Electronic Supplementary Material (ESI) for Green Chemistry.

Metal-Free Regioselective Bromination of Imidazo-Heteroarenes: Dual Role of Organic Bromide Salt in Electrocatalysis

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1. General information:

Electrochemical reactions were conducted using IKA Electrasyn 2.0 (at room temperature) and Keithley 2231A-30-3 triple channel DC power supply (at 50-60 ºC). Commercially available reaction vials and electrodes were purchased from IKA. All the reactions were performed without taking any necessary precaution to exclude air or moisture. Cyclic voltammetry (CV) experiments were also conducted in IKA Electrasyn 2.0 using CV glassy carbon electrode, CV reference electrode and Platinum plated electrode purchased from IKA. Chromatographic purification of products was accomplished by Column chromatography on silica gel (230-400 mesh). For thin layer chromatography (TLC) analysis throughout this work, Merck pre-coated TLC plates (silica gel 60 GF_{254}, 0.25 mm) were employed, using UV light as the visualizing agent. Organic solutions were concentrated under reduced pressure on a Heidolph rotary evaporator. The products obtained were characterised using ^{1}H NMR,^{13}C NMR, FT-IR (ATR) and ESI-HRMS. NMR spectra were recorded at 400 MHz and 500 MHz for ^{1}H, 101 MHz and 126 MHz for ^{13}C. The chemical shift (δ) for ^{1}H and ^{13}C are given in ppm relative to internal standard/residual signals of the solvents (tetramethylsilane @ 0 ppm ^{1}H NMR and $CDCl_3$ @ 77.00 ppm ^{13}C NMR). Coupling constants are given in Hertz. The following abbreviations are followed to indicate the multiplicity: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; dd, doublet of doublets; ddd, doublet of doublets of doublets. IR measurements were carried out on the Agilent ATR FT-IR spectrophotometer and the representative data are reported in terms of frequency (cm^{-1}) of absorption. High-resolution mass spectra (HRMS) were obtained from the High-Resolution Mass Spectrometry unit on MicroTOF Focus with electrospray ionization. Gas chromatography measurements were performed on a Shimadzu Chromatograph Nexis GC-2030 equipped with a Shimadzu SH-Rxi-5ms 30 meter capillary column and an FID detector.

Materials:

Synthesis grade solvents like acetonitrile (MeCN) and *N*,*N*-dimethylformamide (DMF) were used as purchased. Double distilled water was used as a solvent. 2-bromoacetophenones, 2-aminopyridines, tetra-*n*-butylammonium bromide (TBAB, ≥98%) and tetraethylammonium chloride (TEAC, ≥98%) were purchased from Sigma-Aldrich. All the other commercial grade reagents and solvents were purchased from Sigma-Aldrich at the highest commercial quality and used without further purification, unless otherwise stated. All the starting materials were prepared using the literature procedures.[1]

Reaction setup:

The reaction setups are detailed in Figure S-01 and S-02. To perform electrolysis, Electrsyn vial of 5 mL capacity was used. Two Graphite SK-50 electrodes (0.8 cm × 0.2 cm × 5.2 cm) were inserted into the ElectraSyn vial cap. This vial cap was then fitted tightly to the reaction vial consisting of reaction mixture and a magnetic stirring bead.

Figure S-01: Reaction vial, vial cap and electrodes.

Electrasyn 2.0 was used for the electrochemical bromination at room temperature (Figure S-02a). However, for higher temperature Keithley 2231A-30-3 triple channel DC power supply was used as a source of DC supply (Figure S-02b).

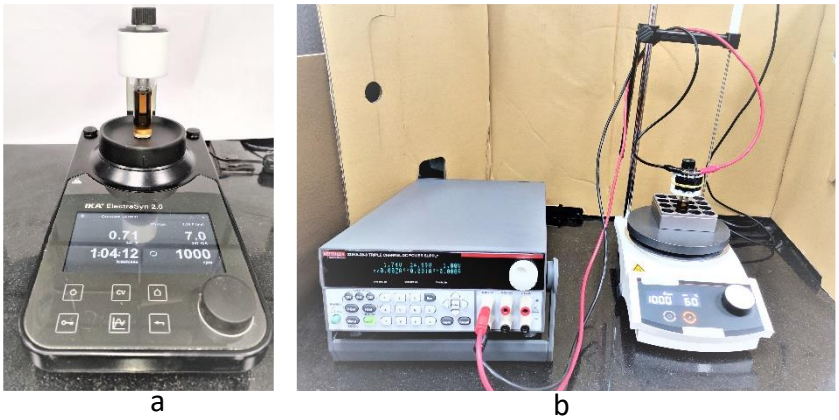


Figure S-02: (a) Reaction setup at room temperature, (b) Reaction setup at 50-60 ºC.

2. General procedure for the electrochemical bromination:

(a) Electrochemical bromination at room temperature:

Without taking any precaution to remove air or moisture, an oven dried ElectraSyn vial (5 mL) equipped with magnetic stirring bar was charged with 0.2 mmol appropriate imidazo-heteroarenes (**1a-i**, **1k**, **1m-n**, **1r**, **1u-w**) and TBAB (3.0 equiv., 0.6 mmol, 193 mg). Exact 4 mL of MeCN (or in some cases a mixture of MeCN/DMF in a ratio of 3:1) was added to the ElectraSyn vial. An ElectraSyn vial cap equipped with Graphite SK-50 as an anode and the same as cathode was then fitted tightly to the reaction vial. The whole reaction mixture was the stirred vigorously for 10 minutes to make the mixture homogenous. After 10 minutes of pre-stirring, the complete setup was connected to the vial holder of Electrasyn 2.0. The reaction mixture was then electrolysed for 4 h by applying 7.0 mA constant current with 1000 rpm magnetic stirring (Figure S-02a). After completion, saturated sodium chloride solution (4.0 mL) was added to the reaction mixture and was extracted with ethyl acetate (3 × 5.0 mL), dried using anhydrous sodium sulfate, concentrated in vacuo. The residue was finally purified through silica gel (230-400 mesh) column chromatography using ethyl acetate/hexane (1:10) as eluent.

NOTE: For electrochemical chlorination rection same procedure was followed, only TEAC was used instead of TBAB.

(b) Electrochemical bromination at 60 ºC:

Without taking any necessary precaution to remove air or moisture, an oven dried ElectraSyn vial (5 mL) equipped with magnetic stirring bar was charged with 0.2 mmol appropriate imidazo-heteroarenes (**1j**, **1l**, **1o-q**, **1s-t**) and TBAB (3.0 equiv., 0.6 mmol, 193 mg). 4 mL of MeCN (or in some cases a mixture of MeCN/DMF in a ratio of 3:1) was added to the ElectraSyn vial. An ElectraSyn vial cap equipped with Graphite SK-50 as an anode and the same as cathode was then fitted tightly to the reaction vial. The vial was then placed into a heating block equipped with a temperature controlling probe. The reaction mixture was simultaneously stirred and heated for 10 minutes till the temperature of the mixture reaches 60 ºC. With Keithley 2231A-30-3 triple channel DC power supply, the reaction mixture was next electrolysed for 4 h by applying 7 mA constant current with 1000 rpm magnetic stirring (Figure S-02b). After completion of the reaction, the mixture was left to cool down at room temperature. When the reaction mixture reached room temperature, saturated sodium chloride solution (4.0 mL) was added to the reaction mixture and was extracted with ethyl acetate (3 × 5.0 mL), dried using anhydrous sodium

sulfate, concentrated in vacuo. The residue was finally purified through silica gel (230-400 mesh) column chromatography using ethyl acetate/hexane (1:10) as eluent.

3. General procedure for domino organo-electrochemical bromination:

Without taking any necessary precaution to remove air or moisture, an oven dried ElectraSyn vial (5 mL) equipped with magnetic stirring bar was charged with 0.2 mmol of appropriate 2-bromoacetophenone (**4a**-**h**), 0.5 mmol (2.5 equiv.) of 2-aminopyridine (**5a**-**b**) and 30 mol% TBAB (0.06 mmol, 19 mg). 4 mL of mixed solvent system containing MeCN/water in the ratio of 3:1 was added to the reaction vial. After inserting a Electrasyn vial cap equipped with Graphite SK-50 as an anode and the same as cathode to the reaction vial, the whole system was placed in a heating block equipped with a temperature controlling probe for simultaneous pre-stirring and heating at 50 ºC for 10 minutes. After that, the mixture was electrolysed at 50 ºC for 7 h by applying a constant current supply of 6 mA from Keithley 2231A-30-3 triple channel DC power supply. After completion, the reaction mixture was left to settle down at room temperature. Then saturated sodium chloride solution (4.0 mL) was added to the mixture and was extracted with ethyl acetate (3 × 5.0 mL), dried using anhydrous sodium sulfate, concentrated in vacuo. The residue was finally purified using silica gel (230-400 mesh) column chromatography using ethyl acetate/hexane (1:10) as eluent.

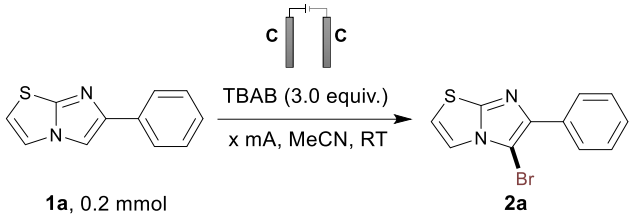
4. Resistance measurement of the reaction mixture:

Resistance measurement was conducted using IKA Electrasyn 2.0. ElectraSyn vial (5 mL) equipped with magnetic stirring bar was charged with 0.2 mmol 6-phenylimidazo[2,1-b]thiazole (**1a**) and 4 mL MeCN. After inserting a Electrasyn vial cap equipped with Graphite SK-50 as an anode and the same as cathode to the reaction vial, the whole system was stirred for 10 minutes to attain homogeneity. Then the resistance of that solution was measured by applying a constant voltage of 2.0 V (Figure S-03a). Next, 0.2 mmol (1.0 equiv.) of TBAB was added to the same vial and resistance was measured at the same voltage after 5 minutes of pre-stirring (Figure S-03b). To the similar vial another 2.0 equivalent of TBAB was added and resistance was measured in a similar fashion (Figure S-03c).

a b c

Figure S-03: Measured resistance of **1a** and TBAB in 4 mL MeCN at a constant voltage of 2.0 V, (a) resistance of the solution of 0.2 mmol **1a,** (b) resistance of the solution of 0.2 mmol **1a** + 0.2 mmol (1 eqiuv.) TBAB, (c) resistance of resistance of 0.2 the solution of mmol **1a** + 0.6 mmol (3.0 eqiuv.) TBAB.

5. Voltage (V) vs Time (h) plot for the electrochemical bromination reaction:



For the above reaction, change in the voltage was recorded at several time intervals during the electrolysis with constant current of 3 mA, 7 mA and 10 mA respectively. When we applied 3 mA current for the model reaction, after 4 h **2a** was formed in only 62% yield. On the other hand, when we have increased the current supply from 7 mA to 10 mA almost same amount (~90%) of the final product **2a** was formed in 3.5 h instead of 4 h. A plot of voltage (V) versus time (h) is shown below:

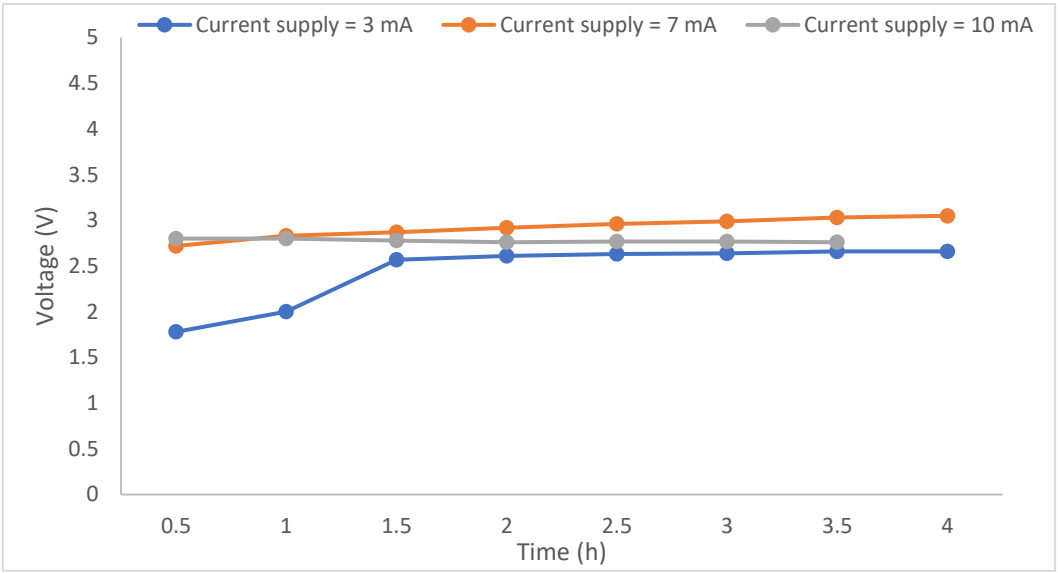
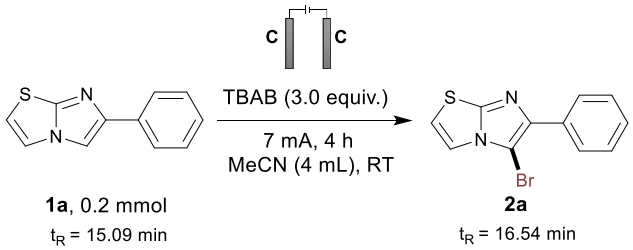


Figure S-04: Voltage vs time plot at several time intervals by applying different amount of constant current.

6. GC analysis to confirm exclusive regioselectivity:



After completion of the above model electrolysis reaction, an aliquot portion (100 µL) was taken from the reaction mixture using a micro-pipette and the analytical sample solution was prepared in MeCN (1 mL). From the resulting solution, 2 µL solution was then subjected to GC analysis. The GC analysis (Fig S-05) reveals the formation of mono-brominated product **2a** (t_R = 16.54 min) exclusively. No other regioisomeric product was observed. It is also important to mention that there was no peak related to the cyanomethylated imidazothiazole was observed.

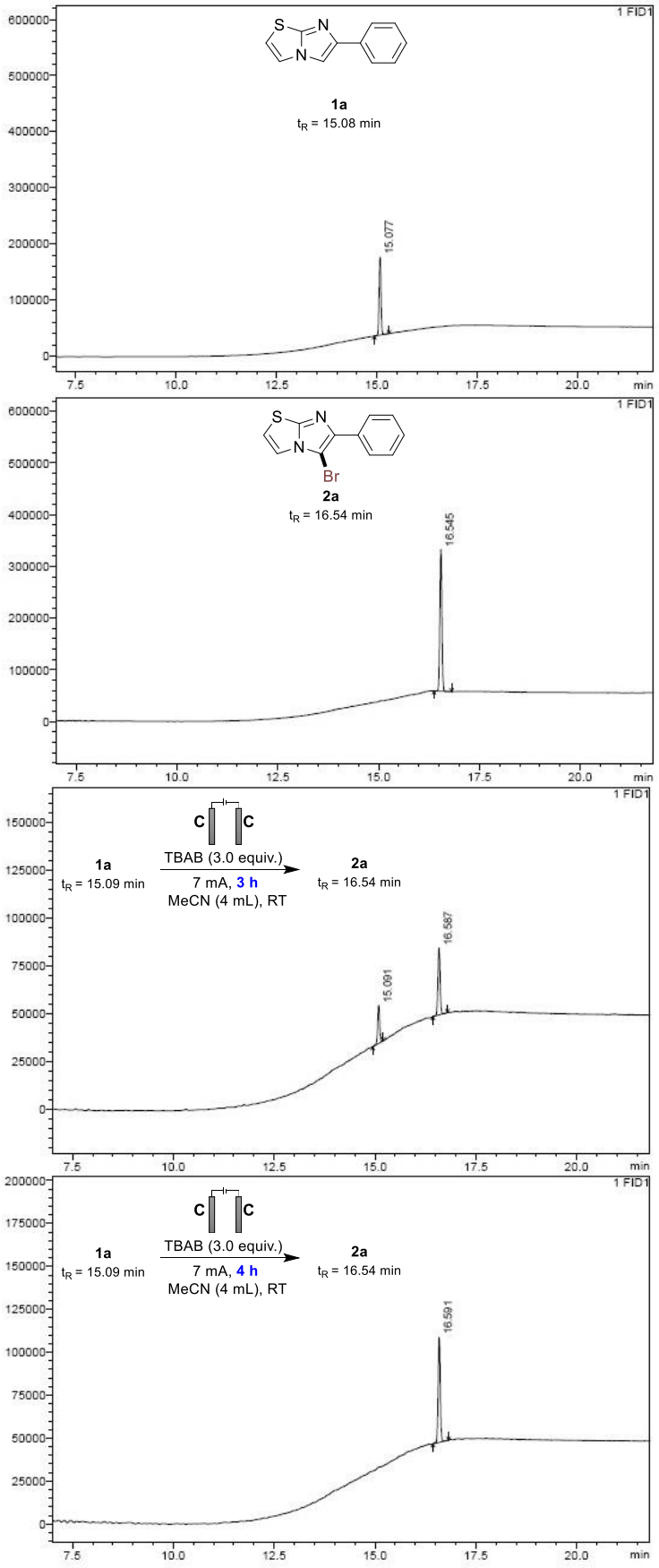


Figure S-05: GC analysis of crude reaction mixture at 3 h and 4 h.

We have also carried out the GC analysis of the crude reaction mixture for the following two reactions using the same sampling process mentioned above and got the desire single mono brominated regioisomer exclusively as mentioned in the Figure S-06 and Figure S-07:

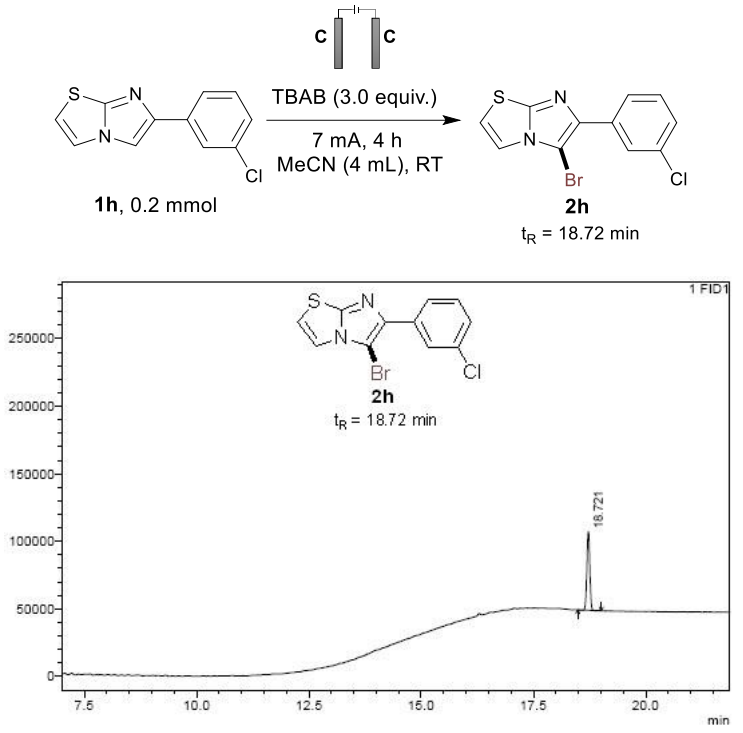


Figure S-06: GC analysis of crude reaction mixture after 4 h.

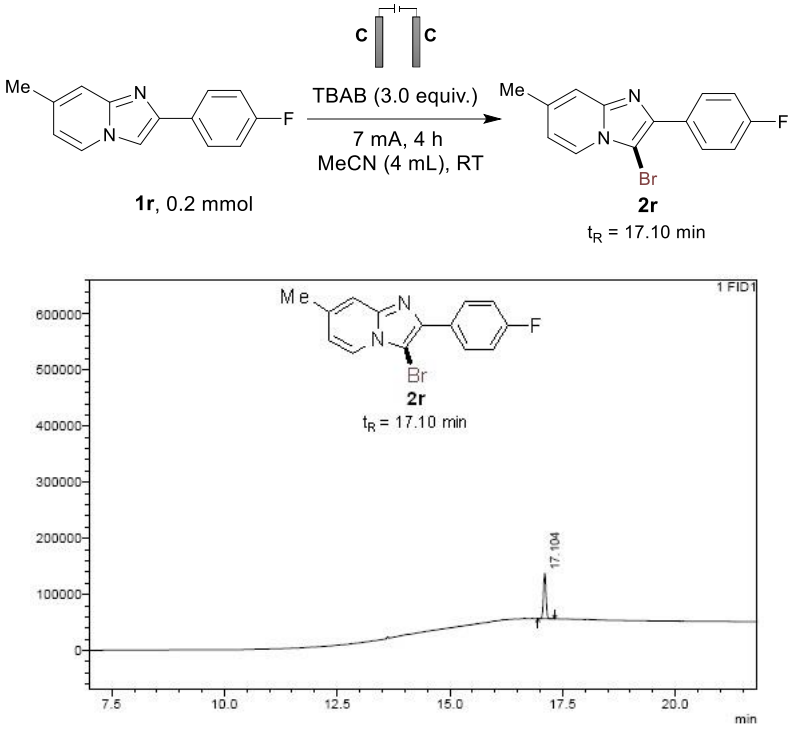


Figure S-07: GC analysis of crude reaction mixture after 4 h.

7. Reusability of the electrodes:

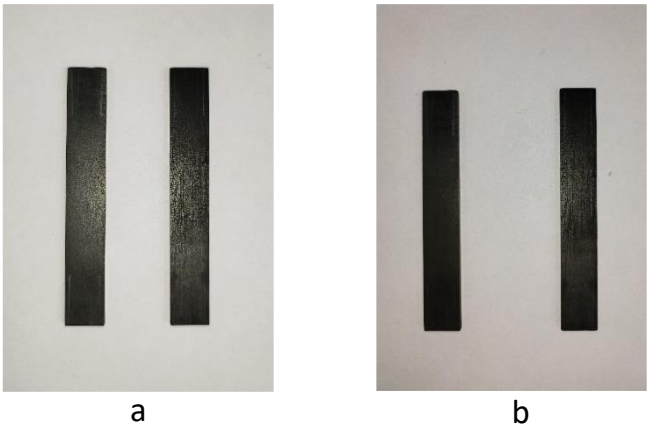


Figure S-08: (a) Electrodes before one pot scale up reaction, (b) Electrodes after one pot scale up reaction.

8. Controlled experiment using sodium thiosulfate:

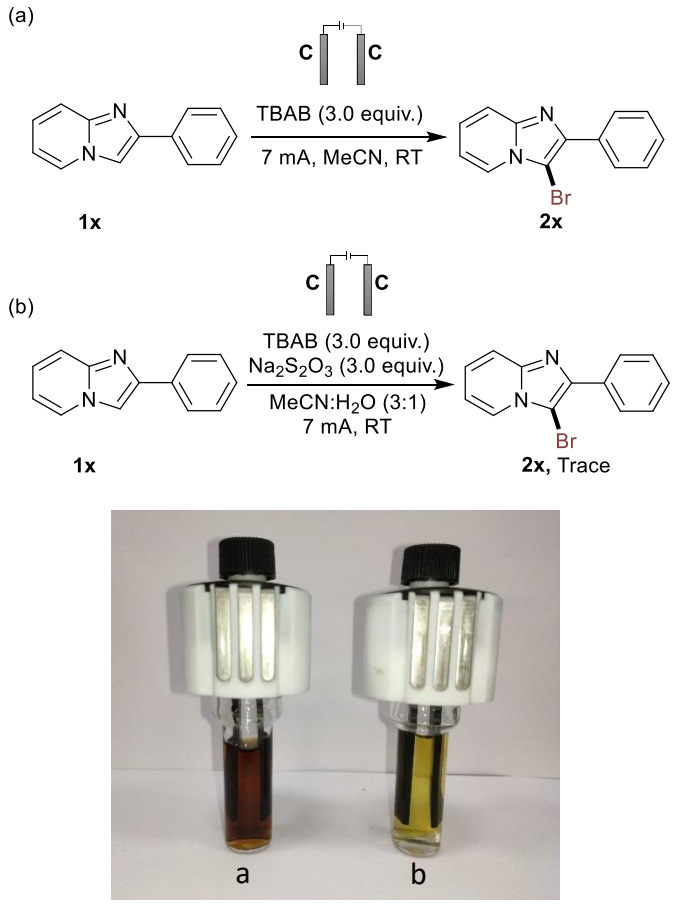


Figure S-09: (a) Reaction mixture after standard electrochemical bromination of **1x**, (b) Reaction mixture after standard electrochemical bromination of **1x** in presence of 3.0 equivalent sodium thiosulfate.

9. Cyclic voltammetry experiments:

All the cyclic voltammetry (CV) experiments were performed using Electrsyn (segment = 3, initial voltage = 0.0 V, final voltage = 2.0 V, sweep = 200 mV/s) in a vial of 5 mL capacity using 0.1 M $^{n}Bu_4NPF_6$ (in MeCN).

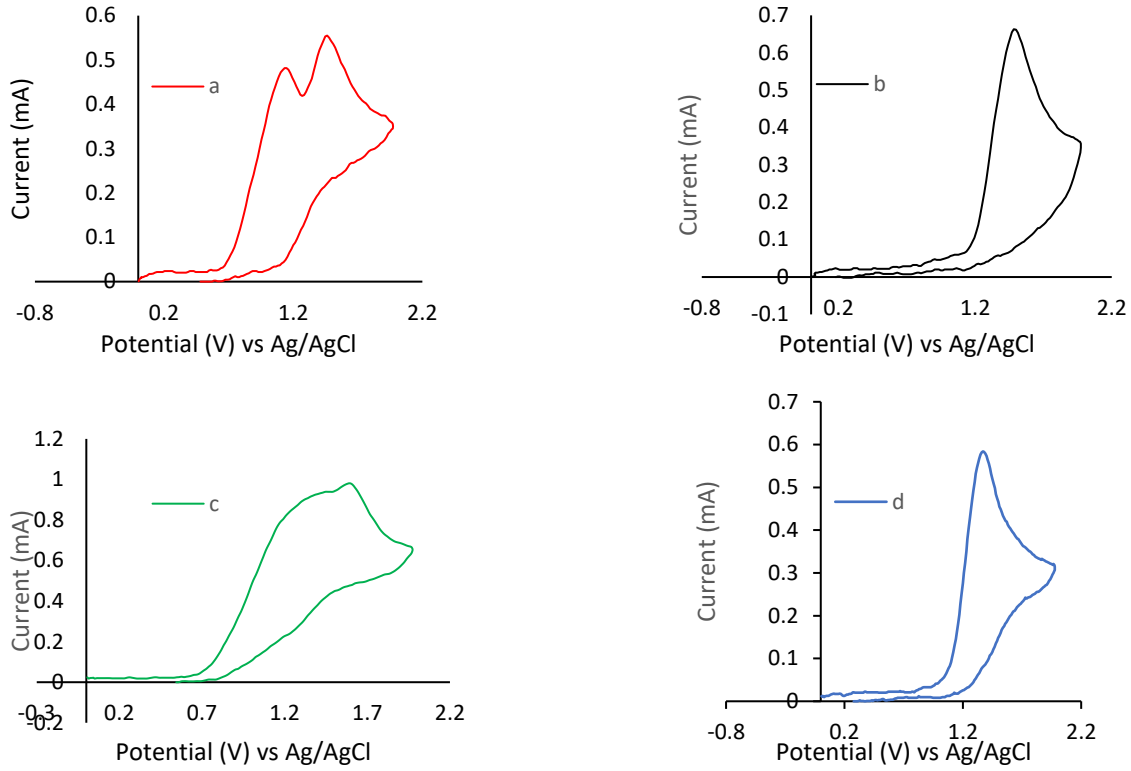


Figure S-10: (a) 0.02 M TBAB, (b) 0.02 M **1a**, (c) 0.02 M **1a** + 0.02 M TBAB, (d) 0.02 M **1x**

10. Characterization data of the synthesized compounds:

5-bromo-6-phenylimidazo[2,1-b]thiazole (2a):[2] white solid, 51.4 mg, 92% yield, ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.02 – 8.00 (m, 1H), 7.44 – 7.41s (m, 1H), 7.34 – 7.30 (m, 1H), 6.81 (d, *J* = 4.5 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 148.6, 143.7, 132.9, 128.3, 127.6, 126.7, 117.3, 112.8, 90.0.

5-bromo-6-(*p*-tolyl)imidazo[2,1-b]thiazole (2b):[3] yellow solid, 44.0 mg, 75% yield, ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.90 (d, *J* = 8.0 Hz, 2H), 7.39 (dd, *J* = 4.4, 2.7 Hz, 1H), 7.25 (d, *J* = 7.8 Hz, 2H), 6.88 (dd, *J* = 4.4, 2.7 Hz, 1H), 2.39 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 148.6, 144.0, 137.6, 130.2, 129.1, 126.8, 117.5, 112.7, 89.7, 21.3.

5-bromo-6-(4-methoxyphenyl)imidazo[2,1-b]thiazole (2c): off-white solid, 48.2 mg, 78% yield, mp = 125 ºC, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, *J* = 8.7 Hz, 2H), 7.37 (d, *J* = 4.5 Hz, 1H), 6.98 (d, *J* = 8.7 Hz, 2H), 6.86 (d, *J* = 4.4 Hz, 1H), 3.84 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.2, 148.5, 143.8, 128.2, 125.7, 117.4, 113.8, 112.6, 89.1, 55.2. ATR FT-IR υ (cm^{-1}): 652, 816, 950, 1126, 1158, 1306, 1464, 2884, 2929, 2969. HRMS (ESI^{+}) m/z: $[M+H]^{+}$ calcd for $C_{12}H_{10}BrN_2OS$, 308.9692; found, 308.9702.

5-bromo-6-(4-(trifluoromethyl)phenyl)imidazo[2,1-b]thiazole (2d): white solid, 48.6 mg, 70% yield, mp = 165 ºC, ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.15 (d, *J* = 8.1 Hz, 2H), 7.68 (d, *J* = 8.2 Hz, 2H), 7.42 (d, *J* = 4.5 Hz, 1H), 6.94 (d, *J* = 4.5 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 149.1, 142.4, 136.5,

129.3 (q, J_{C-F} = 32.8 Hz), 126.9, 125.4 (q, J_{C-F} = 3.8 Hz), 124.2 (q, J_{C-F} = 272.2 Hz), 117.5, 113.6, 91.1. ATR FT-IR υ (cm^{-1}): 512, 598, 650, 842, 1062, 1101, 1251, 1322, 1473, 1544, 1612, 3123, 3150. HRMS (ESI^+) m/z: $[M+H]^+$ calcd for $C_{12}H_7BrF_3N_2S$, 346.9460; found, 346.9468.

4-(5-bromoimidazo[2,1-b]thiazol-6-yl)benzonitrile (2e): white solid, 40.8 mg, 67% yield, mp = 206 ºC, ^1H NMR (500 MHz, $CDCl_3$) δ 8.17 (d, *J* = 8.6 Hz, 2H), 7.72 – 7.71 (m, 2H), 7.44 (d, *J* = 4.5 Hz, 1H), 6.98 (d, *J* = 4.5 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 149.4, 141.9, 137.5, 132.3, 127.0, 119.00, 117.5, 114.0, 110.9, 91.6. ATR FT-IR υ (cm^{-1}): 542, 660, 710, 813, 845, 968, 1124, 1245, 1319, 1397, 1467, 1533, 1603, 2219, 2853, 2923, 3109, 3145. HRMS (ESI^+) m/z: $[M+H]^+$ calcd for $C_{12}H_7BrN_3S$, 303.9539; found, 303.9546.

5-bromo-6-(4-fluorophenyl)imidazo[2,1-b]thiazole (2f):[1a] white solid, 47.5 mg, 80% yield, ^1H NMR (400 MHz, $CDCl_3$) δ 8.00 – 7.97 (m, 2H), 7.39 (d, *J* = 4.5 Hz, 1H), 7.12 (t, *J* = 8.8 Hz, 2H), 6.90 (d, *J* = 4.5 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 162.4 (d, J_{C-F} = 247.0 Hz), 148.7, 143.1, 129.2 (d, J_{C-F} = 3.8 Hz), 128.6 (d, J_{C-F} = 7.6 Hz), 117.5, 115.3 (d, J_{C-F} = 21.4 Hz), 113.0, 89.8.

5-bromo-6-(4-chlorophenyl)imidazo[2,1-b]thiazole (2g):[3] white solid, 52.0 mg, 83% yield, ^1H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, *J* = 8.6 Hz, 2H), 7.41 – 7.39 (m, 3H), 6.90 (d, *J* = 4.5 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 148.9, 142.8, 133.5, 131.5, 128.6, 128.0, 117.4, 113.2, 90.2.

5-bromo-6-(3-chlorophenyl)imidazo[2,1-b]thiazole (2h): white solid, 53.3 mg, 85% yield, mp = 126 ºC, ^1H NMR (500 MHz, $CDCl_3$) δ 8.03 (t, *J* = 1.8 Hz, 1H), 7.92 – 7.90 (m, 1H), 7.38 (d, *J* = 4.5 Hz, 1H), 7.35 (t, *J* = 7.9 Hz, 1H), 7.29 (ddd, *J* = 8.0, 2.0, 1.1 Hz, 1H), 6.90 (d, *J* = 4.5 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 148.9, 142.3, 134.8, 134.4, 129.6, 127.6, 126.7, 124.7, 117.4, 113.3, 90.5. ATR FT-IR υ (cm^{-1}): 652, 689, 786, 817, 852, 897, 1078, 1132, 1462, 1593, 2922, 3125. HRMS (ESI^+) m/z: $[M+H]^+$ calcd for $C_{11}H_7BrClN_2S$, 312.9196; found, 312.9211.

5-bromo-6-(4-bromophenyl)imidazo[2,1-b]thiazole (2i): yellowish solid, 63.0 mg, 88% yield, mp = 136 ºC, ^1H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, *J* = 8.5 Hz, 2H), 7.55 (d, *J* = 8.5 Hz, 2H), 7.39 (d, *J* = 4.5 Hz, 1H), 6.91 (d, *J* = 4.5 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 148.9, 142.8, 132.0, 131.5, 128.3, 121.8, 117.5, 113.2, 90.2. ATR FT-IR υ (cm^{-1}): 661, 709, 823, 965, 1006, 1099, 1245, 1324, 1393, 1462, 1514, 2854, 2922, 3101, 3127. HRMS (ESI^+) m/z: $[M+H]^+$ calcd for $C_{11}H_7Br_2N_2S$, 358.8691; found, 358.8681.

5-bromo-6-(4-chlorophenyl)-2-methylimidazo[2,1-b]thiazole (2j): off-white solid, 34.0 mg, 52% yield, mp = 160 ºC, ^1H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, *J* = 8.6 Hz, 2H), 7.39 (d, *J* = 8.6 Hz, 2H), 7.12 (d, *J* = 1.3 Hz, 1H), 2.45 (d, *J* = 1.3 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 148.3, 141.5, 133.3, 131.7, 128.5, 127.9, 127.3, 114.0, 89.8, 14.5. ATR FT-IR υ (cm^{-1}): 679, 714, 747, 821, 965, 1090, 1339, 1464, 1515, 2922, 3741. HRMS (ESI^+) m/z: $[M+H]^+$ calcd for $C_{12}H_9BrClN_2S$, 326.9353; found, 326.9376.

3-bromo-2-(4-chlorophenyl)imidazo[1,2-a]pyridine (2k):[4] white solid, 46.1 mg, 75% yield, ^1H NMR (500 MHz, $CDCl_3$) δ 8.16 (d, *J* = 6.7 Hz, 1H), 8.08 (d, *J* = 8.2 Hz, 2H), 7.63 (d, *J* = 8.9 Hz, 1H), 7.45 (d, *J* = 8.2 Hz, 2H), 7.27 (t, *J* = 7.5 Hz, 1H), 6.94 (t, *J* = 6.5 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 145.5, 141.5, 134.2, 131.4, 129.0, 128.7, 125.3, 124.0, 117.6, 113.2, 91.7.

3-bromo-2-(4-bromophenyl)imidazo[1,2-a]pyridine (2l):[5] white solid, 56.32 mg, 80% yield, ^1H NMR (500 MHz, $CDCl_3$) δ 8.16 (d, *J* = 6.8 Hz, 1H), 8.02 (d, *J* = 8.4 Hz, 2H), 7.63 – 7.59 (m, 3H), 7.27 (t, *J* = 7.6 Hz, 1H), 6.94 (t, *J* = 6.6 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 145.5, 141.5, 131.8, 131.6, 129.3, 125.3, 124.0, 122.5, 117.6, 113.2, 91.8.

3-bromo-2-(4-fluorophenyl)imidazo[1,2-a]pyridine (2m):[4] white solid, 42.5 mg, 73% yield, ^1H NMR (500 MHz, $CDCl_3$) δ 8.17 (d, *J* = 6.9 Hz, 1H), 8.13 – 8.10 (m, 2H), 7.63 (d, *J* = 9.1 Hz, 1H), 7.28 – 7.25 (m, 1H), 7.17 (t, *J* = 8.7 Hz, 2H), 6.94 (dd, *J* = 9.9, 3.7 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ

162.8 (d, J_{C-F} = 249.5 Hz), 145.4, 141.8, 129.6 (d, J_{C-F} = 7.6 Hz), 129.0 (d, J_{C-F} = 3.8 Hz), 125.2, 123.9, 117.6, 115.4 (d, J_{C-F} = 21.4 Hz), 113.1, 91.4.

3-bromo-7-methyl-2-(4-(trifluoromethyl)phenyl)imidazo[1,2-a]pyridine (2n): off-white solid, 54.7 mg, 77% yield, mp = 111 ºC, ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.24 (d, *J* = 8.1 Hz, 2H), 8.02 (d, *J* = 7.0 Hz, 1H), 7.71 (d, *J* = 8.2 Hz, 2H), 7.38 (s, 1H), 6.76 (dd, *J* = 7.0, 1.5 Hz, 1H), 2.43 (d, *J* = 0.7 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 145.9, 140.7, 136.7, 136.6, 129.8 (q, J_{C-F} = 32.8 Hz), 127.80, 125.3 (q, J_{C-F} = 3.8 Hz), 124.5 (q, J_{C-F} = 289 Hz), 123.13, 116.12, 116.00, 91.56, 21.29. ATR FT-IR υ (cm^{-1}): 600, 650, 690, 843, 1063, 1106, 1158, 1321, 1615, 2925. HRMS (ESI^+) m/z: $[M+H]^+$ calcd for $C_{15}H_{11}BrF_3N_2$, 355.0052; found, 355.0054.

4-(3-bromo-7-methylimidazo[1,2-a]pyridin-2-yl)benzonitrile (2o): white solid, 37.4 mg, 60% yield, mp = 192 ºC, ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.27 (dd, *J* = 8.3, 1.5 Hz, 2H), 8.06 (d, *J* = 7.0 Hz, 1H), 7.74 (dd, *J* = 8.4, 1.8 Hz, 2H), 7.39 (s, 1H), 6.81 (d, *J* = 7.0 Hz, 1H), 2.45 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 146.0, 140.1, 137.6, 137.1, 132.2, 128.0, 123.2, 119.0, 116.3, 116.2, 111.3, 92.1, 21.4. ATR FT-IR υ (cm^{-1}): 599, 669, 767, 845, 1020, 1091, 1349, 1469, 1534, 1644, 2218, 2853, 2919, 3060, 3741. HRMS (ESI^+) m/z: $[M+H]^+$ calcd for $C_{15}H_{11}BrN_3$, 312.0131; found, 312.0136.

3-bromo-2-(4-methoxyphenyl)-7-methylimidazo[1,2-a]pyridine (2p):[6] white solid, 44.4 mg, 76% yield, ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.07 – 8.04 (m, 2H), 8.02 (d, *J* = 7.0 Hz, 1H), 7.37 (s, 1H), 7.01 (d, *J* = 8.8 Hz, 2H), 6.74 (dd, *J* = 7.0, 1.2 Hz, 1H), 3.86 (s, 3H), 2.43 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.6, 145.7, 142.2, 135.9, 129.1, 125.6, 123.0, 115.8, 115.4, 113.8, 89.9, 55.3, 21.3.

3-bromo-2-(4-chlorophenyl)-7-methylimidazo[1,2-a]pyridine (2q): white solid, 47.0 mg, 73% yield, mp = 147 ºC, ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.06 (d, *J* = 8.5 Hz, 2H), 8.02 (d, *J* = 7.0 Hz, 1H), 7.43 (d, *J* = 8.5 Hz, 2H), 7.37 (s, 1H), 6.75 (dd, *J* = 7.0, 1.0 Hz, 1H), 2.43 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 145.8, 141.2, 136.4, 134.0, 131.5, 128.9, 128.6, 123.1, 116.0, 115.8, 90.8, 21.3. ATR FT-IR υ (cm^{-1}): 598, 664, 719, 771, 827, 1015, 1091, 1159, 1346, 1642, 1727, 2853, 2918, 3062, 3740. HRMS (ESI^+) m/z: $[M+H]^+$ calcd for $C_{14}H_{11}BrClN_2$, 320.9789; found, 320.9760.

3-bromo-2-(4-fluorophenyl)-7-methylimidazo[1,2-a]pyridine (2r): white solid, 42.7 mg, 70% yield, mp = 110 ºC, ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.10 – 8.07 (m, 2H), 8.02 (d, *J* = 7.0 Hz, 1H), 7.37 (s, 1H), 7.17 – 7.14 (m, 2H), 6.75 (dd, *J* = 7.0, 1.3 Hz, 1H), 2.42 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 162.7 (d, J_{C-F} = 248.2 Hz), 145.8, 141.5, 136.3, 129.5 (d, J_{C-F} = 7.6 Hz), 129.2 (d, J_{C-F} = 3.8 Hz), 123.1, 115.9, 115.7, 115.5 (d, J_{C-F} = 21.4 Hz), 90.5, 21.3. ATR FT-IR υ (cm^{-1}): 605, 662, 764, 826, 988, 1018, 1151, 1216, 1479, 2852, 2922, 3037, 3745. HRMS (ESI^+) m/z: $[M+H]^+$ calcd for $C_{14}H_{11}BrFN_2$, 305.0084; found, 305.0083.

3-bromo-7-chloro-2-(4-fluorophenyl)imidazo[1,2-a]pyridine (2s): white solid, 46.9 mg, 72% yield, mp = 143 ºC, ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.09 – 8.06 (m, 3H), 7.61 (d, *J* = 1.4 Hz, 1H), 7.18 – 7.15 (m, 2H), 6.91 (dd, *J* = 7.3, 2.0 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 162.9 (d, J_{C-F} = 249.5 Hz), 145.0, 142.7, 131.8, 129.6 (d, J_{C-F} = 7.6 Hz), 128.6 (d, J_{C-F} = 3.8 Hz), 124.2, 116.3, 115.5 (d, J_{C-F} = 21.4 Hz), 114.7, 91.6. ATR FT-IR υ (cm^{-1}): 597, 654, 730, 770, 800, 830, 932, 985, 1066, 1143, 1216, 1348, 1478, 1625, 3033, 3103. HRMS (ESI^+) m/z: $[M+H]^+$ calcd for $C_{13}H_8BrClFN_2$, 324.9538; found, 324.9540.

3,6-dibromo-2-(4-chlorophenyl)imidazo[1,2-a]pyridine (2t): white solid, 50.2 mg, 65 % yield, mp = 186 ºC, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32 (d, *J* = 0.7 Hz, 1H), 8.06 (d, *J* = 8.5 Hz, 2H), 7.52 (d, *J* = 9.5 Hz, 1H), 7.45 (d, *J* = 8.5 Hz, 2H), 7.33 (dd, *J* = 9.5, 1.7 Hz, 1H)**.** ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.9, 142.4, 134.6, 130.9, 129.0, 128.9, 128.8, 124.2, 118.2, 108.1, 92.0. ATR FT-IR υ (cm^{-1}): 722, 793, 1080, 1322, 1456, 1517, 2922, 3071. HRMS (ESI^+) m/z: $[M+H]^+$ calcd for $C_{13}H_8Br_2ClN_2$, 386.8717; found, 386.8718.

5-bromo-6-(tert-butyl)imidazo[2,1-b]thiazole (2u):[7a] white solid, 41.4 mg, 80% yield, ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32 (d, *J* = 4.5 Hz, 1H), 6.83 (d, *J* = 4.5 Hz, 1H), 1.44 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 153.0, 146.5, 117.3, 112.0, 88.2, 33.4, 29.89.

5-bromo-6-methylimidazo[2,1-b]thiazole (2v):[7a] off white solid, 32.1 mg, 74% yield, ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29 (d, *J* = 4.5 Hz, 1H), 6.83 (d, *J* = 4.5 Hz, 1H), 2.32 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 147.9, 142.5, 117.3, 111.9, 91.1, 13.6

3-bromo-2-(tert-butyl)imidazo[1,2-a]pyridine (2w):[8a] brown oil, 39.5 mg, 78% yield, ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.12 (d, *J* = 6.9 Hz, 1H), 7.59 (d, *J* = 9.0 Hz, 1H), 7.20-7.17 (m, 1H), 6.88-6.86 (m, 1H), 1.53 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 152.0, 143.8, 124.0, 123.2, 117.3, 112.5, 90.0, 33.1, 29.7.

3-bromo-2-phenylimidazo[1,2-a]pyridine (2x):[4] white solid, 35.5 mg, 65% yield, ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.14 – 8.12 (m, 2H), 7.98 (d, *J* = 6.9 Hz, 1H), 7.55 (d, *J* = 9.0 Hz, 1H), 7.45 (t, *J* = 7.7 Hz, 2H), 7.34 (t, *J* = 7.4 Hz, 1H), 7.12 – 7.09 (m, 1H), 6.74 (dd, *J* = 10.0, 3.6 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 145.0, 142.2, 132.6, 128.1, 127.9, 127.5, 124.7, 123.5, 117.1, 112.6, 91.3.

4-(3-bromoimidazo[1,2-a]pyridin-2-yl)benzonitrile (2y):[7b] white solid, 29.8 mg, 50% yield, ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.30 – 8.28 (m, 2H), 8.20 (dt, *J* = 6.9, 1.0 Hz, 1H), 7.77 – 7.75 (m, 2H), 7.65 (dd, *J* = 9.1, 0.9 Hz, 1H), 7.32 (ddd, *J* = 9.1, 6.8, 1.2 Hz, 1H), 6.99 (td, *J* = 6.8, 1.0 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 145.7, 140.5, 137.4, 132.2, 128.1, 125.9, 124.1, 118.9, 117.9, 113.6, 111.5, 92.9.

3-bromo-2-(4-(trifluoromethyl)phenyl)imidazo[1,2-a]pyridine (2z):[4] white solid, 38.2 mg, 56% yield, ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.27 (d, *J* = 8.1 Hz, 2H), 8.19 (d, *J* = 6.9 Hz, 1H), 7.73 (d, *J* = 8.2 Hz, 2H), 7.65 (d, *J* = 9.1 Hz, 1H), 7.30 (ddd, *J* = 9.0, 6.8, 1.1 Hz, 1H), 6.97 (td, *J* = 6.8, 0.8 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 145.6, 141.1, 136.4, 130.0 (q, J_{C-F} = 32.8 Hz), 128.0, 125.6, 125.4 (q, J_{C-F} = 3.8 Hz), 124.2 (q, J_{C-F} = 272.2 Hz), 124.1, 117.8, 113.4, 92.5.

3-bromo-7-methyl-2-phenylimidazo[1,2-a]pyridine (2aa):[8b] white solid, 47.1 mg, 62% yield, ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.12 – 8.11 (m, 2H), 8.03 (d, *J* = 7.0 Hz, 1H), 7.49 – 7.46 (m, 2H), 7.39 – 7.36 (m, 2H), 6.74 (dd, *J* = 7.0, 1.4 Hz, 1H), 2.43 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 145.8, 142.3, 136.1, 133.0, 128.4, 128.1, 127.8, 123.1, 116.0, 115.1, 90.8, 21.3.

3-bromo-7-methyl-2-(*p*-tolyl)imidazo[1,2-a]pyridine (2ab):[6] white solid, 40.4 mg, 67% yield, ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.01 (d, *J* = 8.2 Hz, 2H), 7.92 (d, *J* = 0.9, 1H), 7.52 (d, *J* = 9.1 Hz, 1H), 7.28 (d, *J* = 7.9 Hz, 2H), 7.08 (dd, *J* = 9.1, 1.6 Hz, 1H), 2.40 (s, 3H), 2.37 (d, *J* = 0.9 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 144.4, 142.4, 138.0, 130.1, 129.1, 128.1, 127.6, 122.7, 121.6, 116.8, 90.9, 21.3, 18.3.

5-chloro-6-phenylimidazo[2,1-b]thiazole (3a):[1] white solid, 36.6 mg, 77% yield, ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.02 – 7.99 (m, 2H), 7.46 – 7.43 (m, 2H), 7.39 (d, *J* = 4.5 Hz, 1H), 7.35 – 7.31 (m, 1H), 6.89 (d, *J* = 4.5 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 147.3, 141.0, 132.8, 128.5, 127.6, 126.5, 116.6, 113.2, 106.1.

5-chloro-6-(4-fluorophenyl)imidazo[2,1-b]thiazole (3b): white solid, 39.9 mg, 79% yield, mp = 112 ºC, ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.99 – 7.96 (m, 2H), 7.38 (d, *J* = 4.4 Hz, 1H), 7.14 – 7.11 (m, 2H), 6.90 (d, *J* = 4.4 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 162.3 (d, J_{C-F} = 249.2 Hz), 147.3, 140.2, 128.9 (d, J_{C-F} = 2.5 Hz), 128.3 (d, J_{C-F} = 7.6 Hz), 116.6, 115. (d, J_{C-F} = 21.4 Hz), 113.3, 105.8. ATR FT-IR υ (cm^{-1}): 600, 661, 710, 773, 826, 980, 1088, 1219, 1328, 1464, 1535, 1608, 2922, 2957, 3046, 3100, 3138. HRMS (ESI^+) m/z: $[M+H]^+$ calcd for $C_{11}H_7ClFN_2S$, 252.9997; found, 252.9996.

3-chloro-2-phenylimidazo[1,2-a]pyridine (3c):[9] yellow solid, 36.6 mg, 80% yield, ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.15– 8.13 (m, 2H), 8.09 (dt, *J* = 6.9, 1.1 Hz, 1H), 7.63 (dt, *J* = 9.1, 0.9 Hz, 1H), 7.50 – 7.47 (m, 2H), 7.40 – 7.36 (m, 1H), 7.23 (ddd, *J* = 9.0, 6.8, 1.2 Hz, 1H), 6.91 (td, *J* = 6.8, 1.0 Hz, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 143.7, 139.8, 132.5, 128.5, 128.2, 127.4, 124.8, 122.6, 117.6, 112.8, 105.6.

3-chloro-7-methyl-2-(4-(trifluoromethyl)phenyl)imidazo[1,2-a]pyridine (3d): white solid, 46.0 mg, 74% yield, mp = 102 ºC, ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.24 (d, *J* = 8.2 Hz, 2H), 7.95 (d, *J* = 7.0 Hz, 1H), 7.70 (d, *J* = 8.3 Hz, 2H), 7.37 (s, 1H), 6.76 (dd, *J* = 7.0, 1.3 Hz, 1H), 2.42 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 144.2, 137.8, 136.5, 136.2, 129.7 (q, J_{C-F} =32.8 Hz), 128.7, 127.8, 127.4, 125.35 (q, J_{C-F} = 3.8 Hz), 124.4 (q, J_{C-F} = 272.2 Hz), 121.9, 116.1, 115.9, 105.8, 21.3. ATR FT-IR υ (cm^{-1}): 685, 767, 840, 1008, 1064, 1099, 1322, 1164, 1322, 1616, 2923, 2962, 3036. HRMS (ESI^+) m/z: $[M+H]^+$ calcd for $C_{15}H_{11}ClF_3N_2$, 311.0557; found, 311.0556.

2-(tert-butyl)-3-chloroimidazo[1,2-a]pyridine (3e):[8a] yellow oil, 27.5 mg, 66% yield, ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.04 (d, *J* = 6.9 Hz, 1H), 7.58 (d, *J* = 9.1 Hz, 1H), 7.18 – 7.15 (m, 1H), 6.88-6.86 (m, 1H), 1.50 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 149.5, 142.2, 123.7, 122.0, 117.3, 112.4, 104.4, 32.9, 29.5.

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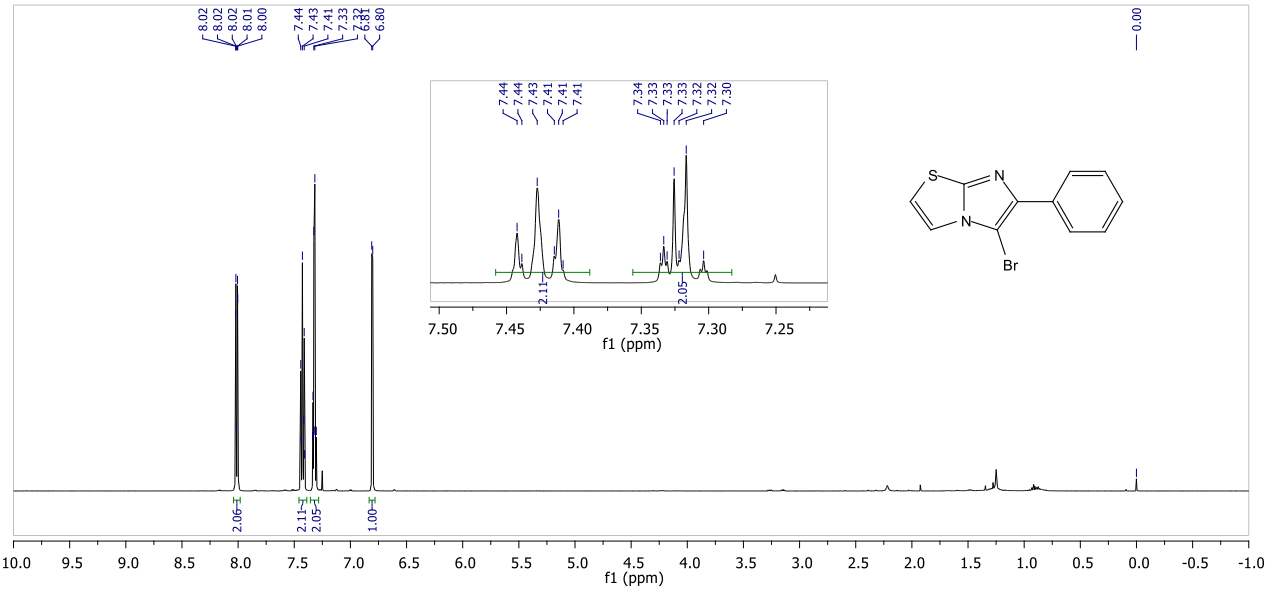
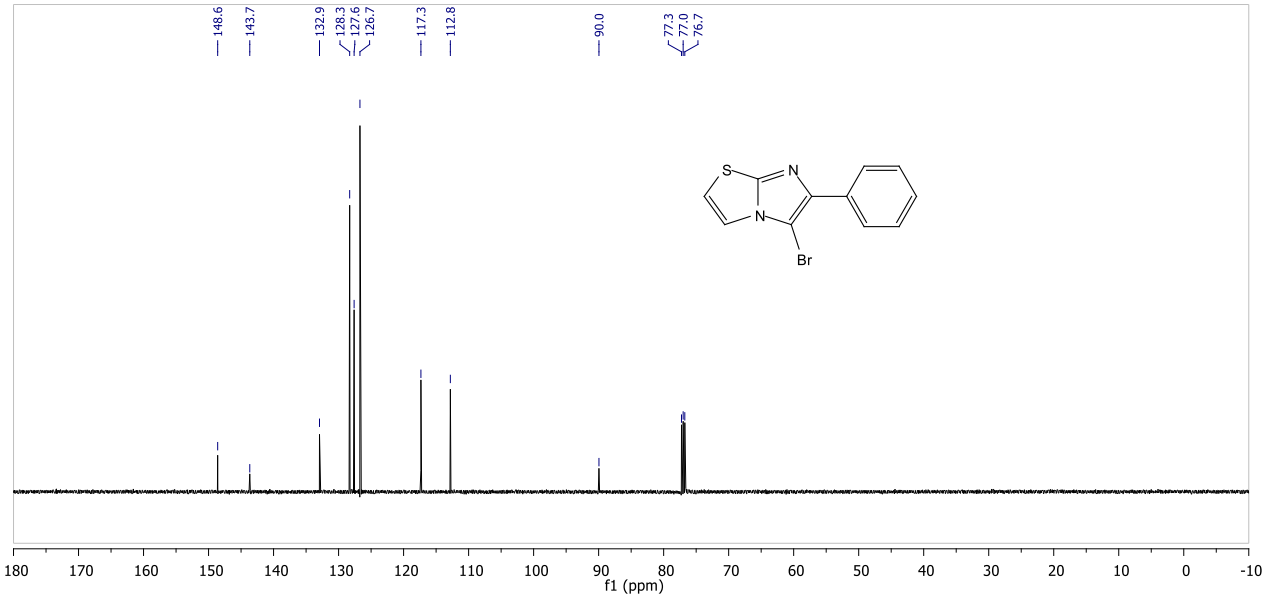
12. ^{1}H and ^{13}CNMR Spectra:

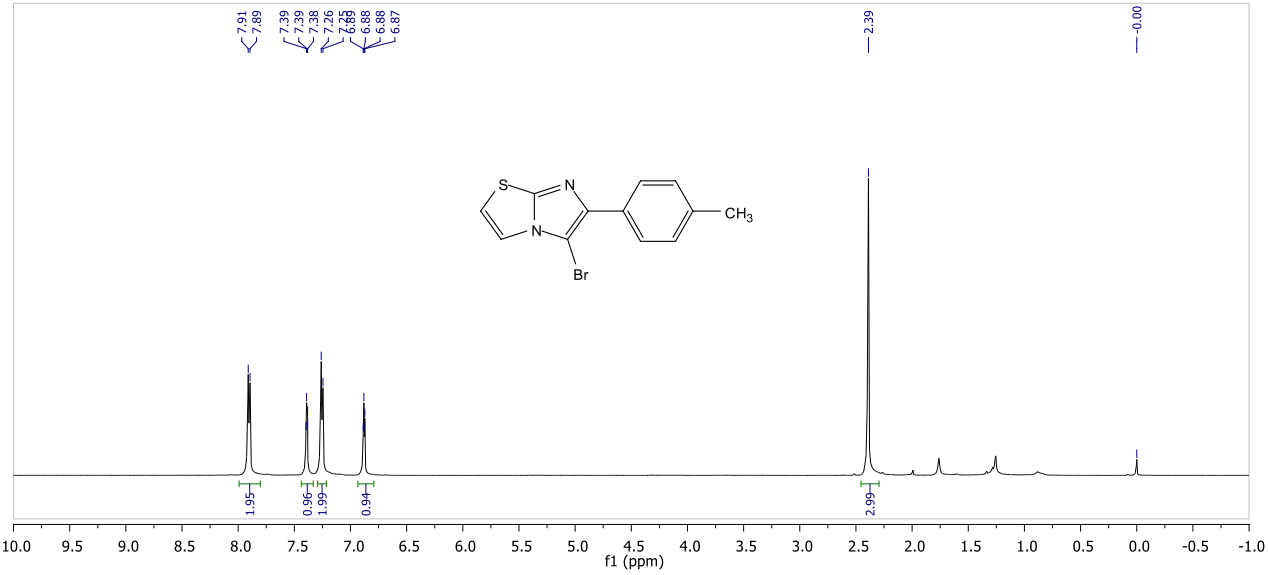
^{1}H NMR (500 MHz, $CDCl_3$) of compound **2a**



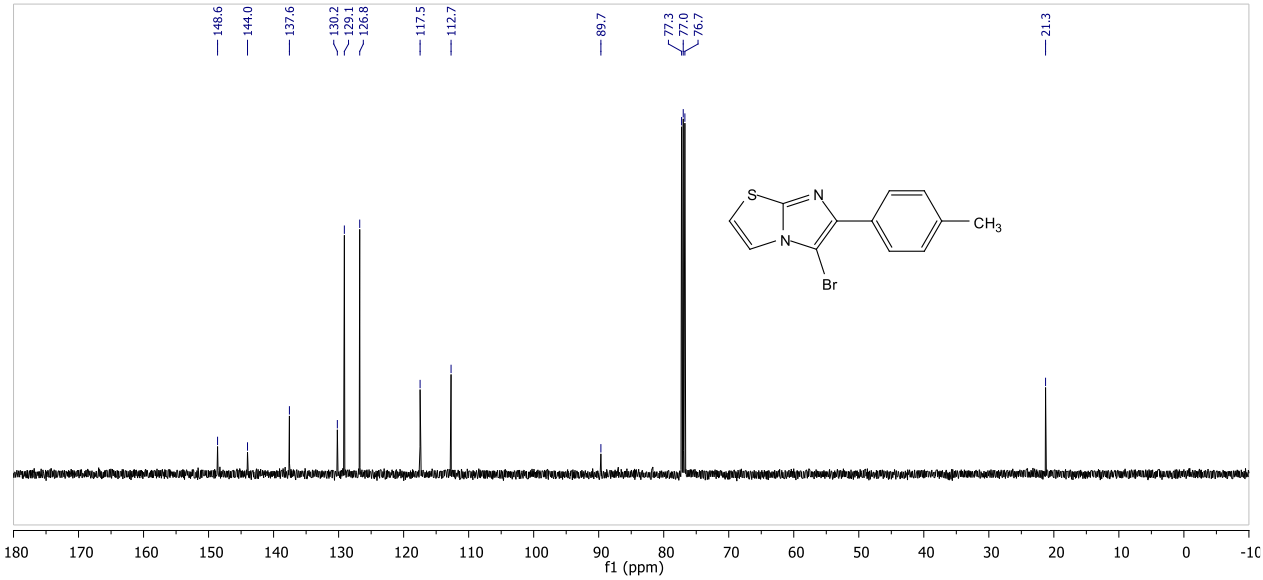
^{13}C NMR (126 MHz, $CDCl_3$) of compound **2a**



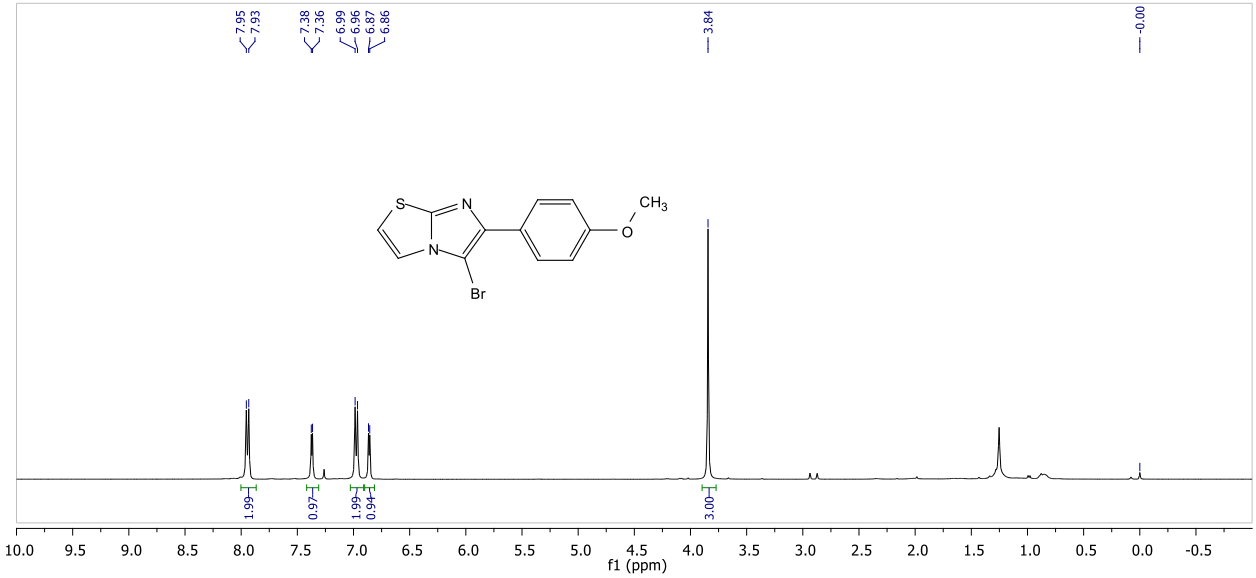
^{1}H NMR (500 MHz, $CDCl_3$) of compound **2b**



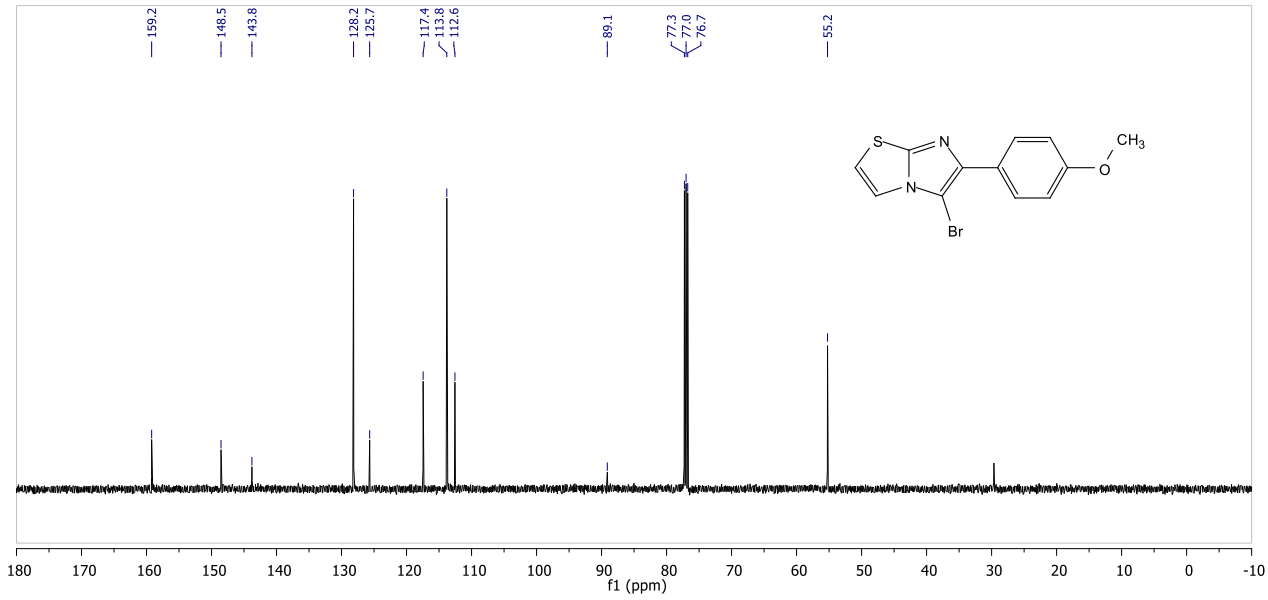
^{13}C NMR (126 MHz, $CDCl_3$) of compound **2b**



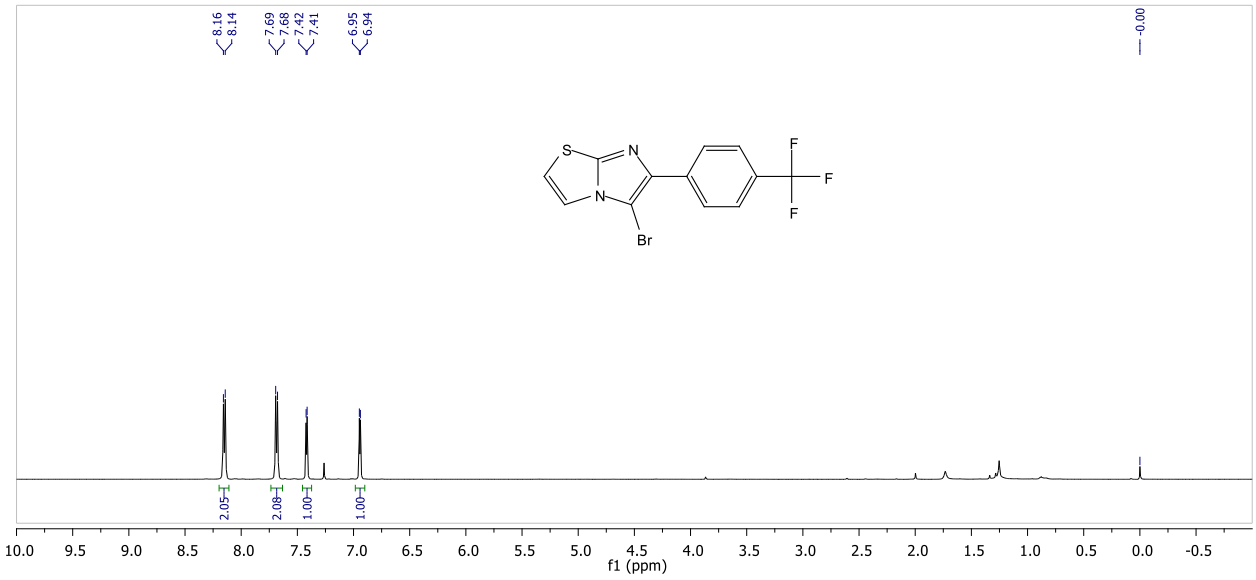
^{1}H NMR (400 MHz, $CDCl_3$) of compound **2c**



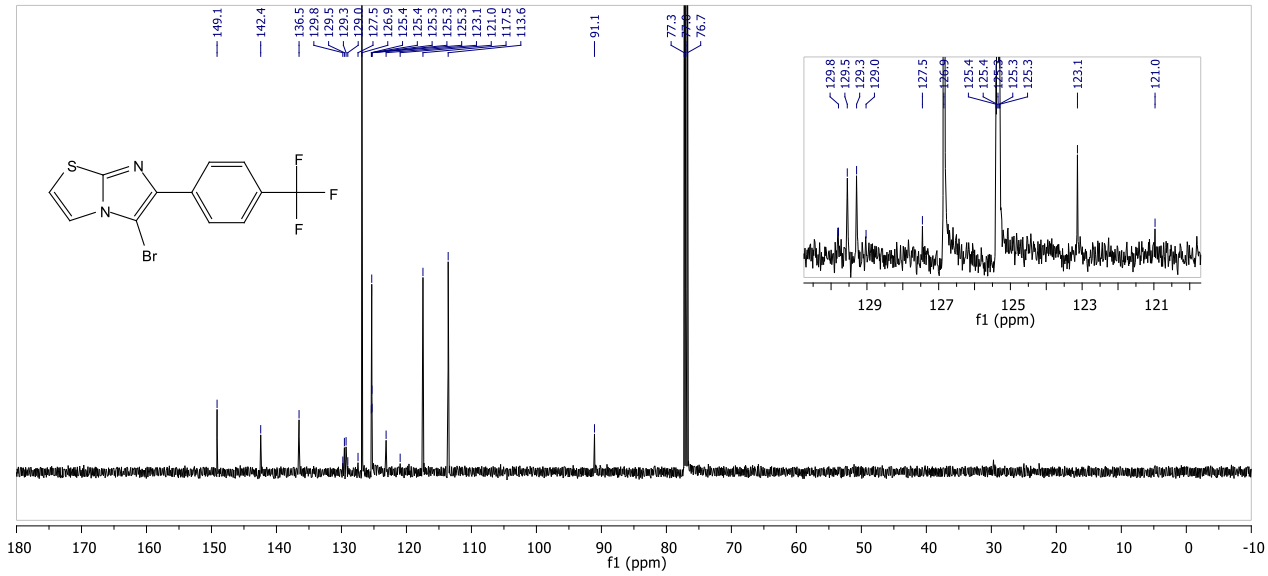
^{13}C NMR (126 MHz, $CDCl_3$) of compound **2c**



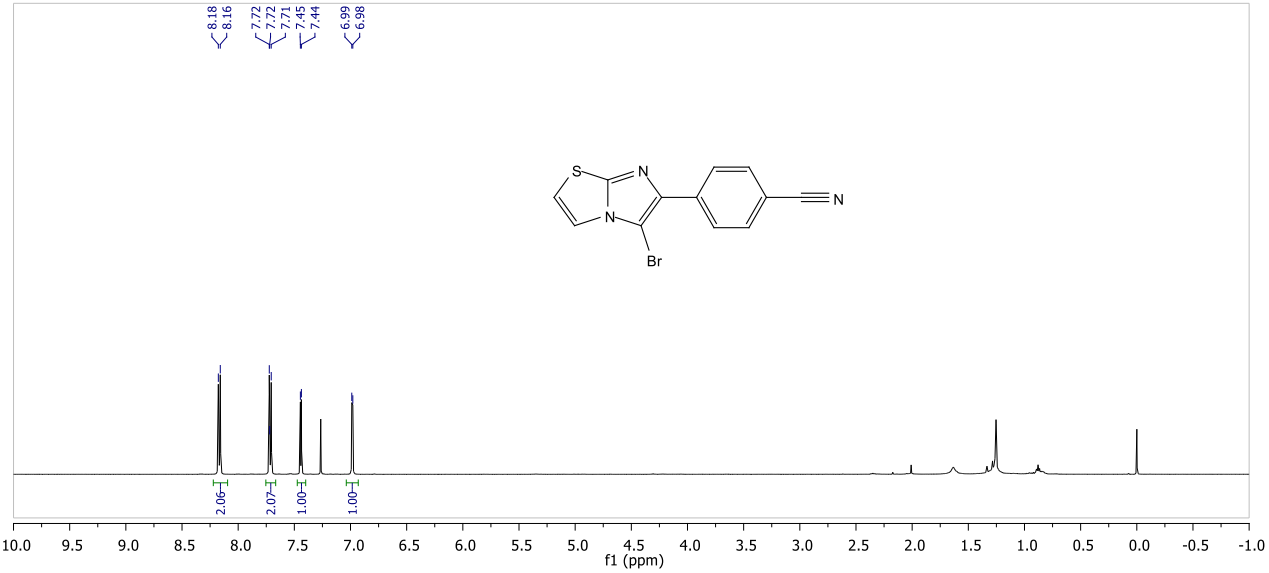
^{1}H NMR (500 MHz, $CDCl_3$) of compound **2d**



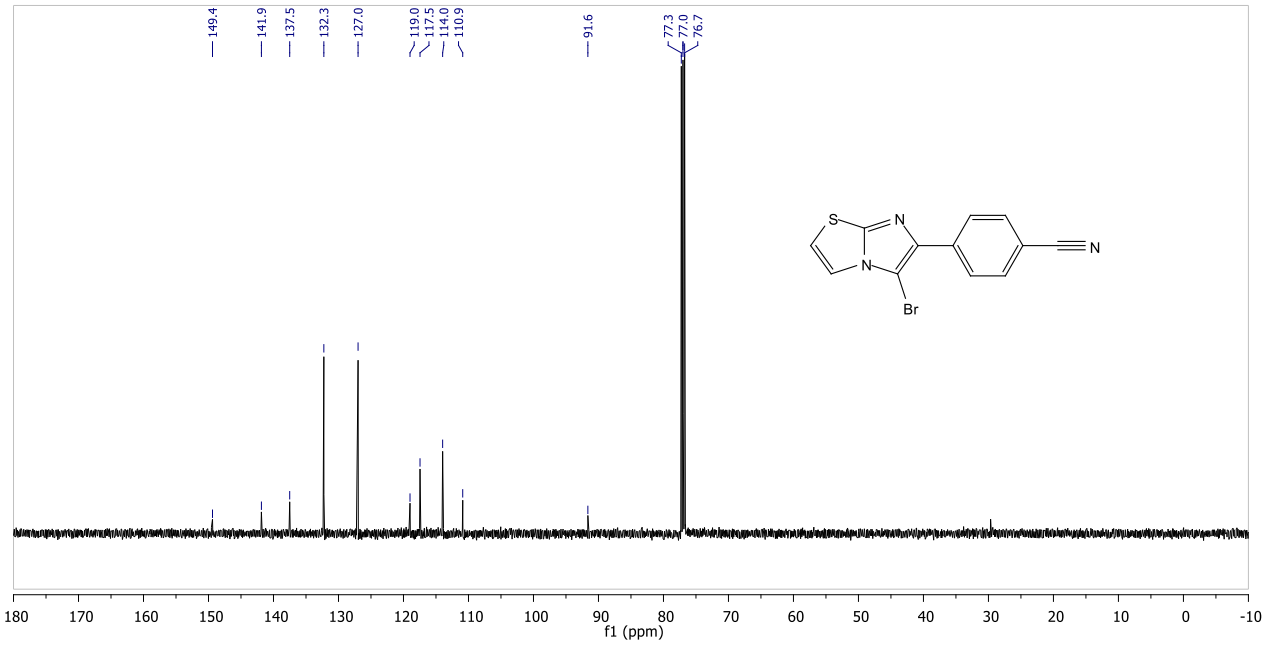
^{13}C NMR (126 MHz, $CDCl_3$) of compound **2d**



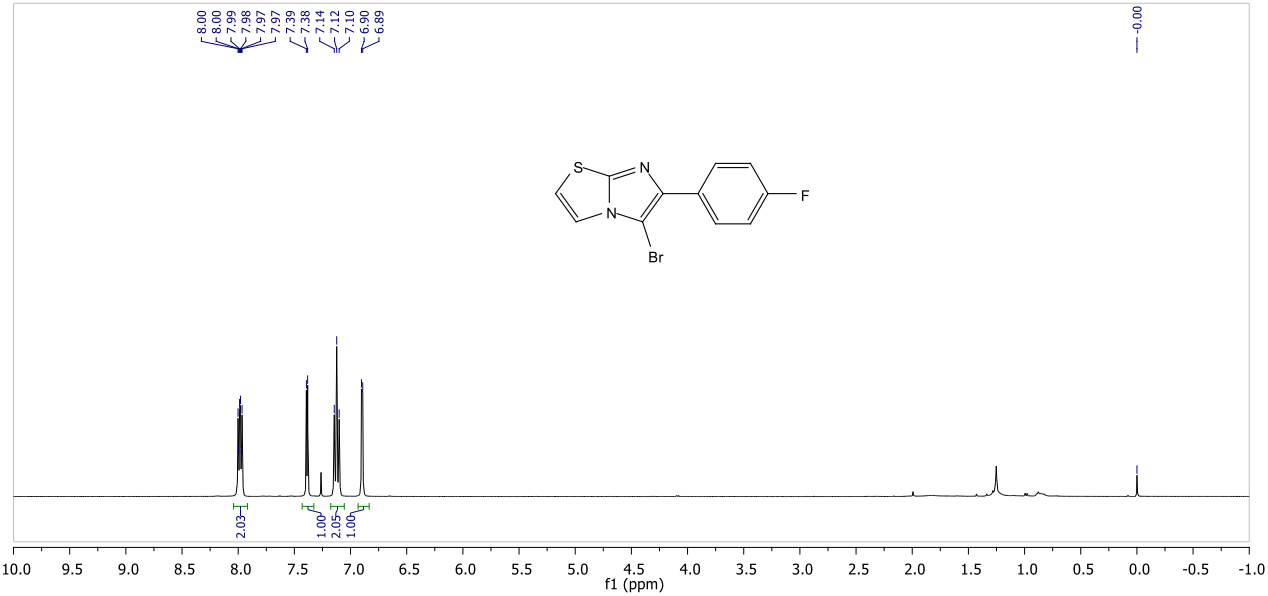
^{1}H NMR (500 MHz, $CDCl_3$) of compound **2e**



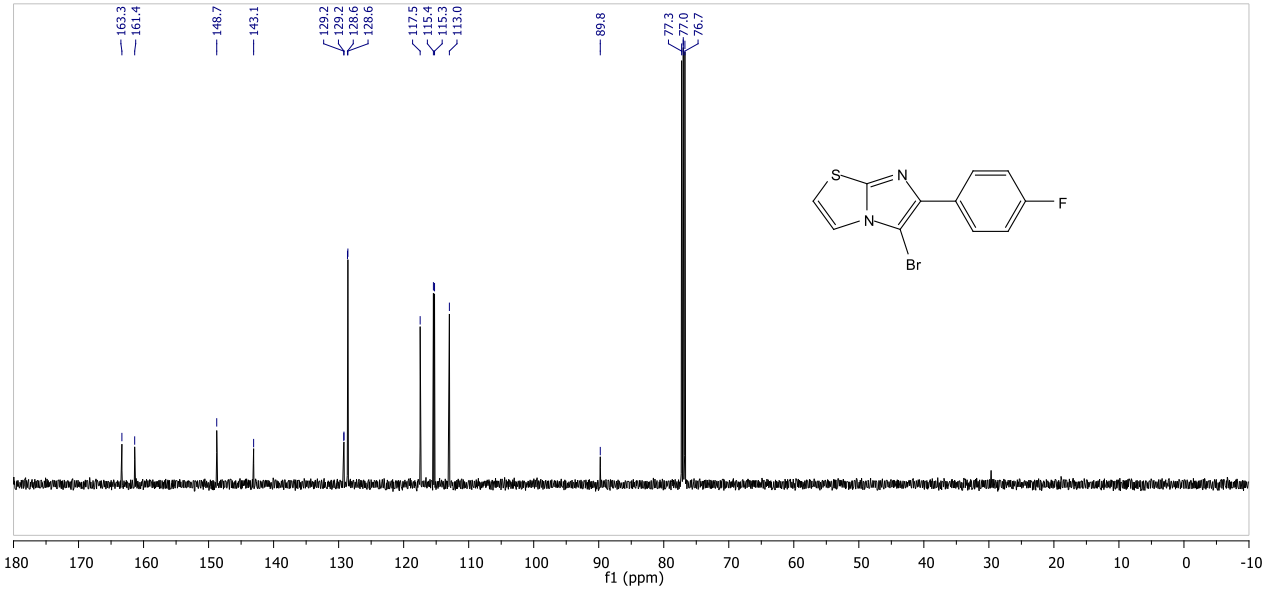
^{13}C NMR (126 MHz, $CDCl_3$) of compound **2e**



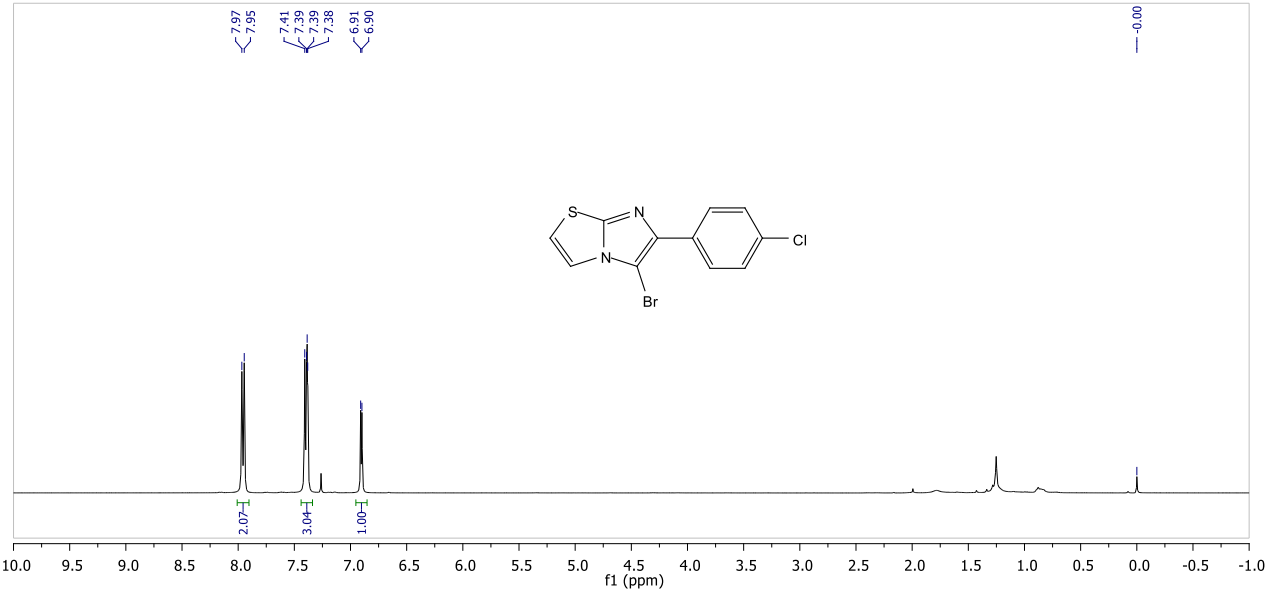
^{1}H NMR (400 MHz, $CDCl_3$) of compound 2f



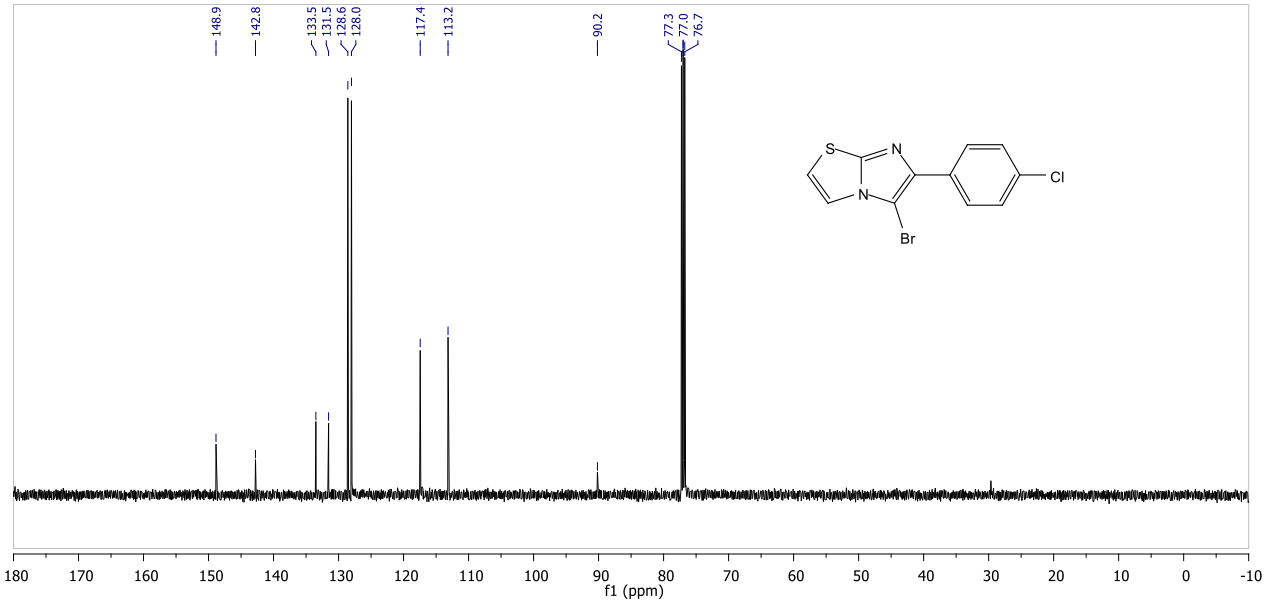
^{13}C NMR (126 MHz, $CDCl_3$) of compound **2f**



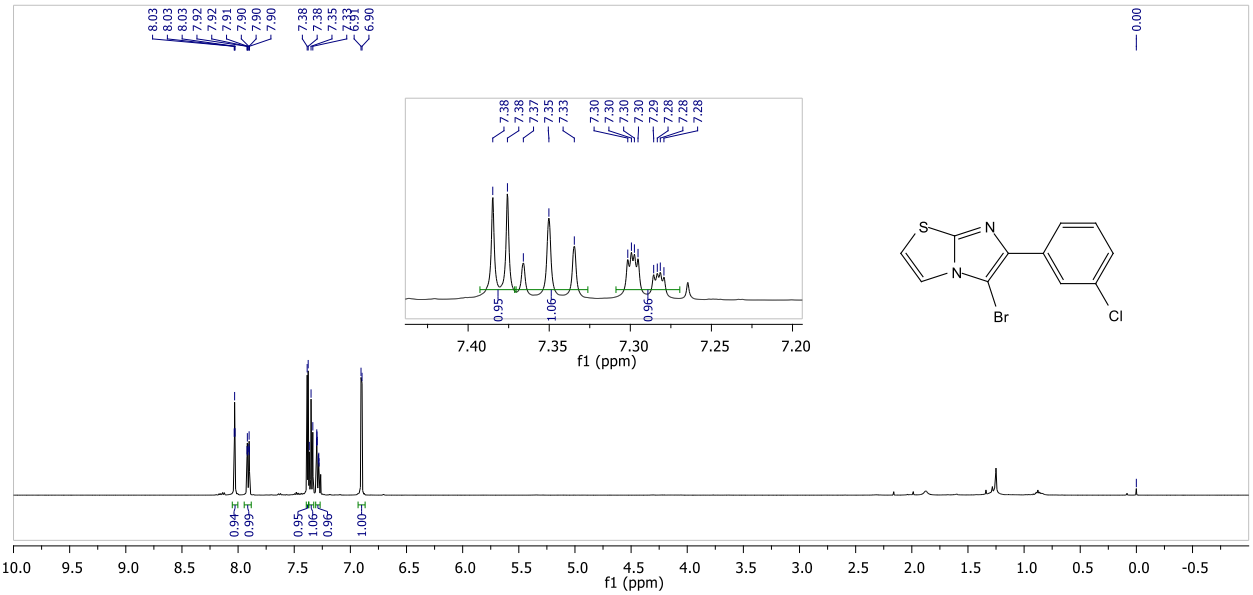
^{1}H NMR (400 MHz, $CDCl_3$) of compound **2g**



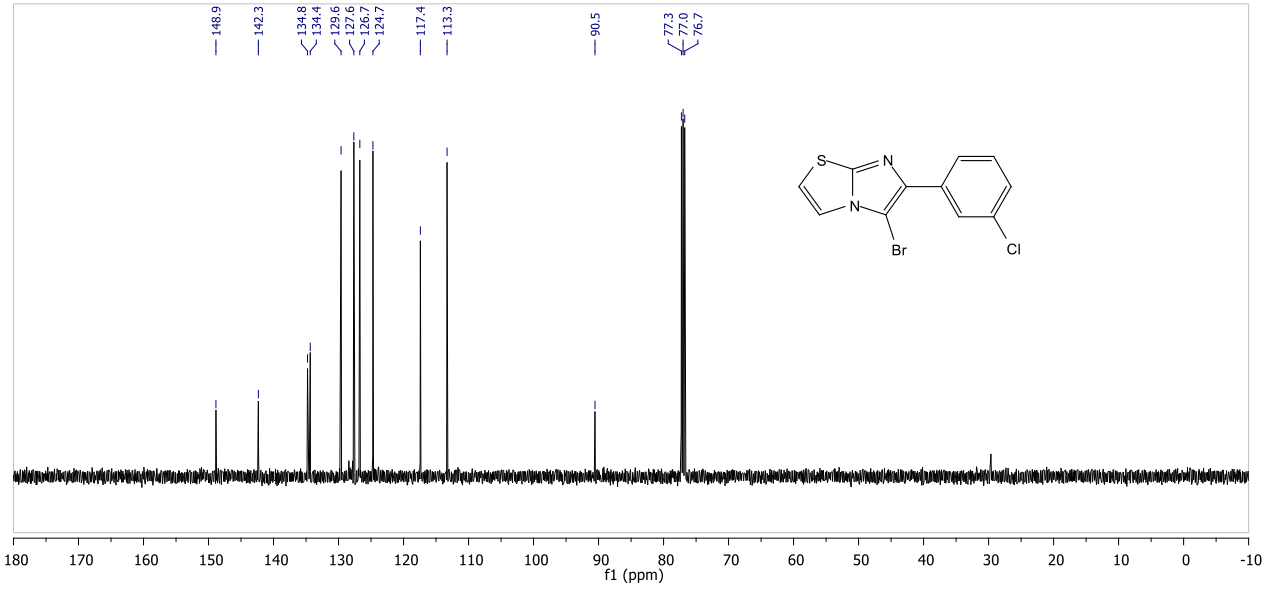
^{13}C NMR (126 MHz, $CDCl_3$) of compound **2g**



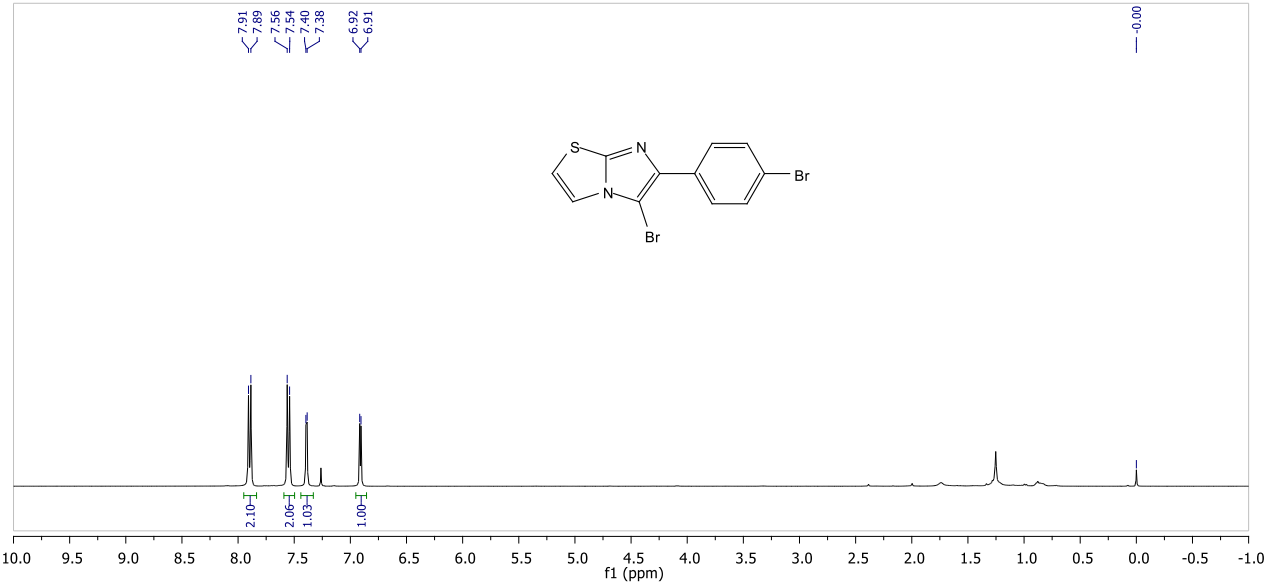
^{1}H NMR (500 MHz, $CDCl_3$) of compound **2h**



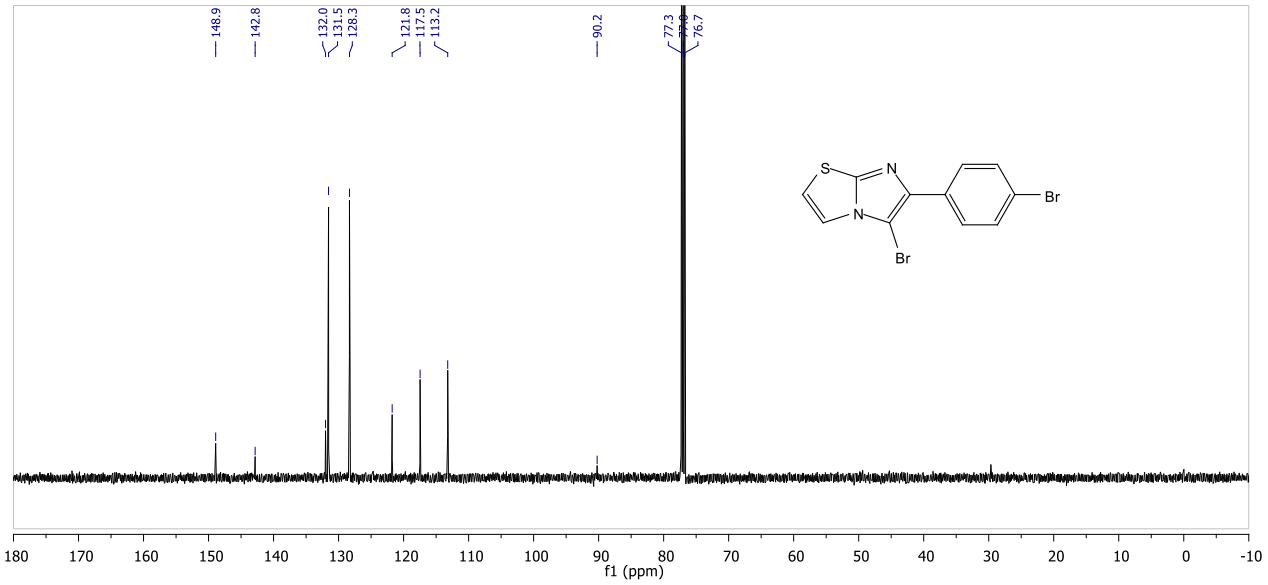
^{13}C NMR (126 MHz, $CDCl_3$) of compound **2h**



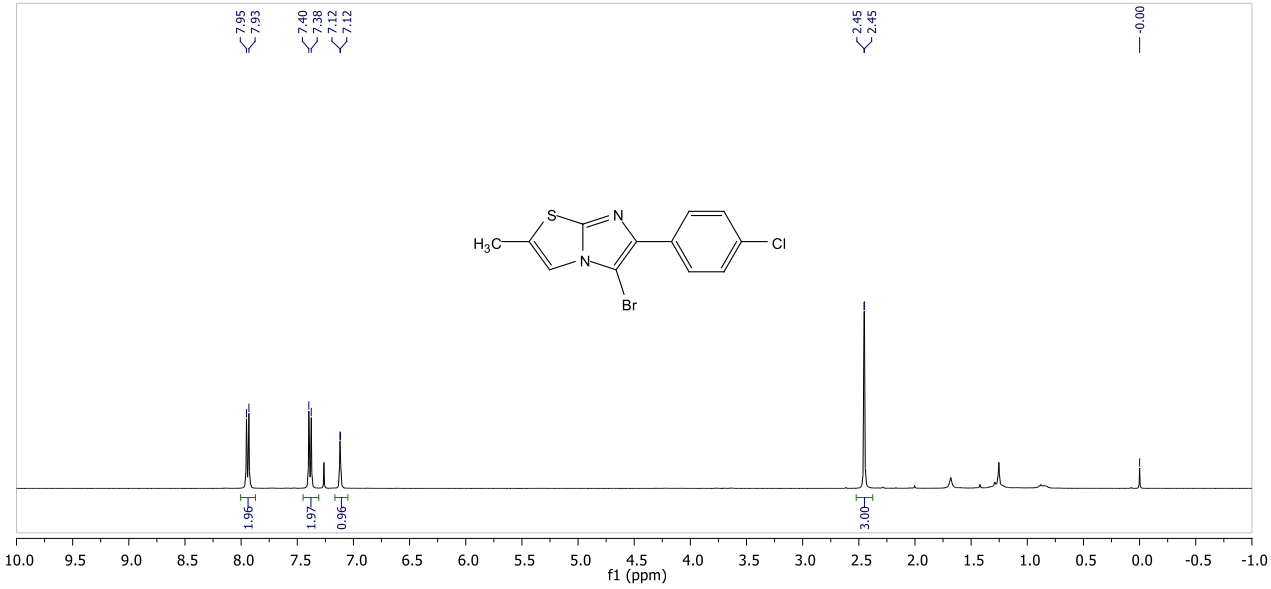
^{1}H NMR (400 MHz, $CDCl_3$) of compound **2i**



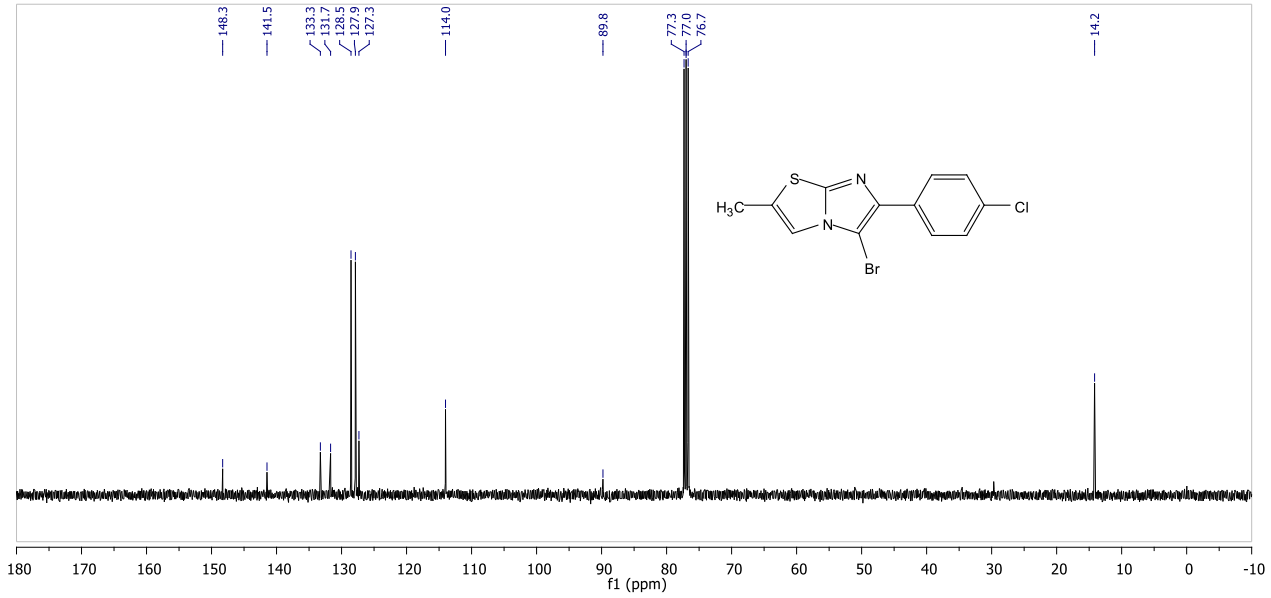
^{13}C NMR (126 MHz, $CDCl_3$) of compound **2i**



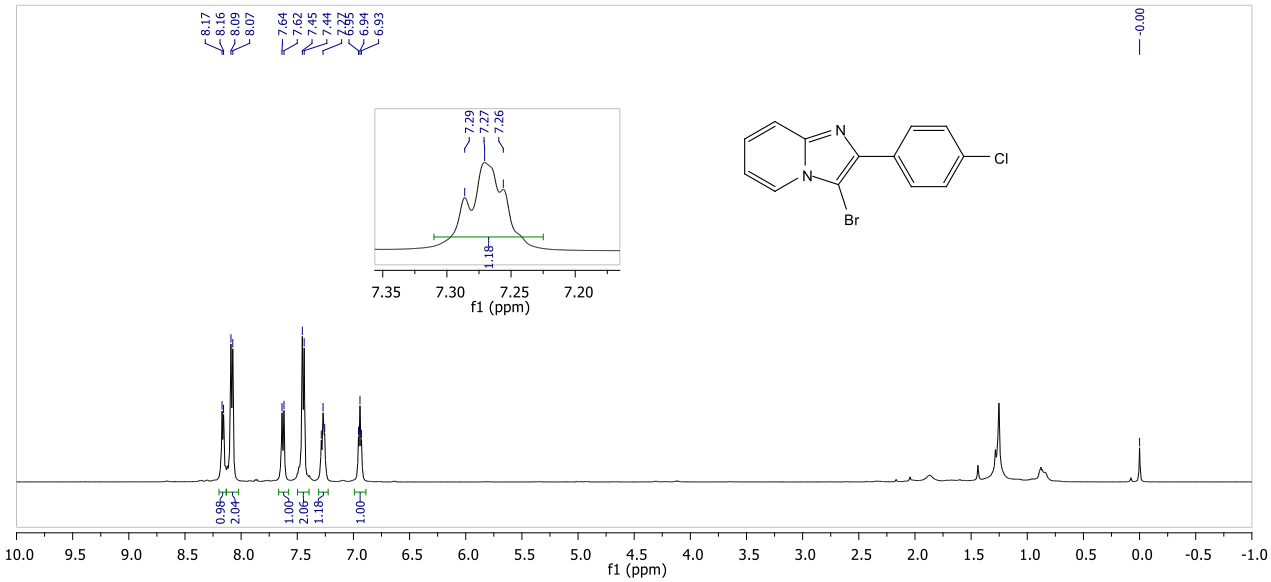
^{1}H NMR (400 MHz, $CDCl_3$) of compound **2j**



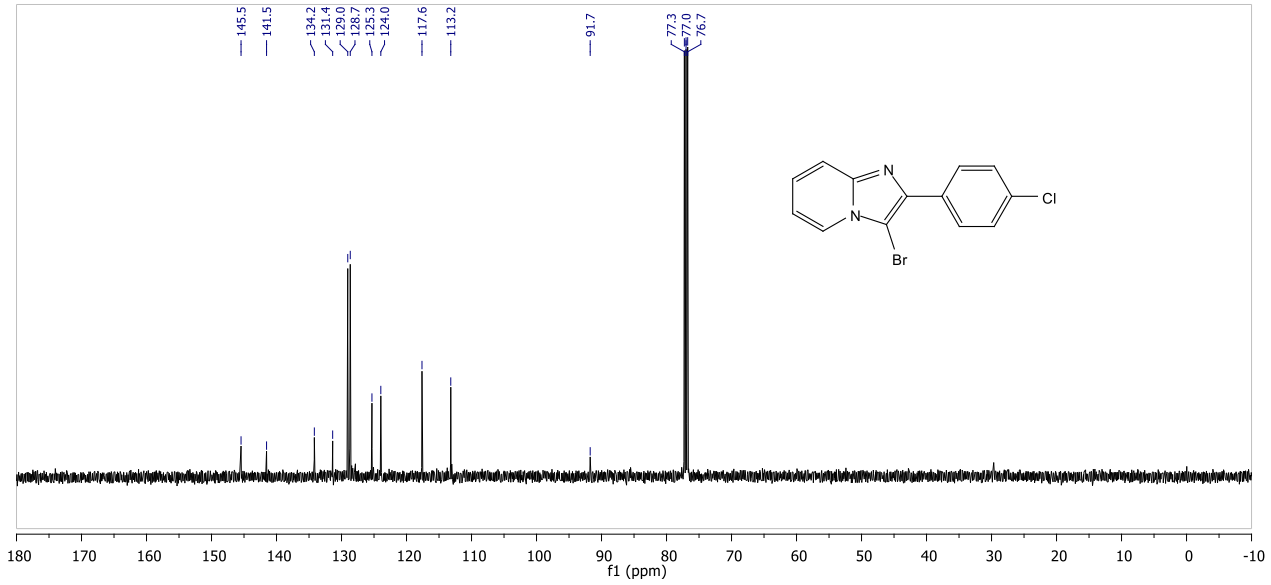
^{13}C NMR (101 MHz, $CDCl_3$) of compound **2j**



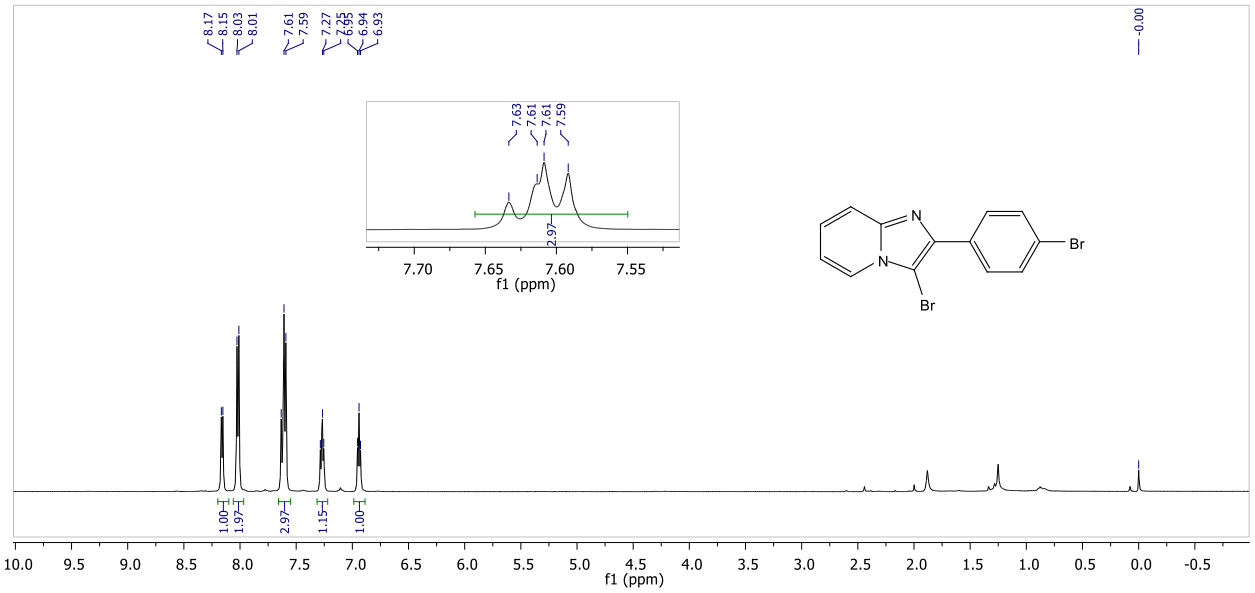
^{1}H NMR (500 MHz, $CDCl_3$) of compound **2k**



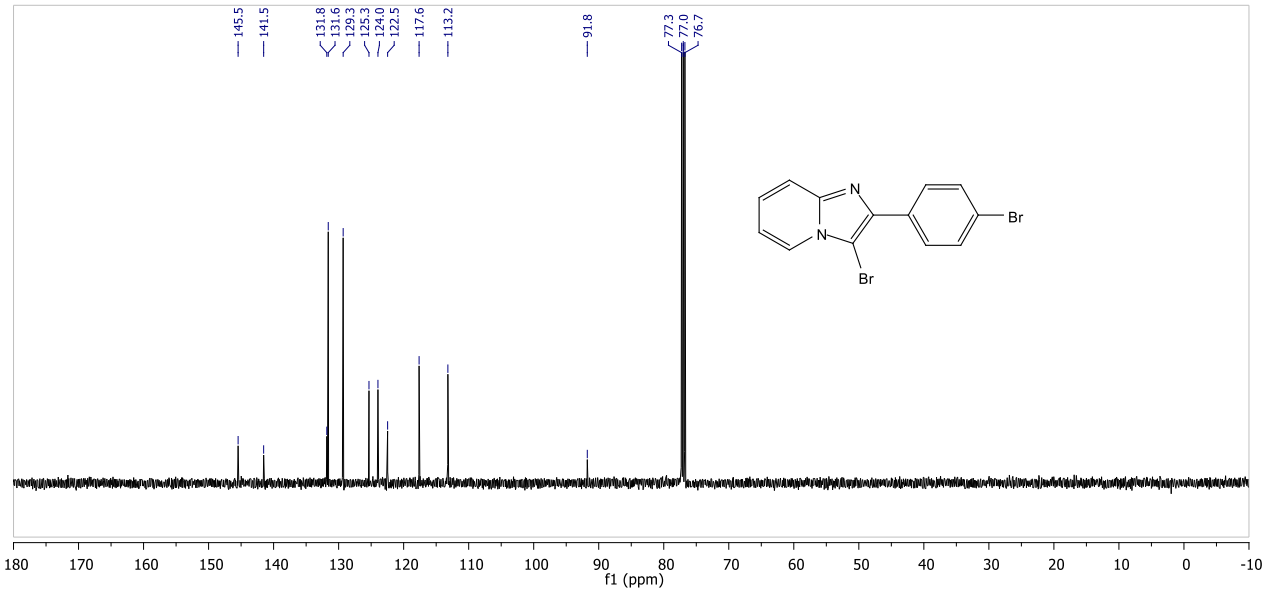
^{13}C NMR (126 MHz, $CDCl_3$) of compound **2k**



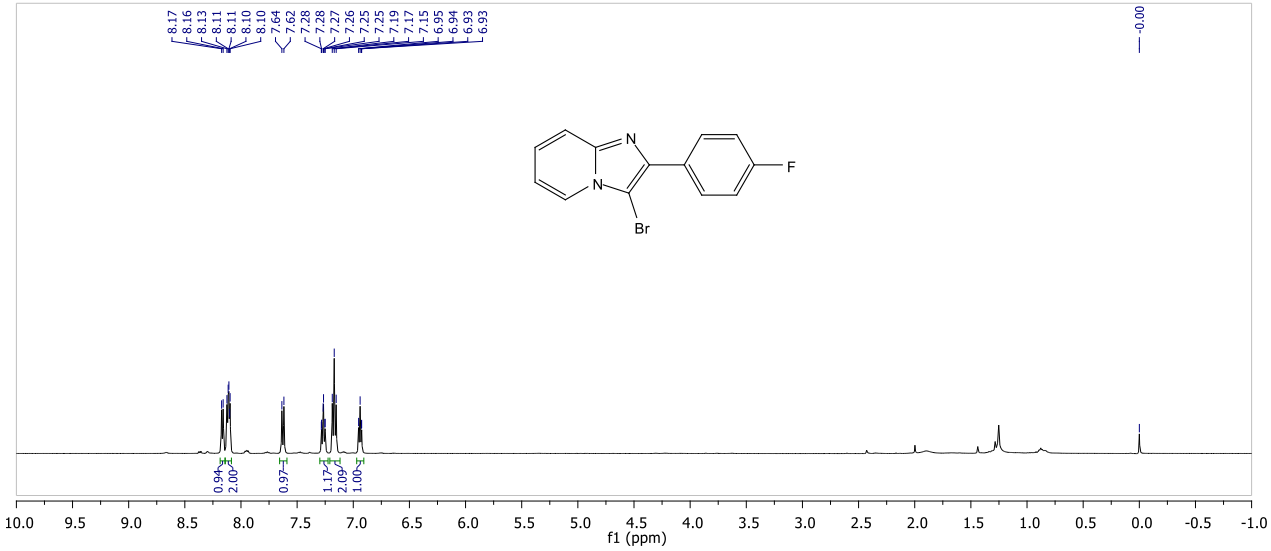
^{1}H NMR (500 MHz, $CDCl_3$) of compound **2l**



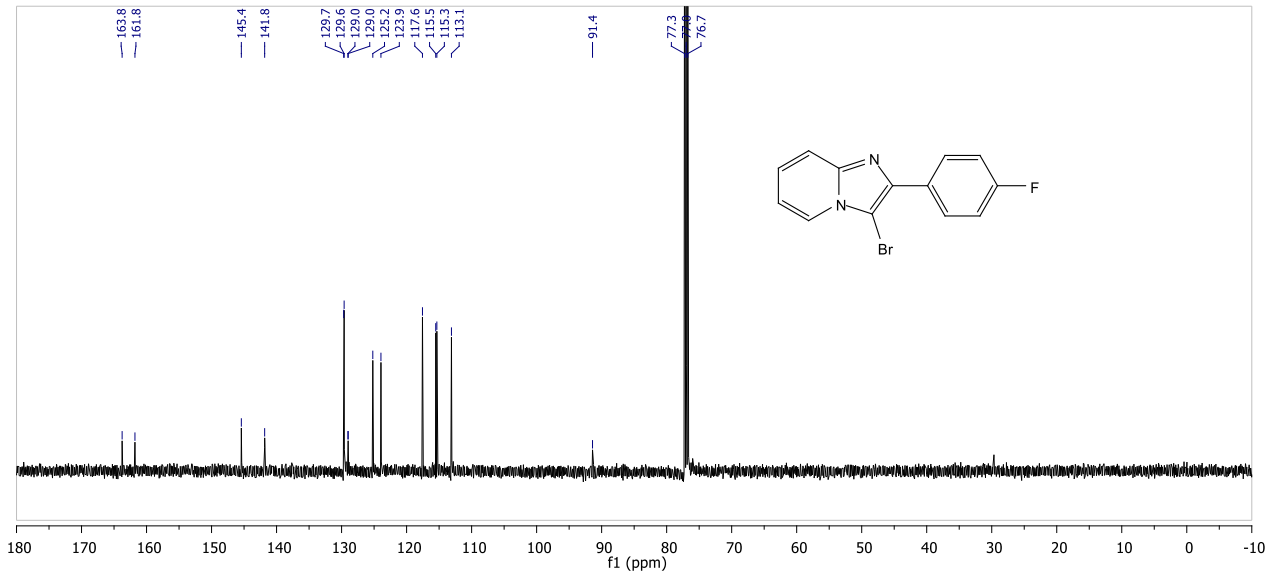
^{13}C NMR (126 MHz, $CDCl_3$) of compound **2l**



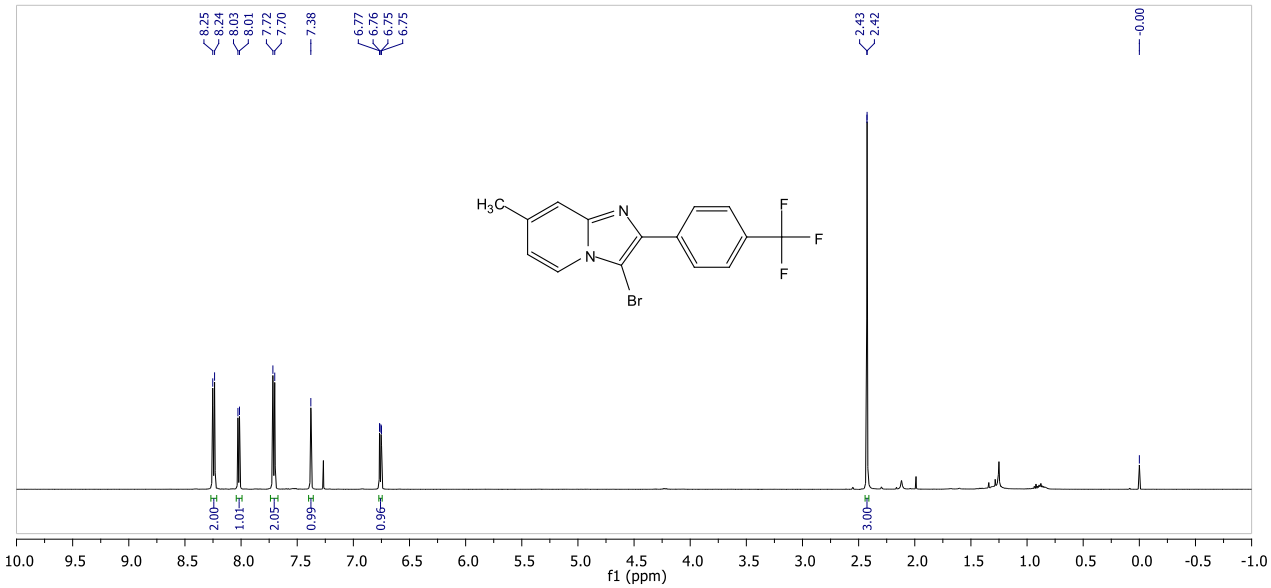
^{1}H NMR (500 MHz, $CDCl_3$) of compound **2m**



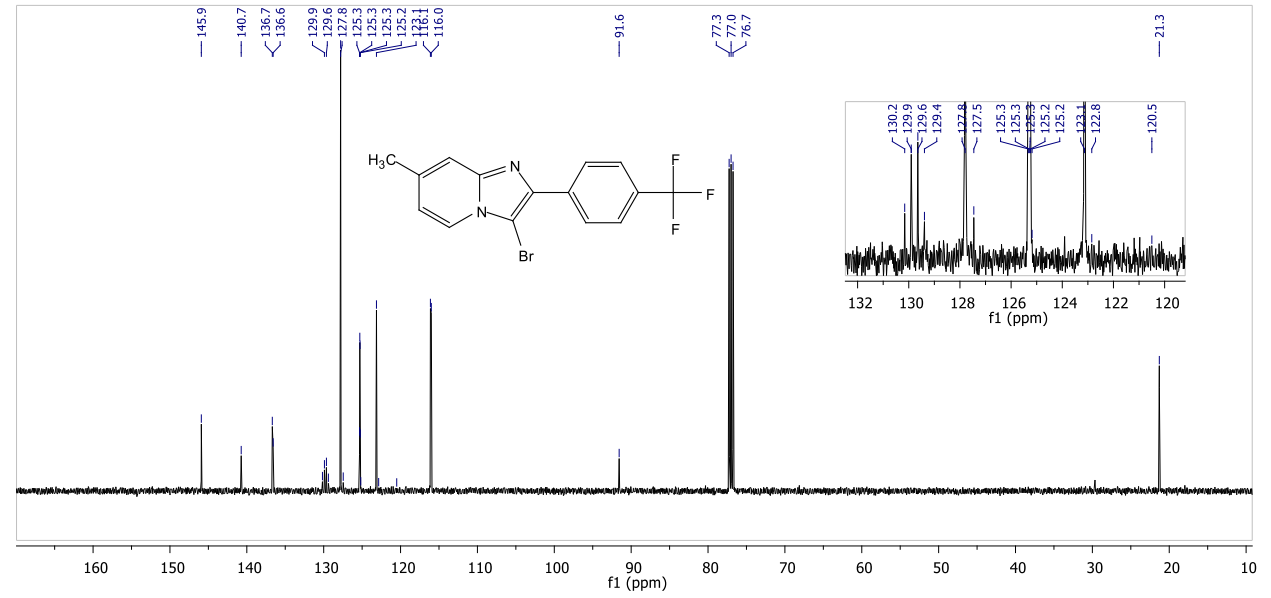
^{13}C NMR (126 MHz, $CDCl_3$) of compound **2m**



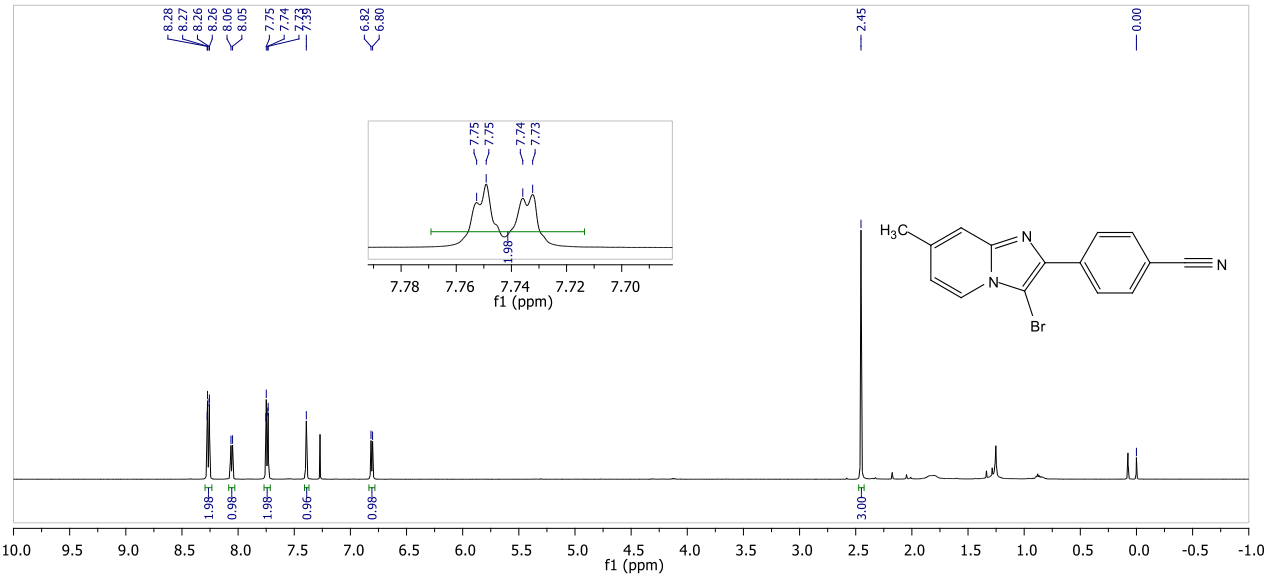
^{1}H NMR (500 MHz, $CDCl_3$) of compound **2n**



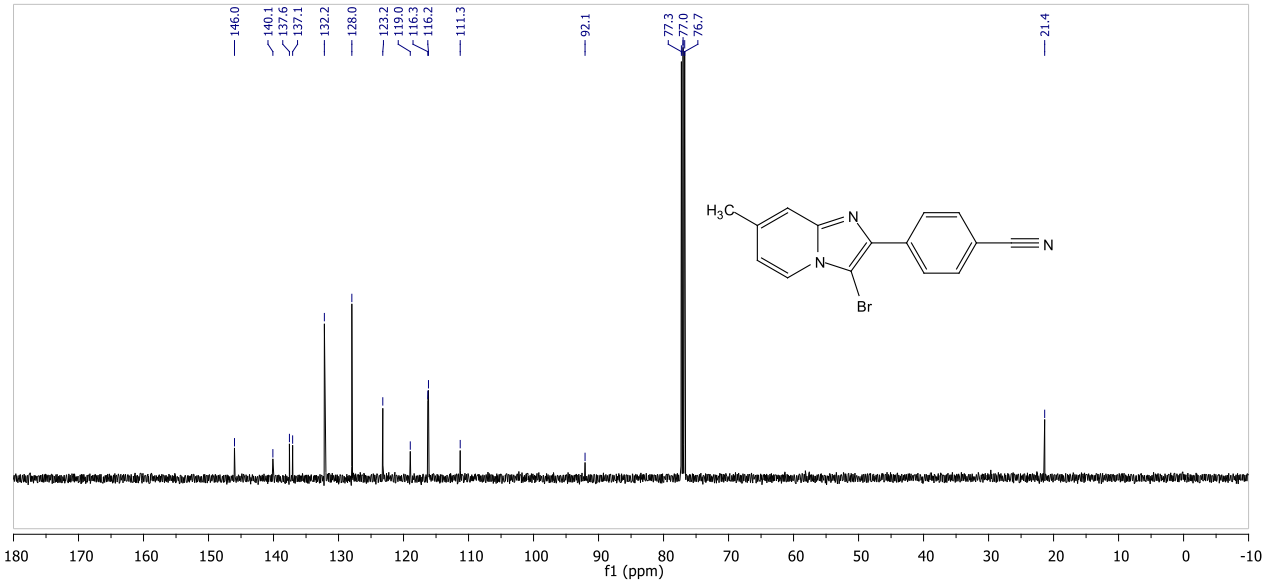
^{13}C NMR (126 MHz, $CDCl_3$) of compound **2n**



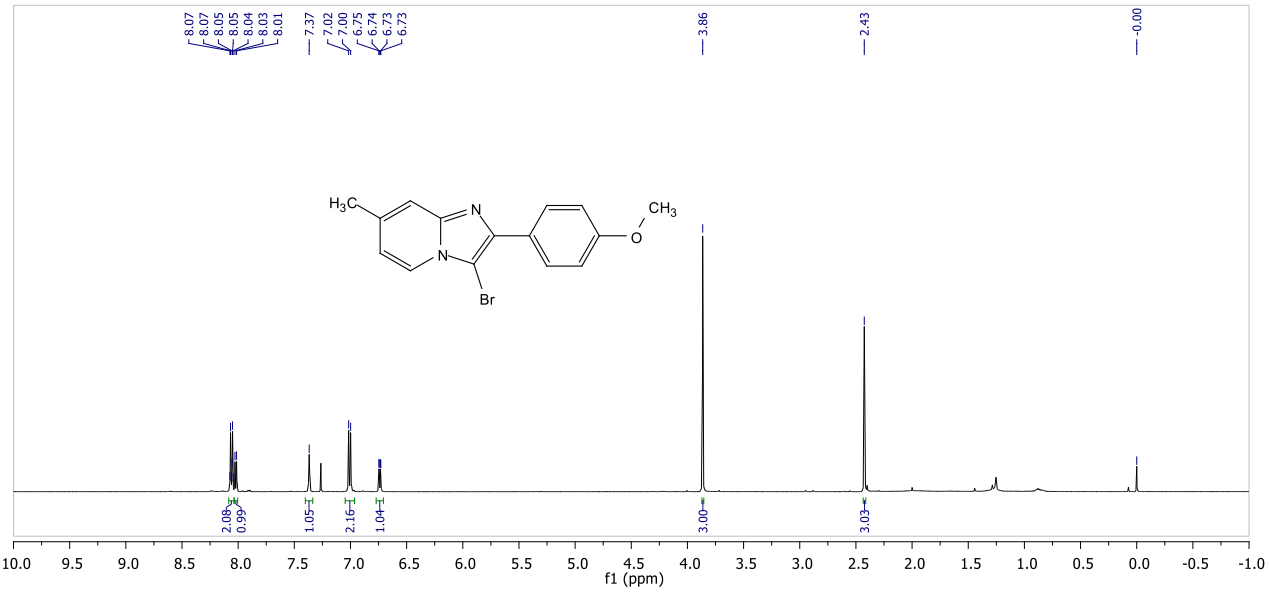
^{1}H NMR (500 MHz, $CDCl_3$) of compound **2o**



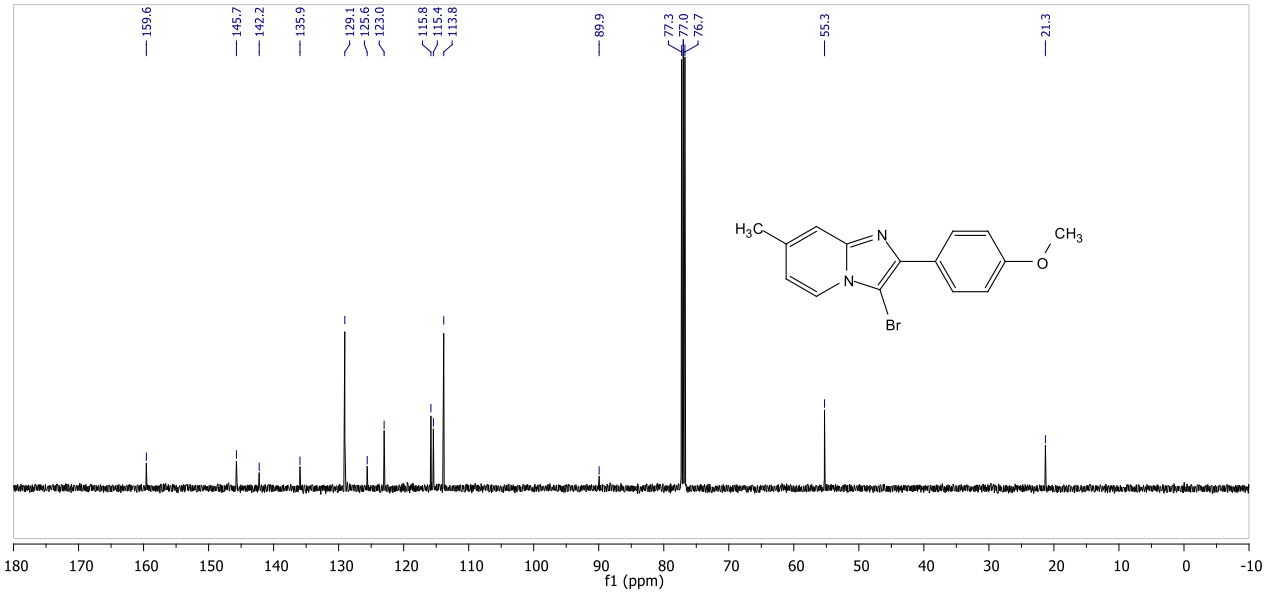
^{13}C NMR (126 MHz, $CDCl_3$) of compound **2o**



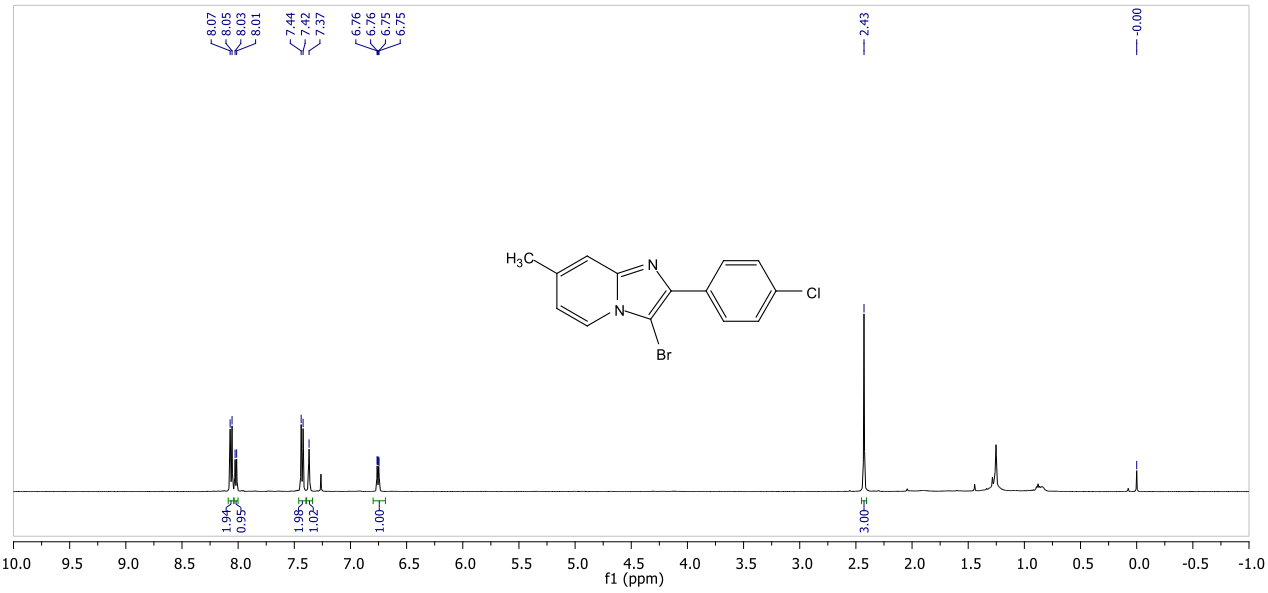
^{1}H NMR (500 MHz, $CDCl_3$) of compound **2p**



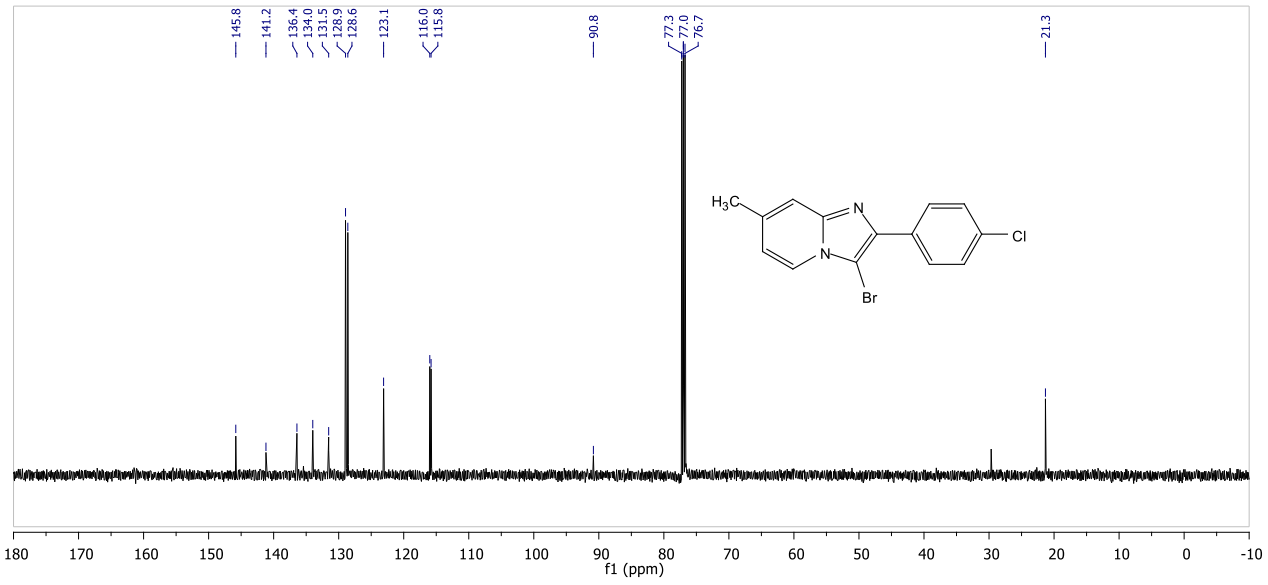
^{13}C NMR (126 MHz, $CDCl_3$) of compound **2p**



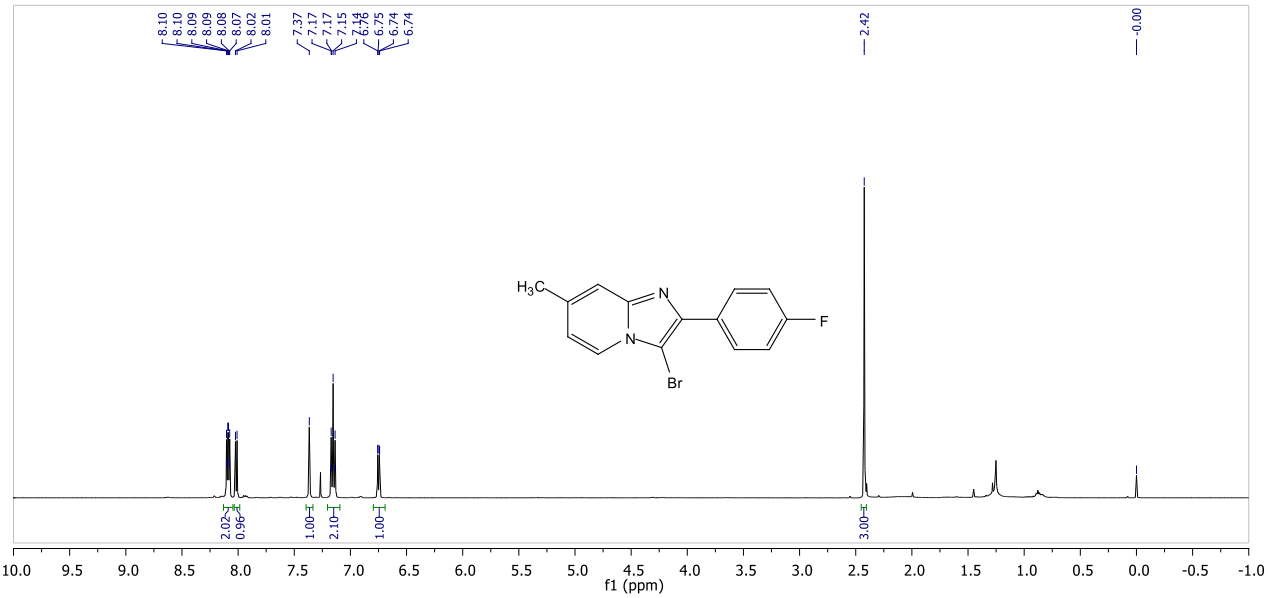
^{1}H NMR (500 MHz, $CDCl_3$) of compound **2q**



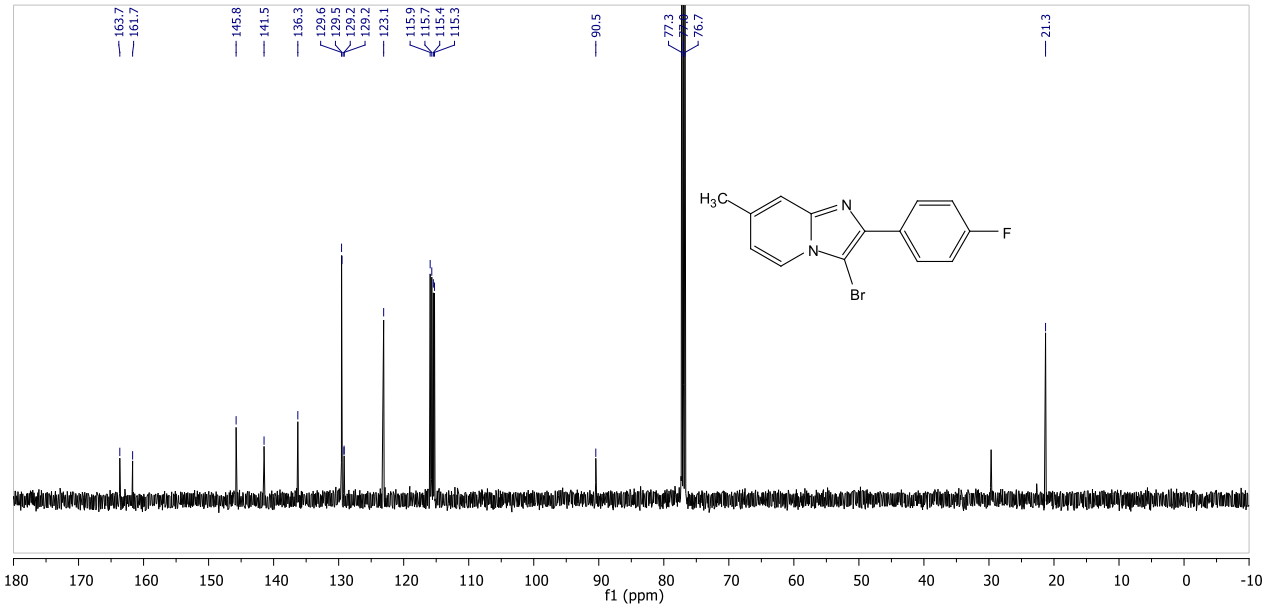
^{13}C NMR (126 MHz, $CDCl_3$) of compound **2q**



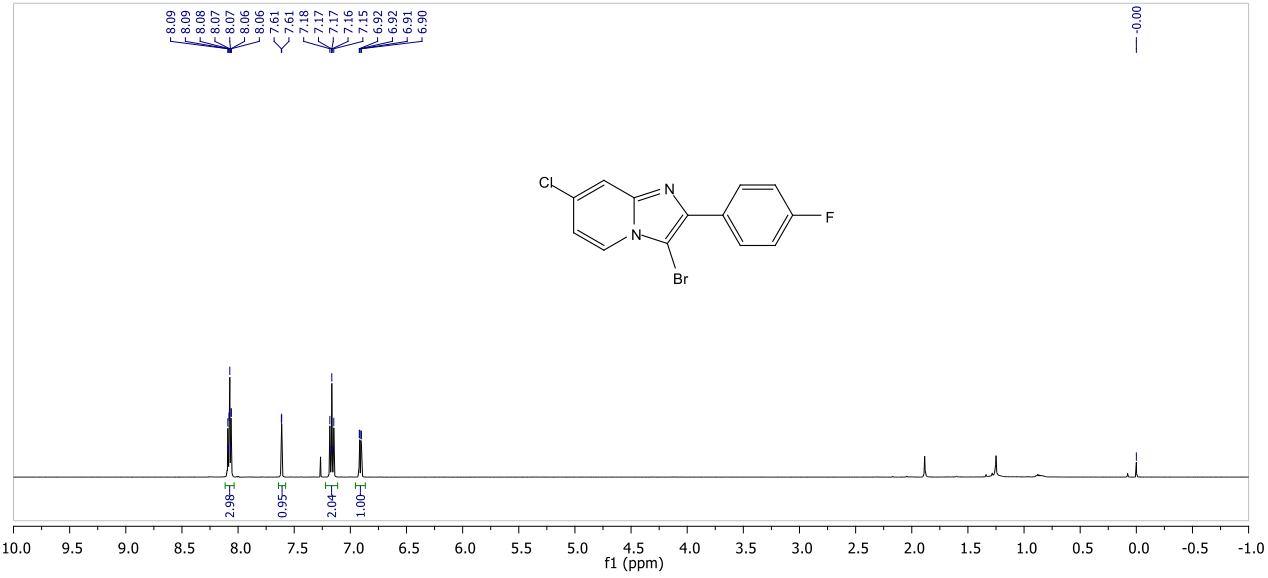
^{1}H NMR (500 MHz, $CDCl_3$) of compound **2r**



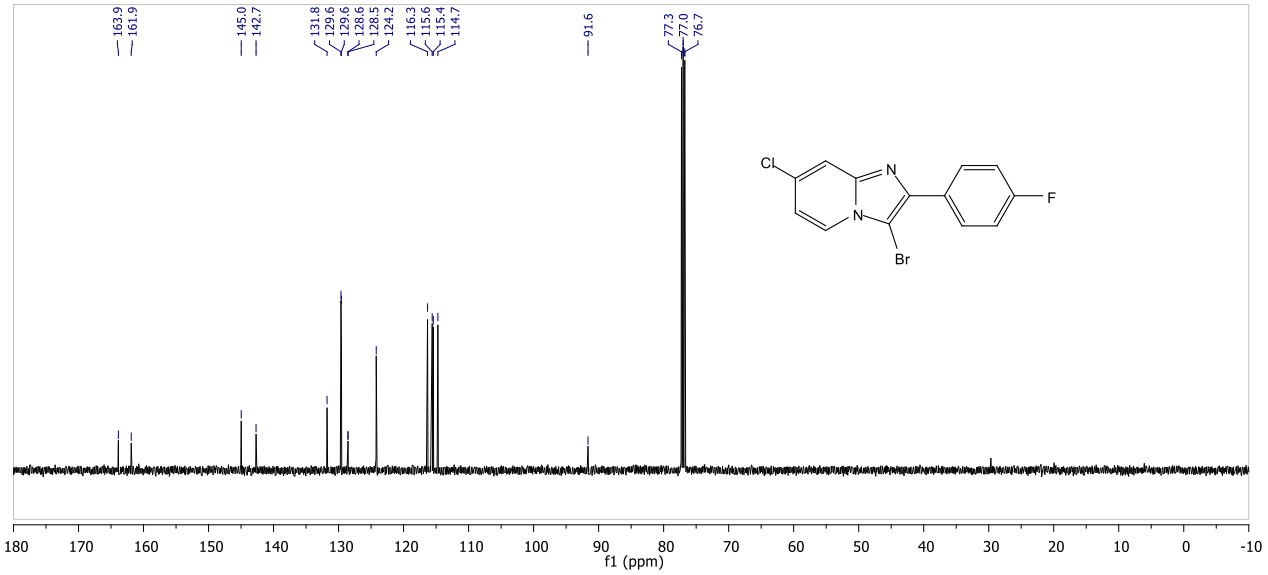
^{13}C NMR (126 MHz, $CDCl_3$) of compound **2r**



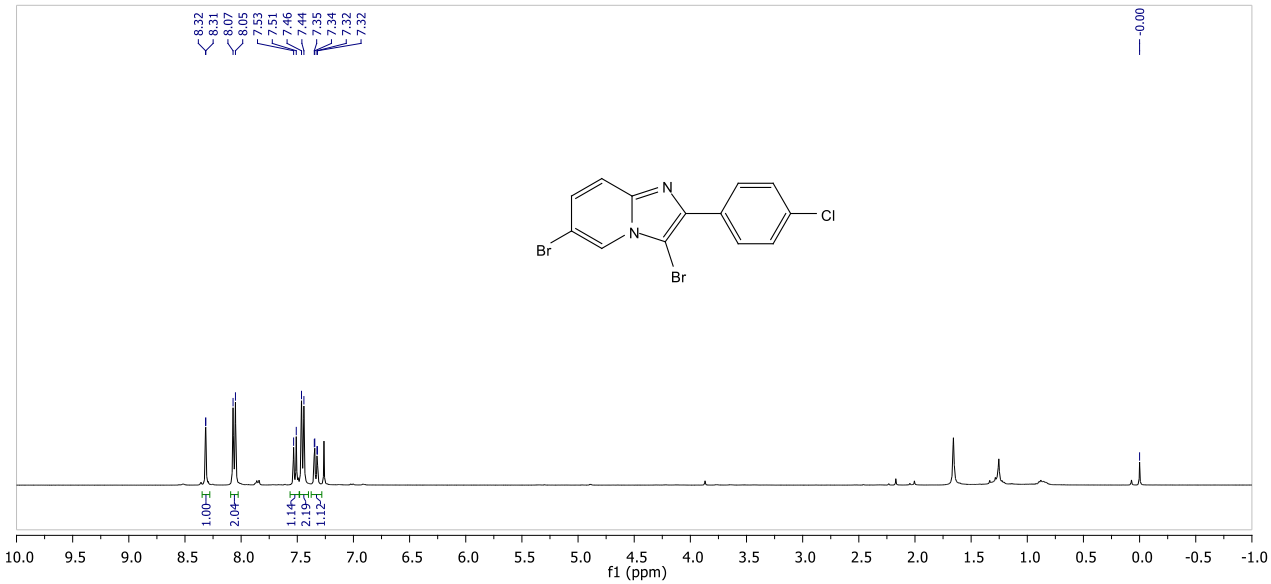
^{1}H NMR (500 MHz, $CDCl_3$) of compound **2s**



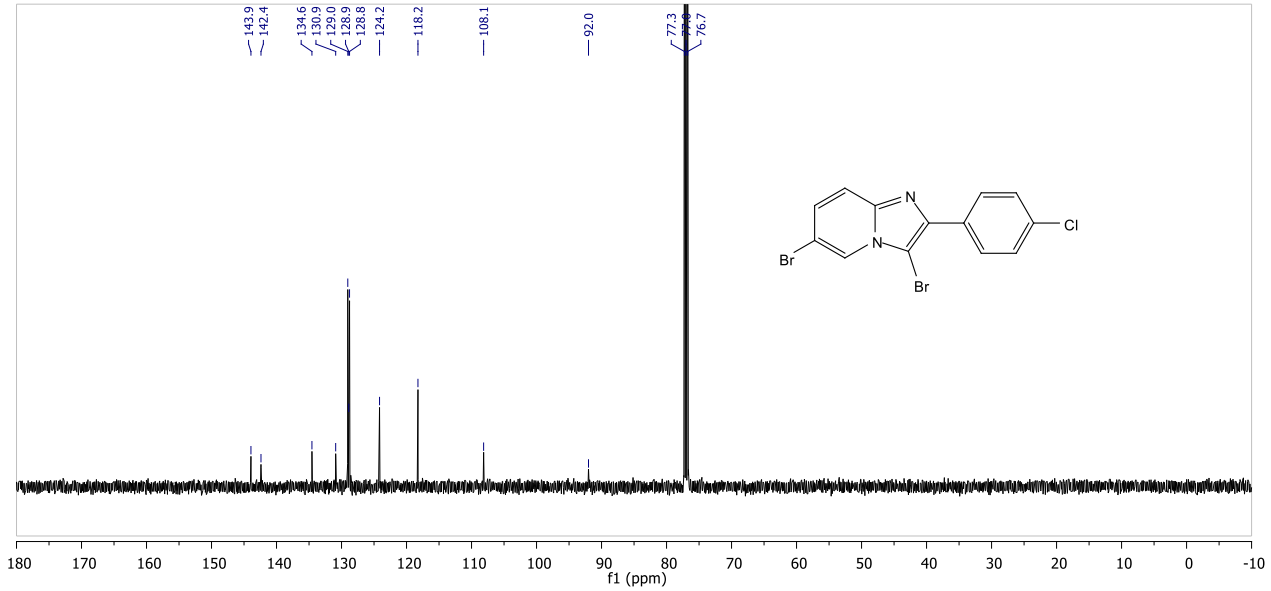
^{13}C NMR (126 MHz, $CDCl_3$) of compound **2s**



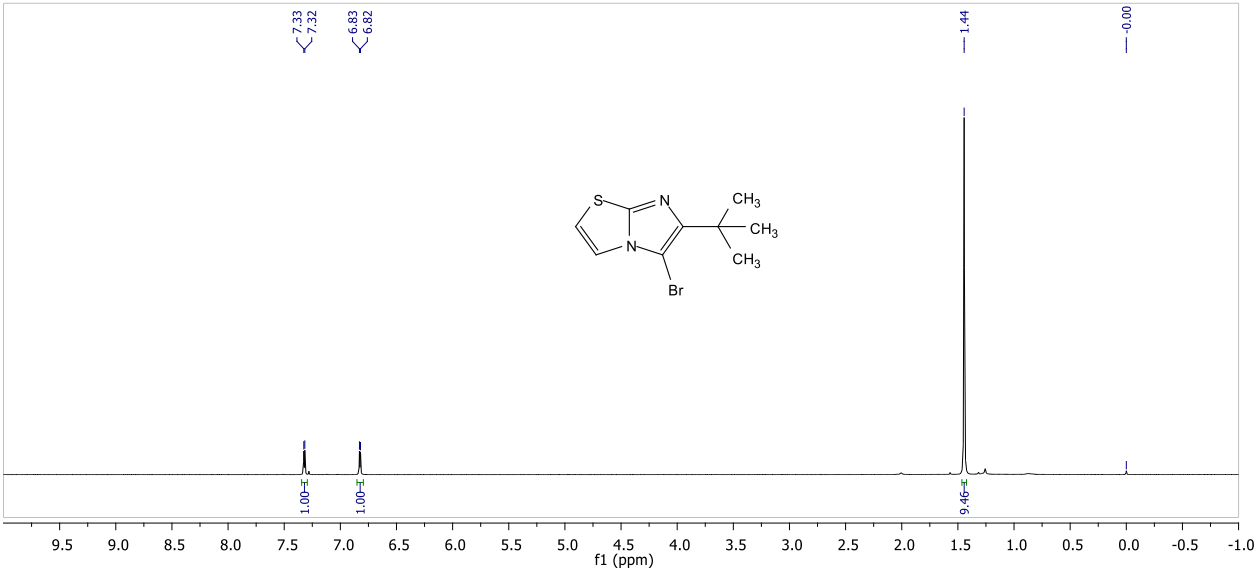
^{1}H NMR (500 MHz, $CDCl_3$) of compound **2t**



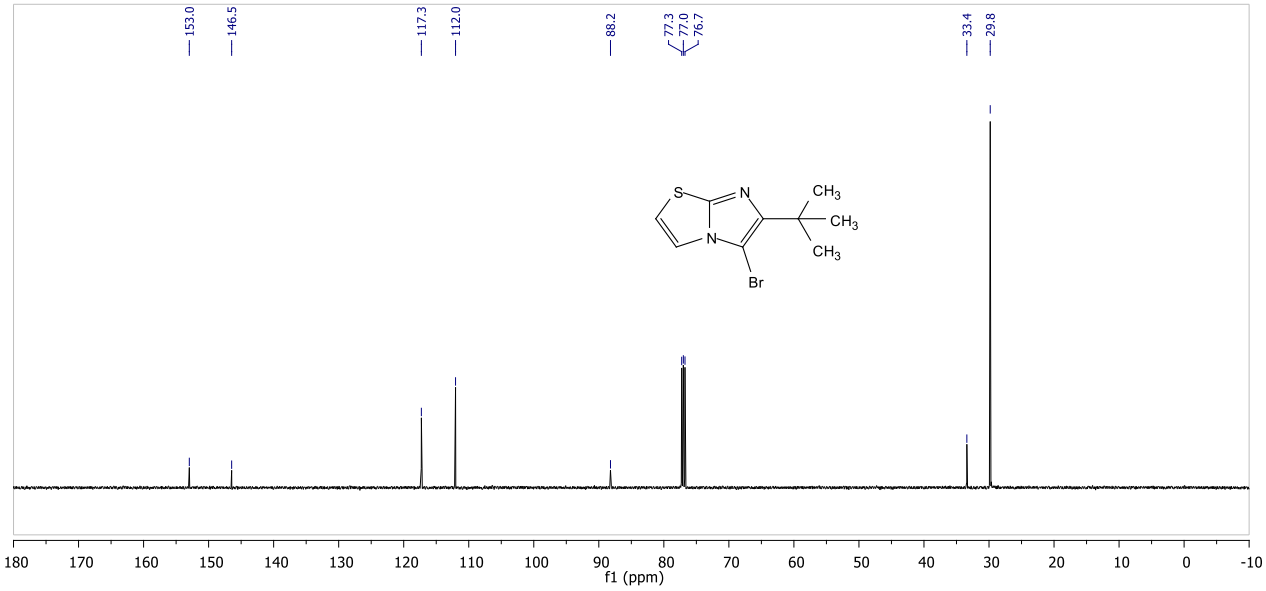
^{13}C NMR (126 MHz, $CDCl_3$) of compound **2t**



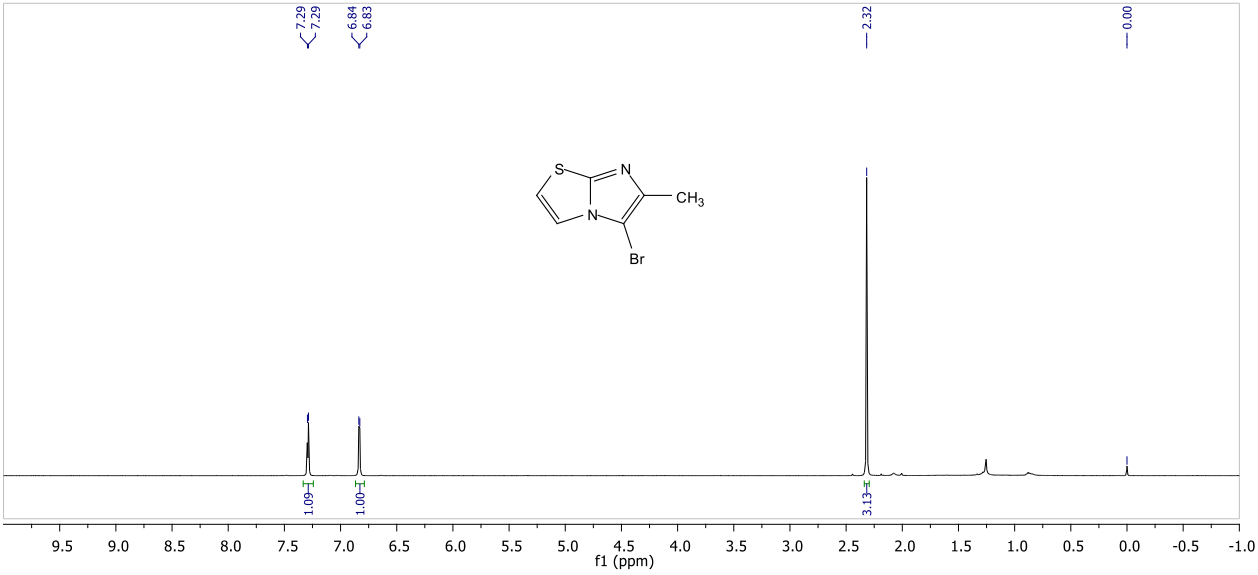
^{1}H NMR (500 MHz, $CDCl_3$) of compound **2u**



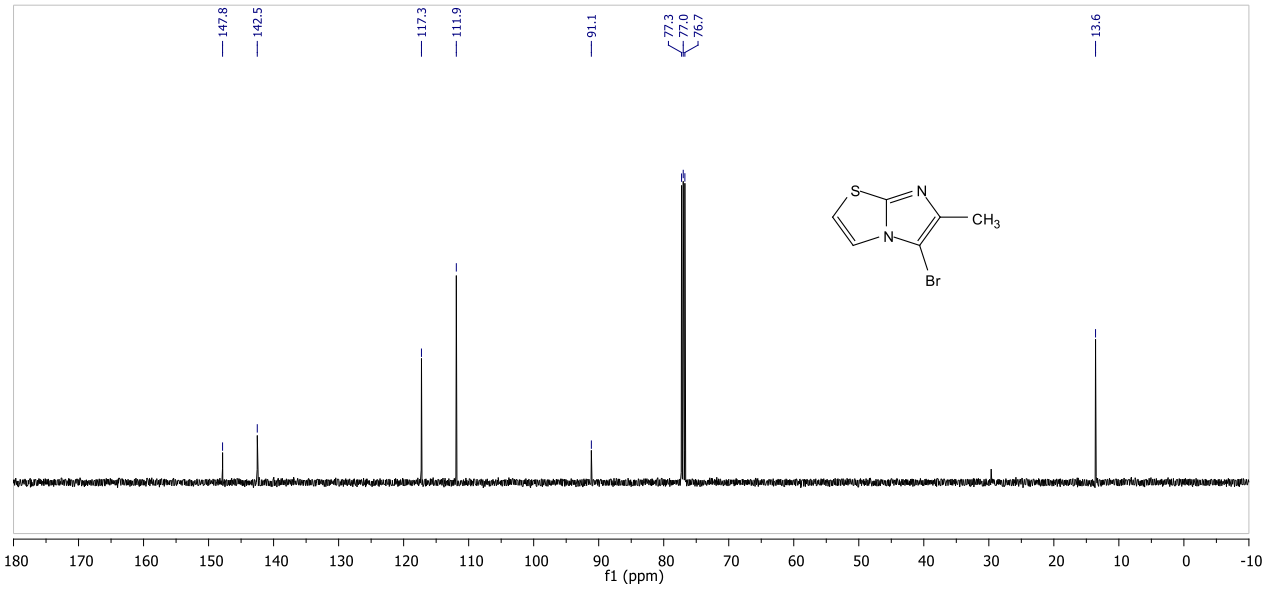
^{13}C NMR (126 MHz, $CDCl_3$) of compound **2u**



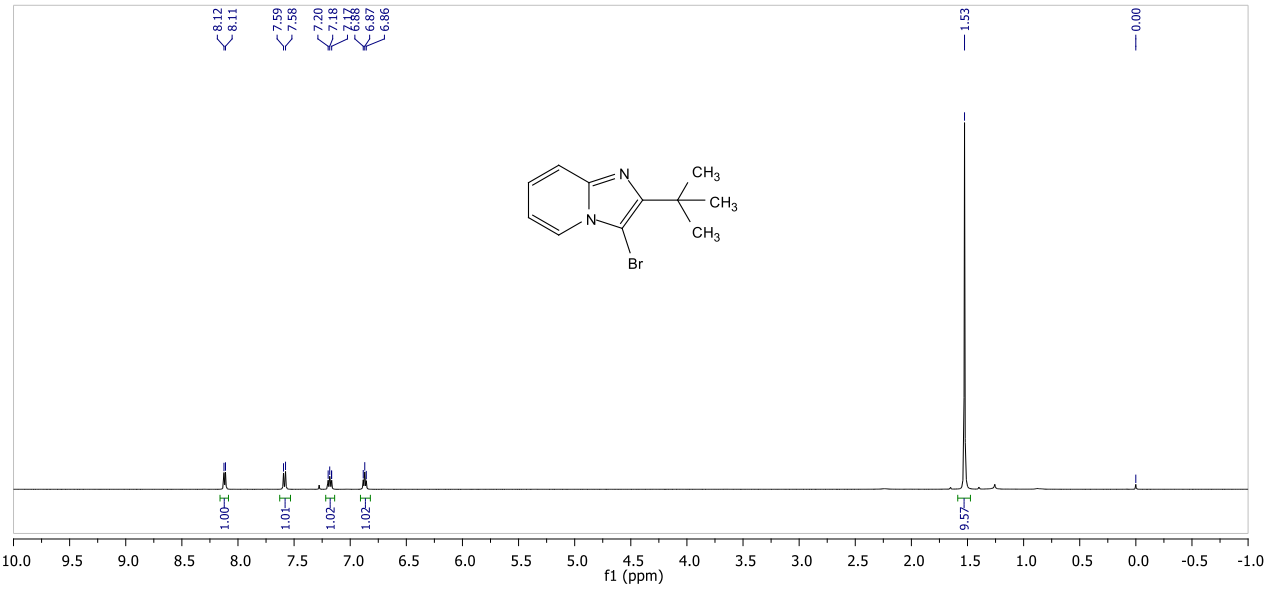
^{1}H NMR (500 MHz, $CDCl_3$) of compound **2v**



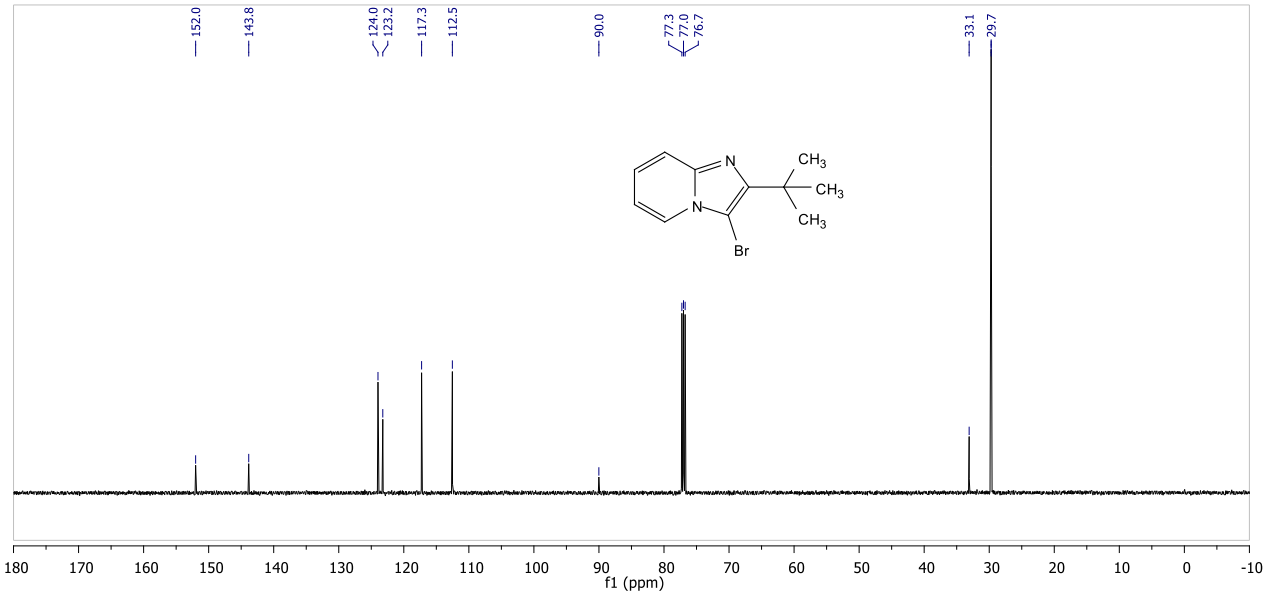
^{13}C NMR (126 MHz, $CDCl_3$) of compound **2v**



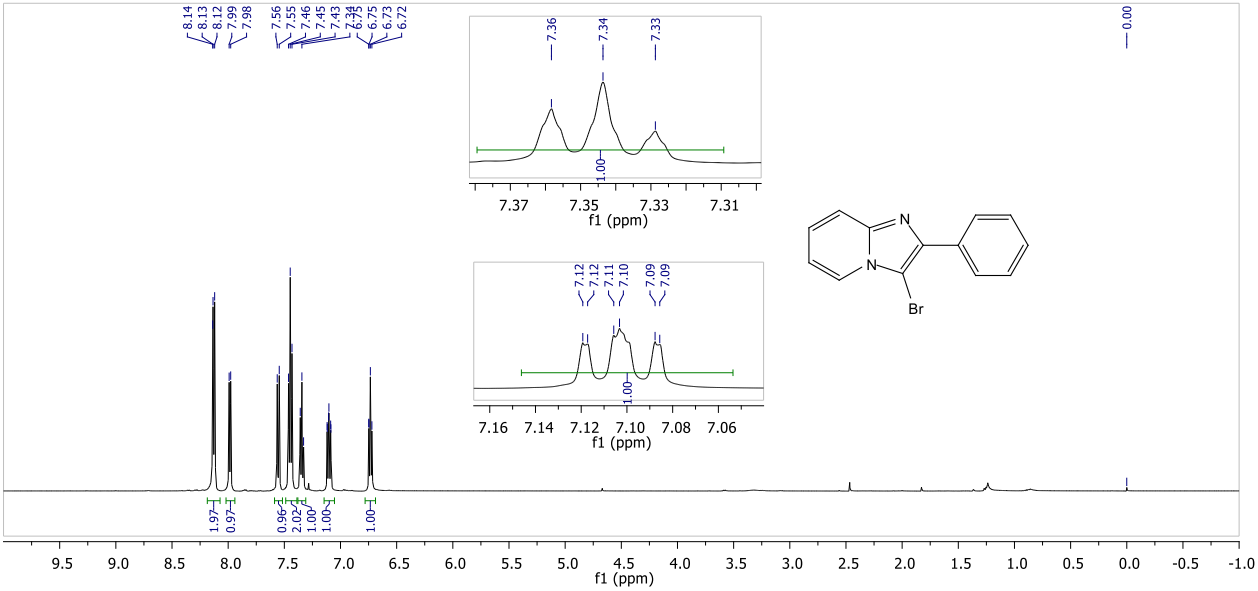
^{1}H NMR (500 MHz, $CDCl_3$) of compound **2w**



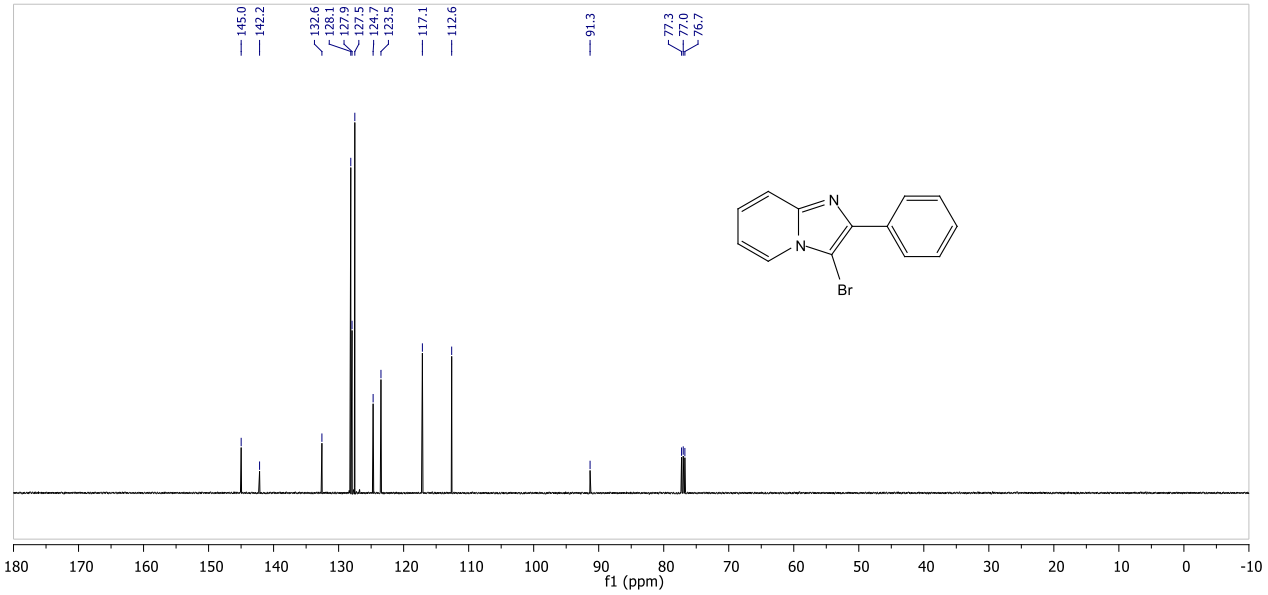
^{13}C NMR (126 MHz, $CDCl_3$) of compound **2w**



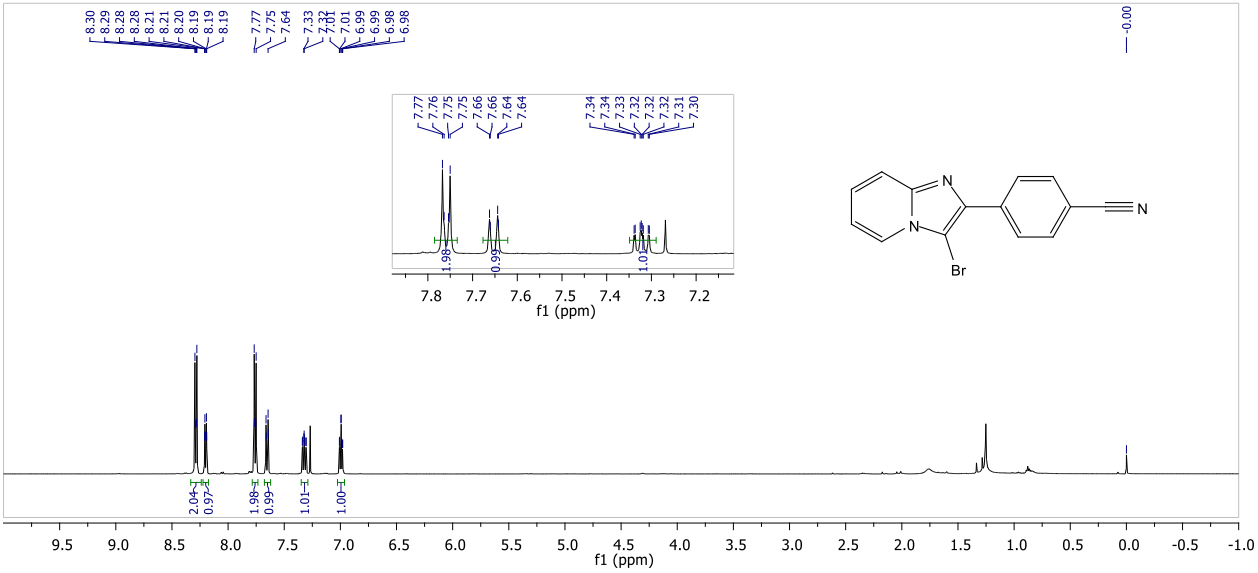
^{1}H NMR (500 MHz, $CDCl_3$) of compound **2x**



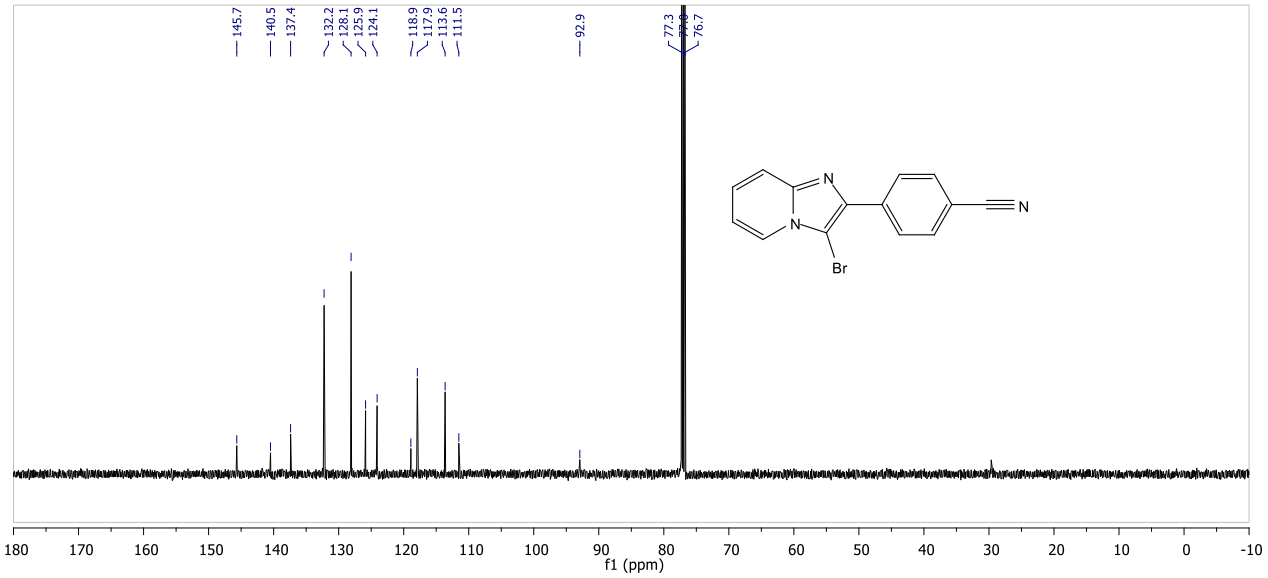
^{13}C NMR (126 MHz, $CDCl_3$) of compound **2x**



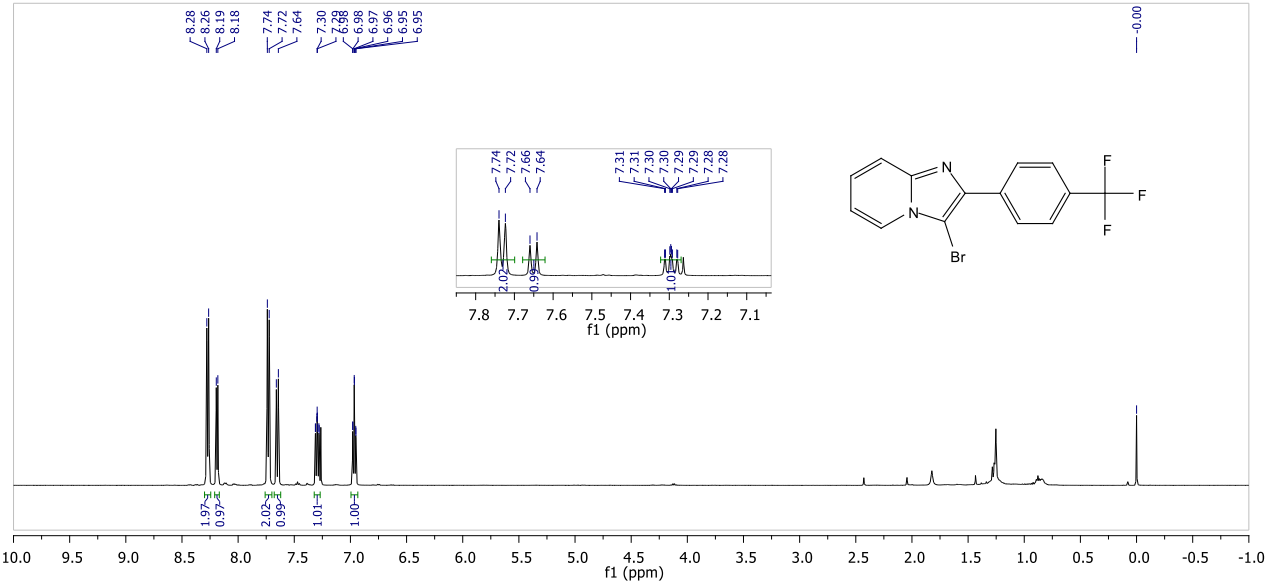
^{1}H NMR (500 MHz, $CDCl_3$) of compound **2y**



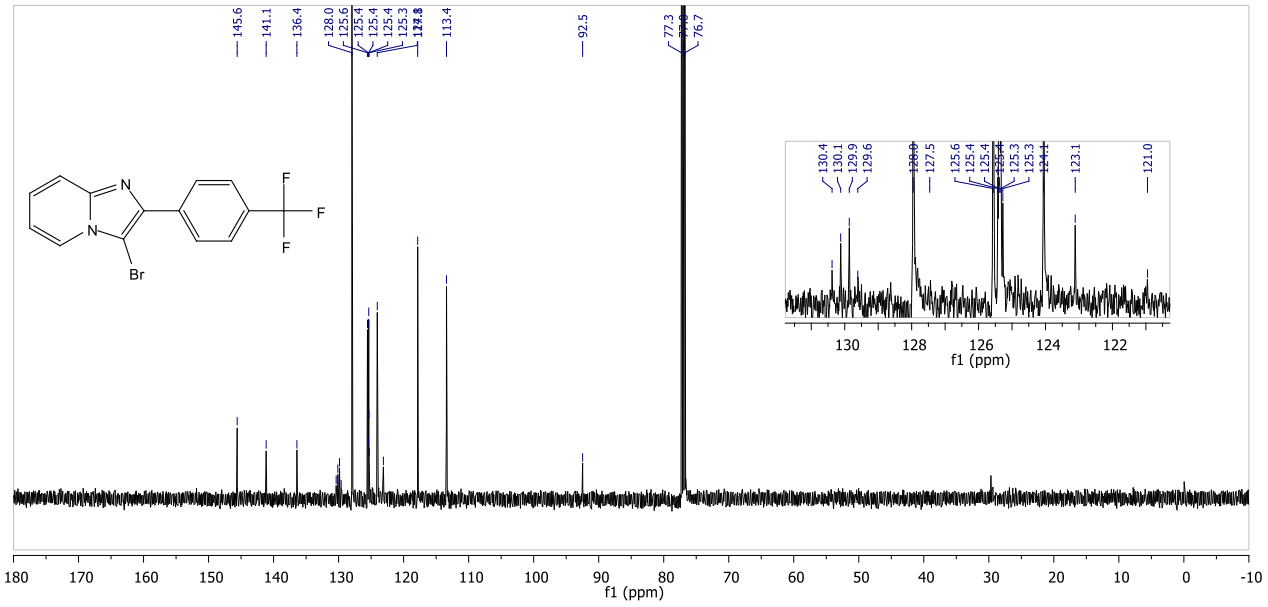
^{13}C NMR (126 MHz, $CDCl_3$) of compound **2y**



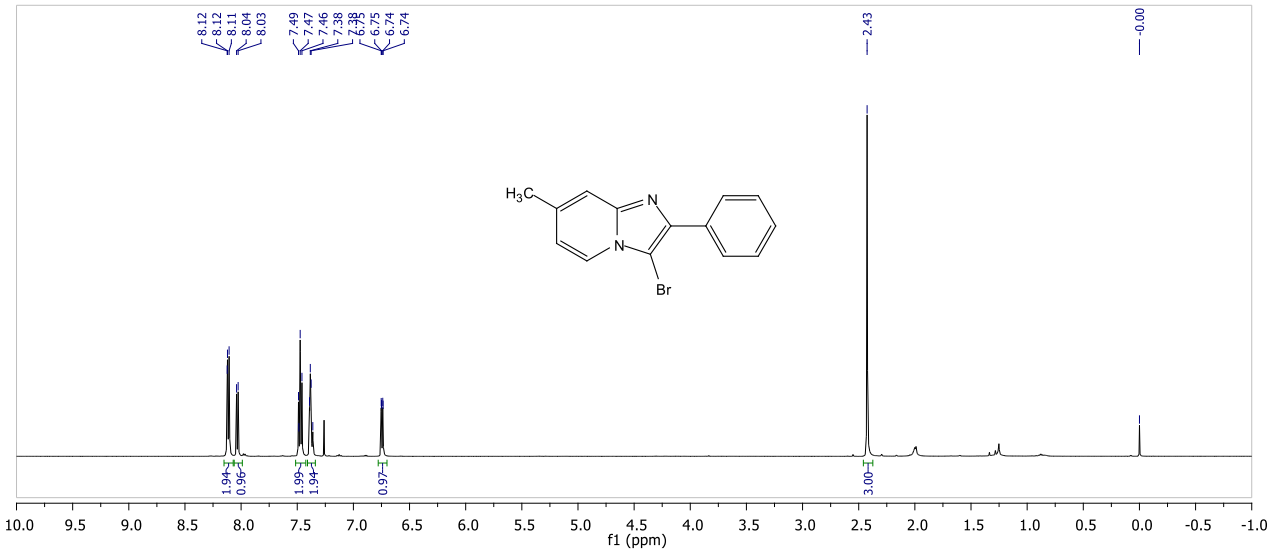
^{1}H NMR (500 MHz, $CDCl_3$) of compound **2z**



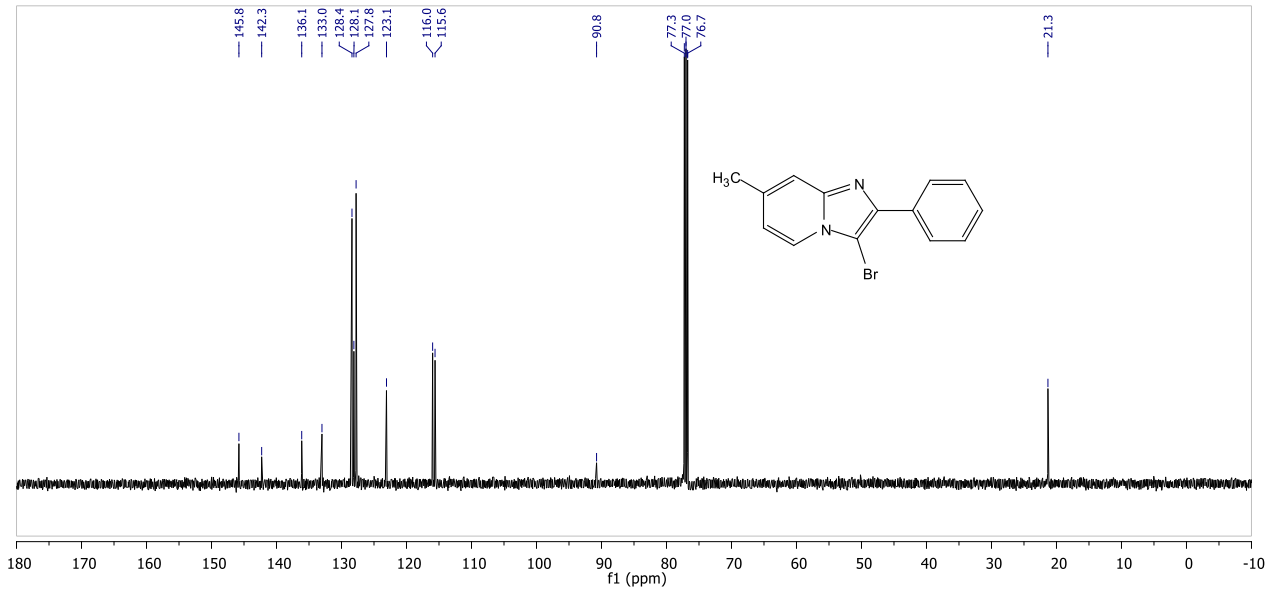
^{13}C NMR (126 MHz, $CDCl_3$) of compound **2z**



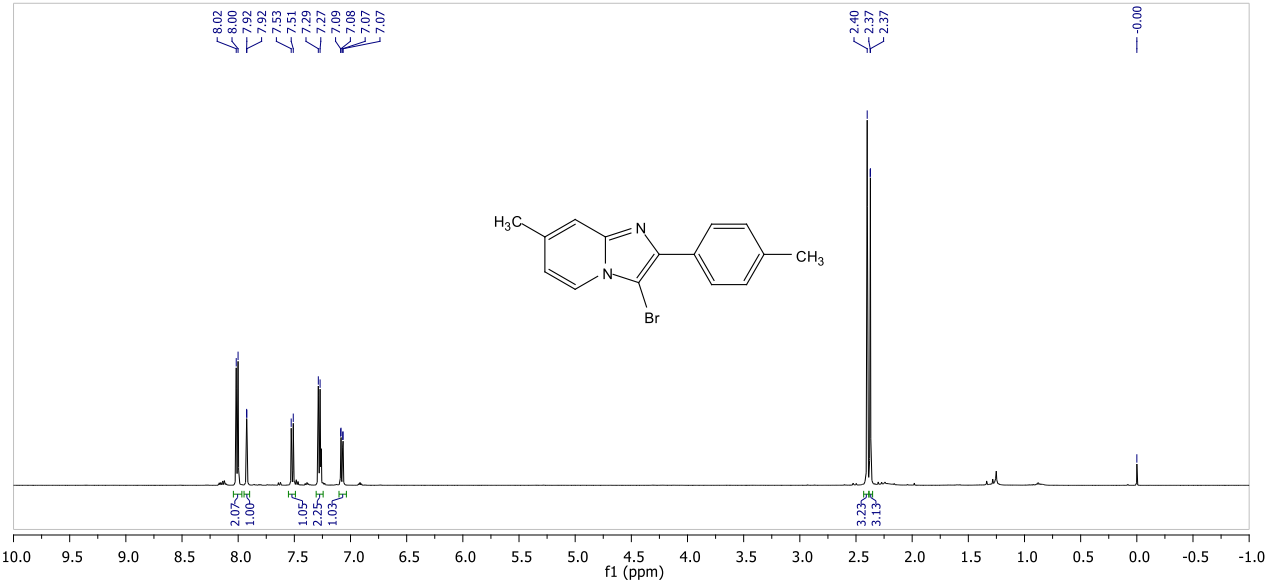
^{1}H NMR (500 MHz, $CDCl_3$) of compound **2aa**



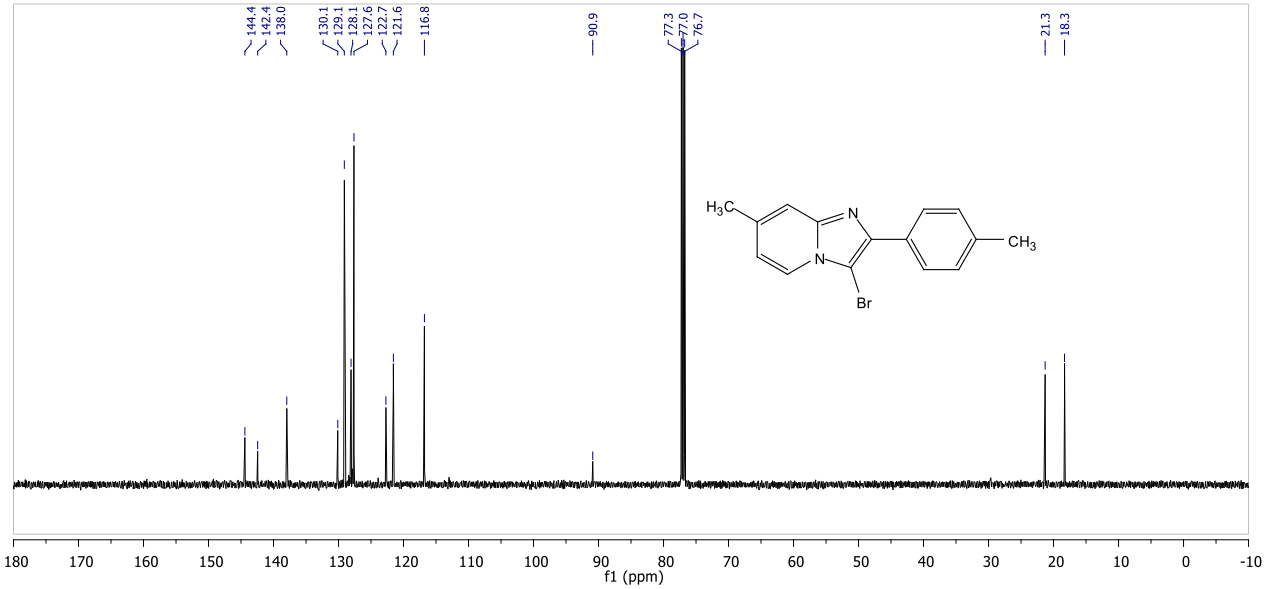
^{13}C NMR (126 MHz, $CDCl_3$) of compound **2aa**



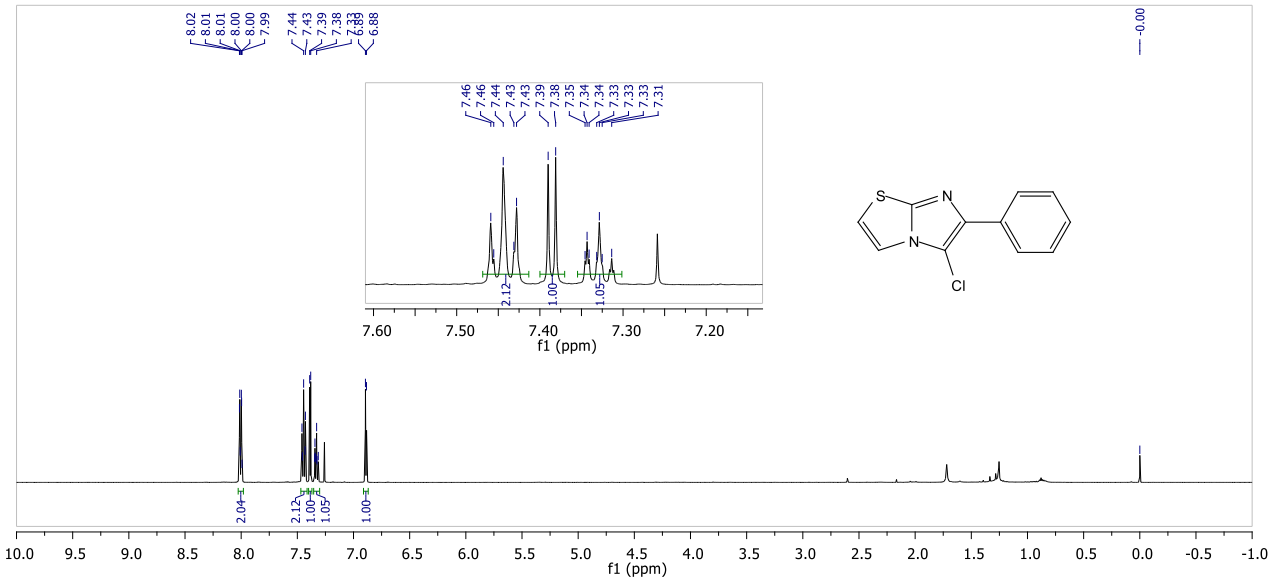
^{1}H NMR (500 MHz, $CDCl_3$) of compound **2ab**



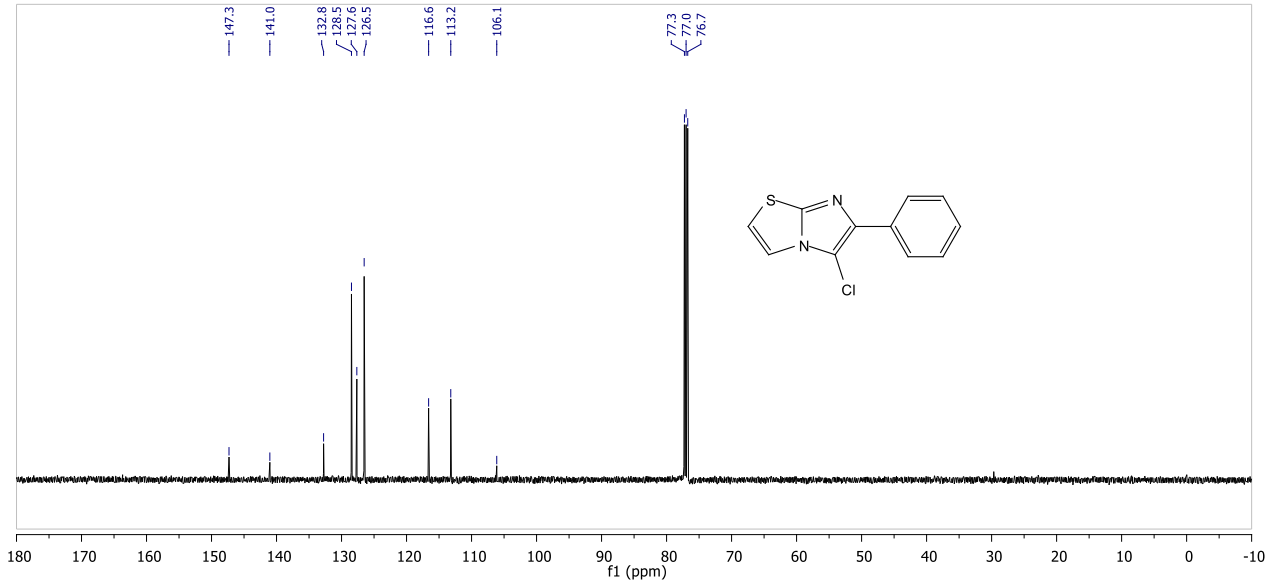
^{13}C NMR (126 MHz, $CDCl_3$) of compound **2ab**



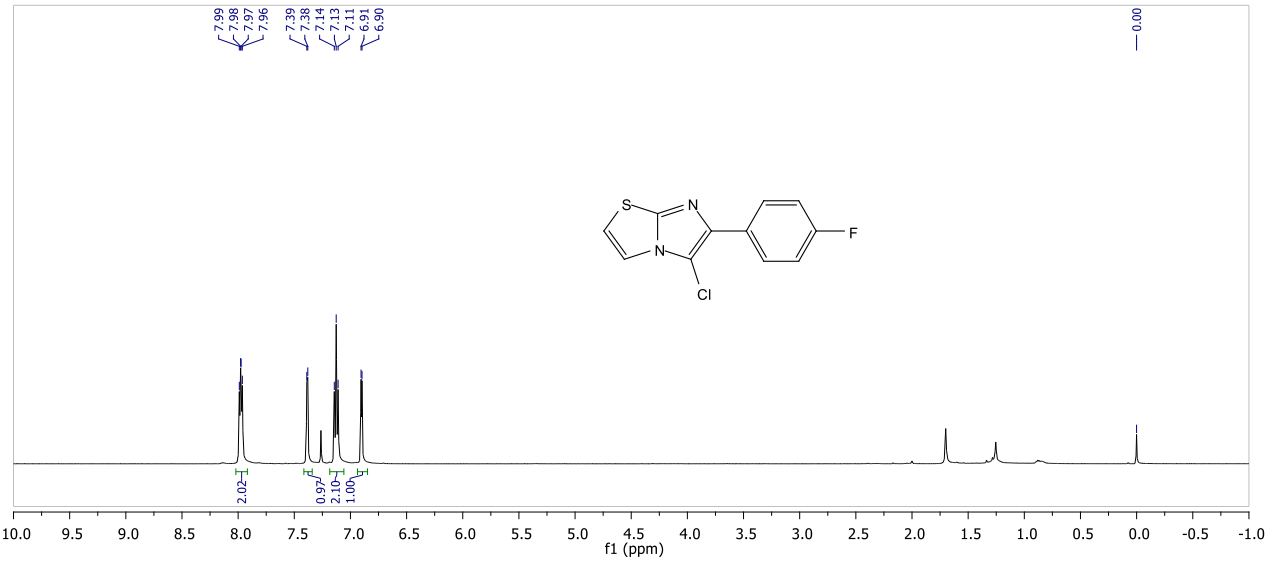
^{1}H NMR (500 MHz, $CDCl_3$) of compound **3a**



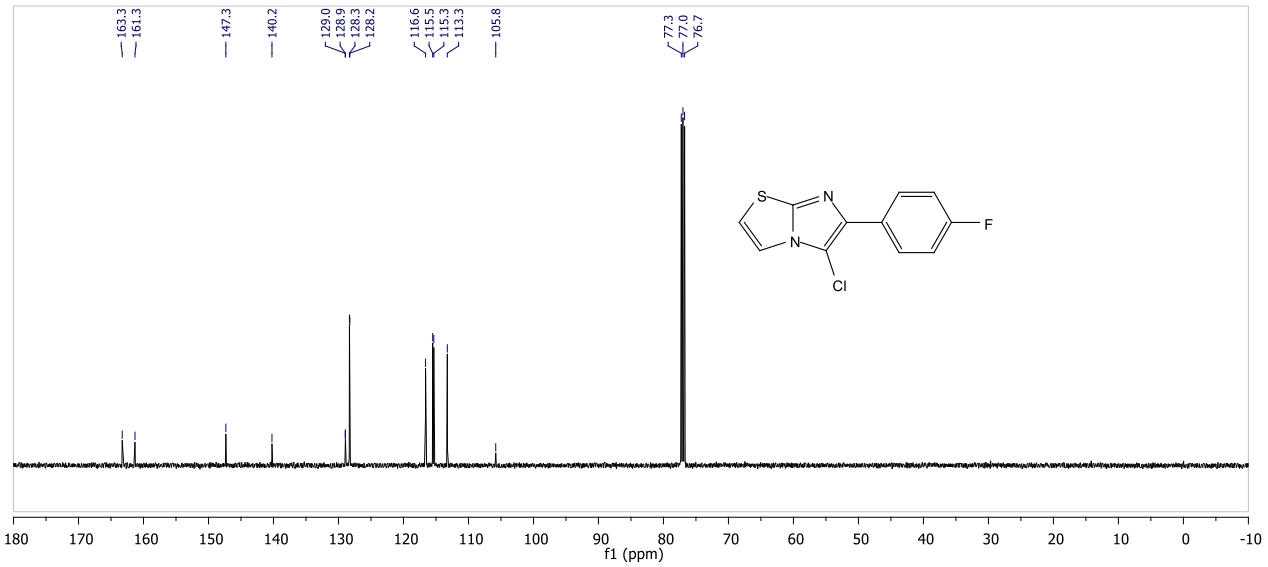
^{13}C NMR (126 MHz, $CDCl_3$) of compound **3a**



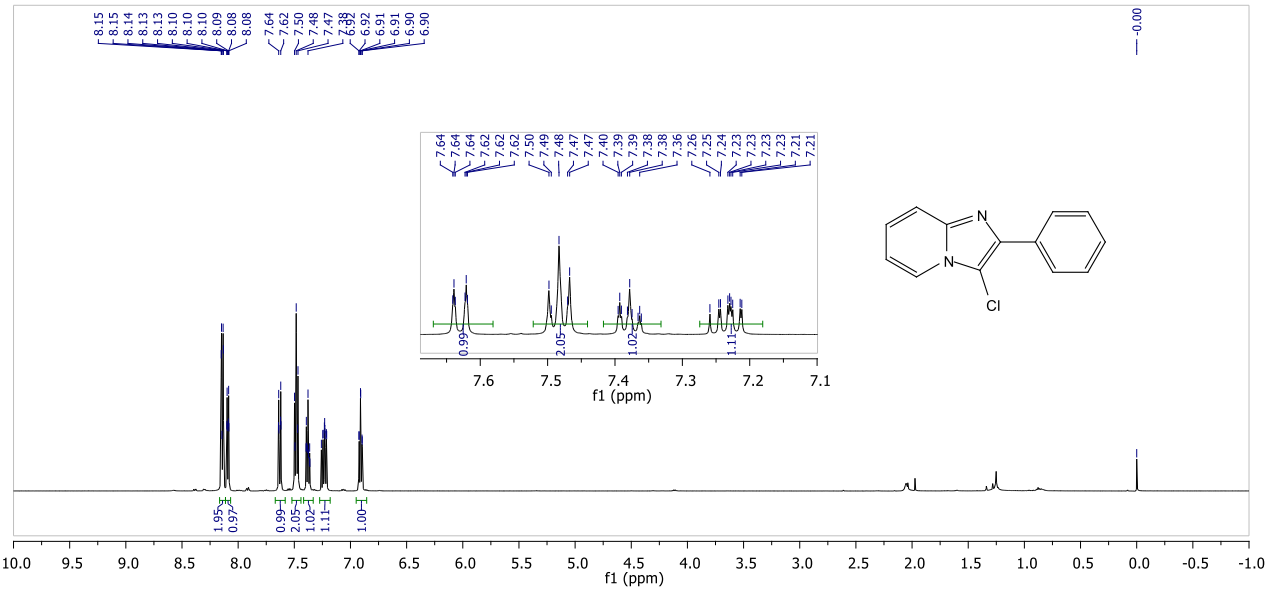
^{1}H NMR (500 MHz, $CDCl_3$) of compound **3b**



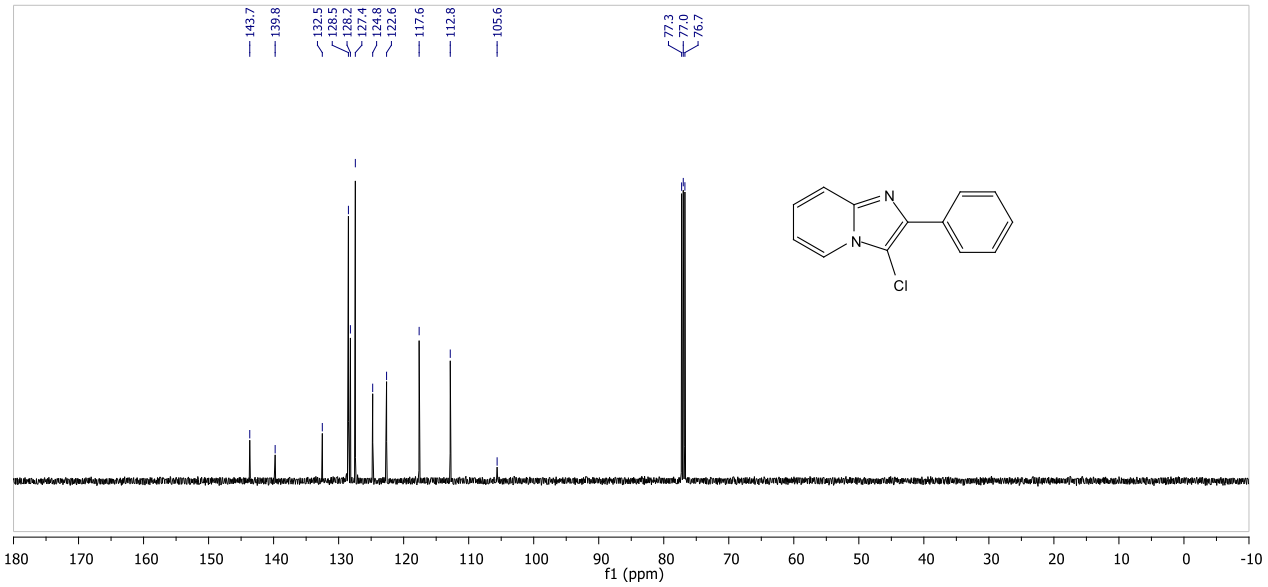
^{13}C NMR (126 MHz, $CDCl_3$) of compound **3b**



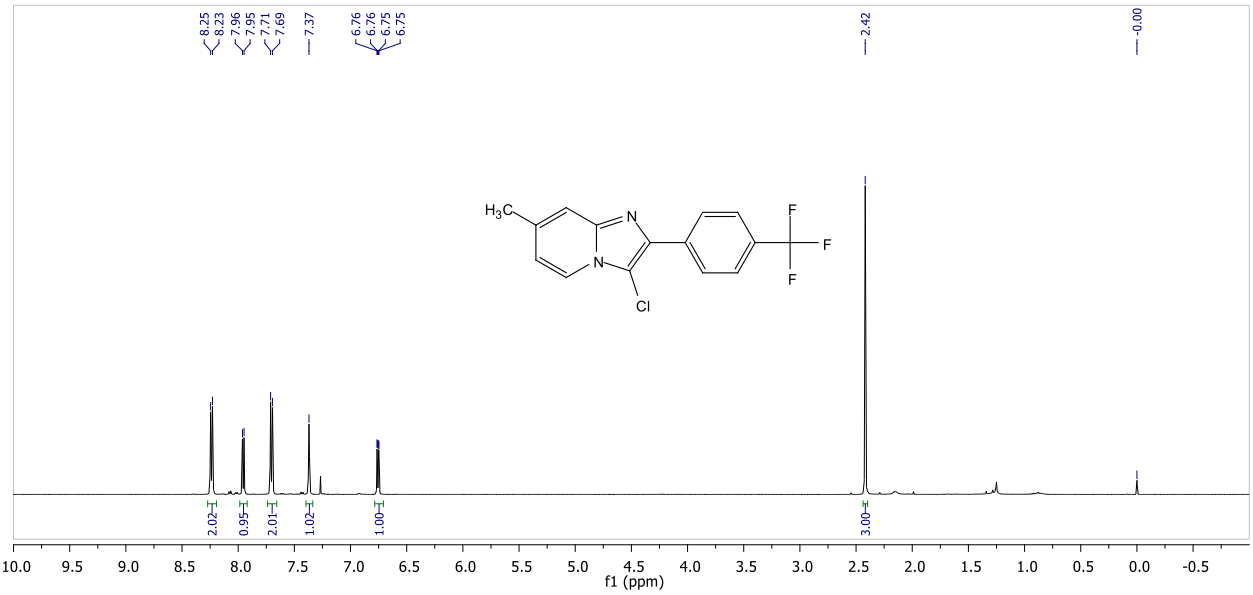
^{1}H NMR (500 MHz, $CDCl_3$) of compound **3c**



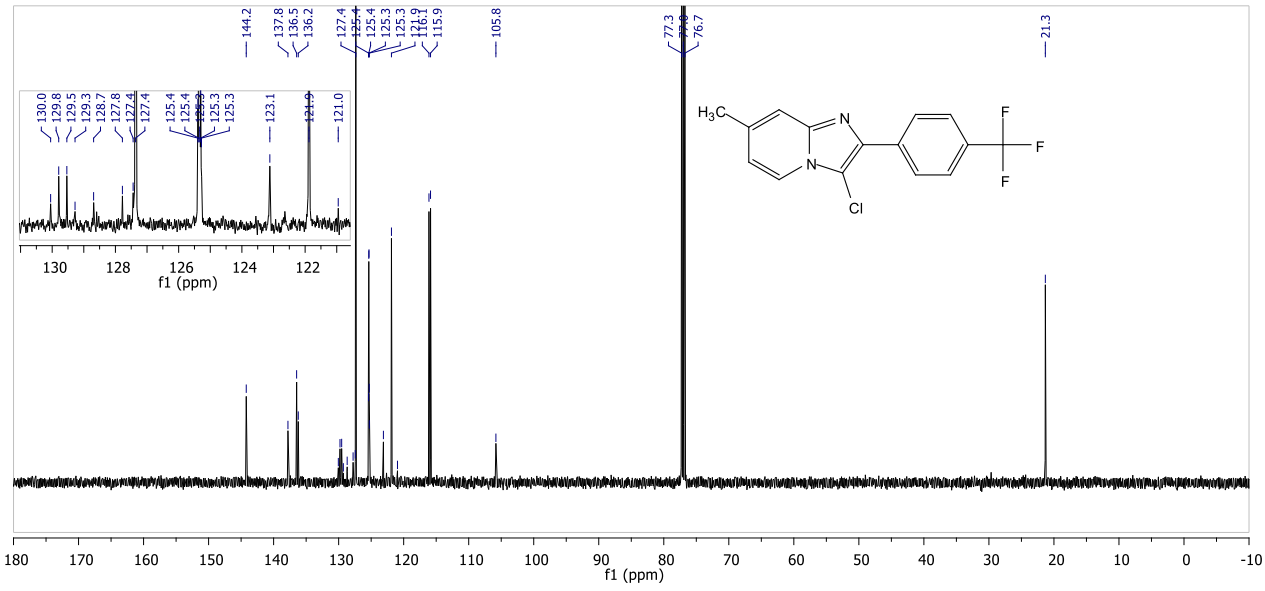
^{13}C NMR (126 MHz, $CDCl_3$) of compound **3c**



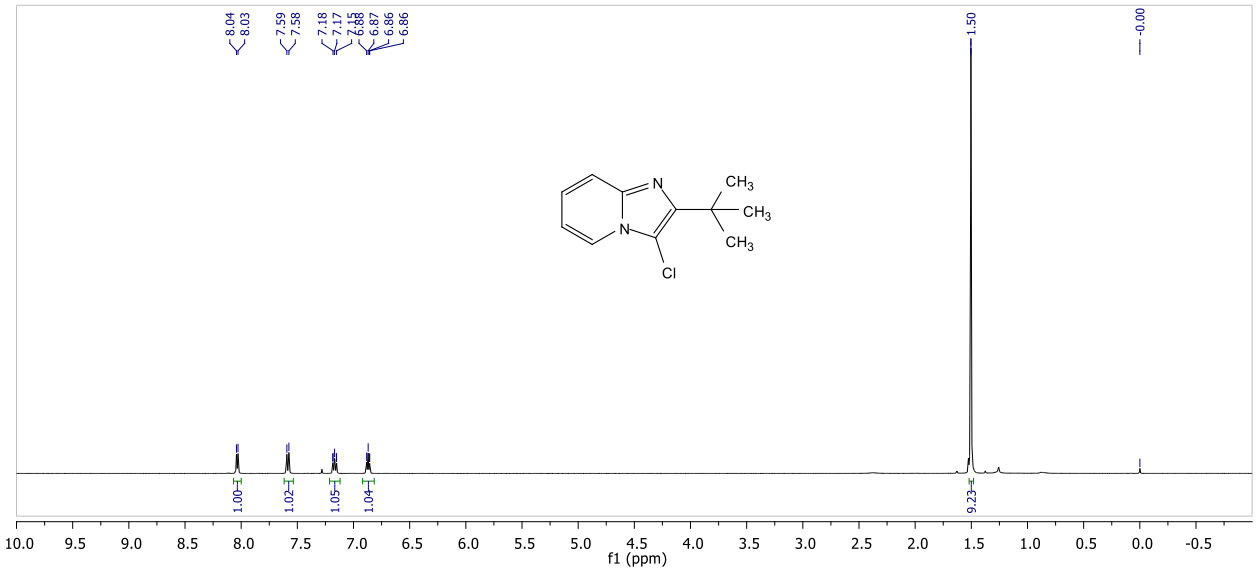
^{1}H NMR (500 MHz, $CDCl_3$) of compound **3d**



^{13}C NMR (126 MHz, $CDCl_3$) of compound **3d**



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



^{13}C NMR (126 MHz, $CDCl_3$) of compound **3e**