Palladium-Catalyzed Benzylation of Heterocyclic Aromatic Compounds

David Lapointe, and Keith Fagnou*

Centre for Catalysis Research and Innovation, Department of Chemistry, University of Ottawa,

10 Marie Curie, Ottawa, ON K1N 6N5, Canada

keith.fagnou@uottawa.ca

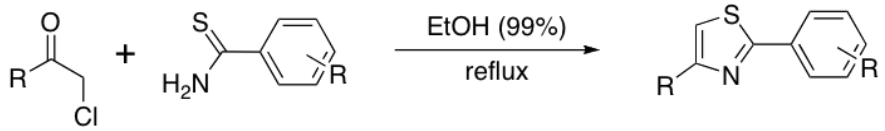
Supporting Information

General Considerations

^{1}H and ^{13}C NMR spectra were recorded using Bruker Avance 300 MHz or 400 MHz spectrometers. High-resolution mass spectra were obtained on a Kratos Concept IIH mass spectrometer. Infra-red analysis was performed with a Bruker EQUINOX 55 Fourier-Transform IR spectrometer. $Pd(OPiv)_2$ was prepared according to literature procedures.[i] $Pd(OPiv)_2$ and 2-(diphenylphosphino)-2'-(N,N-dimethylamino)biphenyl[ii] were stored in the desiccator and were weighed to air. Unless otherwise stated, all other reagents and solvents were used without further purification. Ethyl indolizine-2-carboxylate,[iii] 2-methylindolizine,[iv] 2-(4-methoxyphenyl)imidazo[1,2-a]pyrimidine,[v] 4-butyl-1-phenyl-1,2,3-triazole[vi] and 2-phenyloxazole[vii] were synthesized according to literature procedures and exhibited identical spectral data to previous reports.

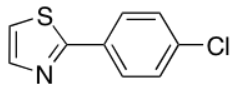
General Procedures

General procedure for the direct benzylation of heterocycles. $Pd(OPiv)_2$ (2 or 5 mol%), 2-Ph_2P-2'-(Me_2N)biphenyl (4 or 10 mol%), Cs_2CO_3 (1.5 equiv.) and PivOH (20 mol%) are weighed to air and placed in a screw-cap vial equipped with a magnetic stir bar. The heterocycle (1 equiv.), if a solid is then added at that point. The vial is purged with argon and a solution of the benzyl chloride (1.5 or 2.0 equiv.) in degassed toluene (0.5 M) is added to the mixture. The reaction mixture is then stirred vigorously at 110 °C for 16 to 24 hours. The solution is then cooled to ambient temperature, diluted with ethyl acetate, then filtered and evaporated under reduced pressure. The crude product is purified by silica gel column chromatography to afford the corresponding product.

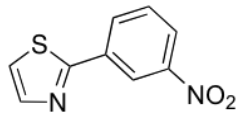


General procedure for the preparation of the 2-aryl and 3- substituted thiazole.[viii] Thioamide (3,0 mmol), a-chloro ketone (3,6 mmol) are weighed to air and placed in a round bottom flask equipped with a magnetic stir bar and a reflux condenser. Ethanol (99%, 1 M) is then added and the mixture is heated to reflux until full consumption of the thioamide as judge by TLC (~1 hour). The mixture is then evaporated under reduced pressure. The crude product is purified by silica gel column chromatography to afford the corresponding product.

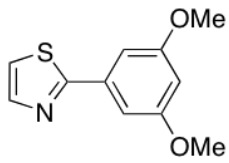
Characterization of Starting Materials



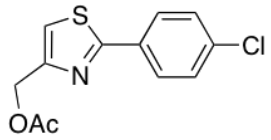
2-(4-chlorophenyl)thiazole. Synthesized according to the general procedure of thiazole synthesis. Brown solid; mp 32-34 °C; R_f 0.35 (petroleum ether/ethyl acetate 80/20); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (dt, J = 8.7, 2.0 Hz, 2H), 7.86 (d, J = 3.3 Hz, 1H), 7.42 (dt, J = 8.7, 2.0 Hz, 1H), 7.34 (d, J = 3.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.9, 143.7, 135.8, 132.0, 129.1, 127.7, 119.0; IR (ν_{max}) 3121, 3081, 2047, 1249,1146, 1014, 974, 831 cm^{-1}; HRMS Calcd for C_9H_6ClNS (M^+) 194.9909, Found 194.9924.



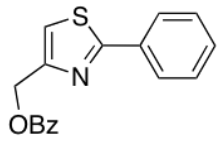
2-(3-nitrophenyl)thiazole. Synthesized according to the general procedure of thiazole synthesis. Yellow solid; mp 94-97 °C; R_f 0.33 (petroleum ether/ethyl acetate 80/20); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.82 (t, J = 2.0 Hz, 1H), 8.31 (dt, J = 6.6, 1.2 Hz, 1H), 8.28 (ddd, J = 8.2, 2.1, 0.9 Hz, 1H), 7.95 (d, J = 3.2 Hz, 1H), 7.65 (t, J = 8.0 Hz, 1H), 7.46 (d, J = 3.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.4, 148.7, 144.2, 135.1, 132.1, 130.0, 124.3, 121.4, 120.2; IR (ν_{max}) 3128, 3039, 2049, 1534, 1249, 611 cm^{-1}; HRMS Calcd for $C_9H_6N_2O_2S$ (M^+) 206.0150, Found 206.0166.



2-(3,5-dimethoxyphenyl)thiazole. Synthesized according to the general procedure of thiazole synthesis. Pale yellow oil; R_f 0.30 (petroleum ether/ethyl acetate 80/20); ^{1}H NMR (400 MHz, CDCl3) δ 7.86 (d, *J* = 3.3 Hz, 1H), 7.32 (d, *J* = 3.3 Hz, 1H), 7.13 (d, *J* = 2.3 Hz, 2H), 6.53 (t, *J* = 2.3 Hz, 1H), 3.86 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.3, 161.1, 143.5, 135.3, 119.0, 104.5, 102.5, 55.6; IR (ν_{max}) 1595, 1457, 1427, 1206, 1157, 1062, 1024, 808 cm^{-1}; HRMS Calcd for $C_9H_6N_2O_2S$ (M^+) 221.0510, Found 221.0492.



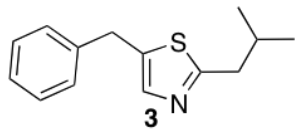
(2-(4-chlorophenyl)thiazol-4-yl)methyl acetate. Synthesized according to the general procedure of thiazole synthesis. Pale yellow solid; mp 52-55 °C; R_f 0.41 (petroleum ether/ethyl acetate 80/20); ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 7.89 (d, *J* = 8.8 Hz, 2H), 7.41 (d, *J* = 8.8 Hz, 2H), 7.30 (s, 1H), 5.25 (s, 2H), 2.14 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 170.6, 167.3, 152.3, 136.1, 131.8, 129.1, 127.8, 117.7, 61.7, 20.9; IR (ν_{max}) 3106, 3036, 1737, 1247, 837, 607 cm^{-1}; HRMS Calcd for $C_{12}H_{10}ClNO_2S$ (M^+) 267.0121, Found 267.0069.



(2-phenylthiazol-4-yl)methyl benzoate. Synthesized according to the general procedure of thiazole synthesis. Yellow solid; mp 68-70 °C; R_f 0.39 (petroleum ether/ethyl acetate 80/20); ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 8.11 (d, *J* = 7.2 Hz, 2H), 8.01-7.90 (m, 2H), 7.57 (t, *J* = 7.4 Hz, 1H), 7.51-7.40 (m, 5H), 7.36 (s, 1H), 5.54 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 168.6, 166.2, 152.3, 133.4, 133.1, 130.1, 129.9, 129.7, 128.9, 128.3, 126.6, 117.3, 62.3; IR (ν_{max}) 3120, 3069,

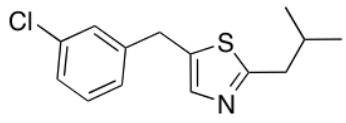
3037, 2972, 1790, 1725, 1266, 1104 cm^{-1}; HRMS Calcd for $C_{17}H_{13}NO_2S$ (M^+) 295.0667, Found 295.0653.

Characterization of Coupling Products



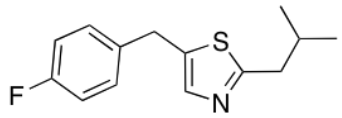
3

5-Benzyl-2-isobutylthiazole 3. Synthesized according to the general procedure. Colorless oil; R_f 0.31 (petroleum ether/ethyl acetate 80/20); ^1H NMR (400 MHz, $CDCl_3$) δ 7.36 (s, 1H), 7.34-7.27 (m, 2H), 7.23 (m, 3H), 4.10 (s, 2H), 2.79 (d, J = 7.2 Hz, 2H), 2.05 (hept, J = 6.8 Hz, 1H), 0.97 (d, J = 6.6 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.8, 139.6, 139.5, 137.5, 128.7, 128.5, 126.8, 42.5, 33.3, 29.7, 22.3; IR (ν_{max}) 3032, 2960, 2928, 2869, 1225 cm^{-1}; HRMS Calcd for $C_{14}H_{17}NS$ (M^+) 231.1082, Found 231.1076.



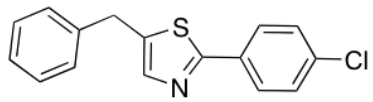
4

5-(4-Fluorobenzyl)-2-isobutylthiazole 4. Synthesized according to the general procedure. Colorless oil; R_f 0.31 (petroleum ether/ethyl acetate 80/20); ^1H NMR (400 MHz, $CDCl_3$) δ 7.35 (s, 1H), 7.21-7.14 (m, 2H), 7.03-6.95 (m, 2H), 4.07 (s, 2H), 2.79 (d, J = 7.2 Hz, 2H), 2.06 (hept, J = 6.8 Hz, 1H), 0.97 (d, J = 6.6 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.9, 161.7 (d, J = 245.0 Hz), 139.6, 137.3, 135.3 (d, J = 3.2 Hz), 129.9 (d, J = 8.0 Hz), 115.5 (d, J = 21.4 Hz), 42.5, 32.4, 29.7, 22.3; ^{19}F NMR (377 MHz, $CDCl_3$) δ -116.2; IR (ν_{max}) 2963, 2931, 2869, 834 cm^{-1}; HRMS Calcd for $C_{14}H_{16}FNS$ (M^+) 249.0987, Found 249.1013.



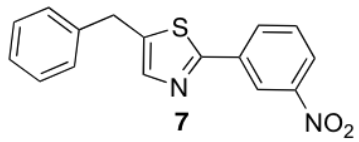
5

5-(4-Fluorobenzyl)-2-isobutylthiazole 5. Synthesized according to the general procedure. Colorless oil; R_f 0.31 (petroleum ether/ethyl acetate 80/20); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 (s, 1H), 7.21-7.14 (m, 2H), 7.03-6.95 (m, 2H), 4.07 (s, 2H), 2.79 (d, J = 7.2 Hz, 2H), 2.06 (hept, J = 6.8 Hz, 1H), 0.97 (d, J = 6.6 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.9, 161.7 (d, J = 245.0 Hz), 139.6, 137.3, 135.3 (d, J = 3.2 Hz), 129.9 (d, J = 8.0 Hz), 115.5 (d, J = 21.4 Hz), 42.5, 32.4, 29.7, 22.3; ^{19}F NMR (377 MHz, $CDCl_3$) δ -116.2; IR (ν_{max}) 2963, 2931, 2869, 834 cm^{-1}; HRMS Calcd for $C_{14}H_{16}FNS$ (M^+) 249.0987, Found 249.1013.



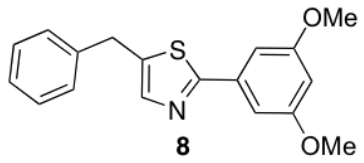
6

5-Benzyl-2-(4-chlorophenyl)thiazole 6. Synthesized according to the general procedure. Yellow solid; mp 80-81 °C; R_f 0.50 (petroleum ether/ethyl acetate 80/20); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, J = 8.5 Hz, 2H), 7.57 (s, 1H), 7.37 (d, J = 8.6 Hz, 2H), 7.35-7.30 (m, 2H), 7.26 (m, 3H), 4.18 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.2, 141.3, 139.3, 139.1, 135.6, 132.3, 129.1, 128.8, 128.4, 127.4, 126.9, 33.3; IR (ν_{max}) 3022, 2932, 2907, 972 cm^{-1}; HRMS Calcd for $C_{16}H_{12}ClNS$ (M^+) 285.0379, Found 285.0357.



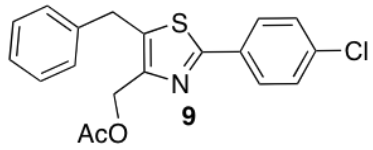
7

5-Benzyl-2-(3-nitropheny)thiazole 7. Synthesized according to the general procedure. Pale yellow solid; mp 100-103 °C; R_f 0.18 (petroleum ether/ethyl acetate 80/20); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.71 (s, 1H), 8.21 (t, J = 8.0 Hz, 2H), 7.65 (s, 1H), 7.59 (t, J = 8.0 Hz, 1H), 7.39-7.32 (m, 2H), 7.31-7.25 (m, 3H), 4.22 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.4, 148.7, 141.7, 140.6, 139.0, 135.4, 131.7, 129.9, 128.9, 128.5, 127.1, 124.0, 121.0, 33.4; IR (ν_{max}) 3066, 3035, 2925, 2863, 1226 cm^{-1}; HRMS Calcd for $C_{16}H_{12}N_2O_2S$ (M^+) 296.0619, Found 296.0612.



8

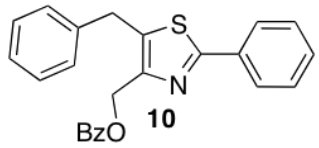
5-Benzyl-2-(3,5-dimethoxypheny)thiazole 8. Synthesized according to the general procedure. Yellow solid; mp 56-58 °C; R_f 0.24 (petroleum ether/ethyl acetate 80/20); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (s, 1H), 7.38-7.30 (m, 2H), 7.29-7.23 (m, 3H), 7.04 (d, J = 2.0 Hz, 2H), 6.49 (d, J = 2.0 Hz, 1H), 4.18 (s, 2H), 3.83 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.5, 161.1, 141.1, 139.4, 138.9, 135.6, 128.8, 128.5, 126.9, 104.1, 102.5, 55.5, 33.3; IR (ν_{max}) 2969, 2935, 2835, 1204, 1026 cm^{-1}; HRMS Calcd for $C_{18}H_{17}NO_2S$ (M^+) 311.0980, Found 311.0976.



9

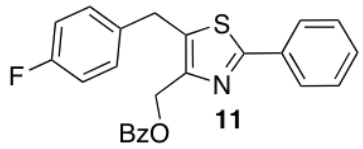
(5-Benzyl-2-(4-chlorophenyl)thiazol-4-yl)methyl acetate 9. Synthesized according to the general procedure. Pale yellow solid; mp 88-92°C; R_f 0.48 (petroleum ether/ethyl acetate 80/20); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84-7.75 (m, 2H), 7.39-7.34 (m, 2H), 7.34-7.29 (m, 2H), 7.28-7.21 (m, 3H), 5.24 (s, 2H), 4.23 (s, 2H), 2.08 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.8, 164.6, 147.3, 139.2, 138.3, 135.9, 131.9, 129.1, 128.8, 128.4, 127.5, 127.0, 59.5, 32.3, 20.9;

IR (ν_{max}) 3032, 2966, 2935, 2052, 1710, 831 cm^{-1}; HRMS Calcd for $C_{19}H_{16}ClNO_2S$ (M^+) 357.0590, Found 357.0564.



10

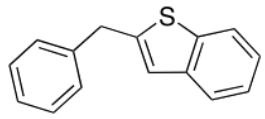
(5-benzyl-2-phenylthiazol-4-yl)methyl benzoate 10. Synthesized according to the general procedure. White solid; mp 78-80 °C; R_f 0.55 (petroleum ether/ethyl acetate 80/20); ^1H NMR (400 MHz, $CDCl_3$) δ 8.08-8.01 (m, 2H), 7.90-7.86 (m, 2H), 7.58-7.51 (m, 1H), 7.45-7.37 (m, 5H), 7.32-7.20 (m, 5H), 5.50 (s, 2H), 4.31 (s, 2H) ; ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.5, 165.8, 147.3, 139.4, 138.1, 133.5, 133.0, 123.0, 129.9, 129.8, 128.9, 128.8, 128.4, 128.3, 126.9, 126.4, 60.2, 32.4; IR (ν_{max}) 3067, 3028, 2964, 1718, 1266 cm^{-1}; HRMS Calcd for $C_{24}H_{19}NO_2S$ (M^+) 385.1136, Found 385.1143.



11

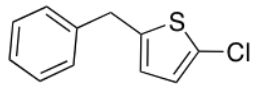
(5-(4-fluorobenzyl)-2-phenylthiazol-4-yl)methyl benzoate 11. Synthesized according to the general procedure. White solid; mp 80-83 °C; R_f 0.52 (petroleum ether/ethyl acetate 80/20); ^1H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, J = 7.2 Hz, 2H), 7.88 (dd, J = 6.7, 3.0 Hz, 2H), 7.55 (t, J = 7.4 Hz, 1H), 7.46-7.36 (m, 5H), 7.22 (dd, J = 8.5, 5.4 Hz, 2H), 6.97 (t, J = 8.6 Hz, 2H), 5.49 (s, 2H), 4.28 (s, 2H) ; ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.3, 165.8, 161.7 (d, J = 245.4 Hz), 147.3, 137.8, 135.1 (d, J = 3.3 Hz), 133.3, 133.0, 123.0, 129.8 (d, J = 8.0 Hz), 129.8, 129.7, 128.8, 128.3, 126.3, 115.6, 115.4, 60.0, 31.5; ^{19}F NMR (377 MHz, $CDCl_3$) δ -115.7; IR (ν_{max}) 3068,

3040, 2960, 2915, 1720, 1504, 1268, 1219 cm^{-1}; HRMS Calcd for $C_{24}H_{18}FNO_2S$ (M^+) 403.1042, Found 403.1069.



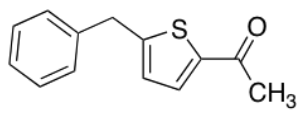
12

2-Benzylbenzothiophene 12. Synthesized according to the general procedure. White solid; mp 76-78 °C; R_f 0.30 (petroleum ether/diethyl ether 90/10); ^1H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, J = 7.8 Hz, 1H), 7.65 (d, J = 7.8 Hz, 1H), 7.39-7.16 (m, 7H), 7.00 (s, 1H), 4.22 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.1, 140.0, 139.5, 128.8, 128.6, 126.7, 124.1, 123.6, 122.9, 122.1, 121.6, 37.0; IR (ν_{max}) 3060, 3032, 2966 cm^{-1}; HRMS Calcd for $C_{15}H_{12}S$ (M^+) 224.0660, Found 224.0636.



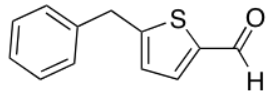
13

2-benzyl-5-chlorothiophene 13. Synthesized according to the general procedure. Oil; R_f 0.46 (petroleum ether 100%); ^1H NMR (400 MHz, $CDCl_3$) δ 7.36-7.27 (m, 2H), 7.27-7.18 (m, 3H), 6.71 (d, J = 3.7 Hz, 1H), 6.56 (dt, J = 3.7, 1.0 Hz, 1H), 4.04 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.9, 139.5, 128.6, 128.5, 127.9, 126.7, 125.7, 124.3, 36.4; IR (ν_{max}) 3090, 3067, 3034, 2906, 2843, 1453,1219, 992 cm^{-1}; HRMS Calcd for $C_{11}H_9ClS$ (M^+) 208.0113, Found 208.0115.



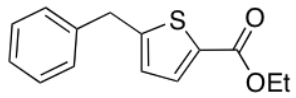
14

1-(5-Benzylthiophen-2-yl)ethanone 14. Synthesized according to the general procedure. Oil; R_f 0.46 (petroleum ether/ethyl acetate 80/20); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (d, J = 3.8 Hz, 1H), 7.35-7.27 (m, 2H), 7.27-7.20 (m, 3H), 6.81 (dt, J = 3.8, 0.9 Hz, 1H), 4.14 (s, 2H), 2.48 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 190.3, 153.9, 142.8, 138.9, 132.7, 128.6, 128.5, 126.8, 126.3, 36.6, 26.3; IR (ν_{max}) 3063, 3032, 2925, 1655, 1276 cm^{-1}; HRMS Calcd for $C_{13}H_{12}OS$ (M^+) 216.0609, Found 216.0612.



15

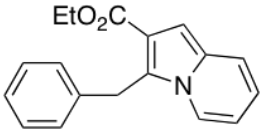
5-Benzylthiophene-2-carbaldehyde 15. Synthesized according to the general procedure. Pale brown oil; R_f 0.20 (petroleum ether/ethyl acetate 90/10); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.80 (s, 1H), 7.60 (d, J = 3.8 Hz, 1H), 7.37-7.29 (m, 2H), 7.29-7.21 (m, 3H), 6.90 (dt, J = 3.7, 0.8 Hz, 1H), 4.18 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 182.7, 155.8, 142.4, 138.7, 136.9, 128.8, 128.7, 127.1, 126.6, 36.9; IR (ν_{max}) 3091, 3066, 3032, 2926, 2847, 2810, 1664, 1451 cm^{-1}; HRMS Calcd for $C_{12}H_{10}OS$ (M^+) 202.0452, Found 202.0451.



16

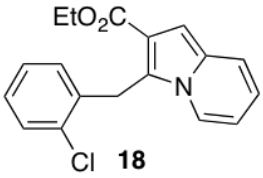
Ethyl 5-benzylthiophene-2-carboxylate 16. Synthesized according to the general procedure. Colorless oil; R_f 0.64 (petroleum ether/ethyl acetate 80/20); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (d, J = 3.7 Hz, 1H), 7.35-7.28 (m, 2H), 7.28-7.19 (m, 3H), 6.79 (d, J = 3.6 Hz, 1H), 4.30 (q, J = 7.1 Hz, 2H), 4.14 (s, 2H), 1.33 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.3, 152.0,

139.2, 133.5, 132.1, 128.7, 128.6, 126.9, 126.0, 60.9, 36.5, 14.3; IR (ν_{max}) 3032, 2985, 2935, 1698, 1279, 1254, 1223 cm^{-1}; HRMS Calcd for $C_{14}H_{14}O_2S$ (M^+) 246.0715, Found 246.0714.



17

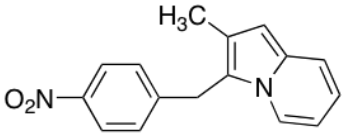
Ethyl 3-benzylindolizine-2-carboxylate 17. Synthesized according to the general procedure. Gray solid; mp 70-73 °C; R_f 0.56 (petroleum ether/ethyl acetate 80/20); ^1H NMR (400 MHz, $CDCl_3$) δ 7.63 (d, J = 7.2 Hz, 1H), 7.37 (d, J = 9.0 Hz, 1H), 7.29-7.20 (m, 2H), 7.20-7.08 (m, 3H), 6.92 (s, 1H), 6.65 (dd, J = 9.0, 6.5 Hz, 1H), 6.46 (t, J = 6.8 Hz, 1H), 4.70 (s, 2H), 4.36 (q, J = 7.1 Hz, 2H), 1.37 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.8, 137.6, 131.6, 128.6, 128.0, 126.3, 126.1, 122.4, 120.4, 117.5, 117.4, 112.0, 100.7, 60.1, 30.4, 14.4; IR (ν_{max}) 3069, 3032, 2985, 2903, 2049, 1226, 1163, 1031 cm^{-1}; HRMS Calcd for $C_{18}H_{17}NO_2$ (M^+) 279.1259, Found 279.1247.



18

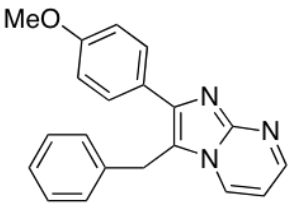
Ethyl 3-(2-chlorobenzyl)indolizine-2-carboxylate 18. Synthesized according to the general procedure. Gray solid; mp 53-56 °C; R_f 0.67 (petroleum ether/ethyl acetate 80/20); ^1H NMR (400 MHz, $CDCl_3$) δ 7.53 (d, J = 7.2 Hz, 1H), 7.45-7.35 (m, 2H), 7.12 (td, J = 7.8, 1.2 Hz, 1H), 7.01 (td, J = 7.7, 0.8 Hz, 1H), 6.95 (s, 1H), 6.68 (dd, J = 8.8, 6.5 Hz, 1H), 6.59 (d, J = 7.6 Hz, 1H), 6.53-6.43 (m, 1H), 4.79 (s, 2H), 4.33 (q, J = 7.1 Hz, 2H), 1.34 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.6, 135.1, 133.7, 131.8, 129.4, 128.8, 127.7, 127.0, 124.8, 122.3, 120.4,

118.0, 117.7, 112.3, 100.8, 60.1, 27.7, 14.3; IR (ν_{max}) 3060, 2988, 2932, 1701, 1232, 1163 cm^{-1}; HRMS Calcd for $C_{18}H_{16}ClNO_2$ (M^+) 313.0870, Found 313.0877.



19

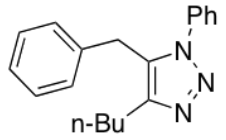
2-Methyl-3-(4-nitrobenzyl)indolizine 19. Synthesized according to the general procedure. Orange solid (light sensitive); mp 100-104 °C; R_f 0.55 (petroleum ether/ethyl acetate 80/20); ^1H NMR (400 MHz, $CDCl_3$) δ 8.10 (d, J = 8.5 Hz, 2H), 7.41 (d, J = 7.0 Hz, 1H), 7.32 (d, J = 8.9 Hz, 1H), 7.19 (d, J = 8.4 Hz, 2H), 6.61 (t, J = 7.7 Hz 1H), 6.41-6.30 (m, 2H), 4.32 (s, 2H), 2.35 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.7, 146.2, 132.3, 128.6, 123.9, 123.5, 121.3, 118.5, 117.1, 116.2, 109.9, 99.8, 29.7, 11.8; IR (ν_{max}) 2931, 2866, 1345, 1223 cm^{-1}; HRMS Calcd for $C_{16}H_{14}N_2O_2$ (M^+) 266.1055, Found 266.1070.



20

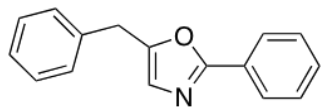
3-Benzyl-2-(4-methoxyphenyl)imidazo[1,2-*a*]pyrimidine 20. Synthesized according to the general procedure. Brown solid; mp 124-129°C; R_f 0.46 (Dichloromethane/methanol 95/5); ^1H NMR (400 MHz, $CDCl_3$) δ 8.50 (dd, J = 4.1, 2.0 Hz, 1H), 7.96 (dd, J = 6.8, 1.9 Hz, 1H), 7.80 (d, J = 8.8 Hz, 2H), 7.36-7.21 (m, 3H), 7.13 (d, J = 6.9 Hz, 2H), 6.97 (d, J = 8.8 Hz, 2H), 6.73 (dd, J = 6.8, 4.1 Hz, 1H), 4.49 (s, 2H), 3.83 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.7, 149.0, 148.0, 145.6, 136.1, 130.6, 129.6, 129.2, 127.6, 127.2, 126.5, 115.5, 114.1, 108.2, 55.3, 29.7;

IR (ν_{max}) 3032, 2960, 2938, 2841, 1251, 1176 cm^{-1}; HRMS Calcd for $C_{20}H_{17}N_3O$ (M^+) 315.1372, Found 315.1373.



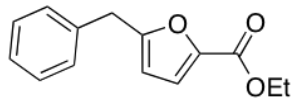
21

5-Benzyl-4-butyl-1-phenyl-1*H*-1,2,3-triazole 21. Synthesized according to the general procedure. White solid; mp 46-47 °C; R_f 0.36 (chloroform/diethyl ether 90/10); ^1H NMR (400 MHz, $CDCl_3$) δ 7.47-7.38 (m, 3H), 7.32-7.27 (m, 2H), 7.27-7.16 (m, 3H), 6.92 (d, J = 6.5 Hz, 2H), 4.01 (s, 2H), 2.71-2.60 (m, 2H), 1.69 (dt, J = 15.4, 7.6 Hz, 2H), 1.45-1.31 (m, 2H), 0.91 (t, J = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.2, 136.9, 136.6, 131.9, 129.3, 129.2, 128.6, 127.9, 126.7, 125.4, 77.0, 31.5, 28.6, 24.9, 22.5, 13.8; IR (ν_{max}) 3032, 2960, 2935, 2869, 759 cm^{-1}; HRMS Calcd for $C_{19}H_{21}N_3$ (M^+) 291.1735, Found 291.1726.



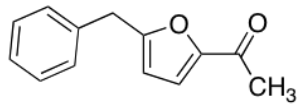
22

2-Benzyl-2-phenyloxazole 22. Synthesized according to the general procedure. Pale yellow oil; R_f 0.52 (petroleum ether/ethyl acetate 80/20); ^1H NMR (400 MHz, $CDCl_3$) δ 8.01-7.96 (m, 2H), 7.45-7.37 (m, 3H), 7.37-7.21 (m, 5H), 6.86 (t, J = 1.0 Hz, 1H), 4.06 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.2, 151.4, 136.6, 130.1, 128.7, 128.7, 127.6, 126.9, 126.1, 124.8, 32.1; IR (ν_{max}) 3066, 3035, 2922, 1701, 1241 cm^{-1}; HRMS Calcd for $C_{16}H_{13}NO$ (M^+) 235.0997, Found 235.0996.



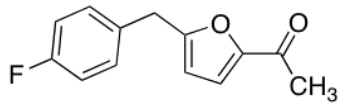
23

Ethyl 5-benzylfuran-2-carboxylate 23. Synthesized according to the general procedure. Colorless oil; R_f 0.58 (petroleum ether/ethyl acetate 80/20); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35-7.28 (m, 2H), 7.28-7.20 (m, 3H), 7.08 (d, J = 3.4 Hz, 1H), 6.05 (d, J = 3.4 Hz, 1H), 4.34 (q, J = 7.1 Hz, 2H), 4.04 (s, 2H), 1.36 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.6, 158.9, 143.7, 136.7, 128.9, 128.7, 126.9, 119.0, 108.8, 60.8, 34.8, 14.4; IR (ν_{max}) 3031, 2985, 2931, 1701, 1029 cm^{-1}; HRMS Calcd for $C_{14}H_{14}O_3$ (M^+) 230.0943, Found 230.0969.



24

1-(5-Benzylfuran-2-yl)ethanone 24. Synthesized according to the general procedure. Yellow oil; R_f 0.42 (petroleum ether/ethyl acetate 80/20); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36-7.29 (m, 2H), 7.29-7.22 (m, 3H), 7.09 (d, J = 3.5 Hz, 1H), 6.10 (d, J = 3.5 Hz, 1H), 4.04 (s, 2H), 2.43 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 186.2, 160.1, 151.8, 136.4, 128.7, 128.6, 126.8, 119.0, 109.2, 34.7, 25.6; IR (ν_{max}) 3126, 3088, 3066, 3035, 2925, 1673, 1507, 1295 cm^{-1}; HRMS Calcd for $C_{13}H_{12}O_2$ (M^+) 200.0837, Found 200.0851.



25

1-(5-(4-Fluorobenzyl)furan-2-yl)ethanone 25. Synthesized according to the general procedure. Colorless oil; R_f 0.35 (petroleum ether/ethyl acetate 80/20); ^{1}H NMR (400 MHz,

$CDCl_3$) δ 7.25-7.17 (m, 2H), 7.10 (d, J = 3.5 Hz, 1H), 7.06-6.96 (m, 2H), 6.10 (dt, J = 3.5, 0.8 Hz, 1H), 4.01 (s, 2H), 2.43 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 186.2, 161.9 (d, J = 245.2 Hz), 159.8, 152.0, 132.2 (d, J = 3.3 Hz), 130.4 (d, J = 8.0 Hz), 119.0, 115.6 (d, J = 21.5 Hz), 109.3, 34.0, 25.8; ^{19}F NMR (377 MHz, $CDCl_3$) δ -115.8; IR (ν_{max}) 312, 3076, 3048, 3013, 2929, 1677, 1507, 1298, 1223 cm^{-1}; HRMS Calcd for $C_{13}H_{11}FO_2$ (M^+) 218.0743, Found 218.0734

Experimental References

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This ligand is commericially available from Strem Chemicals.

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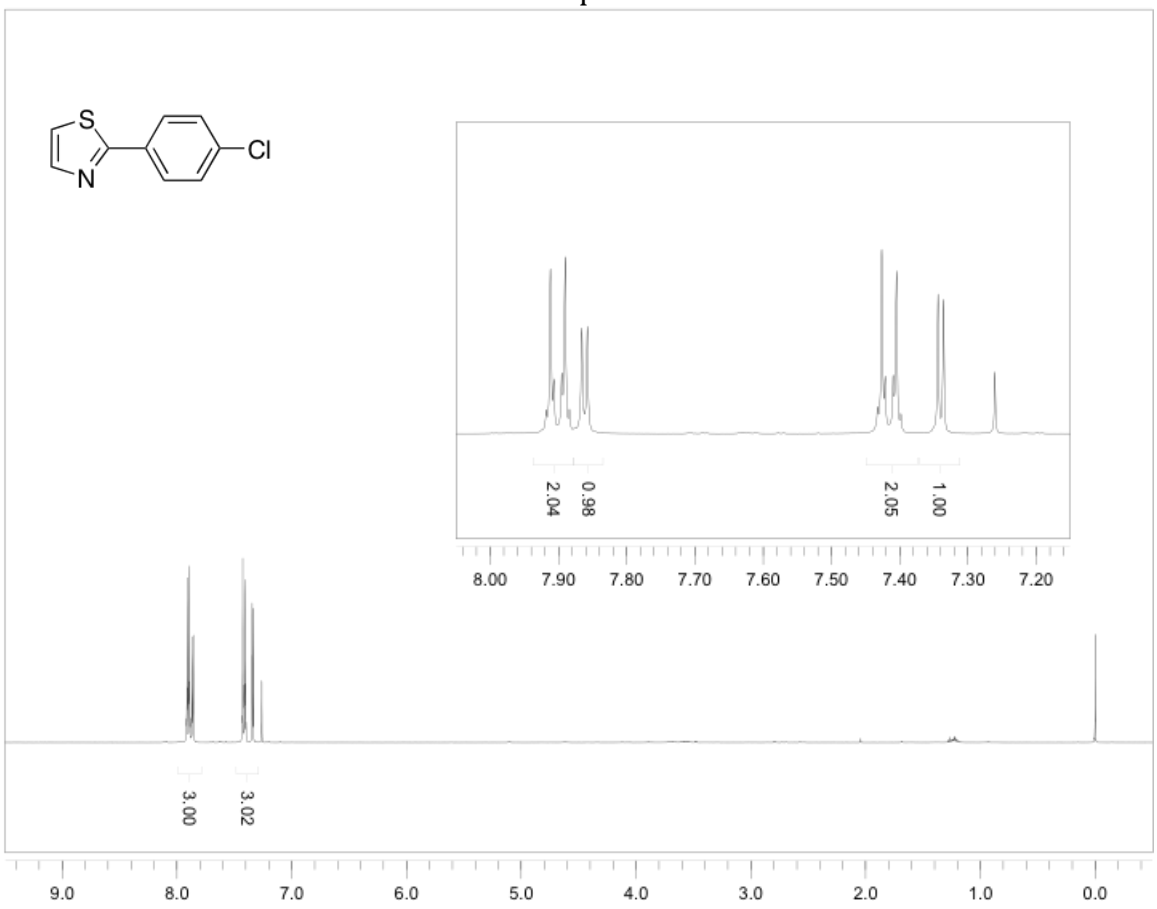
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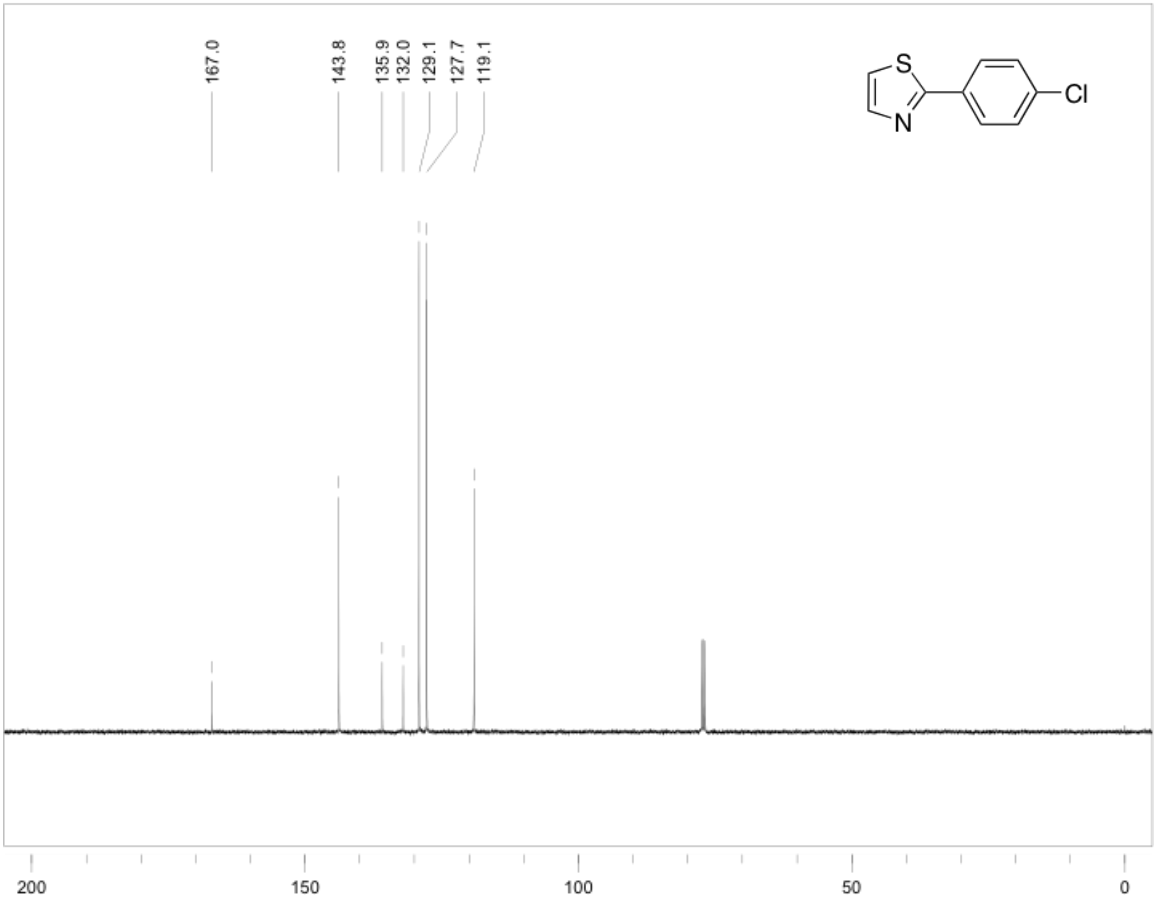
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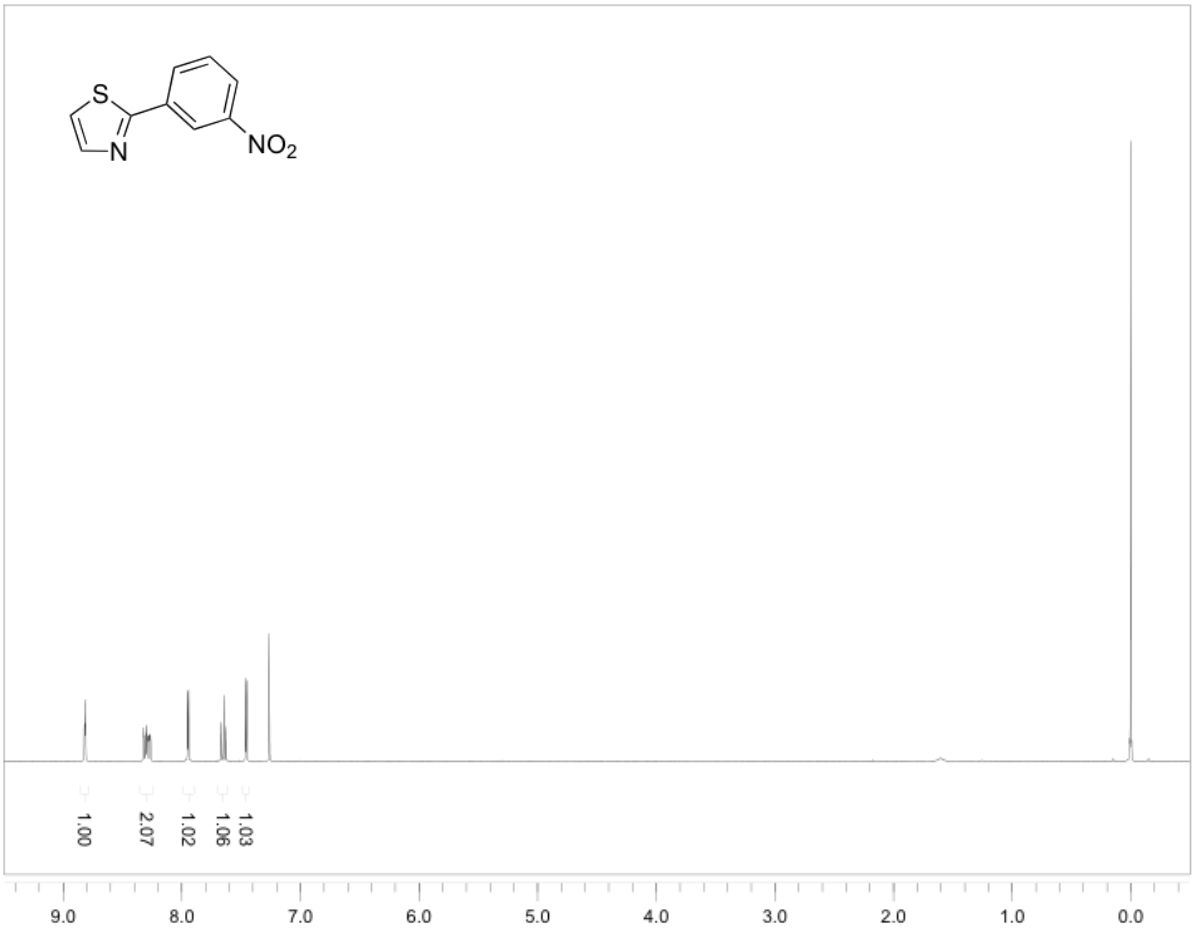
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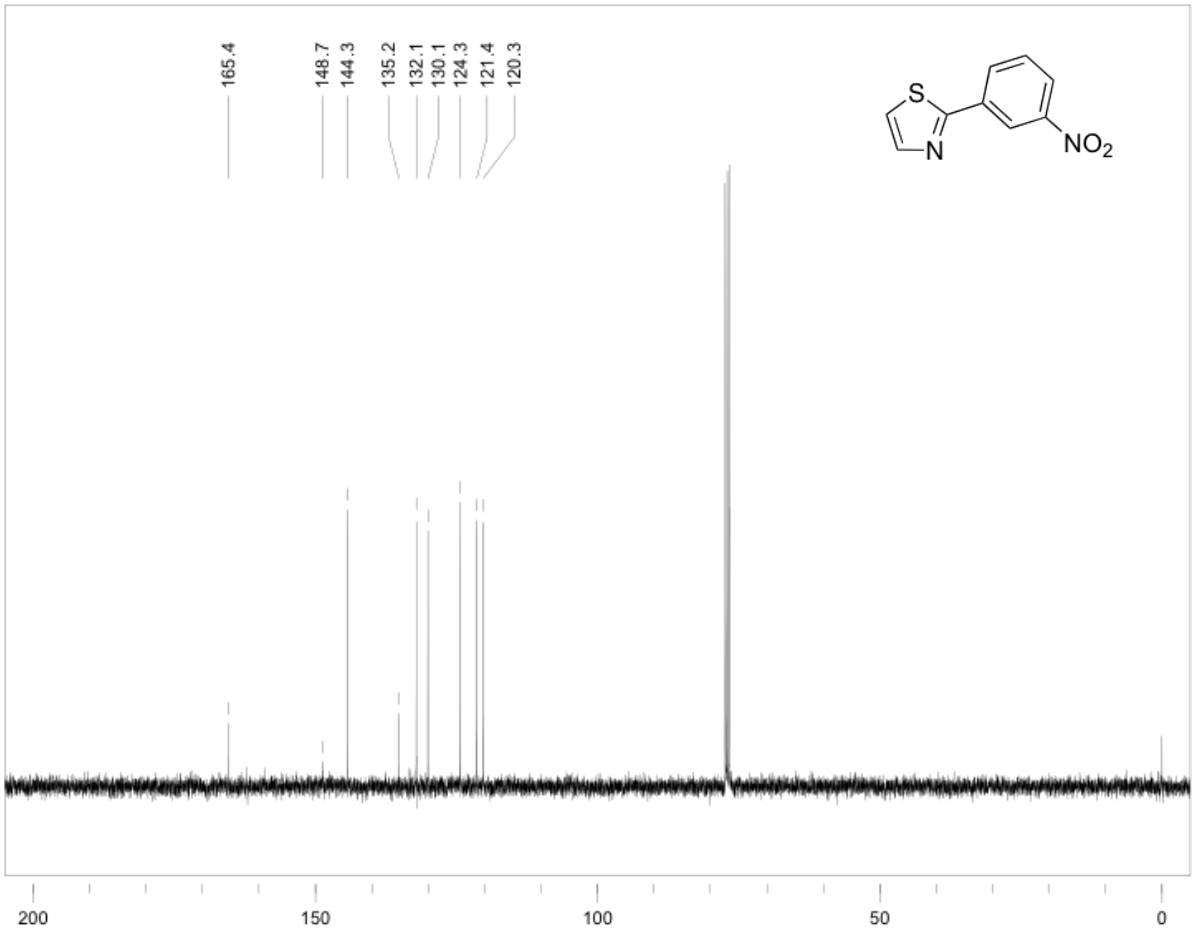
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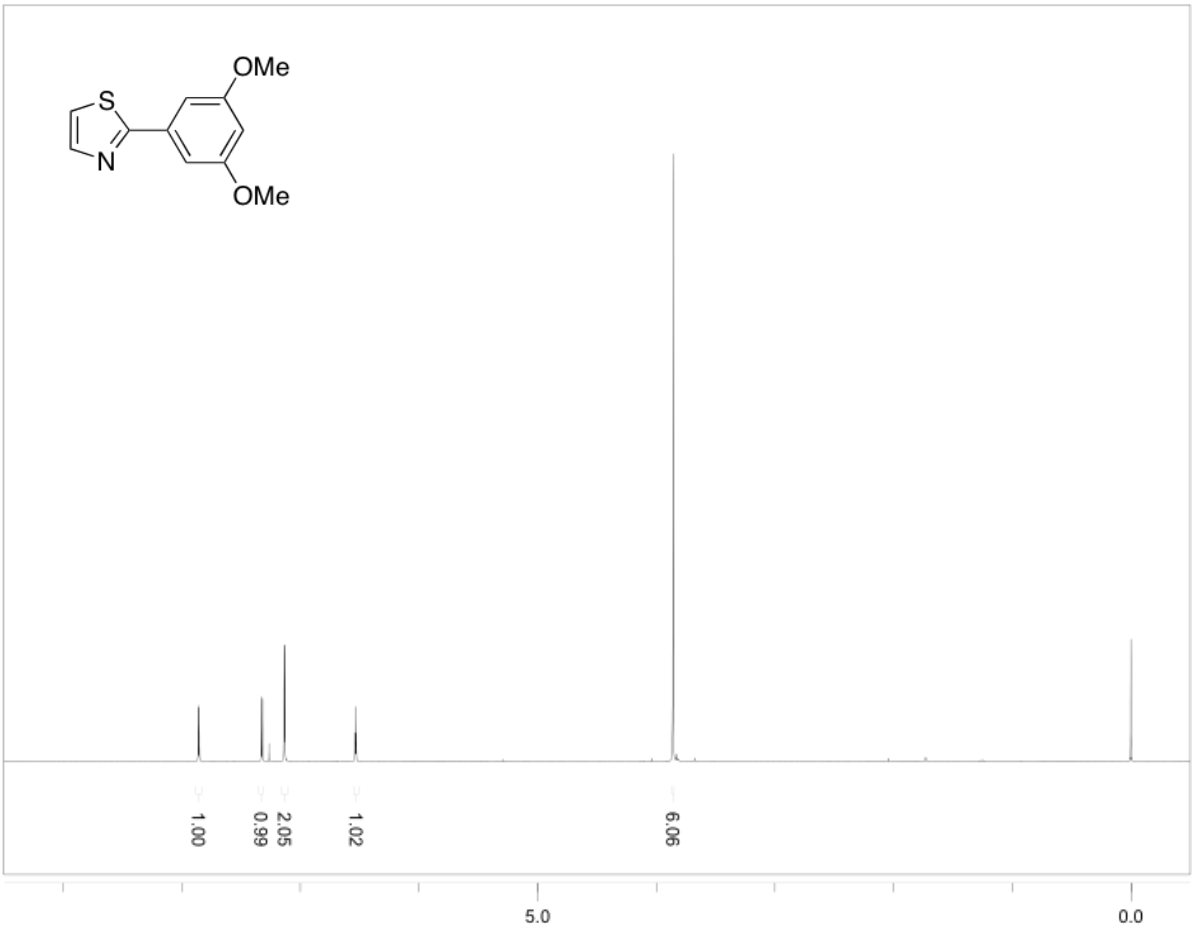
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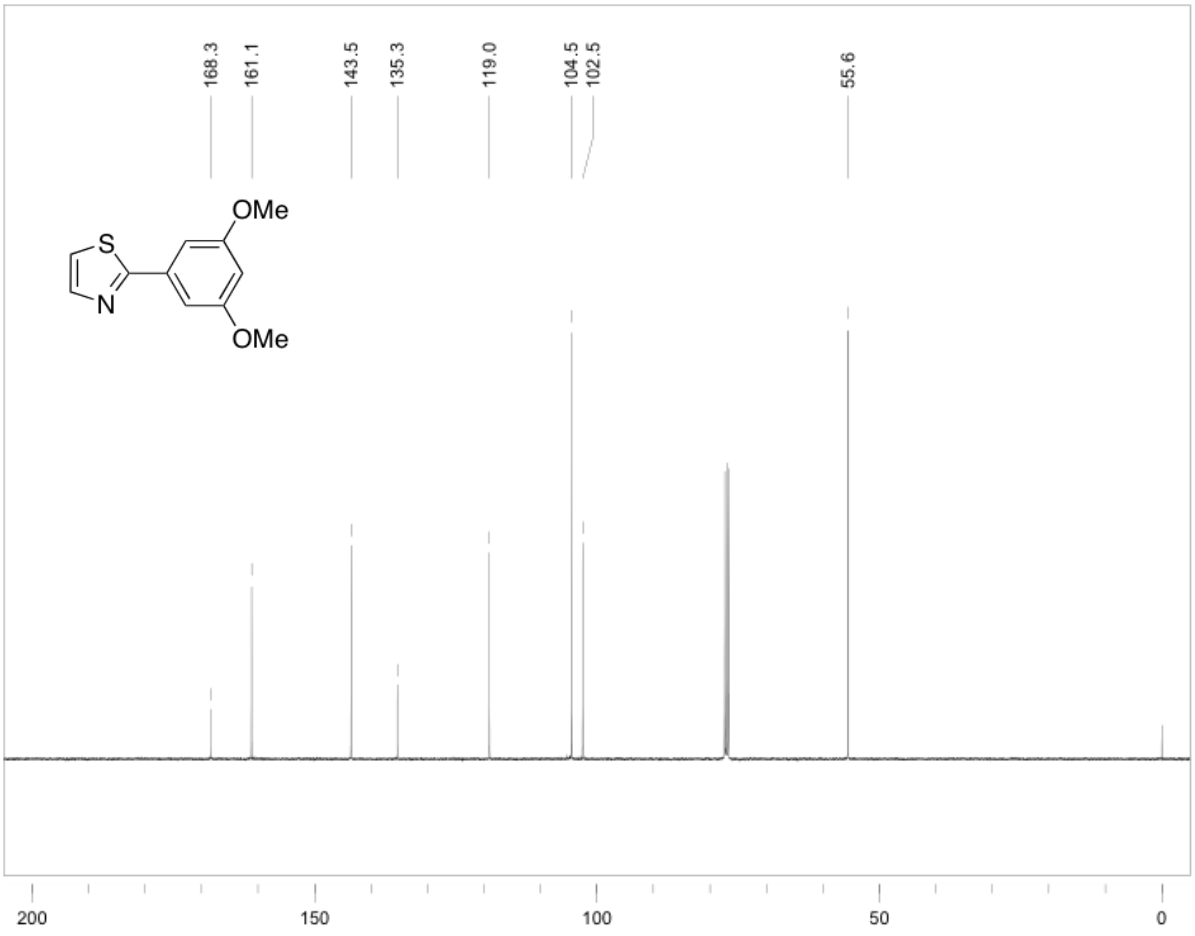
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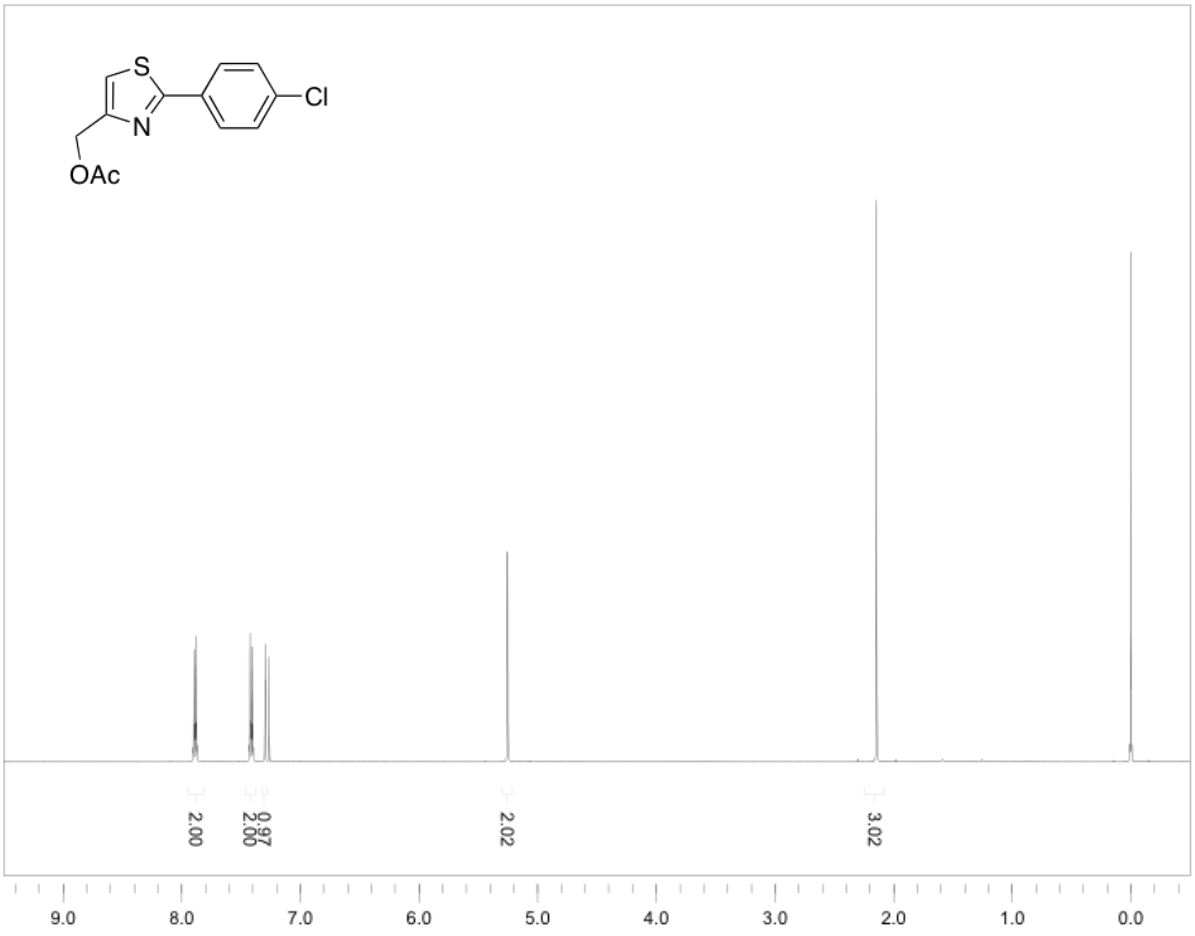
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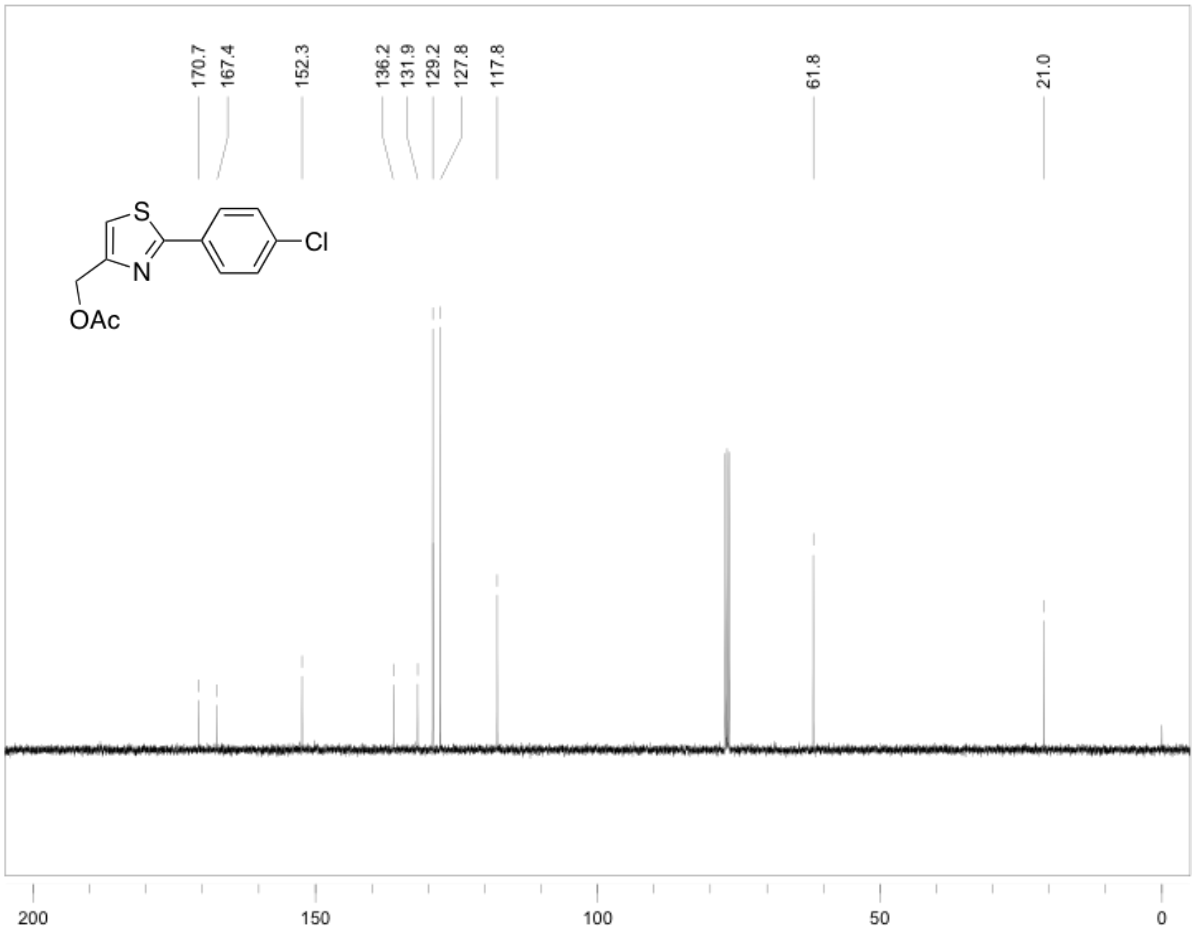
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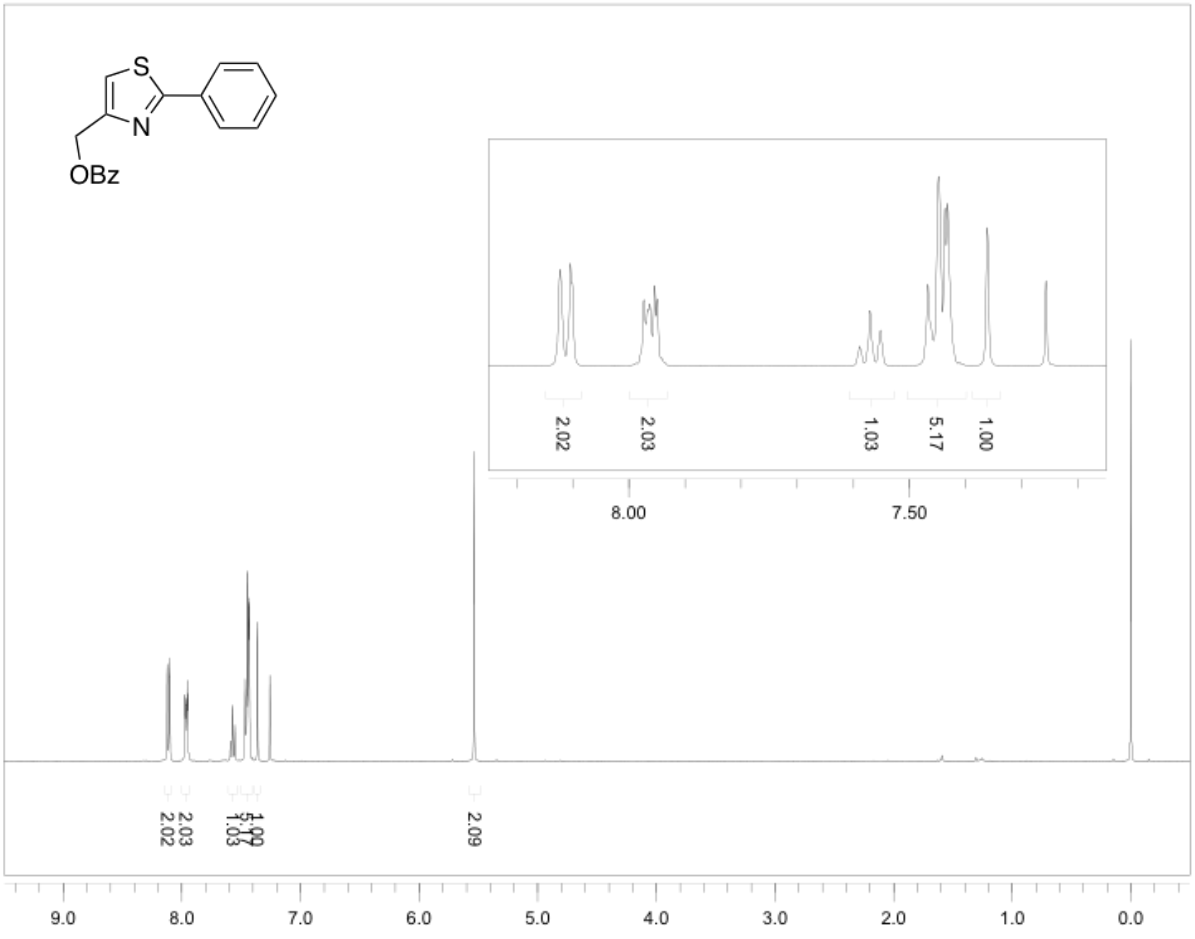
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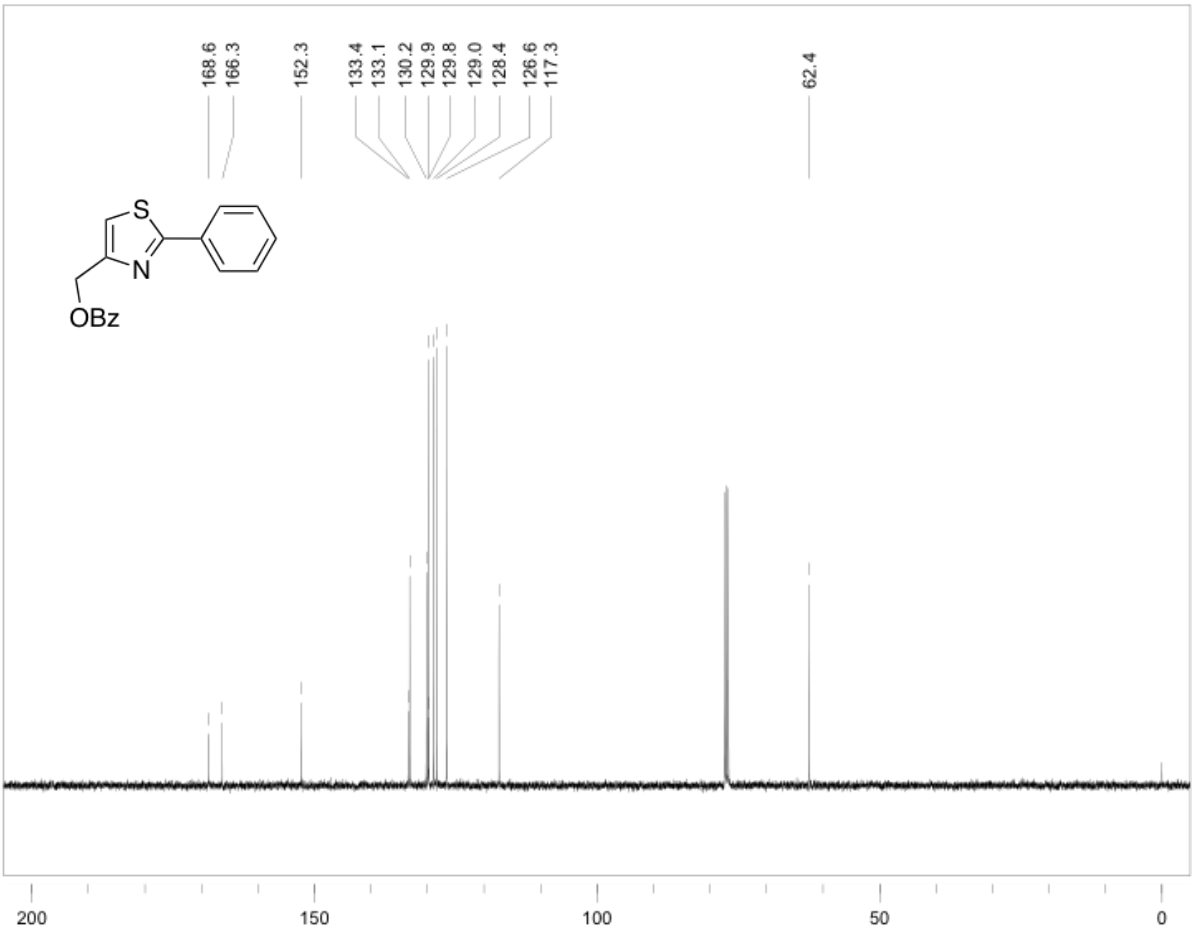
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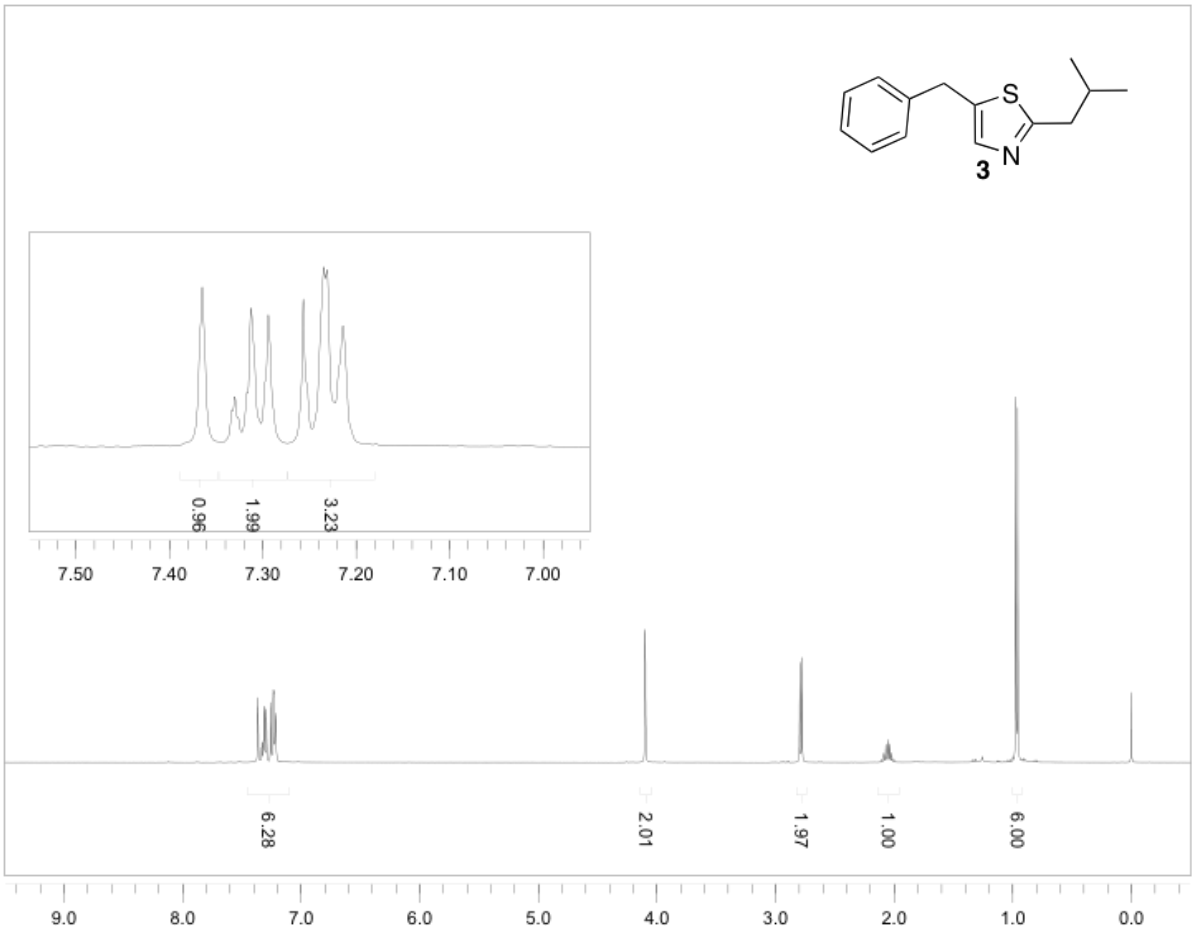
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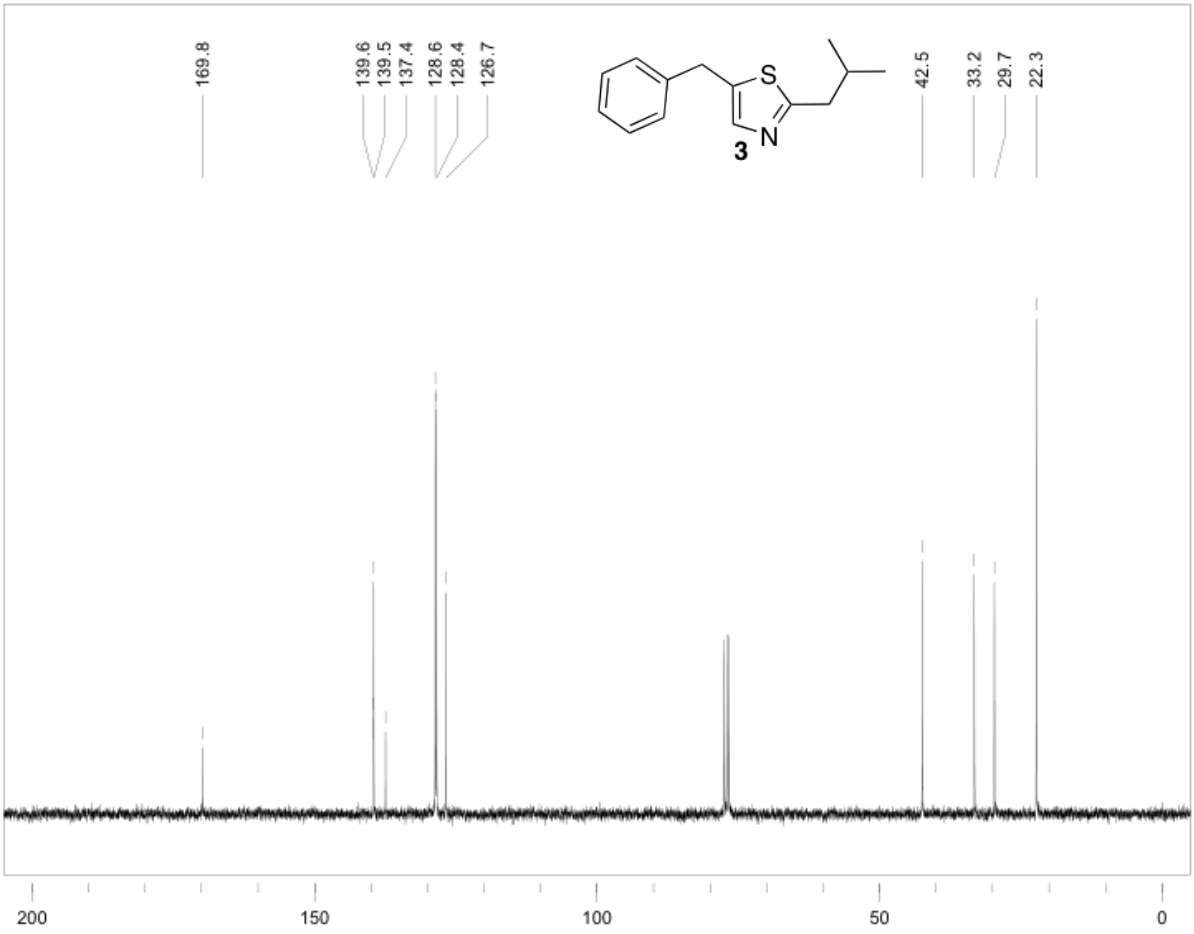
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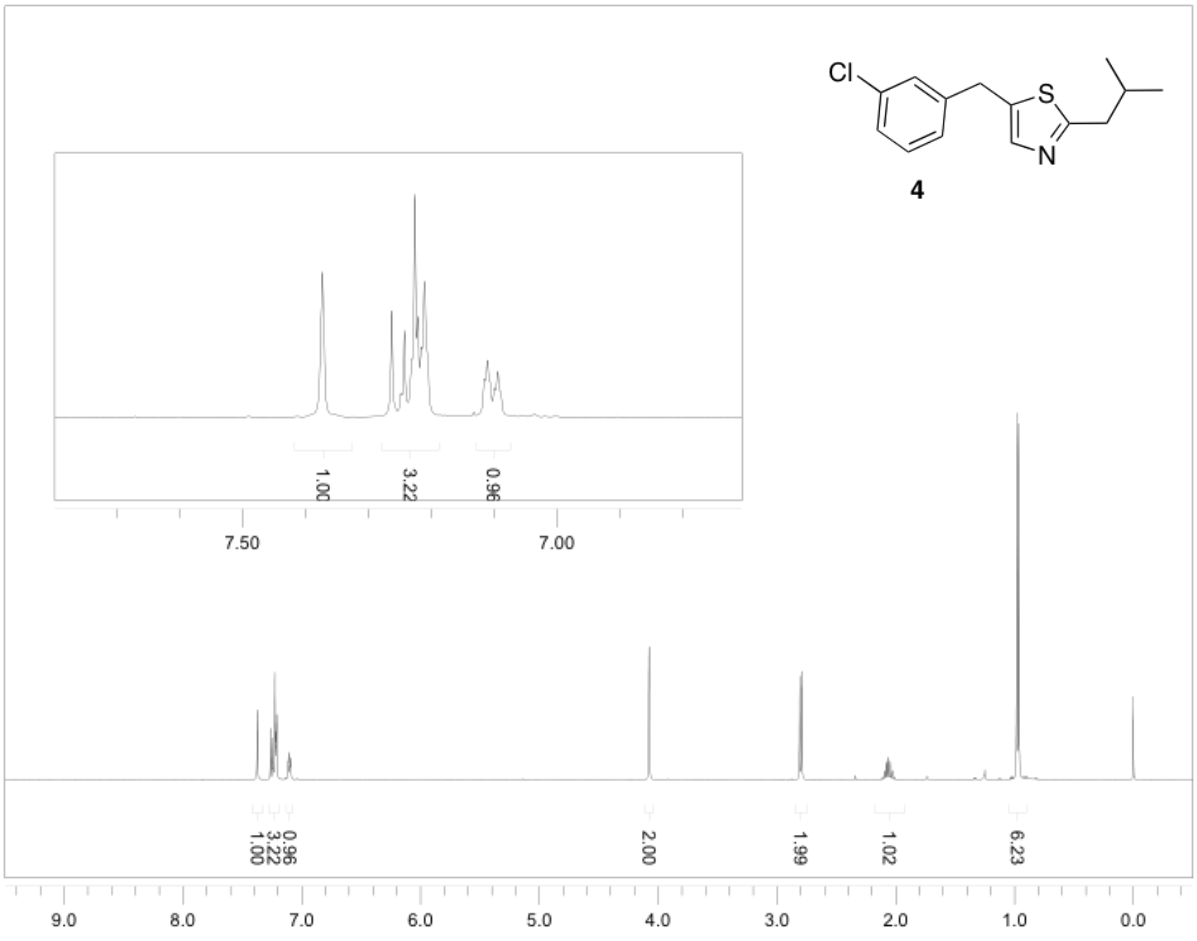
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1.00
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0.96
2.00
1.99
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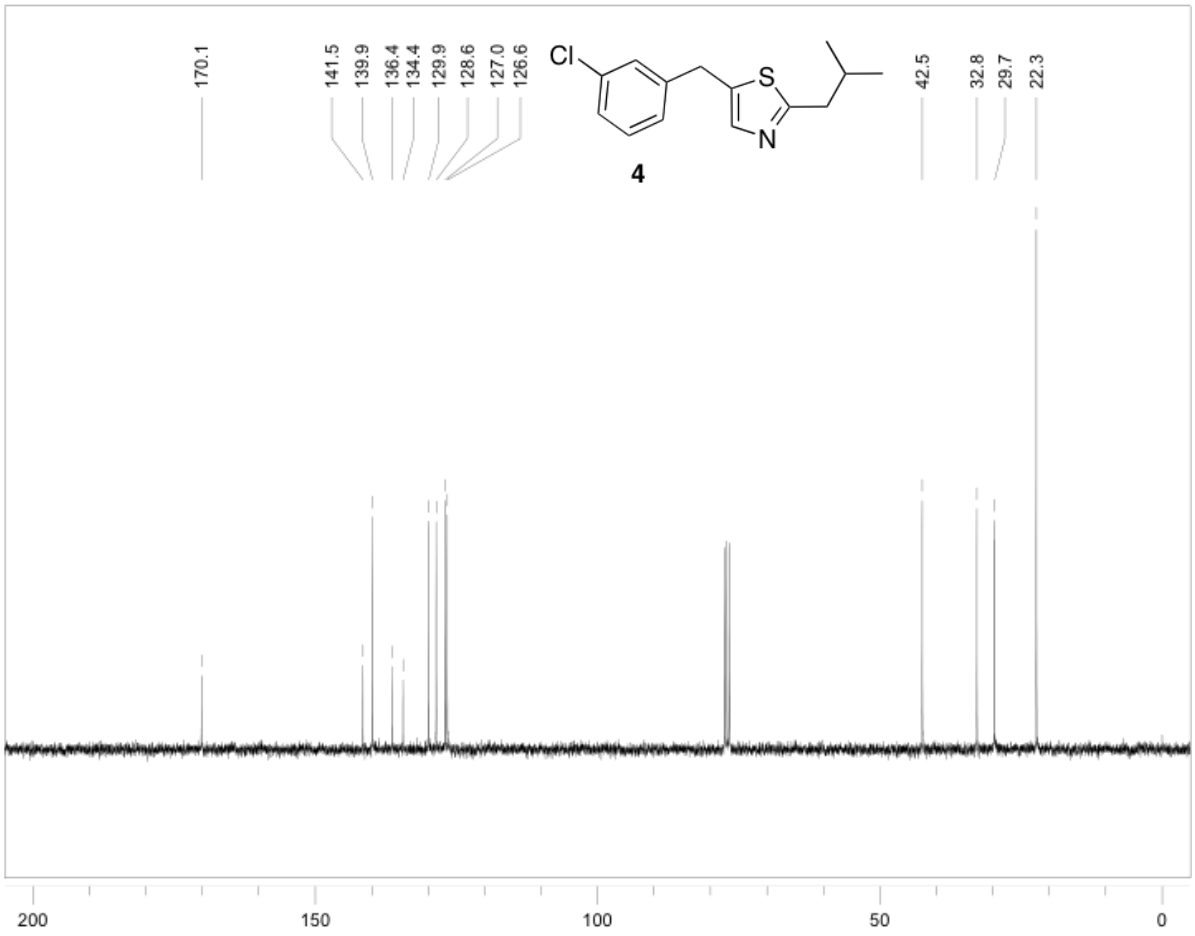
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129.9
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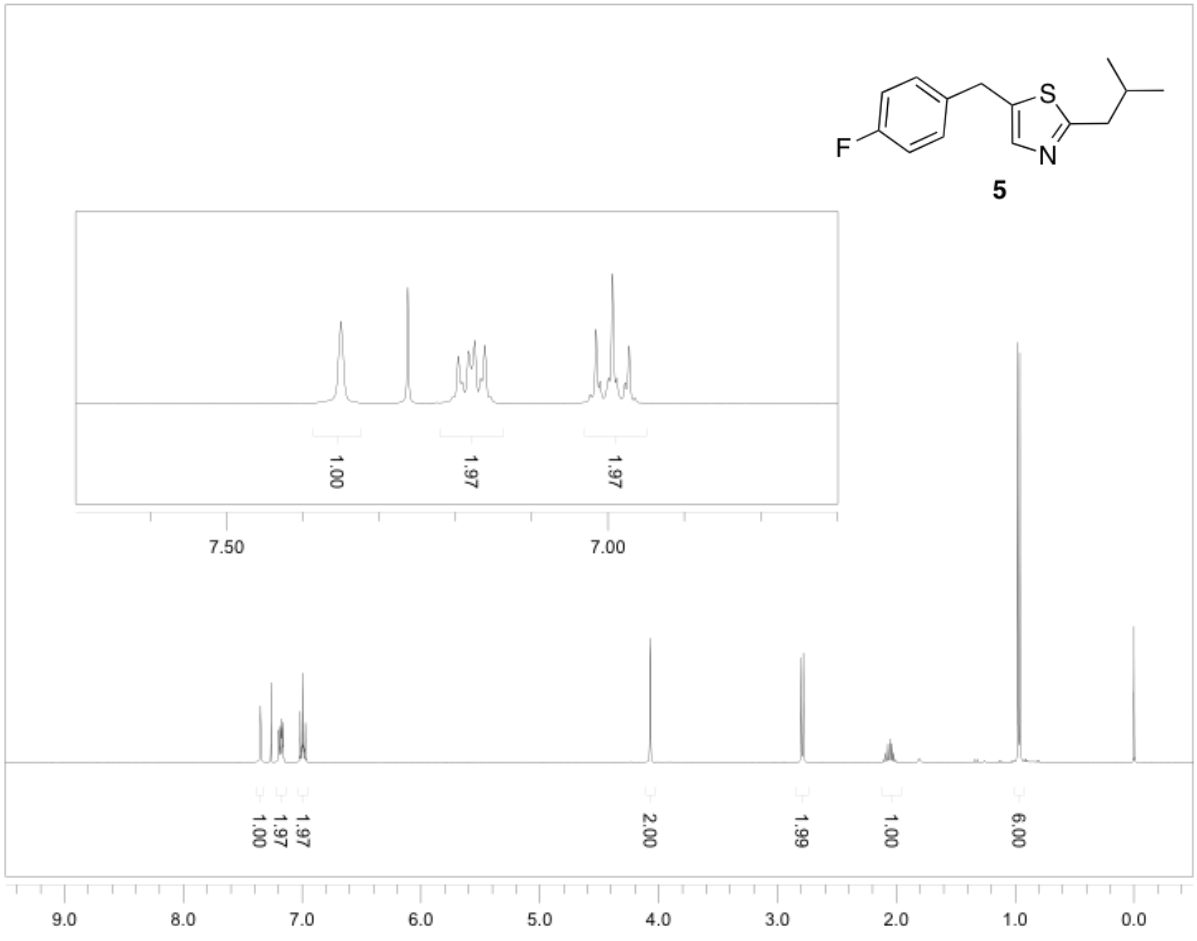
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1.00
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1.97
2.00
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7.0
6.0
5.0
4.0
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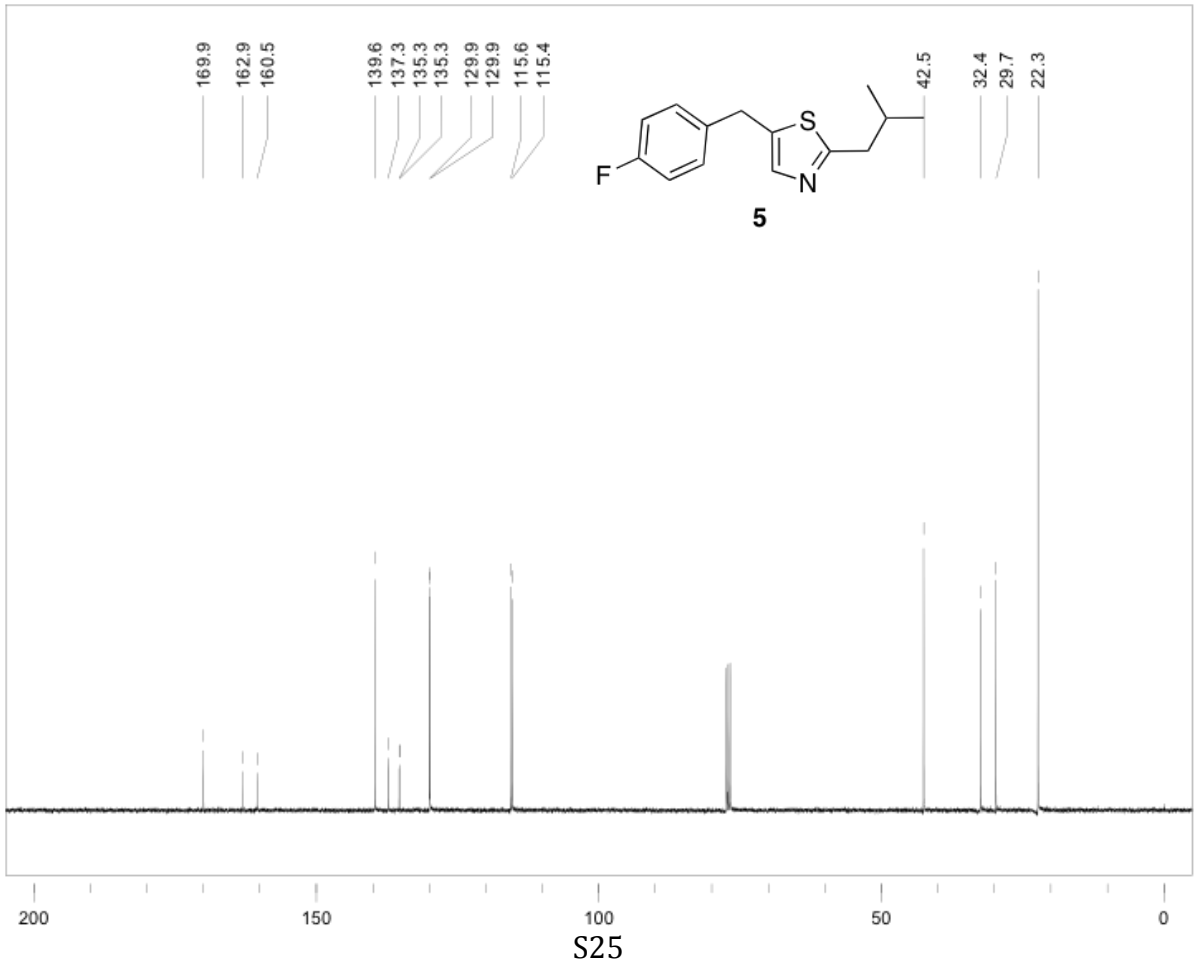
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129.9
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42.5
32.4
29.7
22.3
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S
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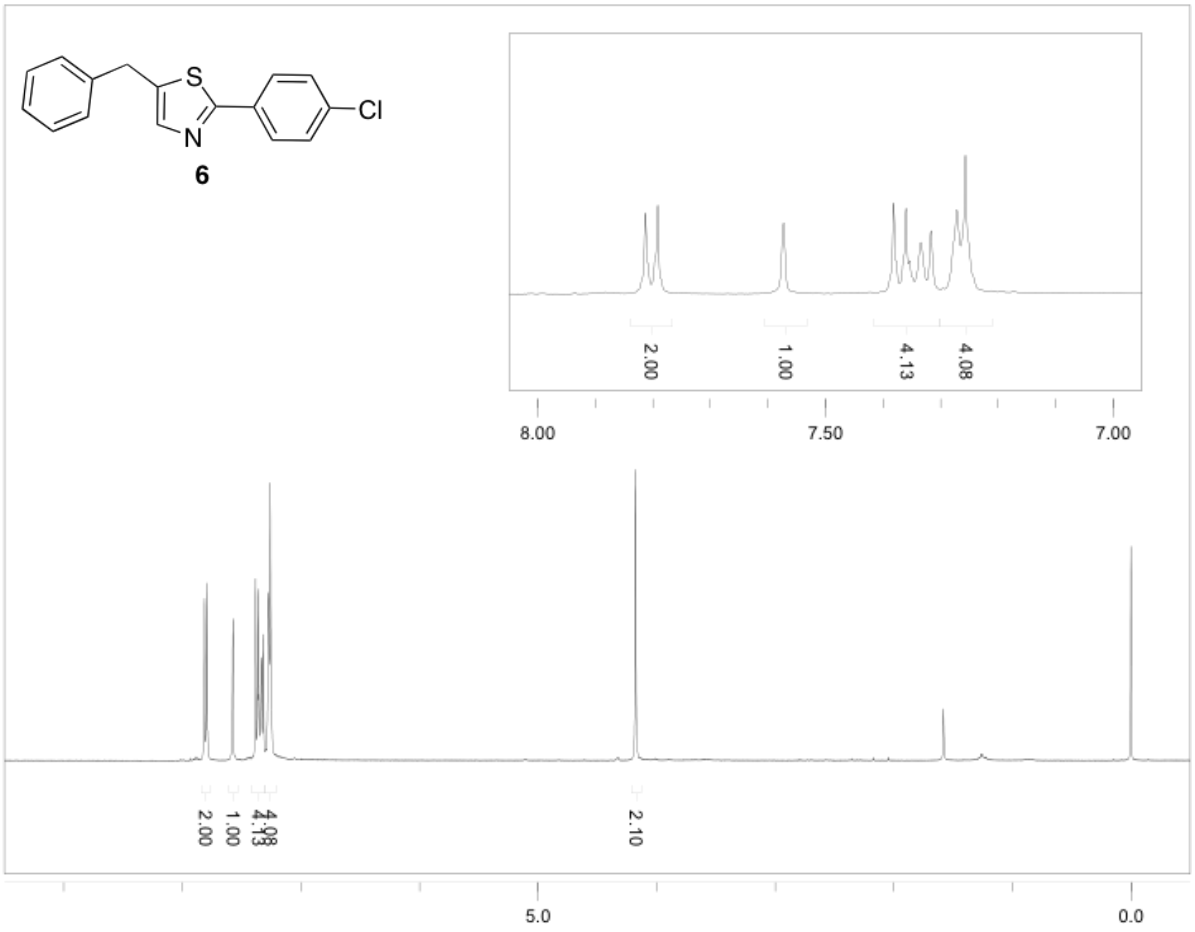
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2.00
1.00
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2.10
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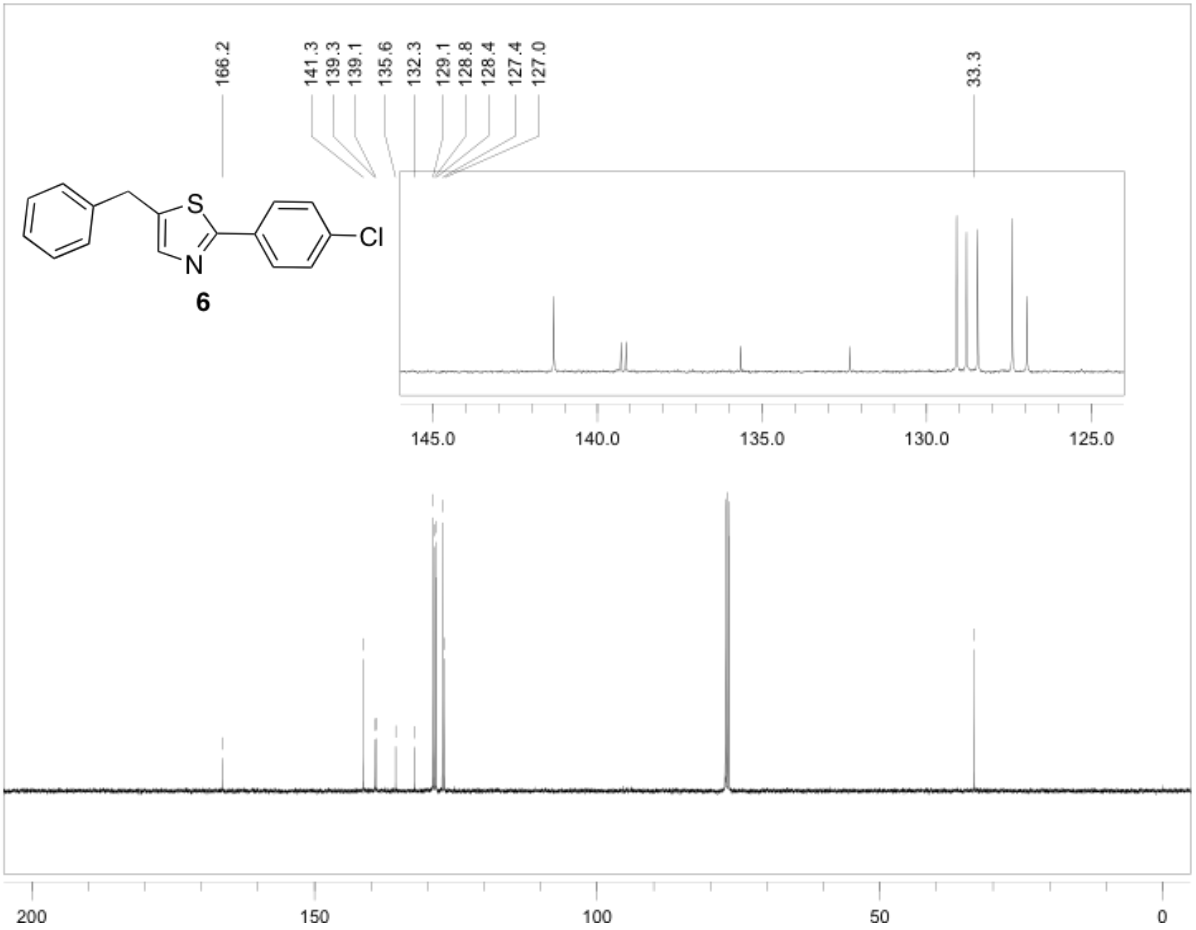
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127.4
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Cl
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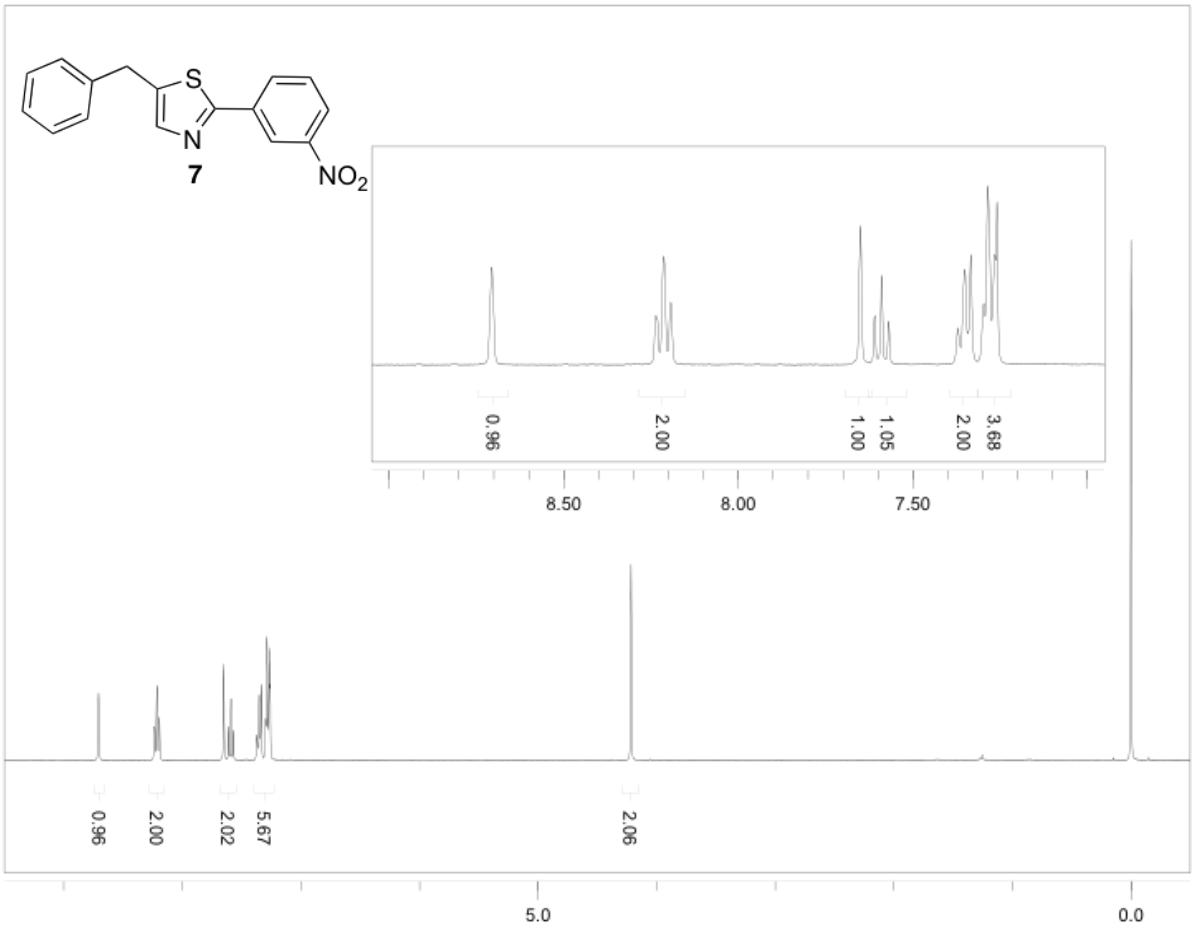
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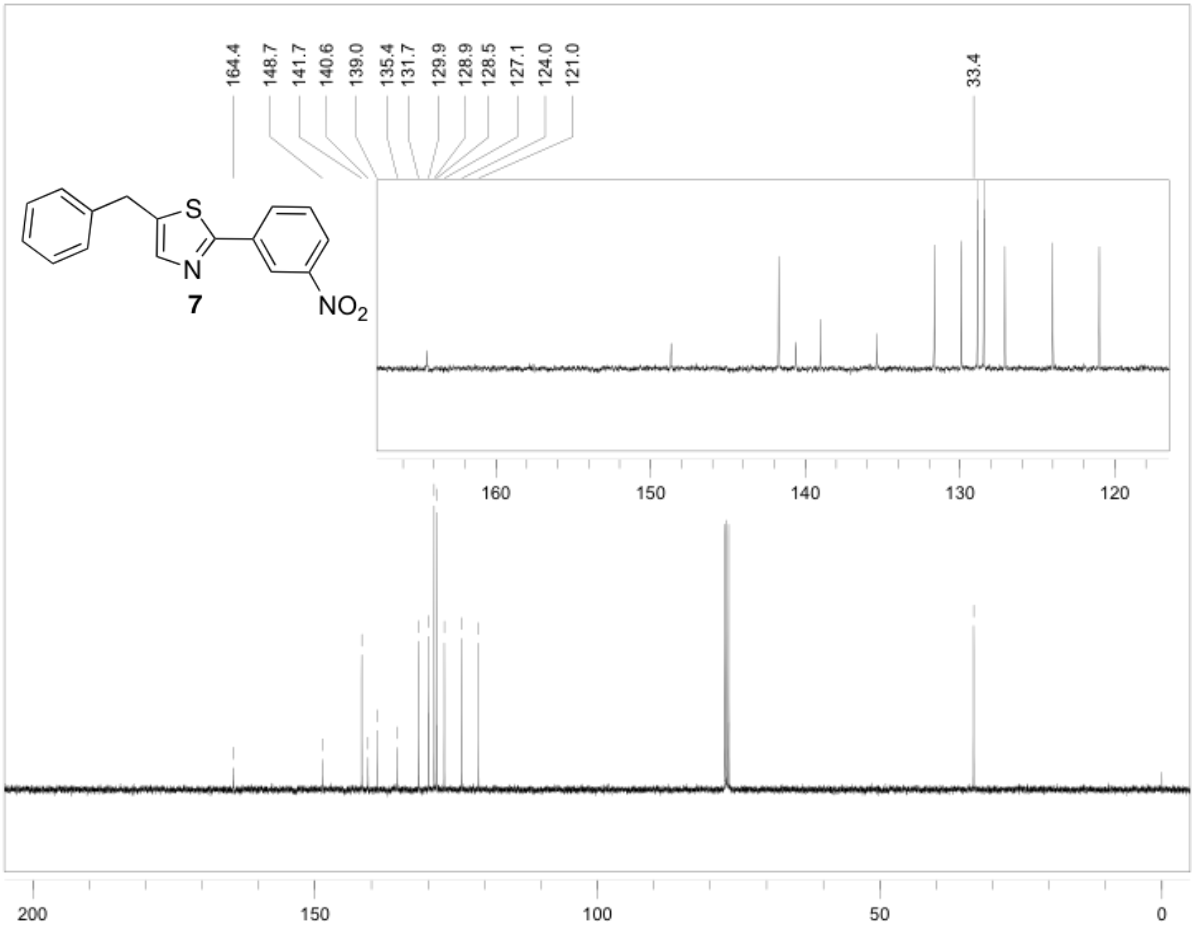
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141.7
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129.9
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NO2
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130
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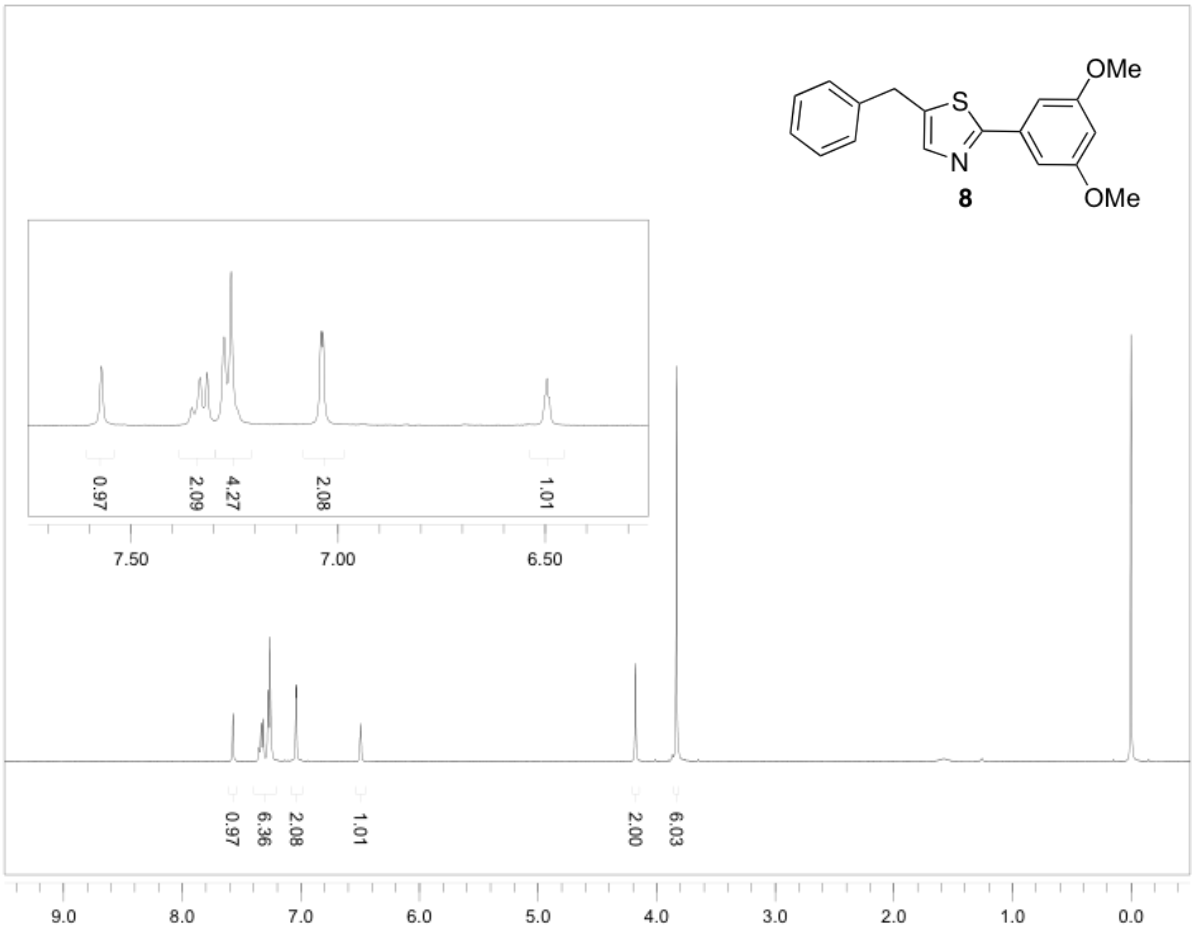
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7.00
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2.08
1.01
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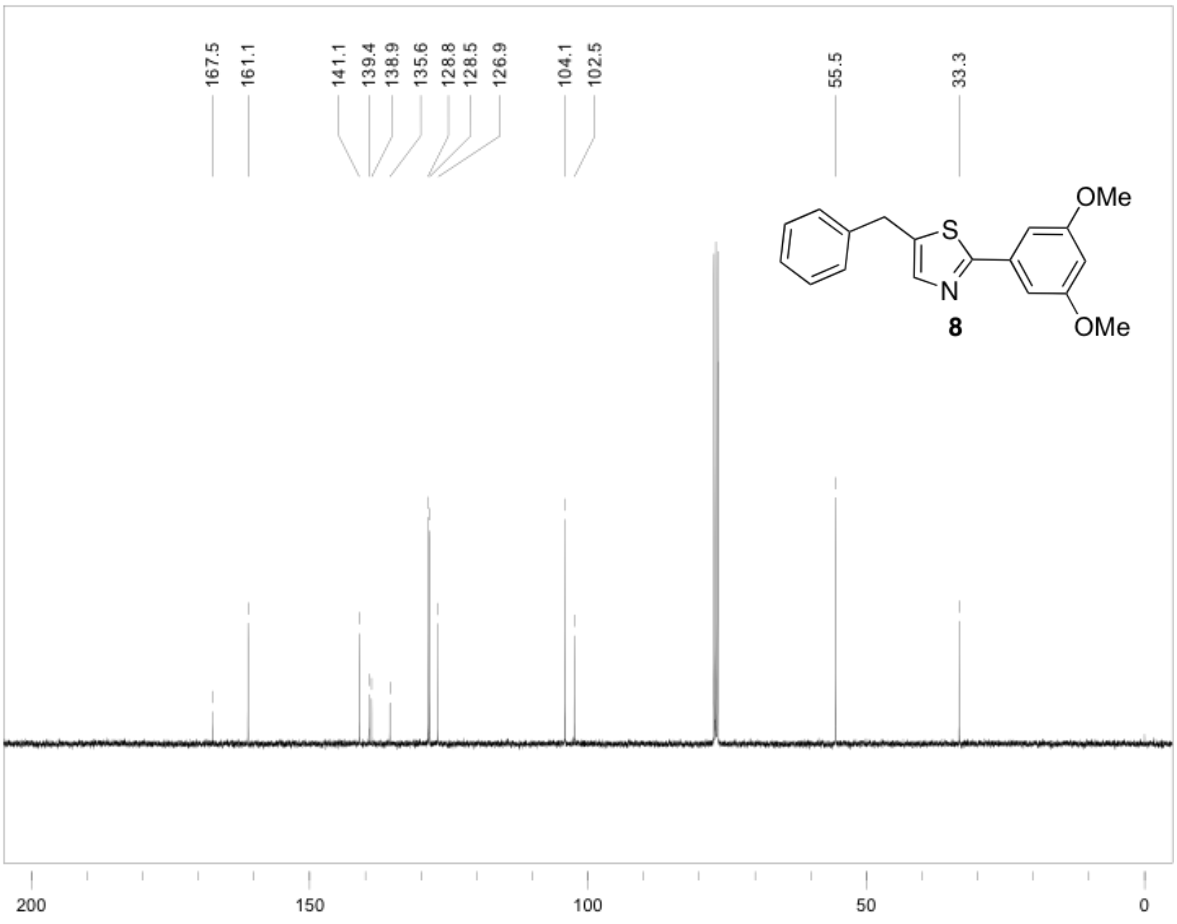
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135.6
128.8
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33.3
OMe
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N
OMe
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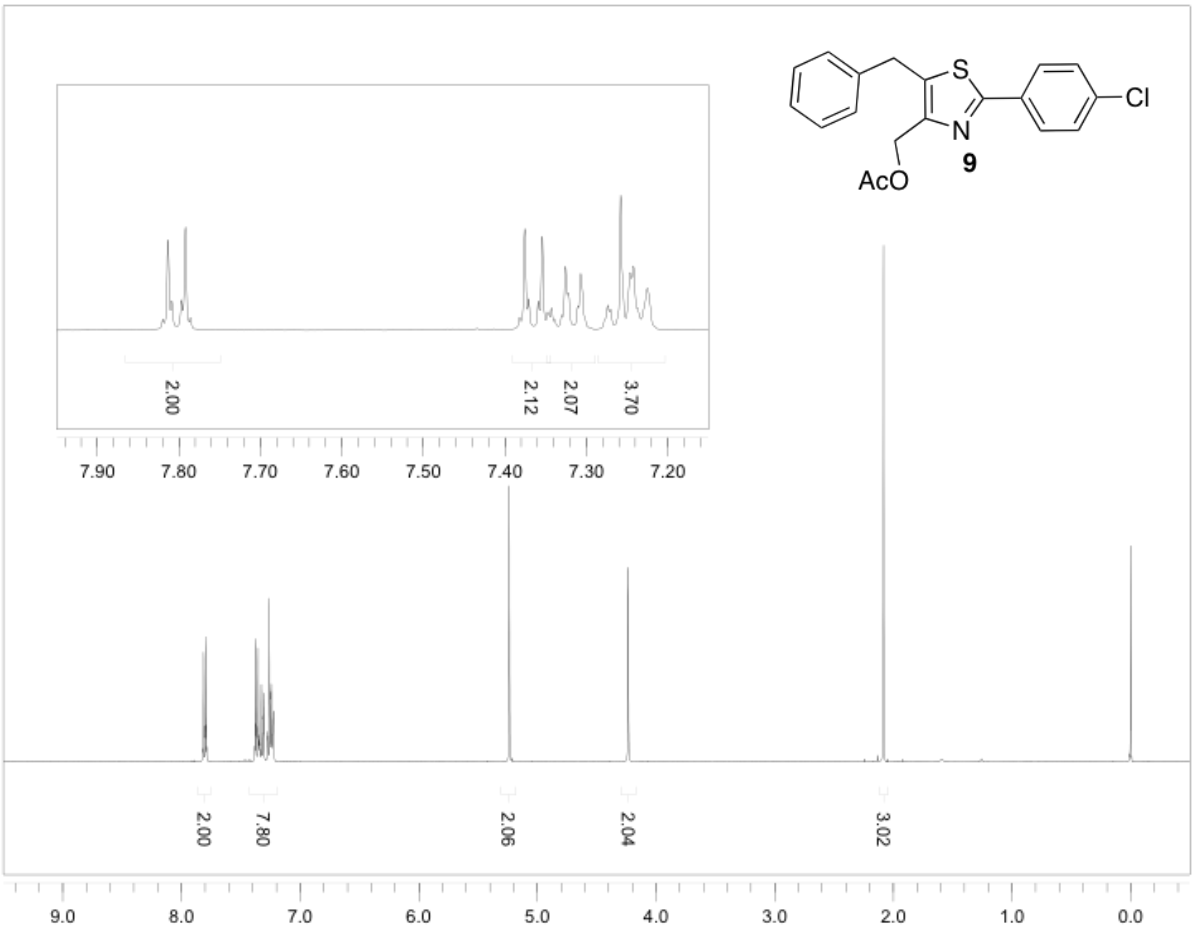
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Cl
AcO
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7.70
7.60
7.50
7.40
7.30
7.20
2.00
7.80
2.06
2.04
3.02
9.0
8.0
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5.0
4.0
3.0
2.0
1.0
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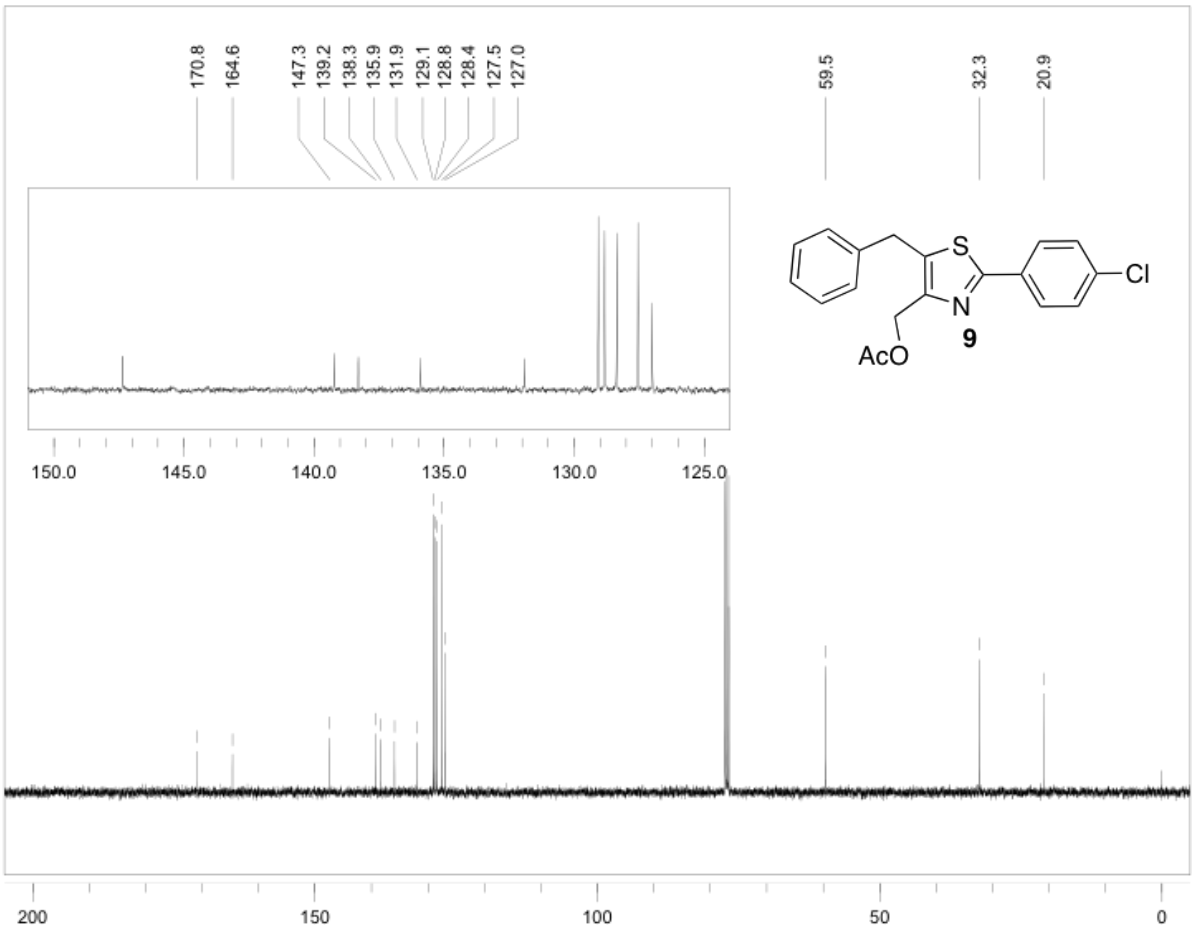
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128.4
127.5
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32.3
20.9
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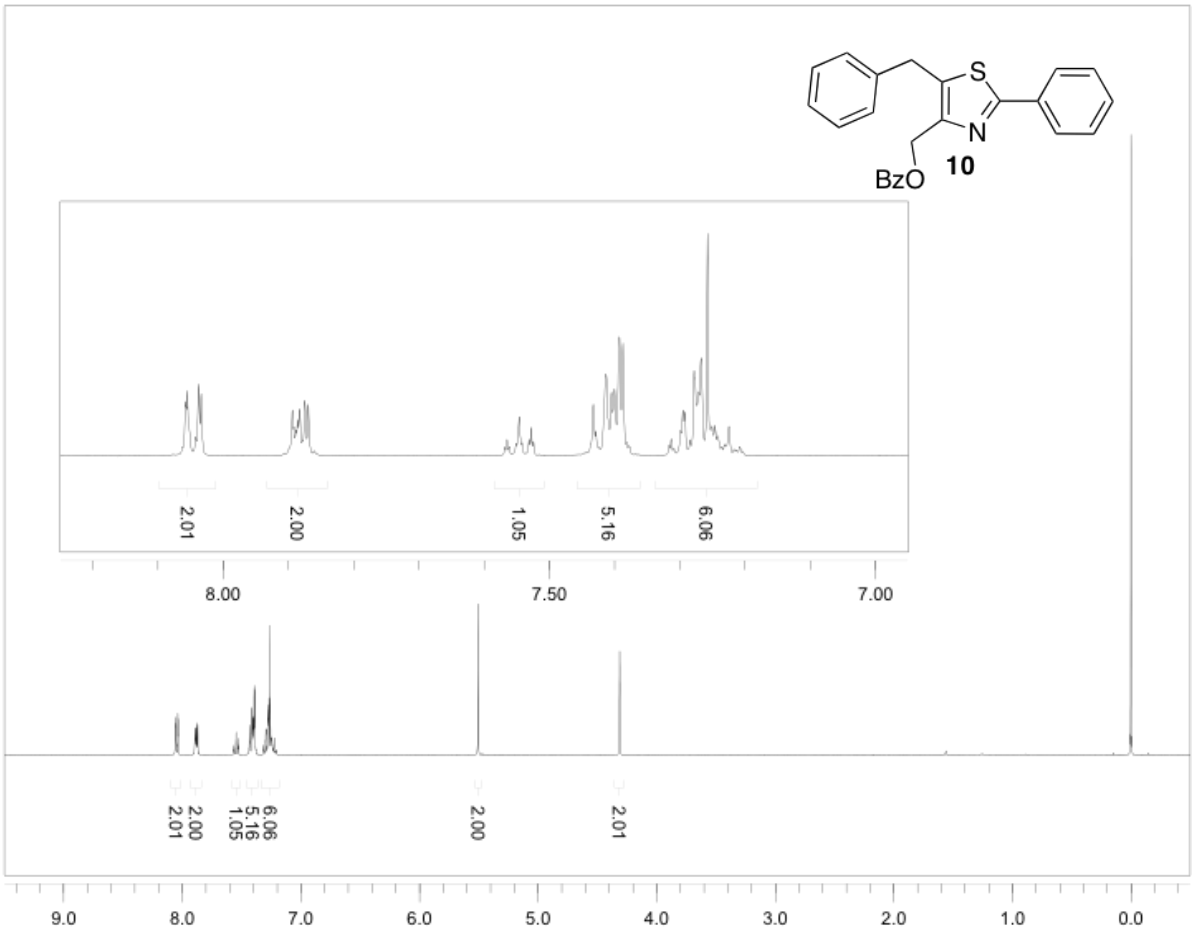
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7.00
2.01
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1.05
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6.06
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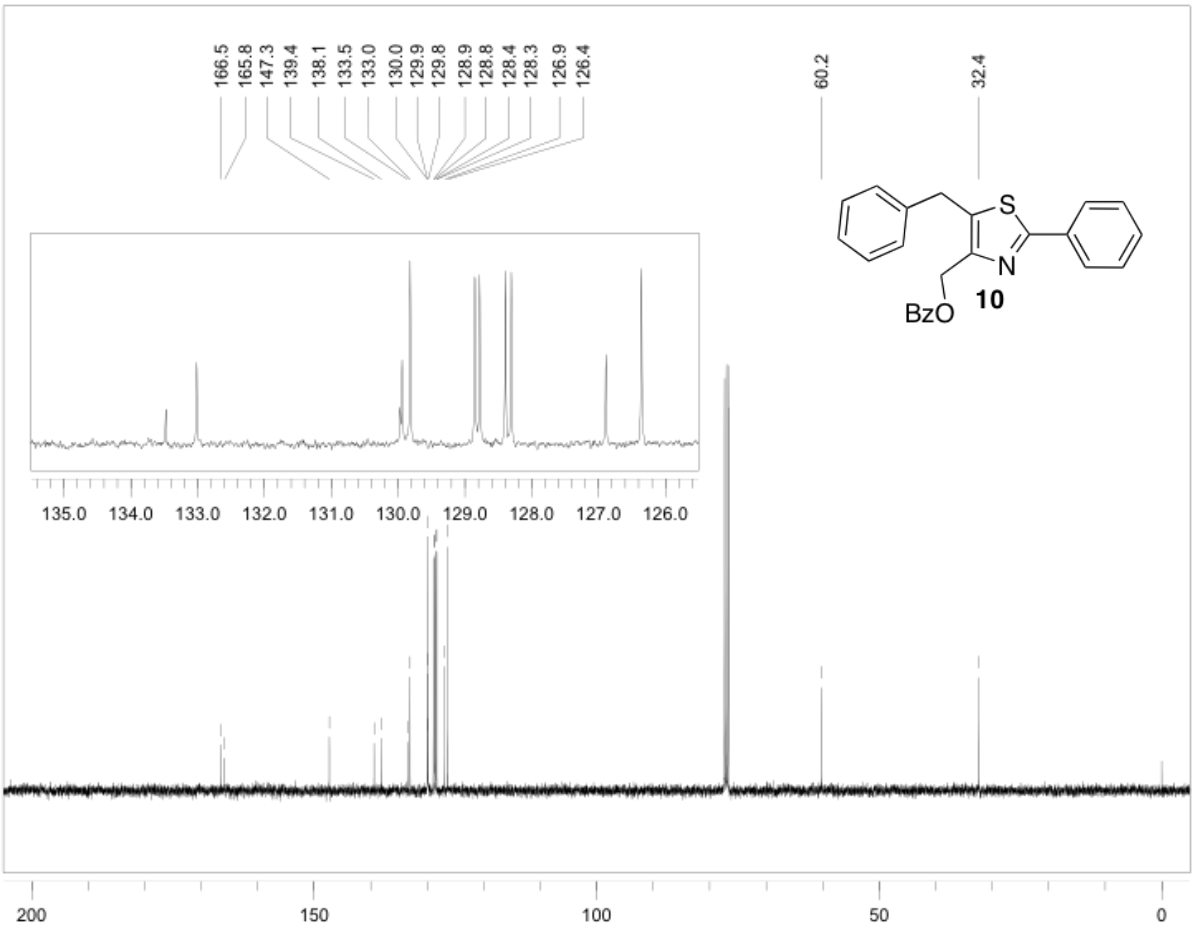
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129.8
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128.8
128.4
128.3
126.9
126.4
60.2
32.4
S
N
BzO
10
135.0
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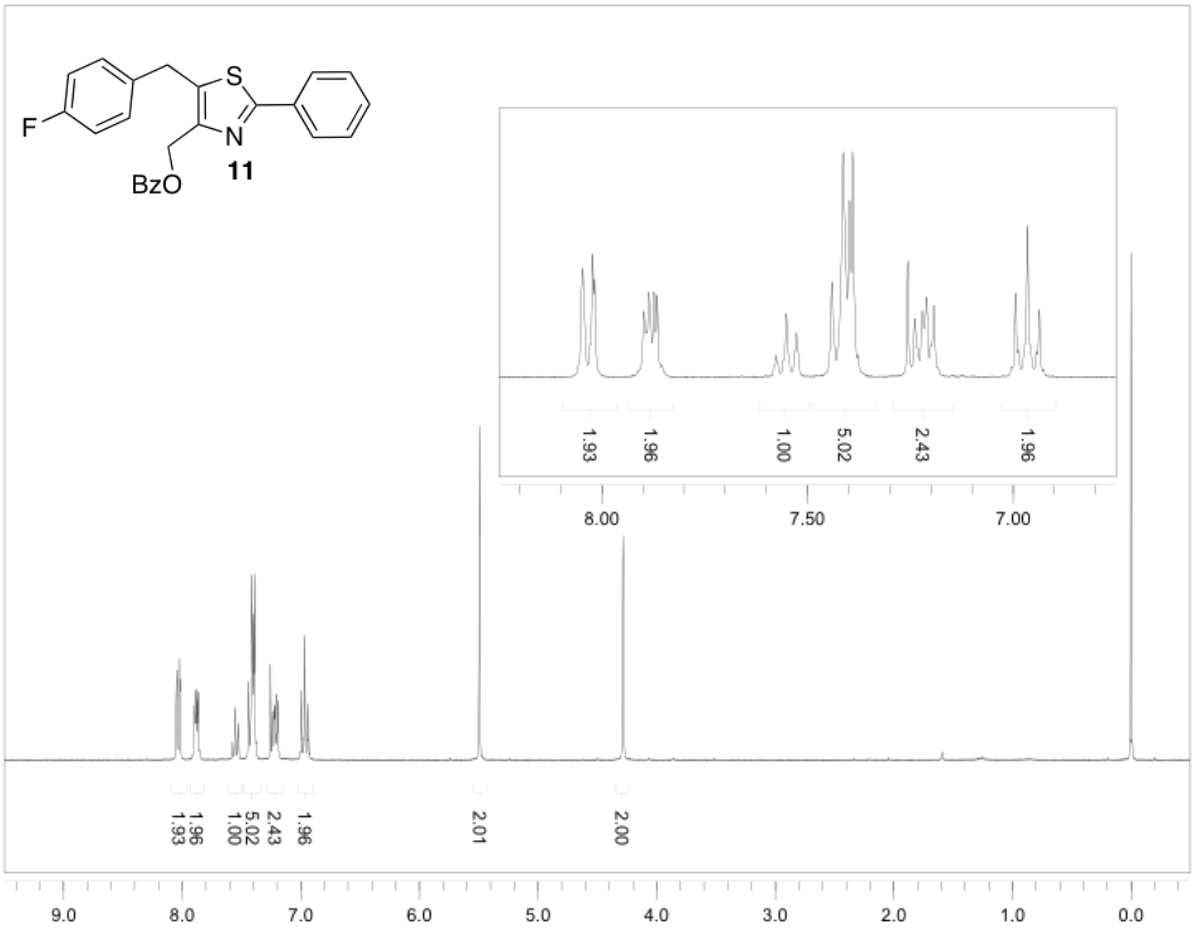
0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BzO
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1.96
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6.0
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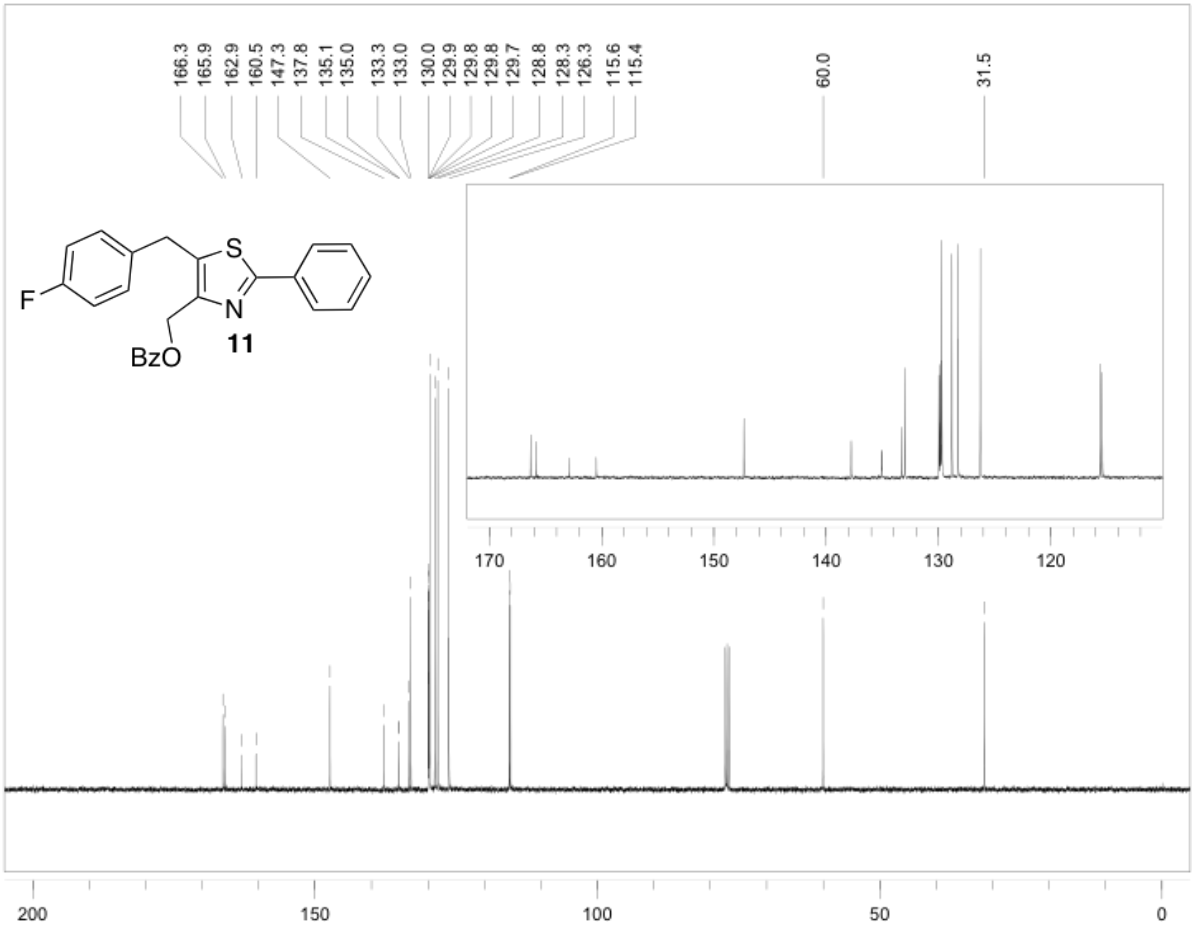
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129.8
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129.7
128.8
128.3
126.3
115.6
115.4
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F
S
N
BzO
11
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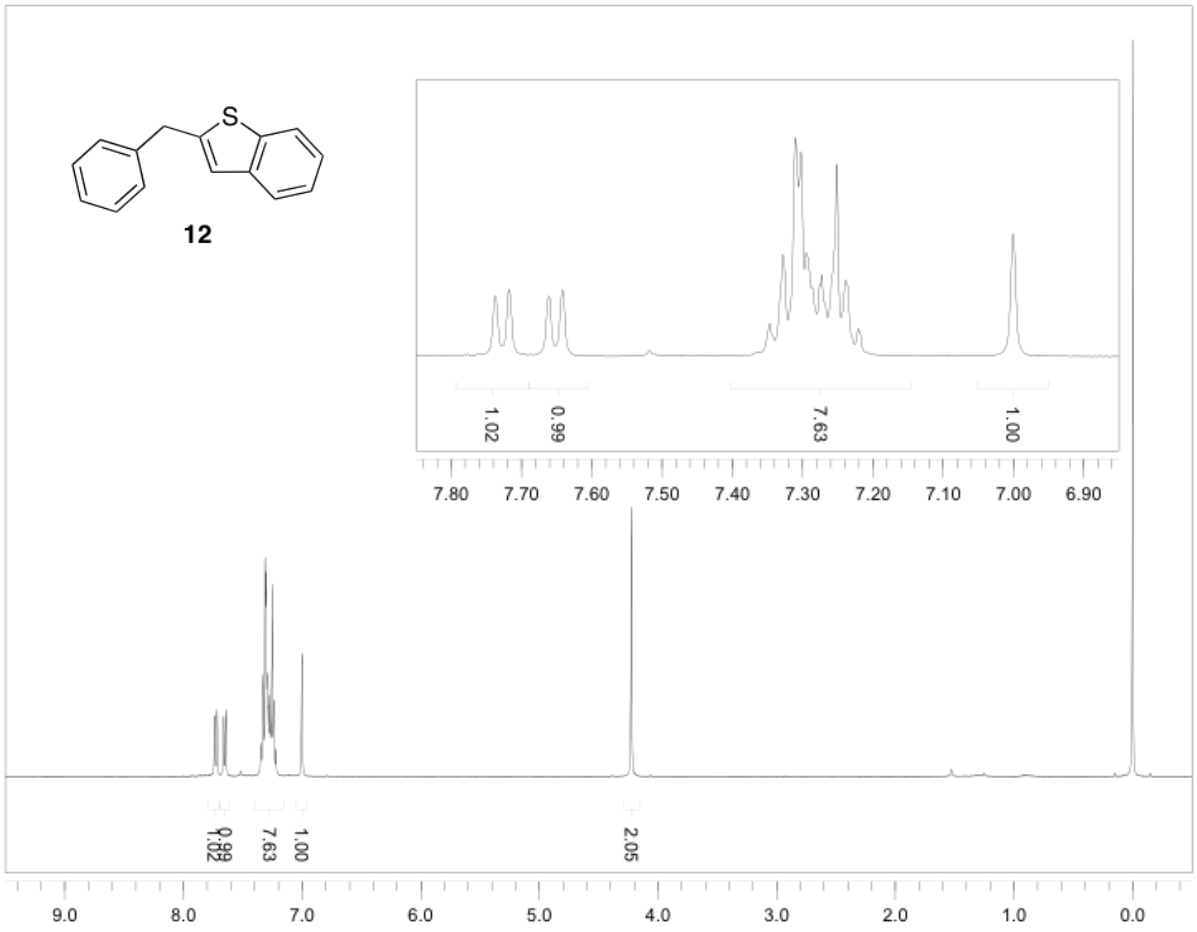
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7.10
7.00
6.90
1.02
0.99
7.63
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6.0
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4.0
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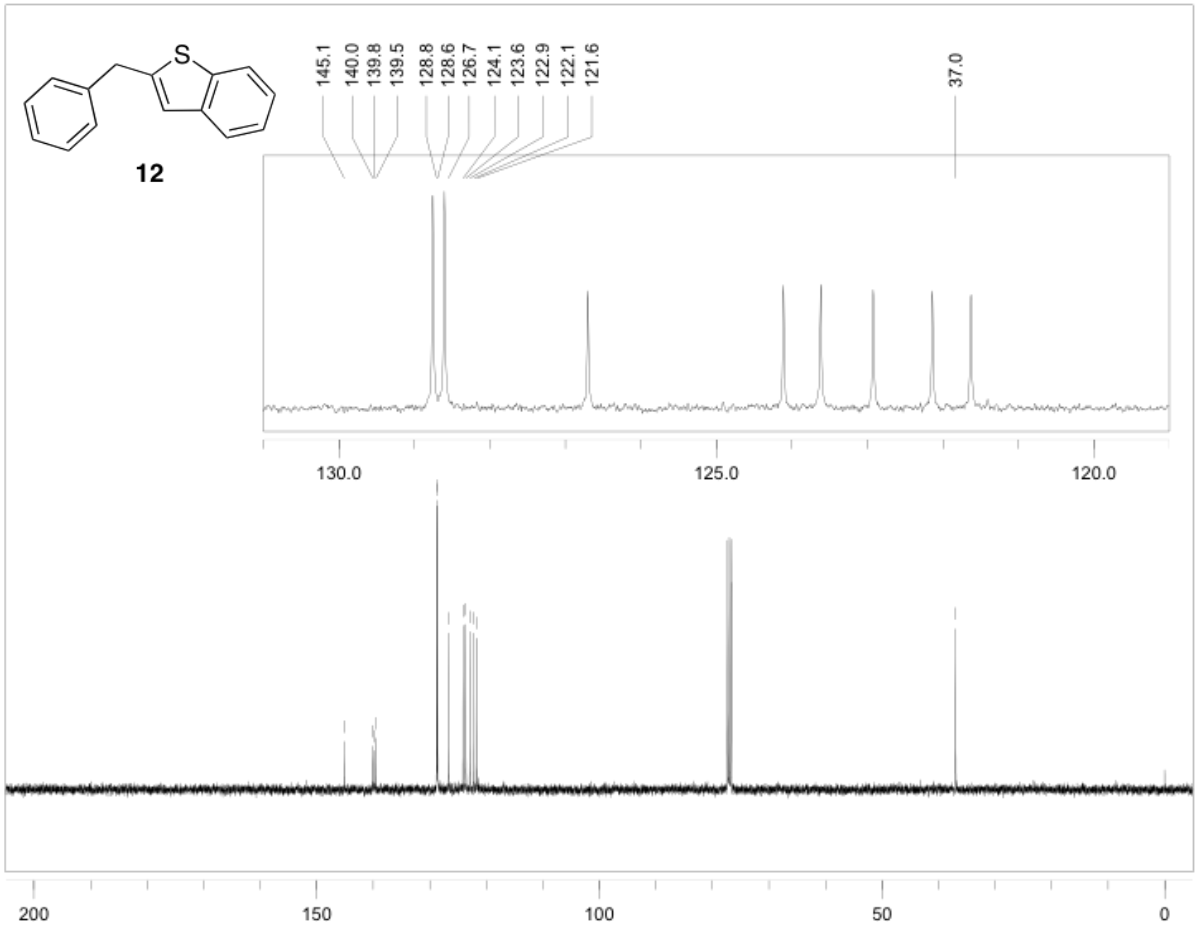
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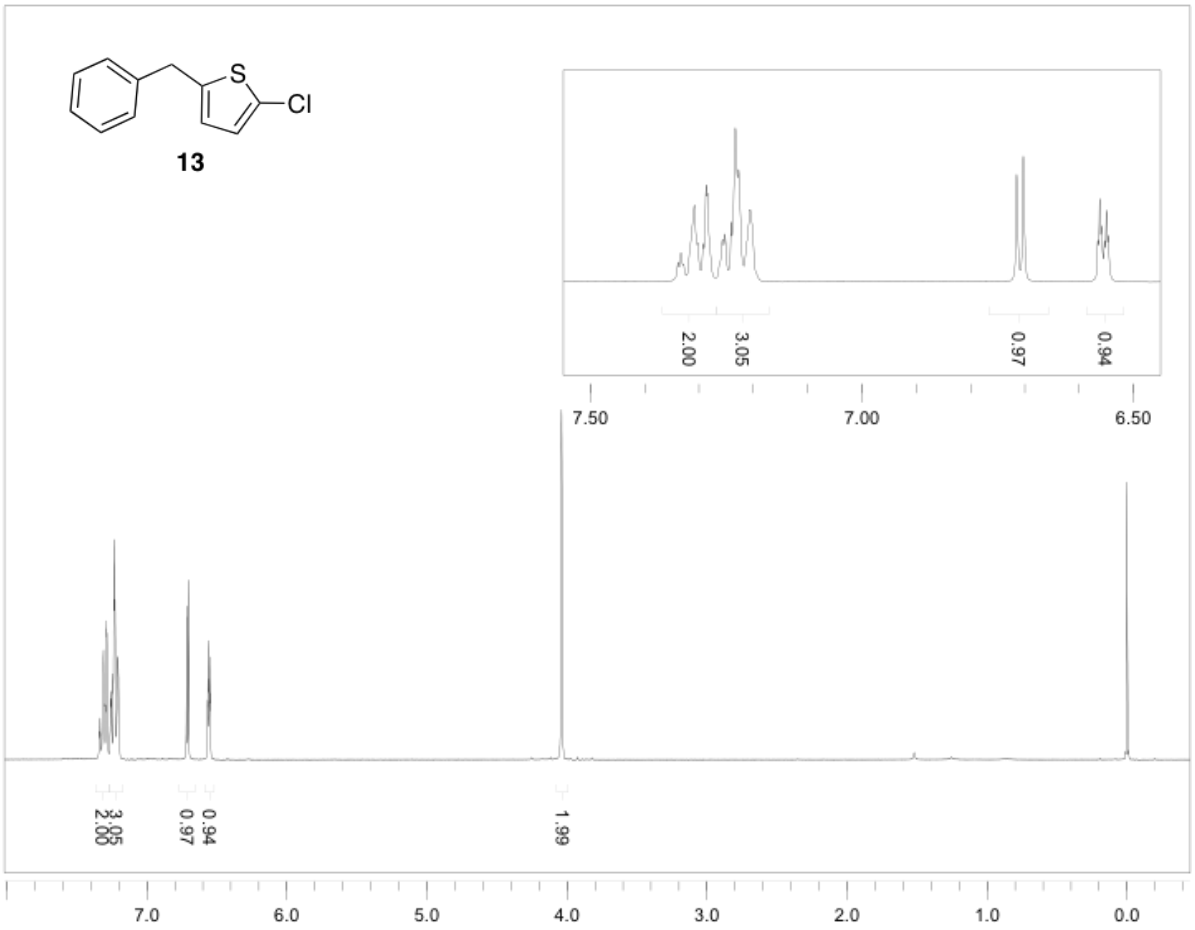
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7.00
6.50
2.00
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1.99
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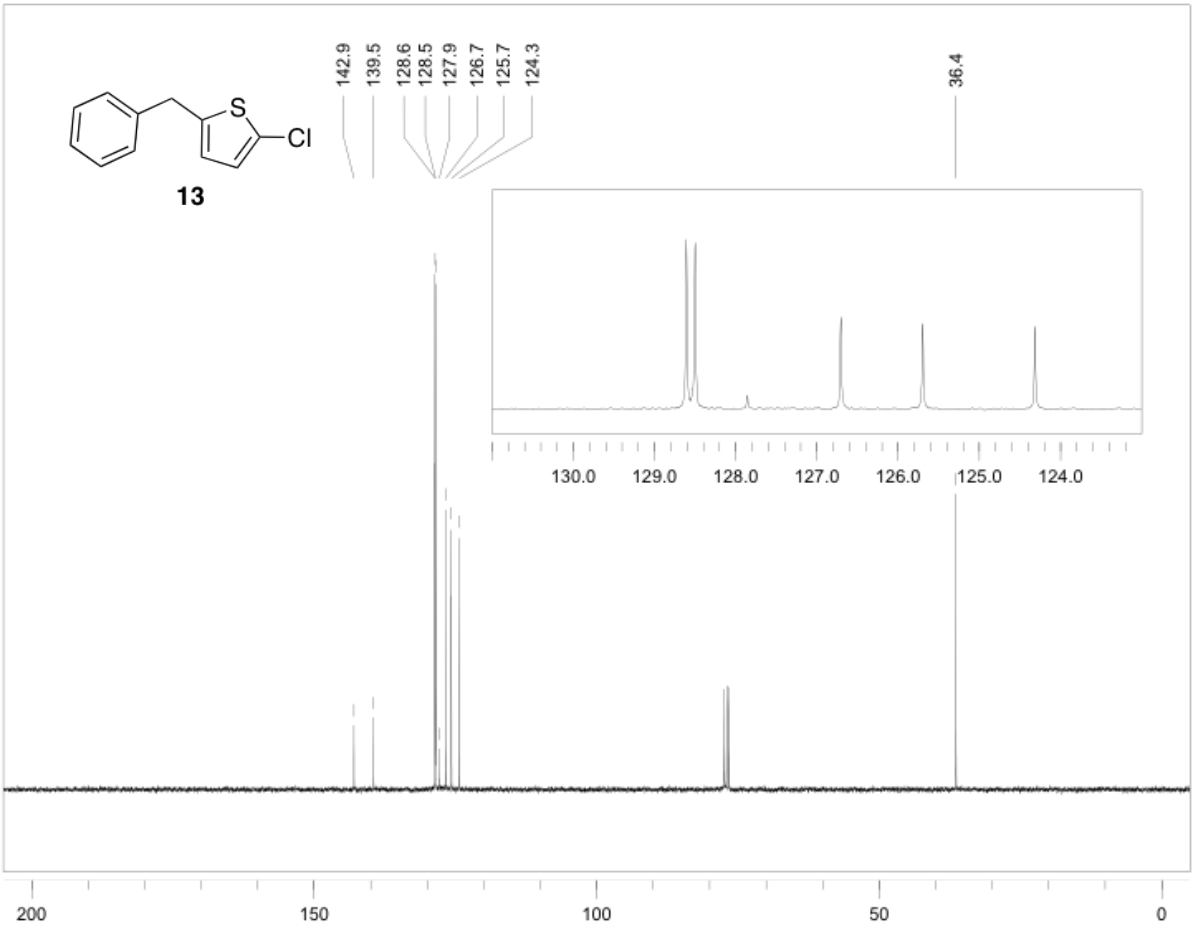
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126.7
125.7
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125.0
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50
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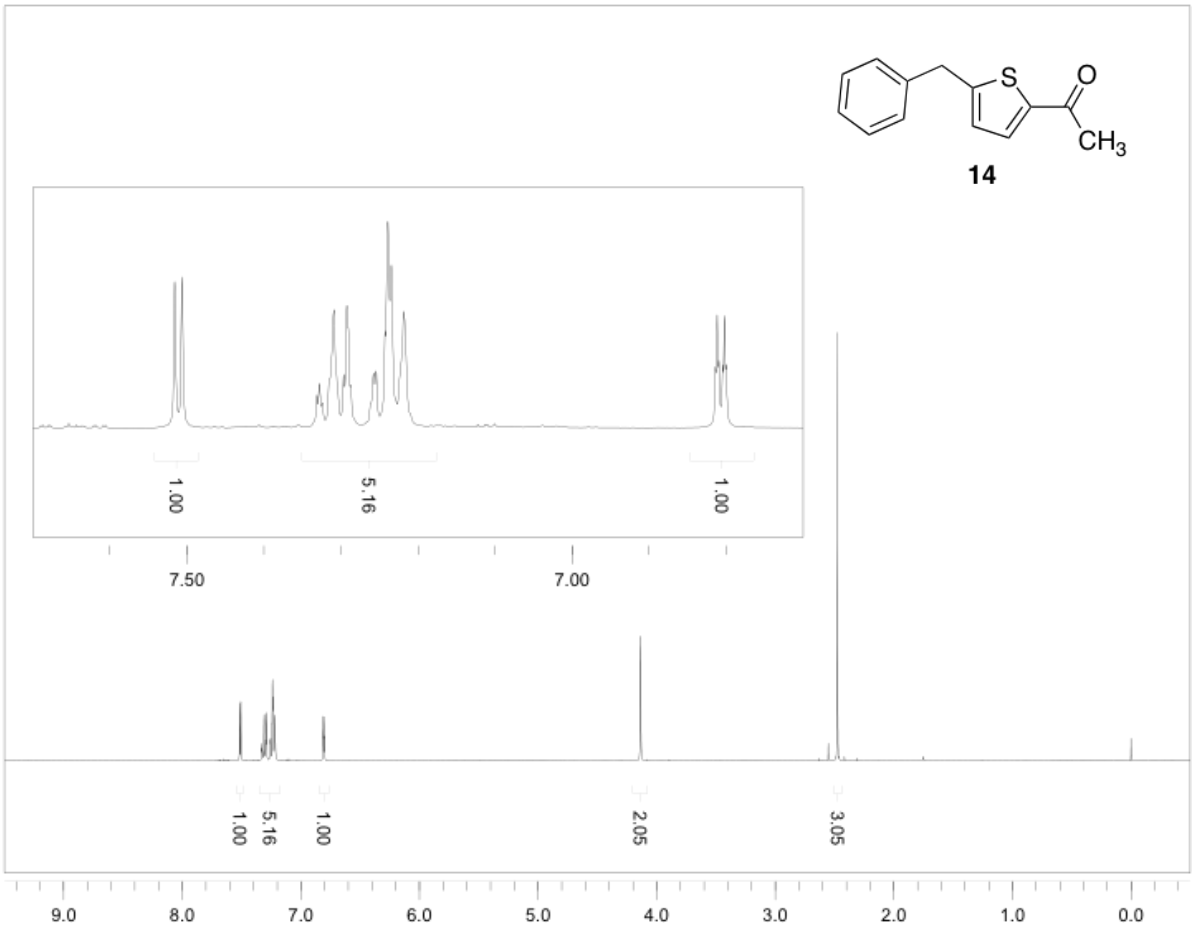
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O
CH3
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1.00
5.16
1.00
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4.0
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2.0
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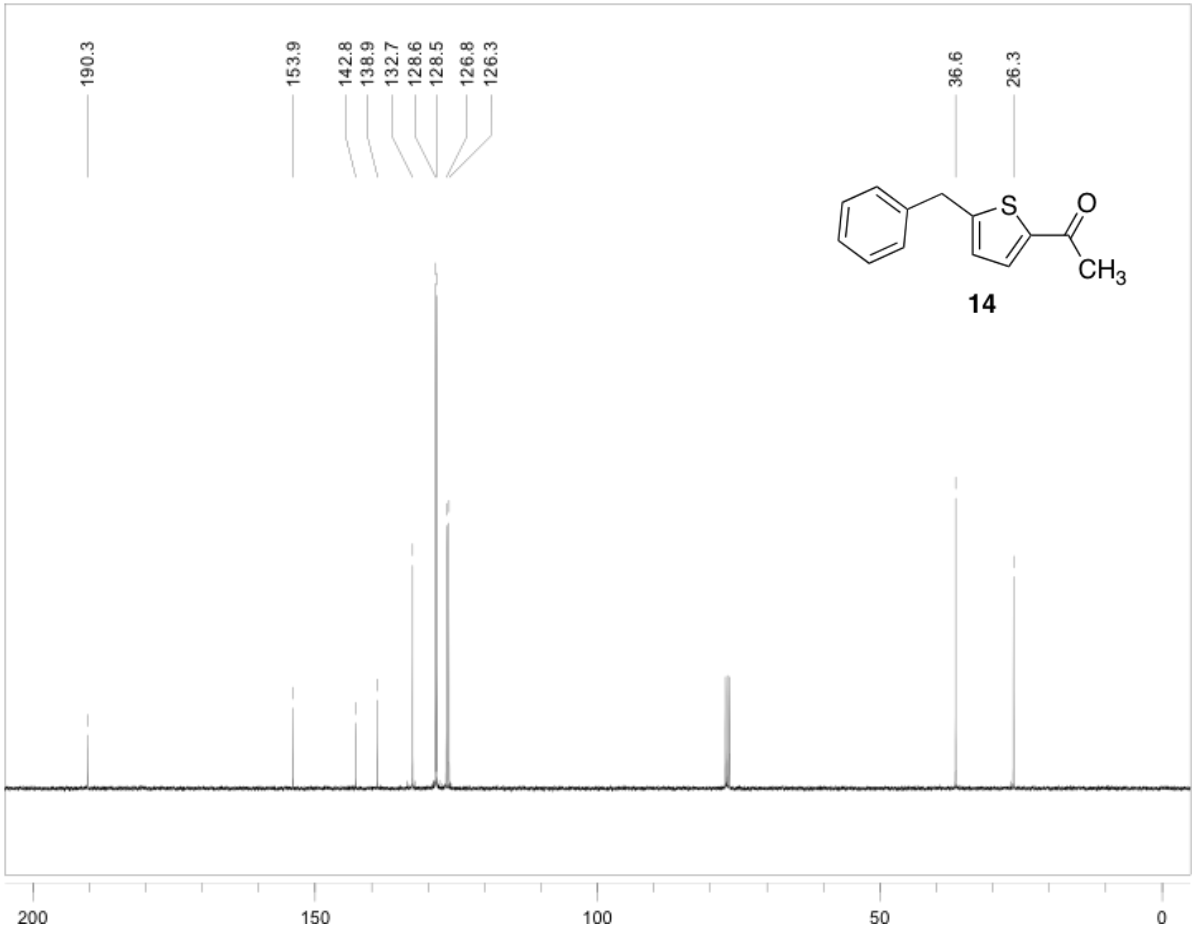
190.3
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126.8
126.3
36.6
26.3
S
O
CH3
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50
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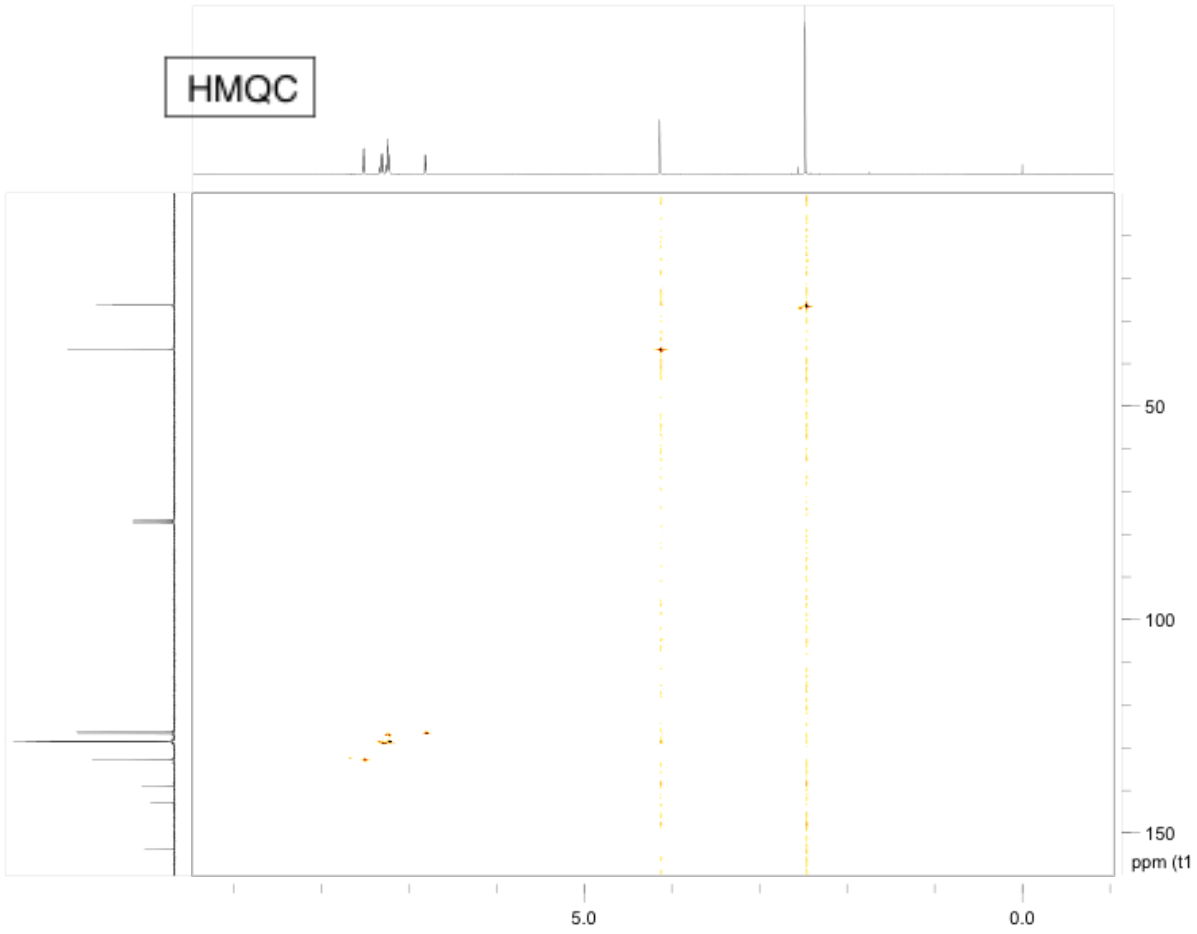
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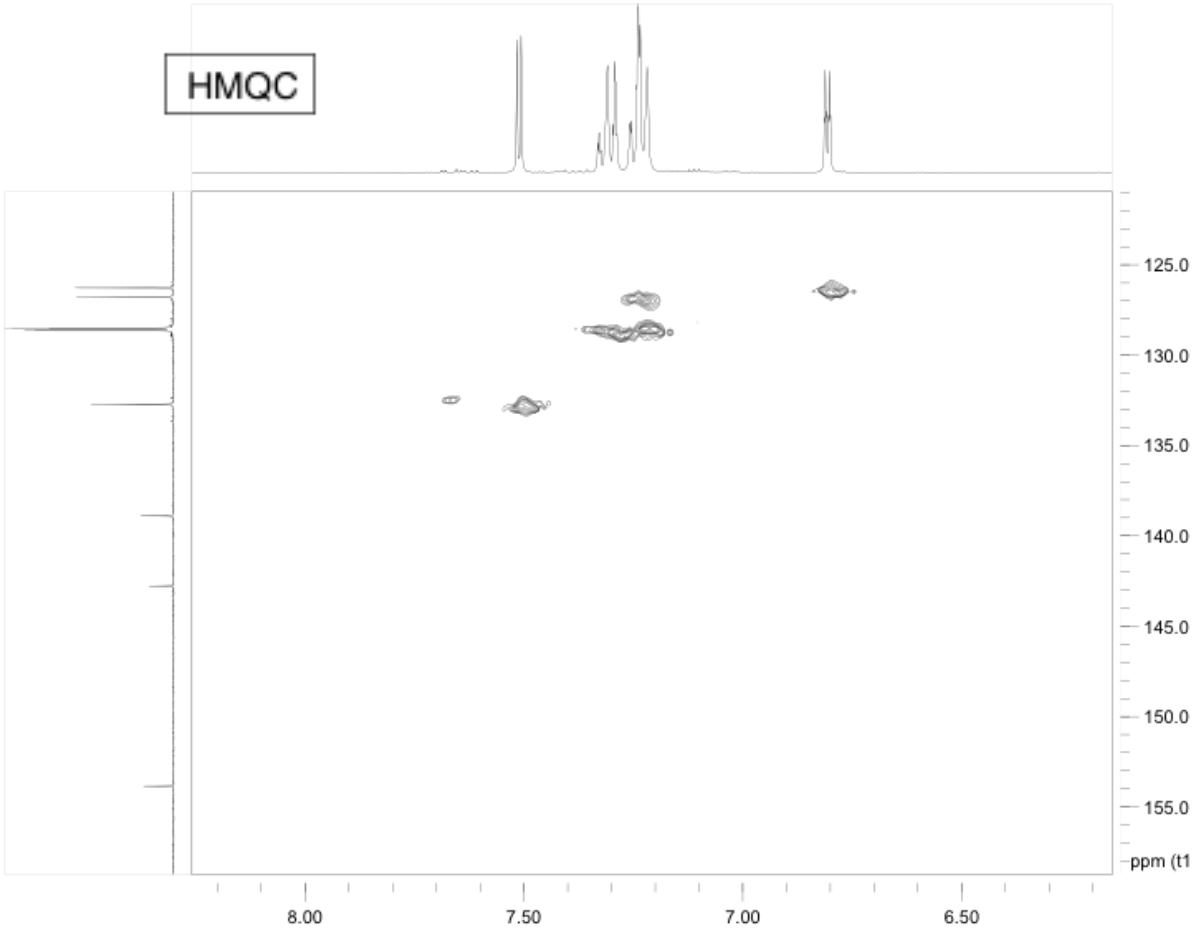
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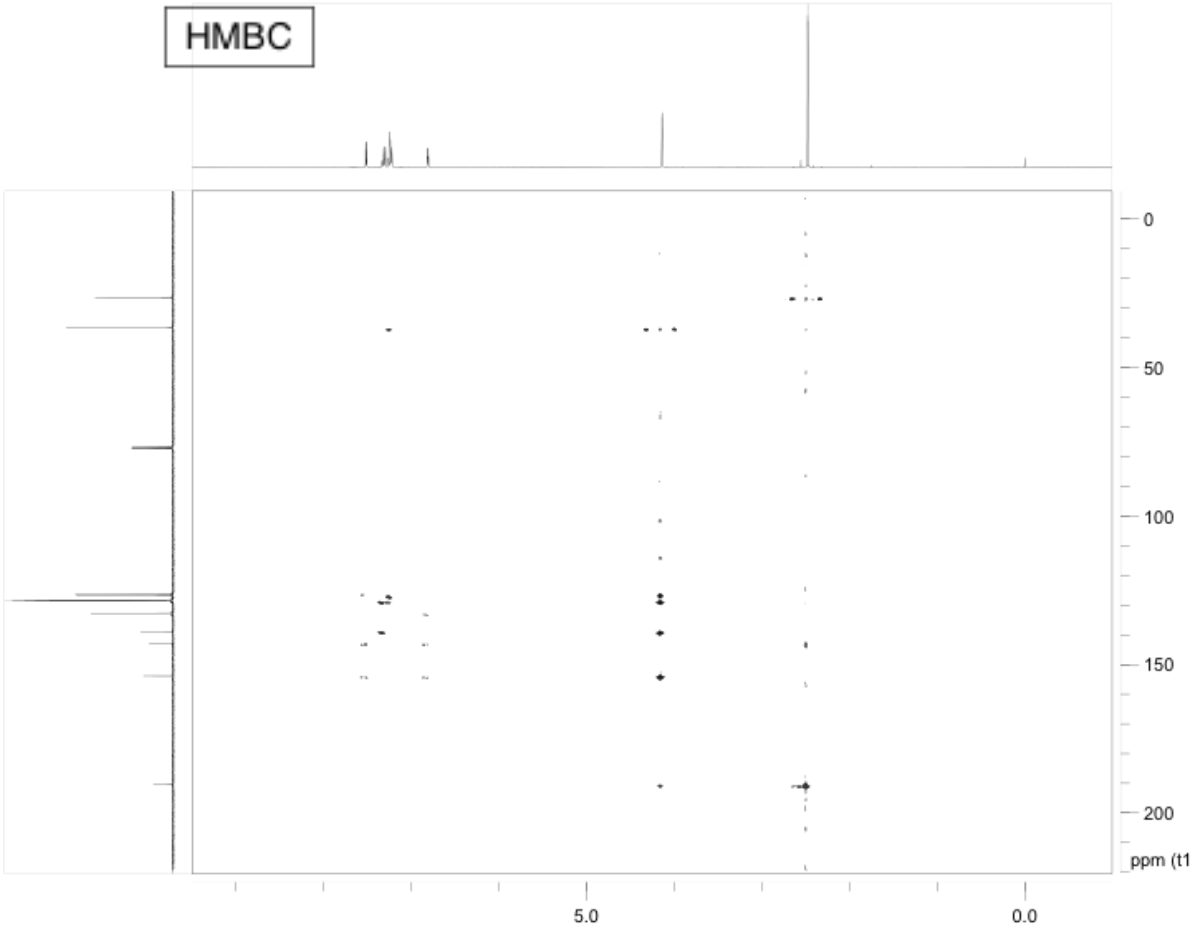
7.00
6.50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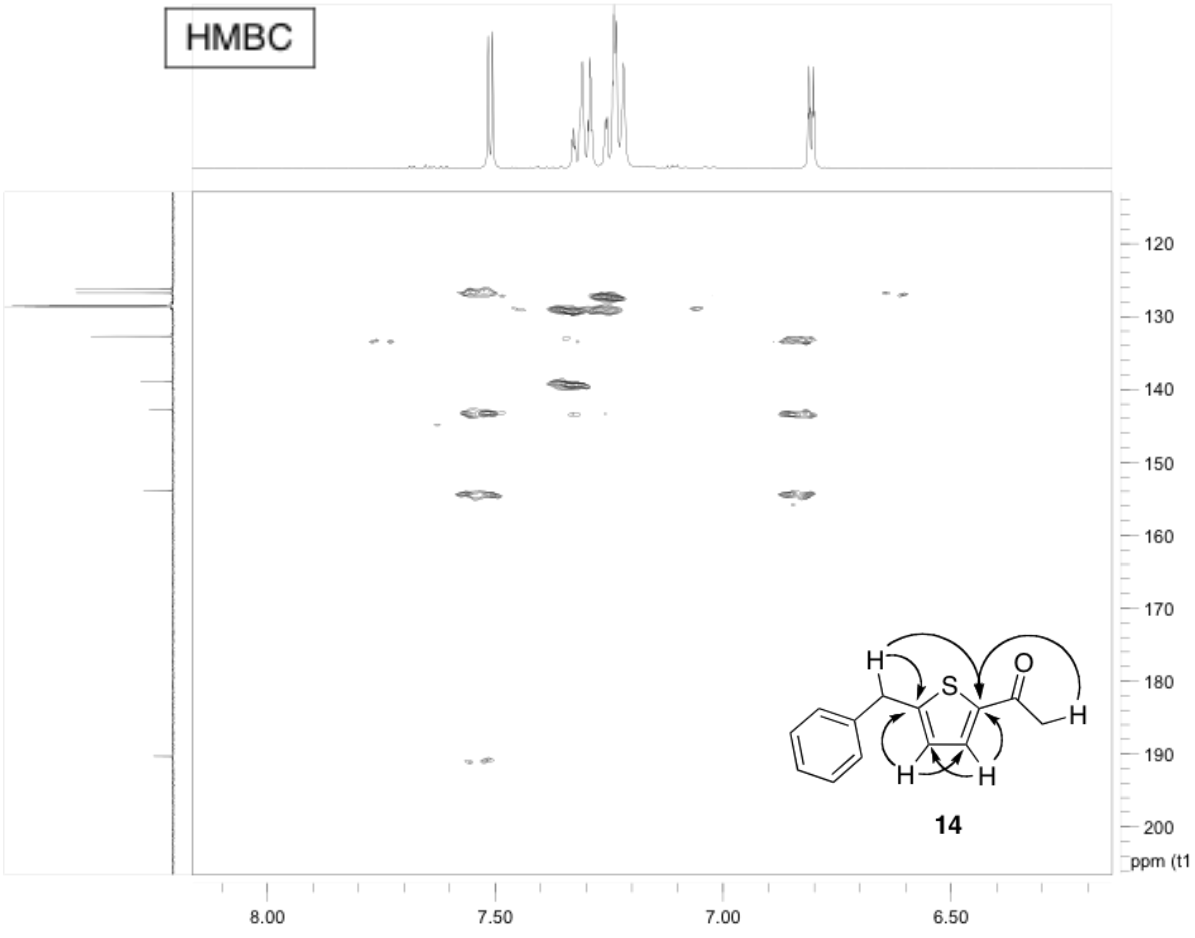
HMBC
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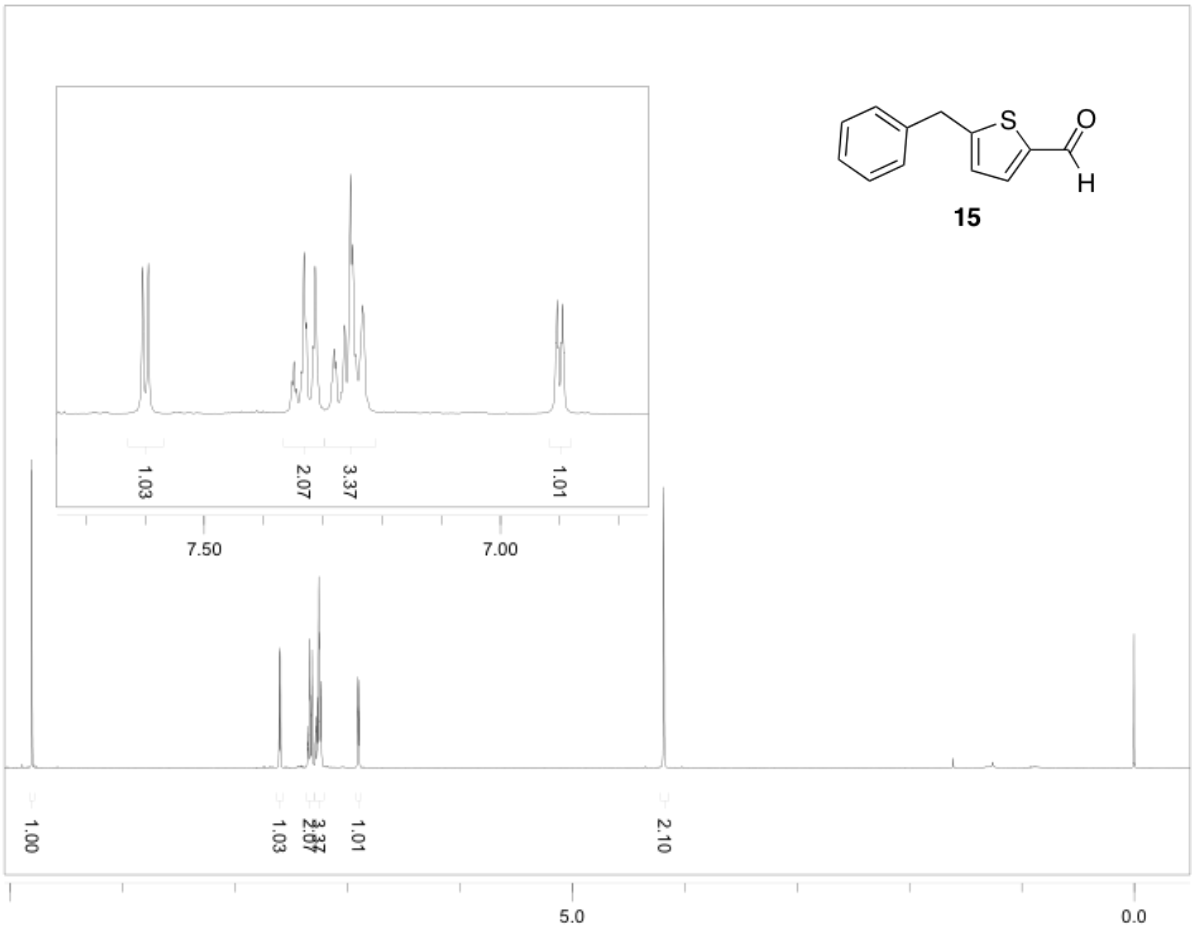
7.00
6.50
H
S
O
H
H
H

14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H
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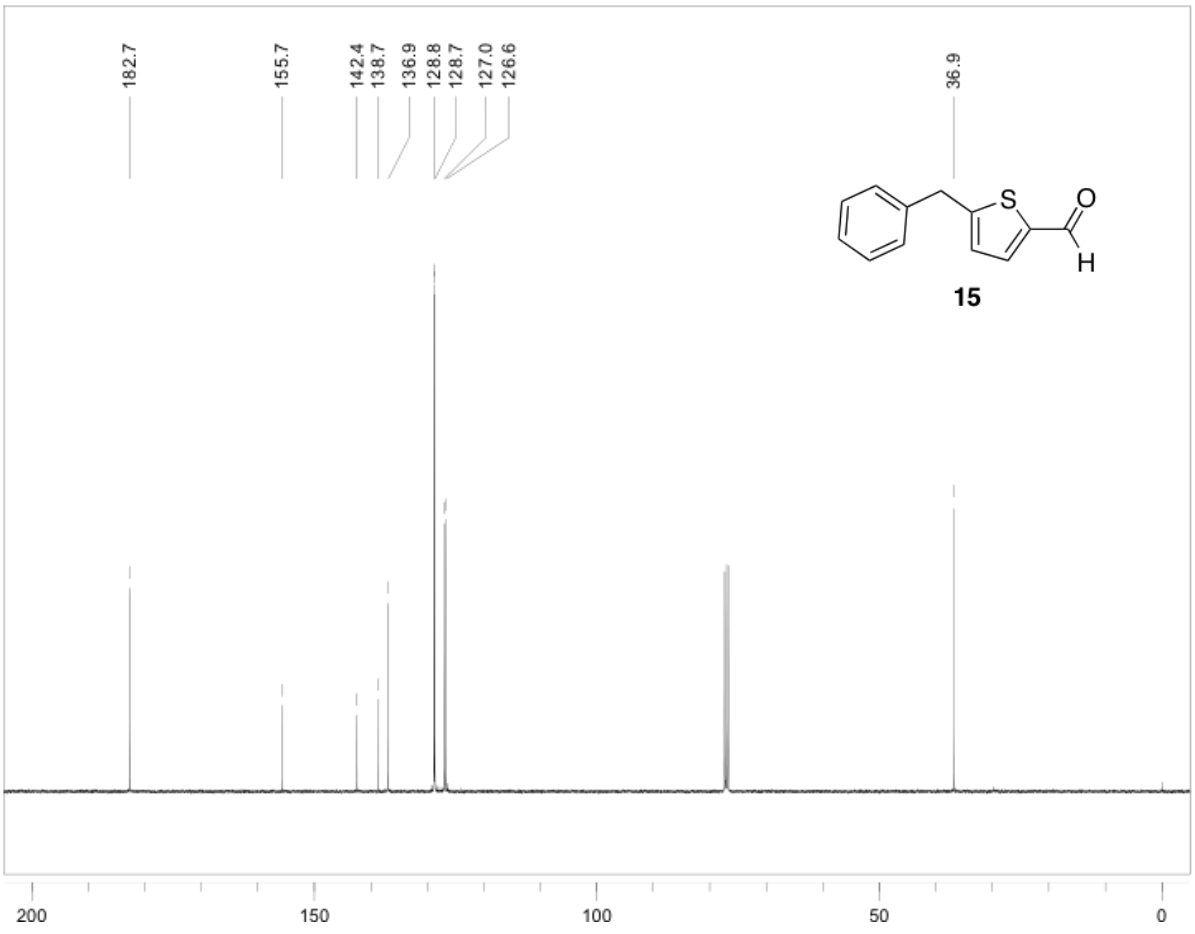
1.00
1.03
2.07
3.37
1.01
2.10
5.0
0.0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136.9
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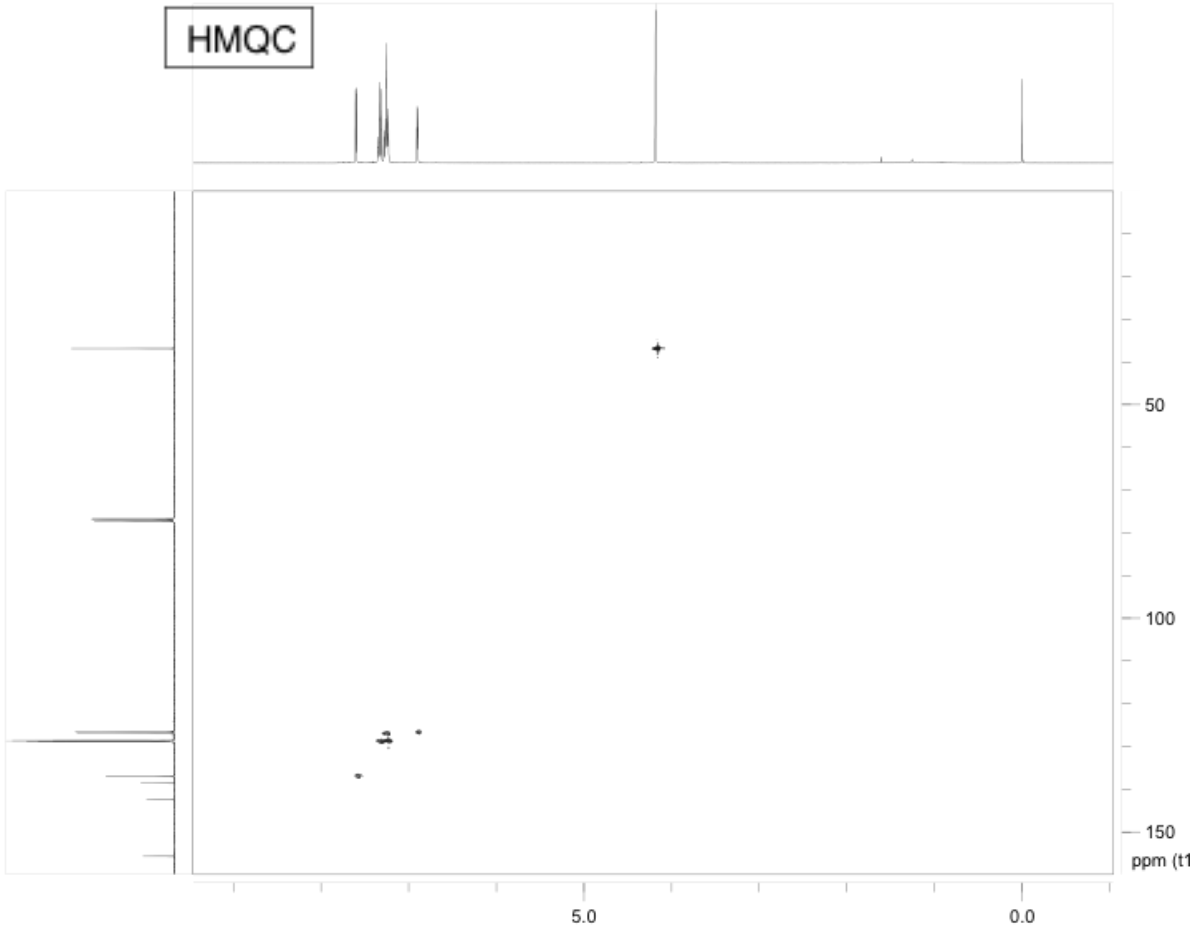
128.7
127.0
126.6
36.9
S
O
H
15
200
150
100
50
0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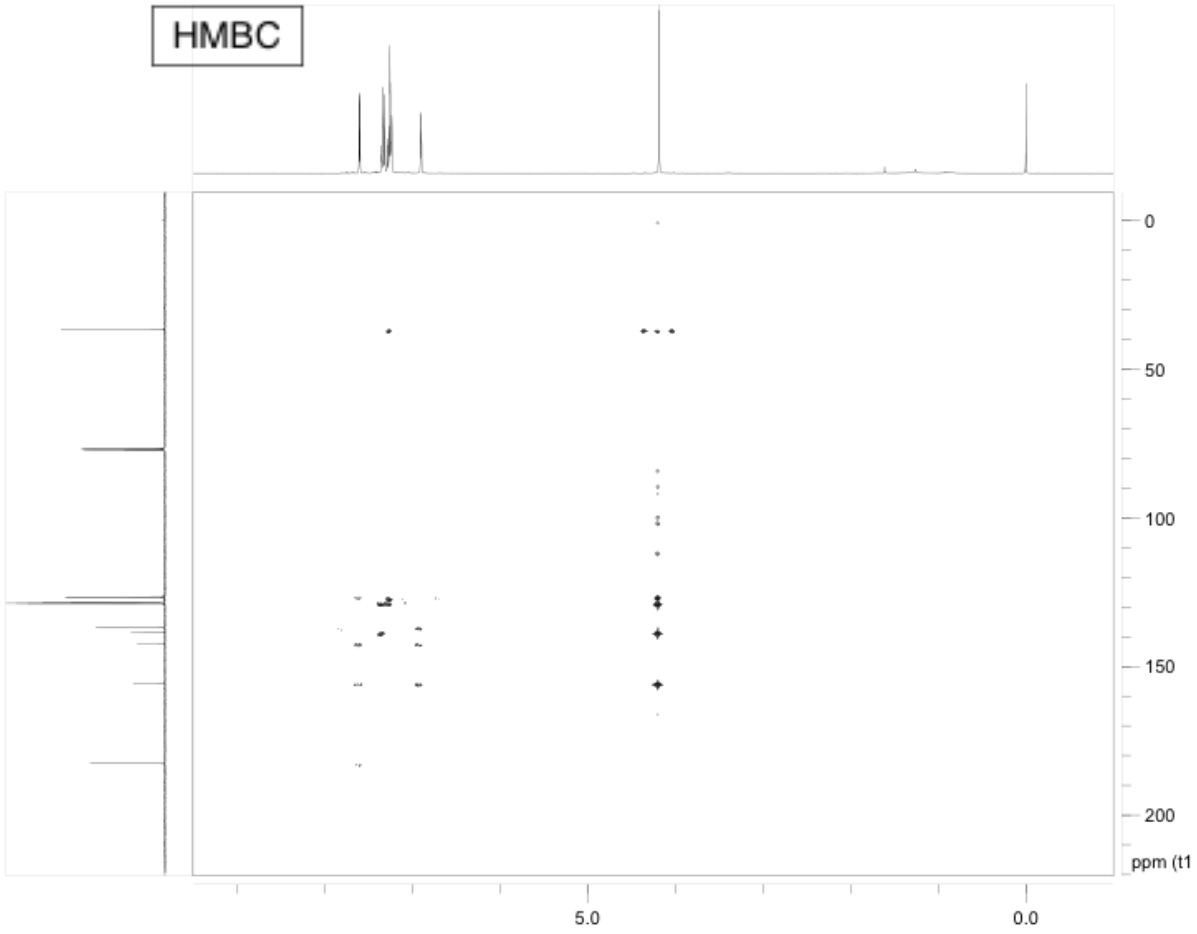
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ppm (t1
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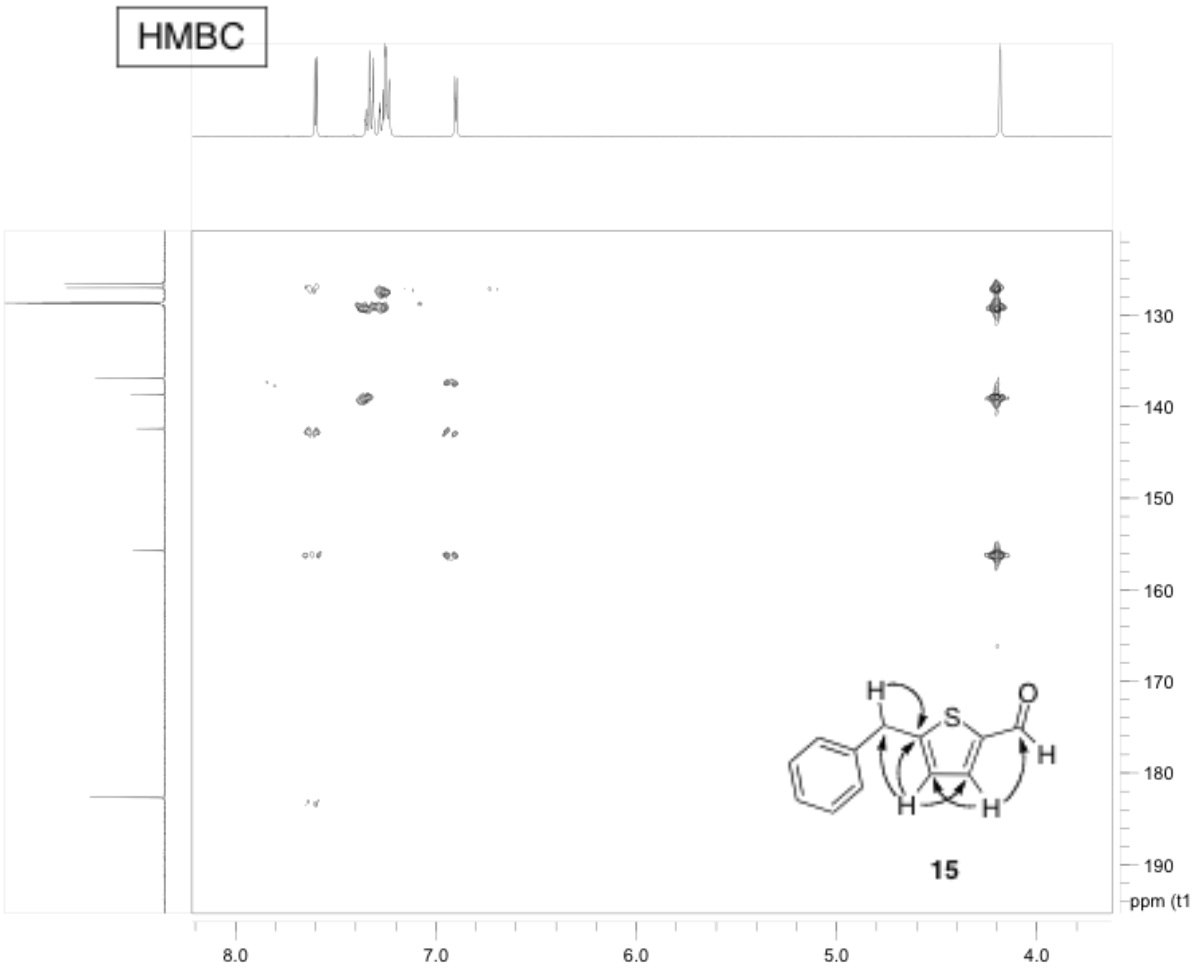
HMBC
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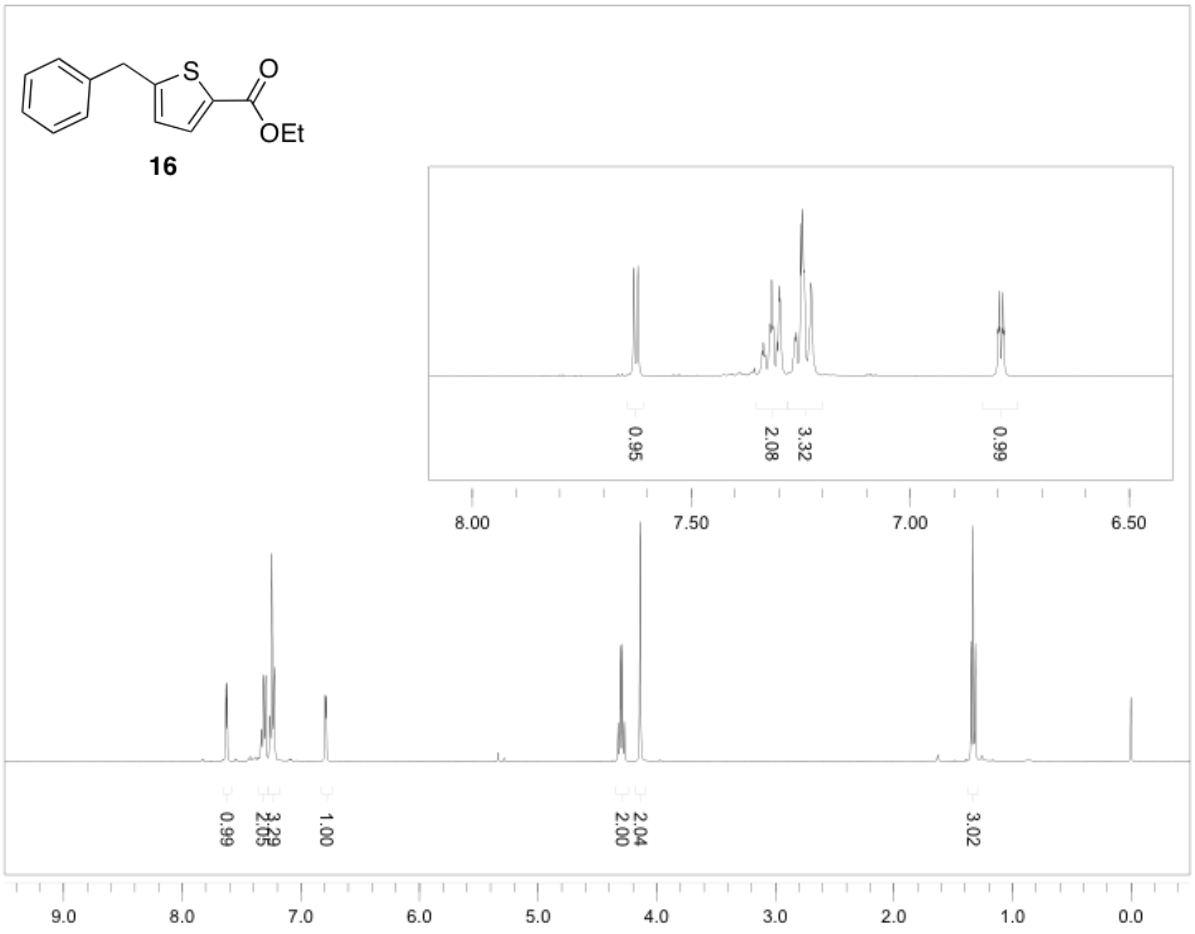
6.0
5.0
4.0
H
S
O
H
H
H
15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OEt
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7.00
6.50
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2.29
2.05
1.00
2.04
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8.0
7.0
6.0
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2.0
1.0
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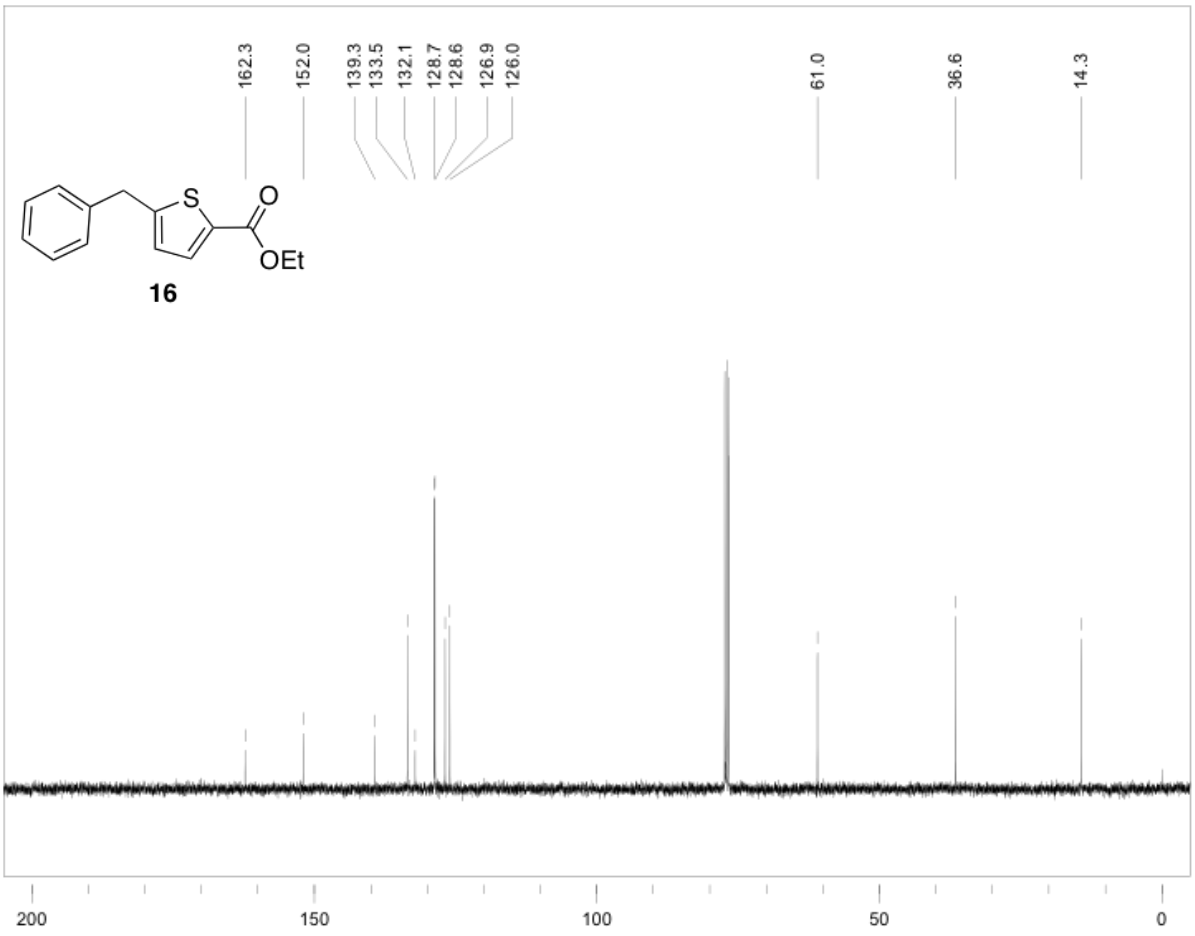
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133.5
132.1
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61.0
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14.3
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O
OEt
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50
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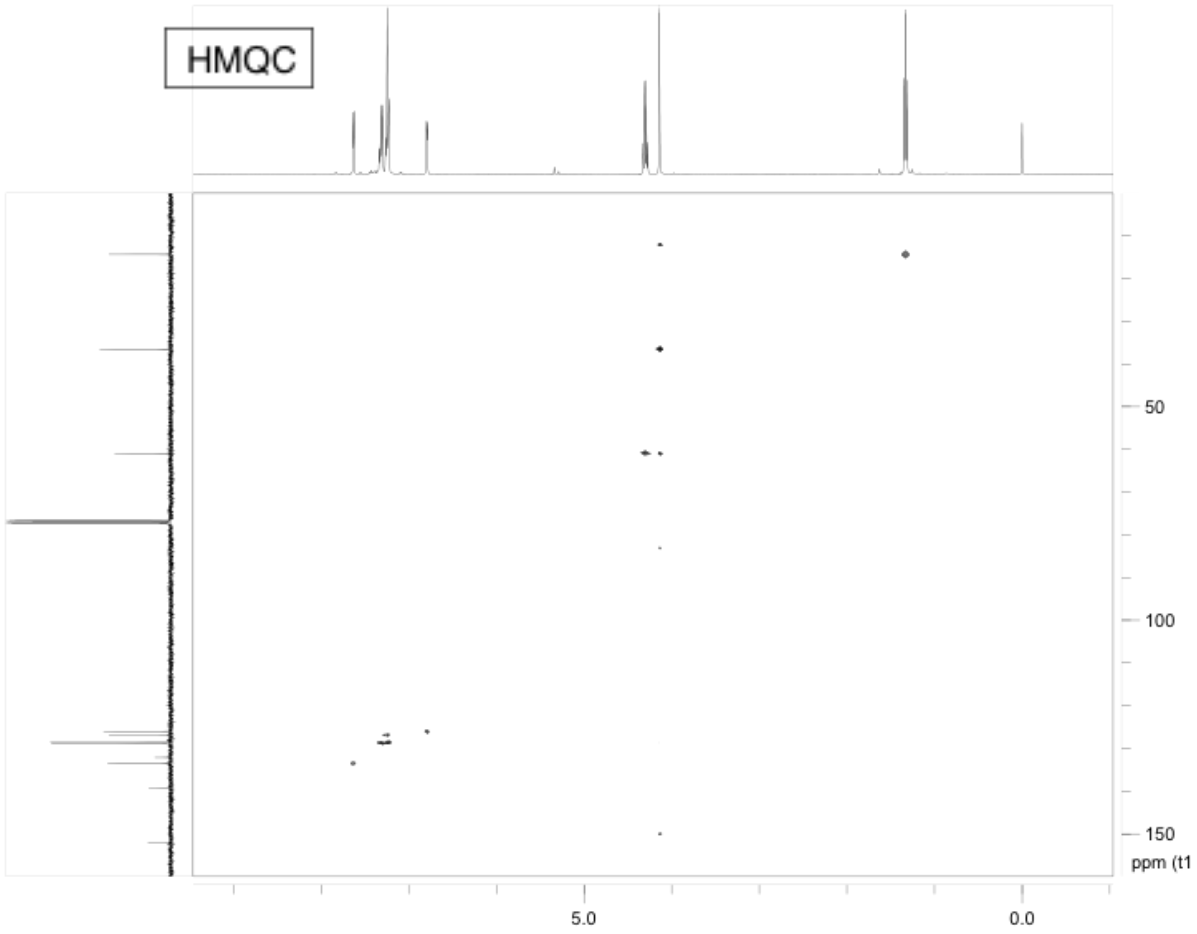
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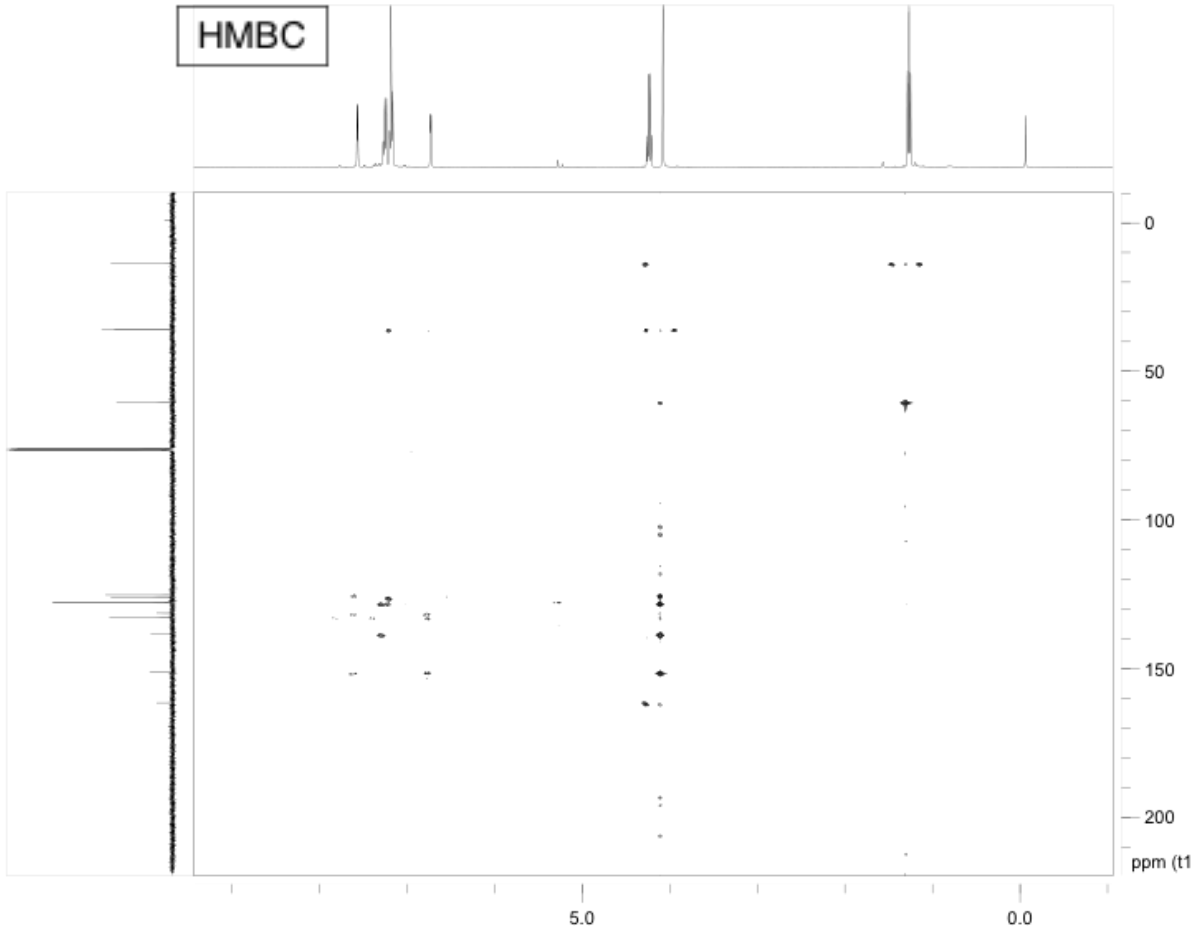
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ppm (t1
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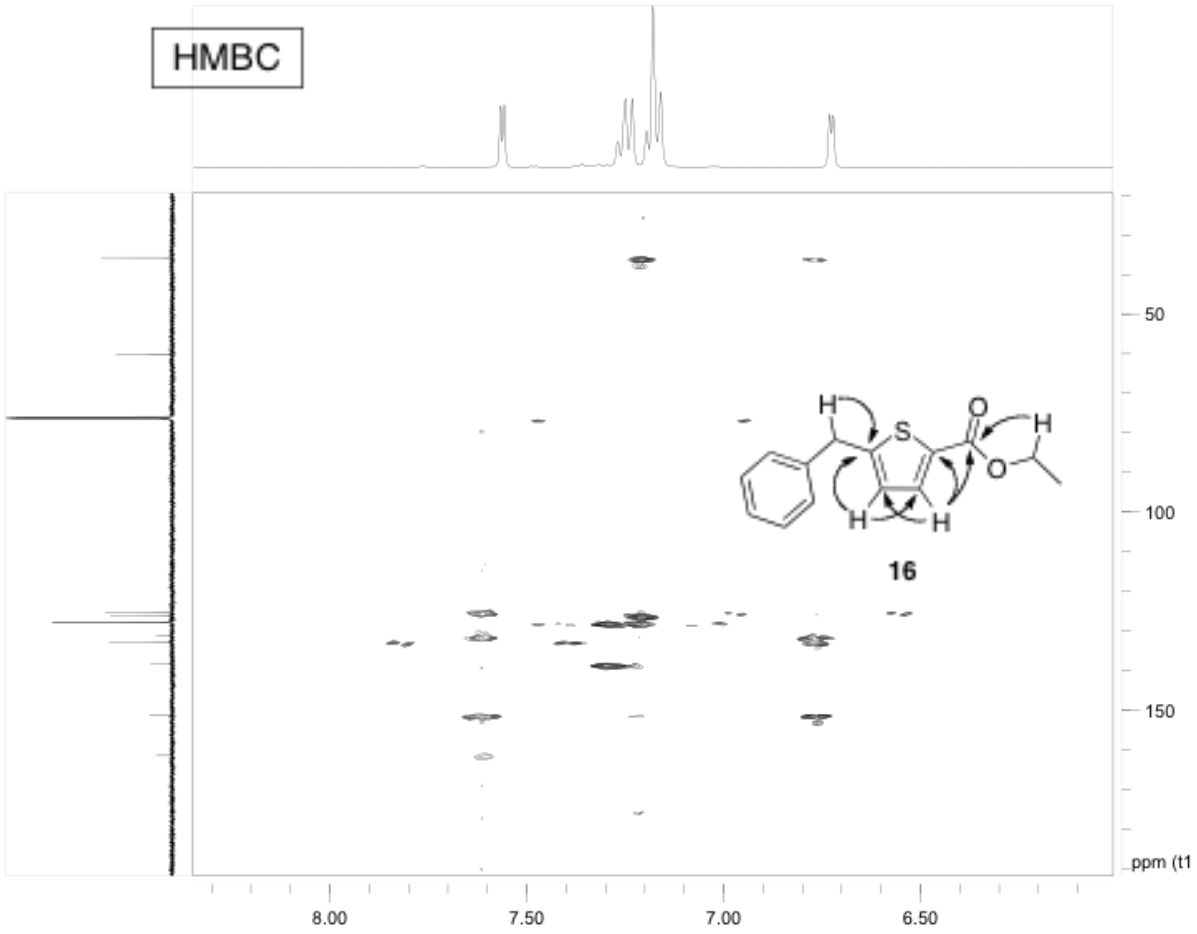
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ppm (t1
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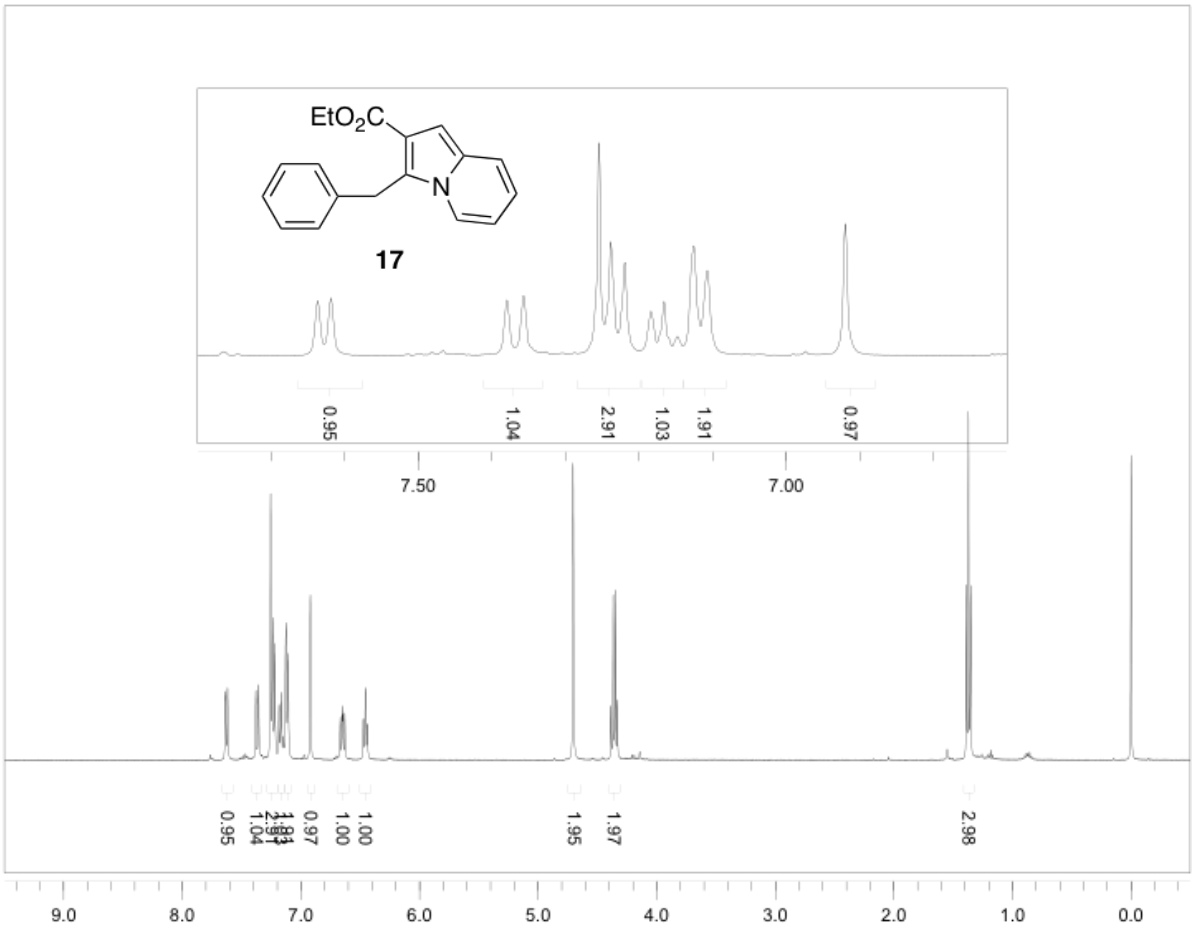
7.00
6.50
H
S
O
H
O
H
H
16


EtO2C
N
17
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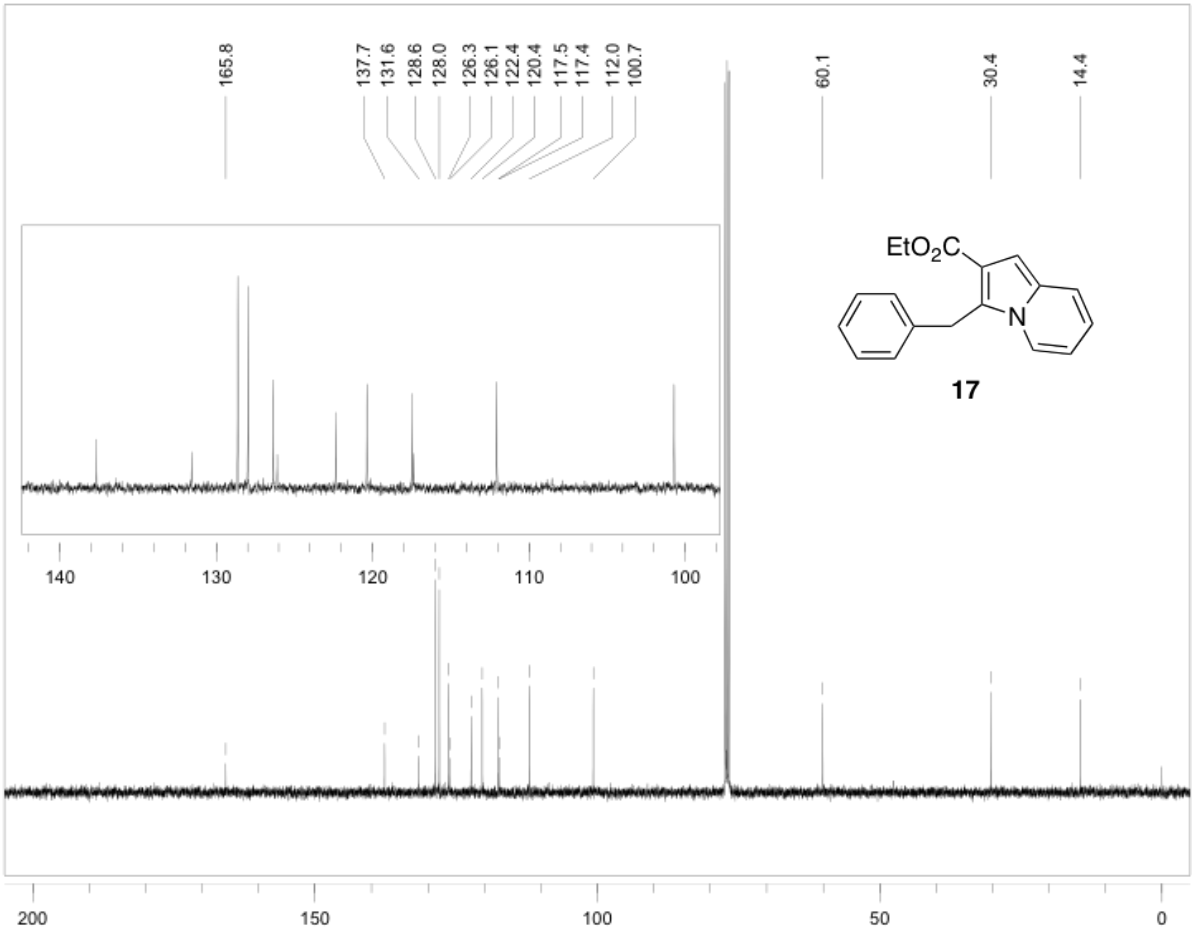
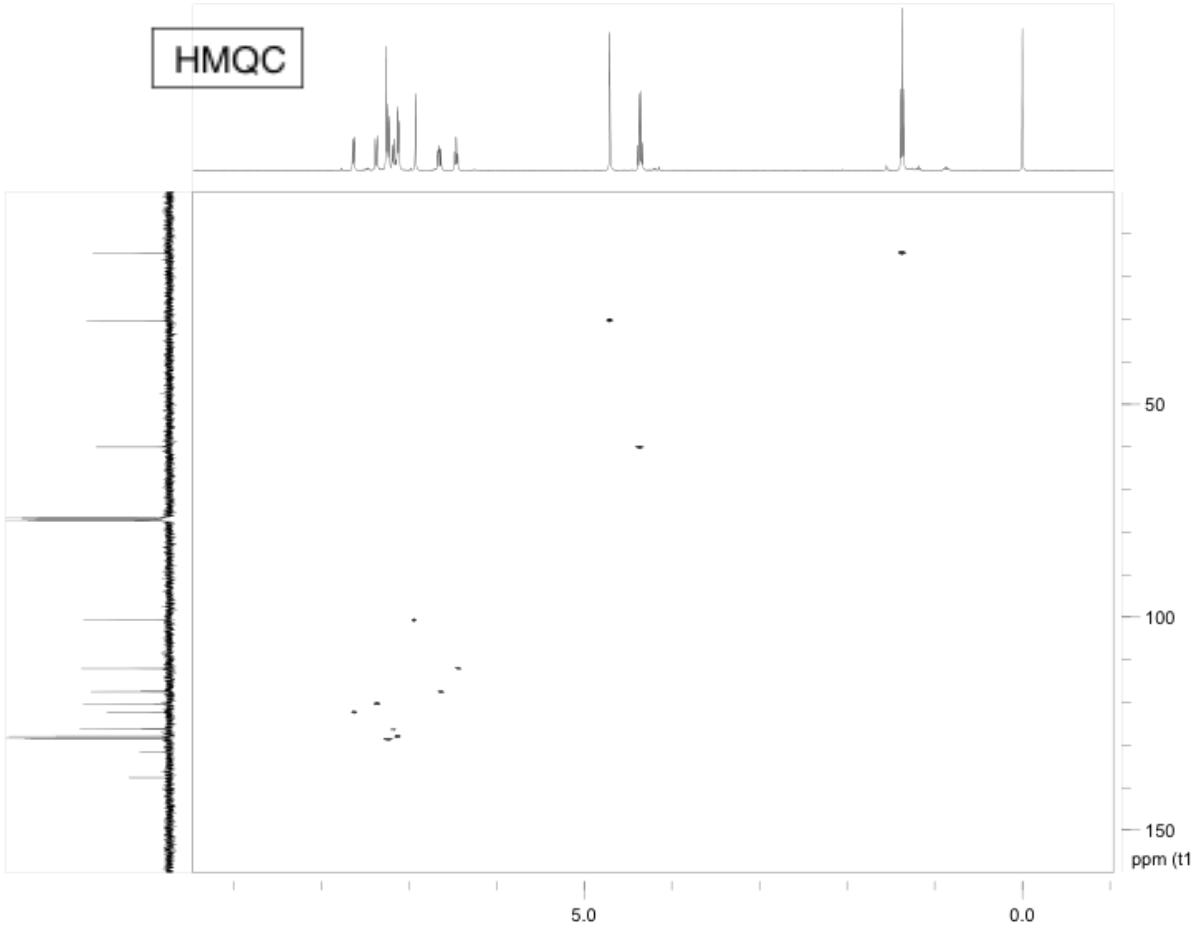
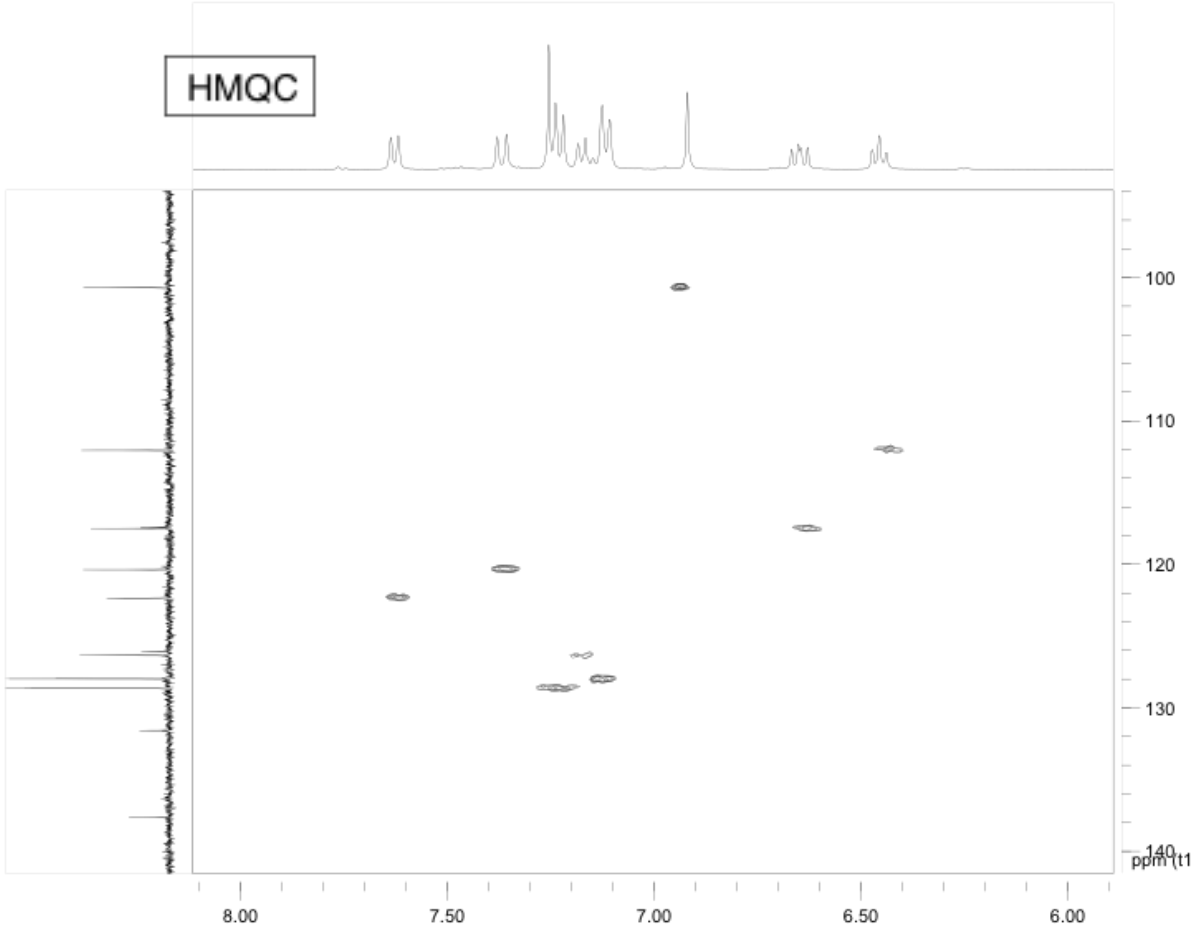
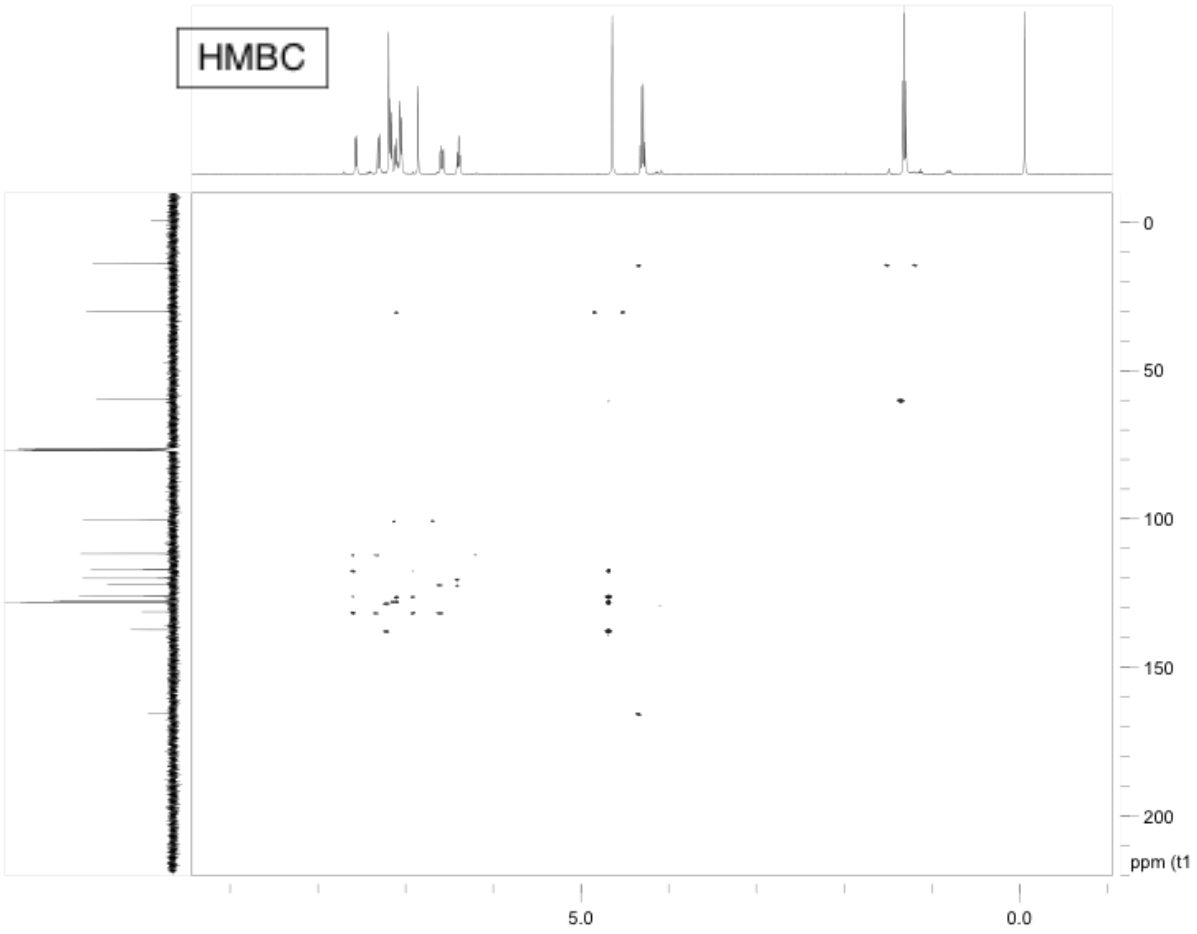
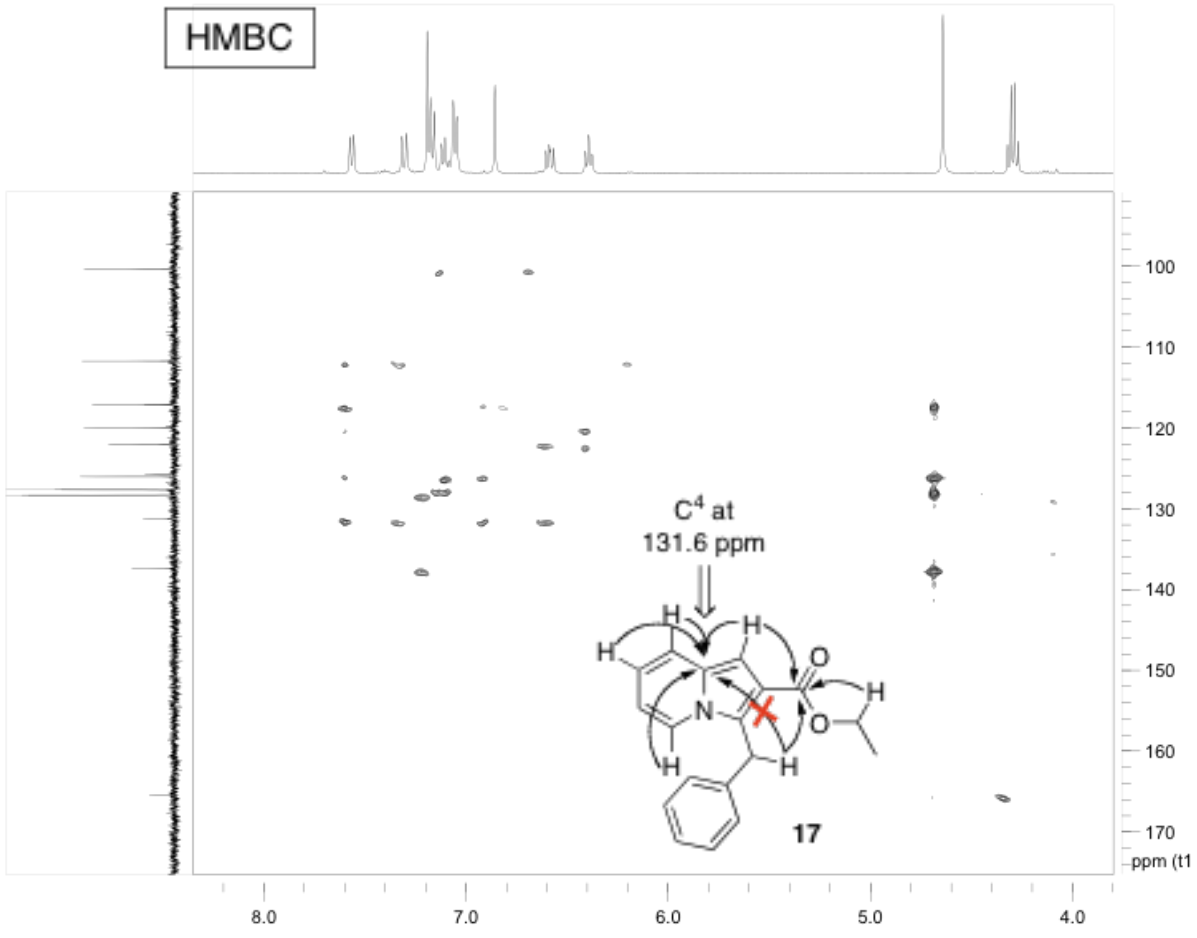
1.04
2.91
1.03
1.91
0.97
7.50
7.00
0.95
1.04
0.97
1.00
1.00
1.95
1.97
2.98
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0

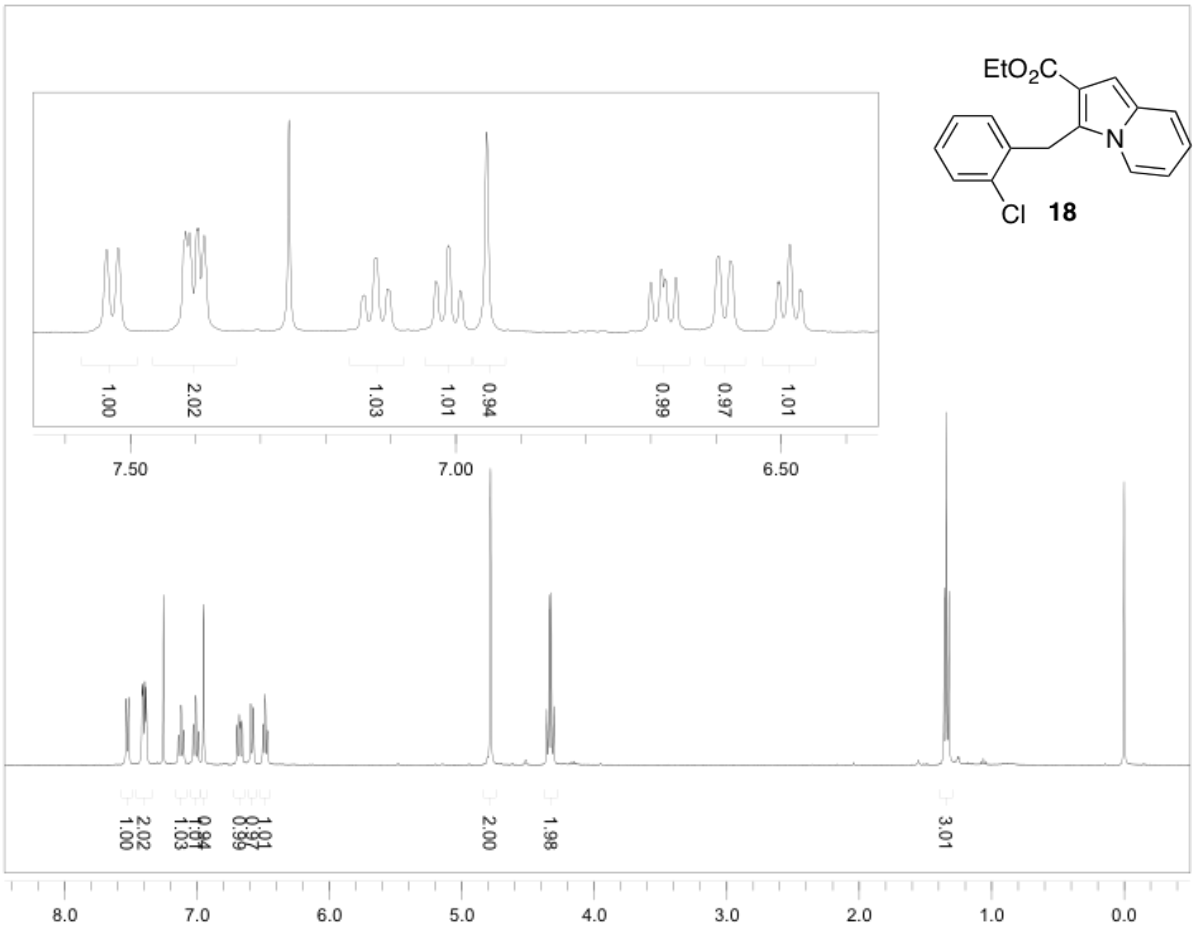

165.8
137.7
131.6
128.6
128.0
126.3
126.1
122.4
120.4
117.5
117.4
112.0
100.7
60.1
30.4
14.4
EtO2C
N
17
140
130
120
110
100
200
150
100
50
0

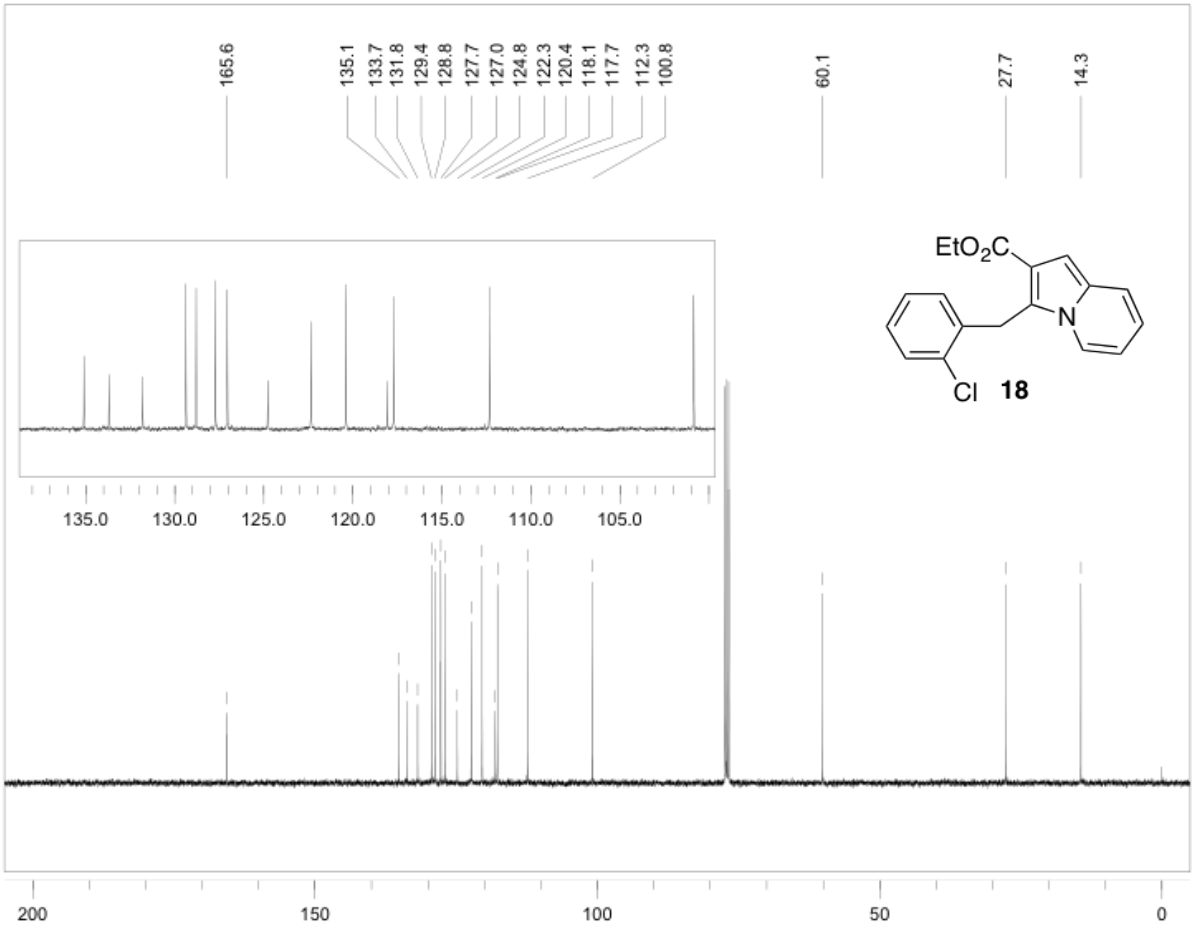

HMQC
50
100
150
ppm (t1
5.0
0.0

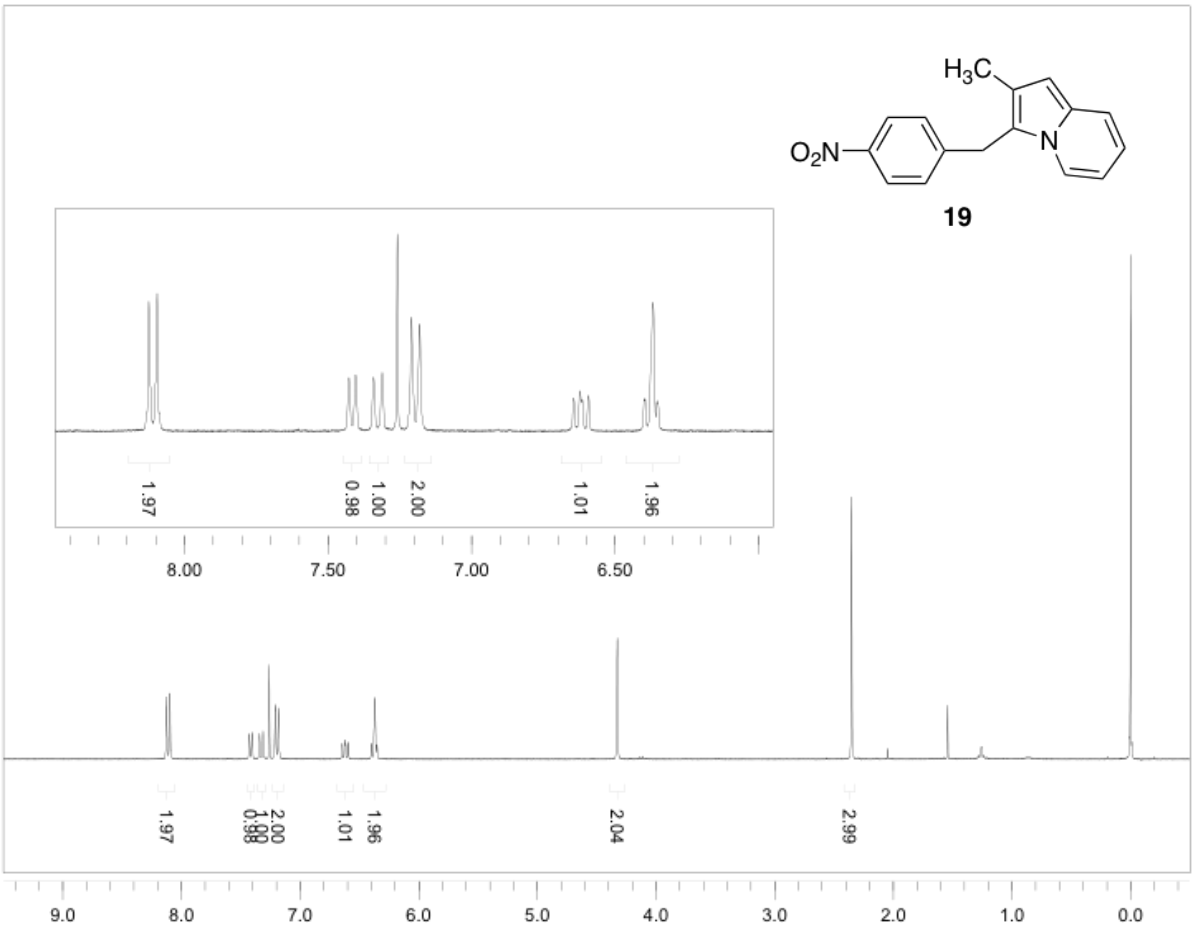

HMQC
100
110
120
130
140
ppm (t1
8.00
7.50
7.00
6.50
6.00


HMBC
0
50
100
150
200
ppm (t1
5.0
0.0


HMBC
C4 at
131.6 ppm
H
H
H
O
H
N
O
H
H
17
100
110
120
130
140
150
160
170
ppm (t1
8.0
7.0
6.0
5.0
4.0


EtO2C
N
Cl
18
1.00
2.02
1.03
1.01
0.94
0.99
0.97
1.01
7.50
7.00
6.50
2.00
1.98
3.01
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0


165.6
135.1
133.7
131.8
129.4
128.8
127.7
127.0
124.8
122.3
120.4
118.1
117.7
112.3
100.8
60.1
27.7
14.3
EtO2C
N
Cl
18
135.0
130.0
125.0
120.0
115.0
110.0
105.0
200
150
100
50
0


H3C
O2N
N
19
1.97
0.98
1.00
2.00
1.01
1.96
8.00
7.50
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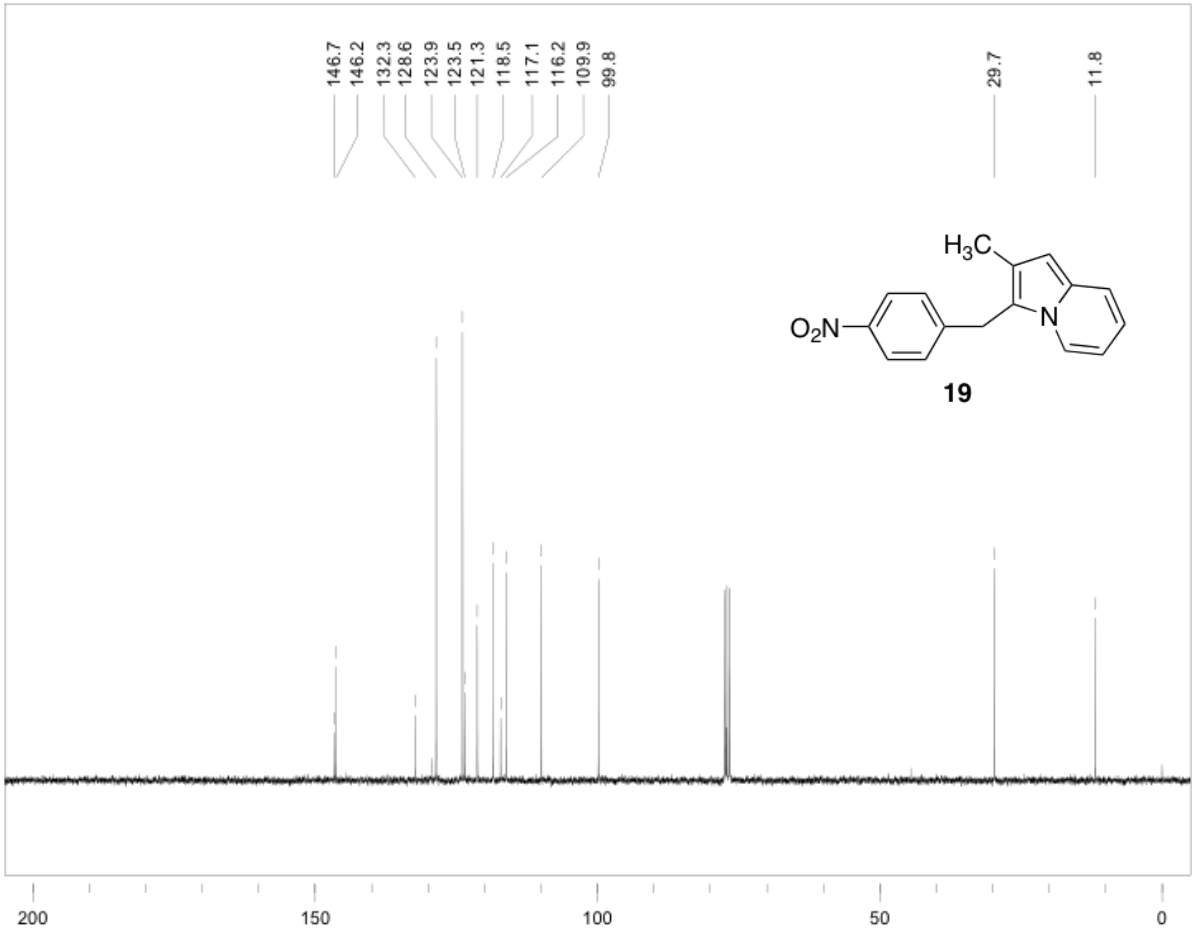
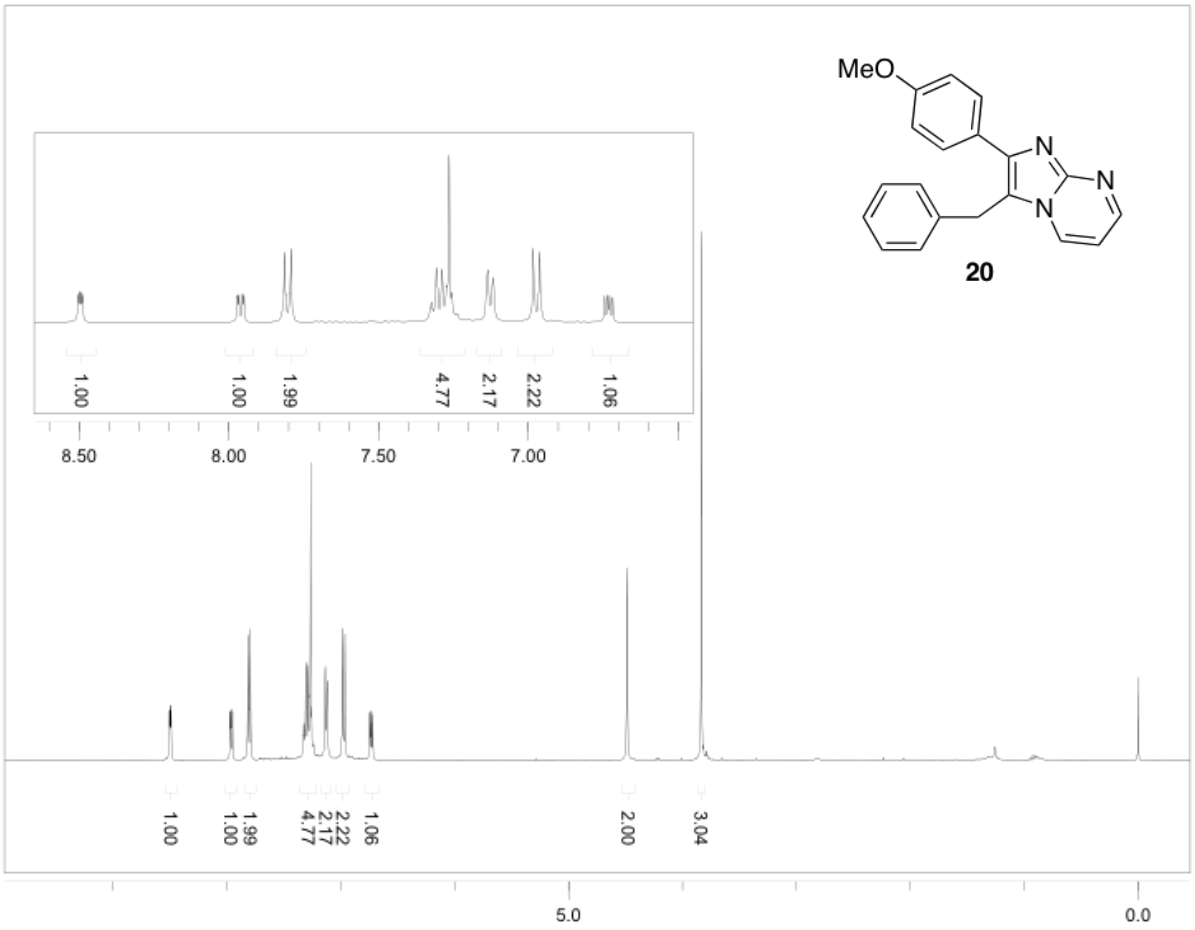
6.50
1.97
2.00
1.01
1.96
2.04
2.99
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0


146.7
146.2
132.3
128.6
123.9
123.5
121.3
118.5
117.1
116.2
109.9
99.8
29.7
11.8
H3C
O2N
N
19
200
150
100
50
0


MeO
N
N
N
20
1.00
1.00
1.99
4.77
2.17
2.22
1.06
8.50
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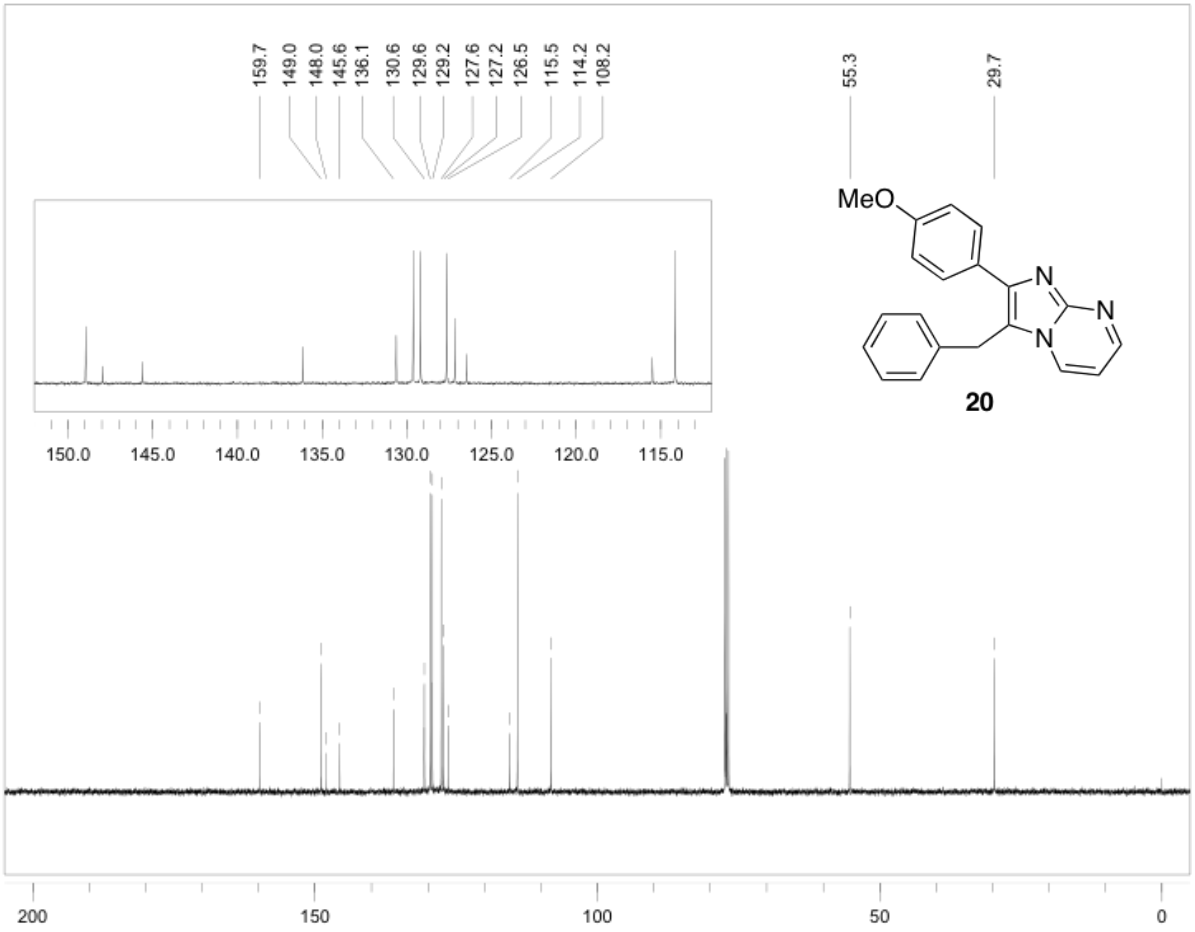
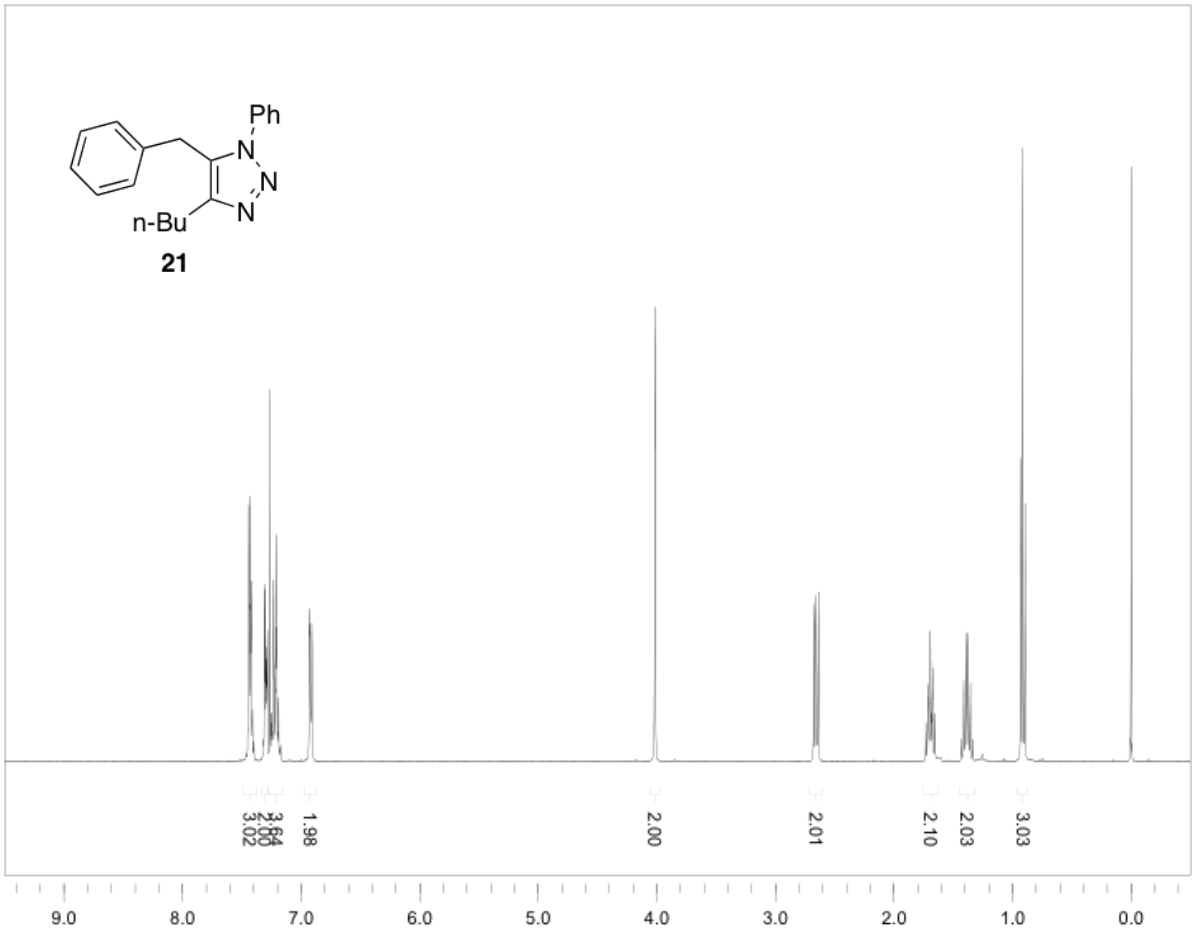
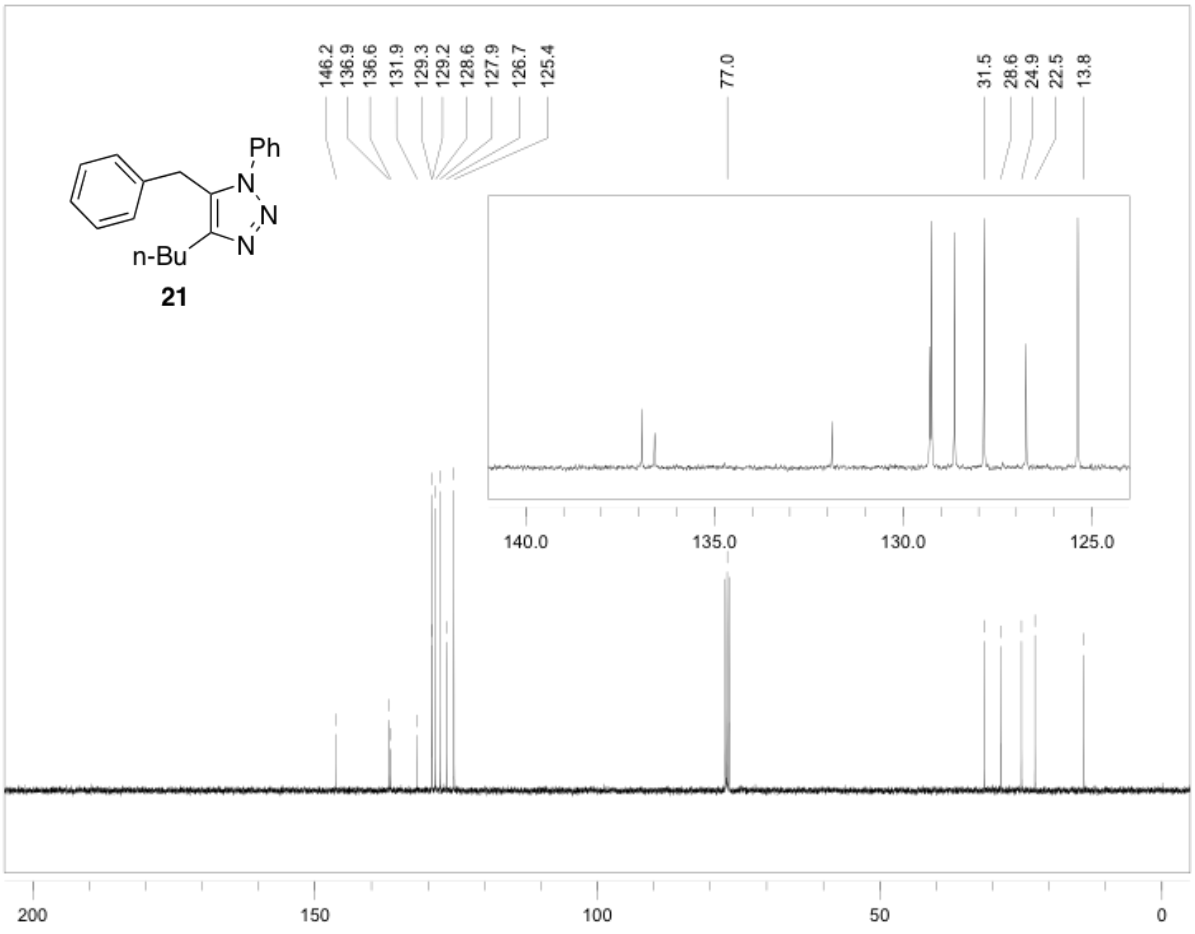
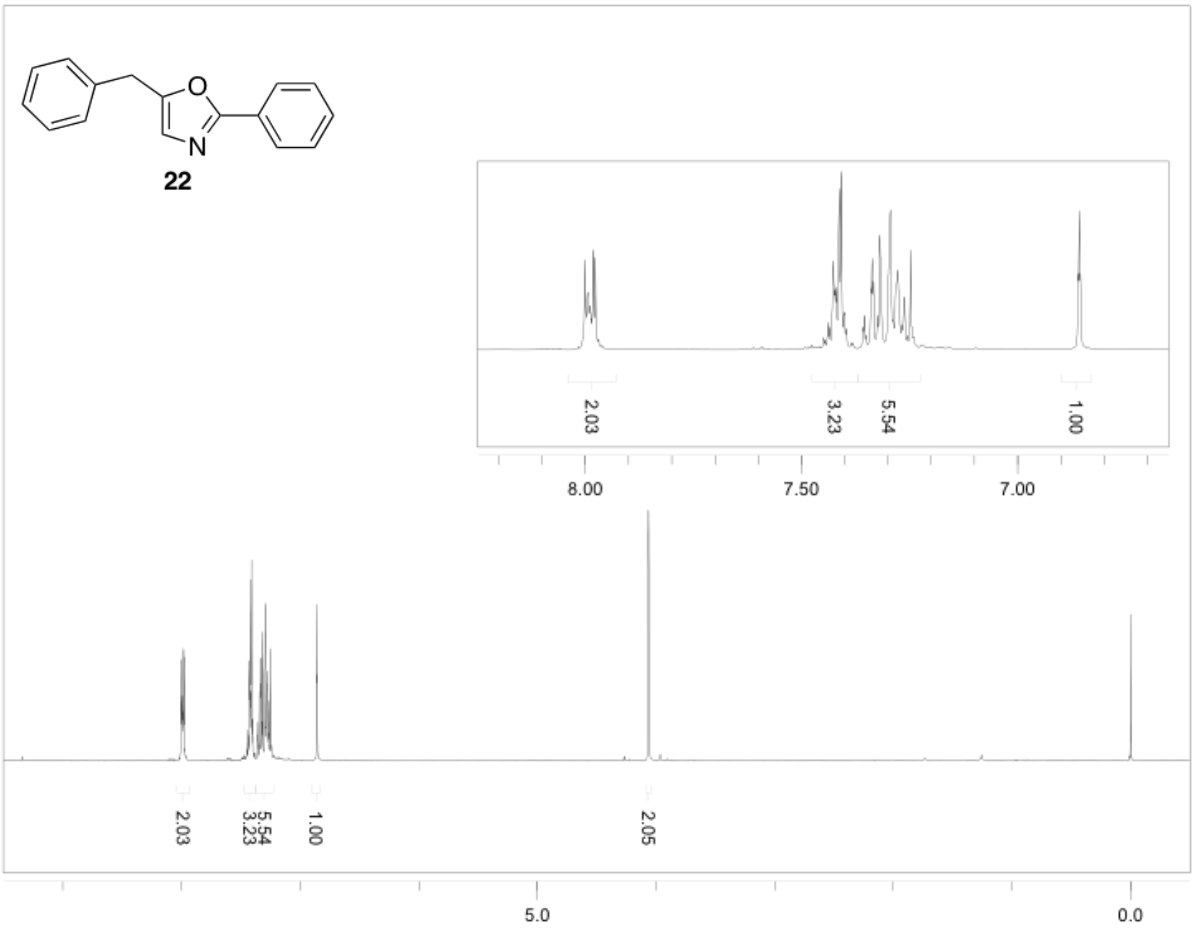
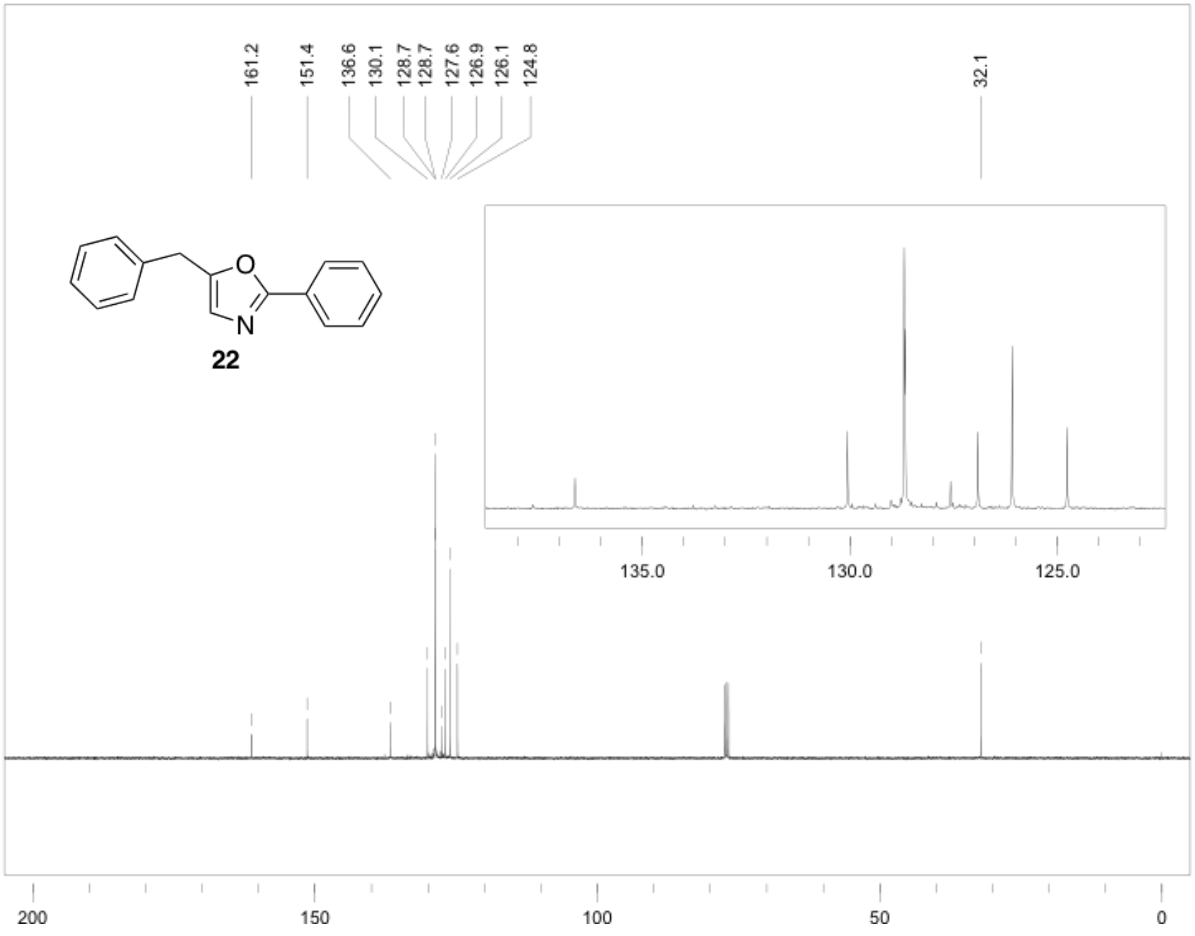
7.50
7.00
1.00
1.00
1.99
4.77
2.17
2.22
1.06
2.00
3.04
5.0
0.0

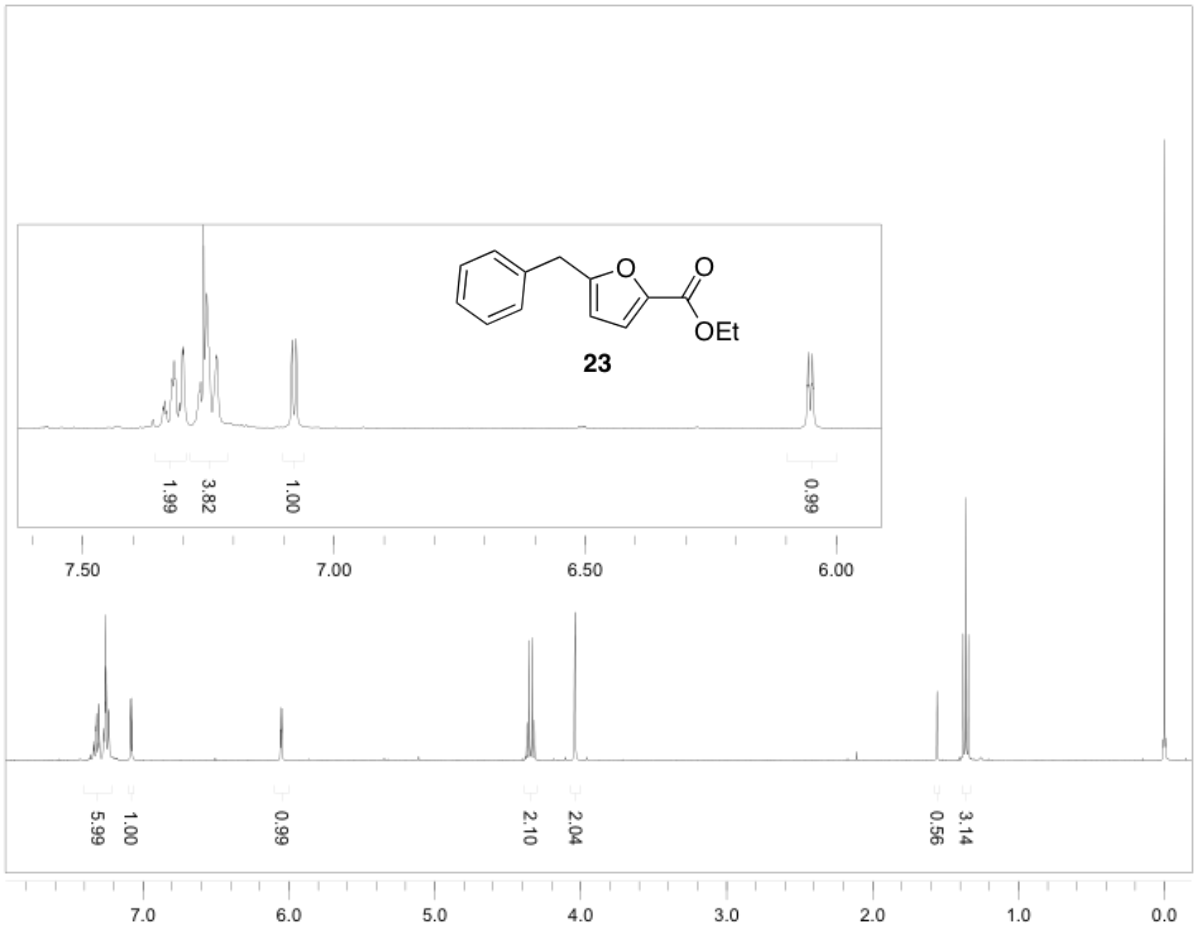

159.7
149.0
148.0
145.6
136.1
130.6
129.6
129.2
127.6
127.2
126.5
115.5
114.2
108.2
55.3
29.7
MeO
N
N
N
20
150.0
145.0
140.0
135.0
130.0
125.0
120.0
115.0
200
150
100
50
0


Ph
N
N
N
n-Bu
21
3.02
2.00
1.98
2.00
2.01
2.10
2.03
3.03
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0


146.2
136.9
136.6
131.9
129.3
129.2
128.6
127.9
126.7
125.4
77.0
31.5
28.6
24.9
22.5
13.8
Ph
N
N
N
n-Bu
21
140.0
135.0
130.0
125.0
200
150
100
50
0


22
2.03
3.23
5.54
1.00
8.00
7.50
7.00
2.03
3.23
5.54
1.00
2.05
5.0
0.0


161.2
151.4
136.6
130.1
128.7
128.7
127.6
126.9
126.1
124.8
32.1
22
135.0
130.0
125.0
200
150
100
50
0


O
O
OEt
23
1.99
3.82
1.00
0.99
7.50
7.00
6.50
6.00
5.99
1.00
0.99
2.10
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3.14
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6.0
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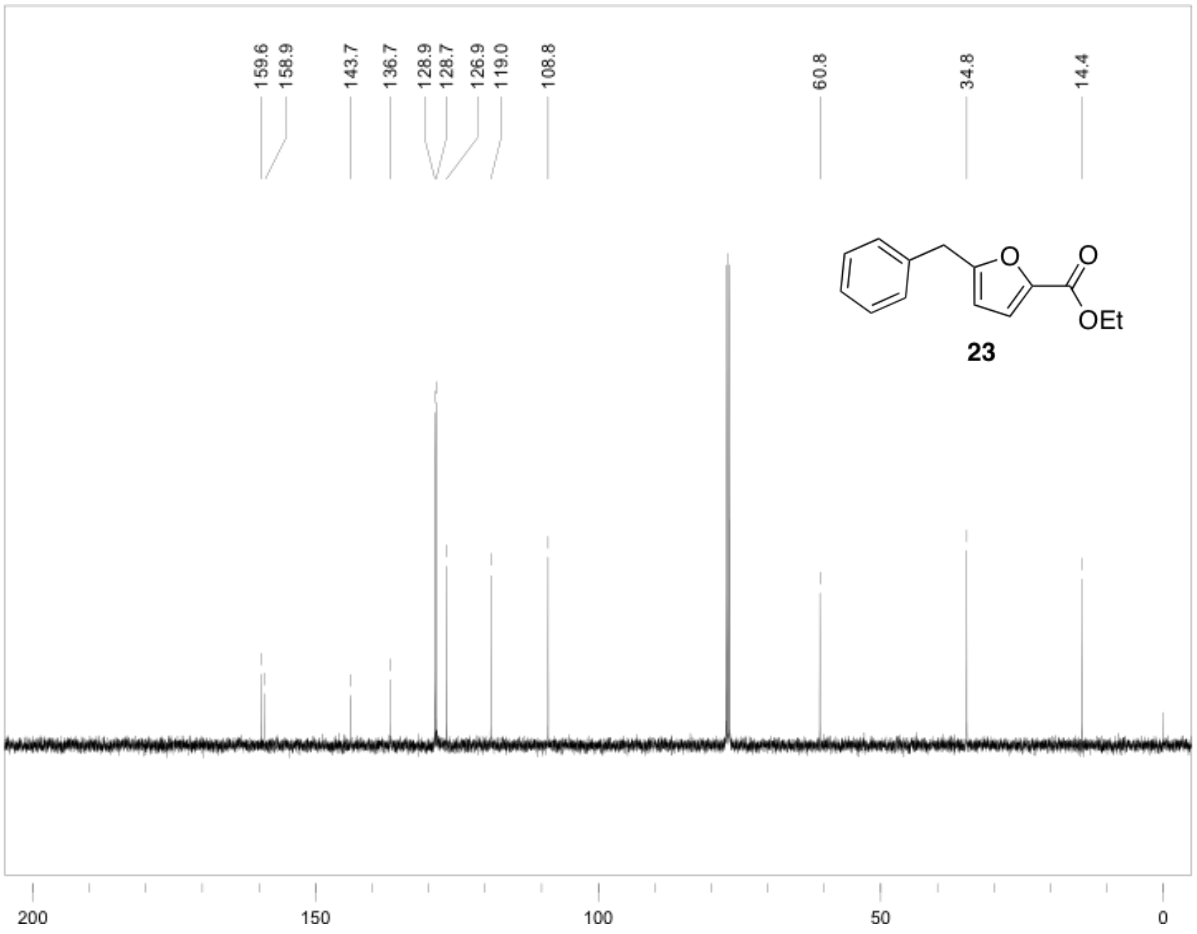
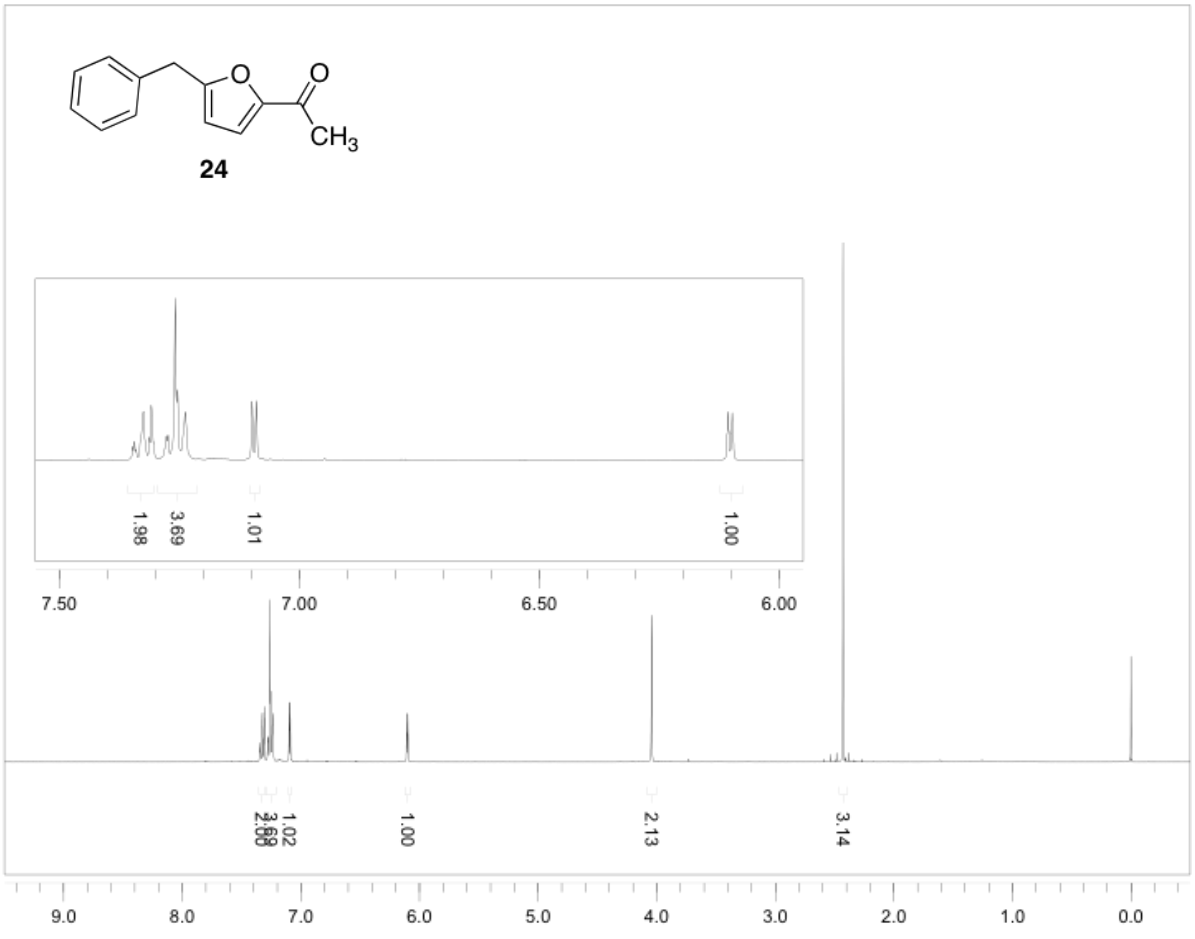
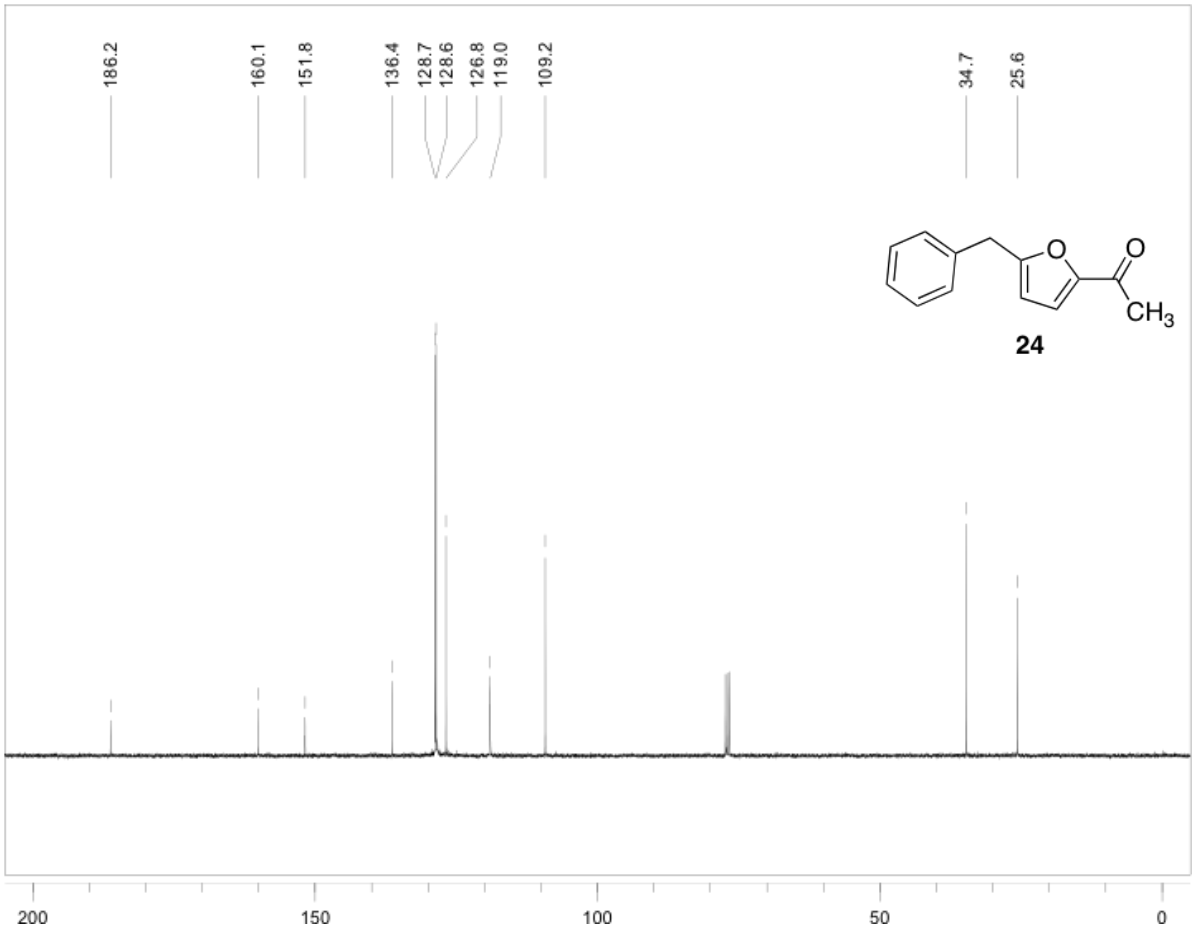
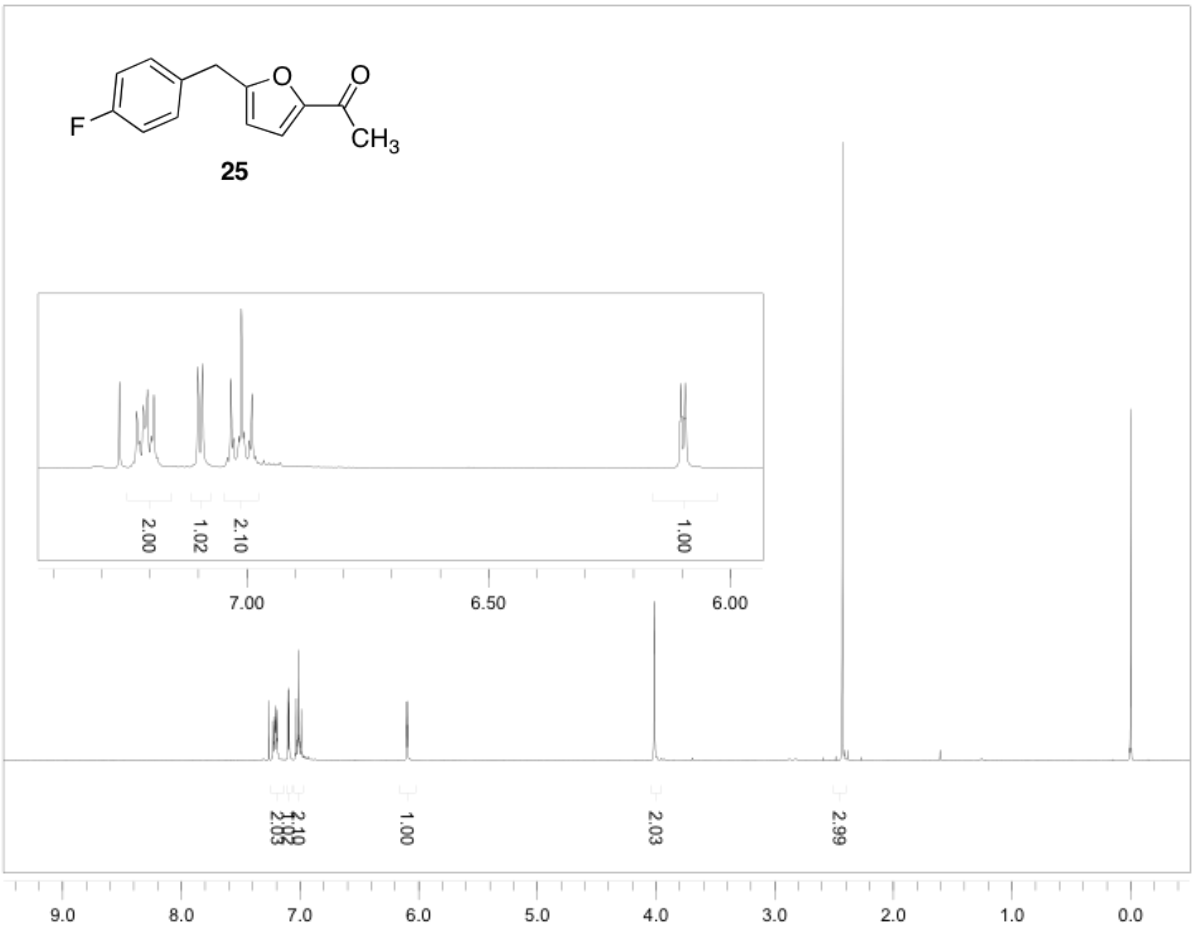
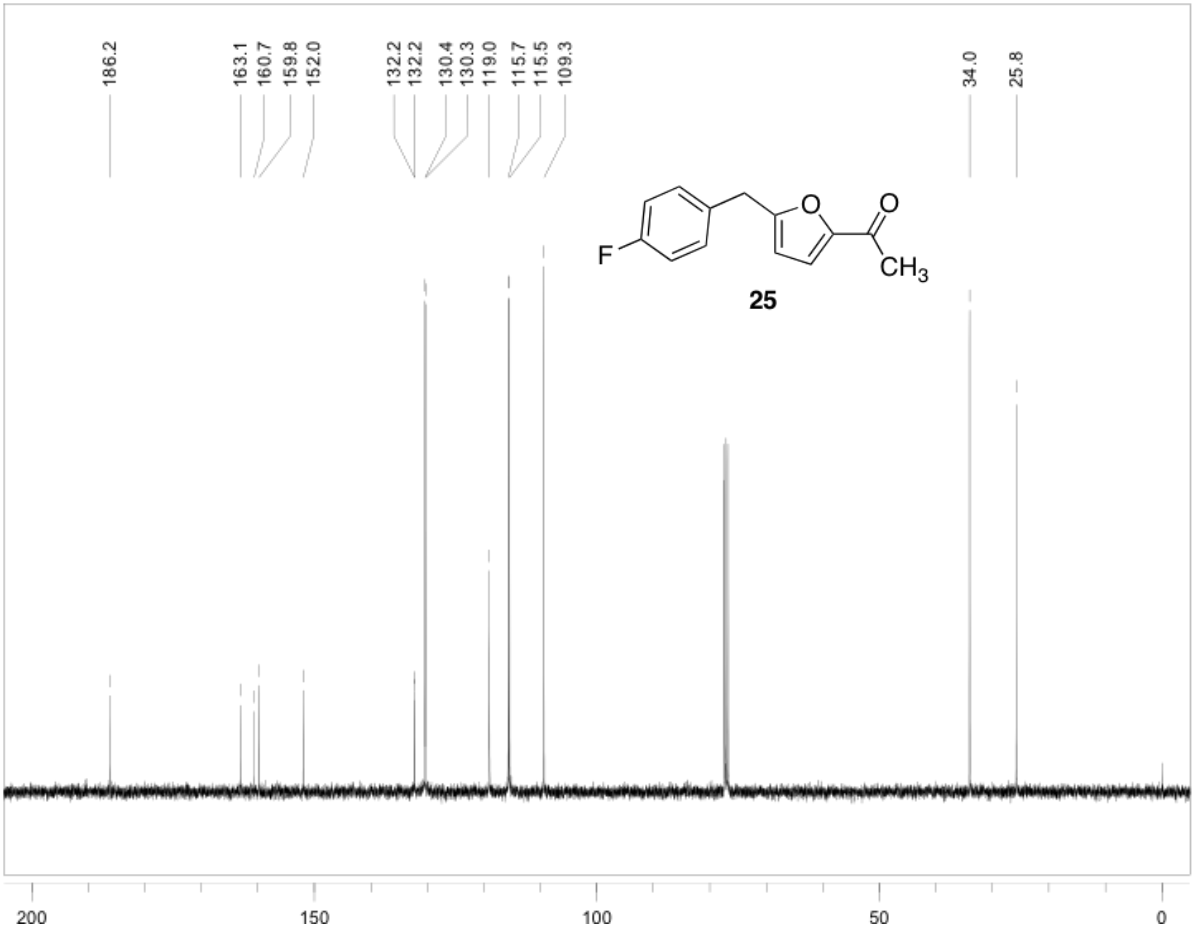
4.0
3.0
2.0
1.0
0.0


159.6
158.9
143.7
136.7
128.9
128.7
126.9
119.0
108.8
60.8
34.8
14.4
O
O
OEt
23
200
150
100
50
0


O
O
CH3
24
1.98
3.69
1.01
1.00
7.50
7.00
6.50
6.00
1.00
2.13
3.14
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0


186.2
160.1
151.8
136.4
128.7
128.6
126.8
119.0
109.2
34.7
25.6
O
O
CH3
24
200
150
100
50
0


F
O
O
CH3
25
2.00
1.02
2.10
1.00
7.00
6.50
6.00
1.00
2.03
2.99
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0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163.1
160.7
159.8
152.0
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132.2
130.4
130.3
119.0
115.7
115.5
109.3
34.0
25.8
F
O
O
CH3
25
200
150
100
50
0