Supporting Information to Accompany:

Expedient Synthesis of a 72-Membered Isoxazolo-β-ketoamide Library by a 2•3-Component Reaction

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General Procedures. All chemicals were purchased from commercial suppliers and used without further purification. Analytical thin layer chromatography was carried out on pre-coated plates (silica gel 60 F254, 250 µm thickness) and visualized with UV light or I_2 chamber. Flash chromatography was performed using 60 Å, 32-63 µm silica gel (Scientific Adsorbents). ^{1}H NMR spectra were recorded at 600 or 400MHz at ambient temperature with DMSO-*d6*, $CDCl_3$, acetone-*d6* or CD_3CN as solvent. ^{13}C NMR spectra were recorded at 151 or 101MHz at ambient temperature with DMSO-*d6* or $CDCl_3$ as solvent. Chemical shifts are reported in parts per million (ppm) relative to the residual solvent peak. Infrared spectra were recorded on an ATI-FTIR spectrometer and frequency is reported in cm^{-1}. The specifications of the LC/MS are as follows: electrospray (+) ionization, mass range 150 - 1500 Da, 20 V cone voltage, and Xterra® MS C18 column (2.1 mm x 50 mm x 3.5 µm). Preparative HPLC specifications are as follows: 15 mL/min flow rate, Xterra Prep MS C18 OBD column (19 mm x 100 mm) and dual wavelength absorbance detector.

5-(Hydroxy(4-methoxyphenyl)methylene)-2,2-dimethyl-1,3-dioxane-4,6-dione (1{2}). Compound was prepared following known protocol. Yamamoto, Y.; Watanabe, Y.; Ohnishi, S. 1,3-Oxazines and related compounds. XIII. Reactions of acyl Meldrum's acids with Schiff bases giving 2,3-disubstituted 5-acyl-3,4,5,6-tetrahydro-2H-1,3-oxazine-4,6-diones and 2,3,6-trisubstituted 2,3-dihydro-1,3-oxazin-4-ones. *Chem. Pharm. Bul*. **1987**, *35*, 1860-1870.

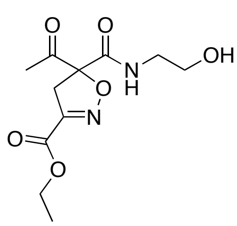
5-(Cyclopropyl(hydroxy)methylene)-2,2-dimethyl-1,3-dioxane-4,6-dione (1{3}). Compound was prepared following known protocol. Beyer, W. R. C.; Woithe, K.; Luke, B.; Schindler, M.; Antonicek, H.; Scherkenbeck, J. Asymmetric total synthesis of the indole alkaloid cyclopiazonic acid and first structure-activity data. *Tetrahedron*, **2011**, *67*, 3062-3070.

Ethyl 2-chloro-2-(hydroxyimino)acetate (4{1}). Compound was prepared following known protocol. Kozikowski, A. P.; Tapadar, S; Luchini, D. N.; Kim, K. H.; Billadeau, D. D. Use of the nitrile oxide cycloaddition (NOC) reaction for molecular probe generation: a wew class of enzyme selective Histone Deacetylase inhibitors (HDACIs) showing picomolar activity at HDAC6. *J. Med. Chem.* **2008,** *51,* 4370–4373.

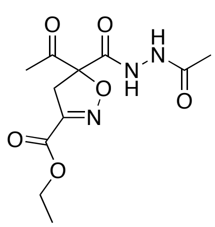
***N*-Hydroxypicolinimidoyl chloride (4{2}).** Compound was prepared following known protocol. Grob, J. E.; Nunez, J.; Dechantsreiter, M. A.; Hamann, L. G. Regioselective synthesis and slow-release Suzuki-Miyaura cross-coupling of MIDA boronate-functionalized isoxazoles and triazoles. *J. Org. Chem*. **2011**, *76*, 10241-10248.

***N*-Hydroxy-2-(trifluoromethyl)benzimidoyl chloride (4{3}).** Compound was prepared following known protocol. Guggenheim, K. G.; Butler, J. D.; Painter, P. P.; Lorsbach, B. A.; Tantillo, D. J.; Kurth, M. J. Synthesis of spiro-fused pyrazolidoylisoxazolines. *J. Org. Chem*. **2011**, *76*, 5803-5812.

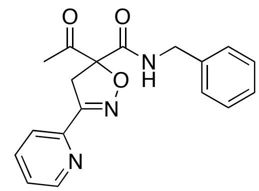
General Procedure for multicomponent reactions. The acylketene precursor (2 mmol) and amine (2 mmol) were dissolved in dry DMF (5 mL) in a 20mL microwave vial. The reaction was heated and stired at 125 ˚C for 10 min. Upon cooling to room temperature, Eshenmoser's salt (2 mmol) and the chlorooxime (4.1 mmol) where added, followed by $KHCO_3$ (10 mmol). The reaction was heated with stirring at 125˚C for 30 min. DMF was removed under reduced pressure and crude material was purified by column chromatography with a steady gradient from 100% hexane to 100% ethyl acetate.



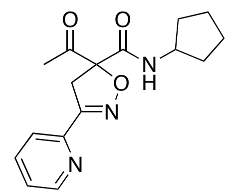
Ethyl 5-acetyl-5-((2-hydroxyethyl)carbamoyl)-4,5-dihydroisoxazole-3-carboxylate 5{1,1,5}. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.49 (t, J = 5.3, 1H), 4.30 (q, J = 7.3, 2H), 3.97 (d, J = 18.2, 1H), 3.73 – 3.66 (m, 2H), 3.52 – 3.46 (m, 1H), 3.44 (d, J = 18.2, 1H), 3.41 – 3.36 (m, 1H), 2.29 (s, 3H), 1.32 – 1.30 (t, *J* = 7.2, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.54, 167.87, 159.18, 152.65, 94.89, 62.85, 61.06, 42.45, 39.51, 25.15, 14.38. IR (neat): 3346, 2937, 2878, 1728, 1659, 1529.



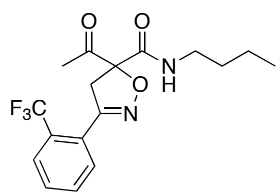
Ethyl 5-acetyl-5-(2-acetylhydrazinecarbonyl)-4,5-dihydroisoxazole-3-carboxylate 5{1,1,6}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.29 (q, J = 7.1, 2H), 3.99 (d, J = 18.9, 1H), 3.45 (d, J = 18.9, 1H), 2.33 (s, 3H), 2.02 (s, 3H), 1.30 (t, J = 7.1, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 196.61, 168.17, 165.22, 158.90, 152.93, 94.25, 63.15, 40.11, 25.44, 20.91, 14.09. IR (neat): 3250, 2967, 2853, 1731, 1673, 1505.



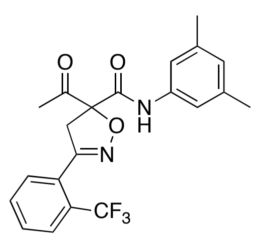
5-Acetyl-*N*-benzyl-3-(pyridin-2-yl)-4,5-dihydroisoxazole-5-carboxamide 5{1,2,7}. ^{1}H NMR (600 MHz, CDCl$_3$) δ 8.57 (dtd, J = 4.8, 1.9, 1.0, 1H), 7.84 – 7.82 (m, 1H), 7.69 – 7.65 (m, 1H), 7.37 (s, 1H), 7.30 – 7.25 (m, 4H), 7.24 – 7.18 (m, 3H), 4.55 (dd, J = 14.7, 6.4, 1H), 4.36 (dd, J = 14.7, 5.5, 1H), 4.26 (dd, J = 18.6, 2.0, 1H), 3.77 (dd, J = 18.6, 2.0, 1H), 2.27 (s, 3H). ^{13}C NMR (101 MHz, CDCl$_3$) δ 198.15, 168.21, 159.64, 149.94, 147.93, 137.44, 136.84, 129.07, 128.05, 128.03, 125.31, 122.19, 93.67, 43.85, 41.04, 25.56. IR (neat): 3060, 3029, 2924, 2852, 1730, 1666, 1522.



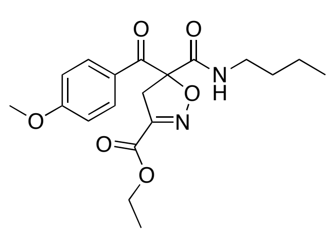
5-Acetyl-*N*-cyclopentyl-3-(pyridin-2-yl)-4,5-dihydroisoxazole-5-carboxamide 5{1,2,8}. ^{1}H NMR (600 MHz, CDCl$_3$) δ 8.59 (d, J = 2.8, 1H), 7.86 (d, , J = 7.8, 1H), 7.70 (t, J = 7.8, 1H), 7.31 (m, 1H), 6.85 (d, J = 6.7, 1H), 4.26 (d, J = 18.6, 1H), 4.18 (sextet, J = 6.8, 1H), 3.73 (d, J = 18.6, 1H), 2.30 (s, 3H), 2.04 – 1.98 (m, 1H), 1.98 – 1.91 (m, 1H), 1.68 (m, 2H), 1.61 – 1.54 (m, 2H), 1.48 – 1.41 (m, 1H), 1.37 (m, 1H). ^{13}C NMR (151 MHz, CDCl$_3$) δ 197.94, 167.41, 159.34, 149.70, 147.75, 136.48, 124.97, 121.94, 93.30, 51.28, 40.47, 32.96, 32.77, 25.10, 23.71. IR (neat): 3011, 2957, 2868, 1732, 1668, 1584, 1518.



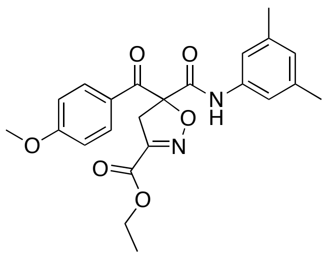
5-Acetyl-*N*-butyl-3-(2-(trifluoromethyl)phenyl)-4,5-dihydroisoxazole-5-carboxamide 5{1,3,1}. ^{1}H NMR (600 MHz, CDCl$_3$) δ 7.70 (d, J = 7.6, 1H), 7.56 (t, J = 7.4, 1H), 7.53 (t, J = 7.5, 1H), 7.41 (d, J = 7.4, 1H), 7.12 (s, 1H), 4.12 (d, J = 18.3, 1H), 3.51 (d, J = 18.3, 1H), 3.30 (q, J = 6.6, 2H), 2.30 (s, 3H), 1.49 (p, J = 6.8, 2H), 1.31(sextet, J = 7.5, 2H), 0.88 (t, J = 7.4, 3H). ^{13}C NMR (151 MHz, CDCl$_3$) δ 197.64, 167.85, 157.42, 132.08 (q, J = 25.4), 130.37, 130.22, 128.65 (q, J = 30.9), 126.87, 126.70, 123.44 (q, J = 276.2), 93.09, 44.38, 39.17, 31.31, 25.16, 19.86, 13.68. IR (neat): 3331, 2958, 2934, 2873, 1731, 1666, 1528.



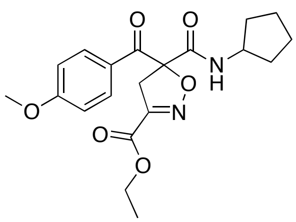
5-Acetyl-*N*-(3,5-dimethylphenyl)-3-(2-(trifluoromethyl)phenyl)-4,5-dihydroisoxazole-5-carboxamide 5{1,3,2}. ^{1}H NMR (600 MHz, CDCl$_3$) δ 8.62 (s, 1H), 7.77 – 7.75 (d, J = 7.6, 1H), 7.63 – 7.57 (m, 2H), 7.48 (d, J = 7.9 1H), 7.26 (s, 2H), 6.84 (s, 1H), 4.25 (d, J = 18.4, 1H), 3.67 (d, J = 18.4, 1H), 2.42 – 2.41 (s, 3H), 2.32 (s, 6H). ^{13}C NMR (101 MHz, CDCl$_3$) δ 197.52, 166.15, 158.08, 139.26, 139.04, 136.43, 132.38, 130.70, 130.60, 127.40, 127.17, 123.82 (q, J = 277.15), 118.21, 118.03, 93.51, 93.40, 44.79, 21.51. IR (neat): 3021, 2923, 2854,1734, 1680, 1613, 1542.



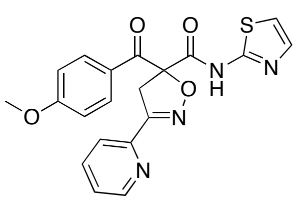
Ethyl 5-(butylcarbamoyl)-5-(4-methoxybenzoyl)-4,5-dihydroisoxazole-3-carboxylate 5{2,1,1}. ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.01 (d, *J* = 8.9 Hz, 2H), 6.91 (d, *J* = 9.0 Hz, 2H), 6.82 (t, *J* = 5.6 Hz, 1H), 4.43 (d, *J* = 19.0 Hz, 1H), 4.35 (q, *J* = 7.1 Hz, 2H), 3.86 (s, 3H), 3.57 (d, *J* = 19.0 Hz, 1H), 3.44 – 3.28 (m, 1H), 3.31 – 3.11 (m, 1H), 1.58 – 1.43 (m, 2H), 1.32-1.17 (m, 5H), 0.89 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (101 MHz, CDCl$_3$) δ 187.88, 168.05, 164.41, 159.44, 152.88, 132.44, 126.24, 114.13, 94.81, 62.85, 55.77, 41.77, 39.62, 31.49, 20.19, 14.27, 13.88. IR (neat): 3349, 3010, 2934, 2863, 1725, 1681, 1599, 1512.



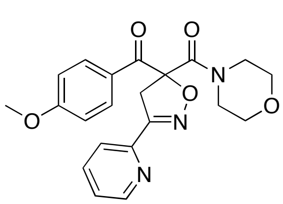
Ethyl 5-((3,5-dimethylphenyl)carbamoyl)-5-(4-methoxybenzoyl)-4,5-dihydroisoxazole-3-carboxylate 5{2,1,2}. ^{1}H NMR (600 MHz, CDCl$_3$) δ 8.28 (s, 1H), 7.95 (d, *J* = 8.5Hz, 2H), 7.09 (s, 1H), 6.83 (d, *J* = 8.6Hz, 2H), 6.71 (s, 1H), 4.43 (d, *J* = 19.1Hz, 1H), 4.27 (q, *J* = 7.1Hz, 2H), 3.75 (s, 3H), 3.60 (d, *J* = 19.1Hz, 1H), 2.19 (s, 6H), 1.27 (t, *J* = 7.5, 3H); ^{13}C NMR (151 MHz, CDCl$_3$) δ 187.27, 165.79, 164.28, 159.04, 152.93, 139.03, 136.11, 132.19, 127.13, 125.86, 117.65, 114.13, 94.45, 62.72, 55.54, 41.86, 21.31, 14.04. IR (neat): 3549, 3425, 3331, 3263, 2959, 2923, 1725, 1686, 1598, 1548, 1548, 1511.



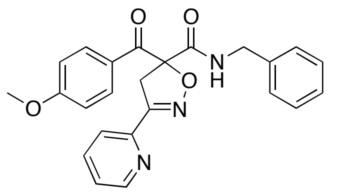
Ethyl 5-(cyclopentylcarbamoyl)-5-(4-methoxybenzoyl)-4,5-dihydroisoxazole-3-carboxylate 5{2,1,8}. ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.00 (d, *J* = 8.9, 2H), 6.91 (d, *J* = 8.9, 2H), 6.72 (d, *J* = 1H), 4.44 (d, *J* = 19.0, 1H), 4.35 (q, *J* = 7.1, 2H), 4.11 (sextet, *J* = 6.9, 1H), 3.86 (s, 3H), 3.56 (d, *J* = 19.0, 1H), 1.97-1.82 (m, 2H), 1.70-1.59 (m, 2H), 1.59-1.51 (m, 2H), 1.41-1.33 (m, 2H), 1.30 (t, *J* = 7.1, 3H). ^{13}C NMR (101 MHz, CDCl$_3$) δ 187.85, 167.62, 164.54, 159.45, 152.90, 132.46, 126.27, 114.10, 94.65, 62.86, 55.81, 51.72, 41.63, 33.01, 32.85, 29.95, 23.92, 14.29. IR (neat): 3528, 3334, 2940, 2871, 1727, 1682, 1599, 1512.



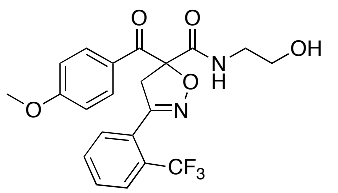
5-(4-Methoxybenzoyl)-3-(pyridin-2-yl)-*N*-(thiazol-2-yl)-4,5-dihydroisoxazole-5-carboxamide 5{2,2,3}. ^{1}H NMR (600 MHz, CDCl$_3$) δ 8.67 (d, *J* = 4.4, 1H), 8.10 (d, *J* = 8.8, 2H), 8.06 (d, *J* = 7.9, 1H), 7.81 (t, *J* = 7.8, 1H), 7.52 (d, *J* = 3.8, 1H), 7.40 (m, 1H), 7.10 (t, *J* = 3.9, 1H), 6.93 (d, *J* = 8.8, 2H), 4.74 (d, *J* = 18.7, 1H), 4.15 (d, *J* = 18.8, 1H), 3.86 (s, 3H). ^{13}C NMR (151 MHz, CDCl$_3$) δ 187.93, 168.43, 164.40, 160.07, 158.42, 149.17, 147.24, 137.21, 132.78, 132.51, 125.89, 125.34, 122.68, 114.66, 114.13, 93.51, 55.57, 43.46. IR(neat): 3196, 3126, 3019, 2923, 2854, 2923, 2854, 2341, 1969, 1775, 1676, 1536, 1520.



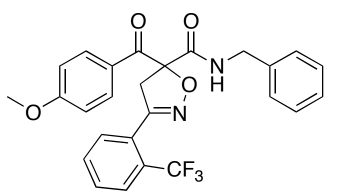
(5-(4-Methoxybenzoyl)-3-(pyridin-2-yl)-4,5-dihydroisoxazol-5-yl)(morpholino)methanone 5{2,2,4}. ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.66 (d, *J* = 4.3 Hz, 1H), 8.06 (m, 3H), 7.81 (t, *J* = 4.5 Hz, 1H), 7.40 (t, *J* = 6Hz, 1H), 6.93 (d, *J* = 5.9 Hz, 2H), 4.83 (d, *J* = 18.2 Hz, 1H), 3.97 (d, *J* = 18.41, 1H), 3.86 (s, 3H), 3.74 – 3.70 (m, 1H), 3.65 – 3.57 (m, 4H), 3.55 – 3.50 (m, 2H), 3.43 – 3.36 (m, 1H). ^{13}C NMR (101 MHz, cdcl3) δ 191.20, 165.64, 164.73, 157.56, 148.83, 147.61, 137.87, 132.44, 125.44, 125.31, 122.79, 114.49, 94.76, 66.83, 66.70, 55.81, 47.05, 44.07, 43.15. ^{13}C NMR (151 MHz, DMSO *d*-6) δ 189.34, 169.23, 164.29, 159.00, 150.46, 148.01, 139.45, 137.85, 132.53, 128.88, 128.85, 128.06, 127.50, 126.45, 126.05, 122.36, 114.58, 92.96, 56.29, 43.05, 42.47. IR (neat): 3196, 3015, 2962, 2924, 2853, 1648, 1598, 1511, 1439.



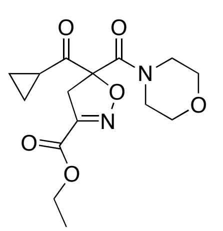
***N*-Benzyl-5-(4-methoxybenzoyl)-3-(pyridin-2-yl)-4,5-dihydroisoxazole-5-carboxamide 5{2,2,7}**. ^{1}H NMR (600 MHz, DMSO *d*-6) δ 9.43 (t, *J* = 6.4, 1H), 8.74 (d, *J* = 4.5, 1H), 7.97 (m, 4H), 7.56 (t, *J* = 5.5, 1H), 7.31 (m, 3H), 7.28 (d, *J* = 7.3, 2H), 7.02 (d, *J* = 8.8, 2H), 4.64 (d, *J* = 18.3, 1H), 4.44 (dd, *J* = 6.6, 14.9, 1H), 4.30 (dd, *J* = 5.9, 14.8, 1H), 3.89 (s, 3H), 3.75 (d, *J* = 18.3, 1H). ^{13}C NMR (151 MHz, DMSO *d*-6) δ 189.34, 169.23, 164.29, 159.00, 150.46, 148.01, 139.45, 137.85, 132.53, 128.88, 128.85, 128.06, 127.50, 126.45, 126.05, 122.36, 114.58, 92.96, 56.29, 43.05, 42.47. IR (neat): 3263, 3248, 3236, 2964, 2961, 2929, 2910, 1679, 1594, 1535.



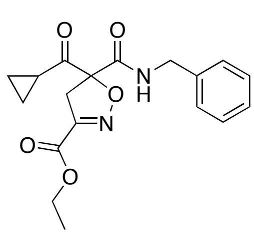
***N*-(2-Hydroxyethyl)-5-(4-methoxybenzoyl)-3-(2-(trifluoromethyl)phenyl)-4,5-dihydroisoxazole-5-carboxamide 5{2,3,5}.** ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (d, J = 8.9, 2H), 7.75 (d, J = 7.0, 1H), 7.64 – 7.53 (m, 2H), 7.48 (d, J = 7.4, 1H), 6.91 (d, J = 8.9, 2H), 4.61 (d, J = 18.5, 1H), 3.84 (s, 3H), 3.71 (t, J = 5.0, 2H), 3.66 (d, J = 18.5, 1H), 3.57 – 2.51 (m, 1H), 3.49 – 3.40 (m, 1H), 2.40 (s, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 188.19, 170.11, 164.16, 157.58, 132.26, 132.15, 130.45, 130.31, 128.74 (q, *J* = 31.5), 126.86, 126.39, 123.65 (q, *J* = 277.0), 113.91, 92.96, 61.60, 55.52, 46.83, 42.13. IR (neat): 3360.89, 3333.96, 3195.44, 3018.35, 2923.44, 2854.11, 1681.00, 1598.48, 1574.75, 1513.06.



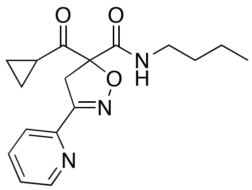
***N*-Benzyl-5-(4-methoxybenzoyl)-3-(2-(trifluoromethyl)phenyl)-4,5-dihydroisoxazole-5-carboxamide 5{2,3,7}.** ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, *J* = 7.8 Hz, 2H), 7.72 (d, *J* = 6.8Hz, 1H), 7.58 – 7.50 (m, 2H), 7.41 (d, *J* = 6.2 Hz, 1H), 7.29 – 7.25 (m, 3H), 7.24 – 7.20 (m, 2H), 6.81 (d, *J* = 7.8 Hz, 2H), 4.63-4.584(m, 2H), 4.37 – 4.30 (dd, *J* = 13.5, 4.9, 1H), 3.81 (s Hz, 3H), 3.66 (d, *J* = 18.4 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 188.32, 169.33, 164.31, 157.89, 137.52, 132.52, 132.38, 130.70, 130.57, 128.96, 128.28, 127.98, 127.07 (q, *J* = 5.3), 126.60, 123.76 (q, *J* = 274.4), 114.10, 93.25, 55.97, 46.96, 43.73. IR (neat): 3381, 3367, 3359, 2919, 1677, 1601, 1515.



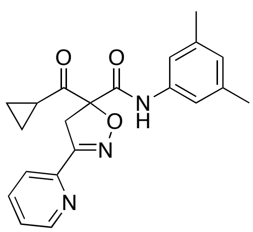
Ethyl 5-(cyclopropanecarbonyl)-5-(morpholine-4-carbonyl)-4,5-dihydroisoxazole-3-carboxylate 5{3,1,4}. ^{1}H NMR (600 MHz, $CDCl_3$) δ 4.56 (d, *J* = 18.3, 1H), 4.35 (q, *J* = 7.2, 2H), 3.76 – 3.68 (m, 2H), 3.67 - 3.62 (m, 2H), 3.62 – 3.53 (m, 3H), 3.41 (d, *J* = 18.8, 1H), 3.32 – 3.27 (m, 1H), 2.21 – 2.14 (m, 1H), 1.36 (t, *J* = 7.1, 3H), 1.21 – 1.13 (m, 2H), 1.13 – 1.04 (m, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 203.44, 163.77, 159.28, 151.64, 96.17, 66.61, 66.32, 62.56, 46.93, 43.83, 41.72, 15.93, 14.04, 13.49, 13.11. IR (neat): 3017, 2968, 2924, 2924, 2857, 1722, 1652, 1603, 1438.



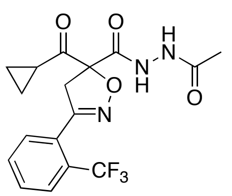
Ethyl 5-(benzylcarbamoyl)-5-(cyclopropanecarbonyl)-4,5-dihydroisoxazole-3-carboxylate 5{3,1,7}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 (s, 1H), 7.26 (m, 5H), 4.59 (dd, *J* = 14.7, 6.5, 1H), 4.36 (dd, *J* = 14.2, 5.5, 1H), 4.28 (q, 2H), 3.97 (d, *J* = 18.9, 1H), 3.57 (d, *J* = 18.9, 1H), 2.191-2.112 (m, 1H), 1.31 (t, *J* = 6.9, 3H), 1.15 – 1.05 (m, 2H), 1.02 – 0.94 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 200.11, 167.14, 159.34, 152.76, 137.51, 128.96, 128.00, 127.97, 95.41, 62.79, 43.84, 39.88, 17.45, 14.24, 13.93, 12.86. IR (neat): 3374, 3352, 2983, 2936, 1716, 1716, 1672, 1601, 1524.



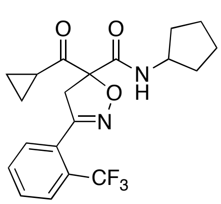
***N*-Butyl-5-(cyclopropanecarbonyl)-3-(pyridin-2-yl)-4,5-dihydroisoxazole-5-carboxamide 5{3,2,1}**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.62 (d, *J* = 4.1, 1H), 7.91 (d, *J* = 8.0, 1H), 7.72 (t, *J* = 4.0, 1H), 7.32 (t, *J* = 4.9, 1H), 6.91 (s, 1H), 4.26 (d, *J* = 18.6, 1H), 3.91 (d, *J* = 18.6, 1H), 3.46-3.33 (quint, J = 6.3, 1H), 3.33 – 3.20 (quint, J = 6.3, 1H), 2.36 – 2.25 (m, 1H), 1.53 (quint, *J* = 6.6, 2H), 1.36 (sext, *J* = 7.8, 2H), 1.21 – 1.13 (m, 2H), 1.10 – 1.01 (m, 2H), 0.91 (t, *J* = 7.3, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 201.27, 168.04, 159.40, 150.06, 136.77, 125.15, 122.48, 94.25, 41.25, 39.55, 31.65, 20.17, 17.45, 13.90, 13.57, 12.65. IR (neat): 3380, 3345, 3297, 3007, 2961, 2960, 2873, 1713, 1667, 1584, 1512.



5-(Cyclopropanecarbonyl)-*N*-(3,5-dimethylphenyl)-3-(pyridin-2-yl)-4,5-dihydroisoxazole-5-carboxamide 5{3,2,2}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.76 (s, 1H), 8.60 (d, *J* = 4.6, 1H), 7.91 (d, *J* = 7.8, 1H), 7.70 (t, *J* = 7.7, 1H), 7.31 (t, J = 5.1, 1H), 7.22 (s, 2H), 6.77 (s, 1H), 4.36 (d, *J* = 18.7, 1H), 4.04 (d, *J* = 18.7, 1H), 2.43 – 2.31 (m, 1H), 2.27 (s, 6H), 1.23 – 1.15 (m, 2H), 1.08 – 1.03 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 200.93, 166.32, 159.76, 149.88, 147.94, 139.01, 136.75, 136.70, 127.04, 125.24, 122.19, 117.91, 94.08, 41.52, 21.54, 17.70, 13.73, 12.83. IR (neat): 3600, 3554, 3495, 3326, 3286, 1710, 1664, 1664, 1612, 1540.



***N'*-Acetyl-5-(cyclopropanecarbonyl)-3-(2-(trifluoromethyl)phenyl)-4,5-dihydroisoxazole-5-carbohydrazide 5{3,3,6}.** ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.55 (s, 1H), 9.23 (s, 1H), 7.69 (d, J = 7.2, 1H), 7.58 – 7.50 (m, 2H), 7.46 (d, *J* = 7.1, 1H), 4.11 (d, *J* = 18.2, 1H), 3.70 (d, *J* = 18.2, 1H), 2.43 (m, 1H), 2.02 (s, 3H), 1.16-1.09 (m, 2H), 1.08-1.01 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 200.96, 168.47, 166.08, 157.57, 132.37, 130.81, 130.59, 128.79 (q, *J* = 27.4), 126.97 (q, *J* = 5.1), 126.80, 123.77 (q, *J* = 274.6), 93.17, 45.27, 20.72, 17.52, 13.90, 13.37. IR (neat): 3312, 3247, 3155, 2768, 1699, 1670, 1488.



***N*-Cyclopentyl-5-(cyclopropanecarbonyl)-3-(2-(trifluoromethyl)phenyl)-4,5-dihydroisoxazole-5-carboxamide 5{3,3,8}**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, *J* = 7.4, 1H), 7.61 – 7.53 (m, 2H), 7.44 (d, *J* = 8.0, 1H), 6.97 (d, *J* = 7.6, 1H), 4.27 (sext, *J* = 7.2, 1H), 4.12 (d, *J* = 18.3, 1H), 3.61 (d, *J* = 18.3, 1H), 2.25-2.20 (m, 1H), 2.06 – 1.96 (m, 2H), 1.74 - 1.66 (m, 2H), 1.65 – 1.56 (m, 2H), 1.53 – 1.39 (m, 2H), 1.23 – 1.11 (m, 2H), 1.10 – 1.00 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 200.75, 167.61, 157.66, 132.30, 130.52, 130.48, 128.97 (q, *J* = 31.2), 127.28 (q, *J* = 2.0), 127.05 (q, *J* = 275.8), 123.72 (q, *J* = 275.8), 93.64, 51.61, 44.76, 33.19, 33.08, 23.94, 23.90, 17.53, 13.59, 12.56. IR (neat): 3524, 3512, 3387, 2969, 2928, 2877, 1710, 1669, 1517.

ESI-MS values and yields for the entire library:

Compound	ESI-MS m/z [M+H]+	Yield
5{1,1,1)	285.1	80%
5{1,1,2)	333.11	79%
5{1,1,3}	312.01	30%
5{1,1,4}	299.01	40%
5{1,1,5}	273.03	40%
5{1,1,6}	286.02	51%
5{1,1,7}	319.06	76%
5{1,1,8}	297.89	88%
5{1,2,1)	290.18	75%
5{1,2,2)	338.12	76%
5{1,2,3}	317.02	31%
5{1,2,4}	304.16	44%
5{1,2,5}	278.11	31%
5{1,2,6}	291.11	50%
5{1,2,7}	324.08	78%
5{1,2,8}	302.11	83%
5{1,3,1)	357.12	81%
5{1,3,2)	405.15	80%
5{1,3,3}	384.04	19%
5{1,3,4}	371.11	48%
5{1,3,5}	345.12	41%
5{1,3,6}	358.11	38%
5{1,3,7}	391.16	75%
5{1,3,8}	369.13	75%
5{2,1,1)	377.16	30%
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5{2,1,3}	404.09	8%
5{2,1,4}	391.16	15%
5{2,1,5}	365.17	35%
5{2,1,6}	378.1	44%
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5{2,1,8}	389.68	64%
5{2,2,1)	382.19	60%
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5{3,2,1)	316.16	77%
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5{3,2,3}	343.07	18%
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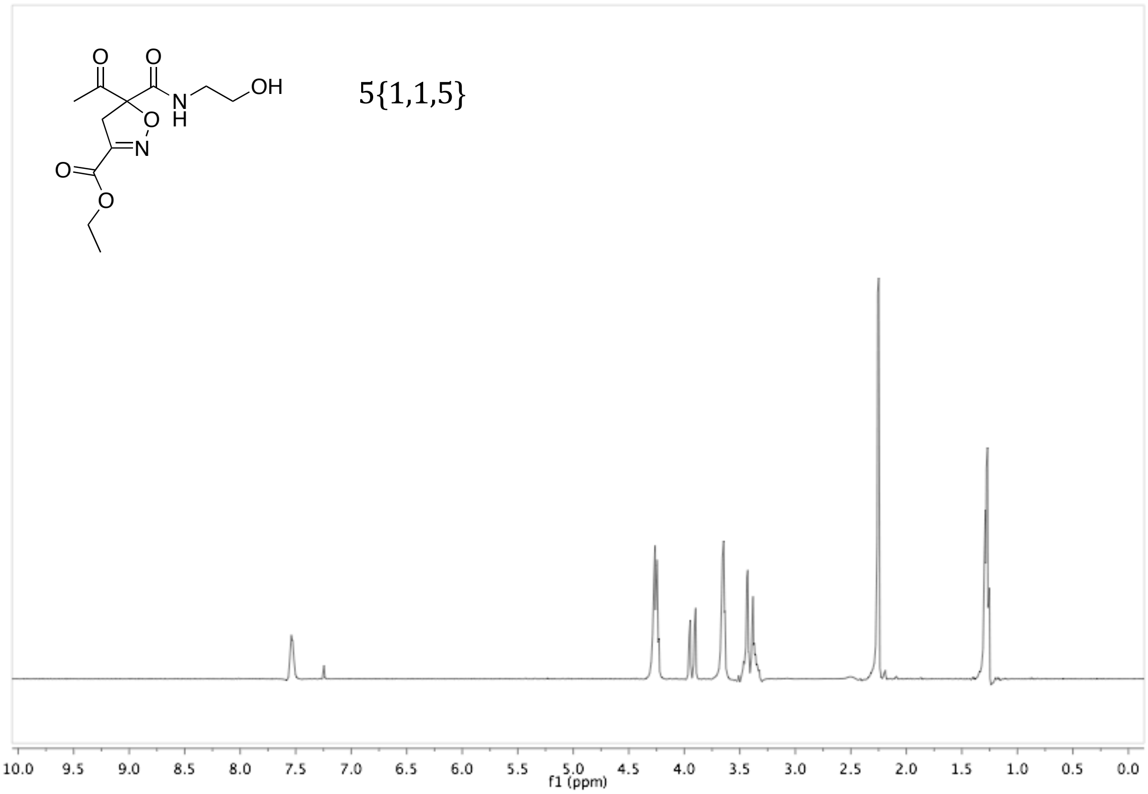
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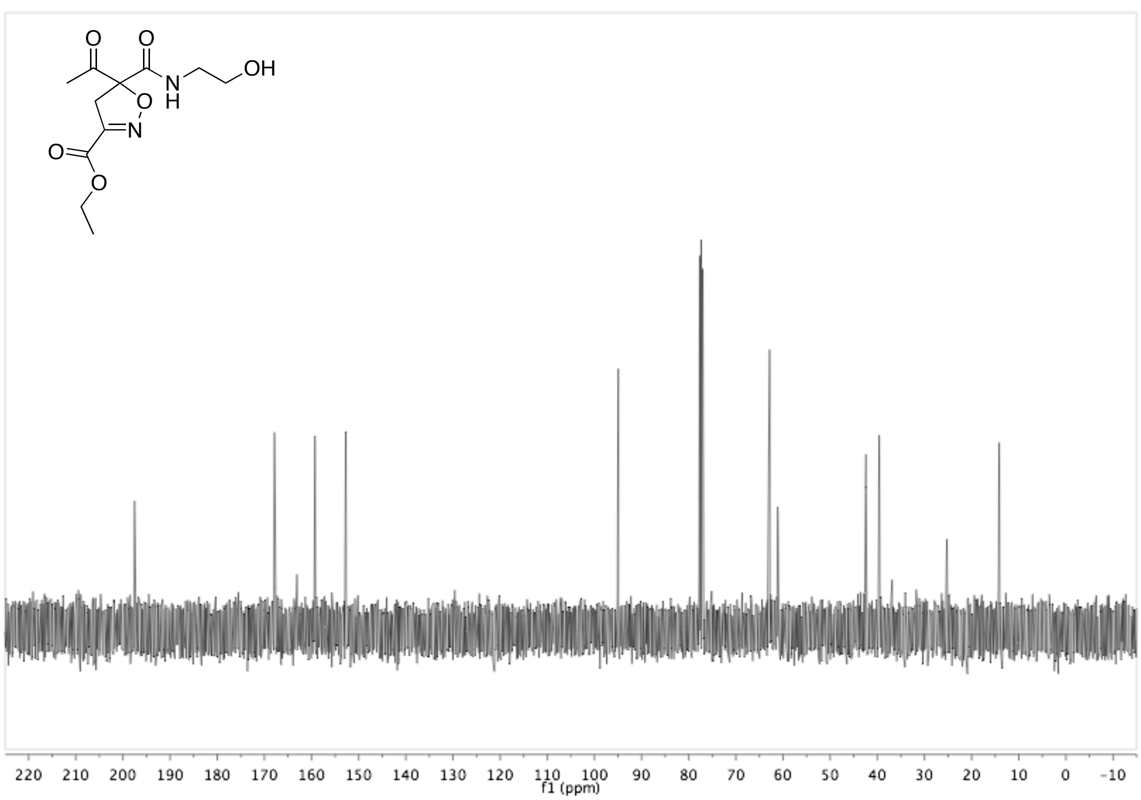
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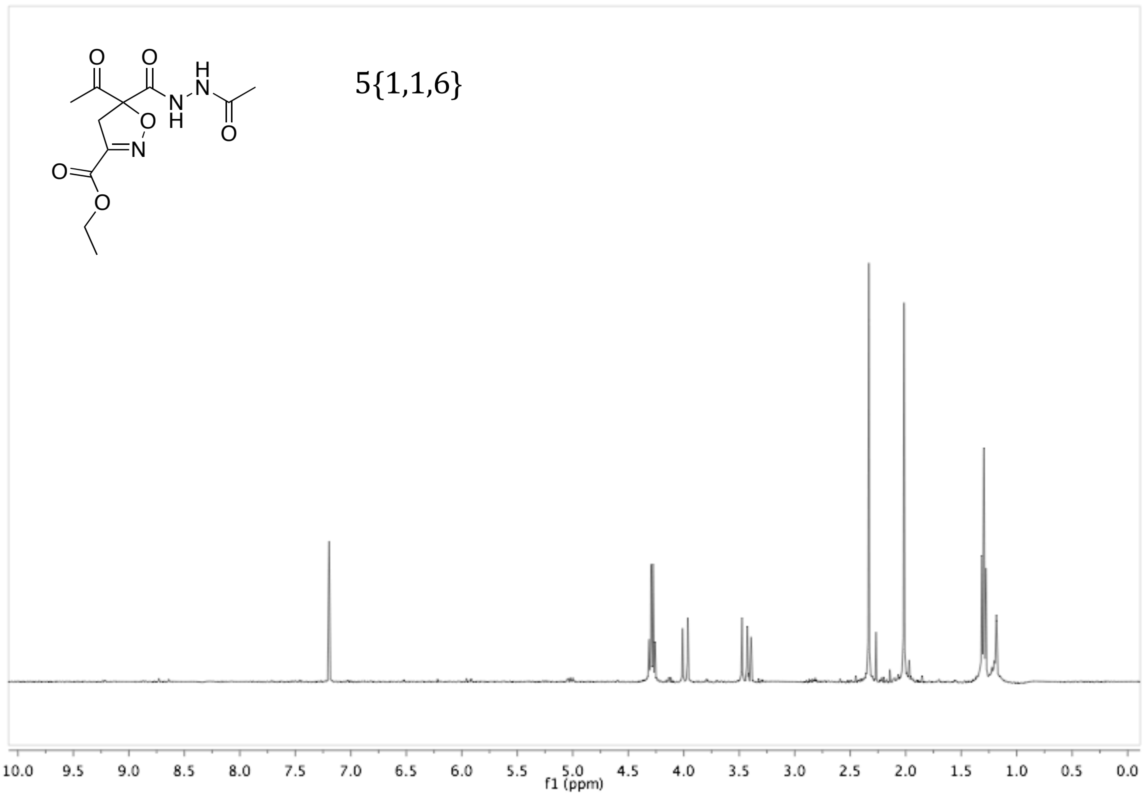

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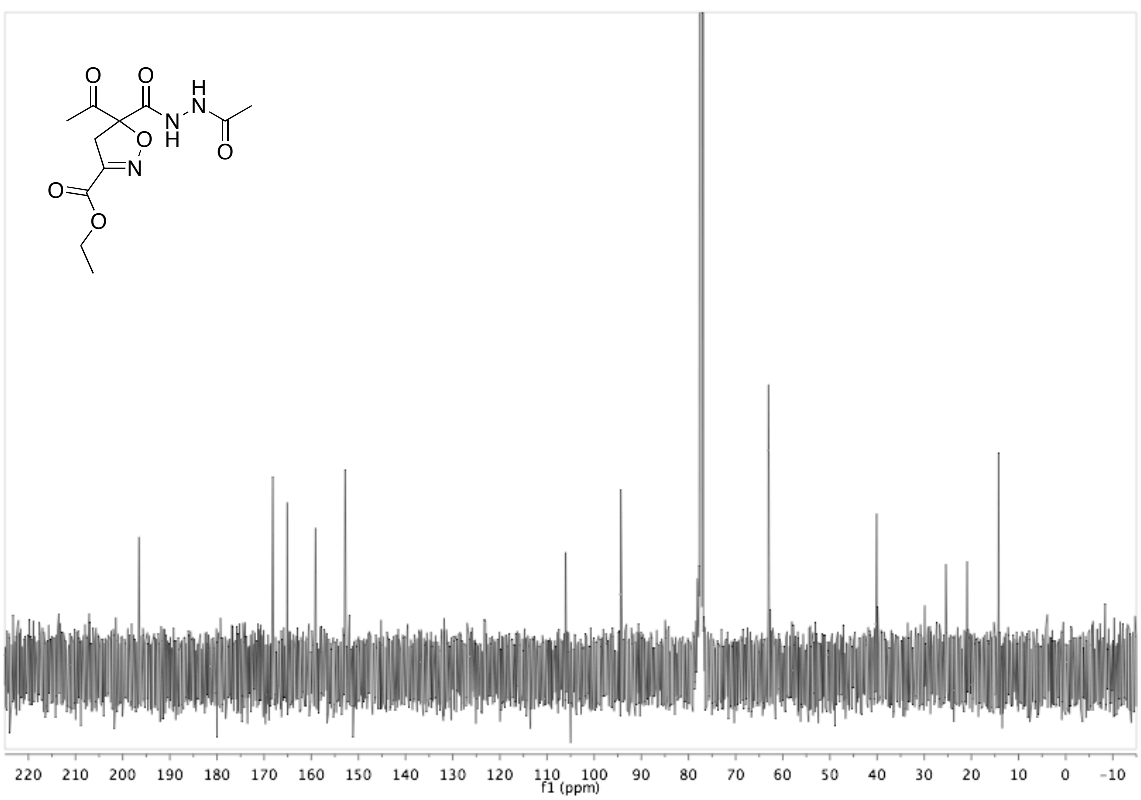
f1 (ppm)



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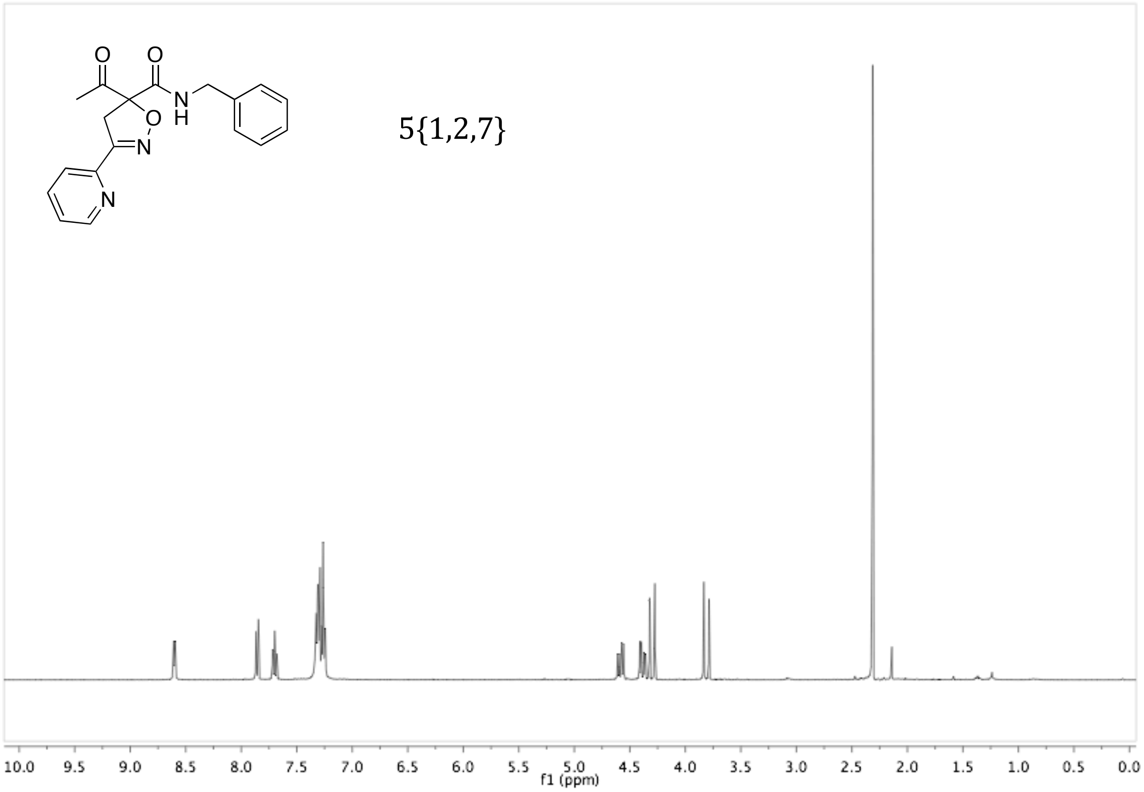
f1 (ppm)

5{1,2,7}



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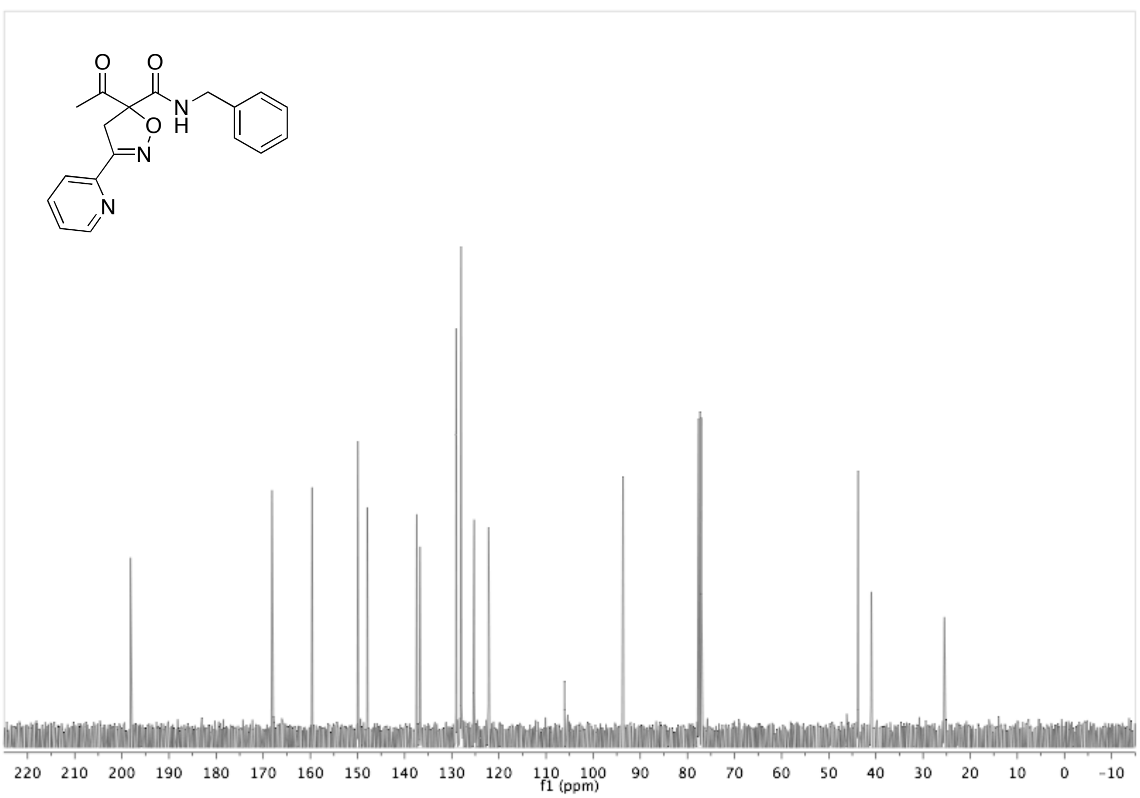

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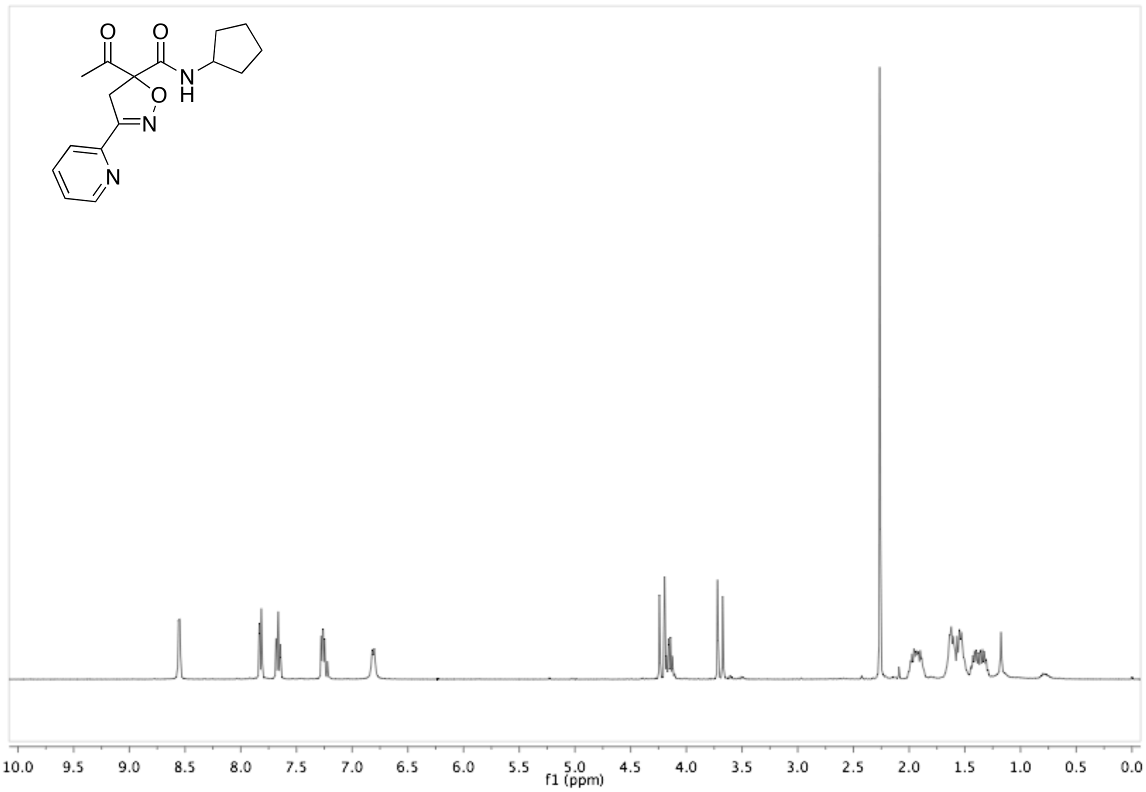
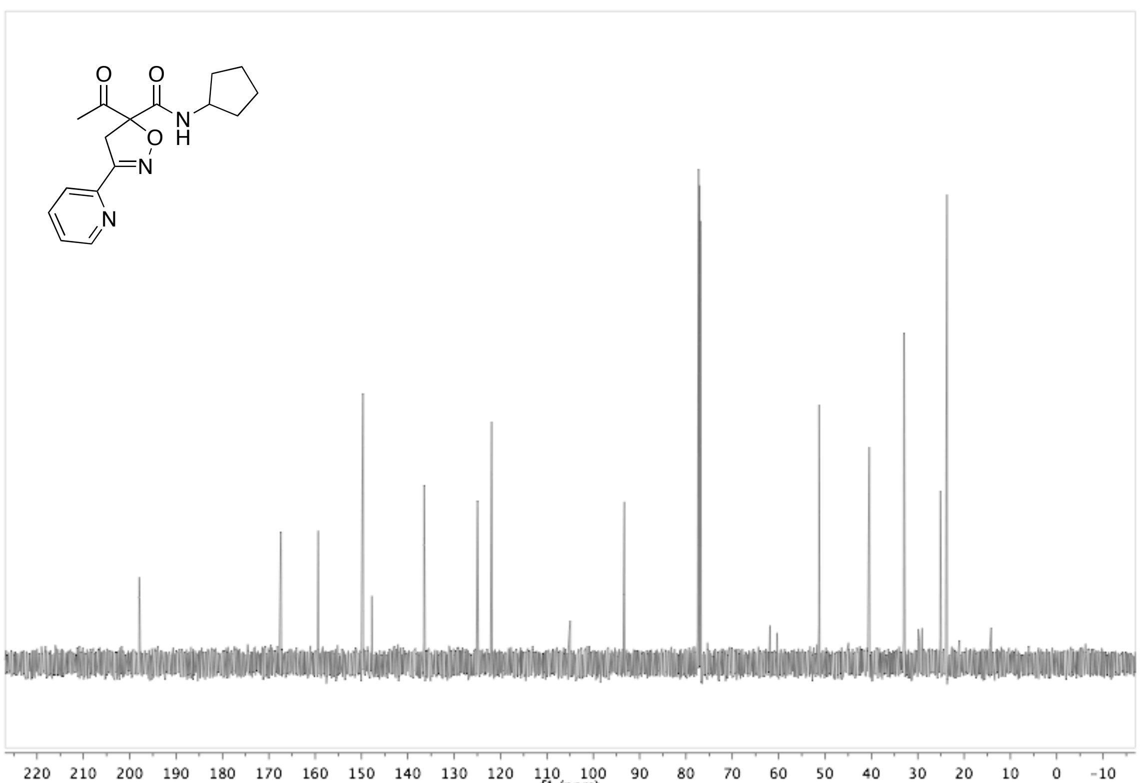
5{1,2,8}





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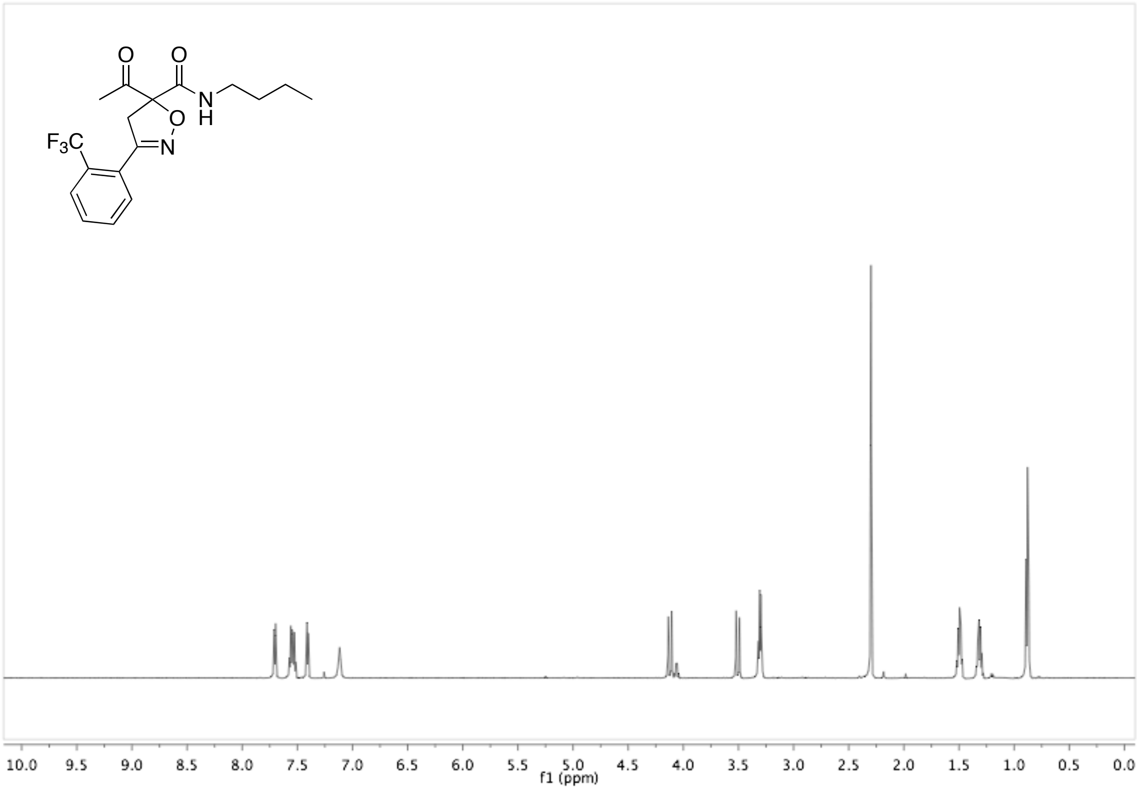

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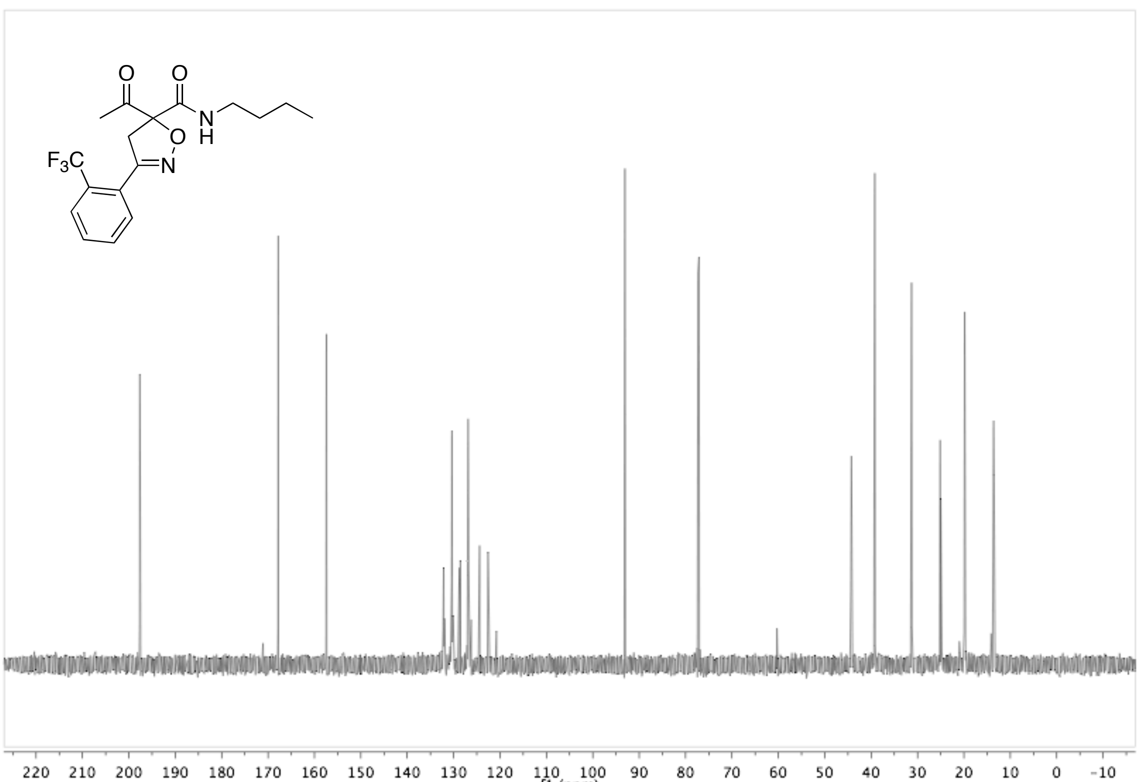
f1 (ppm)



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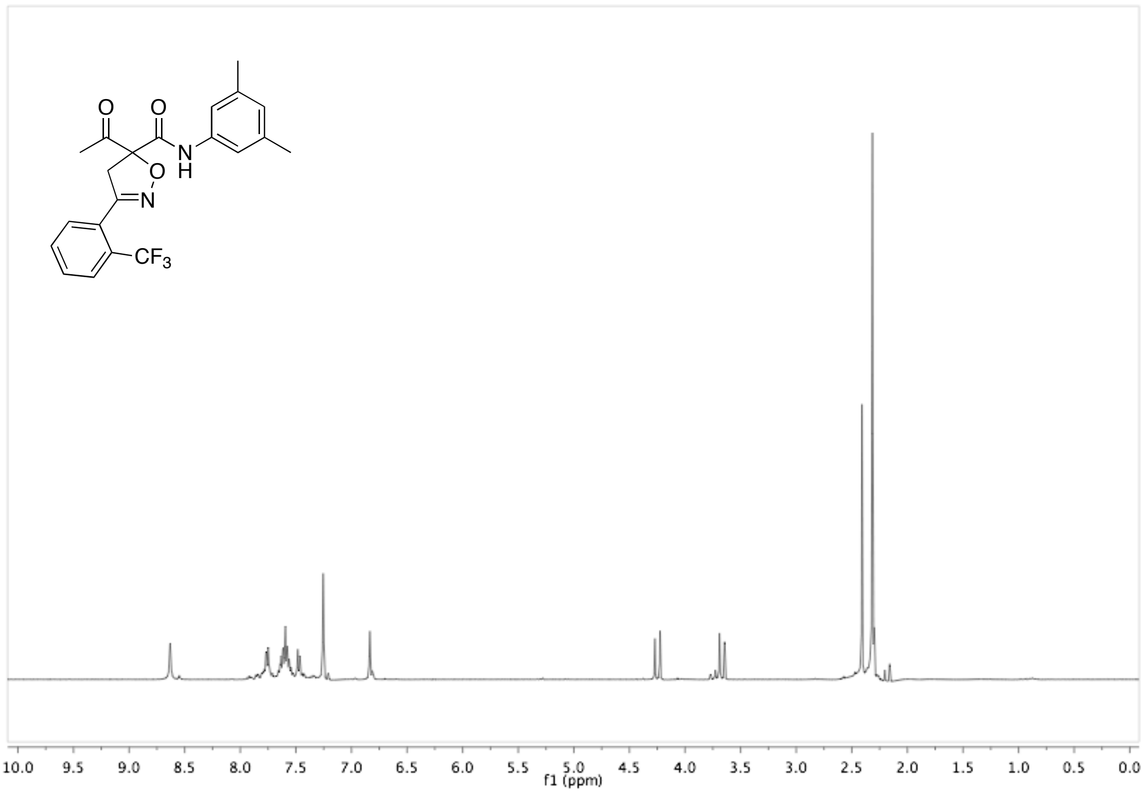
f1 (ppm)

5{1,3,2}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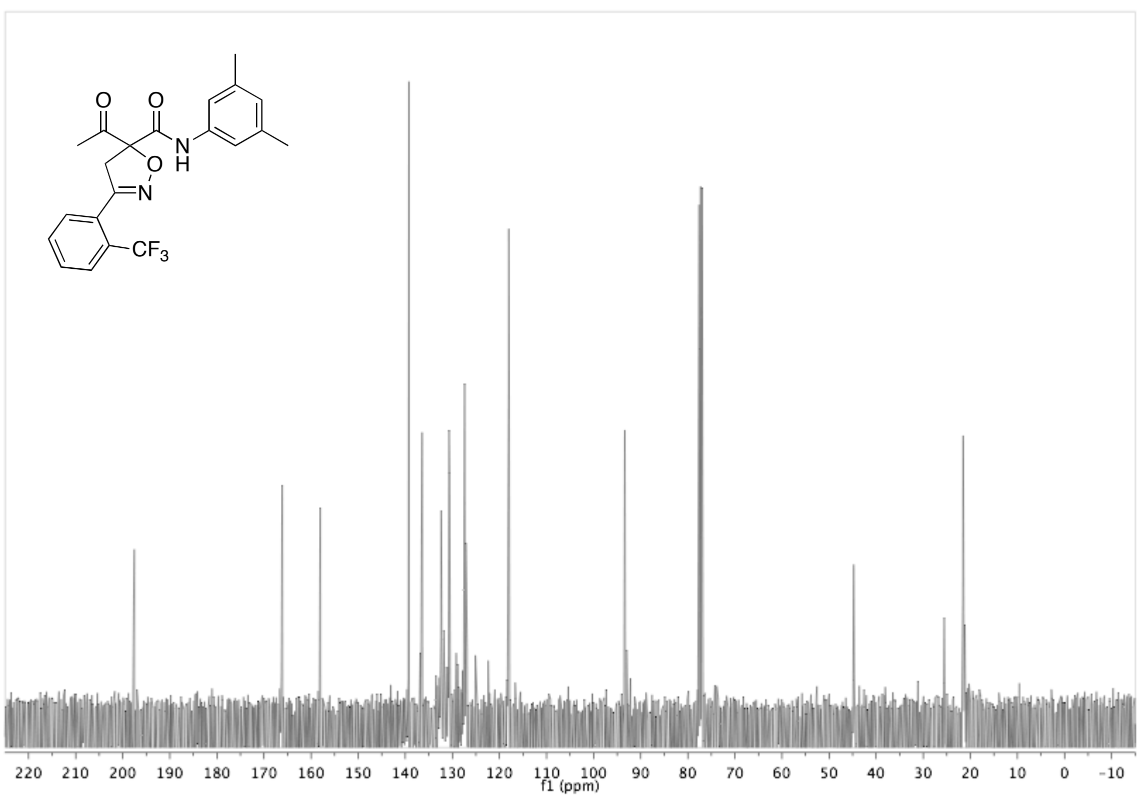
f1 (ppm)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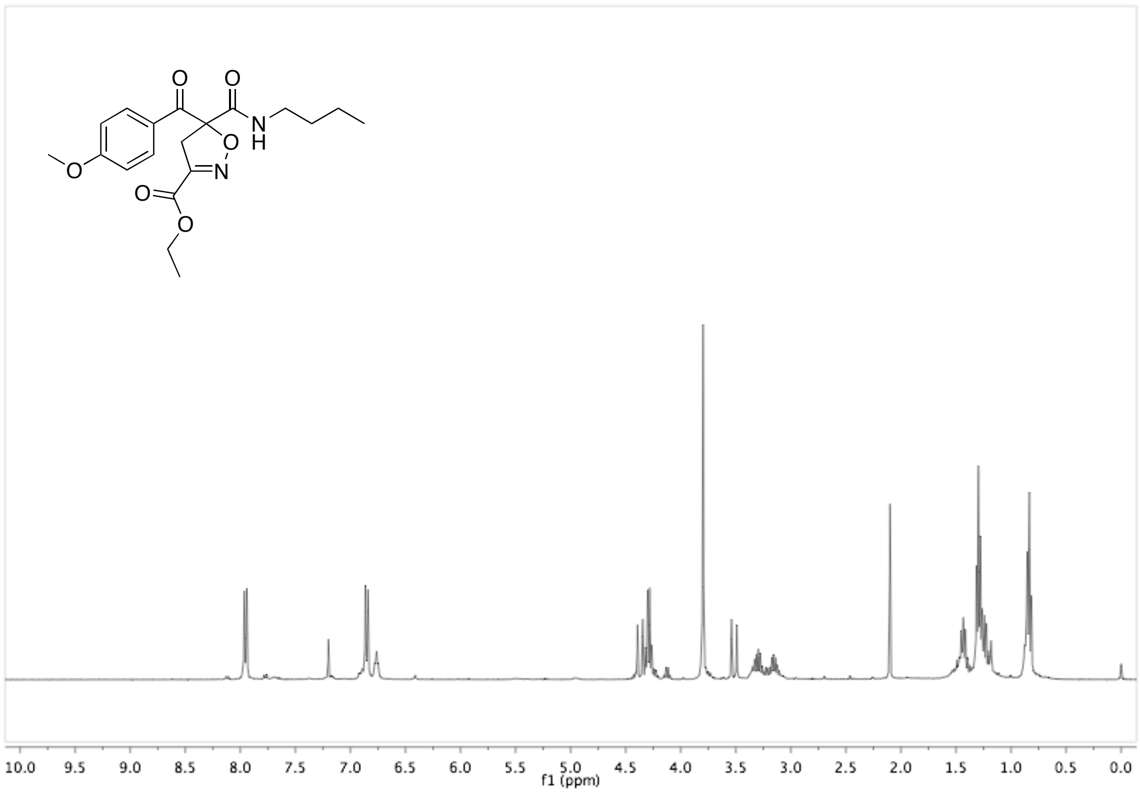
f1 (ppm)

5{2,1,1}



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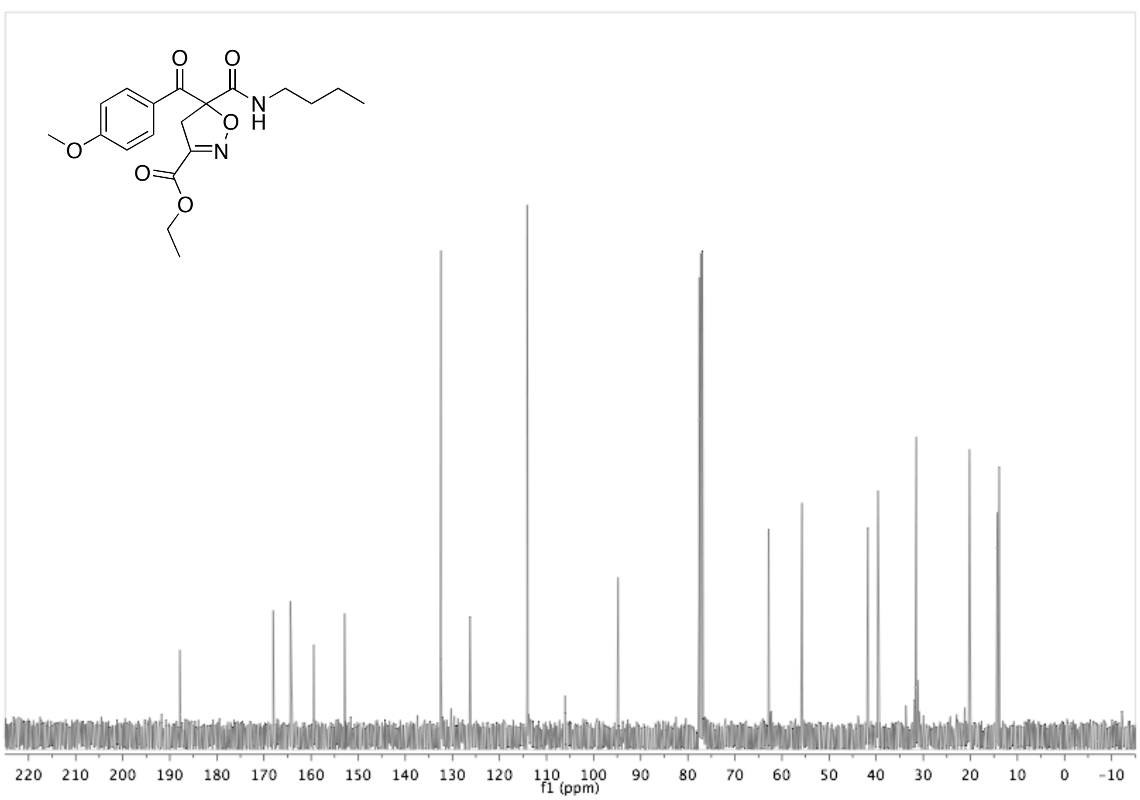
f1 (ppm)



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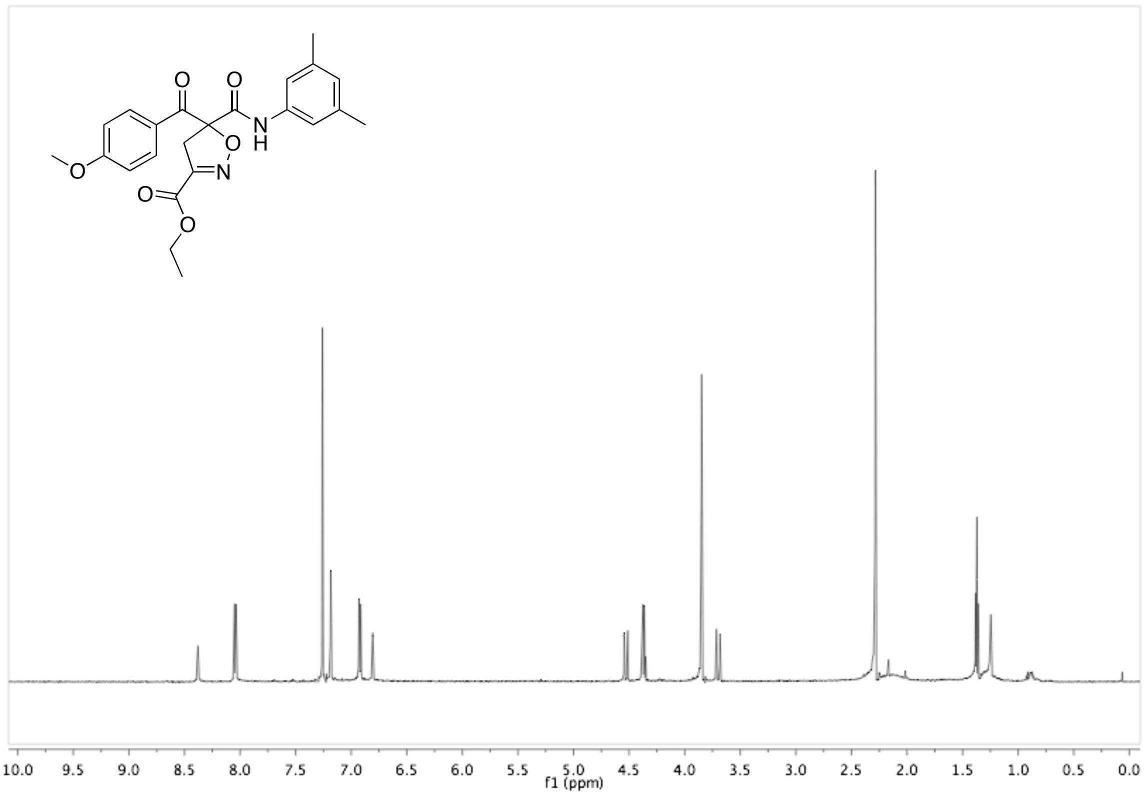
f1 (ppm)

5{2,1,2}



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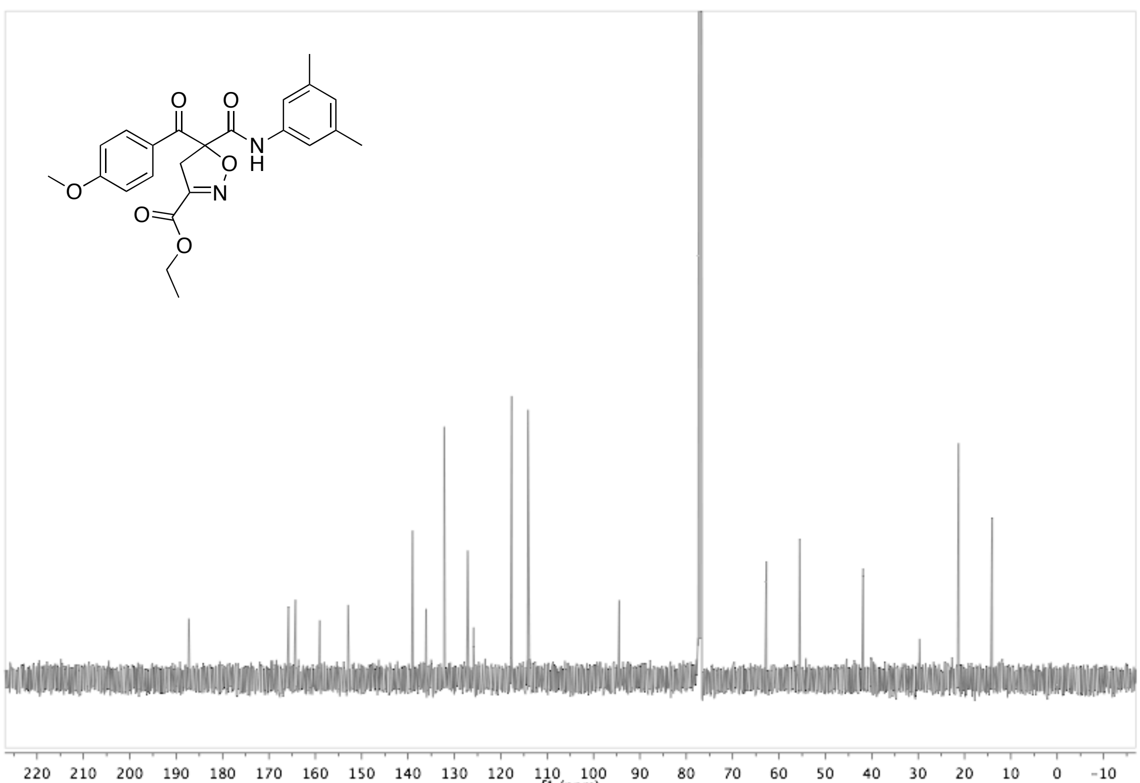
f1 (ppm)



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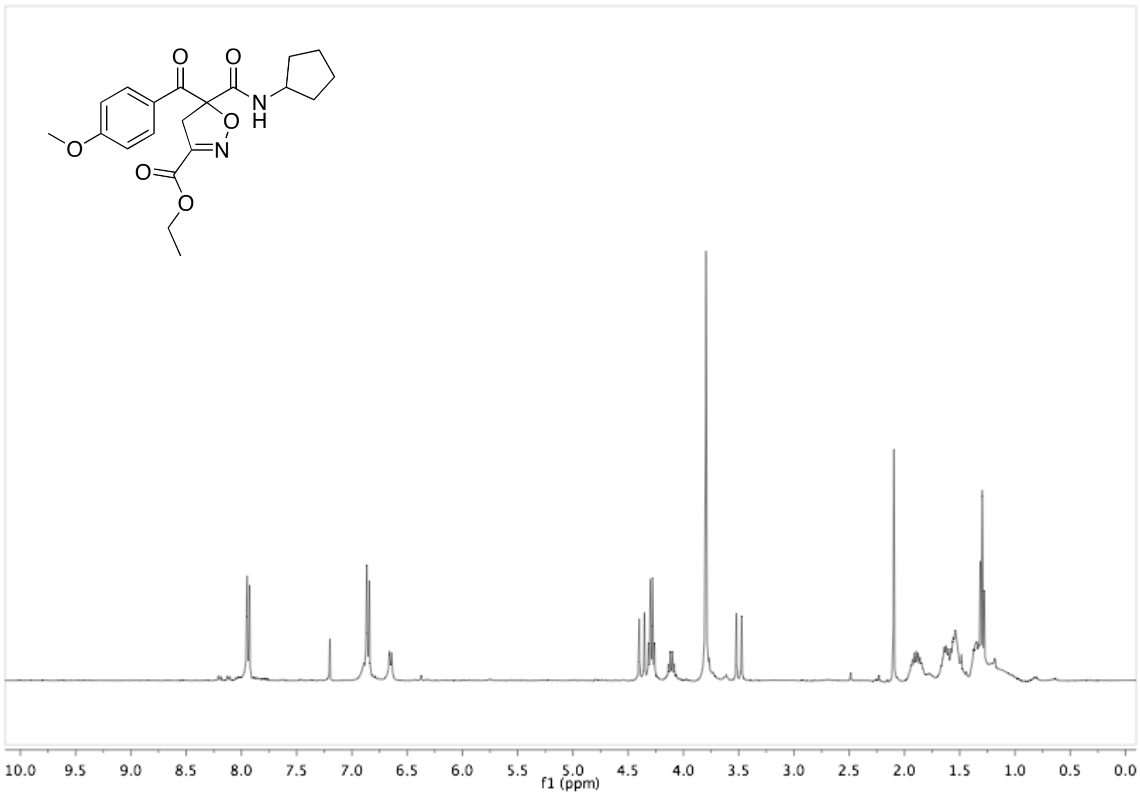
f1 (ppm)

5{2,1,8}



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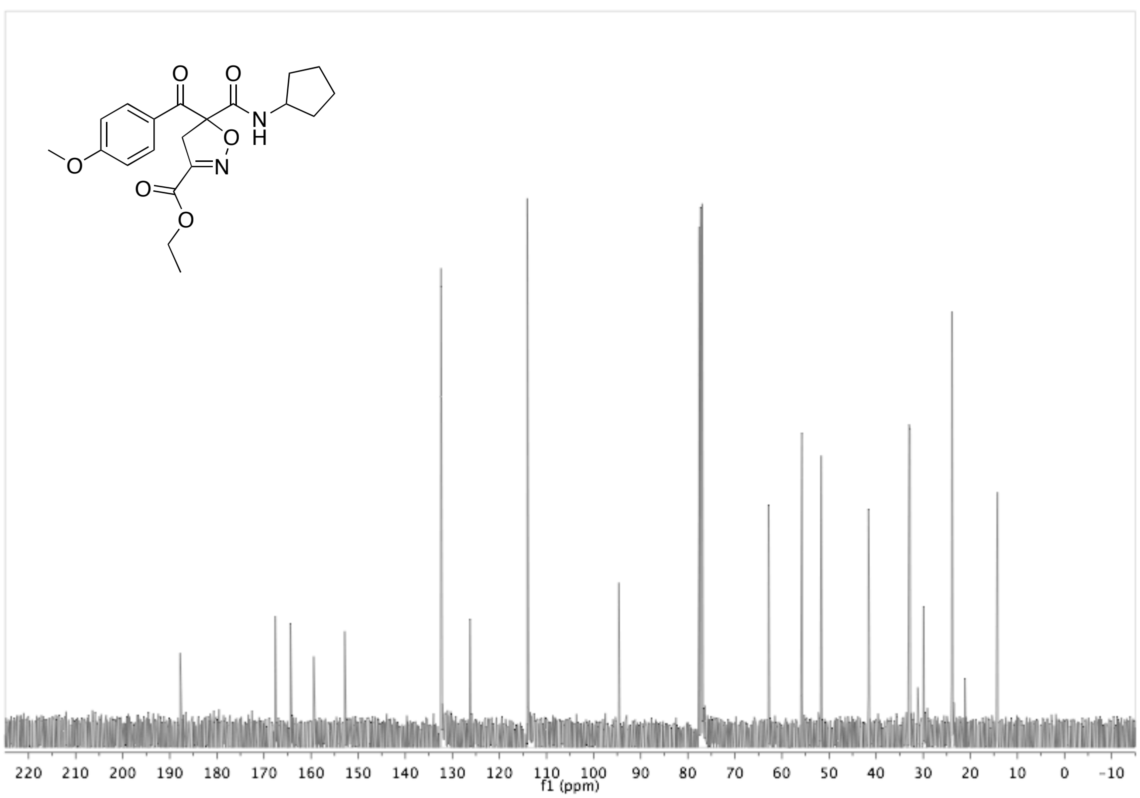
f1 (ppm)



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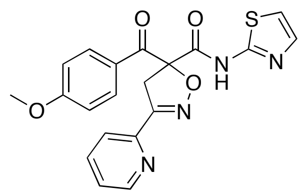
f1 (ppm)

5{2,2,3}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O
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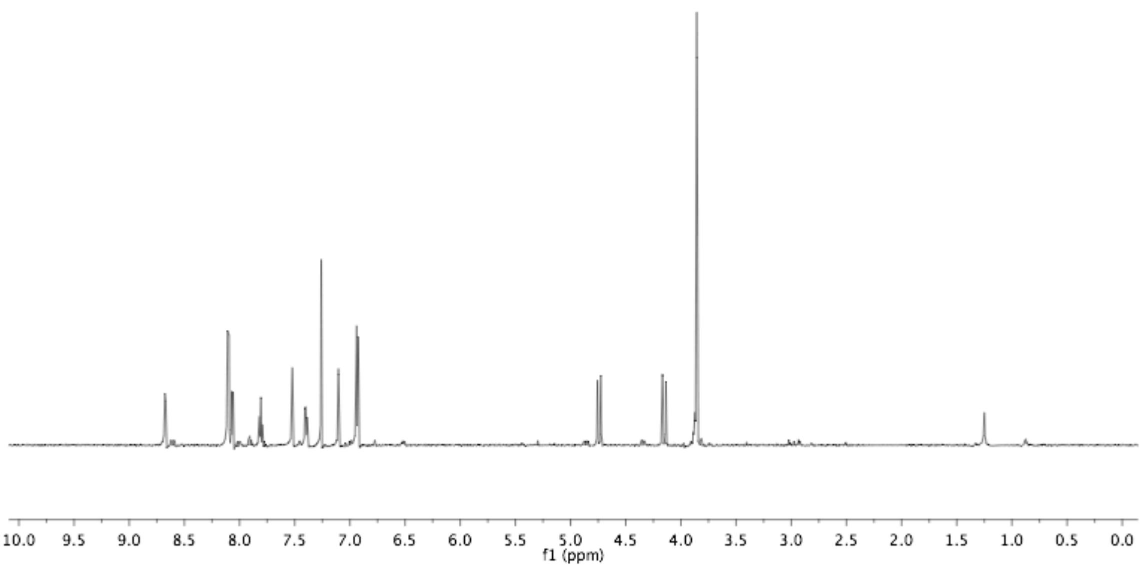
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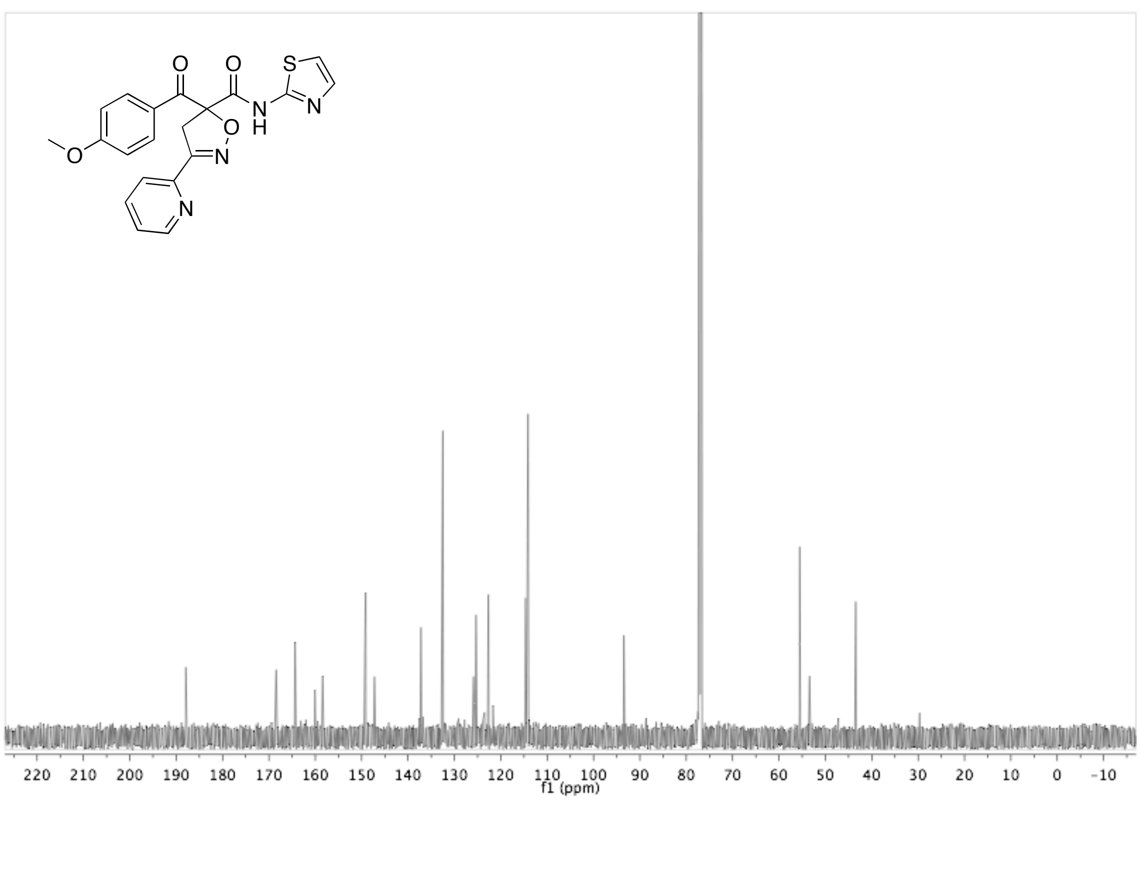
f1 (ppm)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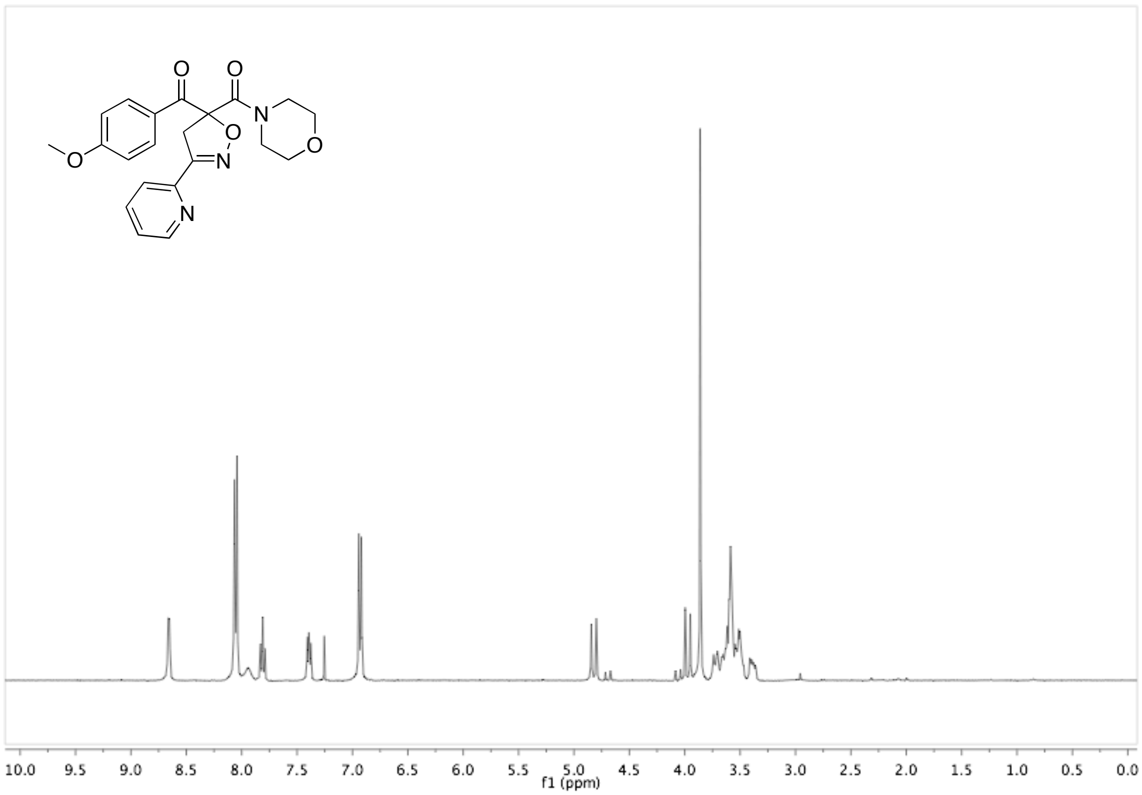
f1 (ppm)

5{2,2,4}



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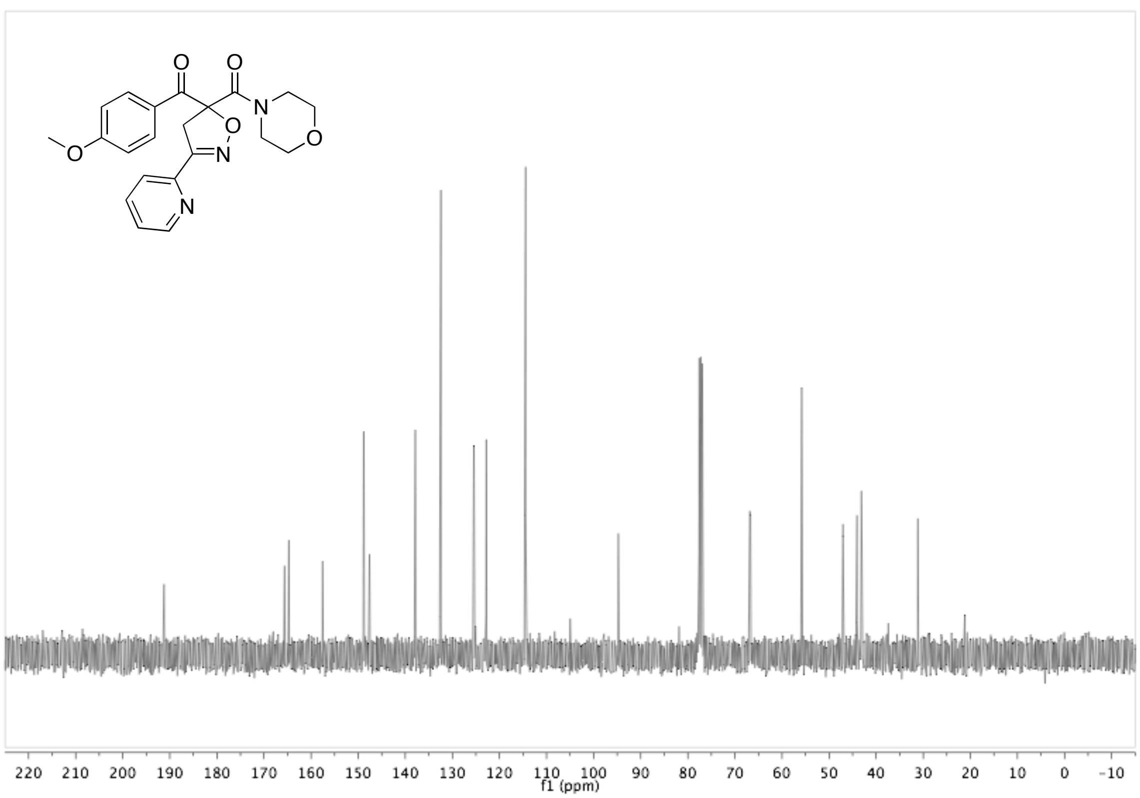
f1 (ppm)



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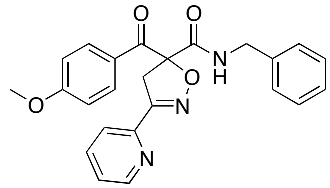
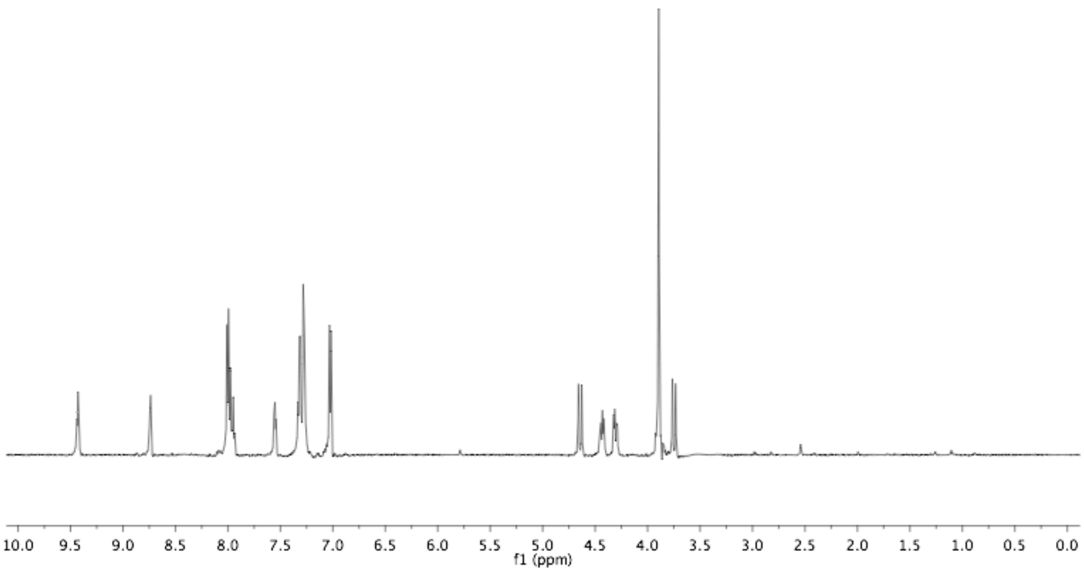
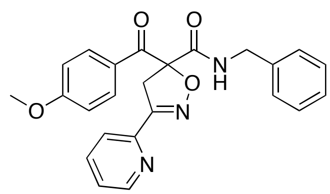
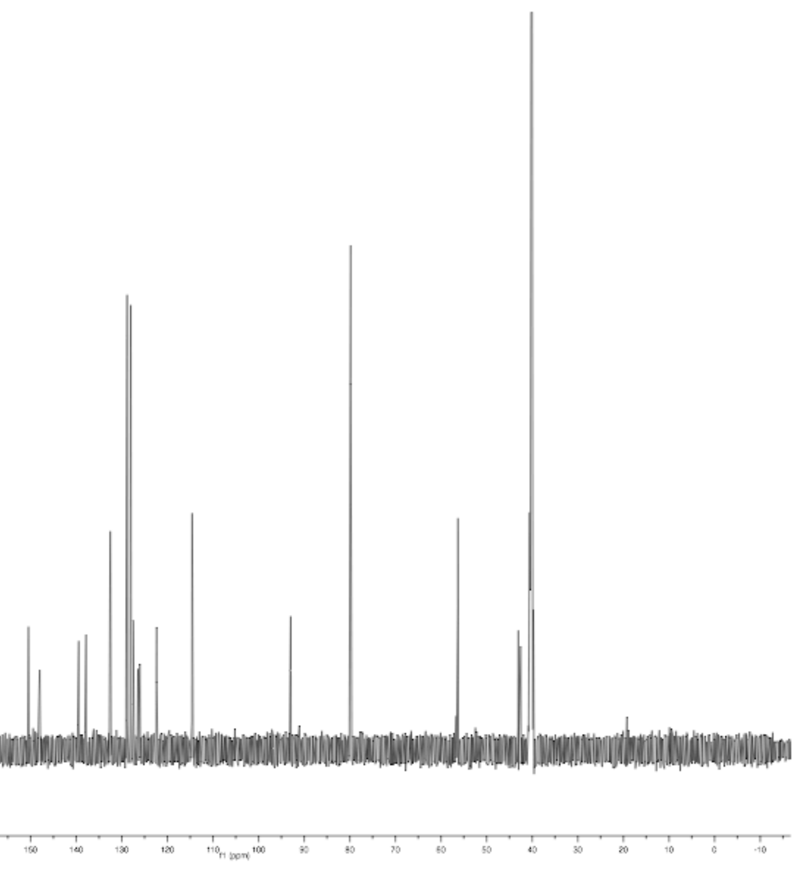
5{2,2,7}

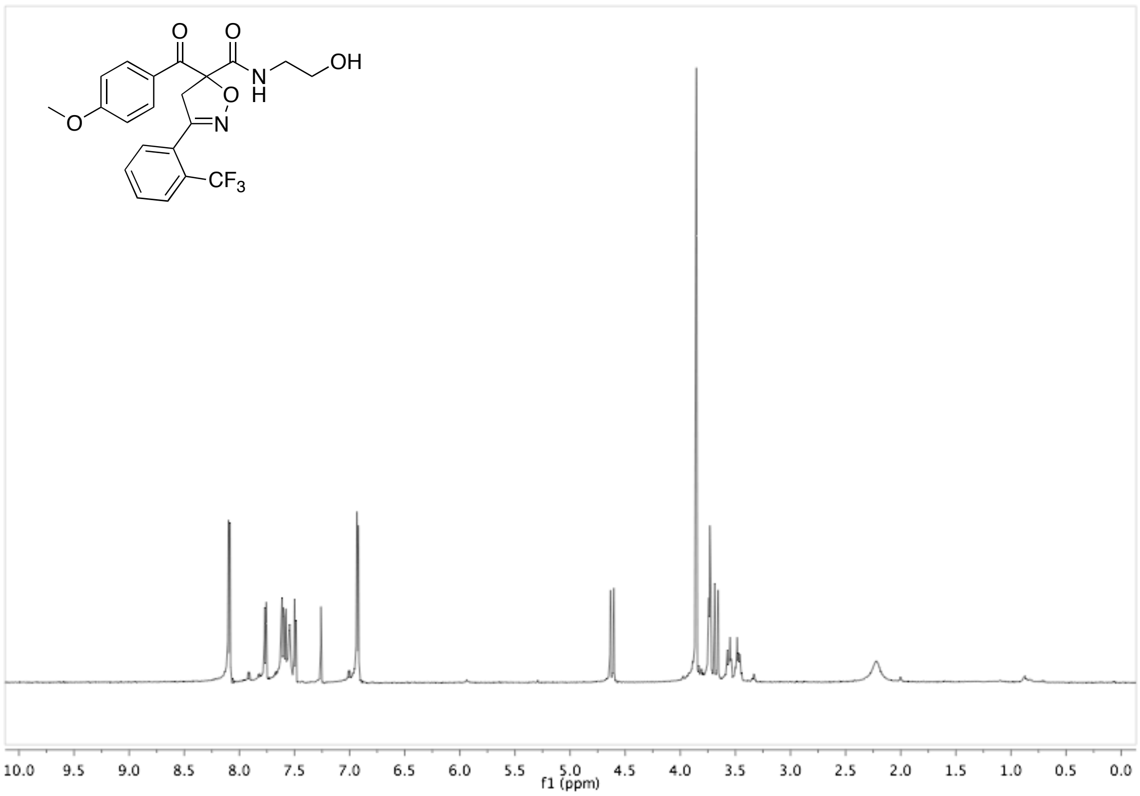


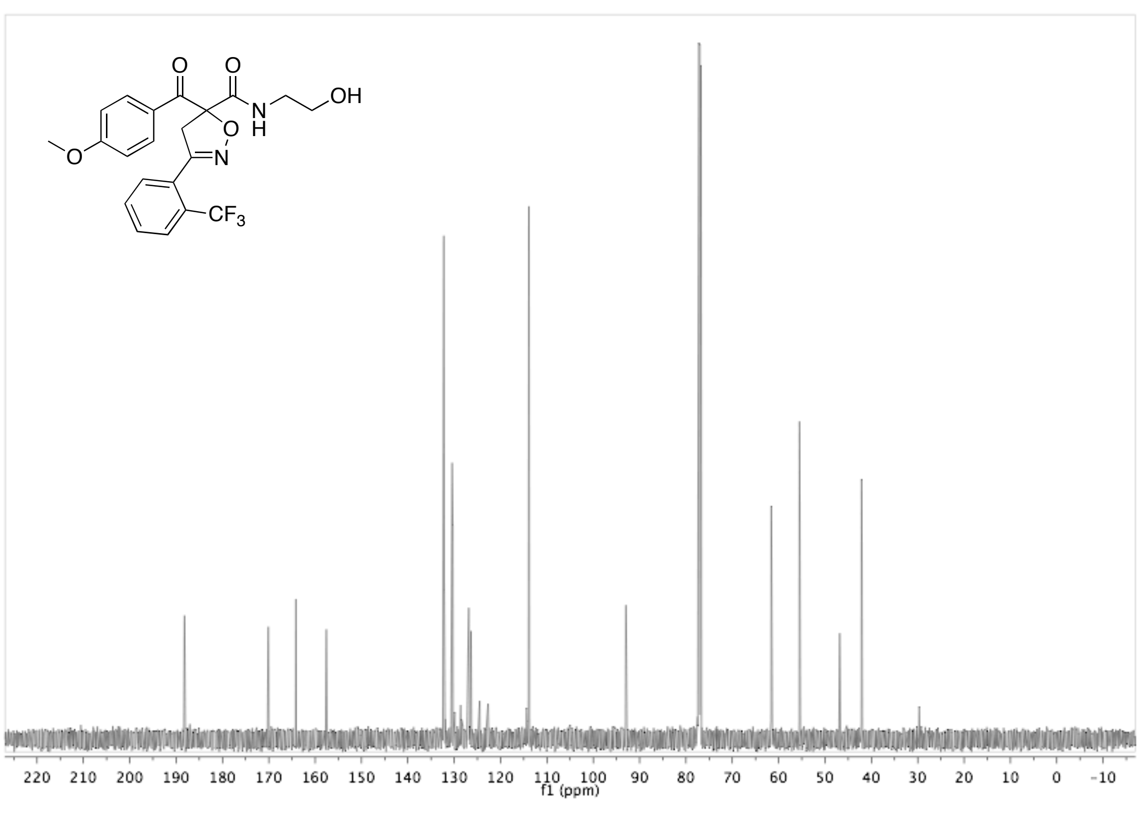




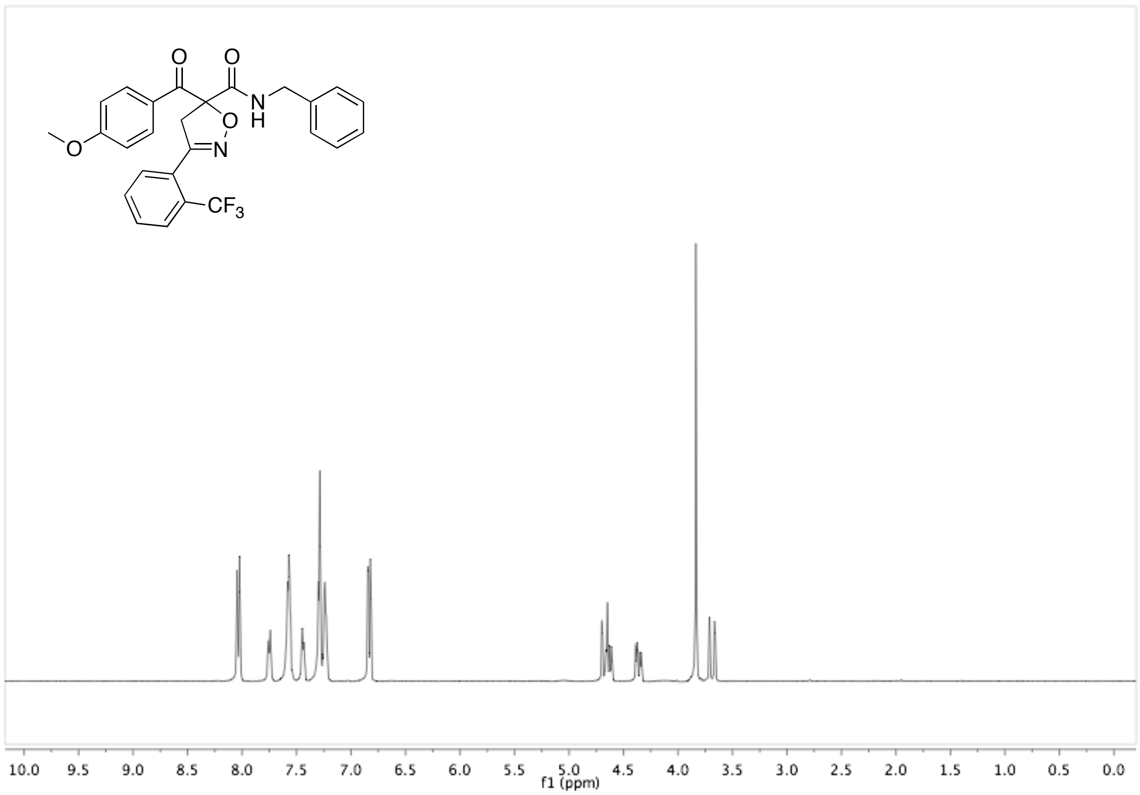


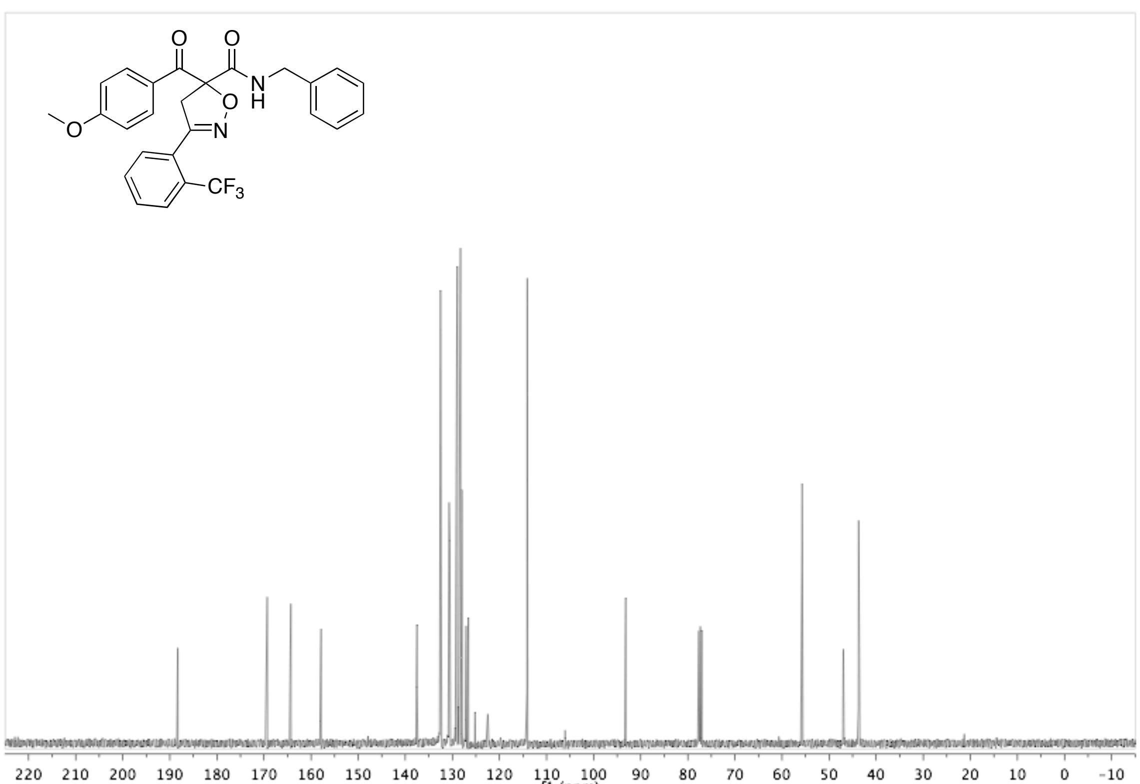
5{2,3,5}


O
O
N
H
OH
O
N
O
CF3
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)

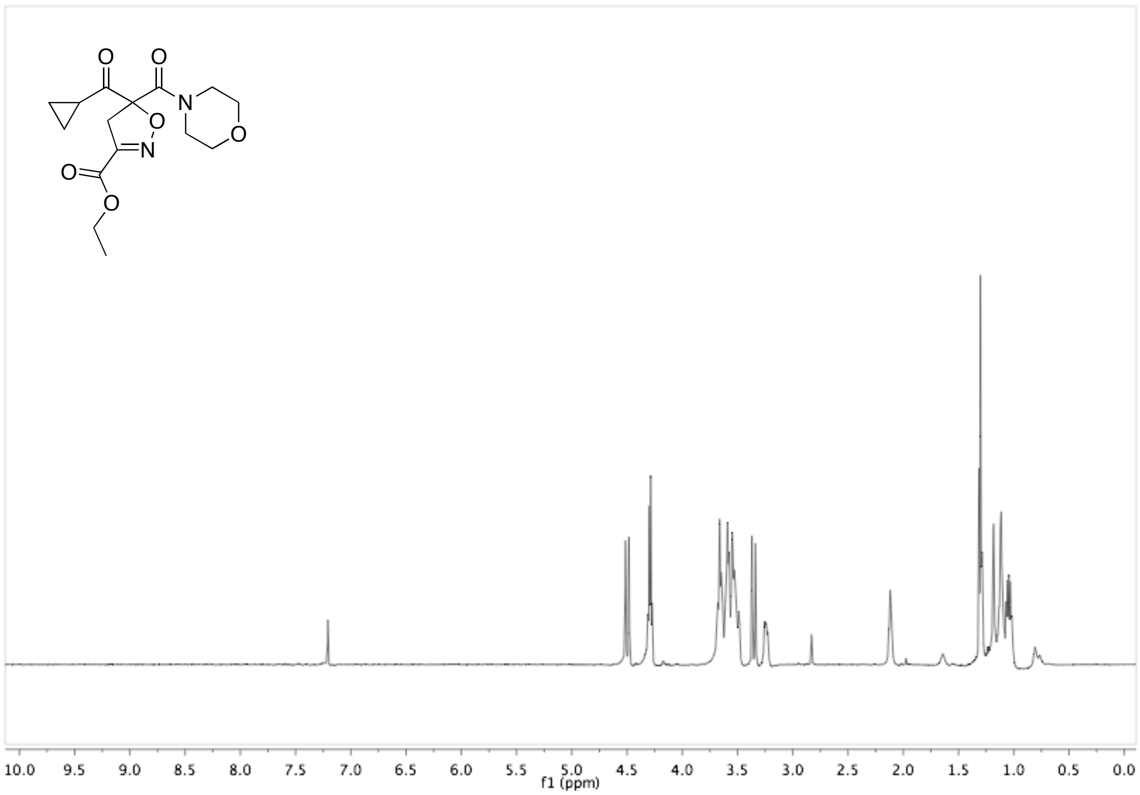

O
O
N
H
OH
O
N
O
CF3
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

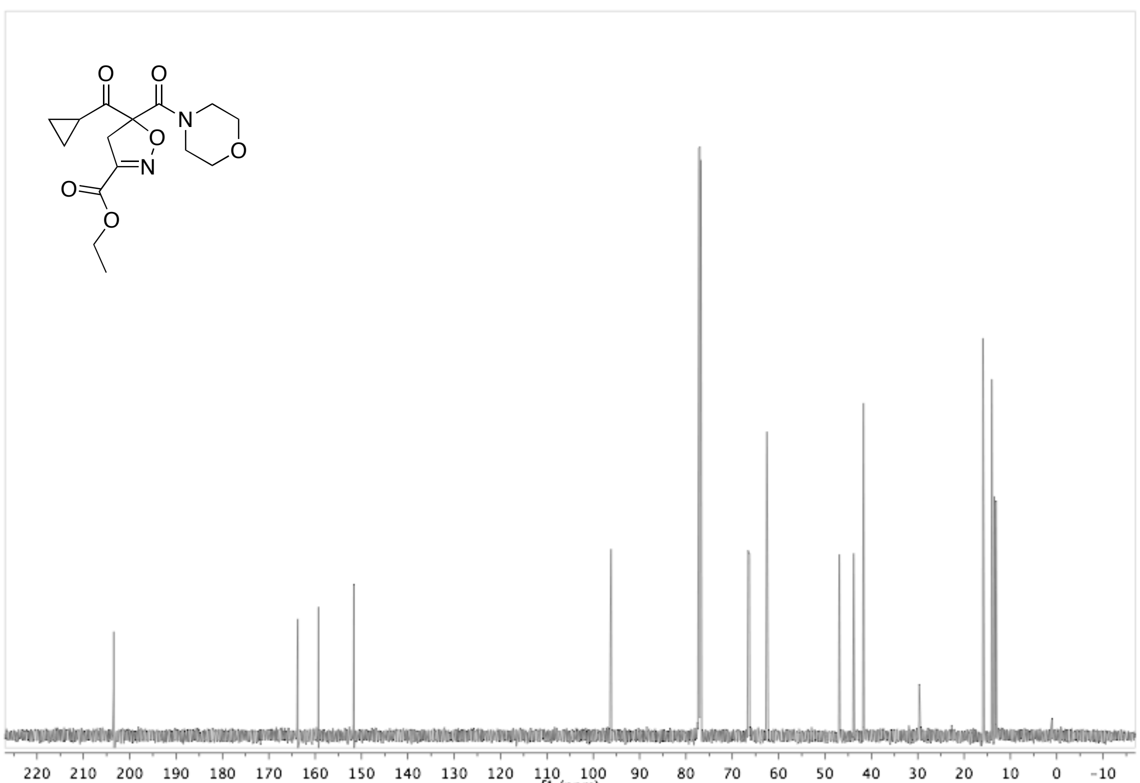
5{2,3,7}



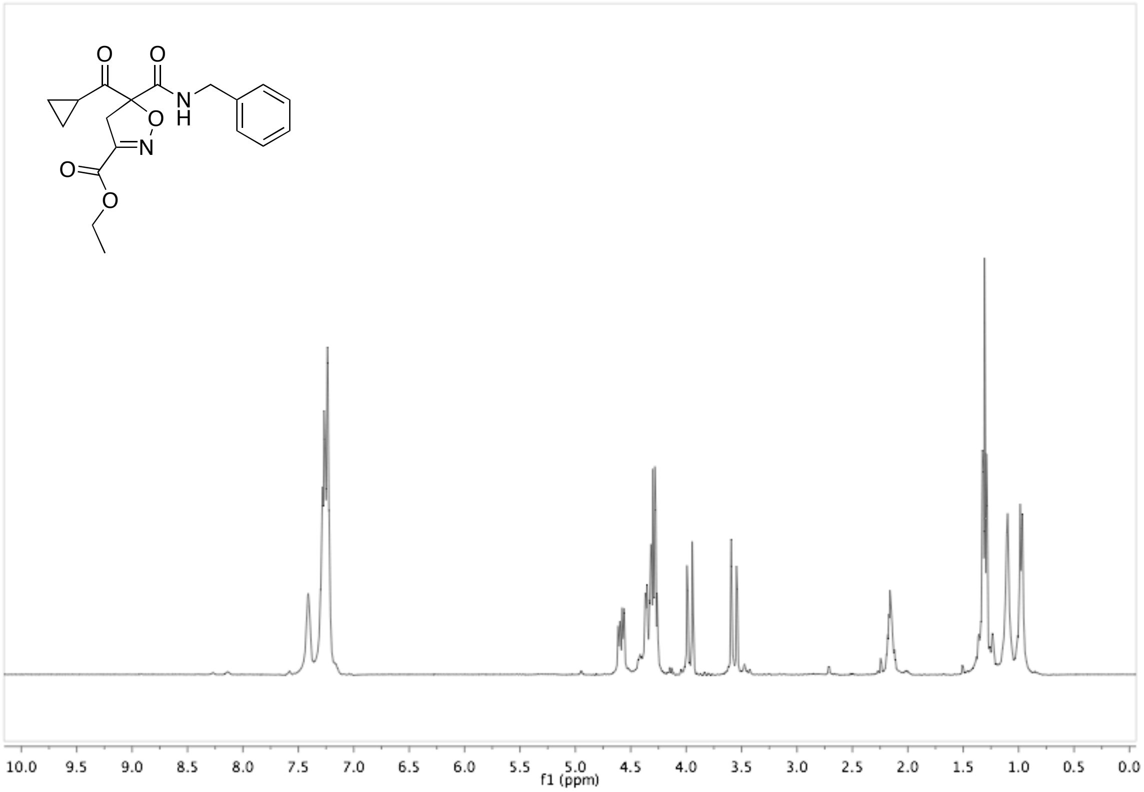


5{3,1,4}

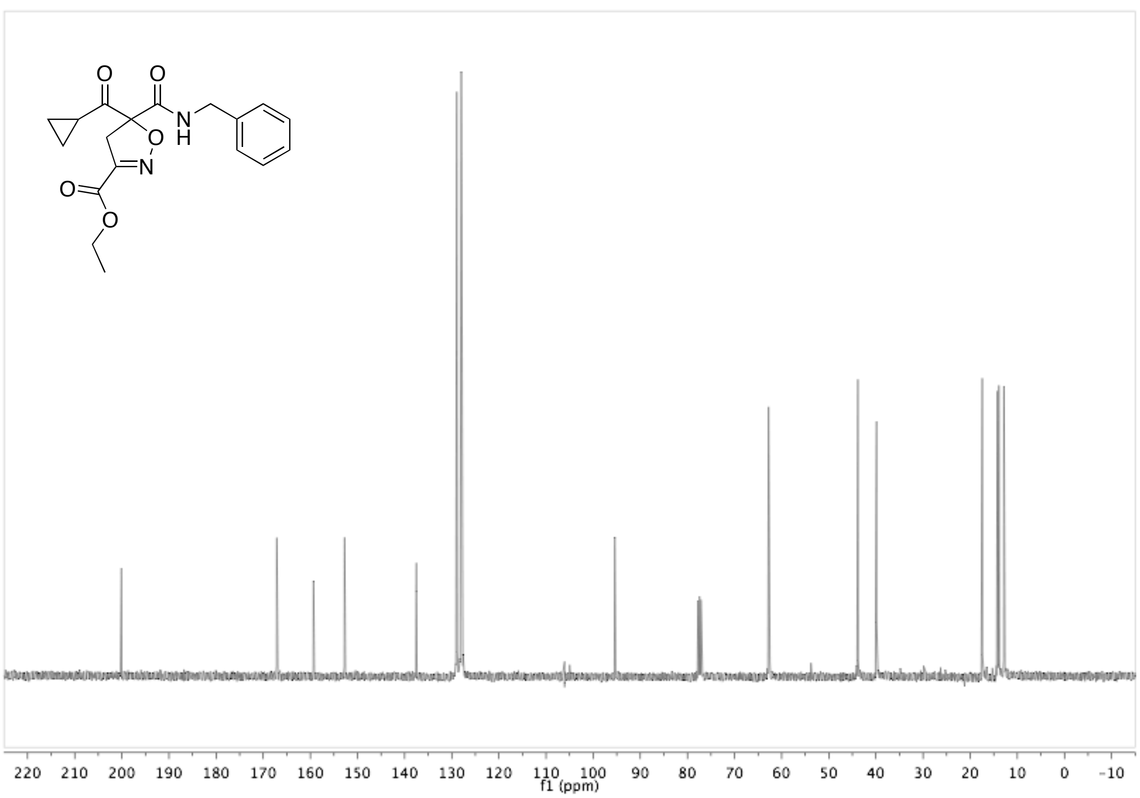




5{3,1,7}

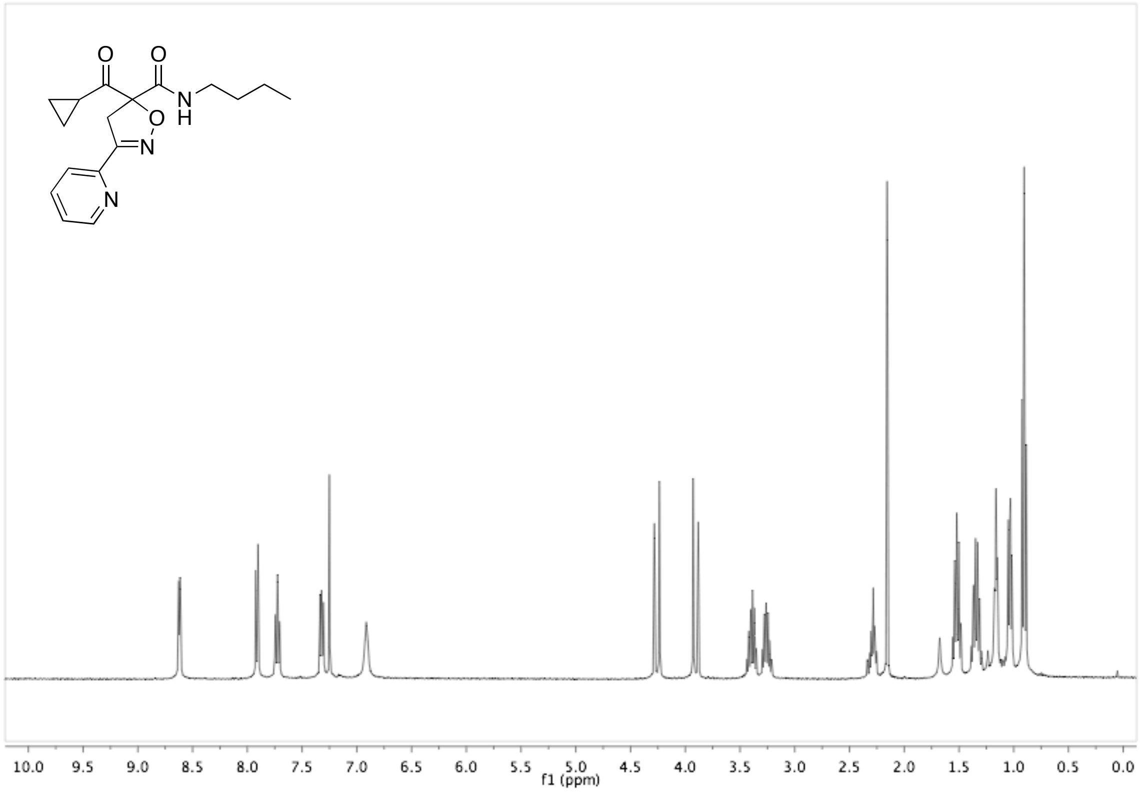


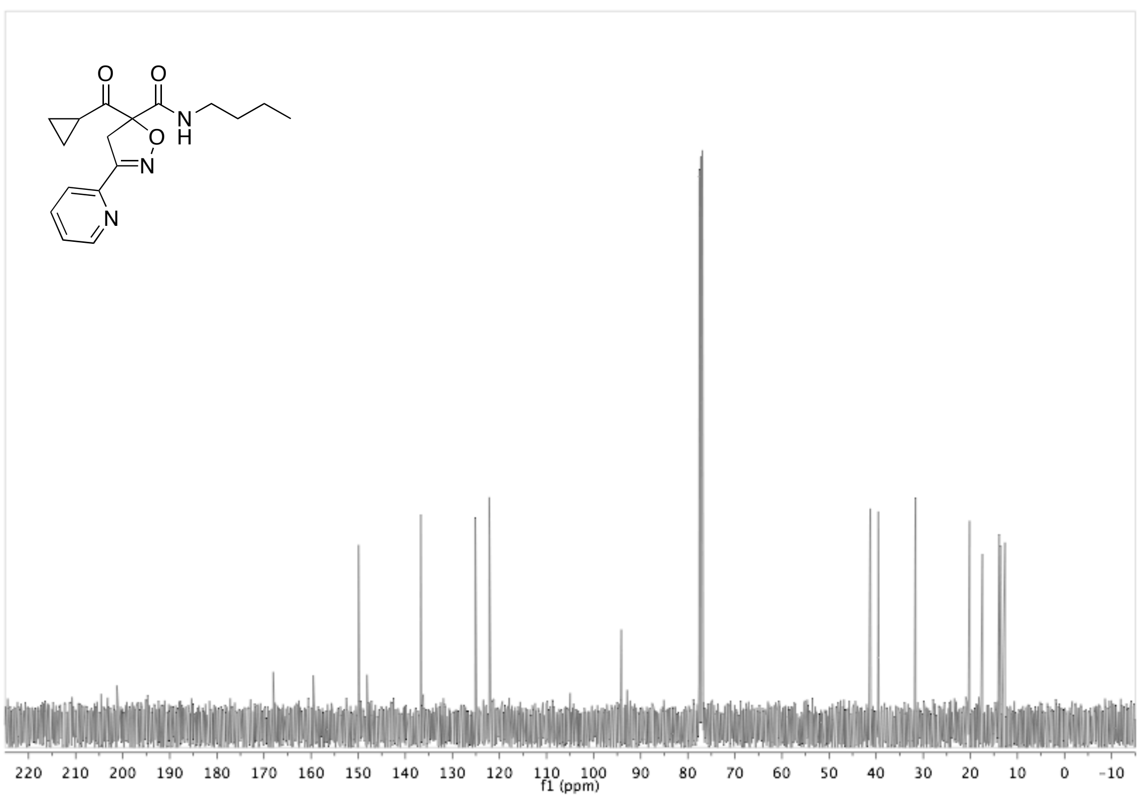
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)



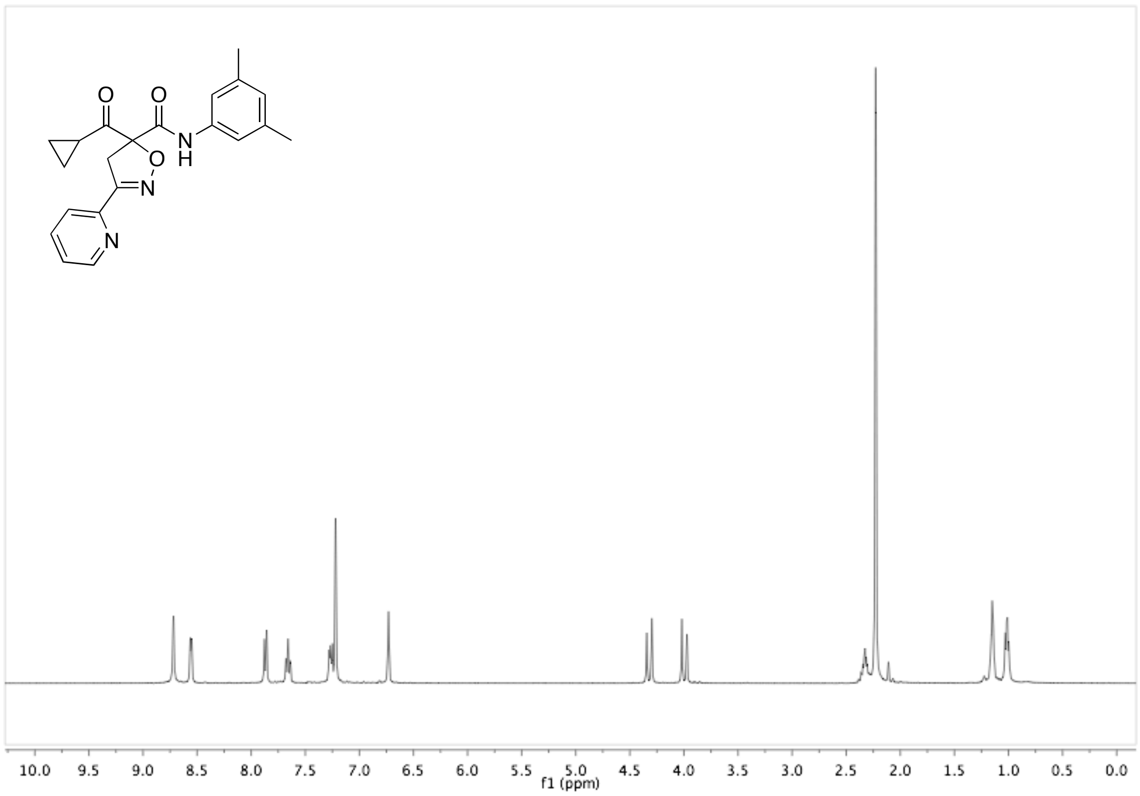
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

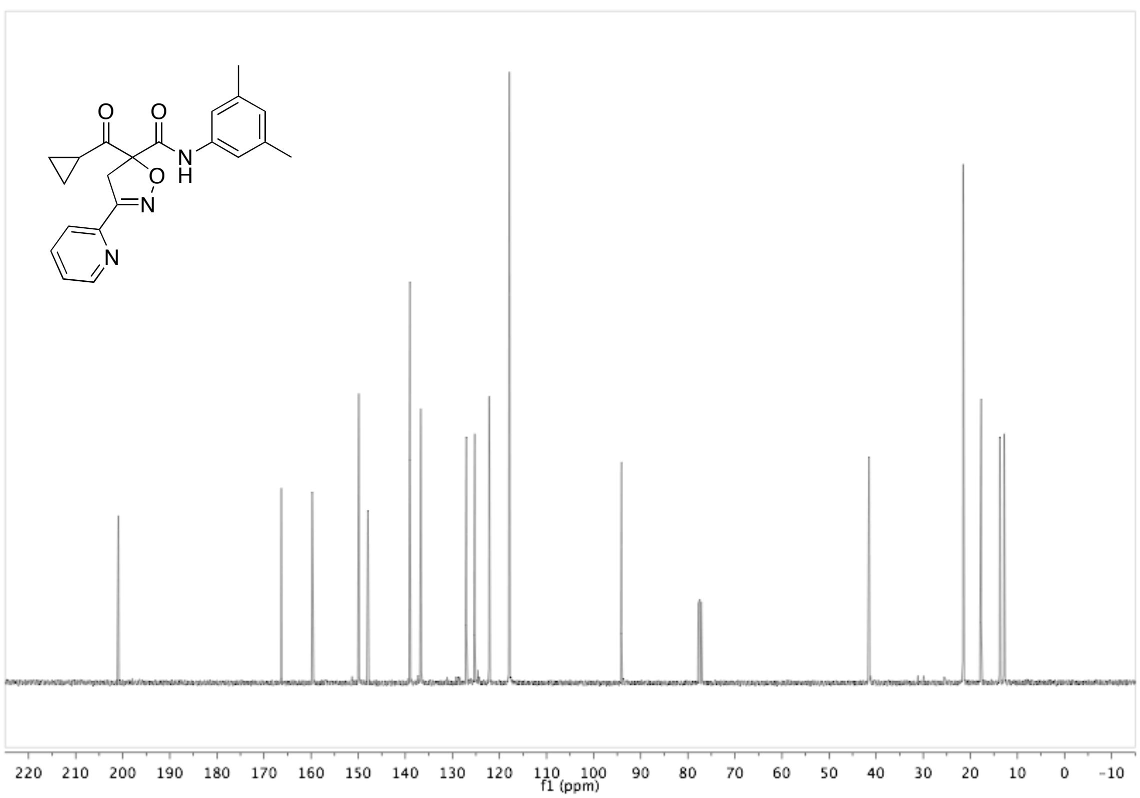
5{3,2,1}


O
O
N
H
O
N
N
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)

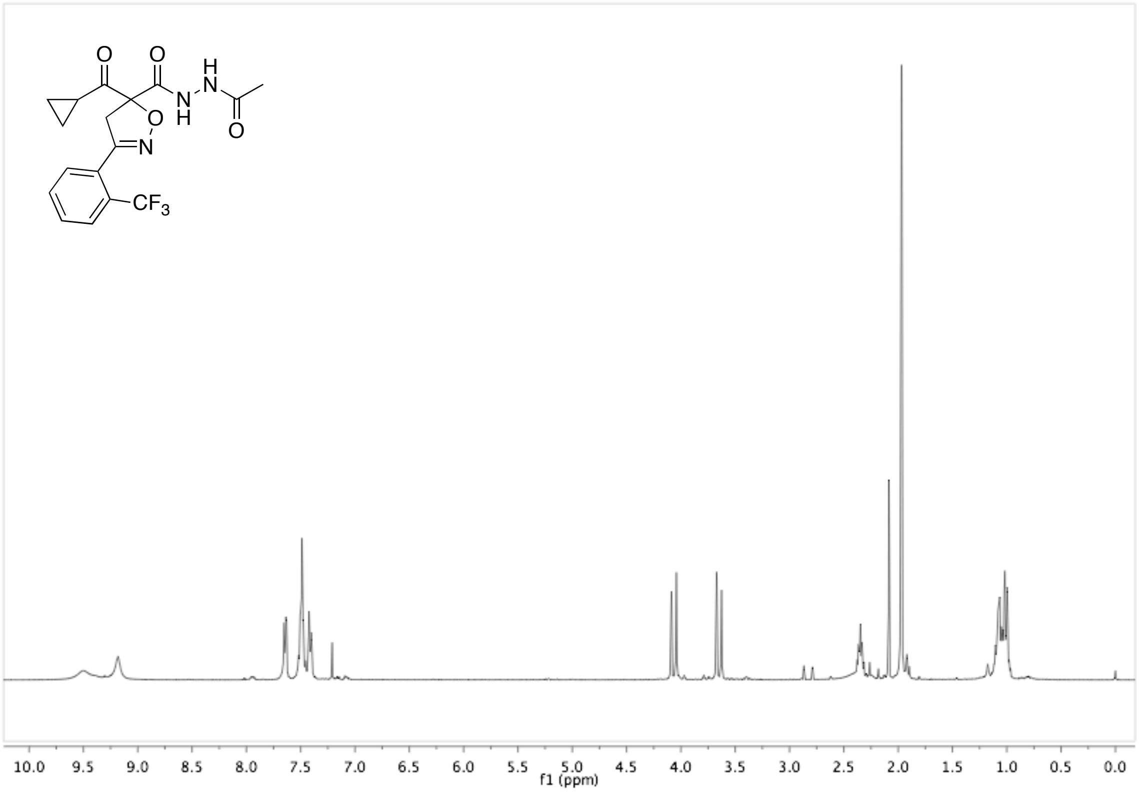

O
O
N
H
O
N
N
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

5{3,2,2}

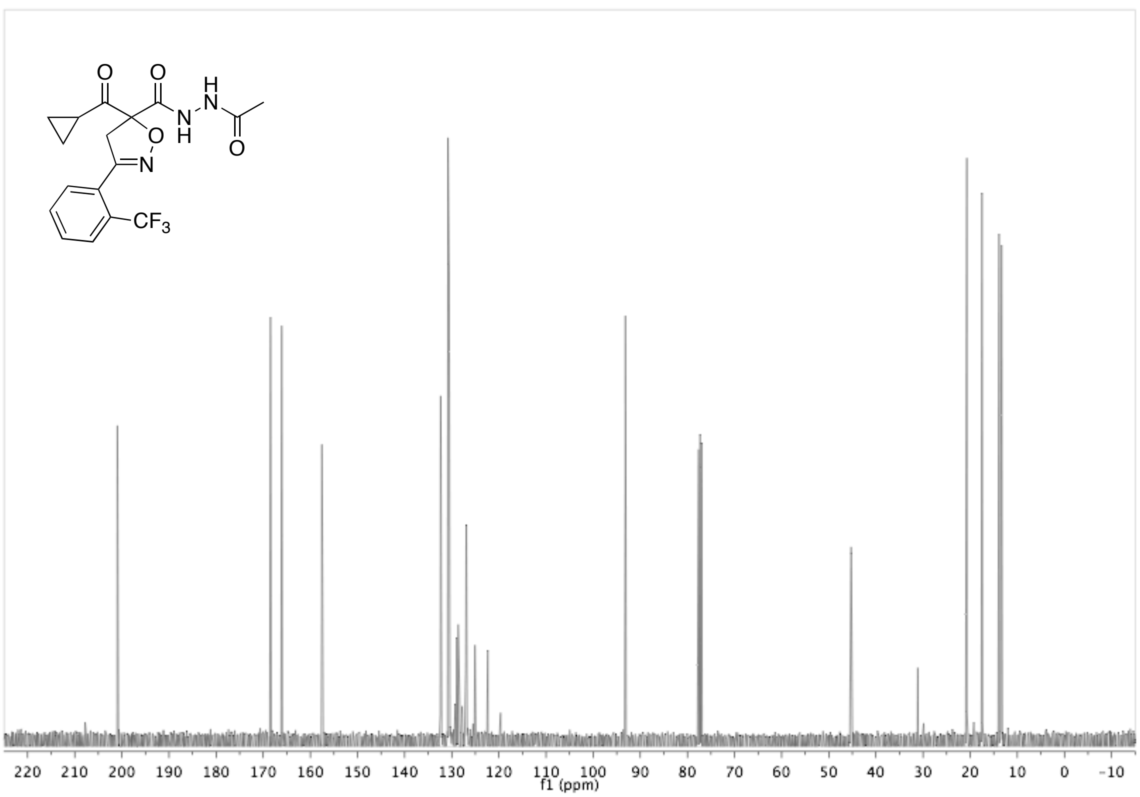

O
O
N
H
O
N
N
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


O
O
N
H
O
N
N
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

5{3,3,6}



CF3
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)



CF3
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

5{3,3,8}