Electronic Supplementary Material (ESI) for RSC Advances.

Supporting information for

Pd/Cu-Cocatalyzed Regioselective Arylation of Thiazole Derivatives at 2-Position under Ligand-Free Conditions

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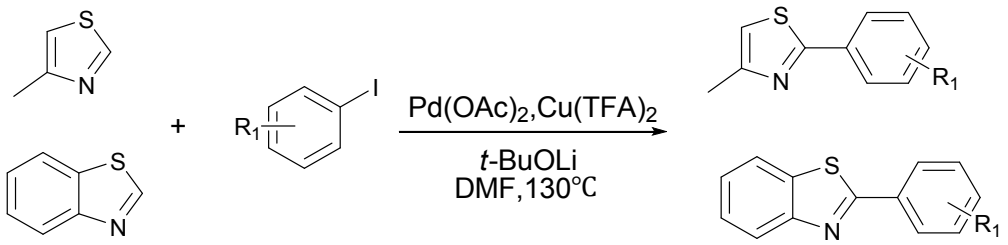


1 Experimental

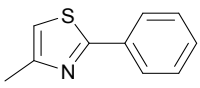
1.1 General

All chemical reagents are obtained from commercial suppliers and used without further purification. All known compounds are identified by appropriate technique such as ^{1}H NMR, ^{13}C NMR and compared with previously reported data. Analytical thin- layer chromatography are performed on glass plates precoated with silica gel impregnated with a fluorescent indicator (254 nm), and the plates are visualized by exposure to ultraviolet light. ^{1}H NMR and ^{13}C NMR spectra are recorded on an AVANCE 500 Bruker spectrometer operating at 500 MHz and 125 MHz in $CDCl_3$, respectively, and chemical shifts are reported in ppm. GC analyses are performed on an Agilent 7890A instrument (Column: Agilent 19091J-413: 30 m × 320 μm × 0.25 μm, carrier gas: H_2 , FID detection. Mass spectra are taken on a Thermo Scientific ISQ LT GC-MS instrument in the electron ionization (EI) mode. Elemental analyses are performed on a Yanagimoto MT3CHN recorder.

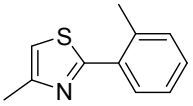
1.2 Experimental Procedure

General Procedure for the Arylation of Thiazole Derivatives： A mixture of 4-methylthiazole (1.0 mmol), iodobenzene (1.0 mmol), $Pd(OAc)_2$ (0.01 mmol), $Cu(TFA)_2$ (0.2 mmol) and *t*-BuOLi (2.0 mmol) in DMF (3.0 mL) was stirred at 130^{o}C for 3 h. After the completion of the reaction, the mixture was cooled to 25 ^{o}C and then EtOAc and H_2O were added to it. The organic layer was separated and washed with brine, dried over Na_2SO_4. The volatiles were removed under vacuum to afford the crude product, and analyzed by GC. The crude product was purified by column chromatography on silica gel and eluted with EtOAc/hexanes (10/90) to afford the desired pure product.

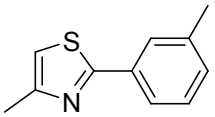
2. Characterization Data



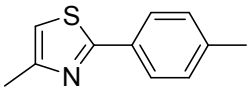
4-methyl-2-phenylthiazole (**3a**)[1]: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.93 (dd, J = 7.9, 1.5 Hz, 2H), 7.46 – 7.38 (m, 3H), 6.87 (d, J = 0.8 Hz, 1H), 2.51 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.73 (s), 152.71 (s), 130.17 (s), 128.93 (s), 127.93 (s), 125.54 (s), 112.48 (s), 16.23 (s).



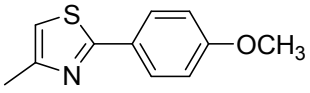
4-methyl-2-*o*-tolylthiazole (**3b**)[2]: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.69 (dd, *J* = 7.5, 1.1 Hz, 1H), 7.32 – 7.25 (m, 3H), 6.94 (dd, *J* = 1.9, 0.9 Hz, 1H), 2.57 (s, 3H), 2.53 (d, *J* = 1.0 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.09 (s), 153.13 (s), 136.65 (s), 133.41 (s), 131.39 (s), 130.01 (s), 129.31 (s), 126.10 (s), 114.14 (s), 21.38 (s), 17.39 (s).



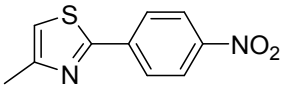
4-methyl-2-*m*-tolylthiazole (**3c**): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.78 (s, 1H), 7.71 (d, *J* = 7.7 Hz, 1H), 7.31 (t, *J* = 7.6 Hz, 1H), 7.22 (d, *J* = 7.6 Hz, 1H), 6.86 (s, 1H), 2.51 (d, *J* = 0.8 Hz, 3H), 2.41 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.97 (s), 153.83 (s), 138.78 (s), 133.79 (s), 130.72 (s), 128.88 (s), 127.04 (s), 123.83 (s), 113.39 (s), 21.43 (s), 17.41 (s). MS (EI) m/z: 189 [M+]. Anal. Calcd for $C_{11}H_{11}NS$: C, 69.80; H, 5.86, N, 7.40. Found: C, 69.85; H, 5.89; N, 7.36.



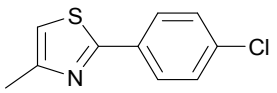
4-methyl-2-*p*-tolylthiazole (**3d**)[3]: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.78 (d, *J* = 8.1 Hz, 2H), 7.18 (d, *J* = 7.9 Hz, 2H), 6.78 (d, *J* = 0.7 Hz, 1H), 2.45 (d, *J* = 0.7 Hz, 3H), 2.34 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.92 (s), 153.73 (s), 140.08 (s), 131.28 (s), 129.66 (s), 126.49 (s), 113.03 (s), 21.49 (s), 17.39 (s).



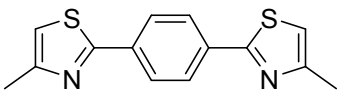
2-(4-methoxyphenyl)-4-methylthiazole(**3e**): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.82 (d, *J* = 8.7 Hz, 2H), 6.89 (d, *J* = 8.7 Hz, 2H), 6.75 (s, 1H), 3.80 (s, 3H), 2.44 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.64 (s), 161.10 (s), 153.57 (s), 128.04 (s), 114.32 (s), 112.55 (s), 55.49 (s), 17.36 (s). MS (EI) m/z: 205 [M+]. Anal. Calcd for $C_{11}H_{11}NOS$: C, 64.36; H, 5.40, N, 6.82. Found: C, 64.32; H, 5.43; N, 6.80.



4-methyl-2-(4-nitrophenyl)thiazole (**3f**): ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.30 – 8.21 (m, 2H), 8.12 – 8.02 (m, 2H), 7.01 (s, 1H), 2.51 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.48 (s), 155.19 (s), 148.34 (s), 139.35 (s), 127.07 (s), 124.40 (s), 115.89 (s), 17.32 (s). MS (EI) m/z: 220 [M+]. Anal. Calcd for $C_{10}H_8N_2O_2S$: C, 54.53; H, 3.66, N, 12.72. Found: C, 54.55; H, 3.70; N, 12.68.

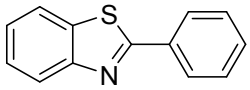


2-(4-chlorophenyl)-4-methylthiazole (**3g**)[4]: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.94 – 7.88 (m, 2H), 7.14 – 7.08 (m, 2H), 6.85 (d, *J* = 0.9 Hz, 1H), 2.50 (d, *J* = 0.9 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.49 (s), 164.82 (s), 162.83 (s), 153.98 (s), 130.26 (s), 128.47 (s), 116.13 (s), 115.95 (s), 113.52 (s), 17.34 (s).

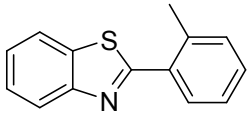


1,4-bis(4-methylthiazol-2-yl)benzene (**3h**): ^{1}H NMR (500 MHz,

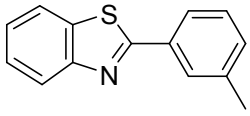
$CDCl_3$) δ 7.95 (s, 4H), 6.86 (s, 2H), 2.48 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.77 (s), 154.27 (s), 134.92 (s), 126.99 (s), 114.03 (s), 17.36 (s). MS (EI) m/z: 272 [M+]. Anal. Calcd for $C_{14}H_{12}N_2S_2$: C, 61.73; H, 4.44, N, 10.28. Found: C, 61.77; H, 4.50; N, 10.25.



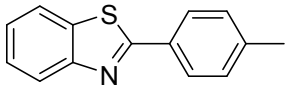
2-phenylbenzo[*d*]thiazole (**8a**)[5]: ^1H NMR (500 MHz, $CDCl_3$) δ 8.13 – 8.07 (m, 3H), 7.90 (d, *J* = 8.0 Hz, 1H), 7.53 – 7.47 (m, 4H), 7.41 – 7.37 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.19 (s), 154.27 (s), 135.19 (s), 133.75 (s), 131.08 (s), 129.14 (s), 127.69 (s), 126.43 (s), 125.31 (s), 123.36 (s), 121.74 (s).



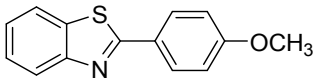
2-o-tolylbenzo[*d*]thiazole (**8b**)[5]: ^1H NMR (500 MHz, $CDCl_3$) δ 8.08 (ddd, *J* = 8.2, 1.0, 0.6 Hz, 1H), 7.90 (ddd, *J* = 7.9, 1.1, 0.6 Hz, 1H), 7.73 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.48 (ddd, *J* = 8.3, 7.2, 1.2 Hz, 1H), 7.40 – 7.26 (m, 4H), 2.64 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.13 (s), 153.93 (s), 137.38 (s), 135.73 (s), 133.21 (s), 131.68 (s), 130.68 (s), 130.14 (s), 126.25 (s), 125.22 (s), 123.51 (s), 121.50 (s), 21.50 (s).



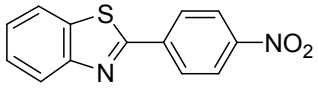
2-m-tolylbenzo[*d*]thiazole (**8c**)[5]: ^1H NMR (500 MHz, $CDCl_3$) δ 8.04 (d, *J* = 8.1 Hz, 1H), 7.90 (s, 1H), 7.84 (dd, *J* = 12.4, 8.0 Hz, 2H), 7.45 (t, *J* = 7.6 Hz, 1H), 7.34 (t, *J* = 7.6 Hz, 2H), 7.26 (d, *J* = 7.5 Hz, 1H), 2.41 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.51 (s), 154.14 (s), 139.00 (s), 135.10 (s), 133.56 (s), 131.98 (s), 129.06 (s), 128.12 (s), 126.44 (s), 125.13 (d, *J* = 34.7 Hz), 123.26 (s), 121.74 (s), 21.49 (s).



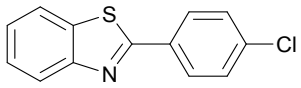
2-p-tolylbenzo[*d*]thiazole (**8d**)[5]: ^1H NMR (500 MHz, $CDCl_3$) δ 8.04 (d, *J* = 8.2 Hz, 1H), 7.95 (d, *J* = 8.0 Hz, 2H), 7.83 (d, *J* = 8.0 Hz, 1H), 7.44 (t, *J* = 7.7 Hz, 1H), 7.32 (t, *J* = 7.6 Hz, 1H), 7.24 (d, *J* = 7.9 Hz, 2H), 2.37 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.33 (s), 154.33 (s), 141.49 (s), 135.10 (s), 131.10 (s), 129.82 (s), 127.61 (s), 126.35 (s), 125.11 (s), 123.18 (s), 121.68 (s), 21.63 (s).



2-(4-methoxyphenyl)benzo[*d*]thiazole (**8e**) [6]: ^1H NMR (500 MHz, $CDCl_3$) δ 8.01 (dd, *J* = 8.5, 3.3 Hz, 3H), 7.86 (d, *J* = 7.9 Hz, 1H), 7.47 – 7.43 (m, 1H), 7.36 – 7.32 (m, 1H), 7.01 – 6.96 (m, 2H), 3.87 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.99 (s), 162.05 (s), 154.30 (s), 134.95 (s), 129.24 (s), 128.16 (s), 126.43 (d, *J* = 25.2 Hz), 124.92 (s), 122.93 (s), 121.62 (s), 114.49 (s), 55.59 (s).



2-(4-nitrophenyl)benzo[*d*]thiazole (**8f**)[7]: ^1H NMR (500 MHz, $CDCl_3$) δ 8.34 (d, *J* = 8.8 Hz, 2H), 8.25 (d, *J* = 8.8 Hz, 2H), 8.11 (d, *J* = 8.1 Hz, 1H), 7.94 (d, *J* = 8.0 Hz, 1H), 7.54 (t, *J* = 7.4 Hz, 1H), 7.45 (t, *J* = 7.4 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.95 (s), 154.20 (s), 149.13 (s), 139.28 (s), 135.59 (s), 128.35 (s), 127.04 (s), 126.34 (s), 124.24 (d, *J* = 49.7 Hz), 124.01 – 123.62 (m), 121.96 (s).



2-(4-chlorophenyl)benzo[*d*]thiazole (**8g**)[7]: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.13 – 7.98 (m, 3H), 7.85 (d, J = 8.0 Hz, 1H), 7.54 – 7.43 (m, 1H), 7.41 – 7.31 (m, 1H), 7.14 (t, J = 8.6 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.78 (s), 165.53 (s), 163.52 (s), 154.19 (s), 135.15 (s), 130.03 (s), 129.58 (s), 126.50 (s), 125.33 (s), 123.29 (s), 121.70 (s), 116.31 (s), 116.14 (s).

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[2] Campeau, L.C.; *J. Am. Chem. Soc.* **2009**, 131, 3291-3306
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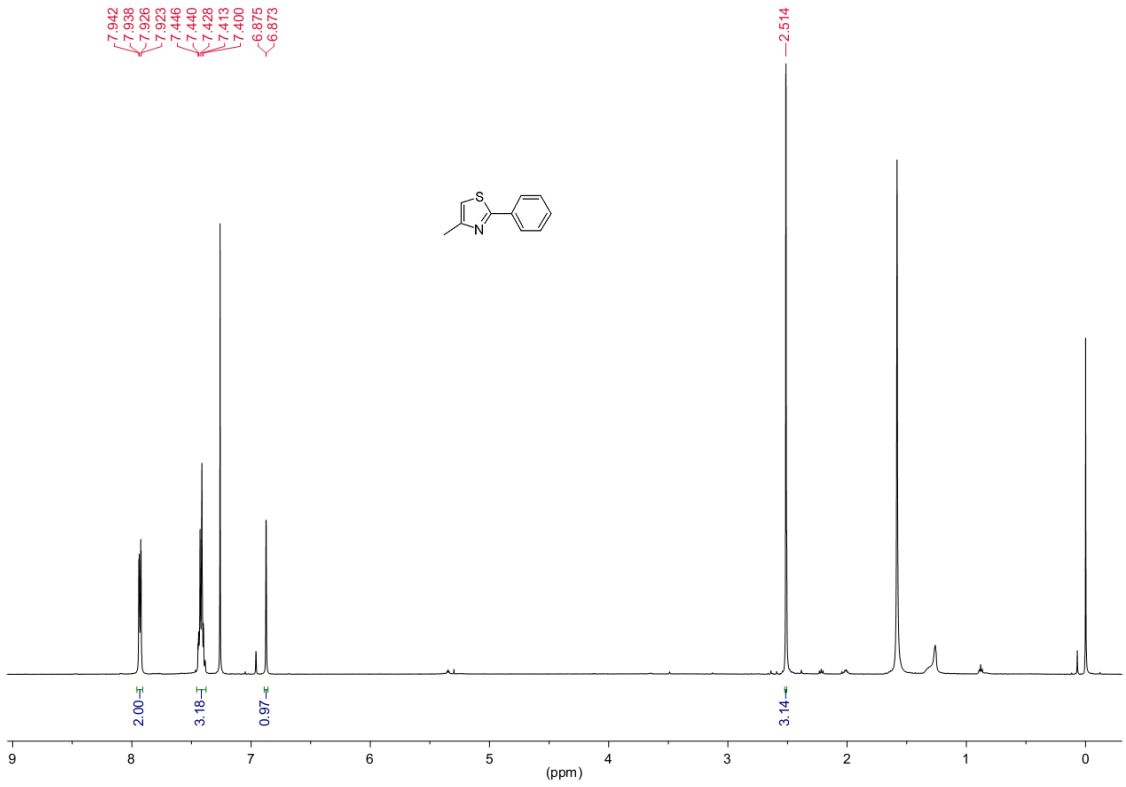
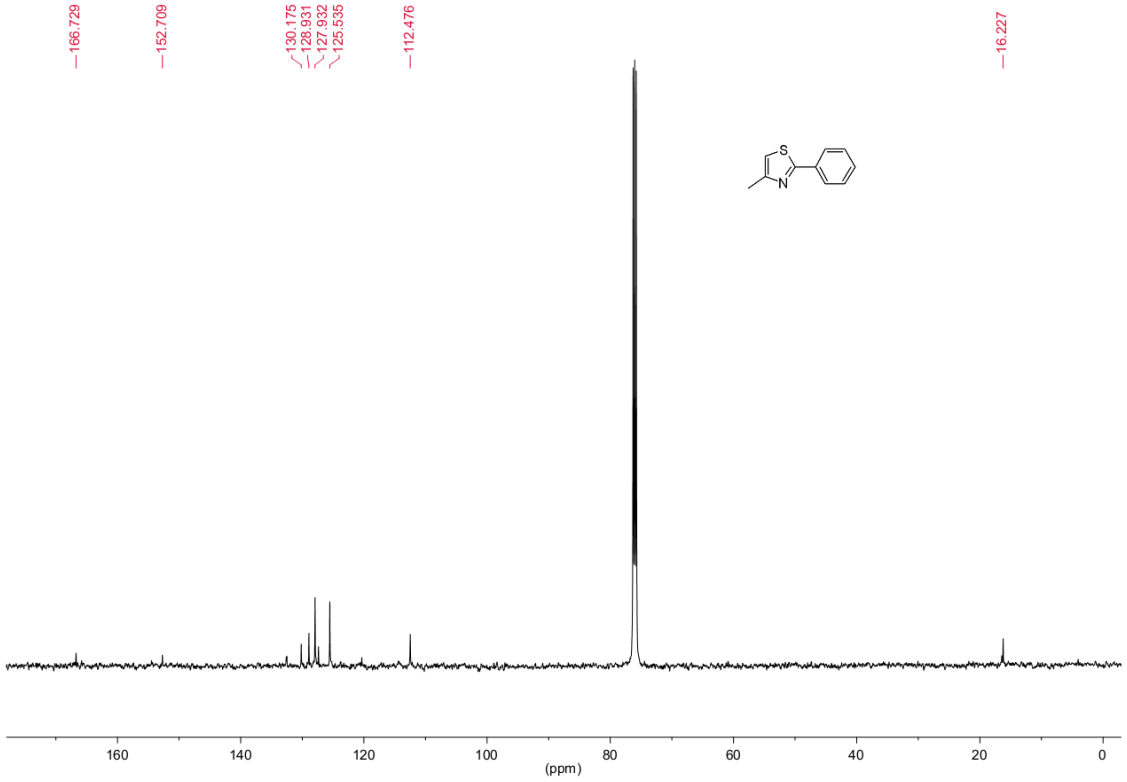
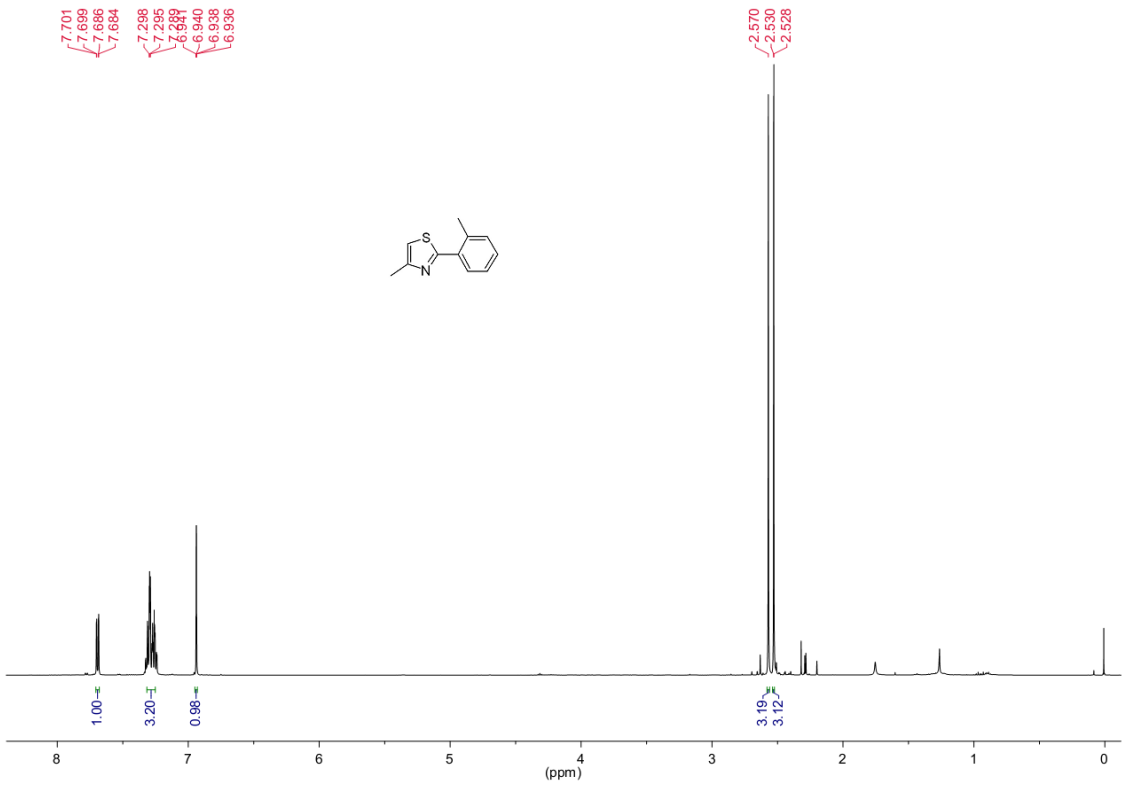
Copies of products ^{1}H NMR and ^{13}C NMR



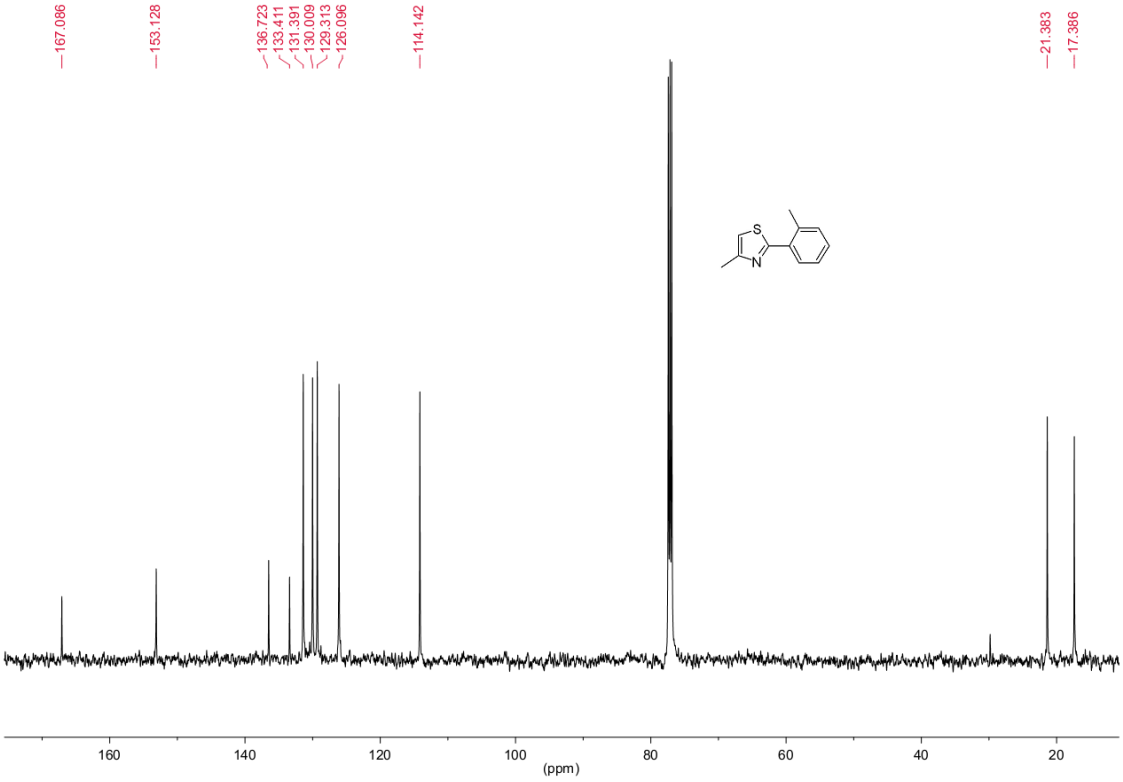
^{1}H NMR spectrum (500 MHz, $CDCl_3$) of **3a**



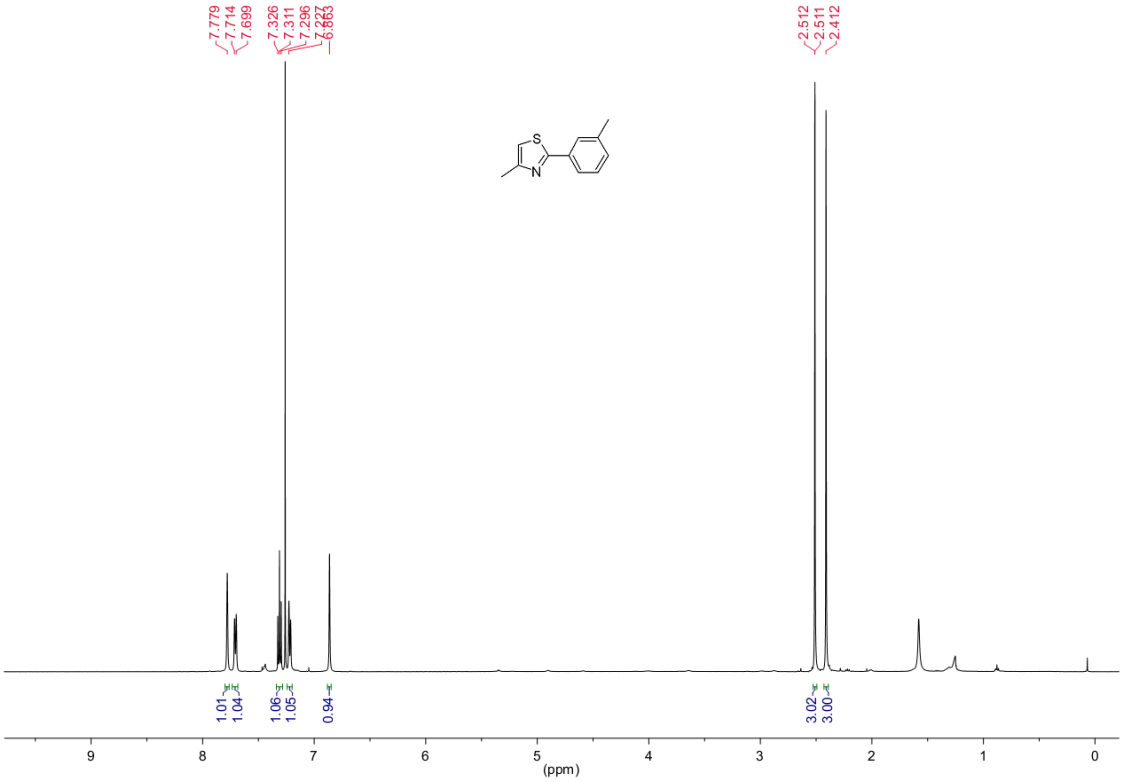
^{13}C NMR spectrum (125 MHz, $CDCl_3$) of **3a**



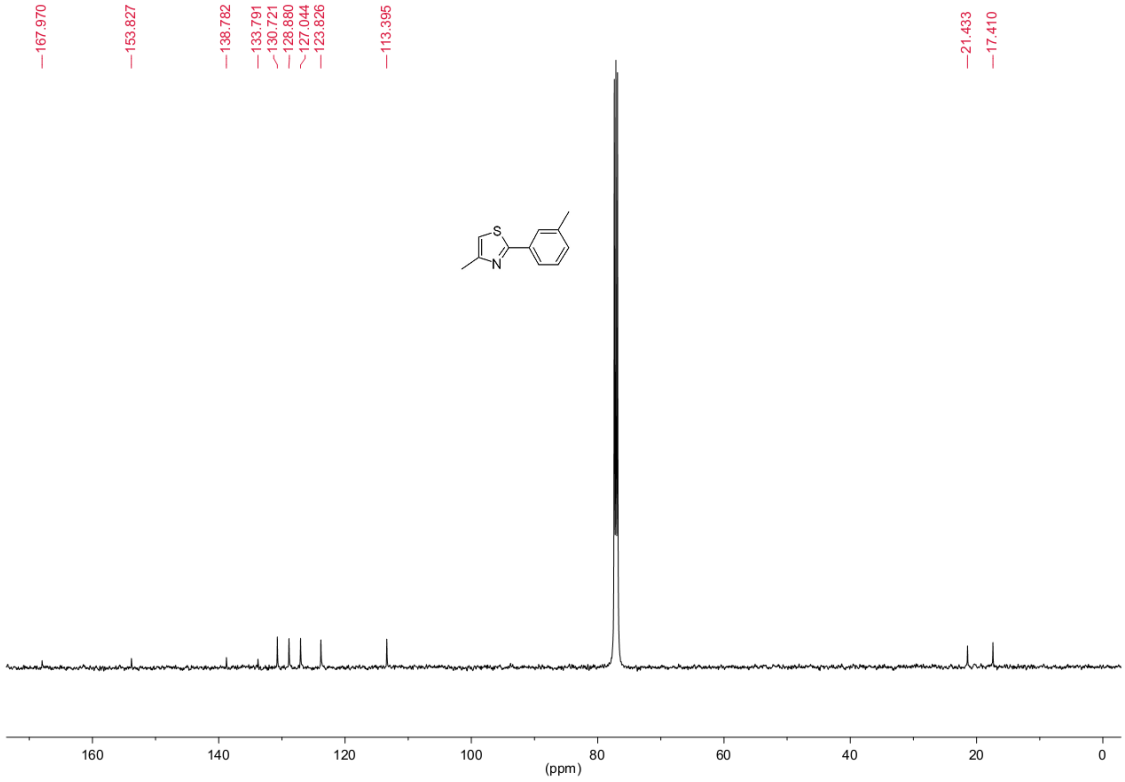
^{1}H NMR spectrum (500 MHz, $CDCl_3$) of **3b**



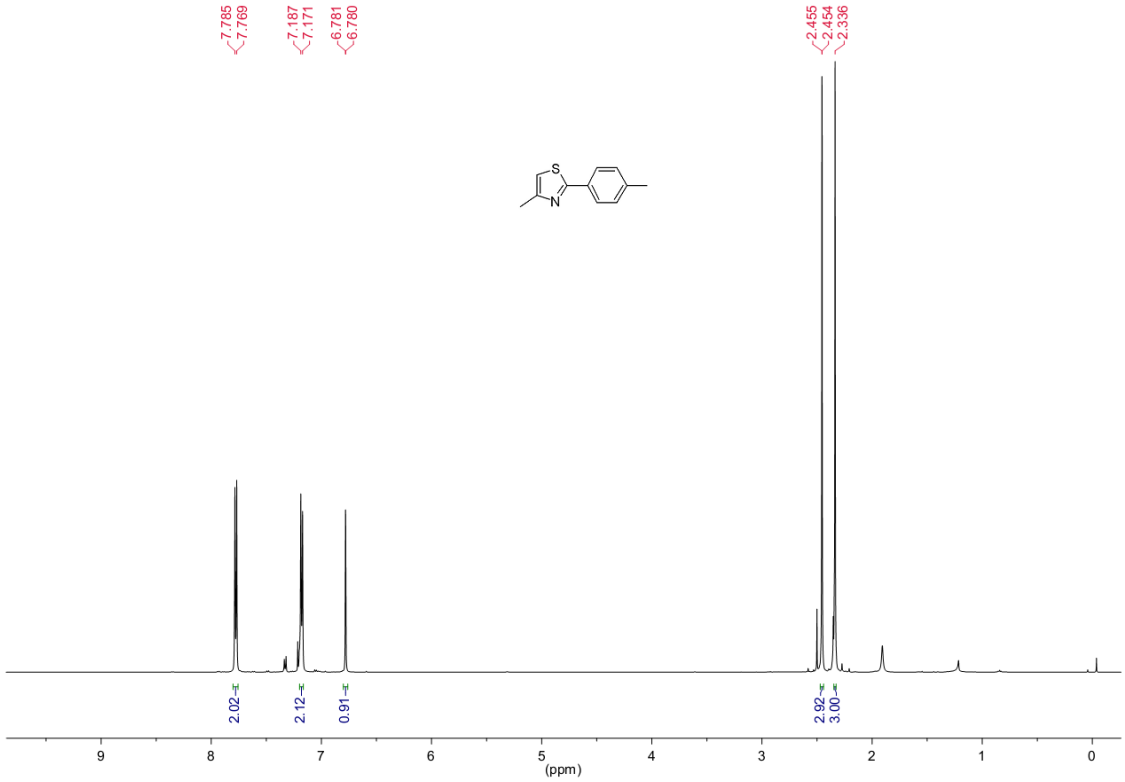
^{13}C NMR spectrum (125 MHz, $CDCl_3$) of **3b**



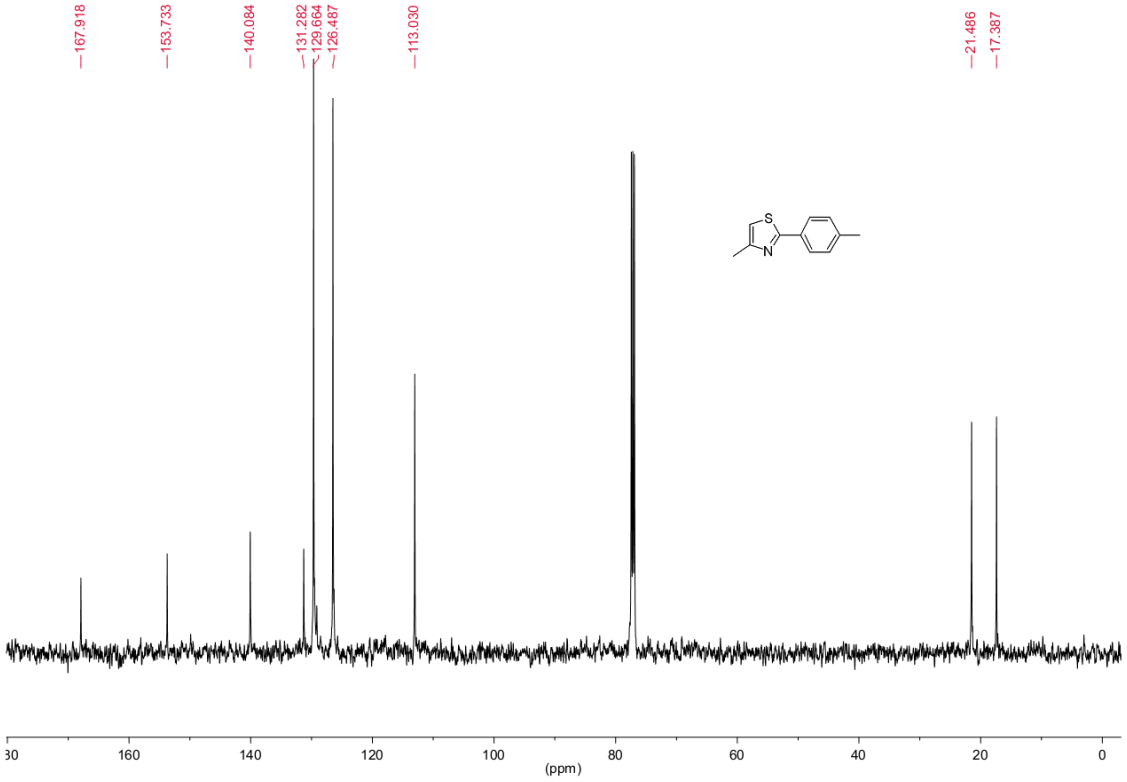
^{1}H NMR spectrum (500 MHz, $CDCl_3$) of **3c**



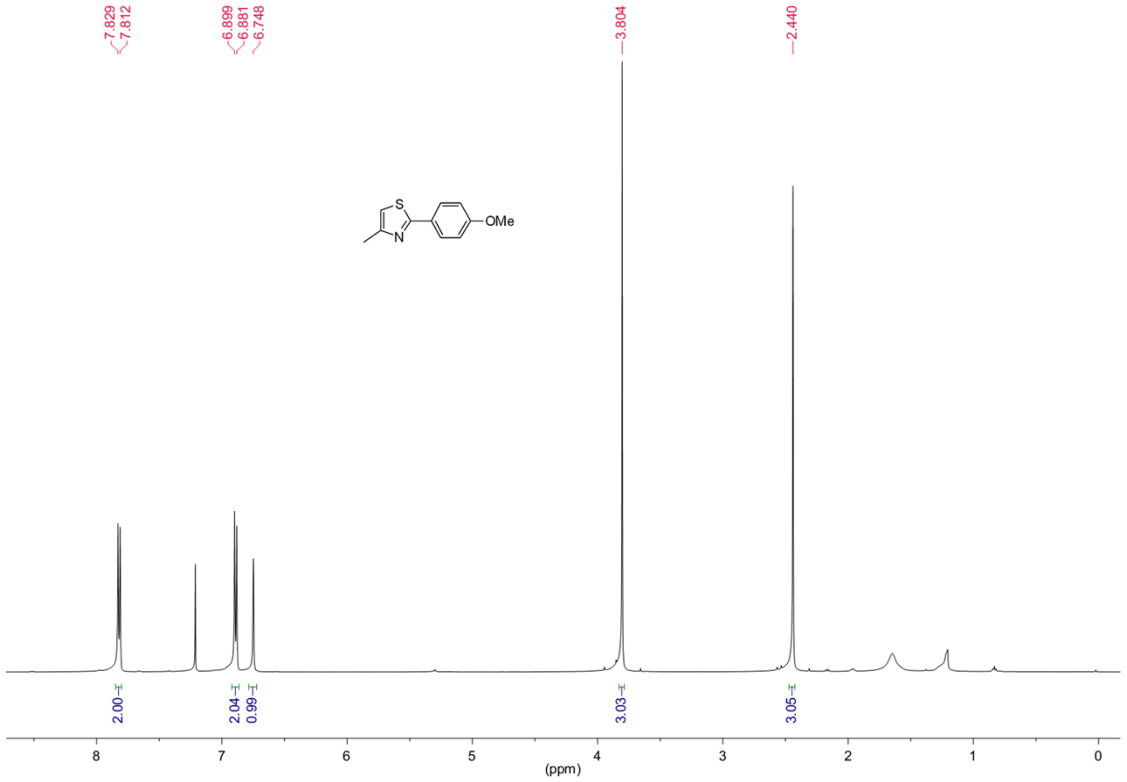
^{13}C NMR spectrum (125 MHz, $CDCl_3$) of **3c**



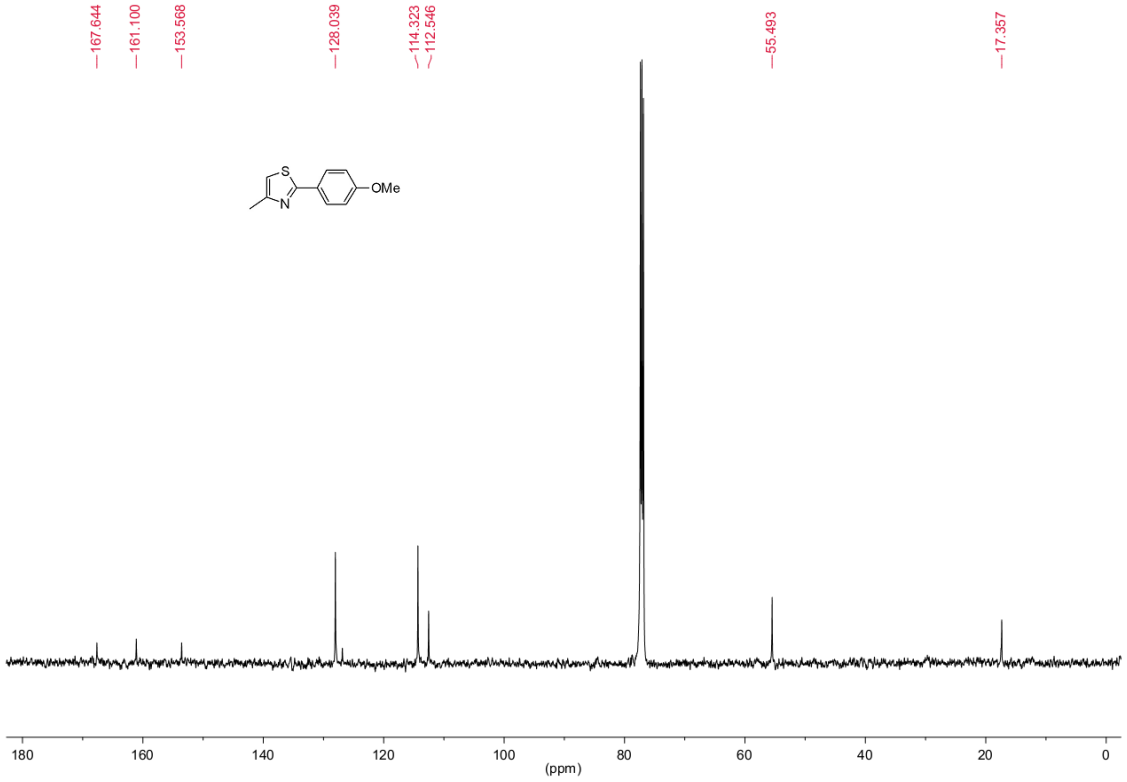
^{1}H NMR spectrum (500 MHz, $CDCl_3$) of **3d**



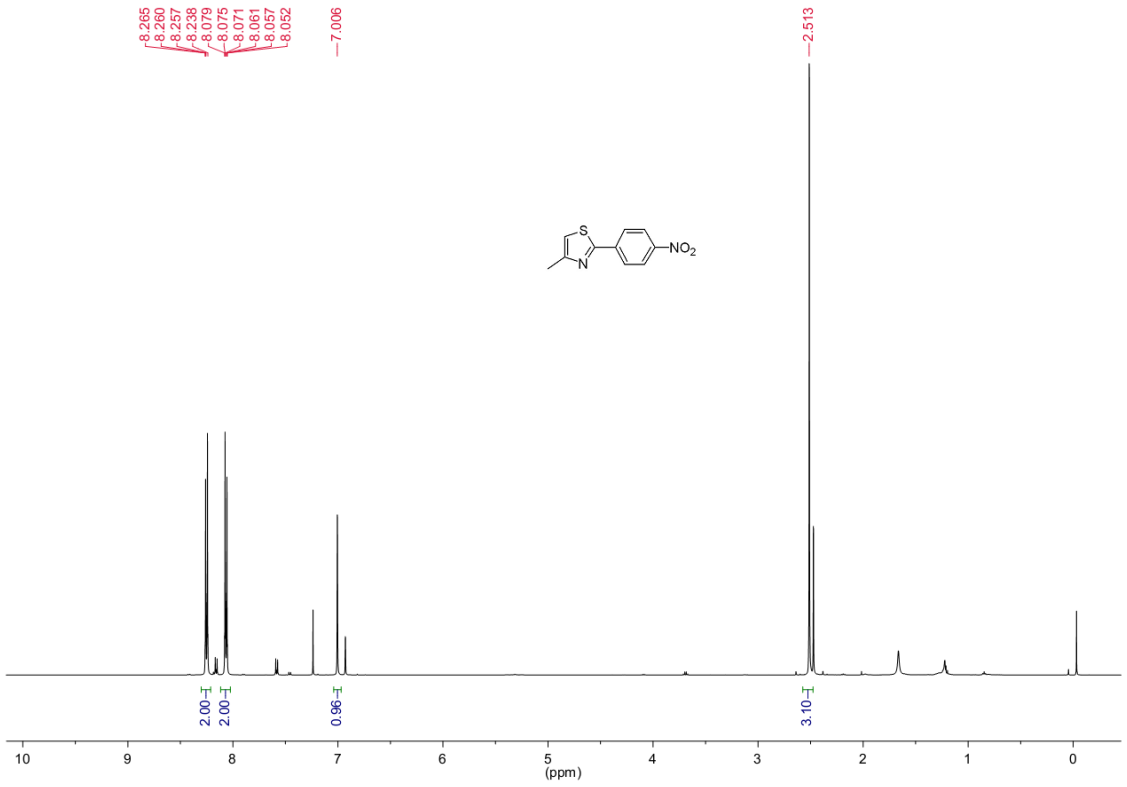
^{13}C NMR spectrum (125 MHz, $CDCl_3$) of **3d**



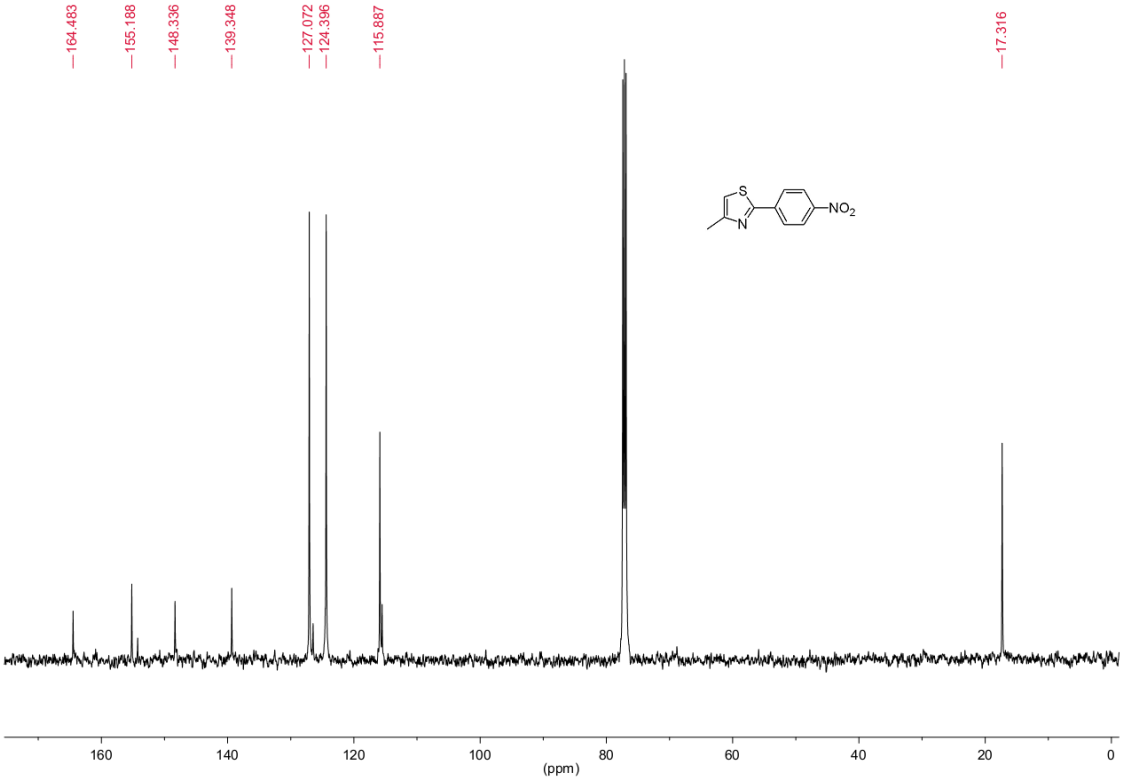
^{1}H NMR spectrum (500 MHz, $CDCl_3$) of **3e**



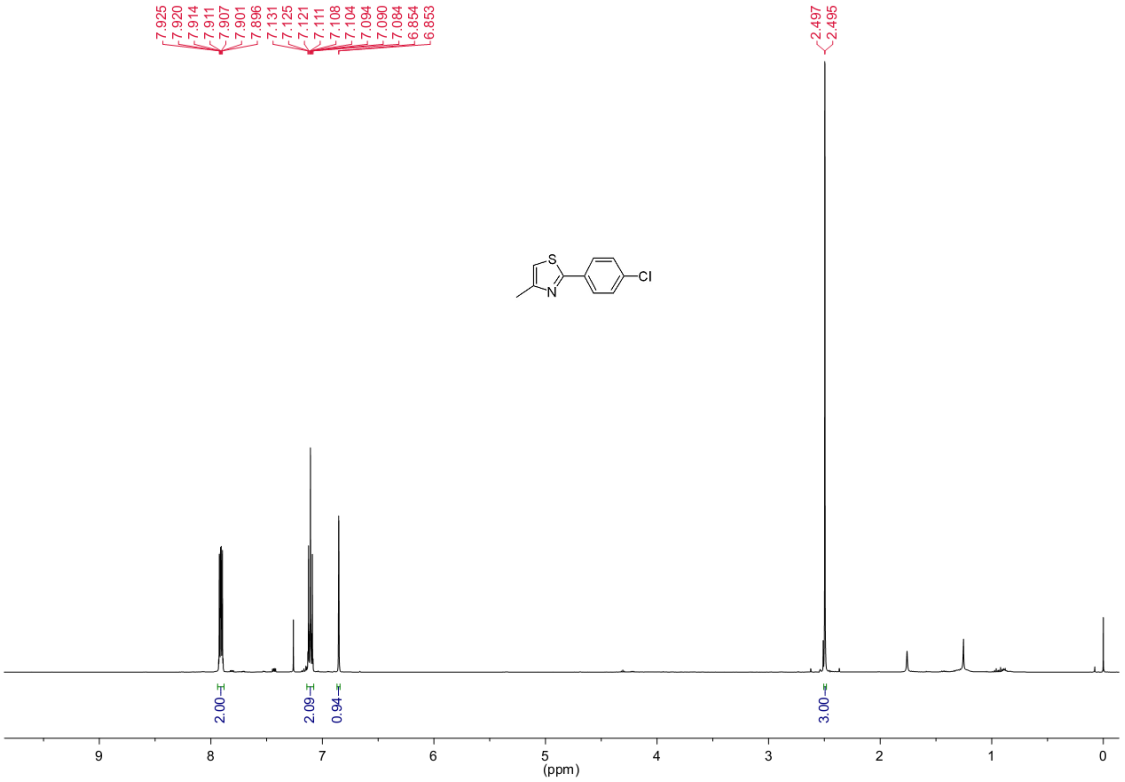
^{13}C NMR spectrum (125 MHz, $CDCl_3$) of **3e**



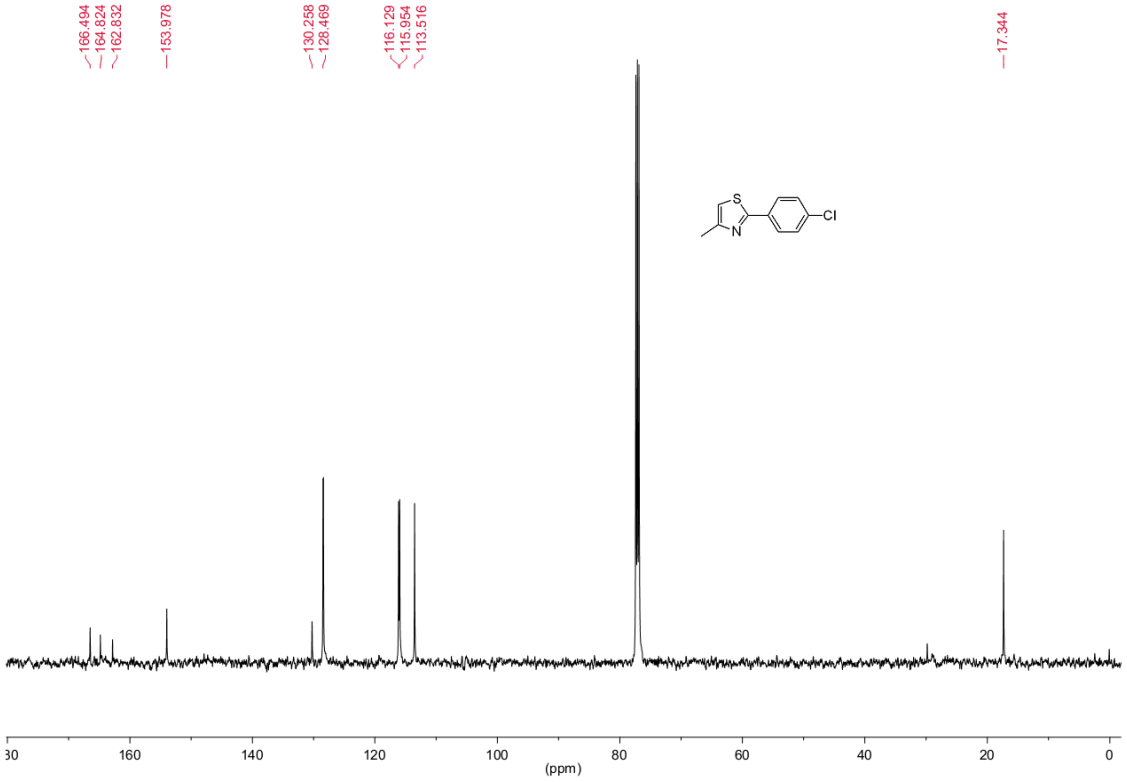
^{1}H NMR spectrum (500 MHz, $CDCl_3$) of **3f**



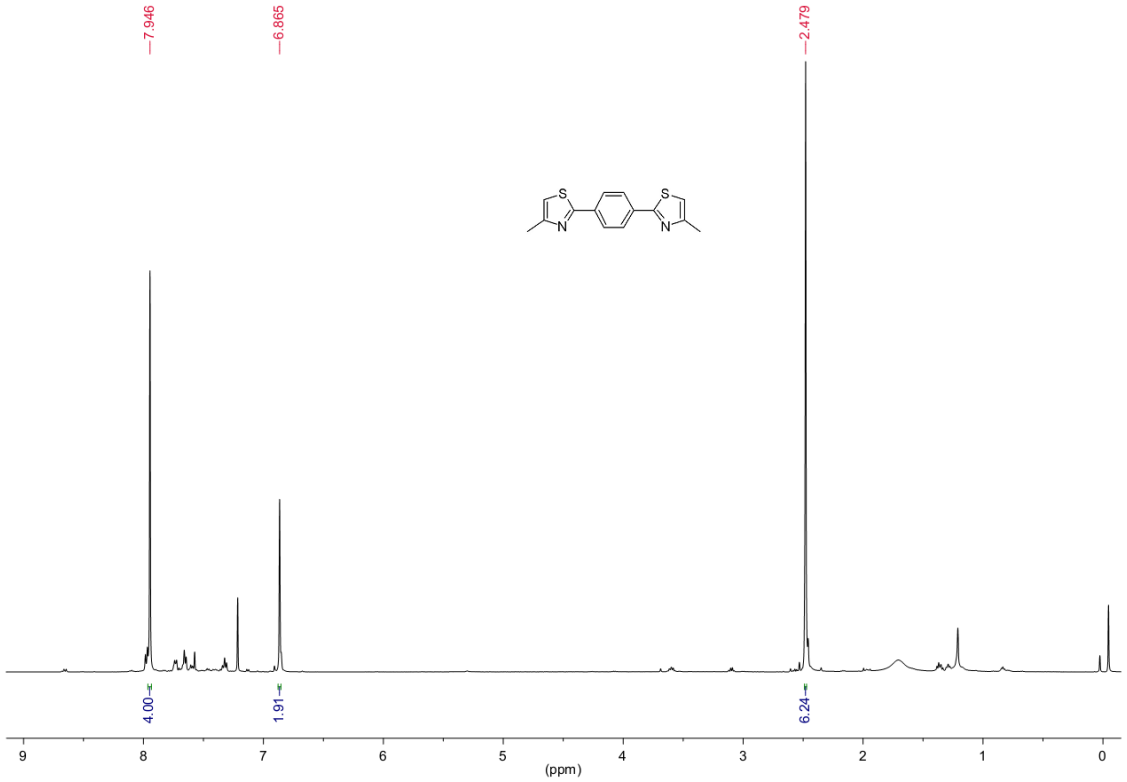
^{13}C NMR spectrum (125 MHz, $CDCl_3$) of **3f**



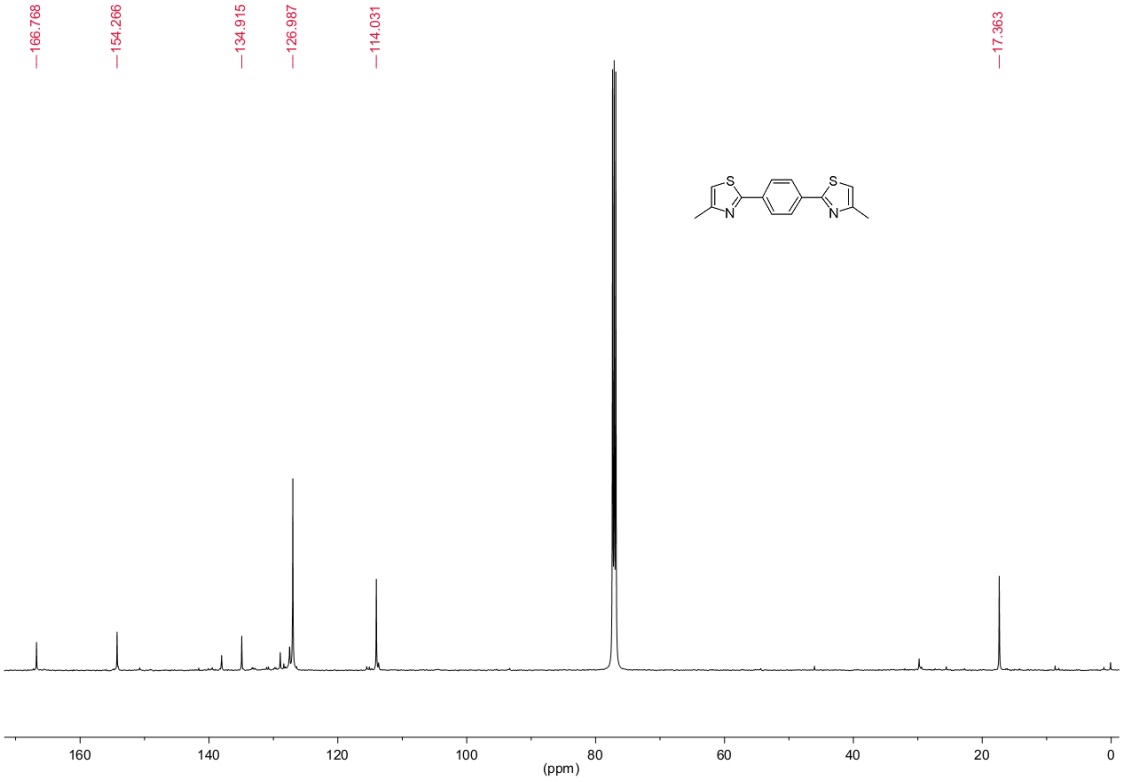
^{1}H NMR spectrum (500 MHz, $CDCl_3$) of **3g**



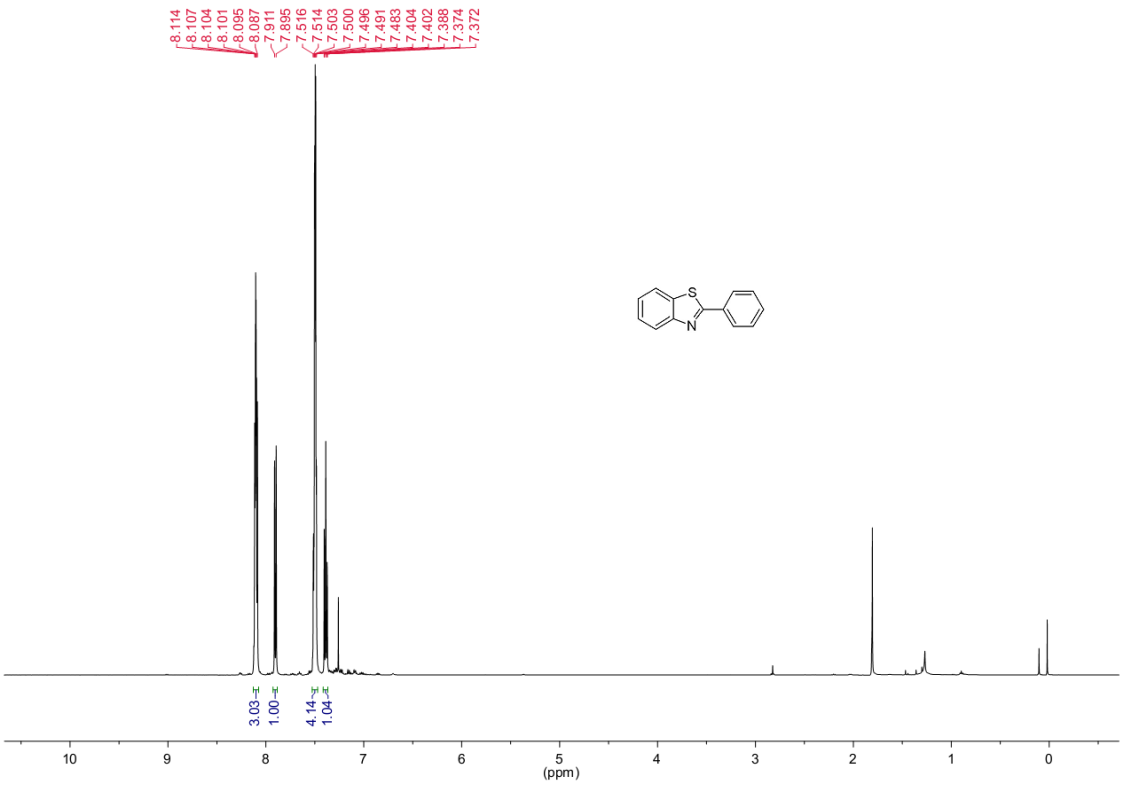
^{13}C NMR spectrum (125 MHz, $CDCl_3$) of **3g**



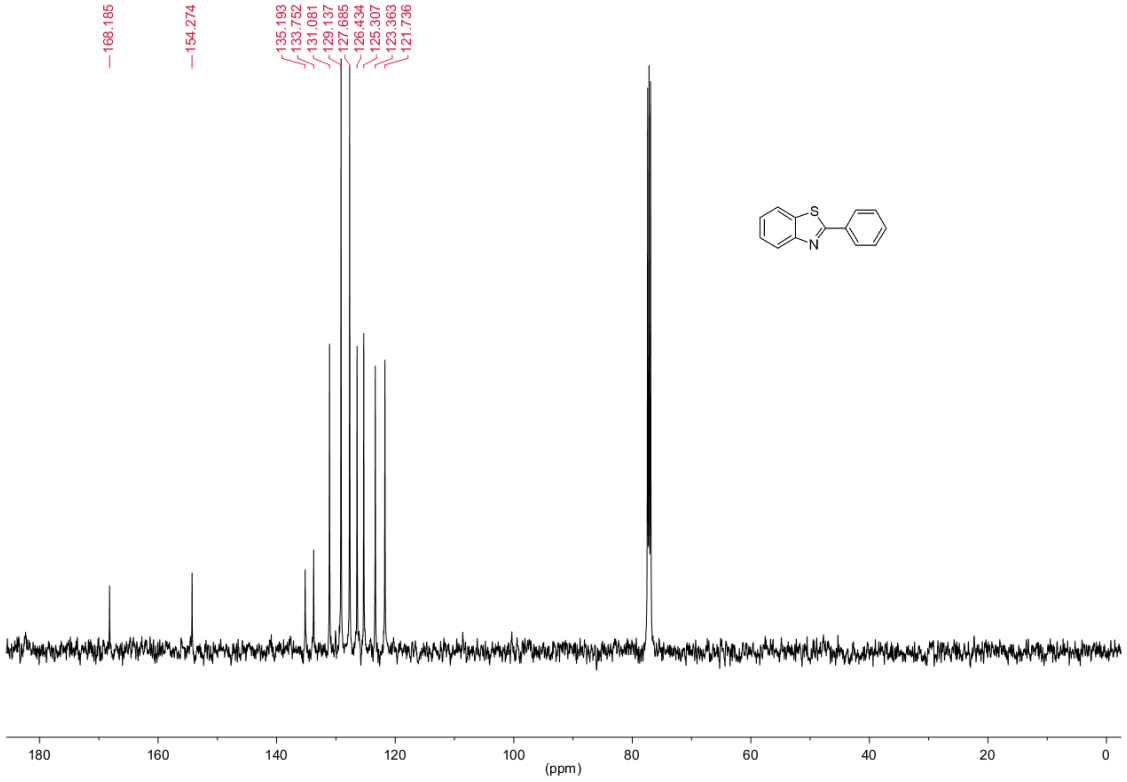
^{1}H NMR spectrum (500 MHz, $CDCl_3$) of **3h**



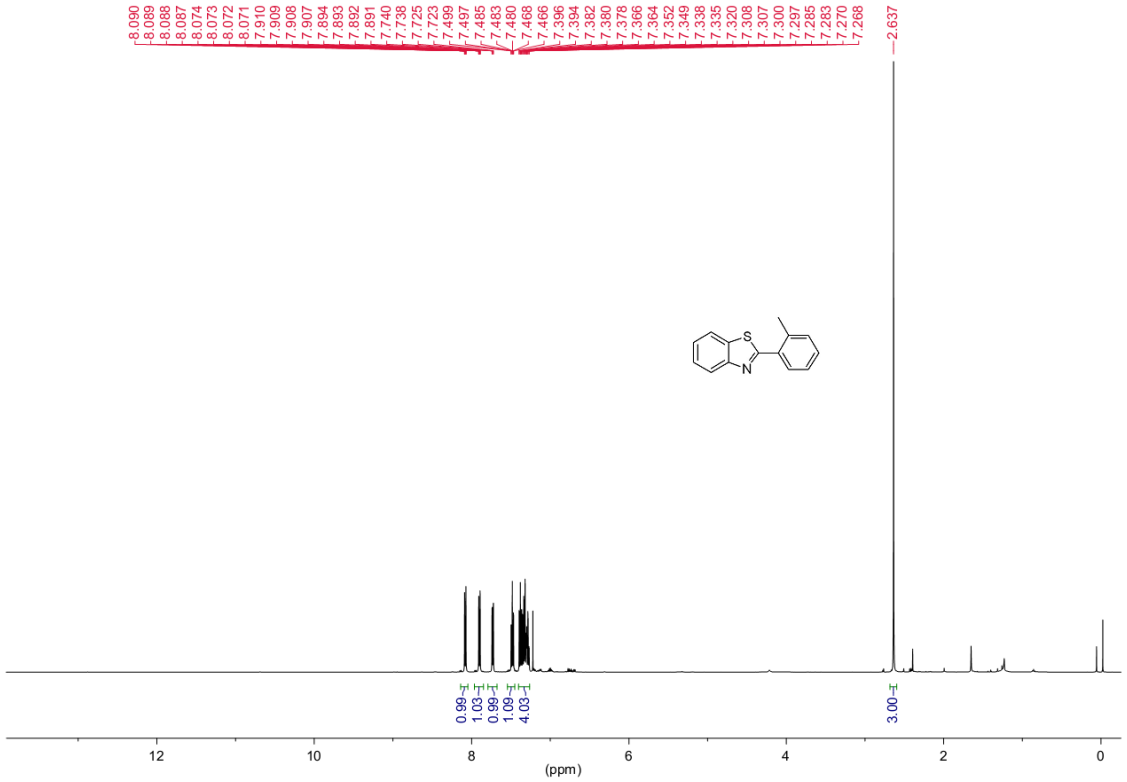
^{13}C NMR spectrum (125 MHz, $CDCl_3$) of **3h**



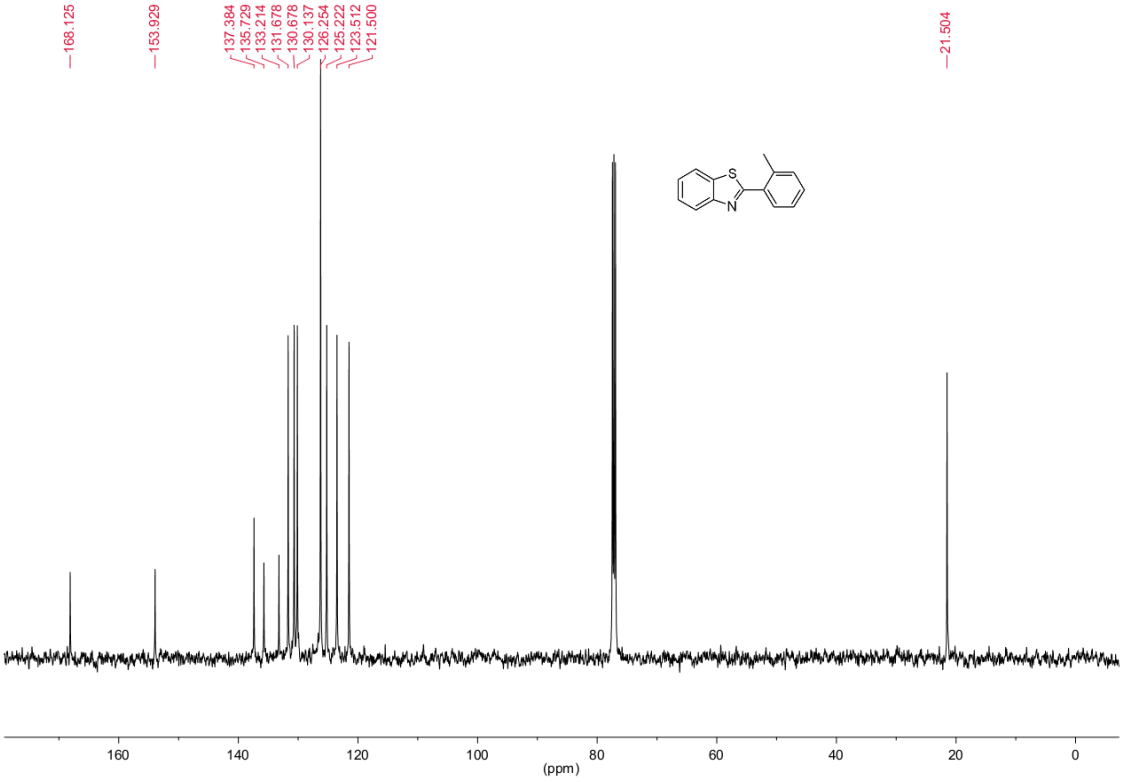
^{1}H NMR spectrum (500 MHz, $CDCl_3$) of **8a**



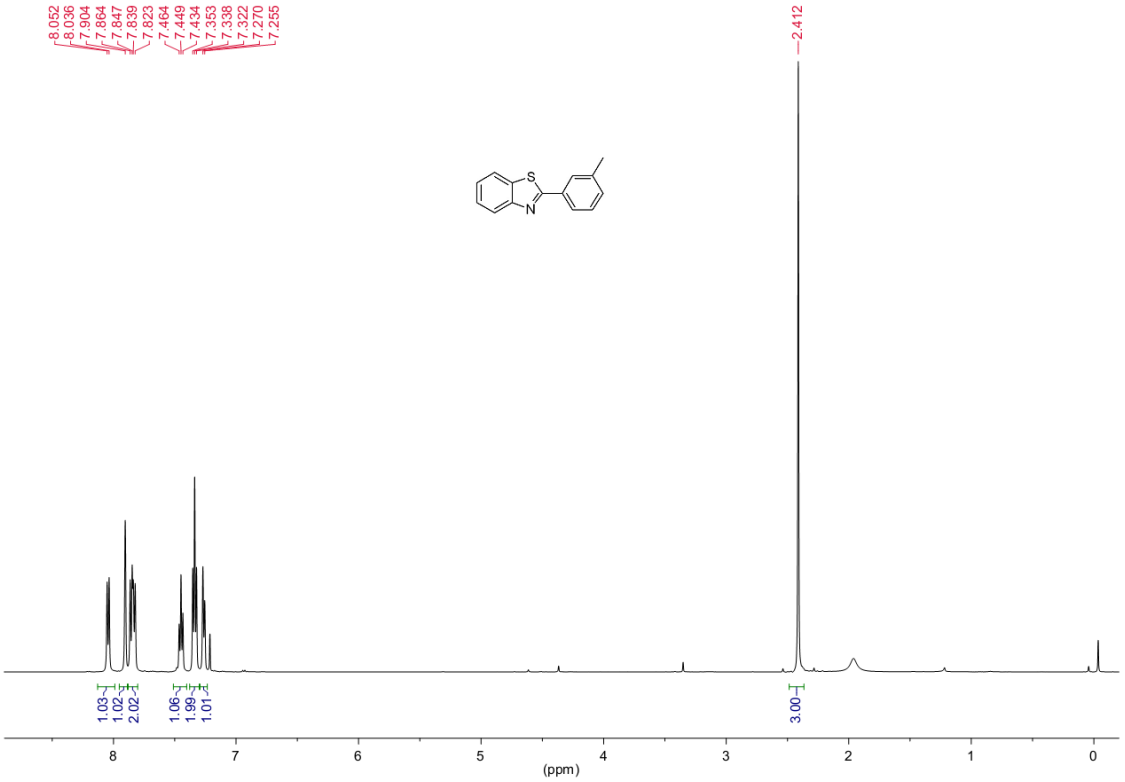
^{13}C NMR spectrum (125 MHz, $CDCl_3$) of **8a**



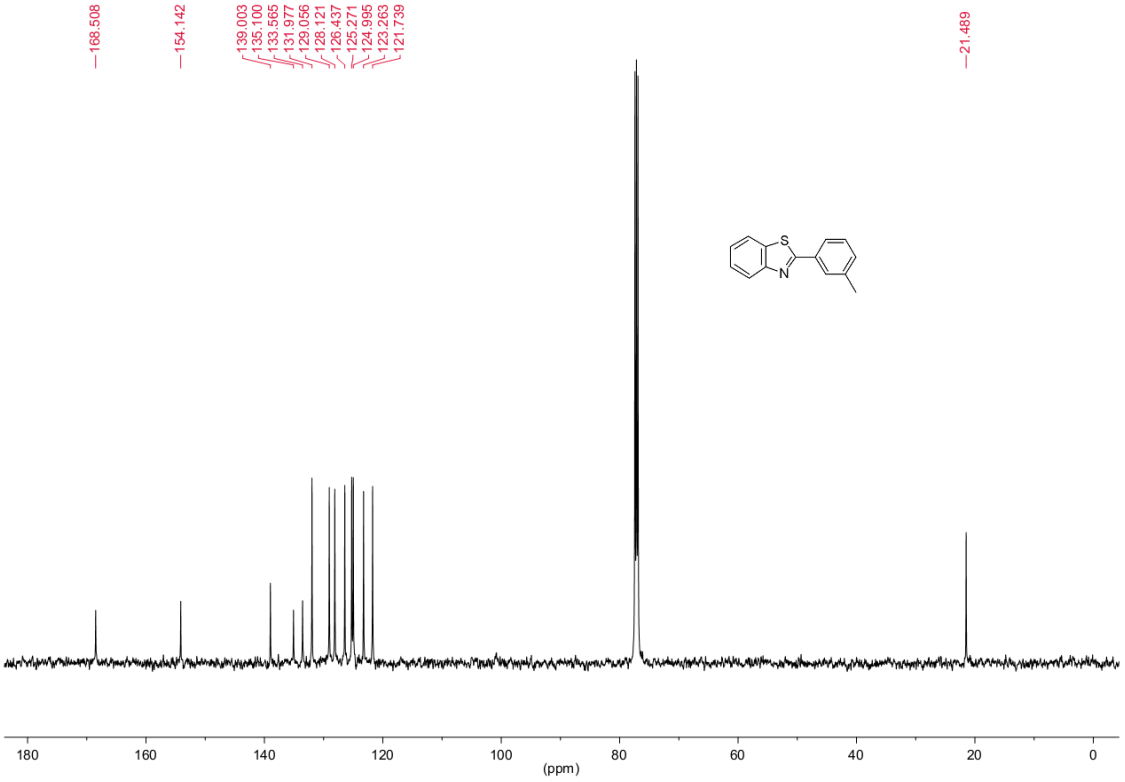
^{1}H NMR spectrum (500 MHz, $CDCl_3$) of **8b**



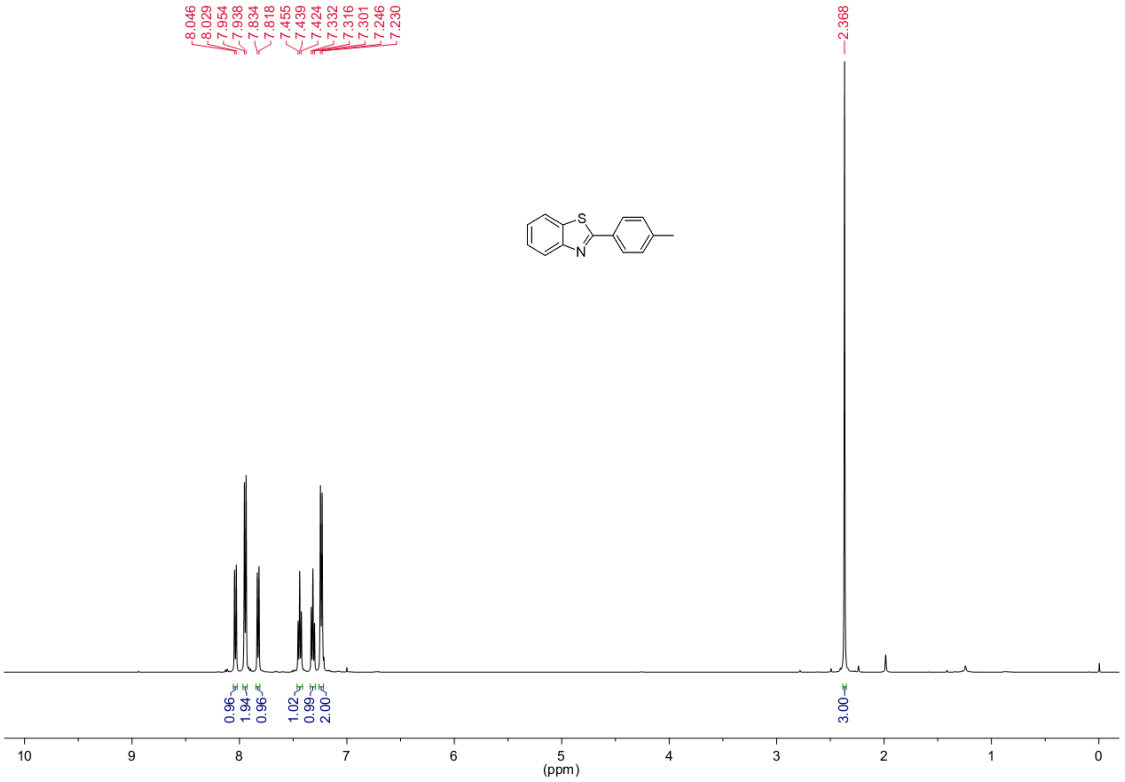
^{13}C NMR spectrum (125 MHz, $CDCl_3$) of **8b**



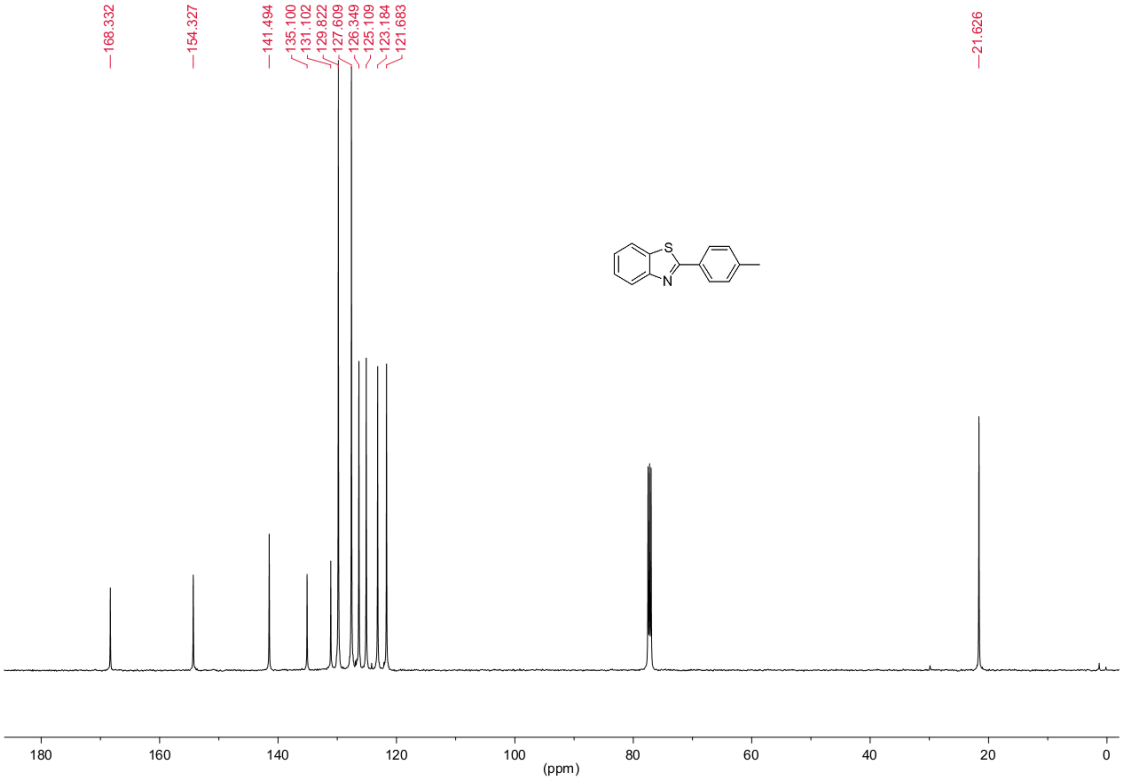
^{1}H NMR spectrum (500 MHz, $CDCl_3$) of **8c**



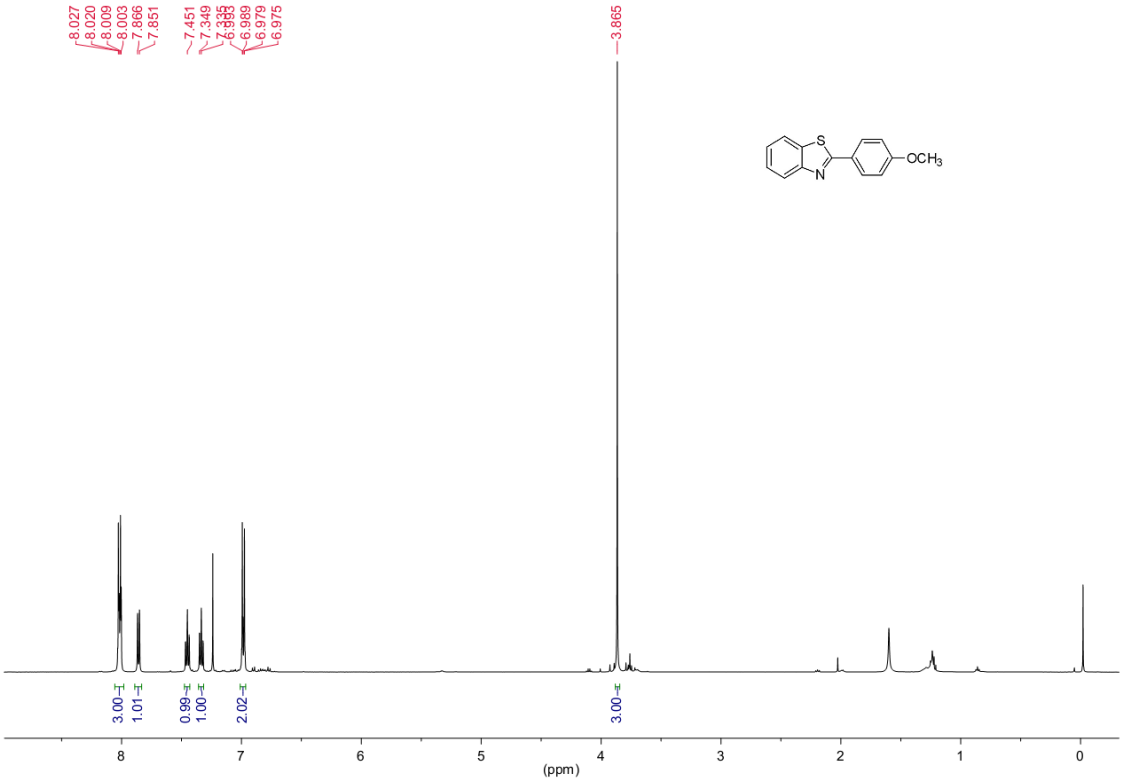
^{13}C NMR spectrum (125 MHz, $CDCl_3$) of **8c**



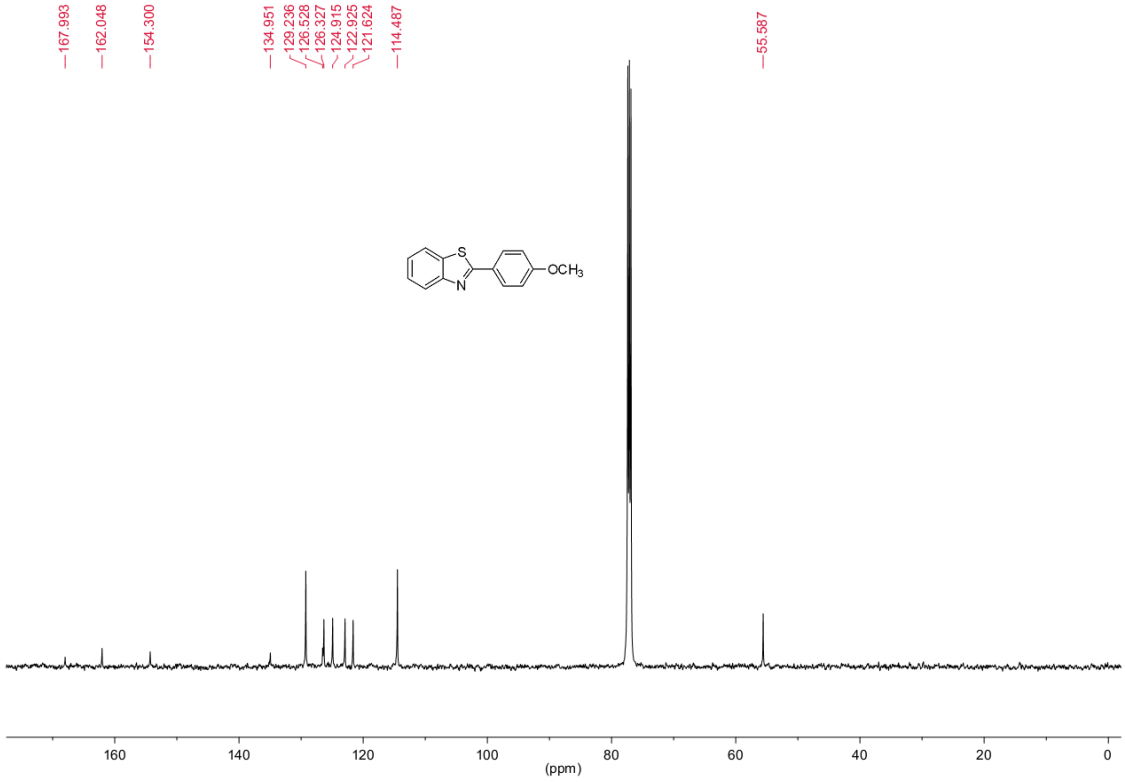
^{1}H NMR spectrum (500 MHz, $CDCl_3$) of **8d**



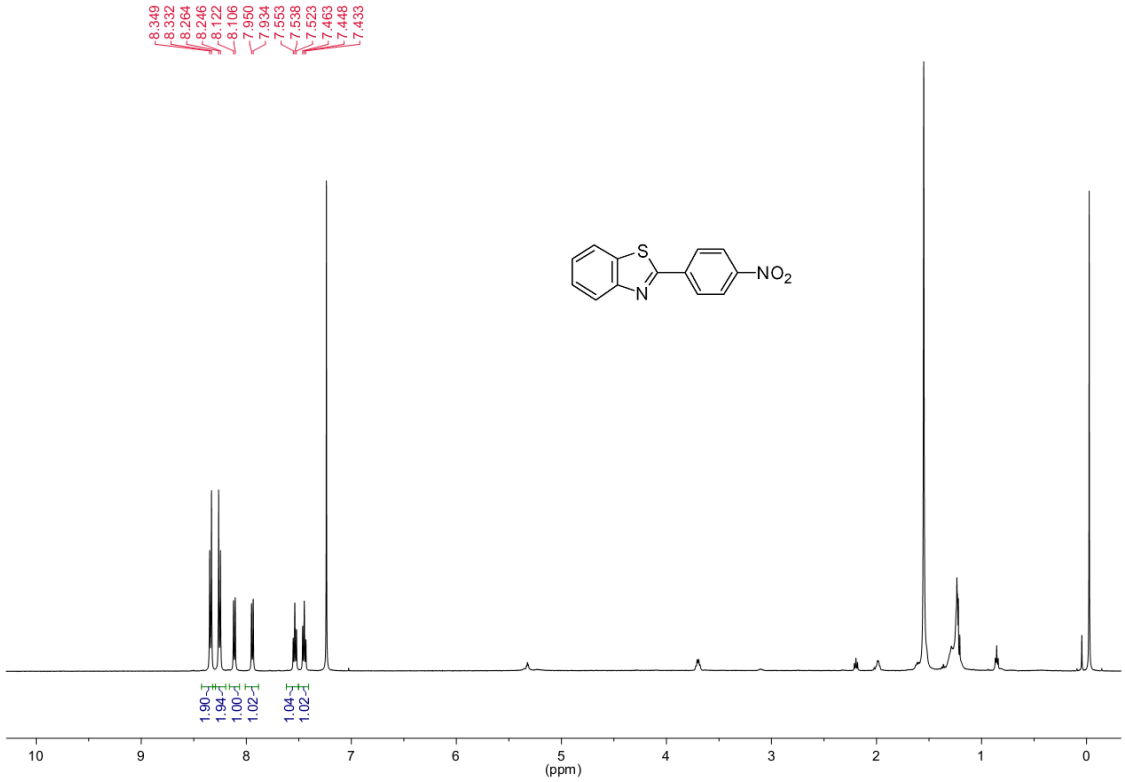
^{13}C NMR spectrum (125 MHz, $CDCl_3$) of **8d**



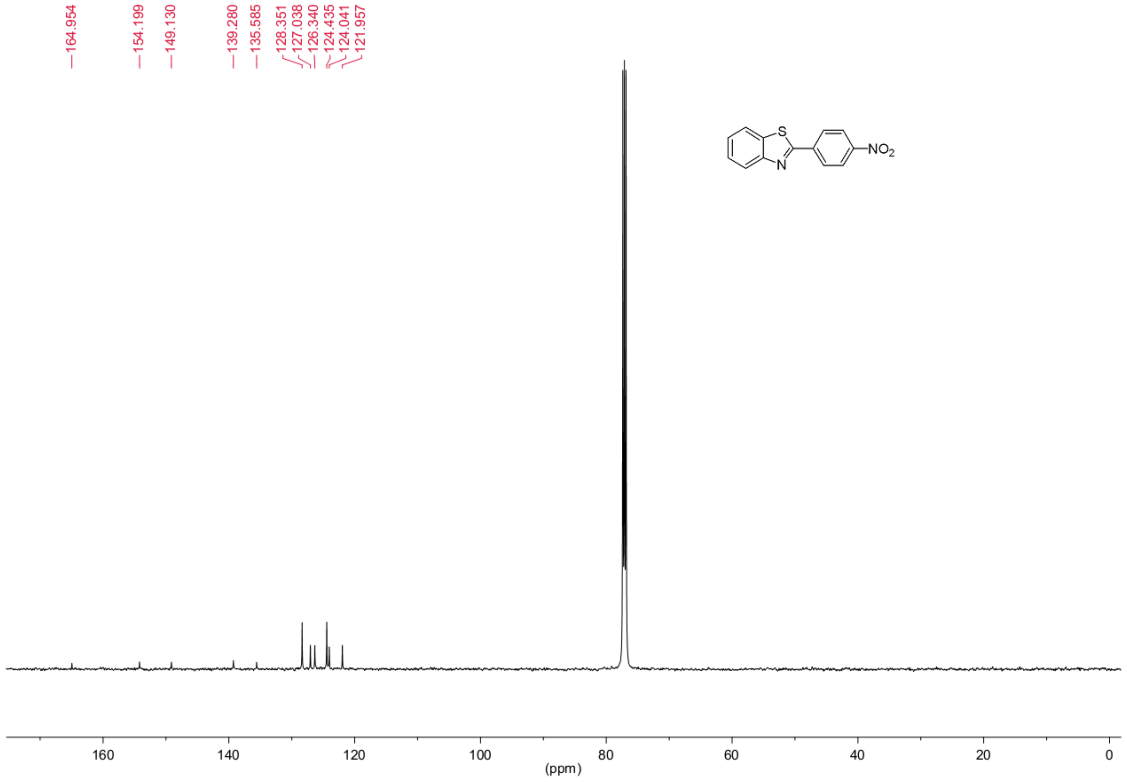
^{1}H NMR spectrum (500 MHz, $CDCl_3$) of **8e**



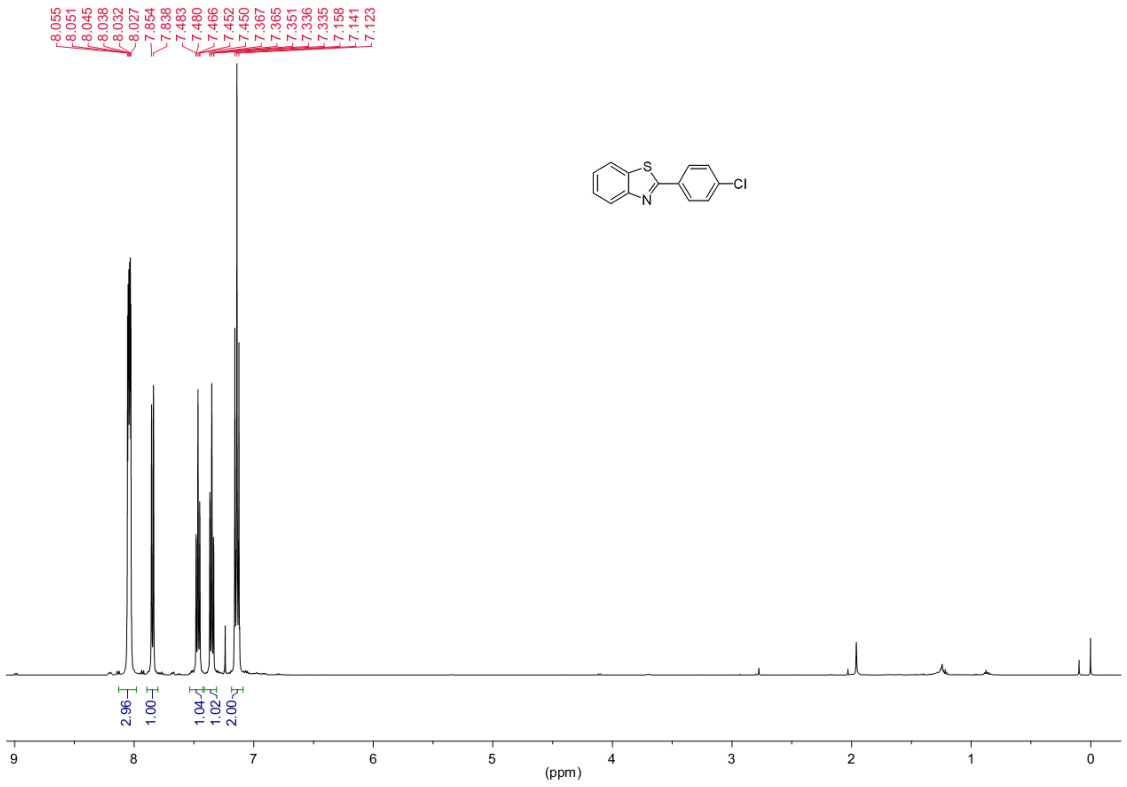
^{13}C NMR spectrum (125 MHz, $CDCl_3$) of **8e**



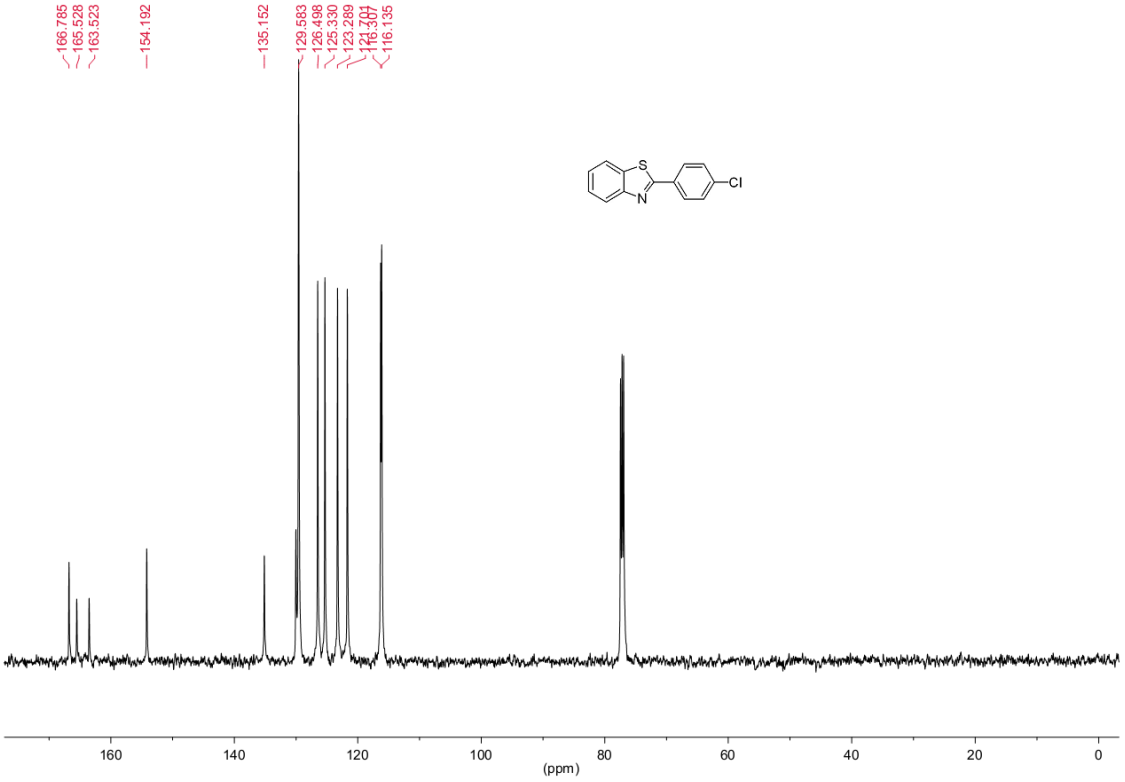
^{1}H NMR spectrum (500 MHz, $CDCl_3$) of **8f**



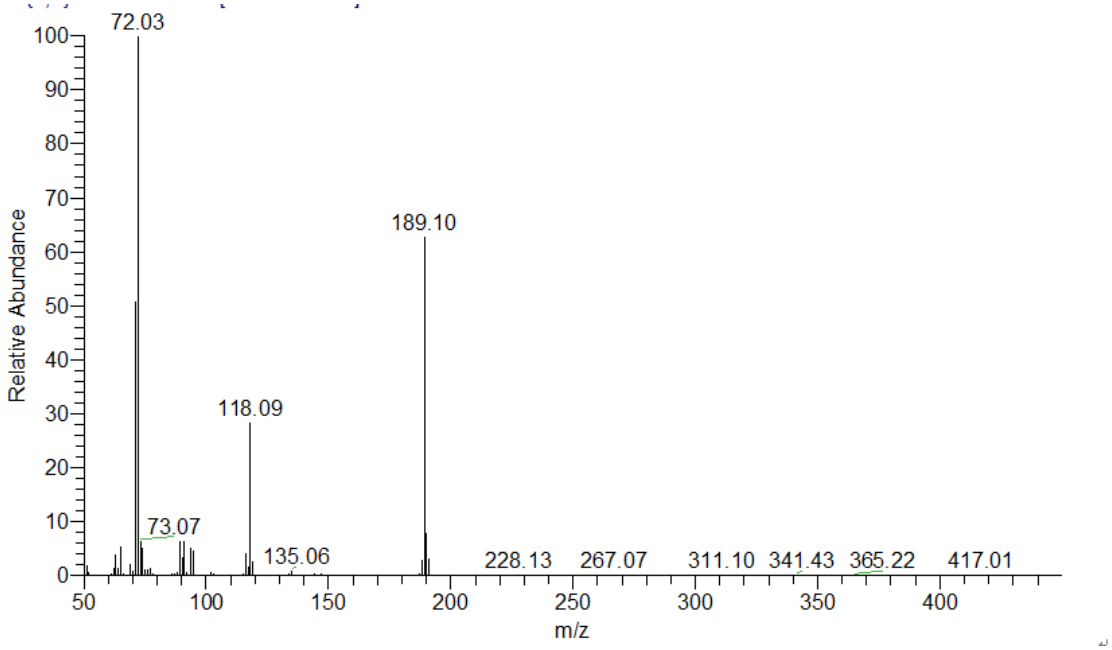
^{13}C NMR spectrum (125 MHz, $CDCl_3$) of **8f**



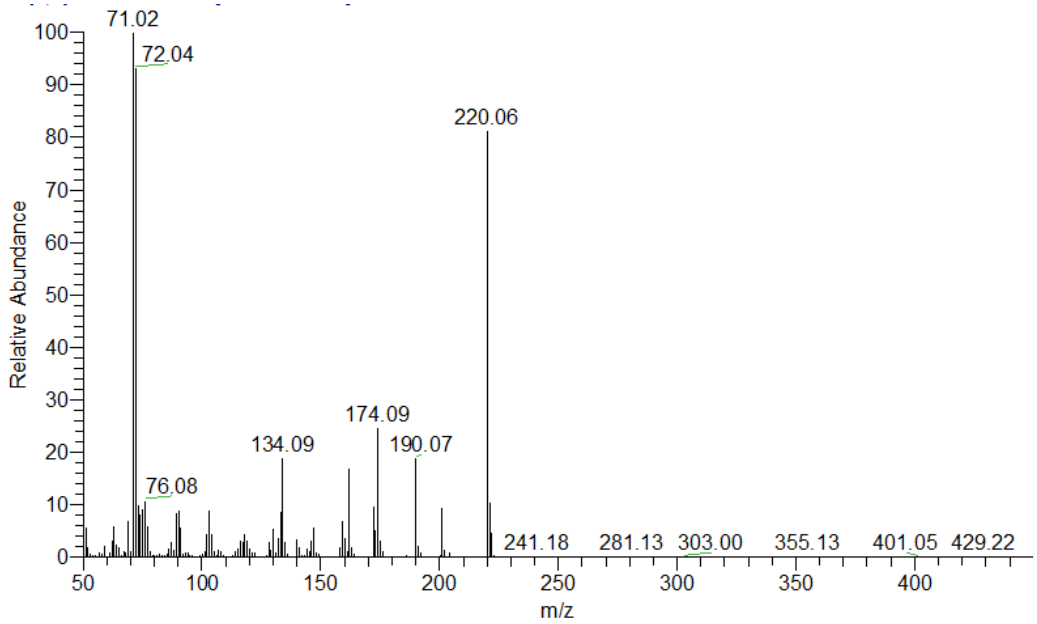
^{1}H NMR spectrum (500 MHz, $CDCl_3$) of **8g**



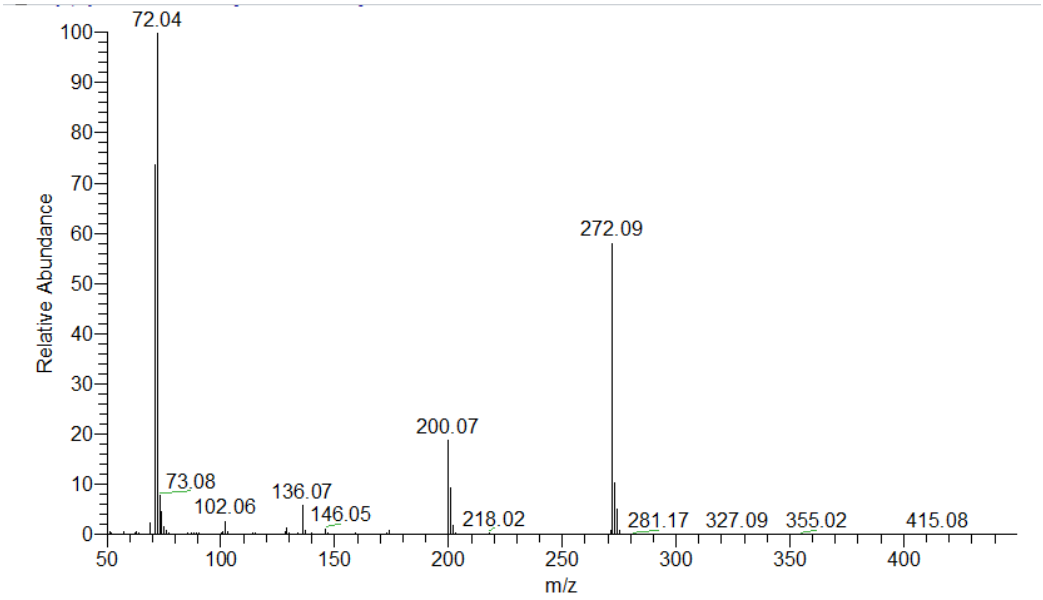
^{13}C NMR spectrum (125 MHz, $CDCl_3$) of **8g**



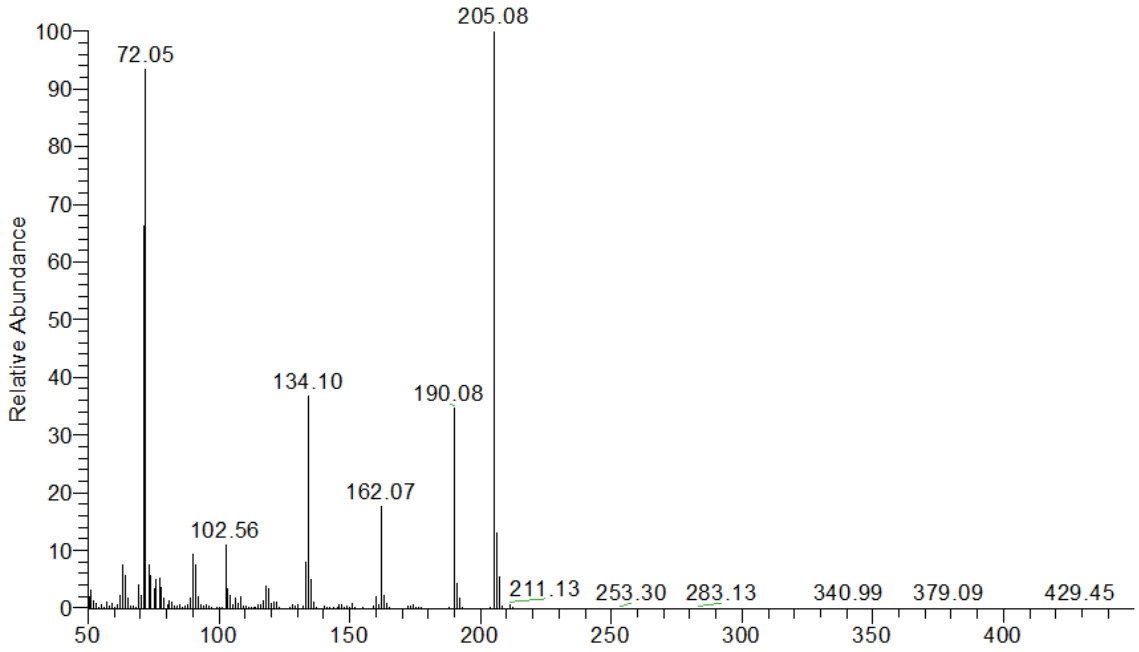
MS 3c


71.02
72.04
220.06
174.09
134.09
190.07
76.08
241.18
281.13
303.00
355.13
401.05
429.22
Relative Abundance
m/z

MS 3f


72.04
272.09
200.07
73.08
102.06
136.07
146.05
218.02
281.17
327.09
355.02
415.08
Relative Abundance
m/z

MS 3h


205.08
72.05
100
90
80
70
60
50
40
30
20
10
0
Relative Abundance
134.10
190.08
162.07
102.56
211.13
253.30
283.13
340.99
379.09
429.45
50
100
150
200
250
300
350
400

MS 3e