Supporting Information

6π-Electrocyclization in Water: Microwave-Assisted Synthesis of Polyheterocyclic-Fused Quinoline-2-Thiones

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Table of Contents

1. General Information

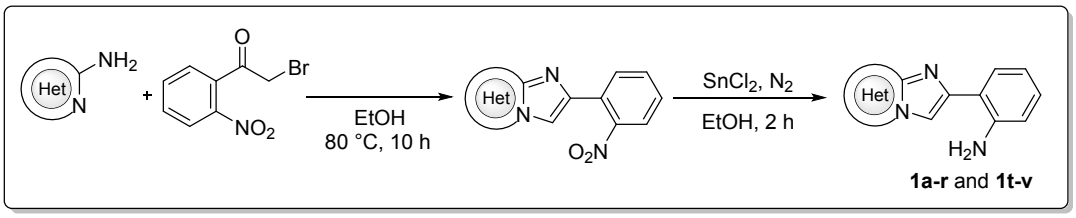
All reagents were purchased and used without further purification. TLC was performed on silica gel plates (F254, 200-300 mesh) using UV light (254/366 nm) for detection and column chromatography was performed on silica gel (200-300 mesh). ^{1}H, ^{13}C and ^{19}F NMR spectra were measured on a Bruker Avance 400 MHz spectrometer operating at 400 MHz, 101 MHz and 376 MHz, respectively. All NMR spectra were recorded in $CDCl_3$ or DMSO at room temperature (20 ± 2 °C). To display multiplicities and signal forms correctly the following abbreviations were used: s = singlet, d = doublet, t = triplet, m = multiplet. ^{1}H and ^{13}C chemical shifts are quoted in parts per million downfield from TMS. High resolution mass spectra (HRMS) were obtained with a Waters Micromass Q-Tof Micro instrument using the ESI technique. X-ray single-crystal diffraction data were collected on a Bruker SMART1000 CCD diffractometer with Mo-Kα radiation (λ = 0.71073 Å) at variable temperatures. Microwave-assisted reactions were conducted in the microwave reactor (2.45 GHz, maximum power 300 W) using a focused single-mode microwave synthesis system (Discover, CEM, USA) (Figure S1).

Figure S1. Pictures of 10 mL microwave reaction vial (Left) and 30 mL microwave reaction vial (Center) used in the experiment and the irradiation by microwave reactor (Right).

2. Experimental Procedures

2.1 Preparation of Starting Materials

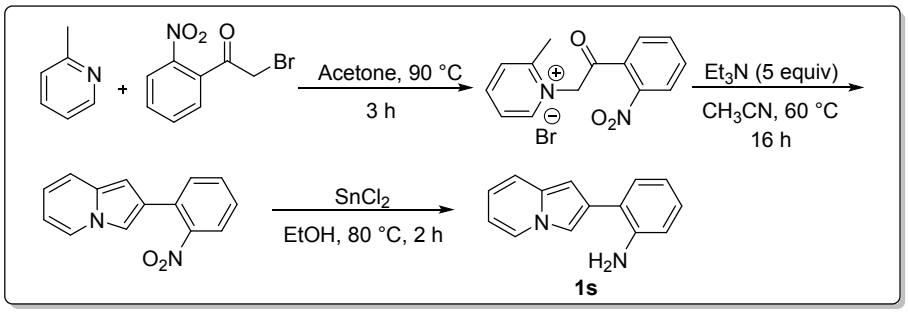
2.1.1 General Procedures for the Synthesis of 2-(imidazo[1,2-*a*]pyridin-2-yl)anilines (1a-r and 1t-v)[1]



A solution of 2-amino-pyridine (7.0 mmol, 0.66 g) and 2-bromo-1-(2-nitrophenyl)ethan-1-one (7.0 mmol, 1.70 g) in ethanol (28.0 mL) were added to the sealed tube for 10 h. Afterward, the mixture was basified to pH 8 with $NaHCO_3$ solution and extracted with DCM (60.0 mL). The organic layer

was washed with water (30.0 mL) and brine (30.0 mL) and dried over anhydrous Na_2SO_4. The organic layer was evaporated under reduced pressure. The residue was purified by silica gel chromatography using petroleum ether/ethyl acetate (70/30, v/v) to afford the expected product. A solution of 2-(2-nitrophenyl)imidazo[1,2-*a*]pyridine (5.0 mmol, 1.19 g) and $SnCl_2$ (25.0 mmol, 4.74 g) in ethanol (100.0 mL) was refluxed under nitrogen for 2 h. After cooled to room temperature, the residue was basified to pH 8 with $NaHCO_3$ solution and extracted with EtOAc (100.0 mL), and it was filtered through a bed of celite. The organic layer was finally washed with water (80.0 mL) and brine (80.0 mL) and dried over anhydrous Na_2SO_4. The organic layer was evaporated under reduced pressure. The residue was purified by silica gel chromatography using petroleum ether/ethyl acetate (75/25, v/v) to afford 2-(imidazo[1,2-*a*]pyridin-2-yl)anilines (**1a-r** and **1t-v**).

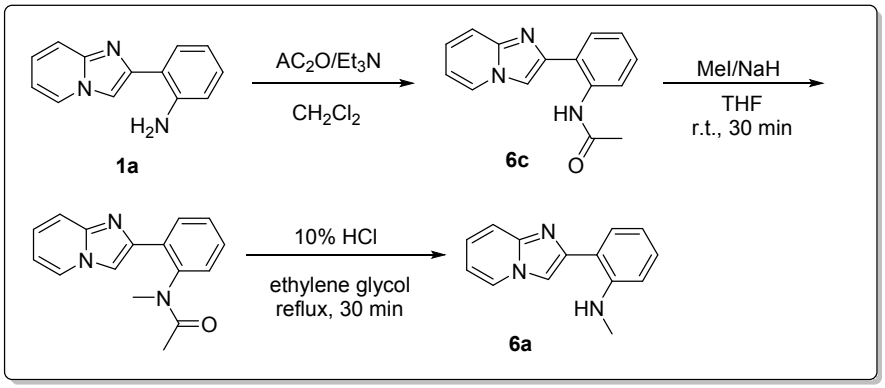
2.1.2 General Procedures for the Synthesis of 2-(indolizin-2-yl)aniline (1s)[2]



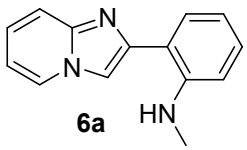
To a mixture of 2-bromo-1-(2-nitrophenyl)ethan-1-one (5.0 mmol, 1.21 g) in acetone (10.0 mL), 2-methylpyridine (6.5 mmol, 0.60 g) was added to the sealed tube. Then, the reaction mixture stirred at 90 °C for 3 h. After cooled to room temperature, the reaction mixture was suction-filtered and washed with CH_2Cl_2 (15.0 mL). The solid was used directly for the next step without further purification. To a mixture of indolizinium salt (5.0 mmol, 1.68 g) and Et_3N (25.0 mmol) in CH_3CN (20.0 mL) were stirred at 60 °C for 16 h. After cooled to room temperature, solvent was removed under reduced pressure. The residue was purified by column chromatography to afford the expected product. A solution of 2-(2-nitrophenyl)indolizine (5.0 mmol, 1.19 g) and $SnCl_2$ (25.0 mmol, 4.74 g) in ethanol (100.0 mL) was refluxed under nitrogen for 2 h. The solution was allowed to cool down, and then the pH was made slightly basic (pH 8) by addition of saturated $NaHCO_3$ solution. EtOAc (100.0 mL) was added to the mixture, and it was filtered through a bed of celite. The organic layer was finally washed with water (80.0 mL) and brine (80.0 mL) and dried over anhydrous Na_2SO_4. The organic layer was evaporated to dryness under reduced pressure. The residue was purified by silica gel chromatography using petroleum ether/ethyl acetate (80/20, v/v) to afford 2-(indolizin-2-yl)aniline (**1s**).

*2.2 General Procedures for the Synthesis of 2-(imidazo[1,2-a]pyridin-2-yl)aniline with Different Protecting Groups (**6a-6d**)*

2.2.1 General Procedures for the Synthesis of 2-(imidazo[1,2-*a*]pyridin-2-yl)-*N*-methylaniline (6a)[3]



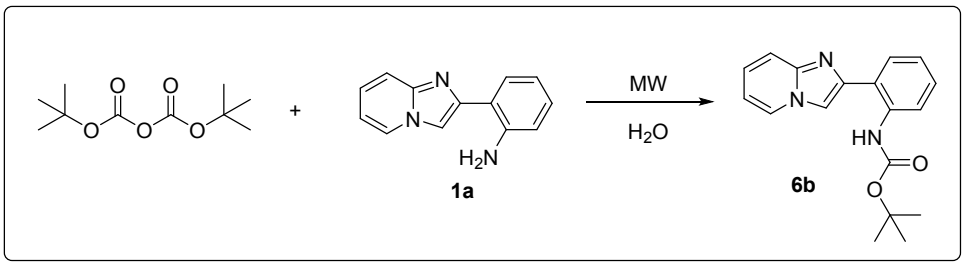
A solution of acetic anhydride (1.2 mmol) was added dropwise over 15 min to a magnetically stirred solution of 2-(imidazo[1,2-*a*]pyridin-2-yl)aniline **1a** (1.0 mmol) and triethylamine (1.2 mmol) in dry CH_2Cl_2 (15.0 mL). The reaction was monitored by TLC. After the reaction was completed, the solvent was evaporated under reduced pressure. Water was added to wash the resulting solid, and the mixture was filtered to give the *N*-(2-(imidazo[1,2-*a*]pyridin-2-yl)phenyl)acetamide **6c**. Sodium hydride (1.2 mmol) was added to the magnetically stirred *N*-(2-(imidazo[1,2-*a*]pyridin-2-yl)phenyl)acetamide (**6c**, 1.0 mmol) in anhydrous THF, and iodomethane (1.2 mmol) was added dropwise to the mixture, which was maintained below 5 °C for 0.5 h, and stirred at room temperature. The reaction was monitored by TLC. After the reaction was completed, the reaction mixture was extracted between saturated aqueous NH_4Cl and ethyl acetate for three times. The organic layers were combined, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by flash chromatography with petroleum ether/ethyl acetate to give the *N*-(2-(imidazo[1,2-*a*]pyridin-2-yl)phenyl)-*N*-methylacetamide. Concentrated HCl (0.25 mL) was added to a stirred solution of *N*-(2-(imidazo[1,2-*a*]pyridin-2-yl)phenyl)-*N*-methylacetamide (1.0 mmol) in ethylene glycol (0.75 mL). The reaction mixture was heated to reflux and the reaction was monitored by TLC. When the reaction was completed, the reaction mixture was extracted between water and ethyl acetate. The combined organic layers, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by flash chromatography with petroleum ether/ethyl acetate to give 2-(imidazo[1,2-*a*]pyridin-2-yl)-*N*-methylaniline (**6a**).



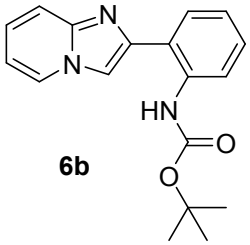
2-(imidazo[1,2-a]pyridin-2-yl)-N-methylaniline (6a): white solid (34.81 mg, 78% yield). ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.55 (m, J = 6.7, 1.1 Hz, 1H), 8.34 (s, 1H), 8.26 (m, J = 4.8 Hz, 1H), 7.65 – 7.60 (m, 2H), 7.27 (m, J = 9.0, 6.8, 1.2 Hz, 1H), 7.20 – 7.15 (m, 1H), 6.95 (m, J = 6.8, 1.1 Hz, 1H), 6.69 – 6.61 (m, 2H), 2.88 (d, J = 5.1 Hz, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 147.96, 146.11, 143.85, 129.46, 127.98, 126.78, 125.10, 116.61, 115.98, 115.51, 113.05, 110.65, 109.38, 30.11. HRMS Calcd for $C_{14}H_{14}N_3$ $[M + H]^+$: 224.1182, found: 224.1181.

2.2.2 General Procedures for the Synthesis of Boc-, Ac- and Ts- Protecting 2-(imidazo[1,2-

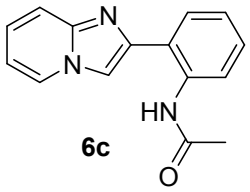
***a*]pyridin-2-yl)aniline (exampled by 6b)**[4]



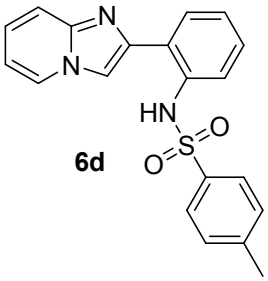
A mixture of 2-(imidazo[1,2-*a*]pyridin-2-yl)aniline **1a** (0.2 mmol, 41.82 mg), di-*tert*-butyl dicarbonate (0.22 mmol) and H_2O (0.5 mL) were added to a 10 mL microwave reaction vial and the reaction mixture was heated to 80 °C by using a focused single-mode microwave synthesis system (Discover, CEM, USA) under air and then irradiated a further 10 minutes. Afterward, the product was suction-filtered and washed with CH_2Cl_2 (3×5.0 mL) without further purification.



tert-butyl (2-(imidazo[1,2-a]pyridin-2-yl)phenyl)carbamate (6b): white solid (59.37 mg, 96% yield). ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.84 (s, 1H), 8.60 (d, J = 6.7 Hz, 1H), 8.47 (s, 1H), 8.27 (d, J = 8.3 Hz, 1H), 7.81 (dd, J = 7.8, 1.2 Hz, 1H), 7.63 (d, J = 9.0 Hz, 1H), 7.38 – 7.28 (m, 2H), 7.10 – 7.05 (m, 1H), 7.04 – 6.98 (m, 1H), 1.50 (s, 9H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 153.06, 144.25, 143.92, 137.54, 128.92, 127.99, 127.26, 126.26, 122.52, 119.80, 119.29, 116.72, 113.60, 110.75, 79.67, 28.50. HRMS Calcd for $C_{18}H_{20}N_3O_2$ $[M + H]^+$: 310.1550, found: 310.1558.

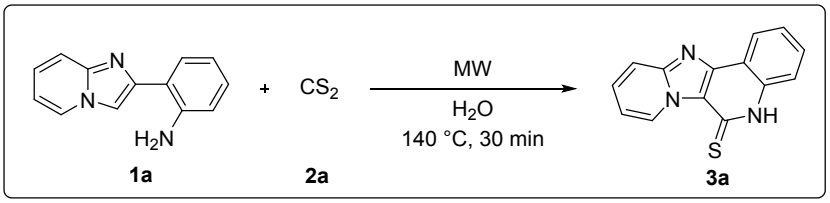


N-(2-(imidazo[1,2-a]pyridin-2-yl)phenyl)acetamide (6c): green solid (45.70 mg, 91% yield). ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.51 (s, 1H), 8.63 – 8.57 (m, 1H), 8.48 (d, J = 8.7 Hz, 2H), 7.87 (d, J = 7.6 Hz, 1H), 7.70 (d, J = 9.0 Hz, 1H), 7.33 (m, J = 18.1, 7.6 Hz, 2H), 7.14 (t, J = 7.3 Hz, 1H), 7.01 (t, J = 6.5 Hz, 1H), 2.20 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 168.51, 144.00, 128.78, 127.90, 127.27, 126.24, 123.57, 120.94, 120.52, 116.90, 113.62, 110.96, 25.46. HRMS Calcd for $C_{15}H_{14}N_3O$ $[M + H]^+$: 252.1131, found: 252.1128.



N-(2-(imidazo[1,2-a]pyridin-2-yl)phenyl)-4-methylbenzenesulfonamide (6d): purple solid (69.72 mg, 96% yield). ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.71 (s, 1H), 8.58 (d, J = 6.8 Hz, 1H), 8.38 (s, 1H), 7.78 – 7.71 (m, 2H), 7.56 – 7.49 (m, 3H), 7.41 (m, J = 9.0, 6.8, 1.1 Hz, 1H), 7.30 – 7.25 (m, 1H), 7.17 – 7.10 (m, 3H), 7.05 (m, J = 6.8, 1.0 Hz, 1H), 2.24 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 143.81, 143.27, 136.58, 135.97, 129.90, 129.14, 127.96, 127.34, 127.04, 126.79, 124.57, 121.56, 120.61, 116.72, 113.89, 110.85, 21.33. HRMS Calcd for $C_{20}H_{18}N_3O_2S$ $[M + H]^+$: 364.1114, found: 364.1117.

*2.3 General Procedure for the Synthesis of imidazopyridine fused quinoline-2-thiones (exampled by **3a**)*



A mixture of 2-(imidazo[1,2-*a*]pyridin-2-yl)aniline **1a** (0.2 mmol, 41.82 mg), carbon disulfide **2a** (0.4 mmol) and H_2O (1.0 mL) were added to a 10 mL microwave reaction vial and the reaction mixture was heated to 140 °C by using a focused single-mode microwave synthesis system (Discover, CEM, USA) under air and then irradiated a further 30 minutes. Afterward, the product was isolated by simple filtration and dried in a vacuum drying oven.

2.4 General Procedure for Gram-scale Reaction

A mixture of 2-(imidazo[1,2-*a*]pyridin-2-yl)aniline **1a** (4.5 mmol, 0.94 g), carbon disulfide **2a** (9.0 mmol) were added in a 30 mL microwave reaction vial. Then, H_2O (20.0 mL) was added into this reaction system. The reaction vial was sealed under air and stirred under irradiation of microwave at 140 °C for 30 min. Afterward, the product was isolated by simple filtration and dried in a vacuum drying oven.

*2.5 General Procedure for the Synthesis of 6-(methylthio)pyrido[2',1':2,3]imidazo[4,5-c]quinoline (**4**)*[5]

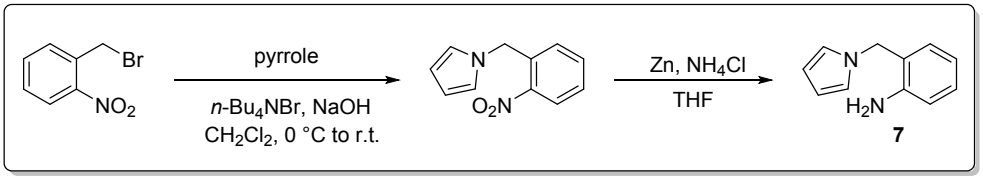
Pyrido[2',1':2,3]imidazo[4,5-*c*]quinoline-6(5*H*)-thione **3a** (0.3 mmol, 75.30 mg), MeI (0.36 mmol), K_2CO_3 (0.45 mmol, 62.20 mg), EtOH (1.0 mL) was added by dropper and the mixture was stirred at 80 °C for 5 h. And the progress of the reaction was monitored by TLC (silica gel). After completion of the reaction, mixture was cooled to ambient temperature, quenched by addition of saturated NH_4Cl (2.0 mL), and extracted with DCM (3×10.0 mL). The organic layers were combined and dried with

anhydrous Na_2SO_4 and concentrated in vacuo, the resulting residue was purified by silica gel column chromatography using petroleum ether/ethyl acetate (20:1) as eluent to afford the product.

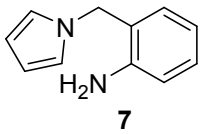
*2.6 General Procedure for the Synthesis of 6-(piperidin-1-yl)pyrido[2',1':2,3]imidazo[4,5-c]quinoline (**5**)*[6]

Pyrido[2',1':2,3]imidazo[4,5-*c*]quinoline-6(5*H*)-thione **3a** (0.3 mmol, 75.30 mg), and piperidine (1.2 mmol) in DMA (2.0 mL) was stirred under an oxygen atmosphere at 110 °C for 24 h. After completion of the reaction, the reaction mixture was cooled to room temperature and then added H_2O (5.0 mL). The aqueous solution was extracted with DCM (3×10.0 mL) and the combined extracts were dried with anhydrous Na_2SO_4. The solvent was removed under reduced pressure by rotary evaporation. Then, the pure product was obtained by flash column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 20:1).

*2.7 General Procedure for the Synthesis of 2-((1H-pyrrol-1-yl)methyl)aniline （**7**）*[7]



A mixture of 1-(bromomethyl)-2-nitrobenzene (5.0 mmol, 1.08 g), pyrrole (10.0 mmol) and tetrabutylammonium bromide (10.0 mmol) were added in 10.0 mL CH_2Cl_2. Then, NaOH (10.0 mmol) was added into this reaction system for 30 min. The reaction vessel was stirred at 25 °C for 2 h. Afterward, the mixture was extracted with DCM and water. The organic layers were combined, dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure by rotary evaporation. Then, the pure product was obtained by flash column chromatography on silica gel. A suspension of 1-(2-nitrobenzyl)-1*H*-pyrrole (5.0 mmol, 1.01 g), zinc powder (45.0 mmol, 2.93 g) and ammonium chloride (30.0 mmol, 1.60 g) in THF (45.0 mL) were refluxed for 10 h under N_2 atmosphere. The resulting suspension was filtered and the solid was washed with dichloromethane. The organic layer was then dried over Na_2SO_4, concentrated under reduced pressure to give crude product. The crude product was purified through silica gel column chromatography using petroleum ether/ethyl acetate as eluent to give pure 2-((1*H*-pyrrol-1-yl)methyl)aniline (**7**).



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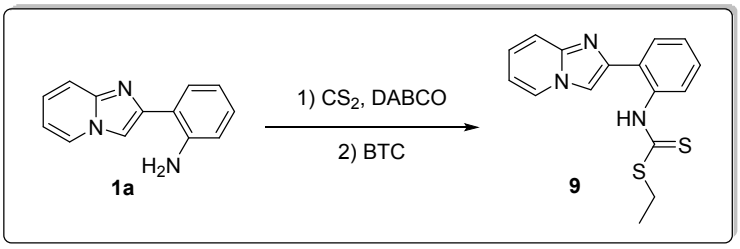
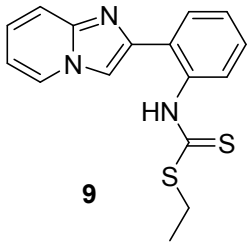
2-((1H-pyrrol-1-yl)methyl)aniline (7): white solid (28.22 mg, 82% yield). ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.01 – 6.95 (m, 1H), 6.79 (t, J = 2.1 Hz, 2H), 6.66 (d, J = 8.0 Hz, 2H), 6.53 – 6.47 (m, 1H), 6.02 (t, J = 2.1 Hz, 2H), 5.03 (s, 2H), 4.95 (s, 2H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 146.24, 128.69, 128.59, 122.39, 121.50, 116.62, 115.37, 108.10, 49.23. HRMS Calcd for $C_{11}H_{13}N_2$ $[M + H]^+$: 173.1073, found: 173.1081.

*2.8 General Procedure for the Synthesis of (2-(imidazo[1,2-a]pyridin-2-yl)phenyl)carbamodithioate (**9**)*[8]

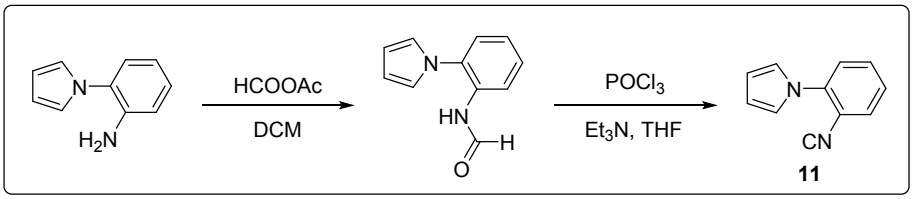


Under an ambient atmosphere, a 25 mL round-bottom flask was charged with 2-(imidazo[1,2-*a*]pyridin-2-yl)aniline **1a** (2.0 mmol, 0.42 g), DABCO (8.0 mmol, 0.90 g), and toluene (4.0 mL) with stirring. CS_2 (4.0 mmol) was added dropwise. The mixture was kept at room temperature overnight. The precipitates were filtered, washed with toluene (3×3.0 mL), and dissolved in $CHCl_3$ (5.0 mL) with stirring. Then, a solution of BTC (1.0 mmol, 0.30 g) in $CHCl_3$ (2.5 mL) was added dropwise at 0 °C. The mixture was stirred at 0 °C for 1 h and heated at reflux for 2 h. The solvent was removed under reduced pressure. The residue was purified by column chromatography on silica gel using a mixture of petroleum ether and ethyl acetate as eluents to afford (2-(imidazo[1,2-*a*]pyridin-2-yl)phenyl)carbamodithioate (**9**).



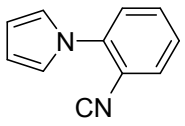
ethyl (2-(imidazo[1,2-a]pyridin-2-yl)phenyl)carbamodithioate (9): white solid (16.28 mg, 26% yield). ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.96 (s, 1H), 8.59 (d, J = 6.8 Hz, 1H), 8.47 (s, 1H), 8.25 (d, J = 8.3 Hz, 1H), 7.83 (d, J = 7.8 Hz, 1H), 7.65 (d, J = 9.1 Hz, 1H), 7.38 – 7.30 (m, 2H), 7.13 – 7.08 (m, 1H), 7.01 (m, J = 6.8, 3.4 Hz, 1H), 4.17 (q, J = 7.1 Hz, 2H), 1.27 (t, J = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 153.86, 144.08, 143.97, 137.12, 129.04, 128.03, 127.27, 126.42, 122.93, 119.98, 119.41, 116.72, 113.90 – 113.31 (m), 110.95 – 110.58 (m), 60.88, 15.00. HRMS Calcd for $C_{16}H_{16}N_3S$ $[M + H]^+$: 314.0780, found: 314.0786.

*2.9 General Procedure for the Synthesis of 1-(2-isocyanophenyl)-1H-pyrrole (**11**)*[9]



To a stirring solution of 2-(1*H*-pyrrol-1-yl)aniline (3.0 mmol, 0.47 g) in DCM (6.0 mL) was added dropwise acetic formic anhydride (7.8 mmol, 0.62 mL) at 0 °C. The mixture was stirred for 2 h at

room temperature. Then, the mixture was quenched with saturated Na_2CO_3 solution and extracted with DCM for three times. The organic layers were combined, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to give the crude formamides. The crude product was used for next dehydration without further purification. The formamides and Et_3N (3.0 mL) were dissolved in THF (6.0 mL) under nitrogen atmosphere. $POCl_3$ (5.2 mmol, 0.49 mL) in THF (1.0 mL) was added slowly to the solution via syringe for a period of 1 h at 0 °C. The reaction mixture was then stirred for another 2 h at 0 °C. After that, the reaction mixture was diluted with 5.0 mL ethyl acetate at 0 °C and slowly quenched with saturated Na_2CO_3 solution with continuous stirring for another 30 min. The crude products were then purified through silica gel column chromatography using petroleum ether/ethyl acetate as eluent to give 1-(2-isocyanophenyl)-1*H*-pyrrole (**11**).



11

***1-(2-isocyanophenyl)-1H-pyrrole (11)*:** yellow oil (16.28 mg, 36% yield). ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.41 – 7.33 (m, 2H), 7.27 – 7.20 (m, 2H), 6.91 (d, *J* = 2.0 Hz, 2H), 6.31 – 6.26 (m, 2H). ^{13}C NMR (151 MHz, Chloroform-*d*) δ 169.14 – 167.84 (m), 136.07, 129.31, 127.60, 126.18, 125.14, 120.29, 109.51. HRMS Calcd for $C_{11}H_9N_2$ $[M + H]^+$: 169.0760, found: 169.0766.

2.10 Calculation for E-factor and EcoScale Score

Table S1. E-factor of Synthesis of Quinoline-2-Thiones System

Item	Reactant 1	Reactant 2	Product
	1a	**2a**	**3a**
Mmol	0.2 mmol	0.4 mmol	0.198 mmol
MW	209.09	76.14	251.05
Mass	41.82 mg	30.46 mg	49.71 mg

$$\text{E-factor} = \frac{\Sigma\text{MW of stiochiometric reactants} + \Sigma\text{MW of desired products}}{\Sigma\text{MW of desired products}}$$

$$= \frac{41.82 + 30.46 - 49.71}{49.71}$$

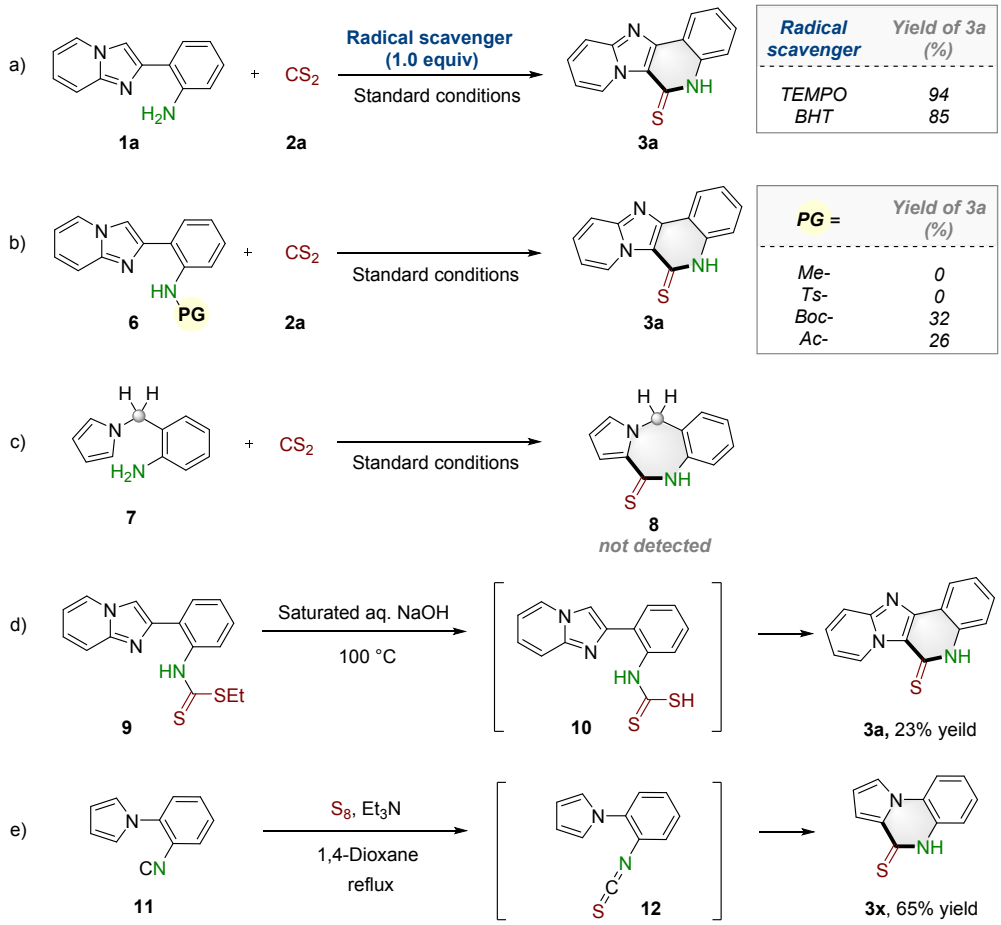
$$= 0.45$$

Table S2. Penalty Points for the Synthesis of Quinoline-2-Thiones System

EcoScale penalty points	Factor	Penalty
1.yield	99%	0.5
2.price	2-(imidazo[1,2-*a*]pyridin-2-yl)aniline	0
	carbon disulfide	0
	H_2O	0
3.safety	2-(imidazo[1,2-*a*]pyridin-2-yl)aniline	0
	carbon disulfide (F, T)	10
	H_2O	0

4.technical setup	microwave heating	2
5.temperature/time	heating, <1 h	2
6.workup and purification	simple filtration	0
total penalty points		***14.5***
EcoScale score		***85.5***

2.11 Mechanistic Studies



Scheme S1. Mechanistic Studies

In order to have a deeper mechanistic insight into this microwave-assisted cyclization reaction, several control experiments were carried out (Scheme S1). Initially, when the well-known radical scavengers, *i.e.*, 2, 2, 6, 6-tetramethylpiperidine 1-oxyl (TEMPO) or 2, 6-di-*tert*-butyl-4-methylphenol (BHT) was added to the model reaction under standard conditions, no obvious declines in yields were observed, ruling out the radical process in this transformation (Scheme S1a). Afterward, the reactivities of *N*-protected 2-(imidazo[1,2-*a*]pyridin-2-yl)anilines **6** were tested. When *N*-methyl and -Ts substituted substates were reacted with CS_2 under standard conditions, no desired product **3a** was detected. While, the *N*-Boc and -Ac protected ones only provided deprotected product **3a** in significantly decreased yields of 32% and 26%, respectively, which implying the condensation of amino group with carbon disulfide could be hindered by *N*-protected groups (Scheme S1b). Next,

the 2-((1*H*-pyrrol-1-yl)methyl)aniline **7** with the insertion of a methylene group between benzene and pyrrole was synthesized to block the 6π-electron conjugated system. Predictably, it failed to give any desired seven-membered cyclic product **8** when reacting with CS_2 under standard conditions (Scheme S1c). Despite considerable efforts have been made to synthesize the key intermediates **A** and **B** which are involved in our proposed mechanism, unfortunately, we are not yet able to obtain them, and there are no previous literatures reporting the successful cases of preparing them. However, a one-pot formation of the cyclization products **3a** and **3x** was observed during the synthesis of corresponding intermediates carbamodithioic acid **10** and thioisocyanate **12** from ethyl carbamodithioate **9** and isocyanide **11** (Scheme S1d-e), which evidently supports our proposed mechanism that the formation of intermediates carbamodithioic acid and thioisocyanate is necessary in this reaction.

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3. Crystal Data and Structure Refinement for 3q

Identification code	1967133
Empirical formula	$C_{17}H_{15}F_3N_3OS_2$
Formula weight	398.44
Temperature/K	298.15
Crystal system	triclinic
Space group	P-1
a/Å	7.1450(6)
b/Å	10.3161(9)
c/Å	12.2769(11)
α/°	101.410(3)
β/°	103.927(3)
γ/°	93.498(2)
Volume/Å^3	855.32(13)
Z	2
ρ_{calc}g/cm^3	1.547
μ/mm^{-1}	0.354
F(000)	410.0
Crystal size/mm^3	0.42 × 0.21 × 0.13
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	5.912 to 50.196
Index ranges	$-8 \le h \le 8$, $-12 \le k \le 12$, $-14 \le l \le 14$
Reflections collected	4416
Independent reflections	3001 [R_{int} = 0.0303, R_{sigma} = 0.0458]
Data/restraints/parameters	3001/0/238
Goodness-of-fit on F^2	1.029
Final R indexes [I>=2σ (I)]	R_1 = 0.0520, wR_2 = 0.1399
Final R indexes [all data]	R_1 = 0.0629, wR_2 = 0.1501
Largest diff. peak/hole / e Å^{-3}	0.52/-0.36

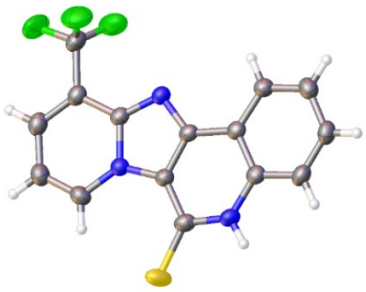
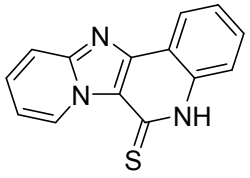


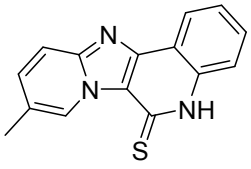
Figure S1. ORTEP view (30% ellipsoid contour probability) of X-crystal structure of **3q**.

4. Characterization Data



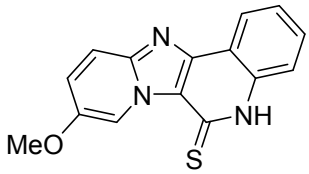
3a

Pyrido[2',1':2,3]imidazo[4,5-c]quinoline-6(5H)-thione (3a): red solid (49.70 mg, 99% yield), mp > 300 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 13.37 (s, 1H), 10.85 (d, J = 6.9 Hz, 1H), 8.42 (d, J = 7.9 Hz, 1H), 8.03 (d, J = 9.1 Hz, 1H), 7.88 (dd, J = 17.3, 8.0 Hz, 2H), 7.71 (t, J = 7.7 Hz, 1H), 7.53 (t, J = 7.5 Hz, 1H), 7.41 (t, J = 6.9 Hz, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 169.26, 162.74, 150.54, 144.60, 138.24, 132.26, 130.59, 127.72, 124.54, 123.32, 122.21, 117.75, 117.30, 114.03. HRMS Calcd for $C_{14}H_{10}N_3S$ $[M + H]^+$: 252.0590, found: 252.0595.



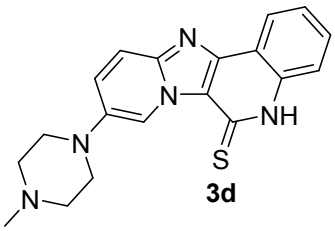
3b

9-methylpyrido[2',1':2,3]imidazo[4,5-c]quinoline-6(5H)-thione (3b): red solid (51.95 mg, 98% yield), mp > 300 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 13.26 (s, 1H), 10.67 (s, 1H), 8.37 (d, J = 7.8 Hz, 1H), 7.91 (d, J = 9.1 Hz, 1H), 7.83 (d, J = 8.3 Hz, 1H), 7.74 (d, J = 9.2 Hz, 1H), 7.68 (t, J = 7.6 Hz, 1H), 7.49 (t, J = 7.5 Hz, 1H), 2.51 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 169.19, 149.52, 144.46, 138.12, 135.02, 130.52, 125.28, 124.57, 123.54, 123.27, 122.01, 117.80, 117.26, 116.62, 18.50. HRMS Calcd for $C_{15}H_{12}N_3S$ $[M + H]^+$: 266.0746, found: 266.0752.



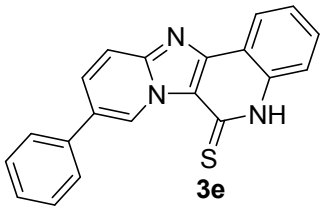
3c

9-methoxypyrido[2',1':2,3]imidazo[4,5-c]quinoline-6(5H)-thione (3c): pink solid (55.09 mg, 98% yield), mp > 300 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 13.30 (s, 1H), 10.66 (d, J = 2.3 Hz, 1H), 8.37 (d, J = 7.6 Hz, 1H), 7.96 (d, J = 9.7 Hz, 1H), 7.83 (d, J = 8.3 Hz, 1H), 7.72 – 7.66 (m, 2H), 7.50 (t, J = 7.3 Hz, 1H), 3.94 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 169.31, 149.23, 147.37, 144.43, 138.04, 130.37, 126.14, 124.61, 123.12, 122.72, 118.07, 117.55, 117.34, 110.05, 56.77. HRMS Calcd for $C_{15}H_{12}N_3OS$ $[M + H]^+$: 282.0696, found: 282.0701.



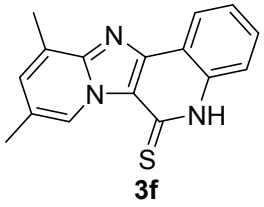
3d

9-(4-methylpiperazin-1-yl)pyrido[2',1':2,3]imidazo[4,5-c]quinoline-6(5H)-thione (3d): red solid (68.43 mg, 98% yield), mp 277.2 - 278.5 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 13.21 (s, 1H), 10.46 (s, 1H), 8.35 (d, J = 7.5 Hz, 1H), 7.89 (s, 2H), 7.81 (d, J = 8.3 Hz, 1H), 7.68 – 7.63 (m, 1H), 7.48 (t, J = 7.5 Hz, 1H), 3.23 – 3.17 (m, 4H), 2.59 – 2.54 (m, 4H), 2.27 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 169.15, 146.90, 144.26, 140.56, 138.04, 130.22, 127.42, 124.50, 123.09, 122.57, 118.14, 117.29, 116.89, 112.29, 54.74, 49.48, 46.13. HRMS Calcd for $C_{19}H_{20}N_5S$ [M + H]$^+$: 350.1434, found: 350.1429.



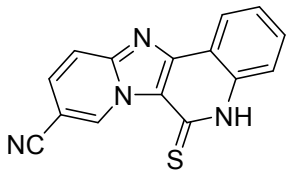
3e

9-phenylpyrido[2',1':2,3]imidazo[4,5-c]quinoline-6(5H)-thione (3e): red solid (62.79 mg, 96% yield), mp > 300 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 13.38 (s, 1H), 11.21 (s, 1H), 8.38 (d, J = 7.8 Hz, 1H), 8.20 (dd, J = 9.4, 1.8 Hz, 1H), 8.06 (d, J = 9.4 Hz, 1H), 7.83 (d, J = 8.3 Hz, 1H), 7.78 (d, J = 7.4 Hz, 2H), 7.71 – 7.66 (m, 1H), 7.58 (t, J = 7.6 Hz, 2H), 7.49 (m, J = 7.8 Hz, 2H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 169.26, 149.75, 145.07, 138.29, 136.54, 131.81, 130.70, 129.90, 128.74, 127.12, 126.84, 124.66, 124.56, 123.35, 122.35, 117.84, 117.37, 117.33. HRMS Calcd for $C_{20}H_{14}N_3S$ [M + H]$^+$: 328.0903, found: 328.0906.



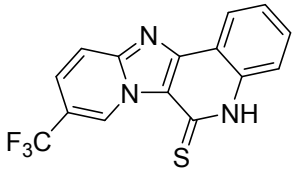
3f

9,11-dimethylpyrido[2',1':2,3]imidazo[4,5-c]quinoline-6(5H)-thione (3f): yellow solid (37.95 mg, 68% yield), mp > 300 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 13.24 (s, 1H), 10.51 (s, 1H), 8.39 (d, J = 7.2 Hz, 1H), 7.82 (d, J = 8.3 Hz, 1H), 7.70 – 7.64 (m, 1H), 7.55 – 7.46 (m, 2H), 2.67 (s, 3H), 2.43 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 169.33, 149.71, 144.00, 138.10, 133.64, 130.39, 126.13, 124.51, 123.30, 123.10, 122.54, 117.98, 117.26, 18.52, 17.19. HRMS Calcd for $C_{16}H_{14}N_3S$ [M + H]$^+$: 280.0903, found: 280.0907.



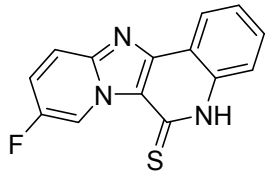
3g

6-thioxo-5,6-dihydropyrido[2',1':2,3]imidazo[4,5-c]quinoline-9-carbonitrile (3g): red solid (52.45 mg, 95% yield), mp > 300 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 13.61 (s, 1H), 11.28 (s, 1H), 8.36 (d, J = 7.8 Hz, 1H), 8.10 (s, 2H), 7.84 (d, J = 8.3 Hz, 1H), 7.74 (t, J = 7.6 Hz, 1H), 7.53 (t, J = 7.4 Hz, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 169.38, 149.87, 145.64, 138.47, 133.40, 131.82, 131.37, 125.01, 123.47, 121.97, 118.31, 117.47, 117.35, 117.11, 98.47. HRMS Calcd for $C_{15}H_9N_4S$ $[M + H]^+$: 277.0542, found: 277.0534.



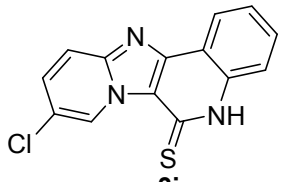
3h

9-(trifluoromethyl)pyrido[2',1':2,3]imidazo[4,5-c]quinoline-6(5H)-thione (3h): white solid (52.96 mg, 83% yield), mp > 300 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 13.64 (s, 1H), 11.40 (s, 1H), 8.44 (d, J = 7.6 Hz, 1H), 8.23 – 8.12 (m, 2H), 7.88 (d, J = 8.4 Hz, 1H), 7.80 – 7.73 (m, 1H), 7.57 (t, J = 7.6 Hz, 1H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 169.54, 150.49, 145.77, 138.49, 131.29, 127.55, 126.50, 125.07, 123.51, 122.45, 118.60, 117.64, 117.55, 115.93, 55.38. ^{19}F NMR (376 MHz, DMSO-d_6) δ -60.07. HRMS Calcd for $C_{15}H_9F_3N_3S$ $[M + H]^+$: 320.0464, found: 320.0461.



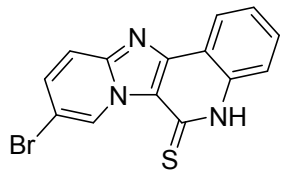
3i

9-fluoropyrido[2',1':2,3]imidazo[4,5-c]quinoline-6(5H)-thione (3i): green solid (46.27 mg, 86% yield), mp > 300 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 13.45 (s, 1H), 10.94 (dd, J = 4.7, 2.5 Hz, 1H), 8.40 (d, J = 7.7 Hz, 1H), 8.11 (dd, J = 9.8, 5.3 Hz, 1H), 8.04 – 7.99 (m, 1H), 7.85 (d, J = 8.3 Hz, 1H), 7.74 – 7.69 (m, 1H), 7.53 (t, J = 7.4 Hz, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 169.56, 152.64 (d, J = 234.6 Hz), 148.30, 145.25, 138.22, 130.80, 124.83, 123.63 (d, J = 25.4 Hz), 123.28, 122.75, 118.20 (d, J = 8.9 Hz), 117.88, 117.45, 114.42 (d, J = 45.2 Hz). ^{19}F NMR (376 MHz, DMSO-d_6) δ -136.90. HRMS Calcd for $C_{14}H_9FN_3S$ $[M + H]^+$: 270.0496, found: 270.0497.



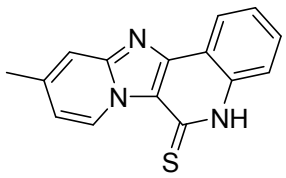
3j

9-chloropyrido[2',1':2,3]imidazo[4,5-c]quinoline-6(5H)-thione (3j): yellow solid (45.60 mg, 80% yield), mp > 300 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 13.48 (s, 1H), 10.98 (s, 1H), 8.38 (d, J = 8.0 Hz, 1H), 8.05 (d, J = 9.6 Hz, 1H), 7.97 – 7.92 (m, 1H), 7.85 (d, J = 8.4 Hz, 1H), 7.72 (t, J = 7.7 Hz, 1H), 7.53 (t, J = 7.5 Hz, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 169.42, 148.96, 144.92, 138.24, 132.75, 130.91, 125.09, 124.86, 123.36, 122.01, 120.39, 118.22, 117.68, 117.43. HRMS Calcd for $C_{14}H_9ClN_3S$ $[M + H]^+$: 286.0200, found: 286.0193.



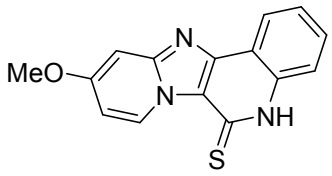
3k

9-bromopyrido[2',1':2,3]imidazo[4,5-c]quinoline-6(5H)-thione (3k): red solid (61.18 mg, 93% yield), mp > 300 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 13.50 (s, 1H), 11.08 (s, 1H), 8.41 (d, J = 7.8 Hz, 1H), 8.02 (d, J = 2.0 Hz, 2H), 7.86 (d, J = 8.3 Hz, 1H), 7.76 – 7.71 (m, 1H), 7.54 (t, J = 7.5 Hz, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 169.37, 149.06, 144.72, 138.25, 134.93, 130.97, 127.21, 124.92, 123.41, 121.86, 118.48, 117.65, 117.44, 107.39. HRMS Calcd for $C_{14}H_9BrN_3S$ $[M + H]^+$: 329.9695, found: 329.9691.



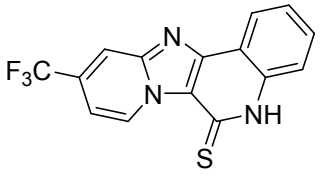
3l

10-methylpyrido[2',1':2,3]imidazo[4,5-c]quinoline-6(5H)-thione (3l): red solid (51.95 mg, 98% yield), mp > 300 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 13.28 (s, 1H), 10.67 (d, J = 7.0 Hz, 1H), 8.39 (d, J = 7.8 Hz, 1H), 7.84 (d, J = 8.4 Hz, 1H), 7.80 (s, 1H), 7.69 (t, J = 7.5 Hz, 1H), 7.50 (t, J = 7.5 Hz, 1H), 7.25 (d, J = 6.9 Hz, 1H), 2.55 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 168.76, 151.05, 144.86, 143.73, 138.28, 130.55, 126.87, 124.50, 123.34, 122.20, 117.81, 117.30, 116.37, 115.82, 21.82. HRMS Calcd for $C_{15}H_{12}N_3S$ $[M + H]^+$: 266.0746, found: 266.0745.



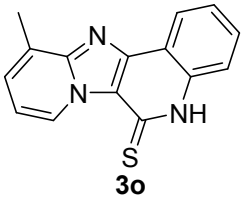
3m

10-methoxypyrido[2',1':2,3]imidazo[4,5-c]quinoline-6(5H)-thione (3m): red solid (55.08 mg, 98% yield), mp > 300 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 13.21 (s, 1H), 10.60 (d, J = 7.6 Hz, 1H), 8.34 (d, J = 7.9 Hz, 1H), 7.83 (d, J = 8.3 Hz, 1H), 7.68 (t, J = 7.5 Hz, 1H), 7.49 (t, J = 7.5 Hz, 1H), 7.40 (d, J = 2.2 Hz, 1H), 7.07 (dd, J = 7.6, 2.4 Hz, 1H), 3.99 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 172.61, 158.00, 150.07, 143.05, 135.20, 133.37, 133.05, 129.18, 127.98, 126.93, 122.40, 122.04, 112.51, 100.58, 61.51. HRMS Calcd for $C_{15}H_{12}N_3OS$ $[M + H]^+$: 282.0696, found: 282.0692.



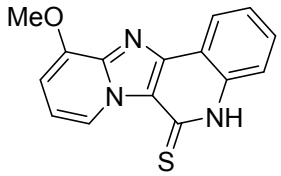
3n

10-(trifluoromethyl)pyrido[2',1':2,3]imidazo[4,5-c]quinoline-6(5H)-thione (3n): yellow solid (48.49 mg, 76% yield), mp 286.2 - 287.5 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 13.53 (s, 1H), 10.95 (d, J = 7.3 Hz, 1H), 8.46 (s, 1H), 8.36 (d, J = 7.4 Hz, 1H), 7.83 (d, J = 8.3 Hz, 1H), 7.73 – 7.64 (m, 2H), 7.53 – 7.49 (m, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 170.03, 148.87, 145.32, 138.28, 131.07, 128.97, 124.88, 123.36, 122.42, 117.50, 117.40, 115.34, 115.30, 109.33, 109.30. ^{19}F NMR (376 MHz, DMSO-d_6) δ -61.88. HRMS Calcd for $C_{15}H_9F_3N_3S$ $[M + H]^+$: 320.0464, found: 320.0468.



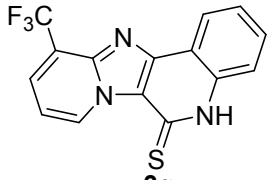
3o

11-methylpyrido[2',1':2,3]imidazo[4,5-c]quinoline-6(5H)-thione (3o): yellow solid (48.77 mg, 92% yield), mp > 300 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 13.34 (s, 1H), 10.72 (d, J = 6.8 Hz, 1H), 8.46 – 8.43 (m, 1H), 7.86 (d, J = 8.3 Hz, 1H), 7.73 – 7.68 (m, 2H), 7.54 – 7.50 (m, 1H), 7.31 (t, J = 7.0 Hz, 1H), 2.74 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 169.42, 150.80, 144.16, 138.25, 130.85, 130.57, 126.93, 125.53, 124.60, 123.41, 122.76, 117.93, 117.33, 114.01, 17.33. HRMS Calcd for $C_{15}H_{12}N_3S$ $[M + H]^+$: 266.0746, found: 266.0744.



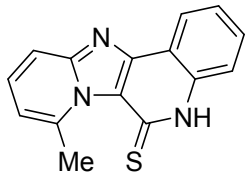
3p

11-methoxypyrido[2',1':2,3]imidazo[4,5-c]quinoline-6(5H)-thione (3p): yellow solid (55.08 mg, 98% yield), mp > 300 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 13.35 (s, 1H), 10.42 (dd, J = 6.2, 1.6 Hz, 1H), 8.42 (d, J = 7.0 Hz, 1H), 7.84 (d, J = 8.3 Hz, 1H), 7.72 – 7.67 (m, 1H), 7.54 – 7.49 (m, 1H), 7.33 – 7.26 (m, 2H), 4.08 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 169.67, 148.43, 144.73, 143.60, 138.21, 130.51, 124.69, 123.30, 123.07, 120.27, 118.04, 117.29, 114.08, 109.03, 56.70. HRMS Calcd for $C_{15}H_{12}N_3OS$ $[M + H]^+$: 282.0696, found: 282.0697.



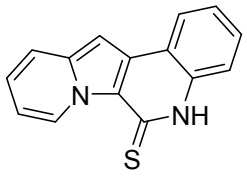
3q

11-(trifluoromethyl)pyrido[2',1':2,3]imidazo[4,5-c]quinoline-6(5H)-thione (3q): yellow solid (59.98 mg, 94% yield), mp > 300 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 13.61 (s, 1H), 11.10 (d, J = 6.9 Hz, 1H), 8.47 – 8.44 (m, 1H), 8.35 (d, J = 7.3 Hz, 1H), 7.89 (d, J = 8.3 Hz, 1H), 7.78 – 7.74 (m, 1H), 7.58 – 7.52 (m, 2H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 169.74, 146.08, 144.83, 138.45, 131.43, 131.20, 126.11, 124.99, 123.60, 122.39, 117.52, 117.44, 112.89, 55.37. ^{19}F NMR (376 MHz, DMSO-d_6) δ -61.55. HRMS Calcd for $C_{15}H_9F_3N_3S$ $[M + H]^+$: 320.0464, found: 320.0464.



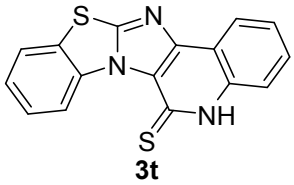
3r

8-methylpyrido[2',1':2,3]imidazo[4,5-c]quinoline-6(5H)-thione (3r): brown solid (49.30 mg, 93% yield), mp 291.8 – 293.1 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 13.07 (s, 1H), 8.34 (d, J = 7.7 Hz, 1H), 7.77 (dd, J = 4.5, 3.0 Hz, 3H), 7.68 – 7.63 (m, 1H), 7.47 – 7.42 (m, 1H), 7.15 – 7.11 (m, 1H), 3.34 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 171.44, 153.24, 146.82, 142.89, 138.69, 132.85, 130.81, 126.36, 124.14, 123.46, 117.59, 116.84, 116.68, 114.70, 27.00. HRMS Calcd for $C_{15}H_{12}N_3S$ $[M + H]^+$: 266.0746, found: 266.0754.



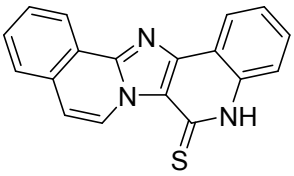
3s

indolizino[3,2-c]quinoline-6(5H)-thione (3s): brown solid (49.30 mg, 99% yield), mp >300 °C. ^{1}H NMR (400 MHz, DMSO-d6) δ 12.87 (s, 1H), 11.29 (d, J = 7.2 Hz, 1H), 8.32 (d, J = 7.3 Hz, 1H), 7.91 (d, J = 8.9 Hz, 1H), 7.79 (d, J = 8.1 Hz, 1H), 7.61 – 7.56 (m, 1H), 7.50 – 7.41 (m, 3H), 7.11 (m, J = 7.0, 1.2 Hz, 1H). ^{13}C NMR (101 MHz, DMSO-d6) δ 185.51, 168.24, 140.89, 136.20, 129.25, 128.77, 127.08, 126.50, 124.72, 124.07, 119.05, 118.34, 117.00, 112.13, 93.62. HRMS Calcd for $C_{15}H_{11}N_2S$ $[M + H]^+$: 251.0637, found: 251.0628.



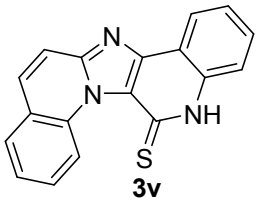
3t

benzo[4',5']thiazolo[2',3':2,3]imidazo[4,5-c]quinoline-6(5H)-thione (3t): green solid (18.42 mg, 30% yield), mp > 300 °C. ^{1}H NMR (400 MHz, DMSO-d6) δ 13.48 (s, 1H), 10.77 – 10.74 (m, 1H), 8.32 – 8.28 (m, 1H), 8.16 (dd, J = 7.9, 1.1 Hz, 1H), 7.84 (d, J = 8.3 Hz, 1H), 7.64 (m, J = 22.5, 8.5, 7.3, 1.4 Hz, 2H), 7.56 – 7.48 (m, 2H). ^{13}C NMR (101 MHz, DMSO-d6) δ 168.47, 159.00, 147.62, 138.03, 134.42, 130.44, 130.39, 129.13, 126.32, 126.08, 125.19, 124.88, 122.90, 120.58, 117.56, 116.99. HRMS Calcd for $C_{16}H_{10}N_3S_2$ $[M + H]^+$: 308.0311, found: 308.0324.



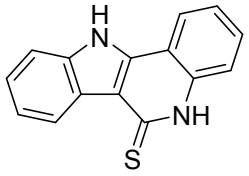
3u

isoquinolino[1',2':2,3]imidazo[4,5-c]quinoline-6(5H)-thione (3u): gray solid (49.98 mg, 83% yield), mp > 300 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 13.51 (s, 1H), 10.54 (d, J = 7.4 Hz, 1H), 8.88 – 8.83 (m, 1H), 8.53 – 8.48 (m, 1H), 8.10 (d, J = 7.2 Hz, 1H), 7.89 (m, J = 14.6, 7.2, 3.7 Hz, 3H), 7.74 – 7.67 (m, 2H), 7.59 – 7.54 (m, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 169.51, 148.99, 143.26, 138.07, 131.98, 131.36, 130.35, 129.14, 127.91, 125.01, 124.83, 123.97, 123.83, 123.16, 122.28, 118.00, 117.38, 113.73. HRMS Calcd for $C_{18}H_{12}N_3S$ $[M + H]^+$: 302.0746, found: 302.0745.



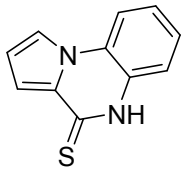
3v

imidazo[1,2-a:5,4-c']diquinoline-6(5H)-thione (3v): yellow solid (54.79 mg, 91% yield), mp > 300 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 13.42 (s, 1H), 9.60 (d, J = 8.5 Hz, 1H), 8.43 (d, J = 7.3 Hz, 1H), 8.29 (d, J = 9.3 Hz, 1H), 8.13 – 8.09 (m, 1H), 7.89 (dd, J = 8.8, 5.9 Hz, 2H), 7.78 (m, J = 8.6, 7.2, 1.5 Hz, 1H), 7.74 – 7.64 (m, 2H), 7.55 – 7.50 (m, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 171.01, 151.76, 146.28, 138.48, 134.76, 133.28, 130.63, 128.75, 128.31, 127.51, 126.03, 125.21, 125.03, 124.59, 123.29, 117.68, 116.91, 116.70. HRMS Calcd for $C_{18}H_{12}N_3S$ $[M + H]^+$: 302.0746, found: 302.0754.



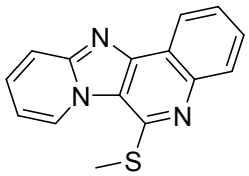
3w

5,11-dihydro-6H-indolo[3,2-c]quinoline-6-thione (3w): white solid (35.01 mg, 70% yield), mp 270.4 – 271.3 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 13.07 (s, 1H), 12.90 (s, 1H), 9.09 (d, J = 7.9 Hz, 1H), 8.36 (d, J = 7.9 Hz, 1H), 7.85 (d, J = 8.3 Hz, 1H), 7.70 – 7.63 (m, 2H), 7.49 (t, J = 7.5 Hz, 2H), 7.37 (t, J = 7.5 Hz, 1H).^{13}C NMR (101 MHz, DMSO-d_6) δ 176.69, 139.02, 138.17, 137.83, 130.30, 125.64, 125.62, 124.03, 122.82, 122.76, 121.70, 117.36, 116.01, 113.80, 112.12. HRMS Calcd for $C_{15}H_{11}N_2S$ $[M + H]^+$: 251.0637, found: 251.0631.



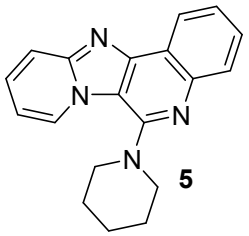
3x

pyrrolo[1,2-a]quinoxaline-4(5H)-thione (3x): white solid (9.20 mg, 23% yield), mp 208.0 – 209.2 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.92 (s, 1H), 8.36 (dd, J = 2.5, 1.5 Hz, 1H), 8.17 – 8.12 (m, 1H), 7.61 – 7.57 (m, 1H), 7.41 – 7.35 (m, 2H), 7.32 (dd, J = 3.9, 1.3 Hz, 1H), 6.84 – 6.80 (m, 1H).^{13}C NMR (101 MHz, DMSO-d_6) δ 174.53, 129.73, 128.14, 126.38, 125.20, 124.60, 119.02, 117.56, 116.17, 115.73, 114.97. HRMS Calcd for $C_{11}H_9N_2S$ $[M + H]^+$: 201.0481, found: 201.0484.



4

6-(methylthio)pyrido[2',1':2,3]imidazo[4,5-c]quinoline (4): white solid (48.51 mg, 61% yield), mp 123.4 – 124.2 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.17 (d, J = 6.9 Hz, 1H), 8.49 (d, J = 7.6 Hz, 1H), 7.96 (dd, J = 19.0, 8.7 Hz, 2H), 7.75 – 7.69 (m, 2H), 7.60 (t, J = 7.4 Hz, 1H), 7.28 (t, J = 6.8 Hz, 1H), 2.87 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 148.97, 146.68, 145.64, 144.87, 130.75, 129.13, 128.70, 128.13, 125.70, 122.80, 120.33, 120.28, 117.77, 113.75, 12.46. HRMS Calcd for $C_{15}H_{12}N_3S$ $[M + H]^+$: 266.0746, found: 266.0745.

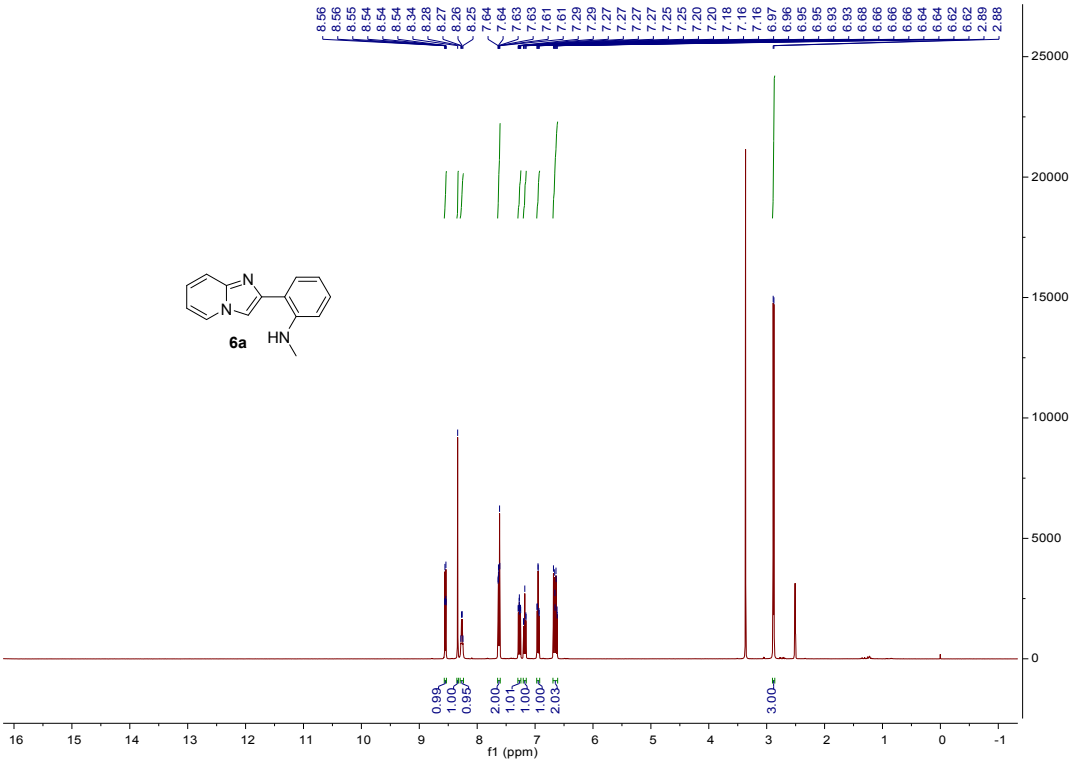


5

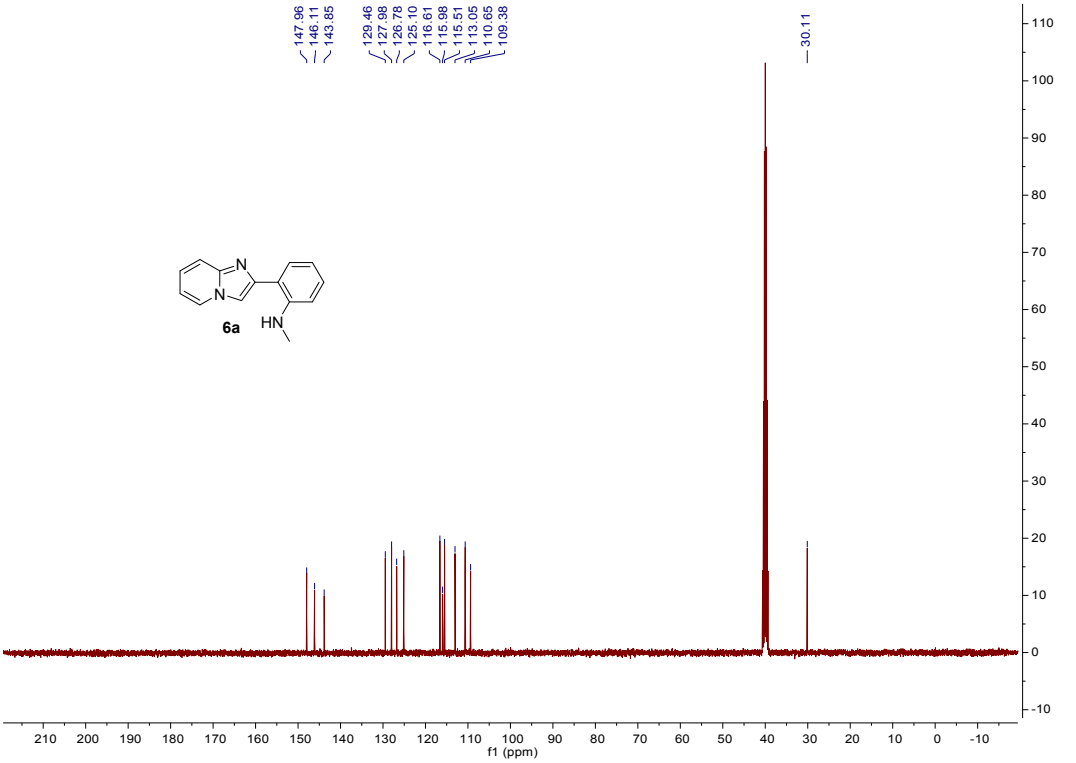
6-(piperidin-1-yl)pyrido[2',1':2,3]imidazo[4,5-c]quinoline (5): white solid (48.04 mg, 53% yield), mp > 300 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.88 (d, J = 6.9 Hz, 1H), 8.52 – 8.47 (m, 1H), 7.95 (dd, J = 14.6, 8.7 Hz, 2H), 7.78 – 7.66 (m, 2H), 7.59 – 7.54 (m, 1H), 7.38 – 7.32 (m, 1H), 3.18 (d, J = 4.3 Hz, 4H), 1.90 – 1.54 (m, 6H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 152.65, 148.78, 147.97, 144.42, 130.25, 128.90, 128.43, 128.24, 124.86, 122.59, 120.84, 117.60, 115.48, 113.58, 51.26, 25.66, 24.42. HRMS Calcd for $C_{19}H_{19}N_4$ $[M + H]^+$: 303.1604, found: 303.1605.

5. ^{1}H NMR, ^{13}C NMR and ^{19}F NMR Spectra

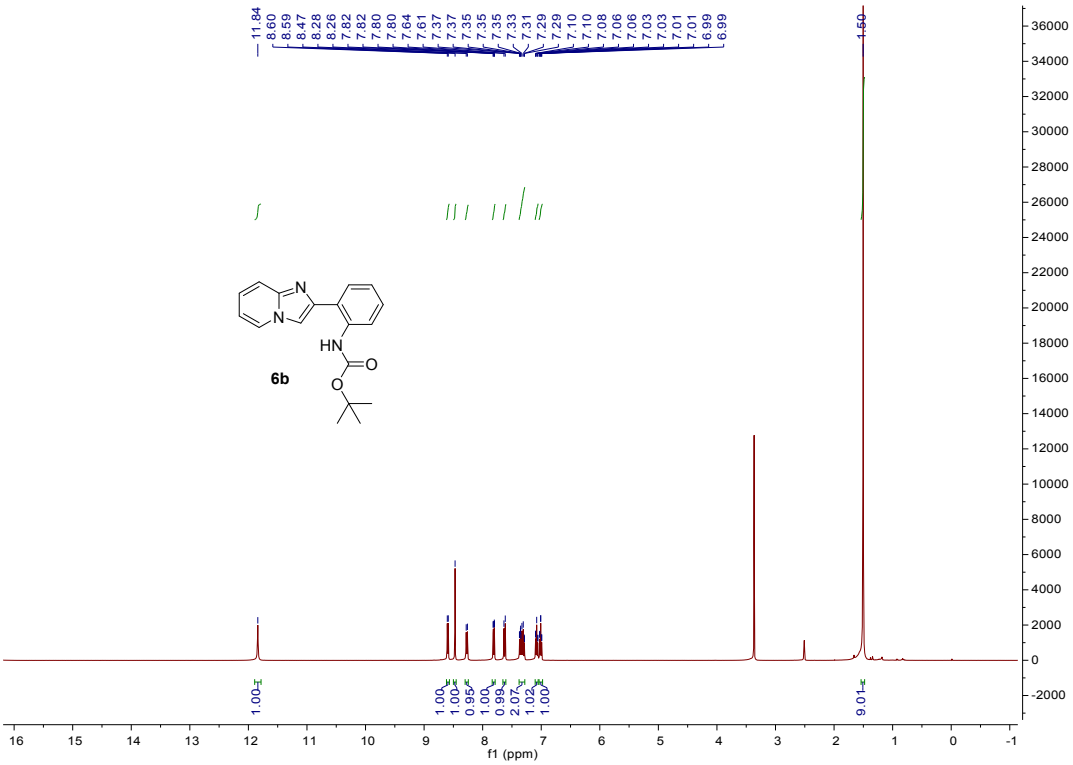
^{1}H NMR spectrum of 6a



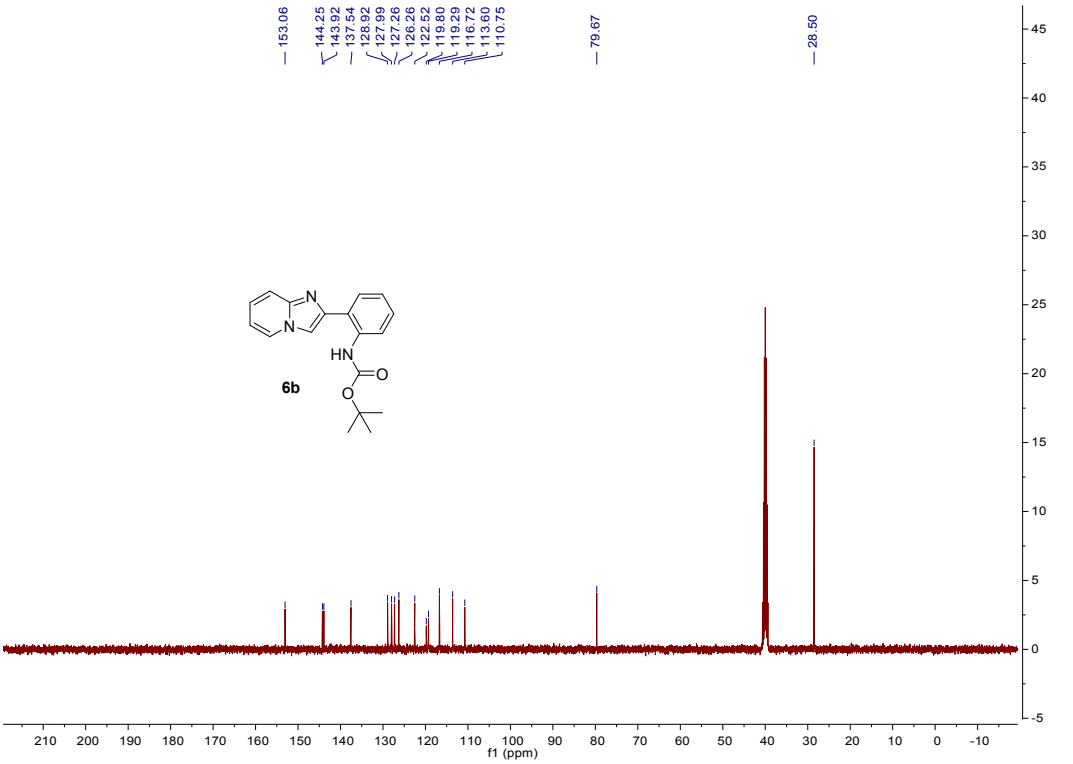
^{13}C NMR spectrum of 6a



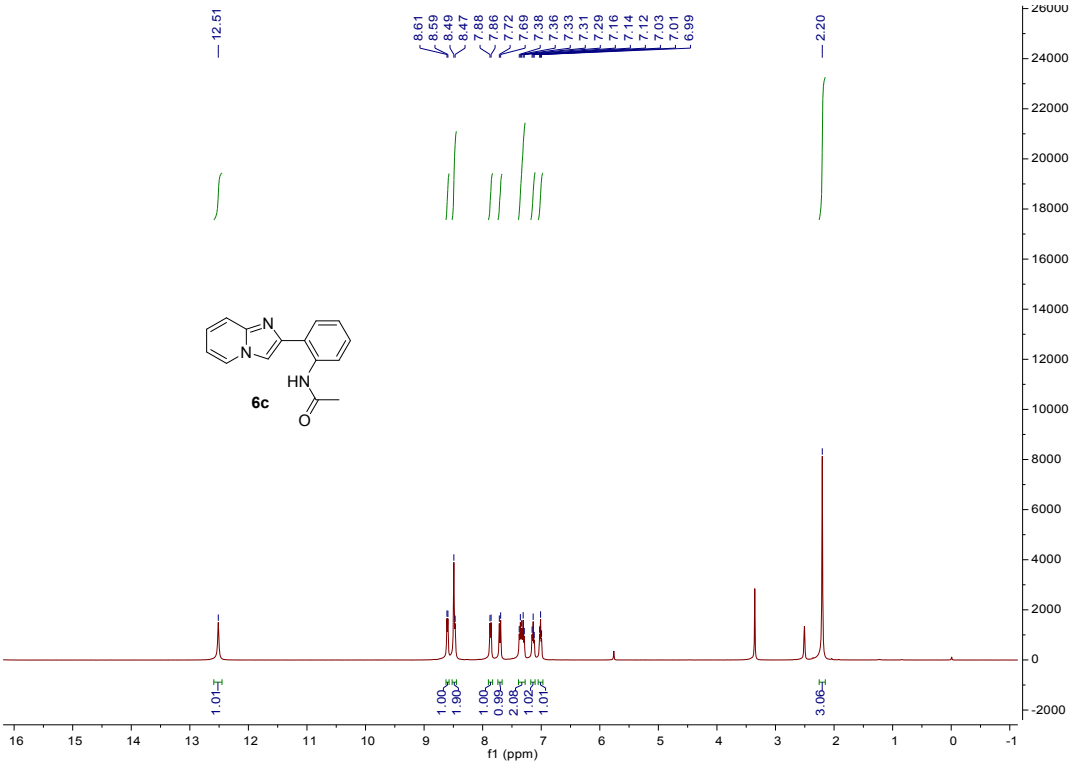
^{1}H NMR spectrum of 6b



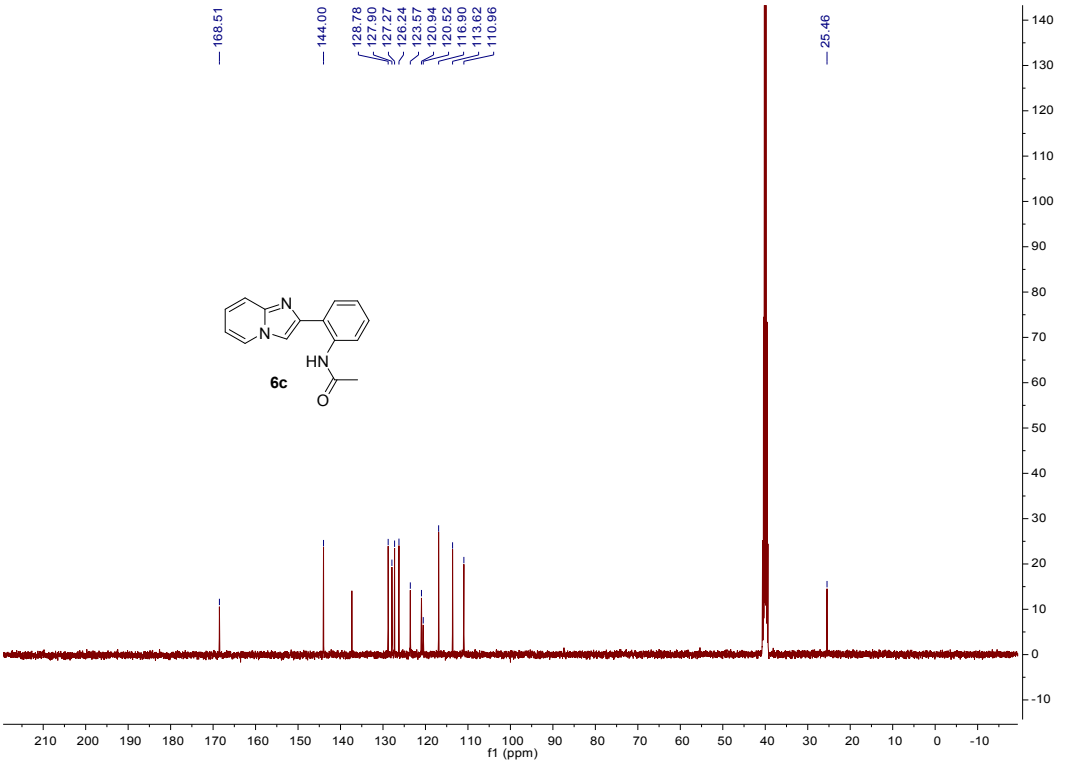
^{13}C NMR spectrum of 6b



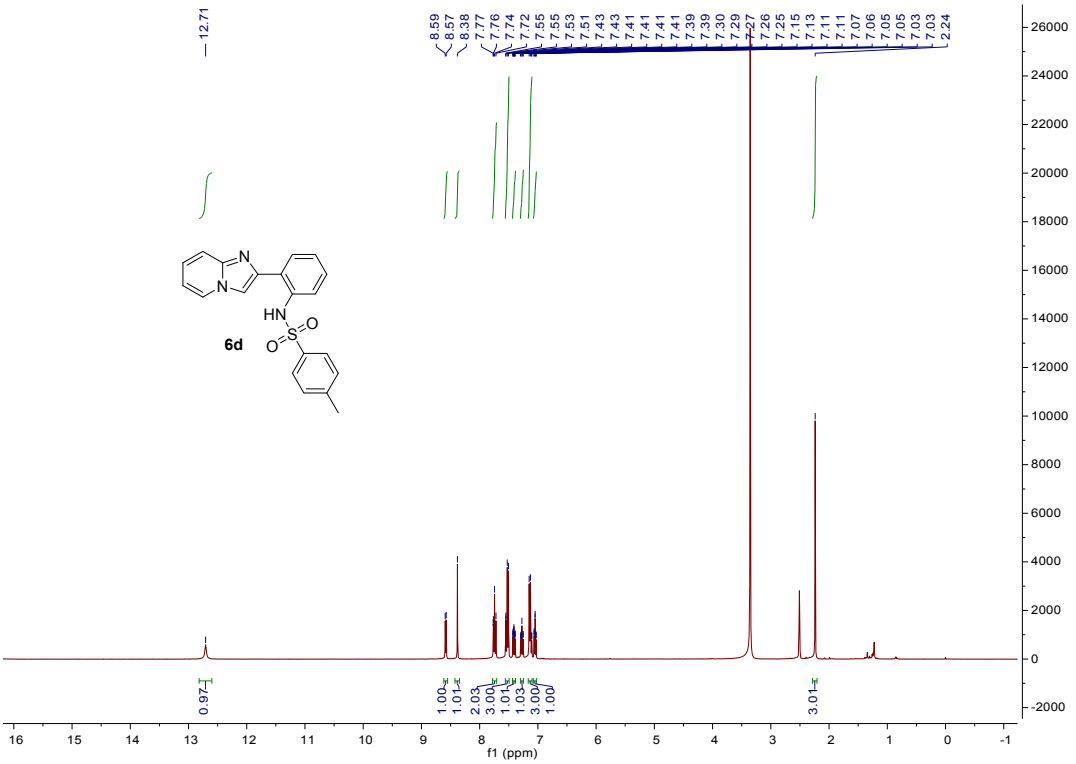
^{1}H NMR spectrum of 6c



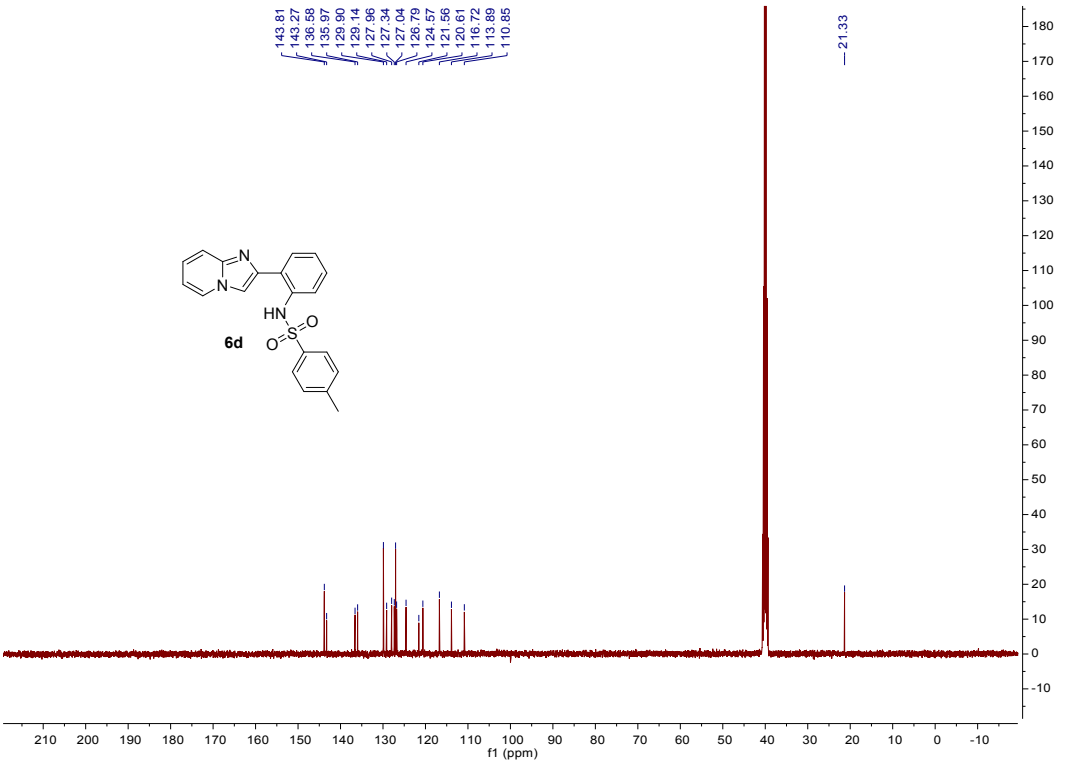
^{13}C NMR spectrum of 6c



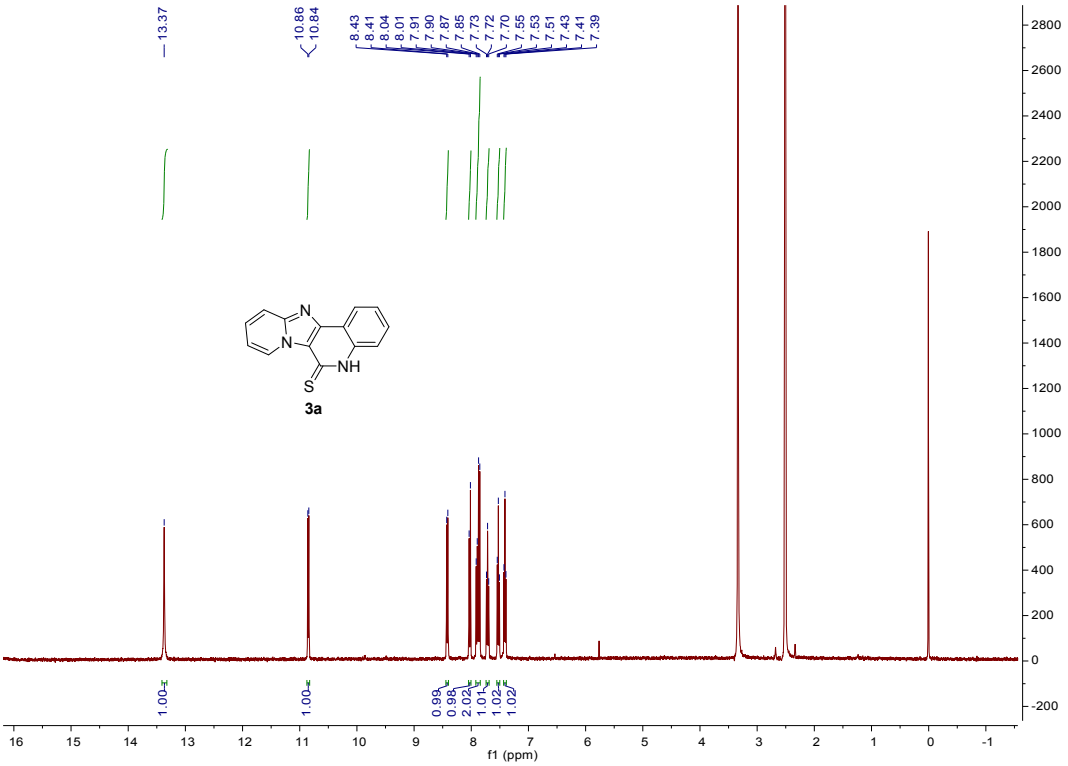
^{1}H NMR spectrum of 6d



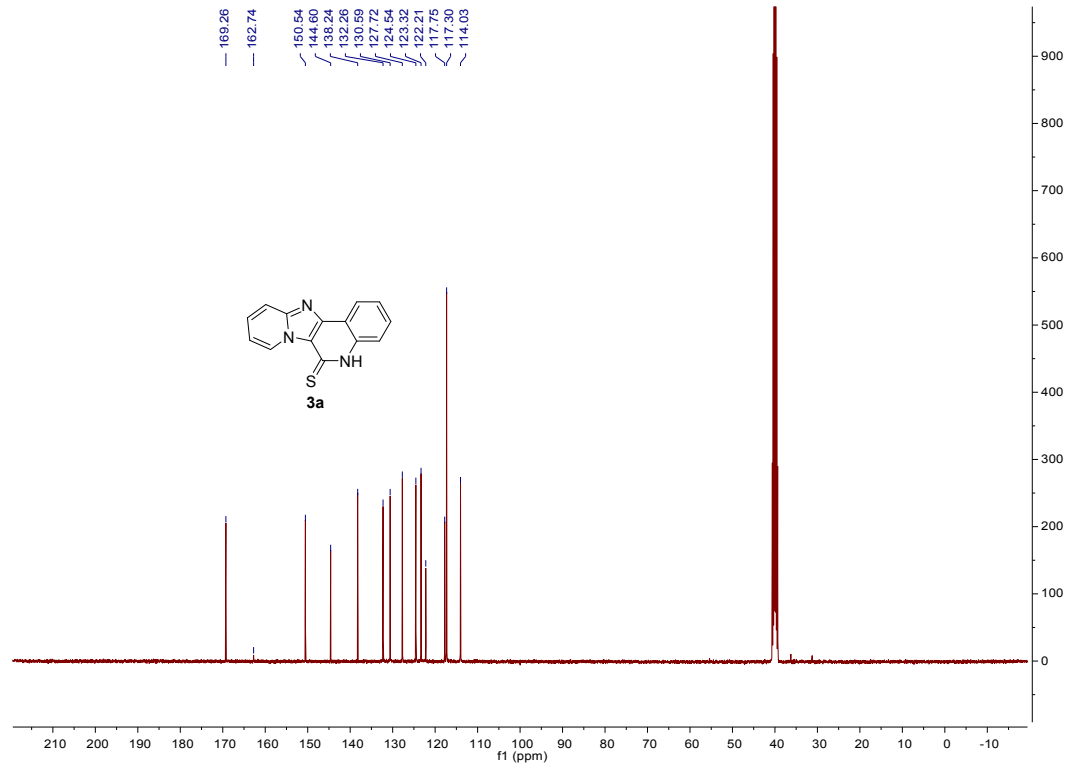
^{13}C NMR spectrum of 6d



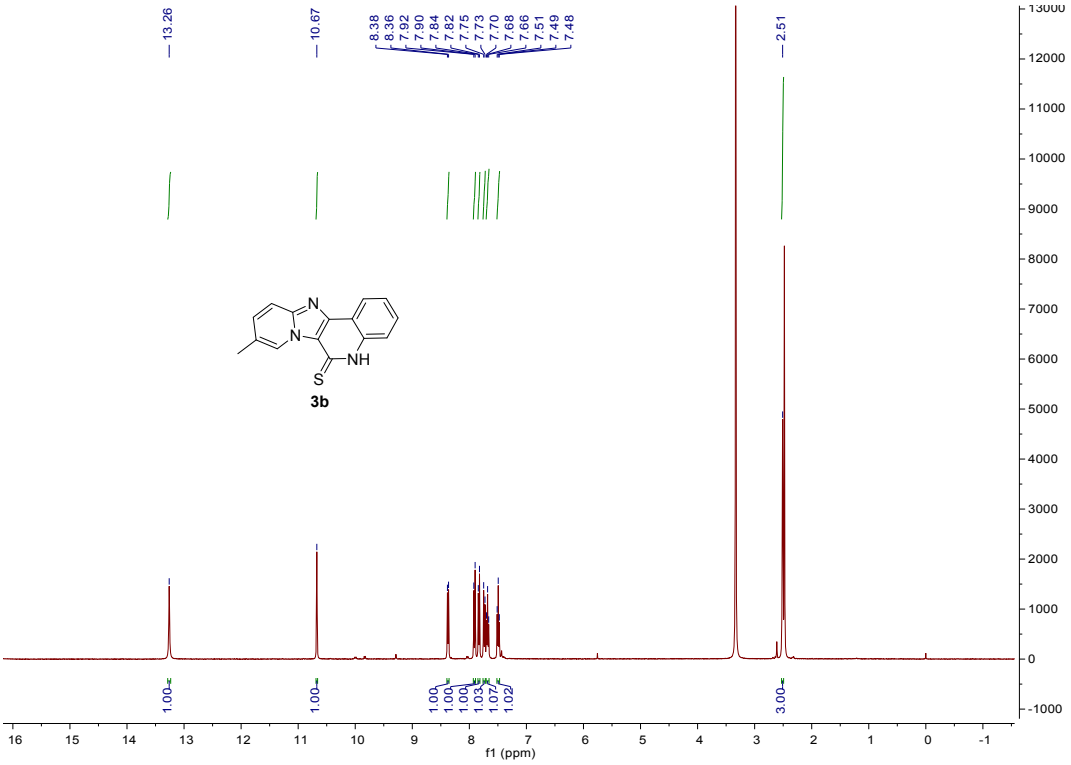
^{1}H NMR spectrum of 3a



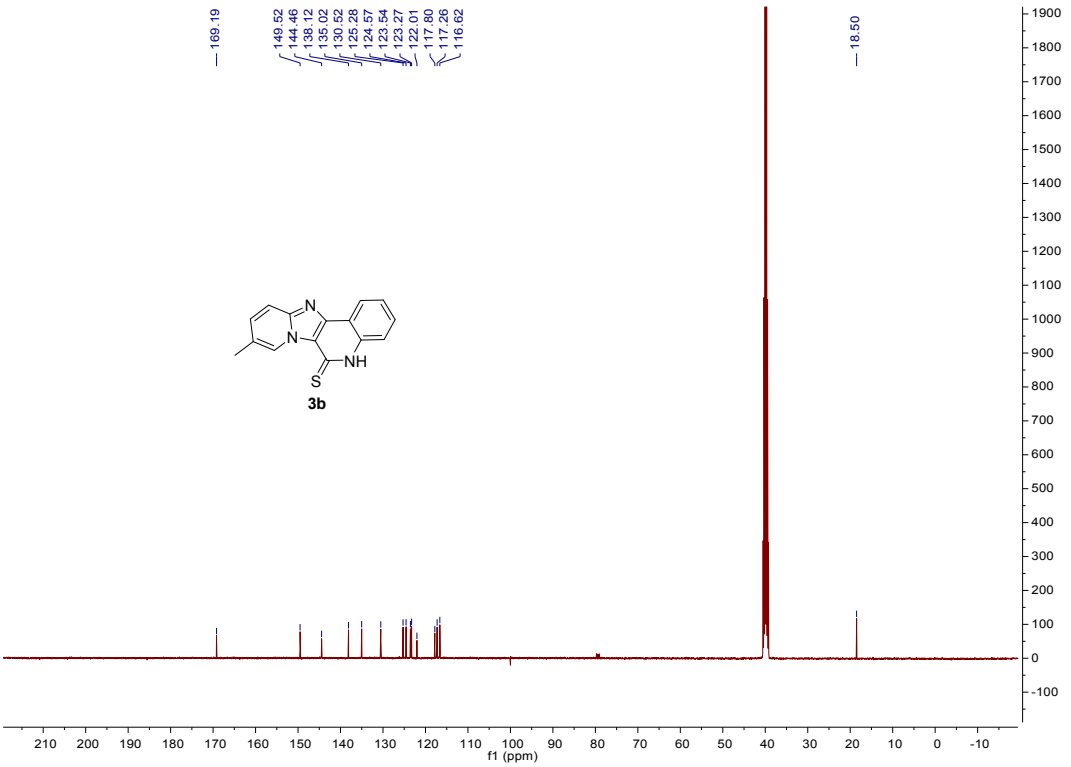
^{13}C NMR spectrum of 3a



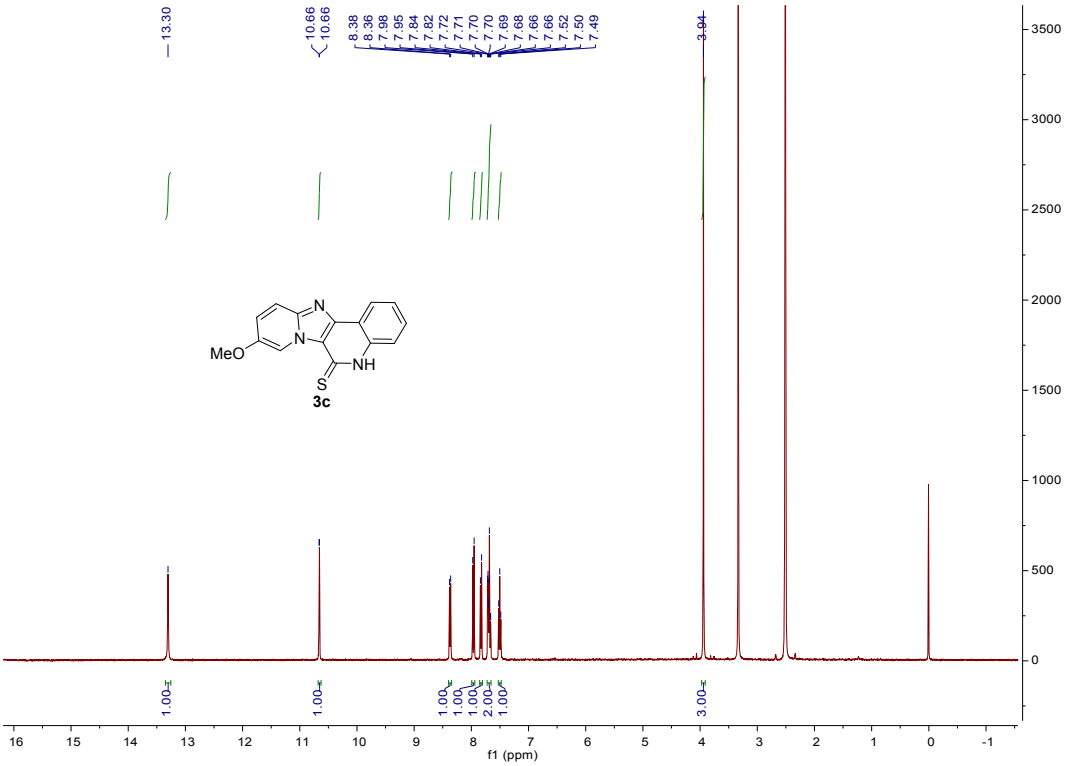
^{1}H NMR spectrum of 3b



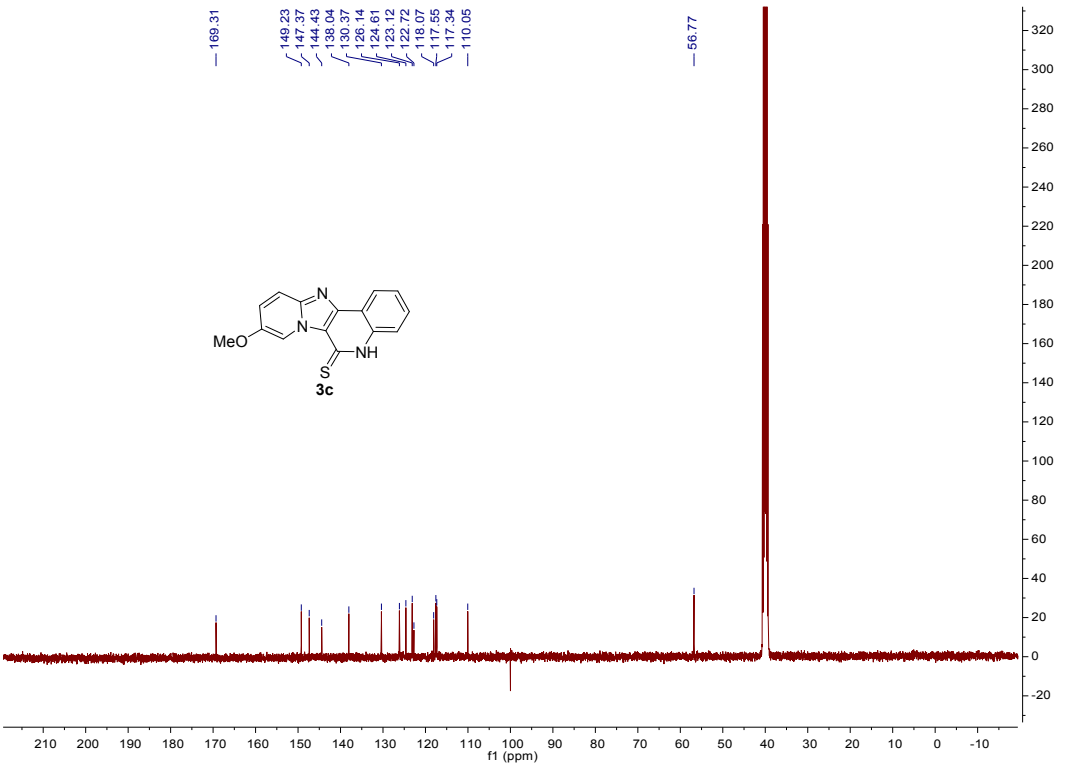
^{13}C NMR spectrum of 3b



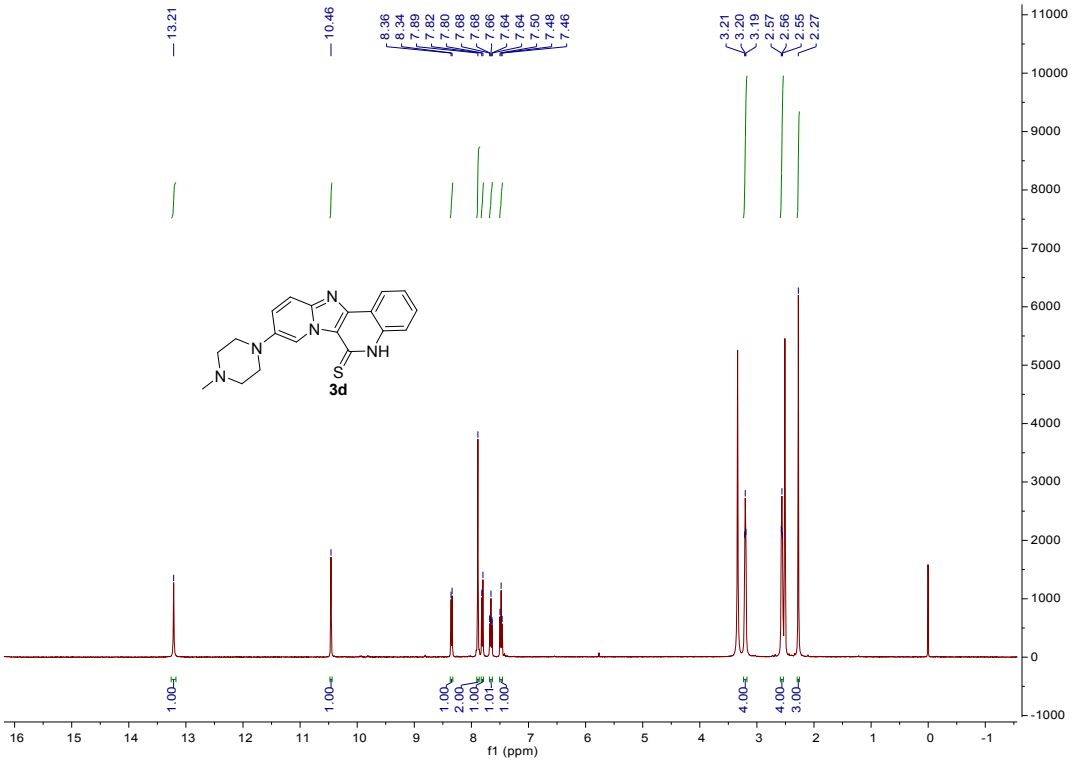
^{1}H NMR spectrum of 3c



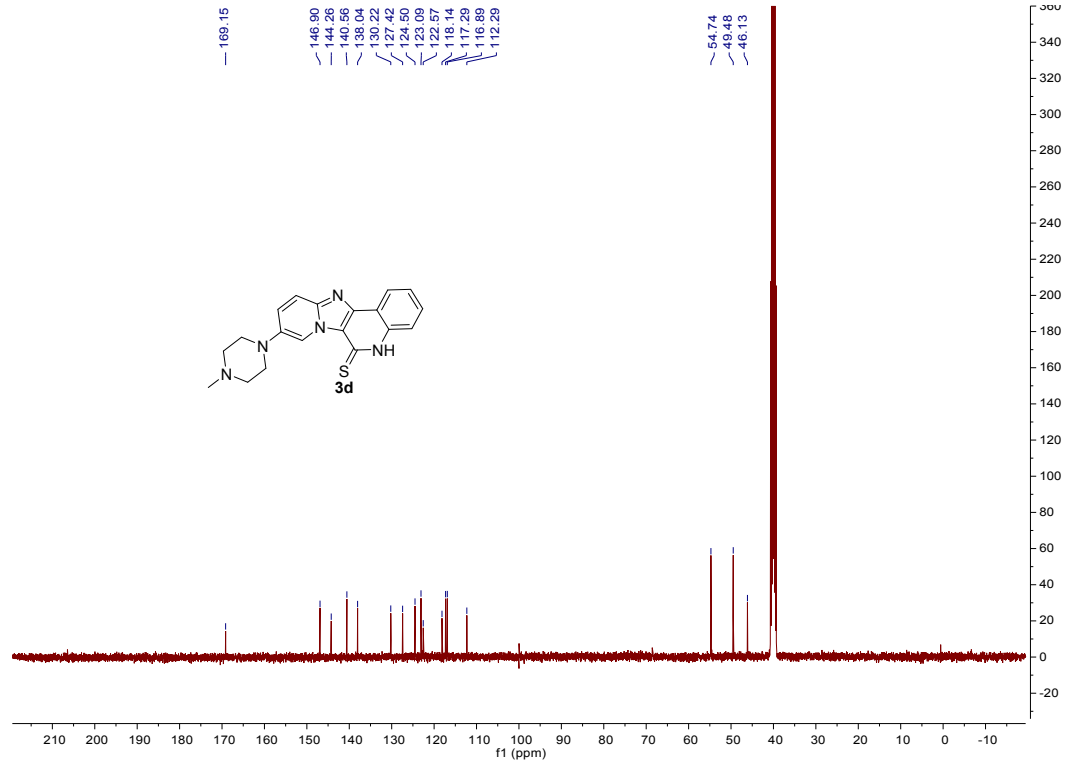
^{13}C NMR spectrum of 3c



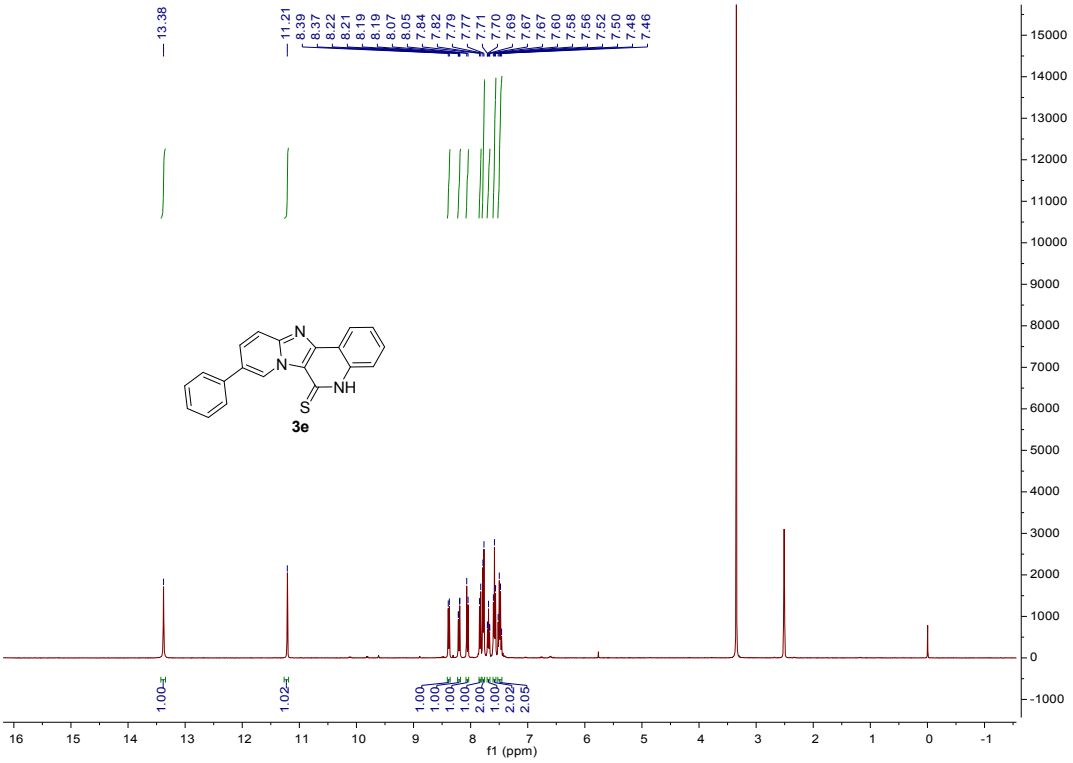
^{1}H NMR spectrum of 3d



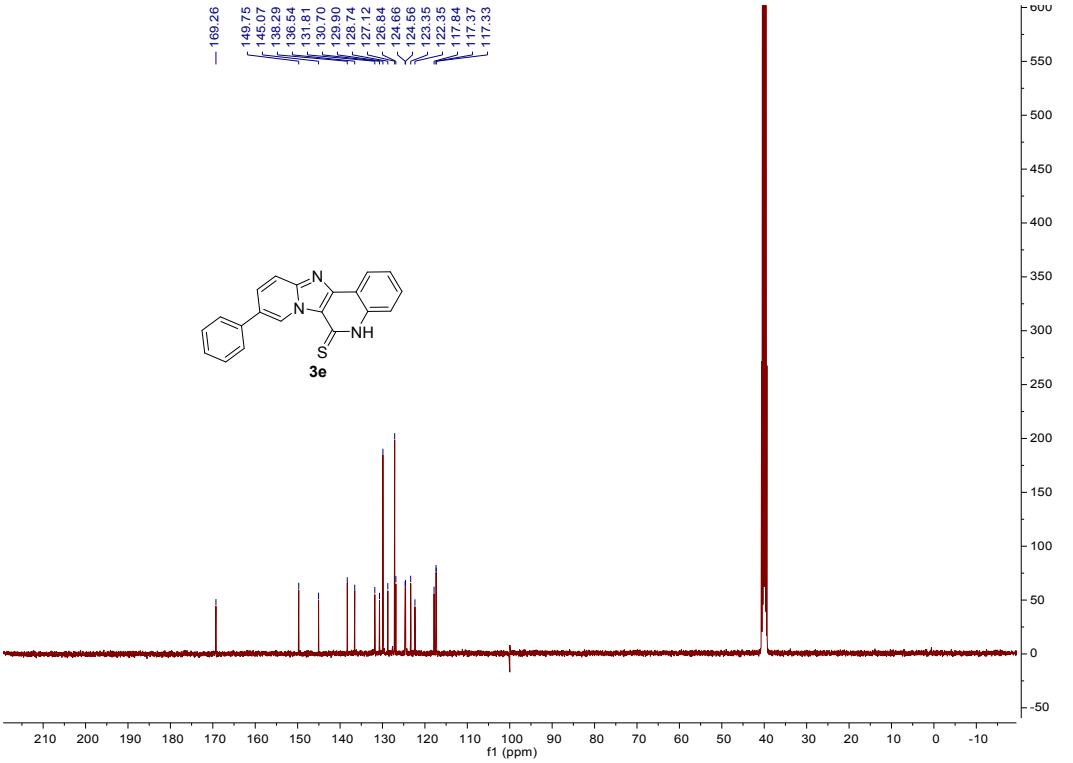
^{13}C NMR spectrum of 3d



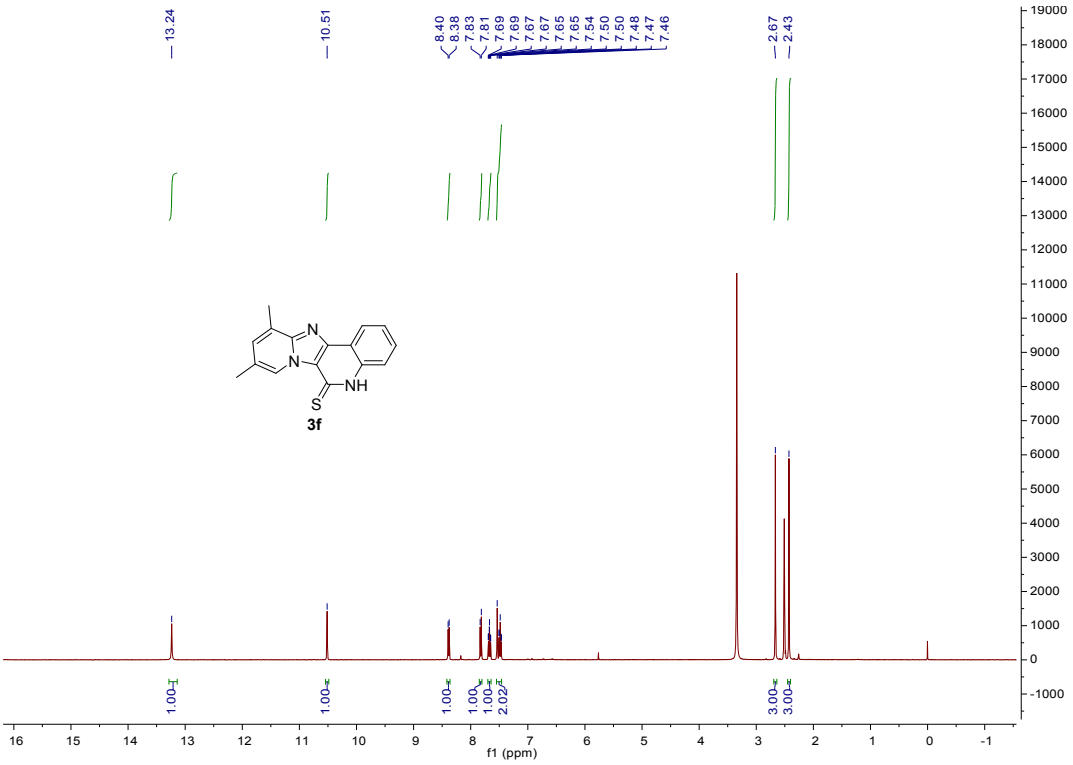
^{1}H NMR spectrum of 3e



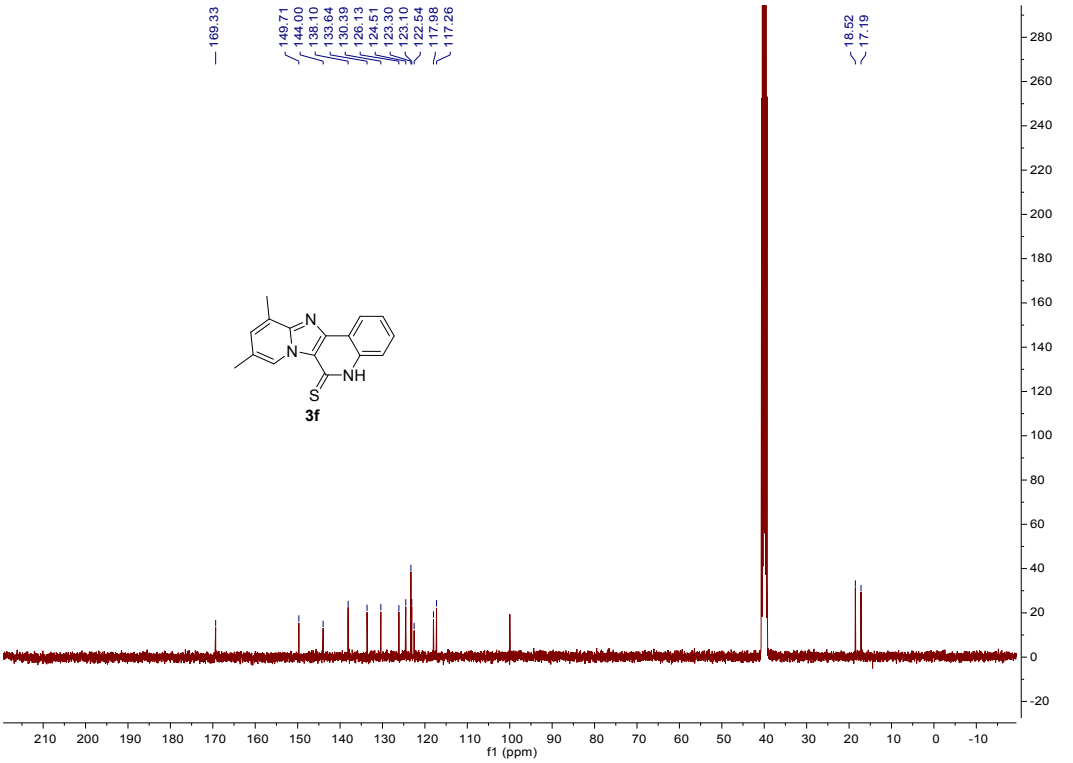
^{13}C NMR spectrum of 3e



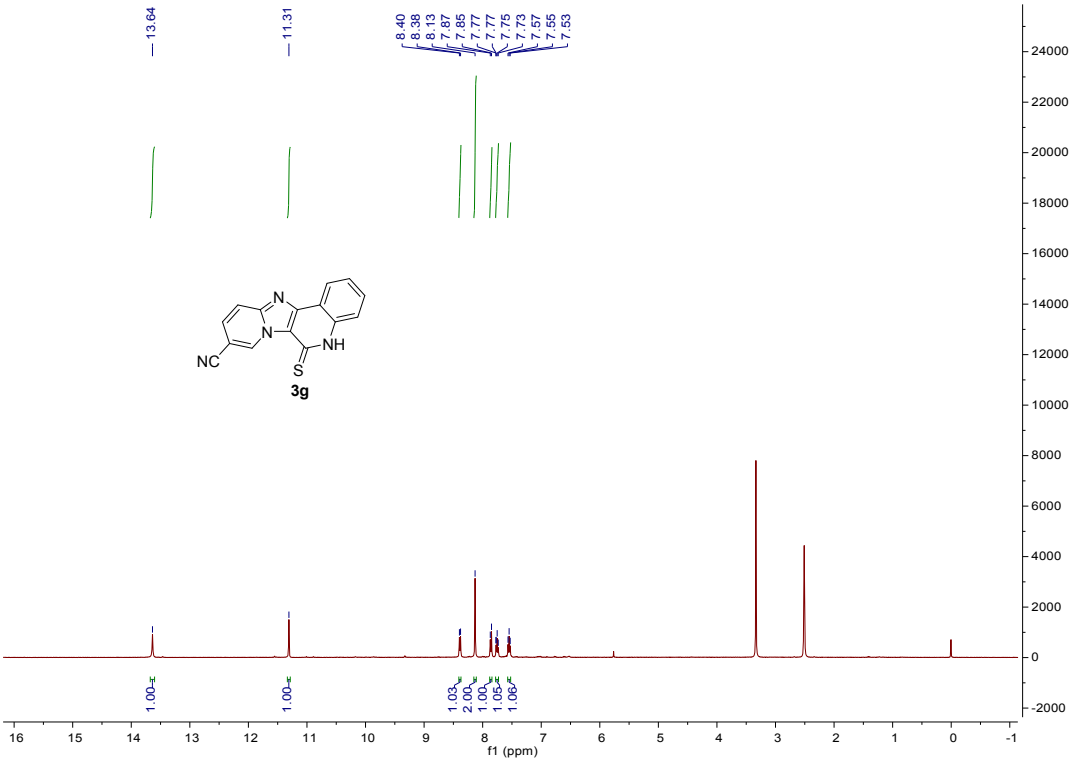
^{1}H NMR spectrum of 3f



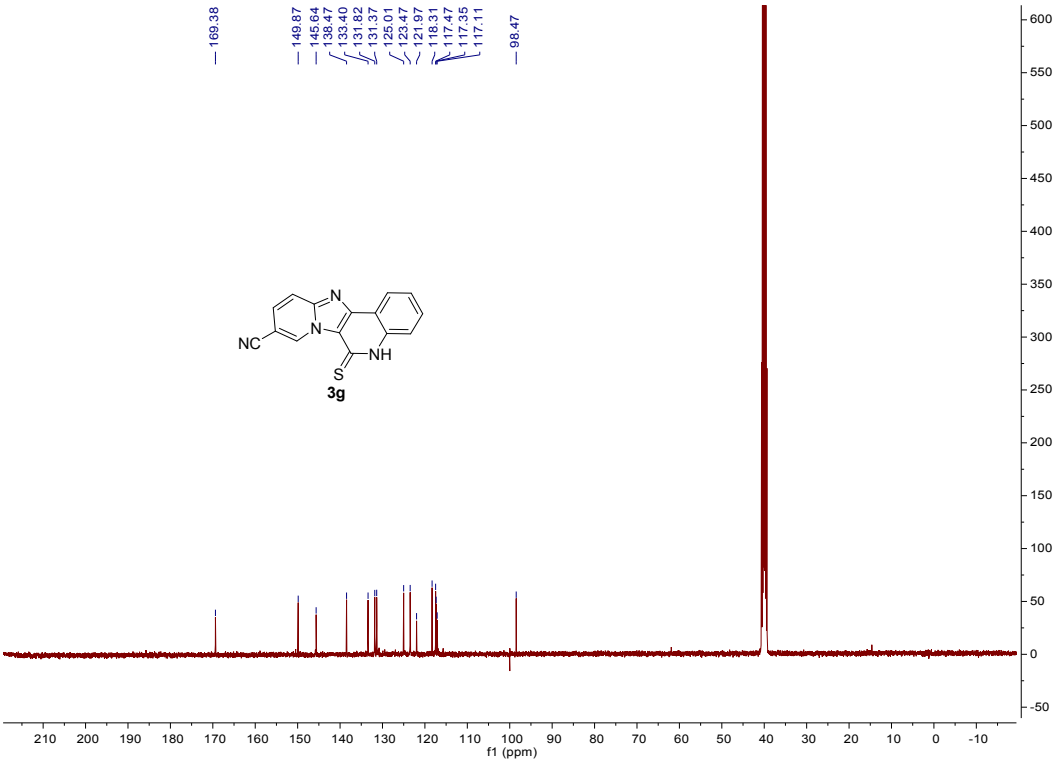
^{13}C NMR spectrum of 3f



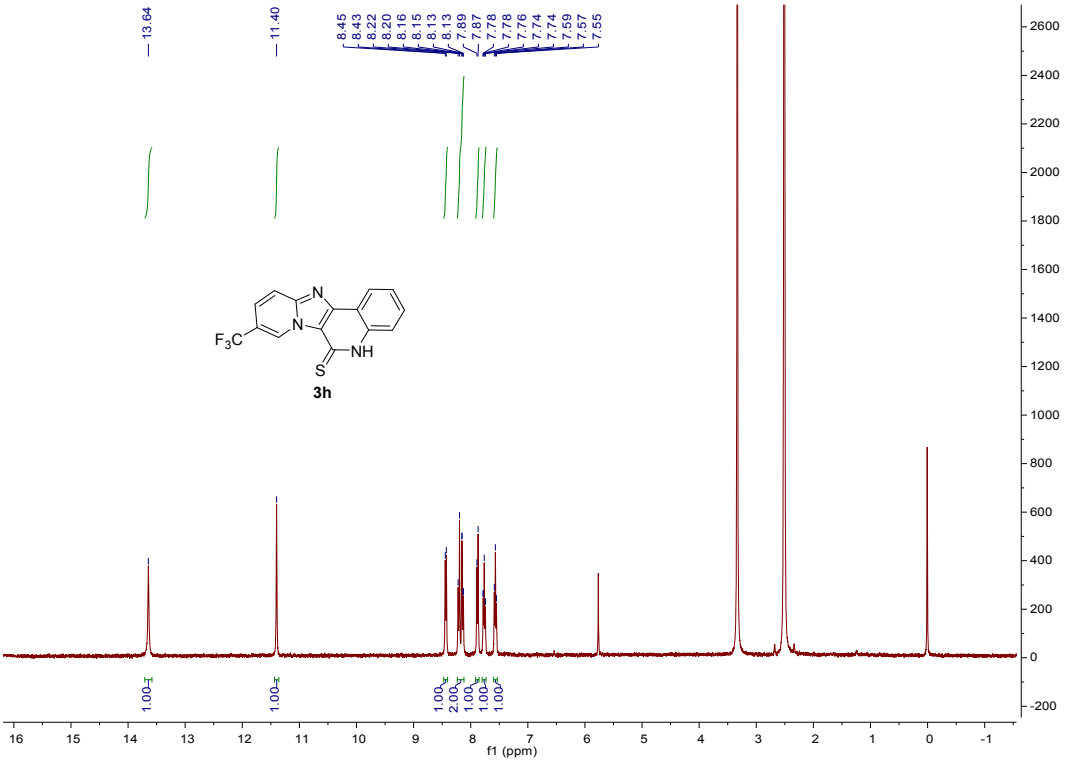
^{1}H NMR spectrum of 3g



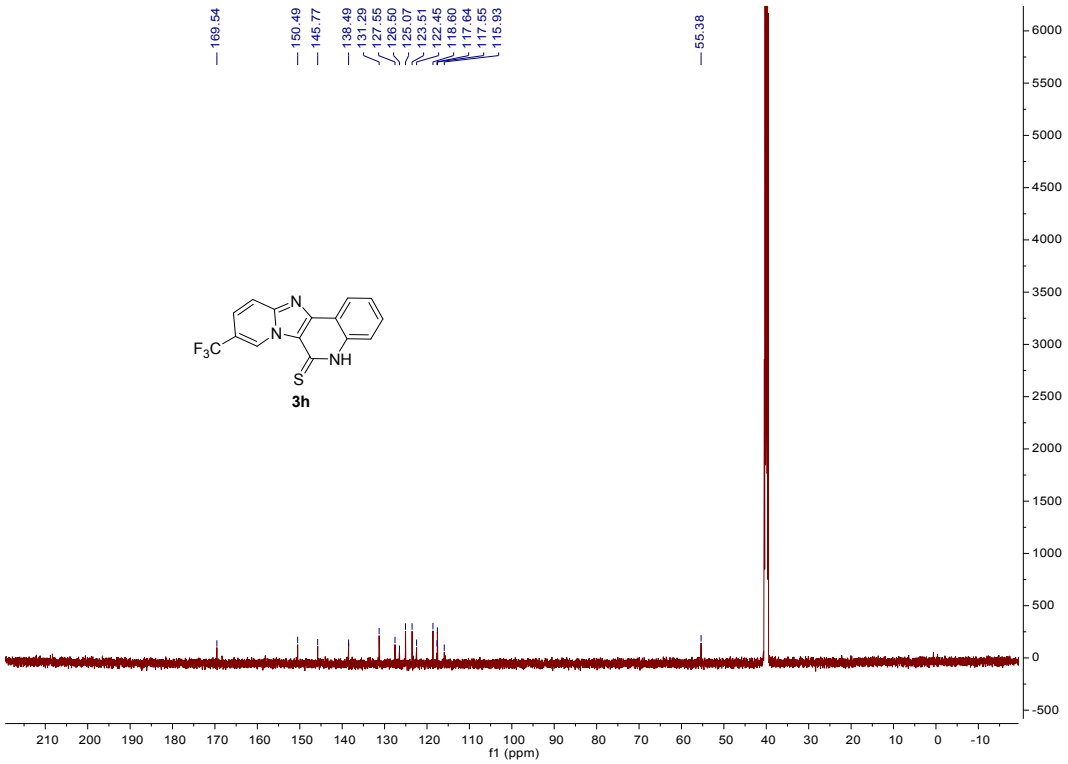
^{13}C NMR spectrum of 3g



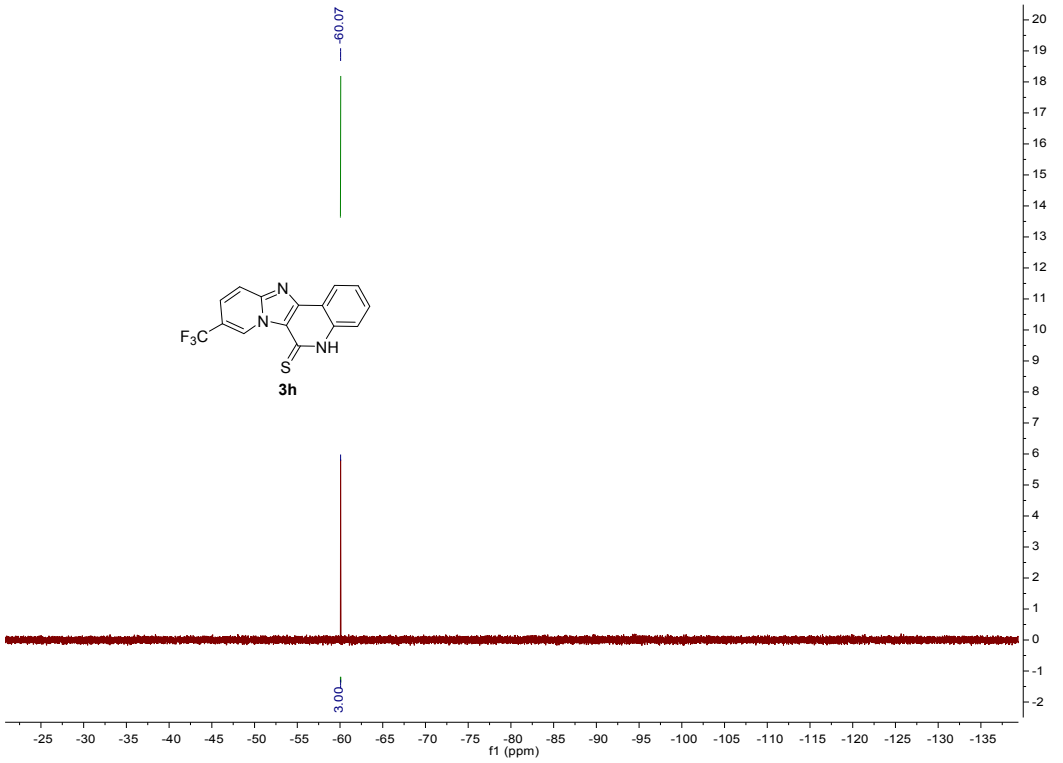
^{1}H NMR spectrum of 3h



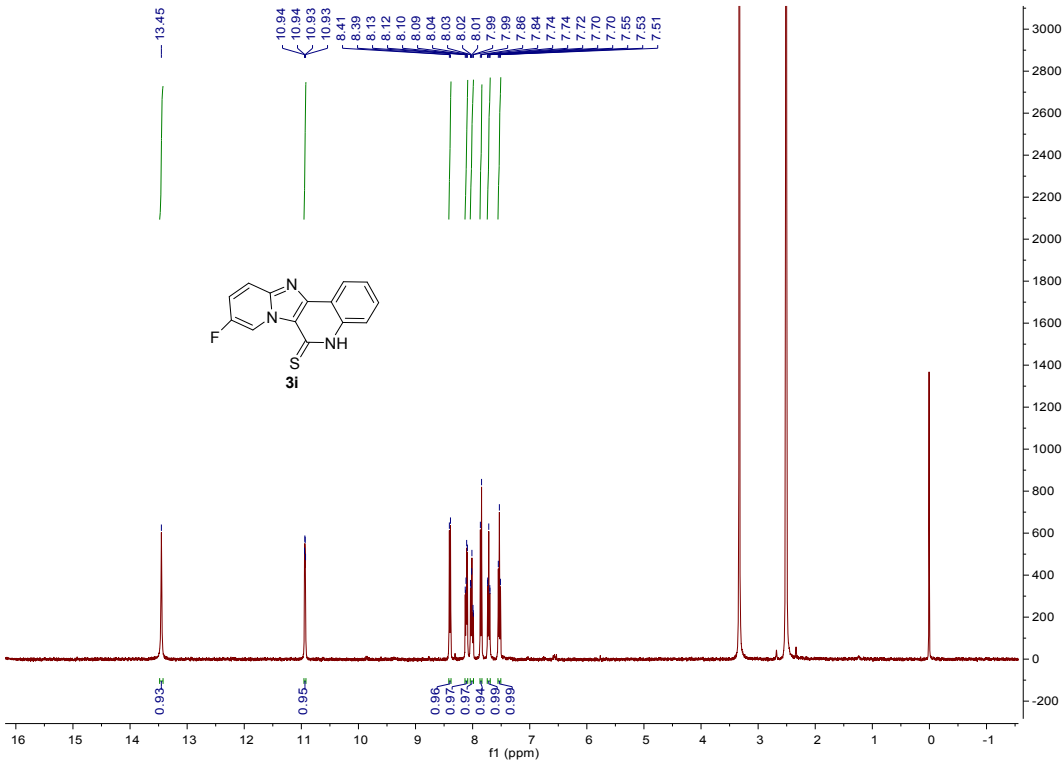
^{13}C NMR spectrum of 3h



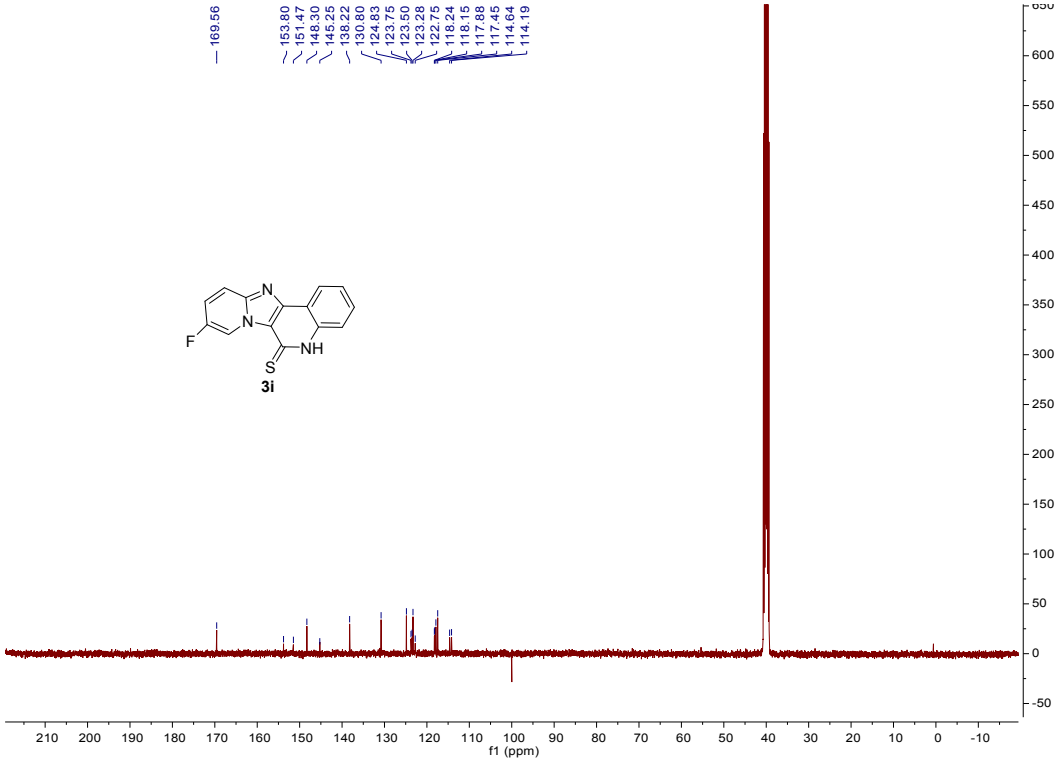
^{19}F NMR spectrum of 3h



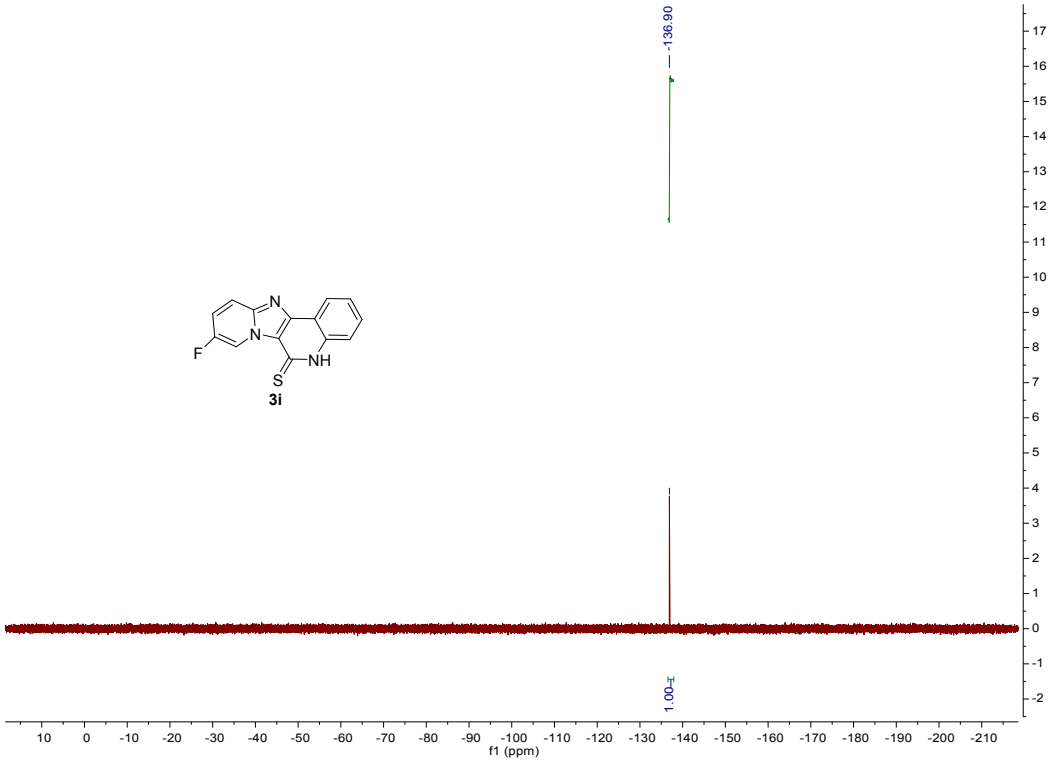
^{1}H NMR spectrum of 3i



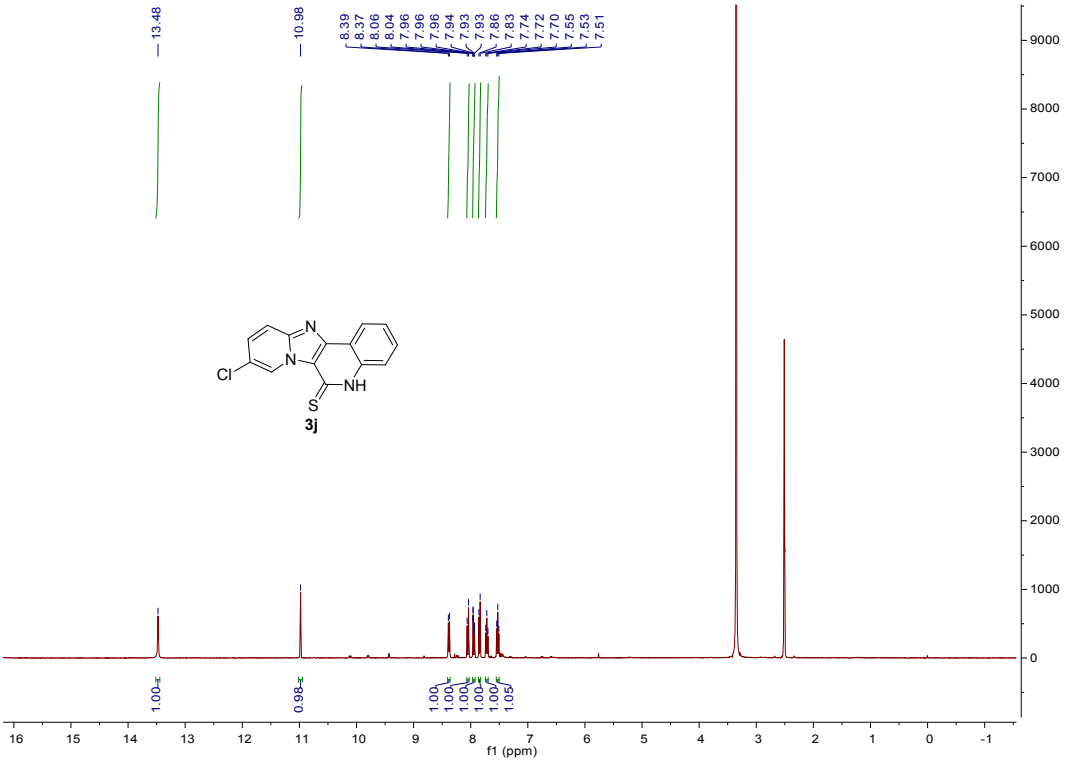
^{13}C NMR spectrum of 3i



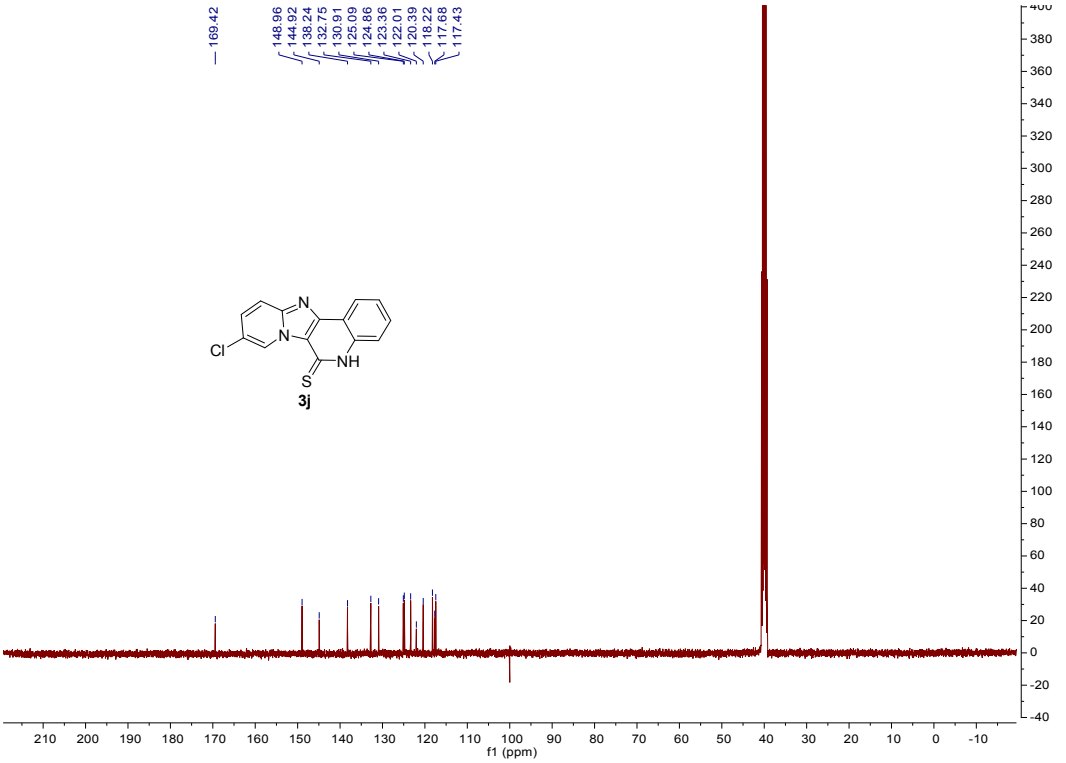
^{19}F NMR spectrum of 3i



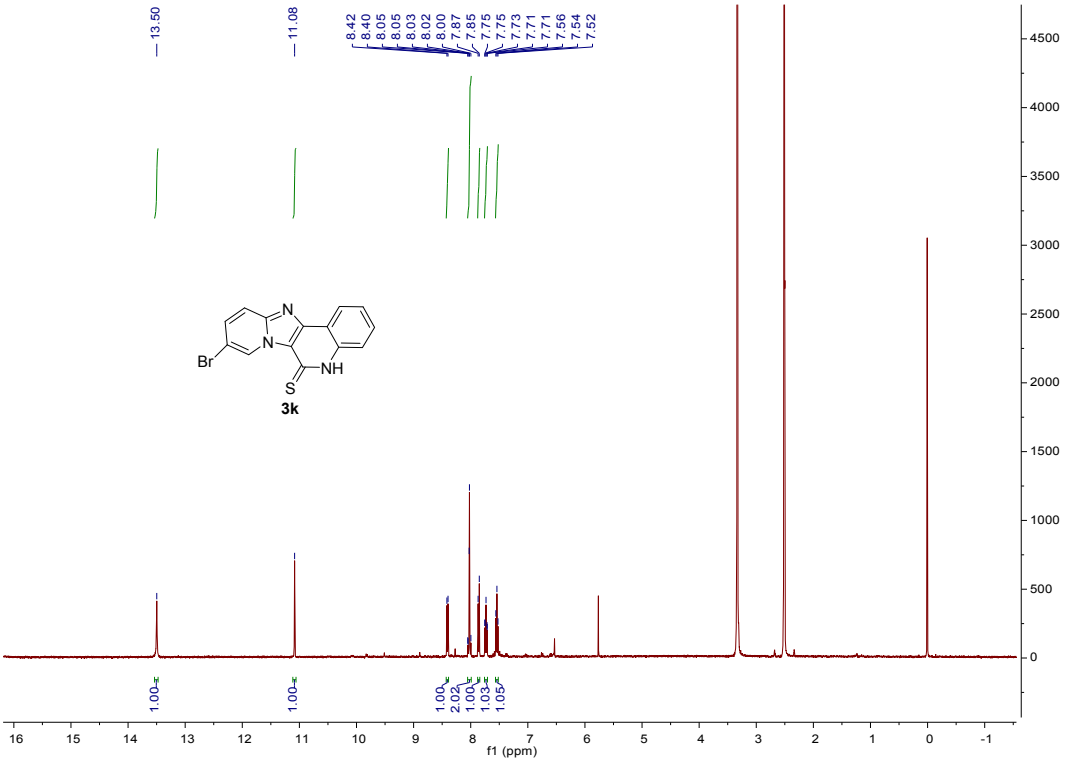
^{1}H NMR spectrum of 3j



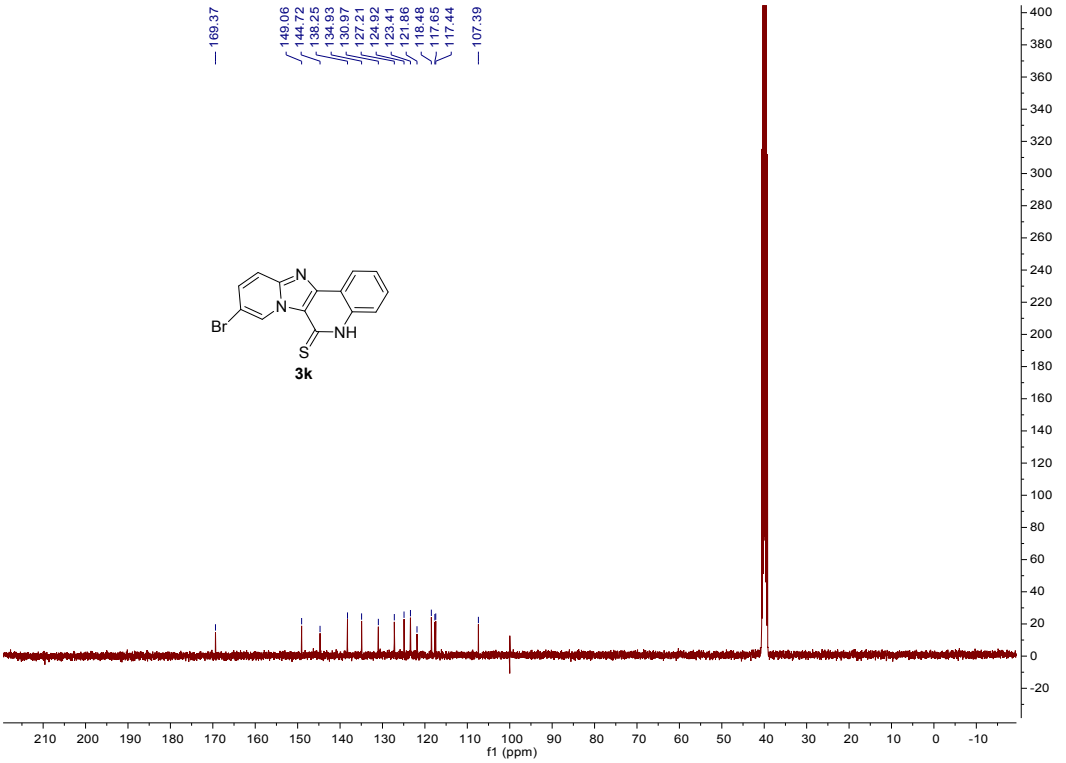
^{13}C NMR spectrum of 3j



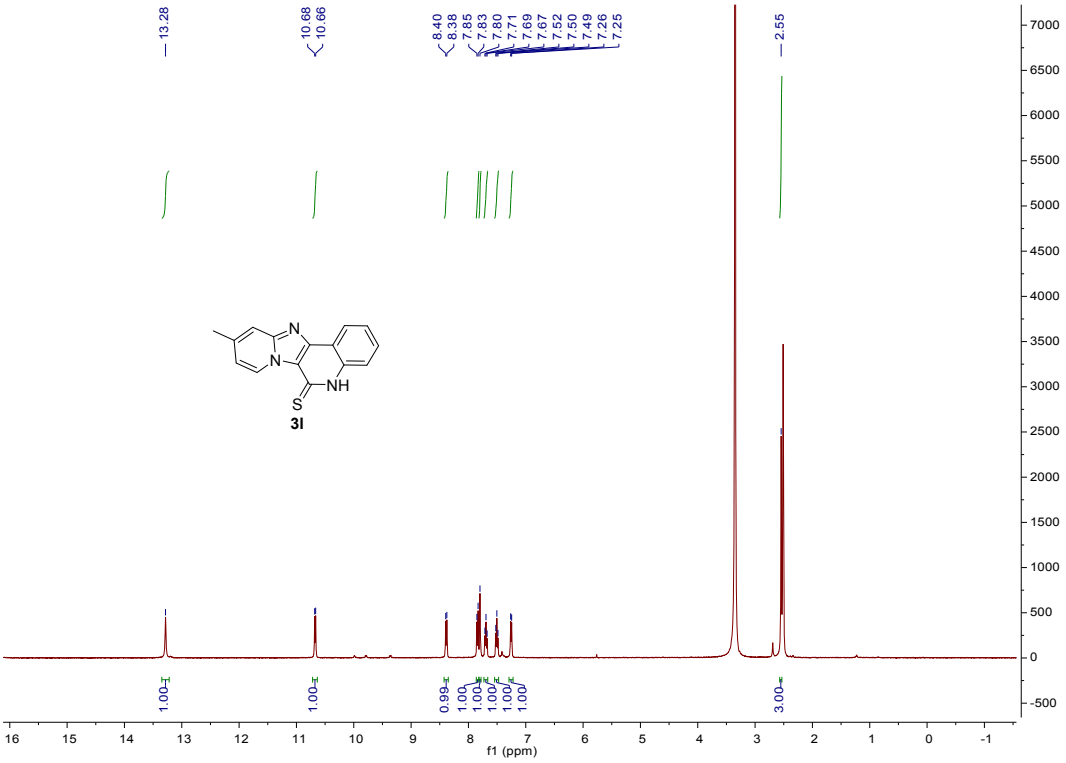
^{1}H NMR spectrum of 3k



^{13}C NMR spectrum of 3k

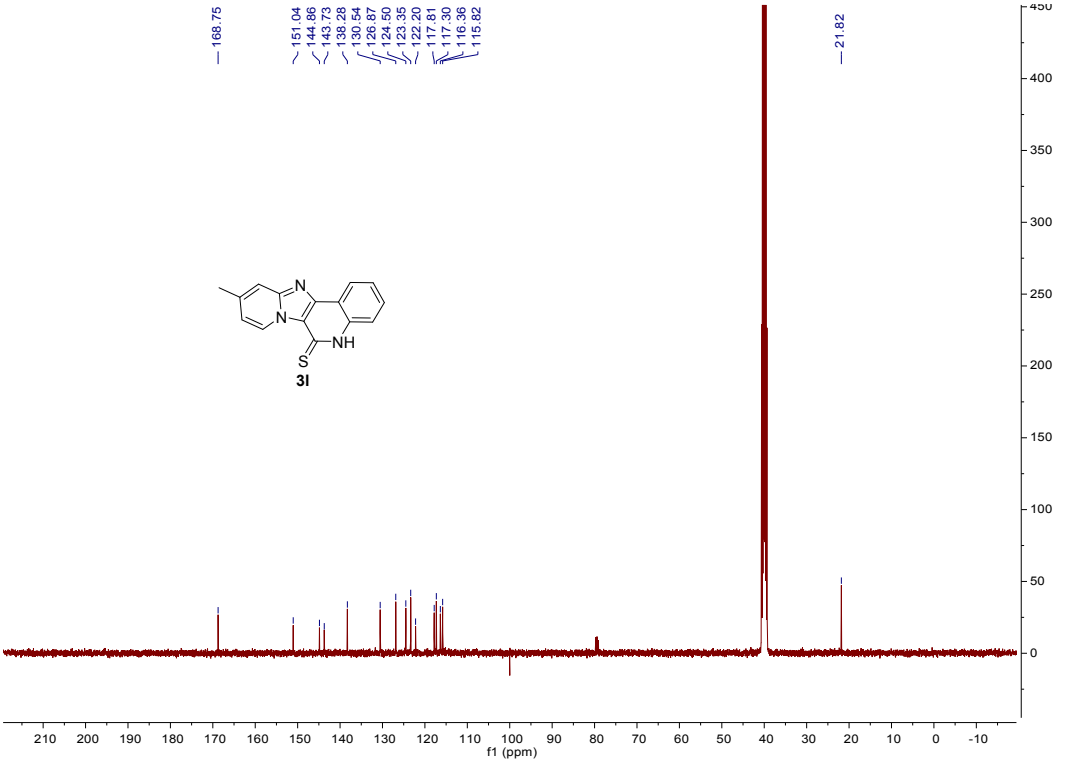


^{1}H NMR spectrum of 3l



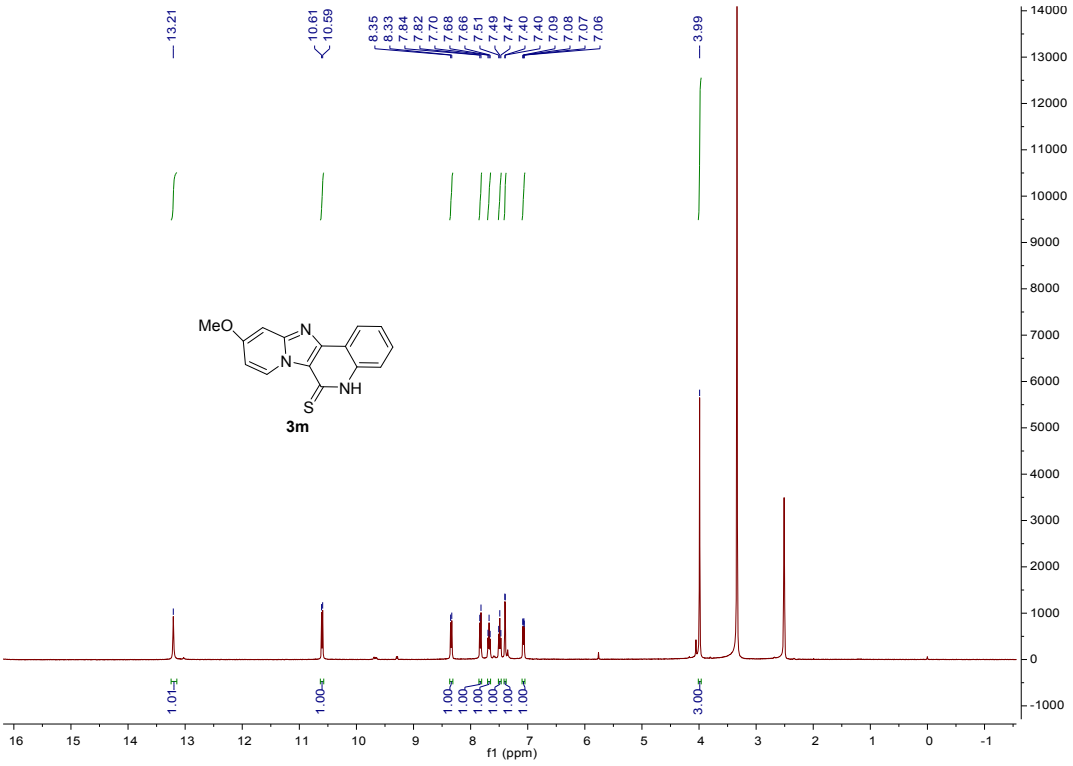
3l

^{13}C NMR spectrum of 3l

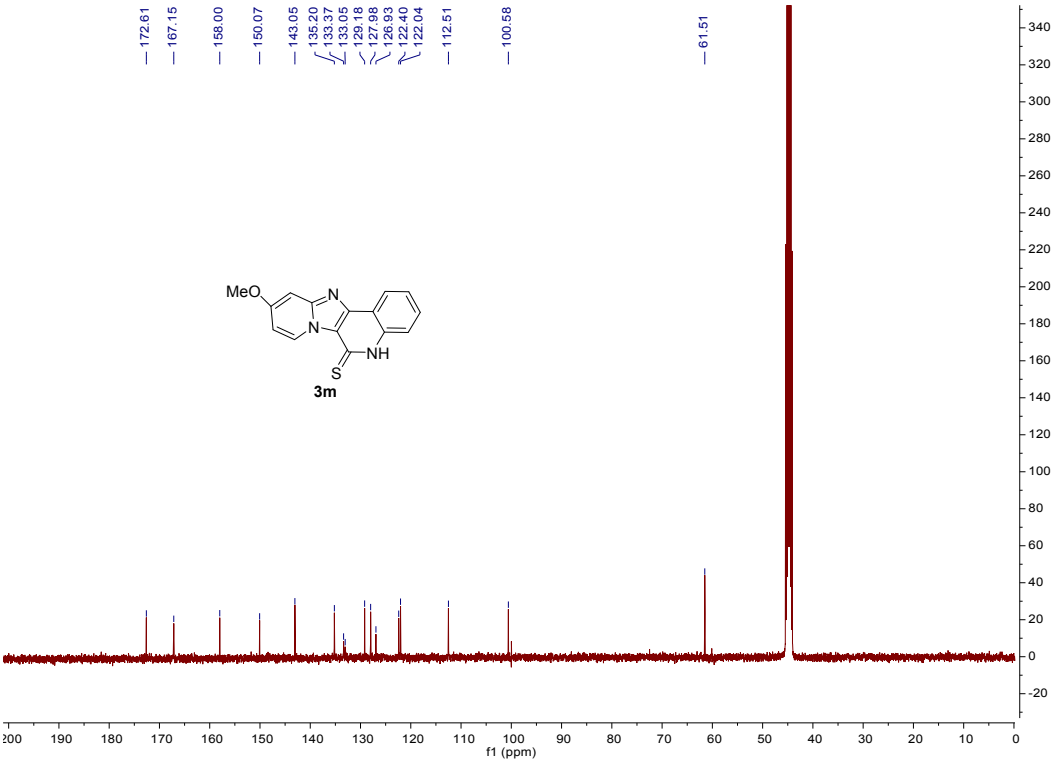


3l

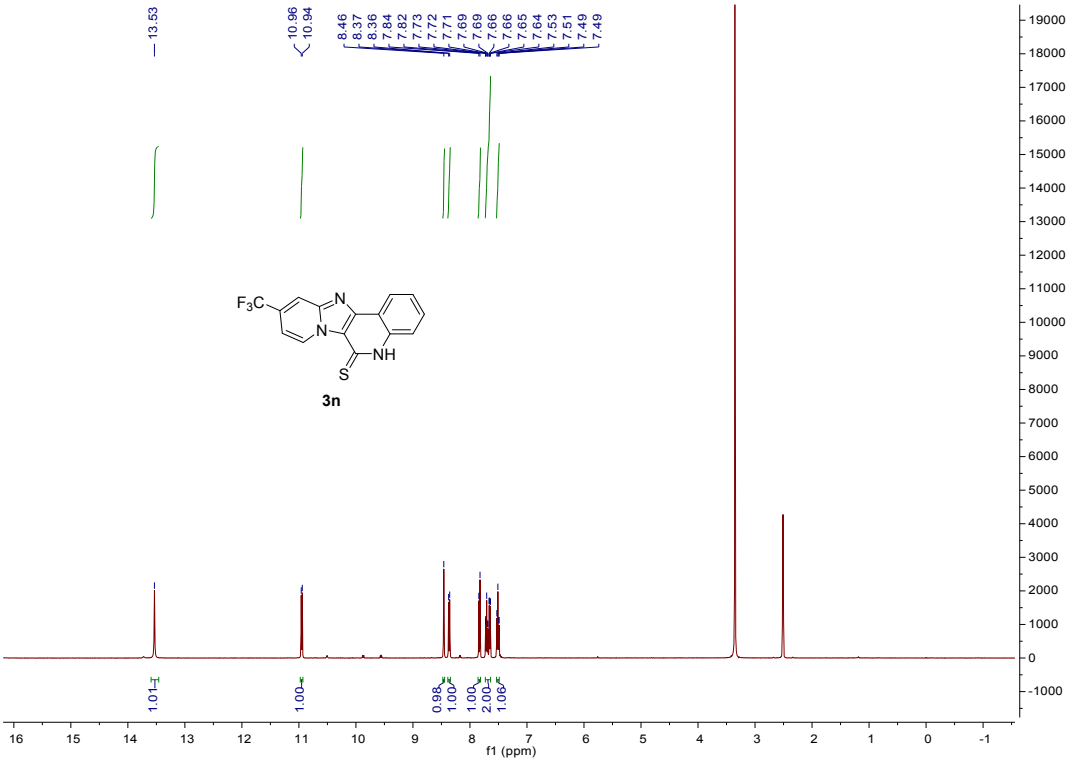
^{1}H NMR spectrum of 3m



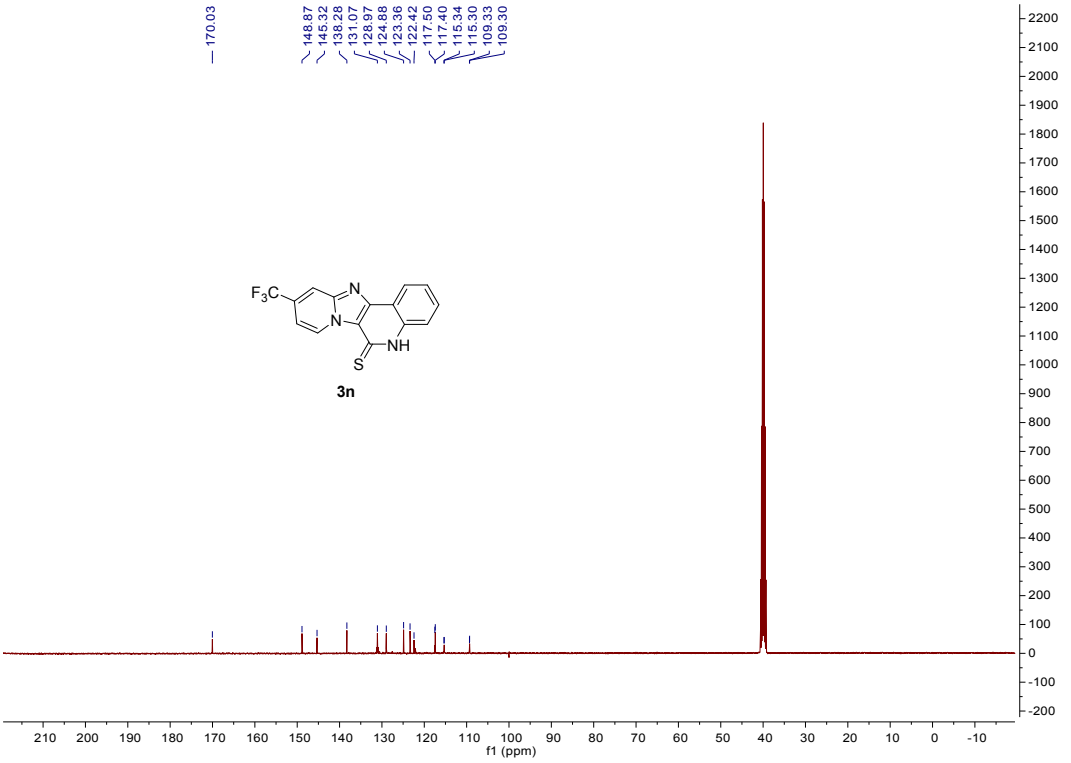
^{13}C NMR spectrum of 3m



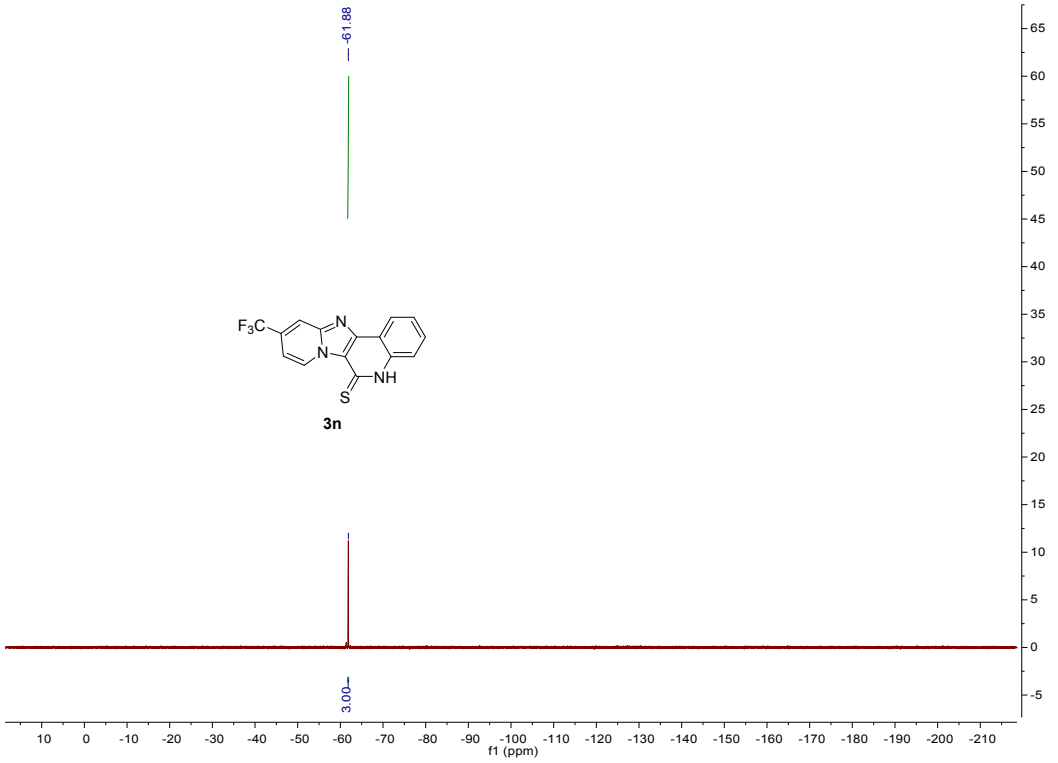
^{1}H NMR spectrum of 3n



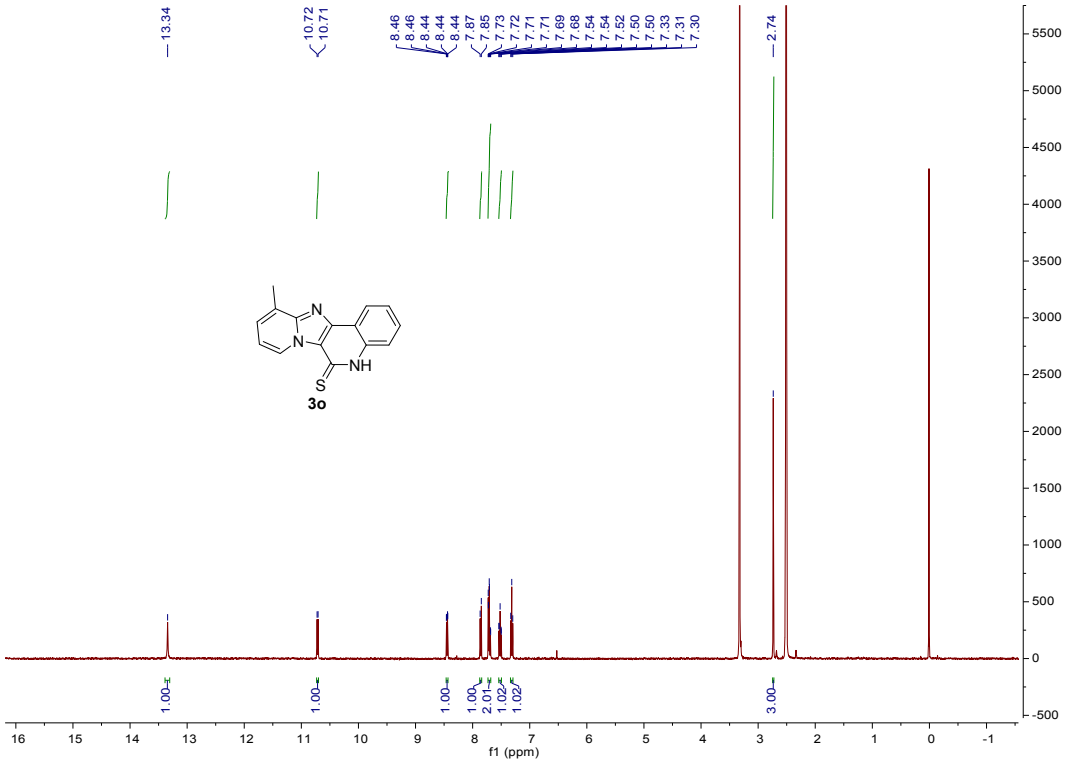
^{13}C NMR spectrum of 3n



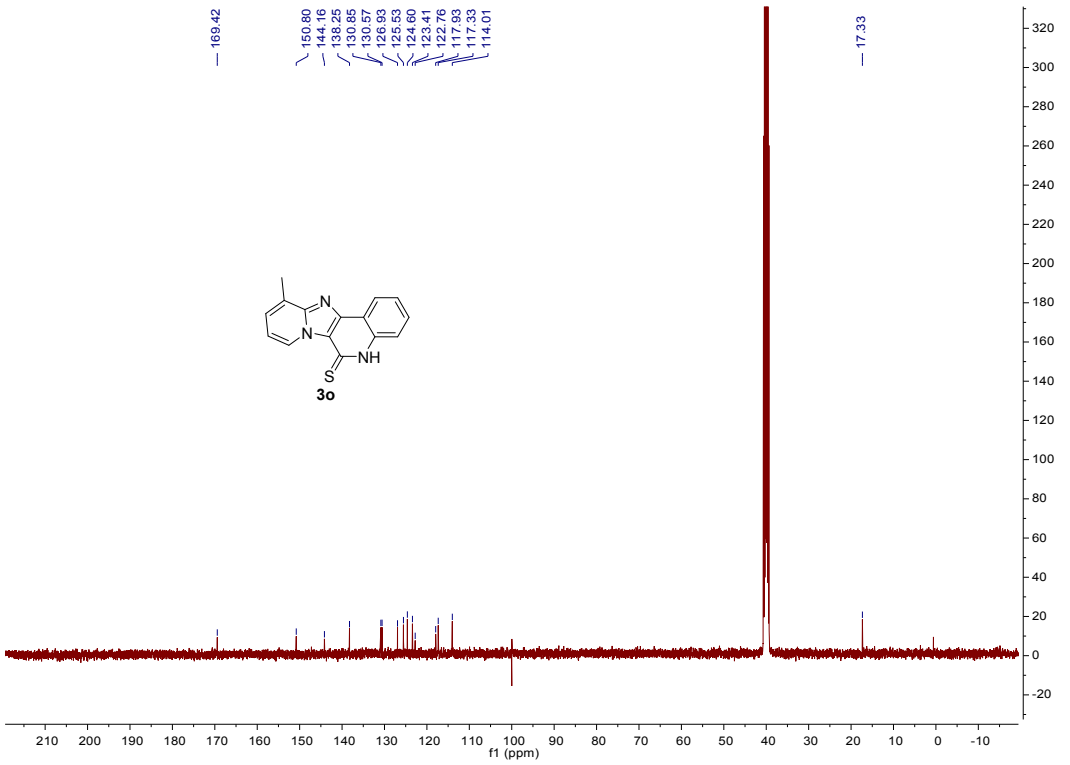
^{19}F NMR spectrum of 3n



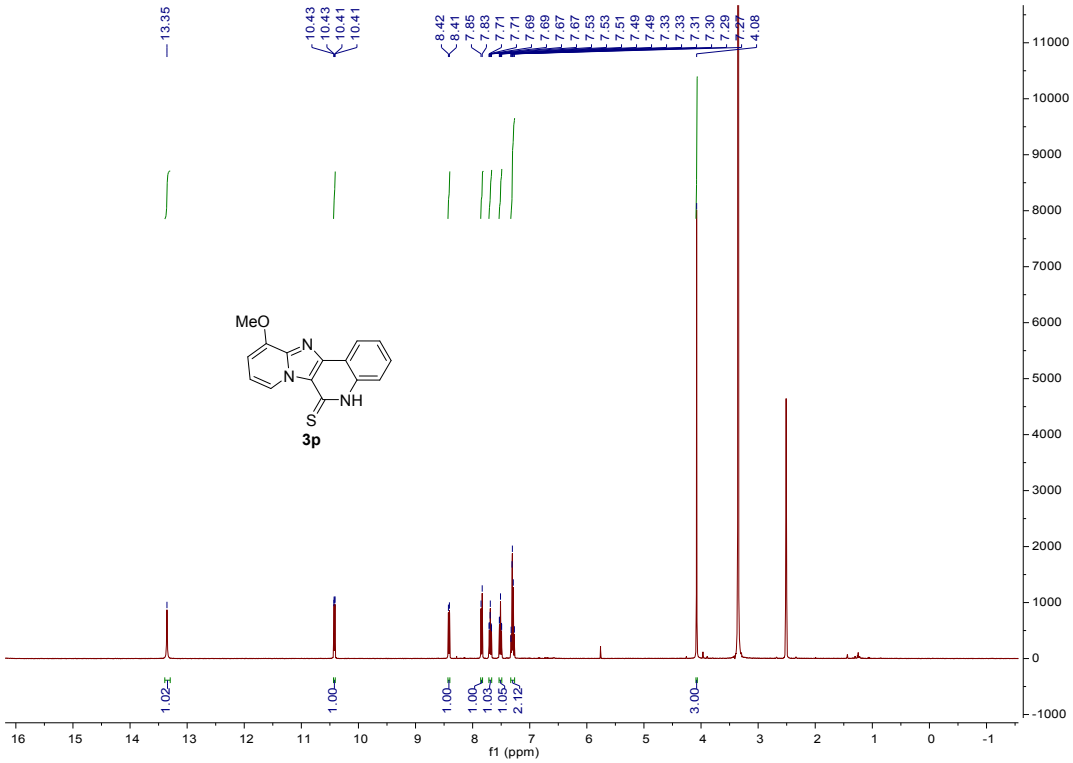
^{1}H NMR spectrum of 3o



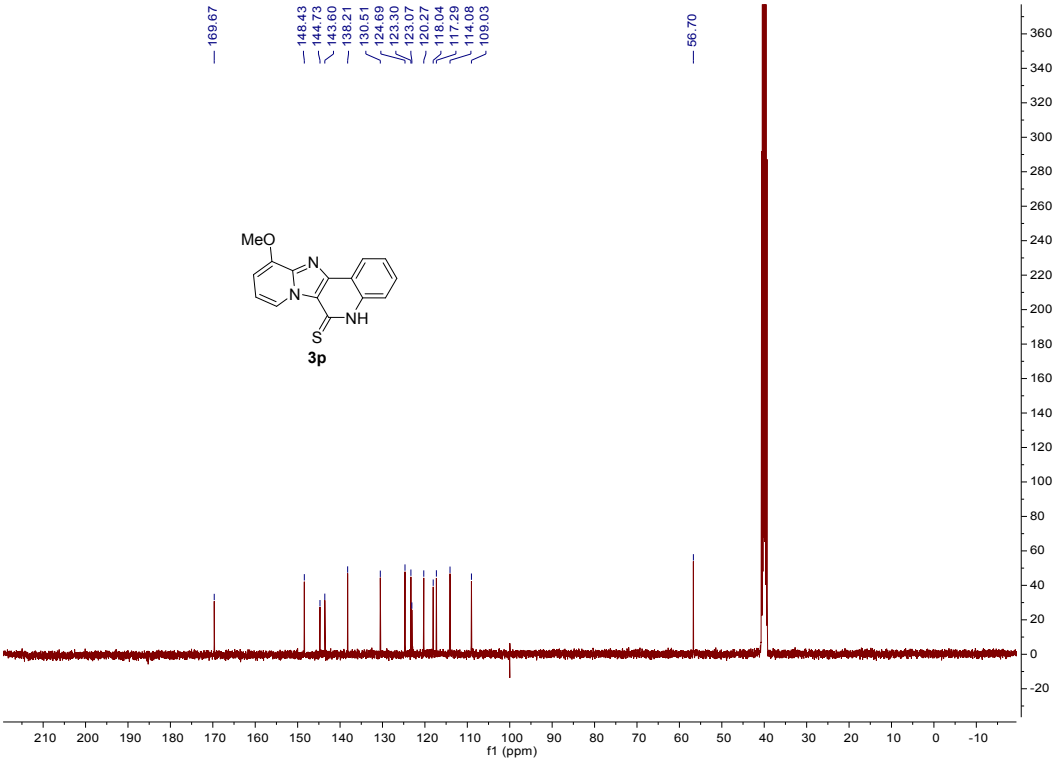
^{13}C NMR spectrum of 3o



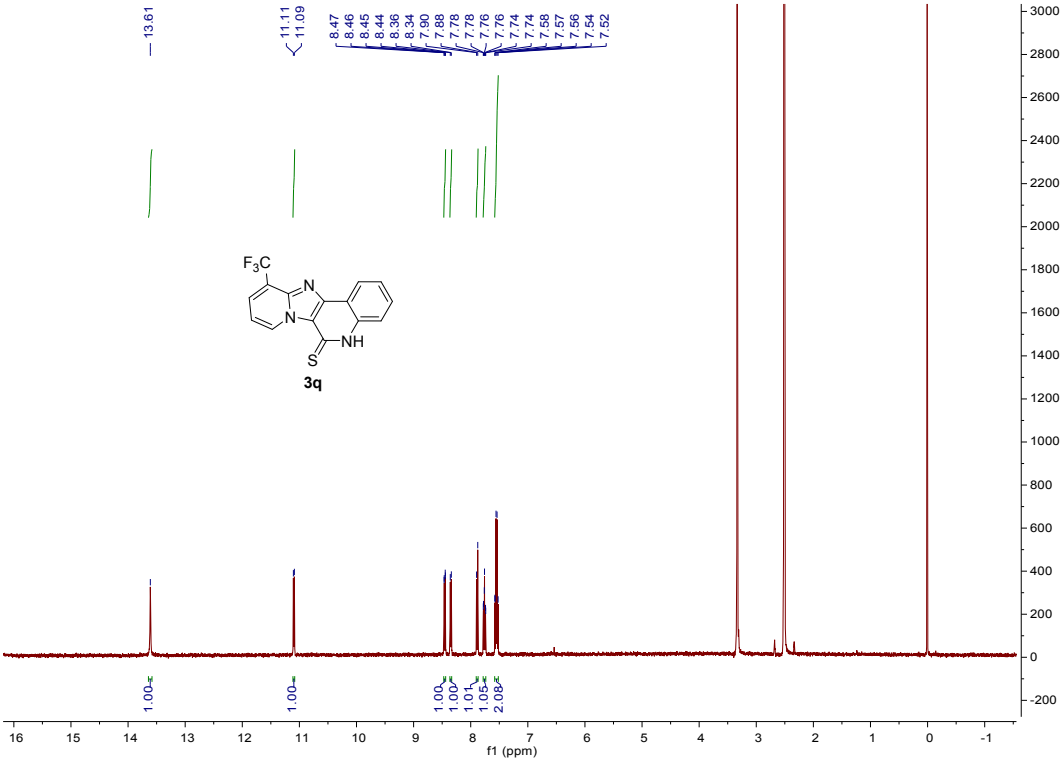
^{1}H NMR spectrum of 3p



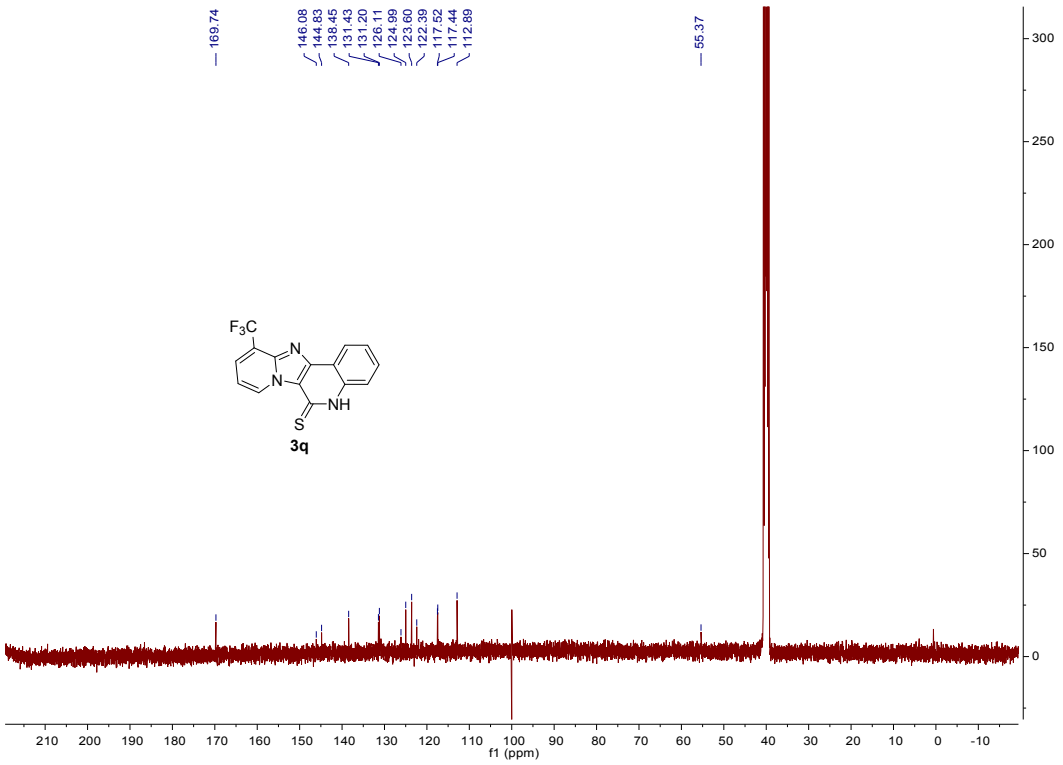
^{13}C NMR spectrum of 3p



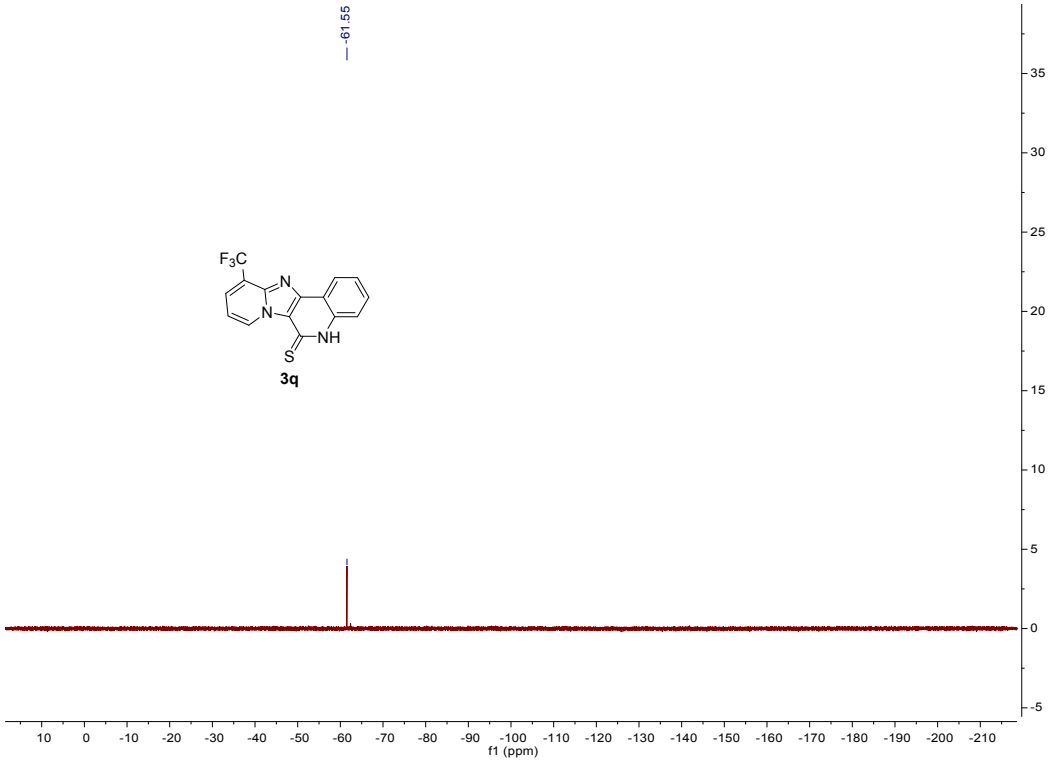
^{1}H NMR spectrum of 3q



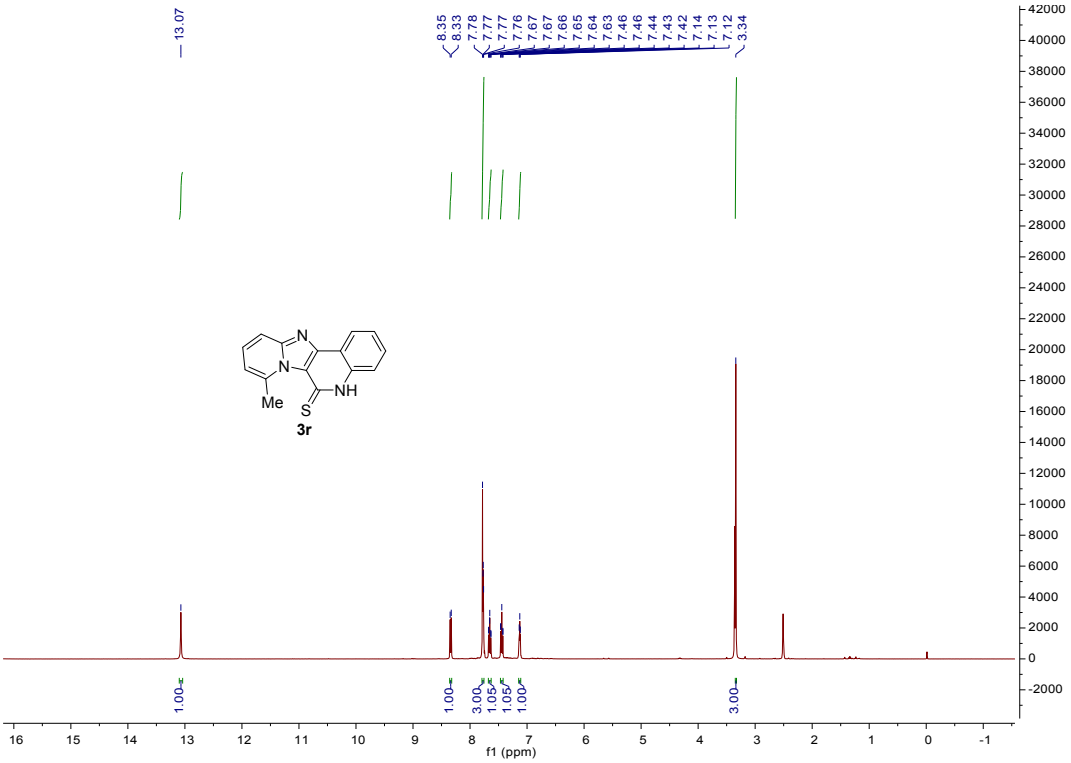
^{13}C NMR spectrum of 3q



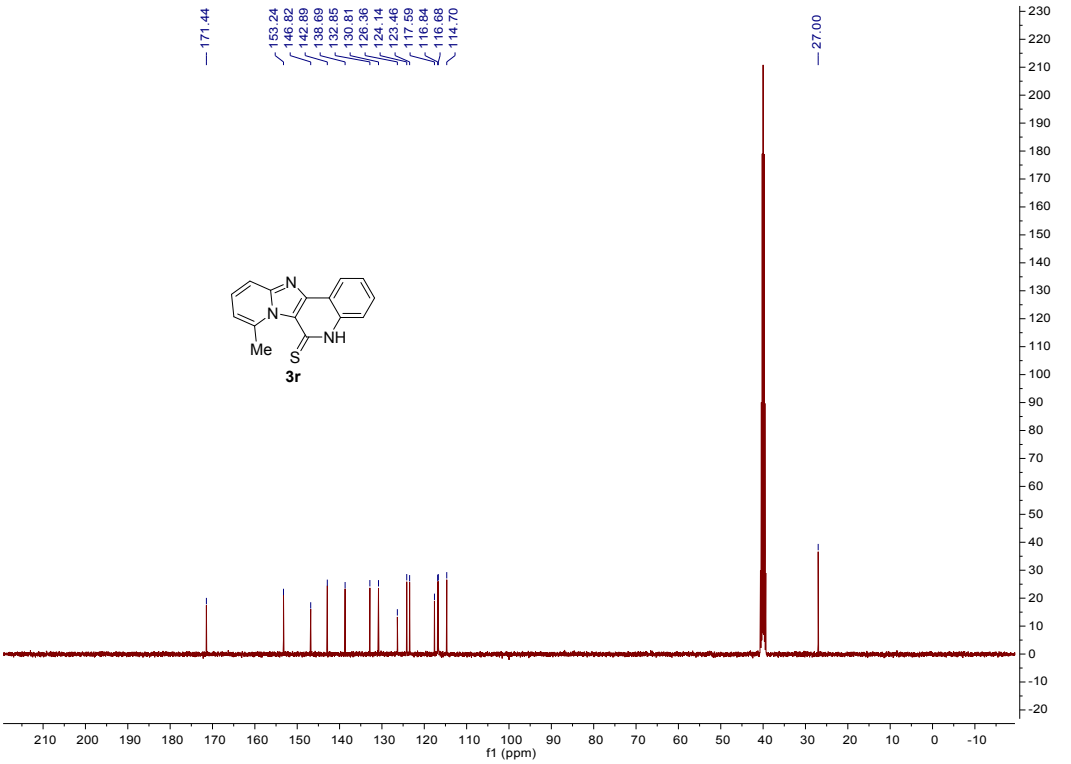
^{19}F NMR spectrum of 3q



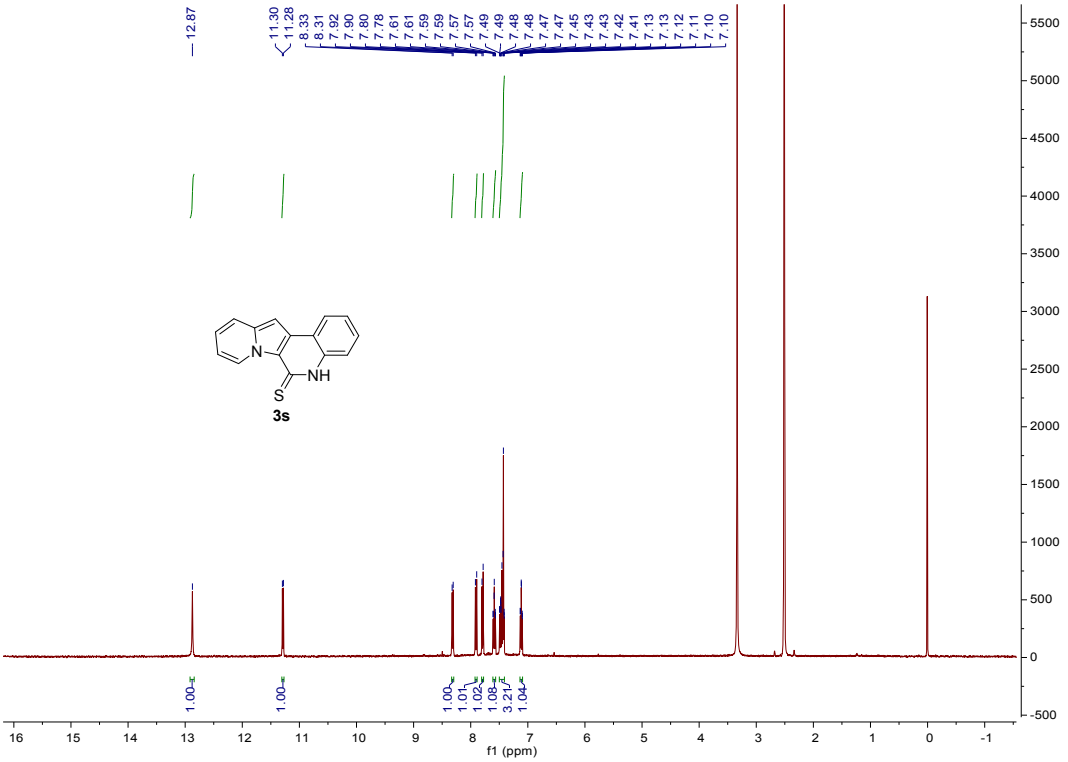
^{1}H NMR spectrum of 3r



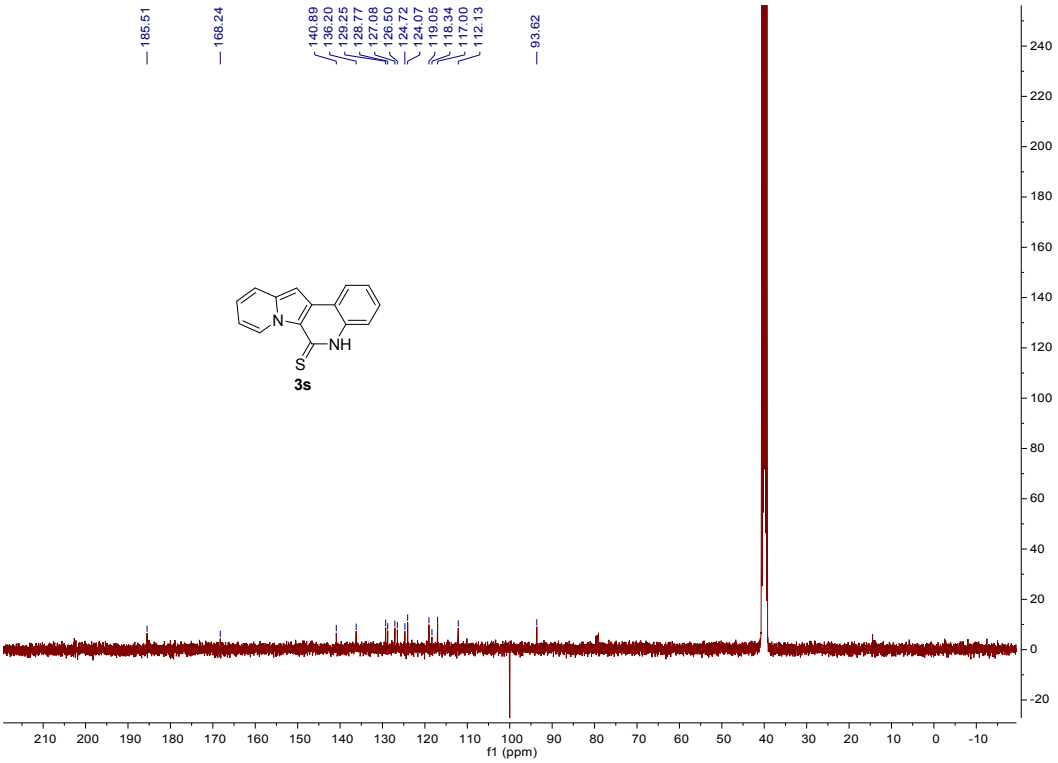
^{13}C NMR spectrum of 3r



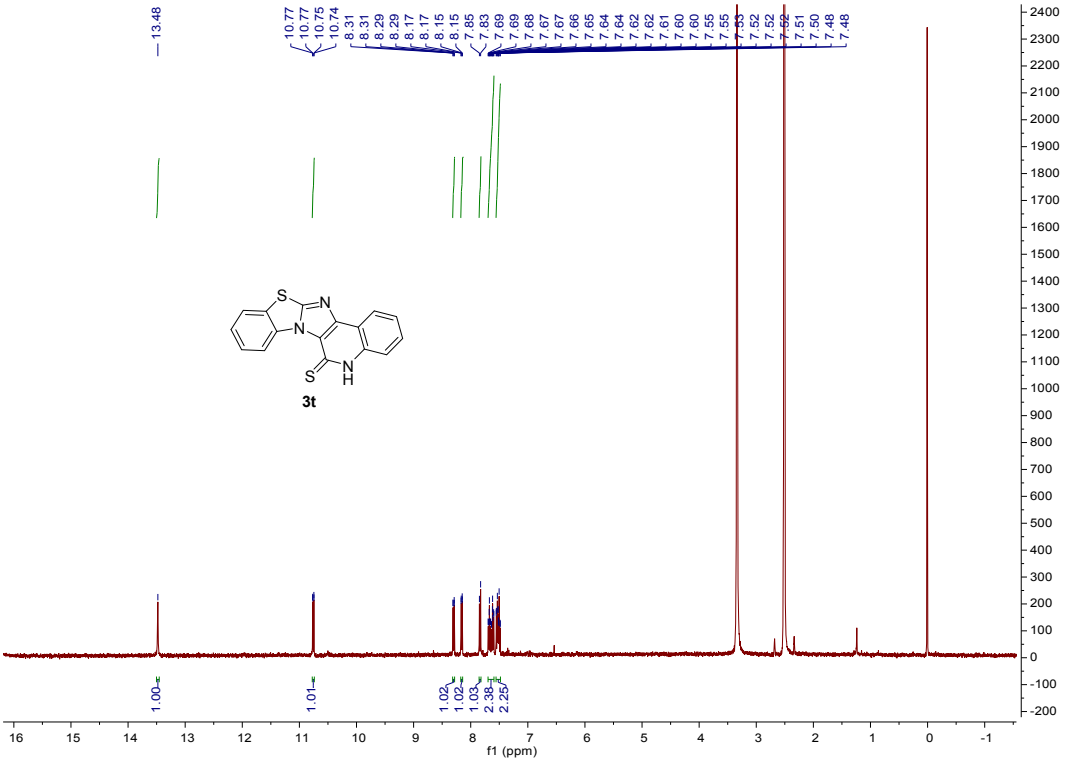
^{1}H NMR spectrum of 3s



^{13}C NMR spectrum of 3s

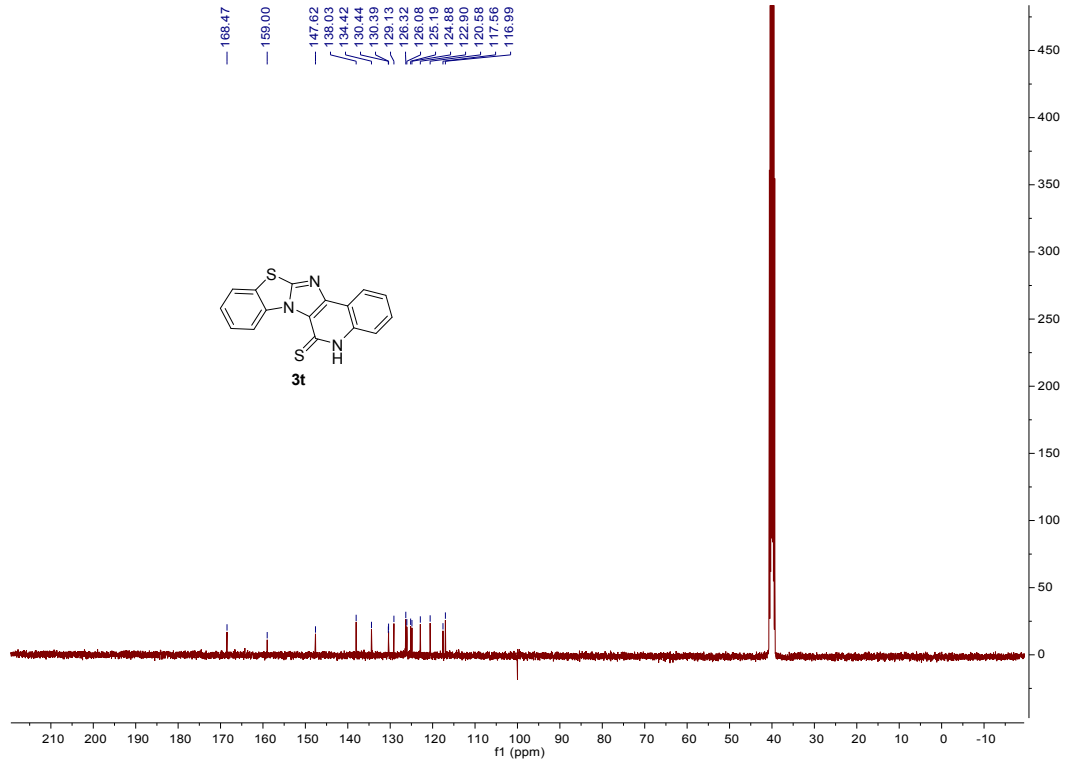


^{1}H NMR spectrum of 3t



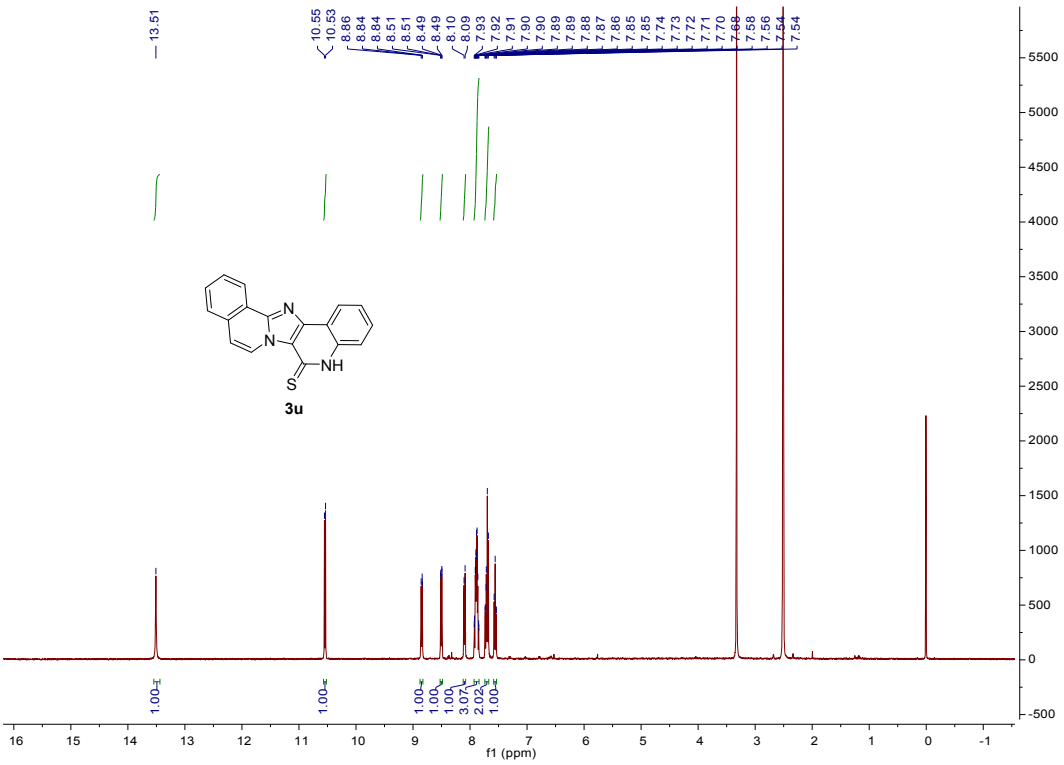
3t

^{13}C NMR spectrum of 3t

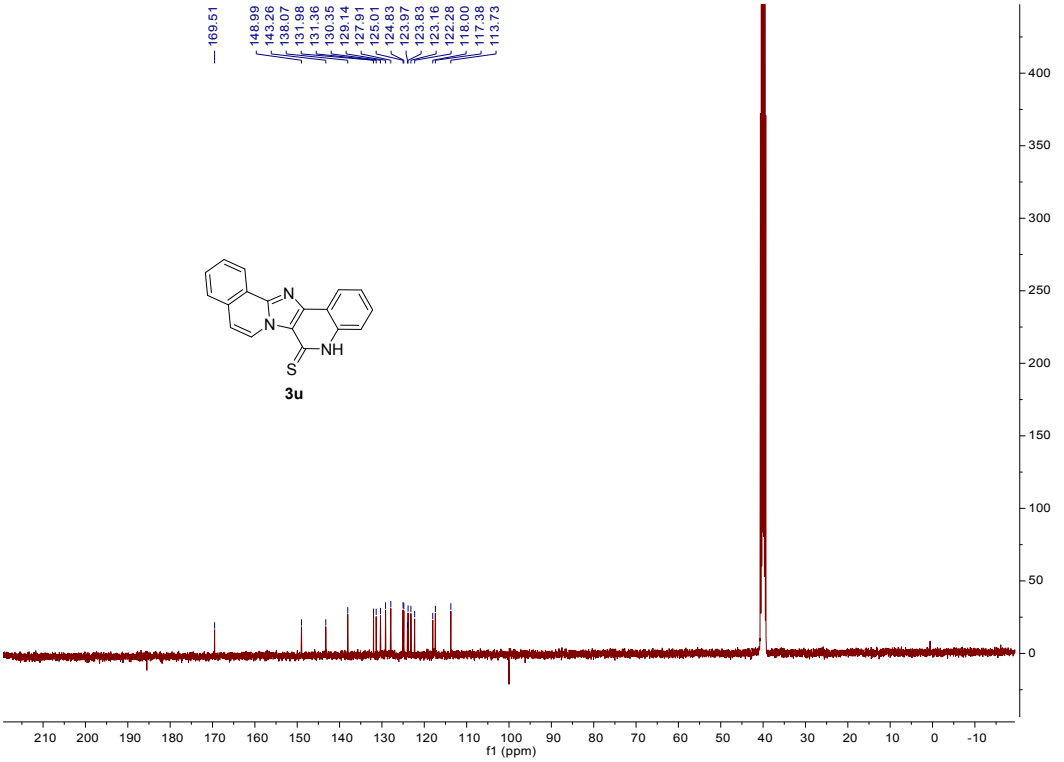


3t

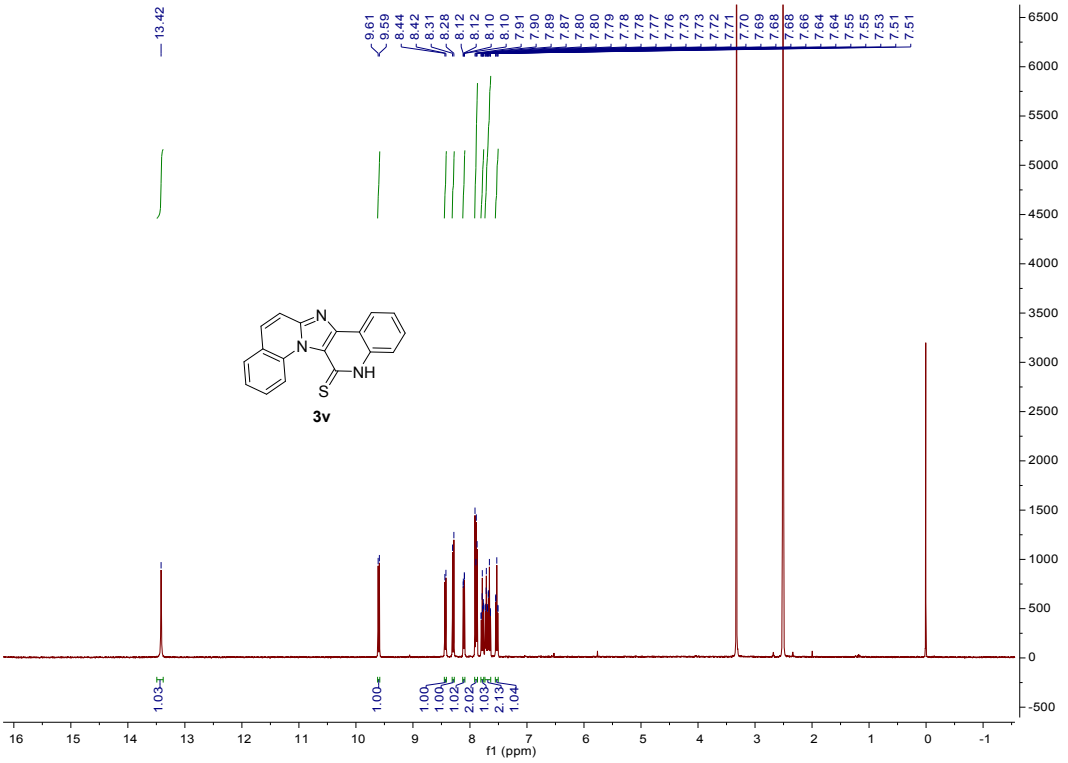
^{1}H NMR spectrum of 3u



^{13}C NMR spectrum of 3u

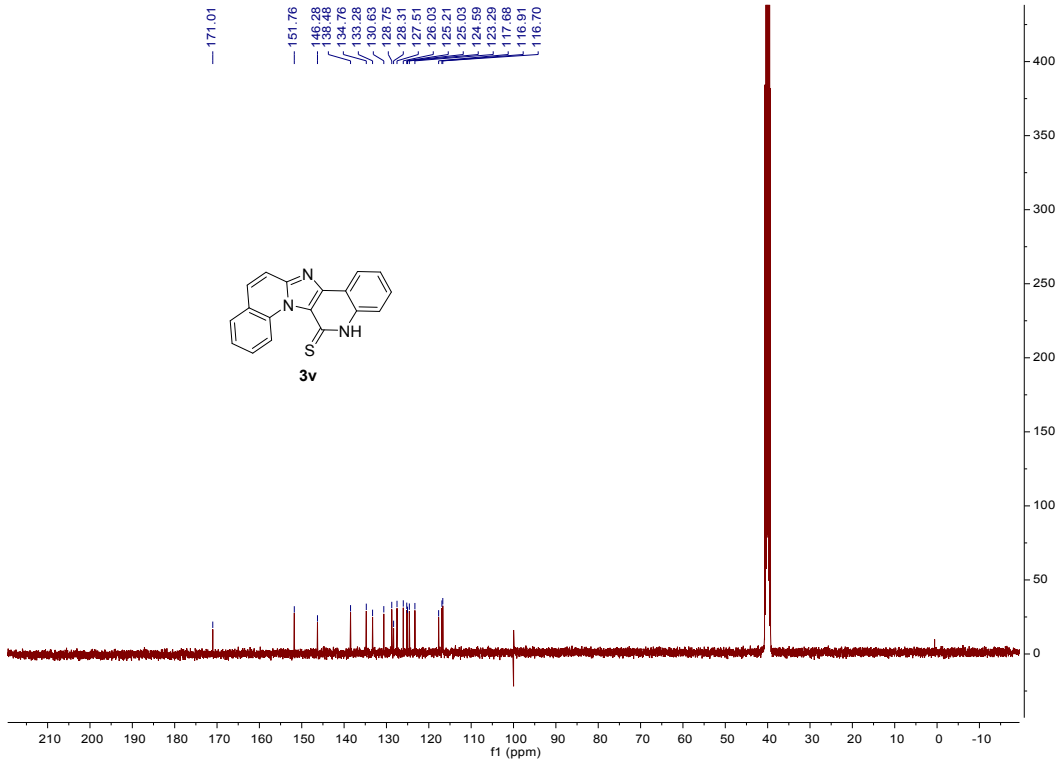


^{1}H NMR spectrum of 3v



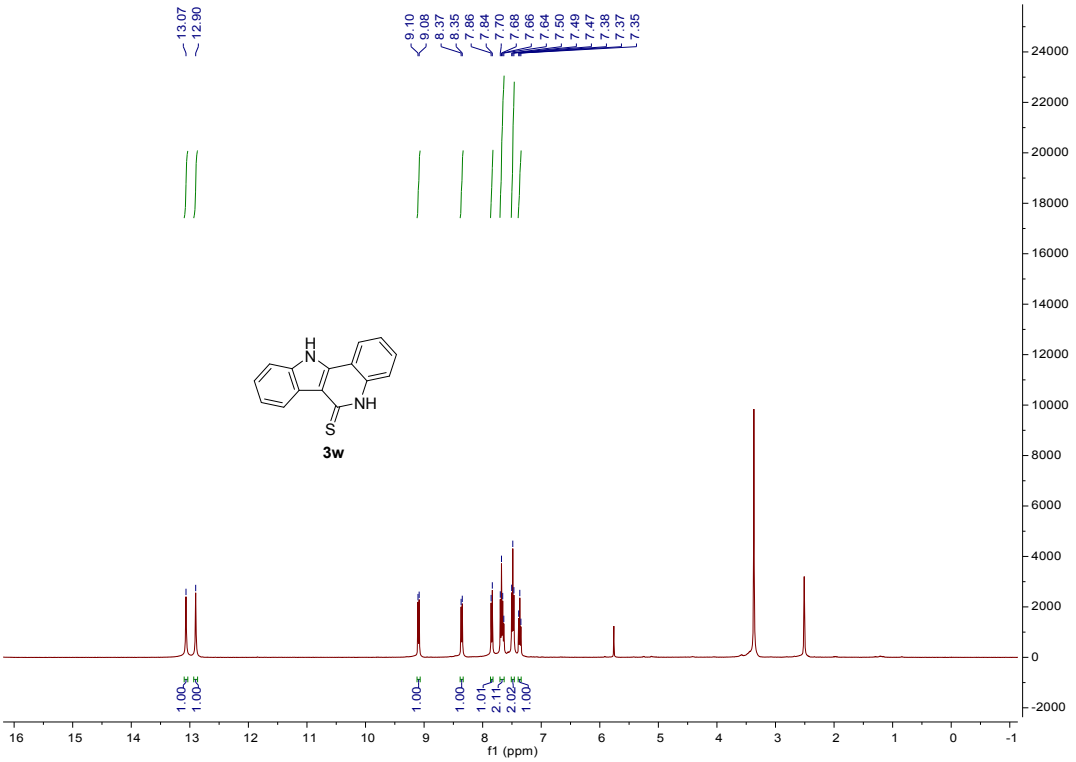
3v

^{13}C NMR spectrum of 3v

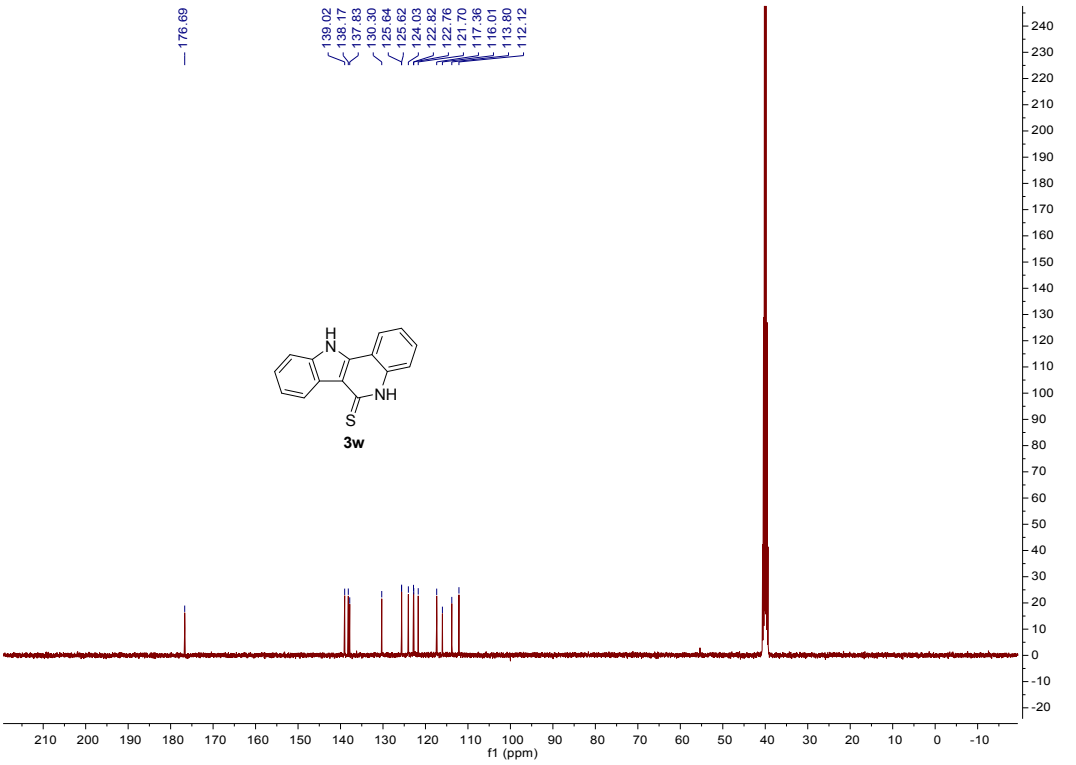


3v

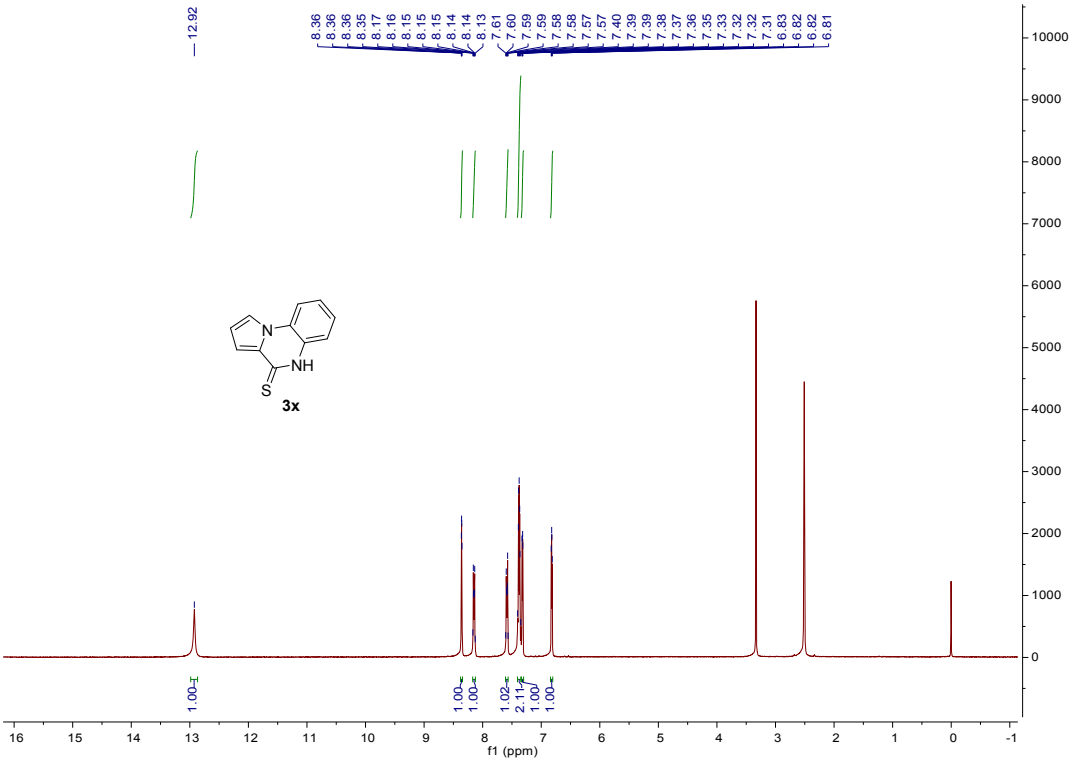
^{1}H NMR spectrum of 3w



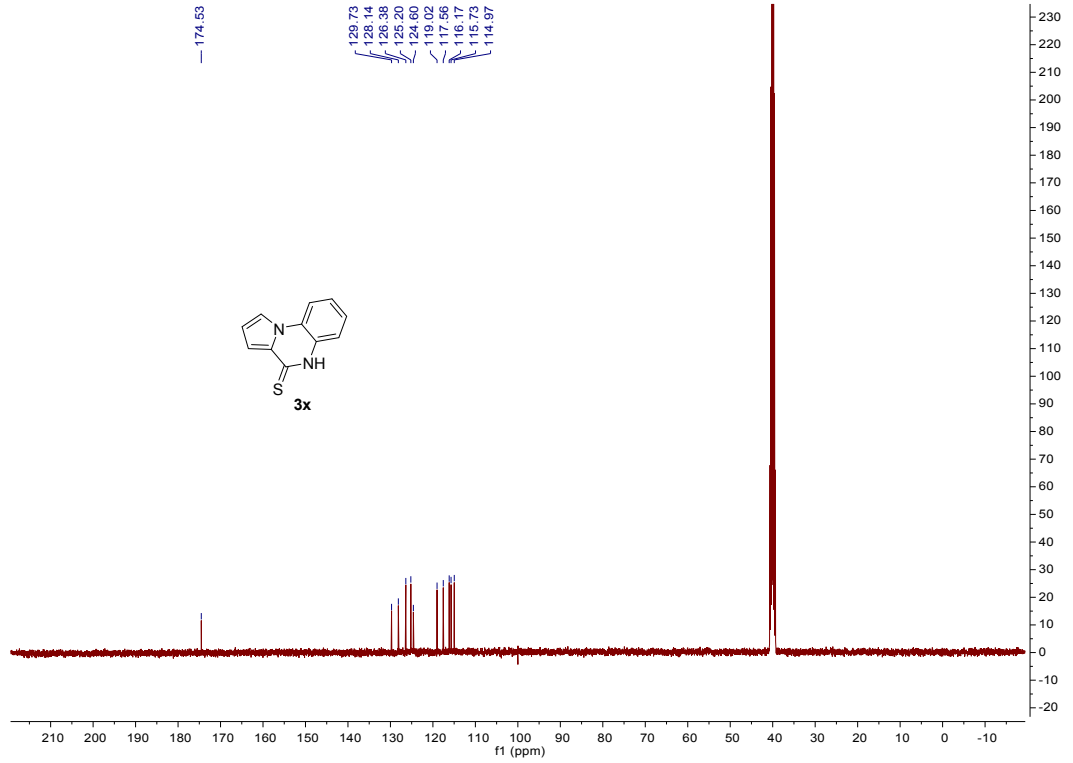
^{13}C NMR spectrum of 3w



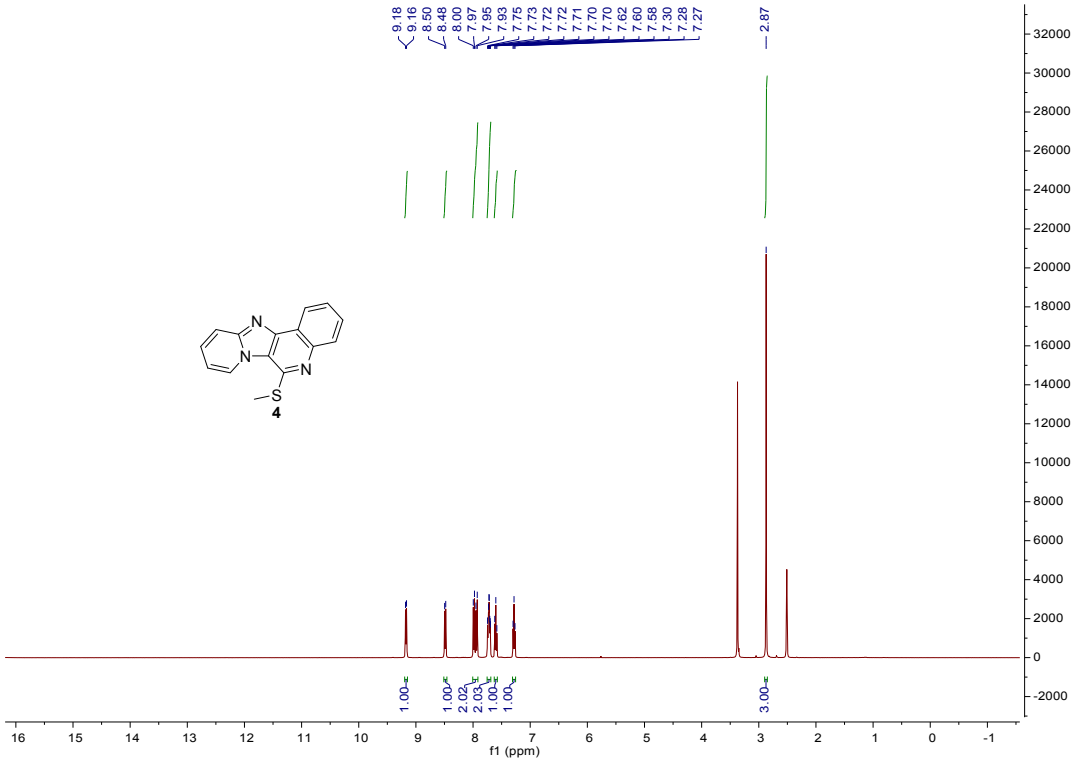
^{1}H NMR spectrum of 3x



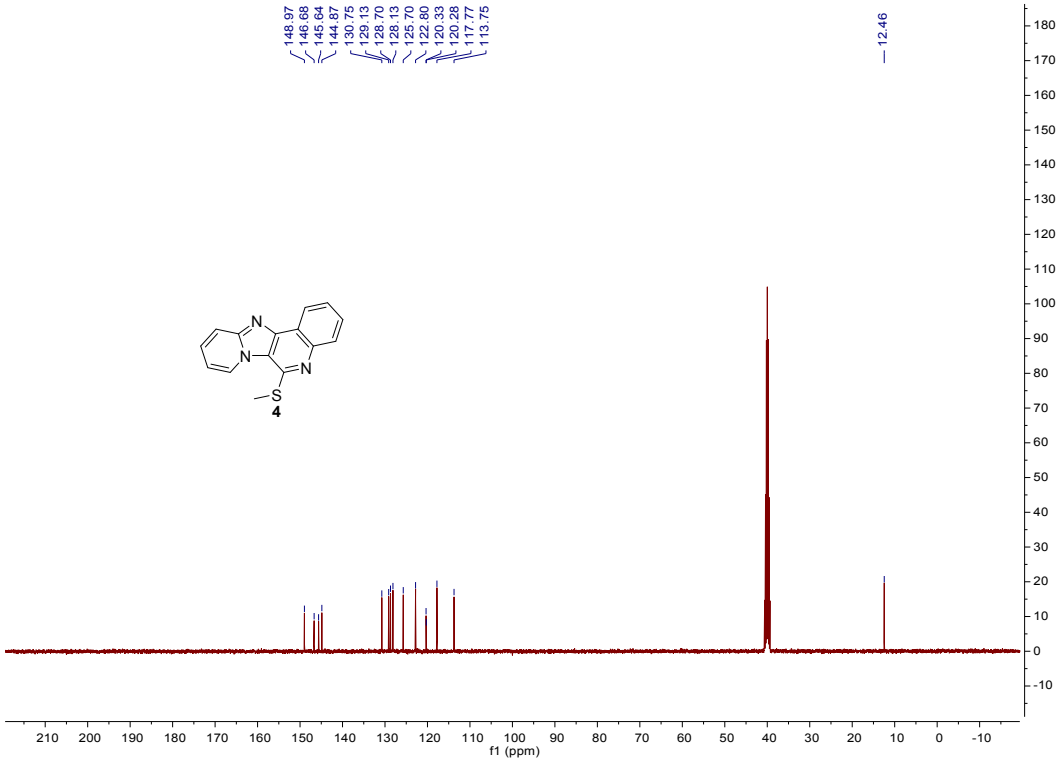
^{13}C NMR spectrum of 3x



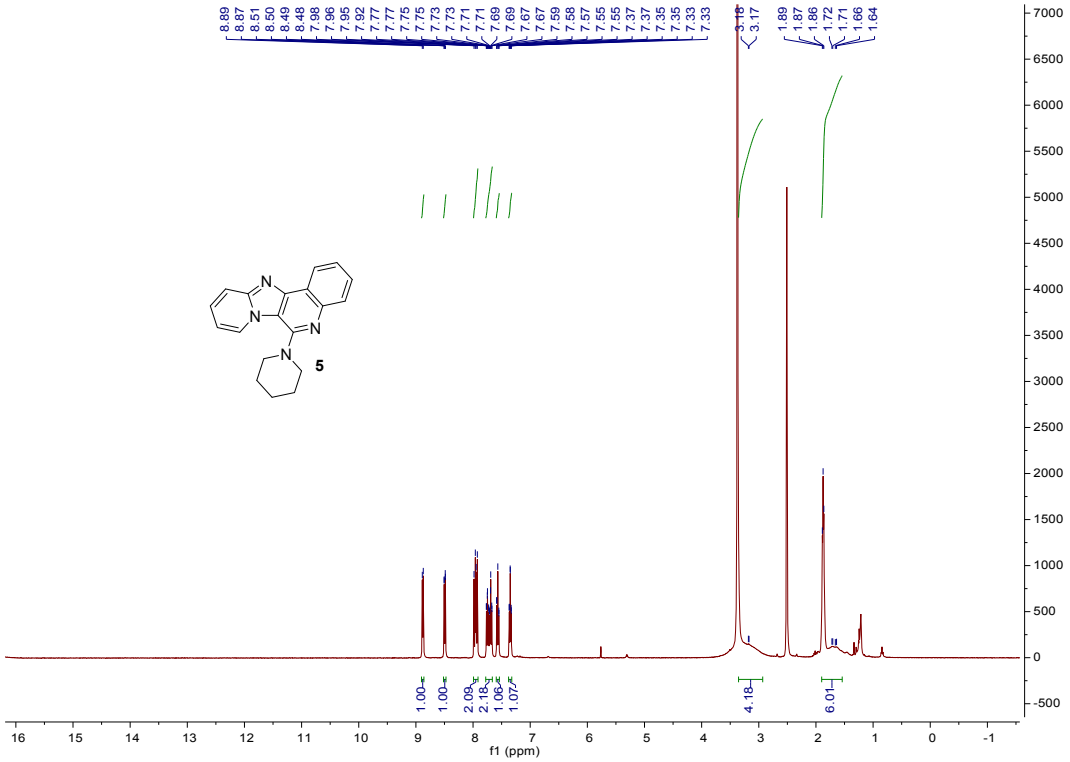
^{1}H NMR spectrum of 4



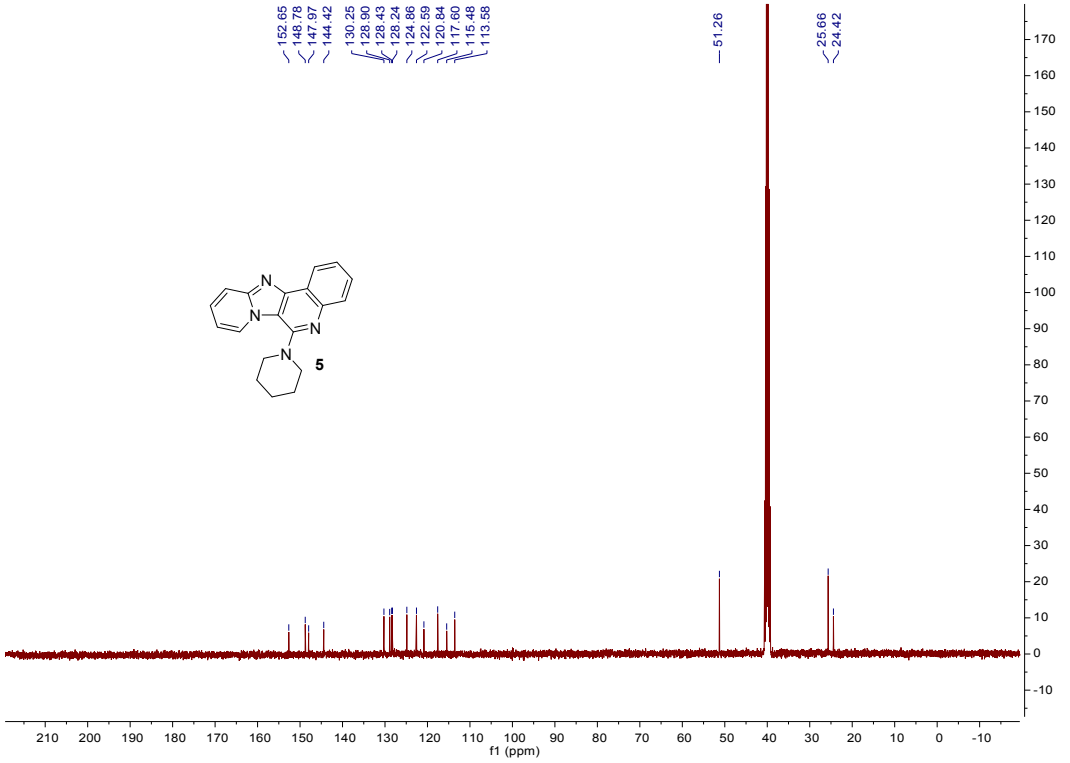
^{13}C NMR spectrum of 4



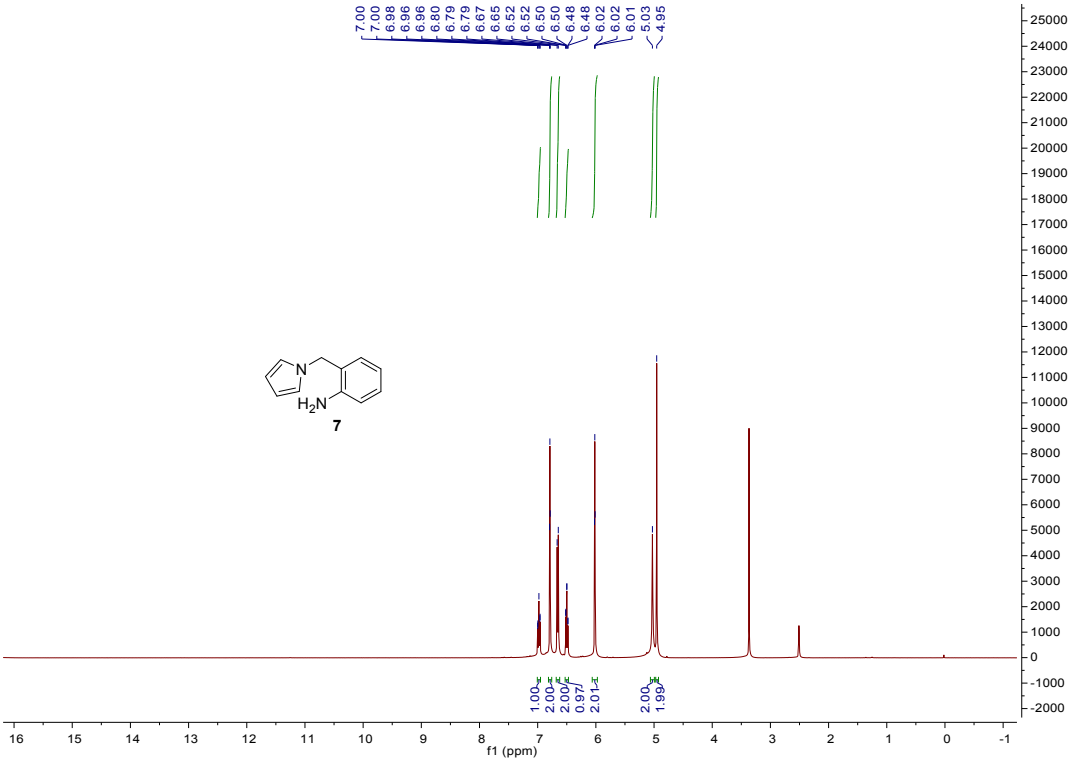
^{1}H NMR spectrum of 5



^{13}C NMR spectrum of 5

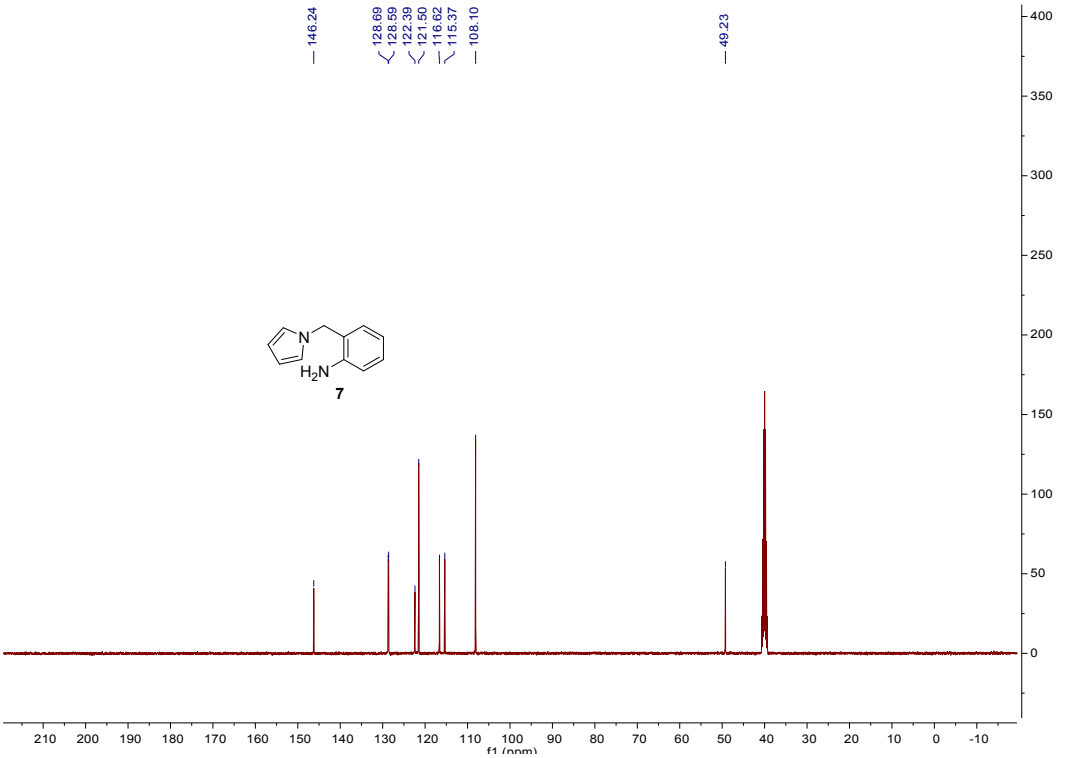


^{1}H NMR spectrum of 7



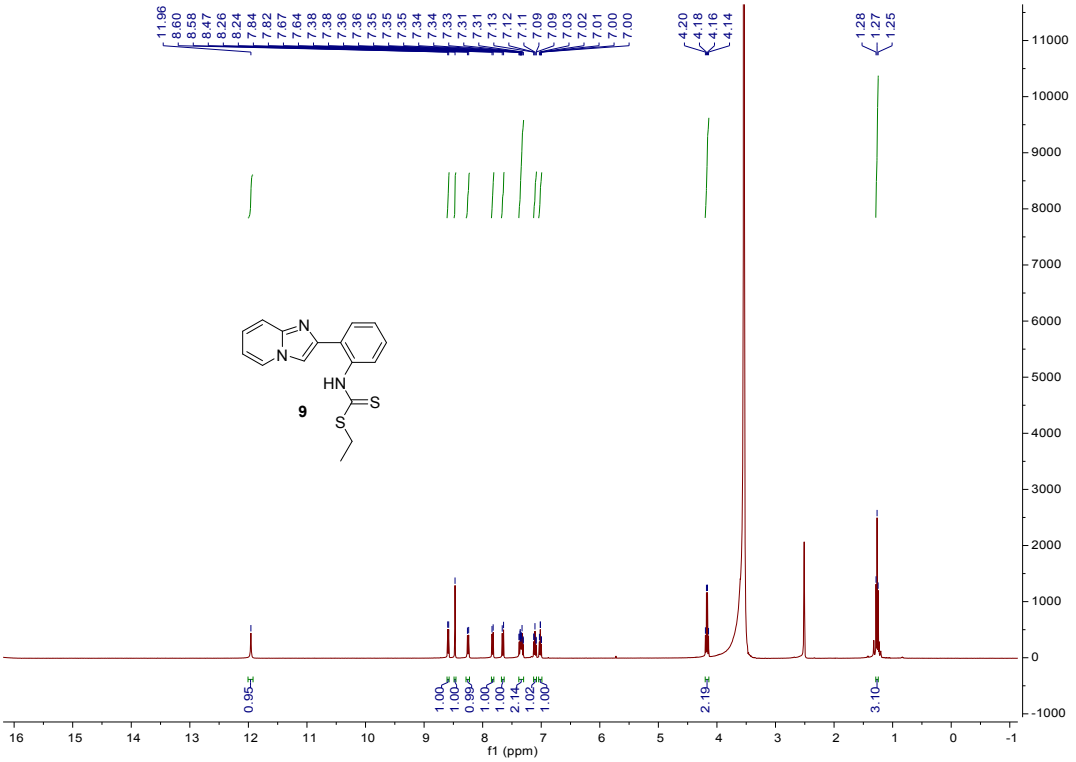
7

^{13}C NMR spectrum of 7

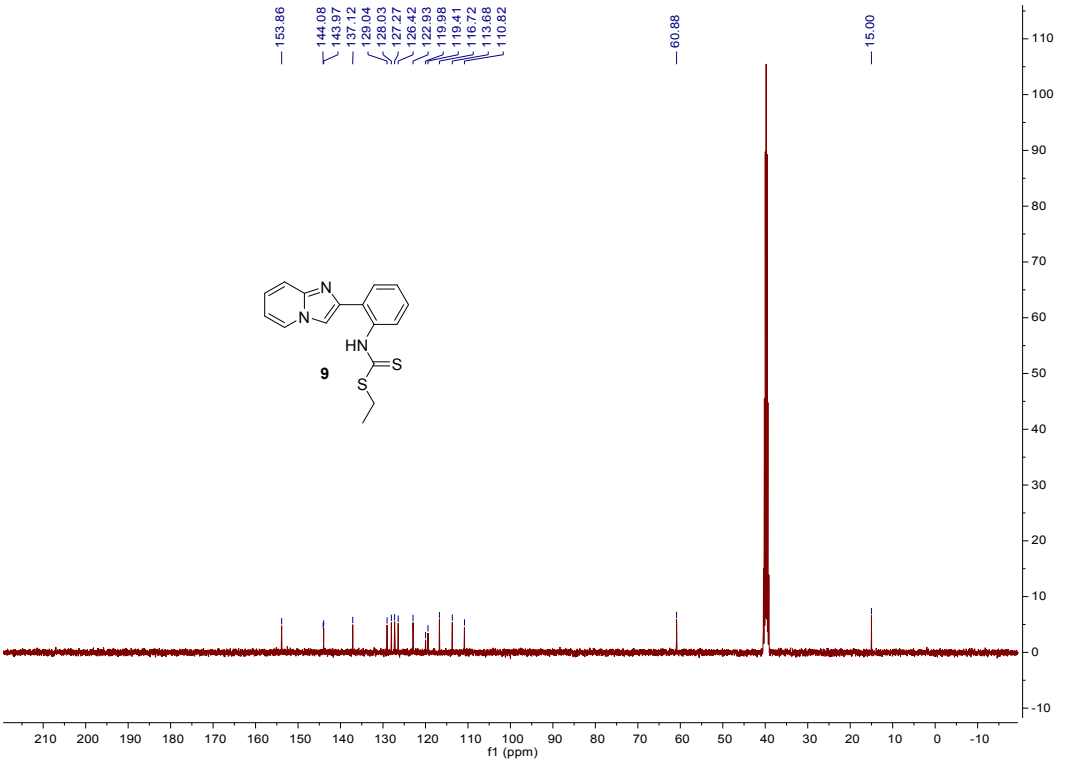


7

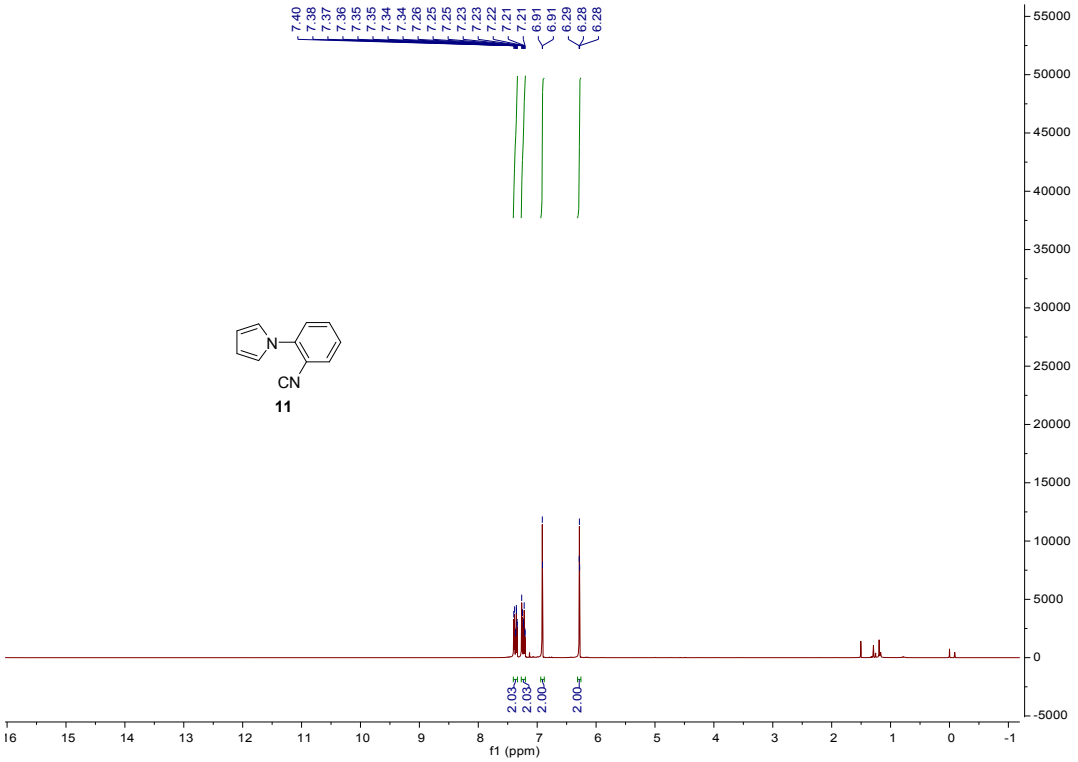
^{1}H NMR spectrum of 9



^{13}C NMR spectrum of 9



^{1}H NMR spectrum of 11



^{13}C NMR spectrum of 11