

Supporting Information

Palladium-Catalyzed *Ortho*-Selective C–H Oxidative Carbonylation of *N*-Substituted Anilines with CO and Primary Amines for the Synthesis of *o*-Aminobenzamides

Xiaopeng Zhang,* Shuxiang Dong, Xueli Niu, Zhengwei Li, Xuesen Fan, and Guisheng Zhang*

†Collaborative Innovation Center of Henan Province for Green Manufacturing of Fine Chemicals, Key Laboratory of Green Chemical Media and Reactions, Ministry of Education, School of Chemistry and Chemical Engineering, Henan Normal University, Xinxiang 453007, P. R. China

E-mail: zhangxiaopengv@sina.com; zgs6668@yahoo.com

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General Information

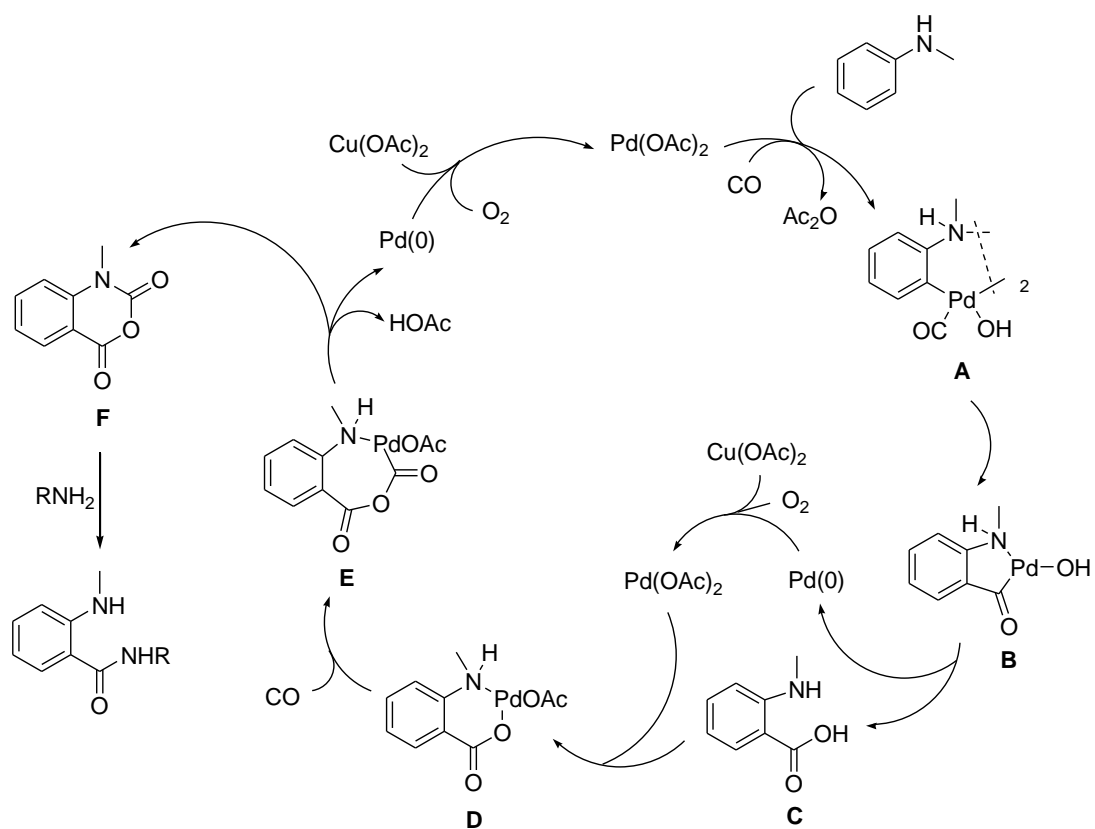
All reactions were carried out in a 50 mL round-bottom flask. Copper acetate was dried by heating at 110 °C to a constant weight under reduced pressure. Unless otherwise stated, all reagents and materials were obtained from commercial suppliers and used without further purification. The conversion of starting materials was monitored by thin layer chromatography (TLC) using silica gel plates (silica gel 60 F254 0.25 mm) and components were visualized by observation under UV light. Flash column chromatography was performed with 200-300 mesh silica gel. All new compounds were characterized by ^1H NMR, ^{13}C NMR and High resolution mass spectra (HRMS). The known compounds were characterized by ^1H NMR and ^{13}C NMR. ^1H and ^{13}C NMR data were recorded with AVANCE 400 Spectrometer and AVANCE III HD 600 Spectrometer with tetramethylsilane (TMS) as an internal standard. All chemical shifts (δ) were reported in ppm and were referenced to residual solvent or TMS peaks. HRMS were obtained by using a MicrOTOF mass spectrometer.

General Procedure for the Synthesis of *o*-Aminobenzamides

N-Substitutedaniline (1.5 mmol), RNH_2 (3.0 mmol), $\text{Pd}(\text{OAc})_2$ (0.075 mmol, 16.8 mg), $\text{Cu}(\text{OAc})_2$ (2.3 mmol, 417 mg), KI (0.3 mmol, 49.8 mg), toluene (4 mL), CH_3CN (4 mL) and AcOH (4.5 mmol, 270 mg) were charged in a 50 mL round-bottom flask equipped with stir bar. Then, the flask was evacuated and back-filled with CO/O_2 (5:1) (3-times, balloon) and stirred at 70 °C for 18 h. Then the mixture was cooled to room temperature and vented to discharge the excess balloon gas. Subsequently, the reaction was quenched with H_2O (50 mL) and extracted with EtOAc (3×10 mL). The combined organic layers were dried over anhydrous Na_2SO_4 and then evaporated in vacuo. The residue was purified by column chromatography on silica gel to afford the corresponding *o*-aminobenzamide **3** with petroleum ether/ethyl acetate as the eluent.

Mechanism Investigation

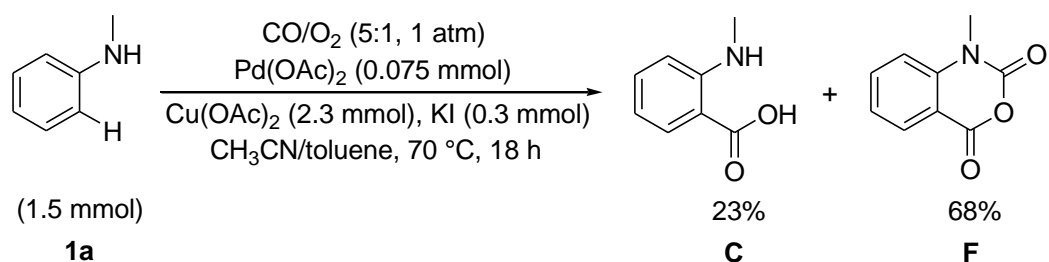
1) Proposed Mechanism



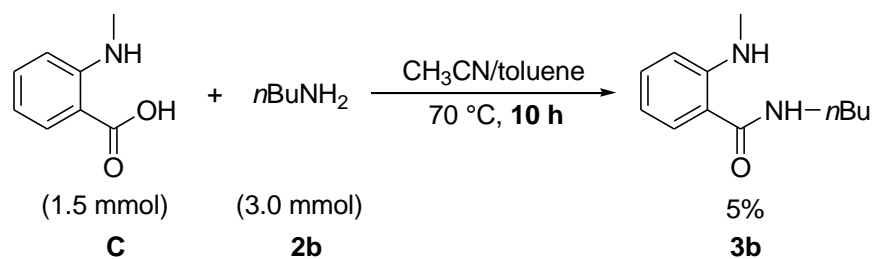
Reference: Guan, Z. H.; Chen, M.; Ren, Z. H., *J. Am. Chem. Soc.* **2012**, *134*, 17490–17493.

2) Control Experiments

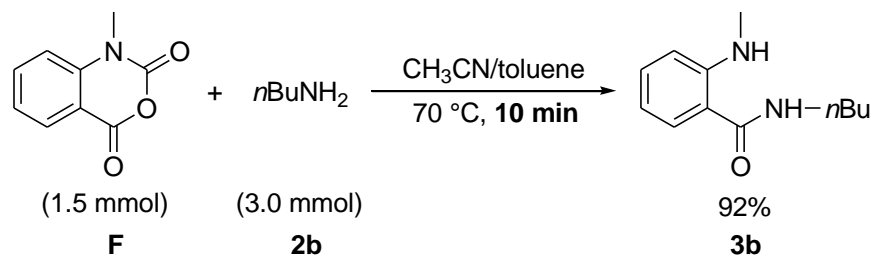
(1) Palladium-Catalyzed *Ortho*-Selective C–H Carbonylation of *N*-Methylaniline



(2) Transformation of *N*-Methylantranilic Acid (**C**) to *N*-Butyl-2-(methylamino)benzamide (**3b**)

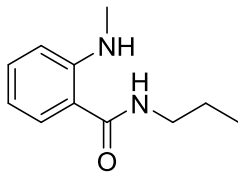


(3) Transformation of Isatoic Anhydride (**F**) to *N*-Butyl-2-(methylamino)benzamide (**3b**)



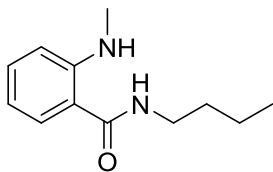
Characterization of Synthesized Compounds

2-(methylamino)-*N*-propylbenzamide (3a)



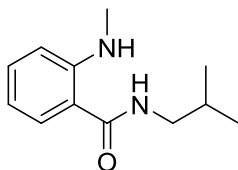
Yield: 87% (250.9 mg), colorless liquid; CAS registry number: 116465-89-5; $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.42 (s, 1H), 7.35 – 7.29 (m, 2H), 6.66 (d, $J = 8.1$ Hz, 1H), 6.58 (t, $J = 8.0$ Hz, 1H), 6.04 (s, 1H), 3.37 (dd, $J = 13.0, 7.1$ Hz, 2H), 2.85 (d, $J = 4.7$ Hz, 3H), 1.61 (dd, $J = 8.2, 6.2$ Hz, 2H), 0.98 (t, $J = 7.4$ Hz, 3H); $^{13}\text{C NMR}$ (151 MHz, CDCl_3) δ 169.9, 150.5, 132.7, 127.0, 115.5, 114.4, 111.1, 41.4, 29.7, 23.0, 11.5.

N-butyl-2-(methylamino)benzamide (3b)



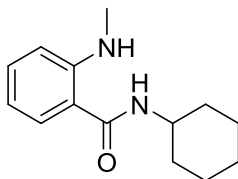
Yield: 78% (241.4 mg), colorless liquid; CAS registry number: 53693-72-4; $^1\text{H NMR}$ (600 MHz, CDCl_3) δ 7.41 (s, 1H), 7.33 – 7.25 (m, 2H), 6.63 (d, $J = 8.3$ Hz, 1H), 6.57 – 6.50 (m, 1H), 6.27 (s, 1H), 3.45 – 3.23 (m, 2H), 2.81 (d, $J = 6.2$ Hz, 3H), 1.58 – 1.49 (m, 2H), 1.42 – 1.32 (m, 2H), 0.92 (t, $J = 7.3$ Hz, 3H); $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 169.9, 150.5, 132.7, 127.0, 115.5, 114.4, 111.1, 39.4, 31.8, 29.7, 20.2, 13.8.

N-isobutyl-2-(methylamino)benzamide (3c)



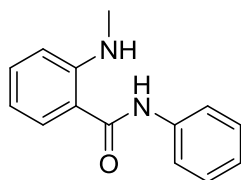
Yield: 69% (213.5 mg), colorless liquid; CAS registry number: 348611-91-6; $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.33 (s, 1H), 7.28 – 7.22 (m, 2H), 6.60 (d, $J = 8.0$ Hz, 1H), 6.52 (t, $J = 7.0$ Hz, 1H), 6.02 (s, 1H), 3.20 – 3.11 (m, 2H), 2.78 (s, 3H), 1.88 – 1.73 (m, 1H), 0.91 (d, $J = 6.7$ Hz, 6H); $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 169.9, 150.5, 132.7, 127.0, 115.6, 114.4, 111.1, 47.0, 29.7, 28.7, 20.2.

N-cyclohexyl-2-(methylamino)benzamide (3e)



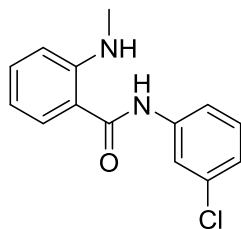
Yield: 70% (243.9 mg), white solid, mp. 164-168 °C; CAS registry number: 348612-65-7; $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.40 (s, 1H), 7.35 – 7.27 (m, 2H), 6.65 (d, $J = 8.2$ Hz, 1H), 6.58 (t, $J = 8.0$ Hz, 1H), 5.90 (s, 1H), 3.90 (tdt, $J = 11.6, 7.9, 3.9$ Hz, 1H), 2.85 (d, $J = 5.1$ Hz, 3H), 2.00 (dd, $J = 12.4, 3.4$ Hz, 2H), 1.81 – 1.69 (m, 2H), 1.69 – 1.58 (m, 2H), 1.42 (dd, $J = 25.2, 12.0$ Hz, 2H), 1.31 – 1.11 (m, 3H); $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 169.0, 150.5, 132.6, 127.0, 115.7, 114.4, 111.0, 48.3, 33.3, 29.7, 25.6, 24.9.

2-(methylamino)-*N*-phenylbenzamide (3f)



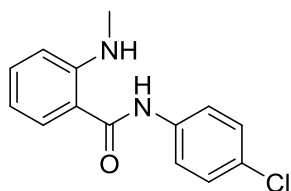
Yield: 89% (302.1 mg), white solid, mp. 123-124 °C (Lit.¹ 121-122 °C); CAS registry number: 21258-59-3; ¹H NMR (400 MHz, CDCl₃) δ 7.73 (s, 1H), 7.55 (d, *J* = 7.6 Hz, 2H), 7.48 (d, *J* = 7.8 Hz, 1H), 7.41 – 7.34 (m, 4H), 7.15 (t, *J* = 7.4 Hz, 1H), 6.71 (d, *J* = 8.4 Hz, 1H), 6.65 (t, *J* = 7.9 Hz, 1H), 2.88 (d, *J* = 5.1 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 168.2, 150.9, 137.9, 133.4, 129.1, 127.2, 124.5, 120.5, 115.1, 114.7, 111.4, 29.7.

N-(3-chlorophenyl)-2-(methylamino)benzamide (3h)



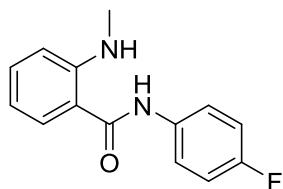
Yield: 60% (234.6 mg), white solid, mp. 119-122 °C; CAS registry number: 348612-38-4; ¹H NMR (400 MHz, CDCl₃) δ 7.74 – 7.67 (m, 2H), 7.45 (d, *J* = 7.9 Hz, 1H), 7.41 – 7.38 (m, 3H), 7.31 – 7.23 (m, 1H), 7.11 (d, *J* = 7.9 Hz, 1H), 6.72 (d, *J* = 8.4 Hz, 1H), 6.65 (t, *J* = 7.9 Hz, 1H), 2.88 (d, *J* = 5.1 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 168.1, 151.0, 139.1, 134.7, 133.6, 130.0, 127.2, 124.4, 120.5, 118.3, 114.7, 114.5, 111.6, 29.7.

N-(4-chlorophenyl)-2-(methylamino)benzamide (3i)



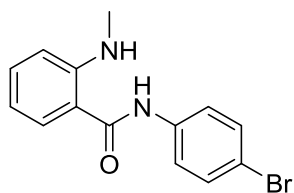
Yield: 76% (297.2 mg), white solid, mp. 129-131 °C; CAS registry number: 1025-38-3; ¹H NMR (400 MHz, CDCl₃) δ 7.73 (s, 1H), 7.60 – 7.46 (m, 3H), 7.43 – 7.29 (m, 4H), 6.72 (d, *J* = 8.4 Hz, 1H), 6.65 (t, *J* = 7.5 Hz, 1H), 2.88 (d, *J* = 5.1 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 168.1, 150.9, 136.5, 133.6, 129.4, 129.1, 127.2, 121.7, 114.7, 114.6, 111.5, 29.7.

N-(4-fluorophenyl)-2-(methylamino)benzamide (3j)



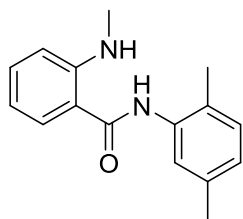
Yield: 80% (293.1 mg), white solid, mp. 140-143 °C; CAS registry number: 348612-12-4; ¹H NMR (400 MHz, CDCl₃) δ 7.69 (s, 1H), 7.53 – 7.45 (m, 3H), 7.38 (t, *J* = 8.4 Hz, 2H), 7.07 (t, *J* = 8.7 Hz, 2H), 6.72 (d, *J* = 8.4 Hz, 1H), 6.65 (t, *J* = 8.0 Hz, 1H), 2.88 (d, *J* = 5.1 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 168.1, 150.9, 133.5, 127.2, 122.5, 122.4, 115.8, 115.6, 114.7, 114.7, 111.5, 29.7.

N-(4-bromophenyl)-2-(methylamino)benzamide (3k)



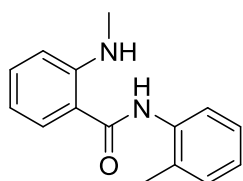
Yield: 72% (329.6 mg), white solid, mp. 137-139 °C(Lit.² 138-139 °C); CAS registry number: 35727-69-6; ¹H NMR (400 MHz, CDCl₃) δ 7.72 (s, 1H), 7.50 – 7.43 (m, 5H), 7.38 (t, *J* = 8.4 Hz, 2H), 6.72 (d, *J* = 8.4 Hz, 1H), 6.65 (t, *J* = 7.9 Hz, 1H), 2.88 (d, *J* = 5.1 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 168.1, 150.9, 137.0, 133.6, 132.0, 127.2, 122.0, 117.0, 114.7, 114.6, 111.5, 29.7.

N-(2, 5-dimethylphenyl)-2-(methylamino)benzamide (3l)



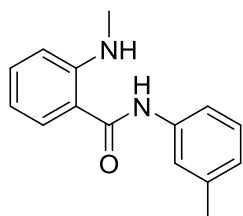
Yield: 50% (190.7 mg), white solid, mp. 129-133 °C; CAS registry number: 348613-26-3; ¹H NMR (400 MHz, CDCl₃) δ 7.64 (s, 1H), 7.53 – 7.45 (m, 3H), 7.39 (t, *J* = 8.4 Hz, 1H), 7.12 (d, *J* = 7.7 Hz, 1H), 6.94 (d, *J* = 7.9 Hz, 1H), 6.72 (d, *J* = 8.4 Hz, 1H), 6.66 (t, *J* = 7.9 Hz, 1H), 2.88 (d, *J* = 5.1 Hz, 3H), 2.35 (s, 3H), 2.27 (s, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 168.2, 151.0, 136.5, 135.5, 133.3, 130.4, 127.2, 126.8, 126.1, 124.0, 115.1, 114.6, 111.4, 29.7, 21.2, 17.5.

2-(methylamino)-N-(*o*-tolyl)benzamide (3m)



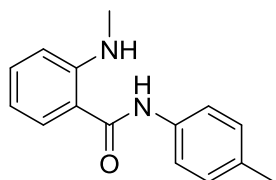
Yield: 60% (216.3 mg), white solid, mp. 152-154 °C(Lit.² 154-155 °C); CAS registry number: 35833-79-5; ¹H NMR (400 MHz, CDCl₃) δ 7.79 (d, *J* = 7.9 Hz, 1H), 7.58 – 7.46 (m, 3H), 7.39 (t, *J* = 8.4 Hz, 1H), 7.30 – 7.22 (m, 3H), 7.13 (t, *J* = 8.0 Hz, 1H), 6.73 (d, *J* = 8.4 Hz, 1H), 6.66 (t, *J* = 8.0 Hz, 1H), 2.88 (d, *J* = 5.1 Hz, 3H), 2.32 (s, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 168.2, 151.0, 135.7, 133.4, 130.6, 130.0, 127.2, 126.8, 125.4, 123.5, 115.0, 114.6, 111.4, 29.7, 18.0.

2-(methylamino)-N-(*m*-tolyl)benzamide (3n)



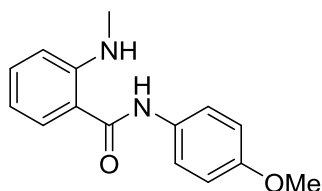
Yield: 72% (259.5 mg), white solid, mp. 128-130 °C(Lit.² 136-137 °C); CAS registry number: 35833-80-8; ¹H NMR (400 MHz, CDCl₃) δ 7.68 (s, 1H), 7.47 (d, *J* = 9.2 Hz, 1H), 7.43 – 7.34 (m, 3H), 7.32 (d, *J* = 8.2 Hz, 1H), 7.29 – 7.22 (m, 2H), 6.97 (d, *J* = 7.4 Hz, 1H), 6.71 (d, *J* = 8.4 Hz, 1H), 6.65 (t, *J* = 7.9 Hz, 1H), 2.88 (d, *J* = 5.1 Hz, 3H), 2.37 (s, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 168.1, 150.9, 139.0, 137.8, 133.3, 128.9, 127.2, 125.3, 121.1, 117.6, 115.2, 114.6, 111.4, 29.7, 21.6.

2-(methylamino)-*N*-(*p*-tolyl)benzamide (3o)



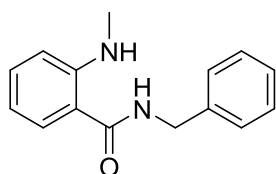
Yield: 80% (288.4 mg), white solid, mp. 131-133 °C (Lit.² 130-132 °C); CAS registry number: 35833-81-9; ¹H NMR (400 MHz, CDCl₃) δ 7.67 (s, 1H), 7.51 – 7.33 (m, 5H), 7.17 (d, *J* = 8.2 Hz, 2H), 6.71 (d, *J* = 8.4 Hz, 1H), 6.65 (t, *J* = 7.9 Hz, 1H), 2.87 (d, *J* = 5.1 Hz, 3H), 2.34 (s, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 168.1, 150.8, 135.3, 134.2, 133.2, 129.6, 127.2, 120.7, 115.2, 114.6, 111.4, 29.7, 20.9.

N-(4-methoxyphenyl)-2-(methylamino)benzamide (3p)



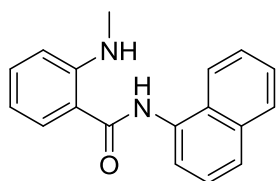
Yield: 76% (292.2 mg), white solid, mp. 132-134 °C; CAS registry number: 1029-08-9; ¹H NMR (400 MHz, CDCl₃) δ 7.66 (s, 1H), 7.48 – 7.28 (m, 5H), 6.90 (d, *J* = 9.0 Hz, 2H), 6.70 (d, *J* = 8.4 Hz, 1H), 6.63 (t, *J* = 7.0 Hz, 1H), 3.81 (s, 3H), 2.86 (d, *J* = 5.1 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 168.2, 156.6, 150.8, 133.2, 130.8, 127.2, 122.6, 115.2, 114.6, 114.2, 111.3, 55.5, 29.7.

N-benzyl-2-(methylamino)benzamide (3q)



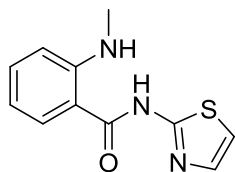
Yield: 25% (90.1 mg), white solid, mp. 93-95 °C (Lit.¹ 94-96 °C); CAS registry number: 56042-78-5; ¹H NMR (600 MHz, CDCl₃) δ 7.52 (s, 1H), 7.39 – 7.21 (m, 7H), 6.68 (d, *J* = 8.3 Hz, 1H), 6.56 (t, *J* = 7.5 Hz, 1H), 6.30 (s, 1H), 4.60 (d, *J* = 5.6 Hz, 2H), 2.87 (d, *J* = 5.0 Hz, 3H); ¹³C NMR (151 MHz, CDCl₃) δ 169.7, 150.7, 138.3, 133.0, 128.8, 127.8, 127.6, 127.1, 114.7, 114.4, 111.2, 43.7, 29.7.

2-(methylamino)-*N*-(naphthalen-1-yl)benzamide (3r)



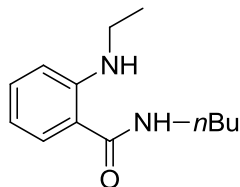
Yield: 33% (136.8 mg), white solid, mp. 190-192 °C (Lit.¹ 185-187 °C); CAS registry number: 53693-71-3; ¹H NMR (600 MHz, CDCl₃) δ 8.09 (s, 1H), 7.94 – 7.86 (m, 3H), 7.76 (d, *J* = 8.2 Hz, 1H), 7.69 (d, *J* = 7.7 Hz, 1H), 7.56 – 7.48 (m, 4H), 7.43 (t, *J* = 7.8 Hz, 1H), 6.76 (d, *J* = 8.4 Hz, 1H), 6.72 (t, *J* = 7.5 Hz, 1H), 2.89 (d, *J* = 5.1 Hz, 3H); ¹³C NMR (151 MHz, CDCl₃) δ 151.2, 134.3, 133.5, 132.6, 128.8, 128.0, 127.4, 126.5, 126.1, 125.7, 121.7, 121.1, 114.7, 114.7, 111.6, 29.7.

2-(methylamino)-*N*-(thiazol-2-yl)benzamide (3s)



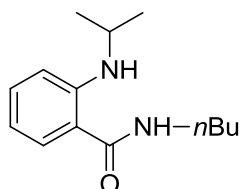
Yield: 52% (182.0 mg), light yellow solid, mp. 155-156 °C; CAS registry number: 21258-68-4; $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 11.09 (s, 1H), 7.65 (d, $J = 6.5$ Hz, 2H), 7.42 (t, $J = 7.1$ Hz, 1H), 7.27 (d, $J = 3.6$ Hz, 1H), 6.93 (d, $J = 3.6$ Hz, 1H), 6.75 (d, $J = 8.3$ Hz, 1H), 6.64 (t, $J = 7.5$ Hz, 1H), 2.93 (d, $J = 4.9$ Hz, 3H); $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 167.2, 159.3, 151.6, 137.5, 134.4, 128.3, 114.7, 113.1, 112.0, 111.6, 29.6.

***N*-butyl-2-(ethylamino)benzamide (3bb)**



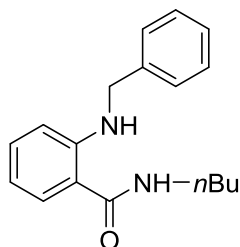
Yield: 70% (231.3 mg), colorless liquid; CAS registry number: 1249561-72-5; $^1\text{H NMR}$ (600 MHz, CDCl_3) δ 7.38 (s, 1H), 7.33 – 7.27 (m, 2H), 6.67 (d, $J = 8.3$ Hz, 1H), 6.56 (t, $J = 7.5$ Hz, 1H), 6.01 (s, 1H), 3.40 (dd, $J = 13.0, 7.0$ Hz, 2H), 3.17 (q, $J = 7.3$ Hz, 2H), 1.59 (dd, $J = 15.0, 7.5$ Hz, 2H), 1.42 (dq, $J = 14.7, 7.4$ Hz, 2H), 1.32 – 1.21 (m, 5H), 0.96 (t, $J = 7.4$ Hz, 3H); $^{13}\text{C NMR}$ (151 MHz, CDCl_3) δ 169.9, 149.6, 132.7, 127.1, 115.3, 114.4, 111.6, 39.4, 37.6, 31.8, 20.2, 14.6, 13.8.

***N*-butyl-2-(isopropylamino)benzamide (3bc)**



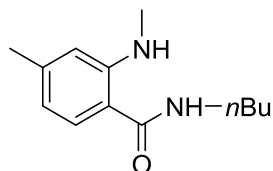
Yield: 27% (94.9 mg), colorless liquid; CAS registry number: 1281631-01-3; $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.44 (s, 1H), 7.32 – 7.14 (m, 2H), 6.68 (d, $J = 8.4$ Hz, 1H), 6.52 (t, $J = 7.5$ Hz, 1H), 6.04 (s, 1H), 3.65 (dt, $J = 12.5, 6.2$ Hz, 1H), 3.39 (dd, $J = 12.9, 7.1$ Hz, 2H), 1.58 (dt, $J = 14.9, 7.3$ Hz, 2H), 1.41 (dq, $J = 14.4, 7.3$ Hz, 2H), 1.24 (d, $J = 6.3$ Hz, 6H), 0.95 (t, $J = 7.3$ Hz, 3H); $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 169.9, 148.9, 132.6, 127.4, 115.2, 114.1, 112.1, 43.4, 39.4, 31.7, 22.8, 20.2, 13.8.

2-(benzylamino)-*N*-butylbenzamide (3bd)



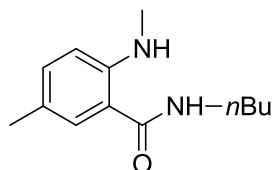
Yield: 21% (89.0 mg), colorless liquid; CAS registry number: 92944-80-4; $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 8.01 (s, 1H), 7.41 – 7.26 (m, 5H), 7.21 (dd, $J = 17.0, 8.1$ Hz, 2H), 6.60 (d, $J = 8.3$ Hz, 1H), 6.56 (t, $J = 8.0$ Hz, 1H), 6.12 (s, 1H), 4.38 (s, 2H), 3.38 (dd, $J = 12.9, 7.1$ Hz, 2H), 1.57 (dt, $J = 14.8, 7.4$ Hz, 2H), 1.40 (dq, $J = 14.4, 7.3$ Hz, 2H), 0.95 (t, $J = 7.3$ Hz, 3H); $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 169.9, 149.4, 139.2, 132.6, 128.6, 127.2, 127.1, 127.0, 115.7, 115.0, 112.1, 47.2, 39.5, 31.8, 20.2, 13.8.

***N*-butyl-4-methyl-2-(methylamino)benzamide (3bh)**



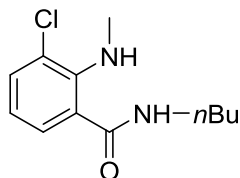
Yield: 50% (165.2 mg), colorless liquid; CAS registry number: 1505257-68-0; $^1\text{H NMR}$ (600 MHz, CDCl_3) δ 7.50 (s, 1H), 7.19 (d, $J = 7.9$ Hz, 1H), 6.46 (s, 1H), 6.38 (d, $J = 7.9$ Hz, 1H), 6.04 (s, 1H), 3.36 (dd, $J = 13.2, 6.8$ Hz, 2H), 2.83 (s, 3H), 2.30 (s, 3H), 1.59 – 1.53 (m, 2H), 1.43 – 1.35 (m, 2H), 0.94 (t, $J = 7.4$ Hz, 3H); $^{13}\text{C NMR}$ (151 MHz, CDCl_3) δ 169.9, 150.6, 143.2, 127.1, 115.5, 112.7, 111.5, 39.4, 31.8, 29.6, 21.9, 20.2, 13.8.

***N*-butyl-5-methyl-2-(methylamino)benzamide (3bi)**



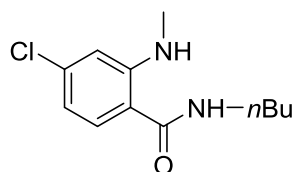
Yield: 62% (204.9 mg), colorless liquid; CAS registry number: 1249799-25-4; $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.15 – 7.10 (m, 3H), 6.59 (d, $J = 8.4$ Hz, 1H), 6.05 (s, 1H), 3.39 (dd, $J = 12.9, 7.1$ Hz, 2H), 2.83 (s, 3H), 2.24 (s, 3H), 1.58 (dt, $J = 14.8, 7.4$ Hz, 2H), 1.41 (dq, $J = 14.4, 7.3$ Hz, 2H), 0.95 (t, $J = 7.3$ Hz, 3H); $^{13}\text{C NMR}$ (151 MHz, CDCl_3) δ 169.9, 148.4, 133.4, 127.3, 123.5, 115.7, 111.3, 39.4, 31.8, 29.9, 20.3, 20.2, 13.8.

***N*-butyl-3-chloro-2-(methylamino)benzamide (3bj)**



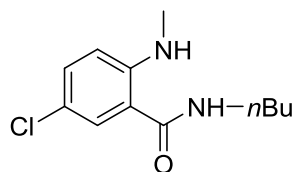
Yield: 20% (72.2 mg), colorless liquid; $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.42 (s, 1H), 7.35 – 7.27 (m, 2H), 6.66 (d, $J = 8.2$ Hz, 1H), 6.57 (t, $J = 7.5$ Hz, 1H), 6.02 (s, 1H), 3.39 (dd, $J = 12.9, 7.1$ Hz, 2H), 2.85 (s, 3H), 1.58 (dt, $J = 14.9, 7.3$ Hz, 2H), 1.41 (dq, $J = 14.4, 7.3$ Hz, 2H), 0.96 (t, $J = 7.3$ Hz, 3H); $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 169.9, 150.5, 132.7, 127.0, 115.5, 114.4, 111.1, 39.4, 31.8, 29.7, 20.2, 13.8; **HRMS** (ESI^+) calculated for $\text{C}_{12}\text{H}_{18}\text{ClN}_2\text{O}$ $[\text{M}+\text{H}]^+$: 241.1108; found: 241.1102.

***N*-butyl-4-chloro-2-(methylamino)benzamide (3bk)**



Yield: 52% (187.7 mg), white solid, mp. 101-103 °C; $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.60 (s, 1H), 7.21 (d, $J = 8.3$ Hz, 1H), 6.61 (s, 1H), 6.53 (d, $J = 8.3$ Hz, 1H), 5.95 (s, 1H), 3.38 (dd, $J = 13.0, 7.1$ Hz, 2H), 2.83 (d, $J = 5.1$ Hz, 3H), 1.63 – 1.52 (m, 2H), 1.48 – 1.33 (m, 2H), 0.96 (t, $J = 7.3$ Hz, 3H); $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 169.1, 151.4, 138.8, 128.1, 114.3, 113.8, 110.8, 39.5, 31.7, 29.6, 20.2, 13.8; **HRMS** (ESI^+) calculated for $\text{C}_{12}\text{H}_{18}\text{ClN}_2\text{O}$ $[\text{M}+\text{H}]^+$: 241.1108; found: 241.1102.

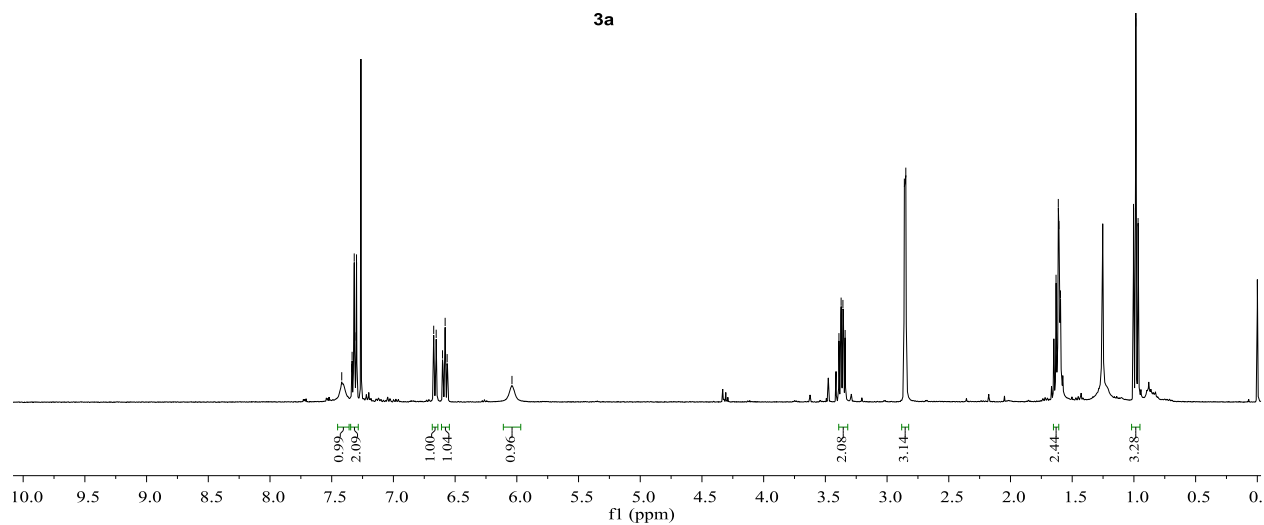
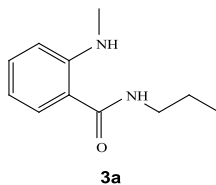
***N*-butyl-5-chloro-2-(methylamino)benzamide (3bl)**



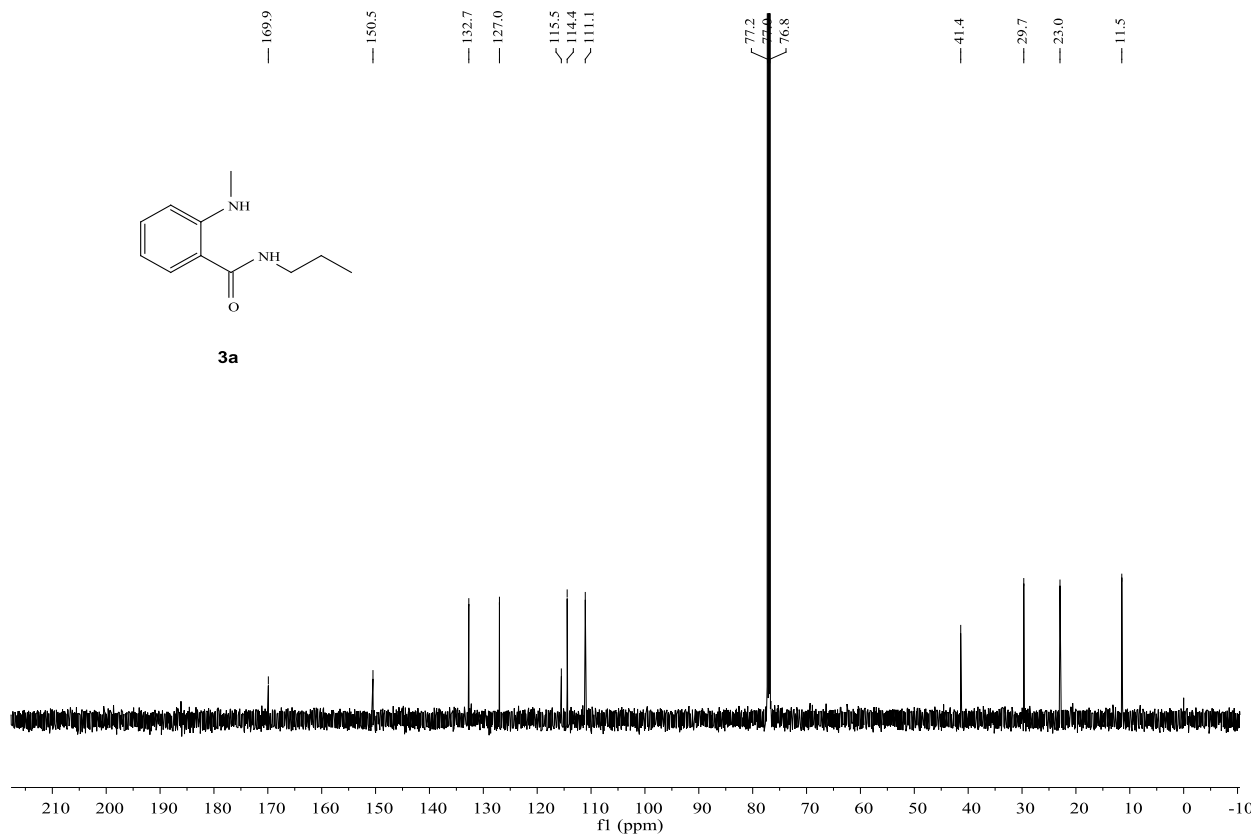
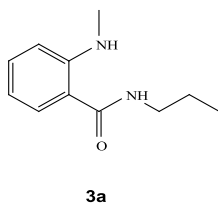
Yield: 58% (209.4 mg), white solid, mp. 110-112°C; CAS registry number: 1247473-47-7; $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.33 (s, 1H), 7.26 – 7.22 (m, 2H), 6.58 (d, $J = 9.0$ Hz, 1H), 5.98 (s, 1H), 3.38 (dd, $J = 13.0, 7.1$ Hz, 2H), 2.83 (d, $J = 5.1$ Hz, 3H), 1.61 – 1.51 (m, 2H), 1.50 – 1.32 (m, 2H), 0.96 (t, $J = 7.3$ Hz, 3H); $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 168.7, 149.0, 132.4, 126.7, 119.0, 116.5, 112.4, 39.5, 31.7, 29.8, 20.2, 13.8.

NMR Spectra

7.419
7.339
7.335
7.318
7.303
7.299
6.674
6.653
6.602
6.581
6.565
— 6.039
3.390
3.372
3.358
3.340
2.860
2.848
1.631
1.613
1.607
1.595
1.003
0.985
0.966



169.9
150.5
132.7
127.0
115.5
114.4
111.1
77.2
77.0
76.8
41.4
29.7
23.0
11.5

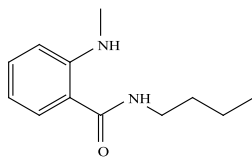


7.405
7.311
7.308
7.298
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7.278
7.261
6.636
6.622
6.540
6.530
6.521
6.272

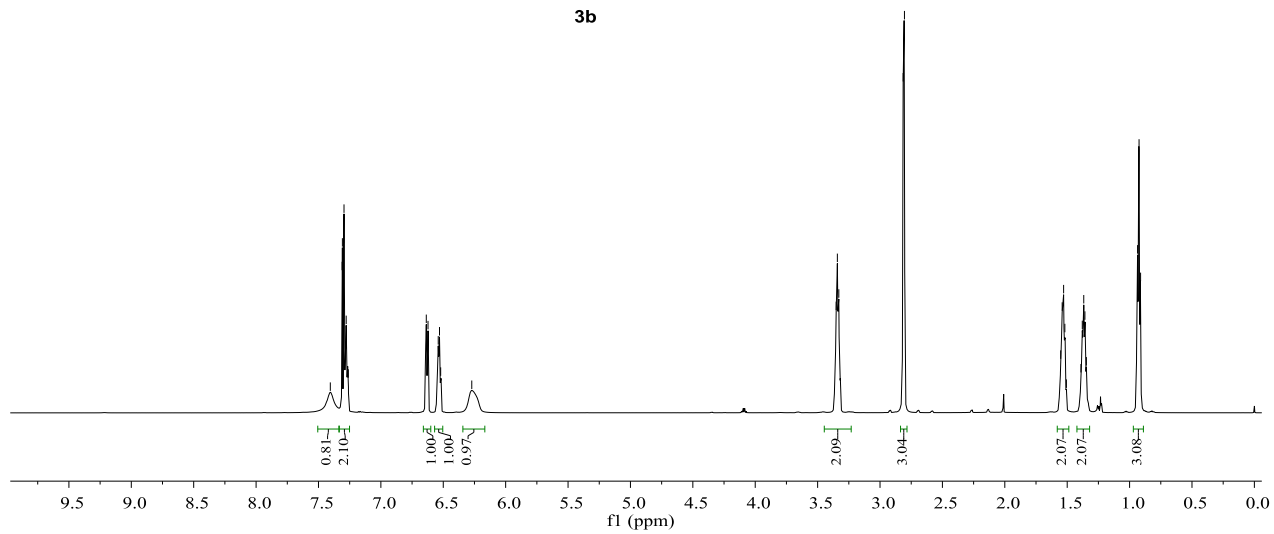
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3.330

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2.804

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1.367
1.358
1.346
0.936
0.924
0.912



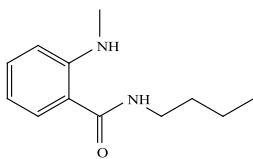
3b



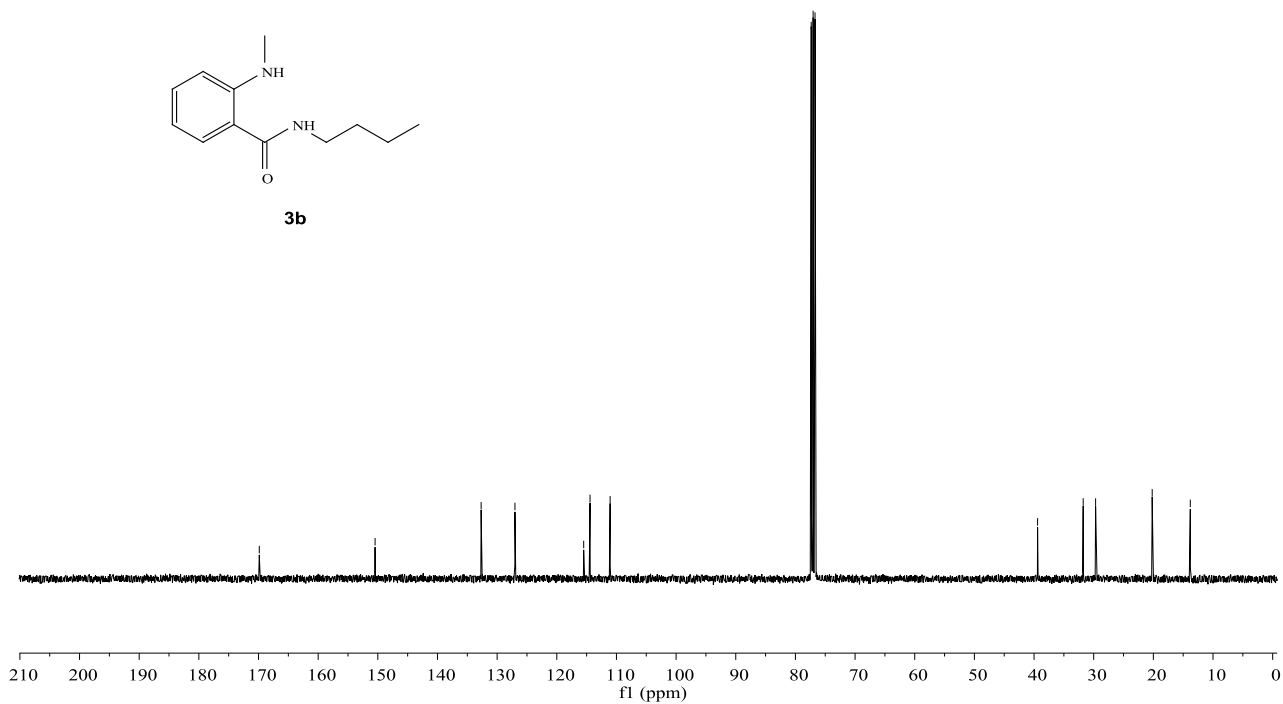
169.9
150.5
132.7
127.0
115.5
114.4
111.1

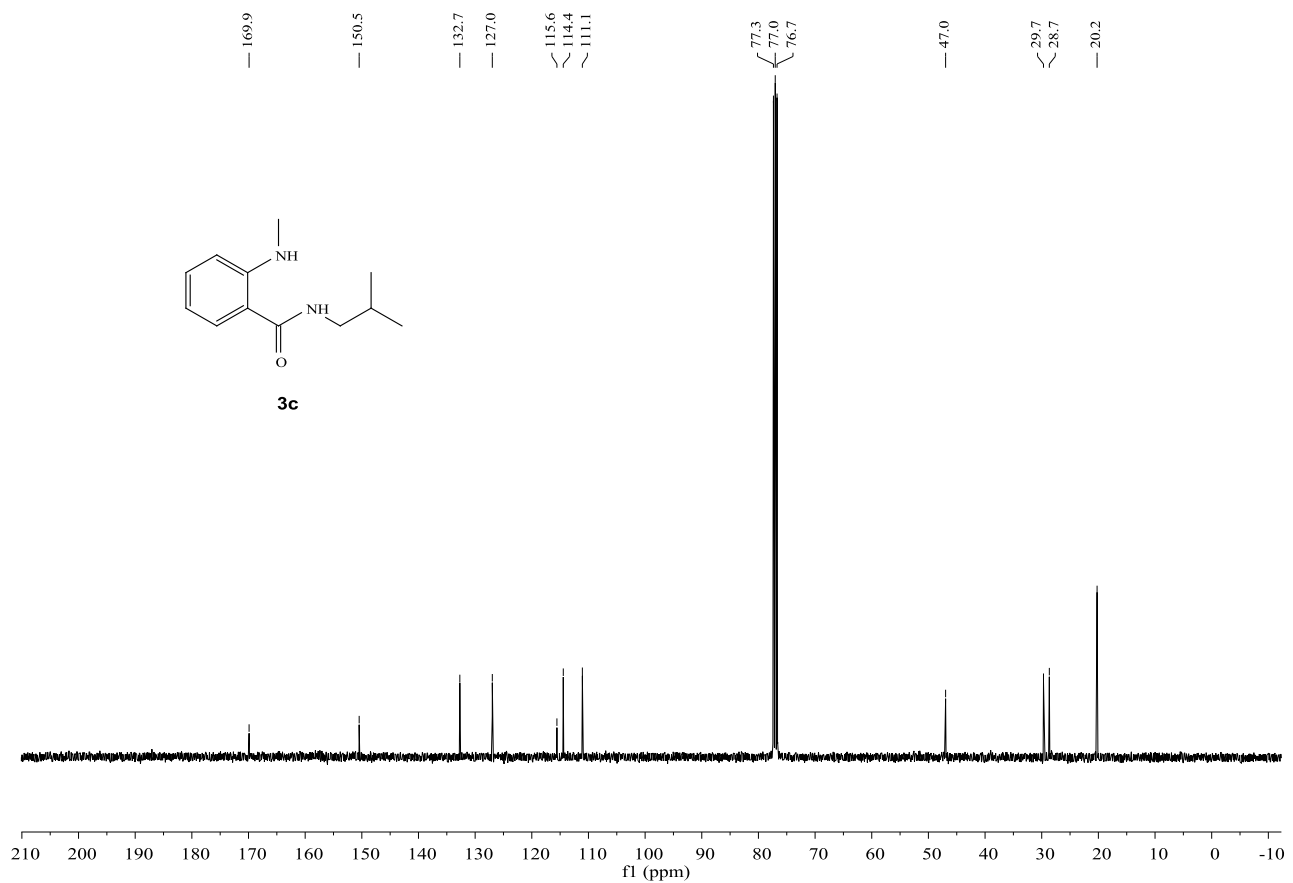
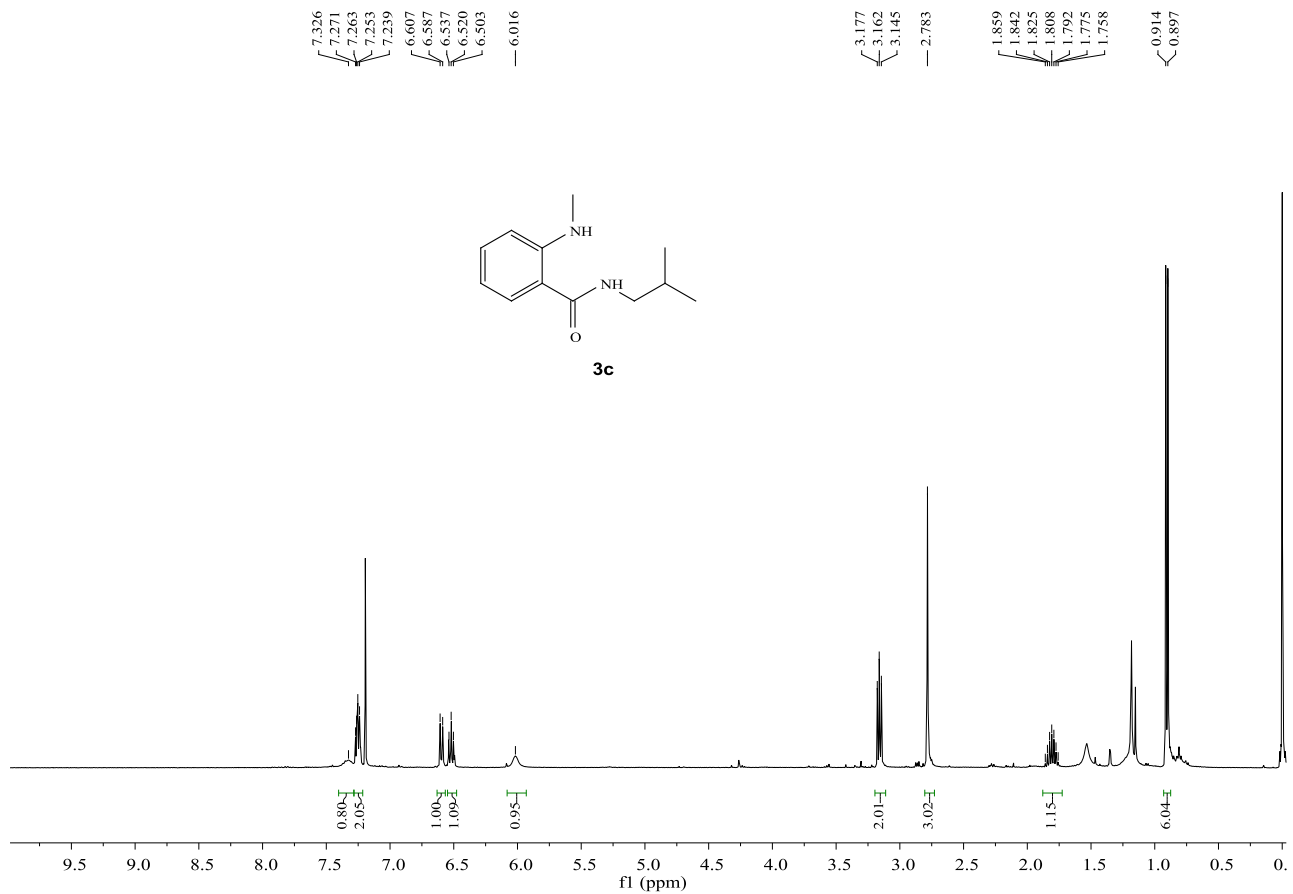
77.4
77.0
76.7

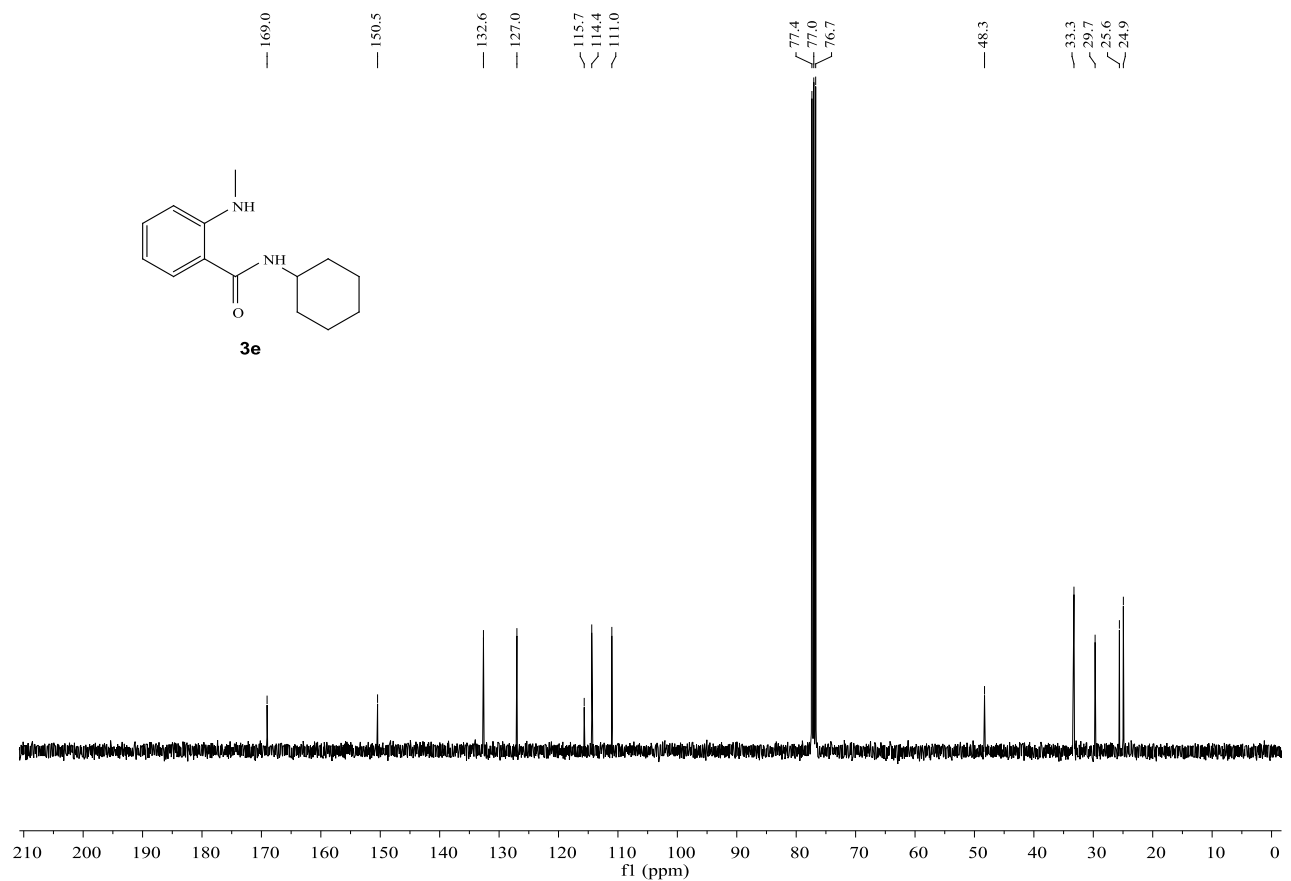
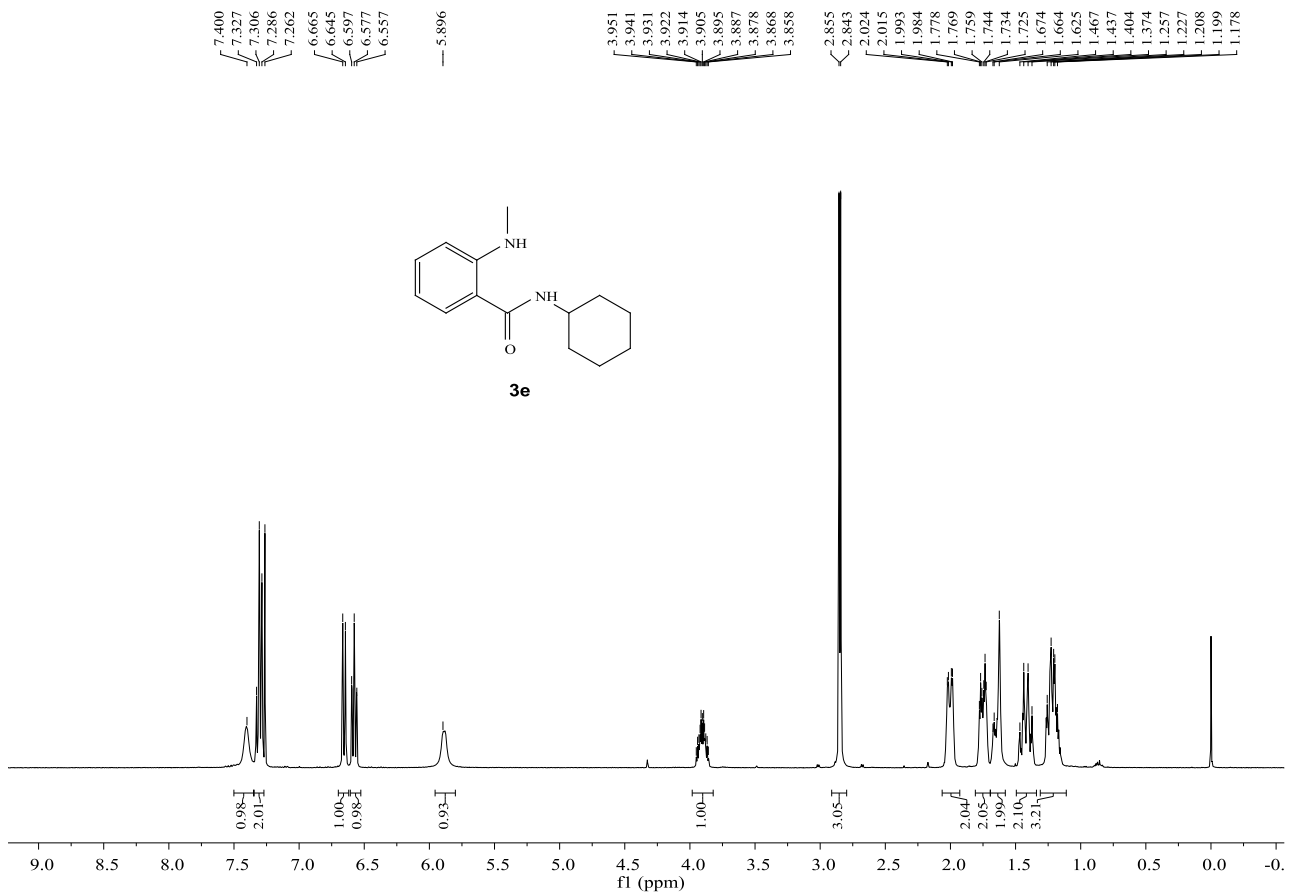
39.4
31.8
29.7
20.2
13.8

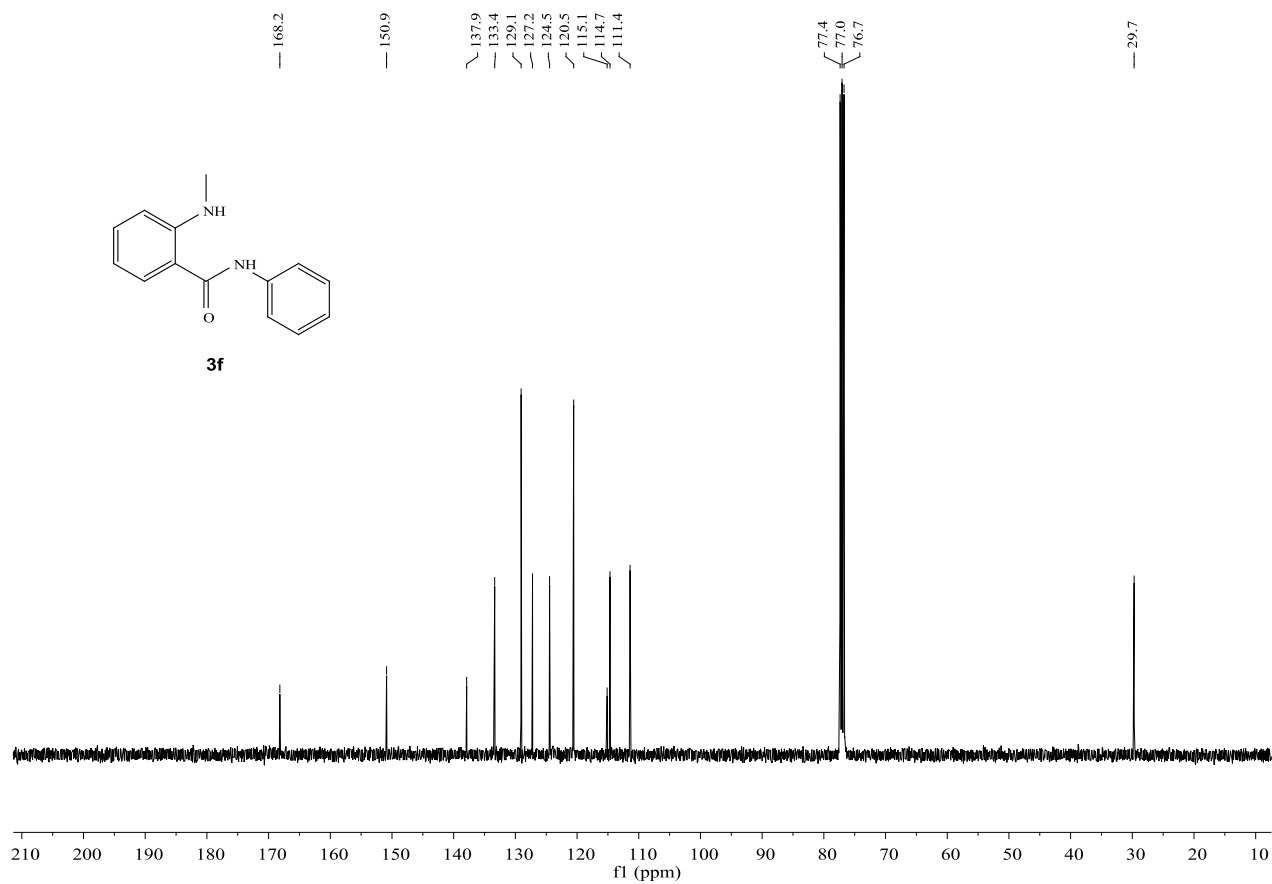
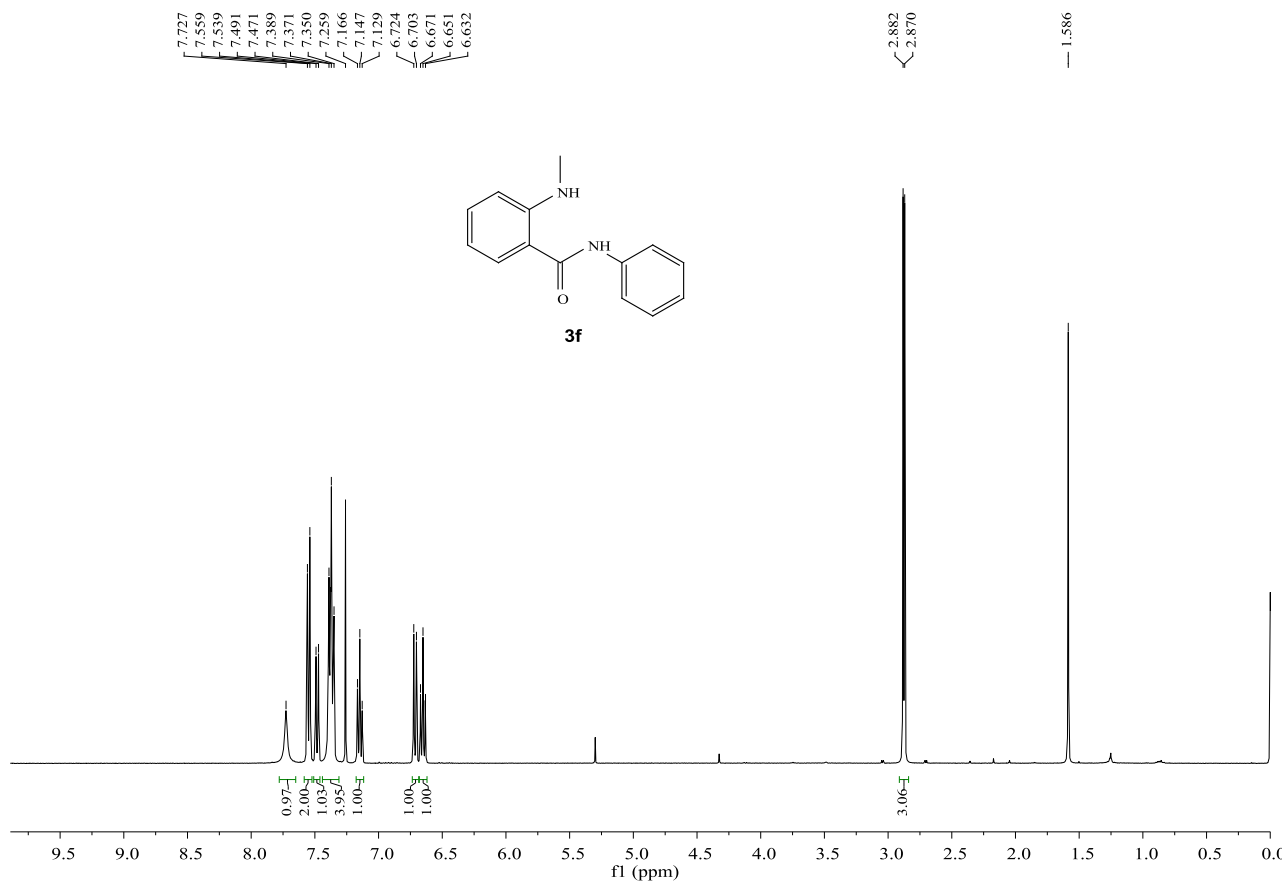


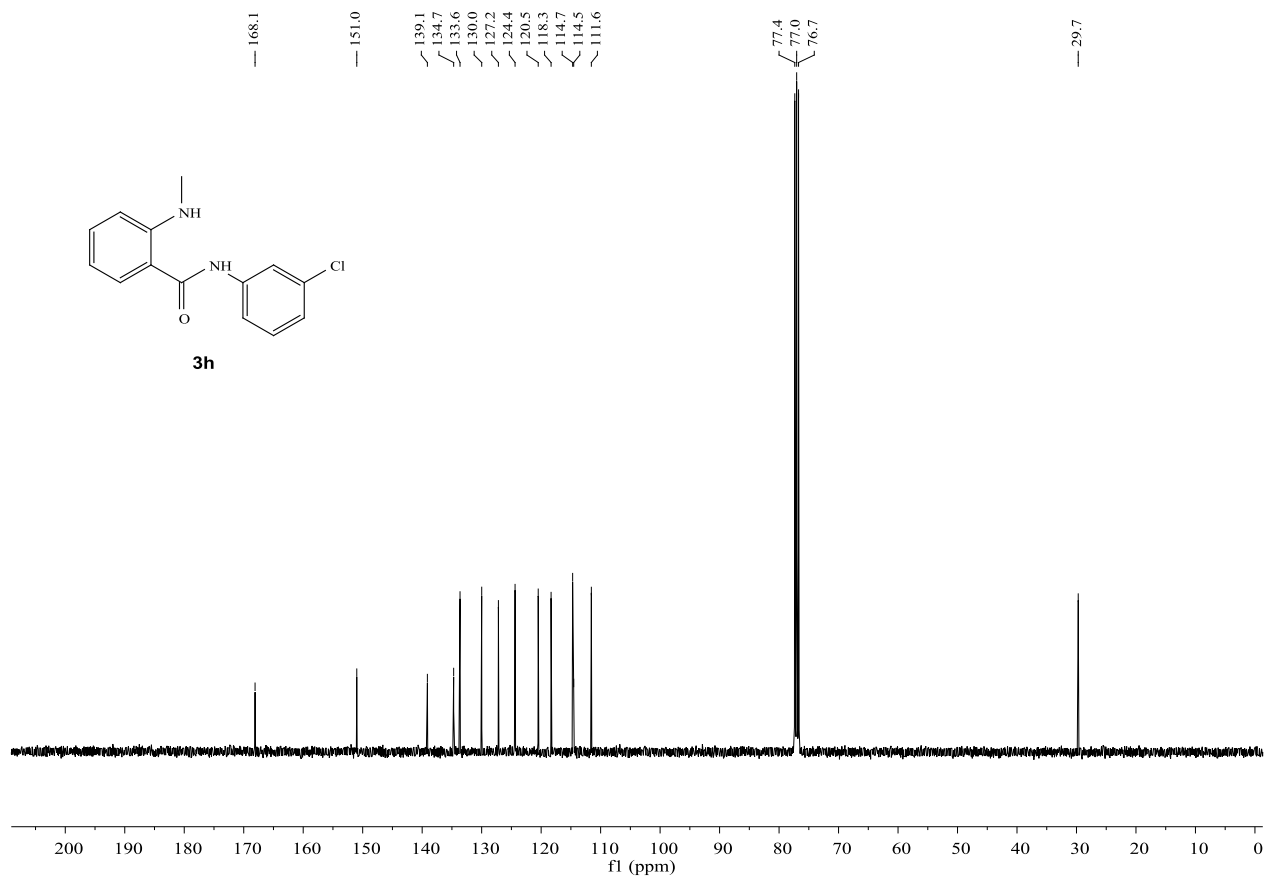
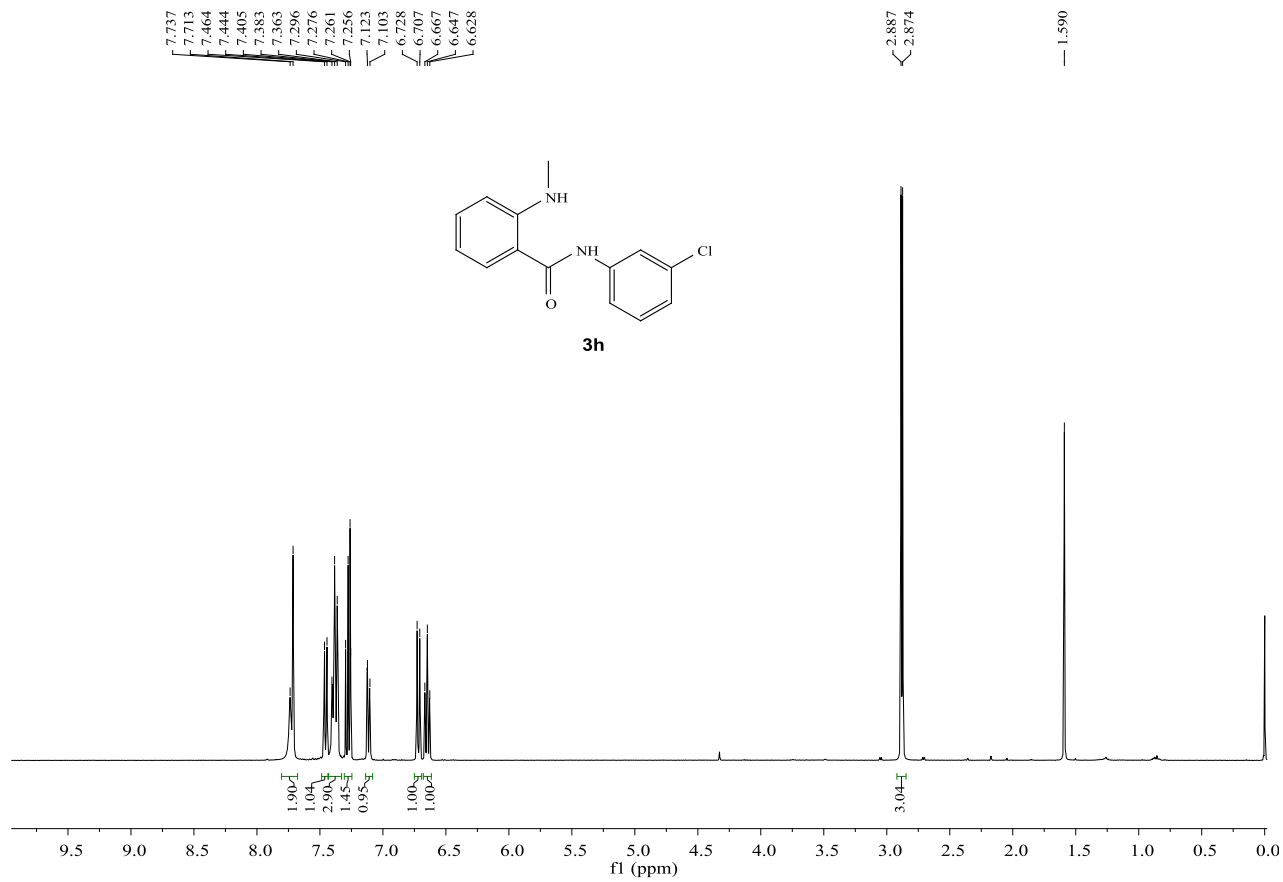
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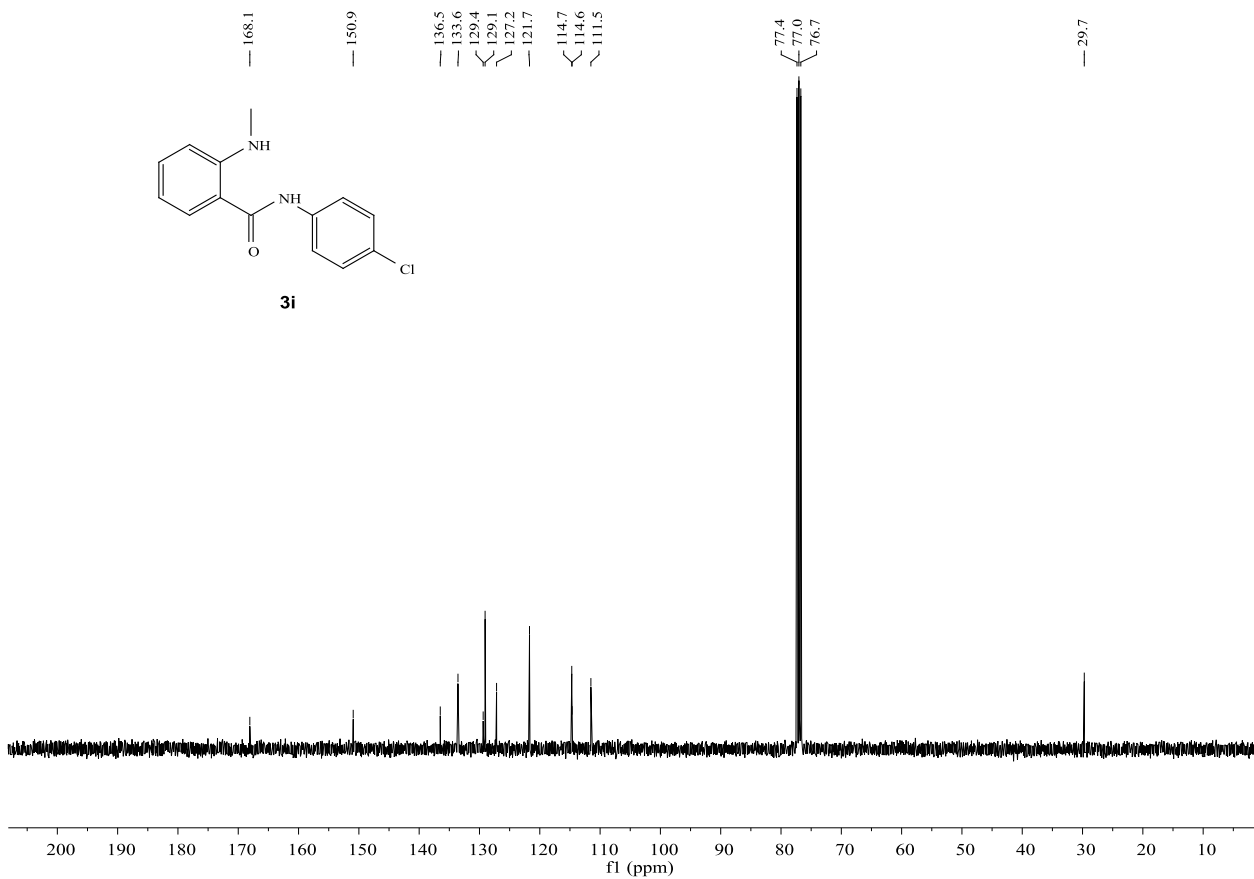
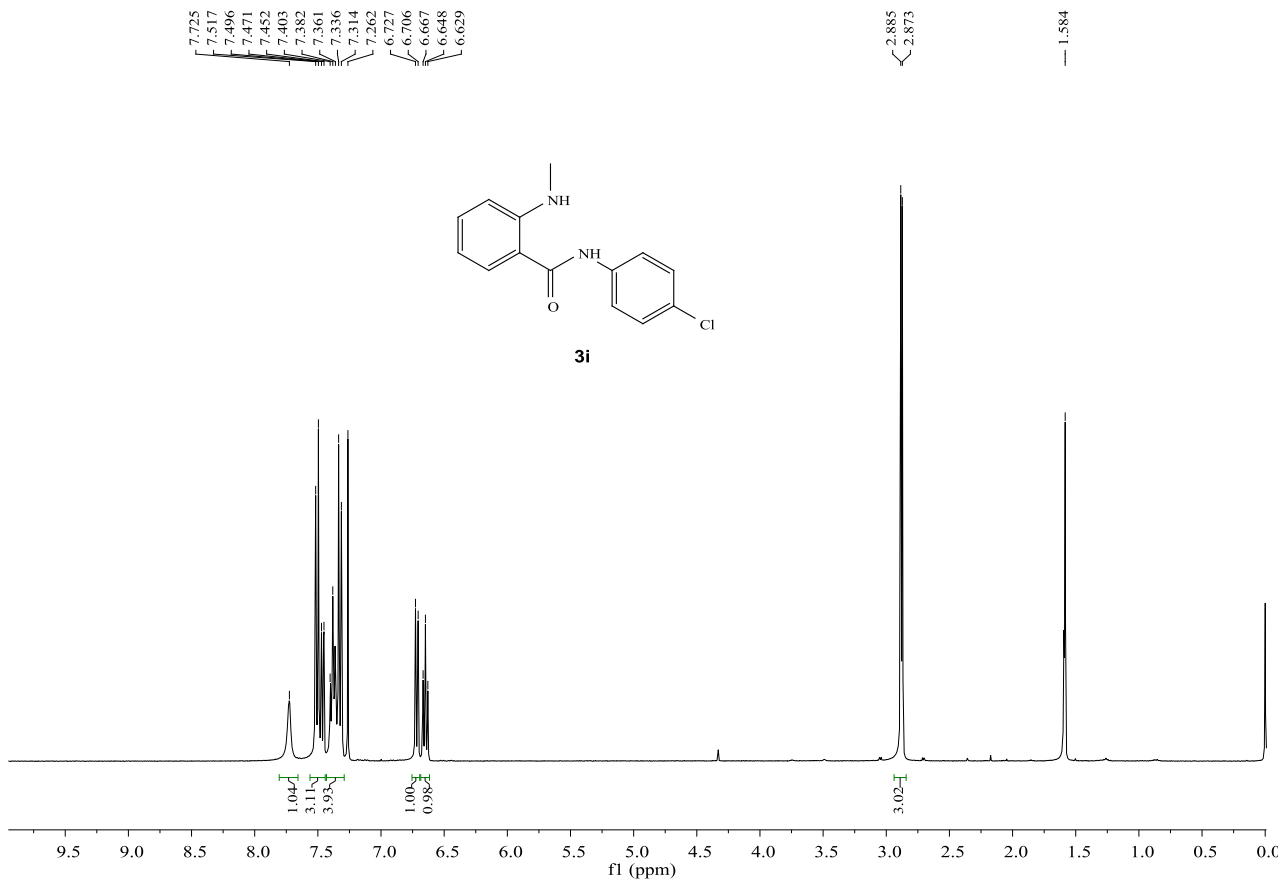






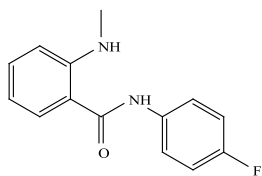




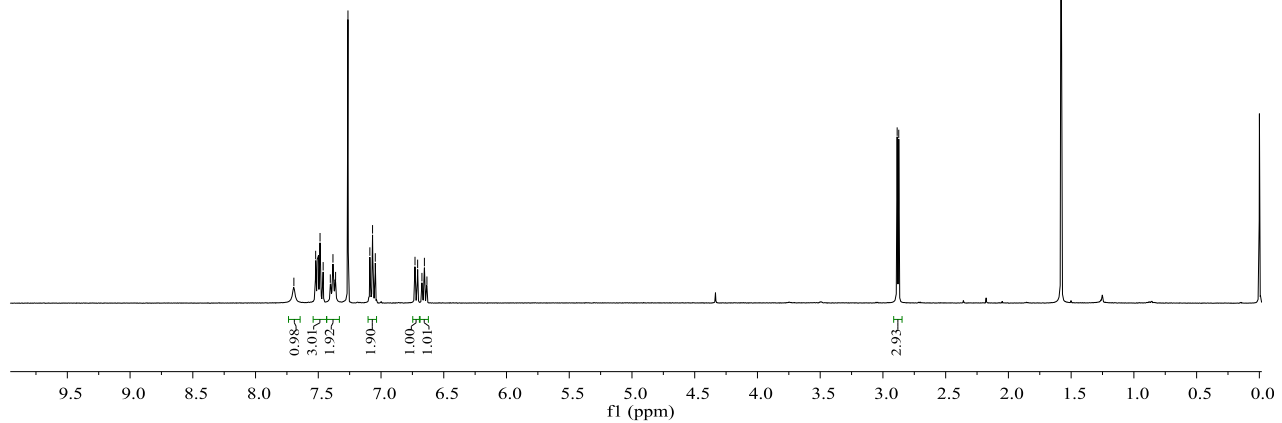


7.694
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6.654
6.634

2.887
2.874



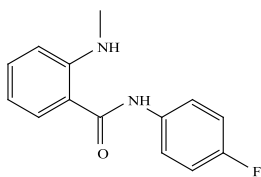
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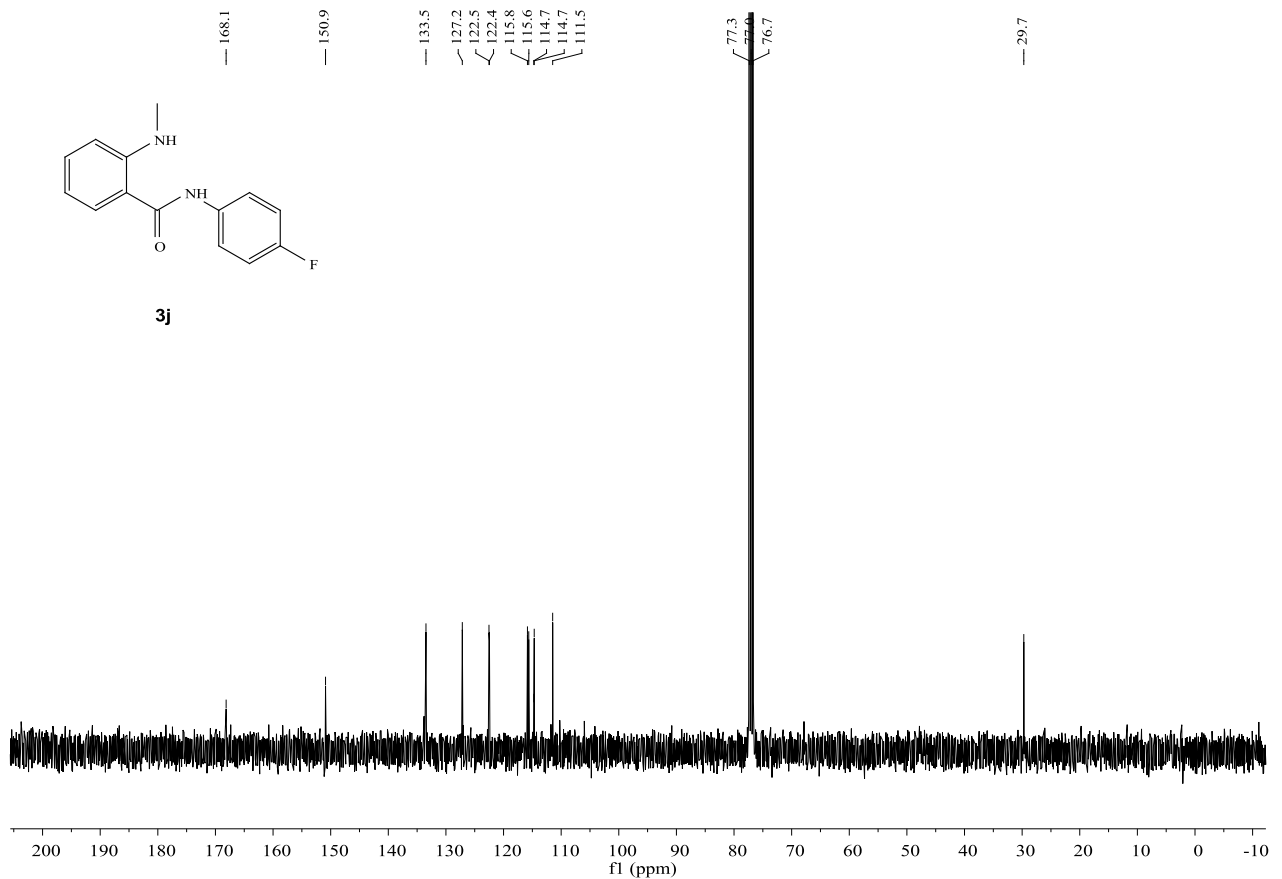
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133.5
127.2
122.5
122.4
115.8
115.6
114.7
114.7
111.5

77.3
77.0
76.7

29.7



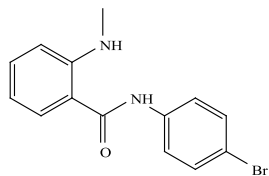
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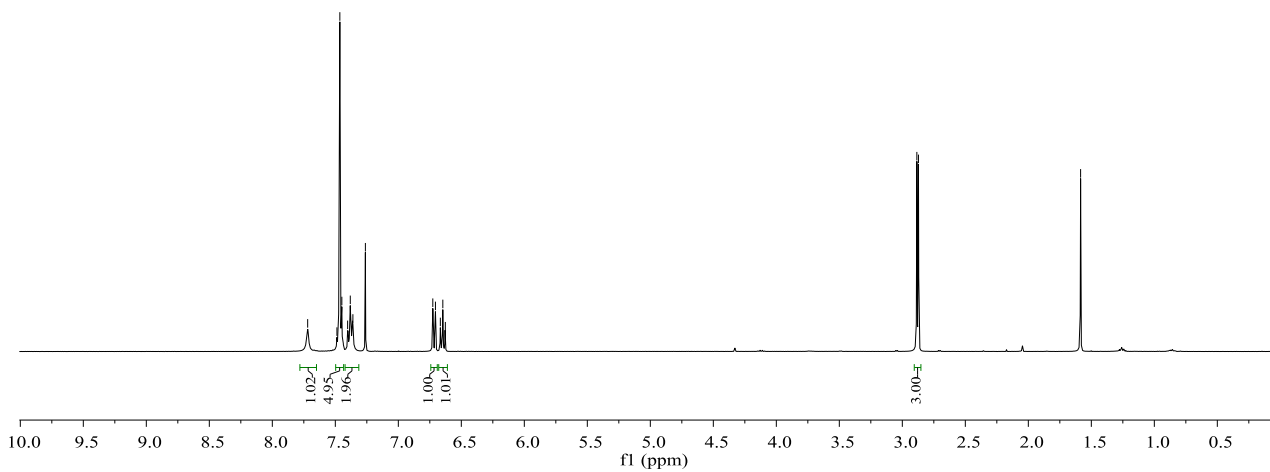
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7.261
6.726
6.705
6.666
6.647
6.627

2.885
2.872

1.585



3k



168.1

150.9

137.0

135.6

132.0

127.2

122.0

117.0

114.7

114.6

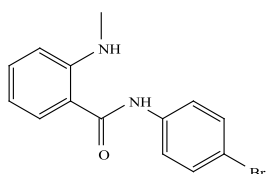
111.5

77.4

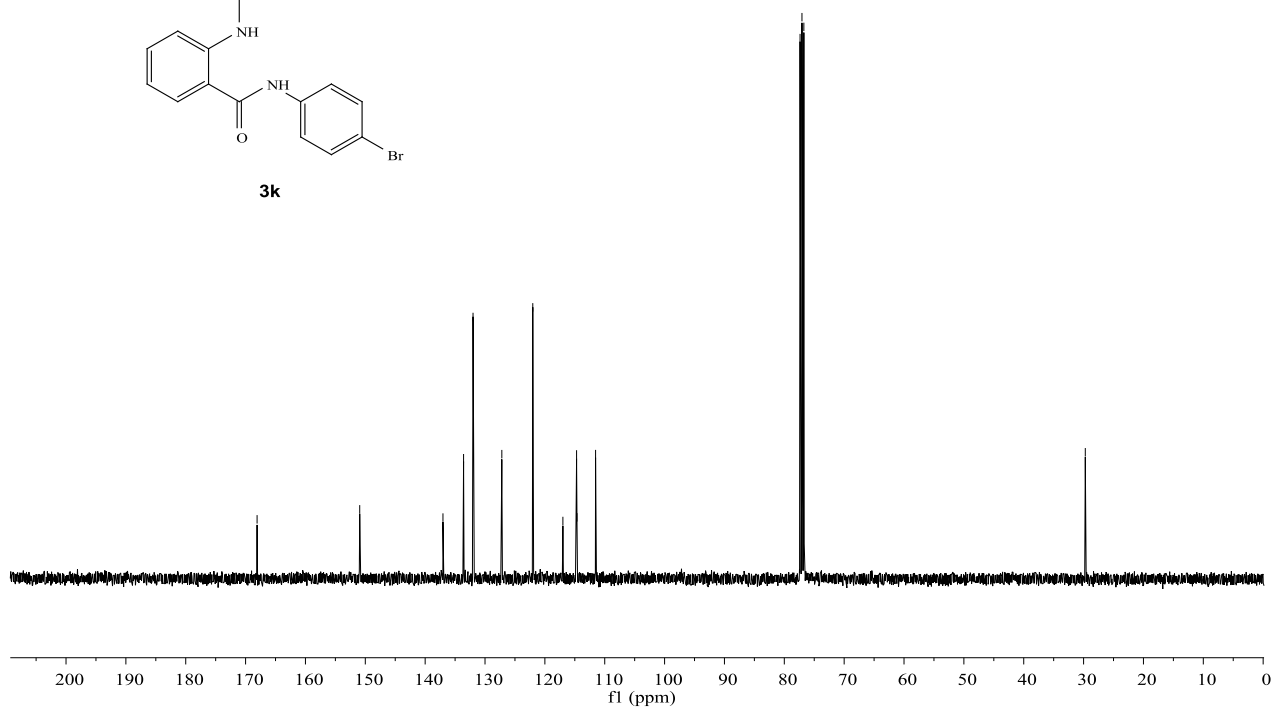
77.0

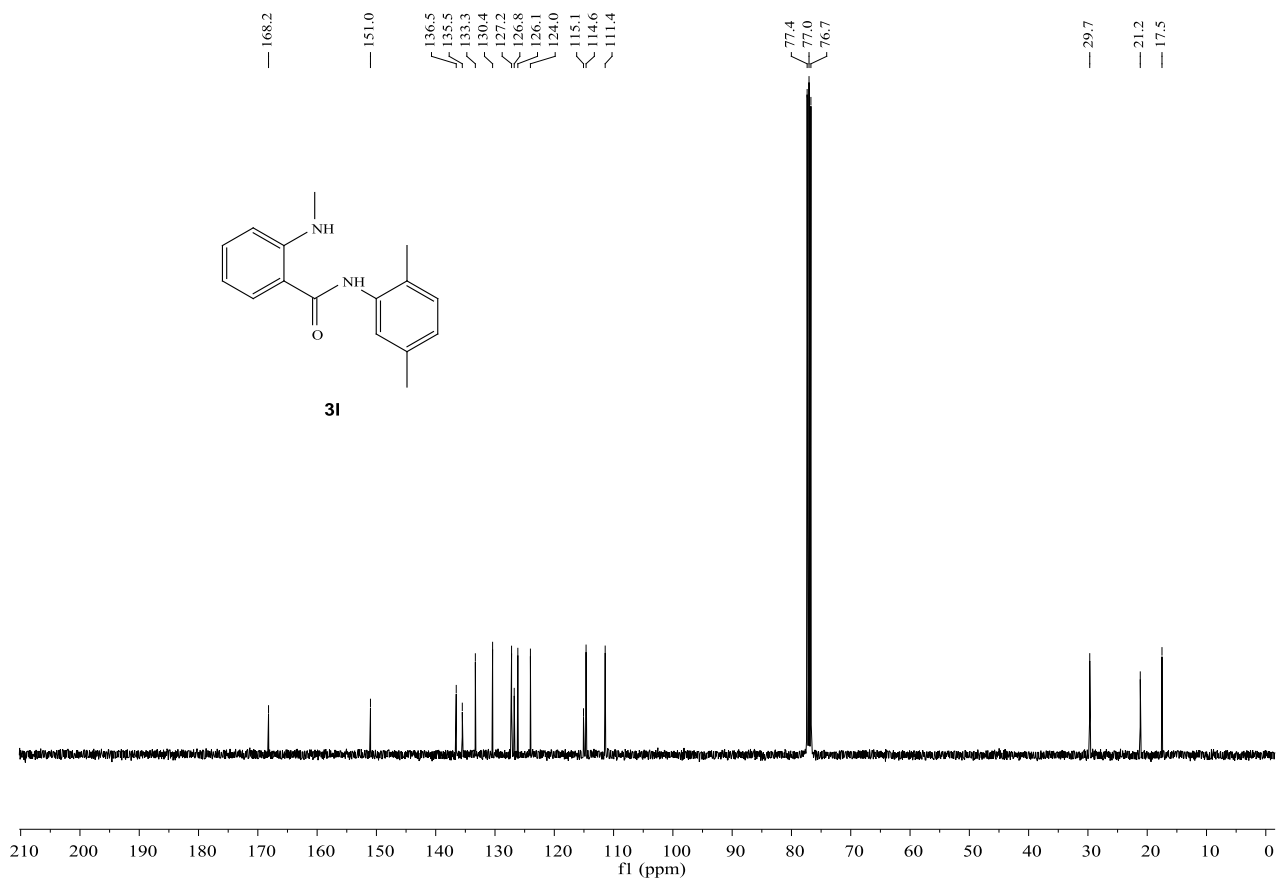
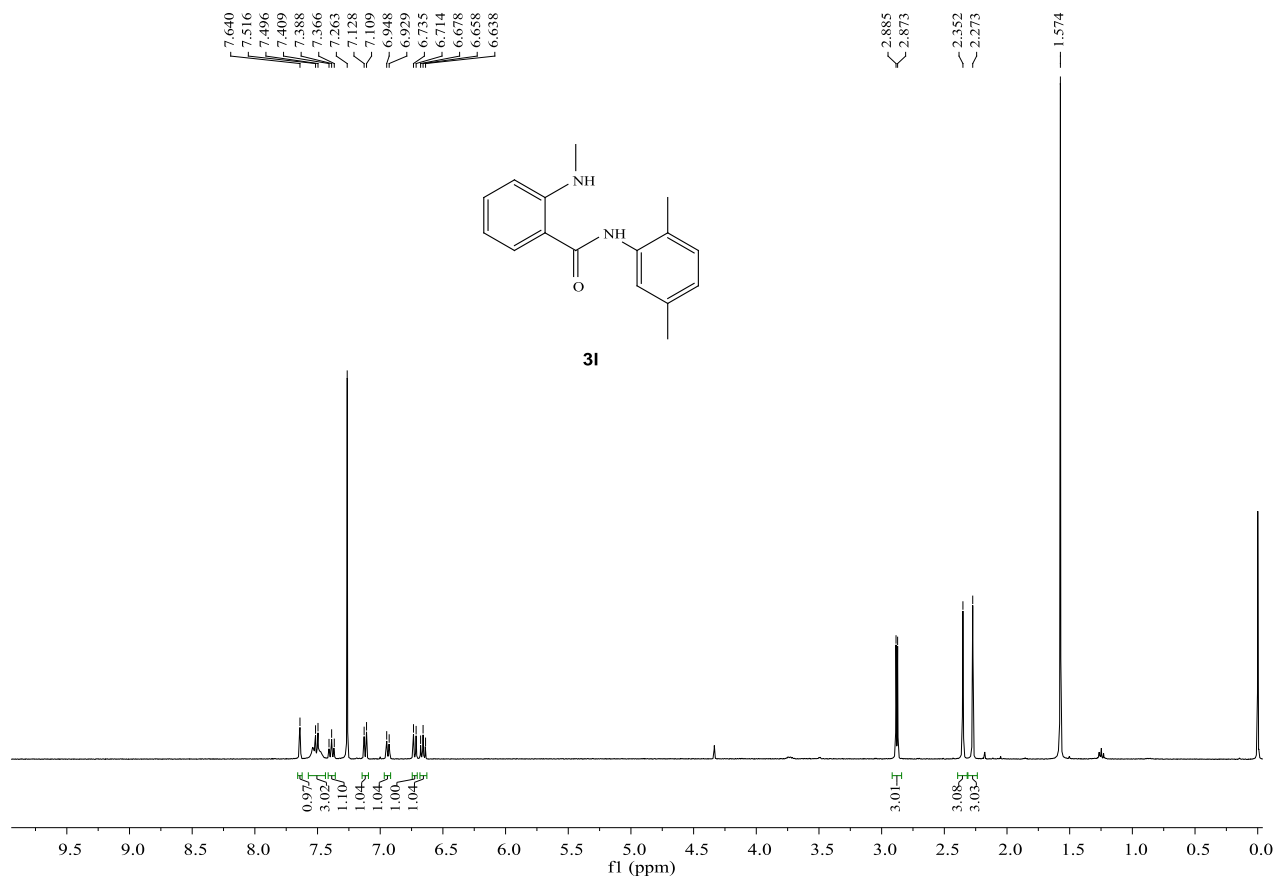
76.7

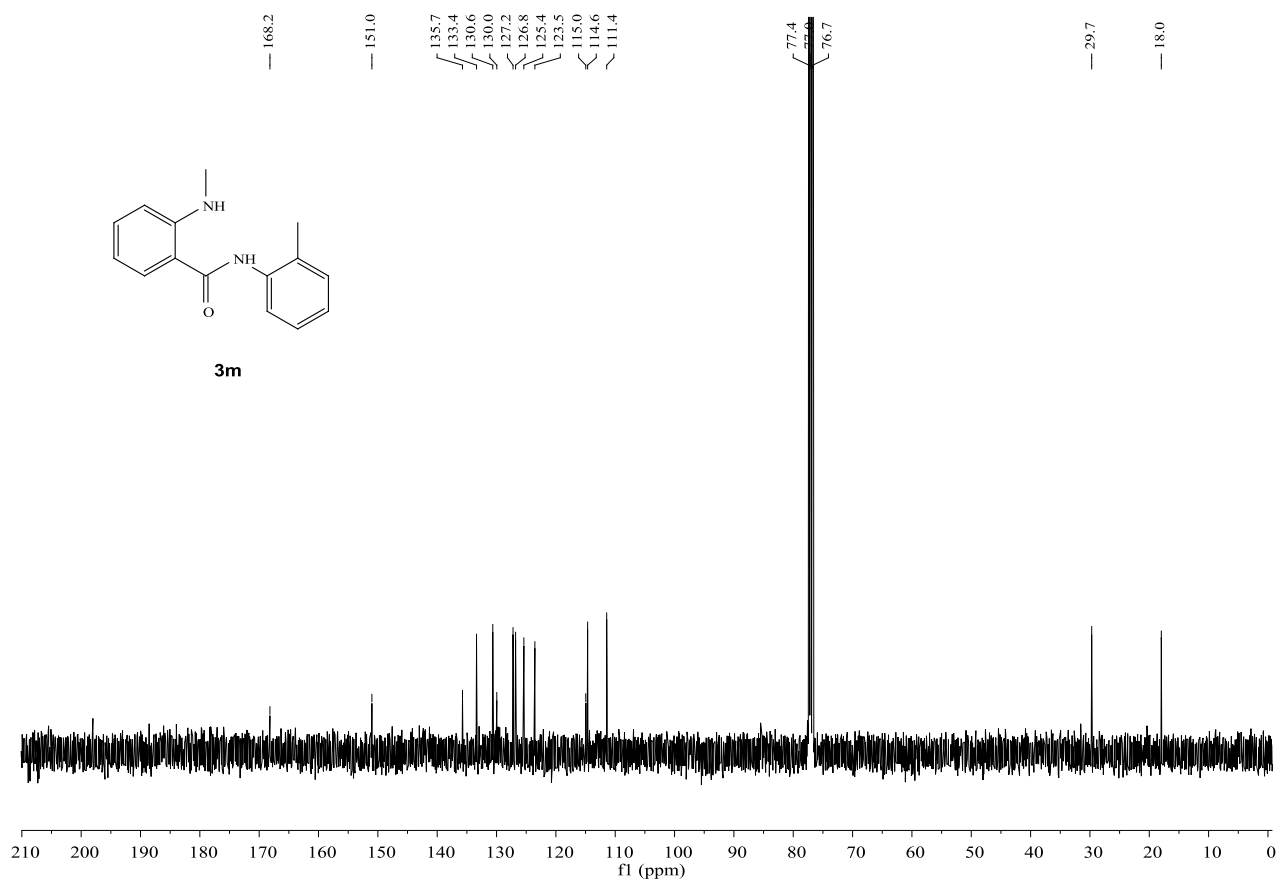
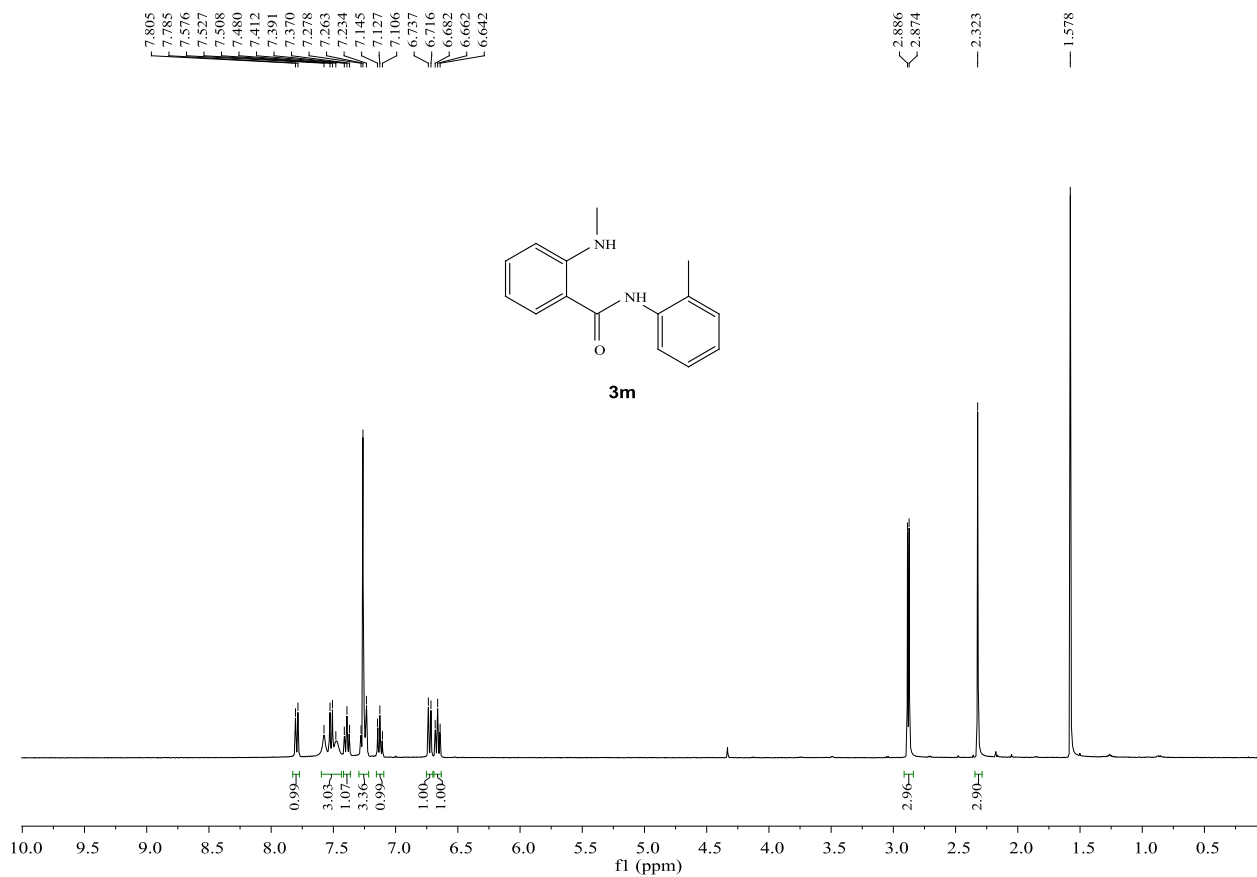
29.7

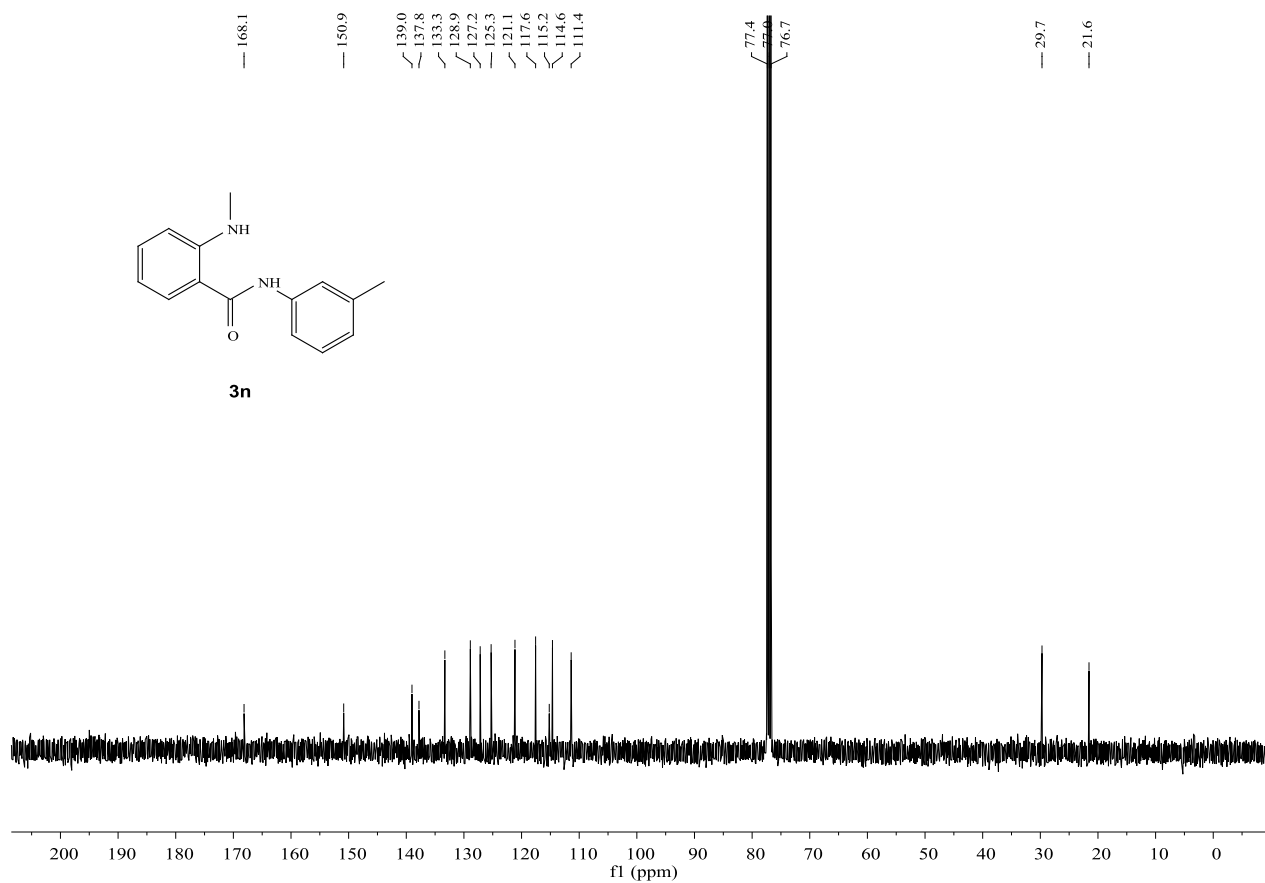
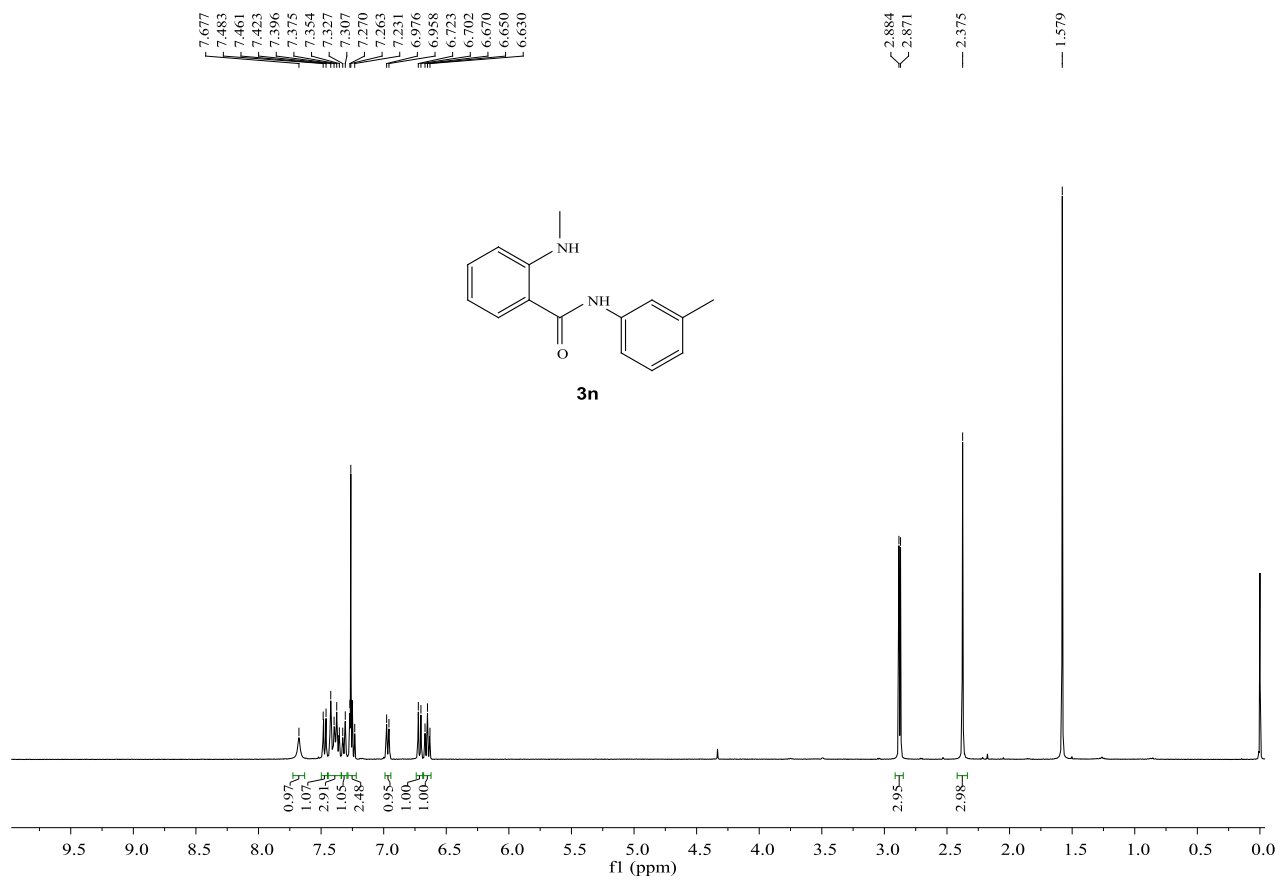


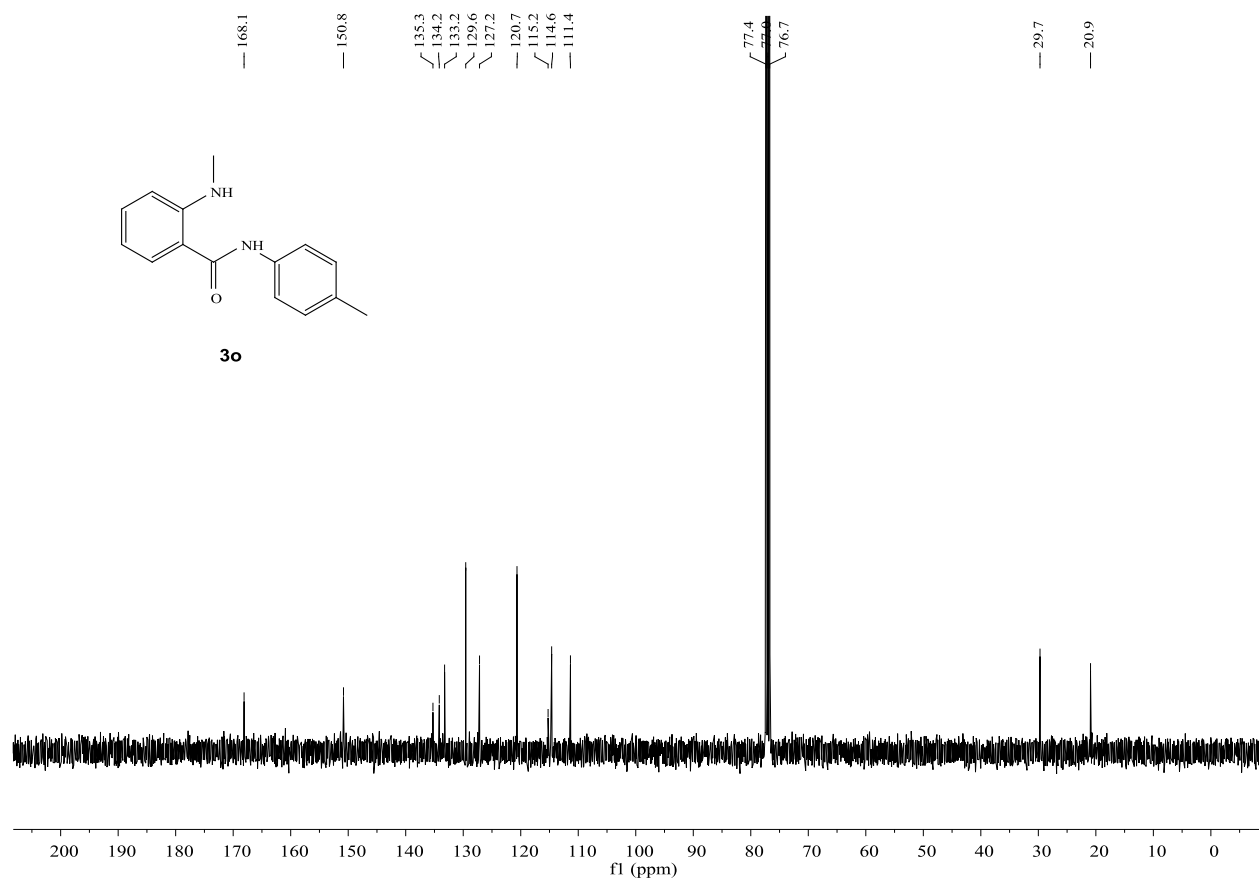
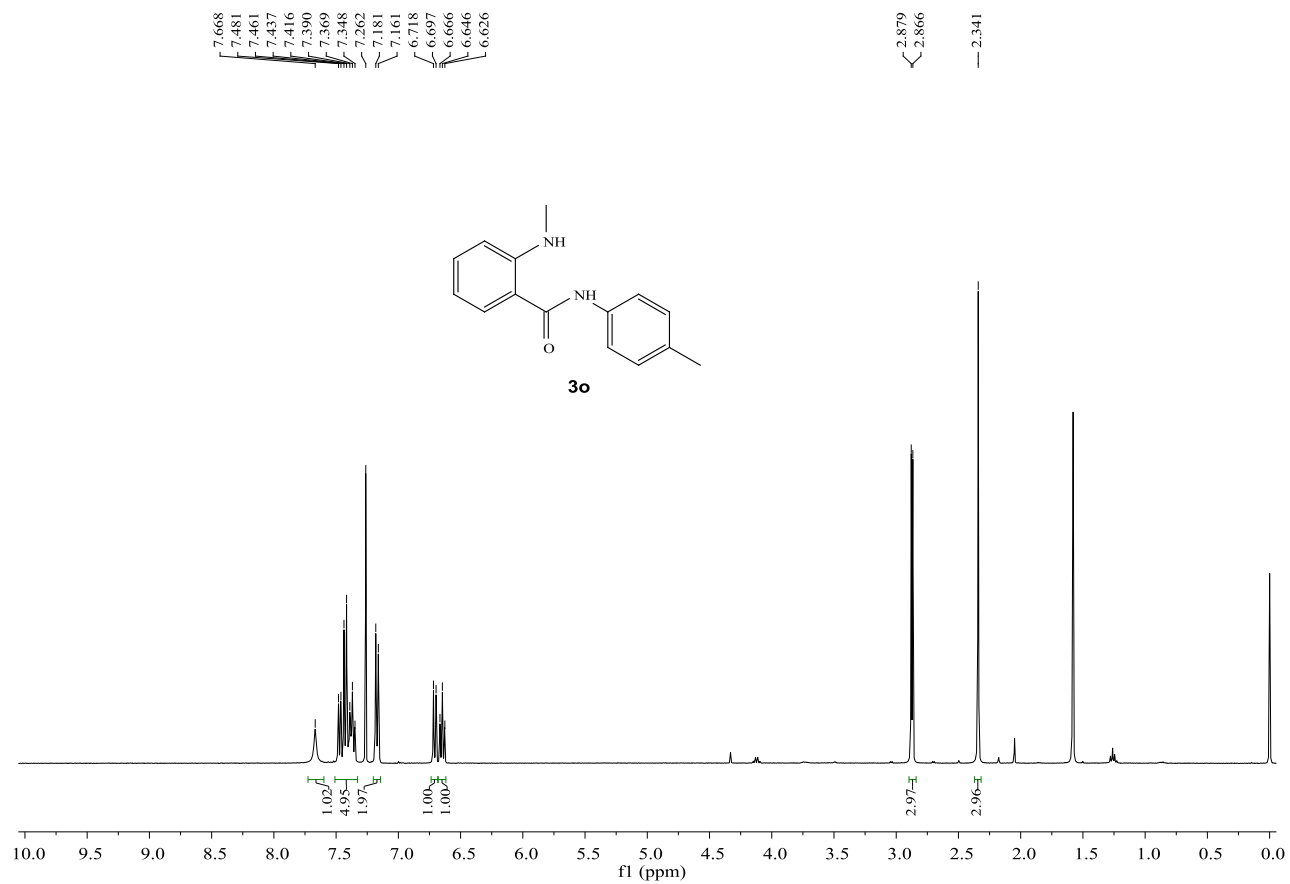
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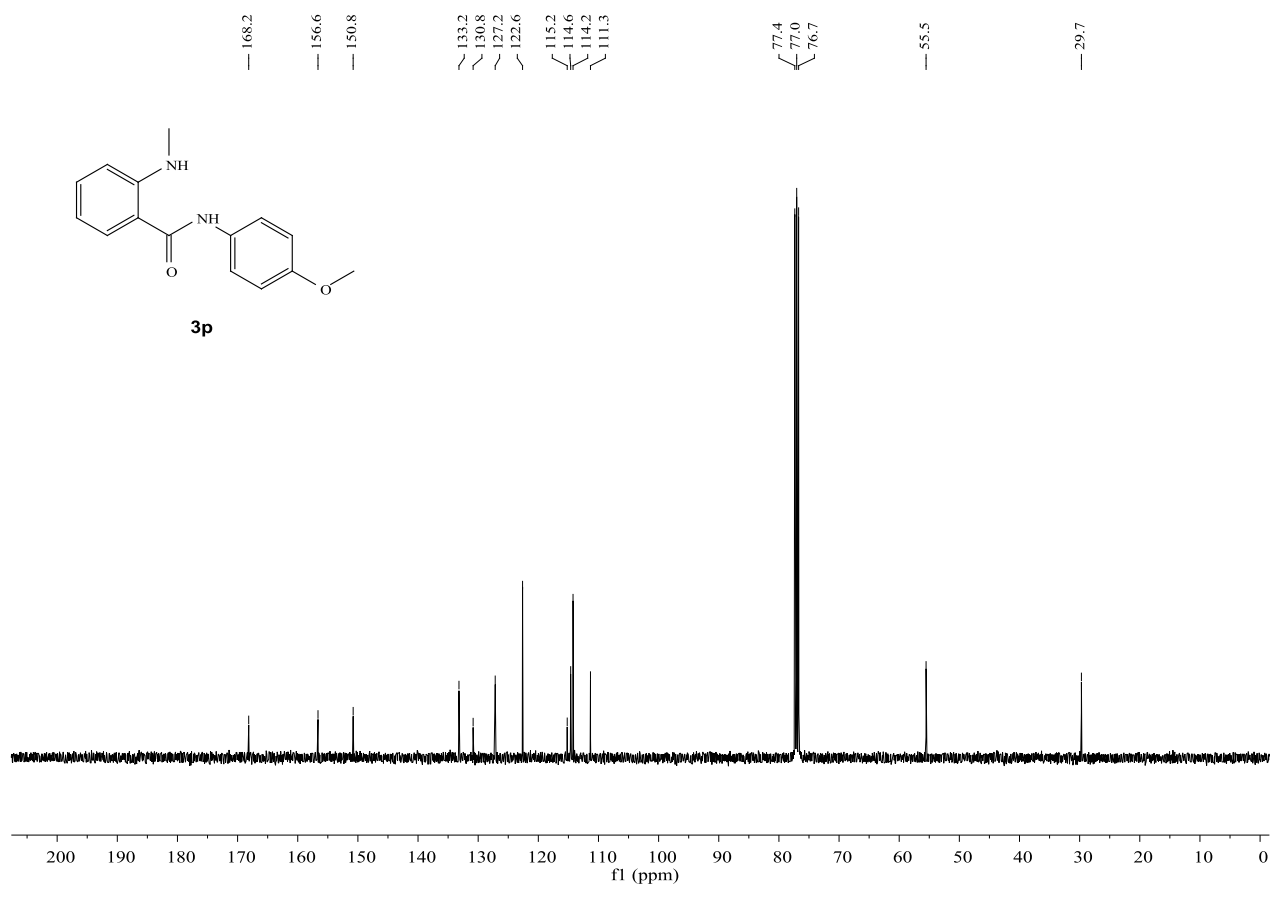
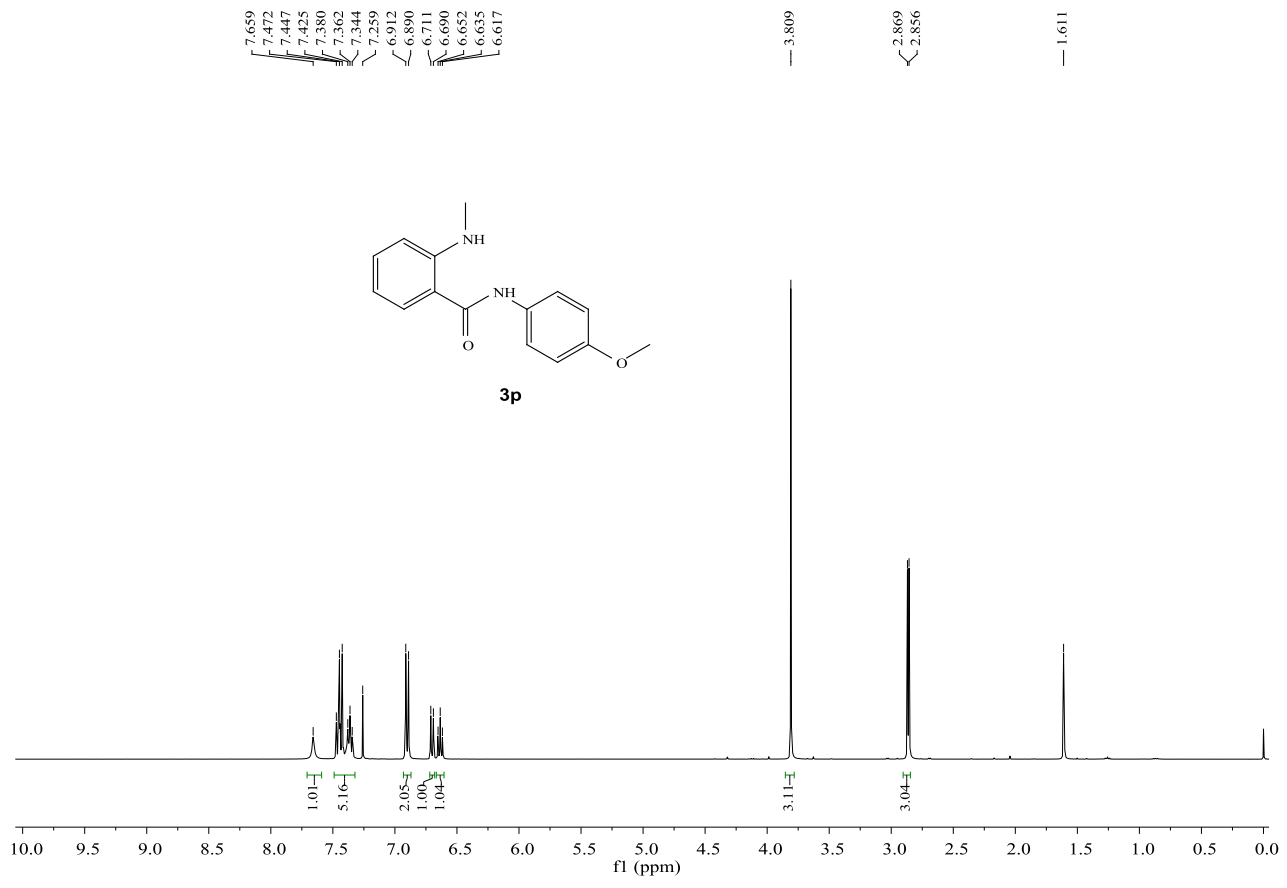


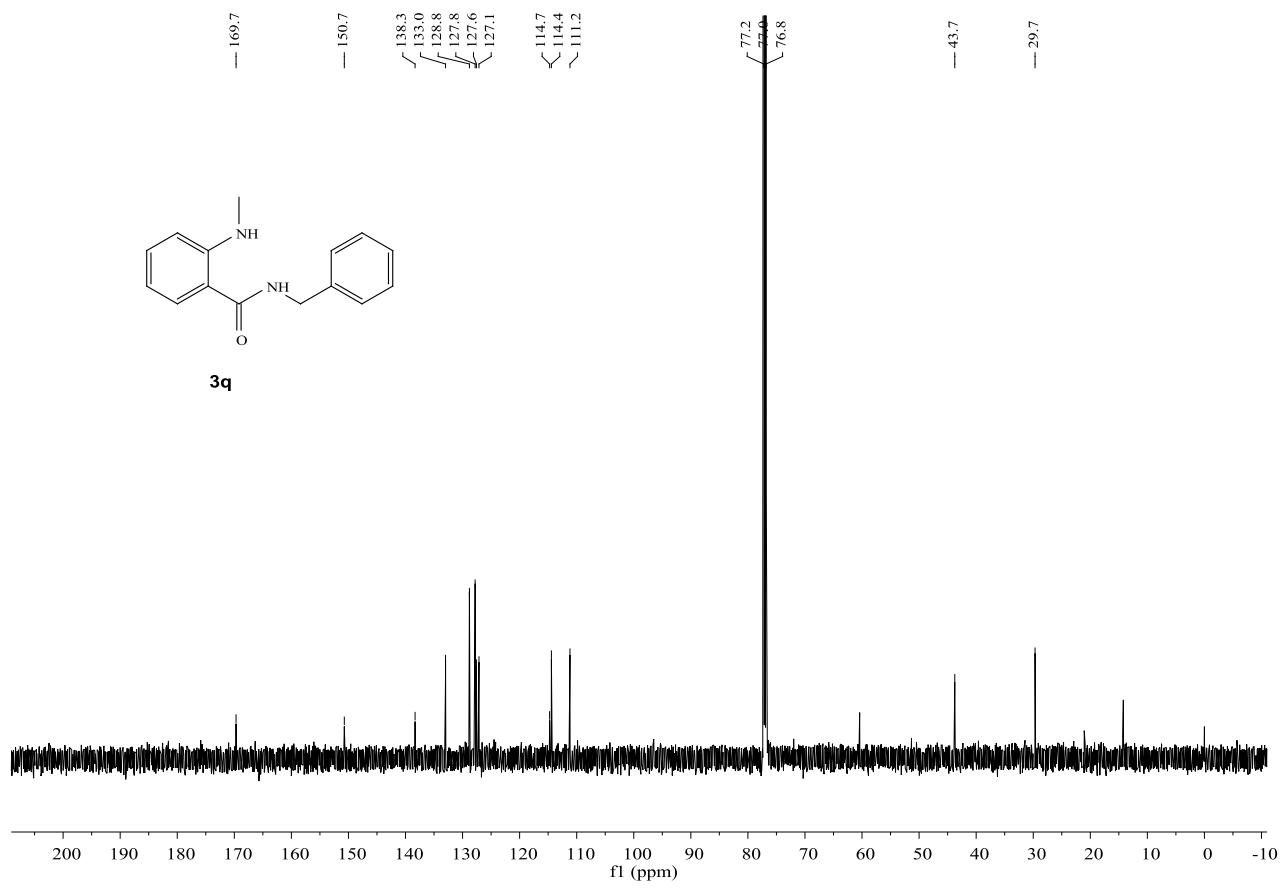
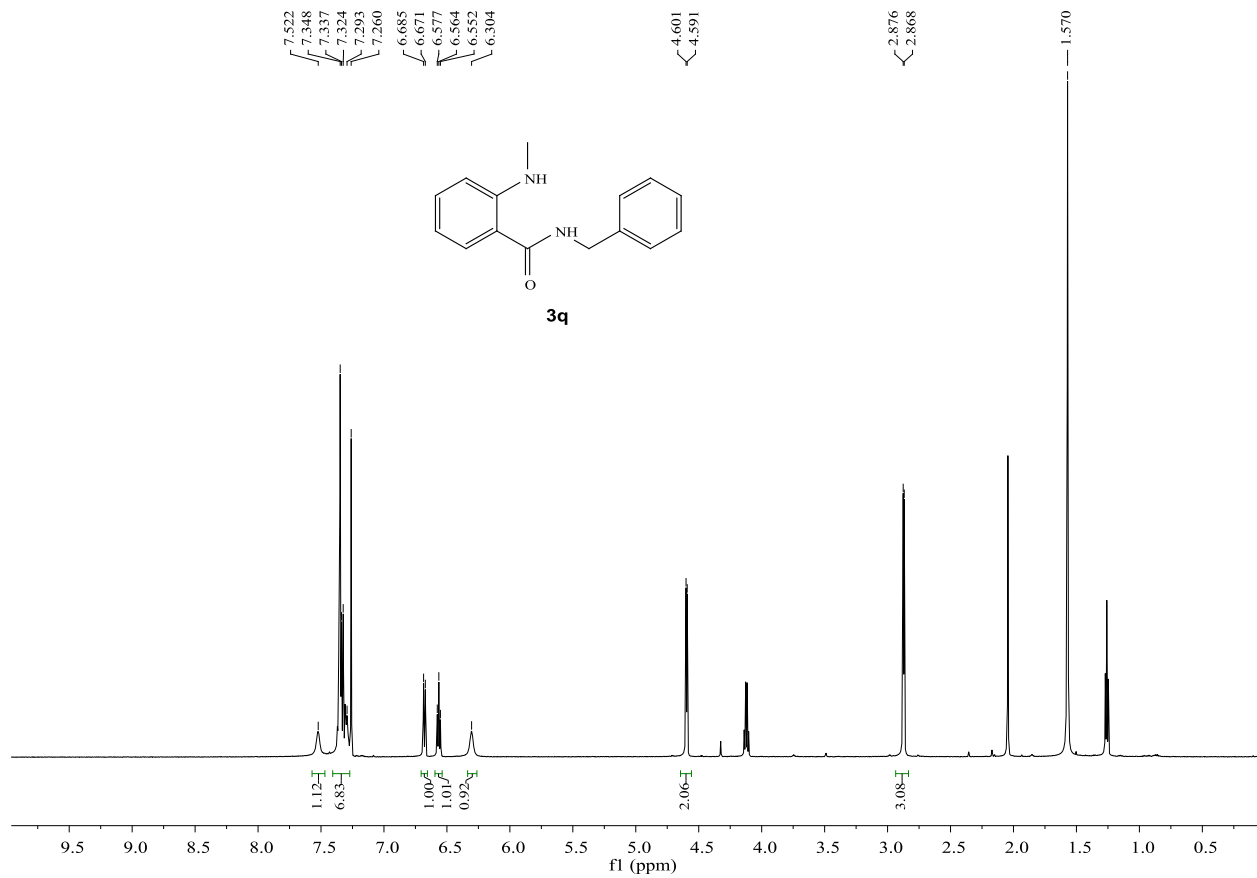


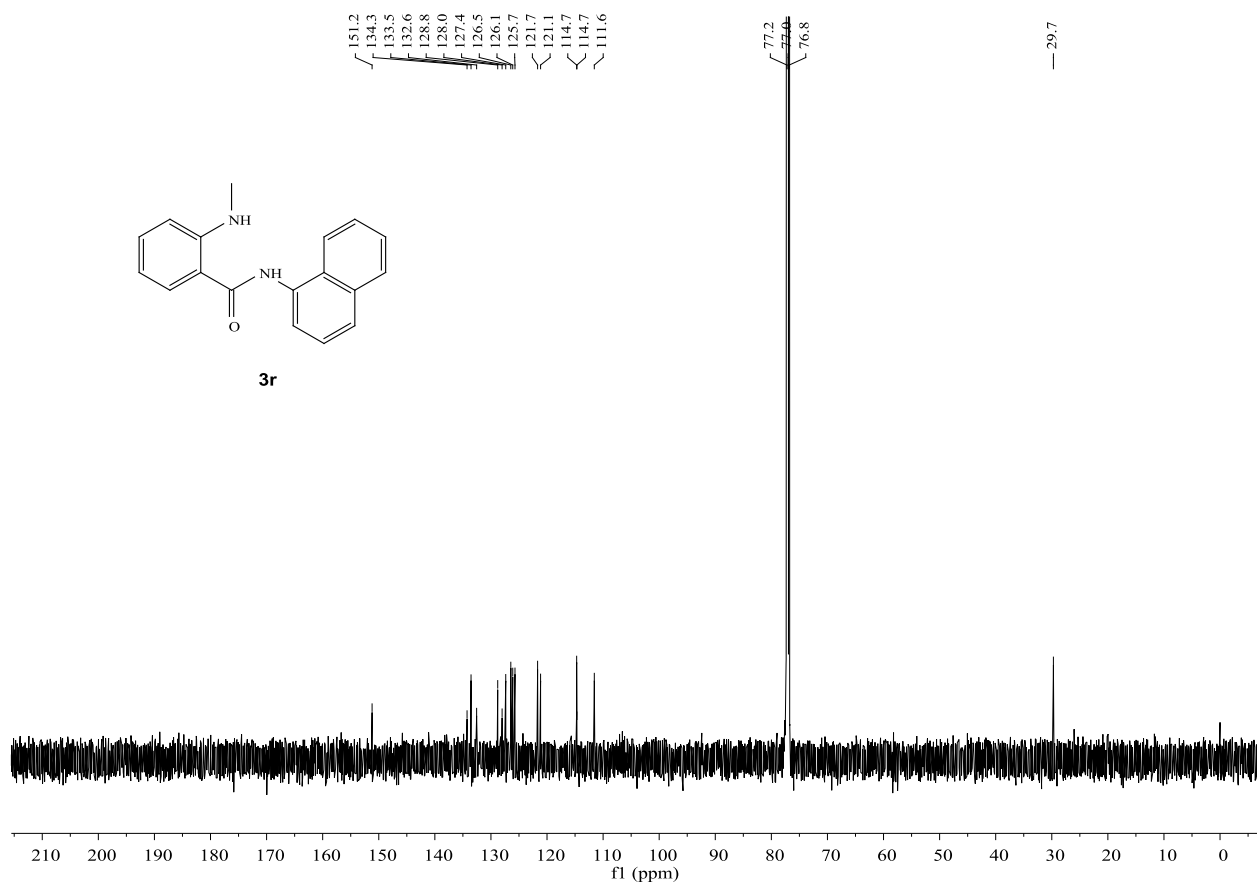
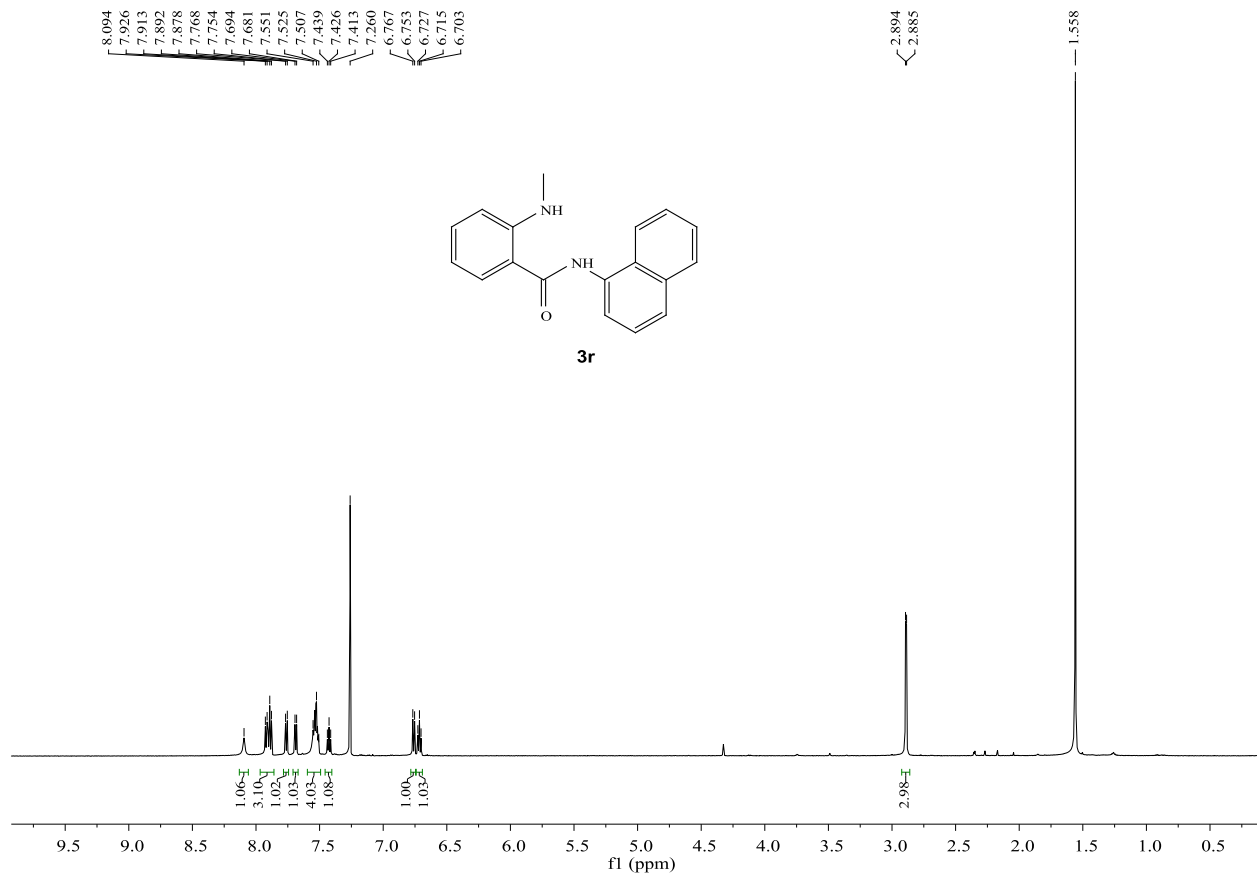


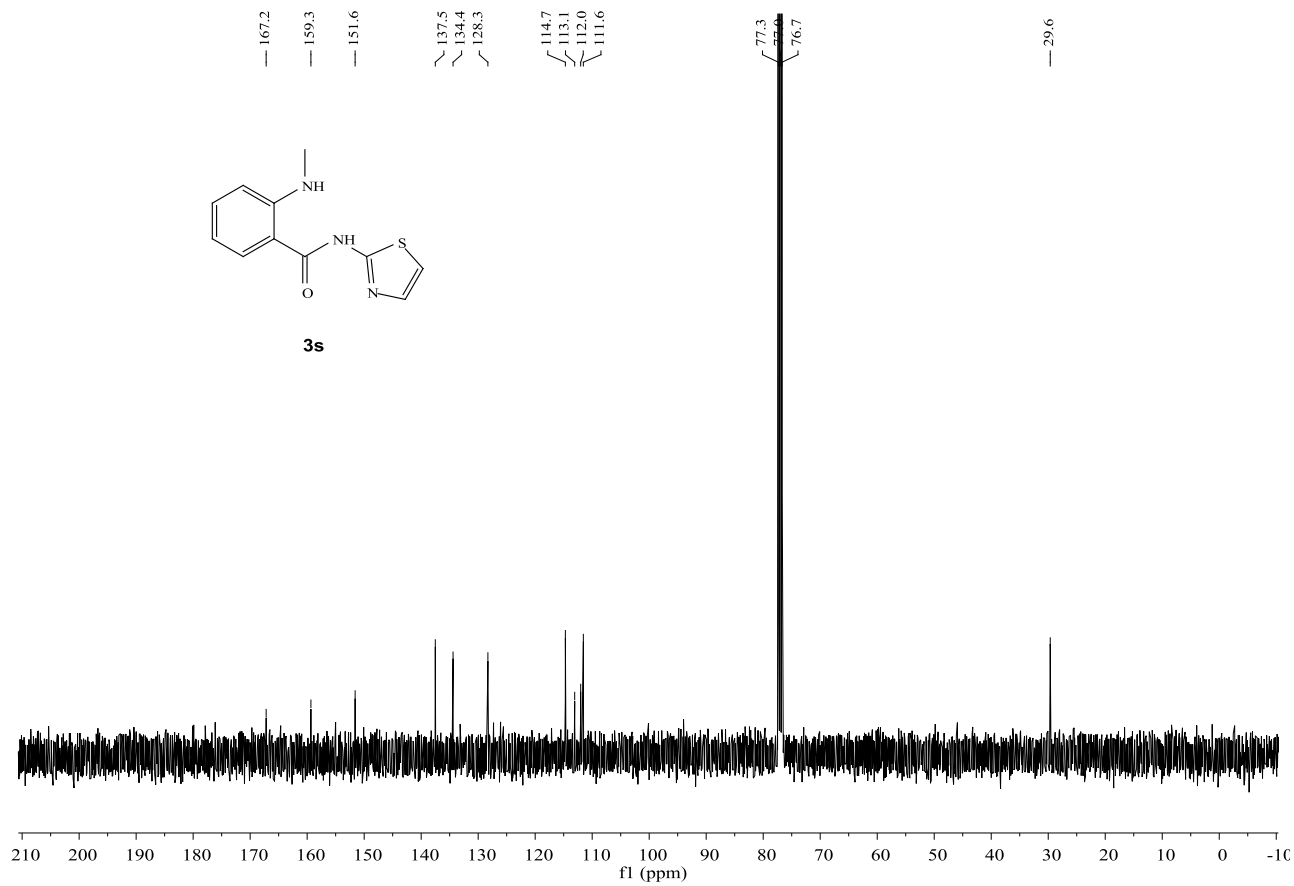
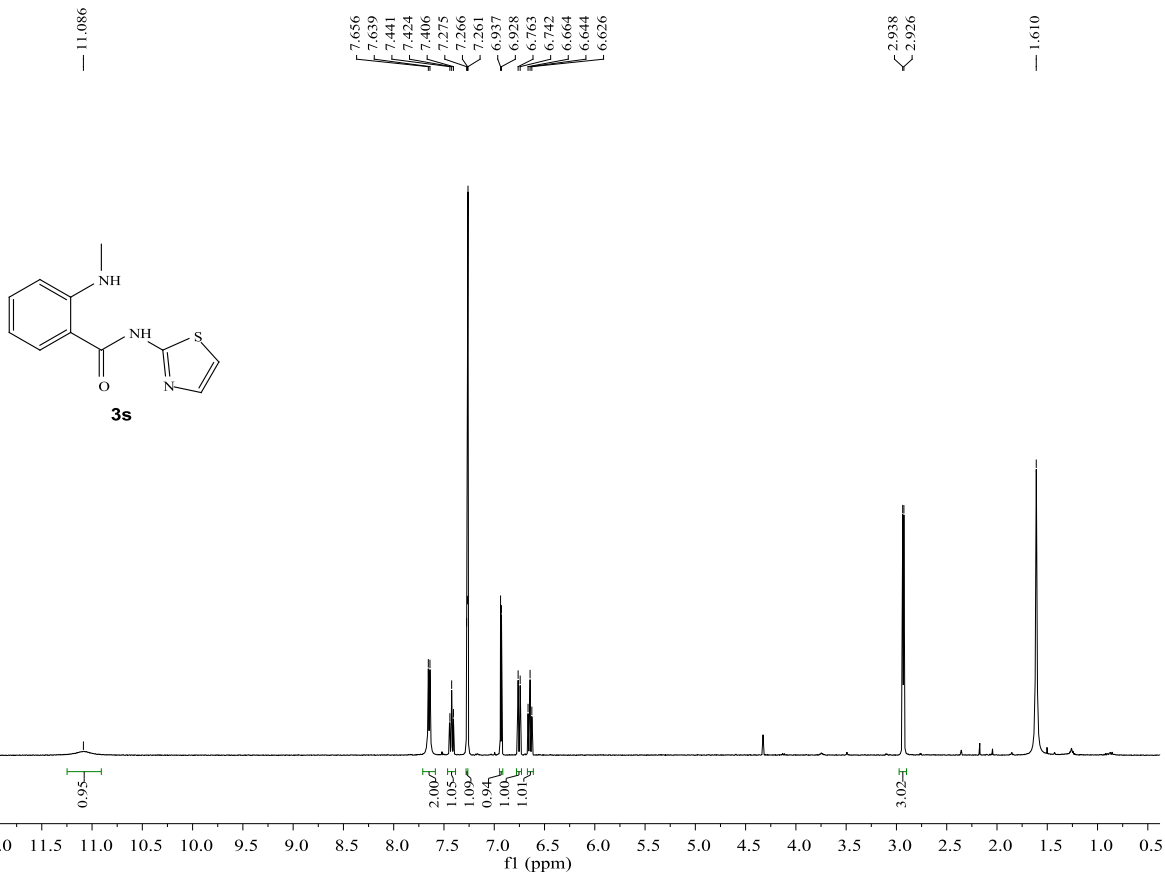


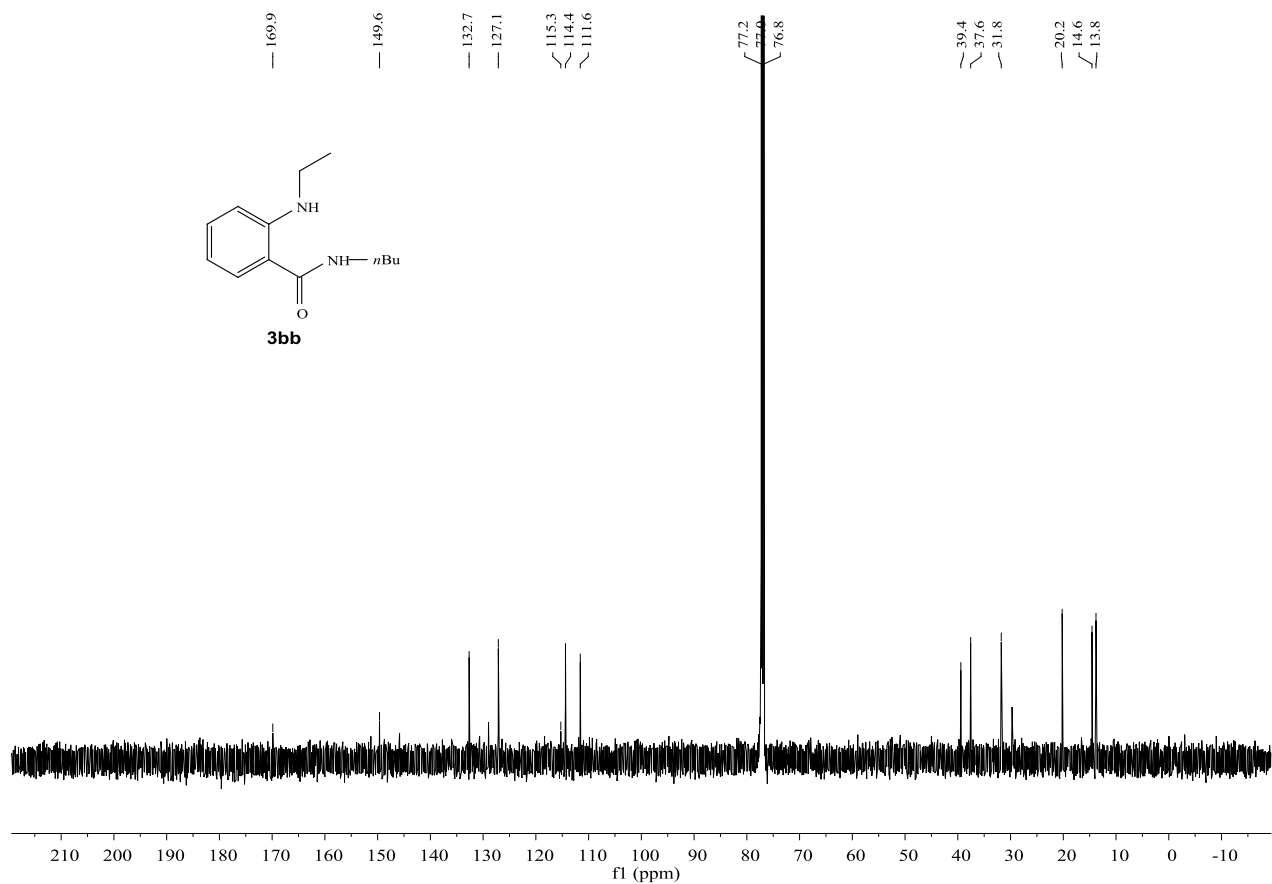
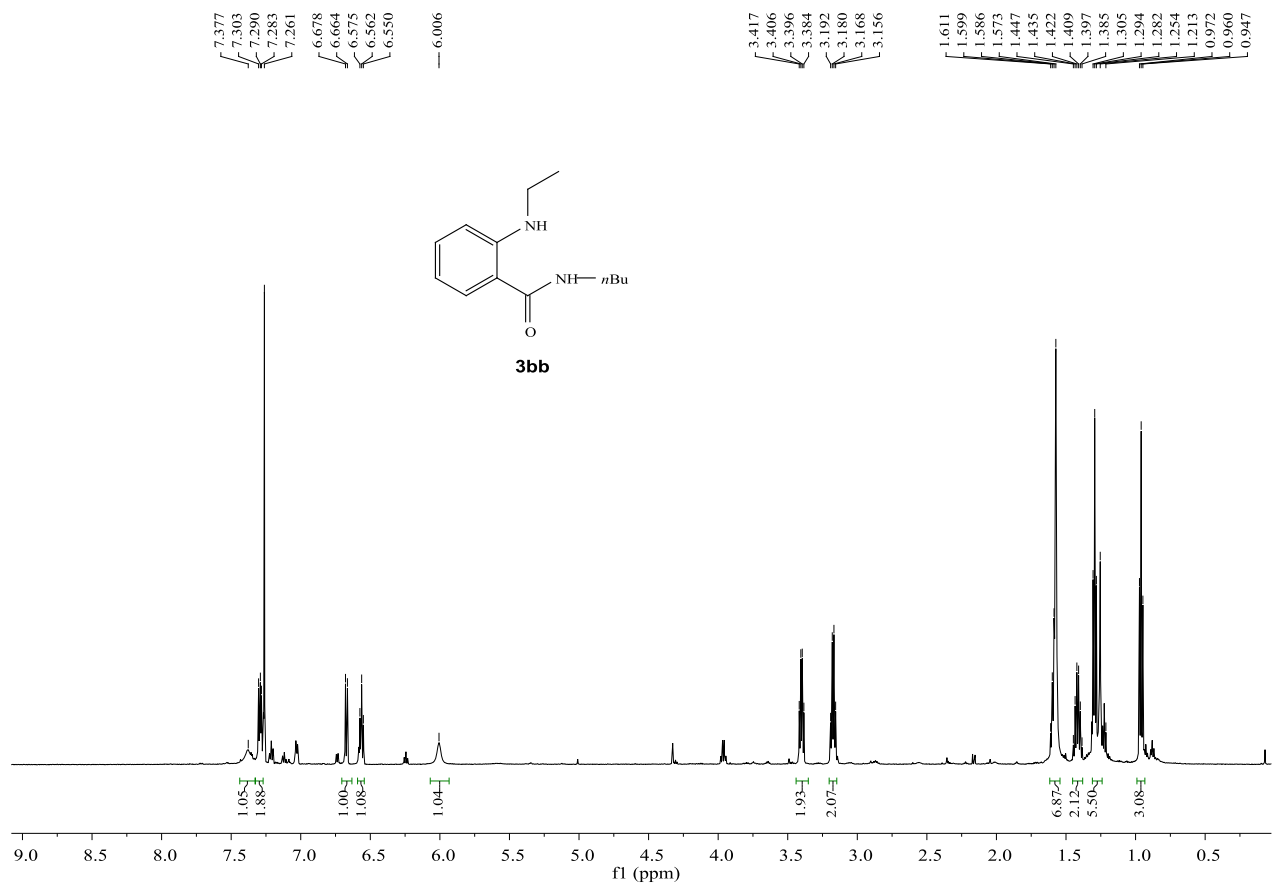


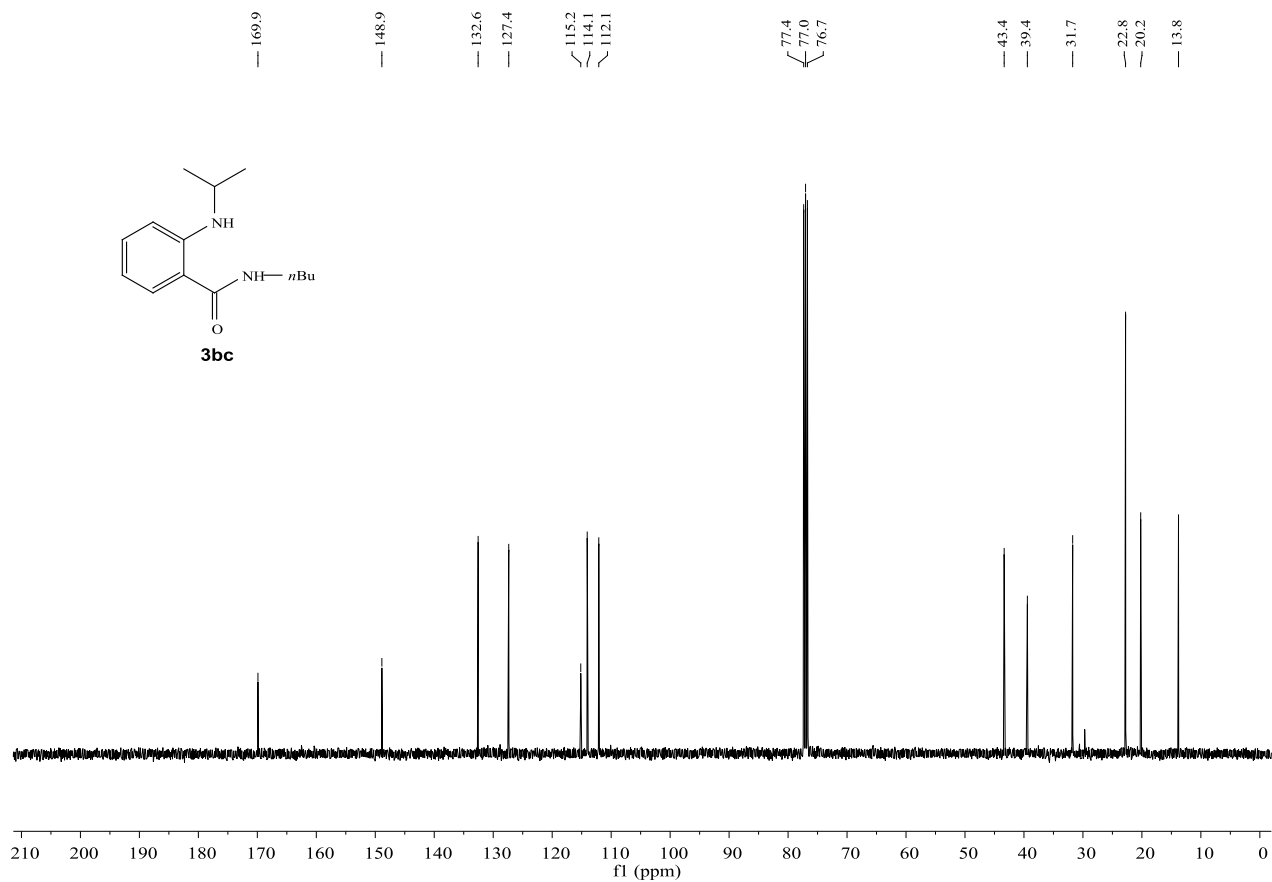
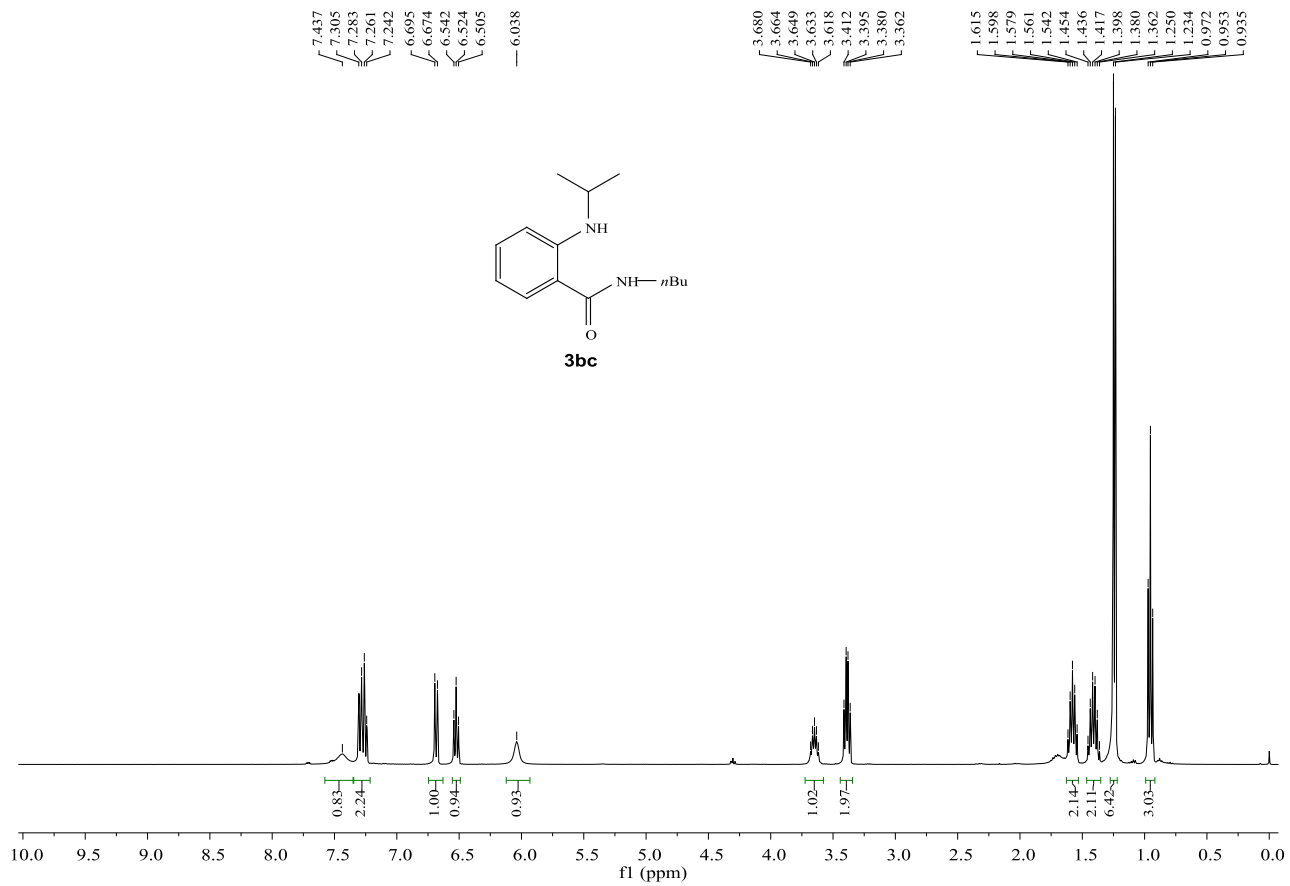


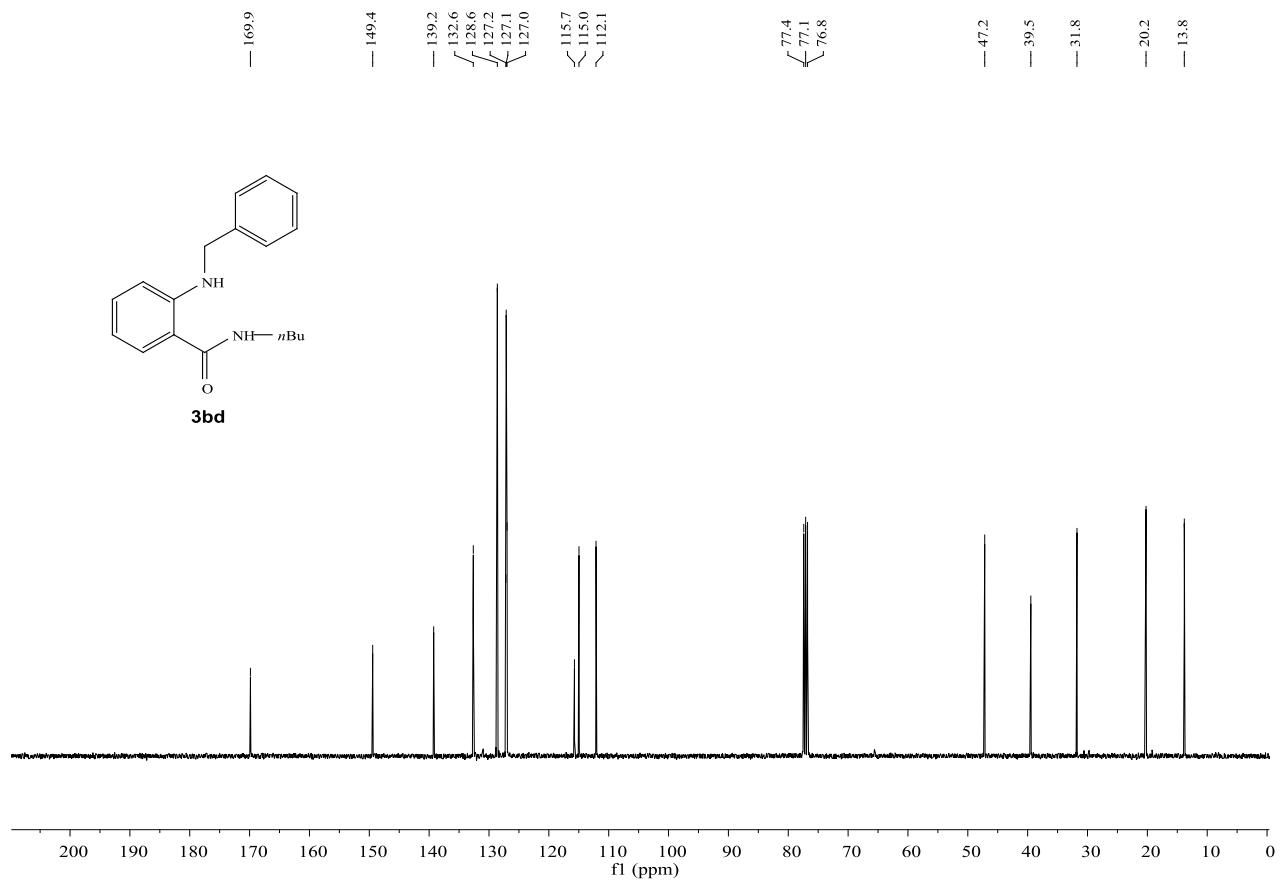
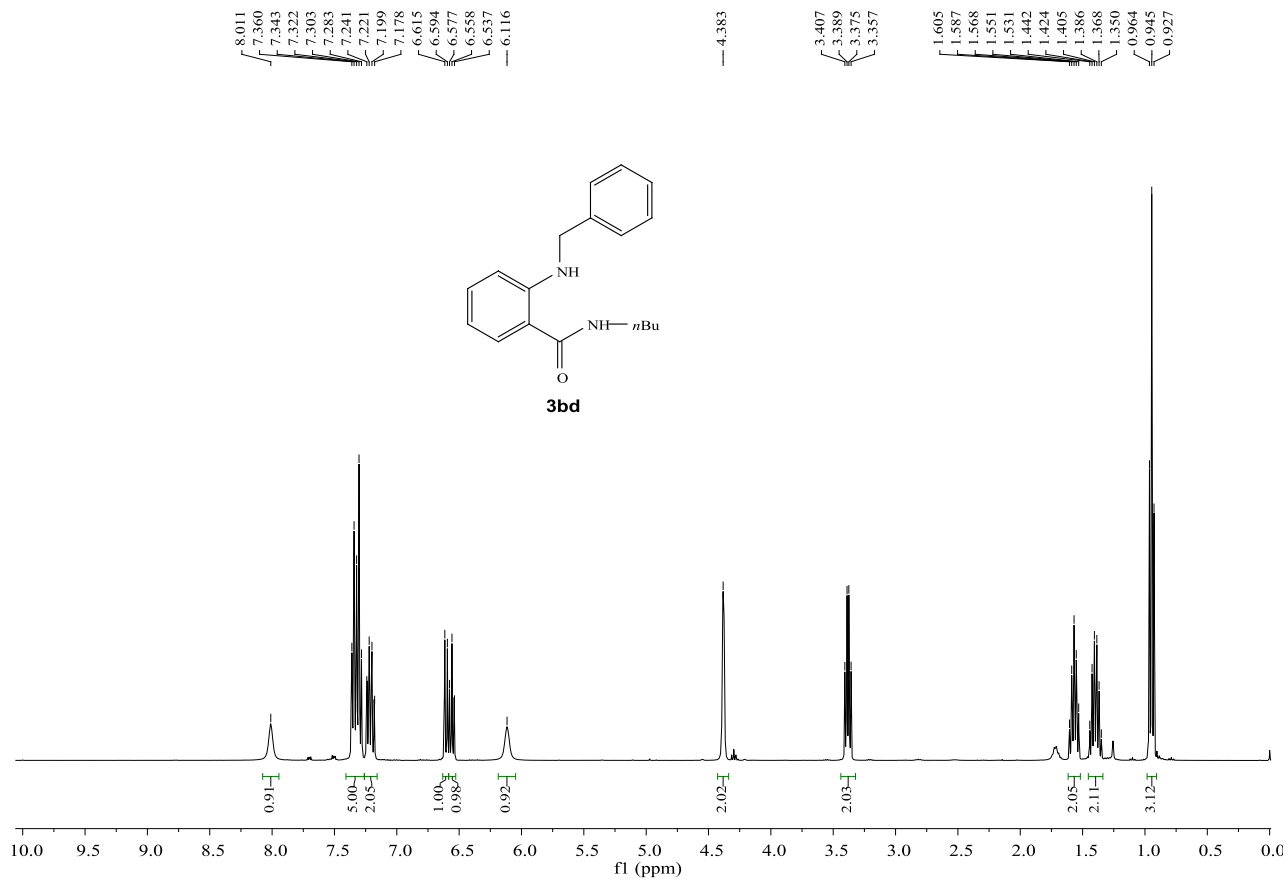


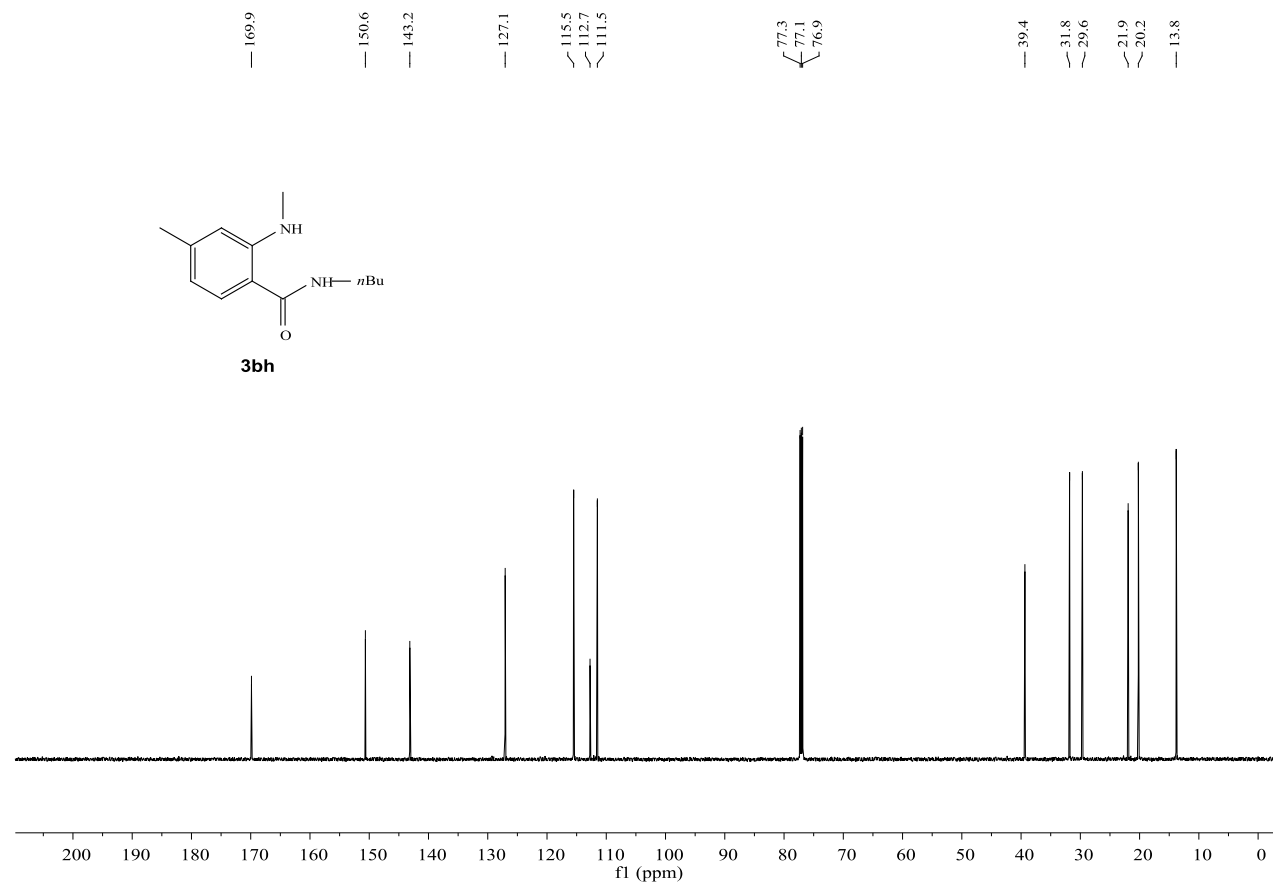
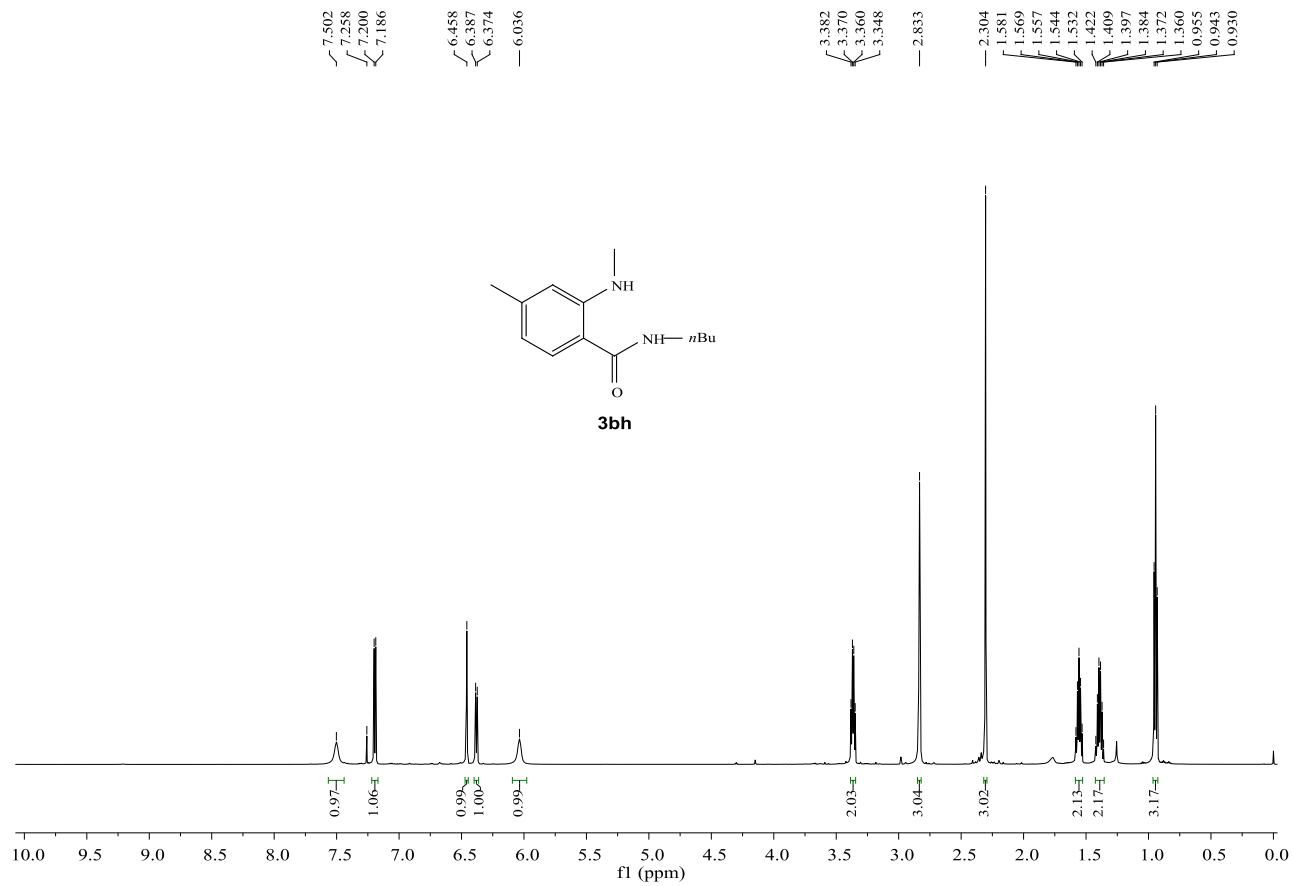


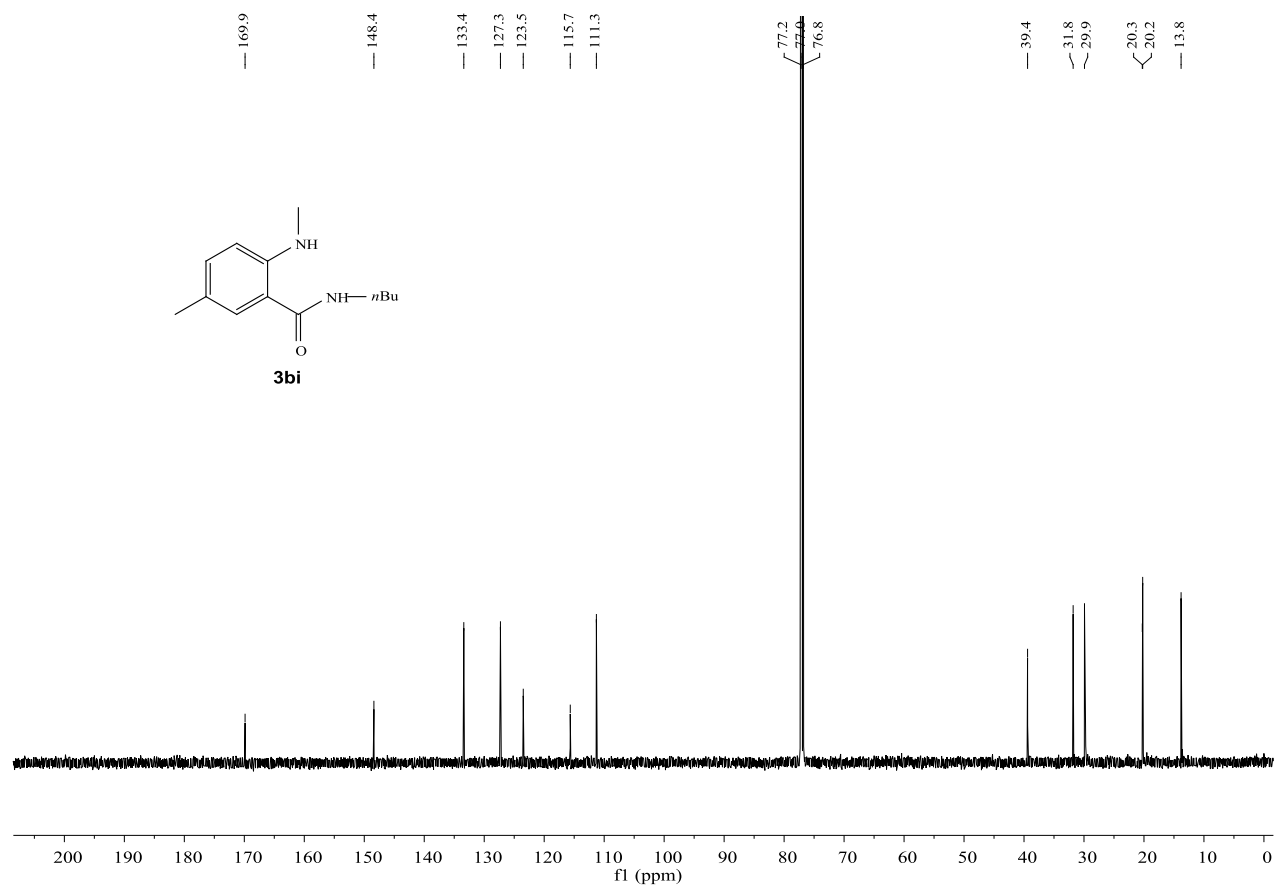
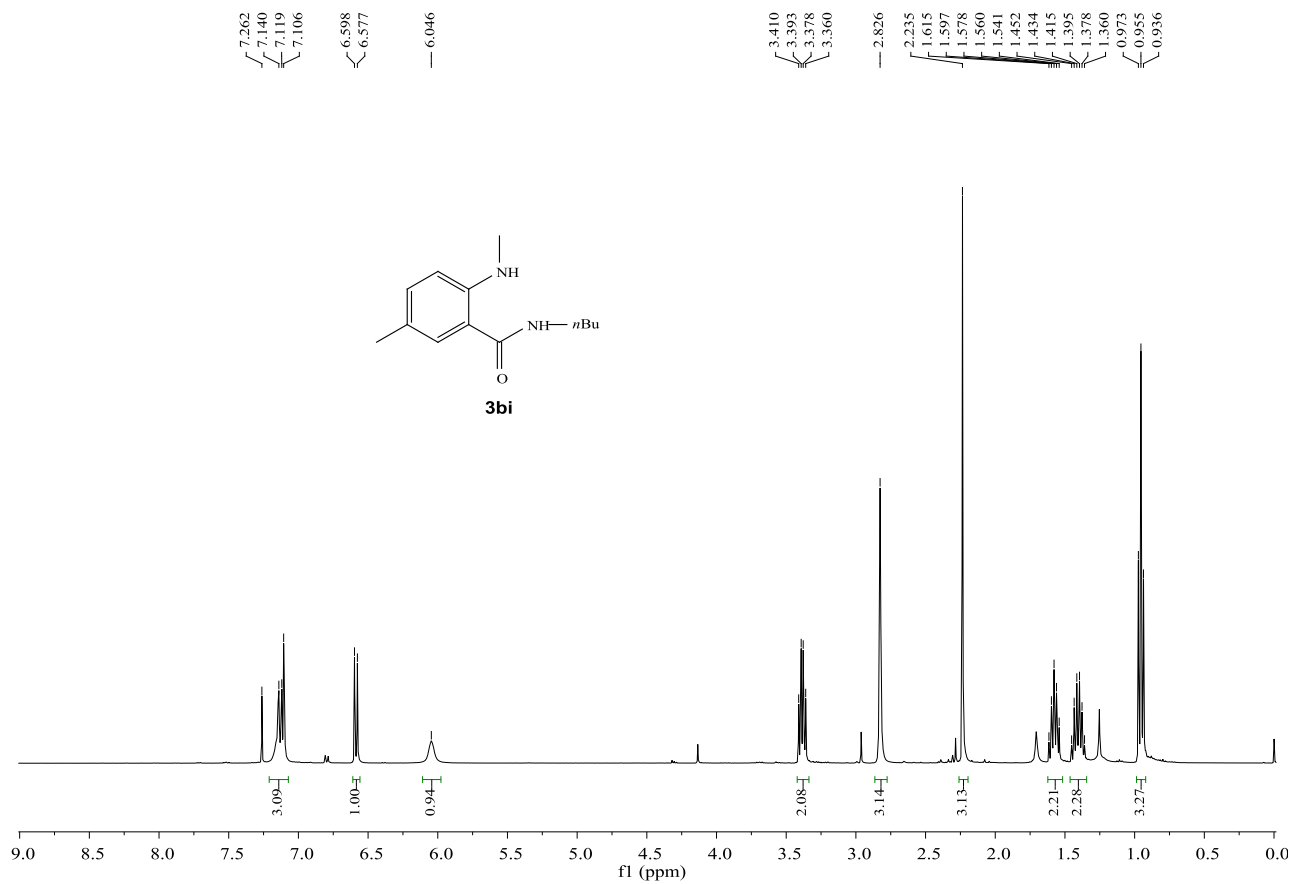


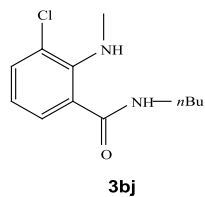






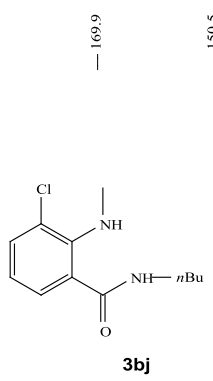
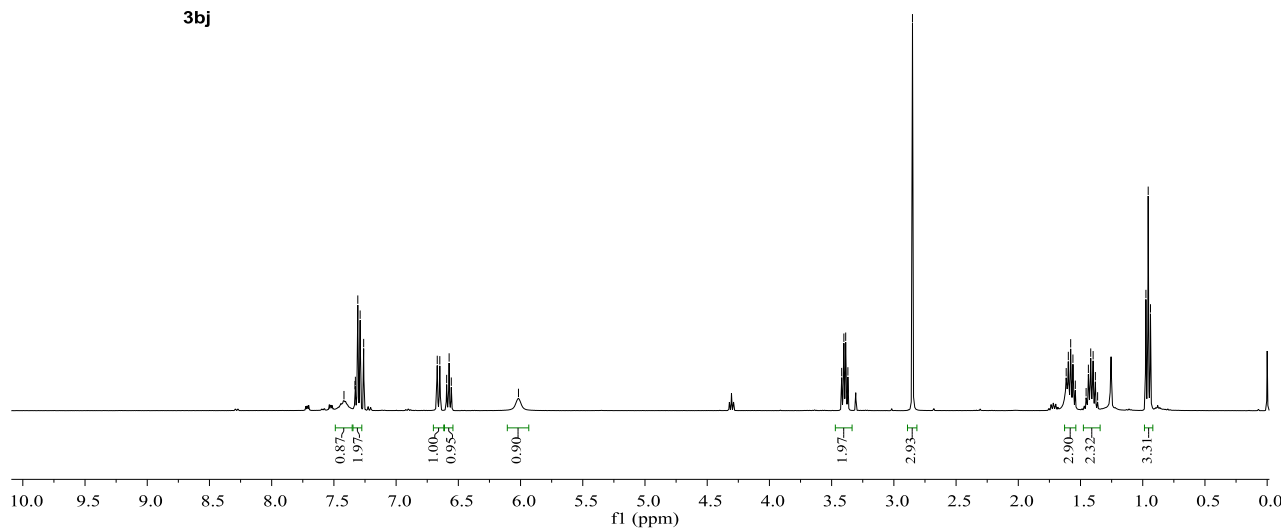




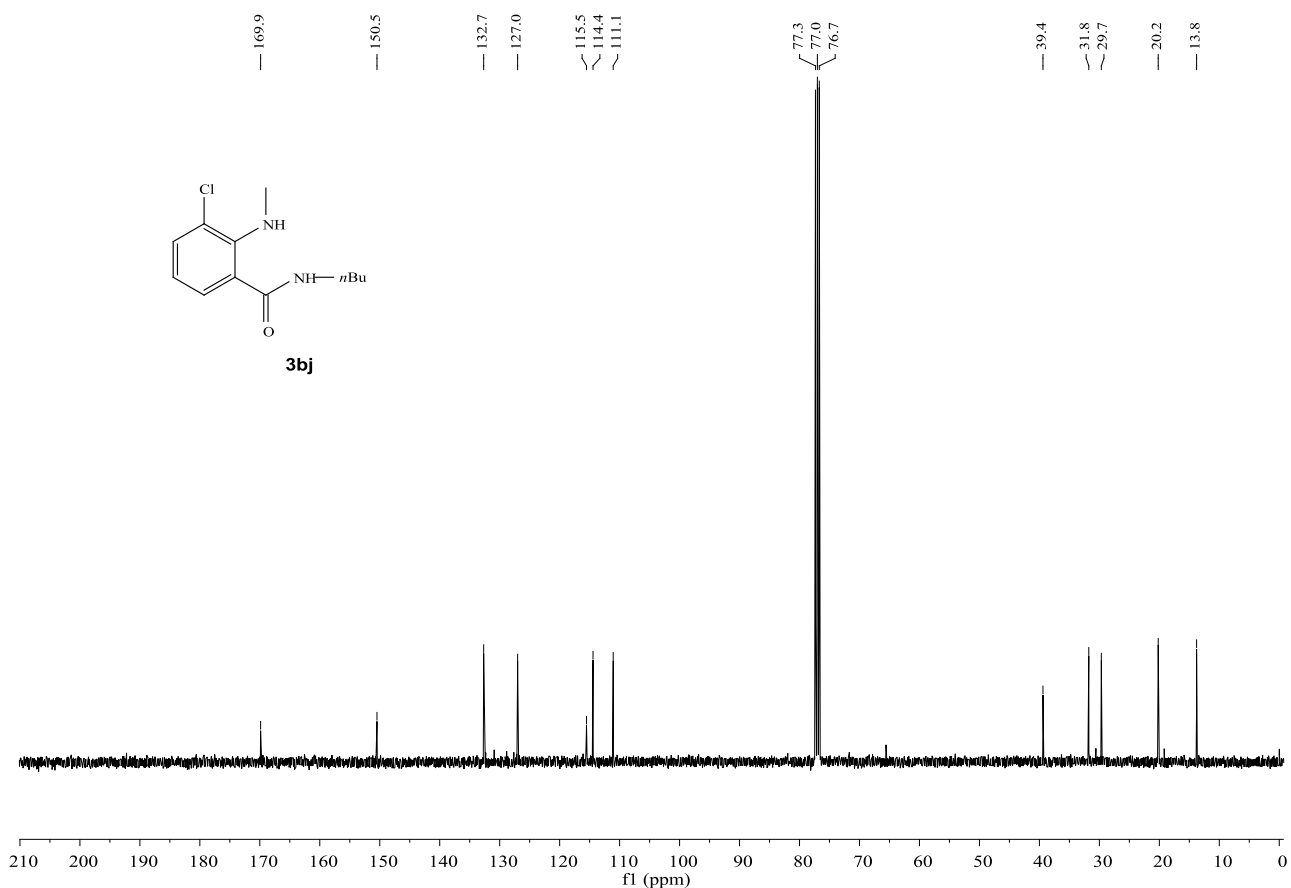


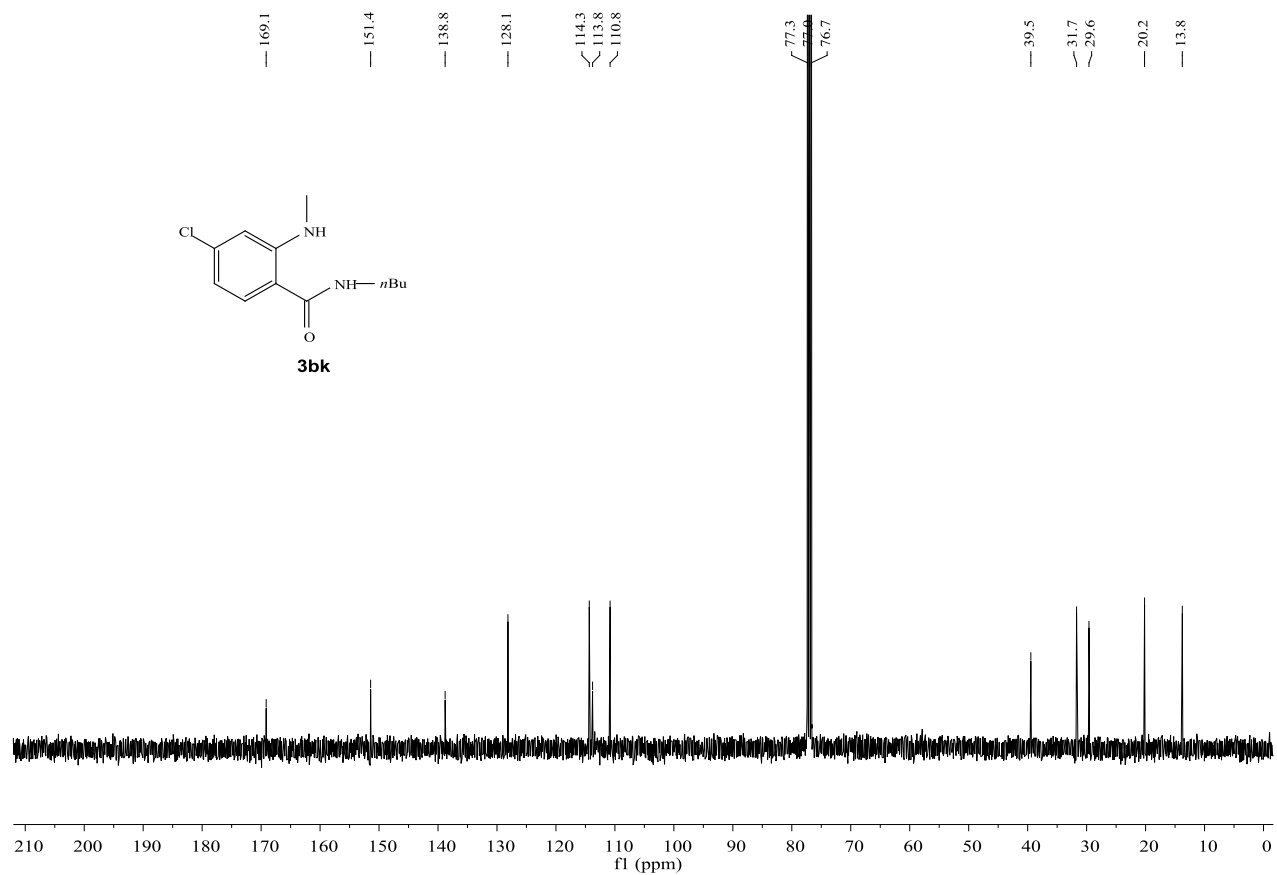
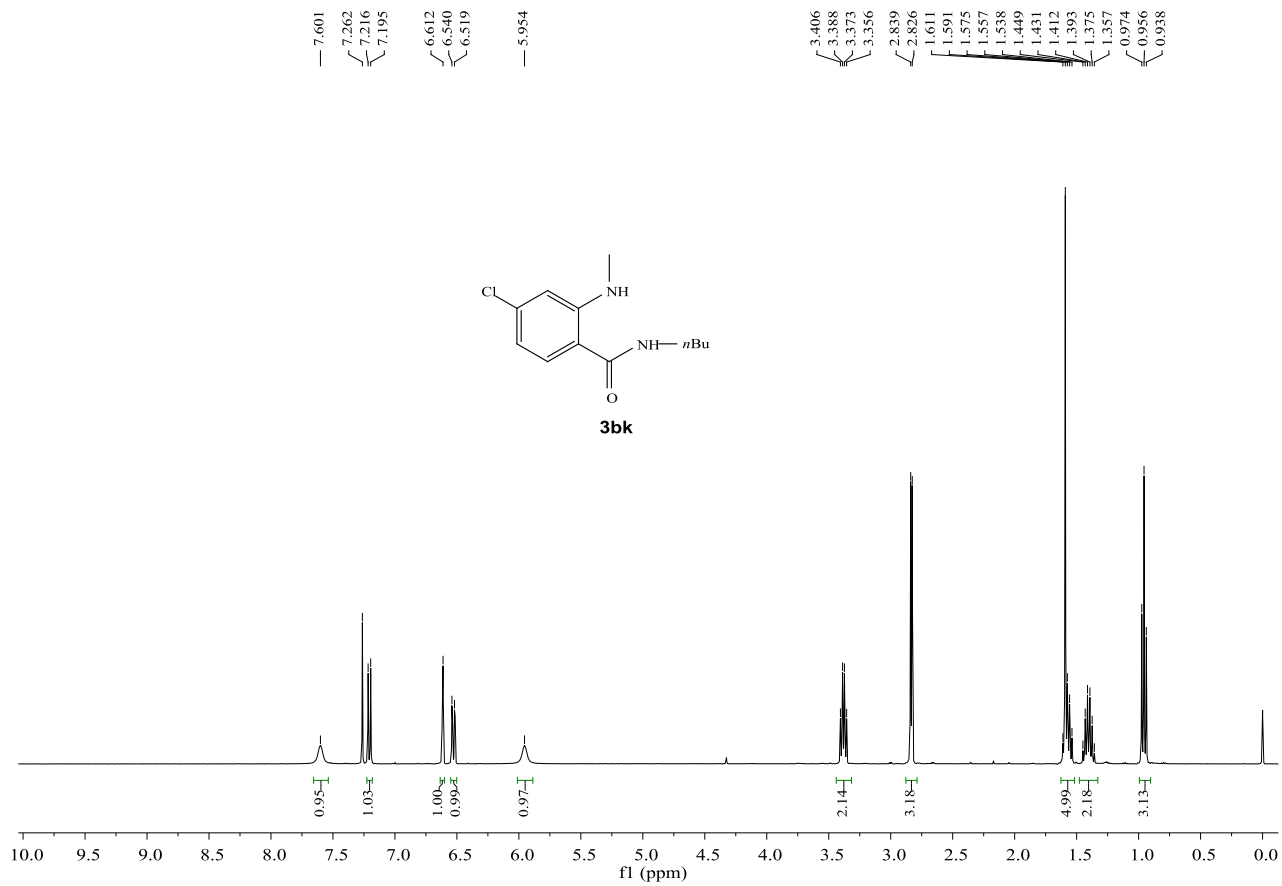
7.419
7.331
7.327
7.308
7.289
7.261
6.669
6.649
6.594
6.574
6.557
— 6.017

3.419
3.402
3.387
3.369
— 2.850
1.615
1.598
1.579
1.561
1.542
1.455
1.437
1.418
1.399
1.381
1.363
0.974
0.956
0.938

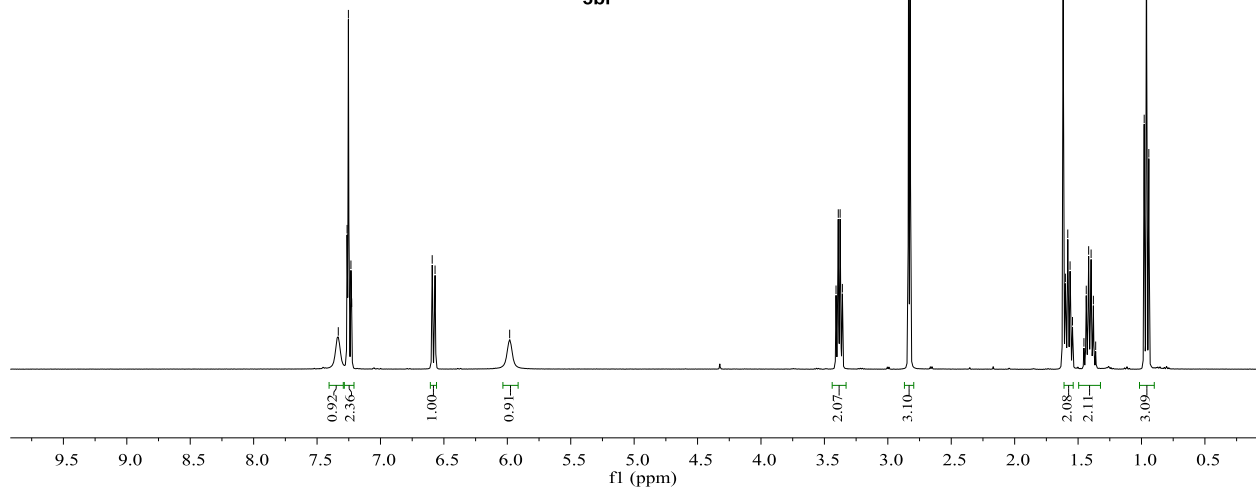
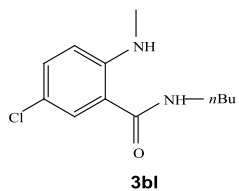


169.9
150.5
132.7
127.0
115.5
114.4
111.1
77.3
77.0
76.7
39.4
31.8
29.7
20.2
13.8

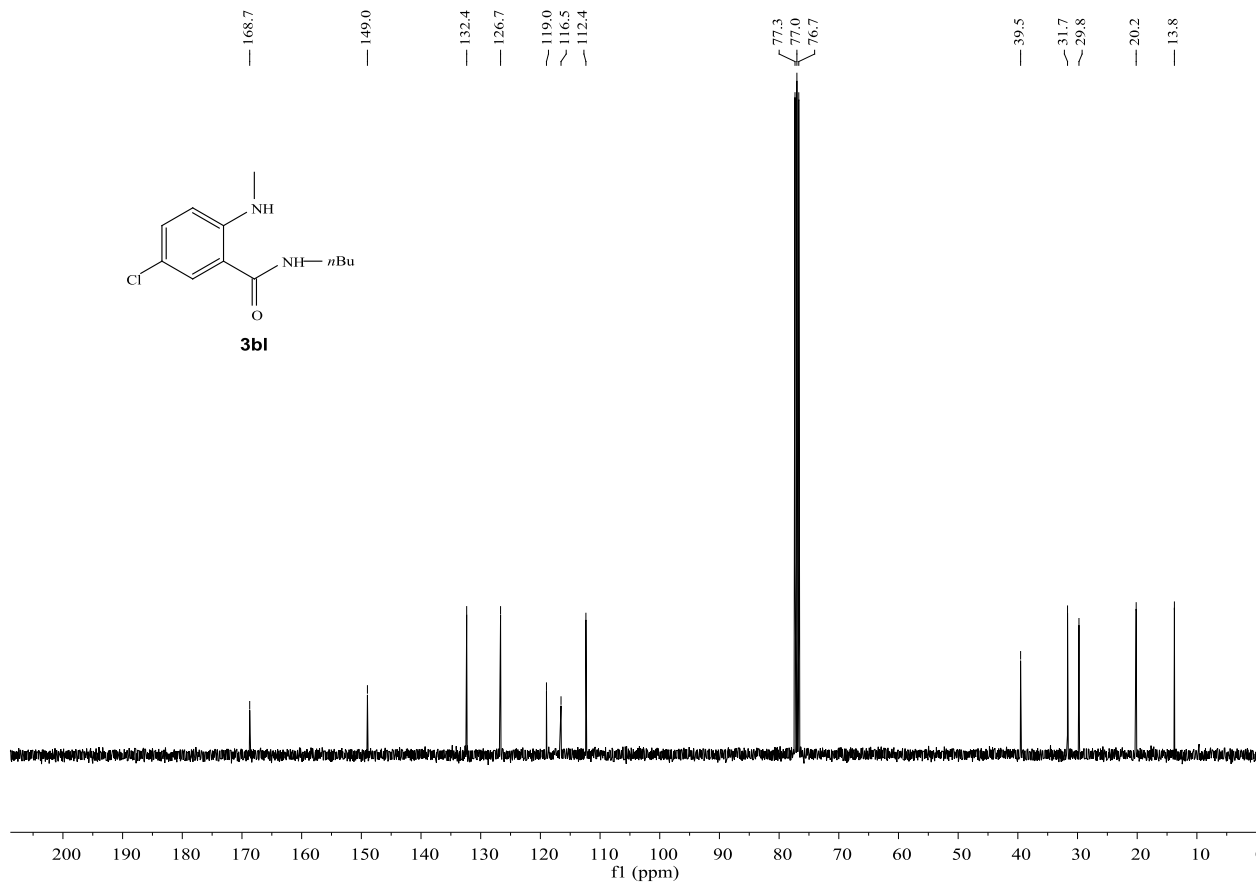
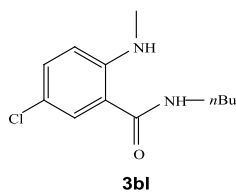




7.333
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7.253
7.233
7.227
6.592
6.570
5.982
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3.391
3.376
3.358
2.836
2.823
1.618
1.600
1.581
1.563
1.544
1.454
1.435
1.417
1.397
1.379
1.361
0.979
0.960
0.942



168.7
149.0
132.4
126.7
119.0
116.5
112.4
77.3
77.0
76.7
39.5
31.7
29.8
20.2
13.8



References

1. Correa, A.; Tellitu, I.; Dominguez, E.; SanMartin, R., *J. Org. Chem.* **2006**, *71*, 3501–3505.
2. Bogentoft, C.; Ericsson, O.; Kvist, M.; Danielsson, B., *Acta Pharm. Suecica* **1971**, *8*, 667–670.