Nickel-catalyzed Reductive Amidation of Aryl-triazine Ethers

Outline

1. Experimental section

1.1. General

Chemicals were purchased from Fluka, Merck and Aldrich chemical companies and used without further purification. The known products were characterized by comparison of their spectral and physical data with those reported in the literature. ^{1}H (400 and 500 MHz) and ^{13}C NMR (100 and 126 MHz) spectra were recorded on a Bruker Advance spectrometer in $CDCl_3$ solution with tetramethylsilane (TMS) as the internal standard. FT-IR spectroscopy (Shimadzu FT-IR 8300 spectrophotometer) was employed for characterization of the products. Melting points were determined in open capillary tubes in a Barnstead electro-thermal 9100 BZ circulating oil melting point apparatus. The reaction monitoring was accomplished by TLC on silica gel PolyGram SILG/UV254 plates. Column chromatography was carried out on columns of silica gel 60 (70–230 mesh).

1.2. General procedure for the synthesis of 2,4,6-triaryloxy-1,3,5-triazine (TAT)

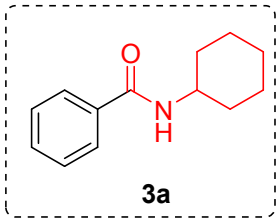
Into a canonical flask (50 mL), a mixture of phenol (3.3 mmol), and sodium hydride (3.6 mmol, 0.087 g) was stirred in THF (5 mL) for 1.5 h at room temperature. Then cyanuric chloride (1.0 mmol, 0.184 g) was added and the reaction media was refluxed for 5 h. The reaction was then allowed to cool down to room temperature. The precipitate was filtered, washed with THF and dried in vacuum to afford the product TAT.

1.3. General procedure for nickel-catalyzed reductive amidation of aryl-triazine ethers

An oven-dried reaction tube containing a stirring bar was charged with aryl-triazine ether (0.2 mmol), $NiCl_2$.dmg (10 mol%, 15 mg), dppf (20 mol%, 66 mg), Zn (1.2 mmol, 78 mg) and K_2HPO_4 (1.2 mmol, 210 mg). Afterward, the reaction tube was evacuated and back-filled with dry argon (this sequence was repeated three times). Dry DMF (2 mL) and isocyanate/carbodiimide (1.0 mmol) were subsequently added under argon atmosphere by syringe. The reaction mixture was warmed up to 90 °C and stirred for 24h. After completion of the reaction, the mixture was cool down to room temperature and quenched with 5% aq. HCl (2 mL) and it was extracted with ethyl acetate (3 x 10 mL). The organic layer was dried over anhydrous Na_2SO_4, filtered, and then concentrated in vacuum. The crude product was purified by column chromatography, eluting with n-hexane/ EtOAc, to afford the title compound.

2. Spectral data for synthesized compounds

2.1. N-cyclohexylbenzamide (3a)[1]



3a

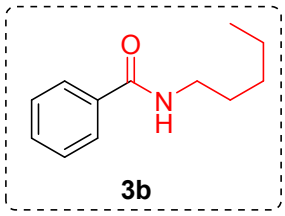
Yield: 91% (111 mg)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 – 7.70 (m, 1H), 7.49 – 7.44 (m, 1H), 7.40 (ddd, *J* = 6.5, 4.5, 1.4 Hz, 1H), 6.06 (s, 1H), 4.04 – 3.88 (m, 1H), 2.02 (dq, *J* = 11.7, 3.8 Hz, 1H), 1.85 – 1.70 (m, 1H), 1.69 – 1.58 (m, 1H), 1.49 – 1.35 (m, 1H), 1.32 – 1.12 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 166.71, 135.19, 131.26, 128.54, 126.91, 48.77, 33.28, 25.65, 24.98.

Anal. Cal. For $C_{13}H_{17}NO$ (203.29): C, 76.81; H, 8.43; N, 6.89; Found: C, 76.75; H, 8.37; N, 6.81.

2.2. N-pentylbenzamide (3b)[2]



3b

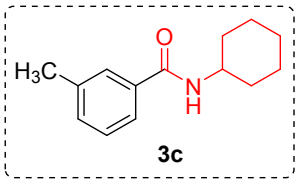
Yield: 88% (101 mg)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (ddd, *J* = 6.9, 3.4, 1.7 Hz, 1H), 7.45 – 7.40 (m, 1H), 7.37 – 7.32 (m, 1H), 6.76 (s, 1H), 3.38 (dd, *J* = 12.1, 7.3 Hz, 1H), 1.61 – 1.52 (m, 1H), 1.35 – 1.26 (m, 2H), 0.89 – 0.83 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 167.71, 134.79, 131.19, 128.39, 126.96, 40.15, 29.31, 29.15, 22.37, 13.95.

Anal. Cal. For $C_{12}H_{17}NO$ (191.27): C, 75.35; H, 8.96; N, 7.32; Found: C, 75.28; H, 8.91; N, 7.25.

2.3. N-cyclohexyl-3-methylbenzamide (3c)[3]



3c

Yield: 86% (112 mg)

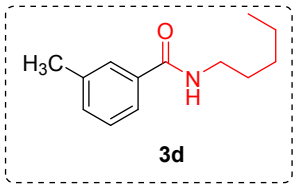
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (dt, *J* = 3.2, 1.3 Hz, 1H), 7.53 – 7.49 (m, 1H), 7.33 – 7.28 (m, 1H), 5.92 (s, 1H), 4.04 – 3.91 (m, 1H), 2.40 (s, 1H), 2.09 – 1.97 (m, 1H), 1.76 (dt, *J* = 13.5, 3.9 Hz, 1H), 1.71 – 1.62 (m, 1H), 1.51 – 1.36 (m, 1H), 1.30 – 1.15 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 166.89, 138.46, 135.28, 132.02, 128.47, 127.69, 123.84, 48.70, 33.37, 25.72, 25.01, 21.43.

Anal. Cal. For $C_{14}H_{19}NO$ (217.31): C, 77.38; H, 8.81; N, 6.45; Found: C, 77.30; H, 8.75; N, 6.38.

2.4. 3-methyl-N-pentylbenzamide (3d)

[1] A. Correa and R. Martin, *J. Am. Chem. Soc.* 2014, **136**, 7253–7256.
[2] R. N. Lima, V. R. Silva, L. de S. Santos, D. P. Bezerra, M. B. P. Soares, A. L. M. Porto , *RSC Adv.* , 2017 , **7** , 56566.
[3] C. Chen, Y. Miao, K. D. Winter, H.-J. Wang, P. Demeyere, Y. Yuan, and F. Verpoort, *Molecules* 2018, **23**, 2413.



3d

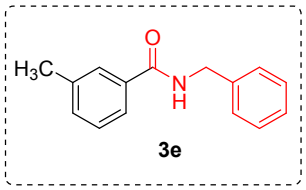
Yield: 85% (104 mg)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (td, *J* = 2.0, 1.2 Hz, 1H), 7.54 – 7.50 (m, 1H), 7.26 – 7.24 (m, 2H), 6.43 (s, 1H), 3.40 (td, *J* = 7.2, 5.8 Hz, 2H), 2.34 (d, *J* = 0.5 Hz, 3H), 1.63 – 1.54 (m, 2H), 1.32 (ddt, *J* = 7.2, 5.5, 1.7 Hz, 4H), 0.91 – 0.85 (m, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 167.83, 138.30, 134.86, 131.97, 128.34, 127.70, 123.87, 40.11, 29.38, 29.17, 22.39, 21.30, 13.97.

Anal. Cal. For $C_{13}H_{19}NO$ (205.30): C, 76.06; H, 9.33; N, 6.82; Found: C, 75.98; H, 9.25; N, 6.76.

2.5. N-benzyl-3-methylbenzamide (3e)[4]



3e

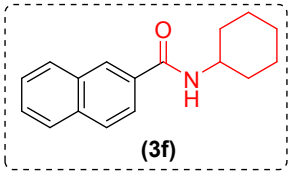
Yield: 88% (119 mg)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (dq, *J* = 1.5, 1.0 Hz, 1H), 7.59 – 7.55 (m, 1H), 7.37 – 7.35 (m, 4H), 7.31 – 7.29 (m, 3H), 6.46 (s, 1H), 4.64 (d, *J* = 5.6 Hz, 2H), 2.39 (t, *J* = 0.5 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 167.66, 138.53, 138.35, 134.47, 132.34, 130.72, 128.85, 128.53, 128.00, 127.81, 127.67, 127.35, 124.00, 44.21, 21.39.

Anal. Cal. For $C_{15}H_{15}NO$ (225.29): C, 79.97; H, 6.71; N, 6.22; Found: C, 79.90; H, 6.62; N, 6.16.

2.6. N-cyclohexyl-2-naphthamide (3f)



(3f)

Yield: 84% (127 mg)

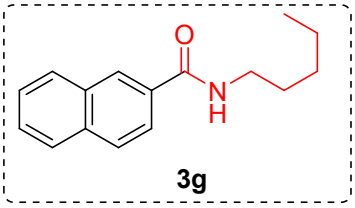
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35 – 8.19 (m, 1H), 7.99 – 7.77 (m, 4H), 7.53 (m, 2H), 6.16 (d, *J* = 7.4 Hz, 1H), 4.14 – 3.96 (m, 1H), 2.13 – 2.02 (m, 2H), 1.78 (ddd, *J* = 13.7, 7.4, 3.4 Hz, 2H), 1.72 – 1.61 (m, 1H), 1.52 – 1.37 (m, 2H), 1.35 – 1.10 (m, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 166.77, 134.74, 132.75, 132.43, 128.93, 128.45, 127.81, 127.56, 127.24, 126.76, 123.72, 48.93, 33.38, 25.70, 25.03.

Anal. Cal. For $C_{17}H_{19}NO$ (253.35): C, 80.60; H, 7.56; N, 5.53; Found: C, 80.52; H, 7.50; N, 5.45.

2.7. N-pentyl-2-naphthamide (3g)

[4] S. L. Yedage, D. S. D'silvaa and B. M. Bhanage, *RSC Adv.*, 2015, **5**, 80441-80449



3g

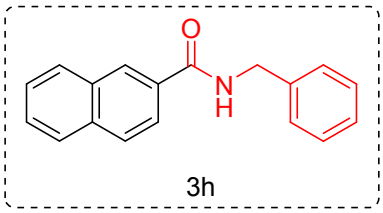
Yield: 80% (116 mg)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 (d, *J* = 1.5 Hz, 1H), 7.94 – 7.79 (m, 5H), 7.58 – 7.50 (m, 2H), 6.30 (s, 1H), 3.51 (td, *J* = 7.2, 5.7 Hz, 2H), 1.67 (tdd, *J* = 7.2, 6.0, 3.8 Hz, 2H), 1.45 – 1.32 (m, 5H), 0.99 – 0.88 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 167.64, 134.78, 132.78, 132.22, 128.97, 128.51, 127.83, 127.63, 127.30, 126.80, 123.68, 40.33, 29.53, 29.29, 22.50, 14.07.

Anal. Cal. For $C_{16}H_{19}NO$ (241.15): C, 79.63; H, 7.94; N, 5.80; Found: C, 79.55; H, 7.88; N, 5.73.

2.8. N-pentyl-2-naphthamide (3h)



3h

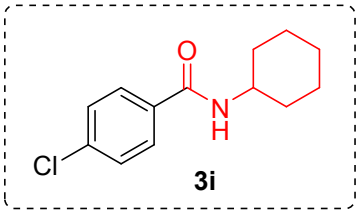
Yield: 83% (130 mg)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (s, 1H), 7.88 (m, 2H), 7.59 – 7.50 (m, 1H), 7.43 – 7.28 (m, 2H), 6.62 (s, 1H), 4.71 (d, *J* = 5.6 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 167.51, 138.33, 134.88, 132.89, 132.74, 131.70, 129.00, 128.91, 128.58, 128.08, 127.83, 127.75, 127.54, 126.85, 123.68, 44.39.

Anal. Cal. For $C_{18}H_{15}NO$ (261.32): C, 82.73; H, 5.79; N, 5.36; Found: C, 82.66; H, 5.71; N, 5.27.

2.9. 4-chloro-N-cyclohexylbenzamide (3i)[5]



3i

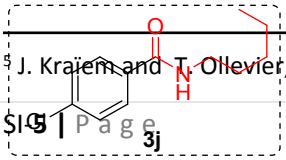
Yield: 89% (127 mg)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 – 7.65 (m, 1H), 7.40 – 7.36 (m, 1H), 5.94 (d, *J* = 5.3 Hz, 1H), 4.01 – 3.91 (m, 1H), 2.07 – 1.97 (m, 1H), 1.81 – 1.70 (m, 1H), 1.69 – 1.60 (m, 1H), 1.46 – 1.37 (m, 1H), 1.30 – 1.17 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 165.63, 137.54, 133.58, 128.83, 128.38, 48.95, 33.30, 25.64, 24.98.

Anal. Cal. For $C_{13}H_{16}ClNO$ (237.73): C, 65.68; H, 6.78; N, 5.89; Found: C, 65.60; H, 6.72; N, 5.81.

2.10. 4-chloro-N-pentylbenzamide (3j)



3j

[5] J. Kraïem and T. Ollevier, *Green Chem.*, 2017, **19**, 1263-1267

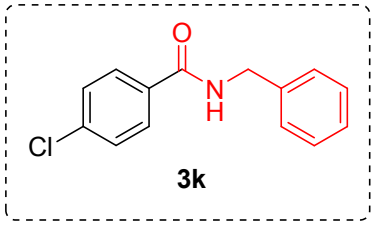
Yield: 88% (120 mg)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 – 7.63 (m, 1H), 7.43 – 7.31 (m, 1H), 6.28 (s, 1H), 3.41 (dd, *J* = 12.6, 6.7 Hz, 1H), 1.70 – 1.51 (m, 1H), 1.44 – 1.27 (m, 2H), 0.90 (td, *J* = 6.8, 3.4 Hz, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 166.56, 137.59, 133.31, 128.82, 128.39, 40.28, 29.39, 29.21, 22.43, 14.02.

Anal. Cal. For $C_{12}H_{16}ClNO$ (225.72): C, 63.86; H, 7.15; N, 6.21; Found: C, 63.78; H, 7.06; N, 6.15.

2.11. N-benzyl-4-chlorobenzamide (3k)[6]



3k

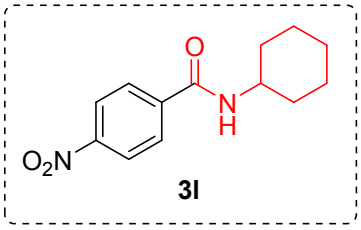
Yield: 90% (132 mg)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 – 7.68 (m, 1H), 7.40 – 7.27 (m, 3H), 6.50 (s, 1H), 4.62 (d, *J* = 5.6 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 166.44, 138.04, 137.90, 132.83, 131.95, 128.91, 128.86, 128.51, 128.00, 127.80, 44.32.

Anal. Cal. For $C_{14}H_{12}ClNO$ (245.71): C, 68.44; H, 4.92; N, 5.70; Found: C, 68.37; H, 4.86; N, 5.63.

2.12. N-cyclohexyl-4-nitrobenzamide (3l)[7]



3l

Yield: 90% (134 mg)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29 – 8.23 (m, 2H), 7.94 – 7.85 (m, 2H), 6.04 (d, *J* = 7.1 Hz, 1H), 4.06 – 3.87 (m, 1H), 2.05 (dq, *J* = 11.7, 3.8 Hz, 2H), 1.77 (ddd, *J* = 13.5, 7.1, 3.4 Hz, 2H), 1.72 – 1.60 (m, 1H), 1.51 – 1.34 (m, 2H), 1.35 – 1.14 (m, 3H).

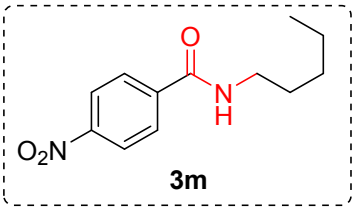
^{13}C NMR (101 MHz, $CDCl_3$) δ 164.66, 149.59, 140.80, 128.13, 123.84, 49.33, 33.20, 25.57, 24.94.

Anal. Cal. For $C_{13}H_{16}N_2O_3$ (248.28): C, 62.89; H, 6.50; N, 11.28; Found: C, 62.81; H, 6.63; N, 11.22.

2.13. 4-nitro-N-pentylbenzamide (3m)

[6] J. Luo and W. Huang, *Mol Divers*, 2003, **6**, 33-41

[7] D. C. Lenstra, F. P. J. T. Rutjes and J. Mecinović, *Chem. Commun.*, 2014, **50**, 5763-5766



3m

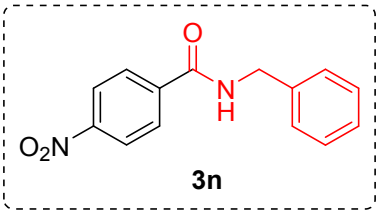
Yield: 83% (118 mg)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.25 (d, *J* = 9.0 Hz, 1H), 7.92 (d, *J* = 9.0 Hz, 1H), 6.39 (s, 1H), 3.60 – 3.35 (m, 1H), 1.63 (dd, *J* = 8.7, 5.8 Hz, 1H), 1.43 – 1.30 (m, 2H), 1.00 – 0.82 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 165.57, 149.60, 140.55, 128.64, 128.15, 126.85, 123.83, 40.53, 29.29, 29.18, 22.41, 14.00.

Anal. Cal. For $C_{12}H_{16}N_2O_3$ (236.27): C, 61.00; H, 6.83; N, 11.86; Found: C, 60.93; H, 6.77; N, 11.78.

2.14. N-cyclohexyl-4-nitrobenzamide (3n)[8]



3n

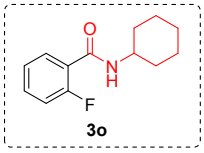
Yield: 87% (134 mg)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.25 (d, *J* = 9.0 Hz, 1H), 7.94 (d, *J* = 9.0 Hz, 1H), 7.41 – 7.29 (m, 2H), 6.64 (s, 1H), 4.65 (d, *J* = 5.7 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 165.47, 149.75, 140.00, 137.54, 131.79, 131.26, 129.01, 128.28, 128.05, 128.02, 124.23, 123.90, 123.65, 44.56.

Anal. Cal. For $C_{14}H_{12}N_2O_3$ (256.26): C, 65.62; H, 4.72; N, 10.93; Found: C, 65.55; H, 4.65; N, 10.86.

2.15. N-cyclohexyl-2-fluorobenzamide (3o)[9]



3o

Yield: 81% (107 mg)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (td, *J* = 7.9, 1.9 Hz, 1H), 7.44 (dddd, *J* = 8.3, 7.2, 5.2, 1.9 Hz, 1H), 7.27 – 7.21 (m, 1H), 7.09 (ddd, *J* = 12.1, 8.3, 1.1 Hz, 1H), 6.60 (s, 1H), 4.08 – 3.96 (m, 1H), 2.03 (dq, *J* = 11.9, 3.7 Hz, 1H), 1.79 – 1.69 (m, 1H), 1.68 – 1.59 (m, 1H), 1.47 – 1.37 (m, 1H), 1.34 – 1.21 (m, 1H).

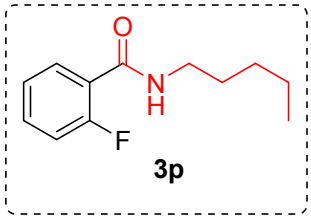
^{13}C NMR (101 MHz, $CDCl_3$) δ 162.35 (d, *J* = 3.2 Hz), 160.66 (d, *J* = 246.6 Hz), 133.03 (d, *J* = 9.3 Hz), 132.98, 124.82 (d, *J* = 3.2 Hz), 121.66 (d, *J* = 11.5 Hz), 115.98 (d, *J* = 24.9 Hz), 48.73, 33.07, 25.69, 24.82.

Anal. Cal. For $C_{13}H_{16}FNO$ (221.28): C, 70.57; H, 7.29; N, 6.33; Found: C, 70.49; H, 7.21; N, 6.26.

2.16. 2-fluoro-N-pentylbenzamide (3p)

[8] D. C. Lenstra, F. P. J. T. Rutjes and J. Mecinović, *Chem. Commun.*, 2014, **50**, 5763-5766

[9] P. Sureshbabu, S. Azeez, P. Chaudhary and J. Kandasamy, *Org. Biomol. Chem.*, 2019, **17**, 845-850



3p

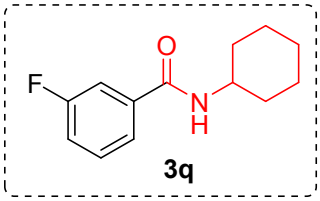
Yield: 83% (104 mg)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 – 7.98 (m, 1H), 7.43 – 7.36 (m, 1H), 7.23 – 7.16 (m, 1H), 7.09 – 7.02 (m, 1H), 6.74 (s, 1H), 3.46 – 3.39 (m, 1H), 1.63 – 1.54 (m, 1H), 1.36 – 1.29 (m, 1H), 0.91 – 0.84 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 163.21 (d, *J* = 3.2 Hz), 160.54 (d, *J* = 246.8 Hz), 132.95 (d, *J* = 9.3 Hz), 131.94 (d, *J* = 2.3 Hz), 124.68 (d, *J* = 3.3 Hz), 121.41 (d, *J* = 11.7 Hz), 115.87 (d, *J* = 24.9 Hz), 40.03, 29.15, 29.10, 22.32, 13.91.

Anal. Cal. For $C_{12}H_{16}FNO$ (209.26): C, 68.88; H, 7.71; N, 6.69; Found: C, 68.80; H, 7.65; N, 6.62.

2.17. N-cyclohexyl-3-fluorobenzamide (3q)



3q

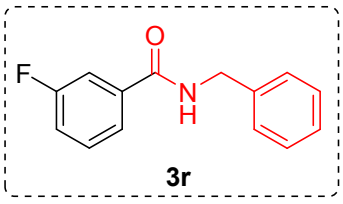
Yield: 85% (113 mg)

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47 (ddd, *J* = 9.4, 8.0, 4.8 Hz, 2H), 7.36 (td, *J* = 8.0, 5.6 Hz, 1H), 7.15 (td, *J* = 8.2, 2.5 Hz, 1H), 6.13 (s, 1H), 3.94 (tdt, *J* = 11.7, 8.0, 4.0 Hz, 1H), 2.06 – 1.95 (m, 2H), 1.73 (ddd, *J* = 10.6, 7.2, 3.4 Hz, 2H), 1.67 – 1.58 (m, 1H), 1.45 – 1.32 (m, 2H), 1.28 – 1.10 (m, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 165.48 (d, *J* = 2.5 Hz), 162.78 (d, *J* = 247.5 Hz), 137.42 (d, *J* = 6.8 Hz), 130.17 (d, *J* = 7.9 Hz), 122.38 (d, *J* = 3.0 Hz), 118.24 (d, *J* = 21.3 Hz), 114.38 (d, *J* = 22.8 Hz), 48.98, 33.17, 25.56, 24.95.

Anal. Cal. For $C_{13}H_{16}FNO$ (221.28): C, 70.57; H, 7.29; N, 6.33; Found: C, 70.49; H, 7.22; N, 6.25.

2.18. N-benzyl-3-fluorobenzamide (3r)[10]



3r

Yield: 81% (111 mg)

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.56 – 7.47 (m, 1H), 7.39 – 7.26 (m, 3H), 7.21 – 7.14 (m, 1H), 6.76 (s, 1H), 4.59 (d, *J* = 5.7 Hz, 1H).

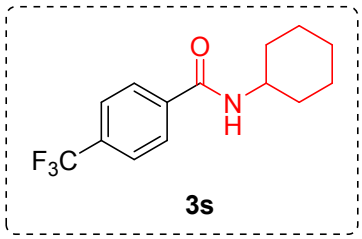
^{13}C NMR (126 MHz, $CDCl_3$) δ 166.27 (d, *J* = 2.6 Hz), 162.77 (d, J = 248.2 Hz), 137.97, 136.67 (d, *J* = 6.7 Hz), 130.25 (d, *J* = 8.8 Hz), 128.83, 127.91, 127.70, 122.53 (d, *J* = 3.1 Hz), 118.56 (d, *J* = 21.3 Hz), 114.50 (d, *J* = 22.9 Hz), 44.22.

^{19}F NMR (471 MHz, $CDCl_3$) δ -111.45 – -112.60 (m).

Anal. Cal. For $C_{14}H_{12}FNO$ (229.25): C, 73.35; H, 5.28; N, 6.11; Found: C, 73.26; H, 5.22; N, 6.03.

2.19. N-cyclohexyl-4-(trifluoromethyl)benzamide (3s)[11]

[10] C. Chen, Y. Miao, K. D. Winter, H.-J. Wang, P. Demeyere, Y. Yuan, and F. Verpoort, *Molecules* 2018, **23**, 2413.
[11] A. Mishra, S. Chauhan, P. Verma, S. Singh, V. Srivastava, *Asian J. Org. Chem.* 2019, **8**, 853-857.



3s

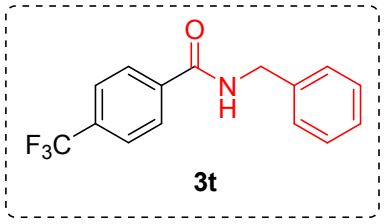
Yield: 88% (143 mg)

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.85 (d, *J* = 8.2 Hz, 2H), 7.67 (d, *J* = 8.3 Hz, 2H), 6.09 (d, *J* = 6.7 Hz, 1H), 3.98 (tdt, *J* = 11.7, 8.0, 4.0 Hz, 1H), 2.08 – 2.00 (m, 2H), 1.76 (ddd, *J* = 10.6, 7.2, 3.4 Hz, 2H), 1.70 – 1.63 (m, 1H), 1.49 – 1.37 (m, 2H), 1.29 – 1.18 (m, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 165.55, 138.43 (d, *J* = 1.0 Hz), 133.11 (d, *J* = 32.7 Hz), 127.43, 125.63 (q, *J* = 3.8 Hz), 123.77 (d, *J* = 272.6 Hz), 49.13, 33.21, 25.58, 24.96.

Anal. Cal. For $C_{14}H_{16}F_3NO$ (271.28): C, 61.98; H, 5.95; N, 5.16; Found: C, 61.89; H, 5.86; N, 5.08.

2.20. N-benzyl-4-(trifluoromethyl)benzamide (3t)[12]



3t

Yield: 89% (149 mg)

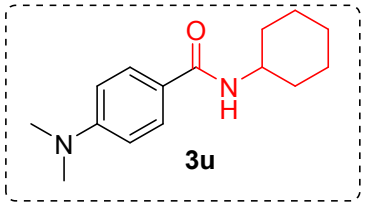
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.90 (d, *J* = 8.2 Hz, 1H), 7.69 (d, *J* = 8.3 Hz, 1H), 7.40 – 7.29 (m, 2H), 6.46 (s, 1H), 4.66 (d, *J* = 5.6 Hz, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 166.16, 137.78, 137.73, 133.43 (q, *J* = 32.7 Hz), 131.05, 130.60, 129.01, 129.00, 128.99, 128.09, 128.08, 128.07, 127.96, 127.55, 127.54, 127.53, 125.77 (q, *J* = 3.8 Hz), 44.45.

^{19}F NMR (471 MHz, $CDCl_3$) δ -62.98.

Anal. Cal. For $C_{15}H_{12}F_3NO$ (279.26): C, 64.51; H, 4.33; N, 5.02; Found: C, 64.44; H, 4.26; N, 4.96.

2.21. N-cyclohexyl-4-(dimethylamino)benzamide (3u)[13]



3u

Yield: 78% (115 mg)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 – 7.60 (m, 1H), 6.69 – 6.64 (m, 1H), 5.84 (d, *J* = 7.4 Hz, 1H), 3.97 (ttd, *J* = 11.8, 8.0, 3.9 Hz, 1H), 3.05 (s, 2H), 2.02 (dt, *J* = 8.1, 3.3 Hz, 1H), 1.79 – 1.69 (m, 1H), 1.68 – 1.59 (m, 1H), 1.49 – 1.35 (m, 1H), 1.28 – 1.15 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 166.64, 152.40, 128.33, 122.20, 110.79, 48.44, 40.11, 33.51, 25.77, 25.05.

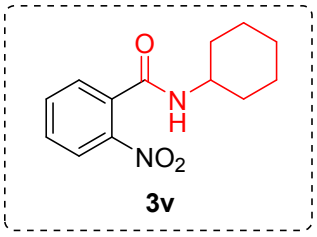
Anal. Cal. For $C_{15}H_{22}N_2O$ (246.35): C, 73.13; H, 9.00; N, 11.37; Found: C, 73.05; H, 5.91; N, 11.30.

2.22. N-cyclohexyl-2-nitrobenzamide (3v)[14]

[12] D. C. Lenstra, F. P. J. T. Rutjes and J. Mecinović, *Chem. Commun.*, 2014, **50**, 5763-5766

[13] W. S. Bechara, G. Pelletier & A. B. Charette, *Nature Chemistry* 2012, **4**, 228–234.

[14] J. Kraïem and T. Ollevier, *Green Chem.*, 2017, **19**, 1263-1267



3v

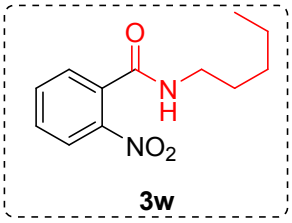
Yield: 80% (119 mg)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 – 8.02 (m, 1H), 7.65 (td, *J* = 7.5, 1.2 Hz, 1H), 7.52 (dddd, *J* = 7.8, 4.5, 1.9, 0.9 Hz, 2H), 5.70 (d, *J* = 6.6 Hz, 1H), 3.97 (tdt, *J* = 10.6, 8.1, 4.0 Hz, 1H), 2.08 (dq, *J* = 13.9, 3.8 Hz, 2H), 1.79 – 1.70 (m, 2H), 1.69 – 1.60 (m, 1H), 1.49 – 1.36 (m, 2H), 1.28 – 1.16 (m, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 165.75, 146.53, 133.72, 133.45, 130.32, 128.89, 124.55, 49.16, 32.81, 25.58, 24.87.

Anal. Cal. For $C_{13}H_{16}N_2O_3$ (248.28): C, 62.89; H, 6.50; N, 11.28; Found: C, 62.81; H, 6.44; N, 11.21.

2.23. 2-nitro-N-pentylbenzamide (3w)



3w

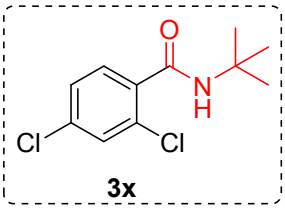
Yield: 82% (116 mg)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (dd, *J* = 8.2, 1.2 Hz, 1H), 7.70 – 7.62 (m, 1H), 7.57 – 7.52 (m, 1H), 7.48 (dd, *J* = 7.5, 1.5 Hz, 1H), 5.98 (s, 1H), 3.42 (ddd, *J* = 13.1, 8.4, 4.8 Hz, 2H), 1.61 (tdd, *J* = 7.2, 6.0, 3.5 Hz, 2H), 1.41 – 1.32 (m, 5H), 0.94 – 0.88 (m, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 166.50, 146.58, 133.67, 133.30, 130.36, 128.82, 124.53, 40.37, 29.09, 28.98, 22.38, 14.02.

Anal. Cal. For $C_{12}H_{16}N_2O_3$ (236.27): C, 61.00; H, 6.83; N, 11.86; Found: C, 60.53; H, 6.75; N, 11.80.

2.24. N-(tert-butyl)-2,4-dichlorobenzamide (3x)



3x

Yield: 85% (125 mg)

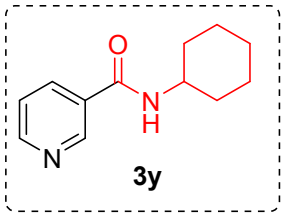
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (d, *J* = 8.3 Hz, 1H), 7.38 – 7.38 (m, 1H), 7.27 (dd, *J* = 8.3, 2.0 Hz, 1H), 5.95 (s, 1H), 1.46 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 164.90, 136.30, 134.88, 131.36, 130.95, 129.92, 127.51, 52.47, 28.84.

Anal. Cal. For $C_{11}H_{13}C_{12}NO$ (246.13): C, 53.68; H, 5.32; N, 5.69; Found: C, 53.59; H, 5.25; N, 5.60.

2.25. N-cyclohexylnicotinamide (3y)[15]

[15] M. Largeron, N. Auzeil, E. Bacqué and M.-B. Fleury *J. Chem. Soc., Perkin Trans. 2*, 1997, 495-501.



3y

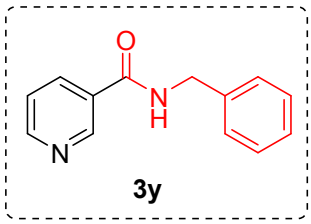
Yield: 80% (98 mg)

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.97 (d, *J* = 1.8 Hz, 1H), 8.72 (dd, *J* = 4.8, 1.4 Hz, 1H), 8.14 (dt, *J* = 7.9, 1.9 Hz, 1H), 7.40 (dd, *J* = 7.9, 4.9 Hz, 1H), 6.05 (s, 1H), 4.04 – 3.94 (m, 1H), 2.07 – 2.01 (m, 2H), 1.80 – 1.75 (m, 2H), 1.69 – 1.63 (m, 1H), 1.43 (dt, *J* = 22.2, 7.8 Hz, 2H), 1.32 – 1.17 (m, 4H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 164.61, 151.79, 147.48, 135.62, 130.98, 123.73, 53.07, 49.11, 33.24, 25.59, 24.97.

Anal. Cal. For $C_{12}H_{16}N_2O$ (204.27): C, 70.56; H, 7.90; N, 13.71; Found: C, 70.48; H, 7.83; N, 13.63.

2.26. N-benzylnicotinamide (3z)[16]



3y

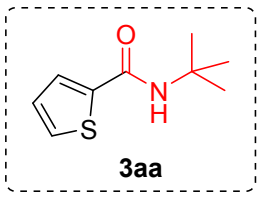
Yield: 78% (99 mg)

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.98 (d, *J* = 2.0 Hz, 1H), 8.71 (dd, *J* = 4.8, 1.6 Hz, 1H), 8.15 (dt, *J* = 7.9, 2.0 Hz, 1H), 7.43 – 7.35 (m, 2H), 7.33 – 7.28 (m, 1H), 6.62 (s, 1H), 4.66 (d, *J* = 5.7 Hz, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 165.46, 152.21, 147.77, 137.77, 135.49, 130.26, 128.98, 128.08, 127.93, 123.71, 44.34.

Anal. Cal. For $C_{13}H_{12}N_2O$ (212.25): C, 73.56; H, 5.70; N, 13.20; Found: C, 73.48; H, 5.65; N, 13.27.

2.27. N-(tert-butyl)thiophene-2-carboxamide (3ab)[17]



3aa

Yield: 75% (82 mg)

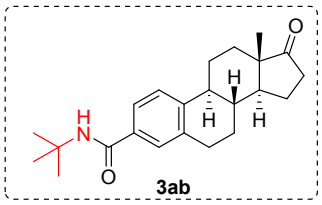
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49-7.47 (m, 1H), 7.44-7.42 (m, 1H), 6.99-6.96 (m, 1H), 6.24 (s, 1H), 1.50 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 161.21, 140.51, 129.31, 127.46, 127.31, 51.86, 28.88.

Anal. Cal. For $C_9H_{13}NOS$ (183.27): C, 58.98; H, 7.15; N, 7.64; S, 17.49; Found: C, 58.91; H, 7.19; N, 7.69; S, 17.41.

2.28. (8R,9S,13S,14S)-N-(tert-butyl)-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthrene-3-carboxamide (3ac)

[16] E. Eidia and M. Z. Kassaee, *RSC Adv.*, 2016, **6**, 106873-106879.
[17] T. Tang, L. Zhang, H. Dong, Z. Fang, W. Fu, Q. Yu and T. Tang, *RSC Adv.* 2017, **7**, 7711-7717.



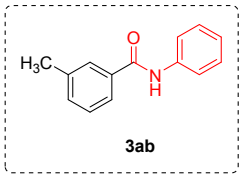
Yield: 76% (161 mg)

^{1}H NMR (250 MHz, DMSO-d_6) δ 7.76 (d, J = 10.0 Hz, 1H), 7.22-7.13 (m, 3H), 3.43 (d, *J* = 5.0 Hz, 1H), 2.78-2.75 (m, 2H), 2.49-2.27 (m, 2H), 2.10-187 (m, 4H), 1.50 (s, 9H), 1.52-129 (m, 6H), 0.78 (s, 3H).

^{13}C NMR (62.9 MHz, $CDCl_3$) δ 219.71, 165.37, 143.29, 136.09, 132.24, 119.13, 118.97, 60.38, 54.76, 52.51, 48.62, 40.55, 36.54, 34.24, 31.32, 30.74, 29.35, 26.32, 18.70.

Anal. Cal. For $C_{23}H_{31}NO_2$ (353.5060): C, 78.15; H, 8.84; N, 3.96; Found: C, 78.02; H, 8.75; N, 3.88.

2.29. 3-methyl-N-phenylbenzamide (3ad)[18]



Yield: 30% (38 mg) using isocyanatobenzene

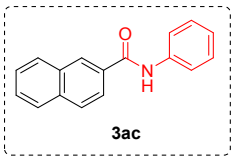
Yield: 82% (104 mg) using diphenylmethanediimine

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, *J* = 0.8 Hz, 1H), 7.69 – 7.62 (m, 4H), 7.38 – 7.33 (m, 4H), 7.17 – 7.11 (m, 1H), 2.41 (s, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 166.10, 138.73, 138.11, 135.09, 132.60, 129.11, 128.67, 127.89, 124.55, 124.06, 120.34, 21.41.

Anal. Cal. For $C_{14}H_{13}NO$ (211.26): C, 79.59; H, 6.20; N, 6.63; Found: C, 79.67; H, 6.17; N, 6.55.

2.30. N-phenyl-2-naphthamide (3ae)



Yield: 84% (125 mg)

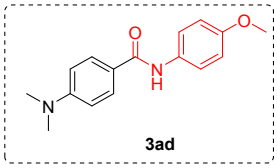
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (d, *J* = 0.6 Hz, 1H), 8.02 (s, 1H), 7.96 – 7.87 (m, 4H), 7.73 – 7.68 (m, 2H), 7.63 – 7.53 (m, 2H), 7.44 – 7.35 (m, 2H), 7.21 – 7.14 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 165.89, 138.13, 134.98, 132.74, 132.33, 129.22, 129.06, 128.84, 127.99, 127.91, 127.61, 127.03, 124.70, 123.64, 120.37.

Anal. Cal. For $C_{17}H_{13}NO$ (247.30): C, 82.57; H, 5.30; N, 5.66; Found: C, 82.51; H, 5.23; N, 5.61.

2.31. 4-(dimethylamino)-N-(4-methoxyphenyl)benzamide (3af)

[18] X. Guo, L. Tang, Y. Yang, Z. Zha and Z. Wang, *Green Chem.*, 2014, **16**, 2443-2447.



3ad

Yield: 89% (144 mg)

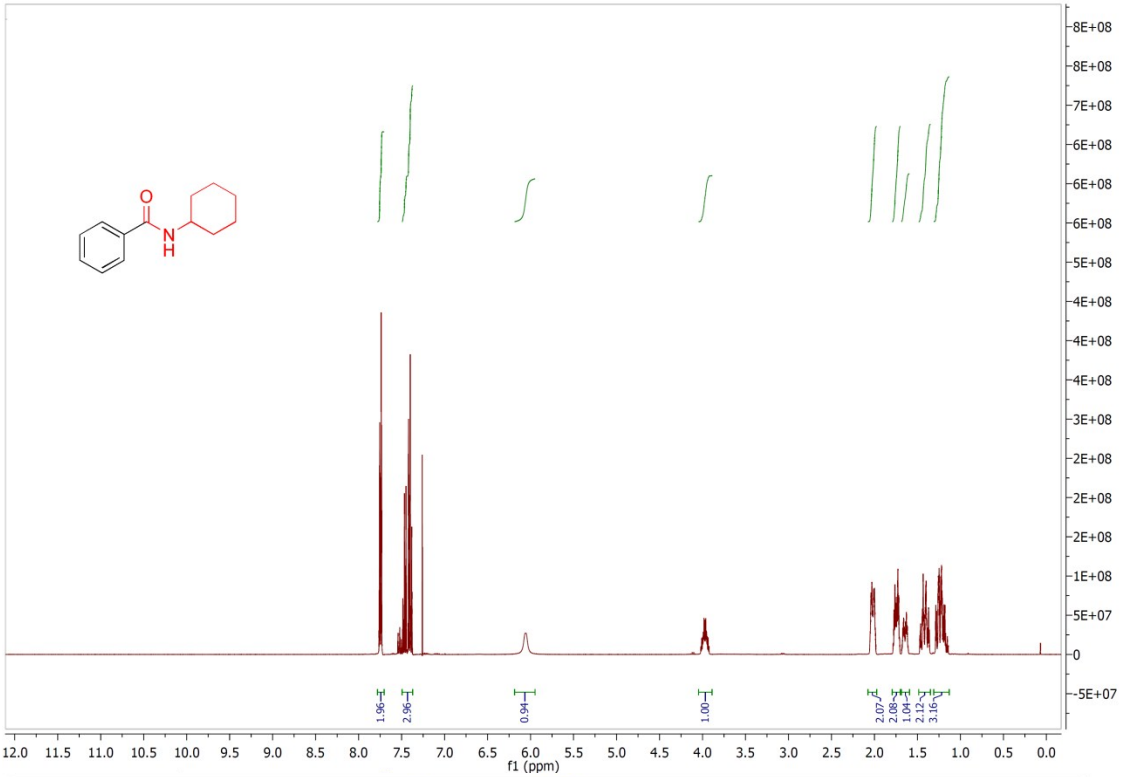
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.79 – 7.75 (m, 1H), 7.72 (s, 1H), 7.55 – 7.50 (m, 1H), 6.90 – 6.85 (m, 1H), 6.69 – 6.67 (m, 1H), 3.80 (s, 1H), 3.03 (s, 1H).

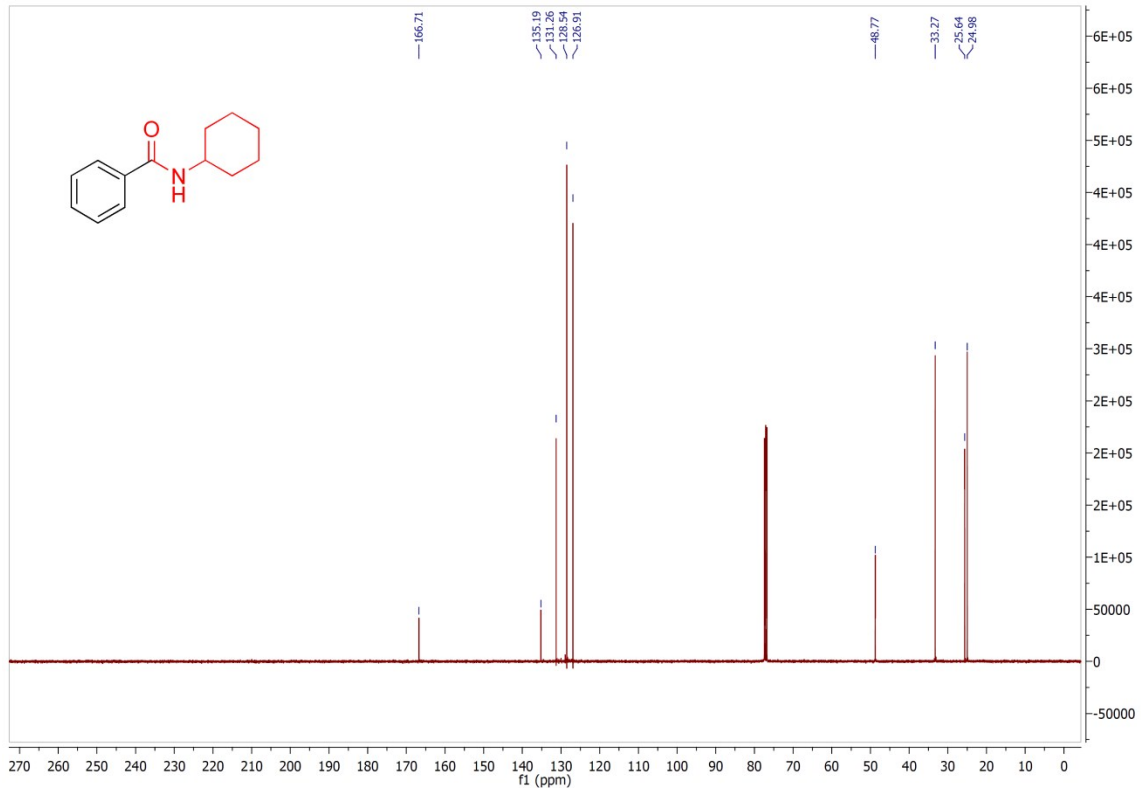
^{13}C NMR (126 MHz, $CDCl_3$) δ 165.64, 156.25, 152.64, 131.75, 128.62, 122.03, 114.21, 111.21, 55.56, 40.17.

Anal. Cal. For $C_{16}H_{18}N_2O_2$ (270.33): C, 71.09; H, 6.71; N, 10.36; Found: C, 71.00; H, 6.64; N, 10.31.

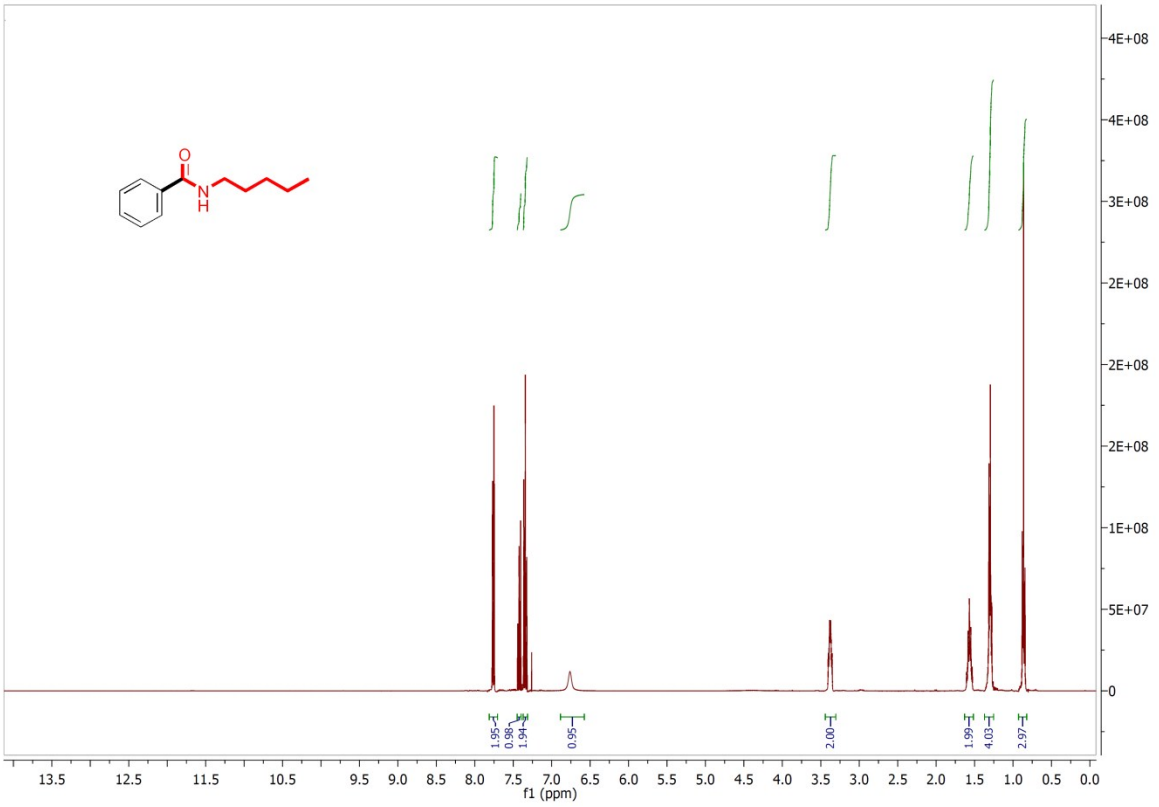
3. Copy of ^{1}HNMR and ^{13}CNMR of synthesized compounds

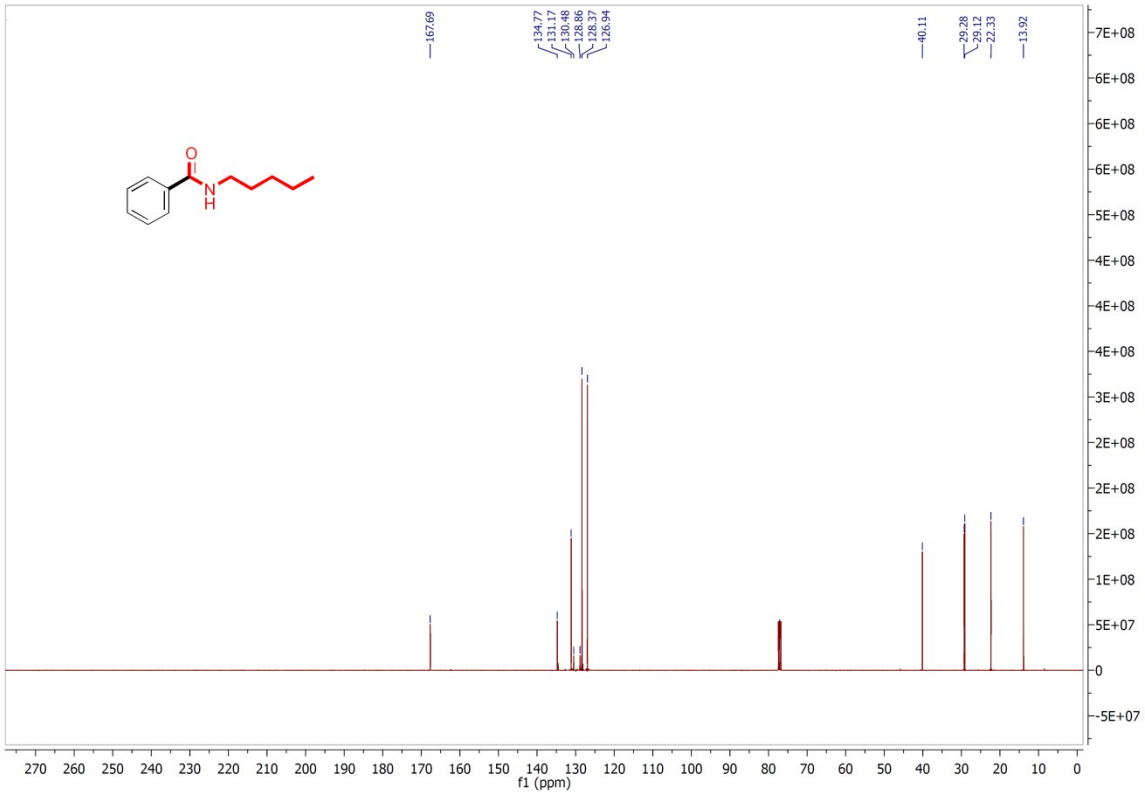
3.1. N-cyclohexylbenzamide (3a)



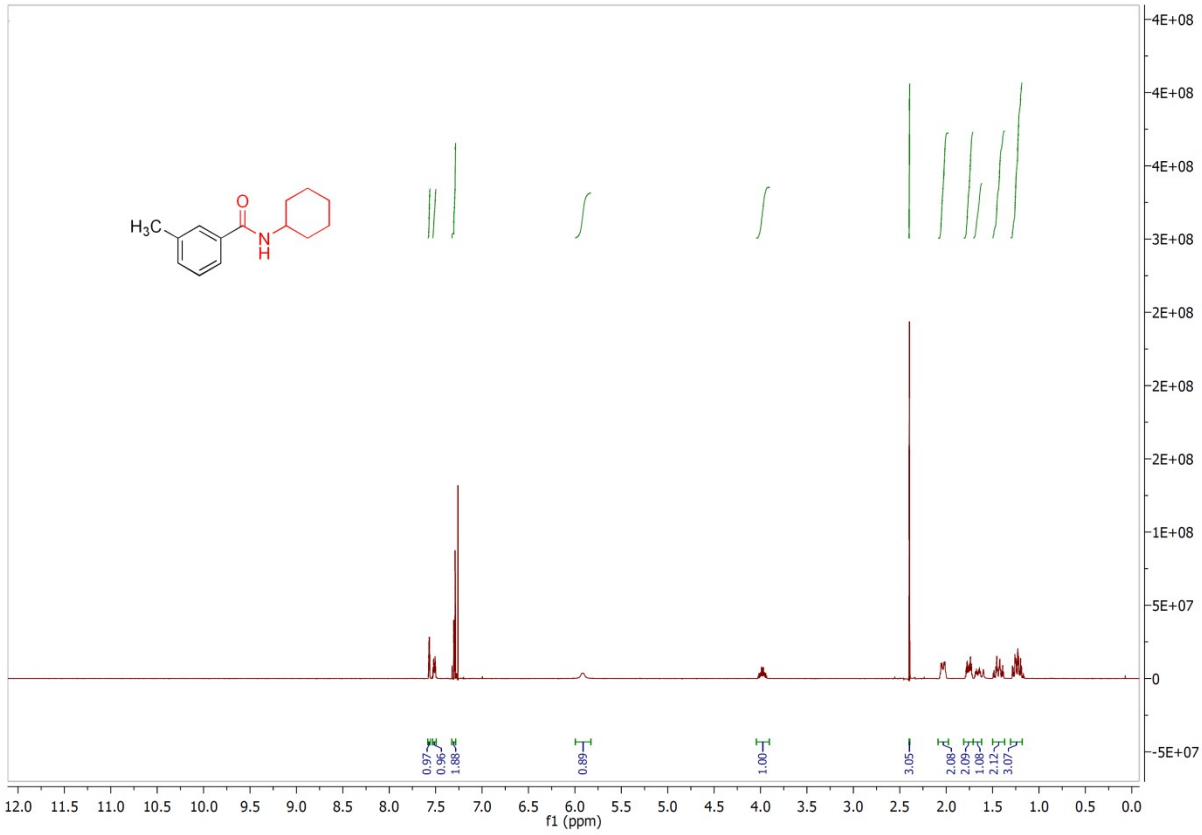


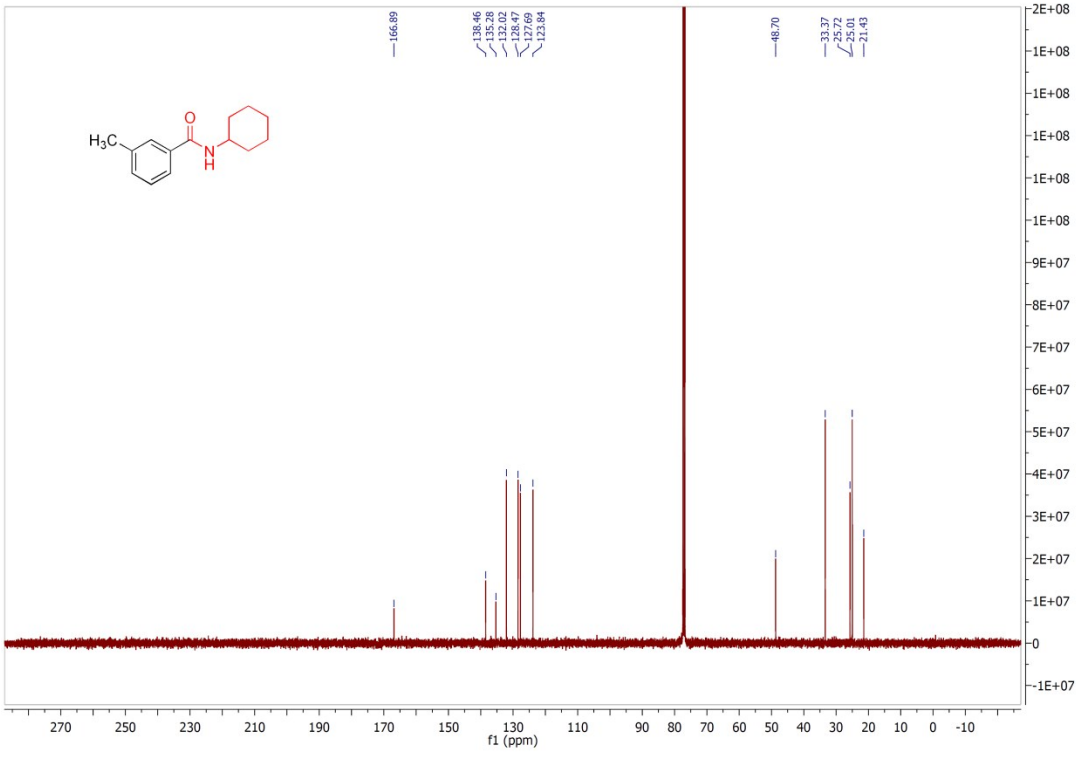
3.2. N-pentylbenzamide (3b)



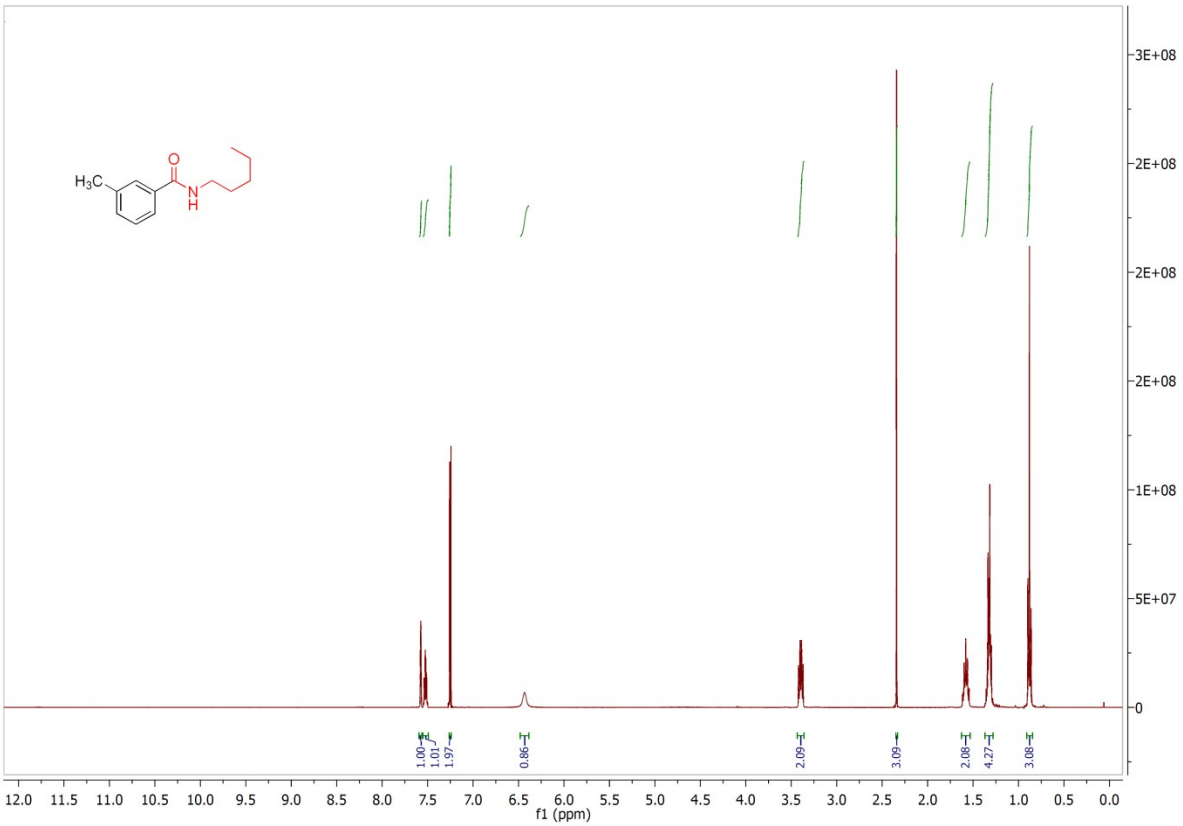


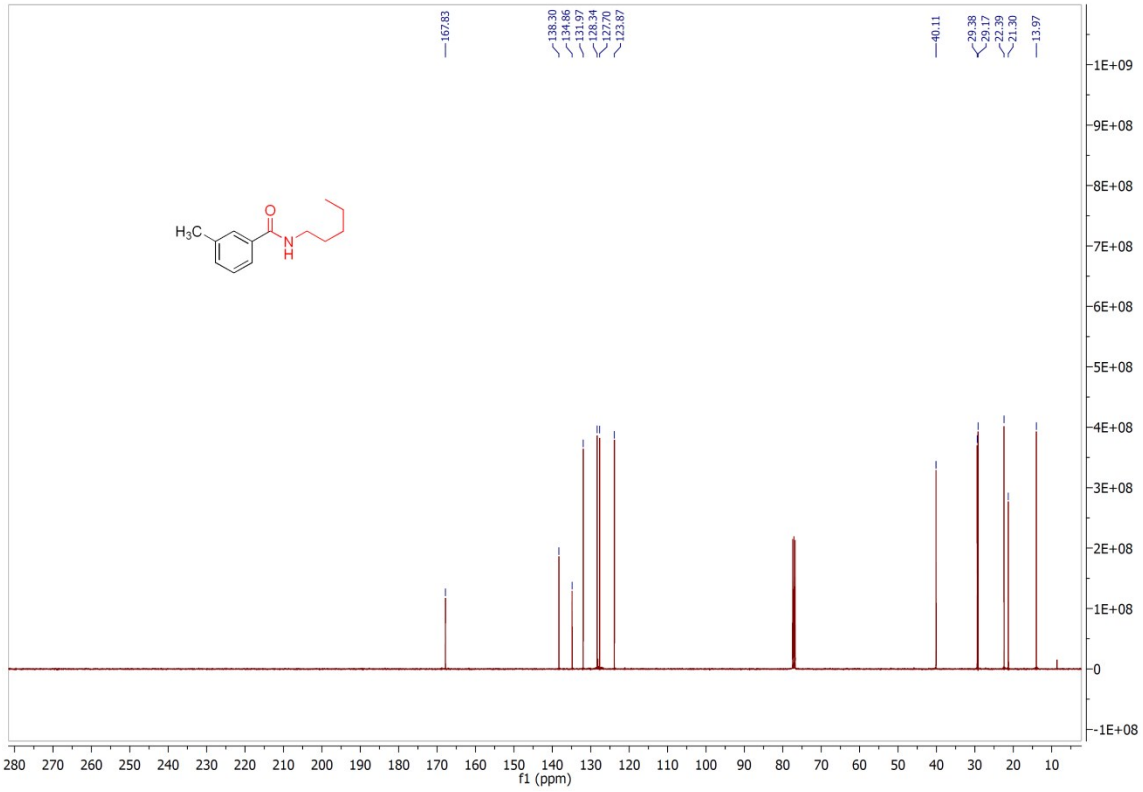
3.3. N-cyclohexyl-3-methylbenzamide (3c)



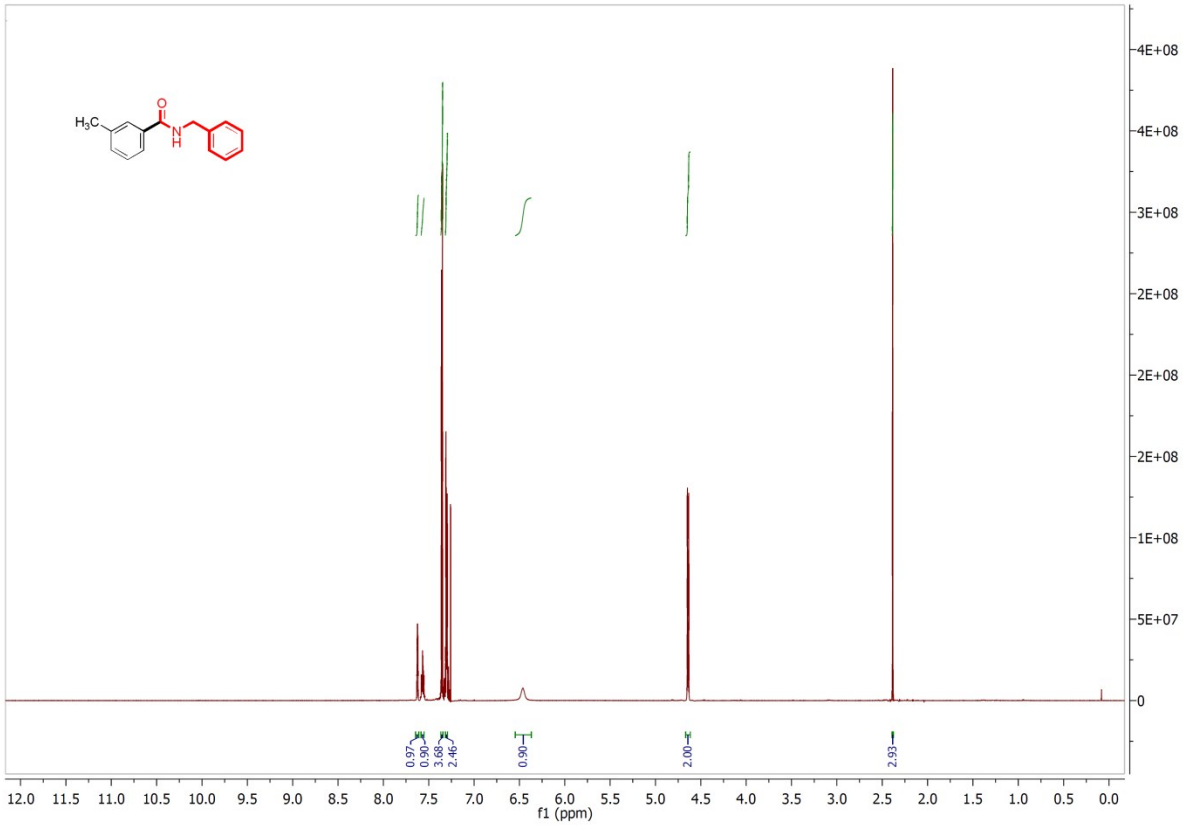


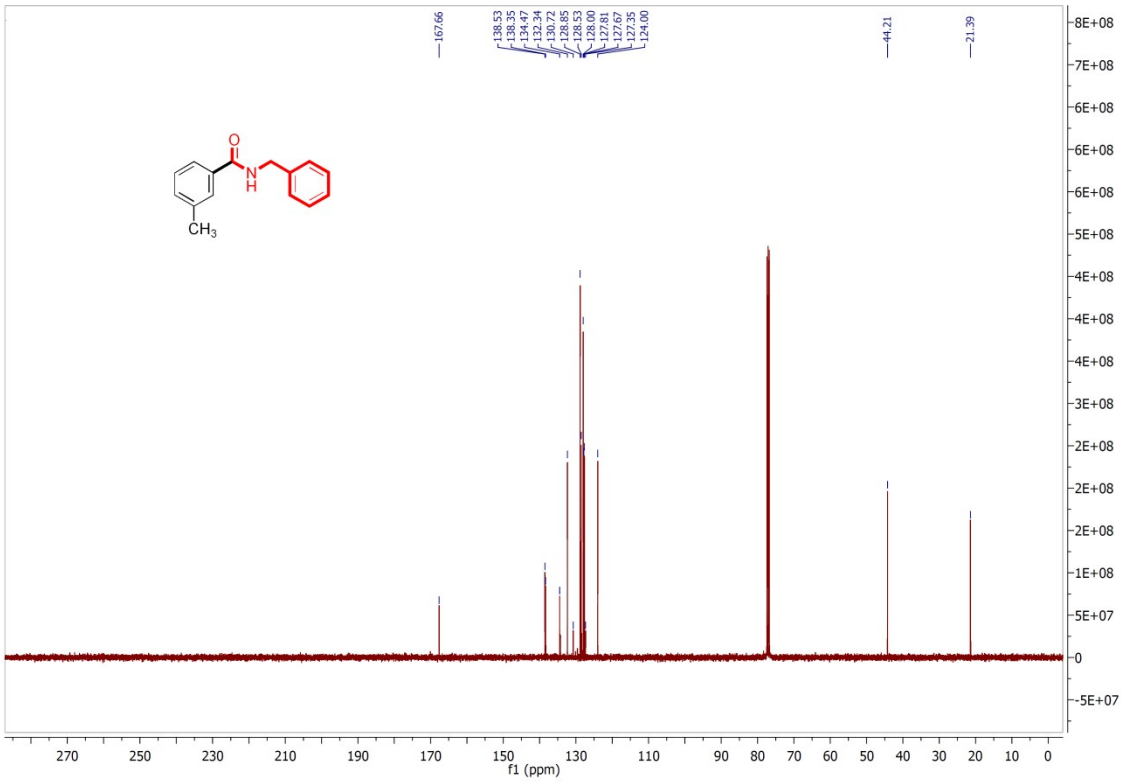
3.4. 3-methyl-N-pentylbenzamide (3d)



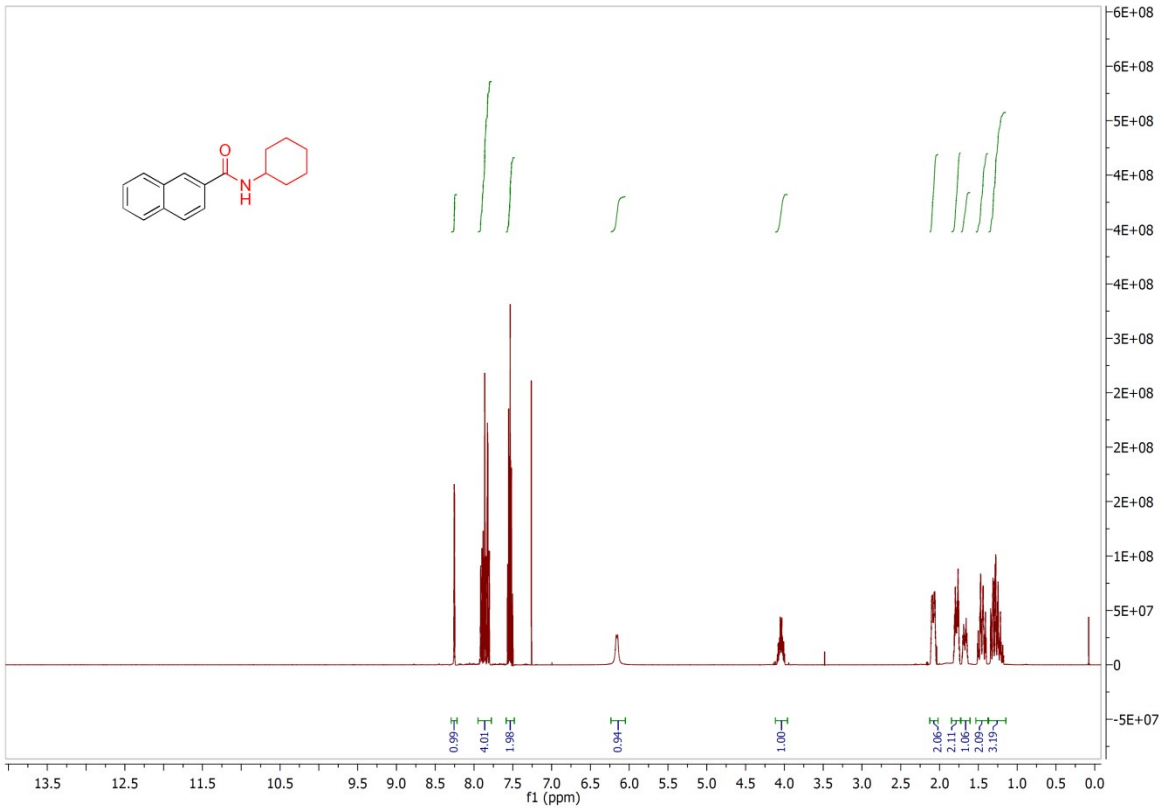


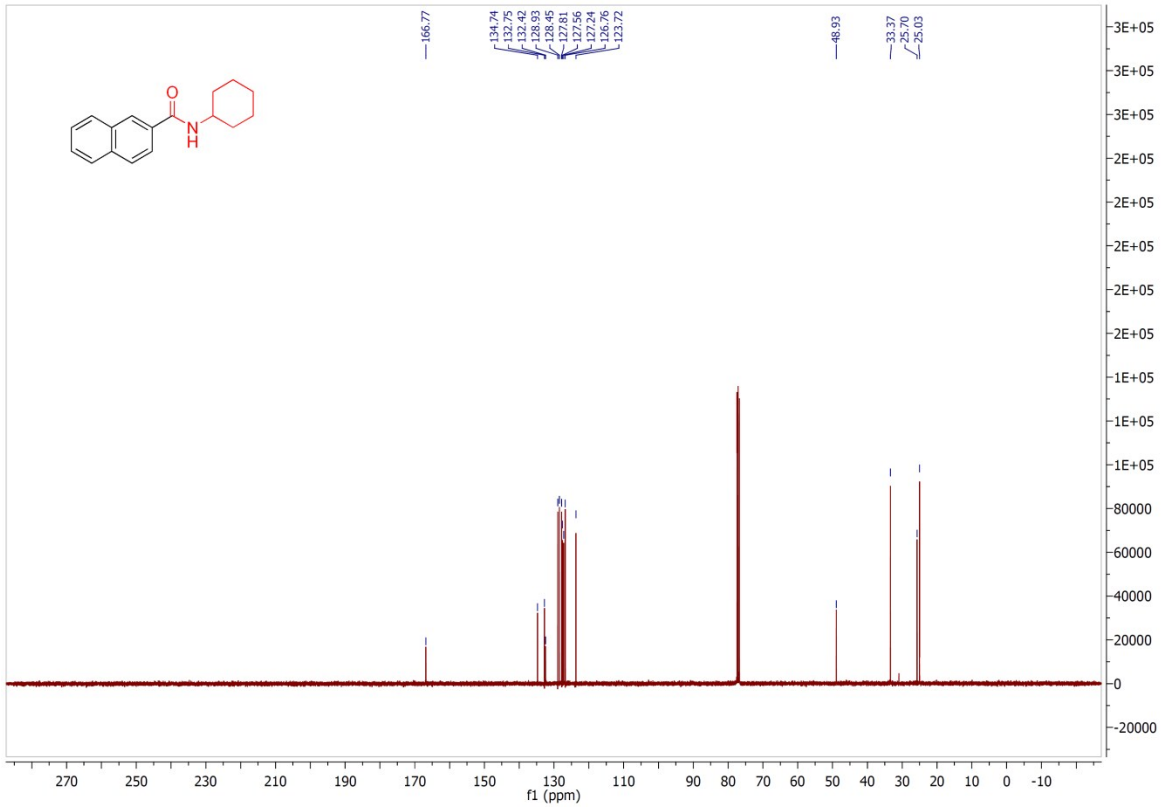
3.5. N-benzyl-3-methylbenzamide (3e)



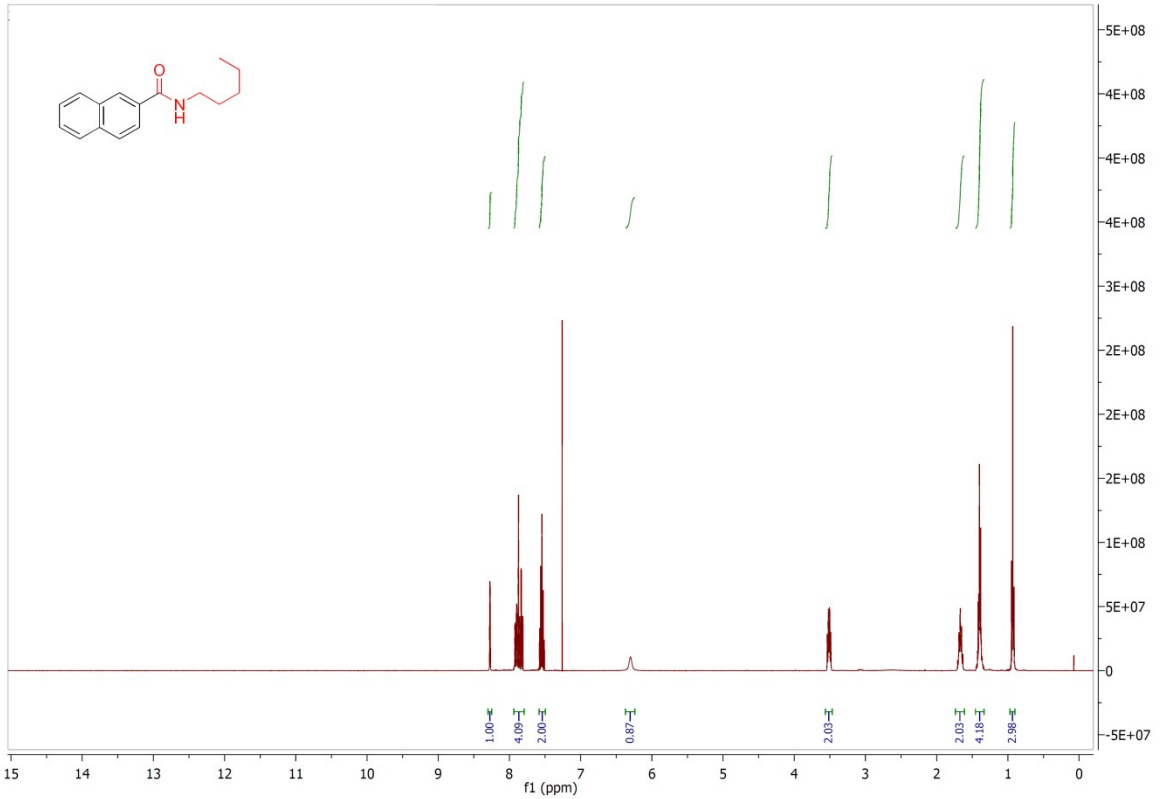


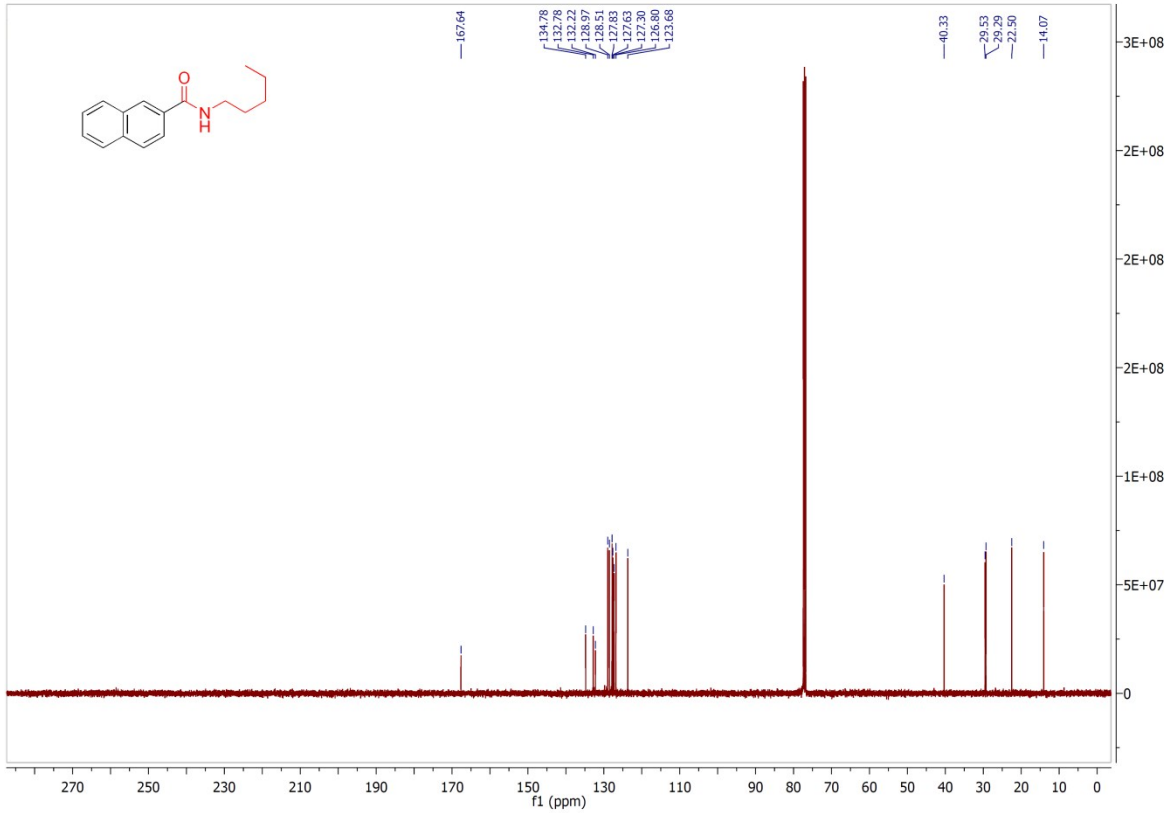
3.6. N-cyclohexyl-2-naphthamide (3f)



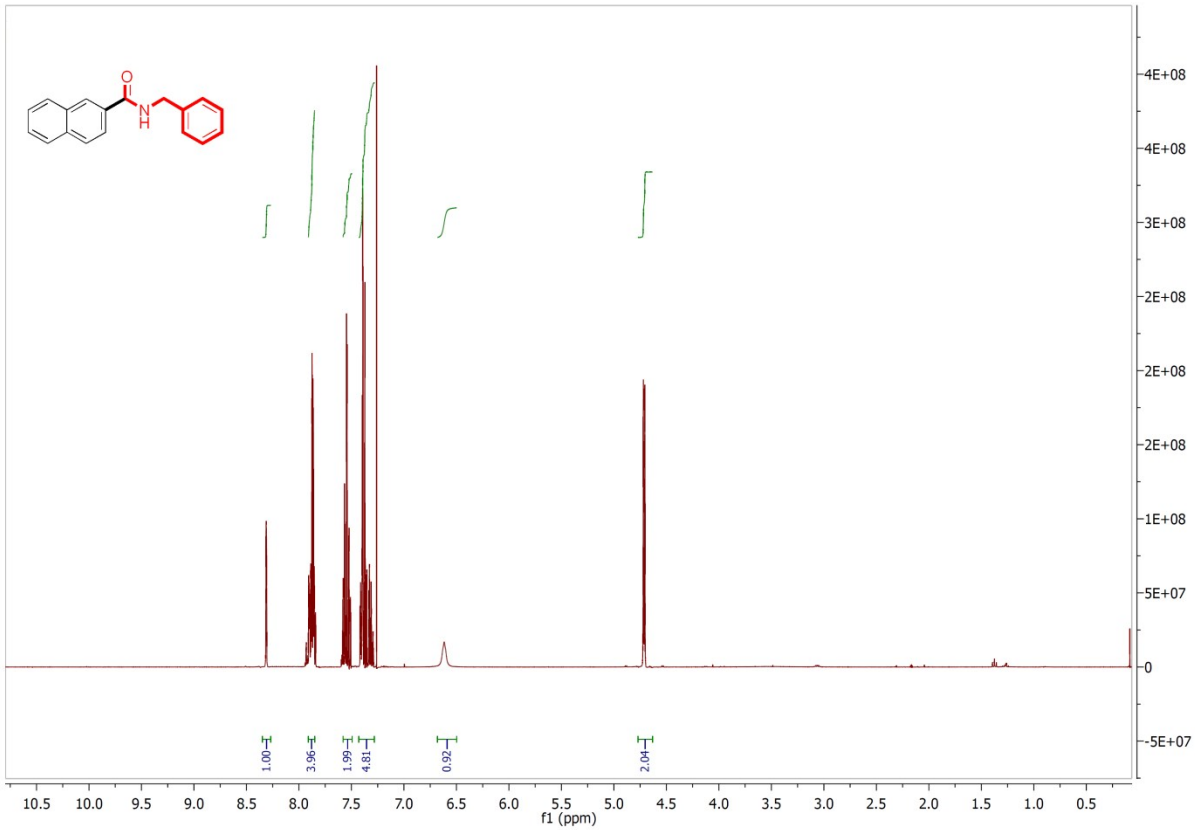


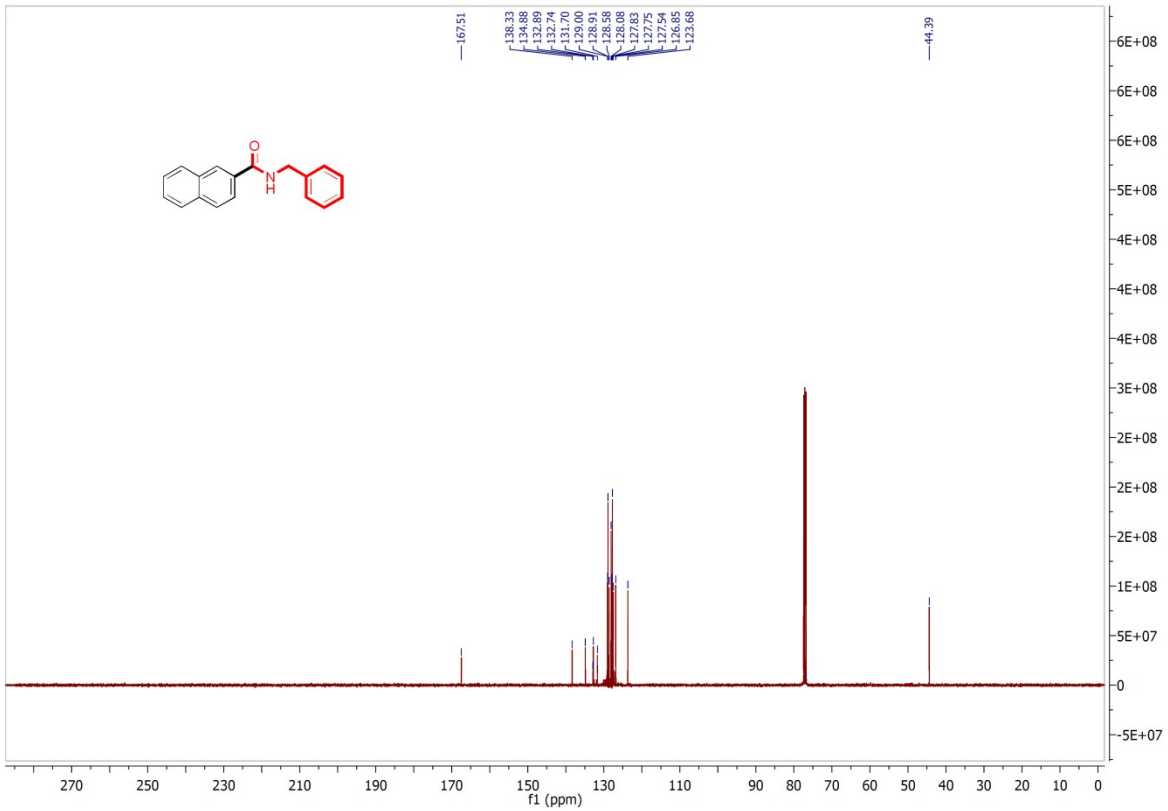
3.7. N-pentyl-2-naphthamide (3g)



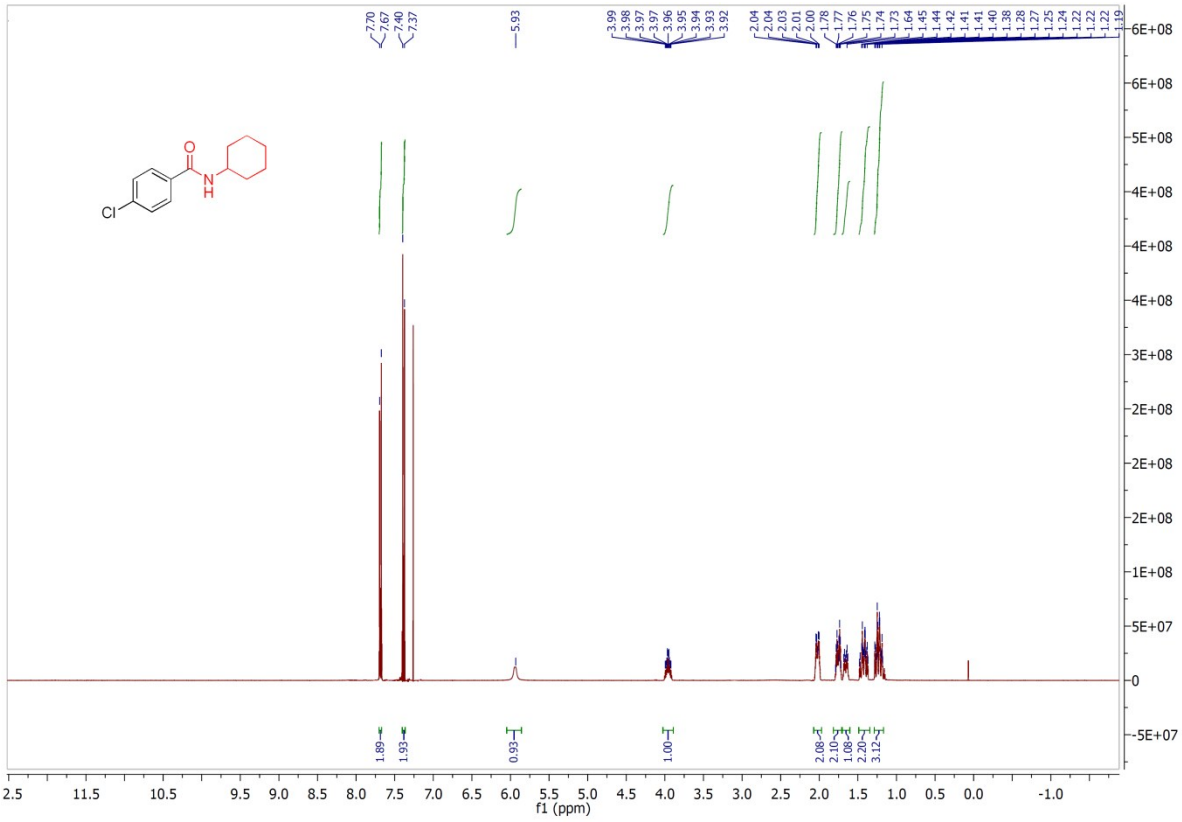


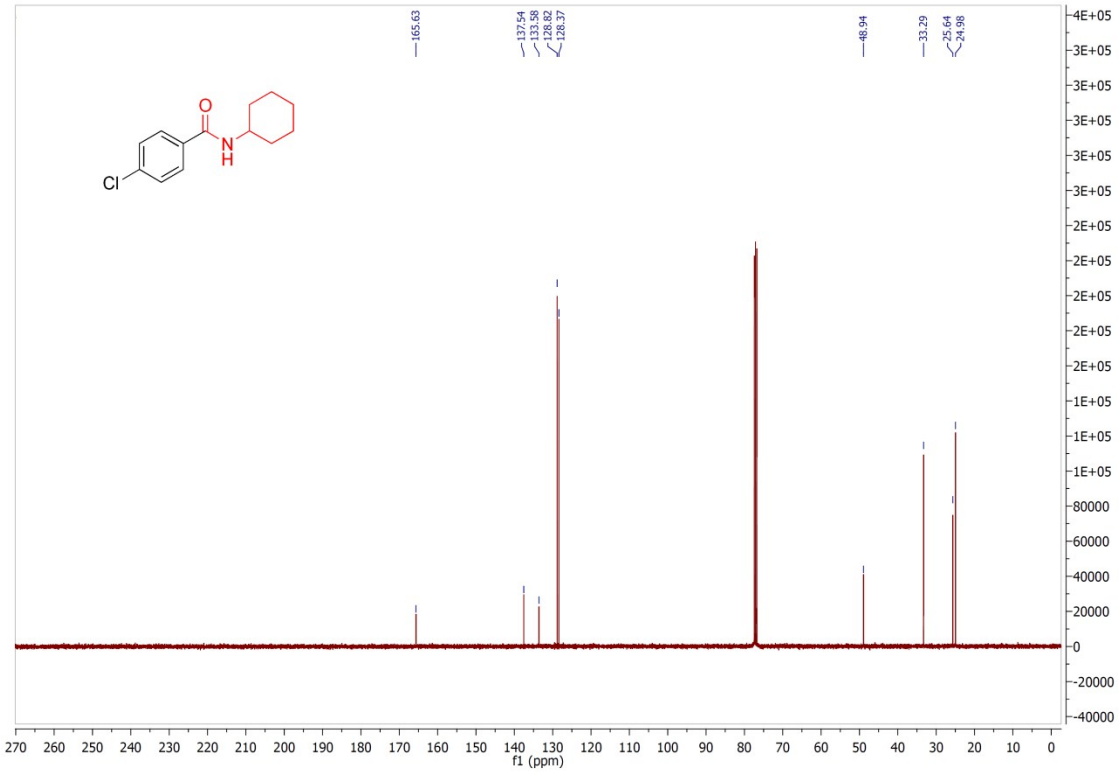
3.8. N-pentyl-2-naphthamide (3h)



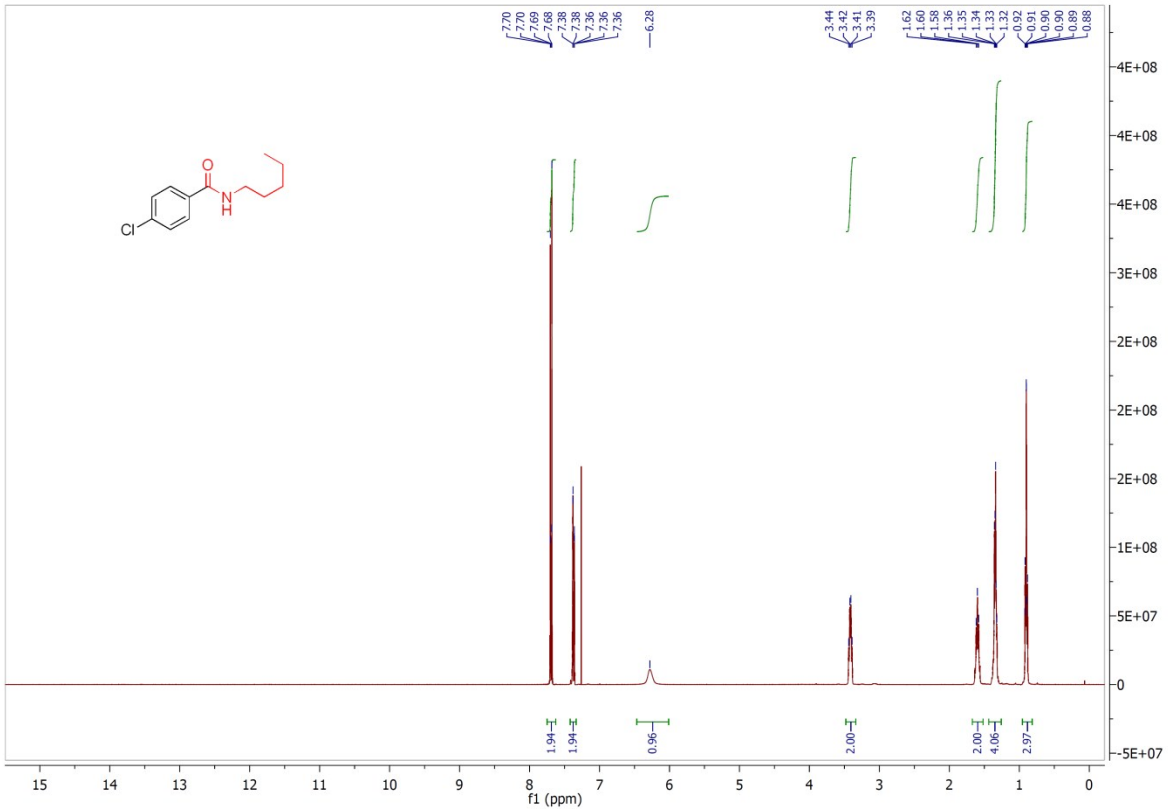


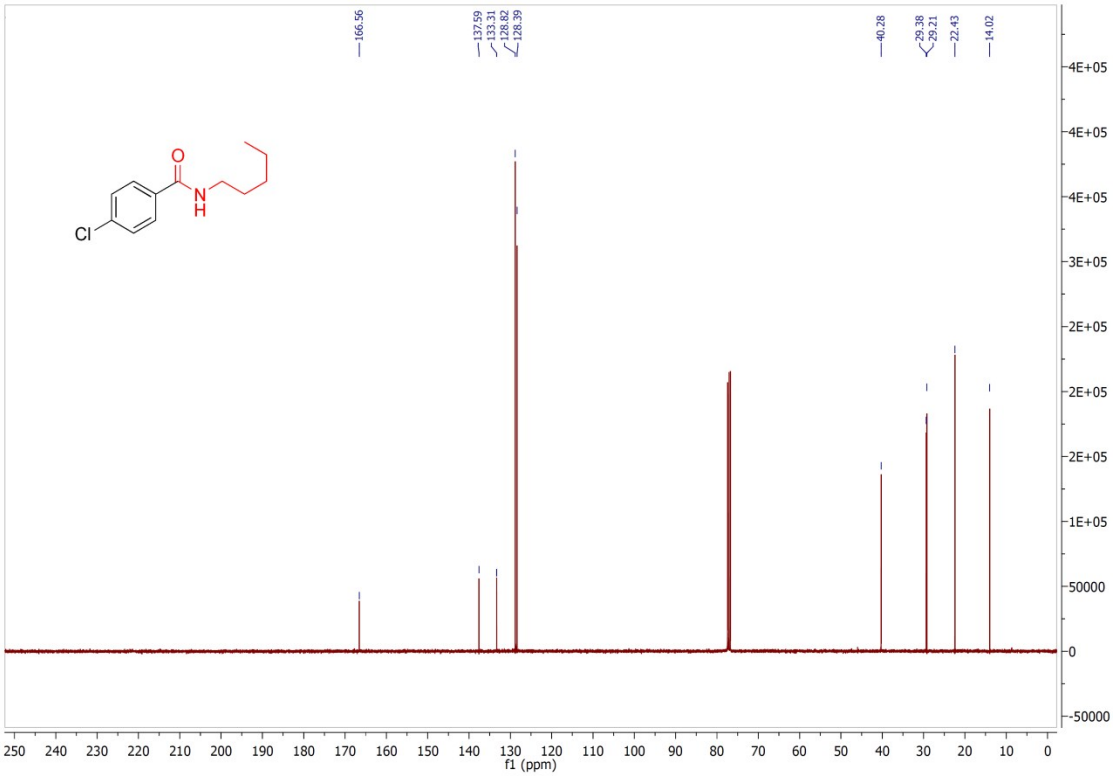
3.9. 4-chloro-N-cyclohexylbenzamide (3i)



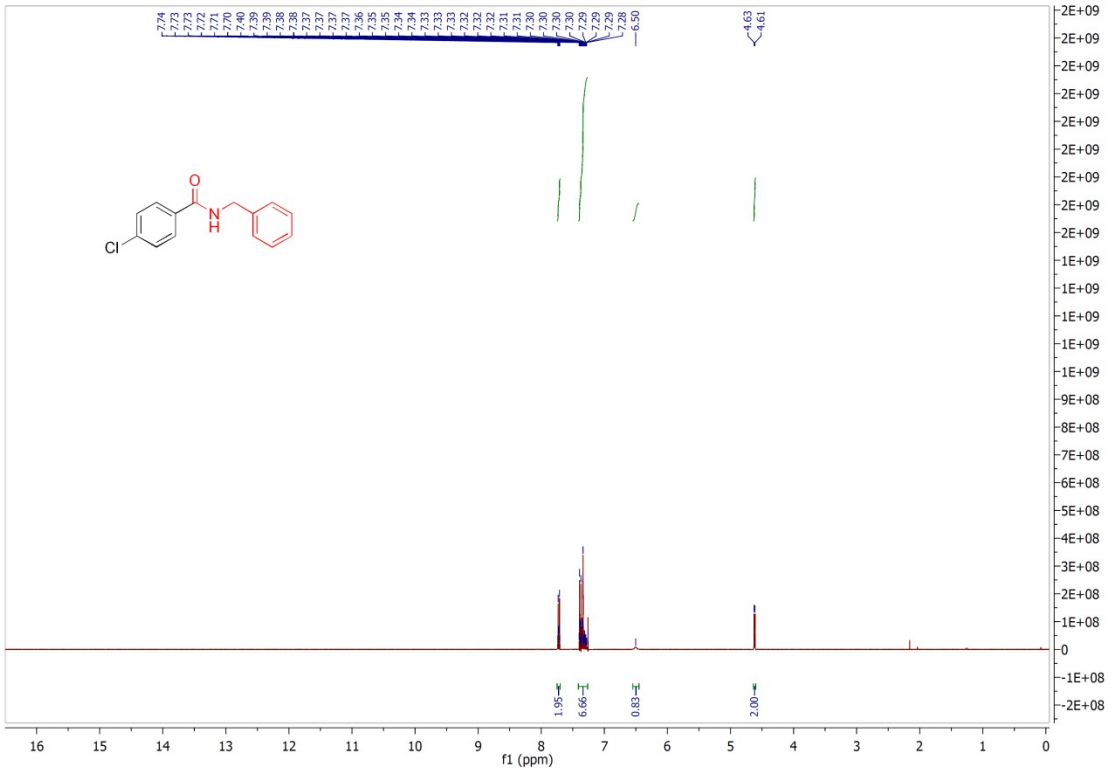


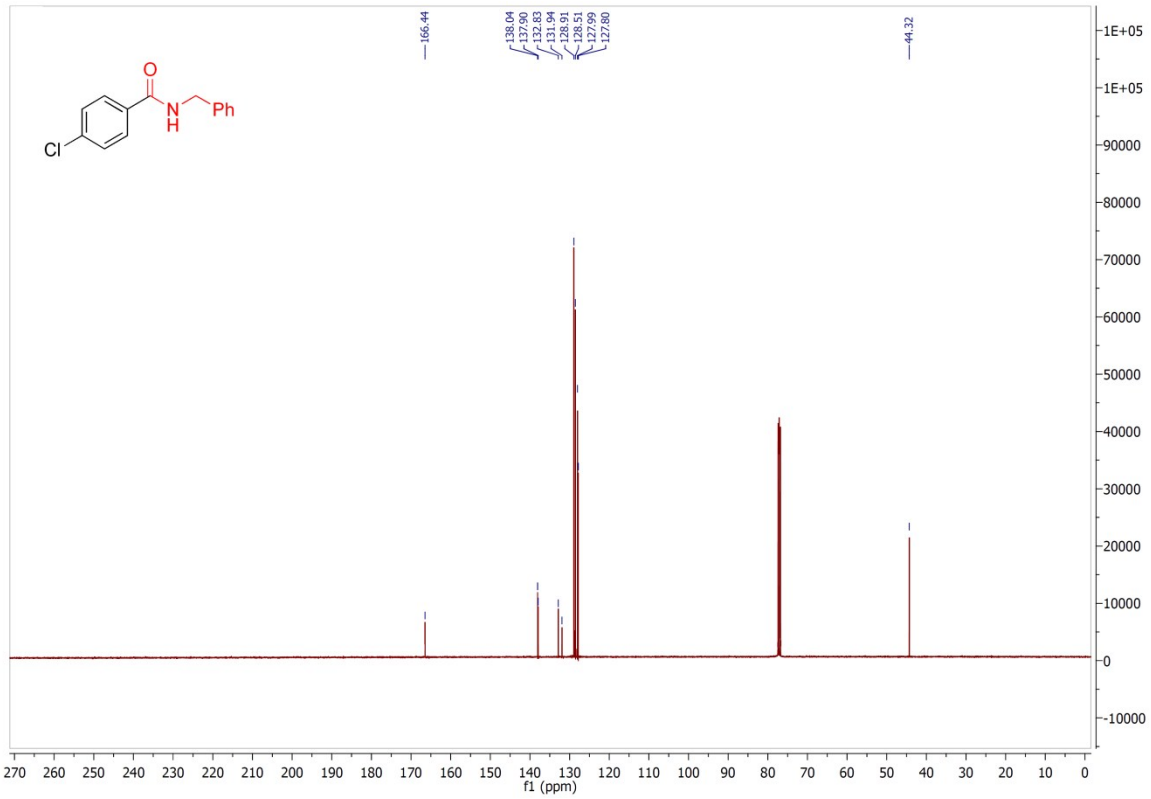
3.10. 4-chloro-N-pentylbenzamide (3j)



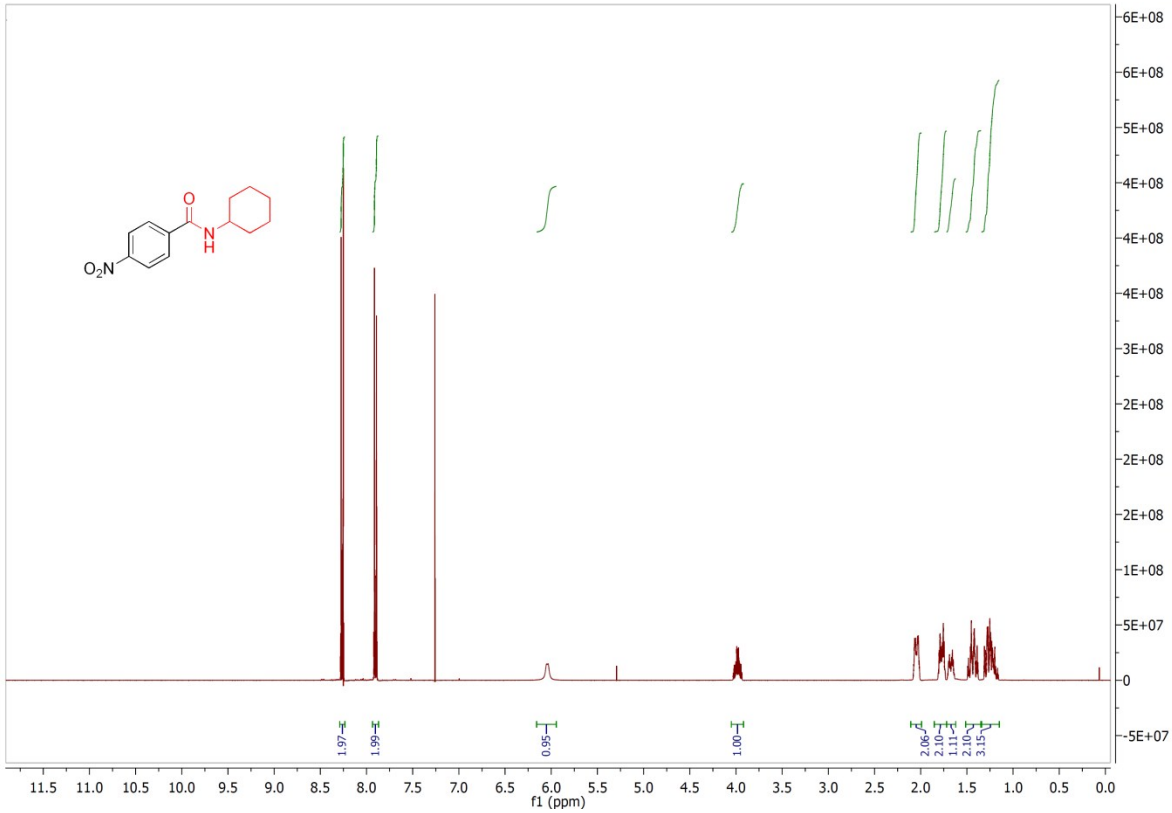


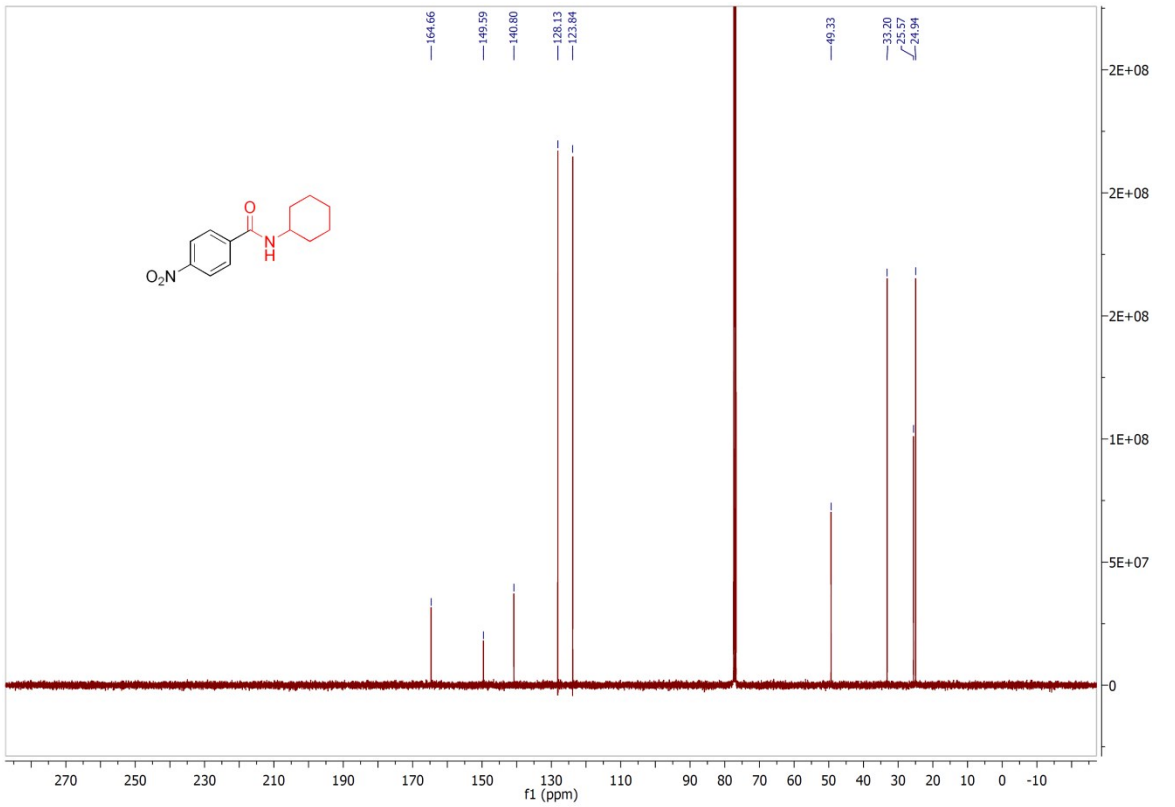
3.11. N-benzyl-4-chlorobenzamide (3k)



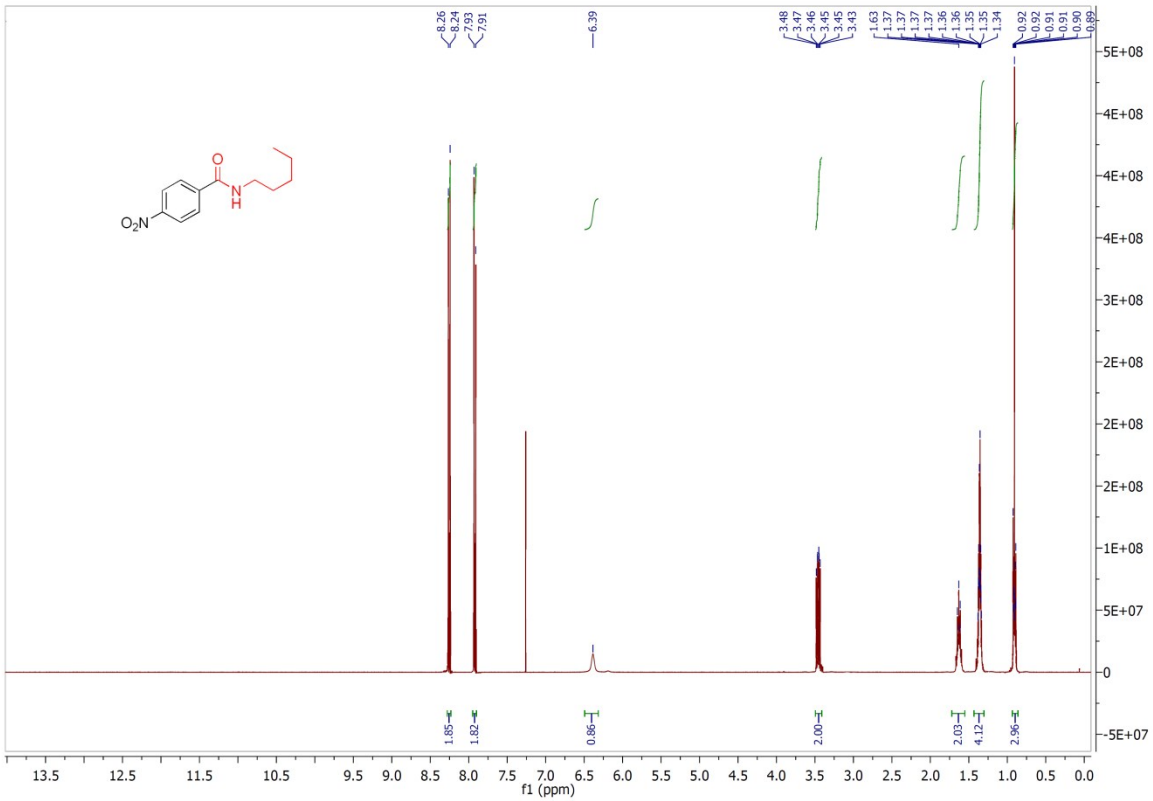


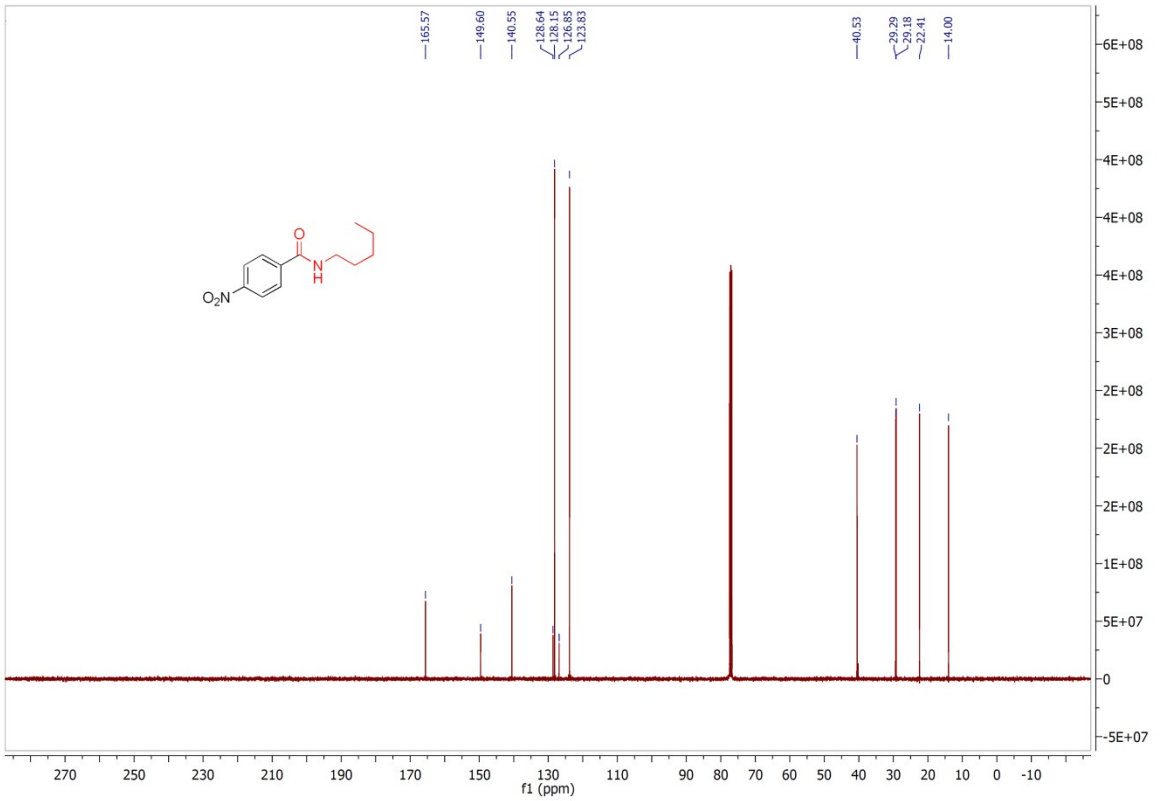
3.12. N-cyclohexyl-4-nitrobenzamide (3l)



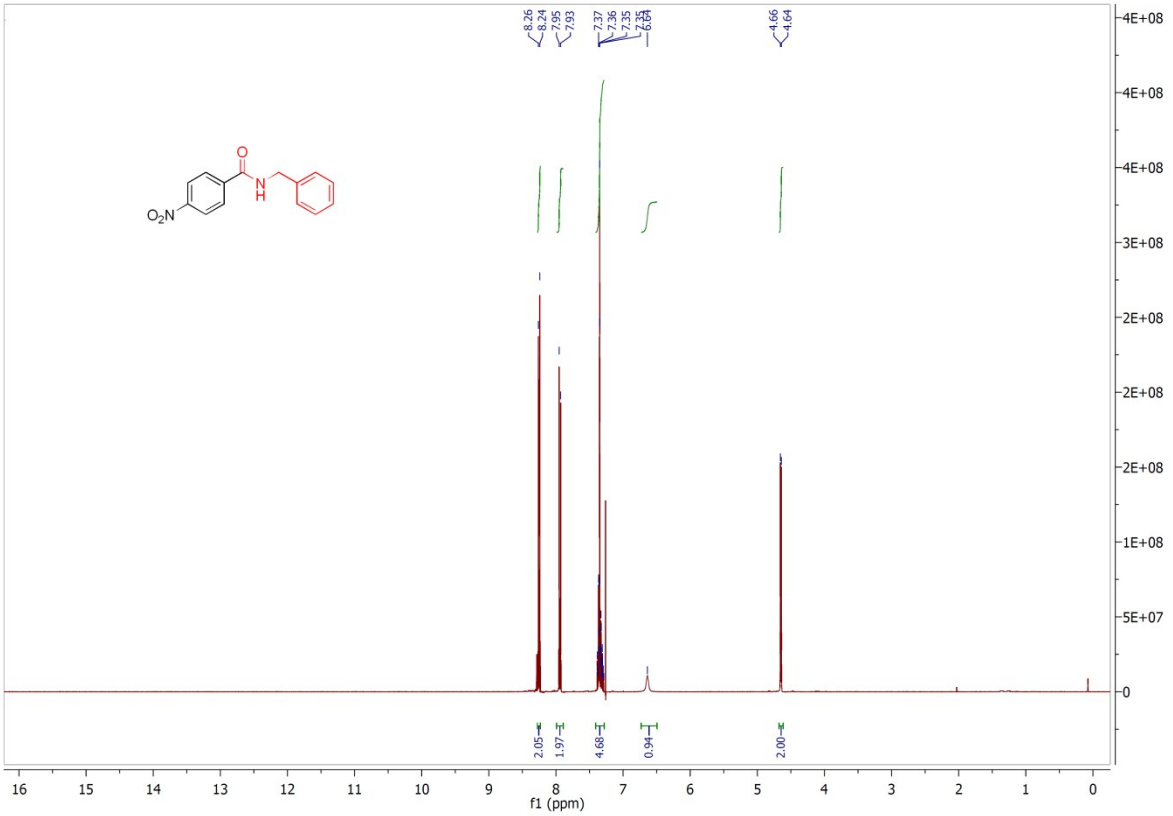


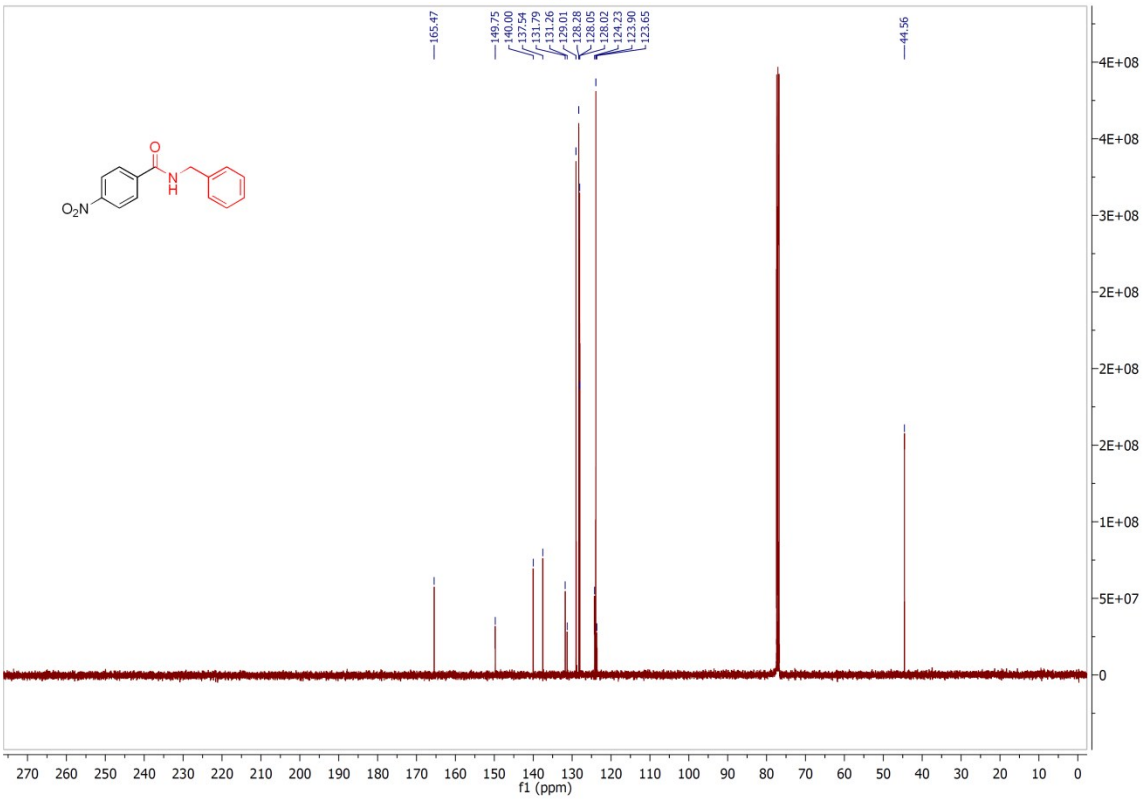
3.13. N-cyclohexyl-4-nitrobenzamide (3m)



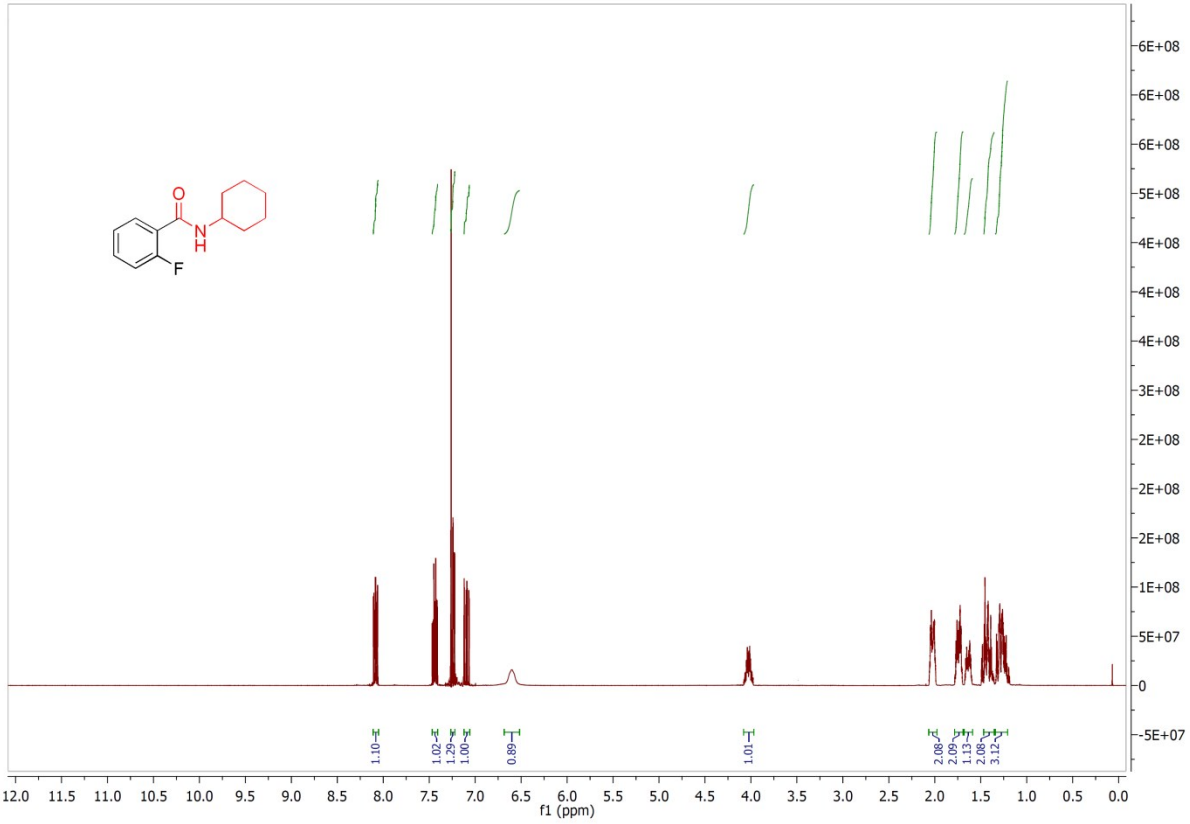


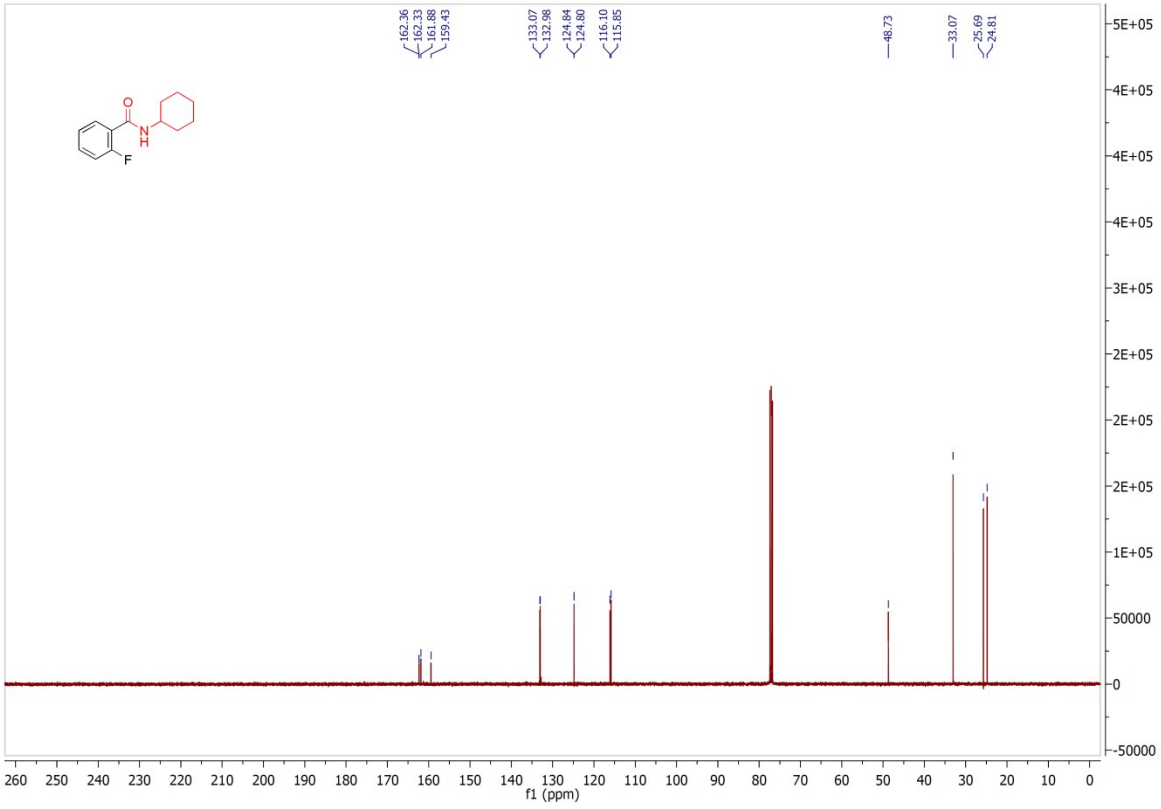
3.14. N-cyclohexyl-4-nitrobenzamide (3n)



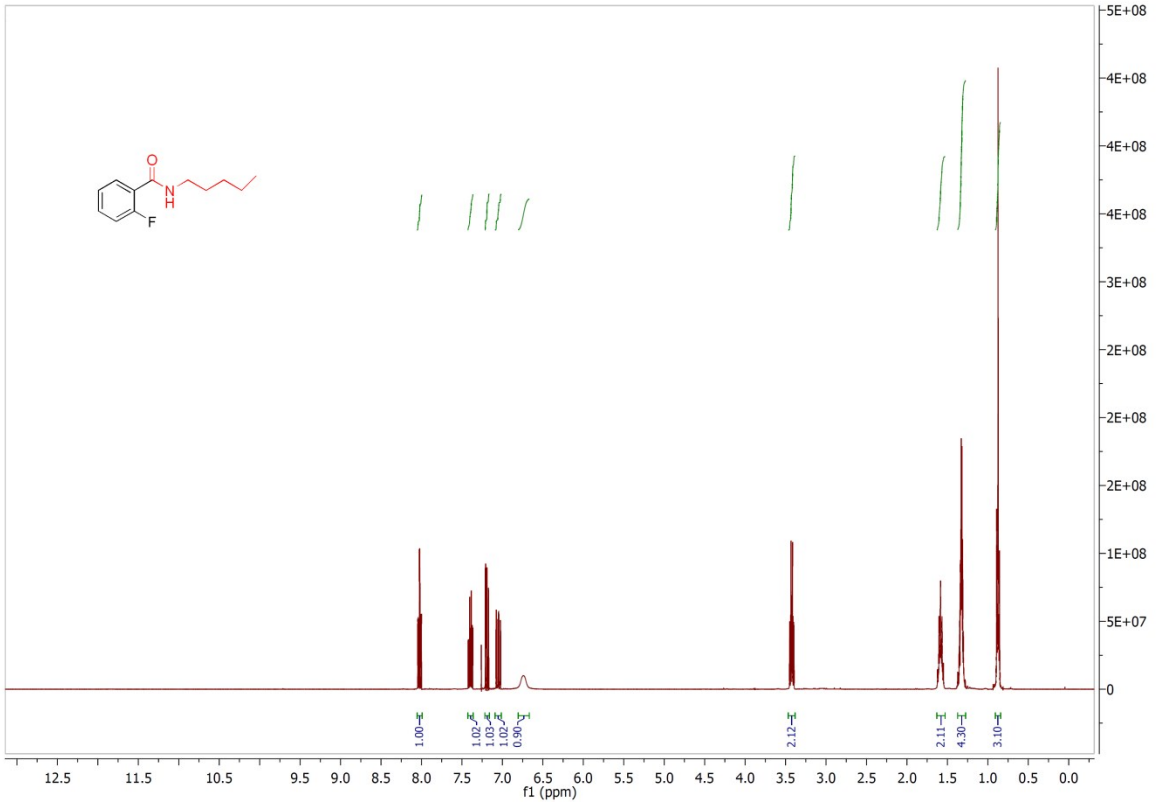


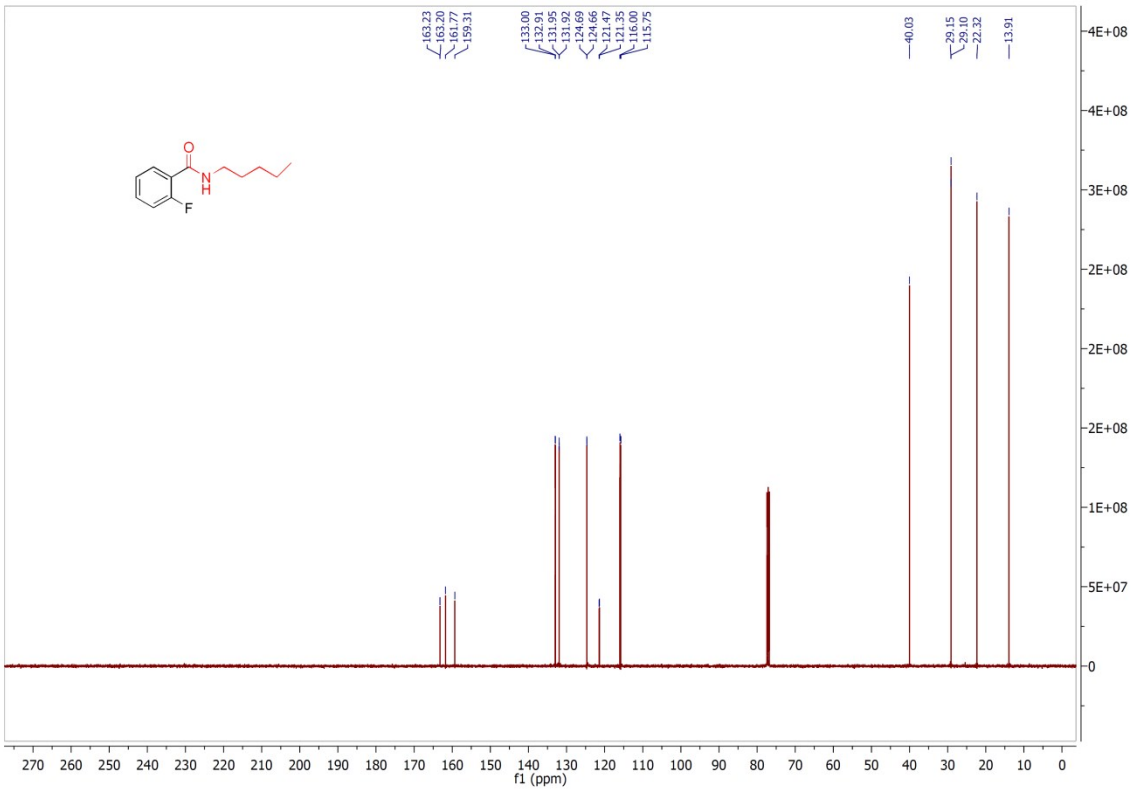
3.15. N-cyclohexyl-2-fluorobenzamide (3o)

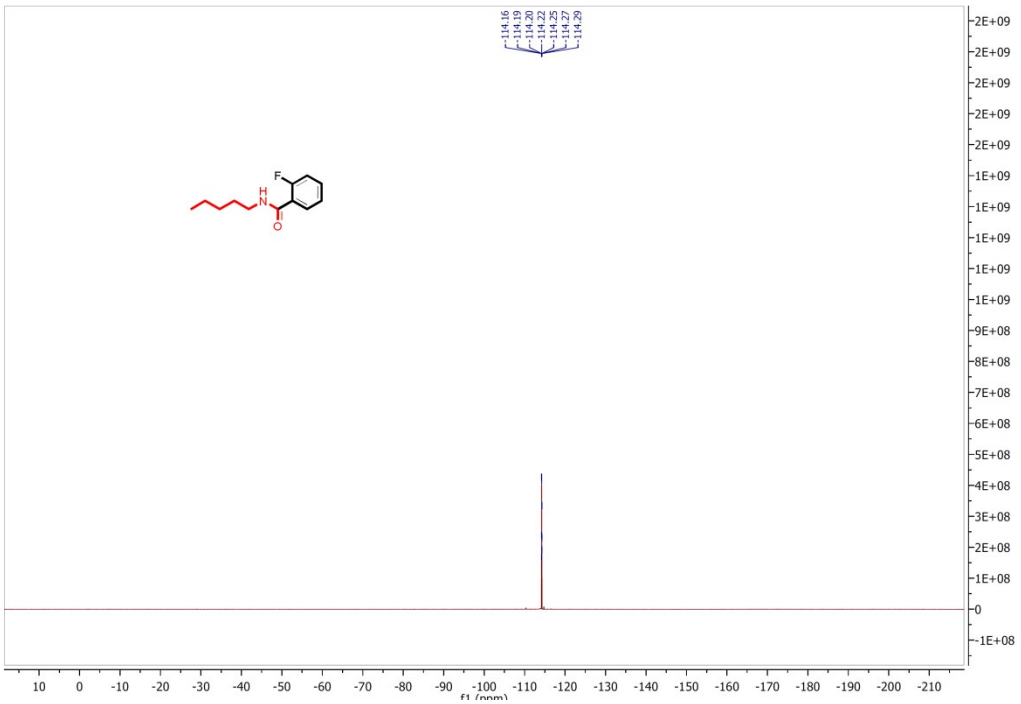

O
N
H
F
6E+08
6E+08
6E+08
5E+08
4E+08
4E+08
4E+08
4E+08
3E+08
2E+08
2E+08
2E+08
2E+08
1E+08
5E+07
0
-5E+07
1.10
1.02
1.29
1.00
0.89
1.01
2.08
2.09
1.13
2.08
3.12
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


162.36
162.33
161.88
159.43
133.07
132.98
124.84
124.80
116.10
115.85
48.73
33.07
25.69
24.81
O
N
H
F
5E+05
4E+05
4E+05
4E+05
3E+05
2E+05
2E+05
2E+05
1E+05
50000
0
-50000
260 250 240 230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

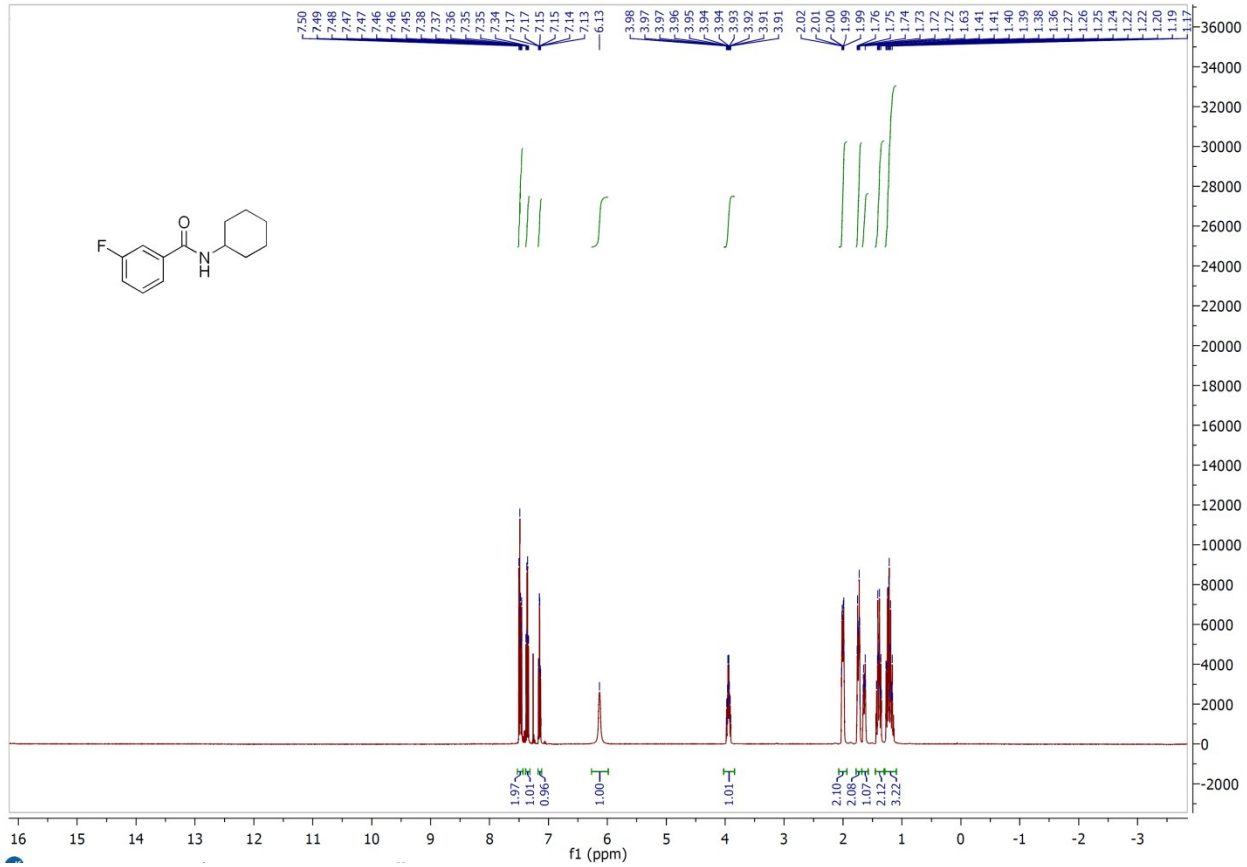
3.16. 2-fluoro-N-pentylbenzamide (3p)

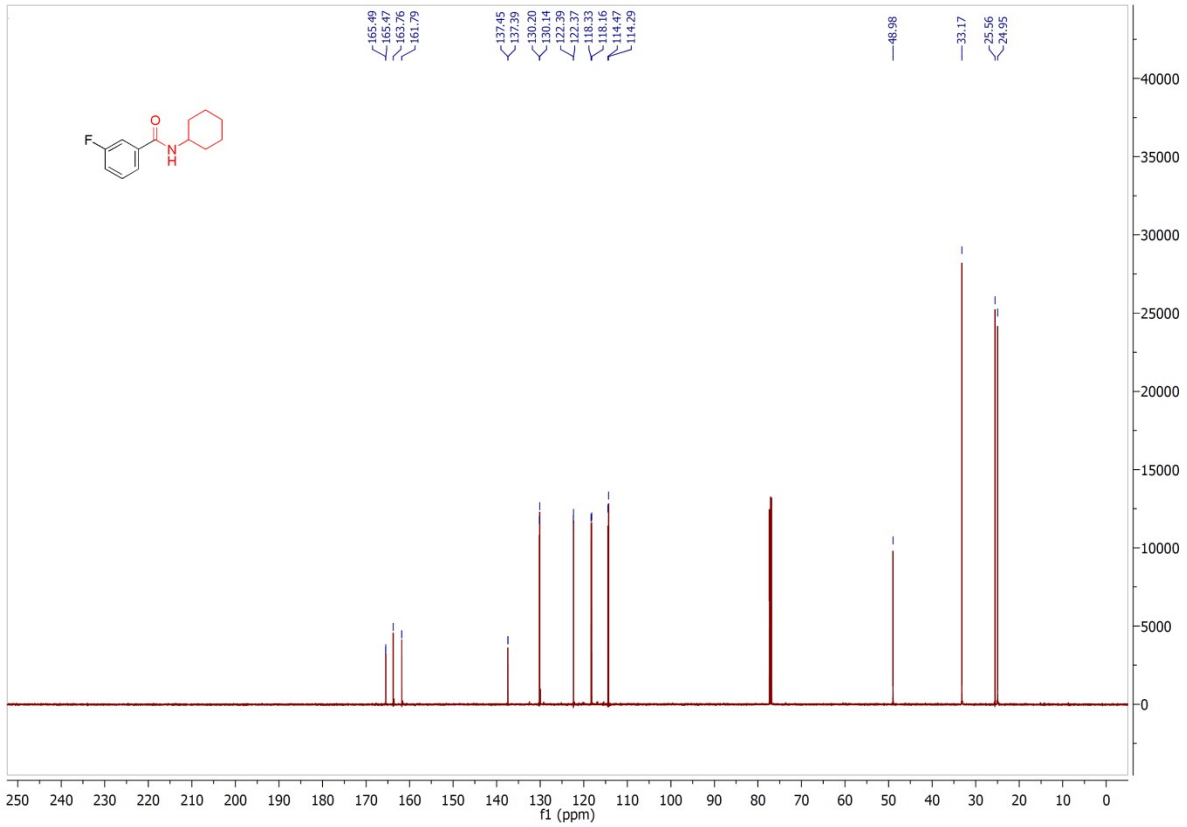




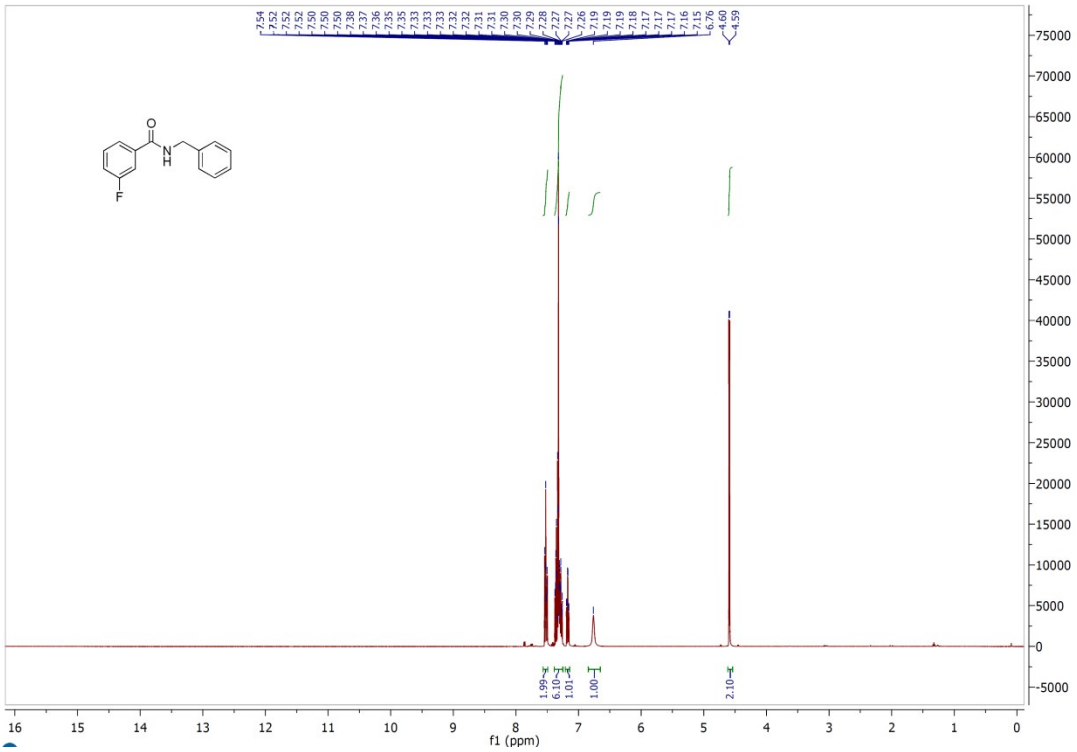


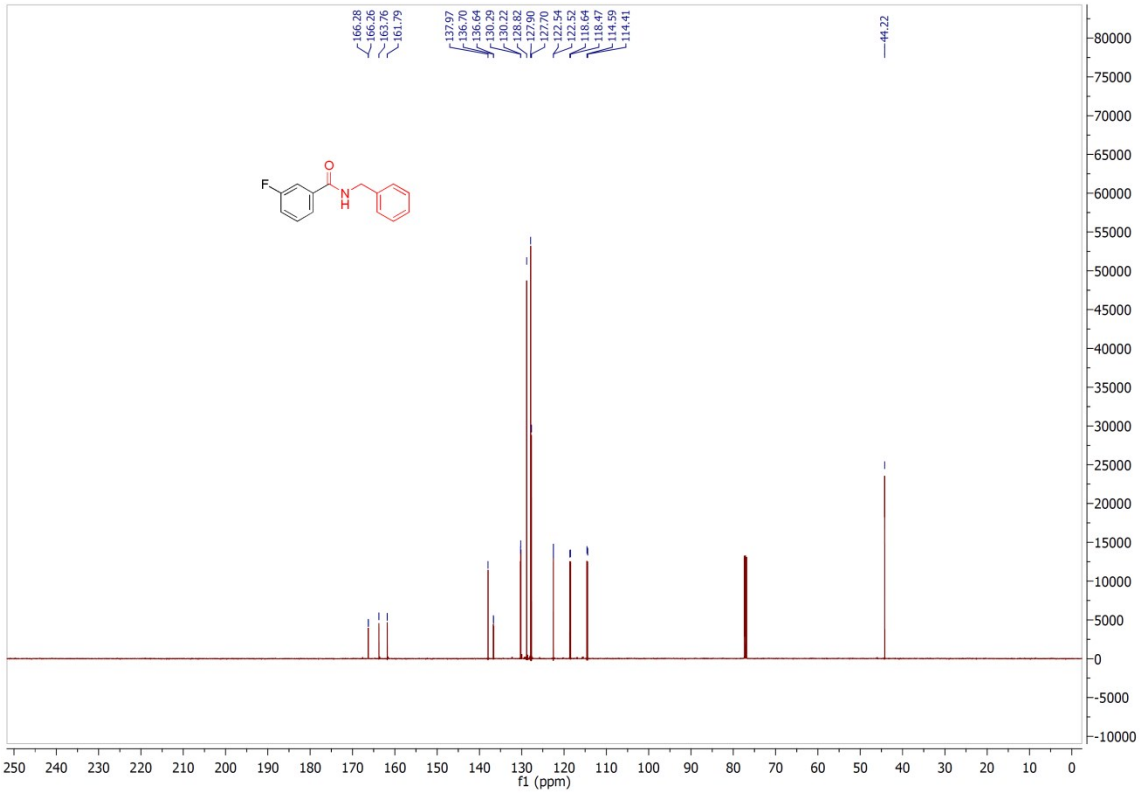
3.17. N-cyclohexyl-3-fluorobenzamide (3q)

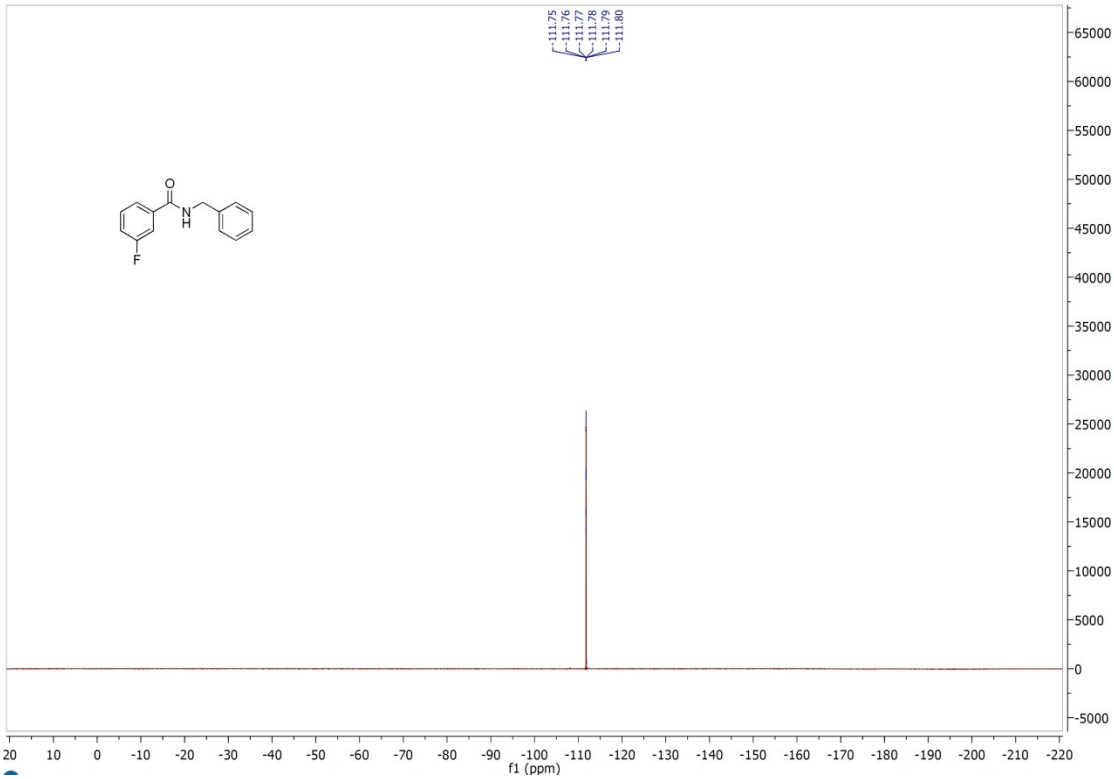




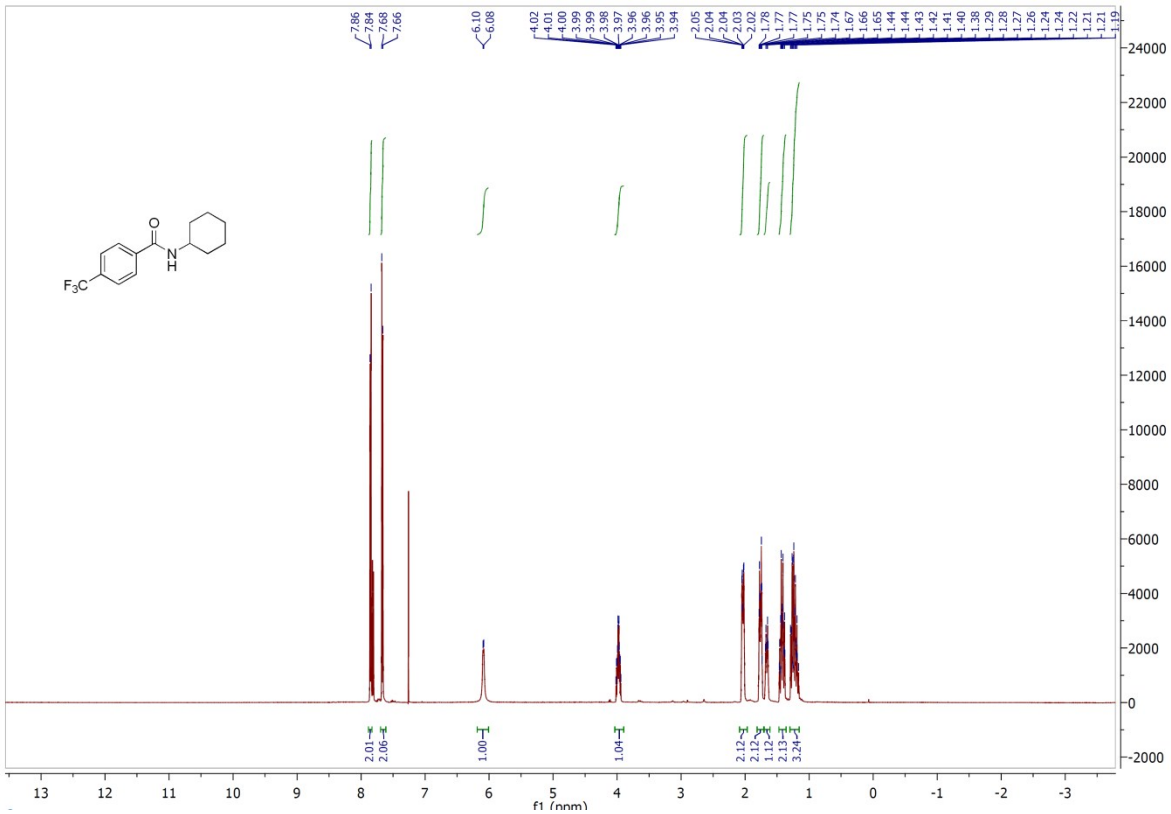
3.18. N-benzyl-3-fluorobenzamide (3r)

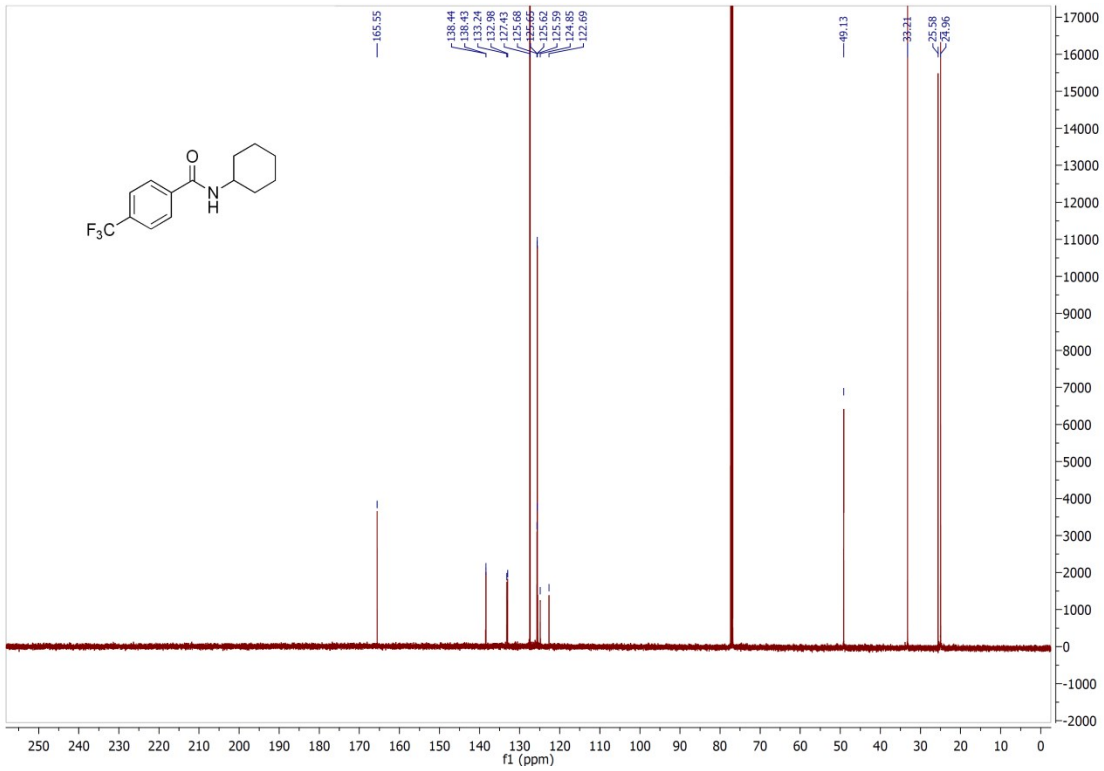



166.28
166.26
163.76
161.79
137.97
136.70
136.64
130.39
130.22
128.82
127.90
127.70
122.54
122.52
118.64
118.47
114.59
114.41
44.22
F
O
N
H
f1 (ppm)

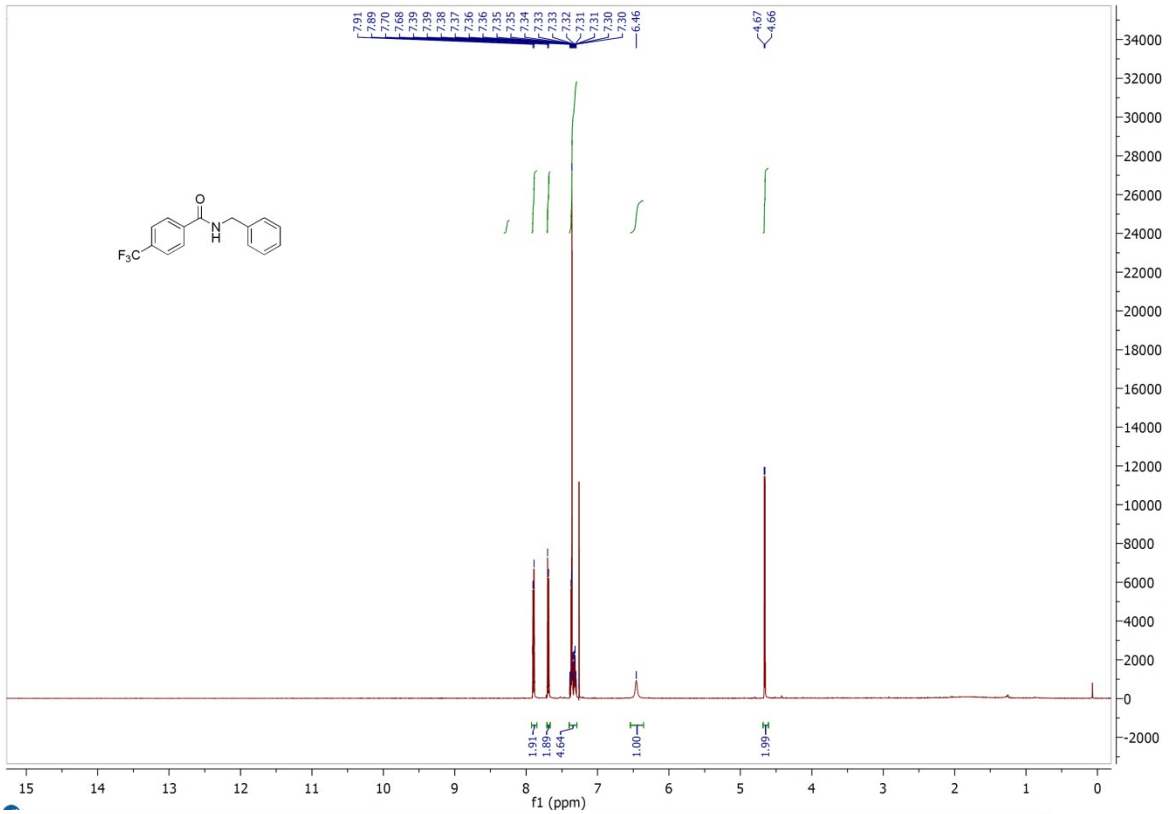

111.75
111.76
111.77
111.78
111.79
111.80
O
N
H
F
f1 (ppm)

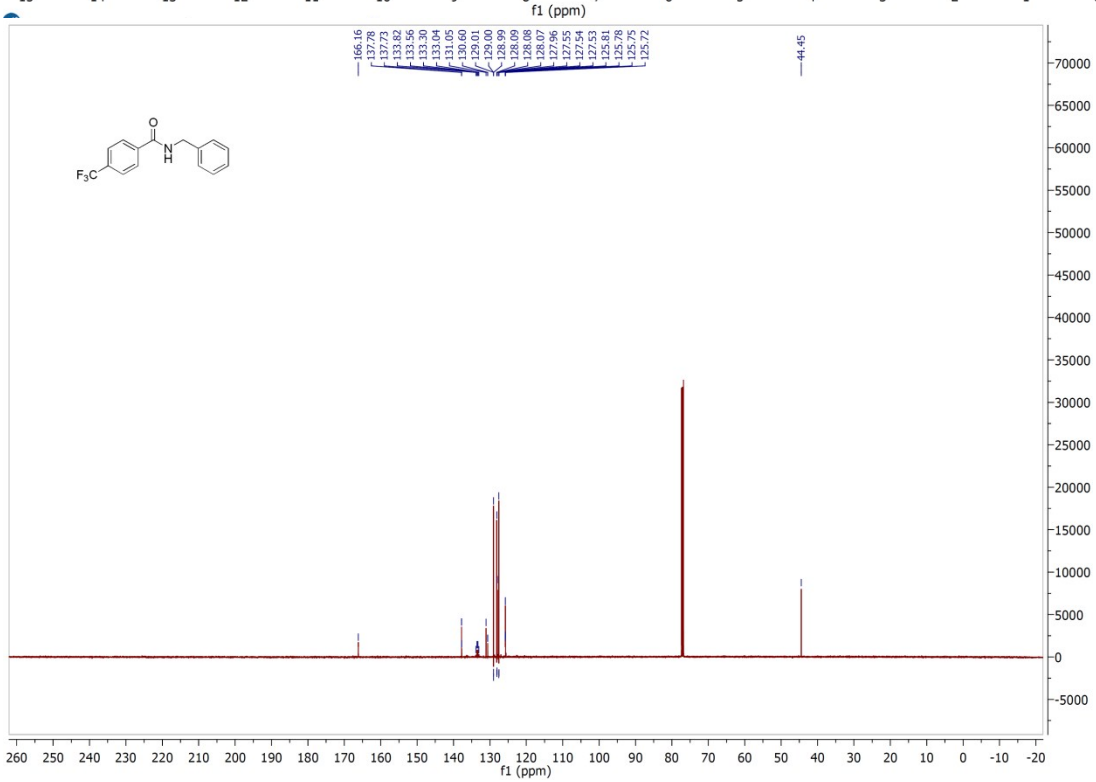
3.19. N-cyclohexyl-4-(trifluoromethyl)benzamide (3s)

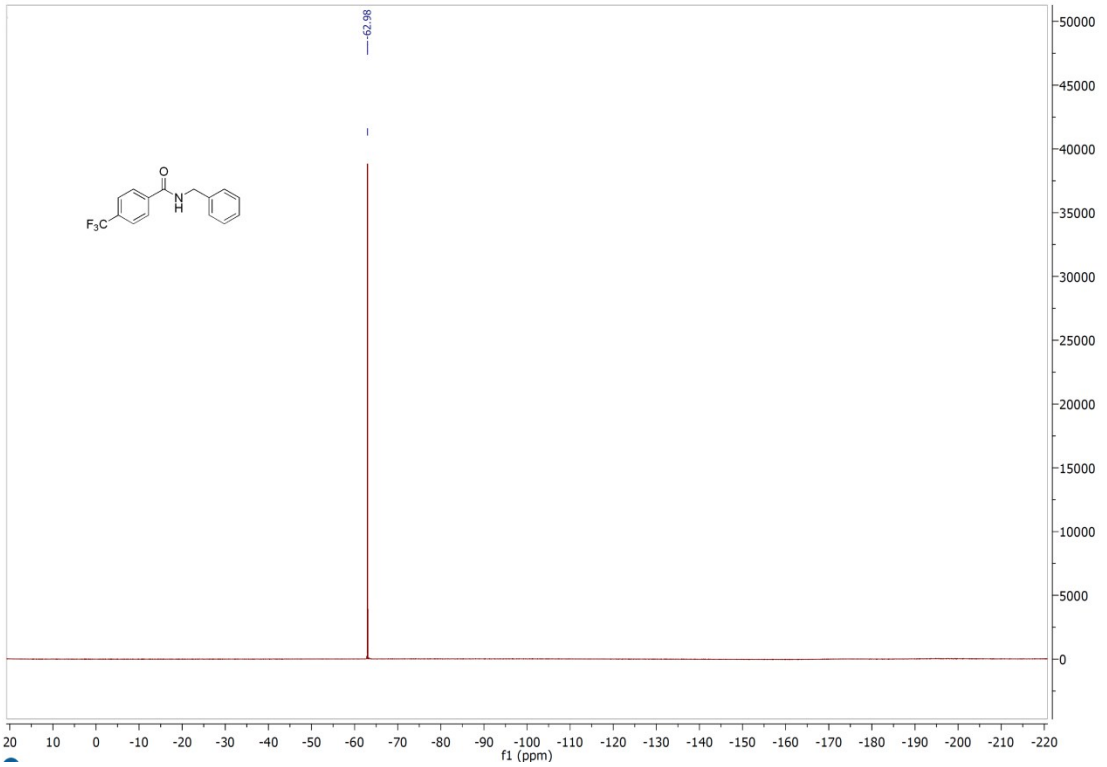




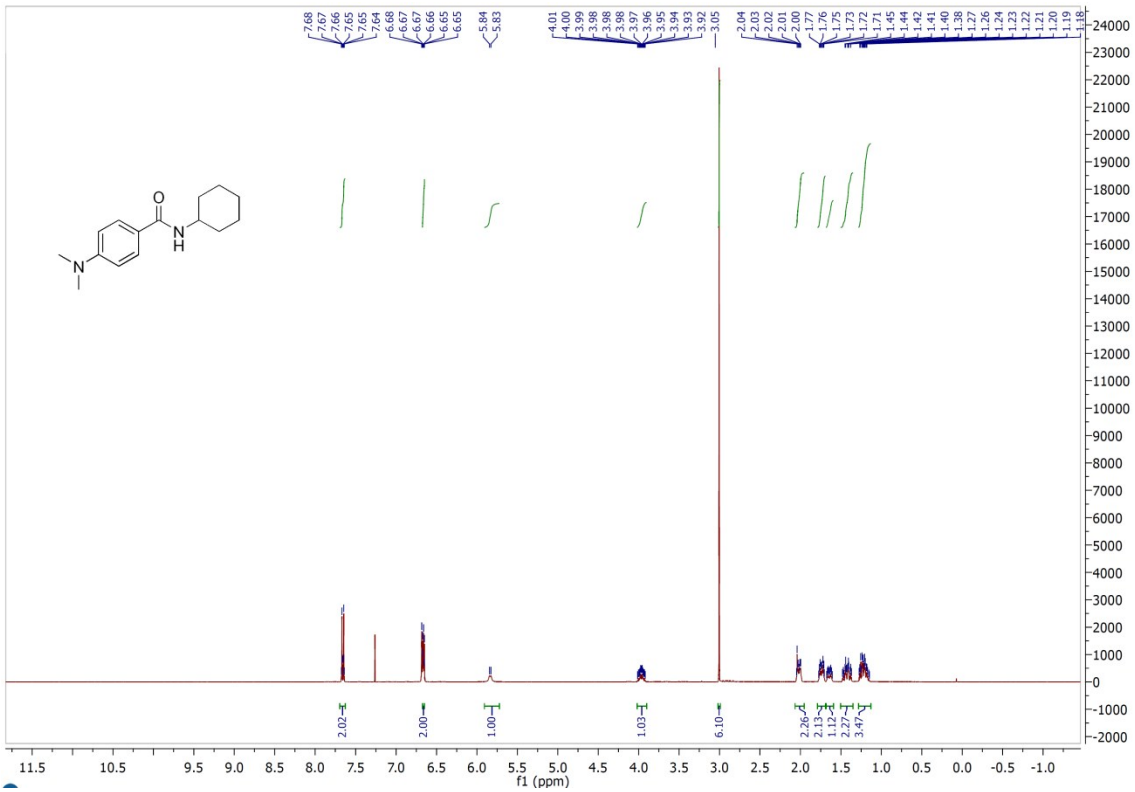
3.20. N-benzyl-4-(trifluoromethyl)benzamide (3t)

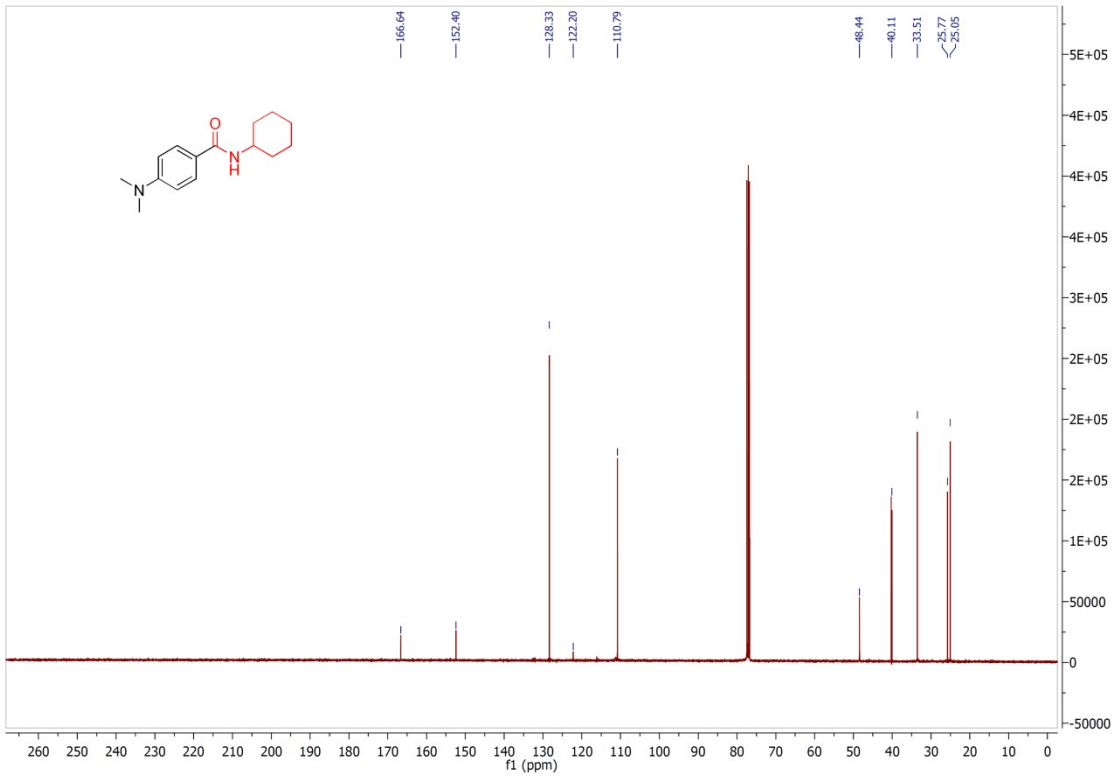




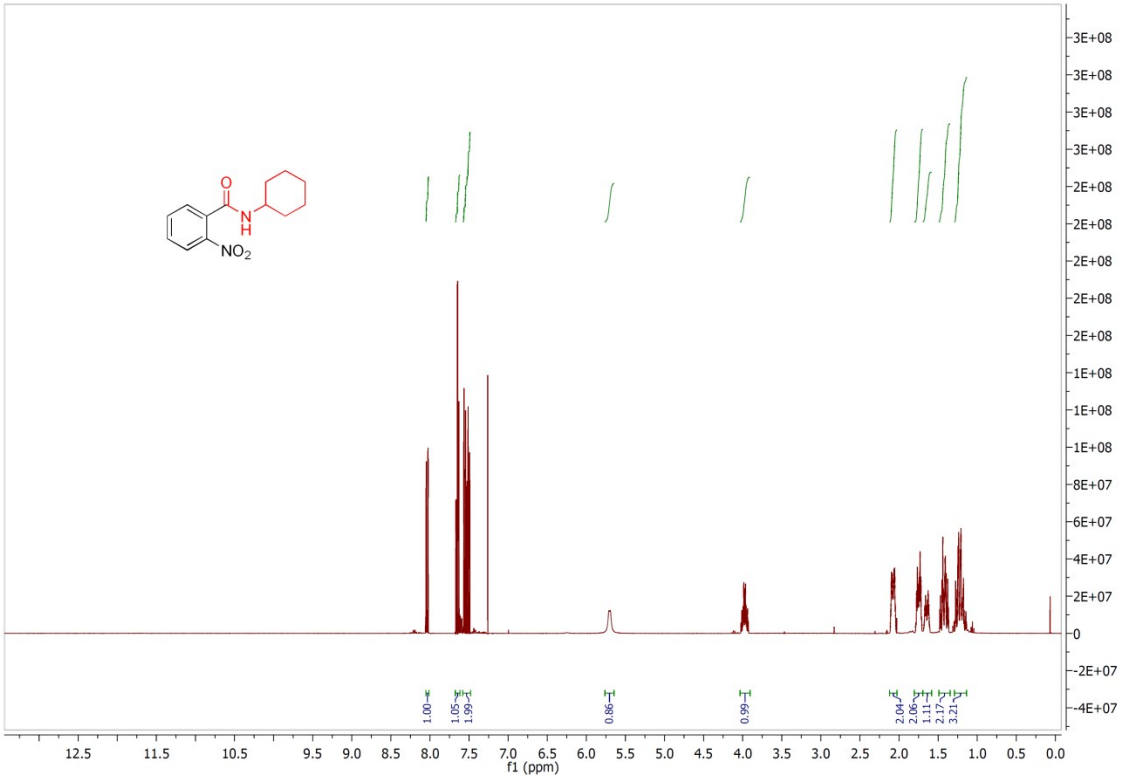


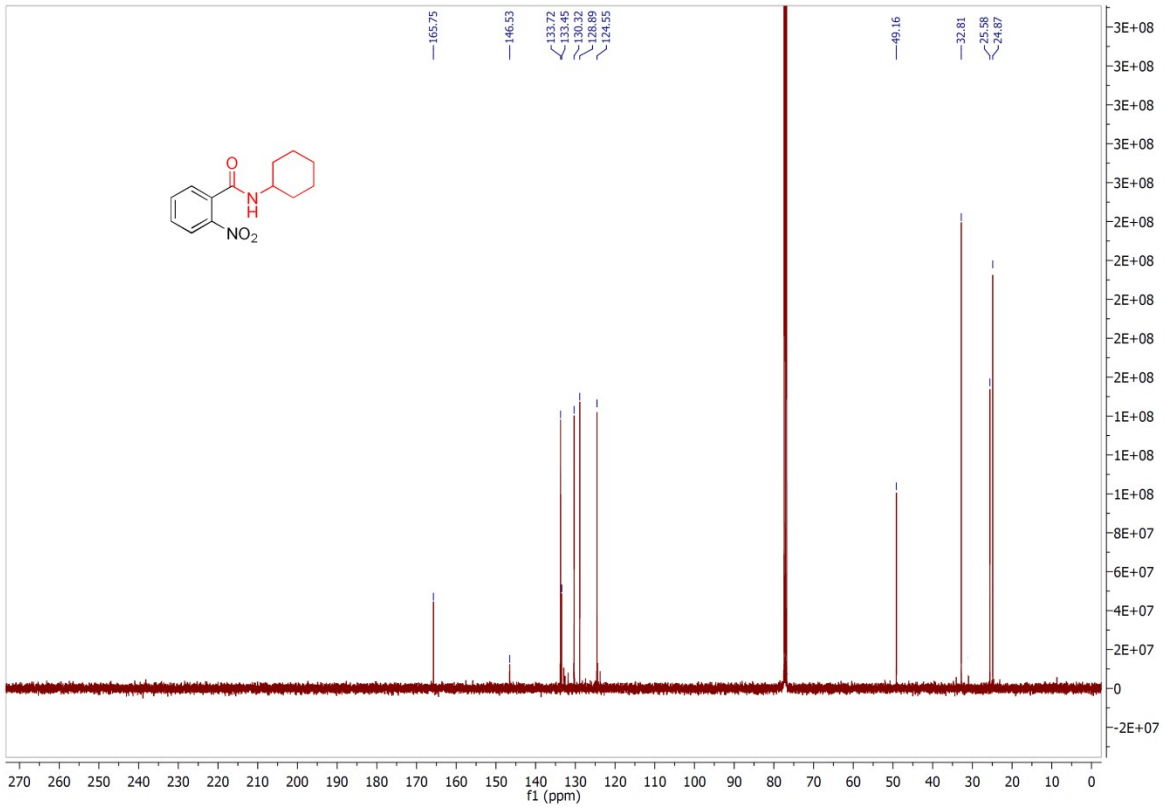
3.21. N-cyclohexyl-4-(dimethylamino)benzamide (3u)



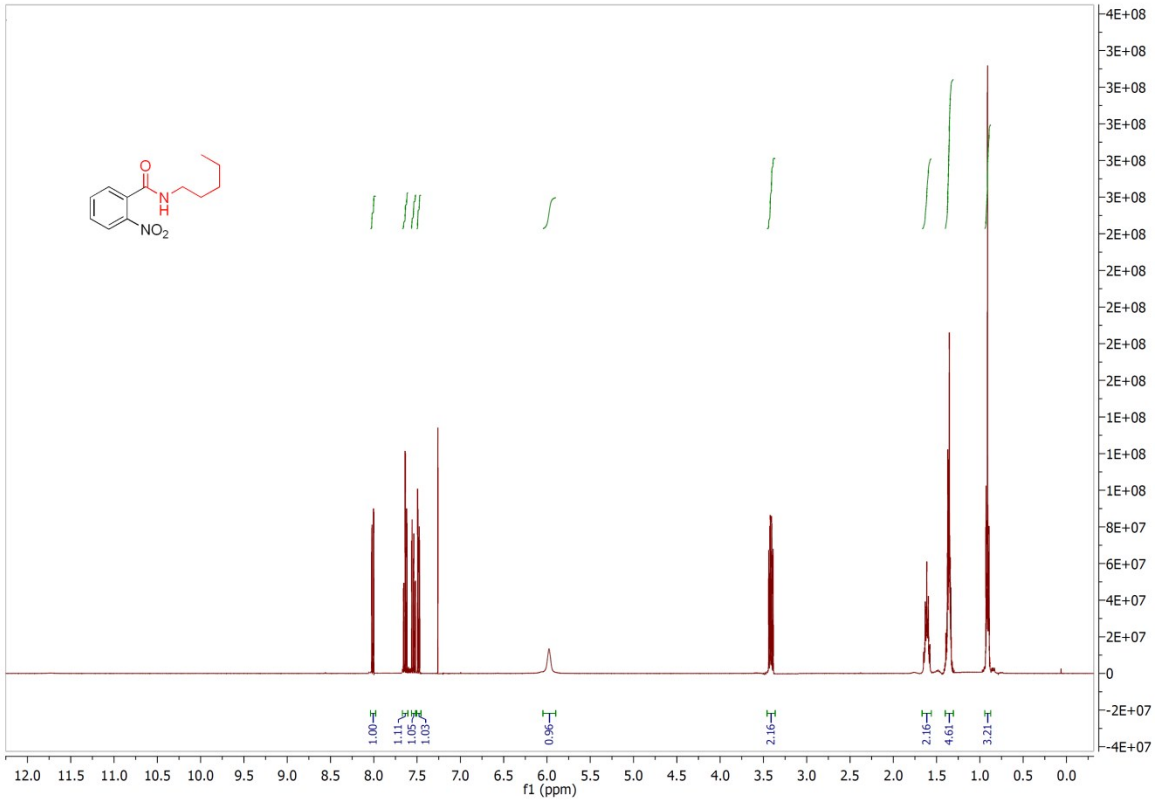


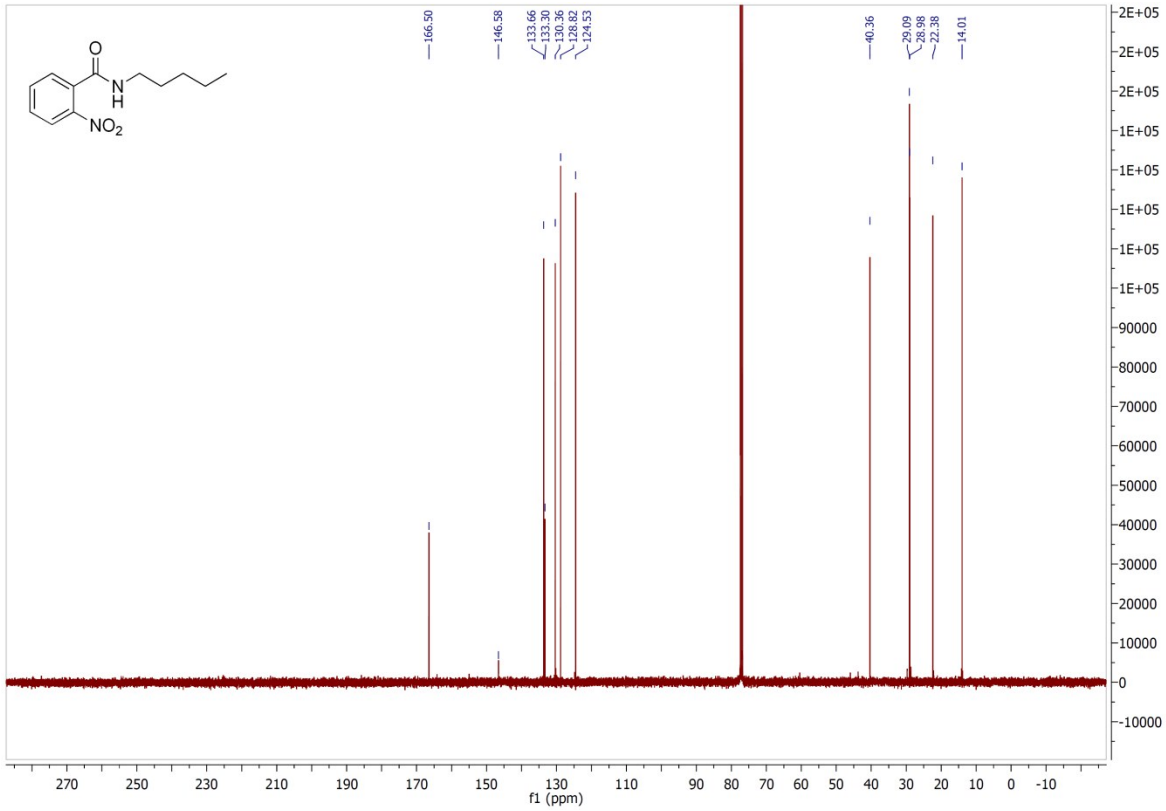
3.22. N-cyclohexyl-2-nitrobenzamide (3v)



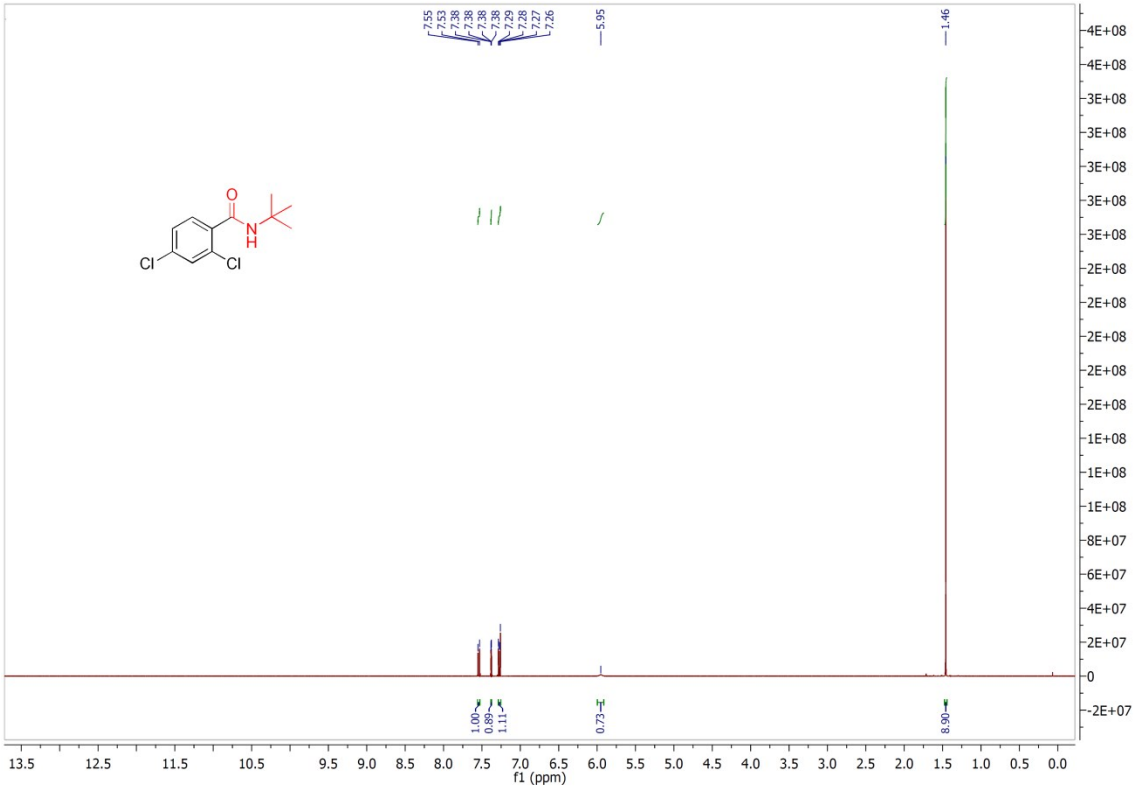


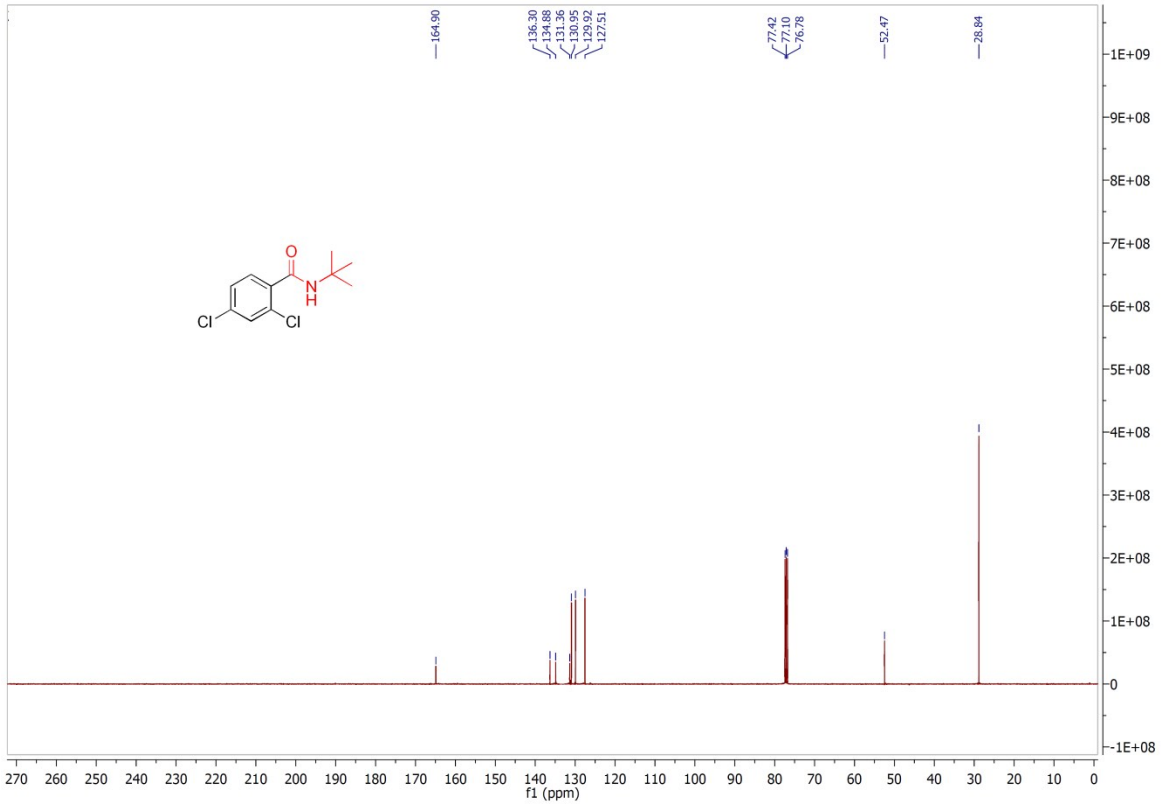
3.23. 2-nitro-N-pentylbenzamide (3w)



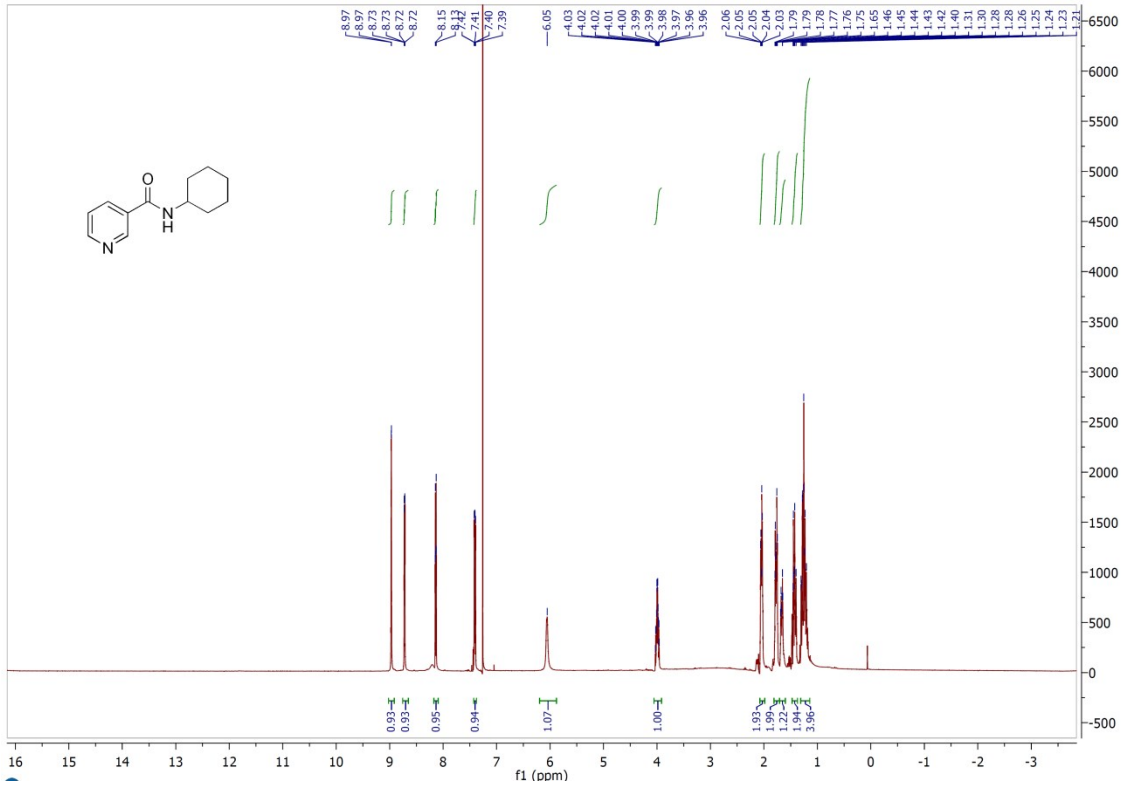


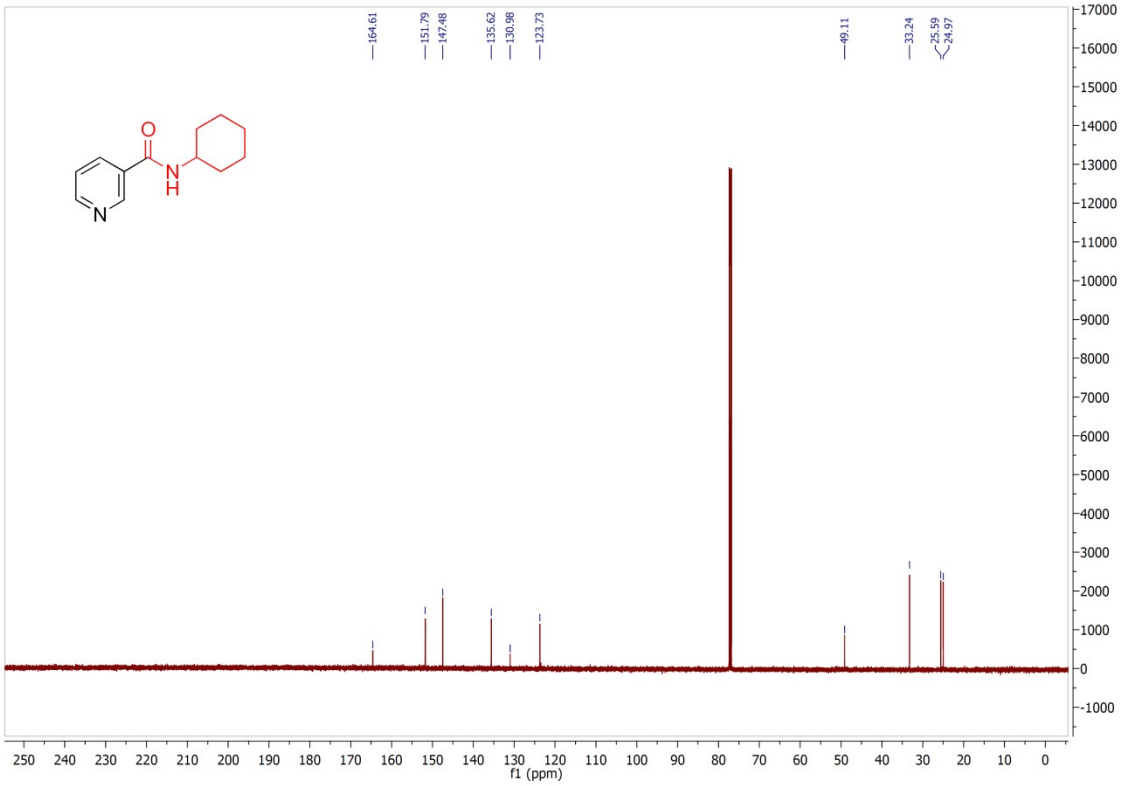
3.24. N-(tert-butyl)-2,4-dichlorobenzamide (3x)



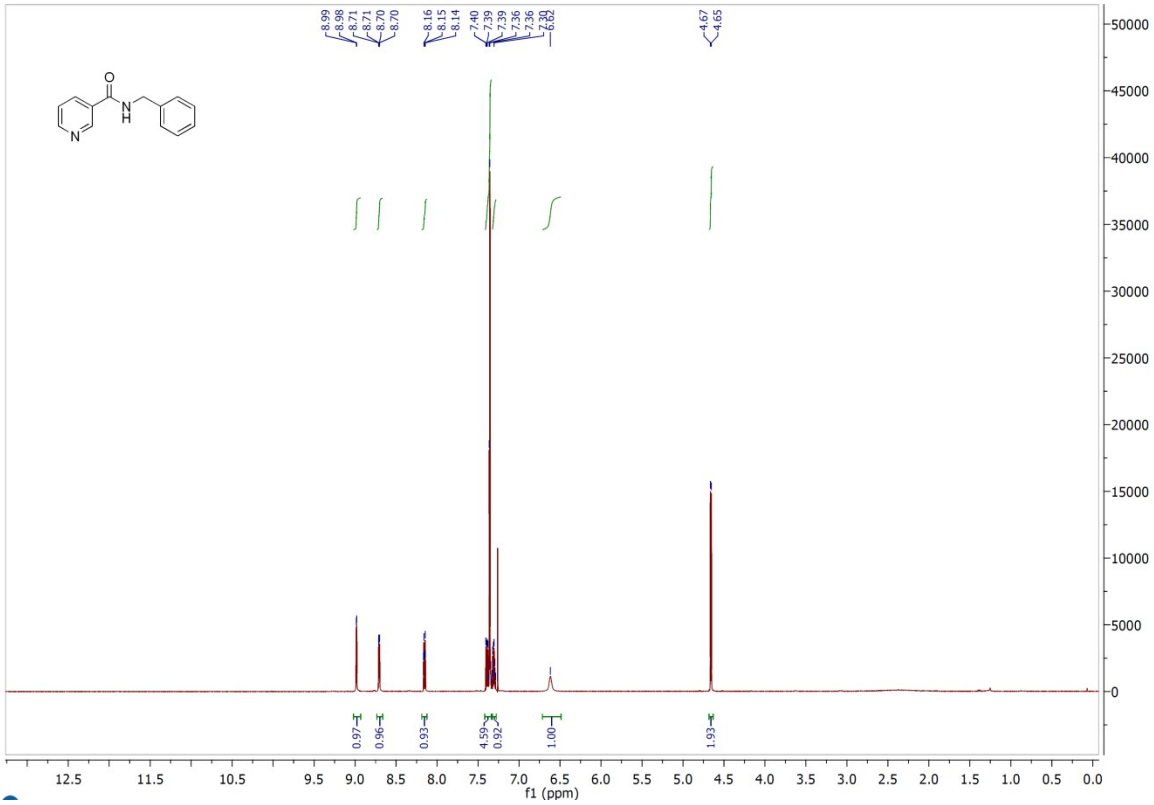


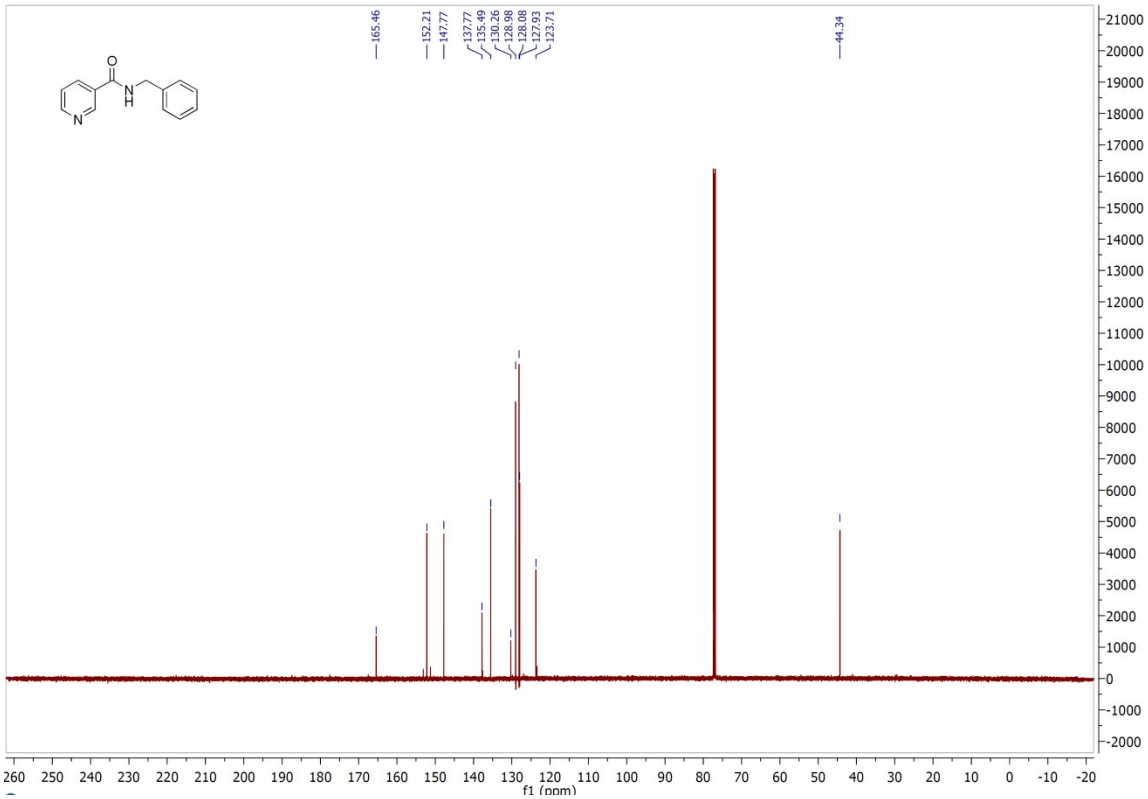
3.25. N-cyclohexylnicotinamide (3y)



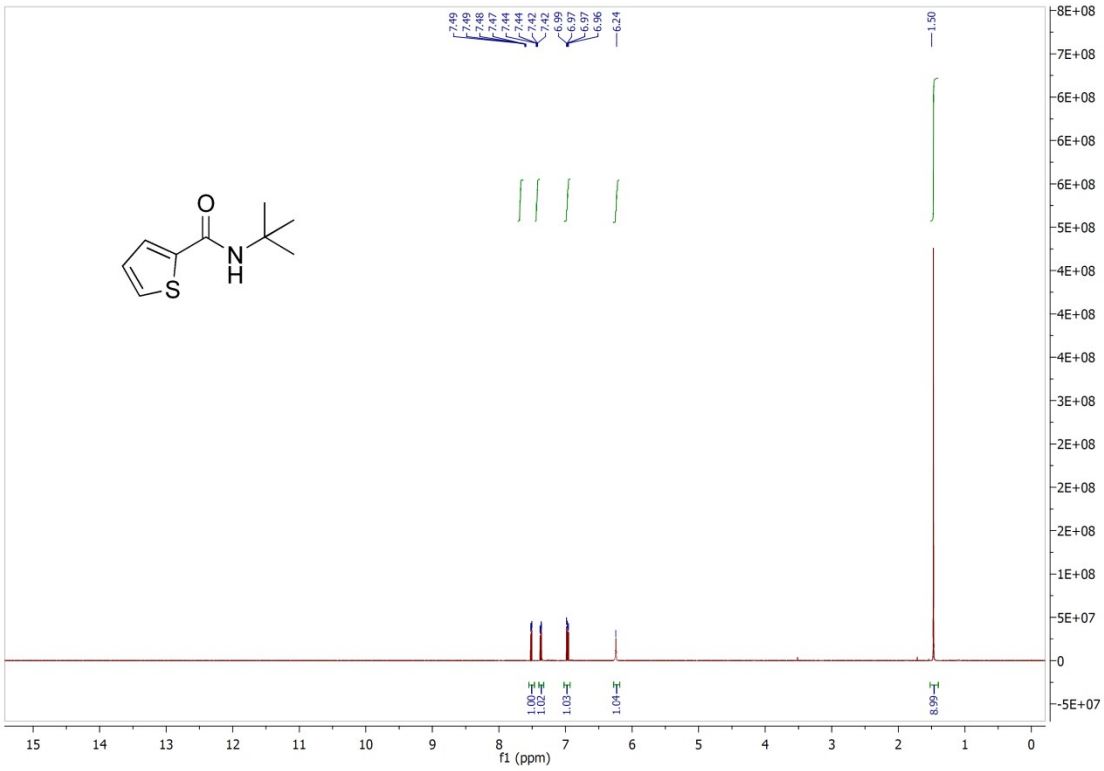


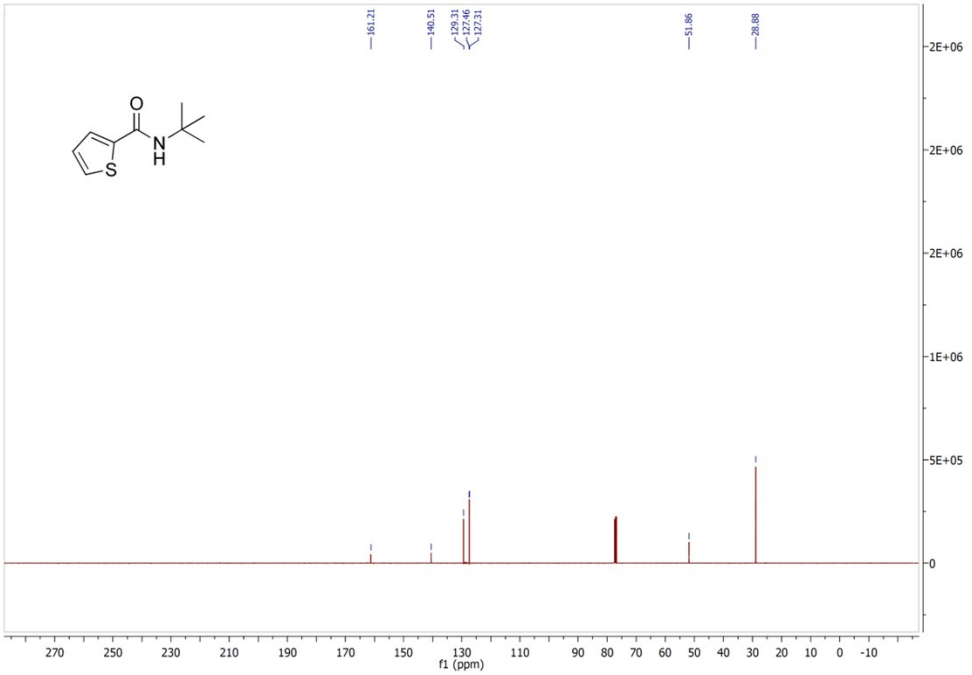
3.26. N-benzylnicotinamide (3z)



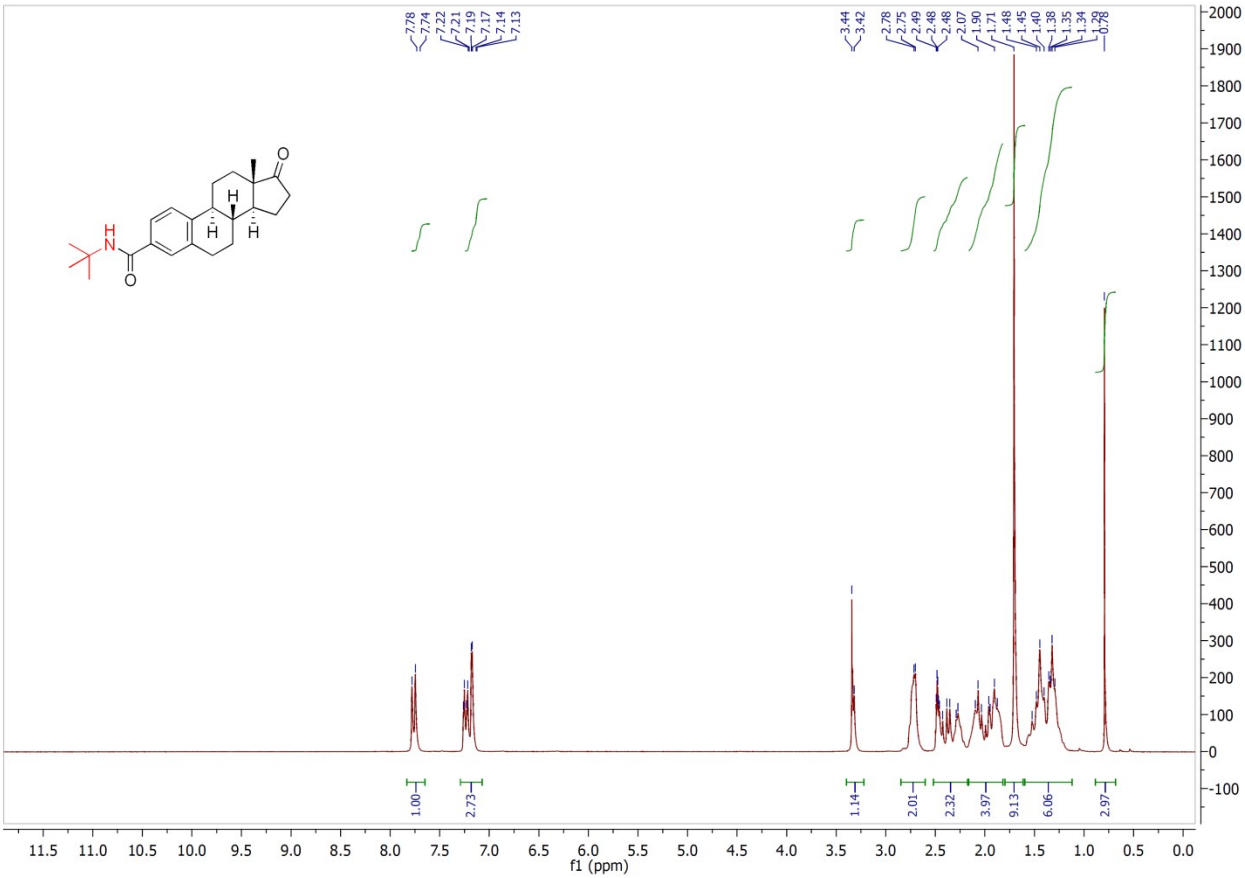


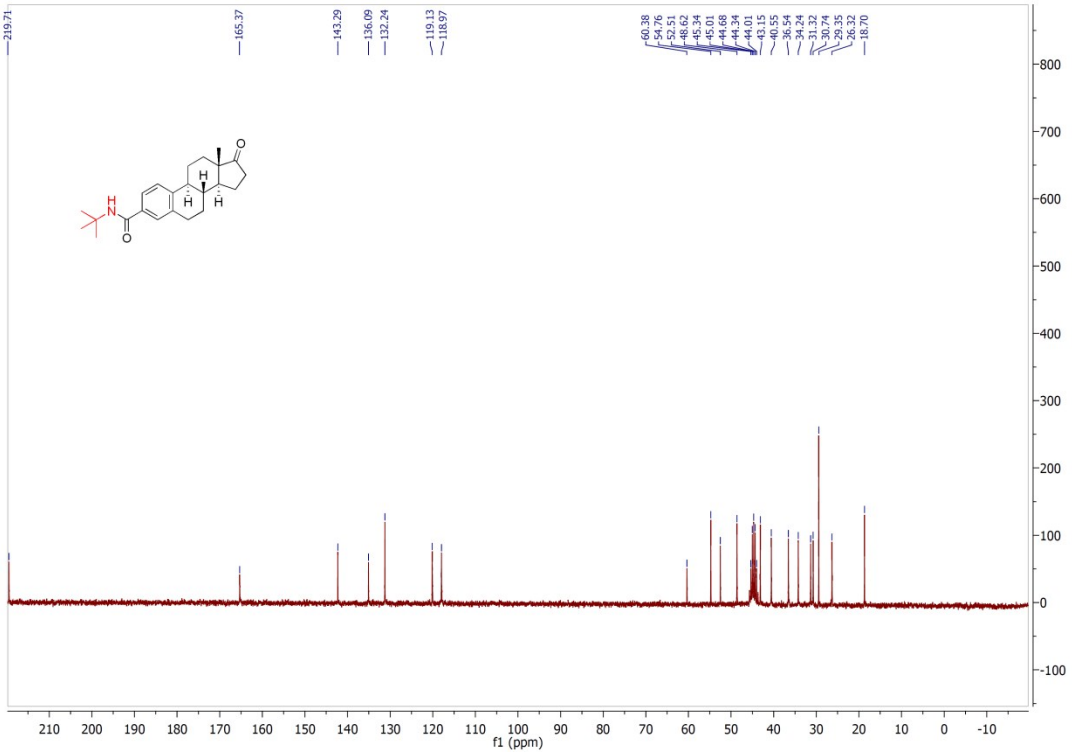
3.27. N-(tert-butyl)thiophene-2-carboxamide (3ab)



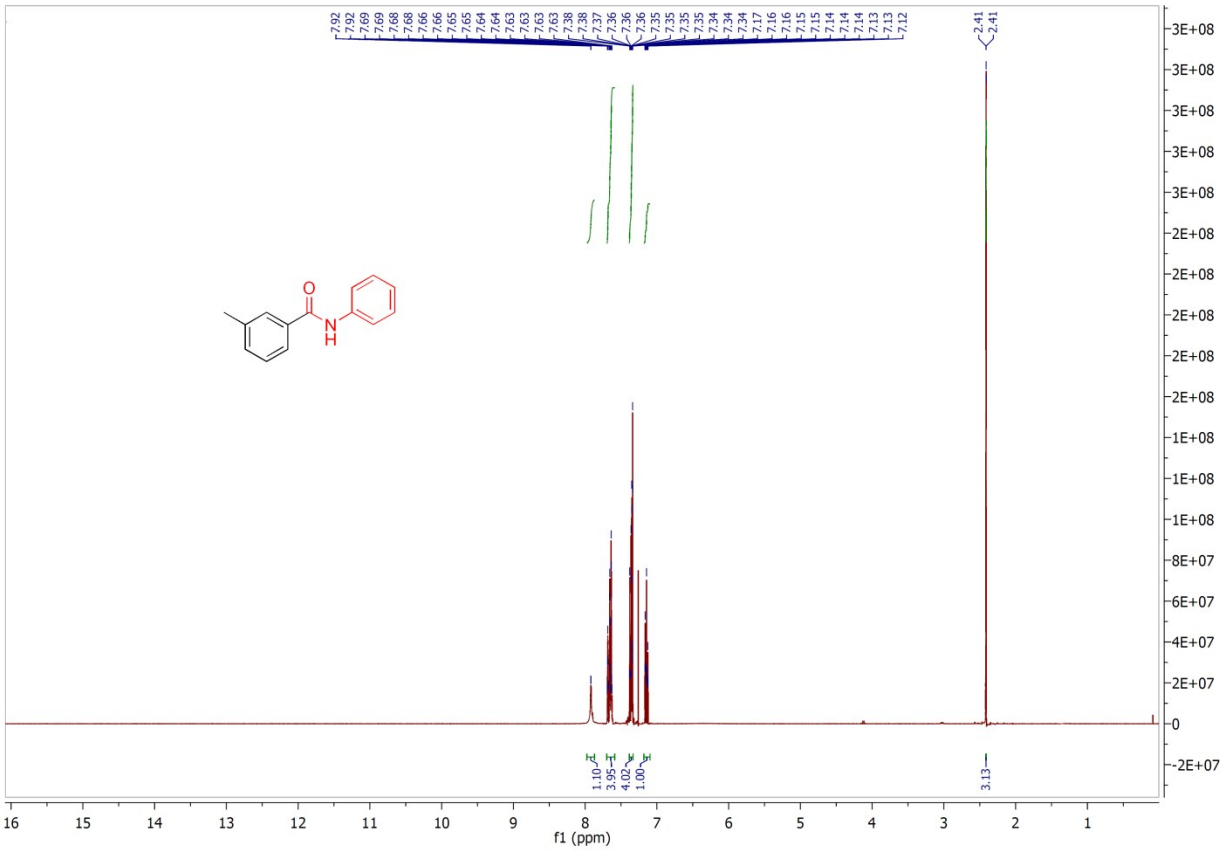


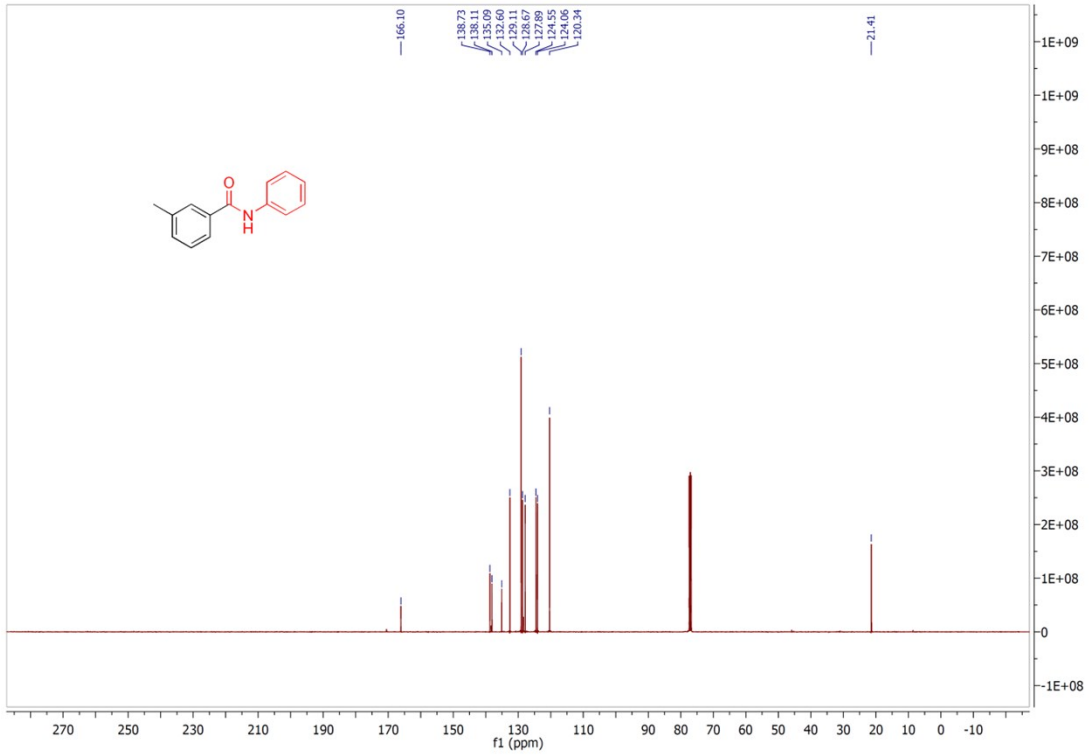
2.28. (8R,9S,13S,14S)-N-(tert-butyl)-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthrene-3-carboxamide (3ac)



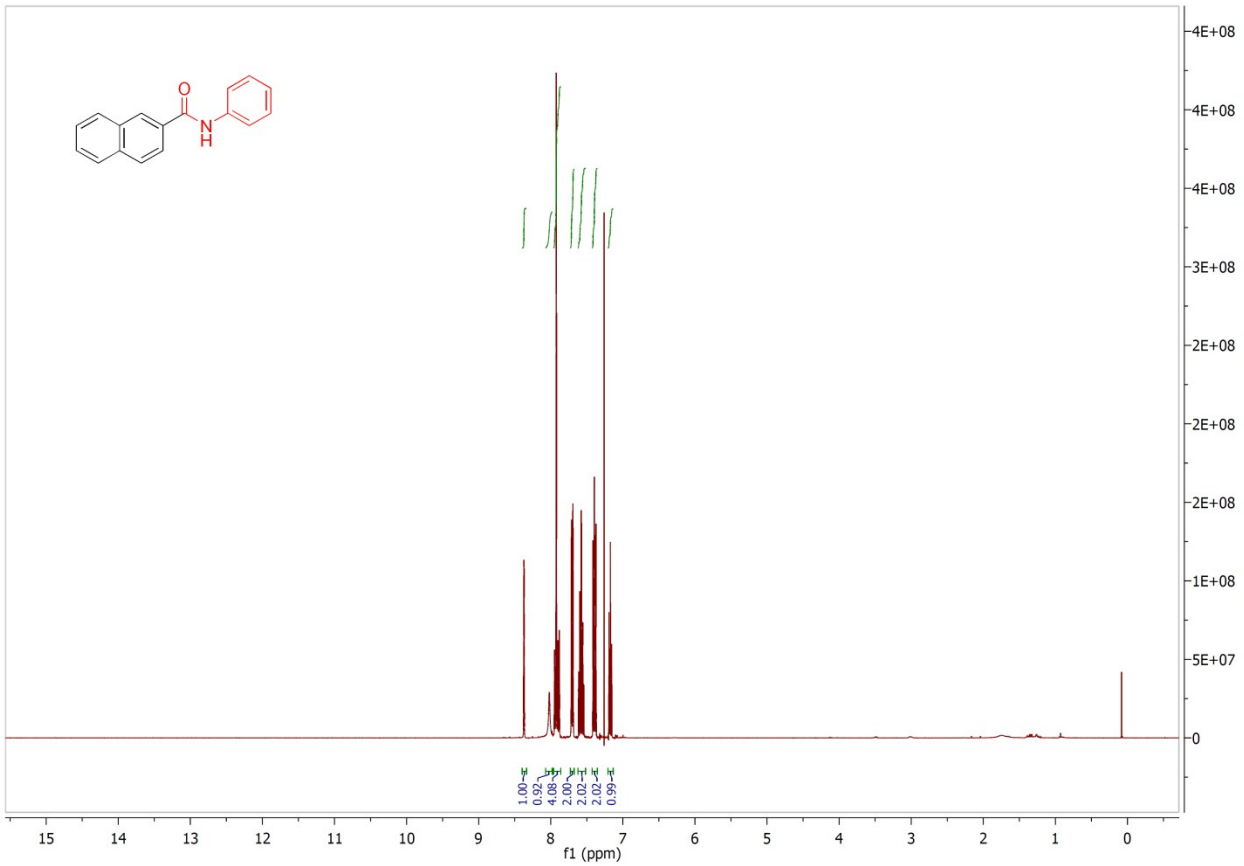


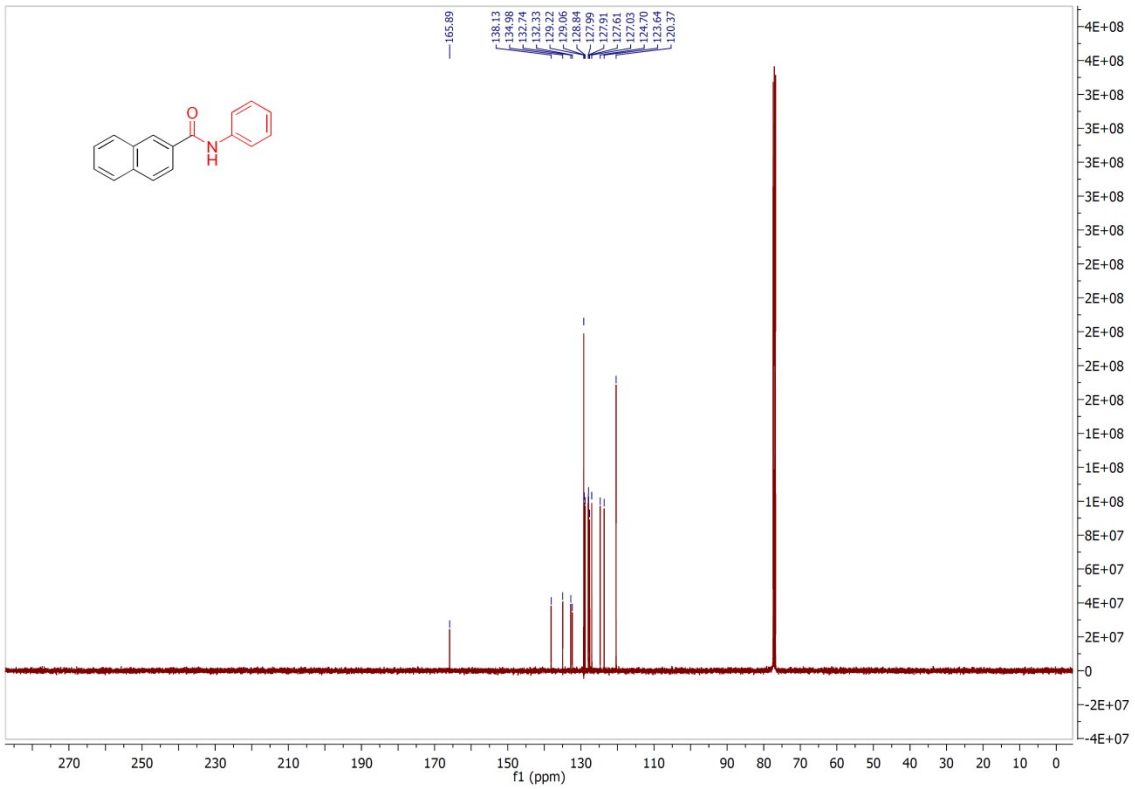
3.29. 3-methyl-N-phenylbenzamide (3ad)



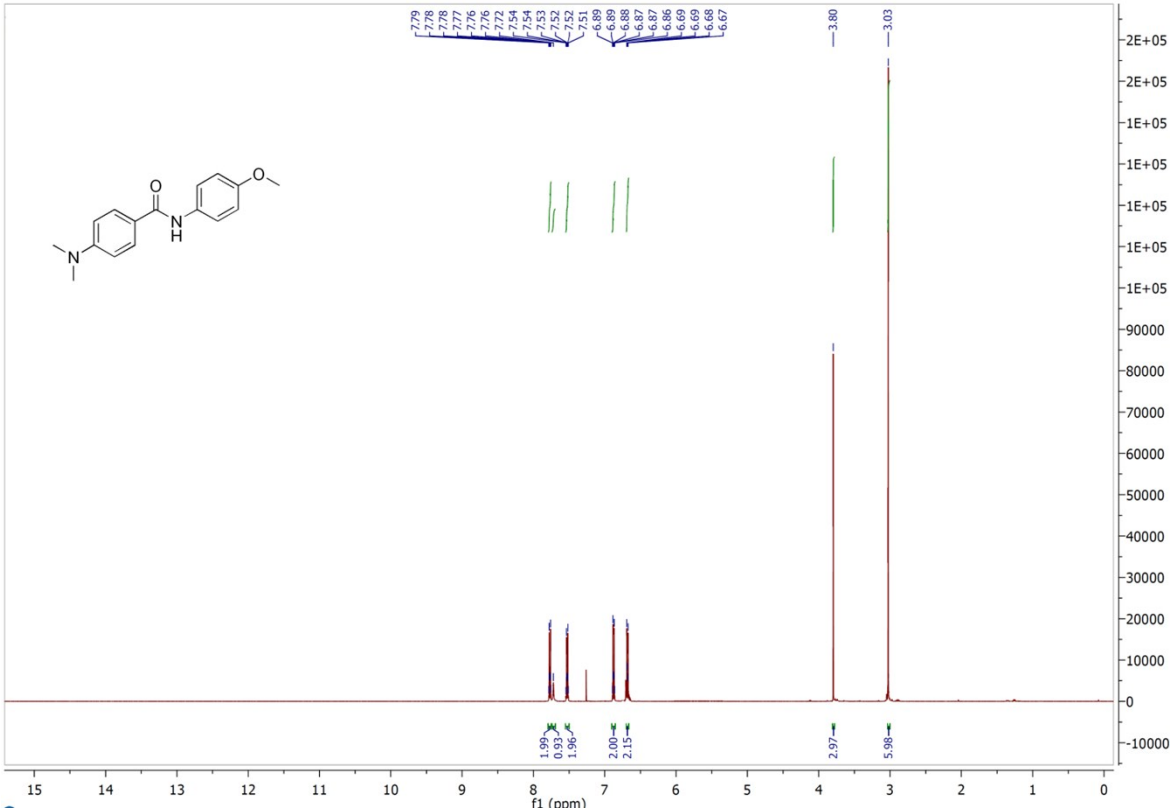


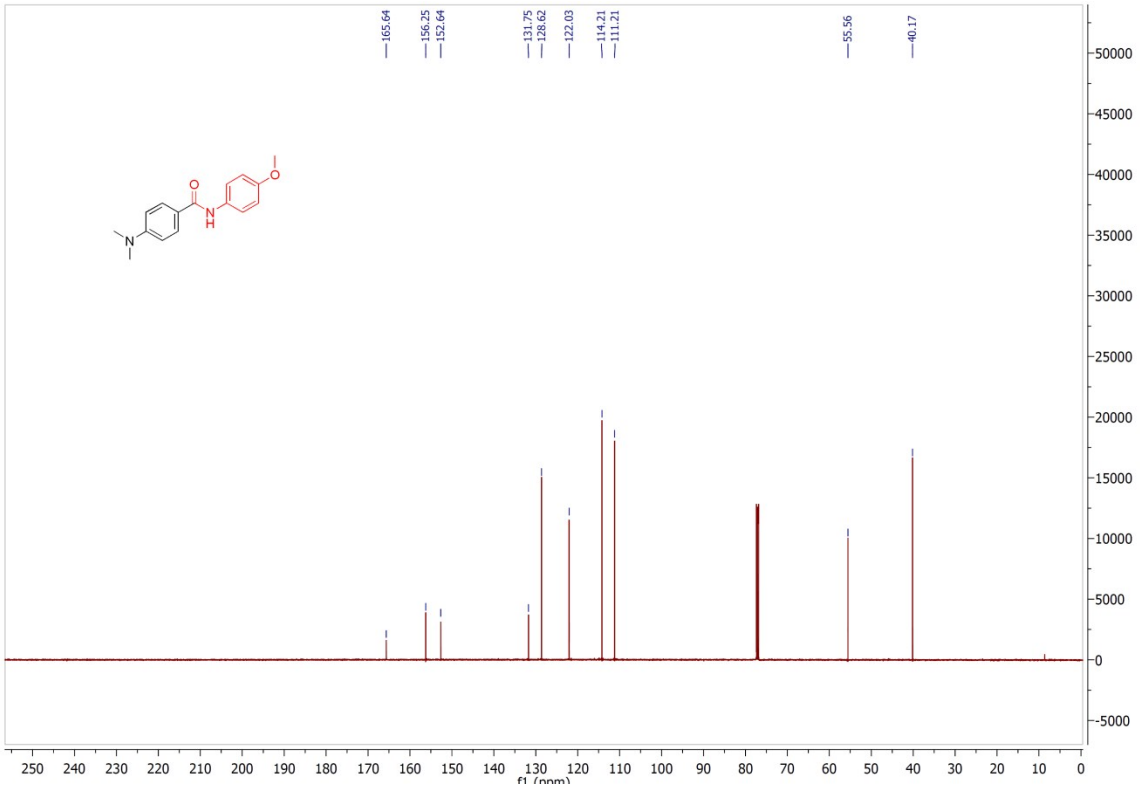
3.30. N-phenyl-2-naphthamide (3ae)





3.31. N-phenyl-2-naphthamide (3ae)

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152.64
131.75
128.62
122.03
114.21
111.21
55.56
40.17
50000
45000
40000
35000
30000
25000
20000
15000
10000
5000
0
-5000
250 240 230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)