Supporting Information

Synthesis of Various Acylating Agents Directly from Carboxylic Acids

Fathima Pilathottathil,‡ Doppalapudi Vineet Kumar,‡ Alagiri Kaliyamoorthy*

*School of Chemistry, Indian Institute of Science Education and Research, Thiruvananthapuram, Vithura, Kerala 695551, India.

Contents

EXPERIMENTAL SECTION

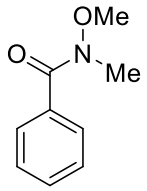
General information. Unless otherwise noted, all reactions were carried out in a reaction vessel with a teflon coated magnetic stirring bar under open atmosphere. Reagents and solvents were obtained from commercial suppliers and used without further purification. Literature procedures were followed for the synthesis of carboxylic acid precursors for **2v**,[1] **2w**,[2] **3f**,[3] *N*-methyl-2-amino pyridine.[4] Merck silica gel aluminium plates with F-254 indicator was used to perform analytical thin layer chromatography (TLC) and examined under UV. Column chromatography was performed with Finar silica gel 230-400 mesh. ^{1}H and ^{13}C NMR were recorded in $CDCl_3$ on Brucker spectrometer (500 and 125 MHz) using tetramethylsilane as the internal standard. Spin multiplicities were described as s (singlet), d (doublet), dd (double doublet), t (triplet), and m (multiplet). IR was recorded using Brucker Alpha spectrometer. HRMS was recorded using Thermo Scientific Q Exactive TM Bench top LC-HRMS instrument. Melting points were uncorrected and determined using Stuart Melting Point SMP50 apparatus.

A. General procedure for the synthesis of Weinreb amides. To a mixture of benzoic acid (50 mg, 0.41 mmol, 1 equiv), PPh_3 (160 mg, 0.61 mmol, 1.5 equiv) and NBS (108.5 mg, 0.61 mmol, 1.5 equiv), CH_2Cl_2 (2 ml) was added and the reaction was stirred at 0 °C for 15 min. The reaction was brought to room temperature and *N,O*-dimethylhydroxylamine hydrochloride (59.5 mg, 0.61 mmol, 1.5 equiv) and Et_3N (45.5 mg, 63 µl, 0.45 mmol, 1.1 equiv) were added and reaction was stirred for 1 h at room temperature. The reaction mixture was quenched with aqueous sodium bicarbonate solution and diluted with CH_2Cl_2. The bicarbonate washings were again extracted with CH_2Cl_2 and the combined organic layers were dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. Column chromatography was performed using EtOAc/Petroleum ether (1:5).

Procedure for a gram-scale synthesis of Weinreb amide (2a). To a mixture of benzoic acid (1 g, 8.1 mmol), PPh_3 (3.18 g, 12.15 mmol, 1.5 equiv) and NBS (2.16 g, 12.15 mmol, 1.5 equiv), CH_2Cl_2 (40 ml) was added and the reaction was stirred at 0 °C for 15 min. The reaction was brought to room temperature and *N,O*-dimethylhydroxylamine hydrochloride (1.18 g, 12.15 mmol, 1.5 equiv) and Et_3N (0.9 g, 1.24 ml, 8.91 mmol, 1.1 equiv) were added and reaction was stirred for 1 h at room temperature. The reaction mixture was quenched with aqueous sodium bicarbonate solution and diluted with CH_2Cl_2. The bicarbonate washings were again extracted with CH_2Cl_2 and the combined organic layers were dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. Column chromatography was performed using EtOAc/Petroleum ether (1:5). The product **2a** was obtained as a clear oil in 75% (1.002 g) yield.

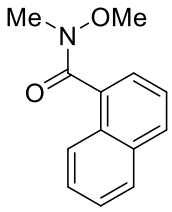
Characterization data of synthesized compounds.

N-methoxy-N-methylbenzamide (2a).[5]



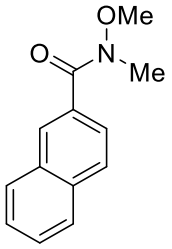
Prepared according to the general procedure A using benzoic acid (50 mg, 0.41 mmol). Yield: 97% (66 mg). The title compound was obtained as a pale yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.60-7.58 (m, 2H), 7.39 - 7.31 (m, 3H), 3.47 (s, 3H), 3.28 (s, 3H). ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$): δ (ppm) 170.1, 134.2, 130.6, 128.2, 128.1, 61.1, 33.9. HRMS (m/z): calculated for $C_9H_{11}NO_2$ (M + H): 166.0860, found (M + H) 166.0825. The data is in accordance with reported literature.

N-methoxy-N-methyl-1-naphthamide (2b).[6]



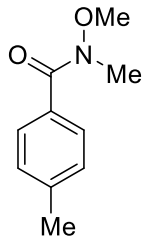
Prepared according to the general procedure A using 1-naphthoic acid (50 mg, 0.29 mmol). Yield: 93% (49 mg). The title compound was obtained as a pale yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.82-7.78 (m, 3H), 7.46-7.38 (m, 4H), 3.30 (brs, 6H). HRMS (m/z): calculated for $C_{13}H_{13}NO_2$ (M + H): 216.1019, found (M + H) 216.1017. The data is in accordance with reported literature.

N-methoxy-N-methyl-2-naphthamide (2c).[7a]



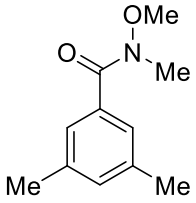
Prepared according to the general procedure A using 2-naphthoic acid (50 mg, 0.29 mmol). Yield: 93% (57.8 mg). The title compound was obtained as a pale yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 8.22 (s, 1H), 7.90 (d, J = 7.5 Hz, 1H), 7.86 (d, J = 8.5 Hz, 2H), 7.75 (d, J = 7.5 Hz, 1H), 7.56-7.52 (m, 2H), 3.56 (s, 3H), 3.41 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 170.0, 134.3, 132.6, 131.5, 128.9, 128.8, 127.8, 127.7, 127.5, 126.5, 125.1, 61.2, 33.9. HRMS (m/z): Calculated for $C_{13}H_{13}NO_2$ (M+H): 216.1019, found (M+H) 216.1017. The data is in accordance with reported literature.

N-methoxy-N,4-dimethylbenzamide (2d).[5]



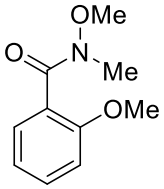
Prepared according to the general procedure A using 4-methylbenzoic acid (50 mg, 0.37 mmol). Yield: 81% (54 mg). The title compound was obtained as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.59 (d, *J* = 8.0 Hz, 2H), 7.19 (d, *J* = 7.5 Hz, 2H), 3.55 (s, 3H), 3.34 (s, 3H), 2.38 (s, 3H). HRMS (m/z): calculated for $C_{10}H_{13}NO_2$ (M + H): 180.1033, found (M + H) 180.1035. The data is in accordance with reported literature.

N-methoxy-N,3,5-trimethylbenzamide (2e).[8]



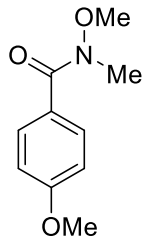
Prepared according to the general procedure A using 3,5-dimethylbenzoic acid (50 mg, 0.33 mmol). Yield: 62% (38 mg). The title compound was obtained as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.23 (s, 2H), 7.07 (s, 1H), 3.57 (s, 3H), 3.33 (s, 3H), 2.33 (s, 6H). HRMS (m/z): calculated for $C_{11}H_{15}NO_2$ (M + H): 194.1175, found (M + H) 194.1190. The data is in accordance with reported literature.

N,2-dimethoxy-N-methylbenzamide (2f).[9]



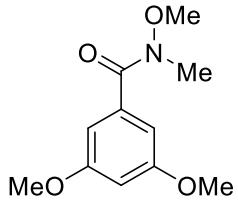
Prepared according to the general procedure A using 2-methoxybenzoic acid (50 mg, 0.32 mmol). Yield: 86% (53.7 mg). The title compound was obtained as a pale yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.36 (d, *J* = 7.5 Hz, 1H), 7.26 (s, 1H), 6.98 (d, *J* = 6.5 Hz, 1H), 6.92 (d, *J* = 8.0 Hz, 1H), 3.84 (s, 3H), 3.48 (brs, 3H), 3.31 (brs, 3H). HRMS (m/z): Calculated for $C_{10}H_{13}NO_3$ (M+H): 196.0968, found (M+H) 196.0966. The data is in accordance with reported literature.

N,4-dimethoxy-N-methylbenzamide (2g).[5]



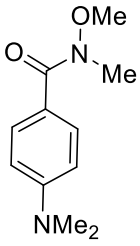
Prepared according to the general procedure A using 4-methoxybenzoic acid (50 mg, 0.32 mmol). Yield (52.9 mg, 82%). The title compound was obtained as a colourless oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.71 (d, *J* = 8.5 Hz, 2H), 6.89 (d, *J* = 8.5 Hz, 2H), 3.83 (s, 3H), 3.55 (s, 3H), 3.34 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 169.5, 161.6, 130.6, 126.1, 113.3, 60.9, 55.4, 34.0. HRMS (m/z): Calculated for $C_{10}H_{13}NO_3$ (M+H): 196.0968, found (M+H) 196.0966. The data is in accordance with reported literature.

N,3,5-trimethoxy-N-methylbenzamide (2h).[6]



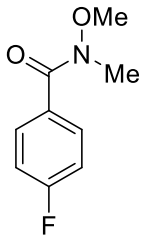
Prepared according to the general procedure A using 3,5-dimethoxybenzoic acid (50 mg, 0.27 mmol). Yield: 87% (52.9 mg). The title compound was obtained as a pale yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 6.78 (s, 2H), 6.53 (s, 1H), 3.80 (s, 6H), 3.59 (s, 3H), 3.33 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 169.7, 160.5, 136.1, 106.0, 102.9, 61.2, 55.6, 34.1. HRMS (m/z): Calculated for $C_{11}H_{15}NO_4$ (M+H) 226.1073, found (M+H) 226.1070. The data is in accordance with reported literature.

4-(dimethylamino)-N-methoxy-N-methylbenzamide (2i).[10]



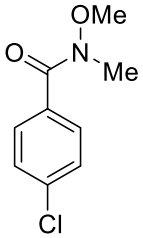
Prepared according to the general procedure A using 4-dimethylaminobenzoic acid (50 mg, 0.30 mmol). Yield: 77% (49 mg). The title compound was obtained as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.72 (d, *J* = 8.5 Hz, 2H), 6.65 (d, *J* = 8.5 Hz, 2H), 3.59 (s, 3H), 3.34 (s, 3H), 3.01 (s, 6H). HRMS (m/z): calculated for $C_{11}H_{16}N_2O_2$ (M + H): 209.1384, found (M + H) 209.1301. The data is in accordance with reported literature.

4-fluoro-N-methoxy-N-methylbenzamide (2j).[11b]



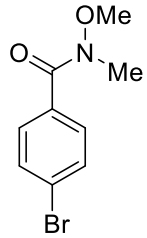
Prepared according to the general procedure A using 4-flourobenzoic acid (50 mg, 0.36 mmol). Yield: 75% (49 mg). The title compound was obtained as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.68 - 7.65 (m, 2H), 7.01 (t, *J* = 8.5 Hz, 2H), 3.46 (s, 3H), 3.29 (s, 3H). HRMS (m/z): calculated for $C_9H_{10}FNO_2$ (M + H): 184.0768, found (M + H) 184.0768. The data is in accordance with reported literature.

4-chloro-N-methoxy-N-methylbenzamide (2k).[5]



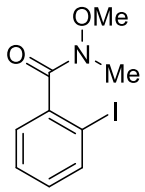
Prepared according to the general procedure A using 4-chlorobenzoic acid (50 mg, 0.32 mmol). Yield: 85% (42 mg). The title compound was obtained as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.65 (d, *J* = 8.5 Hz, 2H), 7.38 (d, *J* = 8.5 Hz, 2H), 3.53 (s, 3H), 3.35 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 168.8, 136.9, 132.4, 130.0, 128.4, 61.2, 33.6. HRMS (m/z): calculated for $C_9H_{10}ClNO_2$ (M + H): 200.0478, found (M + H) 200.0482. The data is in accordance with reported literature.

4-bromo-N-methoxy-N-methylbenzamide (2l).[11b]



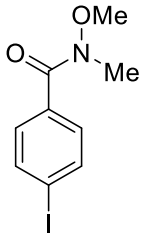
Prepared according to the general procedure A using 4-bromobenzoic acid (50 mg, 0.25 mmol). Yield: 83% (42 mg). The title compound was obtained as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.58 (d, *J* = 8.5 Hz, 2H), 7.53 (d, *J* = 8.5 Hz, 2H), 3.53 (s, 3H), 3.35 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 168.8, 132.9, 131.4, 130.1, 125.3, 61.2, 33.6. HRMS (m/z): calculated for $C_9H_{10}BrNO_2$ (M + H): 243.9967, found (M + H) 243.9969. The data is in accordance with reported literature.

2-iodo-N-methoxy-N-methylbenzamide (2m).[11a]



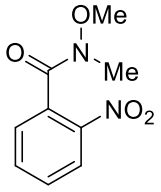
Prepared according to the general procedure A using 2-iodobenzoic acid (50 mg, 0.20 mmol). Yield: 97% (43 mg). The title compound was obtained as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.75 (d, *J* = 8.0 Hz, 1H), 7.31 (t, *J* = 7.5 Hz, 1H), 7.19 (d, *J* = 7.5 Hz, 1H), 7.02 (t, *J* = 8.0 Hz, 1H), 3.39 (m, 1+2 H), 3.32 (m, 2+1 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 170.8, 141.7, 138.9, 130.3, 127.7, 127.2, 92.5, 61.5, 32.6. HRMS (m/z): calculated for $C_9H_{10}INO_2$ (M + H): 291.9828, found (M + H) 291.9847. The data is in accordance with reported literature.

4-iodo-N-methoxy-N-methylbenzamide (2n).[12]



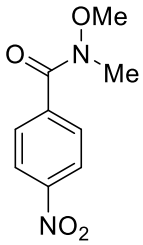
Prepared according to the general procedure A using 4-iodobenzoic acid (50 mg, 0.20 mmol). Yield: 81% (48 mg). The title compound was obtained as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.75 (d, *J* = 8.5 Hz, 2H), 7.43 (d, *J* = 8.0 Hz, 2H), 3.53 (s, 3H), 3.35 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 169.0, 137.3, 133.5, 130.1, 97.4, 61.2, 33.6. HRMS (m/z): calculated for $C_9H_{10}INO_2$ (M + H): 291.9834, found (M + H) 291.9841. The data is in accordance with reported literature.

N-methoxy-N-methyl-2-nitrobenzamide (2o).[6]



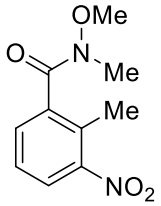
Prepared according to the general procedure A using 2-nitrobenzoic acid (50 mg, 0.30 mmol). Yield: 78% (49.3 mg). The title compound was obtained as a brown oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 8.15 (d, *J* = 8.0 Hz, 1H), 7.72 (t, *J* = 7.5 Hz, 1H), 7.58 (t, *J* = 8.0 Hz, 1H), 7.53 (d, *J* = 7.5 Hz, 1H), 3.36 (s, 3H), 3.33 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 168.9, 145.9, 134.0, 131.6, 130.1, 128.5, 124.0, 61.4, 33.5. HRMS (m/z): Calculated for $C_9H_{10}N_2O_4$ (M+H): 211.0713, found (M+H) 211.0712. The data is in accordance with reported literature.

N-methoxy-N-methyl-4-nitrobenzamide (2p).[11b]



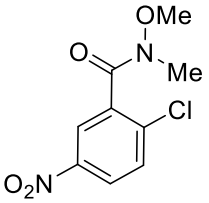
Prepared according to the general procedure A using 4-nitrobenzoic acid (50 mg, 0.30 mmol). Yield: 97% (61.7 mg). The title compound was obtained as a yellow solid, mp = 71.8 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 8.26 (d, *J* = 7.0 Hz, 2H), 7.83 (d, *J* = 7.5 Hz, 2H), 3.52 (s, 3H), 3.39 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 167.7, 148.8, 140.0, 129.2, 123.2, 61.3, 33.1. HRMS (m/z): Calculated for $C_9H_{10}N_2O_4$ (M + H): 211.0713, found (M+H) 211.0711. The data is in accordance with reported literature.

N-methoxy-N,2-dimethyl-3-nitrobenzamide (2q).[12]



Prepared according to the general procedure A using 2-methyl-3-nitrobenzoic acid (50 mg, 0.28 mmol). Yield: 74% (44.8 mg). The title compound was obtained as a pale yellow solid, mp = 53.0 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.90 (d, *J* = 8.5 Hz, 1H), 7.50 (d, *J* = 7.5 Hz, 1H), 7.39 (t, *J* = 7.8 Hz, 1H), 3.41 (s, 3H), 3.40 (s, 3H), 2.48 (s, 3H). HRMS (m/z): Calculated for $C_{10}H_{12}N_2O_4$ (M+H): 225.0870, found (M+H): 225.0864. The data is in accordance with reported literature.

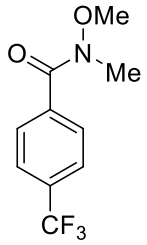
2-chloro-N-methoxy-N-methyl-5-nitrobenzamide (2r).



Prepared according to the general procedure A using 2-chloro-5-nitrobenzoic acid (50 mg, 0.25 mmol). Yield: 94% (57 mg).The title compound was obtained as a yellow solid, mp = 101.6 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 8.23 - 8.20 (m, 2H), 7.60 (d, *J* = 8.5 Hz, 1H), 3.50 (s, 3H), 3.41 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 165.9, 146.3, 138.0, 136.7, 130.7, 125.0, 123.1, 61.7, 32.4. IR (ATR,

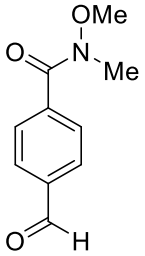
cm^{-1}): 2928, 2863, 1665, 1459, 1358, 745. HRMS (m/z): calculated for $C_9H_9ClN_2O_4$ (M + H): 245.0323, found (M + H) 245.0341.

N-methoxy-N-methyl-4-(trifluoromethyl)benzamide (2s).[5]



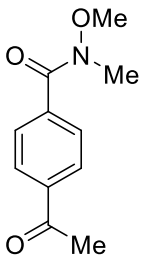
Prepared according to the general procedure A using 4-trifluoromethylbenzoic acid (50 mg, 0.26 mmol). Yield: 95% (57.7 mg). The title compound was obtained as a pale yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.78 (d, *J* = 8.0 Hz, 2H), 7.67 (d, *J* = 7.5 Hz, 2H), 3.53 (s, 3H), 3.38 (s, 3H). HRMS (m/z): Calculated for $C_{10}H_{10}F_3NO_2$ (M+H) 234.0736, found (M+H) 234.0733. The data is in accordance with reported literature.

4-formyl-N-methoxy-N-methylbenzamide (2t).[13]



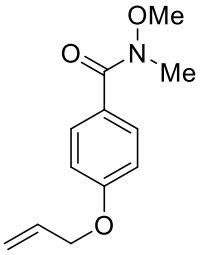
Prepared according to the general procedure A using 4-formylbenzoic acid (50 mg, 0.33 mmol). Yield: 82% (48 mg). The title compound was obtained as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 10.07 (s, 1H), 7.93 (d, *J* = 8.0 Hz, 2H), 7.81 (d, *J* = 8.0 Hz, 2H), 3.54 (s, 3H), 3.38 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 191.7, 168.8, 139.8, 137.5, 129.4, 128.7, 61.3, 31.0. HRMS (m/z): calculated for $C_{10}H_{11}NO_3$ (M + H): 194.0811, found (M + H) 194.0828. The data is in accordance with reported literature.

4-acetyl-N-methoxy-N-methylbenzamide (2u).[7a]



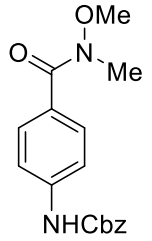
Prepared according to the general procedure A using 4-acetylbenzoic acid. (50 mg, 0.30 mmol). Yield: (50.1 mg, 81%). The title compound was obtained as a pale yellow solid, mp = 41.7 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.97 (d, *J* = 8.0 Hz, 2H), 7.73 (d, *J* = 8.5 Hz, 2H), 3.52 (s, 3H), 3.36 (s, 3H), 2.62 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 197.6, 169.0, 138.54, 138.47, 128.45, 128.07, 61.3, 33.5, 26.8. HRMS (m/z): Calculated for $C_{11}H_{13}NO_3$ (M+H) 208.0968, found (M+H) 208.0966. The data is in accordance with reported literature.

4-(allyloxy)-N-methoxy-N-methylbenzamide (2v).



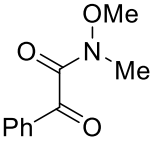
Prepared according to the general procedure A using 4-allyloxybenzoic acid (50 mg, 0.28 mmol). Yield (41.8 mg, 67%). The title compound was obtained as an orange oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.70 (d, *J* = 8.5 Hz, 2H). 6.90 (d, *J* = 8.5 Hz, 2H), 6.01- 6.08 (m, 1H), 5.41 (dd, *J* = 17.5,1.5 Hz, 1H), 5.29 (dd, *J* = 10.5, 1 Hz, 1H), 4.56 - 4.57 (m, 2H), 3.55 (s, 3H), 3.34 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 169.5, 160.6, 132.9, 130.6, 126.2, 118.1, 114.1, 68.9, 61.0, 34.0. IR (ATR, cm^{-1}): 2903, 1638, 1596, 1415, 1292, 1239, 787. HRMS (m/z): Calculated for $C_{12}H_{15}NO_3$ (M+H) 222.1124, found (M+H) 222.1124.

benzyl (4-(methoxy(methyl)carbamoyl)phenyl)carbamate (2w).



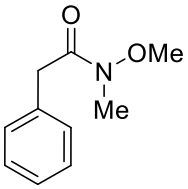
Prepared according to the general procedure A using 4-cbzaminobenzoic acid (50 mg, 0.18 mmol). Yield: 83% (47 mg). The title compound was obtained as a pale yellow solid, mp = 118.5 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.62 (d, *J* = 8.5 Hz, 2H), 7.23-7.41 (m, 7H), 6.91 (s, 1H), 5.13 (s, 2H), 3.47 (s, 3H), 3.27 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 169.2, 153.2, 140.2, 135.9, 129.9, 128.7, 128.6, 128.5, 128.4, 117.6, 67.3, 61.1, 33.9. IR (ATR, cm^{-1}): 1732, 1610, 1534, 1224, 1060, 750. HRMS (m/z): Calculated for $C_{17}H_{18}N_2O_4$ (M + H): 315.1339, found (M + H) 315.1333.

N-methoxy-N-methyl-2-oxo-2-phenylacetamide (2x).[14]



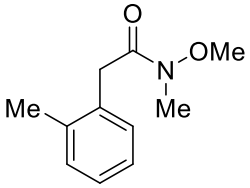
Prepared according to the general procedure A using 2-oxo-2-phenylacetic acid (50 mg, 0.33 mmol). Yield: 75% (48 mg). The title compound was obtained as a white solid, mp = 68.8 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.90 (d, *J* = 8.0 Hz, 2H), 7.62 (d, *J* = 7.5 Hz, 1H), 7.50 (t, *J* = 7.5 Hz, 2H), 3.65 (s, 3H), 3.36 (s, 3H). ^{13}C NMR (125 MHz, CDCl3): δ (ppm) 190.9, 167.3, 134.5, 132.9, 129.5, 129.04, 62.2, 31.5. HRMS (m/z): calculated for $C_{10}H_{11}NO_3$ (M + H): 194.0811, found (M + H) 194.0827. The data is in accordance with reported literature.

N-methoxy-N-methyl-2-phenylacetamide (3a).[5]



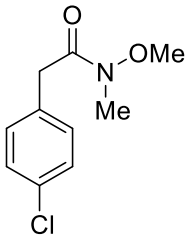
Prepared according to the general procedure A using phenylacetic acid (50 mg, 0.37 mmol). Yield: 94% (66 mg). The title compound was obtained as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.24-7.14 (m, 5H), 3.69 (s, 2H), 3.51 (s, 3H), 3.11 (s, 3H). HRMS (m/z): calculated for $C_{10}H_{13}NO_2$ (M + H): 180.1034, found (M + H) 180.1033. The data is in accordance with reported literature.

N-methoxy-N-methyl-2-(o-tolyl)acetamide (3b).[15]



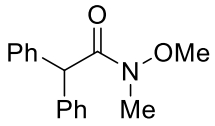
Prepared according to the general procedure A using o-tolylacetic acid (50 mg, 0.33 mmol). Yield: 80% (51.3 mg). The title compound was obtained as a pale yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.19 - 7.14 (m, 4H), 3.77 (s, 2H), 3.60 (s, 3H), 3.20 (s, 3H), 2.31 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 172.7, 136.9, 133.7, 130.3, 130.0, 127.1, 126.1, 61.3, 37.2, 32.5, 19.8. HRMS (m/z): Calculated for $C_{11}H_{15}NO_2$ (M+H) 194.1175, found (M+H) 194.1173. The data is in accordance with reported literature.

2-(4-chlorophenyl)-N-methoxy-N-methylacetamide (3c).[16]



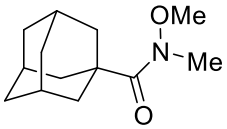
Prepared according to the general procedure A using 4-chlorophenylacetic acid (50 mg, 0.29 mmol). Yield: 80% (50 mg). The title compound was obtained as a pale yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.28 (d, *J* = 8.0 Hz, 2H), 7.22 (d, *J* = 7.5 Hz, 2H), 3.73 (s, 2H), 3.63 (s, 3H), 3.18 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 171.9, 133.4, 132.8, 130.8, 128.7, 61.4, 38.7, 32.3. HRMS (m/z): Calculated for $C_{10}H_{12}ClNO_2$ (M+H) 214.0629, found (M+H) 214.0627. The data is in accordance with reported literature.

N-methoxy-N-methyl-2,2-diphenylacetamide (3d).[13]



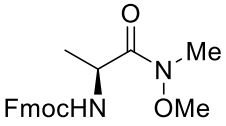
Prepared according to the general procedure A using diphenylacetic acid (50 mg, 0.23 mmol). Yield: 82% (47.9 mg). The title compound was obtained as a pale yellow solid, mp = 110.0 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.31 - 7.29 (m, 8H), 7.25-7.23 (m, 2H), 5.54 (s, 1H), 3.48 (s, 3H), 3.23 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 173.2, 139.5, 129.1, 128.5, 127.0, 61.5, 52.9, 32.5. HRMS (m/z): Calculated for $C_{16}H_{17}NO_2$ (M+H) 256.1332, found (M+H) 256.1328. The data is in accordance with reported literature.

(3r, 5r, 7r)-N-methoxy-N-methyladamantane-1-carboxamide (3e).[5]



Prepared according to the general procedure A using 1-adamantanecarboxylic acid (50 mg, 0.28 mmol). Yield: 68% (42.4 mg). The title compound was obtained as a pale yellow solid, mp = 45.0 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 3.66 (s, 3H), 3.15 (s, 3H), 1.98 (s, 9H), 1.70 (s, 6H). HRMS (m/z): Calculated for $C_{13}H_{21}NO_2$ (M+H) 224.1645, found (M+H) 224.1641. The data is in accordance with reported literature.

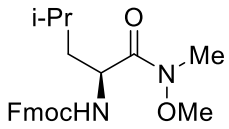
(9H-fluoren-9-yl)methyl (S)-(1-(methoxy(methyl)amino)-1-oxopropan-2-yl)carbamate (3f).[17a]



Prepared according to the general procedure A using Fmoc L-alanine (50 mg, 0.16 mmol). Yield: 80% (46 mg). The title compound was obtained as a colourless oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.76 - 7.75 (m, 2H), 7.62 - 7.59 (m, 2H), 7.41 - 7.38 (m, 2H), 7.32 - 7.29 (m, 2H), 5.64 (d, *J* = 7.0 Hz, 1H), 4.76 (s, 1H), 4.36 - 4.35 (m, 2H), 4.23 - 4.21 (m, 1H), 3.77 (s, 3H), 3.22 (s, 3H), 1.38 - 1.36 (m,

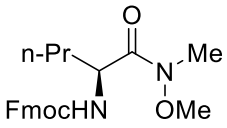
3H). HRMS (m/z): calculated for $C_{20}H_{22}N_2O_4$ (M + H): 355.1658, found (M + H) 355.1647. $[\alpha]_D^{25}$ = +1.9 (*c* 0.68, $CHCl_3$). lit.[16] $[\alpha]_D^{20}$ = +2.1 (*c* 0.68, $CHCl_3$). The data is in accordance with reported literature.

(9H-fluoren-9-yl)methyl (S)-(1-(methoxy(methyl)amino)-4-methyl-1-oxopentan-2-yl)carbamate (3g).[18]



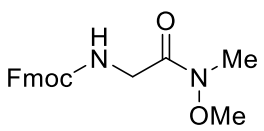
Prepared according to the general procedure A using Fmoc L-leucine (50 mg, 0.14 mmol). Yield: 89% (50 mg). The title compound was obtained as a colourless oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.76 - 7.75 (m, 2H), 7.62 - 7.58 (m, 2H), 7.41 - 7.38 (m, 2H), 7.32 - 7.29 (m, 2H), 5.41 (d, *J* = 9.0 Hz, 1H), 4.81 (d, *J* = 7.0 Hz, 1H), 4.37 - 4.35 (m, 2H), 4.23 - 4.22 (m, 1H), 3.79 (s, 3H), 3.21 (s, 3H), 1.75 - 1.70 (m, 2H), 1.51 - 1.49 (m, 2H), 0.99 - 0.94 (m, 6H). HRMS (m/z): calculated for $C_{23}H_{28}N_2O_4$ (M + H): 397.2121, found (M + H) 397.2117. The data is in accordance with reported literature. $[\alpha]_D^{20}$ = +2.537 (*c* 0.1, CH_2Cl_2).

(9H-fluoren-9-yl)methyl (S)-(1-(methoxy(methyl)amino)-1-oxopentan-2-yl)carbamate (3h).[17b]



Prepared according to the general procedure A using Fmoc L-norvaline (50 mg, 0.15 mmol). Yield: 94% (53 mg). The title compound was obtained as a colourless oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.76 - 7.75 (m, 2H), 7.61 - 7.59 (m, 2H), 7.40 - 7.37 (m, 2H), 7.32 - 7.29 (m, 2H), 5.49 (d, *J* = 8.8 Hz, 1H), 4.77 (s, 1H), 4.39 - 4.33 (m, 2H), 4.22 (t, *J* = 7.05 Hz, 1H), 3.78 (s, 3H), 3.22 (s, 3H), 1.75 -1.69 (m, 1H), 1.62 - 1.55 (m, 1H), 1.47 -1.42 (m, 2H), 0.94 (t, *J* = 7.25 Hz, 3H). HRMS (m/z): calculated for $C_{22}H_{26}N_2O_4$ (M + H): 383.1965, found (M + H) 383.1961. The data is in accordance with reported literature. $[\alpha]_D^{20}$ = -2.920 (*c* 0.1, CH_2Cl_2).

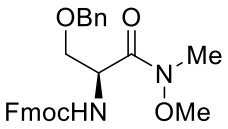
(9H-fluoren-9-yl)methyl (2-(methoxy(methyl)amino)-2-oxoethyl)carbamate (3i).[18]



Prepared according to the general procedure A using Fmoc glycine (50 mg, 0.15 mmol). Yield: 78% (45 mg). The title compound was obtained as a colourless gummy oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.77 – 7.75 (m, 2H), 7.62 – 7.61 (m, 2H), 7.41 – 7.38 (m, 2H), 7.33 – 7.30 (m, 2H), 5.59 (s, 1H),

4.39 (d, *J* = 7 Hz, 2H), 4.25 – 4.23 (m, 1H), 4.17 (d, *J* = 3 Hz, 2H), 3.73 (s, 3H), 3.22 (s, 3H). HRMS (m/z): calculated for $C_{19}H_{20}N_2O_4$ (M + H): 341.1495, found (M + H) 341.1491. The data is in accordance with reported literature.

(9H-fluoren-9-yl)methyl (S)-(3-(benzyloxy)-1-(methoxy(methyl)amino)-1-oxopropan-2-yl)carbamate (3j).

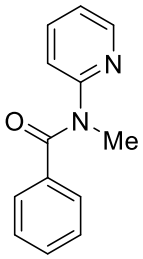


Prepared according to the general procedure A using Fmoc L-O-benzyl serine (50 mg, 0.12 mmol). Yield: 89% (49 mg). The title compound was obtained as a white solid, mp = 95.0 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.77 - 7.75 (m, 2H), 7.63 - 7.60 (m, 2H), 7.41 - 7.38 (m, 2H), 7.34 - 7.27 (m, 7H), 5.77 (d, *J* = 8.5 Hz, 1H), 4.95 (s, 1H), 4.60 - 4.51 (m, 2H), 4.36 (d, *J* = 7.0 Hz, 2H), 4.24 - 4.21 (m, 1H), 3.72 (s, 5H), 3.23 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 156.1, 144.0, 143.9,141.4, 137.8, 128.5, 127.9, 127.2, 125.36, 125.33, 120.0, 69.6, 67.3, 61.6, 51.5, 47.2, 32.3. IR (ATR, cm^{-1}): 3856, 3749, 3311, 3055, 2936, 1716, 1658, 1517, 1450, 1240, 1102, 742, 617, 551. HRMS (m/z): calculated for $C_{27}H_{28}N_2O_5$ (M + H): 461.2070, found (M + H) 461.2068. $[\alpha]_D^{20}$ = +4.804 (*c* 0.1, CH_2Cl_2).

B. General procedure for synthesis of *N*-methyl-2-amino pyridine amides. To a mixture of benzoic acid (50 mg, 0.41 mmol, 1 equiv), PPh_3 (160 mg, 0.61 mmol, 1.5 equiv) and NBS (108.5 mg, 0.61 mmol, 1.5 equiv), CH_2Cl_2 (1.5 ml) was added and the reaction was stirred at 0 °C for 30 min. The reaction was brought to room temperature and DMAP (10 mg, 0.08 mmol, 0.20 equiv) was added and stirred for 10 min. The mixture of *N*-methyl-2-amino pyridine (49 mg, 0.45 mmol, 1.1 equiv), Et_3N (45.5 mg, 63 µl, 0.45 mmol, 1.1 equiv) and CH_2Cl_2 (0.5 ml) were added and the reaction was stirred for 1 h at room temperature. The reaction mixture was diluted with EtOAc and washed with aqueous sodium bicarbonate solution. The bicarbonate washings were again extracted with EtOAc and the combined organic layers were dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. Column chromatography was performed using EtOAc/Petroleum ether (1:5).

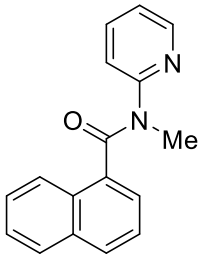
Characterization data of synthesized compounds

N-methyl-N-(pyridin-2-yl)benzamide (4a).[7]



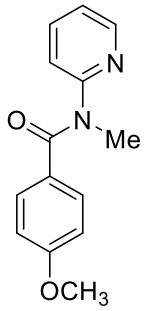
Prepared according to the general procedure B using benzoic acid (50 mg, 0.41 mmol). Yield: 86% (75 mg). The title compound was obtained as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 8.37 - 8.36 (m, 1H), 7.37 - 7.34 (m, 1H), 7.27 - 7.22 (m, 3H), 7.16 - 7.13 (m, 2H), 6.97 - 6.95 (m, 1H), 6.73 (d, *J* = 8.0 Hz, 1H), 3.51 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 171.1, 156.9, 148.8, 137.4, 136.1, 130.2, 128.6, 128.1, 121.7, 121.0, 36.1. HRMS (m/z): calculated for $C_{13}H_{12}N_2O$ (M + H): 213.1022, found (M + H) 213.1023. The data is in accordance with reported literature.

N-methyl-N-(pyridine-2-yl)-1-naphthamide (4b).[7]



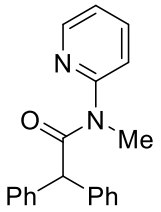
Prepared according to the general procedure B using 1-naphthoic acid (50 mg, 0.29 mmol). Yield: 74% (46 mg). The title compound was obtained as a white solid mp = 170.0 °C . ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 8.38 (d, *J* = 4.0 Hz, 1H), 8.08 (d, *J* = 8.5 Hz, 1H), 7.83 - 7.78 (m, 2H), 7.55 - 7.47 (m, 2H), 7.32 - 7.26 (m, 3H), 6.95 (t, *J* = 5.7 Hz, 2H), 3.60 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 170.9, 155.8, 148.5, 137.3, 134.5, 133.5,130.1, 129.7, 128.4, 127.2, 126.4, 125.6, 125.2, 124.8, 121.0, 120.7, 35.7. HRMS (m/z): calculated for $C_{17}H_{14}N_2O$ (M + H): 263.1178, found (M + H) 263.1172. The data is in accordance with reported literature.

4-methoxy-N-methyl-N-(pyridine-2-yl)benzamide (4c).[7]



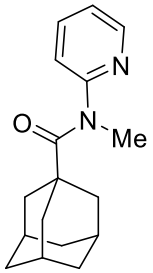
Prepared according to the general procedure B using 4-methoxybenzoic acid (50 mg, 0.33 mmol). Yield: 68% (40 mg). The title compound was obtained as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 8.36 (s, 1H), 7.36 (t, *J* = 7.5 Hz, 1H), 7.23 - 7.21 (m, 2H), 6.96-6.94 (m, 1H), 6.69 (d, *J* = 8 Hz, 1H), 6.64 - 6.63 (m, 2H), 3.68 (s, 3H), 3.49 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 170.8, 161.2, 157.4, 148.8, 137.4, 130.8, 128.1, 121.7, 120.7, 113.4, 55.3, 36.1. HRMS (m/z): calculated for $C_{14}H_{14}N_2O_2$ (M + H): 243.1128, found (M + H) 243.1126.

N-methyl-2,2-diphenyl-N-(pyridine-2-yl)acetamide (4d).[19]



Prepared according to the general procedure B using 2,2-diphenylacetic acid (50 mg, 0.23 mmol). Yield: 58% (25 mg). The title compound was obtained as an off white solid, mp = 122.7 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 8.52 (s, 1H), 7.64 - 7.61 (m, 1H), 7.25 - 7.19 (m, 12H), 5.21 (s, 1H), 3.40 (s, 3H). HRMS (m/z): calculated for $C_{20}H_{18}N_2O$ (M + H): 303.1491, found (M + H) 303.1478. The data is in accordance with reported literature.

(3r,5r,7r)-N-methyl-N-(pyridine-2-yl)adamantane-1-carboxamide (4e).

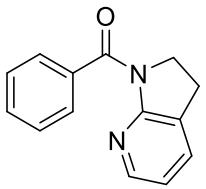


Prepared according to the general procedure B using 1-adamantane carboxylic acid (50 mg, 0.28 mmol). Yield: 81% (62 mg). The title compound was obtained as a white solid, mp = 95.1°C. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 8.50 - 8.49 (m, 1H), 7.76 - 7.73 (m, 1H), 7.26 - 7.23 (m, 1H), 7.20 (d, *J* = 7.9 Hz, 1H), 3.25 (s, 3H), 1.86 (s, 3H), 1.76 (s, 6H), 1.60 - 1.51 (m, 6H). ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 179.3, 158.0, 149.1, 138.4, 122.6, 122.4, 44.0, 39.9, 39.5, 36.5, 28.5. IR (ATR, cm^{-1}): 2909, 2855, 1645, 1585, 1468, 1348, 1281, 1149, 1042, 751, 659, 585. HRMS (m/z): calculated for $C_{17}H_{22}N_2O$ (M + H): 271.1804, found (M + H) 271.1799.

C. General procedure for the synthesis of 2,3-Dihydro-7-azaindole amides. A reaction tube with a teflon coated magnetic stir bar was charged with benzoic acid (50 mg, 0.41 mmol, 1 equiv), PPh_3 (160 mg, 0.61 mmol, 1.5 equiv) and NBS (108.5 mg, 0.61 mmol, 1.5 equiv). CH_2Cl_2 (2 ml) was added and the reaction was stirred at 0 °C for 30 min. The reaction was brought to room temperature and 2,3-dihydro-7-azaindole (54 mg, 0.45 mmol, 1.1 equiv) and Et_3N (45.5 mg, 63 µl, 0.45 mmol, 1.1 equiv) were added and the reaction was stirred for 1 h at room temperature. The reaction mixture was diluted with EtOAc and washed with aqueous sodium bicarbonate solution. The bicarbonate washings were again extracted with EtOAc and the combined organic layers were dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. Column chromatography was performed using EtOAc/Petroleum ether (1:5).

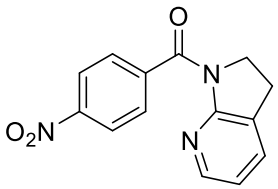
Characterization data of synthesized compounds.

(2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-1-yl)(phenyl)methanone (5a).



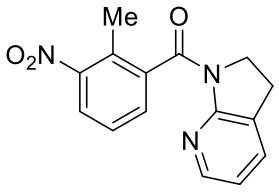
Prepared according to the general procedure C using benzoic acid (50 mg, 0.41 mmol). Yield: 73% (66.8 mg). The title compound was obtained as a white solid, mp = 114.0 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.85 (d, *J* = 5.0 Hz, 1H), 7.59 (d, *J* = 7.0 Hz, 2H), 7.48 - 7.45 (m, 2H), 7.38 (t, *J* = 7.5 Hz, 2H), 6.81 (dd, *J* = 7.5, 5 Hz, 1H), 4.22 (t, *J* = 8.0 Hz, 2H), 3.11 (t, *J* = 8.5 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 169.3, 156.2, 146.3, 136.1, 133.3, 130.7, 128.5, 127.8, 125.8, 118.5, 47.9, 25.1. IR (ATR, cm^{-1}): 1643, 1593, 1420, 1379, 1347, 1245, 790, 712. HRMS (m/z): Calculated for $C_{14}H_{12}N_2O$ (M+H) 225.1022, found (M+H) 225.1022.

(2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-1-yl)(4nitrophenyl)methanone (5b).



Prepared according to the general procedure C using 4-nitrobenzoic acid (50 mg, 0.30 mmol). Yield: 71% (57.7 mg). The title compound was obtained as an off-white solid, mp = 158.4 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 8.24 (d, *J* = 9.0 Hz, 2H), 7.76 (d, *J* = 5.0 Hz, 1H), 7.70 (d, *J* = 8.5 Hz, 2H), 7.50 (dd, *J* = 7.5, 1.5 Hz, 1H), 6.85 (dd, *J* = 7.5, 5.0 Hz, 1H), 4.28 (t, *J* = 8.0 Hz, 2H), 3.17 (t, *J* = 8.5 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 167.1, 155.3, 148.9, 146.2, 142.4, 133.8, 129.4, 125.8, 123.1, 119.2, 47.2, 24.9. IR (ATR, cm^{-1}): 1650, 1595, 1512, 1426, 1344, 1240, 852, 701. HRMS (m/z): Calculated for $C_{14}H_{11}N_3O_3$ (M+H) 270.0873, found (M+H) 270.0870.

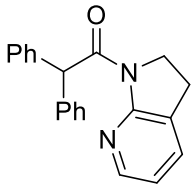
(2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-1-yl)(2-methyl-nitrophenyl)methanone (5c).



Prepared according to the general procedure C using 2-methyl-3-nitrobenzoic acid (50 mg, 0.27 mmol). Yield: 75% (45.4 mg). The title compound was obtained as a yellow solid, mp = 153.5 °C. ^{1}H NMR

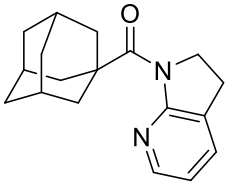
(500 MHz, $CDCl_3$): δ (ppm) 7.94 (d, *J* = 8.1 Hz, 1H), 7.71 (s, 1H), 7.48 - 7.43 (m, 2H), 7.37 - 7.34 (m, 1H), 6.83 - 6.81 (m, 1H), 4.31 (s, 2H), 3.18 (t, *J* = 8.5 Hz, 2H), 2.41 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 166.8, 154.67, 150.0, 146.71, 141.0, 133.7, 130.8, 130.4, 126.5, 125.5, 124.8, 119.1, 46.0, 24.5, 16.5. IR (ATR, cm^{-1}) = 1642, 1591, 1526, 1422, 1346, 797, 733. HRMS (m/z): Calculated for $C_{15}H_{14}N_3O_3$ (M+H) 284.1030, found (M+H) 284.1020.

1-(2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-1-yl)-2,2-diphenylethan-1-one (5d).



Prepared according to the general procedure C using diphenylacetic acid (50 mg, 0.23 mmol). Yield: 62% (44.5 mg). The title compound was obtained as a pale yellow solid, mp = 170.8 °C. ^1H NMR (500 MHz, $CDCl_3$): δ (ppm) 8.13 (d, *J* = 3.5 Hz, 1H), 7.44-7.41 (m, 5H), 7.37 (s, 1H), 7.29-7.25 (m, 4H), 7.21-7.18 (m, 2H), 6.85 (t, *J* = 5.5 Hz, 1H), 4.16 (t, *J* = 8.5 Hz, 2H), 3.01 (t, *J* = 8.0 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 171.9, 155.7, 146.1, 140.2, 133.6, 129.6, 128.3, 126.8, 126.3, 118.2, 54.6, 46.2, 24.0. IR (ATR, cm^{-1}): 1655, 1595, 1420, 1236, 805, 706. HRMS (m/z): Calculated for $C_{21}H_{18}N_2O$ (M+H) 315.1491 , found (M+H) 315.1481.

((3r,5r,7r)-adamantan-1-yl)(2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-1-yl)methanone (5e).



Prepared according to the general procedure C using 1-adamantanecarboxylic acid (50 mg, 0.28 mmol). Yield (58.7 mg, 75%). The title compound was obtained as a yellow solid, mp = 125.6 °C. ^1H NMR (500 MHz, $CDCl_3$): δ (ppm) 8.12-8.11 (m, 1H), 7.40 (dd, *J* = 7.25, 1 Hz, 1H), 6.82 (dd, *J* = 7.5, 5.0 Hz, 1H), 4.10 (t, *J* = 8.5 Hz, 2H), 2.98 (t, *J* = 8.5 Hz, 2H), 2.31 (d, *J* = 2 Hz, 6 H), 2.04 (s, 3H), 1.91 (d, *J* = 2.5 Hz, 1H), 1.81 (d, *J* = 11.5 Hz, 3H), 1.71 (d, *J* = 11.5 Hz, 4H). ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 179.1, 156.0, 145.4, 133.0, 126.5,117.6, 49.0, 43.6, 38.7, 36.84, 36.81, 36.56, 28.7, 27.9, 24.8. IR (ATR, cm^{-1}): 2904, 2853, 1640, 1597, 1416, 1294, 1240, 787. HRMS (m/z): Calculated for $C_{18}H_{22}N_2O$ (M+H) 283.1804, found (M+H) 283.1799.

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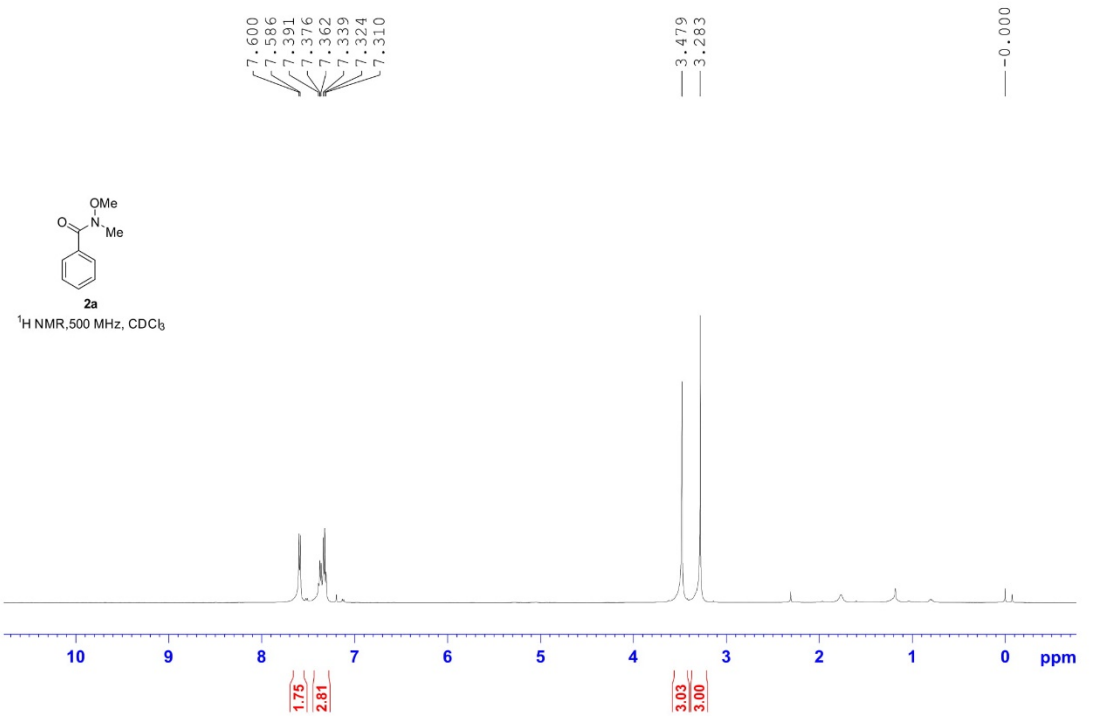
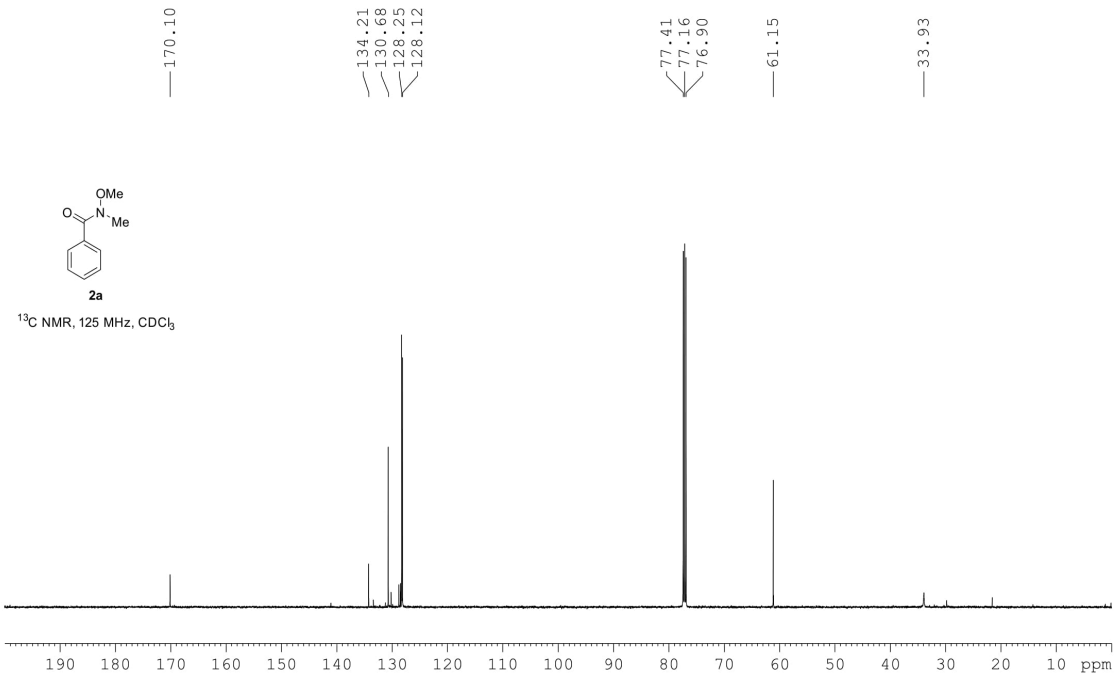
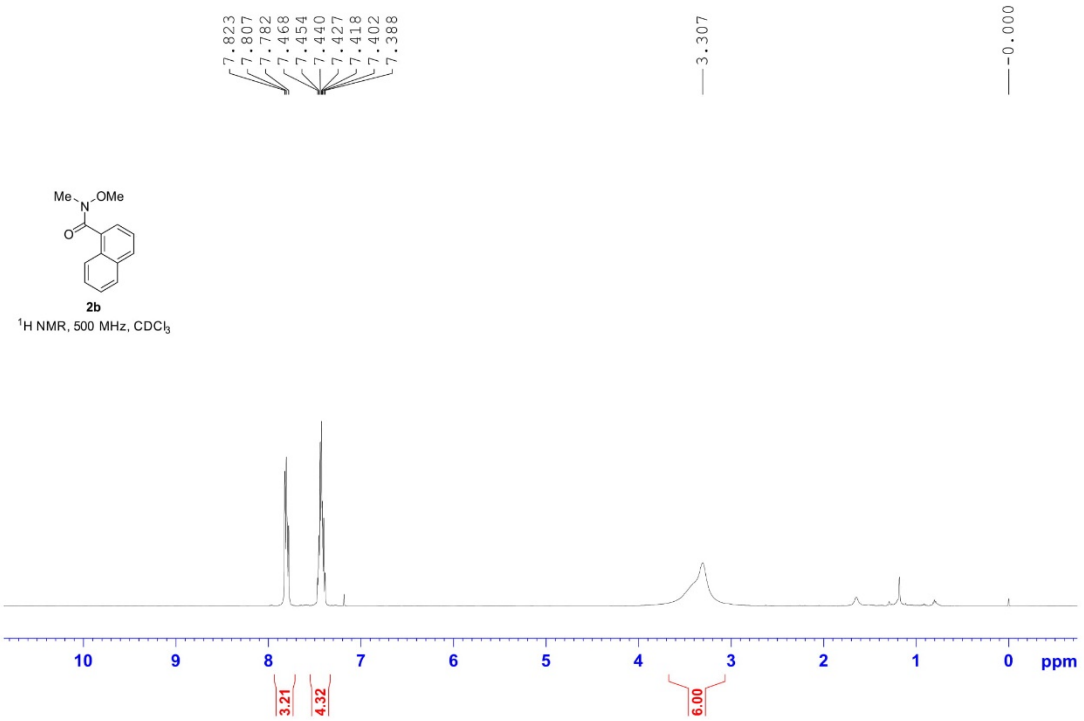
^{1}H and ^{13}C NMR of products



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7.454
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7.388
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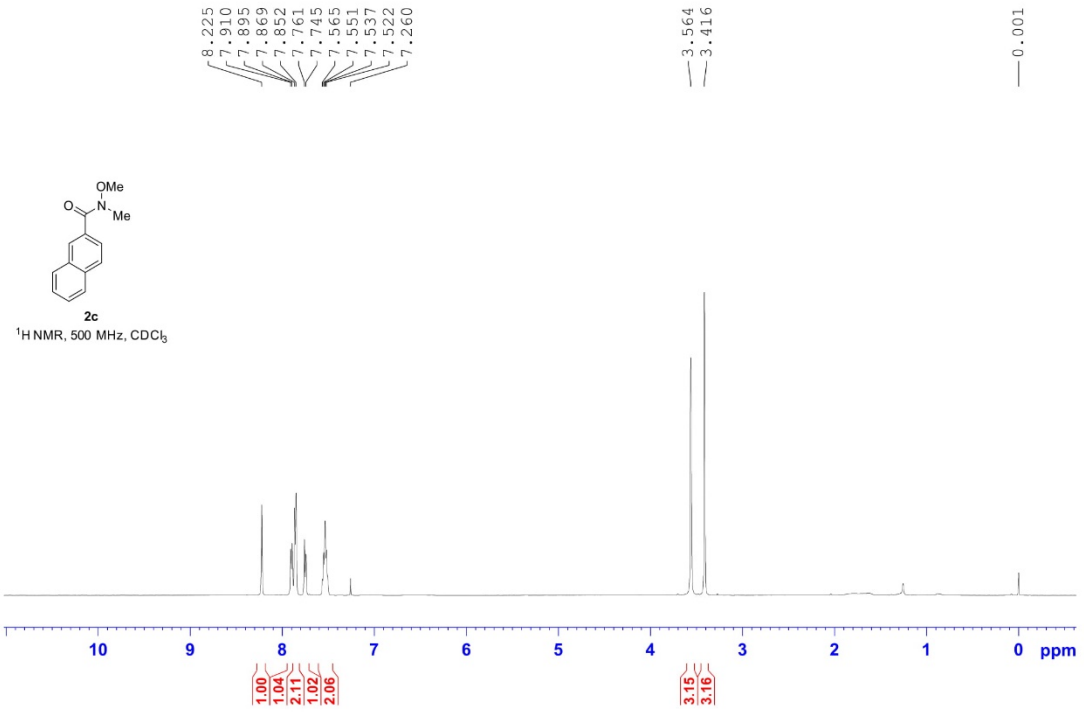
0.000
Me
N
OMe
O
2b
1H NMR, 500 MHz, CDCl3
10
9
8
7
6
5
4
3
2
1
0
ppm
3.21
4.32
6.00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7.537
7.522
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3.416
0.001
OMe
O
N
Me
2c
1H NMR, 500 MHz, CDCl3
10
9
8
7
6
5
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3
2
1
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ppm
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1.04
2.11
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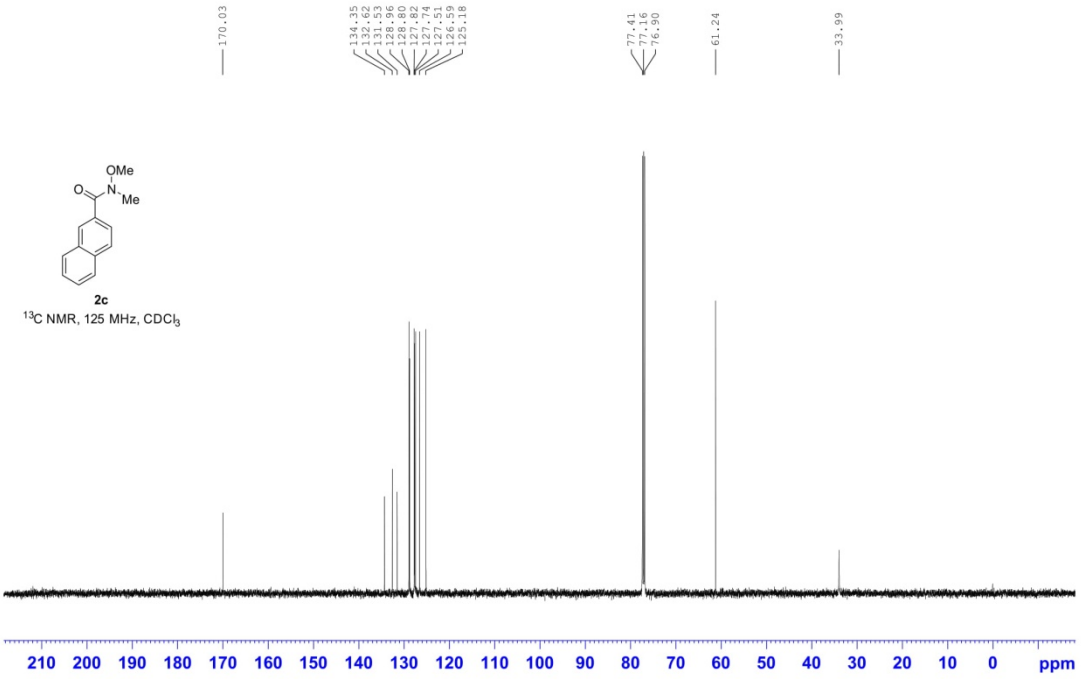
3.15
3.16



2c

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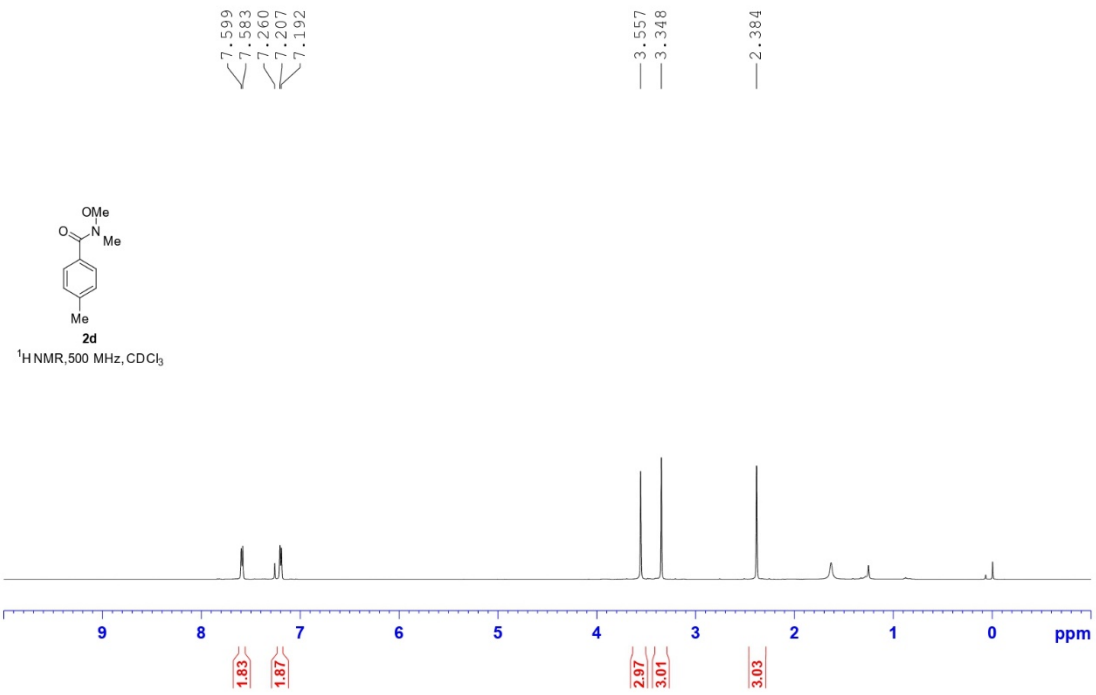
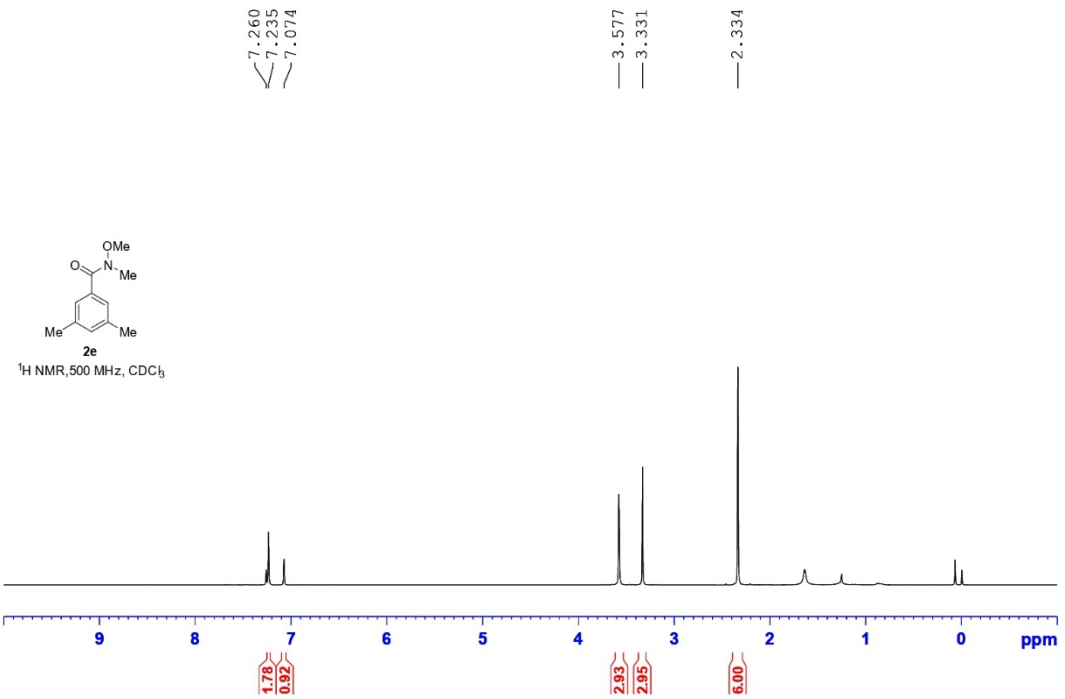


2d

^{1}H NMR,500 MHz, $CDCl_3$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6
5
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2
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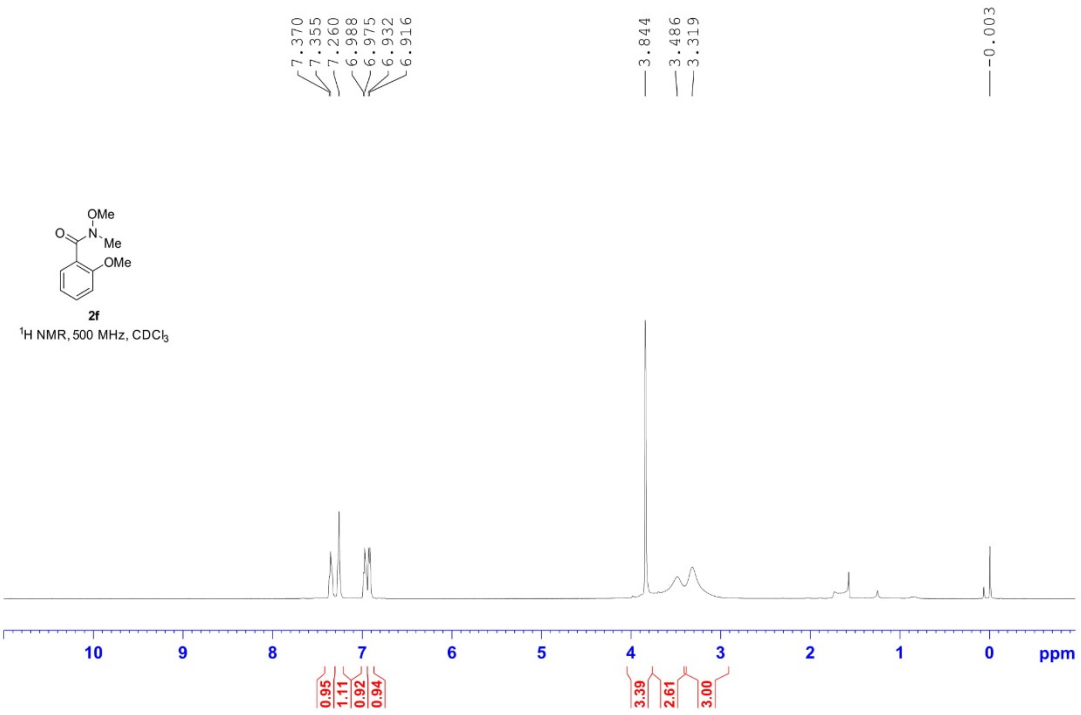
2.95
6.00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Me
OMe
2f
^{1}H NMR, 500 MHz, $CDCl_3$
10
9
8
7
6
5
4
3
2
1
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ppm
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1.11
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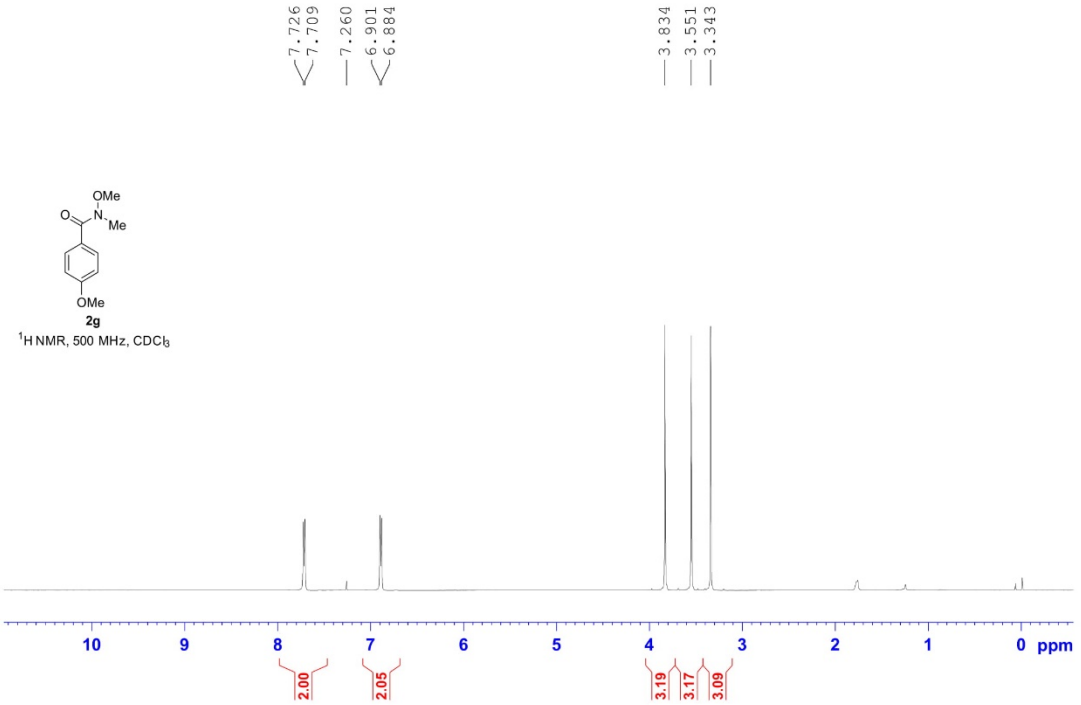
3.00



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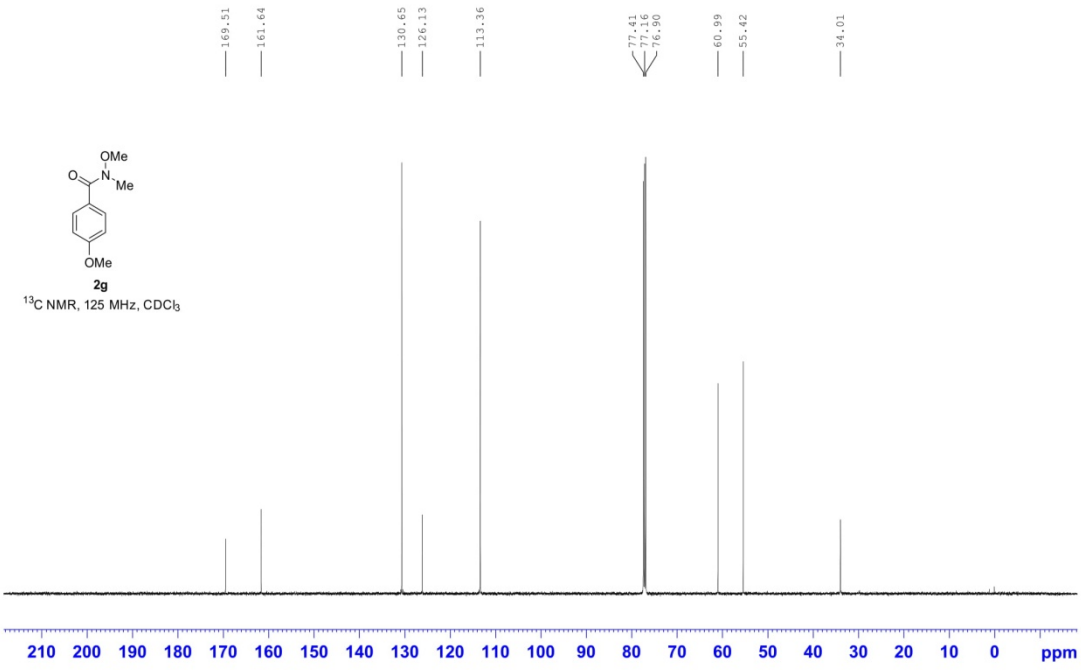

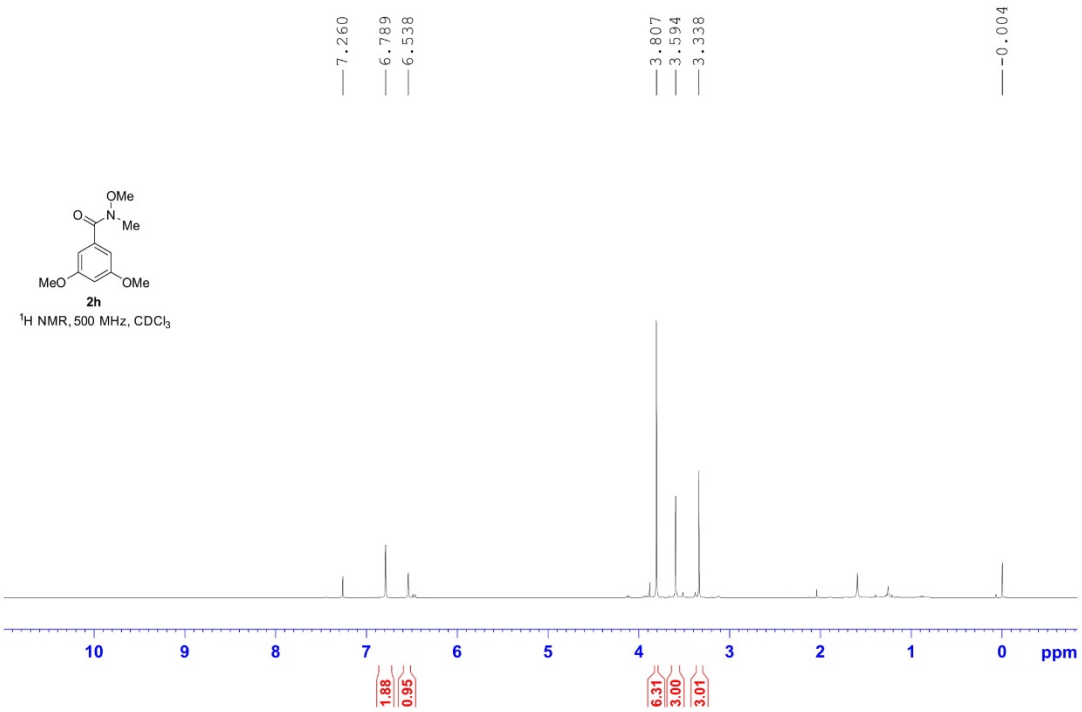
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ppm
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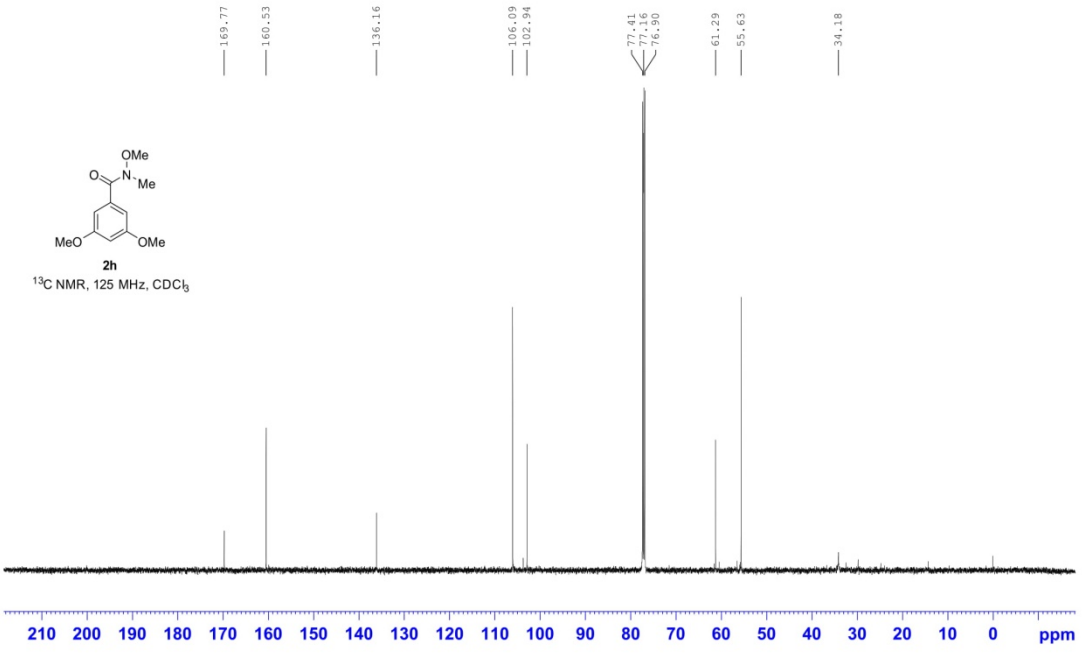
3.01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Me
O
MeO
OMe
2h
13C NMR, 125 MHz, CDCl3
210
200
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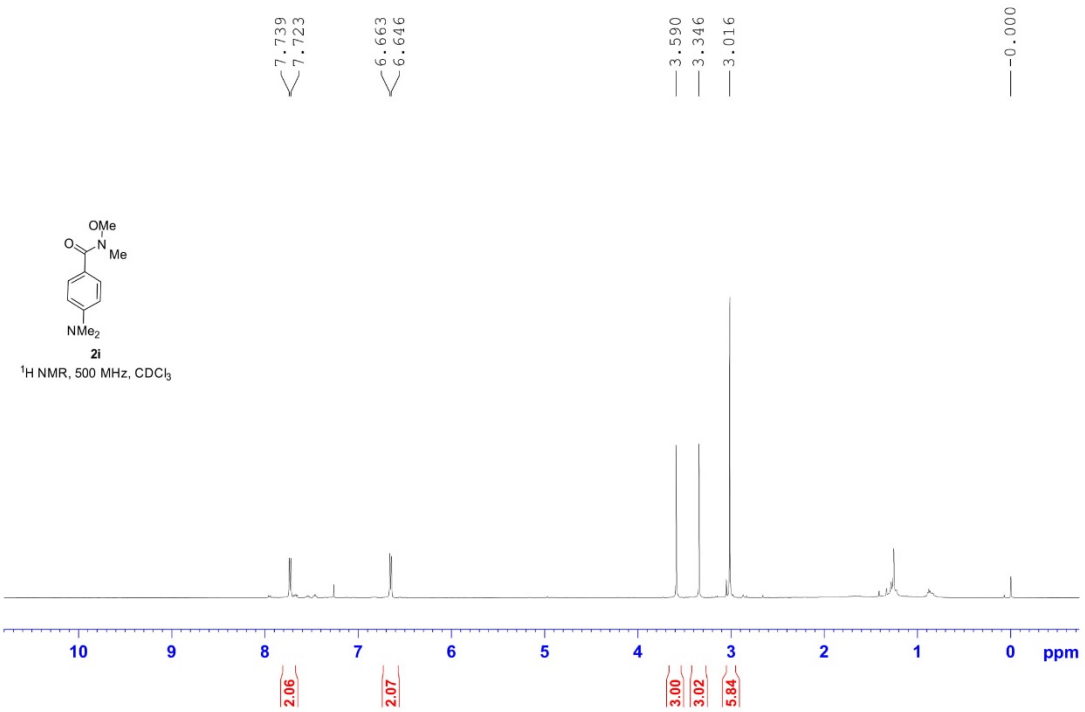
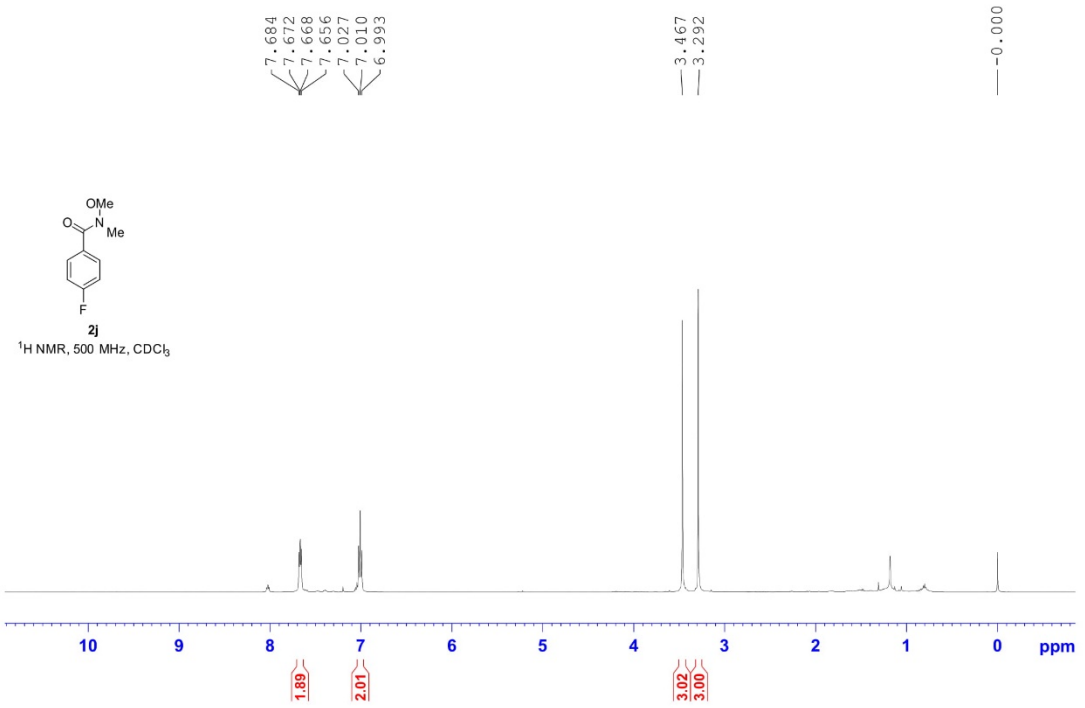


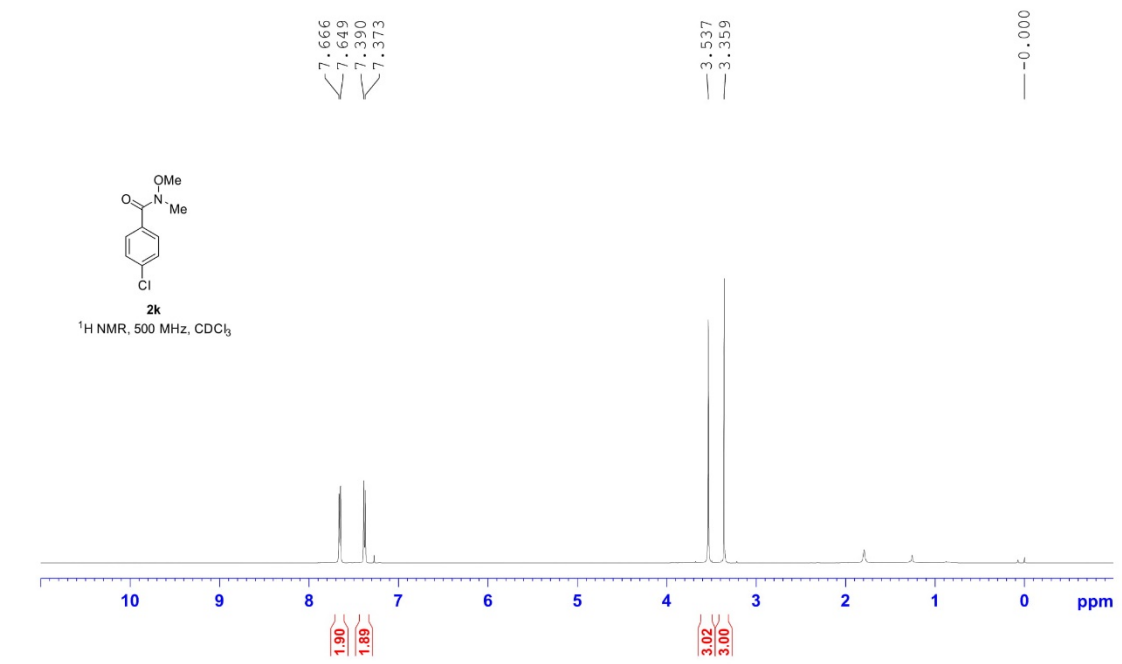
2i

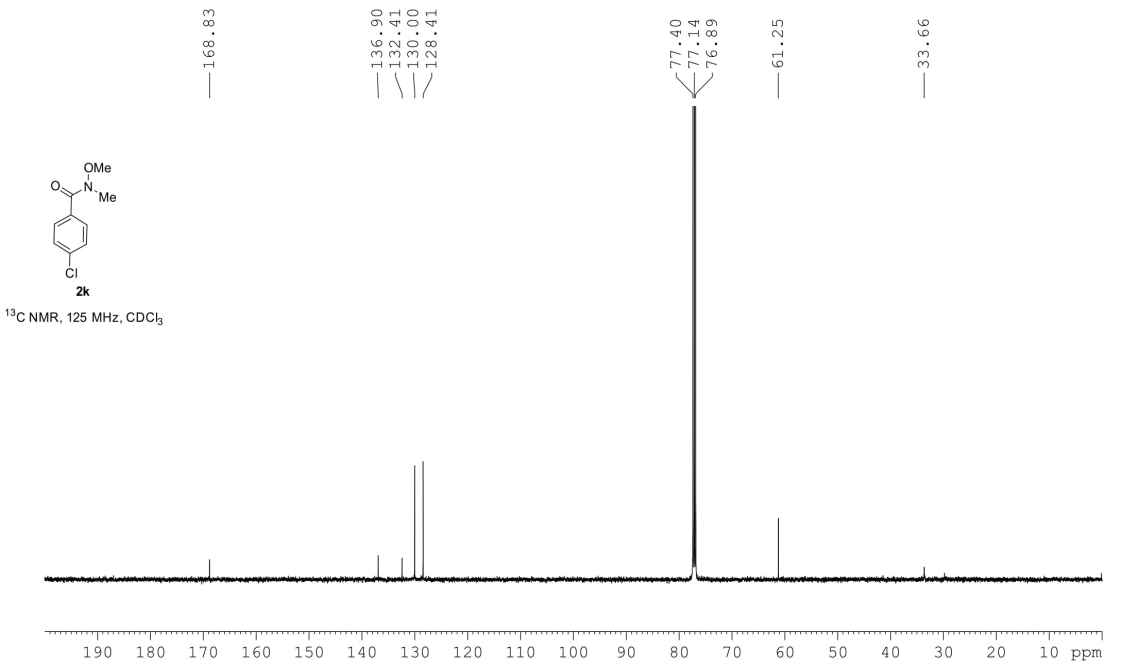
^{1}H NMR, 500 MHz, $CDCl_3$

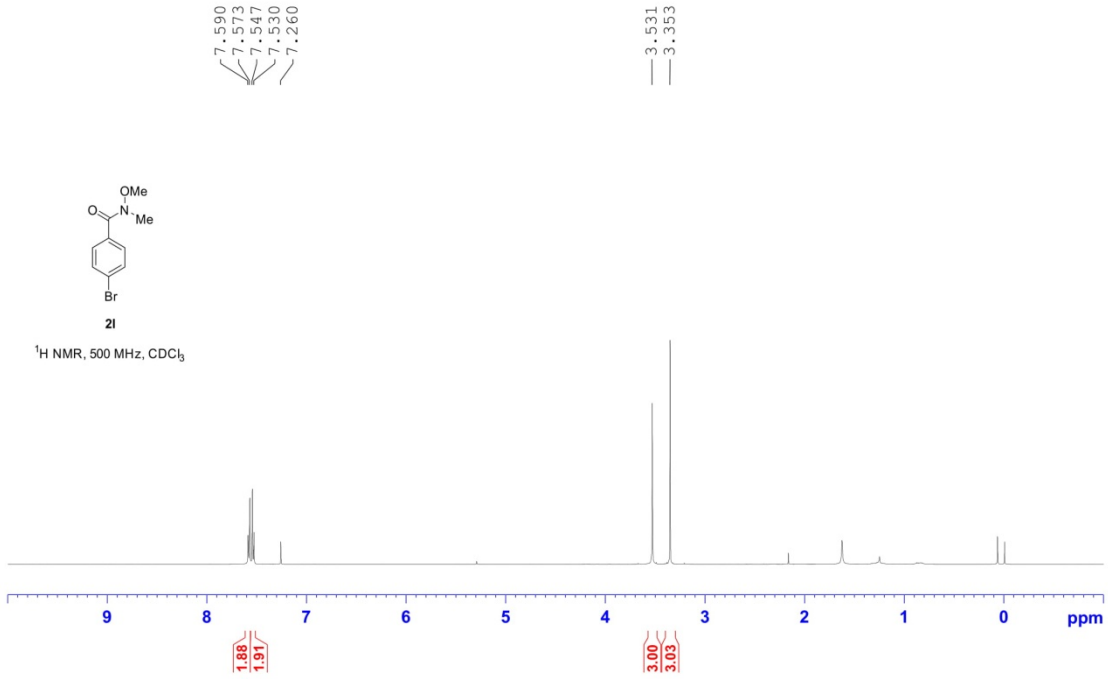


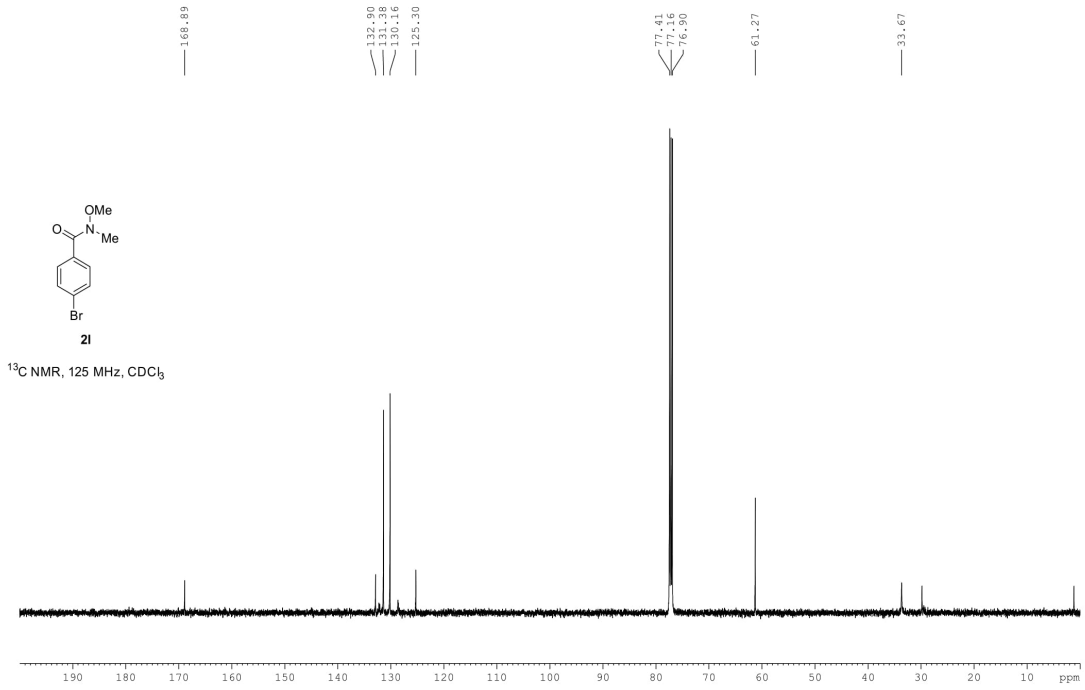
2j

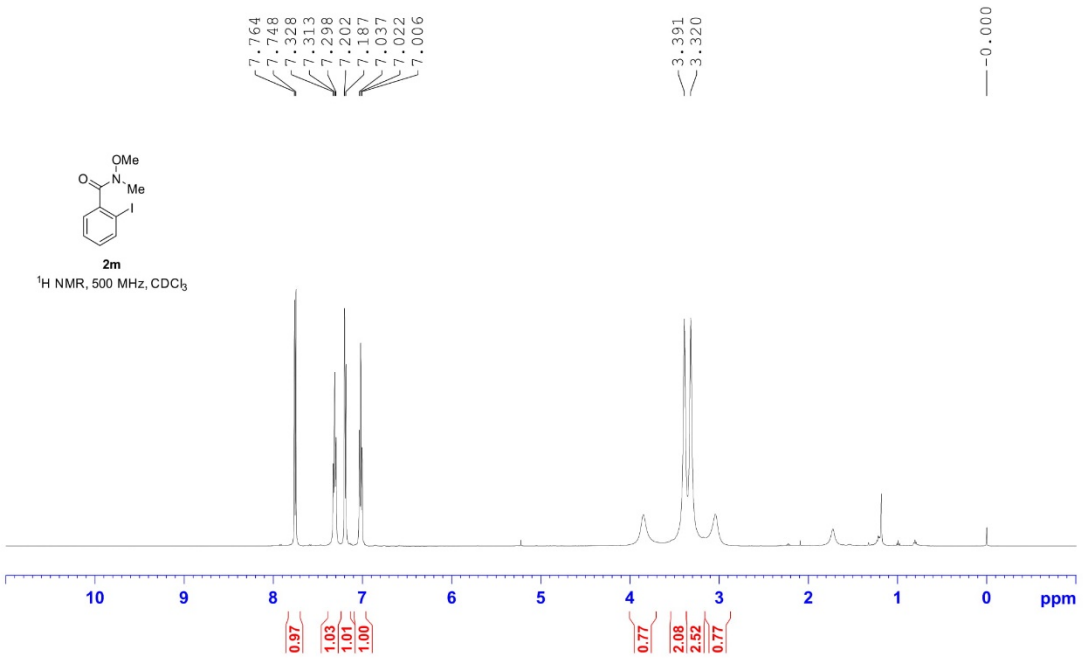
^{1}H NMR, 500 MHz, $CDCl_3$

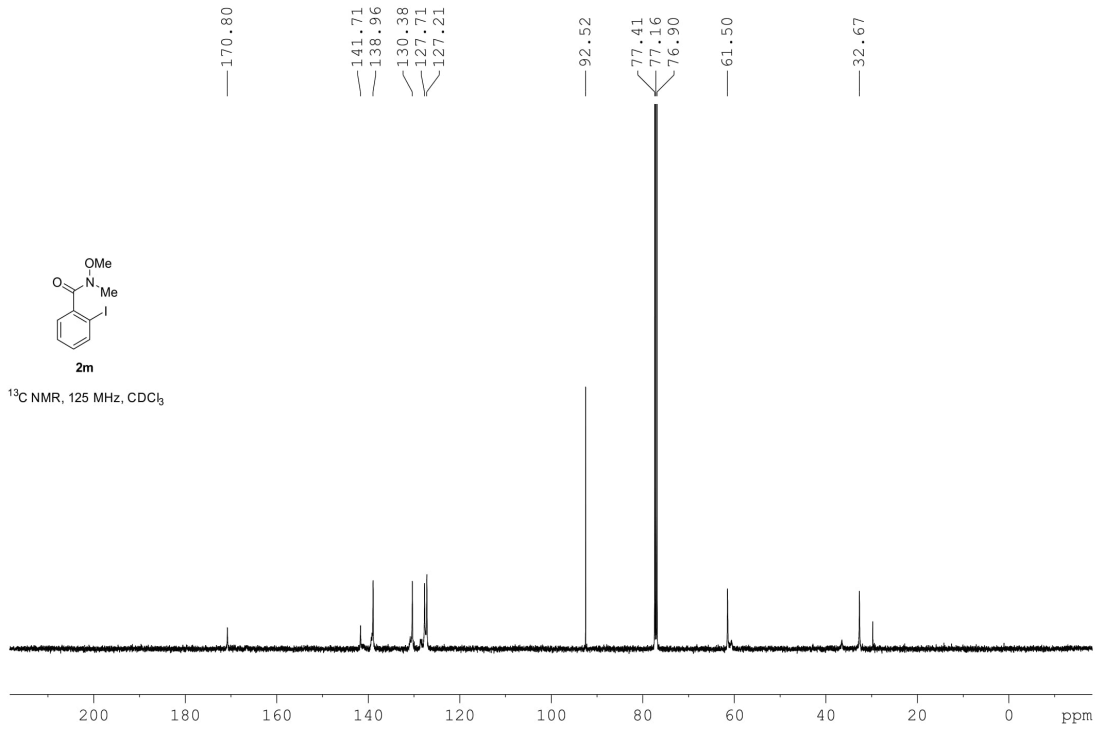

7.666
7.649
7.390
7.373
3.537
3.359
-0.000
OMe
N
Me
O
Cl
2k
1H NMR, 500 MHz, CDCl3
10
9
8
7
6
5
4
3
2
1
0
ppm
1.90
1.89
3.02
3.00

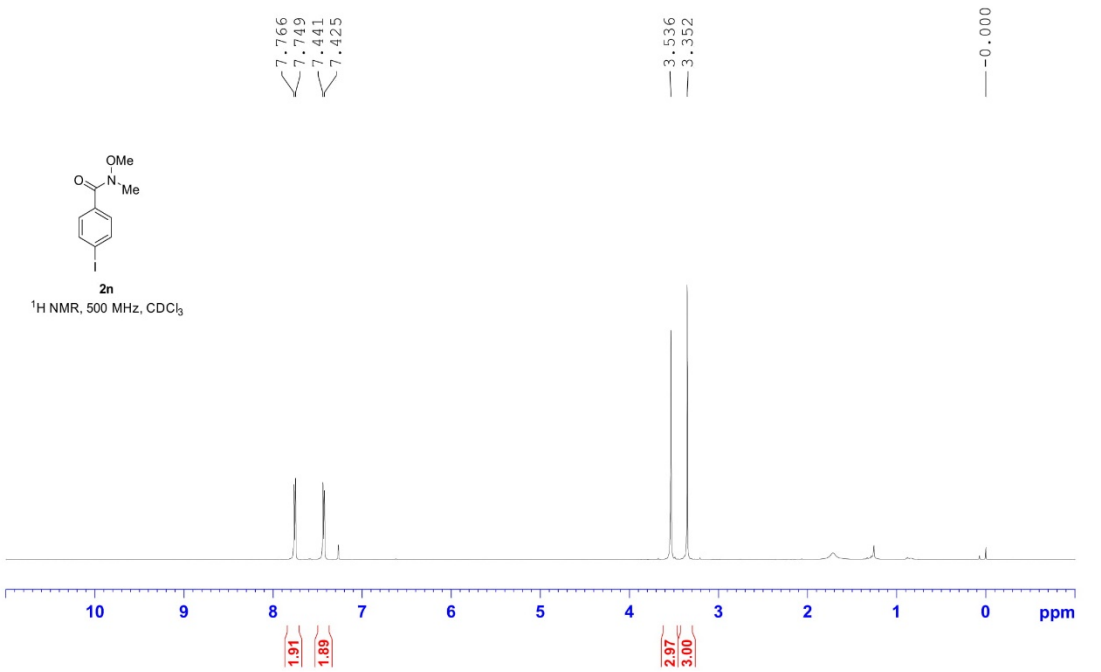

168.83
136.90
132.41
130.00
128.41
77.40
77.14
76.89
61.25
33.66
OMe
N
Me
O
Cl
2k
13C NMR, 125 MHz, CDCl3
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

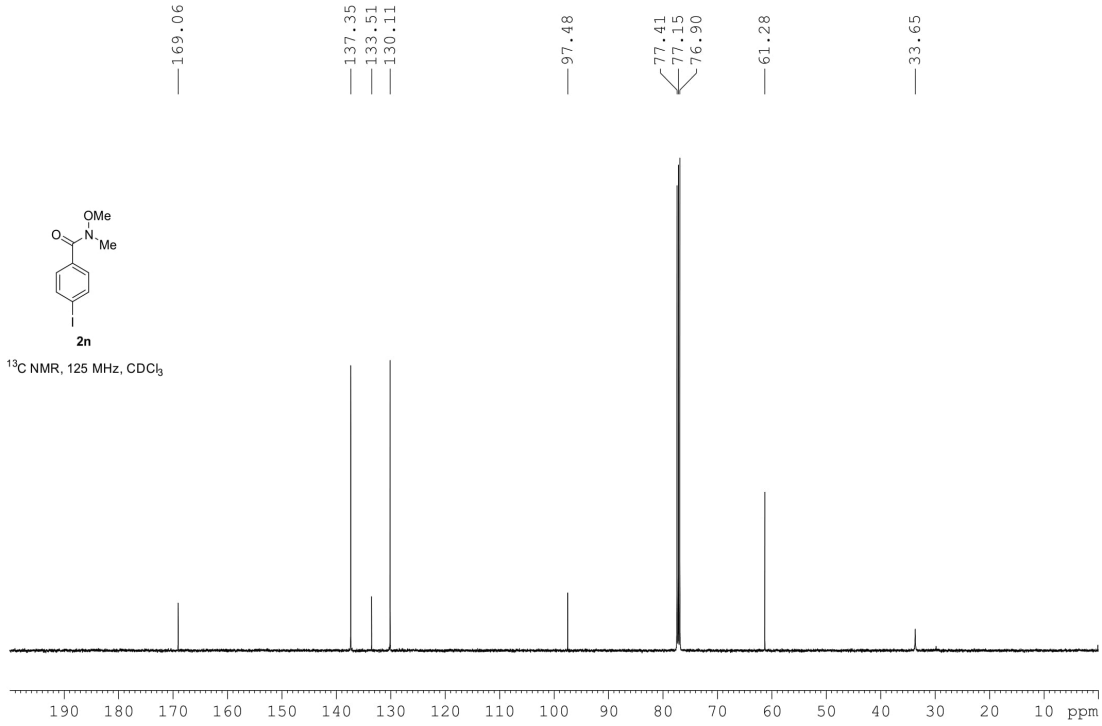

7.590
7.573
7.547
7.530
7.260
3.531
3.353
OMe
N
Me
O
Br
2l
1H NMR, 500 MHz, CDCl3
9
8
7
6
5
4
3
2
1
0
ppm
1.88
1.91
3.00
3.03

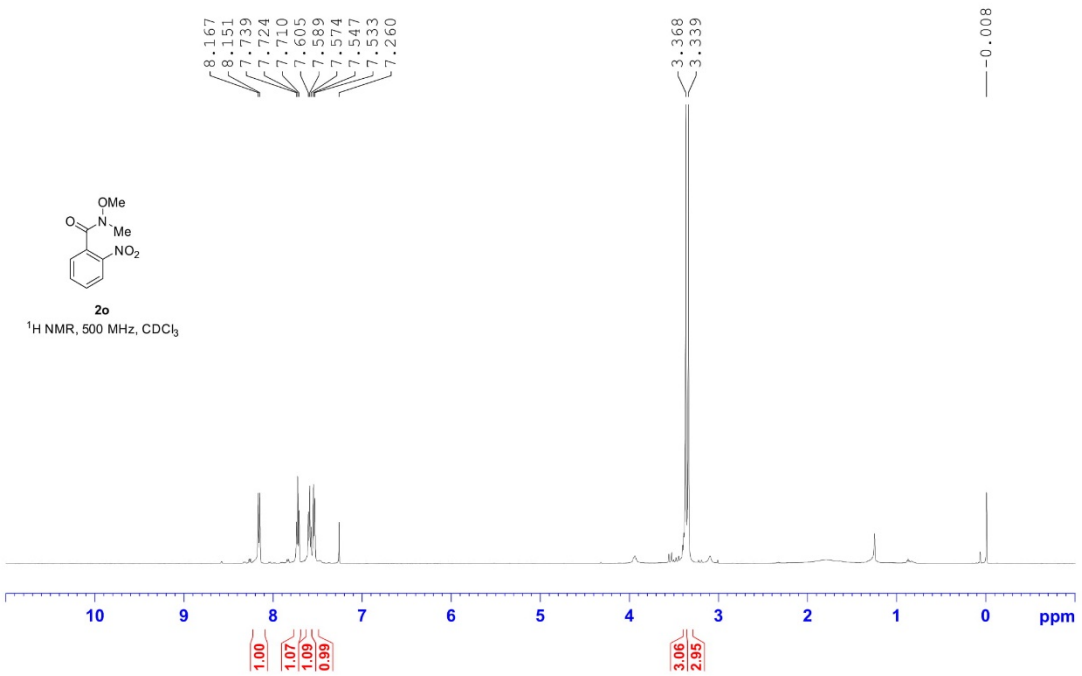

168.89
132.90
131.38
130.16
125.30
77.41
77.16
76.90
61.27
33.67
OMe
N
Me
O
Br
2l
13C NMR, 125 MHz, CDCl3
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


7.764
7.748
7.328
7.313
7.298
7.202
7.187
7.037
7.022
7.006
3.391
3.320
0.000
OMe
N
Me
O
I
2m
1H NMR, 500 MHz, CDCl3
10
9
8
7
6
5
4
3
2
1
0
ppm
0.97
1.03
1.01
1.00
0.77
2.08
2.52
0.77


170.80
141.71
138.96
130.38
127.71
127.21
92.52
77.41
77.16
76.90
61.50
32.67
OMe
N
Me
O
I
2m
13C NMR, 125 MHz, CDCl3
200
180
160
140
120
100
80
60
40
20
0
ppm

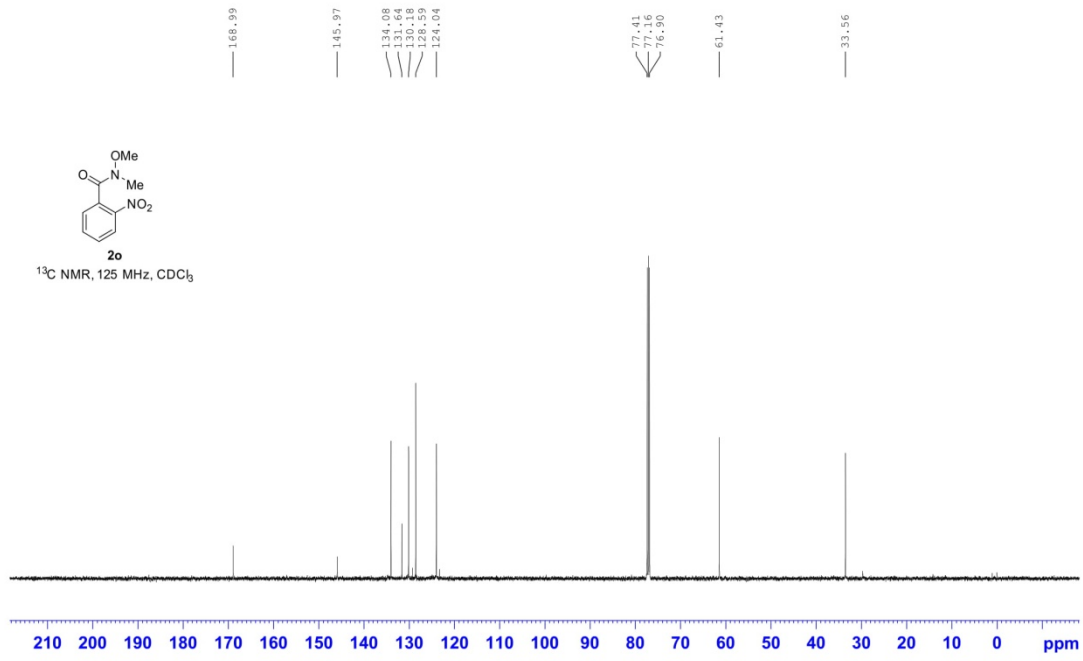

7.766
7.749
7.441
7.425
3.536
3.352
0.000
OMe
N
Me
O
2n
1H NMR, 500 MHz, CDCl3
10
9
8
7
6
5
4
3
2
1
0
ppm
1.91
1.89
2.97
3.00


169.06
137.35
133.51
130.11
97.48
77.41
77.15
76.90
61.28
33.65
OMe
N
Me
O
2n
13C NMR, 125 MHz, CDCl3
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm



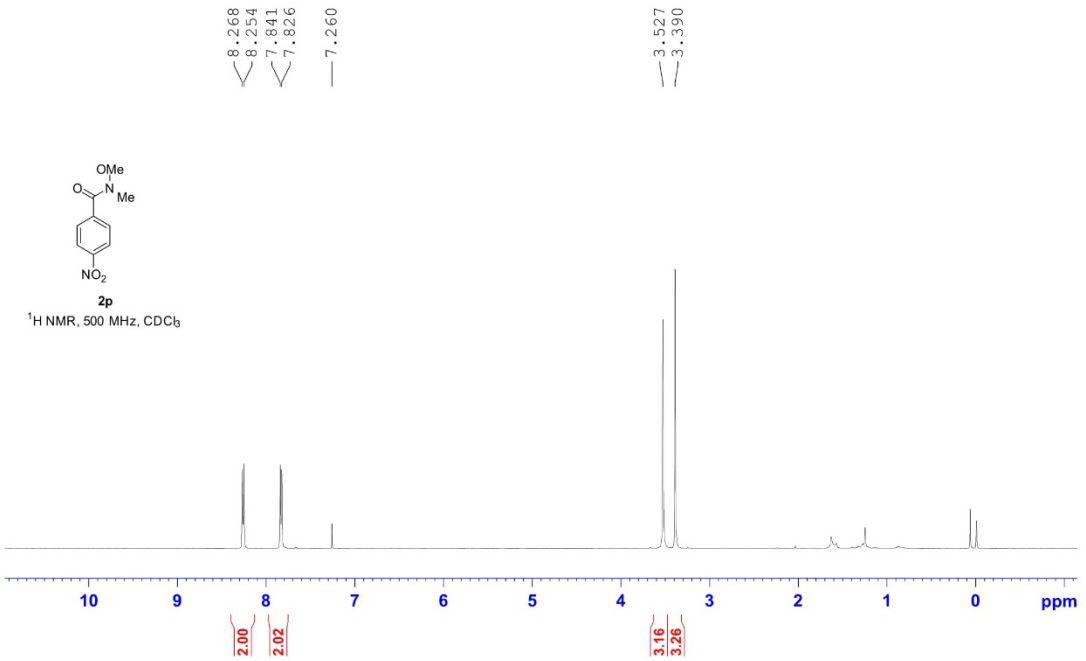
2o

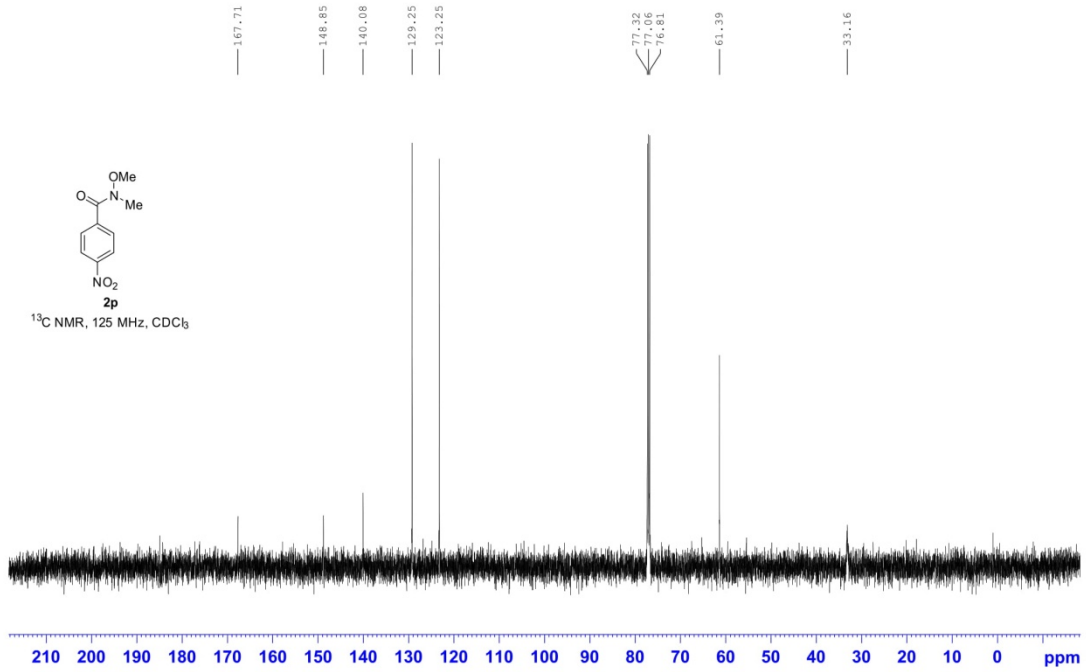
^{1}H NMR, 500 MHz, $CDCl_3$

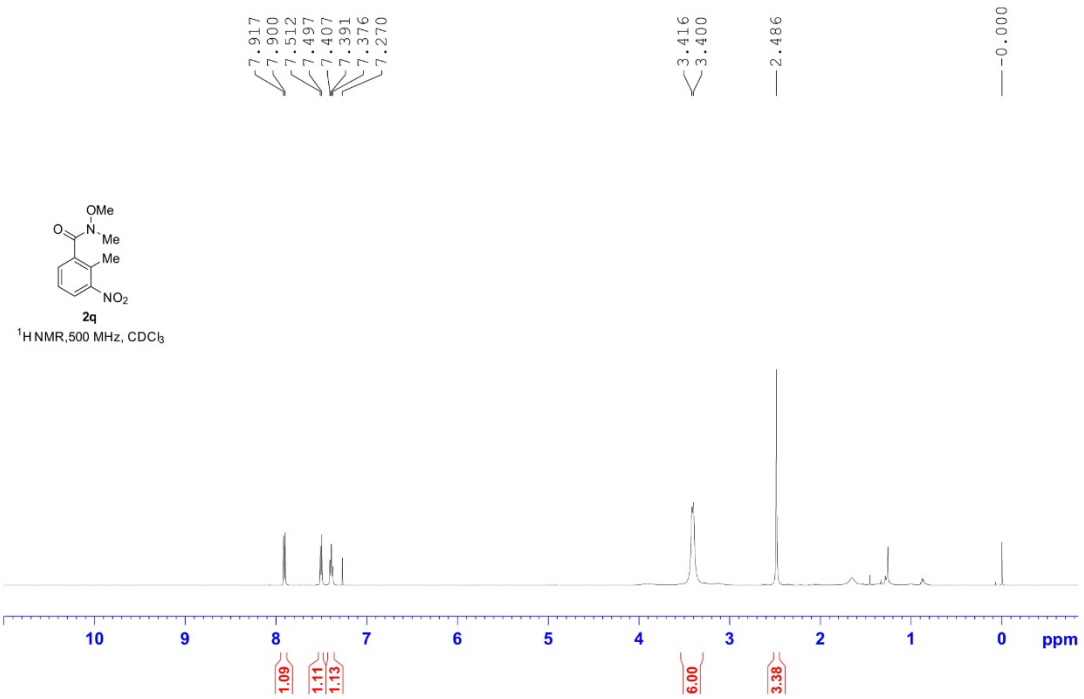


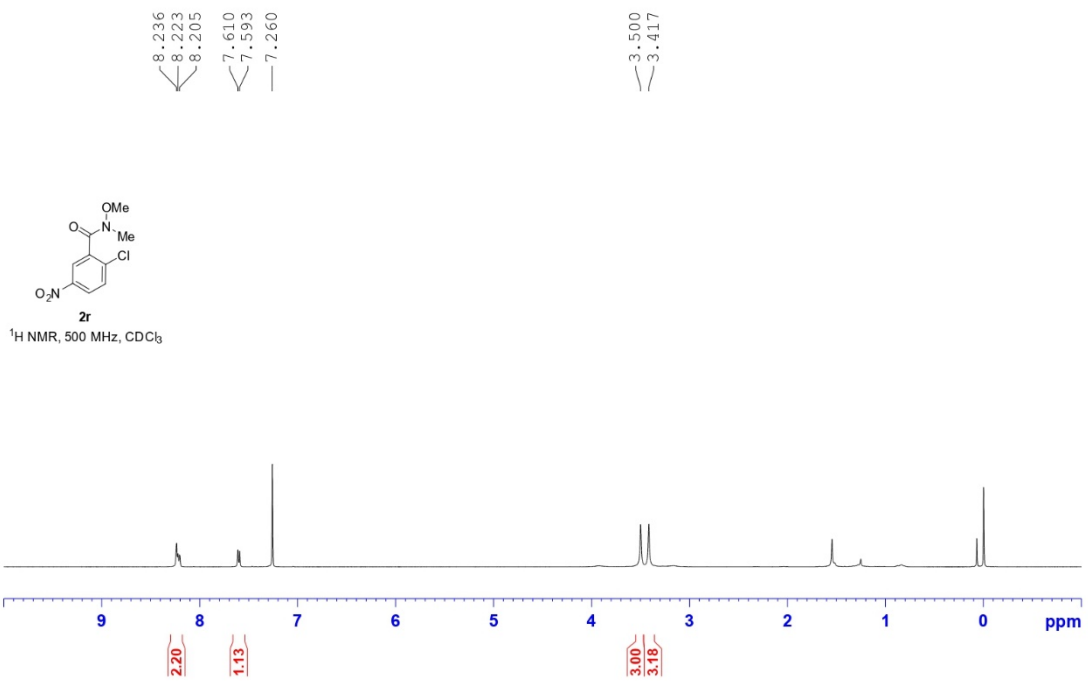
2o

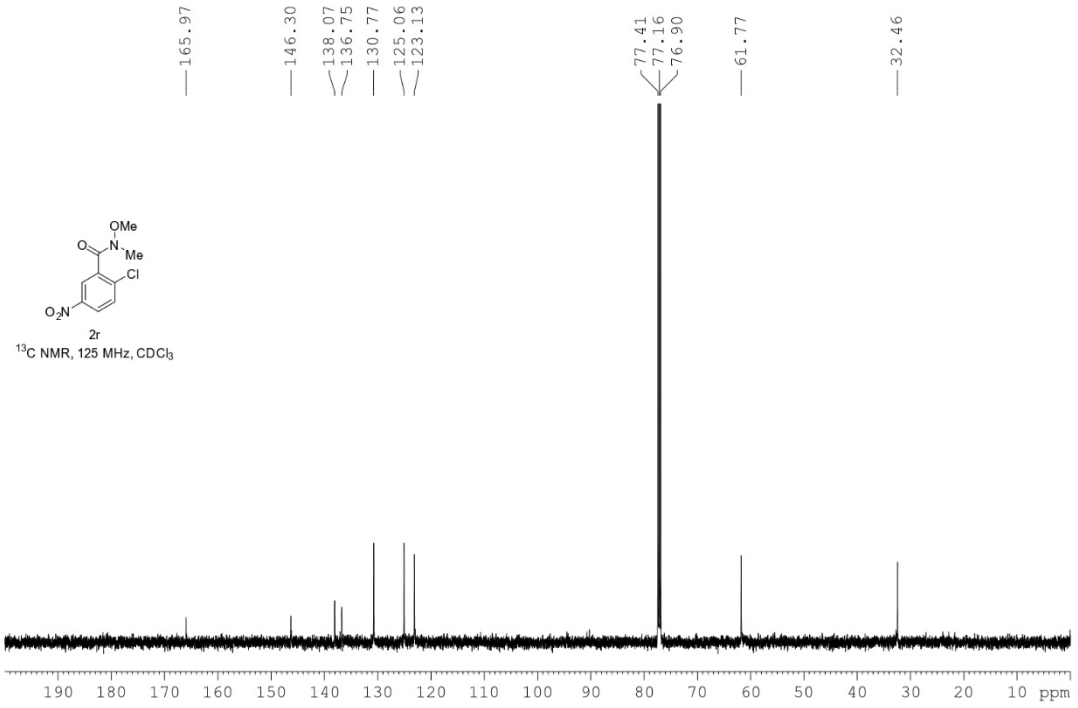
^{13}C NMR, 125 MHz, $CDCl_3$


8.268
8.254
7.841
7.826
7.260
3.527
3.390
OMe
N
Me
O
NO2
2p
1H NMR, 500 MHz, CDCl3
10
9
8
7
6
5
4
3
2
1
0
ppm
2.00
2.02
3.16
3.26


167.71
148.85
140.08
129.25
123.25
77.32
77.06
76.81
61.39
33.16
OMe
N
Me
O
NO2
2p
13C NMR, 125 MHz, CDCl3
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

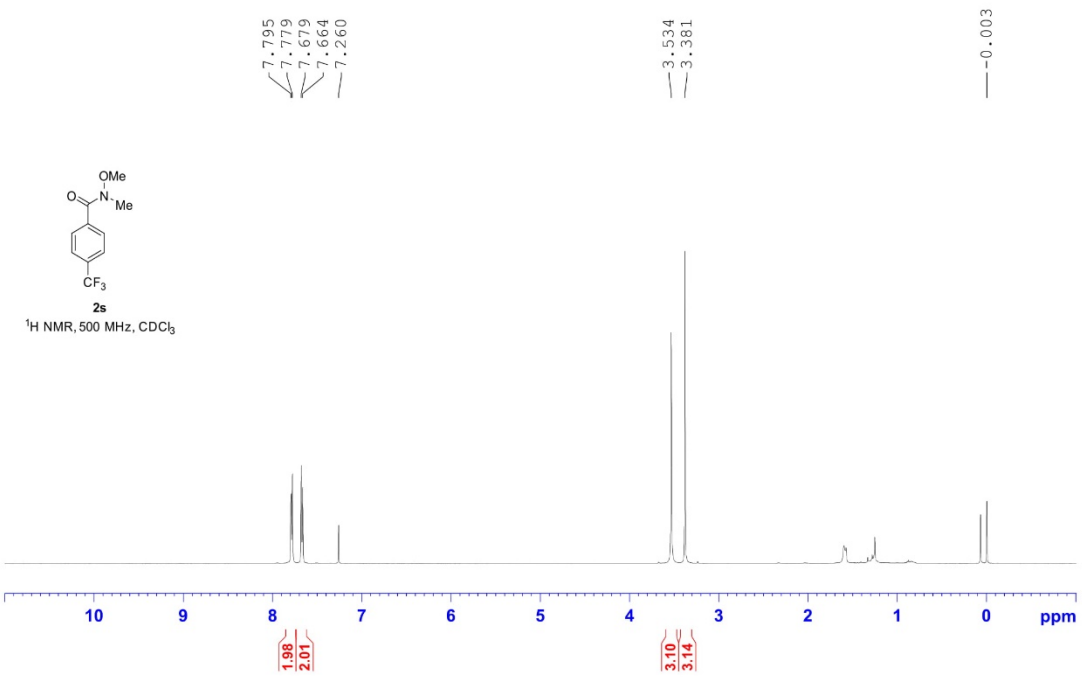

7.917
7.900
7.512
7.497
7.407
7.391
7.376
7.270
3.416
3.400
2.486
0.000
OMe
N
Me
Me
NO2
2q
1H NMR,500 MHz, CDCl3
10
9
8
7
6
5
4
3
2
1
0
ppm
1.09
1.11
1.13
6.00
3.38


8.236
8.223
8.205
7.610
7.593
7.260
3.500
3.417
OMe
N
Me
Cl
O2N
2r
1H NMR, 500 MHz, CDCl3
9
8
7
6
5
4
3
2
1
0
ppm
2.20
1.13
3.00
3.18



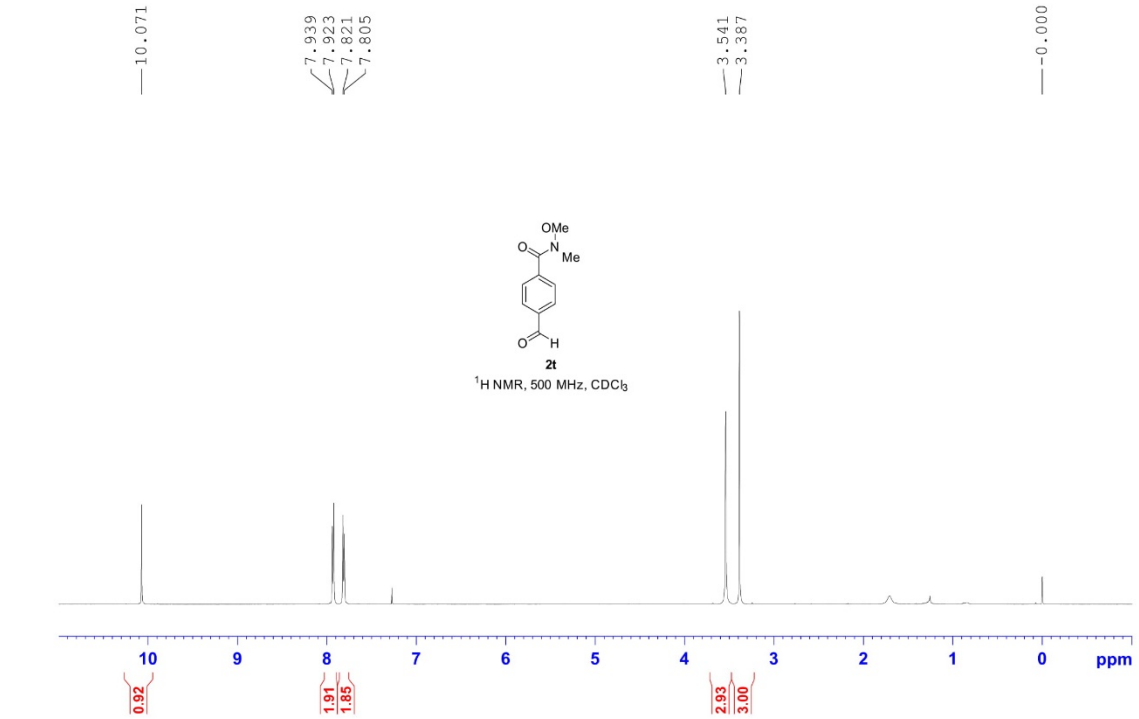
2r

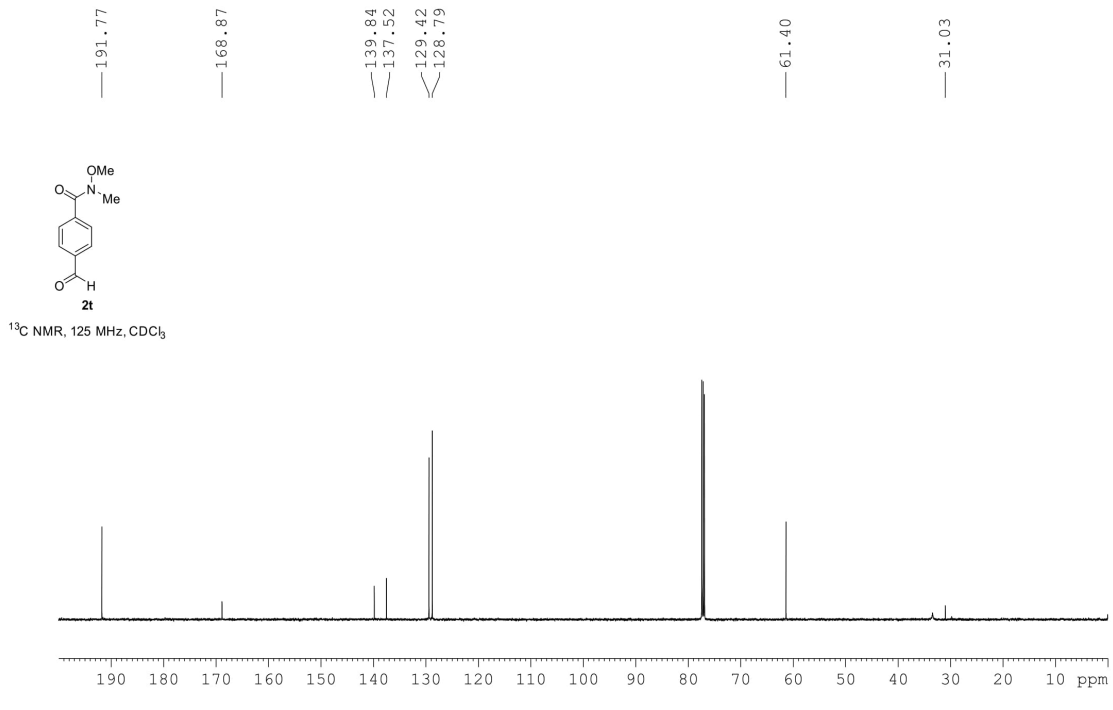
^{13}C NMR, 125 MHz, $CDCl_3$

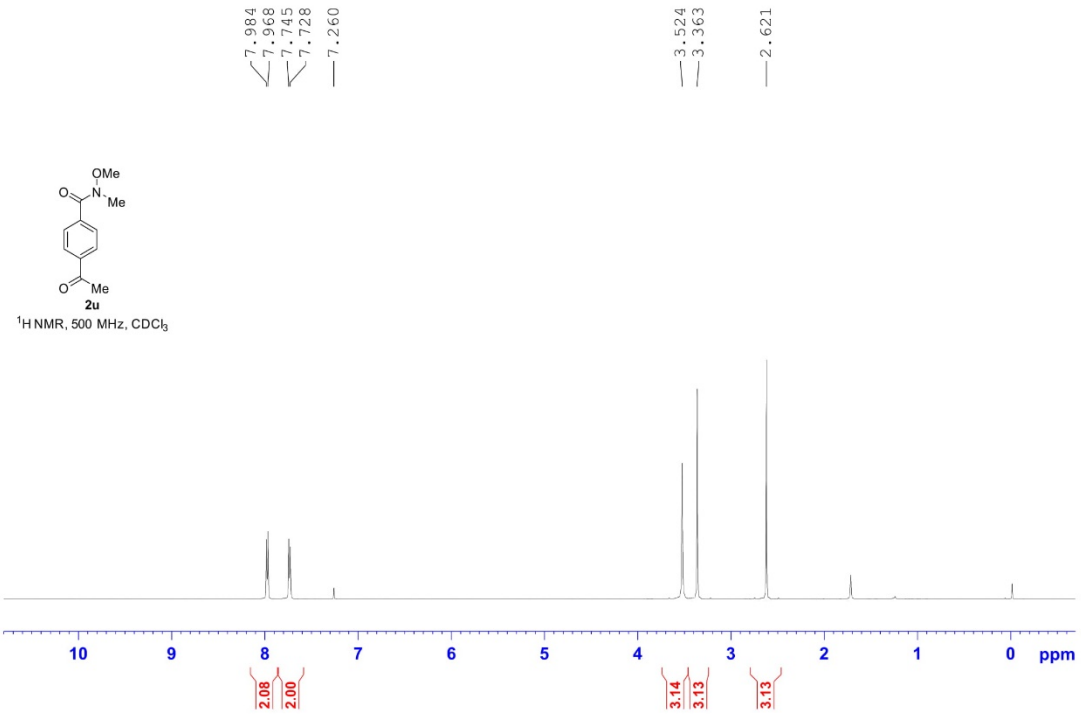


2s

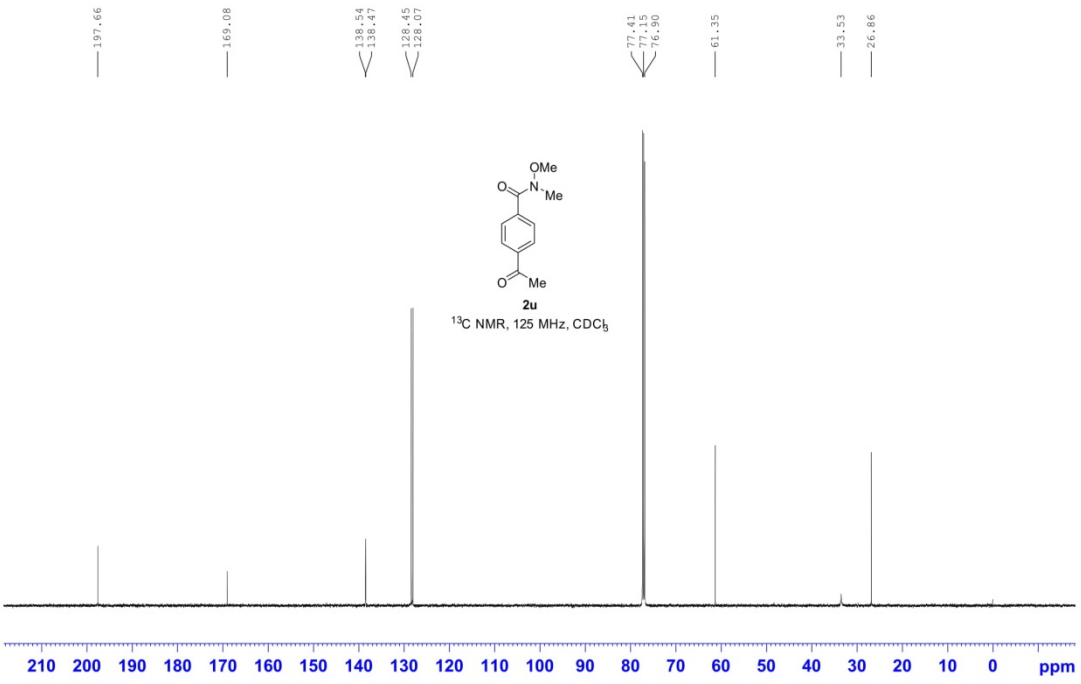
^{1}H NMR, 500 MHz, $CDCl_3$

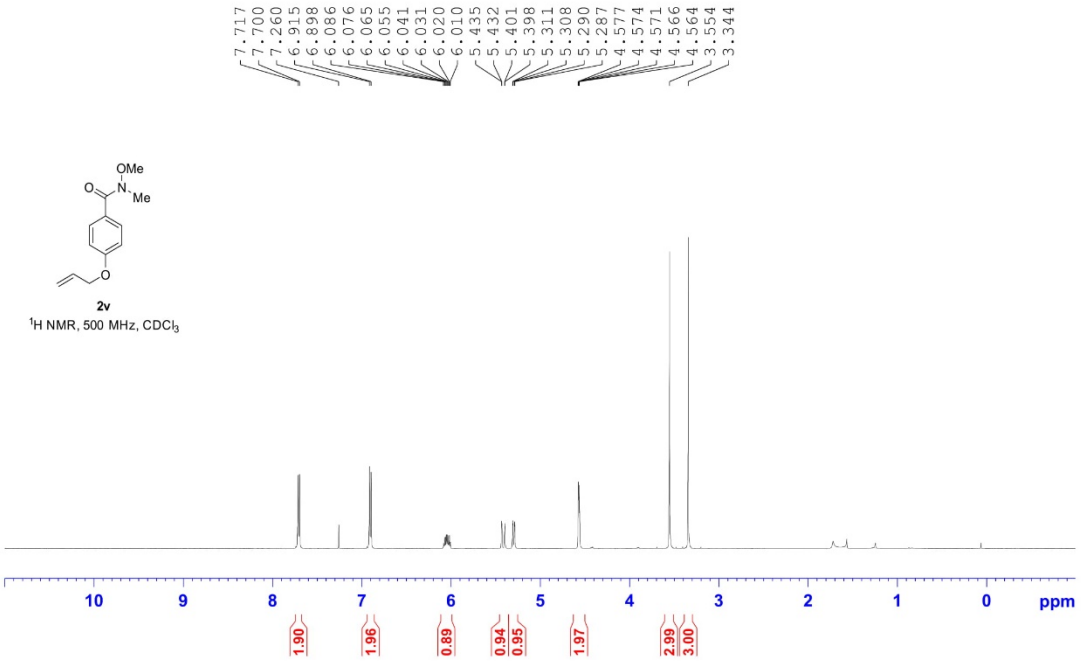

10.071
7.939
7.923
7.821
7.805
3.541
3.387
0.000
OMe
N
Me
O
H
2t
1H NMR, 500 MHz, CDCl3
10
9
8
7
6
5
4
3
2
1
0
ppm
0.92
1.91
1.85
2.93
3.00

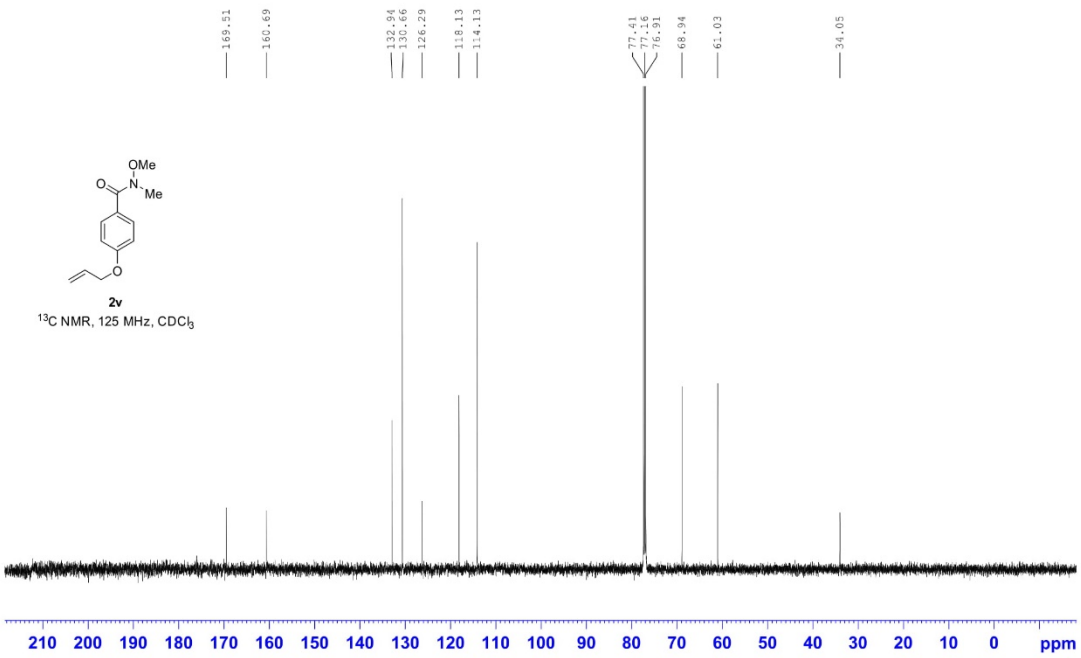

191.77
168.87
139.84
137.52
129.42
128.79
61.40
31.03
OMe
N
Me
O
H
2t
13C NMR, 125 MHz, CDCl3
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

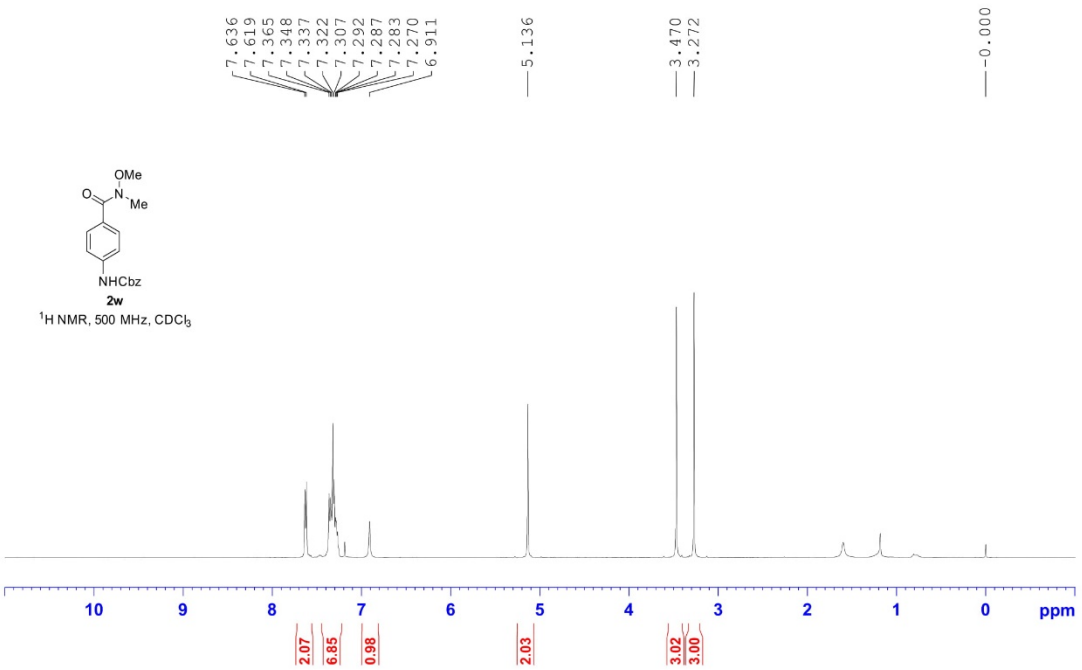


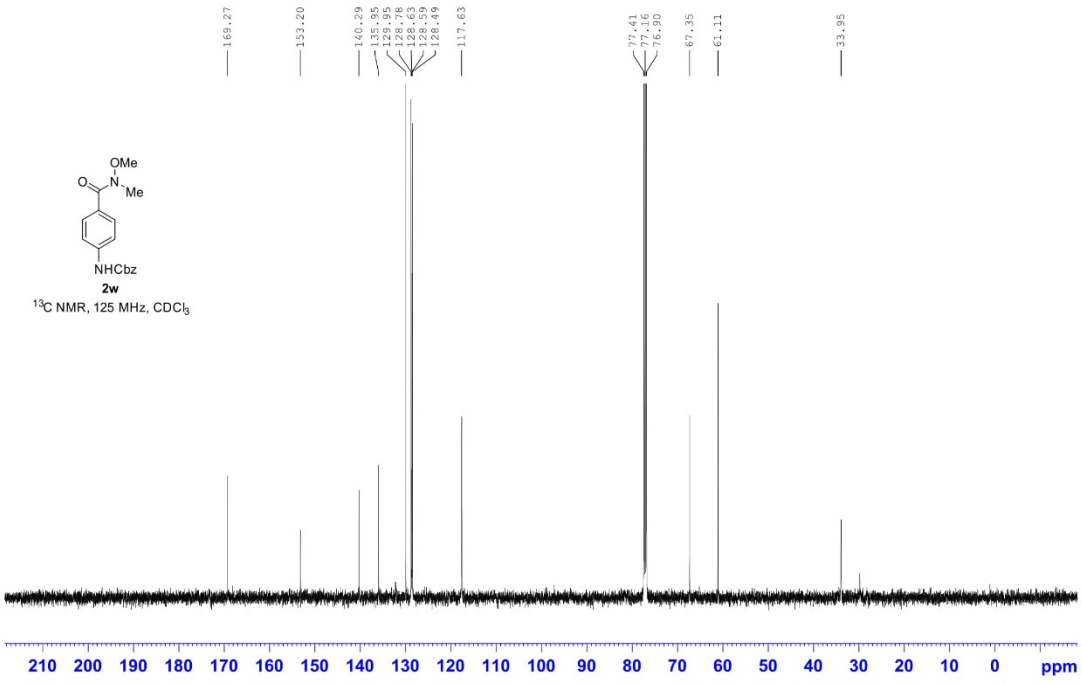
AK-DVK-137
C13CPD CDCl3 {C:\Bruker\TopSpin3.2} nmr 56

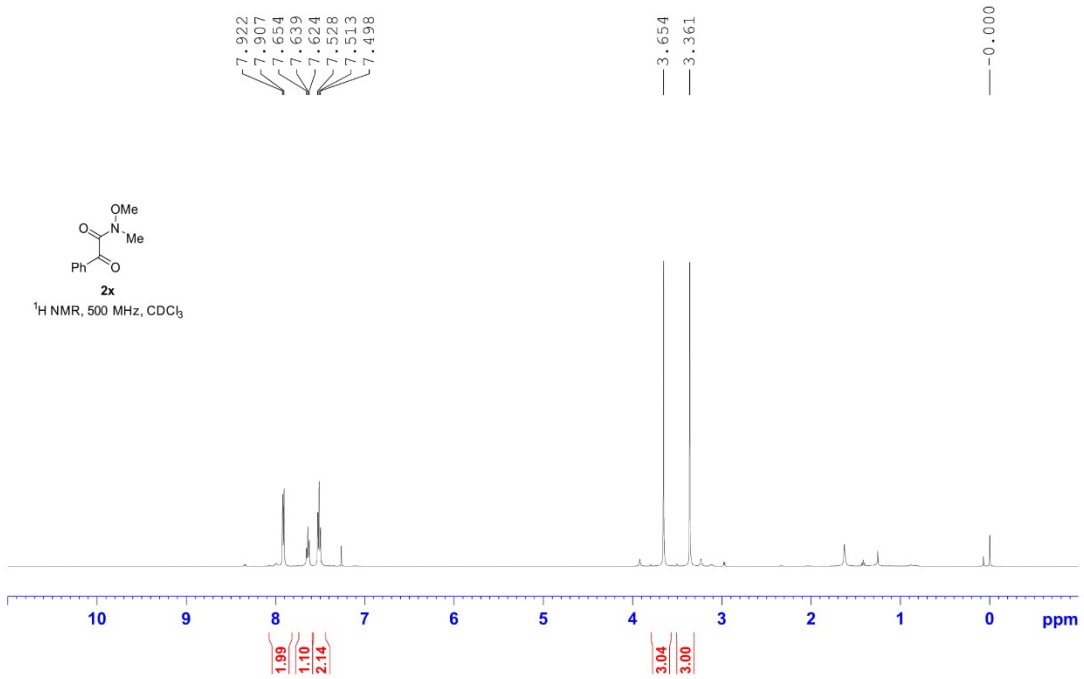


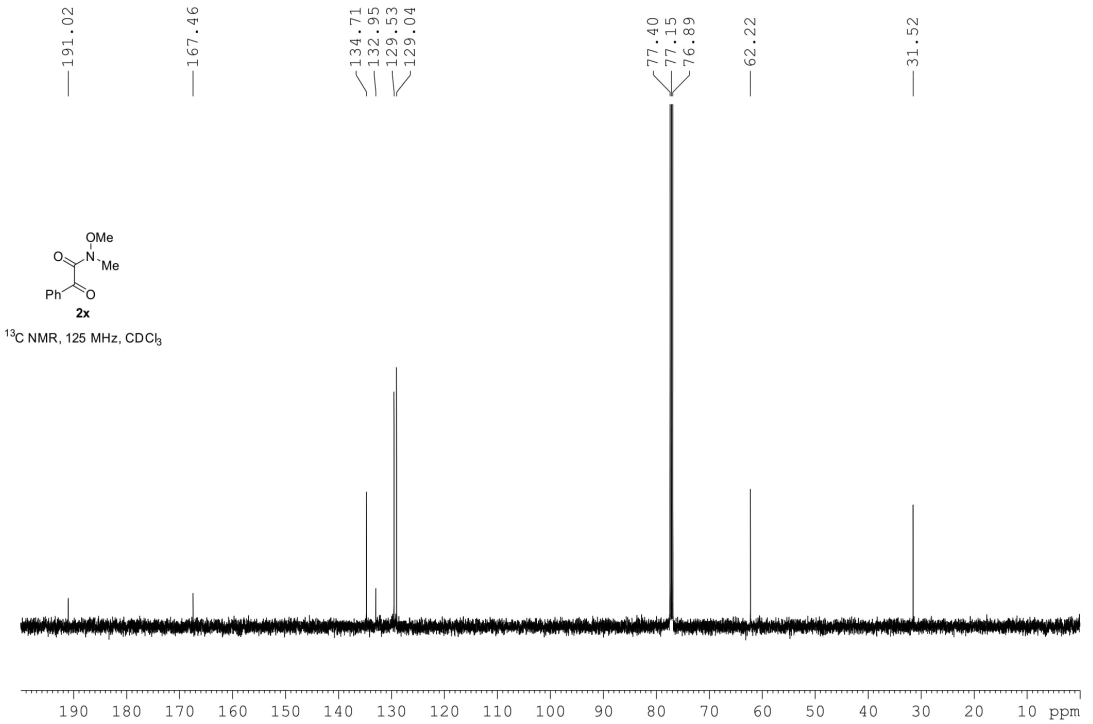

7.717
7.700
7.260
6.915
6.898
6.086
6.076
6.065
6.055
6.041
6.031
6.020
6.010
5.435
5.432
5.401
5.398
5.311
5.308
5.290
5.287
4.577
4.574
4.571
4.566
4.564
3.554
3.344
OMe
N
Me
O
O
2v
1H NMR, 500 MHz, CDCl3
10
9
8
7
6
5
4
3
2
1
0
ppm
1.90
1.96
0.89
0.94
0.95
1.97
2.99
3.00

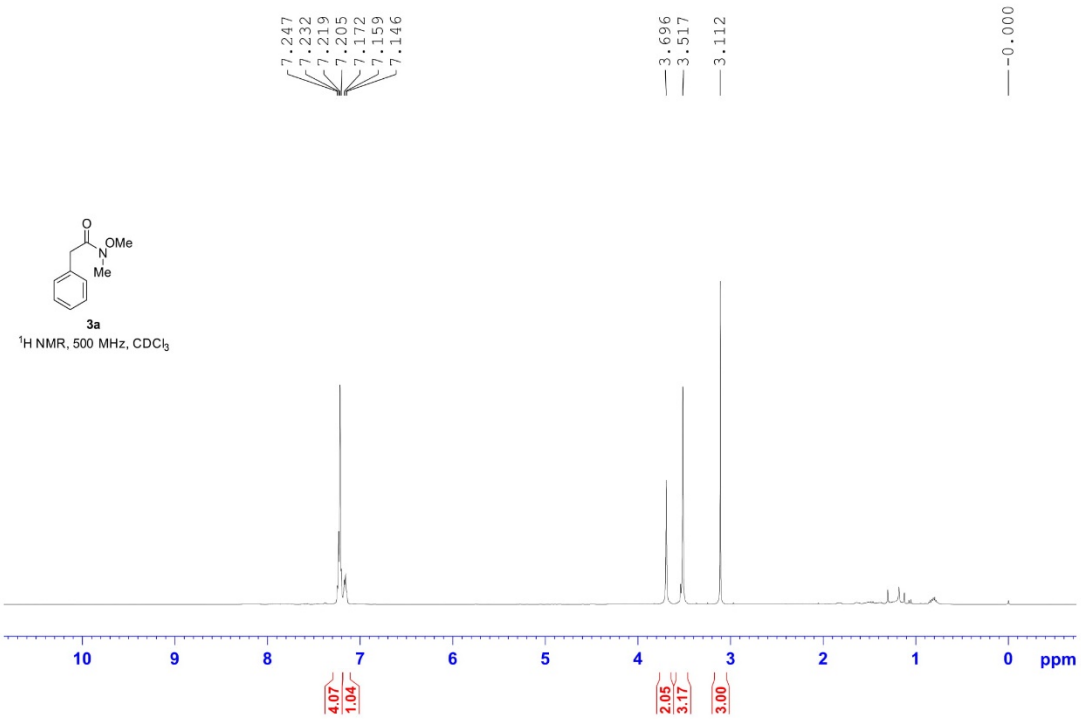

169.51
160.69
132.94
130.66
126.29
118.13
114.13
77.41
77.16
76.91
68.94
61.03
34.05
OMe
N
Me
O
O
2v
13C NMR, 125 MHz, CDCl3
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm


7.636
7.619
7.365
7.348
7.337
7.322
7.307
7.292
7.287
7.283
7.270
6.911
5.136
3.470
3.272
0.000
OMe
N
Me
O
NHCbz
2w
1H NMR, 500 MHz, CDCl3
10 9 8 7 6 5 4 3 2 1 0 ppm
2.07
6.85
0.98
2.03
3.02
3.00


169.27
153.20
140.29
135.95
129.95
128.78
128.63
128.59
128.49
117.63
77.41
77.16
76.90
67.35
61.11
33.95
OMe
N
Me
O
NHCbz
2w
13C NMR, 125 MHz, CDCl3
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

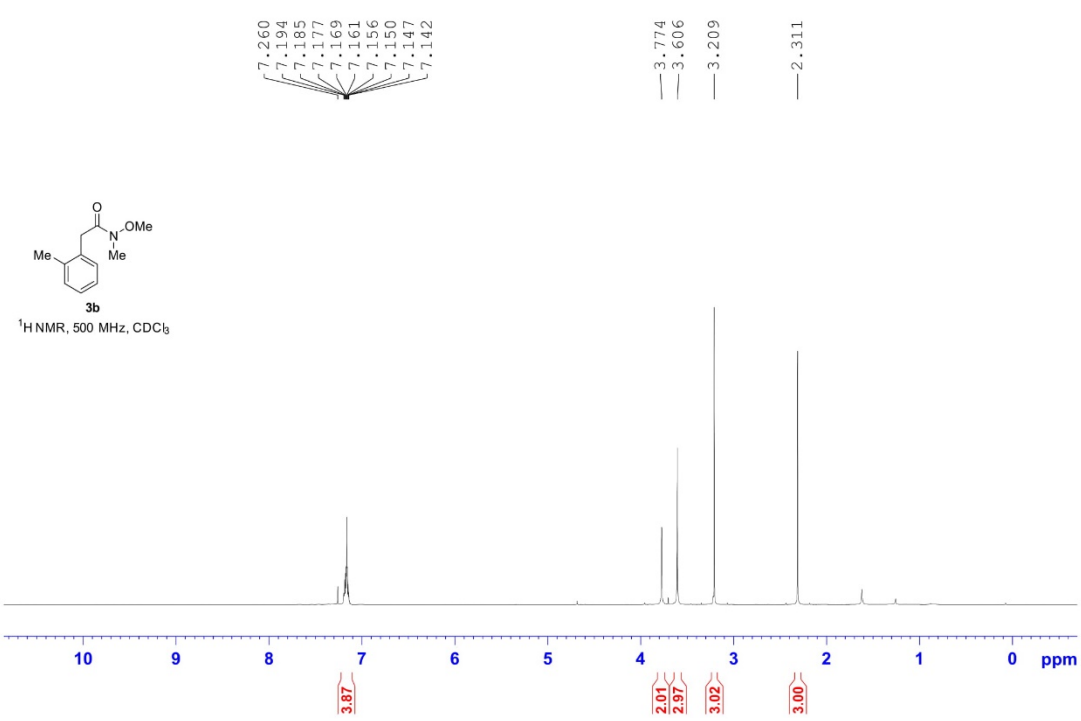

7.922
7.907
7.654
7.639
7.624
7.528
7.513
7.498
3.654
3.361
0.000
OMe
N
Me
O
O
Ph
2x
1H NMR, 500 MHz, CDCl3
10
9
8
7
6
5
4
3
2
1
0
ppm
1.99
1.10
2.14
3.04
3.00


191.02
167.46
134.71
132.95
129.53
129.04
77.40
77.15
76.89
62.22
31.52
OMe
N
Me
O
O
Ph
2x
13C NMR, 125 MHz, CDCl3
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm



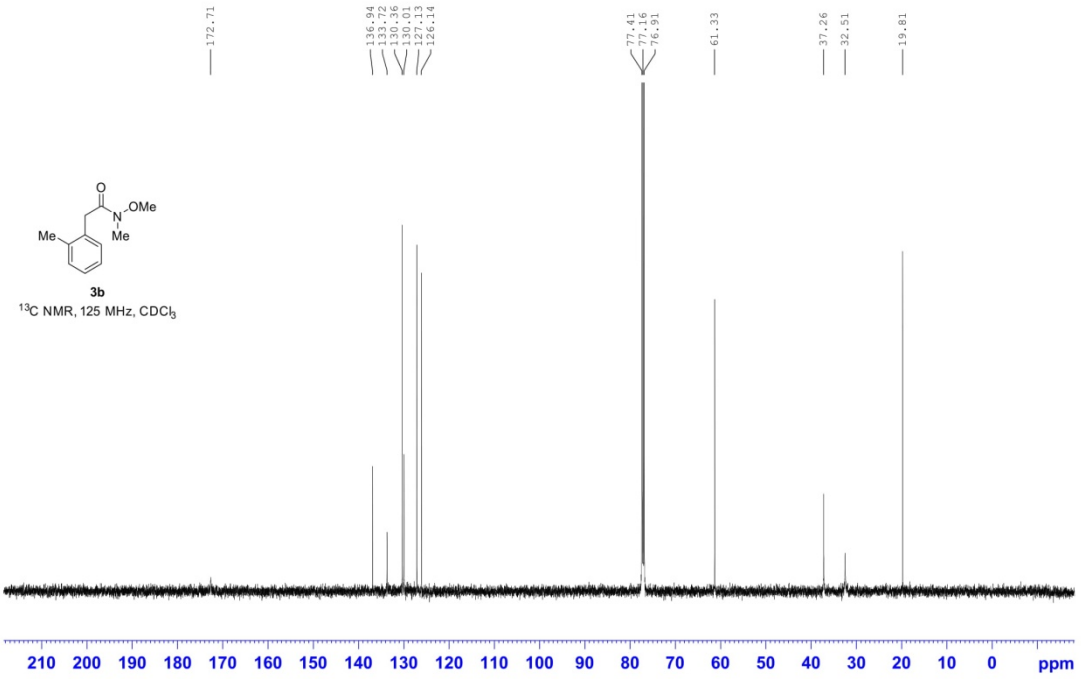
3a

^{1}H NMR, 500 MHz, $CDCl_3$



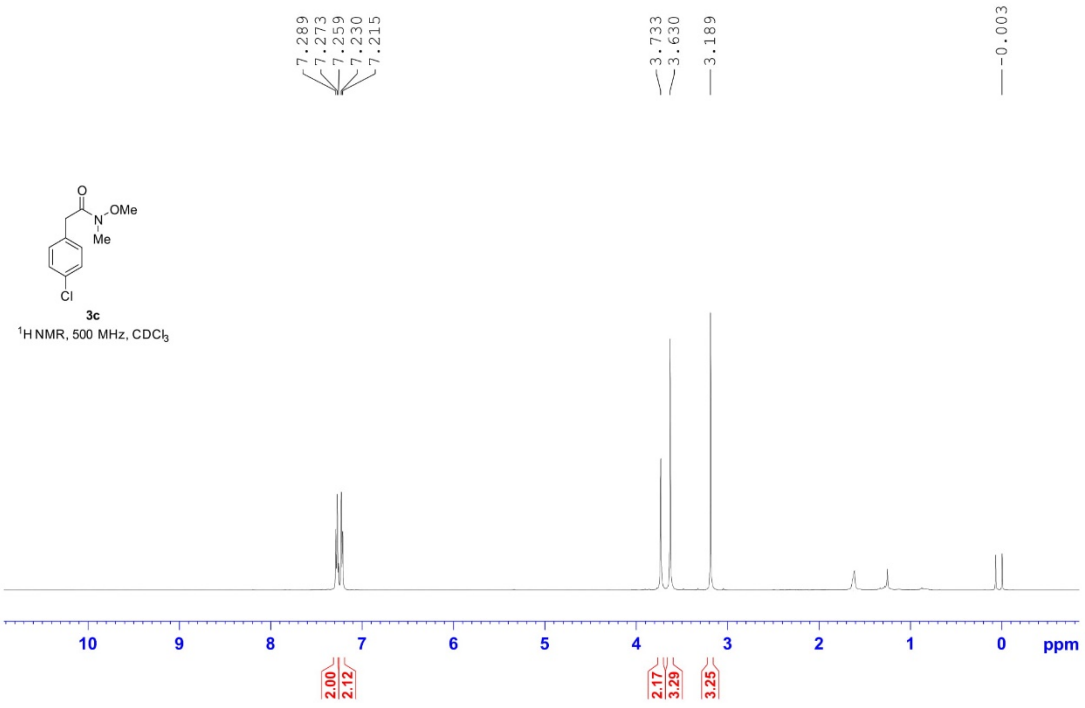
3b

^{1}H NMR, 500 MHz, $CDCl_3$



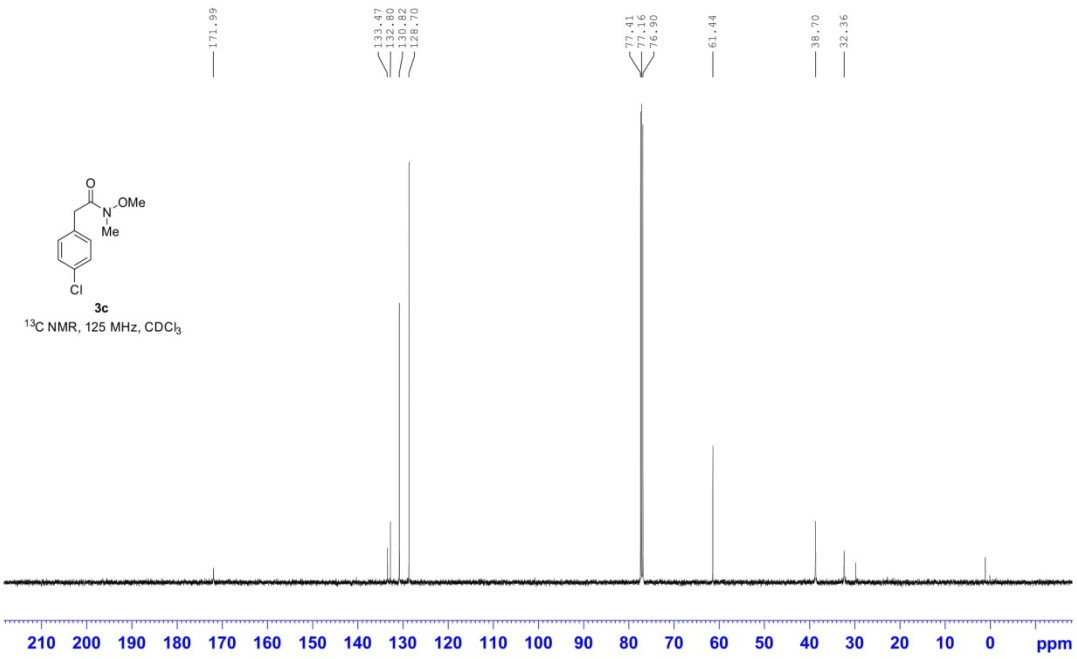
3b

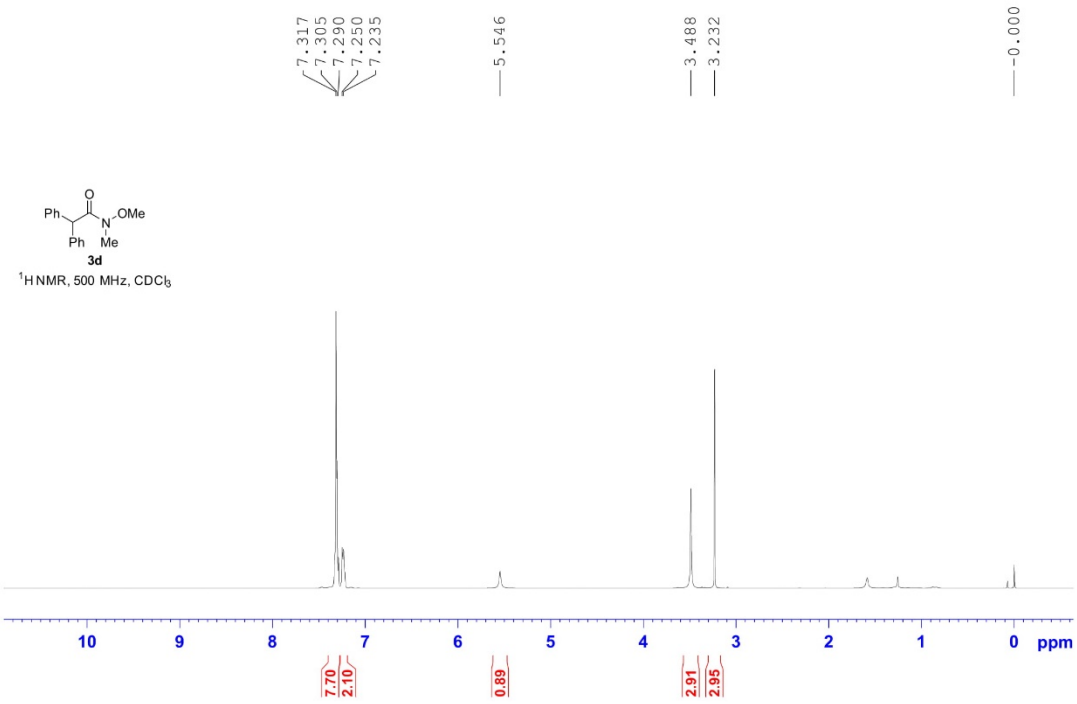
^{13}C NMR, 125 MHz, $CDCl_3$

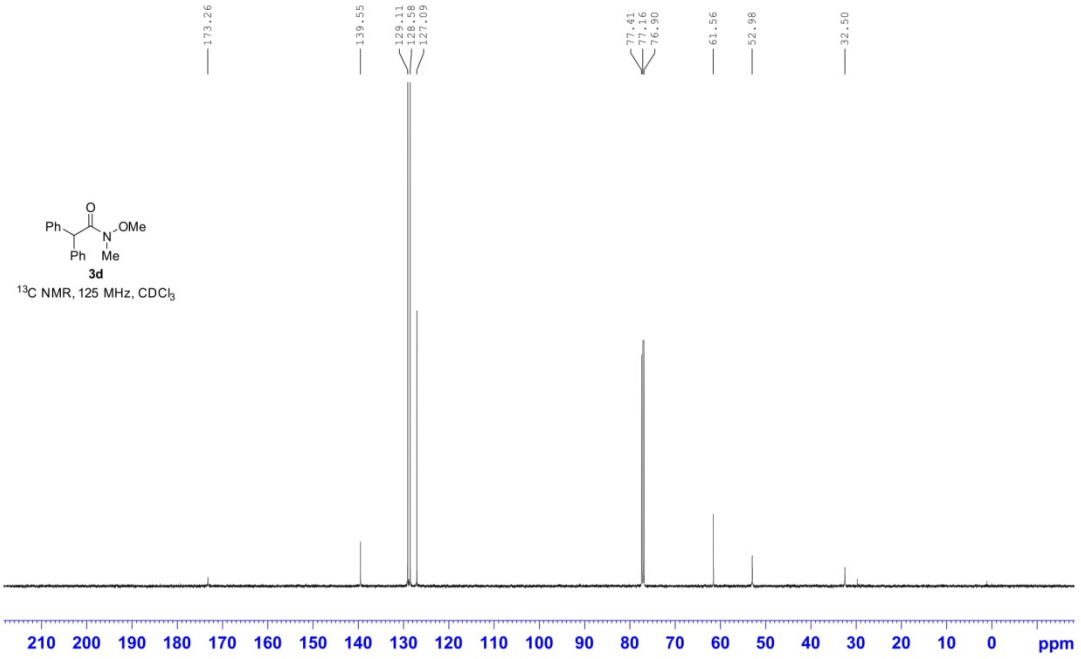


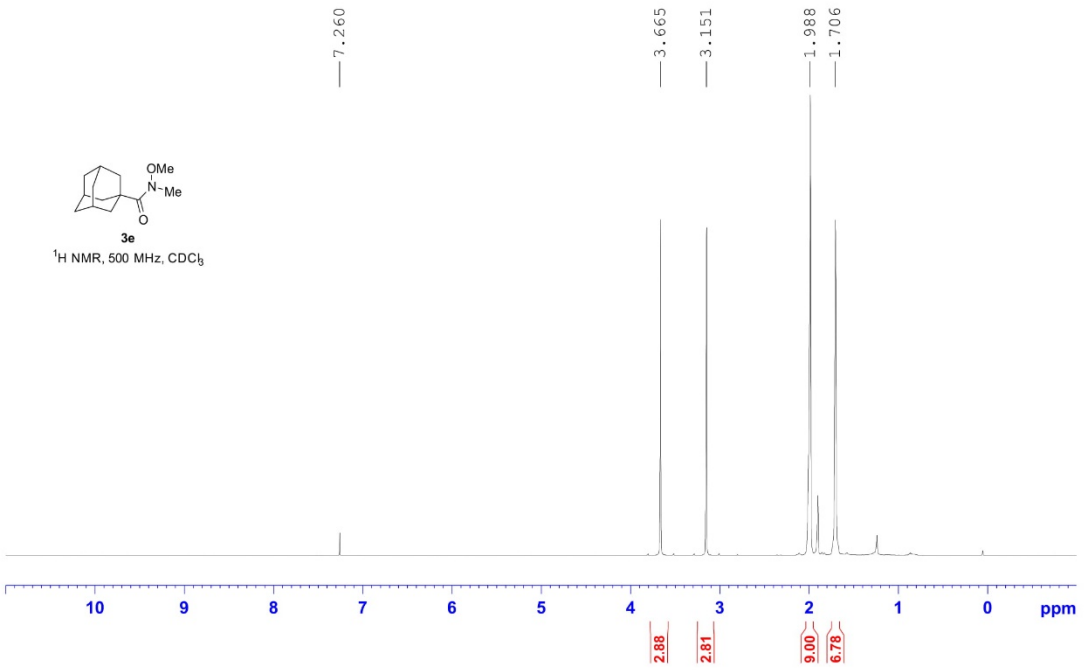
3c

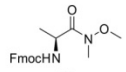
^{1}H NMR, 500 MHz, $CDCl_3$


171.99
133.47
132.80
130.22
128.70
77.41
77.16
76.90
61.44
38.70
32.36
O
N
OMe
Me
Cl
3c
13C NMR, 125 MHz, CDCl3
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


7.317
7.305
7.290
7.250
7.235
5.546
3.488
3.232
0.000
O
Ph
N
OMe
Ph
Me
3d
1H NMR, 500 MHz, CDCl3
10 9 8 7 6 5 4 3 2 1 0 ppm
7.70
2.10
0.89
2.91
2.95

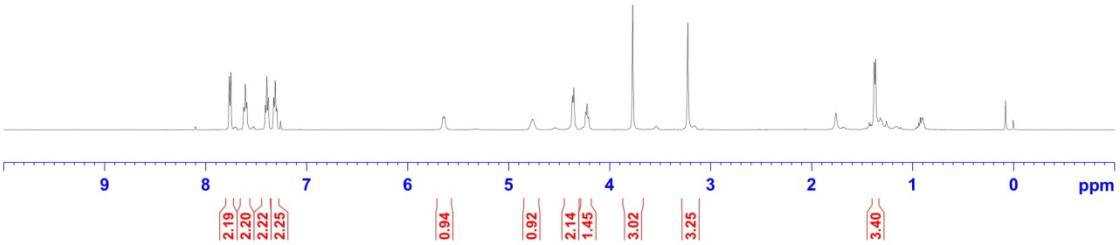

173.26
139.55
129.11
128.58
127.09
77.41
77.16
76.90
61.56
52.98
32.50
Ph
Ph
N
OMe
Me
O
3d
13C NMR, 125 MHz, CDCl3
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

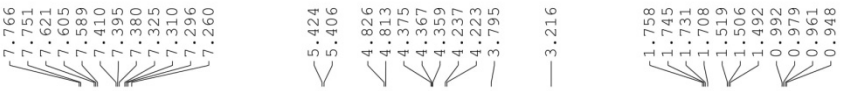

7.260
3.665
3.151
1.988
1.706
OMe
N
Me
O
3e
1H NMR, 500 MHz, CDCl3
10 9 8 7 6 5 4 3 2 1 0 ppm
2.88
2.81
9.00
6.78

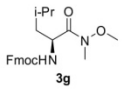


3f

^{1}H NMR, 500 MHz, $CDCl_3$

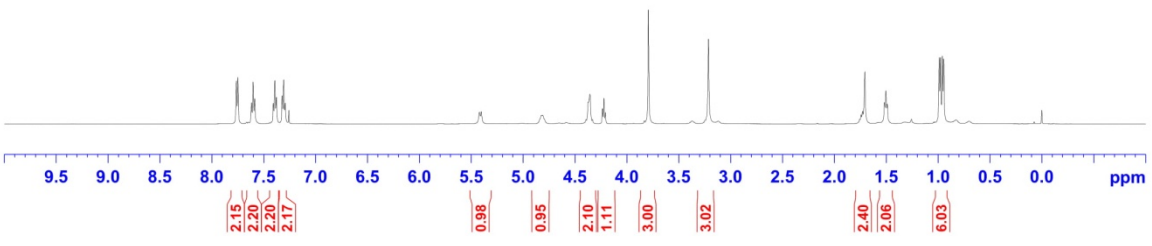


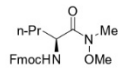




3g

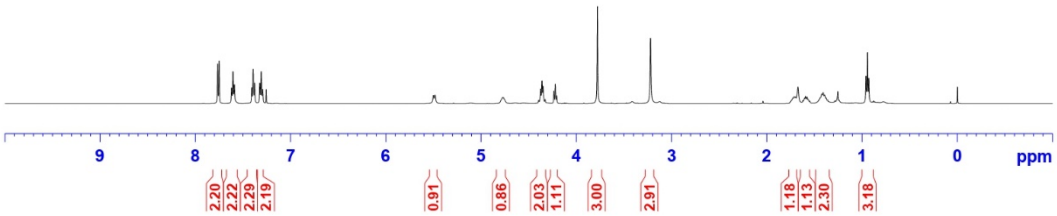
^{1}H NMR, 500 MHz, $CDCl_3$

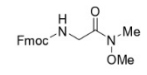




3h

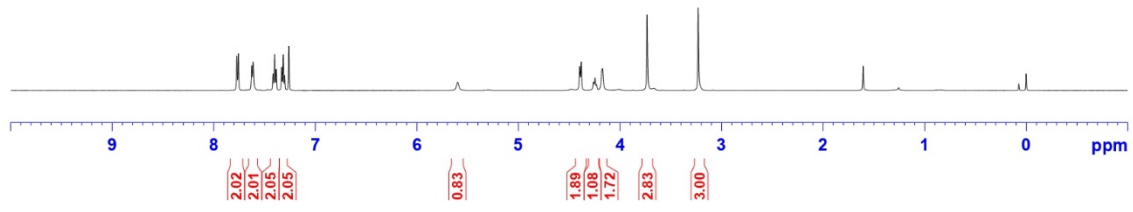
^{1}H NMR, 500 MHz, $CDCl_3$

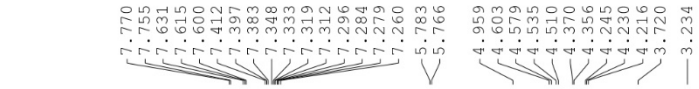


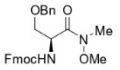


3i

^{1}H NMR, 500 MHz, $CDCl_3$

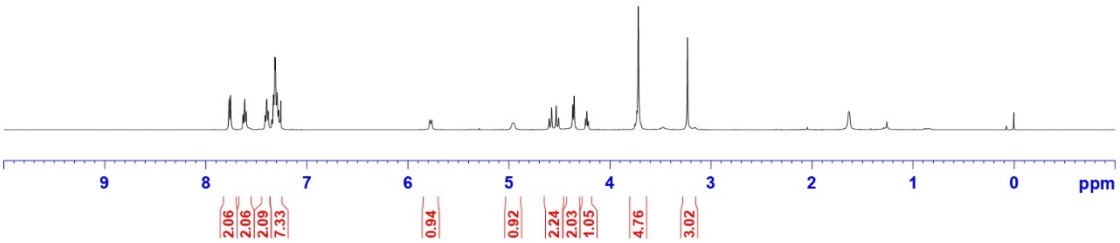


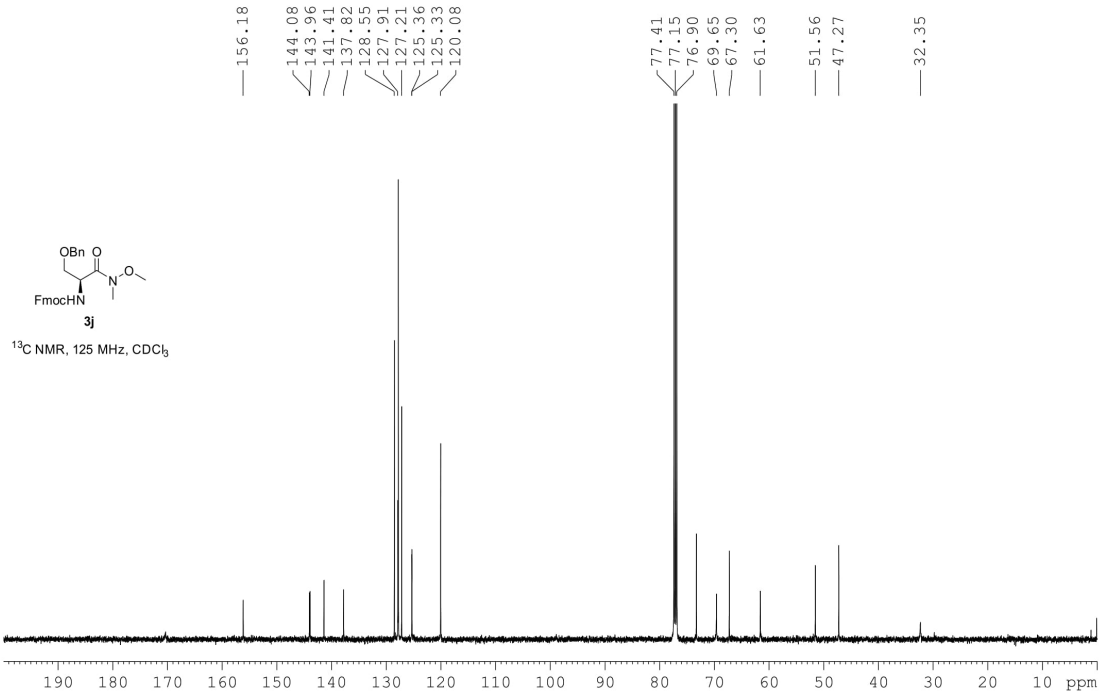




3j

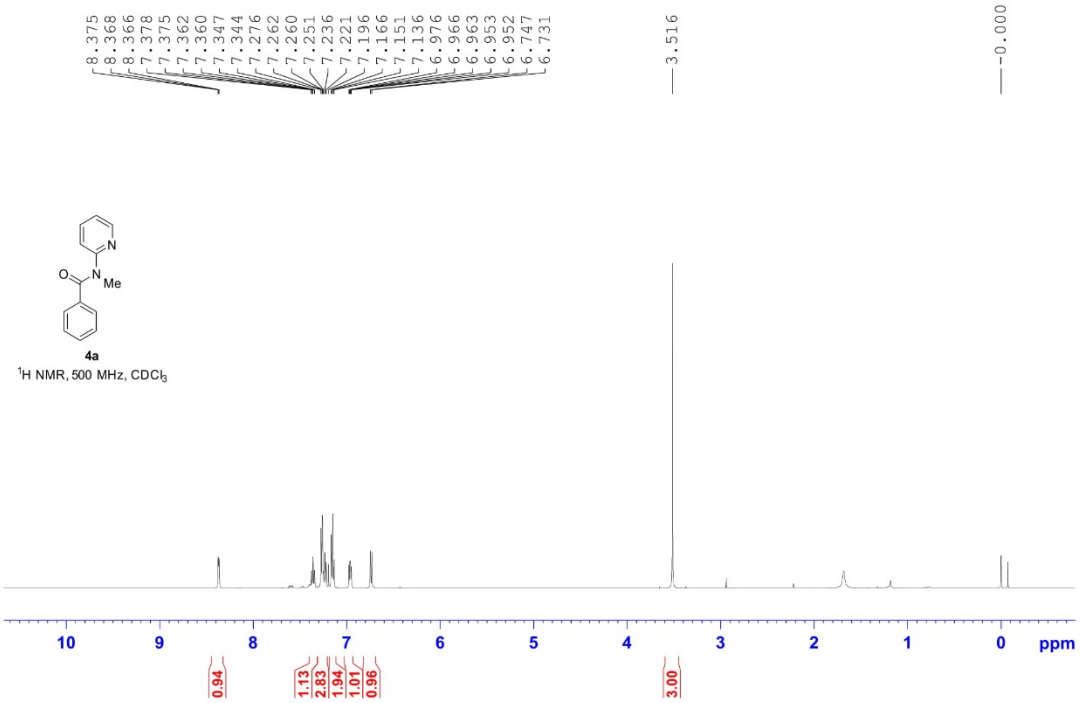
^{1}H NMR, 500 MHz, $CDCl_3$





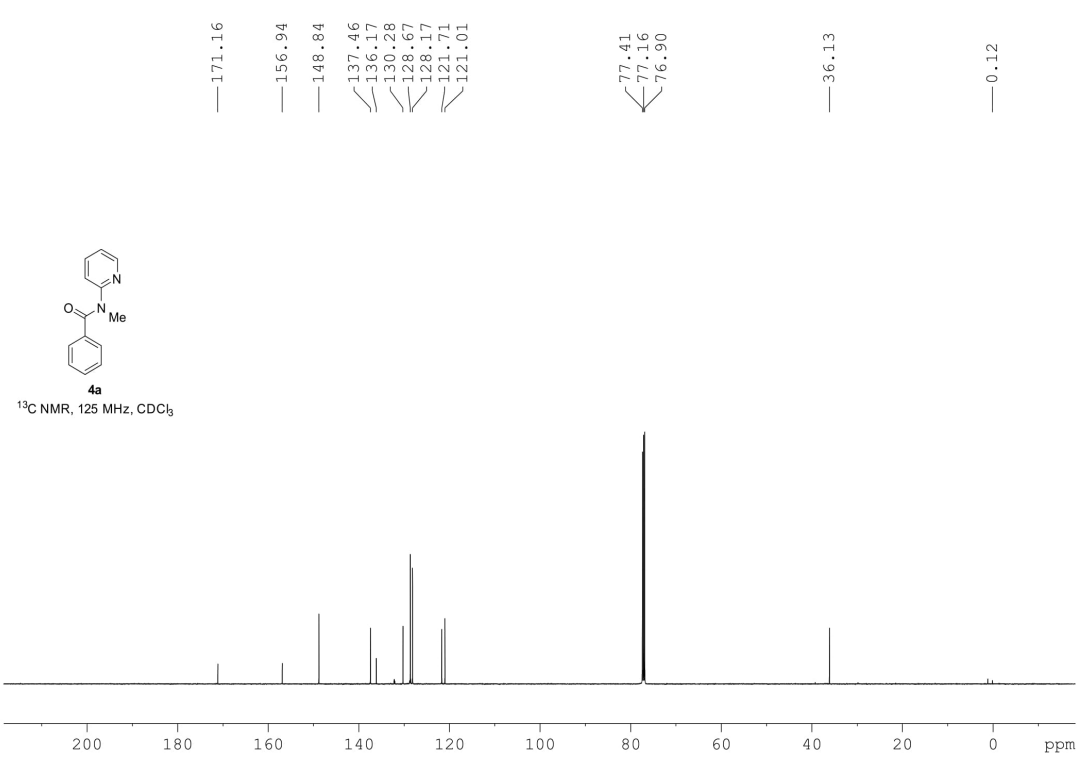
3j

^{13}C NMR, 125 MHz, $CDCl_3$



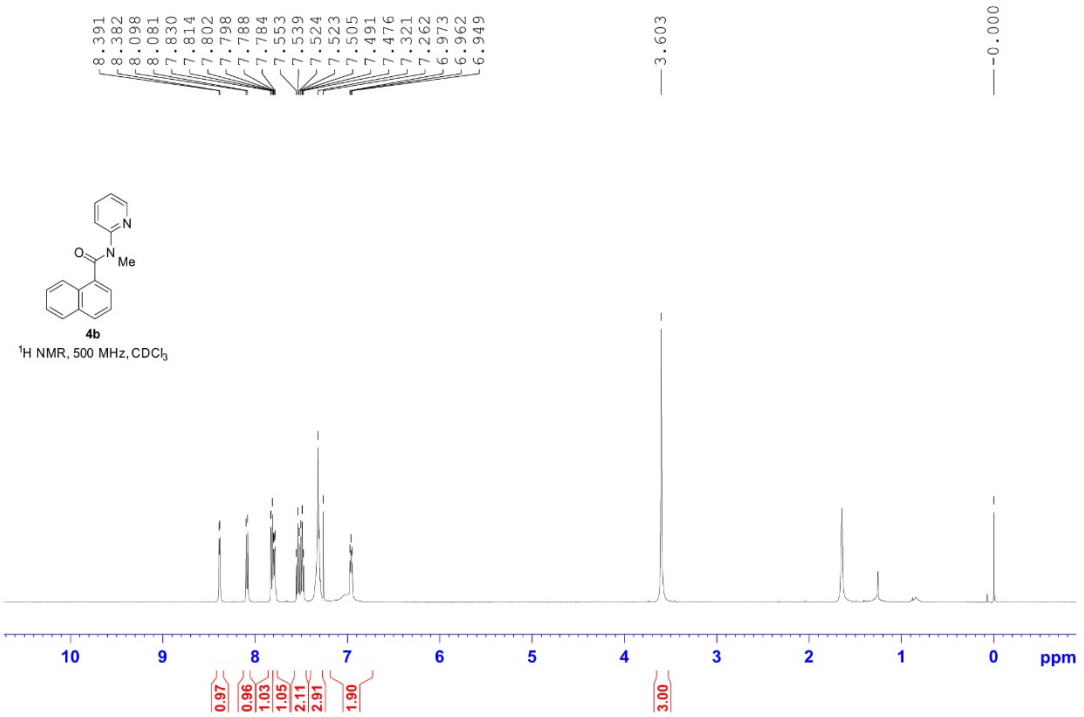
4a

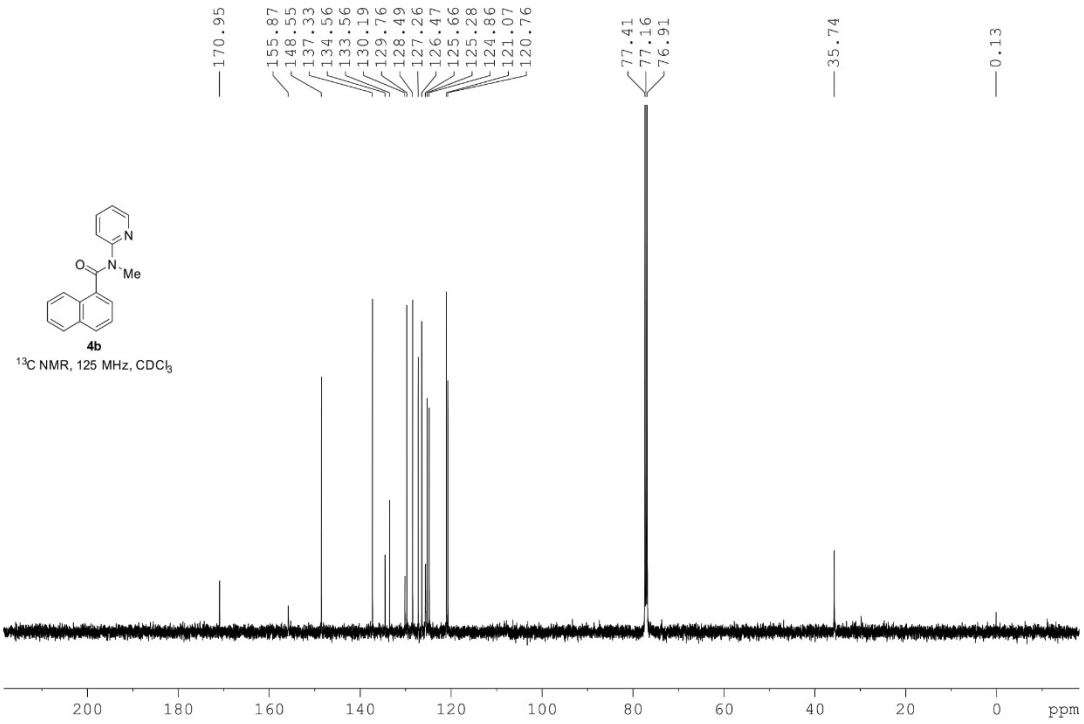
^{1}H NMR, 500 MHz, $CDCl_3$

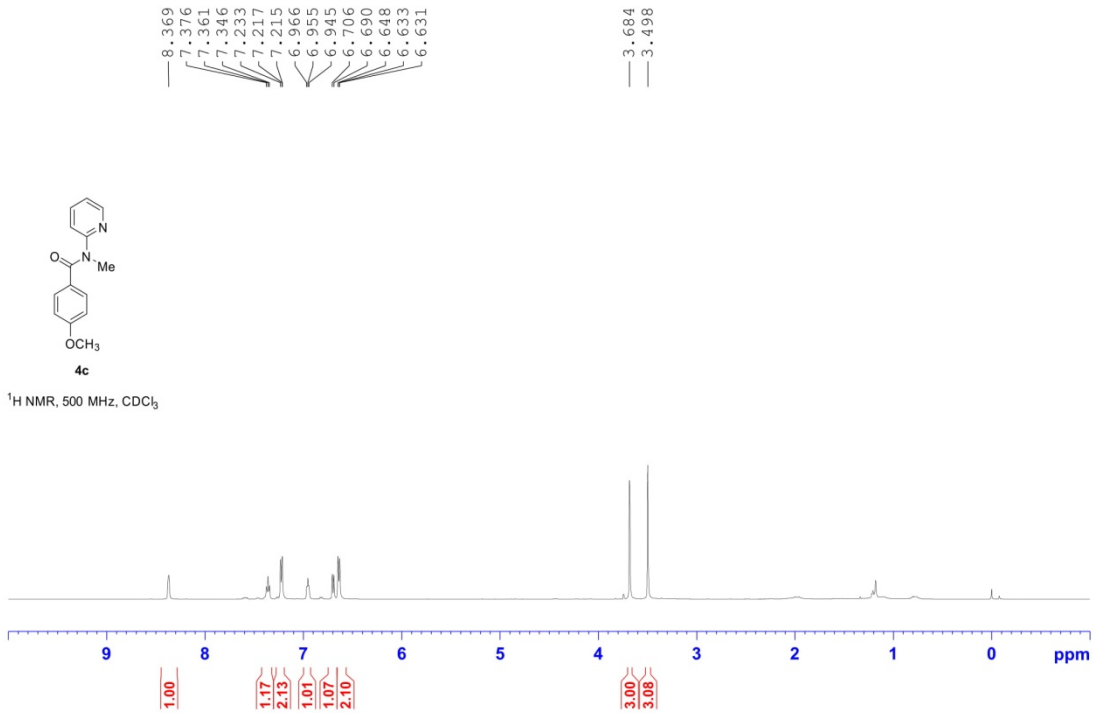


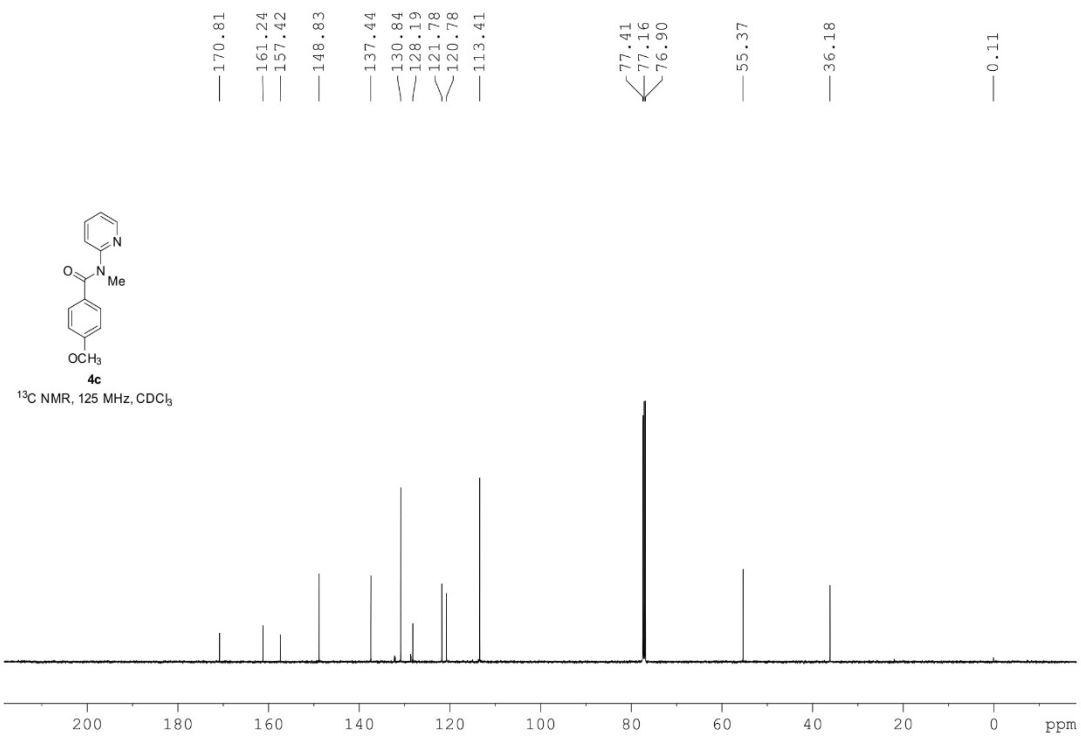
4a

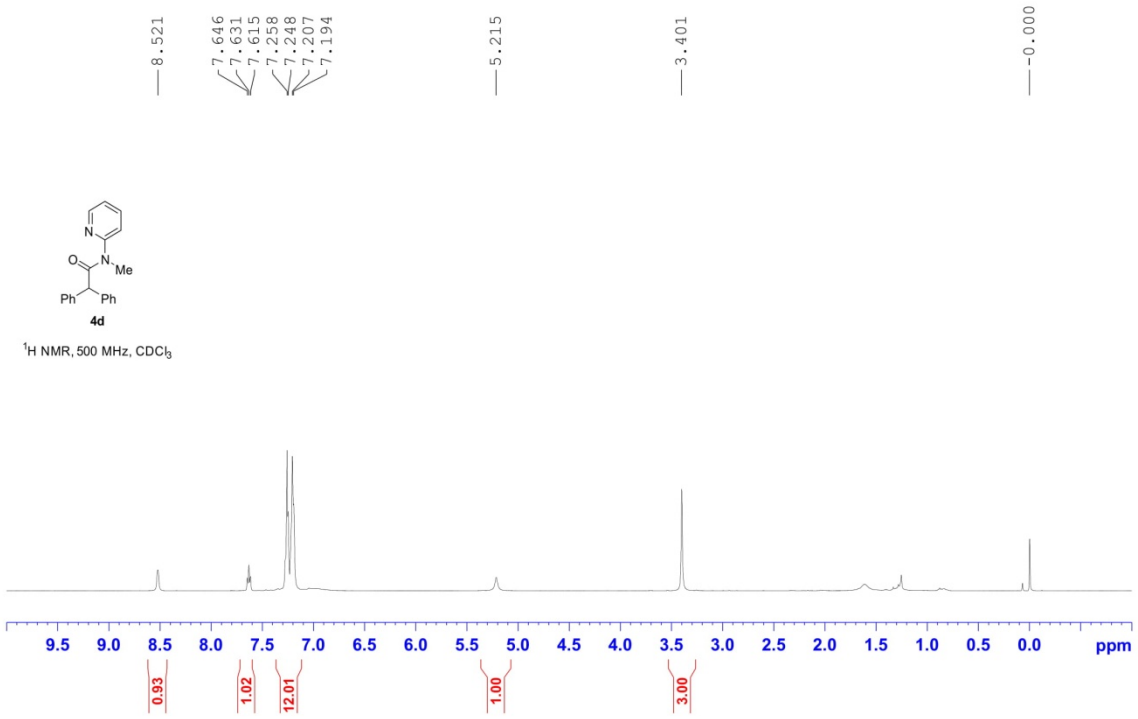
^{13}C NMR, 125 MHz, $CDCl_3$

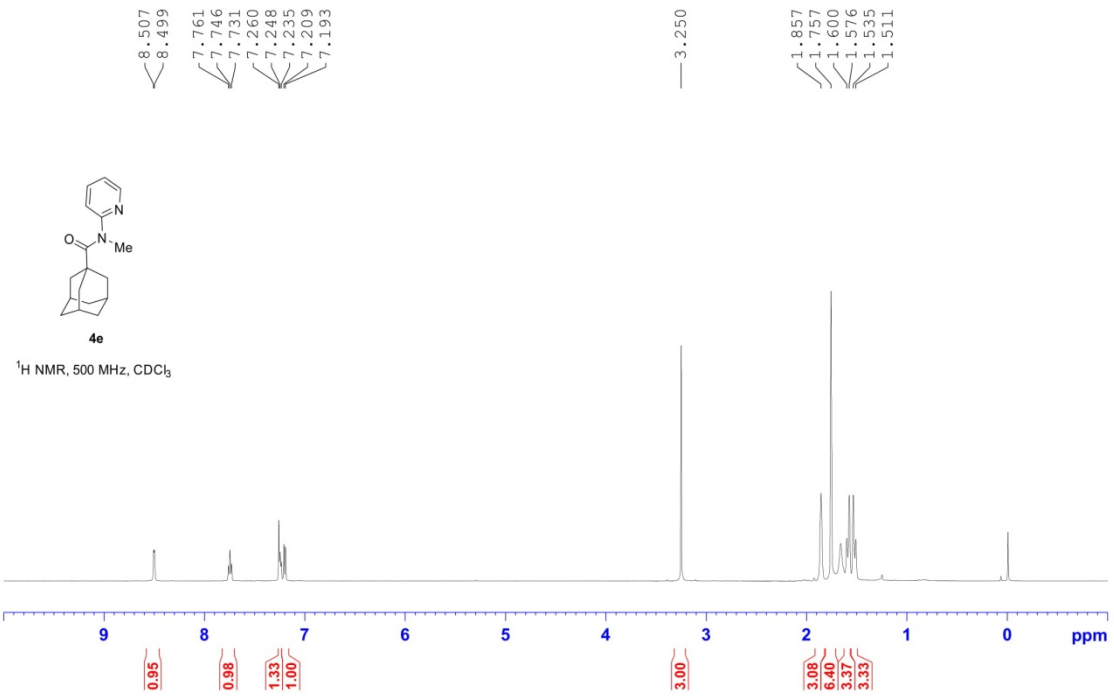

8.391
8.382
8.098
8.081
7.830
7.814
7.802
7.798
7.788
7.784
7.553
7.539
7.524
7.523
7.505
7.491
7.476
7.321
7.262
6.973
6.962
6.949
3.603
0.000
N
O
N
Me
4b
1H NMR, 500 MHz, CDCl3
10
9
8
7
6
5
4
3
2
1
0
ppm
0.97
0.96
1.03
1.05
2.11
2.91
1.90
3.00

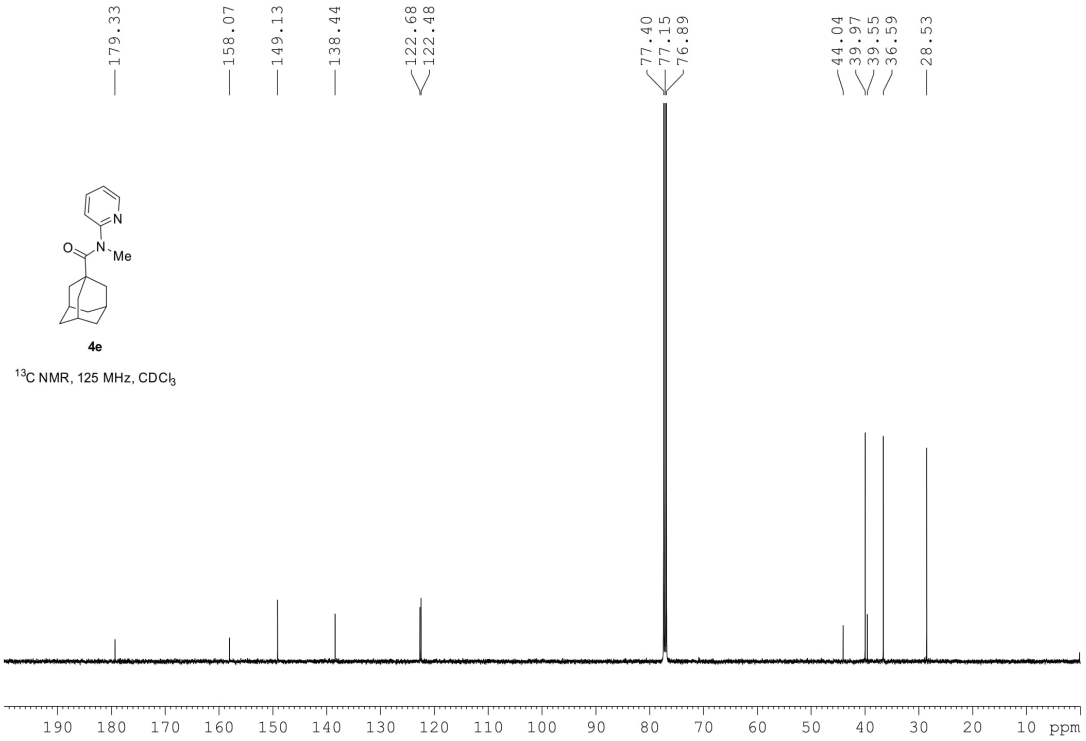

170.95
155.87
148.55
137.33
134.56
133.56
130.19
129.76
128.49
127.26
126.47
125.66
125.28
124.86
121.07
120.76
77.41
77.16
76.91
35.74
0.13
N
O
N
Me
4b
13C NMR, 125 MHz, CDCl3
200
180
160
140
120
100
80
60
40
20
0
ppm


8.369
7.376
7.361
7.346
7.233
7.217
7.215
6.966
6.955
6.945
6.706
6.690
6.648
6.633
6.631
3.684
3.498
N
O
N
Me
OCH3
4c
1H NMR, 500 MHz, CDCl3
9
8
7
6
5
4
3
2
1
0
ppm
1.00
1.17
2.13
1.01
1.07
2.10
3.00
3.08


170.81
161.24
157.42
148.83
137.44
130.84
128.19
121.78
120.78
113.41
77.41
77.16
76.90
55.37
36.18
0.11
N
O
N
Me
OCH3
4c
13C NMR, 125 MHz, CDCl3
200
180
160
140
120
100
80
60
40
20
0
ppm

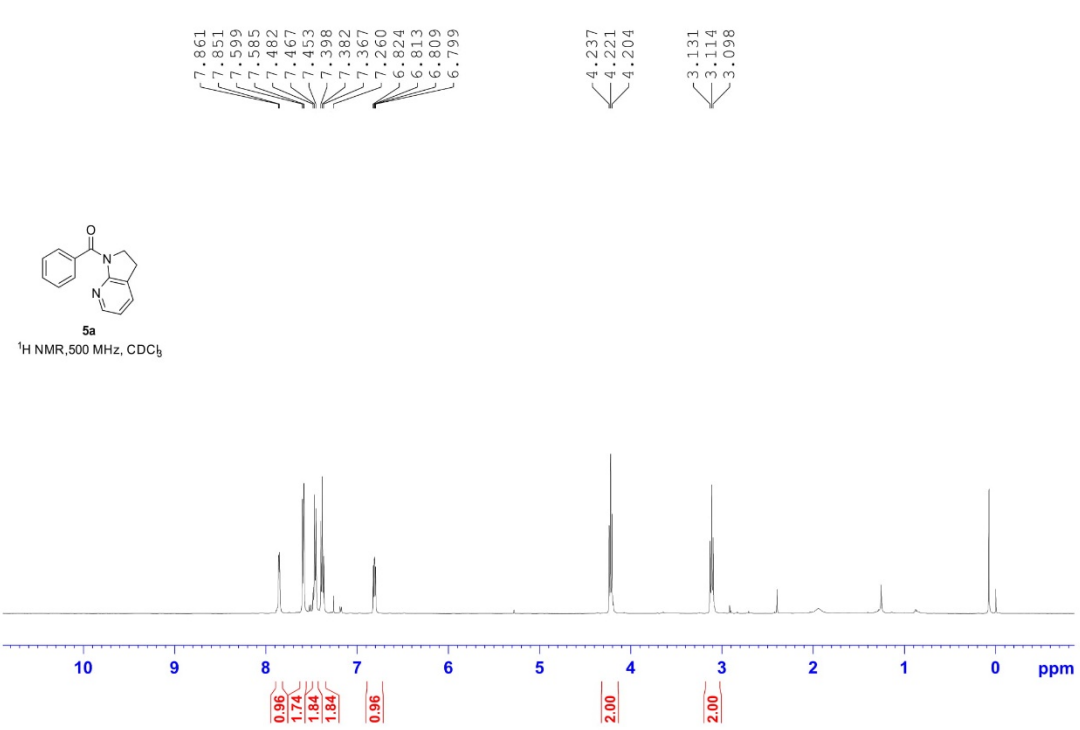

8.521
7.646
7.631
7.615
7.258
7.248
7.207
7.194
5.215
3.401
0.000
N
O
N
Me
Ph
Ph
4d
^{1}H NMR, 500 MHz, CDCl$_3$
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
0.93
1.02
12.01
1.00
3.00


8.507
8.499
7.761
7.746
7.731
7.260
7.248
7.235
7.209
7.193
3.250
1.857
1.757
1.600
1.576
1.535
1.511
N
O
N
Me
4e
^{1}H NMR, 500 MHz, CDCl$_3$
9 8 7 6 5 4 3 2 1 0 ppm
0.95
0.98
1.33
1.00
3.00
3.08
6.40
3.37
3.33



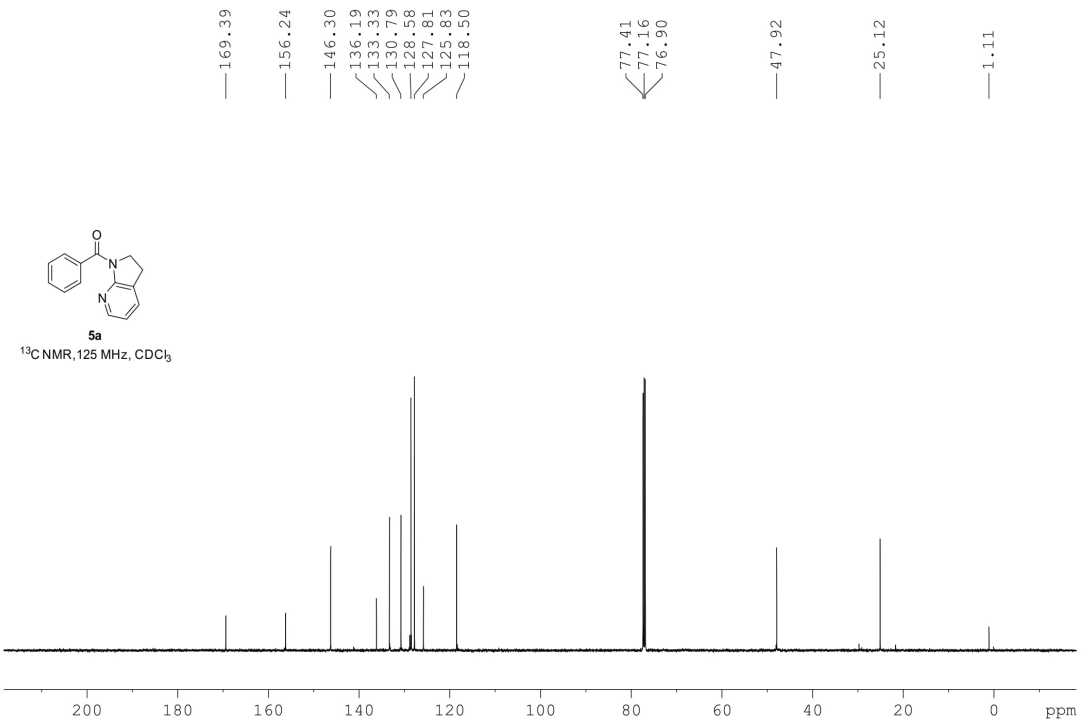
4e

^{13}C NMR, 125 MHz, $CDCl_3$



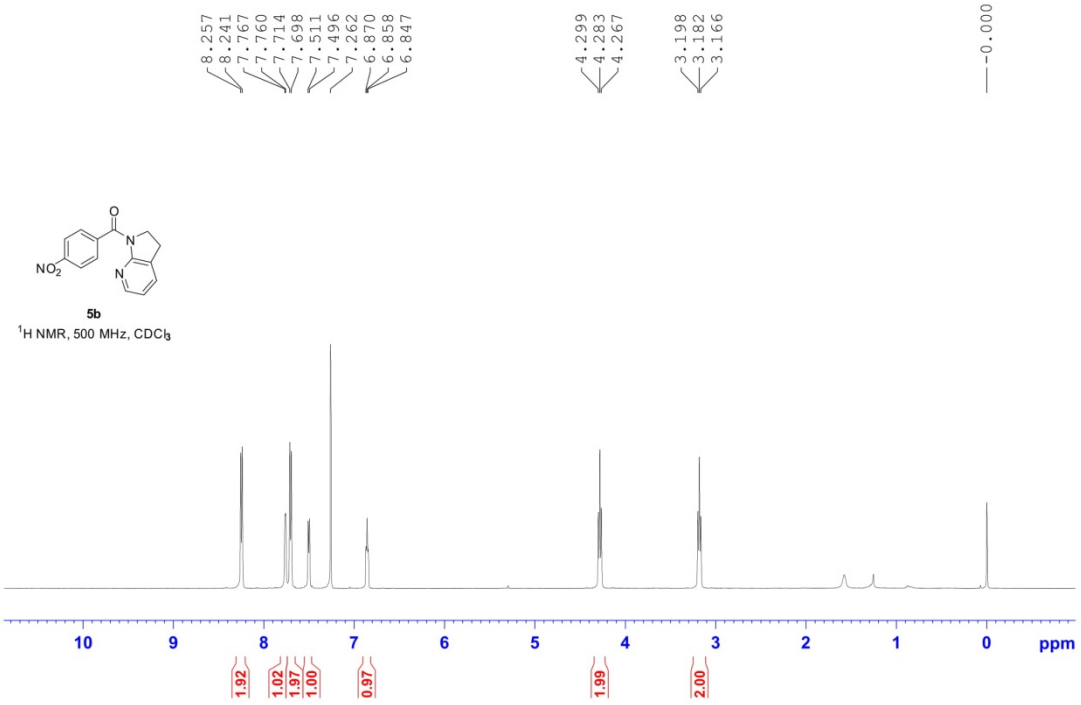
5a

^{1}H NMR,500 MHz, $CDCl_3$



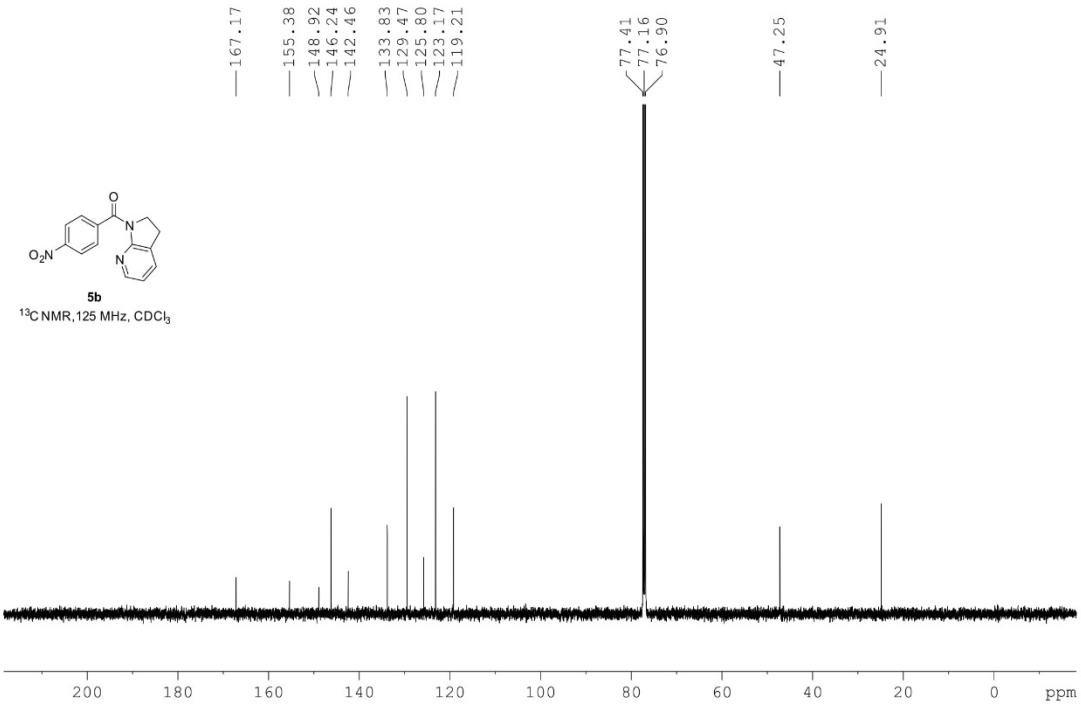
5a

^{13}C NMR, 125 MHz, $CDCl_3$



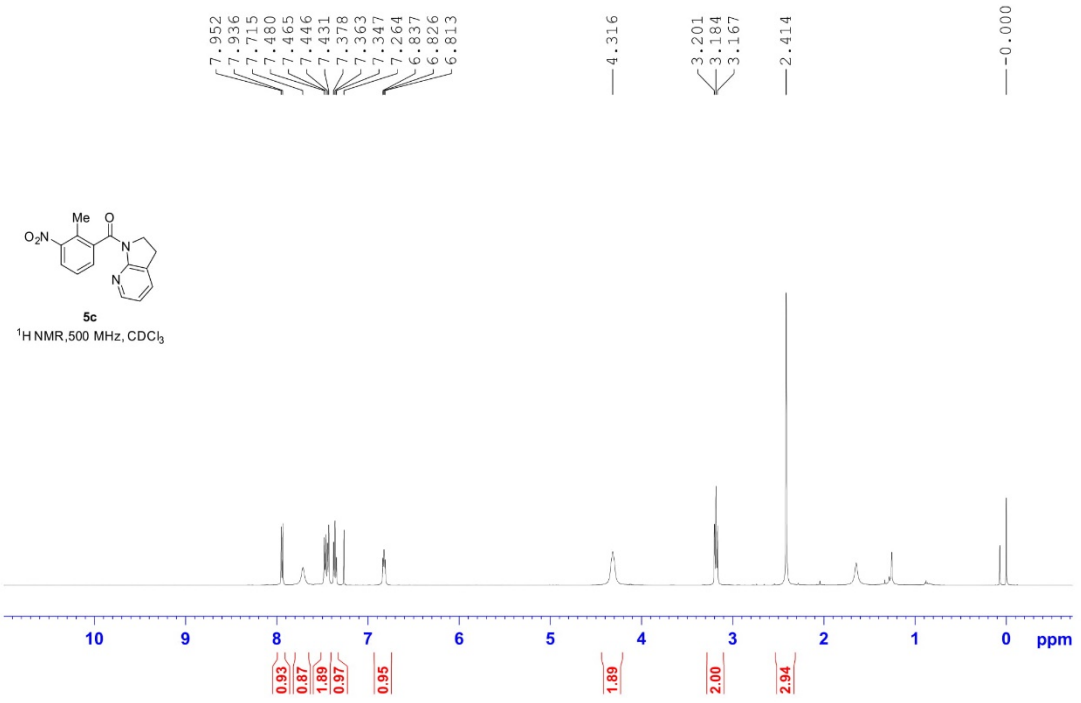
5b

^{1}H NMR, 500 MHz, $CDCl_3$



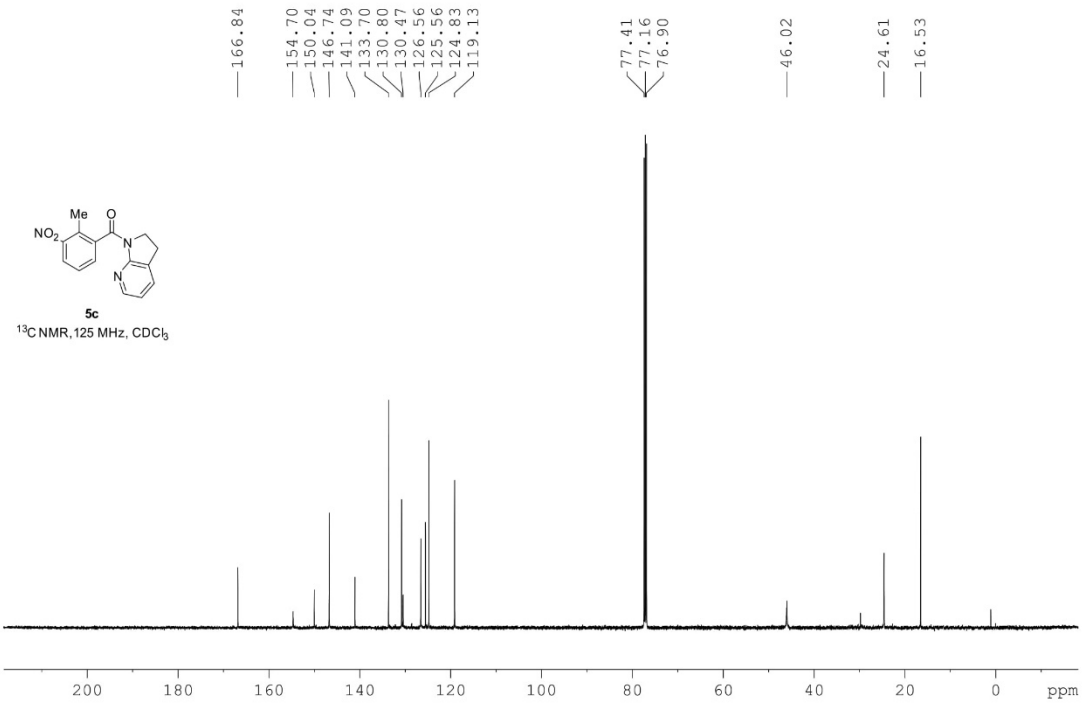
5b

^{13}C NMR,125 MHz, $CDCl_3$



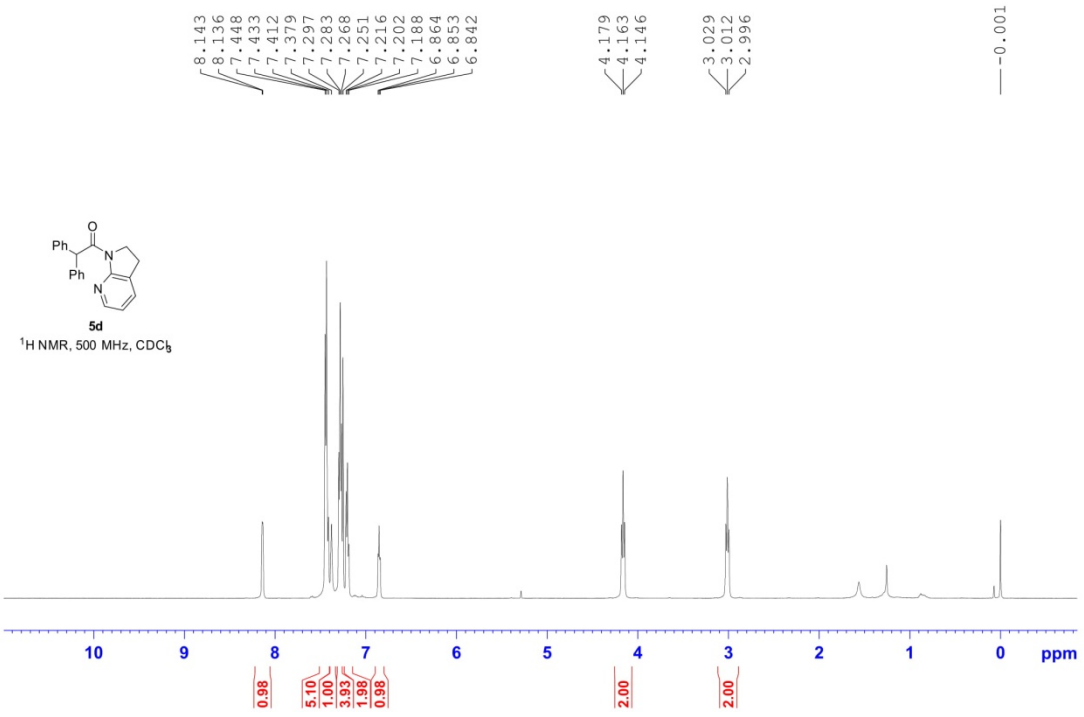
5c

^{1}H NMR,500 MHz, $CDCl_3$



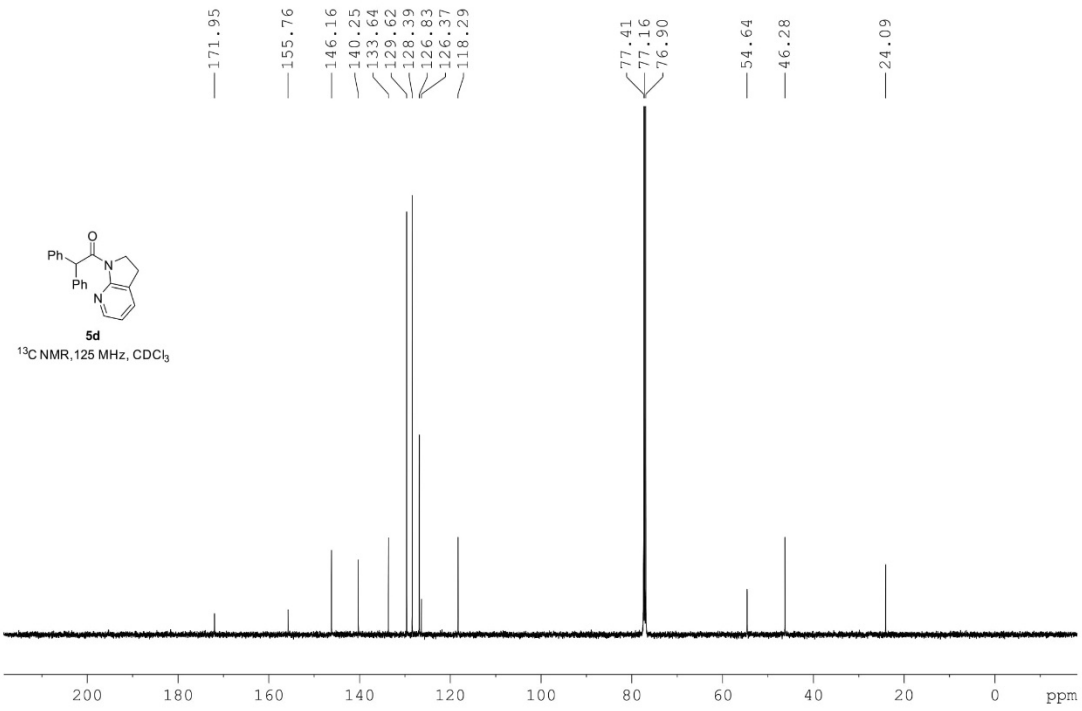
5c

^{13}C NMR, 125 MHz, $CDCl_3$



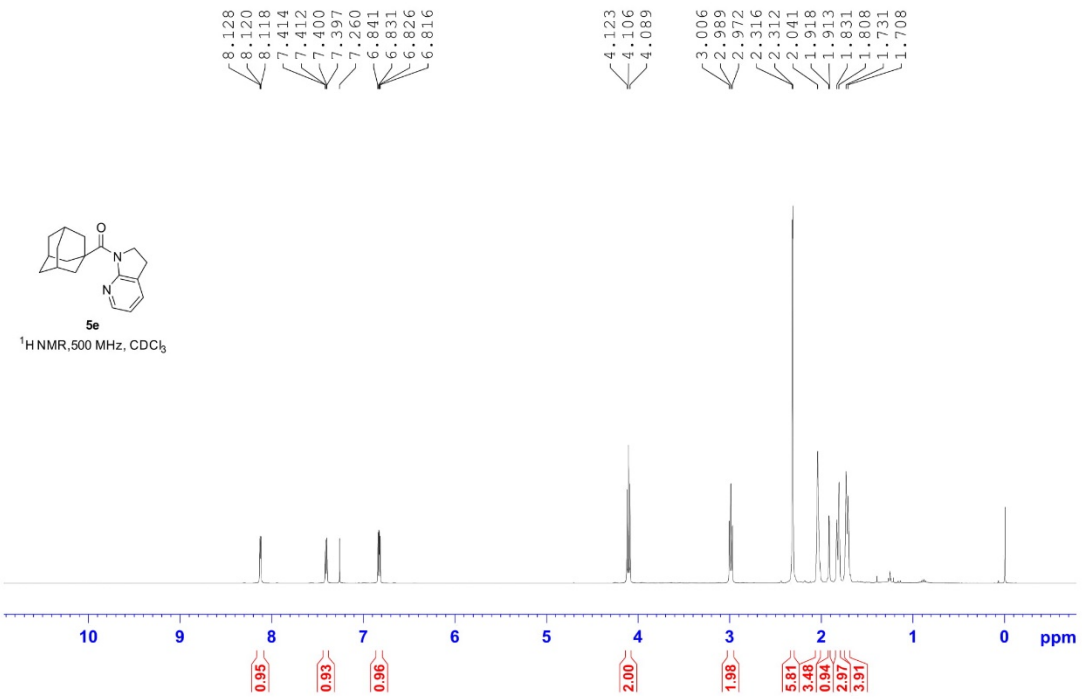
5d

^{1}H NMR, 500 MHz, $CDCl_3$



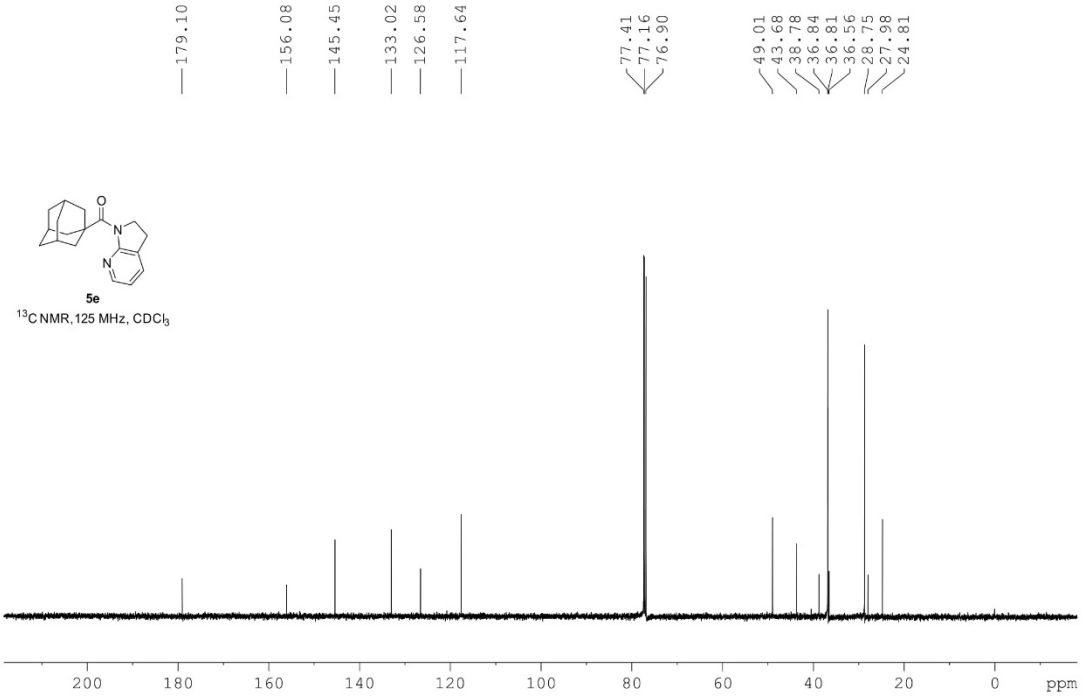
5d

^{13}C NMR,125 MHz, $CDCl_3$



5e

^{1}H NMR,500 MHz, $CDCl_3$



5e

^{13}C NMR, 125 MHz, $CDCl_3$