Synthesis of 4-Amino Pyrrolo and Indolo[1,2-a]quinoxalines via Copper-Catalyzed Insertion of *O*-benzoylhydroxylamines into Isocyanide

Chaeeun Lee, [§,a] Kyung Ah Kim,[§,a] Nayoung Lim,[§,a] Bomcha Park,[a] Jiwoo Lee,[b] Ki Bum Hong,*[,b], and Sungwook Choi*[,a]

[a]*Department of New Drug Discovery and Development, Chungnam National University, Daejeon, Korea*
Email: swchoi2010@cnu.ac.kr
[b]*New Drug Development Center (NDDC), Daegu-Gyeongbuk Medical Innovation Foundation (DGMIF), 80 Cheombok-ro, Dong-gu, Daegu, Republic of Korea*
Email: kbhong@kmedihub.re.kr

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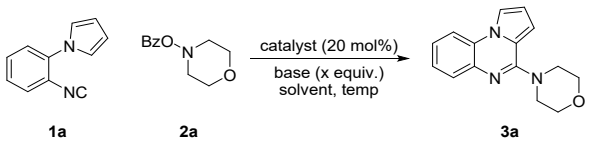
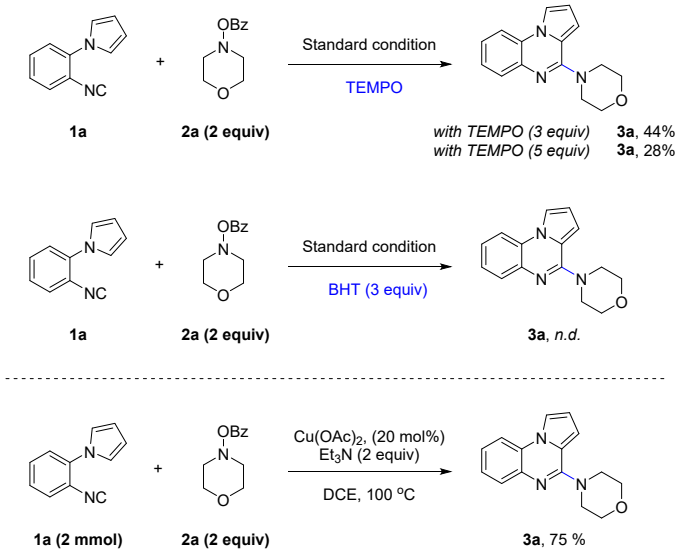
Table S1. Optimization

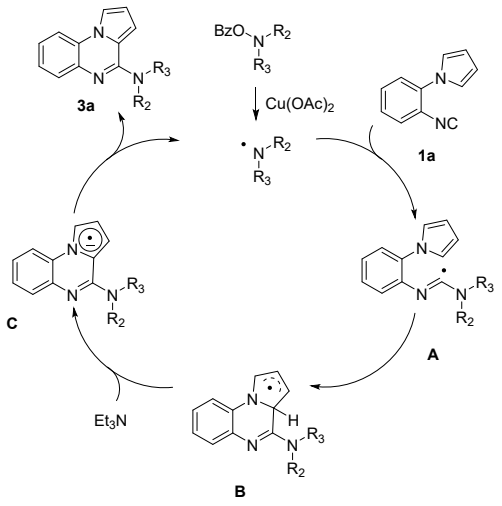


entry[a]	catalyst	Base (equiv.)	solvent	temp	Yield (%) [b]
9	$Cu(OAc)_2$	Et_3N	DCE	100	78
15	$Cu(OAc)_2$	Et_3N	DCE	60	51
16	$Cu(OAc)_2$	Cs_2CO_3 (2)	DCE	100	56
17	$Cu(OAc)_2$	DBU (2)	DCE	100	52
18	$Cu(OAc)_2$	DIEA (2)	DCE	100	58
19	$Cu(OAc)_2$	K_2CO_3 (2)	DCE	100	56
20	$Cu(OAc)_2$	Na_2CO_3 (2)	DCE	100	67
21	$Cu(OAc)_2$	$NaHCO_3$ (2)	DCE	100	68

Scheme S1. Mechanistic investigation and large-scale reaction



Scheme S2. Plausible Mechanism



Addition of a dialkylamine radical (R_2R_3N•) to the isonitrile unit of **1a** furnishes imidoyl radical **A**, which undergoes intramolecular cyclization to give radical **B**. Owing to the pronounced acidity of the α-proton, **B** is deprotonated by triethylamine to afford radical anion **C**. Single-electron transfer from **C** to a O-benzoylhydroxylamines then delivers product **3a** and regenerates dialkylamine radical, thereby sustaining the radical-chain propagation.

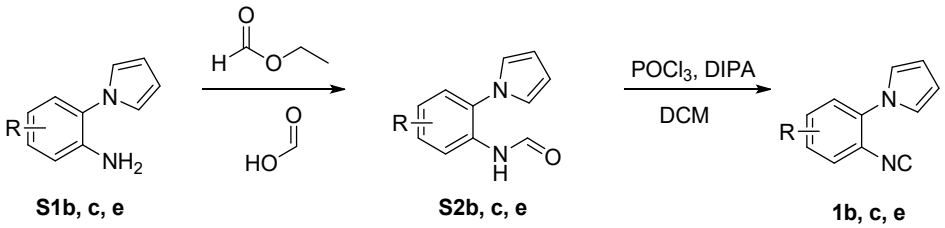
1. Generals

Unless otherwise noted, all solvents and reagents were purchased from commercial suppliers (Sigma-Aldrich, TCI, and Alfa-Aesar) and used without further purification. Thin Layer Chromatography (TLC) was performed on Merck (Silica gel 60, F-254, 0.25 mm). Chromatographic purifications were performed under gradient using a Biotage® system and prepacked disposable silica cartridges using commercial 60 Å silica gel. NMR spectra were recorded on a Bruker 400-, 600-MHz spectrometers. Chemical shifts are reported as δ values in parts per million downfield from solvents as internal standards ($CDCl_3$: 7.26 ppm for ^1H NMR and 77.04 ppm for ^{13}C NMR). Mass spectra were obtained in positive electrospray ionization (ESI+) using an AB SCIEX (1290 infinity II/Triple TOF 5600 plus). *O*-Benzoyl hydroxylamines (**2a-q**) were synthesized in accordance with previously described methods.[1-4] High resolution mass spectra (HRMS) were obtained by AB SCIEX Triple TOF 5600 Plus System at Chungnam National University.

2. Synthesis and characterization of Starting Arylisocyanides

Compounds **1a**[5], **1d**[6], **1i**[7], **1j**[7], **1k**[6] and **4**[7] are adapted in accordance to literature procedures, while substrates **1b**, **1c**, and **1e-i** were prepared as described below.

Method 1:

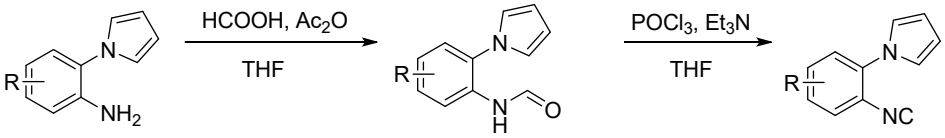


S1b, c, e **S2b, c, e** **1b, c, e**

A solution of **S1** (1.0 equiv) in ethyl formate (78.0 equiv) and formic acid (22.0 equiv) was heated at reflux overnight. After cooling to room temperature, the solvent was removed under reduced pressure to afford N-(2-pyrrolyl)phenyl formamide quantitatively. The crude product was used directly in the next step without further purification.

To a solution of the above crude **S2** (1.0 equiv) in dichloromethane (0.135 M) at 0 °C was added N,N-diisopropylamine (DIPA) (6.0 equiv), followed by dropwise addition of phosphoryl trichloride ($POCl_3$) (2.0 equiv). The reaction mixture was stirred at 0 °C for 30 min and then at room temperature for 2 h. The mixture was cooled again to 0 °C and quenched by slow addition of a 20% aqueous sodium carbonate solution, followed by dilution with dichloromethane (DCM, 5 mL). The organic layer was separated, washed sequentially with 20% aqueous sodium carbonate ($NaHCO_3$) and brine, dried over anhydrous sodium sulfate (Na_2SO_4), and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (n-hexane/ethyl acetate (EtOAc)) to yield the title compound.

Method 2:



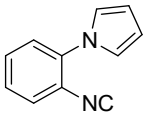
S1f-i **S2f-i** **1f-i**

Acetic formic anhydride, prepared in situ from acetic anhydride (2.0 equiv) and formic acid (2.0 equiv) by stirring at 55 °C for 2 h, was added dropwise to a stirred solution of **S1** (1.0 equiv) in tetrahydrofuran (THF, 0.52 M) at 0 °C. The reaction mixture was stirred at room temperature for 30 min. After completion, volatiles were removed under reduced pressure to afford N-(2-pyrrolyl)phenyl formamide quantitatively. The crude product was used directly in the subsequent dehydration without further purification.

A solution of the crude **S2** (1.0 equiv) and triethylamine (Et_3N) (5.0 equiv) in THF (0.5 M) was cooled to 0 °C. $POCl_3$ (1.5 equiv) was then added dropwise, and the reaction mixture was stirred at 0 °C for 15 min. Upon completion of the reaction, the mixture was quenched by the addition of saturated ammonium chloride (NH_4Cl) solution and extracted with EtOAc (3 ×). The combined organic extracts were dried over anhydrous Na_2SO_4 and concentrated under reduced

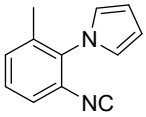
pressure. The residue was purified by column chromatography on silica gel (n-hexane/EtOAc) to afford the title compound.

1-(2-Isocyanophenyl)-1*H*-pyrrole (1a)[5]



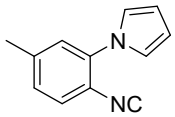
Compound **1a** was prepared in accordance with the literature known procedure in 73% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53-7.44 (m, 2H), 7.39-7.31 (m, 2H), 7.02 (t, *J* = 2.2 Hz, 2H), 6.39 (t, *J* = 2.2 Hz, 2H). The spectral data are in accordance with the literature.

1-(2-Isocyano-6-methylphenyl)-1*H*-pyrrole (1b)



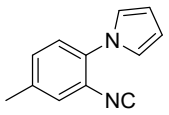
Compound **1b** was prepared in accordance with the general procedure for the synthesis of arylisocyanides by using **S1b**[8] (3-methyl-2-(1*H*-pyrrol-1-yl)aniline, 1.25 mmol) as the starting material and purified by flash chromatography on silica gel (Biotage®, gradient elution: 2→20% EtOAc in n-hexane) as a brown solid (Method 1, 173 mg, 75% yield, M.P. 50-51 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 (d, *J* = 8.1 Hz, 1H), 7.17 (s, 1H), 7.13 (d, *J* = 8.1 Hz, 1H), 7.00 (t, *J* = 2.1 Hz, 2H), 6.37 (t, *J* = 2.1 Hz, 2H), 2.41 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.0, 141.1, 136.9, 128.4, 127.9, 126.7, 121.3, 110.4, 21.3; HRMS (ESI) m/z: [M+H$^+$] Calcd for $C_{12}H_{11}N_2$ 183.0917; found 183.0918

1-(2-Isocyano-5-methylphenyl)-1*H*-pyrrole (1c)



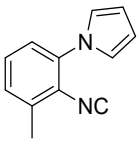
Compound **1c** was prepared in accordance with the general procedure for the synthesis of arylisocyanides by using **S1c**[8] (4-methyl-2-(1*H*-pyrrol-1-yl)aniline, 1.47 mmol) as the starting material and purified by flash chromatography on silica gel (Biotage®, gradient elution: 2→20% EtOAc in n-hexane) as a light yellow solid (Method 1, 190 mg, 75% yield, M.P. 93-94 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37-7.28 (m, 3H), 6.70 (t, *J* = 2.1 Hz, 2H), 6.39 (t, *J* = 2.1 Hz, 2H), 2.13 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.4, 138.0, 137.1, 131.6, 128.5, 125.1, 121.4, 109.9, 17.5; HRMS (ESI) m/z: [M+H$^+$] Calcd for $C_{12}H_{11}N_2$ 183.0917; found 183.0917

1-(2-Isocyano-4-methylphenyl)-1*H*-pyrrole (1d)[6]



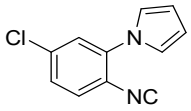
Compound **1d** was prepared in accordance with the literature known procedure in 33% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 (s, 1H), 7.25 (s, 2H), 6.98 (t, *J* = 2.2 Hz, 2H), 6.37 (t, *J* = 2.1 Hz, 2H), 2.40 (s, 3H). The spectral data are in accordance with the literature.

1-(2-Isocyano-3-methylphenyl)-1*H*-pyrrole (1e)



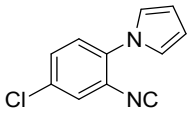
Compound **1e** was prepared in accordance with the general procedure for the synthesis of arylisocyanides by using **S1e**[9] (2-methyl-6-(1*H*-pyrrol-1-yl)aniline, 1.74 mmol) as the starting material and purified by flash chromatography on silica gel (Biotage®, gradient elution: 2→20% EtOAc in n-hexane) as a light-yellow solid (115 mg, 36% yield, M.P. 68-69 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39-7.32 (m, 1H), 7.25-7.17 (m, 2H), 6.99 (t, *J* = 2.2 Hz, 2H), 6.38 (t, *J* = 2.1 Hz, 2H), 2.51 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.7, 137.4, 137.2, 129.5, 128.4, 123.7, 121.5, 110.3, 19.3; HRMS (ESI) m/z: [M+H$^+$] $C_{12}H_{11}N_2$ 183.0917; found 183.092

1-(5-Chloro-2-isocyanophenyl)-1*H*-pyrrole (1f)



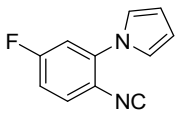
Compound **1f** was prepared in accordance with the general procedure for the synthesis of arylisocyanides by using **S1f**[8] (4-chloro-2-(1*H*-pyrrol-1-yl)aniline, 0.5 mmol) as the starting material and purified by flash chromatography on silica gel (Biotage®, gradient elution: 2→20% EtOAc in n-hexane) as a brown liquid (89 mg, 87% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48-7.36 (m, 2H), 7.34-7.27 (m, 1H), 7.02 (t, *J* = 2.1 Hz, 2H), 6.40 (t, *J* = 2.1 Hz, 2H); ^{13}C NMR (101MHz, $CDCl_3$) δ 171.2, 138.0, 136.1, 129.7, 127.3, 126.3, 121.2, 111.2; HRMS (ESI) m/z: [M$^+$] Calcd for $C_{11}H_7ClN_2$ 203.0371; found 202.0381

1-(4-Chloro-2-isocyanophenyl)-1*H*-pyrrole (1g)



Compound **1g** was prepared in accordance with the general procedure for the synthesis of arylisocyanides by using **S1g**[8] (5-chloro-2-(1*H*-pyrrol-1-yl)aniline, 0.86 mmol) as the starting material and purified by flash chromatography on silica gel (Biotage®, gradient elution: 2→20% EtOAc in n-hexane) as a brown liquid (Method 2, 150 mg, 86% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (d, *J* = 2.3 Hz, 1H), 7.49-7.42 (m, 1 H), 7.35-7.29 (m, 1H), 6.98 (t, *J* = 2.2 Hz, 2H), 6.40 (t, *J* = 2.2 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.5, 135.9, 132.6, 130.7, 128.5, 127.2, 121.3, 111.0; HRMS (ESI) m/z: [M+H$^+$] Calcd for $C_{11}H_8ClN_2$ 203.0371; found 203.0369

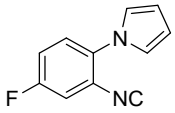
1-(5-Fluoro-2-isocyanophenyl)-1*H*-pyrrole (1h)



Compound **1h** was prepared in accordance with the general procedure for the synthesis of arylisocyanides by using **S1h**[8] (4-fluoro-2-(1*H*-pyrrol-1-yl)aniline, 1.17 mmol) as the starting material and purified by flash chromatography on silica gel (Biotage®, gradient elution: 2→20% EtOAc in n-hexane) as a green liquid (Method 2, 183 mg, 84% yield). ^{1}H NMR

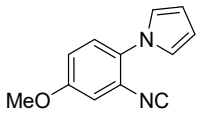
(400 MHz, $CDCl_3$) δ 7.51 (dd, *J* = 5.5, 8.9 Hz, 1H), 7.10 (dd, *J* = 2.8, 8.9 Hz, 1H), 7.07-7.04 (m, 1H), 7.04-7.01 (m, 2H), 6.40 (t, *J* = 2.2 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.2, 163.6, 161.1, 138.8, 138.7, 130.5, 130.4, 121.2, 114.4, 114.2, 113.5, 113.3, 111.2; HRMS (ESI) m/z: [M+H$^+$] Calcd for $C_{11}H_8FN_2$ 187.0666; found 187.0673

1-(4-Fluoro-2-isocyanophenyl)-1*H*-pyrrole (1i)[7]



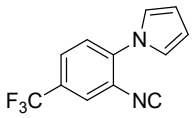
Compound **1i** was prepared in accordance with the literature known procedure in 87% yield. ^1H NMR (400 MHz, $CDCl_3$) δ 7.36 (dd, *J* = 5.3, 8.9 Hz, 1H), 7.26-7.18 (m, 2H), 6.95 (t, *J* = 2.2 Hz, 2H), 6.39 (t, *J* = 2.2 Hz, 2H). The spectral data are in accordance with the literature.

1-(2-Isocyano-4-methoxyphenyl)-1*H*-pyrrole (1j)[7]



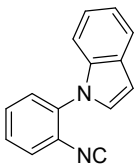
Compound **1j** was prepared in accordance with the literature known procedure in 79% yield. ^1H NMR (400 MHz, $CDCl_3$) δ 7.31-7.26 (m, 1H), 7.03-6.97 (m, 2H), 6.92 (t, *J* = 2.1 Hz, 2H), 6.36 (t, *J* = 2.1 Hz, 2H), 3.85 (s, 3H). The spectral data are in accordance with the literature.

1-(2-Isocyano-4-(trifluoromethyl)phenyl)-1*H*-pyrrole (1k)[6]



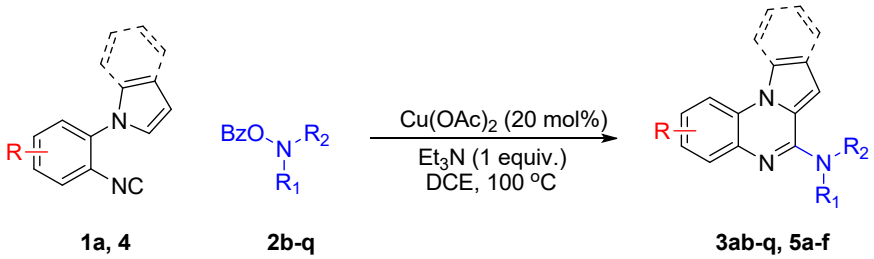
Compound **1k** was prepared in accordance with the literature known procedure in 83% yield. ^1H NMR (400 MHz, $CDCl_3$) δ 7.79 (s, 1H), 7.73 (dd, *J* = 1.6, 8.4 Hz, 1H), 7.51 (d, *J* = 8.5 Hz, 1H), 7.07 (t, *J* = 2.2 Hz, 2H), 6.44 (t, *J* = 2.2 Hz, 2H). The spectral data are in accordance with the literature.

1-(2-Isocyanophenyl)-1*H*-indole (4)[7]



Compound **4** was prepared in accordance with the literature known procedure in 91% yield. ^1H NMR (400 MHz, $CDCl_3$) δ 7.74-7.67 (m, 1H) 7.60 (d, *J* = 7.8 Hz, 1H) 7.57-7.52 (m, 2H) 7.48-7.41 (m, 1H) 7.33 (d, *J* = 3.4 Hz, 1H) 7.25-7.17 (m, 3H), 6.75 (d, *J* = 3.3 Hz, 1H). The spectral data are in accordance with the literature.

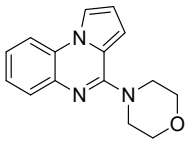
3. General procedure for the synthesis of pyrrolo[1,2-a]quinoxaline derivatives



1a, 4 **2b-q** **3ab-q, 5a-f**

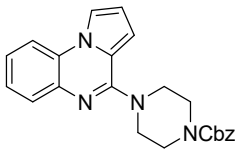
A mixture of compound **1a**, **4** (0.2 mmol, 1.0 equiv), O-benzoylhydroxylamine (0.4 mmol, 2.0 equiv), $Cu(OAc)_2$ (7.4 mg, 0.04 mmol, 0.2 equiv), and Et_3N (56 μL, 0.4 mmol, 2.0 equiv) in DCM (2–4 mL, 0.05–0.1 M) was heated at 100 °C and stirred for 3–24 h. After completion, the reaction mixture was diluted with EtOAc and washed sequentially with saturated $NaHCO_3$ solution and brine. The organic layer was dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by column chromatography on silica gel (n-hexane/EtOAc) to afford the desired amination product.

4-(Pyrrolo[1,2-a]quinoxalin-4-yl)morpholine (3a)



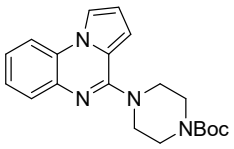
Compound **3a** was prepared in accordance with the general procedure for the synthesis of pyrrolo[1,2-a]quinoxaline derivatives and purified by flash chromatography on silica gel (Biotage®, gradient elution: 6→50% EtOAc in n-hexane) as a yellow solid (35 mg, 69% yield, M.P. 76-77 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84-7.81 (m, 1H), 7.76-7.66 (m, 2H), 7.36-7.26 (m, 2H), 6.79-6.73 (m, 2H), 3.93-3.87 (m, 4H), 3.82-3.76 (m, 4H); ^{13}C NMR (101MHz, $CDCl_3$) δ 152.7, 136.0, 127.6, 125.9, 125.2, 124.3, 120.1, 114.5, 113.3, 112.5, 106.6, 67.0, 48.7; HRMS (ESI) m/z: [M+H$^+$] Calcd for $C_{15}H_{16}N_3O$ 254.1293; found 254.1268.

Benzyl 4-(pyrrolo[1,2-a]quinoxalin-4-yl)piperazine-1-carboxylate (3b)



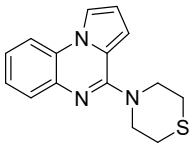
Compound **3b** was prepared in accordance with the general procedure for the synthesis of pyrrolo[1,2-a]quinoxaline derivatives and purified by flash chromatography on silica gel (Biotage®, gradient elution: 6→50% EtOAc in n-hexane) as a yellow solid (55 mg, 71% yield, M.P. 98-99 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87-7.81 (m, 1H), 7.78-7.71 (m, 1H), 7.67 (dd, J = 1.6, 7.8 Hz, 1H), 7.41-7.27 (m, 7H), 6.81-6.74 (m, 2H), 5.19 (s, 2H), 3.84-3.67 (m, 8H); ^{13}C NMR (101MHz, $CDCl_3$) δ 155.4, 152.6, 136.7, 135.9, 128.6, 128.1, 128.0, 127.7, 125.9, 125.2, 124.4, 120.2, 114.6, 113.3, 112.6, 106.6, 67.3, 47.9, 43.8; HRMS (ESI) m/z: [M+H$^+$] Calcd for $C_{23}H_{23}N_4O_2$ 387.1816; found 387.1802.

tert-Butyl 4-(pyrrolo[1,2-a]quinoxalin-4-yl)piperazine-1-carboxylate (3c)



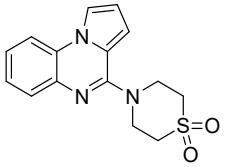
Compound **3c** was prepared in accordance with the general procedure for the synthesis of pyrrolo[1,2-a]quinoxaline derivatives and purified by flash chromatography on silica gel (Biotage®, gradient elution: 6→50% EtOAc in n-hexane) as a yellow solid (43 mg, 66% yield, M.P. 124-126 °C). ^{1}H NMR (400MHz, $CDCl_3$) δ 7.83 (t, J = 2.0 Hz, 1H), 7.74 (dd, J = 1.6, 7.8 Hz, 1H), 7.67 (dd, J = 1.6, 7.8 Hz, 1H), 7.31 (ddd, J = 1.6, 7.8, 9.7 Hz, 2H), 6.79-6.75 (m, 2H), 3.79-3.73 (m, 4H), 3.67-3.62 (m, 4H), 1.50 (s, 9H); ^{13}C NMR (101MHz, $CDCl_3$) δ 154.9, 152.7, 136.0, 127.6, 125.9, 125.2, 124.3, 120.2, 114.5, 113.3, 112.6, 106.6, 79.9, 47.9, 28.5, 28.4; HRMS (ESI) m/z: [M+H$^+$] Calcd for $C_{20}H_{25}N_4O_2$ 353.1972; found 353.1961.

4-(Pyrrolo[1,2-a]quinoxalin-4-yl)thiomorpholine (3d)



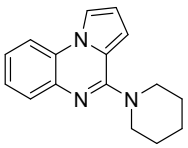
Compound **3d** was prepared in accordance with the general procedure for the synthesis of pyrrolo[1,2-a]quinoxaline derivatives and purified by flash chromatography on silica gel (Biotage®, gradient elution: 6→50% EtOAc in n-hexane) as a light yellow solid (34 mg, 63% yield, M.P. 139-140 °C). ^{1}H NMR (400MHz $CDCl_3$) δ 7.82 (dd, J = 1.3, 2.8 Hz, 1H), 7.73 (dd, J = 1.4, 7.8 Hz, 1H), 7.66 (dd, J = 1.6, 7.8 Hz, 1H), 7.36-7.26 (m, 2H), 6.79-6.70 (m, 2H), 4.14-4.01 (m, 4H), 2.93-2.76 (m, 4H); ^{13}C NMR (101MHz, $CDCl_3$) δ 152.6, 136.0, 127.5, 125.8, 125.2, 124.2, 120.2, 114.5, 113.3, 112.5, 106.6, 50.6, 27.4; HRMS (ESI) m/z: [M+H$^+$] Calcd for $C_{15}H_{16}N_3S$ 270.1059; found 270.1062.

4-(Pyrrolo[1,2-a]quinoxalin-4-yl)thiomorpholine 1,1-dioxide (3e)



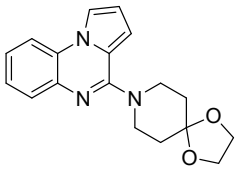
Compound **3e** was prepared in accordance with the general procedure for the synthesis of pyrrolo[1,2-a]quinoxaline derivatives and purified by flash chromatography on silica gel (Biotage®, gradient elution: 6→50% EtOAc in n-hexane) as a brown solid (11 mg, 18% yield, M.P. 240-241 °C). ^{1}H NMR (400MHz ,$CDCl_3$) δ 7.89 (d, J = 1.5 Hz, 1H), 7.82-7.74 (m, 1H), 7.69 (dd, J = 3.3, 6.3 Hz, 1H), 7.43-7.33 (m, 2H), 6.85-6.74 (m, 2H), 4.40-4.24 (m, 4H), 3.33-3.18 (m, 4H); ^{13}C NMR (101MHz, $CDCl_3$) δ 150.9, 135.2, 128.1, 126.0, 125.5, 125.4, 119.4, 115.2, 113.5, 113.1, 106.6, 51.5, 46.6; HRMS (ESI) m/z: [M+H$^+$] Calcd for $C_{15}H_{16}N_3O_2S$ 302.0958; found 302.0966.

4-(Piperidin-1-yl)pyrrolo[1,2-a]quinoxaline (3f)



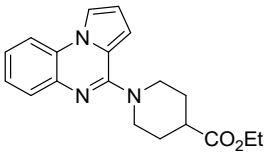
Compound **3f** was prepared in accordance with the general procedure for the synthesis of pyrrolo[1,2-a]quinoxaline derivatives and purified by flash chromatography on silica gel (Biotage®, gradient elution: 4→34% EtOAc in n-hexane) as a yellow solid (28 mg, 55% yield, M.P. 101-103 °C). ^{1}H NMR (400MHz , $CDCl_3$) δ 7.79 (d, *J* = 1.4 Hz, 1H), 7.73-7.69 (m, 1H), 7.67-7.63 (m, 1H), 7.34-7.26 (m, 1H), 7.25-7.21 (m, 1H), 6.80-6.71 (m, 2H), 3.73 (d, *J* = 5.6 Hz, 4H), 1.84-1.67 (m, 6H); ^{13}C NMR (101MHz, $CDCl_3$) δ 153.2, 136.5, 127.3, 125.8, 125.1, 123.6, 120.6, 114.2, 113.2, 112.3, 106.8, 49.3, 26.1, 25.1; HRMS (ESI) m/z: [M+H$^+$] Calcd for $C_{16}H_{17}N_3$ 252.1495; found 252.1499.

8-(Pyrrolo[1,2-a]quinoxalin-4-yl)-1,4-dioxa-8-azaspiro[4.5]decane (3g)



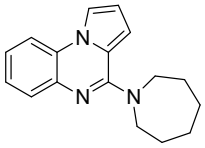
Compound **3g** was prepared in accordance with the general procedure for the synthesis of pyrrolo[1,2-a]quinoxaline derivatives and purified by flash chromatography on silica gel (Biotage®, gradient elution: 6→50% EtOAc in n-hexane) as a yellow syrup (43 mg, 70% yield). ^{1}H NMR (400MHz ,$CDCl_3$) δ 7.81 (dd, *J* = 1.3, 2.6 Hz, 1H), 7.72 (dd, *J* = 1.3, 7.9 Hz, 1H), 7.66 (dd, *J* = 1.5, 7.9 Hz, 1H), 7.34-7.24 (m, 2H), 7.24 (d, *J* = 1.4 Hz, 1H), 6.82-6.72 (m, 2H), 4.02 (s, 4H), 3.95-3.85 (m, 4H), 1.94-1.89 (m, 4H); ^{13}C NMR (101MHz, $CDCl_3$) δ 152.4, 136.3, 127.4, 125.8, 125.1, 123.8, 120.3, 114.3, 113.2, 112.4, 107.7, 106.7, 64.4, 46.1, 35.2; HRMS (ESI) m/z: [M+H$^+$] Calcd for $C_{18}H_{20}N_3O_2$ 310.1550; found 310.1552.

Ethyl 1-(pyrrolo[1,2-a]quinoxalin-4-yl)piperidine-4-carboxylate (3h)



Compound **3h** was prepared in accordance with the general procedure for the synthesis of pyrrolo[1,2-a]quinoxaline derivatives and purified by flash chromatography on silica gel (Biotage®, gradient elution: 6→50% EtOAc in n-hexane) as a yellow syrup (45 mg, 69% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (dd, *J* = 1.4, 2.6 Hz, 1H), 7.73 (dd, *J* = 1.5, 7.9 Hz, 1H), 7.67 (dd, *J* = 1.5, 7.9 Hz, 1H), 7.35-7.25 (m, 2H), 6.80-6.73 (m, 2H), 4.40 (td, *J* = 3.2, 13.5 Hz, 2H), 4.18 (q, *J* = 7.1 Hz, 2H), 3.23-3.10 (m, 2H), 2.61 (tt, *J* = 4.1, 11.1 Hz, 1H), 2.13-1.88 (m, 4H), 1.36-1.20 (m, 3H); ^{13}C NMR (101MHz, $CDCl_3$) δ 174.8, 153.0, 136.2, 127.5, 125.9, 125.1, 124.0, 120.4, 114.3, 113.3, 112.5, 106.6, 60.5, 47.8, 41.8, 28.3, 14.3, 0.0; HRMS (ESI) m/z: [M+H$^+$] Calcd for $C_{19}H_{22}N_3O_2$ 324.1707; found 324.1711.

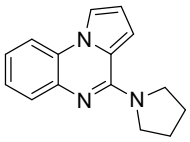
4-(Azepan-1-yl)pyrrolo[1,2-a]quinoxaline (3i)



Compound **3i** was prepared in accordance with the general procedure for the synthesis of pyrrolo[1,2-a]quinoxaline derivatives and purified by flash chromatography on silica gel (Biotage®, gradient elution: 2→20% EtOAc in n-hexane) as a yellow syrup (30 mg, 57% yield). ^{1}H NMR (400MHz ,$CDCl_3$) δ 7.81 (dd, *J* = 1.1, 2.7 Hz, 1H), 7.66 (d, *J* = 8.0 Hz,

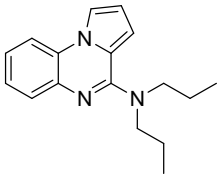
1H), 7.56 (d, *J* = 8.0 Hz, 1H), 7.28-7.24 (m, 1H), 7.17-7.11 (m, 1H), 6.87 (d, *J* = 3.5 Hz, 1H), 6.74-6.69 (m, 1H), 4.05-3.89 (m, 4H), 1.95 (br. s., 4H), 1.74-1.59 (m, 4H); ^{13}C NMR (101MHz, $CDCl_3$) δ 151.3, 137.0, 126.5, 125.1, 125.0, 122.1, 119.6, 114.3, 113.0, 111.9, 107.7, 49.3, 29.1, 27.5; HRMS (ESI) m/z: [M+H$^+$] Calcd for $C_{17}H_{20}N_3$ 266.1652 found 266.1652.

4-(Pyrrolidin-1-yl)pyrrolo[1,2-a]quinoxaline (3j)



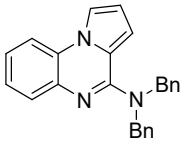
Compound **3j** was prepared in accordance with the general procedure for the synthesis of pyrrolo[1,2-a]quinoxaline derivatives and purified by flash chromatography on silica gel (Biotage®, gradient elution: 6→50% EtOAc in n-hexane) as a yellow syrup (35 mg, 74% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (dd, *J* = 1.3, 2.8 Hz, 1H), 7.64 (dd, *J* = 1.3, 8.1 Hz, 1H), 7.56 (dd, *J* = 1.3, 8.1 Hz, 1H), 7.28-7.22 (m, 1H), 7.12 (dt, *J* = 1.4, 7.6 Hz, 1H), 6.93 (dd, *J* = 1.3, 4.1 Hz, 1H), 6.70 (dd, *J* = 2.9, 4.0 Hz, 1H), 4.01-3.88 (m, 4H), 2.08-1.95 (m, 4H); ^{13}C NMR (101MHz, $CDCl_3$) δ 149.8, 137.5, 126.2, 125.2, 124.9, 121.9, 120.2, 114.2, 113.1, 111.9, 107.6, 48.8, 25.6; HRMS (ESI) m/z: [M+H$^+$] Calcd for $C_{15}H_{16}N_3$ 238.1339 found 238.1344.

***N,N*-dipropylpyrrolo[1,2-a]quinoxalin-4-amine (3k)**



Compound **3k** was prepared in accordance with the general procedure for the synthesis of pyrrolo[1,2-a]quinoxaline derivatives and purified by flash chromatography on silica gel (Biotage®, gradient elution: 2→22% EtOAc in n-hexane) as a light yellow solid (47 mg, 88% yield, M.P. 73-75 °C). ^{1}H NMR (400MHz ,$CDCl_3$) δ 7.80 (dd, *J* = 1.2, 2.7 Hz, 1H), 7.68-7.64 (m, 1H), 7.55 (dd, *J* = 1.2, 8.1 Hz, 1H), 7.28-7.24 (m, *J* = 1.3 Hz, 1H), 7.17-7.12 (m, 1H), 6.77-6.70 (m, 2H), 3.76-3.61 (m, 4H), 1.85-1.76 (m, 4H), 0.99 (t, *J* = 7.4 Hz, 6H); ^{13}C NMR (101MHz, $CDCl_3$) δ 150.6, 136.9, 126.6, 125.0, 125.0, 122.2, 119.7, 114.1, 113.0, 112.0, 107.0, 51.8, 21.8, 11.4; HRMS (ESI) m/z: [M+H$^+$] Calcd for $C_{17}H_{22}N_3$ 268.1808; found 268.1813.

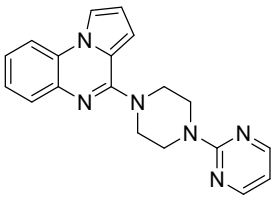
***N,N*-dibenzylpyrrolo[1,2-a]quinoxalin-4-amine (3l)**



Compound **3l** was prepared in accordance with the general procedure for the synthesis of pyrrolo[1,2-a]quinoxaline derivatives and purified by flash chromatography on silica gel (Biotage®, gradient elution: 2→20% EtOAc in n-hexane) as a brown syrup (44 mg, 60% yield). ^{1}H NMR (400MHz ,$CDCl_3$) δ 7.83 (dd, *J* = 1.2, 2.7 Hz, 1H), 7.71 (dd, *J* = 1.1, 8.0 Hz, 1H), 7.63 (dd, *J* = 1.3, 8.0 Hz, 1H), 7.41-7.37 (m, 4H), 7.36-7.30 (m, 5H), 7.30-7.26 (m, 2H), 7.25-7.20 (m, 1H), 6.69-6.60 (m, 2H), 5.01 (s, 4H); ^{13}C NMR (101MHz, $CDCl_3$) δ 151.6, 138.4, 136.6, 128.6, 127.8, 127.1, 127.0, 125.4,

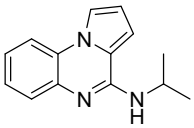
125.2, 123.0, 119.1, 114.6, 113.1, 112.4, 107.7, 51.6; HRMS (ESI) m/z: [M+H$^+$] Calcd for $C_{25}H_{22}N_3$ 364.1808; found 364.1812.

4-(4-(Pyrimidin-2-yl)piperazin-1-yl)pyrrolo[1,2-a]quinoxaline (3m)



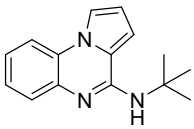
Compound **3m** was prepared in accordance with the general procedure for the synthesis of pyrrolo[1,2-a]quinoxaline derivatives and purified by flash chromatography on silica gel (Biotage®, gradient elution: 6→50% EtOAc in n-hexane) as a brown solid (47 mg, 71% yield, M.P. 120-121 °C). ^{1}H NMR (400MHz ,$CDCl_3$) δ 8.36 (d, *J* = 4.8 Hz, 2H), 7.84 (dd, *J* = 1.2, 2.7 Hz, 1H), 7.77-7.66 (m, 2H), 7.36-7.26 (m, 2H), 6.84 (dd, *J* = 1.1, 4.0 Hz, 1H), 6.79 (dd, *J* = 2.9, 3.9 Hz, 1H), 6.53 (t, *J* = 4.7 Hz, 1H), 4.11-4.00 (m, 4H), 3.96-3.85 (m, 4H); ^{13}C NMR (101MHz, $CDCl_3$) δ 161.8, 157.8, 152.7, 136.1, 127.6, 125.9, 125.2, 124.1, 120.3, 114.5, 113.3, 112.6, 110.1, 106.8, 47.8, 43.7; HRMS (ESI) m/z: [M+H$^+$] Calcd for $C_{19}H_{19}N_6$ 331.1666; found 331.1665.

***N*-Isopropylpyrrolo[1,2-a]quinoxalin-4-amine (3n)**



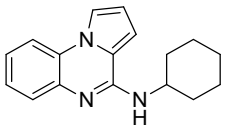
Compound **3n** was prepared in accordance with the general procedure for the synthesis of pyrrolo[1,2-a]quinoxaline derivatives and purified by flash chromatography on silica gel (Biotage®, isocratic elution: 1% EtOAc in n-hexane) as a brown solid (17 mg, 38% yield, M.P. 115-116 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (dd, *J* = 1.3, 2.7 Hz, 1H), 7.69 (dd, *J* = 1.2, 8.1 Hz, 1H), 7.64 (dd, *J* = 1.3, 8.1 Hz, 1H), 7.34-7.27 (m, 1H), 7.23-7.17 (m, 1H), 6.71 (dd, *J* = 2.8, 3.8 Hz, 1H), 6.60 (dd, *J* = 1.3, 3.9 Hz, 1H), 4.71 (d, *J* = 7.0 Hz, 1H), 4.65-4.53 (m, 1H), 1.35 (s, 3H), 1.34 (s, 3H); ^{13}C NMR (101MHz, $CDCl_3$) δ; HRMS (ESI) m/z: [M+H$^+$] Calcd for $C_{14}H_{16}N_3$ 226.1339; found 226.1343.

***N*-(*tert*-Butyl)pyrrolo[1,2-a]quinoxalin-4-amine (3o)**



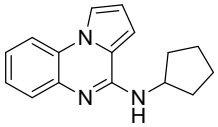
Compound **3o** was prepared in accordance with the general procedure for the synthesis of pyrrolo[1,2-a]quinoxaline derivatives and purified by flash chromatography on silica gel (Biotage®, isocratic elution: 1% EtOAc in n-hexane) as a brown solid (7 mg, 16% yield, M.P. 98-99 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (dd, *J* = 1.2, 2.6 Hz, 1H), 7.70-7.61 (m, 2H), 7.31-7.27 (m, 1H), 7.22-7.16 (m, 1H), 6.72-6.64 (m, 1H), 6.53 (dd, *J* = 1.0, 3.9 Hz, 1H), 4.75 (br. s., 1H), 1.61 (s, 9H); ^{13}C NMR (101MHz, $CDCl_3$) δ 148.5, 137.1, 127.3, 125.1, 125.0, 122.5, 120.0, 114.0, 113.2, 112.0, 101.4, 52.1, 29.5; HRMS (ESI) m/z: [M+H$^+$] Calcd for $C_{15}H_{18}N_3$ 240.1495; found 240.1502.

_N_-Cyclohexylpyrrolo[1,2-a]quinoxalin-4-amine (3p)



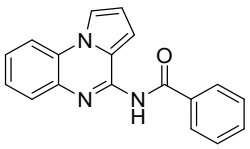
Compound **3p** was prepared in accordance with the general procedure for the synthesis of pyrrolo[1,2-a]quinoxaline derivatives and purified by flash chromatography on silica gel (Biotage®, isocratic elution: 1% EtOAc in n-hexane) as a yellow solid (23 mg, 43% yield, M.P. 83-84 °C). ^{1}H NMR (400MHz, $CDCl_3$) δ 7.77 (d, *J* = 1.5 Hz, 1H), 7.69 (dd, *J* = 1.1, 8.1 Hz, 1H), 7.64 (dd, *J* = 1.1, 8.0 Hz, 1H), 7.34-7.25 (m, 1H), 7.23-7.16 (m, 1H), 6.73-6.68 (m, 1H), 6.60 (d, *J* = 3.1 Hz, 1H), 4.80 (d, *J* = 7.3 Hz, 1H), 4.35-4.22 (m, 1H), 2.24-2.13 (m, 2H), 1.79 (td, *J* = 3.6, 13.4 Hz, 2H), 1.69 (td, *J* = 3.8, 12.9 Hz, 1H), 1.58-1.45 (m, 2H), 1.36-1.27 (m, 3H); ^{13}C NMR (101MHz, $CDCl_3$) δ 148.5, 137.2, 126.8, 125.3, 125.1, 122.6, 119.6, 114.3, 113.3, 112.2, 102.0, 48.8, 33.6, 25.9, 25.1; HRMS (ESI) m/z: [M+H$^+$] Calcd for $C_{17}H_{20}N_3$ 266.1652; found 266.1657.

_N_-Cyclopentylpyrrolo[1,2-a]quinoxalin-4-amine (3q)



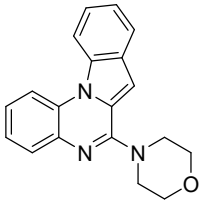
Compound **3q** was prepared in accordance with the general procedure for the synthesis of pyrrolo[1,2-a]quinoxaline derivatives and purified by flash chromatography on silica gel (Biotage®, isocratic elution: 1% EtOAc in n-hexane) as a yellow solid (10 mg, 20% yield, M.P. 159-160 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (dd, *J* = 1.2, 2.6 Hz, 1H), 7.73-7.61 (m, 2H), 7.36-7.27 (m, 1H), 7.23-7.15 (m, 1H), 6.75-6.66 (m, 1H), 6.63-6.54 (m, 1H), 4.86 (d, *J* = 6.6 Hz, 1H), 4.77-4.61 (m, 1H), 2.37-2.08 (m, 2H), 1.84-1.64 (m, 4H), 1.61-1.50 (m, 2H); ^{13}C NMR (101MHz, $CDCl_3$) δ 149.0, 137.3, 126.9, 125.3, 125.1, 122.6, 119.7, 114.2, 113.3, 112.2, 101.9, 52.2, 33.7, 23.9; HRMS (ESI) m/z: [M+H$^+$] Calcd for $C_{16}H_{18}N_3$ 252.1495; found 252.1500.

_N_-(Pyrrolo[1,2-a]quinoxalin-4-yl)benzamide (3r)



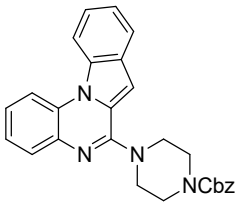
Compound **3s** was prepared in accordance with the general procedure for the synthesis of pyrrolo[1,2-a]quinoxaline derivatives and purified by flash chromatography on silica gel (Biotage®, gradient elution: 5→40% EtOAc in n-hexane) as a brown solid (32 mg, 55% yield, M.P. 167-168 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ 14.55 (s., 1H), 8.41 (br. s., 2H), 7.87 (s., 1H), 7.84-7.68 (m, 1H), 7.57 (d, *J* = 8.1 Hz, 1H), 7.55-7.45 (m, 3H), 7.37 (d, *J* = 3.9 Hz, 3H), 6.93-6.77 (m, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 137.9, 131.9, 129.4, 129.1, 128.1, 127.5, 125.9, 125.3, 120.4, 117.6, 114.4, 114.2, 112.9, 29.7; HRMS (ESI) m/z: [M+H$^+$] Calcd for $C_{18}H_{14}N_3O$ 288.1131; found 288.1130

4-(Indolo[1,2-a]quinoxalin-6-yl)morpholine (5a)



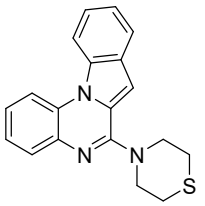
Compound **5a** was prepared in accordance with the general procedure for the synthesis of indolo[1,2-a]quinoxaline derivatives and purified by flash chromatography on silica gel (Biotage®, gradient elution: 6→50% EtOAc in n-hexane) as a light brown solid (43 mg, 71% yield, M.P. 168-169 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.47-8.40 (m, 2H), 7.90 (d, *J* = 7.9 Hz, 1H), 7.76 (dd, *J* = 1.6, 7.8 Hz, 1H), 7.51 (dt, *J* = 1.1, 7.8 Hz, 1H), 7.45-7.39 (m, 2H), 7.38-7.32 (m, 1H), 7.07 (s, 1H), 3.99-3.93 (m, 4H), 3.82-3.75 (m, 4H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.9, 135.9, 133.3, 128.9, 128.9, 128.0, 125.2, 124.8, 124.2, 123.9, 122.6, 122.3, 114.6, 114.5, 100.2, 67.0, 49.2; HRMS (ESI) m/z: [M+H$^+$] Calcd for $C_{19}H_{18}N_3O$ 304.1444; found 304.1446

Benzyl 4-(indolo[1,2-a]quinoxalin-6-yl)piperazine-1-carboxylate (5b)



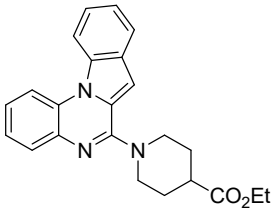
Compound **5b** was prepared in accordance with the general procedure for the synthesis of indolo[1,2-a]quinoxaline derivatives and purified by flash chromatography on silica gel (Biotage®, gradient elution: 6→50% EtOAc in n-hexane) as a yellow solid (60 mg, 69% yield, M.P. 143-145 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.43 (t, *J* = 8.4 Hz, 2H), 7.91 (d, *J* = 7.9 Hz, 1H), 7.75 (dd, *J* = 1.3, 7.9 Hz, 1H), 7.54-7.49 (m, 1H), 7.45-7.43 (m, 1H), 7.42-7.41 (m, 1H), 7.40-7.37 (m, 4H), 7.37-7.32 (m, 2H), 7.06 (s, 1H), 5.20 (s, 2H), 3.78 (s, 8H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.4, 153.8, 136.7, 135.8, 133.3, 129.0, 128.8, 128.6, 128.1, 128.1, 128.0, 125.3, 124.8, 124.2, 124.0, 122.6, 122.4, 114.6, 114.5, 100.2, 67.3, 48.4, 43.8; HRMS (ESI) m/z: [M+H$^+$] Calcd for $C_{27}H_{25}N_4O_2$ 437.1972; found 437.1965

4-(Indolo[1,2-a]quinoxalin-6-yl)thiomorpholine (5c)



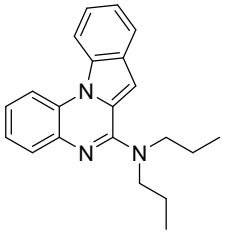
Compound **5c** was prepared in accordance with the general procedure for the synthesis of indolo[1,2-a]quinoxaline derivatives and purified by flash chromatography on silica gel (Biotage®, gradient elution: 2→100% EtOAc in n-hexane) as a light yellow solid (40 mg, 63% yield, M.P. 166-167 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.43 (t, *J* = 9.3 Hz, 2H), 7.90 (d, *J* = 8.0 Hz, 1H), 7.74 (dd, *J* = 1.5, 7.8 Hz, 1H), 7.53-7.47 (m, 1H), 7.41 (t, *J* = 7.6 Hz, 2H), 7.37-7.32 (m, 1H), 7.02 (s, 1H), 4.14-4.01 (m, 4H), 2.97-2.85 (m, 4H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.0, 135.9, 133.3, 128.8, 128.8, 127.9, 125.1, 125.0, 124.2, 123.9, 122.6, 122.3, 114.5, 114.5, 100.1, 51.0, 27.5; HRMS (ESI) m/z: [M+H$^+$] Calcd for $C_{19}H_{18}N_3S$ 320.1216; found 320.1221

Ethyl 1-(indolo[1,2-a]quinoxalin-6-yl)piperidine-4-carboxylate (5d)



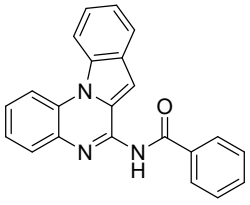
Compound **5d** was prepared in accordance with the general procedure for the synthesis of indolo[1,2-a]quinoxaline derivatives and purified by flash chromatography on silica gel (Biotage®, gradient elution: 3→28% EtOAc in n-hexane) as a light brown solid (55 mg, 74% yield, M.P. 94-96 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.46-8.38 (m, 2H), 7.90 (d, *J* = 8.0 Hz, 1H), 7.74 (dd, *J* = 1.6, 7.8 Hz, 1H), 7.49 (dt, *J* = 1.2, 7.8 Hz, 1H), 7.43-7.37 (m, 2H), 7.36-7.30 (m, 1H), 7.06 (s, 1H), 4.37 (td, *J* = 3.0, 13.3 Hz, 2H), 4.20 (q, *J* = 7.1 Hz, 2H), 3.24-3.13 (m, 2H), 2.64 (tt, *J* = 4.2, 11.0 Hz, 1H), 2.17-2.10 (m, 2H), 2.08-1.97 (m, 2H), 1.30 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.8, 154.2, 136.1, 133.3, 128.9, 127.9, 125.1, 124.9, 124.1, 123.8, 122.5, 122.3, 114.5, 114.5, 100.2, 60.5, 48.3, 41.8, 28.3, 14.3, 0.0 HRMS (ESI) m/z: [M+H$^+$] Calcd for $C_{23}H_{24}N_3O_2$ 374.1863; found 374.1857

***N*,*N*-dipropylindolo[1,2-a]quinoxalin-6-amine (5e)**



Compound **5e** was prepared in accordance with the general procedure for the synthesis of indolo[1,2-a]quinoxaline derivatives and purified by flash chromatography on silica gel (Biotage®, gradient elution: 3→24% EtOAc in n-hexane) as a light yellow solid (45 mg, 71% yield, M.P. 131-132 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.44 (d, *J* = 8.6 Hz, 1H), 8.41-8.34 (m, 1H), 7.89 (d, *J* = 8.0 Hz, 1H), 7.71-7.58 (m, 1H), 7.47 (ddd, *J* = 1.3, 7.1, 8.5 Hz, 1H), 7.43-7.33 (m, 1H), 7.33 - 7.26 (m, 2H), 7.07 (s, 1H), 3.81-3.57 (m, 4H), 1.95-1.74 (m, 4H), 1.01 (t, *J* = 7.4 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 152.1, 136.8, 133.1, 128.8, 128.1, 126.9, 125.0, 124.1, 123.6, 123.3, 122.2, 122.2, 114.5, 114.3, 100.3, 52.0, 21.6, 11.5; HRMS (ESI) m/z: [M+H$^+$] Calcd for $C_{21}H_{24}N_3$ 318.1965; found 318.1966

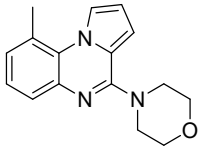
***N*-(Indolo[1,2-a]quinoxalin-6-yl)benzamide (5f)**



Compound **5f** was prepared in accordance with the general procedure for the synthesis of indolo[1,2-a]quinoxaline derivatives and purified by flash chromatography on silica gel (Biotage®, gradient elution: 1→8% EtOAc in n-hexane) as a brown solid (26 mg, 38% yield, M.P. 121-122 °C) ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.70 (d, *J* = 8.3 Hz, 1H), 7.85-7.71 (m, 1H), 7.62-7.49 (m, 2H), 7.46-7.35 (m, 2H), 7.32-7.27 (m, 2H), 7.26-7.19 (m, 5H), 7.19-7.14 (m,

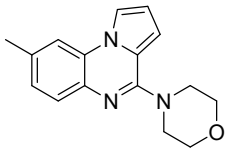
1H), 6.79 (d, J = 3.1 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.1, 136.6, 134.9, 134.2, 131.9, 129.4, 128.7, 128.7, 128.5, 128.0, 126.7, 124.6, 123.2, 121.6, 121.5, 120.9, 110.5, 104.6; MS (ESI) m/z 338.21

4-(9-Methylpyrrolo[1,2-a]quinoxalin-4-yl)morpholine (6b)



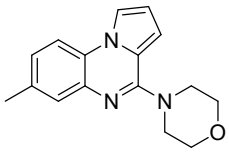
Compound **6b** was prepared in accordance with the general procedure for the synthesis of pyrrolo[1,2-a]quinoxaline derivatives and purified by flash chromatography on silica gel (Biotage®, gradient elution: 2→22% EtOAc in n-hexane) as a yellow solid (38 mg, 71% yield, M.P. 113-114 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84-7.77 (m, 1H), 7.64-7.47 (m, 2H), 7.15 (dd, J = 1.3, 8.2 Hz, 1H), 6.78-6.69 (m, 2H), 3.94-3.89 (m, 4H), 3.80-3.66 (m, 4H), 2.49 (s, 3H); ^{13}C NMR (101MHz, $CDCl_3$) δ 152.4, 134.5, 133.7, 127.5, 126.4, 125.7, 120.3, 114.2, 113.5, 112.5, 106.3, 67.0, 48.9, 21.6; HRMS (ESI) m/z: [M+H$^+$] Calcd for $C_{16}H_{18}N_3O$ 268.1444; found 268.1449.

4-(8-Methylpyrrolo[1,2-a]quinoxalin-4-yl)morpholine (6c)



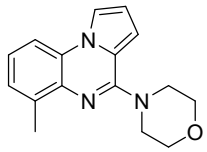
Compound **6c** was prepared in accordance with the general procedure for the synthesis of pyrrolo[1,2-a]quinoxaline derivatives and purified by flash chromatography on silica gel (Biotage®, gradient elution: 2→22% EtOAc in n-hexane) as a yellow solid (39 mg, 73% yield, M.P. 97-98 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (dd, J = 1.3, 2.9 Hz, 1H), 7.63-7.50 (m, 1H), 7.22 (t, J = 7.7 Hz, 1H), 7.13-7.06 (m, 1H), 6.82-6.68 (m, 2H), 3.99-3.81 (m, 4H), 3.81-3.64 (m, 4H), 2.87 (s, 3H); ^{13}C NMR (101MHz, $CDCl_3$) δ 152.8, 137.5, 128.2, 126.2, 126.2, 124.8, 124.6, 121.3, 120.0, 111.8, 105.8, 67.0, 48.9, 23.6; HRMS (ESI) m/z: [M+H$^+$] Calcd for $C_{16}H_{18}N_3O$ 268.1444; found 268.1456.

4-(7-Methylpyrrolo[1,2-a]quinoxalin-4-yl)morpholine (6d)



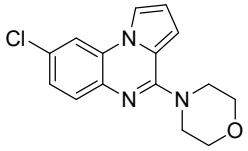
Compound **6d** was prepared in accordance with the general procedure for the synthesis of pyrrolo[1,2-a]quinoxaline derivatives and purified by flash chromatography on silica gel (Biotage®, gradient elution: 2→22% EtOAc in n-hexane) as a yellow solid (36 mg, 67% yield, M.P. 113-114 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (t, J = 2.1 Hz, 1H), 7.62 (d, J = 8.3 Hz, 1H), 7.50 (s, 1H), 7.11 (dd, J = 1.8, 8.3 Hz, 1H), 6.78-6.69 (m, 2H), 3.95-3.85 (m, 4H), 3.81-3.72 (m, 4H), 2.44 (s, 3H); ^{13}C NMR (101MHz, $CDCl_3$) δ 152.8, 135.9, 134.9, 127.6, 125.4, 123.8, 120.0, 114.3, 113.0, 112.3, 106.4, 67.0, 48.8, 21.1; HRMS (ESI) m/z: [M+H$^+$] Calcd for $C_{16}H_{18}N_3O$ 268.1444; found 268.1442.

4-(6-Methylpyrrolo[1,2-a]quinoxalin-4-yl)morpholine (6e)



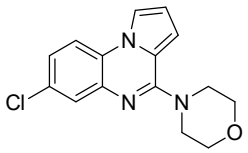
Compound **6e** was prepared in accordance with the general procedure for the synthesis of pyrrolo[1,2-a]quinoxaline derivatives and purified by flash chromatography on silica gel (Biotage®, gradient elution: 2→22% EtOAc in n-hexane) as a light yellow solid (36 mg, 68% yield, M.P. 94-95 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (t, *J* = 2.0 Hz, 1H), 7.60 (dd, *J* = 1.3, 7.8 Hz, 1H), 7.24-7.14 (m, 2H), 6.82-6.68 (m, 2H), 3.96-3.88 (m, 4H), 3.84-3.75 (m, 4H), 2.63 (s, 3H); ^{13}C NMR (101MHz, $CDCl_3$) δ 151.3, 136.1, 134.2, 126.1, 125.6, 123.6, 119.9, 114.6, 112.4, 111.1, 106.1, 66.9, 48.6, 18.0; HRMS (ESI) m/z: [M+H$^+$] Calcd for $C_{16}H_{18}N_3O$ 268.1444; found 268.1442

4-(8-Chloropyrrolo[1,2-a]quinoxalin-4-yl)morpholine (6f)



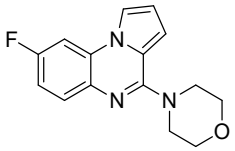
Compound **6f** was prepared in accordance with the general procedure for the synthesis of pyrrolo[1,2-a]quinoxaline derivatives and purified by flash chromatography on silica gel (Biotage®, gradient elution: 2→22% EtOAc in n-hexane) as a brown solid (32 mg, 56% yield, M.P. 162-163 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79-7.64 (m, 2H), 7.58 (d, *J* = 8.6 Hz, 1H), 7.33-7.26 (m, 1H), 6.81-6.73 (m, 2H), 3.94-3.85 (m, 4H), 3.83-3.74 (m, 4H); ^{13}C NMR (101MHz, $CDCl_3$) δ 152.5, 134.7, 129.2, 128.6, 126.4, 125.4, 119.9, 114.7, 113.5, 113.0, 107.2, 66.9, 48.5; HRMS (ESI) m/z: [M+H$^+$] Calcd for $C_{15}H_{15}ClN_3O$ 288.0898; found 288.0902

4-(7-chloropyrrolo[1,2-a]quinoxalin-4-yl)morpholine (6g)



Compound **6g** was prepared in accordance with the general procedure for the synthesis of pyrrolo[1,2-a]quinoxaline derivatives and purified by flash chromatography on silica gel (Biotage®, gradient elution: 2→22% EtOAc in n-hexane) as a brown solid (27 mg, 47% yield, M.P.138-139 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (dd, *J* = 1.3, 2.6 Hz, 1H), 7.69-7.60 (m, 2H), 7.22 (dd, *J* = 2.3, 8.7 Hz, 1H), 6.84-6.70 (m, 2H), 3.92-3.86 (m, 4H), 3.85-3.79 (m, 4H); ^{13}C NMR (101MHz, $CDCl_3$) δ 152.9, 137.2, 130.3, 126.8, 124.4, 123.9, 119.7, 114.8, 114.3, 112.8, 107.3, 66.9, 48.4; HRMS (ESI) m/z: [M+H$^+$] Calcd for $C_{15}H_{15}ClN_3O$ 288.0898; found 288.0904

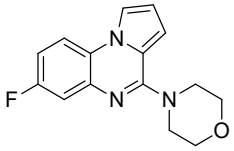
4-(8-Fluoropyrrolo[1,2-a]quinoxalin-4-yl)morpholine (6h)



Compound **6h** was prepared in accordance with the general procedure for the synthesis of pyrrolo[1,2-a]quinoxaline derivatives and purified by flash chromatography on silica gel (Biotage®, gradient elution: 2→22% EtOAc in n-hexane)

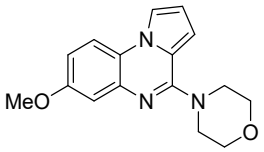
as a yellow solid (31 mg, 56% yield, M.P. 126-127 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (dd, *J* = 1.4, 2.5 Hz, 1H), 7.64 (dd, *J* = 5.8, 8.9 Hz, 1H), 7.42 (dd, *J* = 2.7, 9.3 Hz, 1H), 7.06 (dt, *J* = 2.8, 8.6 Hz, 1H), 6.84-6.73 (m, 2H), 3.95-3.86 (m, 4H), 3.80-3.70 (m, 4H); ^{13}C NMR (101MHz, $CDCl_3$) δ 160.7, 158.3, 152.2, 132.4, 132.4, 129.1, 129.0, 126.3, 126.2, 120.0, 114.6, 113.0, 112.9, 112.6, 106.9, 100.4, 100.1, 66.9, 48.7; HRMS (ESI) m/z: [M+H$^+$] Calcd for; HRMS (ESI) m/z: [M+H+] Calcd for $C_{15}H_{15}FN_3O$ 272.1194; found 272.1202

4-(7-Fluoropyrrolo[1,2-a]quinoxalin-4-yl)morpholine (6i)



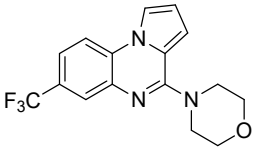
Compound **6i** was prepared in accordance with the general procedure for the synthesis of pyrrolo[1,2-a]quinoxaline derivatives and purified by flash chromatography on silica gel (Biotage®, gradient elution: 2→22% EtOAc in n-hexane) as a brown solid (30 mg, 55% yield, M.P. 123-124 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (dd, *J* = 1.3, 2.6 Hz, 1H), 7.66 (dd, *J* = 5.2, 8.9 Hz, 1H), 7.33 (dd, *J* = 2.8, 9.9 Hz, 1H), 7.00 (dt, *J* = 2.9, 8.5 Hz, 1H), 6.81-6.71 (m, 2 H), 3.93-3.86 (m, 4H), 3.86-3.78 (m, 4H); ^{13}C NMR (101MHz, $CDCl_3$) δ 161.4, 159.0, 153.1, 137.6, 137.5, 122.4, 119.6, 114.7, 114.2, 114.1, 112.9, 112.7, 112.6, 111.5, 111.2, 107.1, 66.9, 48.4; HRMS (ESI) m/z: [M+H$^+$] Calcd for $C_{15}H_{15}FN_3O$ 272.1194; found 272.1199

4-(7-Methoxypyrrolo[1,2-a]quinoxalin-4-yl)morpholine (6j)



Compound **6j** was prepared in accordance with the general procedure for the synthesis of pyrrolo[1,2-a]quinoxaline derivatives and purified by flash chromatography on silica gel (Biotage®, gradient elution: 4→40% EtOAc in n-hexane) as a yellow solid (36 mg, 64% yield, M.P. 144-145 °C). ^{1}H NMR (400MHz, $CDCl_3$) δ 7.75 (dd, *J* = 1.4, 2.4 Hz, 1H), 7.64 (d, *J* = 9.0 Hz, 1 H), 7.17 (d, *J* = 2.8 Hz, 1H), 6.90 (dd, *J* = 2.8, 8.9 Hz, 1H), 6.84-6.62 (m, 2H), 3.96 - 3.89 (m, 4H), 3.89 (s, 3H), 3.83-3.75 (m, 4H); ^{13}C NMR (101MHz, $CDCl_3$) δ 157.4, 153.1, 137.2, 120.2, 119.7, 114.2, 112.9, 112.2, 109.5, 106.3, 67.0, 55.7, 48.7; HRMS (ESI) m/z: [M+H$^+$] Calcd for $C_{16}H_{18}N_3O_2$ 284.1394; found 284.1399

4-(7-(Trifluoromethyl)pyrrolo[1,2-a]quinoxalin-4-yl)morpholine (6k)



Compound **6k** was prepared in accordance with the general procedure for the synthesis of pyrrolo[1,2-a]quinoxaline derivatives and purified by flash chromatography on silica gel (Biotage®, gradient elution: 2→20% EtOAc in n-hexane) as a yellow solid (33 mg, 52% yield, M.P. 164-165 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98-7.90 (m, 1H), 7.85 (dd, *J* = 1.3, 2.7 Hz, 1H), 7.80 (d, *J* = 8.5 Hz, 1H), 7.49 (dd, *J* = 1.5, 8.5 Hz, 1H), 6.89-6.73 (m, 2H), 3.93-3.87 (m, 4H), 3.87-3.82

(m, 4H); ^{13}C NMR (101MHz, $CDCl_3$) δ 153.0, 136.1, 127.8, 127.5, 127.2, 124.8, 120.3-120.0, 115.2, 113.8, 113.3, 107.8, 66.9, 48.3; HRMS (ESI) m/z: [M+H$^+$] Calcd for $C_{16}H_{15}F_3N_3O$ 322.1162; found 322.1165

4. Synthesis of compound 3a (2 mmol scale)

The mixture of compound **1a** (336 mg, 2mmol, 1.0 equiv.), morpholino benzoate (829 mg, 4 mmol, 2.0 equiv.), $Cu(OAc)_2$ (74 mg, 0.4 mmol, 0.2 equiv.), and Et_3N (0.56 mL, 4 mmol, 2.0 equiv.) in dichloroethane (20 mL, 0.1 M) was heated to 100 ℃ and stirred for 3 h. The reaction mixture was diluted with EtOAc, and then the solution was washed with a saturated solution of $NaHCO_3$ and brine. The organic phase was dried over Na_2SO_4, and the product was purified by column chromatography on silica gel (n-hexane/EtOAc) to afford the title compound as a colorless foam (984 mg, 75% yield).

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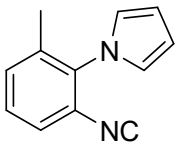
6. ^{1}H NMR and ^{13}C NMR spectra of all new product



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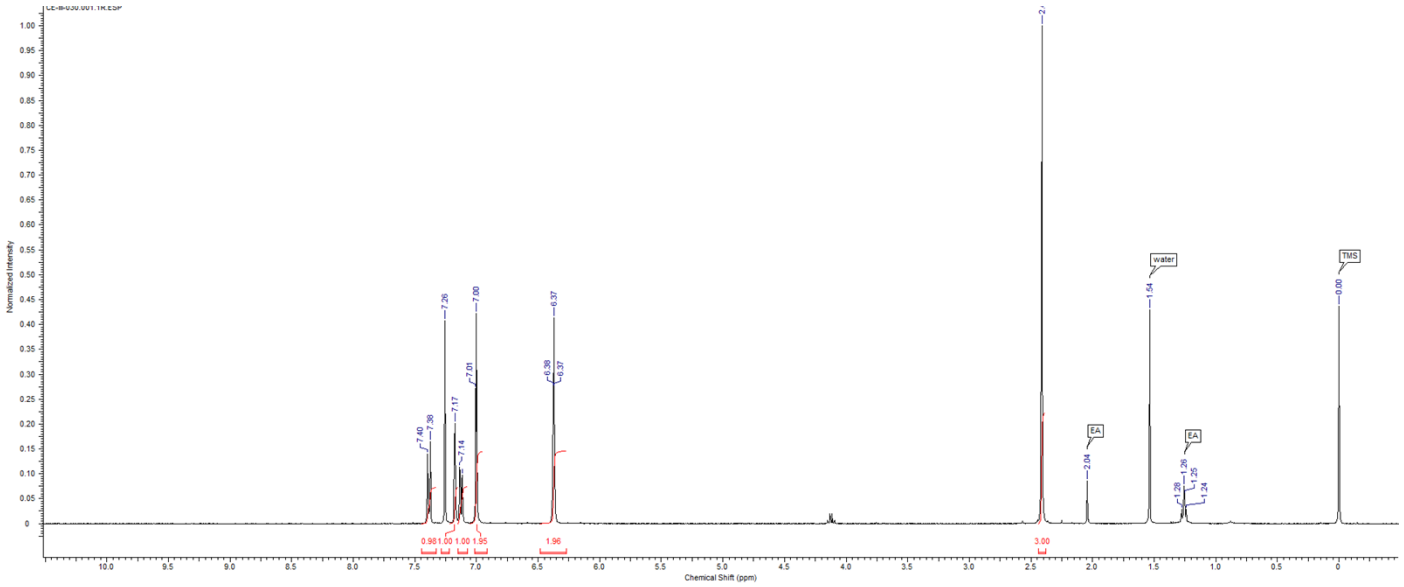


(b)

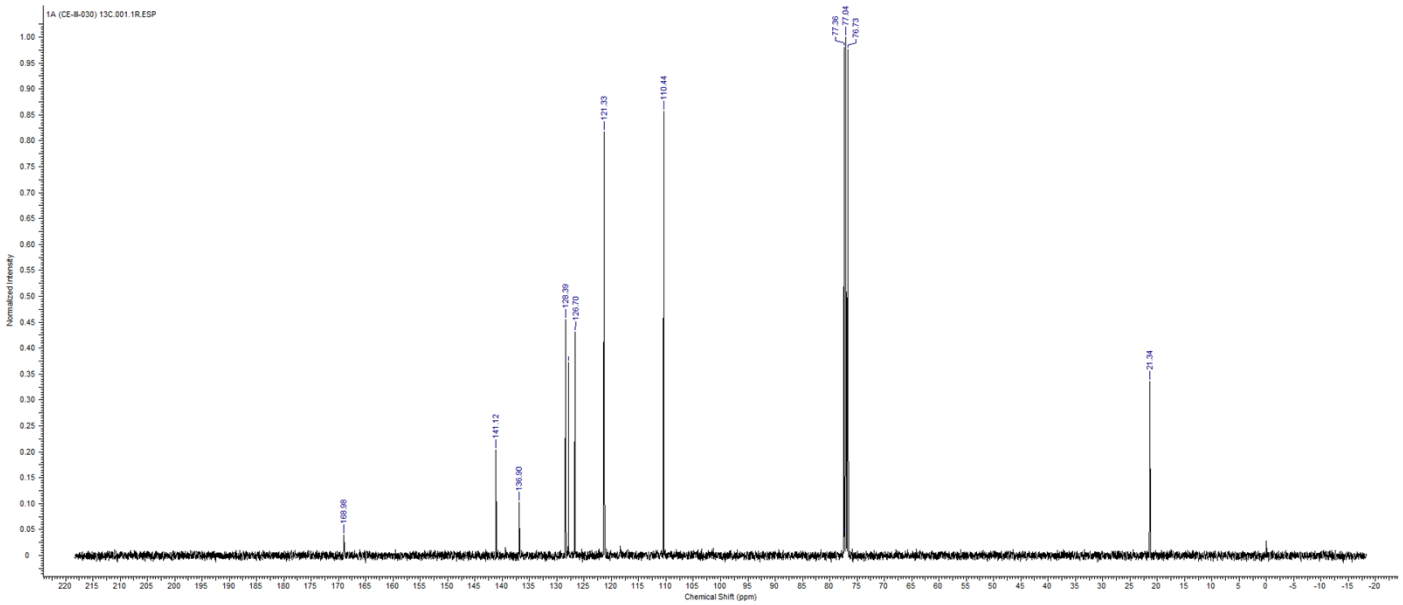
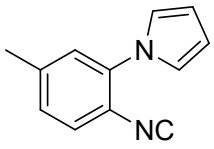


Figure S1. (a) ^{1}H NMR (400 MHz, $CDCl_3$) and (b) ^{13}C NMR (101 MHz, $CDCl_3$) spectra of **1b**



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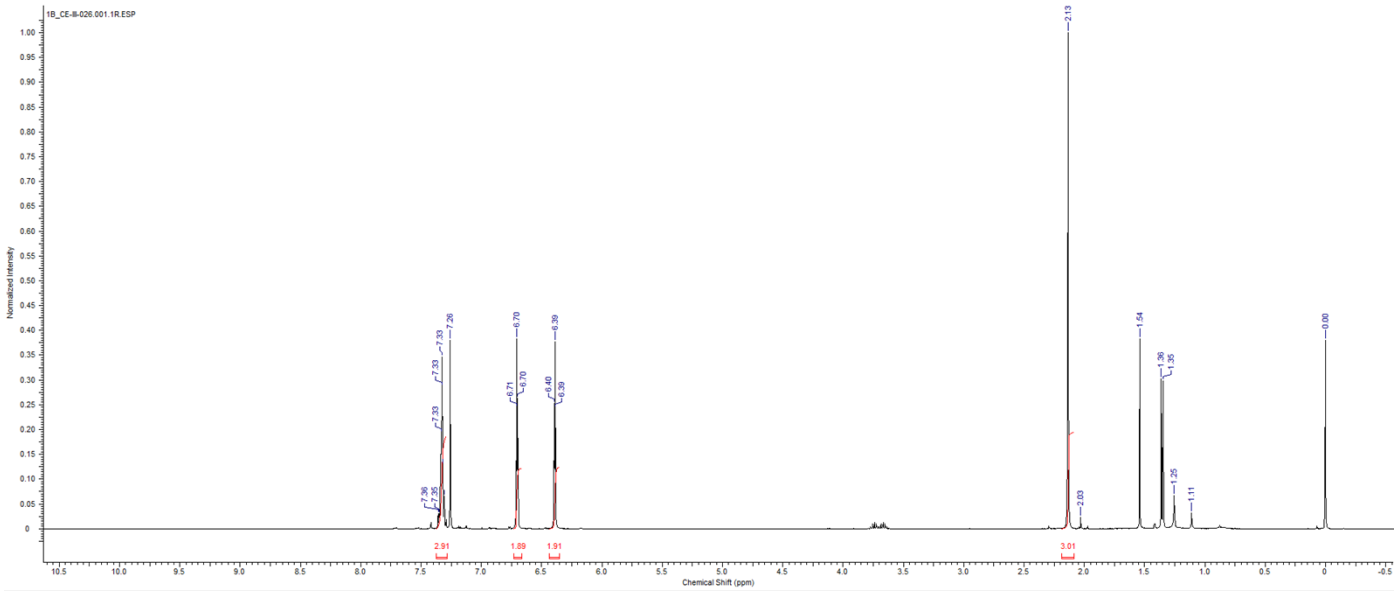

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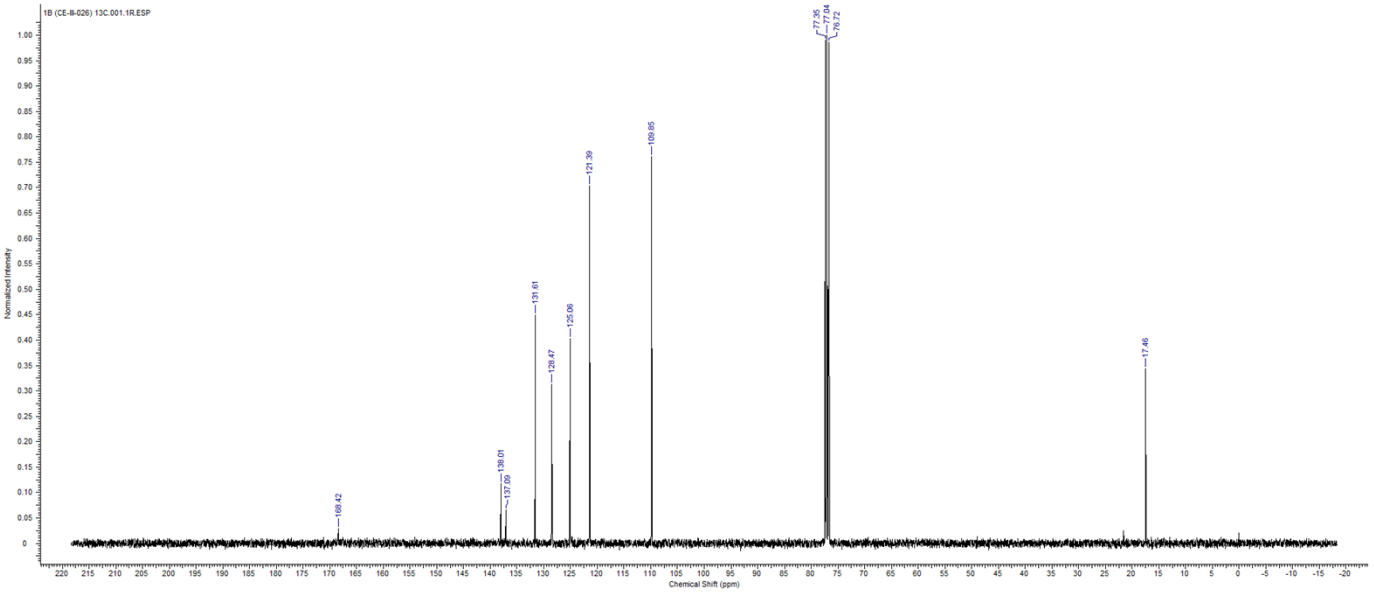
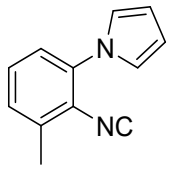


Figure S2. (a) ^{1}H NMR (400 MHz, $CDCl_3$) and (b) ^{13}C NMR (101 MHz, $CDCl_3$) spectra of **1c**



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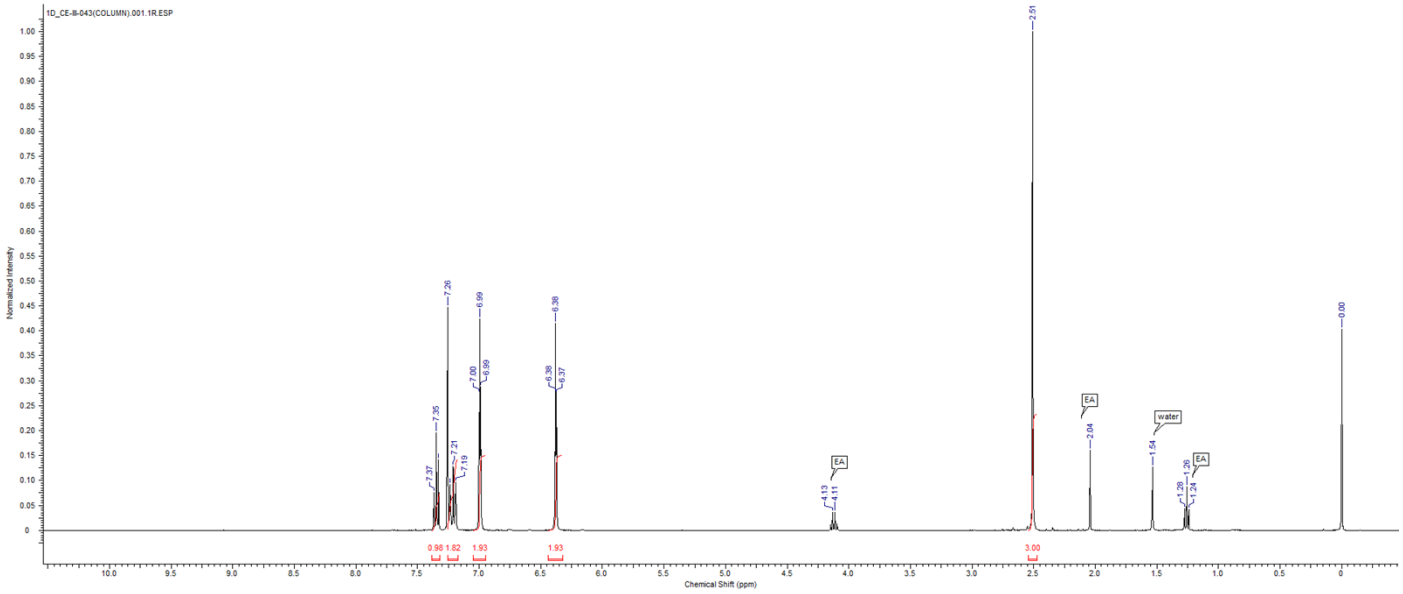

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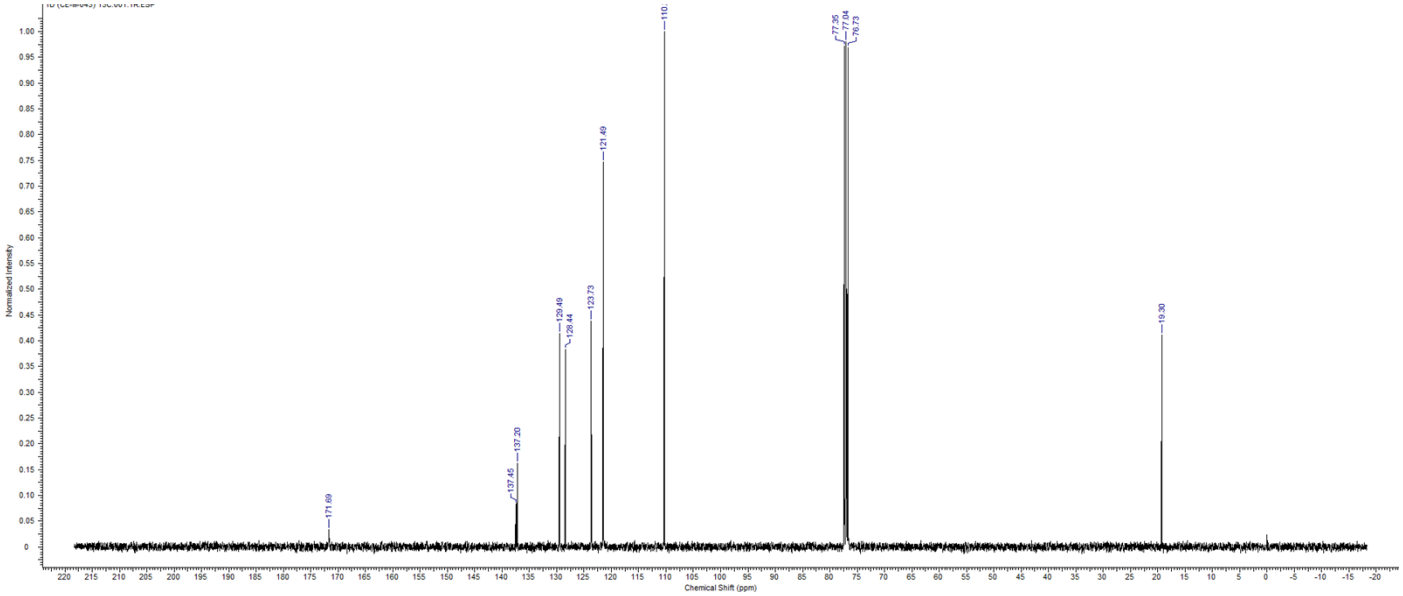
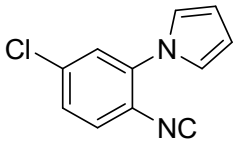


Figure S4. (a) ^{1}H NMR (400 MHz, $CDCl_3$) and (b) ^{13}C NMR (101 MHz, $CDCl_3$) spectra of **1e**



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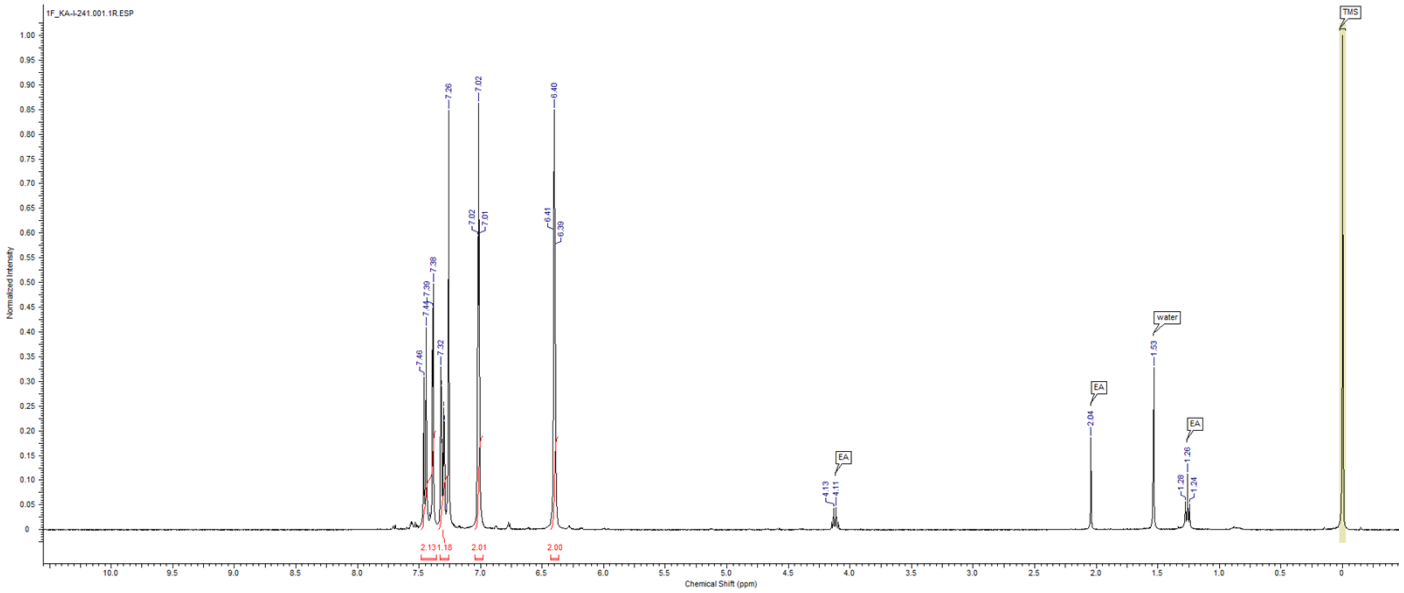

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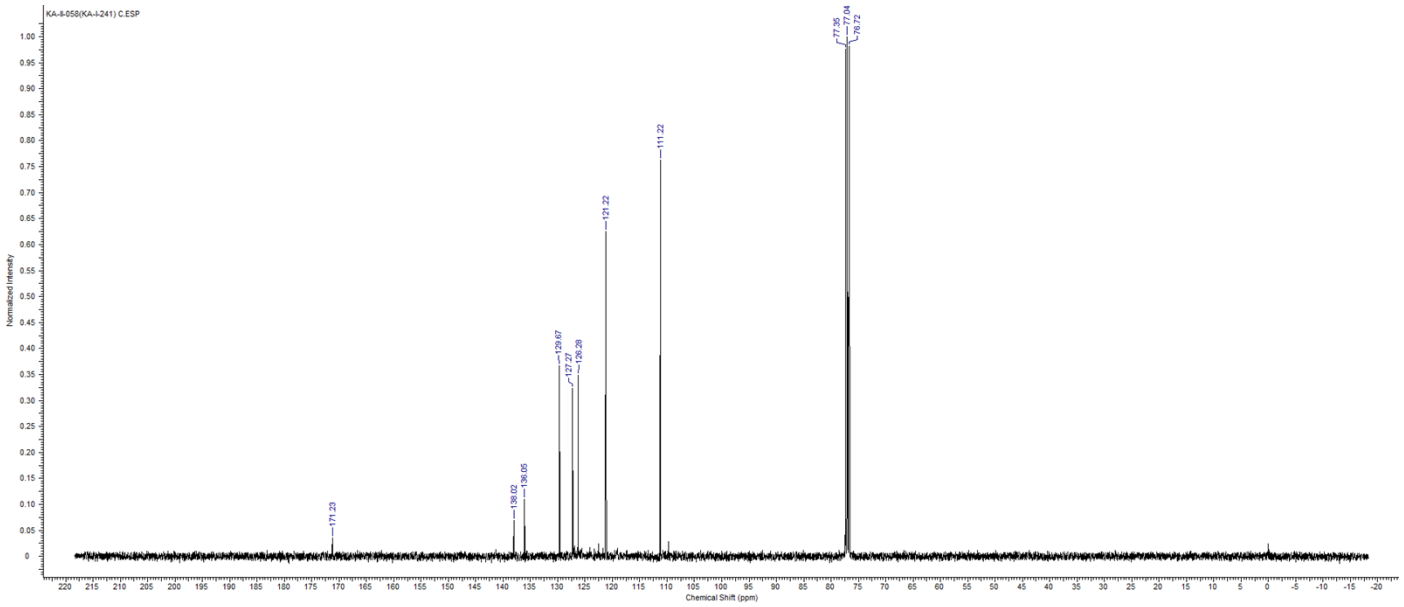
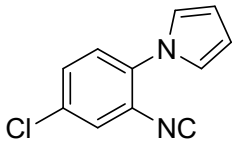


Figure S5. (a) ^{1}H NMR (400 MHz, $CDCl_3$) and (b) ^{13}C NMR (101 MHz, $CDCl_3$) spectra of **1f**



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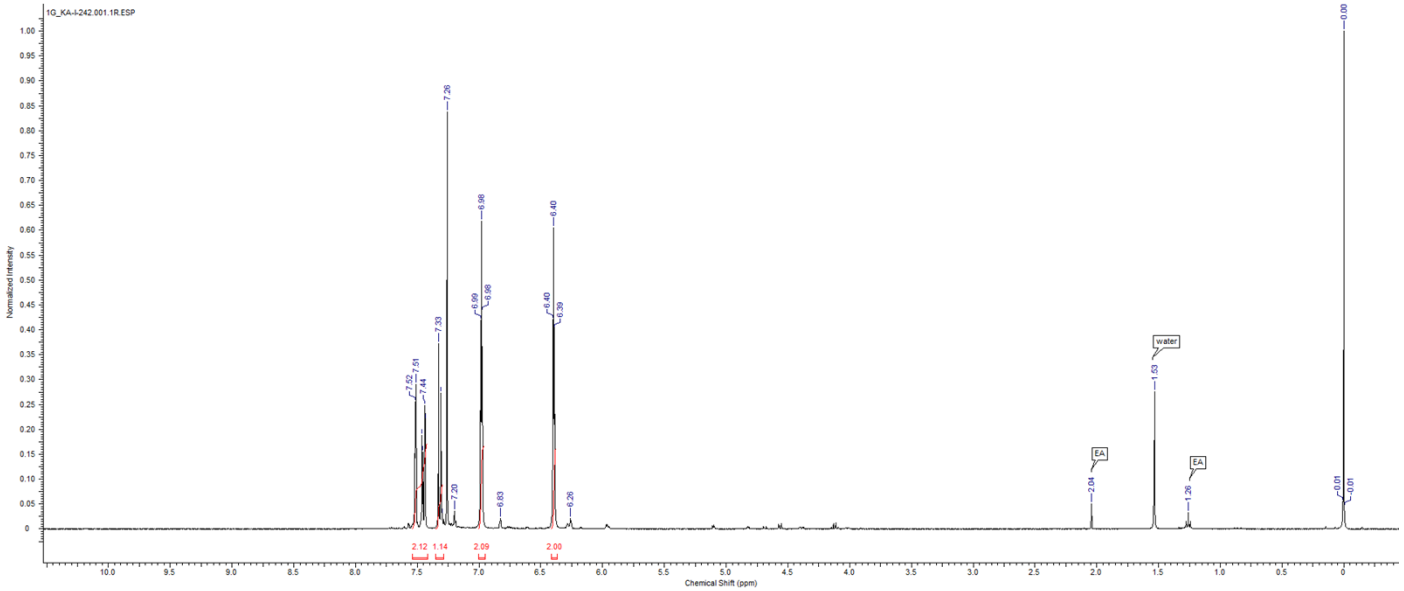

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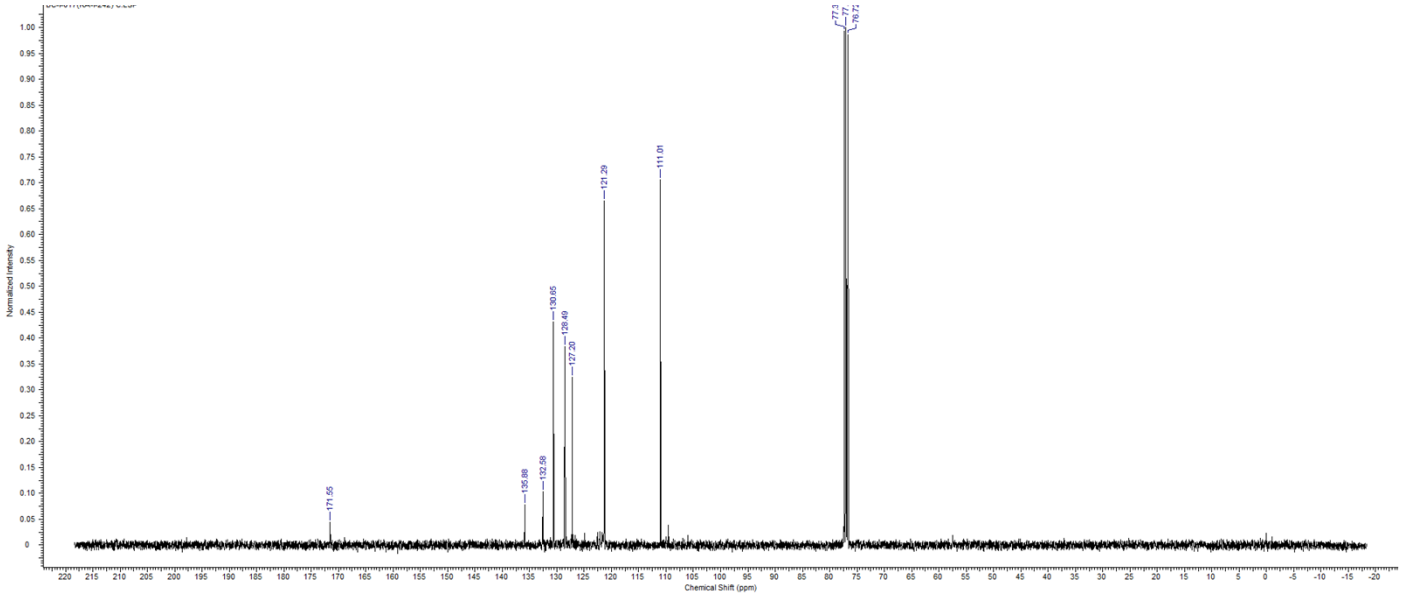
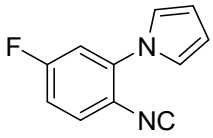
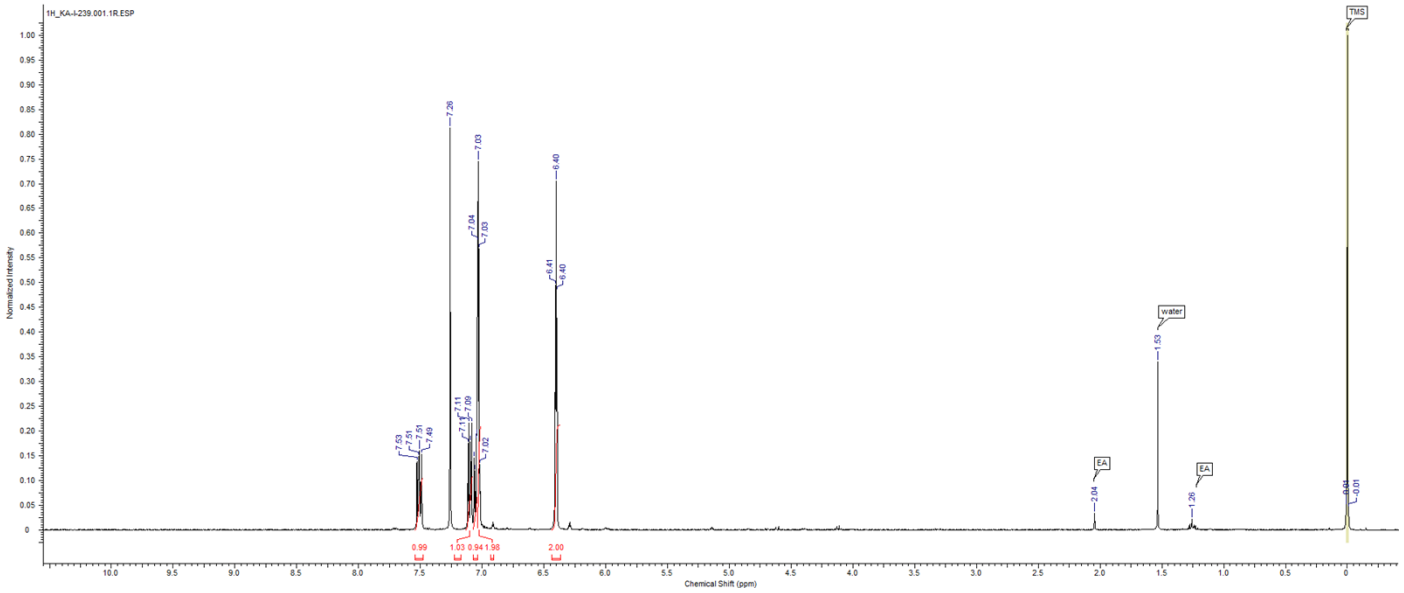


Figure S6. (a) ^{1}H NMR (400 MHz, $CDCl_3$) and (b) ^{13}C NMR (101 MHz, $CDCl_3$) spectra of **1g**



(a)



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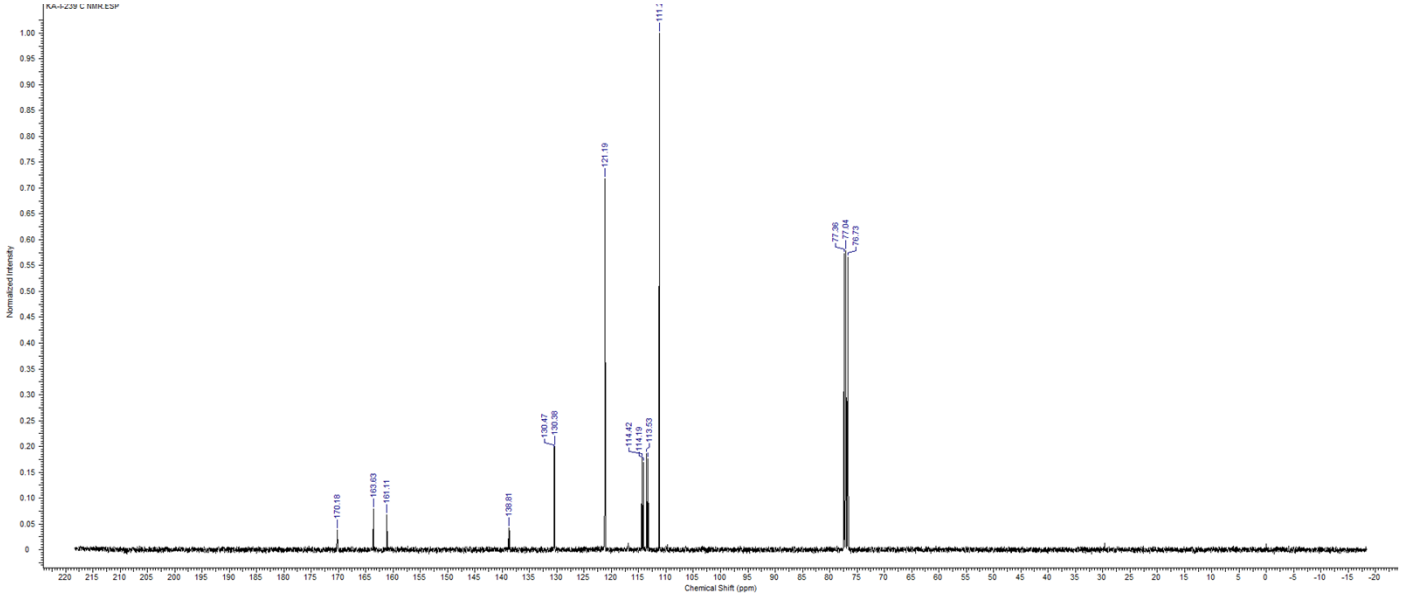
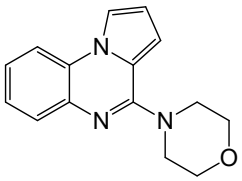


Figure S7. (a) ^{1}H NMR (400 MHz, $CDCl_3$) and (b) ^{13}C NMR (101 MHz, $CDCl_3$) spectra of **1h**



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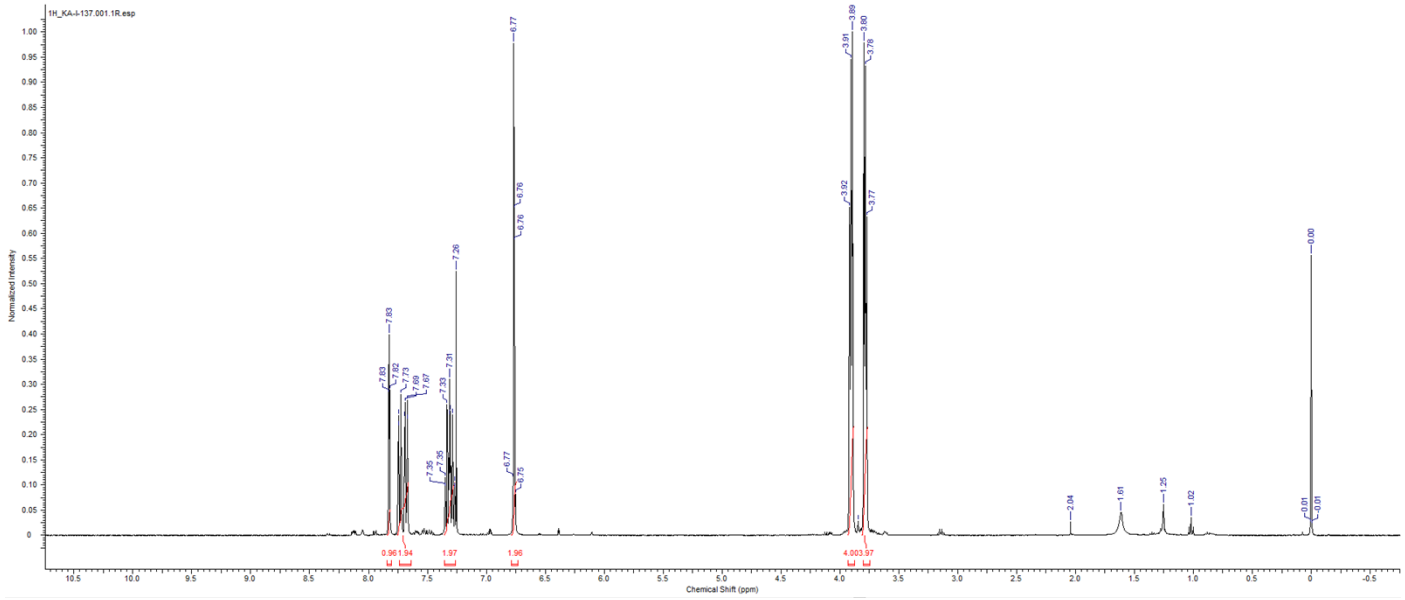

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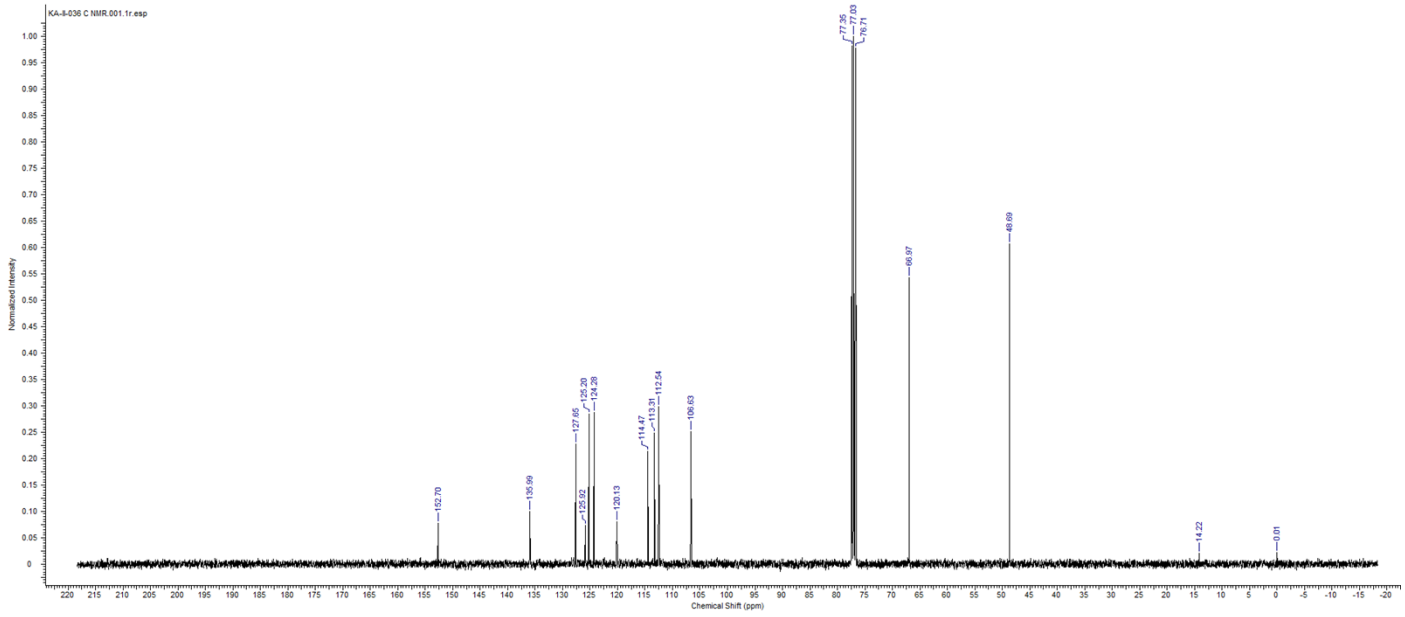
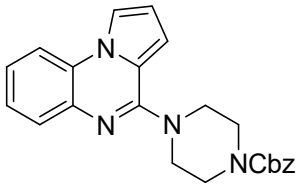
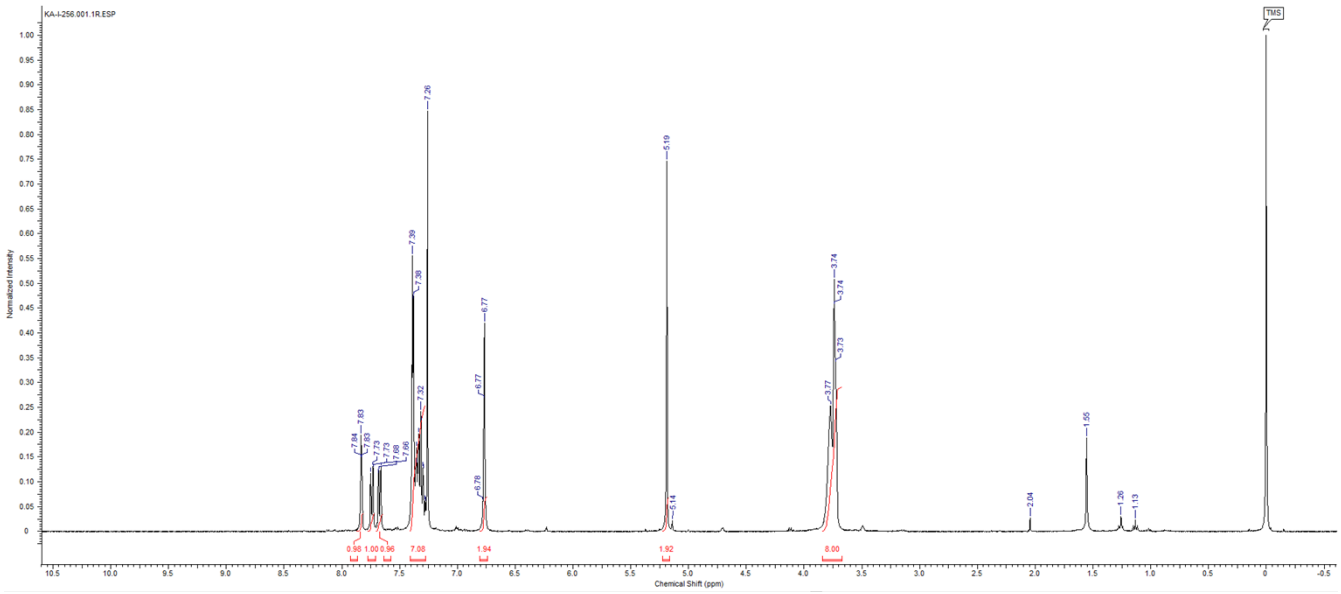


Figure S8. (a) ^{1}H NMR (400 MHz, $CDCl_3$) and (b) ^{13}C NMR (101 MHz, $CDCl_3$) spectra of **3a**



(a)



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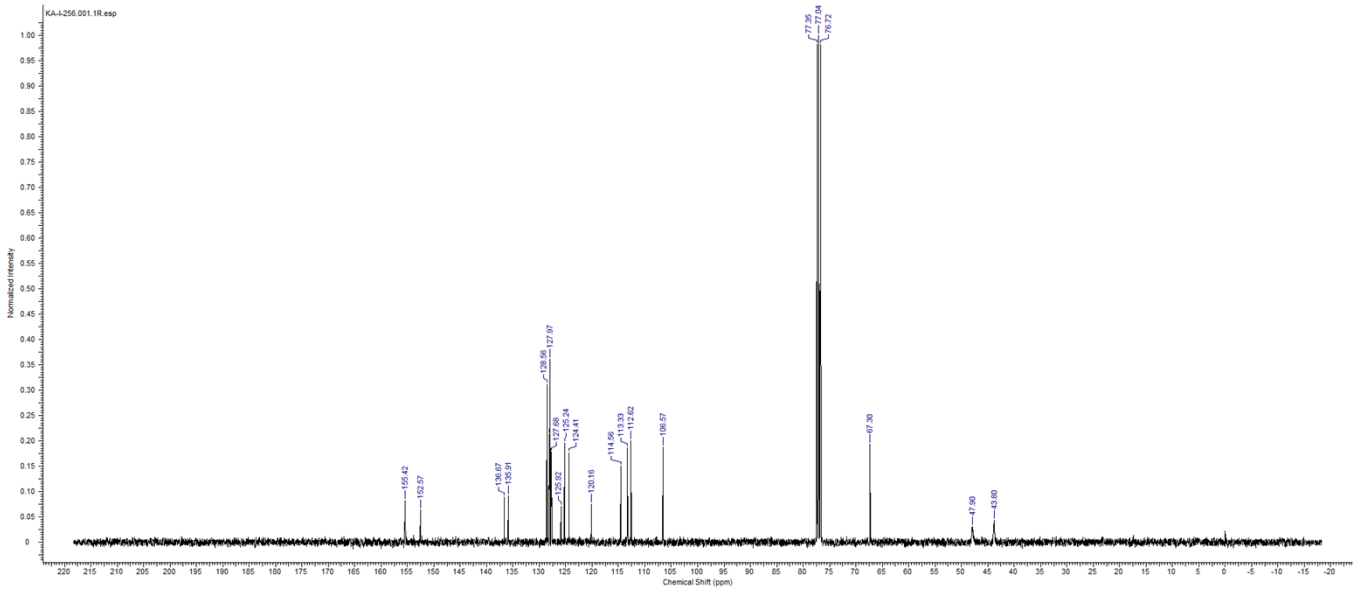
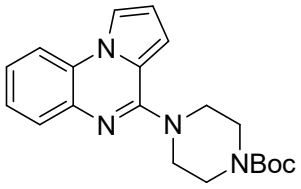


Figure S9. (a) ^{1}H NMR (400 MHz, $CDCl_3$) and (b) ^{13}C NMR (101 MHz, $CDCl_3$) spectra of **3b**



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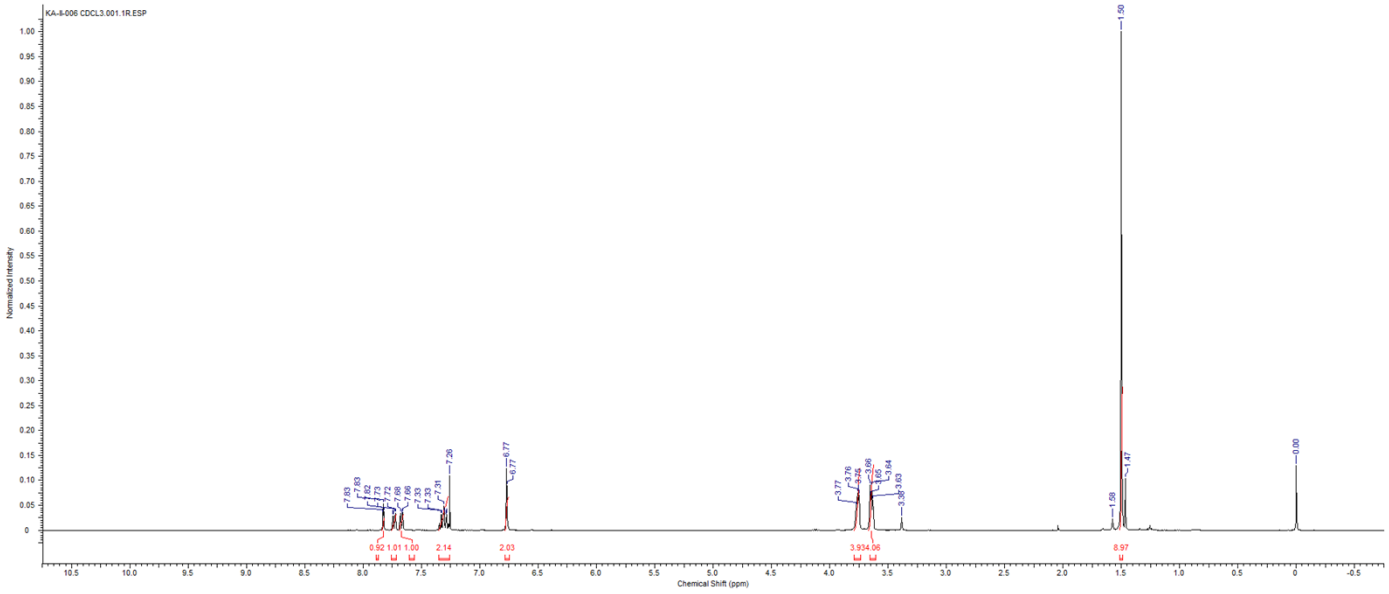

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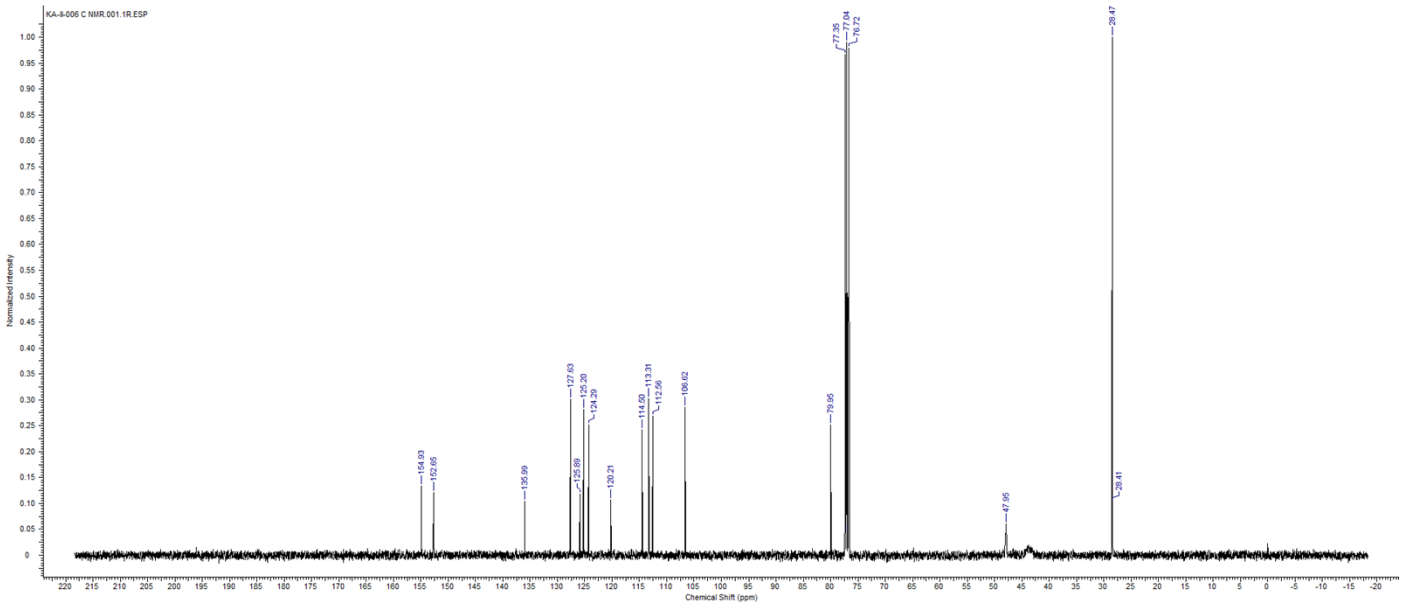
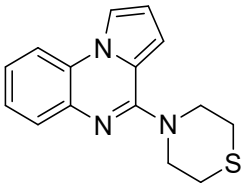


Figure S10. (a) ^{1}H NMR (400 MHz, $CDCl_3$) and (b) ^{13}C NMR (101 MHz, $CDCl_3$) spectra of **3c**



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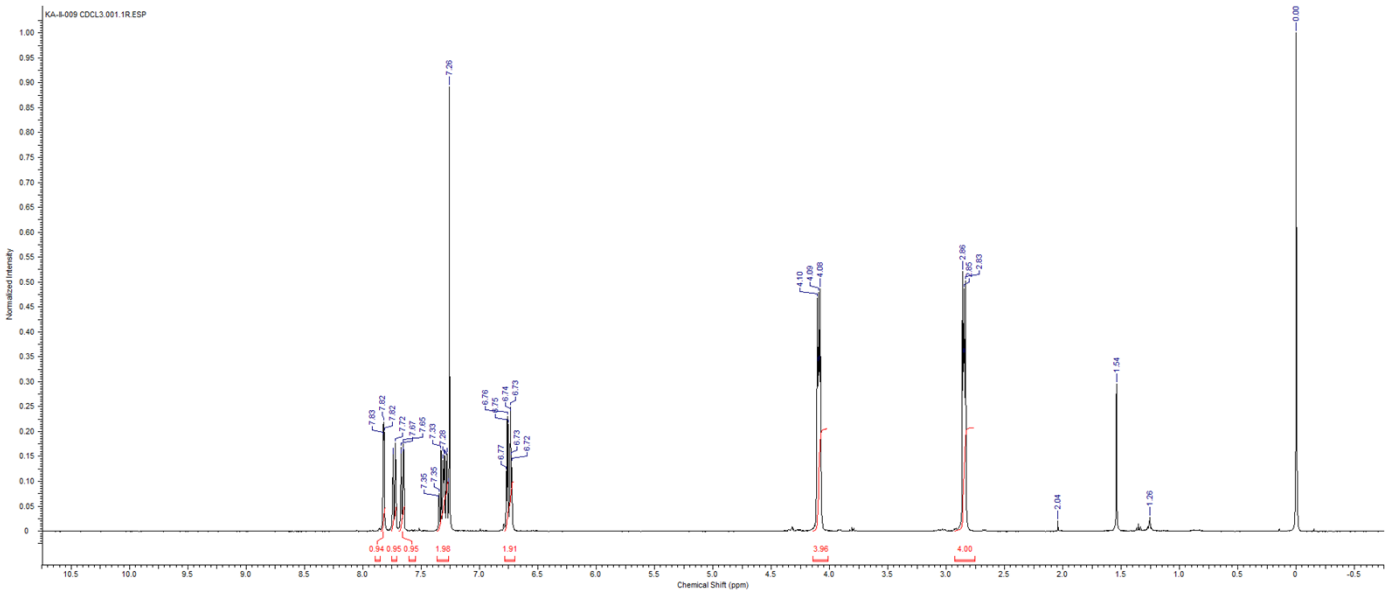

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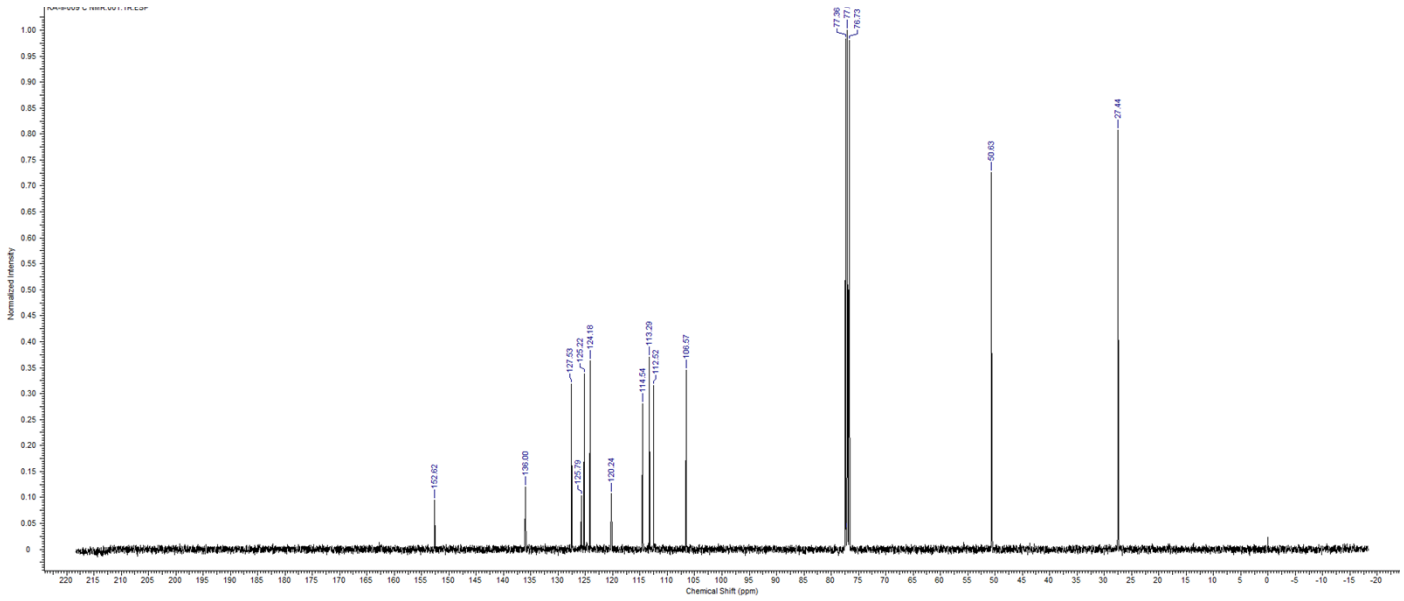
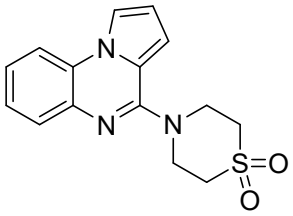


Figure S11. (a) ^{1}H NMR (400 MHz, $CDCl_3$) and (b) ^{13}C NMR (101 MHz, $CDCl_3$) spectra of **3d**



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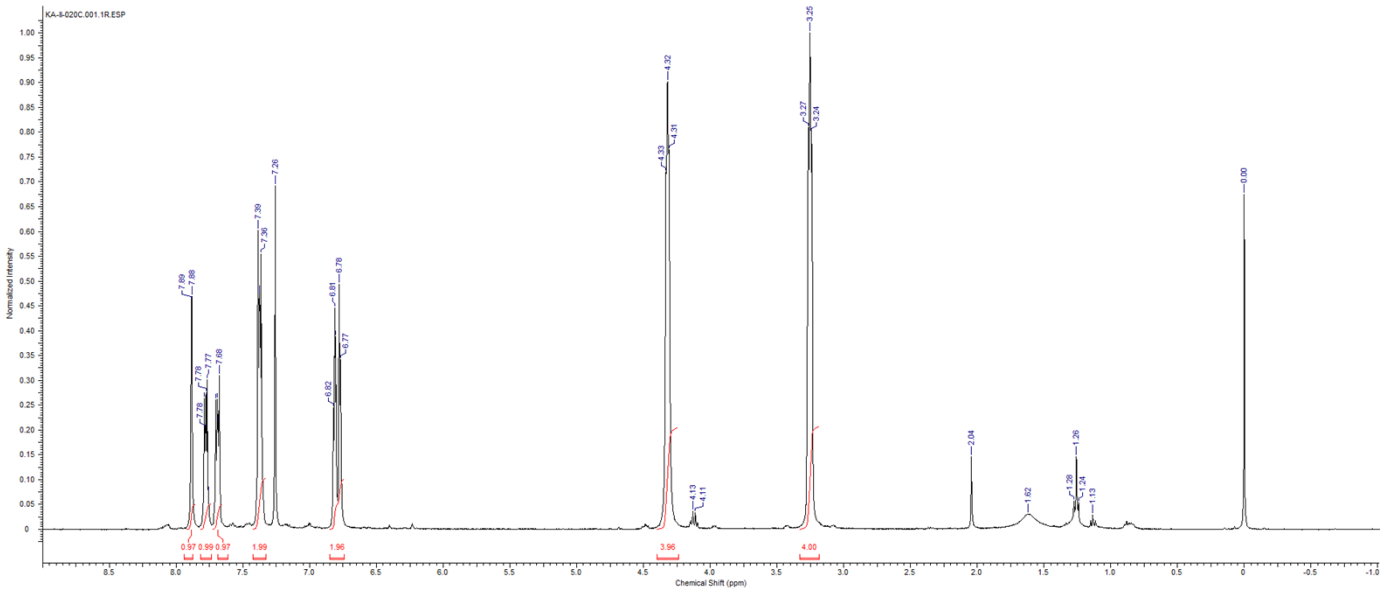

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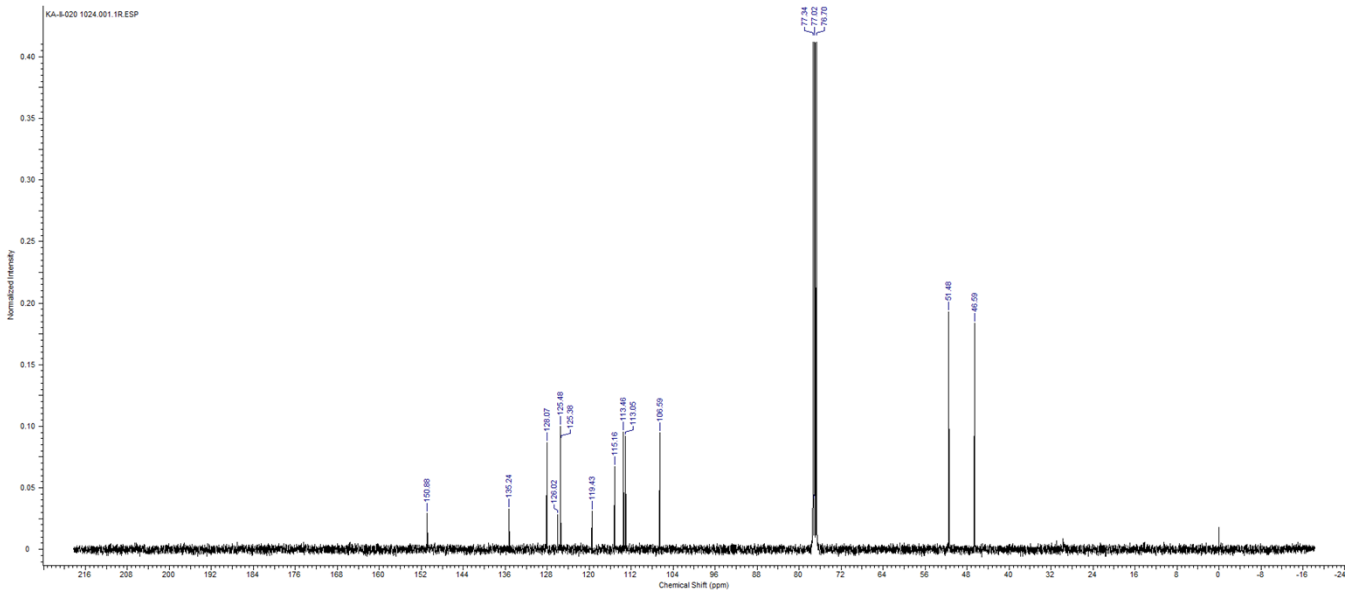
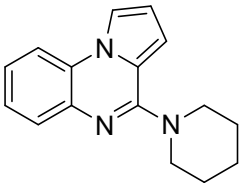


Figure S12. (a) ^{1}H NMR (400 MHz, $CDCl_3$) and (b) ^{13}C NMR (101 MHz, $CDCl_3$) spectra of **3e**



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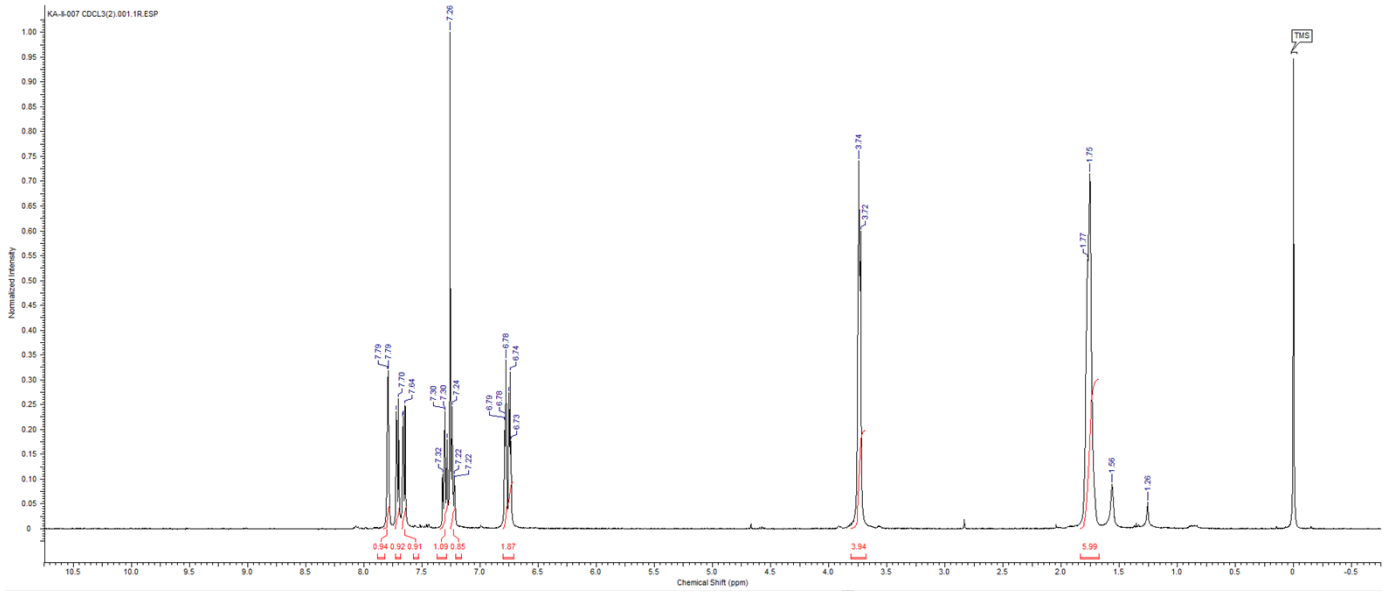

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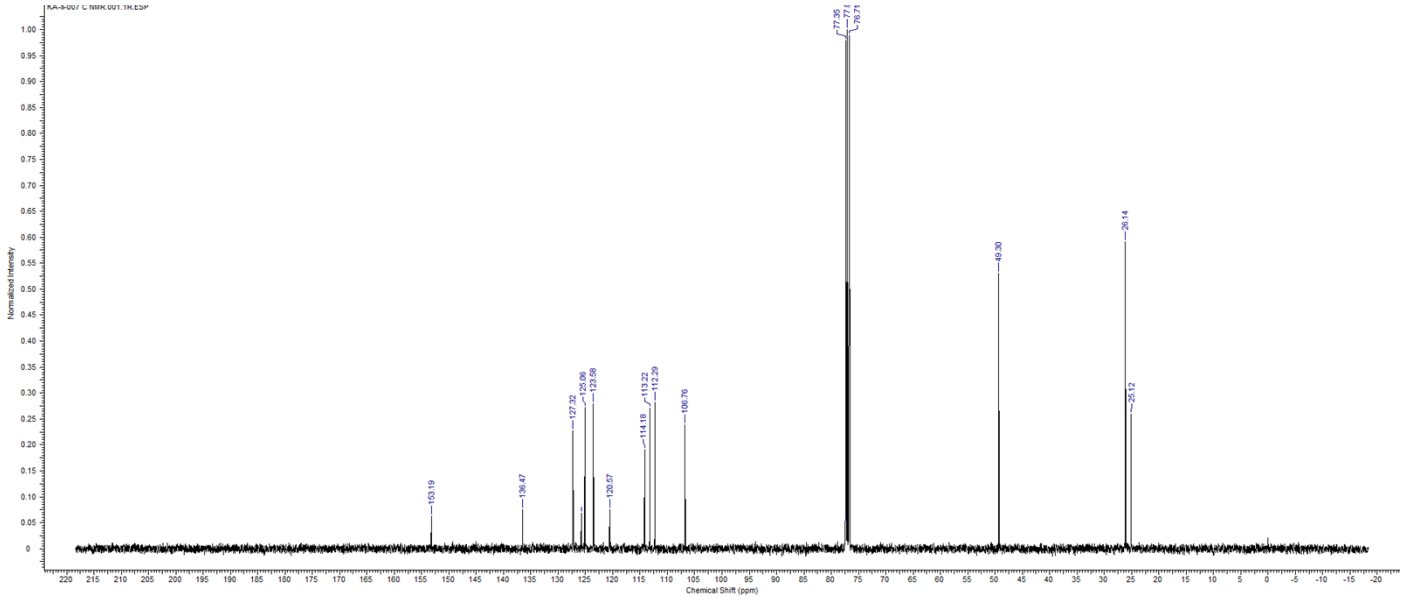
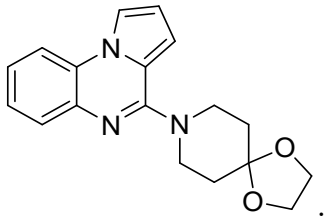
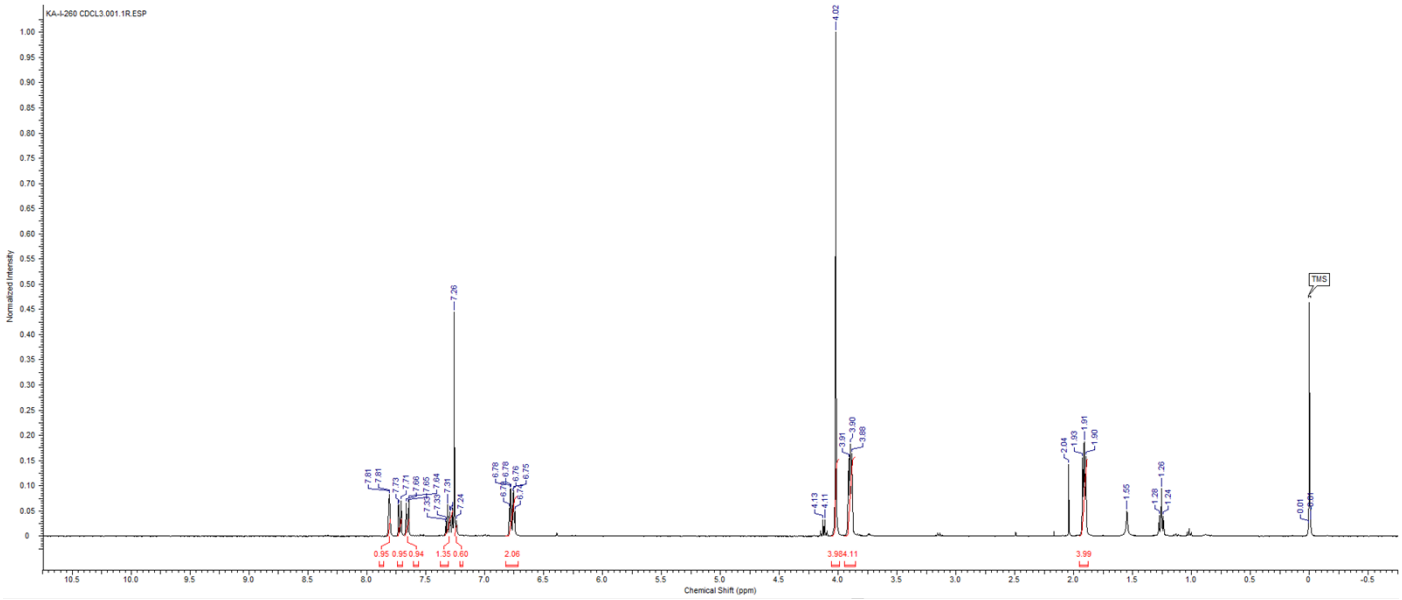


Figure S13. (a) ^{1}H NMR (400 MHz, $CDCl_3$) and (b) ^{13}C NMR (101 MHz, $CDCl_3$) spectra of **3f**



(a)



(b)

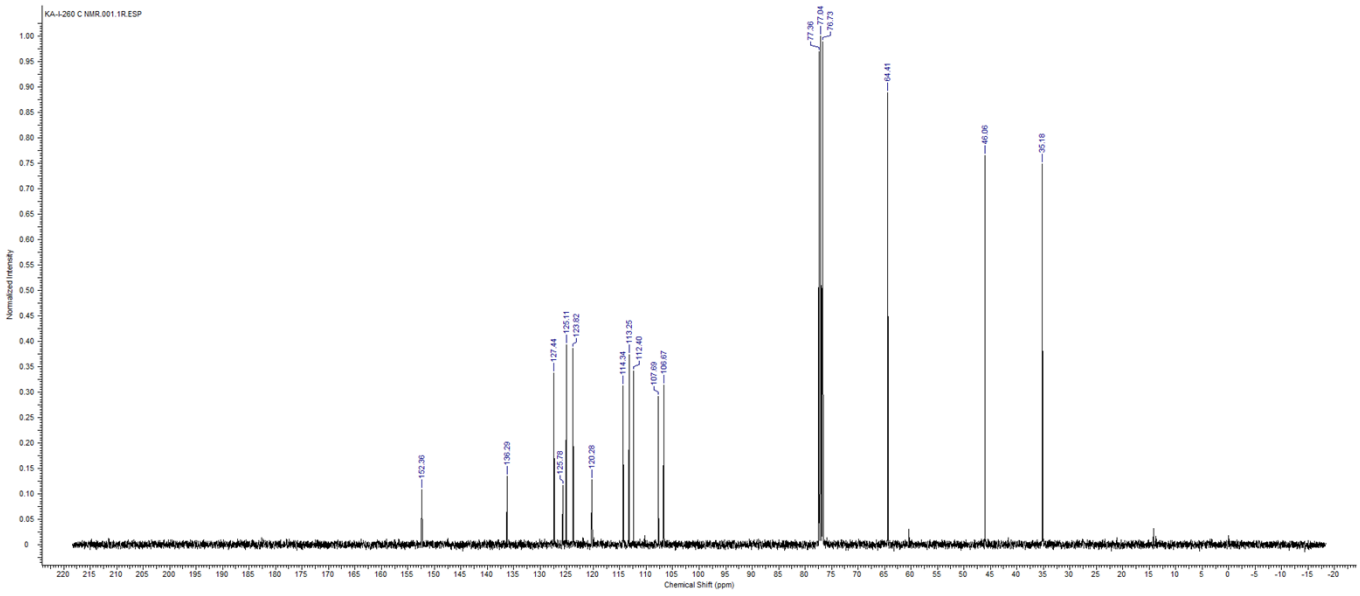
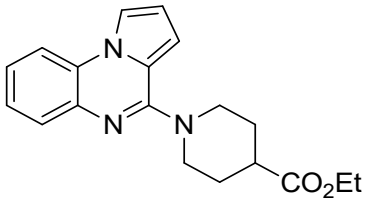
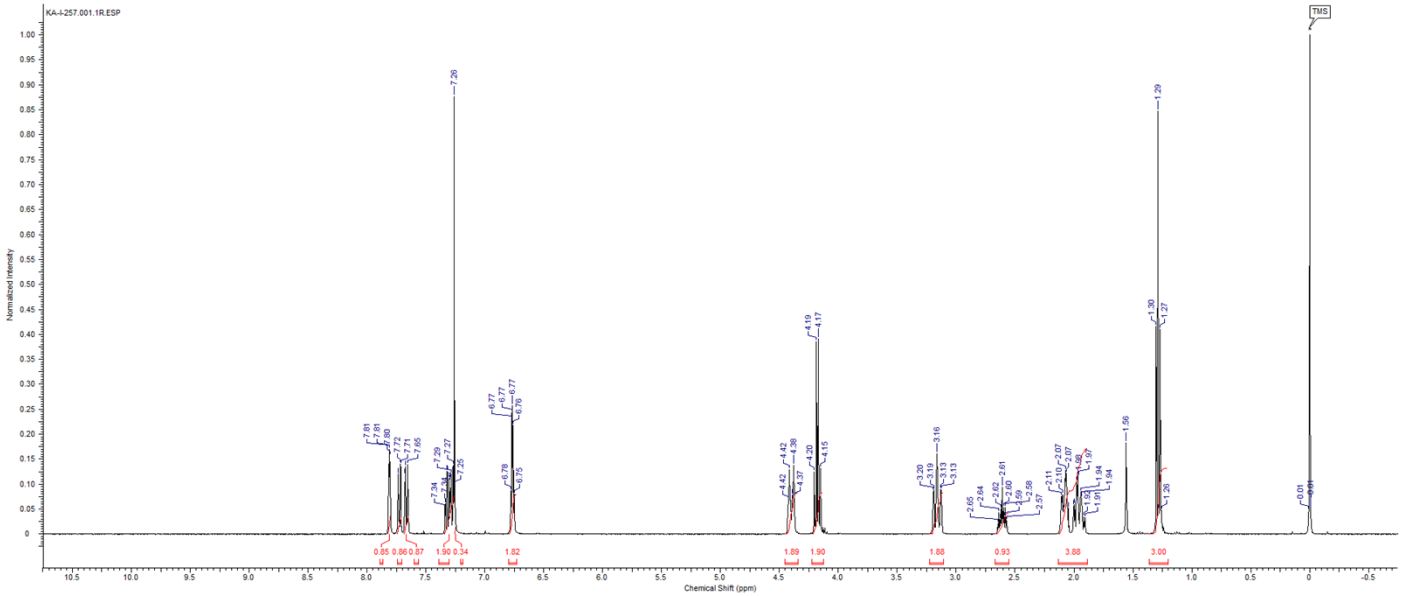


Figure S14. (a) ^{1}H NMR (400 MHz, $CDCl_3$) and (b) ^{13}C NMR (101 MHz, $CDCl_3$) spectra of **3g**



(a)



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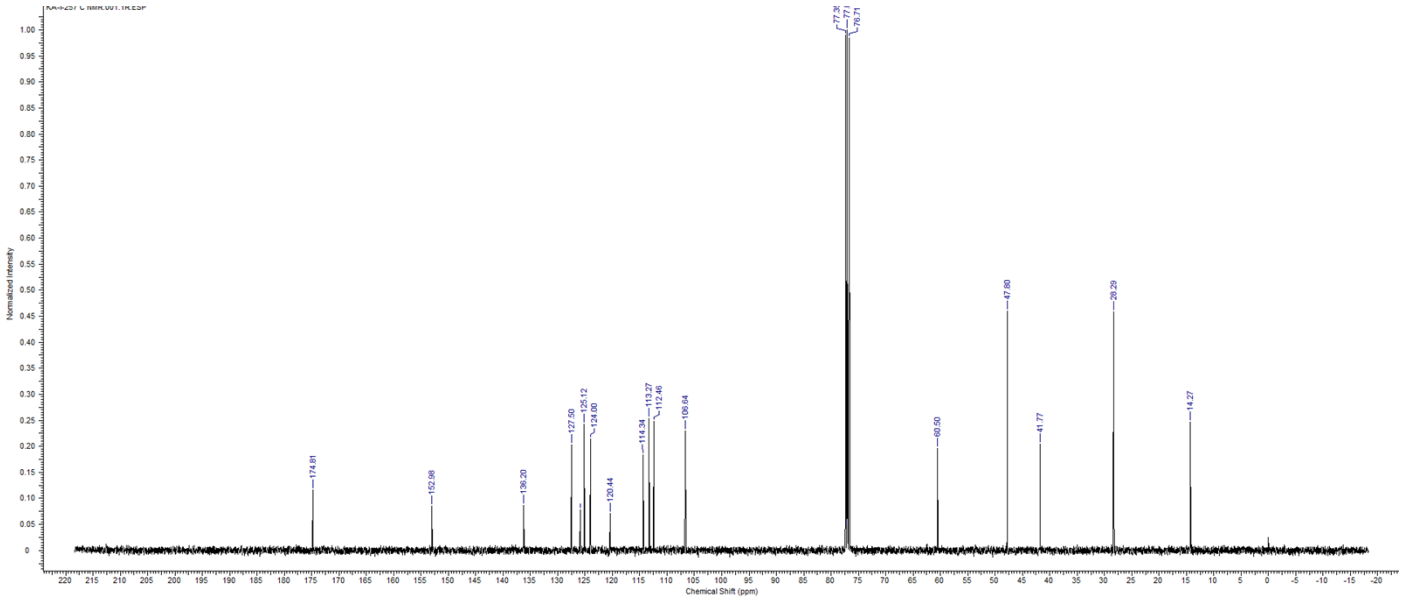
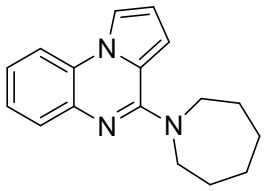
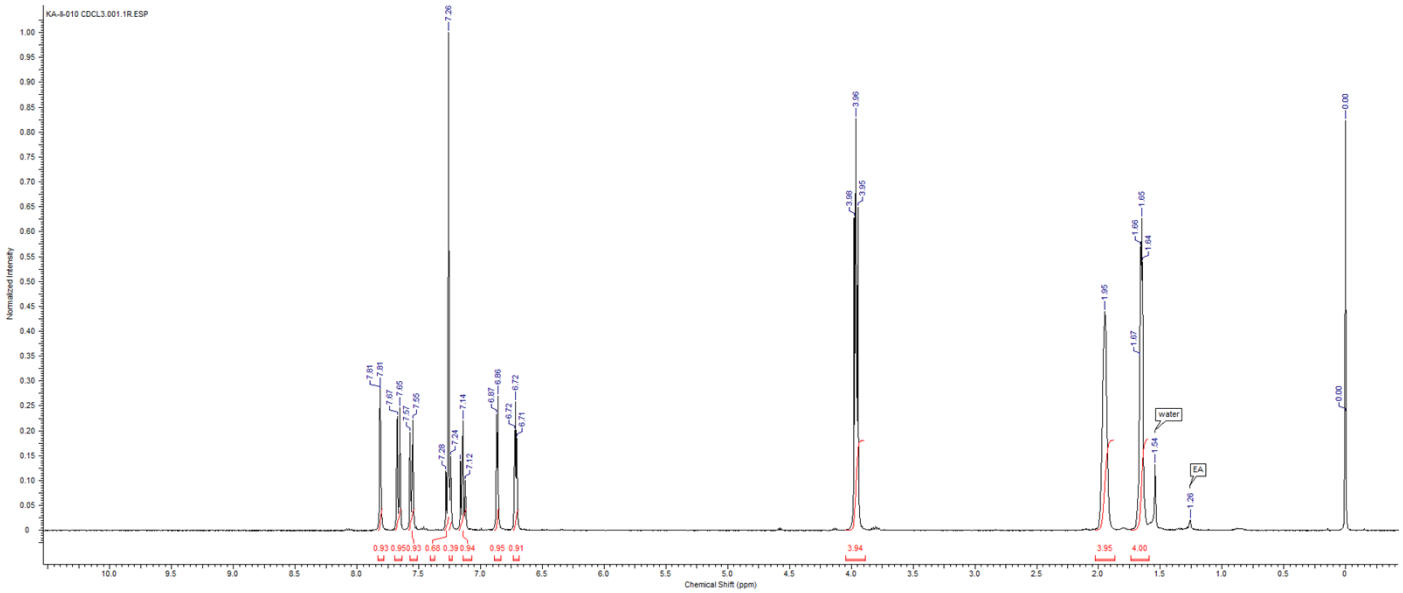


Figure S15. (a) ^{1}H NMR (400 MHz, $CDCl_3$) and (b) ^{13}C NMR (101 MHz, $CDCl_3$) spectra of **3h**



(a)



(b)

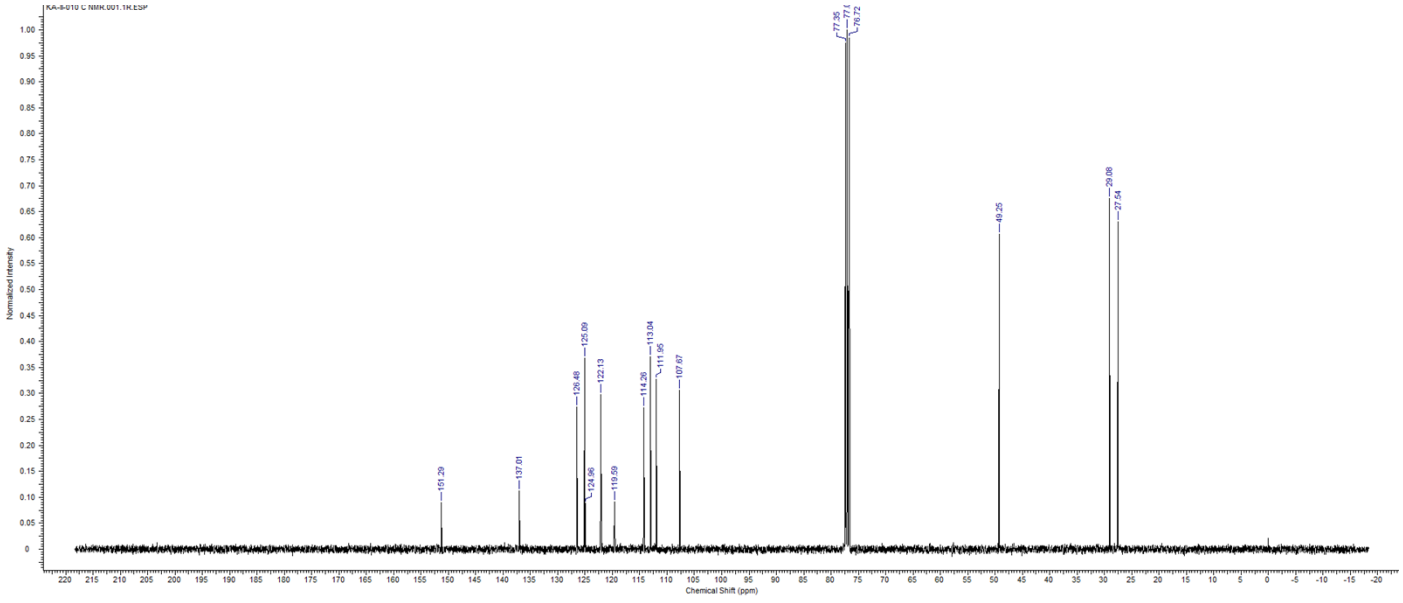
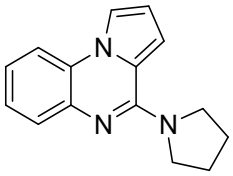
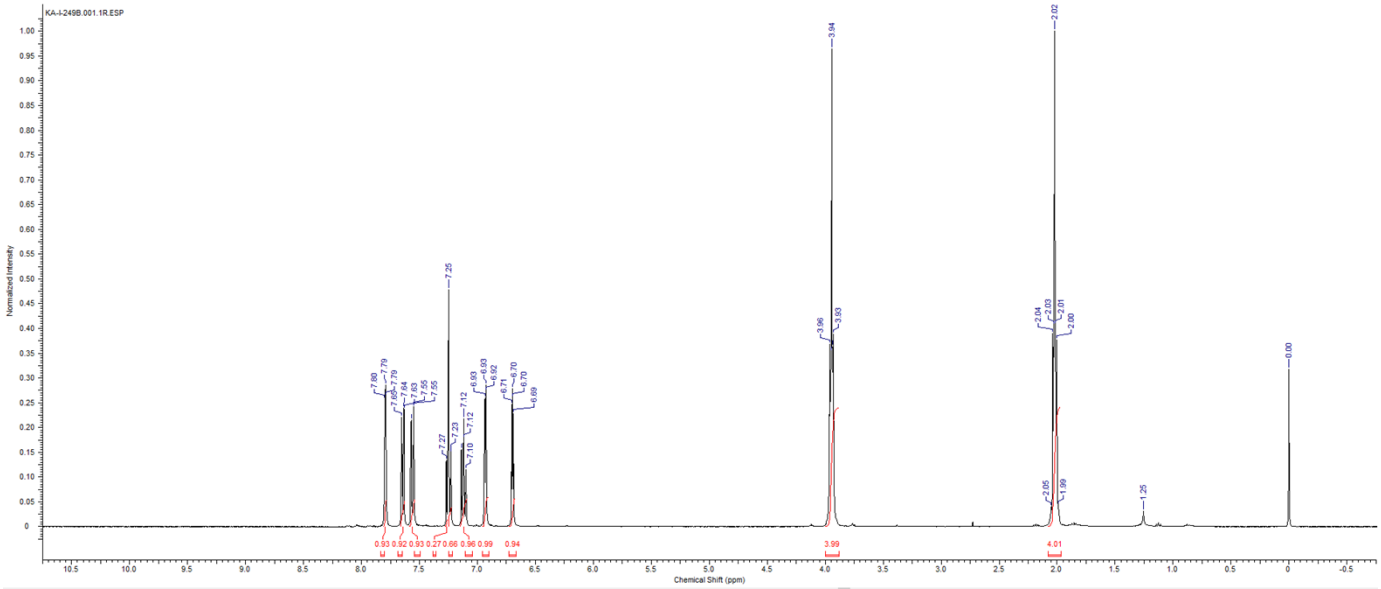


Figure S16. (a) ^{1}H NMR (400 MHz, $CDCl_3$) and (b) ^{13}C NMR (101 MHz, $CDCl_3$) spectra of **3i**



(a)



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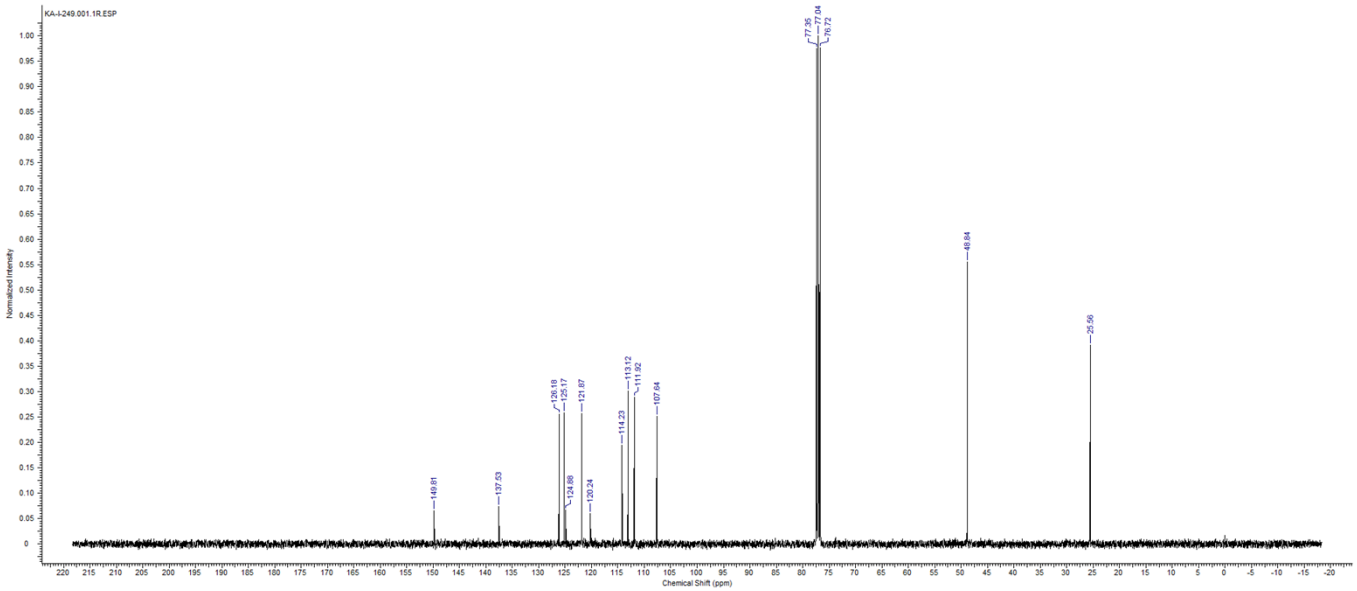
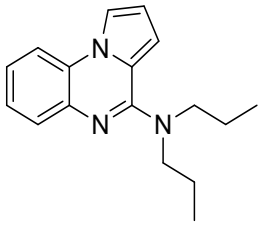
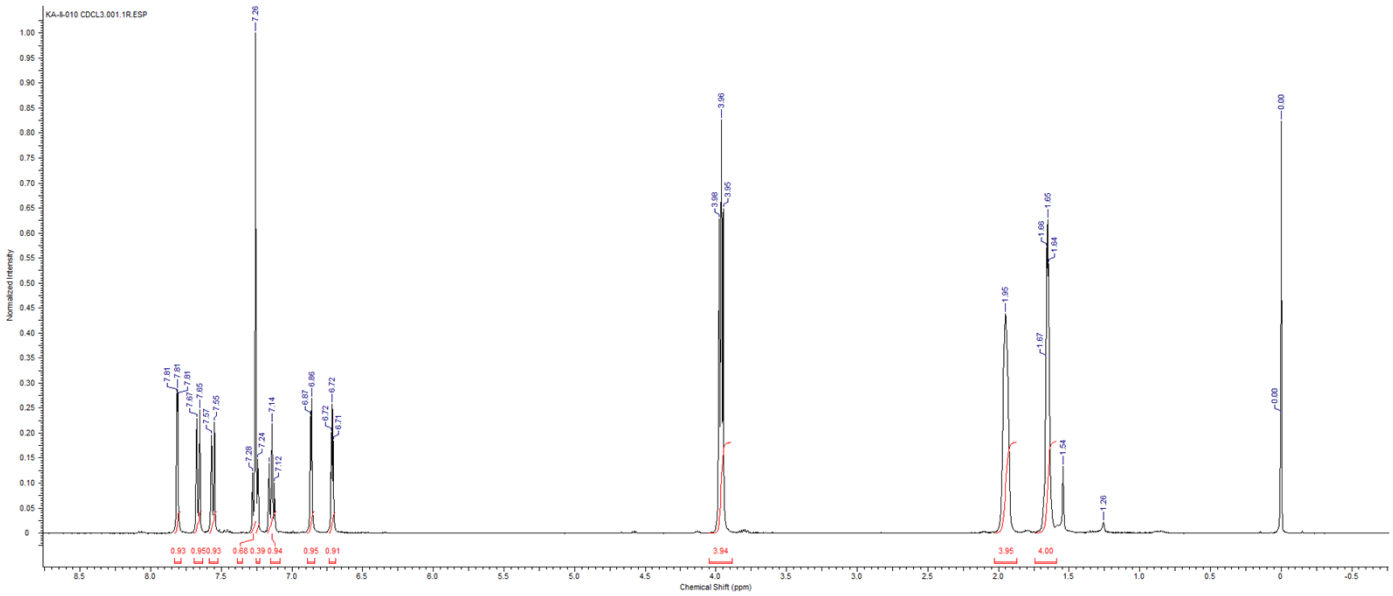


Figure S17. (a) ^{1}H NMR (400 MHz, $CDCl_3$) and (b) ^{13}C NMR (101 MHz, $CDCl_3$) spectra of **3j**



(a)



(b)

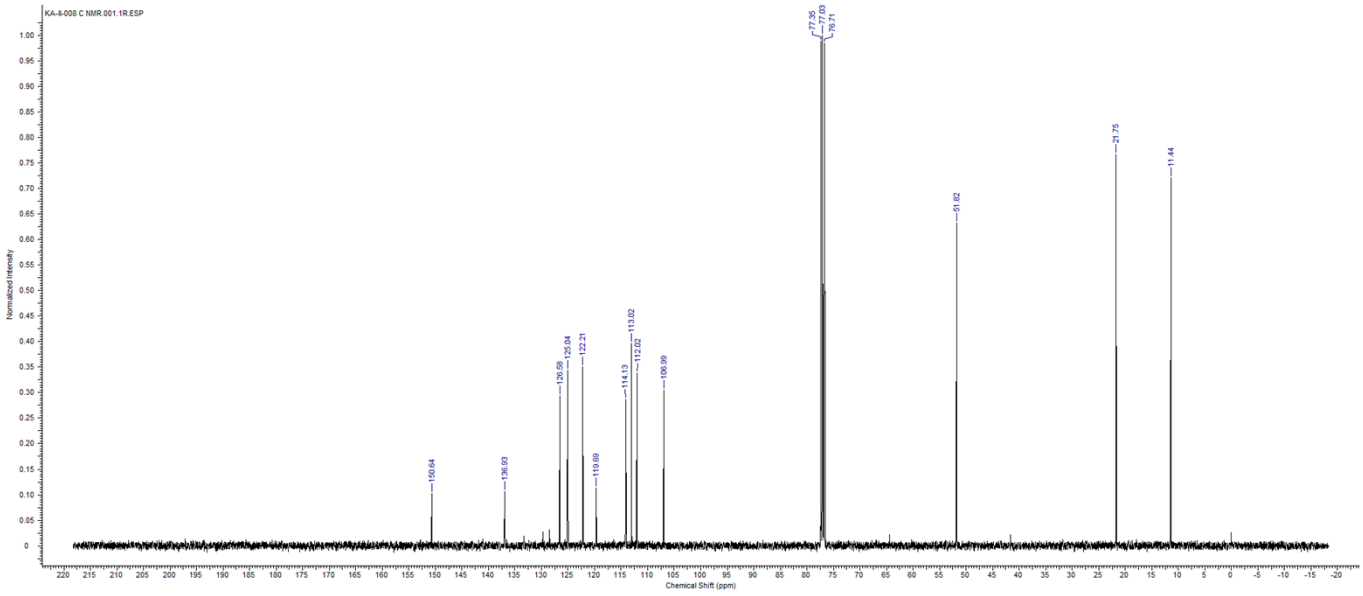
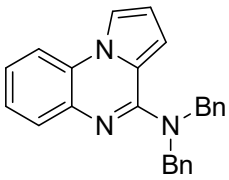
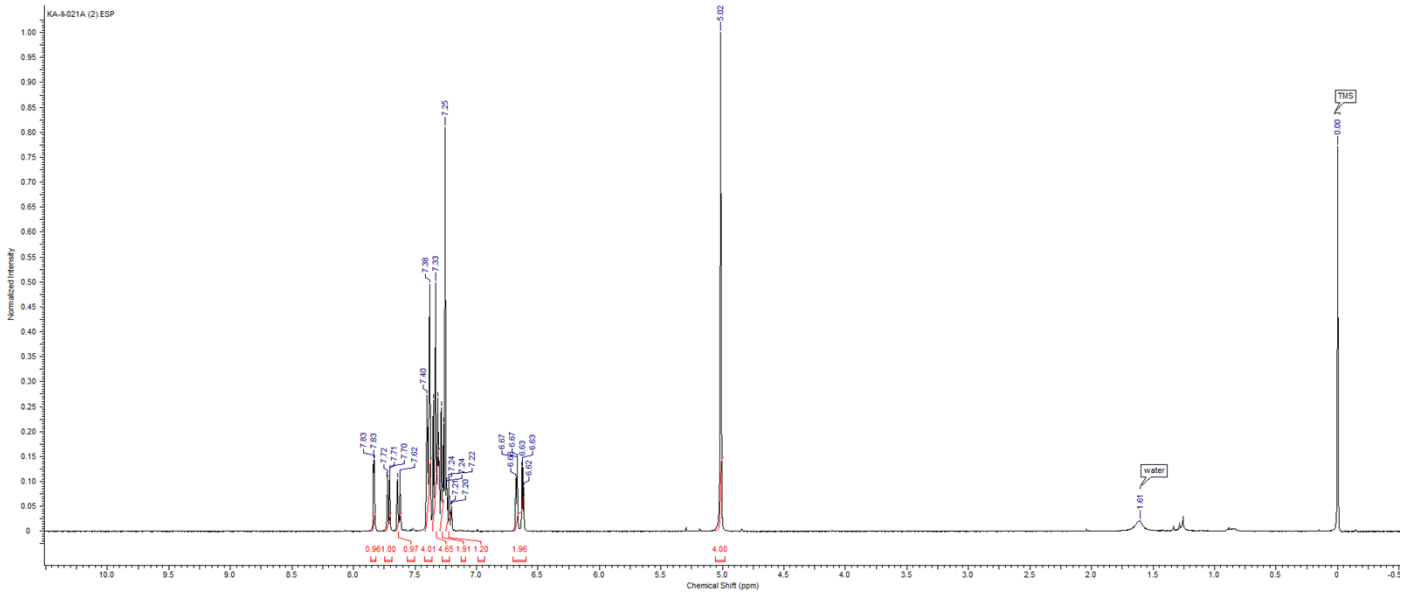


Figure S18. (a) ^{1}H NMR (400 MHz, $CDCl_3$) and (b) ^{13}C NMR (101 MHz, $CDCl_3$) spectra of **3k**



(a)



(b)

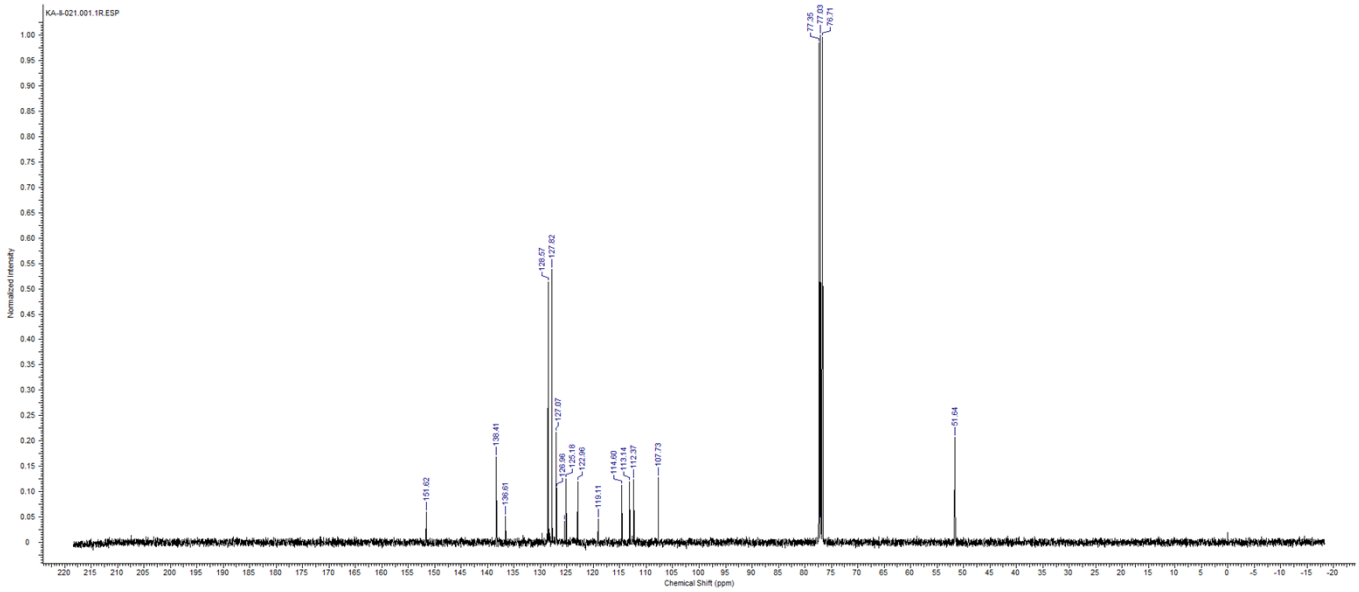
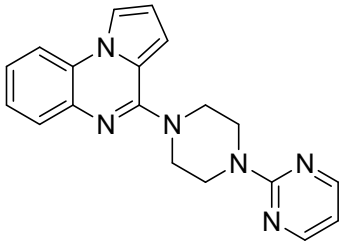
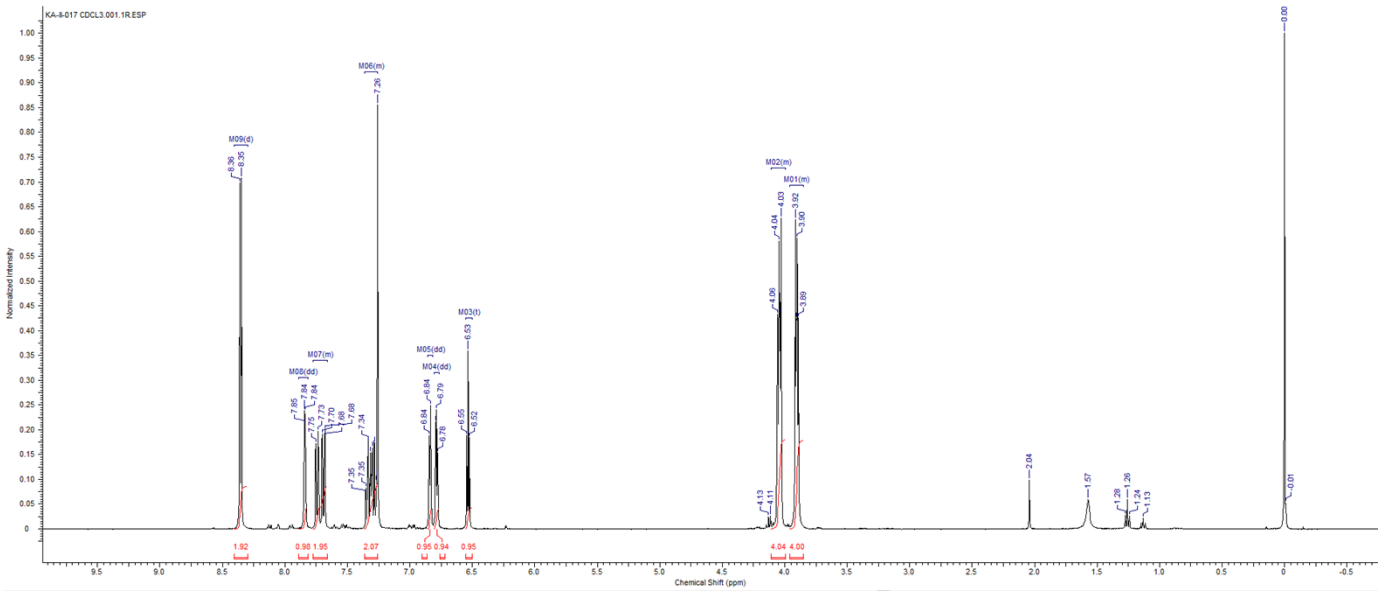


Figure S19. (a) ^{1}H NMR (400 MHz, $CDCl_3$) and (b) ^{13}C NMR (101 MHz, $CDCl_3$) spectra of **3l**



(a)



(b)

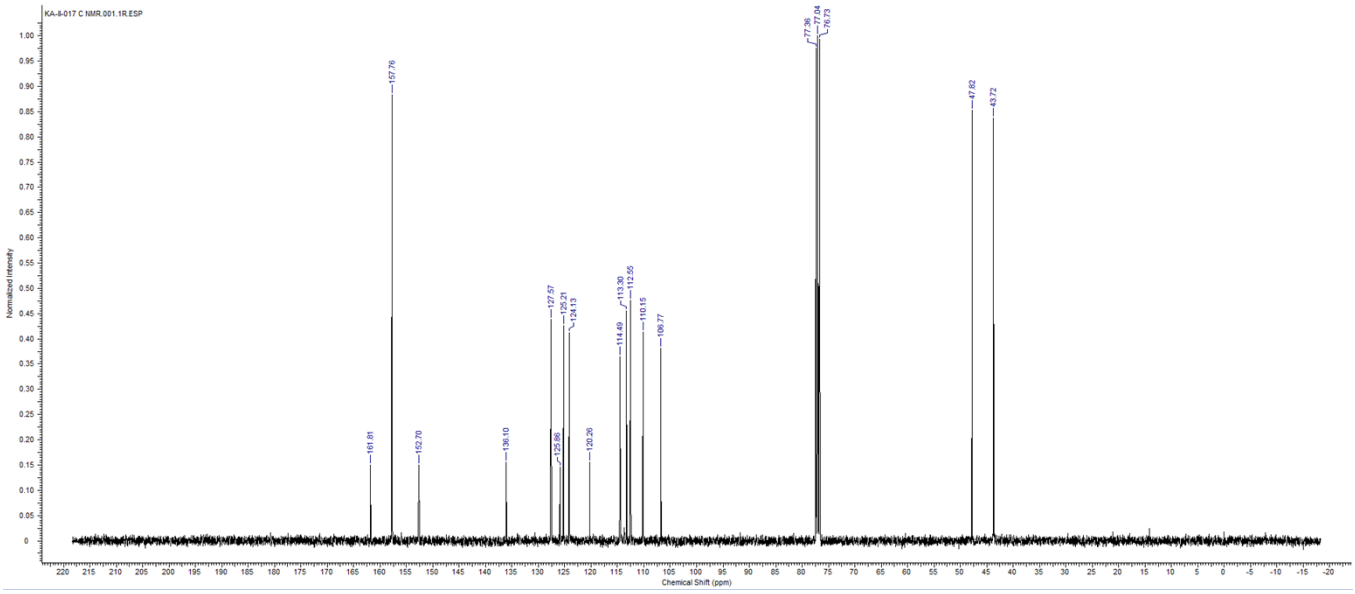
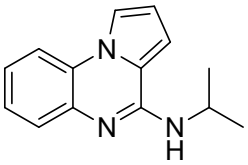
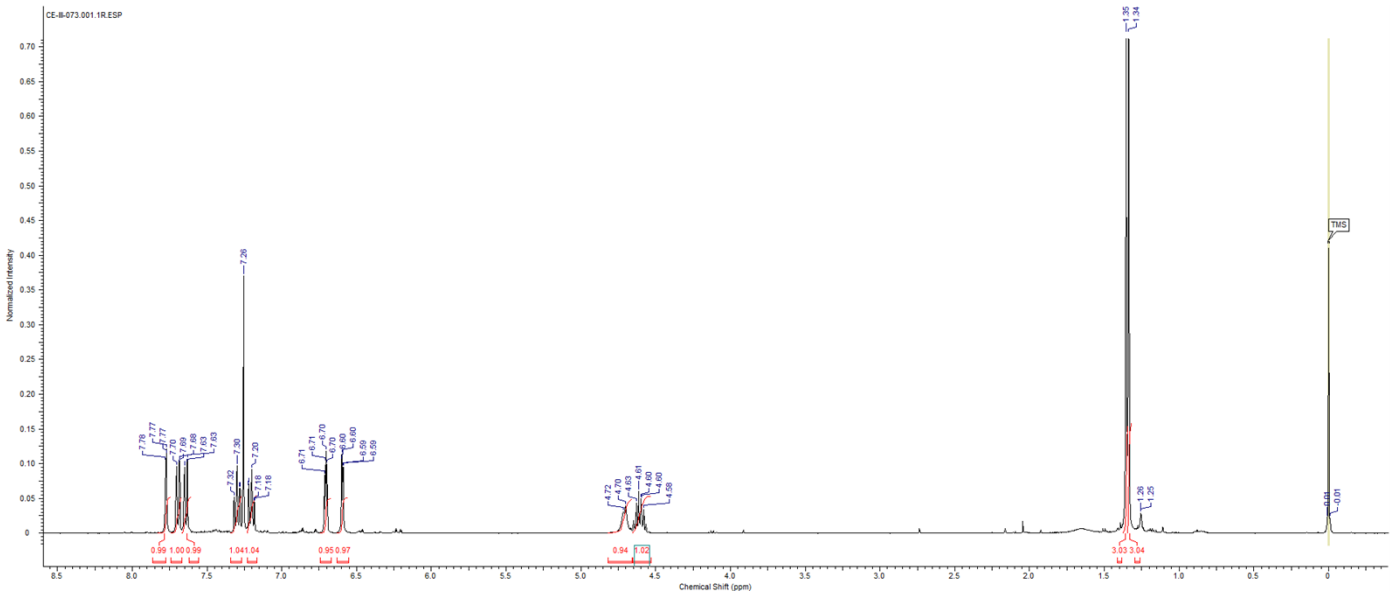


Figure S20. (a) ^{1}H NMR (400 MHz, $CDCl_3$) and (b) ^{13}C NMR (101 MHz, $CDCl_3$) spectra of **3m**



(a)



(b)

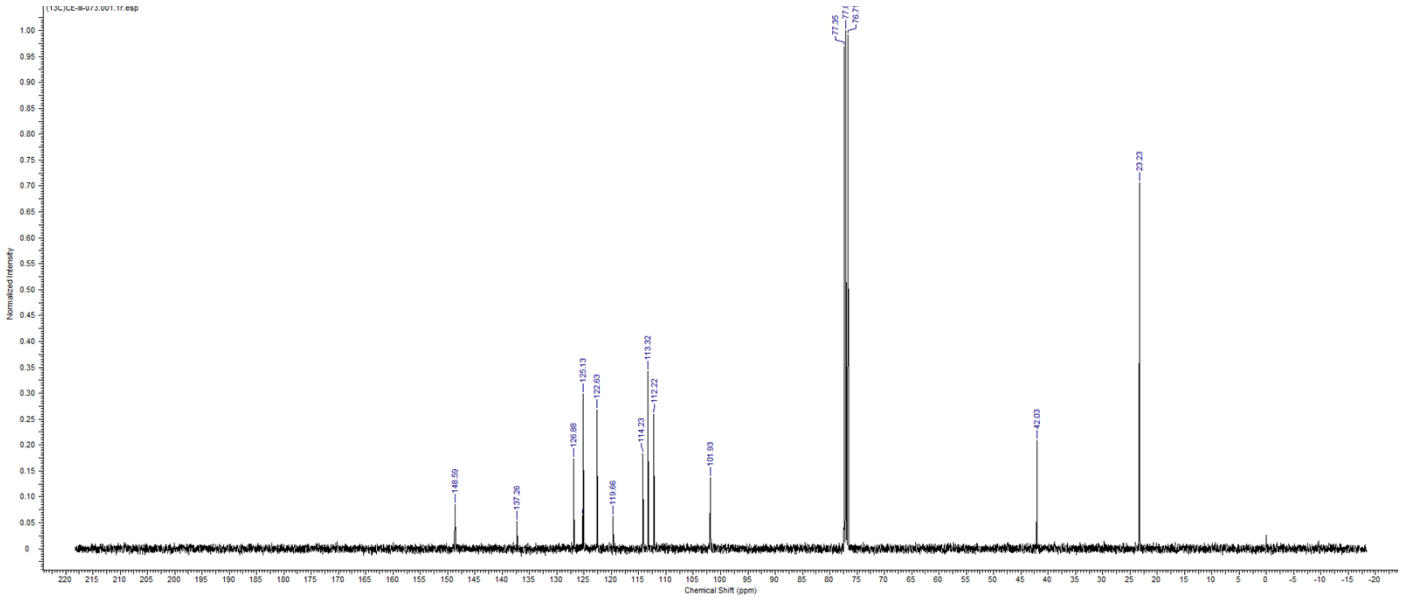
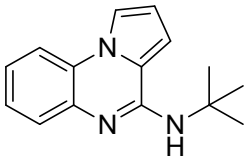
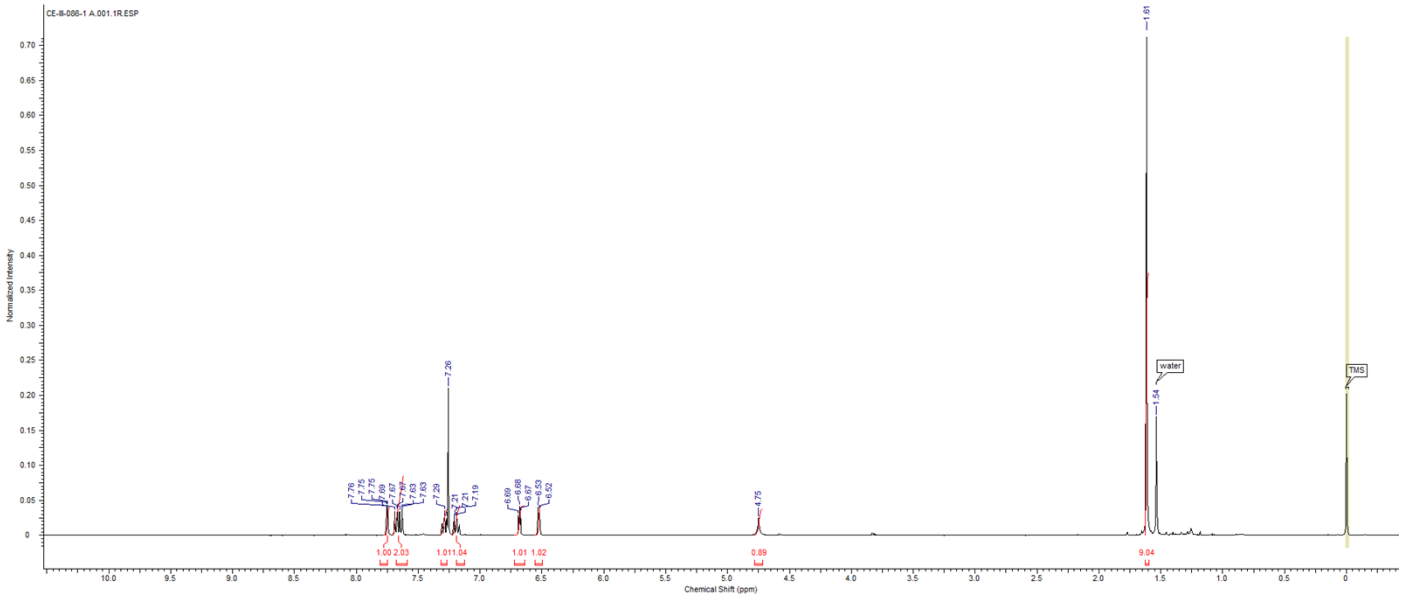


Figure S21. (a) ^{1}H NMR (400 MHz, $CDCl_3$) and (b) ^{13}C NMR (101 MHz, $CDCl_3$) spectra of **3n**



(a)



(b)

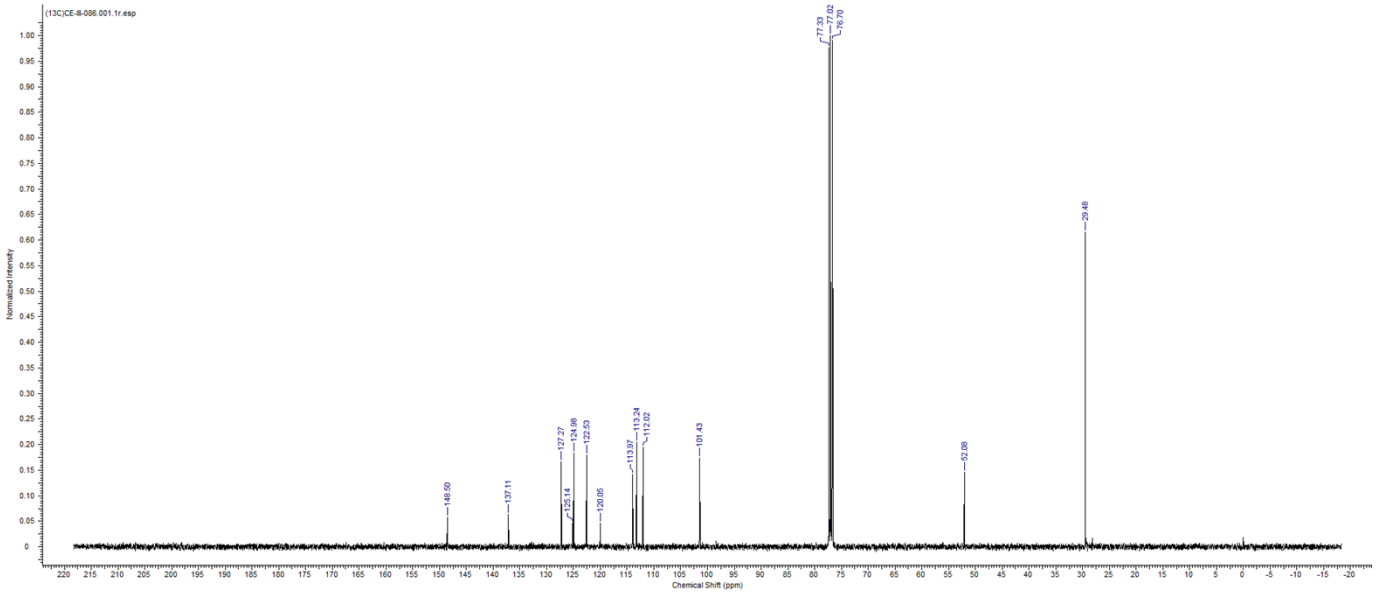
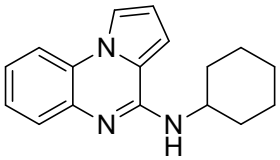
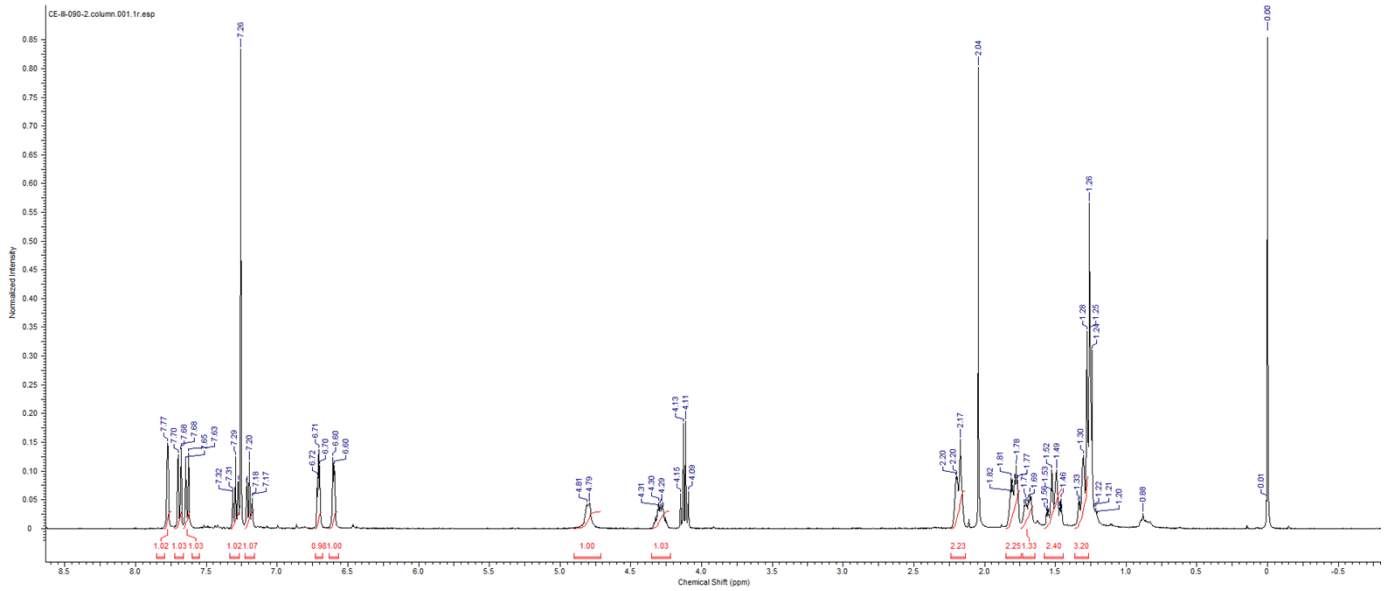


Figure S22. (a) ^{1}H NMR (400 MHz, $CDCl_3$) and (b) ^{13}C NMR (101 MHz, $CDCl_3$) spectra of **3o**



(a)



(b)

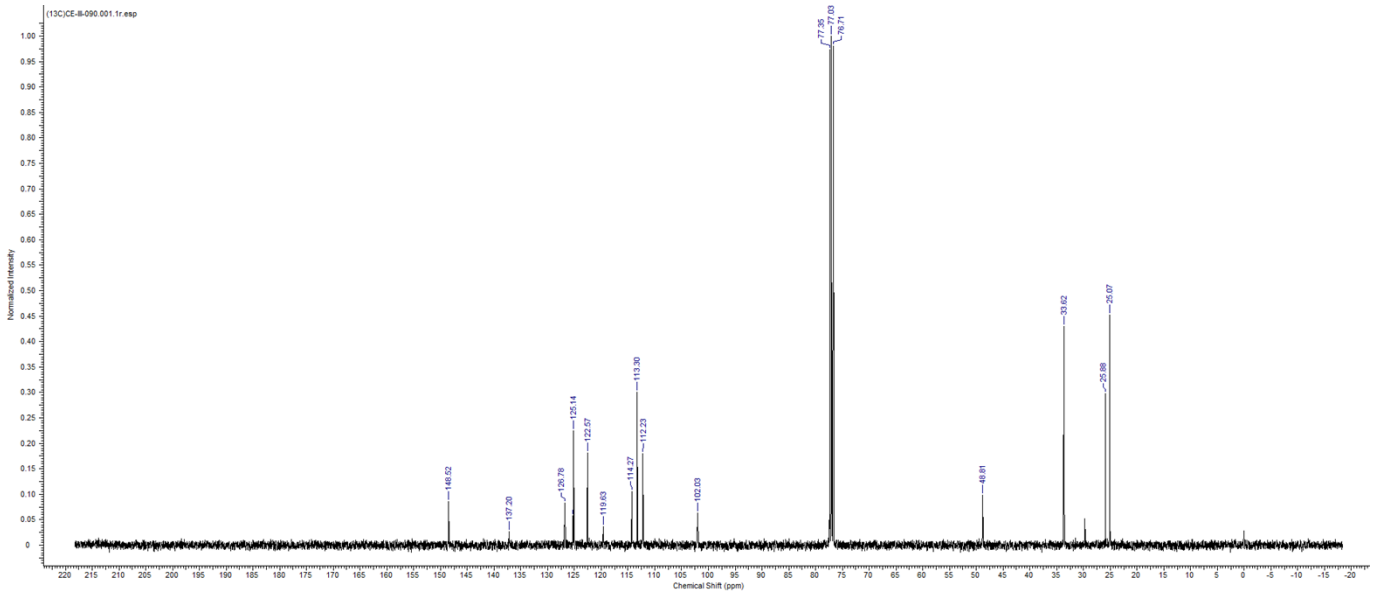
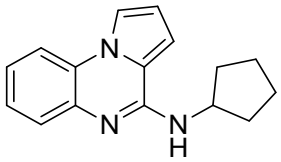
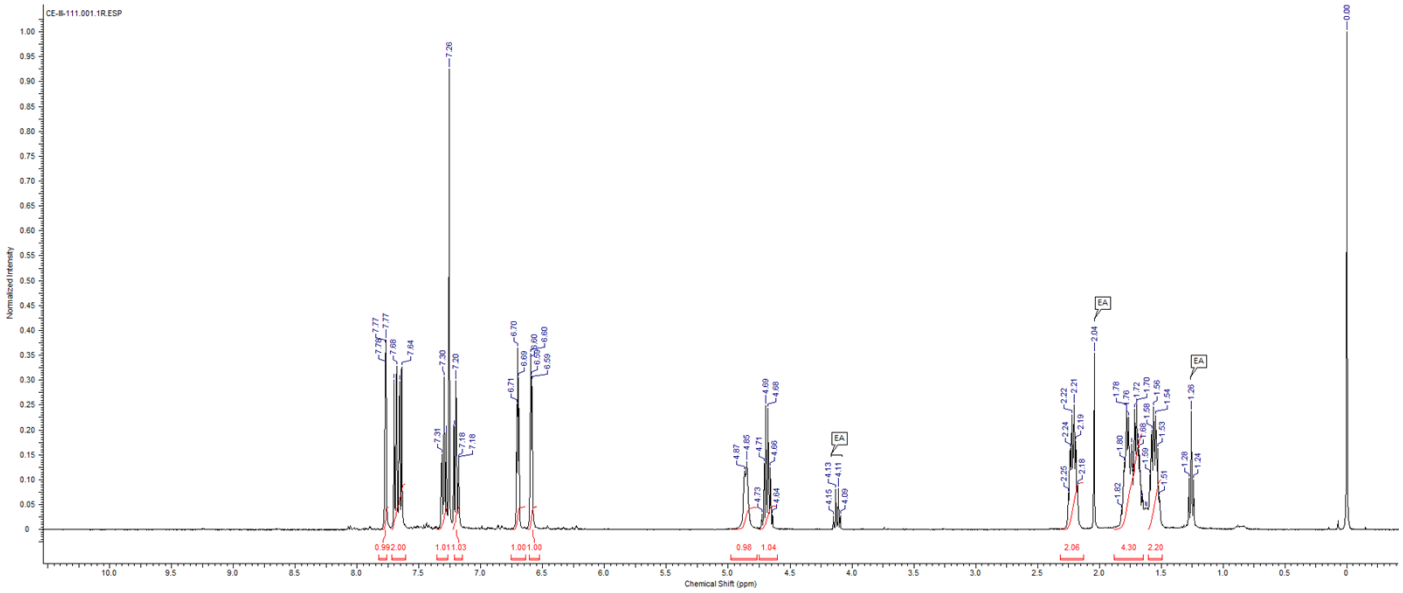


Figure S23. (a) ^{1}H NMR (400 MHz, $CDCl_3$) and (b) ^{13}C NMR (101 MHz, $CDCl_3$) spectra of **3p**



(a)



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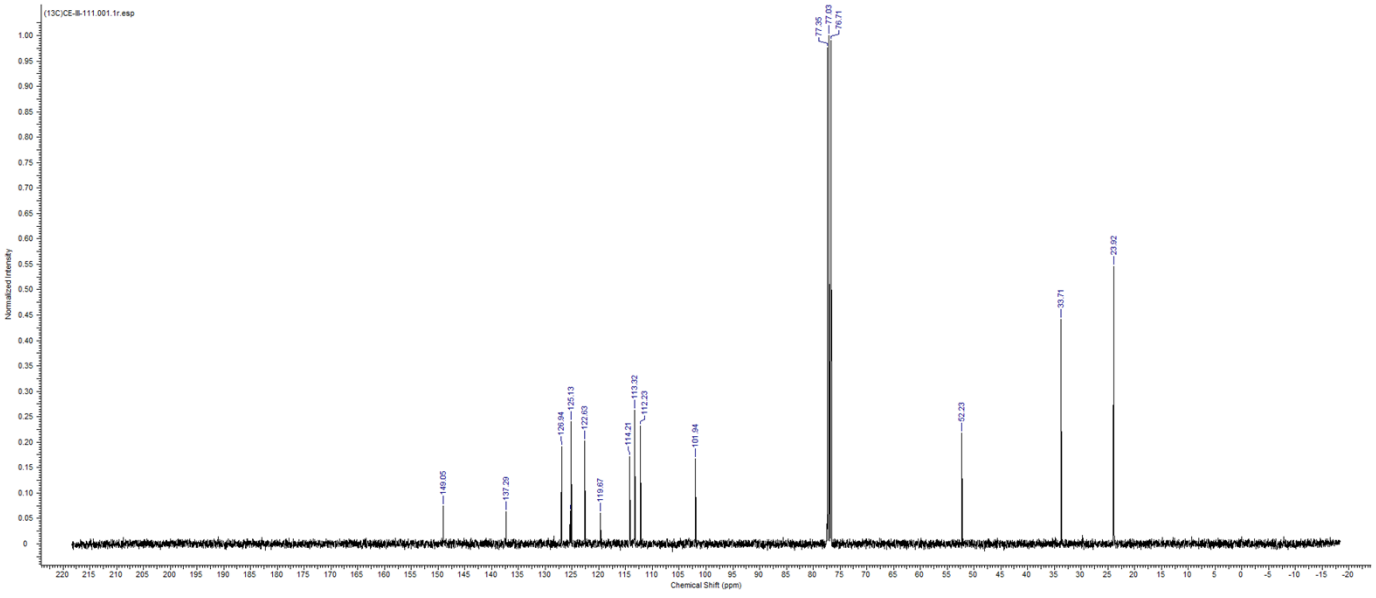
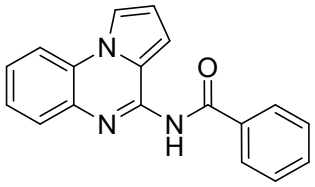
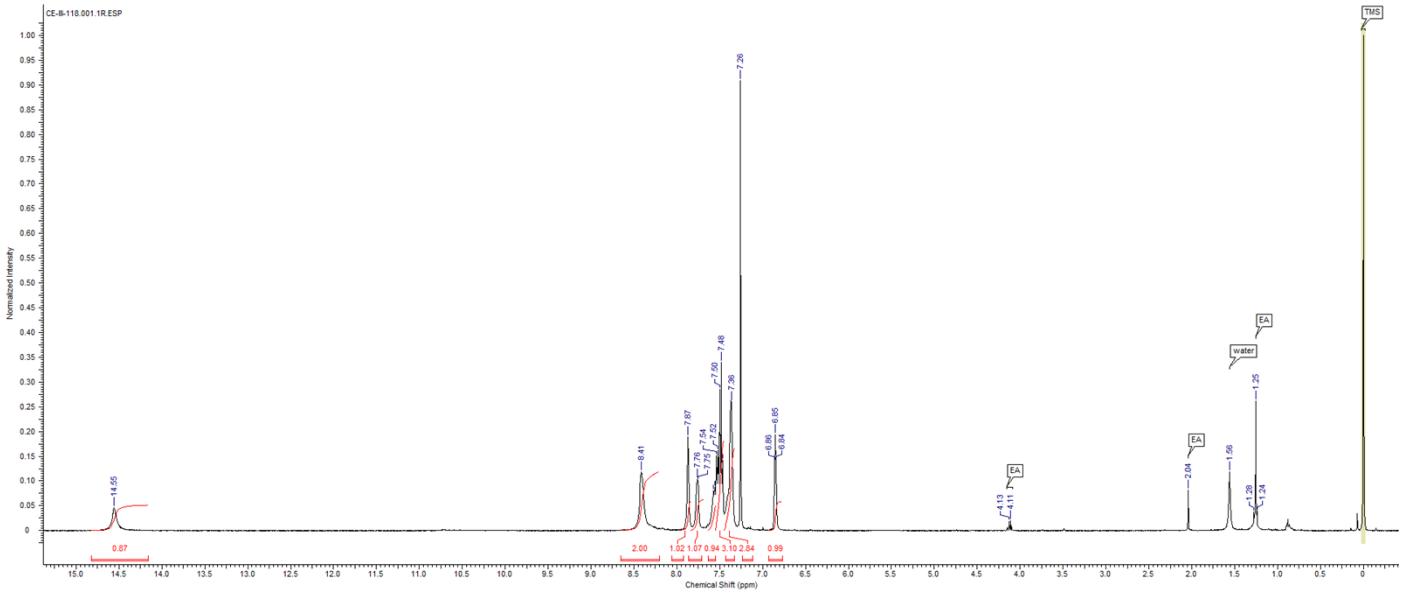


Figure S24. (a) ^{1}H NMR (400 MHz, $CDCl_3$) and (b) ^{13}C NMR (101 MHz, $CDCl_3$) spectra of **3q**



(a)



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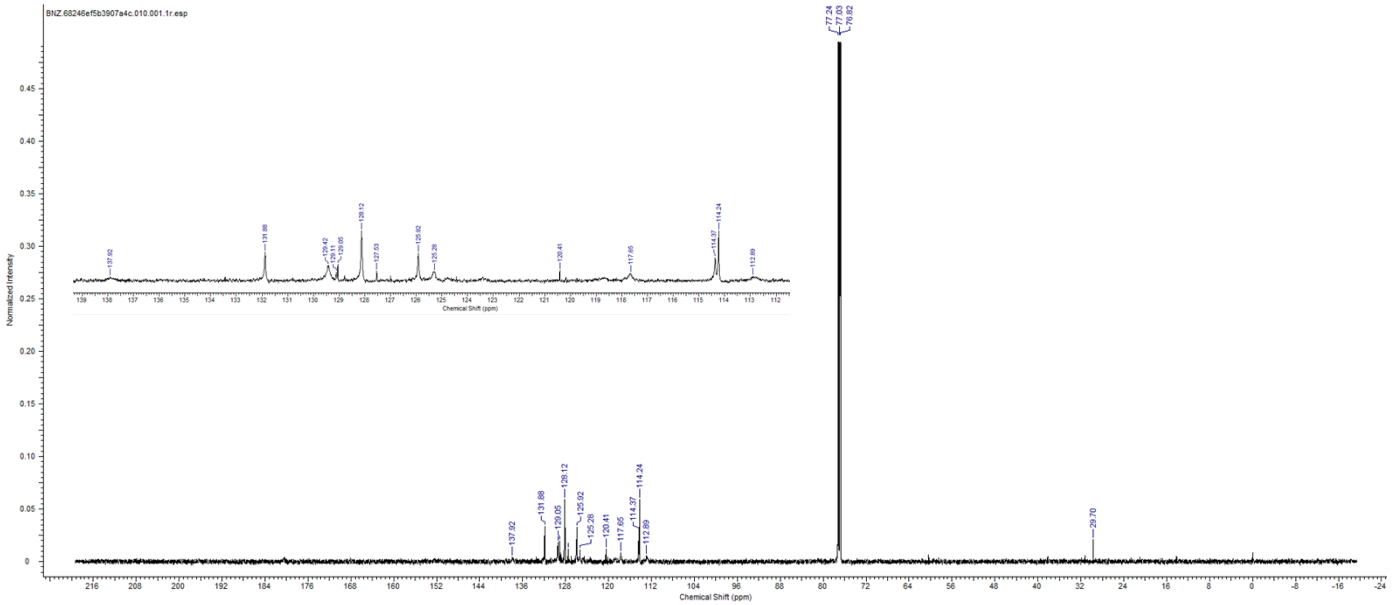
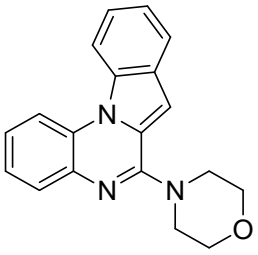
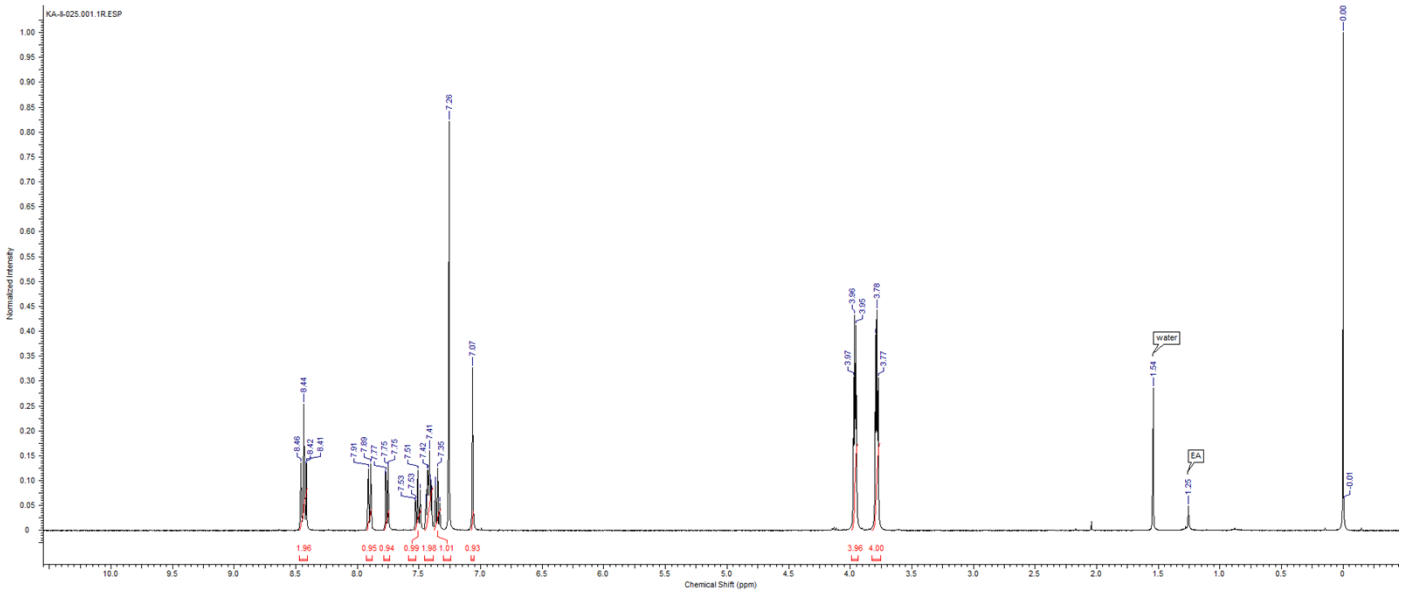


Figure S25. (a) ^{1}H NMR (400 MHz, $CDCl_3$) and (b) ^{13}C NMR (150 MHz, $CDCl_3$) spectra of **3r**



(a)



(b)

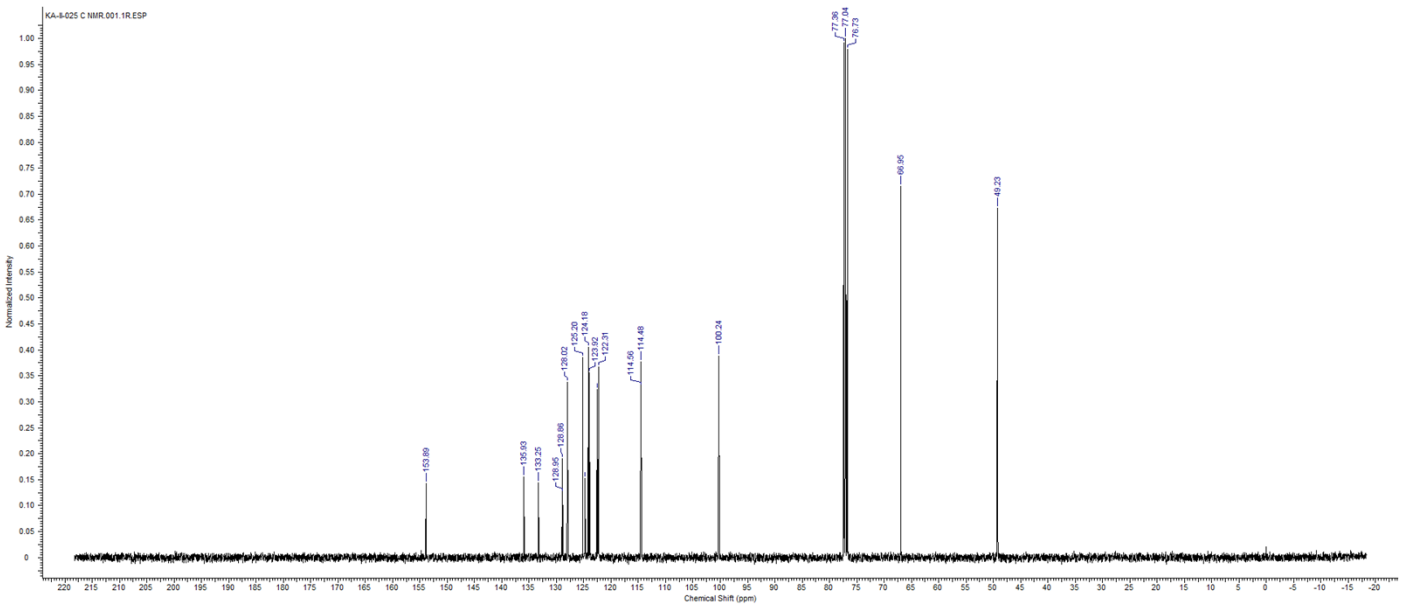
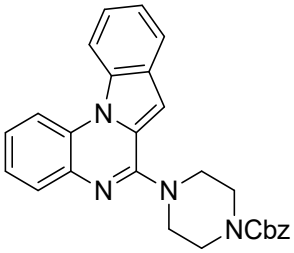
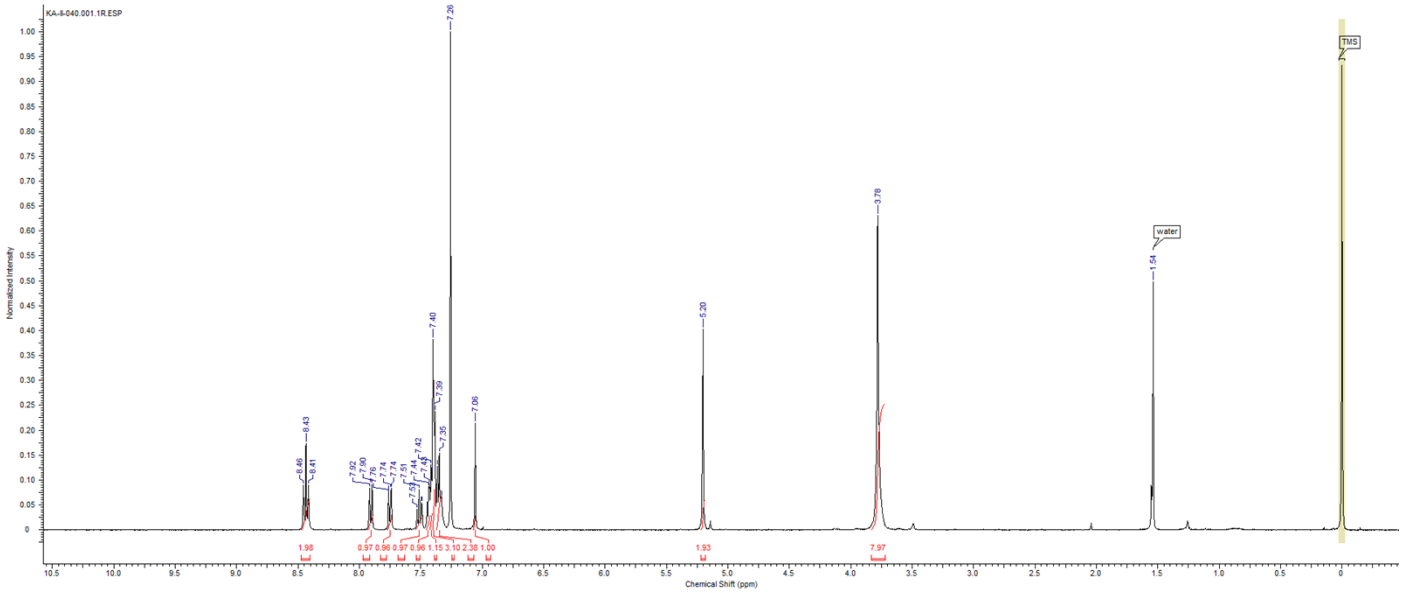


Figure S26. (a) ^{1}H NMR (400 MHz, $CDCl_3$) and (b) ^{13}C NMR (101 MHz, $CDCl_3$) spectra of **5a**



(a)



(b)

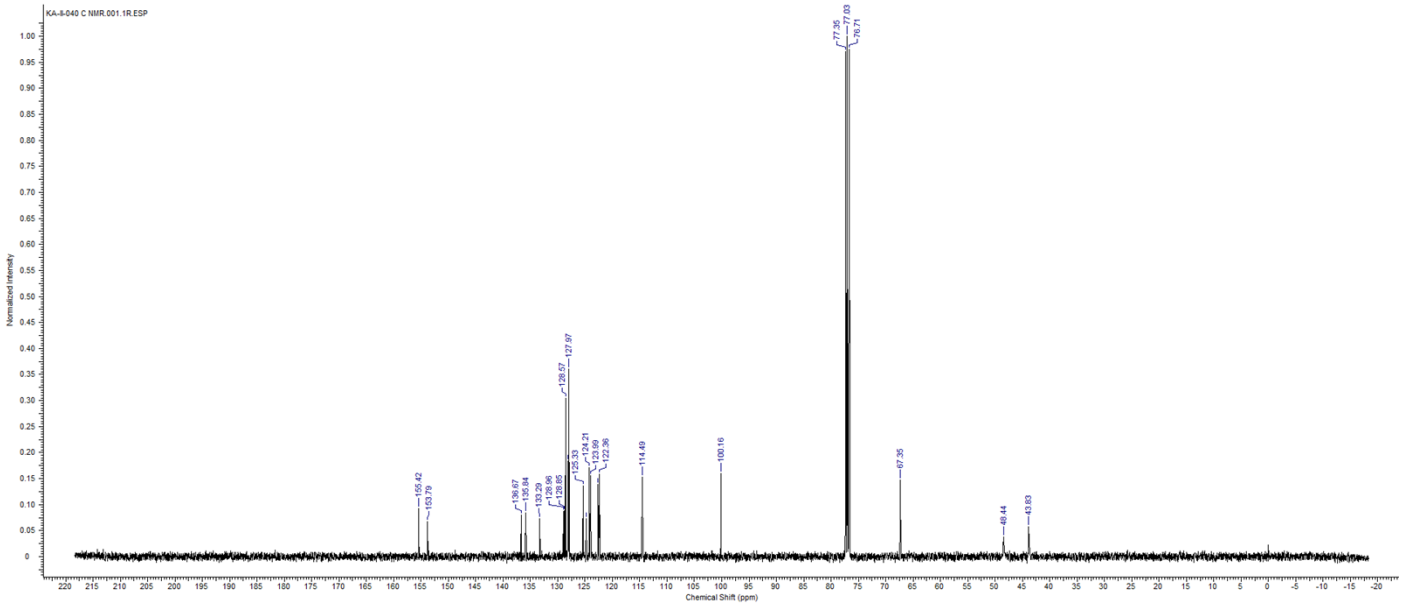
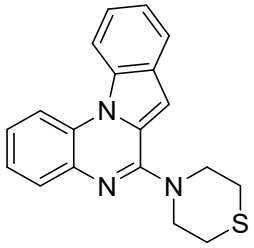
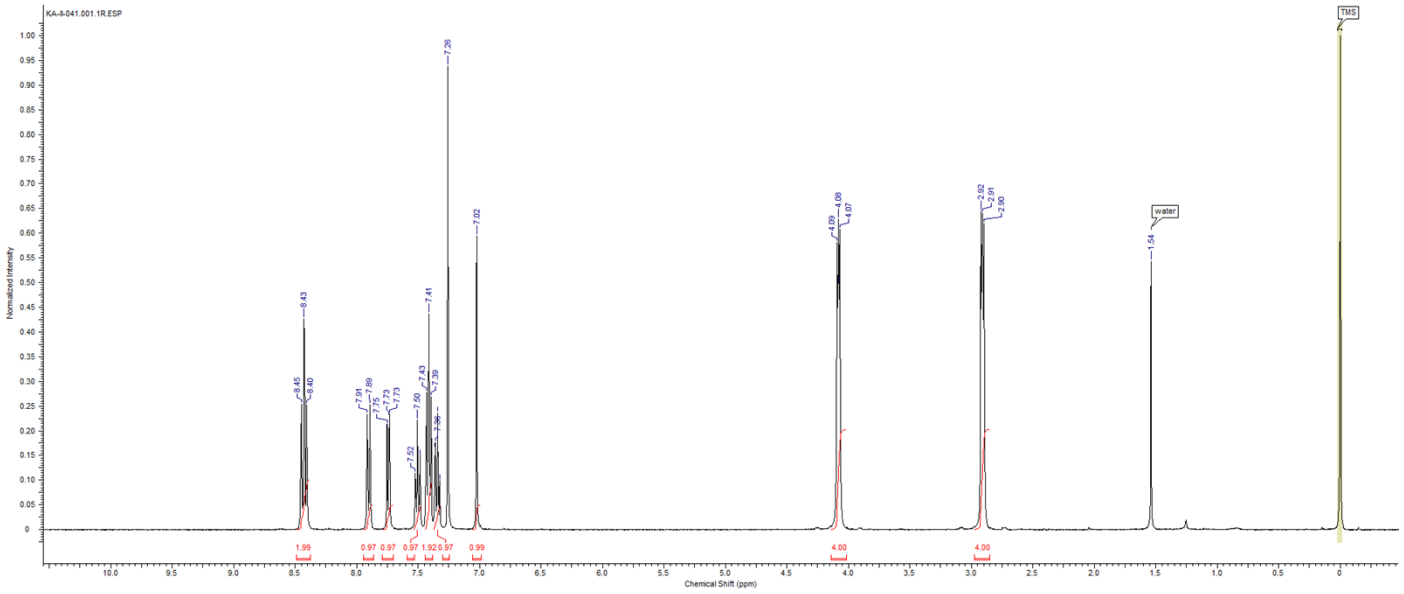


Figure S27. (a) ^{1}H NMR (400 MHz, $CDCl_3$) and (b) ^{13}C NMR (101 MHz, $CDCl_3$) spectra of **5b**



(a)



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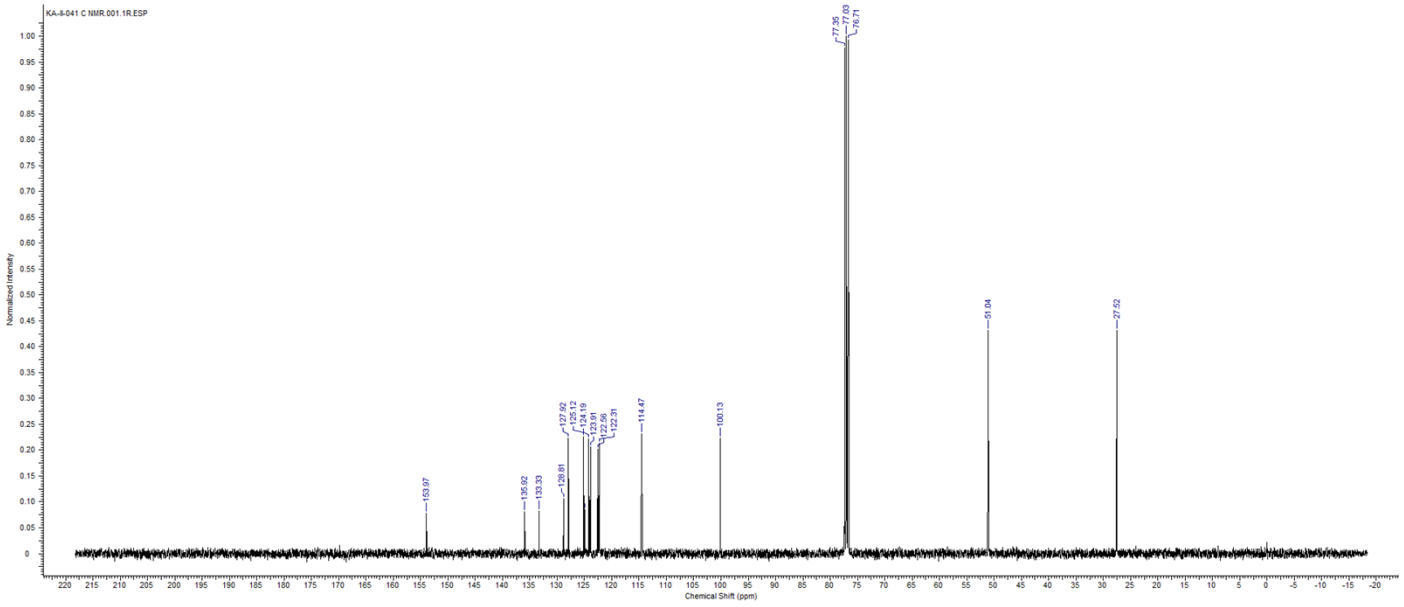
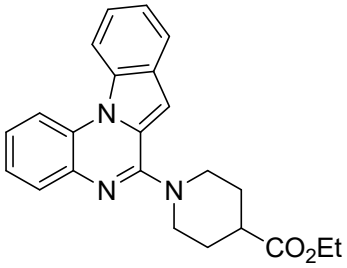
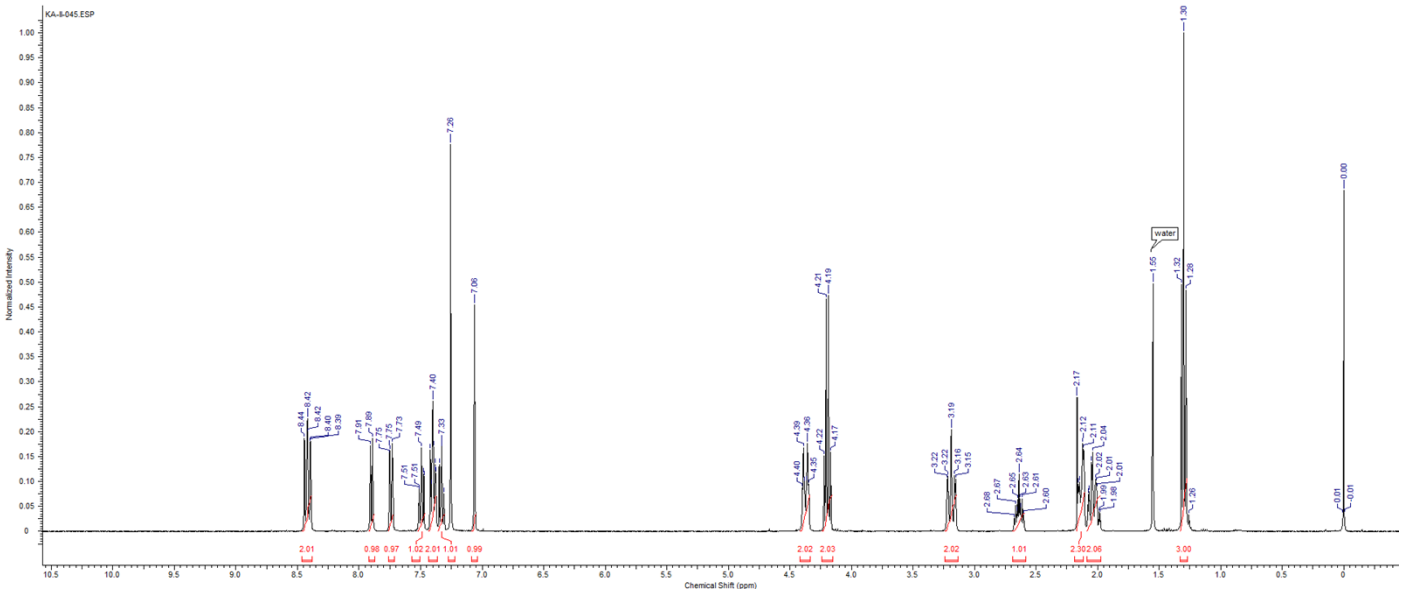


Figure S28. (a) ^{1}H NMR (400 MHz, $CDCl_3$) and (b) ^{13}C NMR (101 MHz, $CDCl_3$) spectra of **5c**



(a)



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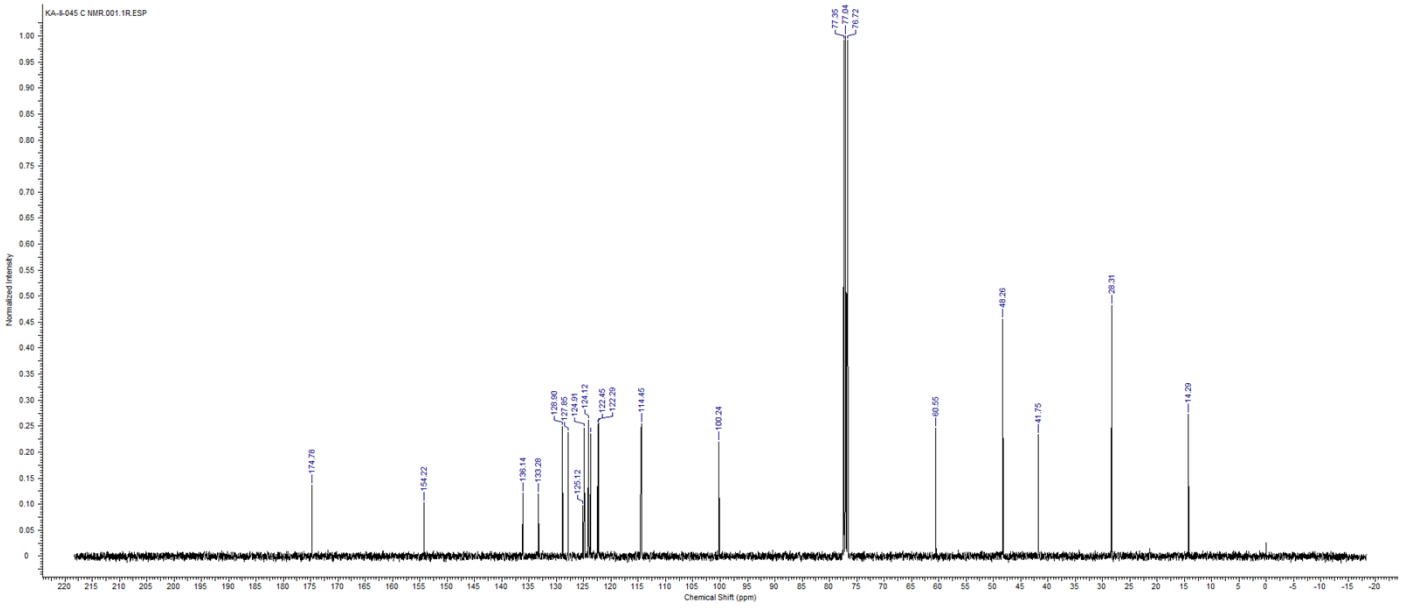
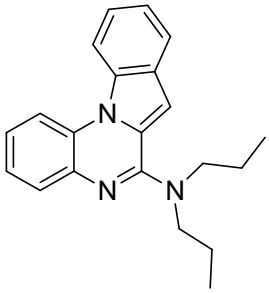
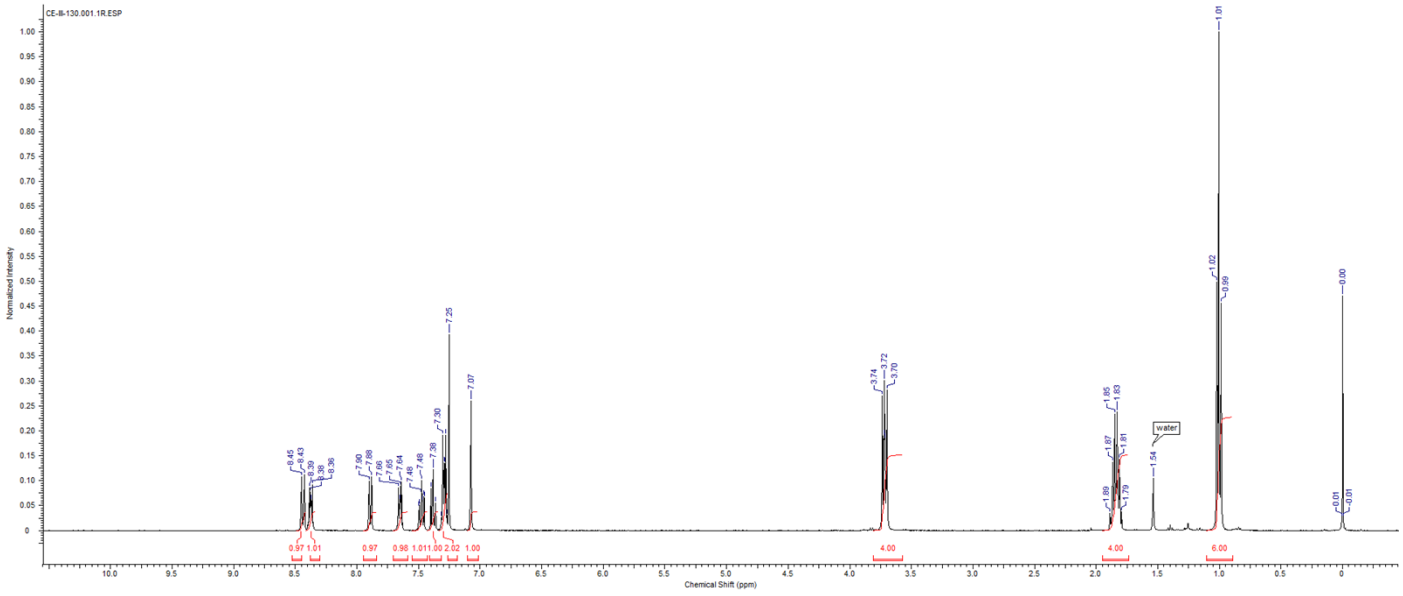


Figure S29. (a) ^{1}H NMR (400 MHz, $CDCl_3$) and (b) ^{13}C NMR (101 MHz, $CDCl_3$) spectra of **5d**



(a)



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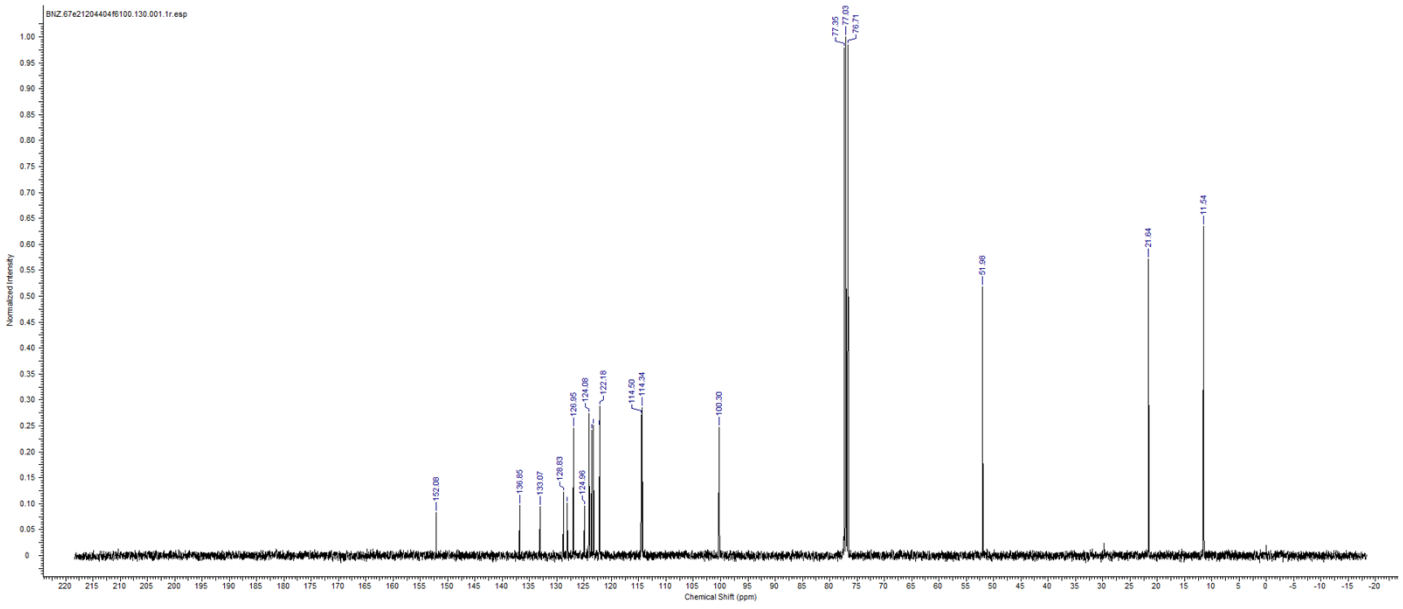
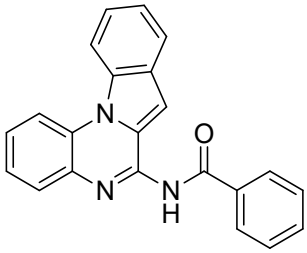
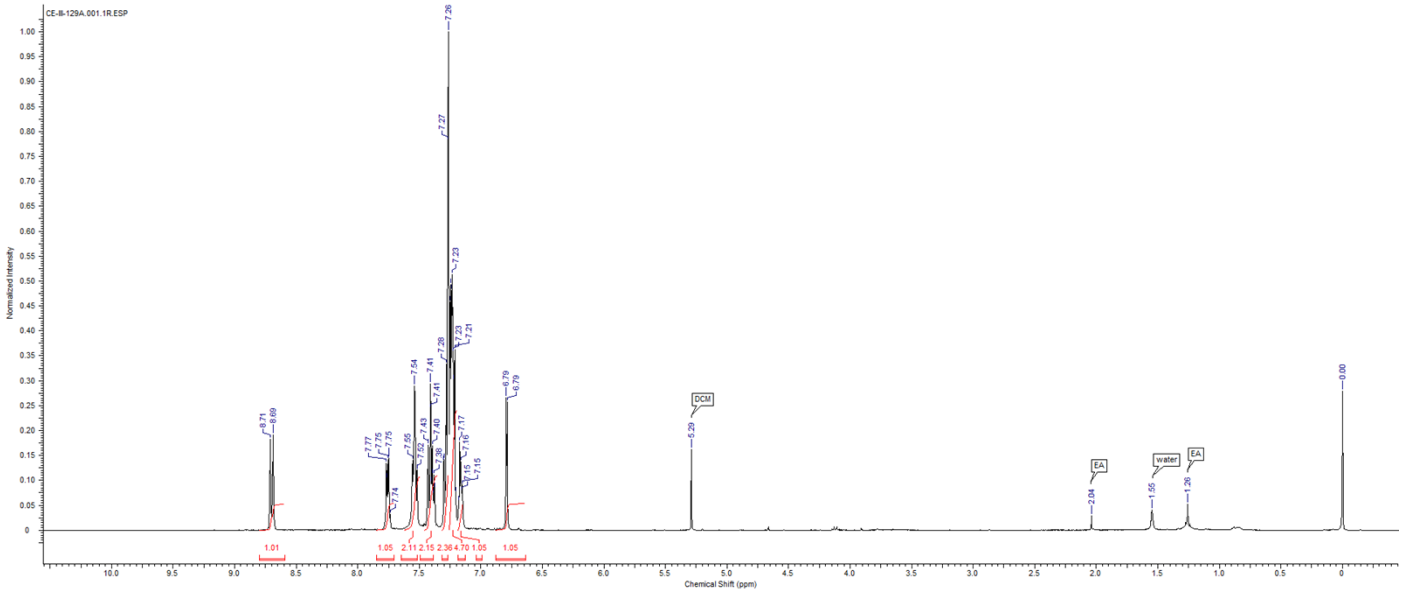


Figure S30. (a) ^{1}H NMR (400 MHz, $CDCl_3$) and (b) ^{13}C NMR (101 MHz, $CDCl_3$) spectra of **5e**



(a)



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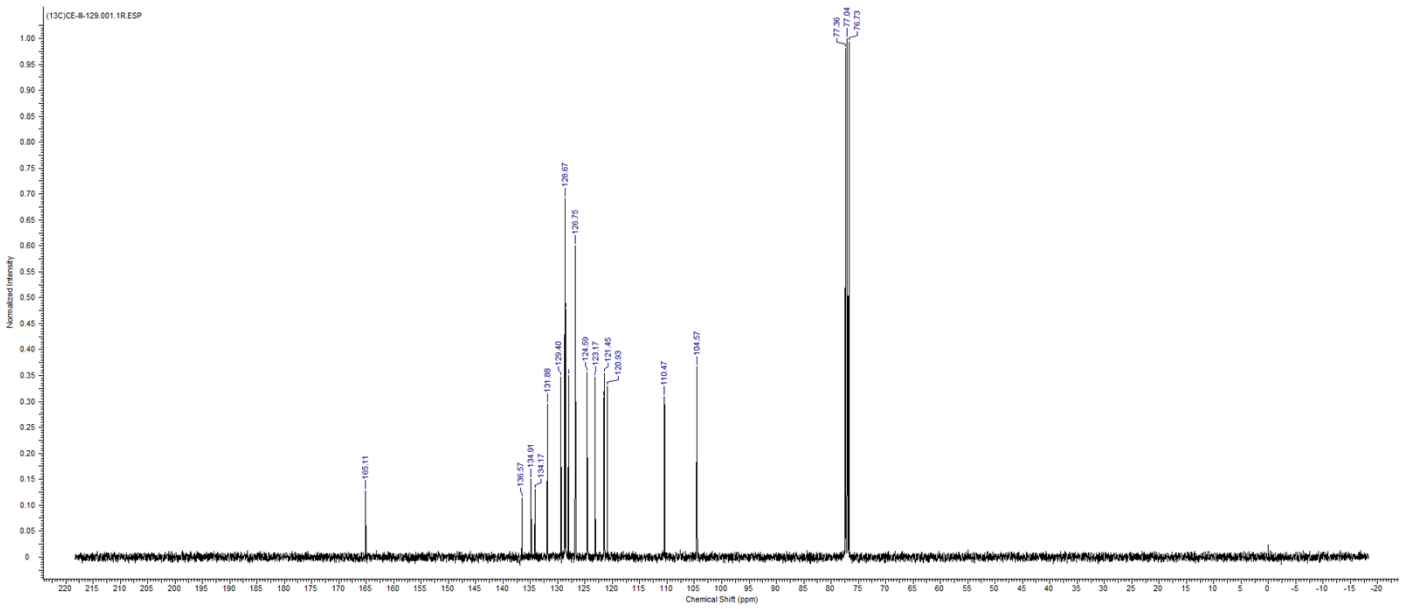
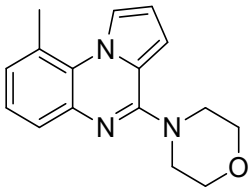
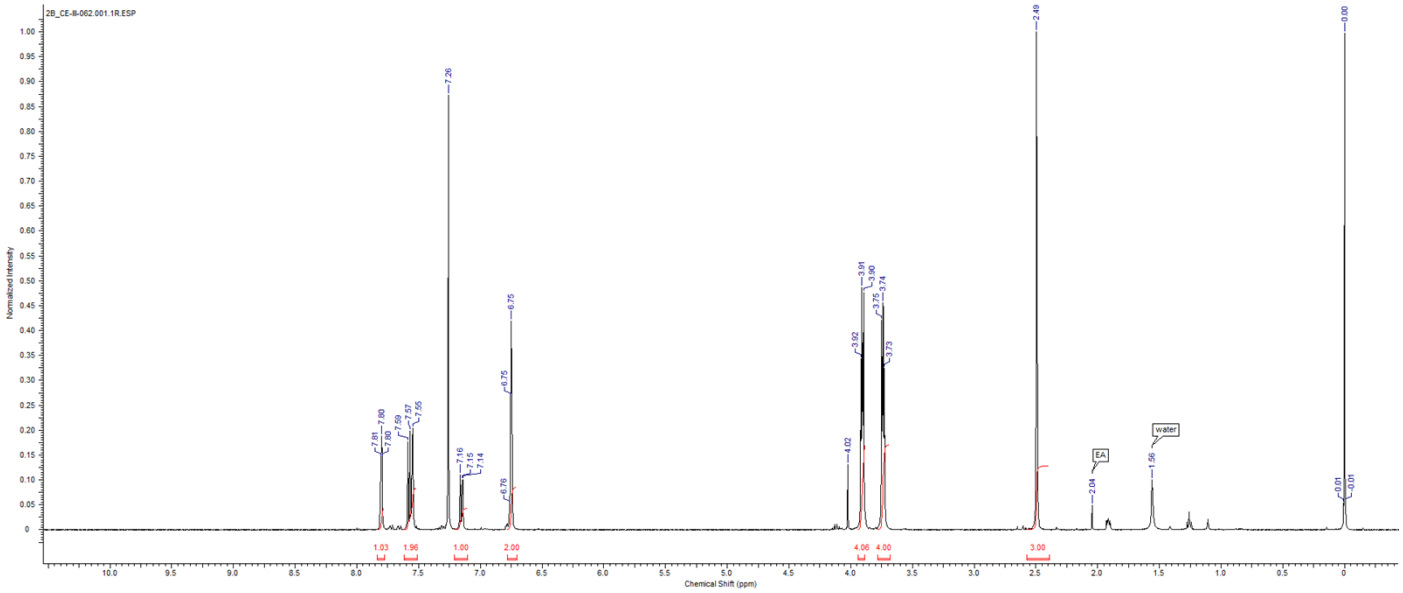


Figure S31. (a) ^{1}H NMR (400 MHz, $CDCl_3$) and (b) ^{13}C NMR (101 MHz, $CDCl_3$) spectra of **5f**



(a)



(b)

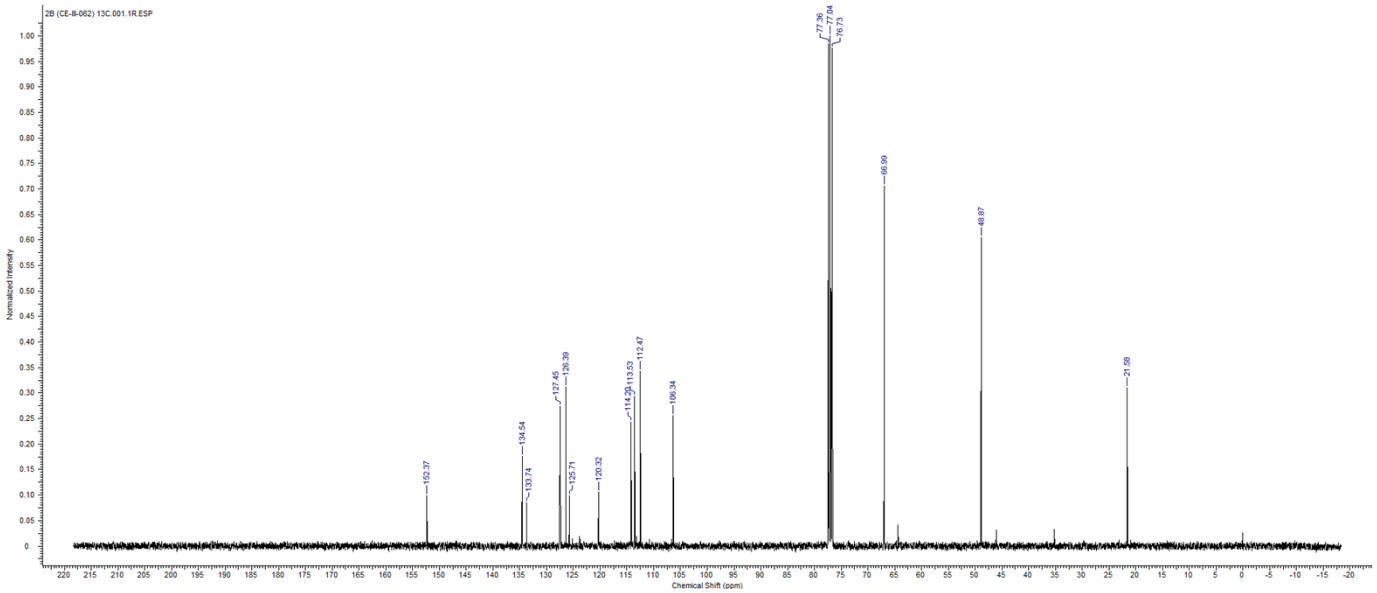
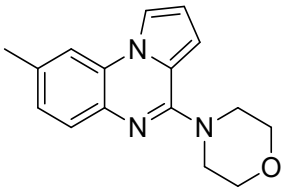
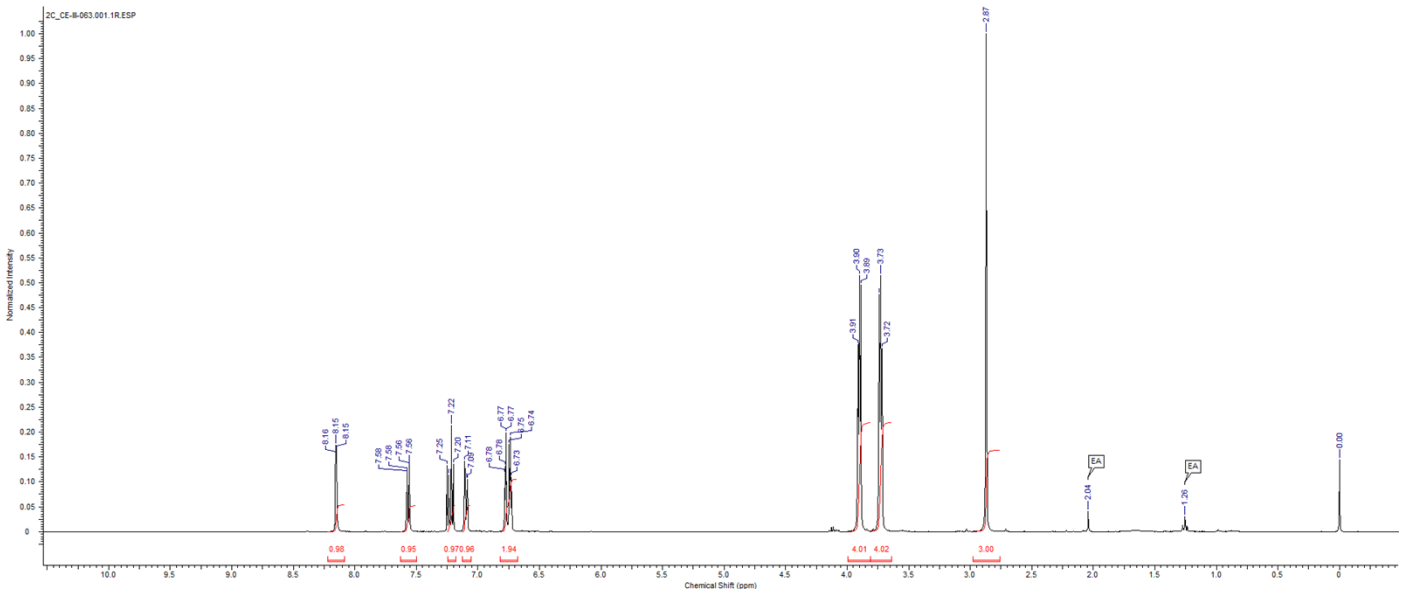


Figure S32. (a) ^{1}H NMR (400 MHz, $CDCl_3$) and (b) ^{13}C NMR (101 MHz, $CDCl_3$) spectra of **6b**



(a)



(b)

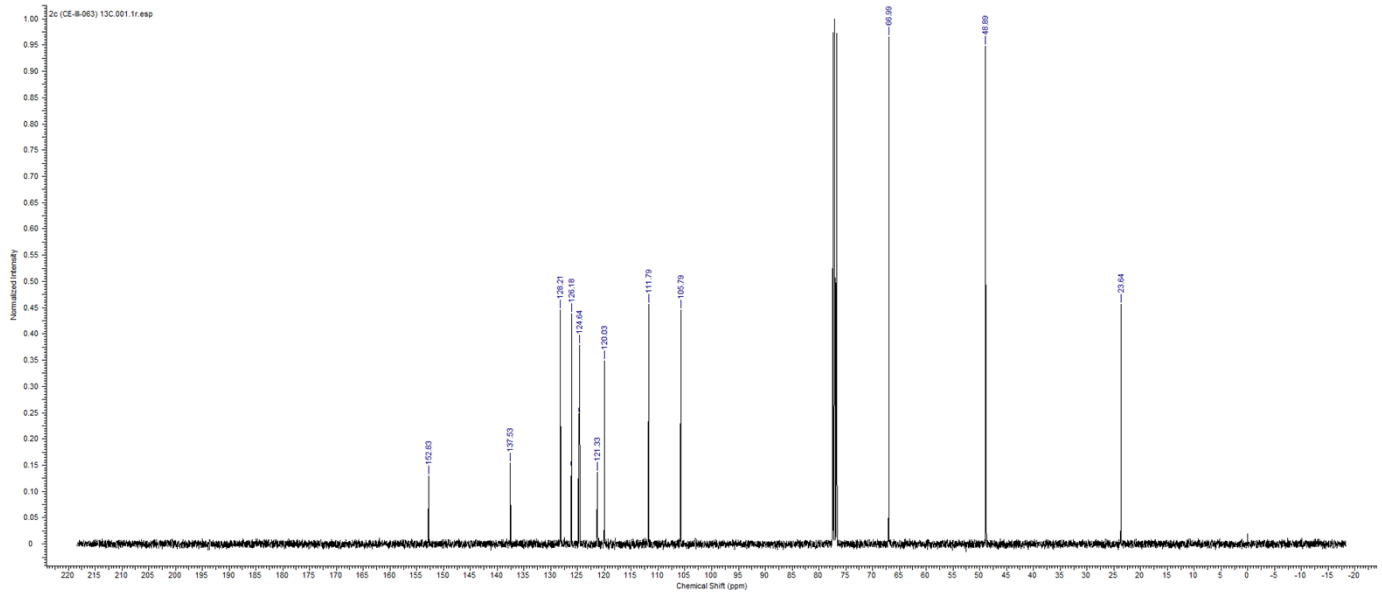
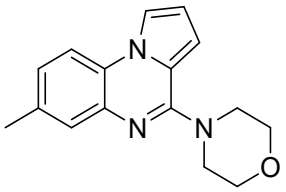
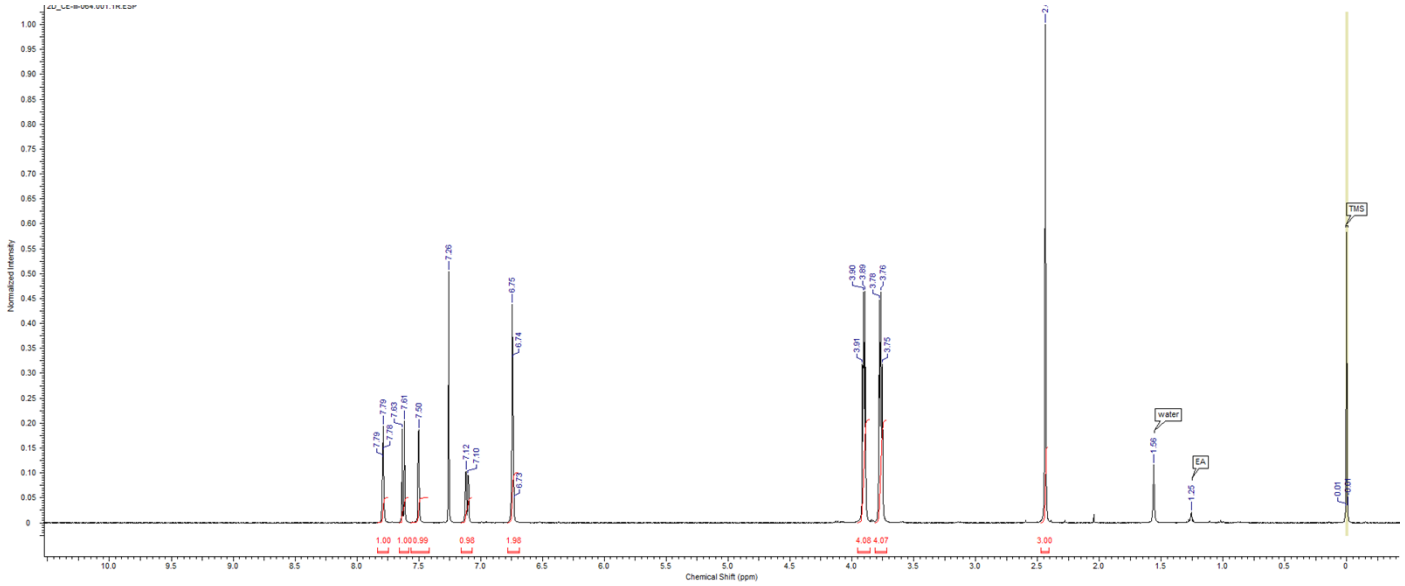


Figure S33. (a) ^{1}H NMR (400 MHz, $CDCl_3$) and (b) ^{13}C NMR (101 MHz, $CDCl_3$) spectra of **6c**



(a)



(b)

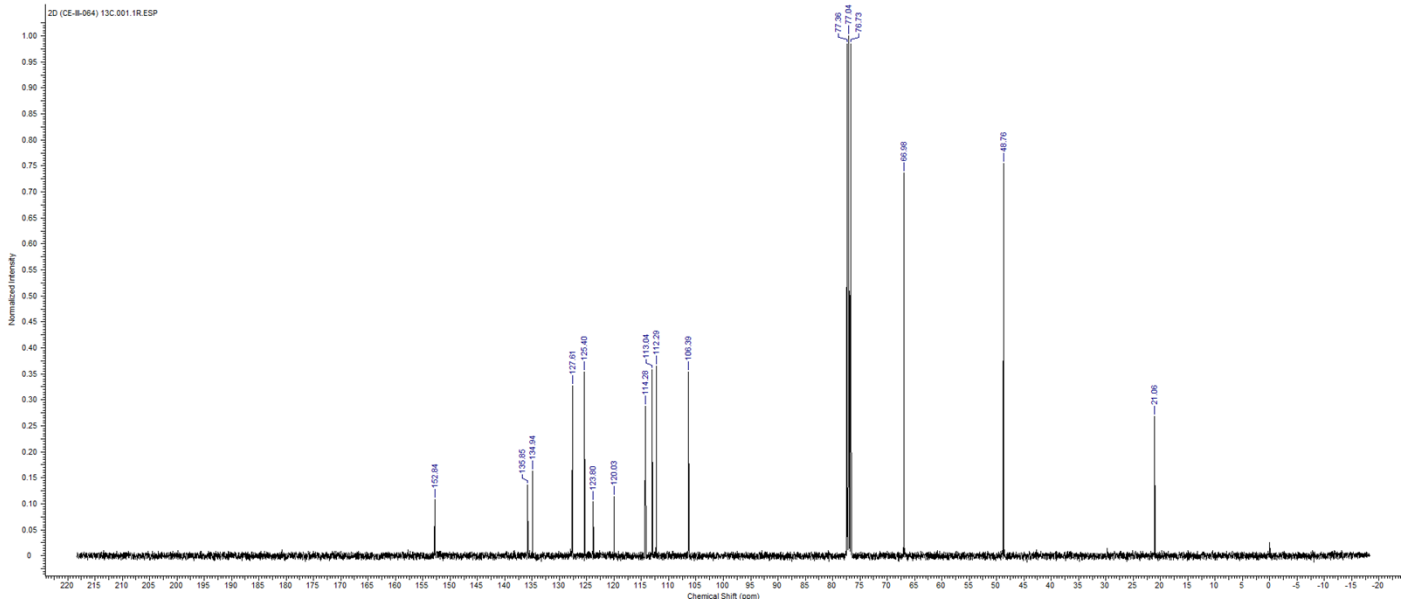
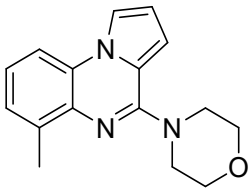
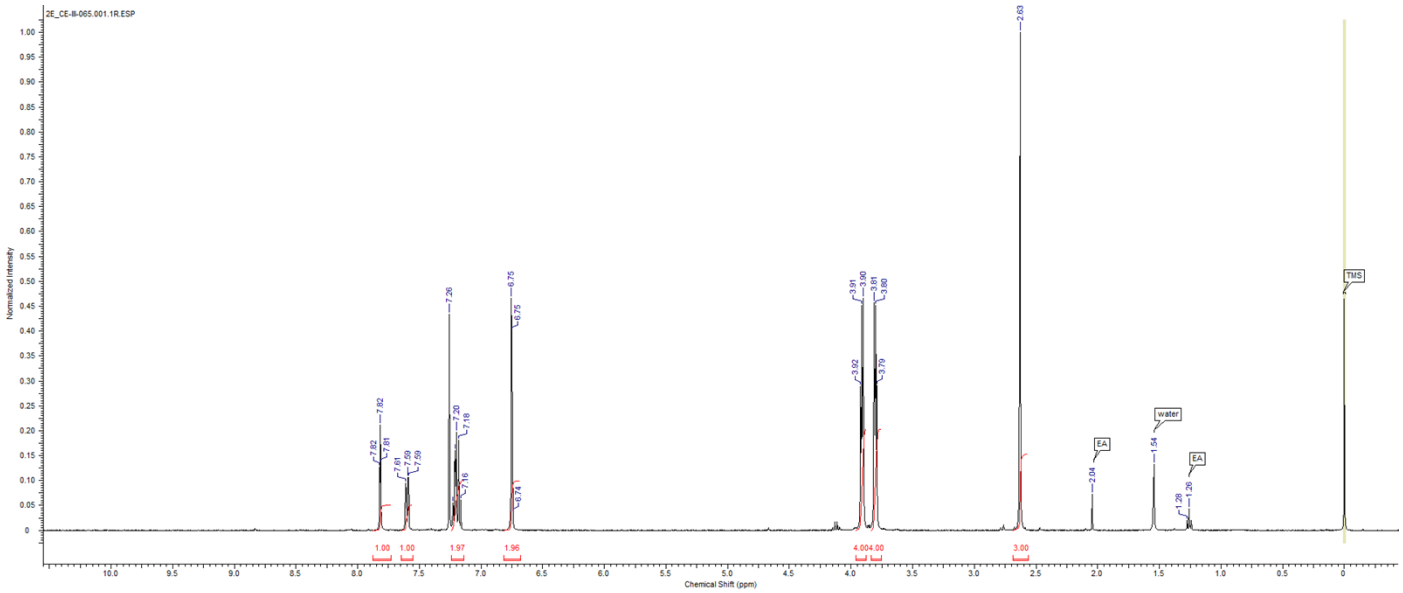


Figure S34. (a) ^{1}H NMR (400 MHz, $CDCl_3$) and (b) ^{13}C NMR (101 MHz, $CDCl_3$) spectra of **6d**



(a)



(b)

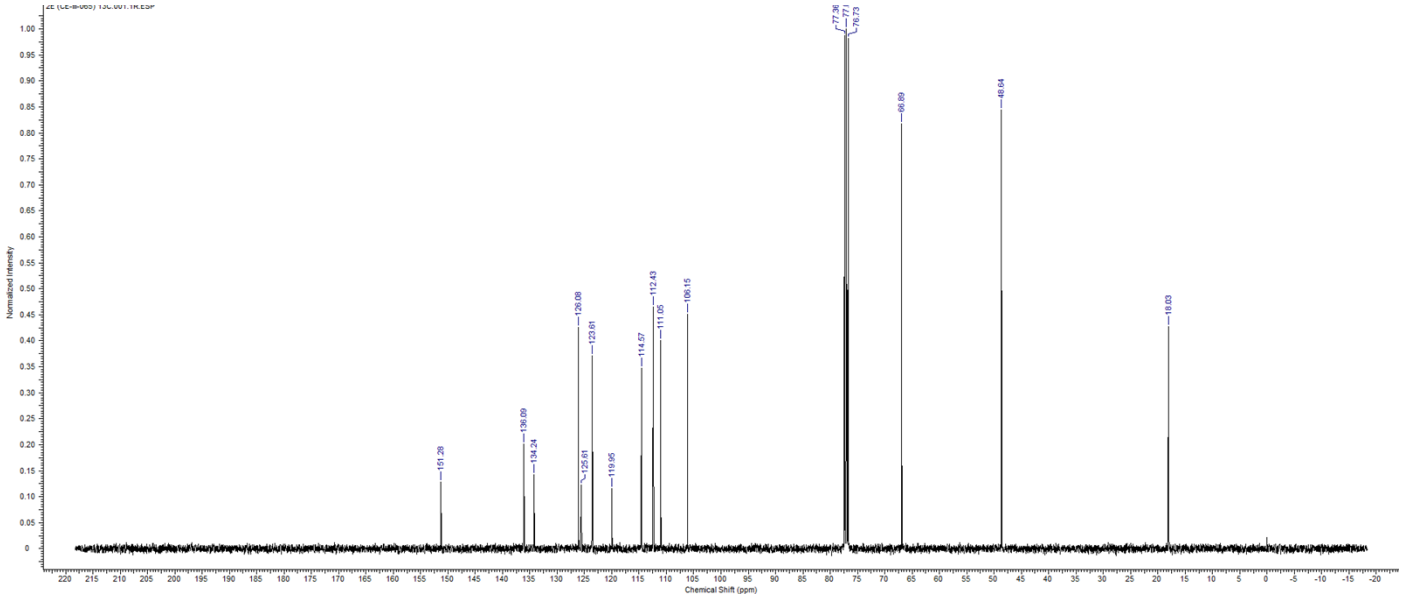
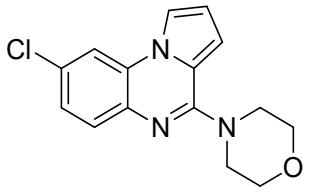
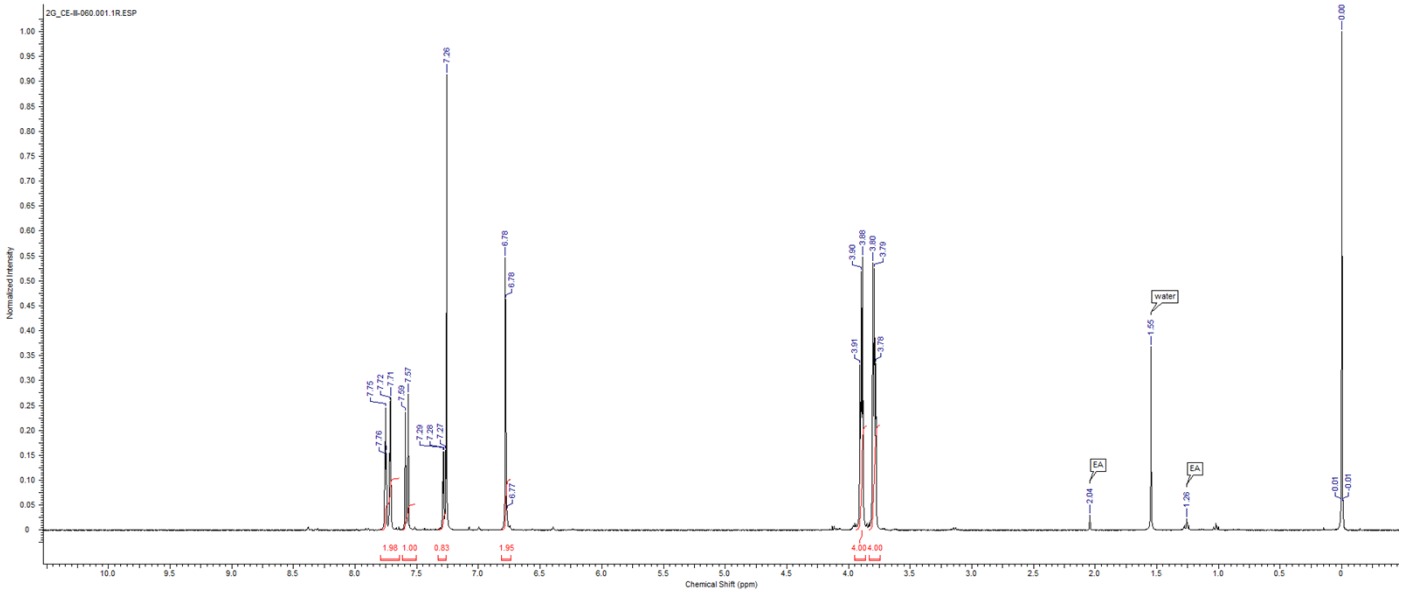


Figure S35. (a) ^{1}H NMR (400 MHz, $CDCl_3$) and (b) ^{13}C NMR (101 MHz, $CDCl_3$) spectra of **6e**



(a)



(b)

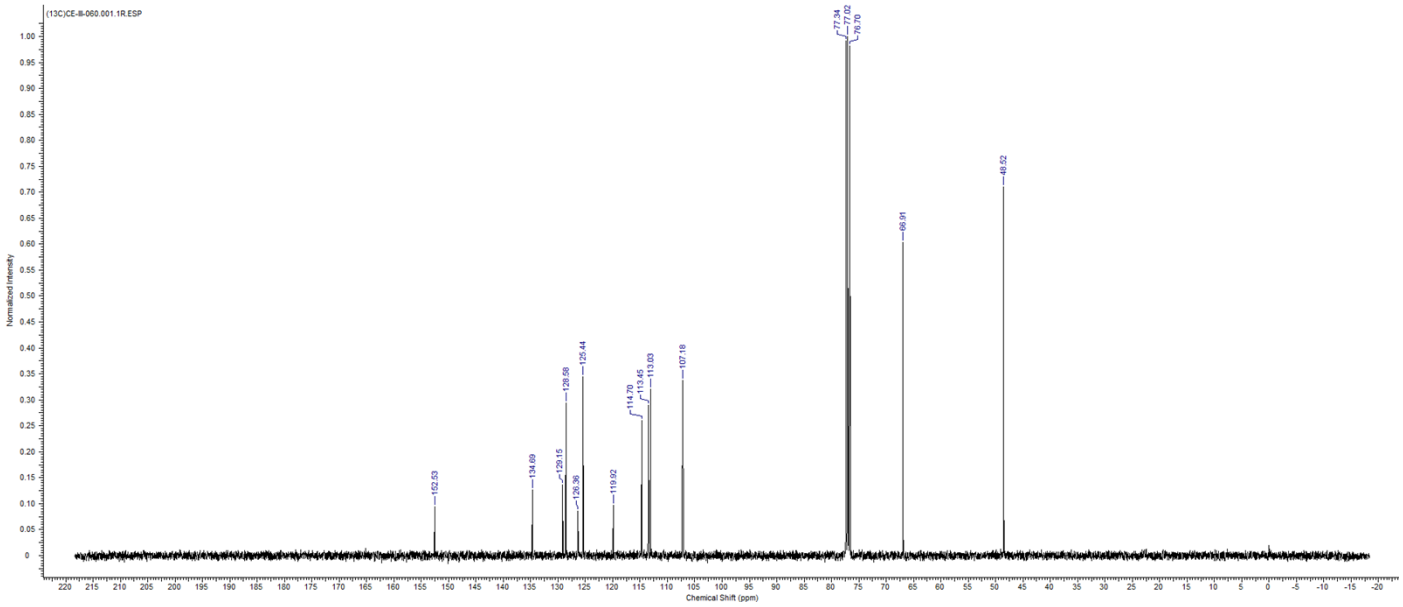
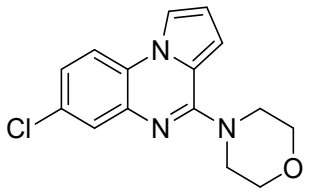
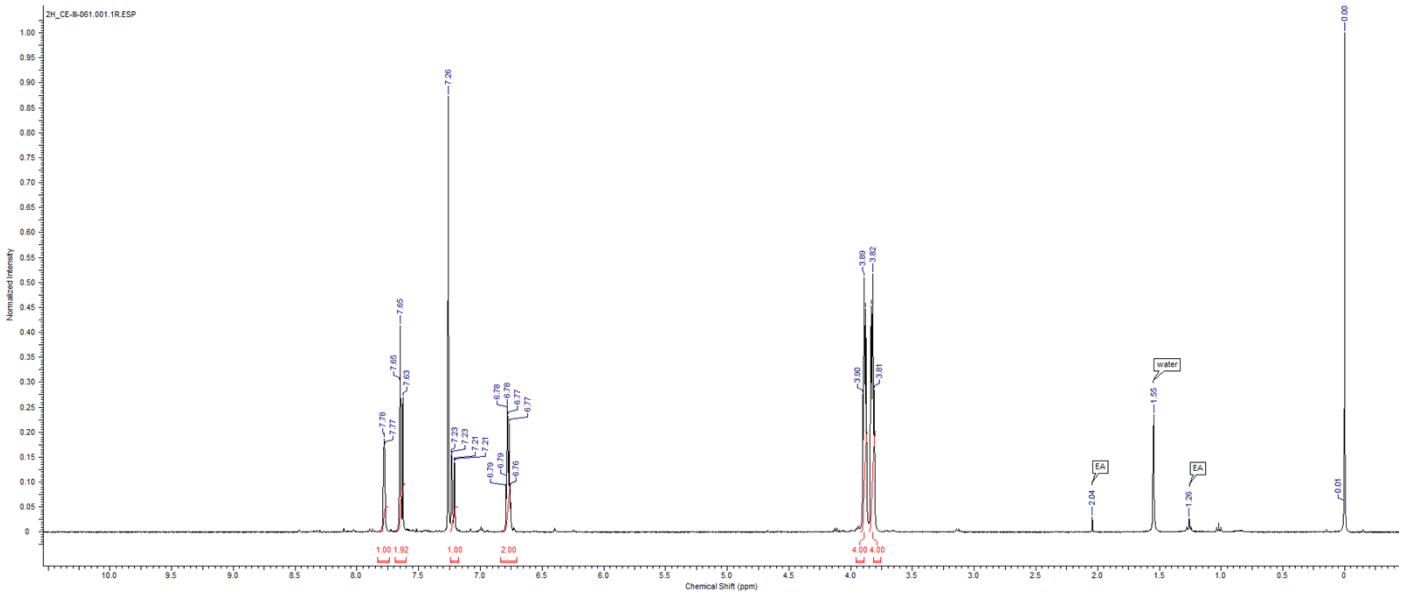


Figure S36. (a) ^{1}H NMR (400 MHz, $CDCl_3$) and (b) ^{13}C NMR (101 MHz, $CDCl_3$) spectra of **6f**



(a)



(b)

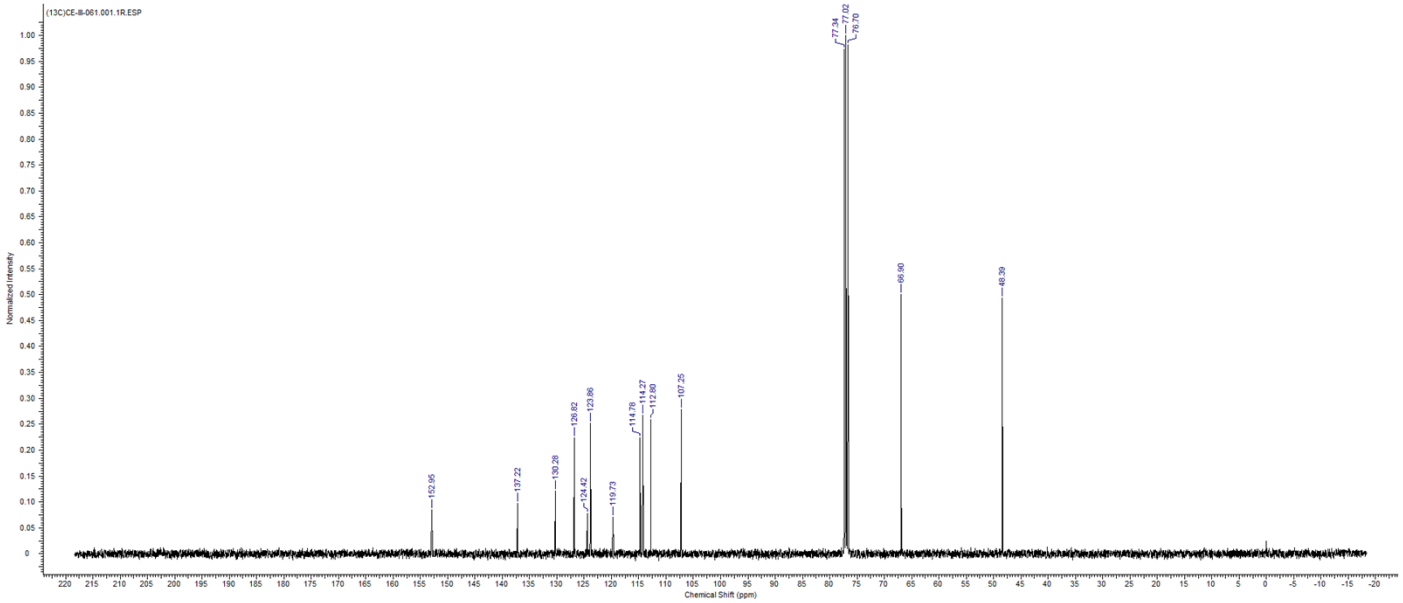
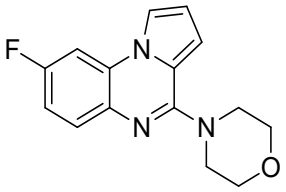
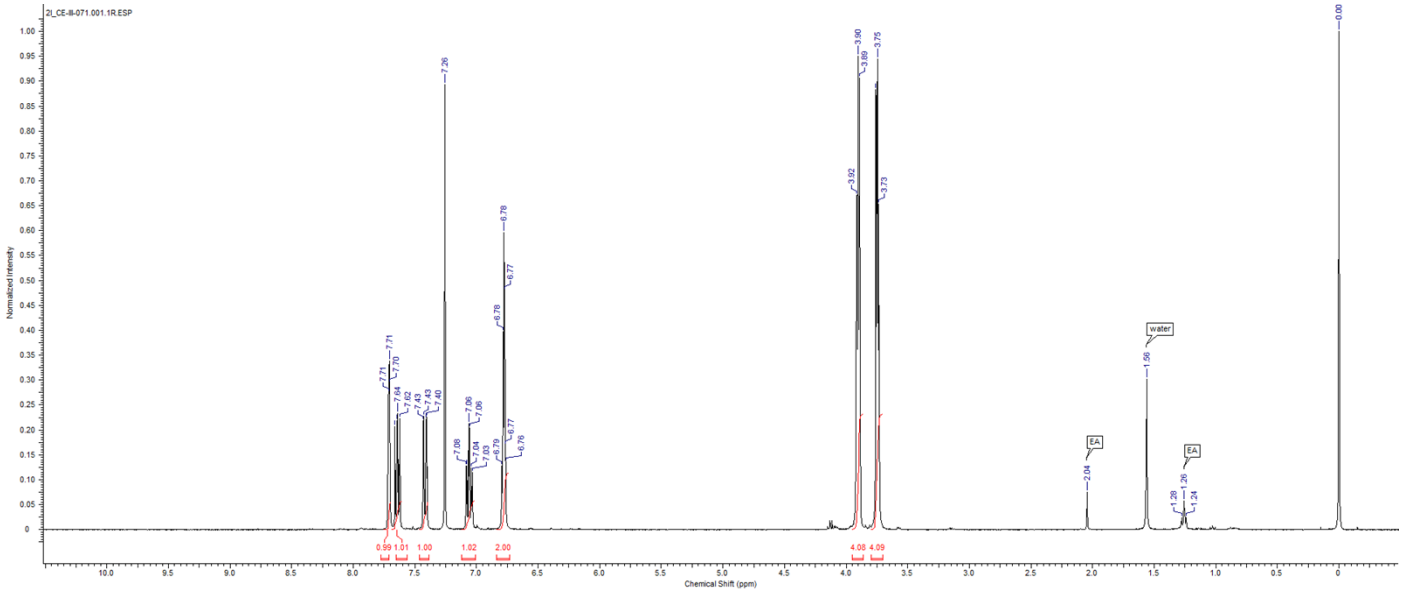


Figure S37. (a) ^{1}H NMR (400 MHz, $CDCl_3$) and (b) ^{13}C NMR (101 MHz, $CDCl_3$) spectra of **6g**



(a)



(b)

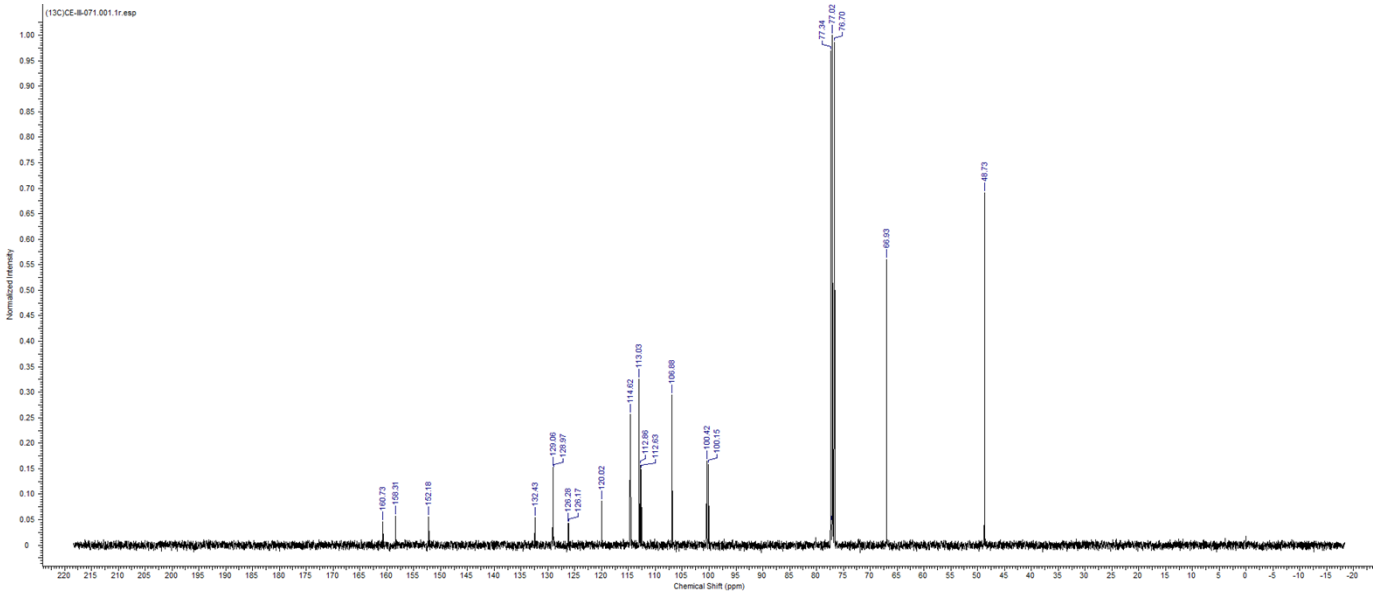
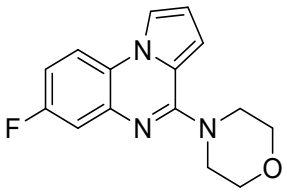
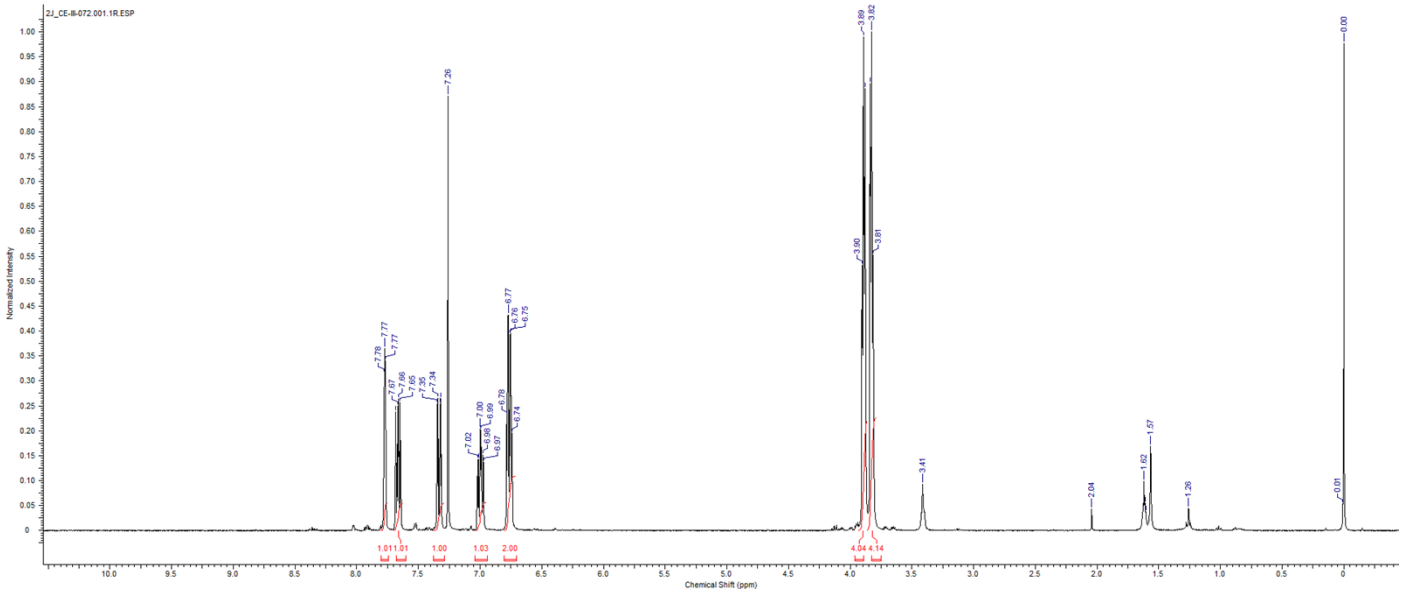


Figure S38. (a) ^{1}H NMR (400 MHz, $CDCl_3$) and (b) ^{13}C NMR (101 MHz, $CDCl_3$) spectra of **6h**



(a)



(b)

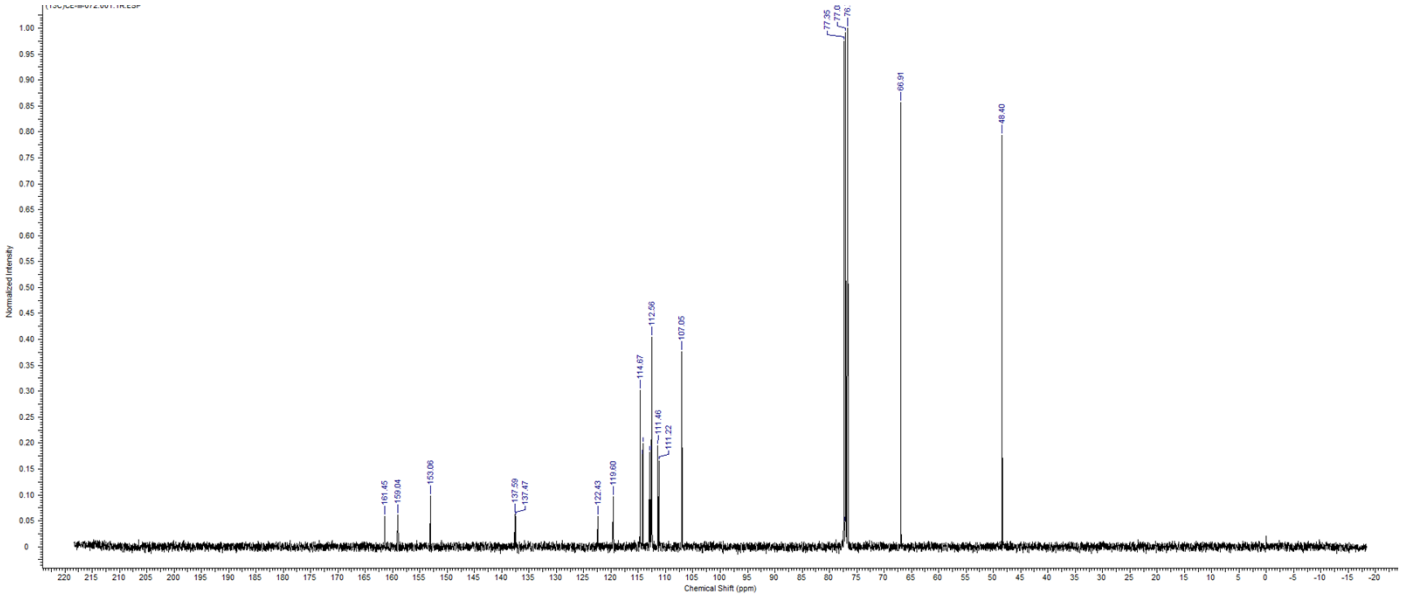
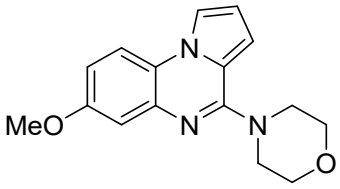
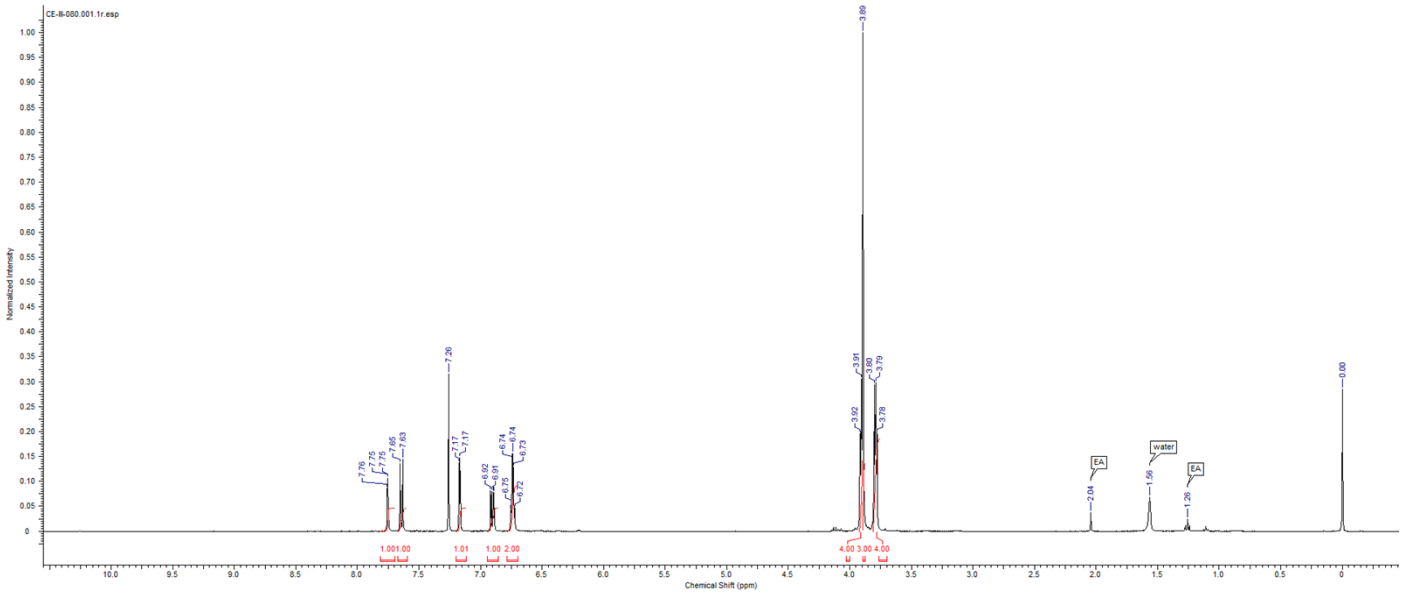


Figure S39. (a) ^{1}H NMR (400 MHz, $CDCl_3$) and (b) ^{13}C NMR (101 MHz, $CDCl_3$) spectra of **6i**



(a)



(b)

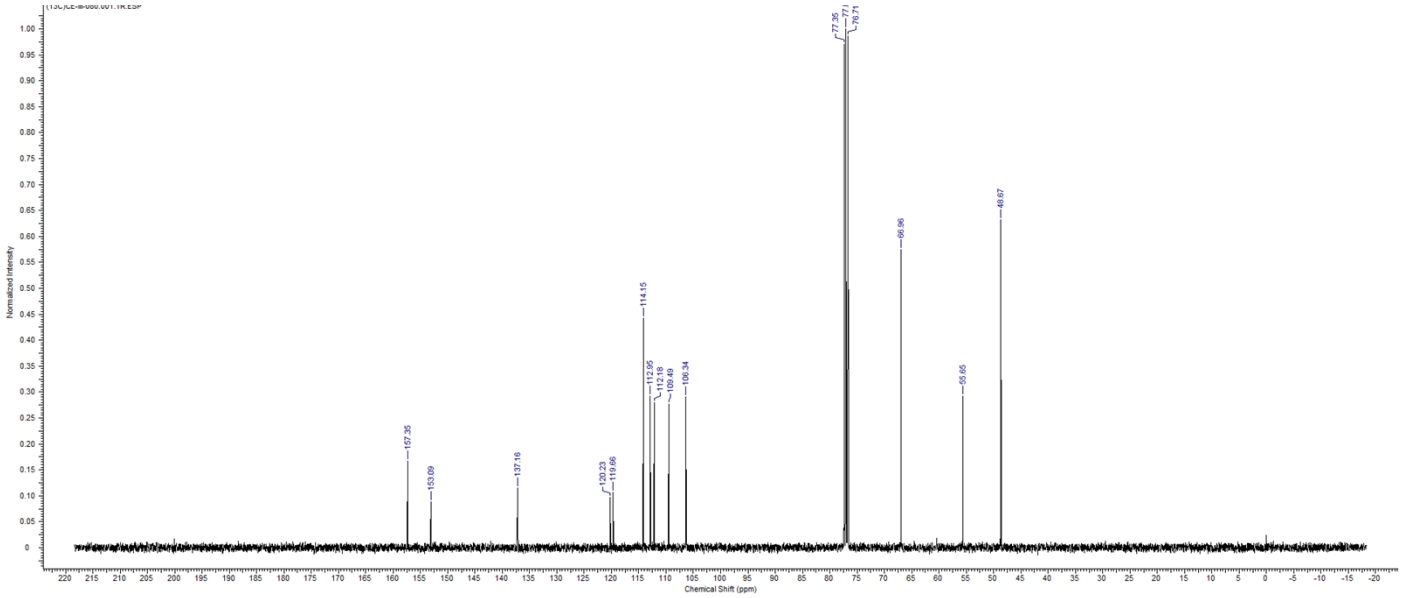
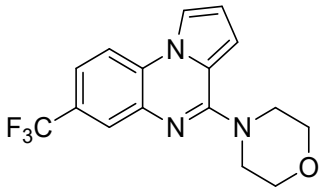
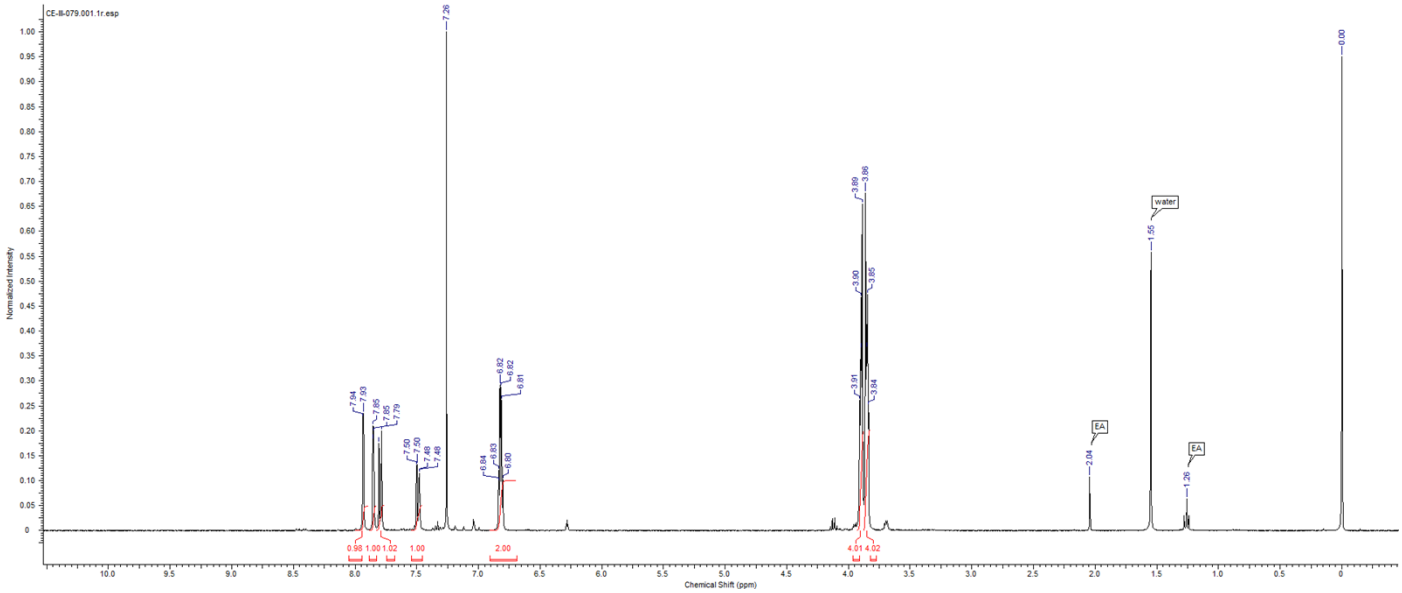


Figure S40. (a) ^{1}H NMR (400 MHz, $CDCl_3$) and (b) ^{13}C NMR (101 MHz, $CDCl_3$) spectra of **6j**



(a)



(b)

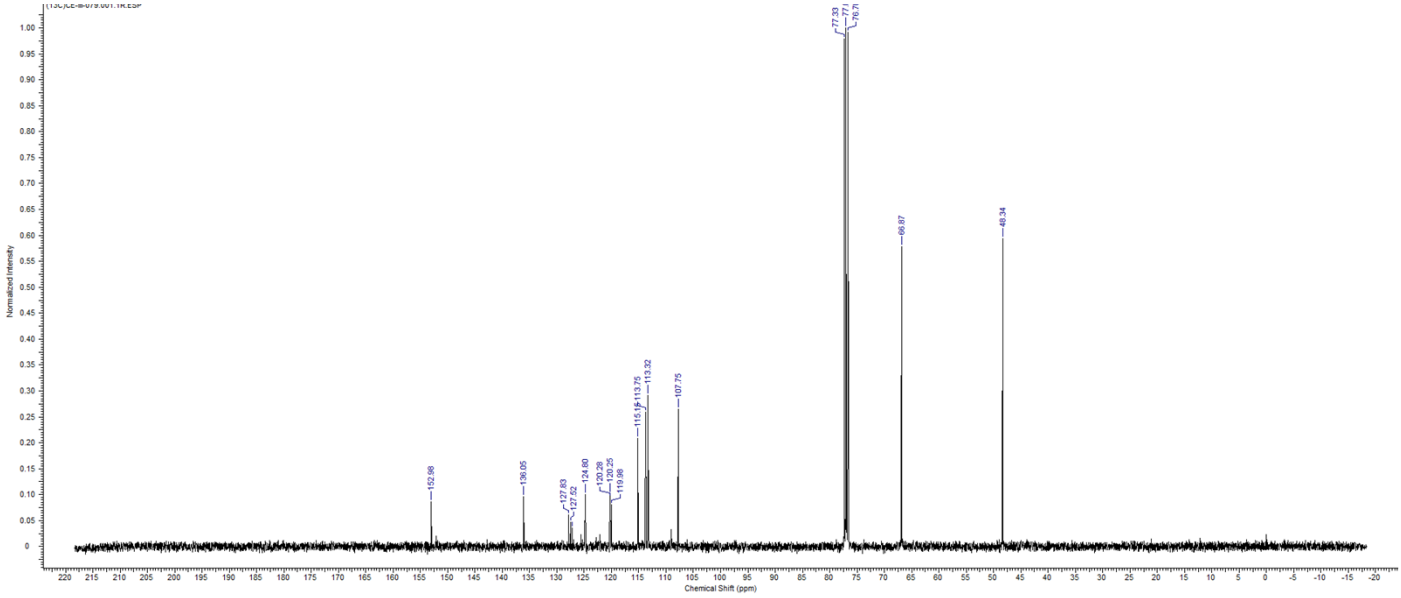


Figure S41. (a) ^{1}H NMR (400 MHz, $CDCl_3$) and (b) ^{13}C NMR (101 MHz, $CDCl_3$) spectra of **6k**