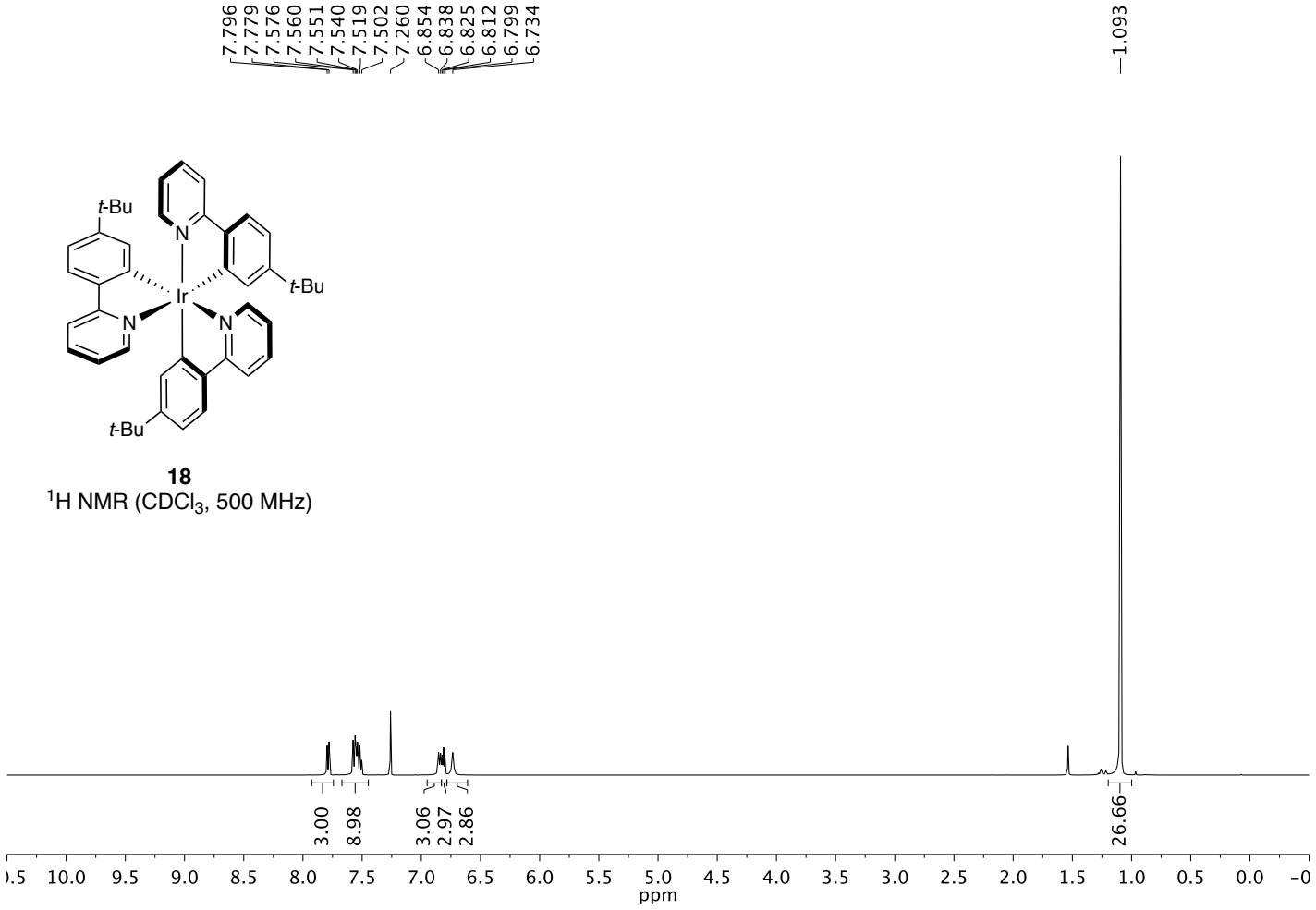
^{13}C NMR (CD_2Cl_2, 126 MHz)



^{1}H NMR ($CDCl_3$, 500 MHz)

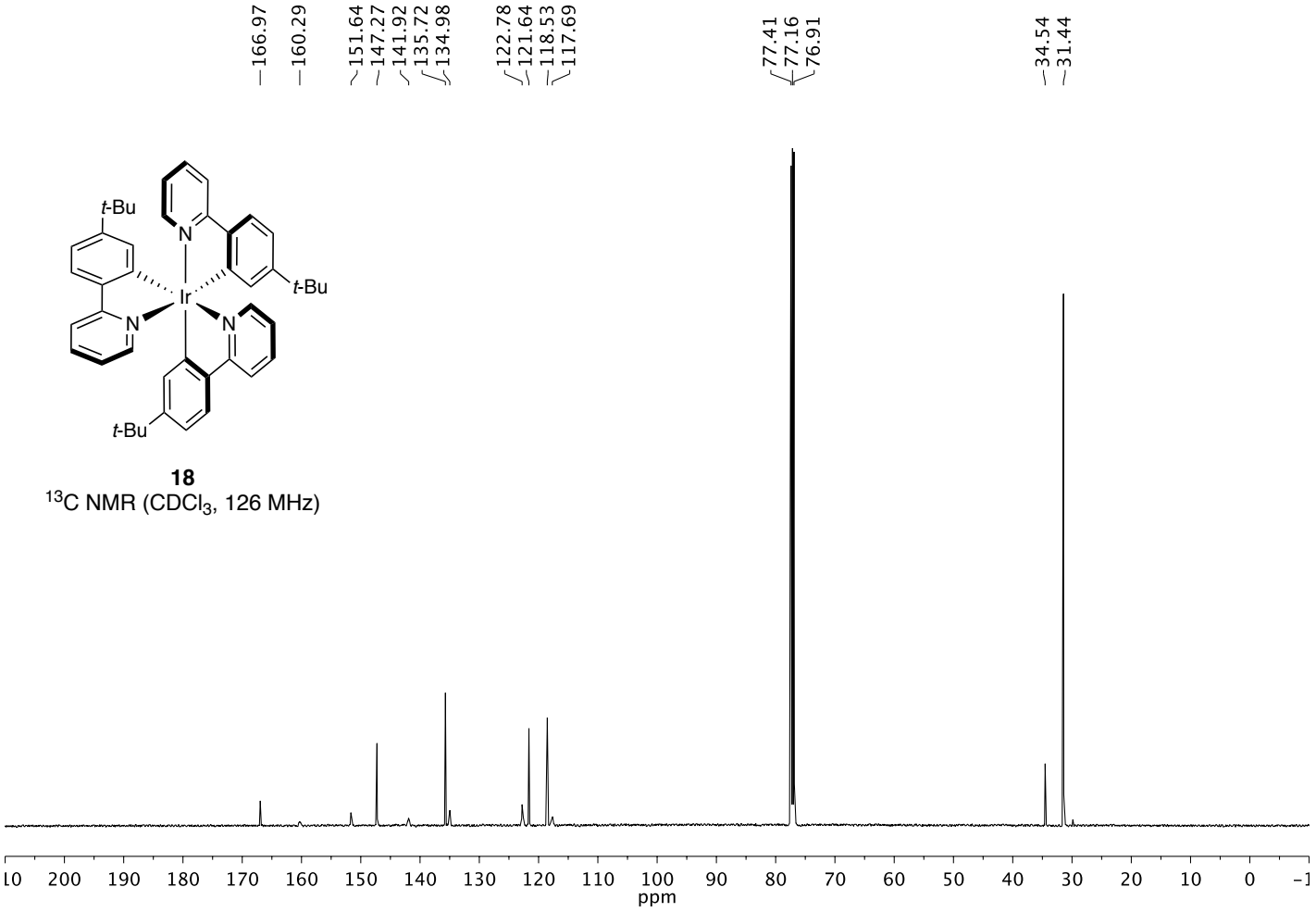


^{13}C NMR ($CDCl_3$, 126 MHz)



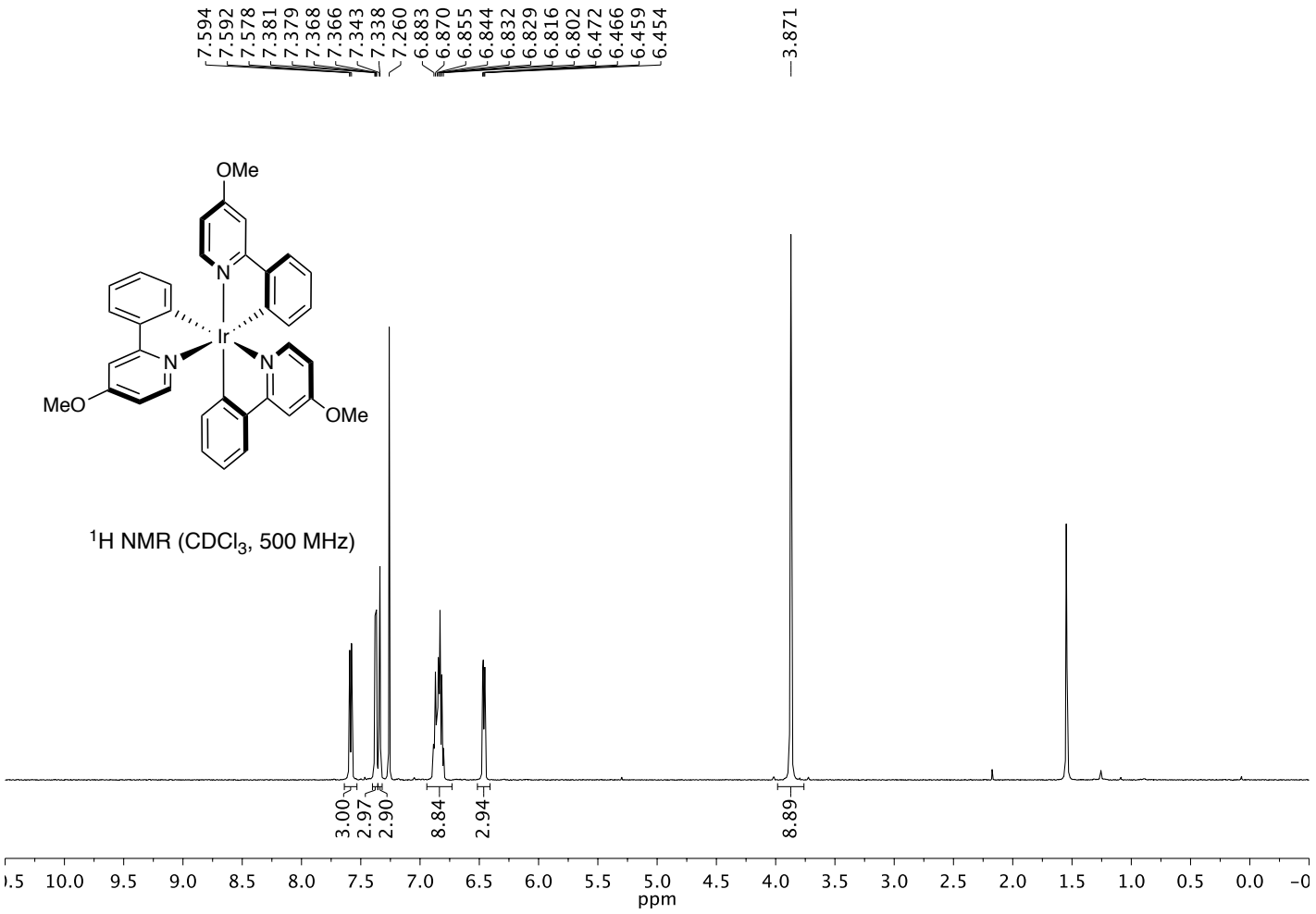
18

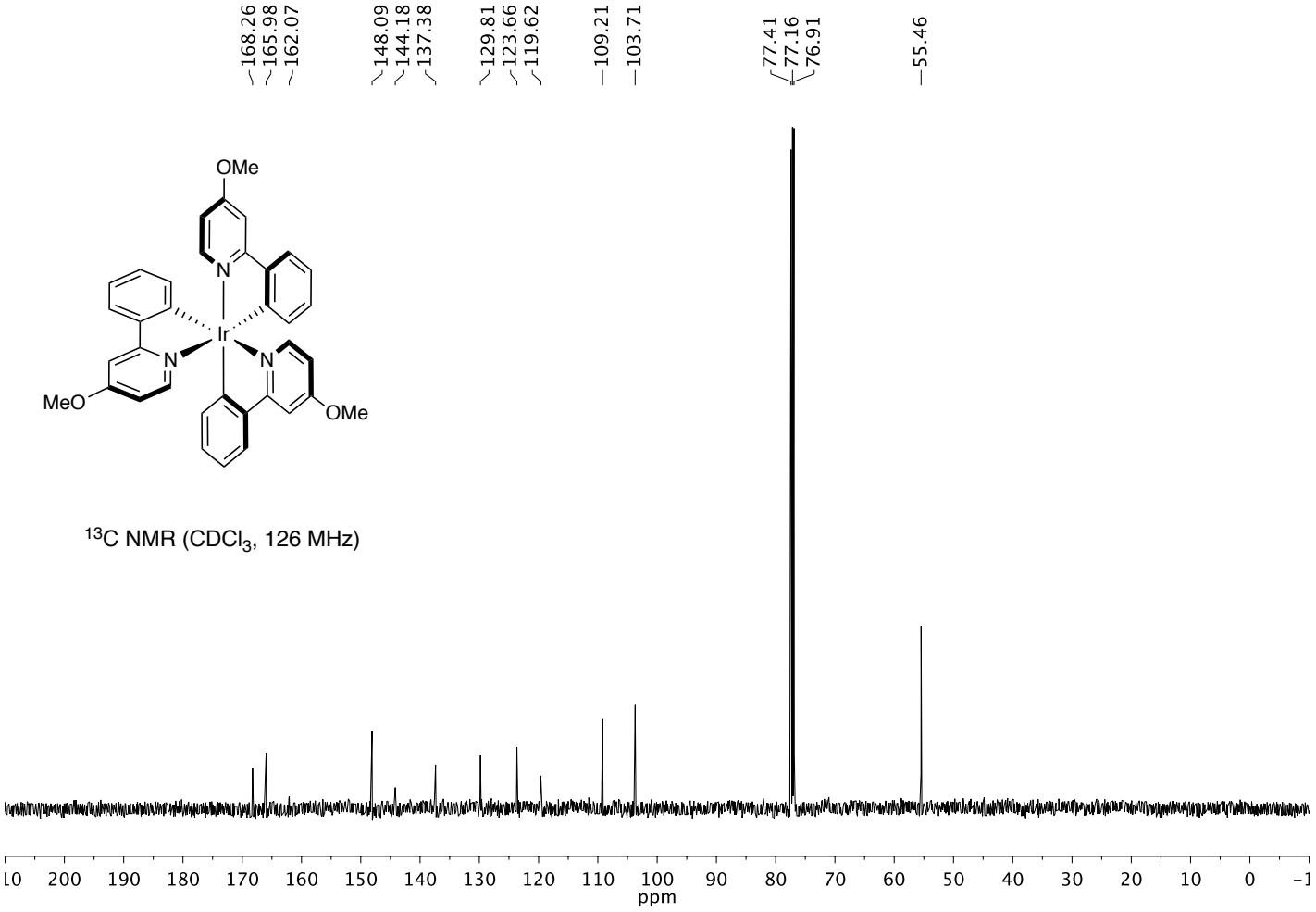
^{1}H NMR ($CDCl_3$, 500 MHz)



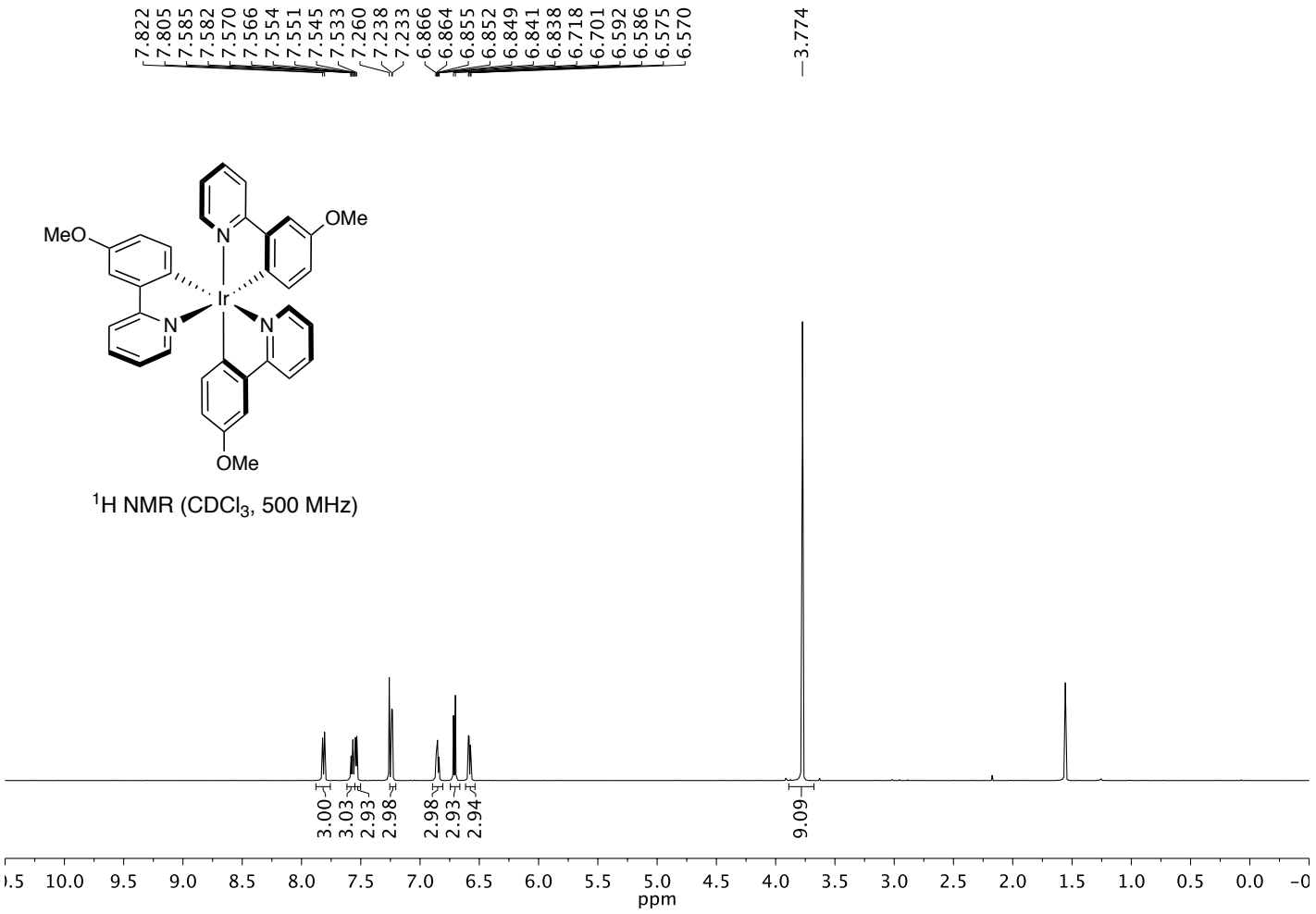
18

^{13}C NMR ($CDCl_3$, 126 MHz)

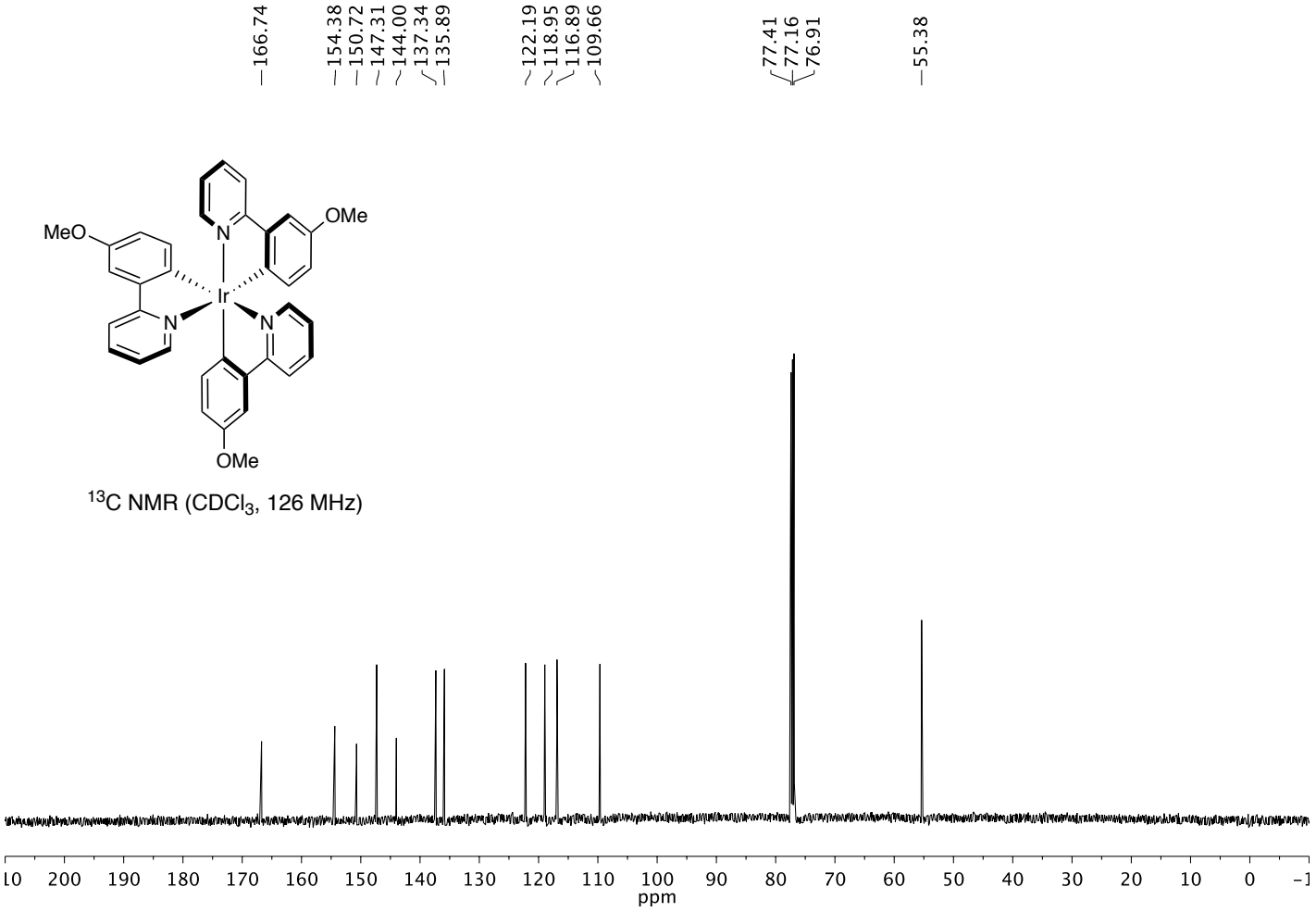

7.594
7.592
7.578
7.381
7.379
7.368
7.366
7.343
7.338
7.260
6.883
6.870
6.855
6.844
6.832
6.829
6.816
6.802
6.472
6.466
6.459
6.454
3.871
OMe
N
Ir
N
N
MeO
OMe
1H NMR (CDCl3, 500 MHz)
3.00
2.97
2.90
8.84
2.94
8.89
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm



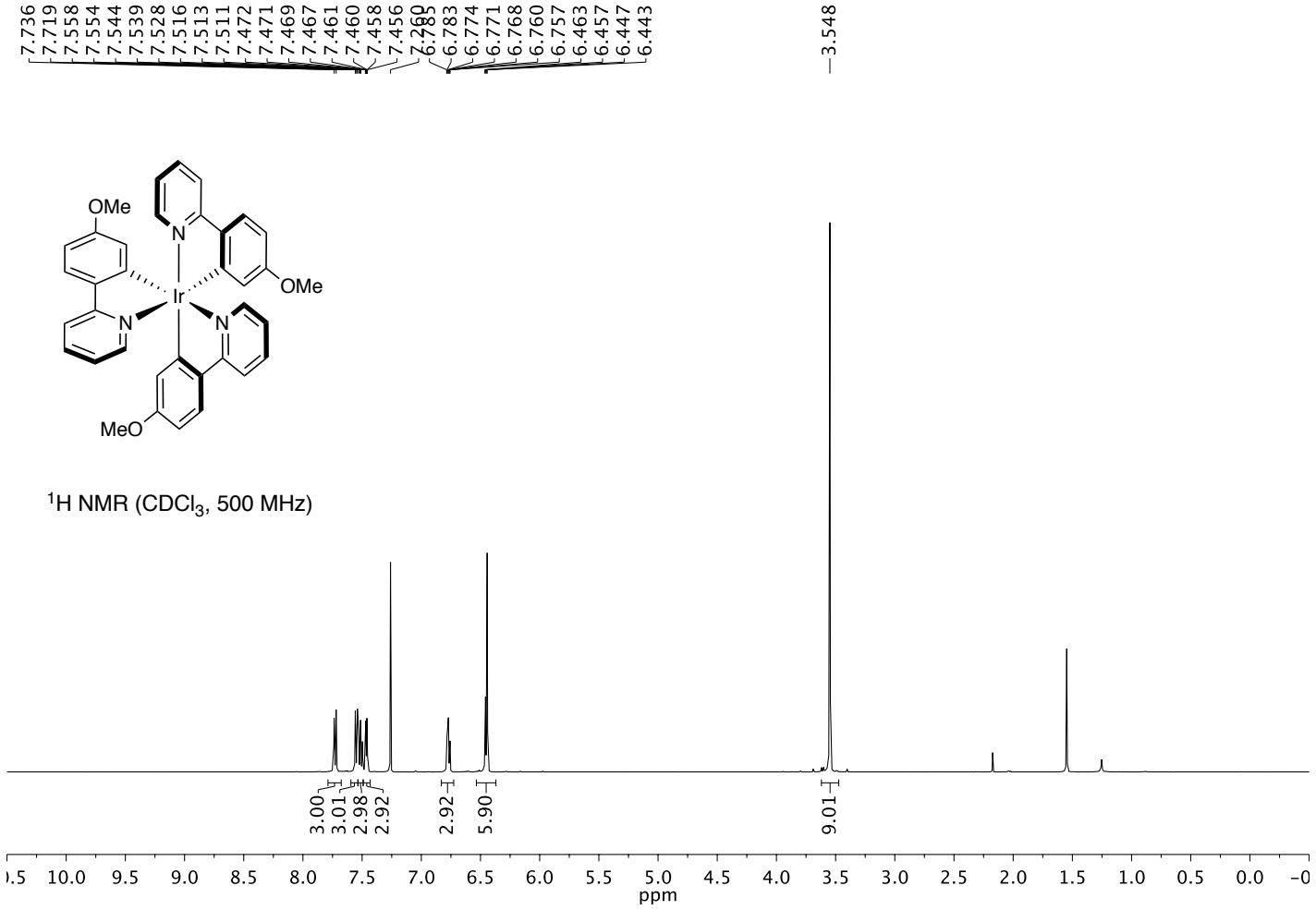
^{13}C NMR ($CDCl_3$, 126 MHz)

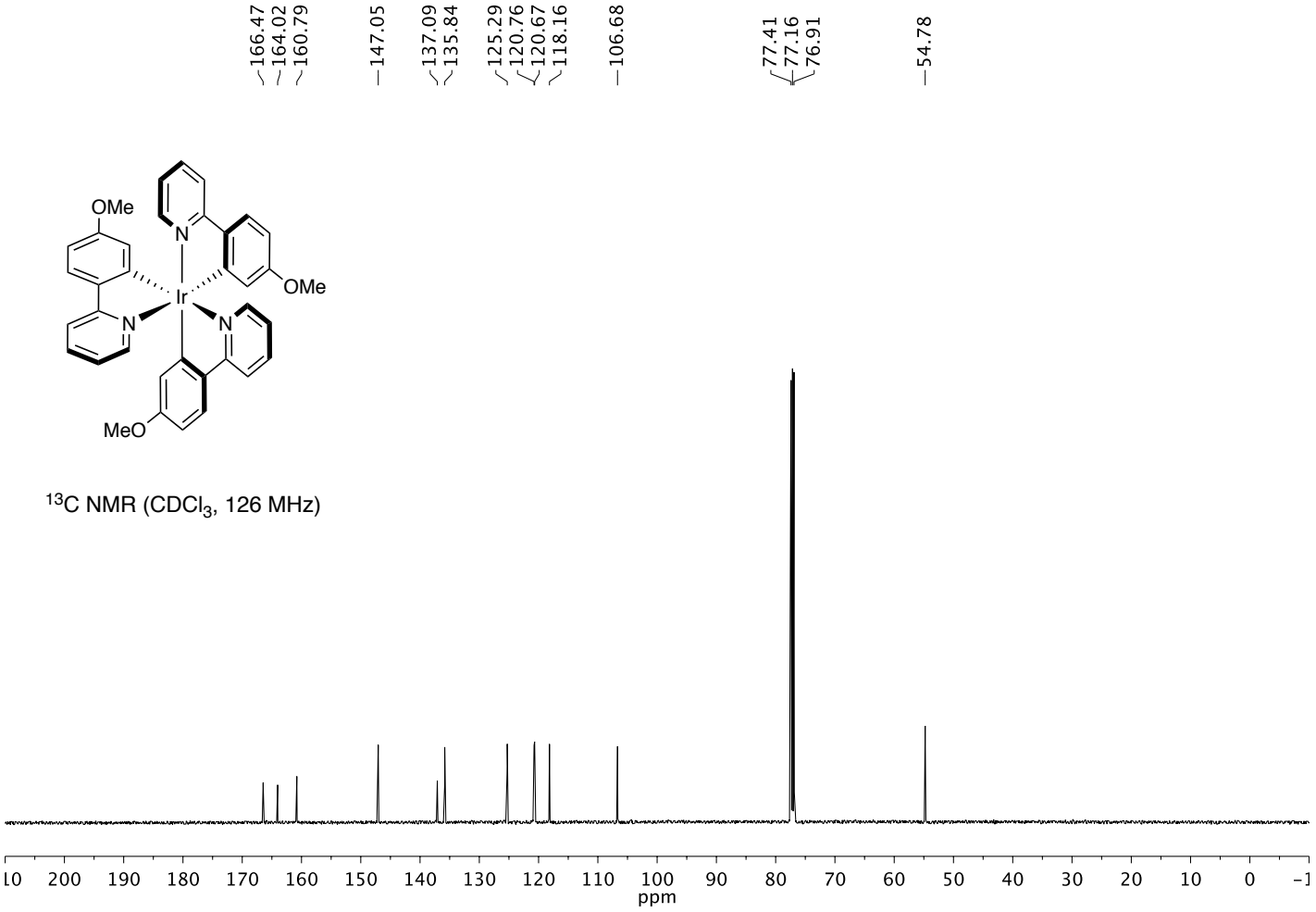


^{1}H NMR ($CDCl_3$, 500 MHz)

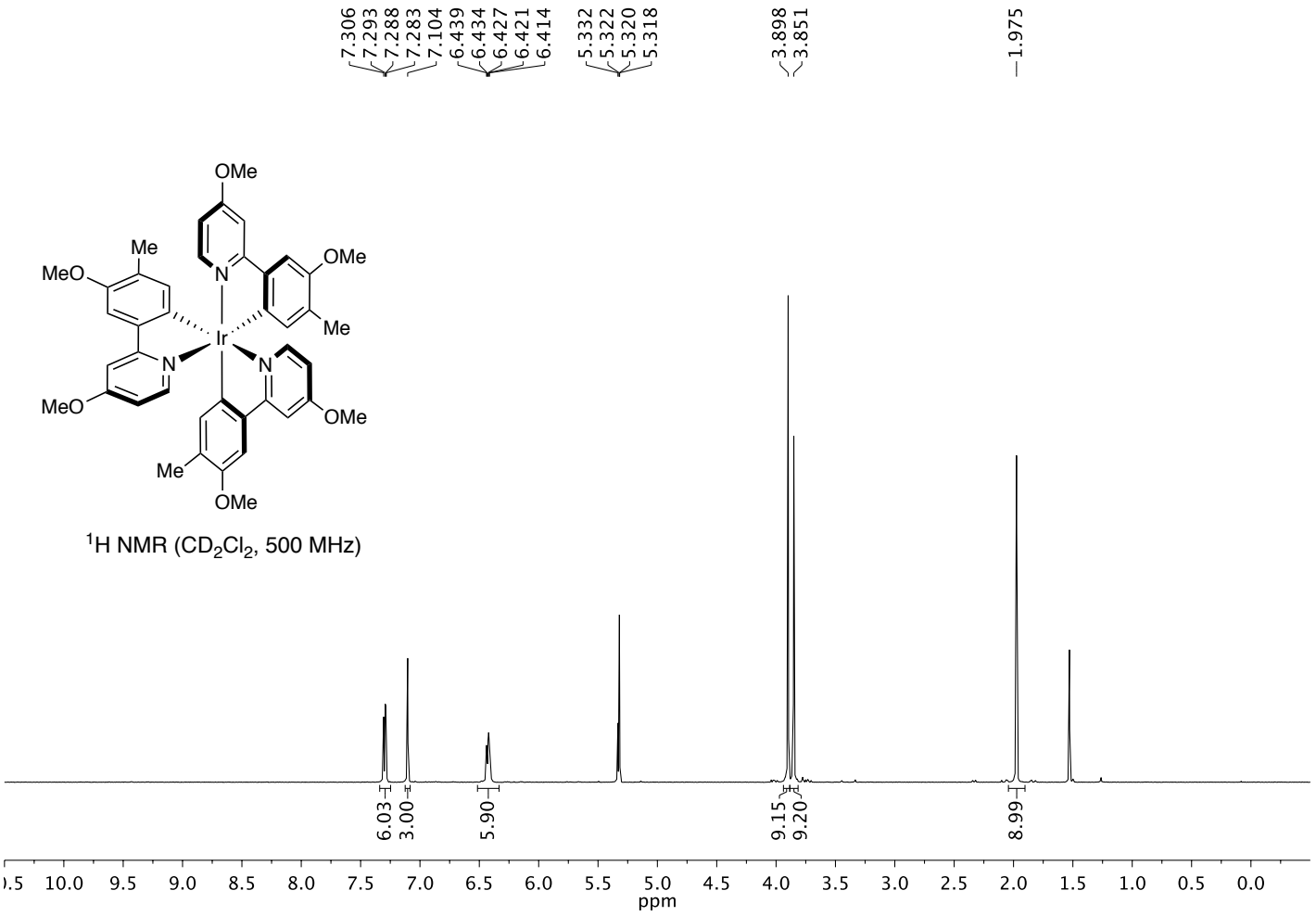


^{13}C NMR ($CDCl_3$, 126 MHz)

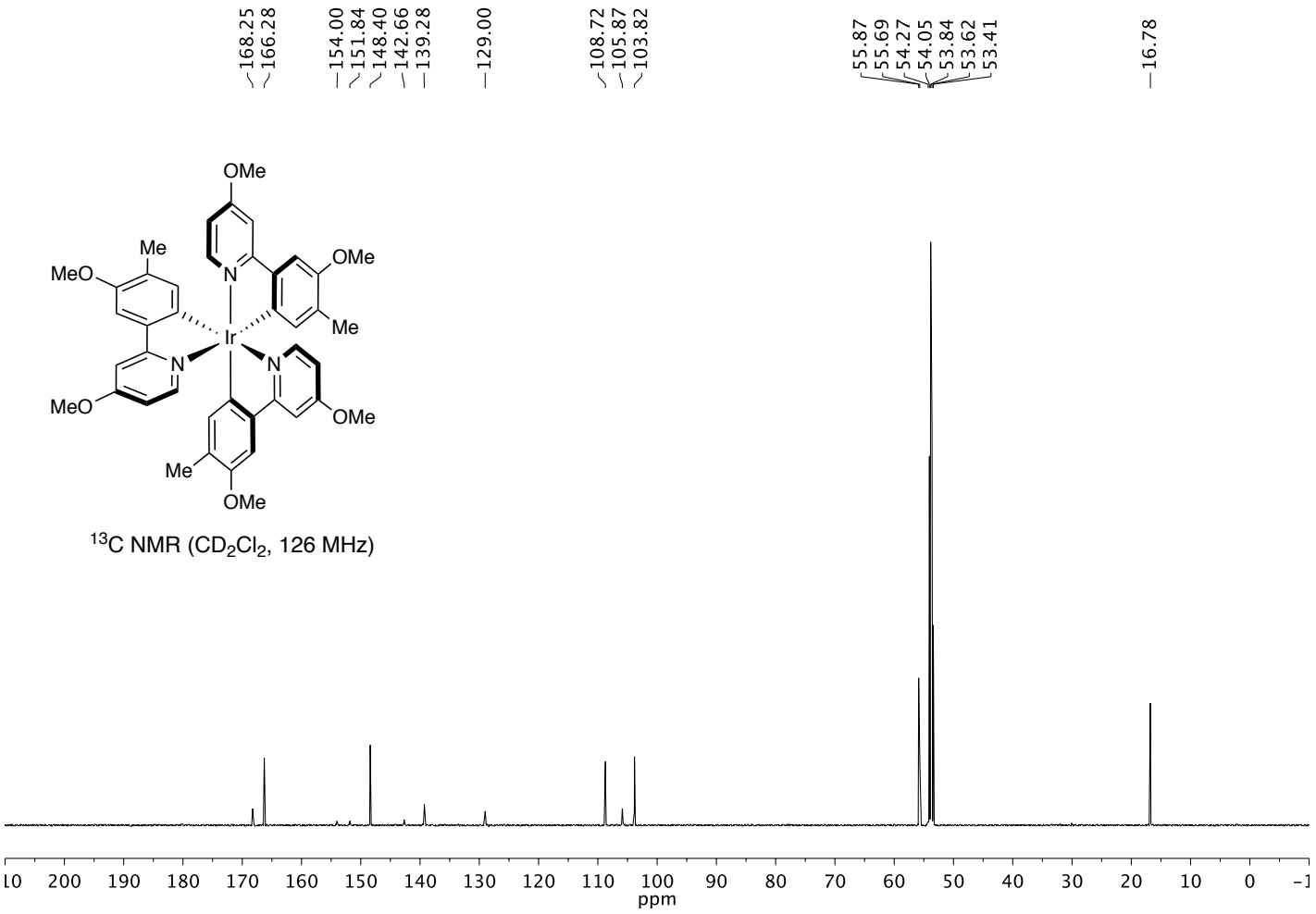

7.736
7.719
7.558
7.554
7.544
7.539
7.528
7.516
7.513
7.511
7.472
7.471
7.469
7.467
7.461
7.460
7.458
7.456
6.783
6.774
6.771
6.768
6.760
6.757
6.463
6.457
6.447
6.443
3.548
OMe
N
OMe
Ir
N
N
MeO
1H NMR (CDCl3, 500 MHz)
3.00
3.01
2.98
2.92
2.92
5.90
9.01
ppm



^{13}C NMR ($CDCl_3$, 126 MHz)



^{1}H NMR (CD_2Cl_2, 500 MHz)



^{13}C NMR (CD_2Cl_2, 126 MHz)