Rhodium(III)-Catalyzed Oxidative Carbonylation of Benzamides with Carbon Monoxide

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Supporting Information

General Information

Solvents were obtained from Sigma-Aldrich and used directly without further purification. Carboxylic acids were obtained from commercial sources and used to prepare the corresponding amides. Column chromatography was performed on SiliCycle® Silica Flash® 40-63μm 60A. Thin Layer chromatography was performed on SiliCycle® 250 μm 60A plates. Visualization was accomplished with UV light (254 nm). ^{1}H NMR and ^{13}C NMR spectra were recorded on Varian 300 spectrometers at ambient temperature. ^{1}H NMR data are reported as the following: chemical shift in parts per million (δ, ppm) from chloroform ($CHCl_3$) taken as 7.26 ppm, integration, multiplicity (s=singlet, d=doublet, t=triplet, q=quartet, m=multiplet, dd=doublet of doublets) and coupling constant (Hz). ^{13}C NMR data are reported as the following: chemical shifts are reported in ppm from $CDCl_3$ taken as 77.0 ppm. Mass spectra were obtained on a Fisons VG Autospec. Infrared spectra (IR) were obtained on Bruker Tensor 27 FT-IR spectrometer and only selected absorbance was reported. Melting points (mp) were determined with a melting point apparatus (MEL-TEMP II).

Procedure of catalyst preparation and characterization

$[Cp^*RhCl_2]_2$: The known title complex was prepared as follows.[1] To $RhCl_3 \cdot 3H_2O$ (1.02 g, 3.89 mmol) in 25 mL of methanol was added excess pentamethylcyclopentadiene (1.0 mL). The mixture was stirred under reflux for 21 h. After the mixture was cooled to room temperature, the product was isolated by filtration and washing with ether. Yield 1.02 g (85%).

A 1.5 dram vial is charged with $AgSbF_6$ or $AgClO_4$ (4.0 equiv), MeCN (0.2 M), and a stirbar. The reaction was purged with Argon. $[Cp^*RhCl_2]_2$ (1.0 equiv) was added in one portion. The reaction mixture immediately turned yellow. The reaction was allowed to stir at room temperature for 4 hours and then the reaction mixture was placed in a centrifuge and spun for 2 minutes. The yellow supernatant was collected and 1 mL of MeCN was added to the flask and spun in the centrifuge. This was repeated until the supernatant lost its yellow color. The solution was concentrated to yield the yellow solid. $RhCp^*(MeCN)_3[SbF_6]_2$ 85% yield, $RhCp^*(MeCN)_3[ClO_4]_2$ 90% yield.

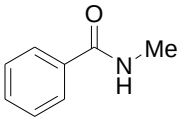
$RhCp^*(MeCN)_3[SbF_6]_2$ **^{1}HNMR** (300 MHz, $CDCl_3$) δ ppm 2.03 (s, 9H), 1.7 (s, 15H).

$RhCp^*(MeCN)_3[ClO_4]_2$ **^{1}HNMR** (300 MHz, $CDCl_3$) δ ppm 2.03 (s, 9H), 1.7 (s, 15H).

General procedure of amide preparation and characterization

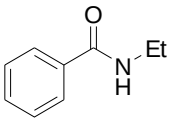
The amides were prepared from the corresponding acid chloride and amine or amine hydrochloride salt and matched the literature data. A round bottom flask was charged with carboxylic acids (20 mmol) and thionyl chloride (10 mL) was charged and reflux for 2 hours. The solvent was removed in vacuo to give crude acid chloride.

A round bottom flask charged with a magnetic stir bar was added the acid chloride (1 equiv), potassium carbonate (2.5 equiv) and ether or tetrahydrofuran (1M) and the flask placed in an ice bath. To the cooled mixture was added the amine hydrochloride salt in one portion or amine in several portions. The flask was capped with septum and the reaction was allowed to stir for 12 hours and quenched with 1M HCl carefully and extracted with ether (3×30 mL) or ethyl acetate (3×30mL), washed with $NaHCO_3$ and brine subsequently and dried with $MgSO_4$, and concentrated to yield the crude product. The crude amide was purified by column and used for coupling reaction with CO subsequently.



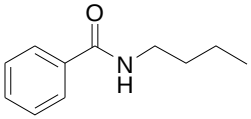
***N*-Methyl-benzamide 1a**

^{1}HNMR (300 MHz, $CDCl_3$) δ ppm 7.77-7.74 (m, 2H), 7.49-7.39 (m, 3H), 6.19 (brs, 1H), 3.02 (d, 3H, J=6.0 Hz)



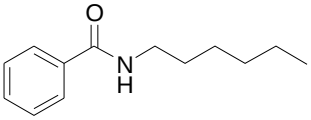
***N*-Ethyl-benzamide 1b**

^{1}HNMR (300 MHz, $CDCl_3$) δ ppm 7.77-7.74 (m, 2H), 7.52-7.39 (m, 3H), 6.11 (brs, 1H), 3.55-3.46 (m, 2H), 1.25 (t, 3H, *J*=7.5 Hz)



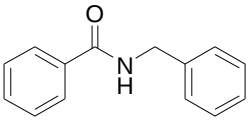
***N*-Butyl-benzamide 1c**

^{1}HNMR (300 MHz, $CDCl_3$) δ ppm 7.79-7.75 (m, 2H), 7.52-7.40 (m, 3H), 6.12 (brs, 1H), 3.50-3.43 (m, 2H), 1.66-1.56 (m, 2H), 1.48-1.36 (m, 2H), 0.96 (t, 3H, *J*=7.5 Hz)



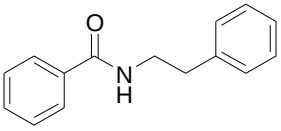
***N*-Hexyl-benzamide 1d**

^{1}HNMR (300 MHz, $CDCl_3$) δ ppm 7.78-7.74 (m, 2H), 7.52-7.40 (m, 3H), 6.10 (brs, 1H), 3.49-3.42 (m, 2H), 1.69-1.62 (m, 2H), 1.41-1.29 (m, 6H), 0.89 (t, 3H, *J*=7.5 Hz)



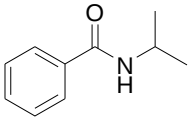
***N*-Benzyl-benzamide 1e**

^{1}HNMR (300 MHz, $CDCl_3$) δ ppm 7.81-7.78 (m, 2H), 7.51-7.29 (m, 8H), 6.37 (brs, 1H), 4.66 (d, 2H, *J*=6.0 Hz)



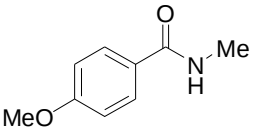
***N*-Phenethyl-benzamide 1f**

^{1}HNMR (300 MHz, $CDCl_3$) δ ppm 7.70 (d, 2H, *J*=7.5 Hz), 7.50-7.23 (m, 8H), 6.11 (brs, 1H), 3.74 (q, J=6.6 Hz, 2H), 2.94 (t, *J*=9.0 Hz, 2H)



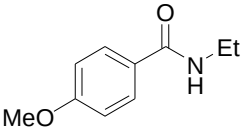
***N*-Isopropyl-benzamide 1g**

^{1}HNMR (300 MHz, $CDCl_3$) δ ppm 7.77-7.74 (m, 2H), 7.54-7.40 (m, 3H), 5.94 (brs, 1H), 4.35-4.21 (m, 1H), 1.27 (d, 6H, *J*=6.0 Hz)



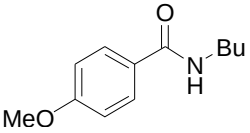
4-Methoxy-*N*-methyl-benzamide 1h

^{1}HNMR (300 MHz, $CDCl_3$) δ ppm 7.72 (d, 2H, *J*=9.0 Hz), 6.93 (d, 2H, *J*=9.0 Hz), 6.08 (s, 1H), 3.84 (s, 3H), 3.0 (d, 3H, *J*=6.0 Hz), 1.25 (t, 3H, *J*=7.5 Hz)



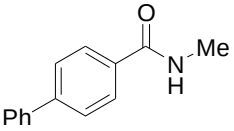
***N*-Ethyl-4-methoxy-benzamide 1i**

^{1}HNMR (300 MHz, $CDCl_3$) δ ppm 7.73 (d, 2H, *J*=9.0 Hz), 6.92 (d, 2H, *J*=9.0 Hz), 6.01 (brs, 1H), 3.84 (s, 3H), 3.53-3.44 (m, 2H), 1.24 (t, 3H, *J*=9.0 Hz)



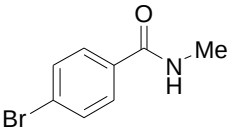
***N*-Butyl-4-methoxy-benzamide 1j**

^{1}HNMR (300 MHz, $CDCl_3$) δ ppm 7.72 (d, 2H, *J*=9.0 Hz), 6.91 (d, 2H, *J*=9.0 Hz), 6.08 (brs, 1H), 3.84 (s, 3H), 3.44 (q, 2H, *J*=6.0 Hz), 1.64-1.54 (m, 2H), 1.47-1.37 (m, 2H), 0.95 (t, 3H, 6.0 Hz).



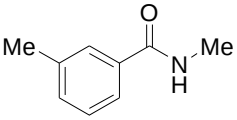
Biphenyl-4-carboxylic acid methylamide 1k

^{1}HNMR (300 MHz, $CDCl_3$) δ ppm 7.83 (d, 2H, *J*=9.0 Hz), 7.67-7.60 (m, 4H), 7.46 (t, 3H, *J*=7.5 Hz), 7.41-7.36 (m, 1H), 6.19 (brs, 1H), 3.05 (d, *J*=3.0 Hz).



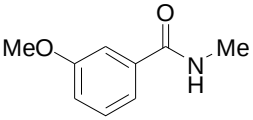
4-Bromo-*N*-ethyl-benzamide 1l

^{1}HNMR (300 MHz, $CDCl_3$) δ ppm 7.64-7.55 (m, 4H), 6.10 (brs, 1H), 3.01 (d, 3H, *J*=5.1 Hz).



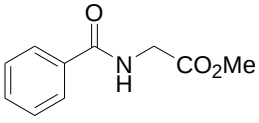
3,*N*-Dimethyl-benzamide 1m

^{1}HNMR (300 MHz, $CDCl_3$) δ ppm 7.60 (s, 1H), 7.55-7.52 (m, 1H), 7.34-7.29 (m, 2H), 6.18 (brs, 1H), 3.01 (d, 3H, *J*=6.0 Hz), 2.39 (s, 3H)



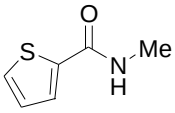
3-Methoxy-*N*-methyl-benzamide 1n

^{1}HNMR (300 MHz, $CDCl_3$) δ ppm 7.36-7.35 (m, 1H), 7.33 (s, 0.5H), 7.30 (s, 0.5H), 7.27-7.25 (m, 1H), 7.05-7.01 (m, 1H), 6.18 (brs, 1H), 3.85 (s, 3H), 3.01 (d, 3H, *J*=3.0 Hz)



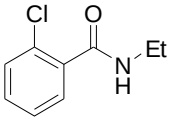
Benzoylamino-acetic acid methyl ester 1o

^{1}HNMR (300 MHz, $CDCl_3$) δ ppm 7.82 (d, 2H, *J*=6.0 Hz), 7.56-7.43 (m, 3H), 6.65 (brs, 1H), 4.26 (d, 2H, *J*=3.0 Hz), 3.81 (s, 3H).

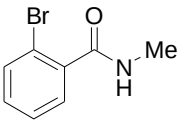


Thiophene-2-carboxylic acid methylamide 1p

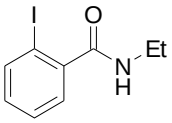
^{1}HNMR (300 MHz, $CDCl_3$) δ ppm 7.48 (d, 1H, *J*=3.0 Hz), 7.45 (d, 1H, *J*=3.0 Hz), 7.0 (t, 1H, *J*=4.5 Hz), 6.02 (brs, 1H), 2.99 (d, 3H, *J*=3.0 Hz).



2-Chloro-*N*-ethyl-benzamide **^{1}HNMR** (300 MHz, $CDCl_3$) δ ppm 7.67-7.64 (m, 1H), 7.41-7.37 (m, 1H), 7.35-7.28 (m, 2H), 6.13 (brs, 1H), 3.55-3.47 (m, 2H), 1.26 (t, 3H, *J*=7.5 Hz)



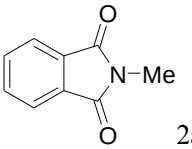
2-Bromo-*N*-methyl-benzamide **^{1}HNMR** (300 MHz, $CDCl_3$) δ ppm 7.60-7.52 (m, 2H), 7.35-7.33 (t, 1H, *J*=7.2 Hz), 7.29-7.24 (m, 1H), 5.90 (brs, 1H), 3.01(d, 3H, *J*=4.8 Hz)



***N*-Ethyl-2-iodo-benzamide** **^{1}HNMR** (300 MHz, $CDCl_3$) δ ppm 7.85 (d, 1H, *J*=8.1Hz), 7.44-7.34 (m, 2H), 7.11-7.06 (m, 1H), 5.70 (brs, 1H), 3.55-3.44 (m, 2H),1.27 (t, 3H, *J*=7.5 Hz)

General procedure for phthalimides synthesis and characterization

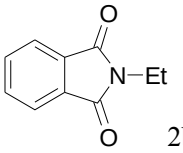
All reactions were carried out in 16×150 mm test tubes sealed with CO balloons with magnetic stirring at 600 rpm in oil bath. To the test tubes, $RhCp^*(MeCN)_3(ClO_4)_2$ (6.5 mg, 0.01mmol) followed by substrate **1a** (27.0 mg, 0.2 mmol), Ag_2CO_3 (115.8 mg, 0.42 mmol), KH_2PO_4 (57.2 mg, 0.42 mmol), and *t*-AmOH solvent (0.37 mL) was added. The reaction mixture bubbled with CO and then was sealed with CO balloons and heated to 100 °C for 24 hours under vigorous stirring. Upon completion, the reaction mixture was cooled to room temperature and diluted with ethyl acetate and then filtered through a small pad of Celite. The filtrate was concentrated *in vacuo*. The NMR yield of desired product **2a** was determined by integration using an internal standard (1, 3, 5-trimethoxyl benzene).



2a

2-Methyl-isoindole-1, 3-dione

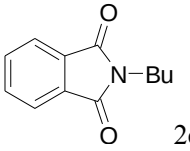
^{1}HNMR (300 MHz, $CDCl_3$) δ ppm 7.85-7.83 (m, 2H), 7.72-7.69(m, 2H), 3.18 (s, 3H); **^{13}CNMR** (75 MHz, $CDCl_3$) δ ppm 168.5, 133.9, 132.2, 123.2, 23.9. IR(thin film): 3020, 1711, 1434, 1006, 748, 669. MP=132-133 (lit: 135 ^oC [2]). R_f=0.45 (hexane:ethyl acetate=2:1)



2b

2-Ethyl-isoindole-1, 3-dione

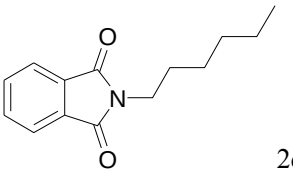
[1] **HNMR** (300 MHz, $CDCl_3$) δ ppm 7.85-7.83 (m, 2H), 7.72-7.69 (m, 2H), 3.74 (q, *J*=7.5 Hz, 2H), 1.27 (t, *J*=7.5 Hz, 3H); [13] **CNMR** (75 MHz, $CDCl_3$) δ ppm 168.5, 134.1, 132.4, 123.4, 33.1, 14.2. GC-MS 175, 160, 146, 133, 118, 105, 76, 66, 56, 50, 42, 36. IR(thin film): 2981, 2942, 2841, 1766, 1710, 1618, 1490, 1397, 1217, 1037, 908, 771, 669. MP=76-78 °C (lit: 79 °C[3]). R_f=0.40 (hexane:ethyl acetate=4:1)



2c

2-Butyl-isoindole-1,3-dione

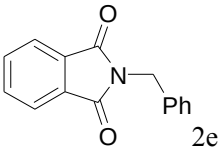
[1] **HNMR** (300 MHz, $CDCl_3$) δ ppm 7.84-7.80 (m, 2H), 7.72-7.08 (m, 2H), 3.68 (t, 2H, *J*=7.5 Hz), 1.70-1.60 (m, 2H), 1.42-1.29 (m, 2H), 0.93 (t, 3H, *J*=7.5 Hz); [13] **CNMR** (75 MHz, $CDCl_3$) δ ppm 168.5, 133.8, 132.1, 123.1, 37.7, 30.6, 20.1, 13.6. IR (thin film):2964, 2875, 1771, 1709, 1468, 1398, 1053, 932, 771, 669. MP= 35-36°C (lit: 134-135 °C [4]). R_f=0.43 (hexane:ethyl acetate=4:1).



2d

2-Hexyl-isoindole-1, 3-dione[5]

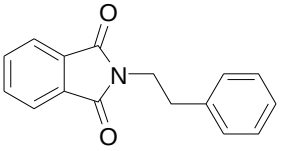
[1] **HNMR** (300 MHz, $CDCl_3$) δ ppm 7.85 (m, 2H), 7.71-7.69 (m, 2H), 3.67 (t, *J*=6.0 Hz, 2H), 1.68-1.62 (m, 2H), 1.36-1.24 (m, 6H), 0.87 (t, *J*=6.0 Hz, 3H); [13] **CNMR** (75 MHz, $CDCl_3$) δ ppm 168.5, 133.8, 132.1, 123.1, 38.1, 31.2, 28.6, 26.5, 22.5, 14.0. IR (thin film): 3023, 2931, 2859, 1773, 1714, 1467, 1438, 1396, 1367, 1219, 1187, 1062, 1004, 771, 719, 668. MP=37-38 °C. R_f=0.58 (hexane:ethyl acetate=2:1).



2e

2-Benzyl-isoindole-1, 3-dione[6]

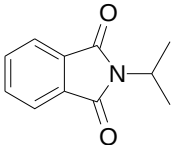
[1] **HNMR** (300 MHz, $CDCl_3$) δ ppm 7.76-7.74 (m, 2H), 7.62-7.59 (m, 2H), 7.36-7.34 (m, 2H), 7.26-7.15 (m, 3H), 4.76 (s, 2H). [13] **CNMR** (75 MHz, $CDCl_3$) δ ppm 167.9, 136.3, 133.9, 132.0, 128.6, 128.5, 127.7, 123.2, 41.5. IR (thin film): 1715, 1524, 1431, 1395, 1045, 928, 757, 669. MP=115-116 °C. R_f=0.37 (hexane:ethyl acetate=4:1)



2f

2-Phenethyl-isoindole-1,3-dione[7]

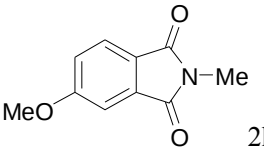
^{1}HNMR (300 MHz, $CDCl_3$) δ ppm 7.83-7.80 (m, 2H), 7.71-7.68 (m, 2H), 7.31-7.18 (m, 5H), 3.92 (t, *J*=7.5 Hz, 2H), 2.98 (t, *J*= 7.5 Hz, 2H), **^{13}CNMR** (75 MHz, $CDCl_3$) δ ppm 168.1, 137.9, 133.8, 131.9, 128.7, 128.4, 126.5, 123.1, 39.2, 34.5. IR (thin film): 3020, 1772, 1713, 1639, 1523, 1476, 1423, 1397, 1362, 1045, 910, 849, 746, 669. MP=104-105^{o}C. R_f=0.50 (hexane:ethyl acetate=4:1)



2g

2-Isopropyl-isoindole-1,3-dione

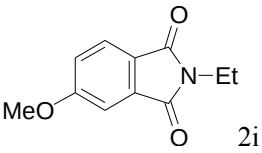
^{1}HNMR (300 MHz, $CDCl_3$) δ ppm 7.82-7.77 (m, 2H), 7.71-7.67 (m, 2H), 4.60-4.46 (m, 1H), 1.48 (d, *J*=7.2 Hz, 6H), **^{13}CNMR** (75 MHz, $CDCl_3$) δ ppm 168.3, 133.7, 132.1, 122.9, 42.9, 20.1. IR (thin film): 1710, 1703, 1525, 1477, 1424, 1386, 1369, 1045, 928, 876, 669. MP=83.5-84.3 (lit. 85^{o}C[8]). R_f=0.50 (hexane:ethyl acetate=4:1)



2h

5-Methoxy-2-methyl-isoindole-1, 3-dione

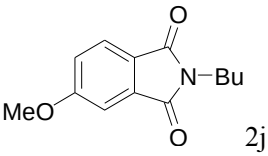
^{1}HNMR (300 MHz, $CDCl_3$) δ ppm 7.74 (d, 1H, *J*=8.4 Hz), 7.32 (d, 1H, *J*=2.4 Hz), 7.14 (dd, 1H, J=8.1 Hz, J=2.4Hz), 3.92 (s, 3H), 3.15 (s, 3H); **^{13}CNMR** (75 MHz, $CDCl_3$) δ ppm 168.6, 168.5, 164.8, 135.1, 125.1, 124.4, 119.7, 108.3, 56.3, 24.2. IR (thin film): 3020, 1766, 1709, 1603, 1489, 1434, 1382, 1288, 1215, 1024, 928, 772, 669. MP=155-157 ^{o}C. R_f=0.32 (hexane:ethyl acetate=4: 1). HRMS (ESI-APCI) Calcd for $C_{10}H_{10}NO_3$ (M+H): 192.0665; found: 192.0675.



2i

2-Ethyl-5-methoxy-isoindole-1, 3-dione

^{1}HNMR (300 MHz, $CDCl_3$) δ ppm 7.71(d, 1H, *J*=9.0 Hz), 7.29 (d, 1H, *J*=3.0Hz), 7.12 (dd, 1H, *J*=9.0 Hz, *J*=3.0 Hz), 3.01 (s, 3H), 3.70 (2H, q, *J*=7.5 Hz), 1.24 (3H, t, *J*=7.5 Hz); **^{13}CNMR** (75 MHz, $CDCl_3$) δ ppm 168.0(2C), 164.5, 134.8, 124.8, 124.1, 119.5, 107.9, 56.0, 32.8, 13.9. IR (thin film) 2981, 2942, 2841, 1766, 1710, 1618, 1490, 1440, 1397, 1351, 1287, 1250, 1094, 1037, 908, 844, 771, 669. MP=82-83 (lit. 81^{o}C). R_f=0.31 (hexane:ethyl acetate=4:1). HRMS (ESI-APCI) Calcd for $C_{11}H_{12}NO_3$ (M+H): 206.0812; found: 206.0817.

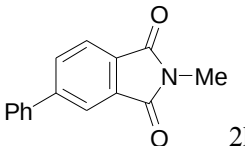


2j

2-Butyl-5-methoxy-isoindole-1, 3-dione

^{1}HNMR (300 MHz, $CDCl_3$) δ ppm 7.72 (d, 1H, *J*=9.0 Hz), 7.29 (d, 1H, *J*=3.0 Hz), 7.12 (dd, 1H, *J*=3.0 Hz, *J*=9.0 Hz), 3.90 (s, 3H), 3.63 (t, 2H, 7.5 Hz), 1.67-1.57 (m, 2H), 1.40-1.28 (m, 2H), 0.92 (t, 3H, *J*=7.5 Hz); **^{13}CNMR** (75 MHz, $CDCl_3$) δ ppm 168.2, 164.5, 134.7, 124.7, 124.0, 119.4, 107.9, 56.0, 37.7, 30.6, 20.0, 13.6. IR (thin film): 3020, 2964, 2942, 2875, 1768, 1707, 1619, 1490, 1456, 1438, 1396, 1371, 1287, 1250, 1078, 1053, 1022, 908, 844, 743, 669.2. MP=68-69 ^{o}C.

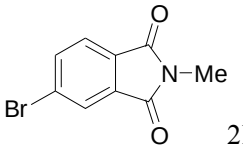
R_f=0.34 (hexane:ethyl acetate=4:1). HRMS (ESI-APCI) Calcd for $C_{13}H_{16}NO_3$ (M+H): 234.1125; found: 234.1122.



2k

2-Methyl-5-phenyl-isoindole-1, 3-dione

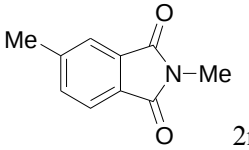
^{1}HNMR (300 MHz, $CDCl_3$) δ ppm 8.06 (s, 1H), 7.90 (s, 2H), 7.63-7.66 (m, 2H), 7.42-7.54 (m, 3H), 3.21(s, 3H); **^{13}CNMR** (75 MHz, $CDCl_3$) δ ppm 168.4, 168.3, 147.3, 139.0, 133.0, 132.4, 130.6, 129.1, 128.8, 127.2, 123.6, 121.7, 24.0. IR (thin film): 3020, 1775, 1707, 1619, 1522, 1475, 1439, 1382, 1008, 928, 850, 746, 669. MP=144-145 ^{o}C. R_f=0.53 (hexane:ethyl acetate=4:1). HRMS (ESI-APCI) Calcd for $C_{15}H_{12}NO_2$ (M+H): 238.0863; found: 238.0860



2l

5-Bromo-2-methyl-isoindole-1,3-dione

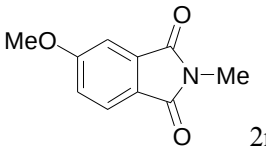
^{1}HNMR (300 MHz, $CDCl_3$) δ ppm 7.97 (d, 1H, *J*=1.5 Hz), 7.84 (dd, 1H, *J*=7.8 Hz, *J*=1.5 Hz), 7.71 (d, 1H, *J*=8.1 Hz), 3.17 (s, 3H); **^{13}CNMR** (75 MHz, $CDCl_3$) δ ppm 167.6, 167.1, 136.8, 133.8, 130.7, 128.8, 126.5, 124.5, 24.1. IR (thin film): 1778, 1718, 1436, 1381, 1009, 929, 757, 669. MP=143-145 ^{o}C. R_f=0.57 (hexane:ethyl acetate=4:1). HRMS (ESI-APCI) Calcd for $C_{10}H_{11}BrNO_3$ (M+CH_5O): 271.9917; found: 271.9923.



2m

2,5-Dimethyl-isoindole-1,3-dione

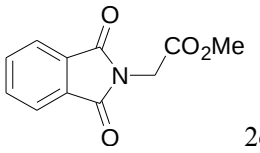
^{1}HNMR (300 MHz, $CDCl_3$) δ ppm 7.72 (d, 1H, *J*=9.0 Hz), 7.64 (s, 1H), 7.48 (d, 1H, *J*=9.0 Hz), 3.16 (s, 3H), 2.50 (s, 3H); **^{13}CNMR** (75 MHz, $CDCl_3$) δ ppm 168.7, 168.6, 145.1, 134.3, 132.5, 129.6, 123.7, 123.1, 23.8, 21.9. GC-MS 175, 161, 146, 131, 118, 89, 78, 73, 63, 57, 51, 44, 38. IR (thin film): 3020, 1714, 1431, 1381, 1016, 928, 747, 669. mp= 128-130 ^{o}C (lit. 126-128 ^{o}C[9]). R_f=0.34 (hexane: ethyl acetate=4:1).



2n

5-Methoxy-2-methyl-isoindole-1,3-dione

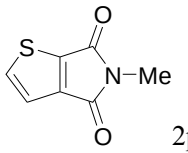
^{1}HNMR (300 MHz, $CDCl_3$) δ ppm 7.74 (d, 1H, *J*=8.4 Hz), 7.32 (d, 1H, *J*=2.4 Hz), 7.14 (dd, 1H, J=8.1 Hz, J=2.4Hz), 3.92 (s, 3H), 3.15 (s, 3H); **^{13}CNMR** (75 MHz, $CDCl_3$) δ ppm 168.6, 168.5, 164.8, 135.1, 125.1, 124.4, 119.7, 108.3, 56.3, 24.2. IR (thin film): 3020, 1766, 1709, 1603, 1489, 1434, 1382, 1288, 1215, 1024, 928, 772, 669. MP=155-157 ^{o}C. R_f=0.32 (hexane:ethyl acetate=4:1). HRMS (ESI-APCI) Calcd for C10H10NO3 (M+H): 192.0665; found: 192.0675.



2o

1, 3-Dioxo-1, 3-dihydro-isoindole-2-carboxylic acid methyl ester

^{1}HNMR (300 MHz, $CDCl_3$) δ ppm 7.91-7.88 (m, 2H), 7.77-7.74 (m, 2H), 4.46 (s, 2H), 3.77 (s, 3H), **^{13}CNMR** (75 MHz, $CDCl_3$) δ ppm 167.9, 167.6, 132.2, 123.8, 52.9, 39.0. IR (thin film): 1754, 1724, 1419, 1395, 1115, 956, 929, 669. MP=111-112 °C (lit: 112-114[10]). R_f=0.24 (hexane: ethyl acetate=4: 1)

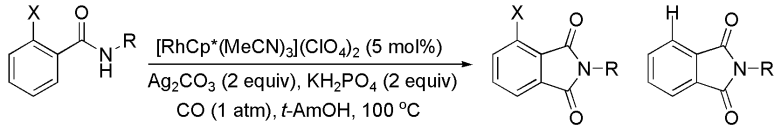


2p

5-Methyl-thieno[2,3-c]pyrrole-4,6-dione

^{1}HNMR (300 MHz, $CDCl_3$) δ ppm 7.30 (d, 1H, *J*=6.0 Hz), 6.98 (d, 1H, *J*=6.0 Hz), 3.11 (s, 3H)**;** **^{13}CNMR** (75 MHz, $CDCl_3$) δ ppm 164.0, 162.8, 144.7, 137.2, 121.1, 24.3. IR (thin film): 1712, 1520, 1427, 1382, 1363, 1045, 928, 757, 669. MP=91-92 °C. R_f=0.37 (hexane: ethyl acetate=4: 1). HRMS (ESI-APCI) Calcd for C7H6NO2S (M+H): 168.0114; found: 168.0112.

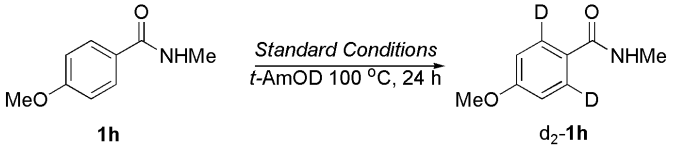
General Procedure for formation of dehalogenated phthalimides from *Ortho* Cl, Br, I amides to and Characterization



X=Cl, R=Et	4%	9%
X=Br, R=Me	5%	40%
X=I, R=Et	trace	70%

To the test tube, $RhCp^*(MeCN)_3(ClO_4)_2$ (6.5 mg, 0.01mmol) followed by substrate **1a** (36.7 mg, 0.2 mmol), Ag_2CO_3 (115.8 mg, 0.42 mmol), KH_2PO_4 (57.2 mg, 0.42 mmol), and *t*-AmOH solvent (0.37 mL) was added. The reaction mixture bubbled with CO and then was sealed with CO balloon and heated to 100 °C for 24 hours under vigorous stirring. Upon completion, the reaction mixture was cooled to room temperature and purified to give the mixture of 4-chloro-2-ethyl-isoindole-1,3-dione and 2-ethyl-isoindole-1,3-dione.

Deuterium incorporation experiments

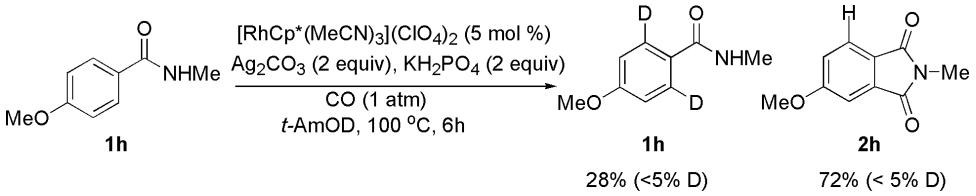


1h **d_2-1h**

>99% (19% D)

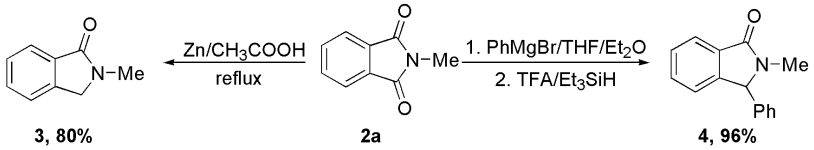
To the test tube, $RhCp^*(MeCN)_3(ClO_4)_2$ (6.5 mg, 0.01mmol) followed by substrate **1h** (33.0 mg, 0.2 mmol), Ag_2CO_3 (115.8 mg, 0.42 mmol), KH2PO4 (57.2 mg, 0.42 mmol), and *t*-AmOD solvent (0.37 mL) was added. The reaction mixture was sealed and heated to 100 °C for 24 hours under vigorous stirring. Upon completion, the reaction mixture was cooled to room temperature and

diluted with ethyl acetate and then filtered through a small pad of Celite. The filtrate was concentrated to yield the deuterated amide in 95% yield and 19% deuterium incorporation at the two ortho positions as judged by ^{1}H NMR.



To the test tube, RhCp*$(MeCN)_3(ClO_4)_2$ (6.5 mg, 0.01mmol) followed by substrate **1h** (33.0 mg, 0.2 mmol), Ag_2CO_3 (115.8 mg, 0.42 mmol), KH_2PO_4 (57.2 mg, 0.42 mmol), and *t*-AmOD solvent (0.37 mL) was added. The reaction mixture bubbled with CO and then was sealed with CO balloons and heated to 100 °C for 6 hours under vigorous stirring. The reaction mixture was cooled to room temperature and purified to give **2h** and recover **1h**. No deuterium incorporation happened at any position of **2h** and **1h**.

Product derivatization



A round bottom flask charged with a magnetic stir bar was added the phthalimide **2a** (48.3mg, 0.3 mmol), Zn dust (149 mg, 2.3 equiv) and acetic acid (3 mL) and the flask was heated to flux for 6 h. The reaction mixture was cooled to room temperature and purified to give **3** in 80% yield. **2-Methyl-2, 3-dihydro-isoindol-1-one ^{1}HNMR** (300 MHz, $CDCl_3$) δ ppm 7.80 (d, *J*=7.5 Hz, 1H), 7.53-7.40 (m, 3H), 4.35 (s, 2H), 3.17 (s, 3H), **^{13}CNMR** (75 MHz, $CDCl_3$) δ ppm 168.9, 141.1, 131.3, 128.2, 123.7, 122.7, 52.2, 29.7. IR (thin film): 1685, 1485, 1425, 1400, 1096, 909, 739. MP=97-99 °C. R_f=0.18. (hexane:ethyl acetate=1: 1)

To a well stirred and cold solution of phthalimide **2a** (483 mg, 3 mmol) under dry Argon atmosphere in a mixture of anhydrous diethyl ether and anhydrous THF (15 mL) was added slowly in dropwise, over a period of 40 min, a 0.5 M solution of Grignard reagent (phenylmagnesium bromide (4.5 mmol)) in dry THF. After 3 h of reaction at room temperature, the reaction was hydrolysed under stirring with water (13 mL) then with 0.5 M NH_4Cl solution (13 mL), and the solution was passed through Celite. After separation, the organic layer was washed with water, brine, dried over $MgSO_4$ and concentrated under reduced pressure to give 3-hydroxy-2-methyl-3-phenyl-2, 3-dihydro-isoindol-1-one in quantitive yield.

To a solution of 3-hydroxy-2-methyl-3-phenyl-2, 3-dihydro-isoindol-1-one (717.8 mg, 3 mmol) in 18 mL of dry dichloromethane, was added on stirring and cooling at 0 °C dropwise 5 mL of TFA. After 5 min of reaction, triethylsilane (1.53 mL, 10 mmol) dissolved in 10 mL of anhydrous dichloromethane was added slowly over a period of 5 min. After 4 h of the reaction at room temperature, the solvent was evaporated under reduced pressure. The residue was diluted with 30 mL of dichloromethane and 30 mL of saturated sodium hydrogenocarbonate solution. The organic layer was separated, washed twice with water, brine, dried over $MgSO_4$ and concentrated under reduced pressure and purified to give **4** in 96% yield as white crystals. **3-Phenyl-2, 3-dihydro-isoindol-1-one ^{1}HNMR** (300 MHz, $CDCl_3$) δ ppm 7.88-7.85 (m, 1H), 7.44-7.41 (m,

2H), 7.36-7.32 (m, 3H), 7.16-7.11 (m, 3H), 5.32 (s, 1H), 2.96 (s, 3H). **^{13}CNMR** (75 MHz, $CDCl_3$) δ ppm 168.6, 145.9, 136.8, 131.5, 129.0, 128.5, 128.1, 127.2, 123.3, 122.8, 66.5, 27.4. IR (thin film): 3033, 2253, 1794, 1684, 1473, 1456, 1423, 1393, 1093, 1047, 912, 743. MP=97-98 ^{o}C. R_f=0.25. (hexane:ethyl acetate=2:1)

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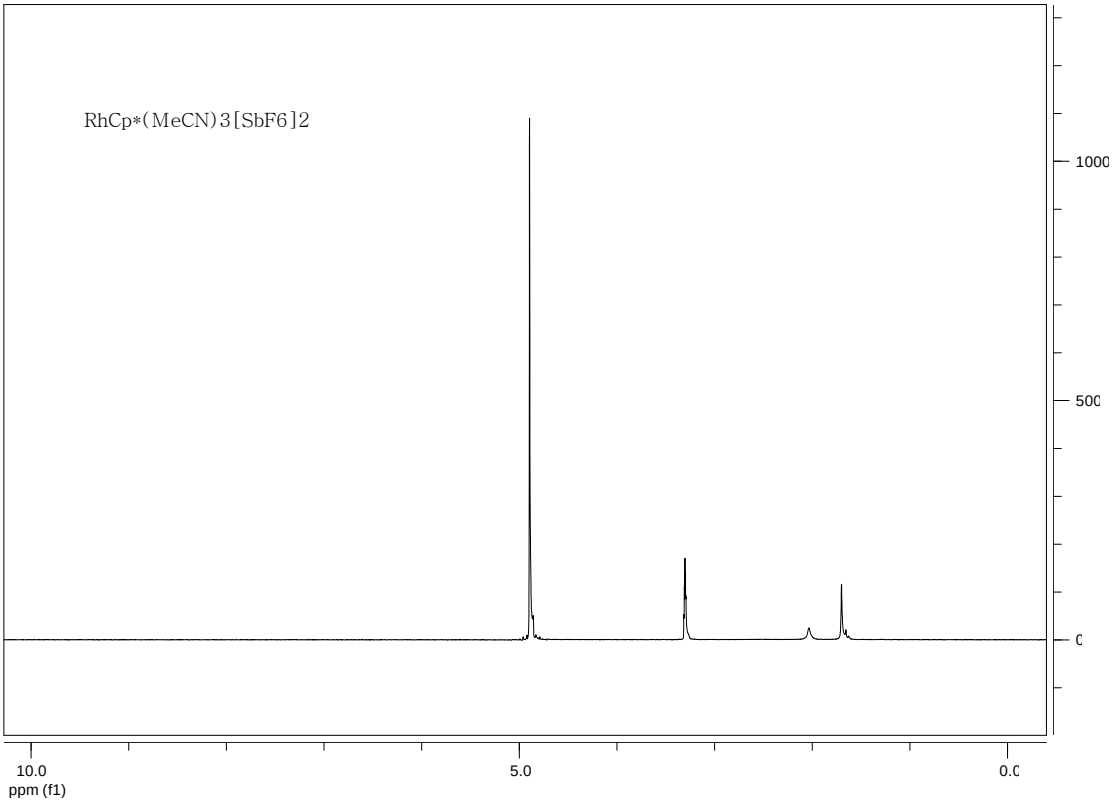
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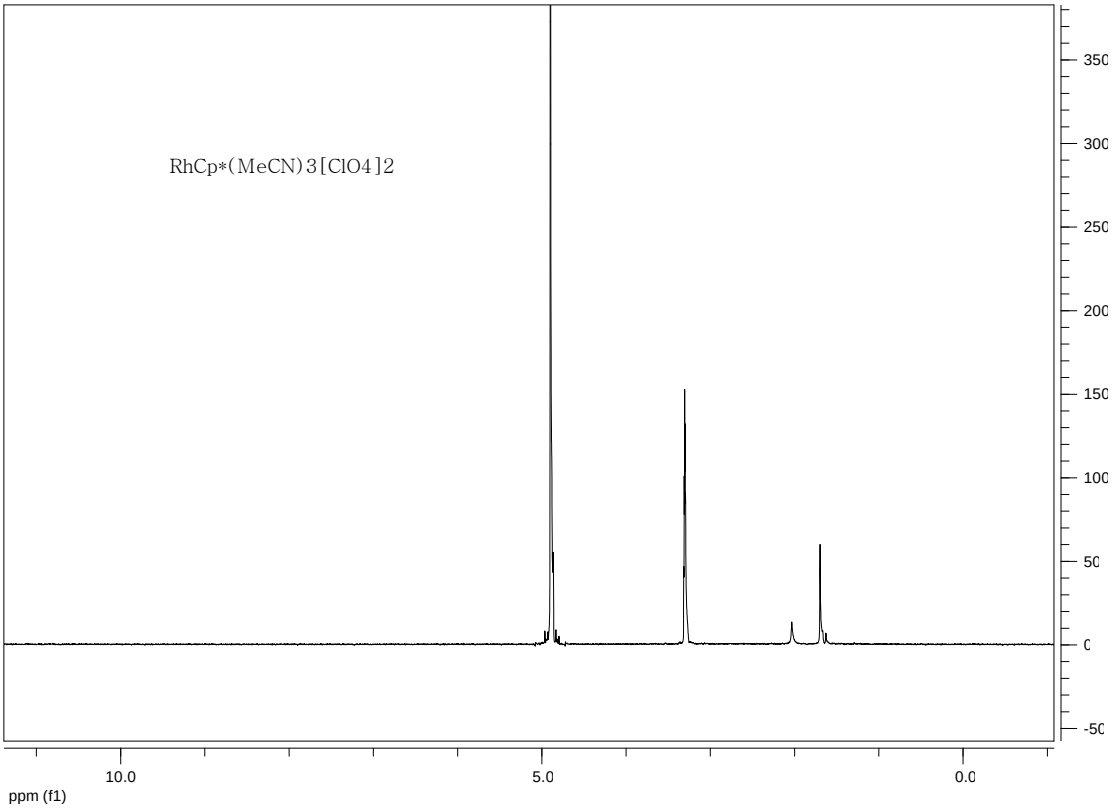
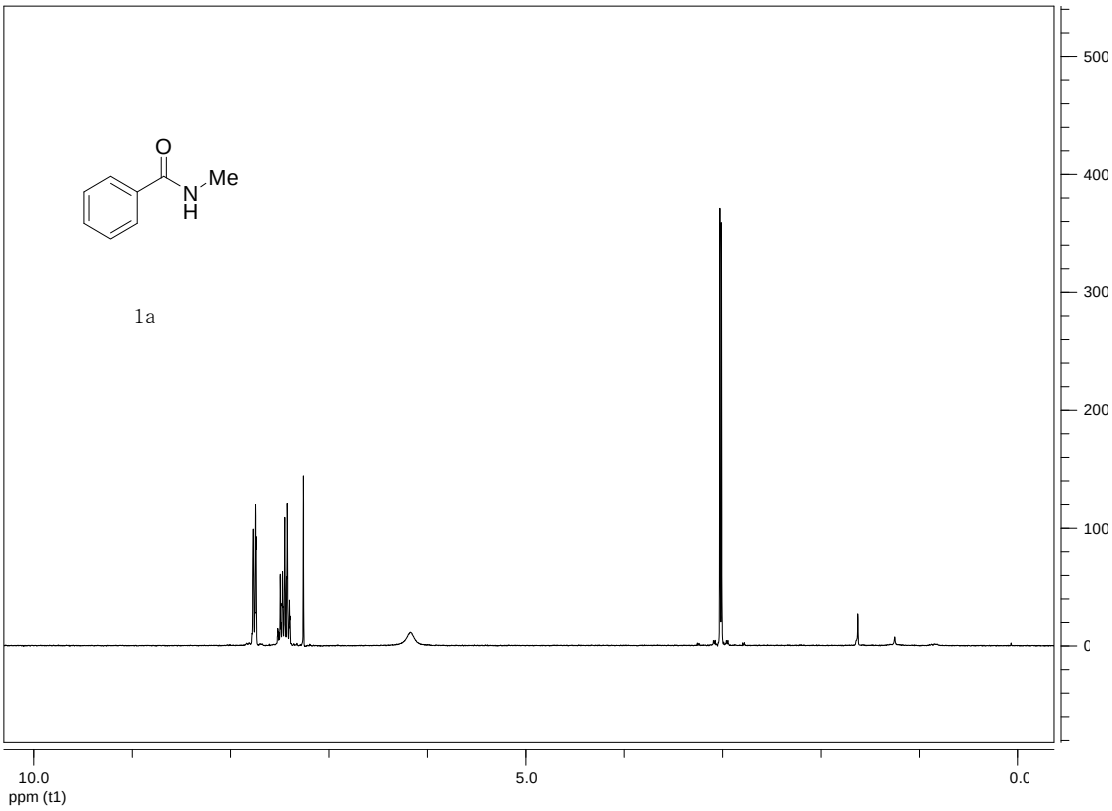
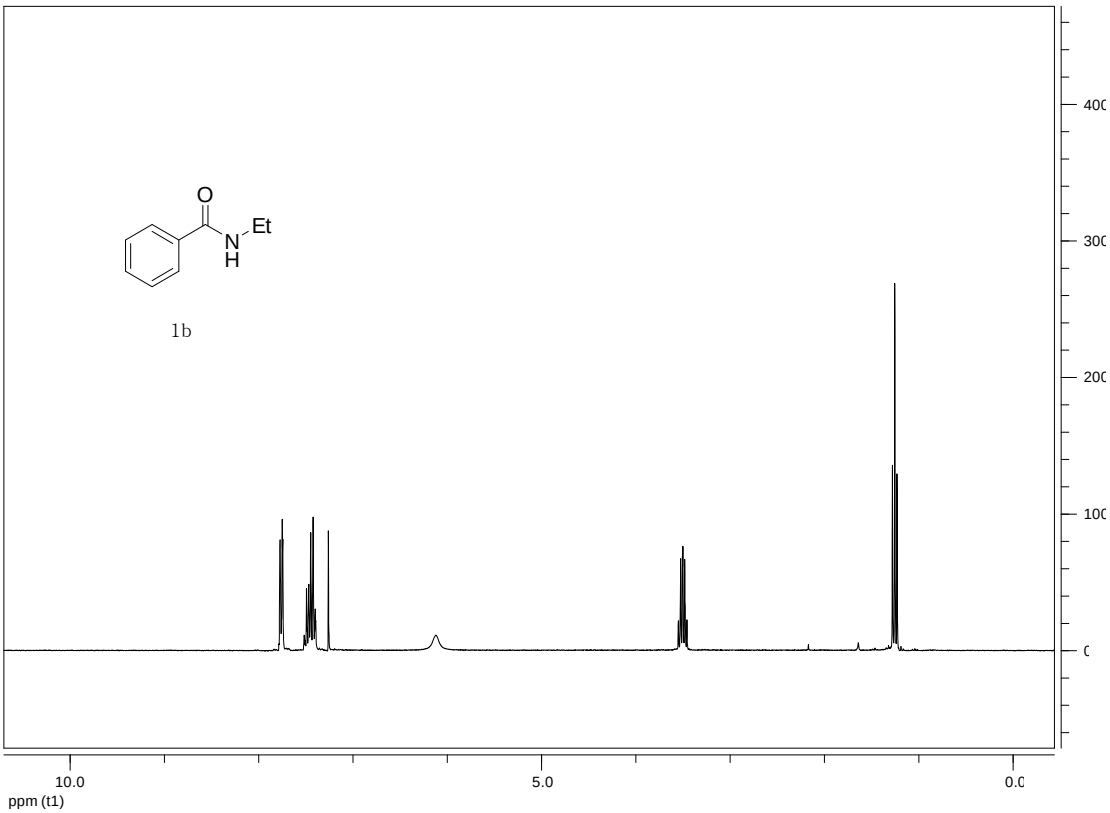
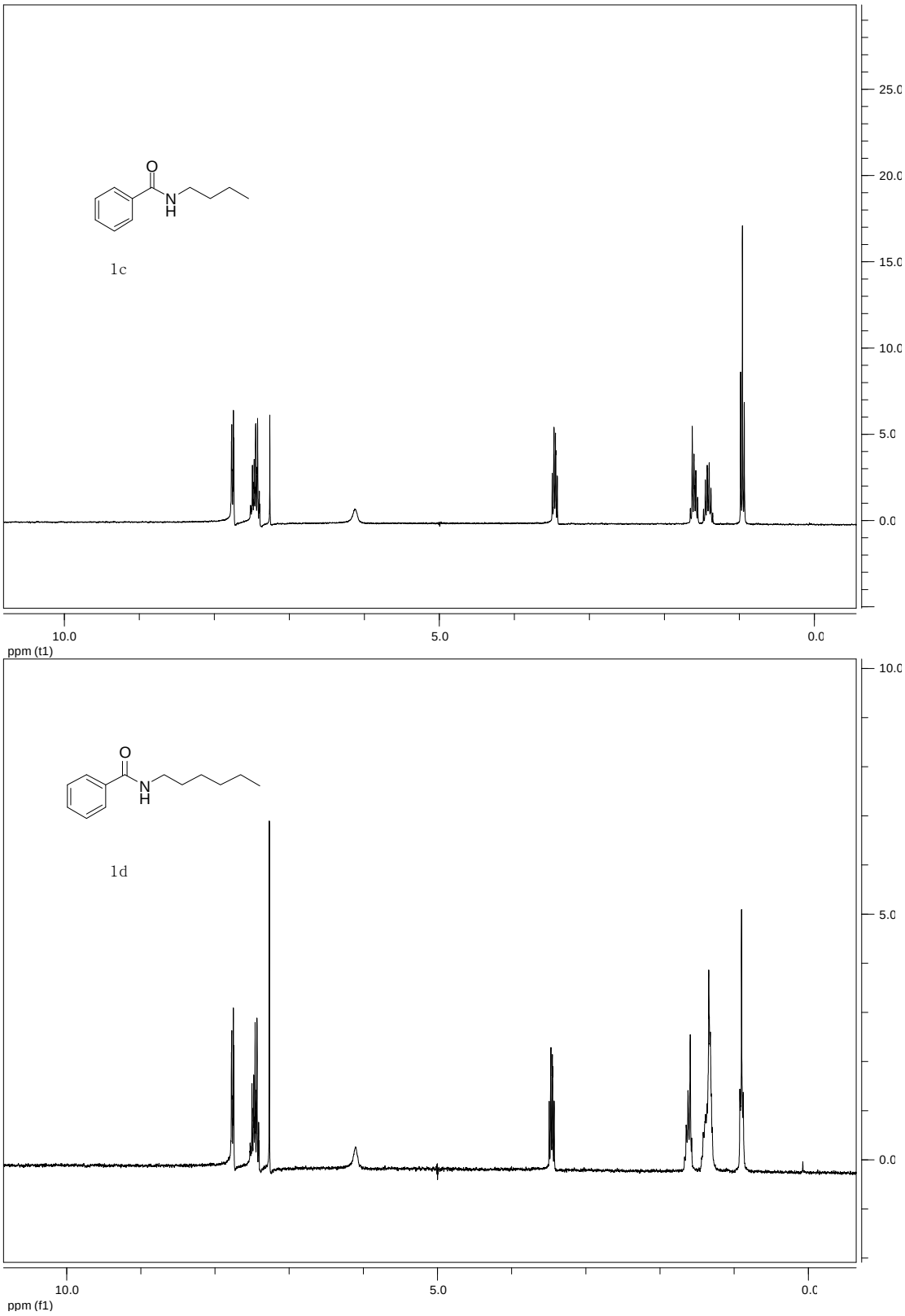
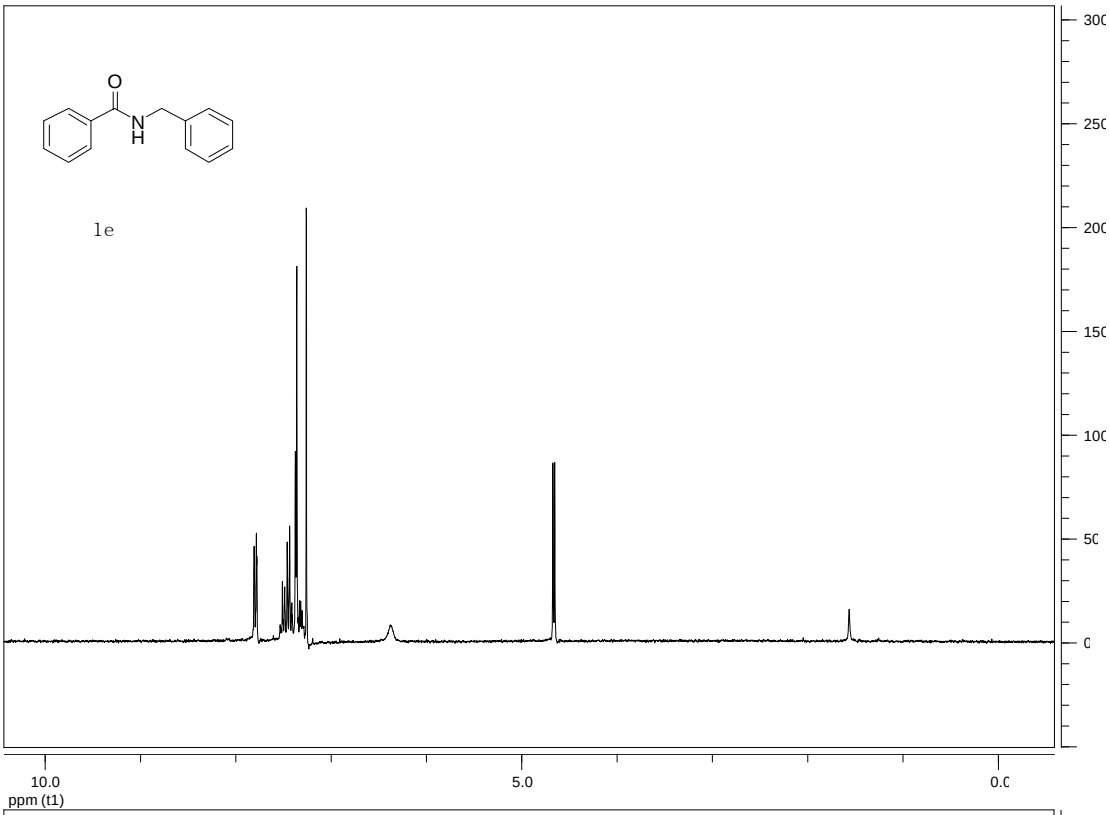
1000
500
0
10.0
5.0
0.0
ppm (f1)

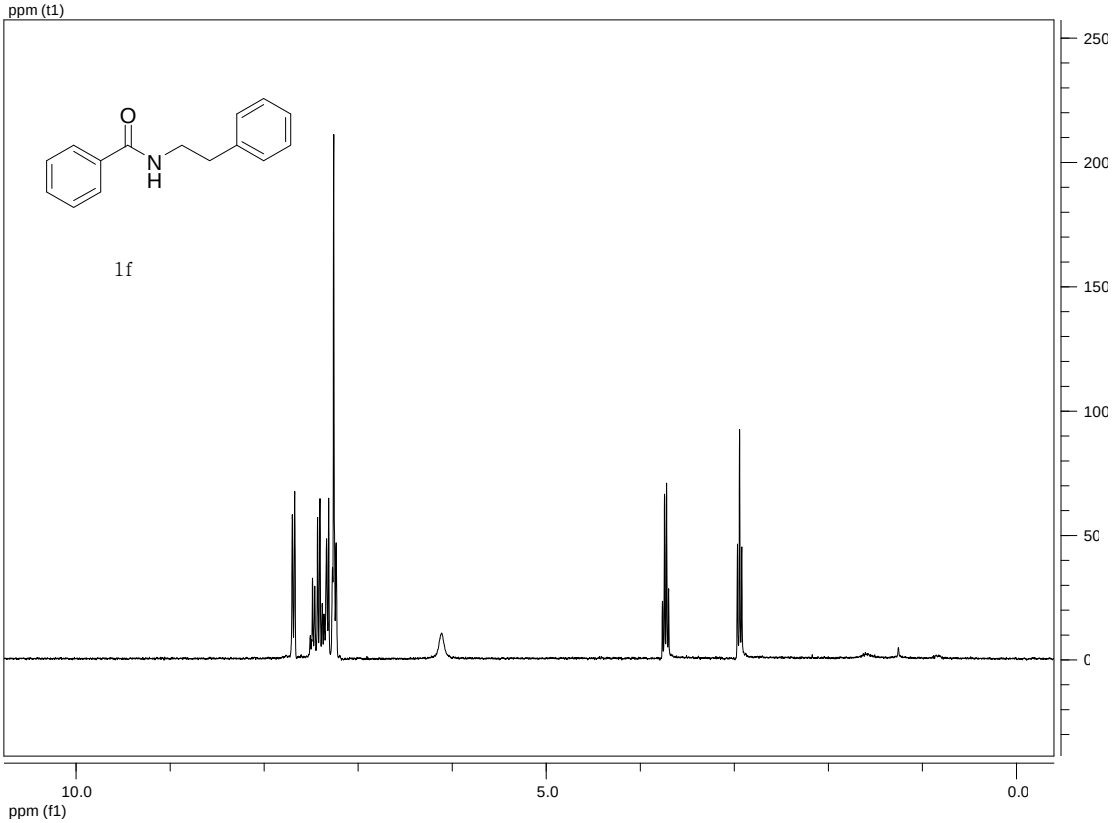

RhCp*(MeCN)3[ClO4]2
350
300
250
200
150
100
50
0
-50
10.0
5.0
0.0
ppm (f1)

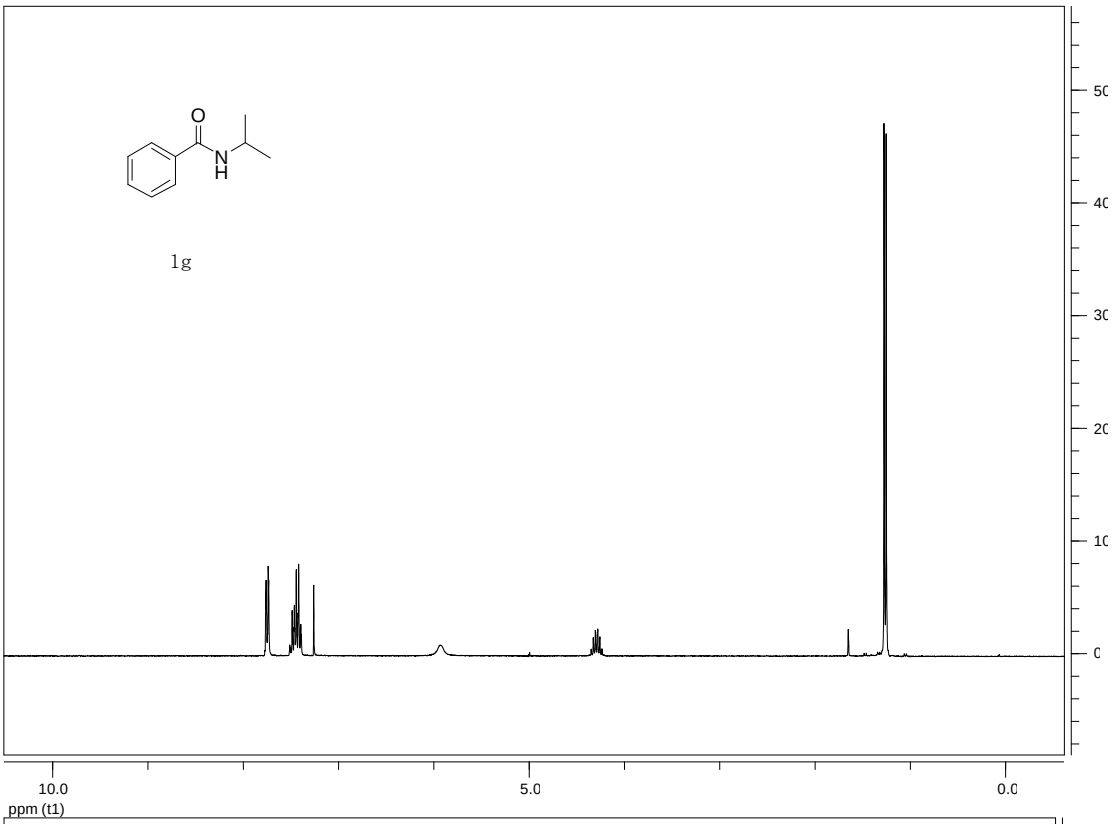

O
N
H
Me
1a
500
400
300
200
100
0
10.0
5.0
0.0
ppm (t1)

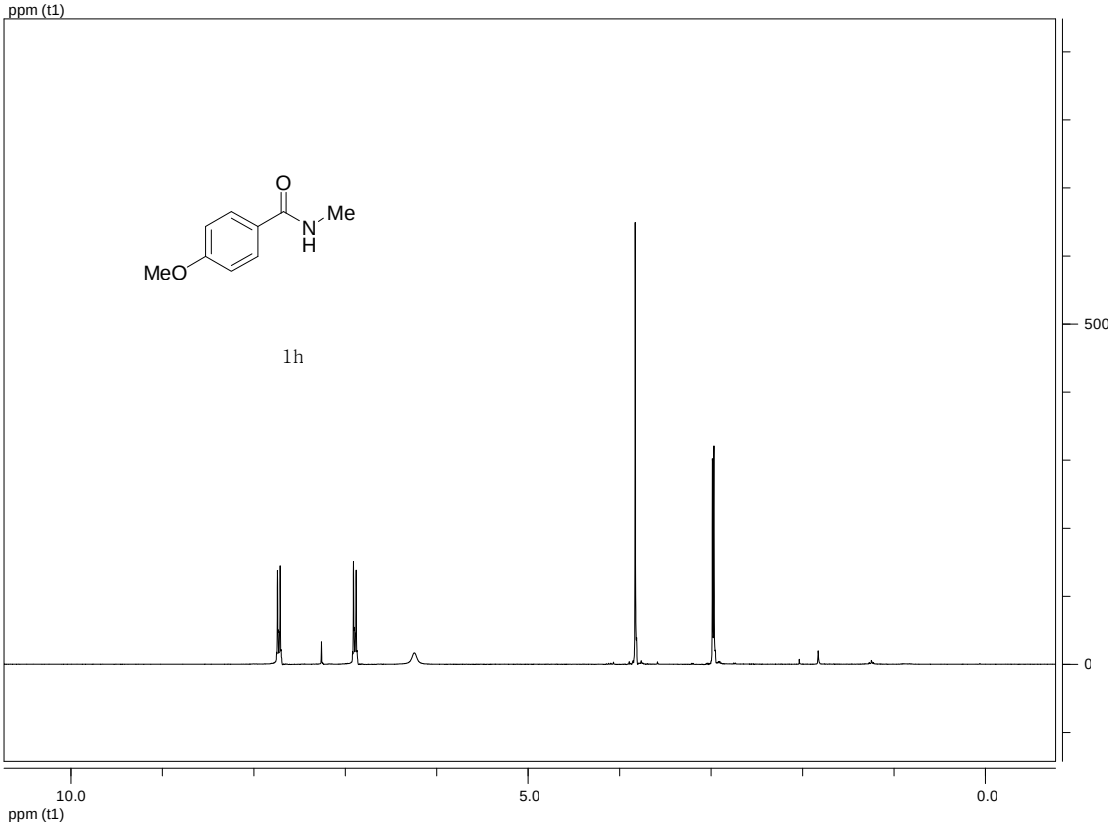

O
N
H
Et
1b
400
300
200
100
0
10.0
5.0
0.0
ppm (t1)

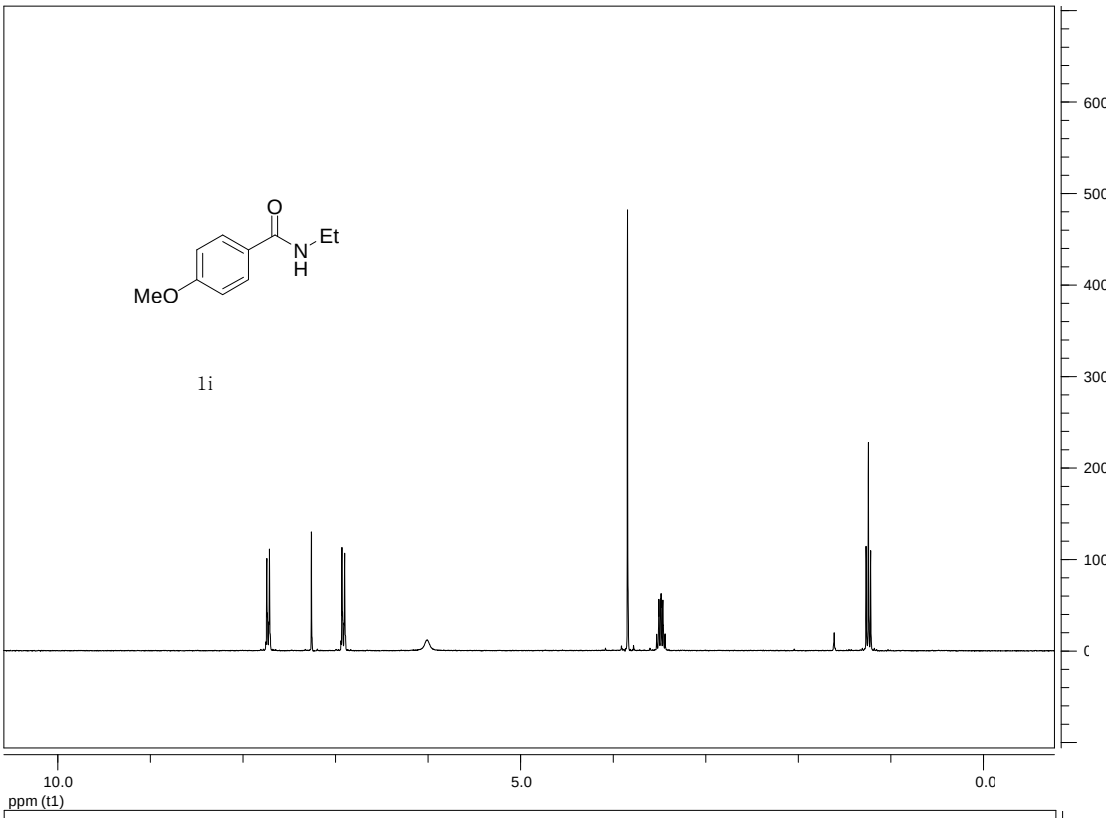

O
N
H
1c
25.0
20.0
15.0
10.0
5.0
0.0
10.0
5.0
0.0
ppm (t1)
O
N
H
1d
10.0
5.0
0.0
10.0
5.0
0.0
ppm (f1)


O
N
H
1e
10.0
5.0
ppm (t1)

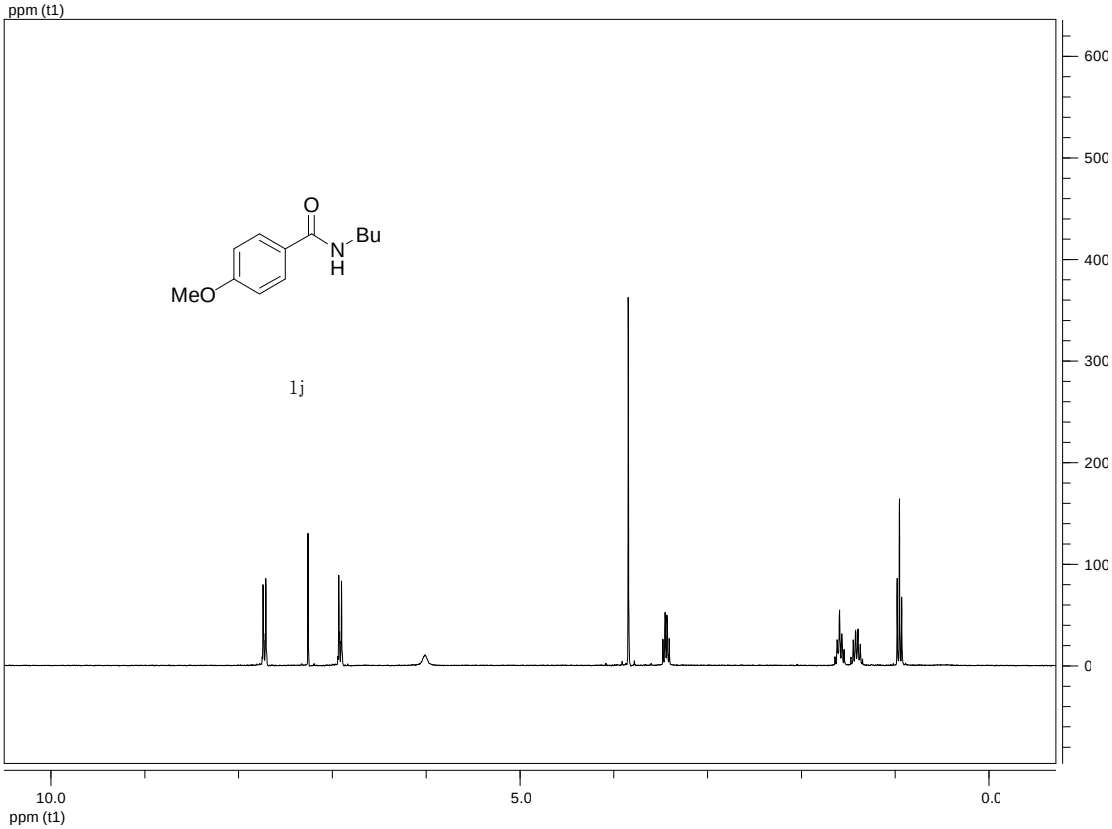

O
N
H
1f
10.0
5.0
0.0
ppm (f1)


O
N
H
1g
10.0
5.0
0.0
ppm (t1)

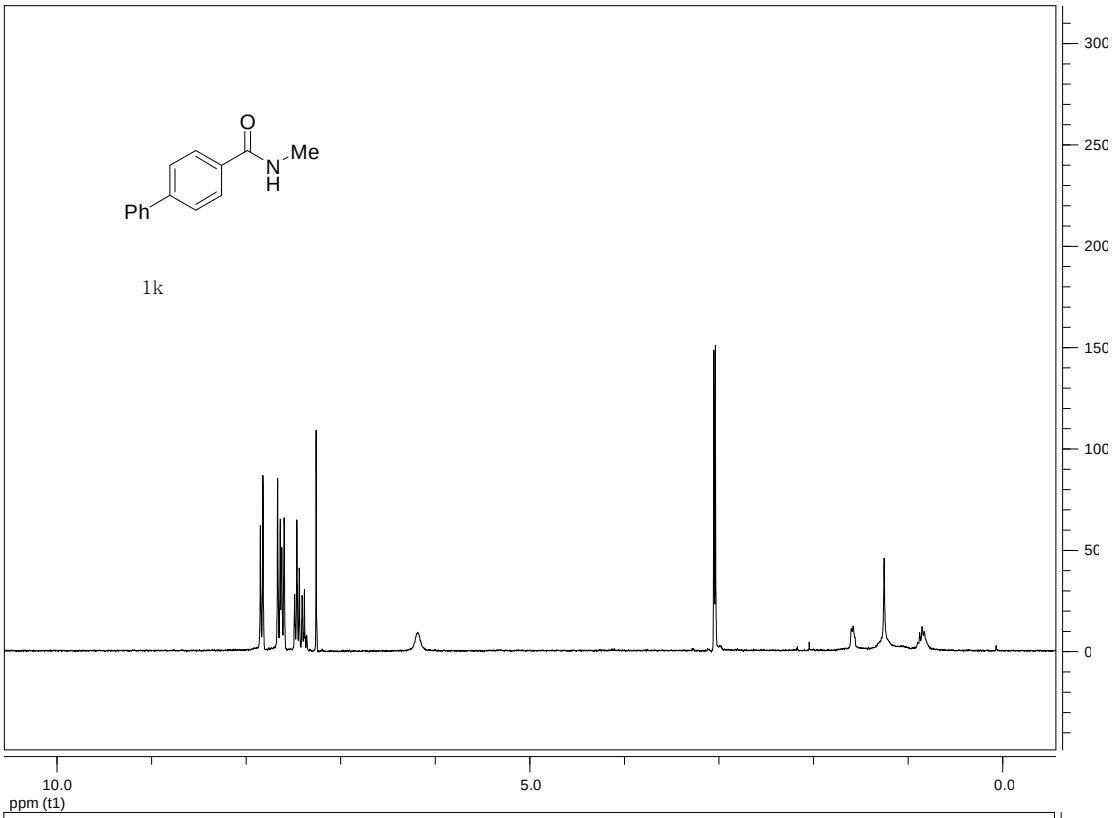

O
N
H
Me
MeO
1h
10.0
5.0
0.0
ppm (t1)

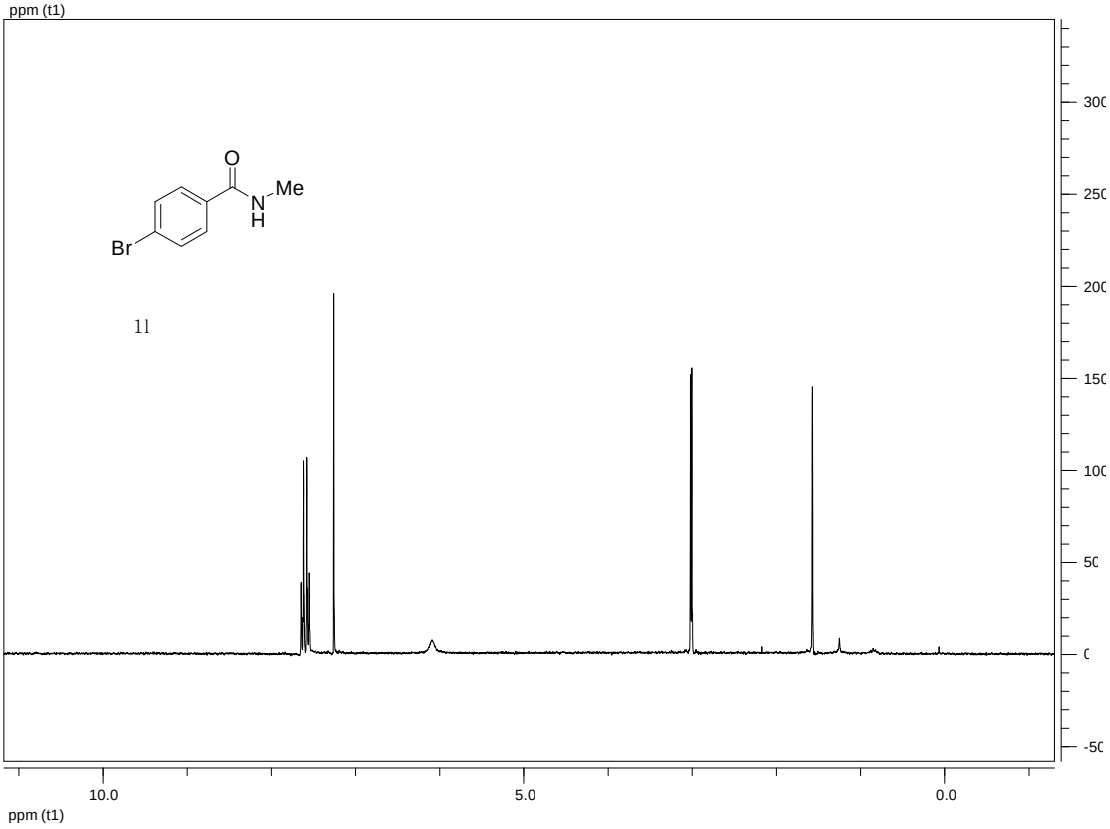


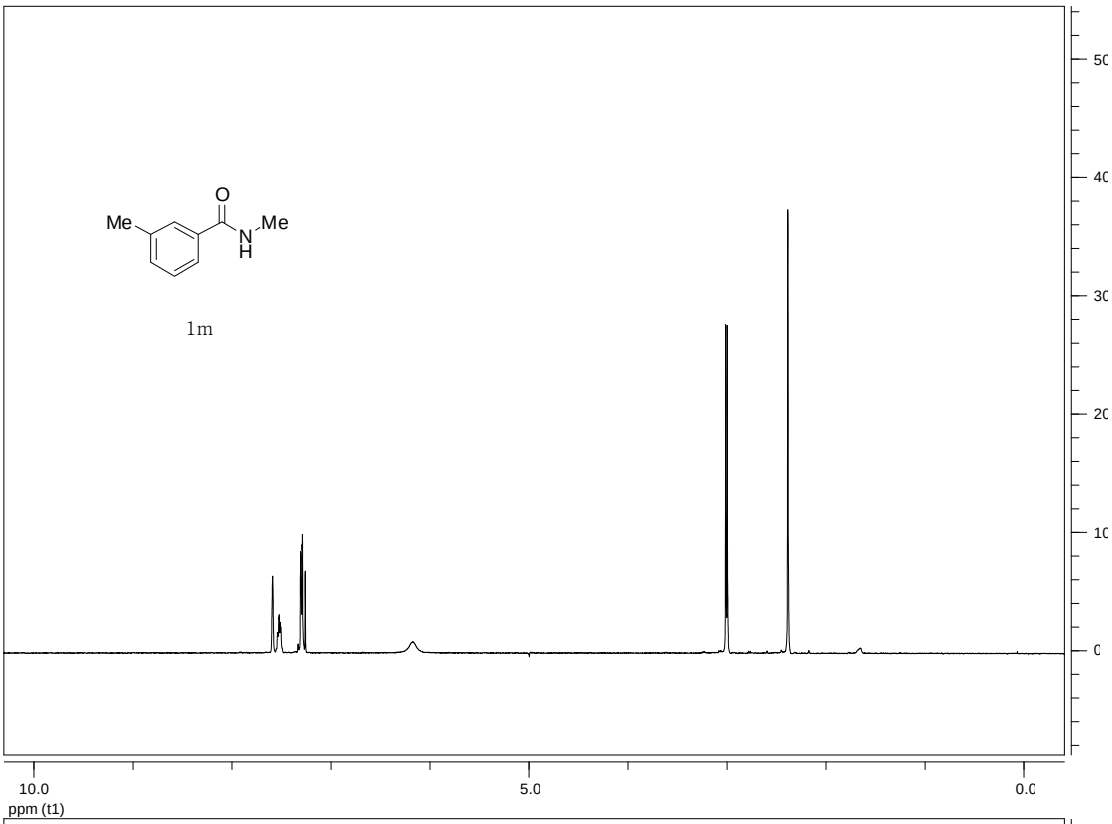
1i

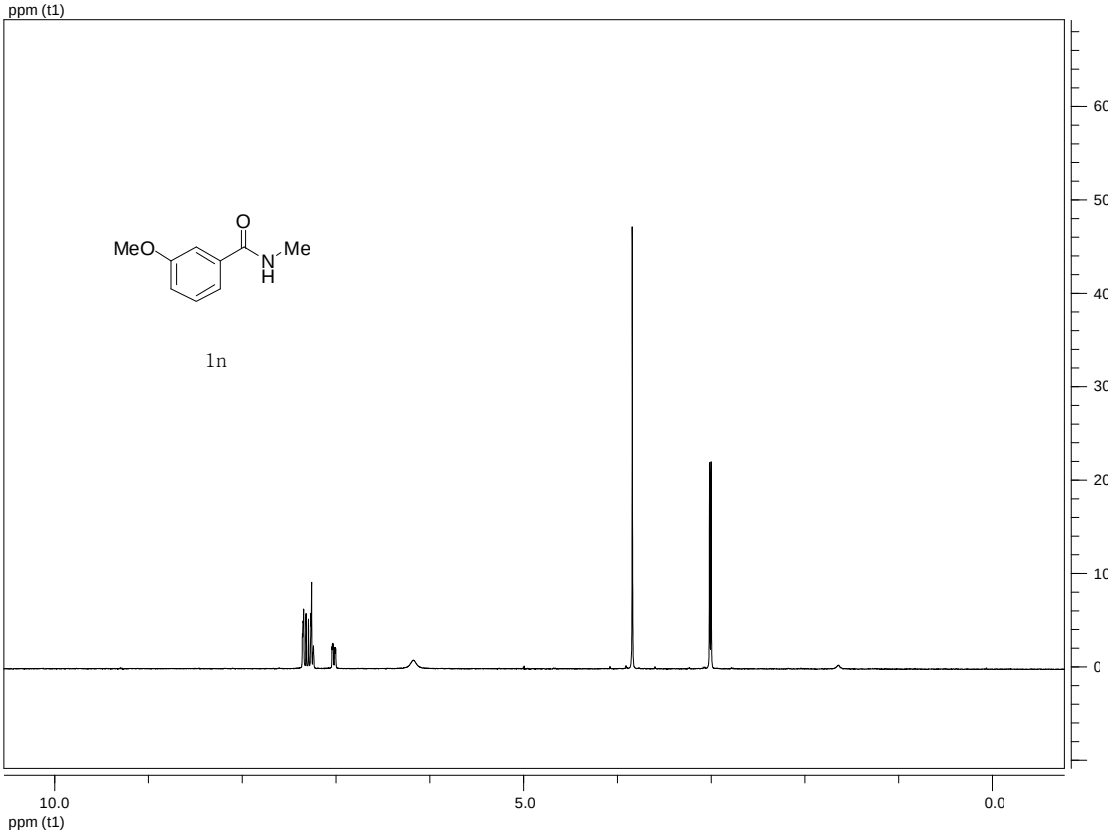


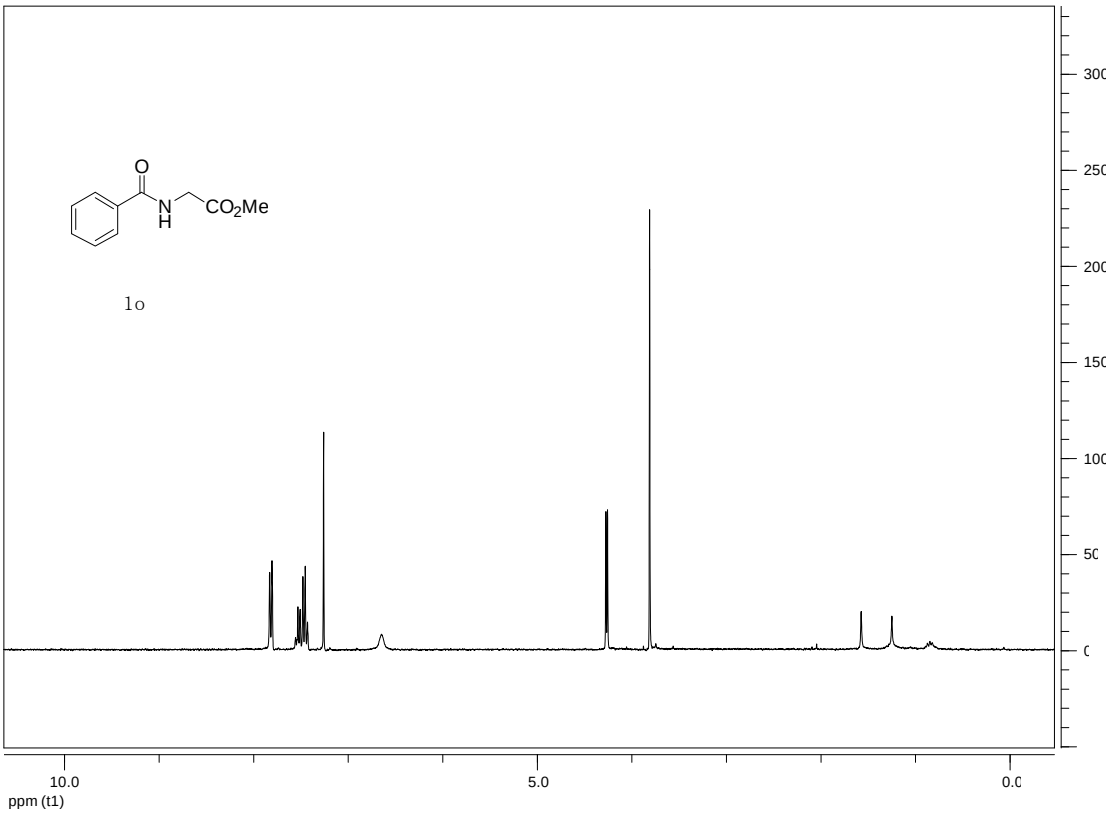
1j


O
N
Me
H
Ph
1k
10.0
5.0
0.0
ppm (t1)

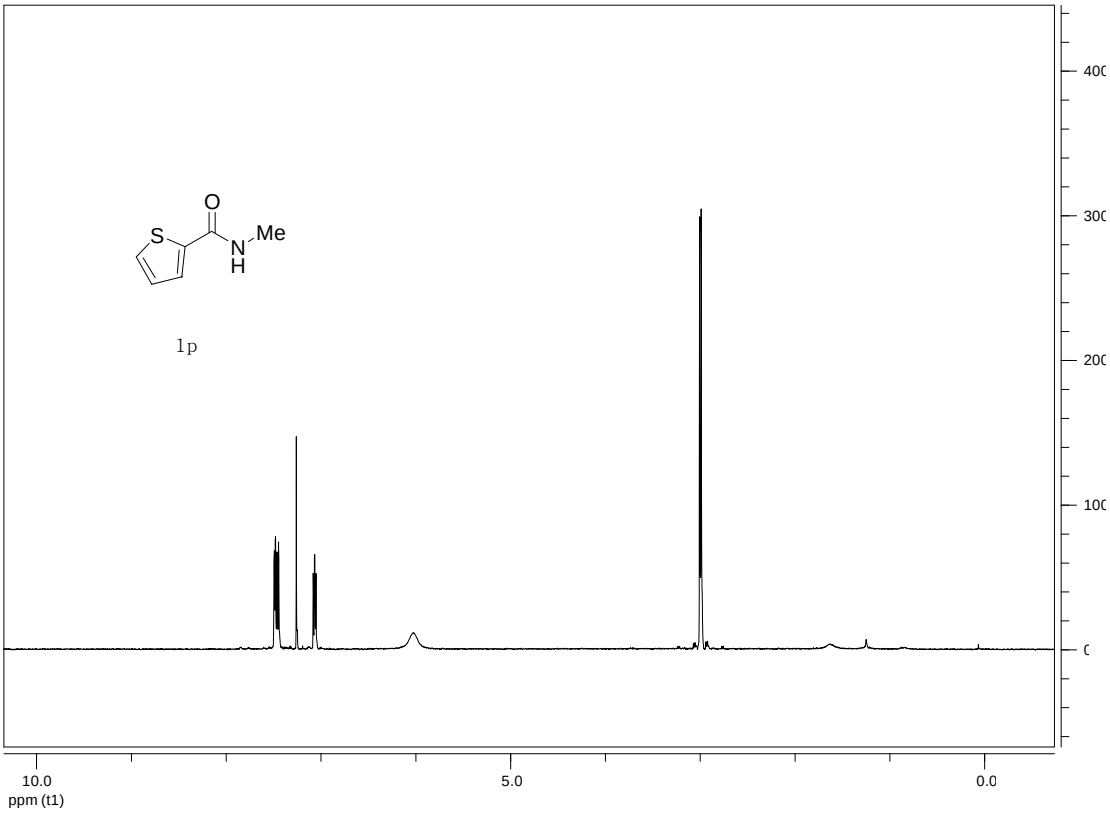

O
N
Me
H
Br
1l
10.0
5.0
0.0
ppm (t1)


Me
O
N
H
Me
1m
10.0
5.0
0.0
ppm (t1)

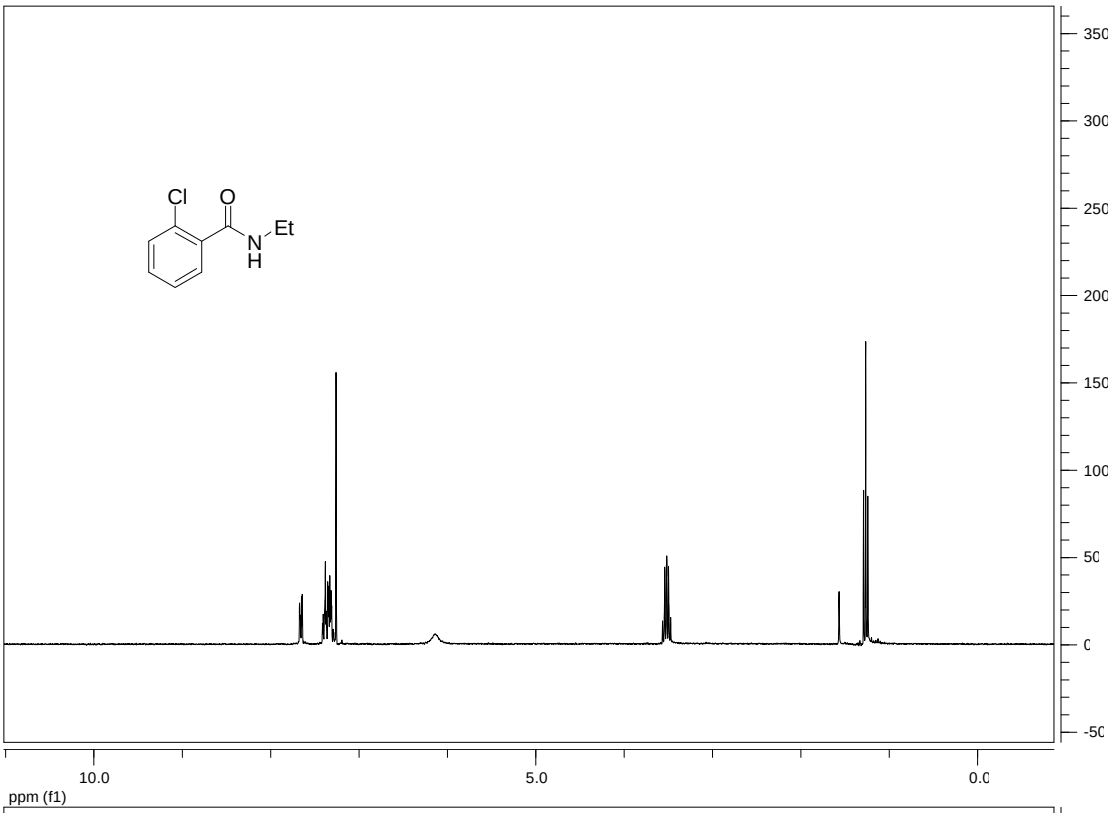

MeO
O
N
H
Me
1n
10.0
5.0
0.0
ppm (t1)

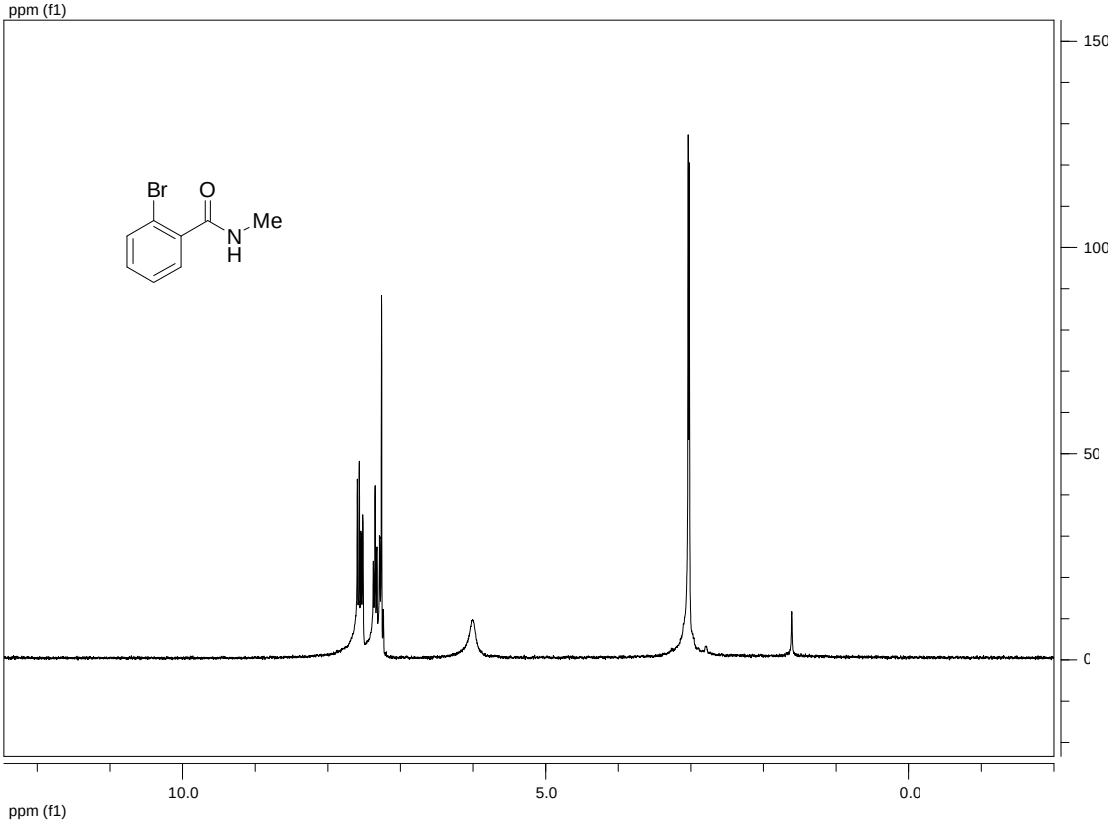


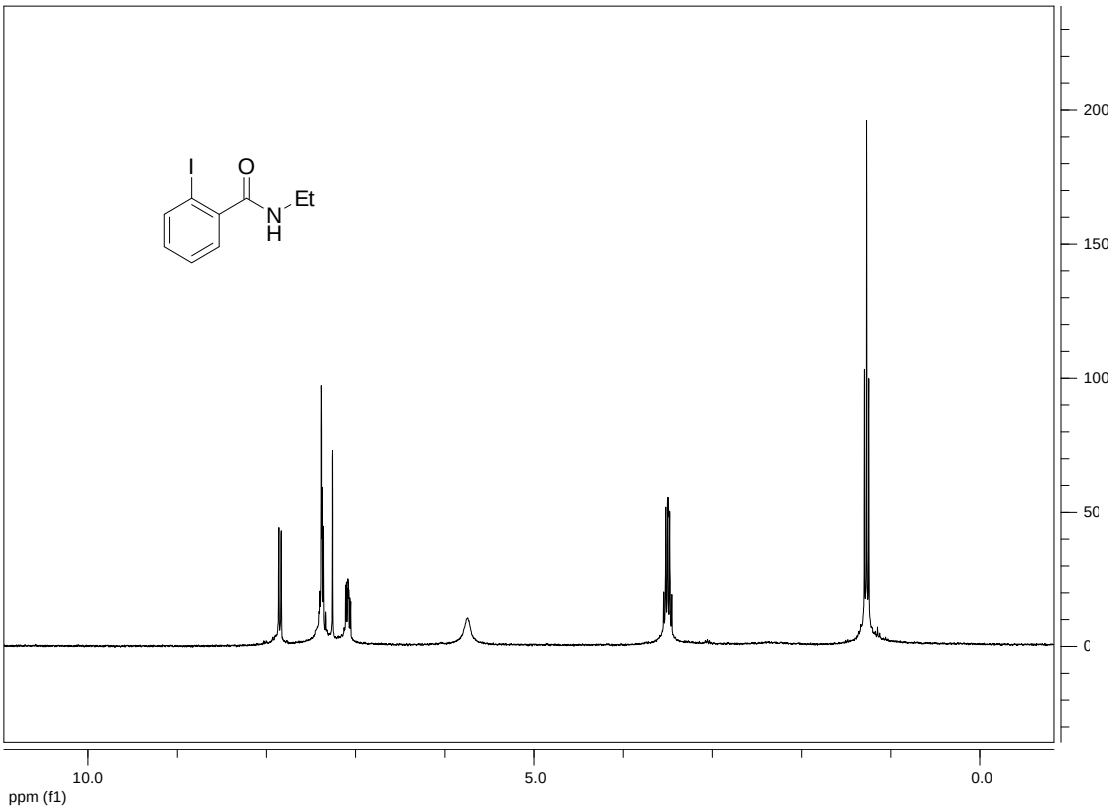
1o

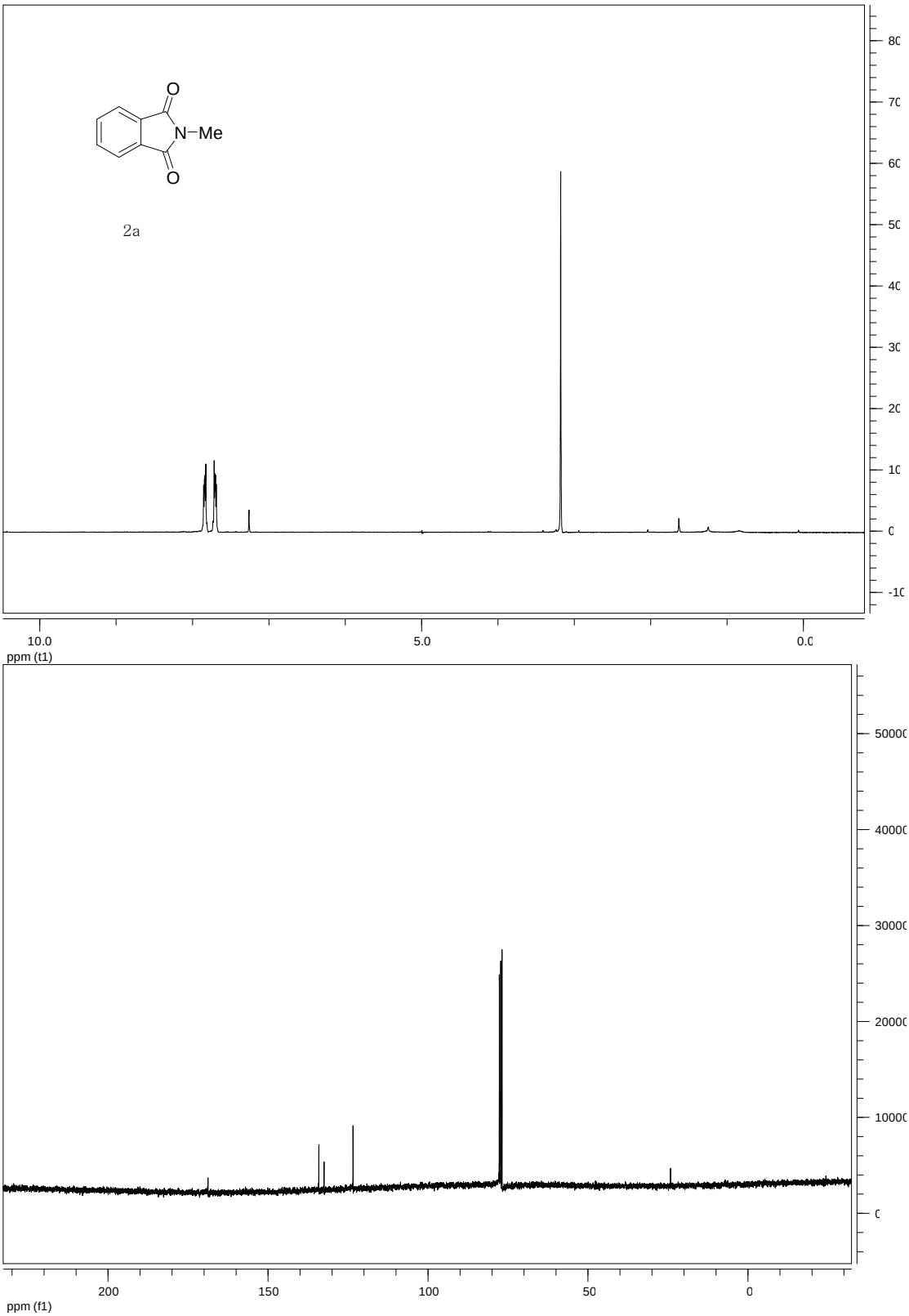


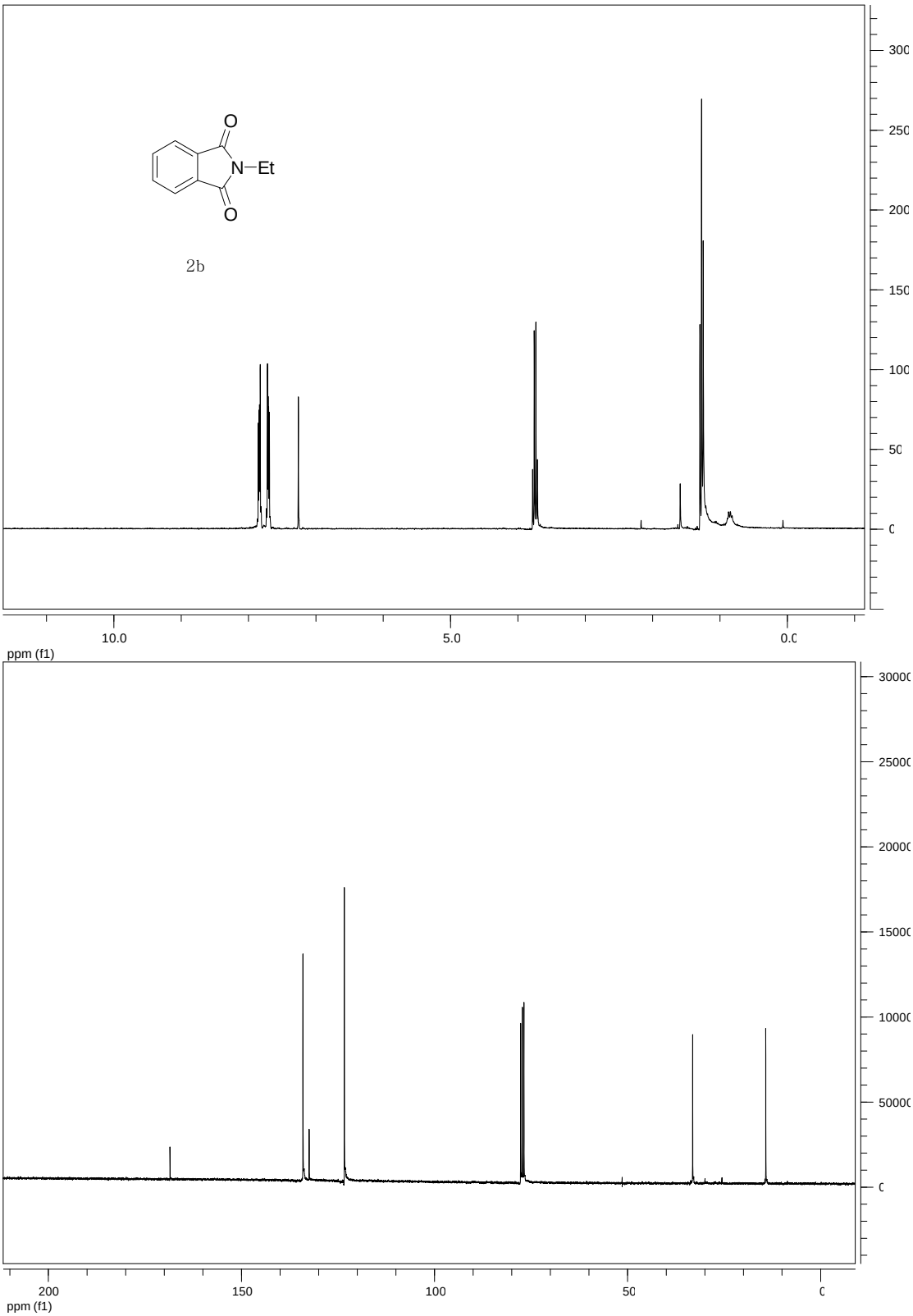
1p

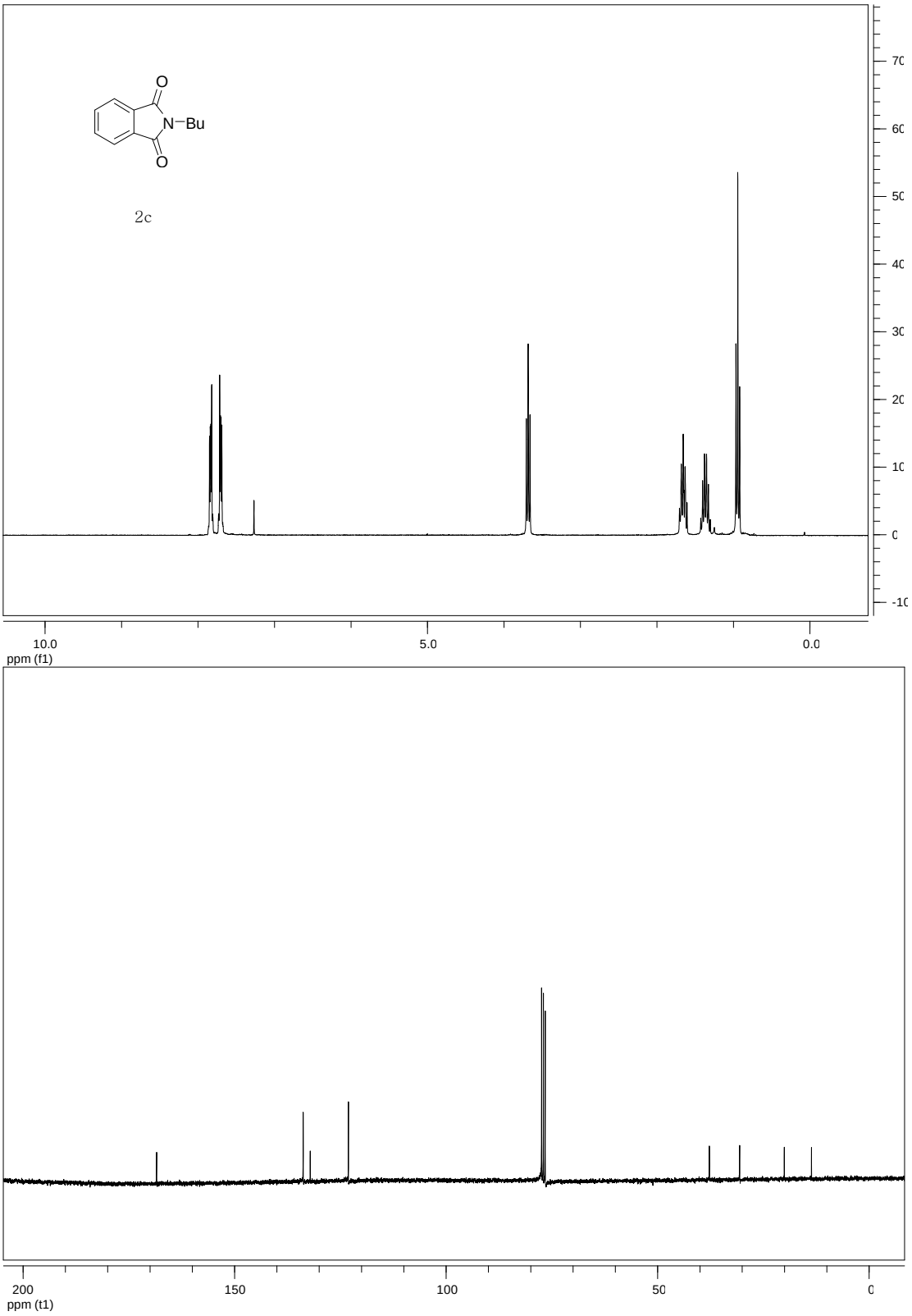

Cl
O
N
H
Et
350
300
250
200
150
100
50
0
-50
10.0
5.0
0.0
ppm (f1)

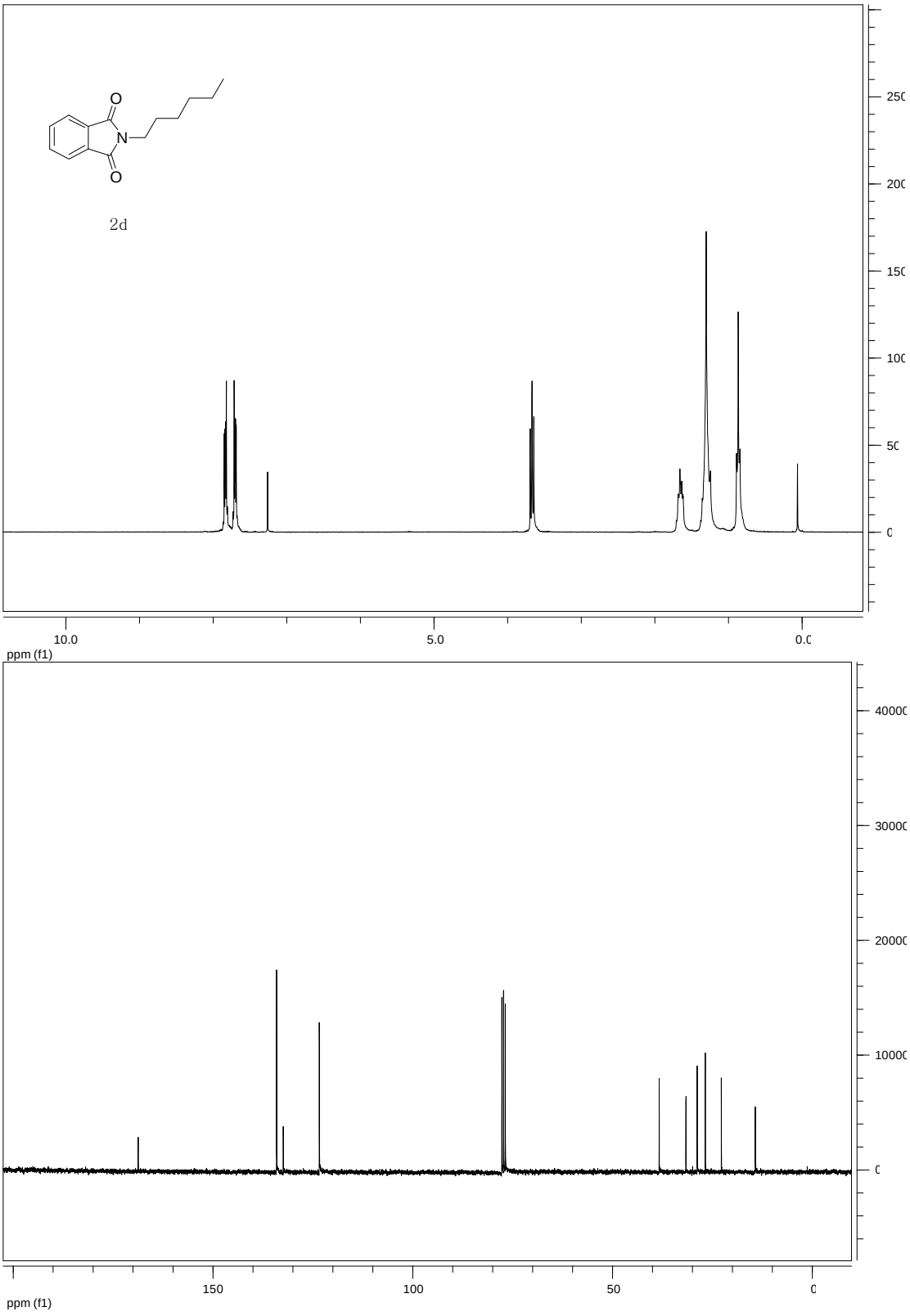

Br
O
N
H
Me
150
100
50
0
10.0
5.0
0.0
ppm (f1)

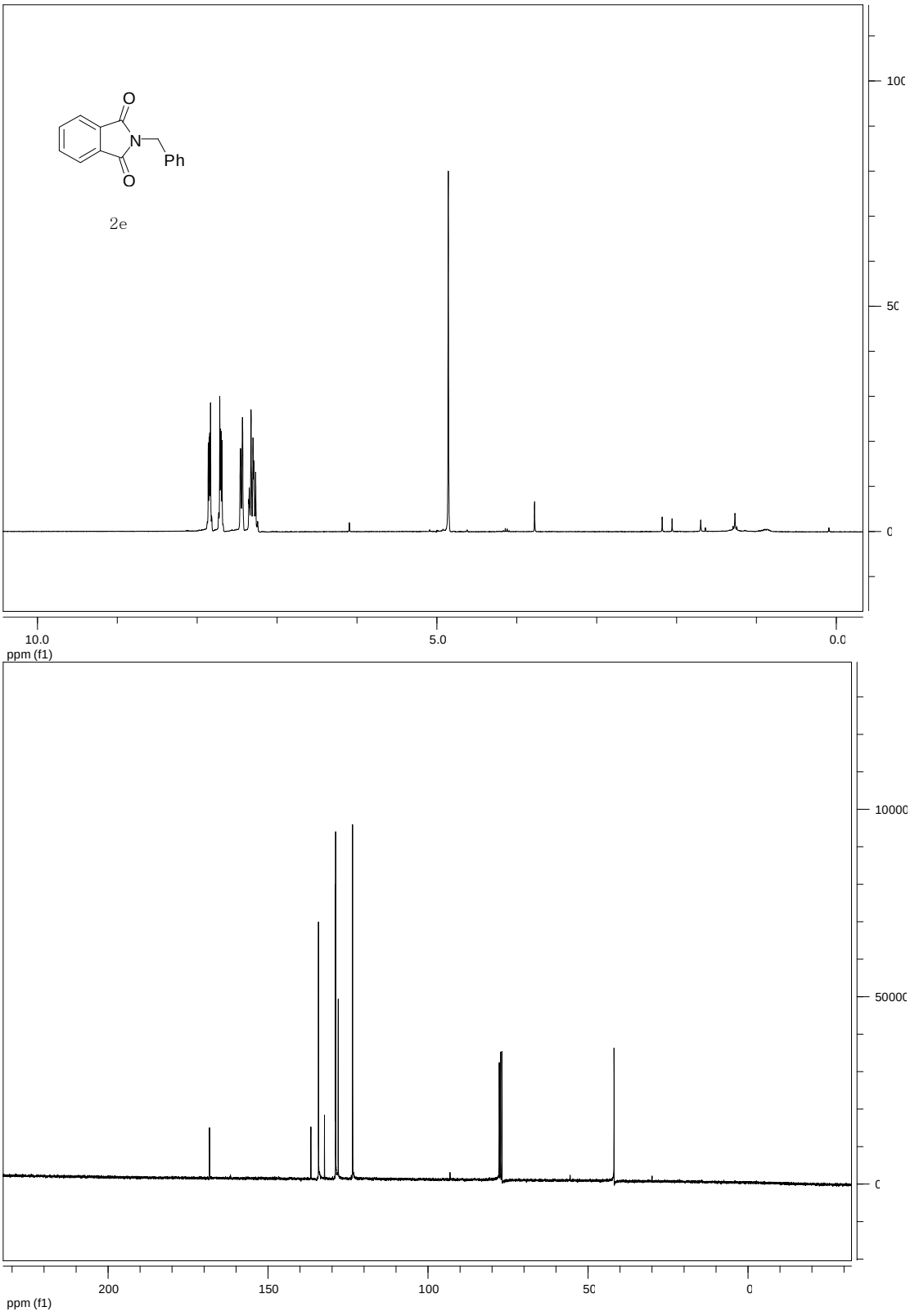

I
O
N
H
Et
200
150
100
50
0
10.0
5.0
0.0
ppm (f1)

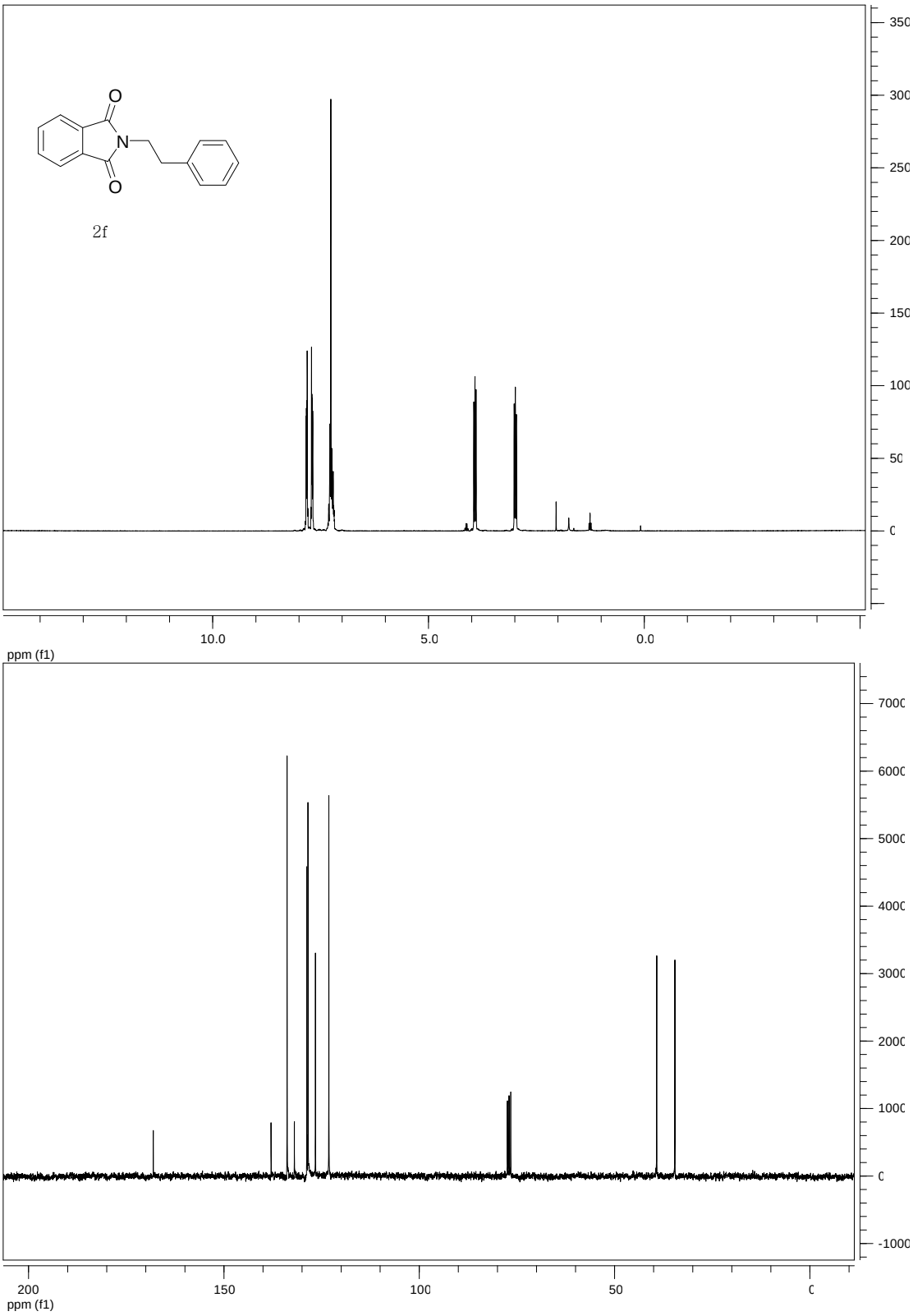

O
N–Me
O
2a
10.0
5.0
0.0
ppm (t1)
200
150
100
50
0
ppm (f1)

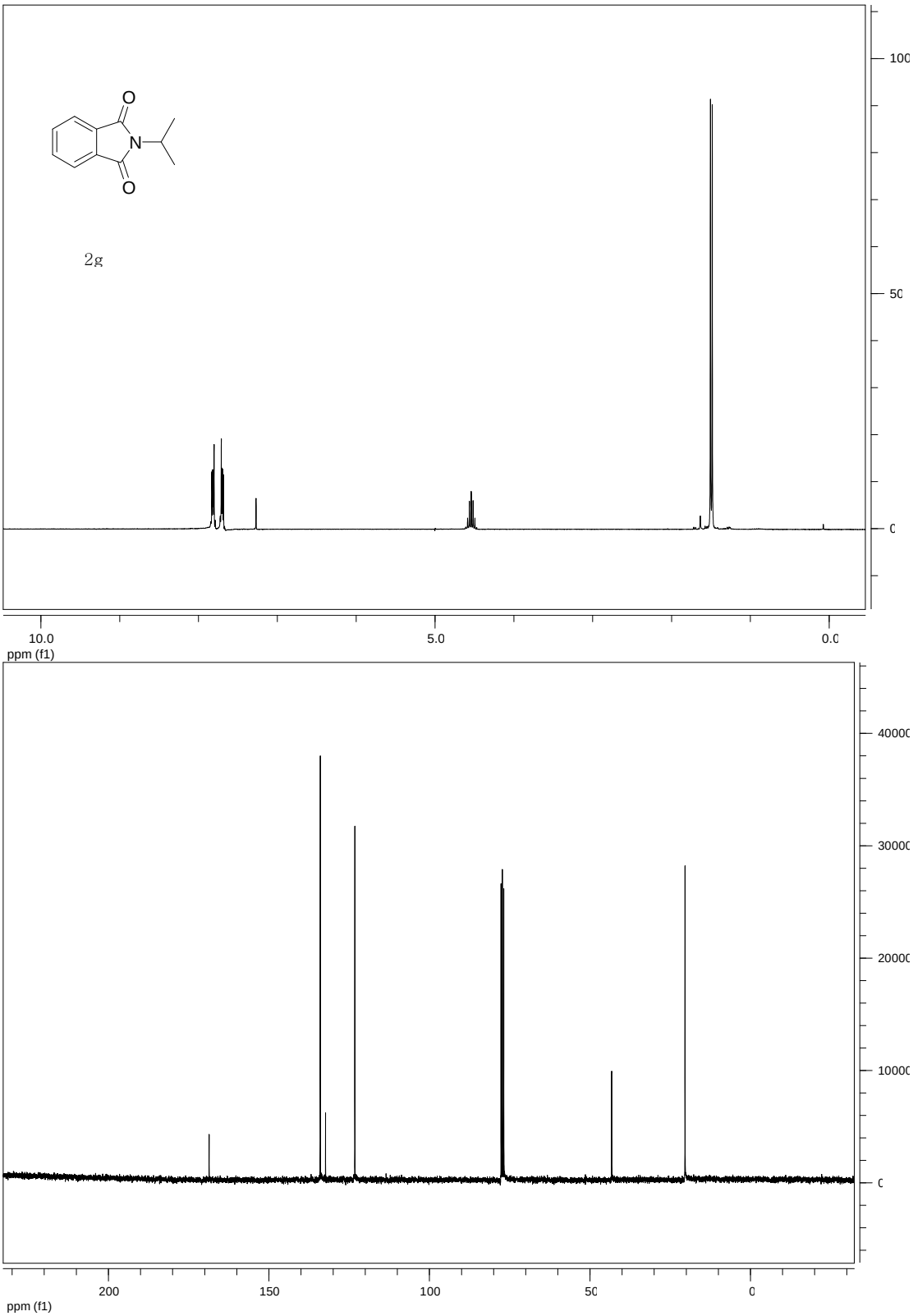

O
N—Et
O
2b
300
250
200
150
100
50
0
10.0
5.0
0.0
ppm (f1)
30000
25000
20000
15000
10000
5000
0
200
150
100
50
0
ppm (f1)

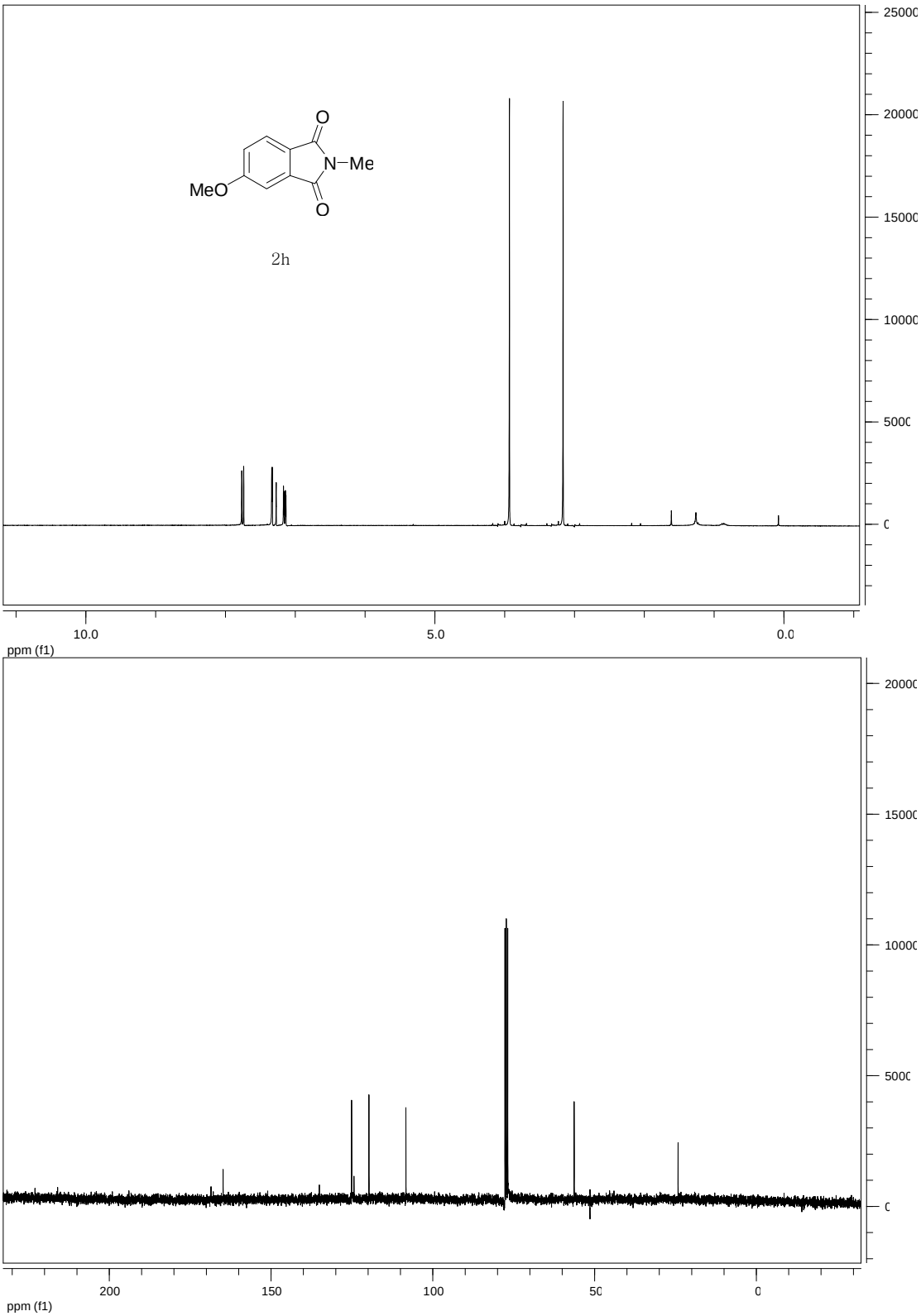

O
N–Bu
O
2c
10.0
5.0
0.0
ppm (f1)
200
150
100
50
0
ppm (t1)

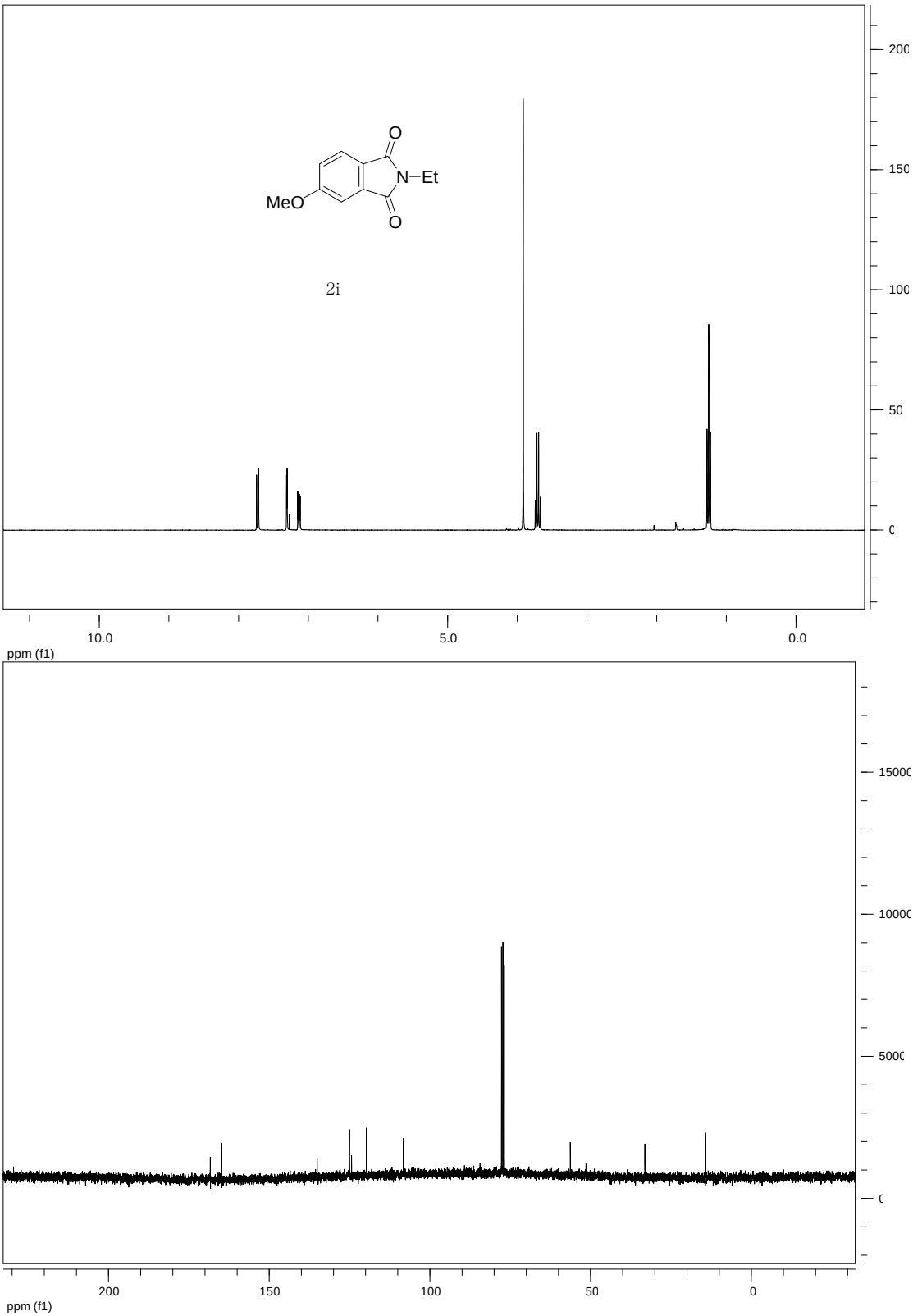

O
N
O
2d
250
200
150
100
50
0
10.0
5.0
0.0
ppm (f1)
40000
30000
20000
10000
0
150
100
50
0
ppm (f1)

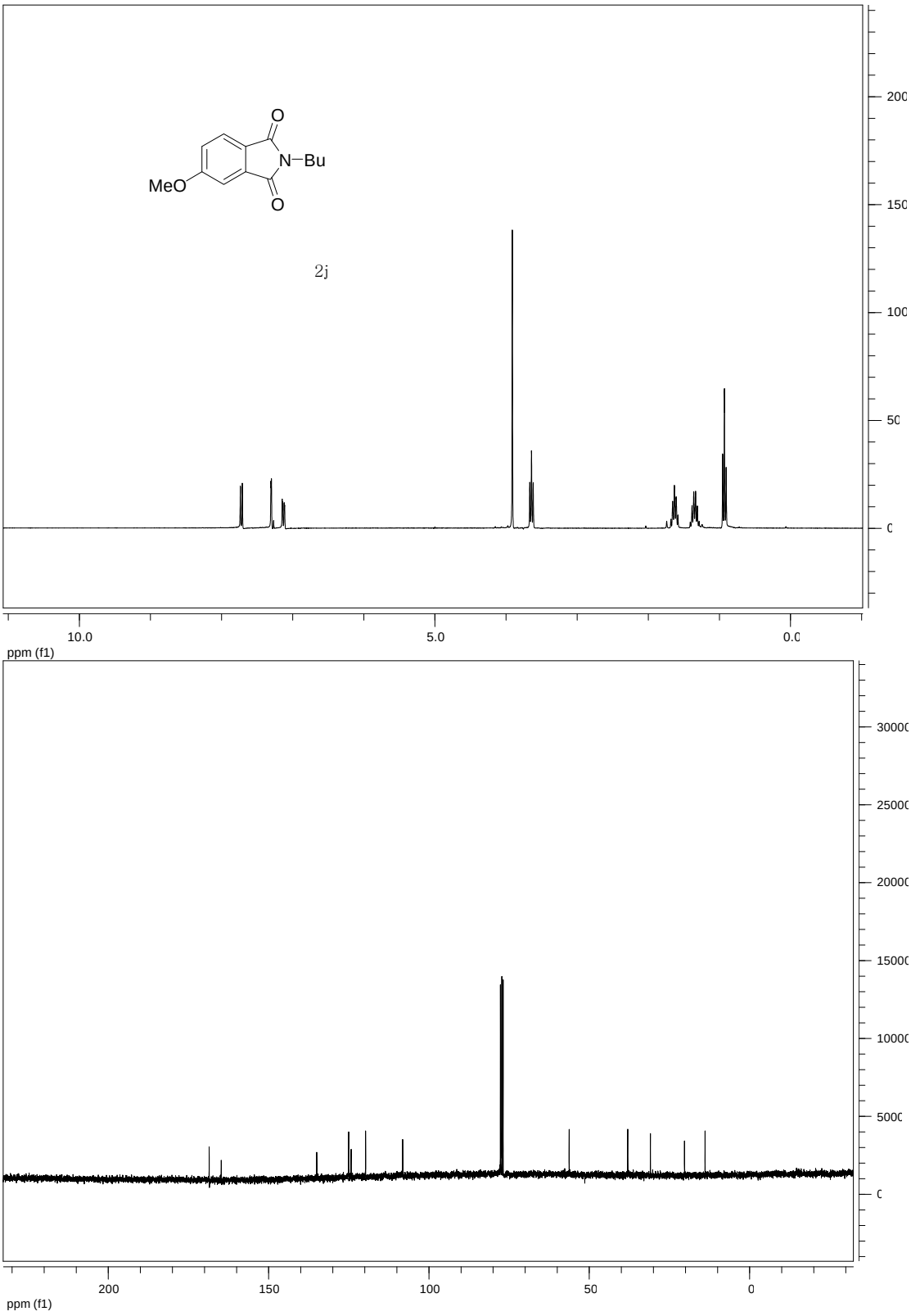

O
N
Ph
O
2e
10.0
5.0
0.0
ppm (f1)
200
150
100
50
0
ppm (f1)

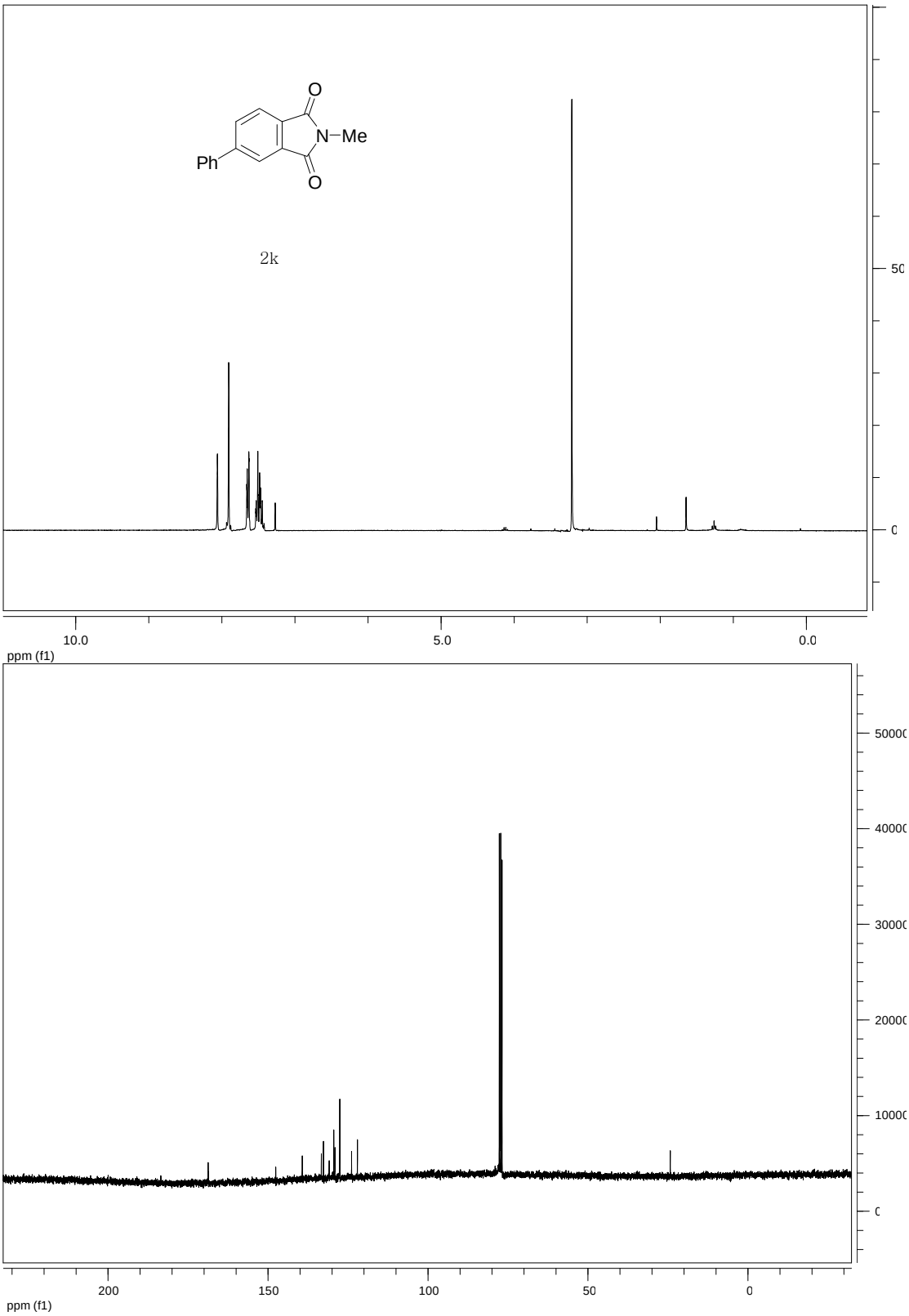

O
N
O
2f
350
300
250
200
150
100
50
0
10.0
5.0
0.0
ppm (f1)
7000
6000
5000
4000
3000
2000
1000
0
-1000
200
150
100
50
0
ppm (f1)

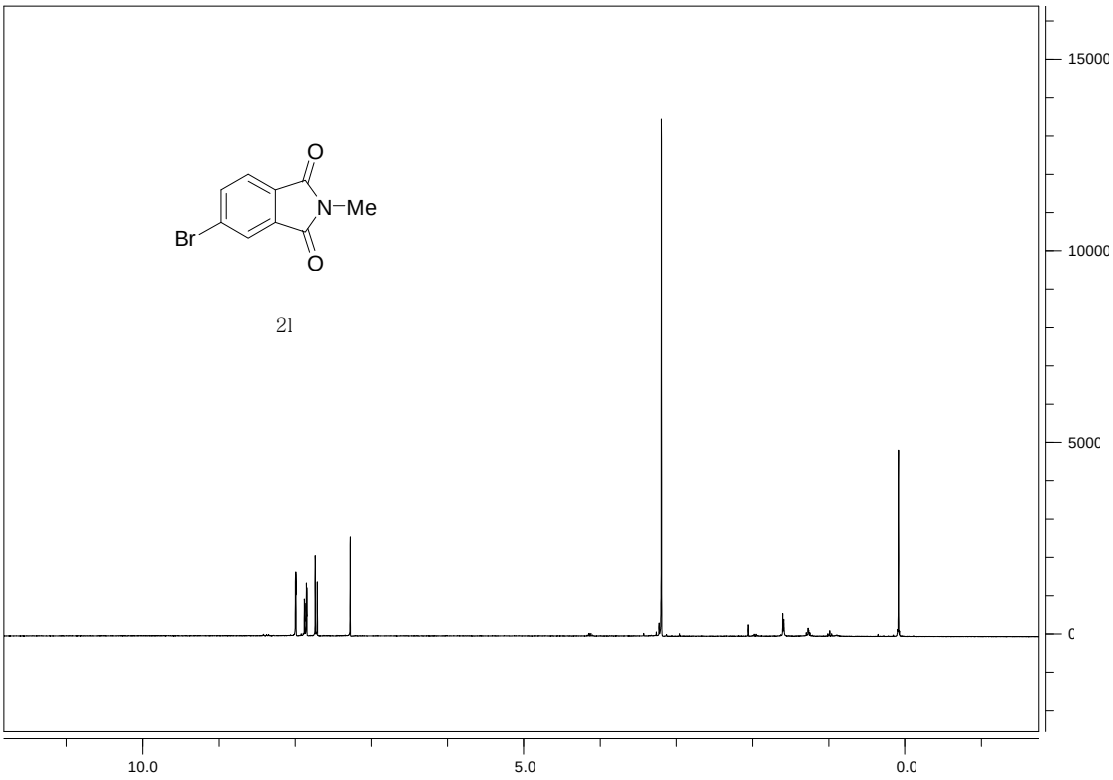

O
N
O
2g
10.0
5.0
0.0
ppm (f1)
200
150
100
50
0
ppm (f1)

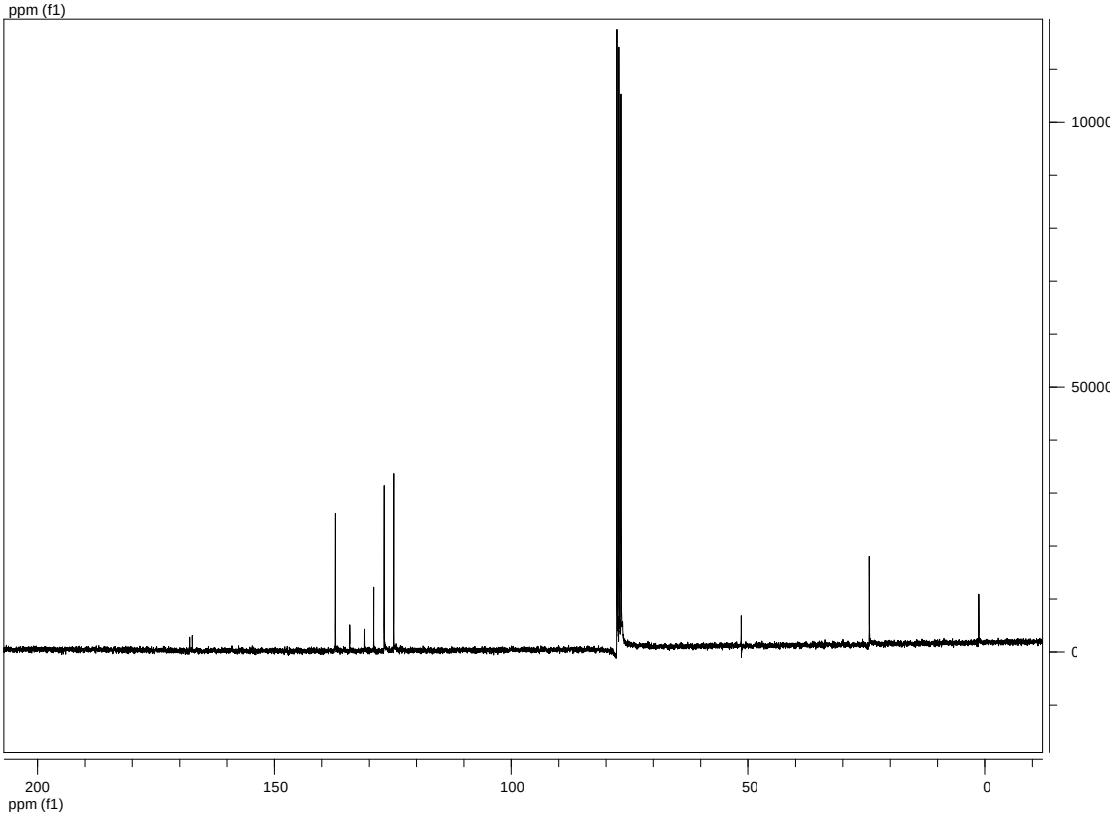

O
N–Me
MeO
O
2h
25000
20000
15000
10000
5000
0
10.0
5.0
0.0
ppm (f1)
20000
15000
10000
5000
0
200
150
100
50
0
ppm (f1)

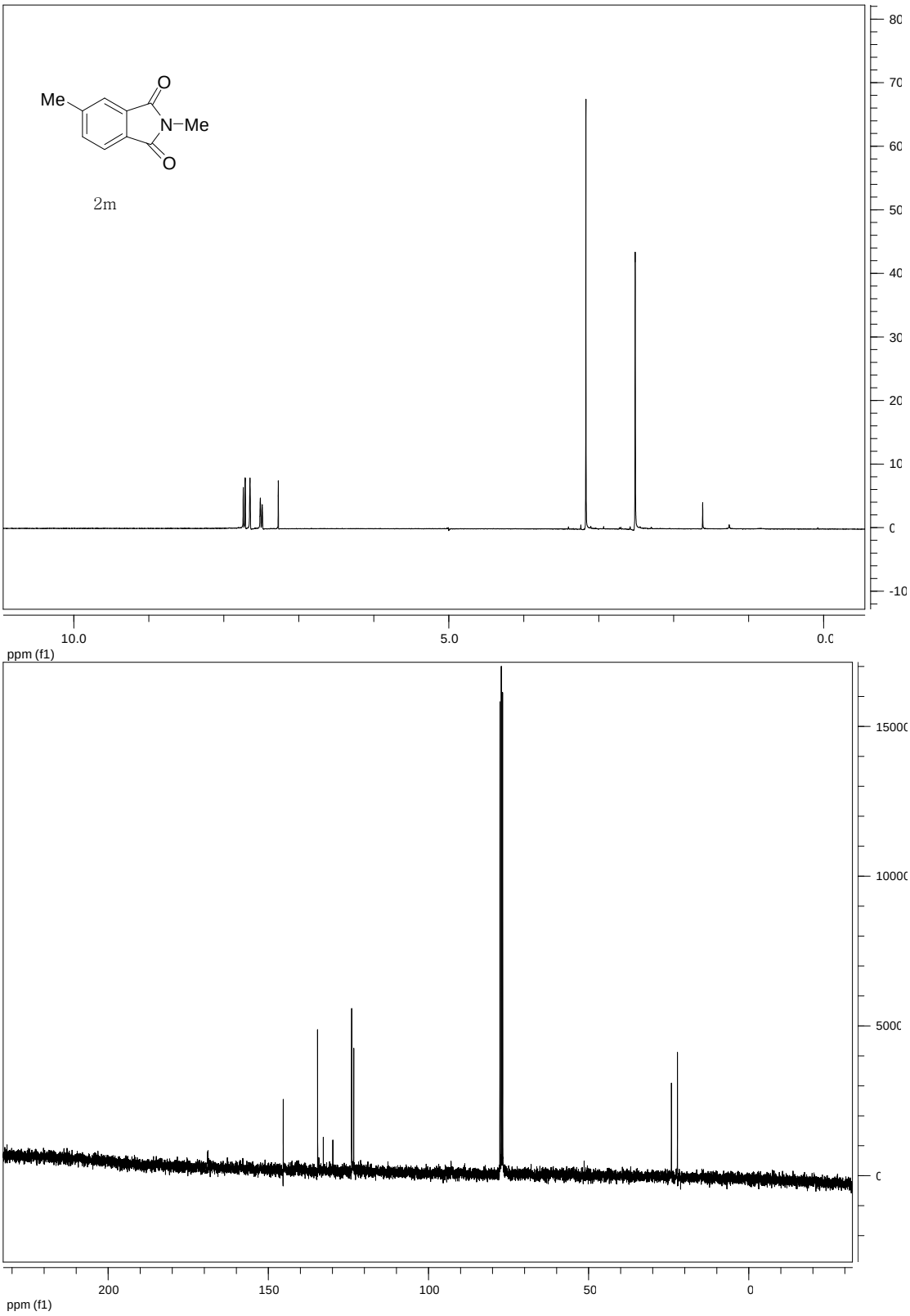

O
N–Et
MeO
O
2i
200
150
100
50
0
10.0
5.0
0.0
ppm (f1)
15000
10000
5000
0
200
150
100
50
0
ppm (f1)

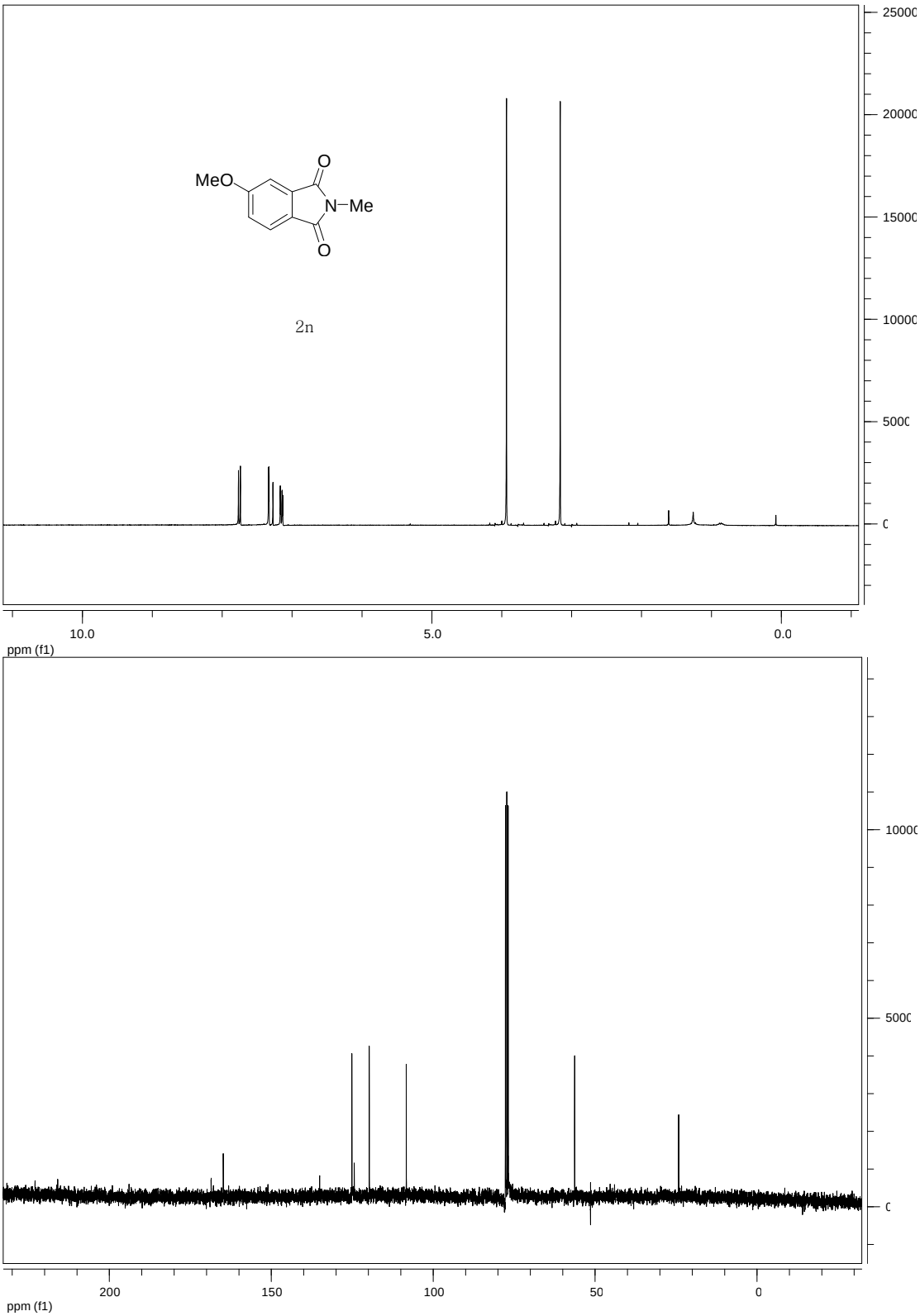

O
N–Bu
MeO
O
2j
200
150
100
50
0
10.0
5.0
0.0
ppm (f1)
30000
25000
20000
15000
10000
5000
0
200
150
100
50
0
ppm (f1)

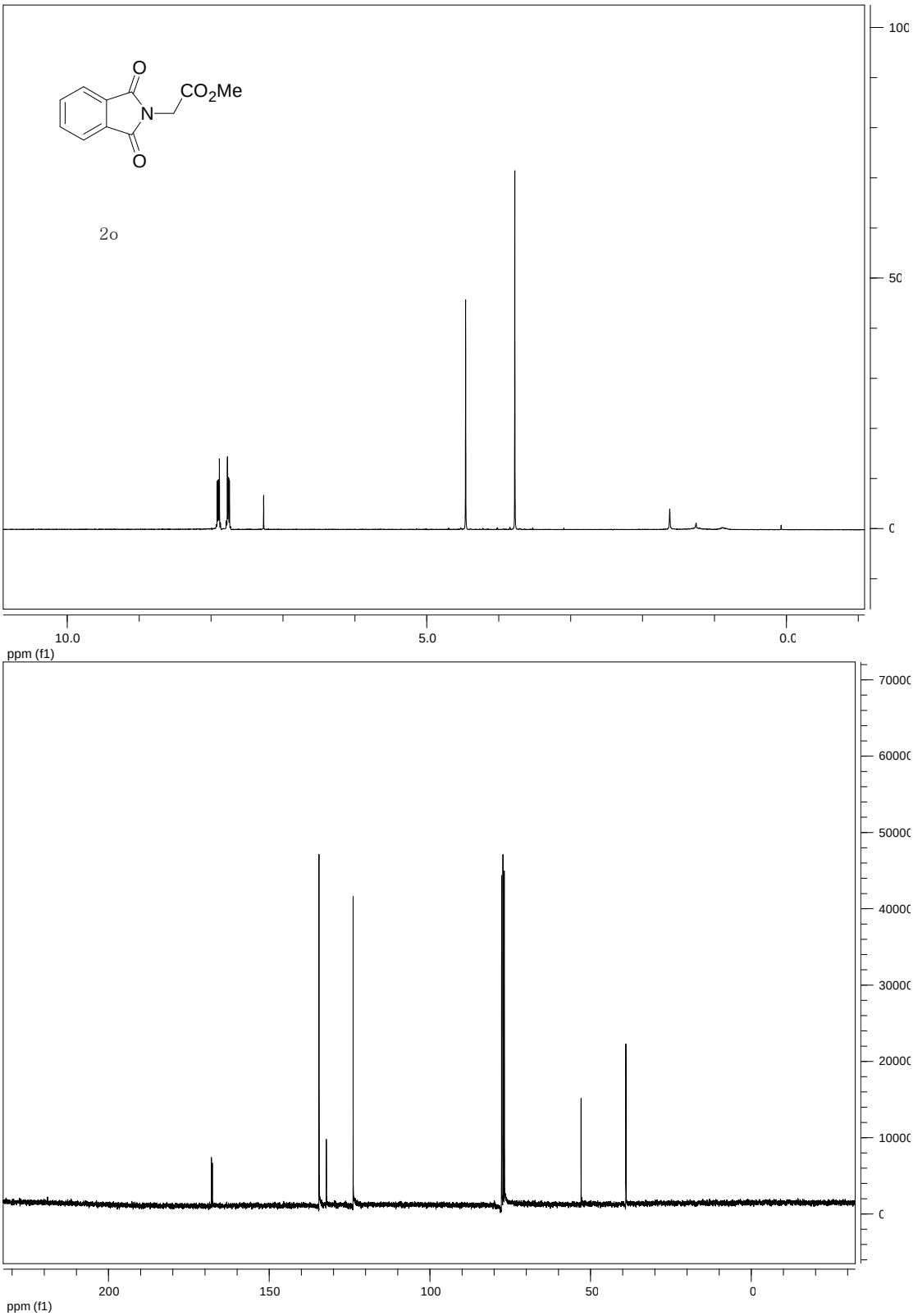

O
N–Me
Ph
O
2k
50
0
10.0
5.0
0.0
ppm (f1)
50000
40000
30000
20000
10000
0
200
150
100
50
0
ppm (f1)

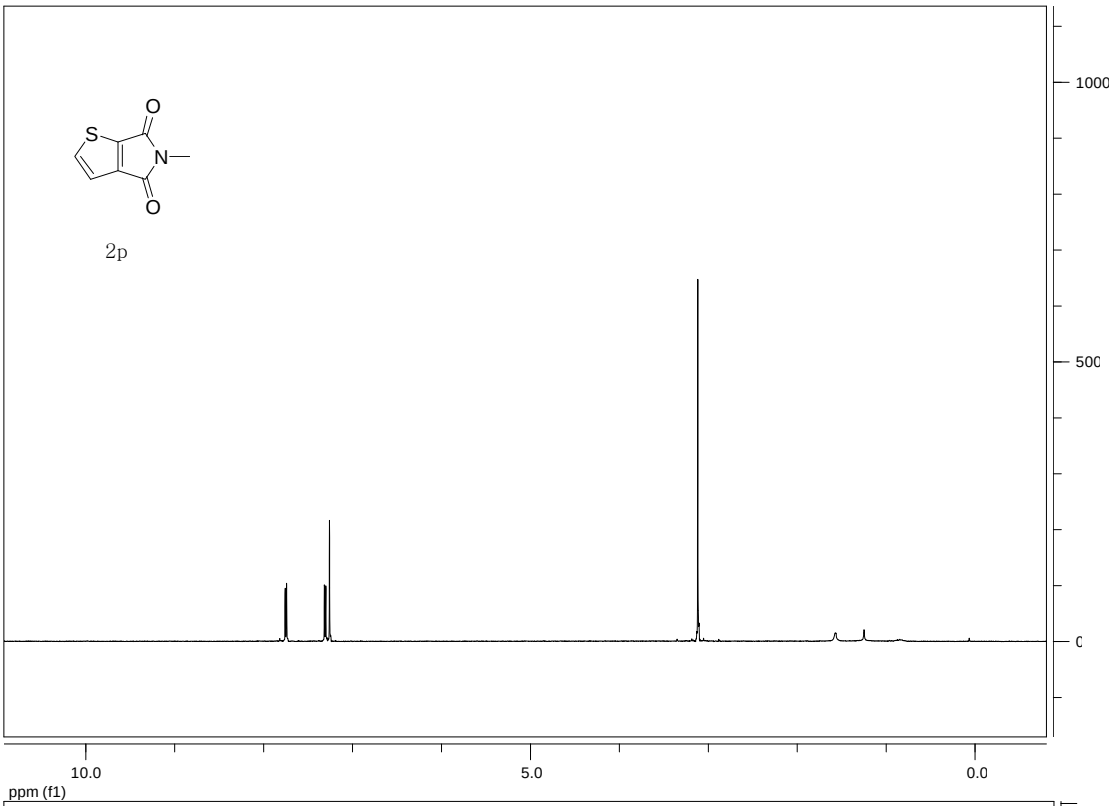

O
N−Me
Br
O
21
15000
10000
5000
0
10.0
5.0
0.0
ppm (f1)


10000
5000
0
200
150
100
50
0
ppm (f1)

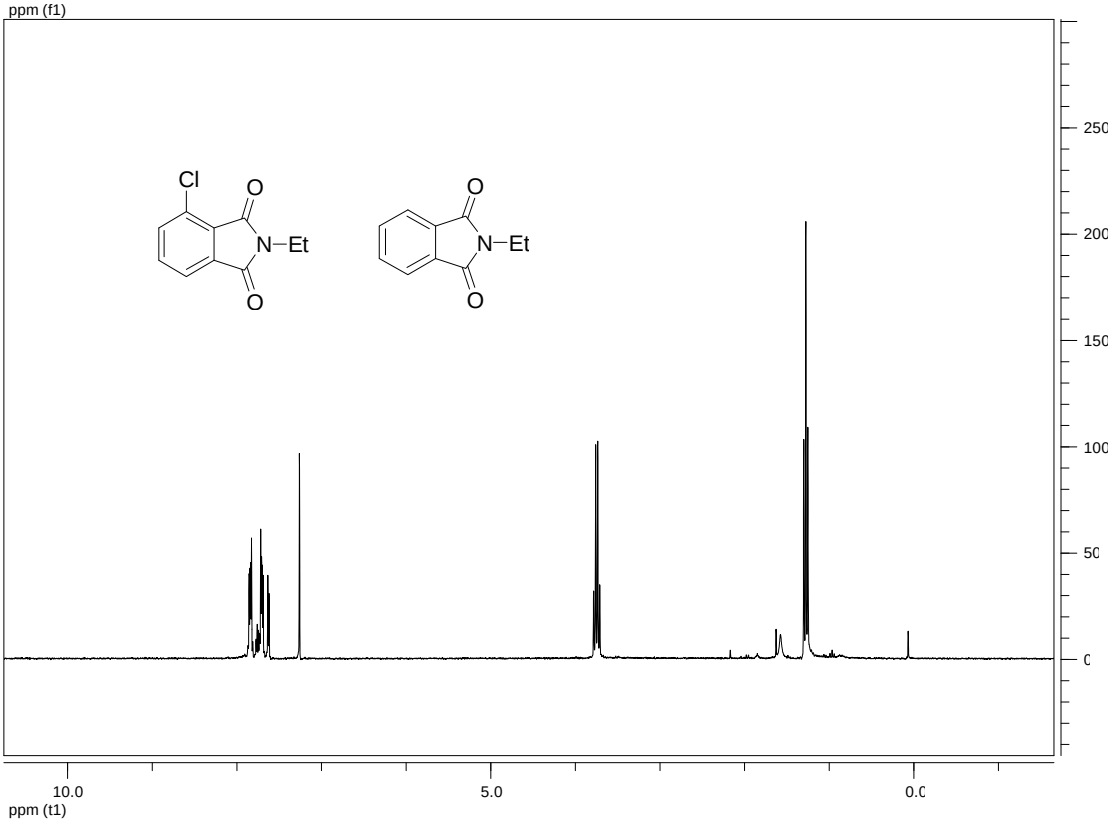

Me
O
N–Me
O
2m
10.0
5.0
0.0
ppm (f1)
200
150
100
50
0
ppm (f1)

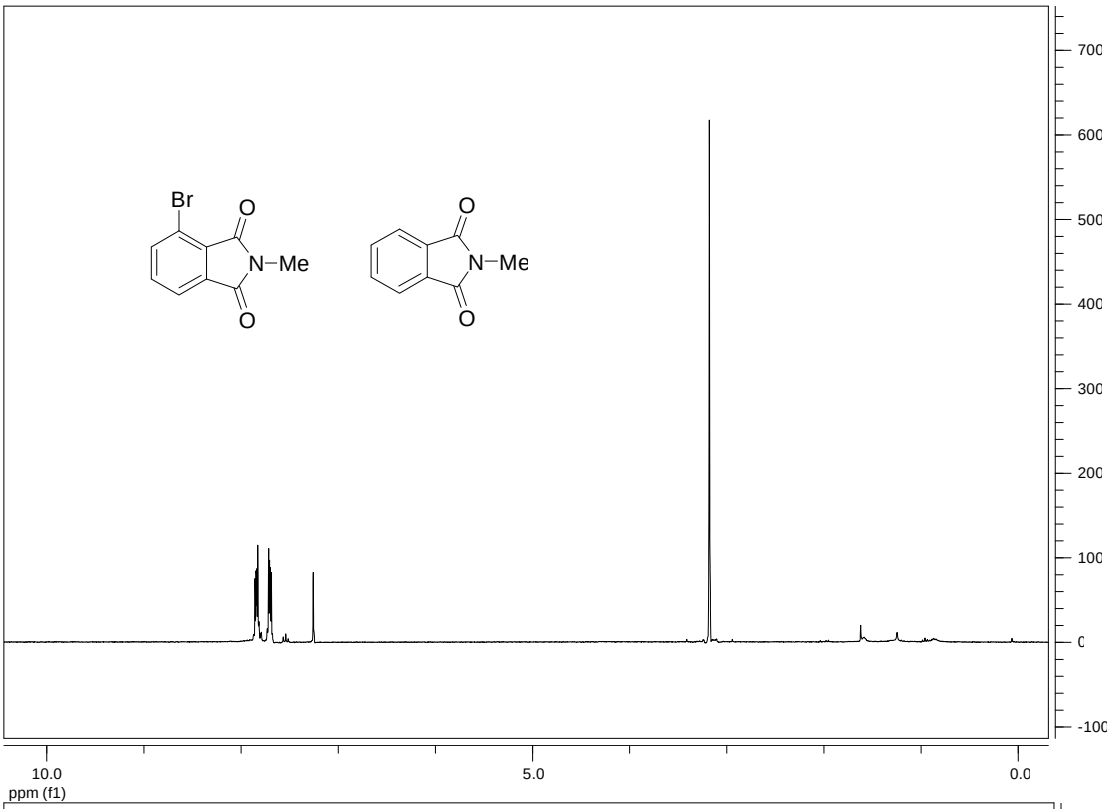

MeO
O
N–Me
O
2n
25000
20000
15000
10000
5000
0
10.0
5.0
0.0
ppm (f1)
10000
5000
0
200
150
100
50
0
ppm (f1)

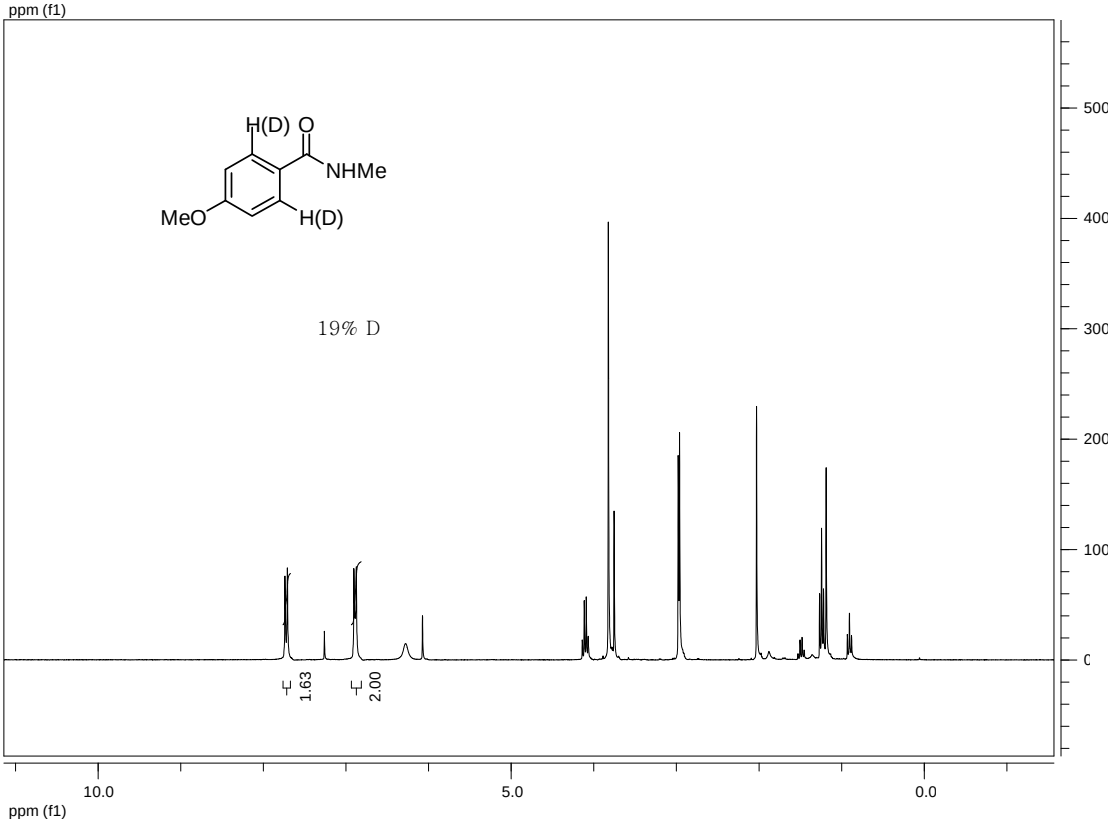

O
N
CO2Me
O
2o
10.0
5.0
0.0
ppm (f1)
200
150
100
50
0
ppm (f1)

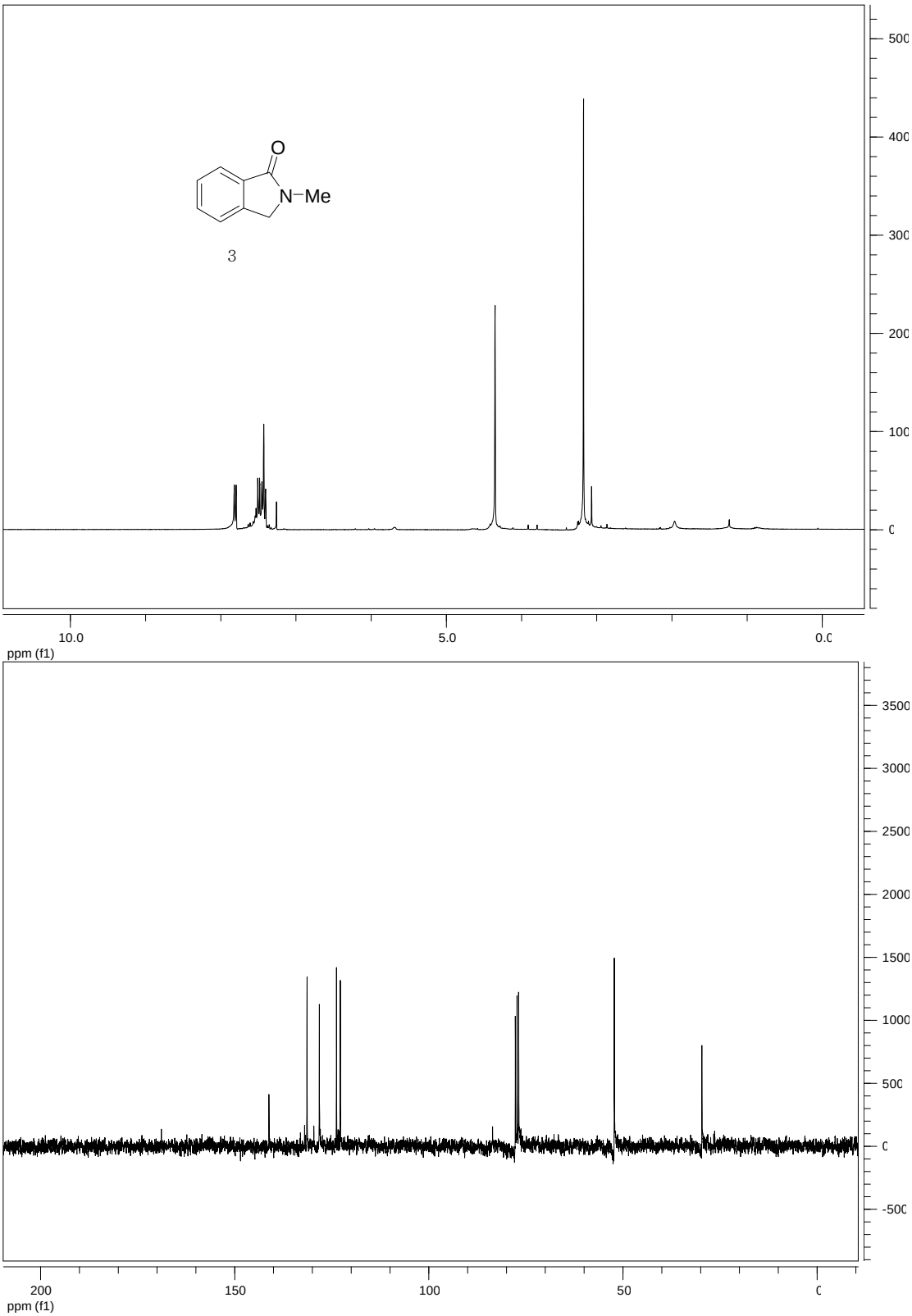

O
S
N
O
1000
500
0
10.0
5.0
0.0
ppm (f1)

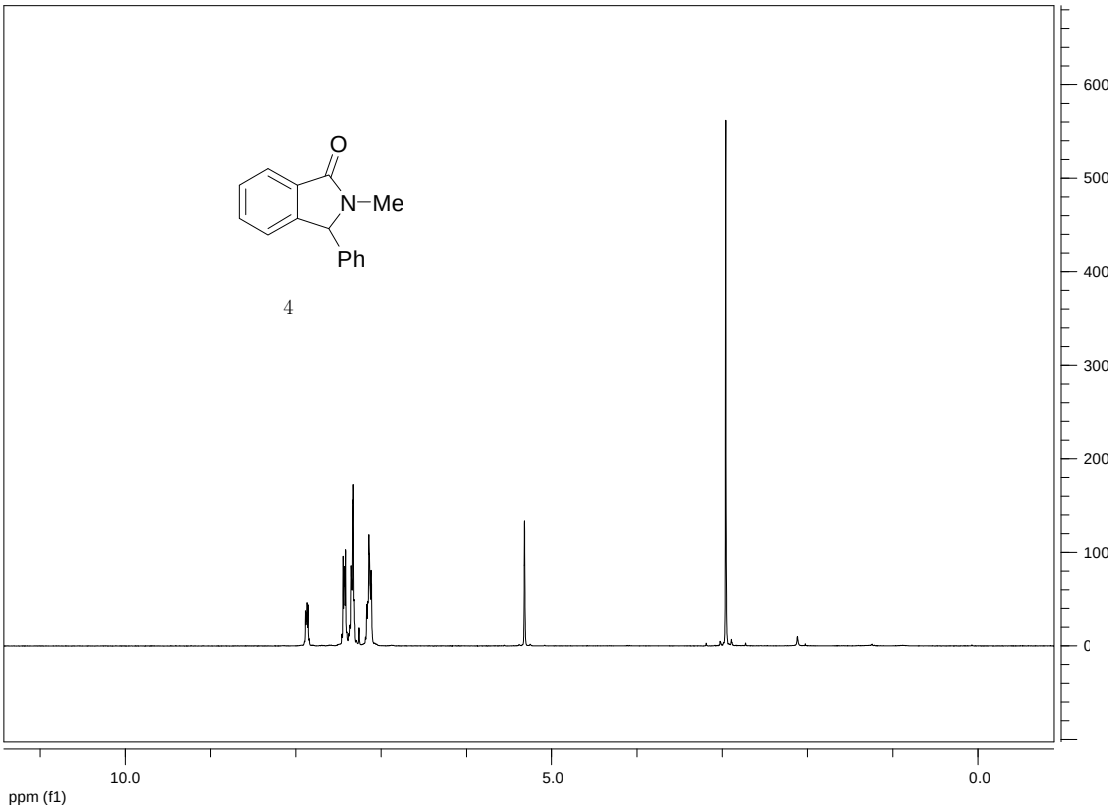
2p


Cl
O
N–Et
O
O
N–Et
O
250
200
150
100
50
0
10.0
5.0
0.0
ppm (t1)

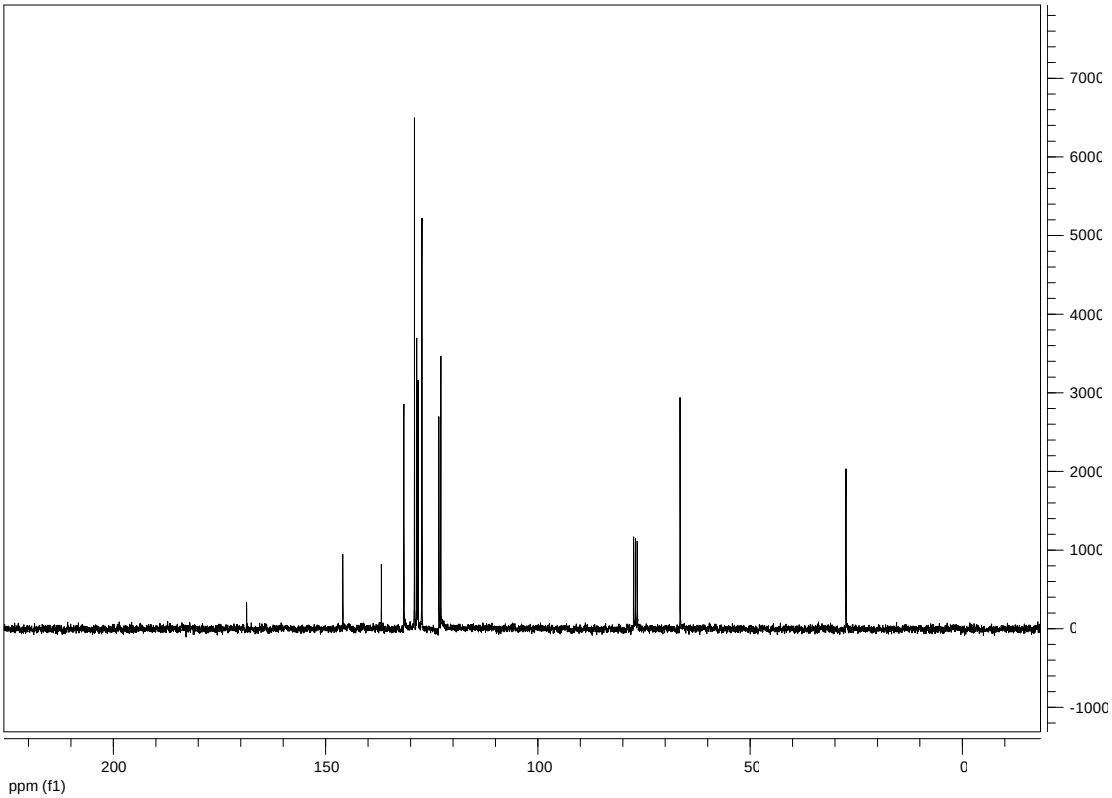

Br
O
N–Me
O
O
N–Me
O
700
600
500
400
300
200
100
0
-100
10.0
5.0
0.0
ppm (f1)


H(D)
O
NHMe
MeO
H(D)
19% D
1.63
2.00
500
400
300
200
100
0
10.0
5.0
0.0
ppm (f1)


O
N–Me
3
500
400
300
200
100
0
10.0
5.0
0.0
ppm (f1)
3500
3000
2500
2000
1500
1000
500
0
-500
200
150
100
50
0
ppm (f1)


O
N–Me
Ph
600
500
400
300
200
100
0
10.0
5.0
0.0
ppm (f1)

4


7000
6000
5000
4000
3000
2000
1000
0
-1000
200
150
100
50
0
ppm (f1)