Regioselective Bromination of Fused Hetereocyclic *N*-Oxides

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Supporting Information

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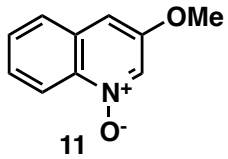
General Experimental

All reactions were either carried out under air (oxidation of azines) or in flame-dried glassware under an atmosphere of argon (bromination of azine *N*-oxides). All reagents

were purchased at the highest commercial quality and used without further purification, except for of *p*-toluenesulfonic anhydride (recrystallized from benzene/Et_2O) and tetrabutylammonium bromide (recrystallized from benzene/hexanes). Starting materials including 6-methoxyquinoline *N*-oxide, quinolone *N*-oxide, 8-methoxyisoquinoline *N*-oxide, and isoquinoline *N*-oxide were purchased from commercial sources and used without further purification. Yields refer to chromatographically and spectroscopically pure material (^{1}H NMR, ^{13}C NMR). Reactions were monitored by thin layer chromatography (TLC) carried out on 0.25 mm E. Merck silica plates (60F-254), using ultra violet light (UV) as the visualizing agent. Flash silica gel chromatography was performed using E. Merck silica gel (60, partical size 0.043-0.063 mm). Nuclear magnetic resonance spectra (NMR) were recorded on Bruker AV-400, DRX-500, and DRX-600 instruments and were calibrated using residual undeuterated solvent as an internal reference (^{1}H NMR: $CHCl_3$ 7.26 ppm, ^{13}C NMR: $CDCl_3$ 77.16) or an internal instrument calibration for ^{19}F. The following abbreviations were used to indicate multiplicities: *s* = singlet, *d* = doublet. High resolution mass spectra (HRMS) were recorded on an Agilent LC/MSD TOF mass spectrometer by electrospray ionization time of flight reflectron experiments. Infrared spectra (IR) were recorded on a Perkin Elmer Spectrum BX FTIR spectrometer. Melting points were recorded on a Fisher-Johns 12-144 melting point apparatus and are uncorrected.

General Procedure I: Oxidation of azines

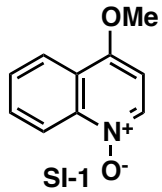
To a 0 °C solution of the appropriate azine in CH_2Cl_2 (0.5M) is added *m*CPBA (2.0 equiv) and the reaction is allowed to stir at room temperature overnight. The reaction mixture is diluted with CH_2Cl_2 and washed with aq. KOH (6N, 3x), the organic layer is dried over Na_2SO_4 and the solvent is evaporated under reduced pressure. The azine *N*-oxides are obtained as white solids and used without further purification unless stated otherwise.



11

3-Methoxyquinoline *N*-oxide (11)

Using 3-methoxyquinoline in accordance with General Procedure I, the title compound was obtained (76% yield) as an off-white solid. **Mp**: 55 °C (CH_2Cl_2); **IR** (neat): υ_{max} 2362, 2340, 1593, 1470, 1385, 1346, 1211, 1141, 1085, 671, 655 cm^{-1}; **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.67 – 8.57 (m, 1H), 8.37 (d, *J* = 2.2 Hz, 1H), 7.80 – 7.67 (m, 1H), 7.64 – 7.52 (m, 2H), 7.10 (d, *J* = 2.3 Hz, 1H), 3.95 (d, *J* = 1.3 Hz, 3H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 153.6, 137.8, 130.2, 129.8, 129.4, 127.8, 127.3, 119.8, 105.4, 56.2; **HRMS** (ESI-TOF) calcd for $C_9H_9NO_2H^+$ [$(M+H)^+$] 176.0706, found 176.0709.



SI-1

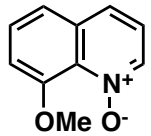
4-Methoxyquinoline *N*-oxide (SI-1)

Using 4-methoxyquinoline in accordance with General Procedure I, the title compound was obtained (41% yield) as a red solid. **Mp**: 39 °C; **IR** (neat): υ_{max} 2361, 2339, 2598, 1573, 1462, 1394, 1323, 1284, 1210, 1194, 11168, 1095, 968, 752 cm^{-1}; **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.64 (d, *J* = 8.8 Hz, 1H), 8.38 (d, *J* = 6.8 Hz, 1H), 8.12 (d, *J* = 8.5 Hz, 1H), 7.71 (ddd, *J* = 8.3, 6.8, 1.2 Hz, 1H), 7.55 (dd, *J* = 7.6, 7.6 Hz, 1H), 6.54 (d, *J* = 6.8 Hz, 1H), 3.96 (s, 3H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 154.8, 141.2, 136.3, 131.1, 128.4, 128.1, 122.7, 119.9, 99.6, 56.4; **HRMS** (ESI-TOF) calcd for $C_{10}H_9NO_2^+$ [$(M+H)^+$] 176.0706, found 176.0703.

SI-2

5-Methoxyquinoline *N*-oxide (SI-2)

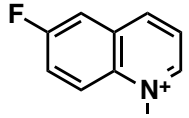
Using 5-methoxyquinoline in accordance with General Procedure I, the title compound was obtained (80% yield) as an off-white solid. **Mp**: 74–76 °C (CH_2Cl_2); $\mathbf{R_f}$ = 0.27 (CH_2Cl_2:MeOH 20:1); **IR** (neat): υ_{max} 2361, 2240, 1553, 1403, 1377, 1268, 1208, 1044, 779, 671 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.53 (d, *J* = 4.6 Hz, 1H), 8.30 (d, *J* = 8.8 Hz, 1H), 8.13 (d, *J* = 8.7 Hz, 1H), 7.66 (dd, *J* = 8.2, 8.2 Hz, 1H), 7.24 (m, 1H), 7.10 (dd, *J* = 7.8, 7.8 Hz, 1H), 4.12 (s, 3H) ppm; **^{13}C NMR** (151 MHz, $CDCl_3$) δ 155.7, 142.5, 136.4, 130.8, 123.4, 121.3, 119.9, 111.7, 106.6, 56.2; **HRMS** (ESI-TOF) calcd for $C_{10}H_9NO_2H^+$ [$(M+H)^+$] 176.0706, found 176.0711.



SI-3

8-Methoxyquinoline *N*-oxide (SI-3)

Using 8-methoxyquinoline in accordance with General Procedure I, the title compound was obtained (68% yield) as an off-white solid. **Mp**: 58 °C (CH_2Cl_2); **IR** (neat): υ_{max} 2361, 2340, 1571, 1461, 1388, 1284, 1265, 1082, 813, 727, 699, 539 cm^{-1}; **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.40 (dd, *J* = 6.1, 1.2 Hz, 1H), 7.60 (d, *J* = 8.4 Hz, 1H), 7.46 (dd, *J* = 8.0, 8.0 Hz, 1H), 7.37 (d, *J* = 8.2 Hz, 1H), 7.18 (dd, *J* = 8.3, 6.2 Hz, 1H), 7.06 (d, *J* = 7.9 Hz, 1H), 4.01 (s, 3H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 153.8, 138.2, 134.3, 133.8, 128.8, 125.6, 121.4, 120.6, 111.0, 57.2; **HRMS** (ESI-TOF) calcd for $C_{10}H_9NO_2H^+$ [$(M+H)^+$] 176.0706, found 176.0714.

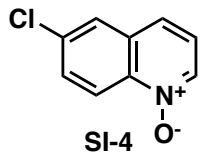


10

6-Fluoroquinoline *N*-oxide (10)

Using 6-fluoroquinoline in accordance with General Procedure I, the title compound was obtained (55% yield) as a white solid. **Mp**: 90 °C (CH_2Cl_2); $\mathbf{R_f}$ = 0.22 (CH_2Cl_2:MeOH 20:1);

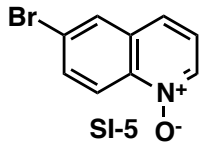
IR (neat): υ_{max} 2361, 2340, 1629, 1572, 1512, 1381, 1238, 1265, 1199, 1176, 850, 788, 731, 453 cm^{-1}; **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.77 (dd, *J* = 9.3, 5.2 Hz, 1H), 8.48 (d, *J* = 6.0 Hz, 1H), 7.67 (d, *J* = 8.5 Hz, 1H), 7.53 – 7.47 (m, 2H), 7.32 (dd, *J* = 8.2, 6.5 Hz, 1H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 161.9, 138.9, 135.1, 131.8, 125.2, 123.1, 122.4, 120.5, 111.6 ; ^{19}F NMR (376 MHz, $CDCl_3$) δ -110.6. **HRMS** (ESI-TOF) calcd for $C_9H_6FNOH^+$ [$(M+H)^+$] 164.0506, found 164.0508.



SI-4

6-Chloroquinoline *N*-oxide (SI-4)

Using 6-chloroquinoline in accordance with General Procedure I, the title compound was obtained (93% yield) as a white solid. **Mp**: 108 °C (CH_2Cl_2); **R_f** = 0.25 (CH_2Cl_2:MeOH 20:1); **IR** (neat): υ_{max} 2360, 2340, 1561, 1503, 1441, 1424, 1359, 1301, 1264, 1222, 1175, 1141, 1095, 1073, 829, 791, 733, 579 cm^{-1}; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.71 (d, *J* = 9.3 Hz, 1H), 8.50 (d, *J* = 6.2 Hz, 1H), 7.87 (d, *J* = 2.2 Hz, 1H), 7.69 (dd, *J* = 9.3, 2.2 Hz, 1H), 7.65 (d, *J* = 8.5 Hz, 1H), 7.33 (dd, *J* = 8.5, 6.0 Hz, 1H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 140.3, 135.8, 135.2, 131.4, 131.3, 126.9, 124.8, 122.4, 121.9; **HRMS** (ESI-TOF) calcd for $C_9H_6ClNOH^+$ [$(M+H)^+$] 180.0211, found 180.0209.

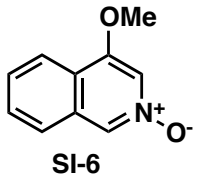


SI-5

6-Bromoquinoline *N*-oxide (SI-5)

Using 6-bromoquinoline in accordance with General Procedure I, the title compound was obtained (94% yield) as a white solid. **Mp**: 110 °C (CH_2Cl_2); **R_f** = 0.22 (CH_2Cl_2:MeOH 20:1); **IR** (neat): υ_{max} 2360, 2338, 1565, 1501, 1422, 1357, 1299, 1264, 1223, 1173, 1141, 1065, 822, 792, 729, 700 cm^{-1}; **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.63 (d, *J* = 9.3 Hz, 1H), 8.52 (dd, *J* = 6.2, 1.1 Hz, 1H), 8.04 (s, 1H), 7.83 (dd, *J* = 9.3, 1.9 Hz, 1H), 7.64 (d, *J* = 8.5 Hz, 1H),

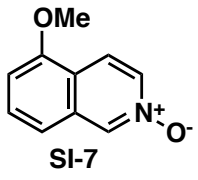
7.33 (dd, *J* = 8.4, 6.1 Hz, 1H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 140.6, 135.9, 133.9, 131.8, 130.3, 124.7, 123.4, 122.4, 121.9; **HRMS** (ESI-TOF) calcd for $C_9H_6BrNOH^+$ [$(M+H)^+$] 223.9711, found 223.9699.



SI-6

4-Methoxyisoquinoline *N*-oxide (SI-6)

Using 4-methoxyisoquinoline in accordance with General Procedure I, the title compound was obtained (76% yield) as a white solid. **Mp**: 176 °C (CH_2Cl_2); $\mathbf{R_f}$ = 0.19 (CH_2Cl_2:MeOH 20:1); **IR** (neat): υ_{max} 2360, 2340, 1395, 1339, 1171, 1138, 1089, 978, 864, 771, 669, 656 cm^{-1}; **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.45 (d, *J* = 1.5 Hz, 1H), 8.08 (d, *J* = 7.9 Hz, 1H), 7.76 (d, *J* = 1.4 Hz, 1H), 7.66 (d, *J* = 8.1 Hz, 1H), 7.61 (ddd, *J* = 8.2, 6.9, 1.2 Hz, 1H), 7.56 (ddd, *J* = 8.2, 6.8, 1.3 Hz, 1H), 4.01 (s, 3H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 153.7, 130.1, 130.0, 128.4, 124.8, 123.1, 121.8, 119.4, 56.7; **HRMS** (ESI-TOF) calcd for $C_{10}H_9NO_2H^+$ [$(M+H)^+$] 176.0706, found 176.0710.

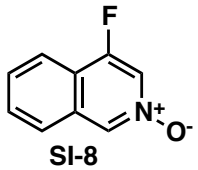


SI-7

5-Methoxyisoquinoline *N*-oxide (SI-7)

Using 5-methoxyisoquinoline in accordance with General Procedure I, the title compound was obtained (93% yield) as a white solid. **Mp**: 148 °C (CH_2Cl_2); $\mathbf{R_f}$ = 0.22 (CH_2Cl_2:MeOH 20:1); **IR** (neat): υ_{max} 2359, 2340, 1628, 1596, 1468, 1440, 1389, 1323, 1273, 1250, 1206, 1193, 1157, 1103, 994, 960, 782, 730 cm^{-1}; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.70 (d, *J* = 1.3 Hz, 1H), 8.10 (dd, *J* = 7.3, 1.7 Hz, 1H), 8.04 (d, *J* = 7.2 Hz, 1H), 7.52 (t, *J* = 8.1 Hz, 1H), 7.27 (d, *J* = 8.3 Hz, 1H), 6.91 (d, *J* = 7.8 Hz, 1H), 4.01 (s, 3H); **^{13}C NMR** (151

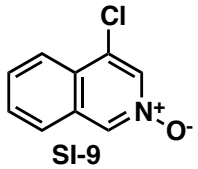
MHz, $CDCl_3$) δ 154.9, 136.1, 135.8, 130.8, 130.4, 121.1, 119.5, 116.9, 116.9, 107.1, 55.9; **HRMS** (ESI-TOF) calcd for $C_{10}H_9NO_2H^+$ [$(M+H)^+$] 176.0706, found 176.0710.



SI-8

4-Fluoroisoquinoline *N*-oxide (SI-8)

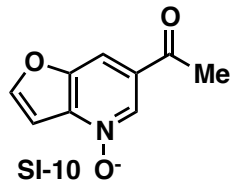
Using 4-fluoroisoquinoline in accordance with General Procedure I, the title compound was obtained (88% yield) as a white solid. **Mp**: 164 °C (CH_2Cl_2); $\mathbf{R_f}$ = 0.22 (CH_2Cl_2:MeOH 20:1); **IR** (neat): υ_{max} 2361, 2340, 1601, 1402, 1331, 1156, 1126, 1081, 773 cm^{-1}; **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.62 (s, 1H), 8.11 (dd, *J* = 5.3, 1.5 Hz, 1H), 7.99 (d, *J* = 8.1 Hz, 1H), 7.74 (d, *J* = 8.1 Hz, 1H), 7.68 (dd, *J* = 7.6, 7.6 Hz, 1H), 7.65 (dd, *J* = 7.5, 7.5 Hz, 1H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 156.7, 133.3, 130.9, 129.6, 129.3, 124.9, 124.8, 121.0, 120.4; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -132.91; **HRMS** (ESI-TOF) calcd for C9H6FNOH$^+$ [$(M+H)^+$] 164.0506, found 164.0503.



SI-9

4-Chloroisoquinoline *N*-oxide (SI-9)

Using 4-chloroisoquinoline in accordance with General Procedure I, the title compound was obtained (88% yield) as a white solid. **Mp**: 174 °C (CH_2Cl_2); $\mathbf{R_f}$ = 0.22 (CH_2Cl_2:MeOH 20:1); **IR** (neat): υ_{max} 2361, 2341, 1621, 1590, 1555, 1487, 1373, 1327, 1225, 1175, 1129, 951, 762, 741, 644 cm^{-1}; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.69 (s, 1H), 8.29 (d, *J* = 1.7 Hz, 1H), 8.19 – 8.09 (m, 1H), 7.78 – 7.64 (m, 3H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 136.0, 135.3, 130.9, 130.6, 129.9, 129.5, 127.4, 125.4, 123.9; **HRMS** (ESI-TOF) calcd for C9H6ClNOH$^+$ [$(M+H)^+$] 180.0211, found 180.0215.



SI-10

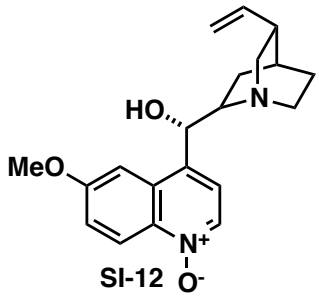
6-Acetylfuro[3,2-b]pyridine 4-oxide (SI-10)

Using 1-(furo[3,2-b]pyridin-6-yl)ethanone in accordance with General Procedure I, the title compound was obtained (99% yield) as an off-white solid. **Mp**: 182 °C (CH_2Cl_2); **IR** (neat): υ_{max} 2361, 2340, 1692, 1613, 1511, 1395, 1370, 1351, 1323, 1220, 1072, 878, 780, 616 cm^{-1}; **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.78 (s, 1H), 7.99 (s, 1H), 7.91 (d, *J* = 2.3 Hz, 1H), 7.28 (d, *J* = 2.1 Hz, 1H), 2.64 (s, 3H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 193.6, 150.9, 150.4, 141.1, 135.5, 130.9, 110.3, 103.3, 27.1; **HRMS** (ESI-TOF) calcd for $C_9H_7NO_3H^+$ [$(M+H)^+$] 178.0499, found 178.0506.

SI-11

***N1*-1,10-phenanthrolein-*N*-oxide (SI-11)**

Using 1,10-phenanthrolein, the title compound was prepared according to a literature procedure[1]. Spectroscopic data was identical to that previously reported.[2]



SI-12

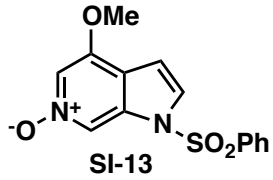
Quinine *N*-oxide (SI-12)

Using quinine, **SI-12** was prepared in accordance with a literature procedure[3], and the title compound was obtained (78 % yield) as an off-white solid. **Mp**: 103-107 °C (CH_2Cl_2); **IR** (neat): υ_{max} cm^{-1} 3075, 2921, 1615, 1570, 1430, 1250, 1194, 1165, 1021, 825; **^{1}H NMR**

(400 MHz, $CDCl_3$) δ 8.43 (d, *J* = 9.5 Hz, 1H), 7.88 (d, *J* = 6.3 Hz, 1H), 7.22 - 7.10 (m, 2H), 6.93 (d, *J* = 2.6 Hz, 1H), 5.74 (ddd, *J* = 17.5, 10.3, 7.5 Hz, 1H), 5.03 - 4.79 (m, 2H), 3.87 (s, 3H), 3.08 (dd, *J* = 13.6, 10.1 Hz, 1H), 2.99 - 2.82 (m, 1H), 2.68-2.59 (m, 2H), 2.29 (s, 1H), 1.88 - 1.71 (m, 4H), 1.67 - 1.56 (m, 1H), 1.54-1.46 (m, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 159.8, 142.4, 136.1, 136.0, 134.5, 129.4, 123.6, 121.9, 119.3, 115.4, 102.6, 71.5, 61.1, 57.6, 56.8, 43.9, 40.6, 28.6, 28.2, 22.9; **HRMS** (ESI-TOF) calcd for $C_{20}H_{24}N_2O_3H^+$ [$(M+H)^+$] 341.1860, found 341.1864

General Procedure II: Protection and oxidation of azaindoles

To a mixture of the appropriate azaindole and K_2CO_3 (1.5 equiv) in MeCN (10 mL/g) was added benzenesulfonyl chloride (0.95 equiv.) drop-wise while maintaining the internal temperature below 25 °C. After the addition, the heterogeneous mixture was further agitated at room temperature until the *N*1- protection reached completion (about 1 hour). The crude reaction mixture was concentrated under reduced pressure. Ethyl acetate (10 mL/g) was added, followed by water (20 mL/g). The layers were separated, and the organic layer was dried over sodium sulfate, filtered and concentrated under reduced pressure. The crude solid was subjected to the oxidation step without further purification. The crude solid was dissolved in DCM (25 mL/g). To the solution was added aqueous hydrogen peroxide (35 wt%, 2.0 equiv) and MTO (2 mol%). The resulting mixture was further stirred at room temperature until *N*-oxide formation was complete (6 to 12 hours). Excess of hydrogen peroxide was quenched by slow addition of sat. $NaHSO_3$ solution (5 mL/g). The crude mixture was agitated for 30 minutes before layers were separated. The aqueous layer was tested for residue peroxide before discarded. The organic layer was dried over sodium sulfate, filtered and swapped into methyl *t*-butyl ether (20 mL/g). The resulting white slurry was filtered, and the cake was dried in vacuum oven to provide *N*1-benzenesulfonyl-azaindole *N*-oxides without further purification.



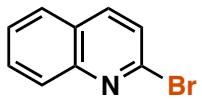
SI-13

***N*1-benzenesulfonyl-4-methoxy-6-azainole *N*6-oxide (SI-13)**

Using *N*1-benzenesulfonyl-4-methoxy-6-azainole in accordance with General Procedure II, the title compound was obtained (83% yield) as an off-white solid. **Mp**: 145 °C (CH_2Cl_2); **IR** (neat): υ_{max} 1578, 1491, 1445, 1424, 1188, 1158, 1116, 1088, 1067, 980, 840, 725, 685, 628 cm^{-1}; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.82 – 8.65 (m, 1H), 7.97 – 7.84 (m, 2H), 7.78 (s, 1H), 7.66 – 7.59 (m, 1H), 7.58 (dd, *J* = 3.6, 0.9 Hz, 1H), 7.55 – 7.48 (m, 2H), 6.73 (d, *J* = 3.6 Hz, 1H), 3.90 (s, 3H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 150.2, 137.4, 134.9, 132.0, 129.9, 128.4, 127.2, 120.9, 120.4, 119.9, 105.9, 56.7; **HRMS** (ESI-TOF) calcd for $C_{14}H_{12}N_2O_4SH^+$ [$(M+H)^+$] 305.0517, found 305.0595.

General Procedure III: Bromination of azine *N*-oxides

To a mixture of tetrabutylammonium bromide (1.5 equiv), 4 Å molecular sieves and the appropriate azine *N*-oxide is added CH_2Cl_2 (0.01M) and the mixture is stirred at room temperature for 10 min. *p*-Toluenesulfonic anhydride (1.5 equiv) is added and the reaction is stirred at room temperature overnight. The reaction mixture is filtrated and concentrated under reduced pressure. The crude product is purified by flash column chromatography using hexanes/CH_2Cl_2 and hexanes/EtOAc solvent mixtures.

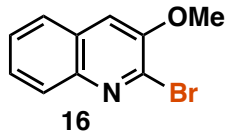


15

2-Bromoquinoline (15)

Using quinoline *N*-oxide, in accordance with General Procedure III, the title compound was obtained (35% yield) as a white solid. The spectroscopic data were consistent with those of a commercial sample. **^{1}H NMR** (150 MHz, $CDCl_3$) δ 8.02 (d, *J*=9.0 Hz, 1H), 7.97 (d, *J*=8.4 Hz, 1H), 7.79 (d, *J*= 7.8 Hz, 1H), 7.73–7.71 (m, 1H), 7.57–7.55 (m, 1H), 7.50 (d,

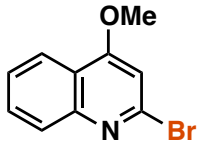
J=8.4 Hz, 1H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 148.7, 141.9, 138.5, 130.7, 127.8, 127.1, 125.9;



16

2-Bromo-3-methoxyquinoline (16)

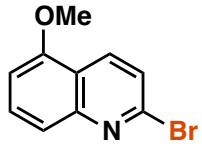
Using 3-methoxyquinoline *N*-oxide (**11**) in accordance with General Procedure III, the title compound was obtained (63% yield) as a white solid. **Mp**: 58 °C (CH_2Cl_2); **R_f** = 0.36 (hexanes:EtOAc 7:1); **IR** (neat): υ_{max} 2360, 2334, 1588, 1404, 1348, 1222 1199, 1051, 772, 748 cm^{-1}; **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.99 (dd, *J* = 8.2, 0.7 Hz, 1H), 7.73 (d, *J* = 8.1 Hz, 1H), 7.57 (ddd, *J* = 8.4, 6.9, 1.5 Hz, 1H), 7.53 (ddd, *J* = 8.2, 7.0, 1.4 Hz, 1H), 7.36 (d, *J* = 1.5 Hz, 1H), 4.02 (s, 3H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 150.0, 143.3, 136.4, 128.7, 128.5, 127.8, 127.7, 126.5, 113.5, 56.5; **HRMS** (ESI-TOF) calcd for $C_{10}H_8BrNOH^+$ $[(M+H)^+]$ 237.9862, found 237.9863.



17

2-Bromo-4-methoxyquinoline (17)

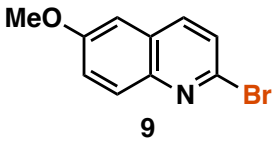
Using 4-methoxyquinoline *N*-oxide (**SI-1**) in accordance with General Procedure III, the title compound was obtained (42% yield) as a white solid. **R_f** = 0.35 (hexanes:EtOAc 5:1); **Mp**: 75 °C (CH_2Cl_2); **IR** (neat): υ_{max} 2360, 2340, 1563, 1507, 1458, 1412, 131, 1260, 1110, 1092, 1019, 987, 880, 764, 730 cm^{-1}; **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.14 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.95 (d, *J* = 8.4 Hz, 1H), 7.70 (ddd, *J* = 8.4, 6.9, 1.5 Hz, 1H), 7.55 – 7.49 (m, 2H), 6.88 (s, 1H), 4.06 (d, *J* = 1.2 Hz, 3H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 163.2, 148.9, 142.6, 130.9, 128.3, 126.3, 122.2, 120.7, 104.8, 56.3; **HRMS** (ESI-TOF) calcd for $C_{10}H_8BrNOH^+$ $[(M+H)^+]$ 237.9789, found 237.9866.



18

2-Bromo-5-methoxyquinoline (18)

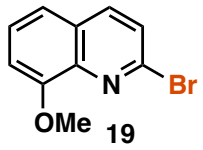
Using 5-methoxyquinoline *N*-oxide (**SI-2**) in accordance with General Procedure III, the title compound was obtained (55% yield) as a white solid. $\mathbf{R_f}$ = 0.30 (hexanes:EtOAc 5:1); **Mp**: 58-60 °C (CH_2Cl_2); **IR** (neat): υ_{max} 2360, 2340, 1563, 1507, 1458, 1412, 131, 1260, 1110, 1092, 1019, 987, 880, 764, 730 cm^{-1}; **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.40 (d, *J* = 8.7, 1H), 7.63-7.62 (m, 2H), 7.49 (d, *J* = 8.7 Hz, 1H), 6.89 (dd, *J* = 6.2, 2.5 Hz, 1H), 4.01 (s, 3H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 155.5, 149.6, 142.6, 133.6, 130.9, 124.8, 120.8, 119.7, 105.1, 56.0; **HRMS** (ESI-TOF) calcd for $C_{10}H_8BrNOH^+$ [$(M+H)^+$] 237.9789, found 237.9866.



9

2-Bromo-6-methoxyquinoline (9)

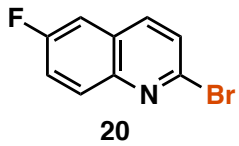
Using 6-methoxyquinoline *N*-oxide (**8**) in accordance with General Procedure III, the title compound was obtained (97% yield) as a white solid. For the large-scale reaction setup (1.05 g, 6.00 mmol) the reaction was scaled up according to General Procedure II and the product was obtained (70%) as a white solid. **Mp**: 110 °C (CH_2Cl_2); $\mathbf{R_f}$ = 0.52 (hexanes:EtOAc 5:1); **IR** (neat): υ_{max} 2360, 2340, 1618, 1562, 1494, 1452, 1376, 1337, 1229, 1292, 1090, 1025, 910, 838, 802, 669 cm^{-1}; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.86 (d, *J* = 9.2 Hz, 1H), 7.78 (d, *J* = 8.5 Hz, 1H), 7.37 (d, *J* = 8.6 Hz, 1H), 7.30 (d, *J* = 7.5 Hz, 1H), 6.96 (s, 1H), 3.86 (s, 3H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 158.1, 144.6, 138.8, 137.2, 129.9, 128.1, 125.8, 123.1, 105.3, 55.6; **HRMS** (ESI-TOF) calcd for $C_{10}H_8BrNOH^+$ [$(M+H)^+$] 237.9862, found 237.9854.



19

2-Bromo-8-methoxyquinoline (19)

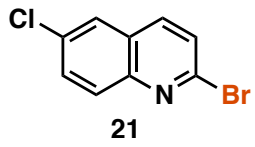
Using 8-methoxyquinoline *N*-oxide (**SI-3**) in accordance with General Procedure III, the title compound was obtained (71% yield) as an orange-colored solid. **Mp**: 72 °C. $\mathbf{R_f}$ = 0.30 (hexanes:EtOAc 5:1); **IR** (neat): υ_{max} 2361, 2338, 1584, 1562, 1492, 1465, 1416, 1374, 1322, 1299, 1261, 1112, 1095, 991, 828, 751, 713 cm^{-1}; **^{1}H NMR** (600 MHz, $CDCl_3$)) δ 7.95 (d, *J* = 8.5 Hz, 1H), 7.54 (d, *J* = 8.4 Hz, 1H), 7.49 (dd, *J* = 7.9, 7.9 Hz, 1H), 7.36 (dd, *J* = 8.1, 1.2 Hz, 1H), 7.08 (dd, *J* = 7.8, 1.1 Hz, 1H), 4.06 (s, 3H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 154.8, 141.0, 140.4, 138.4, 128.3, 127.5, 126.7, 119.4, 108.9, 56.2; **HRMS** (ESI-TOF) calcd for $C_{10}H_8BrNOH^+$ [$(M+H)^+$] 237.9862, found 237.9859.



20

2-Bromo-6-fluoroquinoline (20)

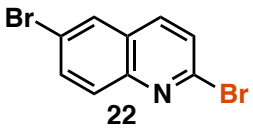
Using 6-fluoroquinoline *N*-oxide (**10**) in accordance with General Procedure III, the title compound was obtained (71% yield) as a white solid. **Mp**: 128 °C (CH_2Cl_2); $\mathbf{R_f}$ = 0.53 (hexanes:EtOAc 7:1); **IR** (neat): υ_{max} 2360, 2340, 1580, 1563, 1485, 1442, 1330, 1282, 1129, 1083, 874, 825, 811 cm^{-1}; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.99 (dd, *J* = 9.2, 5.2 Hz, 1H), 7.89 (d, *J* = 8.6 Hz, 1H), 7.49 (s, 1H), 7.45 (dd, *J* = 8.8, 2.5 Hz, 1H), 7.37 (dd, *J* = 8.5, 2.8 Hz, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 160.6, 145.6, 141.1, 137.7, 131.2, 127.0, 126.6, 120.7, 111.1; **HRMS** (ESI-TOF) calcd for $C_9H_5BrFNH^+$ [$(M+H)^+$] 225.9662, found 225.9662.



21

2-Bromo-6-chloroquinoline (21)

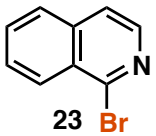
Using 6-chloroquinoline *N*-oxide (**SI-4**) in accordance with General Procedure III, the title compound was obtained (58% yield) as a white solid. **Mp**: 128 °C (CH_2Cl_2); $\mathbf{R_f}$ = 0.53 (hexanes:EtOAc 7:1); **IR** (neat): υ_{max} 2361, 2339, 1580, 1486, 1282, 1129, 1083, 875, 825, 671, 653 cm^{-1}; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.92 (d, *J* = 9.0 Hz, 1H), 7.85 (d, *J* = 8.6 Hz, 1H), 7.72 (d, *J* = 2.3 Hz, 1H), 7.62 (dd, *J* = 9.0, 2.4 Hz, 1H), 7.49 (d, *J* = 8.6 Hz, 1H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 146.9, 142.2, 137.3, 132.9, 131.5, 130.3, 127.6, 126.8, 126.5; **HRMS** (ESI-TOF) calcd for $C_9H_5BrClNH^+$ [$(M+H)^+$] 241.9367, found 241.9367.



22

2,6-Dibromoquinoline (22)

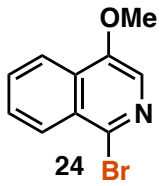
Using 6-bromoquinoline *N*-oxide (**SI-5**) in accordance with General Procedure III, the title compound was obtained (63% yield) as a white solid. **Mp**: 151 °C (CH_2Cl_2); $\mathbf{R_f}$ = 0.53 (hexanes:EtOAc 7:1); **IR** (neat): υ_{max} 2361, 2338, 1576, 1543, 1480, 1439, 1327, 1279, 1127, 1082, 589, 821, 671 cm^{-1}; **^{1}H NMR** (125 MHz, $CDCl_3$) δ 7.97 (d, *J* = 2.2 Hz, 1H), 7.93 – 7.87 (m, 2H), 7.80 (dd, *J* = 8.9, 2.1 Hz, 1H), 7.54 (d, *J* = 8.5 Hz, 1H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 147.3, 142.4, 137.4, 134.2, 130.5, 129.9, 128.2, 126.9, 121.1; **HRMS** (ESI-TOF) calcd for $C9H5Br_2NH^+$ [$(M+H)^+$] 285.8861, found 285.8858.



23

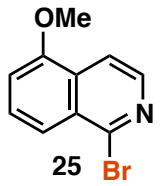
1-Bromoisoquinoline (23)

Using isoquinoline *N*-oxide in accordance with General Procedure III, the title compound was obtained (55% yield) as a white solid. All spectroscopic data were consistent with a commercial sample. **^{1}H NMR** (100 MHz, $CDCl_3$) δ 8.31 (d, *J* = 8.0 Hz, 1H), 8.27 (d, *J*= 5.6 Hz, 1H), 7.83 (d, *J*= 10.0 Hz, 1H), 7.73 – 7.68 (m, 2H), 7.62 (d, *J* = 6.8 Hz, 1H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 145.2, 141.8, 137.6, 131.6, 129.1, 128.9, 127.2, 121.4.



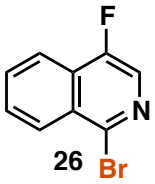
1-Bromo-4-methoxyisoquinoline (24)

Using 4-methoxyisoquinoline *N*-oxide (**SI-1**) in accordance with General Procedure III, the title compound was obtained (97% yield) as a white solid. **Mp**: 70 °C (CH_2Cl_2); $\mathbf{R_f}$ = 0.27 (hexanes:EtOAc 7:1); **IR** (neat): υ_{max} 2361, 2340, 1580, 1556, 1503, 1454, 1315, 1278, 1099, 989, 929, 876, 756, 623, 606 cm^{-1}; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.20 (dd, *J* = 9.2, 9.2 Hz, 2H), 7.81 (s, 1H), 7.76 – 7.66 (m, 2H), 4.05 (s, 3H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 150.9, 135.6, 130.4, 130.2, 129.1, 128.9, 128.3, 122.2, 121.9, 56.3; **HRMS** (ESI-TOF) calcd for $C_{10}H_8BrNOH^+$ [$(M+H)^+$] 237.9862, found 237.9877.



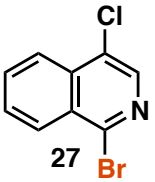
1-Bromo-5-methoxyisoquinoline (25)

Using 5-methoxyisoquinoline *N*-oxide (**SI-2**) in accordance with General Procedure III, the title compound was obtained (50% yield) as a white solid. **Mp**: 113 °C (CH_2Cl_2); $\mathbf{R_f}$ = 0.40 (hexanes:EtOAc 7:1); **IR** (neat): υ_{max} 2359, 2339, 1579, 1487, 1461, 1376, 1327, 1317, 1264, 1005, 834, 789, 773, 740 cm^{-1}; **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.14 (d, *J* = 5.7 Hz, 1H), 7.91 (d, *J* = 5.7 Hz, 1H), 7.75 (d, *J* = 8.6 Hz, 1H), 7.49 (dd, *J* = 8.6, 7.8 Hz, 1H), 6.95 (dd, *J* = 7.8, 0.9 Hz, 1H), 3.92 (s, 3H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 154.8, 144.9, 141.7, 130.2, 129.8, 128.8, 120.4, 115.8, 108.5, 56.1; **HRMS** (ESI-TOF) calcd for $C_{10}H_8BrNOH^+$ [$(M+H)^+$] 237.9862, found 237.9865.



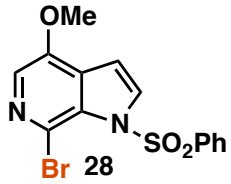
1-Bromo-4-fluoroisoquinoline (26)

Using 4-fluoroisoquinoline *N*-oxide (**SI-8**) in accordance with General Procedure III, the title compound was obtained (87% yield) as a white solid. **Mp**: 62 °C (CH_2Cl_2); $\mathbf{R_f}$ = 0.60 (hexanes:EtOAc 7:1); **IR** (neat): υ_{max} 2361, 2338, 1592, 1504, 1417, 1378, 1310, 1261, 1068, 948, 880, 762, 670 cm^{-1}; **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.24 (d, *J* = 9.0 Hz, 1H), 8.14 (s, 1H), 8.06 (d, *J* = 8.3 Hz, 1H), 7.81 (dd, *J* = 8.5, 7.0 Hz, 1H), 7.74 (dd, *J* = 8.5, 7.0 Hz, 1H); **^{13}C NMR** (600 MHz, $CDCl_3$) δ 155.31, 138.8, 131.6, 129.8, 128.6, 128.3, 127.6, 127.5, 120.4; **^{19}F NMR** (376 MHz, $CDCl_3$) δ -140.34; **HRMS** (ESI-TOF) calcd for $C_9H_2BrNFH^+$ $[(M+H)^+]$ 225.9662, found 225.9663.



1-Bromo-4-chloroisoquinoline (27)

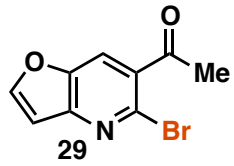
Using 4-chloroisoquinoline *N*-oxide (**SI-9**) in accordance with General Procedure III, the title compound was obtained (85% yield) as a white solid. **Mp**: 72 °C (CH_2Cl_2); $\mathbf{R_f}$ = 0.63 (hexanes:EtOAc 7:1); **IR** (neat): υ_{max} 2361, 2340, 1563, 1316, 1293, 1217, 980, 758, 678, 563 cm^{-1}; **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.34 (s, 1H) 8.33 (d, *J* = 9.4 Hz, 1H), 8.22 (d, *J* = 8.1 Hz, 1H), 7.88 (ddd, *J* = 8.4, 7.0, 1.3 Hz, 1H), 7.78 (ddd, *J* = 8.3, 7.1, 1.3 Hz, 1H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 143.67, 140.8, 135.0, 132.3, 129.8, 129.6, 129.3, 128.9, 124.3; **HRMS** (ESI-TOF) calcd for $C_9H_5BrClNH^+$ $[(M+H)^+]$ 241.9367, found 241.9370.



28

_N_1-benzenesulfonyl-7-bromo-4-methoxy-6-azainole (28)

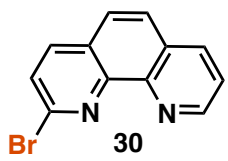
Using _N_1-benzenesulfonyl-4-methoxy-6-azainole _N_6-oxide (**SI-10**) in accordance with General Procedure III, the title compound was obtained (65% yield) as a white solid. **Mp**: 122 °C (CH_2Cl_2); $\mathbf{R_f}$ = (CH_2Cl_2:MeOH 20:1); **IR** (neat): υ_{max} 2360, 2340, 1513, 1453, 1360, 1290, 1174, 1116, 927, 753, 726, 684, 614, 593, 570 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.99 (d, *J* = 3.8 Hz, 1H), 7.82 (dd, *J* = 8.5, 1.3 Hz, 2H), 7.67 – 7.57 (m, 1H), 7.51 (dd, *J* = 8.4, 7.2 Hz, 2H), 6.87 (d, *J* = 3.8 Hz, 1H), 3.99 (s, 3H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 149.4, 139.8, 134.2, 132.4, 131.4, 129.5, 127.4, 123.8, 116.0, 103.9, 99.7, 56.5; **HRMS** (ESI-TOF) calcd for $C_{14}H_{11}BrN_2O_3SH^+$ [$(M+H)^+$] 366.9674, found 366.9747.



29

1-(5-bromofuro[3,2-b]pyridin-6-yl)ethanone (29)

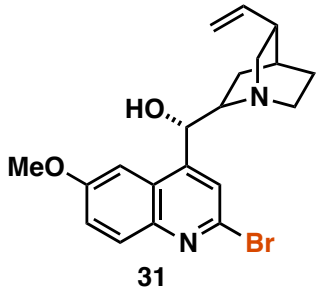
Using 6-acetylfuro[3,2-b]pyridine 4-oxide (**SI-11**) in accordance with General Procedure III, the title compound was obtained (92% yield) as a white solid. **Mp**: 35 °C (CH_2Cl_2); $\mathbf{R_f}$ = 0.28 (hexanes:EtOAc 7:1); **IR** (neat): υ_{max} 2361, 2340, 1697, 1610, 1367, 1318, 1280, 1220, 1119, 1101, 1022, 786, 750, 649 cm^{-1}; **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.97 (d, *J* = 2.3 Hz, 1H), 7.90 (s, 1H), 7.31 – 7.20 (m, 1H), 6.99 (d, *J* = 2.3 Hz, 1H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 199.6, 176.8, 152.5, 149.7, 146.6, 133.6, 133.4, 120.2, 108.0, 30.8; **HRMS** (ESI-TOF) calcd for $C_9H_6BrNO_2H^+$ [$(M+H)^+$] 239.9655, found 239.9664.



30

2-Bromo-1,10-phenanthroline (30)

Using 1,10-phenanthroline *N*-oxide (**SI-11**) in accordance with General Procedure III, the title compound was obtained (70% yield) as a white solid. **Mp**: °C (CH_2Cl_2); $\mathbf{R_f}$ = (CH_2Cl_2:MeOH 20:1); **IR** (neat): υ_{max} cm^{-1} 3041, 2921, 1576, 1486, 1379, 1060, 1032, 840, 724; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.21 (dd, *J* = 4.3, 1.8 Hz, 1H), 8.24 (dd, *J* = 8.1, 1.8 Hz, 1H), 8.06 (d, *J* = 8.4 Hz, 1H), 7.81 (d, *J* = 8.8 Hz, 1H), 7.78 – 7.72 (m, 2H), 7.64 (dd, *J* = 8.1, 4.3 Hz, 1H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 150.9, 146.7, 145.0, 142.7, 138.3, 136.3, 129.1, 128.1, 127.6, 127.2, 126.0, 123.6; **HRMS** (ESI-TOF) calcd for $C_{12}H_7BrN_2H^+$ [$(M+H)^+$] 258.9793, found 258.9871.



31

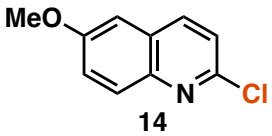
2-Bromoquinine (31)

To a mixture of quinine *N*-oxide (**SI-12**), tetrabutylammonium bromide (4.0 equiv), and 4 Å molecular sieves is added CH_2Cl_2 (0.01M) and the mixture is stirred at room temperature for 10 min. *p*-Toluenesulfonic anhydride (2.0 equiv) is added and the reaction is stirred at room temperature overnight. The reaction mixture is filtrated, the organic layer washed twice with LiCl (sat. aq.), dried over $MgSO_4$ and concentrated under reduced pressure. The crude product is purified by flash column chromatography using a gradient of DCM to 10% MeOH/DCM to give the title compound (63%) as a white solid. **Mp**: 125-130°C (CH_2Cl_2); $\mathbf{R_f}$ =0.4 (CH_2Cl_2:MeOH 10:1); **IR** (neat): υ_{max} cm^{-1} 3254, 2923, 2549, 1618, 1503, 1286, 1233, 1092, 1024, 896, 830, 726; **^{1}H NMR** (100 MHz, $CDCl_3$) δ 7.74 (s, 1H), 7.58 (d, *J* = 9.2 Hz, 1H), 7.02 (dd, *J* = 9.2, 2.6 Hz, 1H), 6.84 (d, *J* = 2.7 Hz, 1H), 6.39 (s, 1H), 5.53 (ddd, *J* = 17.2, 10.5, 6.7 Hz, 1H), 5.05 – 4.91 (m, 2H), 4.50 (s, 1H), 3.76 (s, 3H), 3.41 (dd, *J* = 13.6, 10.7 Hz, 1H), 3.38 – 3.33 (m, 1H), 3.31 – 3.24 (m, 1H), 3.10 (td, *J* = 11.9, 5.3 Hz, 1H), 3.03 (ddd, *J* = 13.7, 5.3, 2.7 Hz, 1H), 2.68 (s, 1H), 2.26 –

2.17 (m, 1H), 2.10 – 2.02 (m, 2H), 1.88 – 1.80 (m, 1H), 1.70-1.64 (m, 1H); **^{13}C NMR** ($CDCl_3$, 151 MHz) δ 159.4, 147.5, 144.9, 139.5, 138.0, 131.5, 124.9, 124.2, 123.7, 118.2, 100.9, 66.7, 60.8, 58.3, 55.8, 45.2, 38.0, 27.7, 25.1, 25.1, 20.6. **HRMS** (ESI-TOF) calcd for $C_{20}H_{23}BrN_2O_2H^+$ [$(M+H)^+$] 403.1016, found 403.1011.

Procedure for chlorination of 6-methoxyquinoline *N*-oxide (8)

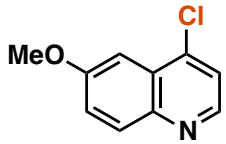
A solution of 6-methoxyquinoline *N*-oxide (18 mg, 0.10 mmol, 1.00 equiv) and tetrabutylammonium chloride hydrate (42 mg, 0.15 mmol, 1.50 equiv) and 4 Å molecular sieves in CH_2Cl_2 (10 mL) was stirred at room temperature for 10 min, then *p*-toluenesulfonic anhydride (49 mg, 0.15 mmol, 1.50 equiv) was added and the mixture was stirred at room temperature overnight. The solution was filtered and the solvent was evaporated. The crude reaction mixture was purified by flash column chromatography using hexanes/EtOAc as the solvent mixture. The two regioisomers (**C2**:**C4** 10:1) were obtained as white solids.



14

2-Chloro-6-methoxyquinoline (14)

The title compound was obtained (87% yield) as a white solid. Mp: 86 °C (CH_2Cl_2); $\mathbf{R_f}$ = 0.47 (hexanes:EtOAc 5:1); **IR** (neat): υ_{max} 2361, 2340, 1622, 1584, 1496, 1470, 1376, 1342, 1295, 1244, 1230, 1161, 1127, 1092, 1018, 954, 918, 849, 824, 799 cm^{-1}; **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.95 (d, *J* = 8.5 Hz, 1H), 7.88 (d, *J* = 9.2 Hz, 1H), 7.35 (dd, *J* = 9.2, 2.8 Hz, 1H), 7.30 (d, *J* = 8.6 Hz, 1H), 7.03 (d, *J* = 2.8 Hz, 1H), 3.89 (s, 3H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 158.1, 148.1, 143.8, 137.7, 129.9, 127.9, 123.1, 122.5, 105.3, 55.7; **HRMS** (ESI-TOF) calcd for $C_{10}H_8ClNO^+$ [$(M+H)^+$] 194.0367, found 194.0374.

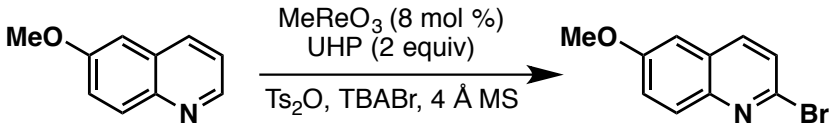


SI-14

4-Chloro-6-methoxyquinoline (SI-14)

The title compound was obtained (9% yield) as a white solid. Mp: 51 °C (CH_2Cl_2); $\mathbf{R_f}$ = 0.37 (hexanes:EtOAc 5:1); **IR** (neat): υ_{max} 2361, 2340, 1621, 1579, 1497, 1424, 1295, 1264, 1193, 1162, 1064, 1032, 848, 826, 717, 673 cm^{-1}; **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.63 (d, *J* = 4.7 Hz, 1H), 8.01 (d, *J* = 9.1 Hz, 1H), 7.46 (d, *J* = 4.7 Hz, 1H), 7.44 (d, *J* = 2.8 Hz, 1H), 7.41 (dd, *J* = 9.1, 2.8 Hz, 1H), 3.98 (s, 3H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 158.9, 147.4, 145.4, 141.1, 131.5, 127.7, 123.5, 121.6, 101.7, 55.9; **HRMS** (ESI-TOF) calcd for $C_{10}H_8ClNO^+$ [$(M+H)^+$] 194.0367, found 194.0376.

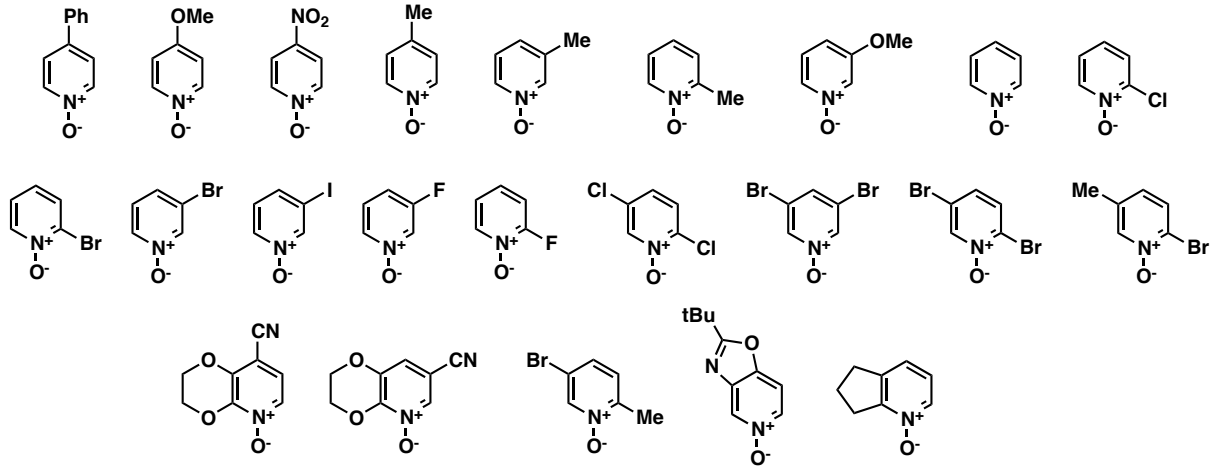
Procedure for One-Pot Oxidation/Bromination Sequence



8 **9**

To a solution of 6-methoxyquinoline (28 μL, 0.200 mmol) in DCM (0.2 mL) was added UHP (37.6 mg, 0.400 mmol) and MTO (4 mg, 0.016 mmol) and the mixture capped and stirred 24 h. At this time the mixture was diluted to 20 mL with DCM and molecular sieves were added. After stirring 5 min, TBABr (96.5 mg, 0.300 mmol) followed by Ts_2O (98 mg, 0.300 mmol) were added and the mixture stirred 12 h. The mixture was then filtered, quenched with 1M NaOH, the aqueous layer extracted twice with DCM, the combined organic extracts dried over Mg_2SO_4 and concentrated to yield a yellow oil. Silica gel chromatography (1:10 EtOAc:Hex) yielded **9** as a while solid (34 mg, 70%).

Table of Pyridines Screened in Attempted Bromination



References

1. Sun, W. H.; He, S. Y.; Zhang, S.; Zhang, W.; Song, Y. X.; Ma, H. W. *Organomet.* **2006,** *25* (3), 666-677.
2. Engel, Y.; Dahan, A.; Rozenshine-Kemelmakher, E.; Gozin, M. *J. Org. Chem.* **2007,** *72* (7), 2318-2328.
3. Wu, Y. W.; Singh, R. P.; Deng, L. *J. Am. Chem. Soc.* **2011,** *133* (32), 12458-12461.

Regioselective Bromination of Fused Hetereocyclic *N*-Oxides

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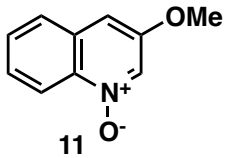
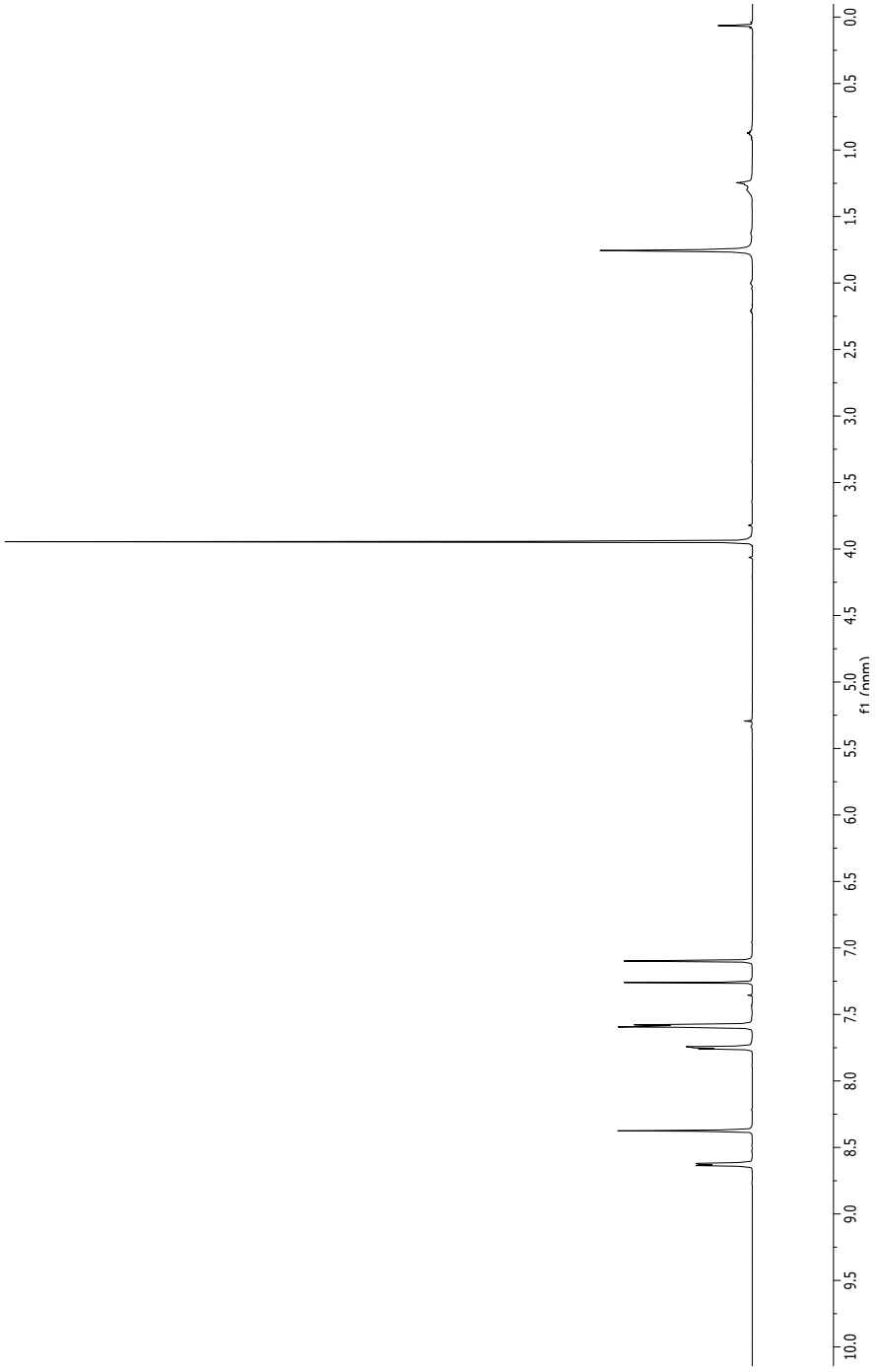
Chemical Development, Bristol-Myers Squibb, One Squibb Drive, New Brunswick, New Jersey, 08903, United States

Spectral File


OMe
N+
O-

11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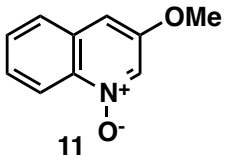
f1 (ppm)



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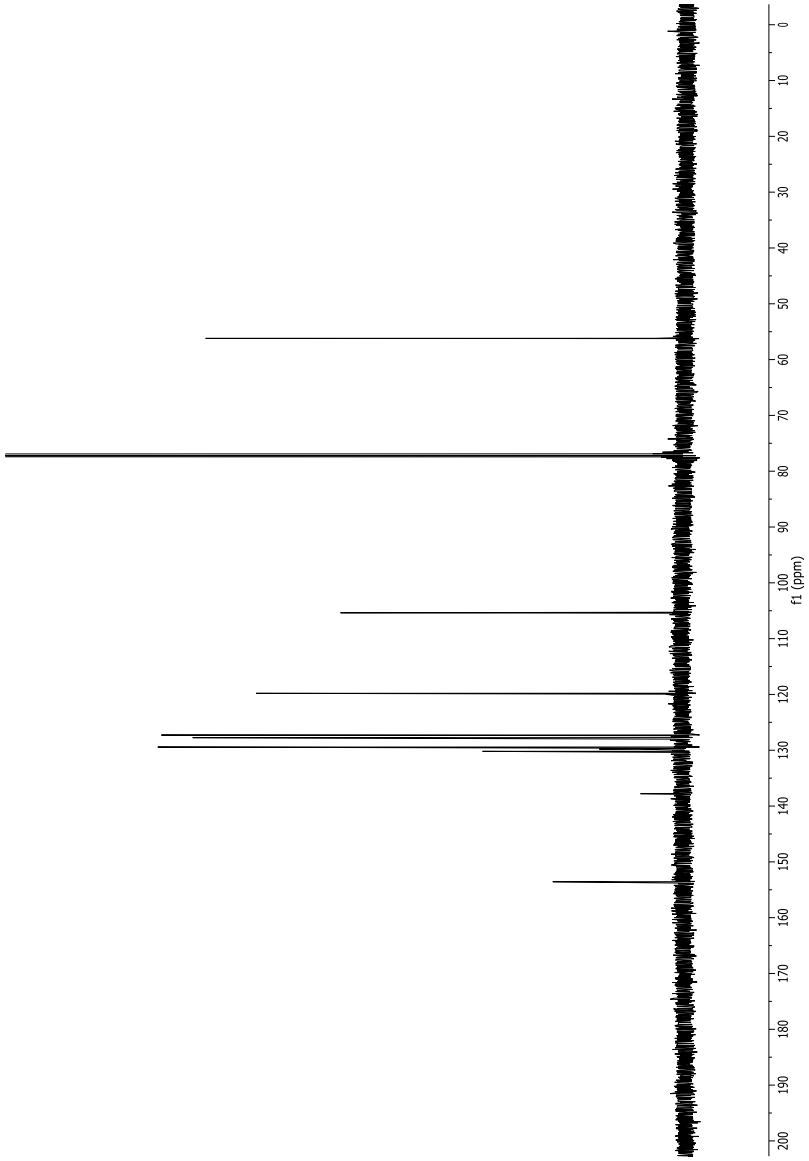

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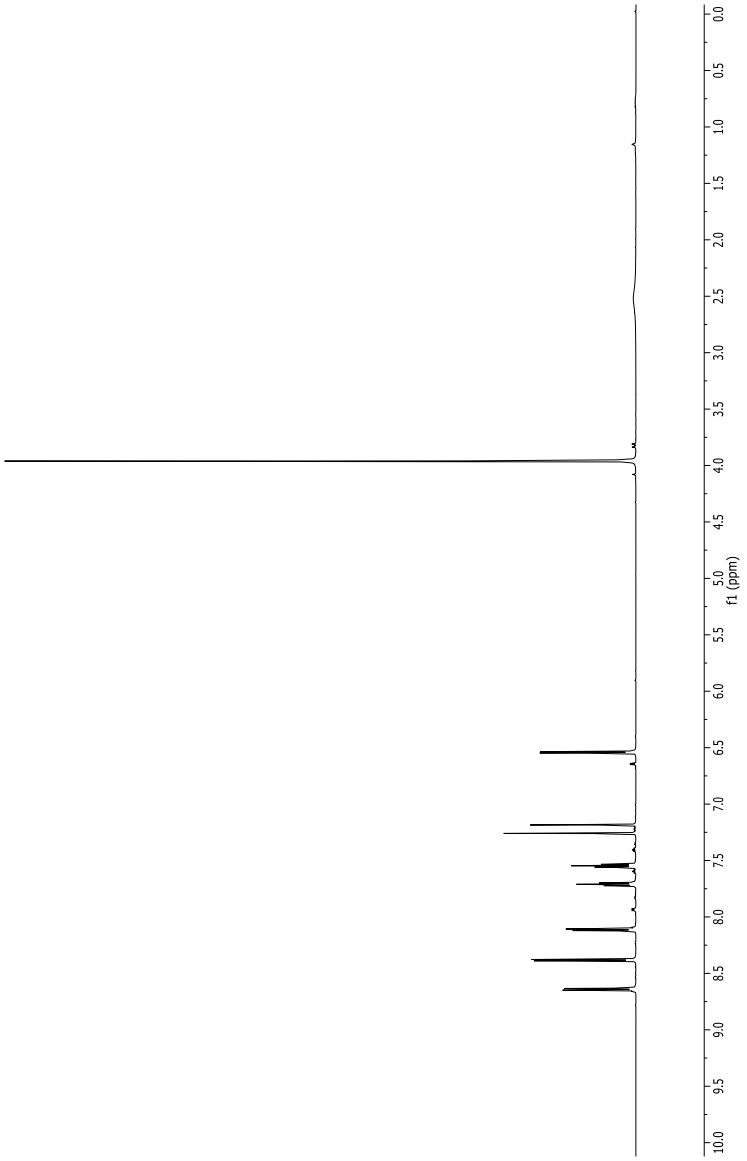

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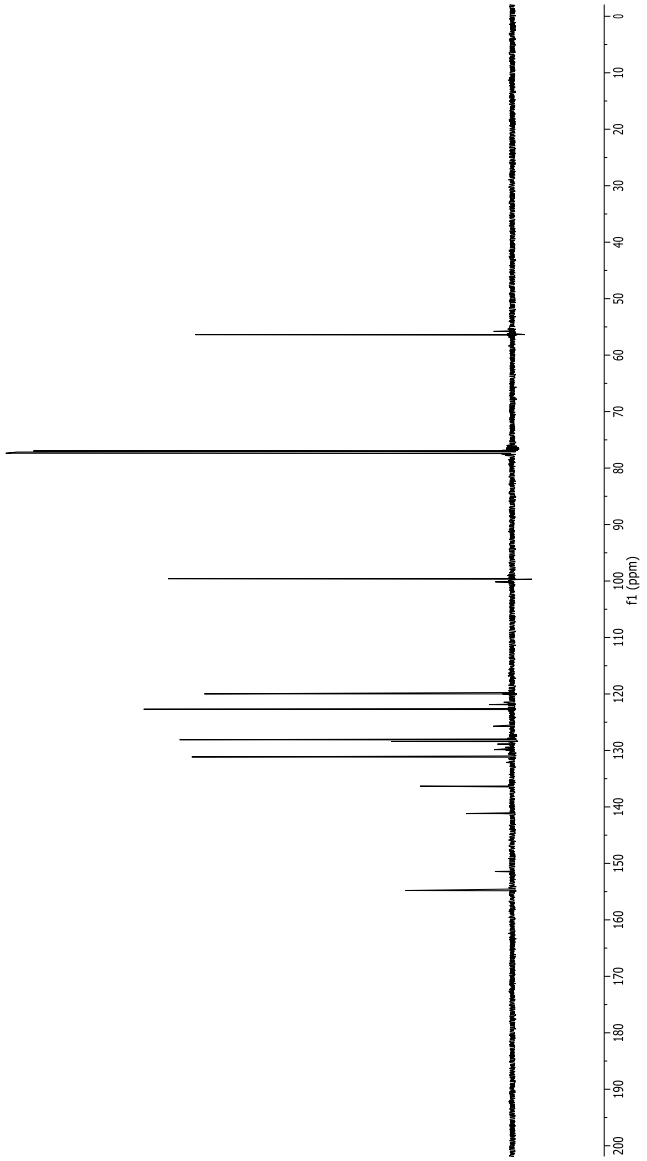

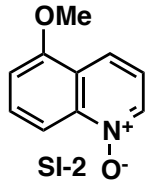

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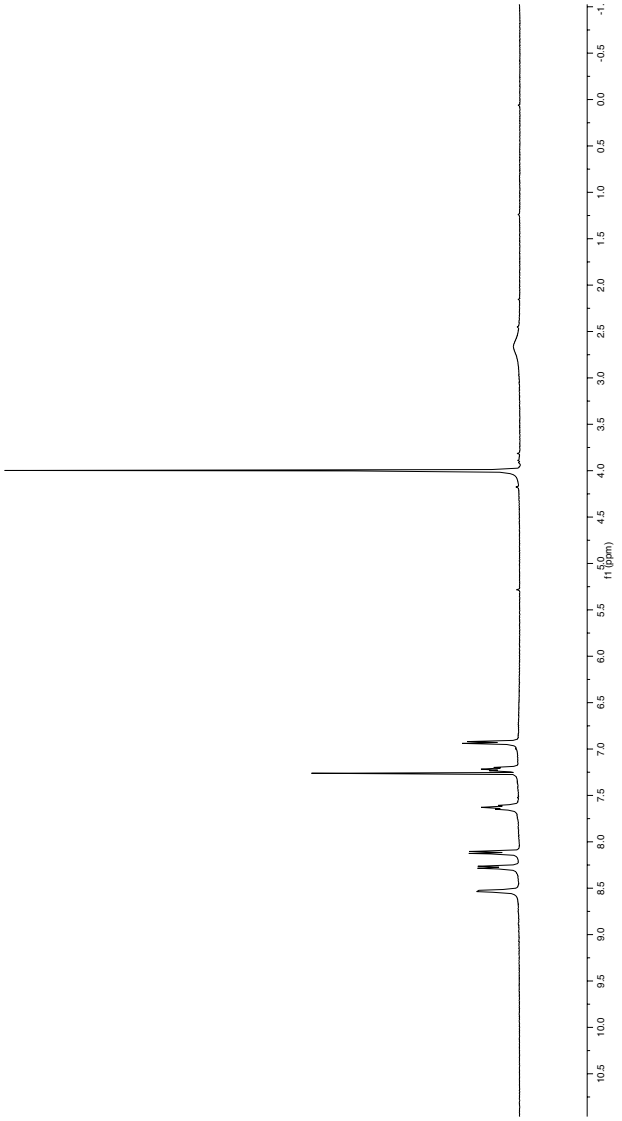
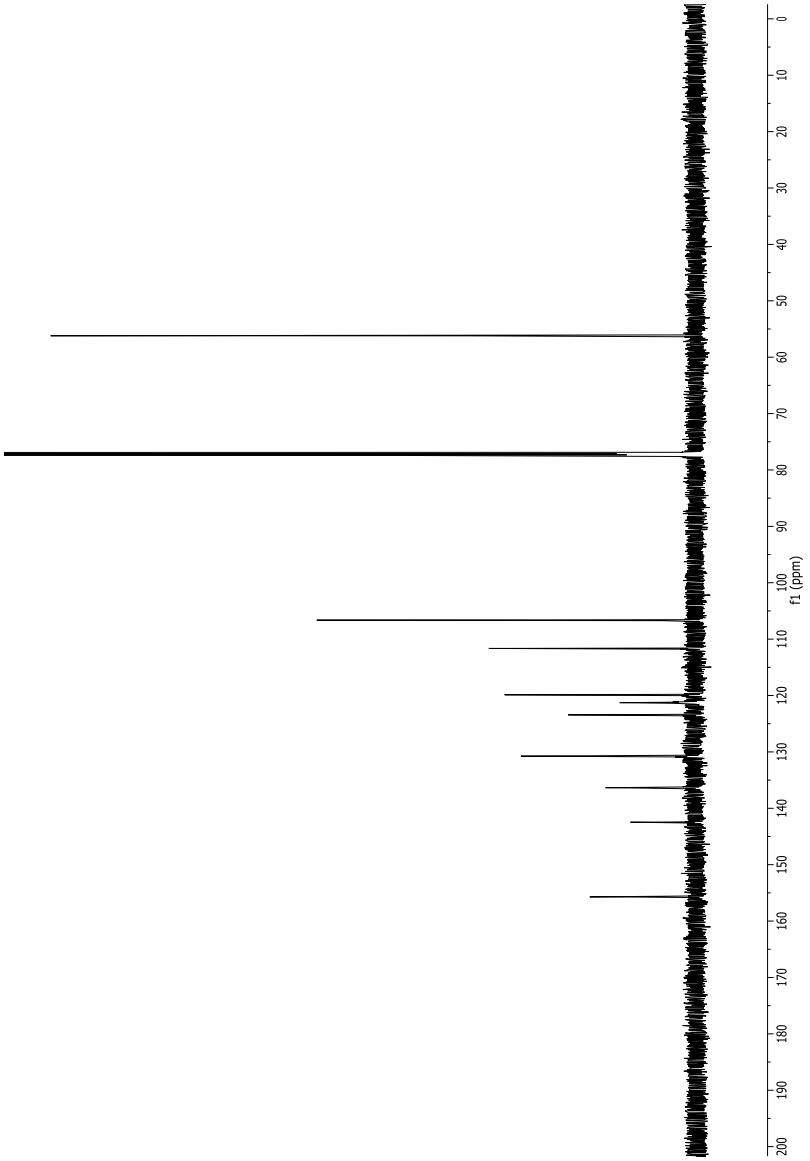
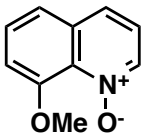


SI-2





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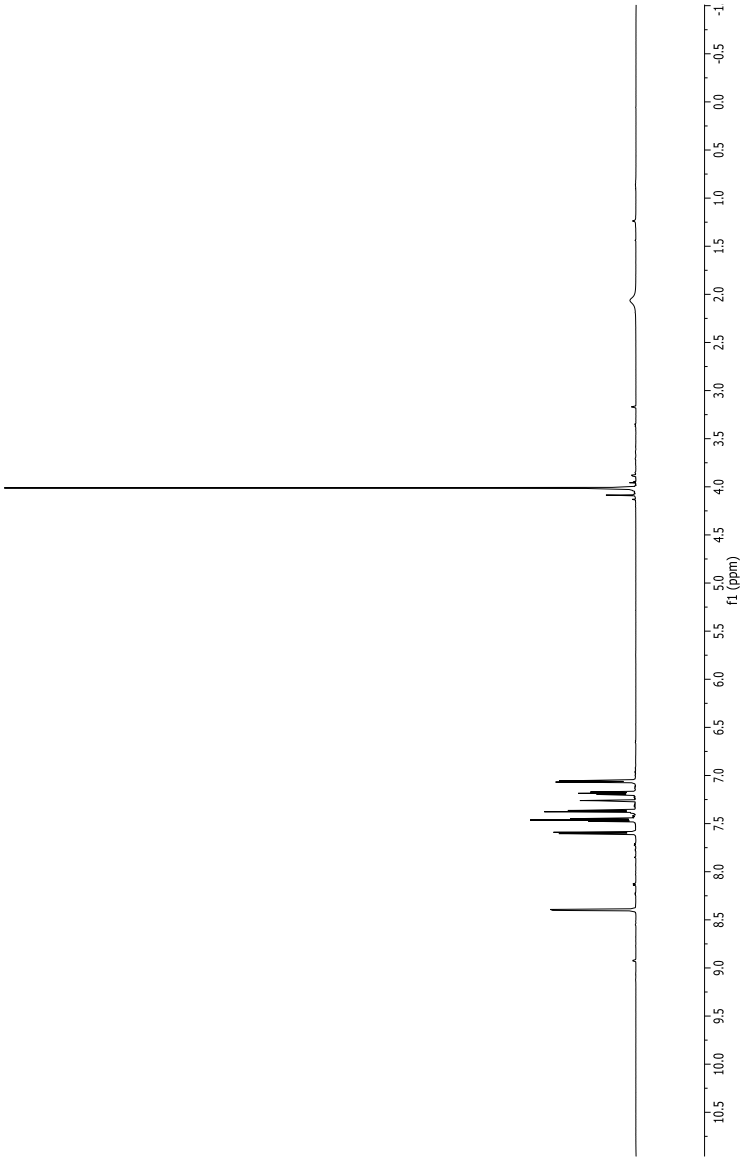
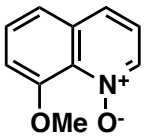
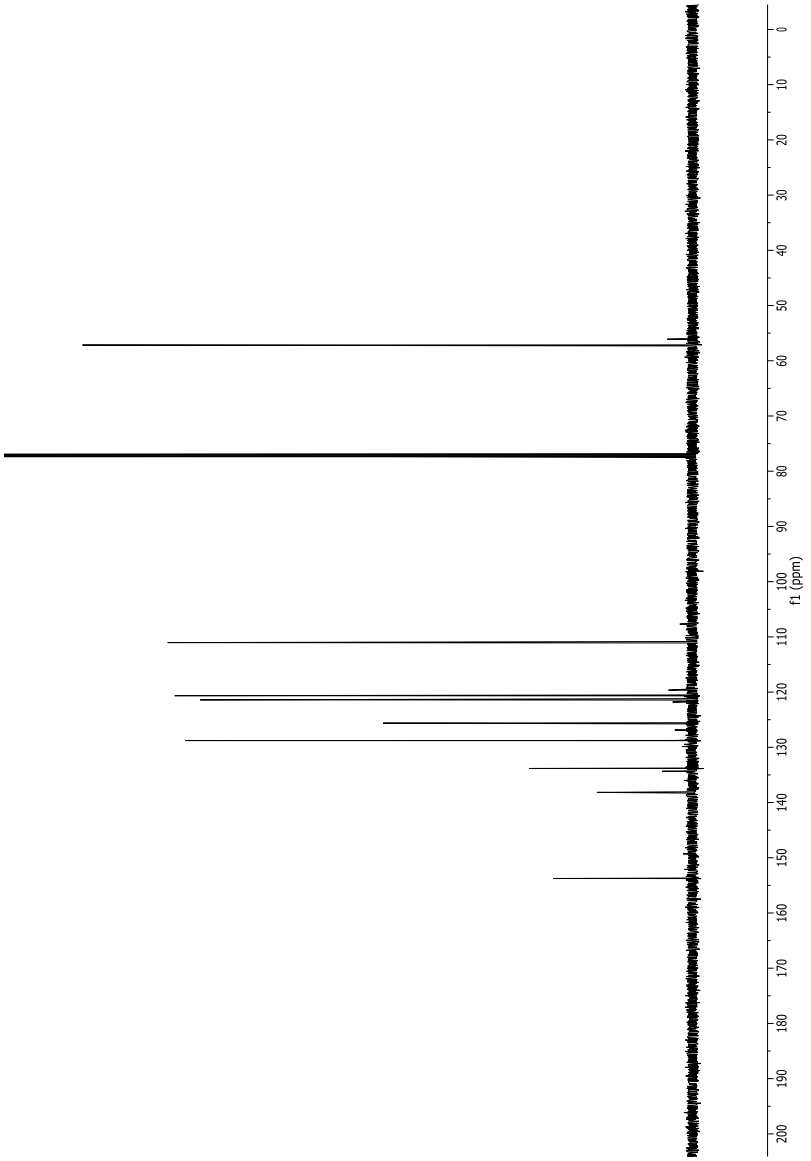
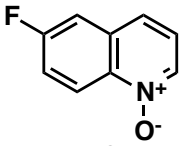




SI-3





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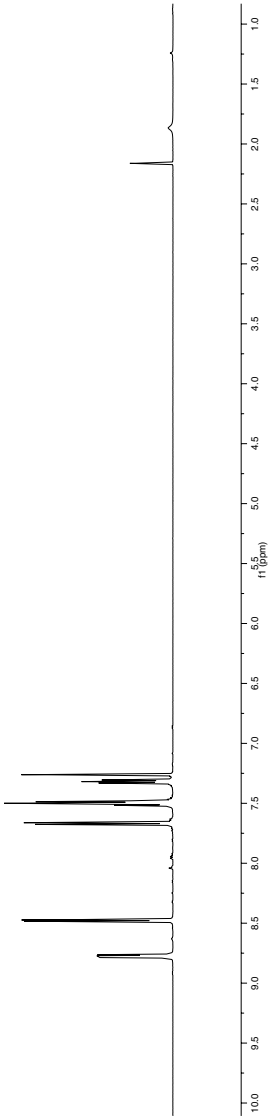

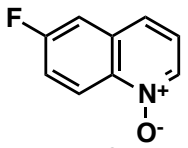

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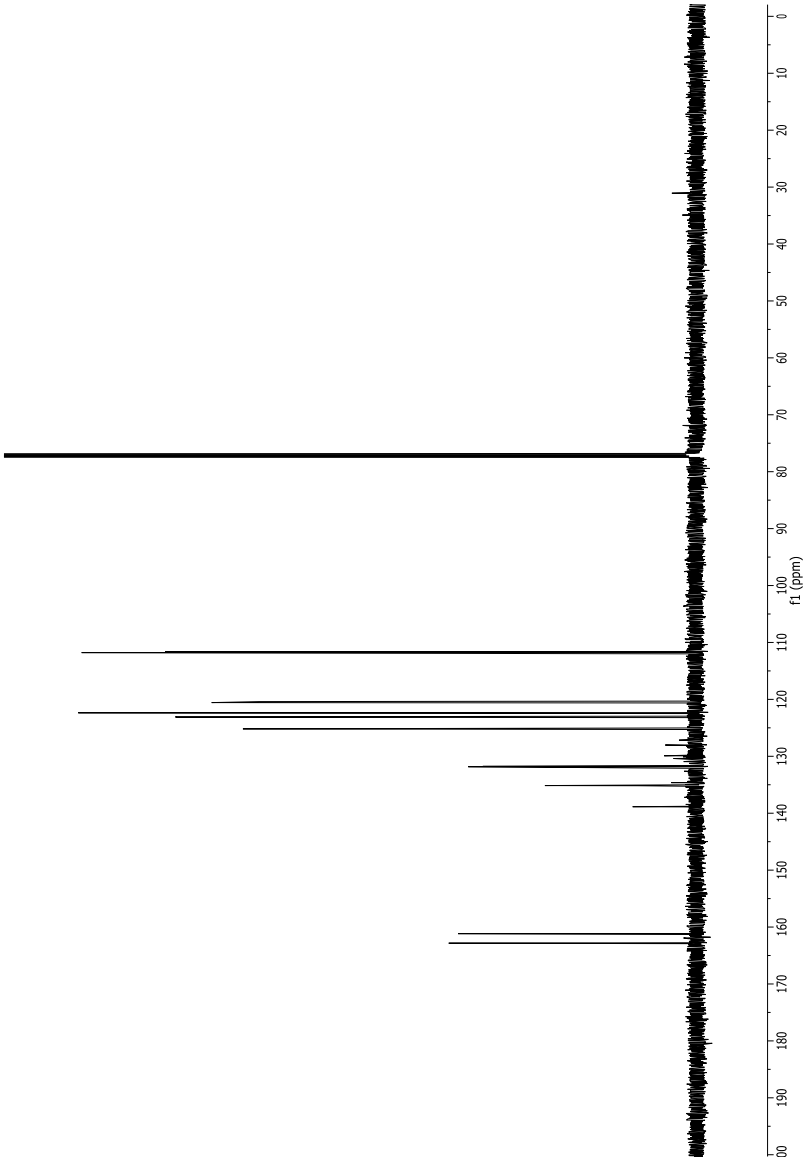
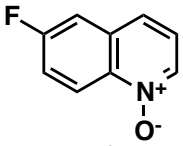
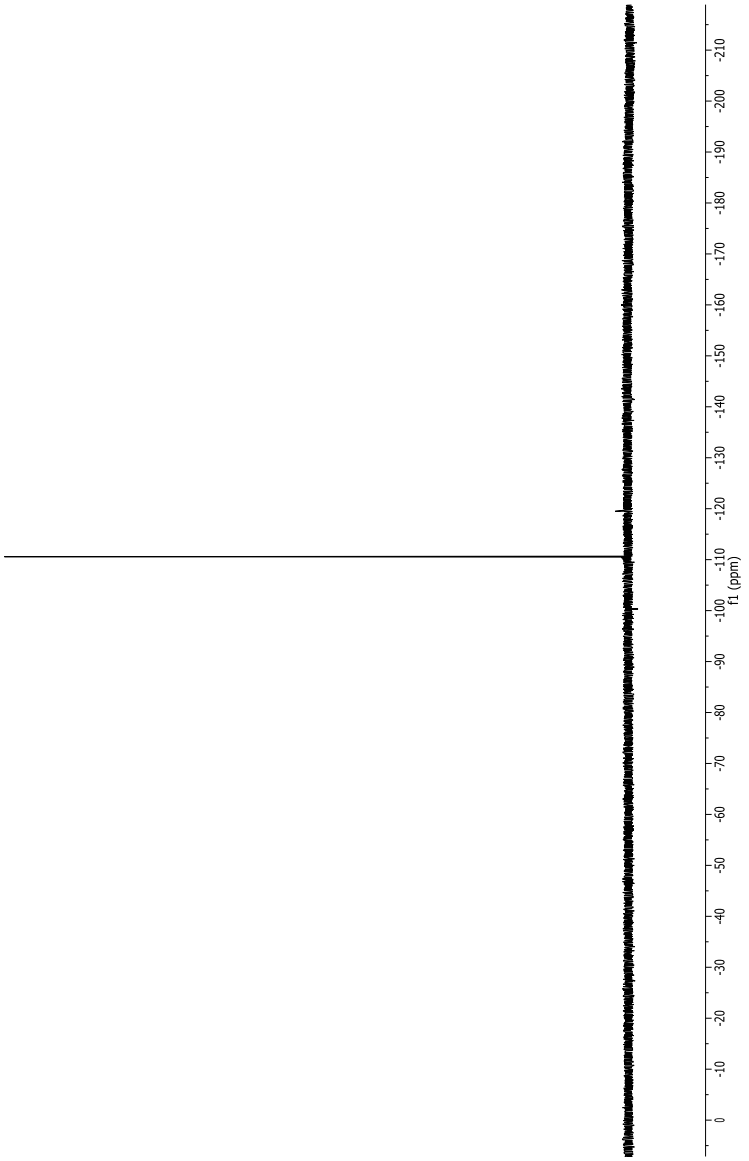



F
N+
O-

10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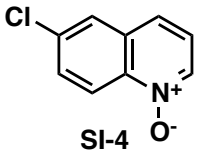

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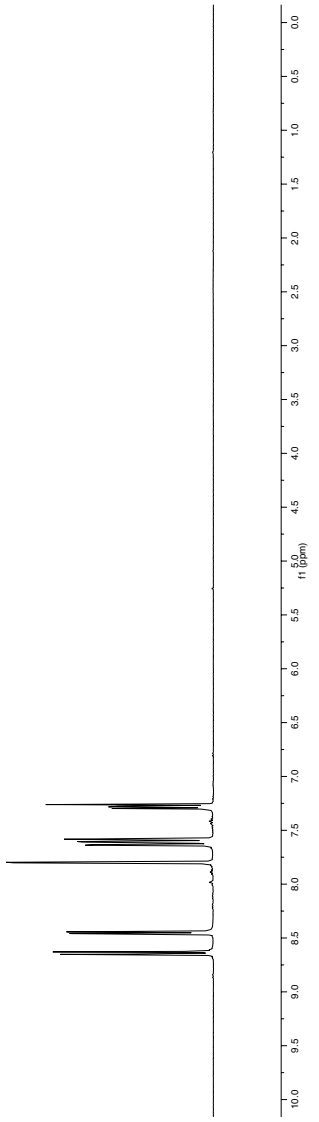

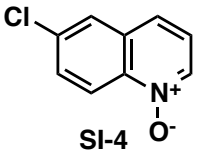

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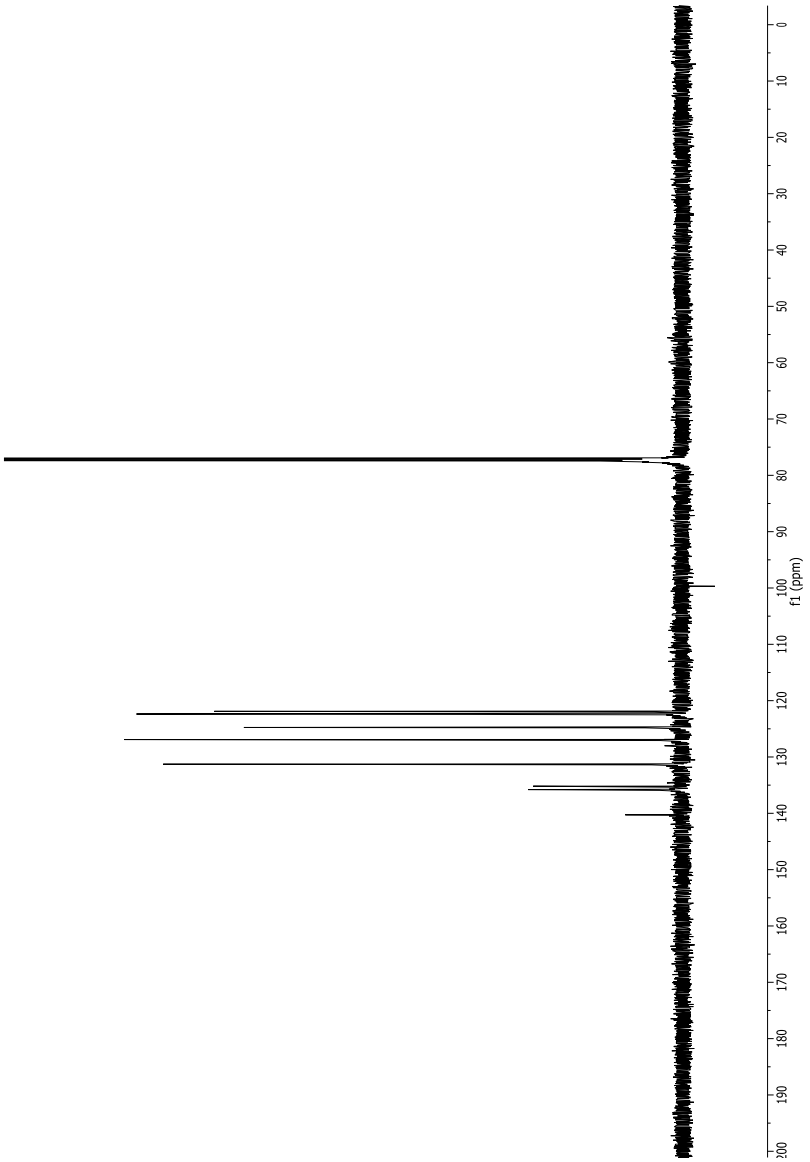
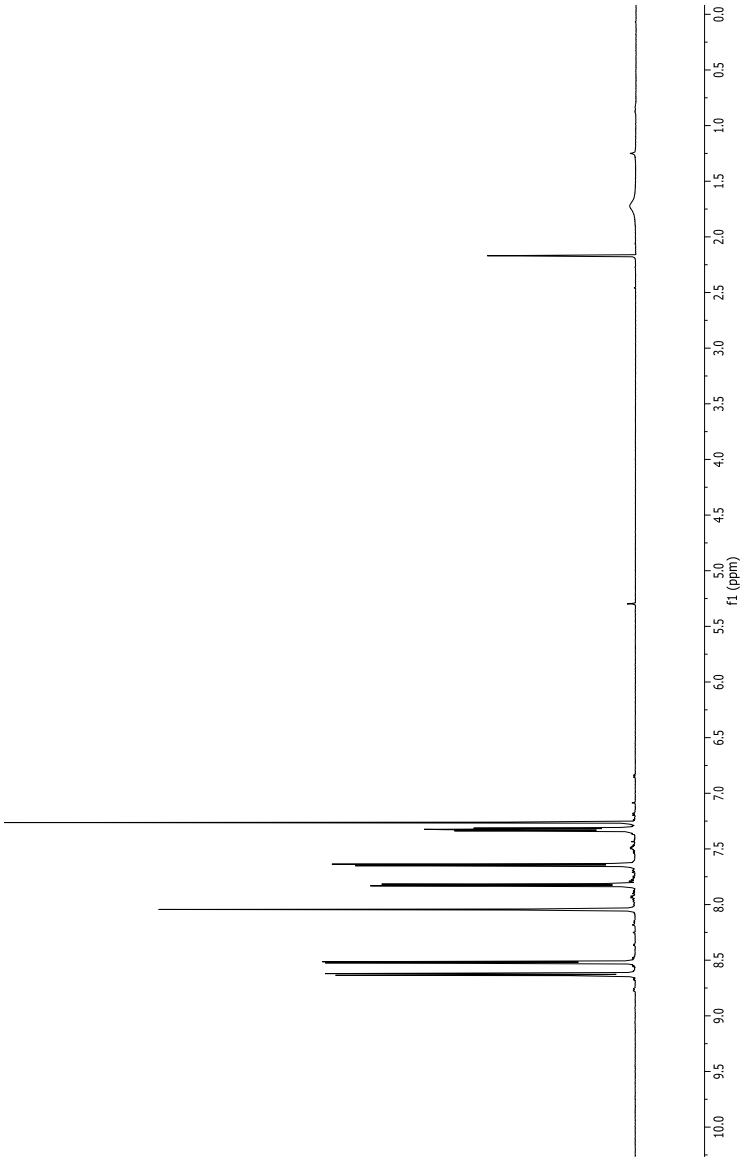



Br
N+
O-

SI-5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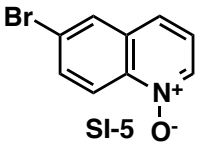

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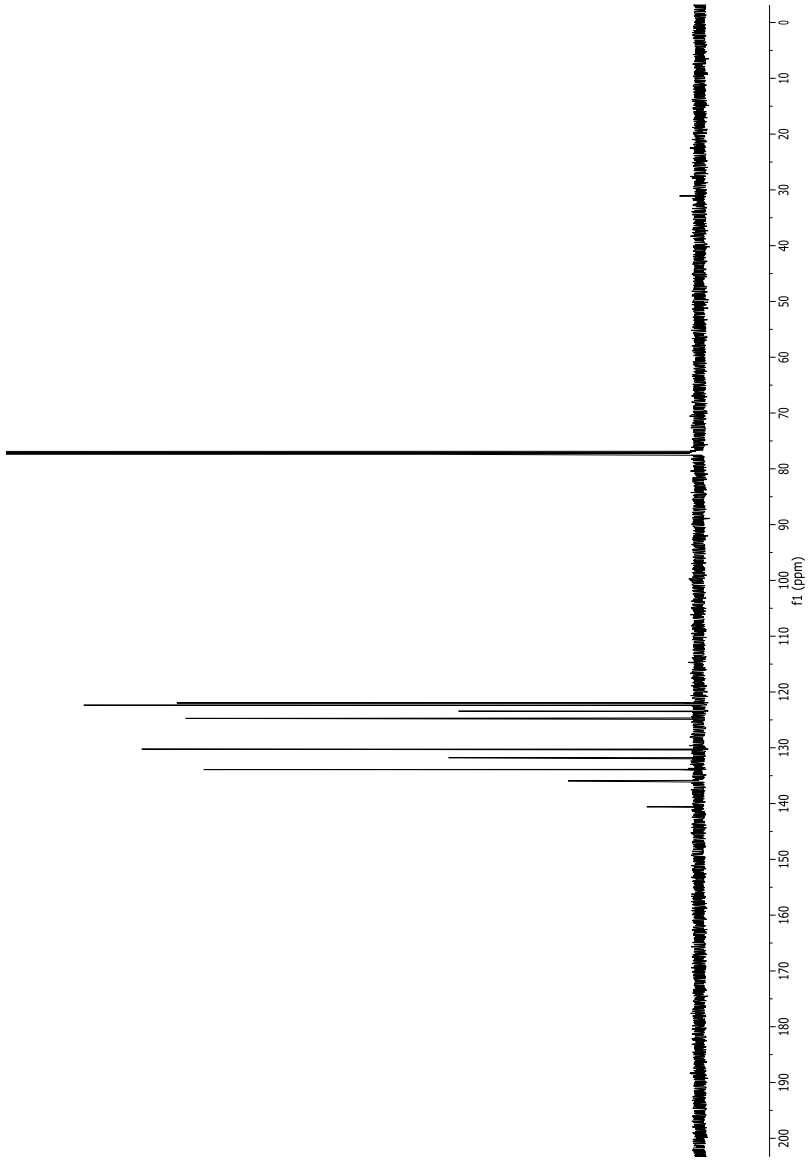
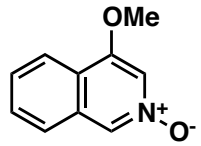
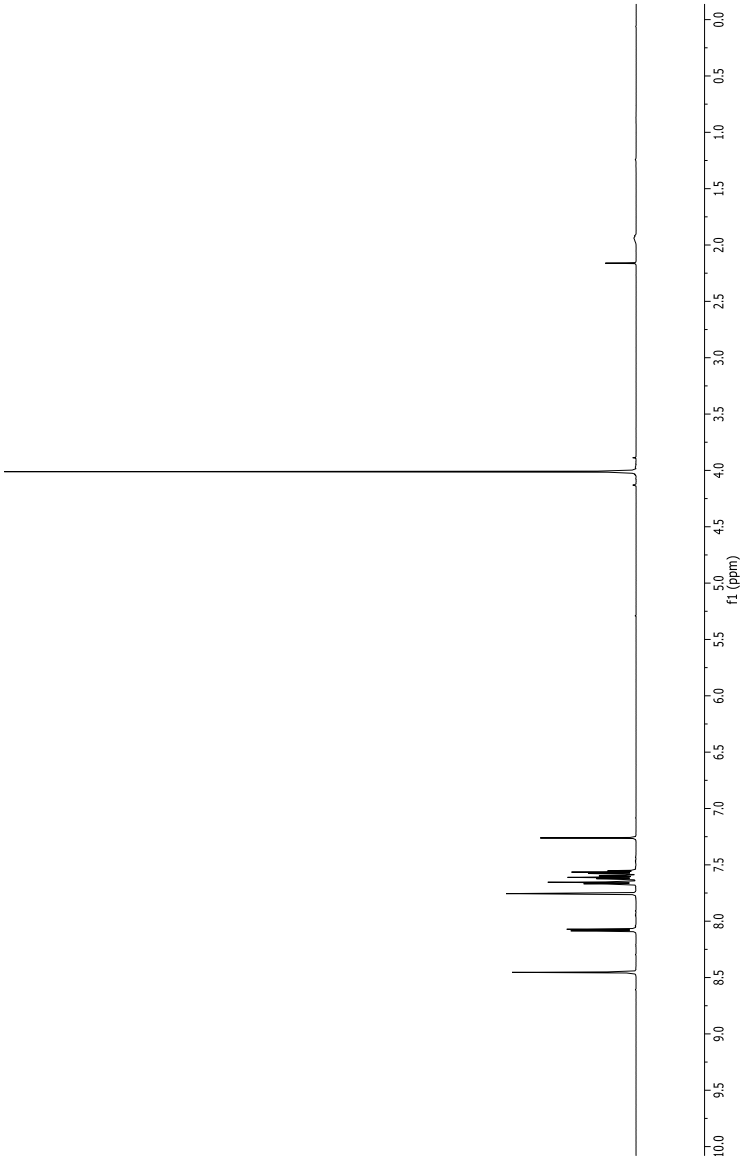



OMe
N+
O-

SI-6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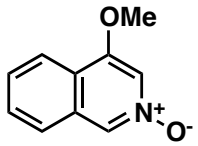
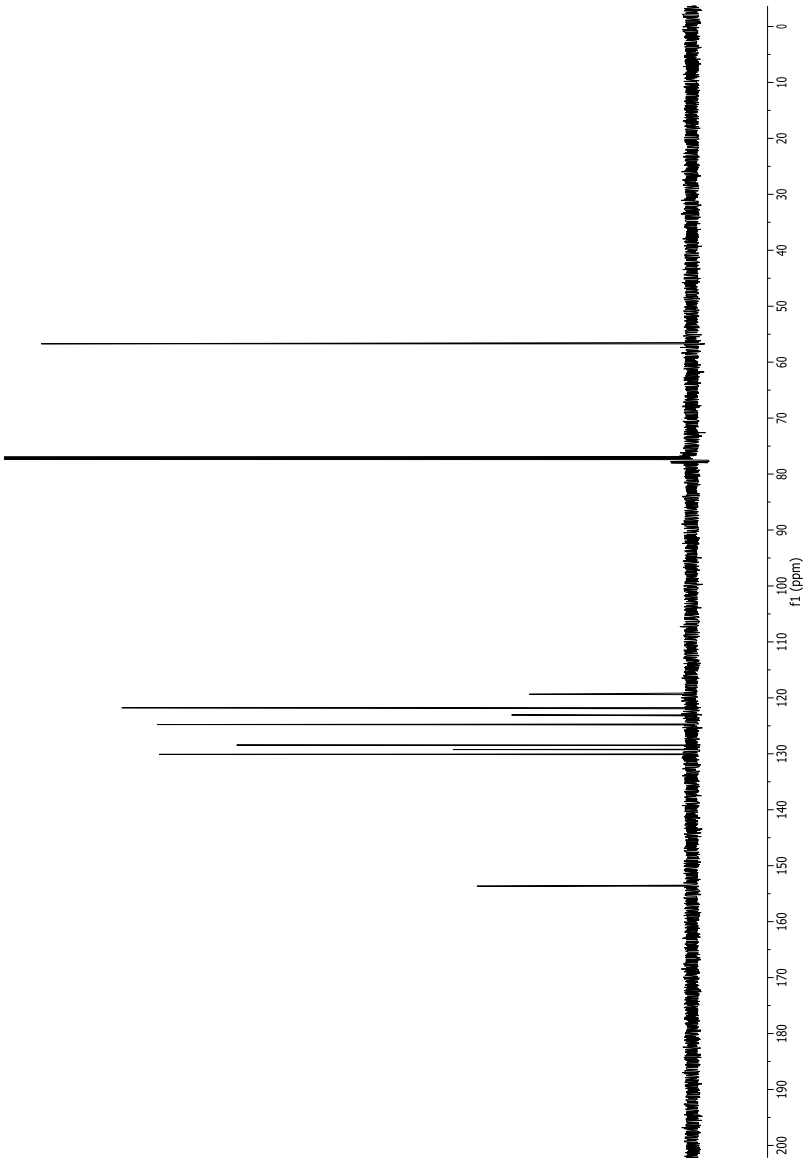
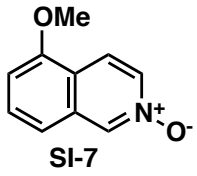


SI-6





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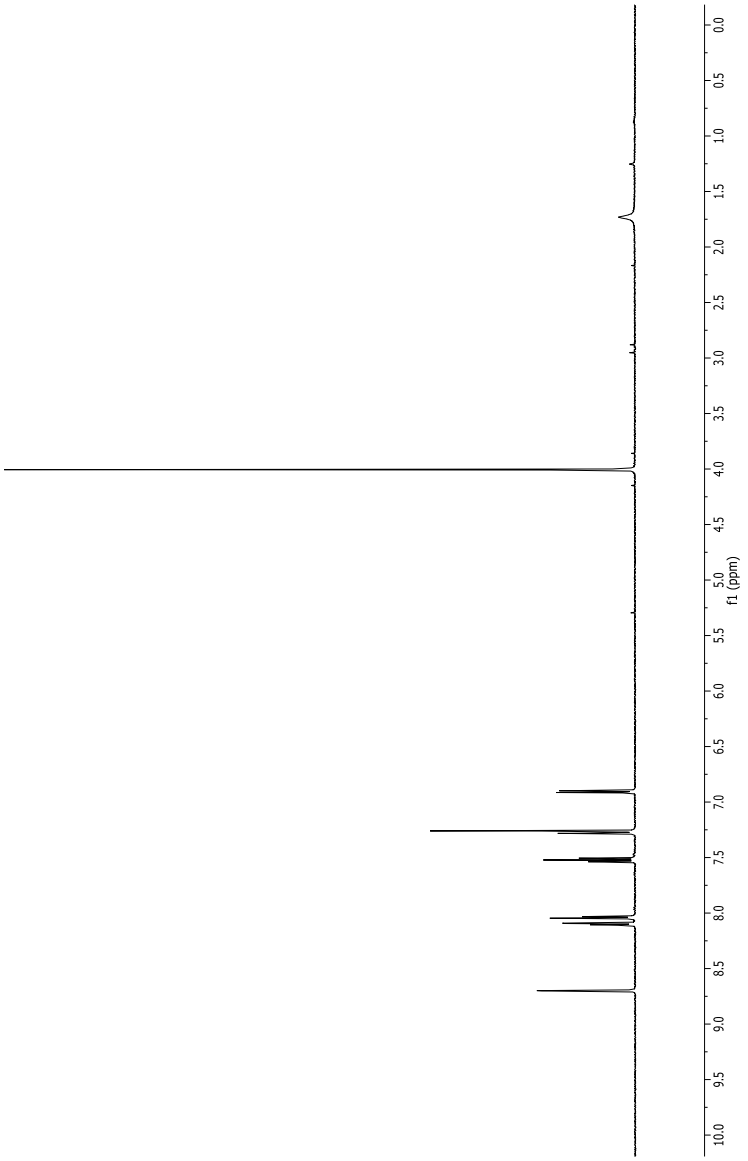

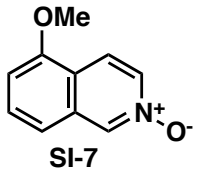

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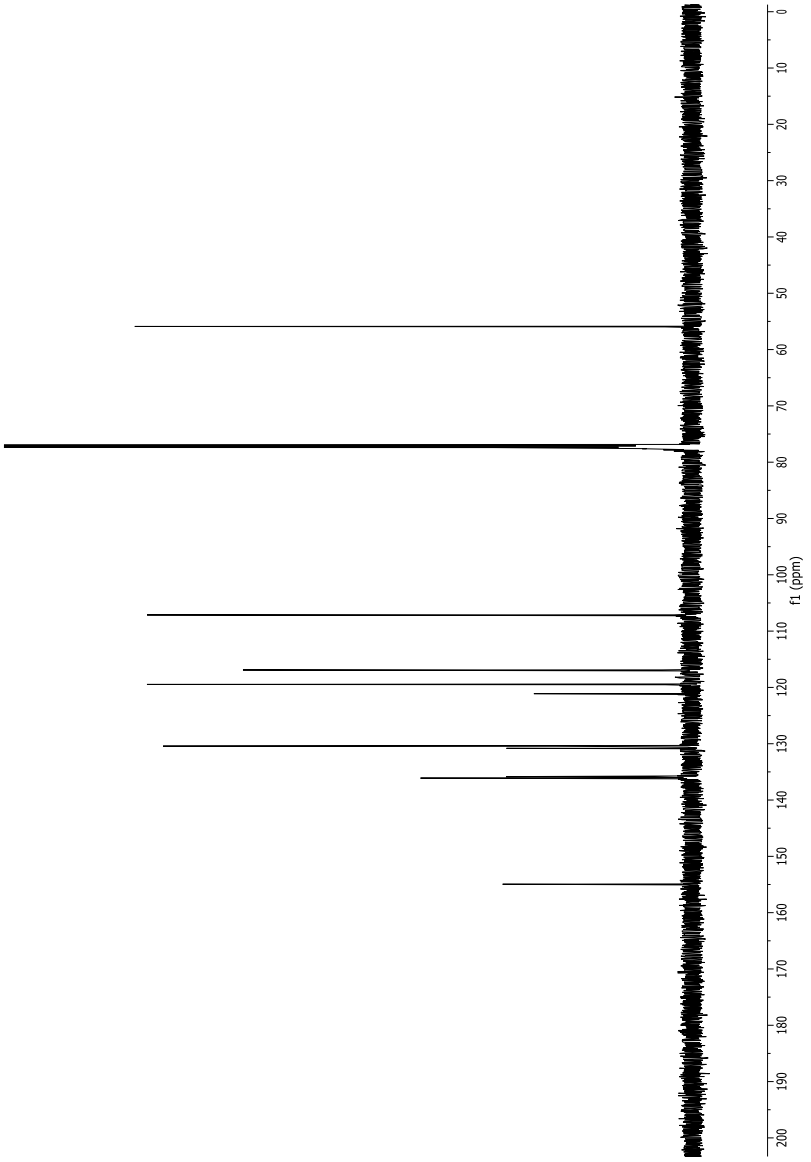

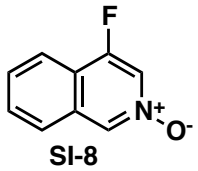

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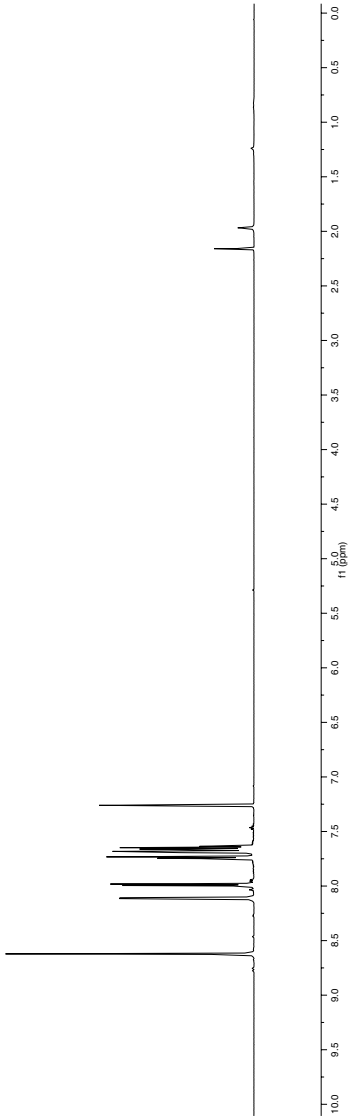

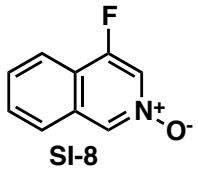

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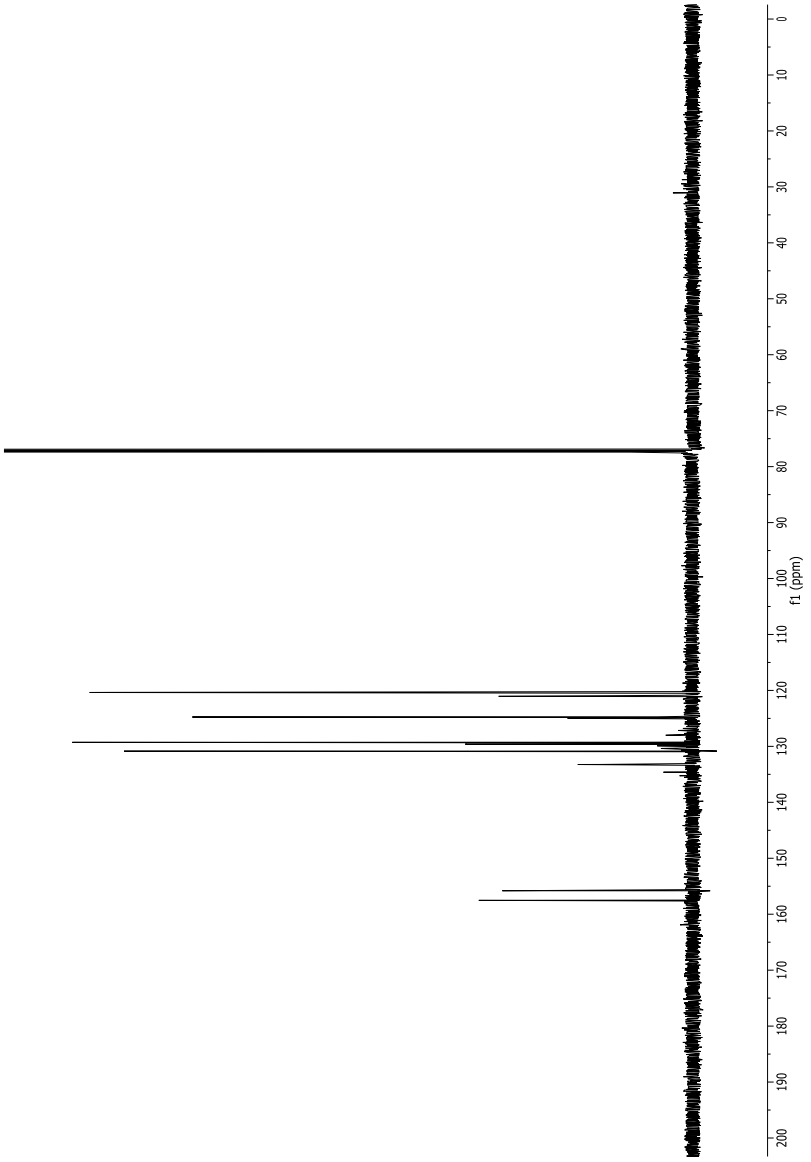

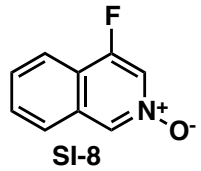
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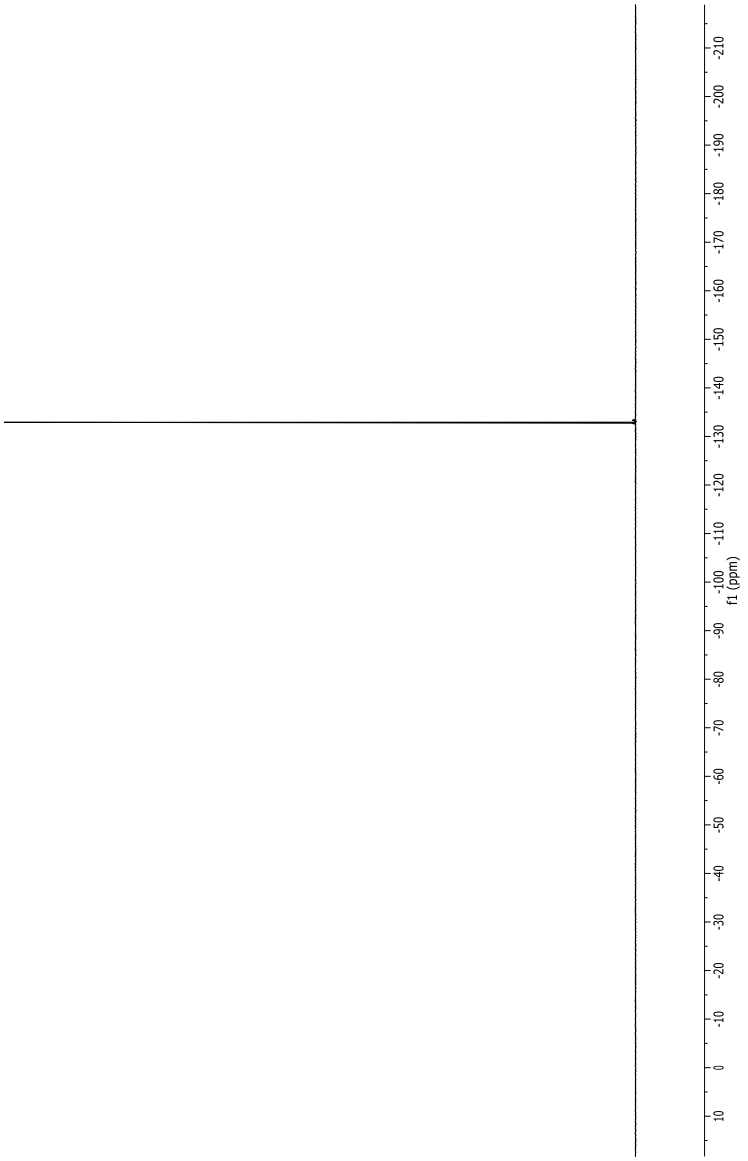
SI-8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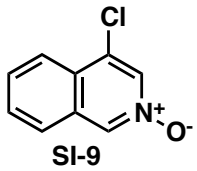

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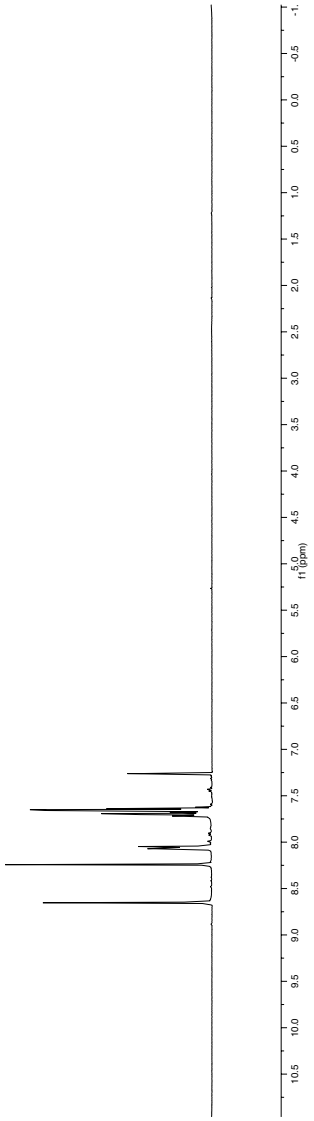

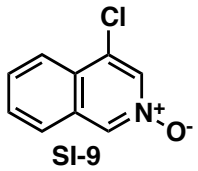

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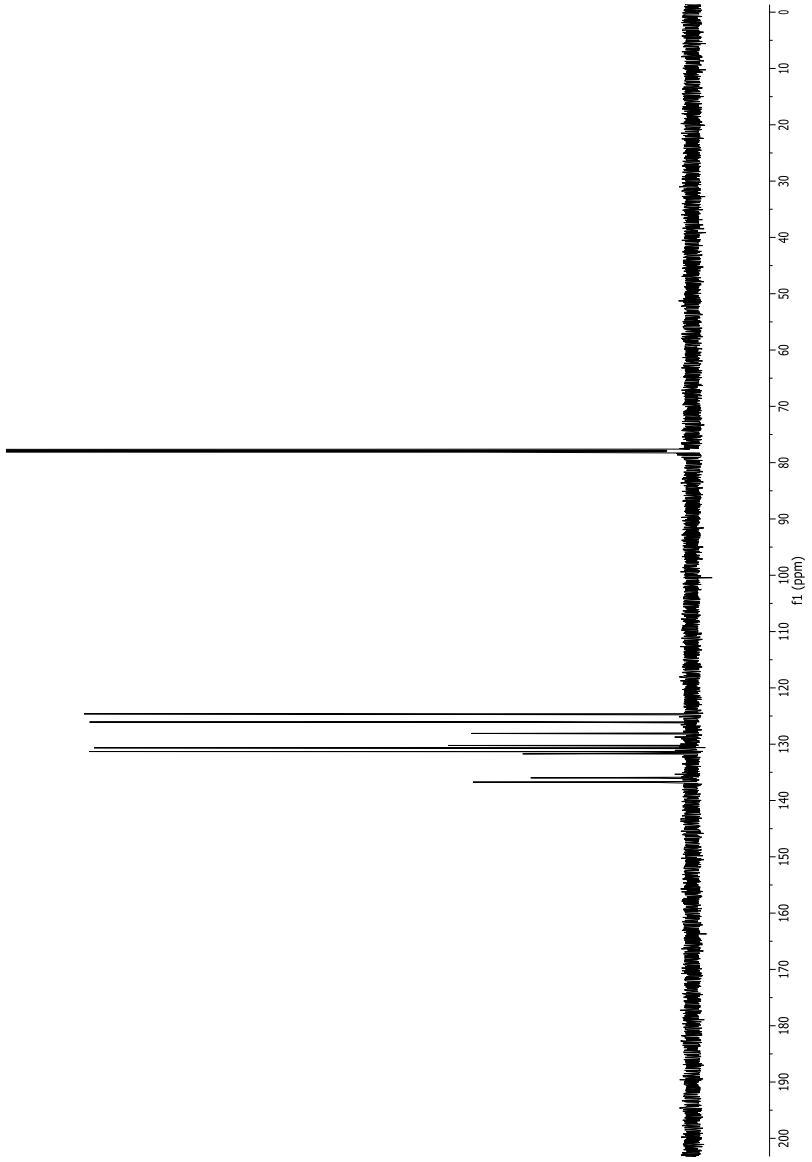

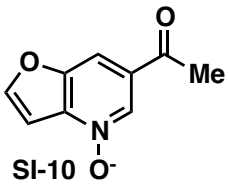

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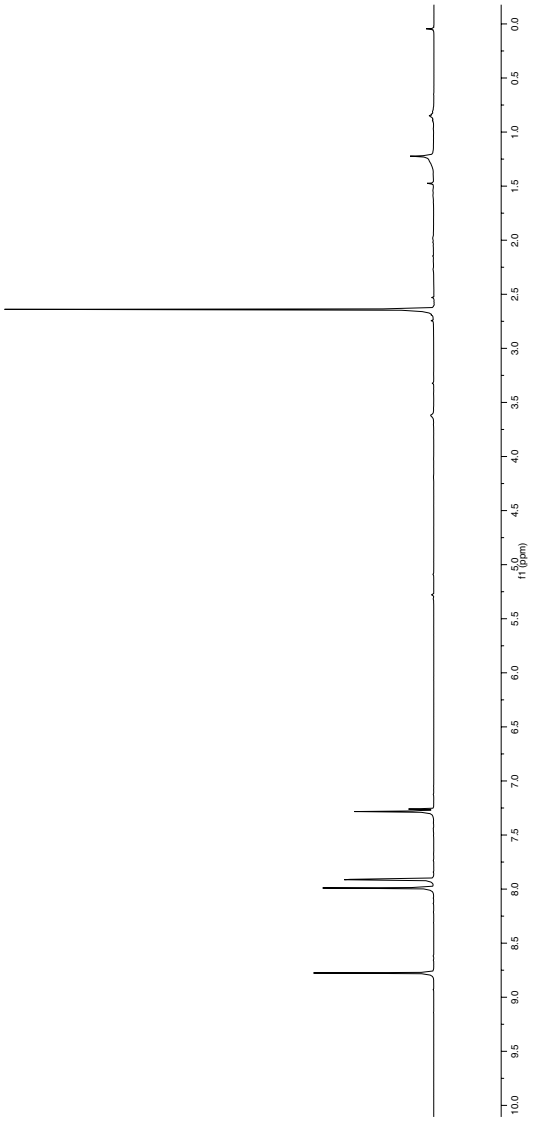

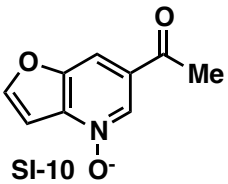

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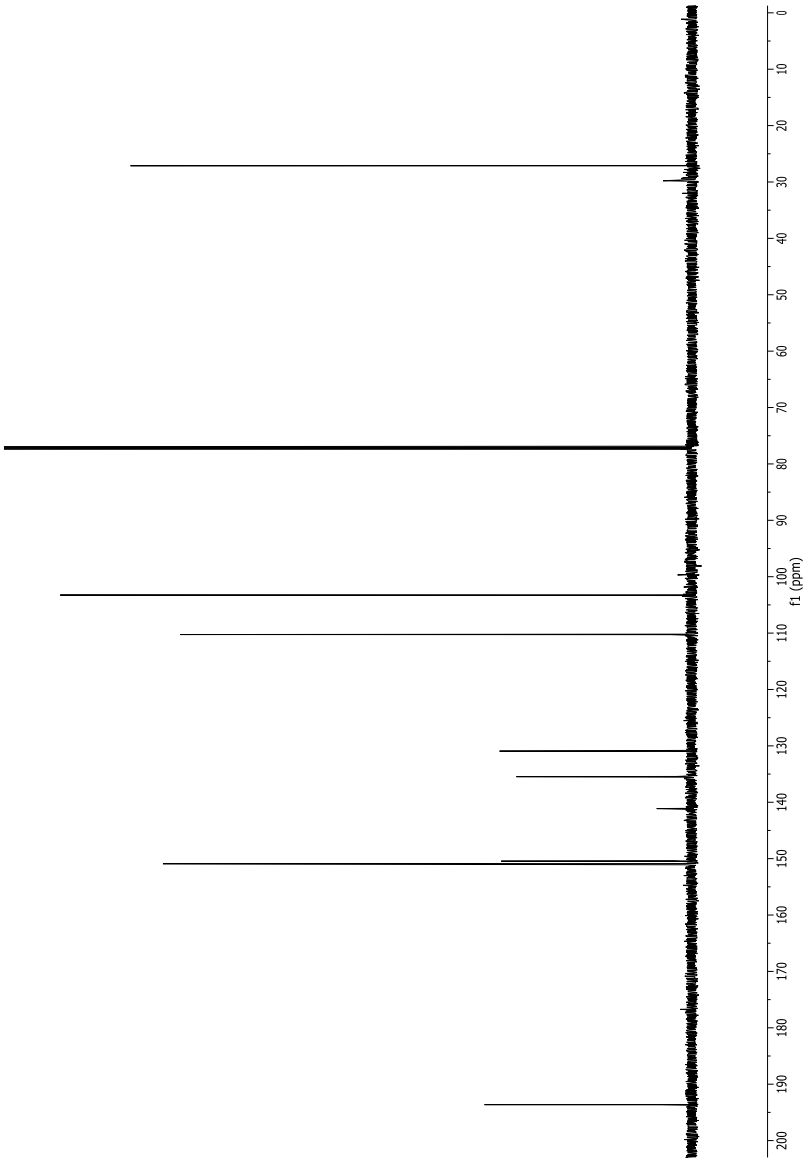

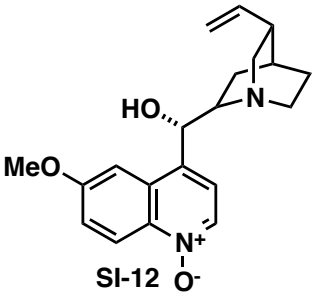

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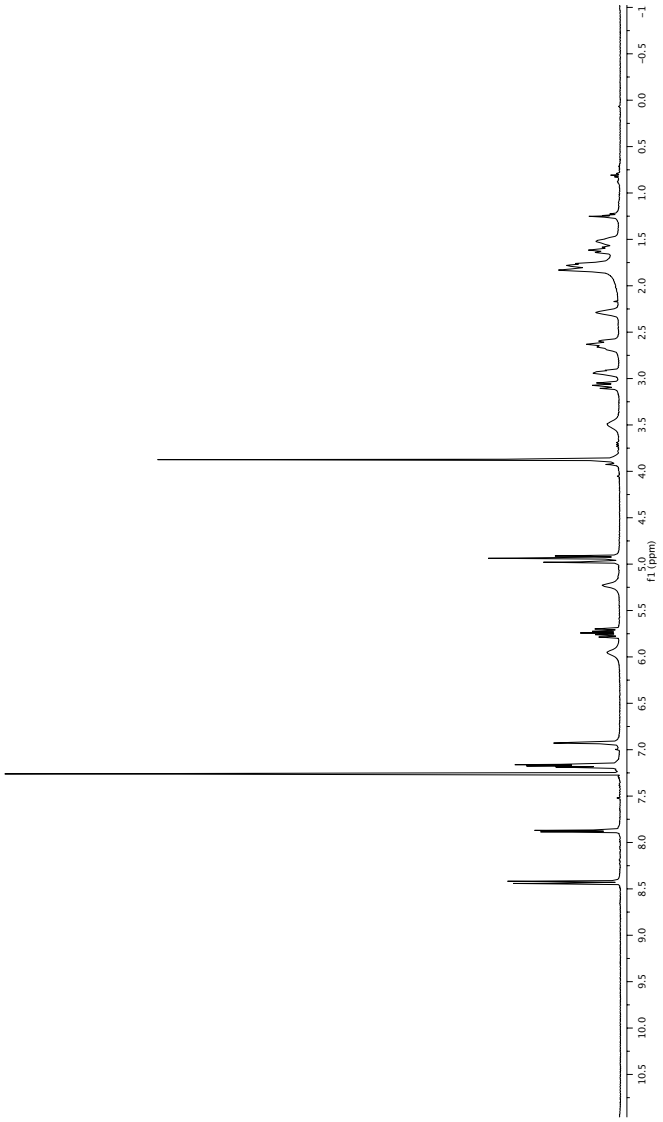

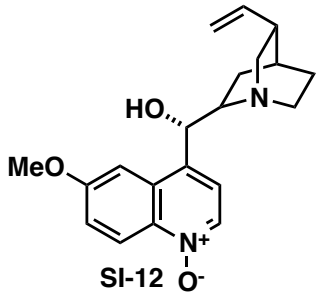

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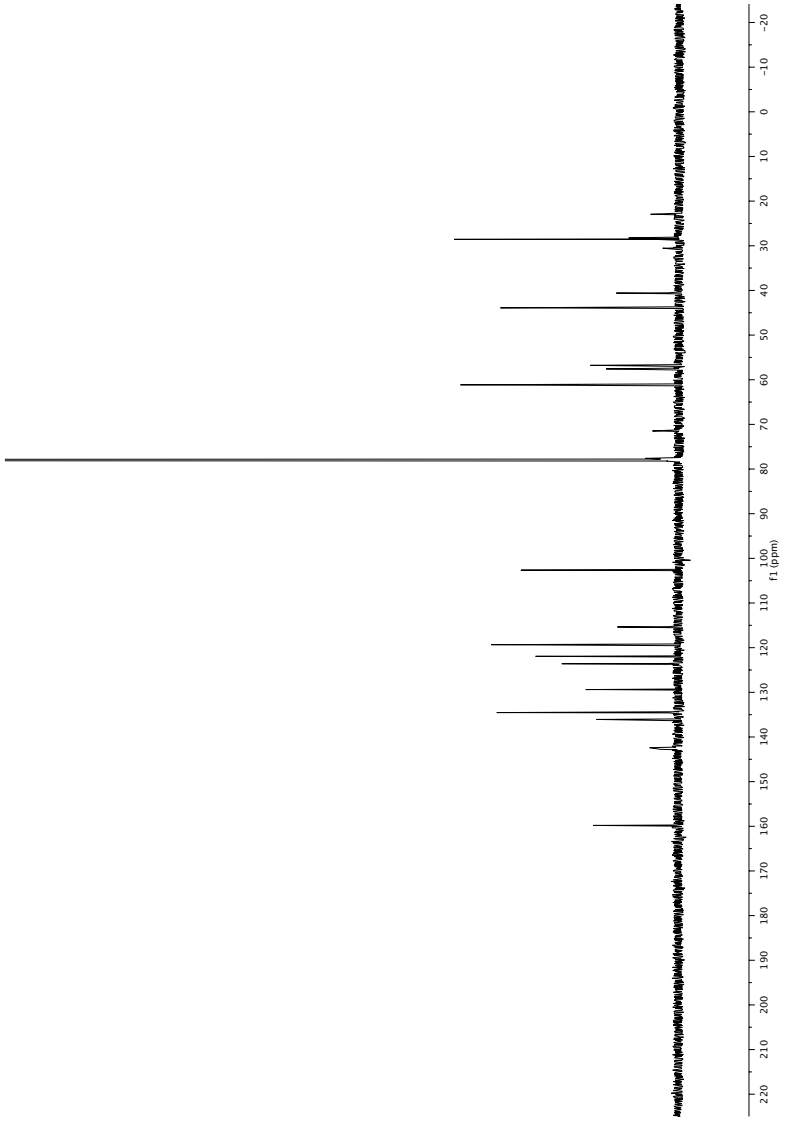

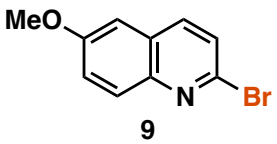

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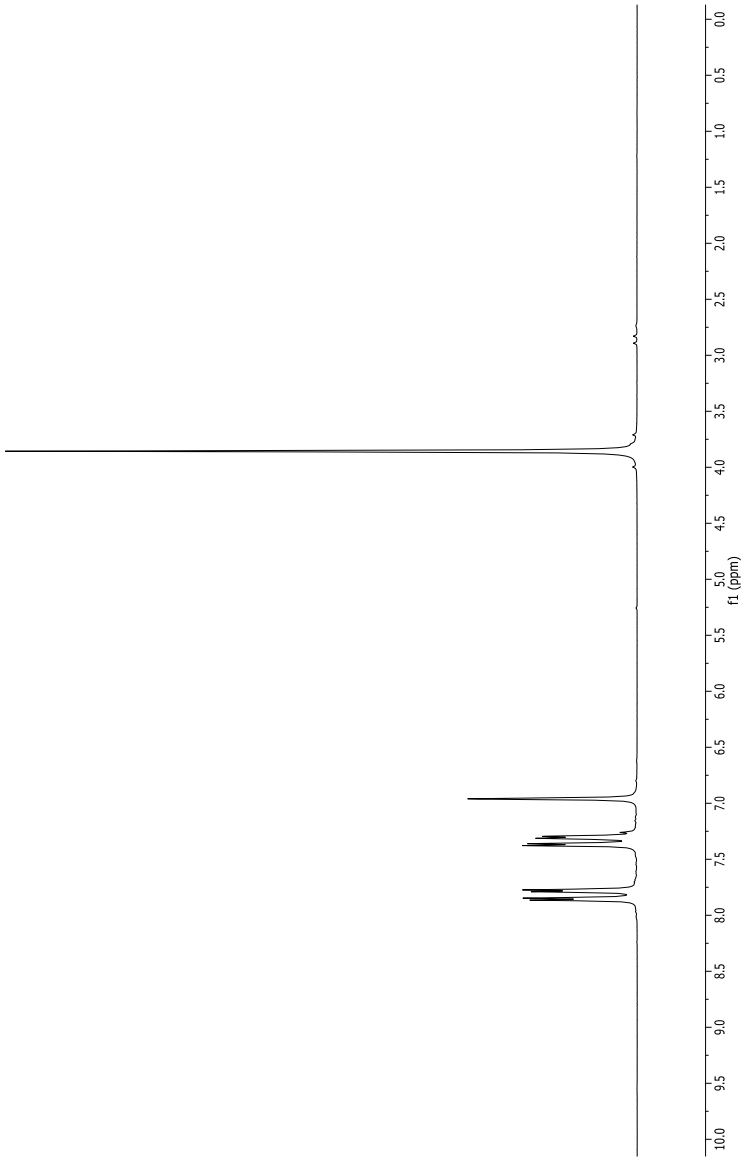

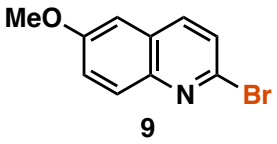

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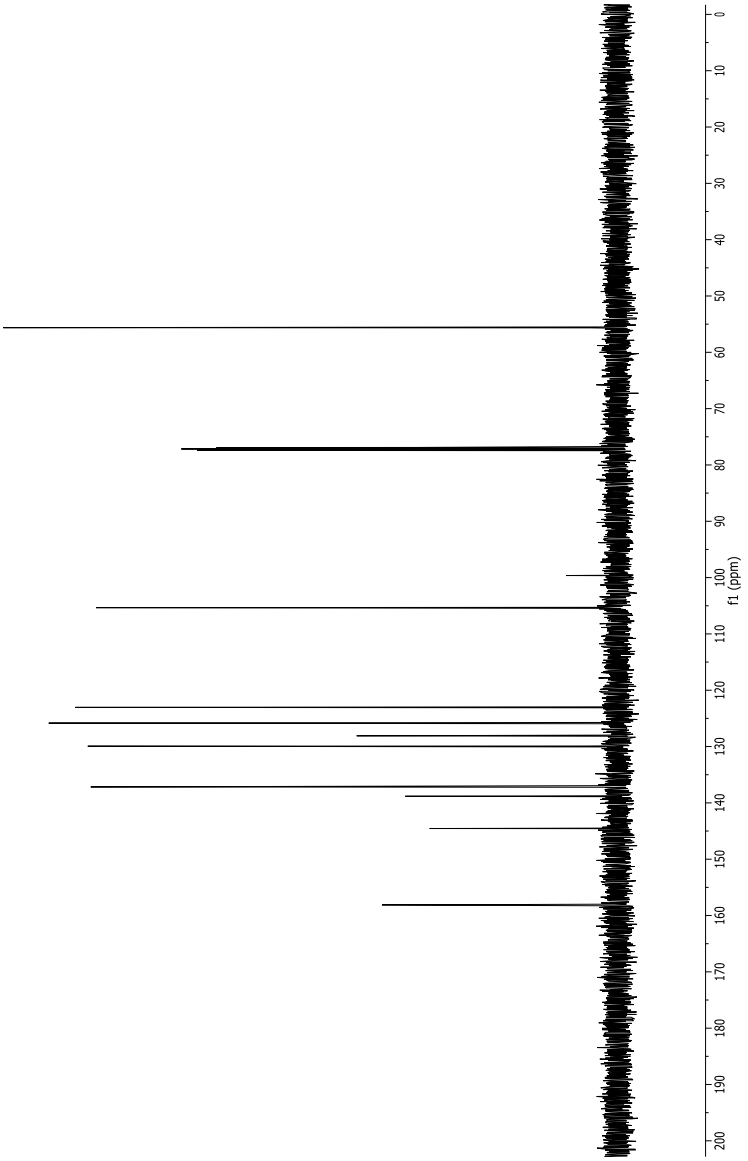

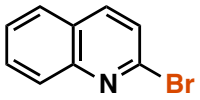

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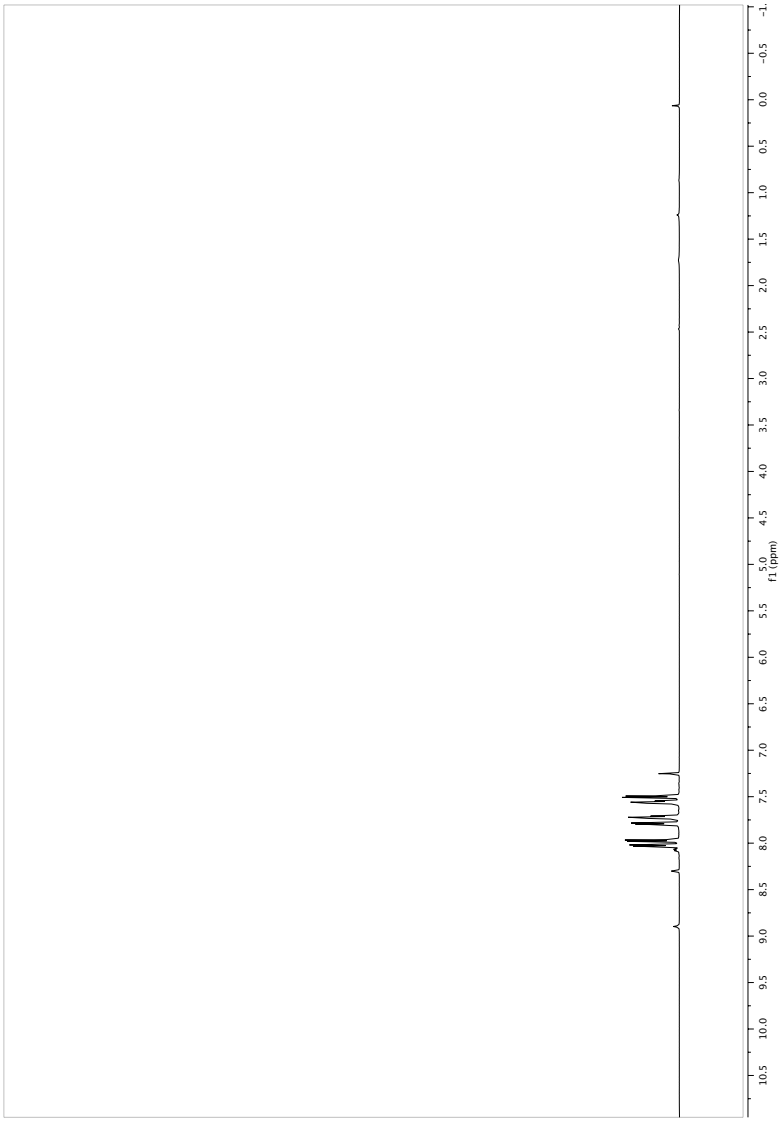

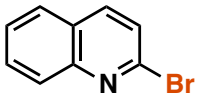

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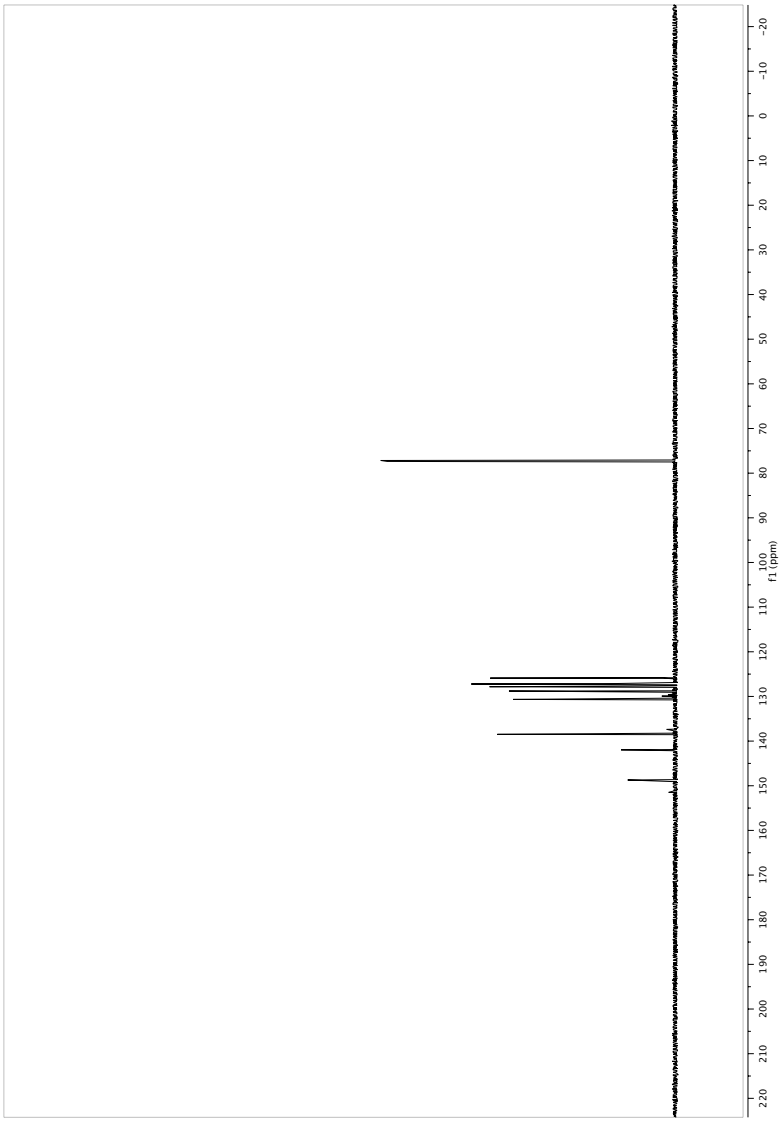

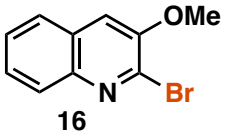
OMe
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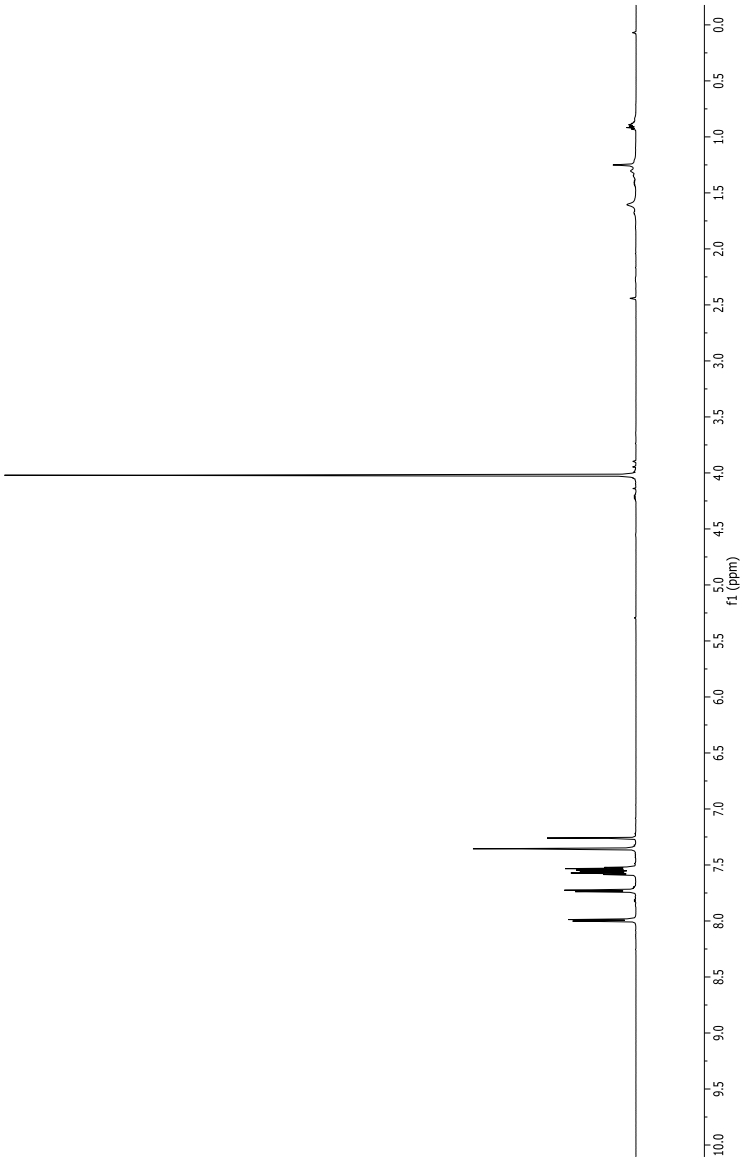
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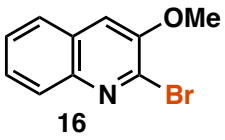
f1 (ppm)



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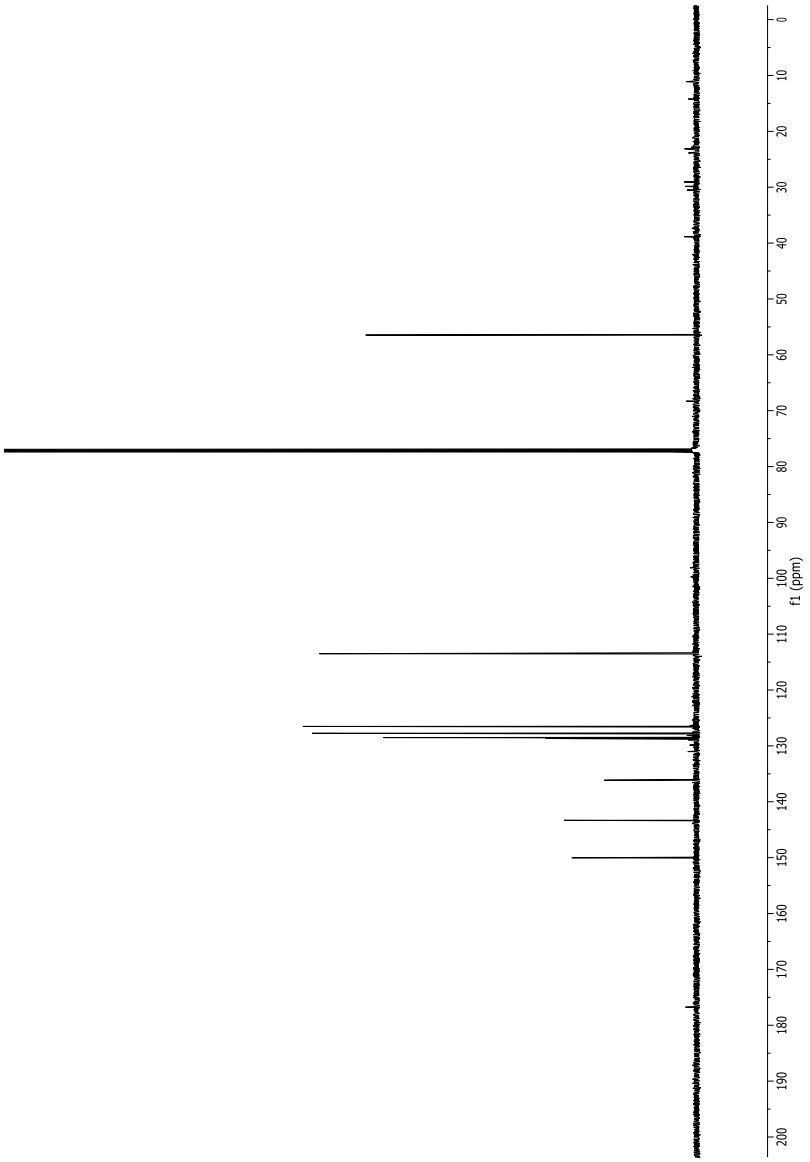

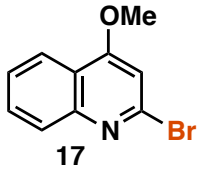

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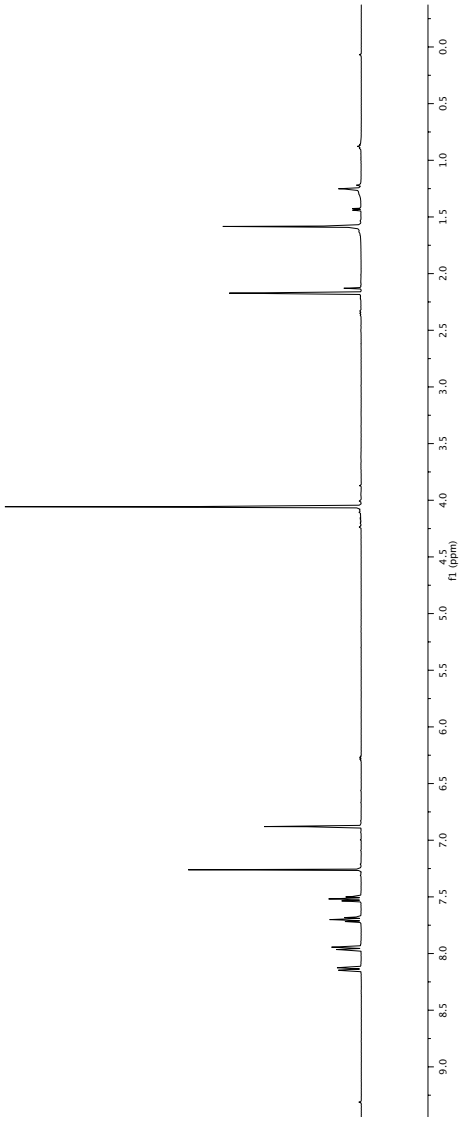

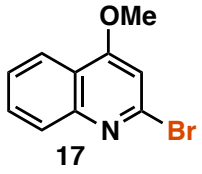

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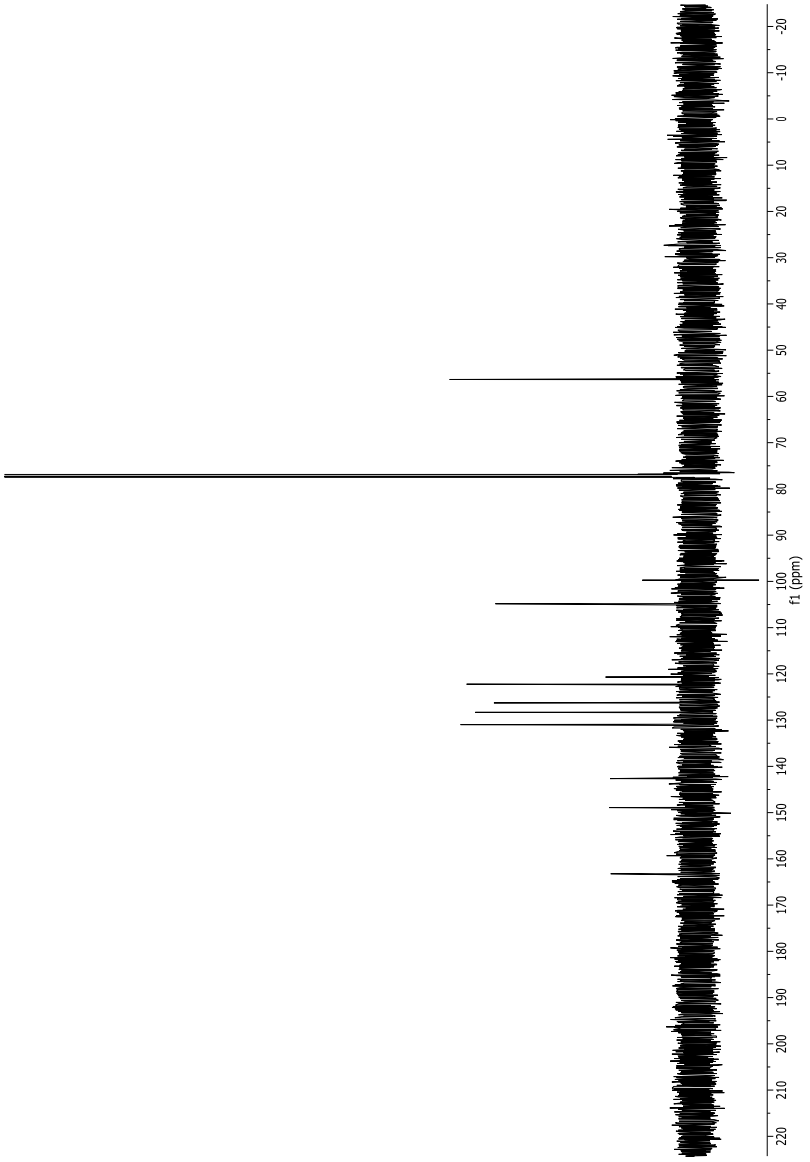

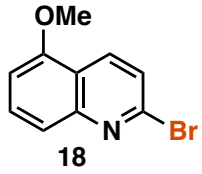

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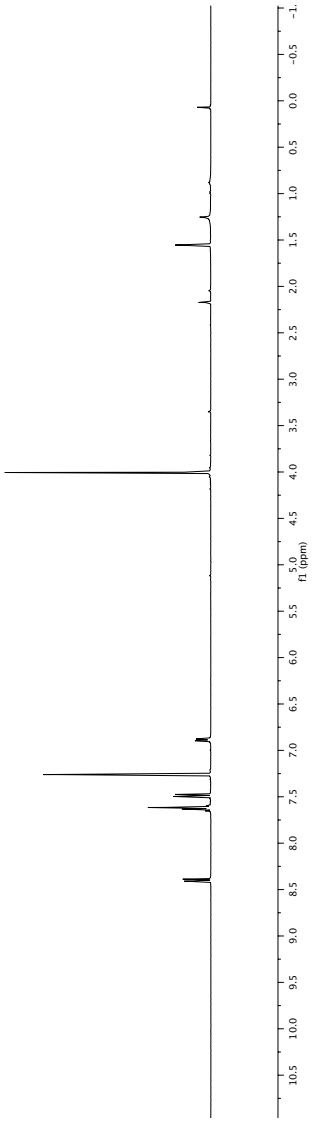

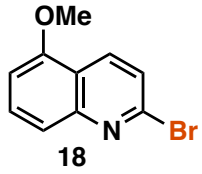

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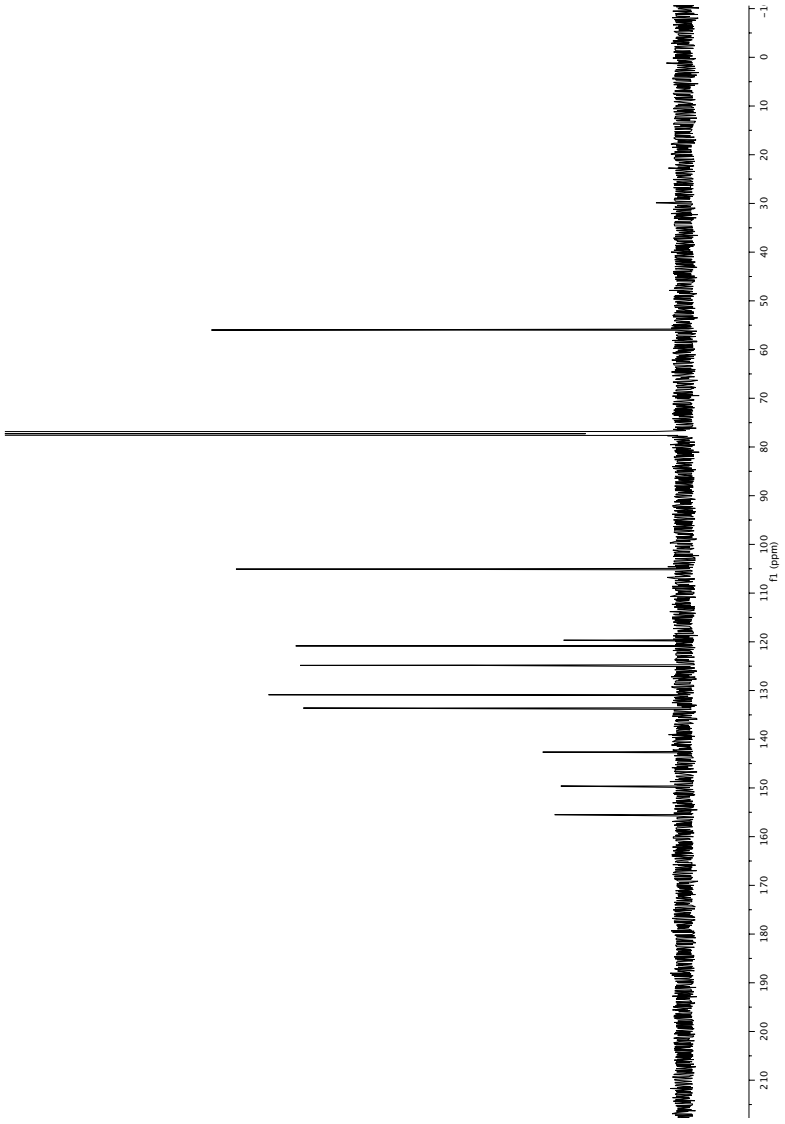

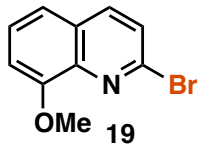

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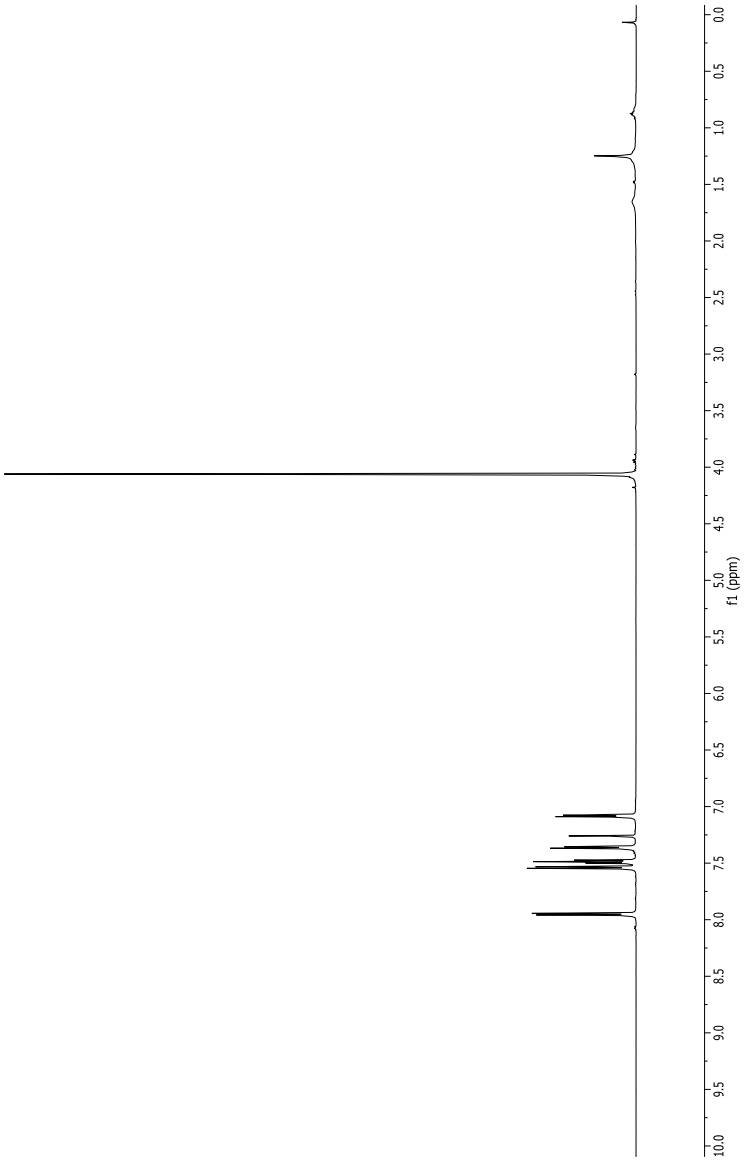

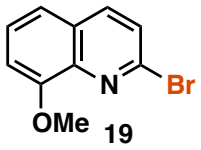

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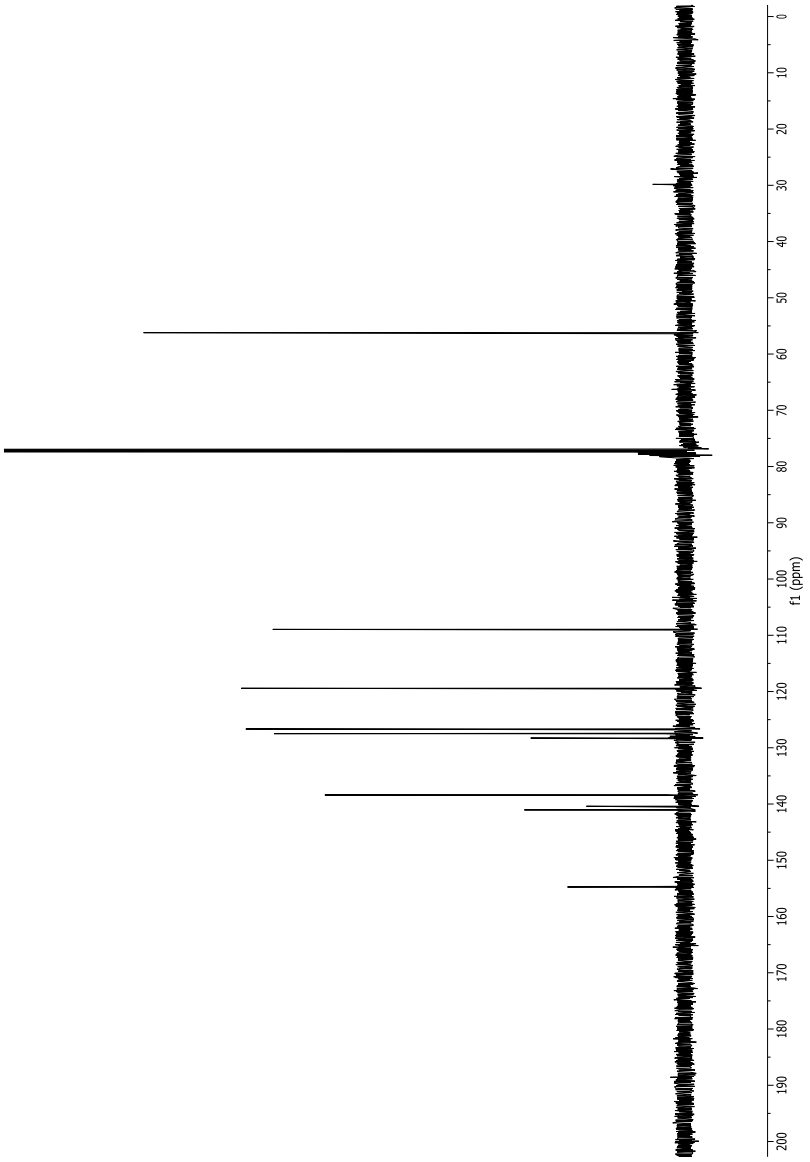

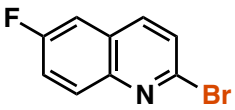

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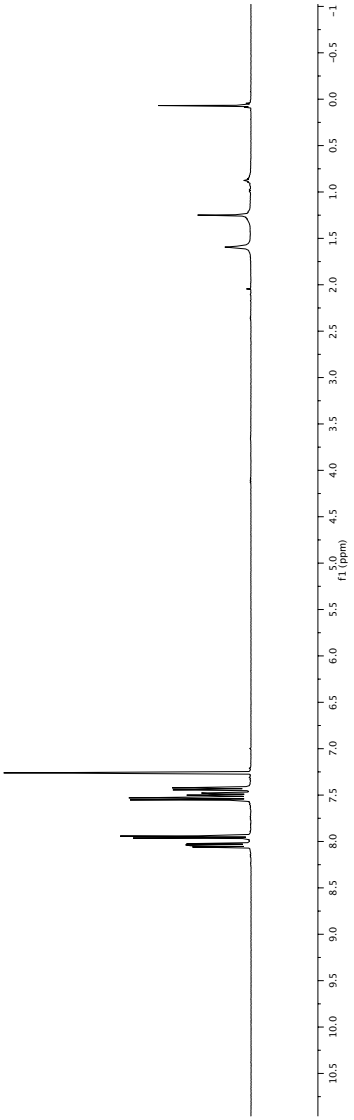

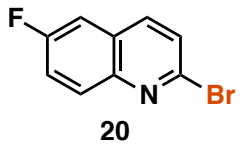
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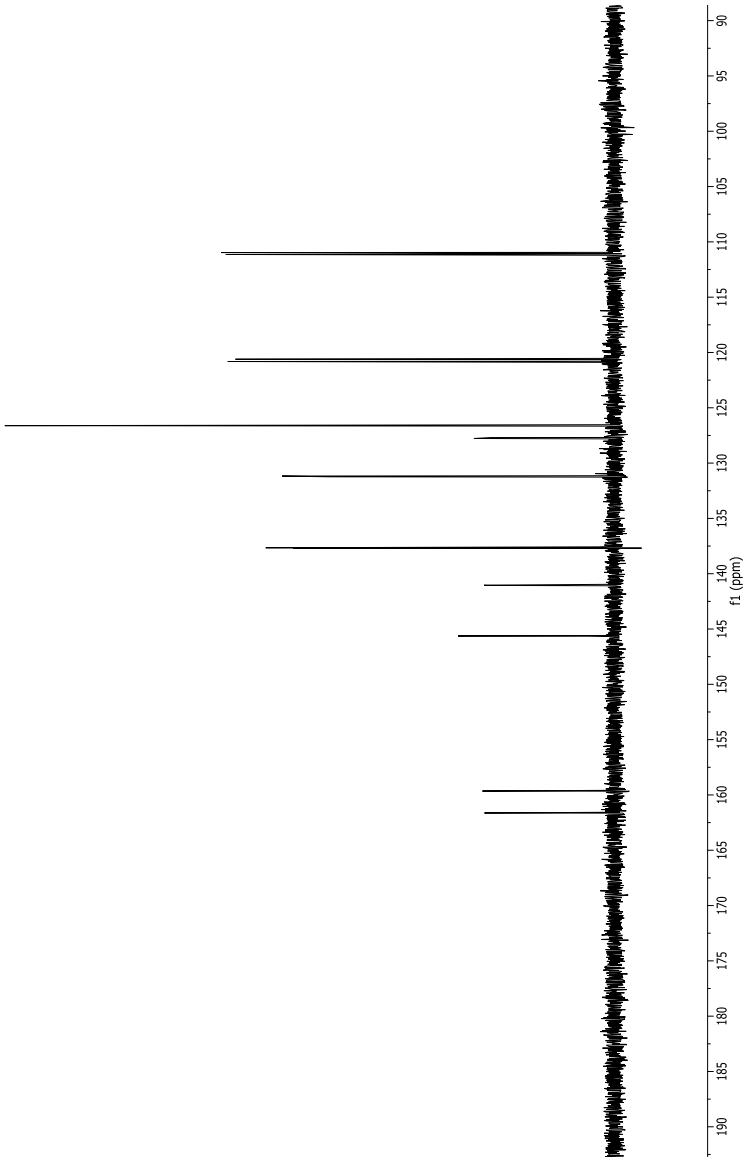
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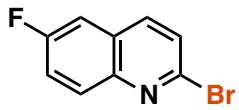

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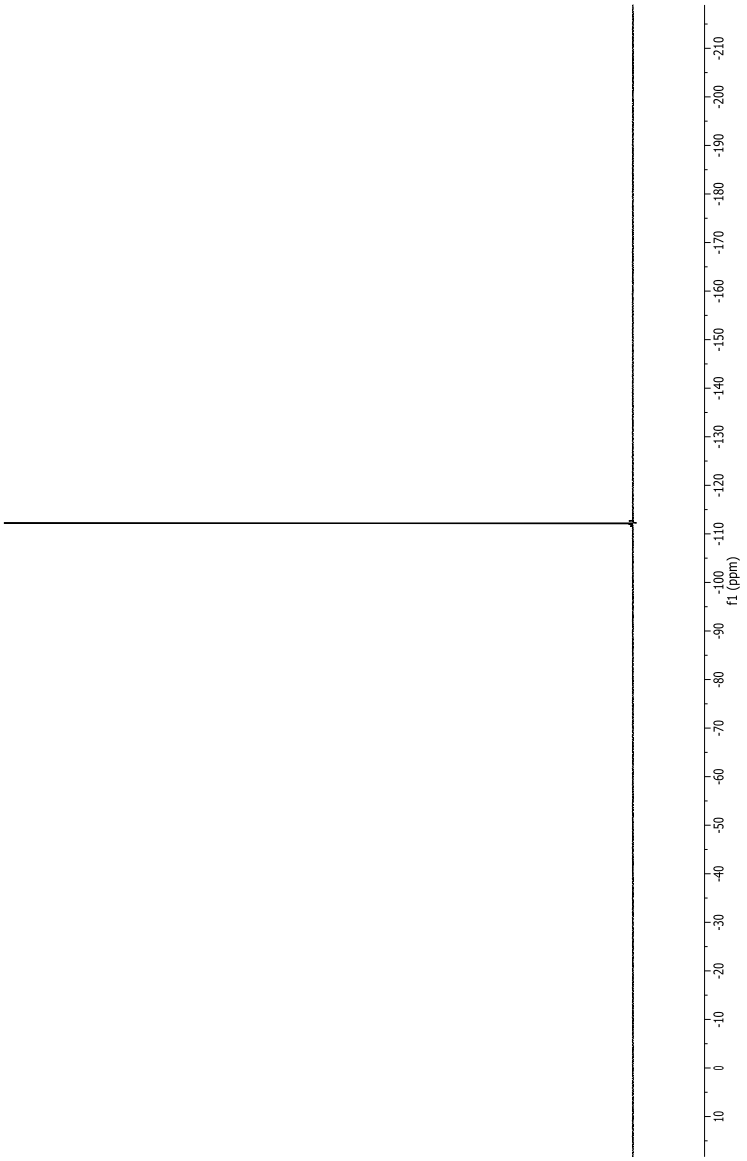

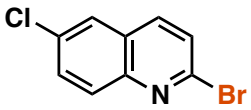

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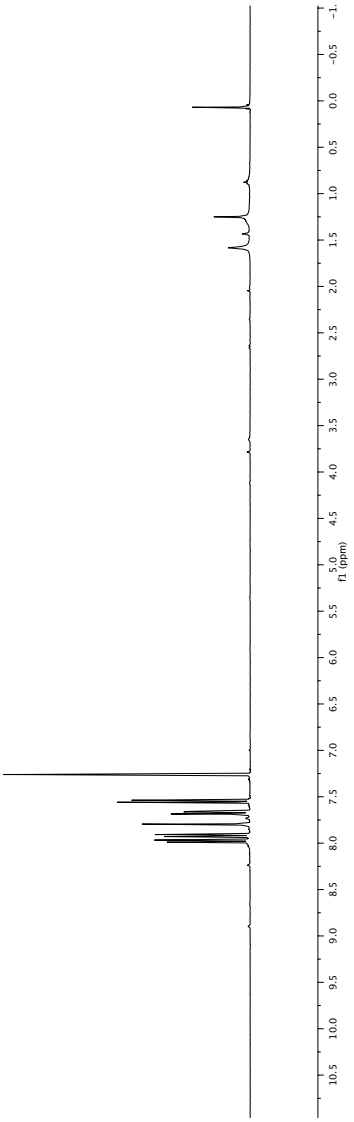

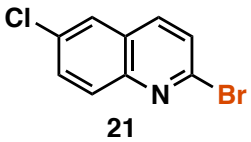

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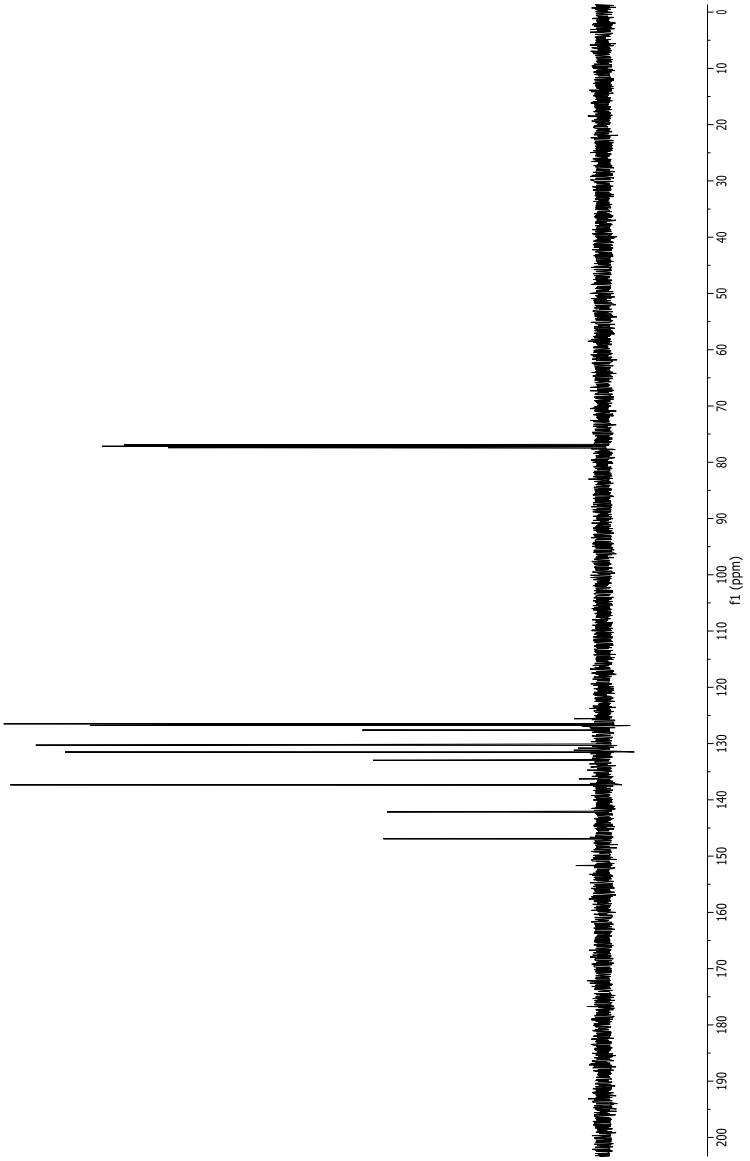

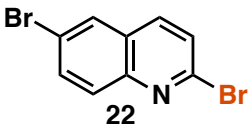

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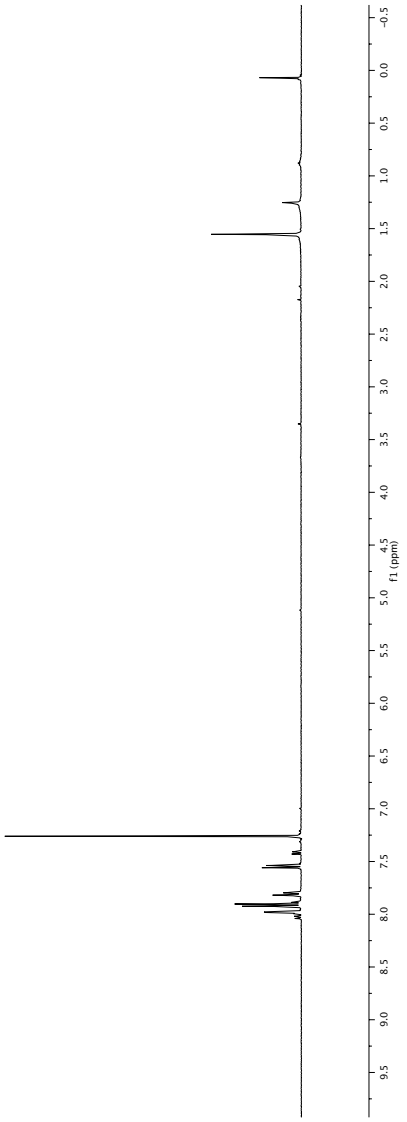

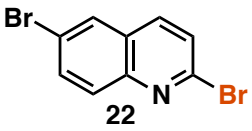

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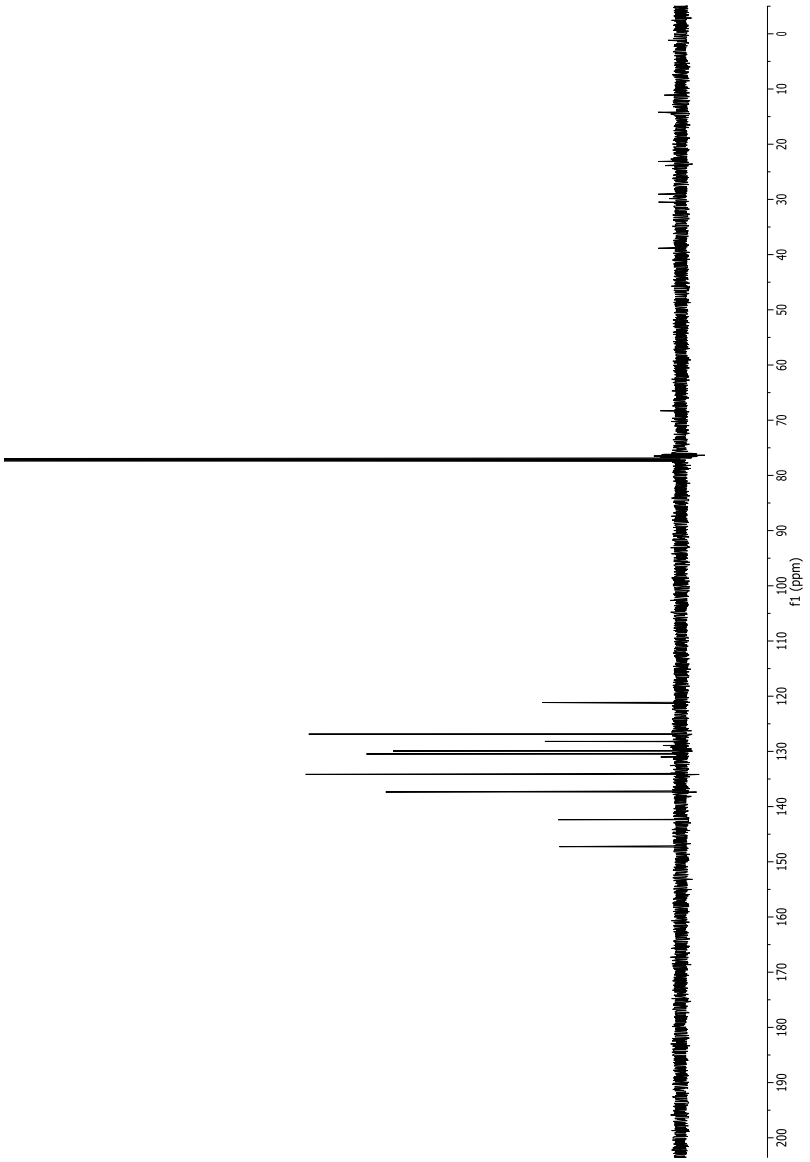

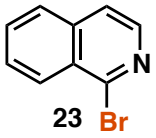
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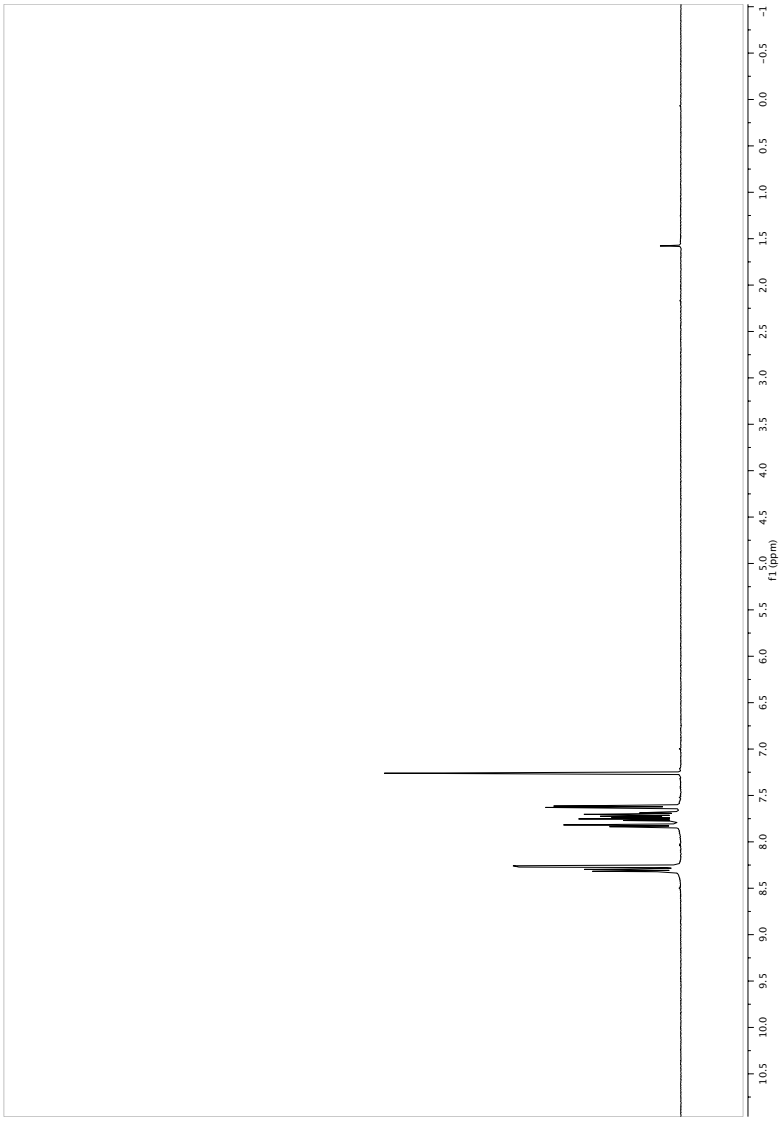
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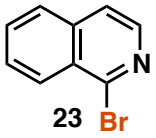
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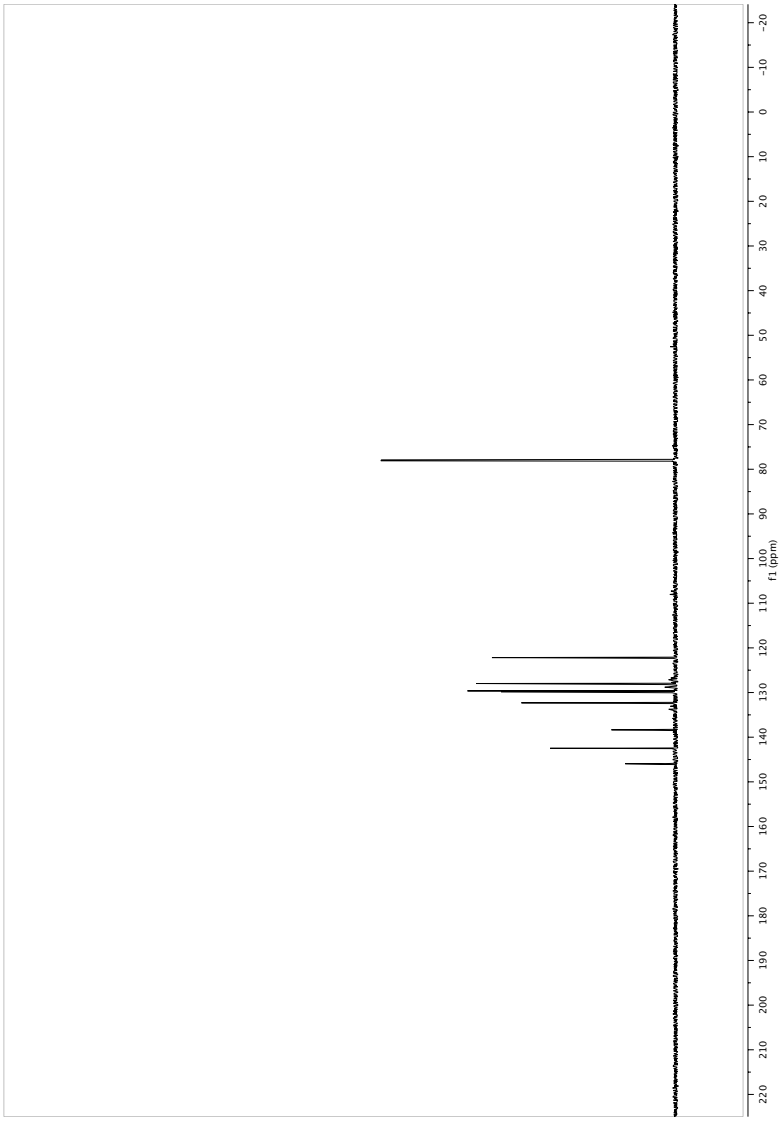
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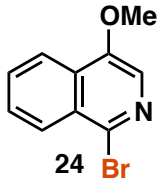
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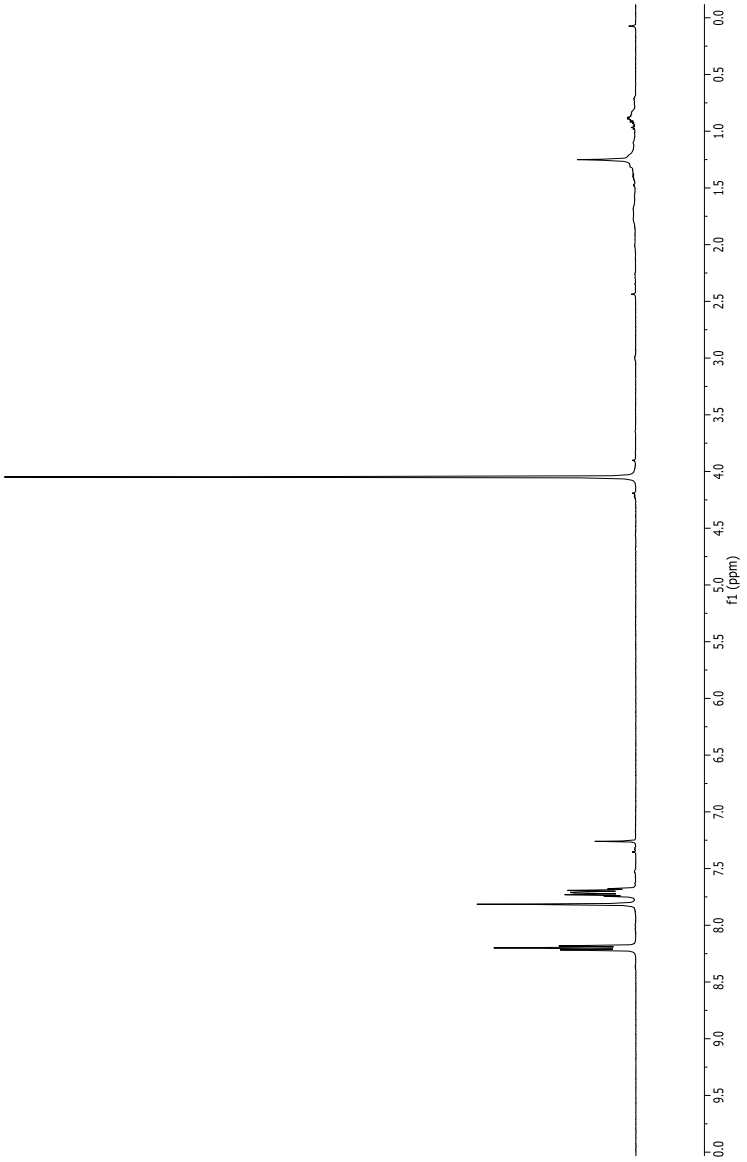
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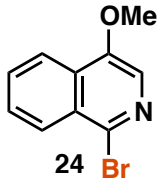
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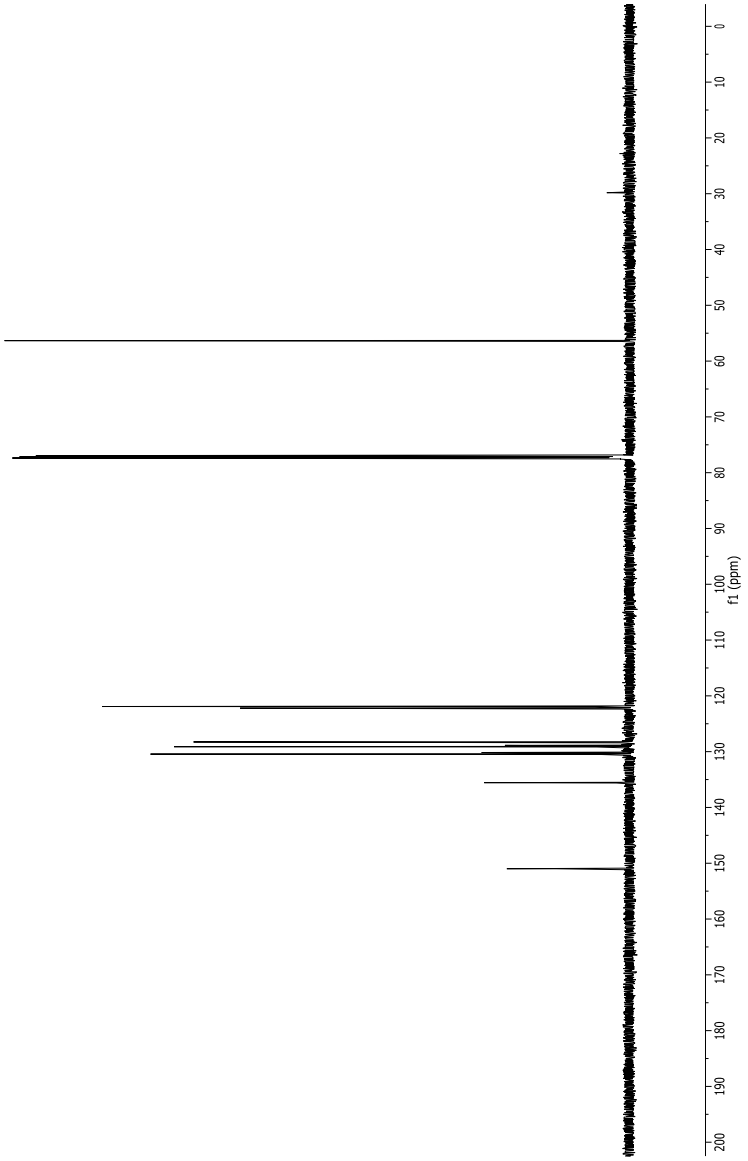
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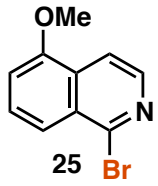
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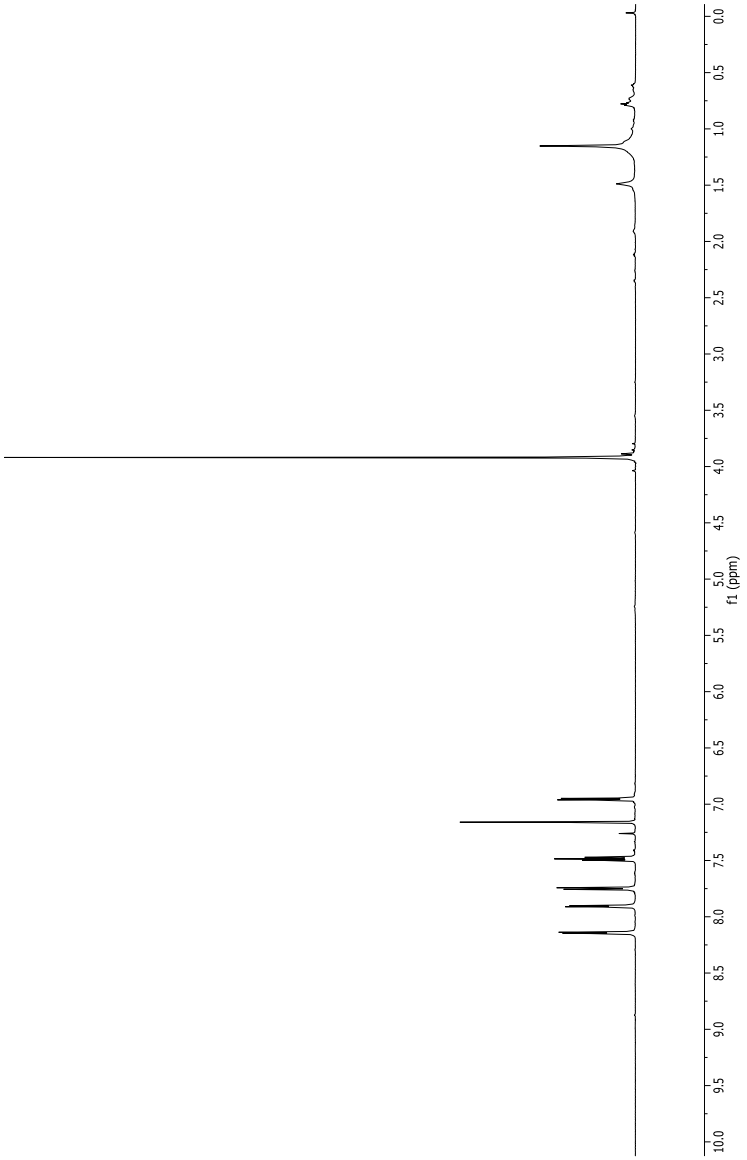
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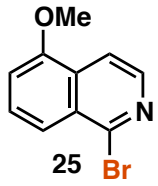
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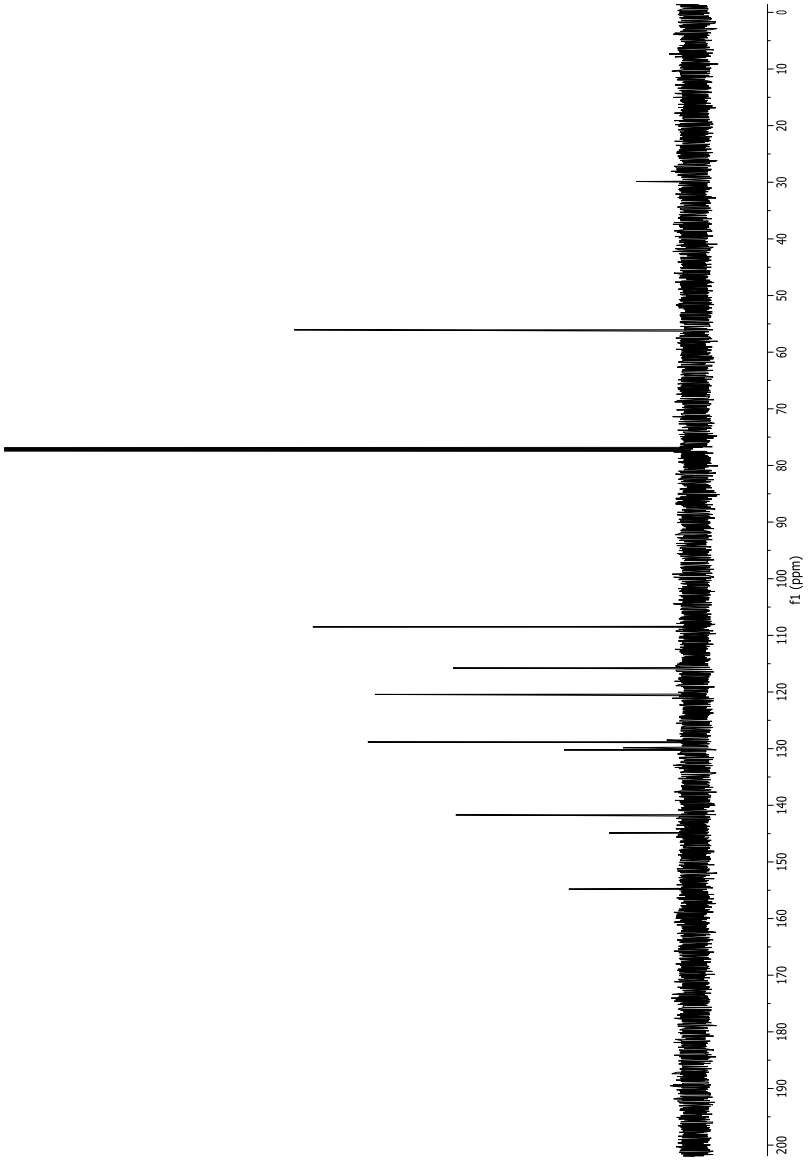
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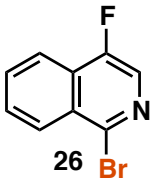
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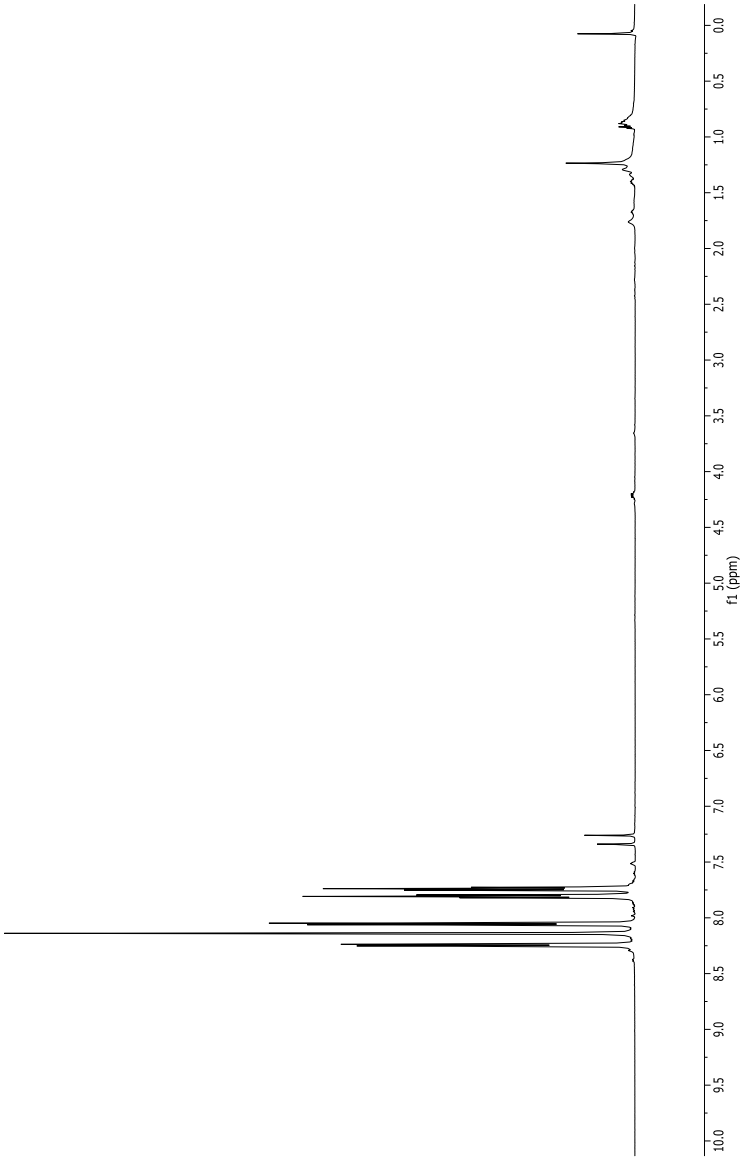
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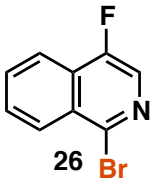
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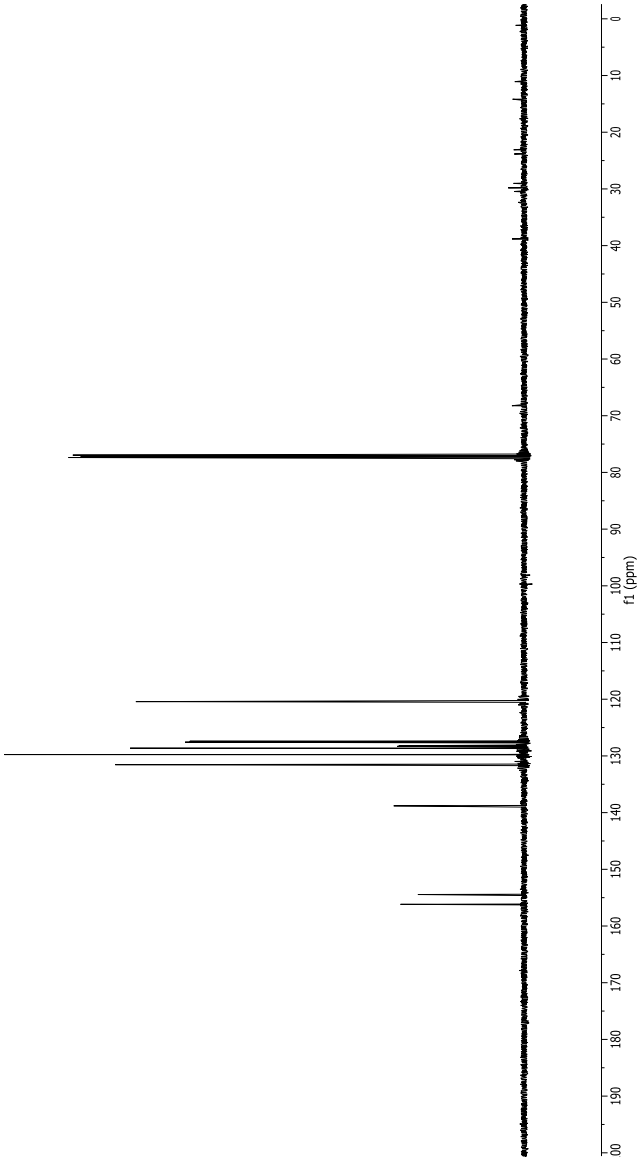
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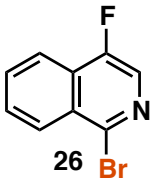
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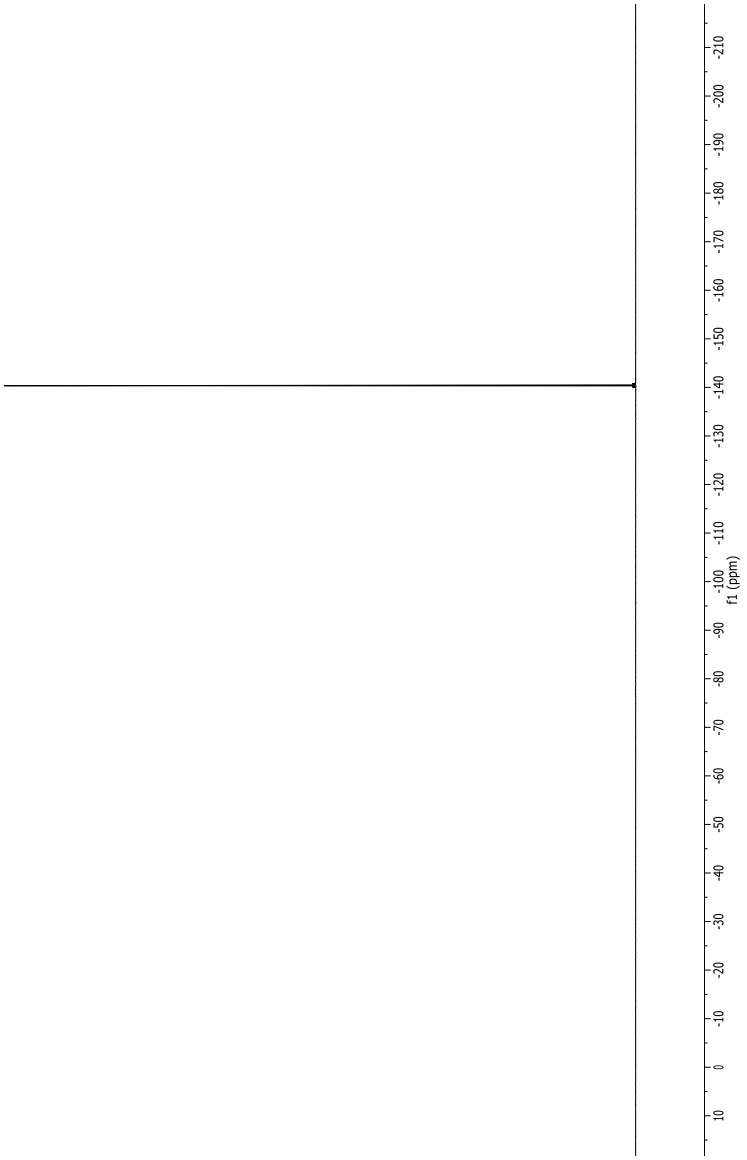
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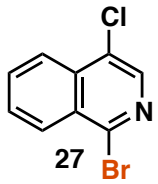
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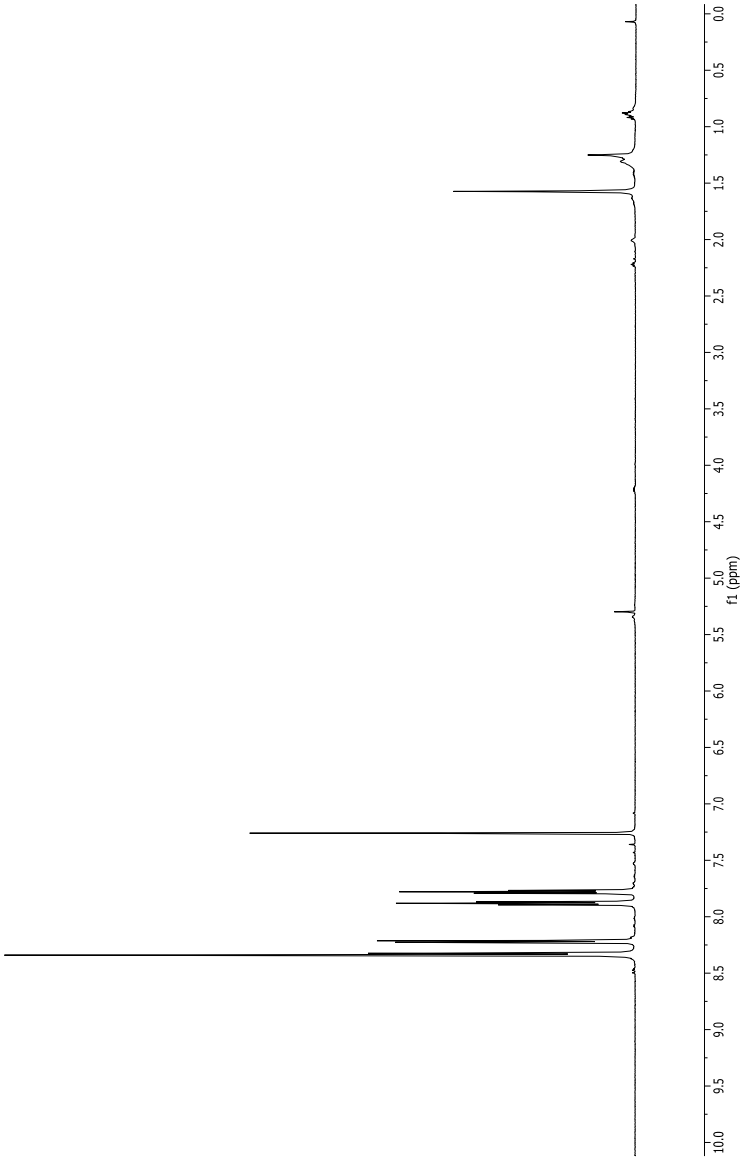
27
Br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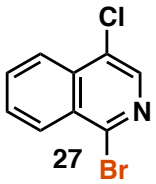
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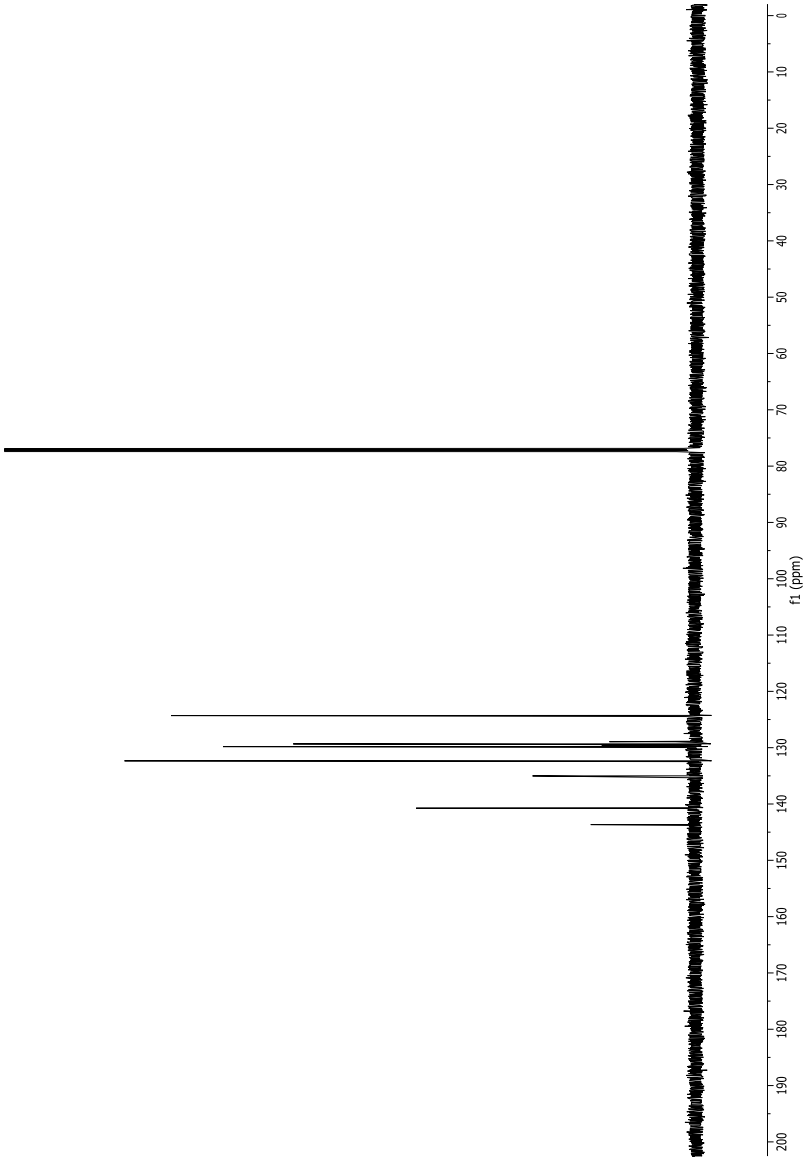
Br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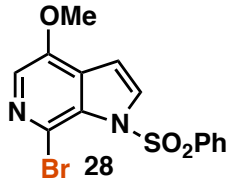
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SO2Ph
Br

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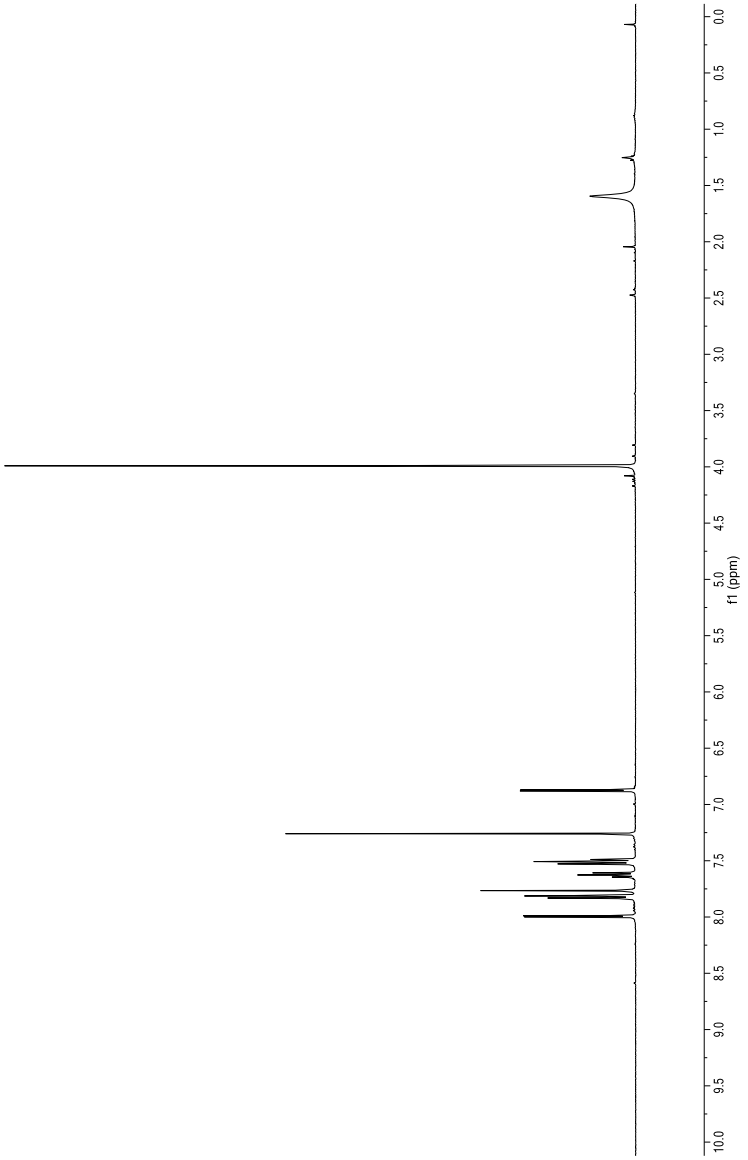
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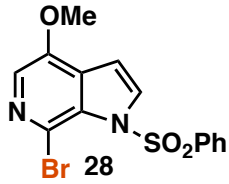

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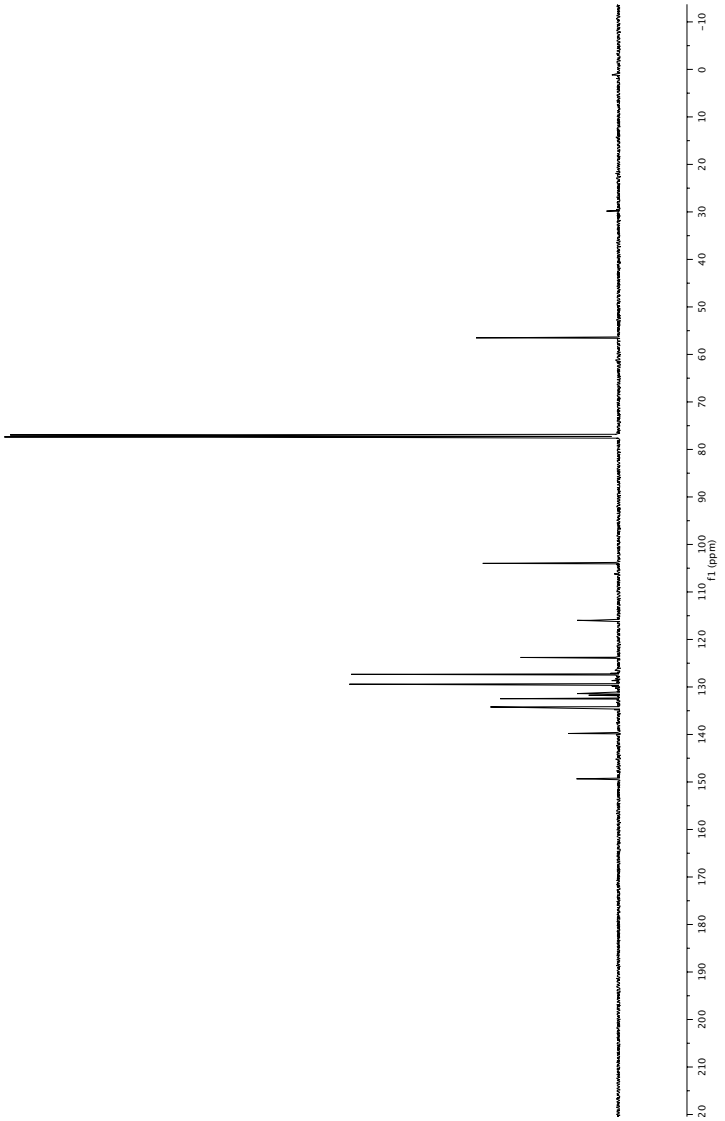

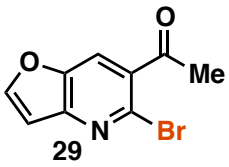

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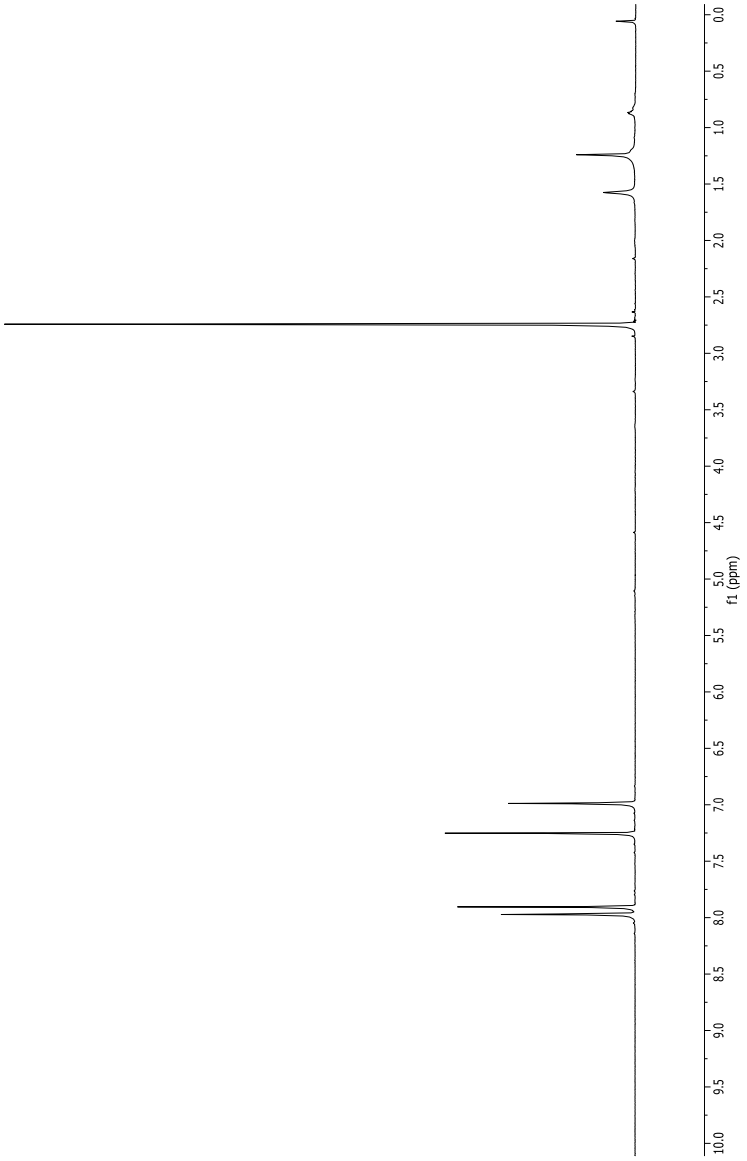

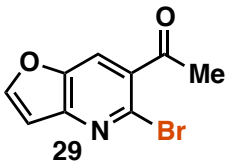
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Me
O
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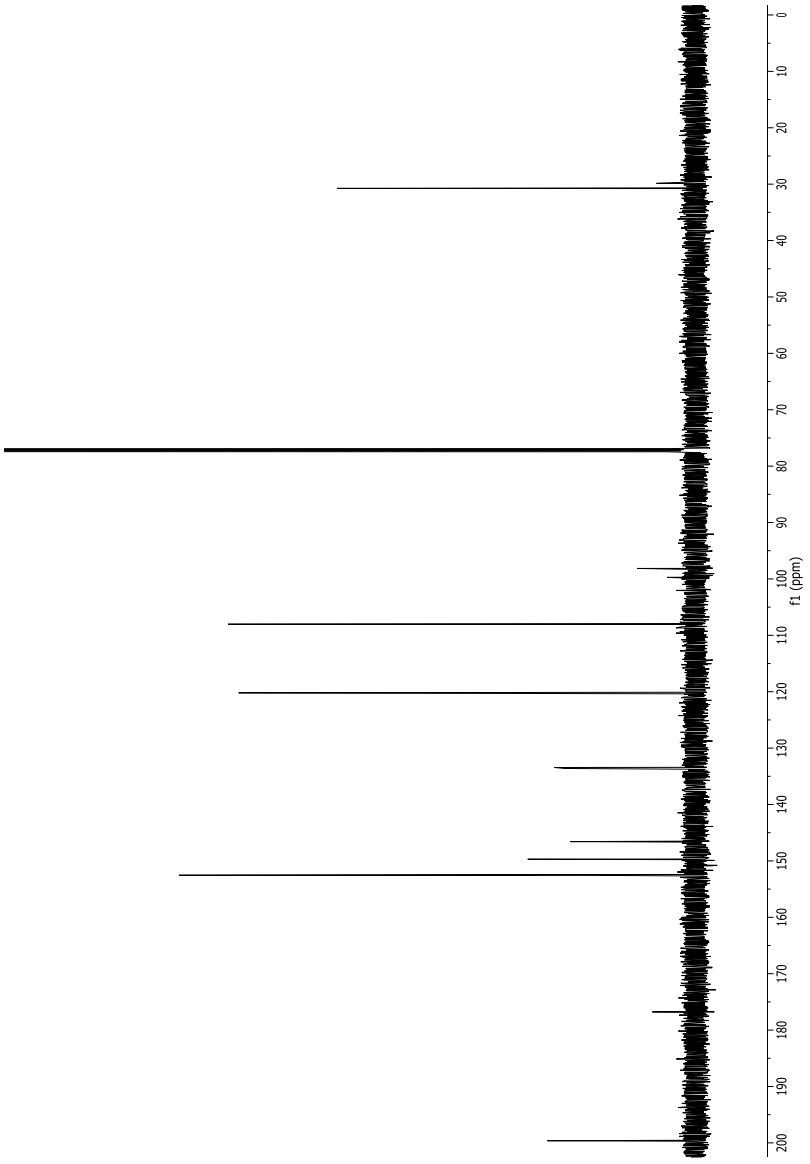
Br
29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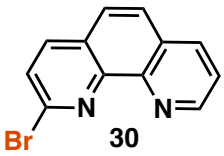

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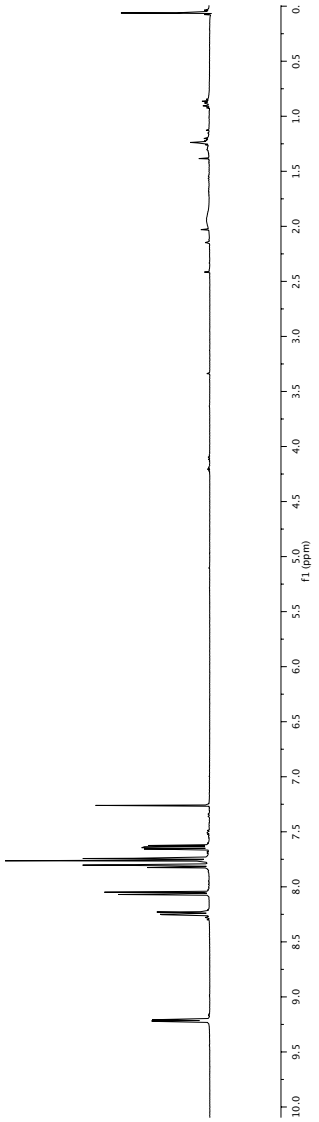

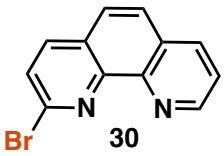

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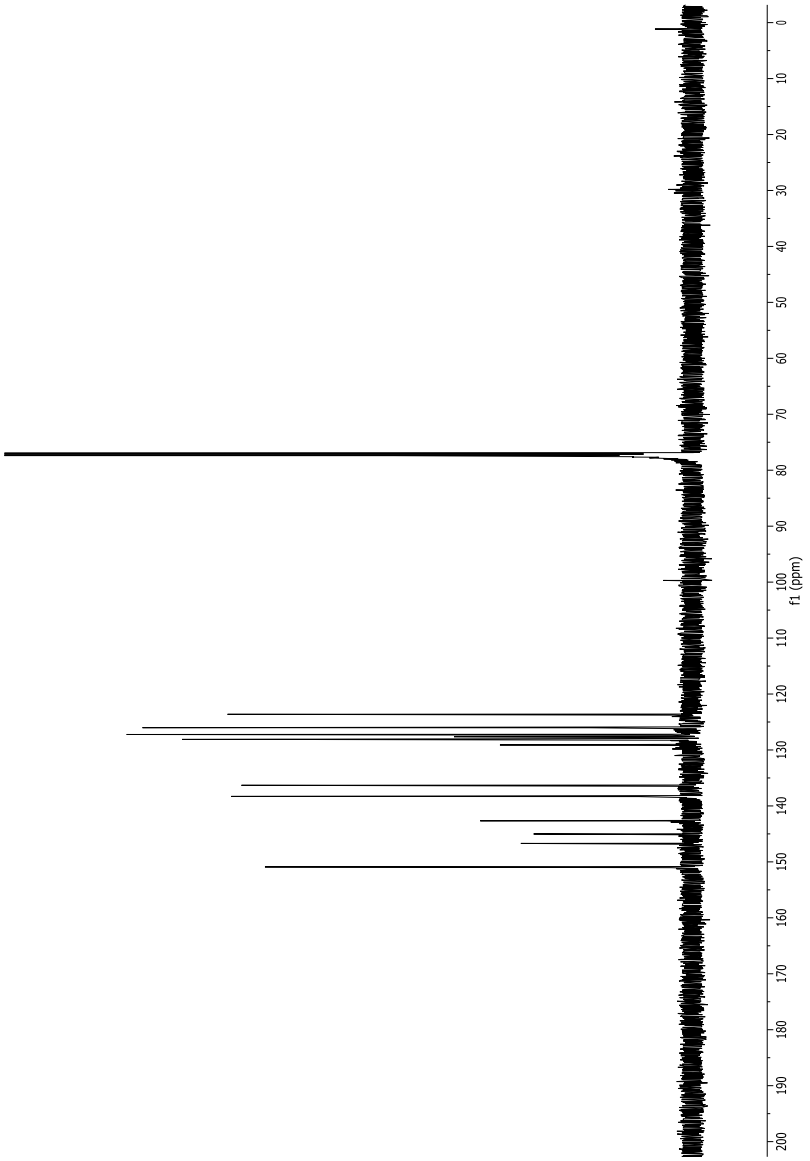

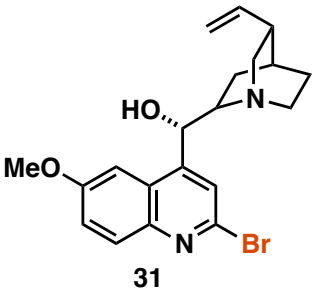

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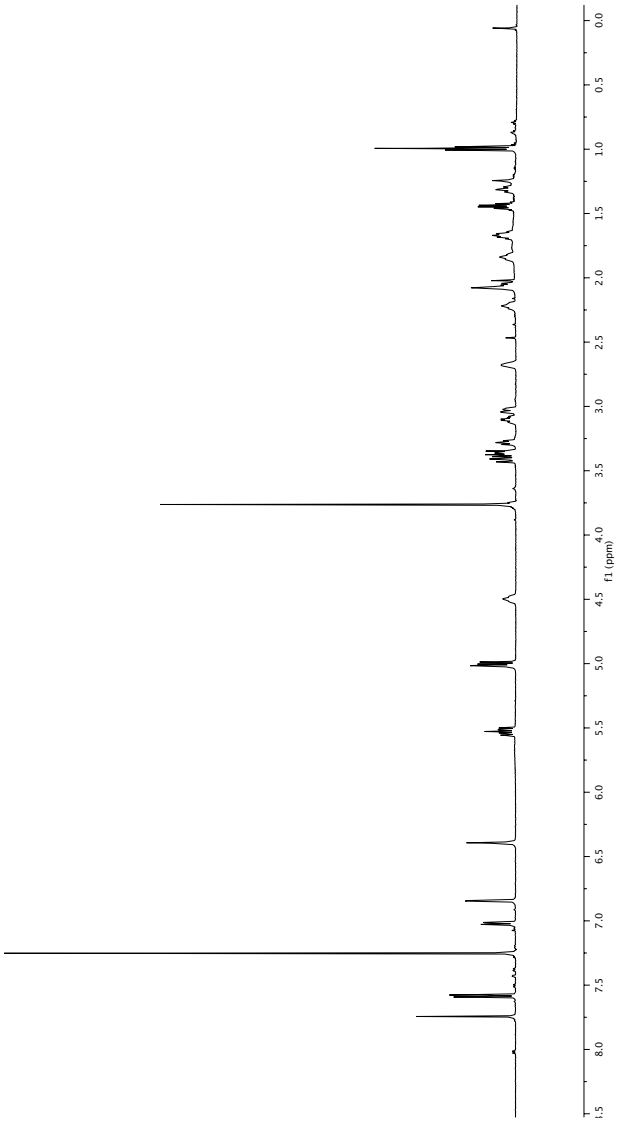

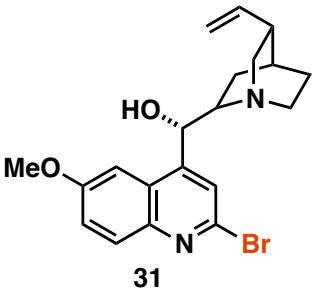

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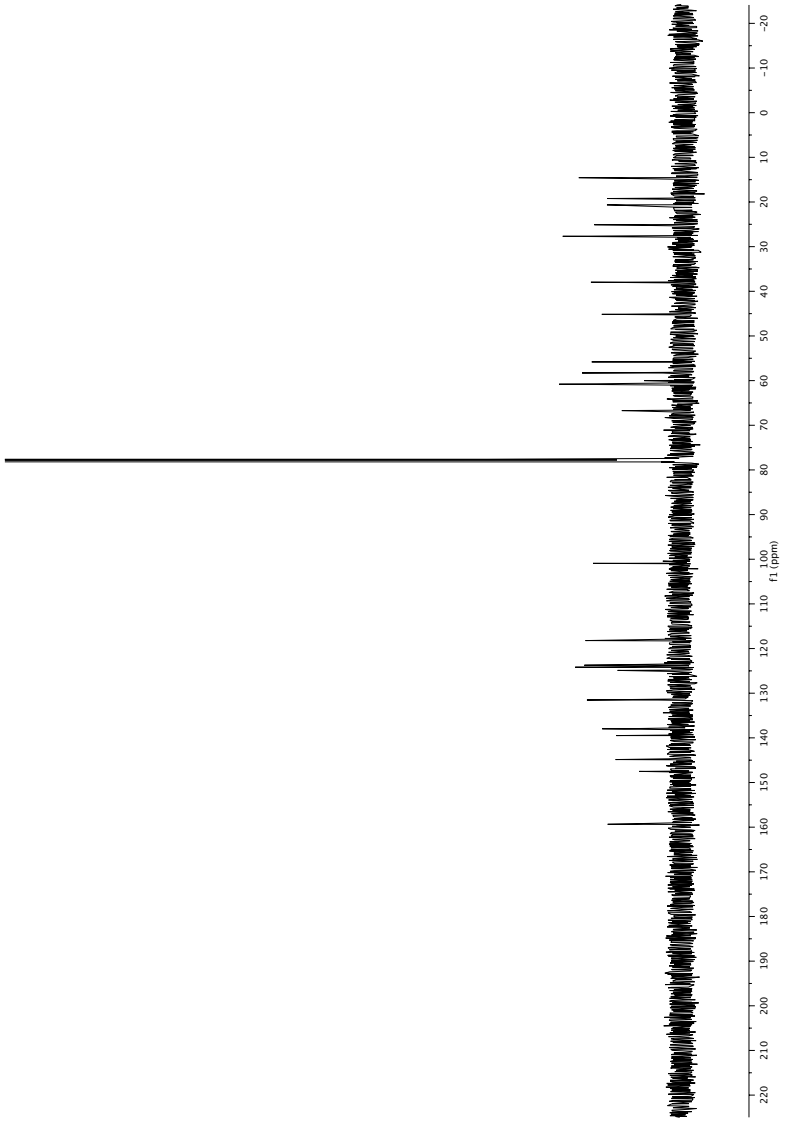

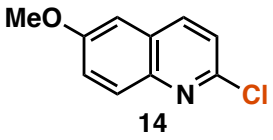

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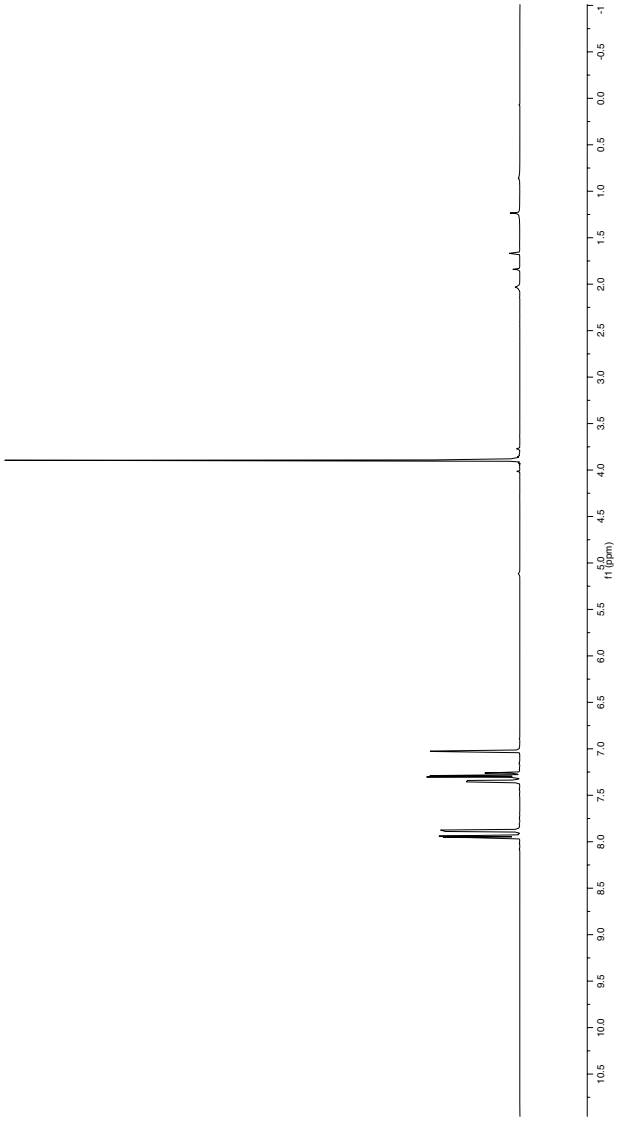

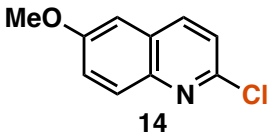

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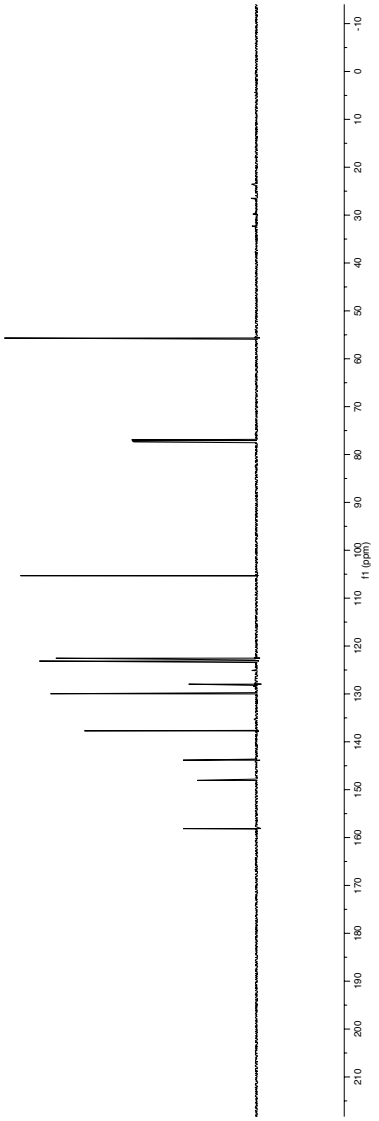

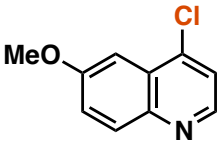

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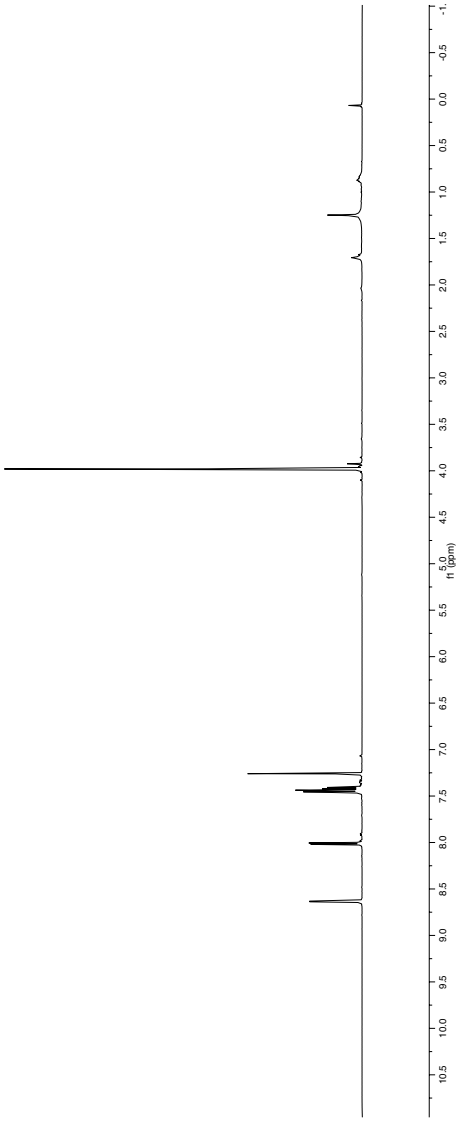

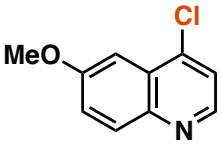

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