Direct α-Heteroarylation of Amides (α to Nitrogen) and Ethers through a Benzaldehyde-Mediated Photoredox Reaction

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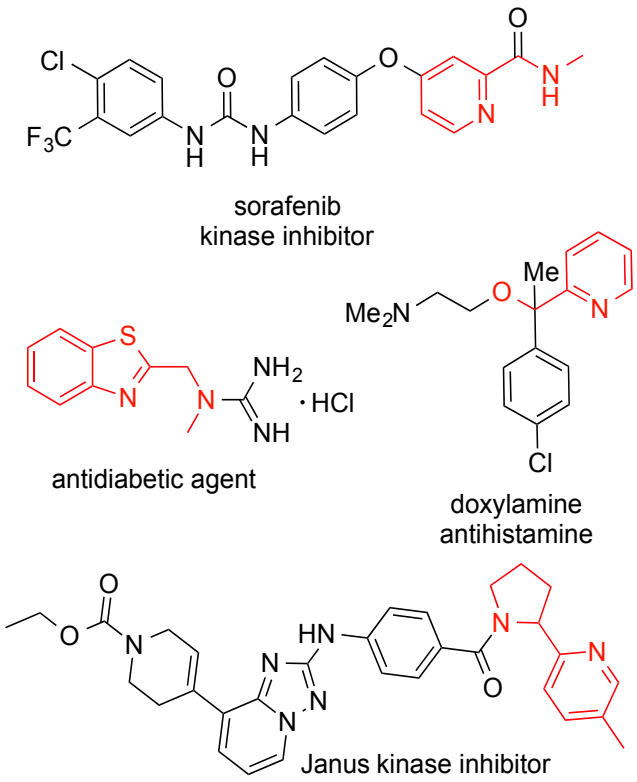


Figure S1. Bioactive compounds that contain a heteroaryl α-amine/ether functionality

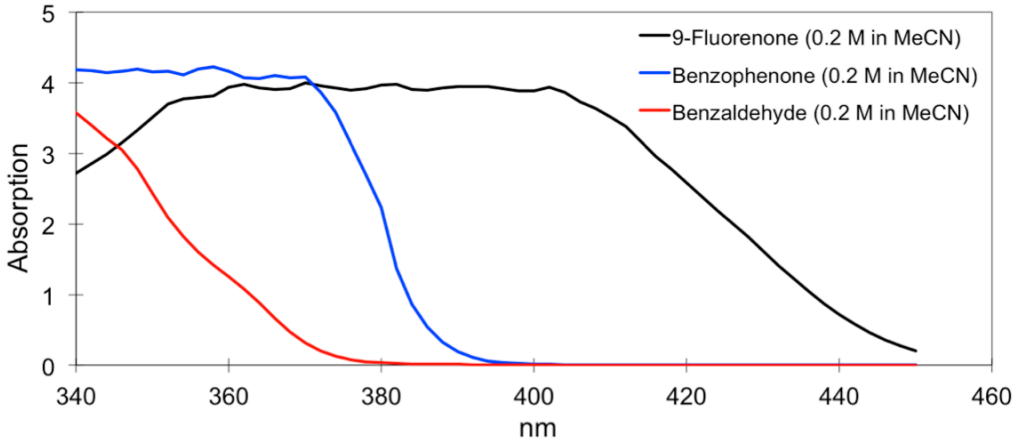


Figure S2. UV-Vis absorption spectra of photosensitizers

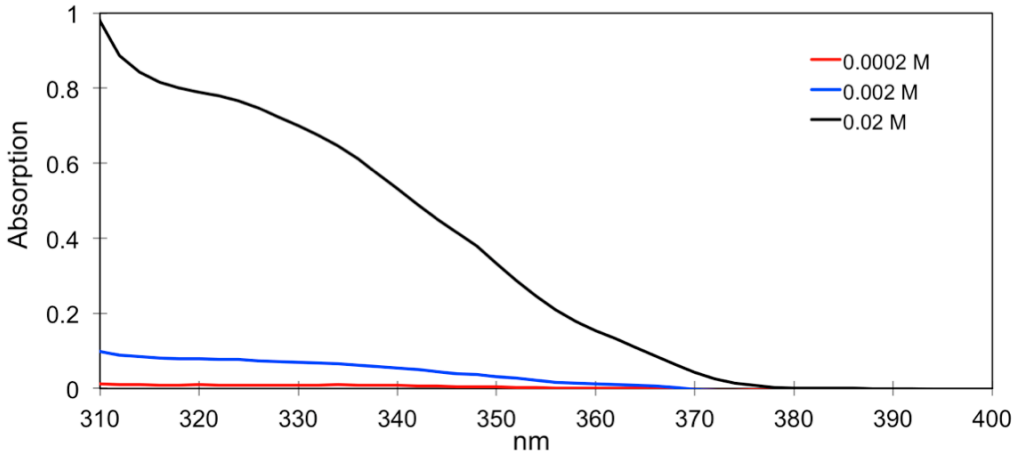


Figure S3. UV-Vis absorption spectra of different concentrations of benzaldehyde in the reaction solvent, EtOAc:$HCONH_2$ = 1:1.

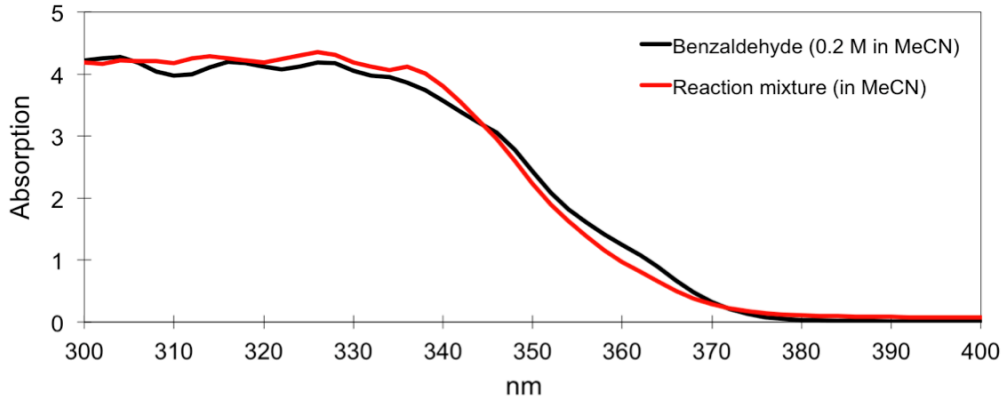
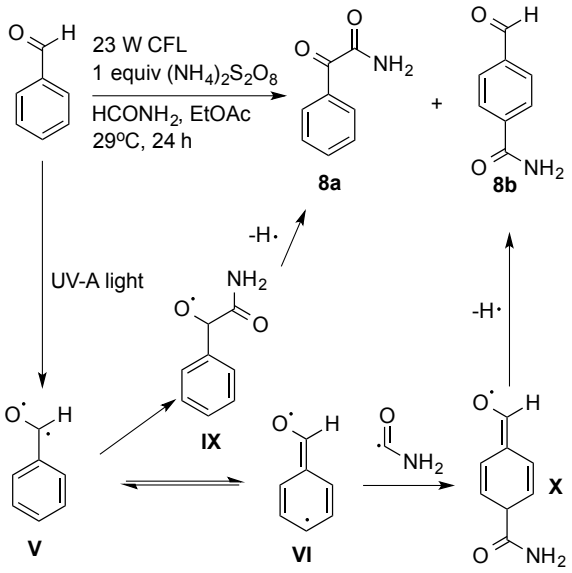


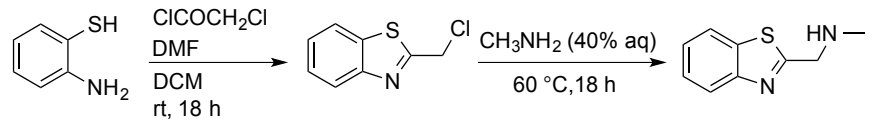
Figure S4. UV-Vis absorption spectra of benzaldehyde and the reaction mixture in acetonitrile.

Scheme S1. Plausible Mechanism for the Decomposition of Benzaldehyde



Scheme S2. Comparison of Two Routes towards the Synthesis of a Key Intermediate for an Antidiabetic Agent

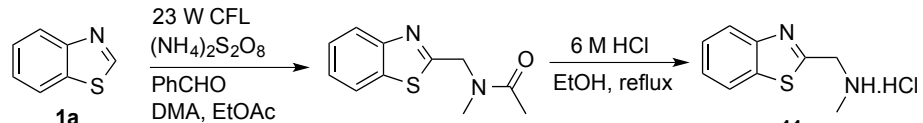
Reported synthetic route (*ref.1*):



Sigma-Aldrich
1 g/0.45 USD

57% overall yield

Our new method:



1a

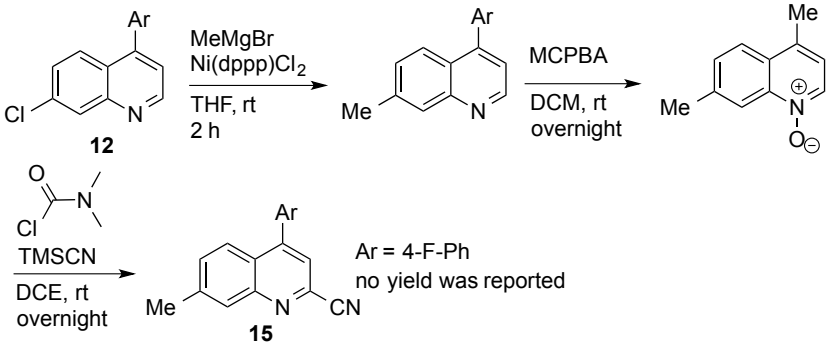
Sigma-Aldrich
1 g/0.09 USD

6c

11
62% overall yield

Scheme S3. Comparison of Two Methods to Install a Cyan Group at Quinoline in the Synthesis of a Leukotriene Biosynthesis Inhibitor

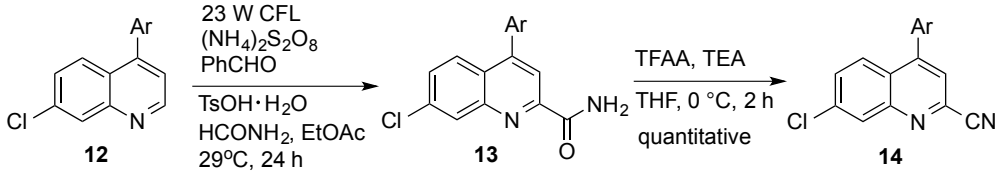
Reported synthetic route (*ref.2*):



12

15

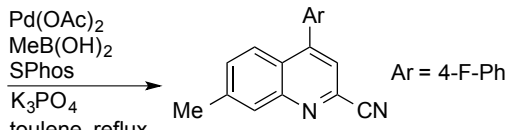
Our new method:



12

13

14



15
75% overall yield

Experiment Procedures and Product Characterization

Commercial reagents and solvents were used as received, unless otherwise stated. Organic solution was concentrated under reduced pressure on a Büchi rotary evaporator using an isopropyl alcohol-dry ice bath. Analytical thin layer chromatography (TLC) was performed on 0.25 mm silica gel plates (SiliCycle Inc., Canada), and the compounds were visualized with a UV light at 254 nm. Further visualization was achieved by staining with iodine. Flash chromatography was performed on silica gel 230–400 mesh (SiliCycle Inc., Canada) with commercial solvents. The ^{1}H and ^{13}C NMR spectra were recorded on a Varian Unity 300 Spectrometer (300 and 75 MHz for ^{1}H and ^{13}C NMR, respectively) or a VXR 500 Spectrometer (500 and 125 MHz for ^{1}H and ^{13}C NMR, respectively) and are internally referenced to residual solvent signals (note: d^{6}-DMSO referenced at 2.50 and 39.52 ppm in ^{1}H and ^{13}C NMR, respectively). Multiplicities were given as s (singlet), d (doublet), t (triplet), dd (double of doublet), and m (multiplets). Coupling constants were reported in Hertz (Hz). Data for ^{13}C NMR are reported in terms of chemical shift. High-resolution mass spectrometry (HRMS) was recorded on Waters LCT Premier XE TOF with Acquity Classic UPLC ToF High Resolution Exact Mass.

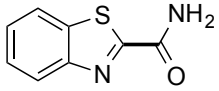
General procedure for the carbamoylation of heteroaromatics.

Method A (with TsOH•H_2O): To a 10 mL (or 20 mL) schlenk tube equipped with a magnetic stir bar was charged a heteroarene (0.22 mmol, 1.0 equiv), $(NH_4)_2S_2O_8$ (0.15 g, 0.66 mmol, 3.0 equiv), TsOH•H_2O (0.042 g, 0.22 mmol, 1.0 equiv), benzaldehyde (0.023 g, 0.22 mmol, 1.0 equiv), 1.5 mL ethyl acetate, and 1.5 mL formamide. The reaction mixture was degassed via freeze pump thaw (× 3 times) and refilled with argon. After the reaction mixture was thoroughly degassed, the vial was sealed and positioned approximately 10 cm away from the light source. Two household full-spectrum 23 W CFL bulbs were used to irradiate the reaction mixture. Water bath was used to keep the reaction temperature at 29 °C. After stirring for the indicated time, the resulting mixture was diluted with water (20 mL). The pH value was then adjusted to 9–10 with NaOH (1 M), extracted with ethyl acetate (15 mL × 3), dried over Na_2SO_4, and concentrated under vacuum. Purification of the crude product by flash chromatography on silica gel using the indicated solvent system afforded the desired product.

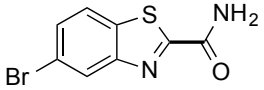
Method B (without TsOH•H_2O): To a 10 mL (or 20 mL) schlenk tube equipped with a magnetic stir bar was charged a heteroarene (0.22 mmol, 1.0 equiv), $(NH_4)_2S_2O_8$ (0.15 g, 0.66 mmol, 3.0 equiv), benzaldehyde (0.023 g, 0.22 mmol, 1.0 equiv), 1.5 mL ethyl acetate, and 1.5 mL formamide. The reaction mixture was degassed via freeze pump thaw (× 3 times) and refilled with argon. After the reaction mixture was thoroughly degassed, the vial was sealed and positioned approximately 10 cm away from the light source. Two household full-spectrum 23 W CFL bulbs were used to irradiate the reaction mixture. Water bath was used to keep the reaction temperature at 29 °C. After stirring for the indicated time, the resulting mixture was diluted with ethyl acetate (30 mL), washed with brine (10 mL × 3), dried over Na_2SO_4, and concentrated under vacuum. Purification of the crude product by flash chromatography on silica gel using the indicated solvent system afforded the desired product.

Method C: To a 10 mL (or 20 mL) schlenk tube equipped with a magnetic stir bar was charged a heteroarene (0.22 mmol, 1.0 equiv), $(NH_4)_2S_2O_8$ (0.15 g, 0.66 mmol, 3.0 equiv), benzaldehyde (0.023 g, 0.22 mmol, 1.0 equiv), 1.5 mL amide, and 1.5 mL ethyl acetate. The reaction mixture was degassed via freeze pump thaw (× 3 times) and refilled with argon. After the reaction mixture was thoroughly degassed, the vial was sealed and positioned approximately 10 cm away from the light source. Two household full-spectrum 23 W CFL bulbs were used to irradiate the reaction mixture. Water bath was used to keep the reaction temperature at 29 °C. After stirring for the indicated time, the resulting mixture was diluted with ethyl acetate (30 mL), washed with brine (10 mL × 3), dried over Na_2SO_4, and concentrated under vacuum. Purification of the crude product by flash chromatography on silica gel using the indicated solvent system afforded the desired product.

Method D: To a 10 mL (or 20 mL) schlenk tube equipped with a magnetic stir bar was charged a heteroarene (0.22 mmol, 1.0 equiv), $(NH_4)_2S_2O_8$ (0.15 g, 0.66 mmol, 3.0 equiv), benzaldehyde (0.023 g, 0.22 mmol, 1.0 equiv), 1.5 mL ether, and 1.5 mL water. The reaction mixture was degassed via freeze pump thaw (× 3 times) and refilled with argon. After the reaction mixture was thoroughly degassed, the vial was sealed and positioned approximately 10 cm away from the light source. Two household full spectrum 23 W CFL bulbs were used to irradiate the reaction mixture. Water bath was used to keep the reaction temperature at 29 °C. After stirring for the indicated time, the resulting mixture was diluted with ethyl acetate (30 mL), washed with brine (10 mL × 3), dried over Na_2SO_4, and concentrated under vacuum. Purification of the crude product by flash chromatography on silica gel using the indicated solvent system afforded the desired product.

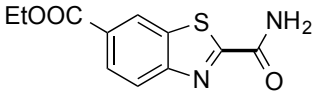


Benzo[d]thiazole-2-carboxamide (2a): According to the general procedure (method A), benzothiazole (0.030 g, 0.22 mmol, 1.0 equiv), $(NH_4)_2S_2O_8$ (0.15 g, 0.66 mmol, 3.0 equiv), TsOH•H_2O (0.042 g, 0.22 mmol, 1.0 equiv), benzaldehyde (0.023 g, 0.22 mmol, 1.0 equiv), 1.5 mL ethyl acetate, and 1.5 mL formamide were used. After 24 h, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified through flash chromatography (hexanes:acetone = 8:1–6:1) to provide the title compound as white solid (37 mg, 94%). ^{1}H NMR (500 MHz, d^6-DMSO) δ ppm 8.47 (brs, 1H), 8.19 (d, J = 8.0 Hz, 1H), 8.10 (d, J = 8.0 Hz, 1H), 8.07 (brs, 1H), 7.60 (t, J = 8.0 Hz, 1H), 7.55 (t, J = 8.0 Hz, 1H); ^{13}C NMR (125 MHz, d^6-DMSO) δ ppm 165.57, 162.00, 153.52, 137.06, 127.69, 127.52, 124.68, 123.66; HRMS (ESI) Calcd. for $C_8H_6N_2OS$ $(M + Na)^+$ 201.0099, found 201.0099.

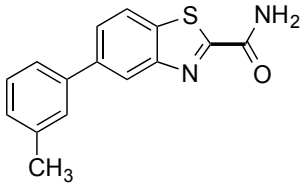


5-Bromobenzo[d]thiazole-2-carboxamide (2b): According to the general procedure (method A), 5-bromobenzothiazole (0.050 g, 0.23 mmol, 1.0 equiv), $(NH_4)_2S_2O_8$ (0.16 g, 0.69 mmol, 3.0

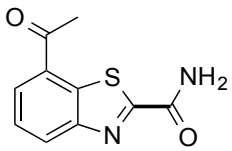
equiv), TsOH•H_2O (0.044 g, 0.23 mmol, 1.0 equiv), benzaldehyde (0.024 g, 0.23 mmol, 1.0 equiv), 2.5 mL ethyl acetate, and 2.5 mL formamide were used. After 24 h, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified through flash chromatography (hexanes:acetone = 8:1–6:1) to provide the title compound as white solid (50 mg, 85%). ^{1}H NMR (500 MHz, d^6-DMSO) δ ppm 8.50 (brs, 1H), 8.25 (d, *J* = 2.0 Hz, 1H), 8.16 (d, *J* = 8.5 Hz, 1H), 8.13 (brs, 1H), 7.70 (dd, *J* = 2.0, 8.0 Hz, 1H); ^{13}C NMR (125 MHz, d^6-DMSO) δ ppm 167.74, 161.64, 154.66, 136.25, 130.30, 126.86, 125.55, 120.43; HRMS (ESI) Calcd. for $C_8H_5BrN_2OS$ $(M + Na)^+$ 278.9204, found 278.9204.



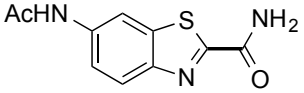
Ethyl 2-carbamoylbenzo[d]thiazole-6-carboxylate (2c): According to the general procedure (method A), ethyl benzo[d]thiazole-6-carboxylate (0.050 g, 0.24 mmol, 1.0 equiv), $(NH_4)_2S_2O_8$ (0.17 g, 0.72 mmol, 3.0 equiv), TsOH•H_2O (0.045 g, 0.24 mmol, 1.0 equiv), benzaldehyde (0.025 g, 0.24 mmol, 1.0 equiv), 2.5 mL ethyl acetate, and 2.5 mL formamide were used. After 24 h, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified through flash chromatography (hexanes:acetone = 8:1–6:1) to provide the title compound as white solid (30 mg, 50%). ^{1}H NMR (300 MHz, d^6-DMSO) δ ppm 8.89 (s, 1H), 8.59 (brs, 1H), 8.22 (d, *J* = 8.0 Hz, 1H), 8.18 (brs, 1H), 8.15 (d, *J* = 8.0 Hz, 1H), 4.38 (q, *J* = 7.2 Hz, 2H), 1.34 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, d^6-DMSO) δ ppm 169.45, 165.87, 161.69, 156.33, 137.25, 128.50, 128.02, 125.77, 124.72, 61.89, 14.85; HRMS (ESI) Calcd. for $C_{11}H_{10}N_2O_3S$ $(M + Na)^+$ 273.0310, found 273.0310.



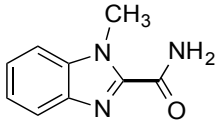
5-(*m*-tolyl)benzo[d]thiazole-2-carboxamide (2d): According to the general procedure (method A), 5-(m-tolyl)benzo[d]thiazole (0.050 g, 0.22 mmol, 1.0 equiv), $(NH_4)_2S_2O_8$ (0.15 g, 0.66 mmol, 3.0 equiv), TsOH•H_2O (0.042 g, 0.22 mmol, 1.0 equiv), benzaldehyde (0.023 g, 0.22 mmol, 1.0 equiv), 2.5 mL ethyl acetate, and 2.5 mL formamide were used. After 24 h, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified through flash chromatography (hexanes:acetone = 8:1–6:1) to provide the title compound as white solid (46 mg, 78%). ^{1}H NMR (500 MHz, d^6-DMSO) δ ppm 8.46 (brs, 1H), 8.27 (d, *J* = 2.0 Hz, 1H), 8.23 (d, *J* = 8.5 Hz, 1H), 8.13 (brs, 1H), 7.81 (dd, *J* = 2.0, 8.5 Hz, 1H), 7.55 (s, 1H), 7.51 (d, *J* = 8.0 Hz, 1H), 7.35 (t, *J* = 8.0 Hz, 1H), 7.18 (d, *J* = 7.5 Hz, 1H), 2.37 (s, 3H); ^{13}C NMR (125 MHz, d^6-DMSO) δ ppm 166.39, 161.95, 154.27, 140.25, 140.05, 138.94, 136.06, 129.63, 129.10, 128.45, 126.67, 124.89, 123.98, 122.11, 21.83; HRMS (ESI) Calcd. for $C_{15}H_{12}N_2OS$ $(M + Na)^+$ 291.0568, found 291.0573.



7-Acetylbenzo[d]thiazole-2-carboxamide (2e): According to the general procedure (method A), 1-(benzo[d]thiazol-7-yl)ethanone (0.050 g, 0.28 mmol, 1.0 equiv), $(NH_4)_2S_2O_8$ (0.19 g, 0.84 mmol, 3.0 equiv), TsOH•H_2O (0.053 g, 0.28 mmol, 1.0 equiv), benzaldehyde (0.030 g, 0.28 mmol, 1.0 equiv), 2.5 mL ethyl acetate, and 2.5 mL formamide were used. After 24 h, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified through flash chromatography (hexanes:acetone = 6:1–4:1) to provide the title compound as white solid (41 mg, 66%). ^{1}H NMR (300 MHz, d^6-DMSO) δ ppm 8.50 (brs, 1H), 8.39 (d, *J* = 8.1 Hz, 1H), 8.37 (d, *J* = 8.1 Hz, 1H), 8.08 (brs, 1H), 7.80 (t, *J* = 8.1 Hz, 1H), 2.76 (s, 3H); ^{13}C NMR (75 MHz, d^6-DMSO) δ ppm 197.62, 169.20, 162.33, 154.55, 134.28, 131.63, 130.47, 129.94, 128.00, 26.87; HRMS (ESI) Calcd. for $C_{10}H_8N_2O_2S$ $(M + Na)^+$ 243.0204, found 243.0204.

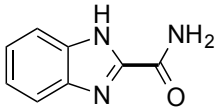


6-Acetamidobenzo[d]thiazole-2-carboxamide (2f): According to the general procedure (method A), *N*-(benzo[d]thiazol-6-yl)acetamide (0.040 g, 0.21 mmol, 1.0 equiv), $(NH_4)_2S_2O_8$ (0.14 g, 0.63 mmol, 3.0 equiv), TsOH•H_2O (0.040 g, 0.21 mmol, 1.0 equiv), benzaldehyde (0.022 g, 0.21 mmol, 1.0 equiv), 2.5 mL ethyl acetate, and 2.5 mL formamide were used. After 24 h, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified through flash chromatography (hexanes:acetone = 3:1–1:1) to provide the title compound as white solid (15 mg, 30%). ^{1}H NMR (500 MHz, d^6-DMSO) δ ppm 10.26 (s, 1H), 8.54 (d, *J* = 2.0 Hz, 1H), 8.34 (brs, 1H), 8.00 (d, *J* = 8.5 Hz, 1H), 7.95 (brs, 1H), 7.60 (dd, *J* = 2.0, 9.0 Hz, 1H), 2.08 (s, 3H); ^{13}C NMR (125 MHz, d^6-DMSO) δ ppm 169.40, 163.84, 162.06, 149.30, 138.89, 137.99, 124.79, 120.10, 111.94, 24.77; HRMS (ESI) Calcd. for $C_{10}H_9N_3O_2S$ $(M + Na)^+$ 258.0313, found 258.0314.

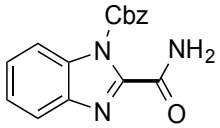


1-Methyl-1H-benzo[d]imidazole-2-carboxamide (2g): According to the general procedure (method A), 1-methyl-1H-benzo[d]imidazole (0.050 g, 0.38 mmol, 1.0 equiv), $(NH_4)_2S_2O_8$ (0.26 g, 1.13 mmol, 3.0 equiv), TsOH•H_2O (0.072 g, 0.38 mmol, 1.0 equiv), benzaldehyde (0.040 g, 0.38 mmol, 1.0 equiv), 2.5 mL ethyl acetate, and 2.5 mL formamide were used. After 24 h, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified through flash chromatography (hexanes:acetone = 5:1–3:1) to provide the title compound as white solid (42 mg, 64%). ^{1}H NMR (500 MHz, d^6-DMSO) δ ppm 8.26 (brs, 1H), 7.82 (brs, 1H), 7.71 (d, *J* = 8.0 Hz, 1H), 7.63 (d, *J* = 8.0 Hz, 1H), 7.36 (t, *J* = 8.0 Hz, 1H), 7.29 (t,

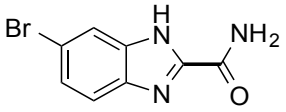
J = 8.0 Hz, 1H), 4.10 (s, 3H); ^{13}C NMR (125 MHz, d^6-DMSO) δ ppm 162.16, 144.57, 141.31, 137.34, 124.74, 123.51, 120.67, 111.91, 32.52; HRMS (ESI) Calcd. for $C_9H_9N_3O$ $(M + Na)^+$ 198.0643, found 198.0643.



1H-benzo[d]imidazole-2-carboxamide (2h): According to the general procedure (method A), benzo[d]imidazole (0.050 g, 0.43 mmol, 1.0 equiv), $(NH_4)_2S_2O_8$ (0.30 g, 1.30 mmol, 3.0 equiv), TsOH•H_2O (0.081 g, 0.43 mmol, 1.0 equiv), benzaldehyde (0.045 g, 0.43 mmol, 1.0 equiv), 2.5 mL ethyl acetate, and 2.5 mL formamide were used. After 24 h, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified through flash chromatography (hexanes:acetone = 3:1–2:1) to provide the title compound as white solid (46 mg, 67%). ^{1}H NMR (500 MHz, d^6-DMSO) δ ppm 13.17 (s, 1H), 8.24 (brs, 1H), 7.80 (brs, 1H), 7.69 (d, *J* = 7.0 Hz, 1H), 7.50 (d, *J* = 7.0 Hz, 1H), 7.28 – 7.24 (m, 2H); ^{13}C NMR (125 MHz, d^6-DMSO) δ ppm 161.37, 146.49, 143.28, 135.20, 124.73, 123.12, 120.61, 113.16; HRMS (ESI) Calcd. for $C_8H_7N_3O$ $(M + Na)^+$ 184.0487, found 184.0489.

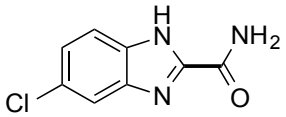


Benzyl 2-carbamoyl-1H-benzo[d]imidazole-1-carboxylate (2i): According to the general procedure (method A), benzyl 1H-benzo[d]imidazole-1-carboxylate (0.050 g, 0.20 mmol, 1.0 equiv), $(NH_4)_2S_2O_8$ (0.14 g, 0.60 mmol, 3.0 equiv), TsOH•H_2O (0.038 g, 0.20 mmol, 1.0 equiv), benzaldehyde (0.021 g, 0.20 mmol, 1.0 equiv), 2.5 mL ethyl acetate, and 2.5 mL formamide were used. After 24 h, the reaction mixture was subjected to workup protocol outlined in the general procedure and purified through flash chromatography (hexanes:acetone = 5:1–4:1) to provide the title compound as white solid (38 mg, 64%). ^{1}H NMR (500 MHz, d^6-DMSO) δ ppm 11.00 (brs, 1H), 7.80 – 7.50 (m, 2H), 7.47 (d, J = 7.0 Hz, 2H), 7.38 (t, J = 7.0 Hz, 2H), 7.34 – 7.31 (m, 3H); ^{13}C NMR (125 MHz, d^6-DMSO) δ ppm 157.99, 151.16, 144.56, 136.48, 129.06, 128.72, 128.38, 67.28; HRMS (ESI) Calcd. for $C_{16}H_{13}N_3O_3$ $(M + Na)^+$ 318.0855, found 318.0855.

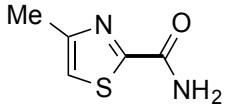


6-Bromo-1H-benzo[d]imidazole-2-carboxamide (2j): According to the general procedure (method A), 6-bromo-1H-benzo[d]imidazole (0.050 g, 0.25 mmol, 1.0 equiv), $(NH_4)_2S_2O_8$ (0.17 g, 0.75 mmol, 3.0 equiv), TsOH•H_2O (0.048 g, 0.25 mmol, 1.0 equiv), benzaldehyde (0.027 g, 0.25 mmol, 1.0 equiv), 2.5 mL ethyl acetate, and 2.5 mL formamide were used. After 24 h, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified through flash chromatography (hexanes:acetone = 3:1–2:1) to provide the title compound as white solid (51 mg, 85%). Both the Z and E isomers were obtained (E:Z = 1:1). ^{1}H

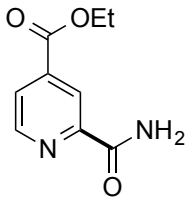
NMR (500 MHz, d^6-DMSO) δ ppm 13.40 (s, 1H, rotamer A), 13.33 (s, 1H, rotamer B), 8.29 (brs, 2H), 7.89 (s, 1H), 7.87 (brs, 2H), 7.66 (d, *J* = 7.5 Hz, 1H), 7.65 (s, 1H), 7.47 (d, *J* = 8.5 Hz, 1H), 7.42 (d, *J* = 8.5 Hz, 1H), 7.37 (d, *J* = 7.5 Hz, 1H); ^{13}C NMR (125 MHz, d^6-DMSO) δ ppm 161.51, 148.28, 147.96, 145.24, 142.92, 136.95, 134.83, 128.14, 126.79, 123.50, 123.04, 117.63, 116.29, 115.87, 115.61; HRMS (ESI) Calcd. for $C_8H_6BrN_3O$ (M + Na)$^+$ 261.9592, found 261.9598.



5-Chloro-1H-benzo[d]imidazole-2-carboxamide (2k): According to the general procedure (method A), 5-chloro-1H-benzo[d]imidazole (0.050 g, 0.33 mmol, 1.0 equiv), $(NH_4)_2S_2O_8$ (0.23 g, 0.99 mmol, 3.0 equiv), TsOH•H_2O (0.063 g, 0.33 mmol, 1.0 equiv), benzaldehyde (0.035 g, 0.33 mmol, 1.0 equiv), 2.5 mL ethyl acetate, and 2.5 mL formamide were used. After 24 h, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified through flash chromatography (hexanes:acetone = 3:1–2:1) to provide the title compound as white solid (50 mg, 78%). Both the Z and E isomers were obtained (E:Z = 1:1). ^{1}H NMR (500 MHz, d^6-DMSO) δ ppm 13.40 (s, 1H, rotamer A), 13.33 (s, 1H, rotamer B), 8.30 (brs, 1H), 8.28 (brs, 1H), 7.88 (brs, 2H), 7.54 (s, 1H), 7.71 (d, *J* = 8.5 Hz, 1H), 7.52 (d, *J* = 9.0 Hz, 1H), 7.51 (s, 1H), 7.31 (d, *J* = 8.5 Hz, 1H), 7.26 (d, *J* = 9.0 Hz, 1H); ^{13}C NMR (125 MHz, d^6-DMSO) δ ppm 160.74, 147.71, 147.37, 143.88, 141.88, 135.66, 133.76, 128.87, 127.27, 124.82, 123.41, 121.86, 119.68, 114.39, 112.52; HRMS (ESI) Calcd. for $C_8H_6ClN_3O$ (M + Na)$^+$ 218.0097, found 218.0102.

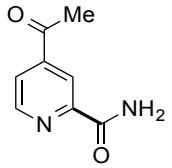


4-Methylthiazole-2-carboxamide (2m): According to the general procedure (method A), 5-chloro-1H-benzo[d]imidazole (0.050 g, 0.50 mmol, 1.0 equiv), $(NH_4)_2S_2O_8$ (0.34 g, 1.50 mmol, 3.0 equiv), TsOH•H_2O (0.095 g, 0.50 mmol, 1.0 equiv), benzaldehyde (0.053 g, 0.50 mmol, 1.0 equiv), 2.5 mL ethyl acetate, and 2.5 mL formamide were used. After 24 h, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified through flash chromatography (hexanes:acetone = 8:1–6:1) to provide the title compound as white solid (38 mg, 54%). ^{1}H NMR (500 MHz, d^6-DMSO) δ ppm 8.06 (brs, 1H), 7.76 (brs, 1H), 7.55 (s, 1H), 2.40 (s, 3H); ^{13}C NMR (125 MHz, d^6-DMSO) δ ppm 164.02, 161.64, 154.18, 121.05, 17.48; HRMS (ESI) Calcd. for $C_5H_6N_2OS$ (M + Na)$^+$ 165.0099, found 165.0101.

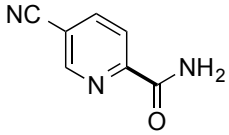


Ethyl isonicotinate (4a): According to the general procedure (method A), ethyl

9H-pyrido[3,4-b]indole-3-carboxylate (0.050 g, 0.33 mmol, 1.0 equiv), $(NH_4)_2S_2O_8$ (0.23 g, 0.99 mmol, 3.0 equiv), TsOH•H_2O (0.063 g, 0.33 mmol, 1.0 equiv), benzaldehyde (0.035 g, 0.33 mmol, 1.0 equiv), 2.5 mL ethyl acetate, and 2.5 mL formamide were used. After 24 h, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified through flash chromatography (hexanes:acetone = 5:1–3:1) to provide the title compound as white solid (43 mg, 67%). ^{1}H NMR (500 MHz, d^6-DMSO) δ ppm 8.81 (dd, *J* = 0.5, 5.0 Hz, 1H), 8.39 (dd, *J* = 0.5, 1.5 Hz, 1H), 8.23 (brs, 1H), 7.98 (dd, *J* = 1.5, 5.5 Hz, 1H), 7.81 (brs, 1H), 4.35 (q, *J* = 7.0 Hz, 2H), 1.33 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, d^6-DMSO) δ ppm 165.88, 164.81, 152.16, 150.51, 139.22, 125.73, 121.21, 62.53, 14.65; HRMS (ESI) Calcd. for $C_9H_{10}N_2O_3$ $(M + Na)^+$ 217.0589, found 217.0586.

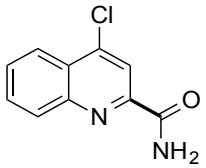


4-Acetylpicolinamide (4b): According to the general procedure (method A), 4-acetylpyridine (0.050 g, 0.41 mmol, 1.0 equiv), $(NH_4)_2S_2O_8$ (0.28 g, 1.24 mmol, 3.0 equiv), TsOH•H_2O (0.078 g, 0.41 mmol, 1.0 equiv), benzaldehyde (0.043 g, 0.41 mmol, 1.0 equiv), 2.5 mL ethyl acetate, and 2.5 mL formamide were used. After 24 h, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified through flash chromatography (hexanes:acetone = 5:1–3:1) to provide the title compound as white solid (40 mg, 60%). ^{1}H NMR (300 MHz, d^6-DMSO) δ ppm 8.83 (d, *J* = 5.1 Hz, 1H), 8.36 (s, 1H), 8.23 (brs, 1H), 7.98 (dd, *J* = 1.5, 4.8 Hz, 1H), 7.81 (brs, 1H), 2.66 (s, 3H); ^{13}C NMR (75 MHz, d^6-DMSO) δ ppm 198.29, 166.12, 152.24, 150.53, 144.63, 124.55, 120.06, 17.71; HRMS (ESI) Calcd. for $C_8H_8N_2O_2$ $(M + Na)^+$ 187.0483, found 187.0482.

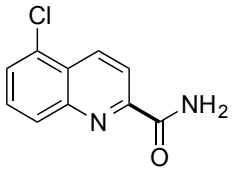


5-Cyanopicolinamide (4c): According to the general procedure (method A), 3-cyanopyridine (0.050 g, 0.48 mmol, 1.0 equiv), $(NH_4)_2S_2O_8$ (0.40 g, 1.44 mmol, 3.0 equiv), TsOH•H_2O (0.091 g, 0.48 mmol, 1.0 equiv), benzaldehyde (0.051 g, 0.48 mmol, 1.0 equiv), 2.5 mL ethyl acetate, and 2.5 mL formamide were used. After 24 h, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified through flash chromatography (hexanes:acetone = 5:1–3:1) to provide the title compound as white solid (46 mg, 65%). Regioselectivity ratio (r.r.), C-6:C-2:C-4 = 16.5:5.5:1. Major isomer (C-2): ^{1}H NMR (300 MHz, d^6-DMSO) δ ppm 9.08 (dd, *J* = 0.9, 2.1 Hz, 1H), 8.48 (dd, *J* = 2.1, 8.4 Hz, 1H), 8.31 (brs, 1H), 8.15 (dd, *J* = 0.9, 8.1 Hz, 1H), 7.92 (brs, 1H); Minor isomer (C-6): ^{1}H NMR (300 MHz, d^6-DMSO) δ ppm 8.85 (dd, J = 1.5, 4.8 Hz, 1H), 8.43 (dd, J = 1.5, 7.8 Hz, 1H), 8.31 (brs, 1H), 7.96 (brs, 1H), 7.77 (dd, J = 4.8, 8.1 Hz, 1H); isomers, C-6 and C-2, ^{13}C NMR (75 MHz, d^6-DMSO) δ ppm 165.35, 164.95, 153.51, 152.66, 152.26, 152.23, 144.31, 142.49, 126.79,

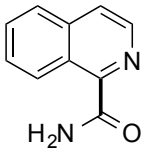
122.57, 117.37, 117.23; HRMS (ESI) Calcd. for $C_7H_5N_3O$ $(M + Na)^+$ 170.0330, found 170.0336.



4-Chloroquinoline-2-carboxamide (4d): According to the general procedure (method B), 4-chloroquinoline (0.030 g, 0.18 mmol, 1.0 equiv), $(NH_4)_2S_2O_8$ (0.12 g, 0.54 mmol, 3.0 equiv), benzaldehyde (0.019 g, 0.18 mmol, 1.0 equiv), 1.5 mL ethyl acetate, and 1.5 mL formamide were used. After 6 h, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified through flash chromatography (hexanes:acetone = 10:1–8:1) to provide the title compound as white solid (35 mg, 95%). ^{1}H NMR (300 MHz, d^6-DMSO) δ ppm 8.35 (brs, 1H), 8.23 (d, *J* = 8.4 Hz, 1H), 8.20 (s, 1H), 8.16 (d, *J* = 8.4 Hz, 1H), 7.95 (t, *J* = 8.4 Hz, 1H), 7.91 (brs, 1H), 7.84 (t, *J* = 8.4 Hz, 1H); ^{13}C NMR (75 MHz, d^6-DMSO) δ ppm 165.77, 151.28, 147.63, 143.47, 132.30, 130.64, 130.34, 126.89, 124.42, 119.42; HRMS (ESI) Calcd. for $C_{10}H_7ClN_2O$ $(M + Na)^+$ 229.0145, found 229.0142.

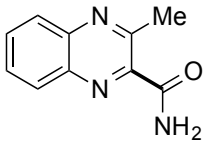


5-Chloroquinoline-2-carboxamide (4e): According to the general procedure (method B), 5-chloroquinoline (0.030 g, 0.18 mmol, 1.0 equiv), $(NH_4)_2S_2O_8$ (0.12 g, 0.54 mmol, 3.0 equiv), benzaldehyde (0.019 g, 0.18 mmol, 1.0 equiv), 1.5 mL ethyl acetate, and 1.5 mL formamide were used. After 12 h, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified through flash chromatography (hexanes:acetone = 10:1–8:1) to provide the title compound as white solid (35 mg, 95%). ^{1}H NMR (500 MHz, d^6-DMSO) δ ppm 8.71 (d, *J* = 8.5 Hz, 1H), 8.33 (brs, 1H), 8.26 (d, *J* = 9.0 Hz, 1H), 8.09 (d, *J* = 8.0 Hz, 1H), 7.88 (d, *J* = 7.5 Hz, 1H), 7.87 (brs, 1H), 7.84 (t, *J* = 7.5 Hz, 1H); ^{13}C NMR (125 MHz, d^6-DMSO) δ ppm 166.36, 151.91, 147.50, 134.78, 131.25, 130.99, 129.67, 128.90, 127.03, 120.65; HRMS (ESI) Calcd. for $C_{10}H_7ClN_2O$ $(M + Na)^+$ 229.0145, found 229.0145.

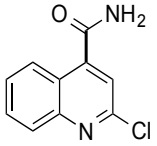


Isoquinoline-1-carboxamide (4f): According to the general procedure (method B), isoquinoline (0.050 g, 0.39 mmol, 1.0 equiv), $(NH_4)_2S_2O_8$ (0.26 g, 1.16 mmol, 3.0 equiv), benzaldehyde (0.041 g, 0.39 mmol, 1.0 equiv), 2.5 mL ethyl acetate, and 2.5 mL formamide were used. After 12 h, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified through flash chromatography (hexanes:acetone = 8:1–5:1) to provide the title compound as white solid (58 mg, 87%). ^{1}H NMR (300 MHz, d^6-DMSO) δ ppm 8.94 (d, *J* = 8.4

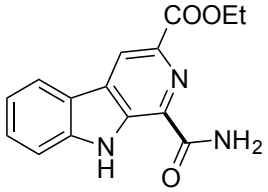
Hz, 1H), 8.50 (d, *J* = 5.7 Hz, 1H), 8.26 (brs, 1H), 8.00 (d, *J* = 8.1 Hz, 1H), 7.96 (d, *J* = 5.4 Hz, 1H), 7.80 (brs, 1H), 7.78 (t, *J* = 8.4 Hz, 1H), 7.69 (t, *J* = 8.4 Hz, 1H); ^{13}C NMR (75 MHz, d^6-DMSO) δ ppm 169.16, 152.06, 141.51, 137.19, 131.24, 128.96, 127.75, 127.40, 126.12, 123.92; HRMS (ESI) Calcd. for $C_{10}H_8N_2O$ (M + Na)$^+$ 195.0534, found 195.0536.



3-Methylquinoxaline-2-carboxamide (4g): According to the general procedure (method B), 2-methylquinoxaline (0.030 g, 0.21 mmol, 1.0 equiv), $(NH_4)_2S_2O_8$ (0.14 g, 0.63 mmol, 3.0 equiv), benzaldehyde (0.022 g, 0.21 mmol, 1.0 equiv), 1.5 mL ethyl acetate, and 1.5 mL formamide were used. After 24 h, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified through flash chromatography (hexanes:acetone = 8:1–5:1) to provide the title compound as white solid (28 mg, 71%). ^{1}H NMR (500 MHz, d^6-DMSO) δ ppm 8.24 (brs, 1H), 8.07 (d, *J* = 8.0 Hz, 1H), 8.03 (d, J = 8.0 Hz, 1H), 7.88 (brs, 1H), 7.87 (t, *J* = 8.0 Hz, 1H), 7.82 (t, *J* = 8.0 Hz, 1H), 2.81 (s, 3H); ^{13}C NMR (125 MHz, d^6-DMSO) δ ppm 189.54, 168.37, 152.87, 148.24, 142.23, 139.52, 131.83, 130.51, 129.55, 128.80; HRMS (ESI) Calcd. for $C_{10}H_9N_3O$ (M + Na)$^+$ 210.0643, found 210.0644.

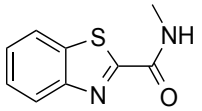


2-Chloroquinoline-4-carboxamide (4h): According to the general procedure (method B), 2-chloroquinoline (0.030 g, 0.18 mmol, 1.0 equiv), $(NH_4)_2S_2O_8$ (0.12 g, 0.54 mmol, 3.0 equiv), benzaldehyde (0.019 g, 0.18 mmol, 1.0 equiv), 1.5 mL ethyl acetate, and 1.5 mL formamide were used. After 12 h, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified through flash chromatography (hexanes:acetone = 5:1–3:1) to provide the title compound as white solid (6 mg, 15%). ^{1}H NMR (500 MHz, d^6-DMSO) δ ppm 8.32 (brs, 1H), 8.18 (d, *J* = 8.5 Hz, 1H), 8.02 (brs, 1H), 7.99 (d, *J* = 8.5 Hz, 1H), 7.85 (t, *J* = 8.5 Hz, 1H), 7.70 (t, *J* = 8.5 Hz, 1H), 7.62 (s, 1H); ^{13}C NMR (125 MHz, d^6-DMSO) δ ppm 167.71, 150.05, 148.33, 146.57, 131.88, 128.97, 128.57, 126.44, 123.89, 120.56; HRMS (ESI) Calcd. for $C_{10}H_7ClN_2O$ (M + Na)$^+$ 229.0145, found 229.0138.

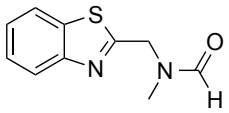


Ethyl 1-carbamoyl-9H-pyrido[3,4-b]indole-3-carboxylate (4i): According to the general procedure (method A), ethyl 9H-pyrido[3,4-b]indole-3-carboxylate (0.050 g, 0.21 mmol, 1.0 equiv), $(NH_4)_2S_2O_8$ (0.14 g, 0.63 mmol, 3.0 equiv), TsOH•H_2O (0.039 g, 0.21 mmol, 1.0 equiv), benzaldehyde (0.022 g, 0.21 mmol, 1.0 equiv), 2.5 mL ethyl acetate, and 2.5 mL formamide

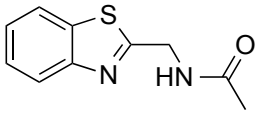
were used. After 24 h, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified through flash chromatography (CH_2Cl_2:MeOH = 80:1–50:1) to provide the title compound as pale yellow solid (30 mg, 50%). Both the Z and E isomers were obtained. (E:Z = 1:1). ^{1}H NMR (500 MHz, d^6-DMSO) δ ppm 12.48 (s, 1H, rotamer A), 12.07 (s, 1H, rotamer B), 11.29 (brs, 1H), 9.06 (s, 1H), 8.42 (d, *J* = 8.0 Hz, 1H), 8.18 (d, *J* = 8.0 Hz, 1H), 7.98 (d, J = 9.0 Hz, 2H), 7.90 (s, 1H), 7.85 (d, *J* = 8.5 Hz, 1H), 7.60 (t, *J* = 7.5 Hz, 1H), 7.55 (d, *J* = 8.0 Hz, 1H), 7.44 (t, *J* = 8.0 Hz, 1H), 7.31 (t, *J* = 7.5 Hz, 1H), 7.24 (t, *J* = 7.5 Hz, 1H), 4.40 (q, *J* = 7.0 Hz, 2H), 4.33 (q, *J* = 7.0 Hz, 2H), 1.39 (t, *J* = 7.0 Hz, 3H), 1.34 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, d^6-DMSO) δ ppm 167.55, 165.30, 161.98, 155.19, 142.49, 139.82, 136.09, 135.67, 132.62, 131.53, 131.39, 129.69, 127.21, 125.31, 123.01, 122.63, 122.47, 122.05, 121.09, 120.74, 120.43, 113.89, 113.28, 106.57, 61.88, 61.38, 14.78, 14.60; HRMS (ESI) Calcd. for $C_{15}H_{13}N_3O_3$ $(M + Na)^+$ 306.0855, found 306.0861.



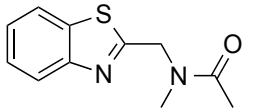
***N*-Methylbenzo[d]thiazole-2-carboxamide (5a):** According to the general procedure (method C), benzothiazole (0.030 g, 0.22 mmol, 1.0 equiv), $(NH_4)_2S_2O_8$ (0.15 g, 0.66 mmol, 3.0 equiv), benzaldehyde (0.023 g, 0.22 mmol, 1.0 equiv), 1.5 mL ethyl acetate, and 1.5 mL *N*-methylformamide were used. After 24 h, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified through flash chromatography (hexanes:acetone = 8:1–6:1) to provide the title compound as colorless oil (37 mg, 88%). ^{1}H NMR (500 MHz, d^6-Acetone) δ ppm 8.25 (brs, 1H), 8.15 (d, *J* = 8.0 Hz, 1H), 8.05 (d, *J* = 8.5 Hz, 1H), 7.59 (t, *J* = 8.0 Hz, 1H), 7.55 (t, *J* = 8.0 Hz, 1H), 3.03 (d, *J* = 5.0 Hz, 3H); ^{13}C NMR (125 MHz, d^6-Acetone) δ ppm 164.91, 160.24, 153.41, 136.97, 127.03, 126.89, 124.88, 122.82, 25.87; HRMS (ESI) Calcd. for $C_9H_8N_2OS$ $(M + Na)^+$ 215.0255, found 215.0255.



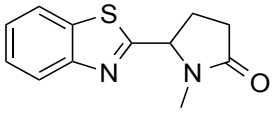
***N*-(Benzo[d]thiazol-2-ylmethyl)-*N*-methylformamide (6a):** According to the general procedure (method C), benzothiazole (0.030 g, 0.22 mmol, 1.0 equiv), $(NH_4)_2S_2O_8$ (0.15 g, 0.66 mmol, 3.0 equiv), benzaldehyde (0.023 g, 0.22 mmol, 1.0 equiv), 1.5 mL ethyl acetate, and 1.5 mL *N*, *N*-dimethylformamide were used. After 24 h, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified through flash chromatography (hexanes:acetone = 5:1–3:1) to provide the title compound as colorless oil (36 mg, 80%). Both the Z and E isomers were obtained. (E:Z = 1:1) ^{1}H NMR (500 MHz, d^6-Acetone) δ ppm 8.38 (s, 1H, rotamer A), 8.22 (s, 1H, rotamer B), 8.05 (d, *J* = 8.5 Hz, 1H), 8.02 (d, *J* = 8.0 Hz, 1H), 7.99 (d, *J* = 8.5 Hz, 1H), 7.97 (d, *J* = 8.5 Hz, 1H), 7.54 (t, *J* = 8.5 Hz, 1H), 7.51 (t, *J* = 8.5 Hz, 1H), 7.46 (t, *J* = 8.5 Hz, 1H), 7.43 (t, *J* = 8.5 Hz, 1H), 4.97 (s, 2H), 4.91 (s, 2H), 3.12 (s, 3H), 2.92 (s, 3H); ^{13}C NMR (125 MHz, d^6-Acetone) δ ppm 168.78, 167.56, 162.92, 162.65, 153.71, 153.40, 135.74, 135.50, 126.49, 126.29, 125.61, 125.45, 123.17, 123.02, 122.30, 122.17, 51.05, 45.84, 34.07, 29.52; HRMS (ESI) Calcd. for $C_{10}H_{10}N_2OS$ $(M + Na)^+$ 229.0412, found 229.0412.



***N*-(Benzo[d]thiazol-2-ylmethyl)acetamide (6b):** According to the general procedure (method C), benzothiazole (0.060 g, 0.44 mmol, 1.0 equiv), $(NH_4)_2S_2O_8$ (0.30 g, 1.32 mmol, 3.0 equiv), benzaldehyde (0.046 g, 0.44 mmol, 1.0 equiv), 2.5 mL ethyl acetate, and 2.5 mL *N*-methylformamide were used. After 24 h, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified through flash chromatography (hexanes:acetone = 3:1–2:1) to provide the title compound as white solid (74 mg, 82%). ^{1}H NMR (300 MHz, d^6-DMSO) δ ppm 8.86 (t, *J* = 6.0 Hz, 1H), 8.04 (d, *J* = 7.8 Hz, 1H), 7.92 (d, *J* = 7.8 Hz, 1H), 7.49 (t, *J* = 7.8 Hz, 1H), 7.39 (t, *J* = 7.8 Hz, 1H), 4.63 (d, *J* = 6.0 Hz, 2H), 1.92 (s, 3H); ^{13}C NMR (75 MHz, d^6-DMSO) δ ppm 172.23, 170.51, 153.40, 135.23, 126.79, 125.65, 123.01, 122.91, 41.74, 23.08; HRMS (ESI) Calcd. for $C_{10}H_{10}N_2OS$ $(M + Na)^+$ 229.0412, found 229.0408.

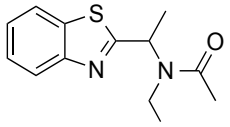


***N*-(benzo[d]thiazol-2-ylmethyl)-*N*-methylacetamide (6c):** According to the general procedure (method C), benzothiazole (0.030 g, 0.22 mmol, 1.0 equiv), $(NH_4)_2S_2O_8$ (0.15 g, 0.66 mmol, 3.0 equiv), benzaldehyde (0.023 g, 0.22 mmol, 1.0 equiv), 1.5 mL ethyl acetate, and 1.5 mL *N*, *N*-dimethylacetamide were used. After 24 h, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified through flash chromatography (hexanes:acetone = 5:1–3:1) to provide the title compound as colorless oil (42 mg, 87%). Both the Z and E isomers were obtained (E:Z = 2.4:1). Major isomer, ^{1}H NMR (500 MHz, d^6-Acetone) δ ppm 8.00 (d, *J* = 8.0 Hz, 1H), 7.95 (d, *J* = 8.0 Hz, 1H), 7.50 (t, *J* = 8.0 Hz, 1H), 7.41 (t, *J* = 8.0 Hz, 1H), 4.92 (s, 2H), 3.17 (s, 3H), 2.13 (s, 3H); ^{13}C NMR (125 MHz, d^6-Acetone) δ ppm 170.36, 169.05, 153.4, 135.78, 126.17, 125.29, 122.92, 122.12, 49.18, 36.04, 20.92; HRMS (ESI) Calcd. for $C_{11}H_{12}N_2OS$ $(M + Na)^+$ 243.0568, found 243.0566.

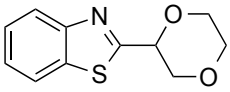


5-(Benzo[d]thiazol-2-yl)-1-methylpyrrolidin-2-one [(±)-6d]: According to the general procedure (method C), benzothiazole (0.030 g, 0.22 mmol, 1.0 equiv), $(NH_4)_2S_2O_8$ (0.15 g, 0.66 mmol, 3.0 equiv), benzaldehyde (0.023 g, 0.22 mmol, 1.0 equiv), 1.5 mL ethyl acetate, and 1.5 mL 1-methylpyrrolidin-2-one were used. After 24 h, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified through flash chromatography (hexanes:acetone = 5:1–3:1) to provide the title compound as colorless oil (45 mg, 89%). ^{1}H NMR (300 MHz, d^6-Acetone) δ ppm 8.06 (d, *J* = 8.1 Hz, 1H), 8.00 (d, *J* = 7.8 Hz, 1H), 7.54 (t, *J* = 7.8 Hz, 1H), 7.45 (t, *J* = 7.8 Hz, 1H), 5.09 (dd, *J* = 3.9, 8.7 Hz, 1H), 2.80 (s, 3H), 2.74 – 2.05 (m, 4H); ^{13}C NMR (75 MHz, d^6-Acetone) δ ppm 174.32, 173.19, 153.61, 135.18, 126.53, 125.68, 123.27, 122.47, 62.28, 28.23, 26.61; HRMS (ESI) Calcd. for $C_{12}H_{12}N_2OS$ $(M + Na)^+$ 255.0568,

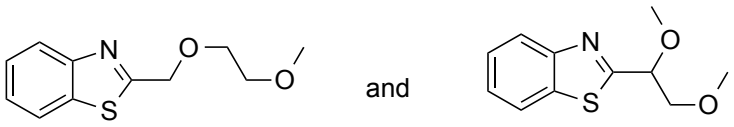
found 255.0564.



***N*-(1-(Benzo[d]thiazol-2-yl)ethyl)-*N*-ethylacetamide [(±)-6e]:** According to the general procedure (method C), benzothiazole (0.060 g, 0.44 mmol, 1.0 equiv), $(NH_4)_2S_2O_8$ (0.30 g, 1.32 mmol, 3.0 equiv), $TsOH•H_2O$ (0.081 g, 0.44 mmol, 1.0 equiv), benzaldehyde (0.046 g, 0.44 mmol, 1.0 equiv), 2.5 mL ethyl acetate, and 2.5 mL *N*, *N*-dimethylacetamide were used. After 24 h, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified through flash chromatography (hexanes:acetone = 8:1–6:1) to provide the title compound as pale yellow oil (28 mg, 25%). Both the Z and E isomers were obtained (E:Z = 2.5:1). Major isomer, ^{1}H NMR (500 MHz, d^6-Acetone) δ ppm 7.99 (d, *J* = 8.0 Hz, 1H), 7.96 (d, *J* = 8.0 Hz, 1H), 7.49 (t, *J* = 8.0 Hz, 1H), 7.41 (t, *J* = 8.0 Hz, 1H), 5.95 (q, *J* = 7.5 Hz, 1H), 3.51 (dt, *J* = 7.5, 23.0 Hz, 1H), 3.35 (dt, *J* = 7.5, 23.0 Hz, 1H), 2.15 (s, 3H), 1.74 (d, *J* = 7.0 Hz, 3H), 1.16 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, d^6-Acetone) δ ppm 173.32, 169.96, 153.24, 135.79, 126.07, 125.30, 122.99, 122.03, 51.87, 40.35, 21.21, 16.79, 15.67; HRMS (ESI) Calcd. for $C_{13}H_{16}N_2OS$ $(M + Na)^+$ 271.0881, found 271.0884.



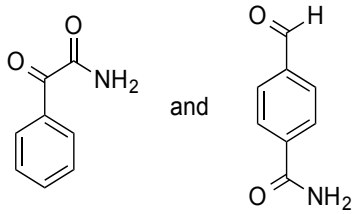
2-(1,4-Dioxan-2-yl)benzo[d]thiazole [(±)-7a]: According to the general procedure (method D), benzothiazole (0.060 g, 0.44 mmol, 1.0 equiv), $(NH_4)_2S_2O_8$ (0.30 g, 1.32 mmol, 3.0 equiv), benzaldehyde (0.046 g, 0.44 mmol, 1.0 equiv), 2.5 mL 1,4-dioxane, and 2.5 mL water were used. After 48 h, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified through flash chromatography (hexanes:ethyl acetate = 30:1–20:1) to provide the title compound as colorless oil (60 mg, 62%). ^{1}H NMR (500 MHz, d^6-Acetone) δ ppm 8.07 (d, *J* = 8.0 Hz, 1H), 7.98 (d, *J* = 8.0 Hz, 1H), 7.52 (t, *J* = 8.0 Hz, 1H), 7.44 (t, *J* = 8.0 Hz, 1H), 5.01 (dd, *J* = 3.0, 9.5 Hz, 1H), 4.21 (dd, *J* = 3.0, 11.5 Hz, 1H), 3.99 (dd, *J* = 3.0, 12.0 Hz, 1H), 3.94 – 3.91 (m, 1H), 3.82 – 3.79 (m, 1H), 3.71 – 3.66 (m, 1H), 3.63 (dd, *J* = 9.5, 11.5 Hz, 1H); ^{13}C NMR (125 MHz, d^6-Acetone) δ ppm 169.65, 153.59, 134.84, 126.28, 125.33, 123.10, 122.22, 75.39, 70.25, 67.00, 66.33; HRMS (ESI) Calcd. for $C_{11}H_{11}NO_2S$ $(M + Na)^+$ 244.0408, found 244.0409.



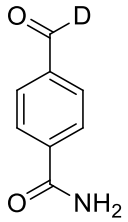
7b and **7c**

2-((2-Methoxyethoxy) methyl) benzo[d]thiazole (7b) and 2-(1,2-dimethoxyethyl) benzo[d]thiazole (7c): According to the general procedure (method D), benzothiazole (0.060 g, 0.44 mmol, 1.0 equiv), $(NH_4)_2S_2O_8$ (0.30 g, 1.32 mmol, 3.0 equiv), benzaldehyde (0.046 g, 0.44

mmol, 1.0 equiv), 2.5 mL glycol dimethyl ether, and 2.5 mL water were used. After 48 h, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified through flash chromatography (hexanes:ethyl acetate = 15:1, 10:1 to 4:1) to provide **7b** and **7c** as colorless oil (62 mg, 68%) with a ratio of 1:1 (regioselectivity ratio). **7b:** ^{1}H NMR (500 MHz, d^{6}-Acetone) δ ppm 8.05 (d, *J* = 8.0 Hz, 1H), 7.95 (d, *J* = 8.0 Hz, 1H), 4.95 (s, 2H), 3.80 (t, *J* = 4.5 Hz, 2H), 3.60 (t, *J* = 4.5 Hz, 2H), 3.34 (s, 3H); ^{13}C NMR (125 MHz, d^{6}-Acetone) δ ppm 170.73, 153.57, 135.26, 126.16, 125.19, 122.98, 122.17, 71.93, 70.84, 70.57, 58.27; HRMS (ESI) Calcd for $C_{11}H_{13}NO_2S$ $(M+Na)^+$ 246.0565, found 246.0558. **7c:** ^{1}H NMR (500 MHz, d^{6}-Acetone) δ ppm 8.06 (d, *J* = 8.0 Hz, 1H), 7.97 (d, *J* = 8.0 Hz, 1H), 7.51 (t, *J* = 8.0 Hz, 1H), 7.44 (t, *J* = 8.0 Hz, 1H), 4.83 (dd, *J* = 4.0, 6.5 Hz, 1H), 3.84 (dd, *J* = 4.0, 10.5 Hz, 1H), 3.75 (dd, *J* = 6.5, 10.5 Hz, 1H), 3.51 (s, 3H), 3.62 (s, 3H); ^{13}C NMR (125 MHz, d^{6}-Acetone) δ ppm 172.03, 153.61, 135.33, 126.15, 125.30, 123.09, 122.23, 81.19, 75.30, 58.63, 57.94; HRMS (ESI) Calcd for $C_{11}H_{13}NO_2S$ $(M+Na)^+$ 246.0565, found 246.0560.

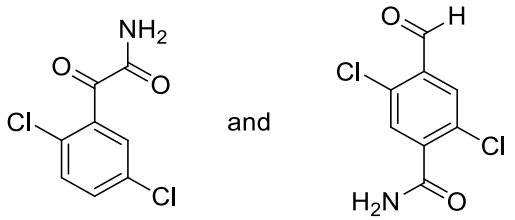


2-Oxo-2-phenylacetamide (8a) and 4-formylbenzamide (8b): According to the general procedure (method B), $(NH_4)_2S_2O_8$ (0.30 g, 1.32 mmol, 1.0 equiv), benzaldehyde (0.14 g, 1.32 mmol, 1.0 equiv), 1.5 mL ethyl acetate, and 1.5 mL formamide were mixed. After 24 h, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified through flash chromatography (hexanes:acetone = 10:1–5:1–3:1) to provide the title compounds **12** (8 mg, 4%) and **13** (5 mg, 2.5%) as white solid. Compound **8a**: ^{1}H NMR (300 MHz, d^{6}-DMSO) δ ppm 8.32 (brs, 1H), 8.01 (brs, 1H), 7.95 (d, *J* = 7.2 Hz, 2H), 7.72 (t, *J* = 7.2 Hz, 1H), 7.57 (t, *J* = 7.2 Hz, 2H); ^{13}C NMR (75 MHz, d^{6}-DMSO) δ ppm 191.52, 167.85, 135.16, 133.41, 130.30, 129.64; GCMS (EI) acquisition time, 15.86 min, m/z = 149.0 (5.23%), m/z = 104.9 (100%), m/z = 77.0 (53.85%). Compound **8b**: ^{1}H NMR (300 MHz, d^{6}-DMSO) δ ppm 10.06 (s, 1H), 8.18 (brs, 1H), 8.04 (d, *J* = 8.1 Hz, 2H), 7.97 (d, *J* = 8.1 Hz, 2H), 7.61 (brs, 1H); GCMS (EI) acquisition time, 18.19 min, m/z = 148.9 (91.79%), m/z = 132.9 (100%), m/z = 77.0 (33.44%).

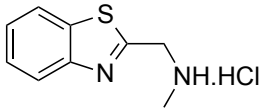


Deuterated-4-formylbenzamide (9). It was prepared by the same procedure as compound **8b**, white solid (4 mg, 2.0%). ^{1}H NMR (300 MHz, d^{6}-DMSO) *δ* ppm 8.16 (brs, 1H), 8.03 (d, *J* = 8.1 Hz, 2H), 7.97 (d, *J* = 8.1 Hz, 2H), 7.60 (brs, 1H); GCMS (EI) acquisition time, 18.19 min, m/z =

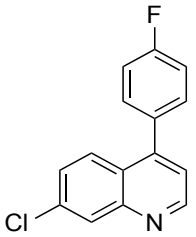
149.9 (89.73%), m/z = 133.9 (100%), m/z = 78.0 (26.41/%).



2-(2,5-Dichlorophenyl)-2-oxoacetamide (10a) and 2,5-dichloro-4-formylbenzamide (10b). These two compounds were prepared through the same procedure as compounds **8a** and **8b**. Compound **10a**, white solid (28.2 mg, 19%). ^{1}H NMR (500 MHz, d^{6}-DMSO) δ ppm 8.40 (brs, 1H), 8.05 (brs, 1H), 7.72 (d, J = 3.0 Hz, 1H), 7.66 (dd, J = 3.0, 8.5 Hz, 1H), 7.58 (d, J = 8.5 Hz, 1H); ^{13}C NMR (125 MHz, d^{6}-DMSO) δ ppm 190.23, 164.23, 136.97, 133.58, 132.61, 132.45, 130.97, 130.60; GCMS (EI) acquisition time, 19.82 min, m/z = 216.8 (1.81%), m/z = 104.9 (100%), m/z = 172.8 (100%). Compound **10b** (14.0 mg, 9% yield): ^{1}H NMR (500 MHz, d^{6}-DMSO) δ ppm 10.23 (s, 1H), 8.12 (brs, 1H), 7.87 (brs, 1H), 7.86 (s, 1H), 7.72 (s, 1H); GCMS (EI) acquisition time, 21.43 min, m/z = 216.8 (64.20%), m/z = 200.8 (100%).

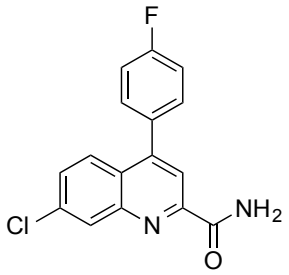


1-(Benzo[*d*]thiazol-2-yl)-*N*-methylmethanamine hydrochloride (11): To a solution of compound **6c** (0.042 g, 0.19 mmol) in 5 mL of ethanol was added 5 mL HCl (6M). The resulting mixture was heated to gentle reflux overnight. Then the mixture was diluted with water (20 mL). The pH value of the solution was adjusted to 10–11, extracted with ethyl acetate (20 mL × 3), dried over Na_2SO_4, and concentrated to give the crude product. The crude product was then dissolved into dichloromethane (10 mL), treated with 1 mL HCl (4M in dioxane). The resulting mixture was further stirred for 10 min, and the solvent was removed under vacuum to give the crude product, which was further dissolved into deionized water (10 mL), washed with ethyl acetate (20 mL × 3), and lyophilized to give the product as white solid (30 mg, 74%). ^{1}H NMR (300 MHz, CD_3OD) δ ppm 8.06 (d, J = 7.2 Hz, 1H), 8.03 (d, J = 7.2 Hz, 1H), 7.56 (t, J = 7.2 Hz, 1H), 7.49 (t, J = 7.2 Hz, 1H), 4.87 (s, 2H), 2.91 (s, 3H); ^{13}C NMR (75 MHz, CD_3OD) δ ppm 161.18, 152.62, 135.53, 126.67, 126.11, 123.07, 122.03, 49.06; HRMS (ESI) Calcd. for $C_9H_{11}ClN_2S$ $(M + H)^+$ 179.0643, found 179.0644.

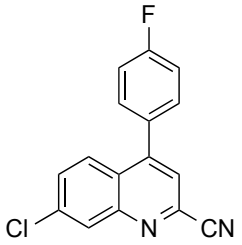


7-Chloro-4-(4-fluorophenyl)quinoline (12): It was prepared according to the reported procedure [2,3]. ^{1}H NMR (500 MHz, d^{6}-Acetone) δ ppm 8.98 (d, J = 4.0 Hz, 1H), 8.13 (d, J = 2.5

Hz, 1H), 7.92 (d, J = 9.0 Hz, 1H), 7.65 – 7.62 (m, 2H), 7.59 (dd, J = 2.0, 9.0 Hz, 1H), 7.47 (d, J = 4.5 Hz, 1H), 7.40 – 7.36 (m, 2H); ^{13}C NMR (75 MHz, d^6-DMSO) δ ppm 163.12 (d, $J_{C\text{-}F}$ = 244.5 Hz), 152.13, 149.21, 147.23, 134.81, 133.80, 132.30 (d, $J_{C\text{-}F}$ = 8.2 Hz), 128.77, 128.29, 128.15, 125.25, 122.68, 116.50 (d, $J_{C\text{-}F}$ = 21.7 Hz); HRMS (ESI) Calcd. for $C_{15}H_9ClFN$ (M + H)$^+$ 258.0486, found 258.0486.

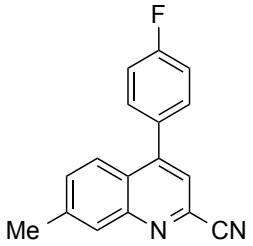


7-Chloro-4-(4-fluorophenyl)quinoline-2-carboxamide (13): According to the general procedure (method A), compound **12** (0.050 g, 0.19 mmol, 1.0 equiv), $(NH_4)_2S_2O_8$ (0.13 g, 0.58 mmol, 3.0 equiv), TsOH•H_2O (0.036 g, 0.19 mmol, 1.0 equiv), benzaldehyde (0.020 g, 0.19 mmol, 1.0 equiv), 2.5 mL formamide, and 2.5 mL water were used. After 24 h, the reaction mixture was subjected to the workup protocol outlined in the general procedure and purified through flash chromatography (hexanes:acetone = 10:1–8:1) to provide the title compound as white solid (50 mg, 88%). ^{1}H NMR (500 MHz, d^6-DMSO) δ ppm 8.33 (brs, 1H), 8.19 (s, 1H), 8.00 (s, 1H), 7.90 (brs, 1H), 7.89 (d, J = 9.0 Hz, 1H), 7.71 (dd, J = 2.5, 9.0 Hz, 1H), 7.65 – 7.62 (m, 2H), 7.42 (t, J = 9.0 Hz, 2H); ^{13}C NMR (125 MHz, d^6-DMSO) δ ppm 166.36, 163.24 (d, $J_{C\text{-}F}$ = 245.0 Hz), 151.77, 149.01, 147.87, 135.63, 133.65 (d, $J_{C\text{-}F}$ = 3.1 Hz), 132.35 (d, $J_{C\text{-}F}$ = 8.5 Hz), 129.69, 129.02, 128.21, 126.11, 119.75, 116.60 (d, $J_{C\text{-}F}$ = 21.5 Hz); HRMS (ESI) Calcd. for $C_{16}H_{10}ClFN_2O$ (M + Na)$^+$ 323.0363, found 323.0368.



7-Chloro-4-(4-fluorophenyl)quinoline-2-carbonitrile (14): It was prepared according to the reported procedure.[4] To a solution of compound **13** (0.030 g, 0.10 mmol, 1 equiv) and triethylamine (0.031 g, 0.15 mmol, 1.5 equiv) in 3 mL of tetrahydrofuran was added the solution of trifluoroacetic anhydride (0.020 g, 0.20 mmol, 2 equiv) in 2 mL tetrahydrofuran at 0–5 °C. The resulting mixture was stirred for another 2 h at the same temperature. Then, the solution was diluted with ethyl acetate (30 mL), washed with brine (15 mL × 3), dried over Na_2SO_4, and concentrated to give the pure product as white solid (28 mg, 100%). ^{1}H NMR (300 MHz, d^6-DMSO) δ ppm 8.27 (d, J = 2.1 Hz, 1H), 8.04 (s, 1H), 7.92 (d, J = 9.0 Hz, 1H), 7.79 (dd, J = 2.1, 9.0 Hz, 1H), 7.68 – 7.63 (m, 2H), 7.44 (t, J = 8.7 Hz, 2H); ^{13}C NMR (75 MHz, d^6-DMSO) δ ppm 163.51 (d, $J_{C\text{-}F}$ = 245.5 Hz),149.67, 148.95, 136.80, 134.57, 132.65 (d, $J_{C\text{-}F}$ = 8.5 Hz), 132.33 (d, $J_{C\text{-}F}$ = 3.2 Hz), 131.23, 128.95, 128.42, 126.12, 125.00, 117.94, 116.68 (d, $J_{C\text{-}F}$ = 21.7

Hz); HRMS (ESI) Calcd. for $C_{16}H_8ClFN_2$ $(M + H)^+$ 283.0438, found 283.0438.

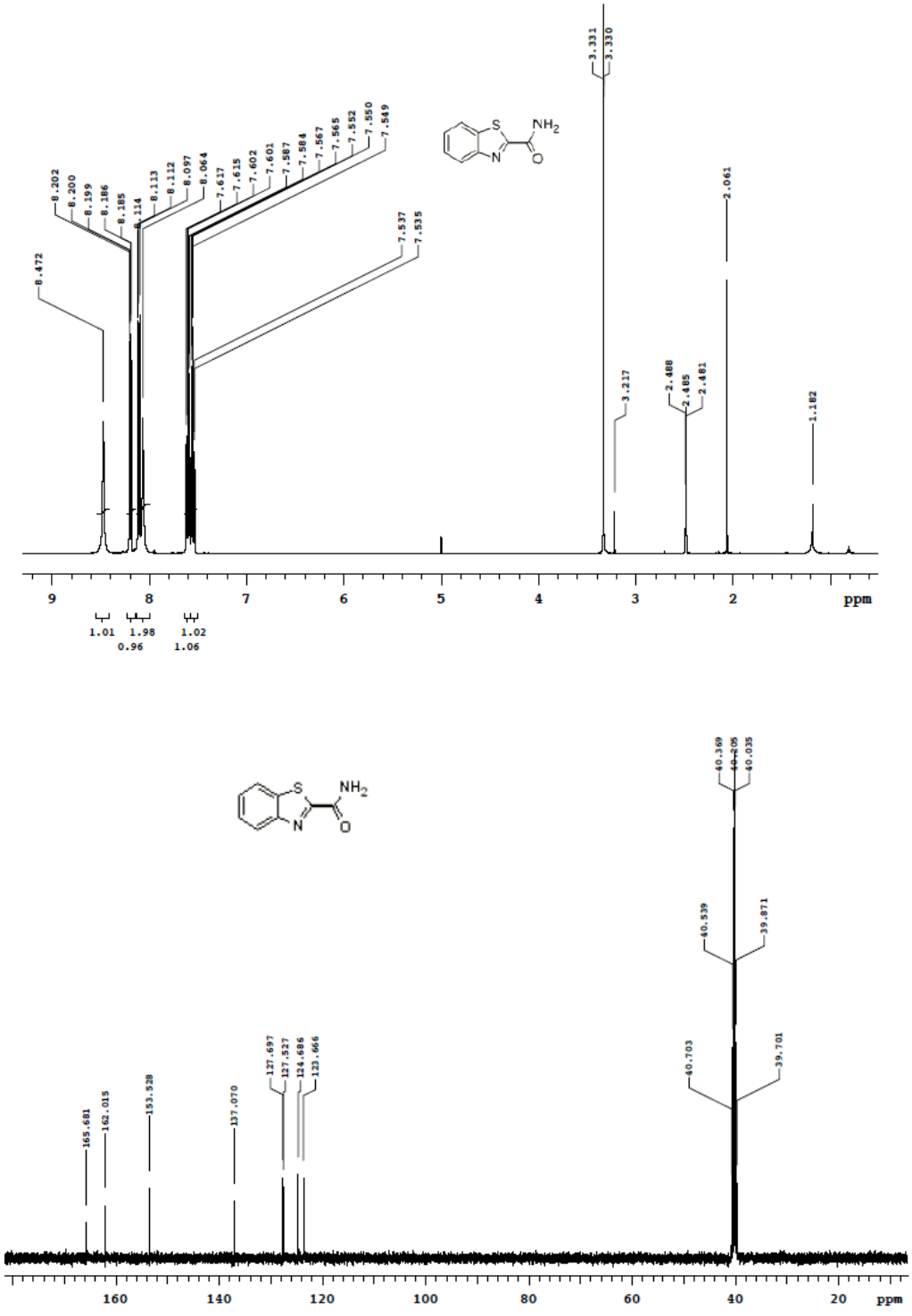


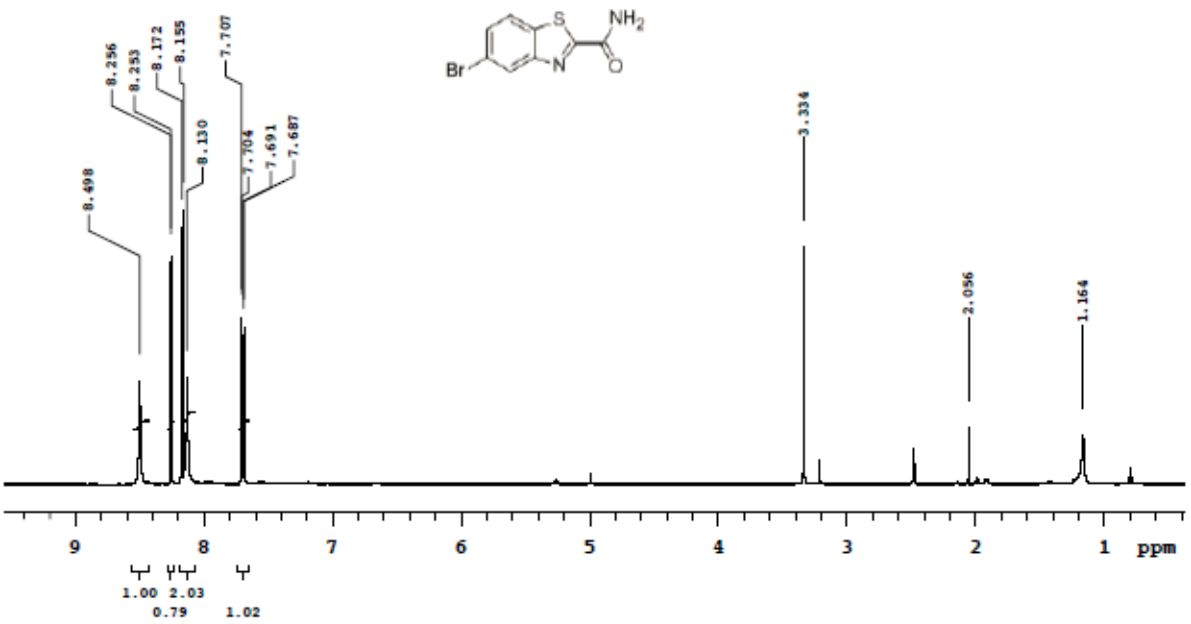
4-(4-Fluorophenyl)-7-methylquinoline-2-carbonitrile (15): It was prepared according to the reported procedure.[5] To a solution of **14** (0.030 g, 0.10 mmol, 1 equiv), potassium phosphate (0.042 g, 0.20 mmol, 2 equiv), 2-dicyclohexylphosphino-2',6'-dimethoxybiphenyl (0.010 g, 0.025 mmol, 0.25 equiv), methylboronic acid (0.018 mg, 0.30 mmol, 3 equiv) in 3 mL of toulene was added palladium acetate (2.00 mg, 0.010 mmol, 0.1 equiv). The resulting mixture was heated to gentle reflux for 24 h under argon. Then, the solution was cooled to room temperature and was diluted with ethyl acetate (30 mL), washed with brine (15 mL × 3), dried over Na_2SO_4, and concentrated to give the crude product. It was purified through flash chromatography (hexanes:ethyl acetate = 80:1–60:1) to provide the title compound as white solid (22 mg, 85%). ^{1}H NMR (500 MHz, d^6-acetone) δ ppm 7.96 (s, 1H), 7.88 (d, J = 8.5 Hz, 1H), 7.78 (s, 1H), 7.69–7.66 (m, 2H), 7.62 (d, J = 8.5 Hz, 1H), 7.40 (t, J = 9.0 Hz, 2H), 2.60 (s, 3H); ^{13}C NMR (125 MHz, d^6-acetone) δ ppm 163.49 (d, $J_{C\text{-}F}$ = 246.50 Hz),149.17, 149.06, 142.08, 133.52, 132.91 (d, $J_{C\text{-}F}$ = 3.4 Hz), 132.23, 132.00 (d, $J_{C\text{-}F}$ = 8.5 Hz), 129.12, 125.57, 125.46, 123.20, 117.82,116.80 (d, $J_{C\text{-}F}$ = 21.7 Hz), 20.95; HRMS (ESI) Calcd. for $C_{17}H_{11}FN_2$ $(M + H)^+$ 263.0979, found 263.0980.

Supplementary References:

1. (a) Martin, I.; Anvelt, J.; Vares, L.; Kühn, I.; Claesson, A. *Acta. Chem. Scand.* **1995**, *49*, 230–232; (b) Moinet, G.; Cravo, D. U.S. Patent 7,491,733, February 17, 2009.
2. Ducharme, Y.; Wu, T. Y.-H.; Frenette, R. PCT Int. Appl. WO 2007038865 A1, 2007.
3. Friesen, R. W.; Trimble, L. A. *Can. J. Chem.* **2004**, *82*, 206–214.
4. Wendt, M. D.; Rockway, T. W.; Geyer, A.; McClellan, W.; Weitzberg, M.; Zhao, X.; Mantei, R.; Nienaber, V. L.; Stewart, K.; Klinghofer, V.; Giranda, V. L. *J. Med. Chem.* **2004**, *47*, 303–324.
5. Minutolo, F.; Bellini, R.; Bertini, S.; Carboni, I.; Lapucci, A.; Pistolesi, L.; Prota, G.; Rapposelli, S.; Solati, F.; Tuccinardi, T.; Martinelli, A.; Stossi, F.; Carlson, K. E.; Katzenellenbogen, B. S.; Katzenellenbogen, J. A.; Macchia, M. *J. Med. Chem.* **2008**, *51*, 1344–1351.

Spectral Data for the Products

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8
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5
4
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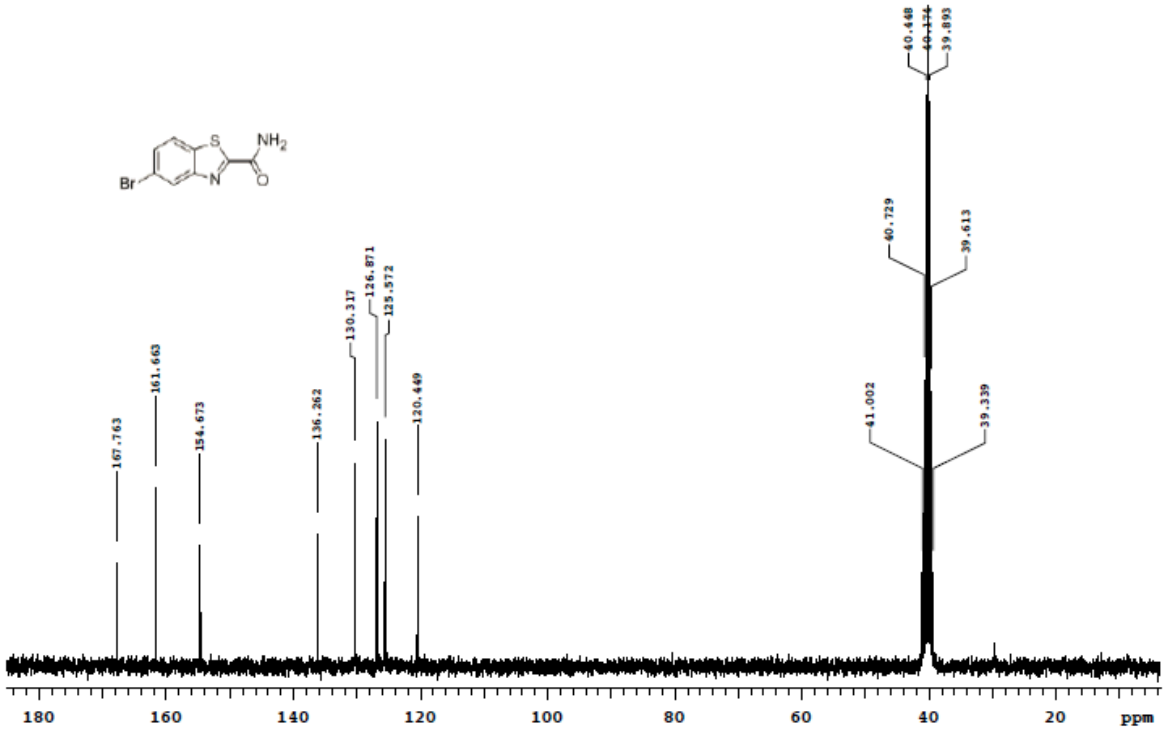
1.02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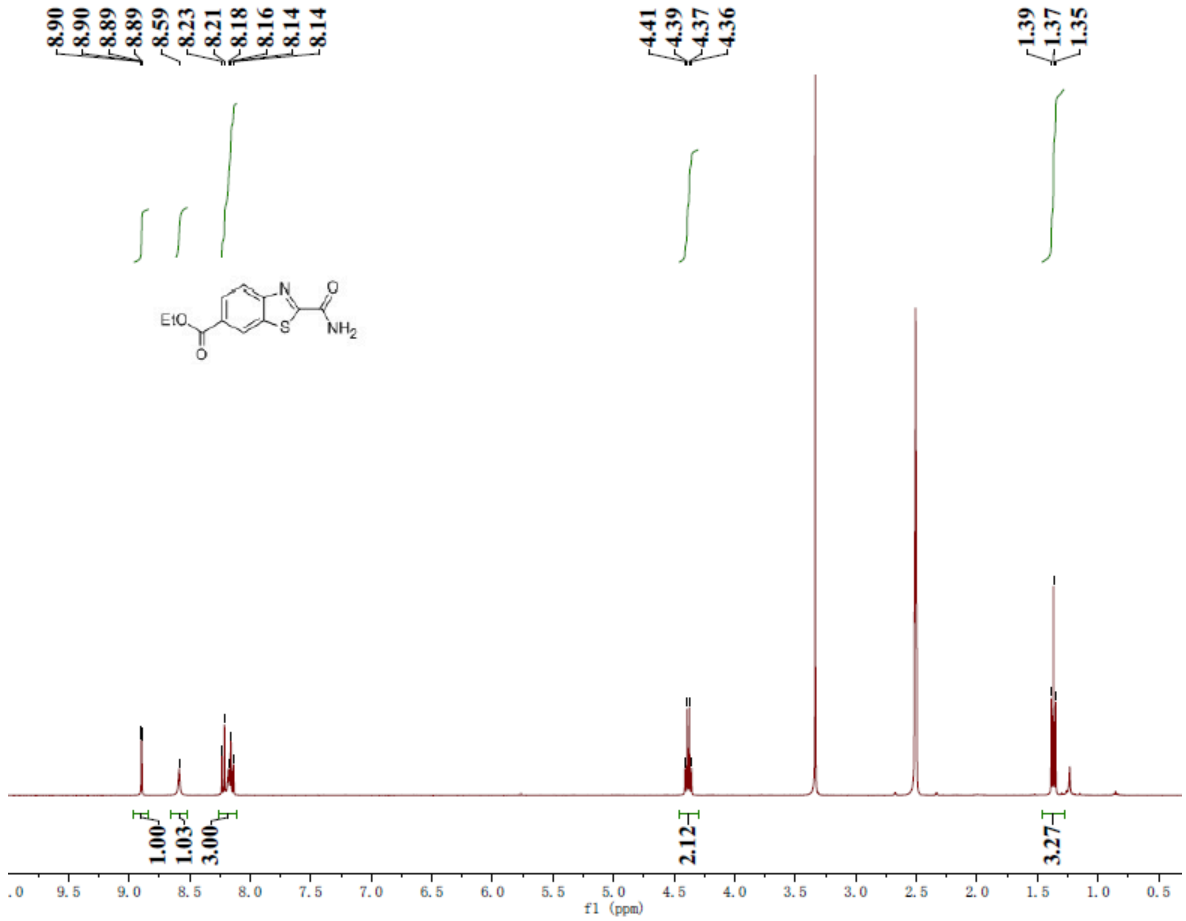
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4.39
4.37
4.36
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S
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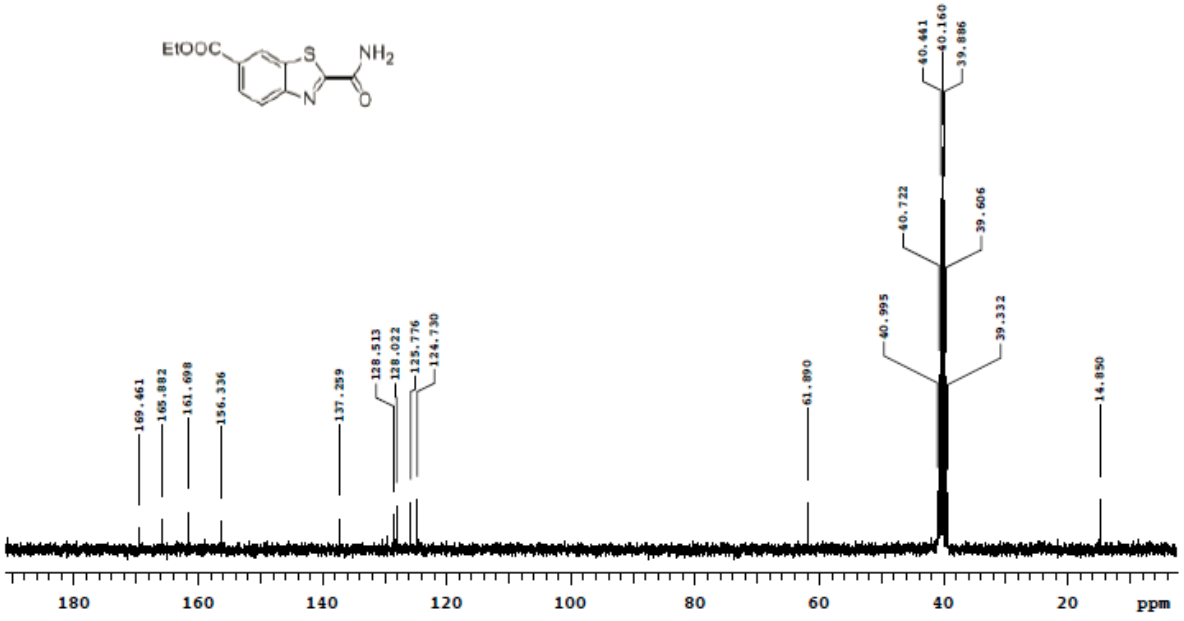
f1 (ppm)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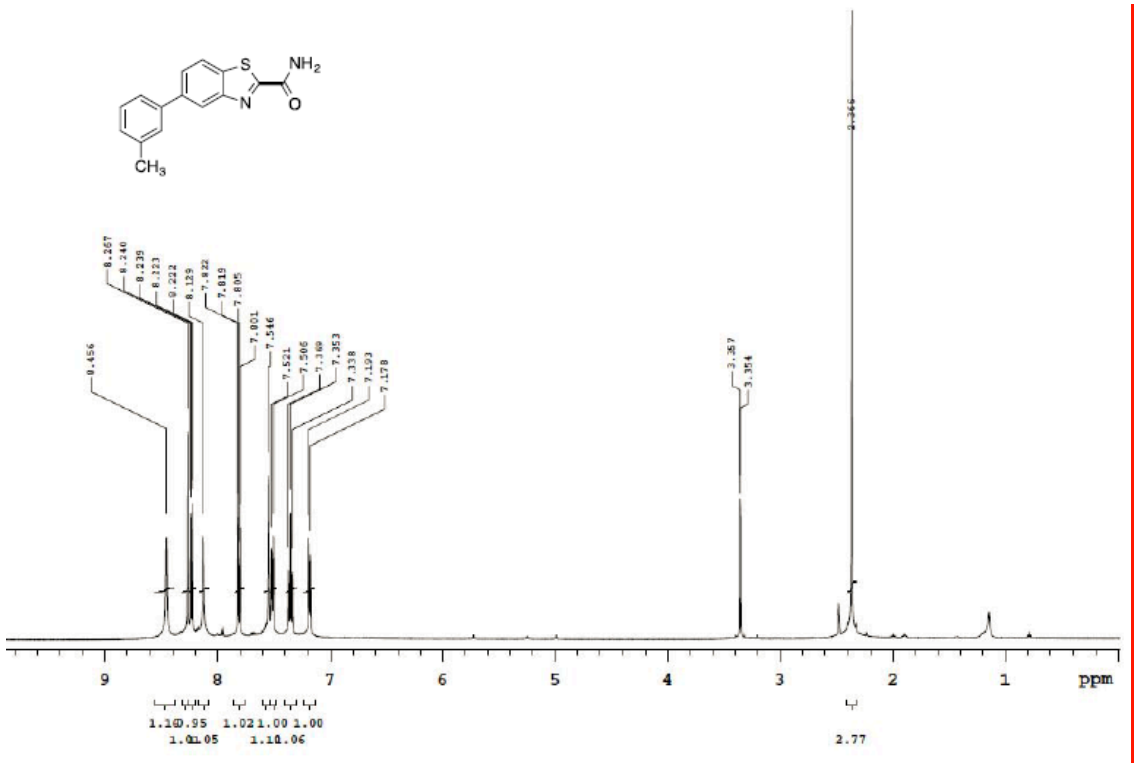
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7
6
5
4
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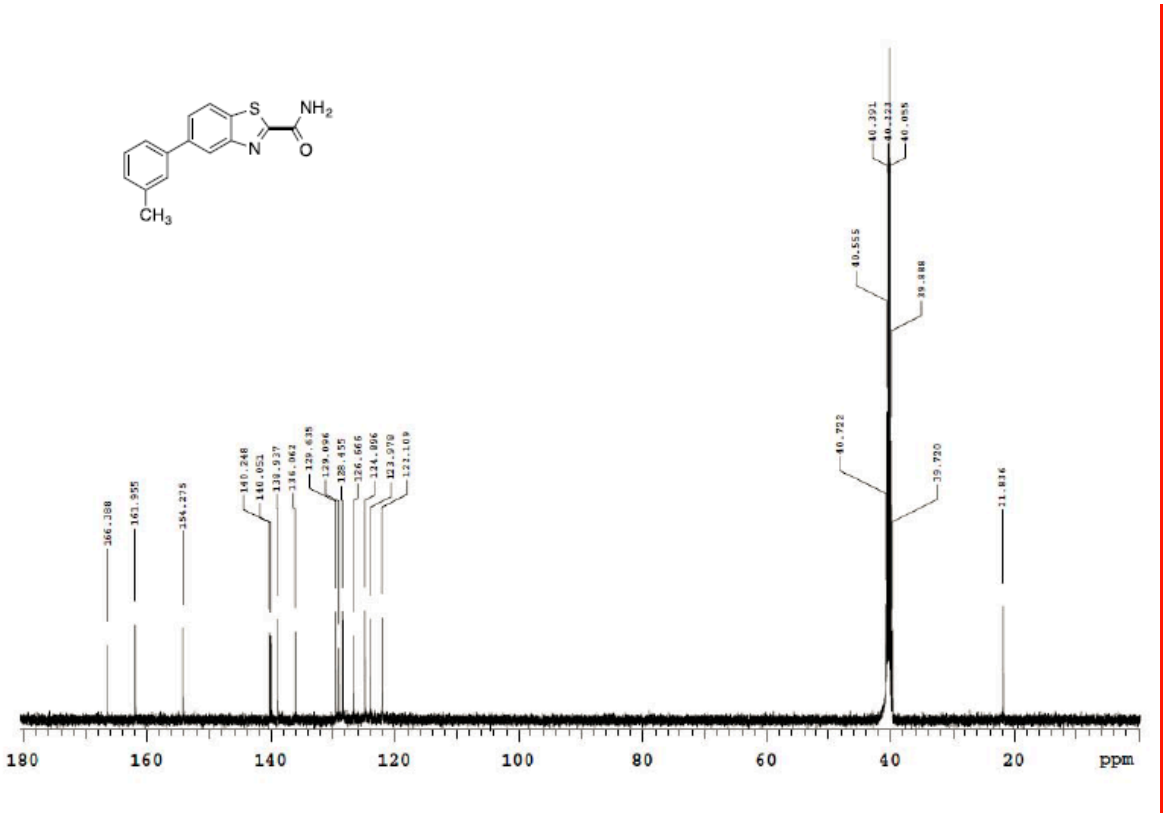
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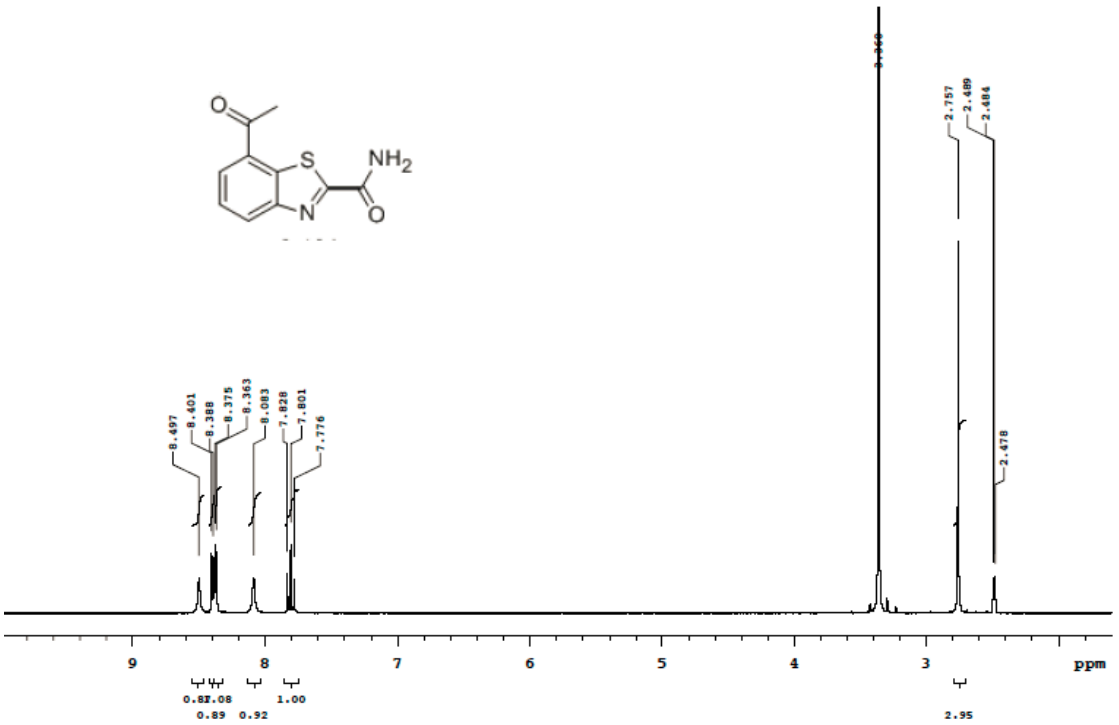
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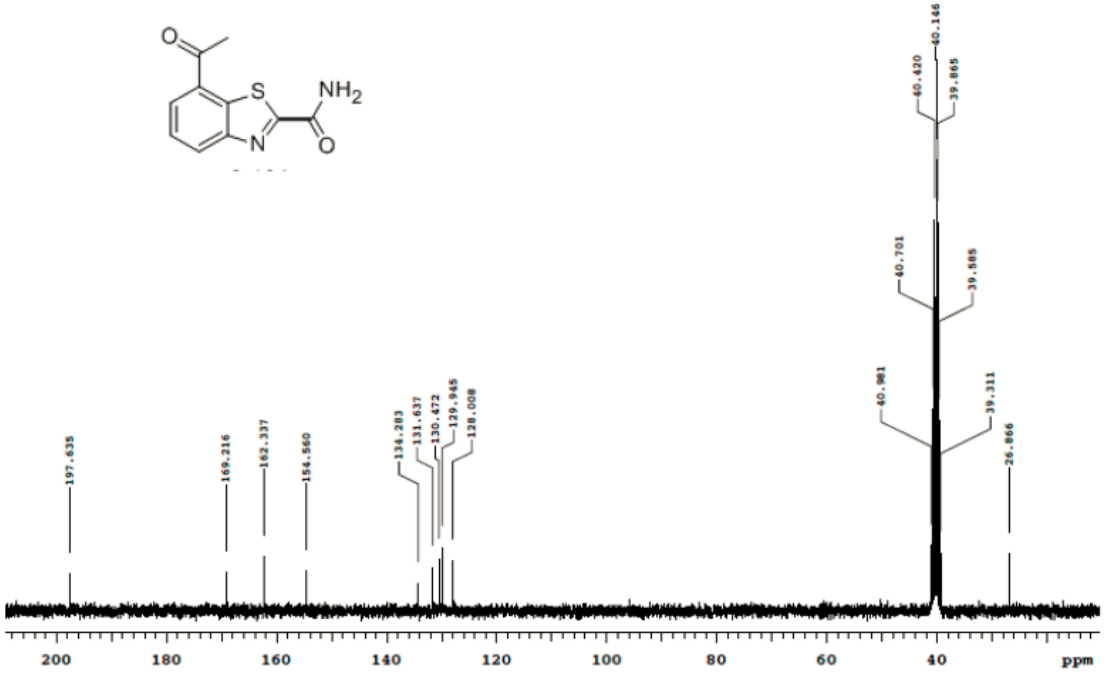
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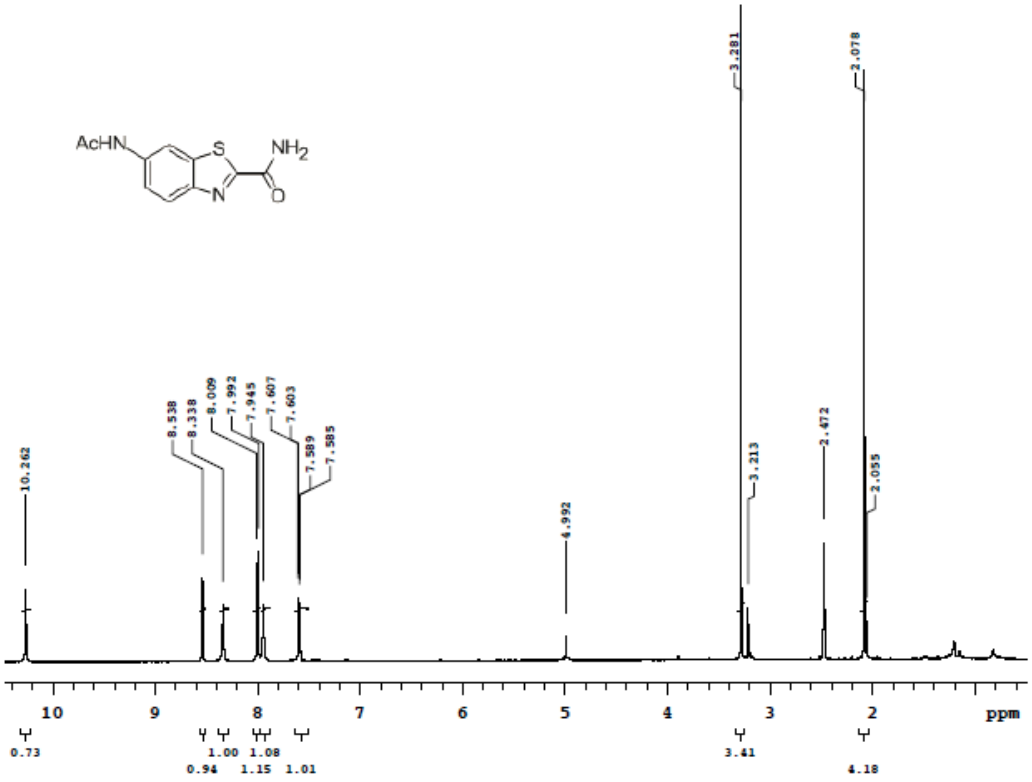
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9
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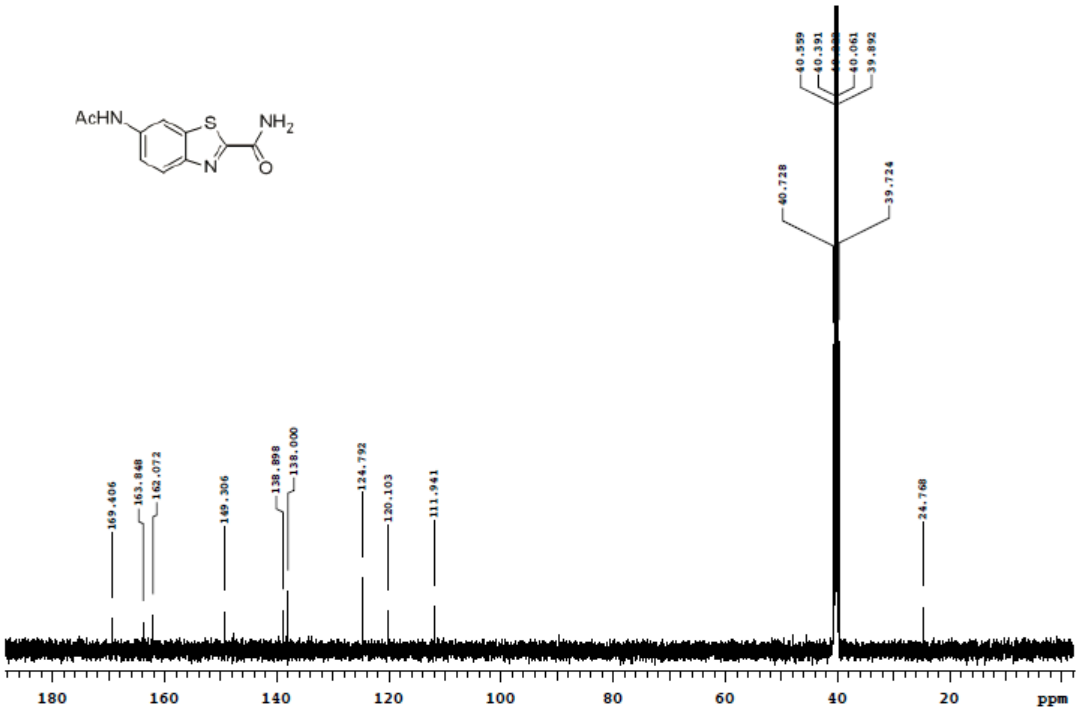
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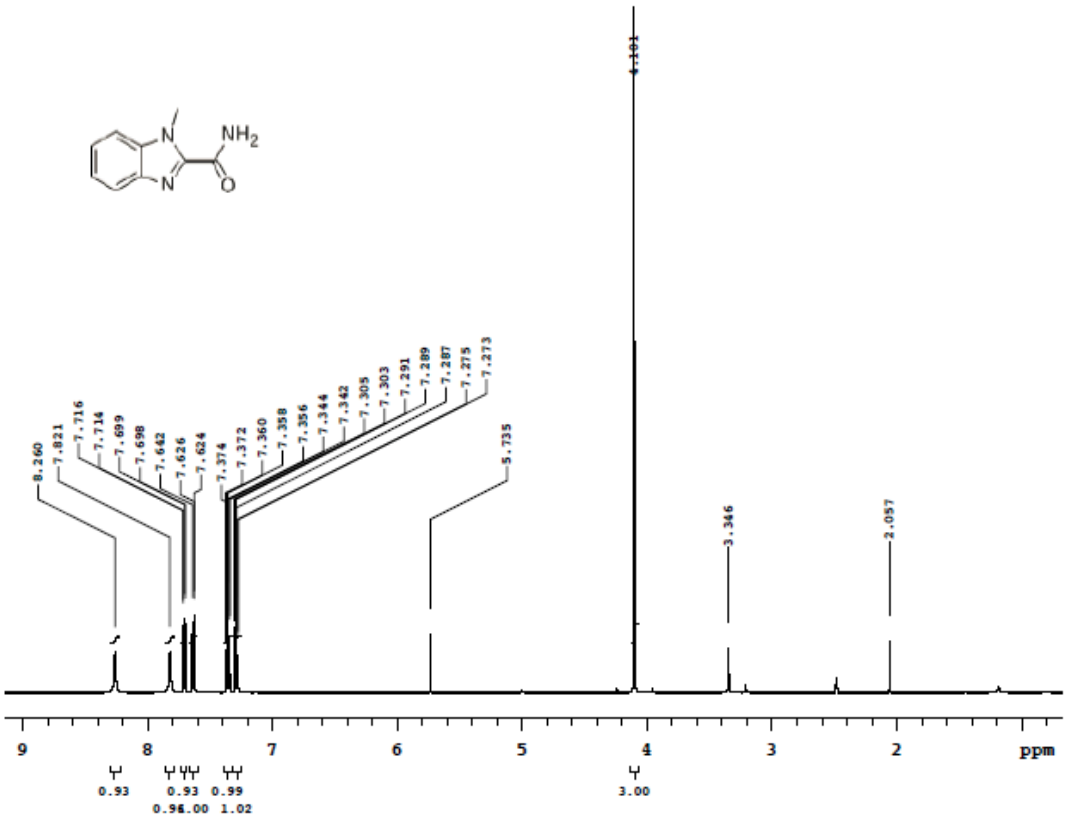
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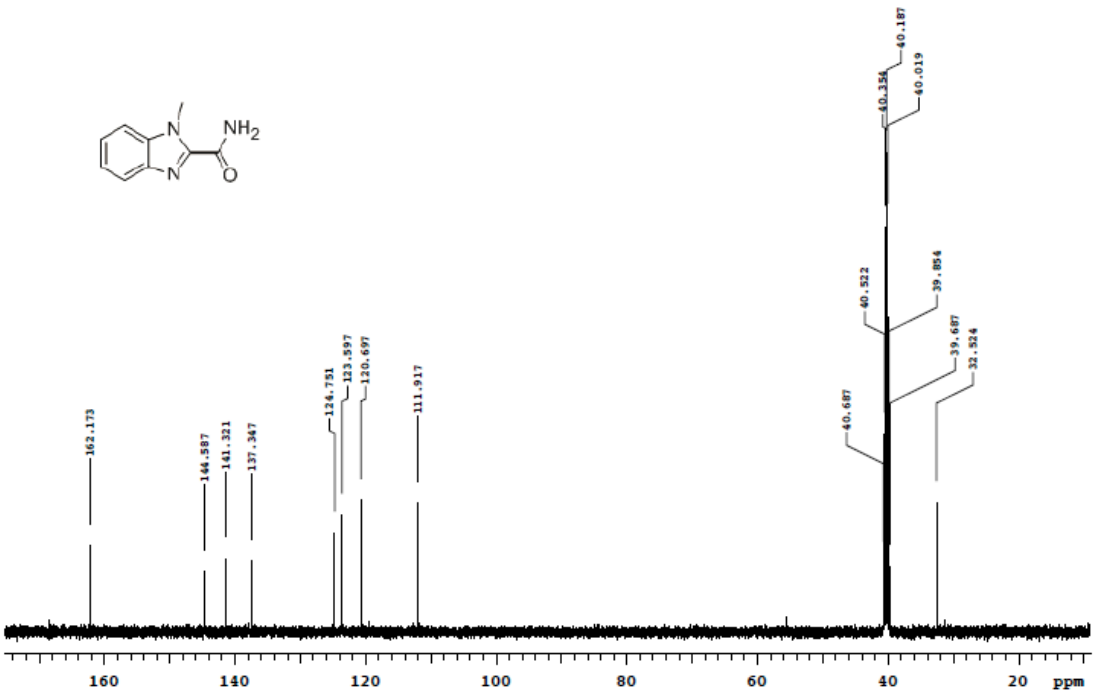
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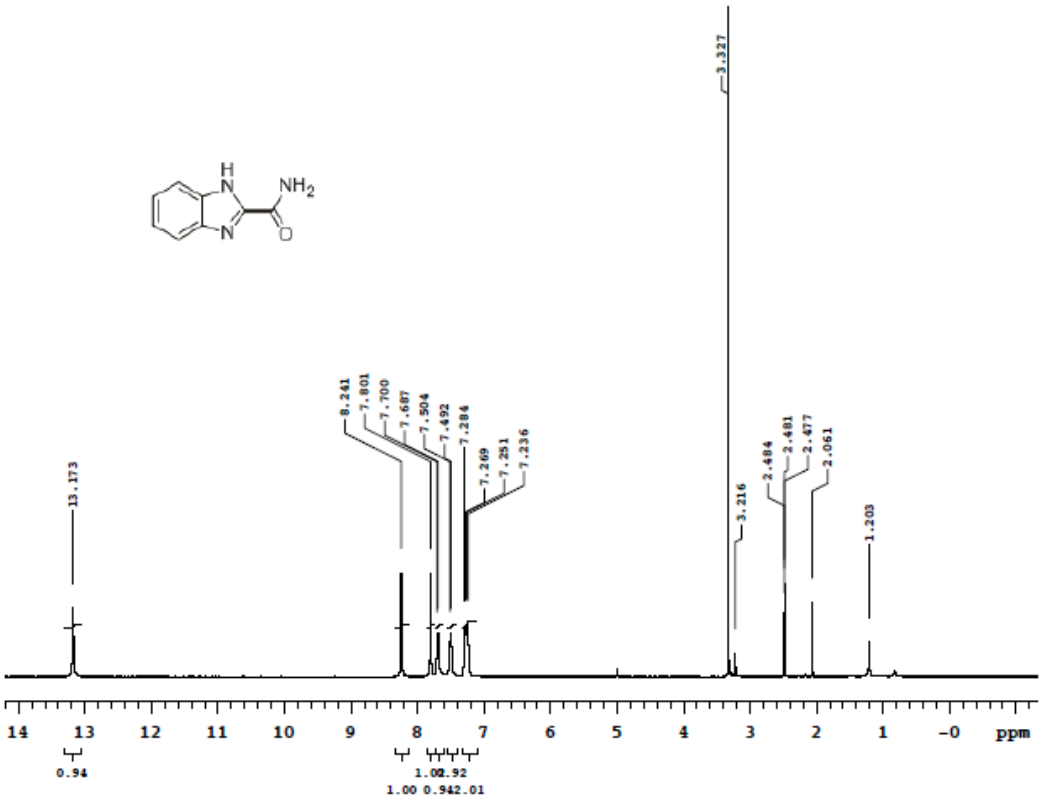
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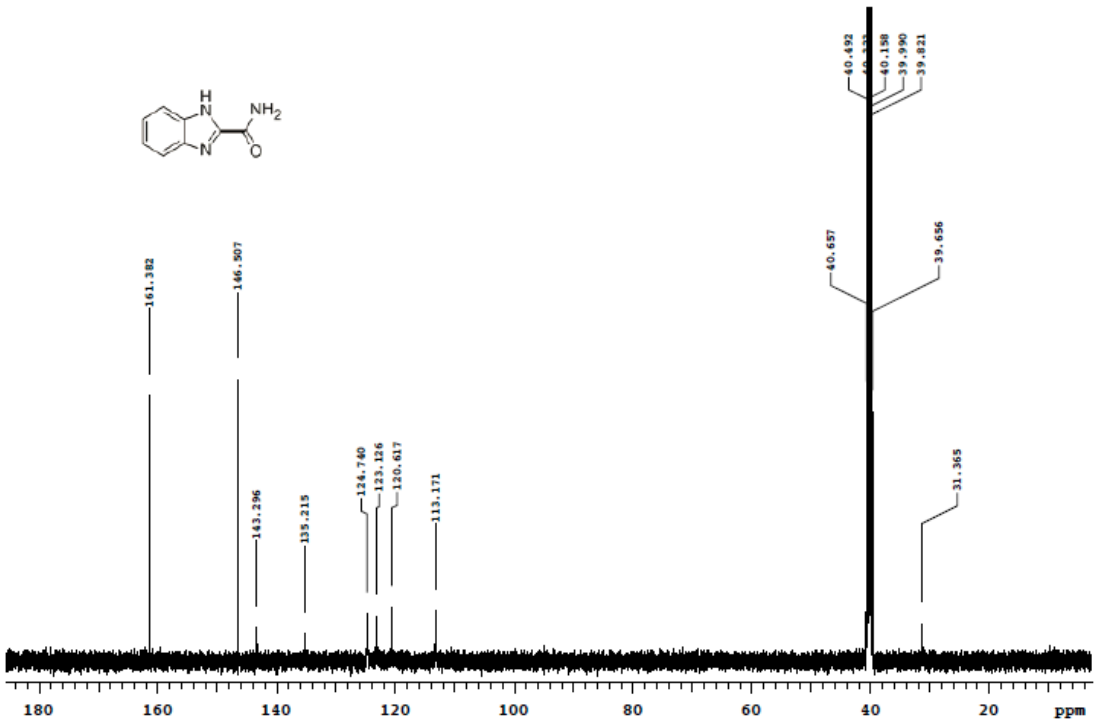
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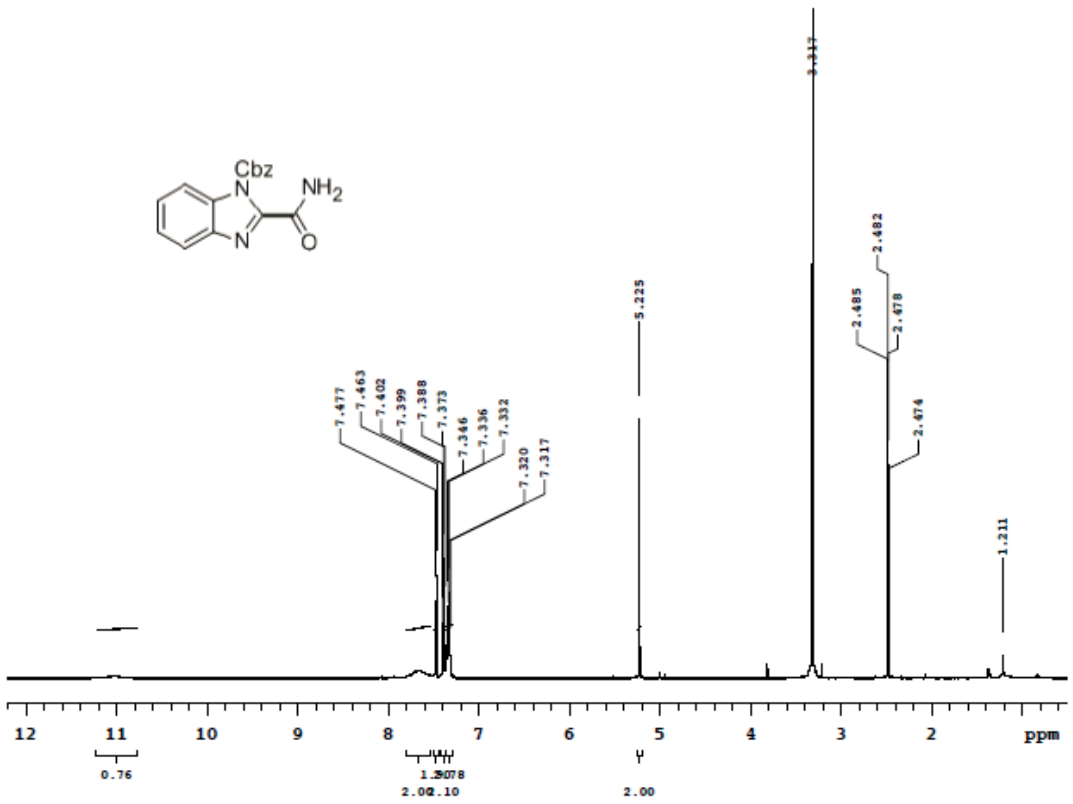
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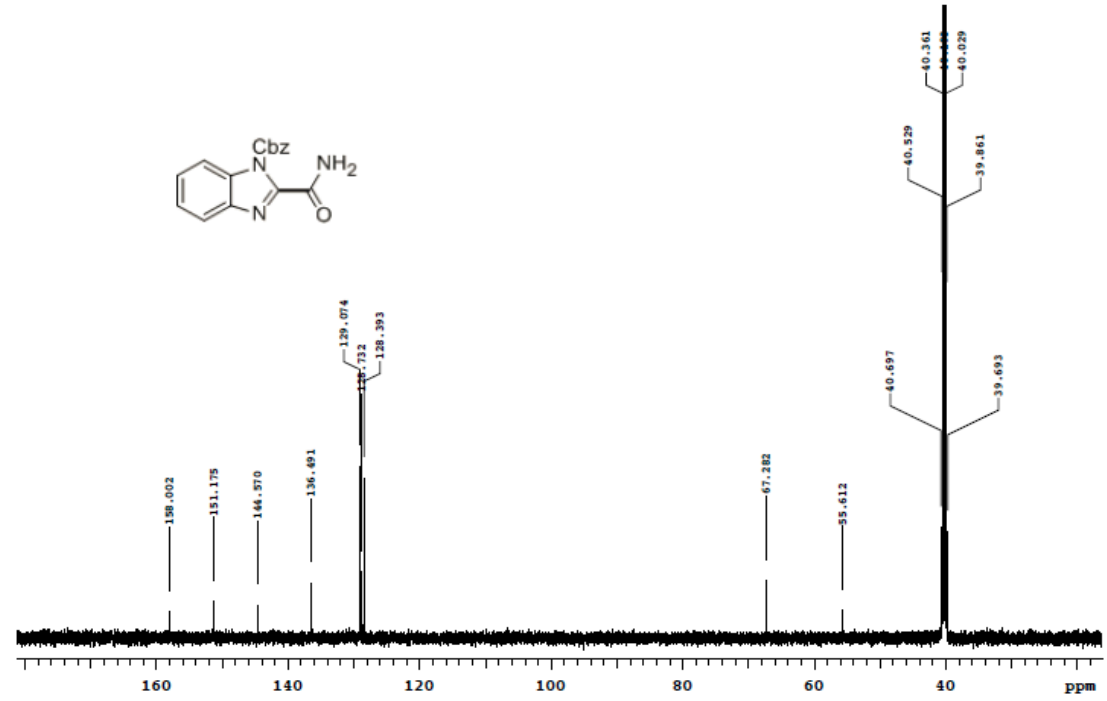
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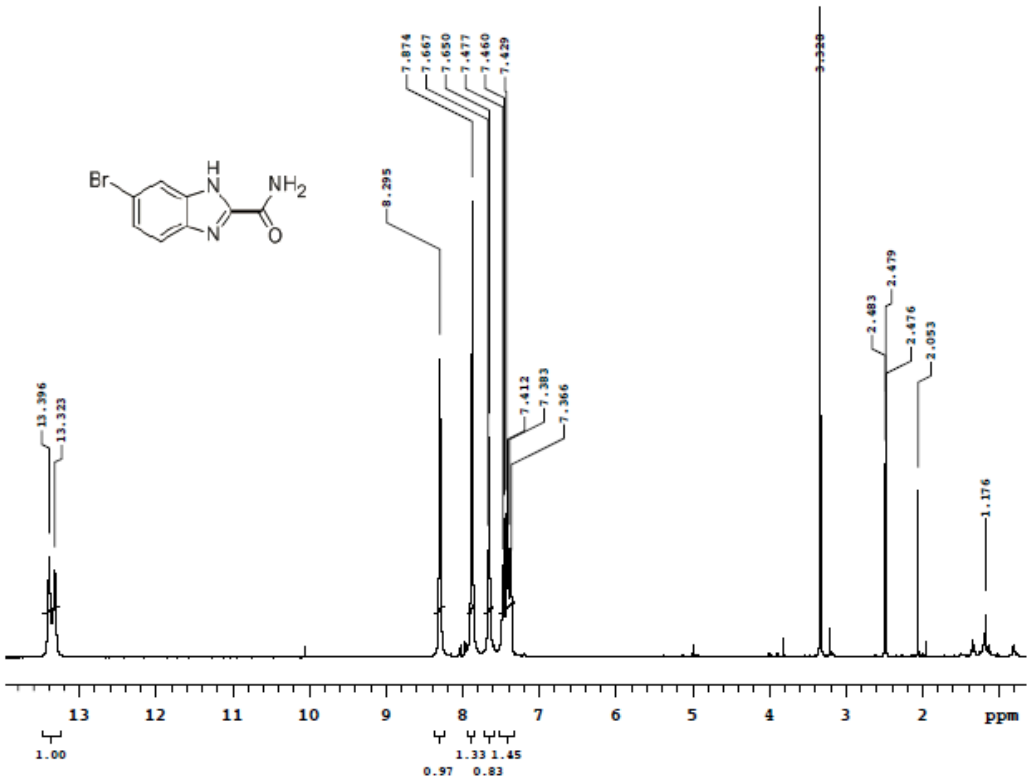
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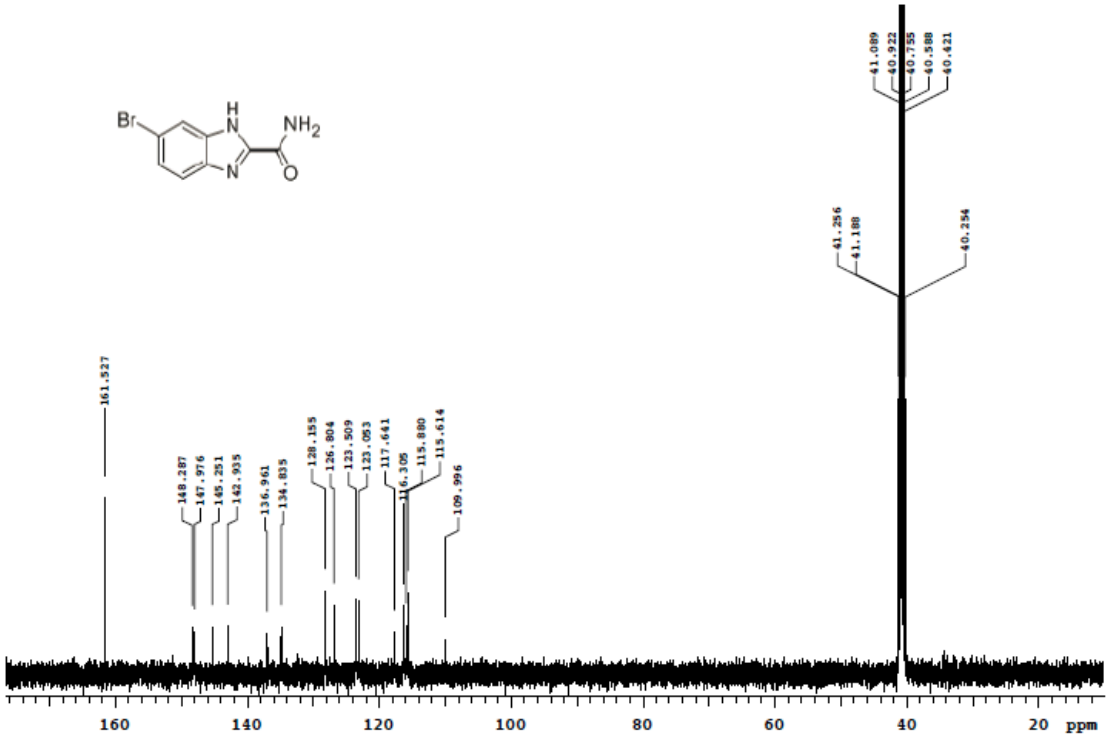
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20
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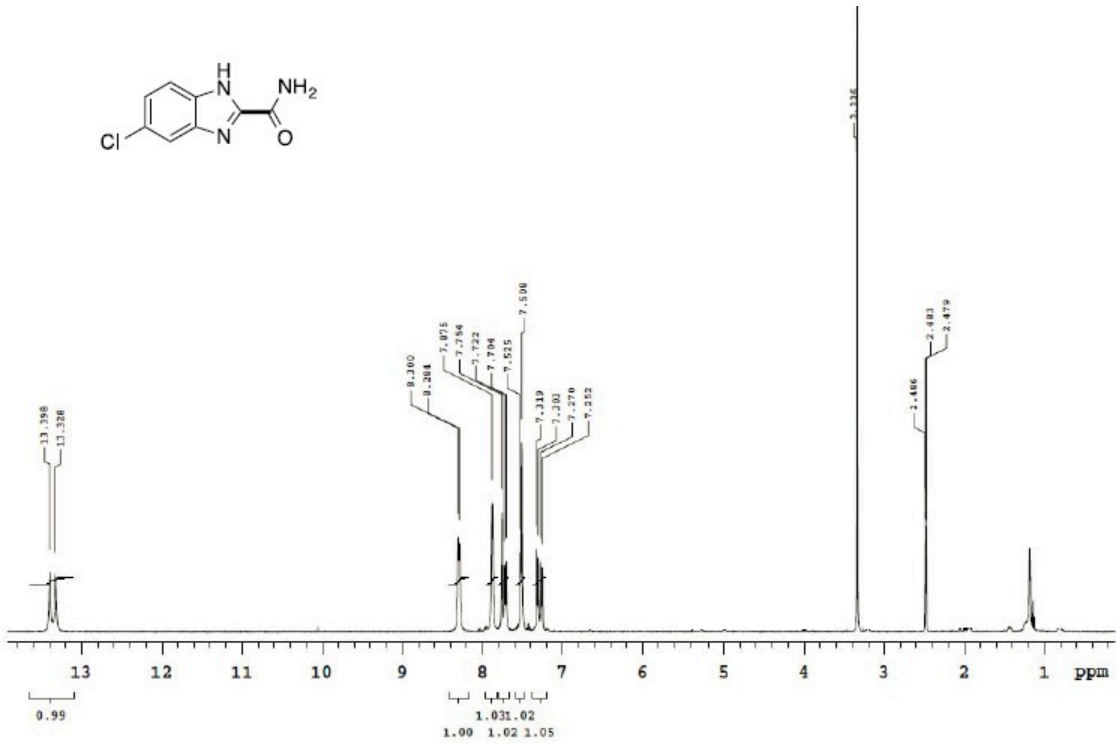
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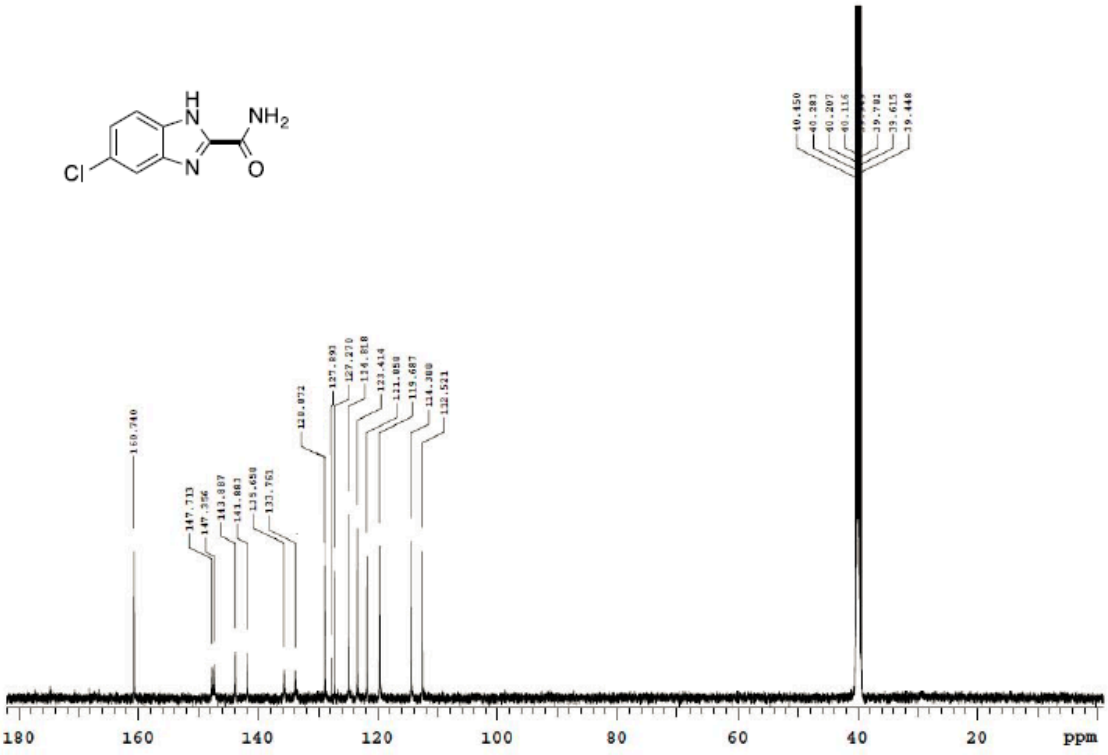
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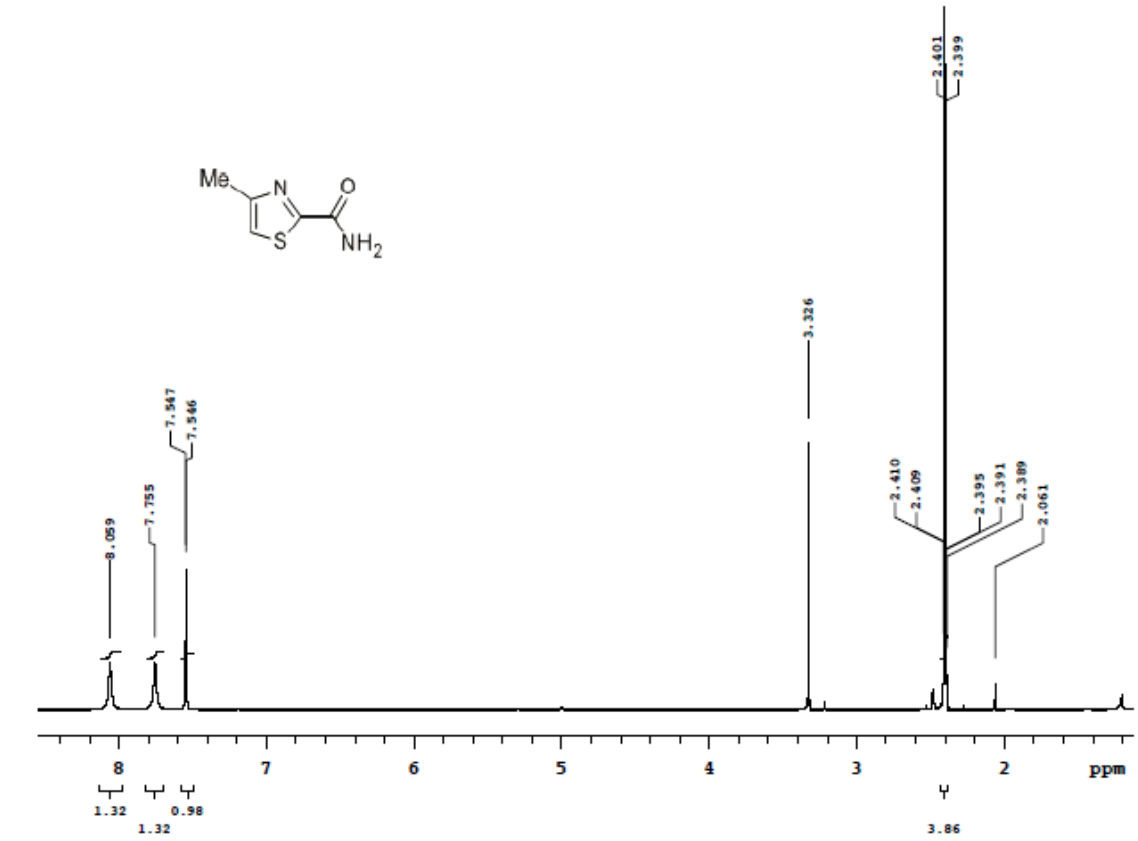
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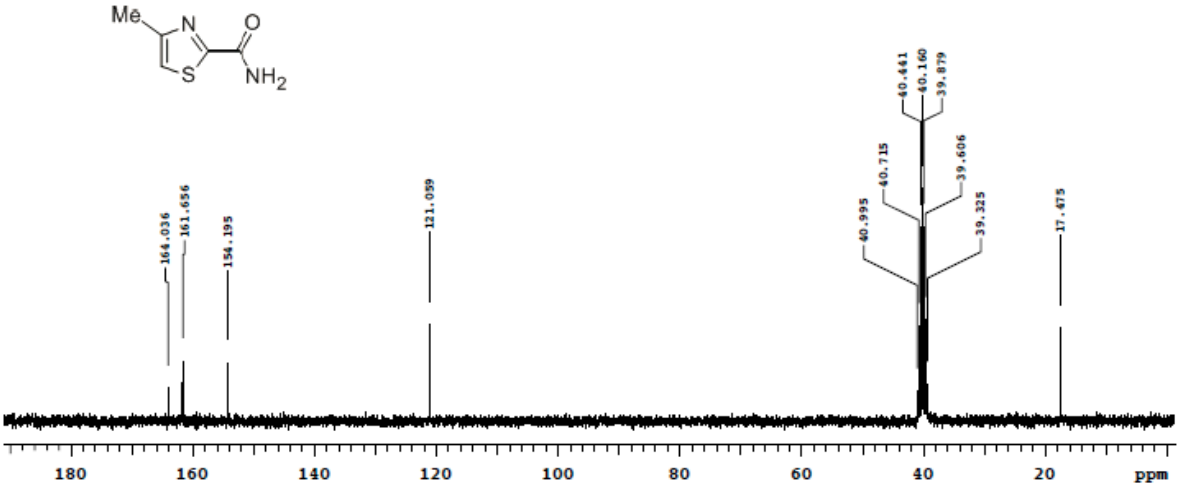
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N
O
S
NH2
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39.606
39.325
17.475
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140
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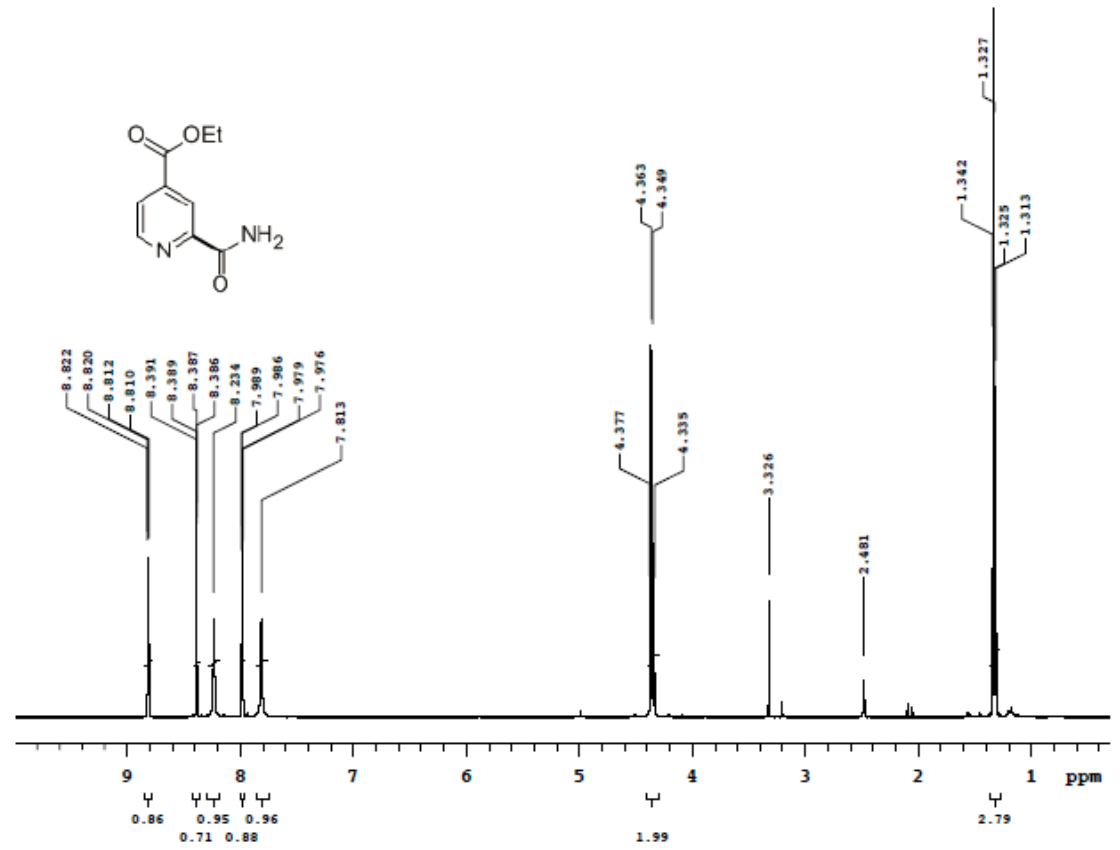
60
40
20
ppm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OEt
N
NH2
O
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8.812
8.810
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8.389
8.387
8.386
8.234
7.989
7.986
7.979
7.976
7.813
4.363
4.349
4.377
4.335
3.326
2.481
1.342
1.327
1.325
1.313
9
8
7
6
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3
2
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ppm
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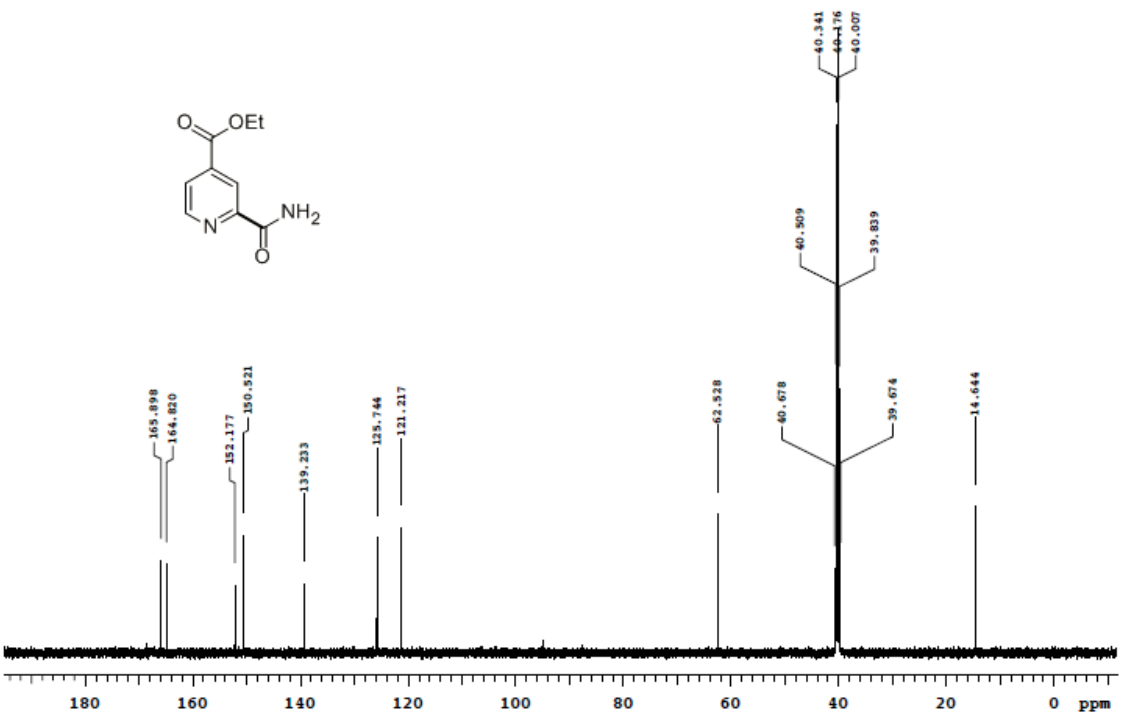
0.96
0.71
0.88
1.99
2.79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OEt
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NH2
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139.233
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121.217
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40.678
40.509
40.341
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39.839
39.674
14.644
180
160
140
120
100
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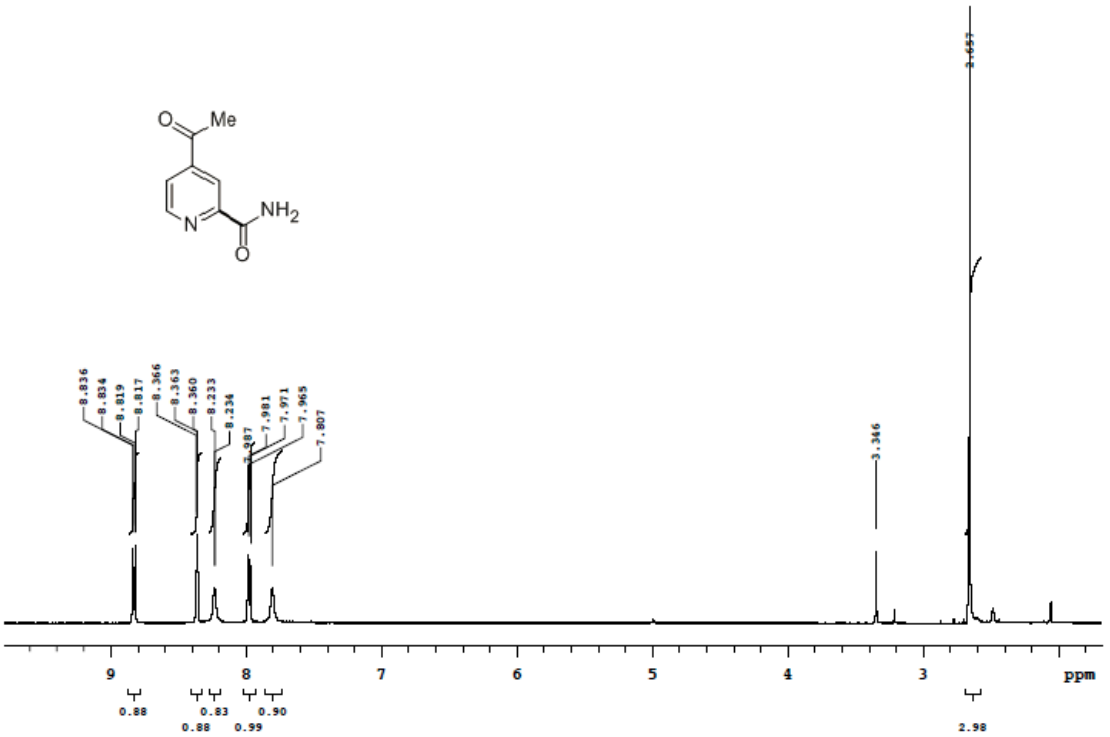
60
40
20
0
ppm


O
Me
N
NH2
O
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8.819
8.817
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8.363
8.360
8.233
8.234
7.981
7.971
7.965
7.807
3.346
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8
7
6
5
4
3
ppm
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0.88
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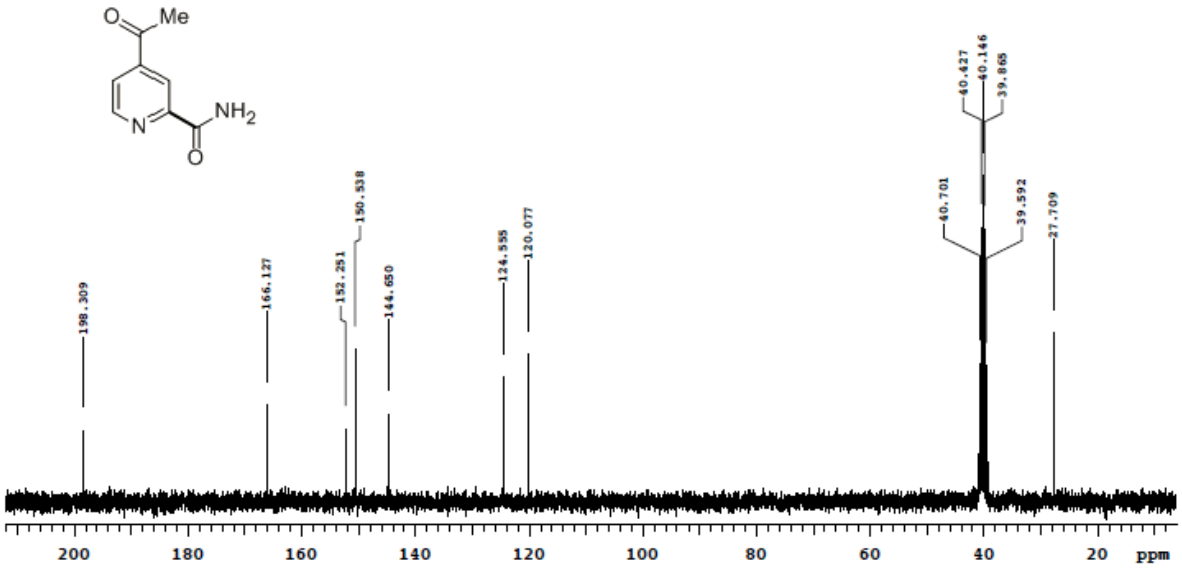
0.90
2.98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Me
N
NH2
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150.538
144.650
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120.077
40.427
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40.701
39.592
27.709
200
180
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140
120
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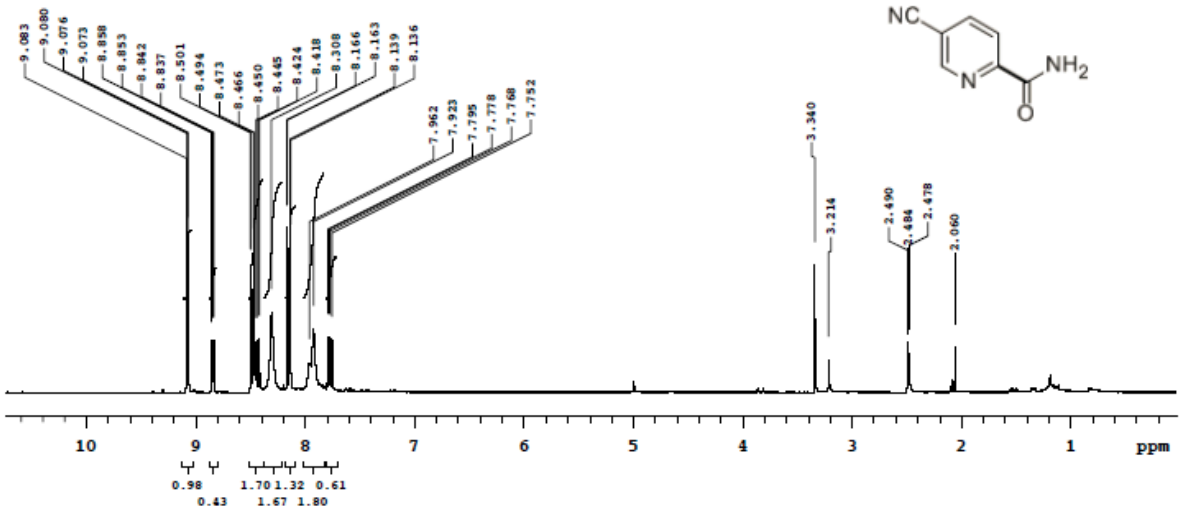
80
60
40
20
ppm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8.466
8.450
8.445
8.424
8.418
8.308
8.166
8.163
8.139
8.136
7.962
7.923
7.795
7.778
7.768
7.752
3.340
3.214
2.490
2.484
2.478
2.060
NC
NH2
N
O
10
9
8
7
6
5
4
3
2
1
ppm
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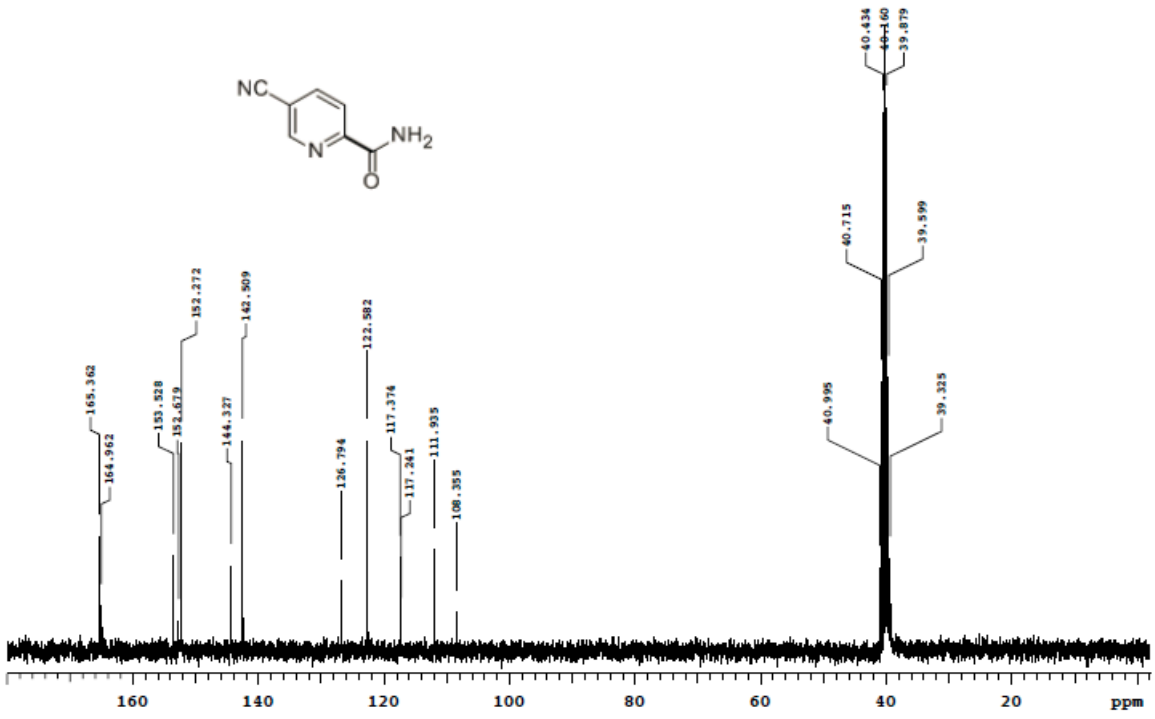
1.32
1.80
0.61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NH2
N
O
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153.528
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152.272
144.327
142.509
126.794
122.582
117.374
117.241
111.935
108.355
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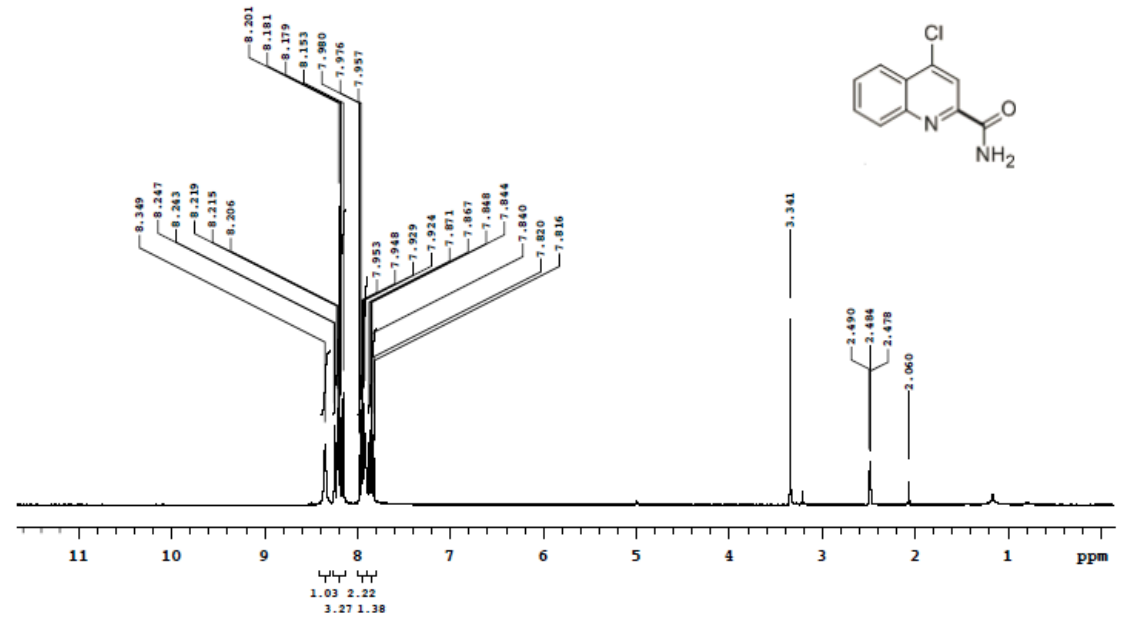
40.160
39.879
40.715
39.599
40.995
39.325
160
140
120
100
80
60
40
20
ppm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8.181
8.179
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7.976
7.957
8.349
8.247
8.243
8.219
8.215
8.206
7.953
7.948
7.929
7.924
7.871
7.867
7.848
7.844
7.840
7.820
7.816
3.341
2.490
2.484
2.478
2.060
Cl
N
O
NH2
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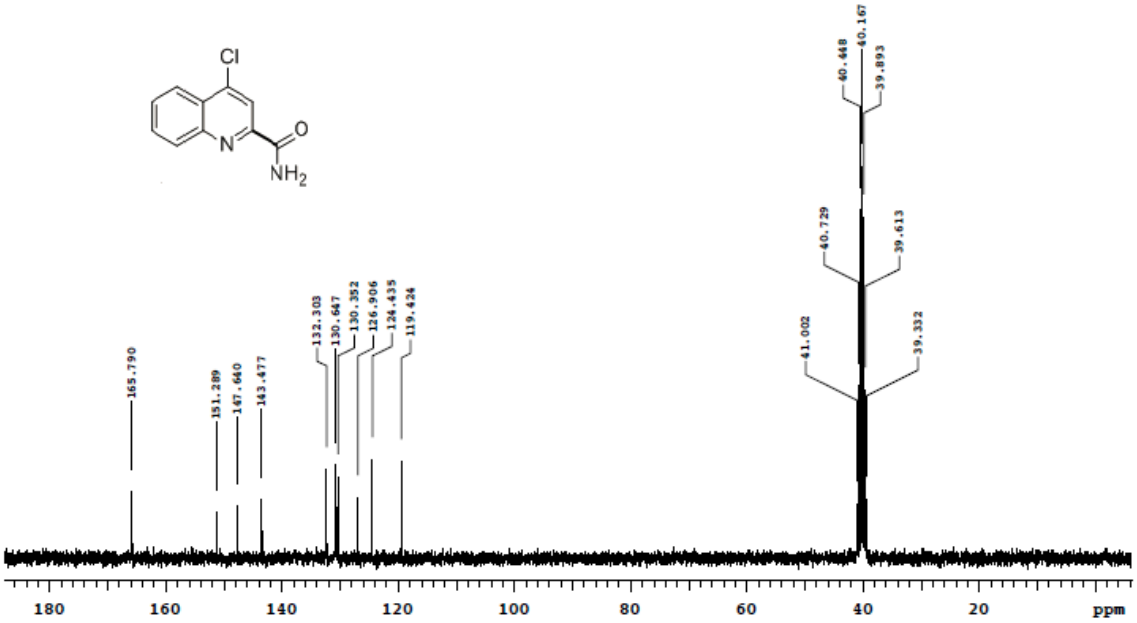
10
9
8
7
6
5
4
3
2
1
ppm
1.03 2.22
3.27 1.38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O
NH2
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147.640
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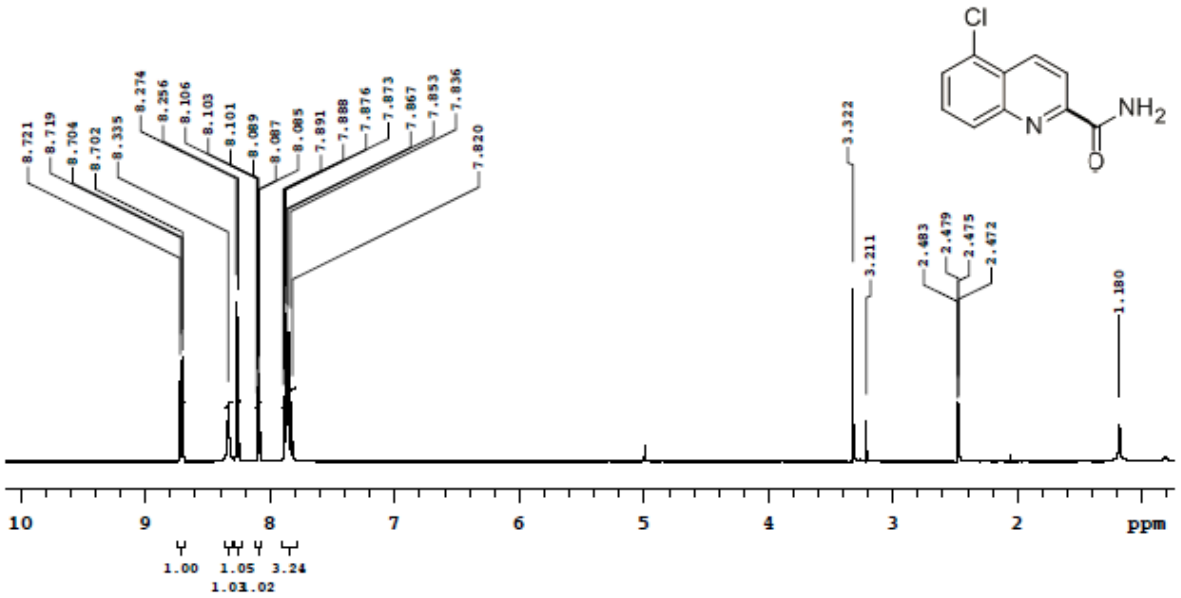
132.303
130.647
130.352
126.906
124.435
119.424
40.448
40.167
39.893
40.729
39.613
41.002
39.332
180
160
140
120
100
80
60
40
20
ppm


Cl
NH2
N
O
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8.704
8.702
8.335
8.274
8.256
8.106
8.103
8.101
8.089
8.087
8.085
7.891
7.888
7.876
7.873
7.867
7.853
7.836
7.820
3.322
3.211
2.483
2.479
2.475
2.472
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10
9
8
7
6
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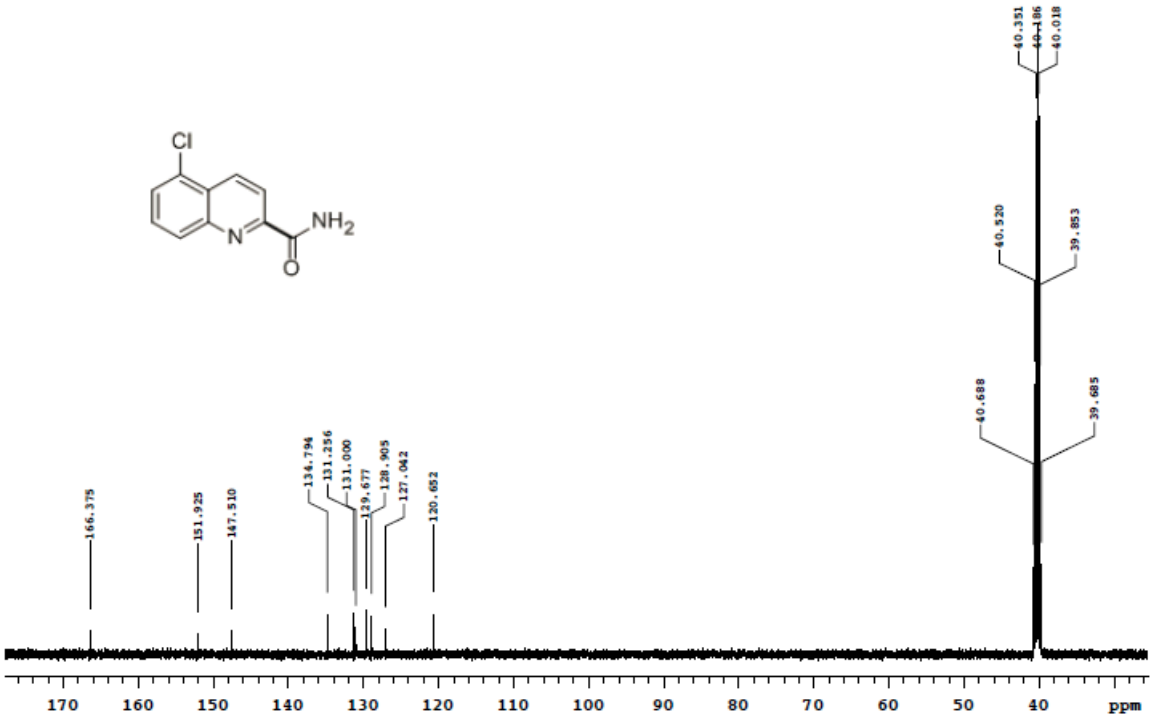
ppm
1.00
1.05
3.24
1.01
1.02


Cl
NH2
N
O
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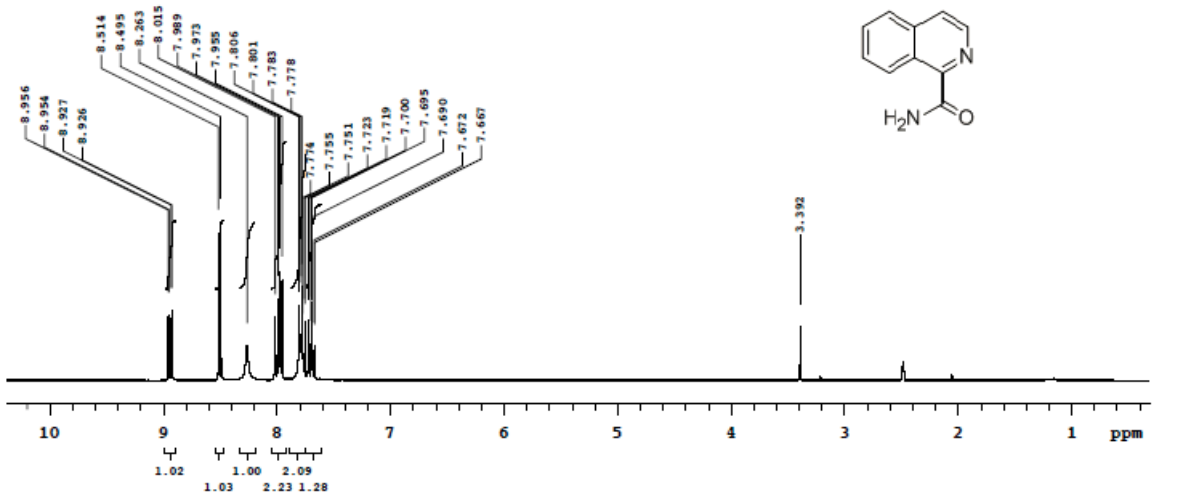
40.018
40.520
39.853
40.688
39.685
166.375
151.925
147.510
134.794
131.256
131.000
129.677
128.905
127.042
120.652
170
160
150
140
130
120
110
100
90
80
70
60
50
40
ppm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8.927
8.926
8.514
8.495
8.263
8.015
7.989
7.973
7.955
7.806
7.801
7.783
7.778
7.774
7.755
7.751
7.723
7.719
7.700
7.695
7.690
7.672
7.667
3.392
N
H2N
O
10
9
8
7
6
5
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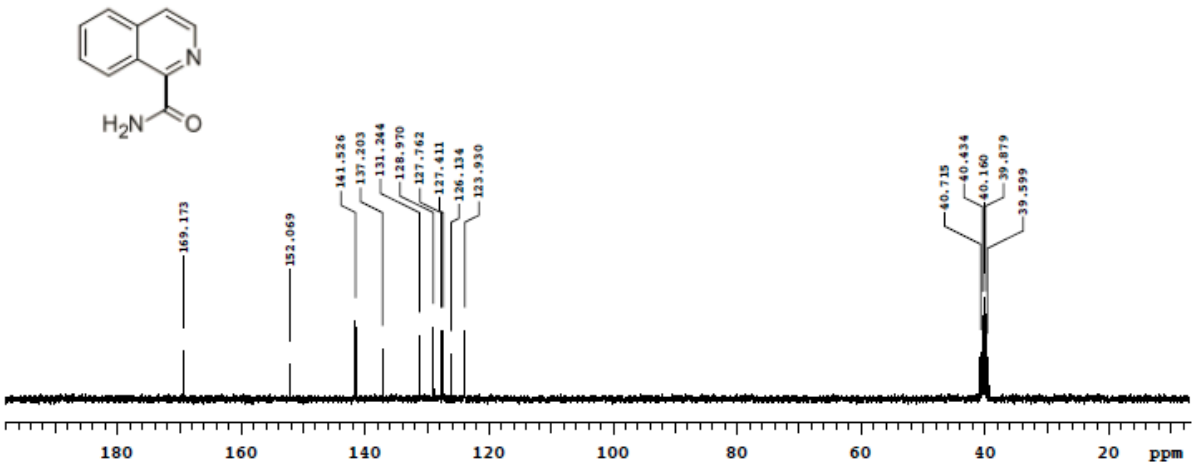
1.02
1.03
1.00
2.23
2.09
1.28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H2N
O
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127.411
126.134
123.930
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40.160
39.879
39.599
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160
140
120
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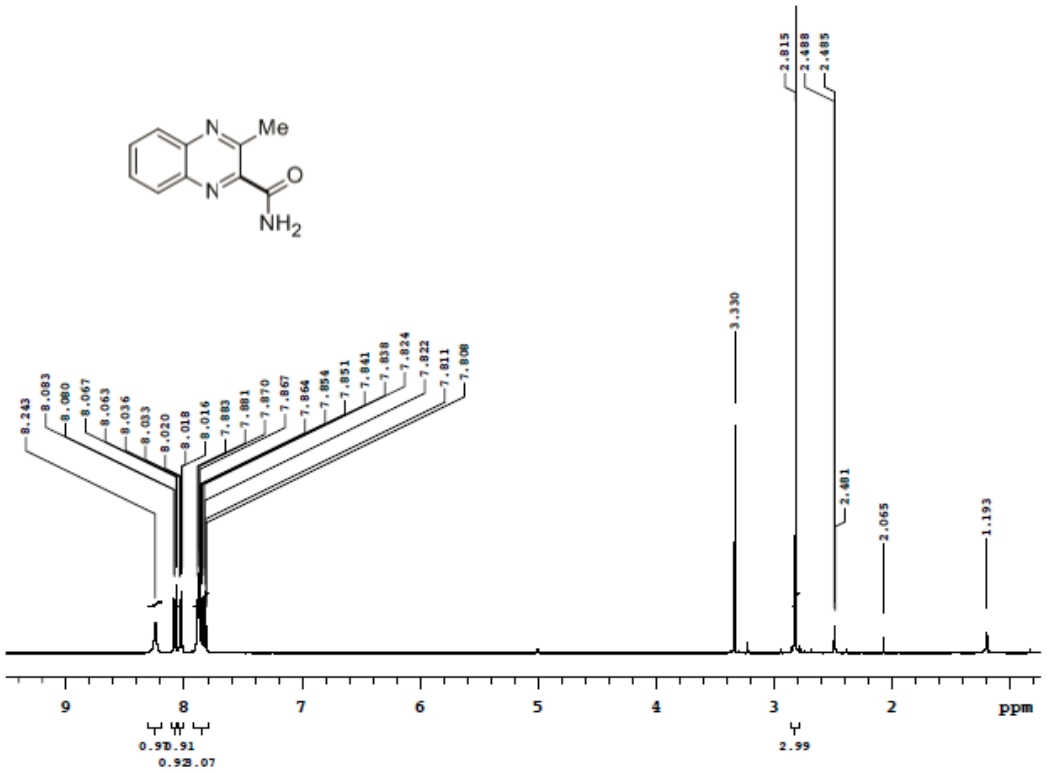
80
60
40
20
ppm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N
O
NH2
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8.063
8.036
8.033
8.020
8.018
8.016
7.883
7.881
7.870
7.867
7.864
7.854
7.851
7.841
7.838
7.824
7.822
7.811
7.808
3.330
2.815
2.488
2.485
2.481
2.065
1.193
9
8
7
6
5
4
3
2
ppm
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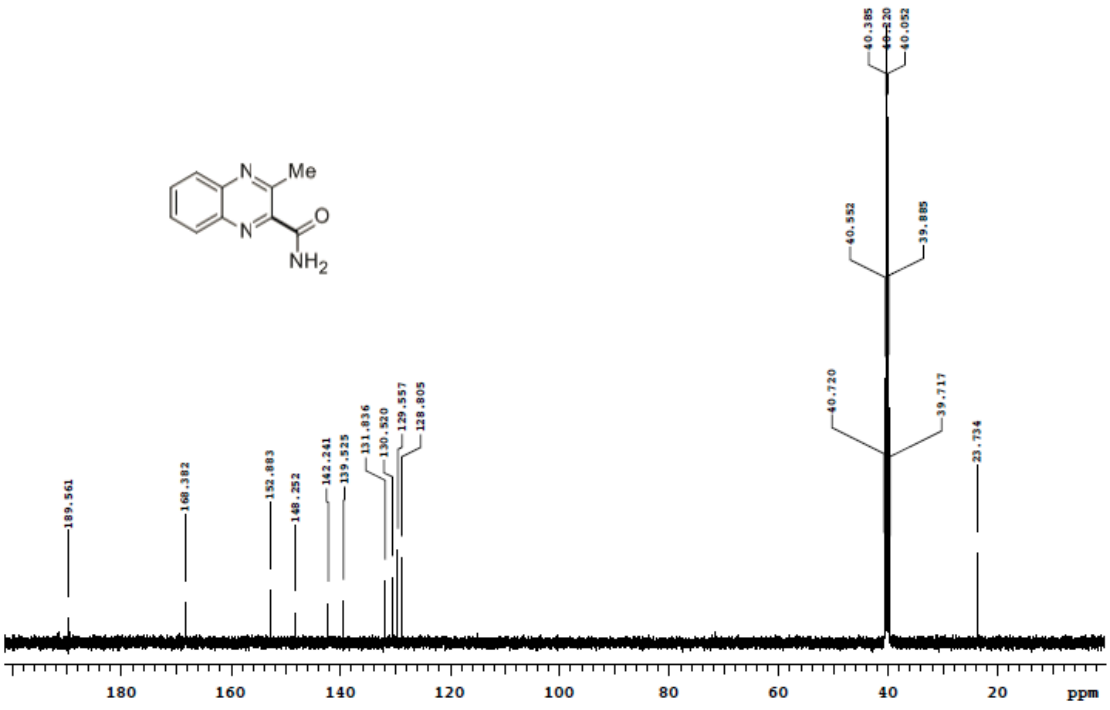
0.92
3.07
2.99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N
O
NH2
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39.717
23.734
189.561
168.382
152.883
148.252
142.241
139.525
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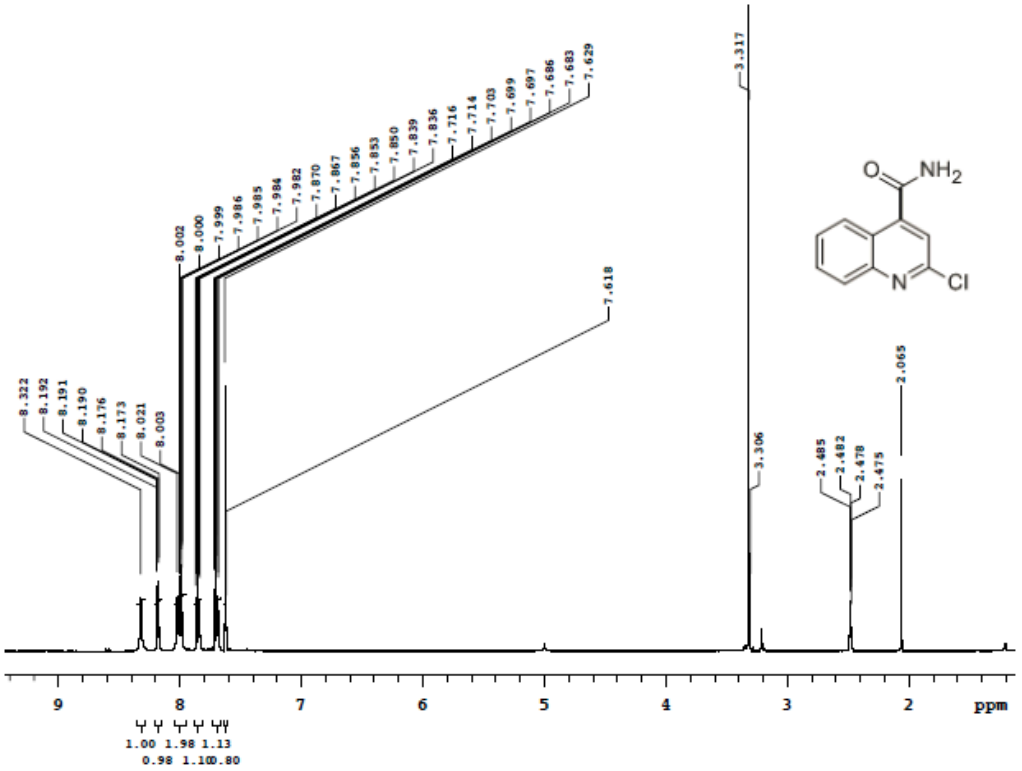
130.520
129.557
128.805
180
160
140
120
100
80
60
40
20
ppm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8.190
8.176
8.173
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8.003
8.002
8.000
7.999
7.986
7.985
7.984
7.982
7.870
7.867
7.856
7.853
7.850
7.839
7.836
7.716
7.714
7.703
7.699
7.697
7.686
7.683
7.629
7.618
3.317
3.306
2.485
2.482
2.478
2.475
2.065
O
NH2
N
Cl
9
8
7
6
5
4
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2
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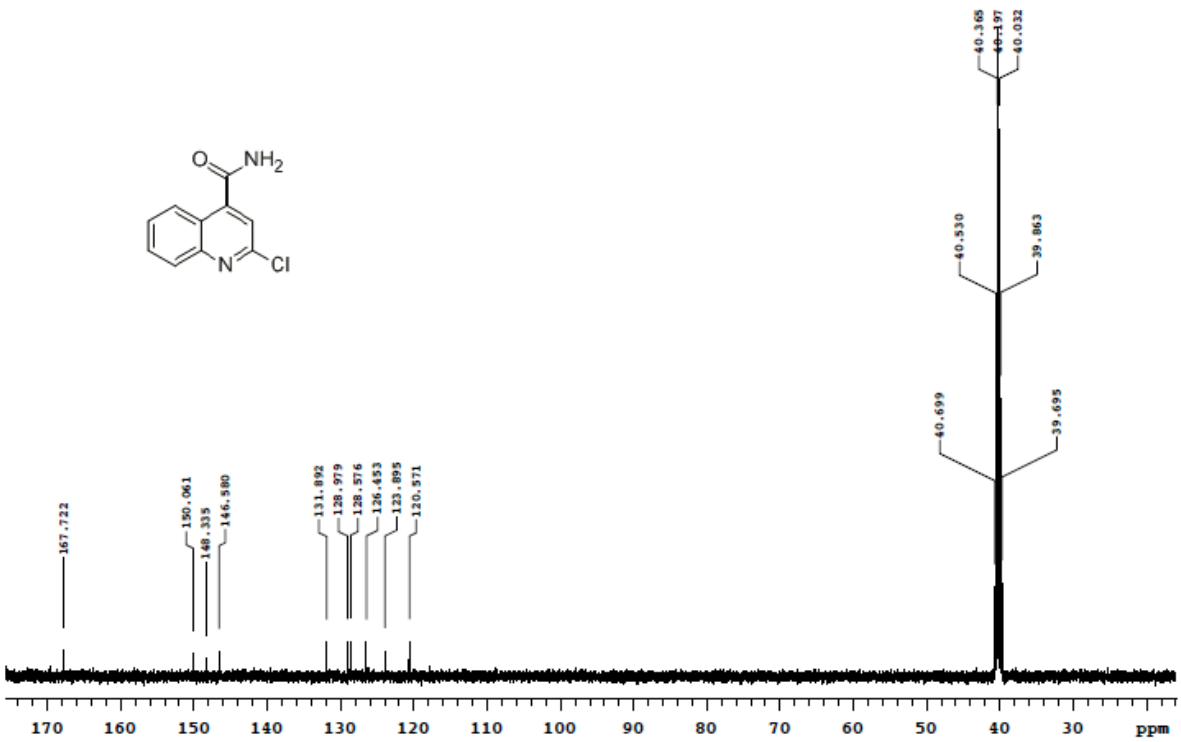
0.98 1.10 0.80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150.061
148.335
146.580
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128.979
128.576
126.453
123.895
120.571
O
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N
Cl
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160
150
140
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120
110
100
90
80
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60
50
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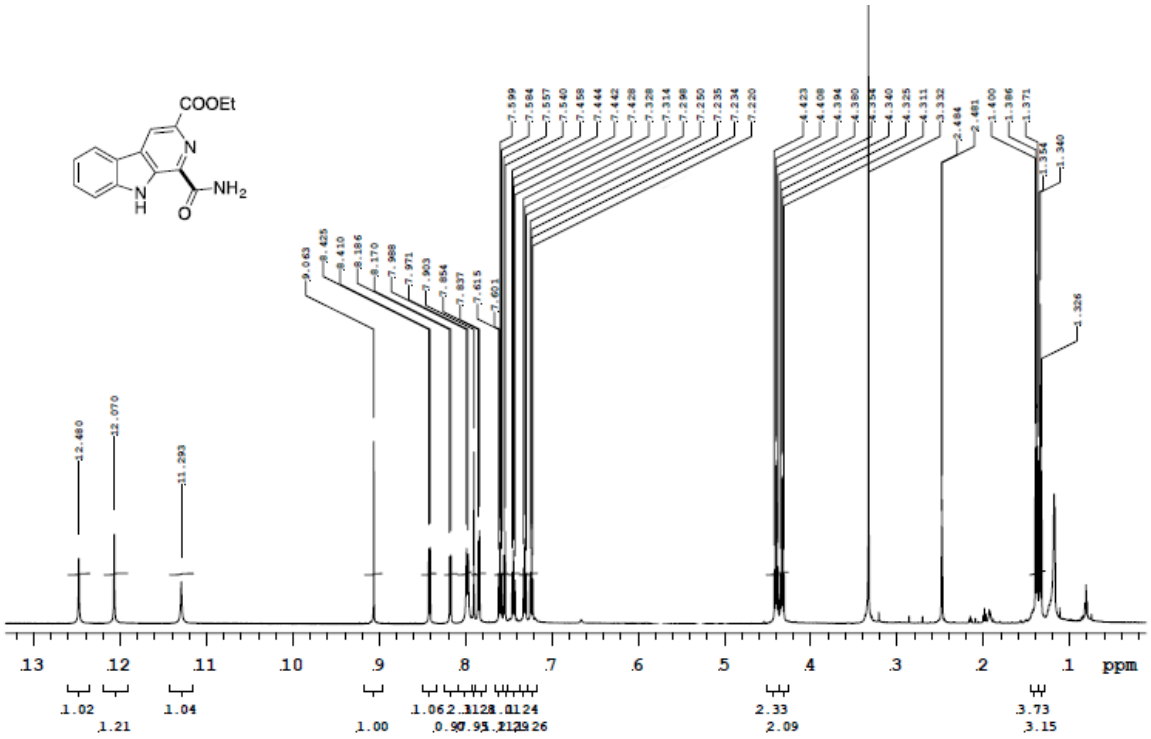
30
ppm


COOEt
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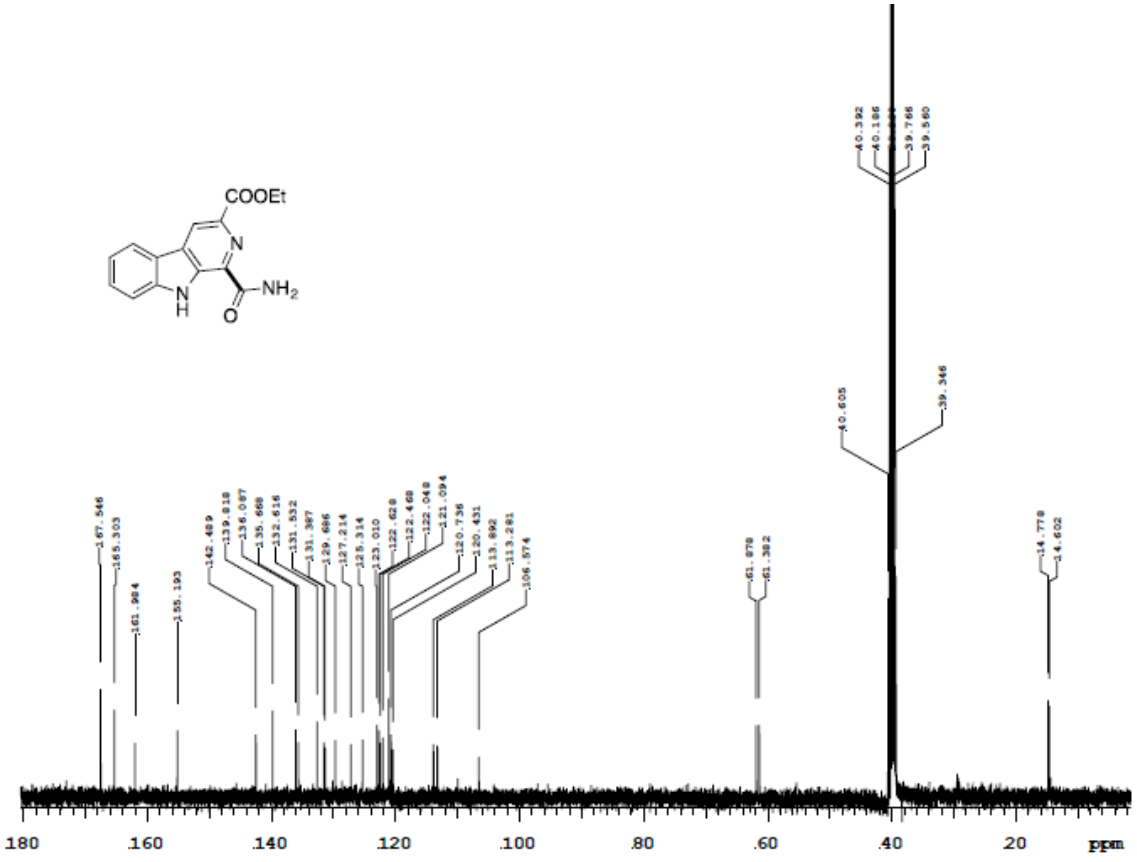
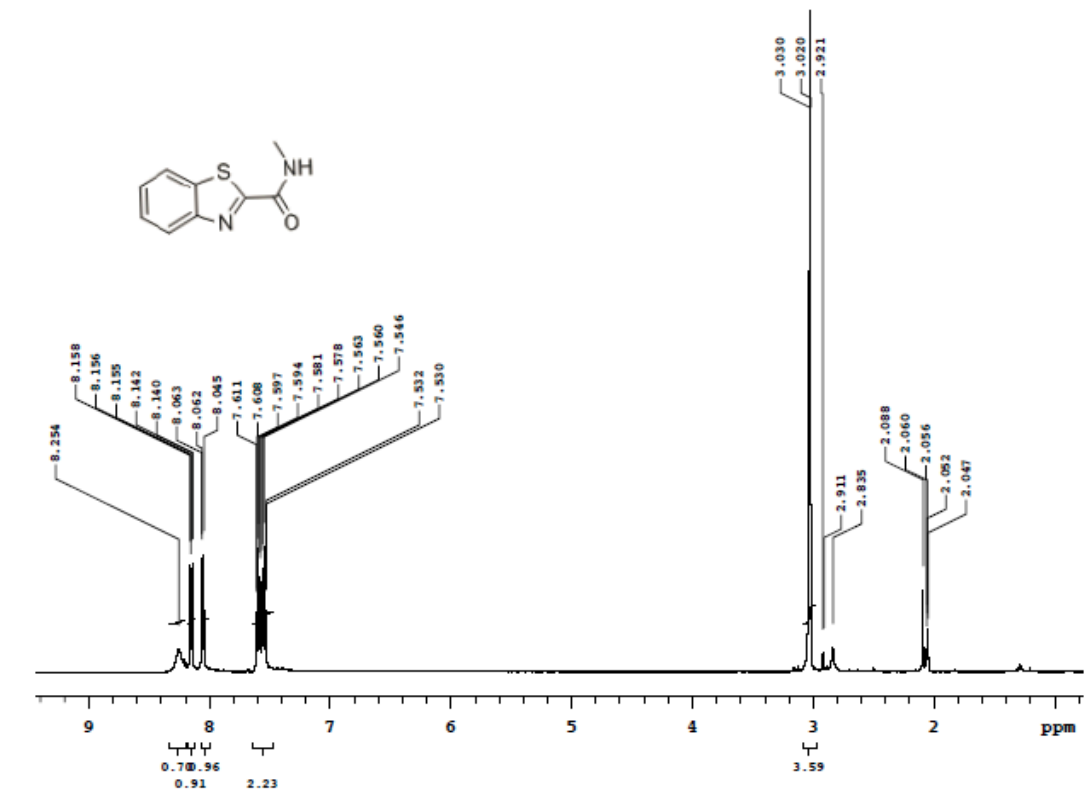
N
H
NH2
O
ppm


COOEt
N
N
H
NH2
O
ppm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S
N
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8.140
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8.062
8.045
7.611
7.608
7.597
7.594
7.581
7.578
7.563
7.560
7.546
7.532
7.530
3.030
3.020
2.921
2.911
2.835
2.088
2.060
2.056
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8
7
6
5
4
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2
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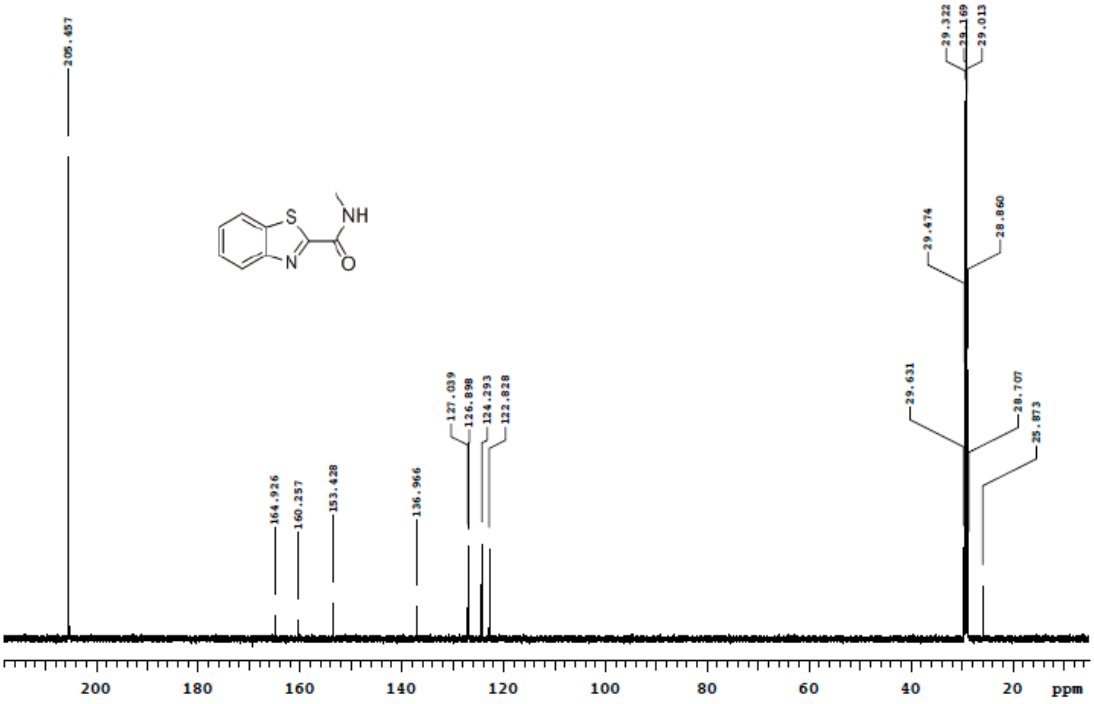
3.59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S
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126.898
124.293
122.828
29.322
29.169
29.013
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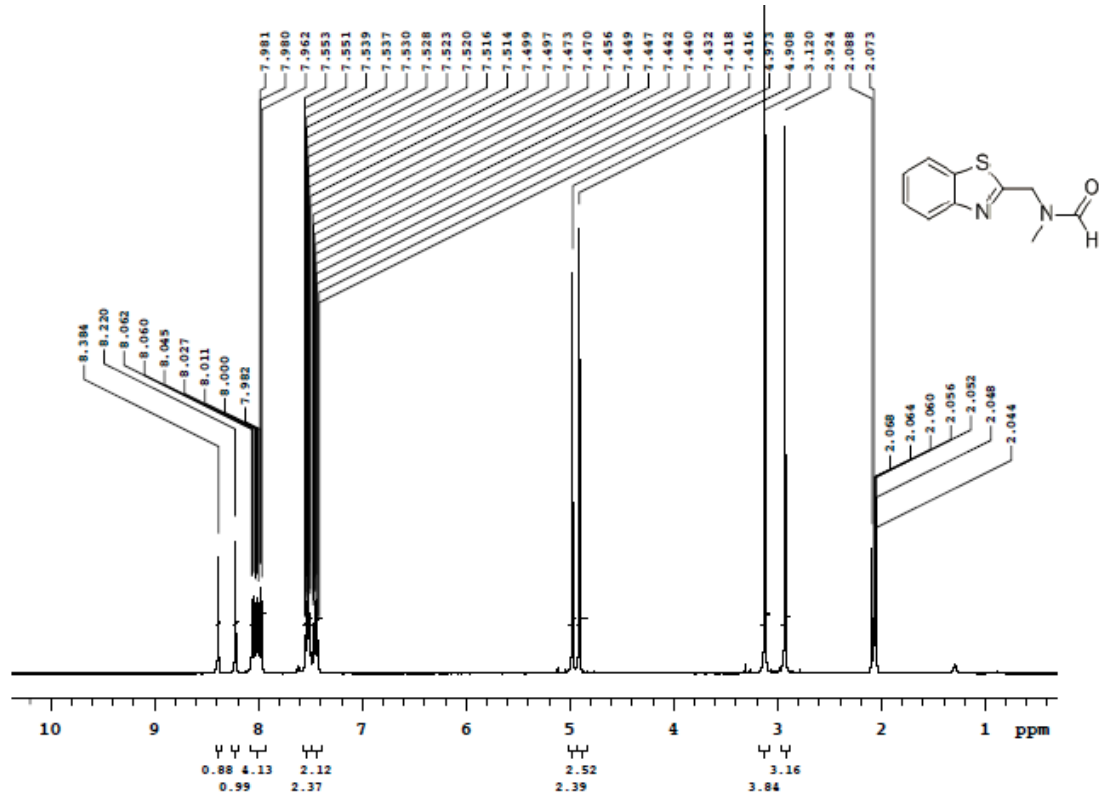
29.631
28.707
25.873
200
180
160
140
120
100
80
60
40
20
ppm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7.523
7.520
7.516
7.514
7.499
7.497
7.473
7.470
7.456
7.449
7.447
7.442
7.440
7.432
7.418
7.416
4.973
4.908
3.120
2.924
2.088
2.073
8.384
8.220
8.062
8.060
8.045
8.027
8.011
8.000
7.982
2.068
2.064
2.060
2.056
2.052
2.048
2.044
S
N
O
N
H
10
9
8
7
6
5
4
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ppm
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3.16
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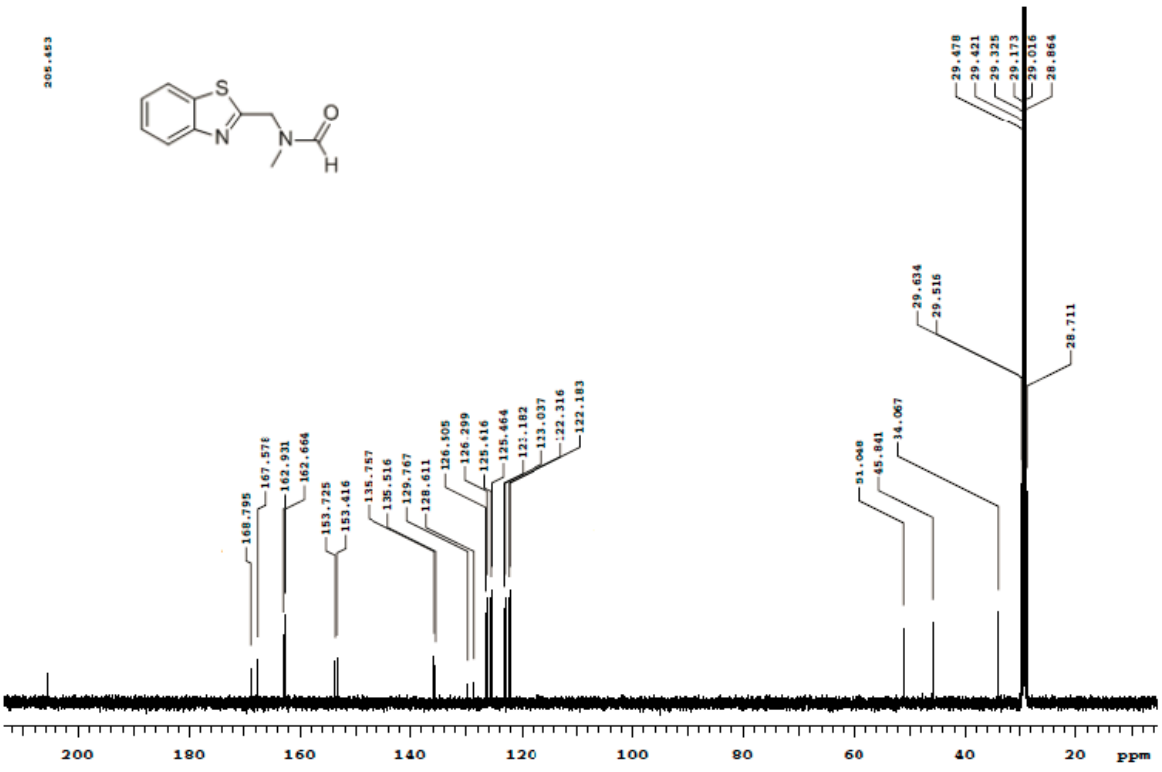
3.84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29.516
28.711
168.795
167.578
162.931
162.664
153.725
153.416
135.757
135.516
129.767
128.611
126.105
126.299
125.416
125.464
123.182
123.037
122.316
122.183
51.048
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S
N
O
N
H
200
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140
120
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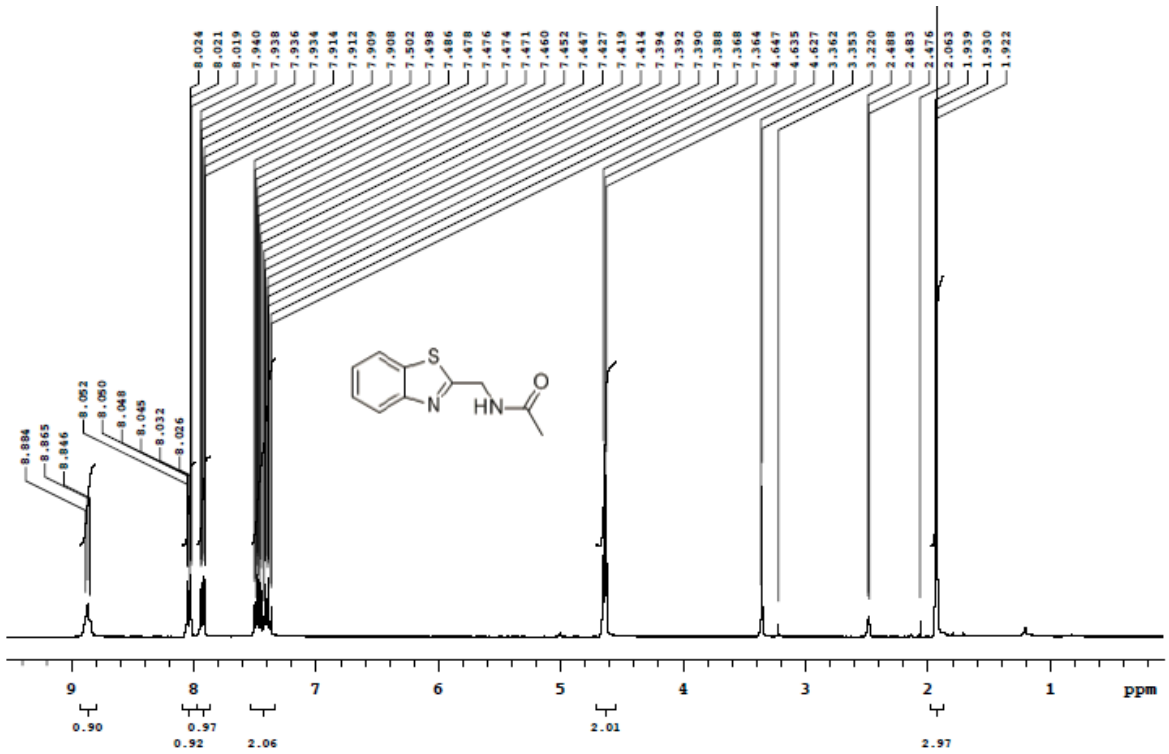
60
40
20
ppm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7.486
7.478
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7.474
7.471
7.460
7.452
7.447
7.427
7.419
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7.394
7.392
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7.388
7.368
7.364
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4.635
4.627
3.362
3.353
3.220
2.488
2.483
2.476
2.063
1.939
1.930
1.922
8.884
8.865
8.846
8.052
8.050
8.048
8.045
8.032
8.026
S
N
HN
O
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4
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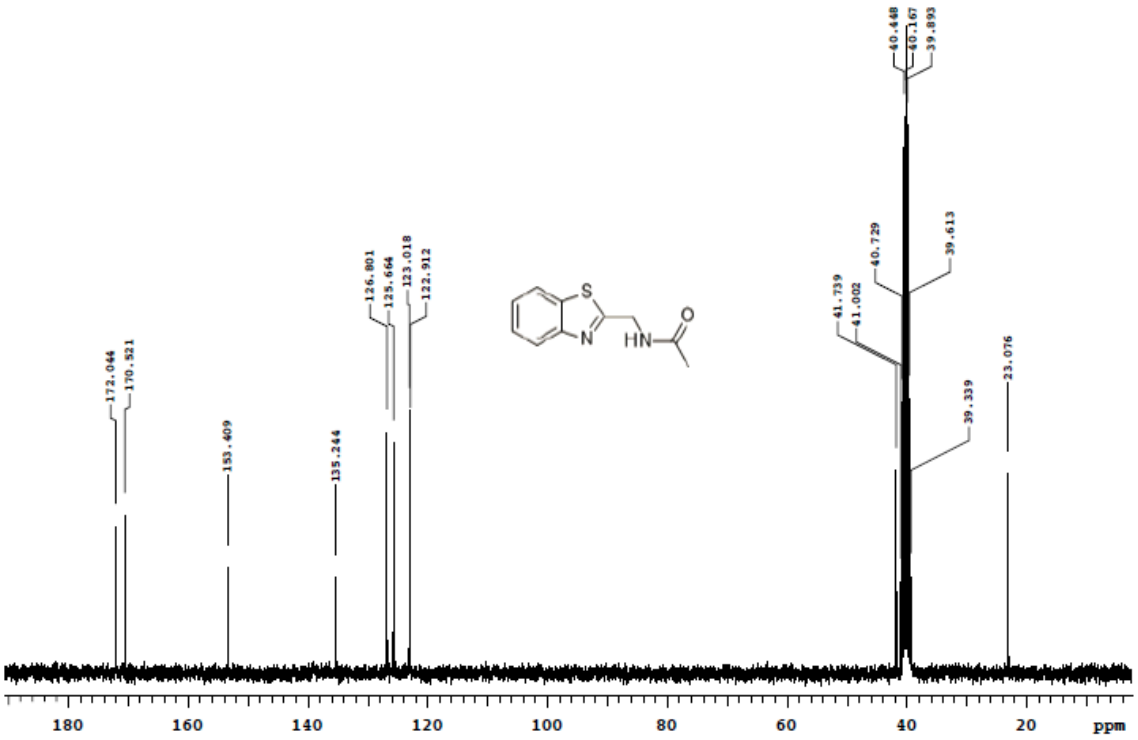
2.97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153.409
135.244
126.801
125.664
123.018
122.912
40.448
40.167
39.893
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41.002
40.729
39.613
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23.076
S
N
HN
O
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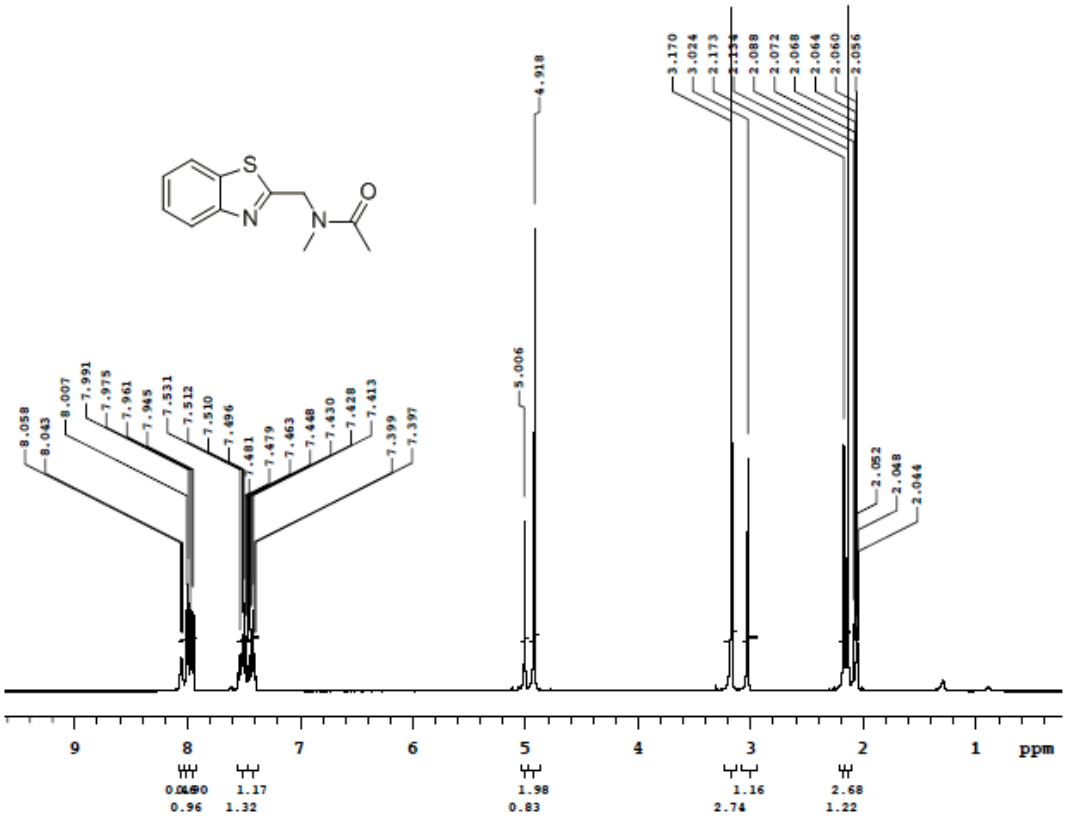
160
140
120
100
80
60
40
20
ppm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7.531
7.512
7.510
7.496
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7.479
7.463
7.448
7.430
7.428
7.413
7.399
7.397
5.006
4.918
3.170
3.024
2.173
2.131
2.088
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2.064
2.060
2.056
2.052
2.048
2.044
9
8
7
6
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ppm
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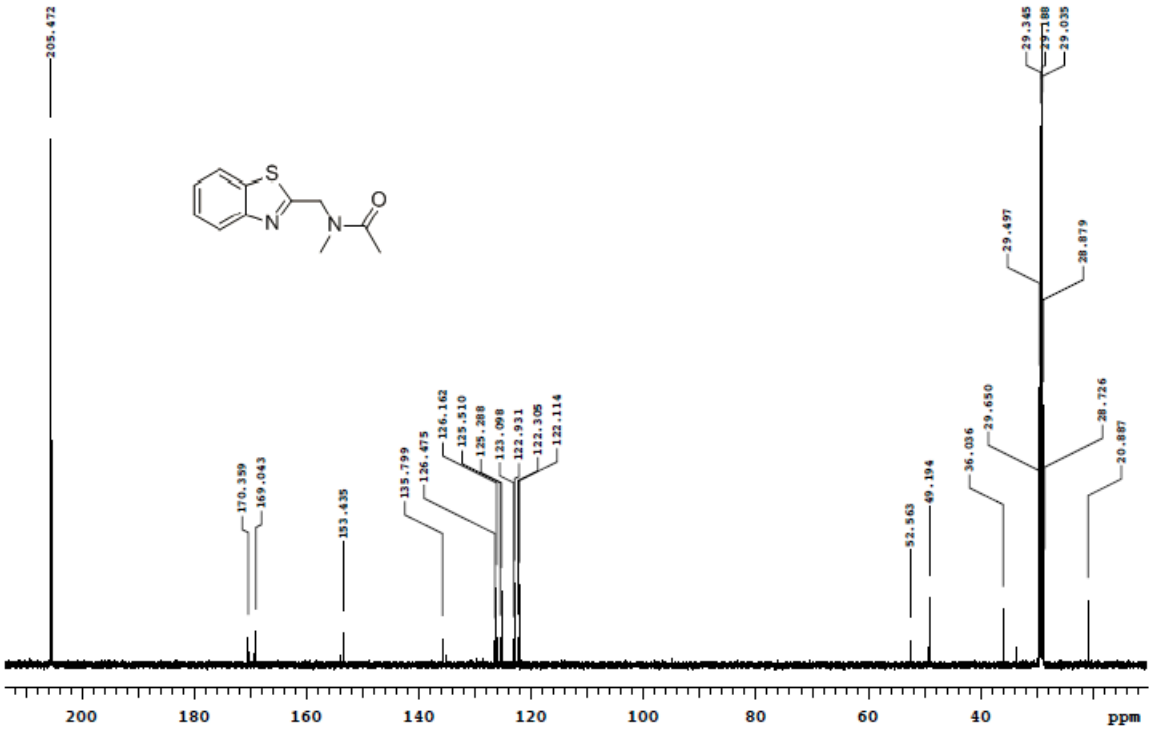
2.68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125.510
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122.931
122.305
122.114
52.563
49.194
36.036
29.650
29.497
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40
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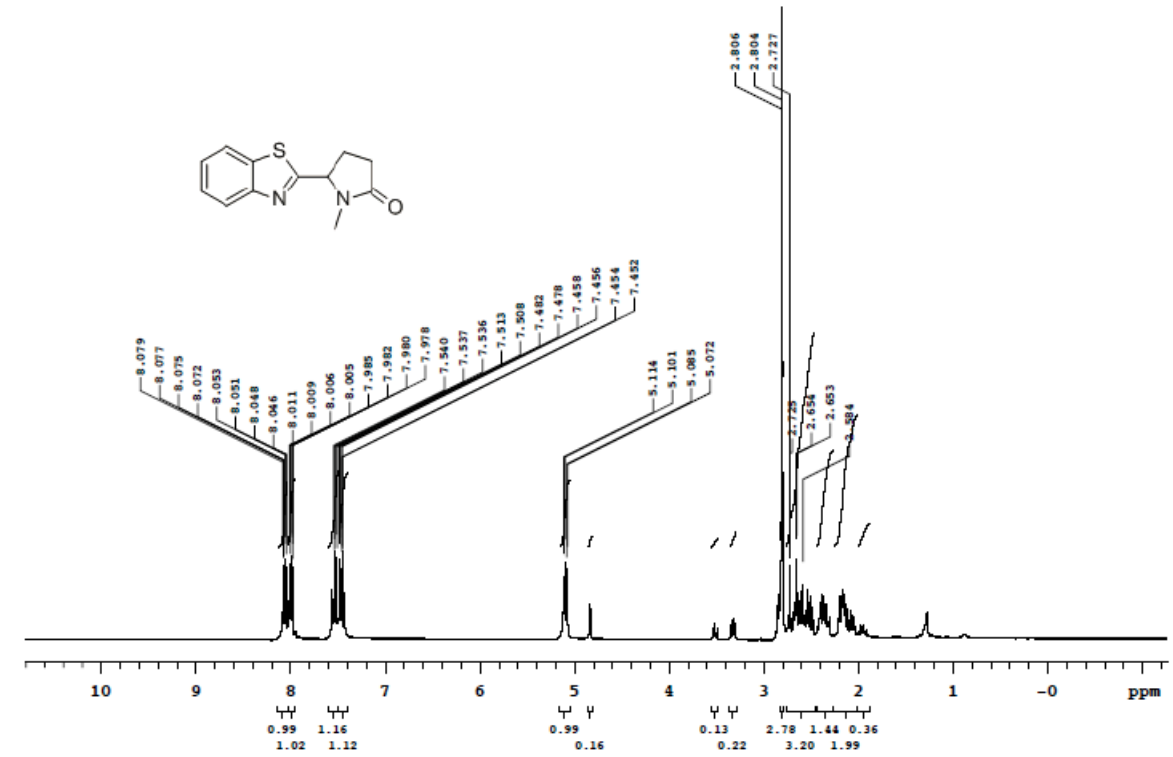
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7.980
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7.536
7.513
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7.458
7.456
7.454
7.452
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5.101
5.085
5.072
2.806
2.804
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2.725
2.654
2.653
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9
8
7
6
5
4
3
2
1
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ppm
0.99
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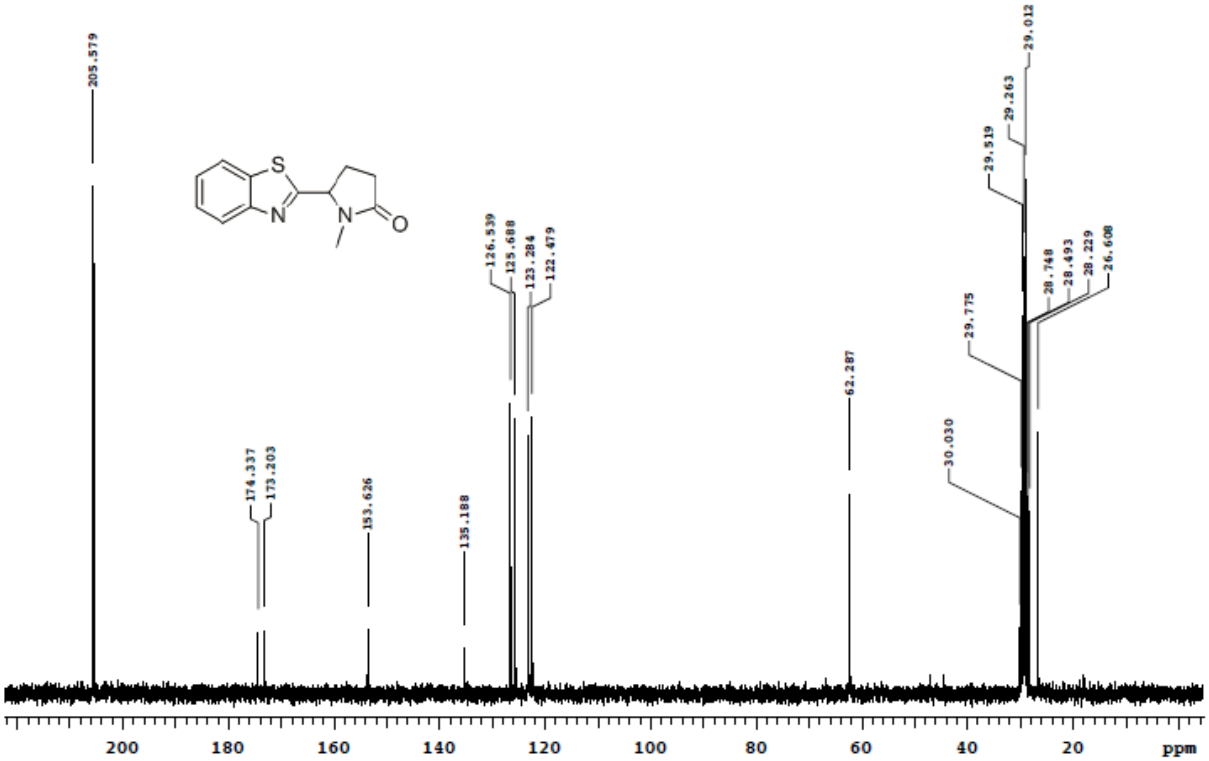
1.99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29.519
29.263
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26.608
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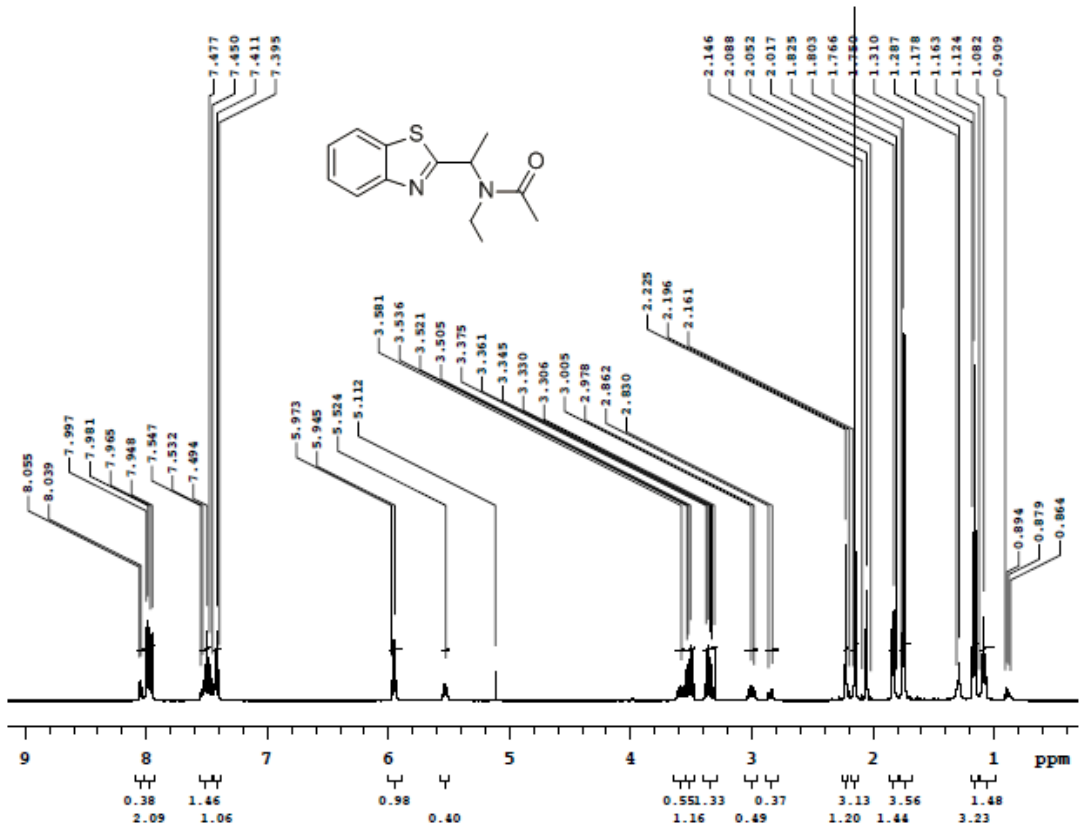
20
ppm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7.494
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5.524
5.112
3.581
3.536
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3.361
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3.306
3.005
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2.830
2.225
2.196
2.161
2.146
2.088
2.052
2.017
1.825
1.803
1.766
1.310
1.287
1.178
1.163
1.124
1.082
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0.894
0.879
0.864
S
N
O
9
8
7
6
5
4
3
2
1
ppm
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1.46
1.06
0.98
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1.33
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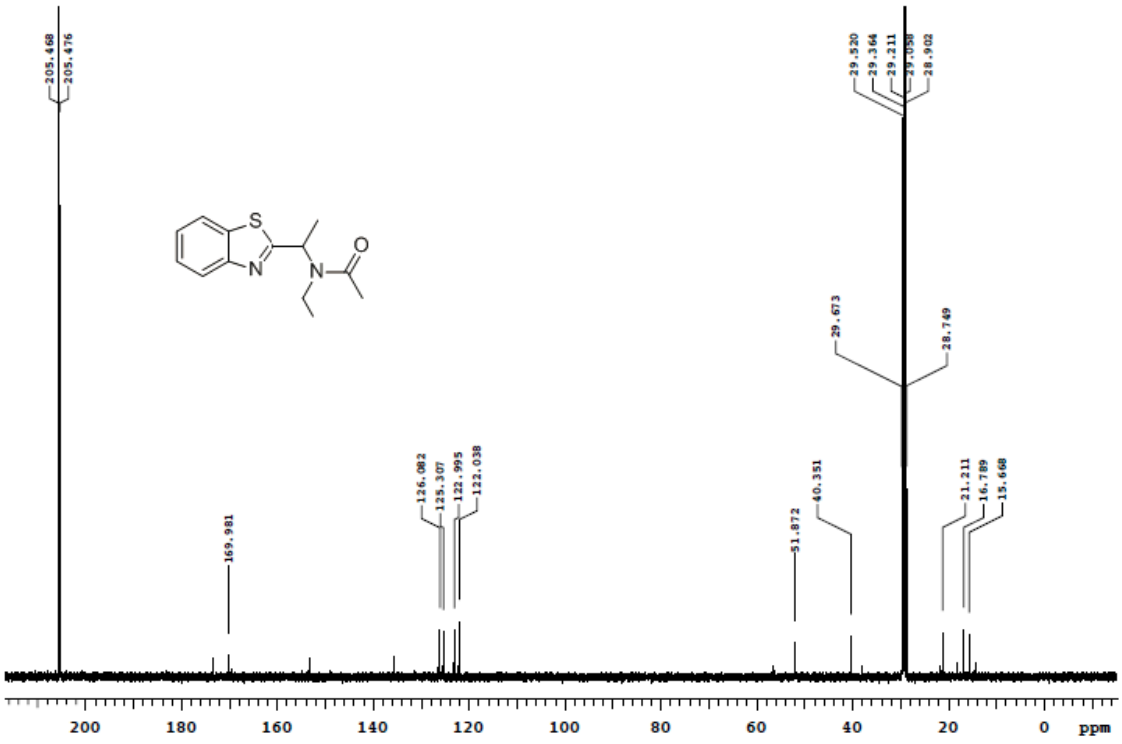
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122.038
51.872
40.351
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N
O
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120
100
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60
40
20
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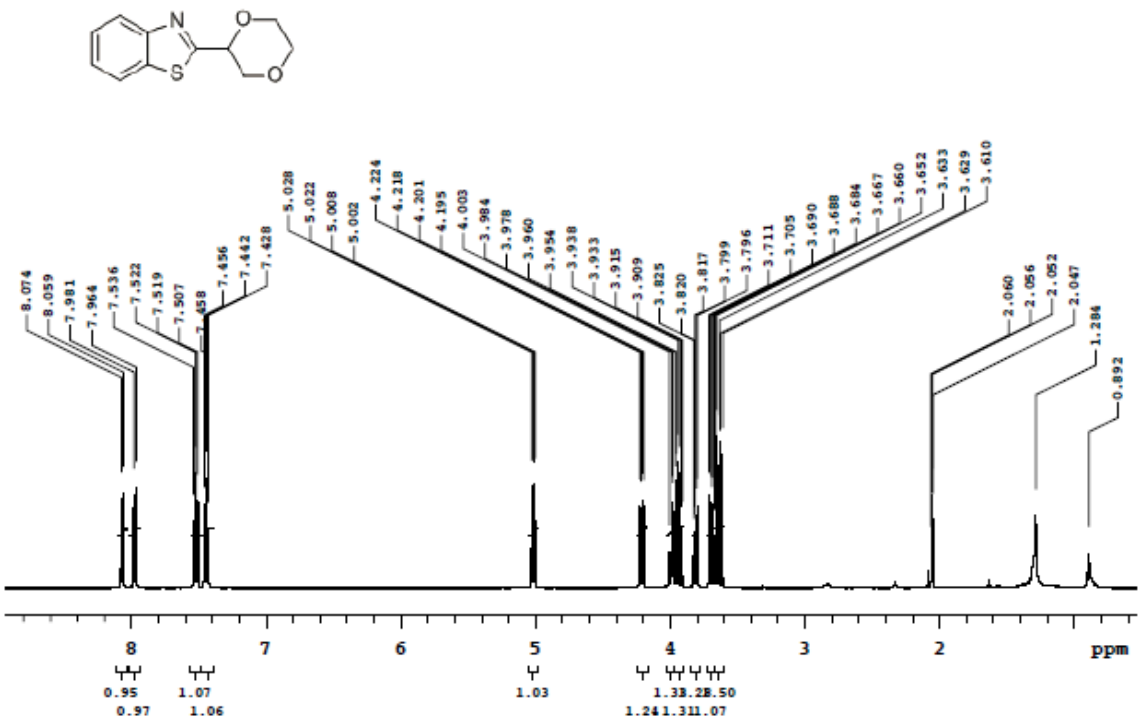
ppm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7.442
7.428
5.028
5.022
5.008
5.002
4.224
4.218
4.201
4.195
4.003
3.984
3.978
3.960
3.954
3.938
3.933
3.915
3.909
3.825
3.820
3.817
3.799
3.796
3.711
3.705
3.690
3.688
3.684
3.667
3.660
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3.633
3.629
3.610
2.060
2.056
2.052
2.047
1.284
0.892
8
7
6
5
4
3
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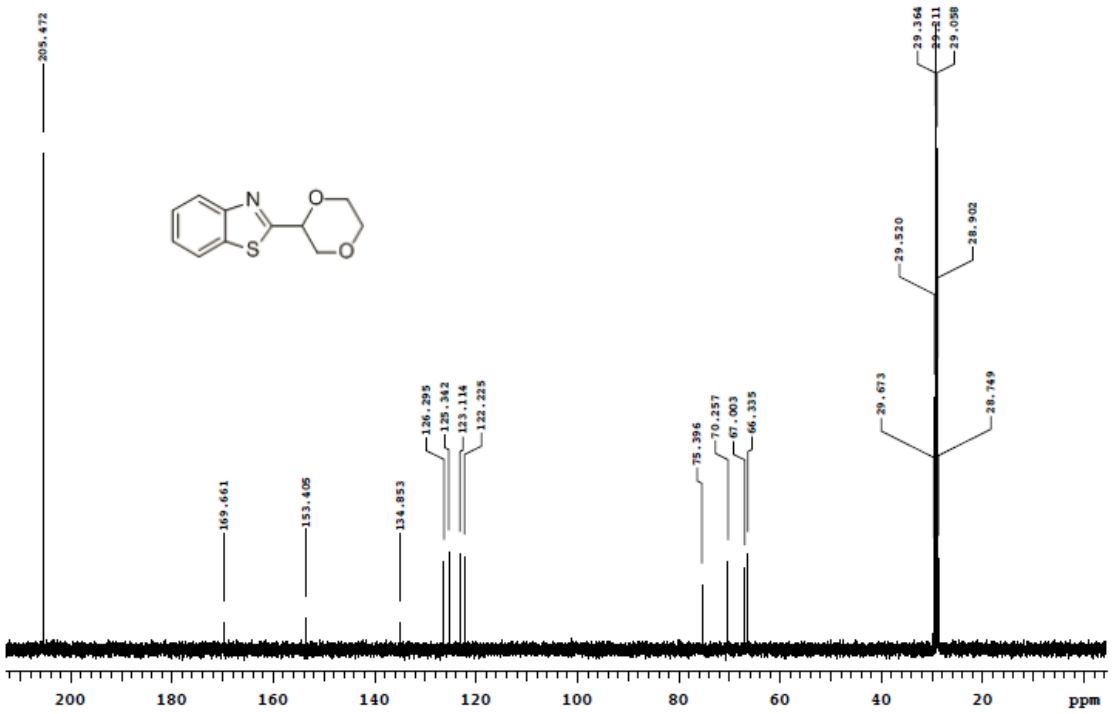
1.50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123.114
122.225
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70.257
67.003
66.335
29.364
29.211
29.058
29.520
28.902
29.673
28.749
200
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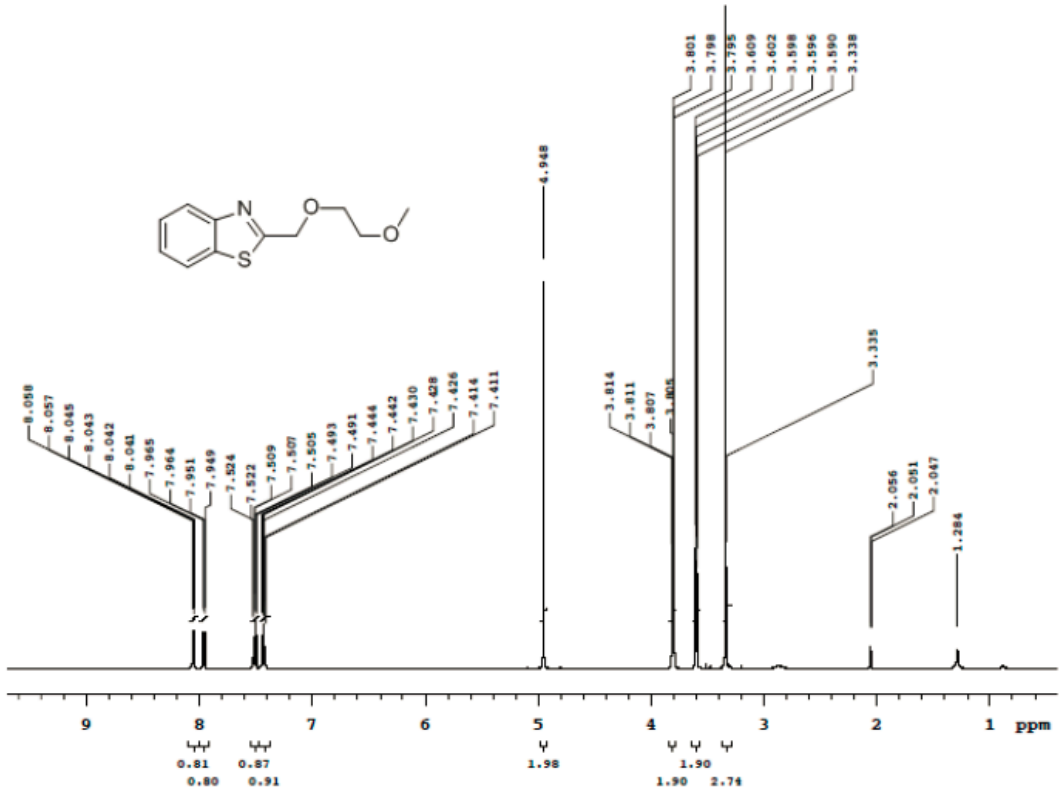
140
120
100
80
60
40
20
ppm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7.964
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7.949
7.524
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7.509
7.507
7.505
7.493
7.491
7.444
7.442
7.430
7.428
7.426
7.414
7.411
4.948
3.814
3.811
3.807
3.801
3.798
3.795
3.609
3.602
3.598
3.596
3.590
3.338
3.335
2.056
2.051
2.047
1.284
9
8
7
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2
1
ppm
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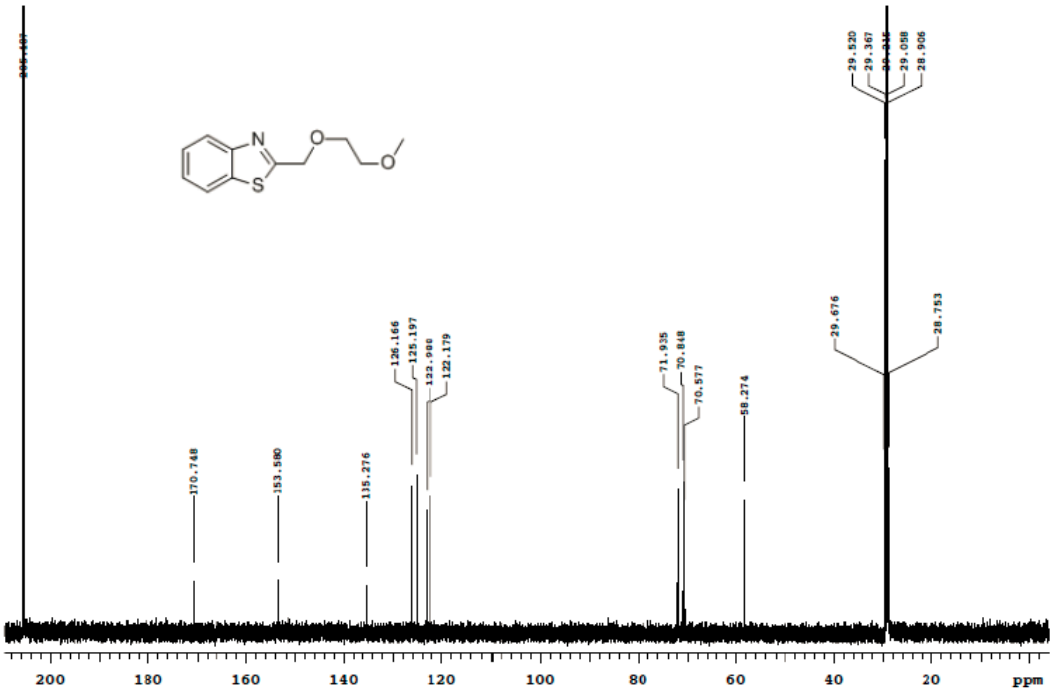
1.90
2.74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122.179
71.935
70.848
70.577
58.274
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29.367
29.058
28.906
28.753
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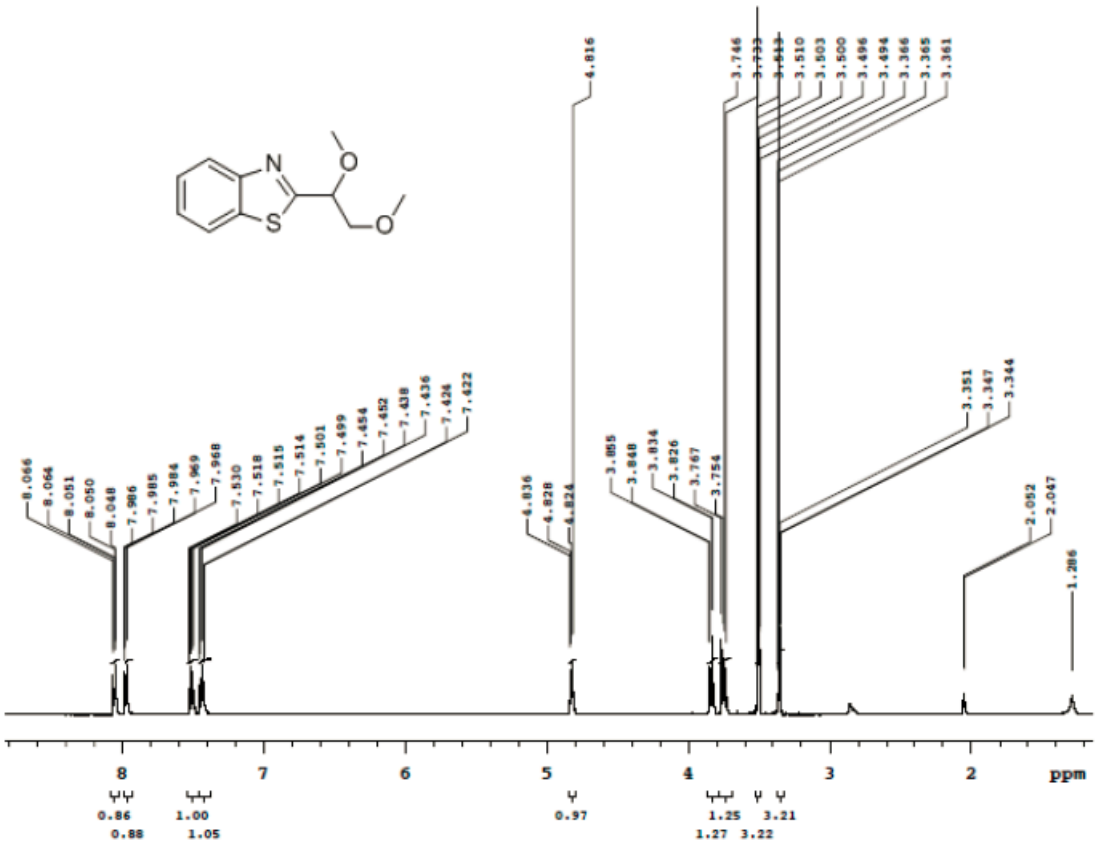
140
120
100
80
60
40
20
ppm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7.515
7.514
7.501
7.499
7.454
7.452
7.438
7.436
7.424
7.422
4.836
4.828
4.824
4.816
3.885
3.848
3.834
3.826
3.767
3.754
3.746
3.733
3.513
3.510
3.503
3.500
3.496
3.494
3.366
3.365
3.361
3.351
3.347
3.344
2.052
2.047
1.286
8
7
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1.05
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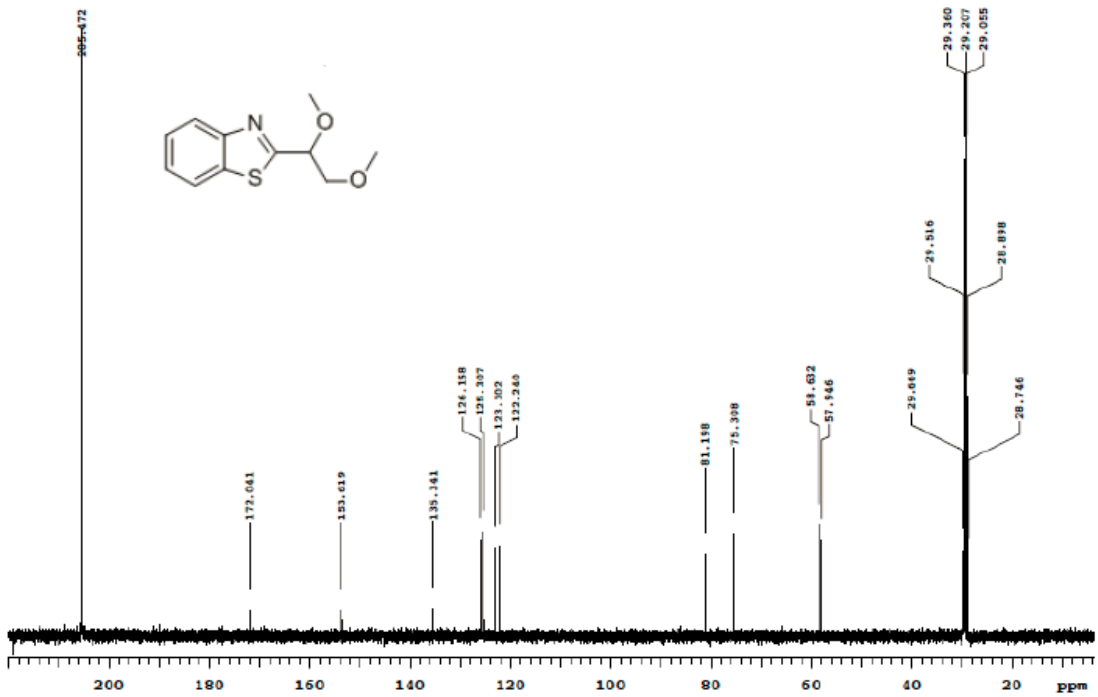
3.22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123.307
123.302
122.249
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75.398
59.632
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29.360
29.207
29.055
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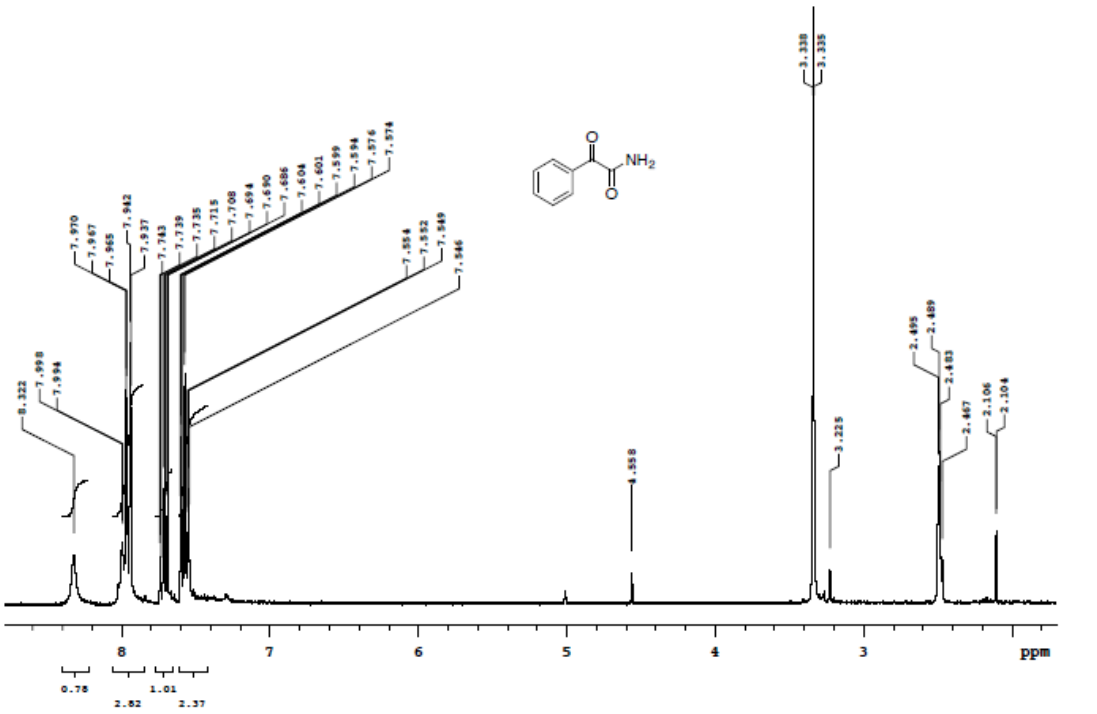
20.898
29.649
28.746
200
180
160
140
120
100
80
60
40
20
ppm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O
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7.967
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7.937
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7.739
7.735
7.715
7.708
7.694
7.690
7.686
7.604
7.601
7.599
7.594
7.576
7.574
7.554
7.552
7.549
7.546
4.558
3.338
3.335
3.225
2.495
2.489
2.483
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2.104
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2.82
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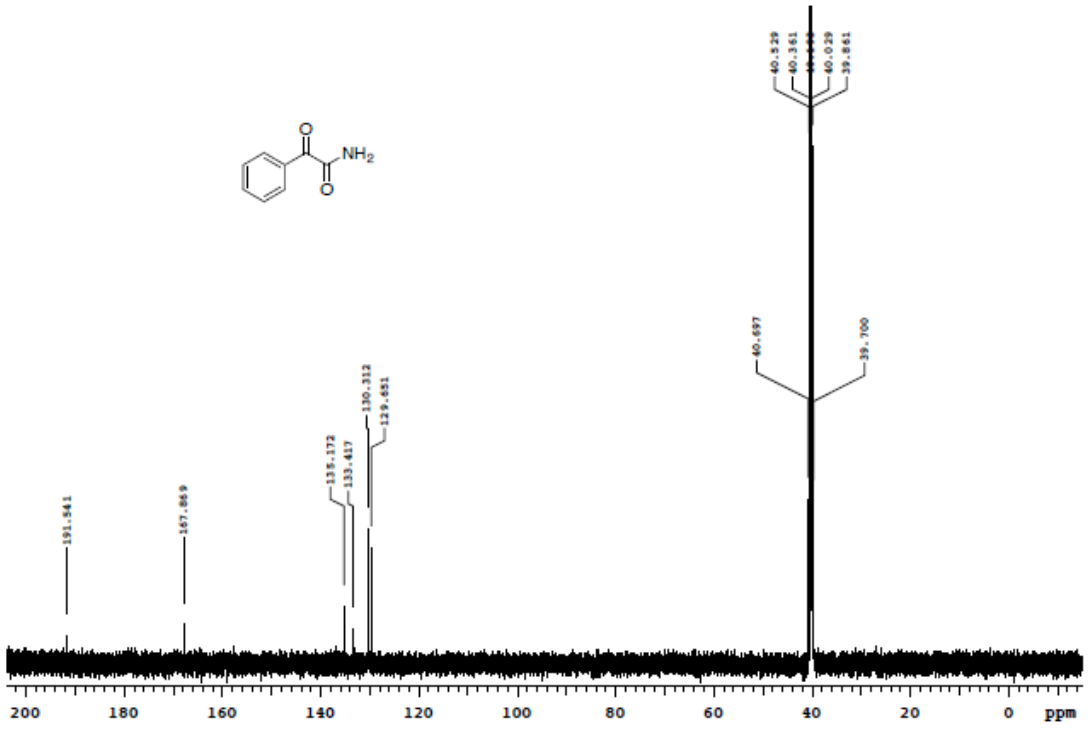
5
4
3
ppm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O
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129.651
40.529
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40.697
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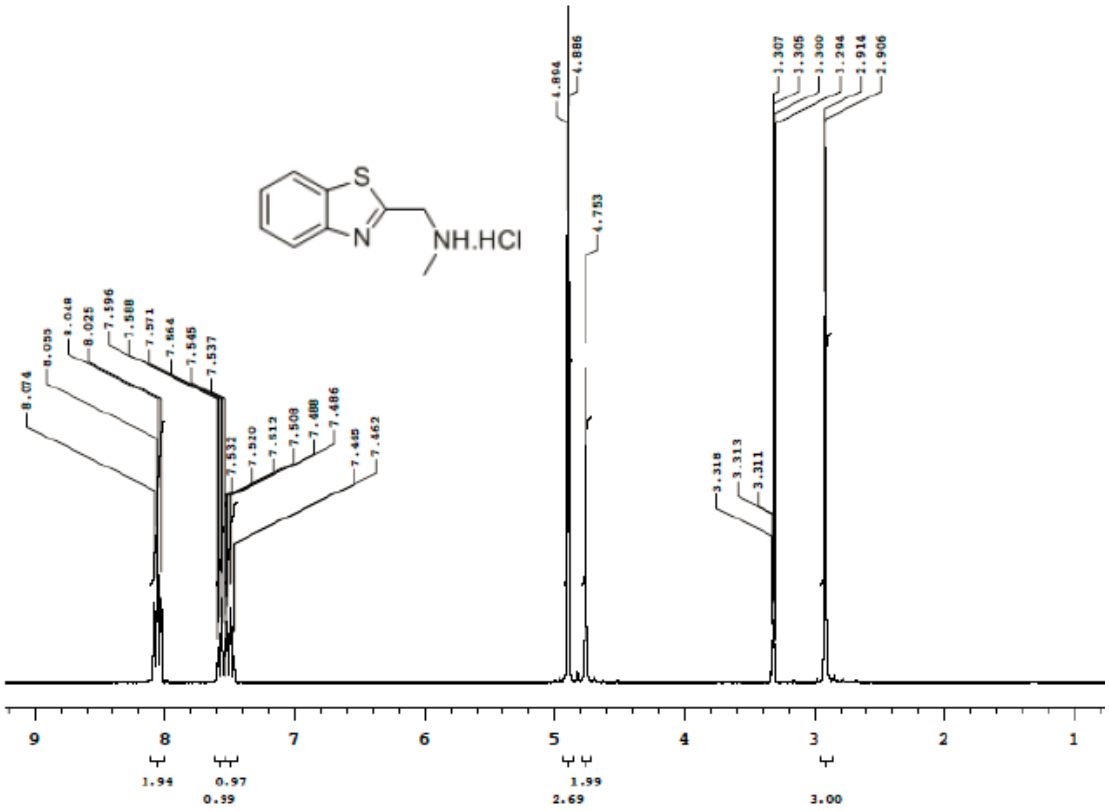
120
100
80
60
40
20
0
ppm


S
N
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7.588
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7.545
7.537
7.533
7.520
7.512
7.508
7.488
7.486
7.465
7.462
4.864
4.886
4.753
3.318
3.313
3.311
3.307
3.305
3.300
3.294
2.914
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6
5
4
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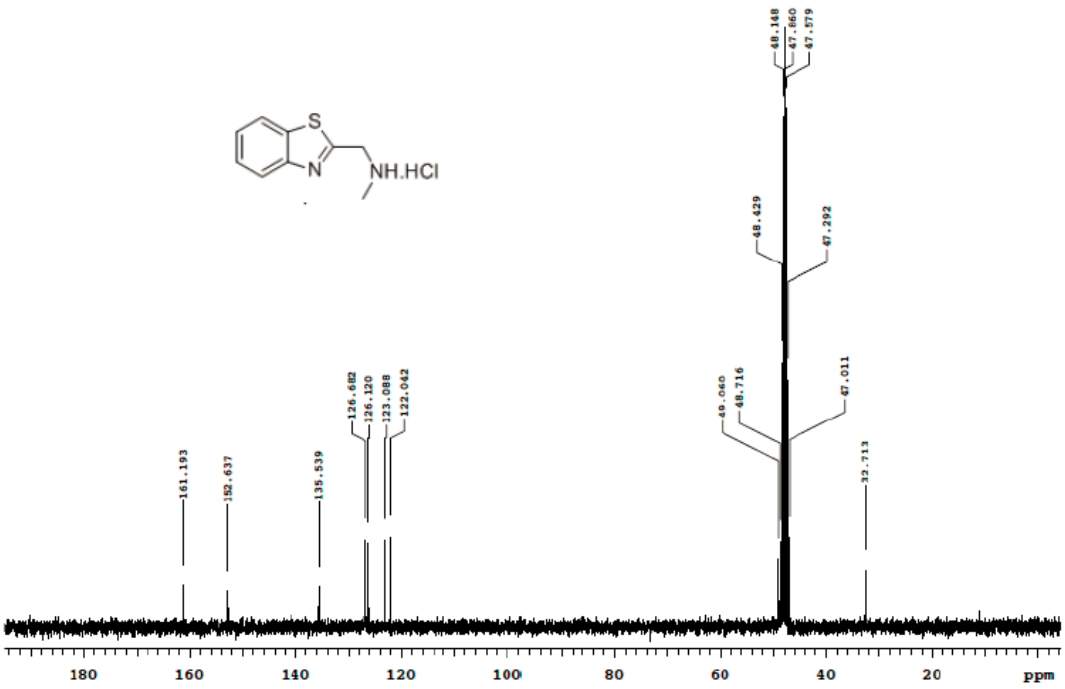
3.00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47.011
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140
120
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40
20
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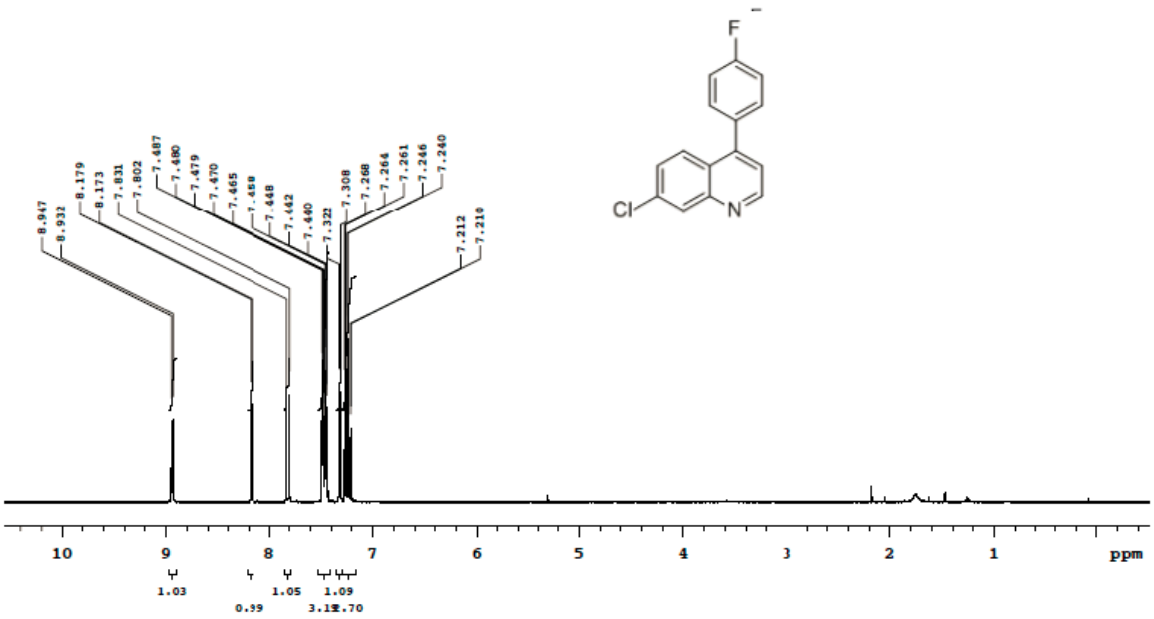
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Cl
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7.470
7.465
7.458
7.448
7.442
7.440
7.322
7.308
7.268
7.264
7.261
7.246
7.240
7.212
7.210
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5
4
3
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1.09
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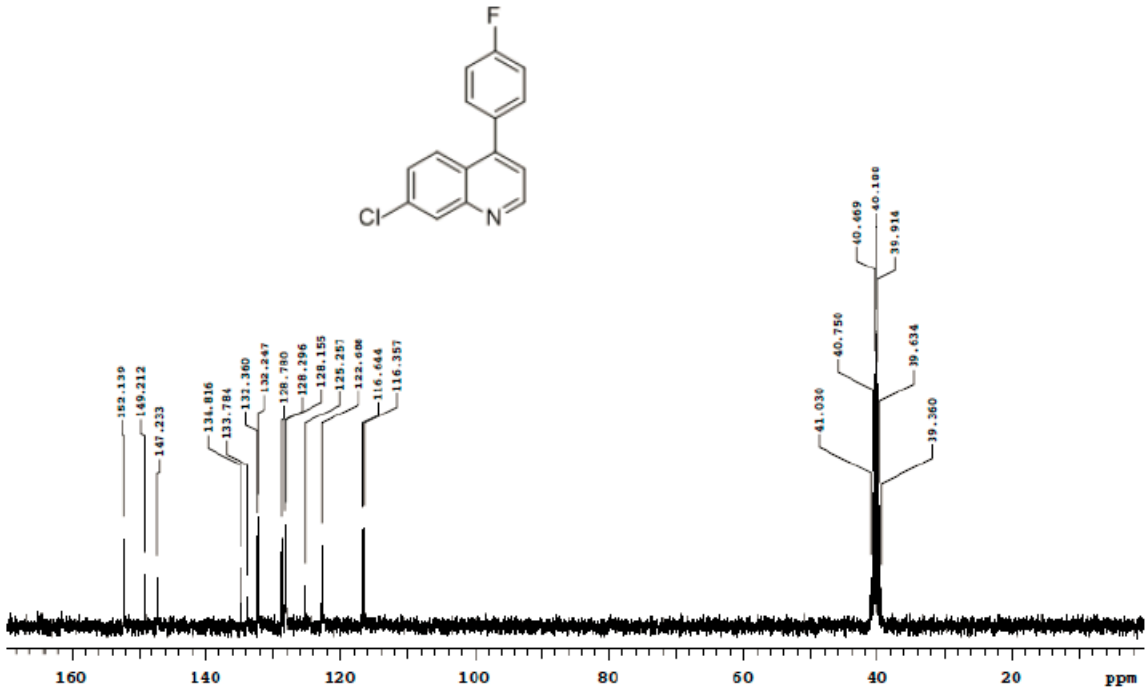
2.70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128.296
128.155
125.257
122.608
116.644
116.357
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140
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20
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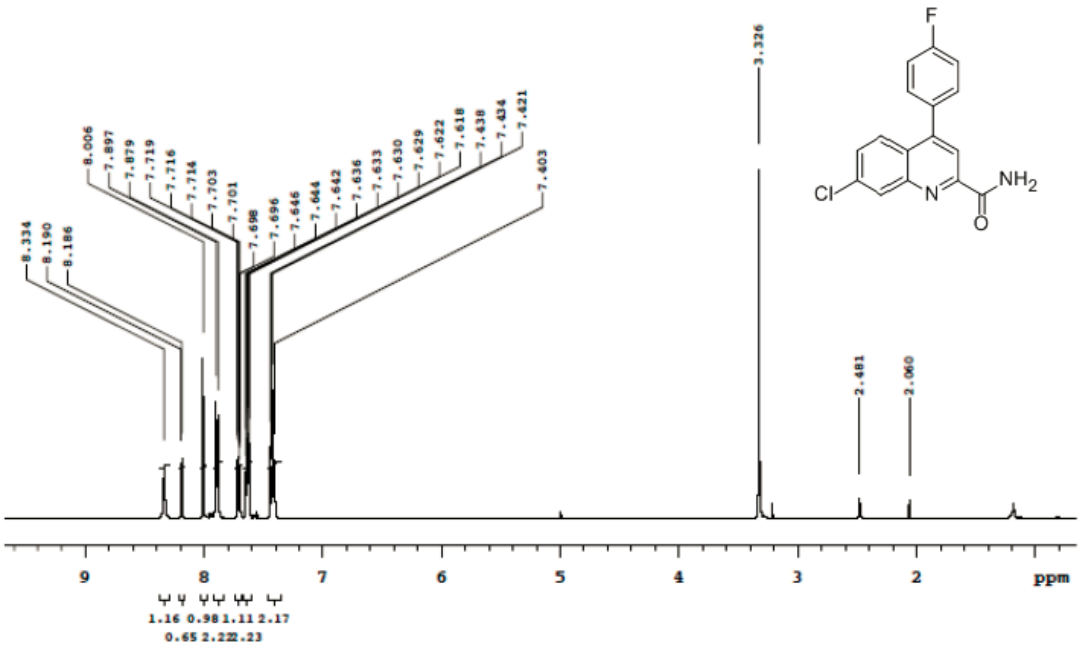
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Cl
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O
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7.879
7.719
7.716
7.714
7.703
7.701
7.698
7.696
7.646
7.644
7.642
7.636
7.633
7.630
7.629
7.622
7.618
7.438
7.434
7.421
7.403
3.326
2.481
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8
7
6
5
4
3
2
ppm
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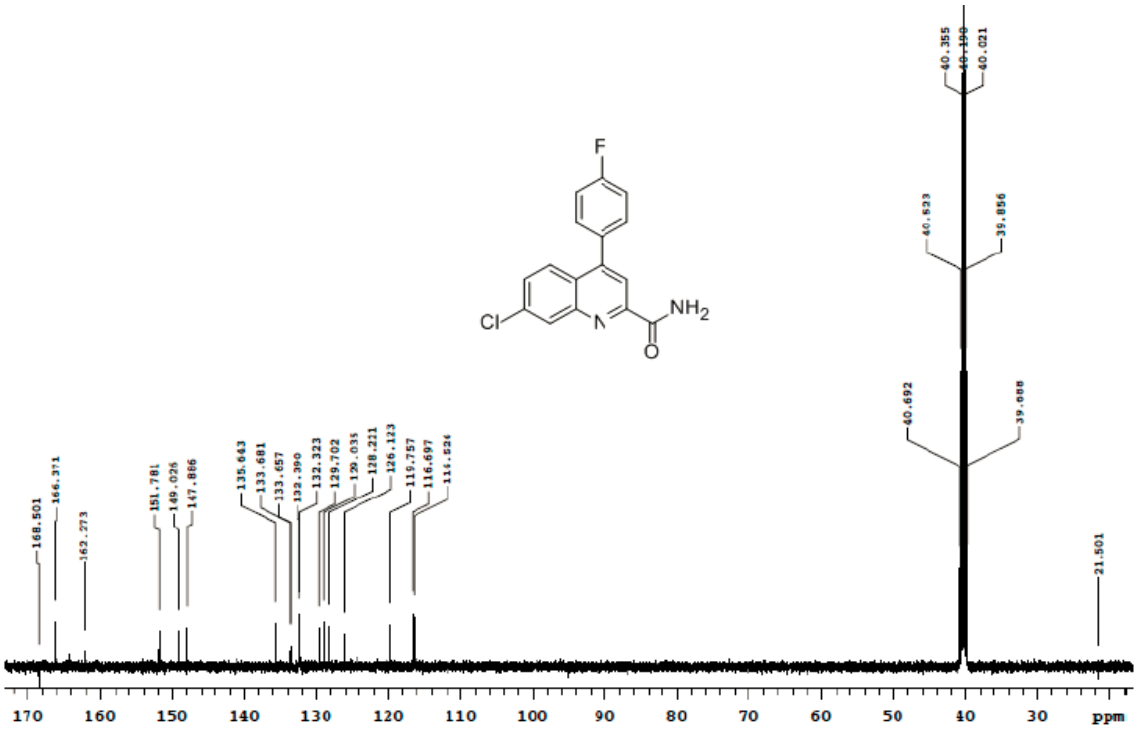
0.65 2.22 2.23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O
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149.026
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135.643
133.681
133.657
132.390
132.323
129.702
129.035
128.221
126.123
119.757
116.697
114.824
40.355
40.190
40.021
40.523
39.856
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100
90
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30
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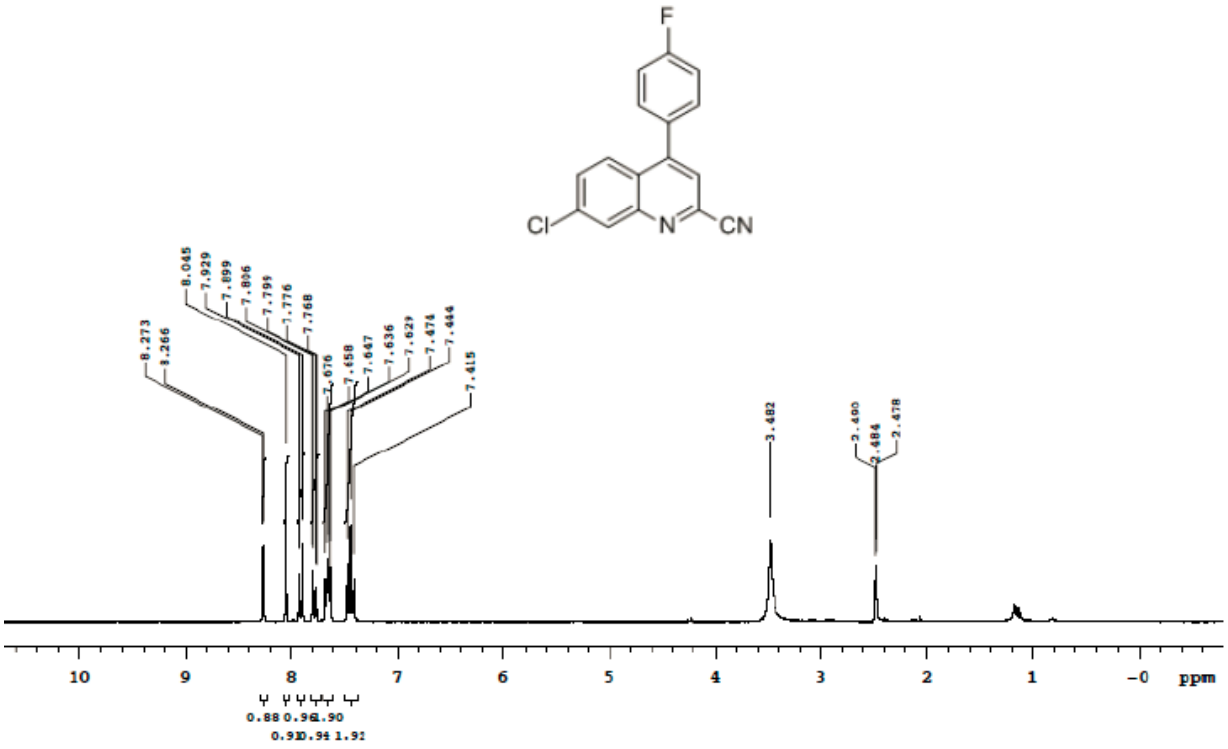
F
Cl
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CN
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7.896
7.795
7.776
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7.658
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7.636
7.629
7.474
7.444
7.415
3.482
2.490
2.484
2.478
10
9
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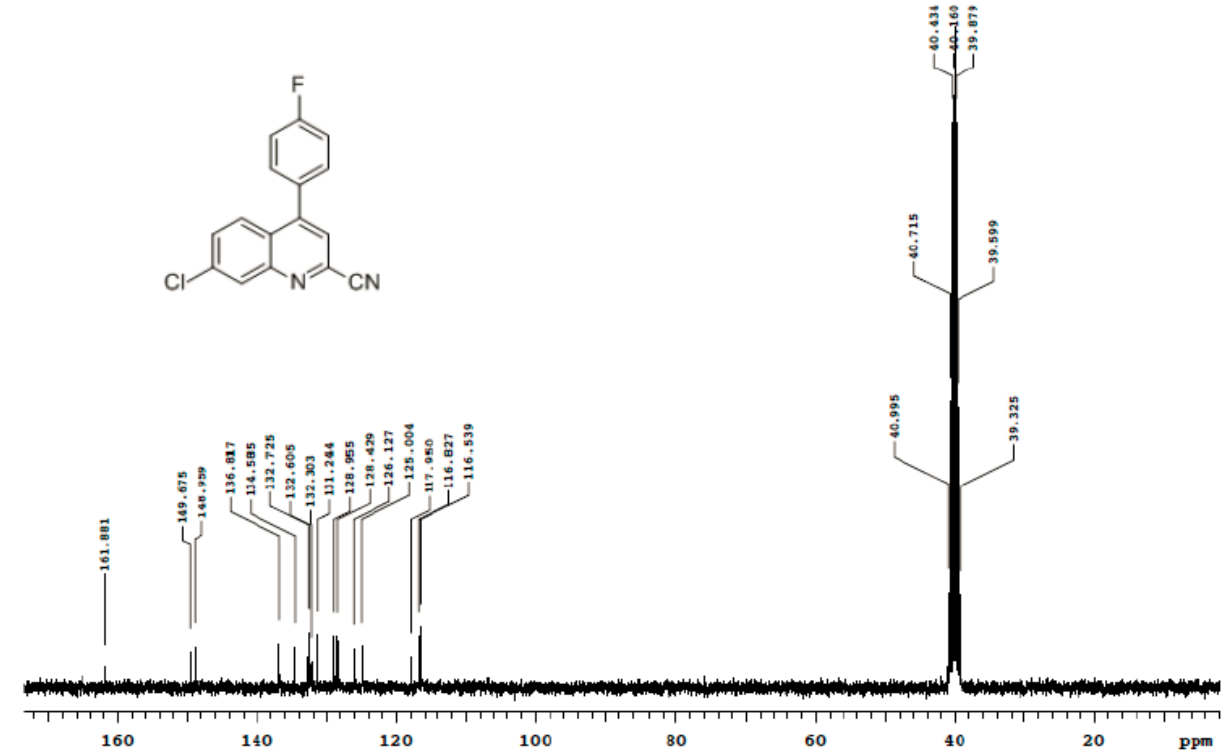
1.91


F
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132.725
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132.303
131.244
128.955
128.429
126.127
125.004
117.950
116.827
116.539
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40.715
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40.995
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140
120
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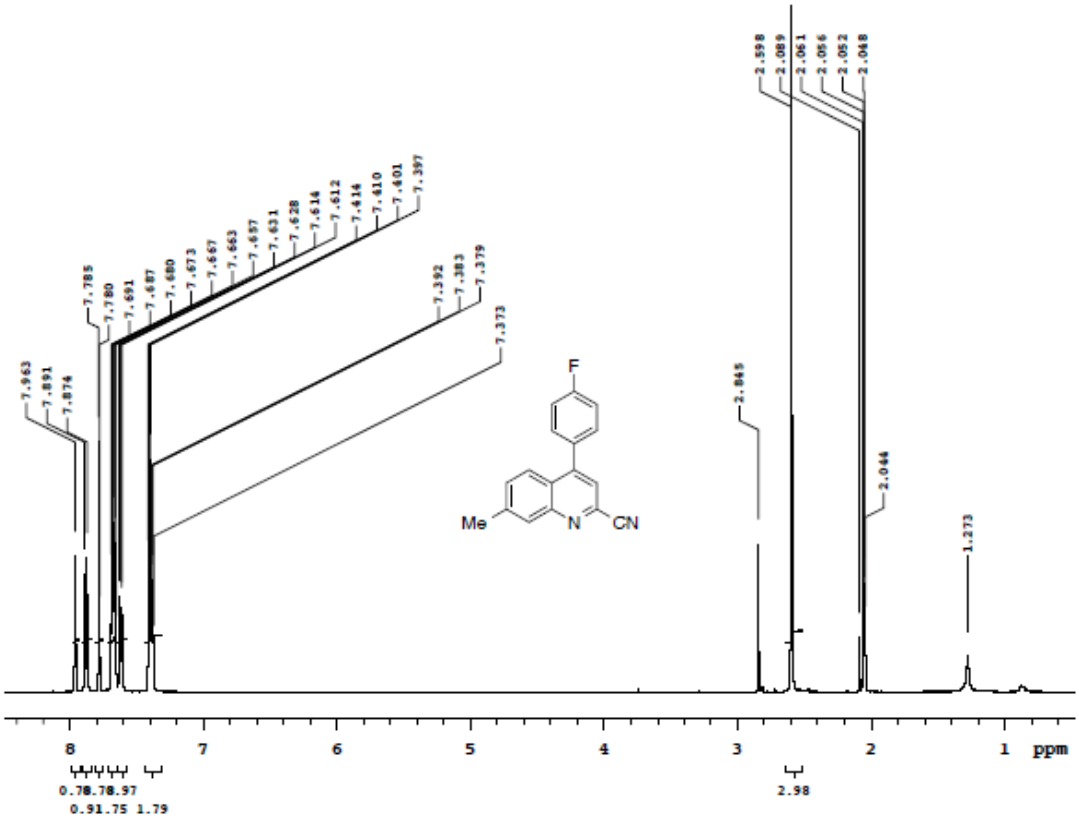
40
20
ppm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7.663
7.657
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7.628
7.614
7.612
7.414
7.410
7.401
7.397
7.392
7.383
7.379
7.373
2.598
2.089
2.061
2.056
2.052
2.048
2.845
2.044
1.273
F
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CN
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6
5
4
3
2
1
ppm
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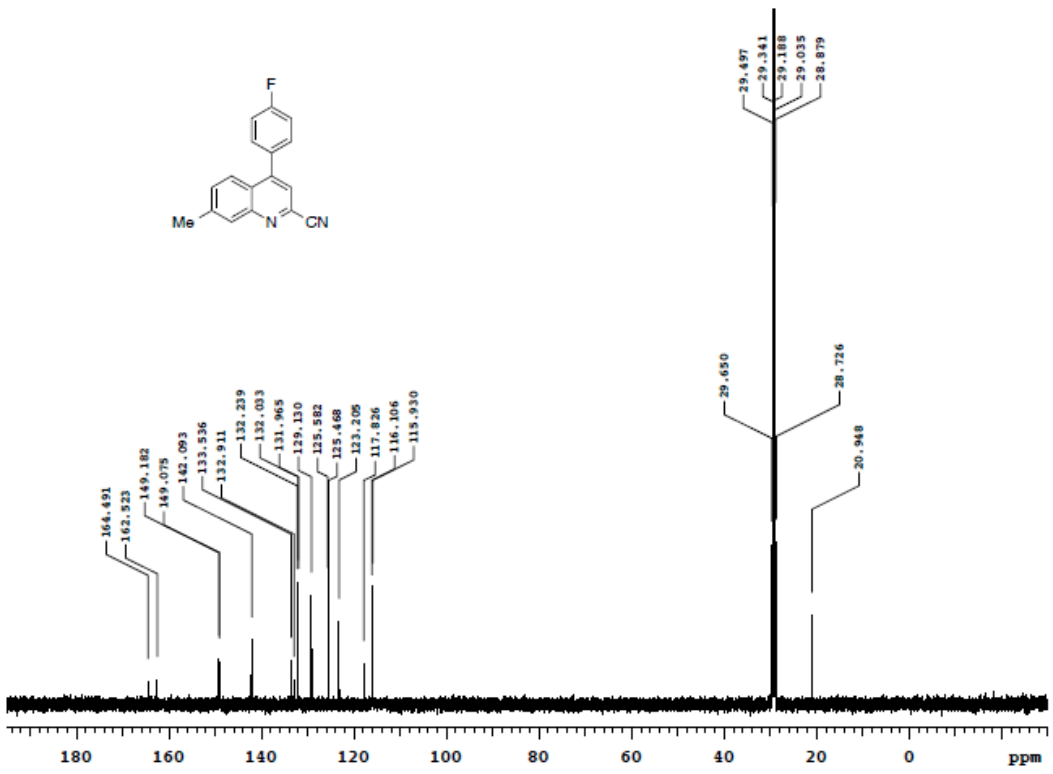
0.91 1.75 1.79
2.98


F
Me
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CN
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29.650
28.726
20.948
164.491
162.523
149.182
149.075
142.093
133.536
132.911
132.239
132.033
131.965
129.130
125.582
125.468
123.205
117.826
116.106
115.930
180
160
140
120
100
80
60
40
20
0
ppm