Appendix A. Supplementary data

Tuning the Sensitivity towards Mercury via Cooperative Binding to D-Fructose: Dual Fluorescent Chemosensor Based on 1,8-Naphthyridin-boronic Acid Derivative

E. Ramanjaneya Reddy and Marina Rajadurai*.

Dr. Reddy's Institute of Life Sciences, University of Hyderabad Campus, Gachibowli, Hyderabad 500046, Telangana, India.

Buffers and Samples Preparation for Fluorescence Studies

1. Buffer Preparation for Fluorescence Studies:

Fluorescence studies were performed using aqueous methanolic buffer (pH 8.20), which was prepared according to Perrin and Dempsey protocol:[1] 8 g of NaCl, 0.2 g of KCl, 1.44 g of Na_2HPO_4, 0.24 g of KH_2PO_4 were dissolved in 800 mL of distilled water and adjust pH by adding a solution of 5 M NaOH and finally make a total volume of 1 L with additional distilled water.

2. Sample Preparation for Fluorescence Binding Studies with Metal Ions:

A known amount of various metal ions (Hg^{2+}, Cu^{+1}, Ag^{+1}, Mg^{+2}, Pb^{+2}, Cd^{+2}, Hg^{+2}, Li^{+1} and Fe^{+3}) was added from 4.86×10^{-4} M stock solution to a solution of compound **1.1 (**30 μL of 10^{-3} M). The volume of the prepared solution was adjusted to 3mL with buffer to achieve final concentration 10 μM in respect to compound **1.1**. The fluorescence measurements were made for each solution.

3. Stoichiometry Determination Using Jobs Plot:

In Job method, solutions of Hg^{2+} and **1.1** with equal concentrations were prepared in MeOH/H_2O (v/v=1:1, 5 mM, pH 7.50), and mixed in different proportions maintaining a total volume of 3 mL and total concentration of 10 μM of the mixture. Then emission of these solutions was recorded, and a graph of the emission intensity (fixed at 408 nm) versus a mole fraction of compound **1.1** was plotted**.** The stoichiometry of the complex was determined by the point of the maximum emission intensity.

4. Sample Preparation for Fluorescence Binding Studies with D-Mono Saccharides:

A known amount of D-monosaccharides (D-glucose, D-galactose, D-mannose and D-fructose) was added from 0.3 M stock solution to a solution of compound **1.1** (30 μL of 10^{-3} M). The volume of the prepared solution was adjusted to 3mL with buffer to achieve final concentration 10 μM in respect to compound **1.1**. The fluorescence measurements were made for each solution and I/I_0 was plotted at 409, 410, 408 and 403 nm respectively.

5. Sample Preparation for Fluorescence Binding Studies of D-Fructose at Various pH Solutions:

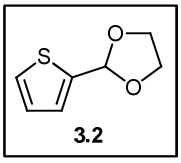
A known amount of D-fructose was added from 0.3 M stock solution to a solution of compound **1.1** (30 μL of 10^{-3} M). The volume of the prepared solution was adjusted to 3mL with buffer (pH 2, 3, 4, 5, 7.5, 9, 10, 11, 12 respectively) to achieve final concentration 10 μM in respect to compound **1.1**. The fluorescence measurements were made for each solution and I/I_0 was plotted at 403 nm.

6. Sample Preparation for Competitive Binding Studies of D-Monosaccharides and Hg^{2+}:

A known amount of D-monosaccharides (from 0.3 M stock solution), Hg^{2+} (from 4.86×10^{-4} M stock solution) and 30 μL of a 10^{-3} M of compound **1.1** was placed in 3mL buffer to give a final concentration of 10 μM. The fluorescence measurements were made for each solution.

Synthesis of the intermediates via Routes II-IV

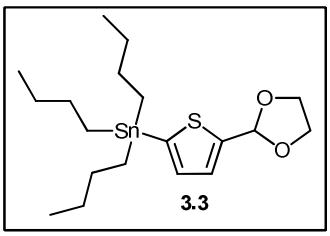
Route-II; Scheme 3a:



3.2

2-(Thiophen-2-yl)-1,3-dioxolane (3.2):[2]

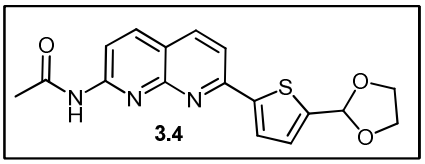
Thiophene-2-carbaldehyde **3.1** (1.35 g, 12.05 mmol), ethylene glycol (2.68 mL, 48.2 mmol) and p-toluenesulfonic acid (0.01 g, 0.06 mmol) were dissolved in toluene (60 mL) in one neck round bottom flask. A Dean Stark apparatus was fitted and the reaction mixture was heated at 160 ^{o}C for 16 h. The reaction mixture cooled to room temperature and washed with 10% NaOH solution and extracted with DCM. The organic phase was dried with anhydrous sodium sulphate, filtered and solvent was evaporated to provide compound **3.2** as brown oil (1.64 g, 88%) which was used without further purification. Spectroscopic data matches with the one from reported procedure. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.33 (1H, d, J = 3.2 Hz), 7.17 (1H, d, J = 3.2 Hz), 7.01 (1H, m), 6.13 (1H, s), 4.11 (2H, m), 4.01 (2H, m).



3.3

(5-(1,3-Dioxolan-2-yl)thiophen-2-yl)tributylstannane (3.3):[3]

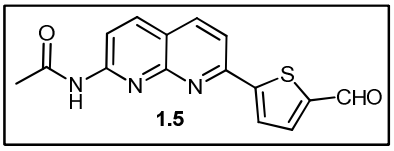
To a solution of compound **3.2** (0.9, 5.76 mmol) in dry THF (30 mL) was added n-butyl lithium (1.6 M in hexane, 7.25 mL, 11.6 mmol) at -78 ^{o}C. After 1 h at -78 ^{o}C, tributyl tin chloride (2.81 mL, 8.64 mmol) was added drop wise to the above reaction mixture. After stirring for 24 h at room temperature, the mixture was quenched with 20 mL of saturated aqueous ammonium chloride solution and extracted with hexane. The organic phase was dried with anhydrous sodium sulphate, concentrated under reduced pressure, and the resulting residue **3.3** was used without further purification (1.08 g, 43%). Spectroscopic data matches with the one from reported procedure. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.27 (1H, d, J = 3.2 Hz), 7.04 (1H, d, J = 3.2 Hz), 6.15 (1H, s), 4.16 (2H, m), 4.02 (2H, m), 1.56 (6H, m), 1.32 (6H, m), 1.09 (6H, m), 0.91 (9H, m).



3.4

N-(7-(5-(1,3-Dioxolan-2-yl)thiophen-2-yl)-1,8-naphthyridin-2-yl)acetamide (3.4):

Compound **3.3 (**5.32 g, 12 mmol), compound **1.4** (2.0 g, 9 mmol) and $PdCl_2(PPh_3)_2$ (0.630 g, 0.9 mmol) were taken in a two necked round bottom flask, degassed with nitrogen and dry 1,4- dioxane (100 mL) under nitrogen atmosphere was added. The reaction mixture was refluxed for 3 h, after that the solvent was removed under reduced pressure, and then the crude residue was dissolved in EtOAc, passed through celite and the solvent was evaporated. The crude residue was purified by column chromatography using 1:1 EtOAc:hexane to give pure compound **3.4** as a yellowish solid (2.0 g, 65%). Mp: 180-190 ^{o}C. TLC (50% EtOAc in Hexane): R_f = 0.26. ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 11.11 (1H, s), 8.37-8.29 (3H, m), 8.04 (1H, d, J = 8.4 Hz), 7.91 (1H, d, J = 3.6 Hz), 7.27-7.26 (1H, m), 6.00 (1H, s), 4.08-4.04 (2H, m), 3.97-3.92 (2H, m), 2.15 (3H, S). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 170.3, 155.1, 154.5, 154.2, 146.1, 144.8, 139.0, 137.0, 132.0, 131.9, 128.4, 128.3, 126.9, 126.4, 119.3, 116.8, 115.0, 24.8. MS (EI, 70*ev*): *m/z* $[M]^+$ calcd for $C_{17}H_{15}N_3O_3S$: 341.0, found 342.0 $[M+1]^+$. Anal. Calcd for $C_{17}H_{15}N_3O_3S$: C, 59.81; H, 4.43; N, 12.31; O, 14.06; S, 9.39, found: C, 59.73; H, 4.41; N, 12.29.

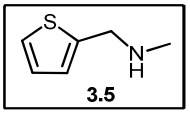


1.5

N-(7-(5-Formylthiophen-2-yl)-1,8-naphthyridin-2-yl)acetamide (1.5):

1M HCl (2 mL) was added dropwise to a solution of compound **3.4** (0.16 g, 0.46 mmol) in dry acetone (30 mL). After complete addition of HCl the reaction mixture was stirred at room temperature for 6 h, then the solvent was removed under reduced pressure and crude residue was extracted with EtOAc. The organic phase was dried with anhydrous sodium sulphate, concentrated under reduced pressure, and the resulting residue **1.5** was used without further purification (0.1 g, 73%). Mp: 270-274 ^{o}C. TLC (50% EtOAc in hexane): R_f = 0.24; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 11.20 (1H, s), 9.98 (1H, s), 8.50-8.36 (3H, m), 8.22-8.20 (2H, m), 8.12 (1H, d, J = 3.6 Hz), 2.18 (3H, s). ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 185.2, 170.6, 155.4, 154.6, 153.8, 153.3, 145.2, 139.7, 139.2, 138.8, 128.7, 120.3, 117.5, 115.4, 24.5. MS (EI, 70*ev*): *m/z* $[M]^+$ calcd for $C_{15}H_{11}N_3O_3S$: 297.0, found 298.1 $[M+1]^+$. Anal. Calcd for $C_{15}H_{11}N_3O_2S$: C, 60.59; H, 3.73; N, 14.13; O, 10.76; S, 10.78, found: C, 60.45; H, 3.68; N, 14.06.

Route-II; Scheme 3b:

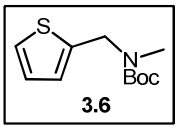


3.5

N-Methyl-1-(thiophen-2-yl)methanamine (3.5):[4]

Thiophene-2-carboxaldehyde **3.1** (0.54 g, 4 mmol) and 40% aqueous methyl amine (0.74 g, 20 mmol) were dissolved in MeOH (20 mL). After 1 h, sodium borohydride was added portion wise at 0 ^{o}C to the reaction mixture. The resulting mixture was stirred at room temperature for 3-4 days. The crude residue was taken up in 200 mL water and extracted with DCM. The organic phase was dried with anhydrous sodium sulphate, concentrated under reduced pressure, and the resulting residue was subjected to column chromatography using 70% EtOAc in hexane to give compound **3.5** (0.30g, 60%).

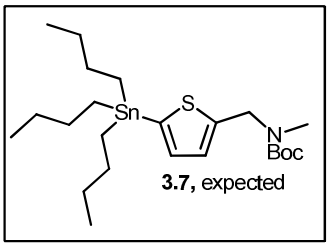
Spectroscopic data matches with the one from reported procedure. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.17 (1H, m), 6.91 (2H, m), 3.90 (2H, s), 2.43 (3H, s), 2.18 (1H, s).



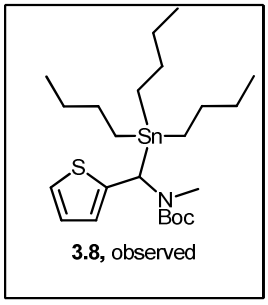
3.6

Tert-butyl methyl(thiophen-2-ylmethyl)carbamate (3.6):[5]

Compound **3.5** (0.2 g, 1.57 mmol) and sodium bicarbonate (0.25 g, 3.14 mmol) were dissolved in dry THF. Boc_2O (0.68 g, 3.14 mmol) was added dropwise to the reaction mixture. The resulting mixture was stirred at room temperature for 3 h. The crude residue was taken up in 100 mL water and extracted with EtOAc. The organic phase was dried with anhydrous sodium sulphate, concentrated under reduced pressure, and the resulting residue was subjected to column chromatography using 10% EtOAc in hexane to give compound **3.6** which was used without further purification (0.34g, 97%). Spectroscopic data matches with the one from reported procedure. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.22 (1H, m), 6.94 (2H, m), 4.54 (2H, s), 2.85 (3H, s), 1.52 (9H, s).



3.7, expected

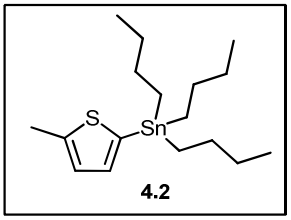


3.8, observed

Tert-butyl methyl((5-(tributylstannyl)thiophen-2-yl)methyl)carbamate (3.7):[6]

n-Butyl lithium (1.6 M in hexane, 2.4 mL, 3.85 mmol) was added to a solution of compound **3.6** (0.4 g, 1.76 mmol) in dry THF (30 mL) at 0 ^{o}C. After 1 h at 0 ^{o}C, tributyl tin chloride (1.26 g, 3.88 mmol) was added to the above reaction mixture. After stirring for 12 h at room temperature, the reaction mixture was quenched with 20 mL of saturated aqueous ammonium chloride solution and extracted with hexane. The organic phase was dried with anhydrous sodium sulphate, concentrated under reduced pressure. Spectroscopic data matches to compound **3.8** (0.58 g, 64%) instead of **3.7**. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 6.99 (1H, d, J = 4.8 Hz), 6.87 (1H, dd, J = 4.8, 3.6 Hz), 6.59 (1H, d, J = 3.2 Hz), 3.96 (1H, s), 2.91 (3H, s), 1.47 (9H, s), 1.41-1.22 (12H, m), 0.94-0.84 (15H, m).

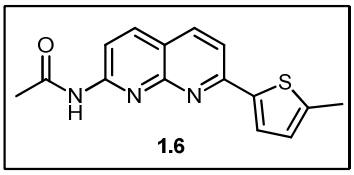
Route-III; Scheme 4:



4.2

Tributyl(5-methylthiophen-2-yl)stannane (4.2): ENREF 22[6]

n-Butyl lithium (1.6 M in hexane, 3.81 mL, 6.11 mmol) was added to a solution of compound **4.1** (0.5 g, 5.09 mmol) in dry THF (30 mL) at 0 ^{o}C. After 1 h at 0 ^{o}C, tributyl tin chloride (1.65 mL, 6.11 mmol) was added drop wise to the above reaction mixture. After stirring over 12 h at room temperature, the reaction mixture was quenched with 20 mL of saturated aqueous ammonium chloride solution and extracted with hexane. The organic phase was dried with anhydrous sodium sulphate, concentrated under reduced pressure, and the resulting residue **4.2** was used without further purification (1.26 g, 64%). Spectroscopic data matches the one from reported procedure. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 6.96 (1H, d, J = 3.2 Hz), 6.88 (1H, dd, J = 5.2, 3.2 Hz), 2.54 (3H, s), 1.56 (6H, m), 1.33 (6H, m), 1.07 (6H, m), 0.89 (9H, m).

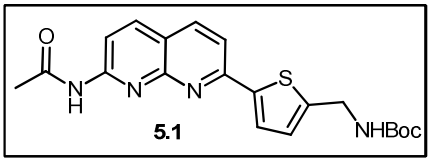


1.6

N-(7-(5-Methylthiophen-2-yl)-1,8-naphthyridin-2-yl)acetamide (1.6):

Compound **4.2 (**2.40 g, 6 mmol), compound **1.4** (1.0 g, 4.5 mmol) and $PdCl_2(PPh_3)_2$ (0.149 g, 0.22 mmol) were taken in a two necked round bottom flask, degassed with nitrogen and 1,4- dioxane (50 mL) was added under nitrogen atmosphere. The reaction mixture was refluxed for 2 h, the solvent was removed under reduced pressure, and the crude residue was dissolved in EtOAc, passed through celite and the solvent was evaporated. The crude residue was purified by column chromatography using 1:1 EtOAc:hexane to give compound **1.6** as a yellowish solid (1.1 g, 65%). Mp: 150-152 ^{o}C. TLC (50% EtOAc in hexane): R_f = 0.28. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.44 (1H, d, J = 8.4 Hz), 8.16 (1H, d, J = 8.8 Hz), 8.08 (1H, d, J = 8.4 Hz), 7.75 (1H, d, J = 8.4 Hz), 7.66 (1H, d, J = 3.6 Hz), 6.84 (1H, m), 2.57 (3H, s), 2.33 (3H, s). ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 170.5, 156.1, 153.7, 145.83, 145.82, 141.5, 139.9, 136.9, 127.8, 126.8, 118.9, 117.3, 114.1, 24.9, 15.8. MS (EI, 70*ev*): *m/z* $[M]^+$ calcd for $C_{15}H_{13}N_3OS$: 283.0, found 284.1 $[M+1]^+$. Anal. Calcd for $C_{15}H_{13}N_3OS$: C, 63.58; H, 4.62; N, 14.83; O, 5.65; S, 11.32, found: C, 63.53; H, 4.63; N, 14.85.

Route-IV; Scheme 5:

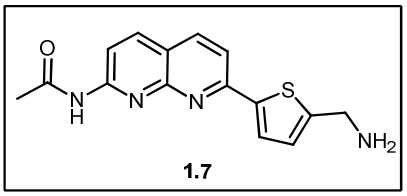


5.1

Tert-butyl ((5-(7-acetamido-1,8-naphthyridin-2-yl)thiophen-2-yl)methyl)carbamate 5.1:

Compound **1.4 (**1.0 g, 4.5 mmol), compound **2.2** (3.0 g, 6 mmol) and $PdCl_2(PPh_3)_2$ (0.157 g, 0.22 mmol) were taken in a two necked round bottom flask, degassed with nitrogen and dry 1,4- dioxane (100 mL) was added under nitrogen atmosphere. The reaction mixture was refluxed for 1 h, the solvent was removed under reduced pressure, and the crude residue was dissolved in EtOAc, passed through celite and the solvent was evaporated. The crude compound was purified by column chromatography using 60% EtOAc in hexane to give compound **5.1** as a yellowish solid (1.5 g, 84%). Mp: 198-200 ^{o}C. TLC (60% EtOAc in hexane): R_f = 0.24. ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 11.09 (1H, s), 8.33 (3H, m), 8.01

(1H, d, *J* = 8.4 Hz), 7.85 (1H, d, *J* = 3.2 Hz), 7.59-7.55 (1H, m), 7.01 (1H, d, *J* = 3.2 Hz), 4.31 (2H, d, *J* = 5.6 Hz), 2.16 (3H, s). ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 170.4, 156.0, 155.2, 155.0, 154.8, 148.8, 143.5, 139.5, 138.0, 127.7, 126.5, 119.2, 116.7, 114.2, 78.5, 44.0, 28.6, 24.5. MS (EI, 70*ev*): *m/z* $[M]^+$ calcd for $C_{20}H_{22}N_4O_3S$: 398.14, found 398.2 $[M+1]^+$. Anal. Calcd for $C_{20}H_{22}N_4O_3S$: C, 60.28; H, 5.56; N, 14.06; O, 12.05; S, 8.05, found: C, 60.15; H, 5.63; N, 14.12.



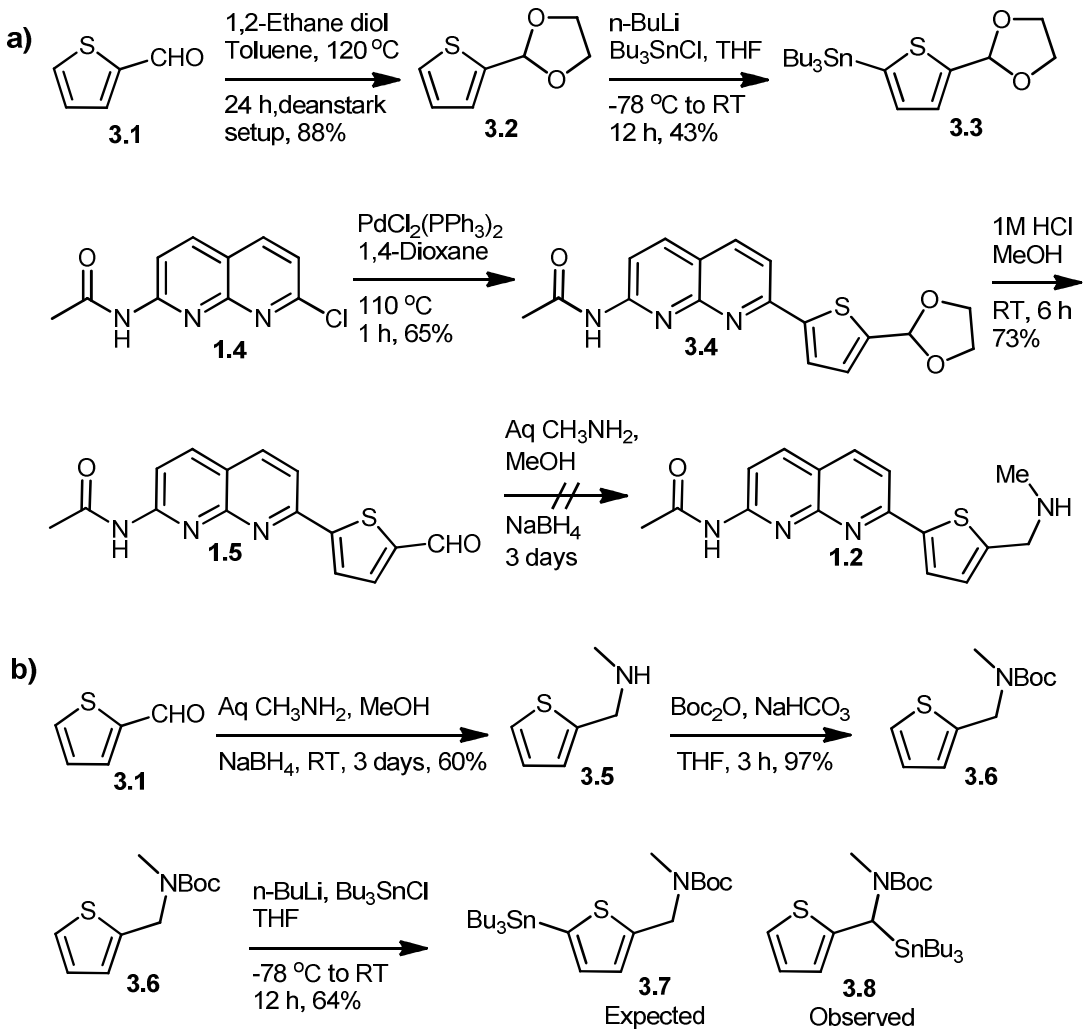
1.7

N-(7-(5-(Aminomethyl)thiophen-2-yl)-1,8-naphthyridin-2-yl)acetamide (1.7):

To a solution of compound **5.1** (0.14 g, 0.35 mmol) in dry DCM (2 mL) trifluoroacetic acid (2 mL) was added at 0 ^{o}C. The reaction mixture was slowly heated to room temperature and stirred at room temperature for 4 h. After 4 h, reaction mixture was quenched with saturated sodium bicarbonate solution followed by extraction with DCM. The organic phase was dried with anhydrous sodium sulphate, concentrated under reduced pressure, and the resulting residue **1.7** (0.11 g, 82%) was used without further purification. Mp: 172-174 ^{o}C. TLC (20% MeOH in DCM): R_f = 0.24. ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 11.10 (1H, s), 8.40-8.33 (3H, m), 8.26 (2H, s), 8.06 (1H, d, *J* = 8.4 Hz), 7.97 (1H, d, *J* = 3.6 Hz), 7.30 (1H, d, *J* = 4.0 Hz), 4.33-4.27 (2H, m), 2.16 (3H, s). ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 170.5, 158.8, 158.5, 155.1, 154.7, 146.0, 139.8, 138.4, 130.6, 127.9, 119.5, 116.8, 114.6, 37.7, 24.6. MS (EI, 70*ev*): *m/z* $[M]^+$ calcd for $C_{15}H_{14}N_4OS$: 298.09, found 299.2 $[M]^+$. Anal. Calcd for $C_{15}H_{14}N_4OS$: C, 60.38; H, 4.73; N, 18.78; O, 5.36, S, 10.75, found: C, 60.26; H, 4.78; N, 18.65.

Discussion of the Routes II-IV

Our attempt to synthesize key intermediate **1.2** following route **II** is outlined in **Scheme S1.** Commercially available starting material thiophene-2-carbaldehyde **3.1** was protected with ethylene glycol to give compound **3.2** in 88% yield.[2] Later, compound **3.2** was subjected to lithiation using n-BuLi followed by treatment with tributyl tin chloride to afford compound **3.3** in good yield. In the next step, compound **3.3** was coupled to compound **1.4** in Stille coupling conditions in THF using palladium (II) catalyst to give compound **3.4** in decent yields. Deprotection of compound **3.4** with 1M HCl led to compound **1.5** in 73% yield.

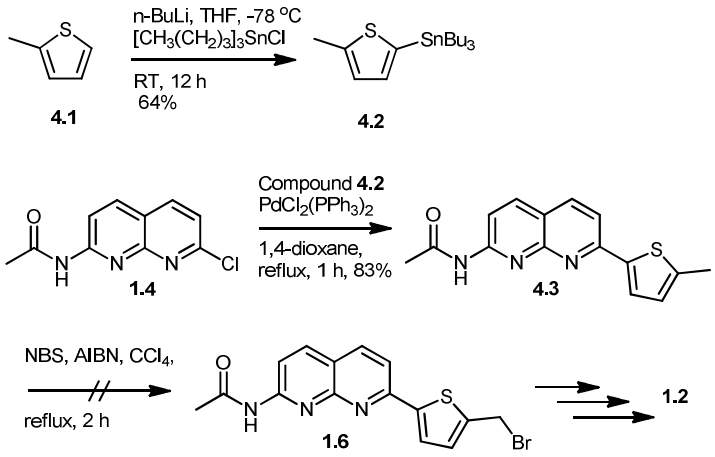


Scheme S1: Route II towards key intermediate **1.2**

We expected to obtain key intermediate **1.2** after treatment of compound **1.5** with methyl amine to obtain corresponding imine, followed by reduction using sodium borohydride. Unfortunately, reaction didn't initiate under these conditions and starting materials were recovered as it is. Therefore, we desired to change the synthetic plan as outlined in **Scheme S1b**. In this case, the same starting material thiophene-2-carbaxaldehyde **3.1** first was subjected to imine formation using methyl amine followed by reduction with sodium borohydride to afford compound **3.5** in 60% yield. In the next step, Boc protection of compound **3.5** gave compound **3.6** in 97% yield, and finally compound **3.6** was subjected to lithiation using n-BuLi followed by treatment with tributyl tin chloride. Unfortunately, instead of **3.7** we obtained unexpected compound **3.8** as a major product. ^{1}H NMR spectroscopy shows three protons in aromatic region and one proton at 3.96 ppm corresponding to **3.8**.[7]

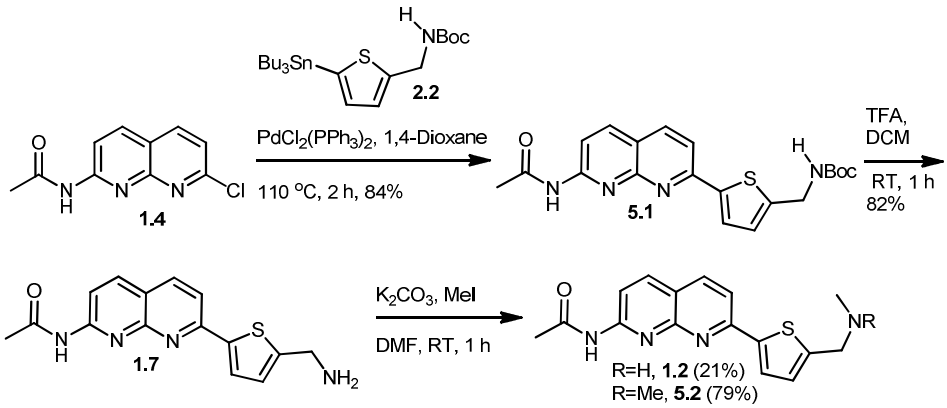
Another attempt towards key intermediate **1.2** was made as described in route **III** and outlined in **Scheme S2**. The synthesis started from lithiation of methyl thiophene **4.1** with n-BuLi, which was further treated with tributyl tin chloride to give compound **4.2** in 64% yield.[6] Subsequently, compound **4.2** was coupled with compound **1.4** in Stille coupling conditions in 1,4-dioxane using palladium (II) catalyst to give compound **4.3** in 83% yield. Next, we were planning partial bromination of compound **4.3** with N-bromosuccinimide using free radical initiator

azobisisobutyronitrile (AIBN). However, this reaction did not lead to compound **1.6**, instead we observe a complex mixture of side products and had to abandon this scheme.



Scheme S2: Route III towards key intermediate **1.2**

Yet another attempt towards key intermediate **1.4** is outlined in **Scheme S3**, route IV. We used compounds **2.2** and **1.4** as our starting materials and subjected them to Stille coupling in 1,4-dioxane using palladium (II) catalyst to obtain compound **5.1** in 84% yield. Boc-deprotection of the later using trifluoroacetic acid resulted in compound **1.7** in 82% yield. Further, in order to attain key starting material **1.2**, compound **1.7** was treated with methyl iodide as a methylating agent and potassium carbonate as a base. Although this step was successful, the yield of compound **1.2** was very poor, only 21%. Such low yield is the result of exclusive formation of over-alkylated product. Therefore, this synthetic pathway was not efficient enough and was abandoned as well.



Scheme S3: Route IV towards key intermediate **1.2**

NMR Spectra of Synthesized Compounds.

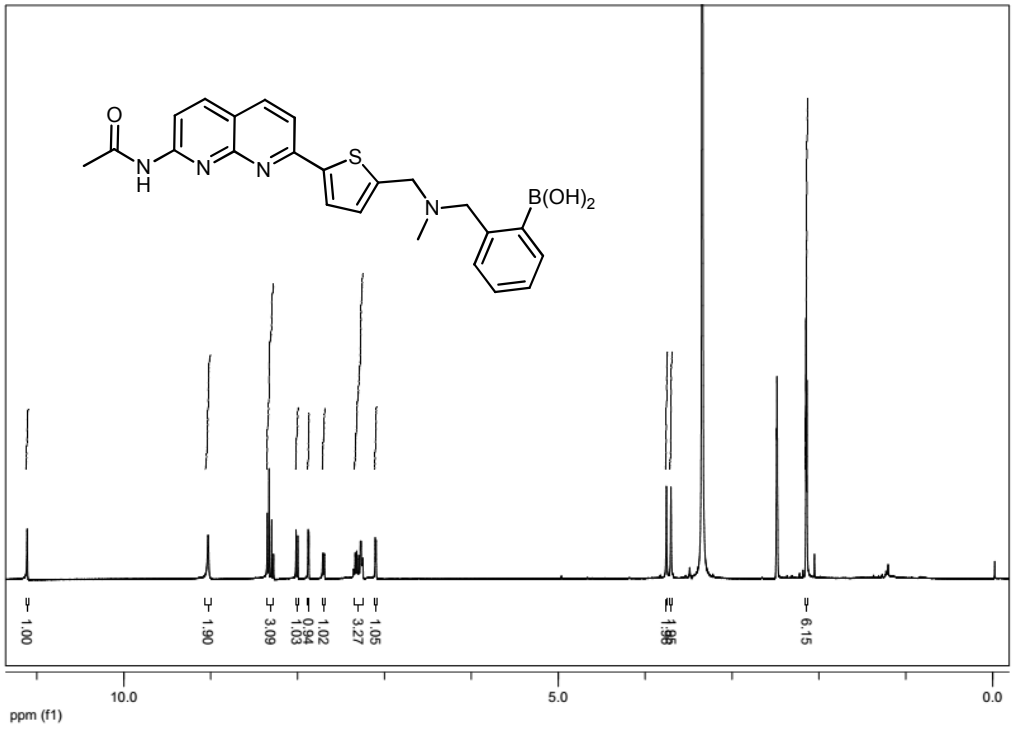


Figure S1: ^{1}H NMR (DMSO-d_6, 400 MHz) of compound **1.1**

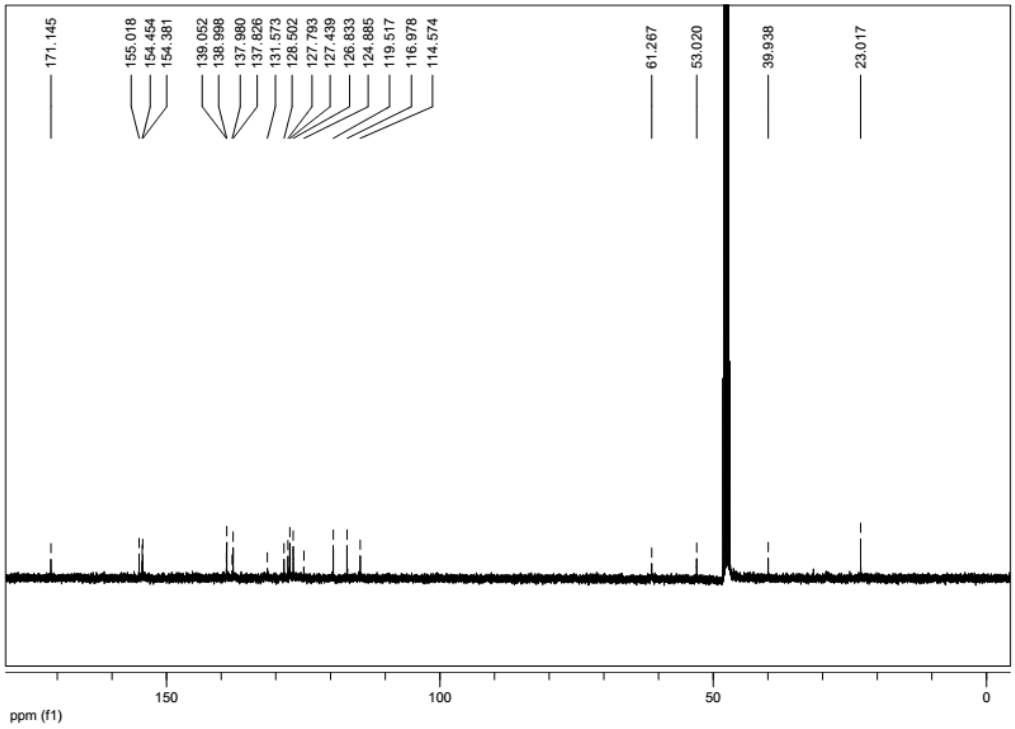


Figure S2: ^{13}C NMR (CD_3OD, 100 MHz) of compound **1.1**

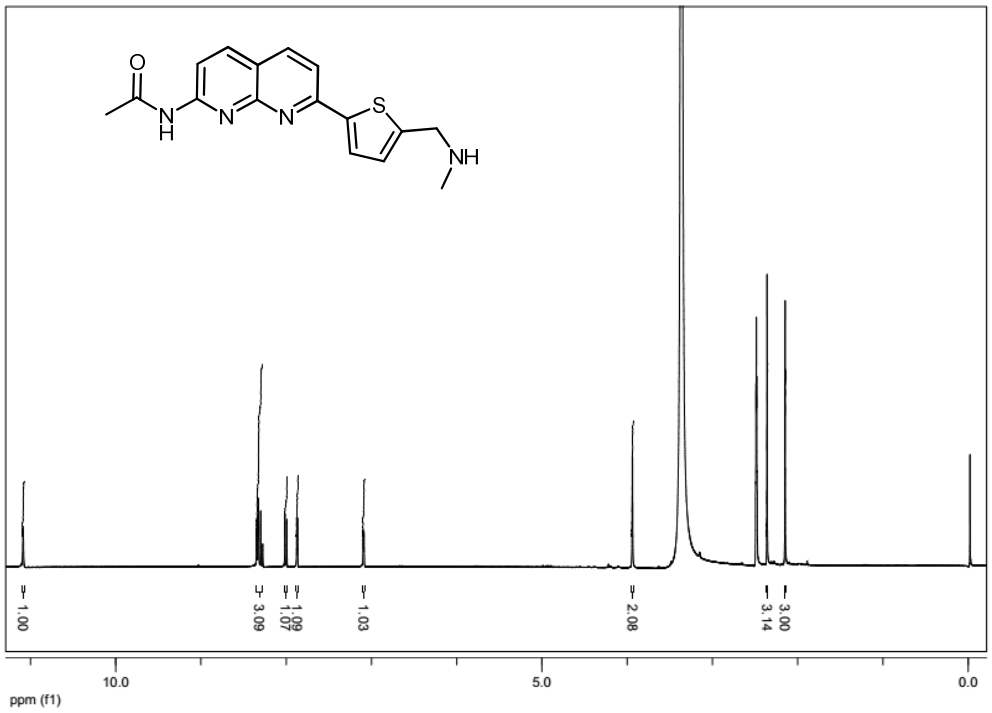


Figure S3: ^{1}H NMR (DMSO-d_6, 400 MHz) of compound **1.2**

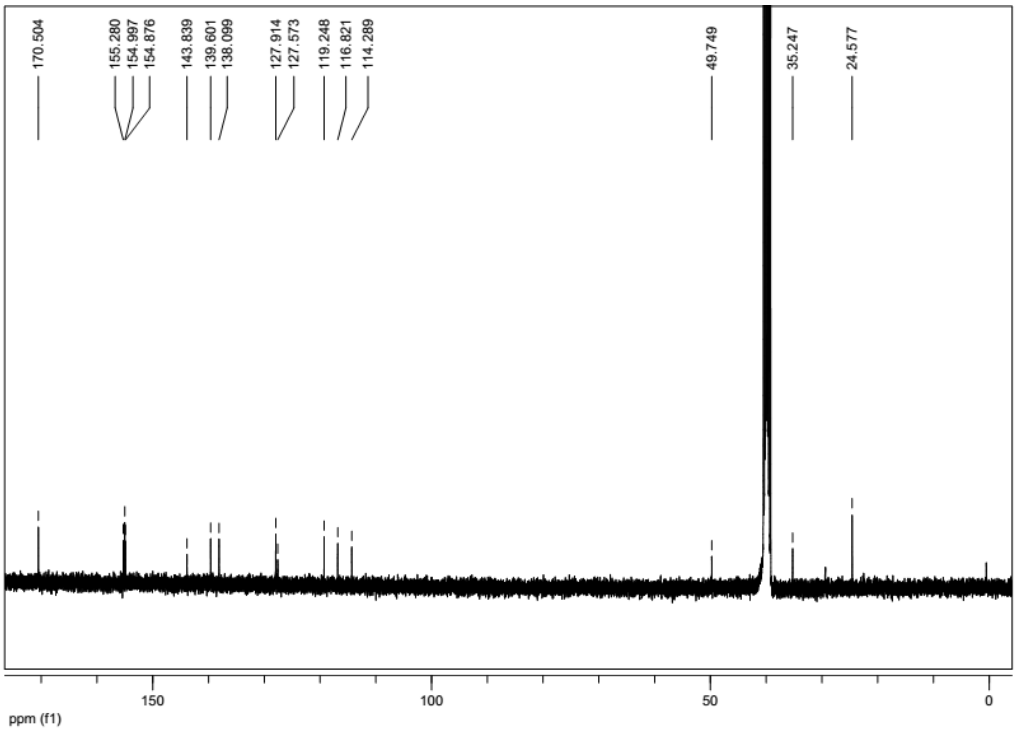


Figure S4: ^{13}C NMR (DMSO-d_6, 100 MHz) of compound **1.2**

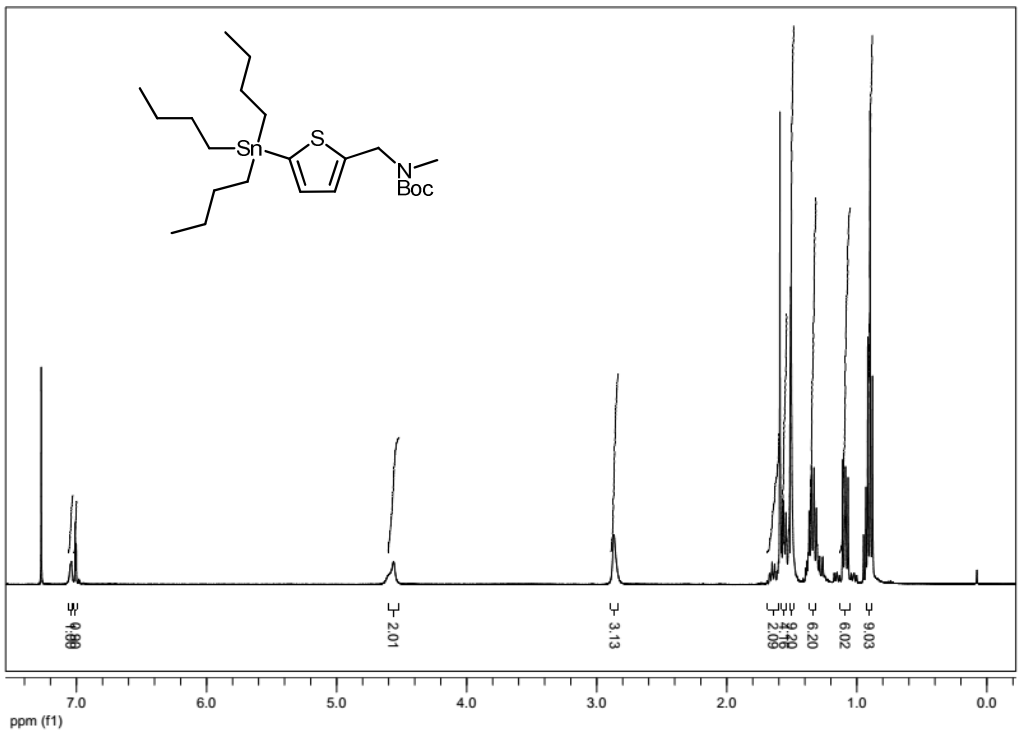


Figure S5: ^{1}H NMR ($CDCl_3$, 400 MHz) of compound **1.3**

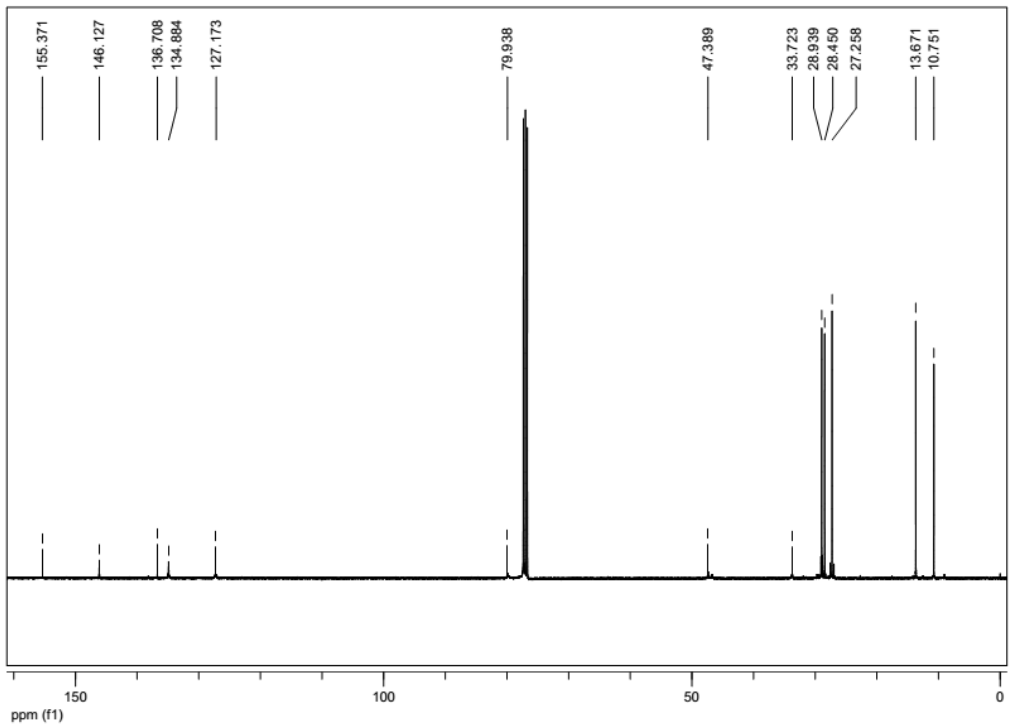


Figure S6: ^{13}C NMR ($CDCl_3$, 100 MHz) of compound **1.3**

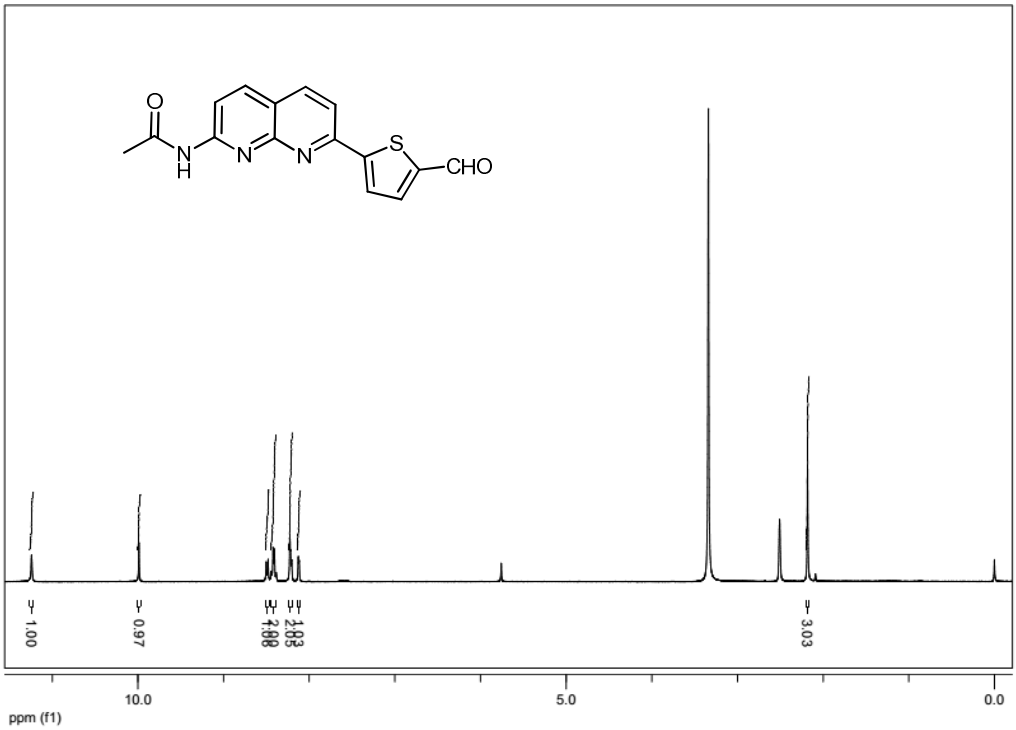


Figure S7: ^{1}H NMR (DMSO-d_6, 400 MHz) of compound **1.5**

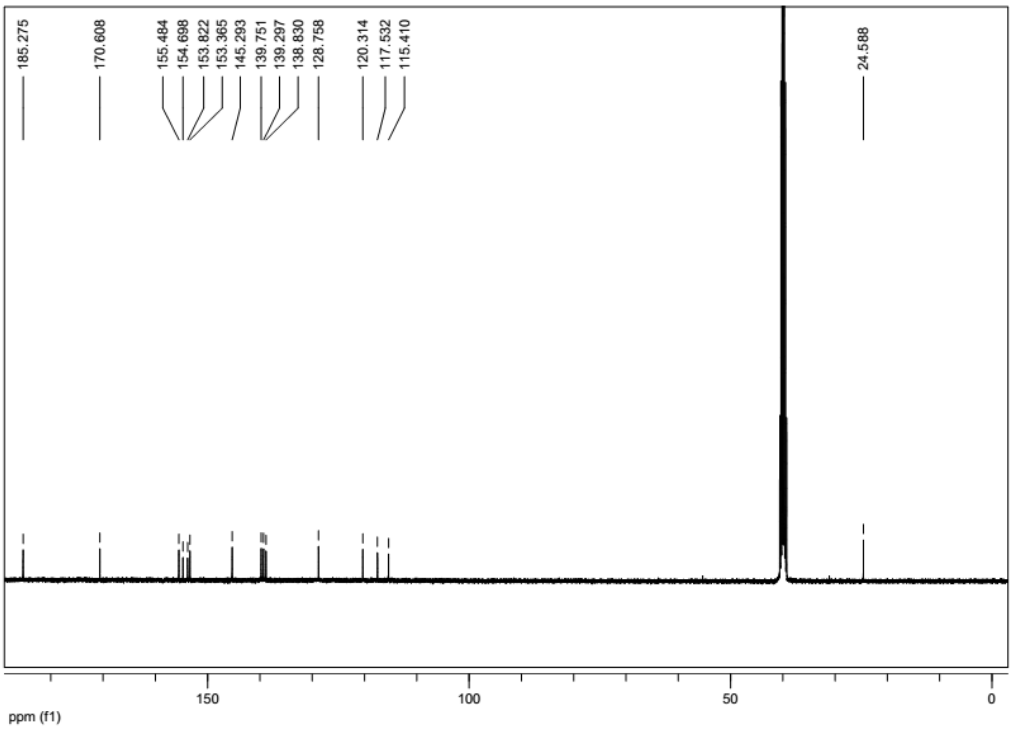


Figure S8: ^{13}C NMR (DMSO-d_6, 100 MHz) of compound **1.5**

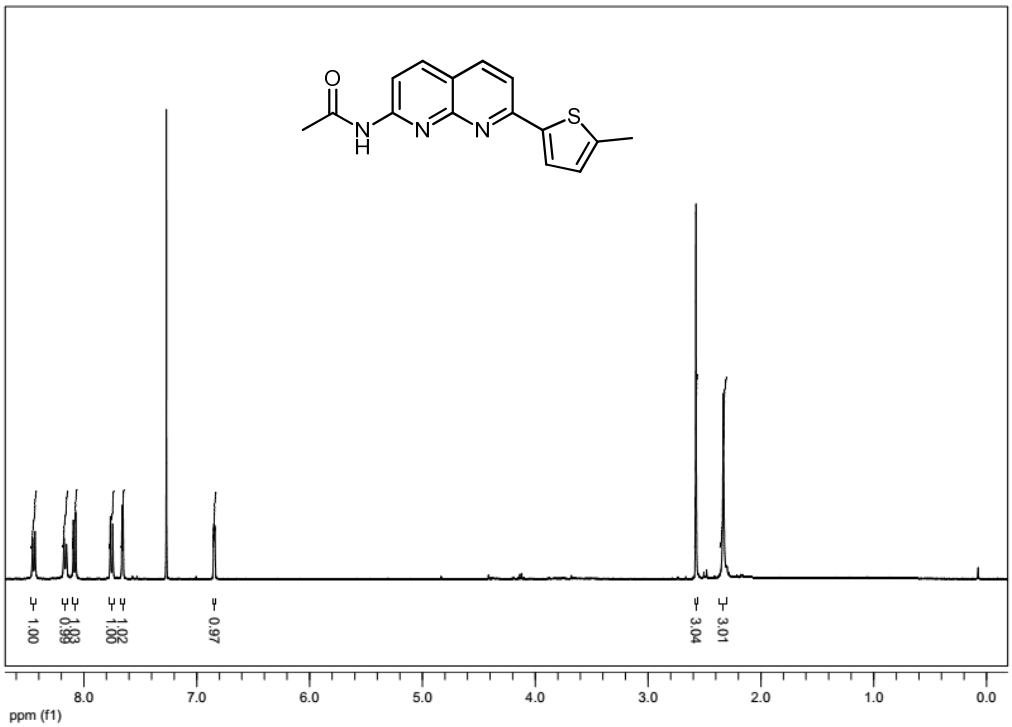


Figure S9: ^{1}H NMR ($CDCl_3$, 400 MHz) of compound **1.6**

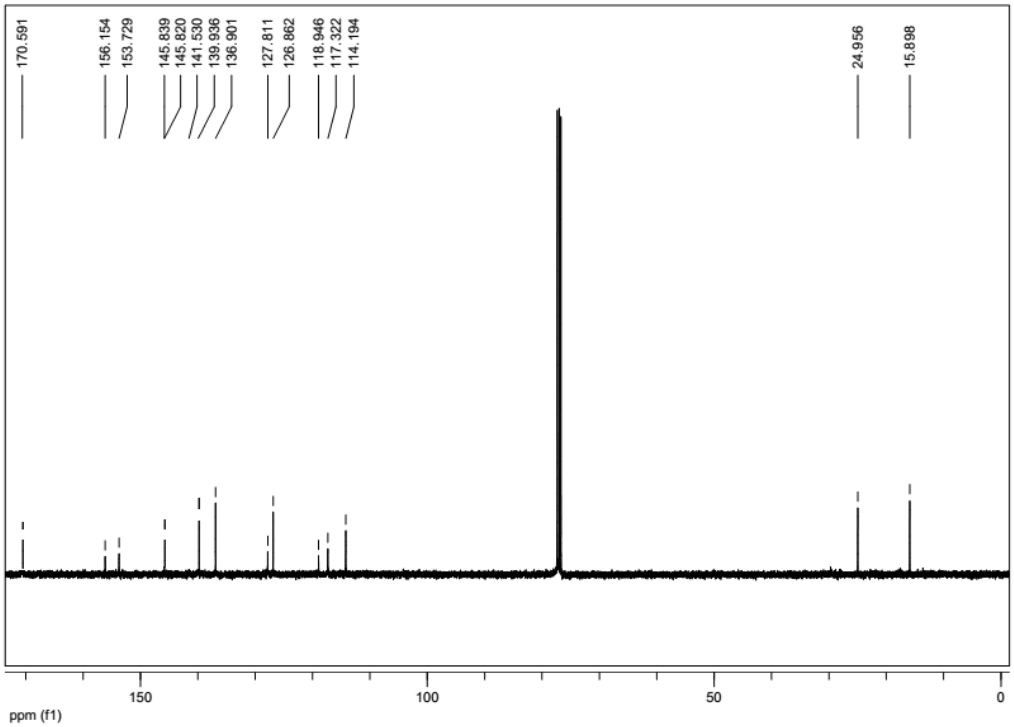


Figure S10: ^{13}C NMR ($CDCl_3$, 100 MHz) of compound **1.6**

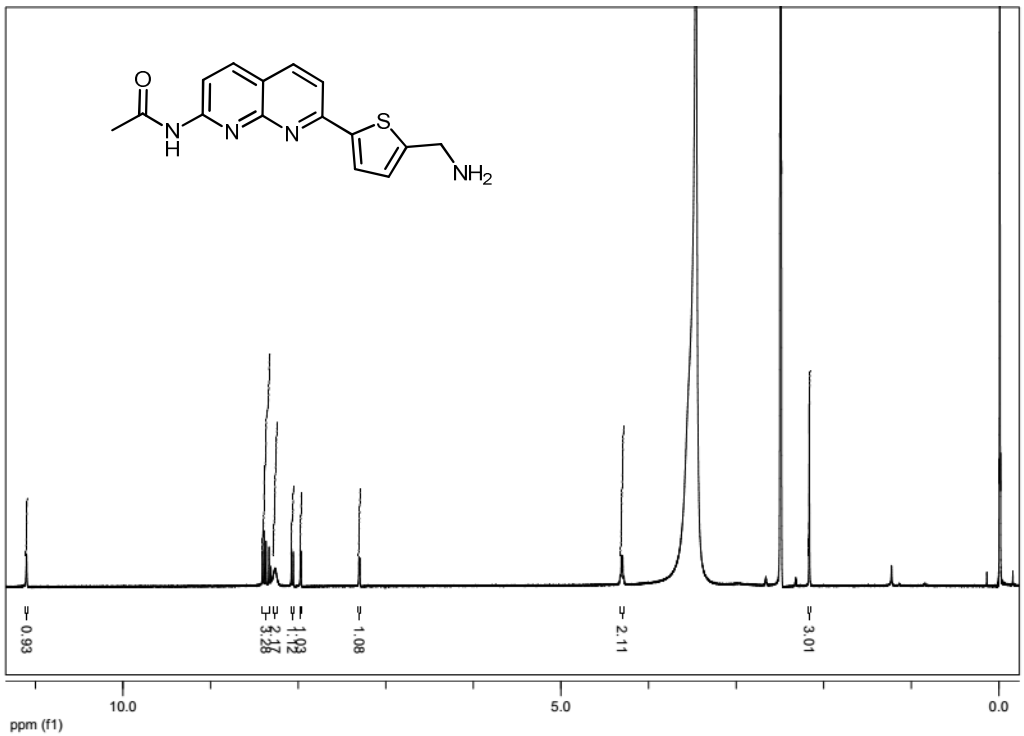


Figure S11: ^{1}H NMR (DMSO-d_6, 400 MHz) of compound **1.7**

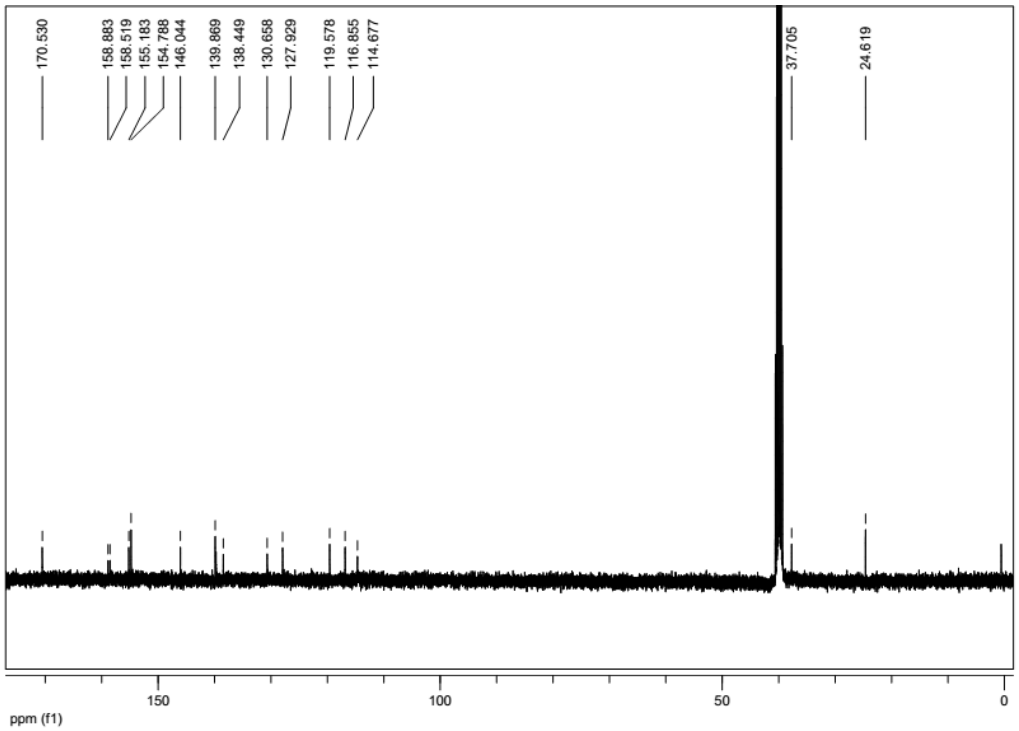


Figure S12: ^{13}C NMR (DMSO-d_6, 100 MHz) of compound **1.7**

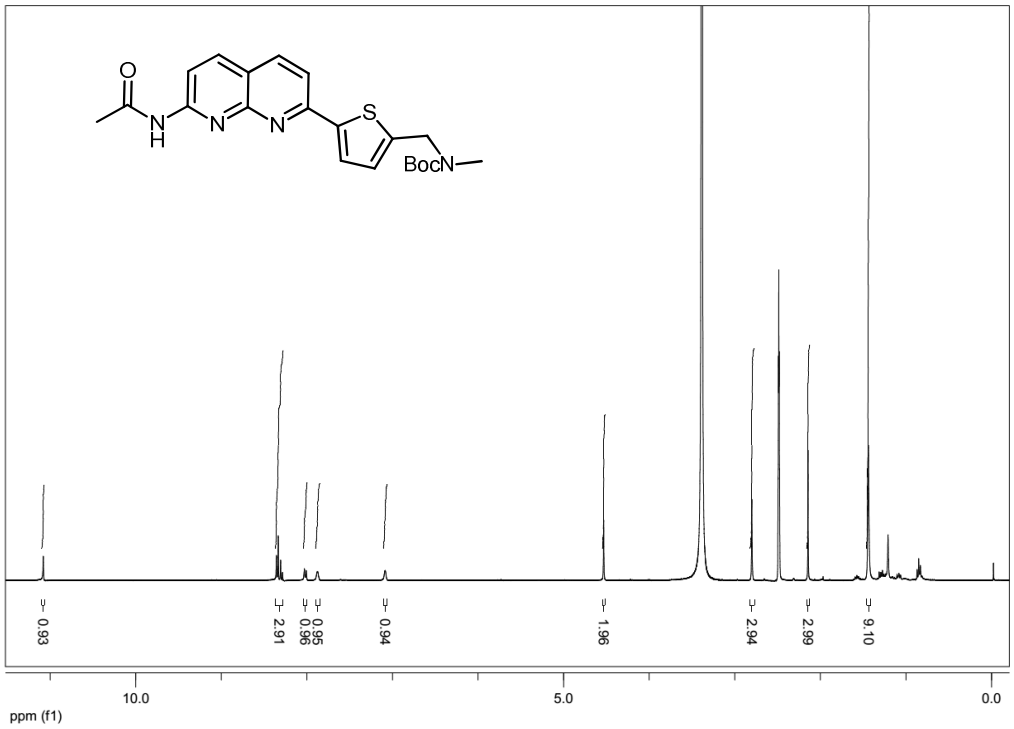


Figure S13: ^{1}H NMR (DMSO-d_6, 400 MHz) of compound **2.6**

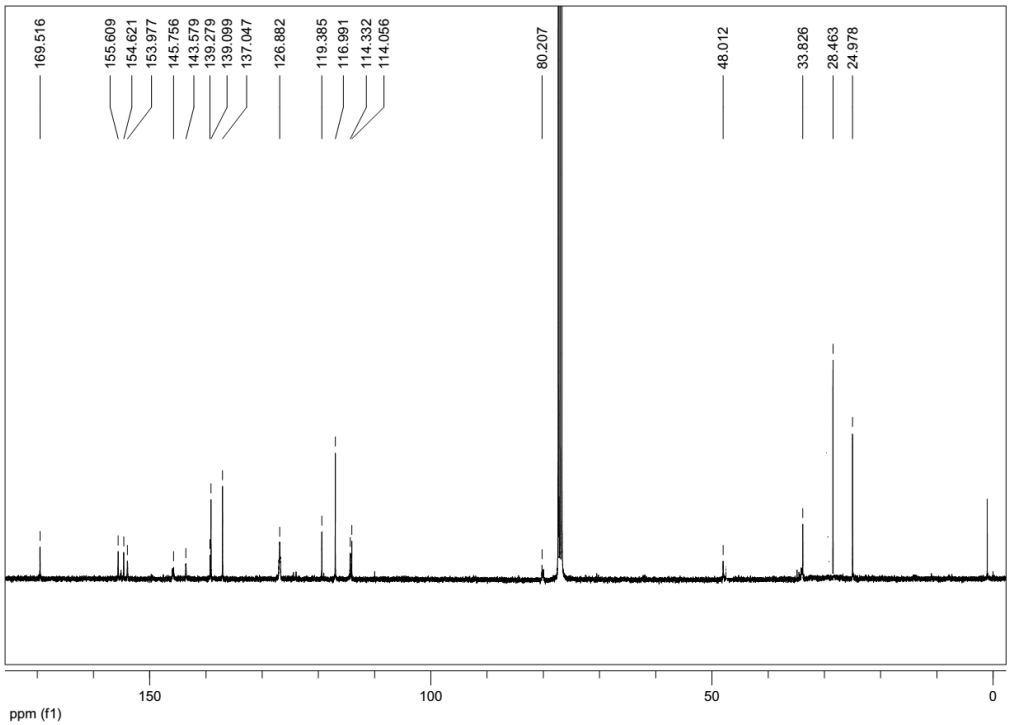


Figure S14: ^{13}C NMR ($CDCl_3$, 100 MHz) of compound **2.6**

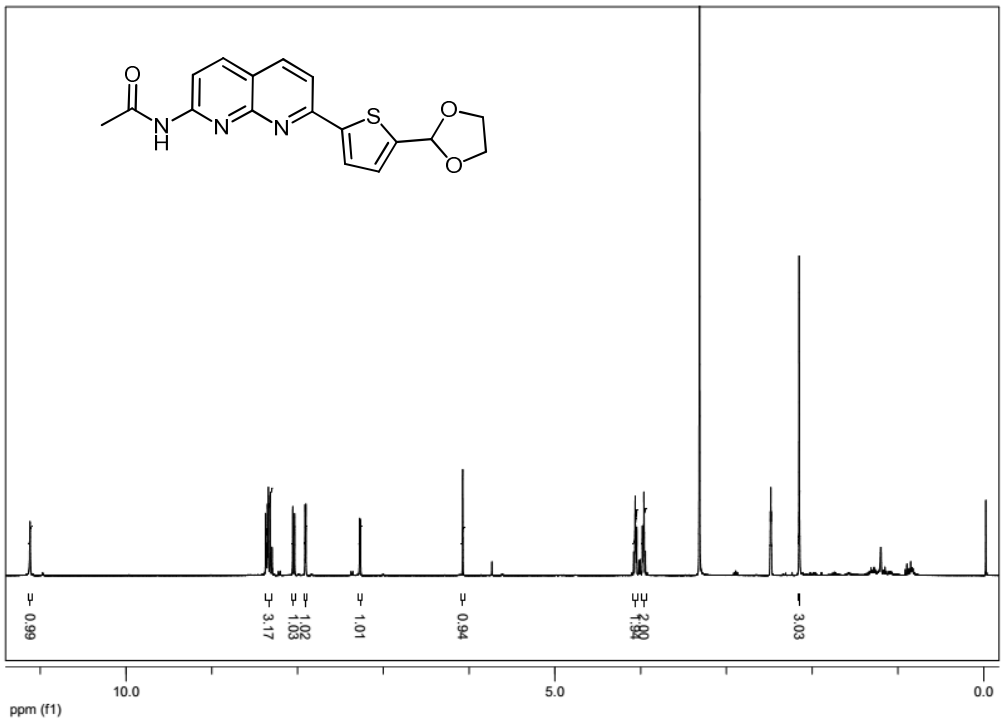


Figure S15: ^{1}H NMR (DMSO-d_6, 400 MHz) of compound **3.4**

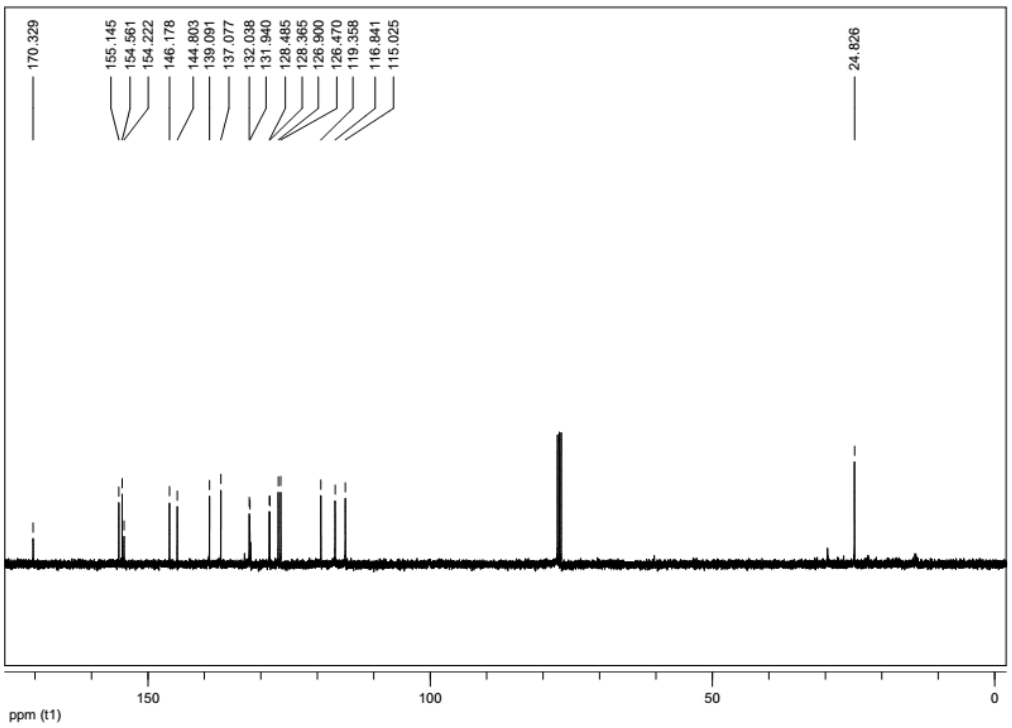


Figure S16: ^{13}C NMR ($CDCl_3$, 100 MHz) of compound **3.4**

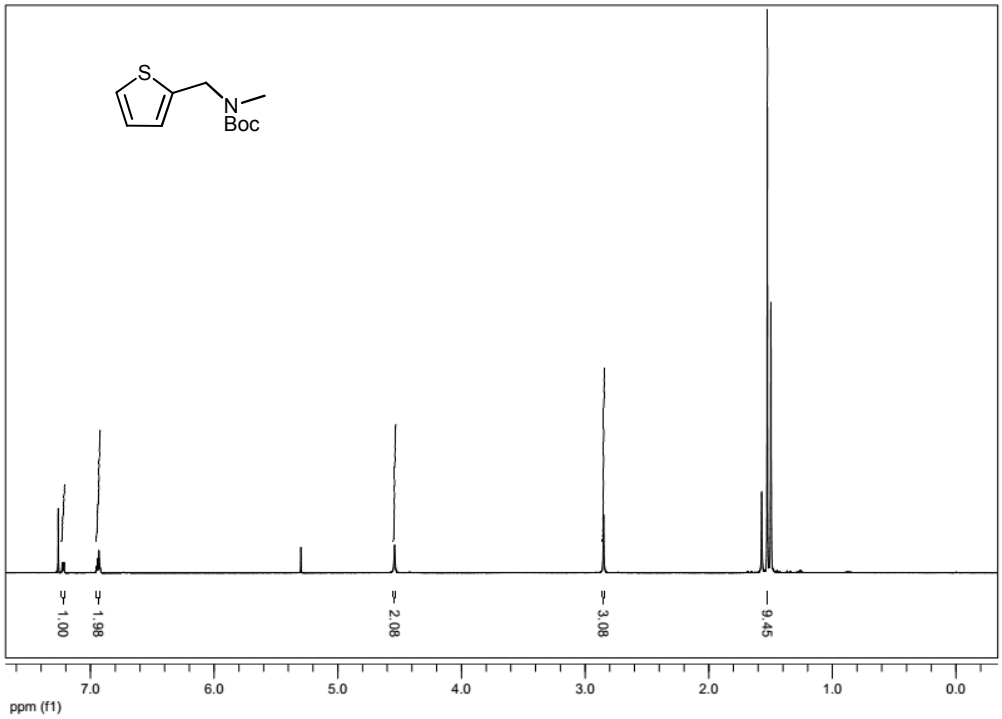


Figure S17: ^{1}H NMR ($CDCl_3$, 400 MHz) of compound **3.6**

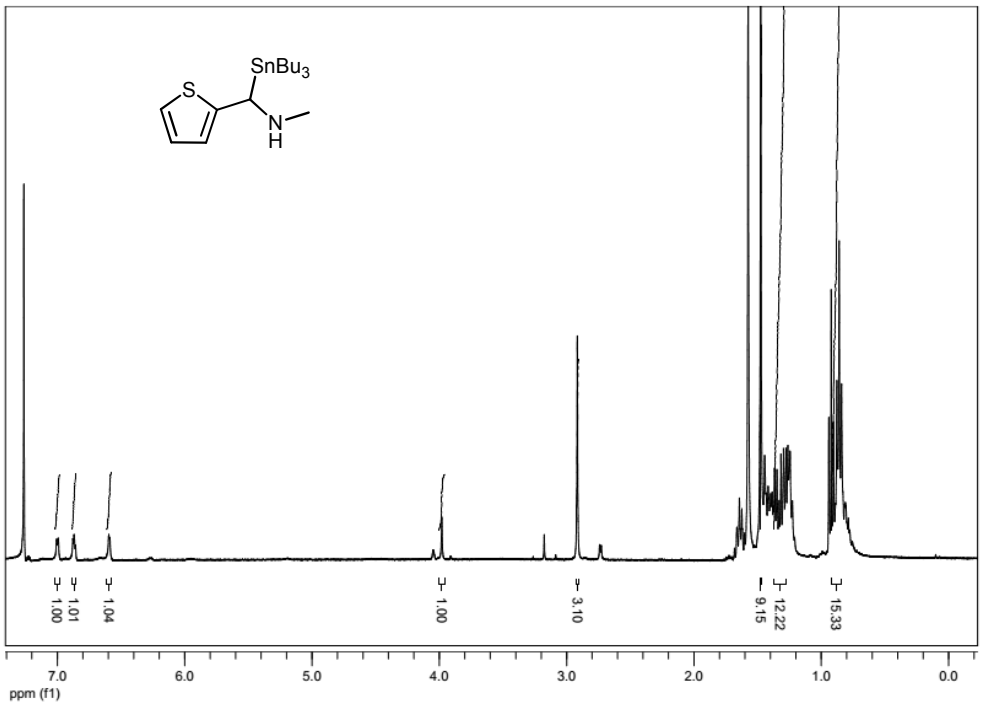


Figure S18: ^{1}H NMR ($CDCl_3$, 400 MHz) of compound **3.8**

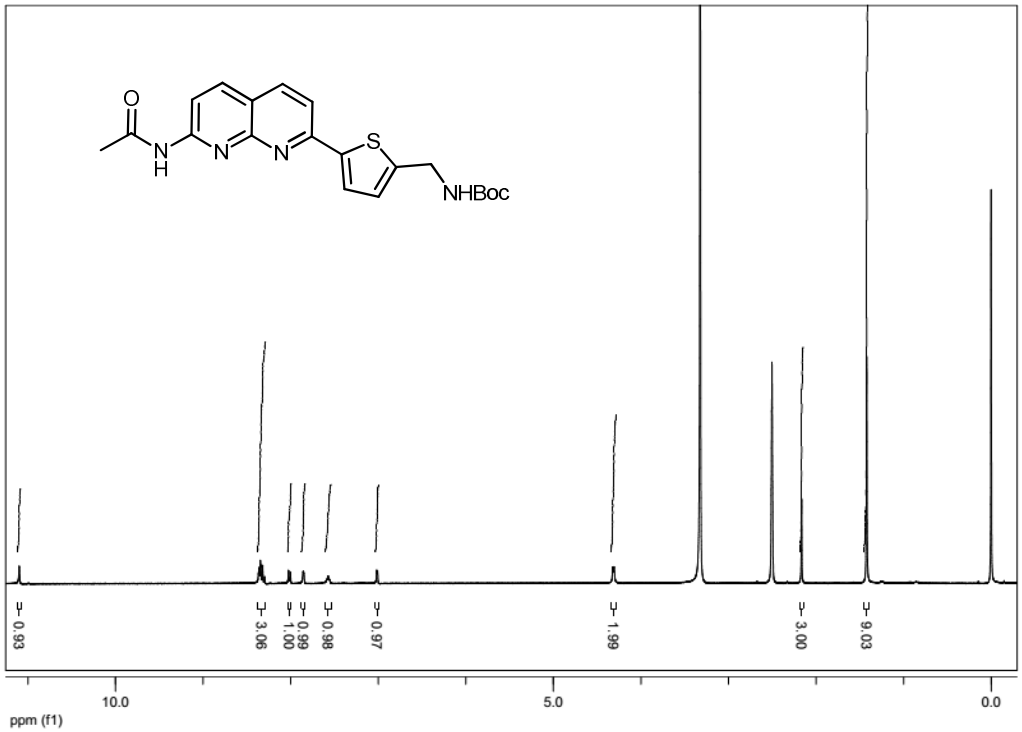


Figure S19: ^{1}H NMR (DMSO-d_6, 400 MHz) of compound **5.1**

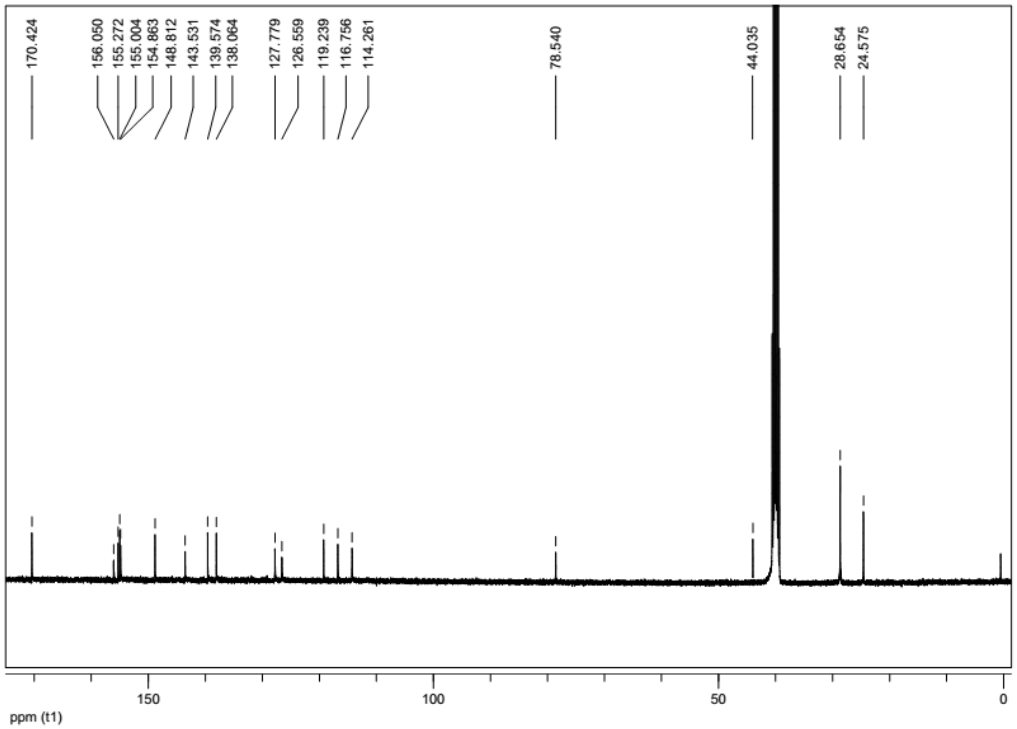


Figure S20: ^{13}C NMR (DMSO-d_6, 100 MHz) of compound **5.1**

Photophysical data and Benesi-Hildebrand association constants of compound 1.1 (10-5 M)

Table S1: Numerical photophysical data of **1.1** in MeOH and MeOH/H_2O at 10^{-5}M

Solvent	$\lambda_{abs,}$ nm	$\lambda_{em,}$ nm	Relative Φ_f with respect to quinine sulphate
MeOH	356, 371	401	0.20
MeOH/H_2O (50:50)	356, 371	403	0.26
MeOH/H_2O (2:98)	356, 371	403	0.25

Table S2: Benesi-Hildebrand association constant for **1.1** with D-fructose.

IF	**IF-IF$_0$ (ΔF)**	**D-Fructo-se (mM)**	**1/D-Fruct-ose**	**1/ΔF**		
185.489	53.750	0.001	1000	0.0186	Ka	Slope
231.690	99.951	0.002	500	0.010	104.91 M^{-1}	1.6873E-5
262.329	130.590	0.003	333.33	0.0076		
289.623	157.884	0.004	250	0.0063		
311.109	179.670	0.005	200	0.0055		
348.621	216.882	0.006	166.66	0.0046	IF_0	Intercept
371.462	239.723	0.007	142.85	0.0041	131.739	0.00177
393.968	262.229	0.008	125	0.0038		
418.180	286.441	0.009	111.11	0.0034		
433.771	302.032	0.10	100	0.0033		

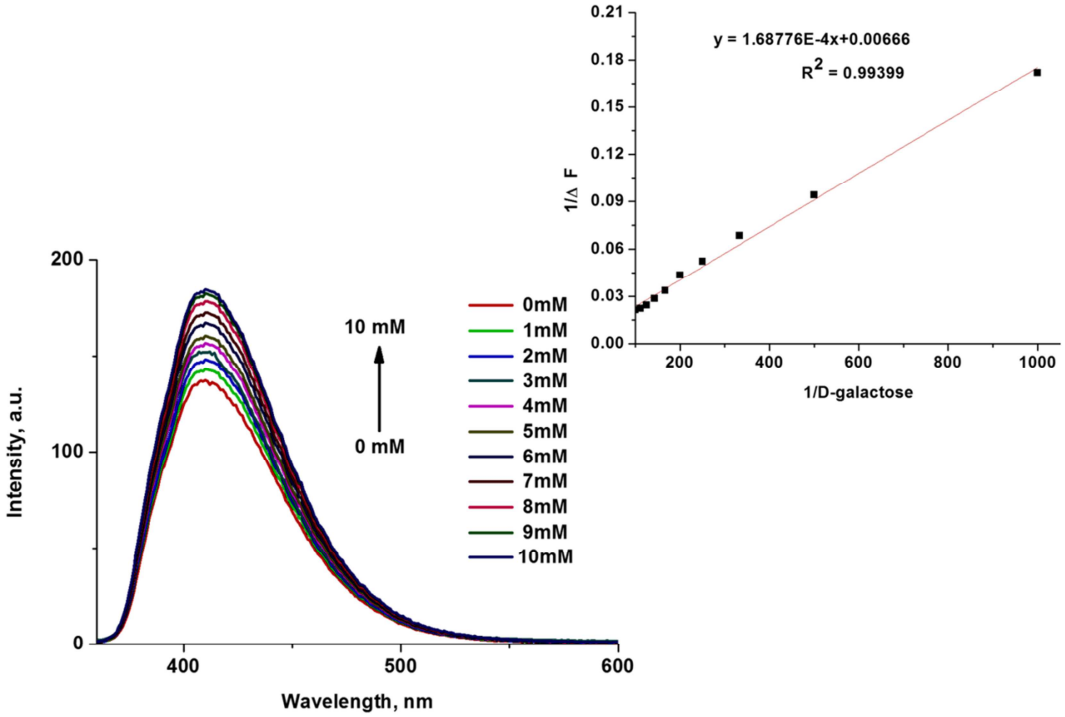


Figure S21: Fluorescence spectra of compound **1.1** (10^{-5} M) in presence of D-galactose at various concentrations (0-10 mM) and inset shows Benesi-Hildebrand plot of the naphthyridine-boronic acid-galactose complex in MeOH/H_2O (v/v=1:1, 5 mM PBS, pH 8.20) solutions. The monitored emission wavelength was 410 nm.

Table S3: Benesi-Hildebrand association constant for **1.1** with D-galactose.

IF	**IF-IF$_0$ (ΔF)**	**D-galactose (mM)**	**1/D-galactose**	**1/ΔF**	Ka 39.46 M^{-1}	Slope 1.68776E-4
143.188	5.808	0.001	1000	0.172		
148.000	10.620	0.002	500	0.0941		
151.999	14.619	0.003	333.33	0.0684		
156.438	19.058	0.004	250	0.0524		
160.275	22.895	0.005	200	0.0436		
166.896	29.516	0.006	166.66	0.0338		
172.338	34.958	0.007	142.85	0.0286	IF_0 137.38	Intercept 0.00666
178.320	40.94	0.008	125	0.0244		
182.142	44.762	0.009	111.11	0.0223		
184.326	46.946	0.10	100	0.0213		

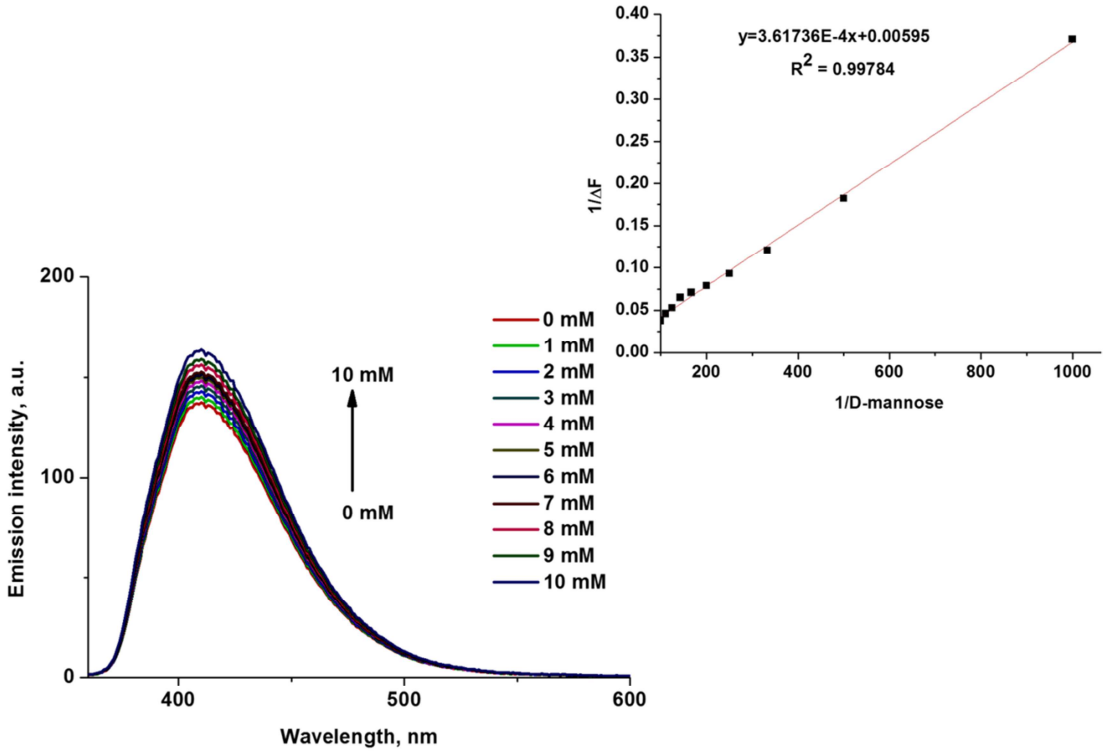


Figure S22: Fluorescence spectra of compound **1.1** (10^{-5}M) in presence of D-mannose at various concentrations (0-10 mM) and inset shows Benesi-Hildebrand plot of the naphthyridine-boronic acid-mannose complex in MeOH/PBS (v/v=1:1, 5 Mm PBS, pH 8.20) solutions. The monitored emission wavelength was 408 nm

Table S4: Benesi-Hildebrand association constant for **1.1** with D-mannose.

IF	**IF-IF$_0$ (ΔF)**	**D-mannose (mM)**	**1/D-mannose**	**1/ΔF**		
139.565	5.808	0.001	1000	0.371	Ka 16.44 M^{-1}	Slope 3.61736E-4
142.364	10.620	0.002	500	0.182		
145.134	14.619	0.003	333.33	0.121		
147.620	19.058	0.004	250	0.093		
149.528	22.895	0.005	200	0.079		
150.954	29.516	0.006	166.66	0.071		
152.254	34.958	0.007	142.85	0.065	IF$_0$ 136.87	Intercept 0.00595
155.730	40.94	0.008	125	0.053		
158.609	44.762	0.009	111.11	0.046		
163.180	46.946	0.10	100	0.038		

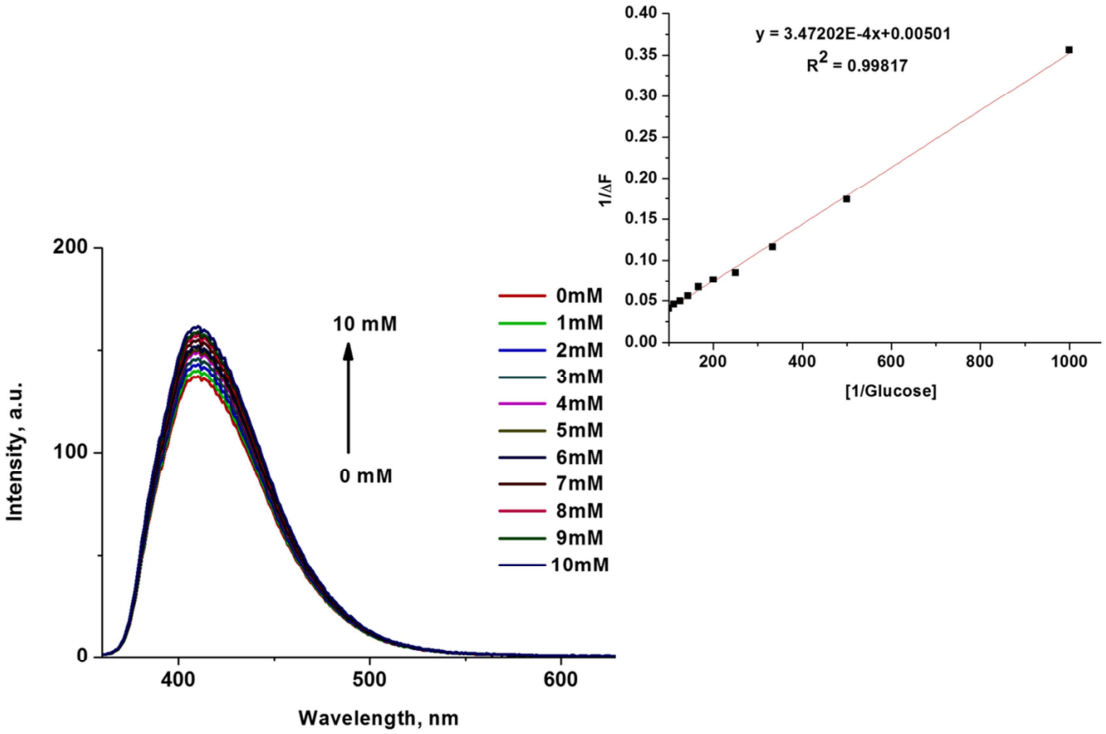


Figure S23: Fluorescence spectra of compound **1.1** (10^{-5} M) in presence of D-glucose at various concentrations (0-10 mM) and inset shows Benesi-Hildebrand plot of the naphthridine-boronic acid-glucose complex in MeOH/H_2O (v/v=1:1, 5 mM, pH 8.20) solutions. The monitored emission wavelength was 409 nm

Table S5: Benesi-Hildebrand association constant for **1.1** with D-glucose.

IF	**IF-IF$_0$ (ΔF)**	**D-glucose (mM)**	**1/D-glucose**	**1/ΔF**	Ka 14.42 M^{-1}	Slope 3.47202E-4
139.444	2.804	0.001	1000	0.356		
142.382	5.742	0.002	500	0.174		
145.251	8.611	0.003	333.33	0.116		
148.367	11.720	0.004	250	0.085	IF_0 136.64	Intercept 0.00501
149.730	13.090	0.005	200	0.076		
151.371	14.731	0.006	166.66	0.067		
154.270	17.630	0.007	142.85	0.056		
156.456	19.810	0.008	125	0.050		
158.096	21.450	0.009	111.11	0.046		
160.651	24.010	0.10	100	0.041		

References

[1] Dempsey, B. *London: Chapman and Hall Ltd* **1974**, *25*, 13.

[2] Chen, H.; Huang, H.; Huang, X.; Clifford, J. N.; Forneli, A.; Palomares, E.; Zheng, X.; Zheng, L.; Wang, X.; Shen, P.; Zhao, B.; Tan, S. *J. Phys. Chem. C* **2010**, *114*, 3280.

[3] Shen, P.; Tang, Y.; Jiang, S.; Chen, H.; Zheng, X.; Wang, X.; Zhao, B.; Tan, S. *Org. Electron.* **2011**, *12*, 125.

[4] Pyun, S. Y.; Lee, D. C.; Seung, Y. J.; Cho, B. R. *J. Org. Chem.* **2005**, *70*, 5327.

[5] Putey, A.; Joucla, L.; Picot, L.; Besson, T.; Joseph, B. *Tetrahedron* **2007**, *63*, 867.

[6] Palamà, I.; Di Maria, F.; Viola, I.; Fabiano, E.; Gigli, G.; Bettini, C.; Barbarella, G. *J. Am. Chem. Soc.* **2011**, *133*, 17777.

[7] Mita, T.; Higuchi, Y.; Sato, Y. *Org. Lett.* **2011**, *13*, 2354.